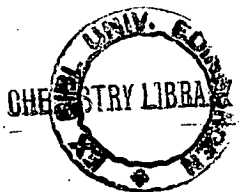


1-ALKYL-1-PHENYLHYDRAZINES: THEIR SYNTHESIS AND
OXIDATIVE REARRANGEMENT

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1977



To my parents

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L.M.

I have composed this thesis which describes
my own work. Where the work of other authors
is referred to, this is clearly indicated.

ABSTRACT OF THESIS

Some historical aspects of the oxidation reactions of 1,1-disubstituted hydrazines are reviewed. In particular, the evidence for the proposed intermediacy of diazenes in these reactions is outlined and the nature of the oxidation products is considered in the broader context of diazene-generating reactions.

The synthesis of 1-alkyl-1-phenylhydrazines has been examined and several preparative procedures are discussed. The alkylation of the sodium salt of phenylhydrazine with the appropriate alkyl halides was found to be the most successful method; the hydrazines prepared in this way all had substituents of the allylic type. Purification (to remove residual phenylhydrazine) can be achieved by selective recrystallisation of the hydrochloride derivative from benzene. Some limitations of this general method are described.

The oxidation studies were carried out using lead tetra-acetate and mercuric oxide. The oxidative rearrangement of 1-allyl-1-phenylhydrazine to 1-phenylazoprop-2-ene was confirmed, and by regarding this as the model system, formation of particular species from the other hydrazines was envisaged. The outcome of each oxidation study is discussed in detail.

The oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine was studied in the context of a proposed method of examining the base-catalysed rearrangement of an optically active azo-compound (formed in the oxidative rearrangement of the optically active hydrazine). Preliminary studies on the racemic hydrazine indicate that the azo-compound is obtained in the form of two geometrical isomers.

The synthesis of 1-phenylazoprop-2-ene by an unambiguous route is described; the method should have wider potential.

A proposed method of determining the electronic character of the diazene involved in the oxidative rearrangement of allylic hydrazines, and difficulties encountered in its application are described.

The attempted interception of the intermediate diazenes by dimethyl sulphoxide and dimethyl sulphide is described.

Oxidation of the hydrazines with cupric chloride was found to give copper-containing solids whose exact composition could not be determined.

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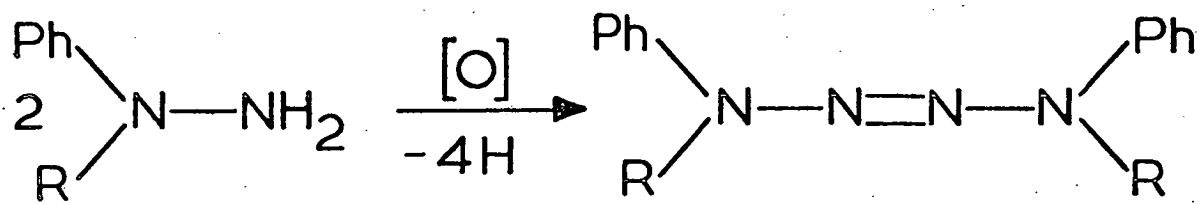
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INTRODUCTION

The oxidation of 1-alkyl-1-phenylhydrazines was first studied towards the end of the nineteenth century. In 1878 Fischer reported the preparation of phenylhydrazine and several of its derivatives.¹ In that same paper, he described the oxidation of 1-methyl-1-phenylhydrazine and 1,1-diphenylhydrazine with yellow mercuric oxide to give products which he suggested were 1,4-dimethyl-1,4-diphenyltetraz-2-ene and 1,1,4,4-tetraphenyltetraz-2-ene respectively (Scheme 1). Later work by Fischer and Troschke² and by Renouf³ confirmed that tetrasubstituted tetraz-2-enes were formed when such hydrazines were oxidised with mercuric oxide. In the light of these results, tetrazene formation came to be regarded as the 'normal' reaction pathway in the mercuric oxide oxidation of 1,1-disubstituted hydrazines. However, it soon became apparent that this was not the only possible pathway.

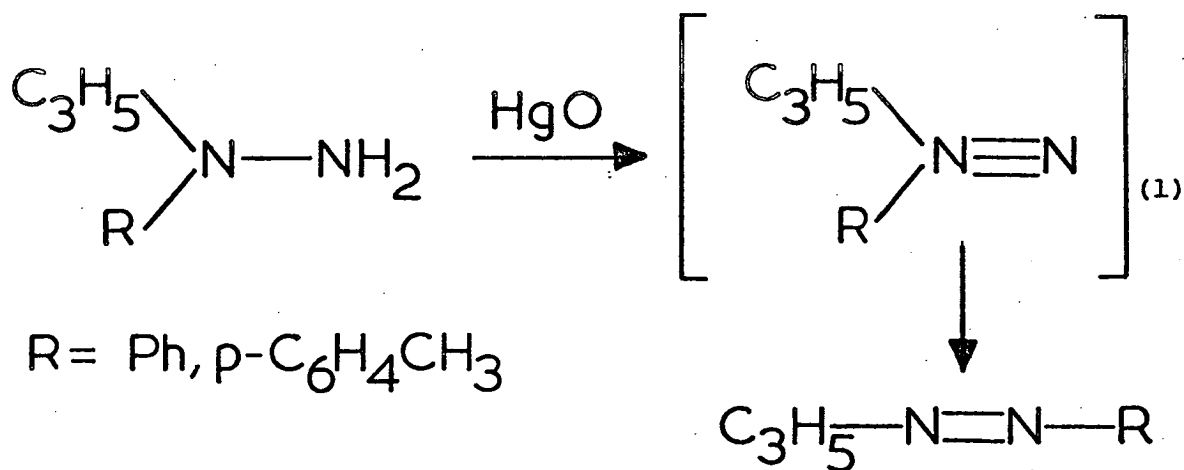
In 1893 Michaelis and Luxemburg⁴ found that the oxidation of 1-allyl-1-phenylhydrazine and 1-allyl-1-*p*-tolylhydrazine with yellow mercuric oxide gave azo-compounds and not the expected tetrazenes. They suggested that the azo-compounds were formed by the rearrangement of an intermediate species (1) having a nitrogen atom bound only to another nitrogen atom (Scheme 2). The same reaction had, in fact, been carried out unwittingly by Fischer and Knoevenagel⁵ some years before.

A further anomalous oxidation pathway in the oxidation of 1,1-disubstituted hydrazines was discovered by Busch and Weiss⁶ in 1900. These authors observed that mercuric oxide oxidation of 1,1-dibenzylhydrazine gave bibenzyl with concomitant evolution of nitrogen (Scheme 3). The reaction proceeds smoothly and has come to be known as the Busch-Weiss reaction.



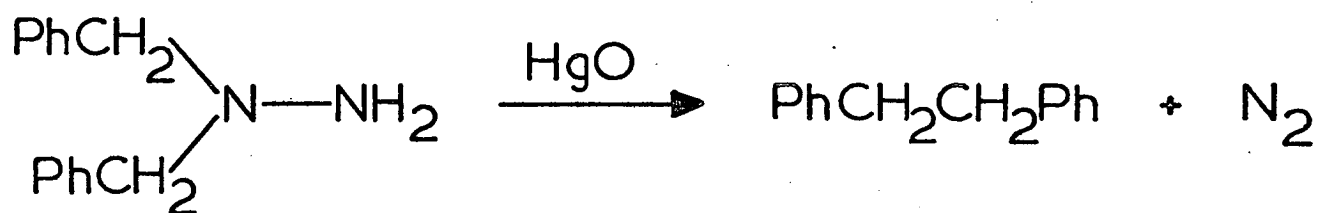
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Scheme 1

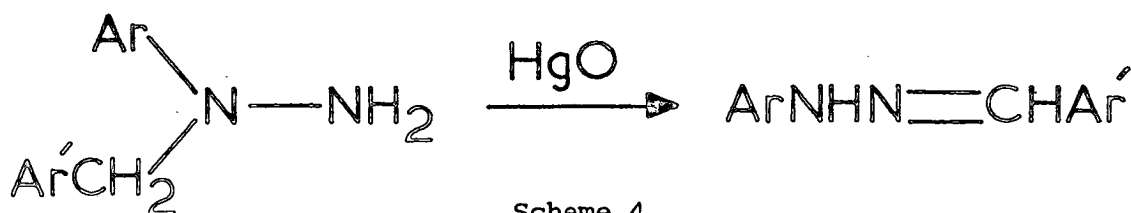


R = Ph, p-C₆H₄CH₃

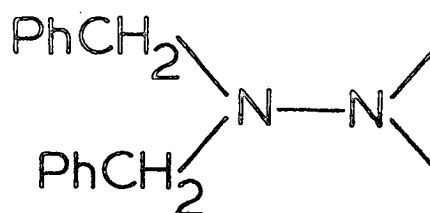
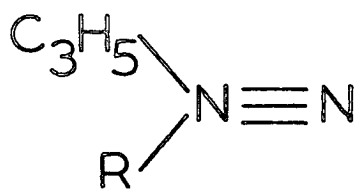
Scheme 2



Scheme 3



Scheme 4



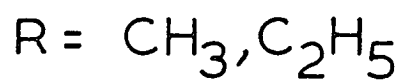
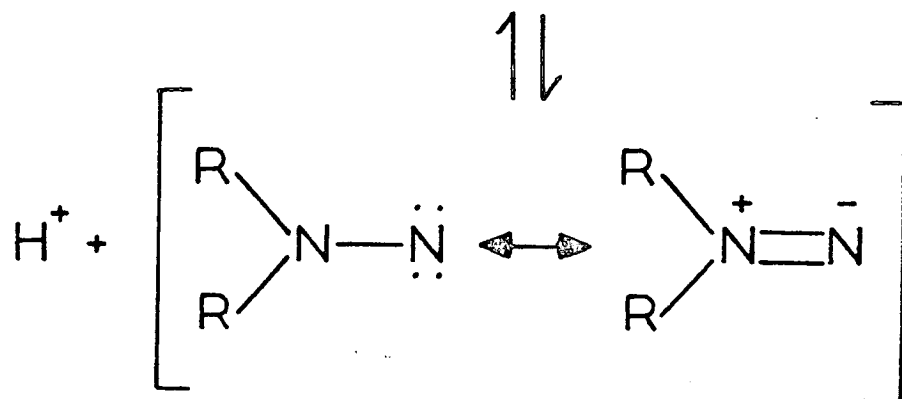
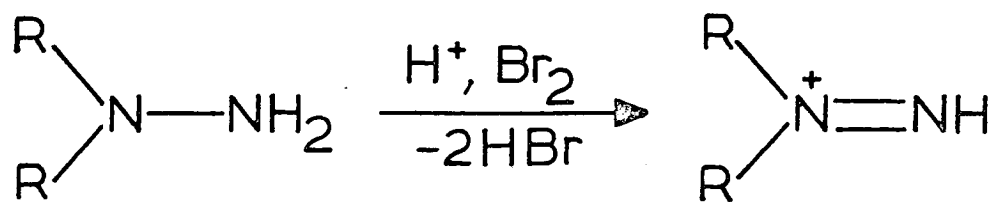
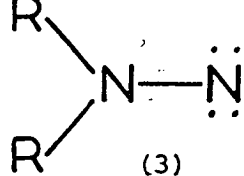
R = Ph, p-C₆H₄CH₃

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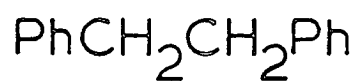
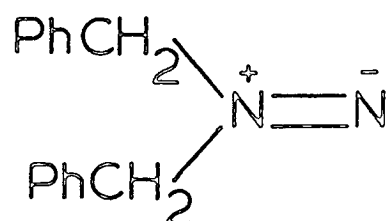
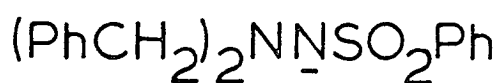
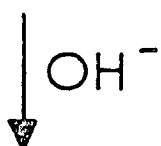
Another anomalous oxidation was reported by Busch and Lang⁷ in 1936; they found that the oxidation of 1-benzyl-1-phenylhydrazines, with substituents in either or both aromatic rings, using mercuric oxides gave arylhydrazones or mixtures of arylhydrazones and the expected tetrazenes. (Scheme 4).

Since that time the oxidation of 1,1-disubstituted hydrazines has been extensively studied and a wide variety of oxidising agents has been used. The most frequently used oxidant is probably mercuric oxide, possibly because of the mildness of the conditions involved and the ease of recovery of the oxidation product. More recently, lead tetra-acetate has become a widely used oxidising agent. Several authors have carried out the oxidation using halogens or alkali metal halates in acidic aqueous solutions. Among the less common oxidising agents used are activated manganese dioxide, nickel dioxide, selenium dioxide, potassium permanganate, N-bromosuccinimide, chlorine, quinone, t-butyl hypochlorite, per-acids and the diethyl ester of azodicarboxylic acid. As a result of this extensive examination, it became apparent that both the 'normal' and the 'anomalous' oxidation pathways unearthed by the early workers (vide supra), were characteristic of the oxidation of 1,1-disubstituted hydrazines as a class, and that the same results could be achieved using oxidising agents other than mercuric oxide.

Until the 1950's, the anomalous oxidations remained relatively unexplored, and little was known of their mechanisms. Although Michaelis and Luxemburg⁴ had proposed an intermediate species (1) to explain the formation of azo-compounds, and Busch and Lang⁷ and Kenner and Knight⁸ had postulated the essentially analogous species (2) to account for the formation of phenylhydrazones and bibenzyls respectively, no firm evidence



Scheme 5



was available to support their existence. In the latter half of the decade, detailed examinations of both existing known reactions, and some new reactions broadly in the field of hydrazine chemistry, supplied a considerable body of evidence in support of the intermediacy of 1,1-diazenes in these reactions. The similarity of the 1,1-diazene (3) to the originally proposed intermediates, (1) and (2), is obvious.

The most fundamental evidence came from the work of McBride and his co-workers^{9,10} and Carpino.¹¹ McBride and Kruse⁹ prepared solutions of 1,1-dialkyldiazenium salts from the oxidation of 1,1-dialkylhydrazines by halogens and by alkali metal halates in strongly acidic media (Scheme 5); they were able to show that two equivalents of oxidant were consumed. Treatment of these solutions with stannous chloride reduced the dialkyldiazenium ions quantitatively to the starting hydrazines, while careful neutralisation of the solutions at low temperature, by the addition of aqueous sodium hydroxide solution gave nearly theoretical yields of the tetra-alkyltetrazenes. The tetrazenes were shown not to be present in protonated form prior to neutralisation by the absence of the characteristic ultraviolet absorption of tetrazenium salts and by the observation that the latter salts were resistant to reduction by stannous chloride; an ultraviolet absorption characteristic of the diazenium salts was observed. McBride and Bens¹⁰ also found that mixtures with a statistical distribution of all possible tetrazenes resulted from the neutralisation of solutions containing a number of different diazenium ions.

Related to the work of McBride and Kruse⁹ was the study of the electrochemical oxidation of 1,1-dimethylhydrazine and 1,1-diphenylhydrazine in acid solutions, by King and Bard¹² and by Cauquis and Genies^{13,14} respectively. This study confirmed the formation of relatively stable

species by a two-electron oxidation, the presence of these species being demonstrated by coulometry, chronopotentiometry and ultraviolet spectroscopy. It was also found¹³ that the original hydrazines could be recovered in up to 95% yield, by electrochemical reduction.

Carpino¹¹ studied the alkaline decomposition of 1,1-disubstituted-2-arenesulphonylhydrazines; his aim was to obtain evidence to support the existence of the species (2) - essentially a 1,1-diazene - by a method directly analogous to the procedure used by Bamford and Stevens¹⁵ for the preparation of diazo-compounds from tosylhydrazones (α -elimination from an anion). He found that the alkaline degradation of 1,1-dibenzyl-2-benzene-sulphonylhydrazines gave bibenzyl in 85% yield and he postulated the mechanism shown in Scheme 6. This suggested that the same intermediate was involved in both the Carpino reaction and the Busch-Weiss reaction.⁶

The same rationale, of similar reaction products implying the intermediacy of the same species, the 1,1-diazene, subsequently provided a rallying point for a number of not obviously related reactions.

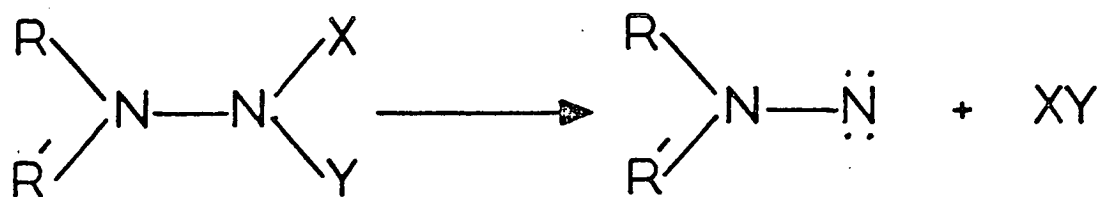
In 1957, Overberger and his co-workers¹⁶ discovered that the reduction of N-nitrosodibenzylamine and its derivatives and analogues with sodium dithionite in alkaline medium gave, not the corresponding 1,1-disubstituted hydrazines, but hydrocarbons of the dibenzyl series. The products were found to be the same as the products of the oxidation of the corresponding hydrazines and the intermediacy of the diazene was proposed. This anomalous reaction, the Overberger-Lombardino reaction, has been observed to occur for a variety of N-nitrosamines other than N-nitrosodibenzylamine.¹⁶⁻²⁰

Lemal and his co-workers^{21,22} studied the reaction of a number of secondary amines with Angeli's salt,²³ $\text{Na}_2\text{N}_2\text{O}_3$. He obtained bibenzyl

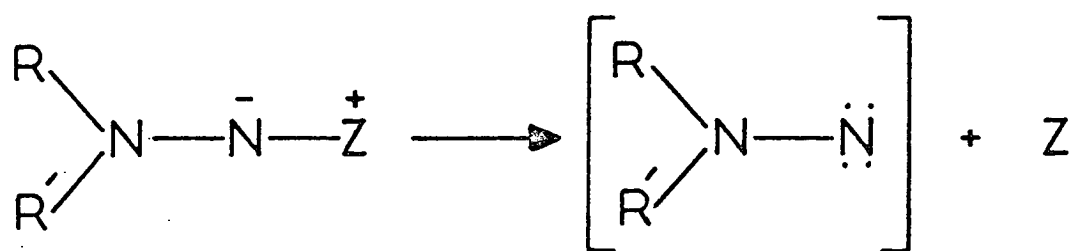
from dibenzylamine; other amino-compounds also gave products identical to the products of the reactions of the corresponding diazenes and the intermediacy of the 1,1-diazene was invoked.

Bumgardner and his co-workers²⁴ examined the reaction of primary and secondary amines with difluoramine using an excess of the amine; dibenzylamine gave bibenzyl and azetidine gave cyclopropane. The reaction of N-nitroso-azetidine with sodium dithionite (the Overberger-Lombardino reaction, vide supra) was studied, and shown to give cyclopropane. This latter finding, together with the earlier reports of bibenzyl formation in the various reactions supposed to generate 1,1-dibenzyl diazene, led these workers to propose the intermediacy of the diazene.

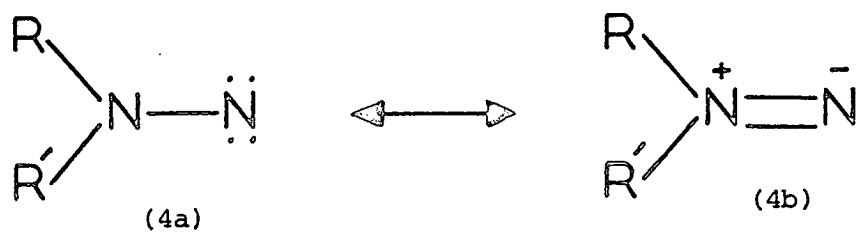
The parallellism in the nature of the products of these several reactions led to the formulation of the 1,1-diazene as the mechanistic common denominator. However, more direct evidence for the intermediacy of 1,1-diazenes, in the oxidation of 1,1-disubstituted hydrazines at least, comes from the fact that certain 1,1-diazenes have been intercepted and isolated in the form of various adducts. The first reported trapping was by Atkinson and Rees²⁵ in 1967. They oxidised 3-aminobenzoxazolinone with lead tetra-acetate in the presence of olefins and dienes and isolated the amino-aziridine adducts in good yield. Since that time a large amount of data has accumulated on the stereospecific addition of 1,1-diazenes across carbon-carbon double bonds.²⁶⁻³⁰ The addition of 1,1-diazenes to $\text{N}=\text{N}$ ³¹ and $\text{C}\equiv\text{C}$ ³² has been reported. To date, only diazenes substituted with electron-withdrawing groups (usually N-amido- and N-imido-diazenes and similar species) have been trapped and the addition of other types of diazenes, such as 1,1-dialkyldiazenes, across multiple bonds has not been observed. Diazenes of similar type to those shown to add across multiple bonds, have been trapped by sulphoxides and isolated as the sulphoximide adducts.^{27,33,34} Photolysis or pyrolysis



Scheme 7



Scheme 8



Scheme 9

of these sulphoximides regenerates the diazene, and provides a convenient method for studying the reactions of these particular diazenes³³. Jones²⁸ has described the regeneration of phthalimidodiazene by the thermally induced dissociation of the aziridine adduct obtained from the reaction of phthalimidodiazene with 2-acetylbenzofuran.

More recently, Boehm et al³⁵ reported the isolation of a copper complex of 1,1-dimethyldiazene by cupric chloride oxidation of 1,1-dimethylhydrazine in acidic solution.

1,1-Diazenium cations, the conjugate acids of the 1,1-diazenes, have also been found to attack unsaturated systems. Since the original report by McBride and his co-workers³⁶ in 1957 who obtained good yields of tetrahydropyridazinium salts from the reaction of dimethyldiazenium bromide with butadiene, many reports of similar addition reactions have appeared.

The considerable number of reactions for which the intermediacy of 1,1-diazenes has been proposed, can be divided into two general categories. The first consists of reactions involving 1,1-disubstituted hydrazines and their derivatives (pre-formed or formed in the course of the reaction) with α -elimination (formally at least), according to Scheme 7. This group includes the oxidation of 1,1-disubstituted hydrazines by various oxidising agents, the alkaline cleavage of the hydrazides of sulphonic acids, the thermal decomposition of their N-sodium derivatives ($XY = \text{NaSO}_2\text{R}''$), the incomplete reduction of N-nitrosamines in alkaline medium ($X = \text{OH}$, $Y = \text{H}$, in the intermediate, the ozonolysis of hydrazones ($X, Y = \text{---}$ of the hydrazone) and possibly the reaction of secondary amines with difluoramine ($X = \text{H}$, $Y = \text{F}$), Angeli's salt²³ and Piloty's acid (N-benzene-sulphonylhydroxylamine).³⁷

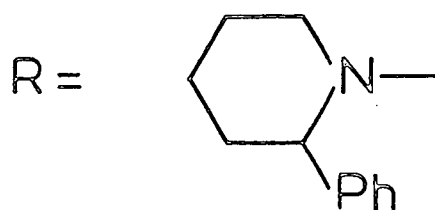
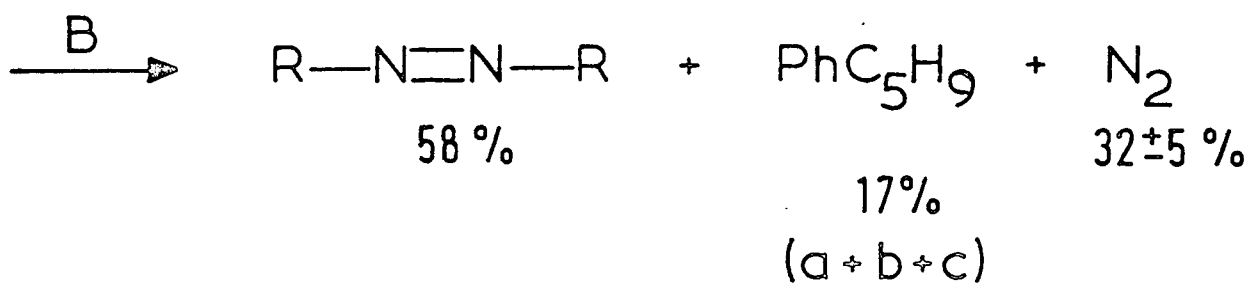
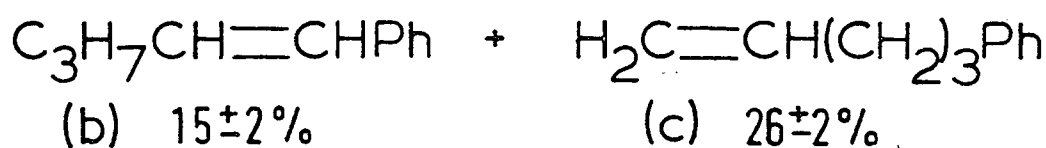
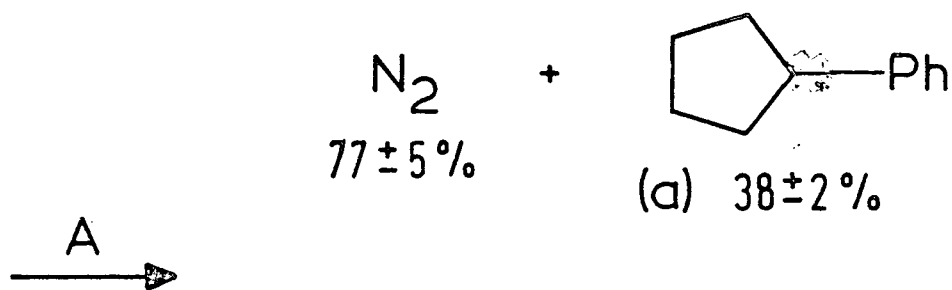
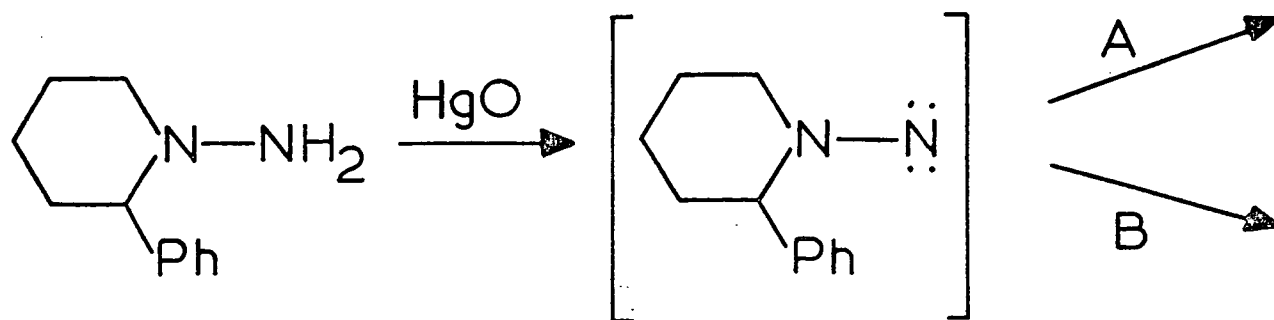
The second, and smaller category consists of reactions involving the decomposition of various ylide-type derivatives of hydrazine according to Scheme 8. This group includes the thermal and photolytic decomposition of sulfoximides³³ ($Z = \text{dimethyl or diphenylsulphoxide}$) and the decomposition of N-azides³⁸ ($Z = \text{N}\equiv\text{N}$).

Thus, the oxidation of 1,1-disubstituted hydrazines is nowadays considered in the wider context of the reactions of 1,1-diazenes. Much information obtained from studies of reactions held to proceed via the intermediacy of 1,1-diazenes (vide supra), has been pooled to develop the present view of the nature and reactivity of 1,1-diazenes. This systematisation of ideas enables predictions, analogies and generalisations to be made in the organic chemistry of hydrazines. However, while the intermediacy of 1,1-diazenes in the various reactions cited above is generally agreed, the mechanism and nature of reaction of the intermediate under the different conditions involved, may not be exactly the same.

The picture which has evolved of the 1,1-diazene is that of a species more stable, and with a longer lifetime than C-nitrenes or carbenes, and having considerable nucleophilic character. The stabilisation and increased lifetime was attributed to mesomerism (Scheme 9). The results of theoretical calculations of the structures of a number of simple 1,1-diazenes³⁹ showed that dihydrodiazene had a planar configuration with N-N bond length of 1.25 Å, and that the terminal nitrogen atom carried an appreciable negative charge (-0.217). The presence of alkyl substituents was shown to increase the negative charge; diazenes in which conjugation was possible between the central nitrogen atom and the substituents (e.g. 1-hydro-1-phenyldiazene) showed a small decrease in the negative charge on the terminal nitrogen atom (-0.204, in this example). The

calculations also showed that the π -bond order of the bond between the nitrogen atoms of these simple diazenes, was in the range 0.81-0.84. Thus, these calculations support the postulated mesomerism, and the view that it is the important contribution of the dipolar structure (4b) which confers nucleophilic character on these diazenes. It is this important characteristic feature which distinguishes them from C-nitrenes and typical carbenes. The dipolar form of the diazene (4b) may be considered as an ylide (5) and indeed much has been made of this (vide infra). Similarly, the formal relationship of diazenes to their symmetrically substituted counterparts, azo compounds (6) is noteworthy; the possibility of decomposition with formation of molecular nitrogen is realised in both cases. The azomethinimine tautomer of the diazene (7) does play a significant role in diazene chemistry principally through its dimerisation in a head-to-tail fashion, but these species are not widely invoked, particularly not in the oxidation reactions of 1,1-disubstituted hydrazines.

The structure of a given diazene and the reaction conditions to which it is subjected, have a great influence over the fate of that diazene, with the result that it may pursue a variety of characteristic reaction pathways. The reactions of 1,1-diazenes can be classified into three categories: decomposition, isomerisation and addition. Examples of the first category are the Busch-Weiss, Carpino, and Overberger-Lombardino reactions in which the diazenes decompose to give hydrocarbons and nitrogen (all analogues of Scheme 3). Examples of diazene isomerisation are the diazene-hydrazone rearrangement (Scheme 4) and the allylic diazene rearrangement which gives azo-compounds (Scheme 2). The third category, addition, includes tetrazene formation (Scheme 1) and the addition across multiple bonds.



Scheme 10

The direction of reaction of any particular diazene is a complex function of many factors, some to do with the inherent nature of the diazene, others to do with the reaction conditions and possibly the reaction medium.

Michaelis and Luxemburg⁴ reported that while oxidation of 1-allyl-1-phenylhydrazine with mercuric oxide gave 1-phenylazoprop-2-ene as the sole product, oxidation of the same hydrazine with ferric chloride gave 1,4-di-allyl-1,4-diphenyltetraz-2-ene as the only product. This is an example of the same diazene giving two very different products under broadly comparable conditions.

Perhaps less surprising is the formation of different products from the same diazene under widely different conditions. An illustrative example is provided by the work of Rees' group.³³ They prepared a series of sulfoximides derived from N-amino-lactams and found that diazenes regenerated photochemically could be intercepted by cyclohexene, but the same diazenes, regenerated by thermal decomposition extruded nitrogen and gave the products of ring contraction.

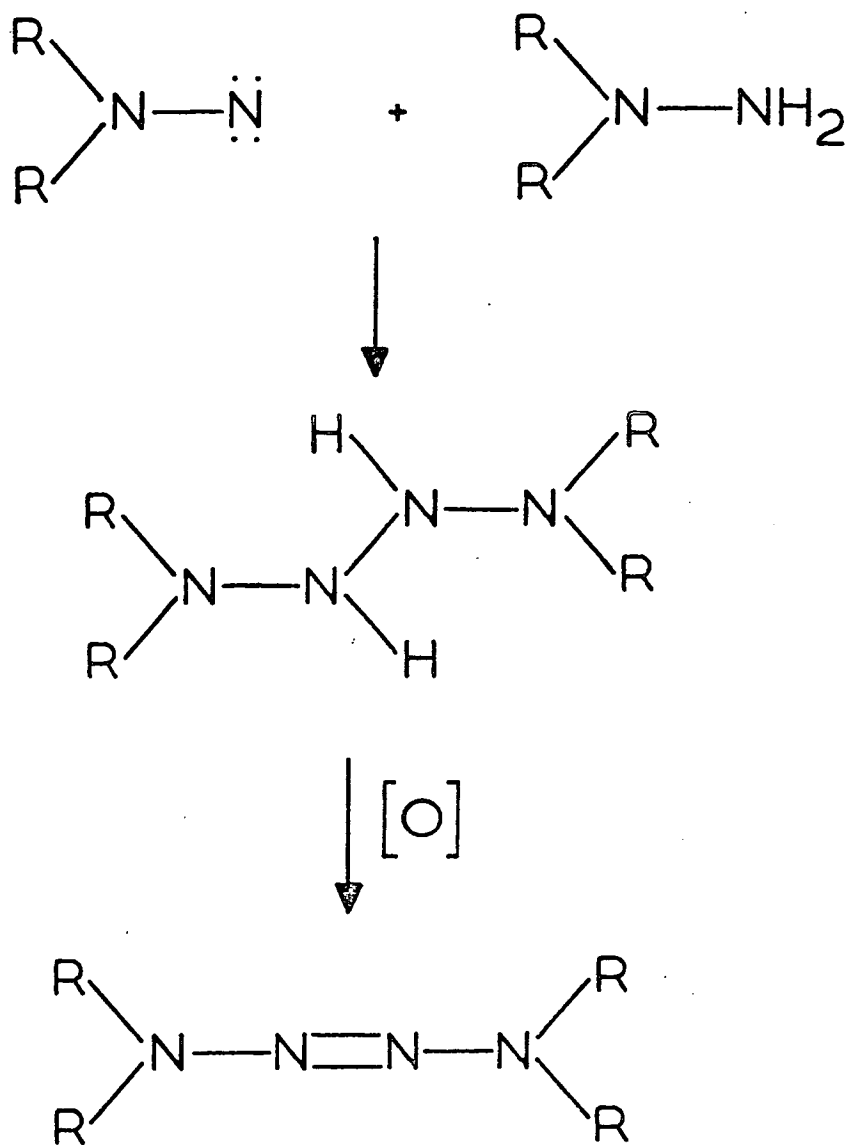
An example of a particular diazene giving a different ratio of products as a result of minor and rather subtle differences in the experimental method and conditions, is afforded by the work of Overberger and Herin.⁴⁰ The scope of reaction open to a given diazene will depend on its lifetime and this lifetime can vary over a wide range, particularly under heterogeneous reaction conditions. Overberger and Herin⁴⁰ examined two modifications of the oxidation of 1-amino-2-phenylpiperidine with mercuric oxide (Scheme 10). They found that rapid addition of the hydrazine to the oxidising agent (path B) gave principally the tetrazene; slow addition of the hydrazine (path A) gave the products of decomposition of the diazene and no tetrazene. They suggested that in the case of rapid addition, the diazene formed reacted with a molecule of unoxidised hydrazine before it could decompose (tetrazene formation), while in the

case of slow addition, the probability of bimolecular reaction was low, enabling decomposition to proceed almost to completion.

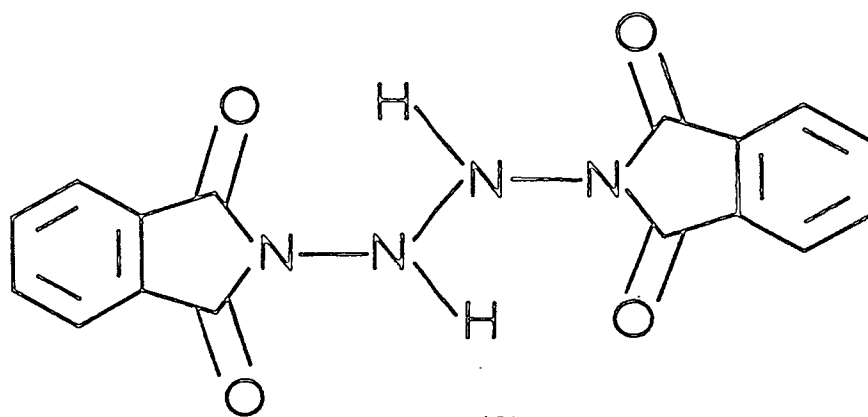
Carpino and his collaborators⁴¹ reported the isolation of dibenzylmercury in 46.5% yield from the mercuric oxide oxidation of 1-n-butyl-1-benzylhydrazine in methylene chloride solution. However, this does not appear to be a common reaction pathway.

The reaction mechanisms of the three primary reaction pathways of 1,1-diazenes, tetrazene formation, decomposition with extrusion of nitrogen and rearrangement, have been widely examined. Although the mechanistic possibilities are many, several useful generalisations have emerged.

The mechanism of tetrazene formation, the 'normal' pathway, is a matter of debate, and while two mechanisms are widely proposed, by no means all authors offer a mechanistic scheme for the observed formation of tetrazenes. The two proposed routes to tetrazenes are a) by dimerisation of the diazenes, and b) by the bimolecular reaction of the diazene with its precursor. The latter is thought to be more probable as it involves the reaction of a short-lived species with a long-lived species, rather than the reaction of two short-lived species. McBride⁹ originally suggested that tetrazene formation by the neutralisation of 1,1-dialkyl-diazenium salt solutions involved dimerisation of the corresponding diazenes but subsequently proposed a mechanism involving the coupling of the diazene with the diazenium ion.¹⁰ Lemal⁴² suggested that head-to-head coupling of diazenes accounts for the formation of tetrazenes in the thermal decomposition of 1,1-dialkyl-2-sulphonylhydrazine salts in aprotic media. Forgione and his co-workers⁴³ suggested that the stereospecific formation of the cis-tetrazene in the oxidation of 3-amino-2-oxazolidinone by mercuric oxide, is due to the dimerisation of the corresponding 1,1-diazenes, adjacently co-ordinated to the oxidant. Diazene dimerisation



Scheme 11

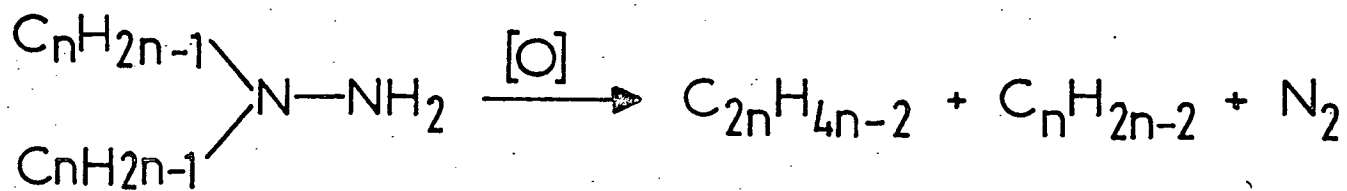


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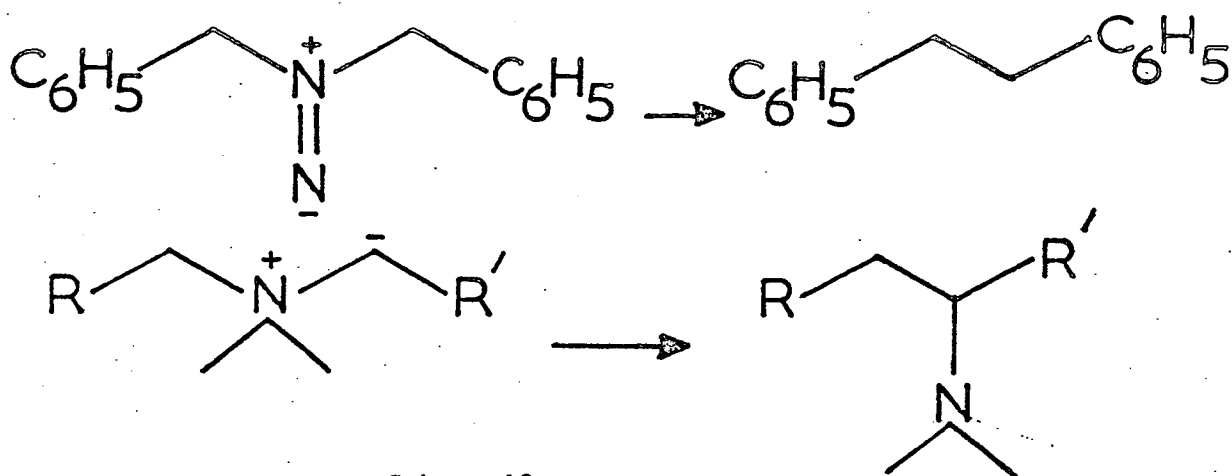
has also been proposed by Koch and Fahr³¹ to account for the formation of tetrazenes in the oxidation of 1,1-disubstituted hydrazines with diethyl hydrazodicarboxylate. The alternative route, not involving dimerisation of 1,1-diazenes, was favoured by Overberger and Herin⁴⁰ to explain the results of the oxidations of 1-amino-2-phenyl-piperidine with mercuric oxide (vide supra, Scheme 10). They proposed the intermediacy of the corresponding tetrazane as shown in Scheme 11. The same intermediate species has been postulated by Hoesch and Dreiding,^{44,45} and by Rees' group,⁴⁶ in the lead tetra-acetate oxidation of N-amino-lactams. Indeed Rees and co-workers⁴⁶ were able to isolate and characterise the tetrazane (8). Lemal and his co-workers,⁴⁷ studying the thermal decomposition of certain 1,1-disubstituted 2-arenesulphonylhydrazine salts in ether solvents, suggested that tetrazene formation might occur by the attack of the diazene on its precursor.

The tetrazenes may be unstable under the conditions of the reaction, but their formation can often be inferred from the nature of the product or products.⁴⁷ Furthermore, tetrazene formation does not exclude the possibility of diazene decomposition and rearrangement occurring concomitantly and such product mixtures have been observed.^{7,40}

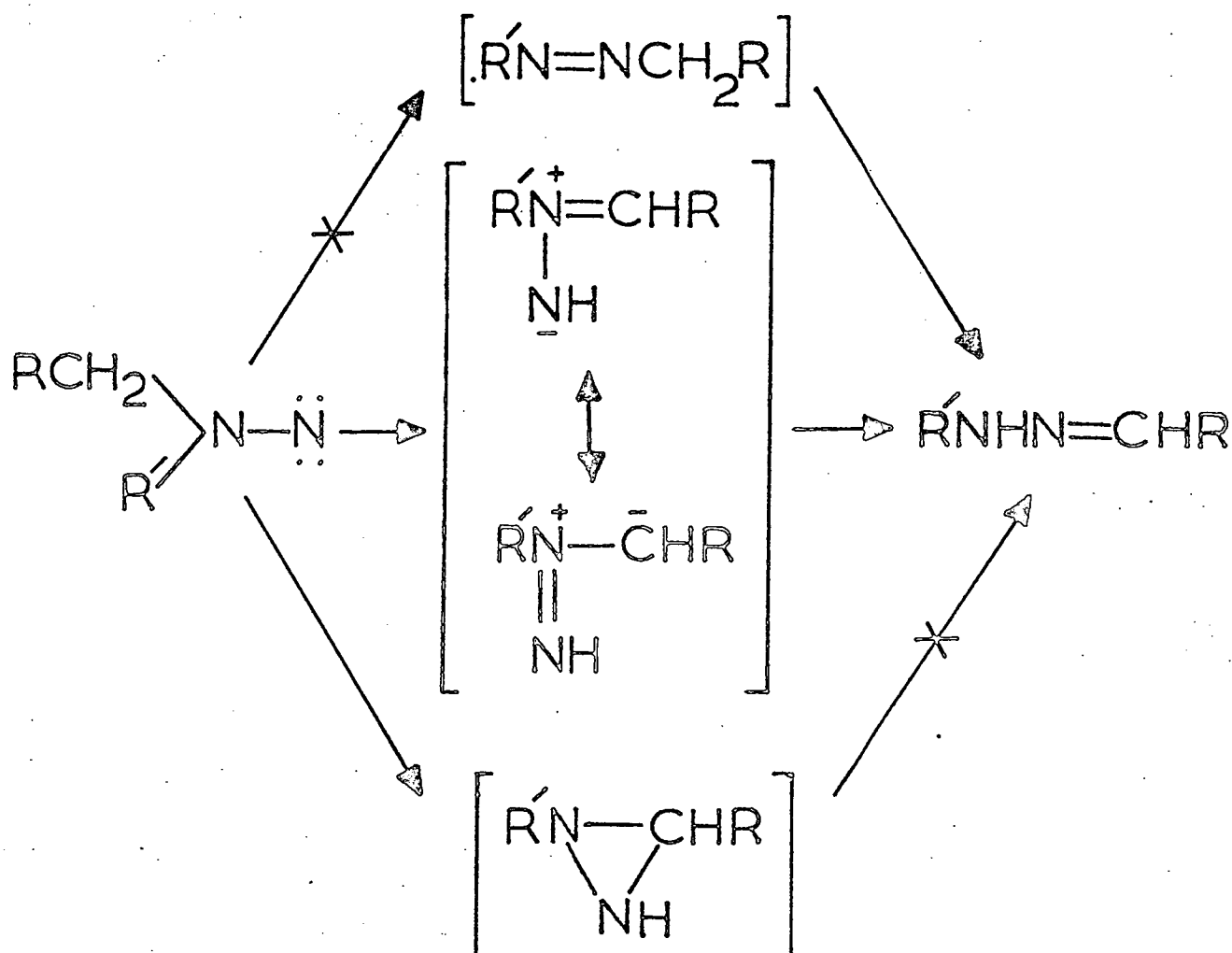
The decomposition of diazenes has been extensively studied and has been observed to occur for diazenes prepared in a wide variety of ways. The fragmentation with extrusion of nitrogen and formation of hydrocarbons was originally observed by Busch and Weiss⁶ in the mercuric oxide oxidation of 1,1-dibenzylhydrazine. This particular example has since been found to be common to nearly all analogous diazene-generating reactions; indeed the formation of bibenzyl has often been taken as diagnostic of diazene intermediacy in those reactions not apparently related to the oxidation of 1,1-dibenzylhydrazine. Many parallel examples were reported,



Scheme 12 (Cf. Scheme 10)



Scheme 13



involving diazenes with substituents analogous to the benzyl radical (e.g. substituents with α -cyano and α -aryl groups) and the decomposition came to be regarded as a substituent-assisted fragmentation. However, in 1963 Lemal and co-workers⁴⁷ reported the first example of decomposition of a diazene with substituents of a non-benzylic type (i.e. substituents unable to stabilise charge or radical character in the transition state). Many examples of this last type have since been cited. Although the reaction has not been widely used as a means of generating carbon-carbon bonds, it does have synthetic potential. The reaction has been used in the preparation of certain strained systems such as benzocyclobutenes from the decomposition of 1,3-dihydroisoindolinodiazene.^{48,49} The decomposition of the diazene derived from 1-amino-benzotriazole to give benzyne has been developed by Rees and his co-workers.⁵⁰

The formation of unsaturated compounds, the products of disproportionation of the diazene substituent residues, was first reported by Overberger and his co-workers^{51,52}, and since that time many more reports have appeared (Scheme 12). The results of the many studies of the decomposition of 1,1-diazenes related to 1,1-dibenzylidiazene (vide supra) suggest that decomposition with combination of the residues requires that both, or at least one, of the substituents be capable of stabilising the intermediate. It has also been suggested⁵³ that in order to obtain a high yield of coupling products (hydrocarbons), the substituents should be of small bulk, otherwise the products of disproportionation (alkenes) are formed preferentially. The effect of experimental procedure on the nature of the product from the oxidation of 1-amino-2-phenylpiperidine with mercuric oxide⁴⁰ has already been described (Scheme 10).

The mechanism of diazene decomposition is a matter for debate, and in many cases, the course of the reaction can be interpreted in terms of

either a radical or a concerted process. In the case of the diazenes with substituents of the benzyl-type (vide supra), Lemal⁵⁴ suggests that a radical mechanism is consistent with all the available evidence. However, the presenters of that evidence, are often divided between the two possibilities. To explain the absence of cross-over products in the decomposition of unsymmetrical diazenes derived from the corresponding N-nitrosamines, Overberger⁵⁵ has suggested that the radicals are not free, but are trapped in a solvent cage.

The formal similarity of diazenes (Scheme 9) to azo-compounds (6) has already been alluded to. It is not surprising therefore that the analogy has been pursued to the formation of hydrocarbons by decomposition of both these species. Parallelism in the isomeric composition of the products of the decomposition of certain diazenes and the corresponding azo compounds, has been taken as indicative of the operation of the same mechanism in each case^{17,55}; the radical mechanism of the decomposition of azo-compounds was established by the work of Overberger and Anselme.⁵⁷

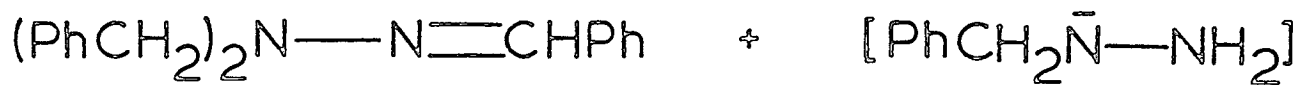
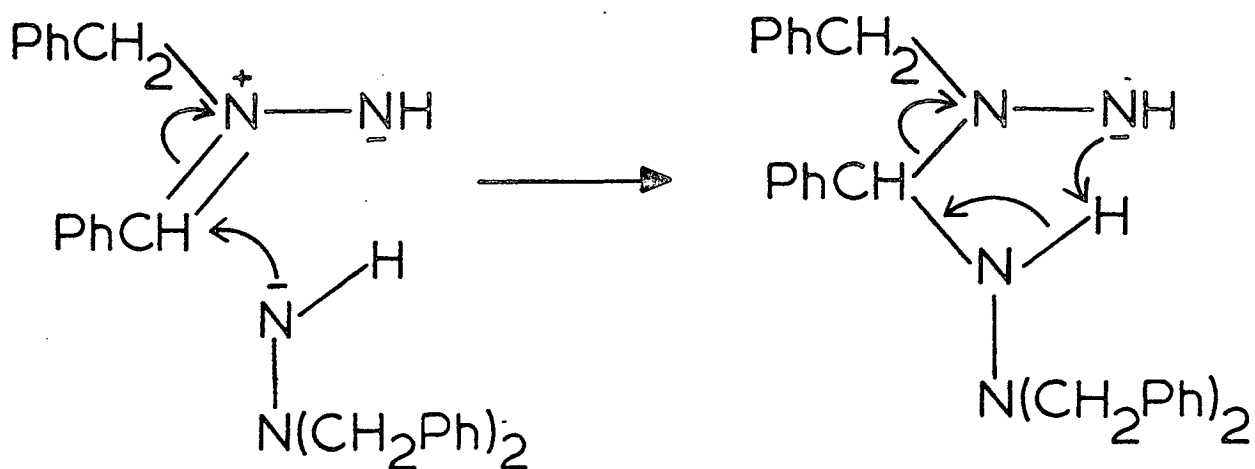
Ollis et al⁵⁸ have noted the formal similarity between the decomposition of dibenzylidiazene to give bibenzyl and the Stevens rearrangement of ammonium ylides (Scheme 13); he interpreted the experimental evidence on the decomposition of 1,1-dibenzylidiazene as indicating a radical mechanism in accord with the known homolytic pathway of the Stevens rearrangement.

Support for a concerted decomposition pathway comes from the work of Lemal⁴⁷ who observed that decomposition of tetramethylene diazene gave nitrogen and ethylene, with no cyclobutane being detected. The decomposition of the diazene derived from cis- and trans-2,5-dimethyl-3- pyrrolidine was shown by Lemal²² to give the diene products predicted by

the Woodward-Hoffmann rules⁵⁹ for concerted processes. The decomposition of the diazenes derived from cis- and trans-2-amino-1,3-dihydro-1-3-diphenylisindoles to give 1,2-diphenylbenzocyclobutenes has also been shown⁶⁰ to obey the Woodward-Hoffmann rules⁵⁹ for concerted processes. This mode of decomposition is generally observed when it is energetically more favourable than the alternative radical process. A common feature of the concerted processes of decomposition of diazenes is the formation of a primary product with greater conjugation than the parent system.

The formation of hydrocarbons by a secondary process can occur in the rearrangement of allylic diazenes (vide infra). The recovery of hydrocarbons rather than the expected azo-compounds may be interpreted in terms of decomposition of the diazene with extrusion of nitrogen, or in terms of decomposition of the azo-product.^{58,61} In the same field, Baldwin et al⁶¹ have suggested that the formation of small amounts of hydrocarbons in the oxidation of certain allylic hydrazines with metal oxides and lead tetra-acetate, was due to some secondary process involving the oxidising agent.

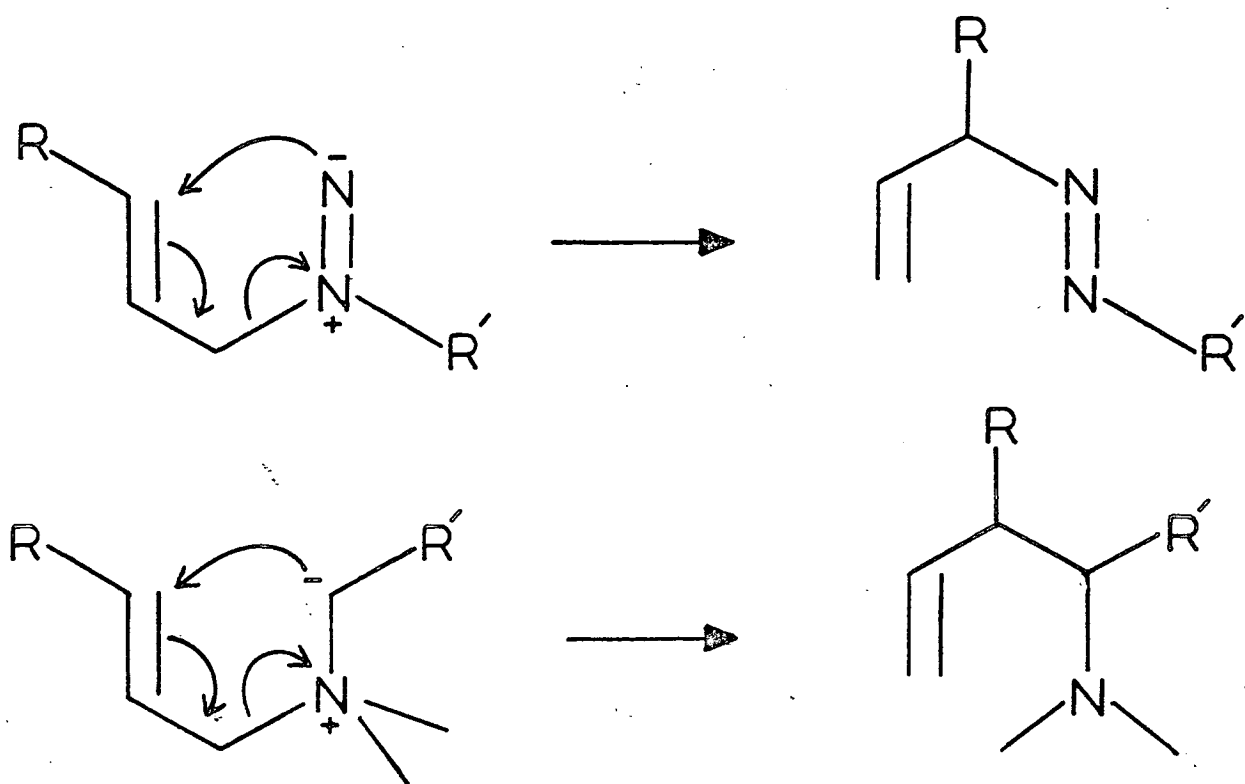
The rearrangement of diazenes to hydrazones, the diazene-hydrazone rearrangement, originally observed in the oxidation of 1-aryl-1-benzyl-hydrazines⁷ with mercuric oxide, was found by Carter and Stevens⁶² to occur in the base catalysed decomposition of 1-aryl-1-benzyl-2-sulphonyl-hydrazines. The rearrangement has been widely studied and examples have been found of aryl, alkyl- and dialkyldiazenes undergoing this rearrangement. Carter and Stevens⁶² showed that the rearrangement was an intramolecular process. Lemal and co-workers⁶³ showed that neither the corresponding azo-compound, nor the diaziridine were intermediates; they tentatively suggested that the rearrangement could be explained in terms of the azomethanimine tautomer (Scheme 14). This mechanistic



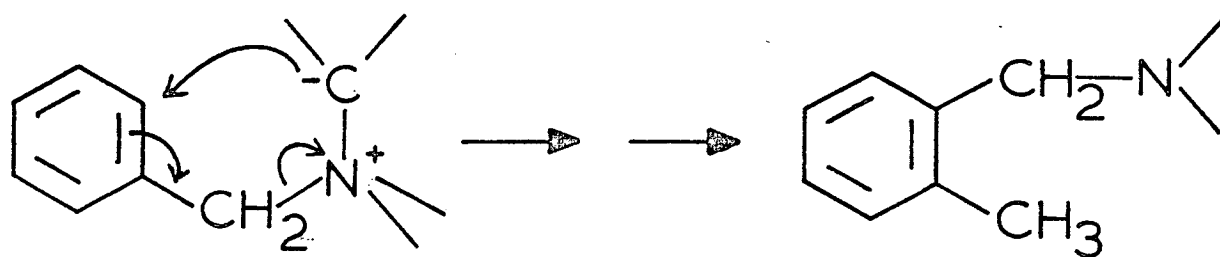
Scheme 15

puzzle was further complicated by the results of Urry and Ikoku⁶⁴ who found that propionaldehyde dipropylhydrazone, as well as propionaldehyde propylhydrazone itself, was a significant product from reactions generating 1,1-dipropyldiazene. Lemal and Underbrink⁶⁵ also found that acetaldehyde diethylhydrazone was a major by-product from the rearrangement of diethyldiazene produced by the thermal decomposition of the sodium salt of 1,1-diethyl-2-benzenesulphonylhydrazine in protic media; tetrazenes were obtained when the reaction was carried out in aprotic media. Koga and Anselme,³⁸ studying the reaction of 1,1-dibenzylhydrazine anions (i.e. in strongly basic medium) with tosyl azide which they suggested generated dibenzylidiazene (cf. Scheme 8), isolated significant quantities of benzaldehyde dibenzylhydrazone. They also showed, by re-examining the literature, that benzaldehyde dibenzylhydrazone had been an unidentified by-product of other reactions generating dibenzylidiazene and its analogues.^{6,17,52,55,62} They considered several mechanisms, but suggested that the most probable pathway was that involving the azomethinimine tautomer of dibenzyl diazene, as shown in Scheme 15. However, the wider applicability of this mechanism is questionable; the exact mechanism of the diazene-hydrazone rearrangement is still a matter for conjecture.

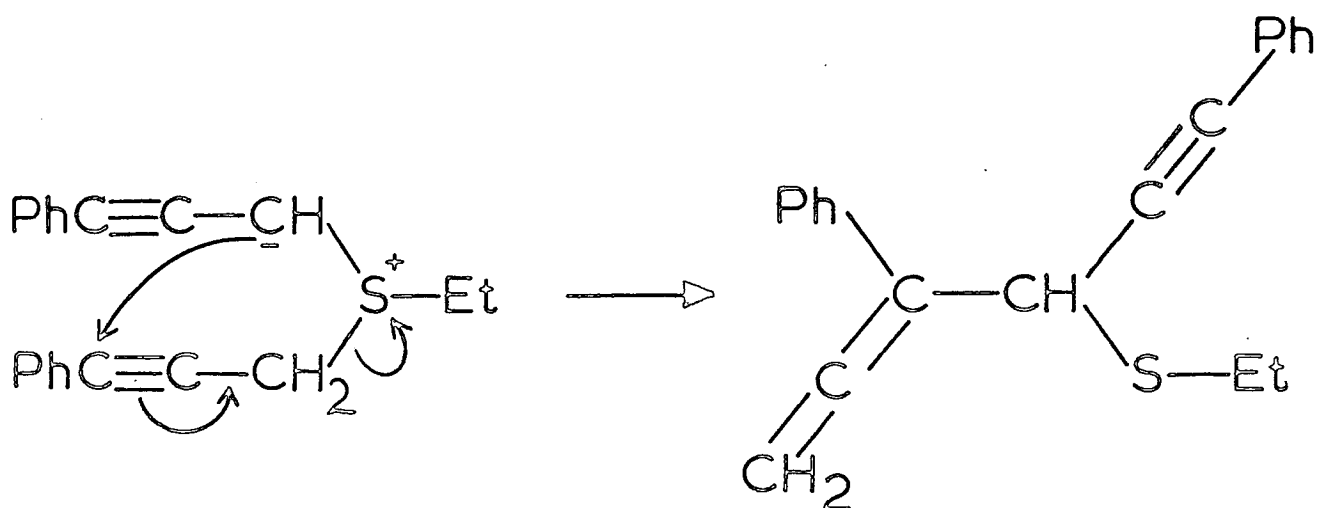
The rearrangement of allylic diazenes to give azo compounds was first discovered in 1893⁴ and although formally analogous rearrangements were observed in the case of the diazenes derived from 1-amino-oxindole⁶⁶ and N-amino-2,3,4,5-tetraphenylpyridone⁶⁷ by oxidation, no other examples of the formation of azo-compounds are known. The rearrangement of allylic diazenes has recently been examined by Ollis⁵⁸ and by Baldwin.⁶¹ Ollis⁵⁸ compared the rearrangement to that of allylic ammonium ylides (Scheme 16) which he had shown⁶⁸ to rearrange by a concerted [2,3]-sigmatropic mechanism as suggested by Scheme 16, rather than by a



Scheme 16



Scheme 17

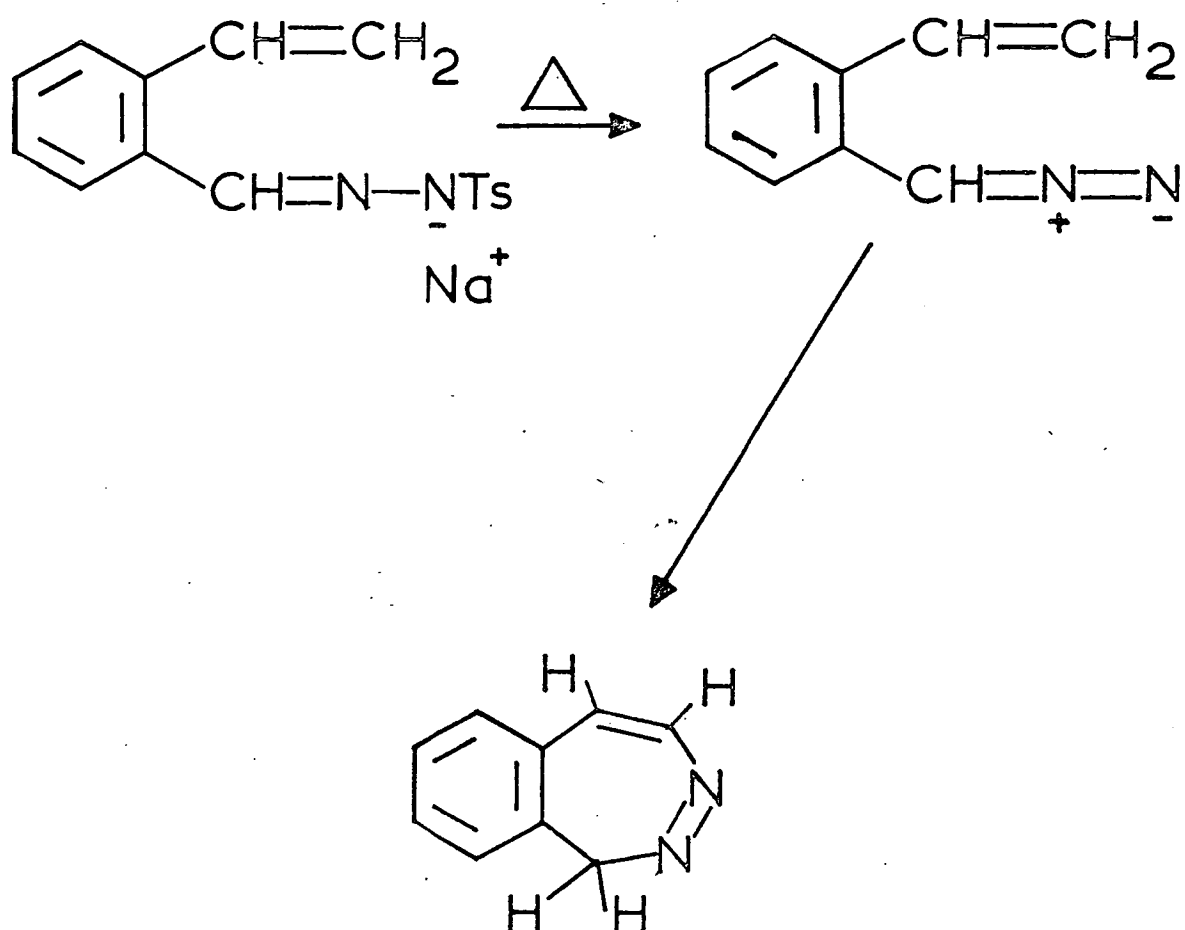


Scheme 18

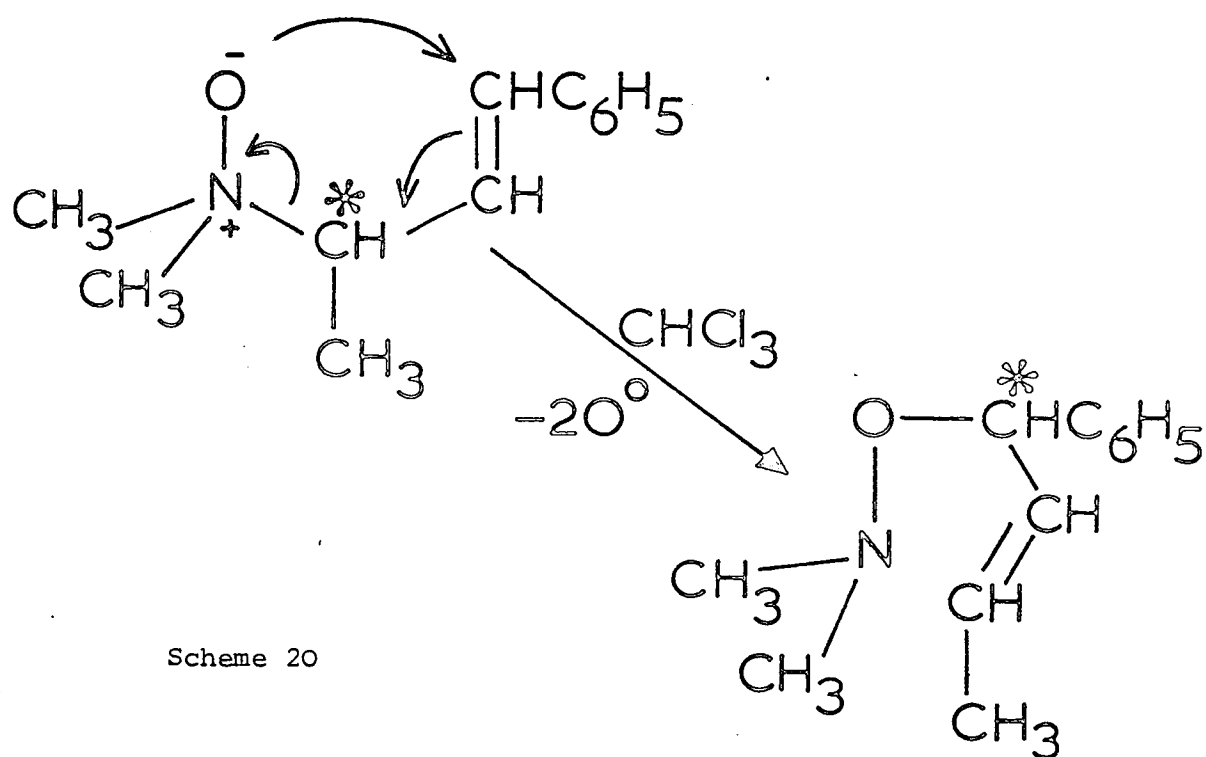
homolytic pathway. However, he found that the allylic diazenes produced by the thermal decomposition of the sodium salts of the corresponding N-toluene-p-sulphonylhydrazines, gave mixtures of hydrocarbons and not the expected azo-compounds. This he interpreted as resulting from the homolytic decomposition of the diazenes with extrusion of nitrogen and combination of the radical residues. Baldwin,⁶¹ working with some of the same diazenes produced by oxidation of the corresponding hydrazines, isolated the expected azo-compounds and only very small amounts of hydrocarbons. He proposed that the rearrangement was a [2,3]-sigmatropic process, and explained the discrepancy between his findings and those of Ollis⁵⁸ in terms of the instability of the azo-compounds under the conditions used by Ollis et al. He was able to support this view in the case of the diazene common to both his study and that of Ollis, benzyl-1-phenylallyldiazene : he showed that the azo-compound which was isolated in the case of the oxidative rearrangement, was thermally unstable and decomposed to give a mixture of hydrocarbons of approximately the same composition as that obtained by Ollis, and which Ollis proposed arose from the decomposition of the diazene.

The prediction of the course of a particular reaction thought to involve diazene formation, is therefore a prediction of the probable reaction pathway of that diazene. This, of necessity, requires that many factors be taken into account, few of which can be quantitatively appraised. The situation can be further complicated by the operation of more than one mechanism and by various secondary processes such as decomposition of the initial product or products.

The aim of the study to be described in this thesis was to examine the oxidation of several hydrazines broadly related to 1-allyl-1-phenylhydrazine,⁴ the intermediacy of the diazene being assumed. In particular,



Scheme 19



Scheme 20

it was hoped to observe diazene rearrangements analogous to (a) the Sommelet-Hauser rearrangement of benzylic ammonium ylides (Scheme 17), (b) the reported rearrangement⁶⁹ of the sulphonium ylide obtained by the deprotonation of the sulphonium cation derived by reaction of di-3-phenylprop-2-yn-1-yl thioether with triethyloxonium bromide (Scheme 18), and (c) the rearrangement observed in the thermal decomposition of the sodium salts of a series of p-tosylhydrazones (Scheme 19).⁷⁰ The possibility of achieving asymmetric induction in the allylic diazene rearrangement, in a manner analogous to that reported for allylic amine oxides (Scheme 20),⁷¹ was also envisaged.

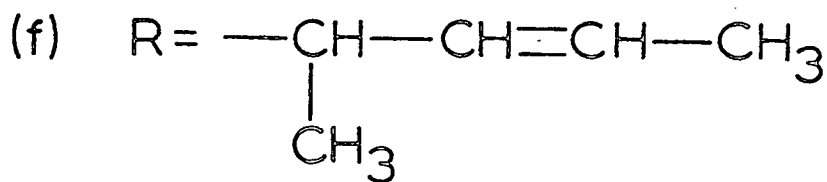
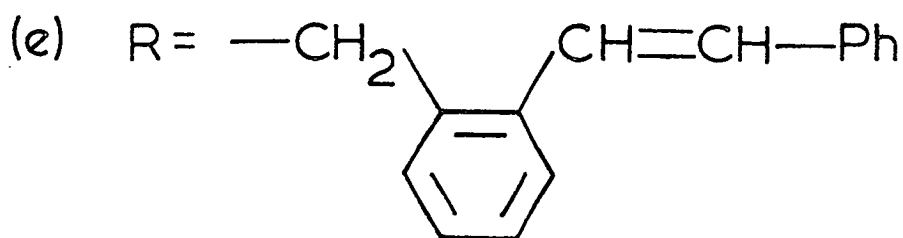
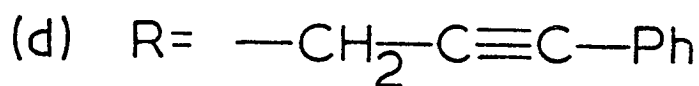
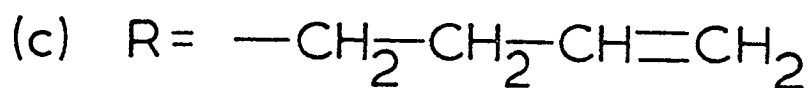
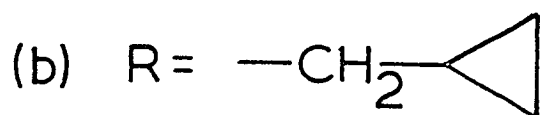
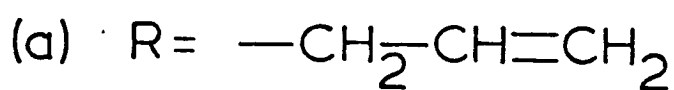
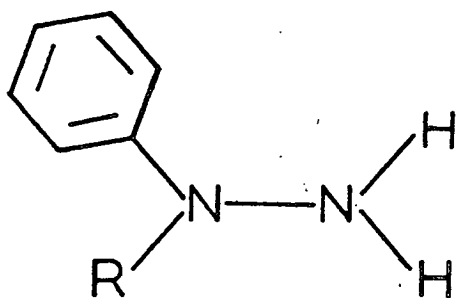


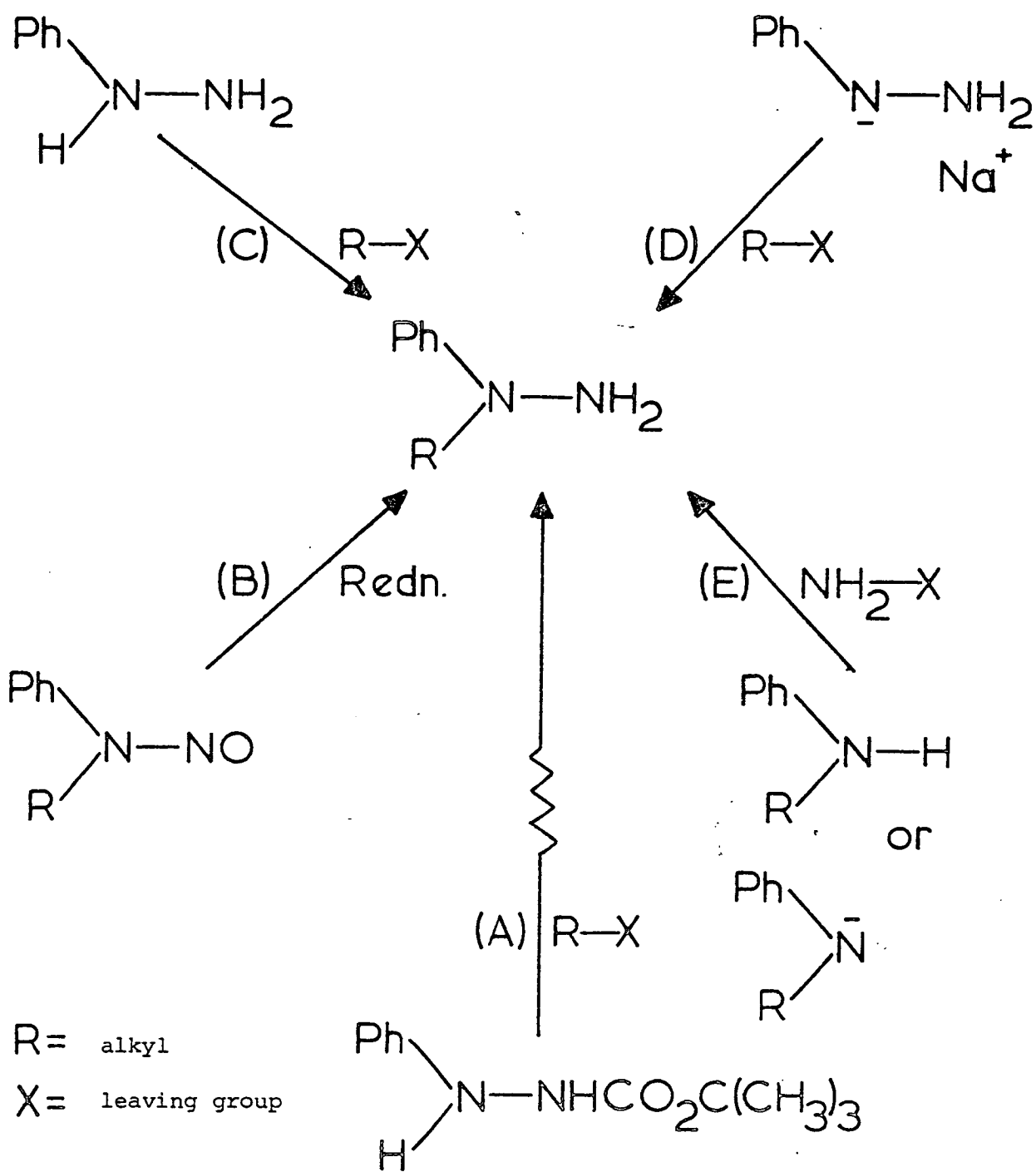
Table 1

DISCUSSION

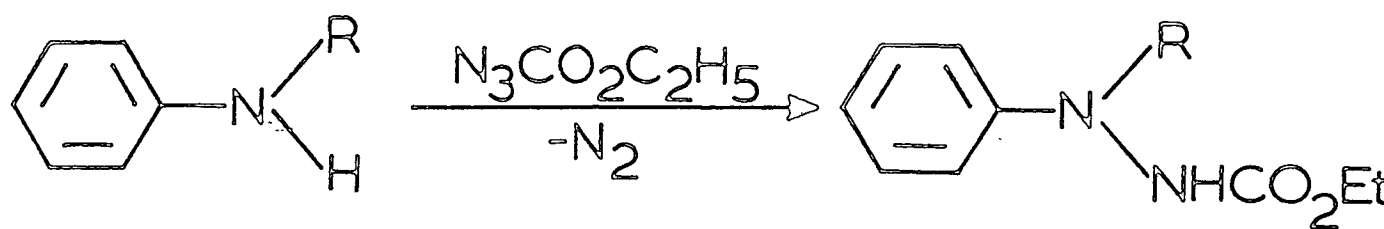
Preparation of 1-Alkyl-1-Phenylhydrazines

Although the intermediacy of 1,1-diazenes in the several supposedly diazene-generating reactions already described (see pages 2 - 5) has never been rigorously proved, the body of evidence in support of their existence is convincing (see Introduction). Perhaps the least ambiguous of these reactions is the mild oxidation of 1,1-disubstituted hydrazines in neutral media with oxidising agents such as mercuric oxide, lead tetra-acetate and t-butyl hypochlorite: least ambiguous in the sense that the basic diazene framework is already formed in the parent hydrazine, and that the possibility of the formation and subsequent reaction of discrete ionic species is not envisaged, except perhaps in the case of oxidation with lead tetra-acetate. As the aim of this study was to examine the reactions of several diazene systems (see p.16) whose formation was to be assumed, it was felt, for the reasons stated above, that the preferred method of generating these systems was by the mild oxidation of the corresponding 1,1-disubstituted hydrazines, shown in Table 1.

The requirements of a potential method of preparing these hydrazines were (a) that it be as direct a method as possible (particularly in those cases where the alkylating agent was not readily available), (b) that a single pure product be obtained, and (c) that it be generally applicable to the preparation of all the required compounds. The first requirement (a) suggested that the initial step of any proposed synthesis should involve a substrate in which the N-phenyl bond was already formed (N-phenylation requires the use of an activated aryl halide, such as 2,4-dinitrochlorobenzene⁷²).



Scheme 21

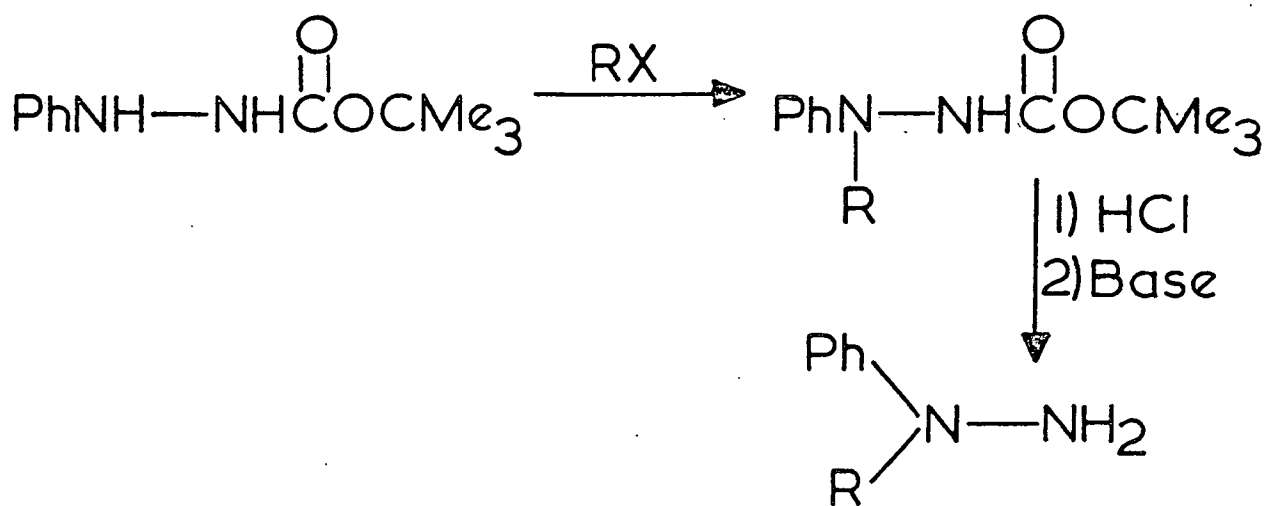


(R = H, 52% ; R = CH₃, 49%)

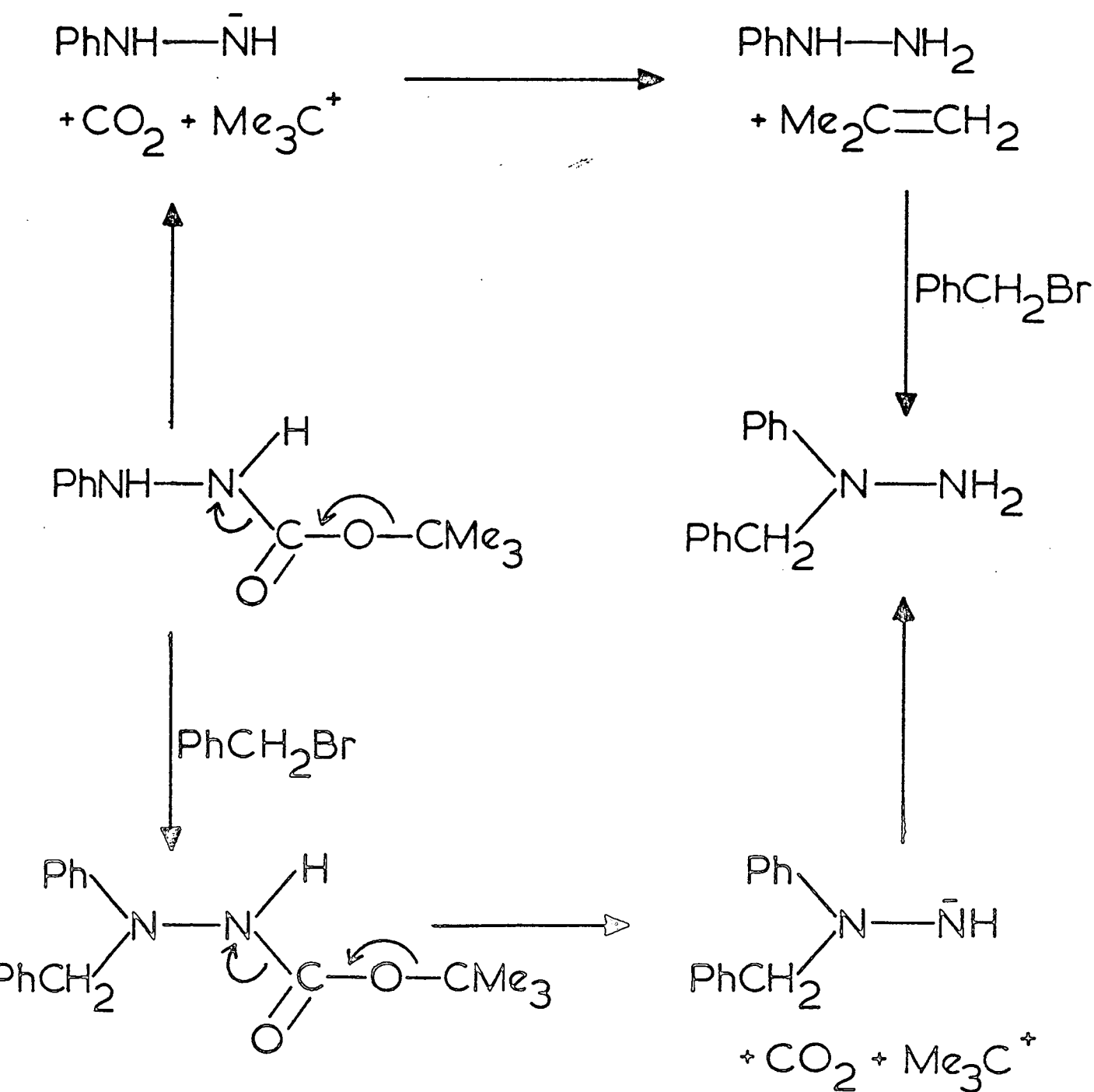
Examination of the literature on the preparation of both 1,1-dialkyl- and 1-alkyl-1-arylhydrazines suggested the possible approaches shown in Scheme 21, each of which appeared to meet the requirements (a), (b), and (c) to some degree at least.

Each of these methods has been examined, with the exception of N-amination (Path E); this method was, however, subsequently employed in a different context (see p. 61 , Experimental p.156). The potential of N-amination has been demonstrated by Schubert et al⁷³ and by Claessen⁷⁴ who prepared substituted 1-alkyl-1-arylhydrazines and substituted phenylhydrazines respectively (the latter in yields of ca. 80%) by the action of ~~chloramine~~ on the corresponding amines. In the preparation of 1,1-disubstituted hydrazines generally, several hydroxylamine derivatives have been used as aminating agents: hydroxylamine-O-sulphonic acid,⁷⁵ O-mesitoylhydroxylamine,^{76,77} and O-2,4-dinitrophenylhydroxylamine.^{77,78} These latter agents are generally reacted with the nitrogen anion of the species to be aminated (see Experimental p.156).

Related to the N-amination route to 1,1-disubstituted hydrazines is the reported reaction of ethoxycarbonylnitrene with aniline and N-methylaniline to give 1-ethoxycarbonyl-2-phenylhydrazine (52%), and 1-ethoxycarbonyl-2-methyl-2-phenylhydrazine (49%) respectively⁷⁹ (Scheme 22). Hydrolysis and decarboxylation of these hydrazines, in a manner analogous to that reported by Al-Sader and Crawford⁸⁰ for the removal of the ethoxycarbonyl groups from 1,2-di-allyl-1,2-di-ethoxycarbonylhydrazine, might be expected to give the products of formal N-amination of aniline and N-methylaniline respectively. However, this extension of the basic nitrene insertion reaction does not appear to have been reported, and, interestingly, the authors of two comprehensive reviews of hydrazine chemistry make no mention of this approach as a means of effecting N-amination of amines to give the corresponding hydrazines.^{81,82}



Scheme 23



Scheme 24

The results of the examination of each proposed approach (Paths A-D in Scheme 21) are now described.

The Attempted Alkylation of t-Butyl 2-Phenylcarbazate. (Method A)

This procedure corresponds to path (A) in Scheme 21. Carpino and his co-workers^{11,41} developed the method of preparing 1,1-dialkylhydrazines (both with equivalent, and with mixed substituents) by the successive alkylation of t-butyl carbazate. The method is advantageous in that alkylation only takes place on the initially unsubstituted nitrogen atom, so avoiding the problem of 1,2-dialkylhydrazine formation. The protecting group is readily removed by treating a solution of the alkylation product in nitromethane with a stream of hydrogen chloride gas to form the hydrochloride of the desired hydrazine; the free base is obtained by treating this hydrochloride with base.

The possibility of adapting this method to the preparation of 1-alkyl-1-phenylhydrazines, using t-butyl 2-phenylcarbazate in place of t-butyl carbazate therefore seemed attractive (Scheme 23) particularly as the preparation of the necessary t-butyl 2-phenylcarbazate had been reported by Carpino.¹¹ He had prepared the compound as an illustrative example of the applicability of t-butyl azidoformate to the acylation of amino compounds, but did not examine it further.

The alkylation of t-butyl 2-phenylcarbazate was attempted according to the procedure of Carpino et al,⁴¹ using allyl bromide and benzyl bromide as alkylating agents. An equimolar mixture of the carbazate and the alkylating agent in dimethyl formamide was heated in an oil bath before adding an equivalent amount of triethylamine. Several different reaction conditions were examined but none of the attempted alkylations gave the precipitation of triethylamine hydrobromide expected from a

successful alkylation (Experimental pp. 120-123).

With allyl bromide, stirring the reaction mixture for ca. 6 h at 25°C gave a mixture of five products, one of which was shown by n.m.r. spectroscopy to be t-butyl 2-phenylcarbazate. The n.m.r. spectrum of the product mixture showed the signals of the allyl moiety, but these were shown to be due to entrained allyl bromide, and not to the presence of the desired alkylation product.

Two modifications of this method, namely, prolonged heating of the reaction mixture at 65-70°C, and heating overnight at 70°C in the presence of a catalytic amount of the silver salt of trifluoroacetic acid, gave a product mixture which was virtually identical to that already described.

Using benzyl bromide, overnight heating of the reaction mixture under reflux gave a red-brown oil whose n.m.r. spectrum showed the almost complete disappearance of the singlet signal attributed to the t-butyl group, and indicated that the oil was a mixture of products. In the light of later work the major part of the n.m.r. spectrum could be interpreted in terms of the formation of 1-benzyl-1-phenylhydrazine. The apparent thermal lability of the protecting group was confirmed by the results of a control experiment in which a solution of t-butyl 2-phenylcarbazate in dimethylformamide was heated under reflux for ca. 20 h; the n.m.r. spectrum of the gum which was recovered showed that the aromatic : methyl proton integral ratio had changed from 5 : 9 to 3 : 1. The possible mechanisms to account for the loss of the protecting group and apparent formation of 1-benzyl-1-phenylhydrazine are shown in Scheme 24; as shown, the possibility of successful alkylation prior to loss of the protecting group is not ruled out.

The alkylation of the anion of t-butyl 2-phenylcarbazate (prepared by the action of sodium hydride on an equimolar amount of the carbazate,

in hot benzene solution), was also examined. (Experimental p.122); using an equivalent amount of allyl bromide as the alkylating agent, the reaction mixture was heated overnight at 50°C. The n.m.r. spectrum of the product gum suggested that cleavage of the protecting group had occurred to a considerable extent. Complete removal of the protecting group gave a liquid which, though very largely 1-allyl-1-phenylhydrazine, also appeared to contain a small amount of the corresponding 1,2-hydrazine (by n.m.r. spectroscopy). The overall yield was, however, only 12%.

The successful alkylation of the sodium salt of t-butyl 2-phenylcarbazate, albeit in very poor yield, suggests that the failure to effect alkylation of t-butyl 2-phenylcarbazate itself is due to its low nucleophilicity and not to steric hindrance. In view of the many reported successful alkylations of t-butylcarbazate itself, using halides of comparable reactivity, this reduced nucleophilicity probably arises from the delocalisation of N-2 lone pair electrons into the aromatic ring. As has been shown (Scheme 24), the formation of 1-benzyl-1-phenylhydrazine in the high temperature alkylation of t-butyl 2-phenylcarbazate, may be explained essentially in terms of the alkylation of phenylhydrazine with benzyl bromide.

Thus, the anticipated mild, selective, and efficient alkylation of t-butyl 2-phenylcarbazate was not achieved and attention was turned to the alternative methods of preparing the desired hydrazines.

The Preparation of N-Nitrosamines and Their Attempted Reduction to 1-Alkyl-1-Phenylhydrazines (Method B).

This method corresponds to path (B) in Scheme 21, and has been widely used in the synthesis of 1,1-disubstituted hydrazines. A wide variety of reducing agents has been employed and hydrazines have also

been obtained on a preparative scale by electrochemical reduction.⁸³ The N-nitrosamines are prepared by the nitrosation of the corresponding secondary amines with nitrous acid. Nitrosation of a crude secondary amine, containing primary and tertiary amine as contaminants, gives the desired nitrosamine which can be readily recovered by ether extraction of the acidic mixture. However, in order to make efficient use of alkylating agents which are not readily synthesised, an efficient preparation of secondary aromatic amines was required.

Hickinbottom⁸⁴ has described the preparation of N-n-propylaniline in 70% yield by the direct alkylation of aniline with n-propyl bromide. He also obtained ca. 6% of the product of dialkylation. Adaptation of this method to the preparation of N-cyclopropylcarbiny l aniline by the reaction of cyclopropylcarbiny l chloride with excess aniline, gave a mixture of the desired amine and the product of dialkylation (ca. 16% of the product, by n.m.r. spectroscopy) in ca. 70% yield. (Nitrosation of this amine mixture by the method of Hickinbottom,⁸⁵ gave the desired nitrosamine in 67% yield.)

Fones⁸⁶ has described the preparation of pure secondary aromatic amines by alkylation of the sodium salt of acetanilide followed by acid hydrolysis of the product. N-Allylaniline was prepared using this route, but in only 53% overall yield (Experimental p.124). This method therefore has little advantage over the procedure of direct alkylation of aniline except in that the secondary amine product may be completely characterised.

N-Nitroso-N-allylaniline was prepared by the action of nitrous acid on N-allylaniline according to the procedure described by Hartman and Roll⁸⁷ (80% yield); satisfactory spectral data was obtained for material prepared in this way. (Experimental p. 125).

The attempted reduction of N-nitrosamines to the corresponding hydrazines was examined using N-nitroso-N-allylaniline and N-nitroso-N-methylaniline (from a commercial source) as model compounds; three common reduction procedures were examined, and the products were analysed by n.m.r. and infra-red spectroscopy.

Hanna and Schueler⁸⁸ described the reduction of several N-nitrosamines with lithium aluminium hydride. A modified version of their procedure gave a complex mixture of products in the case of the N-allyl compound, and a mixture of starting nitrosamine (21%), 1-methyl-1-phenylhydrazine (58%) and N-methylaniline (21%), in the case of the N-methyl compound. Using the method of Poirier and Bennington,⁸⁹ the essential difference being an extended reaction time, N-nitroso-N-allylaniline gave a mixture of 1-allyl-1-phenylhydrazine (83%) and N-allylaniline (17%).

Carpino et al⁴¹ described the preparation of 1-allyl-1-benzylhydrazine by the reduction of the corresponding nitrosamine with aluminium amalgam. The application of this procedure to the reduction of N-nitroso-N-allylaniline gave a mixture of the expected hydrazine and N-allylaniline the former predominating.

Hickinbottom⁹⁰ has reported the reduction of N-nitroso-N-methylaniline with zinc in acetic acid, to give the corresponding hydrazine in 50-56% yield after fractional distillation. This work was repeated and was shown to give a mixture of the expected hydrazine (57%) and N-methylaniline (43%). That Hickinbottom also obtained a mixture of this type may be inferred from the isolation procedure and the reported yield. The reduction of N-nitroso-N-allylaniline by this method gave a similar mixture of 1-allyl-1-phenylhydrazine and N-allylaniline.

These experiments showed that each of the reduction procedures which were examined gave secondary amines, formally the products of further

reduction of the hydrazines, as well as the desired hydrazines.

Carpino and his co-workers⁴¹ reported similar complications in the use of the same methods for the preparation of 1-allyl-1-benzylhydrazine, 1-benzyl-1-n-butylhydrazine and 1-benzyl-1-t-butylhydrazine. They found that the reduction of N-nitroso-N-allylbenzylamine with zinc and acetic acid gave a mixture of the hydrazine and the secondary amine in approximately equal amount (after fractional distillation), that the reduction of N-nitroso-N-t-butyl-benzylamine with lithium aluminium hydride gave a mixture of products which they could not completely identify, and that the reduction of the last-mentioned nitrosamine with aluminium amalgam gave a mixture of the hydrazine (39%) and the secondary amine (40%). Similarly, Carter and Stevens⁶² found that in the preparation of hydrazines such as 1-benzyl-1-o-tolylhydrazine by the reduction of the corresponding N-nitrosamines with zinc and acetic acid, some secondary amine was produced as well.

Thus, while these reductive methods would be expected to give mixtures of products from which the desired hydrazines could be isolated by distillation, in principle at least, the formation of 1-alkyl-1-phenylhydrazines by the reduction of the corresponding N-nitrosamines fell far short of meeting the originally defined requirements of a useful preparative procedure.

Formation of 1-Alkyl-1-Phenylhydrazines by the Reaction of Phenylhydrazine with Alkyl Halides (Method C).

This method corresponds to path (C) in Scheme 21. The usefulness of the direct alkylation of hydrazine as a means of preparing mono-alkyl hydrazines is limited by the tendency for further alkylation to occur at the substituted nitrogen atom. This tendency has its parallel in

the alkylation of phenylhydrazine, and was clearly demonstrated by Hinman⁹¹ who showed that the product of the reaction of phenylhydrazine with excess methyl iodide was 1,1-dimethyl-1-phenyl-hydrazinium iodide. With sufficiently sterically hindered alkylating agents such as triphenylmethyl chloride, phenylhydrazine has been shown to alkylate at the unsubstituted nitrogen⁹² (see p.144). Westphal⁹³ showed that in the alkylation of hydrazine with alkylating agents of intermediate size (e.g. allyl, propyl and butyl halides) the formation of hydrazinium salts is inhibited and 1,1,2-trialkylhydrazines and 1,1,2,2-tetra-alkylhydrazines may be formed instead.

Hinman⁹¹ has suggested that the tendency for alkylation to occur at the substituted nitrogen atom may be due to the ability of alkyl groups to stabilise the positive charge which develops in the transition state (Scheme 25).

The first attempted alkylation procedure paralleled the method which had been used successfully in the alkylation of aniline with cyclopropylcarbinyl chloride (Experimental p. 123). A mixture of cyclopropylcarbinyl chloride and two equivalents of phenylhydrazine was heated at 90°C for ca. 100 h; the alkylation product, a brown liquid was shown by mass spectrometry to contain both the monoalkylated and the dialkylated products. The extent of dialkylation was crudely estimated to be ca. 32% by comparison of the intensities of the peaks at m/e 216 (dialkylated product) and m/e 162 (monoalkylated product) . The n.m.r. spectrum of this material indicated the presence of residual phenylhydrazine, and showed two doublet signals (δ 3.25 and 2.65 p.p.m. with integrals in the ratio of ca. 2:1) which were attributed to the exocyclic methylene protons of the cyclopropylcarbinyl moiety. The doublet at δ 3.25 p.p.m. was attributed to 1-cyclopropylcarbinyl-1-phenylhydrazine (see Experimental p. 126); the doublet at lower frequency was attributed

to 1,2-dicyclopropylcarbiny-1-phenylhydrazine since the mass spectrum had indicated that dialkylation had occurred to a considerable degree, and since the corresponding doublet signal of 2-cyclopropylcarbiny-1-phenylhydrazine was known to occur in the same region of the n.m.r. spectrum (δ 2.62 p.p.m.; Experimental p. 164). The alkylation product was therefore interpreted as being a mixture of phenylhydrazine, with 1-cyclopropylcarbiny-1-phenylhydrazine and 1,2-dicyclopropylcarbiny-1-phenylhydrazine in the ratio 2:1. The possible presence of 2-cyclopropylcarbiny-1-phenylhydrazine as well, cannot be ruled out.

[Westphal⁹³ showed that the reaction of butyl chloride with hydrazine (1.23 equivalents) at 150°C for 16 h. gave a mixture of mono, 1,1-di-, and 1,1,2-tributylhydrazine and the hydrazinium salt (15% of the theoretical). He estimated the yield of 1,1,2-tributylhydrazine to be 36% after fractional distillation.]

Fischer and Knoevenagel⁵ reported the preparation of 2-allyl-1-phenylhydrazine by the reaction of allyl bromide with two equivalents of phenylhydrazine in ether solution. They based their assignment of the product on the results of its oxidation with yellow mercuric oxide; they isolated 1-phenylazoprop-2-ene, the expected product of oxidation of 2-allyl-1-phenylhydrazine. Michaelis and Luxemburg⁴ subsequently showed that the oxidation product which Fischer and Knoevenagel had obtained was indeed 1-phenylazoprop-2-ene, but that it had been formed not from 2-allyl-1-phenylhydrazine but by the oxidative rearrangement of 1-allyl-1-phenylhydrazine.

The alkylation described by Fischer and Knoevenagel⁵ was repeated, and the product was examined by n.m.r. spectroscopy; two multiplet signals attributable to the methylene protons of the allyl group were observed (Experimental p.127).

The spectrum was interpreted in terms of the product being a mixture of 1-allyl-1-phenylhydrazine (78%) and 2-allyl-1-phenylhydrazine (22%). The spectral assignments were confirmed by the subsequent preparation and characterisation of authentic samples of each of the isomeric hydrazines (Experimental p.131 and p. 160).

In contrast to the alkylation of phenylhydrazine with cyclopropyl-carbonyl chloride already described (see p. 26), alkylation according to the procedure of Fischer and Knoevenagel⁵ gave a product in which the presence of only a trace amount of dialkylated material was detectable by mass spectrometry.

These experiments showed that in the direct alkylation of phenylhydrazine with alkyl halides, the problem of dialkylation can be overcome by working in ether solution and at ambient temperature. However the competing formation of the 1,2-isomeric hydrazine to the degree observed represents a serious shortcoming of this method as a means of preparing 1-alkyl-1-phenylhydrazines. The problems of separating the components of such a mixture by distillation, on a small scale, are perhaps exemplified by the very close similarity in the reported boiling points of 1,1- and 1,2-methylphenylhydrazine: 106-109°C/13 mm.⁹⁴ and 110-112°C/12-15 mm.⁹⁵ respectively.

The Preparation of 1-Alkyl-1-Phenylhydrazines by the Alkylation of the Sodium Salt of Phenylhydrazine (Method D).

This method corresponds to path (D) in Scheme 21, and its use was first reported by Michaelis in 1889.⁹⁶ He prepared the sodium salt of phenylhydrazine by distilling an excess of phenylhydrazine with sodium under reduced pressure, the sodium salt being left behind as a fairly

pure, reddish-yellow mass. He showed that alkylation of this material with ethyl bromide gave 1-ethyl-1-phenylhydrazine. He subsequently reported⁹⁷ the preparation of 1-allyl-1-phenylhydrazine by the analogous procedure; he identified two minor impurities (present in ca. 8% amount) as being phenylhydrazine and 2-allyl-1-phenylhydrazine.

Titherley⁹⁸ prepared the sodium-salt by the action of sodamide on an equivalent amount of phenylhydrazine and obtained the compound as a light, golden-yellow precipitate. He showed that the sodium salt was appreciably soluble in benzene and in toluene, and that it could, in fact, be recrystallised from these solvents if large volumes were used. The solid could be stored under vacuum if kept moist with benzene, but was decomposed by exposure to the atmosphere.

More recently, West and Stewart⁹⁹ have described the preparation of 1-methyl-1-m-trifluoromethylphenylhydrazine by the action of methyl iodide on the anion of m-trifluoromethylphenylhydrazine generated by treating the hydrazine with n-butyl-lithium.

In this study, the preparation of the sodium salt of phenylhydrazine according to method of Titherley⁹⁸ was found to be very troublesome in practice. Furthermore, the product which was recovered from the alkylation of the sodium salt prepared in this way, was found by n.m.r. spectroscopy to contain a considerable amount of phenylhydrazine. The possibility of using sodium hydride (a much more convenient reagent) in place of sodamide was examined and with this modification, encouraging results were soon obtained (Experimental p.127). The products of these early alkylation reactions were shown by n.m.r. spectroscopy to be mixtures of the desired 1-alkyl-1-phenylhydrazines and ca. 30% phenylhydrazine. In contrast to the results of Michaelis,⁹⁷ no 2-alkyl-1-phenylhydrazine

was obtained (by n.m.r. spectroscopy); only trace amounts of dialkylated material were detected by mass spectrometry. Unfortunately however, the attempted removal of the phenylhydrazine by distillation from the relatively small amounts of material involved, was unsuccessful.

It was found that the presence of phenylhydrazine could be both identified and quantified by examining the n.m.r. spectrum of the product of reaction of the crude 1-alkyl-1-phenylhydrazine with acetone (Experimental p.128). The method is based on the high reactivity of mono- and 1,1-disubstituted hydrazines towards carbonyl compounds, to give hydrazones. Aldehydes are known to react with 1,2-disubstituted hydrazines as well to give α -hydrazino carbinols which react further,¹⁰⁰ and so a ketone was used in order to avoid this complication. Acetone was chosen because it was known to undergo facile condensation, and because it was anticipated that in the n.m.r. spectrum of the product hydrazones, the signals of the methyl groups would occur at chemical shifts suitably removed from the remainder of the spectrum. The resonances of the syn- and anti-methyl groups of acetone phenylhydrazone in the n.m.r. spectrum of the acetone condensation product mixture, were observed at δ 1.75 and 2.02 p.p.m. (The assignments were confirmed by comparison with the n.m.r. spectrum of the authentic compound). The corresponding signals of the acetone N-alkyl-N-phenylhydrazones were observed as two large singlets in the same region of the spectrum and the phenylhydrazine content was estimated by comparing the ratios of these two pairs of singlets. The same reaction with acetone is also of value in that it can be used to differentiate between the desired 1-alkyl-1-phenylhydrazines and the unwanted 2-alkyl-1-phenylhydrazines.

A possible solution to the problem of the removal of residual phenylhydrazine from the product of alkylation of the sodium salt of phenylhydrazine was suggested by the work of Michaelis and Claessen.⁹⁷ They found that 1-allyl-1-phenylhydrazine could be separated from a mixture

which they had interpreted as being composed of 1-allyl-1-phenylhydrazine and 2-allyl-1-phenylhydrazine, by converting the mixture to its solid hydrochloride derivative and recrystallising this from benzene; the 1,1-isomer separated while the 1,2-isomer stayed in solution. Fortuitously, adaptation of this procedure to the hydrochloride mixture derived from the products of the several alkylations of the sodium salt of phenylhydrazine described here (Experimental p. 1281, gave only the 1-alkyl-1-phenylhydrazine hydrochlorides; phenylhydrazine hydrochloride, which was found to be insoluble in benzene, was removed by hot filtration during the recrystallisation.

The preparation of the crude hydrochlorides also offered a means of identifying the presence of phenylhydrazine in the crude alkylation products: comparison of the infra-red spectra of phenylhydrazine hydrochloride, the crude hydrochloride and the recrystallised material showed that the differences between the spectra of the crude and the recrystallised hydrochlorides could be related to the loss of phenylhydrazine hydrochloride in the recrystallisation process. From these observations, three infra-red absorption bands were found to be diagnostic for the presence of phenylhydrazine hydrochloride in the crude hydrochloride of the alkylation product. These bands were ν (nujol) 887, 857 and 770 cm^{-1} although the latter was not too useful as that region of the spectrum was generally very complex. Although applicable to the particular examples cited here, the observation of these bands can, in the general context, only be considered as a necessary but not sufficient condition for the presence of phenylhydrazine in the crude alkylation product. The reaction of the alkylation product with acetone is probably of greater applicability in identifying the presence of residual phenylhydrazine.

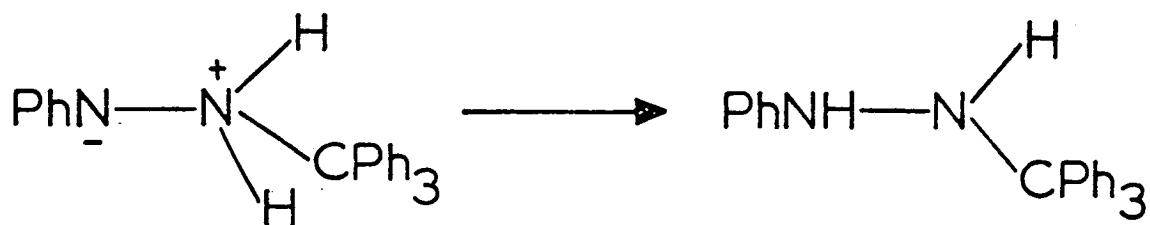
It was subsequently found that by modifying the procedure for the preparation of sodium hydride to enable the use of an exact equivalent of the pure base in the formation of the sodium salt of phenylhydrazine,

complete conversion to 1-alkyl-1-phenylhydrazine could be achieved in most cases, the absence of residual phenylhydrazine being confirmed by applying either or both of the tests described. In such cases, the desired hydrazines were obtained in 80-90% yield.

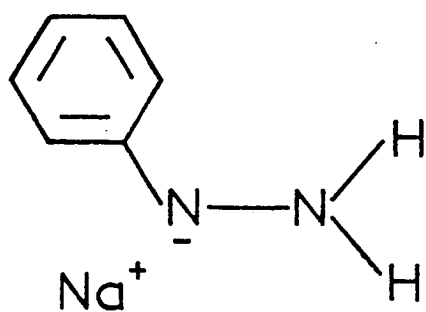
Table 1/^{facing p. 13} lists the 1-alkyl-1-phenylhydrazines which were prepared by the alkylation of the sodium salt of phenylhydrazine with alkyl halides prepared by established methods, the hydrazines were generally stored in the form of the more stable hydrochloride derivatives.

The apparently anomalous results of preliminary experiments on the oxidation of 1-benzyl-1-phenylhydrazine suggested the desirability of preparing analogous hydrazines having complete substitution of the benzylic carbon. However, attempts to prepare 1-cumyl-1-phenylhydrazine and 1-phenyl-1-triphenyl-methylhydrazine by the method described, were unsuccessful (Experimental pp. 140-144).

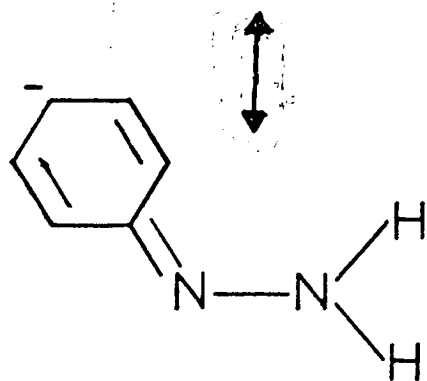
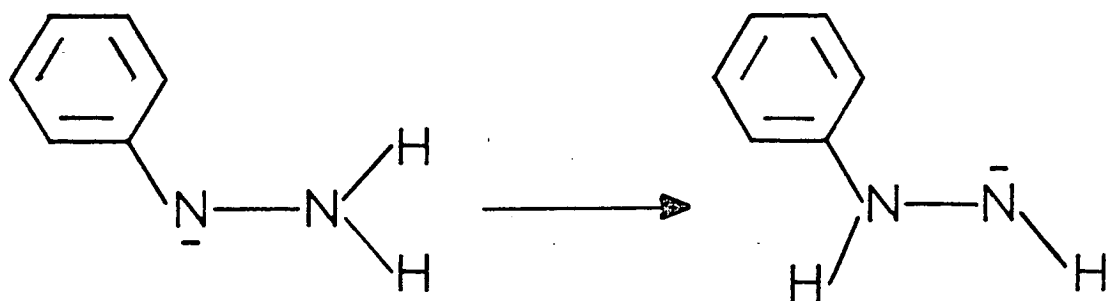
The reaction of the sodium salt of phenylhydrazine with cumyl chloride gave a mixture of α -methylstyrene (formally the product of elimination of hydrogen chloride from cumyl chloride), phenylhydrazine and a product (or products) which could not be identified. The alkylation of phenylhydrazine with cumyl chloride by the method of Fischer and Knoevenagel (see p.142) gave α -methylstyrene and an apparently complex mixture of unidentified basic products. The results of a control experiment showed that a mixture of phenylhydrazine and α -methylstyrene was unchanged after stirring; this suggested that the unidentified products obtained in these attempted alkylations were in fact derived in some way from reaction of the alkylating agent. The formation of α -methylstyrene in both reactions is perhaps not surprising in view of the facile elimination pathway open to the chloride as a result of the ability of the phenyl



Scheme 26



(9)



Etc.

Scheme 27

substituent to stabilise the transition state.

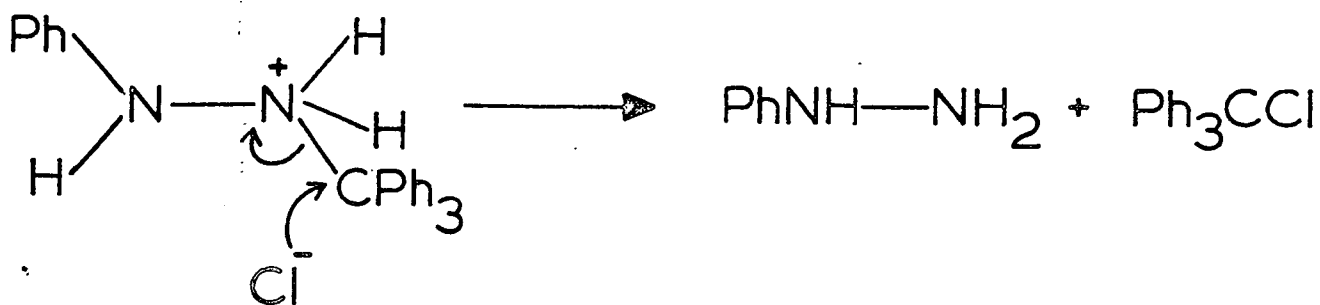
Reaction of the sodium salt of phenylhydrazine with triphenylmethyl chloride gave a yellow gum which, on treating with acetone, gave a small amount of acetone phenylhydrazone and none of the expected acetone 1-phenyl-1-triphenylmethylhydrazone. (The product analysis was done by n.m.r. spectroscopy). The failure to obtain the expected phenylhydrazone in this way suggested that, in the absence of the possibility of elimination of hydrogen chloride from the alkylating agent, the most probable course of reaction was the formation of 1-phenyl-2-triphenylmethylhydrazine. An authentic sample of this latter compound was prepared by the direct alkylation of phenylhydrazine (an example of the influence of steric hindrance on the course of the alkylation of phenylhydrazine) according to the method of Cohen and Wang⁹²; comparison of the n.m.r. spectrum of 1-phenyl-2-triphenylmethylhydrazine with that of the product from the alkylation of the sodium salt of phenylhydrazine supported the view that alkylation had occurred at the unsubstituted nitrogen. The spectra were not identical, however, and indeed the spectrum of the alkylation product showed a weak signal at δ 5.6 p.p.m which was not observed for the authentic 1,2-substituted hydrazine.

The apparent formation of 1-phenyl-2-triphenylmethylhydrazine in the alkylation of the sodium salt of phenylhydrazine may be envisaged as occurring by two possible mechanisms, in which the influence of the bulkiness of the alkylating agent plays an important part. The first possibility is that of direct alkylation followed by the migration of a proton to the anionic centre (Scheme 26); although here represented as an intramolecular process, intermolecular migration of a proton is also conceivable. Edwards and Pearson¹⁰¹ have suggested that the increased nucleophilicity observed when two atoms with unshared electron pairs are

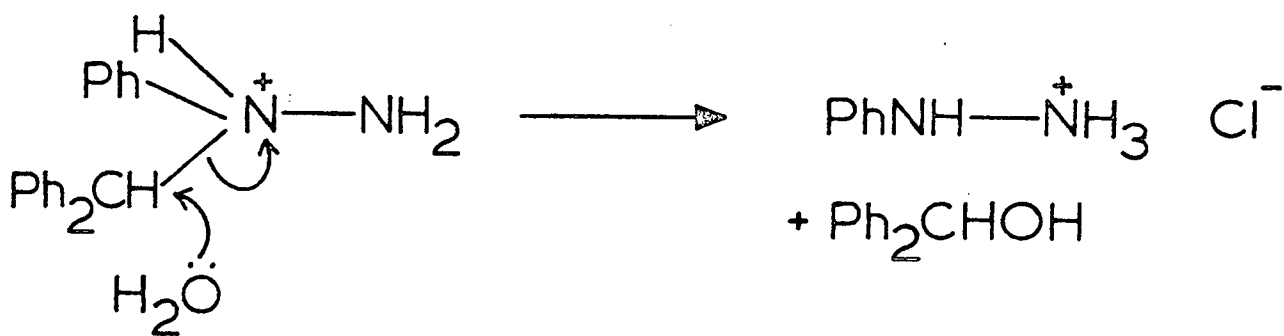
adjacent to one another, can be ascribed to the decreased repulsion between these electron pairs when one pair is involved in bond formation with the electrophilic reagent. Thus, the terminal nitrogen of the sodium salt of phenylhydrazine, generally represented as (9), might be expected to exhibit increased nucleophilicity compared to its situation in phenylhydrazine. Alkylation of the sodium salt of phenylhydrazine with sterically hindered alkylating agents might therefore be expected to give the product of alkylation at the terminal nitrogen atom rather than that of alkylation at the less accessible, though more nucleophilic, anionic centre. The possibility of rearrangement of the phenylhydrazo anion (Scheme 27) followed by alkylation at the new anionic centre, appears less likely, involving as it does, the conversion of a stabilised anion into an unstabilised one.

The alternative mechanism involves initial alkylation at the anionic centre to give the 1,1-disubstituted hydrazine, followed by thermal rearrangement to give the less sterically crowded 1,2-disubstituted hydrazine. No attempt was made to rigorously establish the nature of the actual mechanism involved, although the likelihood of the occurrence of the latter mechanism could presumably be examined by performing the alkylation at low temperature and examining the initially formed product. Carter and Stevens⁶² have shown that 1-diphenylmethyl-1-phenylhydrazine can be prepared by alkylation of the sodium salt of phenylhydrazine with diphenylmethyl bromide; however, the presence of the third phenyl group in the triphenylmethyl moiety may give rise to sufficient steric crowding in the analogous hydrazine to cause rearrangement to occur as suggested. Equally, steric hindrance may prevent formation of 1-phenyl-1-triphenylmethylhydrazine from occurring at all.

Interestingly, the hydrochloride of 1-phenyl-2-triphenylmethylhydrazine prepared by treating a solution of the hydrazine in ether at



Scheme 28



Scheme 29

0°C with gaseous hydrogen chloride was found to be unstable under these conditions, and decomposed to give phenylhydrazine hydrochloride and triphenylmethyl chloride. Likewise, an attempt to prepare the hydrochloride of the crude alkylation product at 0°C gave the same decomposition products. However, the hydrochloride could be isolated when the procedure was carried out at a lower temperature (-5 to -10°C) when only ca. 2% decomposition was observed. The decomposition may be interpreted in terms of the S_N2-type mechanism shown in Scheme 28. An S_N1-type mechanism is also conceivable in view of the highly stabilised nature of the triphenylmethylcarbonium ion which would be formed.

A similar hydrochloride decomposition was reported by Carter and Stevens⁶² to occur in the case of 1-diphenylmethyl-1-phenylhydrazine hydrochloride. They found that this compound was decomposed by water to give diphenylmethanol and phenylhydrazine. They did not give any experimental details and in particular, they did not indicate whether basification was required to isolate free phenylhydrazine or not; neither did they suggest a mechanism for the formation of the observed products. A possible mechanism, based on that described in Scheme 28, is shown in Scheme 29.

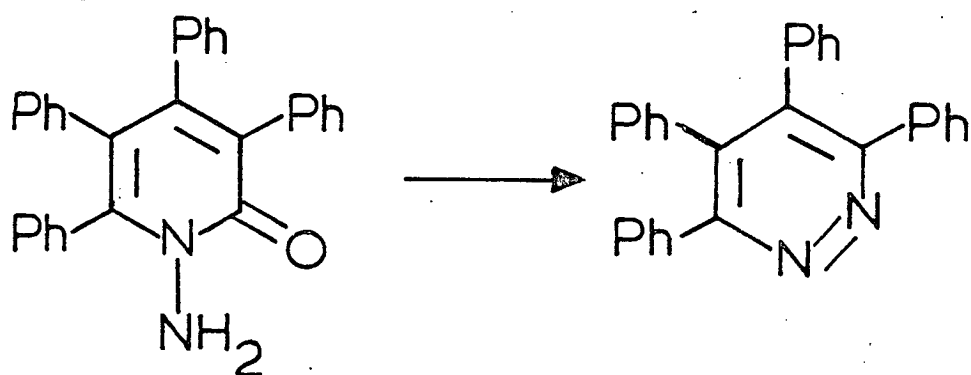
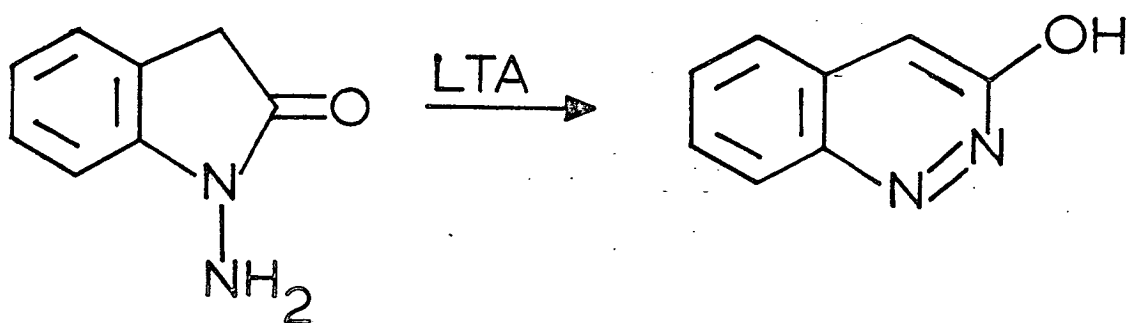
The hydrochloride of 1-pent-3-en-2-yl-1-phenylhydrazine was also found to behave anomalously during its attempted purification by recrystallisation from benzene (see p. 172).

In summary, the sodium salt of phenylhydrazine may be conveniently and efficiently prepared by the action of sodium hydride on phenylhydrazine. The sodium salt can be alkylated readily with alkyl halides to give 1-alkyl-1-phenylhydrazines in high yield. No competing formation of 1-alkyl-2-phenylhydrazines is observed as a rule, and the desired hydrazines are often obtained pure. Two methods have been established to enable the

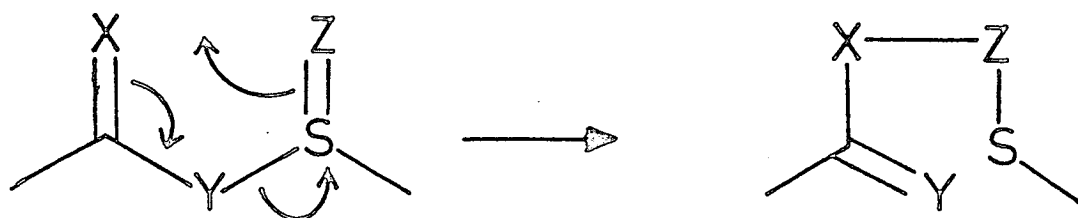
presence of phenylhydrazine to be identified, and the procedure of benzene extraction of the hydrochloride affords a convenient method for its removal.

The alkylation fails for halides which show a tendency to eliminate, but it should be possible to predict such instances in terms of established theory or the known behaviour of the halide in nucleophilic substitution reactions. Similarly, the directing effect of the anionic nitrogen centre is apparently not strong enough to prevent alkylation from occurring preferentially at N-2 in cases where the alkylating agent is severely sterically hindered.

The purification procedure may be limited by the unexpected behaviour of individual hydrochlorides in the course of their preparation (vide supra) or during the benzene extraction process (see p. 174).



Scheme 30



X, Y, Z variously C, O, S

Scheme 31

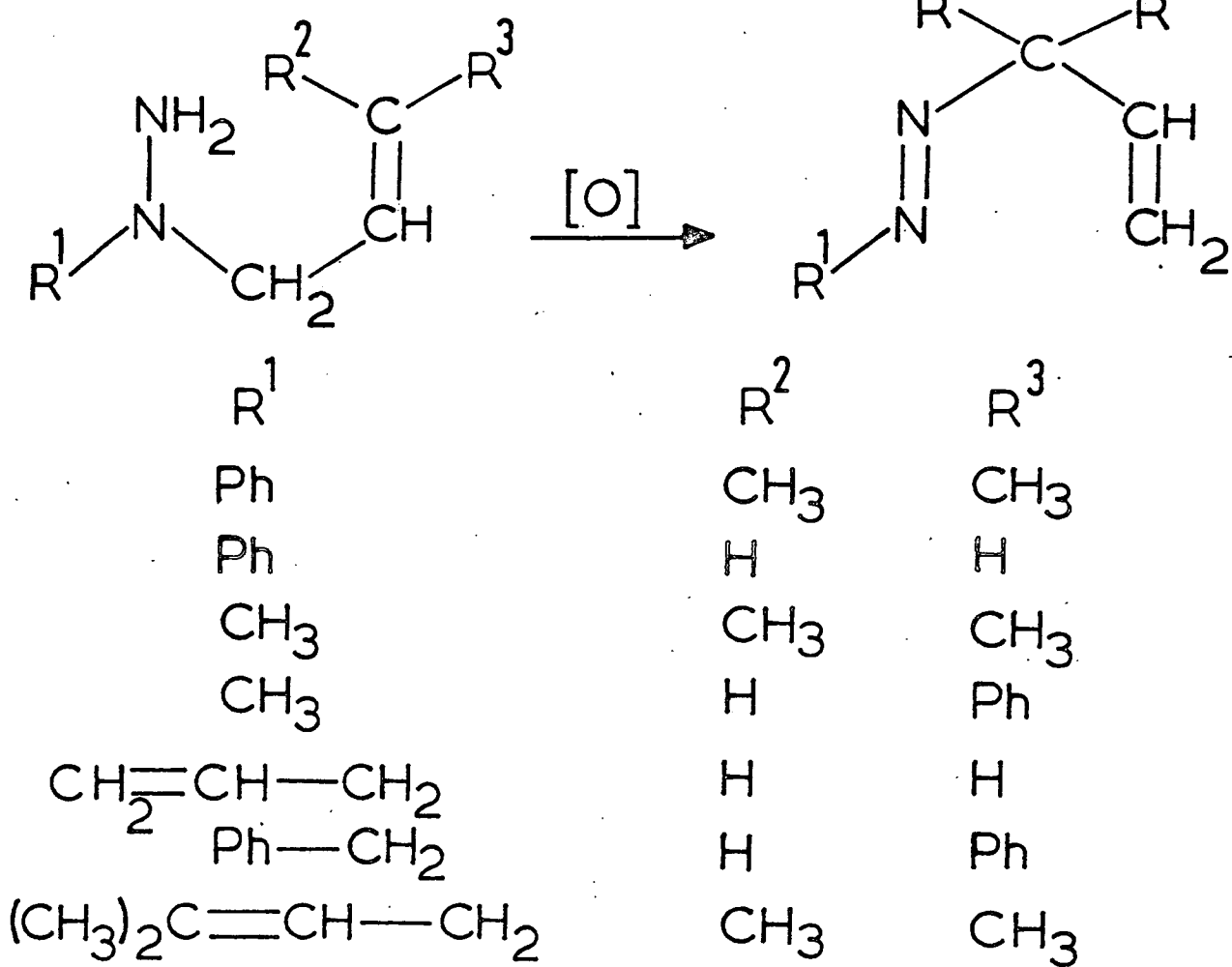
The Oxidation of 1-Alkyl-1-Phenylhydrazines

The hydrazines which were studied were all formally related to 1-allyl-1-phenylhydrazine and the anticipated course of the oxidation was that suggested by analogy with the known rearrangement of allylic diazenes. Before discussing the results of individual oxidations, a brief description of the nature of the allylic diazene rearrangement, and of the mode of action of the oxidising agents used, is given.

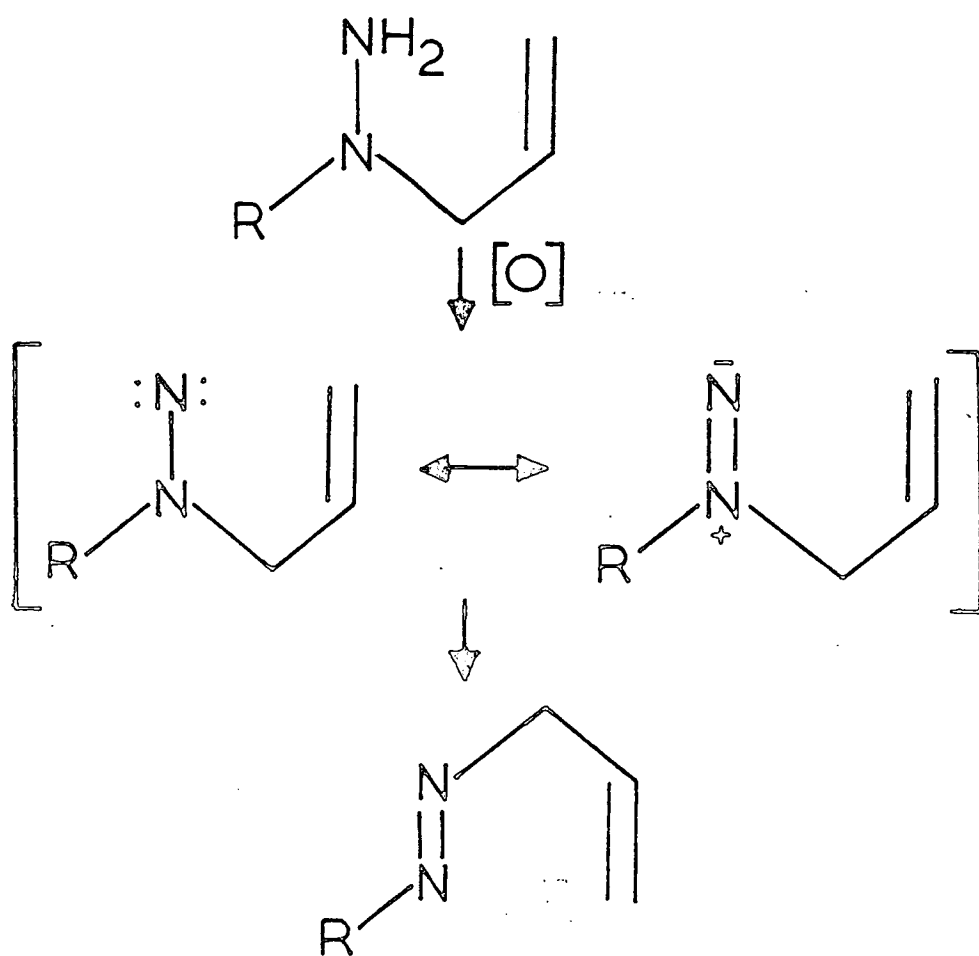
As stated earlier, the oxidation of 1-allyl-1-phenylhydrazine was found by Michaelis and Luxemburg⁴ to give 1-phenylazoprop-2-ene rather than the corresponding tetrazene which they had expected. The important role of the allyl group in this rearrangement is underlined by the fact that only two formally analogous examples of the rearrangement have been reported for hydrazines not containing the allyl substituent: the oxidation of N-amino-oxindole to give 3-cinnolinol⁶⁶ and the oxidation of 1-amino-3,4,5,6-tetraphenylpyrid-2-one to give 3,4,5,6-tetraphenylpyridazine.⁶⁷ (Scheme 30).

In recent years, the development of a general theory of concerted reactions, principally by Woodward and Hoffmann,⁵⁹ has enabled the rationalisation of the stereochemical course of known concerted processes. Furthermore, the theory has enabled the chemist to extrapolate from known reactions and to predict the feasibility of a particular process occurring by a concerted mechanism, and in such instances to predict the stereochemistry of the product, where this applies.

In 1968 Baldwin et al¹⁰² postulated that a number of apparently unrelated reactions in the field of sulphonium ylide chemistry could be rationalised in terms of an electrocyclic mechanism with conservation of orbital symmetry (Scheme 31). Baldwin⁶¹ subsequently examined the scope of this generalised mechanistic scheme and in this



Scheme 32

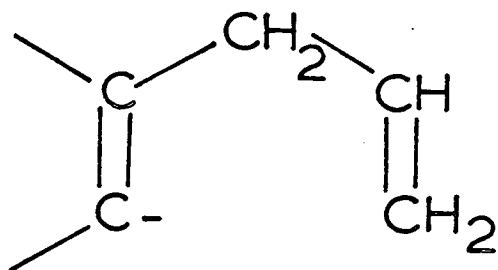
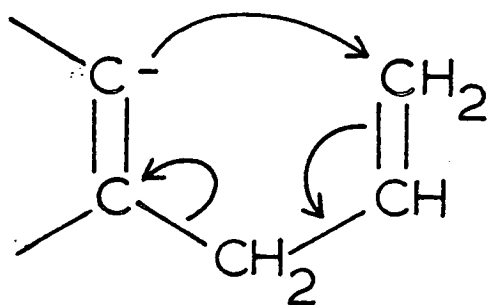


Scheme 33

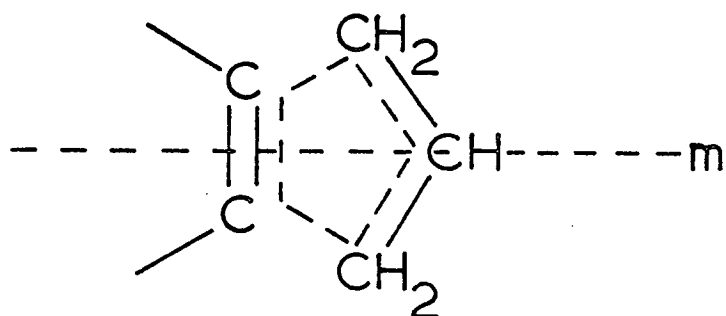
connection he re-examined the oxidation of 1-allyl-1-phenylhydrazine and some related hydrazines (Scheme 32). His work confirmed the observations of Michaelis and Luxemburg⁴, and showed that the oxidation of the allylic hydrazines with mercuric oxide, lead tetra-acetate, manganese dioxide and t-butyl hypochlorite gave the corresponding azo-compounds. Hydrocarbons were obtained in small amount from the oxidations with the metal oxides, but not from those carried out using t-butyl hypochlorite. Hydrocarbon formation was attributed to the formation, and subsequent reaction of an intermediate hydrazinyl radical formed by the one-electron oxidation of the hydrazine; such a stepwise oxidation mechanism was not considered possible in the case of t-butyl hypochlorite..

The formation of the azo-compounds to the almost complete exclusion of hydrocarbon formation led Baldwin to conclude that the rearrangement of allylic diazenes occurred by a [2,3] sigmatropic process; this supported his own prediction that the rearrangement should occur by a concerted suprafacial-suprafacial transformation. Thus the allylic diazene rearrangement could be interpreted in terms of his generalised mechanism (Scheme 33).

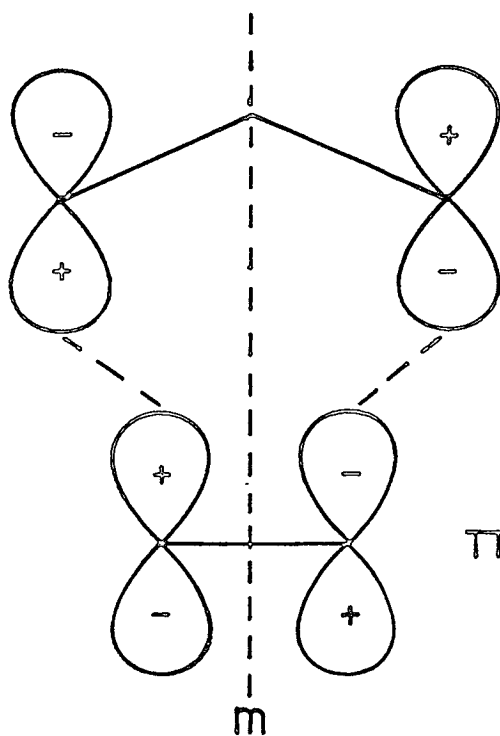
The mechanism is most readily appreciated in terms of the ylide-type representation of the diazene as shown. Support for this representation comes from the results of theoretical calculations (Introduction p. 7) and from the fact that certain 1,1-diazenes, generated by lead tetra-acetate oxidation of the corresponding hydrazines, have been shown to add stereospecifically to electrophilic, as well as to nucleophilic, olefins.^{26,27} Stereospecific addition of diazenes to olefins implies that the reacting diazene is in its singlet ground state; in this state, delocalisation of the lone pair electrons of the N-1 nitrogen into the vacant p-orbital of the N-2 nitrogen can occur to



Scheme 34



Scheme 35



$\Psi_2(A)$

Scheme 36

$\pi^*(A)$

give the dipolar form of the diazene i.e. the ylide-type diazene shown in Scheme 33. It is reasonable to assume that diazenes generated by the use of other oxidising agents such as mercuric oxide, also react in the singlet state.

Consideration of the allylic diazene rearrangement in terms of the Woodward-Hoffmann theory of concerted processes confirms that the [2,3] sigmatropic rearrangement is indeed a 'symmetry-allowed' process. The analysis is simplified if the iso-electronic 'all-carbon' analogue is considered; the rearrangement is then degenerate but is essentially no different from the diazene case (Scheme 34). The transition state for the rearrangement may be considered as two interacting three-electron fragments, an allyl radical and an ethylene-type fragment, as shown in Scheme 35. This transition state has a mirror plane of symmetry (m) with respect to which the participating molecular orbitals must have the same symmetry if the reaction is to be concerted. Using the frontier orbital approach, the relevant orbitals in this case are the singly-occupied π^* anti-bonding orbital of the ethylene-type fragment, and the singly-occupied ψ_2 orbital of the allyl system. For the transition state geometry shown in Scheme 35, it is seen that the interaction between π^* and ψ_2 , in the suprafacial-suprafacial mode shown, is a symmetry allowed process, both orbitals being antisymmetric with respect to the symmetry element, m (Scheme 36).

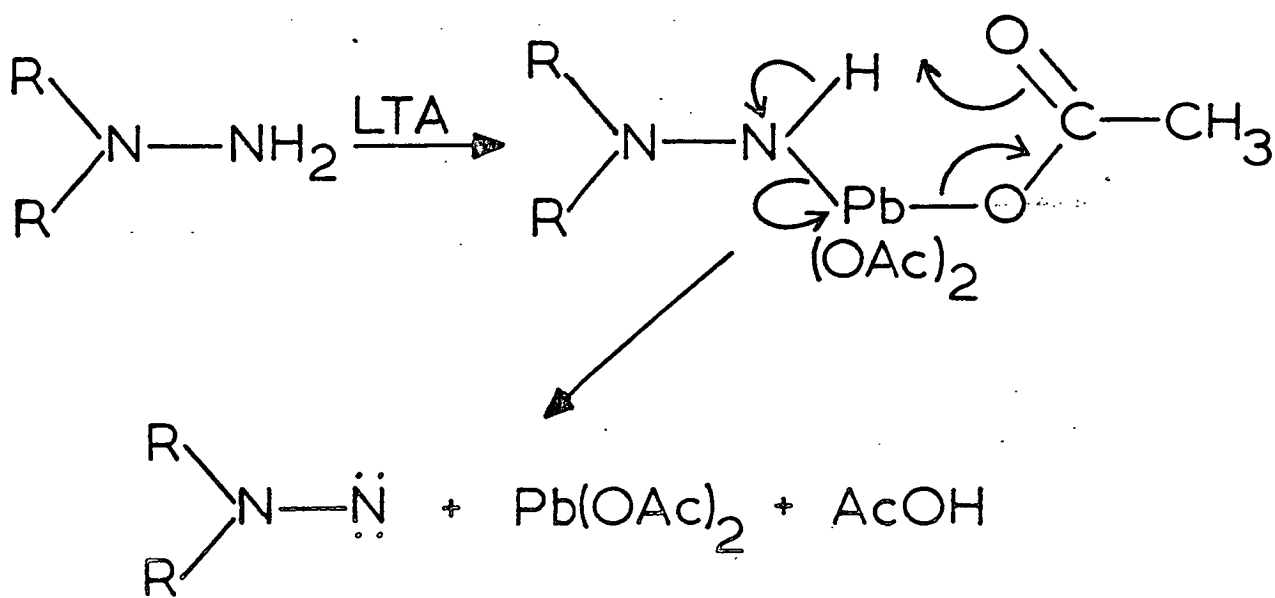
Conservation of orbital symmetry is a necessary but not a sufficient condition for a concerted process to occur. If the required transition state is strained (due to substituent interaction, for example) then reaction will tend to occur by a stepwise pathway of lower energy. Even if the required transition state can be attained, it may well be the case that the activation energy barrier is too high for the concerted process to occur, or the activation energy difference between the concerted

process and the stepwise process may be small enough to allow both mechanisms to operate in competition. Furthermore, the considerations discussed above refer to a specific intramolecular process but in cases where an intermolecular process can compete with intramolecular rearrangement, the task of predicting the nature of the product or products becomes very complex.

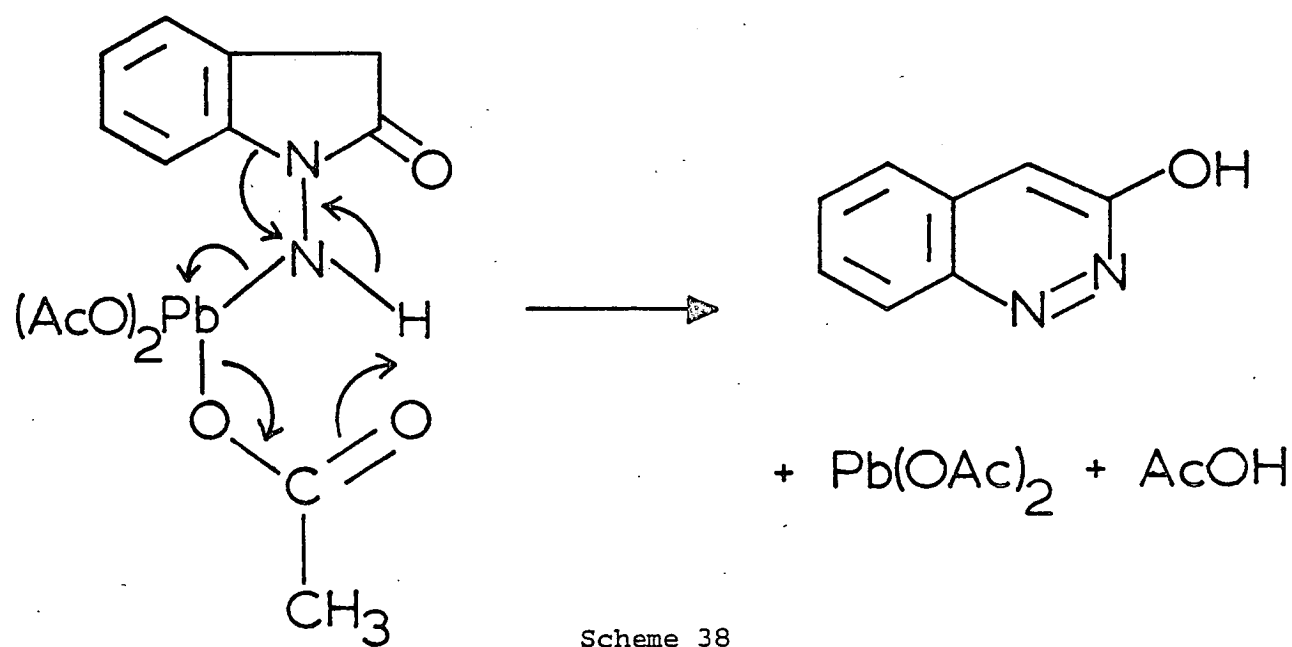
The oxidative rearrangement of allylic 1,1-disubstituted hydrazines to give azo-compounds by a suprafacial-suprafacial rearrangement is therefore a 'symmetry-allowed' concerted process which may be represented as shown in Scheme 33. Predictions of the course of individual oxidation experiments, and therefore of the nature of the anticipated products, were based on this general scheme.

In view of the considerable volume of evidence supporting the formation of diazenes in the oxidation of 1,1-disubstituted hydrazines, their intermediacy was assumed in this study. (Attempts were made to trap the diazenes and although these attempts were unsuccessful, this was not interpreted as denying their formation - see p. 105). Nonetheless, the nature of possible alternative intermediate species in the context of the oxidising agents used (i.e. yellow mercuric oxide, lead tetra-acetate and t-butyl hypochlorite), deserves mention.

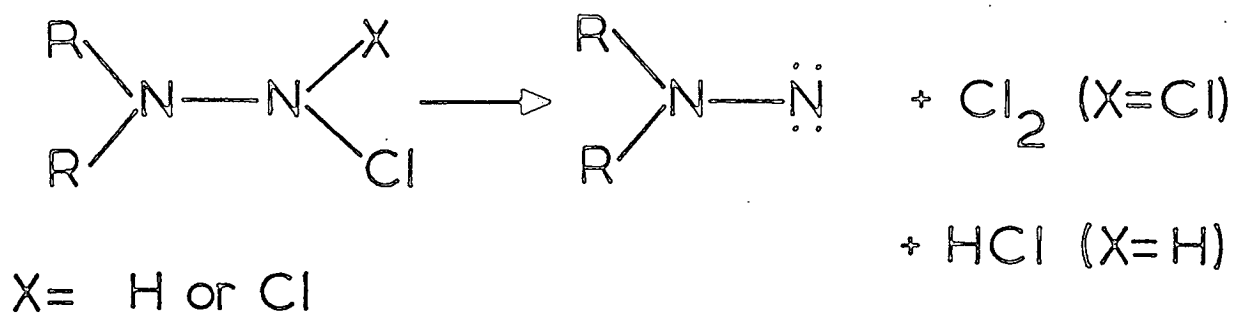
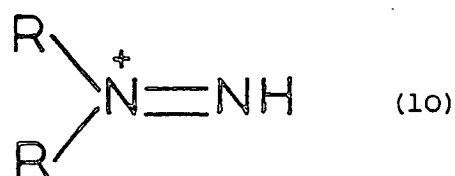
Baldwin⁶¹ has suggested that the overall two-electron oxidation by mercuric oxide is achieved in stepwise fashion, thereby giving rise to a hydrazinyl radical which may decompose with the formation of hydrocarbons, or undergo further oxidation to give the diazene. Heterogeneous oxidation requires that the species to be oxidised become co-ordinated to the oxidant in some way. The surface of the oxidising agent may therefore be regarded as a region of high diazene and high hydrazine concentration, or, if oxidation is instantaneous, as a region of high diazene concentration; both of these situations might be expected to favour tetrazene



Scheme 37



Scheme 38



Scheme 39

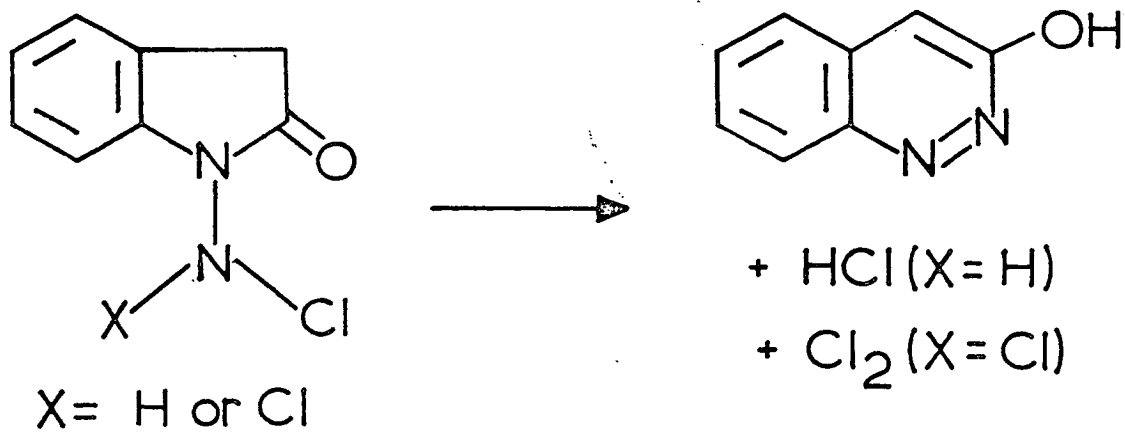
formation (Introduction p. 10). The crystal structure of yellow mercuric oxide is known to be an infinite planar zig-zag chain,¹⁰³ and Forgione et al⁴³ have suggested that the co-ordination which such a structure allows is responsible for the stereospecific oxidation of 3-amino-2-oxazolidinone to the corresponding thermodynamically unfavoured cis-tetraz-2-ene.

Oxidation by lead tetra-acetate is believed to involve the formation of an intermediate complex which then undergoes fragmentation to give the diazene, acetic acid and lead di-acetate (Scheme 37). The possibility of simultaneous rearrangement occurring together with the formation of lead di-acetate and acetic acid, has been suggested in the oxidative rearrangement of N-amino-oxindole;¹⁰⁴ the rearrangement would then involve a diazenoid intermediate rather than a discrete diazene (Scheme 38). The generation of acetic acid in the course of the oxidation allows the possible intermediacy of the conjugate acid of the diazene (10).

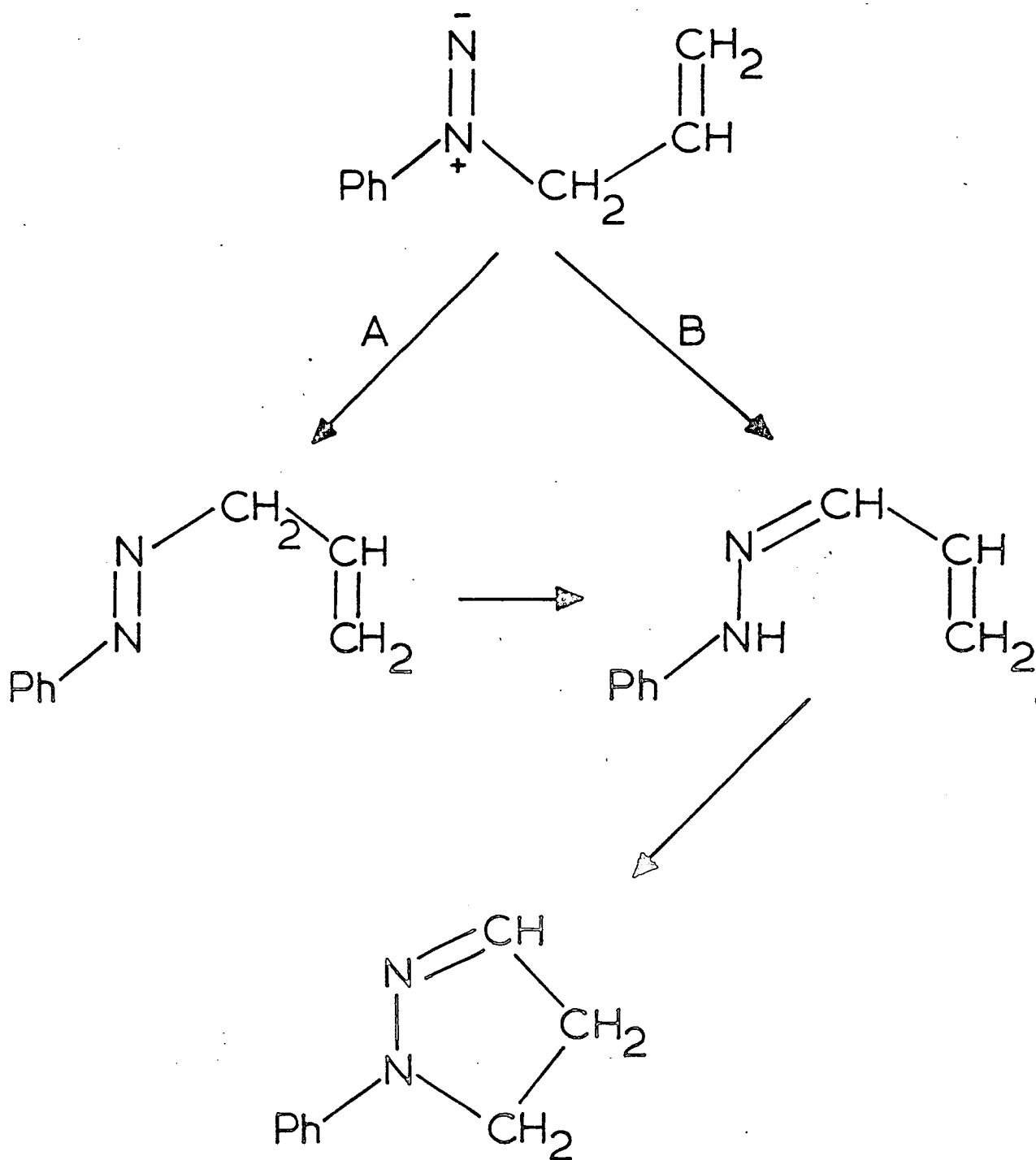
Baldwin⁶¹ has suggested that an intermediate hydrazinyl radical may be involved which can react as such giving rise to hydrocarbons, or be oxidised further to the diazene.

Therefore, the exact nature of the intermediate involved in oxidations with lead tetra-acetate is an open question, but the results of most oxidations of 1,1-disubstituted hydrazines may be satisfactorily rationalised in terms of diazene intermediacy.

Oxidation with t-butyl hypochlorite is believed to involve the formation of an N-chloramine or an N,N-dichloramine which can then decompose to give a diazene (Scheme 39). The common procedure of using one equivalent of the oxidising agent followed by addition of base, probably gives the diazene by the formal α -elimination of hydrogen chloride. Baumgarten et al¹⁰⁴ have suggested that a diazenoid species may be the intermediate in the oxidative rearrangement of N-amino oxindole (Scheme 40).



Scheme 40



The Attempted Oxidation of 1-Allyl-1-Phenylhydrazine with t-Butyl Hypochlorite

The attempted oxidations were carried out on samples of the hydrazine prepared prior to the development of the procedure for their purification described above (see p. 30). The crude hydrazine was distilled and the distillate was collected in four portions; the portions were examined by n.m.r. spectroscopy, and the fraction which appeared least contaminated with phenylhydrazine was used. This distilled material however, was shown still to contain ca. 12% of phenylhydrazine.

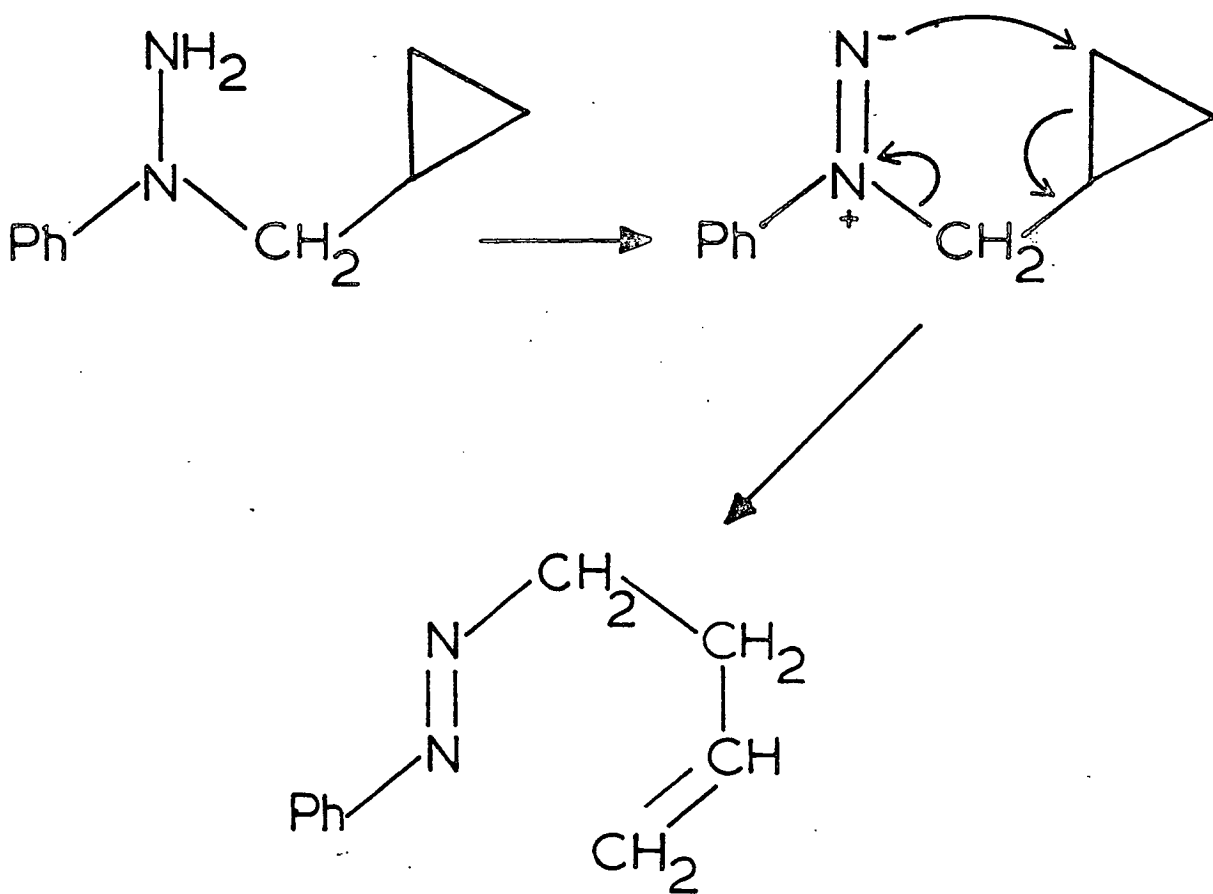
The oxidant was prepared by the methods of Gilliom and Ward,¹⁰⁵ and Mintz and Walling¹⁰⁶; its purity was confirmed by n.m.r. spectroscopy. Three different oxidation procedures were examined (Experimental p. 145) including the use of a 3 mole excess of the oxidising agent. In each case, the oxidation was shown by n.m.r. spectroscopy to give rise to a complex mixture of products. The n.m.r. spectra of these oxidation products could not be reconciled with those of the products of subsequent successful oxidations of the same hydrazine.

While the failure of t-butyl hypochlorite to give the expected product may possibly have been due in some way to the presence of residual phenylhydrazine, the oxidation of the pure 1-alkyl-1-phenylhydrazines with this reagent was not examined, as the use of yellow mercuric oxide and lead tetra-acetate for the oxidation of the pure compounds, had proved satisfactory.

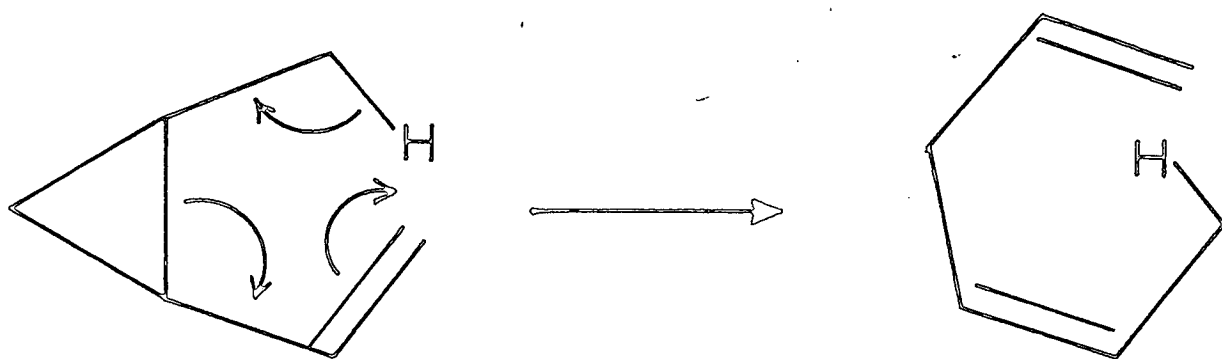
The Oxidation of 1-Allyl-1-Phenylhydrazine with Yellow Mercuric Oxide and with Lead Tetra-acetate

The oxidation was carried out in order to confirm the reported course of the oxidation⁴ and to gain experience of the oxidation methods. Furthermore, while the anticipated product was 1-phenylazoprop-2-ene, the possibility of the formation of 1-phenyl-2-pyrazoline whose presence could be identified by n.m.r. spectroscopy, was also envisaged. Fischer and Knoevenagel¹⁰⁷ and von Auwers and Kreuder¹⁰⁸ have shown that attempts to prepare acrolein phenylhydrazone result in the isolation of the product of internal cyclisation of the hydrazone, 1-phenyl-2-pyrazoline. Formation of this latter compound in the oxidation of 1-allyl-1-phenylhydrazine is conceivable in terms of either of the pathways shown in Scheme 41; path B involves the direct formation of the hydrazone, a possibility which has a close parallel in the observed formation of phenylhydrazones by oxidation of certain 1-aryl-1-benzyl hydrazines.⁷ An attempt to prepare acrolein phenylhydrazone by heating a solution of acrolein and phenylhydrazine (in equimolar ratio) in ethanol under reflux gave a product which was shown by n.m.r. spectroscopy to be very largely 1-phenyl-2-pyrazoline, thus confirming the facile nature of the cyclisation step shown in Scheme 41.

Oxidation of 1-allyl-1-phenylhydrazine with yellow mercuric oxide in methylene chloride and in chloroform (Experimental p. 147) gave 1-phenylazo-prop-2-ene [100%; Identified by comparison with an independently prepared sample of the azo-compound (see pp. 58-62, Experimental p. 160) by chromatography and by n.m.r. and infra-red spectroscopy. Both the oxidation product and the authentic sample of 1-phenylazoprop-2-ene also showed the presence of six identical minor components; the pairing of these components confirmed that the oxidation product contained only phenylazoprop-2-ene and products derived therefrom.]



Scheme 42



Scheme 43

The presence of 1-phenyl-2-pyrazoline could not be detected by n.m.r. spectroscopy.

Oxidation of 1-allyl-1-phenylhydrazine with lead tetra-acetate under homogeneous conditions (Experimental p. 148) was similarly shown to give 1-phenylazoprop-2-ene in 71% yield. The reduced yield with this oxidising agent may be attributed to the more lengthy product isolation procedure. Again, no 1-phenyl-2-pyrazoline could be detected in the product by n.m.r. spectroscopy.

The non-formation of 1,4 di-allyl-1,4-diphenyltetraz-2-ene in these oxidations under conditions which have been suggested to favour tetrazene formation, namely, the generation of 1,1-diazenes in the presence of high hydrazine concentrations (*i.e.* the mixing of the hydrazine and the oxidant in one portion, *c.f.* Overberger and Herin,⁴⁰ Introduction p. 9, Scheme 10), and the generation of high localised diazene concentrations in the case of mercuric oxide (*cf.* Forgione et al⁴³, p. 10), illustrates the highly facile nature of the rearrangement made possible by the close proximity of the allyl group.

The Oxidation of 1-Cyclopropylcarbinyl-1-Phenylhydrazine with Yellow Mercuric Oxide and with Lead Tetra-acetate.

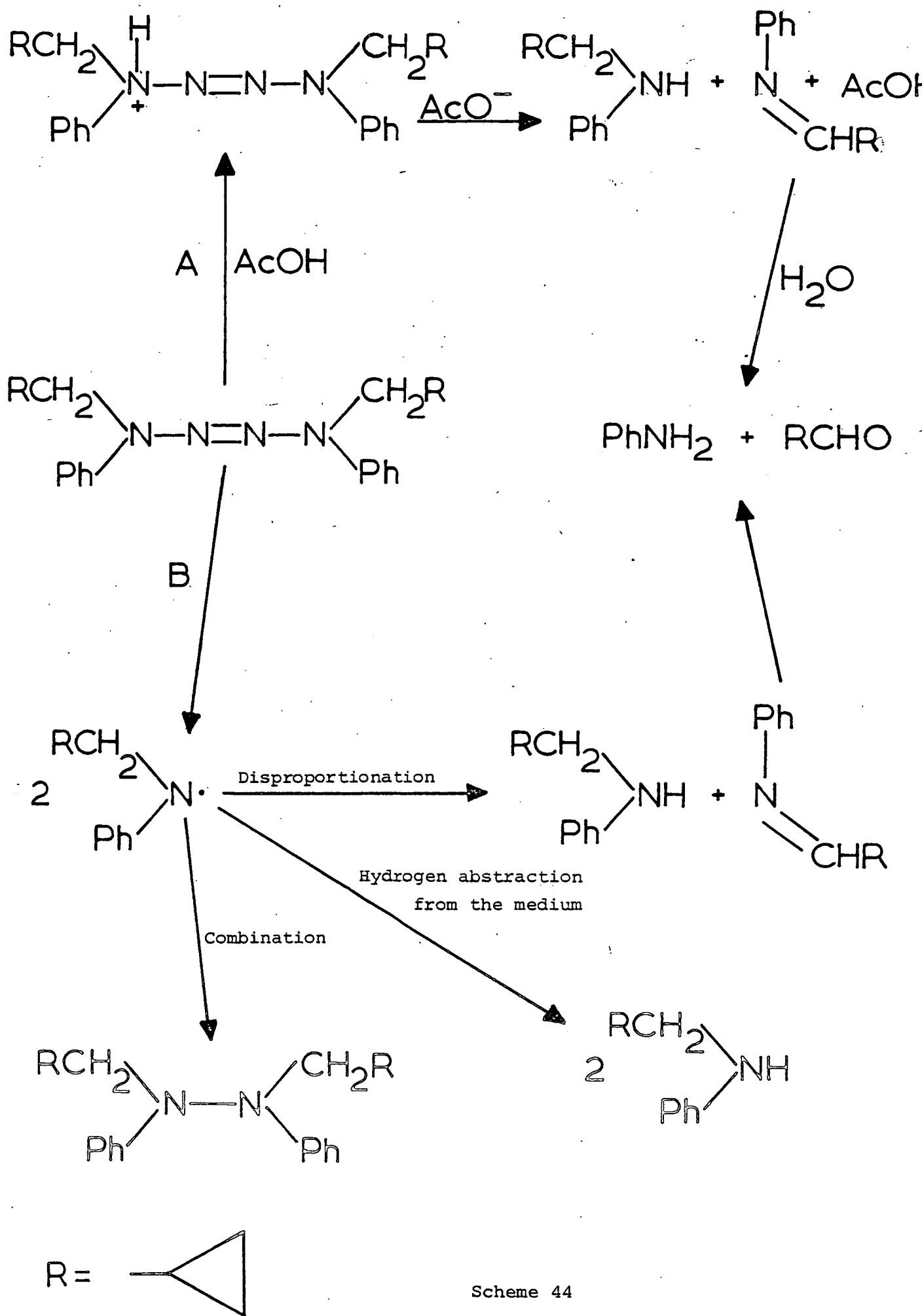
The anticipated reaction pathway to give 1-phenylazobut-3-ene is shown in Scheme 42. The rationale behind the proposed scheme comes from the acknowledged olefin-like character of cyclopropane and its derivatives. Indeed examples are known of the participation of a cyclopropane ring analogously to a double bond, in pericyclic reactions; an example is the [1,5] hydrogen shift shown in Scheme 43.¹⁰⁹

Oxidation of 1-cyclopropylcarbinyl-1-phenylhydrazine with mercuric oxide (Experimental p.160) gave a pale green solid which was characterised after recrystallisation from ethanol. The n.m.r. spectrum of both this material and the crude oxidation product-indicated that the cyclopropyl carbinyl moiety had remained intact, and showed no signals attributable to the anticipated product. The mass spectrum showed a parent ion of m/e 320, and accurate mass measurement established a molecular formula of $C_{20}H_{24}N_4$. On the basis of this evidence, and the compatibility of the observed n.m.r. spectrum, the product (70%) was identified as 1,4-dicyclopropylcarbinyl-1,4-diphenyltetraz-2-ene.

The work of Overberger and Herin⁴⁰ (Introduction p. 9) showed that the rate of addition of 1-amino-2-phenylpiperidine to a suspension of mercuric oxide had considerable influence over the nature of the oxidation products; they suggested that rapid addition of the hydrazine favoured the reaction of the diazene with its precursor to give the tetrazene product, while slow addition favoured the decomposition of the diazene, since the probability of its reaction with the hydrazine was low.

In the light of these observations, the oxidation procedure was repeated with the modification of dropwise addition of a solution of the hydrazine to a suspension of mercuric oxide. However, once again, the only observed product was 1,4-dicyclopropylcarbinyl-1,4-diphenyltetraz-2-ene.

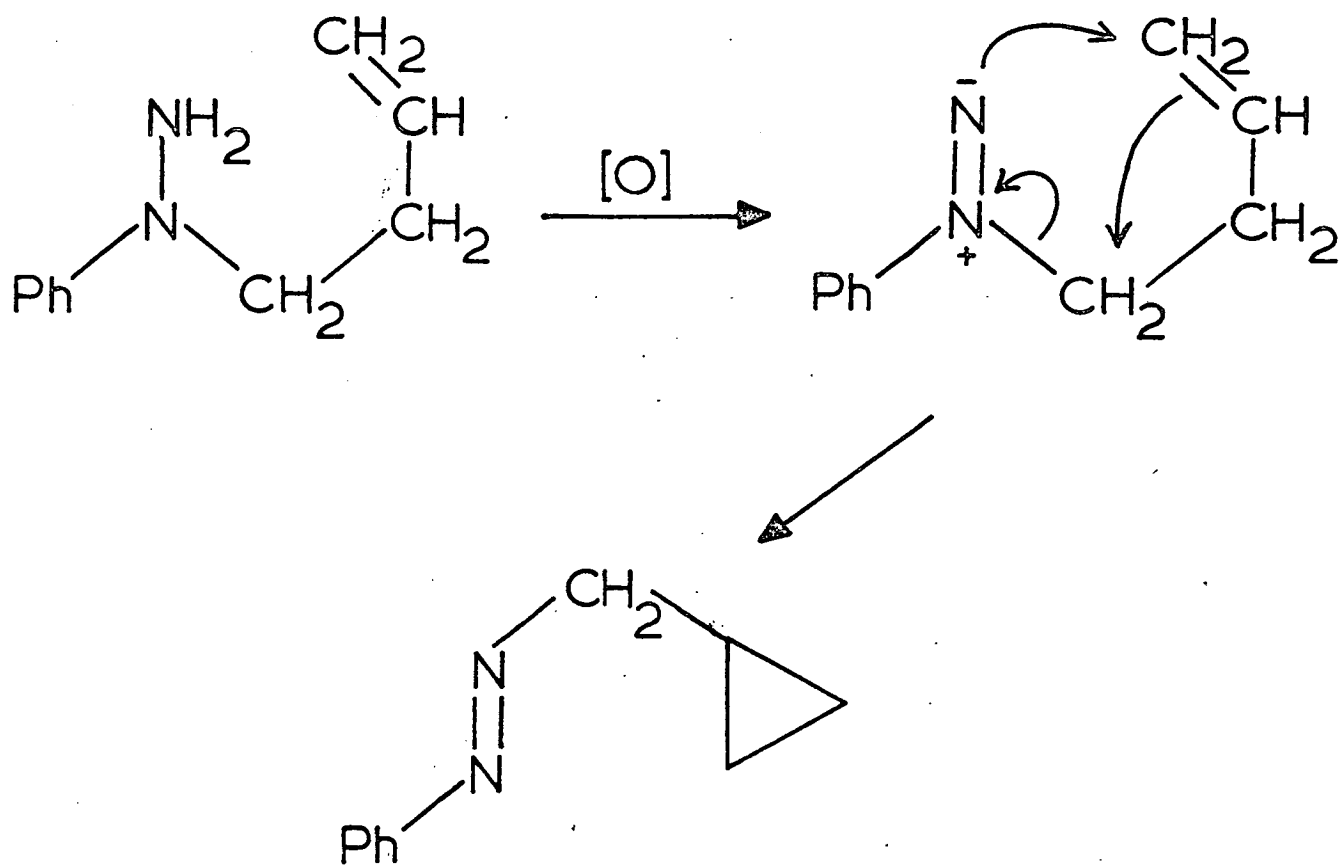
The oxidation with lead tetra-acetate (Experimental p.161) was exothermic and proceeded with the apparent evolution of gas. The n.m.r. spectrum of the concentrated reaction mixture, though complex and poorly resolved, suggested the presence of N-cyclopropylcarbinylaniline, a small amount of the tetrazene, formylcyclopropane (identified by reference to the n.m.r. spectrum of an authentic sample), and further unidentified



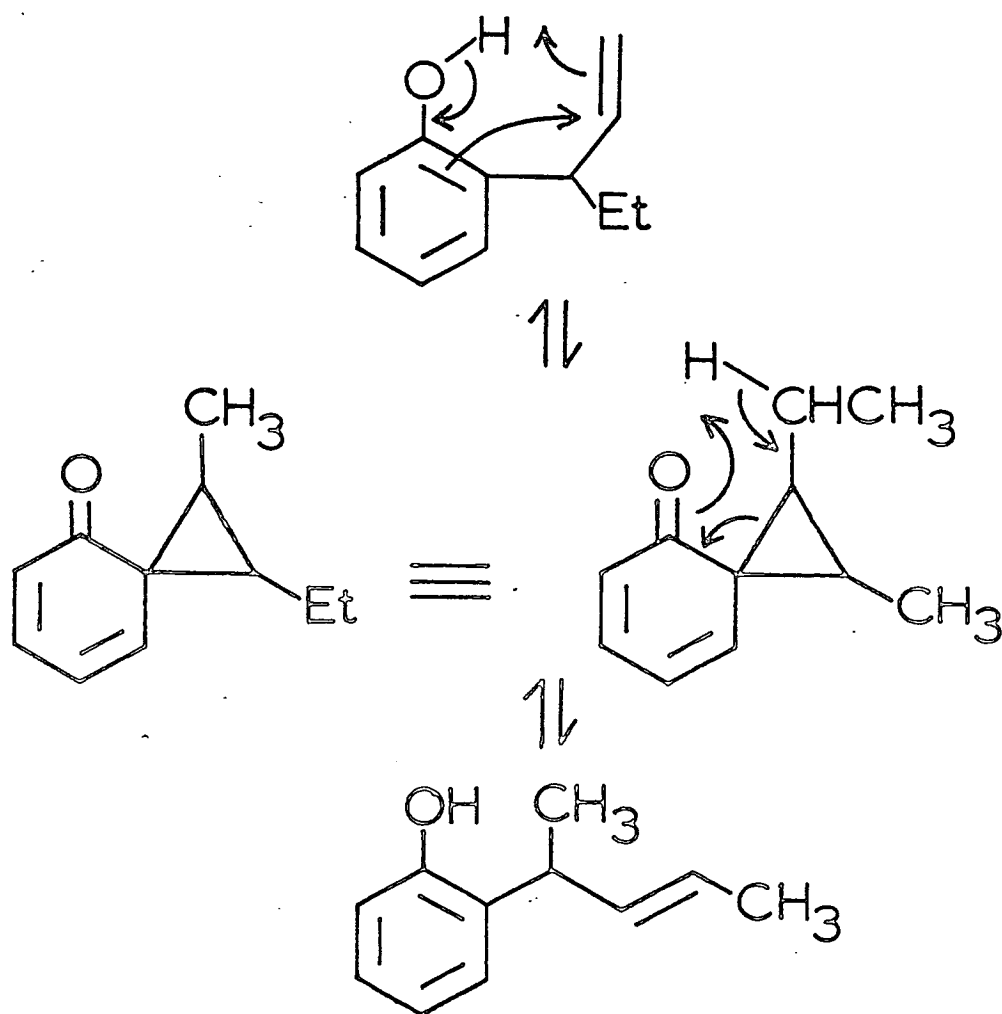
Scheme 44

products; no signals attributable to the anticipated product were observed and the cyclopropylcarbinyl moiety appeared to have again survived the oxidation procedure. The product of complete work-up was examined by column chromatography, but separation of the components could not be achieved. The recovered material, a wine-red liquid, was examined by n.m.r. spectroscopy; the presence of N-cyclopropylcarbinylaniline, a small amount of the corresponding tetrazene, together with a product giving rise to a weak doublet at δ 3.6 p.p.m., was indicated. Evidence from the infra-red spectrum of this material supported the presence of the secondary amine; further support for the n.m.r. spectrum assignments came from the results of thin layer chromatography. It was considered possible that the unassigned signals in the n.m.r. spectrum might be due to 1,2-dicyclopropylcarbinyl-1,2-diphenylhydrazine; such tetrasubstituted hydrazines are known to be formed in the thermal decomposition of tetraz-2-enes. The formation of the assigned products may be accounted for in terms of Scheme 44, which is based in part on the mechanism proposed by Overberger and Marks⁵¹ to explain the formation of the observed products of acid catalysed decomposition of tetrabenzyltetraz-2-ene.

While both amine formation and the apparent formation of formylcyclopropane may be explained in terms of a radical mechanism not involving participation by acetic acid, (path B in Scheme 44), this seems less likely in view of the isolation of the tetrazene from the oxidation with mercuric oxide, in which experiment similar conditions (in terms of solvent and temperature) were employed. Evidence for such a radical pathway has been found in the thermal decomposition of tetramethyltetraz-2-ene.¹¹⁰ The source of the water shown in Scheme 44 would most probably be incompletely dried solvent.



Scheme 45



Scheme 46

The apparent formation of the tetra-substituted hydrazine in the case of oxidation with lead tetra-acetate but not with mercuric oxide may be due to differences in the degree of heating of the oxidation product in the course of the removal of the solvent or to decomposition of the tetrazene during chromatography. In any event, such considerations are not the province of this particular study, and further work would be necessary to confirm or refute the proposed mechanistic scheme.

The oxidations with lead tetra-acetate and with mercuric oxide therefore showed that tetrazene formation was the preferred reaction pathway for 1-cyclopropylcarbiny1-1-phenyldiazene.

The Oxidation of 1-(But-3-en-1-yl)-1-Phenylhydrazine with Yellow Mercuric Oxide

The anticipated product of the oxidative rearrangement of this hydrazine was cyclopropyl(phenylazo)methane, formed by the sequence shown in Scheme 45. An analogous process has been proposed to explain the formation of o-(pent-3-en-2-yl)phenol from o-(pent-1-en-3-yl)-phenol in the course of the Claiesen rearrangement of 1-phenoxy-pent-2-ene (Scheme 46).

The oxidation experiments (Experimental p.162) yielded a brown liquid (quantitative recovery of material) which examination by n.m.r. spectroscopy indicated was a complex mixture of products. Significantly, the characteristic multiplet signal of the cyclopropyl moiety was not observed, indicating that the anticipated rearrangement had not occurred. The infra-red spectrum showed a weak N-H absorption at ν 3400 cm^{-1} which could not be attributed to unoxidised hydrazine (t.l.c. showed that the oxidation product did not contain any residual 1-(but-3-en-1-yl)-1-phenylhydrazine). The mass spectrum of the oxidation product showed a strong parent peak at m/e 320 suggesting the presence of the tetrazene,

and a peak at m/e 147 which, together with N-H absorption observed in the infra-red spectrum of the crude material, suggested the presence of N-(but-3-en-1-yl)aniline. Preliminary examination by t.l.c. revealed seven bands of material, and preparative t.l.c. (silica gel/n-hexane) gave five overlapping bands; the appearance of the developed plate suggested that extensive decomposition was occurring on the adsorbent. Only the leading three bands of material could be isolated cleanly; the products recovered from these bands were examined by mass spectrometry.

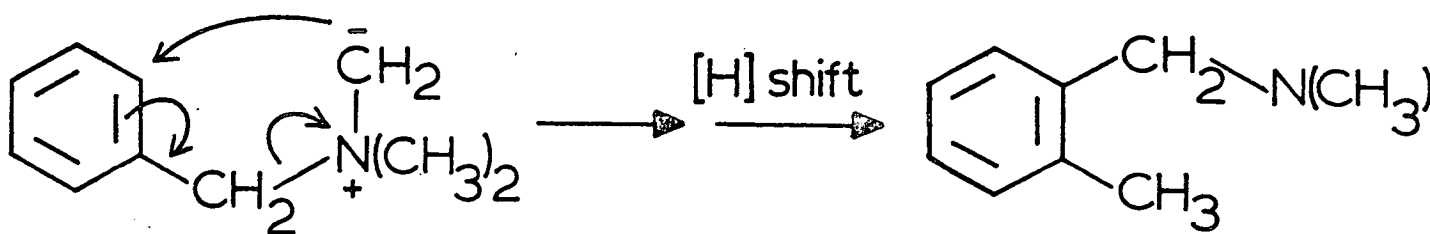
The mass spectra of these products all showed the same peaks although the relative intensities of particular constituent peaks differed from one spectrum to another. A noticeable feature was the markedly diminished intensity of the peak at m/e 320 (earlier attributed to the tetrazene) compared to the same peak in the spectrum of the crude material; this, together with the appearance of the developed t.l.c. plate suggested that the crude product was rich in 1,4-di(but-3-en-1-yl)-1,4-diphenyl-tetraz-2-ene which underwent extensive decomposition during chromatography. Support for this view comes from the observed enhancement of the peaks at m/e 292 and 147. The former may be attributed to 1,2-di(but-3-en-1-yl)-1,2-diphenylhydrazine, the product of extrusion of nitrogen from the tetrazene; the latter to N-(but-3-en-1-yl)aniline formed as a result of hydrogen abstraction by the N-(but-3-en-1-yl)anilino radical derived from the homolytic extrusion of nitrogen from the tetrazene (cf. Wieland and Fressel¹¹²). Fragmentation patterns consistent with these assignments were also observed.

A significant peak was observed at m/e 160 in the spectra of both the crude oxidation product and the material recovered from the third band of the preparative t.l.c. plate; a weak peak at m/e 160 was also observed in the mass spectra of the other t.l.c. products. It seems unlikely that this peak arises from the symmetrical scission of the tetrazene, since the mass spectrum of 1,4-dicyclopropylcarbiny-1,4-diphenyltetrazene (also of

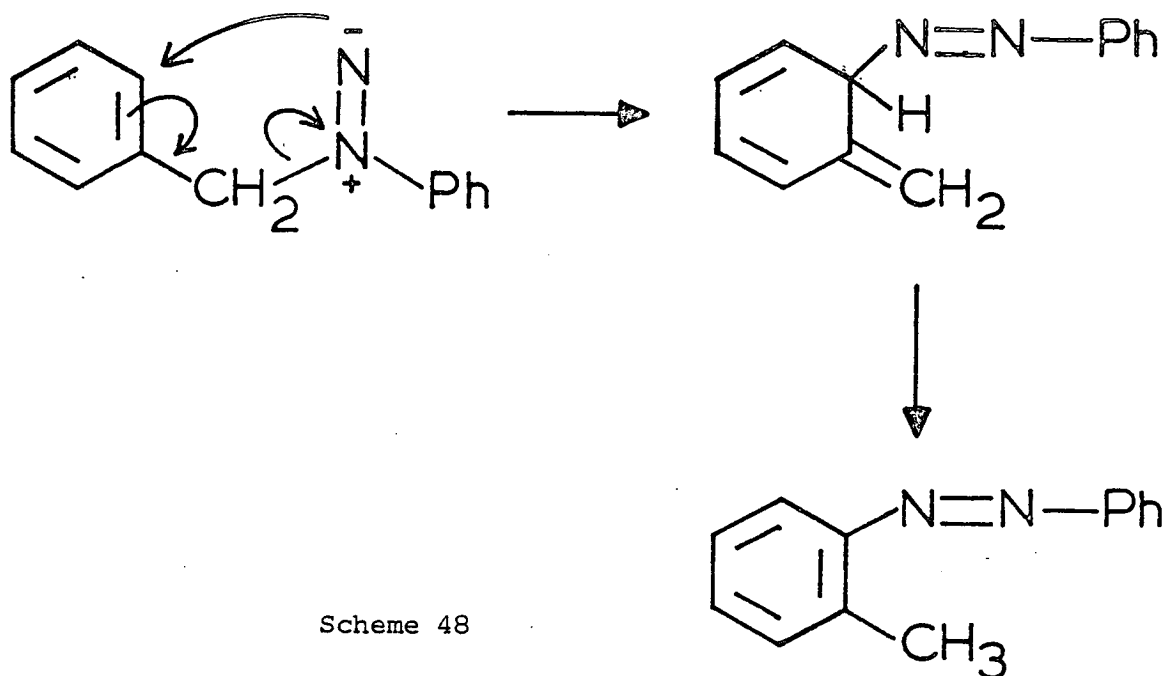
molecular weight 320 a.m.u.) showed only a very weak peak at m/e 160. Furthermore, while the appearance of the peak may be attributed to fragmentation of 1,2-di(but-3-en-2-yl)-1,2-diphenylhydrazine (M.Wt. 292 a.m.u.) with loss of one of each substituent, examination of the mass spectra of the crude oxidation product and the chromatographed materials revealed that when the peak at m/e 292 was large, that at m/e 160 was small, and vice versa; this indicated that the peak at m/e 160 was due to an independent chemical entity.

An alternative explanation for the observation of a peak at m/e 160 is that the peak corresponds to the doubly-charged molecular ion of 1,4-di(but-3-en-1-yl)-1,4-diphenyltetraz-2-ene. However, Beynon¹¹¹ suggests that the intensities of such double-charged ion peaks are only ca. 10% of the base peak height under the most favourable circumstances. In the present case, the peak in question (m/e 160) is considerably more intense, and, in the spectrum of the crude oxidation product, its intensity is ca. 50% of the base peak intensity (m/e 106). As already mentioned, the mass spectra of other tetrazenes examined in this study (1,4-dicyclopropylcarbonyl-1,4-diphenyltetraz-2-ene and 1,4-dibenzyl-1,4-diphenyltetraz-2-ene) show only very weak peaks having a mass to charge ratio of half the molecular ion value. Precedent suggests that the most probable species would be but-3-enal phenylhydrazone. A corroborating C=N infra-red stretch could not be firmly identified; the strong absorption observed at ν 1605 cm^{-1} in the infra-red spectrum of the oxidation product was also displayed by the parent hydrazine.

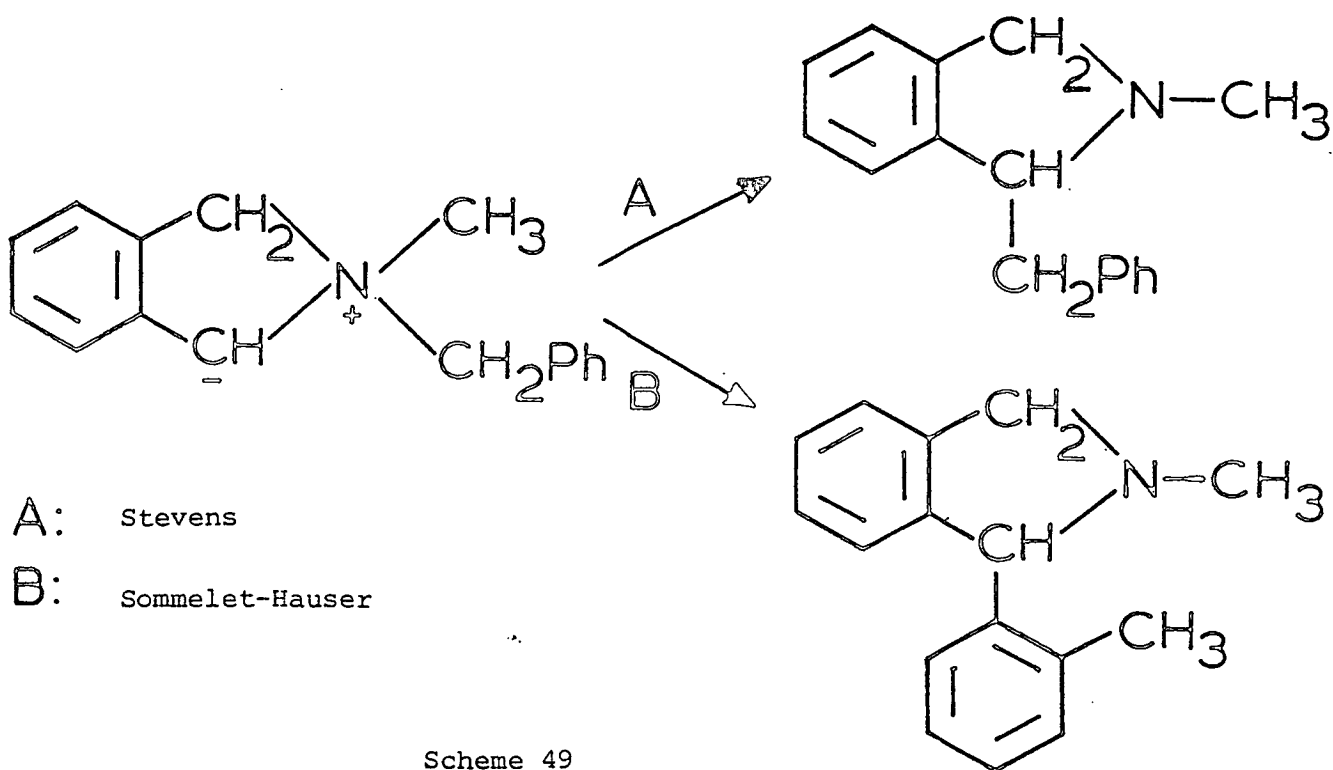
Only a very weak peak was observed at m/e 132 suggesting the hydrocarbon formation (by extrusion of nitrogen from the diazene) had occurred to only a very small extent, if at all.



Scheme 47



Scheme 48



Scheme 49

The material recovered from the third of the bands isolated by preparative t.l.c. (i.e. the slowest moving of these bands) was shown by n.m.r. spectroscopy to be not significantly different from the crude oxidation product, and on rechromatographing, it was found to give rise to six bands of material. This serves as a further illustration of the complex nature, and instability, of the oxidation product.

While the assignment of the components of a complex mixture almost solely on the basis of mass spectral evidence, must be viewed critically, it can be stated categorically that the presence of the anticipated product of oxidative rearrangement could not be detected in any of the oxidations of 1-(but-3-en-1-yl)-1-phenylhydrazine which were carried out.

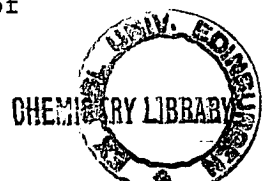
The Oxidation of 1-Benzyl-1-Phenylhydrazine with Mercuric oxide

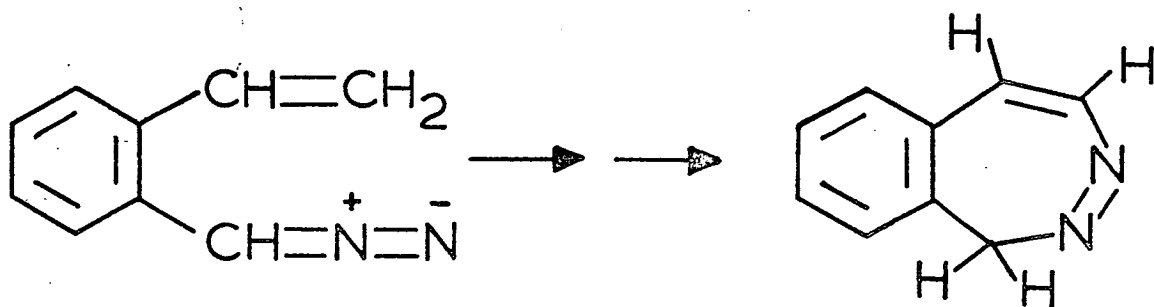
This particular oxidation was first performed by Busch and Lang⁷ who reported the product to be 1,4-dibenzyl-1,4-diphenyltetraz-2-ene. Interestingly, Carter and Stevens⁶² found that the product obtained from the base-catalysed decomposition of 1-benzyl-1-phenyl-2-toluene-p-sulphonylhydrazine was benzaldehyde phenylhydrazone. Both of these reactions are now believed to proceed via the same intermediate diazene and the acute contrast in the nature of the products obtained is surprising. It was thought that a re-investigation of the work of Busch and Lang⁷ might, with the aid of modern techniques, reveal the formation of benzaldehyde phenylhydrazone, to some extent at least, in the oxidation of 1-benzyl-1-phenylhydrazine.

Furthermore, pursuing the analogy between the ylide-type representation of diazenes and allylic ammonium ylides, it was hoped that 1-benzyl-1-phenyldiazene might rearrange to some extent, in a manner analogous to the Sommelet-Hauser rearrangement of benzylic ammonium ylides (Scheme 47) to give 2-phenylazotoluene according to Scheme 48.

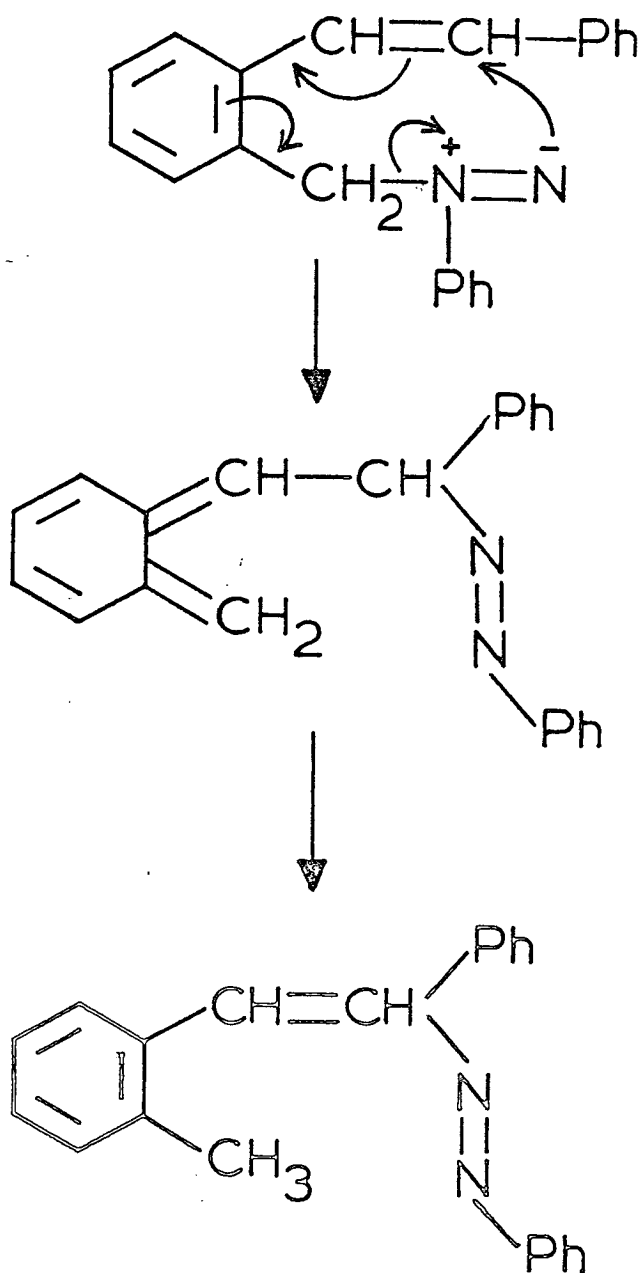
The Sommelet-Hauser Rearrangement of benzylic ammonium ylides occurs in competition with the Stevens Rearrangement which may itself be regarded as having a formal analogue in the formation of aldehyde arylhydrazones by oxidation of substituted 1-benzyl-1-phenylhydrazines (cf. Busch and Lang⁷). Wittig¹¹³ has suggested that the Sommelet-Hauser rearrangement is favoured at low temperatures and that only at higher temperatures does the Stevens rearrangement begin to compete; studying the ylide shown in Scheme 49 he found that no Stevens-type product could be detected when the reaction was carried out in ether at 20-30°C; only the Sommelet Hauser product (69%) was isolated. By reason of the apparently facile nature of the Sommelet-Hauser rearrangement, it was felt that there existed a reasonable possibility that the analogous rearrangement might occur in the oxidation of 1-benzyl-1-phenylhydrazine at ca. 20°C.

The products of preliminary oxidations of 1-benzyl-1-phenylhydrazine with mercuric oxide were found by n.m.r. spectroscopy to be multicomponent mixtures and it was at first thought that the oxidation followed a more complex course than suggested by the original investigators.⁷ However, it was subsequently shown that these mixtures of products arose as a consequence of the thermal lability of the single-component oxidation product. Careful recovery of the oxidation product at, or slightly above, room temperature gave 1,4-dibenzyl-1,4-diphenyltetraz-2-ene in 80% yield (identified by comparison with an independently prepared sample). That the complex products obtained from the preliminary oxidations were derived from the thermal decomposition of the tetrazene was confirmed by n.m.r. spectroscopic examination of the concentrated ethanolic mother liquor of recrystallisation of the tetrazene; the n.m.r. spectrum of this material indicated the presence of all the components formed in the preliminary oxidation experiments. On the basis of the literature reports of the thermal decomposition of





Scheme 50



Scheme 51

tetrazenes such as tetrabenzyltetraz-2-ene,¹¹² these products may be tentatively assumed to be N-benzylaniline, 1,2-dibenzyl-1,2-diphenylhydrazine, and benzaldehyde phenylimine. Indeed, heating a solution of the tetrazene in xylene under reflux was shown to give N-benzylaniline and an unidentified residue (see p. 88 , Experimental p.194).

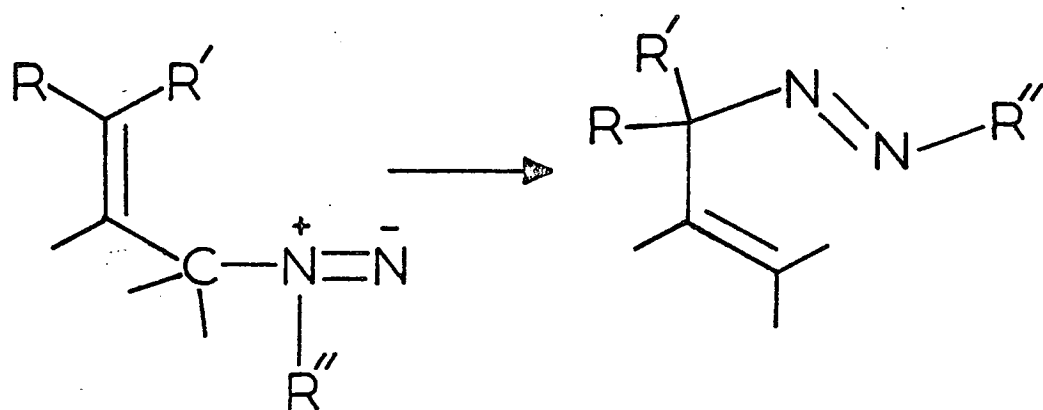
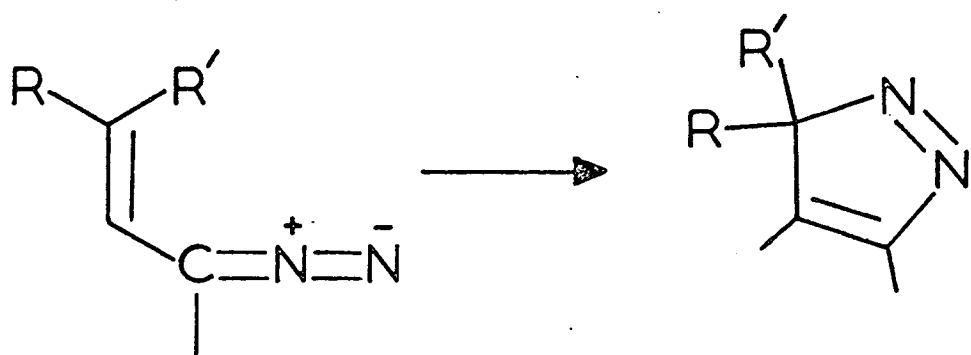
In none of the several oxidations of 1-benzyl-1-phenylhydrazine was any of the anticipated 2-phenylazotoluene detected: the n.m.r. spectrum of an authentic sample of the azo-compound showed the methyl group resonance at δ 2.7 p.p.m., but this characteristic signal was not observed in the n.m.r. spectra of the oxidation products.

Similarly, the possibility of benzaldehyde phenylhydrazone formation was not supported by the results of examination of the oxidation product by n.m.r. spectroscopy.

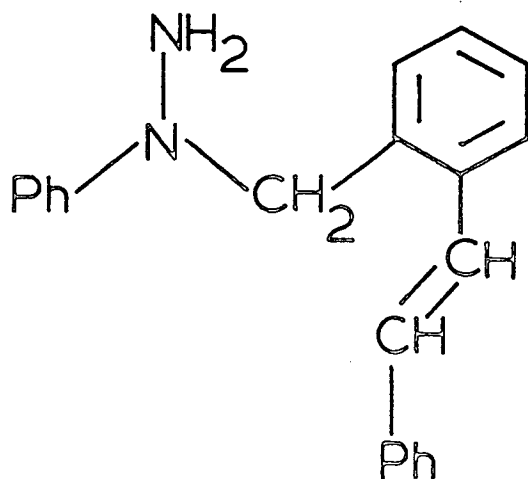
The Oxidation of 1-(2-Styrylphenylmethyl) -1-Phenylhydrazine with Yellow Mercuric Oxide

In this oxidation it was hoped to observe a rearrangement of the intermediate diazene in a manner analogous to that known to occur for the corresponding α -(o-alkenylaryl)diazoalkanes⁷⁰ (Schemes 50 and 51). Support for the proposed reaction pathway came from the fact that the analogy had been demonstrated in the case of unsaturated diazoalkanes^{114,115} and allylic diazenes⁶¹ (Scheme 52).

The hydrazine(11) may also be viewed as a substituted 1-benzyl-1-phenylhydrazine in which case the oxidation product might reasonably be expected to be 2-formylstilbene phenylhydrazone or a mixture of the hydrazone and the corresponding tetrazene, by analogy with the findings of Busch and Lang.⁷



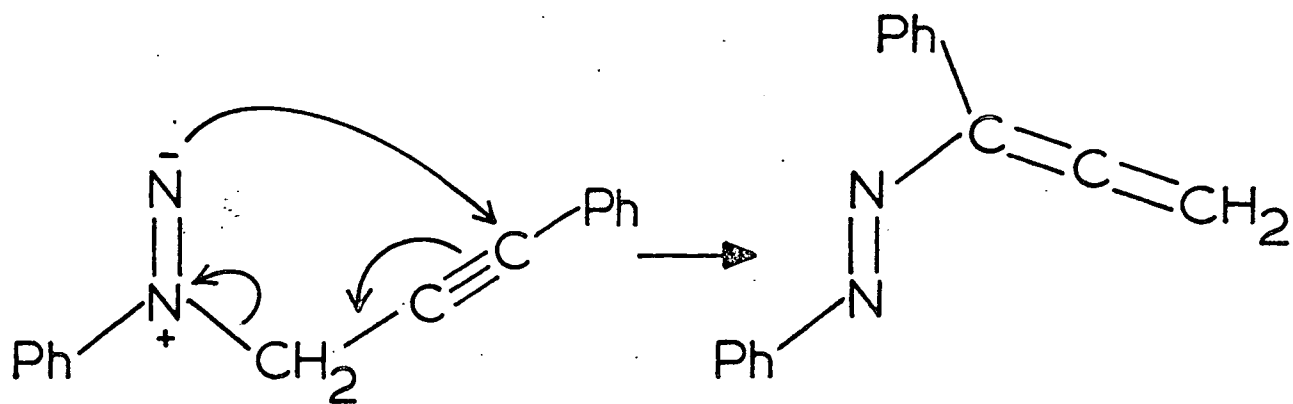
Scheme 52



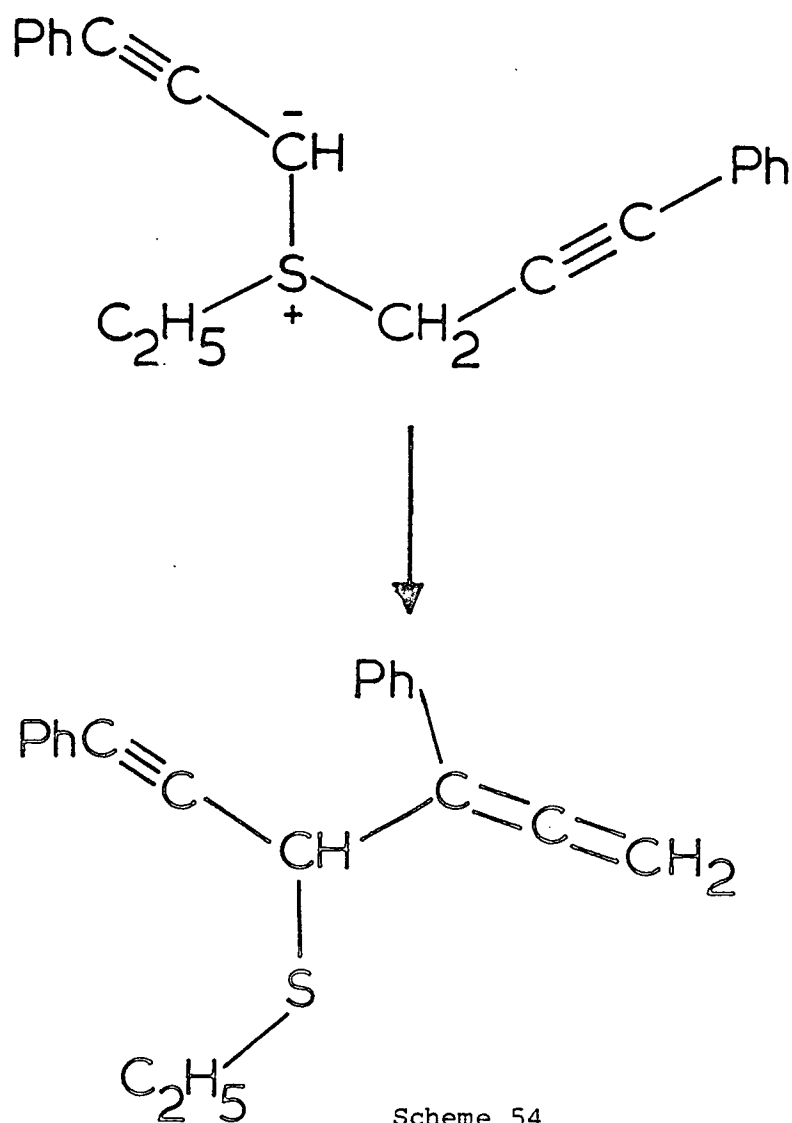
The oxidation experiments (Experimental p.166) gave a brown gum (quantitative recovery of material) which was shown by n.m.r. spectroscopy to be a complex mixture of products: eight poorly resolved singlets could be identified in the range δ 4-5.5 p.p.m., the region where, by comparison with the spectrum of the hydrazine, the benzylic proton resonances would be expected to appear. Indeed, in overall appearance, the n.m.r. spectrum resembled those of the products of the unsuccessful oxidations of 1-benzyl-1-phenylhydrazine; it will be remembered that the mixtures obtained derived from the decomposition of the tetrazene (see p. 51). A successful rearrangement would be immediately apparent by the appearance of a singlet in the methyl region (ca. δ 3.0 p.p.m. by analogy with toluene); three very weak, broad singlets were observed in the range δ 2.8-3.4 p.p.m., and a further very weak singlet was observed at δ 1.25 p.p.m., indicating that the anticipated rearrangement had occurred in only very small part, if at all. An impression of the significance of these singlets may be gained from the integration ratio of aromatic protons to all other protons, which was found to be ca. 15:1.

Examination by t.l.c. showed that up to five different components were present, and the appearance of the developed plate suggested that decomposition was occurring during chromatography. Column chromatography gave a series of four overlapping coloured bands, three of which were shown to account for the weight of material applied to the column.

The recovered fractions were examined by mass spectrometry and n.m.r. spectroscopy. Most of the peaks in the mass spectra were common to each fraction, but the intensities of some of these shared peaks were not necessarily comparable. The mass spectral evidence suggested that tetrazene formation had occurred as the weak peak observed at m/e 596 was attributed to the corresponding tetra-substituted hydrazine.



Scheme 53



Scheme 54

A small amount of a brick-orange solid was recovered from the column, and the n.m.r. spectrum of this material showed only a broad multiplet in the aromatic region. Its mass spectrum showed a significant peak at m/e 298 and this evidence, together with the appearance of the n.m.r. spectrum suggested that the solid was largely 2-formylstilbene phenylhydrazone. An authentic sample of the hydrazone was prepared and its n.m.r. spectrum was shown to be broadly compatible with that of the material under examination; the hydrazone was also shown to be stable to the oxidation conditions. The mass spectrum of the authentic compound showed the parent peak at m/e 298 and fragmentation peaks at m/e 221 and 206; these peaks could also be identified in the mass spectrum of the orange solid.

While the majority of the peaks in the mass spectra of the column fractions could not be readily interpreted in terms of the known behaviour of similar hydrazines on oxidation, the sizeable peak at m/e 490 may possibly be due to 2-formylstilbene 1-(2-styrylphenylmethyl)-1-phenylhydrazone. The formation of such a product has a direct analogue in the reported isolation of benzaldehyde 1,1-dibenzylhydrazone from the oxidation of 1,1-dibenzylhydrazine with several oxidising agents³⁸ (See Introduction p. 15).

The Oxidation of 1-(3-Phenylprop-2-ynyl)-1-Phenylhydrazine with Yellow Mercuric Oxide

The anticipated course of the oxidative rearrangement involved the participation of the acetylenic bond as shown in Scheme 53 to give 1-phenyl-1-phenylazo-allene. The participation of the acetylenic bond in the Diels-Alder reaction is well known, and Baldwin *et al*⁶⁹ showed that this sigmatropic participation could be extended to the rearrangement of the acetylenic sulphonium ylide shown in Scheme 54. The allylic

diazenes⁶¹ and the corresponding allylic sulphonium ylides^{116,117} were known to rearrange in an analogous fashion, and it was hoped that this analogy between diazenes and sulphonium ylides would extend to the system under investigation.

The oxidation experiments gave an almost quantitative recovery of material in the form of a shiny black foam or a black glass. As expected for material of this nature, the n.m.r. and infra-red spectra were ill-defined. The infra-red spectrum showed no N-H absorption, suggesting that complete oxidation had taken place, no $C\equiv C$ absorption could be identified although it should be stated that even in the parent hydrazine, this absorption was very weak. More convincing evidence for the destruction of the 3-phenylprop-2-ynyl substituent was provided by the n.m.r. spectrum which showed no signals attributable to the methylene protons of the substituent; only a multiplet in the aromatic region, and a weak, broad singlet at δ 1.7 p.p.m. were in fact observed. Baldwin et al⁶⁹ reported that the allenic protons of their allene product (Scheme 54) gave rise to a doublet at δ 5.09 p.p.m. in the n.m.r. spectrum. It was therefore concluded that the recovered oxidation product did not contain the anticipated allene.

The mass spectrum of the oxidation product showed a very weak peak at m/e 440 $\pm$ 2 suggesting that a very small amount of the tetrazene was present. The base peak had m/e 220 corresponding to symmetrical scission of the tetrazene; this possibility is however unlikely by analogy with the fragmentations of 1,4 dicyclopropylcarbiny-1,4-diphenyltetraz-2-ene (cf. p. 48) and because of the failure to observe any methylene signals in the n.m.r. spectrum of the oxidation product. The peak at m/e 220 corresponds to the anticipated 1-phenyl-1-phenylazo-allene but in view of the lack of support for this formulation from the n.m.r. spectrum, a better explanation might be the formation of 1-phenylprop-1-yn-3-yl phenylhydrazone.

[By similar reasoning to that described in the case of interpretation of the mass spectrum of the oxidation product from 1-(but-3-en-1-yl)-1-phenylhydrazine (see p. 49), the possibility that the peak at m/e 220 might be due to the doubly-charged molecular ion of the species having molecular weight 440 a.m.u. can be ruled out.]

Baldwin et al⁶⁹ make no mention of any instability associated with their allene (Scheme 54) and in view of the similarity between the reported allene and that anticipated from this oxidation, it may be inferred that 1-phenyl-1-phenylazo-allene would be stable if formed. It can therefore be concluded that the intermediate diazene in this oxidation follows a pathway or pathways other than that proposed in Scheme 53, resulting possibly in the formation of the corresponding tetrazene and, or, phenylhydrazone..

Conclusions

The [2,3] sigmatropic rearrangement of allylic diazenes by a suprafacial-suprafacial migration has been shown to be a 'symmetry-allowed' process (see p. 39).. This merely states, however, that rearrangement by a concerted mechanism is a feasible process; the possibility will only be realised if the necessary transition state can be attained without causing steric strain in the system. Furthermore, the concerted process may occur in competition with stepwise processes which involve comparable activation energies; if the stepwise pathways are of lower energy they will occur in preference to the concerted processes. When the possibility of intermolecular reaction also exists, such pathways will also compete with the concerted process if they are of comparable energy.

Throughout the above work, the analogy between the diazenes and ammonium ylides (and the sulphonium ylide in the case of the proposed acetylenic diazene rearrangement) has been emphasised. However, diazenes differ from typical ylides in the important respect that they may react intramolecularly by several different pathways, and intermolecularly to give tetrazenes by several possible mechanisms (dimerisation, reaction with the hydrazine precursor, or reaction with the diazenium ion in the case of the oxidation with lead tetra-acetate); ylides generally have only one intramolecular pathway open to them (the ammonium ylides are an exception to this in that the Stevens rearrangement can always occur in competition with any other specific process). The possibility of observing the anticipated rearrangement processes for the diazenes in question, therefore requires that the activation energy for the concerted process be at least comparable with the activation energies of all the possible alternative pathways.

Reference to molecular models of the systems examined here, suggests that the required transition state geometry can be achieved without causing steric strain. The failure to observe the anticipated rearrangements may therefore be attributed either to insufficient overlap of the participating π -systems in the transition state, or to the availability of several alternative reaction pathways (e.g. tetrazene formation) of lower energy. The facile rearrangement of 1-allyl-1-phenyldiazene indicates that the concerted process has a lower activation energy than any of the other possible reaction pathways; the most probable explanation for this is that the optimum geometry, and with it the favourable overlap of the participating π -systems, can be achieved in this case. Failure to attain a favourable transition state will result in an increased activation energy for the concerted process; in the case of the other diazenes studied, this increase in the activation energy may be sufficient to make the alternative reaction pathways energetically more favourable.

The Preparation of 1-Phenylazoprop-2-ene

The title compound was required for comparison with the product obtained from the oxidation of 1-allyl-1-phenylhydrazine with yellow mercuric oxide and with lead tetra-acetate.

Examination of the literature revealed only three reports of the preparation of 1-phenylazoprop-2-ene. Two of these reports involved the oxidative rearrangement of 1-allyl-1-phenylhydrazine (Michaelis and Luxemburg,⁴ and Baldwin⁶¹) and the third involved the oxidation of what was shown to be a mixture of 1-allyl-1-phenylhydrazine (the major component) and 2-allyl-1-phenylhydrazine⁴ (Fischer and Knoevenagel⁵). Therefore, as far as the present work was concerned, no independent, unambiguous preparation of 1-phenylazoprop-2-ene was known.

A survey of alternative procedures for the preparation of azo-compounds showed that many were specific to the preparation of particular types of azo-compound or involved multi-step processes (e.g. methods involving the coupling the two substituted nitrogen fragments). It was therefore felt that the oxidation of 2-allyl-1-phenylhydrazine offered the most direct route, and effort was concentrated on this approach.

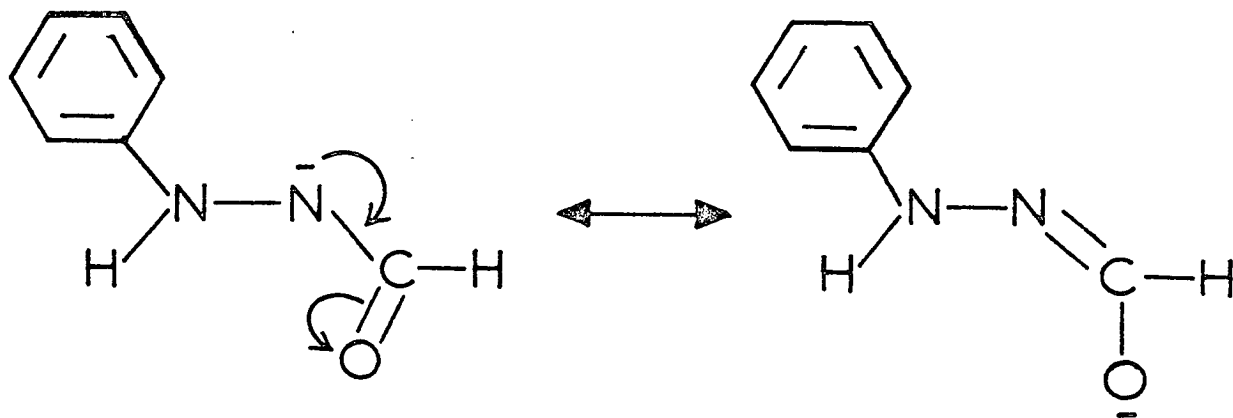
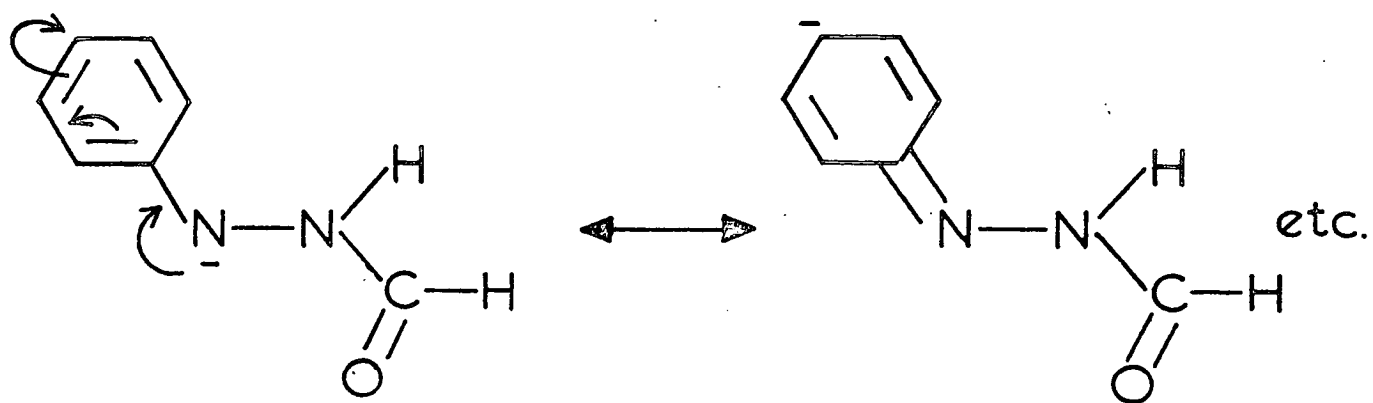
Alkylation of phenylhydrazine with allyl bromide was shown to give a mixture of the 1,1- and 1,2-disubstituted hydrazines (78% and 22% respectively, see p. 28). The preparation of 1,2-disubstituted hydrazines by the reduction of the corresponding hydrazones is limited to compounds with functional groups which are not susceptible to reduction, and so could not be used in this instance; in any case, the isolation of the necessary acrolein phenylhydrazone had been shown to be impossible, as cyclisation to 1-phenyl-2-pyrazoline occurred very readily (see p. 43).

The possibility of using a blocking group or an activating group to prevent alkylation at N-1 was next examined. Freer and Sherman¹¹⁸ reported that 2-ethyl-1-phenylhydrazine could be prepared by the

alkylation of the sodium salt of 2-formyl-1-phenylhydrazine with ethyl iodide, followed by hydrolysis of the product. Adaptation of their procedure to the synthesis of 2-allyl-1-phenylhydrazine (Experimental p. 149) gave a mixture of the 1,1- and the 1,2- disubstituted hydrazines in approximately equal amount (by n.m.r. spectroscopy).

This unexpected result, together with the surprisingly complex n.m.r. spectrum exhibited by 2-formyl-1-phenylhydrazine, suggested the need for more extensive characterisation of the latter material. Its formulation as the 1,2-isomer was supported by the observations that it failed to give the hydrazone derivative with acetone, and that acetylation with acetic anhydride followed by selective hydrolysis, gave 1-acetyl-1-phenylhydrazine (identified by comparison with an independently prepared sample) and no 2-acetyl-1-phenylhydrazine; the attempted reduction to 2-methyl-1-phenylhydrazine was, however, inconclusive (Experimental p. 151). The observed simplification of both the proton and carbon-13 n.m.r. spectra of the prepared 2-formyl-1-phenylhydrazine at elevated temperatures indicated that the material was indeed a single compound in the form of two preferred conformational isomers. A full discussion of these n.m.r. spectra is given on p. 63.

Separation of the product mixture of isomeric disubstituted hydrazines was attempted using three different methods (Experimental p. 153). The common feature of these methods was the attempted formation of a derivative of the 1,1-disubstituted isomer, such that the desired 1,2-disubstituted hydrazine could be selectively isolated. The use of laevulinic acid ($\text{CH}_3\text{COCH}_2\text{CH}_2\text{CO}_2\text{H}$) was based on the ability of keto-carbonyl groups to form hydrazone derivatives with 1,1-disubstituted hydrazines. The dual functionality of this particular reagent enabled the unwanted derivative to be removed by base extraction; the method



Scheme 55

proved to be quite successful, but the recovered 2-allyl-1-phenylhydrazine was contaminated with some unidentified impurities. The rationale for the use of acetophenone in the second method was similar to that for the use of laevulinic acid, except that in this case it was hoped to effect isolation of the desired hydrazine by distillation, leaving the high boiling acetophenone hydrazone derivative behind. In practice, the distillate was found to be contaminated with both acetophenone and the hydrazone derivative. The third method was of a rather speculative nature, and was based on the procedure reported by Hickinbottom⁸⁴ for the separation of aniline from its N-alkyl derivatives. (The method depends on the formation of an almost insoluble complex of zinc chloride and aniline; under the aqueous conditions involved, N-alkylanilines do not form similar complexes.). However, adapting the reported procedure for the present purpose gave back the same mixture of hydrazines, but with an increased proportion of the unwanted component.

The considerable success of the laevulinic acid and the acetophenone methods suggests that, in the general case, and on the larger scale where more refined distillation methods can be employed, the use of these reagents as described can afford a useful means of separating 1,2-disubstituted hydrazines from their 1,1-disubstituted isomers.

The isolation of approximately equal amounts of 1,1- and 1,2-alkylated products from the alkylation of the sodium salt of 2-formyl-1-phenylhydrazine suggests that proton abstraction by the base takes place indiscriminately. This probably reflects the fact that both anionic centres can be stabilised by delocalisation of charge (Scheme 55).

The failure to achieve selective alkylation at N-2 indicated the need for a different approach, and the possibility of preparing and alkylating a suitable 1-acyl-1-phenylhydrazine was examined. Attempts

to prepare such compounds (e.g. 1-acetyl- and 1-ethoxycarbonyl-1-phenylhydrazine) by treatment of the sodium salt of phenylhydrazine with the corresponding acyl chlorides gave mixtures of 1,1- and 1,2-acyl-phenylhydrazines; diacylation was also observed in the case of acetyl chloride. (Michaelis and Schmidt¹¹⁹ reported the formation of a similar mixture of products in the analogous reaction with benzoyl chloride.).

1-Acetyl-1-phenylhydrazine was successfully prepared by treating 2-formyl-1-phenylhydrazine with acetic anhydride and then selectively removing the formyl group (Behrend and Reinsberg¹²⁰). The identity of the product of this procedure was confirmed by comparison with an authentic sample of 1-acetyl-1-phenylhydrazine prepared by the unambiguous, but also less direct, method of N-amination of acetanilide. The absence of any 2-acetyl-1-phenylhydrazine from the product of the former procedure reflects both the purity of the 2-formyl-1-phenylhydrazine with respect to contamination with its 1,1-isomer, and the ability of the formyl group to direct further acylation to N-1 by reducing the nucleophilicity of the nitrogen atom to which it is attached. The alkylation of 1-acetyl-1-phenylhydrazine with allyl bromide was not examined in depth as the desired 2-allyl-1-phenylhydrazine had been prepared by another method (vide infra); however, the results of a cursory examination indicated that alkylation had occurred at N-2, a further example of the directing effect of the acyl substituent.

It therefore appears that 1-acetyl-1-phenylhydrazine may be obtained in pure form by the method of Behrend and Reinsberg,¹²⁰ without the need to resort to direct N-amination as described here (Experimental p.156) or as described by Short¹²¹ (a very cumbersome procedure involving the action of sodamide on N-chloro-aniline). Furthermore, alkylation appears to proceed smoothly at the N-2 position alone. The alkylation of 1-acetyl-1-phenylhydrazine seems to offer a convenient route to 2-alkyl-1-phenylhydrazines and therefore to the corresponding azo-compounds. The mildness of the conditions suggests that the method may succeed where the

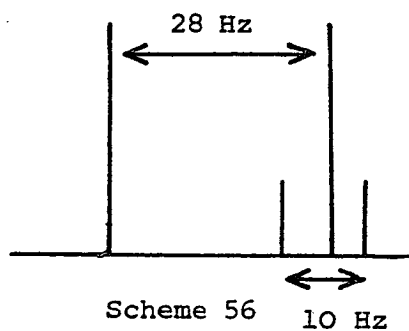
method of alkylation of the sodium salt of 1,2-diformyl-1-phenylhydrazine fails (see below), i.e. in the case of alkylating agents which undergo competing facile elimination.

The use of di-acylated hydrazines for the preparation of 2-alkyl-1-phenylhydrazines was also examined (Experimental p.157). 1,2-Di-acetyl-1-phenylhydrazine was prepared by the method of Widman¹²²; alkylation of the sodium salt of this material gave a complex mixture of products. An unsuccessful attempt was made to separate the components of this mixture by column chromatography, and the method was not examined further.

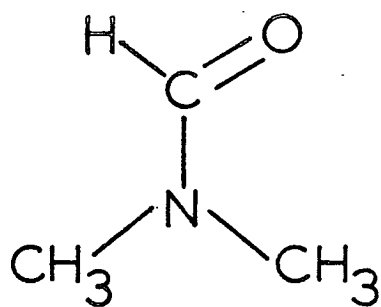
1,2-Diformyl-1-phenylhydrazine was prepared by treating phenylhydrazine with an excess of formic acid.¹²³ The material displayed unexpectedly complex ¹H and ¹³C n.m.r. spectra which could be rationalised in terms of conformational isomerism (see p. 64). Alkylation of the sodium salt of this compound with allyl bromide followed by hydrolysis of the product (Experimental p. 159) gave the desired 2-allyl-1-phenylhydrazine in 85% overall yield.

1-Phenylazoprop-2-ene was readily obtained by the mercuric oxide oxidation of the prepared 2-allyl-1-phenylhydrazine.

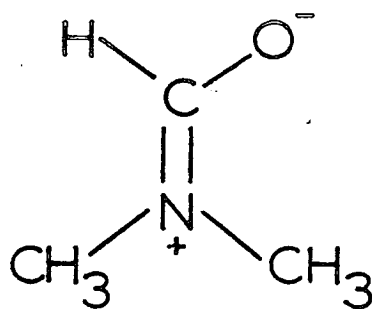
It is felt that the successful preparation of 1-phenylazoprop-2-ene has wider implications as a general means of synthesising 2-alkyl-1-phenylhydrazines and the corresponding azo-compounds. These hydrazines are most often prepared by reduction of the corresponding phenylhydrazones; the alkylation of the sodium salt of 1,2-diformyl-1-phenylhydrazine may offer an efficient and convenient alternative method. The alkylation procedure has been found to fail in the case of 2-chloropent-3-ene, but this is believed to be a reflection of the sensitivity of the alkylating agent towards elimination (see p. 76, Experimental p.189) rather than indicating a significant defect in the general method. The alternative alkylation of 1-acetyl-1-phenylhydrazine may conceivably be successful in such cases.



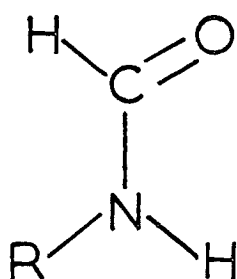
Scheme 56



(12)

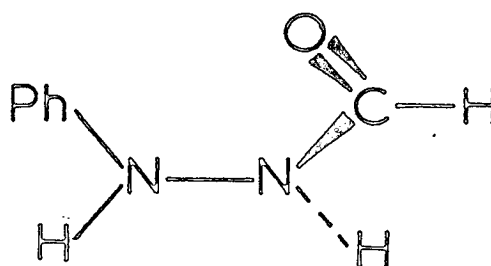
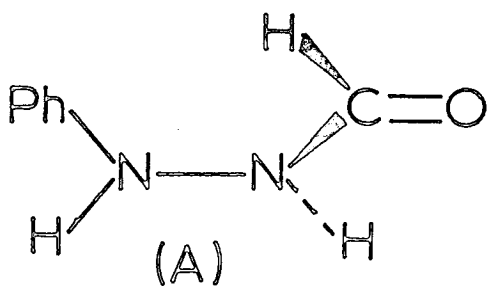


(13)



R = PhNCHO or PhNH

(14)



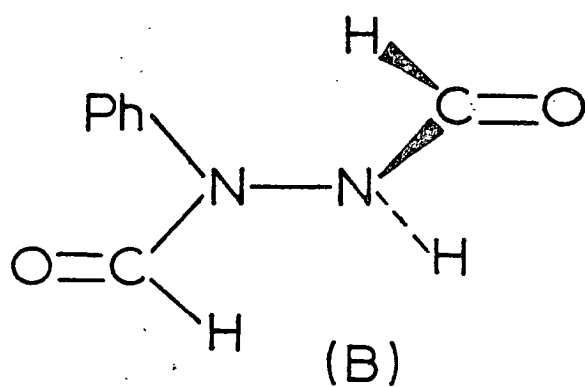
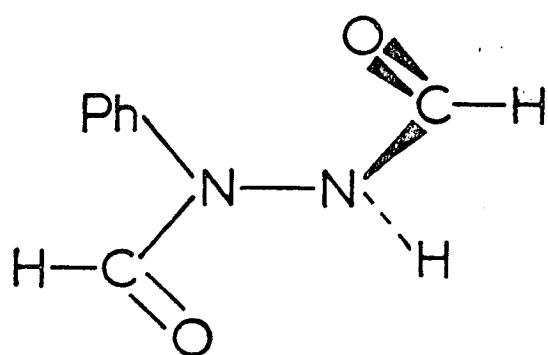
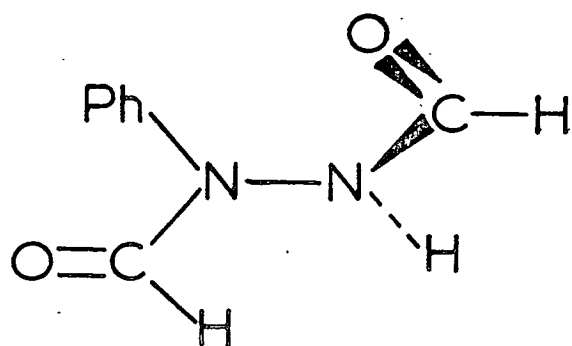
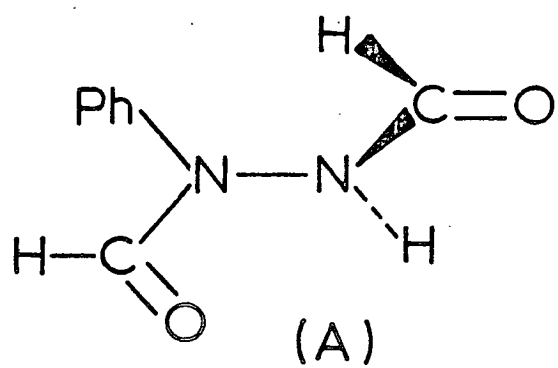
Scheme 57

The ^1H and ^{13}C N.m.r. Spectra of 1,2-Diformyl-1-Phenylhydrazine and 2-Formyl-1-Phenylhydrazine.

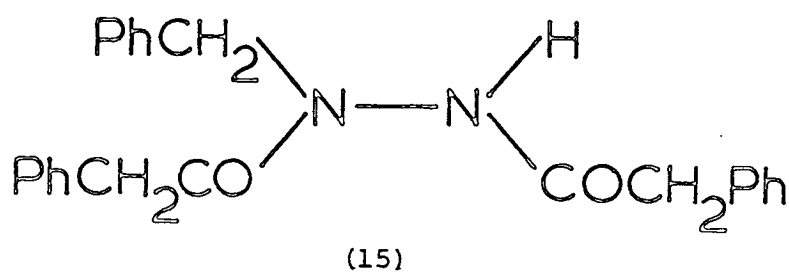
As already mentioned, the ^1H n.m.r. spectra of 1,2-diformyl-1-phenylhydrazine and 2-formyl-1-phenylhydrazine were more complex than expected. The ^1H n.m.r. spectra of 1,2-diformyl-1-phenylhydrazine in a variety of solvents at 25°C showed a common feature in that in each case four singlets were observed between δ 8.0 and 9.0 p.p.m., the region in which the formyl proton resonances were expected to appear. These signals were best resolved when acetic acid was used as solvent, and were observed as two sets of doublets as shown in Scheme 56. The ^1H n.m.r. spectra of 2-formyl-1-phenylhydrazine in the same solvents did not exhibit any identifiable recurring spectral pattern for the formyl proton; the appearance of the spectra was significantly influenced by individual solvents.

The close similarity in the behaviour of these two hydrazines in the n.m.r. experiment was only appreciated by examination of the corresponding ^{13}C n.m.r. spectra. The ^{13}C n.m.r. spectrum of 2-formyl-1-phenylhydrazine at 25°C had ten lines and that of 1,2-diformyl-1-phenylhydrazine showed thirteen distinct lines. The observation that the expected number of resonances were present at suitably elevated temperatures indicated that the complicated n.m.r. spectra displayed by these compounds at room temperature, resulted from the slow inter-conversion of a mixture of conformers rather than from the presence of a mixture of isomers.

This unexpected observation brings to mind the case of the ^1H n.m.r. spectrum of N,N dimethylformamide (12) which shows two methyl group resonances while only one is expected, assuming unrestricted rotation about the N-CO bond. The anomaly is explained in terms of

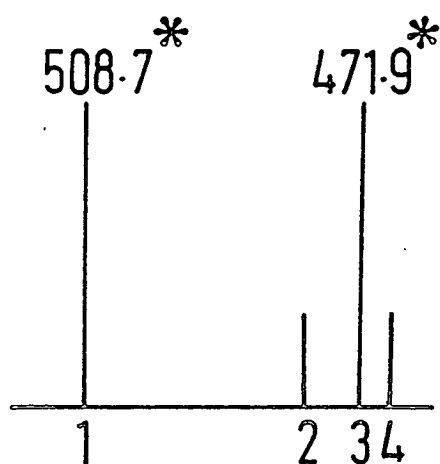


Scheme 58

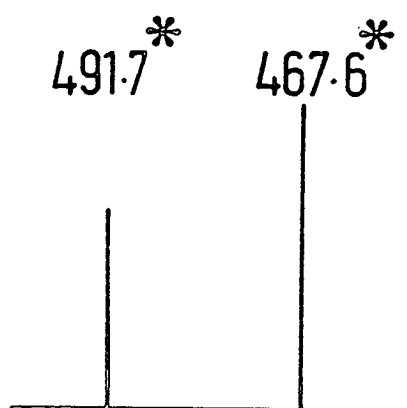


restricted rotation about the N-CO bond which is attributed to a strong contribution of the dipolar form (13). The effect of this is that the methyl groups experience different electronic environments and hence there is a chemical shift difference between them. The barrier to rotation can be overcome by raising the temperature and the methyl group signals are found to coalesce at 148°C (60 MHz).¹²⁴

The formal similarity between the formyl phenylhydrazines and N,N-dimethylformamide is illustrated by comparing (12) and (14). By analogy with N,N-dimethylformamide conformational isomerism is possible for the formyl phenylhydrazines. Assuming unhindered rotation about the N-N bond, two conformations are possible for 2-formyl-1-phenylhydrazine (Scheme 57) and four conformations are possible for 1,2-diformyl-1-phenylhydrazine (Scheme 58). (The assumption of unrestricted rotation about the N-N bond in this case is supported by the observations of Bishop et al.¹²⁵ who reported that there was no barrier to rotation about the N-N bond of (15) at $4 \pm 5^\circ\text{C}$; as the substituents in the present case are significantly less bulky, it might reasonably be expected that the minimum temperature at which free rotation about the N-N bond can occur would be significantly lower.) The presence of only four formyl proton resonances in the spectrum of 1,2-diformyl-1-phenylhydrazine indicates that, in the absence of any accidental equivalence, only two of the conformations contribute. The observation of twice the expected number of ^{13}C resonances also supports this view. The presence of a fifth line in the C=O region of the ^{13}C n.m.r. spectrum suggests that another conformer also contributes but to a minor extent. Accidental equivalence is not a common phenomenon in ^{13}C n.m.r. spectra unlike the case of ^1H n.m.r. spectra where, because of the small range of chemical shifts exhibited by the protons of most organic molecules, the



25°

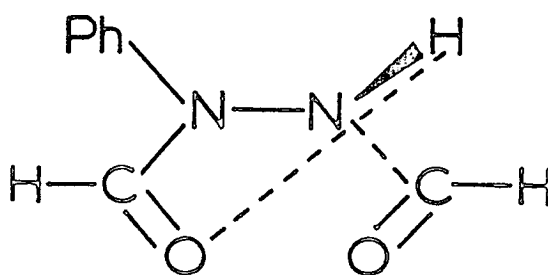
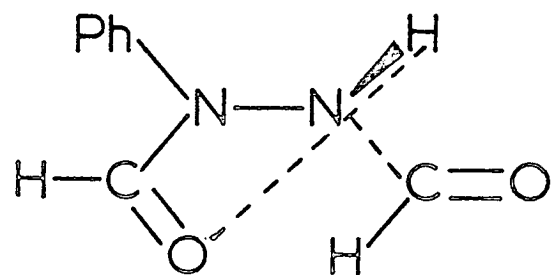


120°

*

Chemical shift from the methylene
proton absorption in $\text{HOCH}_2\text{CH}_2\text{OH}$

Scheme 59



Scheme 60

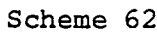
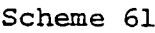
probability of accidental equivalence occurring is much higher.

Reference to a space-filled model of 1,2-diformyl-1-phenylhydrazine incorporating coplanarity of the π -system of the $\ddot{\text{N}}\text{-C=O}$ unit, suggests that the most favourable conformations from steric considerations are (A) and (B) of Scheme 58, (A) being preferred since the substituent interactions are minimised. The only difference between these conformers is in the orientation of the N-1 formyl group. As the temperature is raised to the coalescence temperature (110-120°C), the two pairs of singlets in the ^1H spectrum are replaced by one pair of singlets, the result of surmounting the restrictions on rotation about the N-CO bonds. The chemical shifts of these singlets in the coalesced spectrum enables the formyl proton contributions in the original spectrum to be identified. The changes in the ^1H n.m.r. spectrum of 1,2-diformyl-1-phenylhydrazine in ethylene glycol solution and the assignments of the corresponding protons in the original spectrum, are shown in Scheme 59. The relative intensities of the signals in the proton spectrum at 25°C indicate that resonances 1 and 3 are due to the conformer making the greater contribution, and that resonances 2 and 4 are due to the less favoured conformer. Signals 1 and 2 are due to one of the formyl protons, and signals 3 and 4 are due to the other. These assignments are based on the observed chemical shifts of the formyl protons in the coalesced spectrum: signal 3 cannot be paired with signal 2 since the chemical shift of the resultant singlet after coalescence would be intermediate between the values of 508.7 and 471.9 Hz observed at 25°C, and not outwith that range as found.

The observed ^1H and ^{13}C n.m.r. spectra of 1,2-diformyl-1-phenylhydrazine could also be rationalised in terms of the hydrogen-bonded conformations shown in Scheme 60, and reference to a space-filled model suggests that both conformations are attainable, and that hydrogen

bonding is indeed possible. Analogous conformations are also possible for (15) but Bishop et al.¹²⁵ have shown that unrestricted rotation about the N-N bond of (15) occurs at, and above, $4 \pm 5^\circ\text{C}$. As has already been said, it is reasonable to assume that effectively unhindered rotation can occur in the case of the present hydrazine; the hydrogen-bonded conformers cannot then have any existence over the temperature range of the n.m.r. study at least ($25\text{--}120^\circ\text{C}$). These conformers might, however, be expected to make some contribution to the spectrum at lower temperatures.

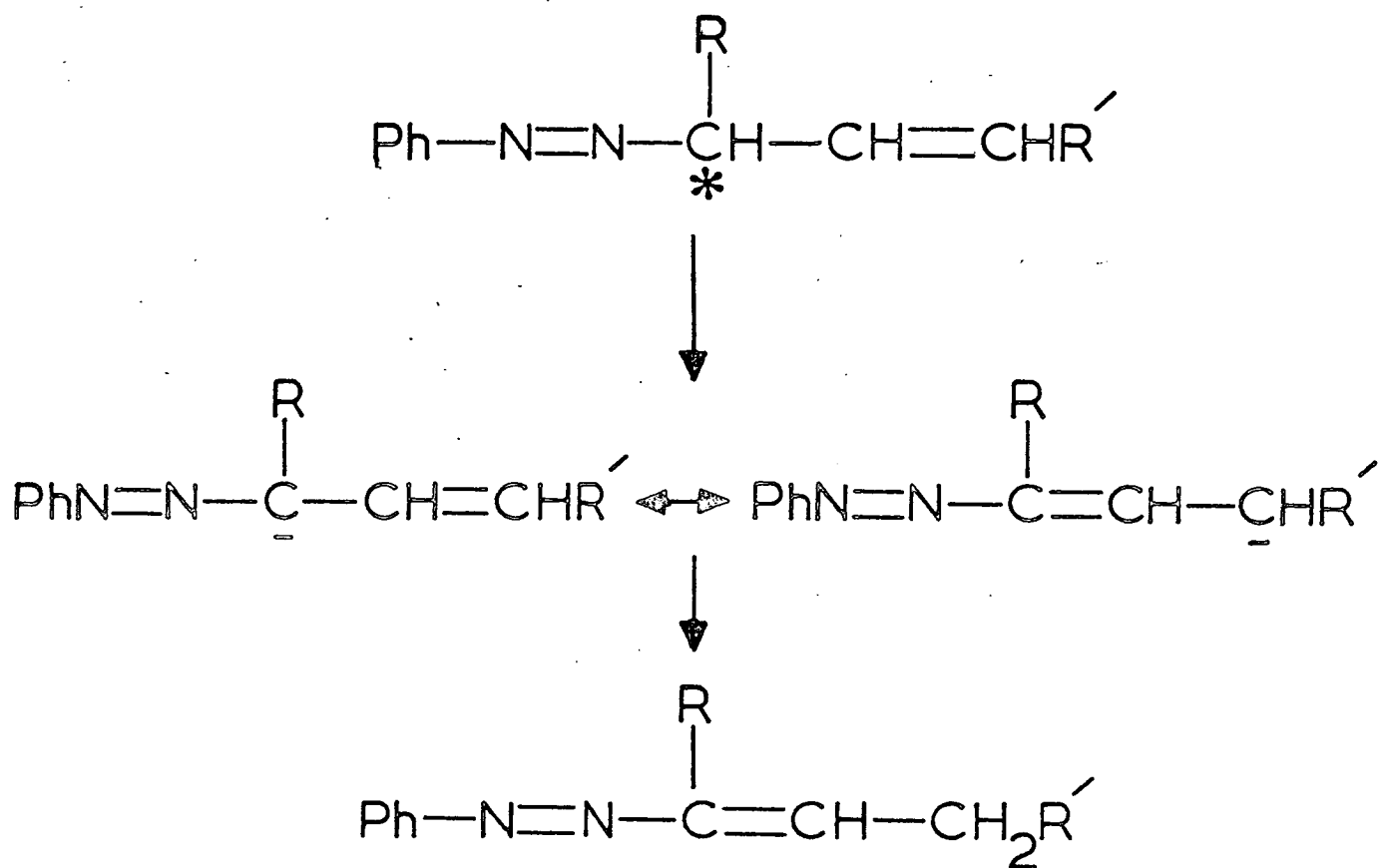
In summary, the ^1H and ^{13}C n.m.r. spectra of 1,2-diformyl-1-phenylhydrazine, may be interpreted in terms of the existence of two preferred conformations which is the result of restricted rotation about the C-N bond of the N-formyl groups. These conformations have been formulated as (A) and (B) of Scheme 58, contributing in the ratio of 2.6:1, based on the integration ratios of the formyl proton signals in the ^1H n.m.r. spectrum at 25°C (100 MHz; acetic acid- d_3). The barrier to free rotation about the N-CO bonds can be surmounted by heating the solution and above the coalescence temperature, the expected spectrum can be observed. Similar arguments apply to the n.m.r. spectra of 2-formyl-1-phenylhydrazine, and again, the expected spectrum is observed at elevated temperatures. The preferred conformation in this case is probably (A) in Scheme 57, with both contributing in a similar ratio to the conformers of 1,2-diformyl-1-phenylhydrazine (based on the less accurate method of comparing the signal ratios of the ^{13}C n.m.r. spectrum with those of the corresponding spectrum of 1,2-diformyl-1-phenylhydrazine).



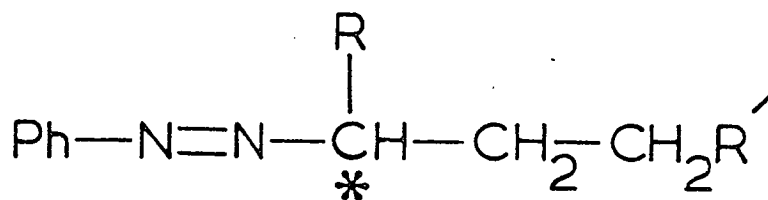
The Preparation and Oxidative Rearrangement of 1-(Pent-3-en-2-yl)-1-Phenylhydrazine

This study was undertaken as a preliminary examination of the possibility of achieving asymmetric induction by rearrangement of the diazene derived from the oxidation of an optically active hydrazine as shown in Scheme 61. The realisation of this aim was of particular interest in that it appeared to offer a solution to the problems encountered by Hunter¹²⁶ in the attempted preparation of a phenylazoalkane having a chiral centre at the α -carbon atom. Hunter's aim in attempting to prepare such a species was to study the kinetics of the base-catalysed isomerisation of this phenylazoalkane to the corresponding phenylhydrazone, believed to occur by the mechanism shown in Scheme 62. By monitoring the decrease in optical rotation by polarimetry, it was envisaged that the progress of the rearrangement could be conveniently followed (N.m.r. and U.V. spectroscopy were considered unsuitable tools for following the course of the isomerisation). Each of the approaches to the problem of synthesising the necessary optically active phenylazoalkane which were examined by Hunter failed in their fundamental stages.

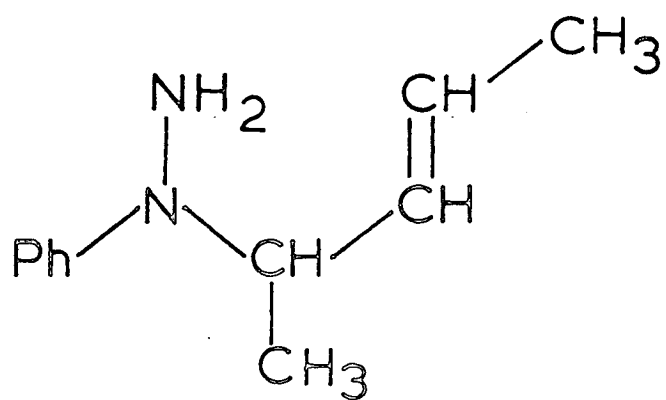
As a compromise, Hunter studied the base-catalysed isomerisation of optically active 2-phenylazobornane (16) [Prepared by the reduction and subsequent oxidation of the phenylhydrazone derivative of (+)-camphor (17)] but this was a far from ideal system, since the product, camphor phenylhydrazone (18), had a non-zero optical rotation and was also unstable under the reaction conditions giving rise to further changes in the optical rotation. In view of the complications in the use of this system, it was felt that a meaningful interpretation of the results of an experiment of this type could only be achieved by the use of a simple phenylazoalkane which would rearrange to give the corresponding phenylhydrazone with complete loss of optical activity; in this case



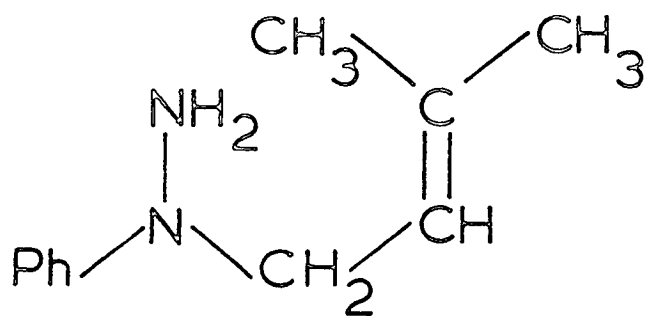
Scheme 63



(19)



(20)



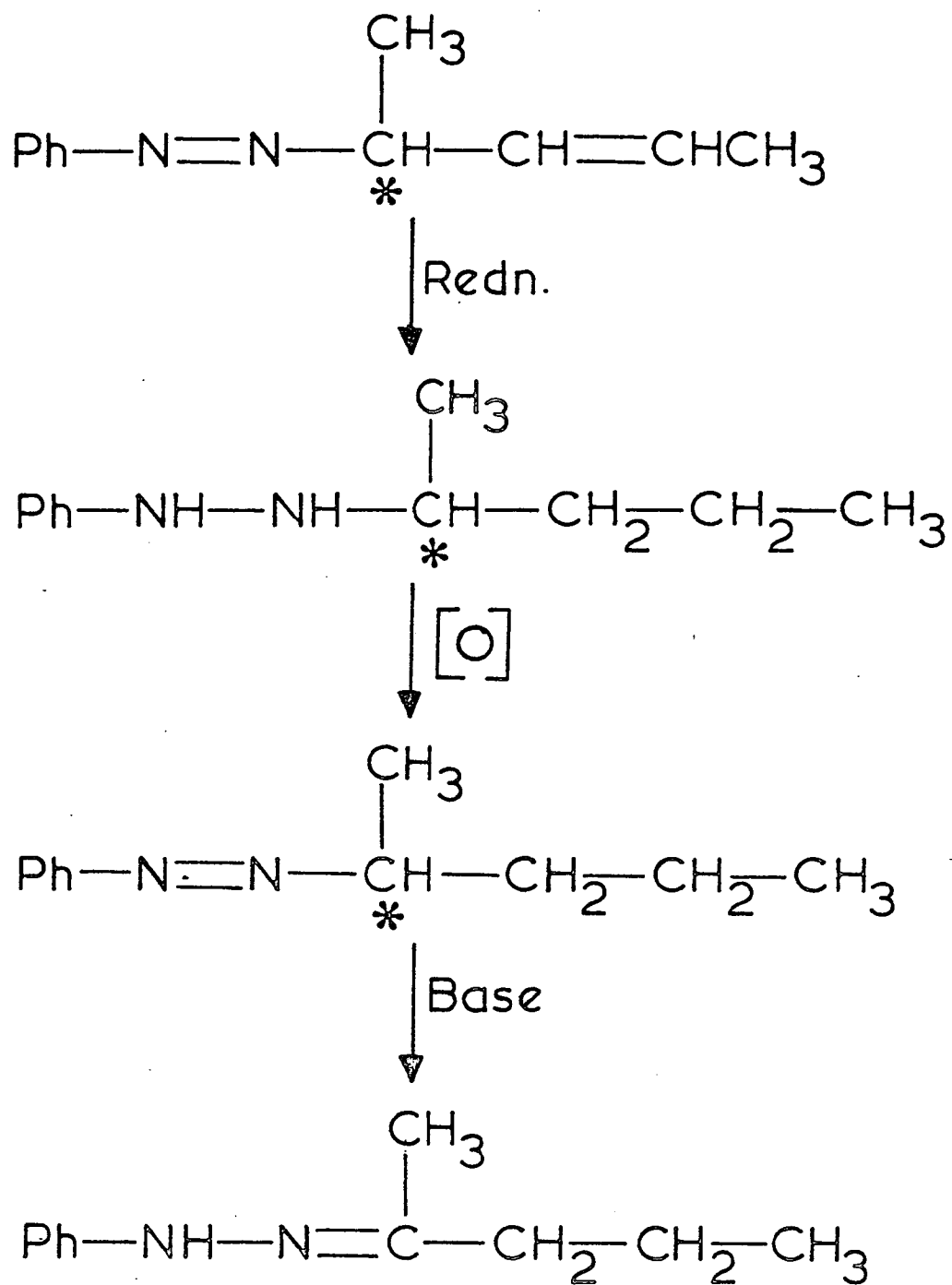
(21)

subsequent reaction of the phenylhydrazone would not affect the optical rotation. In selecting a suitable phenylazoalkane substrate, it was considered important that the proton which was to be abstracted by the base should not be so acidic that rearrangement could occur spontaneously in the absence of base. Thus, the nature of the substituent on the chiral α -carbon atom was important; for example, it was felt that a phenyl substituent was undesirable.

As mentioned in the Introduction, Yamamoto et al⁷¹ in 1973 reported the transfer of chirality from tetrahedral carbon to trigonal carbon in the allylic rearrangement of (R)-N,N-dimethyl-3-(1-phenyl-trans-but-1-enyl)amine oxide as shown in Scheme 20 (see p. 17) and it was hoped that a similar result could be achieved in the case of the chiral diazene as shown in Scheme 61.

It was anticipated that it would be advisable to reduce the carbon-carbon double bond of the allylic azo-compound for two reasons: firstly to avoid the complication of rearrangement of the allylic substituent competing with the rearrangement under examination (Scheme 63), and secondly, to remove the unnecessary complication of potential geometrical isomerism in the C = C bond. The optically active azo-compound prepared by the proposed synthetic route would therefore be of the type (19).

The importance of the nature of the substituent R has already been alluded to above; this consideration therefore influenced the structure of the hydrazine chosen for the proposed oxidative rearrangement, namely 1-(pent-3-en-2-yl)-1-phenylhydrazine (20). It was considered that this choice of allylic substituent in the diazene would not introduce any sterically derived energy barrier to the occurrence of the desired rearrangement, since Baldwin et al⁶¹ had shown that the hydrazine (21) underwent oxidation smoothly to give the corresponding azo-compound in 70% yield.



Scheme 64

It was intended to prepare the required hydrazine by the method which had been successfully applied to the synthesis of a number of related hydrazines (see p. 28), namely by alkylation of the sodium salt of phenylhydrazine with a suitable alkylating agent (Experimental pp.130-131). The preparation of the necessary pure, optically active, alkylating agent, 2-chloropent-3-ene, is well documented in the literature^{127,128} and involves the treatment of the optically active alcohol with phosphorous trichloride. The alcohol may be readily resolved by esterification with phthalic anhydride, formation of the brucine salt of the remaining carboxylic acid moiety^{127,129} (only one enantiomer reacts with brucine under the conditions used), and regeneration of the alcohol from the phthalate by hydrolysis¹²⁷ or by reduction with lithium aluminium hydride.¹²⁹

Scheme 64 summarises the proposed approach for the examination of the kinetics of the base-catalysed isomerisation of phenylazoalkanes to the corresponding phenylhydrazones, following successful stereospecific rearrangement of the diazene.

Preparation of 1-(Pent-3-en-2-yl)-1-Phenylhydrazine

The preliminary experiments on the oxidative rearrangement of 1-(pent-3-en-2-yl)-1-phenylhydrazine described below, were carried out on racemic samples of the hydrazine prepared by alkylation of the sodium salt of phenylhydrazine with a freshly prepared sample of racemic 2-chloropent-3-ene (Experimental p.170). Satisfactory n.m.r. spectral data was obtained for the hydrazine prepared in this way, but on several occasions the n.m.r. spectrum of the alkylation product suggested the presence of residual phenylhydrazine. However, even in those cases where the alkylation product was apparently free from phenylhydrazine it was considered desirable to purify the hydrazine further. To this end, it was hoped to employ the purification procedure already described (Discussion p.30), namely that of hot benzene extraction of the hydrochloride

derivative of the alkylation product.

The hydrochloride derivative was prepared in the usual way by passing a stream of dry hydrogen chloride gas through a solution of the crude hydrazine in ether at 0°C . The infra-red spectrum of the unpurified white solid so obtained showed absorptions in the same region as those taken to be diagnostic for the presence of phenylhydrazine hydrochloride (ν 887 and 857 cm^{-1} ; Discussion p. 31). The intensity of these absorptions appeared to be too great to be due solely to phenylhydrazine hydrochloride since the n.m.r. spectra of the crude hydrazine did not suggest the presence of significant amounts of phenylhydrazine. Furthermore, the possibility that the absorptions were due entirely to phenylhydrazine hydrochloride formed during the preparation of the hydrochloride derivative in a manner analogous to that described earlier (Discussion p. 34) and not to the hydrochloride derivative of the alkylation product, was ruled out on the basis of the outcome of a control experiment in which the crude 1-(pent-3-en-2-yl)-1-phenylhydrazine was recovered unchanged after basic work-up of the hydrochloride derivative prepared at 0°C . The method of establishing the purity of the product obtained from the alkylation of the sodium salt of phenylhydrazine by examination of the infra-red spectrum of the hydrochloride derivative for the presence of absorption bands characteristic of phenylhydrazine hydrochloride, could therefore not be applied to the present case. A further complication arose when it was discovered that the hydrochloride of 1-(pent-3-en-2-yl)-1-phenylhydrazine could not be recrystallised from benzene without undergoing rearrangement and decomposition (Experimental pp. 174-179).

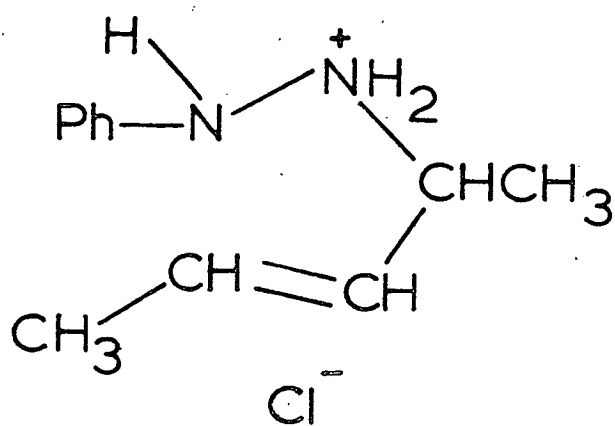
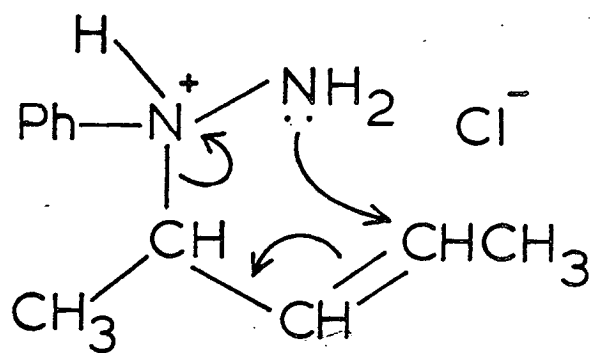
Successive extraction of a sample of the crude hydrochloride with benzene gave a white solid on evaporation of the solvent. Basification of this solid gave a yellow liquid which was shown by n.m.r. spectroscopy

to be a mixture of the expected 1-(pent-3-en-2-yl)-1-phenylhydrazine and another species (the major component) also having the pent-3-en-2-yl substituent. Later observations suggested that this second component was 2-(pent-3-en-2-yl)-1-phenylhydrazine (see below). The residue of the extraction procedure, a white solid, was basified and a brown liquid was recovered which was shown by n.m.r. spectroscopy to be a mixture of phenylhydrazine and a very small amount of 1-(pent-3-en-2-yl)-1-phenylhydrazine. The amount of phenylhydrazine recovered in this way corresponded to a contamination in the crude 1-(pent-3-en-2-yl)-1-phenylhydrazine of 17% by weight (26 mole %). This result contrasted markedly with the appearance of the n.m.r. spectrum of the crude hydrazine; comparison of the integral of the aromatic region with that of the methyl region gave no indication that any significant amount of phenylhydrazine was present.

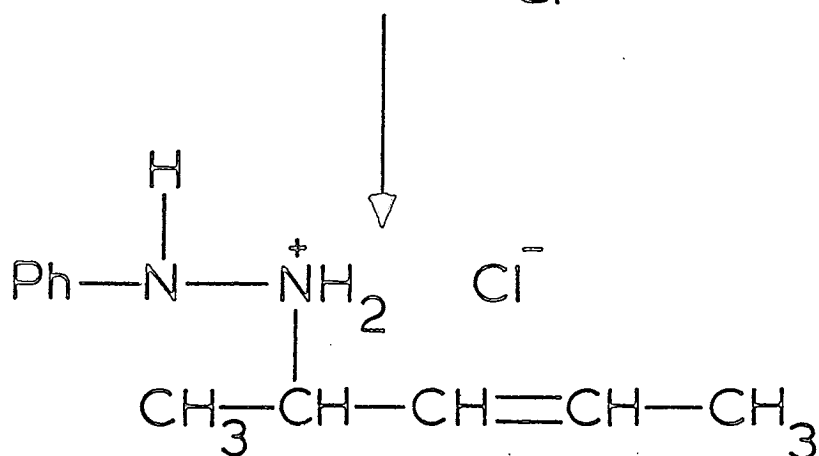
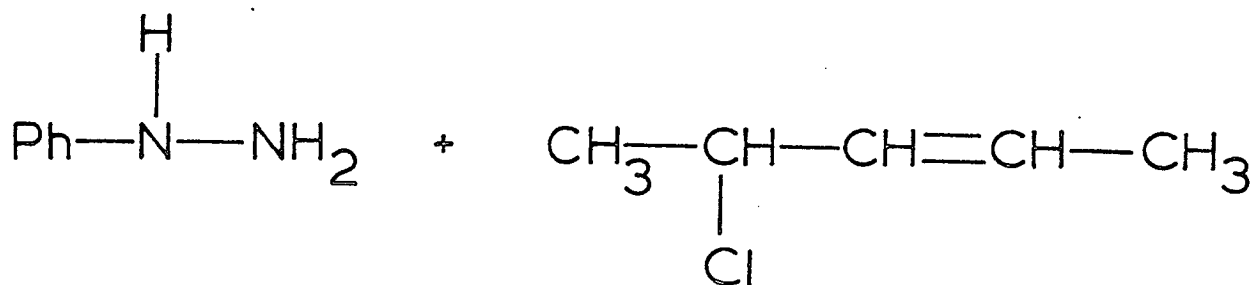
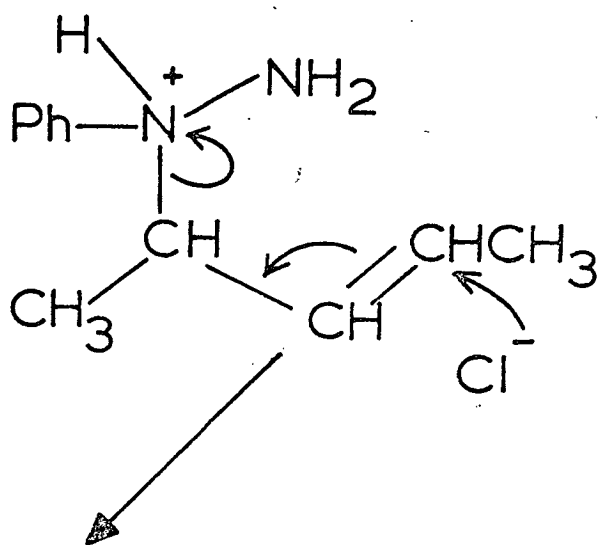
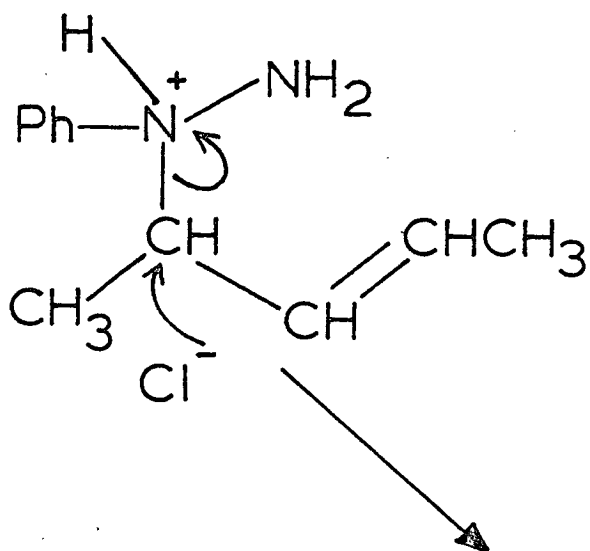
Continuous benzene extraction of another sample of the crude hydrochloride over a period of three days gave a white solid (on evaporation of the solvent) which yielded a yellow-brown liquid after basification. N.m.r. and infra-red data on this liquid, together with the observation that it readily underwent oxidation in air (Experimental p. 176) suggested that it was 2-(pent-3-en-2-yl)-1-phenylhydrazine. The mass spectrum of the liquid showed a parent ion of m/e 174 instead of the expected 176 for the disubstituted hydrazine, a further indication of the ready oxidation of the material. Complete oxidation of the liquid was readily achieved using yellow mercuric oxide; the signals observed in the n.m.r. spectrum of the product were later observed in the spectrum of the oxidation product of 1-(pent-3-en-2-yl)-1-phenylhydrazine and were attributed in both cases to 2-phenylazopent-3-ene. Thus the material recovered from the recrystallised hydrochloride is 2-(pent-3-en-2-yl)-1-phenylhydrazine. Further continuous extraction with benzene for

a period of seven days, failed to produce any more of the white solid; instead, a viscous brown oil was obtained (on evaporation of the solvent) which could not be characterised either in this condition or after treatment with base (Experimental p. 175 and p. 177). However, a brief examination was made into the possible origin of this oil. Benzene solutions of crude 1-(pent-3-en-2-yl)-1-phenylhydrazine and the material recovered after basification of the extraction residue (see below) were heated under reflux, in air, for one week: the former solution gave back the hydrazine unchanged, and the latter gave mainly 2-phenylazopent-3-ene (the product of air oxidation), thereby demonstrating that the oil was not simply derived from the in situ loss of hydrogen chloride from the crude hydrazine hydrochloride or from the 'rearranged' hydrazine hydrochloride (i.e. the extraction residue).

The residue of the extraction procedure was a white solid which, on treatment with base, gave a liquid which was identified by n.m.r. spectroscopy as a mixture of 2-(pent-3-en-2-yl)-1-phenylhydrazine and phenylhydrazine (ca. 30%). The observed phenylhydrazine content corresponded to a contamination of 7% by weight (ca. 11 mole %) in the original crude 1-(pent-3-en-2-yl)-1-phenylhydrazine. This degree of contamination was considered to be greater than that suggested by the appearance of the n.m.r. spectrum of the crude alkylation product, and would appear to support the inference from the results of successive benzene extraction (see p. 70), that phenylhydrazine hydrochloride is generated during the extraction process. Further support for this suggestion came from the results of two more continuous extraction experiments. In these instances, however, no crystalline material was recovered from the benzene extract, instead the residues from the extracts were treated with base, to give liquids which could not be characterised (by n.m.r. and infra-red spectroscopy) in terms of the original material.



Scheme 65

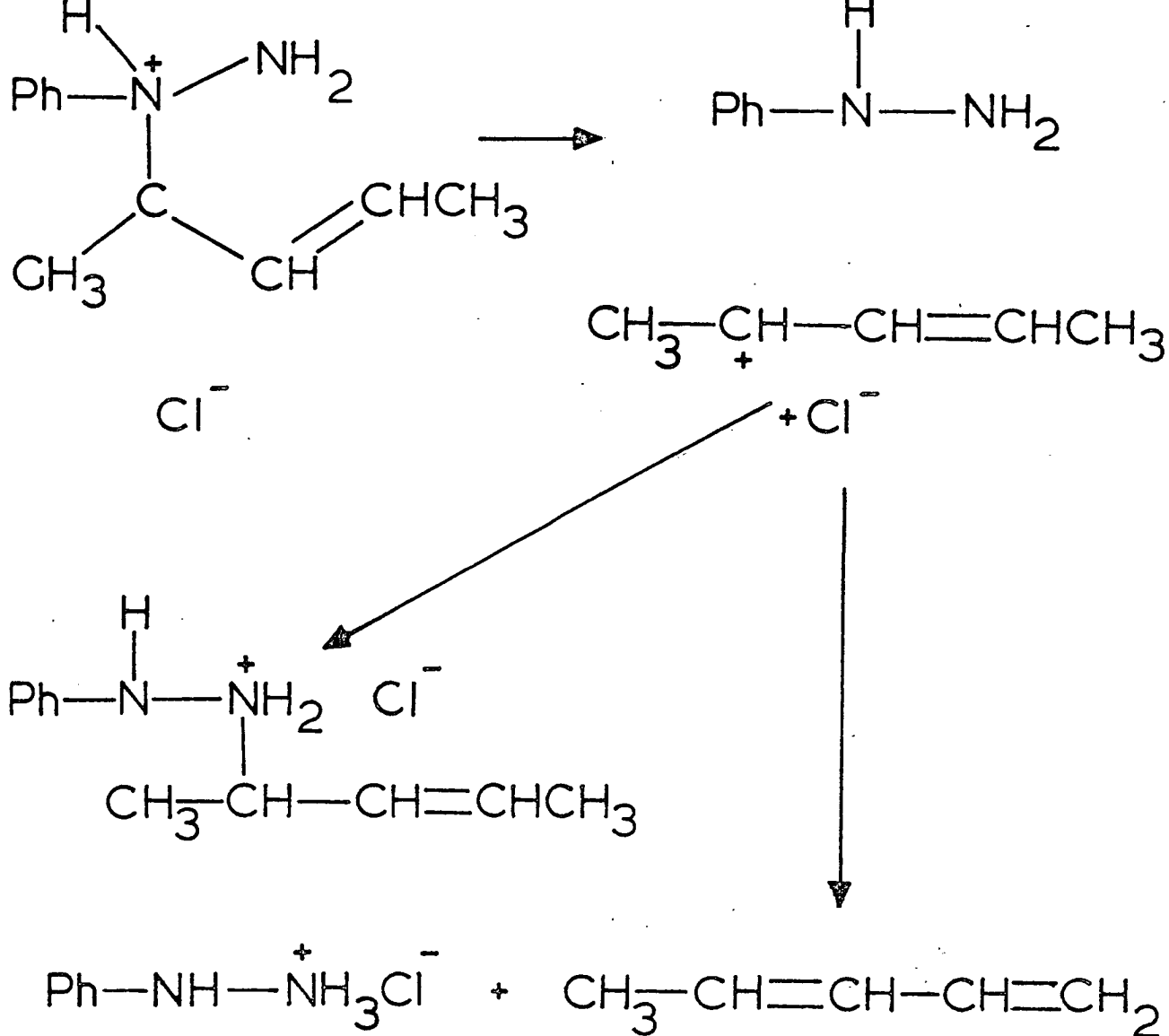


Scheme 66

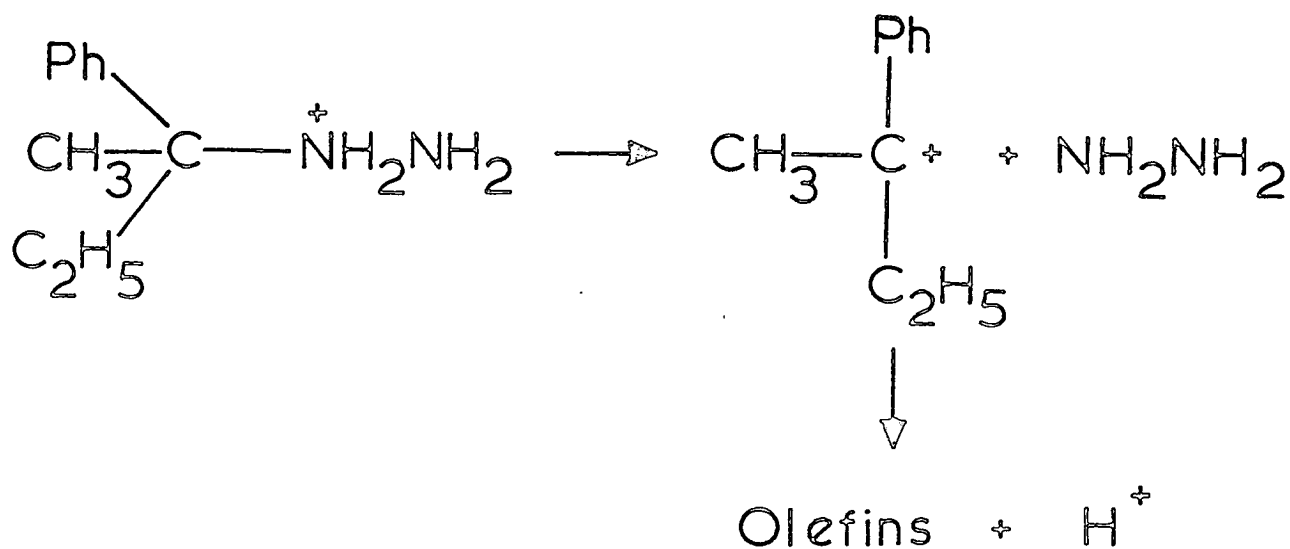
Recrystallisation of the crude hydrochloride from ethanol was also examined (Experimental p. 177). Crystallisation was promoted by the addition of ether; the material precipitated by this process was significantly different to that recovered by evaporation of the mother liquor. Basification of the former gave a liquid whose n.m.r. spectrum suggested the presence of phenylhydrazine and a small amount of material containing the pentenyl substituent, while basification of the latter material gave a liquid which was identified as 2-(pent-3-en-2-yl)-1-phenylhydrazine. The recovery of phenylhydrazine gave further support to the view that phenylhydrazine hydrochloride formation accompanied the rearrangement of 1-(pent-3-en-2-yl)-1-phenylhydrazine hydrochloride to 2-(pent-3-en-2-yl)-1-phenylhydrazine hydrochloride.

The attempted recrystallisation of the crude hydrochloride from water also resulted in the formation of 2-(pent-3-en-2-yl)-1-phenylhydrazine hydrochloride (Experimental p. 179).

This rather superficial examination of the recrystallisation of the crude hydrochloride of 1-(pent-3-en-2-yl)-1-phenylhydrazine from benzene and from ethanol suggests that rearrangement of the hydrochloride takes place to give 2-(pent-3-en-2-yl)-1-phenylhydrazine hydrochloride, and that phenylhydrazine hydrochloride and a mixture of intractable substances are also produced. Three possible mechanisms for the formation of the rearranged hydrochloride are shown in Schemes 65, 66, and 67. In each case it is implied that the hydrochloride of 2-(pent-3-en-2-yl)-1-phenylhydrazine is more stable than the hydrochloride of the 1,1-disubstituted isomer, and that, once formed, it is stable with respect to the reverse rearrangement (Scheme 65), and to the dealkylation process (Schemes 66 and 67). This in turn implies that the driving force for the occurrence of the processes shown in Schemes 65, 66, and 67 is the relief of steric strain in the hydrochloride of 1-(pent-3-en-2-yl)-1-phenylhydrazine. Schemes 66 and 67 allow the formation of phenylhydrazine



Scheme 67



Scheme 68

hydrochloride. Scheme 67 is based on the work of Cram and Sahyun¹³⁰ who found that 2-phenylbut-2-ylhydrazine decomposed in glacial acetic acid at 50°C in the presence of *p*-toluenesulphonic acid to give hydrazine and a mixture of cis- and trans-2-phenyl-but-2-ene and 2-phenylbut-1-ene (Scheme 68). Hegarty¹³¹ suggests that the dealkylation process shown in Scheme 68 is favoured by the ability of the alkyl substituent to form a stable carbonium ion; clearly, this criterion is met in the present case. (This type of dealkylation is also known to occur with the hydrochlorides of *N*-substituted anilines - see below, p. 86). Further detailed examination of the system would be required before it could be decided which of these proposed mechanisms operates.

Further examples of unexpected behaviour involving the pent-3-en-2-yl substituent are given below (see pp. 84-87).

The Oxidative Rearrangement of 1-(Pent-3-en-2-yl)-1-Phenylhydrazine

In view of the repeated failure of the hydrochloride recrystallisation procedure to effect purification of the crude hydrazine, the oxidation experiments were carried out on samples of 1-(pent-3-en-2-yl)-1-phenylhydrazine which were judged by n.m.r. spectroscopy to be pure with respect to contamination with phenylhydrazine.

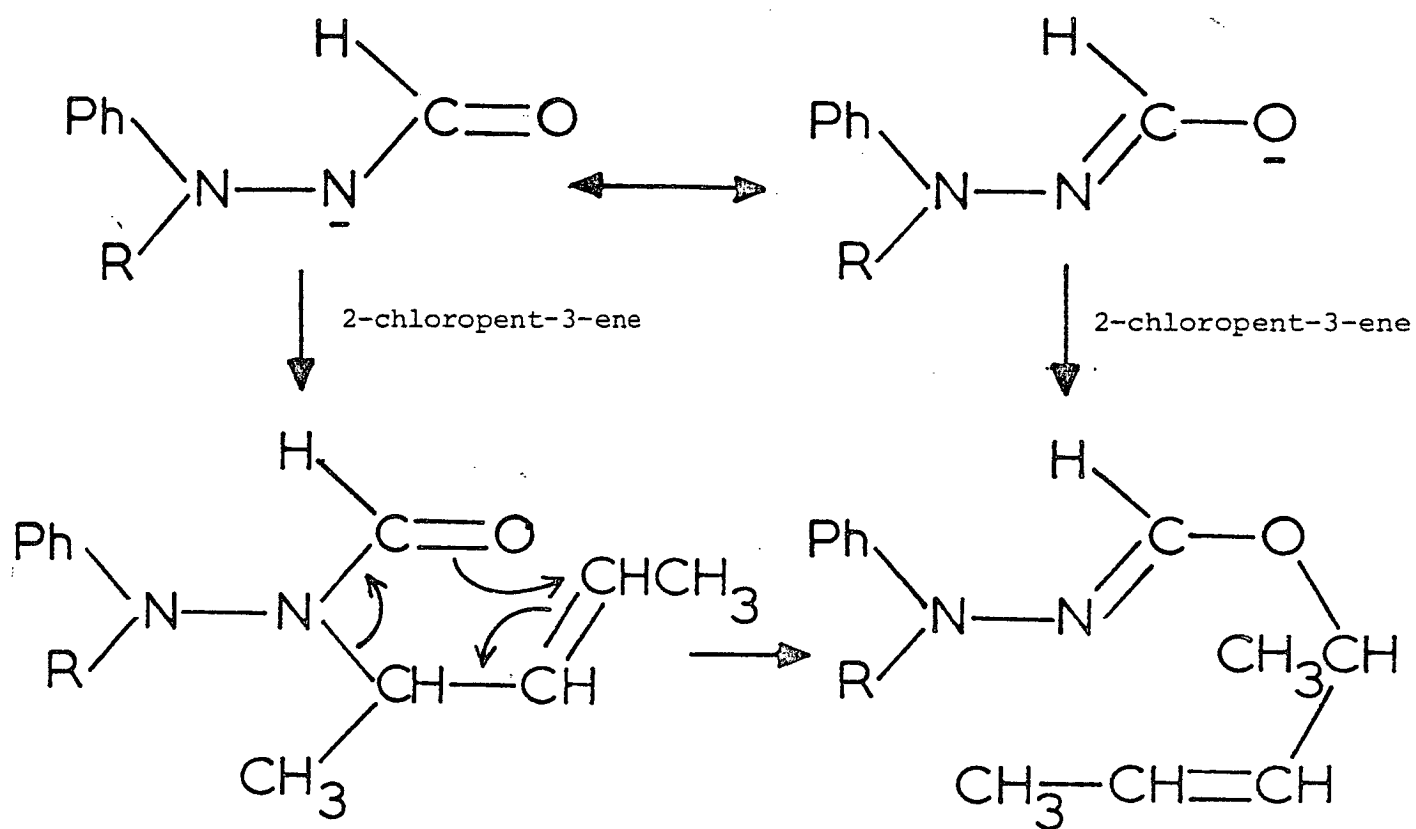
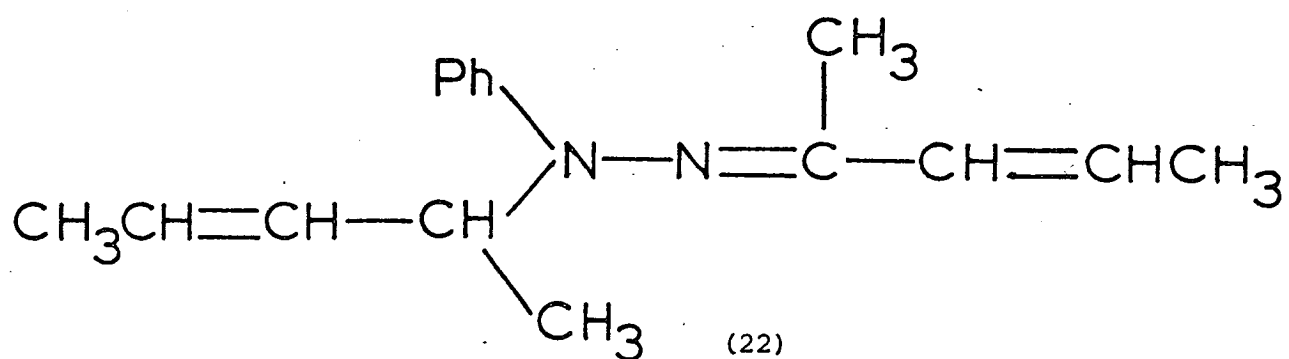
The oxidation with yellow mercuric oxide was first examined, and a mobile orange- yellow liquid was obtained (Experimental p.181). The experiment was repeated several times, and on each occasion oxidation appeared to occur immediately; on several occasions gas appeared to be evolved when the hydrazine was added to the oxidising agent. The same oxidation product was obtained in each case as judged by n.m.r. spectroscopy. The most striking feature of the n.m.r. spectra of these several oxidation products was the presence of two different sets of signals attributable to the pent-3-en-2-yl substituent, indicating that the

oxidation product contained more than one species. All attempts to separate the components of this mixture by conventional column chromatography were unsuccessful. Examination of the material by high pressure liquid chromatography (h.p.l.c.) showed that the mixture consisted of two major components, present in the ratio of 1.35:1, and three very minor components present in less than 1%. The infra-red spectrum of the oxidation product showed no absorption in the N-H region, supporting the view that complete oxidation had been achieved. The mass spectrum supported the presence of the expected product, 2-phenylazopent-3-ene [m/e 174 (P) and 159 (P-CH₃)] but gave no particular indication as to the identity of the second major component; weak peaks were observed at m/e 242 and 227 but these were thought to be due to pent-3-en-2-one 1-(pent-3-en-2-yl)-1-phenylhydrazone (22) formed in the course of the oxidation either from the diazene (cf. Introduction p. 14) or by oxidation of 1,2-di(pent-3-en-2-yl)-1-phenylhydrazine (the mass spectrum of the diazene precursor did show a weak peak at m/e 244, suggesting the presence of the dialkylated phenylhydrazine).

Oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine under homogeneous conditions using lead tetra-acetate (Experimental p. 184) and *p*-benzoquinone (Experimental p.184) gave the same mixture of products as had been obtained from the oxidations with yellow mercuric oxide. (The reasons for the choice of *p*-benzoquinone as an alternative oxidising agent are discussed below - see p. 83).

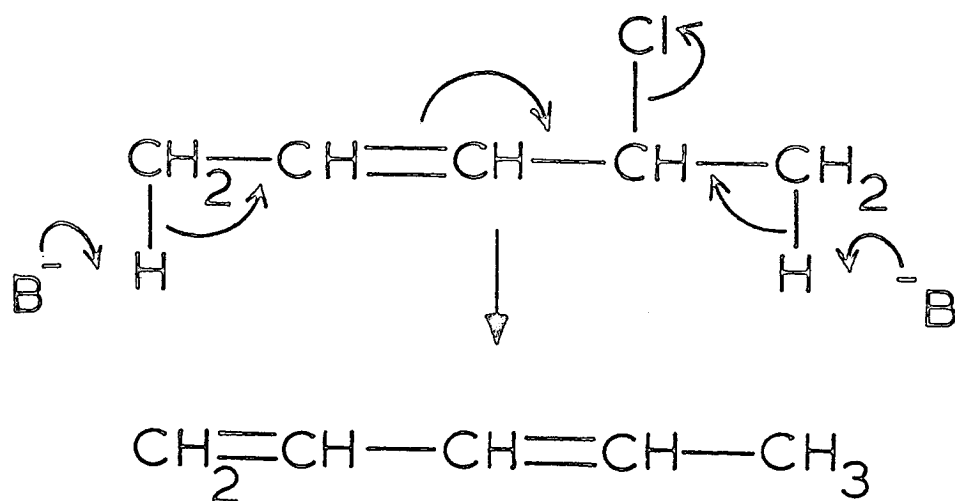
The Attempted Characterisation of the Oxidation Products from 1-Pent-3-en-2-yl-1-Phenylhydrazine

The expected product of oxidative rearrangement was 2-phenylazopent-3-ene and in an attempt to establish the presence of this compound in the oxidation product, two attempts were made to prepare an authentic sample by an unambiguous route. It was intended to prepare the azo-compound by



Scheme 69

$\text{R} = \text{H}, \text{CHO}$



Scheme 70

oxidation of 2-(pent-3-en-2-yl)-1-phenylhydrazine, and it was hoped that, to this end, the hydrazine could be readily obtained via the alkylation of the sodium salt of 1,2-diformyl-1-phenylhydrazine with 2-chloropent-3-ene (This approach had been successfully employed in the preparation of 1-phenylazoprop-2-ene - see p. 62). However, the n.m.r. spectrum of the alkylation product (after removal of the protecting formyl groups) did not give an integration ratio which was consistent with the expected product although it did indicate the presence of the pent-3-en-2-yl substituent; the spectrum could not be reconciled with that of the hydrazine obtained via the rearrangement of 1-(pent-3-en-2-yl)-1-phenylhydrazine hydrochloride (see p. 71). The alkylation of the sodium salt of 2-formyl-1-phenylhydrazine was also unsuccessful (Experimental p. 189).

The contrasting behaviour of allyl bromide and 2-chloropent-3-ene in these two alkylation reactions may conceivably be explained in terms of a tendency for competing O-alkylation to occur in the alkylation with the more bulky 2-chloropent-3-ene: O-alkylation may be seen as occurring either directly, or indirectly by rearrangement of the N-alkylated product (Scheme 69). Hydrolysis of the O-alkylated material would give phenylhydrazine; this would agree with the observation that the integration of the N-H proton signal in the n.m.r. spectrum of the hydrolysis product was larger than expected. (Similar mechanisms have also been invoked to explain the apparently complex course of the alkylation of the sodium salt of acetanilide with 2-chloropent-3-ene - see p. 85). Furthermore, a facile elimination pathway may be envisaged for 2-chloropent-3-ene (Scheme 70) which is not open to simple allyl halides.

Although these attempts to prepare 2-(pent-3-en-2-yl)-1-phenylhydrazine and thence 2-phenylazopent-3-ene by unambiguous methods were

unsuccessful, it will be remembered that these two species had already been obtained via the rearrangement of 1-(pent-3-en-2-yl)-1-phenylhydrazine hydrochloride in benzene solution (see above p. 71). The formulation of the recrystallised hydrochloride as 2-(pent-3-en-2-yl)-1-phenylhydrazine hydrochloride was based on the fact that although the mass spectrum of this recrystallised material showed a parent ion of m/e 176 as expected for the hydrochloride of 1-(pent-3-en-2-yl)-1-phenylhydrazine, basification gave a liquid whose n.m.r. spectrum was quite different to that of the crude 1,1-disubstituted hydrazine but still exhibited the expected integration. Furthermore, this liquid was found to be sensitive to air oxidation giving a mobile liquid having a mass spectral parent ion of m/e 174, suggesting that the oxidation product was 2-phenylazopent-3-ene; the n.m.r. spectrum of the oxidation product supported this assignment.

Comparison of the n.m.r. spectra of the oxidation product of 1-(pent-3-en-2-yl)-1-phenylhydrazine and of the oxidation product referred to in the preceding paragraph (2-phenylazopent-3-ene) showed that all the signals of the latter spectrum also occurred in the former. Thus the formation of 2-phenylazopent-3-ene in the oxidative rearrangement was confirmed. Independent support for the presence of 2-phenylazopent-3-ene was supplied by the results of catalytic hydrogenation of the oxidative rearrangement product (see p. 79).

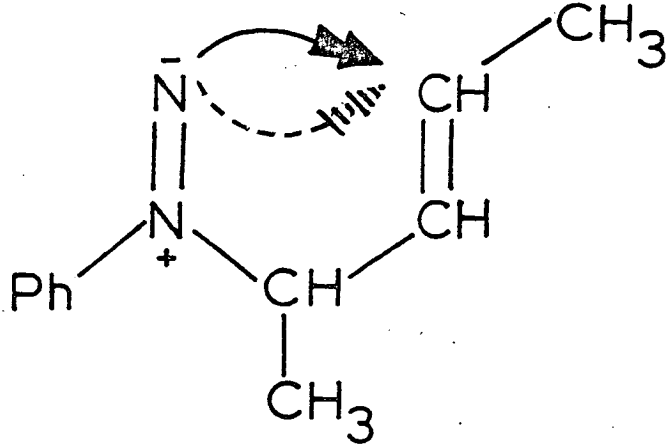
While it is unfortunate that an unambiguously prepared authentic sample of 2-phenylazopent-3-ene was not available, it is felt that the spectral data described above provides sufficiently strong evidence that the oxidative rearrangement of 1-(pent-3-en-2-yl)-1-phenylhydrazine does in fact result in the formation of 2-phenylazopent-3-ene.

Turning to the problem of the second component and its possible relation to 2-phenylazopent-3-ene, a significant pointer was supplied by the n.m.r. spectrum of the oxidation product which indicated that the

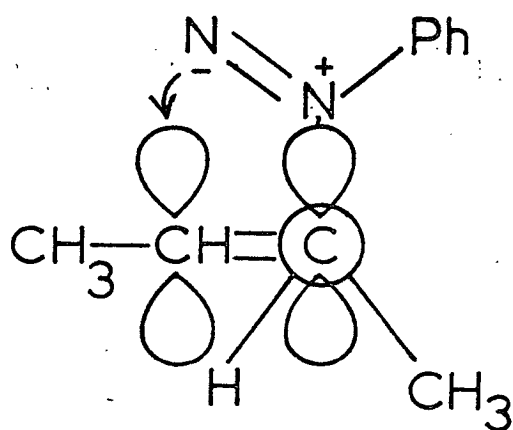
unidentified component contained both the phenyl and the pent-3-en-2-yl substituents in the same ratio as in 2-phenylazopent-3-ene i.e. a 1:1 ratio. In the first approach to the problem, two types of geometrical isomerism were considered.

The possibility that the product was a mixture of the cis- and trans-isomers (with respect to the N=N bond) of 2-phenylazopent-3-ene was considered unlikely as it would involve isomerisation of the initially formed trans-isomer to the thermodynamically less stable cis-isomer. Support for this view came from the fact that oxidation of 2-(pent-3-en-2-yl)-1-phenylhydrazine (see p.71 ; Experimental p. 176) to 2-phenylazopent-3-ene under similar reaction conditions gave only a single species.

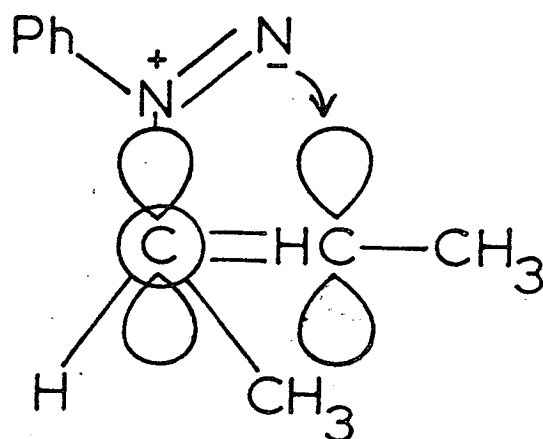
In view of the absence from the literature of reports describing the competing formation of alternative products in the oxidative rearrangement of allylic 1-alkyl-1-phenylhydrazines (i.e. products other than the expected azo-compounds; cf. References 4 and 61), another possibility for geometrical isomerism appeared attractive, namely isomerism about the C=C bond. It was envisaged that such geometrical isomerism about the C=C bond could arise by two distinct suprafacial-suprafacial transformations, which differed only in the direction of the attack by the diazene function on the double bond: one was seen as involving a top-side approach, while the other was seen as involving an under-side approach. These two possibilities are illustrated by the bold arrow and by the dotted arrow respectively in (23); the allylic substituent is represented in its trans-form since the alkylating agent was derived from trans-pent-3-en-2-ol. The use of Newman projections offers a clearer illustration of the two processes, and the preferred conformations (i.e. those which enable the most favourable overlap of the participating orbitals are represented



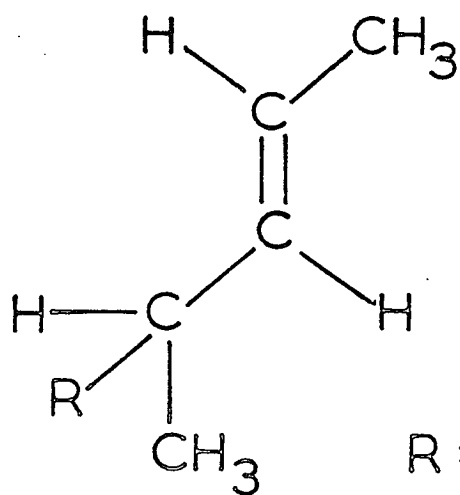
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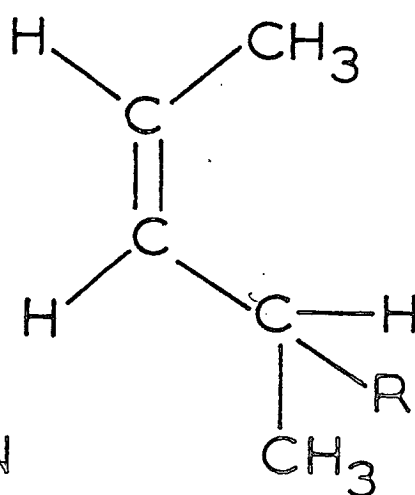
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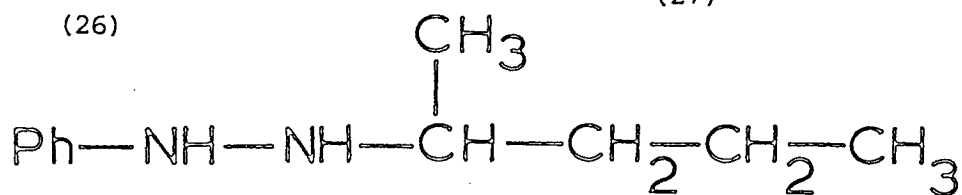
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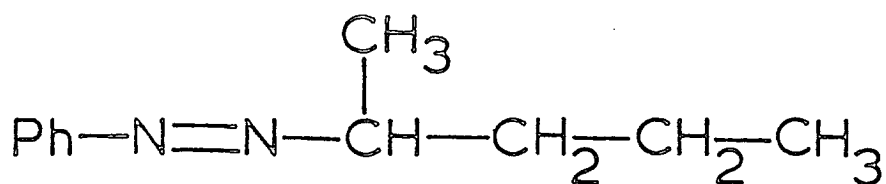
(26)



(27)



(28)

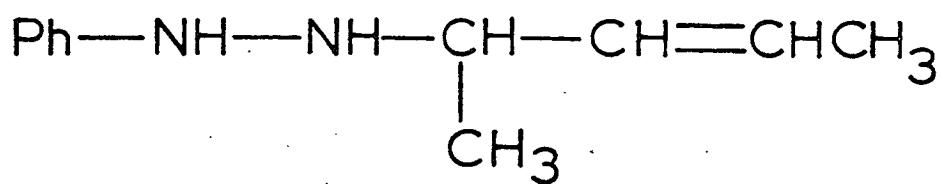


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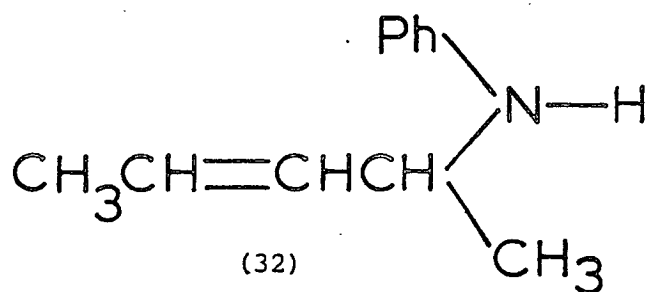
in (24) and (25). The projections are drawn with the C_2-C_3 bond as axis (numbering from $N-1$ of the parent hydrazine), and the conformers may be interconverted by rotation about this bond. The two geometrically isomeric azo-compounds which would be formed in these two competing processes are illustrated as (26) and (27), derived from (24) and (25) respectively. The proton n.m.r. spectra of these species would be expected to be very similar, and to display only small differences in chemical shift values for corresponding protons. The observed n.m.r. spectrum of the oxidation product suggested the presence of two components bearing the pentenyl substituent with the methyl group resonances appearing to be equivalent. Reference to the structures of the proposed azo-compounds (26) and (27) suggest that the most significant differences in electronic environment between one geometrical isomer and the other, will be experienced by the aliphatic methine proton and the olefinic proton on C_3 of the pentenyl moiety. The most significant differences between the two components of the oxidation product in terms of the observed n.m.r. spectrum, were in the chemical shifts of the signals attributed to the aliphatic methine proton (Δ 0.4 p.p.m.) and the olefinic protons (Δ ca. 0.25 p.p.m.). This interpretation is therefore consistent with the experimental evidence so far presented.

It was proposed to test this interpretation further by subjecting the oxidation product to catalytic hydrogenation in order to eliminate the possibility of geometrical isomerism; it was anticipated that this procedure would give 2-(pent-2-yl)-1-phenylhydrazine (28) which could be re-oxidised to give 2-phenylazopentane (29) as the only product.

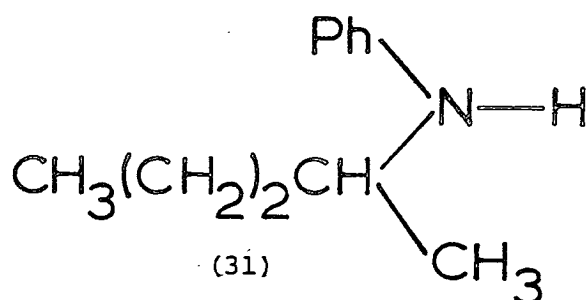
A micro-hydrogenation experiment was performed (Experimental p. 186) and the uptake of hydrogen was found to continue well beyond the volume expected for 2 mole equivalents. It was inferred from the continued uptake of hydrogen beyond the calculated amount, that further reduction



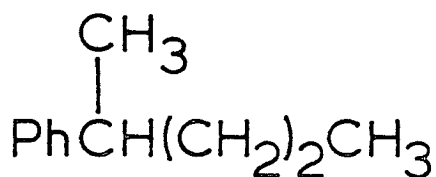
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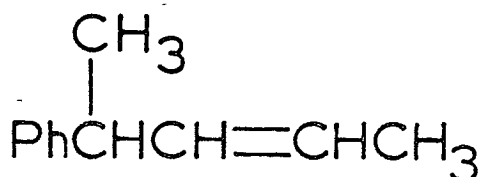
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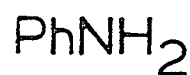
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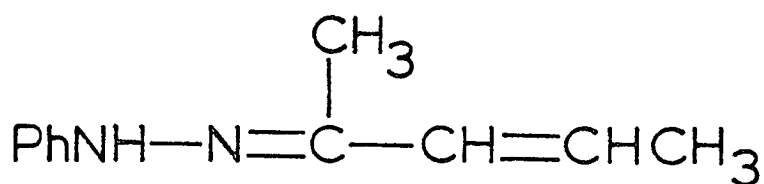
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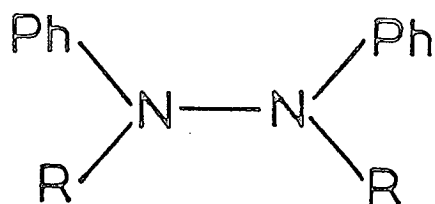
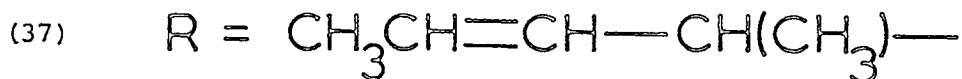
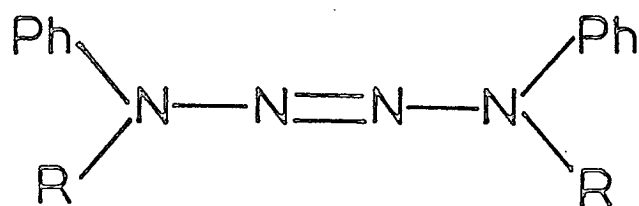
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(36)



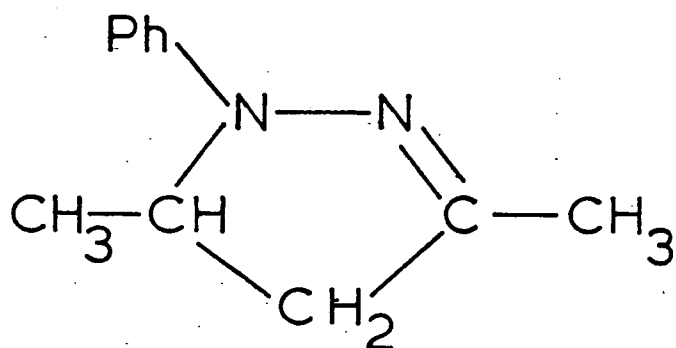
(38)

of the disubstituted hydrazine, probably to give aniline and pent-2-ylamine, was taking place. When the reduction was repeated on a larger scale (Experimental p. 186) the uptake of hydrogen was stopped after two mole equivalents had been consumed. Examination of the product by infra-red and n.m.r. spectroscopy indicated that all the 2-phenylazopent-3-ene (i.e. that component of the oxidation product which had been formulated as being the expected azo-compound on the basis of other evidence - see above p. 77) had been reduced to give 2-(pent-2-yl)-1-phenylhydrazine (28) and 2-phenylazopentane (29), the product of air oxidation of the initially formed hydrazine. (An authentic sample of the saturated hydrazine was found to undergo facile oxidation in air). The n.m.r. spectral evidence also suggested the presence of 2-(pent-3-en-2-yl)-1-phenylhydrazine (30). The fate of the second component of the oxidation mixture, whose identification had been the purpose of this experiment, was unclear as the region of the n.m.r. spectrum in which its most characteristic signals had been observed, was now obscured. However, signals were observed in the olefinic region even after hydrogenation; whether these signals belonged wholly to unreduced 2-(pent-3-en-2-yl)-1-phenylhydrazine or were due in part to the presence of some of the residual second component (or a product derived therefrom) could not be determined. The mass spectrum of the hydrogenation product supported the assignments described: m/e 178 (28), m/e 176, 175 (29 and 30). The other significant peaks could be assigned as follows: m/e 163, 162 (31), m/e 161 (32), m/e 148, 147 (33 ?), m/e 146, 145 (34 ?) and m/e 93, 92 (35 ?). The apparent formation of (31) and (32) in the hydrogenation experiment may be construed as indicating the presence of 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine or the corresponding tetrazene in the oxidation product; however, such assignments, based on mass spectral evidence alone can only be regarded as speculative, and even if the proposed species is present, no reliable inference as to the extent of its presence can be made.

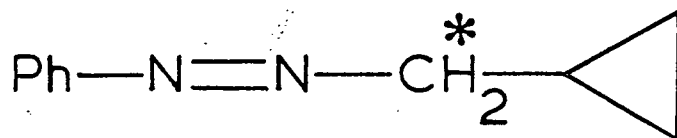
The outcome of this examination of the oxidation product mixture can therefore only be regarded as inconclusive in terms of the original objective. The complex nature of the product obtained, even under the conditions of controlled hydrogenation, suggested that there was little purpose in pursuing this approach further. Thus, the results of this piece of work cannot be regarded as confirming or refuting the original suggestion that the product of oxidative rearrangement of 1-(pent-3-en-2-yl)-1-phenylhydrazine was a mixture of the two geometrical isomers of 2-phenylazopent-3-ene.

In view of the inconclusive outcome of this approach to the problem of identifying the second component of the oxidation product, alternative explanations were considered. Thus several products, which precedent suggested might be formed from the diazene intermediate, either directly or from the decomposition or rearrangement of these primary products, and which were consistent with the inference drawn from the n.m.r. spectrum of the oxidation product (namely, that the second component contained both phenyl and pent-3-en-2-yl substituents in a 1:1 ratio - see p.78) were considered in this context. These were: pent-3-en-2-one phenylhydrazone (36) formed either directly (Introduction p.14) or by rearrangement of the initially formed 2-phenylazopent-3-ene , 1,4-di(pent-3-en-2-yl)-1,4-diphenyltetraz-2-ene (37), N-(pent-3-en-2-yl) aniline (32), 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine (38), and 2-phenylpent-3-ene (34). It was hoped to prepare authentic samples of each of these compounds so that comparisons with the oxidation product could be as direct as possible.

The possibility that the second component of the oxidation product was pent-3-en-2-one phenylhydrazone was supported by the fact that several reports of the rearrangement of diazenes to the corresponding hydrazones appear in the literature^{7,62-65} (Introduction p.14). Hydrazone formation has not however been reported to occur in the rearrangement of allylic diazenes^{4,61} and it will be remembered that

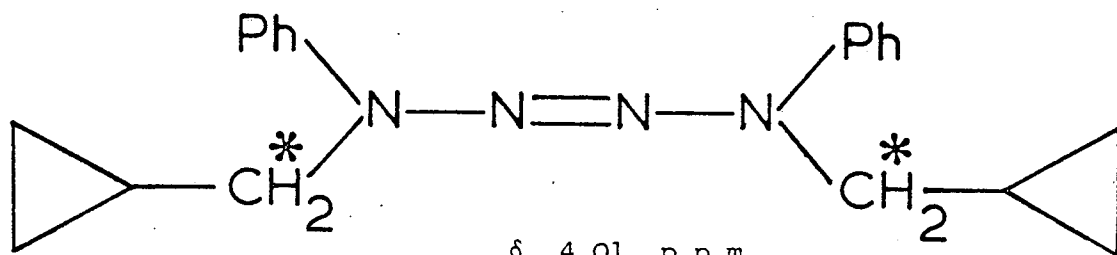


(39)



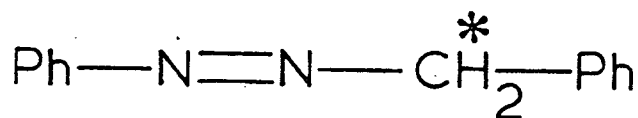
δ 3.82 p.p.m.

(40)



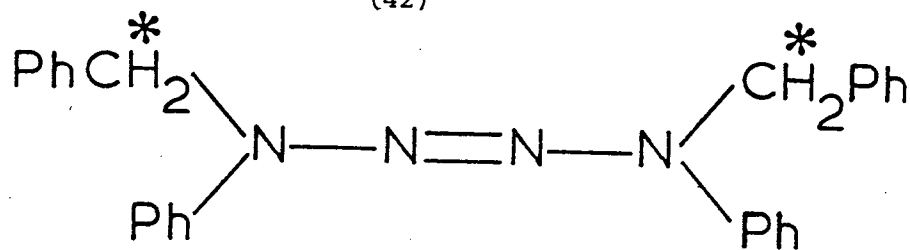
δ 4.01 p.p.m.

(41)



δ 5.08 p.p.m.

(42)



δ 5.3 p.p.m.

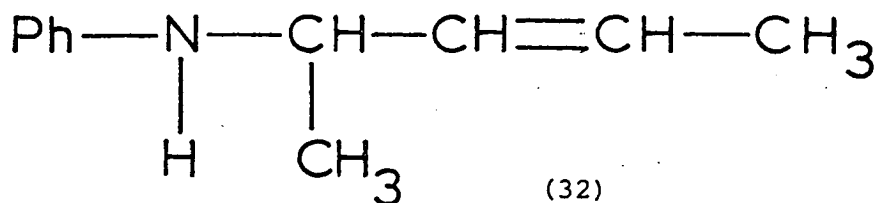
(43)

examination of the product derived from the oxidation of 1-allyl-1-phenyldiazene revealed no trace of the corresponding hydrazone (see p. 43,44) nevertheless it was felt necessary to examine the possibility. It was anticipated that during its formation, the hydrazone might undergo cyclisation to give the corresponding pyrazoline (39); this process is known to occur in the case of acrolein phenylhydrazone (see p. 43). For this reason, and in the belief that the cyclisation might be thermally induced, the authentic sample of 3-pent-en-2-one phenylhydrazone was prepared by carrying out the condensation of pent-3-en-2-one with phenylhydrazine at room temperature (Experimental p.190). The n.m.r. spectrum of the material prepared in this way was quite incompatible with that of the second component of the oxidation product. For example, the single most characteristic signal in the n.m.r. spectrum exhibited by the second oxidation product (in the sense that the other signals of this species were obscured by those of 2-phenylazopent-3-ene) was the multiplet at δ 4.5-5.0 p.p.m. attributed to the aliphatic methine proton ($-\underline{\text{CH}}(\text{CH}_3)-\text{CH}=\text{CH}.\text{CH}_3$); the n.m.r. spectrum of the prepared hydrazone displayed no signals in this region. (The corresponding signal was observed as a multiplet at δ 3.0-3.5 p.p.m.). It was therefore concluded that the unidentified oxidation product was not pent-3-en-2-one phenylhydrazone.

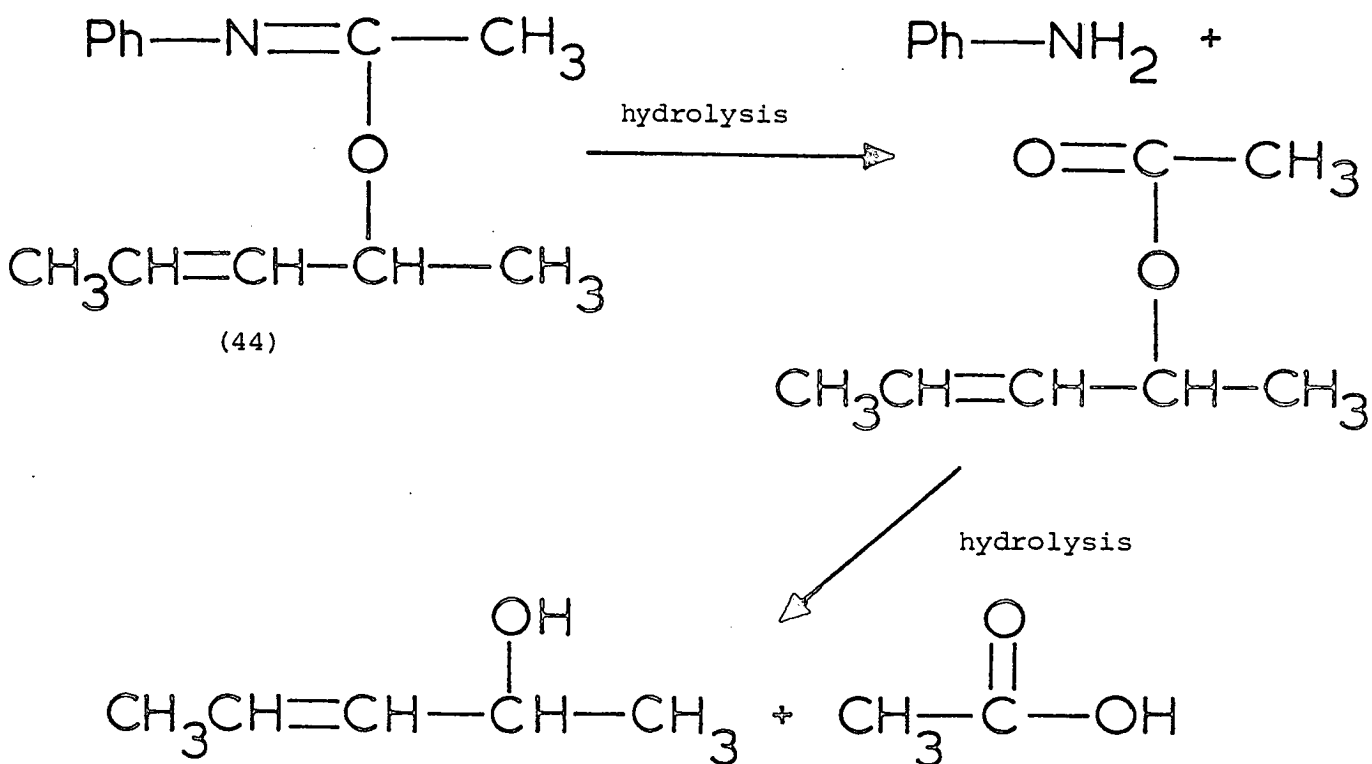
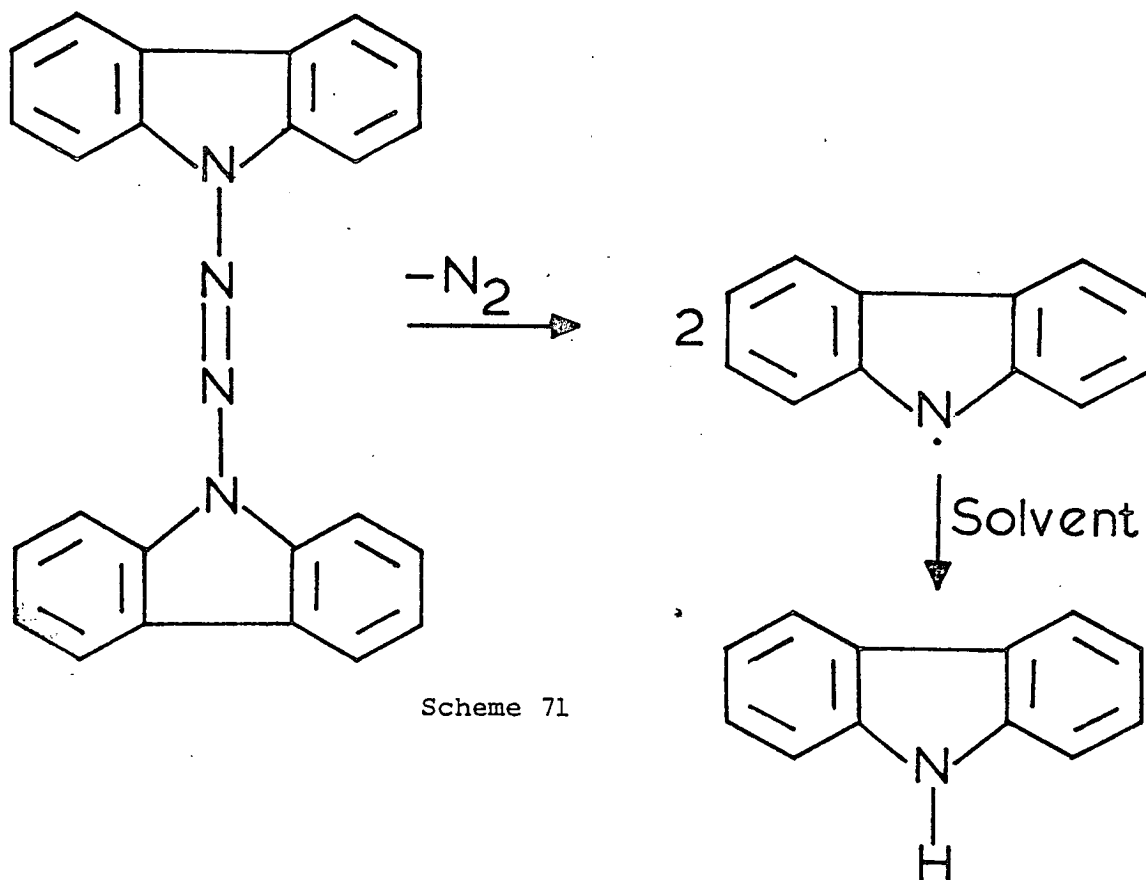
Support for the possibility that the second oxidation product was the corresponding tetrazene (37) came from examination of the n.m.r. spectra of authentic samples of azo-compounds and their corresponding tetrazenes. The compounds which were examined were the azo-compounds (40) and (42) and the tetrazenes (41) and (43). The chemical shifts of the labelled protons in the azo-compound and corresponding tetrazene were compared: as indicated, it was found that the resonances of these protons occurred at slightly higher frequency in the tetrazene compared to the azo-compound. The n.m.r. spectrum of the second oxidation product showed a multiplet, assigned to the proton which would be on the carbon atom α to nitrogen

(N-CH(CH₃)CH=CHCH₃) in the tetrazene, at a slightly higher frequency to that of the corresponding signal in the n.m.r. spectrum of the azo-compound. Thus n.m.r. evidence was in accord with the observed trend, suggesting that further investigation in this direction might be worthwhile. The investigation was, however, hampered by the fact that the only widely reported method of preparing tetrazenes is by oxidation of the corresponding 1,1-disubstituted hydrazines. Clearly in the present case, this approach was inapplicable. A possible solution to this paradoxical problem was suggested by the observation of Wieland and Fressel¹¹² that oxidation of 1,1-dibenzylhydrazine with p-benzoquinone gave 1,1,4,4-tetrabenzyltetraz-2-ene and not bibenzyl which is normally produced in the oxidation of this hydrazine. It was hoped that the oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine with p-benzoquinone would, by analogy, give the corresponding tetrazene; in practice however, oxidation with this reagent (Experimental p.184) gave the same mixture of products as had been obtained using yellow mercuric oxide and lead tetra-acetate.

The evidence in support of the possible presence of the tetrazene in the oxidation product has already been given. However this evidence must be weighed against three observations which question this possibility. Firstly, while the mass spectra of the tetrazenes (41) and (43) both show significant parent ion peaks, the mass spectrum of the oxidation product shows no such peak for the proposed tetrazene (m/e 348); since the tetrazene would be present in 42% (cf. the results of h.p.l.c. analysis of the oxidation product; p. 75) it might be reasonably expected (by analogy with the tetrazenes cited), that a significant parent ion peak would be observed. Secondly, evidence of a more circumstantial nature is provided by the fact that oxidation with lead tetra-acetate gave the same mixture of products as had been obtained with mercuric oxide, with no products of tetrazene decomposition being observed; the tetrazene (41) was found to undergo decomposition under the conditions of lead tetra-acetate oxidation,



(32)



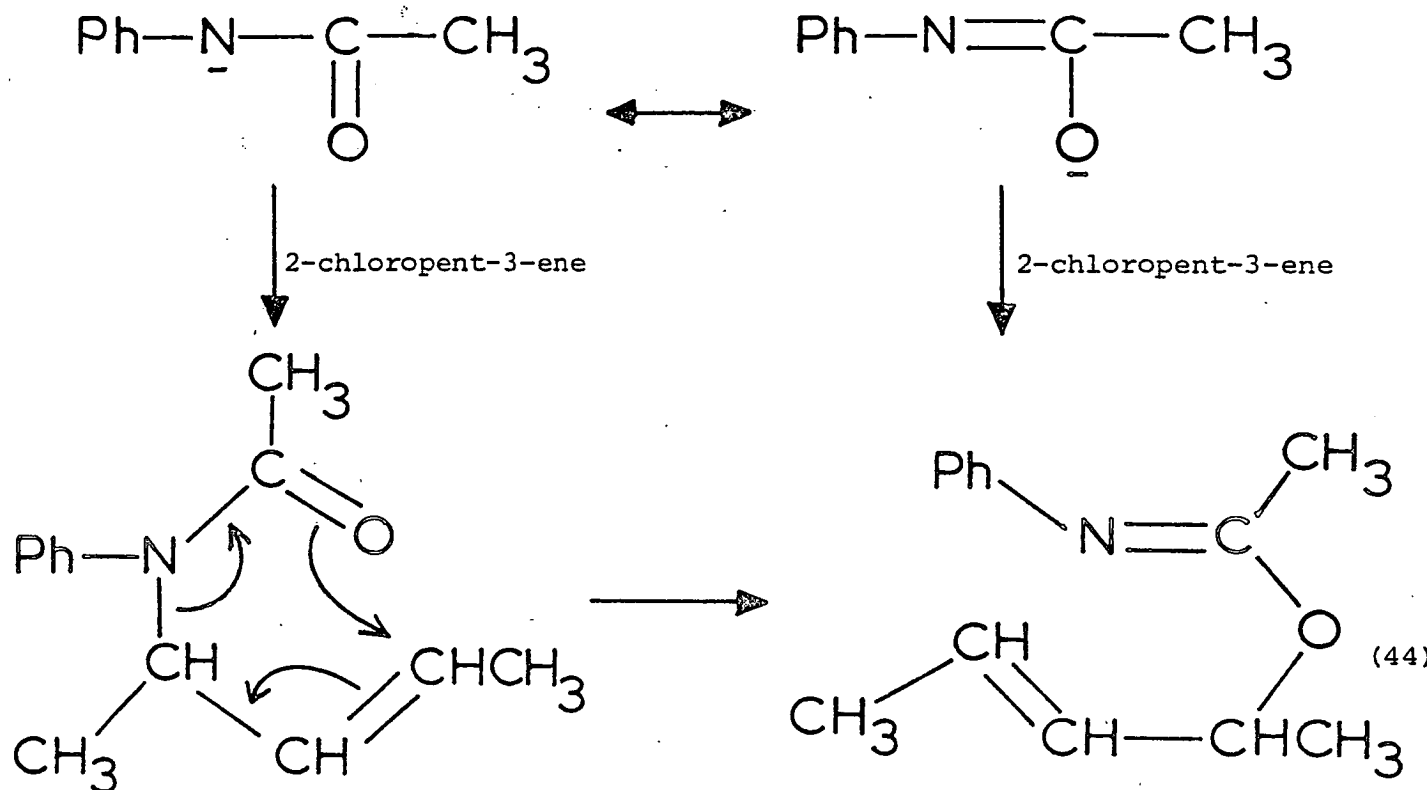
but was isolated cleanly from the oxidation with mercuric oxide.

Thirdly, reduction of tetraz-2-enes (e.g. with hydrogen and palladium) is known to give the corresponding secondary amines; the n.m.r. spectrum of the material obtained from the hydrogenation of the oxidation product did not indicate the presence of any secondary amine. [The mass spectrum of the hydrogenation product did, however, show a weak peak at m/e 161 which could correspond to the parent ion of N-(pent-3-en-2-yl)aniline.]

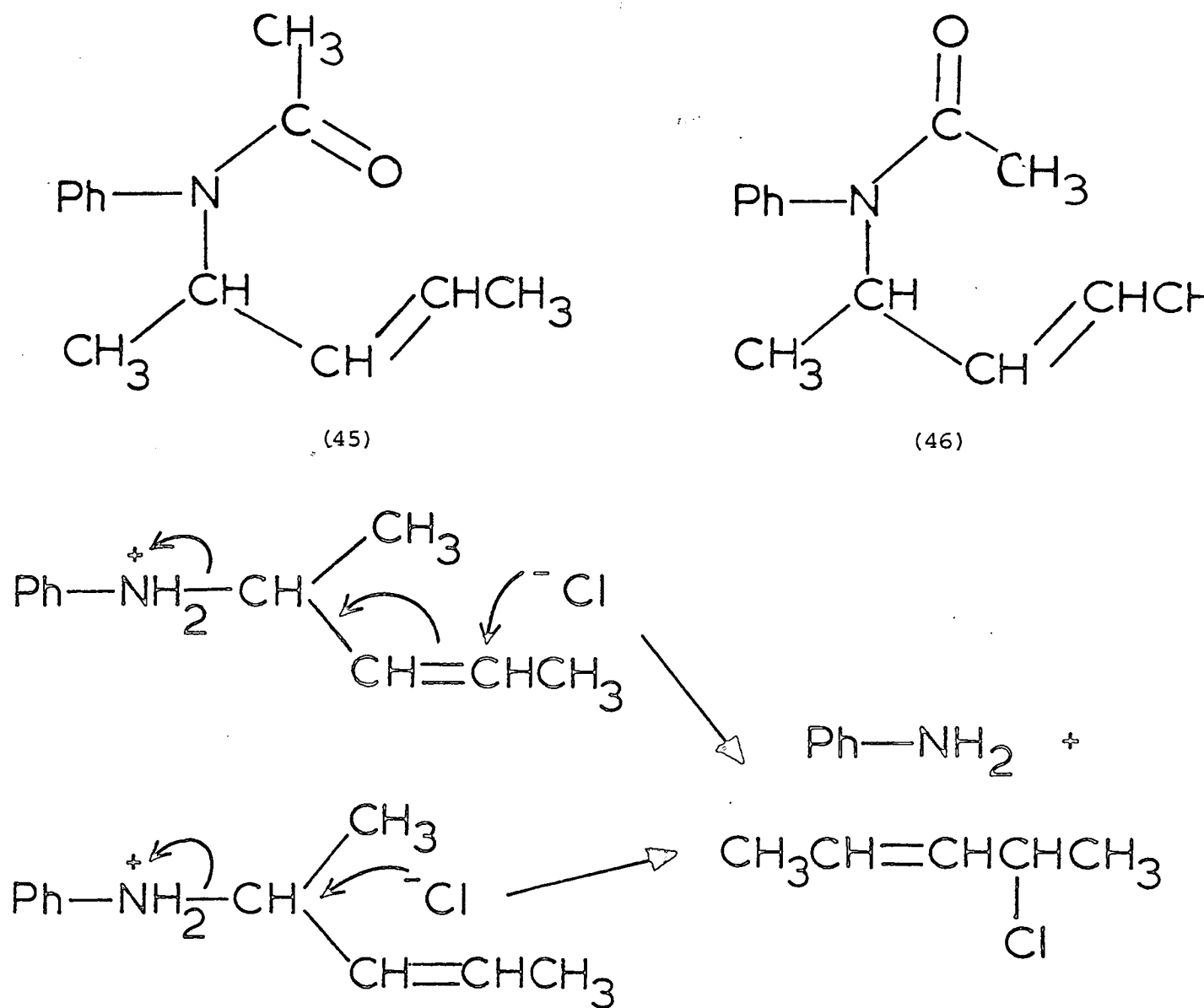
Thus, the possibility that the unidentified oxidation product was 1,4-di(pent-3-en-2-yl)-1,4-diphenyltetraz-2-ene could not be confirmed or denied in terms of the available evidence.

The possibility that N-(pent-3-en-2-yl)aniline (32) was formed in the oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine found support in the work of Lemal et al⁴⁷ who observed that thermal decomposition of the sodium salt of N-benzene sulphonamidocarbazole gave carbazole in 89% yield. These workers proposed (after carrying out the obvious control experiments) that the amine was formed by decomposition of the tetrazene as shown in Scheme 71. Although the infra-red spectrum of the oxidation product showed no N-H absorption to support amine formation, it was considered necessary to examine the possibility more rigorously. It was proposed to do this by first preparing an authentic sample of the amine.

An attempt was made to prepare the desired species by the method which had been successfully employed in the synthesis of N-allylaniline, namely, alkylation of the sodium salt of acetanilide with the appropriate alkylating agent, followed by hydrolysis of the product. However, application of this method to the present case was unsuccessful (Experimental p. 191). Acetanilide was recovered from the alkylation product, and hydrolysis of the remainder was found to give a mixture of aniline and an unidentified material containing the pentenyl substituent.



Scheme 73

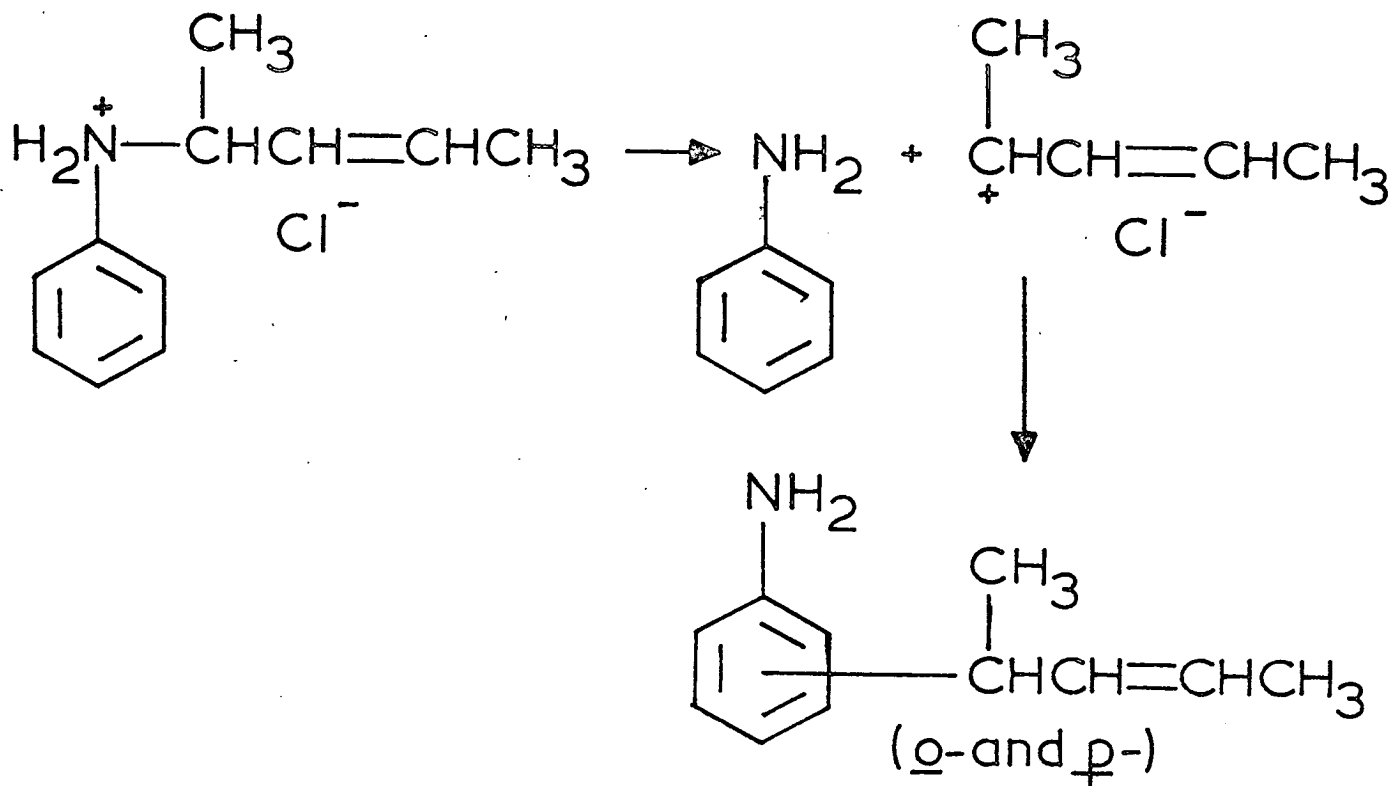
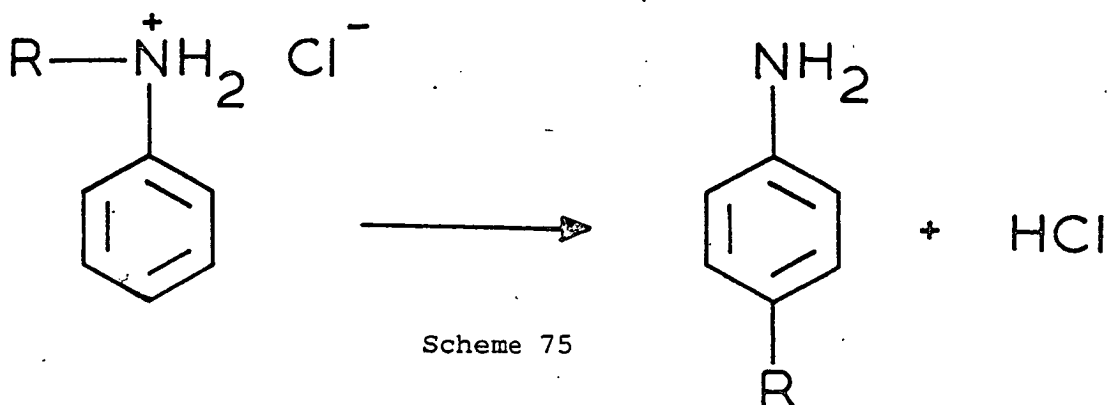


Scheme 74

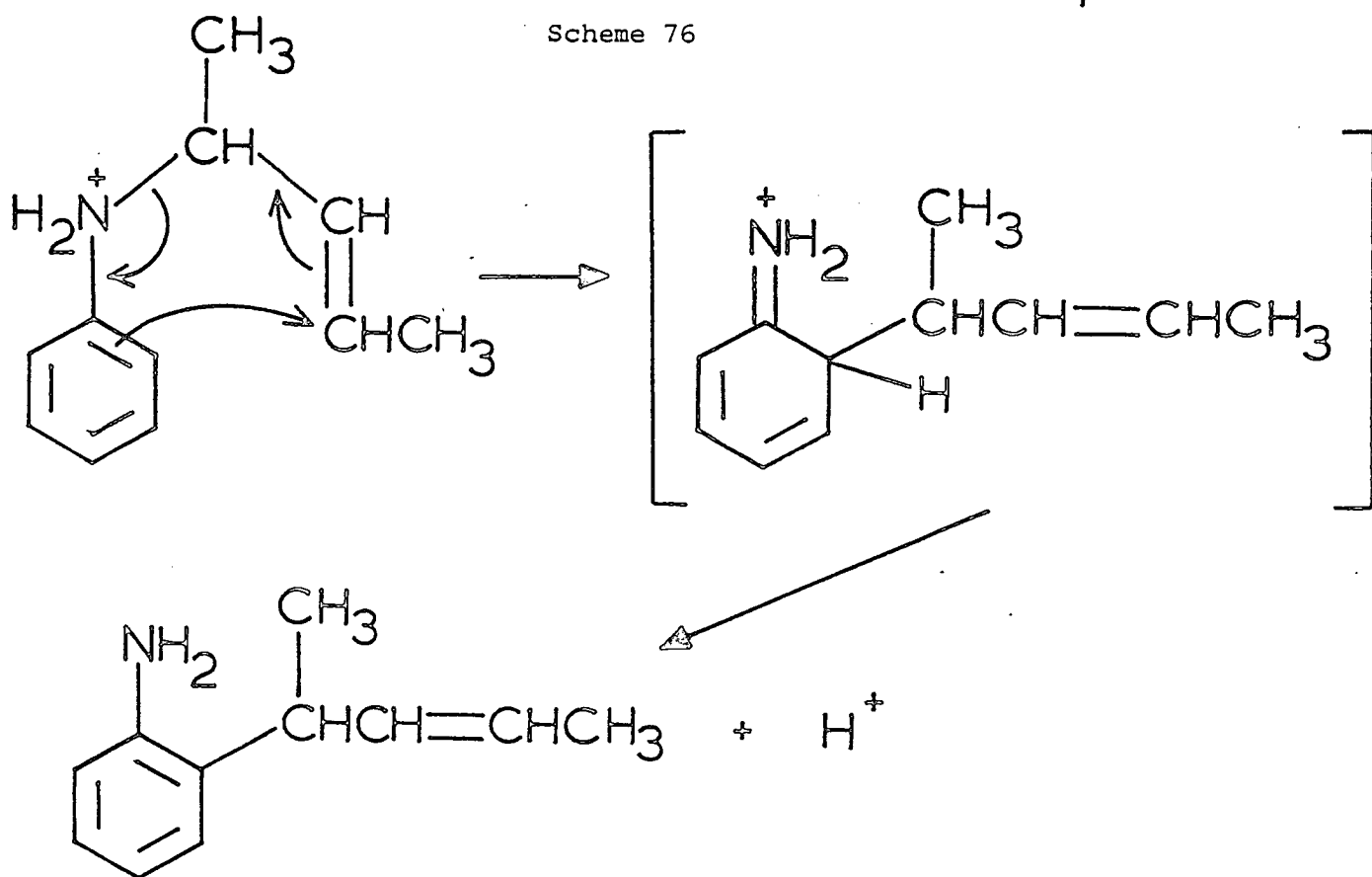
The recovery of acetanilide may be regarded as indicating that elimination from the chloride has occurred as shown in Scheme 70; alternatively, it may indicate that not all the acetanilide was present as its sodium salt in the alkylation process. The recovery of aniline from the hydrolysis of the alkylation product (from which almost all the acetanilide had been removed) suggests that the alkylation procedure gives rise to a product which is sensitive to removal of the introduced substituent under the conditions of acid-catalysed hydrolysis. An obvious explanation would be that alkylation takes place not only on nitrogen but also on oxygen to give the species (44) which may undergo hydrolysis as shown in Scheme 72. The O-alkylated species (44) could be formed either directly or by thermal rearrangement of the N-alkylated product (Scheme 73 - cf. Scheme 69). Support for the presence of both types of alkylation product came from the n.m.r. spectrum of the alkylation product: the appearance of the methyl region indicated the presence of two types of pent-3-en-2-yl substituent. (An alternative interpretation of the observed spectrum might be that the acetanilide derivative exists as a mixture of two conformers (45) and (46); a similar explanation for the observed n.m.r. spectrum of 2-formyl-1-phenylhydrazine has already been discussed - see p. 63).

The most obvious reason for the occurrence of O-alkylation is that it results in the formation of a sterically more stable species. However, reference to a space-filled model of N-(pent-3-en-2-yl)-acetanilide suggests that the molecule should not be particularly strained; certainly not significantly more than N-allylacetanilide which was successfully prepared and isolated in another context (Experimental p. 124).

Formation of aniline may also occur by dealkylation of the N-alkylated species during the hydrolysis procedure, and a possible



Scheme 76



Scheme 77

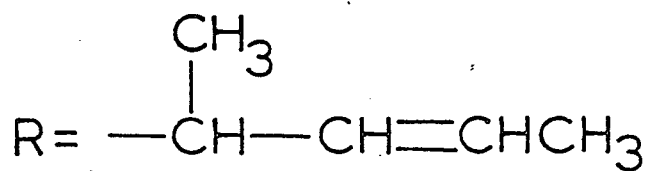
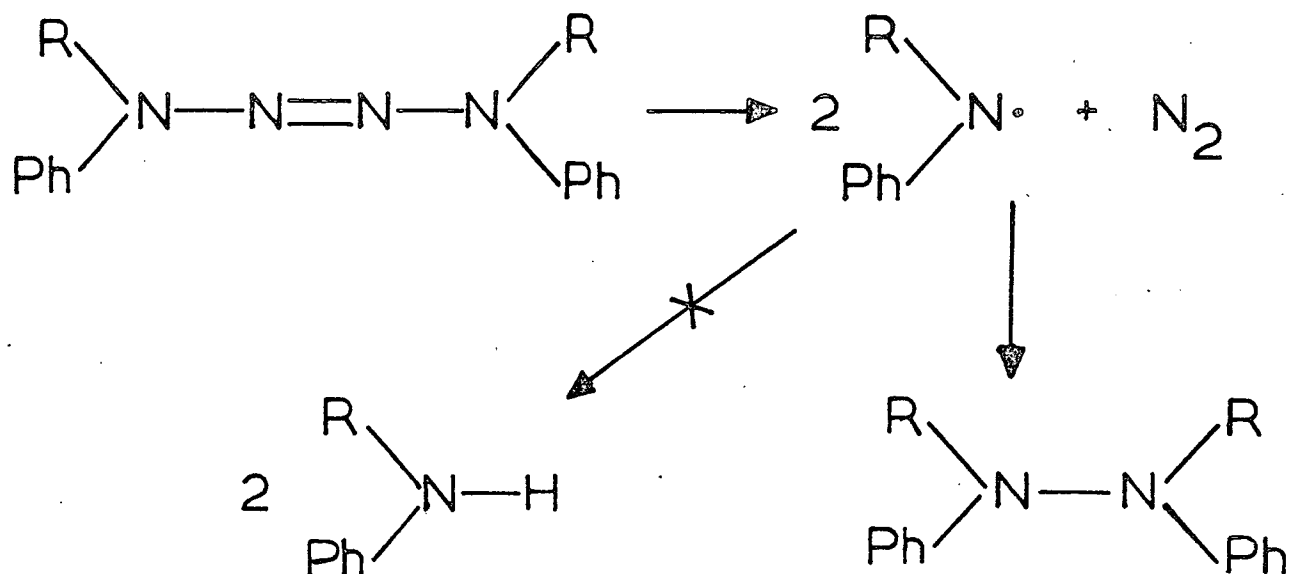
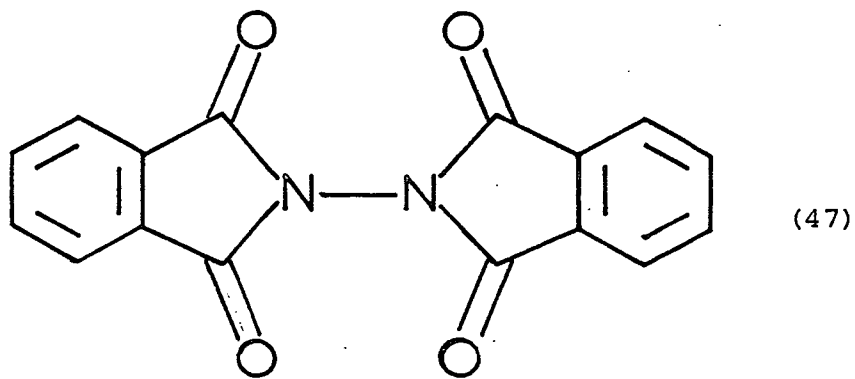
mechanism is suggested in Scheme 74; since the hydrolysis is carried out in an open system the volatile chloride would be lost so that re-alkylation would not occur. A possible pointer to the identity of the unidentified hydrolysis product was suggested by the reported behaviour of the hydrochlorides of N-alkylanilines at temperatures of 200-300°C. The reaction, known as the Hofmann-Martius reaction, involves the migration of an alkyl group onto the aromatic ring, and is known to occur intermolecularly (Scheme 75). For example, Ogata et al¹³² showed that N-methylaniline hydrobromide gave not only both the normal products, o- and p-toluidine, but also aniline and di- and trimethylanilines. When the alkyl substituent is primary, the reaction is thought to proceed with initial generation of the alkyl halide (cf. Scheme 74); when the substituent is secondary or tertiary the reaction may proceed via the carbonium ion rather than the alkyl halide.¹³³ In the present case, the latter mechanism would probably apply (Scheme 76). The nature of the pentenyl substituent may also allow migration to occur by intramolecular process as shown in Scheme 77. (The formation of the sterically favoured p-substituted species is also conceivable in terms of this mechanism).

In order to examine the likelihood that processes of the type shown in Schemes 74, 76, and 77 could occur as proposed in the acid-catalysed hydrolysis of N-(pent-3-en-2-yl)acetanilide, the behaviour of an authentic sample of N-(pent-3-en-2-yl)aniline (see below) under the same conditions as used in the hydrolysis process, was examined (Experimental p. 193). The n.m.r. spectrum of the product (75% recovery by weight) indicated that none of the starting amine remained: in overall appearance it was virtually identical to that of the product obtained from the hydrolysis of the alkylation product. The formation of aniline in both cases suggests that the mechanisms shown in Schemes 74 and 76 may apply. A contribution by the mechanism shown in Scheme 77, cannot however be ruled out.

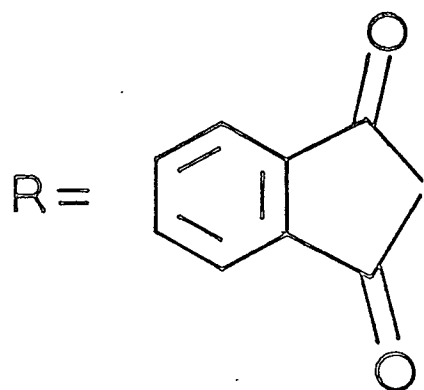
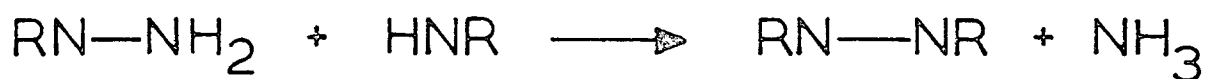
The preparation of N-(pent-3-en-2-yl)aniline was successfully accomplished by the direct alkylation of aniline with 2'-chloropent-3-ene (Experimental p. 192). Comparison of the n.m.r. spectrum of this material with that of the oxidation product from 1-(pent-3-en-2-yl)-1-phenylhydrazine indicated that the second component of that oxidation product was not N-(pent-3-en-2-yl)aniline. A control experiment showed that the amine was stable to the oxidation conditions.

The suggestion that 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine might be formed in the oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine was perhaps speculative inasmuch as the generation of such species during the oxidation of 1,1-disubstituted hydrazines has not been widely suggested. However, in view of the fact that the most widely applicable method of preparing tetrasubstituted hydrazines is by the thermal decomposition of the corresponding tetraz-2-enes (Scheme 78), it might reasonably be expected that these hydrazines could be formed by the decomposition of the tetrazene product from the oxidation of 1,1-disubstituted hydrazines. Although heating to 80°C and above is generally required to initiate decomposition, the possibility that the activation energy barrier could be lower in some instances can be envisaged. It was felt necessary to examine this possibility further, particularly as gas appeared to be evolved in several of the oxidation experiments. Furthermore, Hoesch and Dreiding⁴⁵ recently reported the isolation of N-phthalimidophthalimide (47) in 10% yield from the oxidation product of N-aminophthalimide; significantly however, a temperature of 145°C was required in order to produce a yield of this magnitude.

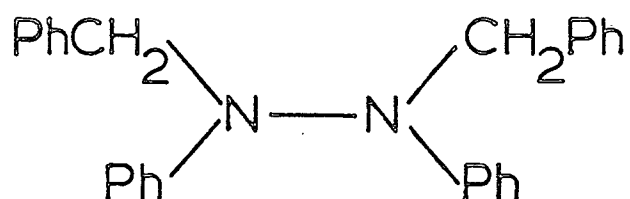
The thermal decomposition of tetrazenes is believed to proceed by a radical mechanism: pyrolysis or photolysis of tetramethyltetraz-2-ene gives nitrogen, tetramethylhydrazine, dimethylamine and a polymer of the imine, $\text{CH}_2=\text{NCH}_3$, and the formation of these species (excepting nitrogen of course) is interpreted in terms of the combination and disproportionation



Scheme 78

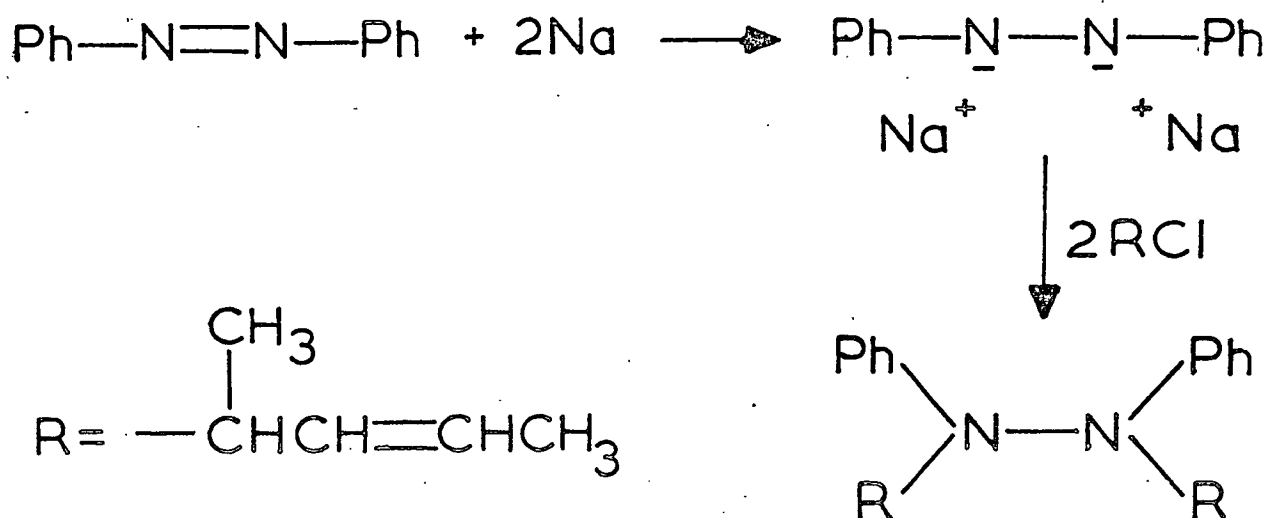


Scheme 79

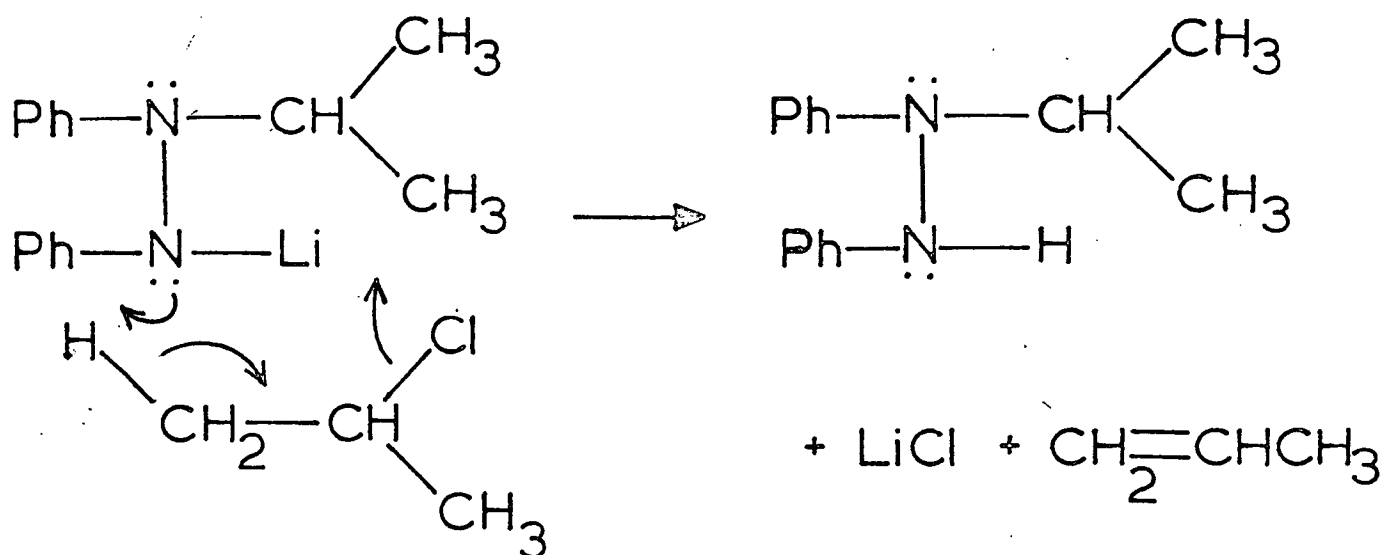


of dimethylamino radicals.¹³⁴ The possible formation of the tetra-substituted hydrazine in the present case may be envisaged as arising by the mechanism shown in Scheme 78 (cf. Scheme 71). The non-formation of N-(pent-3-en-2-yl)aniline (see p. 87) could be explained in terms of the operation of a solvent cage effect which favours the combination of the radical pair. (cf. Introduction p. 13, paragraph 1). The apparent absence of the products of radical disproportionation from the oxidation product is difficult to rationalise in terms of the mechanism of Scheme 78. Hoesch and Dreiding⁴⁵ (see preceding paragraph) have suggested that, while it is not implausible to suggest that tetrasubstituted hydrazines could be formed by a mechanism of the type shown in Scheme 78, an alternative mechanism involving reaction of the secondary amine with the parent 1,1-disubstituted hydrazine (Scheme 79) is also conceivable, and indeed they were able to obtain experimental evidence in favour of the latter proposal.

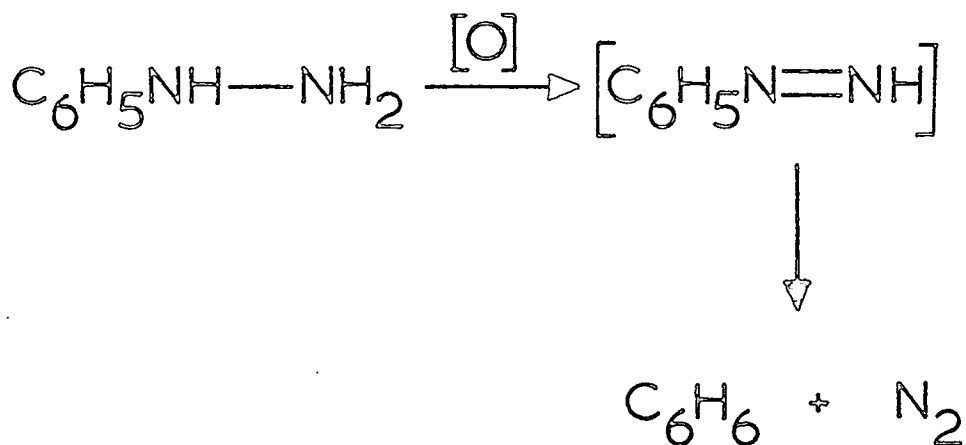
The first approach to an examination of the possibility that the second component of the oxidation product from 1-(pent-3-en-2-yl)-1-phenylhydrazine was 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine, was of an indirect nature. It was proposed to prepare an authentic sample of 1,2-dibenzyl-1,2-diphenylhydrazine (48) and to compare its n.m.r. spectrum with that of an authentic sample of phenylazotoluene (49): in this way it was hoped to ascertain whether or not the n.m.r. spectrum of the second oxidation product was consistent (in terms of the chemical shifts of corresponding protons in the second component and in 2-phenylazopent-3-ene) with the present suggestion. However, the attempted preparation of the tetrasubstituted hydrazine (48) by thermal decomposition of the corresponding tetrazene as reported by Frazen and Zimmerman¹³⁵ was found to give N-benzylaniline, and not the desired hydrazine (Experimental p.194).



Scheme 80



Scheme 81



Scheme 82

Attention was next turned to the preparation of an authentic sample of 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine. Two approaches were examined: firstly, oxidative coupling of N-(pent-3-en-2-yl)-aniline by adaptation of a reported method of preparing 1,1,2,2-tetraphenylhydrazine,¹³⁶ and secondly by alkylation of the di-anion of hydrazobenzene with 2-chloropent-3-ene. The first of these two approaches (Experimental p. 194) was unsuccessful and gave back the amine unchanged; the second approach was more successful. (Experimental p. 194).

Reesor and Wright¹³⁷ in 1957 reported the preparation of di-alkali metal adducts of azobenzene (formally the di-alkali metal salts of hydrazobenzene) and found that these adducts underwent alkylation with suitable alkylating agents. With primary alkyl halides they obtained high yields of the di-alkylated product, but with secondary halides (e.g. 2-chloropropane) the product of monoalkylation was isolated and only a 2% yield of the di-alkylated material was obtained in the most favourable case. While the formal similarity between the alkylating agent of the present example, 2-chloropent-3-ene, and 2-chloropropane was recognised, it was hoped that the desired tetrasubstituted hydrazine could be prepared by the sequence shown in Scheme 80:

The alkylation of the disodium adduct of azobenzene with 2-chloropent-3-^{ene} (1 mole : 2 mole) gave a mixture of products: t.l.c. examination revealed the presence of four components, one of which was shown to be azo-benzene. The work of Reesor and Wright¹³⁷ suggested that the products which might be expected from such an alkylation were azobenzene, the mono- and di-alkylated derivatives, and hydrazobenzene. The mass spectrum of the present alkylation product mixture showed peaks corresponding to the parent ions of each of these species.

The extent to which alkylation had occurred could be estimated from the integration of the n.m.r. spectrum of the alkylation product mixture: the integration ratio of aromatic protons to methyl protons was 5 : 2.9. The n.m.r. spectrum also appeared to support the possibility that the unidentified component of the oxidation product was 1,2-di(pent-3-en-2-yl) 1,2-diphenylhydrazine since the signals of the pent-3-en-2-yl group were observed in similar positions in the n.m.r. spectra of the alkylation and the oxidation product mixtures.

Reesor and Wright separated the mixtures of products which they obtained by careful wet column chromatography, first on silica gel to remove hydrazobenzene (if present), and then on alumina to separate the remaining components. In view of the specialised equipment required, it was felt that in the present case the product mixture could be more conveniently examined using high pressure liquid chromatography. Examination of the present alkylation product by h.p.l.c. revealed the presence of three major components one of which was shown to be

azobenzene. (The presence of two very minor components was also indicated.) Examination by t.l.c. (also on silica) had revealed the presence of four components only three of which were mobile. Reesor and Wright¹³⁷ showed that under similar conditions (i.e. silica gel/n-hexane) hydrazobenzene was immobile while azobenzene and the mono- and di-alkylated hydrazobenzenes could be eluted readily. Taken together with the mass spectral evidence cited above, this suggested that the stationary spot in the t.l.c. experiment was due to hydrazobenzene, and that the three peaks observed in the h.p.l.c. examination were due to azobenzene (confirmed) and the mono- and di-alkylated hydrazobenzenes. Surprisingly however, when the two last-mentioned components were isolated by preparative h.p.l.c., examination by mass spectrometry suggested that both were essentially the same material: both showed the peak corresponding to the parent ion of the mono-alkylated material (m/e 252) and a fragmentation peak (m/e 183; $P - 69$). Neither spectrum showed a peak at m/e 320 corresponding to the parent ion of the di-alkylated material, although the mass spectrum of the crude alkylation product did show this particular peak.

From this, it could be inferred that the two unidentified major components were not the mono- and the di-alkylated materials but hydrazobenzene and the mono-alkylated material. The mass spectra of the fractions obtained from the preparative h.p.l.c. experiment could be interpreted in these terms if it were assumed that less than total separation had been achieved: both spectra would be expected to display the peak at m/e 252, and the observation of a peak at m/e 183 could be interpreted as being due to loss of hydrogen from hydrazobenzene in one case and to loss of the pent-3-en-2-yl substituent from the mono-alkylated product in the other. The actual extent to which di-alkylation occurred may have been very small as the parent ion peak in the mass spectrum of the crude alkylation product was not very large. If this latter suggestion is correct then one of the two minor peaks observed in the h.p.l.c. chromatogram can be assigned to

1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine.

The rather inconclusive and unsatisfactory outcome of the approach described in the preceding paragraph was further complicated by the fact that a subsequent h.p.l.c. experiment suggested that both the present alkylation product and the oxidation product mixture obtained from 1-(pent-3-en-2-yl)-1-phenylhydrazine appeared to share a common component: a mixture of the oxidation and alkylation product mixtures gave a chromatogram having four significant peaks where, in the absence of a common component, five peaks would have been expected. However, this is probably fortuitous since it is unlikely that 1-(pent-3-en-2-yl)-1,2-diphenylhydrazine is one of the oxidation products from the oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine.

Thus the available evidence suggests that alkylation of the di-anion of hydrazobenzene with 2-chloropent-3-ene gives mainly azobenzene, hydrazobenzene and 1-(pent-3-en-2-yl)-1,2-diphenylhydrazine and only a very small amount of 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine. This result is not surprising in view of the fact that Reesor and Wright¹³⁷ found that alkylation of the di-lithium salt of hydrazobenzene with 2-chloropropane gave azobenzene (40%) and the mono-alkylated product (30%). They suggested that the mono-alkylated material was formed by the sequence of relatively rapid alkylation at N-1 followed by a slow replacement of lithium by hydrogen at N-2 as shown in Scheme 81. They suggested that di-alkylation did not occur because of the effect of the covalent character of the N-Li bond in accentuating steric hindrance in the transition state. [Rather surprisingly, alkylation with the more bulky t-butyl chloride was reported to give the di-alkylated product (21%) and hydrazobenzene (25%)]. In the present case, the operation of a mechanism of the type shown in Scheme 81 may be readily envisaged since elimination of the elements of hydrogen chloride from the alkylating agent would be a facile process (cf. Scheme 70).

The results of this attempt to prepare an authentic sample of 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine and to demonstrate its presence in the oxidation product of 1-(pent-3-en-2-yl)-1-phenylhydrazine can only be regarded as inconclusive. However, the fact that the tetra-substituted hydrazine was found to give a parent ion peak (m/e 320) in the mass spectrum of the crude alkylation product is significant since the mass spectrum of the oxidation product showed no peak at m/e 320. The presence of the hydrazine in the oxidation product therefore seems unlikely.

The possible formation of 2-phenylpent-3-ene (34) in the oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine (by extrusion of nitrogen either from 2-phenylazopent-3-ene or from the intermediate diazene) was not investigated. It is considered unlikely in view of the behaviour of the oxidation product on column chromatography (Experimental p. 182). Both components of the oxidation product required a considerable volume of solvent to effect their elution (still as an unresolved mixture), and it is felt that with the conditions used, elution of the hydrocarbon (if present) would have been achieved more rapidly.

CONCLUSIONS: Oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine with either mercuric oxide, lead tetra-acetate, or p-benzoquinone gives a mixture of two components, one of which has been shown to be the expected product, 2-phenylazopent-3-ene. Attempts to identify the second component eliminated two possibilities, namely pent-3-en-2-one phenylhydrazone and N-(pent-3-en-2-yl)aniline, but no firm conclusions could be drawn in respect of the other possibilities which were considered. These were, 2-phenylazo-cis-pent-3-ene, 1,4-di(pent-3-en-2-yl)-1,4-diphenyltetraz-2-ene, 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine, and 2-phenylpent-3-ene. Experimental evidence for and against the formation

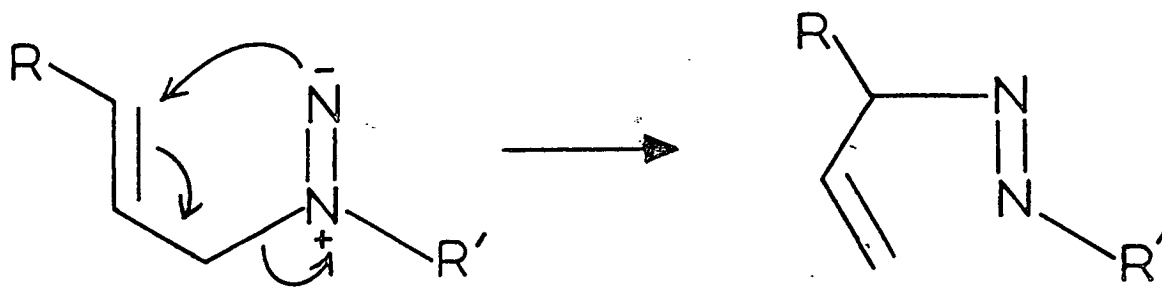
of each of these species has been presented, but, on balance it is felt that the case in favour of 2-phenylazo-cis-pent-3-ene is the strongest.

It will be remembered that the possibility was earlier investigated by a procedure of catalytic hydrogenation, but that, as a complex mixture of products was obtained, the outcome was inconclusive. Unlike the other possibilities which were inconclusively examined, no evidence has been found which undermines the present proposal. In particular the formulation is in accord with the mass spectrum which was observed for the oxidation product (no significant peak was observed above m/e 174 which corresponds to the parent ion of 2-phenylazopent-3-ene). Furthermore, the physical characteristics of the oxidation product (its colour and viscosity) are in accord with those expected of an azo-compound. Tetraz-2-enes are generally pale-yellow, viscous oils or solids (cf. Experimental p.160 and p.164) and tetrasubstituted hydrazines, of comparable molecular weight to the particular example proposed here, are solids (e.g. 1,1,2,2-tetraphenylhydrazine is a solid which melts at 149°C): if either of these species were present in the oxidation product to the extent of 43% as indicated by h.p.l.c., the oxidation product might reasonably be expected to be of a more viscous consistency. The observed evolution of gas during the initial stages of some of the oxidation experiments (to account for which the formation of the tetrasubstituted hydrazine according to Scheme 78 was proposed) may be explained in terms of the oxidation of small amounts of phenylhydrazine present in the samples of 1-(pent-3-en-2-yl)-1-phenylhydrazine as used (Scheme 82).

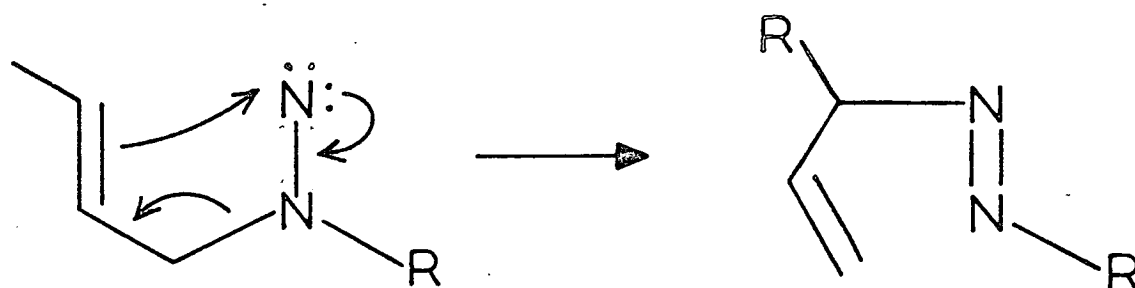
If this interpretation is correct, then the formation of a mixture of oxidation products (of the type inferred) from 1-(pent-3-en-2-yl)-1-phenylhydrazine will not affect the applicability of the proposed method

of examining the base-catalysed rearrangement of phenylazoalkanes to the corresponding phenylhydrazones. The success of the method will probably hinge on being able to reduce 2-phenylazopent-3-ene cleanly to the corresponding fully saturated hydrazine; further reduction to the secondary amine would complicate matters in that it would have to be removed, and its formation would represent wastage of the prepared optically active compound.

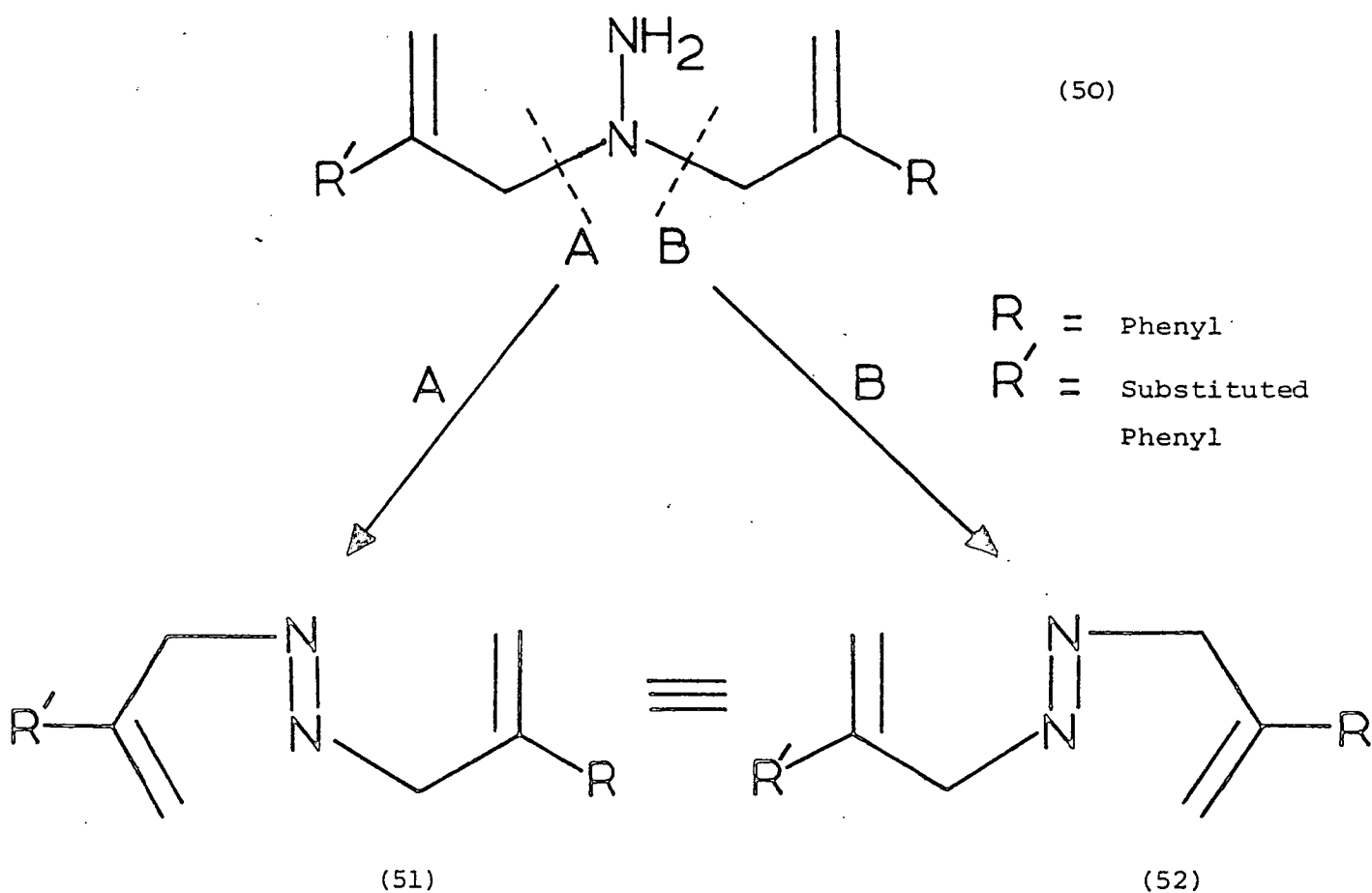
Hunter¹²⁶ showed that phenylazocyclohexane could be cleanly reduced by di-imide and it is conceivable that by using this mild reducing agent, the reduction of 2-phenylazopent-3-ene will be effected cleanly, and without the added complication of further reduction occurring. It is felt that the proposed approach to the preparation of an optically active phenylazoalkane (Scheme 61) merits further examination.



Scheme 16



Scheme 83

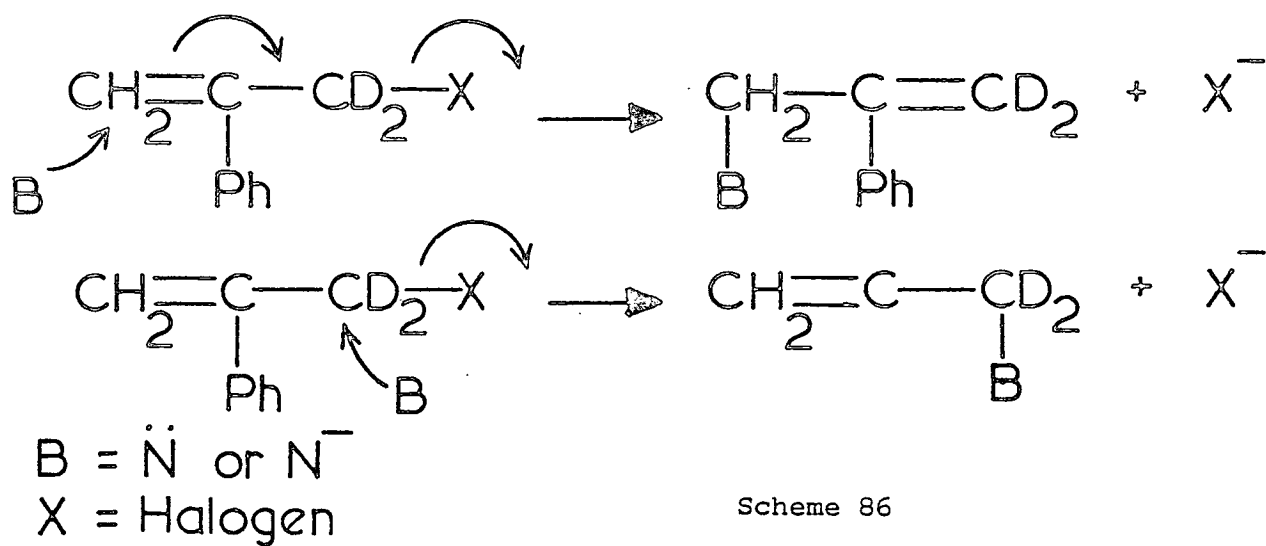
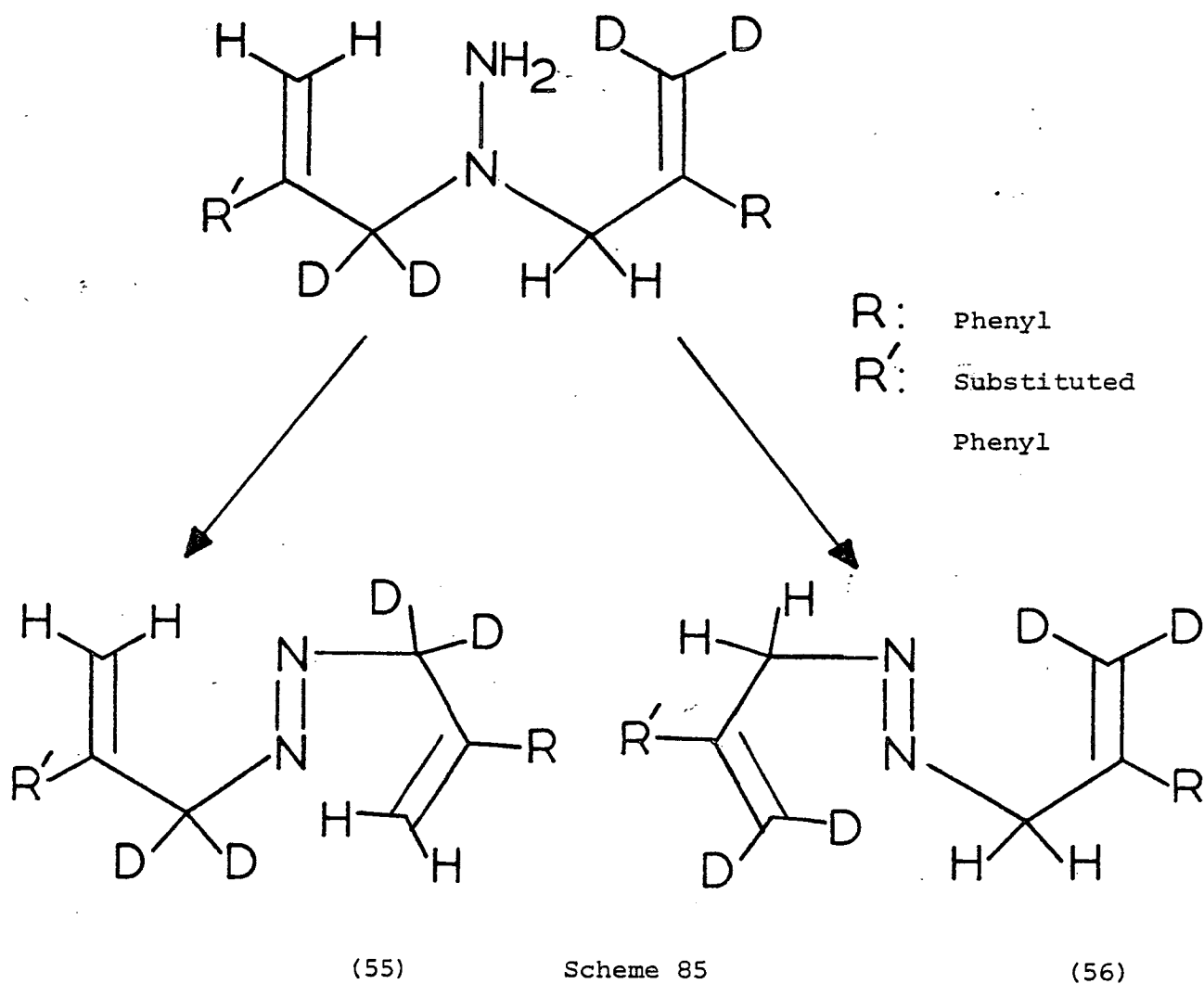
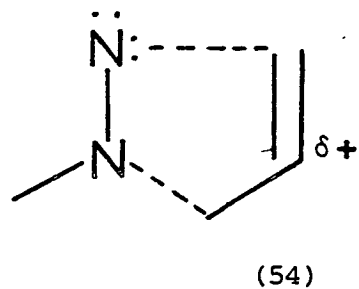
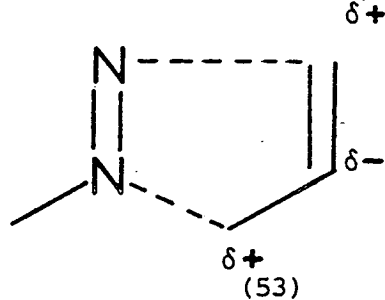


Scheme 84

Preliminary Investigation into a Method for Determining the Electronic Character of the Diazene Involved in the Oxidative Rearrangement of Allylic Hydrazines

As already mentioned, Baldwin⁶¹ has suggested that the rearrangement of allylic diazenes to give azo-compounds may be represented in terms of the concerted mechanism shown in Scheme 16. The evidence which supports the representation of the diazene as a dipolar species has been described already (Introduction p. 7). However, the rearrangement may also be interpreted in terms of the mechanism shown in Scheme 83, and indeed this is perhaps the more obvious one since diazenes are, by first principles, electron deficient species.

Although no evidence existed to suggest that the mechanism of Scheme 16 was inaccurate, it was hoped to develop an experimental method to test the proposal. The mechanism of Scheme 16 implies that as the electrophilic character of the allylic double bond increases, the rearrangement becomes more facile (all other factors remaining unchanged). It was proposed to test this inference by examining the oxidative rearrangement of a series of 1,1-di-allyl hydrazines of the general type (50), in which one of the R groups is held constant while the other is varied in such a way as to influence the character (electrophilic vs. nucleophilic) of the double bond of one of the substituents.

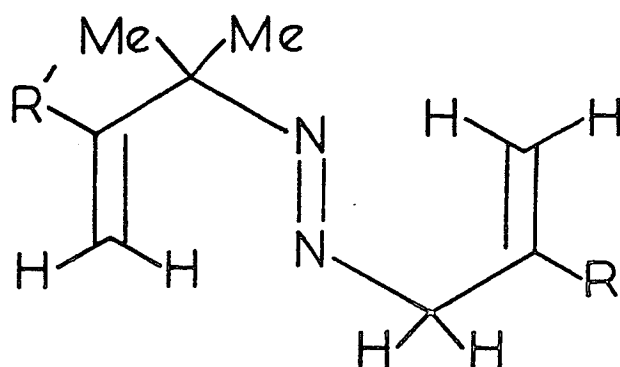


In this way, a situation of internal competition would be created since the diazene may attack (in principle at least) either of the allylic systems as indicated in Scheme 84. However, in the case of a hydrazine of the type (50) the product of attack at one allyl system (path A) is identical to the product of attack at the other allyl system (path B): the azo-compounds (51) and (52) are identical. In order to establish which mode of attack (i.e. path A or path B) predominates it is necessary that each of the possibilities give rise to a different azo-compound i.e. (51) and (52). This in turn requires that the di-allyl hydrazines of the type (50) be unsymmetrically labelled with for example deuterium.

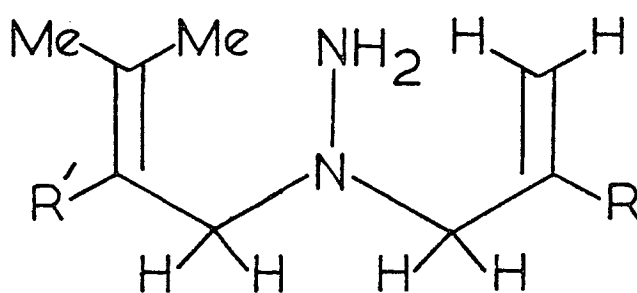
The two possible mechanisms under consideration are shown in Schemes 16 and 83. Although represented as concerted processes, bond cleavage and bond formation may not be synchronous, and, depending on the relative timing of each of the processes indicated by the arrows, the build-up of partial charge at specific centres may be envisaged. This situation (in the general case) is illustrated in (53) and (54), corresponding to Schemes 16 and 83 respectively. Representation in this way, allows prediction of the effect, on the course of the oxidative rearrangement (i.e. whether path A or path B is preferred), of varying one of the R groups in the hydrazines (50). If the mechanism of Scheme 16 operates then introduction of a group R which can stabilise the partial negative charge in (53) will be favourable, while if the mechanism of Scheme 83 operates introduction of such a group will be unfavourable (cf. 54). Thus, by measuring the relative amounts of the product azo-compounds (Scheme 84) and attempting to fit the data obtained to the Hammett equation, it was hoped to obtain evidence to support the mechanism of Scheme 16.

Since it was the aim of the study to examine the influence of electronic effects on the diazene rearrangement, it was important that, in labelling the hydrazines (50), no ambiguity be introduced into the interpretation of experimental observations by, for example, steric effects. For similar reasons, the siting of the R groups as shown (Scheme 84) rather than at the terminal end of the double bond was thus chosen to avoid introducing steric effects which might influence the course of the rearrangement. Furthermore, in view of the difficulties anticipated in attempting to isolate each of the product azo-compounds by physical methods (e.g. fractional distillation or column chromatography), it was proposed to carry out the product analysis by n.m.r. spectroscopy, and this required that the n.m.r. spectra of the azo-compounds (51)/(52) should be significantly different.

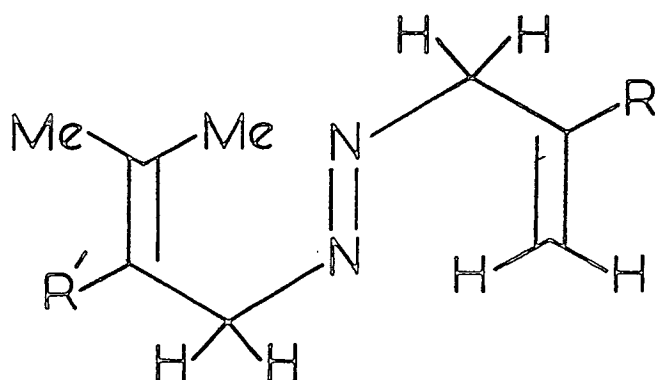
The most desirable method of meeting these two requirements was considered to be the use of deuterium-labelled hydrazines of the type shown in Scheme 85 since this should not introduce any new steric factors. Azo-compound (55), formed by migration of the R-allyl group would show signals in the olefinic region but not in the methylene region while azo-compound (56), formed by migration of the R'-allyl group would show signals in the methylene region, but not in the olefinic region: the relative amounts of (55) and (56) would then be expressed by the integration ratio of olefinic protons to methylene protons. However, it was anticipated that the preparation of the required hydrazines would not be easy. All the established methods of preparing 1,1-di-alkylhydrazines involve at least one alkylation step and with the type of alkylating agent envisaged here, the reaction can proceed in two directions as shown in Scheme 86. This would have the effect of scrambling the deuterium label, and this would complicate the interpretation of the oxidation results and possibly lead to erroneous conclusions. The preparation of pure samples of the labelled alkylating agents would be quite another problem.



(59)



(57)



(58)

R = Phenyl

R = Substituted
Phenyl

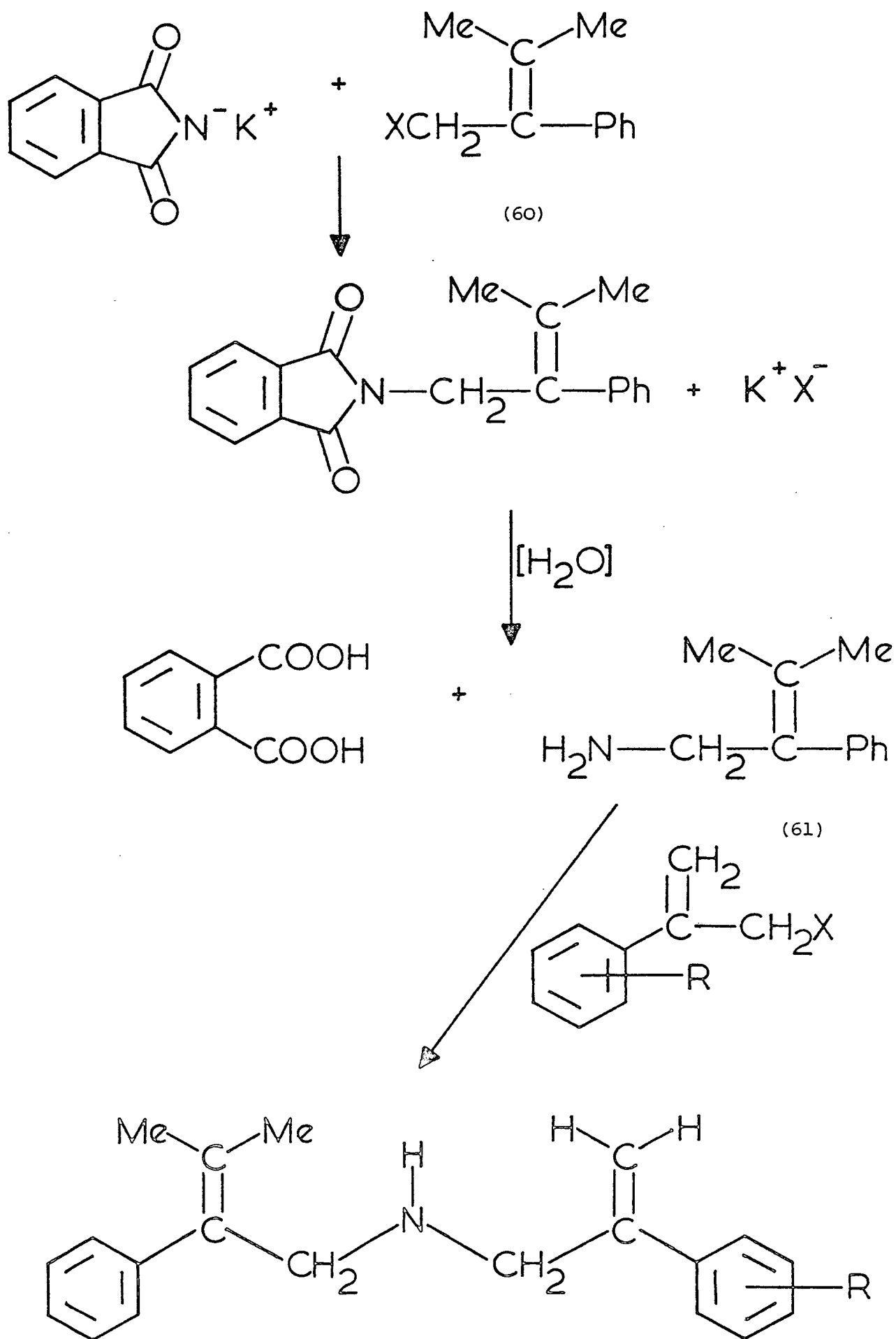
In the face of these considerable problems it was decided, as a compromise, to examine the oxidation of a series of hydrazines of the type (57) as shown in Scheme 87. It was hoped that analysis of the oxidation product could be achieved by calculating the integration ratio of the two types of methyl signals: those of (58) and those of (59) expected in the n.m.r. spectrum of the oxidation product. This approach was very much a compromise since it is conceivable that the methyl substituents might introduce an element of steric control on the course of the oxidative rearrangement.

In view of the reported thermal lability of azo-compounds analogous to those anticipated in the present case,⁶¹ it was felt that preliminary work was required in order to establish that azo-compounds of the type expected would in fact be isolable. Furthermore, an examination of the synthesis and use of the necessary alkylating agents was required.

It was hoped to prepare the necessary series of hydrazines (57) by N-amination of the corresponding secondary amines or by reduction of the N-nitroso derivative of the same amine. Both approaches would require the secondary amines and it was envisaged that these could be prepared by the method of Scheme 88. The preparation of the necessary alkylating agents was first examined.

α -(Bromomethyl)styrene and α -(chloromethyl)styrene were prepared by direct halogenation of α -methylstyrene with N-bromo- and N-chlorosuccinimide respectively, and it was envisaged that the necessary ring-substituted alkylating agents could be prepared in analogous fashion from the corresponding styrene derivatives. α -(Chloromethyl)styrene was also successfully prepared by dehydration of the carbinol obtained from the reaction of phenylmagnesium bromide with chloro-acetone.

The possibility of extending the use of this latter method to the preparation of α -bromomethyl- β,β -dimethylstyrene seemed attractive in

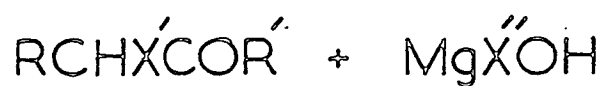
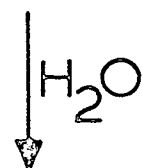
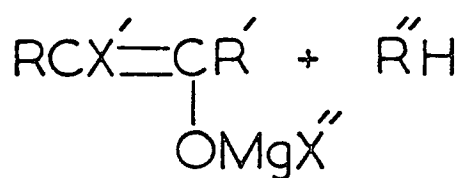
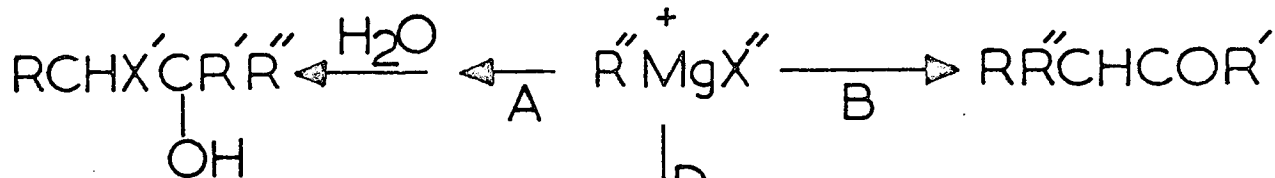
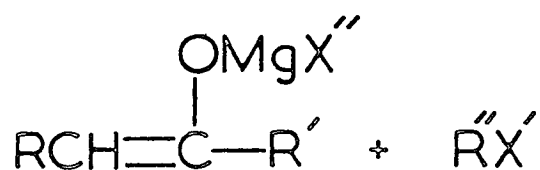
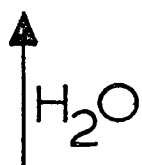
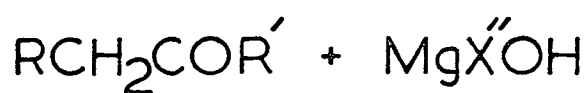


Scheme 88

that the necessary reagents, α -bromo-acetophenone and 2-bromopropane (from which the Grignard reagent would be prepared), were readily available. However when the method was adapted to the preparation of α -bromomethylstyrene (of which an authentic sample had been prepared - see above), examination of the Grignard addition product by infra-red and n.m.r. spectroscopy indicated that it was a complex mixture of products. The infra-red spectrum showed absorptions in the O-H and carbonyl regions; however, the n.m.r. spectrum indicated that no α -bromo-acetophenone was present. The reaction was repeated at low temperature and some of the reaction mixture was worked-up before heating. As before, complex mixtures of products were obtained, and the same O-H and C=O absorptions were observed in the infra-red spectra. Weak signals attributable to α -(bromomethyl)styrene were observed in the n.m.r. spectrum of the product obtained from the portion which was worked-up without heating.

The attempted preparation of α -bromomethyl- β,β -dimethylstyrene (60; X = Br) by addition of the Grignard reagent to α -bromo-acetophenone gave a complex mixture of products. Even with the modified procedures described in the previous paragraph, the reaction product was equally complex, and t.l.c. examination of one particular product mixture showed the presence of at least four components. The only indication as to the nature of the several products came from the infra-red spectra which all showed similar absorptions in the O-H and the carbonyl regions. Evidence from n.m.r. spectroscopy suggested that the products of the low temperature reaction contained an appreciable amount of α -bromo-acetophenone.

Reference to the literature suggests that the clean reaction of chloro-acetone with phenylmagnesium bromide (see above) is an exception to the general tendency for the reaction of α -halo-ketones to give complex mixtures of products. Kharasch and Reinmuth¹³⁸ report that

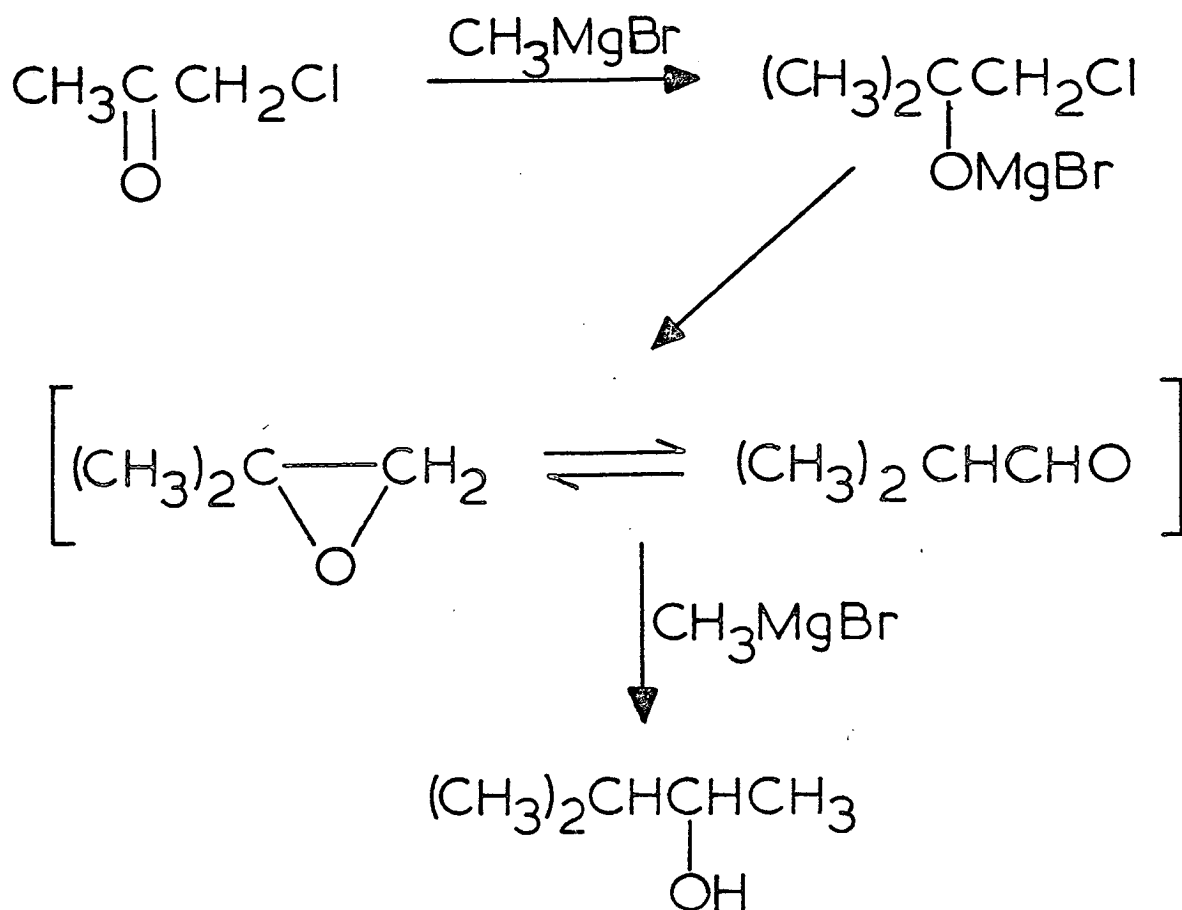


Scheme 89

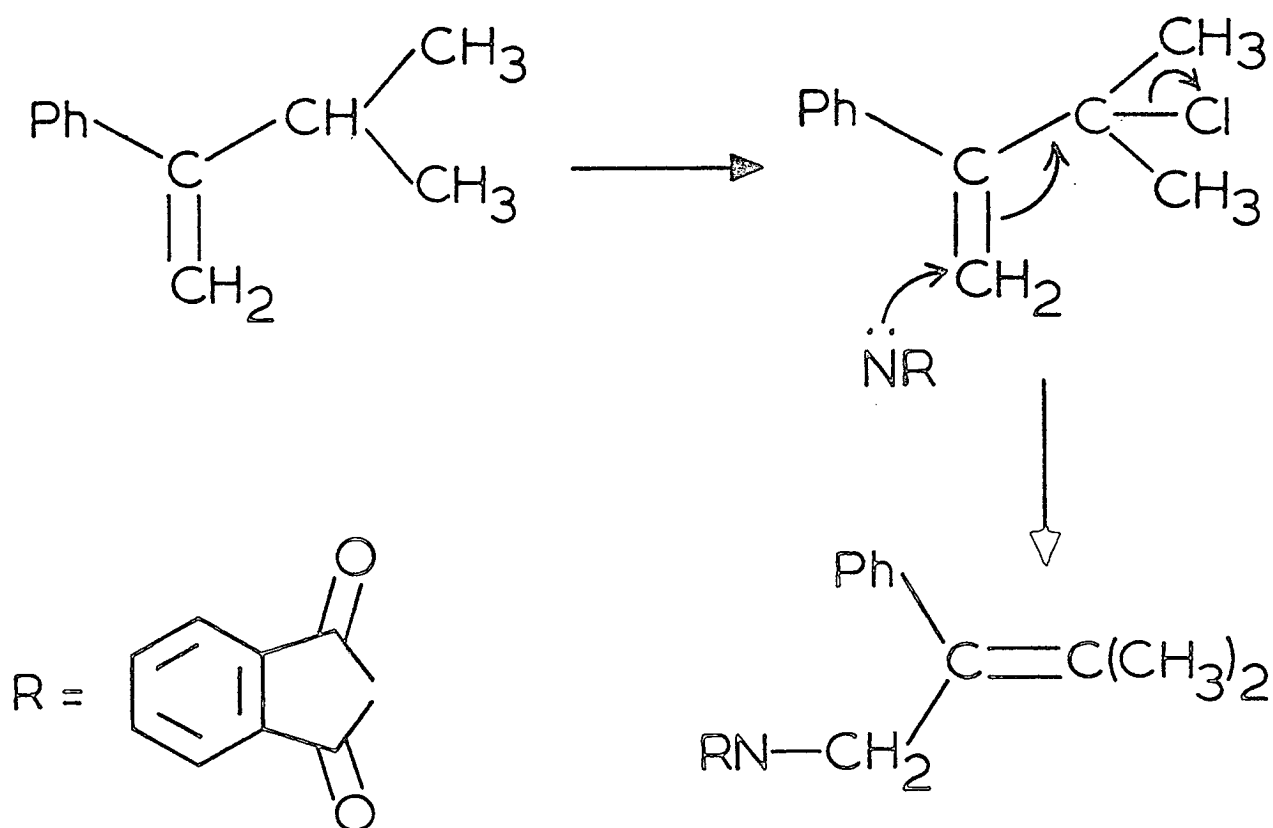
the reaction of saturated α -halo-ketones with Grignard reagents can follow four possible pathways as shown in Scheme 89. These authors suggest that path A (the 'normal' pathway) is followed when there is no significant steric hindrance in the ketone and when the magnesium alkoxide intermediate is stable to the reaction conditions involved. Thus, the observation that the reaction of phenylmagnesium bromide with chloro-acetone gives the carbinol as the only significant product might be interpreted as indicating that there is no steric hindrance. Conversely, the apparently complex course followed by the reaction of Grignard reagents with α -bromo-acetophenone, may be ascribed to the introduction of steric hindrance by the bulky phenyl group and bromine atom. The reaction of phenylmagnesium bromide with chloro-acetone has been shown¹³⁹ to follow path B (Scheme 89) at 130-140°C. Furthermore, the possibility of reaction of the ketone derived from path B with the Grignard reagent may also be envisaged. Henry¹⁴⁰ reported the isolation of the carbinol formed from the addition of two moles of methylmagnesium bromide to chloro-acetone; he proposed the intermediacy of an epoxide as shown in Scheme 90.

The possibility of preparing the desired alkylating agent, α -bromomethyl- β , β -dimethylstyrene, by carrying out the appropriate Wittig-type reaction on α -bromo-acetophenone was not examined.

It was hoped that the required secondary amine (61; Scheme 88) could be prepared by the alternative approach shown in Scheme 91. It was envisaged that attack at the terminal olefinic carbon might be preferred for steric reasons to attack at the carbon atom bearing the chlorine atom. The successful use of N-chlorosuccinimide in the preparation of α -(chloromethyl)styrene made the use of this chlorinating agent attractive for the preparation of the alkylating agent, α -(2-chloroprop-2-yl)styrene, required here. However, in practice (Experimental p. 204), the chlorination



Scheme 90



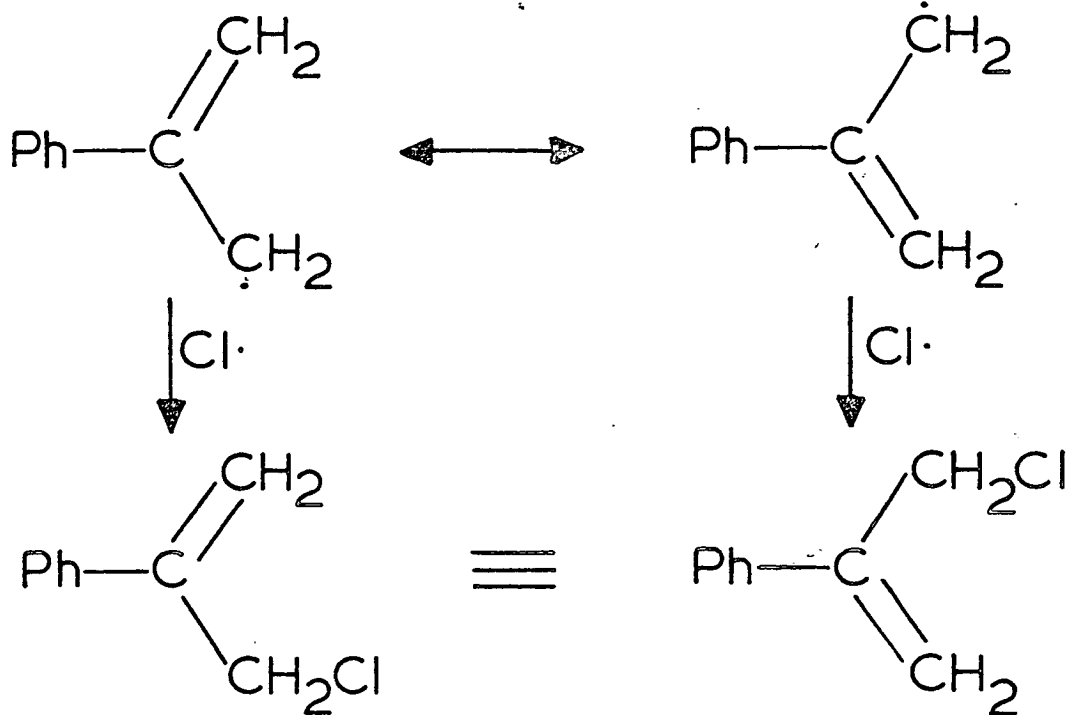
Scheme 91

procedure gave four products. (Unreacted α -prop-2-ylstyrene was also recovered as expected). Attempts to separate the components by fractional distillation were unsuccessful. The complexity of the chlorination product compared to the case of α -methylstyrene may be ascribed in part to the fact that in the case of α -prop-2-ylstyrene the intermediate allyl radical is unsymmetrical so that two different products are obtained where only one is possible in the case of α -methylstyrene; the contrasting situations are illustrated in Schemes 92 and 93. Chlorination of α -methylstyrene with N-chlorosuccinimide gives not only α -(chloromethyl)styrene but also α -methyl- β -chlorostyrene which is probably derived from a rearrangement of the initially formed α -chloromethylstyrene. Clearly, such a process is also possible in the present case: one of the initially formed chlorides (62; Scheme 93) can rearrange to give the isomeric chloride (63) as shown in Scheme 93. Evidence in support of this suggestion was supplied by the fact that the n.m.r. spectrum of the chlorination product showed signals attributable to an aliphatic methine proton in a prop-2-yl group besides that due to the corresponding proton of α -prop-2-ylstyrene. The possibility of the formation of dichloro-derivatives may also be envisaged since the monochloro-compounds (62) and (63) still have allylic hydrogen atoms.

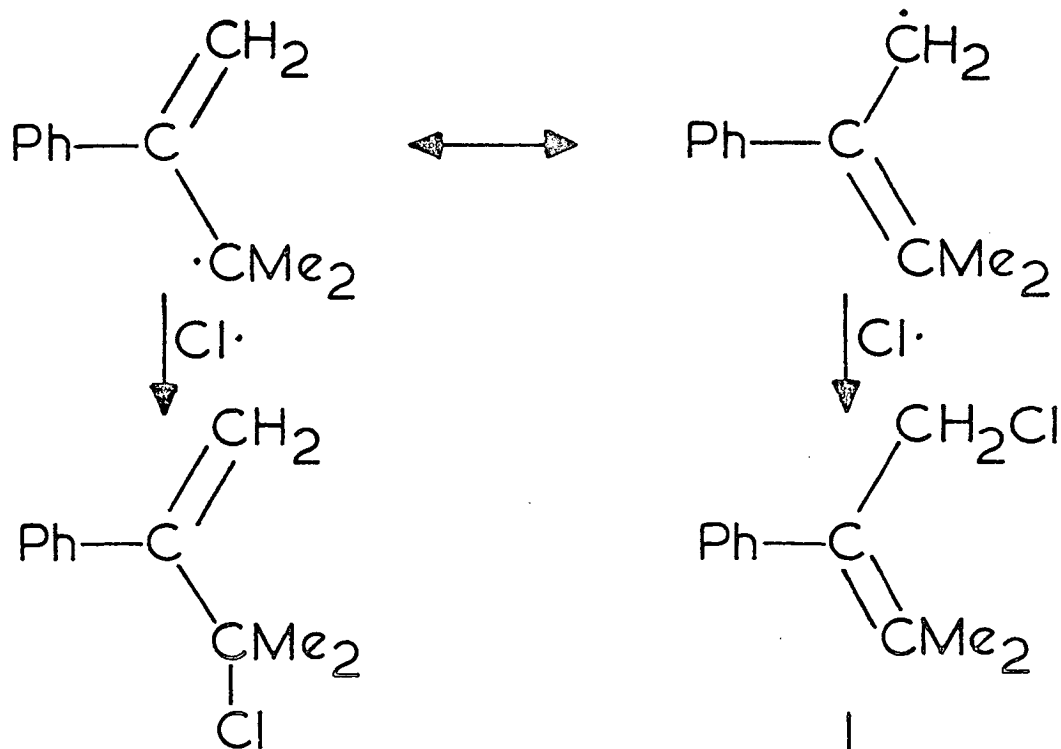
A brief, but unsuccessful investigation was made into the possibility of effecting chlorination using t-butylhypochlorite.

While the attempts to prepare α -bromomethyl- β,β -dimethylstyrene and α -(2-chloroprop-2-yl)styrene were in progress, the behaviour of α -(bromomethyl)styrene and α -(chloromethyl)styrene in several alkylation reactions, was being examined.

The attempted alkylation of phthalimide with α -(bromomethyl)styrene (cf. Scheme 91) gave phthalimide and α -(bromomethyl)styrene as the only identifiable products.

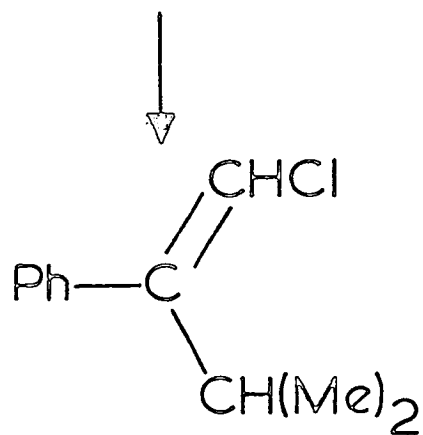


Scheme 92

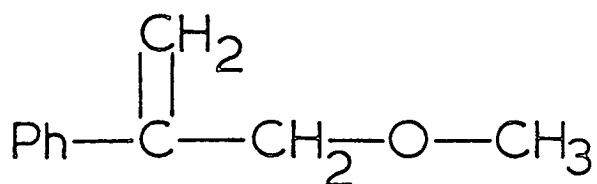


(62)

Scheme 93



(63)



(64)

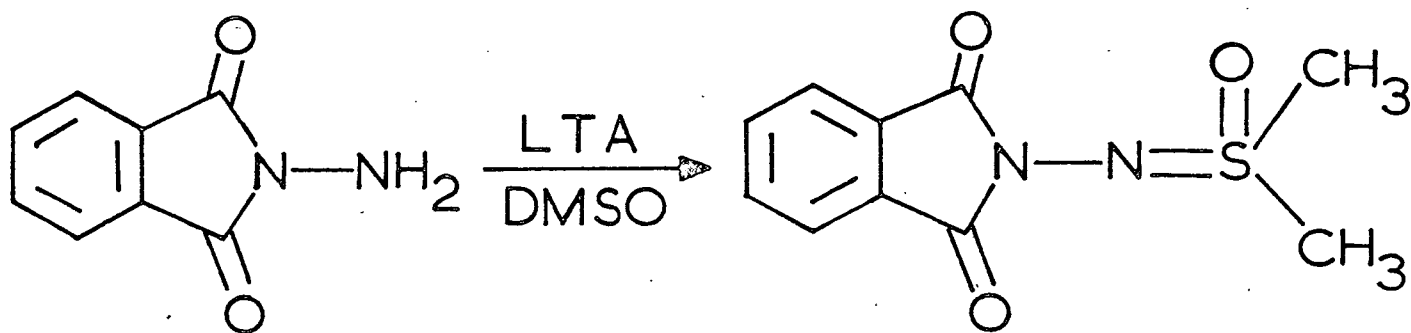
The alkylation of t-butyl carbazate with α -(chloromethyl)styrene and with α -(bromomethyl)styrene was examined in the context of preparing azo-compounds of the type shown in Scheme 84 (see p. 97): oxidative rearrangement of the hydrazines obtained by this method would give the desired azo-compounds. However, while the alkylation of t-butyl carbazate with allyl bromide was found to give the expected product, t-butyl-2-di-allylcarbazate, in 32% yield (after purification), the use of α -chloro- and α -(bromo-methyl)styrene as alkylating agents gave no detectable amount of the desired material. Instead, complex mixtures of products were obtained, and in the case of alkylation with the chloro-compound, examination of the product by t.l.c. indicated the presence of at least four components. A significant feature of this last-mentioned alkylation was that the protecting group appeared to participate in the reaction: by monitoring the course of the reaction by n.m.r. spectroscopy, it was found that the singlet signal due to the t-butyl group disappeared, and was replaced by a multiplet in the same region of the spectrum; the signals due to the olefinic and methylene protons of the chloride also disappeared.

In a further attempt to prepare azo-compounds of the type shown in Scheme 84, the alkylation of the di-sodium salt of di-ethyl hydrazo dicarboxylate with α -(chloromethyl)styrene was attempted. This alkylation procedure was part of a synthetic sequence for the preparation of azo-compound originally by Al-Sader and Crawford.⁸⁰ These authors reported the alkylation of the di-sodium salt with allyl benzenesulphonate to give the di-allyl analogue of the present example. (This work was successfully repeated - Experimental p.217). However, when the alkylation with α -(chloromethyl)-styrene was examined under three different sets of conditions, the most favourable outcome was a mixture of mono- and di-alkylated material.

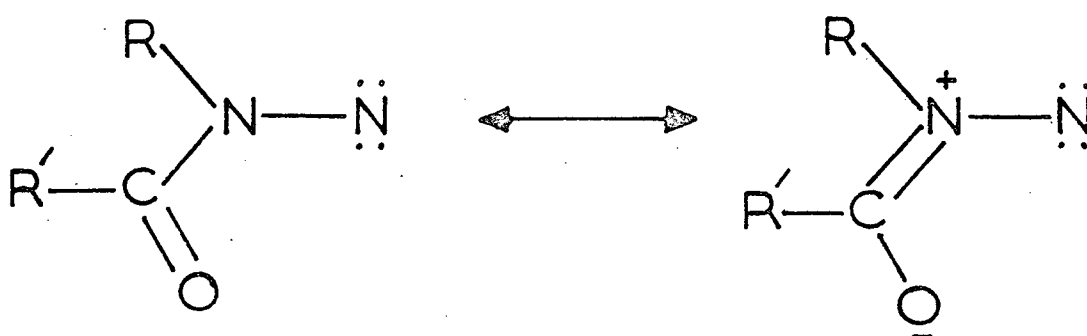
The hydrolysis and decarboxylation of the ~~alkylation~~ product proved appreciably more difficult and less efficient than the original authors had suggested⁸⁰: after subjecting the alkylation product to the hydrolysis and decarboxylation procedure for a period twelve times as long as that used by Al-Sader and Crawford⁸⁰ for the di-allyl case, only a small amount of a yellow liquid was obtained. This material was found not to contain nitrogen, and showed no absorption above ν 3100 cm^{-1} in the infra-red spectrum. The n.m.r. spectrum of the liquid showed the signals expected for the 2-phenylprop-2-en-1-yl group but no exchangeable hydrogen was found. The mass spectrum showed a significant peak at m/e 148 and 147 but no peak at m/e 292 (expected for the di-alkylated product) and the material could be recovered unchanged from mercuric oxide oxidation. In accord with the observed mass spectrum, and the other observations, the product was tentatively formulated as being α -(methoxymethyl)styrene (64).

The alkylation of the di-sodium salt of di-ethylhydrazodicarboxylate with allyl chloride was examined in an attempt to resolve the apparently anomalous course of the alkylation with α -(chloromethyl)styrene. It was found that while alkylation with allyl benzenesulphonate (see above) gave the expected product in high yield, the reaction with allyl chloride was much slower, and a mixture of unreacted, mono-, and di-alkylated di-ethylhydrazodicarboxylate was obtained. Hydrolysis and decarboxylation of an authentic sample of the di-allyl substrate was found to be very inefficient but no product analogous to α -(methoxymethyl)styrene (see previous paragraph) was detected.

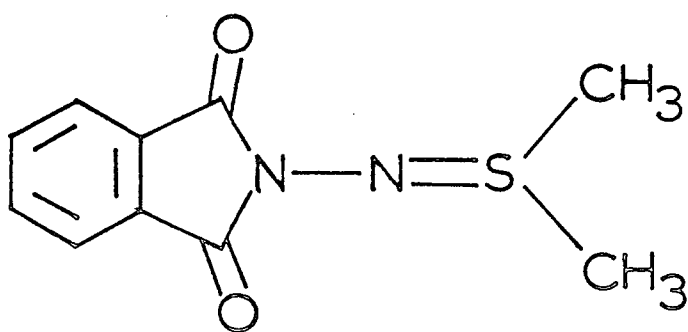
These trial experiments indicated that the preparation of the hydrazines and of authentic samples of the anticipated product azo-compounds required for the study set out at the beginning of this section would be difficult, if not impossible, at least in terms of the procedures described above. No attempt was made to develop alternative methods, and the proposed experimental scheme (Scheme 87) was not examined further.



Scheme 94



Scheme 95



(65)

The Attempted Interception of 1-Alkyl-1-Phenyldiazenes by Dimethyl Sulphoxide, and by Dimethyl Sulphide.

The interception of diazenes by dimethyl sulphoxide to give the sulfoximide adducts was first reported by Rees and his co-workers.¹⁴¹ Since that time many reports of successful trappings of diazenes have appeared, a common feature being the nature of the diazenes involved: the diazenes all carry acyl substituents, the only exception known to the present author being (3-methylindazol-2-yl)diazene. A typical example of diazene interception, the formation of S,S-dimethyl-N-phthalimidodisulfoximide, is represented in Scheme 94. Sulfoximide formation has a dual significance in that the isolation of these adducts is often interpreted as demonstrating the intermediacy of diazenes, and furthermore, the sulfoximides themselves may be used as diazene sources, since they undergo both thermal and photolytic fragmentation to give back the diazene and dimethyl sulphoxide.

The interest in the preparation of sulfoximides in the present study was primarily in their use as diazene sources, and the possible verification of diazene intermediacy in the particular oxidations studied, was regarded as an added bonus. It was hoped that by regenerating the diazenes by photolysis of dilute solutions of the sulfoximides, it would be possible to produce sufficiently low concentrations of the diazenes that the bimolecular reaction pathway (i.e. tetrazene formation) would be effectively eliminated, thereby favouring the rearrangement or decomposition pathway. No examples of the trapping of simple dialkyl- or arylalkyldiazene are known; the procedure outlined by Rees and his co-workers³³ for the preparation of the sulfoximide derivatives of N-amino-lactams was therefore used. (Experimental p.218). The hydrazines which were examined in this connection were 1-allyl-1-

phenylhydrazine, and 1-benzyl-1-phenylhydrazine, and it was anticipated that the successful formation of the sulfoximides would be readily revealed by n.m.r. spectroscopic examination of the reaction product (Rees and his co-workers³³ reported that for S,S-dimethyl-N-naphthalimid.sulphoximide, the methyl proton resonances were observed as a singlet at δ 3.36 p.p.m.).

The lead tetra-acetate oxidation of 1-allyl-1-phenylhydrazine in the presence of excess dimethyl sulphoxide gave an orange-brown liquid, the n.m.r. spectrum of which indicated that the oxidation had followed its normal course to give 1-phenylazoprop-2-ene; no signals attributable to the expected sulfoximide were observed. Dry column chromatography revealed the presence of four components, the major, and only identifiable one being 1-phenylazoprop-2-ene.

The oxidation of 1-benzyl-1-phenylhydrazine in analogous fashion gave a gum from which was recovered a pale brown solid. This solid was shown to be 1,4-dibenzyl-1,4-diphenyltetraz-2-ene by its melting point and n.m.r. spectrum. No trace of the desired sulfoximide adduct could be found by n.m.r. spectroscopy. The oxidation was repeated and in an attempt to inhibit tetrazene formation conditions of high dilution were used; furthermore, the modification of inverse addition (i.e. the addition of the hydrazine to a solution of one equivalent of dimethyl sulphoxide and lead tetra-acetate in methylene chloride) as suggested by Rees and his co-workers,³³ was used. However, the n.m.r. spectrum of the product was found to be virtually identical to that of the product of the previous attempt. No signals attributable to the desired species were observed.

The failure of these attempts to prepare sulfoximide adducts is perhaps not surprising in view of the absence of any reports of the preparation of sulfoximide derivatives of simple 1,1-arylalkyldiazenes. Adduct formation by the acyl-type diazenes may be attributed to the effect of the electron-accepting substituent: delocalisation of the lone pair of the central nitrogen atom resulting in polarisation of the C-N bond as shown in Scheme 95, has the effect of increasing the electrophilicity of the terminal nitrogen atom, so favouring attack by the nucleophilic sulfoxide. The results of theoretical calculations on a number of simple diazenes support the view that electron-withdrawing substituents reduce the nucleophilic nature (and consequently increase the electrophilic nature) of the diazene (Introduction p. 7).³⁹

Failure to effect interception of the diazenes should not be construed as denying their intermediacy in these oxidations. The possibility that the sulfoximides were in fact formed but decomposed under the conditions of the reaction to regenerate the diazenes was not examined as the work of Rees and his co-workers³³ suggested that the adducts were stable enough to survive recrystallisation from ethanol and indeed temperatures of 400-500°C were required to induce thermal fragmentation.

The possibility of isolating the sulphilimide adducts of the diazenes by performing the hydrazine oxidations in the presence of dimethyl sulphide followed from a suggestion by Gilchrist.¹⁴² The procedure employed paralleled that used for the attempted preparation of the sulfoximides.

Oxidation of 1-allyl-1-phenylhydrazine with lead tetra-acetate at 0°C in the presence of three equivalents of dimethyl sulphide gave an orange brown liquid which was shown by n.m.r. spectroscopy to be 1-phenylazoprop-2-ene.

Oxidation of 1-benzyl-1-phenylhydrazine in similar fashion gave an orange-brown solid which was shown to be 1,4-dibenzyl-1,4-diphenyltetraz-2-ene. The n.m.r. spectrum of the product also showed the presence of a very small amount of impurity giving rise to a doublet at δ 2.18 p.p.m.

Subsequent to these attempts to isolate sulphilimide adducts, two reports of the preparation of the sulphilimide (65) have appeared. Gilchrist and his co-workers¹⁴³ report its preparation by the reaction of N-aminophthalimide with N-chlorosuccinimide in the presence of dimethyl sulphide at -25°C , and Jones¹⁴⁴ cites the unpublished observation of Gilchrist et al that the sulphilimide (65) can be prepared by the oxidation of the hydrazine with lead tetra-acetate at -75°C in the presence of dimethyl sulphide. The methyl proton resonances in the n.m.r. spectrum of the adduct (a solid m.p. $133-134^{\circ}\text{C}$) are observed as a singlet at δ 2.67 p.p.m. The doublet signal observed at δ 2.18 p.p.m. in the n.m.r. spectrum of the oxidation product of 1-benzyl-1-phenylhydrazine in the presence of dimethyl sulphide (above) is unlikely to be due to the desired sulphilimide.

It is significant that the only sulphilimide to have been prepared in this way is derived from a diazene which is also known to form a sulphoximide. The failure of the present attempts to isolate the sulphilimide adducts of arylalkyldiazenes may be ascribed to the low electrophilicity of these diazenes compared to diazenes of the acyl-type. While there was a significant temperature difference between the method reported here and conditions quoted by Gilchrist and his co-workers¹⁴³ and by Jones,¹⁴⁴ it is unlikely that this alone accounts for the failure to isolate the desired compounds; this possibility was not examined, however, and cannot be excluded.

The Attempted Preparation of Copper (I) Complexes of 1-Alkyl-1-Phenyldiazenes

Whereas the attempted preparation of the sulphoximide and sulphilimide adducts of the 1-alkyl-1-phenyldiazenes was undertaken with a view to preparing derivatives from which the diazenes could be conveniently regenerated, the attempted diazene-complex formation now described was carried out more as a matter of interest than as a means of generating the diazenes under desirable conditions.

In 1975 Boehm et al³⁵ reported the oxidation of 1,1-dimethylhydrazine in acid solution at 0°C with cupric chloride, and the isolation of a complex of 1,1-dimethyldiazene having the formula $[(CH_3)_2N=N]_2Cu_3Cl_3$. The complex was shown to be diamagnetic, and was characterised by elemental analysis and infra-red spectroscopy. By successively treating the complex with hydrochloric acid and ammonia solution, these workers obtained a 33% yield of 1,1,4,4-tetramethyl-tetraz-2-ene. Furthermore, they found that when they treated a solution of the complex in acid with a solution of 1,1-diethyldiazenium ions and then basified the mixture, they obtained a mixture of the symmetrically substituted, and the mixed tetrazenes in an almost statistical distribution.

Boehm et al interpreted these findings as being indicative of the presence of 1,1-dimethyldiazene rather than that of its formal dimer, 1,1,4,4-tetramethyl-tetraz-2-ene, in the parent complex. The tetrazene is known to be acid labile and they concluded that it could not survive the acidic conditions involved and was therefore not present in the complex; the formation of a crossed-tetrazene product paralleled the results of McBride and Bens¹⁰ (Introduction p. 3) who showed that the same type of experiment with two different diazenium ion solutions (prepared by potassium bromate oxidation of the corresponding hydrazines)

gave a mixture with a statistical distribution of the three possible tetrazenes.

The possibility that it was 1,1-dimethylhydrazine and not 1,1-dimethyldiazene which was present in the complex was ruled out by the failure of the complex to exhibit an absorption above ν 3050 cm^{-1} , the region where, by comparison with the spectra of monosubstituted diazene-cuprous halide complexes and cuprous halide complexes of hydrazines, an N-H stretching vibration would occur.

It was therefore concluded that the complex contained 1,1-dimethyldiazene and not the corresponding hydrazine or tetrazene, and that the diazene was stabilised in some way by co-ordination to copper, probably via interaction of the terminal nitrogen atom with one or two cuprous ions. The low solubility of the complex was seen as indicative of the presence of some type of polymeric CuCl network.

Prior to examining the oxidation of 1-allyl-1-phenylhydrazine and 1-benzyl-1-phenylhydrazine with cupric chloride, the oxidation of 1,1-dimethylhydrazine according to the procedure of Boehm et al³⁵ was examined. The oxidation was found to proceed exactly as had been described, and the product was obtained as a deep-purple solid. The infra-red spectrum of this material was in complete agreement with the reported data, and in particular, the absence of an N-H absorption was confirmed. Successive treatment of the purple solid with 6 M hydrochloric acid and 15 M aqueous ammonia gave 1,1,4,4-tetramethyltetraz-2-ene (25%) which was identified by comparison with an authentic sample. A control experiment showed that the tetrazene was completely destroyed when treated with 6 M hydrochloric acid.

The complex was examined by mass spectrometry but little in the way of meaningful information was obtained using this technique. The mass spectrum was recorded at 80°, 100°, 140° and 160°C but no parent peak

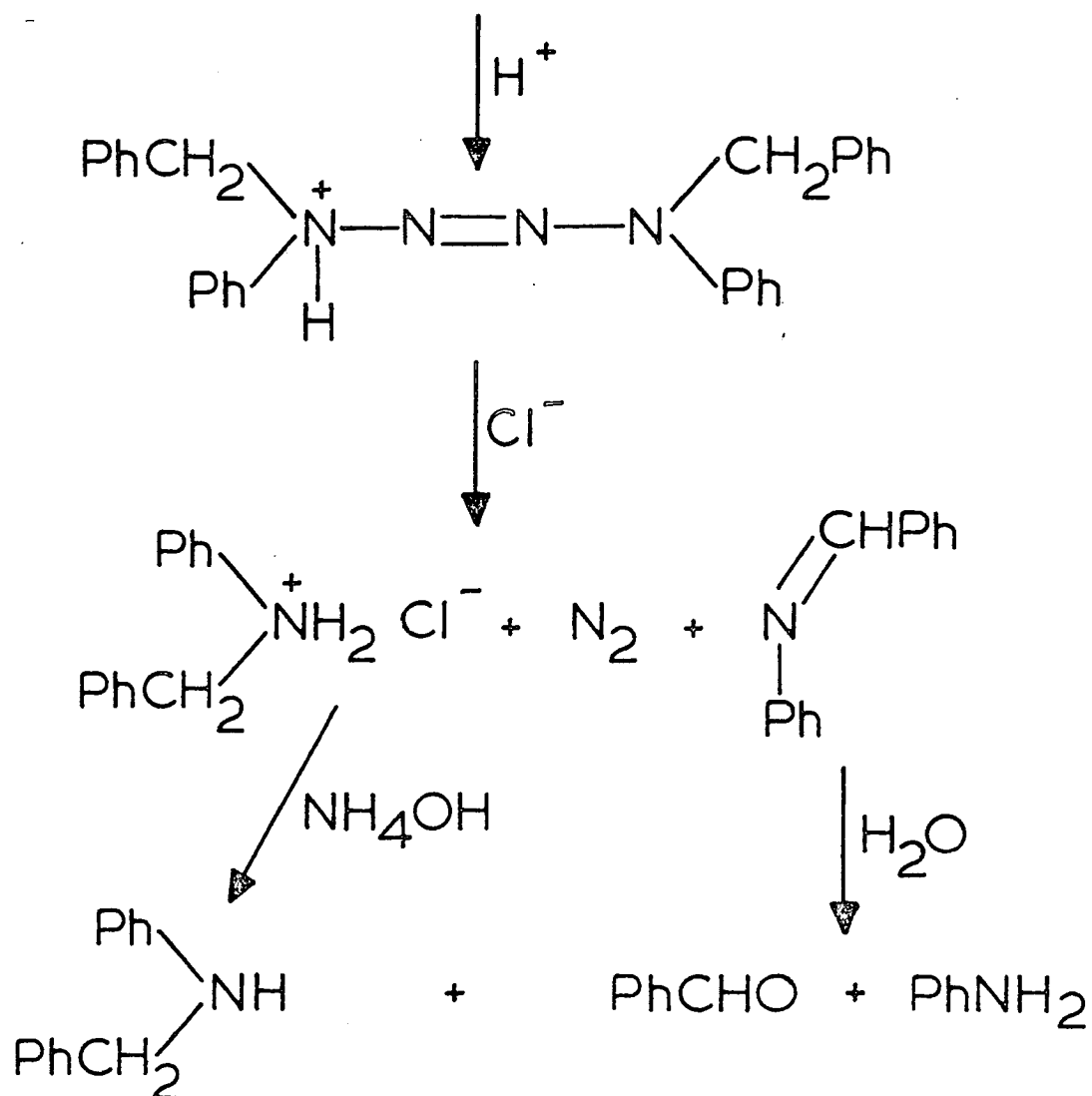
(m/e 413 for the formula proposed by Boehm et al) was observed. The heaviest ion observed had m/e 226 (P-187) which might correspond to loss of both diazene functions and two chlorine atoms from the parent ion. The spectrum at 100°C had a base peak of m/e 116, and this peak was also observed at 80°C and 140°C. The significance of this peak lies in the fact that it corresponds to the parent peak of tetramethyl tetrazene, whose possible presence in the parent complex, Boehm et al had ruled out on the basis of the sensitivity of the tetrazene to acid, and because they were able to obtain the mixed tetrazene by treating an acid solution of the complex with a solution of diethyldiazenium ion (vide infra). In this experiment they used a 1:1 mole ratio of reactants and obtained a mixture of tetramethyltetraz-2-ene, 1,1-di-ethyl-4,4-dimethyltetraz-2-ene and tetra-ethyltetraz-2-ene in the ratio of 1:2.4:1.4; the expected statistical distribution of products being 1:2:1. This departure from the theoretical product distribution is significant in that analysis of the 1:2.4:1.4 ratio in terms of the mole ratios of dimethyldiazene fragments to di-ethyldiazene fragments shows that the latter predominate in the ratio of 5.2:4.4. From this it may be inferred (assuming that conditions are equally favourable to the formation and isolation of both symmetrical tetrazenes), that the complex yields less than the predicted amount of dimethyldiazene. A possible explanation, which finds support in the observation of a peak at m/e 116 in the mass spectrum of Boehm's complex, is that oxidation of 1,1-dimethylhydrazine with cupric chloride gives rise to a complex containing tetramethyltetrazene as ligand, as well as the diazene complex; a complex containing tetramethyltetrazene as the only ligand could not give rise to the mixed tetrazene on treatment with di-ethyldiazenium ion. It is, however, equally conceivable that the apparent presence of tetramethyltetrazene in the complex, might instead be due to dimerisation of the diazene in the spectrometer; an alternative explanation for the results of the cross-coupling experiment would then be required.

The oxidation of 1-allyl-1-phenylhydrazine and 1-benzyl-1-phenylhydrazine with cupric chloride was carried out by a procedure analogous to that outlined by Boehm et al in the case of 1,1-dimethylhydrazine.

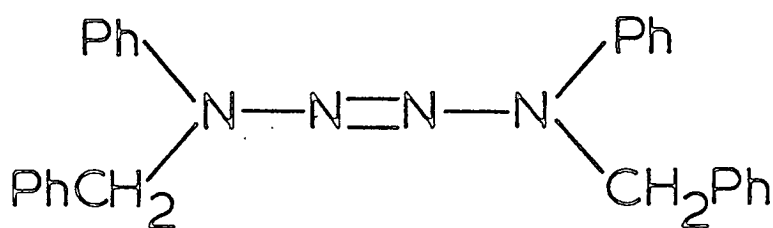
Oxidation of 1-benzyl-1-phenylhydrazine gave a mustard-brown powder which was examined after minimal exposure to the atmosphere. (After standing for several months in a sealed container, the brown solid had decomposed to give a moist brown cake of material which smelled strongly of benzaldehyde.) The mass spectrum of this material showed a parent peak at m/e 364 and the mass spectrum as a whole very closely resembled that of 1,4-dibenzyl-1,4-diphenyltetraz-2-ene - all the corresponding fragmentation peaks were observed. As in the case of the complex derived from 1,1-dimethylhydrazine, the infra-red spectrum of the brown solid showed no absorption in the N-H region. The presence of copper was confirmed by heating a sample of the material in an ignition tube: a film of copper formed on the walls of the tube.

Decomposition of this copper-containing material by the successive treatment with hydrochloric acid and ammonia solution at 0°C was hampered by its very low solubility in acid; the undissolved material was removed by filtration to give a brown residue with the characteristic odour of benzaldehyde. The filtrate was basified to pH 10 and was repeatedly extracted with ether; concentration of these combined extracts gave a red-brown gum which smelled strongly of benzaldehyde. The n.m.r. spectrum of this material suggested the presence of benzaldehyde, N-benzylaniline and 1,4-dibenzyl-1,4-diphenyltetraz-2-ene, and this was confirmed by adding a sample of each in turn to the solution: no new signals appeared, and the expected signal enhancements were observed. Several spurious weak signals were also observed in the range δ 4.0-5.0 p.p.m., and t.l.c. indicated the presence of six components. Four of these were shown to be common to the product of treating a chloroform solution of

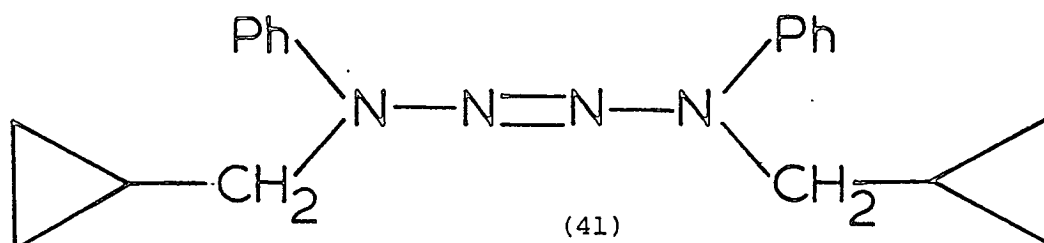
Copper containing
Oxidation Product



Scheme 96



(43)



(41)

1,4-dibenzyl-1,4-diphenyltetrazene with hydrochloric acid of the same strength as that used in the decomposition of the copper-containing material. A possible pathway leading to the observed products is illustrated in Scheme 96.

The mass spectral evidence, and the nature of the decomposition products of the oxidation adduct are compatible with the formulation of the copper-containing material in terms of either the diazene or the tetrazene, or both.

Oxidation of 1-allyl-1-phenylhydrazine by an analogous procedure gave a rust-brown powder which was examined immediately. (The material was found to decompose readily, and after standing for several weeks in a sealed container only a solid, brown mass remained). The presence of copper was again demonstrated by heating a sample of the material in an ignition tube. The mass spectrum of the copper-containing material was recorded at 70°, 150° and 150 + °C. Weak peaks were observed at m/e 334 (Expected parent peak suggested by the formulation of Boehm et al, m/e 589) in the 150+°C spectrum and at m/e 292 in the lower temperature spectra, but the highest significant peak in each of the mass spectra had m/e 264. Both these last-mentioned peaks are consistent with the presence of 1,4-di-allyl-1,4-diphenyltetraz-2-ene (P and P-N₂ respectively). More intense than any of these peaks, however, were those at m/e 148 and 146 which cannot be readily accounted for in terms of fragmentation of the tetrazene although, without reference to the mass spectrum of the authentic compound, the possibility cannot be ruled out. These peaks are consistent with 1-allyl-1-phenylhydrazine and 1-phenylazoprop-2-ene (or its hydrazone tautomer) respectively; the mass spectra of the tetrazenes (41) and (43) do not show peaks attributable to the corresponding hydrazines and azo-compounds. Alternatively, m/e 146 is consistent with the molecular formula of 1-allyl-1-phenyldiazene. The observation

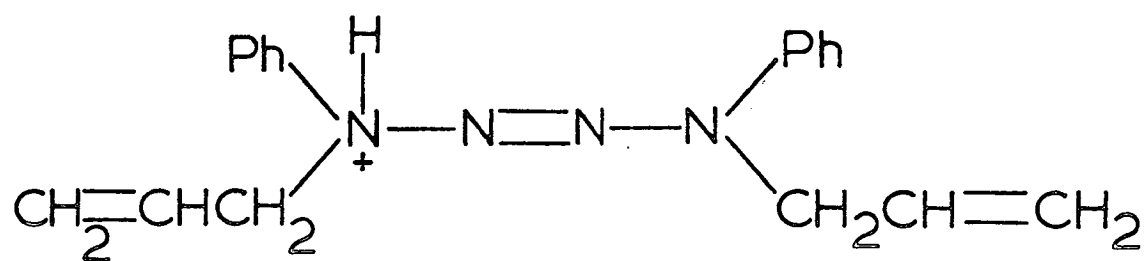
of a peak at m/e 133 (consistent with the molecular ion of N-allylaniline) might be seen as suggesting the presence of N-allylaniline; however, the mass spectra of the tetrazenes (41) and (43) show peaks attributable to the corresponding secondary amines. At 150°C , significant peaks were observed at m/e 107 and 108. These peaks were also observed in the mass spectra of 1-alkyl-1-phenylhydrazines and their hydrochlorides; the significant peak exhibited by tetrazenes in this region had m/e 106.

The mass spectrum of the copper-containing oxidation product of 1-allyl-1-phenylhydrazine could therefore be interpreted as indicating the presence of any, or all, of 1,4-di-allyl-1,4-diphenyltetraz-2-ene, 1-allyl-1-phenylhydrazine, 1-phenylazoprop-2-ene and 1-allyl-1-phenyl-diazene. The infra-red spectrum of this material showed a significant absorption in the N-H region at ν 3250 cm^{-1} . The copper content, estimated by iodometric titration according to the method of Rezintskaya and Burtzeva,¹⁴⁵ was found to be $23.5 \pm 0.03\%$: a complex analogous to that proposed by Boehm et al for the case of 1,1-dimethyl-hydrazine would contain 32% of copper.

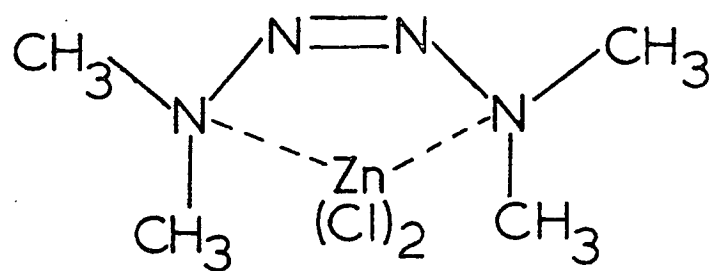
Decomposition of the copper-containing material was again carried out at 0°C by basification of an acid solution of the material. The product was recovered as a brown oil whose n.m.r. spectrum showed two sets of signals attributable to the allylic protons of the allyl group ($\text{CH}_2=\text{CH}-\underline{\text{CH}_2}-$). The position of one set at δ 3.7 p.p.m. suggested the presence of N-allylaniline (Experimental p. 124). The position of the second set at δ 3.95 p.p.m. suggested the presence of 1-allyl-1-phenylhydrazine, (Experimental p. 131) but the spectrum of the olefinic region did not support this; ^{the} signals were attributed to 1,4-di-allyl-1,4-diphenyltetraz-2-ene. No signals attributable to 1-phenylazoprop-2-ene were observed. Thin layer chromatography showed the presence of four components, and dry column chromatography on alumina gave five

overlapping bands. Each of these bands was isolated and the material recovered from each was examined by n.m.r. spectroscopy. Four of the bands gave trace amounts of red-brown gums, while the fifth gave a mobile red-brown liquid whose n.m.r. spectrum resembled that of the material before chromatography in that it showed the signals of N-allylaniline and the corresponding tetrazene, the former being by far the major component; before chromatography, the latter predominated. Several spurious weak signals were also observed. The infra-red spectrum of this liquid closely resembled that of N-allylaniline, but showed a second weak N-H absorption at ν 3315 cm^{-1} . Examination of the liquid by t.l.c. supported the presence of N-allylaniline. Repeated column chromatography of this material, using a short column to enable rapid elution, gave the same series of overlapping bands as had been observed in the original column. The principal band (i.e. the same band as had previously given the major product), which was eluted with carbon tetrachloride, was collected and this solution was immediately examined by n.m.r. spectroscopy. The n.m.r. spectrum was found to be virtually identical to that of the material prior to re-chromatography indicating that the original liquid contained at least one species which underwent extensive decomposition on the column.

The nature of the decomposition products of the copper-containing material, based on mass spectral data, allows certain of the proposals as to the nature of the material to be eliminated. The possible presence of 1-allyl-1-phenylhydrazine is unlikely; the conditions of decomposition of the complex would be expected to lead to the liberation of the free hydrazine, but this was not detected by n.m.r. spectroscopy. Furthermore, Beohm et al state that cuprous-hydrazine complexes are white but the complex isolated in this case was a uniform brown colour. The possibility of a complex containing 1-phenylazoprop-2-ene is also unlikely since no



(66)



(67)

signals attributable to this species were observed in the n.m.r. spectrum of the decomposition product; cuprous complexes of azo-compounds (usually red-brown solids) are known to regenerate the azo-compounds by thermolysis or by treatment with aqueous hydroxide.¹⁴⁶ The possibility of a complex containing N-allylaniline is conceivable, but the m/e (133) peak observed in the mass spectrum of the copper-containing material could also be derived from the tetrazene (vide supra). The most generally consistent proposal is that the copper-containing oxidation adduct contains either the tetrazene, or the diazene, or both, as ligand. The observation of an N-H absorption at ν 3250 cm^{-1} may possibly be ascribed to the protonated form of the tetrazene (66) or perhaps to the presence of N-allylaniline.

CONCLUSION:

The most convincing evidence cited by Boehm et al to support their formulation of their complex as $[(\text{CH}_3)_2\text{N}=\text{N}]_2\text{Cu}_3\text{Cl}_3$, in which 1,1-dimethyldiazene is co-ordinated to copper, is the observed formation of a mixed tetrazene when it is decomposed in the presence of di-ethyldiazenium ions. The recovery of tetramethyltetrazene in 33% yield from the decomposition of the complex is not in itself strong evidence that dimethyldiazene and not tetramethyltetraz-2-ene is the co-ordinated species. Even the results of the cross-coupling experiment leave some room for doubt: the deviation from the statistical product distribution (vide supra) suggests that less than the theoretical yield of dimethyldiazene is liberated from the complex. This deviation may conceivably be due to part of the diazene content of the complex being present in the form of its dimer, tetramethyltetraz-2-ene. However, the observation of a peak in the mass spectrum of the complex, corresponding to the parent ion of the tetrazene is not in itself sufficient evidence in favour of tetrazene co-ordination. Liberation of the

tetrazene from the complex might be expected (under the conditions used) to give a mixture of the tetrazene and its decomposition products; these decomposition products (methylamine, dimethylamine and formaldehyde) would probably be lost during the work-up procedure (concentration of an ether extract of the decomposition product of the complex under vacuum) and so would not have been observed by Boehm et al. The low yield of tetrazene (33%) recovered from the decomposition of the complex contrasts markedly with the high yield of the same tetrazene (60-90%) obtained by McBride and Kruse⁹ from the basification of a solution of dimethyldiazonium ion followed by an analogous work-up procedure. The presence of tetramethyl-tetraz-2-ene in the copper complex derived from 1,1-dimethylhydrazine could explain this discrepancy.

Decomposition of the copper-containing material derived from the oxidation of 1-benzyl-1-phenylhydrazine gave a mixture of the tetrazene and its decomposition products. The mass spectrum of the oxidation adduct showed all the peaks observed in the mass spectrum of the tetrazene; a weak peak attributable to the diazene (m/e 196) was also observed.

The oxidation adduct derived from 1-allyl-1-phenylhydrazine gave a mass spectrum consistent with the presence of both the tetrazene (m/e 292) and the diazene (m/e 146). Decomposition of the copper-containing material gave a mixture of products, one of which was shown to be N-allylaniline; the formation of this compound was ascribed to the acid-catalysed decomposition of the corresponding tetrazene, by a pathway analogous to that shown in Scheme 96.

Decomposition of the copper-containing adducts derived from these 1-alkyl-1-phenylhydrazines gives products which are consistent with the formulation of these adducts in terms of diazene co-ordination as suggested by Boehm et al. However, the results may also be interpreted in terms of tetrazene co-ordination, the occurrence of which to a small degree, may also be accommodated in the work of Boehm et al. The outcome of a

cross-coupling experiment analogous to that carried out by Boehm et al. would indicate whether the diazene was in fact the co-ordinated species in these adducts.

The isolation of a zinc complex of 1,1,4,4,-tetramethyltetraz-2-ene was reported by Noltes and van den Hurk¹⁴⁷ in 1964. Michejda and Campbell¹⁴⁸ have recently re-investigated the complex, which was prepared by mixing an excess of zinc chloride with a solution of tetramethyltetraz-2-ene in tetrahydrofuran, and obtained results in accord with the formulation for the complex proposed by the original workers (67). The formation of analogous complexes by copper might therefore be reasonably expected, especially since tetraz-2-enes may be regarded as being substituted azo-compounds, and cuprous halide complexes of azo-compounds, prepared by the addition of an azo-compound to aqueous solutions of cuprous halides, are well-known.¹⁴⁶

EXPERIMENTAL

¹H Nuclear Magnetic Resonance spectra were recorded on a Varian Associates E.M. 360 (60 MHz) or H.A. 100 (100 MHz) Spectrometer and ¹³C Nuclear Magnetic Resonance spectra were recorded on a Varian Associates XL 100 Spectrometer. Except where indicated otherwise, spectra were recorded at 28°C using deuteriochloroform as solvent. Tetramethylsilane was used as the internal reference unless otherwise stated. All chemical shifts are quoted in p.p.m. (δ scale), with tetramethylsilane as 0 p.p.m. In the description of n.m.r. spectra the following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). J is the coupling constant quoted in Hertz (Hz).

The infra-red spectra were recorded on a Unicam S.P. 200 or on a Perkin Elmer 157G Spectrophotometer. The suffixes to the infra-red bands quoted are abbreviated as follows: (w), weak; (m), medium; (s), strong; (b), broad.

Mass spectra were recorded on an A.E.I. M.S.902 double focussing instrument.

Melting points were determined on a Reichert hot-stage microscope (except those involving the use of sealed tubes) and are uncorrected.

The alumina used in chromatography was of Activity III.

Preparation of 1-Alkyl-1-Phenylhydrazines.

The generally preferred methods of preparing these hydrazines are a) by reduction of the corresponding nitrosamine which can be prepared from the secondary amine, and b) by alkylation of phenylhydrazine or its sodium salt. The preparation of 1,1-dialkylhydrazines can be carried out cleanly and efficiently by the successive alkylation of t-butyl carbazate, and the possibility of adapting this method was examined. The results of this latter approach and the early observations made in the application of methods (a) and (b) above are first described.

Attempted Alkylation of t-Butyl-2-Phenylcarbazate.

t-Butyl-2-phenylcarbazate was prepared by the method of Carpino et al.¹¹ A mixture of t-butyl azidoformate (11.35 g; 0.079 mol), phenylhydrazine (8.58 g; 0.079 mol), triethylamine (11.03 ml), and distilled water (20 ml) was mechanically shaken for ca. 48 h. The reaction mixture was concentrated on a warm water-bath under high vacuum to give an orange-yellow solid. This crude material was washed with water, sucked dry and then recrystallised from petroleum-ether (b.p. 60-80°C). The pure t-butyl-2-phenylcarbazate was obtained as pale orange-brown plates (8.41 g; 52% overall). m.p. 92-93.5°C, lit.¹¹ m.p. 91-93°C; δ 1.45 (s, 9H, -C(CH₃)₃), 5.6-5.75 (s, 1H, Ph-NH-N-), 6.3-6.5 (s, 1H, CO-NH-N-), 6.7-7.4 p.p.m. (m, 5H, aromatic); ν_{max} . (nujol) 3350 (m), 3280 (m), 1735 (m), 1700 (m), 1605 (m), 1530 (w), 1295 (w), 1245 (m), 1150 (m), 750 (m), 690 (m) cm⁻¹.

The attempted alkylations were based on the method of Carpino et al.⁴¹ and the general procedure was as follows. A mixture of t-butyl-2-phenylcarbazate (2.4-9.6 mmole) and alkyl halide (2.4-9.6 mmole) in dry dimethylformamide (15-30 ml) was heated in an oil bath at ca. 55-60°C before adding triethylamine (2.4-9.6 mmole) in one portion. The

reaction time and conditions were different for each attempted alkylation and these are outlined below. The work-up procedure, however, was common to all these reactions: the reaction mixture was treated with water and extracted several times with methylene chloride. The combined extracts were dried (MgSO_4) and the solvent was removed under vacuum.

(a) Using allyl bromide. None of the experiments produced the expected precipitation of triethylamine hydrobromide and in each case work-up produced a red-brown gum or oil.

(i) The reaction mixture was stirred at 25°C for ca. 6 h. Isolation of the product gave a red-brown gum which was shown by t.l.c. (CHCl_3 on silica gel) to contain five components. The n.m.r. spectrum of this material suggested the presence of the allyl moiety. However, these signals were shown to be due to entrained allyl bromide. Wet column chromatography on alumina using 50-50 ether-chloroform afforded a red-brown gum whose n.m.r. spectrum resembled very closely that of t-butyl-2-phenylcarbazate. The gum crystallised on standing.

(ii) The reaction mixture was heated at $65-70^\circ\text{C}$ in a flask equipped with a reflux condenser, for 7 days. Again, a red-brown oil was obtained whose n.m.r. spectrum was identical to that of the crude material of (i) above.

(iii) A small amount of the silver salt of trifluoroacetic acid was added to the reaction mixture which was then heated overnight at ca. 70°C as in (ii). Normal work-up afforded the same red gum with an n.m.r. spectrum identical to those of the crude products of (i) and (ii) above. After attempted trituration with water, petroleum-ether (b.p. $60-80^\circ\text{C}$) and then benzene, a few milligrams of an off-white solid separated (m.p. 138°C). The n.m.r. spectrum (dimethyl sulphoxide d_6) of a weak solution of this solid showed only weak signals in the aromatic region.

(b) Using benzyl bromide. The reaction of benzyl bromide, a more active alkylating agent, at even higher temperatures was also examined. The reaction mixture was prepared as before and was first heated at 30-40°C for 7 h before refluxing overnight with stirring. Work-up afforded a red-brown oil whose n.m.r. spectrum (CCl_4) indicated almost complete disappearance of the singlet signal attributed to the t-butyl group. The remainder of the spectrum: δ 3.3-3.7 (broad s), 4.5 (s), 6.5-7.6 p.p.m. (m), was shown, in the light of later experiments (see the preparation of 1-benzyl-1-phenylhydrazine, p.135) to be not incompatible with the n.m.r. spectrum of 1-benzyl-1-phenylhydrazine. The thermal lability of the carbazate protecting group suggested by this result was confirmed by a control experiment in which a solution of t-butyl-2-phenylcarbazate in dimethyl formamide was refluxed under nitrogen for ca. 20 h. Removal of the solvent afforded an orange gum whose n.m.r. spectrum, compared to that of t-butyl-2-phenylcarbazate, showed a change from 5:9 to 3:1 in the aromatic:methyl proton integral ratio.

Alkylation of the Sodium Salt of t-Butyl-2-Phenylcarbazate.

A solution of t-butyl-2-phenylcarbazate (2.08 g; 0.01 mole) in dry benzene (40 ml) was added in one portion to a stirred suspension of sodium hydride (0.35 g of 80% dispersion in oil; 0.01 mole) and the resulting purple coloured mixture was heated under nitrogen with stirring at ca. 50°C for 4 h. The mixture was cooled before adding allyl bromide (1.21 g; 0.01 mole) in one portion. Heating was resumed and continued overnight before filtering the reaction mixture through a celite pad. The filtrate was washed with water (70 ml) and then dried (MgSO_4) before removing the solvent. Cleavage of the carbazate protecting group was achieved by treating a solution of the product gum in nitromethane (80 ml) with a steady stream of dry

hydrogen chloride gas. No precipitation of hydrochloride occurred. Removal of the solvent produced a dark brown gum which was dissolved in water and washed with ether before basifying with saturated sodium bicarbonate solution. Isolation of the product gave a yellow-brown liquid (0.18 g). In the light of later work (see p 131) the n.m.r. spectrum (CCl_4) of the product suggested it to be a mixture of 1-phenyl-1-allylhydrazine and 1-phenyl-2-allylhydrazine.

Preparation of N-Nitrosamines and Their Attempted Reduction to 1-Alkyl-1-Phenylhydrazines.

This method represents the most unambiguous route to 1-alkyl-1-phenylhydrazines. However, to gain full advantage it is important that the pure N-nitrosamine precursor be obtained. This in turn requires that the secondary aromatic amines from which the N-nitrosamines are prepared be pure.

Preparation of Secondary Aromatic Amines.

(i) N-Cyclopropylcarbinylaniline. The preparation of secondary amines by alkylation of aniline has been described by Hickinbottom⁸⁴ who reports that the tertiary amine is also formed in ca. 6% amount. However, when this method was applied to the preparation of N-cyclopropylcarbinylaniline, the product was shown by n.m.r. (CCl_4) to contain as much as 16% of the tertiary amine. This represents a serious shortcoming as a means of preparing small amounts of pure secondary amines in the cases where the alkylating agent is not readily available.

The use of a blocking group to prevent further alkylation is the basis of the method used by Fones.⁸⁶ Treatment of the sodium salt of acetanilide with an alkyl halide gives the N-alkylacetanilide which can then be hydrolysed to the desired amine. When an attempt was made to prepare N-cyclopropylcarbinylacetanilide, acetanilide was

recovered and n.m.r. evidence suggested that alkylation had occurred to an extent of less than 5%. The method was successfully employed in the preparation of N-allylaniline.

(ii) N-Allylaniline. This was prepared by the method of Fones.⁸⁶

A solution of acetanilide (6.75 g; 0.05 mole) in hot xylene (200 ml) was added in one portion to a suspension of sodium hydride (1.40 g; 0.058 mole) in dry xylene (50 ml), and the mixture was refluxed under nitrogen with stirring for ca. 24 h. A white precipitate separated. The mixture was cooled before adding allyl bromide (17.12 g; 0.141 mole) in one portion. After refluxing for ca. 20 h under dry nitrogen, the mixture was filtered while still hot. Concentration of the filtrate gave a pale yellow solid. Pure N-allylacetanilide was obtained as a white solid by recrystallisation from petroleum-ether (b.p. 40-60°C) (6.62 g; 76%), m.p. 43-45°C, lit.⁸⁶ b.p. 99-103°C/2 mm; δ (CCl₄) 1.8 (s, 3H, -COCH₃), 4.1-4.3 (m, 2H, N-CH₂-), 4.75-5.15 (m, 2H, -CH = CH₂) 5.5-6.2 (m, 1H, -CH = CH₂), 6.9-7.4 p.p.m. (m, 5H, aromatic); $\nu_{\max}$. (nujol) 1690 (s), 1660 (s), 1610 (s), 1280 (s), 950 (s), 790 (s), 740 (s), 700 (s), 660 (s) cm⁻¹; m/e 175 (P), 132 (P-COCH₃).

A solution of N-allylacetanilide (19.92 g; 0.0114 mole) in 3 M hydrochloric acid (150 ml) was refluxed for 2 h. Isolation of the product gave a dark brown liquid which was purified by distillation to give the pure N-allylaniline as a clear colourless liquid (10.64; 70%), b.p. 70-75°C/0.2 mm, lit.⁸⁶ b.p. 62-65°C/1.2 mm; δ (CCl₄) 3.3-3.8 (m, 3H, NH and N-CH₂-), 4.9-5.4 (m, 2H, -CH = CH₂), 5.55-6.2 (m, 1H, -CH = CH₂), 6.3-7.3 p.p.m. (m, 5H, aromatic); $\nu_{\max}$. (film) 3405 (s), 1600 (s), 1500 (s), 1320 (s), 1310 (s), 1260 (s), 1180 (s), 990 (m), 920 (s), 750 (s), 690 (s) cm⁻¹. The colourless distillate turned pale yellow on standing for several weeks.

Preparation of N-Nitroso-N-Allylaniline

This was prepared from N-allylaniline by the method of Hartmann and Roll.⁸⁷ A mixture of N-allylaniline (6.01 g; 0.045 mole), concentrated hydrochloric acid (6.5 ml) and ice (18 g) was cooled to below 10°C before adding a solution of sodium nitrite (3.16 g; 0.045 mole) in water (12 ml) with stirring over a period of ca. 10 min. The temperature was maintained below 10°C by adding ice to the reaction mixture as required. Stirring was continued for a further 1 h before extracting the orange-yellow mixture several times with benzene. Isolation of the product gave an orange oil which distilled as an orange-brown liquid (5.88 g; 80%) b.p. 95-96°C/0.4 mm; δ (CCl₄) 4.4-4.7 (m, 2H, N-CH₂-), 4.75-5.25 (m, 2H, -CH = CH₂), 5.35-6.05 (m, 1H, -CH = CH₂), 7.1-7.6 p.p.m. (m, 5H, aromatic); ν_{max} . (film) 3050 (m), 2900 (m), 1650 (m), 1600 (s), 1500 (s), 1480 (s), 1450 (s), 1420 (s), 1130 (s, broad), 940 (s), 830 (m), 755 (s), 685 (s) cm⁻¹; m/e 162 (P), 132 (P-NO).

Attempted Reduction of N-Nitroso-N-Allylaniline.

(a) Reduction With Lithium Aluminium Hydride. The procedure used was that of Hanna and Schueler,⁸⁸ the only modification being the use of water rather than acetone to decompose the excess of the reducing agent. Isolation of the product gave a viscous brown liquid whose n.m.r. spectrum (CCl₄) indicated that it was a complex mixture of products. When the same procedure was applied to N-nitroso-N-methylaniline (b.p. 84-89°C/0.4 mm, lit.⁸⁷ b.p. 135-137°C/13 mm), the product was shown to be a mixture of starting nitrosamine (21%), 1-methyl-1-phenylhydrazine (58%) and N-methylaniline (21%) by comparison of the n.m.r. spectra (CCl₄) of the product, N-methylaniline and 1-methyl-1-phenylhydrazine.

When the method of Poirier and Bennington⁸⁹ was used (the essential difference being to extend reaction time to 2.5 h), an orange-brown liquid was obtained whose n.m.r. spectrum indicated the

presence of N-allylaniline (ca. 17%) as well as the desired hydrazine. The mass spectrum confirmed the presence of 1-allyl-1-phenylhydrazine (m/e 148).

(b) Reduction with Aluminium Amalgam. Aluminium amalgam was prepared by the method of Vogel¹⁴⁹ and the reduction was carried out using the procedure of Carpino et al.⁴¹ Isolation of the product gave an orange-yellow liquid which was shown by n.m.r. (CCl_4) to be a mixture of the desired hydrazine and N-allylaniline.

(c) Reduction with Zinc and Acetic Acid. The experimental method paralleled that of Hickinbottom.⁹⁰ Isolation of the product gave a yellow-brown liquid, which was shown by n.m.r. (CCl_4) to be a mixture of 1-allyl-1-phenylhydrazine and N-allylaniline. When applied to the reduction of N-nitroso-N-methylaniline, this procedure gave a product mixture which was shown by n.m.r. (CCl_4) to be of similar type, namely 1-methyl-1-phenylhydrazine (57%) and N-methylaniline (43%).

These experiments showed that reduction to the 1-alkyl-1-phenylhydrazine could indeed be achieved, but that in all cases, a considerable degree of further reduction to the secondary amine occurred.

Attempted Preparation of 1-Alkyl-1-Phenylhydrazines by Direct Alkylation.

(i) Alkylation of Phenylhydrazine. Early attempts were based on Hickinbottom's procedure for the alkylation of aniline.⁸⁴ A mixture of phenylhydrazine (2 moles) and cyclopropylcarbonyl chloride (1 mole) was heated under nitrogen at 90°C for ca. 100 h. Phenylhydrazine hydrochloride separated and was filtered off leaving the product as a brown liquid. The mass spectrum of this material suggested that as much as 32% of dialkylation had occurred (m/e 216), and the n.m.r. spectrum supported this.

The alkylation of phenylhydrazine at room temperature in ether solution was reported to give the 1-phenyl-2-alkylhydrazine.⁵

However, when examined in connection with later work (see P. 149), the principal product was found to be the 1-alkyl-1-phenylhydrazine. The molar ratio of phenylhydrazine to alkyl chloride was again 2:1 and under these conditions alkylation with allyl bromide was found by n.m.r. (CCl_4) to give a mixture of 1-allyl-1-phenylhydrazine (78%) and 1-phenyl-2-allylhydrazine (22%). Alkylation with cyclopropyl-carbonyl chloride under these conditions gave only a trace amount of dialkylated material detectable by mass spectrometry.

These experiments showed that while the problem of dialkylation could be overcome by working in ether solution, the formation of 1-phenyl-2-alkylhydrazines was a serious disadvantage.

(ii) Alkylation of the Sodium Salt of Phenylhydrazine. The preparation of the sodium salt by the action of sodium metal on excess phenylhydrazine was described by Michaelis.⁹⁶ Titherley⁹⁸ reported the preparation of sodium phenylhydrazine by treating sodamide with a slight excess of phenylhydrazine. In practice however, this latter method proved very troublesome and the isolated product of alkylation was found to contain a considerable amount of unreacted phenylhydrazine. The use of sodium hydride in place of sodamide proved both convenient and effective.

An equimolar ratio of phenylhydrazine to sodium hydride was used. The sodium hydride was obtained as a 50% dispersion in oil and twice the required amount was weighed out before washing with dry benzene. The sodium salt was formed by heating the mixture of phenylhydrazine and sodium hydride in dry benzene at ca. 40°C under dry nitrogen for ca. 1 h. The mixture was cooled, the alkyl halide was added and the reaction mixture was refluxed for ca. 3 h. Isolation of

the product gave an orange-brown liquid whose n.m.r. spectrum (CCl_4) showed the presence of a considerable amount of phenylhydrazine (typically ca. 30%) in addition to the 1-alkyl-1-phenylhydrazine. Only a trace amount of dialkylated material was detected by mass spectrometry. All attempts to remove the phenylhydrazine by distillation were unsuccessful.

A convenient method of accurately estimating the phenylhydrazine content was found to be the reaction of the alkylation product with acetone. The n.m.r. solution of the alkylation product was dissolved in 'Analar' acetone (ca. 10 ml) and a small amount of anhydrous magnesium sulphate was added. This mixture was heated at ca. 60°C for 2 h before filtering off the magnesium sulphate and removing the solvent. The n.m.r. spectrum of this product (100 MHz, CCl_4) showed two singlets which were assigned to the syn- and anti-methyl signals of acetone phenylhydrazone (δ 1.75, 2.02 p.p.m.) by comparison with the n.m.r. spectrum of authentic acetone phenylhydrazone. The two larger singlets observed in the same region of the spectrum were assigned to the acetone N-alkyl-N-phenylhydrazone. The phenylhydrazine content was estimated by comparing the integration ratios of these two pairs of singlets. This reaction with acetone was also used to differentiate between the 1-alkyl-1-phenylhydrazine and the 1-phenyl-2-alkylhydrazine.

(iii) Removal of Phenylhydrazine. Michaelis and Claessen⁹⁷ found that a mixture of 1-allyl-1-phenylhydrazine and 1-allyl-2-phenylhydrazine could be separated by converting the mixture to the solid hydrochloride and recrystallising this from benzene. The 1,1-isomer separated while the 1,2-isomer stayed in solution. The possibility of using a similar approach to remove the phenylhydrazine from the product of alkylation

of the sodium salt of phenylhydrazine was suggested by the finding that authentic phenylhydrazine hydrochloride was quite insoluble in boiling benzene.

The hydrochloride was prepared by passing a stream of dry hydrogen chloride gas through a solution of the alkylation product in ether at 0°C. The precipitated white solid was collected, washed with ether and sucked dry. Boiling benzene extracts of this material were filtered while hot and the combined filtrates were cooled on ice. The white solid which separated was collected and sucked dry. The hydrazine regenerated from this recrystallised material was shown by n.m.r. to be quite pure and free of phenylhydrazine.

Comparison of the infra-red spectra of authentic phenylhydrazine hydrochloride, the crude hydrochloride and the recrystallised material showed that the differences between the spectra of the crude and the recrystallised hydrochloride could be related to the loss of phenylhydrazine hydrochloride in the recrystallisation process. From these observations three infra-red bands were found to be diagnostic for the presence of phenylhydrazine hydrochloride in the crude hydrochloride of the alkylation product. These were: ν (nujol) 887, 857, 770 cm^{-1} . The latter was not too useful as that region of the spectrum was generally very complex.

Thus the presence of phenylhydrazine could be clearly shown in two ways and the hydrochloride approach appeared to offer a successful method for its removal. It was later found that by weighing out the sodium hydride after washing to remove oil, the problem of residual phenylhydrazine could be avoided. Cases where residual phenylhydrazine was observed, even with this modification, could probably be related to the purity of the sodium hydride. The following general procedure was developed.

Formation of 1-Alkyl-1-Phenylhydrazines by Alkylation of the Sodium Salt of Phenylhydrazine.

(i) Preparation of Sodium Hydride. The sodium hydride oil dispersion was swirled with benzene (dried over sodium) to remove the oil. The grey slurry was then filtered on a sintered funnel under suction. A stream of compressed air (dried by passing through concentrated sulphuric acid) was passed over the pad of sodium hydride by means of an inverted funnel. When dry, the required amount of sodium hydride was quickly weighed into the reaction vessel.

(ii) Preparation and Alkylation of the Sodium Salt of Phenylhydrazine.

An equimolar mixture of sodium hydride and phenylhydrazine in dry benzene (0.1 mole of each reactant in 150 ml of benzene) was stirred under nitrogen at ca. 70°C for 2-7 h. The sodium salt formed as a yellow-brown precipitate. The mixture was cooled at room temperature before adding an equimolar amount of the alkyl halide and this mixture was stirred overnight at room temperature before refluxing for several hours. The precipitated sodium halide was removed by filtration through a celite pad and the filtrate was concentrated. Occasionally the filtration process proved quite difficult as the very fine precipitate blocked the filter. As an alternative procedure, the sodium halide could be removed by washing with water.

(iii) Removal of Phenylhydrazine from the Alkylation Product. A stream of dry hydrogen chloride gas was passed into a solution of the alkylation product in dry ether (typically 0.04 mole in 80 ml of ether) at 0°C for ca. 7-10 min. The precipitated hydrochloride was collected, washed with ether and sucked dry. The filtrate was evaporated to give a further yield of hydrochloride in the form of a dirty white solid or a green-brown gum. The gum could sometimes be induced to solidify by

scratching. In this way the hydrochloride could be obtained in 80-85% yield but only about half the yield was accounted for in the precipitate, the rest being recovered from the filtrate.

Phenylhydrazine contamination was identified by examining the infra-red spectrum of the hydrochloride for the characteristic bands at 887, 857 and 770 cm^{-1} . If these bands were found, the hydrochloride was exhaustively extracted with boiling benzene. The combined extracts were evaporated as the hydrochlorides proved to be surprisingly soluble. The hydrochloride recovered from benzene was basified with dilute aqueous sodium carbonate solution (20%) to give the pure 1-alkyl-1-phenylhydrazine. The residue of the benzene extraction process, when similarly basified, was shown to be mainly phenylhydrazine with a very small amount of the 1-alkyl-1-phenylhydrazine.

The hydrochlorides exhibited peculiar melting point behaviour in unsealed tubes. They appeared to melt, then recrystallise and melt again with decomposition over a large temperature range. The quoted melting points of the hydrochlorides refer to the melting point of the solid in a sealed tube, a much sharper melting point being obtained under these conditions.

a) Preparation of 1-Allyl-1-Phenylhydrazine. The sodium salt of phenylhydrazine was alkylated using allyl bromide. The mixture was refluxed for ca. 5 h to give the product uncontaminated by phenylhydrazine, in 57% yield. (As celite was unavailable, the reaction mixture was filtered through a pad of alumina and this probably accounts for the low yield as the product would be adsorbed to a greater extent than with celite); δ (100 MHz) 3.45 (s, 2H, $-\text{NH}_2$), 3.9-4.0 (m, 2H, $-\text{CH}_2-\text{CH}=\text{CH}_2$), 5.05-5.30 (m, 2H, $-\text{CH}_2-\text{CH}=\text{CH}_2$), 5.6-6.0 (m, 1H, $-\text{CH}_2-\text{CH}=\text{CH}_2$), 6.6-7.3 p.p.m. (m, 5H, aromatic); ν_{max} . (film) 3305 (m), 3040 (m), 1585 (s), 1480 (s), 1340 (m), 1220 (m), 915 (m), 875 (m), 750 (s), 695 (s) cm^{-1} .

The hydrochloride (ex benzene) had m.p. 148-151°C, lit.¹⁵⁰ m.p. 149-150°C ν_{max} . (nujol) 1595 (m), 1585 (m), 1575 (m), 1550 (m), 1500 (m), 930 (m), 915 (m), 760 (s), 740 (m), 730 (m), 720 (m) 690 (m) cm^{-1} . After several weeks the hydrochloride had developed a purple colour where it had been exposed to sunlight.

b) Preparation of 1-Cyclopropylcarbinyl-1-Phenylhydrazine.

(i) Preparation of Cyclopropylcarbinol. This was prepared by the method of Sreen et al.¹⁵¹ A solution of cyclopropanecarboxylic acid (25.80 g; 0.30 mol) in ether (150 ml) was added over a period of ca. 2 h to a stirred suspension of lithium aluminium hydride (14.20 g; 0.375 mole) in ether (500 ml). The mixture was stirred for 1 h and a solution of sodium potassium tartrate (73 g) in water (97 ml) was added. The ether layer was separated and washed with saturated sodium chloride solution. The residue was treated with saturated sodium chloride solution (200 ml) and water (100 ml) and this mixture was extracted with ether. The product isolated from the combined ethereal extracts was distilled to give a clear colourless liquid (15.27 g; 70%). b.p. 121-123°C, lit.¹⁵¹ 123°C; δ 0.0-1.5 (m, 5H, cyclopropyl), 2.55-2.90 (broad, s, 1H, -OH), 3.35-3.50 (d, $J = 7$ Hz, 2H, $-\text{CH}_2-\text{OH}$); ν_{max} . (film) 3350 (broad, s), 2880 (s), 1450 (broad, s), 1260 (m), 1160 (w), 1040 (broad, s), 930 (m), 840 (m), 805 (w) cm^{-1} .

(ii) Preparation of Cyclopropylcarbinyl Chloride. The method of Caserio et al.¹⁵² was employed. A solution of purified thionyl chloride¹⁵³ (46.40 g; 0.39 mole) in dry ether (560 ml) was slowly added to an ice-cooled mixture of cyclopropylcarbinol (28.11 g; 0.39 mole) and tri-n-butylamine (71.40 g; 0.39 mole) keeping the temperature below 6°C. The reaction mixture, consisting of two liquid phases, was then distilled under vacuum and the volatile components were collected in

three traps in series at -78°C . The yield was improved by heating the brown oily distillation residue to ca. 150°C to remove entrained material. The distillate was concentrated and was distilled through a column packed with Fenske helices. Pure cyclopropylcarbinyl chloride was obtained as a clear, colourless, sweet-smelling liquid (21.76 g; 61%, lit.¹⁵² yield 86%; without heating to 150°C in the distillation procedure, yields of 40-50% were obtained). b.p. $82-84^{\circ}\text{C}$, lit.¹⁵² $82.5-85.5^{\circ}\text{C}$; $\delta(\text{CCl}_4)$ 0.1-1.5 (m, 5H, cyclopropyl), 3.3-3.4 (d, $J = 7 \text{ Hz}$, 2H, $-\text{CH}_2-\text{Cl}$); ν_{max} . (film) 3080 (w), 3000 (m), 2950 (m), 2860 (w), 1440 (m), 1370 (w), 1265 (s), 1230 (m), 1035 (w), 1018 (s), 915 (s), 830 (s), 790 (w), 700 (s) cm^{-1} .

(iii) Alkylation of the Sodium Salt of Phenylhydrazine with Cyclopropylcarbinyl Chloride. The mixture was refluxed overnight and the product was isolated in 64% yield. The n.m.r. spectrum indicated the presence of phenylhydrazine and this was confirmed by examination of the infra-red spectrum of the hydrochloride of the crude product. The crude hydrochloride was isolated in 83% yield, half being obtained as a white precipitate, while the other half was obtained by concentration of the filtrate. The infra-red spectrum of this latter half did not exhibit the characteristic absorptions of phenylhydrazine hydrochloride, and was identical to that of the product obtained by extraction of the precipitated hydrochloride with boiling benzene. Pure 1-cyclopropylcarbinyl-1-phenylhydrazine hydrochloride was isolated in 57% yield, and the free base was regenerated on treatment with 20% aqueous sodium carbonate solution (70% recovery); δ (100 MHz, CCl_4) 0.1-1.3 (m, 5H, cyclopropyl), 3.10-3.16 (d, $J = 6 \text{ Hz}$, 2H, $-\text{CH}_2-\text{cyclopropyl}$), 3.40 (s, 2H, $-\text{NH}_2$), 6.50-7.22 (m, 5H, aromatic); ν_{max} . (film) 3335 (w), 3080 (w), 3000 (w), 2920 (w), 1595 (s), 1495 (s), 1450 (w), 1425 (w), 1385 (w), 1340 (broad, w), 1238 (m), 1150 (m), 1018 (m), 985 (m),

930 (w), 870 (m), 828 (m), 750 (s), 690 (s) cm^{-1} . The hydrochloride (ex benzene) had m.p. $135-138^{\circ}\text{C}$; ν_{max} . (nujol) 1600 (s), 1580 (s), 1550 (s), 1500 (s), 1345 (m), 1325 (w), 1250 (w), 1210 (m), 1170 (m), 1105 (w), 1085 (w), 1070 (w), 1055 (w), 1035 (w), 1020 (m), 1000 (w), 940 (m), 925 (m), 835 (m), 795 (m), 760 (s), 735 (m), 690 (s) cm^{-1} .

The hydrochloride developed a pale brown colour after several weeks.

c) Preparation of 1-(But-3-en-1-yl)-1-Phenylhydrazine. The sodium salt was alkylated using 1-bromobut-3-ene. The mixture was stirred for one week at room temperature and the product was isolated as a mobile yellow liquid. (80-87% yield). The infra-red spectrum of the hydrochloride showed that was the alkylation product /uncontaminated by phenylhydrazine; δ (100 MHz)

2.20-2.45 (m, 2H, $-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$), 3.30-3.46 and 3.47 (m and s, $-\text{NH}_2$ and $-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$), 4.92-5.20 (m, 2H, $-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$), 5.58-6.04 (m, 1H, $-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$), 6.58-7.35 p.p.m. (m, 5H, aromatic); ν_{max} . (film) 3340 (w), 3050 (m), 2920 (m), 1645 (m), 1605 (s), 1505 (s), 1460 (m), 1360 (m), 1285 (m), 1210 (m), 1160 (m), 1080 (w), 1030 (w), 995 (m), 920 (m), 880 (m), 750 (s), 690 (s) cm^{-1} ; m/e 162 (P) 121 (P- $\text{CH}_2\text{CH}=\text{CH}_2$).

The hydrochloride (ex benzene) had m.p. $102-105^{\circ}\text{C}$; ν_{max} . (nujol) 2690 (broad m), 1628 (m), 1590 (s), 1485 (s), 1335 (w), 1300 (w), 1270 (w), 1205 (w), 1180 (m), 1145 (w), 1080 (w), 1060 (w), 1025 (m), 995 (m), 920 (s), 890 (w), 760 (s), 738 (m), 725 (w), 690 (s) cm^{-1} .

The n.m.r. spectrum of the butenyl moiety in the hydrazine was different from that in 1-bromobut-3-ene. The splitting pattern of the protons next to bromine and then next to nitrogen ($-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$) changed from a triplet in the bromide to a multiplet of four lines in the hydrazine. The proton assignments were based on the results of decoupling experiments. The identity of the product of alkylation was confirmed by its reaction with acetone (see p.128). The n.m.r. spectrum of the brown, liquid product was as expected for acetone 1-(but-3-enyl)-1-phenylhydrazone.

d) Preparation of 1-Benzyl-1-Phenylhydrazine. The sodium salt of phenylhydrazine was alkylated using benzyl bromide. The mixture was refluxed for 10 h and the product was isolated as a yellow-brown liquid in 87% yield. The hydrochloride was prepared and the absence of phenylhydrazine from the alkylation product was confirmed; $\delta(\text{CCl}_4)$ 3.28 (s, 2H, $-\text{NH}_2$), 4.46 (s, 2H, $-\text{CH}_2\text{-Phenyl}$), 6.5-7.3 p.p.m. (m, 10H, aromatic); ν_{max} . (film) 3340 (w), 3010 (m), 1600 (s), 1505 (s), 1465 (s), 1360 (m), 1300 (w), 1215 (m), 1155 (w), 1080 (m), 1030 (m), 990 (m), 960 (m), 885 (s), 750 (s), 730 (s), 690 (s) cm^{-1} . The hydrochloride (ex benzene) had m.p. 170-172°C, lit.¹⁵⁴ m.p. 176-177°C; ν_{max} . (nujol) 2680 (broad, m), 1600 (m), 1590 (m), 1526 (m), 1490 (m), 1080 (w), 1018 (w), 905 (w), 830 (w), 780 (w), 760 (m), 730 (m), 695 (s) cm^{-1} . After several weeks, the hydrochloride had developed a purple colour where it had been exposed to sunlight.

(e) Preparation of 1-(3-Phenylprop-2-ynyl)-1-Phenylhydrazine

(i) Preparation of 3-Phenylprop-2-yn-1-ol The alcohol was prepared by the method of Schaap et al.¹⁵⁵ by treating the lithium salt of phenylacetylene with paraformaldehyde. When lithium hydride was used as the base, phenylacetylene was recovered unchanged. However, the preparation was achieved smoothly and in good yield using n-butyl-lithium.

Commercial n-butyllithium in hexane (ca. 2.1 M) was added slowly to a stirred solution of phenylacetylene (13.92 g; 0.13 mol) in dry ether (135 ml) containing a crystal of triphenylmethane. The addition was carried out by transferring the hexane solution directly from the bottle via a stainless steel capillary tube under a pressure of dry nitrogen. The addition was continued until the red-brown colour of triphenylmethyl anion appeared, indicating that an excess of base was present. The mixture was refluxed under dry nitrogen for ca. 45 min.

The yellow solution was evaporated under vacuum and the resulting grey solid was quickly dissolved in dry ether (150 ml). This solution was stirred under dry nitrogen and paraformaldehyde (3.94 g; 0.13 mole) was added in small portions. The mixture was refluxed for ca. 25 min. to give a bright yellow solution and a white precipitate. Hydrolysis with an excess of 20% aqueous hydrochloric acid followed by ether extraction gave the product as a red-brown liquid which distilled as a pale yellow mobile liquid. (11.97 g; 67%). b.p. 94-96°C/0.7 mm Hg lit. ¹⁵⁵ b.p. 137-138°C/15 mm Hg; δ 3.75-4.20 (broad, s, 1H, -OH), 4.35-5.52 (broad s, 2H, -CH₂OH), 7.1-7.6 p.p.m. (m, 5H, aromatic); ν_{max} . (film) 3300 (broad s), 2920 (m), 2860 (m), 2230 (w), 1592 (m), 1485 (s), 1438 (m), 1360 (w), 1250 (w), 1220 (w), 1065 (w), 1028 (s), 995 (m), 950 (m), 910 (w), 755 (s), 690 (s) cm⁻¹.

(ii) Preparation of 1-Bromo-3-Phenylprop-2-yne. The compound was prepared by the action of phosphorous tribromide on 3-phenylprop-2-yn-1-ol, using an adaptation of the methods of Bartlett and Rosen ¹⁵⁶ and Smith and Swenson. ¹⁵⁷

Phosphorous tribromide (12.78; 0.047 mole) was added over a period of ca. 2 h to a stirred solution of 3-phenylprop-2-yn-1-ol (12.00 g; 0.091 mole) and dry pyridine (1.50 ml) in dry ether (25 ml) at 0°C. The mixture was stirred at 20°C for ca. 18 h and was then washed with water (100 ml) and extracted with ether. The product was isolated as a brown liquid, which distilled as a very pale yellow liquid. (13.32 g; 75%) b.p. 72-80°C/0.6 mm Hg lit. ¹⁵⁷ b.p. 110-120°C/8 mm Hg; δ 4.10 (s, 2H, -CH₂Br), 7.1-7.55 p.p.m. (m, 5H, aromatic); ν_{max} . (film) 3050 (w), 2950 (w), 2260 (w), 2215 (m), 1590 (m), 1568 (w), 1485 (s), 1438 (s), 1420 (w), 1268 (s), 1200 (s), 1065 (w), 1025 (m), 980 (m), 915 (w), 755 (s), 690 (s) cm⁻¹.

(iii) Alkylation of the Sodium Salt of Phenylhydrazine with 1-Bromo-3-phenylprop-2-yne. The mixture was refluxed overnight and the product was isolated as a viscous brown liquid in 89% yield. The infra-red spectrum of the hydrochloride confirmed the absence of residual phenylhydrazine in the alkylation product; δ 3.76 (s, 2H, $-\text{NH}_2$), 4.35 (s, 2H, $-\text{N}-\text{CH}_2-$), 6.7-7.6 p.p.m. (m, 10H, aromatic); ν_{max} (film) 3315 (m), 3040 (m), 3010 (m), 2905 (w), 2220 (w), 1585 (s), 1480 (s), 1440 (m), 1430 (m), 1315 (s), 1210 (m), 1150 (m), 1135 (m), 1070 (w), 1065 (w), 1020 (m), 985 (w), 950 (m), 930 (m), 880 (s), 755 (s), 690 (s) cm^{-1} .

The hydrochloride (ex benzene) had m.p. 161-164°C; ν_{max} (nujol) 1610 (m), 1590 (m), 1540 (m), 1510 (m), 1340 (w), 1210 (m), 1175 (m), 1110 (w), 1090 (w), 1070 (w), 1035 (w), 1000 (w), 960 (w), 915 (m), 760 (s), 750 (s), 740 (m), 685 (s) cm^{-1} ; m/e 222 (P-HCl), 107 (B).

(f) Preparation of 1-(2-Styrylphenylmethyl)-1-Phenylhydrazine.

The sodium salt of phenylhydrazine was alkylated using 2-styrylphenylmethyl chloride.

(i) Preparation of Benzalphthalide. The method used was that of Weiss.¹⁵⁸ A mixture of phthalic anhydride (50.00 g; 0.33 mol), phenylacetic acid (55.00 g; 0.40 mol) and fused sodium acetate (1.30 g) was heated rapidly to 230°C in a sand bath. When the condensation commenced i.e. water was evolved, the temperature was raised to 238-241°C over a period of ca. 2 h and then maintained at 240°C for a further 1 h. After this time the theoretical volume of water (6 ml) had been collected. The orange-brown mass was cooled to 90-95°C and was dissolved in the minimum volume of hot ethanol (ca. 200 ml). The solution was filtered and allowed to stand overnight. Benzalphthalide was obtained as a sweet-smelling, pale-yellow solid (54.20 g; 74%), m.p. 99-100°C, lit.¹⁵⁸ m.p. 100-101°C; δ 6.4 (s, 1H, $>\text{C} = \text{CH}-$), 7.15-8.0 p.p.m. (m, 9H, aromatic); ν_{max} (nujol) 2910 (m), 2840 (m), 1760 (s), 1650 (w), 1600 (w), 1485 (m),

1460 (m), 1440 (m), 1350 (m), 1270 (m), 1200 (w), 1175 (w), 1160 (w), 1150 (w), 1080 (m), 1000 (w), 980 (s), 965 (s), 870 (m), 865 (m), 855 (m), 850 (m), 775 (s), 770 (s), 760 (m), 710 (m), 690 (s) cm^{-1} .

(ii) Preparation of Benzylphthalide. The method employed was that of Natelson and Gottfried.¹⁵⁹ Benzaldehyde (30.00 g; 0.135 mole) was dissolved in a hot solution of potassium hydroxide (7.83 g) in water (13 ml). The solution, diluted with water to a volume of 210 ml, was added to sodium amalgam, prepared by the addition of mercury (274 g) to molten sodium (9.14 g) under liquid paraffin. Vigorous frothing occurred; after stirring at ca. 100°C for ca. 6 h, the initial orange-pink colour had disappeared. The mixture was allowed to settle and cool before carefully isolating the colourless middle aqueous layer. This was washed with ether before acidifying with dilute sulphuric acid. Benzylphthalide was collected by filtration as a white solid (14.21 g; 47%), m.p. $58-59^{\circ}\text{C}$, lit.¹⁵⁹ m.p. 61°C ; δ 3.18-3.30 (d, J = 7 Hz, 2H, $>\text{CH}-\text{CH}_2-$), 5.6-5.9 (t, 2H, $\text{CH}-\text{CH}_2-$), 7.1-8.0 p.p.m. (m, 9H, aromatic), ν_{max} . (nujol) 1745 (broad, s) 1590 (s), 1490 (s), 1340 (s), 1310 (s), 1285 (s), 1260 (s), 1210 (s), 1190 (m), 1100 (m), 1075 (s), 1060 (s), 1040 (s), 1010 (m), 980 (s), 910 (m), 900 (m), 880 (m), 860 (m), 755 (s), 730 (s), 700 (s), 685 (s) cm^{-1} .

The aqueous filtrate was extracted with ether and the viscous yellow oil obtained by concentrating this extract was found (n.m.r. spectrum) to be wet benzylphthalide (18.63 g). Both fractions of benzylphthalide were used in the next stage without further purification.

(iii) Preparation of Stilbene-2-Carboxylic Acid. The procedure of Natelson and Gottfried¹⁵⁹ was followed. The crude benzylphthalide (30.00 g; 0.135 mole) dissolved in 95% aqueous ethanol (55 ml), was treated with potassium hydroxide (11.86 g). The mixture was gradually heated to 150°C . The alcohol distilled over and the brown residue began to foam. The temperature was raised to 180°C and was kept at $180-200^{\circ}\text{C}$

for ca. 4.5 h during which time water distilled from the mixture. The brown, tarry residue solidified on cooling and was dissolved in water. This solution was washed with ether and then acidified with 20% aqueous hydrochloric acid. The crude stilbene-2-carboxylic acid was collected by filtration and was recrystallised from ethanol, giving the pure compound as white needles (8.20 g; 61%). m.p. 159-160°C, lit.¹⁵⁹ m.p. 160°C; δ 6.8-8.2 (m, 11H, aromatic and olefinic), 10.3-11.4 p.p.m. (broad s, 1H, -OH); ν_{max} . (nujol) 2900 (v. broad, s), 1665 (broad, s) 1615 (m), 1585 (m), 1550 (m), 1480 (m), 1450 (m), 1435 (m), 1400 (m), 1305 (s), 1280 (s), 1245 (s), 1158 (m), 1138 (m), 1075 (m), 1045 (w), 985 (m), 965 (s), 935 (m), 840 (w), 785 (w), 760 (s), 700 (s), 680 (s), 670 (m), 630 (w) cm^{-1} .

(iv) Preparation of 2-Styrylphenylmethyl Alcohol. A solution of stilbene-2-carboxylic acid (13.10 g; 0.058 mole) in dry ether (200 ml) was added over a period of 30 min. to a stirred suspension of lithium aluminium hydride (3.57 g; 0.094 mole) in dry ether (50 ml), at a rate sufficient to maintain gentle boiling. The mixture was refluxed for ca. 3 h before adding a saturated aqueous solution of potassium sodium tartrate. The product was isolated as a white solid which recrystallised from ether as pure white needles (10.02 g; 82%). m.p. 96-97°C lit.¹⁶⁰ m.p. 92-93°C; δ 1.8 (s, 1H, -OH), 4.85 (s, 2H, $-\text{CH}_2\text{-OH}$), 6.9-7.8 p.p.m. (m, 11H, aromatic and olefinic); ν_{max} . (nujol) 3240 (broad, s), 1590 (w), 1570 (w), 1490 (m), 1095 (m), 1045 (m), 1035 (s), 958 (s), 758 (s), 710 (m), 685 (m) cm^{-1} ; m/e 210 (P).

(v) Preparation of 2-Styrylphenylmethyl Chloride. Conversion of 2-styrylphenylmethyl alcohol to 2-styrylphenylmethyl chloride was achieved by the method of Natelson and Gottfried.¹⁶⁰ Thionyl chloride (44 ml; purified by the method of Vogel¹⁵³) was added over 1 h to a stirred

solution of the alcohol (11.00 g; 0.052 mole) in dry ether (120 ml) at 0°C. The solution was then heated under reflux with stirring for ca. 40 min. The solvent and residual thionyl chloride were removed under vacuum and the dark green residue was dissolved in ether. The ether solution was washed with aqueous sodium carbonate solution and the product was isolated as a very pale-yellow, viscous liquid after distillation (10.10 g; 84%). b.p. 148-151°C/0.6 mm Hg, lit.¹⁶⁰ b.p. 170-185°C/15 mm Hg. The chloride turned yellow-orange on standing for several weeks; δ 4.68 (s, 2H, $-\text{CH}_2\text{Cl}$), 6.75-7.75 p.p.m. (m, 11H, aromatic); ν_{max} . (film) 3050 (m), 3020 (m), 2960 (w), 1630 (w), 1595 (m), 1570 (w), 1490 (m), 1445 (m), 1330 (w), 1300 (w), 1255 (s), 1200 (w), 1180 (w), 1070 (w), 980 (w), 960 (s), 850 (w), 835 (w), 780 (w), 760 (s), 730 (m), 690 (s), 665 (s) cm^{-1} .

(vi) Alkylation of the Sodium Salt of Phenylhydrazine with 2-Styrylphenylmethyl Chloride. The mixture was refluxed for 12 h and the product was isolated as a pale-pink solid in 86% yield. The infra-red spectrum of the hydrochloride confirmed the absence of phenylhydrazine from the product. The free hydrazine had m.p. 93-95°C (unrecrystallised); δ 3.45 (s, 2H, $-\text{NH}_2$), 4.6 (s, 2H, $\text{N}-\text{CH}_2-$), 6.7-7.7 p.p.m. (m, 16H, aromatic and olefinic); m/e 300 (P), 193 (B). The hydrochloride (ex benzene) had m.p. 177-179°C; ν_{max} . (nujol) 2680 (s), 1595 (m), 1525 (s), 1490 (s), 1150 (w), 1075 (w), 1045 (w), 1020 (w), 960 (s), 910 (m), 785 (m), 760 (s), 740 (w), 720 (m), 700 (s), 690 (m) cm^{-1} ; m/e 300 (P-HCl), 193.

Attempted Preparation of 1-Cumyl-1-Phenylhydrazine and 1-Phenyl-1-Triphenylmethylhydrazine.

Interest in the preparation of these hydrazines arose from the results of early experiments on the oxidation of 1-benzyl-1-phenylhydrazine.

The oxidation product had been found to be an apparently complex mixture and not the reported tetrazene, and it was thought that complete substitution of the benzylic carbon might eliminate certain possible alternative reaction paths. Although the results of later oxidations of 1-benzyl-1-phenylhydrazine agreed with the literature, making the preparation of these hydrazines unnecessary, the results of the attempts to prepare them are reported.

Attempted Preparation of 1-Cumyl-1-Phenylhydrazine

(i) Preparation of Cumyl Chloride. The method used was that of Brown.¹⁶¹ A stream of dry hydrogen chloride gas was passed over stirred α -methylstyrene (4.74 g; 0.04 mole) for ca. 15 min. The pale-pink liquid was diluted with dry n-pentane (25 ml) and the solution was concentrated under vacuum. The residue was washed with dilute aqueous sodium carbonate solution (2 x 25 ml) and the product was extracted into methylene chloride (30 ml). Removal of the solvent gave cumyl chloride as a clear, colourless liquid (5.92 g; 95%). The n.m.r. spectrum indicated the product to be pure and the material was used without further purification. δ 1.95 (s, 6H, methyls), 7.15-8.70 p.p.m. (m, 5H, aromatic); ν_{max} (film) 3080 (w), 3060 (m), 3020 (w), 2980 (s), 2920 (m), 2860 (w), 1600 (w), 1490 (m), 1445 (s), 1385 (m), 1365 (s), 1355 (m), 1265 (s), 1125 (s), 1095 (s), 1070 (s), 1025 (m), 900 (w), 765 (m), 695 (s) cm^{-1} .

(ii) Attempted Alkylation of the Sodium Salt of Phenylhydrazine with Cumyl Chloride. The mixture was refluxed for 14 h and the product was isolated as a brown oil. The methyl region of the n.m.r. spectrum of this material was complex. The spectrum also showed signals which were attributed to α -methylstyrene, this being formed by elimination of hydrogen chloride from cumyl chloride. The infra-red spectrum showed an absorption in the N-H region (ν_{max} 3340 cm^{-1}).

The procedure used for the formation of the hydrochloride gave a white precipitate which was extracted with boiling benzene. The concentrated extract was a gum whose n.m.r. spectrum still showed the complex signals in the methyl region seen before. The residue of the benzene extraction was basified with aqueous sodium carbonate solution and the product was isolated as a brown oil. The n.m.r. spectrum of this oil indicated it to be largely phenylhydrazine with some other material(s) giving rise to complex signals in the methyl region.

Thus, 1-cumyl-1-phenylhydrazine, if indeed present, could not be identified in the alkylation product.

(iii) Attempted Condensation of Phenylhydrazine with Cumyl Chloride.

A mixture of phenylhydrazine (2.16 g; 0.02 mole) and cumyl chloride (1.55 g; 0.01 mole) dry ether (10 ml) was stirred at room temperature for several days. The precipitate which separated was collected and shown to be phenylhydrazine hydrochloride. Stirring was resumed and more precipitate formed. The cycle of filtration followed by resumed stirring was repeated until after ca. 28 days no further precipitation occurred. The n.m.r. spectrum of the product (1.16 g) indicated the presence of α -methylstyrene. The methyl region contained several small peaks and a large singlet at δ 1.50 p.p.m. with slight shoulders on either side.

α -Methylstyrene was removed by dry column chromatography on alumina with petroleum ether (b.p. 40-60°C) as eluent. The remaining material was extracted with 3 M hydrochloric acid. Basification of the acid extract gave a product (0.25 g) whose n.m.r. spectrum showed four signals in the methyl region, two large signals at δ 2.60 and 2.65 p.p.m. and two smaller signals at δ 2.85 and 2.02 p.p.m. The n.m.r. spectrum of the residue of acid extraction showed two signals at δ 2.55 and

2.65 p.p.m. The aromatic region of the spectrum was quite different from that of the product of acid extraction. A control reaction showed that a mixture of α -methyl styrene and phenylhydrazine was unchanged after stirring for several days. Thus the product of alkylation appeared to be a complex mixture and the desired product was not isolated.

Attempted Preparation of 1-Phenyl-1-Triphenylmethylhydrazine.

(i) Preparation of Triphenylmethyl Chloride. A mixture of triphenylmethanol (20.01 g; 0.077 mole) and acetyl chloride (40 ml) in petroleum ether (100 ml; b.p. 40-60°C) was heated under reflux for ca. 45 min. The mixture was concentrated and the white solid which separated was collected by filtration (19.10 g; 89%) m.p. 112-113°C, lit.¹⁶² m.p. 112-113°C; δ 7.25 (s); $\nu_{\text{max.}}$ (nujol) 1590 (w), 1480 (m), 1460 (m), 1445 (s), 1375 (m), 1320 (m), 1215 (w), 1200 (w), 1180 (w), 1155 (m), 1080 (m), 1030 (m), 1000 (w), 890 (m), 820 (m), 760 (s), 745 (s), 700 (s), 665 (m) cm^{-1} .

(ii) Alkylation of the Sodium Salt of Phenylhydrazine with Triphenylmethyl Chloride. The mixture was refluxed for ca. 62 h and the product was isolated as a yellow gum. The n.m.r. spectrum of this material showed weak signals at δ 5.6 and 4.3 p.p.m. (both broad singlets) and very strong signals in the aromatic region δ 6.6-7.7 p.p.m. The reaction with acetone (see p.128) gave a product whose n.m.r. spectrum did not show the expected strong methyl signals. The weak signals which did appear in the methyl region were shown by the addition of the authentic material to the n.m.r. solution, to be due to acetone phenylhydrazone.

The procedure used for the formation of the hydrochloride at 0°C gave phenylhydrazine hydrochloride as a white precipitate and concentration of the filtrate gave triphenylmethyl chloride, identified

by comparison of infra-red spectra, as a pale brown solid.

To examine the possibility that the product of alkylation was 1-phenyl-2-triphenylmethylhydrazine, an authentic sample of this material was prepared by the method of Cohen and Wang.⁹² A mixture of triphenylmethyl chloride (8.61 g; 0.03 mol) and phenylhydrazine (6.47 g; 0.06 mol) in ether (170 ml) was heated under reflux under nitrogen for 90 min. The mixture was stirred overnight and the white precipitate filtered off. Concentration of the filtrate gave a yellow gum which solidified on standing (11.00 g; 100%). The solid was recrystallised from benzene as a very pale yellow solid, m.p. 136-137°C, lit.⁹² m.p. 136-137°C; δ 4.1 (broad s, 1H, -NH-), 4.5 (broad s, 1H, -NH-), 6.7-7.6 p.p.m. (broad m, 20H, aromatic); m/e 350 (P).

Although the n.m.r. spectrum of this material broadly resembled that of the product of alkylation of the sodium salt of phenylhydrazine, the signal at δ 5.6 p.p.m. was not observed.

The attempted preparation of the hydrochloride of 1-phenyl-2-triphenylmethylhydrazine by treating a solution of the hydrazine in ether at 0°C with hydrogen chloride, gave phenylhydrazine hydrochloride and triphenylmethyl chloride. By cooling the ether solution to between -5 and -10°C before treating with hydrogen chloride, the hydrochloride was successfully prepared with only ca. 2% conversion to phenylhydrazine and triphenylmethyl chloride.

Thus, the alkylation of the sodium salt of phenylhydrazine with triphenylmethyl chloride did not appear to give 1-triphenylmethyl-1-phenylhydrazine. The product broadly resembled 1-phenyl-2-triphenylmethylhydrazine in its n.m.r. spectrum and in its behaviour towards hydrogen chloride. The product was not examined further.

Oxidation of 1-Alkyl-1-Phenylhydrazines.

Of the many possible oxidising agents (see Introduction p.2) only three were used, namely, t-butyl hypochlorite, lead tetra-acetate, and yellow mercuric oxide. The possibility that a heterogeneous oxidation process might influence the course of the reaction against rearrangement (see Discussion p. 40), suggested that t-butyl hypochlorite and lead tetra-acetate would be preferable to mercuric oxide. However, the results of early oxidation experiments with mercuric oxide and with lead tetra-acetate indicated that the oxidation product was the same in both cases; mercuric oxide therefore became the preferred oxidising agent because the product could be isolated cleanly and easily from the reaction mixture.

The results of the attempted oxidations using t-butyl hypochlorite, and the general procedure using lead tetra-acetate and yellow mercuric oxide are first described.

Attempted Oxidation of 1-Alkyl-1-Phenylhydrazines Using t-Butyl Hypochlorite.

t-Butyl hypochlorite was prepared by the method of Gilliom and Ward,¹⁰⁵ and by the method of Mintz and Walling.¹⁰⁶ In both cases a bright yellow liquid was isolated and this was used without further purification, as suggested by Mintz and Walling.¹⁰⁶ The n.m.r. spectrum (CCl_4) of this material showed a sharp singlet at δ 1.3 p.p.m.

Oxidation of 1-allyl-1-phenylhydrazine under the conditions suggested by Baldwin et al.⁶¹ (1 mole of t-butyl hypochlorite to 1 mole of hydrazine) gave a product whose n.m.r. spectrum (CCl_4) indicated that it was a complex mixture. The spectrum could not be reconciled with that of the product of a subsequent successful oxidation using mercuric oxide. The attempted oxidation of the same hydrazine by an adaptation of the method of

Overberger and Marks⁵² (1 mole t-butyl hypochlorite to 1 mole of hydrazine) using triethylamine rather than potassium hydroxide as base appeared to give the hydrazine largely unchanged. The infra-red spectrum of the product in this case showed an absorption in the N-H region ($\nu_{\text{max.}}$ 3320 cm^{-1}), and the n.m.r. spectrum (CCl_4) showed a multiplicity of signals in the methyl region, as well as the signals attributable to the unoxidised hydrazine. When a 3 mole excess of t-butyl hypochlorite was used, the isolated product appeared to be a complex mixture whose n.m.r. spectrum (CCl_4) did not indicate the presence of the expected product of rearrangement.

The use of t-butyl hypochlorite was not examined further as satisfactory results had been obtained with lead tetra-acetate and with yellow mercuric oxide.

Procedure for the Oxidation of 1-Alkyl-1-Phenylhydrazines with Lead Tetra-acetate.

Lead tetra-acetate was supplied as a paste with glacial acetic acid. The acetic acid was removed by suction filtration on a sintered glass funnel under dry nitrogen; the white crystals were washed with dry ether, and the dry oxidising agent was quickly weighed and used immediately. The appearance of a faint brown colouration after some minutes did not seem to affect its reactivity. Methylene chloride was purified by the method of Mathews¹⁶³ by washing with water and aqueous sodium carbonate solution. After drying over calcium chloride, it was distilled and stored over molecular sieve.

A solution of the 1-alkyl-1-phenylhydrazine (3mmole) in methylene chloride (30 ml) was added over a period of 10-15 min. to a stirred solution of lead tetra-acetate (3.5 mmole) in methylene chloride (30 ml).

The reaction mixture was stirred under dry nitrogen in the dark for a further 25 min. before filtering through a celite pad to remove the light brown inorganic precipitate. The orange-brown filtrate was washed with aqueous sodium bicarbonate solution and the product was isolated in the usual way.

Procedure for the Oxidation of 1-Alkyl-1-Phenylhydrazines with Yellow Mercuric Oxide.

A 3:1 molar ratio of yellow mercuric oxide to hydrazine was used and typically the concentration of the hydrazine in the reaction mixture was in the range 0.15-6.5 mmole/ml. The hydrazine was added in one portion to a suspension of the oxidising agent in one of the following solvents, ether, chloroform or methylene chloride. The mercuric oxide soon developed a green colouration and the mixture was stirred under nitrogen with exclusion of light, for not less than 18 h. The mixture was filtered through a celite pad and the product was isolated in high yield. Generally a green powder was collected by filtration and on only one occasion was metallic mercury recovered.

Oxidation of 1-allyl-1-Phenylhydrazine.- The expected product of oxidative rearrangement was 1-phenylazoprop-2-ene.

(a) With Yellow Mercuric Oxide. The mixture of 1-allyl-1-phenylhydrazine (1.51 g; 10 mmole) and yellow mercuric oxide (6.48 g; 30 mmole) in methylene chloride (30 ml) was stirred for ca. 36 h. and the product was isolated as a mobile orange-yellow liquid (1.48 g; 100%). The infra-red and n.m.r. spectra of this liquid indicated that complete oxidation had occurred. The oxidation was also successfully carried out in chloroform; δ 6.55-6.75 (m, 2H, $-\underline{\text{CH}}_2-\text{CH} = \text{CH}_2$), 5.1-5.5 (m, 2H, $-\text{CH}_2-\text{CH} = \underline{\text{CH}}_2$), 5.8-6.6 (m, 1H, $-\text{CH}_2-\underline{\text{CH}} = \text{CH}_2$), 7.1-7.8 (m, 5H, aromatic); ν_{max} . (film) 3100 (m), 2940 (w), 1650 (m), 1610 (s), 1510 (s), 1445 (m), 1440 (m), 1390 (m), 1310 (m), 1280 (w), 1150 (s), 1090 (s), 1020 (w), 1000 (m), 930 (s), 770 (s), 690 (s) cm^{-1} .

The oxidation product was shown to be 1-phenylazoprop-2-ene by comparison of its infra-red and n.m.r. spectra with those of authentic 1-phenylazoprop-2-ene prepared by oxidation of 1-phenyl-2-allylhydrazine with yellow mercuric oxide. T.l.c. (silica gel/benzene) supported the spectral identification but six minor components were also observed; these were also present in the authentic sample of 1-phenylazoprop-2-ene. The main yellow spot had Rf. 0.58.

(b) With Lead Tetra-acetate. The oxidation was carried out as described and an orange-yellow liquid was obtained, the n.m.r. and infra-red spectra of which were identical to those of the product of mercuric oxide oxidation of 1-allyl-1-phenylhydrazine. 1-Phenylazoprop-2-ene was isolated in 71% yield.

The product of both oxidation procedures was examined for the presence of 1-phenyl-2-pyrazoline. An authentic sample of the latter was prepared by yellow mercuric oxide oxidation of 1-phenylpyrazolidine obtained by alkylation of the sodium salt of 1-phenylhydrazine with 1,3-dibromopropane. The crude 1-phenyl-2-pyrazoline was purified by sublimation to give a wine-red solid m.p. 47°C lit.¹⁶⁴ $51-52^{\circ}\text{C}$; δ (100 MHz) 2.6-3.0 (m, 2H, methylene), 3.45-3.7 (m, 2H, methylene), 6.7-7.35 p.p.m. (m, 6H, olefinic and aromatic). The n.m.r. spectra of the product of the oxidations of 1-allyl-1-phenylhydrazine did not show any signals attributable to 1-phenyl-2-pyrazoline.

Preparation of 1-Phenylazoprop-2-ene.- The compound was prepared by yellow mercuric oxide oxidation of 2-allyl-1-phenylhydrazine.

(1) Preparation of 2-Allyl-1-Phenylhydrazine.

A convenient and direct method of preparing 1,2-disubstituted hydrazines is by reduction of the corresponding hydrazones. The method is limited, however, to compounds with functional groups which are not susceptible to reduction. For this reason, the procedure cannot be used to prepare 2-allyl-1-phenylhydrazine. Furthermore free acrolein phenylhydrazone is not known;

rearrangement to 1-phenyl-2-pyrazoline occurs readily,^{107,108} and this was confirmed by experiment.

Direct alkylation of phenylhydrazine with allyl bromide by the method of Fischer and Knoevenagel⁵ was found to give a mixture of the 1,1-isomer (78%) and the 1,2-isomer (22%). (see p.127). Attempts to separate the isomers by distillation were unsuccessful. It was necessary, therefore, to prepare a derivative of phenylhydrazine which would either (A) activate the 2-position towards alkylation or (B) block alkylation at the 1-position.

A) Alkylation of 2-Formyl-1-Phenylhydrazine Followed by Removal of the Formyl Group.

The procedure was based on the method of Freer and Sherman¹¹⁸ who reported the preparation of 2-ethyl-1-phenylhydrazine by the action of ethyl iodide on the sodium salt of 2-formyl-1-phenylhydrazine.

i) Preparation of 2-Formyl-1-Phenylhydrazine.- The method of de Vries¹⁶⁵ was used. Phenylhydrazine (21.60 g; 0.2 mole) was added in one portion to 50% formic acid (73.60 g; 0.8 mole), and the resulting mixture was heated in a water bath (ca. 70°C) for ca. 10 minutes. The reaction mixture was left in the refrigerator for two days. The fawn coloured solid was collected and recrystallised from ethanol, ether being added to lower the solubility of the pure white plates. (19.10; 70%). m.p. 143-144°C; lit.¹⁶⁵ m.p. 144-145°C; $\nu_{\max}$. (nujol) 3270 (s), 3170 (s), 3120 (s), 3050 (s), 3000 (s), 1670 (s), 1640 (s), 1590 (m), 1580 (m), 1540 (w), 1485 (m), 1300 (w) 1260 (w), 1215 (m), 1170 (m), 1155 (m), 1140 (w), 1100 (w), 1080 (s), 1030 (s), 1015 (m), 990 (w), 880 (s), 865 (s), 850 (s), 745 (s), 730 (s), 690 (s) cm^{-1} ; m/e 136 (P), 107 (P-CHO), 77.

The ^1H and ^{13}C N.m.r. Spectra of 2-Formyl-1-Phenylhydrazine.

The unexpected complexity of the ^1H n.m.r. spectrum of 2-formyl-1-phenylhydrazine prompted further examination.

The ^1H N.m.r. Spectrum

(a) In Dimethyl Sulphoxide- d_6 : δ 6.35-7.50 (m), 7.6-8.4 (m), 9.32 (s), 9.54 (s) and 9.68 p.p.m. (broad singlet). Integration ratios - 94 : 35 : 3 : 2 : 9.

(b) In 1,2-Dimethoxyethane: δ 6.25-7.25 (m), 8.04 (s), 8.10 (s), 8.4-8.8 p.p.m. (broad singlet). Integration ratios - 10 : 1 : 1 : 1.

(c) In Glacial Acetic Acid: δ 6.05-7.05 (m), 7.85 p.p.m. (s). Integration ratios - 105 : 17.

(d) In Acetonitrile- d_3 : δ (100 MHz) 6.48 (broad singlet), 6.65 (broad singlet), 6.7-7.0 (m), 7.12-7.35 (m), 8.08 (s), 8.14 (s), and 8.22 p.p.m. (s). Integration ratios - 16 : 46 : 31 : 3 : 11 : 5.

The ^{13}C N.m.r. Spectrum. A variable temperature study was made in which the spectrum of a solution of the hydrazine in dimethyl sulphoxide- d_6 was recorded, first at 25°C , then at 181°C and again at 25°C .

Spectrum at 25°C : Ten lines were observed: δ 167.817, 160.708, 149.571, 148.846, 129.109, 128.865, 119.624, 118.829, 112.515, 112.370 p.p.m.

Spectrum at 181°C : Five lines were observed: δ 163.160, 148.931, 128.814, 119.917, 113.421 p.p.m.

Spectrum after cooling to 25°C: Ten lines were observed and the spectrum was identical to that initially recorded at 25°C.

Characterisation of 2-Formyl-1-Phenylhydrazine - The aim was to establish by chemical means that the prepared hydrazine was the 1,2-isomer and not the 1,1-isomer.

a) Reaction with acetone. A solution of the prepared 2-formyl-1-phenylhydrazine in 'Analar' acetone was refluxed under nitrogen for 16 h. The solvent was removed and the white solid obtained was shown by comparison of infra-red spectra and m.p. (143-144°C) to be unchanged 2-formyl-1-phenylhydrazine.

b) Attempted reduction of the formyl group. The procedure paralleled that of Beltrami and Russel.¹⁶⁶ A solution of the hydrazine (1.90 g; 0.014 mole) in dry 1,2-dimethoxyethane (70 ml) was added dropwise over a period of ca. 30 minutes to a stirred suspension of lithium aluminium hydride (0.62 g; 0.015 mole) in dry dimethoxyethane (30 ml). A vigorous reaction took place on each addition and a pale green colour developed. Work-up with potassium sodium tartrate (60 ml) and chloroform extraction (100 ml) (see p. 132) gave a yellow-brown liquid (1.12 g) from which an off-white solid separated. The solid was removed by filtration and the filtrate was concentrated to give more of the off-white solid. The solid was shown to be 2-formyl-1-phenylhydrazine by its m.p. (144-146°C) and by comparison of infra-red spectra. The filtrate was a cloudy, orange-brown liquid (0.49 g); it was extracted into acid, and after basification with aqueous sodium carbonate solution gave a mobile brown liquid (0.15 g). The infra-red spectrum of this liquid showed a strong absorption at 3250 cm⁻¹. The n.m.r. spectrum showed several signals in the methyl region δ 2.6, 3.02, 3.42, 3.56 and 3.72 with an integration ratio of 56:2:9:7:8. Two overlapping singlets, δ 4.0 and 4.05 p.p.m. were also observed with a combined integration of 48 in the above scheme.

(c) Preparation of 1-Acetyl-1-Phenylhydrazine. See below (p. 155) and Discussion (p. 59).

(ii) Preparation of the Sodium Salt of 2-Formyl-1-Phenylhydrazine.- This was prepared by a method analogous to that used for the preparation of the sodium salt of phenylhydrazine (see p. 130). The solvents used for this reaction were dioxan, ether and 1,2-dimethoxyethane, the latter being preferred because of the increased solubility of 2-formyl-1-phenylhydrazine. 1,2-Dimethoxyethane was dried over activated molecular sieve and then sodium, before distillation from calcium hydride.

A solution of the hydrazine (7.16; 0.06 mole) in hot 1,2-dimethoxyethane (100 ml) was added in one portion to a stirred suspension of sodium hydride (1.44 g, 0.06 mole) in the same solvent (20 ml). A vigorous frothing was seen on mixing and after stirring for ca. 3.5 h under dry nitrogen, a clear bright orange solution had formed.

(iii) Alkylation of the Sodium Salt of 2-Formyl-1-Phenylhydrazine.- Allyl bromide (7.28 g; 0.06 mole) was added in one portion and the mixture was stirred for ca. 26 h to give a heavy, white precipitate and a faintly pink coloured supernatant liquid. Isolation of the product as before (see p.130) gave an orange-yellow gum (10.65 g).

(iv) Removal of the Formyl Group.- The alkylation product (10.65 g) was stirred with concentrated hydrochloric acid (40 ml) for ca. 20 h. The gum dissolved and a precipitate was formed. Water was added to dissolve the precipitated hydrochloride and the solution was extracted with ether to remove any unhydrolysed material. The aqueous solution was basified with 20% aqueous sodium carbonate solution and extracted with chloroform. The product was isolated as a clear, orange-brown liquid (8.12 g), whose n.m.r. spectrum indicated that it was a mixture of 1-allyl-1-phenylhydrazine and 2-allyl-1-phenylhydrazine in approximately equal amounts. The presence of the 1,1-isomer was confirmed by treating

a sample of the product with acetone (see p.128). (Alkylation of the sodium salt of 2-formyl-1-phenylhydrazine with benzyl bromide gave a mixture of the 1,1- and 1,2-isomers in the ratio of ca. 3:2).

(v) Attempted Separation of 2-Allyl-1-phenylhydrazine. Three methods were examined:

(a) Using Laevulinic Acid.-The aim was to selectively prepare a derivative of 1-allyl-1-phenylhydrazine which could be readily separated. It was hoped to form the phenylhydrazone-type derivative of the keto-acid which could be removed by base extraction. A solution of the hydrolysis product (3.00 g; 0.02 mol) and laevulinic acid (2.32 g; 0.02 mole) in absolute alcohol (20 ml) was refluxed under nitrogen for ca. 20 h. Removal of the solvent gave a yellow oil (4.54 g) which had a complex n.m.r. spectrum. Treatment with saturated aqueous potassium carbonate solutions (50 ml) gave an almost colourless, cloudy solution which was extracted with ether. Concentration of the extract gave a yellow-brown liquid (2.09 g). This was distilled to give a mobile, yellow-brown liquid (0.50 g), b.p. 70-72°C/0.05 mm Hg. The n.m.r. spectrum of this liquid indicated that the major product was the desired hydrazine, but the low frequency signals in the region δ 1.04-2.76 p.p.m. indicated the presence of impurities. The ratio of the integration of these signals to that of the signals attributed to the allylic protons ($-\underline{\text{CH}}_2-\text{CH}=\text{CH}_2$) of the desired hydrazine, was 1:3.5. The infra-red spectrum showed absorptions in the carbonyl region at ν_{max} . 1765 and 1720 cm^{-1} . The distillate was washed with saturated aqueous potassium carbonate solution but spectral evidence indicated that the product was unchanged. The mass spectrum showed, inter alia, m/e 274, 234, 188, 148, 107. (When this method was used to separate 2-benzyl-1-phenylhydrazine from 1-benzyl-1-phenylhydrazine, the n.m.r. spectrum of the product displayed similar low frequency signals in the range δ 1.1 - 2.8 p.p.m.).

b) Using Acetophenone.- The aim was to form the acetophenone phenylhydrazone of the 1,1-isomer and to separate the 2-allyl-1-phenylhydrazine by distillation. A mixture of the hydrolysis product (2.97 g; 0.02 mole) and acetophenone (2.39 g; 0.02 mole) in absolute alcohol (16 ml) was refluxed under nitrogen for ca. 10 h. The solvent was removed to give an orange-yellow liquid (4.82 g) which was distilled under vacuum (0.08 mm Hg). Three fractions were collected (i) b.p. 32-38°C, (ii) 40-60°C and (iii) 60-80°C. The n.m.r. spectra of fractions (i) and (ii) were virtually identical and these two fractions were combined (1.42 g). The n.m.r. spectrum of this mobile, bright yellow liquid indicated the presence of acetophenone and of the phenylhydrazone derivative in addition to the desired hydrazine. The higher boiling fraction (iii) was found to be richer in the phenylhydrazone derivative. The combined fractions (i) and (ii) were extracted into 2.5 M hydrochloric acid and the acid solution was washed with ether. The aqueous solution was then basified with 20% aqueous sodium carbonate solution and the product was isolated as a yellow-brown liquid (0.48 g). The n.m.r. spectrum of this liquid (100 MHz) showed it to be very largely 2-allyl-1-phenylhydrazine with a small amount of the phenylhydrazone (ca. 4%).

c) Using Zinc Chloride Solution.- This attempt was based on the method used to separate aniline from its N-alkylated derivative, as described by Hickinbottom.⁸⁴ A solution of zinc chloride (15.00 g) in water (16 ml) was added to the hydrolysis product (1.17 g; 0.008 mole) and the mixture was stirred under nitrogen. A pale brown paste soon formed which prevented further stirring. The mixture was left to stand overnight before decanting off the aqueous layer. The paste was repeatedly extracted with boiling petroleum ether (b.p. 40-60°C) and from the combined extracts a yellow-green liquid was obtained (0.35 g). The n.m.r. spectrum indicated that the product was still a mixture of the two isomers and that the proportion of the 2-allyl-1-phenylhydrazine had decreased.

(B) Alkylation of Phenylhydrazine Derivatives With the 1-Position Blocked, Followed by Removal of the Protecting Group(s). Several derivatives were considered, both 1-substituted phenylhydrazines and 1,2-disubstituted phenylhydrazines.

Monosubstituted Derivatives.-

(i) Attempted Preparation of 1-Ethoxycarbonyl-1-Phenylhydrazine.

A mixture of the sodium salt of phenylhydrazine (see p.130) and ethyl chloroformate (10.90 g; 0.1 mole) in dry benzene (160 mls) was stirred for ca. 48 h at room temperature. The product was isolated as a yellow-brown liquid (17.86 g) whose n.m.r. spectrum indicated that it was a mixture of the 1- and the 2-ethoxycarbonyl-1-phenylhydrazine. Treatment of the mixture with acetone gave an orange-yellow liquid whose n.m.r. spectrum (60 MHz, CDCl_3) confirmed the presence of the 1,1-isomer in the alkylation product, but also indicated the presence of residual phenylhydrazine.

(ii) Preparation of 1-Acetyl-1-phenylhydrazine.-The attempted preparation by the action of acetyl chloride on the sodium salt of phenylhydrazine gave a product whose n.m.r. spectrum indicated that it was a mixture. Three signals were observed in the methyl region suggesting the presence of 1- and 2-acetyl-1-phenylhydrazine and perhaps the product of dialkylation. (The attempted preparation of 1-benzoyl-1-phenylhydrazine by this method is reported to give both monosubstituted isomers and the disubstituted derivative.¹¹⁹).

The compound was successfully prepared by the method of Behrend and Reinsberg.¹²⁰ A mixture of 2-formyl-1-phenylhydrazine (3.72 g; 0.027 mole) and acetic anhydride (2.80 g; 0.027 mole) was heated in a steam bath for ca. 50 min. On cooling a yellow gum was obtained which failed to solidify. Concentrated hydrochloric acid (6 ml) was added to

the yellow gum and the mixture was stirred for ca. 7 h, to give a thick white paste. The mixture was cooled to ca. -15°C and was diluted with water (15 ml) before basifying with concentrated ammonia solution.

The product isolated by filtration was recrystallised from ethanol, ether being added to decrease the solubility of the solid. This gave pure white needles (1.01 g; 28%). (The low yield was due to accidental spillage of the reaction mixture.) m.p. $124-125^{\circ}\text{C}$. lit.¹²⁰ m.p. 124°C ;

δ 2.08 (broad s, 3H, $-\text{CO}-\text{CH}_3$), 4.0-5.1 (broad s, 2H, $-\text{NH}-\text{NH}-$) 7.1-7.6 p.p.m. (broad s, 5H, aromatic); ν_{max} . (nujol) 3340 (m), 3200 (m), 3050 (w), 1650 (broad, s), 1600 (s) 1500 (m), 1470 (m), 1300 (m), 1260 (s), 1195 (m), 1160 (m), 960 (s), 935 (w), 905 (w), 760 (s), 718 (w), 695 (s) cm^{-1} .

The n.m.r. spectrum of the product of reaction with acetone (see p.128) confirmed that the white solid was 1-acetyl-1-phenylhydrazine and not 2-acetyl-1-phenylhydrazine.

1-Acetyl-1-phenylhydrazine was also prepared unambiguously by amination of the sodium salt of acetanilide with O-(2,4-dinitrophenyl) hydroxylamine prepared by the method of Tamura et al.⁷⁷ A solution of O-(2,4-dinitrophenyl)hydroxylamine (2.02 g; 0.01 mole) in dry methylene chloride (65 ml) was added to a suspension of the sodium salt of acetanilide (0.01 mole) in xylene (50 ml) (see p.124). The mixture was a green-brown colour initially, turning to brown after stirring at room temperature for ca. 10 h. The mixture was filtered and the filtrate was concentrated to give a yellow solid (0.97 g). Recrystallisation from ethanol gave a pure white solid (0.77 g) m.p. $125-126^{\circ}\text{C}$; m/e 150 (P), 135, 119, 108 (B). The n.m.r. and infra-red spectra of the white solid were identical to those of the material derived from 2-formyl-1-phenylhydrazine.

Attempted Alkylation of 1-Acetyl-1-Phenylhydrazine Using Allyl Bromide.

Only a cursory examination was made as a successful preparation of 2-allyl-1-phenylhydrazine had already been achieved by another method. The method was analogous to that used in the direct alkylation of phenylhydrazine in ether solution (see p. 127).

A solution of 1-acetyl-1-phenylhydrazine (0.75 g; 0.005 mole) and allyl bromide (0.31 g, 0.0025 mole) in 'Analaar' chloroform (6 ml) was stirred at room temperature under nitrogen for 28 days. The white precipitate which separated was filtered off and the pale brown filtrate was concentrated to give a pale orange solid (0.59 g). The acetyl protecting group was removed by heating a solution of the solid in 3M hydrochloric acid (30 ml) under reflux for 3 h. Isolation of the product gave an orange-brown liquid (0.23 g) whose n.m.r. spectrum showed the signals of the allyl moiety. The product of hydrolysis appeared to be an approximately 50:50 mixture of phenylhydrazine and 2-allyl-1-phenylhydrazine. No attempt was made to separate the desired hydrazine.

Disubstituted Derivatives.-

(i) 1,2-Di-acetyl-1-phenylhydrazine.-This was prepared by the method of Widman.¹²² A mixture of 2-acetyl-1-phenylhydrazine (1.50 g; 0.01 mole) and acetyl chloride (0.81 g; 0.01 mole) in dry benzene (25 ml) was refluxed for 3.5 h. The red solution was concentrated to give a wine red gum which was triturated with ether to give a fawn coloured solid (1.73 g). This was recrystallised from benzene as a pale pink solid (1.61 g). m.p. 105-106°C lit.¹²² m.p. 107-108°C; m/e 192 (P, weak), 150, 108 (B).

The sodium salt of this material was prepared by the action of sodium hydride on a solution of 1,2-di-acetyl-1-phenylhydrazine in benzene. The gum which formed was treated with an equimolar amount of allyl bromide and the mixture was refluxed under dry nitrogen for 2.5 h.

The product was isolated as a red-brown oil whose n.m.r. spectrum indicated it to be a complex mixture. Examination by t.l.c. (alumina/ether) showed five components. An attempt was made to separate the mixture by wet column chromatography (alumina/ether). However, no material was eluted and the applied mixture remained adsorbed on the column.

(ii) 1,2-Diformyl-1-Phenylhydrazine. The hydrazine was prepared by the method of Freund and Horst.¹²³ Phenylhydrazine (10.00 g; 0.092 mole) was added dropwise to formic acid (30.00 g; 0.65 mole) at 0°C. The mixture was refluxed under nitrogen for ca. 7 h and was then left to stand for several days to crystallise. The off-white solid (13.65 g; 90%) was collected and recrystallised first from ethanol and then from benzene as a pure white solid m.p. 125-126°C lit.¹²³ m.p. 126°C; ν_{max} . (nujol) 3140 (s), 3040 (m), 1710 (s), 1700 (s), 1680 (s), 1650 (s), 1580 (s), 1480 (s), 1340 (s), 1320 (m), 1295 (m), 1285 (s), 1268 (s), 1160 (s), 1152 (m), 1020 (m), 1010 (m), 925 (s), 800 (s), 752 (s), 690 (s), 675 (s) cm^{-1} . m/e 164 (P, weak), 136, 107.

The ^1H and ^{13}C N.m.r. Spectra of 1,2-Diformyl-1-Phenylhydrazine.

As in the case of 2-formyl-1-phenylhydrazine, the complex appearance of the ^1H n.m.r. spectrum led to further examination.

The ^1H N.m.r. Spectrum.-

(a) In Dimethyl Sulphoxide- d_6 : δ 7.05-7.60 (m), 8.34 (s), 8.42 (s), 8.84 p.p.m. (s). Integration ratios - 60:8:3:5.

(b) In 1,2-Dimethoxyethane: δ 6.9-7.7 (m), 8.15 and 8.18 (overlapping singlets), 8.23 (s), 8.55 (s), 9.26 (broad singlet) and 9.66 p.p.m. (broad singlet). Integration ratios - 100:22:9:10:6.

(c) In Acetic Acid- d_3 : δ (100 MHz) 7.2-7.6 (m), 8.35 and 8.37 (overlapping singlets), 8.42 (s) and 8.61 p.p.m. (s). Integration ratios - 20:3:1:3. A variable temperature study showed that the three sets of signals in the region δ 8.0-9.0 p.p.m. coalesced and two sharp singlets were observed at 120°C.

(d) In Acetonitrile- d_3 : δ 6.9-7.6 (m), 8.18 and 8.25 (two overlapping singlets), 8.58 (s) 8.70 p.p.m. (broad singlet). Integration ratios - 113:27:30.

(e) In Methanol- d : δ 7.1-7.5 (broad singlet) 8.28 and 8.38 (two overlapping singlets), 8.65 p.p.m. (s). Integration ratios 112:27:15.

The ^{13}C N.m.r. Spectrum. A variable temperature study was made in which a solution of the hydrazine in dimethyl sulphoxide- d_6 was recorded, first at 25°C, then at 152°C, and again at 25°C.

Spectrum at 25°C: Seventeen lines were observed. δ 167.282, 163.850, 161.706 (low intensity), 161.491, 160.013, 159.611, 140.590, 139.452, 129.553, 128.960, 128.444 (low intensity), 126.381, 126.025, 121.420 (low intensity), 121.073, 120.121, 119.723 p.p.m.

Spectrum at 155°C: Six lines were observed. δ 161.450, 161.259, 140.702, 129.109, 126.148. 121.255 p.p.m.

Spectrum after cooling to 25°C: The spectrum was identical to that initially recorded at 25°C.

(a) Alkylation of the Sodium Salt of 1,2-Diformyl-1-Phenylhydrazine With Allyl Bromide. The sodium salt of 1,2-diformyl-1-phenylhydrazine was prepared by adding a solution of the hydrazine (3.28 g; 0.02 mole) in hot 1,2-dimethoxyethane (50 ml) to a stirred suspension of sodium hydride (see p. 130 0.50 g; 0.02 mole) in dimethoxyethane (20 ml). The mixture was refluxed under dry nitrogen for 7 h and was then cooled before adding allyl bromide (2.42 g; 0.02 mole). After stirring under reflux for ca. 6 h, the product was isolated as a brown oil (3.81 g).

(b) Removal of Protecting Groups. A mixture of the alkylation product (3.81 g) and concentrated hydrochloric acid (40 ml) was stirred for ca. 18 h. The mixture was washed with ether and the aqueous solution was basified with 20% aqueous sodium carbonate solution. The product, 2-allyl-1-phenylhydrazine, was isolated as a yellow-brown liquid (2.52 g; 85% overall), b.p. 85-86°C/0.05 mm Hg lit.⁵ b.p. 172°C/60 mm Hg; δ (100 MHz) 3.22-3.45 (m, 2H, $-\underline{\text{CH}}_2-\text{CH}=\text{CH}_2$), 4.0-4.5 (broad singlet, 2H, $-\underline{\text{NH}}_2$) 5.02-5.35 (m, 2H, $-\text{CH}_2-\text{CH}=\underline{\text{CH}}_2$), 5.56-6.04 (m, 1H, $-\text{CH}_2-\underline{\text{CH}}=\text{CH}_2$), 6.65-6.94 and 7.05-7.32 p.p.m. (m, 5H, aromatic); ν_{max} . (film) 3300 (broad, s), 3050 (m), 2920 (m), 2830 (m), 1600 (s), 1495 (s), 1460 (w), 1420 (w), 1310 (m), 1260 (s), 1170 (w), 1155 (w), 1070 (w), 1030 (w), 1000 (m), 930 (s), 890 (m), 760 (s), 700 (s) cm^{-1} ; m/e 148 (P), 107 (B), 77.

(2) Oxidation of 2-Allyl-1-Phenylhydrazine by Yellow Mercuric Oxide.-

The oxidation was carried out on the n.m.r. solution. The solution was made up to a volume of 2.5 ml with 'Analar' chloroform, and to this solution was added yellow mercuric oxide (0.40 g). The mixture was stirred for 3 days and the product was isolated as a mobile red liquid. The infra-red and n.m.r. spectra were identical to those of the product of oxidation of 1-allyl-1-phenylhydrazine (see p. 147).

Oxidation of 1-Cyclopropylcarbiny-1-Phenylhydrazine.- The anticipated product of this oxidation was 1-phenylazobut-3-ene.

(i) With Yellow Mercuric Oxide. The mixture of 1-cyclopropylcarbiny-1-phenylhydrazine (0.54 g; 0.0033 mole) and yellow mercuric oxide (2.16 g; 0.01 mole) in ether (15 ml) was stirred for ca. 70 h and the product was isolated as a pale-green solid (0.37 g). The crude solid recrystallised from ethanol in the form of pale-yellow plates (0.24 g; 65% recovery), m.p. 95.5-96.5°C; δ (100 MHz, CCl_4) 0.0-1.5 (m, 5H, cyclopropyl), 3.98-4.05 (d, J = 6Hz, $-\text{CH}_2\text{-cyclopropyl}$),

6.2-7.4 (m, 5H, aromatic); ν_{max} . (nujol) 1590 (s), 1490 (s), 1320 (w), 1250 (m), 1170 (m), 1120 (s), 1100 (s), 1070 (m), 1020 (w), 980 (m), 830 (w), 795 (w), 745 (s), 690 (s), 650 (s) cm^{-1} ; m/e 320 (P,B), 292 (P-N₂), 237 (P-C₄H₇). Accurate mass measurement 320.200153 (C₂₀H₂₄N₄ requires 320.200087). Thus the product (70%) was identified as 1,4-dicyclopropylcarbinyl-1,4-diphenyltetraz-2-ene. After standing for several months, the tetrazene had decomposed to a black solid.

Overberger and Herin⁴⁰ have shown that under conditions of low hydrazine concentration, tetrazene formation is inhibited and the diazene decomposition pathway is favoured. The oxidation was therefore repeated under conditions in which the hydrazine concentration was low. A solution of 1-cyclopropylcarbinyl-1-phenylhydrazine (0.19 g; 0.00117 mole) in 'Analar' chloroform (10 ml) was added dropwise over a period of 1 h to a stirred suspension of yellow mercuric oxide (0.76 g; 0.0035 mole) in 'Analar' chloroform (13 ml). The mixture was stirred for ca. 48 h and the product was isolated as an orange solid (0.17 g). The crude material recrystallised from ethanol as pale yellow plates (m.p. 96-97°C). The n.m.r. spectrum of the crude product showed the presence of the cyclopropylcarbinyl moiety and no signals attributable to the but-3-enyl moiety were observed. The product was identified as 1,4-dicyclopropylcarbinyl-1,4-diphenyltetraz-2-ene.

(ii) With Lead Tetra-acetate. The oxidation was carried out as described; the reaction mixture became quite warm and appreciable effervescence was observed. The inorganic precipitate was removed and the filtrate was concentrated to give a red-brown liquid. The n.m.r. spectrum showed that it was a complex mixture. No signals attributable to the but-3-enyl moiety were observed. Comparison of n.m.r. spectra suggested that N-cyclopropylcarbinyl-aniline, and small amounts of the corresponding tetrazene and formylcyclopropane were present. Washing with aqueous sodium bicarbonate solution gave a wine red liquid (0.26 g) whose

infra-red spectrum showed an absorption in the N-H region ($\nu_{\text{max.}} 3400 \text{ cm}^{-1}$). Dry column chromatography (alumina/20% ether-benzene) gave a bright yellow band of material from which was recovered a wine-red liquid (0.20 g). The infra-red spectrum showed an absorption in the N-H region ($\nu_{\text{max.}} 3400 \text{ cm}^{-1}$) and comparison of n.m.r. spectra indicated the presence of N-cyclopropylcarbinyllaniline with a small amount of the corresponding tetrazene. T.l.c. (silica gel/benzene) supported the spectral assignments.

Oxidation of 1-cyclopropylcarbinyll-1-phenylhydrazine with lead tetraacetate therefore appeared to give a mixture of 1,4-dicyclopropylcarbinyll-1,4-diphenyltetraz-2-ene and its decomposition products. The anticipated rearrangement product was not observed.

Oxidation of 1-(But-3-en-1-yl)-1-Phenylhydrazine with Yellow Mercuric Oxide.-

The anticipated product of oxidative rearrangement was cyclopropyl (phenylazo)methane.

The mixture of the hydrazine (0.53 g; 0.003 mole) and yellow mercuric oxide (2.12 g; 0.009 mole) in 'Analar' chloroform (13 ml) was stirred for ca. 26 h. Reaction was immediate and the mixture appeared to effervesce. The product was isolated as a brown liquid containing a small amount of the mercuric oxide residue (0.60 g). The n.m.r. spectrum indicated that the product was a complex mixture and in particular, the characteristic signals of the cyclopropyl moiety were not observed. The infra-red spectrum showed a weak absorption at $\nu_{\text{max.}} 3400 \text{ cm}^{-1}$. T.l.c. [silica gel/30% petroleum ether (b.p. 40-60°C)-benzene] showed that the product did not contain any residual 1-(but-3-en-1-yl)-1-phenylhydrazine. The mass spectrum showed (inter alia) m/e 320 (P), 251, 147, 106 (B), suggesting the presence of the tetrazene derivative.

Preliminary examination by t.l.c. (silica gel/n-hexane and silica gel/benzene) revealed seven bands of material. Preparative t.l.c. [silica gel (1 mm)/h-hexane] gave five overlapping bands. The leading grey band had Rf. 0.31 and the appearance of the plate suggested that decomposition was occurring during development. Only the three leading bands in the order (i) grey, (ii) grey-pink and (iii) yellow-green, could be cleanly isolated. Of these, the yellow-green band appeared to be the major component. The material recovered from each band was examined by mass spectrometry:

Band (i). A brown gum was isolated; m/e (inter-alia) 292 (P), 251, 147, 106 (B). The parent peak is consistent with loss of nitrogen from the tetrazene.

Band (ii). A similar brown gum was isolated; m/e (inter alia) 320 (P, v. weak), 292, 251, 147, 106 (B). The spectrum was consistent with decomposition of the tetrazene.

Band (iii). An orange-brown liquid was obtained; m/e (inter alia) 138, 305, 292 (weak), 251 (weak), 160 (B), 159, 106. The peaks at m/e > 160 were only observed after heating the sample. The n.m.r. spectrum of this material was not significantly different from that of the crude oxidation product. When rechromatographed (silica gel/benzene), six bands were observed.

Preparation of Cyclopropyl(phenylazo)methane.

(i) Preparation of Formylcyclopropane. Oxidation of cyclopropylcarbinol by ceric ammonium nitrate according to the method of Young and Trahanovsky¹⁶⁷ gave the aldehyde as a clear colourless liquid in 33% yield, b.p. 96-99°C lit.¹⁶⁷ b.p. 97-99°C.

(ii) Preparation of Formylcyclopropane Phenylhydrazone. An equimolar mixture of the aldehyde and phenylhydrazine in carbon tetrachloride solution was stirred at 0°C for 4 h. The product was isolated as an orange-yellow solid in 83% yield.

(iii) Reduction of Formylcyclopropane Phenylhydrazone with Lithium

Aluminium Hydride. A 2:1 molar ratio of reducing agent to hydrazone was used. The mixture, in tetrahydrofuran was stirred for ca. 14 h and then refluxed for a further 4 h. 2-cyclopropylcarbinyl-1-phenylhydrazine was isolated as a bright yellow liquid in 90% yield.

(iv) Oxidation of 2-Cyclopropylcarbinyl-1-Phenylhydrazine with Yellow

Mercuric Oxide. The normal oxidation procedure (see p. 147) gave cyclopropyl(phenylazo)methane as a bright yellow liquid in 80% yield; δ (CCl_4) 0.2-1.7 (m, 5H, cyclopropyl), 3.75-3.90 (d, $J=7\text{Hz}$, 2H, $-\text{CH}_2$ -cyclopropyl), 7.1-7.8 p.p.m. (m, 5H, aromatic).

Oxidation of 1-Benzyl-1-Phenylhydrazine with Yellow Mercuric Oxide.-

The oxidation product was reported by Busch and Lang⁷ to be 1,4-dibenzyl-1,4-diphenyltetraz-2-ene. The oxidation was repeated in order to ascertain whether any rearrangement to 2-phenylazotoluene occurs.

The mixture of 1-benzyl-1-phenylhydrazine (1.01 g; 0.005 mole) and yellow mercuric oxide (3.23 g; 0.015 mole) in 'Analar' chloroform (30 ml) was stirred for ca. 70 h. The inorganic residue was removed and the filtrate was concentrated at room temperature under vacuum to give an orange yellow solid (1.11 g). The crude material recrystallised from ethanol as pale yellow plates (43% recovery), m.p. 145°C ; δ 5.3 (s, 4H, $-\text{CH}_2$ -Ph), 6.7-7.5 p.p.m. (m, 2OH, aromatic). The product was identified as 1,4-dibenzyl-1,4-diphenyltetraz-2-ene by comparison of its m.p. and n.m.r. spectrum with those of an authentic sample prepared by the method of MacPherson¹⁶⁸ (m.p. 145°C). Thus, the oxidation of 1-benzyl-1-phenylhydrazine, gave 1,4-dibenzyl-1,4-diphenyltetraz-2-ene in 80% yield. No 2-phenylazotoluene was detected by n.m.r. spectroscopy, and no benzaldehyde phenylhydrazone, another possible product, was detected by infra-red and n.m.r. spectroscopy.

Earlier oxidations in which the filtrate was concentrated with heating, gave a brown oil and not the solid tetrazene. The n.m.r. spectrum of this oil indicated that it was a complex mixture. The ethanolic mother liquor of recrystallisation of the product of the successful oxidation (above) was concentrated to give an orange oil. The n.m.r. spectrum of this oil was very similar to that of the product of the early oxidation experiments, suggesting that thermal decomposition was occurring in both cases.

The anticipated rearrangement product, 2-phenylazotoluene, was prepared by the method outlined by Hickinbottom.¹⁶⁹ The condensation of o-toluidine and nitrosobenzene in glacial acetic acid gave a dark wine coloured oil. Wet column chromatography (silica gel/light petroleum, b.p. 40-60°C) gave a bright yellow-red band from which a bright red, mobile liquid was recovered (36%). The n.m.r. spectrum showed a sharp methyl singlet at δ 2.7 p.p.m. This characteristic signal was not observed in the n.m.r. spectra of the product of the several oxidations of 1-benzyl-1-phenylhydrazine.

Oxidation of 1-(3-Phenylprop-2-ynyl)-1-Phenylhydrazine with Yellow Mercuric Oxide.- The anticipated product of oxidative rearrangement was 1-phenyl-1-phenylazo-allene.

The mixture of the hydrazine (0.69 g; 0.003 mole) and yellow mercuric oxide (2.01 g; 0.009 mole) in 'Analar' chloroform (18 ml) was stirred for 5 days. Reaction was immediate and the mixture appeared to effervesce. The mercuric oxide residue was removed and the filtrate was concentrated under vacuum with gentle warming. The product was isolated as a shiny black foam (0.63 g), m.p. 80-90°C. (A subsequent oxidation gave a black glass). The material dissolved in deuterochloroform to give a cloudy brown solution; the n.m.r. spectrum of this solution was

poorly resolved. The spectrum showed a broad multiplet in the aromatic region δ 6.5-8.3 p.p.m. and a weak broad singlet at δ 1.7 p.p.m. with an integration ratio of 39:1. The infra-red spectrum showed no absorptions in the N-H region indicating that oxidation was complete, and no distinct absorption was observed in the $\text{-C}\equiv\text{C-}$ region. The absence of any signal attributable to the 3-phenylprop-2-ynyl moiety ($\text{-CH}_2\text{-C}\equiv\text{C-Ph}$) suggested that the tetrazene was not present in the oxidation product. The mass spectrum had (*inter alia*) $440 + 2$ (very weak), 220 (B), 219, 205 (w), 204 (w), 115 (w). The material was examined by t.l.c. (silica gel with fluorescent indicator/benzene) and the appearance of the plate suggested that decomposition was occurring during development. Under ultraviolet light a series of six overlapping bands and an orange-brown spot at the origin were observed. The leading band had Rf. 0.65 and the band having Rf. 0.47 fluoresced. No attempt was made to isolate the components.

Oxidation of 1-(2-Styrylphenylmethyl)-1-Phenylhydrazine with Yellow Mercuric Oxide.-

The anticipated product of oxidative rearrangement in this case was β -(2-methylphenyl)- α -phenylazostyrene. Other potential products were stilbene-2-aldehyde phenylhydrazone⁷ and the tetrazene.

The mixture of the hydrazine (0.64 g; 0.002 mole) and yellow mercuric oxide (1.41 g; 0.006 mole) in 'Analar' chloroform (15 ml) was stirred for ca. 18 h, and the product was isolated as a brown gum. The n.m.r. spectrum of this gum, though poorly resolved, showed a large multiplet in the aromatic region (δ 6.3-8.1 p.p.m.) and several broad singlets in the methylene region (δ 5.35, 5.3, 5.2, 4.85, 4.8, 4.35, 4.25, 4.05, 3.3, 3.05 and 2.85 p.p.m.), indicating that the product was a complex mixture. The only signal observed in the methyl region was a very weak, broad singlet at δ 1.25 p.p.m. The integration ratio of aromatic to

non-aromatic protons was approximately 15:1. The oxidation was repeated in methylene chloride and in ether, but the same product was obtained. The presence of β -(2-methylphenyl)- α -phenylazostyrene could not be detected by n.m.r. spectroscopy.

T.l.c. (alumina/benzene, petroleum ether, b.p. 40-60°C, and carbon tetrachloride) showed up to five components, and the appearance of the developed plate suggested that decomposition was occurring during development.

Wet column chromatography [alumina, 30 cm x 2 cm/petroleum ether, (b.p. 40-60°C) 80 ml, followed by carbon tetrachloride, 80 ml, and then 20% benzene/carbon tetrachloride, 200 ml] gave four overlapping coloured bands. These were (i) a dark orange-brown at the origin, (ii) a bright yellow band, (iii) a diffuse orange-brown band, and (iv) a diffuse pale-yellow band. As the bands moved very slowly the benzene content of the eluting solvent was increased to 50%. Band (iv) was eluted in the normal way; bands (i) and (ii) were isolated by removing the respective segments of alumina from the top of the column. All the material could be accounted for in bands (i), (ii), and (iv).

Band (i). A film of red-brown material was recovered (0.09 g). The n.m.r. spectrum of this material was poorly resolved and showed a multiplet at δ 6.3-8.2 p.p.m. and weak broad singlets at δ 4.8, 4.75, 4.1 and 3.2 p.p.m.

Band (ii). A brick-orange solid was recovered (0.23 g). The n.m.r. spectrum showed only a broad multiplet in the aromatic region δ 6.5-8.2 p.p.m. The mass spectrum had m/e (inter alia) 374 (weak), 349 (weak), 347, 312, 298, 224, 221, 208 (B), 207, 206, 193, 179, 178.

Band (iv). Elution required 250 ml of solvent and the eluent was collected in two equal portions. A yellow-brown solid (0.06 g) was recovered from the first portion. The n.m.r. spectrum showed a multiplet at δ 6.7-7.7 p.p.m. and a singlet at 5.3 p.p.m. with an integration ratio of 20:1. The mass spectrum had (inter alia) m/e 568 (very weak), 490,

374, 319, 297, 296, 206, 193 (B). The second portion gave a red-brown oil (0.23 g) whose n.m.r. spectrum showed singlet signals at 5.2, 4.7, 4.05, 3.0 and 2.2 (broad). The signals observed in the spectrum of the product recovered from the first portion of eluent were also present, suggesting that the material recovered from the second portion was derived from the decomposition of the material in the first fraction.

Comparison of the n.m.r. spectrum of the crude oxidation product with that of the product of the early oxidations of 1-benzyl-1-phenylhydrazine and that of the material recovered from the mother liquor of recrystallisation of 1,4-dibenzyl-1,4-diphenyltetraz-2-ene (see p 165) showed that a common feature was the multiplicity of signals in the region δ 2.5-5.5 p.p.m.

The formation of 2-formylstilbene phenylhydrazone in the oxidation process was suggested by the presence of peaks at m/e 298 and 221 in the mass spectrum of the material recovered from band (ii). The n.m.r. spectrum of the band (ii) material was not incompatible with that of an authentic sample of 2-formylstilbene phenylhydrazone. T.l.c. (alumina/ CCl_4) supported this possibility. A control experiment showed that 2-formylstilbene phenylhydrazone was stable to the oxidation conditions.

Thus the product of oxidation appeared to be a mixture of the tetrazene, its decomposition products, and 2-formylstilbene phenylhydrazone. Mass spectral data suggested that the order of elution was first the tetrazene and its decomposition products followed by the phenylhydrazone: cf. benzaldehyde phenylhydrazone is eluted slower than 1,4-dibenzyl-1,4-diphenyltetraz-2-ene on t.l.c. (alumina/carbon tetrachloride).

Preparation of 2-Formylstilbene Phenylhydrazone

The hydrazone was prepared in the usual way by the condensation of 2-formylstilbene with phenylhydrazine. The aldehyde was prepared by the method of Dale et al¹⁷⁰ and was obtained as a dark-brown gum.

An attempt to prepare the aldehyde by an adaptation of the method of Kornblum et al.¹⁷¹ was unsuccessful. A mixture of the aldehyde

(0.30 g; 1.4 mmole) and phenylhydrazine (0.155 g; 1.4 mmole)

in absolute alcohol (10 ml) was stirred for ca. 20 h and the product

was isolated by filtration as a bright yellow solid (0.21 g; 50%), m.p. 130-131°C; δ 6.5-8.1 p.p.m. (m); $\nu_{\text{max.}}$ (nujol) 3300 (w), 1600 (s), 1500 (m), 1500 (m), 1340 (w), 1310 (w), 1250 (s), 1170 (w), 1135 (m), 1070 (m), 1040 (w), 965 (s), 920 (m), 890 (m), 740 (s), 720 (m), 685 (s) cm^{-1} ; m/e 298 (P), 221 (-77), 206 (B).

Preparation and Oxidative Rearrangement of 1-(Pent-3-en-2-yl)-1-Phenylhydrazine

Preparation of 1-(Pent-3-en-2-yl)-1-Phenylhydrazine.- The hydrazine was prepared by alkylation of the sodium salt of phenylhydrazine with 2-chloropent-3-ene using the procedure described above (see p. 130).

i) Preparation of trans-Pent-3-en-2-ol.

The alcohol was prepared by the reaction of methylmagnesium chloride with crotonaldehyde using a modification of the method of Coburn.¹⁷³ The Grignard reagent was prepared by passing a steady stream of methyl chloride through a stirred suspension of magnesium metal (60.02 g; 2.50 mol) in dry ether (1700 ml) at a rate sufficient to maintain gentle boiling until all the magnesium had been consumed; the mixture was then stirred for ca. 1 h. A solution of freshly distilled crotonaldehyde (100.00 g; 1.43 mol) in dry ether (300 ml) was added dropwise with stirring, and the mixture was stirred for 1 h. at room temperature. A saturated solution of ammonium chloride (400 ml) was added slowly and the resulting mixture was repeatedly extracted with ether. Concentration of the combined extracts gave a clear, colourless liquid which was distilled through a 6 in. Vigreux column (101.07 g; 82%), b.p. 119-120°C lit.¹⁷² 120°C; δ 1.12-1.20 d, $J = 6\text{Hz}$, 3H, $\text{CH}_3\text{-CH(OH)-}$, 1.65-1.71 (d, $J = 4\text{Hz}$, 3H, $\text{CH}_3\text{-CH=CH-}$), 3.55 (s, 1H, -OH), 3.8-4.35 m, 1H, -CH(OH)-CH_3 , 5.3-5.6 p.p.m. (m, 2H, olefinic); ν_{max} . (film) 3380 (broad, s), 2980 (s), 1680 (w), 1460 (s), 1380 (s), 1300 (m), 1160 (m), 1120 (m), 1065 (s), 970 (s), 920 (s), 870 (w) cm^{-1} .

Although the intended asymmetric induction experiment would require the resolution of this racemic alcohol,¹²⁷ the preliminary experiments were carried out using unresolved pent-3-en-2-ol.

ii) Preparation of 2-Chloropent-3-ene. The compound was prepared from the parent alcohol in two ways:

a) Using Phosphorous Trichloride: The procedure of Balfe et al¹²⁸ was used. A solution of pent-3-en-2-ol (8.15 g; 0.095 mol) in dry pyridine (1.70 g; 0.02 mol) was added dropwise with stirring over a period of ca. 8 min. to neat, freshly distilled phosphorous trichloride (5.00 g; 0.036 mol) at 0°C. The reaction mixture was allowed to stand for ca. 2h

at room temperature, during which time two distinct layers separated. The upper layer was decanted from the lower pale-yellow syrup and was distilled to give the chloride as a clear colourless liquid (6.50 g; 65%); b.p. $20-22^{\circ}\text{C}/32\text{ mm Hg}$; $92-97^{\circ}\text{C}/760\text{ mm Hg}$, lit.¹²⁸ b.p. $20^{\circ}/12\text{ mm Hg}$; δ 1.5-1.9 (m, 6H, methyl), 4.45-4.85 [m, 1H, $-\text{CH}(\text{Cl})-\text{CH}_3$], 5.5-5.85 p.p.m. (m, 2H, olefinic); $\nu_{\text{max.}}$ (film) 3030 (m), 2990 (s), 2960 (s), 2940 (s), 2920 (m), 2890 (m), 2860 (m), 1670 (m), 1450 (s), 1380 (s), 1270 (w), 1215 (s), 1160 (m), 1100 (w), 1050 (w), 1015 (s), 960 (m), 885 (m), 860 (w), 740 (w), 650 (s) cm^{-1} ; m/e 106, 104, 91, 89, 69 (B).

b) Using Hydrogen Chloride: This was the preferred method of preparing 2-chloropent-3-ene since the reaction by-products were readily identifiable and easily removed. A steady stream of dry hydrogen chloride gas was bubbled through the neat alcohol (28.81 g; 0.335 mol) at 0°C for ca. 45 min. The reaction mixture separated into a clear pale brown upper layer and a cloudy grey lower layer. The infra-red spectrum of the upper layer was examined periodically during the reaction and the passage of hydrogen chloride was stopped when the spectrum showed no absorption in the O-H region. The upper layer was separated and warmed gently with stirring for ca. 1 h to remove dissolved hydrogen chloride. Anhydrous potassium carbonate was then added in small portions until no further effervescence was observed. The clear colourless liquid was collected and was used without further purification (28.94 g; 82%). The infra-red and n.m.r. spectra of this material were identical to those of the product obtained from (a).

Examination of the Purity of the Prepared 2-Chloropent-3-ene. The presence of an absorption in the carbonyl region of the infra-red spectrum of the prepared pent-3-en-2-ol ($\nu_{\text{max.}}$ 1680 cm^{-1}) and 2-chloropent-3-ene ($\nu_{\text{max.}}$ 1670 cm^{-1}) cast some doubt as to the purity of these compounds.

Comparison with the infra-red spectra of crotonaldehyde and of pent-3-en-2-one (prepared by the method of House¹⁷³) showed that the absorption could not be attributed to either of these compounds. Similarly, the n.m.r. spectrum of the neat alcohol did not contain any signals attributable to crotonaldehyde or to pent-3-en-2-one. Examination of the chloride by gas chromatography (15% P.E.G.A. at 70°C) indicated that the impurity was present in less than 1%. The retention time of the impurity (7.4 min) was not compatible with that of pent-3-en-2-one (14.3 min) or with that of crotonaldehyde (8.5 min).

The infra-red spectrum suggested that the impurity contained a carbonyl group and an attempt was made to form the phenylhydrazone derivated which it was hoped could be separated from 2-chloropent-3-ene by fractional distillation. A solution of the prepared 2-chloropent-3-ene and excess phenylhydrazine in ethanol was heated under reflux for ca. 3 h. The ethanol was then removed under reduced pressure and the residue was distilled under vacuum. However, the infra-red spectrum of the distillate retained the absorption at 1680 cm^{-1} . No further attempt was made to identify the impurity and in view of its very low estimated concentration (< 1%), the chloride was used as obtained after distillation. The chloride developed a yellow-brown colour after standing for several weeks.

iii) Alkylation of the Sodium Salt of Phenylhydrazine with 2-Chloropent-3-ene.

The alkylation was generally carried out using freshly prepared alkylating agent; otherwise a recently prepared sample was distilled before use. The sodium salt of phenylhydrazine was prepared by the method already described (see p. 130). The reaction time and conditions varied slightly from one preparation to the next and while all gave the required product, the following conditions were most successful.

2-Chloropent-3-ene (10.52 g; 0.1 mol) was added in one portion to the sodium salt of phenylhydrazine (0.1 mol) in dry benzene (150 ml) at room temperature. The mixture was stirred overnight under dry nitrogen before heating at 60-70°C for ca. 40 h. The product hydrazine was isolated as an orange-brown liquid (14.64 g; 83%); δ 1.18 - 1.26 [d, J = 6 Hz, 3H, -CH(CH₃)-CH=CH-CH₃], 1.55-1.75 (m, 3H, -CH=CH-CH₃), 3.15-3.60 (broad s, -NH₂), 4.10-4.65 [m, 1H, -CH(CH₃)-CH=CH-CH₃], 6.55-7.45 p.p.m. (m, 5H, aromatic). The n.m.r. spectrum also showed the presence of much weaker signals usually observed as shoulders at the base of the low frequency doublet signal; these signals were thought to be due to the presence of a small amount of the di-alkylated product (see below). The infra-red spectrum had: $\nu_{\text{max.}}$ (film) 3340 (m), 3015 (m), 2970 (s), 2930 (s), 1598 (s), 1495 (s), 1450 (m), 1375 (m), 1290 (s), 1160 (m), 1030 (m), 975 (s), 880 (s), 840 (m), 760 (s), 695 (s) cm^{-1} . The mass spectrum had m/e (inter alia): 244 (weak), 229 (v.weak), 214 (v.weak), 176, 175, 161, 131, 108, 107, 105, 77, 69. The degree of di-alkylation suggested by the mass spectrum, was not supported by the integration ratios of the n.m.r. spectrum. The hydrochloride was prepared in the usual way (see p. 129) and because of complications in its recrystallisation (see p. 174; Discussion p. 70) it was characterised in its crude form; m.p. 207-209°C (a red-brown colouration developed at ca. 200°C); $\nu_{\text{max.}}$ (nujol) 3230 (s), 2700 (s), 1610 (s), 1590 (s), 1575 (s), 1540 (m), 1500 (s), 1245 (m), 1205 (m), 1170 (w), 1160 (w), 1080 (w), 1050 (w), 970 (w), 895 (s), 865 (s), 770 (s), 730 (m), 690 (s) cm^{-1} .

On several occasions, alkylation gave a product which contained some unreacted phenylhydrazine as judged by the integration of the n.m.r. spectrum. The infra-red spectrum of the hydrochloride contained absorptions in the same region as those taken to be diagnostic for the presence of phenylhydrazine hydrochloride (see p. 129) and so this test could not be applied to establish the purity of the alkylation product.

Attempted Purification of 1-(Pent-3-en-2-yl)-1-Phenylhydrazine Hydrochloride Using the Hydrochloride Procedure.

Although the n.m.r. spectra of the products from the alkylation of the sodium salt of phenylhydrazine indicated a fairly high degree of purity with respect to phenylhydrazine contamination, it was hoped to remove any phenylhydrazine present by selective benzene extraction of the hydrochloride of the crude 1-(pent-3-en-2-yl)-1-phenylhydrazine (see p. 130).

A stream of dry hydrogen chloride was passed through a solution of the crude hydrazine (21.82 g; 0.12 mol) in dry ether (150 ml) at 0°C. The precipitated hydrochloride was recovered in 72% yield (Yields of 65% and 70% were subsequently obtained).

(a) Successive Benzene Extraction: The crude hydrochloride was repeatedly extracted with benzene (ca. 1500 ml in total), and the combined extracts were concentrated to give a white solid. Basification of this solid with aqueous sodium carbonate solution followed by ether extraction gave a yellow liquid after removal of the solvent. The n.m.r. spectrum (CCl_4) of this liquid indicated that it was a mixture of the desired hydrazine and another compound of broadly similar structure, present in apparently equal amount. Later observations [see (b) below] suggested that this second component was 2-(pent-3-en-2-yl)-1-phenylhydrazine.

The residue of the extraction procedure, a white solid, was treated with 10% aqueous sodium hydroxide solution and the mixture was extracted with ether. Concentration of the dried extract gave a brown liquid (1.29 g) which was shown by n.m.r. spectroscopy (CCl_4) to be a mixture of phenylhydrazine and a very small amount of 1-(pent-3-en-2-yl)-1-phenylhydrazine. The recovery of phenylhydrazine was substantially higher than expected; the amount recovered corresponded to a contamination in the crude 1-(pent-3-en-2-yl)-1-phenylhydrazine of 17% by weight and 26 mole %.

(b) Continuous Benzene Extraction.

(i) Extraction of the Crude Hydrochloride with Hot Benzene: The hydrochloride (8.55 g; 0.04 mole), contained in a Soxhlet extractor was continuously extracted with dry benzene for three days. The extract was cooled to room temperature and a white precipitate was collected by filtration (1.22 g); $\nu_{\text{max.}}$ (nujol) 3180 (m), 3120 (w), 2730 (s), 1605 (s), 1585 (m), 1498 (m), 1305 (w), 1235 (w), 1140 (w), 1070 (w), 970 (m), 910 (m), 850 (w), 785 (s), 750 (s), 692 (s) cm^{-1} ; m/e 176, 149, 108, 107 (B).

Continuous extraction was resumed for a further 7 days. However, on cooling the benzene extract, no white precipitate was obtained. The extract was concentrated to give a viscous brown oil (2.30 g) which, unlike the hydrochloride earlier recovered from the benzene extract, was completely soluble in chloroform. The n.m.r. spectrum of this oil was poorly resolved and the complexity of the spectrum, particularly the methyl region, suggested that the material was a multi-component mixture. Although signals which could be attributed to the pentenyl moiety were observed, the complexity of the spectrum suggested that the extraction process was far from straightforward. The residue of the extraction procedure was recovered as a white solid (3.32 g).

(ii) Treatment of the Products and Residue of Continuous Benzene Extraction with Base: Each of the three fractions was treated with 20% aqueous sodium carbonate solution and the product was isolated by ether extraction in the usual way.

The white solid obtained from the benzene extract gave a yellow-brown liquid whose n.m.r. spectrum was significantly different to that of the original crude 1-(pent-3-en-2-yl)-1-phenylhydrazine. The signals of the pent-3-en-2-yl moiety were still present and a broad singlet suggested

the presence of the N-H function. The integration of the n.m.r. spectrum supported the view that the product might be 2-(pent-3-en-2-yl)-1-phenylhydrazine and the spectrum was assigned on that basis as follows:

δ (100 MHz) 1.02-1.08 [d, $J = 6$ Hz, 3H, $-\text{CH}(\underline{\text{CH}_3})-\text{CH}=\text{CH}-\text{CH}_3$], 1.60-1.68 [doublet with fine splitting, $J = 6$ Hz, 3H, $-\text{CH}(\text{CH}_3)-\text{CH}=\text{CH}-\underline{\text{CH}_3}$], 3.05-3.44 [m, 1H, $-\underline{\text{CH}}(\text{CH}_3)-\text{CH}=\text{CH}-\text{CH}_3$], 3.7-4.6 (broad s, 2H, -NH), 5.02-5.80 (m, 2H, olefinic), 6.52-6.90 and 7.02-7.36 p.p.m. (m, 5H, aromatic); $\nu_{\text{max.}}$ (film) 3280 (s, broad), 3005 (m), 2940 (s), 2915 (s), 2855 (m), 1590 (s), 1485 (s), 1455 (m), 1440 (m), 1370 (m), 1300 (w), 1250 (m), 1160 (w), 1145 (w), 1125 (w), 1065 (w), 1020 (w), 965 (m), 875 (w), 765 (s), 750 (s), 690 (s) cm^{-1} .

The mass spectrum recorded after the hydrazine had stood for a few days, had m/e 174, 159, 105, 77 (B). The n.m.r. spectrum of the same solution was recorded again ca. 24 h later and several new signals were observed in addition to those mentioned above. In order to examine the possibility that the changes in the n.m.r. spectrum were due to oxidation of the supposed 2-(pent-3-en-2-yl)-1-phenylhydrazine, the solution was diluted with carbon tetrachloride (2-3 ml) and treated with a small amount of yellow mercuric oxide. The mixture was stirred overnight in the dark under nitrogen, and the product was isolated in the usual way. The n.m.r. spectrum of the resultant liquid showed enhancement of the signals earlier attributed to the product of oxidation; the signals of the parent hydrazine compound had disappeared. The product was thought to be 2-phenylazopent-3-ene and its n.m.r. spectrum was assigned accordingly.

(This view was supported by the fact that the n.m.r. spectrum of the product of mercuric oxide oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine - expected to be 2-phenylazopent-3-ene by oxidative rearrangement - showed the same signals). The mercuric oxide oxidation was repeated on a larger scale: a mixture of the hydrazine (0.68 g; 0.0038 mole) and yellow mercuric oxide

(2.51 g; 0.011 mole) in methylene chloride (34 ml) was stirred at room temperature with exclusion of light for 46 h, before isolating the product in the usual way (see p. 147). Dry column chromatography [alumina, 50 cm x 3 cm/petroleum-ether (b.p. 40-60°C)] gave a diffuse bright-yellow band (Rf. ca. 0.6) from which was recovered a mobile orange-yellow liquid, (0.29 g), with a nauseatingly sweet smell; δ (CCl_4) 1.34-1.52 [d, J = 6 Hz, 3H, $-\text{CH}(\underline{\text{CH}_3})-\text{CH}=\text{CH}-\text{CH}_3$], 1.68-1.8 [d, J = 6 Hz, 3H, $-\text{CH}(\text{CH}_3)-\text{CH}=\text{CH}-\underline{\text{CH}_3}$], 4.05-4.50 [m, 1H, $-\underline{\text{CH}}(\text{CH}_3)-\text{CH}=\text{CH}-\text{CH}_3$], 5.6-5.82 (m, 2H, olefinic), 7.22-7.75 p.p.m. (m, 5H, aromatic); ν_{max} . (film) 3040 (w), 3005 (w), 2960 (s), 2910 (m), 2850 (m), 1585 (s), 1490 (s), 1440 (m), 1370 (w), 1355 (w), 1145 (w), 1015 (w), 960 (s), 765 (s), 745 (s), 690 (s) cm^{-1} .

The brown oil which was obtained from the second extraction was examined after a delay of several months; the n.m.r. spectrum was broadly similar though not identical to that of the freshly-obtained material. As the oil was insoluble in water, a solution in chloroform was treated with an excess of aqueous sodium carbonate solution and the chloroform layer was separated. After drying and concentrating the extract, a red-brown oil was obtained. The n.m.r. spectrum of this oil was not appreciably different to that of the material before treatment with base, and could not be reconciled with the product from the recrystallised hydrochloride (see preceding paragraph).

A portion of the extraction residue (1.02 g) was treated with 20% aqueous sodium carbonate solution and the mixture was extracted with ether. Concentration of the dried extract gave a yellow-brown liquid (0.68 g), the n.m.r. spectrum of which was very similar to that of the initial product from the recrystallised hydrochloride; on the basis of the assignment given to the latter product, the appearance of the spectrum, and its integration, suggested that the liquid was a mixture of 2-(pent-3-en-2-yl)-1-phenylhydrazine and phenylhydrazine (possibly as much as 30%).

A. benzene solution of this material was heated under reflux, with exposure to the atmosphere for one week. The solution was concentrated to give a red-brown liquid whose n.m.r. spectrum showed the same signals as that of the oxidation product derived from the recrystallised hydrochloride. Several other weaker signals were also observed: several spurious peaks in the methyl region (δ 0.9-2.0 p.p.m.), a doublet (δ 2.25 p.p.m., $J = 4\text{Hz}$), a multiplet (δ 5.3 - 5.6 p.p.m.) and a poorly resolved multiplet in the aromatic region. A solution of the crude 1-(pent-3-en-2-yl)-1-phenylhydrazine in benzene was similarly heated under reflux; concentration of this solution gave back the hydrazine unchanged.

These results indicated that the product of the second benzene extraction (the brown oil above, p.175) was not simply derived from the hydrochloride of the crude 1-(pent-3-en-2-yl)-1-phenylhydrazine undergoing in situ loss of hydrogen chloride and reacting further; nor was it derived simply from the "rearranged" hydrochloride (the white solid remaining in the extraction thimble - see above) behaving in similar fashion.

The continuous benzene extraction process was repeated twice more on samples of crude 1-(pent-3-en-2-yl)-1-phenylhydrazine of comparable purity with respect to phenylhydrazine contamination. The only modification was that the Soxhlet extraction was lagged with aluminium foil and cotton wool.

In both cases an orange coloured benzene extract was obtained from which no solid separated on cooling. The benzene extracts were treated with an excess of 20% aqueous sodium carbonate solution and the organic phase was isolated. In both cases, removal of benzene gave brown liquids (0.75 g and 5.02 g from 5.58 g and 19.02 g of crude hydrochloride, respectively), the n.m.r. spectra of which were complex and incompatible with that of 1-(pent-3-en-2-yl)-1-phenylhydrazine. A particular feature

of the n.m.r. spectra was that the integration of the methyl region was 2 to 3 times that of the aromatic region. The residues from these continuous extractions were worked up via aqueous sodium carbonate in the same way. The n.m.r. spectra of the liquids obtained indicated the presence of phenylhydrazine; the n.m.r. spectra also showed weaker complex signals similar to those of the products from the benzene extracts.

Attempted Recrystallisation of the Hydrochloride of Crude 1-(Pent-3-en-2-yl)-1-Phenylhydrazine from Ethanol

The hydrochloride used (0.80 g) was grey in colour, and the recrystallisation solution became red-brown in colour. Ether was added to the cooled solution to encourage crystallisation, and the white solid which separated (0.18 g) was collected by filtration; the filtrate was evaporated to give a brown solid which was washed with petroleum ether (b.p. 40-60°C) to give a light brown solid (0.57 g). Both samples were treated with 20% aqueous sodium carbonate solution and extracted with ether. Concentration of the dried extracts gave an orange-brown liquid (0.13 g) and a more mobile orange-red liquid (0.35 g) respectively. The infra-red spectrum of the former showed a very strong absorption in the N-H region, and the n.m.r. spectrum, though poorly resolved, showed signals attributable to phenylhydrazine, and weaker signals similar to those of the pentenyl moiety. The infra-red spectrum of the latter product also showed a strong N-H absorption; its n.m.r. spectrum closely resembled that of the product of basification of the hydrochloride recrystallised from benzene (successive benzene extraction; see p.174), and was interpreted in terms of a mixture of the 1,1- and 1,2-(pent-3-en-2-yl)-phenylhydrazine, the former predominating.

In another attempted recrystallisation the ethanolic solution was inadvertently allowed to evaporate to dryness. The recrystallisation procedure was repeated; a white solid was precipitated by the addition of ether, and evaporation of the mother liquor gave a further yield of white solid. Work-up, via aqueous sodium carbonate solution and ether extraction, gave a viscous brown oil and a more mobile orange-yellow liquid respectively. The n.m.r. spectrum of the former was complex and uninformative. The spectrum of the latter suggested that the liquid was 2-(pent-3-en-2-yl)-1-phenylhydrazine with no detectable amount of 1-(pent-3-en-2-yl)-1-phenylhydrazine. The N-H signals of the supposed 1,2-hydrazine appeared at different chemical shifts, and were obscured by the signals of the methine and olefinic protons of the pentenyl group; they were identified by exchange with deuterium oxide. (The N-H signals had previously been observed as a very broad singlet - see p176). The mass spectrum of the material had m/e (inter alia) 244 (v. weak), 176, 159, 146, 145, 144, 133, 132, 117, 108, 107, 105, 77, 69. Examination of the n.m.r. spectrum of the liquid after 5 days indicated that aerial oxidation to give 2-phenylazopent-3-ene was occurring (cf. p176).

(A cursory examination of the behaviour of the hydrochloride in boiling aqueous solution was also made. A solution of the hydrochloride (0.59 g) in water (25 ml) was heated under reflux for 6 h; a pale yellow-brown colour soon developed, and a film of brown oil separated. The water-insoluble oil was extracted with chloroform, as was the aqueous residue, after basification with aqueous sodium bicarbonate solution. Concentration of the extracts gave a brown gum (0.21 g) and a viscous orange liquid (0.13 g) respectively. The n.m.r. spectrum of the former, though poorly resolved, suggested that it was a complex mixture. The spectrum of the latter material indicated that it was very largely

2-(pent-3-en-2-yl)-1-phenylhydrazine. The spectrum also suggested the presence of a small amount of 1-(pent-3-en-2-yl)-1-phenylhydrazine and 2-phenylazopent-3-ene; the integration ratio of the aromatic region to the methyl region suggested the presence of some phenylhydrazine.)

Oxidation of 1-(Pent-3-en-2-yl)-1-Phenylhydrazine.

The oxidation was carried out on the crude hydrazine since purification by benzene extraction of the hydrochloride had proved inapplicable (see above).

a) With Yellow Mercuric Oxide. A mixture of the hydrazine (5.00 g; 0.028 mole) and yellow mercuric oxide (18.10 g; 0.083 mole) in 'Analar' chloroform (240 ml) was stirred under nitrogen with exclusion of light for ca. 40 h at room temperature. (The mercuric oxide developed a green colouration very shortly after mixing the reagents). The mixture was filtered to remove the inorganic residue, and the filtrate was concentrated under vacuum at room temperature to give an orange-yellow, mobile liquid (4.61 g; 92% recovery of material), with a nauseating, sweet smell. The n.m.r. spectrum of this material suggested that it was not a single component product; δ 1.38-1.54 [(d, $J = 6$ Hz), 1.65-1.85 (m)], 4.05-5.0 (m), 5.28-5.9 (m), 7.1-7.76 p.p.m. (m, aromatic). The integration of the spectrum was consistent with the original ratio of aromatic to pentenyl protons, and the appearance of the spectrum suggested the presence of two major components (each having the pent-3-en-2-yl substituent) in the ratio of ca. 3:2 [Expansion of the spectrum showed that the doublet in the methyl region was composed of two superimposed doublets each having a coupling constant of 6 Hz, and that the multiplet at δ 4.05-5.0 p.p.m. was in fact due to two separate multiplets of very similar structure both could be ascribed to the aliphatic methine proton, $-\underline{\text{CH}}(\text{CH}_3)\text{CH}=\text{CHCH}_3$, of the 3-penten-2-yl moiety]. A weak and poorly resolved signal with seemingly multiplet structure was

observed at δ 3.2-3.6 p.p.m., which, together with the other weak, apparently spurious signals observed in the methyl region suggested the presence of a further minor component or components (see the mass spectral and chromatographic evidence below).

The infra-red spectrum of the oxidation product showed no absorption in the N-H region and did not suggest any particular functionality:

ν_{max} . (film) 3040 (m), 3005 (m), 2960 (s), 2915 (s), 2850 (m), 1650 (broad, w), 1585 (broad, w), 1470 (m), 1440 (s), 1365 (m), 1285 (w), 1210 (w), 1150 (w), 1065 (m), 1015 (m), 960 (s), 920 (w), 890 (w), 760 (broad, s), 730 (w), 695 (s), 690 (s) cm^{-1} .

T.l.c. (silica gel/benzene) gave a diffuse yellow spot (Rf. 0.68) tailing back to the origin. Wet column chromatography (silica gel; 31 cm x 2.5 cm/benzene) of the oxidation product (4.18 g) gave a continuous band, the head of which was yellow but which became progressively orange-brown towards the origin. The eluent was collected in several portions: (i) 60 ml (ii) 80 ml (iii) 250 ml, and then concentrated.

(i) The n.m.r. spectrum of the mobile orange-yellow liquid (2.48 g) was identical to that of the material prior to chromatography. (This material was subsequently used in the hydrogenation study - see p. 186). The mass spectrum had m/e (inter alia) 174, 159, 105 (B), 77, consistent with 2-phenylazopent-3-ene.

(ii) The n.m.r. spectrum of the mobile orange-yellow liquid (0.75 g) was also virtually identical to that of the crude oxidation product. However, on prolonged heating in a hot water-bath, new signals were observed in the n.m.r. spectrum. [δ 1.22 (d, J = 6 Hz), 1.7 (d, J = 8 Hz), 1.95 - 2.08 (m), 2.2-2.3 (weak, m), 3.9-4.35 (m), 5.75-6.25 (m), 6.7-7.2 p.p.m. (m, aromatic) .] These new signals were consistent with the formation of a species still retaining the pent-3-en-2-yl group.

(iii) A red-brown oil (0.23 g) was recovered which, although it had the same smell as the oxidation product and the products from (i) and (ii), had a quite different n.m.r. spectrum. The spectrum was very poorly resolved, but showed a multiplicity of signals, particularly in the methyl region.

The oxidation was repeated several times using chloroform, methylene chloride and ether as solvent. The n.m.r. spectrum of the oxidation product was invariable and identical to that of the crude product above. Yields, based on the recovery of material, were in the region of 80-94%. On several occasions, it was suspected that the evolution of gas accompanied the addition of the hydrazine to the suspension of mercuric oxide. All attempts to separate the components of the oxidation product by chromatography using both wet column (silica gel/n-hexane) and dry column [6% deactivated alumina/petroleum ether (b.p. 40-60°C)] techniques were unsuccessful.

Examination of a typical sample of the oxidation product by high pressure liquid chromatography ['Wolfson Liquid Chromatography Unit' silica, 7 μ (125 mm x 5 mm); n-hexane; 270 p.s.i.] confirmed the presence of two major components, in the ratio of 1.35:1, with retention times of 11.1 min. and 10.5 min. respectively. Three very minor components (less than 1%) could also be observed in the chromatogram (cf. the n.m.r. spectrum which showed several weak signals attributable to the presence of very minor components).

The mass spectrum of a crude sample of a typical oxidation product showed weak peaks at m/e 242 and 227, in addition to those already ascribed to the expected azo-compound. These may be due to pent-3-en-2-one 1-(pent-3-en-2-yl)-1-phenylhydrazone; m/e 242 (P), m/e 227 (P-CH₃).

Two successive oxidation experiments were found to give a small amount of a white solid (m.p. ca. 230°, sublimation) in addition to the usual orange-yellow liquid. The n.m.r. spectrum of a very dilute solution of the solid, which was only very slightly soluble in deuteriochloroform, showed a large singlet at δ 7.3 p.p.m. and two weak, poorly-resolved multiplets at δ 1.27 and 1.62 p.p.m. The mass spectrum had m/e (inter alia) 406, 358, 314, 279, 202, 186, 172, 154, 112, 77. The same peaks, but of lower intensity, were observed in the mass spectrum of the liquid oxidation product in these two instances. As the solid could not be characterised in terms of the oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine, and since its formation was observed in only two of the several oxidation experiments, it was thought likely that it was derived from the particular batch of celite which had been used in the work-up process of these two oxidation experiments.

(b) With Lead Tetra-acetate. The oxidation was carried out using the method already described (see p. 146). The reaction mixture, consisting of lead tetra-acetate (1.55 g; 3.5 mmole) and the hydrazine (0.52 g; 3 mmole) in methylene chloride (50 ml) was stirred under nitrogen with exclusion of light for 40 min., before filtering to remove the inorganic residue. The filtrate was washed with aqueous sodium bicarbonate solution (2 x 25 ml), dried (MgSO_4), and concentrated to give a wine-red liquid (0.49 g; 94% recovery of material). The n.m.r. spectrum of this material was virtually identical to that of the product of mercuric oxide oxidation from (a), and t.l.c. (silica gel/benzene) gave the same bright yellow spot as previously observed in (a).

(c) With p-Benzoquinone. The use of benzoquinone was suggested by the work of Wieland and Fressel¹¹² who found that oxidation of 1,1-dibenzylhydrazine with benzoquinone gave the tetrabenzyltetraz-2-ene and not

bibenzyl as obtained from the oxidation with mercuric oxide; it was hoped that if the course of the oxidation of 1-(pent-3-en-2-yl)-1-phenylhydrazine could be similarly diverted towards tetrazene formation, the nature of the oxidation products from (a) and (b) could be resolved. The procedure used paralleled that of Wieland and Fressel.¹¹²

A solution of p-benzoquinone (0.40 g; 3.7 mmole) in ethanol (16 ml) at 0°C, was added dropwise under nitrogen, over a period of 25 min., to a stirred solution of the hydrazine (0.65 g; 3.7 mmole) in ethanol (5 ml) cooled in an ice-salt bath. The mixture, which developed an orange-red colour during the addition, was stirred for a further 10 min. A small amount of a green-black solid precipitated and this was collected by suction filtration as a shiny, black paste; it was identified by n.m.r. spectroscopy as being impure hydroquinone - the n.m.r. spectrum did not show any signals attributable to the pentenyl moiety. Concentration of the filtrate at 50°C under vacuum gave a similar paste which was extracted with petroleum ether (b.p. 40-60°C). The insoluble material was removed by filtration and the orange-red filtrate was concentrated at 50°C under vacuum to give a mobile orange-red liquid (0.58 g; 90% recovery of material), with an odour similar to that of the products from mercuric oxide and lead tetra-acetate oxidation. The n.m.r. and infra-red spectra of this material were virtually identical to those of the oxidation products from (a) and (b) above. Examination of the filtration residue by n.m.r. and infra-red spectroscopy, showed that it was very largely hydroquinone. The material was only slightly soluble in deuteriochloroform, but the absence of signals characteristic of the pentenyl moiety in the n.m.r. spectrum indicated that the anticipated tetrazene or its decomposition products were absent.

Hydrogenation of the Oxidation Product of 1-(Pent-3-en-2-yl)-1-phenylhydrazine

Hydrogen uptake was measured using a micro-hydrogenation apparatus operating at atmospheric pressure and 18°C.

A sample of 1-(pent-3-en-2-yl)-1-phenylhydrazine was oxidised with yellow mercuric oxide immediately prior to hydrogenation. The crude oxidation product was applied to a silica gel wet column and was eluted with n-hexane. The leading bright-yellow band which separated was collected and concentrated, to give the familiar mobile orange-yellow liquid which was then subjected to hydrogenation.

The oxidation product (29 mg) was added to a stirred suspension of 10% Pd/C (11.3 mg) in absolute alcohol (40 ml). The uptake of hydrogen was quite rapid initially but soon slowed down and had ceased after 21.5 h, when 16.50 ml (approx.) had been consumed. The volume required for 2 moles of hydrogen per mole of oxidation product (7.26 ml) was taken up within 3 h.

The experiment was repeated on a larger scale [oxidation product (0.425 g) and 10% Pd/C (168 mg) in absolute alcohol (15 ml)] and was stopped after the uptake of 2 mole equivalents of hydrogen. As in the small scale experiment, uptake was rapid initially but moderated after 25 min., and the experiment was stopped after 61 min. when the calculated volume of 107 ml of hydrogen had been consumed.

Isolation of the hydrogenation product gave a yellow-green coloured, mobile liquid (0.340 g). The infra-red spectrum of this material showed a strong absorption in the N-H region (ν 3290 cm^{-1}); the n.m.r. spectrum suggested the presence of three or more products, and had δ 0.7-2.3 (m), 2.6-4.0 (three overlapping multiplets), 4.6-5.1 (broad s), 5.1-5.9 (m), and 6.5-7.7 p.p.m. (m, aromatic). No trace of the signals attributed to 2-phenylazopent-3-ene remained. The signals of 2-(pent-2-yl)-1-phenylhydrazine (see below, p.188) could be identified, but stronger

than these signals were those of 2-phenylazopentane (see below, p. 188), presumably formed by air oxidation of the hydrazine. This result confirmed the identity of one of the components of the oxidation product as 2-phenylazopent-3-ene. Reduction of the second component of the oxidation product could not be confirmed as the broad singlet (δ 4.6-5.1 p.p.m.) obscured the region in which its most characteristic signals had been observed. The residual signals in the olefinic region, however, appeared in the same region as did the olefinic proton resonances of this second component. As stated above, the appearance of the n.m.r. spectrum of the hydrogenation product suggested the presence of at least three components derived from the reduction procedure; two of these were readily identified (above) but the third (giving rise to a multiplet of similar pattern to that observed for the methine proton of the pent-3-en-2-yl and the pent-2-yl groups; δ 3.05-3.45 p.p.m.) could not be firmly identified. Comparison of the spectrum with that of 2-(pent-3-en-2-yl)-1-phenylhydrazine (Experimental p. 176 and p. 180; Discussion p. 71) supported the possibility that the unidentified third product might be this hydrazine, the product of reduction of the N=N bond of 2-phenylazopent-3-ene.

The mass spectrum of the hydrogenation product had m/e (inter alia) 256 (w), 254, 178, 176, 175, 174, 173, 163 (w), 162 (w), 161 (w), 160 (w), 148 (w), 147, 146, 145, 144, 131, 130, 105, 93, 92, 91, 77, 69. The observation of peaks above m/e 178 was surprising in view of the fact that the mass spectrum of the material prior to hydrogenation showed a parent peak having m/e 174.

Preparation of 2-(Pent-2-yl)-1-Phenylhydrazine.

The hydrazine was prepared by reduction of pentan-2-one phenylhydrazone with lithium aluminium hydride.

A solution of pentan-2-one (1.73 g; 0.02 mole) and phenylhydrazine (2.16 g; 0.02 mole) in ethanol (40 ml) was heated under reflux under nitrogen for ca. 3h. The product was isolated as an orange-yellow liquid (3.50 g; 99%); δ (CCl_4) 0.72-2.40 (m, 10H, aliphatic), 6.55-7.35 p.p.m. (m, 6H, aromatic and -NH-) and was used without further purification.

The hydrazone (3.50 g; 0.02 mole) was added dropwise to a stirred suspension of lithium aluminium hydride (1.51 g; 0.04 mole) in ether (50 ml). The mixture was stirred for 1 h and was then heated under reflux under nitrogen for 2.5 h. The product was isolated in the usual way (see p. 132) and was obtained as a bright-yellow liquid (3.04 g; 85%, unpurified). The infra-red spectrum of this material showed a strong absorption in the N-H region [ν (film), 3300 cm^{-1}]. The n.m.r. spectrum had δ (CCl_4) 0.7-1.8 (m, 10H, methyl and methylene protons), 2.6-3.3 [m and broad s, 2H, $-\underline{\text{CH}}(\text{CH}_3)-\underline{\text{CH}}_2-$ and -NH-], 4.75-5.08 (broad s, 1H, -NH-), 6.25-7.75 p.p.m. (m, 5H, aromatic).

Preparation of 2-Phenylazopentane.

A solution of 2-(pent-2-yl)-1-phenylhydrazine in 'Analar' chloroform was oxidised with yellow mercuric oxide on a small scale. The mixture was stirred overnight, and the product was isolated as a mobile orange-yellow liquid; δ (CCl_4) 0.65-2.20 (m, 10H, methyl and methylene protons), 3.35-4.05 [m, 1H, $-\underline{\text{CH}}(\underline{\text{CH}}_3)-\underline{\text{CH}}_2-$], 7.1-7.8 p.p.m. (m, 5H, aromatic).

Attempted Characterisation of the Oxidation Products of 1-(Pent-3-en-2-yl)-1-Phenylhydrazine.

The possible oxidation products which were considered were

(a) those derived from the allylic rearrangement of the intermediate diazene,

and (b) those derived from the 'normal' oxidation pathway, the tetrazene and its decomposition products.

a) Products from the Allylic Rearrangement. The anticipated products were 2-phenylazopent-3-ene and pent-3-en-2-one phenylhydrazone; authentic samples of these compounds were required for comparison.

i) Attempted Preparation of 2-Phenylazopent-3-ene

It was hoped to prepare this compound by the oxidation of 2-(pent-3-en-2-yl)-1-phenylhydrazine. Two attempts were made to prepare the hydrazine: firstly by alkylation of the sodium salt of 2-formyl-1-phenylhydrazine (see p.152) with 2-chloropent-3-ene, and secondly by alkylation of the sodium salt of 1,2-diformyl-1-phenylhydrazine (see p.159) with the same alkylating agent. The former method gave (after removal of the formyl group) a poor yield of a red-brown liquid whose n.m.r. spectrum appeared to show the signals of the pentenyl moiety; however, the integration of the spectrum did not correspond with that expected for the 1,2-disubstituted hydrazine. The second method, which had been successfully used to prepare 2-allyl-1-phenylhydrazine in 85% yield (see p.159), gave (after removal of the formyl groups) a very poor yield of a red-brown liquid (0.49 g from 3.28 g of 2-formyl-1-phenylhydrazine). The n.m.r. spectrum of the product showed several signals in the methyl region and had a much higher N-H integration (based on the integration of the olefinic signals of the pentenyl moiety) than expected for the desired hydrazine. The product from the first continuous benzene extraction of 1-(pent-3-en-2-yl)-1-phenylhydrazine hydrochloride was thought to be the hydrochloride of 2-(pent-3-en-2-yl)-1-phenylhydrazine, formed by rearrangement (see p.175; Discussion p. 73). The n.m.r. spectrum of the free 1,2-disubstituted hydrazine, regenerated from the 'rearranged' hydrochloride, was quite different to those of the products of the attempted preparations described here.

Furthermore, the spectra of the alkylation products were not compatible with the spectra of the corresponding azo-compound formed by oxidation of 2-(pent-3-en-2-yl)-1-phenylhydrazine.

ii) Preparation of Pent-3-en-2-one Phenylhydrazone

Freshly distilled pent-3-en-2-one (2.89 g; 0.034 mole; b.p. 120-122°C), prepared by the method of House et al.,¹⁷³ was added in one portion to a solution of phenylhydrazine (3.71 g; 0.034 mole) in absolute alcohol (20 ml). An exothermic reaction took place on mixing, and the reaction mixture was stirred at room temperature, under nitrogen, for 3 days. The solution was dried over magnesium sulphate, and was concentrated under vacuum at room temperature to give a brown gum. The product was shown by n.m.r. spectroscopy to contain a small amount of residual ethanol, but no attempt was made to purify the product further (e.g. by distillation) in order to avoid possible decomposition or rearrangement. The remainder of the n.m.r. spectrum of this material was consistent with that expected for pent-3-en-2-one phenylhydrazone, although the integration of the aromatic region was larger than expected. (This was thought to be due to the presence of residual phenylhydrazine). The integration ratio of olefinic protons to methyl protons indicated that no cyclisation to give 3,5-dimethyl-1-phenyl-2-pyrazoline had occurred. The observed n.m.r. spectrum had: δ 1.78 (s), 1.88 (s), 3.0-3.5 (m), 5.55-6.6 (m, olefinic; d of q and d), 6.6-7.4 p.p.m. (m, aromatic). The mass spectrum had m/e (inter alia) 174 (P,B) and 159 (P-CH₃), in accord with that expected for pent-3-en-2-one phenylhydrazone.

(b) Products from the 'Normal' Oxidation Pathway.

The species which were examined were N-(pent-3-en-2-yl)aniline and 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine.

i) Preparation of N-(Pent-3-en-2-yl)aniline

Two synthetic routes were examined. Attempted Alkylation of Acetanilide: The method used was that of Fones⁸⁶ and paralleled the procedure which was used successfully to prepare N-allylaniline (Experimental p. 124). A mixture of the sodium salt of acetanilide (0.05 mole) and 2-chloropent-3-ene (14.90 g; 0.14 mole) in xylene (180 ml) was stirred at room temperature under nitrogen for ca. 18 h before heating under reflux for ca. 48 h. The mixture was cooled and filtered to remove a pale brown solid; concentration of the bright-yellow filtrate gave a cloudy yellow-brown oil (6.56 g). The n.m.r. spectrum of this material indicated the presence of the pentenyl moiety, but the multiplicity of signals observed in the methyl region suggested that the product was a multi-component mixture. The infra-red spectrum of the product showed an absorption in the N-H region (ν 3300 cm^{-1}) and a strong, broad absorption in the carbonyl region (ν 1660 cm^{-1}). The mass spectrum of the product had m/e (inter alia) 203 (P), 188, 174, 160, 146, 135, 93 (B); the presence of a peak at m/e 203 indicated that alkylation had occurred. In an attempt to purify the product, the oil was washed with petroleum-ether (50 ml; b.p. 40-60°C): the extract was decanted off leaving a clear, brown, oily residue. A white solid separated from the extract on standing. This solid was collected by filtration and was identified by n.m.r. spectroscopy as being acetanilide (0.28 g); the filtrate was concentrated to give a cloudy yellow-brown oil (3.42 g), the n.m.r. spectrum of which closely resembled that of the crude alkylation product, except that the almost complete disappearance of the signals due to acetanilide was observed. The residue of the petroleum ether extraction, a clear brown oil, gave a tacky solid after cooling to 0°C and scratching with a glass rod. This tacky solid was washed with petroleum ether (b.p. 40-60°C) and examined by n.m.r. spectroscopy.

The spectrum of the washed material (1.86 g) identified it as being very largely acetanilide; the observation of weaker signals attributable to the pentenyl moiety, suggested the possible presence of the desired N-(pent-3-en-2-yl) acetanilide (ca. 25%). Concentration of the petroleum ether washings gave a brown gum (1.00 g), the n.m.r. spectrum of which was virtually identical to that of the brown oil recovered from the original petroleum ether extraction process. Dry column chromatography [silica gel/petroleum ether (b.p. 40-60°C)] gave material which had the following n.m.r. spectrum: δ 0.75-2.4 (m; eight significant peaks could be identified within this multiplet), 3.35-3.9 (m), 5.05-5.7 (m), and 6.9-7.8 p.p.m. (m, aromatic), with integrals in the ratio 17.5:1:4.5:9.2. In brief, the alkylation of the sodium salt of acetanilide with 2-chloropent-3-ene gave a mixture of acetanilide (2.14 g), possibly containing a small amount of N-(pent-3-en-2-yl)acetanilide, and a brown oil (4.42 g) which appeared to be a mixture of components.

A portion of the crude alkylation material (1.72 g) was heated under reflux with 3 M hydrochloric acid (50 ml) for ca. 4 h. The mixture was cooled and washed with ether before basifying by the addition of potassium carbonate. Isolation of the product in the usual way gave a brown liquid (0.72 g) which was shown by n.m.r. spectroscopy to be largely aniline. The spectrum also showed the signals expected for the pent-3-en-2-yl group; comparison with the n.m.r. spectrum of an authentic sample of N-(pent-3-en-2-yl)aniline (see below) indicated that the second component was not the desired amine.

Alkylation of Aniline with 2-Chloropent-3-ene:

The procedure used paralleled that of Hickinbottom.⁸⁴ A mixture of freshly distilled aniline (9.30 g; 0.1 mole) and 2-chloropent-3-ene (4.20 g; 0.04 mole) was heated at 70°C under dry nitrogen for ca. 20 h.

The mixture was filtered to remove the precipitate of aniline hydrochloride and the filtrate was treated with a solution of zinc chloride (7.00 g) in water (7 ml). The resulting thick paste was repeatedly extracted with petroleum ether (b.p. 40-60°C) and the product was isolated from the extract as a mobile brown liquid (4.96 g; 77%). Distillation gave N-(pent-3-en-2-yl) aniline as a faintly yellow, mobile liquid (2.23 g) which became deep yellow coloured after standing for several weeks; b.p. 55-57°C/0.02 mmHg; δ (100 MHz) 1.18-1.25 [d, $J = 6$ Hz, 3H, $-\text{CH}(\text{CH}_3)-\text{CH}=\text{CH}(\text{CH}_3)$], 1.60-1.66 [d, $J = 5$ Hz, 3H, $-\text{CH}(\text{CH}_3)-\text{CH}=\text{CH}(\text{CH}_3)$], 3.24-3.65 (broad s, 1H, $>\text{NH}$), 3.73-4.03 [m, 1H, $-\text{CH}(\text{CH}_3)-$], 5.24-5.82 (m, 2H, olefinic), 6.45-6.72 and 7.01-7.22 p.p.m. (m, 5H, aromatic); ν_{max} . (film) 3400 (s), 3020 (s), 2965 (s), 2920 (s), 1600 (s), 1505 (s), 1450 (m), 1430 (m), 1375 (m), 1320 (s), 1260 (m), 1180 (m), 1160 (m), 1075 (w), 970 (s), 870 (w), 755 (s), 695 (s) cm^{-1} ; m/e 161 (P), 146, 93 (B). Accurate mass measurement 161.120898 ($\text{C}_{11}\text{H}_{15}\text{N}$ requires 161.12044).

In a control experiment to examine the behaviour of N-(pent-3-en-2-yl) aniline under the conditions of acid-catalysed hydrolysis used in the acetanilide alkylation approach (see p. 192), a sample of the amine (0.40 g) was dissolved in 3 M hydrochloric acid (25 ml) and the resulting solution was heated under reflux for 2.5 h. The cooled solution was basified by the addition of solid potassium carbonate, and was then extracted with ether. Isolation of the product gave a yellow-brown liquid (0.32 g), the n.m.r. spectrum of which was very similar to that of the hydrolysis product obtained in acetanilide alkylation.

A further control experiment in which a mixture of N-(pent-3-en-2-yl)-aniline and yellow mercuric oxide in chloroform, was stirred under nitrogen for ca. 48 h, showed that the amine was stable to mercuric oxide oxidation.

(ii) Preparation of 1,2-Di(pent-3-en-2-yl)-1,2-Diphenylhydrazine.

Prior to attempting the synthesis of this compound, an attempt was made to find supporting evidence in favour of its possible presence in the oxidation product of 1-(pent-3-en-2-yl)-1-phenylhydrazine. It was intended to prepare a sample of 1,2-dibenzyl-1,2-diphenylhydrazine, and to compare its n.m.r. spectrum with that of the corresponding azo-compound, phenylazotoluene (Discussion p. 88). The method of Frazen and Zimmerman¹³⁵ was used: a solution of 1,4-dibenzyl-1,4-diphenyltetraz-2-ene in xylene was heated under reflux for 1 h. The resulting orange-brown solution was concentrated under vacuum, and the product was distilled to give a pale yellow-green oil (b.p. 170-180°C/3 mm Hg). This material was identified as being N-benzylaniline by comparison of its n.m.r. spectrum with that of an authentic sample, and by its mass spectrum which showed a parent peak at m/e 183, corresponding to the molecular ion of N-benzylaniline.

The first attempted preparation of the title compound involved adaptation of the method of Wieland and Gambarjan¹³⁶ who reported the preparation of 1,1,2,2-tetraphenylhydrazine by oxidative coupling of N-phenylaniline.

A mixture of N-(pent-3-en-2-yl)aniline (0.81 g; 0.005 mole) and lead dioxide (1.14 g; 0.005 mole) in dry benzene (28 ml) was stirred under nitrogen in the dark for 48 h. The maroon coloured mixture was filtered through a pad of celite and the filtrate was concentrated to give a mobile wine-red liquid (0.79 g). The infra-red and n.m.r. spectra of this liquid indicated that it was N-(pent-3-en-2-yl)aniline.

In an altogether different approach, an attempt was made to prepare the title compound by adaptation of the method of Reesor and Wright,¹³⁷ which involved the alkylation of the di-anion of hydrazobenzene.

A solution of azobenzene (5.46 g; 0.03 mole) in dry 1,2-dimethoxyethane (120 ml) was treated with finely divided sodium metal (2.72 g; 0.12 mole) and the resultant mixture was stirred at room temperature under dry nitrogen for 28 h. The salt, in the form of a red-brown suspension, was transferred to a second reaction vessel under vacuum and was cooled in an ice-salt bath, before adding dropwise a solution of 2-chloropent-3-ene in dimethoxyethane (15 ml). The temperature of the mixture was not allowed to rise above 5°C during the addition process. The reaction mixture was maintained at this temperature for 30 min (during which time the colour changed to blue) and was then warmed to ca. 20°C. After stirring at this temperature for ca. 4 h, an orange-yellow colour had developed and a pale precipitate had separated; stirring, still under nitrogen, was continued for 9 days. The mixture was then concentrated under vacuum, and the residue was treated with ether (90 ml) and water (90 ml): the ether extract was washed with water, and the combined aqueous extracts were extracted further with ether. The combined ether extracts were dried and evaporated under vacuum at 25°C, to give the crude reaction product as an orange-red gum (7.61 g). By analogy with the examples quoted by Reesor and Wright, it was anticipated that the reaction product might be a mixture of azobenzene, 1-(pent-3-en-2-yl)-1,2-diphenylhydrazine, 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine and hydrazobenzene. The mass spectrum of the product showed peaks at m/e 182, 184, 252, and 320 corresponding to the parent ions of these compounds. A peak of appreciable intensity was observed at m/e 183 which could be attributed either to hydrazobenzene (P-1) or to the mono-alkylated product (P-69). The peak intensities decreased in the sequence 182, 183, 184, 252 and 320. A significant feature of the infra-red spectrum of the alkylation product was the presence of a strong N-H absorption at ν 3290 cm^{-1} . The n.m.r. spectrum showed the signals of the pent-3-en-2-yl moiety, but the individual signals of the mono- and di-alkylated products could not be identified. The integration of the n.m.r. spectrum indicated that alkylation had taken place to a considerable extent (the integration

ratio of aromatic protons to methyl protons was 5:2.9). Comparison of the n.m.r. spectrum with that of the oxidation product of 1-(pent-3-en-2-yl)-1-phenylhydrazine showed that the signals due to the aliphatic methine proton $-\underline{\text{CH}}(\text{CH}_3)\text{CH}=\text{CHCH}_3$ of the unidentified oxidation product appeared in very nearly the same region of the spectrum as did the signals of the corresponding proton in the alkylation products: the oxidation product spectrum showed a multiplet at δ 4.5-5.0 p.p.m., and the spectrum of the alkylation product showed a multiplet at δ 4.2-5.0 p.p.m.

T.l.c. examination (silica gel/n-hexane) showed the presence of four components, one of which was shown to be azobenzene: the developed t.l.c. plate showed a spot at the origin and three overlapping spots (one of which was shown to be due to azobenzene) centred at Rf. 0.23. Examination of the product by h.p.l.c. ['Wolfson Liquid Chromatography Unit' silica, 7 μ (125 mm x 5 mm); n-hexane; 270 p.s.i.] showed the presence of three components, one of which was shown to be azobenzene. Azobenzene had a retention time of 3.9 min. and the other two components had retention times of 10.4 min. (A) and 12.0 min. (B).

A mixture of the alkylation product mixture and the oxidation products of 1-(pent-3-en-2-yl)-1-phenylhydrazine was also examined by h.p.l.c. ['Wolfson Liquid Chromatography Unit' silica, 7 μ (125 mm x 5 mm); n-hexane; 400 p.s.i.]. The resultant chromatogram showed four significant peaks suggesting that both these product mixtures shared a common component. The appearance of the chromatogram suggested that the common component was (A), and that this was the major component of the oxidation product.

Preparative h.p.l.c. to isolate each of the unidentified components (A) and (B) gave trace amounts of grey solid material which were examined by mass spectrometry. The mass spectrum of component (A) had m/e (inter alia) 252, 184 and 183; of these, the peak at m/e 183 was the most intense.

The mass spectrum of component (B) was similar to that of (A) and showed the same significant peaks at m/e 252, 184 and 183, with the last-mentioned being by far the most intense. Neither of the mass spectra showed a peak at m/e 320, corresponding to the parent ion of the 1,2-di(pent-3-en-2-yl)-1,2-diphenylhydrazine.

Attempted Preparation of N,N-Di-allylhydrazines and the Corresponding N,N'-Di-allyl Azo-Compounds.

The proposed method of preparing the required hydrazines (57', see Discussion p. 99) was by direct amination of the corresponding secondary amine (prepared by alkylation of 3-methyl-2-phenylbut-2-en-1-ylamine) or by reduction of the N-nitroso derivative of the same amine. It was hoped to prepare the azo-compounds by a method based on the alkylation of diethyl hydrazodicarboxylate.⁸⁰ The synthesis of the necessary alkylating agents was first examined.

A. Preparation of Alkylating Agents.-

Preparation of α -(Chloromethyl)styrene.- The chloride was prepared by two different methods.

(i) From Chloro-acetone. Phenylmagnesium bromide was prepared by the addition of a solution of bromobenzene (7.80 g; 0.05 mole) in ether (60 ml) to a stirred suspension of magnesium (1.20 g; 0.05 mole) in ether (10 ml). The mixture was refluxed for 25 min., cooled on ice, and then treated with a solution of chloro-acetone (4.63 g; 0.05 mole) in ether (15 ml). The mixture was heated under reflux for 15 min. before decomposing the intermediate by addition of a saturated aqueous ammonium chloride solution. The product was isolated as an orange liquid (8.23 g), the infra-red spectrum of which showed a strong absorption in the O-H region ($\nu_{\text{max.}} 3450 \text{ cm}^{-1}$) and also indicated the presence of residual chloro-acetone. The unpurified product (7.26 g) was stirred with warm 18 M sulphuric acid (20 ml) for 20 min, and after normal work up, a mobile dark-brown liquid was obtained; this was distilled to give a pale-pink liquid (1.58 g), b.p. 0.4 mm.Hg/54-56°C. The n.m.r. spectrum (CCl_4) of this material showed signals in the olefinic region and the infra-red spectrum showed only a very weak absorption in the O-H region, indicating successful dehydration. T.l.c. (alumina/n-pentane) showed

three spots, Rf. 0.00, 0.48 and 0.72. The components were separated by dry column chromatography (alumina with fluorescent indicator, 50 cm x 1.3 cm/n-pentane). The band at the origin gave a trace amount of liquid whose n.m.r. spectrum suggested was residual carbinol. Two bands (Rf. 0.52 and 0.75) were isolated and a clear, colourless liquid was recovered from each (0.31 g and 0.32 g respectively). The n.m.r. spectra of these latter fractions suggested that each was a single product. The spectrum of the former agreed exactly with the reported chemical shift data for α -(chloromethyl)styrene.¹⁷⁴ Similarly, the spectrum of the latter agreed with the data reported for β -chloro- α -methylstyrene.¹⁷⁴

(ii) From α -Methylstyrene. Chlorination of α -methylstyrene was achieved by the method of Reed.¹⁷⁴ A mixture of α -methylstyrene (56.63 g; 0.48 mole), N-chlorosuccinimide (40.11 g, 0.30 mole) and carbon tetrachloride (30 ml) was heated under moderate reflux for 2.5 h and the N-chlorosuccinimide eventually dissolved. The mixture was left to stand overnight, and the precipitated succinimide was removed by filtration and washed with petroleum-ether (b.p. 40-60°C). The combined filtrate and washings were concentrated under vacuum to give a cloudy, brown liquid (60.58 g) which was shown by n.m.r. spectroscopy to be a mixture of α -methylstyrene, α -(chloromethyl)-styrene and β -chloro- α -methylstyrene. Fractional distillation on a spinning band column (18 in), monitoring the composition of the distillate by n.m.r. spectroscopy, gave pure β -chloro- α -methylstyrene (9.84 g; b.p. 68°C/5.5 mmHg. lit.¹⁷⁴ b.p. 76°C/4.0 mmHg) and pure α -(chloromethyl)-styrene (11.03 g; b.p. 70-72°C/5.5 mmHg; lit.¹⁷⁴ b.p. 53°C/0.65 mmHg). The n.m.r. spectrum of α -(chloromethyl)styrene agreed with the reported data¹⁷⁴; δ (CCl₄) 4.35 (s, 2H, $-\underline{\text{CH}_2\text{Cl}}$), 5.38 (s, 1H, olefinic), 5.46 (s, 1H, olefinic), 7.1-7.45 p.p.m. (m, 5H, aromatic).

Preparation of α -(Bromomethyl)Styrene.

(i) Attempted Preparation from α -Bromo-acetophenone. The procedure was analogous to that used in the formation of α -(chloromethyl)styrene from chloro-acetone. Methylmagnesium iodide was prepared by the addition of a solution of iodomethane (1.42 g; 0.01 mole) in ether (10 ml) to a stirred suspension of magnesium (0.28 g; 0.01 mole) in dry ether (10 ml). The mixture was heated under reflux for 1 h and then cooled

before the addition of α -bromo-acetophenone (2.00 g; 0.01 mole) in ether (10 ml). Two attempts were made using different conditions:

(a) Addition of α -bromo-acetophenone to the Grignard reagent at room temperature. α -Bromo-acetophenone was added in small portions and the mixture was refluxed for ca. 2h. Normal work-up (see p. 198), gave a red-brown oil (1.74 g). The n.m.r. spectrum of this material showed a multiplicity of signals in the region δ 0.5-3.9 p.p.m. and a multiplet in the aromatic region δ 6.9-8.1 p.p.m. Significantly no signals were observed in the methylene region (Signals due to the expected carbinol were observed in the n.m.r. spectrum of the reaction product of phenylmagnesium bromide with chloro-acetone.). This suggested that neither residual α -bromo-acetophenone nor the expected carbinol was present in the product. No signals were observed in the olefinic region.

The infra-red spectrum showed an absorption in the O-H region and in the carbonyl region; $\nu_{\text{max.}}$ 3400 (s, broad), 1675 (s) cm^{-1} .

b) Addition of α -bromo-acetophenone to the Grignard reagent at -78°C . The Grignard reagent was cooled in an acetone / CO_2 bath before adding the α -bromo-acetophenone solution. The reaction mixture was allowed to warm to room temperature overnight. The mixture, an orange slurry was divided into two portions; portion (i) was worked up immediately and the other (ii) was heated under reflux for ca. 2 h before working up.

In each case, the product was a mixture of two immiscible liquids, one purple and one colourless (0.57 g, and 1.60 g respectively).

Portion (i): the infra-red spectrum showed an absorption in the O-H region and in the carbonyl region; $\nu_{\text{max.}}$ 3400 (s, broad) and 1685 (s) cm^{-1} . The n.m.r. spectrum (CCl_4) showed a greater number of signals than expected, and indicated that very little, if any, residual α -bromo-acetophenone was present. The signals observed at 4.24 (s) and 5.38-5.5 (m) were subsequently shown to be due to α -(bromomethyl)styrene (see p. 202). The rest of the spectrum had δ 0.7-1.85 (m), 2.0-2.35 (m), 2.5 (s), 3.18-4.0 (m), 4.82 (s), 6.7-8.1 p.p.m. (m). Comparison with the spectrum of the product from the reaction of chloro-acetone with phenyl-magnesium bromide, suggested that the singlet at δ 1.65 p.p.m. (part of the multiplet at δ 0.7-1.85 p.p.m.) might be due to the methyl group of the analogous carbinol product.

Portion (ii): the infra-red spectrum showed an absorption in the O-H region and in the carbonyl region; $\nu_{\text{max.}}$ 3420 (s) and 1675 (s) cm^{-1} . The n.m.r. spectrum was more complex than expected and indicated that only very little, if any, α -bromo-acetophenone was present. No signals were observed in the olefinic region although the spectrum did show some points of similarity to that of the product from (i). The spectrum showed δ 0.7-1.6 (m), 1.67 (s), 2.15 (s), 2.60 (s), 2.95 (s), 3.08 (s), 3.3-3.95 (m), 4.34 (s), 6.5 (s), 6.8-8.1 p.p.m. (m). The observation of the singlet at δ 1.67 p.p.m. suggested the possible presence of the expected carbinol product. The n.m.r. solution was shaken with deuterium oxide but no distinct O-H proton assignment could be made; a new signal appeared at δ 4.7 p.p.m.

(ii) From α -Methylstyrene. Bromination of α -methylstyrene was achieved by the method of Reed.¹⁷⁴ A mixture of α -methylstyrene (92.17 g; 0.78 mole), N-bromosuccinimide and (87.92 g; 0.49 mole) and carbon tetrachloride (50 ml) was heated in an oil bath at 160-170°C. The oil bath was removed intermittently to moderate the vigorous foaming which occurred. Refluxing was continued until all the N-bromosuccinimide had dissolved (ca. 4 min.) and the mixture was left to cool slowly over a period of 3 h. The filtrate was removed by suction filtration and the residue was washed with ether. The combined filtrate and washings were concentrated under vacuum and the residual α -methylstyrene was removed by distillation (b.p. 42°C/0.4 mmHg), leaving an orange liquid (103.10 g). The n.m.r. spectrum of this liquid indicated the presence of the two expected isomeric bromides; the presence of a small amount of α -methylstyrene and another impurity, possibly derived from the brominating agent, was also indicated. The product was diluted with petroleum-ether (600 ml; b.p. 40-60°C) and a small amount of a white solid separated. The infra-red spectrum of the solid indicated it to be succinimide.

An attempt was made to distil the product on a spinning band column; the last traces of α -methylstyrene were removed, but because of an electrical fault, the distillation could not be continued. The residue was distilled in the normal way to give a clear, colourless liquid (55.00 g; b.p. 68-80°C/0.4 mmHg). The n.m.r. spectrum of this material indicated that it was a mixture of α -(bromomethyl)styrene (76%) and β -bromo- α -methylstyrene (24%); a small amount of succinimide was also shown to be present. α -(Bromomethyl)styrene had δ (CCl₄) 4.26 (s, $-\text{CH}_2-\text{Br}$), 5.36 (s, 1H, olefinic), 5.52 (s, 1H, olefinic), 7.1-7.7 p.p.m. (m, aromatic). No attempt was made to purify the α -(bromomethyl)styrene further; it was used directly.

Attempted Preparation of α -Bromomethyl- β,β -Dimethylstyrene. The method was based on the successful preparation of α -(chloromethyl)styrene by the action of phenylmagnesium bromide on chloro-acetone.

The Grignard reagent was prepared by the addition of a solution of 2-bromopropane (2.46 g; 0.02 mole) in ether (5 ml) to a stirred suspension of magnesium (0.50 g; 0.02 mole) in ether (15 ml). The mixture was heated under reflux for ca. 1 h before adding a solution of α -bromo-acetophenone (4.00 g; 0.02 mole) in ether (20 ml) over a period of ca. 30 min. The reaction was performed at two different temperatures:

(a) At room temperature: vigorous boiling accompanied each addition and a two-phase mixture of a brown oil and a bright yellow solution, was formed. The mixture was heated under reflux for 6 h, left to stand overnight, and was then worked up (see p. 198). Ether extraction followed by removal of solvent gave a cloudy, viscous, orange liquid (3.46 g). The infra-red spectrum of this liquid showed a strong absorption in the O-H region and in the carbonyl region ($\nu_{\text{max.}}$ 3450 and 1685 cm^{-1}). Its n.m.r. spectrum (CCl_4) showed a multiplicity of signals and indicated that little, if any, α -bromo-acetophenone was present; δ 0.5-1.8 (m), 2.46 (s), 3.0-4.0 (m), 4.25 (s), 5.06 (s), 6.0 (s), 6.36 (s), 6.7-8.1 p.p.m. (m).

(b) At -78°C : the Grignard reagent (0.01 mole) was cooled in an acetone/ CO_2 bath before adding the α -bromo-acetophenone solution (0.01 mole). A yellow precipitate appeared to form and a further portion of ether (10 ml) was added to keep the system homogeneous. The mixture was allowed to warm slowly to room temperature. The reaction mixture, consisting of a brown gum and a cloudy yellow solution, was divided into two portions; portion (i) was worked up immediately, and portion (ii) was heated under reflux for ca. 2 h before working up. In each case, a red-brown oil was obtained (0.88 g and 0.90 g respectively).

Portion (i): the infra-red spectrum was similar to that of the product from (a) and showed a strong absorption in the O-H region and in the carbonyl region (ν_{max} 3450 and 1685 cm^{-1}). The n.m.r. spectrum had δ 0.6-1.5 (m), 2.5 (s), 2.62-2.82 (m), 3.2-4.1 (m), 4.28 (s), 5.1 (s), 6.02 (s), 7.0-8.1 p.p.m. (m). The ratio of the integrations of the singlets (δ 2.5 and 4.28 p.p.m.) and the aromatic multiplet (δ 7.0-8.1 p.p.m.) was 1:5:26. The solution was shaken with deuterium oxide; the singlet at δ 5.1 p.p.m. disappeared, and a new signal was observed at δ 4.6 p.p.m.

Portion (ii): the infra-red spectrum was virtually identical to that of the products from (a) and (i) and showed a strong absorption in the O-H and in the carbonyl region (ν_{max} 3450 and 1690 cm^{-1}). The n.m.r. spectrum broadly resembled that of the product from (i) and had δ 0.6-1.5 (m), 1.9 (s), 2.0 (s), 2.48 (s), 2.65-3.9 (m), 4.25 (s), 4.6-5.1 (m), 6.38 (s), 6.8-8.1 p.p.m. (m). The ratio of the integrations of the singlets (δ 2.48 and 4.25 p.p.m.) and the aromatic multiplet (δ 7.0-8.1 p.p.m.) was 1:2.75:17.5. T.l.c. (alumina/petroleum-ether, b.p. 40-60°C) showed the presence of at least four components.

Attempted Preparation of α -(2-Chloroprop-2-yl)Styrene. The preparation was attempted by the chlorination of α -prop-2-ylstyrene.

(i) Preparation of α -Prop-2-ylstyrene. Two methods were used, both based on the procedure of Klages.¹⁷⁵

Method (a): methylmagnesium iodide was prepared by the addition of a solution of iodomethane (6.42 g; 0.045 mole) in ether (15 ml) to a stirred suspension of magnesium (1.08 g; 0.045 mole); the reaction mixture was then heated under reflux for 1 h. A solution of isobutyrophenone (4.45 g; 0.03 mole) in ether (15 ml) was added dropwise to the Grignard reagent at 0°C. The mixture was allowed to warm to room

temperature during ca. 2 h, with continued stirring. Isolation of the product in the usual way (see p. 198) gave a bright yellow liquid (4.23 g; 86%). The infra-red spectrum of the product showed a strong O-H absorption, with no absorption in the carbonyl region.

A stream of dry hydrogen chloride was passed through the neat carbinol at 0°C for ca. 5 min and a mixture of two immiscible liquids formed. The mixture was extracted with ether and the extract was washed with aqueous sodium bicarbonate solution before concentrating to give the desired chloride as a bright-yellow liquid (4.45 g; 94%). The n.m.r. spectrum (CCl_4) suggested that the material was pure and the infra-red spectrum showed no residual absorption in the O-H region.

A solution of the chloride (4.45 g; 0.024 mole) in dry pyridine (9.60 g; 0.120 mole) was heated under reflux, with stirring, for ca. 4 h. The reaction mixture was cooled, and the white precipitate was removed by filtration. The filtrate was dissolved in ether and successively washed with 2 M hydrochloric acid (3 x 50 ml) and water (50 ml). The product was isolated as a mobile, pale-brown liquid (3.38 g). The n.m.r. spectrum (CCl_4) of the product was consistent with that expected for α -prop-2-ylstyrene, but it did show four seemingly spurious signals (δ 1.4-2.02 p.p.m.). δ 1.0-1.25 (d, $J=8\text{Hz}$, 6H methyls), 2.5-3.1 (m, 1H, $-\text{CH}(\text{CH}_3)_2$), 4.88-5.12 (m, 2H, olefinic), 7.0-7.34 p.p.m. (m, 5H, aromatic); $\nu_{\text{max.}}$ (film) 3050 (m), 2950 (s), 2860 (m), 1635 (m), 1605 (w), 1585 (w), 1505 (m), 1475 (m), 1455 (m), 1390 (m), 1370 (w), 1290 (w), 1265 (w), 1160 (w), 1095 (m), 1070 (w), 1030 (m), 900 (s), 780 (s), 765 (m), 725 (m), 695 (s) cm^{-1} .

In order to examine the possibility that the unassigned signals in the n.m.r. spectrum might be due to α,β -trimethylstyrene, the solution was shaken with a small amount of aluminium trichloride. No

enhancement of these signals was observed; several signals did however appear in the region δ 0.55-1.45 p.p.m. The α -prop-2-ylstyrene was used without further purification.

Method (b): prop-2-ylmagnesium bromide was prepared by the addition of a solution of 2-bromopropane (46.16 g; 0.37 mole) in ether (40 ml) to a stirred suspension of magnesium (9.01 g; 0.37 mole) in ether (50 ml); the reaction mixture was then heated under reflux for 1.5 h. A solution of acetophenone (30.00 g; 0.25 mole) in dry ether (30 ml) was added dropwise to the Grignard reagent at 0°C, and the mixture was refluxed with stirring for ca. 2 h. Normal work up gave a pale, yellow-green liquid (36.21 g).

The procedure outlined in (a) above was then followed and the final product was isolated as a pale-brown liquid (34.52 g). The infra-red and n.m.r. spectra of this material indicated that the product was a mixture of the carbinol with a small quantity of residual acetophenone. The acetophenone was removed by chemical means rather than by distillation (acetophenone b.p. 202°C; α -prop-2-ylstyrene b.p. 192°C/753 mmHg). A solution of 2,4-dinitrophenylhydrazine (4.00 g) in ethanol (100 ml) containing concentrated sulphuric acid (5 ml) was added to the crude α -prop-2-ylstyrene with stirring; the red precipitate was removed by filtration and the red filtrate was washed with water before extracting with ether. The extract was concentrated to give a red liquid. Dry column chromatography [alumina (type H), 62 cm x 3.8 cm/petroleum ether (b.p. 30-40°C)] with complete extraction of all but the red band at the origin gave a mobile pale-yellow liquid (13.50 g). The infra-red and n.m.r. spectra of this material were identical to that of the final product from method (a).

Gas chromatography of the pale-yellow liquid (15% PEGA; 170°C) showed the presence of four components, three of which were present in only very small amounts.

(ii) Chlorination of α -Prop-2-ylstyrene.

a) Using N-Chlorosuccinimide. The procedure used paralleled that of Reed.¹⁷⁴ A mixture of α -isopropylstyrene (3.38 g; 0.023 mole), N-chlorosuccinimide (1.94 g; 0.014 mole) and carbon tetrachloride (1.5 ml) was heated in an oil bath at 150°C. The mixture began to foam and some of the N-chlorosuccinimide became lodged in the condenser. The oil bath temperature was raised to 205-210°C, and the resulting solution was heated under reflux for ca. 1 h. Examination of the product by n.m.r. spectroscopy (CCl_4) suggested that chlorination was not complete. A further portion of N-chlorosuccinimide (1.00 g) was added to the reaction mixture and refluxing was resumed for ca. 1.5 h. After cooling overnight, the mixture was filtered to remove the white solid which separated, and the residue was washed with petroleum-ether (b.p. 40-60°C). The combined filtrate and washings were concentrated to give a mobile brown liquid (3.64 g). The n.m.r. spectrum (CCl_4) of this liquid indicated that the product was a complex mixture. In addition to the signals attributable to excess α -prop-2-ylstyrene, the spectrum showed a multiplicity of signals in the methyl region, a multiplet characteristic of $-\text{CH}(\text{CH}_3)_2$, five signals in the range δ 3.6-4.3 p.p.m., and four signals in the range δ 5.7-6.4 p.p.m. Gas chromatography (10% 'Apiezon L'; 150°C) showed the presence of 5 components, present in the ratio of ca. 18:1:38:2:9 (in order of elution).

Fractional distillation under reduced pressure (2.5 mmHg) gave four fractions: (i) b.p. 50-60°C, (ii) b.p. 68-70°C, (iii) b.p. 75-76°C and (iv) b.p. 100-106°C. The n.m.r. spectra of these fractions suggested that none consisted of a single component. The n.m.r. spectra of

fractions (i), (ii) and (iii) showed all the signals of the spectrum of the crude material, except those in the range δ 3.6-4.3 p.p.m. The spectrum of fraction (iv) showed all the signals of the crude product spectrum but those attributed to residual α -prop-2-ylstyrene were weak.

Examination of the fractions (i)-(iv) by gas chromatography (10% 'Apiezon L'; 150°C) indicated that each was a similar mixture of products. Examination of fraction (iii) (15% PEGA; 170°C) which appeared by n.m.r. spectroscopy to be the least complex mixture of products, showed five components, one of which was identified as α -prop-2-ylstyrene. The other components were present in the ratio of ca. 1:5.7:8.5:1.6 in order of elution.

b) Using t-butyl hypochlorite. The chlorinating agent was prepared by the method of Mintz and Walling¹⁰⁶ and was used immediately. A mixture of α -prop-2-ylstyrene (2.93 g; 0.02 mole) and t-butyl hypochlorite (0.23 g; 0.002 mole) in a firmly sealed test tube was heated at 80°C for 4.5 h. The yellow liquid was diluted with ether and washed with water. Concentration of the organic phase under vacuum gave a mobile yellow liquid (2.86 g) whose n.m.r. spectrum (CCl_4) was virtually identical to that of α -prop-2-ylstyrene. None of the signals shown by the product from (a) were observed.

(B) Attempted Alkylations. α -(Bromomethyl)styrene and α -(chloromethyl)styrene were used as model compounds.

(i) Attempted Alkylation of Phthalimide with α -(Bromomethyl)styrene.

The procedure was based on the method used by Inge and Manske¹⁷⁶ to prepare N-benzylphthalimide, an intermediate in the preparation of benzylamine. An intimate mixture of powdered phthalimide (5.23 g;

0.033 mole) and powdered potassium carbonate (2.61 g; 0.019 mole) was treated with crude α -bromomethylstyrene (10.02 g; 0.05 mole; see p. 202) and the resulting mixture was heated in an oil bath at 180-200°C for ca. 3.5 h. The mixture was cooled to give a tacky brown solid, a white solid in the condenser, and a yellow solid on the walls of the reaction vessel. The white solid was shown to be phthalimide by infra-red spectroscopy. The contents of the reaction vessel were washed with n-pentane to remove the residual bromide and the residue was recovered by filtration as a tacky, brown solid. This solid was dissolved in chloroform and washed with water. Concentration of the chloroform extract gave a tacky brown solid; the washings were neutral or slightly basic to universal indicator.

The infra-red spectrum of the solid material showed an absorption in the O-H region and in the carbonyl region [$\nu_{\text{max.}}$ 3045 and 1740 (v.broad) cm^{-1}], and showed many points of similarity with the infra-red spectrum of phthalimide. Its n.m.r. spectrum showed a large multiplet in the region δ 6.8-8.0 p.p.m and several much weaker signals at lower frequencies. The ratio of the integration of the aromatic signals to the combined integrations of all other signals was ca. 3.5:1. The n-pentane washings of the crude product were concentrated to give a red-brown oil, whose n.m.r. spectrum showed only weak signals attributable to residual crude α -bromomethylstyrene.

The reaction product was not examined further.

ii) Attempted Alkylation of t-Butyl Carbazate with α -(Chloromethyl)styrene and with α -(Bromomethyl)styrene. Although this method was not applicable to the synthesis of the desired mixed 1,1-disubstituted hydrazines (57, see Discussion p.99), it was of interest in that it could provide

information about the stability and other characteristics of these hydrazines. Furthermore, it was hoped that the hydrazines obtained in this way would undergo oxidative rearrangement to the corresponding azo-compounds, and so provide information about unsymmetrical di-allyl azo-compounds (58 and 59 , see Discussion p. 99).

a) With α -(Chloromethyl)Styrene. The procedure used paralleled that of Carpino et al.⁴¹ Preliminary examination of this reaction had suggested that a mixture of products was formed. The experiment was repeated, the course of the alkylation being monitored by n.m.r. spectroscopy. A solution of t-butyl carbazate (1.32 g; 0.01 mole) and α -(chloromethyl)styrene (3.07 g; 0.02 mole) in dry dimethylformamide (15 ml) was heated in an oil bath at 50-56°C and triethylamine (2.03 g; 0.02 mole) was added dropwise, with stirring, over a period of ca. 15 min. The solution was heated to 70°C for ca. 72 h, and a white precipitate separated. [The n.m.r. spectrum (CCl_4) of the reaction mixture after heating at 70°C for 24 h was compared to that of the reaction mixture immediately after the addition of triethylamine: the singlet of the t-butyl group (δ 1.42 p.p.m.) had been replaced by a multiplet (δ 1.15-1.55 p.p.m.) and the signals due to the olefinic and methylene protons of the chloride had been lost. At high spectrum amplitude, the spectrum of the mixture after heating showed five signals in the range δ 4.75-6.2 p.p.m.]

The mixture was filtered to remove the precipitated triethylamine hydrochloride and the residue was washed with methylene chloride. The combined filtrate and washings were washed with water and the product was isolated as a viscous, red-brown liquid (3.12 g). The n.m.r. spectrum (CCl_4) of the product indicated the presence of residual dimethylformamide and that all the chloride had been consumed. It showed a multiplet at δ 0.9-1.8 p.p.m., a broad singlet at δ 3.6-4.2 p.p.m., a pair of signals

in the range δ 5.15-5.5 p.p.m. and a multiplet at δ 6.9-7.7 p.p.m. The spectrum (100 MHz, CCl_4) was also recorded at 75°C; the low frequency multiplet showed improved resolution and several peaks were identifiable within the multiplet (δ 1.1-1.5 p.p.m.). In place of the broad singlet (δ 3.6-4.2 p.p.m.), a sharp singlet was observed (δ 3.9 p.p.m.). A weak new signal was observed at δ 5.65 p.p.m. (broad, s). However, the spectrum integration was incompatible with that of the expected product. The solution was shaken with deuterium oxide but the spectrum remained unchanged. The reaction product was examined by t.l.c. (alumina/benzene) and the presence of at least four components was indicated. Distillation using a cup still under reduced pressure effected removal of residual dimethylformamide but the distillate and the residue were shown to be identical by n.m.r. spectroscopy. The residue formed a yellow glass on standing. Treatment of a solution of the alkylation product in nitromethane with a stream of hydrogen chloride gas (the procedure for removal of the protecting group) did not give the expected precipitate of the hydrazine hydrochloride. The solution was extracted with water and the extract was treated with an excess of aqueous sodium carbonate solution. Isolation of the product with ether gave a red-brown oil whose n.m.r. spectrum indicated the presence of residual nitromethane, and had δ 1.1-1.7 (m), 2.7 (s), 3.38 (s), 3.46 (s), 3.55-3.9 (m), 5.0-5.2 (m), 5.3-5.42 (m) and 6.8-7.5 p.p.m. (m). The residual nitromethane was removed with heating under vacuum to give a red-brown oil whose n.m.r. spectrum, though very poorly resolved, was significantly different to that of the material prior to removal of the nitromethane. The spectrum of the nitromethane-free material was recorded at 70°C, but no change in resolution or appearance was observed. The infra-red spectrum of the product prior to removal of nitromethane showed an absorption in the N-H region ($\nu_{\text{max.}}$ 3250 cm^{-1} , broad) and weak

absorptions in the carbonyl region ($\nu_{\text{max.}}$ 1680 and 1635 cm^{-1}).

(b) With α -(Bromomethyl)styrene. The alkylation was attempted under similar conditions using crude α -(bromomethyl)styrene (see p. 202), and the product obtained was similar to that of the reaction with α -(chloromethyl)-styrene (a). Removal of the protecting group as described gave a brown oil whose infra-red and n.m.r. spectra were virtually identical to those of the analogous product from (a).

[Under similar conditions, t-butyl carbazate was successfully alkylated using allyl bromide. The alkylation mixture was heated overnight at ca. 80°C; the heavy precipitate was removed by filtration and the product was isolated (as described in the case of alkylation with α -(chloromethyl)styrene) as an orange gum. Trituration with water gave a pale yellow solid from which pure t-butyl 2,2-di-allylcarbazate was obtained, in 32% yield, by vacuum sublimation. Removal of the protecting group (see p.122) gave the hydrazine hydrochloride as a brown oil; the free hydrazine was obtained as an orange-yellow liquid.]

(iii) Attempted Alkylation of Diethyl Hydrazodicarboxylate. The procedure was based on the method of Al-Sader and Crawford⁸⁰ who reported the alkylation of diethyl hydrazodicarboxylate with allyl benzenesulphonate.

(a) Preparation of Diethyl Hydrazodicarboxylate. The compound was prepared by the method of Rabjohn.¹⁷⁷ A stirred solution of 99-100% hydrazine hydrate (25.02 g; 0.5 mole) in ethanol (250 ml), cooled to 10°C, was treated dropwise with a solution of ethyl chloroformate (152.51 g; 1 mole), keeping the temperature between 15 and 20°C. When half of the solution had been added, a solution of sodium carbonate (53.00 g;

0.5 mole) in water (250 ml) was added dropwise simultaneously with the remaining ethyl chloroformate. Addition of the base was adjusted to enable the addition of ethyl chloroformate to be completed just before the addition of the base was completed, and to maintain the temperature below 20°C. The mixture was stirred for 30 min. and the heavy white precipitate of diethyl hydrazodicarboxylate was collected by suction filtration, washed with water (400 ml) and dried in an oven at 80°C for ca. 4 h. (74.40 g; 84%); m.p. 132-133°C, lit.¹⁷⁷ 131-133°C. δ 1.25-1.52 (t, 6H, -CH₂-CH₃), 4.1-4.55 (g, 4H, -CH₂-CH₃), 6.68 p.p.m. (broad s, 2H, -NH-NH-); ν_{max.} (nujol), 3220 (broad, s), 3025 (s), 1730 (broad, s), 1675 (broad, s), 1520 (broad, s), 1470 (m), 1440 (broad, s), 1380 (w), 1360 (m), 1250 (broad, s), 1108 (m), 1090 (w), 1080 (m), 1070 (s), 1015 (w), 1000 (w), 895 (m), 795 (m), 780 (m), 755 (m), 655 (broad, s) cm⁻¹.

(b) Attempted Preparation of Diethyl N,N'-Di(2-Phenylprop-2-en-1-yl)-bicarbamate. The procedure used was analogous to that of Al-Sader and Crawford.⁸⁰

A well-stirred slurry of sodium hydride (0.51 g; 0.02 mole; see p.130) in dry 1,2-dimethoxyethane (20 ml), under nitrogen, was treated with diethyl hydrazodicarboxylate (1.76 g; 0.01 mole) added in small portions. A vigorous reaction accompanied each addition, and the mixture was stirred for an additional 3 h. The mixture was cooled to 10°C and a solution α-(chloromethyl)styrene (3.07 g; 0.02 mole) in 1,2-dimethoxyethane (15 ml) was added dropwise with stirring.

Three attempts were made to perform the alkylation; the procedure described was common to all three but the reaction conditions differed in each case.

(i) The mixture was stirred overnight under nitrogen to give a colourless liquid and a white precipitate. Water (30 ml) was added, but the precipitate did not dissolve. This mixture was extracted with benzene to give a pale yellow solution, which was concentrated to give a cloudy, pale-yellow liquid (4.06 g) which smelled strongly of α -(chloromethyl)styrene. The product was diluted with petroleum ether (b.p. 40-60°C) and a white solid was precipitated. The solid was collected by suction filtration and was shown by n.m.r. spectroscopy to be diethyl hydrazodicarboxylate. The filtrate was concentrated to give a yellow liquid whose n.m.r. spectrum indicated that it was a mixture of α -(chloromethyl)styrene and a small amount of material derived from diethyl hydrazodicarboxylate.

(ii) The mixture was heated under reflux overnight to give a pale yellow liquid and an off-white precipitate. Isolation of the product as in (i), gave a cloudy, yellow liquid (4.06 g) which was shown to be of similar composition to the product from (i). The n.m.r. spectrum (CCl_4) showed two overlapping triplets (δ 0.8-1.5 p.p.m.) suggesting that alkylation might have occurred to a small extent.

(iii) The mixture was heated under reflux for ca. 65 h and isolation of the product as in (i) gave a yellow oil (3.91 g). Though poorly resolved, the n.m.r. spectrum (CCl_4) of this oil showed signals attributable to the 2-phenylprop-2-yl moiety and complex signals (possibly two overlapping sets of signals) attributable to the ethoxycarbonyl moiety. Diethylhydrazodicarboxylate was shown to be virtually insoluble in carbon tetrachloride, suggesting that the ethyl group signals observed in the n.m.r. spectrum were not due to unreacted diethyl hydrazodicarboxylate.

The yellow oil was extracted with 2 M hydrochloric acid and the product recovered from the extract after basification with aqueous sodium carbonate solution (100% recovery) was shown by n.m.r. spectroscopy to be identical to the alkylation product. This showed that all the α -(chloromethyl)styrene had reacted.

The product was subjected to the hydrolysis and decarboxylation procedure, the reagent quantities being calculated on the basis of the product being pure diethyl N,N'-di-(2-phenylprop-2-en-1-yl)bicarbamate. A solution of the oil (3.91 g; 0.00958 mole) and potassium hydroxide (2.15 g) in methanol (10 ml) and water (2.5 ml) was heated under reflux under nitrogen for ca. 3 h. The reaction mixture was cooled, washed with water (2 x 50 ml) and extracted with ether. The product was recovered as a yellow-brown oil (2.44 g). The infra-red spectrum of this material showed a strong absorption in the carbonyl region; the hydrolysis/decarboxylation procedure was repeated three times until, after a total of 33.5 h of heating under reflux, the infra-red spectrum of the product, a viscous dark brown liquid, showed only a weak carbonyl absorption ($\nu_{\text{max.}} 1715 \text{ cm}^{-1}$). Distillation of this material gave a mobile yellow liquid (0.13 g); b.p. $40-42^{\circ}\text{C}/0.2 \text{ mmHg}$. Comparison of the n.m.r. spectra (CCl_4) of the distillate and of the undistilled material, showed that no major change had occurred during the distillation. The n.m.r. spectrum (CCl_4) of the distillate showed the signals attributable to the 2-phenylprop-2-yl moiety, a singlet at $\delta 3.28 \text{ p.p.m.}$, and a weak multiplet at $\delta 2.18 \text{ p.p.m.}$ [$\delta 3.28 \text{ (s)}, 4.18 \text{ (s)}, 5.18-5.46 \text{ (m, olefinic)}, 7.06-7.48 \text{ p.p.m. (m)}$; integration ratio 19:11:12:36]. The solution was shaken with deuterium oxide, but no change was observed in the spectrum. The infra-red spectrum showed a weak absorption in the carbonyl region ($\nu_{\text{max.}} 1630 \text{ cm}^{-1}$) but no absorption in the N-H region. Although this evidence did not suggest that the desired hydrazine had been prepared, the

reaction of the material with yellow mercuric oxide was examined. A mixture of the distillate (0.13 g), yellow mercuric oxide (0.48 g) and anhydrous sodium sulphate (0.46 g) in ether (10 ml) at 0°C was stirred overnight. The product, recovered in the usual way (see p. 147), was shown by n.m.r. spectroscopy to be identical to the unoxidised material. The mass spectrum of this material had m/e (inter alia) 198 (v.weak), 196 (v.weak), 154, 152, 148, 147, 133, 118, 117, 103. A Lassaigne test indicated that the material did not contain nitrogen.

Alkylation of Diethyl Hydrazodicarboxylate with Allyl Chloride.

The aim was to examine the alkylation of diethyl hydrazodicarboxylate with allyl chloride, in an attempt to resolve the apparently anomalous course of the attempted alkylation with α -(chloromethyl)styrene. The procedure paralleled that described for the attempted alkylations with α -(chloromethyl)styrene (see p. 210). The stirred alkylation mixture (0.03 mole scale) was heated under reflux overnight and the product was isolated as a yellow paste. Treatment of this paste with petroleum-ether (b.p. 40-60°C) gave a precipitate of diethyl hydrazodicarboxylate (1.21 g; 23% of the amount used) and a yellow solution from which a yellow liquid (2.59 g) has obtained upon evaporation of the solvent. Distillation of this liquid gave a pale-yellow liquid (1.40 g); b.p. 80-83°C/0.2 mmHg. The n.m.r. spectrum of the distillate indicated that it was a mixture of mono-alkylated and di-alkylated material in the ratio of ca. 2:3. The mass spectrum had m/e (inter alia) 256, 216, 211, 128 (B).

Preparation of Authentic Diethyl N,N'-Di-allylbicarbamate.

This was achieved by the method of Al-Sader and Crawford,⁸⁰ allyl benzenesulphonate being prepared according to the procedure of Bergstrom and Siegel.¹⁷⁸ Distillation of the crude product gave the pure bicarbamate as a clear, colourless liquid (10.91; 85%), b.p. 88°C/0.4 mmHg, lit.⁸⁰ b.p. 92-93°C/0.5 mmHg; δ 1.1-1.4 (t, 6H, $-\text{CH}_2-\text{CH}_3$), 3.9-4.4 (m, 8H, $-\text{CH}_2-\text{CH}_3$ and $-\text{CH}_2-\text{CH}=\text{CH}_2$), 4.95-5.38 (m, 4H, $-\text{CH}_2-\text{CH}=\text{CH}_2$), 5.55-6.3 p.p.m. (m, 2H, $-\text{CH}_2-\text{CH}=\text{CH}_2$).

Attempted Hydrolysis and Decarboxylation of Diethyl N,N'-Di-allyl-bicarbamate. The procedure of Al-Sader and Crawford⁸⁰ was used:

a solution of the authentic carbamate (10.91 g; 0.042 mole) and potassium hydroxide (9.63 g; 0.17 mole) in methanol (40 ml) and water (10 ml) was heated under reflux under nitrogen for 3 h. The mixture was left to stand under nitrogen for 40 h, was filtered to remove the white precipitate, and the filtrate was extracted with ether. The extract was concentrated at room temperature under reduced pressure and the product was distilled under vacuum to give a clear, colourless liquid (0.43 g); b.p. 65-67°C/30 mmHg. The n.m.r. spectrum of this material showed a multiplicity of signals in the methyl region and could not be reconciled with that expected for the desired 1,2-di-allylhydrazine.

[The product of alkylation of diethyl hydrazodicarboxylate with allyl chloride (see p.²¹⁶) was subjected to the same hydrolysis/decarboxylation process; the product, a yellow-brown liquid, was distilled under reduced pressure to give a colourless liquid, b.p. 80-90°C/32 mmHg. The n.m.r. spectrum showed that hydrolysis was not complete; the mass spectrum had (inter alia) 256 (v.weak), 230 (v.weak), 202 (v.weak), 184, 170, 143, 128, 129, 110, 83.]

Oxidation of 1-Alkyl-1-Phenylhydrazines: Attempts to Trap the Diazene Intermediate.

Two methods of trapping the diazene were examined. These were (a) by lead tetra-acetate oxidation of the hydrazines in dimethyl sulphoxide or dimethyl sulphide, the adduct being a sulfoximide or a sulphilimide respectively, and (b) by cupric chloride oxidation of the hydrazines in acid solution, the product being a copper complex with co-ordination to the diazene. Although both methods are reversible with respect to the regeneration of the diazene the former method is preferable in that the diazene can be generated under milder and more versatile conditions.

Attempted Preparation of Sulfoximides.- The procedure followed was that of Anderson et al.³³ Lead tetra-acetate was prepared as described (see p.146) and dimethyl sulphoxide was dried by standing over activated molecular sieve. Lead tetra-acetate was added in small portions over a period of several minutes to a stirred solution of the hydrazine in dimethyl sulphoxide and the mixture was stirred for ca. 10 min under nitrogen with exclusion of light. The mixture was poured into water to remove the residual dimethyl sulphoxide and the product was isolated by repeated extraction of this mixture with chloroform.

Attempted Preparation of N-(N'-Allylanilino)S,S-Dimethylsulphoximide.

Lead tetra-acetate (3.07 g; 7 mmole) was added to a solution of 1-allyl-1-phenylhydrazine (0.88 g; 6 mmole) in dimethyl sulphoxide (30 ml) and the product was isolated as an orange-brown liquid (3.69 g). The n.m.r. spectrum of this material indicated the presence of residual dimethyl sulphoxide. Comparison of the spectrum with that of an authentic sample of 1-phenylazoprop-2-ene indicated that the oxidation had followed its normal course and that the diazene had not

been trapped. Dry column chromatography (silica gel, 22 in x 1.5 in/ benzene) gave four bands, all of which were examined. The n.m.r. spectra of the fractions recovered from the column did not show the low-frequency methyl signals expected of the sulfoximide adduct. The only identifiable product was 1-phenylazoprop-2-ene.

Attempted Preparation of N-(N'-Benzylanilino)S,S-Dimethylsulfoximide.-

Lead tetra-acetate (2.92 g; 6.5 mmole) was added to a solution of 1-benzyl-1-phenylhydrazine (1.18 g; 6 mmole) in dimethyl sulphoxide (30 ml). The product was isolated as a brown gum with a strong odour of benzaldehyde. The n.m.r. spectrum of this gum indicated the presence of residual dimethyl sulphoxide, and a singlet, attributed to benzaldehyde, was observed at δ 9.9 p.p.m. The remainder of the spectrum was consistent with the formation of 1,4-dibenzyl-1,4-diphenyltetraz-2-ene and no signals attributable to the sulfoximide were observed. Trituration of the gum with n-pentane gave a pale brown solid (0.57 g) which was recrystallised from ethanol and shown to be the tetrazene by its m.p. (145°C) and n.m.r. spectrum.

The attempted preparation of the sulfoximide was repeated with the modification of inverse addition as described by Anderson et al.³³ Furthermore, in an attempt to inhibit tetrazene formation, conditions of high dilution were used.

A solution of the hydrazine (1.99 g; 10 mmole) in dry methylene chloride (5 ml; see p.146) was added over a period of 50 min, to a stirred mixture of lead tetra-acetate (4.91 g; 11 mmole) and dimethyl sulphoxide (0.78 g; 10 mmole) in dry methylene chloride (100 ml) at 0°C. The mixture was stirred for a further 20 min before removing the inorganic residue. The filtrate was diluted with chloroform and was washed with water. The chloroform solution was concentrated under vacuum with gentle warming (< 40°C) to give an orange-brown oil which

solidified on standing (1.85 g). The n.m.r. spectrum (CCl_4) of this material was virtually identical to that of the crude product of the first attempt to prepare the sulphoximide, although weak signals were also observed at δ 1.7, 1.76, 1.95 and 2.00 p.p.m. Thus it appeared that the sulphoximide was formed to only a small extent, if at all.

Attempted Preparation of Sulphilimides.- The experimental method paralleled that used in the attempts to prepare the sulphoximides.

Attempted Preparation of N-(N'-Allylanilino)S,S-Dimethylsulphilimide.-

Lead tetra-acetate (1.48 g; 3.3 mmole) was added in small portions to a stirred mixture of 1-allyl-1-phenylhydrazine (0.49 g; 3.3 mmole) and dimethylsulphide (6.5 ml; 10 mmole) in dry methylene chloride (30 ml) at 0°C . The reaction was carried out under nitrogen with exclusion of light. The mixture was stirred for 1.5 h before filtering off the inorganic precipitate. The filtrate was washed with sodium carbonate solution and the aqueous phase extracted with ether. The solvent was removed from the combined organic extracts under vacuum with gentle heating (ca. 60°C) to give an orange-brown liquid (0.32 g). This was shown by n.m.r. spectroscopy to be 1-phenylazoprop-2-ene.

Attempted Preparation of N-(N'-Benzylanilino)S,S-Dimethylsulphilimide.-

Lead tetra-acetate (4.91 g; 11 mmole) was added in small portions to a stirred mixture of 1-benzyl-1-phenylhydrazine (1.99 g; 10 mmole) and dimethylsulphide (6.5 ml; 10 mmole) in dry methylene chloride (45 ml) at 0°C . Again the reaction was carried out under nitrogen in the dark. The mixture was stirred for 2 h and the product was isolated as described above. After washing with aqueous sodium bicarbonate solution followed by evaporation of the solvent, an orange-brown solid (1.91 g) was obtained whose n.m.r. spectrum showed, in addition to the signals attributable to the tetrazene, a doublet at δ 2.18 p.p.m. ($J=9\text{Hz}$) and singlets at

4.35, 5.15 and 5.20 p.p.m. The ratio of the integration of the benzylic protons of the tetrazene to that of the doublet signal was 16:6. The solid was recrystallised from ethanol (m.p. 143-144°C; 52% recovery) and was identified as 1,4-dibenzyl-1,4-diphenyltetraz-2-ene (lit.¹⁶⁸ m.p. 145°C); m/e 392 (P), 364, 362, 273, 271, 183 (B). The ethanolic mother liquor was concentrated to give a brown oil whose n.m.r. spectrum (CCl₄) was very similar to those of the products of the early oxidations of 1-benzyl-1-phenylhydrazine using yellow mercuric oxide.

Oxidation of 1-Alkyl-1-Phenylhydrazines with Cupric Chloride: Attempted Preparation of Copper (I) Complexes of 1-Alkyl-1-Phenyldiazenes.

The method employed was that of Boehm et al.³⁵ who reported the oxidation of 1,1-dimethylhydrazine by cupric chloride and the isolation of a complex of 1,1-dimethyldiazene. Before examining the oxidation of 1-alkyl-1-phenylhydrazines, this work was repeated.

Oxidation of 1,1-Dimethylhydrazine by Cupric Chloride.- The reported experimental procedure was followed exactly and the product was isolated as a deep-purple solid, m.p. 75-80°C. The reaction proceeded exactly as described and the infra-red spectrum of the product was in complete agreement with the reported data. As reported the complex was found to decompose rapidly in air, and was therefore stored under vacuum.

The isolation of tetramethyltetraz-2-ene by successive treatment of the complex with 6 M hydrochloric acid and 15 M aqueous ammonia, was achieved in 25% yield using the reported method. Tetramethyltetraz-2-ene was identified by comparison of the n.m.r. spectrum of the product with that of an authentic sample of the tetrazene which was prepared by oxidation of 1,1-dimethylhydrazine¹⁷⁹ [72%; δ 2.8 p.p.m. (s)]. A control experiment showed that tetramethyltetraz-2-ene was completely decomposed when treated with 6 M hydrochloric acid (as used in the decomposition of the complex).

The complex was examined by mass spectrometry; the parent peak (m/e 413) was not observed. The spectrum was recorded at several temperatures and the following peaks (inter alia) were observed:

- i) 80°C m/e 144 (v.w.), 142 (v.w.), 128, 72 (B), 71, 59, 58.
- ii) 100°C m/e 198 (v.w), 186 (v.w), 144 (w), 142 (w), 128, 116 (B), 101, 81, 71 (w), 59, 58.
- iii) 140°C m/e 226, 224 (v.w) 198 (w), 186 (v.w), 128, 116, 59 (B), 58 (w).
- iv) 160°C m/e 186 (v.w), 101 (w), 95 (w), 81 (v.w), 77 (v.w).

The appearance of these spectra suggested that extensive decomposition and rearrangement was occurring in the spectrometer.

All other observations agreed with the reported information and supported the conclusions made by the authors.

Oxidation of 1-Benzyl-1-Phenylhydrazine with Cupric Chloride.- All solutions were cooled in an ice-salt bath before mixing. A solution of the hydrazine (4.03 g; 22.3 mmole) in 5% aqueous hydrochloric acid (200 ml) was filtered to remove the small amount of precipitated hydrochloride before adding a solution of 'Analar' cupric chloride (7.27 g; 42.6 mmole) in water (31 ml), in one portion. The turquoise solution was stirred and saturated aqueous sodium acetate solution was added dropwise to bring the pH to 4. The rust-brown precipitate was collected by suction filtration and washed with 25 ml portions of water, methanol and ether. Efficient drying by suction filtration proved impossible; the moist brown cake of material was dried under vacuum over phosphoric oxide. The product was obtained as a mustard brown powder (6.27 g), m.p. 132-134°C (decomp); ν_{max} . (nujol) 3060 (w), 1600 (m), 1590 (w), 1495 (s), 1428 (s), 1345 (m), 1235 (m), 1160 (m), 1080 (m), 1035 (m), 1020 (m), 1000 (v.w), 920 (m), 835 (w), 785 (s), 765 (s), 735 (s), 700 (s), 640 (w) cm^{-1} ; m/e, 130°C (*inter alia*) 364 (w), 362 (w), 286, 195, 183, 106, 105, 91 (B). The presence of copper in the product was demonstrated by heating a sample of the brown powder in an ignition tube: a film of copper formed on the wall of the tube.

After standing in a sealed container for several months, the brown solid had decomposed to give a moist brown cake of material which smelled of benzaldehyde.

Decomposition of the Copper Complex.- The brown solid (5.28 g) was stirred with 6 M hydrochloric acid (100 ml) cooled in an ice-salt bath. The material proved to be only slightly soluble and the undissolved solid was removed by filtration through celite. The brown residue had the characteristic odour of benzaldehyde. The pale-green filtrate was basified to pH 10 with

15 M ammonia solution keeping the temperature below 5°C. This gave a brown precipitate and a rust-brown aqueous phase. Repeated extraction of this mixture with ether (4 x 100 ml) gave, after removal of the solvent, a red brown gum (0.24 g) which contained some crystalline material and had the characteristic odour of benzaldehyde. The n.m.r. spectrum of this gum suggested the presence of benzaldehyde, N-benzyl-aniline and 1,4-dibenzyl-1,4-diphenyltetraz-2-ene. This was confirmed by adding an authentic sample of each in turn to the n.m.r. solution: no new signals appeared and the expected signal enhancements were observed. T.l.c. (silica/benzene) showed the gum to be a mixture of six components. The leading four spots were also observed when the product of treating a solution of the tetrazene in chloroform with 6 M hydrochloric acid, was examined by t.l.c. (silica/benzene).

The product from the decomposed complex suggested that its constitution was not analogous to that of the reported complex of 1,1-dimethyldiazene.

Oxidation of 1-Allyl-1-Phenylhydrazine with Cupric Chloride.- All solutions were cooled in an ice-salt bath before mixing. A solution of 'Analar' cupric chloride (4.82 g; 35.8 mmole) in water (20 ml) was added in one portion to a stirred solution of 1-allyl-1-phenylhydrazine (2.41 g; 17.9 mmole) in 5% hydrochloric acid. A saturated aqueous sodium acetate solution was added in small portions keeping the temperature of the mixture at -2°C. The pH of the mixture, monitored using a pH meter, was raised to 4.25, at which point the addition was stopped. A brown precipitate was isolated and dried as described above to give a rust-brown powder (4.00 g) which was examined after minimal exposure to the atmosphere, m.p. 65-69°C; $\nu_{\text{max.}}$ (nujol) 3250 (m), 3150 (w), 1595 (s), 1490 (s), 1260 (w), 1225 (w), 1155 (w), 1130 (w), 1070 (w), 1030 (m), 990 (w), 930 (broad, m), 760 (s), 695 (s) cm^{-1} ; m/e (inter alia):

- (i) 70°C 292 (v.w), 264 (v.w), 223 (v.w), 148, 146, 107, 105, 77 (B).
- (ii) 150°C 292 (v.w), 264, 223, 148, 146, 133, 108, 107, 106.
- (iii) 150+°C 334 (w), 264, 223.

Though not evident from the mass spectrum, the presence of copper in the product was demonstrated as above, by heating a sample in an ignition tube. The copper content, estimated by iodometric titration according to the method of Rezintskaya and Burtseva¹⁴⁵ was found to be $23.5 \pm 0.03\%$.

An attempt was made to obtain an X-ray diffraction photograph on a powdered sample of the complex, but the results showed that the material was non-crystalline.

After standing for several weeks in a sealed container, the complex had decomposed to give a brown solid mass.

Decomposition of the Copper Complex.— The brown solid (2.00 g) was stirred with 3 M hydrochloric acid (100 ml) at 0°C. The dark brown solution was filtered to remove undissolved material; the residue formed a blue-black tar after standing in air. The filtrate was basified with 5 M ammonia solution and developed a deep blue colour. Repeated ether extraction gave a brown oil (0.47 g), after removal of the solvent. The n.m.r. spectrum (CCl_4) of this oil indicated the product to be a mixture. A broad multiplet was observed in the aromatic region (δ 6.3–7.6 p.p.m.) and the signals of the allyl moiety were also observed. In particular two multiplets, in similar position and of similar pattern to those attributed to the allyl protons ($-\text{CH}_2-\text{CH}=\text{CH}_2$) in allyl compounds were observed at δ 3.65–3.8 and 3.85–4.05 p.p.m. with an integral ratio of ca. 1:2. A singlet was observed at δ 3.48 p.p.m.

T.l.c. (alumina/benzene) showed four components, and dry column chromatography (alumina, 42 cm x 3 cm/benzene) gave five overlapping bands. These were (i) a dark-brown band at the origin, (ii) a diffuse orange-yellow band, (iii) a pink band, (iv) a bright yellow band and (v) a fawn-coloured leading band. Each band was isolated and the total recovery of material

was 64%. Band (iv) gave a mobile red-brown liquid (0.12 g); the other bands gave red-brown gums, (i) 0.09 g; (ii) 0.02 g; (iii) 0.05 g and (v) 0.02 g.

The infra-red spectrum of the liquid from band (iv) was quite similar to that of N-allylaniline (see p. 124). Two absorptions were seen in the N-H region: ν_{max} . 3415 (s) and 3315 (w) cm^{-1} . Its n.m.r. spectrum broadly resembled that of N-allylaniline although it did show additional weak signals at δ 2.0 (d), 2.4-2.7 (m) and 3.1 p.p.m. (d). The spectrum differed from that of the crude product of the decomposed complex, in that only one multiplet signal attributable to $-\text{CH}_2-\text{CH}=\text{CH}_2$ was observed (δ 3.68-3.82 p.p.m.). A much smaller multiplet was observed at higher frequency (δ 3.9-4.2 p.p.m.) but this was thought to be due in part to spinning side bands. T.l.c. (alumina/benzene) seemed to confirm the presence of N-allylaniline. The liquid was examined by wet column chromatography (alumina, 8 cm x 0.4 cm/carbon tetrachloride); a purple band was observed at the top of the column, and the same series of overlapping coloured bands as seen in the original column, was obtained. The orange-yellow band was collected and the n.m.r. spectrum of this solution was recorded immediately. The spectrum was virtually identical to that of the liquid prior to wet column chromatography. This suggested that the liquid contained at least one species which decomposed on chromatographing.

The n.m.r. spectra of the gums recovered from bands (i), (ii), (iii), and (v) of the dry column were poorly resolved and gave no meaningful information.

The complex and its decomposition product(s) were not examined further.

Bibliography

1. E. Fischer, *Annalen*, 1878, 190, 67.
2. E. Fischer and H. Troschke, *Annalen*, 1879, 199, 294.
3. E. Renouf, *Ber.*, 1880, 13, 2169.
4. A. Michaelis and K. Luxemburg, *Ber.*, 1893, 26, 2174.
5. E. Fischer and O. Knoevenagel, *Annalen*, 1887, 239, 194.
6. M. Busch and B. Weiss, *Ber.*, 1900, 33, 2701.
7. M. Busch and K. Lang, *J. prakt. Chem.*, 1936, 144, 291.
8. J. Kenner and E.C. Knight, *Ber.*, 1936, 69, 341.
9. W.R. McBride and H.W. Kruse, *J. Amer. Chem. Soc.*, 1957, 79, 572.
10. W.R. McBride and E.M. Bens, *J. Amer. Chem. Soc.*, 1959, 81, 5546.
11. L.A. Carpino, *J. Amer. Chem. Soc.*, 1957, 79, 4427.
12. D.M. King and A.J. Bard, *J. Amer. Chem. Soc.*, 1965, 87, 419.
13. G. Cauquis and M. Genies, *Tetrahedron Letters*, 1970, 2903.
14. G. Cauquis and M. Genies, *Tetrahedron Letters*, 1970, 3430.
15. W.R. Bamford and T.S. Stevens, *J. Chem. Soc.*, 1952, 4335.
16. C.G. Overberger, J.G. Lombardino and R.G. Hiskey, *J. Org. Chem.*, 1957, 22, 858.
17. C.G. Overberger, J.G. Lombardino and R.G. Hiskey, *J. Amer. Chem. Soc.*, 1958, 80, 3009.
18. C.G. Overberger, N.P. Marullo and R.G. Hiskey, *J. Amer. Chem. Soc.*, 1959, 81, 1517.
19. C.G. Overberger, N.P. Marullo and R.G. Hiskey, *J. Amer. Chem. Soc.*, 1961, 83, 1374.
20. C.G. Overberger, M. Valentine and J.-P. Anselme, *J. Amer. Chem. Soc.*, 1969, 91, 687.
21. D.M. Lemal and T.W. Rave, *J. Amer. Chem. Soc.*, 1965, 87, 393.
22. D.M. Lemal and S.D. McGregor, *J. Amer. Chem. Soc.*, 1966, 88, 1335.

23. A. Angeli, Chem. Zentr., 1896, 67 (I), 799.
24. C.L. Bumgardner, K.J. Martin and J.P. Freeman, J. Amer. Chem. Soc., 1963, 85, 97.
25. R.C. Atkinson and C.W. Rees, J.C.S. Chem., Comm., 1967, 1230.
26. D.J. Anderson, T.L. Gilchrist, D.C. Horwell, and C.W. Rees, J.Chem.Soc. (C), 1970, 576.
27. M. Baudru and A. Foucaud, Compt. rend. (C), 1970, 270, 104.
28. D.W. Jones, J.C.S. Chem. Comm., 1972, 884.
29. A.G. Anderson and D.R. Fagerburg, Tetrahedron, 1973, 2973.
30. R.S. Atkinson and J.R. Malpass, J.C.S. Chem. Comm., 1975, 555.
31. K.-H. Koch and E. Fahr, Angew. Chem. (Inter.Ed.), 1970, 9, 634.
32. D.J. Anderson, T.L. Gilchrist, and C.W. Rees, J.C.S. Chem. Comm., 1969, 1
33. D.J. Anderson, D.C. Horwell, E. Stanton, T.L. Gilchrist, and C.W. Rees, J.C.S. Perkin I, 1972, 1317.
34. B.M. Adger, M. Keating, C.W. Rees, and R.C. Storr, J.C.S. Perkin I, 1975, 41.
35. J.R. Boehm, A.L. Balch, K.F. Bizot, and J.H. Enemark, J. Amer. Chem. Soc., 1975, 97, 501.
36. W.R. McBride, H.W. Kruse and W.H. Urry, J. Amer. Chem. Soc., 1957, 79, 6568.
37. O. Piloty, Ber., 1896, 29, 2559.
38. G. Koga and J.-P. Anselme, J.Org.Chem., 1970, 35, 960.
39. V. Ya. Bespalov, L.A. Kartsova, V.I. Baranovskii, and B.V. Ioffe, Doklady Akad. Nauk S.S.S.R., 1971, 200, 99.
40. C.G. Overberger and L.P. Herin, J. Org. Chem., 1962, 27, 417.
41. L.A. Carpino, A.A. Santilli, and R.W. Murray, J. Amer. Chem. Soc., 1960, 82, 2728.

42. W. Lwowski, "Nitrenes", J. Wiley, New York, 1970, p. 361.
43. P.S. Forgione, G.S. Sprague, and H.J. Troffkin, J. Amer. Chem. Soc., 1966, 88, 1079.
44. L. Hoesch and A.S. Dreiding, Chimia (Switz.), 1969, 23, 405.
45. L. Hoesch and A.S. Dreiding, Helv. Chim. Acta, 1975, 58, 980.
46. D.J. Anderson, T.L. Gilchrist, and C.W. Rees, J.C.S. Chem. Comm., 1971, 800.
47. D.M. Lemal, T.W. Rave, and S.D. McGregor, J. Amer. Chem. Soc., 1963, 85, 1944.
48. W. Baker, J.F.W. McOmie, and D.R. Preston, J.Chem.Soc., 1961, 2971.
49. L.A. Carpino, J. Amer. Chem. Soc., 1962, 84, 2196.
50. C.D. Campbell and C.W. Rees, J. Chem. Soc. (C), 1969, 742.
51. C.G. Overberger and B.S. Marks, J. Amer. Chem. Soc., 1955, 77, 4097.
52. C.G. Overberger and B.S. Marks, J. Amer. Chem. Soc., 1955, 77, 4104.
53. C.G. Overberger and S. Altscher, J. Org. Chem., 1966, 31, 1728.
54. W. Lwowski, "Nitrenes", J. Wiley, New York, 1970, p. 365.
55. C.G. Overberger and N.P. Marullo, J. Amer. Chem. Soc., 1961, 83, 1378.
56. C.G. Overberger and C. Yaroslavsky, Tetrahedron Letters, 1965, 4395.
57. C.G. Overberger and J.-P. Anselme, J. Amer. Chem. Soc., 1964, 86, 658.
58. W.D. Ollis, I.O. Sutherland and Y. Thebtaranonth, J.C.S. Chem. Comm., 1970, 1199.
59. R.B. Woodward and R.C. Hoffmann, "The Conservation of Orbital Symmetry", Verlag Chemie, Academic Press Inc., 1970.
60. L.A. Carpino, J.C.S. Chem. Comm., 1966, 494.
61. J.E. Baldwin, J.E. Brown, and G. Hofle, J. Amer. Chem. Soc., 1971, 93, 788.
62. P. Carter and T.S. Stevens, J. Chem. Soc., 1961, 1743.

63. D.M. Lemal, F. Menger, and E. Coats, J. Amer. Chem. Soc., 1964, 86, 2395.
64. W.H. Urry and C. Ikoku, Abstracts, 146th National Meeting Amer. Chem. Soc., Denver, Colo., Jan 1964, p. 25 C.
65. W. Lwowski, "Nitrenes", J. Wiley, New York, 1970, p. 389.
66. H.E. Baumgarten, P.L. Creger, and R.L. Zey, J. Amer. Chem. Soc., 1960, 82, 3977.
67. C.W. Rees and M. Yelland, J.C.S. Chem. Comm., 1969, 377.
68. R.W. Jemison and W.D. Ollis, J.C.S. Chem. Comm., 1969, 294.
69. J.E. Baldwin, R.E. Hackler and D.P. Kelly, J.C.S. Chem. Comm., 1968, 1083.
70. A.A. Reid, J.T. Sharp, H.R. Sood, and P.B. Thorogood, J.C.S. Perkin I, 1973, 2543.
71. Y. Yamamoto, J. Oda, and Y. Inouye, J.C.S. Chem. Comm., 1973, 848.
72. B. Vis, Res. Trav. Chim., 1939, 58, 387.
73. H. Schubert, F. Foehringen and H. Noack, Z. angew. Chem., 1970, 10, 68.
74. H. Claessen, Chem. Abs., 1976, 84, 164393r.
75. M. Somei and M. Natsumi, Tetrahedron Letters, 1974, 461.
76. L.A. Carpino, J. Amer. Chem. Soc., 1960, 82, 3133.
77. Y. Tamura, J. Minamikawa, K. Sumoto, S. Fujii and M. Ikeda, J. Org. Chem., 1973, 38, 1239.
78. T. Sheradsky, Tetrahedron Letters, 1968, 1909.
79. K. Hafner, D. Zinser, and K.-L. Moritz, Tetrahedron Letters, 1964, 1733.
80. B.H. Al-Sader and R.J. Crawford, Canad. J. Chem., 1970, 48, 2745.
81. P.A.S. Smith, "The Chemistry of Open Chain Nitrogen Compounds", Vol. 2, W.A. Benjamin Inc., New York, 1966.
82. J.W. Timberlake and J.C. Stowell, "The Chemistry of the Hydrazo, Azo, and Azoxy Groups", Edited by S. Patai, Part. I, J. Wiley and Sons, London, 1975, pp. 69-107.

83. P.E. Iversen, *Acta Chem. Scand.*, 1971, 25, 2337.
84. W.J. Hickinbottom, *J. Chem. Soc.*, 1930, 992.
85. W.J. Hickinbottom, "Reactions of Organic Compounds", Longmans, London,
Third Edition, p. 426.
86. W.S. Fones, *J. Org. Chem.*, 1949, 14, 1099.
87. W.W. Hartman and L.J. Roll, *Org. Synth.*, 1933, 13, 82.
88. C. Hanna and F.W. Schueler, *J. Amer. Chem. Soc.*, 1952, 74, 3693.
89. R.H. Poirier and F. Bennington, *J. Amer. Chem. Soc.*, 1952, 74, 3192.
90. W.J. Hickinbottom, "Reactions of Organic Compounds", Longmans, London,
Third Edition, p. 477.
91. R.L. Hinman, *J. Org. Chem.*, 1958, 23, 1587.
92. S.G. Cohen and C.H. Wang, *J. Amer. Chem. Soc.*, 1953, 75, 5504.
93. O. Westphal, *Ber.*, 1941, 74, 759.
94. W.W. Hartmann and L.J. Roll, *Org. Synth.*, 1933, 13, 66.
95. L. Knorr and A. Wiedel, *Ber.*, 1909, 42, 3523.
96. A. Michaelis, *Annalen*, 1889, 252, 266.
97. A. Michaelis and C. Claessen, *Ber.*, 1889, 22, 2233.
98. A.W. Titherley, *J. Chem. Soc.*, 1897, 71, 460.
99. R. West and H.F. Stewart, *J. Amer. Chem. Soc.*, 1970, 92, 853.
100. B. Rassow and M. Lummerzheim, *J. prakt. Chem.*, 1901, 64, 138.
101. J.O. Edwards and R.G. Pearson, *J. Amer. Chem. Soc.*, 1962, 84, 16.
102. J.E. Baldwin, R.E. Hackler, and D.P. Kelly, *J.C.S. Chem. Comm.*, 1968, 538.
103. D. Gjrdenic, *Quart. Rev.*, 1965, 19, 316.
104. H.E. Baumgarten, W.F. Wittman, and G.J. Lehmann, *J. Heterocyclic Chem.*,
1969, 6, 333.
105. R.D. Gilliom and B.F. Ward, *J. Amer. Chem. Soc.*, 1965, 87, 3944.
106. M.J. Mintz and C. Walling, *Org. Synth.*, 1969, 49, 9.
107. E. Fischer and O. Knoevenagel, *Annalen*, 1887, 239, 194.

108. K. von Auwers and A. Kreuder, Ber., 1925, 58, 1974.
109. R.J. Ellis and H.M. Frey, J. Chem. Soc., 1964, 5578.
110. F.O. Rice and C.J. Grelecki, J. Amer. Chem. Soc., 1957, 79, 2679.
111. J.H. Beynon, "Mass Spectrometry and its Applications in Organic Chemistry", Elsevier, London, 1960.
112. H. Wieland and H. Fressel, Annalen, 1912, 392, 135.
113. G. Wittig and H. Streib, Annalen, 1953, 584, 1.
114. G.L. Closs, L.E. Closs, and W.A. Boll, J. Amer. Chem. Soc., 1963, 85, 3796.
115. R.H. Findlay, J.T. Sharp, and P.B. Thorogood, J.C.S. Chem. Comm., 1970, 909.
116. R.W.C. Cose, A.M. Davies, W.D. Ollis, C. Smith, and I.O. Sutherland, J.C.S. Chem. Comm., 1969, 293.
117. R.B. Bates and D. Feld, Tetrahedron Letters, 1968, 417.
118. P.C. Freer and P.L. Sherman, Amer. Chem. J., 1896, 18, 572.
119. A. Michaelis and F. Schmidt, Annalen, 1889, 252, 310.
120. R. Behrend and W. Reinsberg, Annalen, 1910, 377, 189.
121. W.F. Short, J.Chem.Soc., 1921, 119, 1445.
122. O. Widman, Ber., 1893, 26, 945.
123. M. Freund and F. Horst, Ber., 1895, 28, 944.
124. M.T. Rogers and J.C. Woodbrey, J.Phys.Chem., 1962, 66, 540.
125. G.J. Bishop, B.J. Price, and I.O. Sutherland, J.C.S. Chem. Comm., 1967, 672.
126. J. Hunter, Ph.D. Thesis, Edinburgh, 1975.
127. H.W.J. Hills, J. Kenyon, H. Phillips, and B.C. Platt, J.Chem.Soc., 1936, 576.
128. M.P. Balfe, H.W.J. Hills, J. Kenyon, H. Phillips and B.C. Platt, J.Chem.Soc., 1943, 348.

129. R.K. Hill, R. Soman, and S. Sawada, *J.Org.Chem.*, 1972, 37, 3737.
130. D.J. Cram and M.R.V. Sahyun, *J. Amer. Chem. Soc.*, 1962, 85, 1257.
131. A.F. Hegarty in "The Chemistry of the Hydrazo, Azo and Azoxy Groups", Edited by S. Patai, Part 2, J. Wiley and Sons, London, 1975, pp. 643-723.
132. Y. Ogata, H. Tabuchi, and Y. Yoshida, *Tetrahedron*, 1964, 20, 2717.
133. H. Hart and J.R. Kosak, *J. Org. Chem.*, 1962, 27, 116.
- 134(a) B.R. Cowley and W.A. Waters, *J. Chem.Soc.*, 1961, 1228.
- (b) D. Mackay and W.A. Waters, *J. Chem. Soc. (C)*, 1966, 813.
135. H. Frazen and F. Zimmerman, *Ber.*, 1906, 39, 2567.
136. H. Wieland and S. Gambarjan, *Ber.*, 1906, 39, 1499.
137. J.W.B. Reesor and G.F. Wright, *J. Org. Chem.*, 1957, 22, 375.
138. M.S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances", Prentice-Hall Inc., New York, 1954.
139. Tiffeneau, *Ann. Chim. (France)*, 1907, 8, 10, 322.
140. L. Henry, *Chem. Zentr.*, 1907, 11, 889.
141. D.J. Anderson, T.L. Gilchrist, D.C. Horwell, and C.W. Rees, *J.C.S. Chem. Comm.*, 1969, 146.
142. T.L. Gilchrist, Departmental Seminar, Edinburgh, March 1975.
143. P. Barraclough, M. Edwards, T.L. Gilchrist, and C. John Harris, *J.C.S. Perkin I*, 1976, 716.
144. D.W. Jones, *J.C.S. Perkin I*, 1976, 1150.
145. T.V. Reznitskaya and E.I. Burtseva, *Zh. Analit. Khim.*, 1966, 21 (9), 1132.
146. O. Diels and W. Koll, *Annalen*, 1925, 443, 262.
147. J.G. Noltes and J.W.G. van den Hurk, *J. Organometallic Chem.*, 1964, 1, 377.
148. C.J. Michejda and D.H. Campbell, *J. Amer. Chem. Soc.*, 1974, 96, 929.

149. I. Vogel, J. Chem. Soc., 1927, 129, 524.
150. B.K. Singh, J. Chem. Soc., 1920, 117, 1202.
151. R.A. Aneen, K.M. Lewandowski, I.A.I. Taha, and B.R. Smith,
J. Amer. Chem. Soc., 1961, 83, 4843.
152. M.C. Caserio, W.H. Graham, and J.D. Roberts, Tetrahedron, 1960,
11, 181.
153. A.I. Vogel, "A Text-Book of Practical Organic Chemistry",
Longmans, London, Third Edition, 1956, p. 189.
154. K. von Auwers and G. Wegener, J. prakt. Chem., 1923, 106, 226.
155. A. Schaap, L. Brandsma, and J.F. Arens, Rec. Trav. Chim.,
1965, 84, 1200.
156. P.D. Bartlett and L.J. Rosen, J.Amer.Chem.Soc., 1942, 64, 545.
157. L.I. Smith and J.S. Swenson, J.Amer.Chem.Soc., 1957, 79, 2966.
158. R. Weiss, Org.Synth., 1933, 13, 10.
159. S. Natelson and S.P. Sottfried, J.Amer.Chem.Soc., 1936, 58, 1432.
160. S.P. Natelson and S.P. Gottfried, J.Amer.Chem.Soc., 1942, 64, 2962.
161. H.C. Brown, J.Org.Chem., 1966, 31, 1090.
162. M. Gomberg, Ber., 1900, 33, 3148.
163. J.H. Mathews, J.Amer.Chem.Soc., 1926, 48, 562.
164. A. Michaelis and O. Lampe, Annalen, 1893, 274, 316.
165. H.J.F. de Vries, Ber., 1894, 27, 1521.
166. R.T. Beltrami and E.R. Russel, J.Amer.Chem.Soc., 1956, 78, 2467.
167. L.B. Young and W.S. Trahanovsky, J.Org.Chem., 1967, 32, 2349.
168. W. McPherson, Amer.Chem.J., 1899, 22, 377.
169. W.J. Hickinbottom, "Reactions of Organic Compounds", Longmans,
London, Third Edition, p. 472.

170. W.J. Dale, L. Starr, and C.W. Strobel, J.Org.Chem., 1961,
26, 2225.
171. N. Kornblum, W.J. Jones, and G.J. Anderson, J.Amer.Chem.Soc.,
1959, 81, 4113.
172. E.R. Coburn, Org.Synth., 1947, 27, 65.
173. H.O. House, W.L. Respess and G.M. Whitesides, J.Org.Chem.,
1966, 31, 3128.
174. S.F. Reed, J.Org.Chem., 1965, 30, 3258.
175. A. Klages, Ber., 1903, 36, 3688.
176. H.R. Ing and R.H.F. Manske, J.Chem.Soc., 1926, 2348.
177. N. Rabjohn, Org.Synth., 1948, 28, 58.
178. C.G. Bergstrom and S. Siegel, J.Amer.Chem.Soc., 1952, 74, 255.