PHENYLHYDRAZONES: THEIR FORMATION, ISOMERISATION AND REACTIONS

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1975

To my parents

and my wife, Heather

ACKNOWLEDGEMENTS

I should like to extend my gratitude to Dr. A.J. Bellamy for his encouragement, advice and assistance throughout this project. I also thank Mr. J. Miller for technical assistance with n.m.r. spectra, the staff and fellow students of the Chemistry Department for their general helpfulness and the Science Research Council for financial support.

J.H.

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

ABSTRACT OF THESIS

A brief review of some historical aspects of phenylhydrazone chemistry and of the work of other authors on the formation and isomerisation of phenylhydrazones and related compounds is given in the Introduction. Where appropriate, more detailed reference is made to the work of other authors in the Discussion.

The initial and equilibrated geometric isomer ratios of various phenylhydrazones in several solvents have been examined by ^{1}H n.m.r. spectroscopy and the factors thought to influence these ratios are discussed in the light of the results obtained. In particular, attention has been given to acetaldehyde phenylhydrazone. The anti isomer was found to be isolated due to preferential crystallisation and was only observed as the kinetic product during the formation of acetaldehyde phenylhydrazone in solution under controlled conditions. Isomerisation of solid acetaldehyde phenylhydrazone has been observed and in solution the isomerisation is strongly catalysed by free phenylhydrazine. It is thought that this catalysis extends to other phenylhydrazones, complicating measurement and interpretation of the initial isomer ratios. The structures and possible mechanisms of formation of higher molecular weight products from the condensation of acetaldehyde and formaldehyde with phenylhydrazine are also discussed.

The configurations of the geometric isomers in a series of alkyl phenyl ketone phenylhydrazones have been assigned by a correlation of data from their n.m.r. and ultra-violet spectra and the phenyl group is apparently approximately equal in 'size' to the ethyl group in this system. This is, to a certain extent, consistent with the recent findings of other workers for the 'size' of the phenyl group in a similar system.

continued.....

The mechanism of the oxidative ring closure of adipaldehyde bisphenylhydrazone has been investigated but the experimental evidence did not discriminate between two possible mechanisms previously proposed and a third mechanism has been considered.

The possibility of a Cope rearrangement between the C-C and N-N dimers of benzaldehyde phenylhydrazone was examined and, although the products were not isolated, analysis of equilibrated solutions by chromatography suggested that such a rearrangement does occur. The range of products arising from oxidations of bezaldehyde phenylhydrazone and possible mechanisms for their formation are also discussed.

The kinetics of the base catalysed rearrangement of an optically active phenylazo compound, 2-phenylazobornane, to the corresponding phenylhydrazone have been studied by polarimetry and ultra-violet spectroscopy but complications due to further reactions of the product were encountered. Investigation of these reactions, which appear to be due to oxidation, was inconclusive and preparation of other optically active phenylazoalkanes for kinetic studies proved difficult.

Besides the main topics outlined above, some experiments concerned with other properties and possible reactions (e.g. re-arrangements) of phenylhydrazones and phenylazo compounds are described and discussed.

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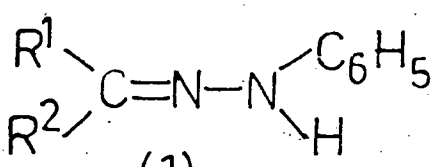
INTRODUCTION

Emil Fischer discovered phenylhydrazine[1] in 1877 and showed [1,2] that it combines with carbonyl compounds to form phenylhydrazones of the general formula (1).

Phenylhydrazones have since formed one of the main classes of crystalline derivatives by means of which carbonyl compounds are commonly characterised. Although phenylhydrazine itself is suitable for the characterisation of many individual aldehydes and ketones, firstly p-nitrophenylhydrazine[3] and then 2,4-dinitrophenylhydrazine[4] replaced phenylhydrazine in routine characterisations because their derivatives are coloured, often more highly crystalline, and less prone to oxidation and cyclisation.

Phenylhydrazones are also important as intermediates in the preparation of many heterocyclic compounds and they undergo a variety of other reactions, some of which are discussed in this thesis.

Most arylhydrazones, are, of course, synthesised by the reaction of the arylhydrazine with the carbonyl compound. The choice of conditions is dependent upon the particular arylhydrazine and the carbonyl compound which are used. Phenylhydrazine is completely miscible with most solvents except light petroleum - ether and water, and phenylhydrazones have been prepared in a variety of solvents, with or without acidic catalyst[2,5,6]. Almost quantitative yields are often obtained in ethanol[5]. Most ring substituted phenylhydrazones can be synthsised by using conditions similar to those for the parent compound, except in the case of 2,4-dinitrophenylhydrazones[7]



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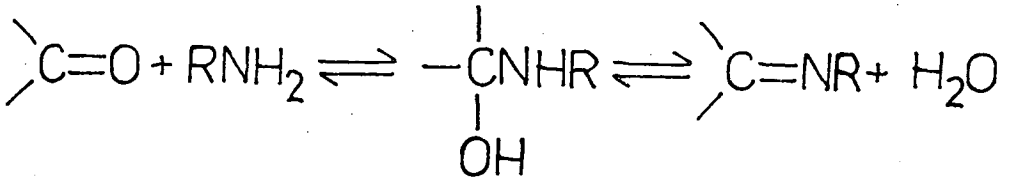
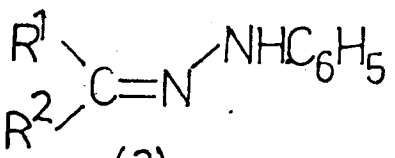


SCHEME 1



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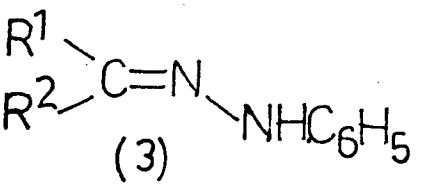

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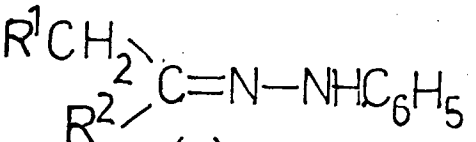

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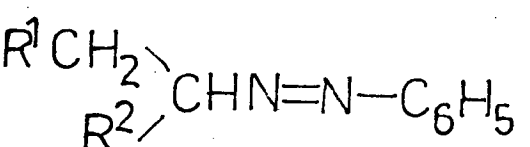

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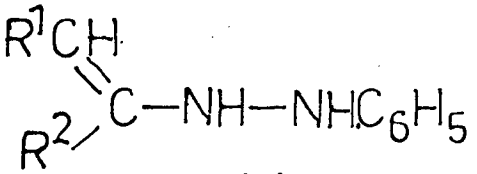

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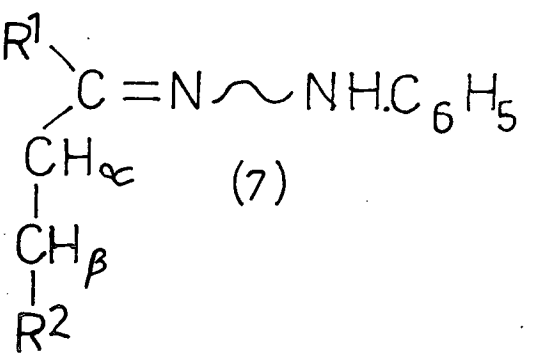


(7)

(D N P's).

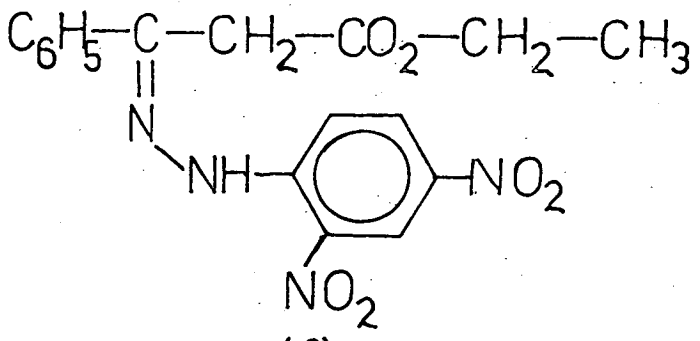
The methods for the preperation of arylhydrazones are well established and the mechanism of their formation under various conditions has been studied in detail, mainly by kinetic experiments[8,9], and has been found to be analogous to that for the formation of oximes, semicarbazones, thiosemicarbazones and Schiff bases[10].

The attack of the nucleophilic reagent (Scheme 1) is rate determining under slightly acidic conditions, and is usually subject to both general acid and specific acid catalysis[10]. Under neutral or basic conditions, dehydration of the carbinolamine becomes the rate determining step. This step is generally subject to strong acid catalysis. It is known[11] that the steric environment of the carbonyl compound involved in the condensation reaction has a marked effect on the overall rate of the reaction.

As rotation is not possible about C = N, and since the arrangement of the bonds around nitrogen is trigonal, two geometrical isomers are possible for phenylhydrazones of unsymmetrical carbonyl compounds, (2) and (3). Both geometrical isomers of numerous phenylhydrazones and D N P's have been isolated[12-16]. Often, however, these are cases where one of the isomers is intramolecularly hydrogen bonded.

It has been concluded by both Bellamy and Guthrie[23], and Karabatsos and Taller[17], that all phenylhydrazones, either in solution or neat, exist in the imine form (4) with no azo (5) or ene-hydrazine (6) forms detectable.

Throughout this thesis the nomenclature for



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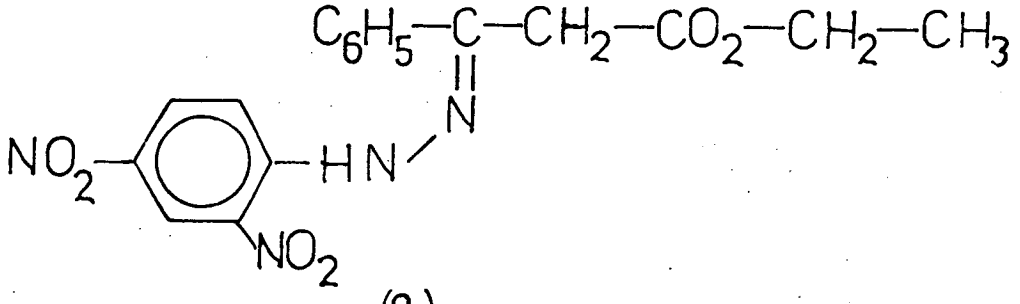

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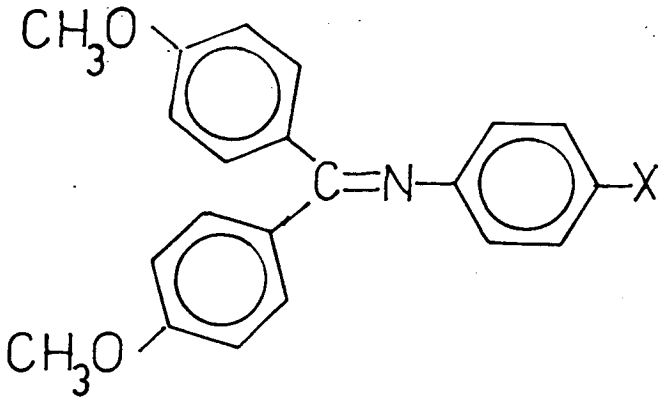


$X = N(CH_3)_2, CH_3, H$ AND $CO_2C_2H_5$

(10)

phenylhydrazones of aldehydes and ketones which was adopted by Karabatsos and co-workers[17] is used, even though this is ambiguous in some cases: the syn isomer (in 7) has the anilino group cis to the smaller R group, and the anti isomer has the anilino group cis to the larger R group e.g. the anti isomer of acetaldehyde phenylhydrazone has the anilino group cis to the methyl group.

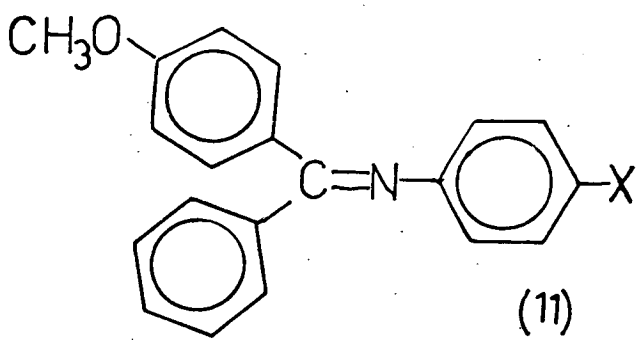
Silverstein and Schoolery[18] were among the first to apply n.m.r. techniques to the studies of D N P's. They noted differences in the aromatic hydrogen resonances of the two geometrical isomers of the D N P derivative of ethyl benzoylacetate and explained the result in terms of an anti form (8) in which the phenyl group is coplanar with the C = N, and a syn form (9) in which the phenyl group is non-coplanar with the C = N.

Karabatsos and his co-workers[17, 19-22] studied the n.m.r. spectra of phenylhydrazones, ring-substituted phenylhydrazones, semicarbazones and thiosemicarbazones of many aldehydes and ketones. Besides assigning n.m.r. absorptions Karabatsos and his co-workers reported a great deal about the configurational stability of phenylhydrazones and related derivatives and in doing so laid the foundation for the major part of the work concerning the formation and isomerisation of phenylhydrazones which is discussed in this thesis.

Various techniques have been used to study the mechanism of the isomerisation of phenylhydrazones and related compounds under a variety of conditions. Since, because of their usefulness in the characterisation of carbonyl compounds, D N P's are probably the most familiar of this class of

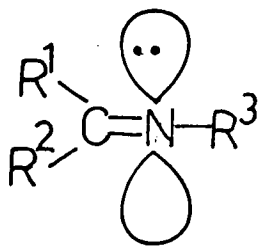
compounds, the question of stereoisomerism and the factors which effect isomerisation in D N P's have received the attention of many workers. The investigation of the syn-anti isomerisation of D N P's of alkyl phenyl ketones by U.V. and infra-red spectroscopy by Ramirez and Kirby[24], the extensive n.m.r. studies on the DNP's ofaliphatic and aliphatic-aromatic aldehydes and ketones by Karabatsos and his co-workers[17,19-21], and the rate studies of the syn-anti isomerisation of alkyl aldehyde D N P's by Hegarty and Scott[25], which occurs during bromination, all suggest that only steric factors are important in determining the stability of the various geometrical isomers in these systems. Karabatsos et al.[20] also point out that in the case of acetaldehyde D N P, the syn isomer is the kinetic product of the condensation, the equilibration of the isomers is acid catalysed, and that solvents capable of hydrogen bonding with the N - H of the D N P increase the syn/anti ratio.

Curtin, Grubbs and McCarty[26] conducted an extensive study of the syn-anti isomerisation of imines, oxime ethers and halo-imines by n.m.r., infra-red and U.V. spectroscopy. The imines (10) were found to have n.m.r. spectra at c.a. 25° C characteristic of structures with the C_6H_4X cis to one of the p-methoxyphenyl groups. Interconversion of stereoisomers was slow on the n.m.r. time scale at this temperature, but isomerisation became more rapid as the temperature was increased. The infra-red spectra of unsymmetrically substituted imines (11) suggested that they crystallise preferentially as a single stereoisomer but isomerise very rapidly, even in non-polar solvents, to a mixture with an equilibrium constant near 1.



$X = N(CH_3)_2, CH_3, Cl.$

(11)



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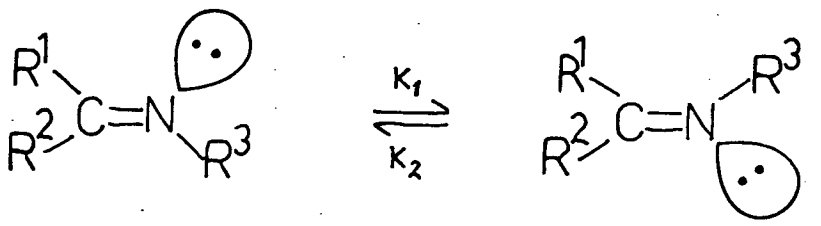
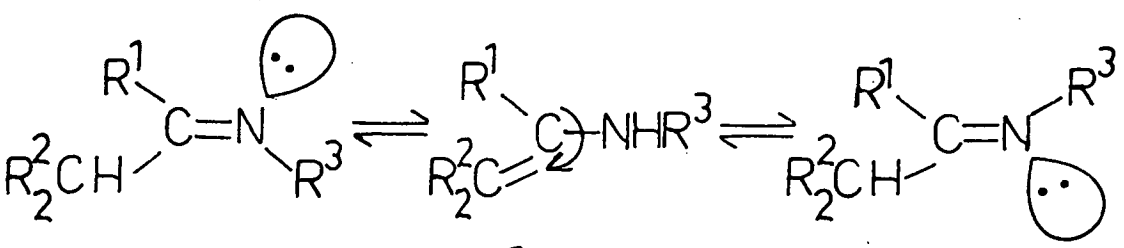


R^1, R^2 = ALKYL OR ARYL $\quad R^3$ = ALKYL

SCHEME 2



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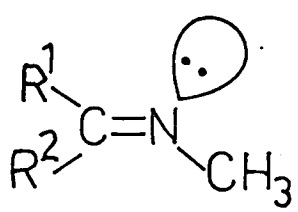

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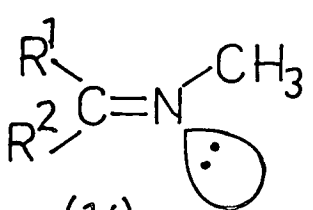


(14)

U.V. kinetic measurements support the n.m.r. results. While oximes were found to be configurationally stable, halo-imines were found to have configurational stability intermediate between the N-arylimines and the oximes. They concluded that the isomerisation of the imines studied is a unimolecular process and suggested that it occurs by a "lateral shift mechanism" which consists of the shift of the substituent attached to nitrogen (12) through a linear transition state, while the π bond remains intact and the unshared electron pair occupies the P orbital orthagonal to the π-bond of the nitrogen. This mechanism is also suggested for the isomerisation of azobenzenes[27] and phenylhydrazones[28].

Jennings and Boyd[29] have recently investigated the mechanism of syn-anti isomerisation of N-alkyl-ketimines by n.m.r. spectroscopy and measured the interconversion rates (see Scheme 2) for a series of N-alkyl-ketimines at 180 - 200°C. The $\Delta G^{\ddagger}$ values obtained from the coalesence temperatures were found to be insensitive to the nature of the substituents (whether alkyl or aryl) on the carbon. This suggests that isomerisation takes place by a mechanism close to pure nitrogen inversion. This mechanism appears to be intermediate between the "lateral shift" mechanism described above and the addition-rotation mechanism described below for acid catalysed isomerisation. Rotation about the C = N is another possible mechanism, but the energy of the dipolar (or di-radical) transition state for this mechanism would be considerably lowered by C-aryl substituents.

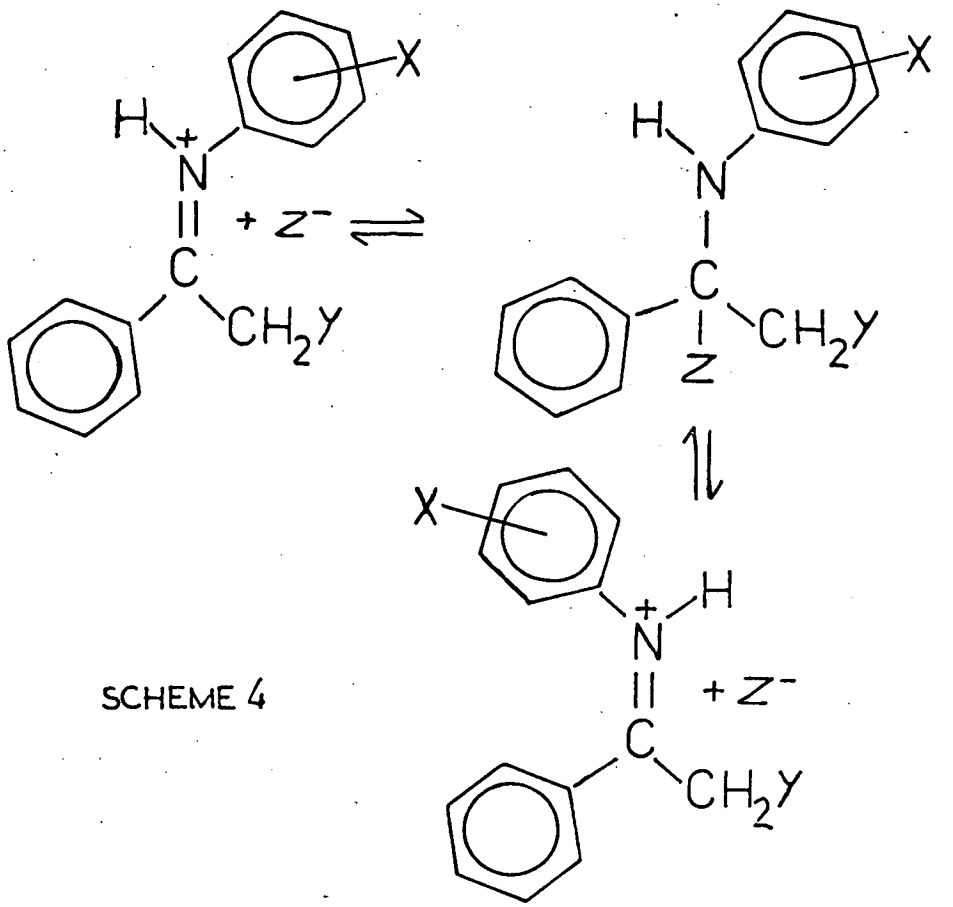
For molecules containing a C-alkyl substituent with at least one α - hydrogen atom they suggested a third

mechanism, involving an enamine intermediate (Scheme 3). In support of this mechanism they cited examples of C-ethyl imines. At temperatures higher than those required for coalescence of the ethyl signals to a single A_2M_3 system due to rapid isomerisation both the methylene quartet and methyl triplet broaden and collapse to singlets due to loss of vincial coupling which is consistent with fast proton exchange during rapid imine-enamine tautomerisation. As more convincing evidence they report deuterium exchange with the protons in the C-methyl group of C-methyl alkylimines in $[^2H_1]$ methanol during isomerisation at ambient temperature.

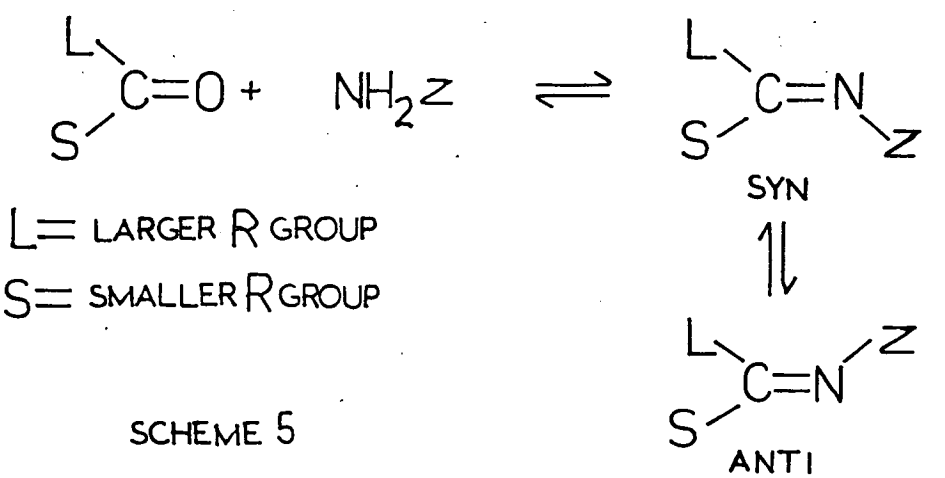
Boyd, Jennings, and co-workers[30], also suggest that interactions involving the nitrogen lone pair might be important in determining imine stereochemistry. Comparison of the equilibrated isomer ratios determined by n.m.r. spectroscopy for N-methyl imines with phenyl and 1-napthyl substituents on carbon (13 and 14) shows that the proportion of (14) increases on substitution of the more bulky 1-napthyl group for a phenyl group at R^1, and also on changing the substituent from 2-napthyl to 1-napthyl. They propose that (13) may be destabalised by an "n - π repulsive interaction" between the non-bonding nitrogen lone pair electrons and the π- electrons of the proximate aryl ring.

More recent work by this group[31], which is dealt with in the discussion section on the alkyl phenyl ketone phenylhydrazone series, substantiates their results which are described immediately above.

A similar controversy concerning the factors which



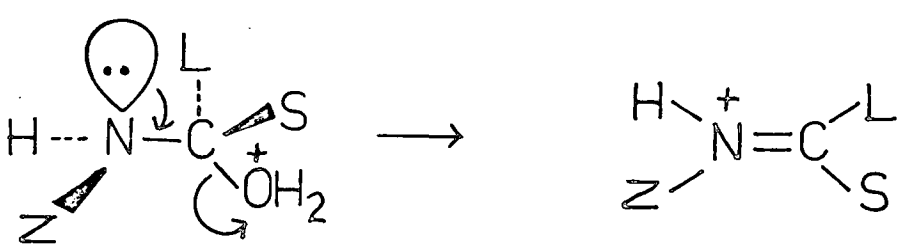
SCHEME 4



L = LARGER R GROUP

S = SMALLER R GROUP

SCHEME 5



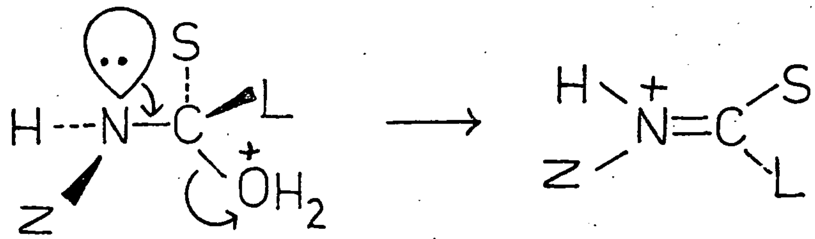
(15)

determine the configurational stability and the mechanism of syn-anti isomerisation of oximes also exists. Several kinetic studies of the syn-anti isomerisation of oximes[19,32-35], and of oxime anions[36] have appeared. However syn-anti isomerisation of phenylhydrazones has not been investigated to the same extent using modern physical techniques.

The mechanism of acid catalysed syn-anti isomerisation of a series of methyl-substituted acetophenone D N P's has been more recently investigated by Idoux and Sikorski[37] who found that the isomerisation was influenced by polar, as well as steric, effects and suggested that polar effects generally play an important role in isomerisation about the C = N bond, though steric factors are the dominant influence. Their results favour an addition-rotation mechanism (Scheme 4) for acid catalysed isomerisation, as suggested earlier by Karabatsos[17,19-21].

The most extensive study of the configurational stability of phenylhydrazones, D N P's and semicarbazones of aliphatic aldehydes and ketones by n.m.r. spectroscopy was that of Karabatsos et al.[17,19-22], whose findings with regard to geometrical isomerisation suggested that the condensation reaction generally gave rise to a single isomer in which the bulky Z group attached to the imino nitrogen bore a syn relationship to the smaller R group (Scheme 5). The isomers equilibrate on standing, or on acidification. At equilibrium, the syn isomer predominates (Bulkiest group trans), the exact isomeric composition of the equilibrium mixture being solvent dependent.

In two cases they found that the anti (thermodynamically



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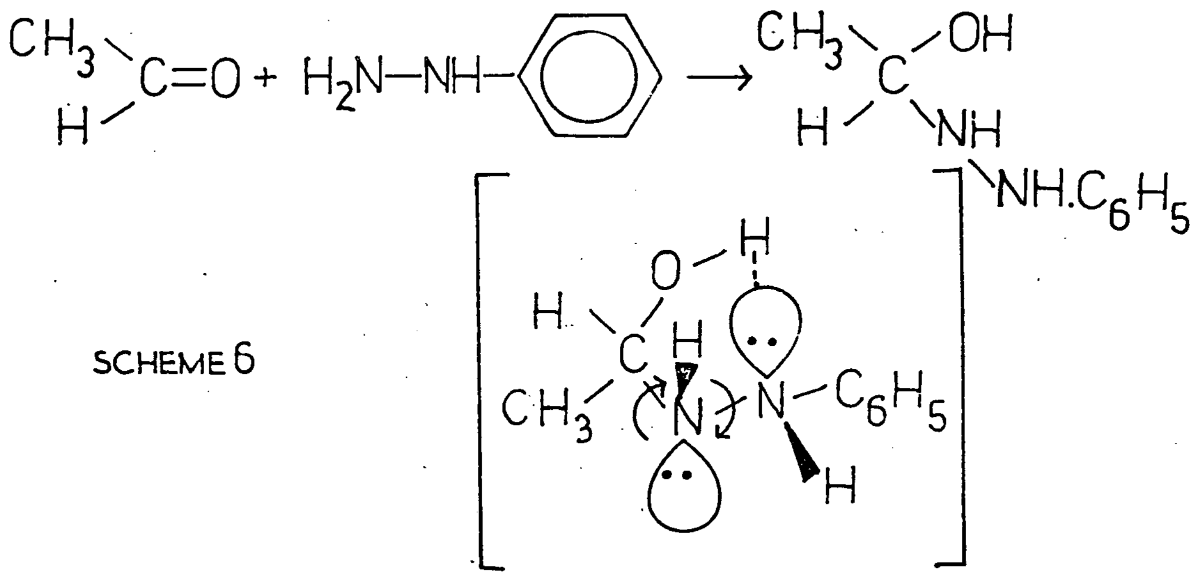
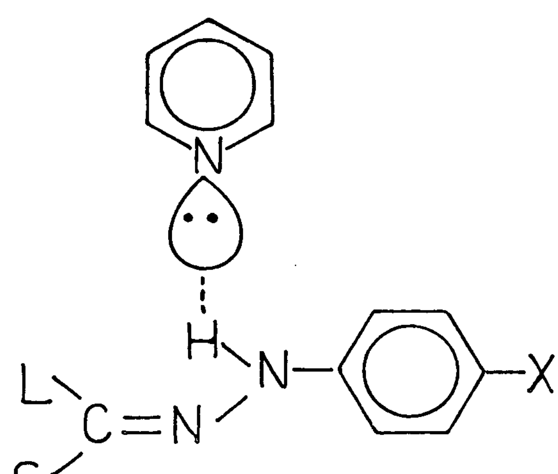


SCHEME 6



(17)

less stable) isomer was isolated (viz. of acetaldehyde phenylhydrazone and p-chlorophenylhydrazone). They suggested that isolation of a single isomer in these cases was the result of either kinetically controlled formation of one isomer only or of rapid isomer equilibration and precipitation of the less soluble one. For aldehyde D N P's, for which isomer equilibration is slow, it has been demonstrated[20] that formation of the thermodynamically more stable isomer is kinetically controlled. The fact that, in general, the thermodynamically most stable isomer has been isolated from preparations of phenylhydrazones and D N P's favours this possibility. Because of steric interactions in the transition state[38] involved in the elimination from the carbinolamine intermediate formation of the thermodynamically more stable isomers is to be expected i.e. reaction (15) should be favoured over (16). In the two cases where the less stable isomers were isolated (see above) the initial product formed was a gum which crystallised only after standing for several hours. The initially formed more stable isomer may have equilibrated and the less stable, perhaps less soluble isomer crystallised out. (This possibility has been investigated further and is dealt with in the discussion.) Karabatsos et al. also discussed the mechanism for the acid catalysed syn-anti isomerisation of D N P's and semicarbazones in terms of the addition-rotation mechanism already described (Scheme 4).

Bellamy and Guthrie[28] also isolated the anti isomer (bulkiest group cis) of acetaldehyde phenylhydrazone and found it to isomerise to an syn-anti equilibrated isomer mixture (3:2) after 42 hours in benzene. By deuterium exchange experiments

using ^{1}H n.m.r. spectroscopy they showed that neither a phenylazoalkane (5) nor an ene-hydrazine (6) was an intermediate in the interconversion of the syn and the anti isomers of phenylhydrazones in neutral solutions. They favoured the "lateral shift" mechanism (described earlier) for the isomerisation of phenylhydrazones under neutral conditions.

In summary, at the commencement of the investigation described in this thesis, it had been established that phenylhydrazones exhibit geometrical isomerism, that they undergo rapid syn-anti isomerisation, and in some cases can be isolated as a single geometrical isomer. It remained a matter for speculation, however, whether steric factors alone, or a combination of steric, electronic and solvent effects are responsible for the ratio of isomers initially formed. The mechanism of phenylhydrazone formation, through a carbinolamine intermediate, was well established, but whether or not the stercochemistry of the carbinolamine controlled the initial product geometry had not been ascertained. It was with a view to investigating further these omissions that the major part of the work concerning the formation and isomerisation of phenylhydrazones discussed in this thesis was undertaken.

DISCUSSION

^{1}H N.M.R. Study of the Formation and Isomerisation of Phenylhydrazones.

The anti (thermodynamically less stable isomer) of acetaldehyde phenylhydrazone had previously been isolated from preparations of acetaldehyde phenylhydrazone, and had been found to isomerise in solution to a syn-anti isomer mixture (3:2) by both Bellamy and Guthrie[28], and Karabatsos et al.[17,21] It was considered that the anti isomer might be the kinetic product of the condensation. (It was later shown, however, (see pages 20 -22) that the anti isomer was isolated due to preferential crystallisation). It was also thought that the thermodynamically less stable isomers of other phenylhydrazones might be kinetically favoured, or at least be more abundant in the initial product mixture formed than in the equilibrated mixture. A consideration of steric effects alone (see page 8 , para. 1) suggests that the thermodynamically favoured (syn) isomer would also be kinetically favoured, but it is possible by taking into account intramolecular hydrogen bonding in the carbinolamine, which is initially formed in the condensation, to devise a mechanism which would lead to the formation of the anti isomer on dehydration.

Hydrogen bonding (Scheme 6) between the hydroxyl proton and the α-nitrogen lone pair, or less likely between the α-N-H and the oxygen lone pair, could hold the carbinolamine in a cyclic arrangement with minimized non-bonded interactions between the methyl group and the α-N-H. If the hydroxyl group was then displaced by the β-nitrogen lone pair,

rotation, as shown, would lead to a trans-antiperiplanar arrangement, and would also bring the methyl and NHPh into a cis arrangement, leading to the least stable geometrical isomer of the phenylhydrazone.

In order to investigate whether or not such a hydrogen bonded carbinolamine did influence the initial products of phenylhydrazone formation, condensations of carbonyl compounds with varying degrees of steric hinderance around the carbonyl group were examined by n.m.r. spectroscopy. The reactions were monitored as soon as solutions of the reagents were mixed, and then at intervals until an equilibrated isomer mixture had been formed. The assignments were made on the basis of the n.m.r. data reported for phenylhydrazones by Karabatsos et al.[17,22] Ring substituted phenylhydrazones (e.g. p-methyl, p-chloro and p-nitro) were used so that comparison could be made of the isomer ratios for phenylhydrazones in which the hydrogen bonding affinity of the nitrogen lone pair described above was either increased or decreased relative to the unsubstituted phenylhydrazone. The solvents used were also varied c.f. pyridine and nitromethane; pyridine[17] would be expected to form intermolecular hydrogen bonds with the carbinolamine and thus prevent formation of the cyclic carbinolamine arrangement described above, whereas with nitromethane intermolecular hydrogen bonding would be greatly decreased or even absent (see below).

The choice of solvents for these experiments was restricted as they had to satisfy the following conditions: (i) the reagents and the products should be soluble enough

in the solvent for 5% M solutions to be formed, (ii) the solvent should be miscible with water (the solutions became 5% M in water formed from the dehydration of the carbinolamine), (iii) the absorptions of the solvent in the n.m.r. spectrum should not interfere with those of the reagents or products being studied (usually methyl or methylene signals in the region of 1 - 2.5 p.p.m. were used in monitoring the reactions). An additional requirement was that they did not show a tendency to form hydrogen bonds with the intermediate carbinolamine.

The experiments were initially conducted with dioxan as the solvent, but a comparison of the basisity of various solvents by measurement of their $\Delta\delta_{\infty}(CH\,Cl_3)$ values (see Experimental, pages 92, 93) suggested that both nitromethane and acetonitrile were much less basic than dioxan. Acetonitrile fulfilled most of the requirements listed above except that the n.m.r. signal for the methyl group (1.34 p.p.m. neat) obscured the absorptions for some of the carbonyl compounds and phenylhydrazones being studied. (This was overcome in most cases by use of $[^2H_3]$ acetonitrile). Acetonitrile had been found by Delpuech[39], using n.m.r. spectroscopy, to exhibit less hydrogen bonding affinity than other common organic solvents (e.g. dioxan, ether and tetrahydrofuran). Nitromethane also fulfilled the requirements listed above, but, from comparison of the result of Delpuech for acetonitrile and that of Martin and Martin[40] for nitromethane, using the same method, nitromethane appeared to have a hydrogen bonding affinity slightly greater than that of acetonitrile. These results were re-investigated using both n.m.r. and infra-red spectroscopy (see Experimental,

pages 89 - 93) and acetonitrile was found to have a greater hydrogen bonding affinity than nitromethane. It was shown that nitromethane did not react with carbonyl compounds under the conditions used for the formation and isomerisation of phenylhydrazones. Nitromethane was found to be the most suitable non-basic solvent for the study of these reactions, although p-nitrophenylhydrazine was not sufficiently soluble in either nitromethane or acetonitrile. (This limitation was not present when p-chlorophenylhydrazine was used.)

The results of these experiments are presented in Table 1. The values reported for the amount of syn isomer are accurate to c.a.$\pm$ 2%, Only the percentage of syn isomer in relation to the total amount of phenylhydrazone in the solution is reported in Table 1. In cases where the carbonyl compound was sterically hindered e.g. benzyl methyl ketone, it was found that formation of the phenylhydrazone was slow, and free carbonyl compound was observed to be present up to 5 hours after mixing the reactants. It was also found that in some solvents e.g. pyridine, p-nitrophenylhydrazine is less reactive than phenylhydrazine itself, which is in turn less reactive than p-methylphenylhydrazine.

Great emphasis cannot be placed on the isomer ratios measured before the solutions were equilibrated since it was discovered, after these experiments had been run, that phenylhydrazine itself greatly catalyses the isomerisation of acetaldehyde phenylhydrazone (see page 30) and it is possible that this catalytic effect extends, to some extent, to the isomerisation of other phenylhydrazones. In order that all the

carbonyl compound would eventually be converted into phenylhydrazone a 25% excess of phenylhydrazine over carbonyl compound was used, but even if equimolar quantities of carbonyl compound and phenylhydrazine had been used, sufficient phenylhydrazine would have been present throughout most of the reaction period to catalyse the syn-anti isomerisation of the phenylhydrazone.

With dioxan (pK - 2.92[41]) and pyridine (pK c.a. 5.2[41]), the more basic solvents used, examination of Tables 1 A, B, C and D shows that the percentage of syn isomer increases as the formation and isomerisation of the phenylhydrazone proceeds, except for the fast reaction of acetaldehyde with p-methylphenylhydrazine (Table 1 D) where condensation and isomerisation were probably complete before the first spectrum (0.5 hr.) was recorded. In nitromethane the initial isomeric composition does not change significantly as the reaction proceeds (Tables 1 G and H), and in $[^2H_3]$ acetonitrile (Tables 1 F and E) an increase in the percentage of syn isomer was observed only in the relatively slow reaction of methyl benzyl ketone with both phenylhydrazine and p-chlorophenylhydrazine. These results indicate that the greater the hydrogen bonding affinity of the solvent, the greater the percentage of anti isomer initially formed. This does not support the hypothesis involving the cyclic carbinolamine intermediate described above. It is possible, however, that isomerisation catalysed by phenylhydrazine is more rapid in solvents which have low hydrogen bonding affinity, and that only equilibrated isomer mixtures were observed in these solvents.

Comparison of the initial isomeric compositions for

p - nitrophenylhydrazones and unsubstituted phenylhydrazones in pyridine (Tables 1 B and C) shows that there is less of the anti isomer present initially with p- nitrophenylhydrazones. The p-nitro substituent would be expected to delocalise the nitrogen lone pair, thus decreasing the strength of the hydrogen bonding in the proposed cyclic carbinolamine (Scheme 6), relative to that for unsubstituted phenylhydrazones, and therefore cause a decrease in the amount of anti isomer initially observed. The results are in agreement with this proposal. The opposite effect should be observed with p-methyl substitution (Table 1 D), but subsititution of a p-methyl group appears to make little difference to the initial isomer ratios (compare Tables 1 B and D). p-Methylphenylhydrazine is more reactive than phenylhydrazine itself, which is in turn more reactive than p-nitrophenylhydrazine. (It may be that, in the experiments with p-methylphenylhydrazine, phenylhydrazone formation and isomerisation was complete before the first spectrum was recorded (0.5 hr.).) In solvents with little hydrogen bonding affinity the effects due to p-substitution should be more marked, but comparison of results in acetonitrile (Tables 1 F and E) and in nitromethane (Tables 1 G and H) (where a p-chloro substituent was used to provide the inductive effect rather than a p-nitro substituent because of solubility problems) shows there is no great difference in the isomeric compositions of the substituted and unsubstituted phenylhydrazones.

Hence, the initial isomer ratios do not, in general, substantiate the hypothesis of the cyclic carbinolamine structure, but the effect of catalysis by phenylhydrazine, or

ring-substituted phenylhydrazines, on these initial ratios is uncertain. The solutions were 1.25% M in phenylhydrazine (or ring-substituted phenylhydrazine) after the phenylhydrazone formation was complete. The equilibrated isomer ratios provide more significant information as these should be unaffected by the catalysis.

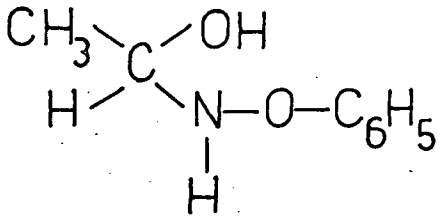
In a p-substituted phenylhydrazone (17) an electron withdrawing substituent (e.g. NO_2 or Cl) should increase the acidity of the NH and favour hydrogen bonding with basic solvents, e.g. pyridine, and this should sterically destabalise the anti isomer relative to the syn isomer. Conversely an electron releasing substituent (e.g. Me) should have the opposite effect and increase the percentage of anti isomer in the equilibrated mixture. For solvents with low hydrogen bonding affinity, e.g. nitromethane and acetonitrile, para-substitution in the phenyl group should have little or no effect on the equilibrated isomer ratios.

Comparison of the equilibrated isomer ratios (after c.a. 200 hours) for substituted and unsubstituted phenylhydrazones substantiates the above hypothesis, i.e. there is less anti isomer at equilibrium in the p-nitro substituted compounds and more in the p-methyl substituted compounds than in the unsubstituted phenylhydrazones for solutions in pyridine (Tables 1 B, C and D). Also, in the non-basic solvents, nitromethane and acetonitrile, substitution of an electron withdrawing substituent (p-chloro) has little effect on the equilibrated isomeric composition (Tables 1 E, F, G and H). For example, with acetaldehyde phenylhydrazone in nitromethane (see

Experimental, pages 88, 86) the equilibrated mixture contains 39% of the anti isomer, whereas with the p-nitrophenylhydrazone in the same solvent 29% of the anti isomer. In pyridine the corresponding figures are 33% and 19% respectively, i.e. in the solvent with greater hydrogen bonding affinity there is less of the anti isomer in an equilibrated solution and this effect is more marked on substitution of an electron withdrawing p-nitro group. Karabatsos and Taller[17] have related chemical shifts in the n.m.r. spectra of phenylhydrazones to hydrogen bonding with solvents such as pyridine, nitrobenzene and methyl benzoate.

Because of complications with catalysis of the isomerisation of phenylhydrazones by free phenylhydrazine the experiments discussed above did not serve the prupose for which they were originally designed i.e. to provide information on isomer ratios of phenylhydrazones as they are formed.

Such catalysis is difficult to avoid entirely but may be minimized by allowing excess of a carbonyl compound to react with small amounts of phenylhydrazine. Experiments of the latter type have been carried out with acetaldehyde and phenylhydrazine, and the results are discussed on page 31 .



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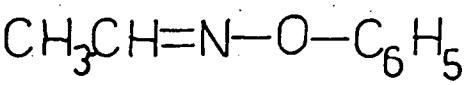

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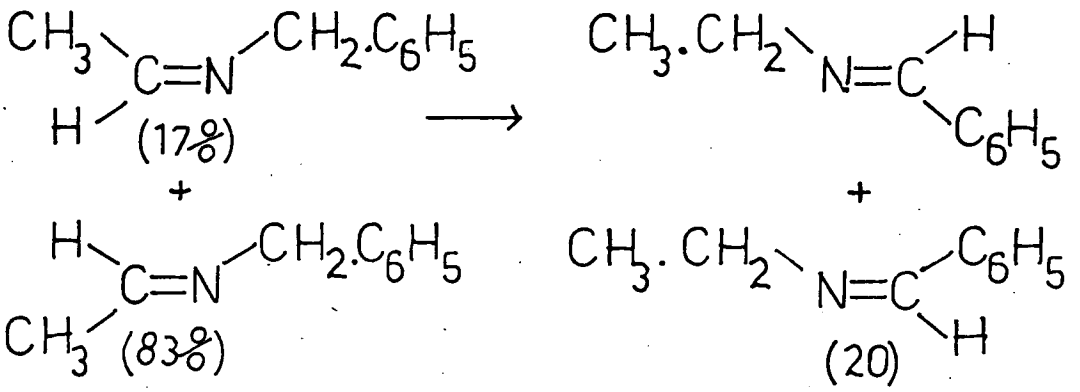
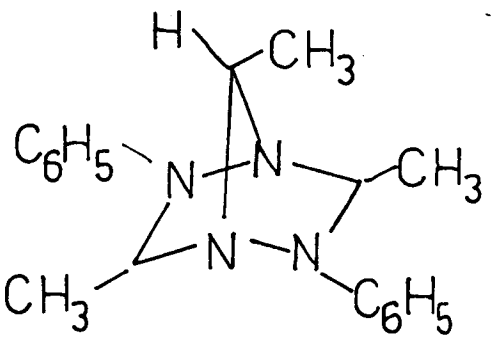


SCHEME 7



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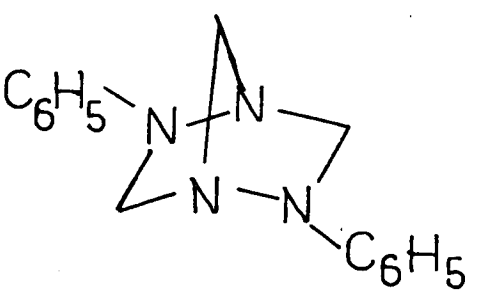


(22)

The Condensations of Acetaldehyde with Amino Derivatives Related to Phenylhydrazine.

Both the hypotheses described earlier in relation to the initial (page 15 , para. 1 , Scheme 6) and equilibrated (page 16 , para. 2 , 17) isomer ratios for phenylhydrazones are dependent upon the basicity of the α - nitrogen in the carbinolamine and the phenylhydrazone respectively. If this basicisity were altered, then, providing the hypotheses were correct, the isomer ratios of the initial and equilibrated products would also be expected to alter. Substitution of the α- nitrogen by oxygen and carbon would be expected to decrease the basicity at the α - position and thus decrease the proportion of anti isomer initially formed and increase the proportion of anti isomer in the equilibrated isomer mixture relative to the proportions observed for a particular phenylhydrazone.

The condensation of O-phenylhydroxylamine with acetaldehyde in dioxan was studied by n.m.r. spectroscopy (Experimental, page 114) in the same way as condensations of carbonyl compounds with phenylhydrazine and substituted phenylhydrazines were followed. The reaction was much slower than that of acetaldehyde with phenylhydrazine. Dehydration of the carbinolamine (1- hydroxy- 1-phenoxyamino-ethane, 18) appeared to be rate determining and absorptions attributed to this intermediate began to decrease in intensity after 5 hours when absorptions for the isomers of O-phenyl acetaldehyde oxime (19) were initially observed. The doublets of the isomers overlapped in dioxan but separated on addition of benzene.

The equilibrated isomer ratio was found to be 53% *syn* and 47% *anti* i.e. more *anti* isomer than for acetaldehyde phenylhydrazone in dioxan (61% *syn*, 39% *anti*). This result supports the hypothesis described earlier in relation to equilibrated isomer ratios. Because of the overlap of signals the initial isomer ratios were not measured.

Similarly, the condensation of acetaldehyde with benzylamine in dioxan was studied (Experimental, page 117). The initial isomeric composition was found to be 83% *syn* and 17% *anti*. The reaction was complicated by rearrangement of the acetaldehyde benzylimine to benzaldehyde ethylimine (20, Scheme 7). The experiment was repeated with pyridine as solvent but separate absorptions for isomers of acetaldehyde benzylimine were not observed. If two isomers were present, their absorptions were co-incident. No evidence of a double bond shift to form benzaldehyde ethylimine was observed in this case.

Experiments with Acetaldehyde Phenylhydrazone.

The Isolation of anti-Acetaldehyde Phenylhydrazone.

Attempts were made to isolate the anti isomer of acetalhyde phenylhydrazone by following the method of Bellamy and Guthrie[28] (Method A; Experimental, page 98), but this method generally yielded an isomeric product mixture containing c.a. 40% anti isomer; 95% was the highest proportion of anti isomer obtained in these mixtures. The method described by Laws and Sidgwick[42] (Method B; Experimental, page 98) also proved unsuccessful. It was apparent from the attempts to prepare the anti isomer by method A that the temperature at which the condensation is carried out is important in determining the nature of the product; higher temperatures favoured the formation of higher molecular weight products. The reaction tended to be more exothermic when redistilled phenylhydrazine and acetaldehyde were used. Pure anti - acetaldehyde phenylhydrazone was obtained by carrying out the reaction at as low a temperature as possible ($< 78^{\circ}C$) in ethanol as solvent (see Experimental, page 99). The solid anti isomer was found to equilibrate when stored under nitrogen at room temperature for c.a. 1 month. In one preparation the yield of crude crystalline product, which was shown by n.m.r. spectroscopy to be 93% anti isomer and 7% syn isomer, before it was further purified by crushing with ice-cold ethanol, was 85%. After purification the yield was 56% and the mixture contained > 98% anti isomer. (For propionaldehyde phenylhydrazone only an equilibrated isomer mixture was obtained using the same method.)

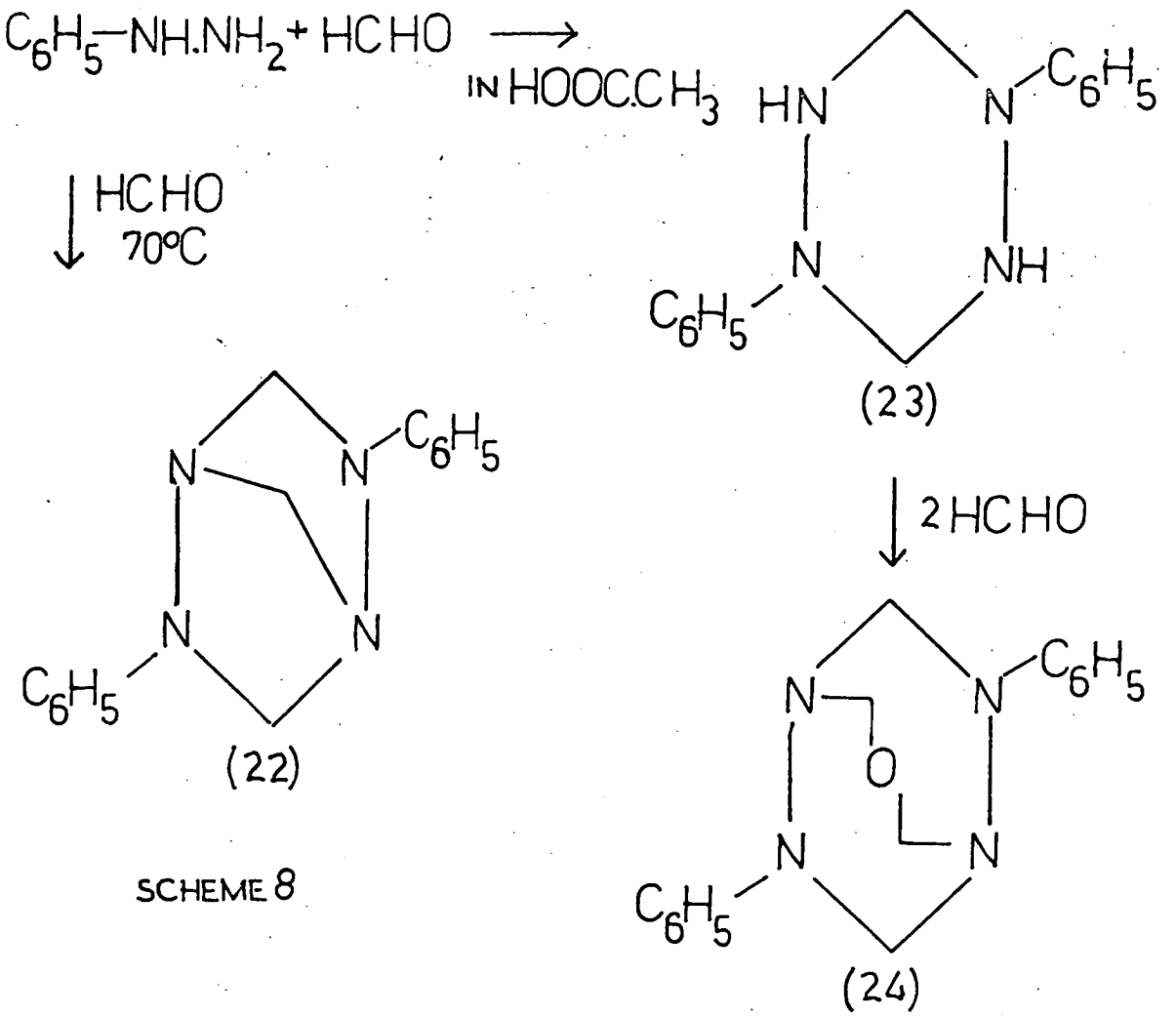
In another preparation (see Experimental, page 100)

in which neat acetaldehyde and phenylhydrazine were allowed to react while cooled on ice, the crude product mixture was shown by n.m.r. spectroscopy to be 69% syn isomer and 31% anti isomer. After purification by crushing with ice-cold ethanol the composition was 40% syn isomer and 60% anti isomer. These results showed that the syn isomer was selectively dissolved in ethanol.

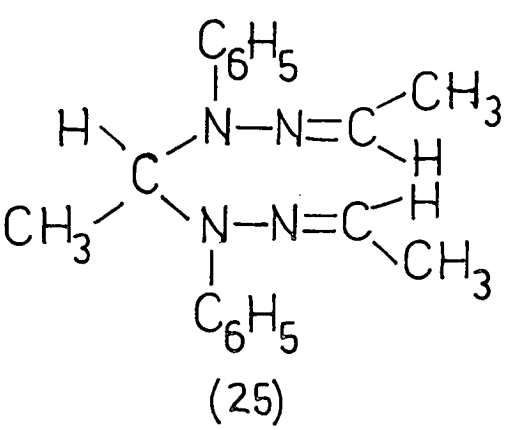
The preferential solubility in ethanol of the syn isomer over the anti isomer is not, however, the reason that the anti isomer was isolated from these preparations. It was shown (Experimental, page 101) that after condensation of acetaldehyde with phenylhydrazine in benzene the solution contained a mixture of 65% syn isomer and 35% anti isomer. After the benzene had been removed in vacuo the n.m.r. spectrum of the crude crystalline product (86.5%) showed it was composed of 13% syn isomer and 87% anti isomer. Conversion of syn isomer to anti isomer must have taken place during crystallisation. During the various attempts to obtain pure anti-acetaldehyde phenylhydrazone by method A it was noted that the lower the temperature during crystallisation, the higher the ratio of anti isomer to syn isomer obtained as crude product. It therefore appears that the anti isomer crystallises out preferentially.

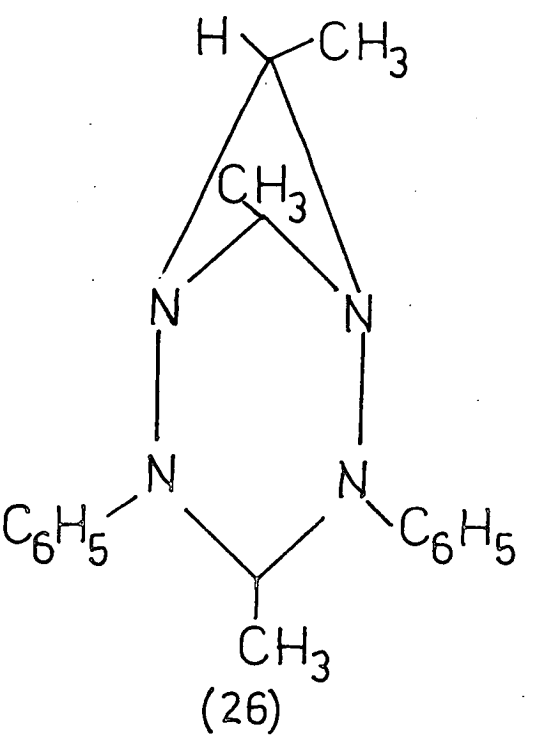
In summary, for acetaldehyde phenylhydrazone the syn isomer is kinetically and thermodynamically favoured in solution. (A mixture of c.a. 65% syn isomer and c.a. 35% anti isomer, i.e. approximately the same as an equilibrated isomer mixture, was observed initially in solution in many preparative

experiments). The anti isomer crystallises out preferentially but the solid product reverts to an equilibrated mixture of c.a. 65% syn isomer on standing (i.e. approximately the same isomer distribution as that of an equilibrated solution.)



SCHEME 8





High Molecular Weight Products from Aldehydes and Phenylhydrazine.

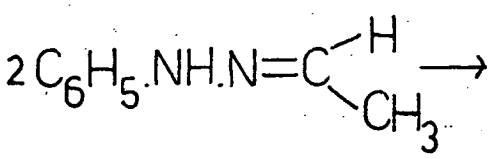
The high molecular weight compound which was isolated from the attempts to prepare anti-acetaldehyde phenylhydrazone by method A was identified as 3, 6, 7 - trimethyl - 2, 5 - diphenyl - 1, 2, 4, 5 - tetra-azabicyclo (2, 2, 1) heptane (21) (Experimental, page 102). Karabatsos and Taller[106] isolated the same compound from their attempts to make acetaldehyde phenylhydrazone and they also isolated the enalogous compound, 2, 5 - diphenyl - 1, 2, 4, 5 - tetra-azabicyclo (2, 2, 1) heptane (22) from their attempts to prepare formaldehyde phenylhydrazone. They made structural assignments by comparison with similar compounds reported by Schmitz and Ohme[43] who showed (Scheme 8) that, in the presence of acetic acid, phenylhydrazine condenses with an equimolar amount of formaldehyde to form 1, 4 - diphenyl - 1, 2, 4, 5 - tetra-azacyclohexane (23) which will condense further with formaldehyde to give 6, 8 - diphenyl - 1, 5, 6, 8 - tetra-aza-3-oxabicyclo (3,2,2) nonane (24) and also that phenylhydrazine condenses with excess formaldehyde at 70°C to form 2, 5 - diphenyl - 1, 2, 4, 5 - tetra-azabicyclo (2, 2, 1) heptane (22).

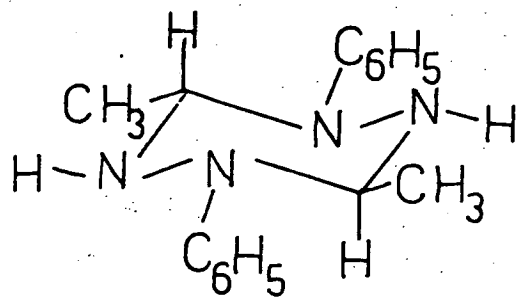
Causse[44] reported isolation of two isomers (m.p. 60°C and 99.5°C) from the treatment of a solution of acetaldehyde in phosphoric acid with phenylhydrazine. He named the lower-melting compound α - triethylidine diphenylhydrazine (25) and the higher-melting compound β - triethylidine diphenylhydrazine (26), and assigned the structures shown. 3, 6, 7 - Trimethyl - 2, 5 - diphenyl - 1, 2, 4, 5 - tetra-azabicyclo

(2, 2, 1) heptane (21) has a similar m.p. (104 - 105°C) to β - triethylidine diphenylhydrazine, and shows the same colour changes (yellow - orange - red - brown), on standing or in solution, as those reported by Causse for β - triethylidine diphenylhydrazine, and appeared to be the same compound. The structure of (26) is very similar to that of (21) proposed by Karabatsos and Taller[106], differing only in the position of the bridge and a phenyl substituent. The α - triethylidine diphenylhydrazine was later shown by Fischer[45] to be the syn isomer of acetaldehyde phenylhydrazone, and, by repetition of Causse's experiments (see Experimental, page 103) in which only isomer mixtures of acetaldehyde phenylhydrazone were obtained, it seems probable that Fischer was correct.

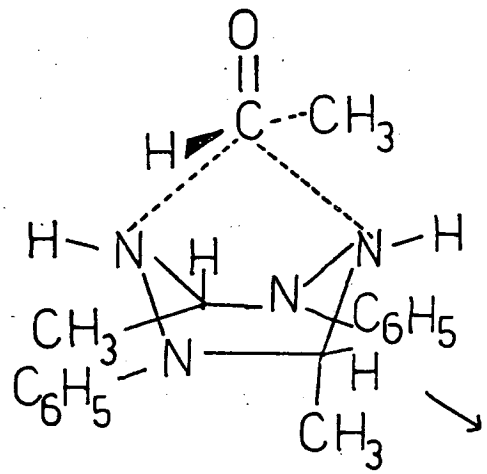
To account for the formation of β - triethylidine diphenylhydrazine, Causse proposed a mechanism involving phosphoric acid, but acid was not present when (21) was isolated from attempted preparations of anti-acetaldehyde phenylhydrazone by method A. In order to obtain further evidence for the structure of (21) and also to investigate the mechanism of its formation, further experiments were carried out on condensations of acetaldehyde and formaldehyde with phenylhydrazine. In the course of this work some of the experiments of Schmitz and Ohme[43], on the basis of which the structure (21) was proposed by Karabatsos and Taller[106], were repeated.

Acetaldehyde was found to condense with anti-acetaldehyde phenylhydrazone (Experimental, pages 104, 105) to form 3, 6, 7 - trimethyl - 2, 5 - diphenyl - 1, 2, 4, 5 - tetra-azabicyclo (2, 2, 1) heptane (21). It was also shown that

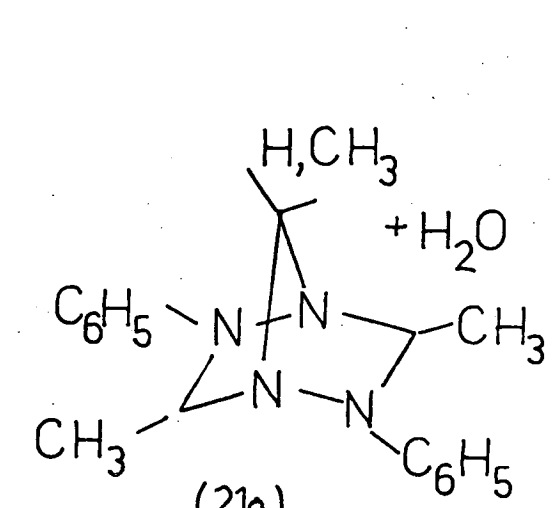




(27) CHAIR

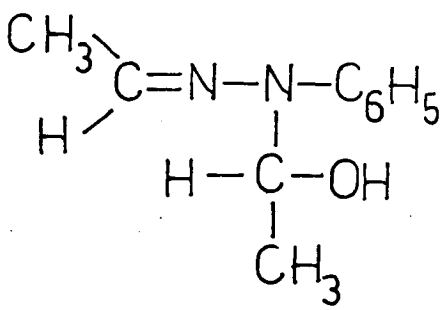


BOAT

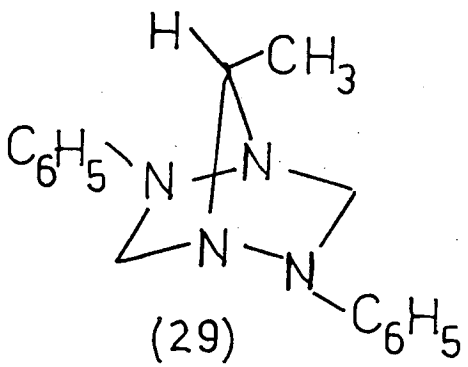


(21a)

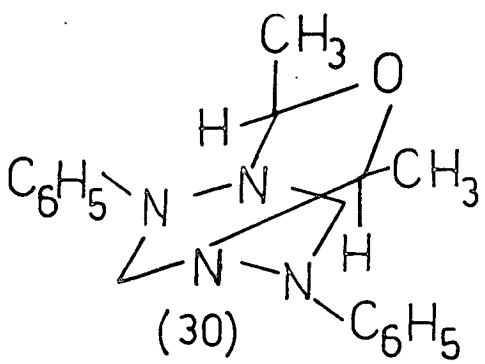
SCHEME 9



(28)



(29)



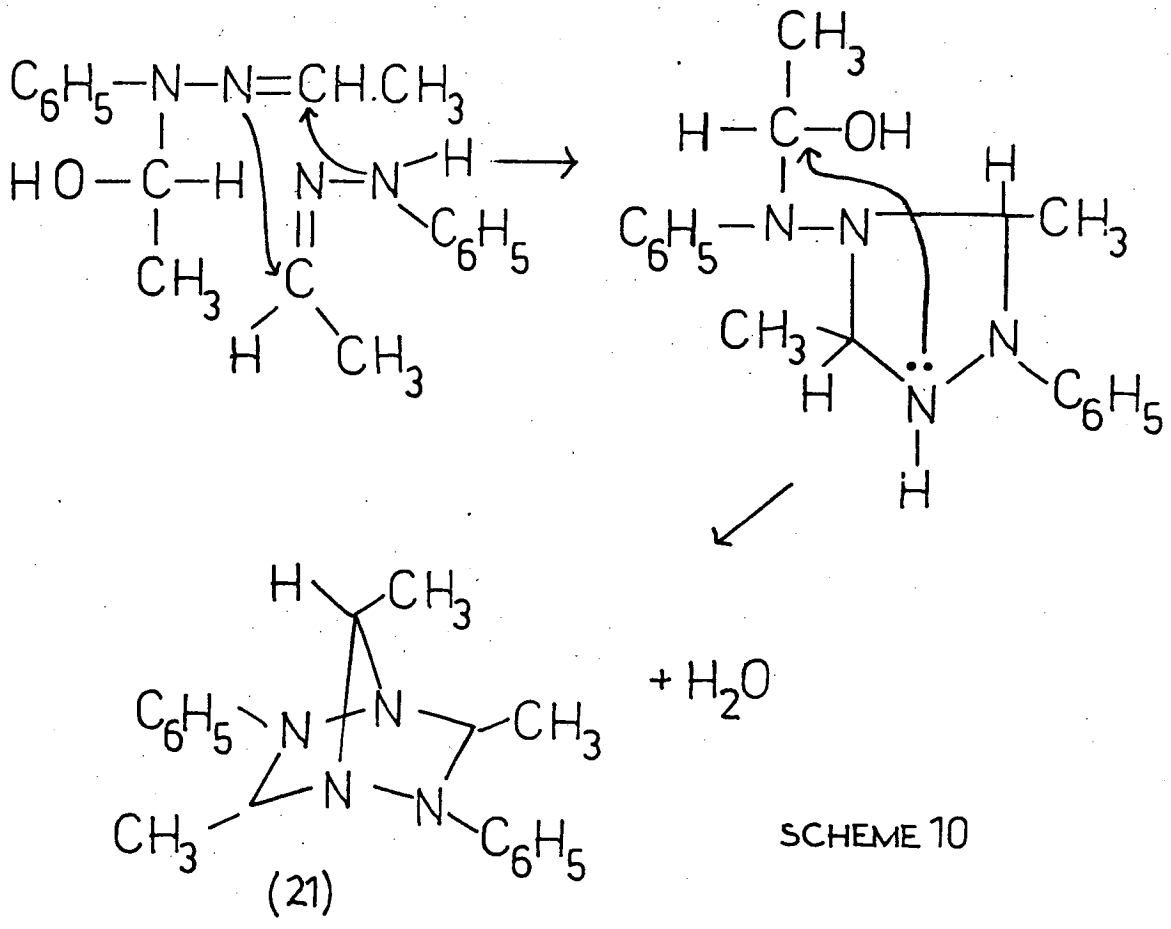
(30)

an isomer mixture of acetaldehyde phenylhydrazone (60% syn, 40% anti) reacted with acetaldehyde to give only one isomer of (21). Whether or not acetaldehyde reacted preferentially with one isomer of the phenylhydrazone was not determined from these experiments as the yields of (21) were poor. Neither acetone nor propionaldehyde were found to react with acetaldehyde phenylhydrazone under similar conditions.

The results suggested that, in the formation of (21) from acetaldehyde and phenylhydrazine, acetaldehyde phenylhydrazone is initially formed, and further condensation of acetaldehyde with acetaldehyde phenylhydrazone may then take place by two routes:-

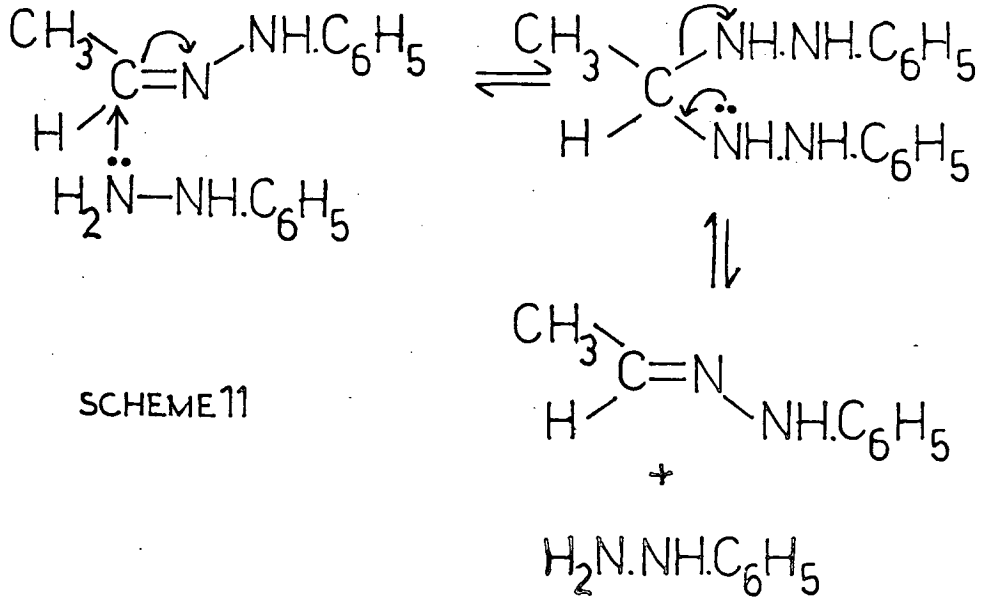
(i.) Two molecules of acetaldehyde phenylhydrazone may react together to form 3, 6 - dimethyl - 1, 4 - diphenyl - 1, 2, 4, 5 - tetra-azacyclohexane (27). (An analogous compound (23) was previously isolated by Schmitz and Ohme[43] from the condensation of formaldehyde with phenylhydrazine). This dimer would be expected to exist in both the chair and the boat forms shown in Scheme 9. Condensation of a molecule of acetaldehyde with the dimer in the boat conformation would lead to a product of configuration (21a), with the position of the final H and Me uncertain.

(ii) A molecule of acetaldehyde may react with one molecule of acetaldehyde phenylhydrazone to give (28) followed by reaction with a further molecule of acetaldehyde phenylhydrazone to give (21) by the



(21)

SCHEME 10



SCHEME 11

mechanism outlined in Scheme 10.

(Simple mechanisms cannot be devised for the reaction of acetaldehyde with acetaldehyde phenylhydrazone under neutral conditions to account for the β - triethylidine structure (26) proposed by Causse, and this suggests that this assignment is incorrect.) Mechanism (ii) is inconsistent with the findings of Schmitz and Ohme[43] for reactions between formaldehyde and phenylhydrazine but, since acetaldehyde phenylhydrazone does not readily dimerise in the absence of acetaldehyde, mechanism (ii) seems more probable than mechanism (i) for the formation of (21). Compound (21) was found to decompose to an equilibrated isomer mixture of acetaldehyde phenylhydrazone on storage in carbon tetrachloride (Experimental, page 106); there was no evidence for acetaldehyde or a dimer of acetaldehyde phenylhydrazone among the products of the decomposition, which appears to be promoted by oxygen rather than by moisture.

The dimer of formaldehyde phenylhydrazone, 1, 4 - diphenyl - 1, 2, 4, 5 - tetra-azacyclohexane (23) was prepared by the method of Schmitz and Ohme[43] and the structure of the product, which decomposed to formaldehyde phenylhydrazone on heating, was shown by n.m.r. spectroscopy to be consistent with structure (23) proposed by Schmitz and Ohme. Reaction of formaldehyde with (23) in the presence of acetic acid, following the method of Schmitz and Ohme[43], yielded a mixture of two products, which was shown by spectroscopy (Experimental, page 109) to be mainly 6, 8 - diphenyl - 1, 5, 6, 8 - tetra-aza-3-oxabicyclo (3, 2, 2) nonane (24), plus a little 2, 5 - diphenyl - 1, 2, 4, 5 -tetra-azabicyclo (2, 2, 1) heptane (22).

(Schmitz and Ohme isolated (24) only from this reaction.) A similar attempt to bridge the dimer of formaldehyde phenylhydrazone (23) with acetaldehyde in the presence of acetic acid was made but the dark brown oil obtained could not be characterised. When the reaction was carried out without acetic acid a mixture of 7 - methyl - 2, 5 - diphenyl - 1, 2, 4, 5 - tetra-azabicyclo (2, 2, 1) heptane (29) (c.a. 20%) and 2, 4 - dimethyl - 6, 8 - diphenyl - 1, 5, 6, 8 - tetra-aza-3-oxa-bicyclo (3, 2,2) nonane (30) (c.a. 80%) was obtained. These compounds are analogous in structure to (22) and (24) which were obtained from the reaction of formaldehyde with (23).

Reaction of excess formaldehyde with acetaldehyde phenylhydrazone in water (Experimental, page 109) produced a mixture of 2, 5 - diphenyl - 1, 2, 4, 5 - tetra-azabicyclo (2, 2, 1) heptane (22) (33%) and 6, 8 - diphenyl - 1, 5, 6, 8 - tetra-aza-3-oxa-bicyclo (3, 2, 2) nonane (24) (67%) i.e. formaldehyde had displaced acetaldehyde from acetaldehyde phenylhydrazone and had subsequently reacted to give the same products as those obtained from the reaction of formaldehyde with the dimer of formaldehyde phenylhydrazone.

These results support the structure of the dimer of formaldehyde phenylhydrazone (23) proposed by Schmitz and Ohme[43] and also the structure of 3, 6, 7 - trimethyl - 2, 5 - diphenyl - 1, 2, 4, 5 - tetra-azabicyclo (2, 2, 1)heptane (21) proposed by Karabatsos and Taller[106]. Whether mechanism (i) or (ii), or both operates in the formation of (21) is debatable, since a dimer of acetaldehyde phenylhydrazone may exist in small quantity in equilibrium with the monomer.

^{1}H N.M.R. Studies on the Formation and Isomerisation of Acetaldehyde Phenylhydrazone.

The isomerisation of pure anti-acetaldehyde phenylhydrazone in nitromethane at 28°C was followed by n.m.r. spectroscopy (Experimental, pages 118 - 120). The results of the two runs that were made are shown in Table 2. These results were plotted according to the equation: $\ln (X_e - X) = -t (k_1 + k_{-1}) + \ln X_e$. ($X_e$ and X were the mole fractions of the syn isomer at equilibrium and time t respectively; k_1 and k_{-1} were the forward and backward rate constants respectively for $Y \rightleftharpoons X$, where Y represents the anti isomer). The equation was derived as follows:

$$\underset{[1 - X]}{Y} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{[X]}{X}$$

$$\frac{dX}{dt} = k_1 (1 - X) - k_{-1} X$$

$$\frac{dX}{X(k_1 + k_{-1}) - k_1} = - dt$$

$$\frac{1}{(k_1 + k_{-1})} \ln (-X (k_1 + k_{-1}) + k_1) = - t + c$$

when $t = 0$, $X = 0$

$$\therefore \quad c = \frac{1}{(k_1 + k_{-1})} \ln k_1$$

$$\ln (-X (k_1 + k_{-1}) + k_1) = -t (k_1 + k_{-1}) + \ln k_1$$

$$\ln \left(-X \frac{(k_1 + k_{-1})}{k_1} + 1\right) = -t (k_1 + k_{-1})$$

At Equilibrium : $k_1 (1 - Xe) = k_{-1} Xe$

$k_1 - k_1 Xe = k_{-1} Xe$

$\therefore \quad \frac{k_1}{k_1 + k_{-1}} = Xe$

$\therefore \quad \ln \left(- \frac{X}{Xe} + 1 \right) = -t (k_1 + k_{-1})$

$\ln \left(\frac{Xe - X}{Xe} \right) = -t (k_1 + k_{-1})$

i.e. $\ln (Xe - X) = -t (k_1 + k_{-1}) + \ln Xe$ - Equation 1.

Since ln (Xe - X) was plotted against t (min.), the gradient was $-(k_1 + k_{-1})$ and the intercept was lnXe. The results calculated from graphs for the two runs are reported in the Experimental section (pages 118 - 120). Since the results differed greatly (e.g. k_1 from Run 1 was 0.0114 $min.^{-1}$ while k_1 from Run 2 was 0.00302 $min.^{-1}$) the results were processed further on a "Wang" calculator using a 'least squares' analysis programme. Both the number of points (values of ln (Xe - X) and t) used and the value of Xe were chosen, as described in the Experimental, to give the smallest errors in the gradient and the intercept. Even after restricting the number of points the values of k_1 and k_{-1} calculated for the two runs still differed greatly, (perhaps due to catalysis by a trace of base) but the equilibrium constants determined were in agreement to within 5%.

The isomerisation of anti-acetaldehyde phenylhydrazone, catalysed by phenylhydrazine, in nitromethane was also investigated by n.m.r. spectroscopy (Experimental, page 123). The isomerisation was found to be too fast for a kinetic treatment of the results to be made. More syn isomer than anti isomer was found to be present after ? min. and the isomeric composition was almost that of an equilibrated mixture after 11 min. The isomerisation in nitromethane was much faster in the presence of phenylhydrazine than in nitromethane alone and it is probable that the excess of phenylhydrazine in the experiments on the formation and isomerisation of phenylhydrazones described earlier acted as a catalyst for the isomerisation of phenylhydrazones.

It seems probable that the rapid catalysis of the isomerisation of acetaldehyde phenylhydrazone by phenylhydrazine occurs by the addition of the free phenylhydrazine across the C = N of the phenylhydrazone (Scheme 11) so the arrangement of bonds to the carbon atom becomes tetrahedral and elimination of a molecule of phenylhydrazine to regenerate the phenylhydrazone can then lead to either isomer. In agreement with this mechanism phenylhydrazine was shown to exchange with o-methylphenylhydrazine in acetaldehyde o-methylphenylhydrazone.

The condensation of acetaldehyde with phenylhydrazine was followed by n.m.r. spectroscopy to determine which isomer was the kinetic product. The experiments were carried out in various solvents at as low a temperature as the viscosity of the cold solutions would allow (Experimental, pages 121, 122). In methanol, the methyl doublets of the isomeric products overlapped, especially at low temperatures, and it was not possible to

determine the isomer ratio. With 1,2-dimethoxyethane as solvent it was difficult to calculate the isomer ratio at temperatures less than +10°C because the broadening of the methyl singlet of the solvent at low temperatures interfered with the methyl doublets of the product. The syn isomer appeared, from these results, to be the kinetic product. (see Table 5A). In nitromethane, the solution was viscous at low temperatures; at -20°C the condensation had gone to completion and the isomeric composition was approximately 60% syn and 40% anti. In 2-methoxyethanol the absorptions were again too broad at temperatures less than -20°C for the isomer ratios to be determined accurately (see Table 5B); the anti isomer did not appear to be the kinetic product.

In order to avoid an excess of phenylhydrazine further low temperature condensation experiments were performed using an excess of acetaldehyde at - 40°C (Experimental, page 127). In nitromethane at -40°C, the results show that, when no excess of phenylhydrazine is present to catalyse the reaction, more anti isomer than syn isomer is initially formed at this temperature. (Table 6). With methanol as solvent satisfactory integrals were not obtained on the methyl doublets of the isomeric phenylhydrazones because of the broad solvent absorption at -40°C. At all times, however, the syn isomer appeared to be present in greater abundance than the anti isomer, and a doublet, attributed to a carbinolamine intermediate was observed. (Experimental, page 128).

Methanol itself it possibly a good enough nucleophile to catalyse the isomerisation (Scheme 12) by the same mechanism as described for phenylhydrazine (Scheme 11). If the doublet, which

was assigned to the carbinolamine, were due to the intermediate (31), it would not be expected to decay and eventually disappear; some (31) would always be present in an equilibrating mixture of isomers.

When the condensation of small amounts of acetaldehyde with an excess of phenylhydrazine in nitromethane was investigated (Experimental, page 129) the solution of phenylhydrazine in nitromethane was too viscous for n.m.r. spectroscopy at low temperatures and the experiment was carried out at +10°C (Table 7). There was never more anti isomer than syn isomer present and the isomeric composition was always close to that of an equilibrated isomer mixture (62% syn, 38% anti).

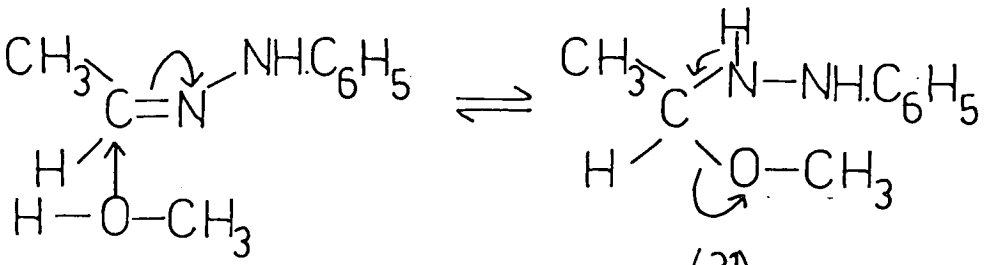
In summary, when an excess of phenylhydrazine is present, or possibly in the presence of other nucleophilic compounds, an almost equilibrated isomer mixture is initially observed during the formation of acetaldehyde phenylhydrazone. This is due to rapid catalysis of the isomerisation, probably by the mechanism described above (Schemes 11 and 12). In the absence of a nucleophilic compound the anti isomer appears to be the kinetically favoured product at -40°C.

The formation and isomerisation of acetaldehyde phenylhydrazone was found to be conveniently studied by the experiments described above since the reactions took place at a suitable rate, even at low temperatures, and the n.m.r. absorptions of the methyl doublets of the two isomers could be easily assigned and were fairly well separated, both from each other and from those of the unreacted aldehyde. It was planned to extend the study to other systems using similar conditions but the condensation and

isomerisation of ketone phenylhydrazones was found to be too slow to follow by the same techniques and few aldehyde phenylhydrazones have suitable n.m.r. absorptions.

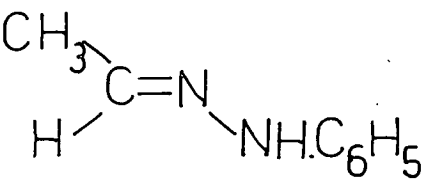
Phenylacetaldehyde phenylhydrazone appeared promising but it was found, however, (Experimental, page 130) that the methylene doublets of the two isomers of phenylacetaldehyde phenylhydrazone were co-incident in both nitromethane and acetonitrile, and that, in benzene, the methylene doublet of phenylacetaldehyde partly obscured that of the anti isomer. Thus phenylacetaldehyde phenylhydrazone was unsuitable and no further systems were studied.

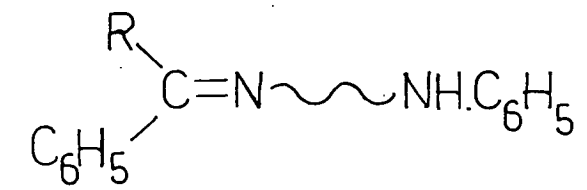
Since absorptions attributed to a carbinolamine intermediate had been observed during the investigation of the formation and isomerisation of acetaldehyde phenylhydrazone in methanol at low temperature (-40°C) it was anticipated that similar absorptions might also be observed during the slower formation of a ketone phenylhydrazone at a higher temperature. However, in the condensation of an excess of methyl benzyl ketone with phenylhydrazine in dioxan at 28°C no signals attributable to the carbinolamine intermediate were observed under fairly neutral conditions where the dehydration of the carbinolamine should be rate determining[10].



(31)

SCHEME 12

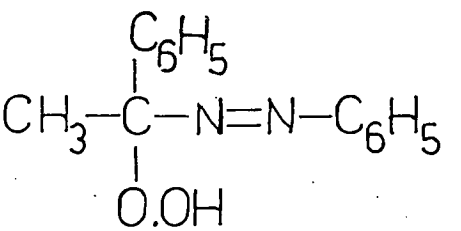




R = CH_3, CH_3-CH_2, i-Pr

OR t-But.

(54)



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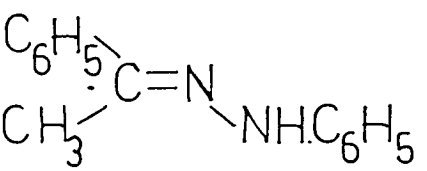

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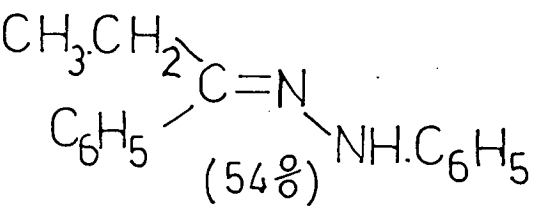

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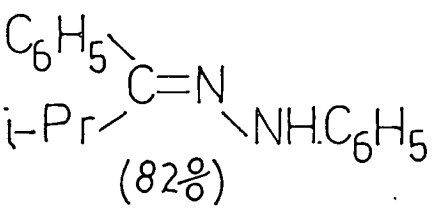

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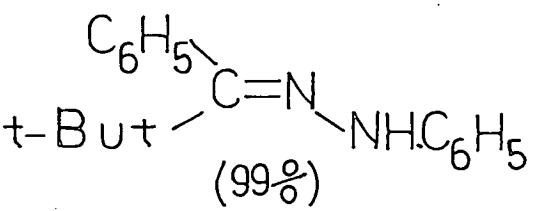


(99%)

(33) IN CCl_4

The Alkyl Phenyl Ketone Phenylhydrazone Series.

It is generally accepted, that, other factors being equal, the alkyl groups increase in bulk in passing from methyl to ethyl to i-propyl to t-butyl. From a consideration of steric effects alone in the corresponding series of alkyl phenyl ketone phenylhydrazones (54) *the amount of the isomer with the R group cis to the anilino group would be expected to decrease as the bulk of the R group was increased from methyl to t-butyl. If any of the R groups in this series were bulkier than the phenyl group then the isomer with the phenyl group cis to the anilino group would be expected to be more abundant than the isomer with the bulkier R group cis to the anilino group. (In discussion of this series the syn and anti nomenclature used in other parts of this thesis is ambiguous, and groups are referred to as cis and trans to the anilino group.)

The isomer ratios within this alkyl phenyl ketone phenylhydrazone series were investigated to find out if they could be correlated on the basis of steric effects alone, and, if so, to determine at which point in the series the alkyl group is bulkier than the phenyl group.

Experiments were carried out to study the formation and isomerisation of the alkyl phenyl ketone phenylhydrazones in pyridine, by n.m.r. spectroscopy (Experimental, page 136) in the same way as the experiments already described for the formation of substituted phenylhydrazones but it was found that the sterically hindered alkyl phenyl ketones did not react readily with phenylhydrazine at 28°C (see Table 8). In the experiments with methyl phenyl ketone and ethyl phenyl ketone unreacted ketone was present

* opposite

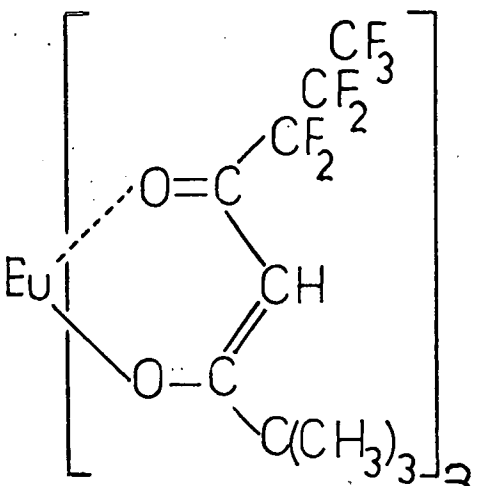
even after c.a. 700 hr. With phenyl i-propyl ketone and t-butyl phenyl ketone, the solutions had to be refluxed overnight before any reaction occurred. These results demonstrate the effect of steric hindrance around the carbonyl group on the rate of the condensation reaction.

The phenylhydrazones of the alkyl phenyl ketones were prepared and their n.m.r. spectra in carbon tetrachloride were recorded (Experimental, pages 133, 134). The solutions were allowed to equilibrate and the isomeric compositions were determined (Table 9). Karabatsos and Taller[17] reported that methyl phenyl ketone phenylhydrazone consisted of a single isomer (with the methyl group cis to the anilino group) in various solvents. They also found that, when oxygen was bubbled through a solution of methyl phenyl ketone phenylhydrazone in benzene, the methyl singlet (1.47 p.p.m.) was replaced by a singlet for the corresponding methyl group of the phenylazohydroperoxide (32) at 1.90 p.p.m. The difference in chemical shift[17] between the absorption of the phenylhydrazone and the phenylazohydroperoxide (0.43 p.p.m.) in benzene is much greater than the difference in chemical shift (0.081 p.p.m.) observed (Experimental, page 139) between the methyl absorptions of the syn (2.179 p.p.m.) and anti (2.26 p.p.m.) isomers of methyl phenyl ketone phenylhydrazone so that it is unlikely that the absorption herein assigned to the anti isomer is that of the phenylazohydroperoxide. (In the case of this phenylhydrazone it is obvious that the syn isomer has the methyl group cis to the anilino group.) It is probable that Karabatsos and Taller did not observe the methyl absorption of the anti isomer, which forms only 4% of the isomeric mixture, on a 60 MHz n.m.r. spectrum.

The results in Table 9 suggest that the point at which the most abundant isomer becomes the one with the phenyl group cis to the anilino group occurs either at the ethyl phenyl ketone or phenyl i-propyl ketone. In order to distinguish which signals in the n.m.r. spectra of the alkyl phenyl ketone phenylhydrazones were those of alkyl groups cis and trans to the anilino groups, the chemical shifts in carbon tetrachloride were compared with the chemical shifts for similar compounds (alkyl ketone and aldehyde phenylhydrazones) reported by Karabatsos and Taller.[17] However the series of configurations, in relation to their abundance (33), derived from this simple comparison of chemical shifts and configurations was not acceptable (see later) in view of the relative 'sizes' of the alkyl groups.

Europium 'shift reagents' were used in experiments to assign the absorptions of the isomeric alkyl phenyl ketone phenylhydrazones. It was found (Experimental, page 138) that significant and reproduceable induced chemical shifts were only obtained when precautions were taken to exclude moisture from these experiments. The absorption of a group in the isomer in which that group is nearest the sight of complexing with europium[46] should have a greater induced chemical shift (usually downfield from tetramethylsilane) than that for the same group in the isomer in which that group is further away from the sight of complexing with europium.

The induced chemical shifts in methyl phenyl ketone phenylhydrazone and methyl phenyl ketone benzylimine were compared to determine which nitrogen of the phenylhydrazone preferentially complexes with europium. The methyl absorption of methyl phenyl



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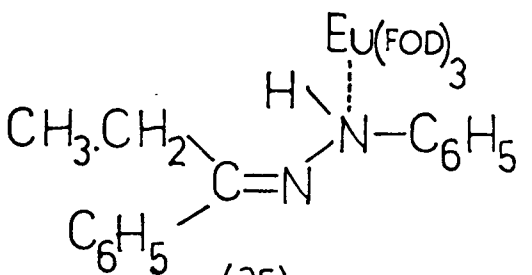

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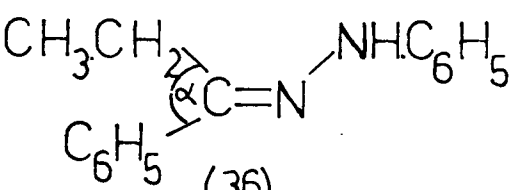

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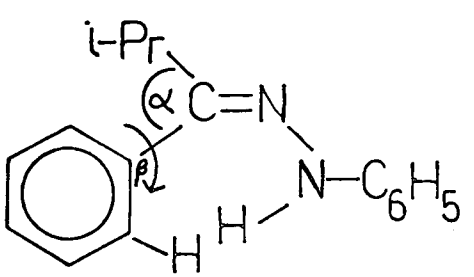

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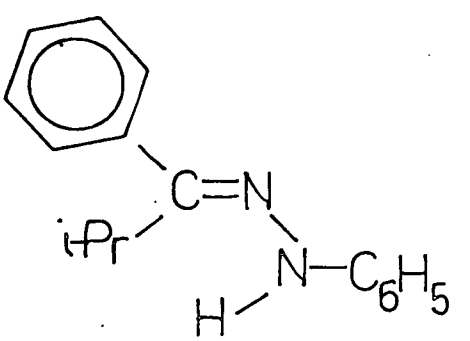
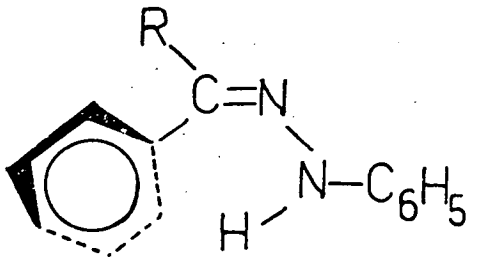


(38)

ketone benzylimine had a greater induced chemical shift at a lower concentration of Eu $(fod)_3$ (34) than that of the corresponding phenylhydrazone. This suggested that for methyl phenyl ketone phenylhydrazone, europium complexes preferentially with the α-nitrogen, which is further from the methyl group than the β-nitrogen, whereas in the benzylimine there is only a β-nitrogen available. The induced chemical shifts for the methylene quartets of the major and minor isomers of ethyl phenyl ketone phenylhydrazones were shown to be 9.0 and 20.2Hz downfield respectively (Experimental, page 140) i.e. the minor isomer had the larger induced chemical shift. If the europium of the Eu $(fod)_3$ (34) were complexed preferentially with the α-nitrogen of the phenylhydrazone in a way similar to that shown in (35), then on average the methylene group cis to the anilino group would be nearer the sight of complexing and therefore have a larger induced chemical shift than that trans to the anilino group. The result of this experiment suggests that the least abundant isomer of ethyl phenyl ketone phenylhydrazone has the ethyl group cis to the anilino group and this assignment is supported by further evidence from the U.V. spectra of the alkyl phenyl ketone phenylhydrazones (see below). Also in agreement with the above assignment, the induced shift for the methyl doublet of the anti isomer of acetaldehyde phenylhydrazone was found to be c.a. 260 Hz downfield whereas that for the syn isomer was only c.a. 98 Hz downfield.

The ultraviolet spectra of the alkyl phenyl ketone phenylhydrazones were recorded (Experimental, page 142, Table 10). The spectrum of acetone phenylhydrazone in ethanol ($\pi \rightarrow \pi^*$

$\lambda_{max.}$ 266.5, ε 9560; $n \longrightarrow \pi^* \lambda_{max.}$ 411, ε 134) was recorded for comparison. The spectra of the alkyl phenyl ketone phenylhydrazones may be compared with those of alkyl phenyl ketones in ethanol[47] (Table 11) for which it has been shown[48] that there is a substantial drop in the intensity of absorbance (due to loss of conjugation) accompanied by a slight shift of $\lambda_{max.}$ to shorter wavelengths as the phenyl group is displaced out of the plane of the carbonyl group to accommodate the bulkier alkyl groups. In the methyl and ethyl ketones the phenyl groups are coplanar with the carbonyl groups, giving good conjugation. This also applies to the corresponding phenylhydrazones; any steric strain in the least stable isomer of ethyl phenyl ketone phenylhydrazone (36) is probably relieved by increasing the angle α so that the phenyl group remains in the plane of the C=N and there is no loss of conjugation. For phenyl i-propyl ketone phenylhydrazone, however, in the isomer with the phenyl group cis to the anilino group (37), increasing the angle α may cause steric interference between the phenyl group and the anilino group. To overcome this the phenyl group must twist out of the plane of the C=N by rotation around the C–C bond, resulting in the loss of conjugation which is reflected in the intensity of absorbance in the U.V. spectrum. Loss of conjugation does not occur with the corresponding ketone (increasing the angle α would not increase any other interactions) and it need not occur in the other isomer of phenyl i-propyl ketone phenylhydrazone (38) either since it is the i-propyl group which would interfere with the anilino group on increasing α . In (37), which is thought to be the most abundant isomer (82%), steric strain is overcome at the expense of resonance stabilization.



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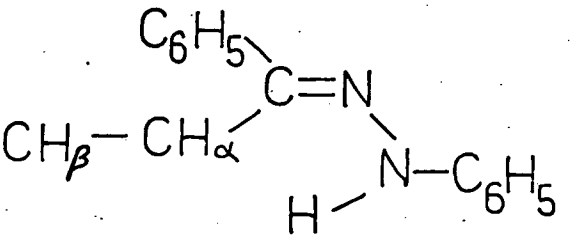

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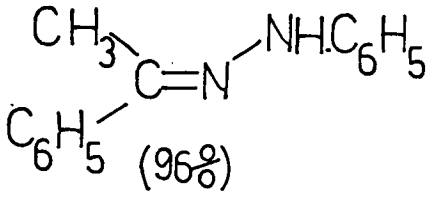

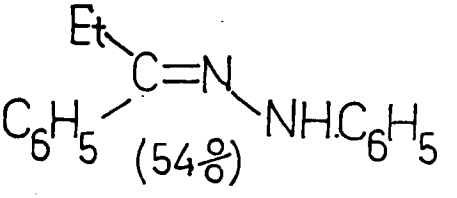

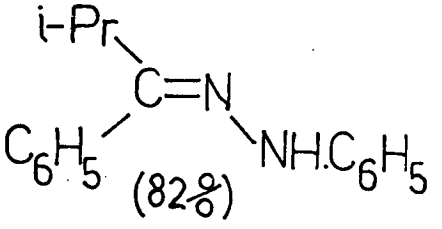

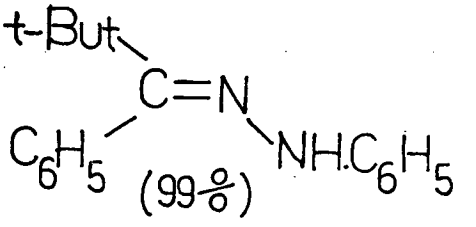

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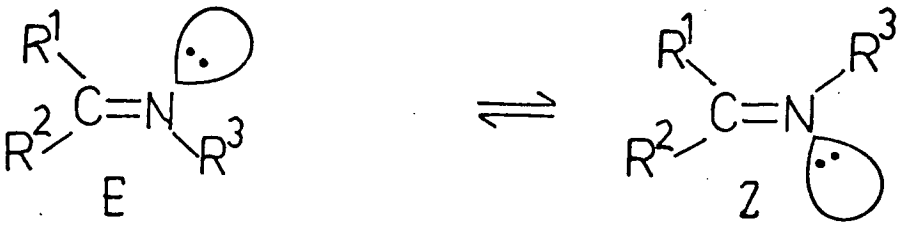
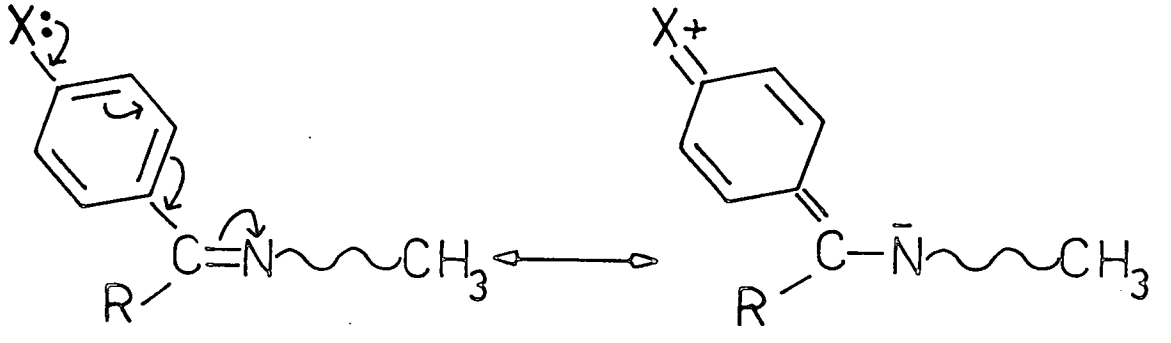


SCHEME 13



SCHEME 14

The chemical shifts of the two isomers (see later) are in agreement with these assignments. Loss of conjugation is also reflected in the U.V. spectrum of t-butyl phenyl ketone phenylhydrazone, which is almost 100% one isomer and has a very similar $\lambda_{max.}$ (267 nm.) to that of acetone phenylhydrazone.

If, in the i-propyl and t-butyl phenyl ketone phenylhydrazones the molecules have a conformation similar to (39), the protons in the alkyl group trans to the anilino group will be shielded and shifted upfield in the n.m.r. spectrum. (The extent to which the protons in the alkyl group cis to the anilino group are shielded will depend on how far the phenyl group in (38) is twisted out of the plane of the C=N, and such a displacement does not appear in phenyl i-propyl ketone.)

The chemical shifts of some alkyl ketone and aldehyde phenylhydrazones reported by Karabatsos and Taller[17] are presented in Table 12 along with those of the alkyl phenyl ketone phenylhydrazones for comparison. The data collected by Karabatsos and Taller shows that generally protons cis to the anilino group (H_α and H_β in (40)) resonate at higher magnetic fields (shielded) than when trans to the anilino group. In methyl phenyl ketone phenylhydrazone, where there is no displacement of the phenyl group from the plane of the C=N, the methyl absorption of the most abundant (syn) isomer (methyl group cis to the anilino group) resonates at 2.179 p.p.m. while that of the anti isomer resonates at 2.26 p.p.m. in keeping with this general trend. The methylene and methyl absorptions of the isomers of ethyl phenyl ketone phenylhydrazone (see Table 12) in which the phenyl group is still co-planar with the C=N, also conform to this trend. In phenyl i-propyl ketone and t-butyl

phenyl ketone phenylhydrazone, however, shielding of the alkyl protons *trans* to the anilino group by the displaced phenyl group causes them to resonate at higher magnetic field than those *cis* to the anilino group (see Table 12) and for these compounds assignments cannot be made in accordance with the general rule described above.

With the interpretation of the combined information from the ultraviolet and n.m.r. spectra described above, the configurations and isomer ratios in the alkyl phenyl ketone phenylhydrazone series can be assigned as indicated in Table 12 and shown in (41) for 5 - 12% molar solutions in carbon tetrachloride.

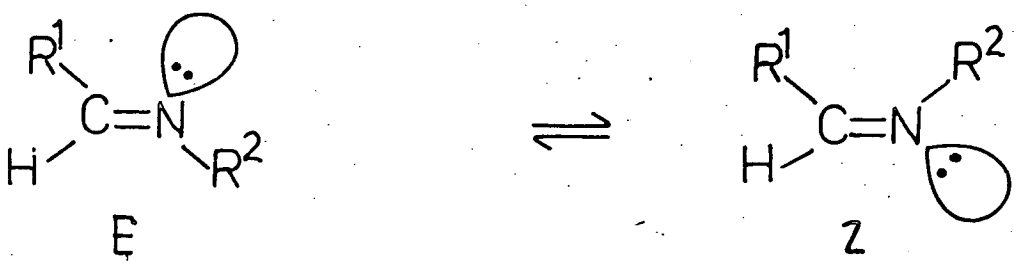
Shortly after this research had been completed Jennings et al.[49] published a paper on the equilibrium distribution of E - Z ketimine isomers in which they used similar arguments to those employed above in the interpretation of the equilibrium distribution of the isomers of alkyl phenyl ketone phenylhydrazones. The equilibrium distribution for a series of E-Z imine isomers (Scheme 13, R^1 = p-X C_6H_4) was measured by multiple integration of the n.m.r. spectra. By varying the 'size' of the groups R^2 and R^3, and with R^1 as phenyl they found the equilibrium isomer distribution to be dominated by classical steric interactions between the *N* - alkyl group and the proximate *C*-alkyl or *C*-phenyl group. A change of R^2 from n-propyl to i-propyl (with R^3=Me) altered the equilibrium in favour of the Z- isomer so that the phenyl group was apparently intermediate in 'size' between n-propyl and i-propyl, whereas in the ethyl phenyl ketone phenylhydrazone system discussed above the phenyl group appeared to be approximately equal in 'size' to the ethyl group. Jennings et al. also point out that, in

cyclohexane systems, where A values reflect mainly (1,3) diaxial interactions, the phenyl group (A value 3.0) appears to be larger than the i-propyl group (A value 2.3).[50]

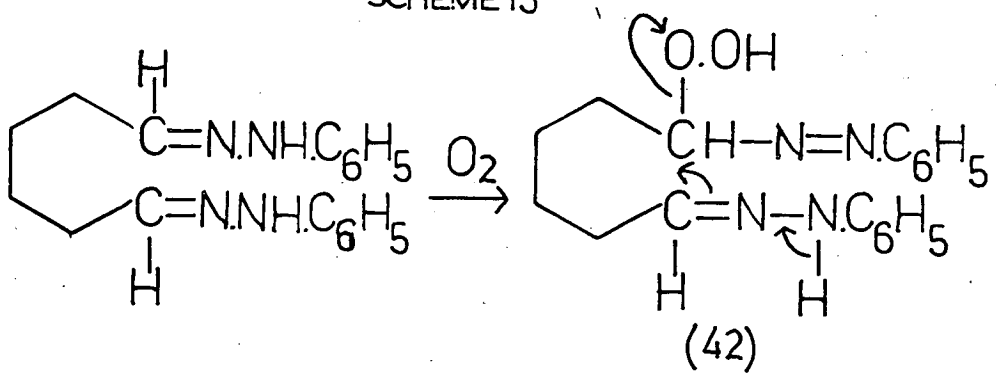
Displacement of the phenyl ring from the plane of the C=N to reduce steric interactions between the ortho-substituents of the phenyl ring and the cis-N-alkyl group in the Z- isomer is also discussed by Jennings et al. This is especially pronounced in cases where an ortho-hydrogen has been replaced by a bulky group. They relate the upfield shift of the position of the N-methyl n.m.r. signals in such compounds to the anisotropic effect of the displaced phenyl group, in much the same way as the upfield shift of the n.m.r. absorptions of alkyl groups in i-propyl and t-butyl phenyl ketone phenylhydrazones have been accounted for above. Jennings et al. also found that electron donating para-substituents on the phenyl ring tended to favour the E isomer, probably through stabilization of the coplanar conformation by increasing the delocalisation energy (Scheme 14) and thus increasing the barrier to rotation around the C-aryl bond. This increased coplanarity is also reflected in the chemical shifts of the N-methyl signals. Solvent effects, n-π repulsion between the nitrogen lone pair and the π cloud of the aryl ring (see Introduction, page 6), and their relationship to the E-Z-isomer distribution of ketimines are also discussed in this paper. They appear to be of less importance than classical non-bonded interactions and a preference for maximum resonance stabilization. It is probable that n-π repulsion is of some importance in determining the equilibrated isomeric composition of the alkyl phenyl ketone phenylhydrazones discussed above but the extent of this effect cannot be easily

estimated.

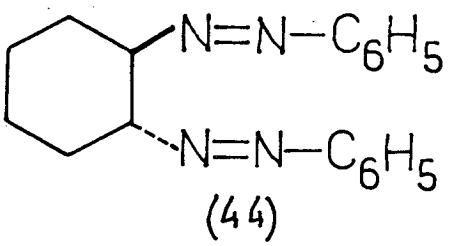
Jennings et al.[51] have more recently investigated E - Z isomerism in a range of C -aryl aldimines, again using n.m.r. spectroscopy. They found that the proportion of the Z - isomer (Scheme 15) at equilibrium in solution was only significant (> 5%) for ortho-disubstituted C -aryl aldimines. They explained their results by the argument used above in relation to the E - Z - isomer distribution of ketimines, and in the ortho-disubstituted C -aryl aldimines the n-π repulsive effect appears to be of greater importance than in the ketimines.

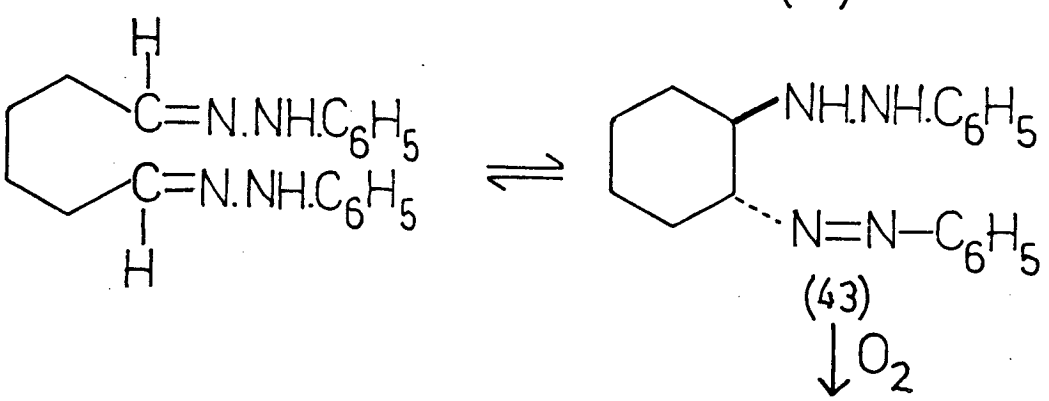


SCHEME 15



SCHEME 16





SCHEME 17

Investigation of the Mechanism of the Oxidative Ring Closure of Adipaldehyde Bisphenylhydrazone.

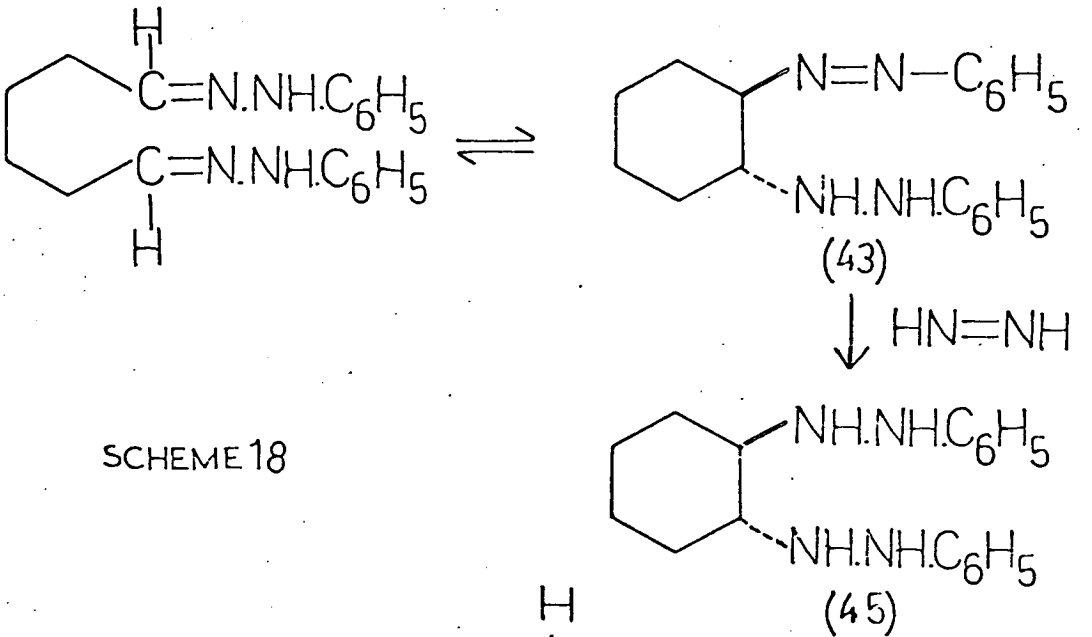
Bellamy, Guthrie and Chittenden[52] found that adipaldehyde bisphenylhydrazone is converted into trans-1,2-bisphenylazocyclohexane by oxidation with yellow mercuric oxide or oxygen. They proposed two possible mechanisms for the reaction. Mechanism (1) (Scheme 16) involves reaction of oxygen with one of the phenylhydrazone groups of adipaldehyde bisphenylhydrazone to give a phenylazohydroperoxide (42) which cyclises, with elimination of a molecule of hydrogen peroxide. (Oxidation of a phenylhydrazone to the corresponding phenylazohydroperoxide is a general reaction.[23]) Mechanism (2) (Scheme 17) involves ring-chain tautomerism between adipaldehyde bisphenylhydrazone and trans-1-phenylazo-2-phenylhydrazocyclohexane (43), perhaps through a cyclic 6-membered transition state. The product (44) could then be formed from (43) by oxidation of the phenylhydrazo group with oxygen.

By oxidation of 1-cyclohexyl-2-phenylhydrazine they showed that one molecule of the phenylhydrazine is oxidized by one molecule of oxygen, liberating hydrogen peroxide. It has been established[53] that hydrogen peroxide can also oxidize phenylhydrazines to phenylazo compounds and this would account for the measured oxygen uptake being less than one mole in the oxidation of adipaldehyde bisphenylhydrazone. Hydrogen peroxide would be liberated by both mechanisms (1) and (2) so that detection of hydrogen peroxide in the reaction mixture when trans-1,2-bisphenylazocyclohexane was formed from adipaldehyde bisphenylhydrazone did not allow a distinction between the two mechanisms.

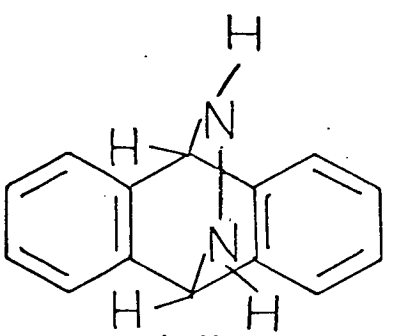
The conversion of adipaldehyde bisphenylhydrazone to

(43) should be accompanied by a yellow coloration and this should occur even in the absence of oxygen, whereas oxygen is required for the formation of the yellow phenylazohydroperoxide compound (42). They found that when a solution of adipaldehyde bisphenylhydrazone in carbon tetrachloride was boiled under nitrogen, the solution became yellow, favouring mechanism (2). The product isolated was still mainly adipladehyde bisphenylhydrazone and the proportion of (43) could not be determined. The fact that yellow mercuric oxide, an efficient reagent in the oxidation of 1-alkyl-2-phenylhydrazines to phenylazoalkanes[23,53] effected the oxidation of adipaldehyde bisphenylhydrazone to trans-1,2-bisphenylazocyclohexane under nitrogen in almost quantitative yield, also favours mechanism (2). The anomolous formation of hexamethylenediamine, which was observed on one occasion in the hydrogenation of trans-1,2-bisphenylazocyclohexane (44), can also be accommodated if trans-1,2-bisphenylazocyclohexane is formed from adipaldehyde bisphenylhydrazone by mechanism (2). The first step in the hydrogenation would be reduction of one of the phenylazo groups to a phenylhydrazo group, thus forming (43). Isomerisation of (43) by ring-chain tautomerism to adipaldehyde bisphenylhydrazone, followed by further hydrogenation would give hexamethylenediamine. Whether hexamethylenediamine or cyclohexane-1,2-diamine was isolated from the hydrogenation of (44) would depend upon the activity of the catalyst. (A more active catalyst would bring about the reduction of (44) to the corresponding phenylhydrazine before formation of (43) occurred.)

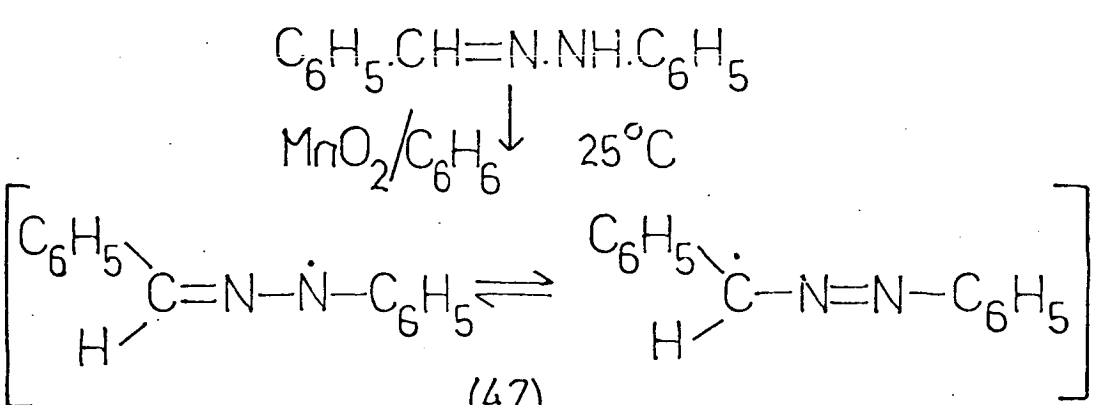
It was with a view to establishing that the ring-chain tautomerism proposed for mechanism (2) did exist, and if so,



SCHEME 18



(46)



SCHEME 19

to determine the detailed mechanism of it, that the investigation of the ring closure of adipaldehyde bisphenylhydrazone was undertaken.

If adipaldehyde bisphenylhydrazone isomerises to (43) by ring-chain tautomerism, then using a reagent which selectively reduces an N=N, and which will not reduce a C=N, it should be possible to reduce the phenylazo group in (43) and thus form trans-1,2-bisphenylhydrazocyclohexane (45) (Scheme 18). Di-imide[54] is known to selectively reduce symmetrical non-polar double bonds, and, in keeping with this selectivity, it was shown (Experimental, pages 146, 147) that di-imide, generated from potassium azodicarboxylate, reduces phenylazocyclohexane to 1-cyclohexyl-2-phenylhydrazine whereas n-propionaldehyde phenylhydrazone was recovered unaltered after similar treatment with di-imide.

Di-imide, generated from potassium azodicarboxylate, also reduced trans-1,2-bisphenylazocyclohexane (44) to trans-1,2-bisphenylhydrazocyclohexane (45) (Experimental, page 149), showing that the presence of a second phenylazo (and probably phenylhydrazo) group at the 2-position of the cyclohexane ring does not interfere with the reduction. The reaction could be reversed by oxidation of (45) to (44) with yellow mercuric oxide.

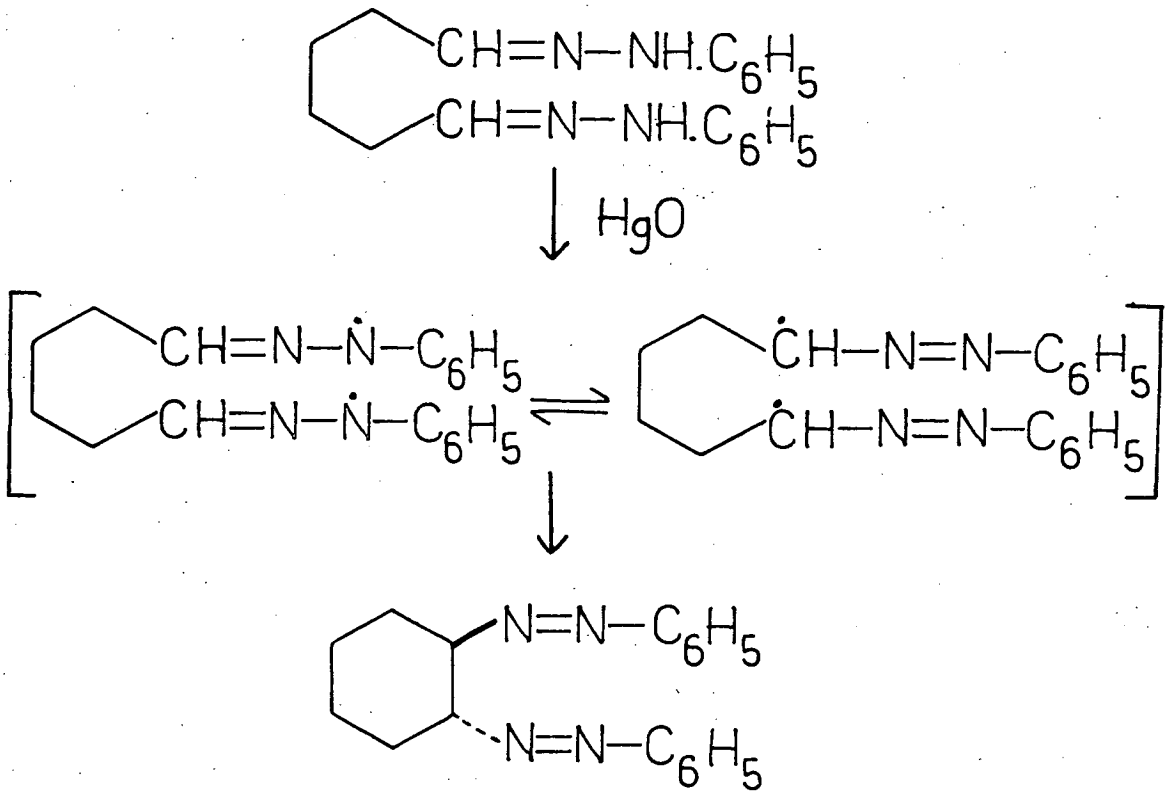
Attempts to reduce adipaldehyde bisphenylhydrazone with di-imide generated from potassium azodicarboxylate, however, were not successful (Experimental, page 148). It was thought that generation of di-imide had been too rapid to reduce the equilibrium concentration of (43).

Further reductions, in which di-imide was generated more slowly from 9,10-dihydro-9,10-bi-imino-anthracene (46)*

* Named as Diels-Alder addition product of anthracene and di-imide.

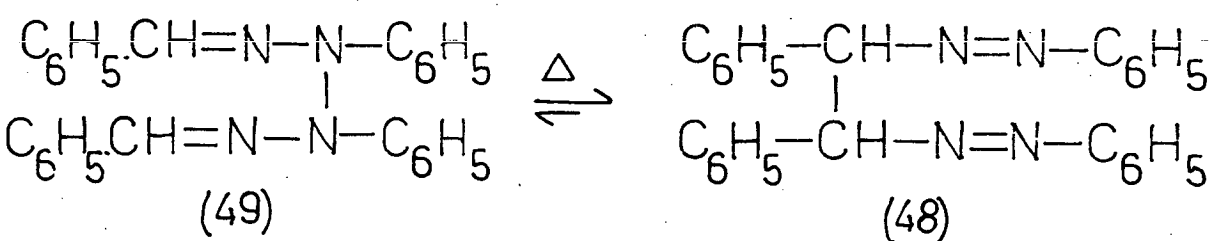
(Experimental, page 151) were attempted, but trans-1,2-bisphenylhydrazocyclohexane was not identified among the products. Since phenylazo compounds can be readily separated from phenylhydrazones by column chromatography, whereas mixtures of phenylhydrazones and phenylhydrazines are difficult to separate, e.g. trans-1,2-bisphenylazocyclohexane[52] can be easily separated from adipaldehyde bisphenylhydrazone, it was considered necessary to oxidise the reduction mixture before chromatography. In exploratory experiments (Experimental, page 152) it was found that 1-cyclohexyl-2-phenylhydrazine is readily oxidized to phenylazocyclohexane on treatment with hydrogen peroxide, whereas adipaldehyde bisphenylhydrazone is recovered unchanged. In order to establish whether or not any trans-1,2-bisphenylhydrazocyclohexane (45) was produced by the treatment of adipaldehyde bisphenylhydrazone with the di-imide precursor (46), the product mixture from this reaction was treated with hydrogen peroxide (Experimental, page 153), but no trans-1,2-bisphenylazocyclohexane was isolated after chromatography, indicating that no trans-1,2-bisphenylhydrazocyclohexane had been present in the product mixture.

The possibility of the ring-chain tautomerism outlined in Scheme (17) was also investigated by the attempted generation of trans-1-phenylazo-2-phenylhydrazocyclohexane (43) by reduction of 1,2-bisphenylazocyclohexane with di-imide generated from (46). If the tautomerism is rapid then adipaldehyde bisphenylhydrazone should be formed. The phenylazo compound (44) was reduced to the corresponding phenylhydrazine (45) (Experimental, page 156), but adipaldehyde bisphenylhydrazone was not identified in the product mixture.



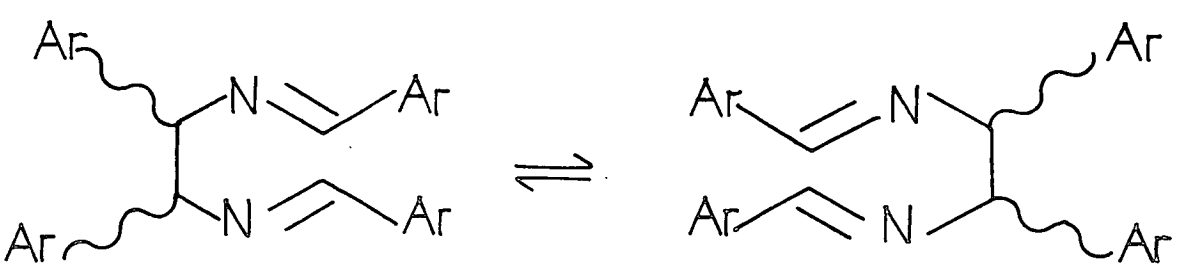
SCHEME 20

[SCHEME 21 — SEE NEXT PAGE]

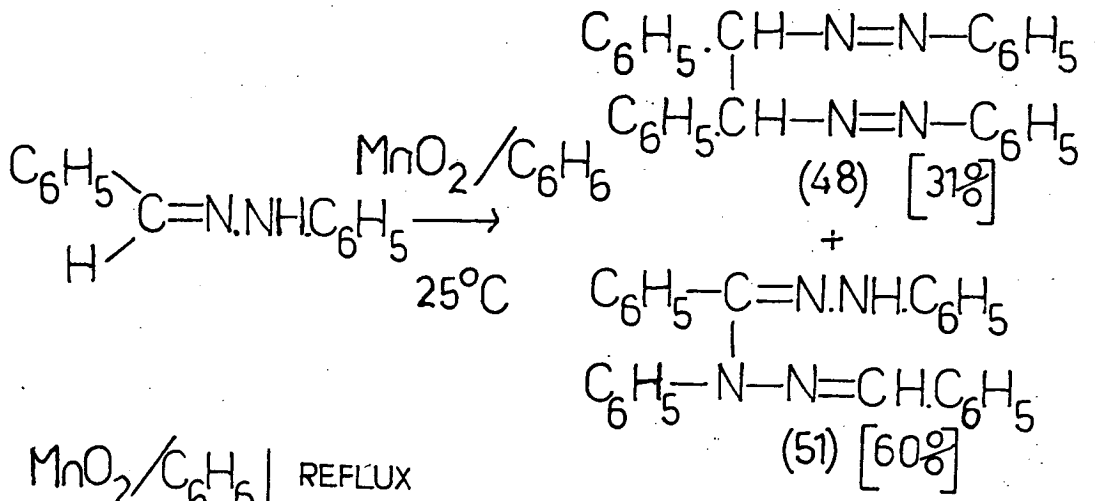


(49) (48)

SCHEME 22



SCHEME 23



SCHEME 21

It was also shown (Experimental, pages 157,158) that, although adipaldehyde bisphenylhydrazone can be converted to trans-1,2-bisphenylazocyclohexane by oxidation with yellow mercuric oxide in dimethyl sulphoxide (the most suitable n.m.r. solvent for adipaldehyde bisphenylhydrazone), no 1-phenylazo-2-phenylhydrazocyclohexane (43) was detected in the n.m.r. spectrum of a sample of adipaldehyde bisphenylhydrazone which had been equilibrated at 100°C in $[^2H_6]$ dimethyl sulphoxide.

The above results suggest that the ring-chain tautomerism (Scheme 17) does not occur to a sufficient extent for (43) to be reduced by di-imide and mechanism (2) appears improbable for the oxidative ring closure of adipaldehyde bisphenylhydrazone.

Besides mechanism (1), another possible mechanism for the oxidative ring closure of adipaldehyde bisphenylhydrazone, analogous to that proposed by Bhatnago and George[55] for the oxidative dimerisation of benzaldehyde phenylhydrazone (compare Schemes 19 and 20) should be considered. Their mechanism involves the coupling of the pseudo-allylic radical (47) which can take place in several ways (see Scheme 21). In support of this third mechanism it was shown (Experimental, page 160) that the oxidation of benzaldehyde phenylhydrazone with yellow mercuric oxide gives both the C-C coupled dimer, 1,2-bisphenylazo-1,2-diphenylethane (48) and the N-N coupled dimer, 2,3-diphenyl-1,4-dibenzaltetrazane (49).

The possibility of extending the oxidative ring-closure reaction of adipaldehyde bisphenylhydrazone to related compounds, so that it might be of more general application in synthesis, was explored. For example adipaldehyde dioxime was recovered unchanged after treatment with both yellow mercuric oxide and manganese

dioxide, and no cyclohexane derivative was isolated on treatment of this compound with dibenzoyl peroxide (Experimental, pages 154, 155). Similarly, adipaldehyde bismethylhydrazone did not undergo oxidative cyclisation.

The Thermal Stability of 1,2-Bisphenylazo-1,2-diphenylethane and 2,3-Diphenyl-1,4-dibenzaltetrazane.

Consideration of the dimers of benzaldehyde phenylhydrazone in connection with oxidative ring closure of adipaldehyde bisphenylhydrazone suggested that a Cope rearrangement of 2,3-diphenyl-1,4-dibenzaltetrazane (49) (Scheme 22) might form 1,2-bisphenylazo-1,2-diphenylethane (48). (The 2,3 bond in tetrazanes is not particularly stable.[77])

Both the expected product (48) and the starting material (49) were obtained from the oxidation of benzaldehyde phenylhydrazone with manganese dioxide in benzene by adaptations of the methods described by Bhatnago and George[55] (Experimental, pages 159 - 162). The two compounds were also obtained from the oxidation of benzaldehyde phenylhydrazone with yellow mercuric oxide (Experimental, page 160) and (48) was also obtained from the oxidation of benzaldehyde phenylhydrazone with dibenzoyl peroxide (Experimental, page 166).

2,3-Diphenyl-1,4-dibenzaltetrazane was heated for several days in refluxing (i) benzene (ii) dimethyldigol and (iii) p-xylene, but no 1,2-bisphenylazo-1,2-diphenylethane was recovered from these reactions (Experimental, pages 163,164). With dimethyldigol (b.p. 164°C) the loss of the characteristic red colour of the tetrazane occurred, but, because of the diversity of products observed, this was thought to be due to decomposition of the tetrazane, catalysed by peroxide impurities in the solvent, rather than rearrangement to (48). With p-xylene (b.p. 138°C) the red colour slowly faded and after 6.5 days, a yellow compound was shown to be present by chromatography, but only the tetrazane

was isolated.

However when 1,2-bisphenylazo-1,2-diphenylethane (48) was heated in refluxing benzene (Experimental, page 164) a red compound with the same Rf value as 2,3-diphenyl-1,4-dibenzal-tetrazane (49) was detected by thin layer chromatography, but this compound was not isolated in sufficient quantity for identification.

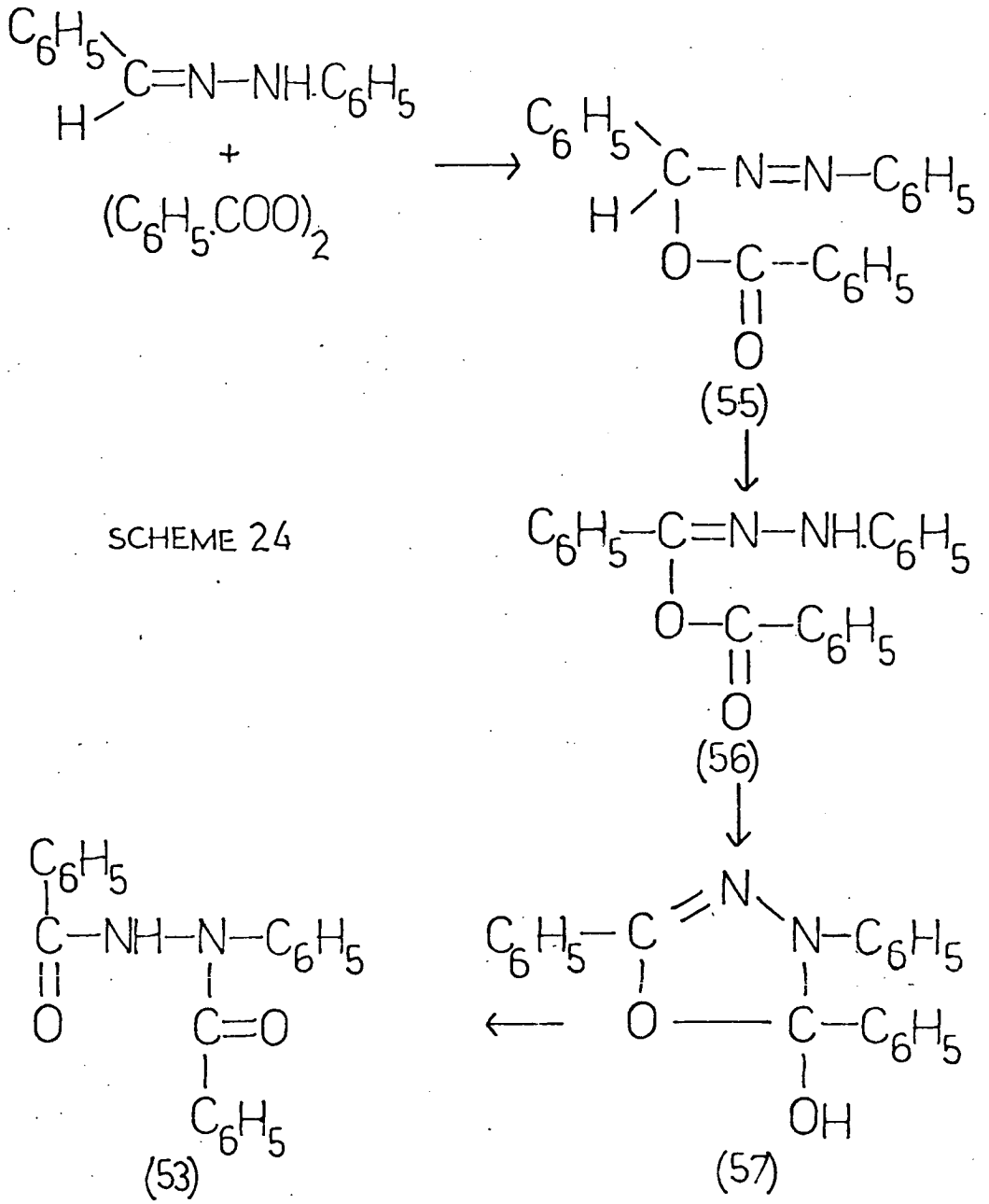
Although no conclusive evidence was obtained from the experiments described above, the results suggest that 1,2-bisphenylazo-1,2-diphenylethane equilibrates, probably by the Cope mechanism outlined in Scheme 22, with 2,3-diphenyl-1,4-dibenzaltetrazane. The equilibration is difficult to observe, especially with 2,3-diphenyl-1,4-dibenzaltetrazane as the starting material, perhaps due to decomposition of these compounds at the temperatures required to bring about equilibration.

A diaza-Cope rearrangement in a system similar to that of 2,3-diphenyl-1,4-dibenzaltetrazane has recently been reported by Vögtle and Goldschmitt[56]. They found that 1,3,4,6-tetra-aryl diazahexa-1,5-dienes isomerise at elevated temperatures (above 120°C in $[^2H_6]$ dimethylsulphoxide) (Scheme 23). By following the reaction by ^1H n.m.r. spectroscopy they found that for N,N'-dibenzylidene diphenylethane-1,2-diamine (Scheme 23, Ar = Ph) an equilibrium was established between the meso- and d,l-valence isomers in the ratio 1:1, irrespective of whether the reaction started from the meso- or the d,l- compound. Introduction of o, m or p-substituents into the four aromatic nuclei led to further degenerate diaza-Cope systems. The difference between these systems and that of 2,3-diphenyl-1,4-dibenzaltetrazane (49) is that, in the tetrazane system, nitrogen replaces carbon at the 3 and 4 positions.

Both (48) and (49) were obtained from oxidations of benzaldehyde phenylhydrazone. During the preparation of these compounds, which were only isolated in small quantities from the oxidation reactions, the diversity of the products reported to have been obtained from oxidations of benzaldehyde phenylhydrazone under various conditions was encountered.

The products obtained by Bhatnago and George[55] from the oxidation of benzaldehyde phenylhydrazone with manganese dioxide in benzene, either at reflux or at 25°C, are shown in Scheme 21. Attempts to repeat their experiments, however, were unsuccessful, possibly because of slight differences in reaction conditions or chromatographic techniques. From the oxidation in refluxing benzene only biphenyl and 2,4,5-triphenyl-1,2,3-triazole (50) were isolated, and no pure products were obtained from the oxidation at 25°C. By modifying their procedures, especially the column chromatography, 2,3-diphenyl-1,4-dibenzaltetrazane (49) was obtained from the oxidation in refluxing benzene, and 1,2-bisphenylazo-1,2-diphenylethane (48), along with 1,3,4,6-tetraphenyl-1,2,4,5-tetra-azahexa-2,5-diene (51), was isolated from the oxidation at 25°C.

Oxidations of benzaldehyde phenylhydrazone have been carried out with various reagents e.g. mercuric oxide[57], oxygen[58], amyl nitrite[59,60], sodium ethoxide and iodine[61], ammonical silver nitrate in dimethylformamide[62] and dibenzoyl peroxide[63]. There has been considerable controversy as to the number and identity of the dimers of benzaldehyde phenylhydrazone of molecular formula $C_{26}H_{22}N_4$ isolated from these reactions, but Bhatnago and George appear to have correctly identified the structures



SCHEME 24

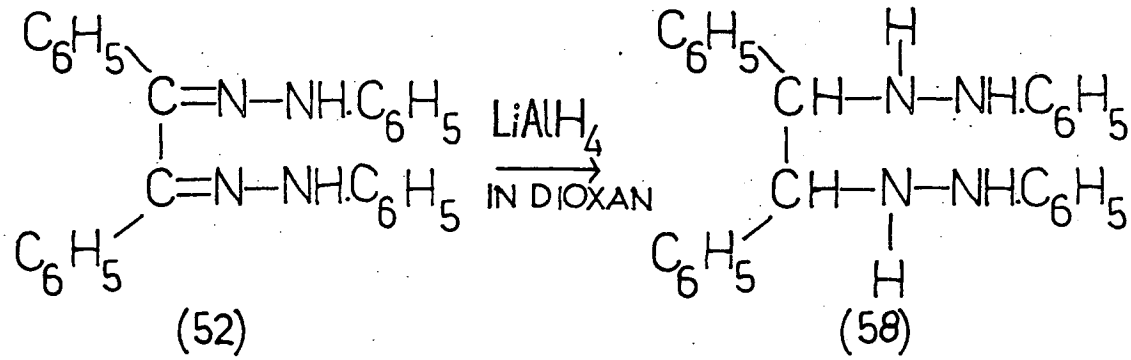
of the compounds obtained from the experiments they performed.

Since (48) and (49) were obtained in poor yield from the oxidation of benzaldehyde phenylhydrazone with manganese dioxide, both yellow mercuric oxide and dibenzoyl peroxide were employed as oxidizing agents.

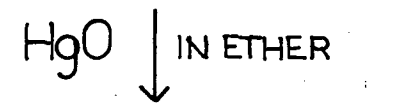
2,3-Diphenyl-1,4-dibenzaltetrazane (49), 1,2-bisphenylazo-1,2-diphenylethane (48) and α-benzil osazone (52) were isolated from the oxidation with yellow mercuric oxide (Experimental, page160). Minnunni[57] appears to have assigned the wrong structures to the compounds he isolated from a similar oxidation.

Oxidation of benzaldehyde phenylhydrazone with dibenzoyl peroxide yielded 1,2-bisphenylazo-1,2-diphenylethane (48), 1,3,4,6-tetraphenyl-1,2,4,5-tetra-azahexa-2,5-diene (51) and α, β -dibenzoylphenylhydrazine (53). Edward and Samad[63] isolated only (53) from a similar oxidation and proposed that it was formed by the mechanism outlined in Scheme 24 ; (55) is initially formed, but, in the presence of benzoic acid it rearranges to (56). (Phenylazo- compounds are known to rearrange to the corresponding phenylhydrazones.[64]) Subsequent migration of the benzoyl group from oxygen to nitrogen via the cyclic intermediate (57) results in formation of (53). The first step in this reaction is again probably formation of the pseudo-allylic radical (47) (Scheme 19) which can couple either with a benzoyloxy radical or dimerize. Isolation of the C-C coupled dimer (48) from this oxidation is therefore consistent with this mechanism. 1,3,4,6-tetraphenyl-1,2,4,5-tetra-azahexa-2,5-diene (51) is also formed by a radical combination.

In oxidations with dibenzoyl peroxide, radicals are



(52) (58)



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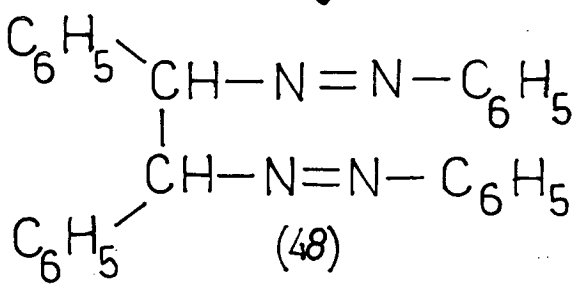
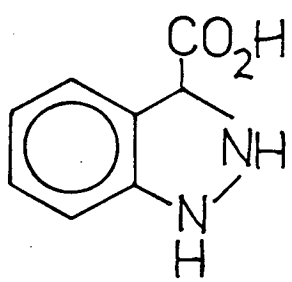
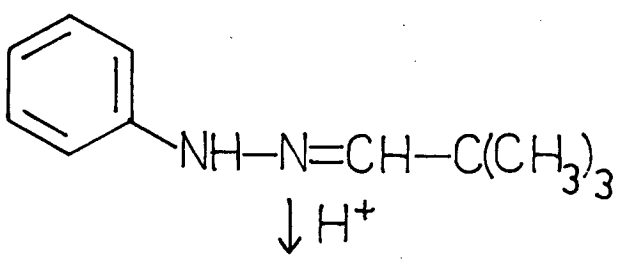
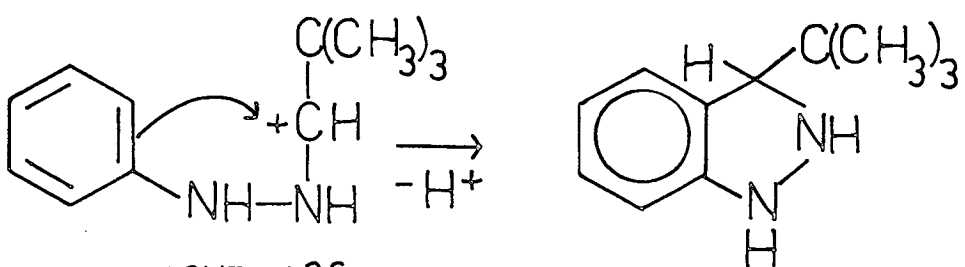


(48)



(59)





SCHEME 26

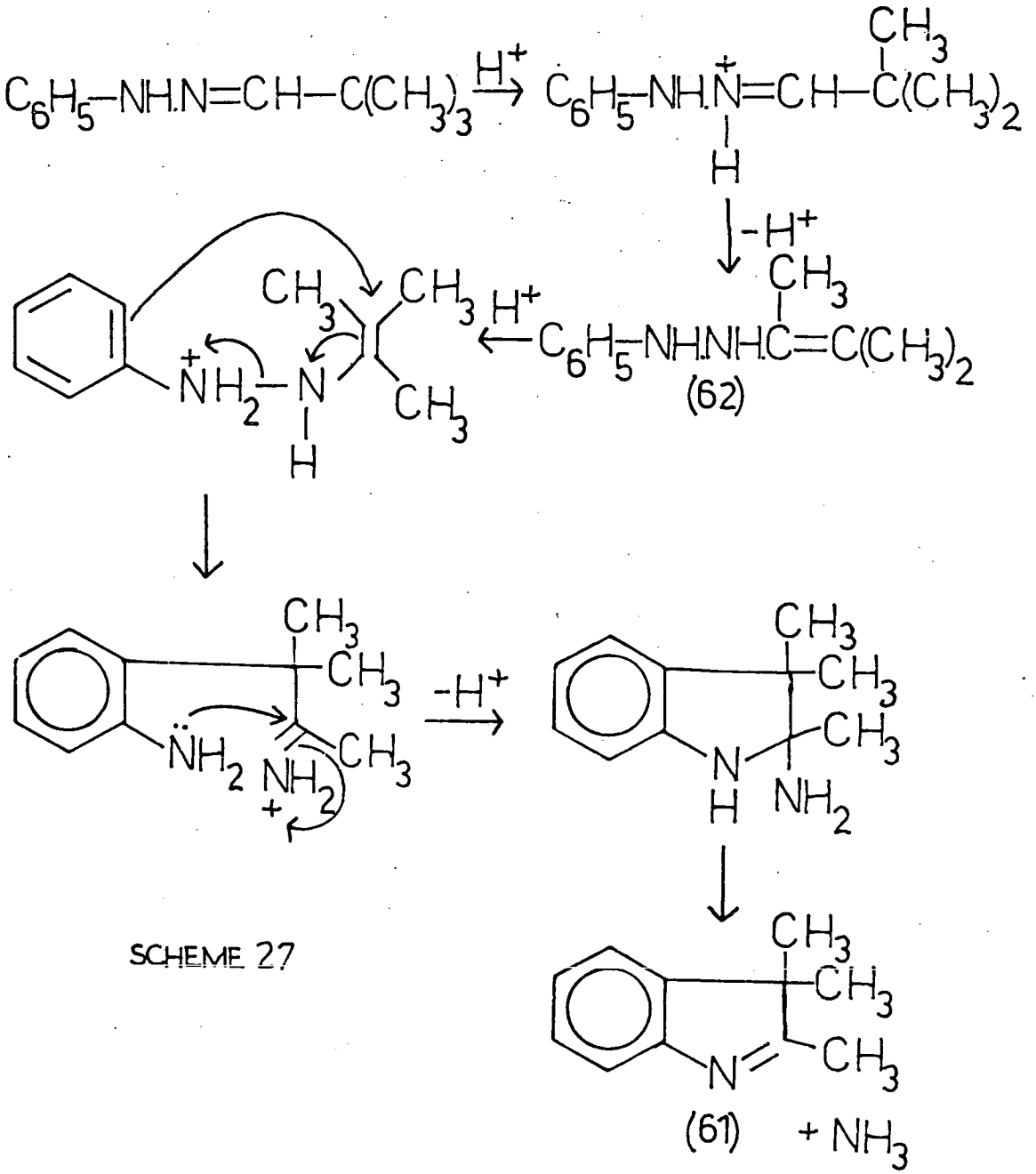
(60)

generated in the free state as opposed to the manganese dioxide case, where they may react on the solid surface. The N-C (51) and C-C (48) coupled dimers of benzaldehyde phenylhydrazone were obtained from oxidation with dibenzoyl peroxide in refluxing benzene, but no N-N coupled dimer (49) was isolated under these conditions, nor was there any evidence to suggest that the N-N coupled dimer was formed (it is deep red in colour and can be readily detected).

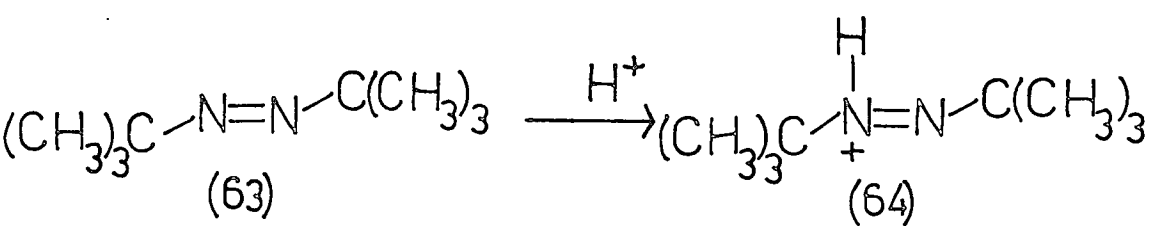
With manganese dioxide the N-C (51) and C-C (48) coupled dimers were obtained at 25°C, whereas biphenyl, the triazole (50), the C-C and the N-N coupled dimers were obtained in refluxing benzene. The similarity of products obtained with the two reagents substantiates the claim of Bhatnago and George[55] that the oxidation with manganense dioxide proceeds by free radical mechanisms. The results indicate that with this reagent the product distribution may be governed by the abosrption of radicals onto the solid surface and the effect of temperature on their orientation, migration, and subsequent dimerisation.

Since the yields of 1,2-bisphenylazo-1,2-diphenylethane (48) from the oxidations of benzaldehyde phenylhydrazone were small, an attempt was made to obtain this compound by reduction of benzil osazone (52) to 1,2-bisphenylhydrazo-1,2-diphenylethane (58), which could then be oxidised to (48) (Scheme 25). Only the starting material and benzaldehyde phenylhydrazone, however, were recovered from the reduction of benzil osazone with lithium aluminium hydride in refluxing dioxan. The same result was observed when the crude product mixture from the above reduction was treated with yellow mercuric oxide in ether (Experimental,

page 169). It was also observed that benzaldehyde phenylhydrazone was not reduced to the corresponding phenylhydrazine either with lithium aluminium hydride or with sodium metal in tetrahydrofuran. Thus lithium aluminium hydride merely cleaves benzil osazone to benzaldehyde phenylhydrazone, which is not readily reduced. Consequently (48) could not be synthesised by the method outlined in Scheme 25.



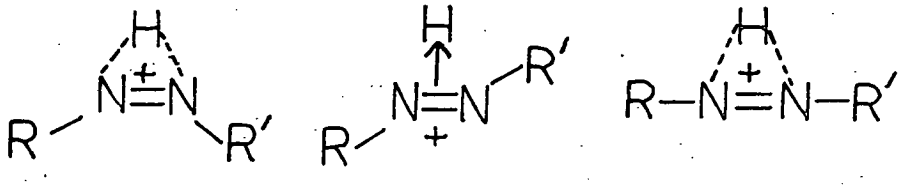
SCHEME 27



Attempted Rearrangement of Trimethylacetaldehyde Phenylhydrazone.

During an attempt to deuterate trimethylacetaldehyde phenylhydrazone, by treatment with $[^2H_2]$ sulphuric acid in $[^2H_1]$ methanol at 25°C, Bellamy[65] isolated an unknown product which was soluble in aqueous hydrochloric acid, but not in aqueous alkali solution. The U.V. spectrum of this unknown compound ($\lambda_{max.}^{CH_3OH}$ 272 nm. (ε 17,170))was similar to that of (59) ($\lambda_{max.}^{H_2O}$ 274 nm. (ε 1,862))[66] and a possible structure for the compound is (60); a possible mechanism for its formation is outlined in Scheme 26. Attempts to oxidise the product with yellow mercuric oxide, however, were inconclusive. Another possible structure (61) can be rationalised by the mechanism in Scheme 27, which, after formation of (62), closely resembles the mechanism of the Fischer indole synthesis[67].

In order to try and establish the identity of this product attempts were made to obtain it by treatment of trimethylacetaldehyde phenylhydrazone with sulphuric acid. However, when the experiment was carried out using either methanol as the solvent or concentrated sulphuric acid alone (Experimental, page 171), only the starting material was recovered.



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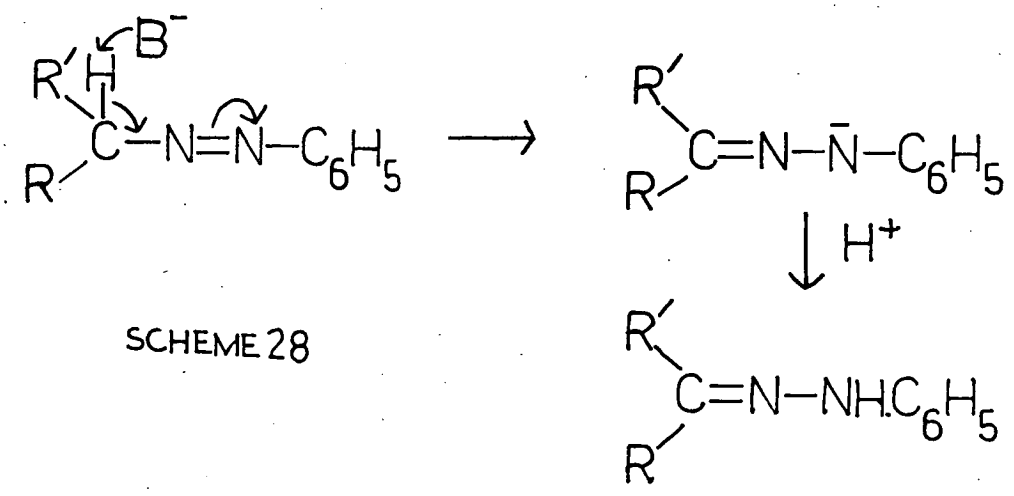
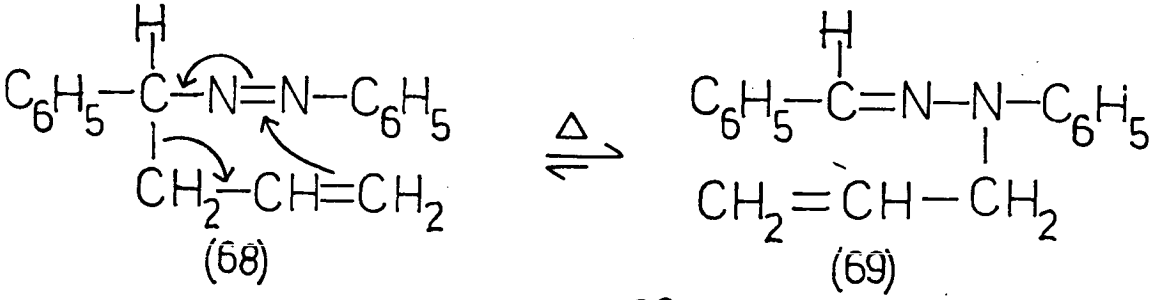


SCHEME 28



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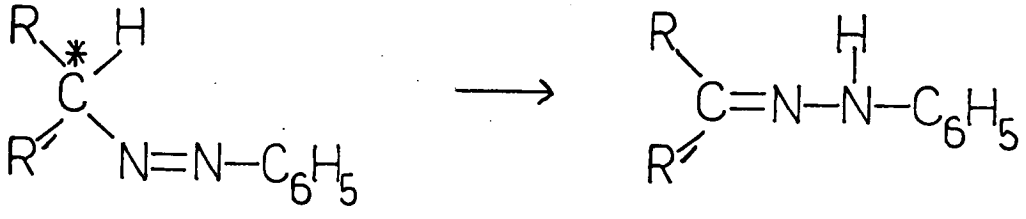
SCHEME 29



SCHEME 30

The Attempted Protonation of 2-Methyl-2-phenylazopropane.

Olah and Mo[68] have studied the protonation of mono- and dihydroxybenzenes and their methyl ethers in superacids by low-temperature n.m.r. spectroscopy. The structures of the ions formed were assigned from their n.m.r. spectra.

It has been shown by Hanselbach and Heilbronner[69] that 2,2'-azoisobutane (63) shows 2 separate signals for t-butyl groups in its n.m.r. spectrum in concentrated sulphuric acid at -10°C. They interpreted this as being due to the unsymmetrical structure (64) with the incoming proton σ-bonded[70] to one or other of the N atoms of the azo compound and dismissed the symmetrical structures (65), (66) and (67) previously assigned to protonated azo compounds.[71,72,73]

It was anticipated, that, under the strong acid conditions used by Olah and Mo[68], 2-methyl-2-phenylazopropane might form a stable cation, enabling its structure, and the position of protonation to be determined by n.m.r. spectroscopy.

2-Methyl-2-phenylazopropane was selected for study in order to avoid acid-catalysed rearrangement of the phenylazoalkane to the corresponding phenylhydrazone.

2-Methyl-2-phenylazopropane was dissolved in fluorosulphonic acid and the solution was studied by n.m.r. spectroscopy, initially at -65°C, and then at 20°C, over a period of c.a. 20 hrs. (Experimental, page 173). No change in the spectrum was observed over this period. The spectrum was similar to that of the neat compound though the 'shape' of the aromatic multiplet was slightly different. The relative values of the electronic integrals of the aromatic multiplet and the t-butyl absorptions were 5:9. The

compound did not appear to be protonated.

The Attempted Rearrangement of 1-Phenyl-1-phenylazobut-3-ene.

Isomerisation of phenylazo compounds to the corresponding phenylhydrazones using acidic, basic and radical initiated conditions takes place readily[64] and the phenylhydrazones are thermodynamically more stable than their phenylazo isomers. The mechanism of the base catalysed rearrangement is most probably that shown in Scheme 28.

Another way in which a phenylazo compound could rearrange to a phenylhydrazone is by a 1,3 shift of an allyl group, rather than a proton (Scheme 29), and it was thought that such a rearrangement might occur under neutral conditions. The stability of 1-phenyl-1-phenlazobut-3-ene (68) in refluxing nonane (b.p. 151°C) under nitrogen was investigated (Experimental, pages 174 - 176) but the expected product of the rearrangement, N-allyl benzaldehyde phenylhydrazone (69), was not observed after 200 hours, although (68) did not appear to be stable under these conditions.

Attempted Preparations of Optically Active Phenylazoalkanes.

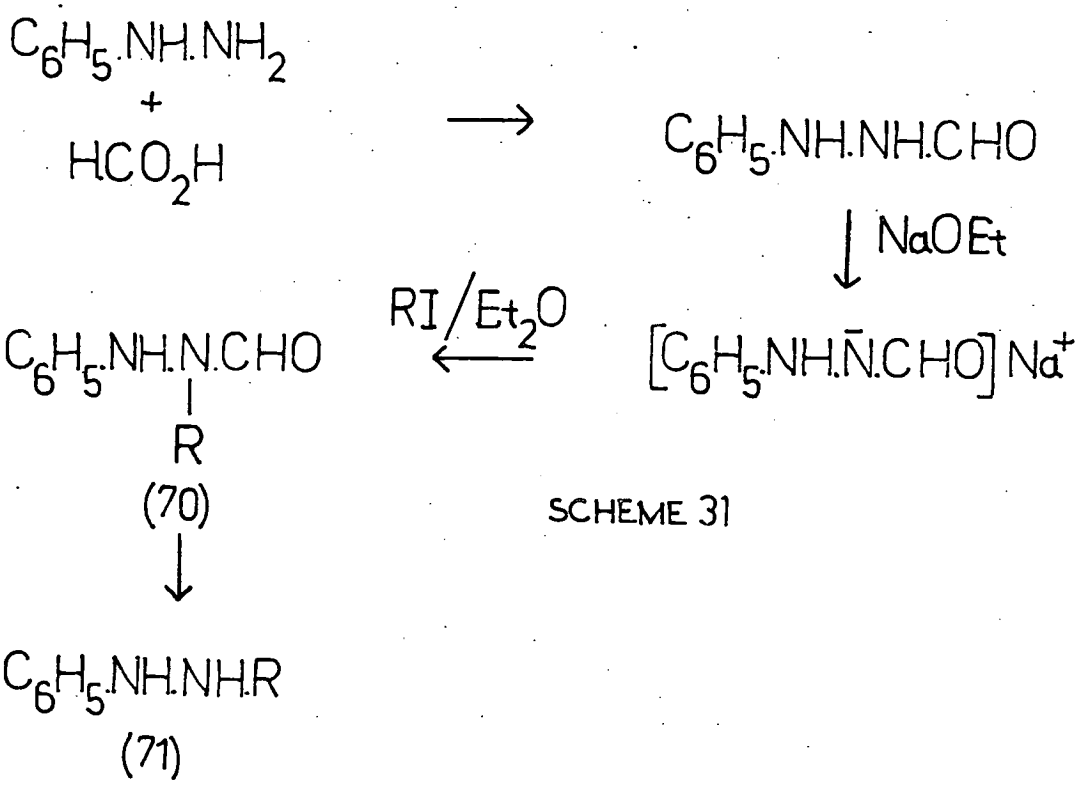
The base catalysed isomerisation of primary and secondary phenylazoalkanes to the corresponding phenylhydrazones has been established[64] (see page 58) but it is difficult to make a kinetic study of this reaction by n.m.r. or U.V. spectroscopy.

With ^{1}H n.m.r. spectroscopy only the migration of one proton to a different position (Scheme 30), which has little effect on the rest of the spectrum, can be observed. In the presence of base the absorption of this proton would be broadened through rapid exchange with the base, so that, even if the signals were well separated from the rest of the spectrum, integrals would not be accurate. U.V. spectroscopy is not particularly suitable because of the ease of oxidation of phenylhydrazones to phenylazohydroperoxides[23] which have U.V. spectra very similar to those of the corresponding phenylazoalkanes and would thus interfere with the absorbance of the phanylazoalkane.

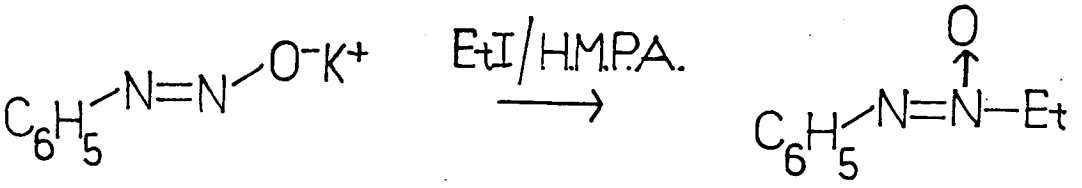
A more suitable tool by which the rearrangement could be studied would be by polarimetry. In a phenylazoalkane with an asymmetric α-carbon atom (Scheme 30) the chirality will be lost on isomerisation to the phenylhydrazone, in which the carbon atom becomes Sp^{2} hybridised.

It was to follow such a rearrangement by measurement of the decrease in optical rotation that a chiral phenylazoalkane was required. The synthesis of several such systems (discussed below) was investigated without success, and eventually 2-phenylazobornane, which did not entirely lose its chirality on rearrangement to the phenylhydrazone, was used.

The first approach tried was the classical method for the resolution of racemic mixtures of optically active bases by

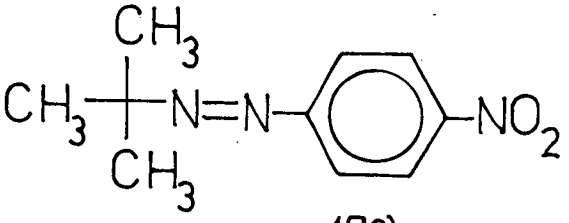


SCHEME 31



SCHEME 32

[SCHEME 33 — SEE NEXT PAGE]



(72)

formation of the salt of an optically active acid. Attempts were made to form the salts of both D-(-)-tartaric acid and L-(-)-malic acid with 1-phenyl-1-phenylhydrazopropane (Experimental, page 177) but no crystalline material was obtained from these reactions.

The second method investigated was the N-alkylation of sodium formylphenylhydrazine, as described by Freer and Sherman[74] (Scheme 31). It was intended to use an optically active alkyl iodide in this reaction and thus produce an optically active 2-N-alkyl formylphenylhydrazine (70), assuming inversion at the reacting carbon, which could be hydrolysed in the presence of acid, or base, to the phenylhydrazo compound (71). The latter could then be readily oxidized to the phenylazoalkane, without interfering with the optical activity.

It was proposed to use optically active 2-iodo-octane as the alkyl halide. This can be obtained from optically active octan-2-ol by the method of Berlak and Gerrad[75] which involves treatment of the alcohol with phosphorous tri-iodide in carbon disulphide. The reaction occurs with inversion at the asymmetric carbon atom. Octan-2-ol may be readily resolved by the method of Kenyon[76], which consists of esterification of the alcohol with phthalic anhydride, formation of the brucine salt of the remaining carboxylic acid moiety (brucine reacts readily with only one enantiomer under the conditions used) and regeneration of the alcohol by reaction with base. Since, however, trial reactions of racemic mixtures of 2-iodo-octane with sodium formylphenylhydrazine (Experimental, page 179) were unsuccessful, this approach to the synthesis of optically active phenylazoalkanes was discontinued before any resolved 2-iodo-octane was required.

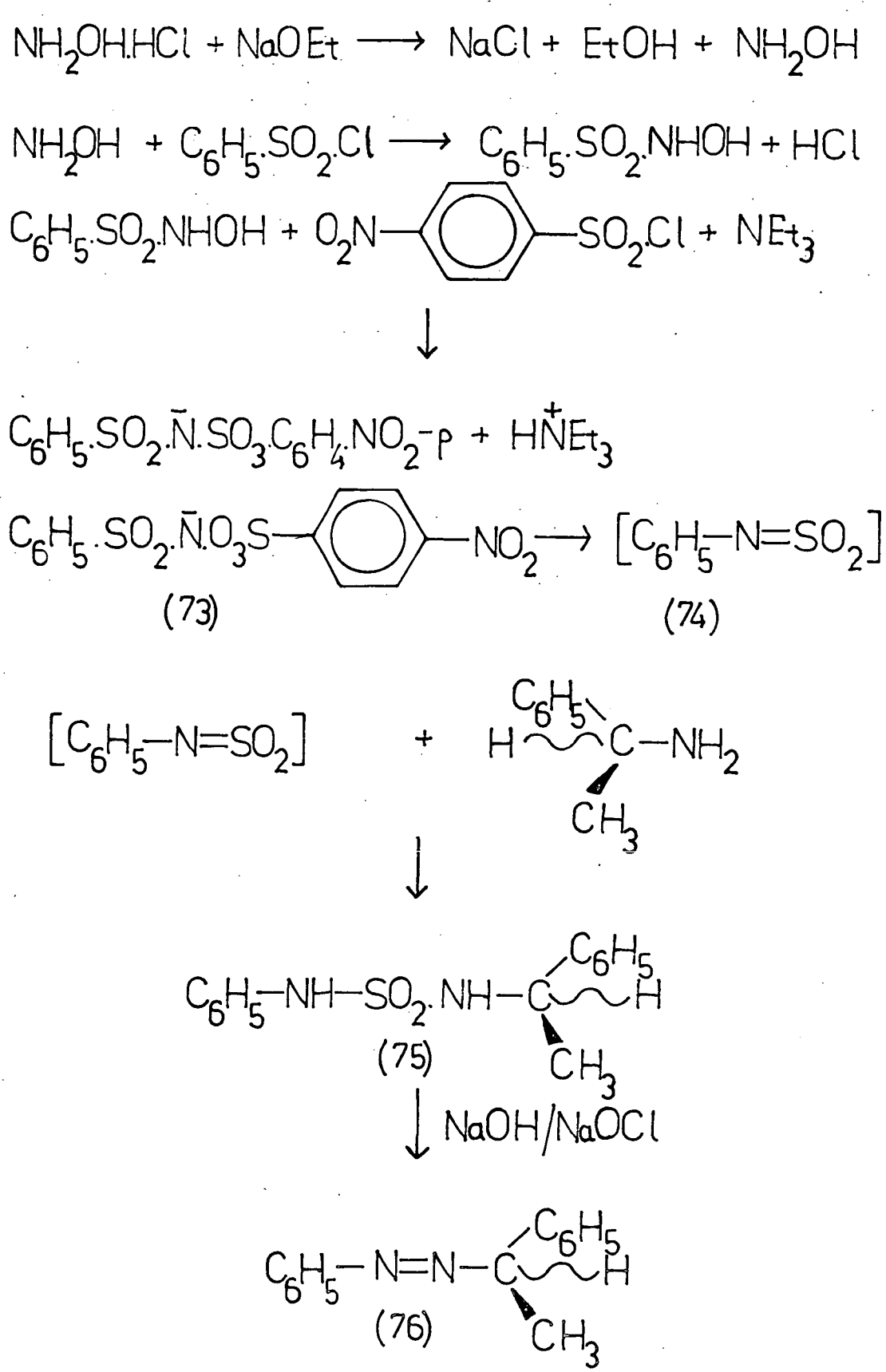
Since only formylphenylhydrazine was recovered from the

attempted reactions of 2-iodo-octane with sodium formylphenylhydrazine, the reaction on which this experiment was based i.e. the reaction of ethyl iodide with sodium formylphenylhydrazine as described by Freer and Sherman[74], was attempted, but again only formylphenylhydrazine was recovered (Experimental, page 180). It was thought that the reactions were unsuccessful because the sodium formylphenylhydrazine used was not pure. (It rapidly decomposes in the presence of air[74].) Analysis by titration (Experimental, page 181) showed that the sodium formylphenylhydrazine used in the experiments described above contained a high percentage (c.a. 70%) of free formylphenylhydrazine, and purer material was not obtained from further preparations.

Attempts to generate the sodium formylphenylhydrazine in situ were unsuccessful, mainly due to deficiencies in the apparatus used (Experimental, page 181).

Another method for the preparation of phenylazoalkanes is alkylation of the potassium salt of phenyldiazotate (Scheme 32) as described by Moss and Love[78]. This reaction is known to occur with retention of the geometry about the N = N and to retain chirality at the carbon atoms α to the azoxy function. The phenyldiazotate produced should be easily reduced to the phenylazoalkane with a limited quantity of lithium aluminium hydride. The alkylation occurs by SN_2 attack (complete inversion) of the diazotate on the alkylating agent. Trial reactions with ethyl iodide and potassium phenyldiazotate (Experimental, page 183) were unsuccessful and this method of synthesis of optically active phenylazoalkanes was not investigated further.

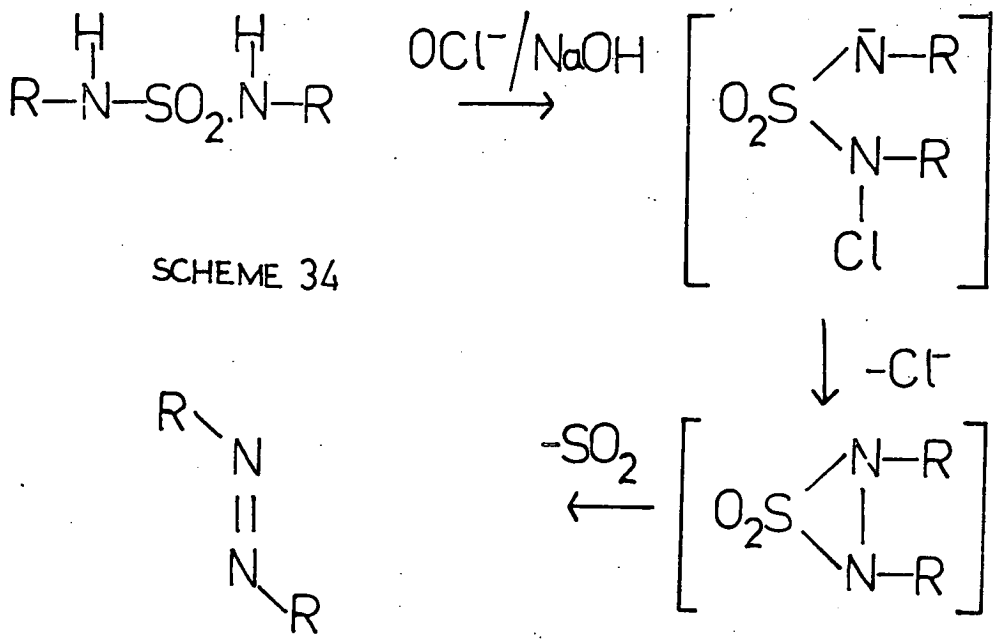
The synthesis of unsymmetrical alkyl-aryl azo compounds via oxidation of unsymmetrical sulphamides or ureas, as described by Porter and Marnett[79] was also attempted. The oxidation



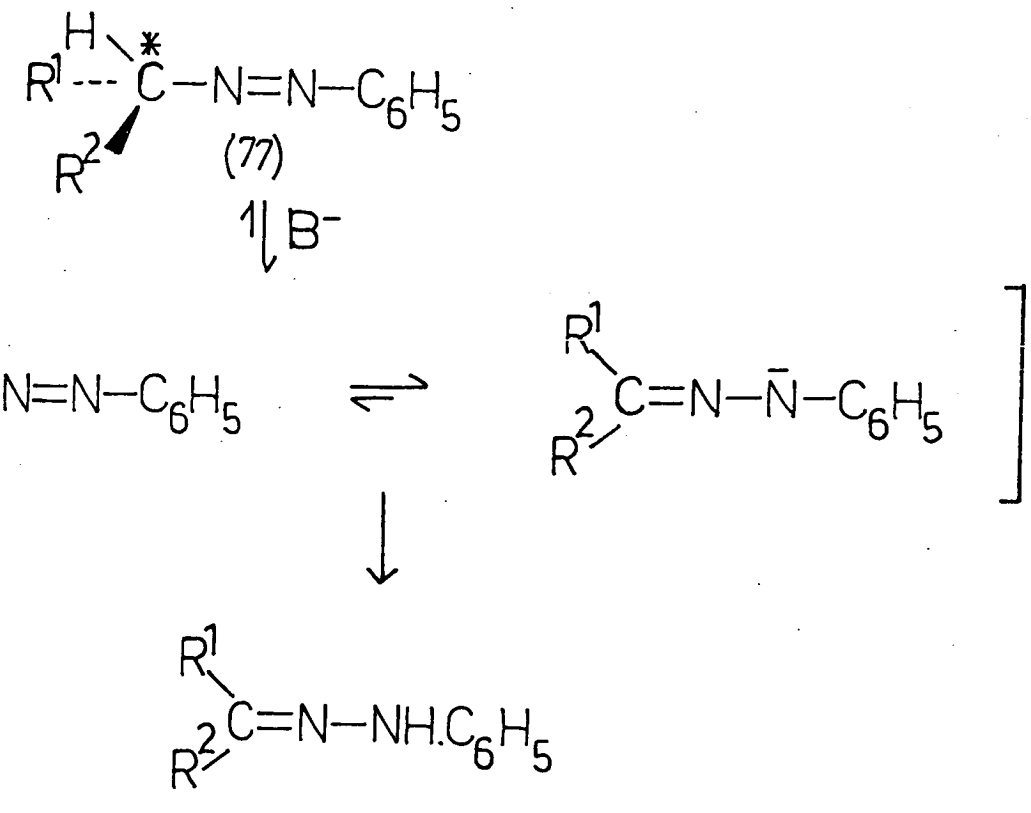
SCHEME 33

of an unsymmetrical sulphamide was first attempted using racemic 1-phenylethylamine (Scheme 33); the use of resolved 1-phenylethylamine should give an optically active phenylazo compound as product. Benzene sulphonyl hydroxylamine was prepared from hydroxylamine and benzene sulphonyl chloride by the method of Piloty.[80] This compound was then reacted with p-nitrobenzene sulphonyl chloride in the presence of triethylamine to give N-(p-nitrophenyl sulphonoxybenzene) sulphonamide (73), the triethylamine salt of which is reported[79] to give the intermediate (74) which will react with amines to form sulphamides, e.g. (75). Since this reaction was unsuccessful , an attempt was made to synthesise 2-methyl-2-phenylazopropane by the same route (Experimental, pages 183-185) but the mass and n.m.r. spectra of the product suggested that it was instead of 2-methyl-2-p-nitrophenylazopropane (72). Attempts to synthesise (72) by an unambiguous route were unsuccessful (see below). The N-(p-nitrophenyl sulphonoxybenzene) sulphonamide (73) used had the same m.p. (179°C) as reported by Lowoski and Schieffele[81], who used the formula (Ph SO_2.NH.OSO_2.$C_6H_4NO_2$p) on the basis of elemental analysis. The production of 2-methyl-2-p-nitrophenylazopropane instead of 2-methyl-2-phenylazopropane in the experiment discussed above appears to be due to the presence of mainly Ph SO_2.$\overline{N}$.SO_2.C_6H_4.NO_2p in the reaction mixture instead of Ph SO_2.$\overline{N}$.OSO_2.C_6H_4.NO_2p but no further explanation can be offered.

The method of synthesis of unsymmetrical alkyl-aryl azo compounds via oxidation of the urea, as developed by Fowler[82], was found by Porter and Marnett[79] to be superior to their own method discussed above. When this method was applied to the synthesis of 1-phenyl-1-phenylazoethane (76) however, very little crude material with the properties of the desired product was isolated. The



SCHEME 34



SCHEME 35

oxidation of the urea formed from 1-phenylethylamine and phenyl-isocyanate, was carried out using t-butyl hypochlorite in a solution of potassium t-butoxide in t-butyl alchohol and it is probable that the alkaline conditions cause the phenylazoalkane, when produced, to rearrange to the corresponding phenylhydrazone. The synthesis of phenylazoalkanes *via* oxidation of substituted ureas had only previously been applied to tertiary amines[79, 82], and it appeared doubtful at the outset that such a route would give primary or secondary phenylazoalkanes in good yield, as they would readily isomerise to the corresponding phenylhydrazones during oxidation under alkaline conditions. The synthesis of phenylazoalkanes *via* oxidation of the sulphamide, however, employs conditions for oxidation similar to those used by Ohme and Schmitz[83] in their successful synthesis of primary and secondary symmetrical azoalkanes (see Scheme 34). For this reason more attention was given to the sulphamide method than the urea method.

Attempts to Synthesise a Sample of 2 - Methyl - 2 - p - nitrophenylazopropane by an Unambiguous Route.

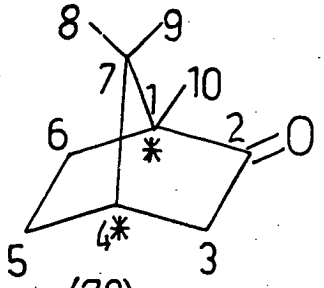
In order to identify the product, thought to be 2-methyl-2-p-nitrophenylazopropane (72), from the attempted synthesis of 2-methyl-2-phenylazopropane by oxidation of the sulphamide (see above), various methods, from established nitrations to unproven routes for the synthesis of phenylazoalkanes, were investigated.

Nitrations of 2-methyl-2-phenylazopropane (Experimental, page 186) under conditions chosen to produce mainly p-nitro substitution in the benzene ring, appeared to cause extensive decomposition of the substrate.

The synthetic route of Curtin and Ursprung[84], reaction of t-butyl zinc chloride with phenyldiazonium fluoroborate, which was convenient for the production of 2-methyl-2-phenylazopropane, was tried using p-nitrophenyldiazonium fluoroborate (Experimental, page 187). Analysis of the product mixture, after chromatography, showed that it contained 1-chloro-4-nitrobenzene, nitrobenzene and possibly 2-methyl-2-p-nitrophenylazopropane (72). The nitrobenzene was removed by distillation and an attempt was made to separate the residual mixture of (72) and 1-chloro-4-nitrobenzene by reacting the 1-chloro-4-nitrobenzene with piperidine. This method of separation was, however, only partially successful (Experimental, page 189) as not all the 1-chloro-4-nitrobenzene present in the mixture reacted with piperidine.

The last three methods attempted for the synthesis of 2-methyl-2-p-nitrophenylazopropane were rather similar in that they all involved reaction of a halide with a hydrazine, from which it was hoped to obtain 2-methyl-2-p-nitrophenylhydrazopropane, which

could be easily oxidised to the azo compound with yellow mercuric oxide. t-Butyl chloride in pyridine and t-butyl iodide in methanol did not react with p-nitrophenylhydrazine (Experimental, pages 191, 192), and attempts to react t-butylhydrazine with 1-chloro-4-nitrobenzene in pyridine were also unsuccessful (Experimental, page 193). No further potential synthetic routes to 2-methyl-2-p-nitrophenylazopropane were investigated.



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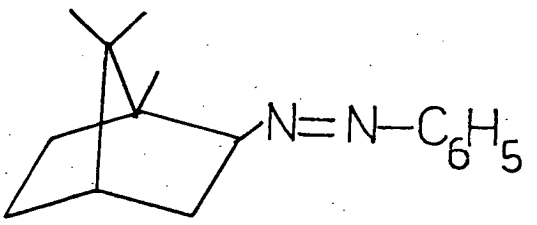

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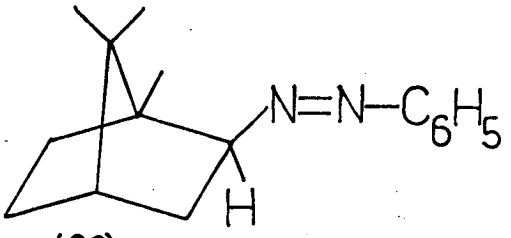

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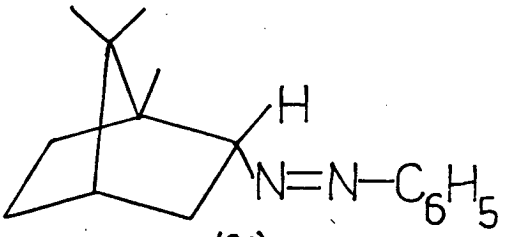

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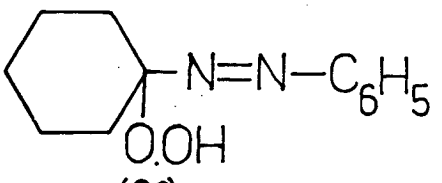

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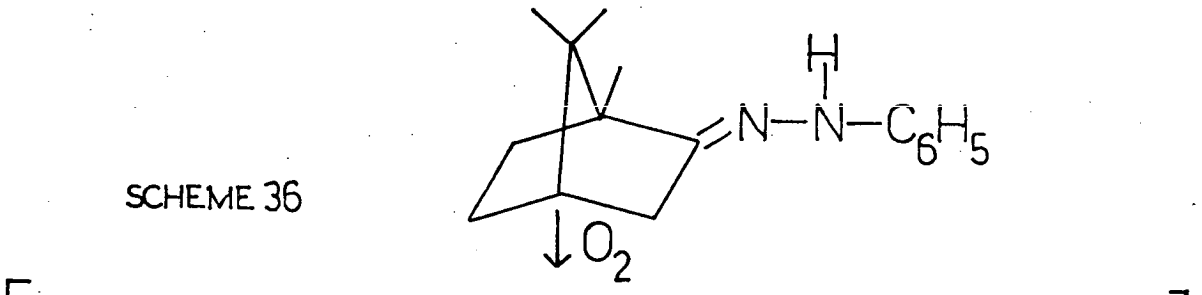
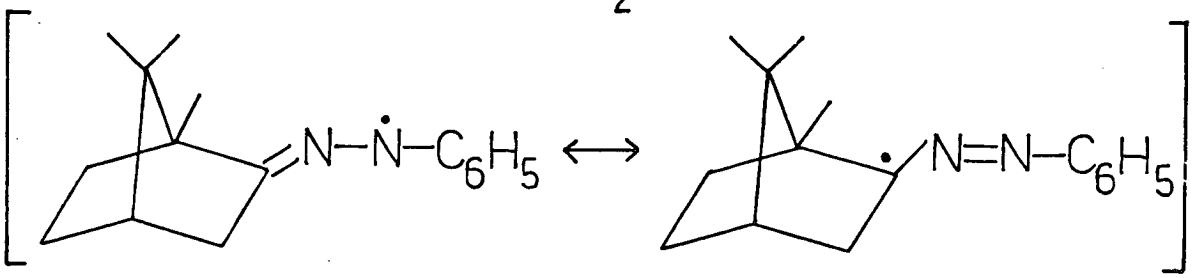
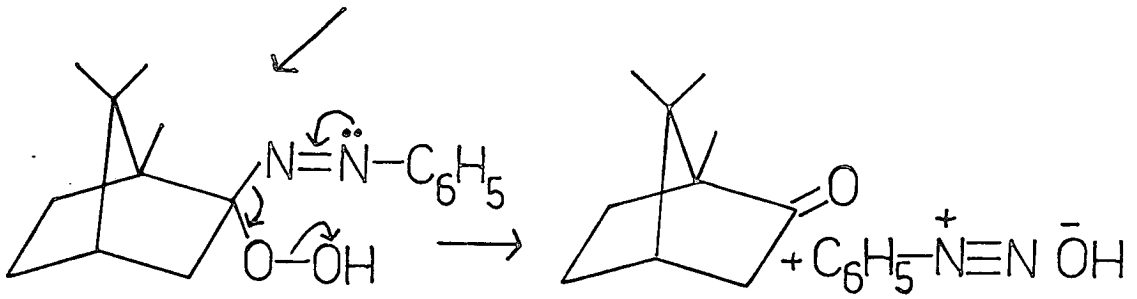
SCHEME 36







The Behaviour of 2-Phenylazobornane and Camphor Phenylhydrazone Under Various Conditions.

Difficulties were encountered in obtaining an optically active phenylazo compound for kinetic studies of the rearrangement to the corresponding phenylhydrazone by measurement of the optical rotation (see pages 59 - 63). The ideal phenylazo compound (77) for such a study should have an asymmetric α-carbon atom to which one proton is bound (an α - C - H is required for rearrangement to the phenylhydrazone) and the molecule should contain no other asymmetric centre, so that there is complete loss of optical activity once the phenylhydrazone has been formed (Scheme 35).

Since such an ideal compound was not obtained from the various synthetic methods investigated, what is perhaps the most reliable method of obtaining phenylazo compounds, reduction of the phenylhydrazone to the phenylhydrazine, which can be easily oxidised to the phenylazoalkane[23], was employed. The obvious fault with this method is that asymmetry at the α-carbon atom can only be created once the phenylhydrazoalkane has been formed, so that the phenylhydrazoalkane would have to be resolved. Resolution of 1-phenyl-1-phenylhydrazopropane had been unsuccessfully attempted with both D-(-)-tartaric and L-(-)-malic acid (Experimental, page 177) . As a compromise (+)-camphor (78), a ketone which itself contains two asymmetric carbon atoms, was used. A third asymmetric centre is produced at carbon 2 when camphor phenylhydrazone is converted to 2-phenylazobornane (79) and loss of this additional asymmetric centre, on isomerisation of 2-phenylazobornane to camphor phenylhydrazone produces a change in optical activity.

Camphor phenylhydrazone could not be prepared by simply

refluxing an equimolar mixture of the ketone and phenylhydrazine either in ethanol or in the absence of solvent. These conditions readily gave the phenylhydrazone of cyclopentanone yet the condensation of camphor with phenylhydrazine required acid catalysis (Experimental, page 195). The ease of formation of cyclopentanone phenylhydrazone shows that there is no difficulty in changing the hybridisation of a carbon atom in a five membered ring from Sp^2 to Sp^3 in the carbinolamine and back to Sp^2 in the phenylhydrazone, so that in the case of camphor other steric factors must make the condensation more difficult. The ease with which 2-phenylazobornane isomerises to camphor phenylhydrazone is shown by the difficulty encountered during purification of 2-phenylazobornane (Experimental, page 197); isomerisation occurred on the chromatographic columns, and in carbon tetrachloride solution (Experimental, page 197). The latter may have been catalysed by traces of acid in the carbon tetrachloride.

Some 100 MHz n.m.r. spectra of the phenylazobornane in carbon tetrachloride show two singlets for each methyl group (see Experimental, page 197). This suggested a mixture of two epimers (80) and (81). The reduction of camphor phenylhydrazone with lithium aluminium hydride to form 2-phenylhydrazobornane is not stereospecific and a mixture of epimers of 2-phenylazobornane was to be expected although the n.m.r. spectra of some batches of product suggested that only one epimer had been obtained. Samples which appeared to contain only one epimer were used in kinetic experiments.

Measurement of Optical Rotations.

Difficulty was encountered in the measurement of the

optical rotations of camphor phenylhydrazone as the observed rotations of fresh solutions in methanol continually decreased (Experimental, page 199), whereas treatment of the solutions with oxygen caused an increase in the observed rotation at all three wavelengths used (Table 14). Thus the continual drift towards lower values was not caused by oxidation of the phenylhydrazone to the phenylazohydroperoxide (see page 59) and must be due to some other chemical change in the solution.

In an experiment to investigate the stability of camphor phenylhydrazone in methanol containing sodium methoxide (Experimental, page 203) the optical rotation of a 1% W/V solution of camphor phenylhydrazone in methanol (+0.035° at 546 nm.) was found to be stable over 40 min. After addition of sodium methoxide solution the reading changed to +0.029° and thereafter remained stable over 2.5 hours. This was therefore taken to be the rotation (at 546 nm.) which a 1% W/V solution of 2-phenylazobornane would reach after rearrangement to camphor phenylhydrazone in methanol with sodium methoxide as catalyst.

The U.V. spectrum of 2-phenylazobornane has λ max. 410 nm., and the absorbances at the wavelengths used to measure the optical rotation on either side of this maximum (436 and 365 nm.) were too strong to allow measurement of the optical rotation at these wavelengths using the concentrations etc. necessary in the kinetic study (Experimental, page 200). (A λ max. in the U.V. spectrum corresponds approximately to the wavelength at which the optical rotation changes sign on a Cotton curve[85] and for 2-phenylazobornane the λ max. in the U.V. spectrum at 410 nm. is reflected in the change of sign in the optical rotation values (Table 15) in passing from 365 to 436 nm.)

The most suitable wavelength for measurement of the optical rotation of 2-phenylazobornane in the kinetic study was found to be 546 nm.

Study of the Base Catalysed Rearrangement of 2-Phenylazobornane in Methanol.

2-Phenylazobornane was shown by n.m.r. spectroscopy to be stable in methanol for up to three days at room temperature (Experimental, page 202). The observed value of the optical rotation of a 1% W/V solution was checked for constancy for 2 hours before sodium methoxide solution was added to the polarimeter cell (Experimental, page 202). The optical rotation then increased steadily (Table 16), indicating that the 2-phenylazobornane was undergoing rearrangement to camphor phenylhydrazone. The rotation reached +0.039°, the value for a 1% W/V solution of camphor phenylhydrazone, after 180 min., and continued to increase to more positive values (+0.095° after 280 min.). After the solution had been stored overnight the rotation had decreased again to +0.014°. This behaviour suggested that more than one reaction had taken place although camphor phenylhydrazone was the only product identified by n.m.r. spectroscopy and this was found to be stable for 2.5 hours under the conditions of the experiment (Experimental, page 203).

In an attempt to determine the cause of the unusual behaviour described above, the isomerisation of 2-phenylazobornane was also followed by U.V. spectroscopy (Experimental, pages 204 - 208).

The decrease of the $n \longrightarrow \pi^*$ absorption of 2-phenylazobornane at λ max. 402* nm. (ε 182) was recorded. Camphor phenylhydrazone also has a very weak $n \longrightarrow \pi^*$ absorption at 402 nm. (ε 11.3) and Equation 2 was used (Experimental, page 206) to allow

* Differs from value of 410 n m. recorded for an earlier sample.

for the absorbance of the product in calculation of the rate constant for the isomerisation of 2-phenylazobornane to camphor phenylhydrazone.

Four successive experiments were performed and the values obtained for the rate constant, k, the intercept, ln (a ($\varepsilon_r - \varepsilon_p$)), and the calculated errors in these values, differed greatly (see Table 18), even though the only modifications made to runs 2 and 3 was sparging of the solutions with dry nitrogen.

In runs 1, 2 and 3 the samples were kept in the cells at 45°C overnight and then rerun. The spectra then showed absorbances with $\lambda_{max.} \sim 390$ nm. which were more intense than the initial absorbances of the 2-phenylazobornane solution. Plots of ln ($A - a\varepsilon p$) v.t for runs 2, 3 and 4, produced curves which indicated that the rate of reaction dropped sharply after 70 - 100 min. Analysis of the results for run 4 over two different periods of time (t = 10 - 100 min. and t = 70 - 160 min.) produced different rate constants (k = 0.00079 ± 0.000063 min.$^{-1}$ and k = 0.00048 ± 0.000046 min.$^{-1}$ respectively). A similar experiment in which phenylazocyclohexane was used as the substrate (Experimental, page209) did not show such anomalous results; treatment of the solution with oxygen, after isomerisation to cyclohexanone phenylhydrazone was complete, resulted in formation of cyclohexane phenylazohydroperoxide (82). (Alkyl phenylazohydroperoxides are normally formed on treatment of phenylhydrazones, in solution, with oxygen[23].) All these factors indicated that the reaction of 2-phenylazobornane was not a simple first order process and that more than one reaction was taking place.

It is possible that the different rate constants obtained

from the four runs were caused by variations in the quality of the catalyst solution used, but titration of five different samples of catalyst solution against standard aqueous hydrochloric acid solution (Experimental, page 209) showed that the base concentration in the catalyst solution was fairly constant. This method of estimation, however, gave the total base concentration and not just the concentration of methoxide ion. No suitable basic, non-ionic catalyst for the reaction was found.

Since 2-phenylazobornane had been shown, by n.m.r. spectroscopy, to rearrange to camphor phenylhydrazone in carbon tetrachloride, and since camphor phenylhydrazone had been isolated after treatment of 2-phenylazobornane with sodium methoxide in methanol, it appeared probable that any side reactions taking place in the U.V. runs described above were reactions of camphor phenylhydrazone and the behaviour of camphor phenylhydrazone under the conditions of these U.V. experiments was investigated (Experimental, pages 210 -211). In the presence of sodium methoxide in methanol (Run 1) a $\lambda_{max.}$ at 388 nm. (A = 1.31) gradually appeared and the solution became yellow in colour. This $\lambda_{max.}$ was at the same wavelength as those observed in the kinetic experiments with 2-pehnylazobornane after the solutions had been allowed to stand overnight (runs 1, 2 and 3). A solution of camphor phenylhydrazone in methanol which had been stored for the same period (26 hr.) at 25°C, and which contained no sodium methoxide, was deep red in colour and the U.V. spectrum was well off scale at wavelengths shorter than 400 nm.

Further investigation of the behaviour of solutions of camphor phenylhydrazone in methanol containing no sodium methoxide (Experimental, page 211) showed that different reactions were

taking place with camphor phenylhydrazone in methanol in the presence of sodium methoxide, compared with those which occurred when the phenylhydrazone in methanol with no base present was exposed to light and air. The reactions in the presence of base precluded the possibility of following the kinetics of the rearrangement of 2-phenylazobornane to camphor phenylhydrazone with sodium methoxide as catalyst. Further experiments (Experimental, page 212), in which unsuccessful attempts were made to identify the products, showed that oxygen was involved in these reactions.

The uptake of oxygen by camphor phenylhydrazone under various conditions was measured (Experimental, pages 214-217), and in some experiments the solutions were examined by spectroscopy (n.m.r., infra-red and U.V.) after treatment with oxygen. Camphor phenylhydrazone in methanol was found to take up more than 2 molar equivalents of oxygen; uptake was slow at first and the reaction appeared to have an induction period. In carbon tetrachloride the phenylhydrazone suddenly took up more than one molar equivalent of oxygen (exceeding the capacity of the apparatus) after c.a. 2.5 hr.; again oxygen uptake was very slow prior to this sudden uptake. The U.V. and n.m.r. spectra suggested that only camphor phenylhydrazone was present after oxygen uptake had ceased. It had been shown (Experimental, page 215) that camphor phenylhydrazone, in a mixture of carbon tetrachloride and water, is hydrolysed to camphor, and the infra-red spectrum of the carbon tetrachloride solution after treatment with oxygen indicated that a mixture of camphor, camphor phenylhydrazone and probably free phenylhydrazine was present. (Camphor in the presence of camphor phenylhydrazone is difficult to detect by n.m.r. spectroscopy due to overlap of signals.) The

amount of camphor in the mixture is calculated to be 22.4% from the intensity of $\nu_{max.}$ C = O (1743 cm.$^{-1}$) i.e.22.4% of the camphor phenylhydrazone had been converted to camphor. The formation of camphor and another product (possibly phenylhydrazine) from the reaction of oxygen with camphor phenylhydrazone does not, however, account for the sudden uptakes of more than one molar equivalent of oxygen.

Hexane has been used as the solvent in the measurement of oxygen absorption by several alkyl phenylhydrazones[23], using the same apparatus as in the present experiments, and no absorption of more than one molar equivalent was observed for the alkyl phenylhydrazones investigated. To ensure that the micro-oxygenation apparatus was functioning properly the oxygen absorption of i-butyraldehyde phenylhydrazone in both carbon tetrachloride and hexane was measured and the results (Experimental, page 217) were consistent with those reported[23] for other aldehyde phenylhydrazones, showing that there was no fault in the apparatus or the method of its operation. Camphor phenylhydrazone in hexane behaved in the same manner as in methanol and carbon tetrachloride i.e. more than one molar equivalent of oxygen was suddenly taken up after c.a. 2.5 hr., showing that camphor phenylhydrazone reacts with oxygen in a different manner to other phenylhydrazones.

In methanol, in the presence of sodium methoxide, more than one molar equivalent of oxygen was taken up after 4 hr. but the uptake was more gradual than in the absence of sodium methoxide. The use of sodium methoxide as catalyst appeared to eliminate the induction period (see above), though the uptake was still slow at first.

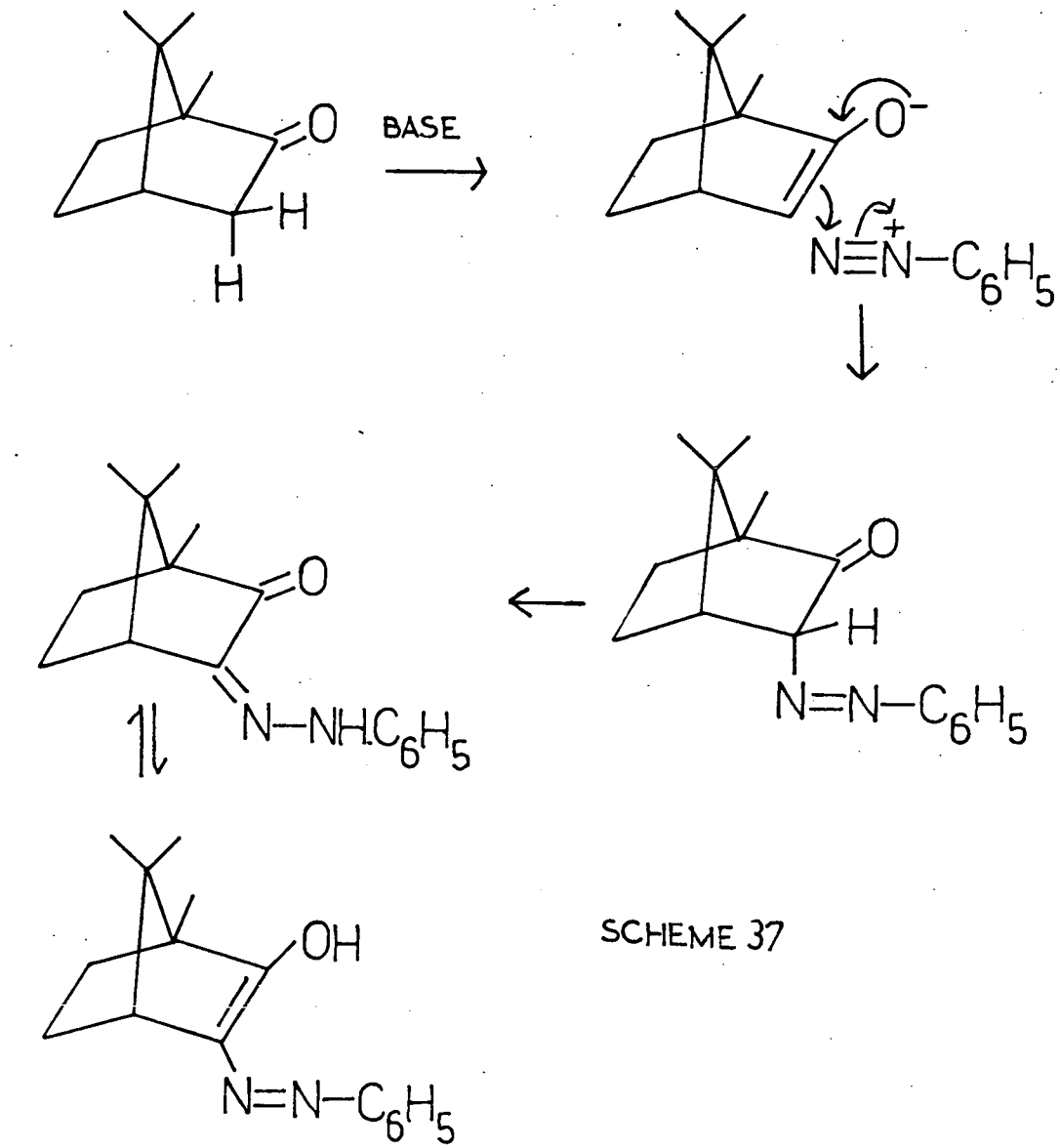
As the production of camphor after treatment of camphor phenylhydrazone with oxygen did not account for the amount of oxygen absorbed in this experiment, it seemed probable that oxygen might also be reacting with phenylhydrazine, or a species closely related to phenylhydrazine, which must be produced along with camphor during the decomposition of the phenylhydrazone. The absorption of oxygen by phenylhydrazine and the phenyldiazonium cation under various conditions, and the products of these reactions, were investigated (Experimental, pages 218 - 221). A possible mechanism to account for the formation of camphor by reaction of oxygen with camphor phenylhydrazone involves formation of a phenyldiazonium cation (Scheme 36).

Phenylhydrazine in carbon tetrachloride was found to suddenly take up more than two molar equivalents of oxygen (in < 2 min.) after c.a. 2 hours and produce a red solution. The infra-red spectrum of this solution showed sharp absorptions at 3600 and 3580 $cm.^{-1}$ which were also observed in the infra-red spectrum of the oxidised solution of camphor phenylhydrazone in carbon tetrachloride. The n.m.r. spectrum of the oxidised solution of phenylhydrazine showed no NH absorption and the aromatic multiplet had collapsed to two singlets. When the reaction was carried out in the presence of water very little oxygen was absorbed. It seems probable that on treatment of camphor phenylhydrazone in carbon tetrachloride with oxygen, camphor is first produced, and further uptake of oxygen occurs by reaction with phenylhydrazine or a related compound. (The presence of water appears to inhibit reaction of phenylhydrazine and also the hydrolysis/oxidation products of camphor phenylhydrazone with oxygen (Experimental, page 219).) When the above experiment

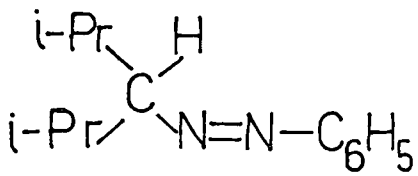
was carried out with methanol as solvent only 1.33 molar equivalents of oxygen were absorbed, but in the presence of sodium methoxide more than two molar equivalents were taken up and the final solution was yellow. In the latter experiment there appeared to be an initial fast uptake of c.a. one molar equivalent of oxygen, followed by a period of no absorption (c.a. 3.5 hr.). The rate of uptake then increased again until more than two molar equivalents had been absorbed. Sodium methoxide apparently acts as a catalyst in an initial step during which one molar equivalent of oxygen is taken up and it also appears to be responsible for subsequent reaction taking place to a greater extent than in methanol alone. Further reaction of phenylhydrazine (or a related compound) must be responsible for the behaviour observed for camphor phenylhydrazone in methanol containing sodium methoxide.

When phenylhydrazine in methanol containing sodium methoxide was treated with oxygen (Experimental, page 222) there was an increase in the intensity of the broad absorption at 350 - 550 nm. This absorption then decreased in intensity, rapidly at first, until after 18 hr. the spectrum had almost reverted to that of the solution before treatment with oxygen. Treatment of a solution of camphor phenylhydrazone with air under the same conditions (Experimental, page 212) produced an increase in intensity which continued to increase on storage. It is therefore improbable that the strong absorption which appeared at 370 nm. when solutions of camphor phenylhydrazone in sodium methoxide/ methanol were exposed to air is due to a product of the oxidation of free phenylhydrazine.

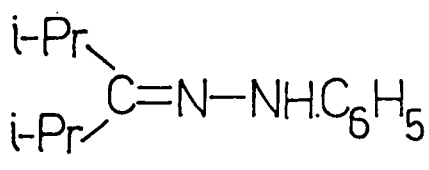
The phenyldiazonium cation in methanol gave oxygen



SCHEME 37



(83)



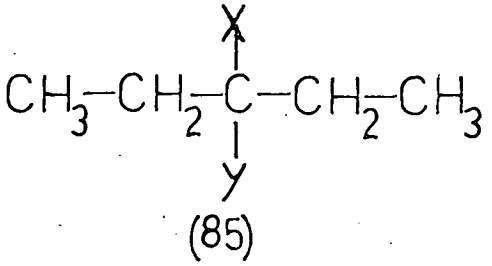
(84)

absorption of less than one molar equivalent, and the uptake in the presence of sodium methoxide was less than that in the absence of the base. The U.V. spectrum of the solution (containing sodium methoxide) after oxygen absorption showed a $\lambda_{max.}$ at a longer wavelength (396 nm.) than that observed for a solution of camphor phenylhydrazone after similar treatment. When the phenyldiazonium cation was subjected to the same conditions as used in the study of the base catalysed rearrangement of 2-phenylazobornane by U.V. spectroscopy, a sample at the same concentration as the phenylazobornane solutions used had to be diluted (X50) to bring the spectrum on scale. A $\lambda_{max.}$ at 396 nm. was observed and this slightly increased in intensity during 3 hr. at 45°C, and then remained steady (ε 2900). (The phenyldiazonium cation does not appear to be stable in solution; probably nitrogen is lost. After storage for c.a. 2 days at 25°C no strong absorption at 396 nm. appears on addition of base.) The $\lambda_{max.}$ at 396 nm. is at a slightly longer wavelength than that produced in solutions of 2-phenylazobornane and camphor phenylhydrazone under similar conditions ($\lambda_{max.} \sim 390$ nm.), however it is possible that the same species might be responsible for both these absorptions.

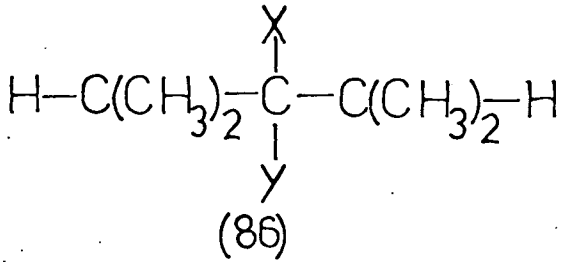
It is conceivable that, under the basic conditions used for the rearrangement of 2-phenylazobornane, a diazonium cation could couple with camphor by a Japp-Klingeman type reaction (Scheme 37) in which the methylene group at the 3 postion will be activated towards electrophilic substitution by enolisation of the carbonyl group. This possibility was investigated (Experimental, page 223) but no reaction between the phenyldiazonium cation and camphor which could be responsible for the absorption observed with camphor phenylhydrazone in sodium methoxide/methanol was found to

take place.

In summary, 2-phenylazobornane readily isomerises to camphor phenylhydrazone on treatment with base. In the presence of oxygen the phenylhydrazone undergoes further reaction and camphor is produced. The other product(s) of this reaction, which requires more than two molar equivalents of oxygen has a strong absorption in the U.V. at 370 - 390 nm. (the wavelength appears to vary). This product was not identified although it is thought to be similar to the oxidation product of the phenyldiazonium cation.



(85)



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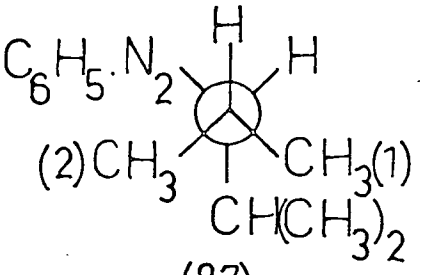
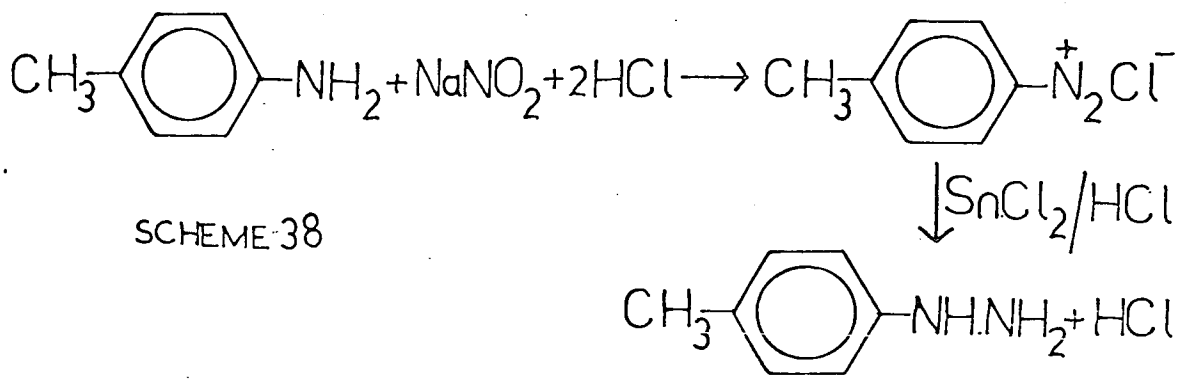
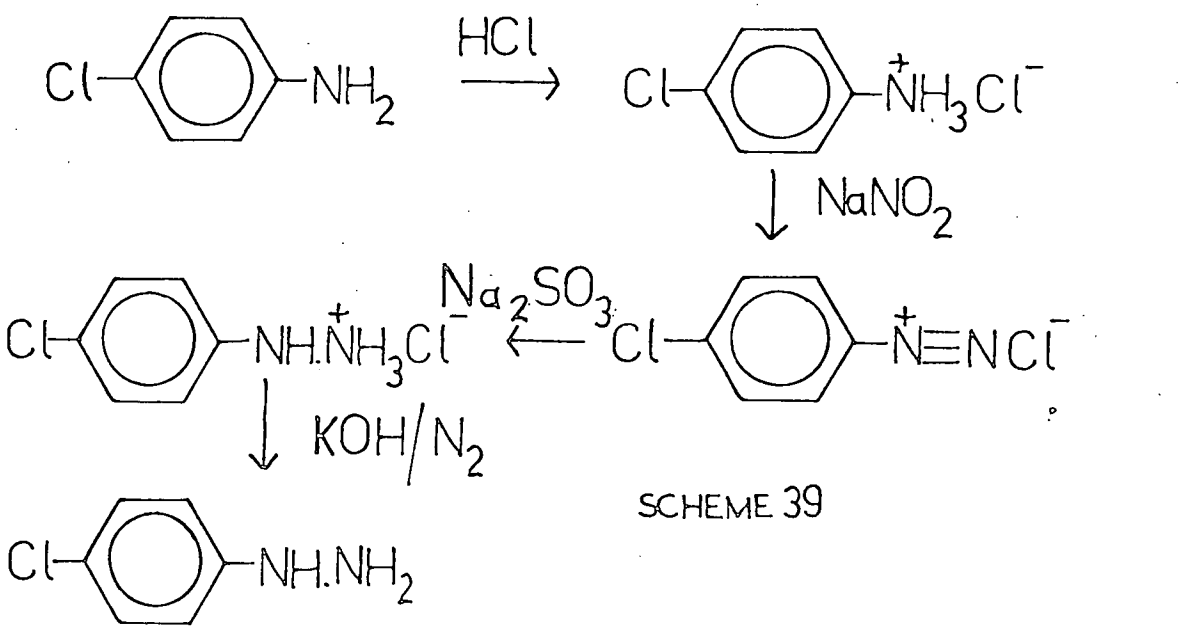


(87)



SCHEME 38



SCHEME 39

The ^{1}H N.M.R. Spectra of Di-isopropyl Ketone Phenylhydrazone and Related Compounds.

The presence of two methyl doublets in the n.m.r. spectrum of 2,4-dimethyl-3-phenylazopentane (83), as opposed to only one in the spectrum of the corresponding phenylhydrazone, di-isopropyl ketone phenylhydrazone (84), had been observed.[65] In order to determine whether this non-equivalence of methyl groups was due to hindered rotation of the isopropyl groups in (83), or to some other factor, these compounds were prepared (Experimental, page 225) and their n.m.r. spectra recorded. The two separate methyl doublets of (83) did not coalesce or even broaden when the compound was heated to 180°C in diphenyl ether. (They did overlap as the temperature was increased but this was merely due to change in chemical shift at higher temperatures.[86]) The non-equivalence was not, therefore, caused by hindered rotation of the i-propyl groups. Further evidence of this is found in the n.m.r. spectrum of 2,4-dimethyl-pentan-3-ol, which, although less sterically hindered, also has two methyl doublets.

Non-equivalence of the methylene protons in ethyl groups[87] in compounds of the general structure (85) is well known[87,88,89,90] and some examples in isopropyl groups have also been observed.[91,92,93] The explanation of this phenomenon in the methylene protons of ethyl groups can also be applied to isopropyl groups by analogy of structure (86) with (85). The methyl protons in (86) are in a similar environment to that of the methylene protons in (85). Me (2) in (87) can never experience the same average magnetic environment as Me(1) even with free rotation about the central C-C bond. The two methyl groups within each isopropyl groups are therefore non-

equivalent, even though the two isopropyl groups are equivalent. Two pairs of doublets are therefore observed if the magnetic anistropy of the other groups (X and Y in (86); Ph N_2 and H in (87)) are sufficiently different to cause a large enough difference in the average environment of Me(1) and Me(2). (Di-isopropyl ketone phenylhydrazone does not have a structure of the type (86) and only one methyl doublet is observed.)

EXPERIMENTAL

^1H Nuclear Magnetic Resonance spectra were run on a Perkin Elmer R.10 Spectrometer (60 MHz) at 33°C, an E.M. 360 (60 MHz) at 33°C, or a Varian Associates H.A. 100 Spectrometer (100 MHz) at 28°C except where other temperatures are indicated. Unless otherwise specified the solvent was carbon tetrachloride and the concentration was 5 - 10% W/V. 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., and adjusted to this where other references have been used. Intensities of absorptions were calculated from an average of three to five electronic integrals on the 100 MHz spectra. In the description of n.m.r. spectra the following abbreviations are used: singlet (s), doublet (d), doublet of doublets (d of d), triplet (t), quartet (q) and multiplet (m). J is the coupling constant quoted in hertz (Hz).

The infra-red spectra were recorded on Unicam S.P. 200, Perkin Elmer 237 and Perkin Elmer 157G Spectrophotometers. The suffixes to the infra-red bands quoted are abbreviated as follows: (w), weak; (m), medium; (s), strong; (b), broad.

Ultraviolet spectra were recorded on a Unicam S.P. 800 A Spectrophotometer, theremostated where indicated using a S.P. 870 constant temperature cell accessory and a S.P. 875 controller.

Optical rotations were determined on a Perkin Elmer 141 Polarimeter theremostated by water circulation around the cell during kinetic runs, and have been corrected for solvent and cell contributions.

Mass spectra were run on an A.E.I. M.S. 902 double

focussing instrument.

All melting points were determined on a Reichert hot-stage microscope and are uncorrected.

The alumina used in all chromatography was of Activity III[94] unless otherwise stated.

NOTE

Due to a typist's misunderstanding, the lay-out of the Experimental Section does not exactly correspond to that of the Discussion. Some experiments are presented on separate pages. References are given in the Discussion to the appropriate pages of the Experimental Section so that no confusion should arise from these slight differences in arrangement.

Solvents

Preparation and Purification of Nitromethane for N.M.R. Spectroscopy

Method A.[95] — Sufficient cold 40% aqueous sodium hydroxide solution (approximately 450 ml.) was added to a mixture of chloroacetic acid (500 g.) and crushed ice (500 g.) to make the resulting solution faintly alkaline to phenolphthalein. The temperature was kept below 20°C during the addition to prevent the formation of sodium glycollate.

The solution was mixed with sodium nitrite (365g.), dissolved in water (500 ml.), in a 3 l. distillation apparatus and then slowly heated to 80°C. The external heating was removed and the reaction was allowed to proceed by itself. Bubbles of carbon dioxide caused effervescence and the reaction mixture became brown. (At 80 - 85°C the exothermic decomposition of sodium nitroacetate becomes so rapid that the temperature rises to 90°C without further application of heat. If heat is applied after the temperature reaches 85°C violent frothing may occur, with loss of nitromethane.)

During spontaneous heating approximately 100 ml. of nitromethane distilled over (b.p. 83°C) accompanied by 120 ml. of water. When the temperature of the mixture had dropped to 85°C heat was again applied until the temperature reached 106°C and a further 100 ml. of liquid, mainly water, distilled over. The distillate was allowed to separate for 30 min. before the nitromethane was run off and dried over calcium chloride. On distillation the fraction b.p. 98 - 103°C was collected as nitromethane (88g; 27%).

The 60 MHz n.m.r. spectrum of the neat liquid showed a singlet for nitromethane (4.3 p.p.m.) plus another singlet (2.1 p.p.m.) due to an impurity. The product was re-distilled through a Vigreux column. Only the fraction b.p. 99 - 102°C was collected. The 60 MHz n.m.r. spectrum of this fraction showed the impurity

was still present although the amount had decreased. Comparison of spectra with and without added acetone suggested that the impurity might be acetone. Subsequent preparations using the above method produced nitromethane without the impurity after one distillation. The nitromethane was stored over molecular sieve (type 4A).

Method B[96]. —— Methyl iodide (42.5g, 0.30 mole) was added to a stirred solution of sodium nitrite (36 g; 0.52 mole) in dimethyl sulphoxide (225 ml.) maintained at 25°C. Stirring was continued for 4 hours before the reaction mixture was poured into a mixture of ice-water (100 ml.) and petroleum-ether (100 ml; b.p. 30 -40°C). After separation the aqueous phase was further extracted with portions of petroleum-ether (4 x 100 ml.), and the combined extracts were washed with water (4 x 100 ml.) and dried ($MgSO_4$). The major part of the petroleum-ether was removed by distillation through a small Vigreux column and the residue was then fractionated at atmospheric pressure. Two fractions were collected, (i) b.p. 60 - 100°C, and (ii) b.p. 100°C. The 60 MHz n.m.r. spectra showed that both fractions were petroleum-ether; no nitromethane was present.

Commercial nitromethane contained impurities which obscured the 0 - 2 p.p.m. region of the n.m.r. spectrum. These impurities could not easily be removed by distillation. The nitromethane used in all experiments has been prepared from chloroacetic acid (method A).

Purification of Chloroform[97]. —— Reagent grade chloroform was washed with concentrated sulphuric acid (4X) in order to remove ethanol, with dilute aqueous sodium hydroxide solution (4X) and finally with water (6X). The chloroform was dried over phosphorous pentoxide and distilled from calcium chloride. The fraction, b.p. 61°C, was collected and stored over molecular sieve (type 4A). The 60 MHz

n.m.r. spectrum of the neat liquid showed only the absorption for chloroform (7.24 p.p.m.).

Purification of Cyclohexane[98]. — Cyclohexane (ex. May and Baker) was washed several times with a cold mixture of concentrated nitric acid and concentrated sulphuric acid in order to nitrate any benzene present, and then washed repeatedly with distilled water. The cyclohexane was distilled from sodium and the fraction b.p. 80 - 81°C was collected and stored over molecular sieve (type 4A).

Preparation of Anhydrous Methanol[99]. — Magnesium turnings (5g.) and iodine (0.5g) were placed in a 2 l. flask, and "AnalaR" methanol (75 ml.) was added through a condenser. The latter was fitted with a drying tube ($CaCl_2$). The mixture was gently heated until the iodine colour had disappeared and hydrogen evolution had ceased, then a further 900 ml. of methanol were added. The mixture was refluxed for 30 min. and then the methanol was distilled; b.p. 65°C. (The first 25 ml. of distillate were discarded.)

Preparation of 'Super Dry' Ethanol[99]. — Absolute ethanol was dried and distilled in the same way as methanol (see above).

Other solvents. — Where other solvents are described as 'dry' analytical grade solvent has been dried either over molecular sieve, or, where possible, with sodium wire.

^{1}H N.M.R. Study of Phenylhydrazone Formation and Isomerisation in Pyridine.

Solutions of phenylhydrazine (4.05g; 37.5 m. mole) in 'AnalaR' pyridine (21.7 ml; 0.27 mole) and of the carbonyl compound (30 m. mole) in 'AnalaR' pyridine (21.7 ml; 0.27 mole) were prepared so that a 5 : 4 excess of phenylhydrazine over carbonyl compound was obtained on mixing equal volumes of each solution. These concentrations also gave a 5% M product solution.

Both solutions were cooled to 0°C before the carbonyl solution (0.75 ml.) was added from a syringe to the phenylhydrazine solution (0.75 ml.) contained in an n.m.r. tube at 0°C. The solutions were thoroughly mixed and the spectra recorded within thirty minutes using an external benzene lock on the 100 MHz spectrometer. The reaction mixtures were stored in the n.m.r. tubes at room temperature under nitrogen and the spectra were recorded again 24 hours, 5 days and 11 days after mixing. No change in the spectra was noted after five days so that the reactants and products had reached equilibrium at that time. The relative amounts of isomers were determined from the electronic integrals.

Experiments to study the formation and isomerisation of phenylhydrazones in dioxan and of para-substituted phenylhydrazones in pyridine were carried out in the same way. Due to the low solubility of p-nitrophenylhydrazine in pyridine only a 4.3% M concentration of product could be obtained though the relative concentrations of reactants remained the same as in other experiments (see Table 1).

Preparation of p-Methylphenylhydrazine.[100] (Scheme 38) —— p-Toludine (5.2g; 0.048 mole) was stirred with concentrated hydrochloric acid (40 ml.) until a thick, yellow paste formed. Diazotization was effected at 0°C with efficient stirring by the addition of a solution of sodium nitrite (3.3g; 0.048 mole) in water (14 ml.).

The diazotised solution was run slowly into a solution of stannous chloride (32.8 g; 0.145 mole) in concentrated hydrochloric acid (28 ml.), at 0°C under nitrogen. A cream coloured solid formed, which became colourless on standing for three hours under nitrogen.

The hydrochloride was filtered off using a sintered funnel and then neutralised with 25% aqueous potassium hydroxide solution (50 ml.) with stirring and cooling under nitrogen. The free base, which precipitated as a solid, was filtered off and dried. It was then dissolved under nitrogen in the minimum quantity of boiling benzene and precipitated as colourless plates by addition of 3x the volume of light petroleum-ether. The arylhydrazine (1.7 g; 28.4%) was filtered off and dried; m.p. 58-60°C (lit.[101] 65-66°C), $\nu_{max.}$ (nujol) 3200 (b), 1610 (m), 1510 (s), 980 (m), 800 $cm.^{-1}$(s). The n.m.r. spectrum (60 MHz) in benzene showed the absorption for the p-methyl group at 2.13 p.p.m. On storage in a vacuum desiccator the crystals became slightly orange in colour.

^{1}H N.M.R. Spectrum of Acetaldehyde p-Nitrophenylhydrazone in Nitromethane.

p-Nitrophenylhydrazine (1.4375 g;0.0094 mole) was added to redistilled acetaldehyde (20 ml.) and the excess of aldehyde was evaporated after 30 min. The compound was recrystallised from nitromethane under nitrogen and the 100 MHz n.m.r. spectrum of a saturated solution in nitromethane was recorded with nitromethane as the internal reference (4.29 p.p.m.). (The arylhydrazone was not sufficiently soluble in nitromethane to allow a 5% M solution to be formed.) In the two methyl doublets the highfield line for the syn isomer (71%) and the lowfield signal for the anti isomer (29%) were co-incident (1.8 p.p.m.). The isomeric composition was determined from the electronic integrals on the other two signals of the doublets.

^{1}H N.M.R. Spectrum of Acetaldehyde Phenylhydrazone in Nitromethane.

Solutions of phenylhydrazine (2.025g; 0.0187 mole) in nitromethane (8.23g; 0.135 mole) and of redistilled acetaldehyde (0.66g; 0.015 mole) in nitromethane (8.23g; 0.135 mole) were prepared so that a 5 : 4 molar excess of phenylhydrazine over acetaldehyde was obtained on mixing equal volumes of the solutions. These concentrations also gave a 5% M product solution. The solutions (0.75 ml. of each) were thoroughly mixed in a n.m.r. tube and set aside under nitrogen to equilibrate. The 100 MHz n.m.r. spectrum recorded after 7 days using nitromethane as the internal reference (4.29 p.p.m.) showed the methyl doublets of the isomeric phenylhydrazones at 1.82 p.p.m. (anti 39%) and a 1.91 p.p.m. (syn 61%).

Comparison of the Basicity of Nitromethane and Acetonitrile by Measurement of their Effects on the Infra-red Hydroxyl Absorption Frequency of p-Fluorophenol.[102] A. Nitromethane.-

The carbon tetrachloride used had been distilled from calcium hydride and stored over molecular sieve (type 4A).

A standard solution of p-fluorophenol (1.0012g.) in dry carbon tetrachloride (100 ml.) was prepared.

Various quantities of nitromethane (ranging from 6 to 41 mg.) were weighed into five 50 ml. volumetric flasks and dry carbon tetrachloride (approximately 40 ml.) was added to each flask to minimise evaporation of the nitromethane. Aliquots (2.00 ml.) of the standard phenol solution were transferred to the five flasks containing nitromethane and also to one empty 50 ml. volumetric flask. The standard phenol solution (1 ml.) was measured into another empty 50 ml. volumetric flask. (The two samples containing no nitromethane were used to determine the extinction coefficient of p-fluorophenol. This did not prove necessary in the experiment with nitromethane.) Each flask was filled to the mark with dry carbon tetrachloride and the contents thoroughly mixed.

The infra-red spectra were recorded at 24°C on a Perkin Elmer 207 Spectrophotometer in a cesium iodide cell (0.5 cm. path-length). The carbon tetrachloride itself and the solutions absorbed a very small amount of moisture on transference to the sample cell. The amount of moisture indicated by the intensity of the infra-red absorption ($\nu_{max.}$ OH, 3704 $cm.^{-1}$) was approximately the same for each sample and did not interfere with the phenol absorption.

In the six solutions containing the same concentration of p-fluorophenol only one hydroxyl group absorbance ($\nu_{max.}$ 3620 $cm.^{-1}$)

was observed. This absorbance was of the same intensity for the 6 solutions including that which contained no nitromethane. In the range of concentrations covered, at 24°C, nitromethane does not therefore form hydrogen-bonds with p-fluorophenol. (see Table 19)

B. Acetonitrile.—The experiment was carried out in the same way as that for nitromethane. The infra-red spectra were recorded at 22°C.

In this case both free hydroxyl absorbances ($\nu_{max.}$ 3625 cm.$^{-1}$) and those of hydroxyl groups hydrogen-bonded to the acetonitrile ($\nu_{max.}$ 3480 cm.$^{-1}$) were observed. $\Delta\nu$, the difference in the frequencies of the free and hydrogen-bonded hydroxyl groups, was 145 cm.$^{-1}$. The formation constant (K_f) for the hydrogen-bonded complex was calculated from the intensities of the free hydroxyl absorbances (see example below) for each of the 5 solutions containing acetonitrile. (see Tables 20 and 21)

An average value for the molar extinction coefficient (ε) for p-fluorophenol in carbon tetrachloride was calculated from the absorbances of the two solutions containing p-fluorophenol but no acetonitrile.

$$\varepsilon = 124.2$$

Solution 1: % transmittance = 60 = 100 I/I_o

$$I_o/I = 1.665$$

$$\log_{10} I_o/I = E = 0.2214$$

where I_o is the intensity of incident radiation.

I is the intensity of transmitted radiation.

E is the absorbance.

$$\varepsilon = \frac{E \times M.W.}{C \times 1}$$

(C is the concentration in g./l.)
(l is the pathlength in cm.)

$$C = \frac{E \times M.W.}{\varepsilon \times l}$$

$$= \frac{0.2214 \times 112}{124.2 \times 0.5} \text{ g./l.}$$

$$= 0.394 \text{ g./l.}$$

$$K_f = \frac{[A_o] - [A]}{[A]([B_o] - [A_o] + [A])}$$

$$= \frac{[C]}{[A]([B_o] - [C])}$$

In this case the proton donor was p-fluorophenol and the free base was acetonitrile.

$[A_o]$ and $[A]$ are the initial and equilibrium concentrations of the proton donor respectively.

$[B_o]$ and $[B]$ are the initial and equilibrium concentrations of the free base respectively.

$[C]$ is the concentration of the hydrogen-bonded complex.

$[A_o] = 0.47$ g./l. $= 0.0042M$

$[A] = 0.394$ g./l. $= 0.00352M$

$[A_o] - [A] = 0.00068M$

$[B_o] = 0.362$ g./l. $= 0.0084M$

$[B_o] + [A] = 0.01192M$

$[B_o] + [A] - [A_o] = 0.00772M$

$$K_f = \frac{0.00068}{0.00352 \times 0.00772} \quad M^{-1}$$

$$= \underline{24.9 \ M^{-1}}$$

(the values for K_f for the other solutions are recorded in Table 21)

The average value of K_f was found to be $26.6 \pm 4.5 \ M^{-1}$ ($\Delta\nu$ 145 cm.$^{-1}$). The results indicate that acetonitrile is more basic than nitromethane, for which no hydrogen-bonding to p-fluorophonol was observed, and suggest acetonitrile is a base of similar strength to that of tetrahydrofuran (K_f 17.7; $\Delta\nu$ 292 cm.$^{-1}$)[102] and cyclohexanone (K_f 20.5; $\Delta\nu$ 429 cm.$^{-1}$).[102]

Comparison of the Basicity of Nitromethane and Acetonitrile by Measurement of their Hydrogen Bonding Affinity for Chloroform by N.M.R. Spectroscopy.[40, 103]

The chloroform, cyclohexane, acetonitrile and nitromethane had been purified, dried and distilled before use. 5% M solutions of chloroform in cyclohexane, nitromethane and acetonitrile (20 ml. of each solvent) were made up. Each solvent contained 3% tetramethylsilane by volume.

The 100 MHz n.m.r. spectrum of each sample ($\frac{1}{2}$ ml.) was scanned with tetramethylsilane as the internal reference. The chloroform absorptions were expanded at 250 Hz sweepwidth and the frequencies determined on a Varian V-4315 frequency counter. A series of dilutions were made on each sample and the frequency of the chloroform absorption determined after each dilution. The absorption frequency for each solvent did not change significantly on dilution to 0.85 ml. The variation was approximately $\pm$ 0.2 Hz about the initial values. The chemical shifts recorded, relative to tetramethylsilane, were therefore taken to be those at infinite dilution. The average values for the chemical shift of chloroform were 757.4 Hz in acetonitrile, 753.2 Hz in nitromethane and 708.7 Hz in cyclohexane.

$\Delta\delta_{\infty}$ ($CH\,Cl_3$) = $\delta_S - \delta_C$ where δ_S and δ_C are the chemical shifts of chloroform at infinite silution in the solvent in question, and in an inert solvent such as cyclohexane, respectively. $\Delta\delta_{\infty}$ ($CH\,Cl_3$) was 0.487 p.p.m. for acetonitrile and 0.445 p.p.m. for nitromethane.

In agreement with the results found by measurement of the effects on the infra-red hydroxyl absorption frequency of p-fluorophenol, nitromethane is a weaker base than acetonitrile.

Previously reported values do not agree with these results: $\Delta\delta_{\infty}(CH\,Cl_3) = 0.31$ p.p.m.[39] for acetonitrile and 0.47 p.p.m.[40] for nitromethane.

Determination of the Stability of Nitromethane towards Carbonyl Compounds.

12.5% M solutions of redistilled phenylhydrazine and collidine (2,4,6-trimethylpyridine), and a 10% M solution of redistilled acetone, were made up in nitromethane. The acetone solution and the collidine solution (0.75 ml. of each) were mixed with separate phenylhydrazine solutions (0.75 ml.) in n.m.r. tubes. The samples were stored under nitrogen at room temperature and the 100 MHz ^{1}H n.m.r. spectra were recorded after 1 hour, 6.5 hours, 30 hours and 5 days with nitromethane (4.2 p.p.m.) as the internal reference.

The spectra of the sample containing acetone and phenylhydrazine showed only acetone phenylhydrazone (two s, 6H, 1.9 p.p.m.) and the excess of phenylhydrazine after 30 hours and 5 days.

The spectra of the sample containing collidine and acetone showed only the absorptions for collidine (s, 3H, p-methyl, 2.16 p.p.m.; s, 6H, o-methyl, 2.29 p.p.m.; s, 2H, aromatic, 6.74 p.p.m.) and for acetone (2 p.p.m.). The spectrum did not change during 5 days. Nitromethane did not react with acetone under these conditions.

Nitromethane does not therefore condense with acetone in the presence of collidine (pK 10.07 at 20°C).[41] It is unlikely that it would condense with acetone in the presence of phenylhydrazine (pK 5.2 at 25°C),[104], and it did not appear to do so.

Preparation of p-Chlorophenylhydrazine.[105] (Scheme 39) ——

A suspension of finely powdered p-chloroaniline (25.5g; 0.2 mole), in an excess of concentrated hydrochloric acid (70 ml.) was heated to approximately 60°C for 1 hour to convert the amine to its hydrochloride. The solution was then cooled in an ice/salt bath and an ice-cold solution of sodium nitrite (20 g.) in water (50 ml.) was added, with vigorous stirring, during 90 mins. The temperature of the reaction mixture remained between 0 - 5°C.

The solution of the diazonium salt was filtered and then added slowly to a solution of sodium sulphite, prepared by passing gaseous sulphur dioxide into a solution of sodium hydroxide (45g.) in water (300 ml.) until an acid reaction was just indicated by phenolphthalein. (Excess sulphur dioxide must be avoided otherwise tars are produced on addition of the diazonium solution and the yield of arylhydrazine is greatly diminished.)

The resulting bright orange solution was heated to approximately 60°C and then made acid to litmus by the addition of concentrated hydrochloric acid (approximately 20 ml.). The colour changed to pale yellow. Heating was continued for 1 hour, concentrated hydrochloric acid (100 ml.) was added, and the mixture was then allowed to cool.

The arylhydrazine hydrochloride which crystallised out was filtered off using a sintered funnel and then neutralized with 25% aqueous potassium hydroxide solution (300 ml.) while cooled in ice. The free hydrazine, which precipitated as pink crystals, was collected, dired, and then recrystallised from benzene by the addition of petroleum-ether (b.p. 60 - 80°C). The cream coloured p- chlorophenylhydrazine (10.87g; 38.5%) was washed with petroleum-ether (b.p. 30 - 40°C) and dried under high vacuum; m.p. 88 - 89°C (lit.[105] m.p. 90°C).

^{1}H N.M.R. Study of the Condensations of p-Chlorophenylhydrazine with Carbonyl Compounds in Nitromethane.

The method described below was used because of the low solubility of p-chlorophenylhydrazine in nitromethane (< 12½% M solution).

A 6.25% M solution of p-chlorophenylhydrazine (6.72g; 0.0442 mole) in nitromethane (43.2g; 0.706 mole) was prepared by stirring the arylhydrazine in nitromethane overnight under nitrogen. Propionaldehyde (0.070 ml.) was added from a syringe to the p-chlorophenylhydrazine solution (1 ml.) contained in an n.m.r. tube to give a 5% M solution of condensation product. The sample was stored under nitrogen and the 100 MHz n.m.r. spectra were recorded, after 30 mins., 5 hours, 25 hours, 5 days and 11 days. The isomer ratios were determined from the electronic integrals on 250 Hz sweepwidth expansions of the methyl triplets.

The experiment was carried out in the same way with ethyl methyl ketone and 1-phenylpropan-2-one. (see Tables 1 G and H)

^{1}H N.M.R. Spectrum of p-Nitrophenylhydrazine in [$^2H_3$] Acetonitrile.

The [$^2H_3$] acetonitrile was dried by storage for 5 days over molecular sieve (type 4A). A small multiplet (2.1 p.p.m.), due to ^{1}H in the methyl group was present in the 100 MHz n.m.r. spectrum. This multiplet was not observed after addition of p-nitrophenylhydrazine. The N-H absorptions for the p-nitrophenylhydrazine were 6.8 p.p.m. and 3.8 p.p.m. Both were diminished, probably through exchange with the ^{2}H in the methyl group of the acetonitrile. The A_2 B_2 aromatic system was at 6.6 - 8.1 p.p.m.

^{1}H N.M.R. Study of the Condensations of p-Chlorophenylhydrazine and Phenylhydrazine with Carbonyl Compounds in [$^2H_3$] Acetonitrile.

p-Chlorophenylhydrazine (0.177 g.) was dissolved in [$^2H_3$] acetonitrile (1 ml.) in a n.m.r. tube to give a 6.25% M solution. 1-Phenylpropan-2-one (0.134 ml.) was added from a syringe to give a 5% M concentration of condensation product. The sample was stored at room temperature under nitrogen and the 100 MHz n.m.r. spectra were recorded after 30 min., 1 hour, 5 hours, 24 hours, 5 days and 11 days. The isomer ratios were determined from the electronic integrals on 250 Hz sweepwidth expansions of the methylene signals; syn isomer 3.72 p.p.m., anti isomer 3.79 p.p.m.

Studies of the condensation of propionaldehyde and ethyl methyl ketone with p-chlorophenylhydrazine in [$^2H_3$] acetonitrile were carried out in the same way, as were the condensations with phenylhydrazine itself. (see Tables 1 E and F)

Experiments with Acetaldehyde Phenylhydrazone

Preparations of Solid Acetaldehyde Phenylhydrazone.

Method A[28]. —— This method was tried several times and only once, when the phenylhydrazine and the acetaldehyde had not been redistilled, was almost pure anti isomer isolated as described below. On the other occasions a compound of higher molecular weight than acetaldehyde phenylhydrazone was also formed (see later).

Phenylhydrazine (9.8 ml.) was slowly added to acetaldehyde (20 ml.), with cooling in ice, and the mixture was set aside for 15 min. The excess of acetaldehyde was evaporated in vacuo, benzene (80 ml.) was added, and the droplets of water were removed. The solution was dried ($MgSO_4$) and the benzene was removed in vacuo leaving a viscous, orange liquid which crystallised on standing. The crude product was purified by washing with cold absolute ethanol; m.p. 75 - 80°C (lit.[42] 98°C). The 60 MHz n.m.r. spectrum in benzene showed the material to be mainly the anti isomer (c.a. 95%), the chemical shift being in agreement with the literature value.[17]

Method B[42]. —— Acetaldehyde (10g.) was dissolved in a mixture of ethanol (40 ml.) and water (7 ml.). The solution was cooled in ice and phenylhydrazine (20g.) was added in small portions, with shaking. The mixture was allowed to cool between additions. After the additions had been completed the mixture was allowed to stand for 1 hour at 20°C then it was cooled to 0°C and the crystals, which had separated, were filtered off. The product was washed with a little cold aqueous ethanol and dried. Three batches of crystals were collected: (i) 6.17 g. m.p. 95 - 100°C (colourless); (ii) 2.79g. m.p. 95 - 100°C (colourless); (iii) 2.06 g. m.p. 69 - 75°C (yellow).

Batches (i) and (iii) were recrystallised from 70% aqueous

ethanol containing a trace of sodium hydroxide, and dried. Batch (ii) was similarly treated, however as its solubility in this medium did not appear to be high, a trace of hydrochloric acid was added. (Laws and Sidgwick[42] stated that the pure syn isomer could be obtained by recrystallisation of crude acetaldehyde phenylhydrazone from slightly acidic aqueous ethanol and the pure anti isomer by recrystallisation of crude acetaldehyde phenylhydrazone from slightly basic aqueous ethanol.) This resulted in a green solution containing no crystalline material. A trace of hydrochloric acid was added to the mother liquors of the other two batches but no further precipitation occurred.

After recrystallisation batches (i) and (iii) had identical infra-red spectra and both melted over a wide range (60 - 98°C).

The 100 MHz n.m.r. spectrum in benzene showed batch (i), after recrystallisation, to be a mixture of the syn isomer (61%) and the anti isomer (39%).

Preparations of Solid Acetaldehyde Phenylhydrazone at Low Temperature.

Phenylhydrazine (9.86g; 0.091 mole) in ethanol (20 ml.) and acetaldehyde (4g; 0.091 mole) in ethanol (20 ml.) were separately cooled in liquid nitrogen. Both solutions solidified. The acetaldehyde solution was allowed to warm until it was just liquid, then it was poured on to the phenylhydrazine solution which was kept frozen in liquid nitrogen. The mixture was allowed to warm, with shaking, until it formed a homogeneous solution still well below room temperature. It was then placed in ice and allowed to warm up slowly, eventually to room temperature. The product separated as colourless crystals.

The ethanol was removed *in vacuo* (while cold) and the product dried (10.41g., 85%), m.p. 89 - 94°C. The 60 MHz n.m.r. spectrum of the crude product, in benzene, showed it to consist of 93% *anti* isomer and 7% *syn* isomer.

The crude product was purified by crushing it twice in ice-cold ethanol, filtering and drying (6.58g., 56%), m.p. 93 - 97°C. The n.m.r. spectrum showed less than 2% *syn* isomer. Subsequent preparations yielded pure *anti* isomer which was found to equilibrate in the solid on storage under nitrogen at room temperature after c.a. 1 month. The sample remained stable for much longer periods when stored at - 15°C.

The preparation was also tried mixing the acetaldehyde and phenylhydrazine neat (i.e. not dissolved in ethanol), but when the mixture was allowed to warm up while cooled in ice, the reaction became so exothermic, that the temperature reached approximately 40°C. The 60 MHz n.m.r. spectrum of the crude product in benzene showed it to consist of 69% *syn* isomer and 31% *anti* isomer. After purification by crushing in ice-cold ethanol, the composition changed to 40% *syn* isomer and 60% *anti* isomer. This suggested the *syn* isomer was selectively dissolved in the ethanol.

Preparation of Propionaldehyde Phenylhydrazone at Low Temperature.

The experiment was carried out in the same way as that for acetaldehyde phenylhydrazone, the reactants being dissolved in ethanol, but only equilibrated isomer mixtures were obtained. The 60 MHz n.m.r. spectra of the neat products was identical to that of a sample equilibrated by distillation; *syn* methyl, 0.92 p.p.m. (t), *anti* methyl, 0.79 p.p.m. (t). The chemical shifts are in agreement with those reported.[17] The isomer ratio could not be determined with any accuracy because of the overlap of the signals.

Investigation of the Isomerisation of Acetaldehyde Phenylhydrazone on Crystallisation.

Acetaldehyde phenylhydrazone was prepared as in method A (see earlier) but with two modifications: (i) only a slight excess of acetaldehyde (0.0945 mole; 5.34 ml.) was used to prevent formation of the high molecular weight condensation product; (ii) the solid product was not purified by crushing with ice-cold ethanol.

The 60 MHz n.m.r. spectrum of the benzene solution, after water had been removed, showed the initial product mixture to be 65% *syn* isomer and 35% *anti* isomer. After the benzene had been removed *in vacuo* the spectrum of the crude product (10.95g; 86.5%) showed it was composed of 13% *syn* isomer and 87% *anti* isomer. Conversion of *syn* isomer to *anti* isomer must have taken place during crystallisation.

Isolation and Identification of the High Molecular Weight Product from Preparations of Acetaldehyde Phenylhydrazone.

In the various attempts to prepare samples of *anti*-acetaldehyde phenylhydrazone by method A, especially in the experiments in which redistilled acetaldehyde and phenylhydrazine had been used, the same absorptions, which were at first attributed to polymeric impurities, were repeatedly present in the n.m.r. spectra. The redistilled acetaldehyde was shown by n.m.r. spectroscopy to be pure. The yields of acetaldehyde phenylhydrazone obtained from these experiments were always very low ($< 5\%$). The absorptions were therefore attributed to a compound formed during the condensation reaction.

During an attempt to determine the kinetic product in the formation of acetaldehyde phenylhydrazone, a colourless compound

(2.67g.) m.p. 101 - 103°C was isolated as the residual crystalline solid after the products had been washed with ice-cold ethanol. Subsequent experiments produced the same compound in slightly higher yield and purity (m.p. 103 - 105°C).

After further recrystallisation from ethanol the m.p. was 104 - 105°C. The compound gave a positive sodium fusion test for nitrogen; it was not reduced by lithium aluminium hydride in boiling tetrahydrofuran. The ^1H n.m.r. spectrum in carbon tetrachloride and the U.V. spectrum were analogous to those reported in the literature[106] for 3,6,7-trimethyl-2,5-diphenyl-1,2,4,5-tetra-azabicyclo (2,2,1) heptane (21). The following spectroscopic data is consistent with this structure. Mass spectrum - P294, 161. Accurate mass measurement P294.184582 ($C_{18}H_{22}N_4$ requires 294.184438), 161.107549 ($C_{10}H_{13}N_2$ requires 161.107868). δ (60 MHz; C_6H_6) 0.65 (d, 3H), 1.4 (d, 3H), 1.5 (d, 3H), 3.4 (q, 1H), 4.0 (q, 1H), 4.3 p.p.m. (q, 1H). Spin-decoupling (100 MHz, CCl_4) showed that the methyl groups were coupled with the corresponding methines in the order of their chemical shifts i.e. the methyl at highest field was coupled with the methine at highest field etc. $\nu_{max.}$ (nujol) 1590(s), 1490(s), 1300(s), 1110(m), 1080 (m), 840 (m), 790 (m), 750 (s), 690 cm^{-1}.(s).

Attempted Preparation of α -Triethylidene Diphenylhydrazine.[44]

Phenylhydrazine (9.86g; 0.091 mole) was dissolved in a solution of sodium thiosulphate (12.5g.) in distilled water (250 ml.). A solution of acetaldehyde (11.8g; 0.27 mole) in aqueous phosphoric acid (118g: from a solution containing 27.4g. of 90% phosphoric acid per 1.) was added in 5 ml. portions from a burrette; c.a. 10 min. were allowed between the addition of each portion. Each drop, on contact with the phenylhydrazine solution, produced a white precipitate, which, during the addition of the first 5 ml., redissolved on shaking. After the addition of 10 ml. the solution was cloudy and a heavy yellow oil was present. When 25 ml. had been added the product began to separate as a yellow solid. The addition was stopped at this stage and a further quantity of colourless crystalline product separated. The solution was allowed to stand overnight and the remainder of the acetaldehyde solution was then added in 10 ml. portions; c.a. 15 min. were allowed between additions. The solid product was collected and recrystallised from ethanol (5.4g.), m.p. 60 - 80°C. The infra-red spectrum was identical to that of a mixture of isomers of acetaldehyde phenylhydrazone. $\nu_{max.}$ (nujol) 3500(b), 1590(s), 1520(m), 1490(s), 1300(s), 1250(s), 1110(m), 1060(m), 880(m), 740(s), 690(s), 670 cm^{-1}. (m).

The experiment was repeated and the addition of acetaldehyde was stopped after only 7.5ml. had been added. The cloudy mixture was left to stand overnight and a yellow oil separated. The 60 MHz n.m.r. spectrum (C_6H_6) showed this to be a mixture of isomers of acetaldehyde phenylhydrazone: 60% syn isomer, 40% anti isomer.

The Condensation of Acetaldehyde with Acetaldehyde Phenylhydrazone.

anti-Acetaldehyde phenylhydrazone (0.5g.) was added to redistilled acetaldehyde (5 ml.) cooled in ice. The mixture was shaken and then set aside for 10 min. The excess of acetaldehyde was evaporated and the residual orange oil was dissolved in ether and dried ($MgSO_4$). When the ether had been removed the residual oil crystallised, and was recrystallised from ethanol to give colourless crystals (0.15g; 13.4%) m.p. 98 - 101°C. Comparison of infra-red spectra identified the product as (21). The low yield obtained was probably due to difficulties encountered in the recrystallisation (see below).

The experiment was repeated with an isomer mixture of acetaldehyde phenylhydrazone (1g; 60% syn isomer, 40% anti isomer) and redistilled acetaldehyde (10 ml.). A viscous orange oil was again obtained as the crude product. Thin layer chromatography on alumina containing fluorescent indicator (green), with benzene as elutent, showed only one spot when the plate was examined under U.V. light. The product could not be crystallised and was therefore chromatographed on a 10 x 1.5 in. dry alumina column with benzene as elutent. The chromatographed material still refused to crystallise.

Subsequent experiments with the expected product (21) showed that it readily decomposed to acetaldehyde phenylhydrazone when it was heated to 60°C in carbon tetrachloride.

The experiment was repeated with both the isomer mixture of acetaldehyde phenylhydrazone and pure anti isomer. Comparison of the infra-red spectra of the crude products indicated that they both contained a high proportion of acetaldehyde phenylhydrazone. Thin layer chromatography on alumina containing fluorescent indicator (green) with benzene: petroleum-ether (b.p. 60 - 80°C)

(1:1) as elutent showed a single spot, with the same Rf. value as (21), from both experiments. This evidence suggested that only one isomer of (21) was produced in the condensation of acetaldehyde with acetaldehyde phenylhydrazone. Whether or not pure anti acetaldehyde phenylhydrazone gave a greater yield of the product than an isomer mixture could not be determined from the chromatograms.

The 60 MHz n.m.r. spectrum of the crude product from the condensation of acetaldehyde with the isomer mixture of acetaldehyde phenylhydrazone showed absorptions for the product (21) and also for unreacted acetaldehyde phenylhydrazone in which the isomer composition had not changed. There was no evidence for an isomer mixture of products. From the composition of the unreacted isomeric mixture of acetaldehyde phenylhydrazones it was not possible to decide whether both isomers reacted at equal rates with acetaldehyde or whether the isomer mixture equilibrated as the anti isomer was removed by reaction with acetaldehyde.

The experiment was performed using acetone and anti-acetaldehyde phenylhydrazone, but no reaction was observed. Neither would propionaldehyde condense with an isomer mixture of acetaldehyde phenylhydrazone under the conditions described above.

Decomposition of 3,6,7-Trimethyl-2,5-diphenyl-1,2,4,5 -tetra-azabicyclo (2,2,1)heptane (21).

A 5% M solution of (21) in carbon tetrachloride was heated under nitrogen at 60°C for 24 hours and then stored at room temperature for 12 days. The 100 MHz n.m.r. spectrum showed that the compound had decomposed to an equilibrated isomer mixture of acetaldehyde phenylhydrazone (65% syn isomer, 35% anti isomer). A further experiment showed that the compound had started (15%) to decompose to an isomer mixture of acetaldehyde phenylhydrazone after 2 days at room temperature. There was no evidence in these spectra for the production of acetaldehyde during the decomposition.

A sample of (21) was thoroughly dried in vacuo and a solution in carbon tetrachloride prepared for spectroscopy in a dry box, where it was stored for 5 days at room temperature before the 100 MHz n.m.r. spectrum was run. 23% of the compound had decomposed during this period and 65% during 13 days.

For another spectroscopic sample, with which no precautions were taken to exclude moisture, only 19.5% of (21) had decomposed after 5 days and 46% after 13 days. These results suggested that moisture was not important for the decomposition.

Another spectroscopic sample was sparged with oxygen for 2 hours and then stored at room temperature for 2 days, after which period the compound was found to be 34% decomposed. This indicated that oxygen was responsible for the decomposition.

A comparison was made of the infra-red spectra (CCl_4) of solutions of: (i) an equilibrated isomer mixture of acetaldehyde phenylhydrazone, (ii) 3,6,7-trimethyl-2,5-diphenyl-1,2,4,5-tetra-azabicyclo (2,2,1) heptane and (iii) a sample of (21) decomposed by

boiling in carbon tetrachloride for 8 hours. This confirmed that the decomposition products of (21) were an isomer mixture of acetaldehyde phenylhydrazone.

Preparation of 1,4-Diphenyl-1,2,4,5-tetra-azacyclohexane.[43]

Glacial acetic acid (25 ml.) was added to phenylhydrazine (54g; 0.5 mole) maintained at 20°C, and formalin solution (30 ml. of 30% W/V aqueous formaldehyde solution) was quickly mixed in. The reaction mixture solidified and water (50 ml.) was added to facilitate stirring. After the mixture had been stirred for 2 hours the orange crystalline product was collected, washed with water and dried; (36.46g.) m.p. 170-175°C. The crude product was mixed with boiling 4N sodium methoxide (200 ml.) for 1.5 hr. (The solution became deep red in colour as impurities dissolved.) The now colourless solid was collected, washed first with ethanol and then with ether, and was finally recrystallised from chlorobenzene (200 ml.) and aniline (7.5 ml.). The crystals which were collected at this stage smelled of aniline. They were washed with ethanol and dried to give colourless crystals (20.78g., 17.4%) m.p. 210-212°C (lit.[43] 210 - 212°C), $\nu_{max.}$ (nujol) 3120(w), 1600(m), 1580(m), 1500(m), 1260(s), 1320(m), 900(s), 750(s), 690 cm^{-1} (s). The compound was not readily soluble in carbon tetrachloride, chloroform or benzene. An attempt to form a saturated solution in $[^2H_6]$ dimethyl sulphoxide decomposed the dimer to formaldehyde phenylhydrazone (100 MHz n.m.r.).

A saturated solution was prepared in hexamethylphosphoramide. The 100 MHz n.m.r. spectrum had the following absorptions: δ 7.1 (m, 10H), 5.4 (t, 2H), 4.45 p.p.m. (d, 4H). On addition of $[^2H_2]$ water the triplet at 5.4 p.p.m. disappeared and the doublet at 4.45 p.p.m. collapsed to a singlet. Mass spectrum:- P 240.

Accurate mass measurement 240.138194, $C_{14}H_{16}N_4$ requires 240.137490. The spectroscopic data was consistent with the proposed structure (23).

The Condensation of Formaldehyde with Acetaldehyde Phenylhydrazone.

Acetaldehyde phenylhydrazone (1g; 0.0075 mole) was mixed with 40% W/V formalin solution (20 ml. containing 0.265 mole of formaldehyde) and the mixture was heated for a few minutes until the phenylhydrazone had dissolved. The product separated as a light red oil. The excess of formaldehyde was evaporated and, when the mixture had cooled, the product was dissolved in ether and dried ($Mg\ SO_4$). The crude product (m.p. 128-131°C) was yellow. Recrystallisation from ethanol yielded colourless crystals (0.28g.), m.p. 128-133°C. The infra-red spectrum (nujol) of the product showed no N - H absorption. (After further recrystallisation it was evident that a mixture of compounds was present; the solid exhibited two melting points 120°C and 130-136°C.)

No methyl absorptions were observed in the 100 MHz n.m.r. spectrum. The spectrum was interpreted as a mixture of 2,5-diphenyl-1,2,4,5-tetra-azabicyclo (2,2,1) heptane (22) (33%), for which the absorptions agreed with those reported in the literature,[106] and 6,8-diphenyl-1,5,6,8-tetra-aza-3-oxabicyclo (3,2,2) nonane (24)[43,107] (67%) which had the following n.m.r. absorptions; δ (CCl_4) 4.37 (s, 1H), 4.47 (s, 1H), 4.72 (m, 5H), 4.98 (s, 1H), and 6.6-7.3 p.p.m. (m, 10H). The mass spectrum of the product mixture (P282, P262) was in agreement with this interpretation.

The Condensation of Formaldehyde with 1,4-Diphenyl-1,2,4,5-tetra-azacyclohexane.[43] (23)

1,4-Diphenyl-1,2,4,5-tetra-azacyclohexane (3.0g; 0.0125 mole) was mixed with 40% W/V formalin solution (10 ml. containing 0.132 mole of formaldehyde), water (10 ml.), and glacial acetic acid (5 ml.). The mixture was stirred overnight at 20°C and the

cream coloured solid, which had separated, was collected, washed with ethanol and then recrystallised from toluene: ?.5g., m.p. 132-137°C. Spectroscopic analysis (mass spectrum,n.m.r. and infra-red) showed the product to be mainly 6,8-diphenyl-1,5,6,8-tetra-aza-3-oxabicyclo (3,?,?) nonane (24), plus a little 2,5-diphenyl-1,?,4,5-tetra-azabicyclo (?,?,1) heptane (22), similar to the mixture obtained from the condensation of formaldehyde with acetaldehyde phenylhydrazone (see earlier).

Heating the reaction mixture at 100°C for 1 hour, as recommended in the literature, did not produce a crystalline product.

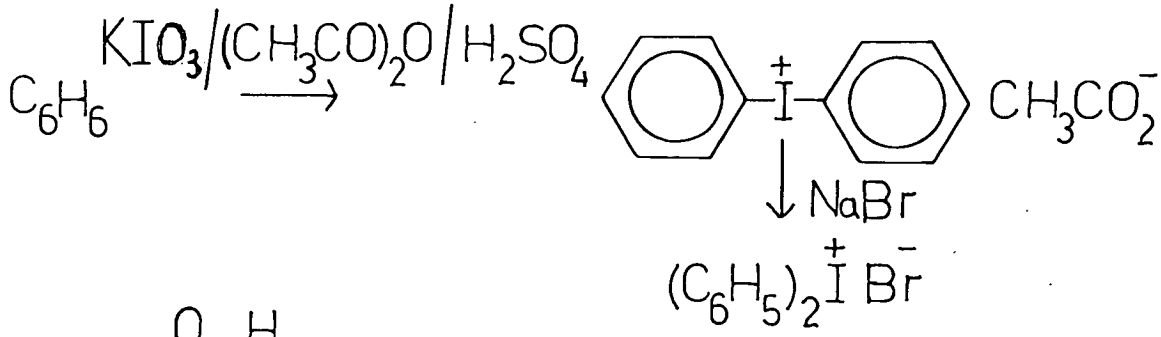
The Condensation of Acetaldehyde with 1,4-Diphenyl-1,?,4,5-tetra-azacyclohexane.(?3)

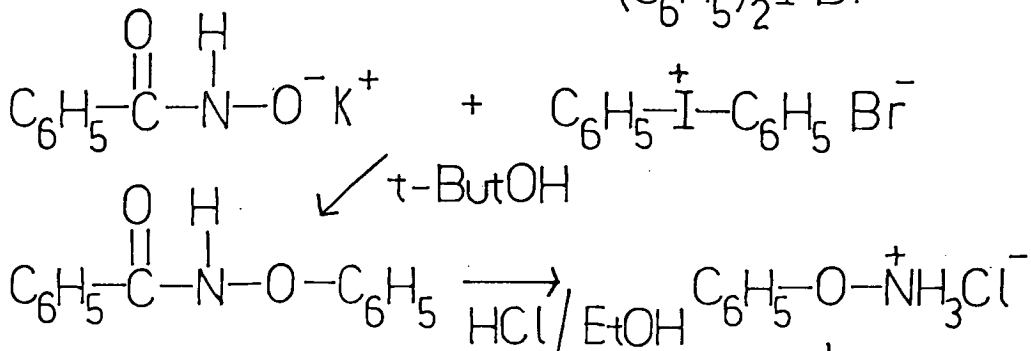
1,4-Diphenyl-1,?,4,5-tetra-azacyclohexane (1.0g; 0.00414 mole) was dissolved in a mixture of redistilled acetaldehyde (20 ml.) and water (10 ml.). The solution was stirred overnight and then the excess of acetaldehyde was evaporated *in vacuo*. The residual solution was extracted with ether and dried ($MgSO_4$). Removal of ether yielded a colourless oil which had the following spectroscopic data: δ (100MHz, CCl_4) 1.32 (d, methyl), 1.45 (d, methyl), 4.15 (d, methylene), 4.4 (d, methylene), 4.76 (d, methylene), 4.98 (d, methylene), 4.65-5 (m, methine), 6.5-7.? p.p.m. (m, aromatic). (The relative values of the integrals are not reported as the oil was found to be a mixture of ? compounds.) Irradiation at 1.32 p.p.m. caused the methine multiplet to collapse to a quartet and a singlet (4.72 p.p.m.); irradiation at 1.45 p.p.m. caused the methine multiplet to collapse to a quartet and a singlet (4.78 p.p.m.); mass spectrum P310, P?60.

The products were a mixture of 7-methyl-?,5-diphenyl-

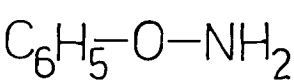
1,2,4,5-tetra-azabicyclo (2,2,1) heptane (29) (c.a. 20%), and 2,4-dimethyl-6,8-diphenyl-1,5,6,8-tetra-aza-3-oxa-bicyclo (3,2,2) nonano (30) (c.a. 80%). The relative amounts were estimated from the electronic integrals on expansions of the n.m.r. absorptions at 250 Hz sweepwidth.

The product mixture could not be effectively separated by chromatography.

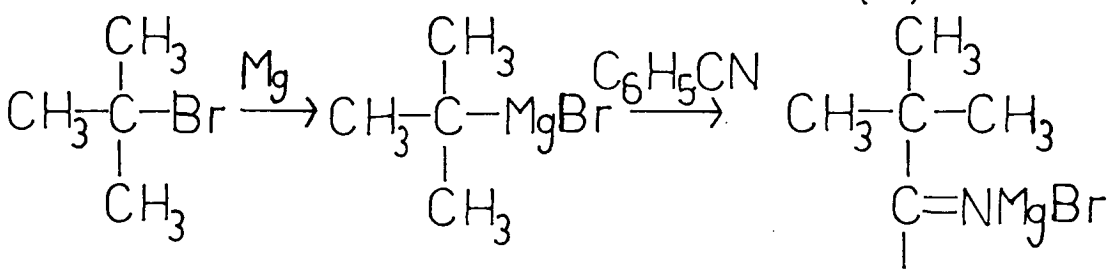




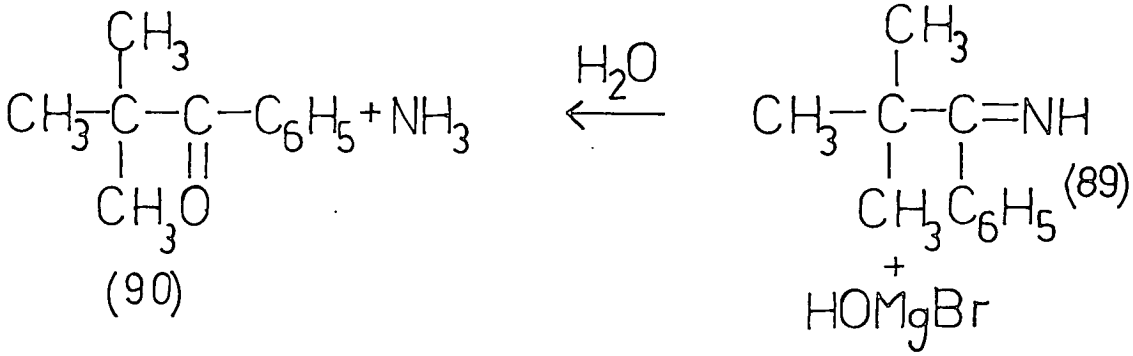
SCHEME 40



(88)



SCHEME 41



Preparation of O-Phenylhydroxylamine Hyrochloride. (Scheme 40)

(i) Preparation of Diphenyl Iodonium Bromide.[108]

A suspension of potassium iodate (200 g; 0.93 mole) in acetic anhydride (200 ml.) and benzene (180 ml. 2.00 mole) was prepared with efficient stirring.

A solution of concentrated sulphuric acid (140 ml., 2.6 mole) in acetic anhydride (200 ml.) was prepared by stirring the acid into the cooled anhydride at such a rate that the temperature of the mixture did not exceed 20°C during the addition.

The cold acetic anhydride/sulphuric acid solution was slowly added to the vigorously stirred benzene/iodate mixture at 0-5°C. (Temperature control at this stage is critical.) The addition took 3 hours. Stirring was continued until the reaction mixture slowly reached 20°C, and then for a further 48 hours.

The reaction mixture was then cooled to 5°C and distilled water (400 ml.) added at such a rate that the temperature did not exceed 10°C. Ether (150 ml.) was added to the mixture which was then stirred for 5 min. and filtered to remove potassium salts. Two further extractions with ether and one with petroleum-ether followed. Sodium bromide (100 g.) in distilled water (300 ml.) was added to the aqueous solution to precipitate the product which was recrystallised from acetic acid, washed with ice cold ethanol, and dried, (131.95 g., 45%) m.p. 232°C (dec.) (lit.[108] m.p. 232°C).

Another method of preparation of diphenyl iodonium bromide[109] was tried but it did not give reasonable yields of pure material.

(ii) Preparation of Phenylbenzhydroxamate.[110]

A mixture of potassium benzhydroxamate (26.1g.), diphenyl iodonium bromide (54.0g.) and t-butyl alcohol (600 ml.) was refluxed

for 4 hours with vigorous stirring, under nitrogen. After filtering off the insoluble material the filtrate was concentrated under reduced pressure, diluted with ether (200 ml.), extracted with 1N sodium hydroxide solution, and then acidified with dilute hydrochloric acid. The crude phenylbenzhydroxamate was collected, and was recrystallised from ethanol, (6.5g., 21%) m.p. 133-136°C (lit.[110] 137.5 - 139°C).

(iii) Cleavage of Phenylbenzhydroxamate to O-Phenylhydroxylamine Hydrochloride.[110]

Phenylbenzhydroxamate (4.09g; 0.0192 mole) and ethanolic hydrochloric acid (45 ml. of 6% W/V) were heated under reflux for 25 min., cooled to 0°C, and then diluted with ether (150 ml.). No product precipitated. Further dilution with ether (1 l) precipitated the crude product which was recrystallised from ethanol/ether (0.59g., 21%), m.p. 136°C (dec.) (lit.[110] m.p. 136°C).

^{1}H N.M.R. Study of the Condensation of Acetaldehyde with O-Phenylhydroxylamine.

Several attempts were made to isolate a sample of the expected condensation product, O-phenyl acetaldehyde oxime (19), without success.

(i) Hydrolysis of O-Phenylhydroxylamine Hydrochloride to the Free Hydroxylamine.

O-Phenylhydroxylamine hydrochloride (200 mg.) was dissolved in 10% aqueous sodium hydroxide solution (2 ml.). The solution was saturated with sodium chloride and then extracted with ether (5X). Evaporation of the dried extracts ($MgSO_4$) yielded a colourless liquid which rapidly became brown. The 60MHz n.m.r. spectrum (CCl_4) was in agreement with the structure of the free hydroxylamine (88):

δ 6.1 (s, 2H), 7.2 p.p.m. (m, 5H).

(ii) Condensation of Acetaldehyde with O-Phenylhydroxylamine.

A fresh sample of the free hydroxylamine was obtained, as described above, in 82.5% yield from its hydrochloride (0.34g.).

A 12.5% M solution of the hydroxylamine (0.0907g.) in dioxan (0.5 ml.) was prepared in an n.m.r. tube, and a 10% M solution of redistilled acetaldehyde in dioxan (0.5 ml.) was added at 0°C. The solutions were thoroughly mixed and the 100MHz n.m.r. spectrum was recorded, with dioxan as the internal reference, after 5 min.:

δ 1.35, (d), methyl; 6.4, (s), excess of N-H; 6.75-7.3 p.p.m., (m), aromatic. There were no absorptions for unreacted acetaldehyde. After 5 hours a weak absorption (t) appeared at 1.9 p.p.m. This signal was much stronger after 3 days storage at 20°C, and it was accompanied by a quartet at 7.8 p.p.m. The intensity of the methyl doublet at 1.35 p.p.m. had greatly diminished after this period.

After 9 days, spin-decoupling showed that the 'triplet' at 1.9 p.p.m. was in fact 2 doublets, one of which was coupled to the quartet at 7.8 p.p.m. (The other doublet was probably coupled to a quartet obscured by the aromatic multiplet.) The spectrum after 9 days suggested the presence of two isomers of O-phenyl acetaldehyde oxime in approximately equal amounts. The original doublet at 1.35 p.p.m. was attributed to 1-hydroxy-1-phenoxyamino-ethane (18), the adduct of the two reactants.

Addition of benzene (0.5 ml.) to the sample separated the two superimposed methyl doublets, and the isomeric composition was determined as 53% *syn* and 47% *anti* from the electronic integrals on a 100Hz sweepwidth expansion.

Preparation of Acetaldehyde Benzylimine.[111]

A solution of benzylamine (20.4g., 0.19 mole) in benzene (25 ml.) was added to a solution of redistilled acetaldehyde (16.8g; 0.38 mole) in benzene (50 ml.). The mixture refluxed for two days while the water from the condensation was removed with a Dean-Stark apparatus. The excess of acetaldehyde and the benzene were evaporated and the residual brown oil was then distilled, to give a colourless liquid (0.53g; 2.1%) b.p. 85°C/10mm.

The 100 MHz n.m.r. spectrum had absorptions for methyl, methylene and phenyl groups, but the integration was not consistent with that expected for the product and spurious absorptions were also observed.

The low yield and purity of the product was attributed to the readiness of benzylimines of low molecular weight aldehydes to polymerize, especially on heating.

Another preparation was attempted without heating but only polymeric material was obtained.

^{1}H N.M.R. Study of the Condensation of Acetaldehyde with Benzylamine.

Equal volumes (0.75 ml.) of a 10% M solution of acetaldehyde in dioxan and a 12.5% M solution of benzylamine in dioxan were mixed in an n.m.r. tube under nitrogen and the 100 M Hz n.m.r. spectra were recorded, with dioxan as internal reference (3.7 p.p.m.), after 30 min., 5 hours and 24 hours: δ (30 min.) 1.40 (d), 2.05 (d), 4.60 (s), 7.35 (m), 7.86 p.p.m. (q). This spectrum was interpreted as an isomer mixture of acetaldehyde benzylimine of composition 83% *syn* and 17% *anti* (from the electronic integrals of the methyl doublets).

After 5 hours the doublets (1.40 and 2.05 p.p.m.) and the quartet (7.86 p.p.m.) had decreased in intensity. Two triplets appeared at 1.25 and 1.43 p.p.m. This trend increased after 24 hours and was interpreted as a double bond shift in the benzylimine to give an isomer mixture of benzaldehyde ethylimine (20, Scheme 7). The isomeric composition could not be determined with any accuracy from the electronic integrals as the signals were broad. The methylene quartets that were expected to accompany the methyl triplets appeared to be obscured by the absorption and spinning side bands of dioxan.

The experiment was repeated with pyridine as solvent. One broad doublet (1.9 p.p.m., 3H) and one broad singlet (4.6 p.p.m.) were initially observed. Expansion at 250Hz sweepwidth and spin-decoupling showed that each line of the methyl doublet at 1.9 p.p.m. was split into a triplet by long range coupling (J = 1 Hz) to the broad methylene singlet. If two isomers were present their absorptions were co-incident.

The spectrum did not change after 24 hours. No evidence of a double bond shift to form benzaldehyde ethylimine was observed with pyridine as solvent.

^{1}H N.M.R. Study of the Isomerisation of anti-Acetaldehyde Phenylhydrazone.

A 5% solution of pure anti-acetaldehyde phenylhydrazone (0.125g; 0.000931 mole) in dry nitromethane (1 ml; 0.01862 mole) was prepared in an n.m.r. tube which was then placed in the n.m.r. probe at 28°C. The 100 M Hz n.m.r. spectrum was recorded. Integrals were recorded on the 100 Hz sweepwidth expansions of the methyl doublets of the two isomers at regular intervals during a period of 105 min. The sample was stored in the dark at 28°C for 67 hours and integrals were again recorded on the expansions of the methyl doublets to obtain the equilibrated isomer ratio.

Since the two methyl doublets partially overlapped, only the highfield and lowfield lines for the anti and syn isomers respectively were used to determine the isomeric compositions. A correction to the ratios, each determined as an average of 5 electronic integrals, was made to compensate for the asymmetry between the highfield and lowfield lines of the doublets caused by coupling to the methine protons. (J = 5.4 Hz, $\nu_0\delta$ = 472 Hz, $J/\nu_0\delta$ = 0.01123). The intensities of the relevant transitions in the AB_3 system were calculated[112] and it was determined that the intensity of the lowfield line of the methyl doublet of the syn isomer should be multiplied by 0.95 to correct for the asymmetry. (The factor of 0.95 which was calculated for this particular AB_3 system was in agreement with similar values reported in the literature[113].)

Run 1.—— The results (see Table 2) were plotted according to the equation $\ln (Xe - X) = -t(k_1 + k_{-1}) + \ln Xe$ (see Discussion, page 28) (Xe and X were the mole fractions of the syn isomer at equilibrium and the time t respectively; k_1 and k_{-1} were the forward and backward rate constants respectively for $\bar{Y} \rightleftharpoons X$ where $\bar{Y}$ represented the anti

isomer.) i.e. ln (Xe - X) was plotted against t (min.) so that the gradient was $(k_1 + k_{-1})$ and the intercept was ln Xe.

from the graph: $(k_1 + k_{-1}) = 0.0181 \text{ min.}^{-1}$

K eq. $= k_1/k_{-1} = Xe/Ye = 0.63/0.37 = 1.70$

$$1.70\ k_{-1} + k_{-1} = 0.0181 \text{ min.}^{-1}$$

$$k_{-1} = 0.0067 \text{ min.}^{-1}$$

$$k_1 = 0.0114 \text{ min.}^{-1}$$

Using the experimental value of 0.63 for Xe, values for the best slope $(k_1 + k_{-1})$, the best intercept (lnXe), and the errors in those, were calculated on a 'Wang' electronic calculator fitted with a 'least squares' analysis programme with the first 5 and 7 values of X and t in chronological order (see Table 3. N, the number of points used, = 5 and 7 respectively.) With an increase in the number of values of X and t used, X approached Xe and the error in ln(Xe - X) became greater. Also the condition that $(k_1 + k_{-1})X < k_1$, used in deriving the equation $\ln(Xe - X) = -t(k_1 + k_{-1}) + \ln Xe$, was not fulfilled. (see Discussion, page 28). Only the first 5 values of X determined (up to t = 75 min.) were used in later calculations.

With N = 5, and varying Xe stepwise by units of + or - 0.005 from the experimental value of 0.63, a 'Wang' calculator was used to determine which values of Xe gave the smallest error in slope and intercept (see Table 4). Xe = 0. 625 gave the minimum errors in slope and intercept. The gradient was 0.01854 and Keq. was 1.668 (k_{-1} = 0.00 695, k_1 = 0.01159) with Xe as 0.625.

Run 2.—— The above experiment was repeated. Measurements were made over a period of 1415 min. and the value of Xe was found to be 0.58 after 6 days. (see Table 2 for results.) From the graph (gradient = 0.0052 min.^{-1}) the values of $k_{-1} = 0.00219 \text{ min.}^{-1}$ and $k_1 = 0.00302 \text{ min.}^{-1}$

were obtained.

The results of this run were also calculated, from graphs, using 5% deviations in the value experimentally determined for Xe (0.58): Xe + 5% = 0.63, k_{-1} = 0.00163 min.$^{-1}$, k_1 = 0.00278 min.$^{-1}$; Xe - 5% = 0.53, k_{-1} = 0.00258 min.$^{-1}$, k_1 = 0.00315 min.$^{-1}$.

Using the 'Wang' calculator the results for Run 2 were treated by the process outlined above for Run 1. It was found that the first 9 values of X and t, with Xe = 0.615 (experimental Xe = 0.58) gave the minimum errors in slope and intercept (see Table 4). Although the rate ($k_1 + k_{-1}$ = 0.00465) was much slower than that determined for Run 1, the equilibrium constants (K eq. = 1.598 for Run 2) were in agreement to within 5%.

N.M.R. Study of the Condensation of Acetaldehyde with Phenylhydrazine in Various Solvents at Low Temperature.

(i) In Methanol.—— Redistilled acetaldehyde (0.070 ml.) was added, from a syringe, to a 6.25% M solution of phenylhydrazine (0.168g.) in methanol (1 ml.), at -78°C, contained in an n.m.r. tube. (This gave a 5% M solution of acetaldehyde.) The contents of the tube were mixed under nitrogen while cold, and then the 100 MHz n.m.r. spectra were recorded at intervals of 10 or 20 min. with the methyl singlet of the methanol (3.34 p.p.m.) as the internal reference, while the temperature of the probe was increased from -80°C to 26°C. (The temperature was calibrated from the chemical shift difference between the hydroxyl and methyl absorptions of methanol.)

The methyl doublets for the product isomers (1.87 and 1.82 p.p.m.) increased in intensity at the expense of the methyl doublet (1.2 p.p.m.) of unreacted acetaldehyde. Because of the overlap of the doublets of the product isomers, especially where the absorptions were broadened at lower temperatures, it was not possible to determine the isomeric compositions.

(ii) In 1,2-Dimethoxyethane. — The experiment was carried out in the same way as described above for methanol as solvent but the temperature ranged from -40°C to + 10°C, with 10°C increases in temperature at 5 min. intervals.

A 250 Hz sweepwidth expansion of the methyl doublets of the isomeric products (c.a. 1.8 p.p.m.) and the unreacted acetaldehyde (1.16 p.p.m.) was recorded at each temperature (see Table 5A).

It was difficult to calculate the isomer ratio of the products accurately at temperatures less than +10°C because the broadening of the methyl singlet of the solvent, at low temperatures, interfered with the methyl doublets of the product. The anti isomer,

however, did not appear to be the kinetic product. The methyl absorptions of the product were a pair of doublets at all times but the rate of equilibration may have been faster than the rate of product formation.

(iii) In Nitromethane.—— At low temperatures the solution was viscous. The n.m.r. spectrum was recorded at -20°C. It was found that the condensation had gone to completion (no unreacted acetaldehyde was observed) and the isomeric composition of the product was approximately 60% syn and 40% anti.

(iv) In 2-Methoxyethanol.——Equal volumes (0.5 ml.) of a 10% M solution of redistilled acetaldehyde in 2-methoxyethanol and a 12.5% M solution of redistilled phenylhydrazine in 2-methoxyethanol were mixed in an n.m.r. tube, under nitrogen, at -78°C. 100 Hz sweepwidth expansions of the methyl doublets of the unreacted acetaldehyde and the product isomers were recorded and integrated at intervals while the temperature was increased from -70°C to +20°C. The product doublets were too broad at temperatures $< -20°C$ for an accurate analysis of the isomeric composition (see Table 5B). Corrections were made in the isomeric composition for asymmetry in the product doublets due to coupling with the methine protons (see page 118, para. 2).

The results showed that the isomeric composition was approximately constant (average: 69% syn, 31% anti) throughout the condensation. A greater percentage of anti isomer than syn isomer was not initially formed.

N.M.R. Study of the Isomerisation of anti-Acetaldehyde Phenylhydrazone Catalysed by Phenylhydrazine in Nitromethane.

Redistilled phenylhydrazine (0.025g; 0.000232 mole) was weighed into an n.m.r. tube. A 5% M solution of anti-acetaldehyde phenylhydrazone (0.125g; 0.00093 mole) in dry nitromethane (1 ml; 0.0186 mole) was measured into the tube (the solution was then 1.25% M in phenylhydrazine) and the 100 MHz n.m.r. spectrum was immediately recorded.

The methyl doublets of the isomers of acetaldehyde phenylhydrazone in the initial spectrum showed that more anti isomer than syn isomer was present (c.a. 70% anti isomer). By the time (< 5 min.) that a 100 Hz sweepwidth expansion of the doublets was scanned and integrated the phenylhydrazone had almost equilibrated (58% syn, 42% anti). Integrals were taken at 1 min. intervals during the next 11 min. but the isomeric composition did not change appreciably over that period. After a further 20 min. it was found to be 60% syn and 40% anti.

A 60 MHz spectrum (CH_3NO_2) of a sample from the same batch of anti isomer as that used in the experiment described above showed the fresh solution to be almost pure anti isomer, which equilibrated on standing overnight.

The experiment was repeated with the spectrometer set to record integrals of the 100 Hz sweepwidth expansions of the methyl doublets. The first integral was taken 2 min. after the anti-acetaldehyde phenylhydrazone solution had been added to the phenylhydrazine in the n.m.r. tube. Because of bubbles in the solution the first integrals were not accurate, but it was evident that more syn isomer than anti isomer was present after 2 min. After 11 min. the

isomeric composition was 57% *syn*, 43% *anti*.

The isomerisation of acetaldehyde phenylhydrazone in nitromethane was much faster when phenylhydrazine was present than when it was absent (see page 118, para. 3 for comparison with isomerisation in nitromethane alone.)

N.M.R. Spectra of Acetaldehyde o-Methylphenylhydrazone in Dioxan.

The o-methylphenylhydrazine used (m.p. 59-60°C, lit.[101] m.p. 59-60°C) was prepared in the same way as p-methylphenylhydrazine (page 87 , para. 1, 2) using o-toludine.

Ice-cold acetaldehyde (0.018 g; 0.0041 mole) was added to a 5% M solution of o-methylphenylhydrazine (0.5g; 0.0041 mole) in dioxan (7 ml; 0.082 mole) contained in a 10ml flask at 0°C. After thorough mixing under nitrogen the solution was set aside for 20 min. at 20°C before the 60 MHz n.m.r. spectrum was recorded: 2 methyl doublets (one for each isomer of acetaldehyde o-methylphenylhydrazone, 3H) overlapping on adjacent lines at 1.85; 2 singlets (the o-methyl groups of the two isomers, 3H) at 2.1 (syn.), and 2.15 (anti); multiplet 6.4 - 7.5 (aromatic and -CH = N, 6H); broad singlet at 7.65 p.p.m. (NH, 1H).

After evaporating the dioxan and dissolving the solid product in benzene, the 60 MHz n.m.r. spectrum showed 2 methyl doublets (anti 1.16 p.p.m., 37%; syn 1.65 p.p.m., 63%) and only one absorption for the co-incident o-methyl groups (1.84 p.p.m.).

Exchange of Phenylhydrazine with the o-Methylphenylhydrazine in Acetaldehyde o-Methylphenylhydrazone.

One drop of phenylhydrazine was added to the n.m.r. sample of acetaldehyde o-methylphenylhydrazine in benzene described above.

The 100 MHz n.m.r. spectrum showed clearly 2 doublets for anti isomers which overlapped on adjacent signals (1.16 p.p.m.) and two doublets, clearly separated, for syn isomers (1.65 and 1.63 p.p.m.) There were 2 distinct o-methyl singlets (free o-methyl, 41.5%, 1.74 p.p.m. (identified by further addition of o-methylphenylhydrazine); o-methyl of the phenylhydrazone, 58.5%, 1.84 p.p.m.) The combined isomeric composition of the substituted and unsubstituted phenylhydrazones was 65% syn and 35% anti. The added phenylhydrazine had displaced some of the substituted phenylhydrazine from the phenylhydrazone.

^{1}H N.M.R. Study of the Condensation of Excess Acetaldehyde with Small Amounts of Phenylhydrazine.

The 100 MHz n.m.r. spectrum of redistilled acetaldehyde (0.052 ml; 0.00093 mole) in nitromethane (0.5 ml.) was recorded. The solution was cooled to -78°C and an aliquot (0.1 ml.) from a cold (just liquid) 5% M solution of phenylhydrazine (0.105g; 0.00093 mole) in nitromethane (1 ml.) was added to the n.m.r. tube. After mixing, the contents of the tube were allowed to warm up until just liquid and then they were mixed by sparging with nitrogen. The 100 MHz n.m.r. spectrum was recorded at -40°C and integrals taken on the 250Hz sweepwidth expansions of the methyl doublts of the isomeric phenylhydrazones and on the methyl doublet of the unreacted aldehyde. The process was repeated for a further 4 additions of cold phenylhydrazine solution. (Throughout the experiment the sample in the n.m.r. tube was kept at, or below, -40°C. Because the doublets of the two isomers overlapped on adjacent lines, the isomer ratios were corrected to allow for asymmetry due to coupling (see page 118, para. 2). After the fifth addition of phenylhydrazine solution, the sample was kept at -40°C for 30 min. and the integrals were recorded again. A further integral was obtained after the sample had been kept at 25°C for 1 hour. (see Table 6)

The results showed that, when no excess of base was present to catalyse isomerisation, more anti isomer than syn isomer was initially formed at -40°C.

The experiment was repeated with dry methanol as solvent. Satisfactory integrals were not obtained on the methyl doublets of the isomeric phenylhydrazones because of the broad spread of the methyl singlet of the methanol at - 40°C. At all times, however,

the syn isomer appeared to be present in greater abundance than the anti isomer. A doublet, which was attributed to the carbinolamine intermediate (1.24 p.p.m.), built up rapidly as a shoulder on the free acetaldehyde doublet, on addition of the first 0.3 ml. of phenylhydrazine solution, decreased while the sample was left for 30 min. at -40°C, and then increased in intensity again when more phenylhydrazine solution was added. (The experiment in methanol was also run on the 60 MHz n.m.r. instrument at 33°C, with similar results, except that no signals from the carbinolamine intermediate were observed.)

Methanol is possibly a strong enough base to catalyse the isomerisation of acetaldehyde phenylhydrazone.

N.M.R. Study of the Condensation of Excess Phenylhydrazine with Small Amounts of Acetaldehyde.

The experiment was carried out as described above for the study of the condensation of excess acetaldehyde with small amounts of phenylhydrazine, except, of course, that the roles and the concentrations of the phenylhydrazine and acetaldehyde solutions in nitromethane were reversed. The 10% M solution of phenylhydrazine in nitromethane was too viscous to give an n.m.r. spectrum at -40°C. The experiment had to be carried out at +10°C. (see Table 7)

There was never more anti isomer than syn isomer present. The isomeric composition was always close to that of an equilibrated isomer mixture (62% syn, 38% anti). This result was in agreement with previous results (page 124, para. 2) which suggested phenylhydrazine was a catalyst in the isomerisation of acetaldehyde phenylhydrazone.

60 MHz N.M.R. Spectrum of Phenylacetaldehyde Phenylhydrazone.

(only the methylene protons are described)

Phenylacetaldehyde phenylhydrazone (m.p. 54 - 60°C, lit.[114] m.p. 62 - 63°C) was prepared by the method of Fischer[114], using redistilled phenylacetaldehyde.

The 60 MHz n.m.r. spectrum (CCl_4) showed the presence of two isomers with methylene doublets at 3.3 (anti 22%) and 3.5 p.p.m. (syn 78%). In both nitromethane and [$^2H_3$] acetonitrile only one methylene doublet (3.7 and 3.6 p.p.m. respectively) was observed i.e. the methylene absorptions of both isomers were co-incident in these solvents.

The n.m.r. spectrum of a sample that had been allowed to equilibrate for 5 days at 20°C in benzene showed the presence of 2 isomers with methylene doublets at 3.50 (syn 82%) and 2.95 p.p.m. (anti 18%). On addition of a few drops of phenylacetaldehyde the methylene doublet of the free phenylacetaldehyde (3.05 p.p.m.) partly obscured the methylene doublet of the anti isomer of the phenylhydrazone.

Investigation of the Carbinolamine Intermediate in Phenylhydrazone Formation.[8]

Equal volumes (0.75 ml.) of a 10% M solution of methyl benzyl ketone in dioxan and a 12.5% M solution of redistilled phenylhydrazine in dioxan were mixed at 0°C in an n.m.r. tube, under nitrogen. The 100 MHz n.m.r. spectrum, recorded after c.a. 10 min., showed only three singlets in the methyl region (0.5 - 2.5 p.p.m.): 1.70 p.p.m. and 1.89 p.p.m., isomeric products; 1.99 p.p.m., unreacted ketone. After 2.5 hours no ketone remained.

The experiment was repeated but 3 volumes of ketone solution were mixed with 2 volumes of phenylhydrazine solution so that the molar ratio of ketone to phenylhydrazine was 6 : 5. No methyl absorptions other than those for the unreacted ketone and isomeric phenylhydrazones were observed. Addition of a small quantity of methyl benzyl ketone after 24 hours confirmed that the signal at 1.99 p.p.m. had been correctly assigned to the unreacted ketone.

In another experiment 5 volumes of ketone solution were mixed with 2 volumes of phenylhydrazine solution but again no methyl absorption that could be attributed to a carbinolamine intermediate was observed.

The Alkyl Phenyl Ketone Phenylhydrazone Series.

Preparation of t-Butyl Phenyl Ketone.[115] (analogous to Scheme 41)

Magnesium turnings (6.9 g; 0.282 mole) were placed in a 250 ml. flask which was equipped with a mechanical stirrer, a reflux condenser, a pressure equilibrated dropping funnel and a nitrogen inlet and outlet. After the system had been flushed with dry nitrogen, a solution of t-butyl chloride (c.a. 0.8 g.) in dry ether (40 ml.) was added. Initiation of the reaction was facilitated by addition of a crystal of iodine.

The remainder of the t-butyl chloride (0.25 mole; 23.2 g. in all) in dry ether (80 ml.) was added very slowly, with stirring, so that the reaction mixture was just boiling. After the addition of the t-butyl chloride solution had been completed, the reaction mixture was refluxed for a further 2 hours.

A solution of benzonitrile (16.6 g; 0.162 mole) in dry ether (30 ml.) was added to the t-butyl magnesium chloride solution (0.2 mole based on an assumed 80% yield from the Grignard preparation) with stirring, over a 1 hour period. The solution, which had become light brown in colour, was refluxed overnight, and then poured into a mixture of 6N sulphuric acid (66 ml.) and ice. This mixture was heated for c.a. 2 hours to distill off the ether and hydrolyse the ketimine (89).

After the mixture had cooled it was extracted with ether (4 x 100 ml.). The combined extracts were washed with saturated sodium bicarbonate solution and dried ($MgSO_4$). The ether was evaporated and the residual oil fractionally distilled: (i) b.p. 80 - 90°C/9 mm. (ii) b.p. 90 - 98°C/9 mm. (iii) b.p. 98 - 106°C/9 mm. The infra-red spectra showed that all three fractions were a mixture of benzonitrile ($\nu_{max.}$ C ≡ N 2200 $cm.^{-1}$) and t-butyl phenyl

ketone (90) ($\nu_{max.}$ C = O 1670 cm.$^{-1}$).

The preparation was repeated with a 3-fold molar excess of Grignard reagent over benzonitrile, but again the ketone, which had been distilled through a small Vigreux column, was contaminated with benzonitrile. G.c. analysis (Apiezon L; Perkin Elmer F11 gas chromatograph; flame ionisation detector) showed that the ratio of benzonitrile to ketone was 5 : 2.

Preparation of Phenyl i-Propyl Ketone.[115]

Phenyl i-propyl ketone was prepared in 72% yield (b.p. 100°C/9 mm., lit.[101] b.p. 95 - 98°C/10 mm.) by the method described above for t-butyl phenyl ketone, using 2-bromopropane instead of t-butyl chloride. It had $\nu_{max.}$ (film) 3050(m), 2950(s), 1690(s), 1610(s), 1590(s), 1470(s), 1390(s), 1290(m), 1230(s), 1165(s), 1100(m), 990(s), 940(w), 880(w), 800(s), 700c m.$^{-1}$(s).

Preparation and N.M.R. Spectra of Phenyl Ketone Phenylhydrazones.

(i) Phenyl i-Propyl Ketone Phenylhydrazone.—— Phenyl i-propyl ketone (1.0 g; 0.00676 mole) was dissolved in ethanol (25 ml.), phenylhydrazine (0.73 g; 0.00676 mole) was added, and the solution was refluxed overnight, under nitrogen. The ethanol was evaporated and the residual oil fractionally distilled. The final fraction (1.19 g; 75%, b.p. 120-130°C/0.01mm.) was a mixture of the two isomers of the phenylhydrazone; δ (CCl_4, 100 MHz) 1.13 (d, Me_2 CH), 1.30 (d, Me_2 CH), 2.77 (septet Me_2 CH), 3.14 (septet, Me_2 CH), 6.5 - 7.5 p.p.m. (m, aromatic and N-H).

(ii) Ethyl Phenyl Ketone Phenylhydrazone.—— Ethyl phenyl ketone phenylhydrazone (b.p. 140 - 144°C/0.02mm.) was prepared, by the method described above for phenyl i-propyl ketone phenylhydrazone, in 67% yield; δ (C_6H_6, 100 MHz) 0.84 (t, Me CH_2), 1.18 (t, Me CH_2), 2.19

(q, Me $\underline{CH}_2$) 2.56 p.p.m. (q, Me $\underline{CH}_2$). The aromatic and N-H absorptions were obscured by the solvent. (In CCl_4 the methyl triplets and methylene quartets of both isomers were co-incident.)

Ethyl phenyl ketone phenylhydrazone was also prepared in 56% yield by an adaptation of the method described below for methyl phenyl ketone phenylhydrazone (iv). The crude product was extracted with ether, washed with aqueous sodium bicarbonate and brine solutions, and then dried ($Mg\ SO_4$) before distillation.

(iii) t-Butyl Phenyl Ketone Phenylhydrazone. — The mixture of t-butyl phenyl ketone and benzonitrile obtained from the preparation of the ketone (see page 132, para. 4) (3.5 g. containing 1 g; 0.0062 mole of ketone) was dissolved in pyridine (25 ml.) and phenylhydrazine (0.67 g; 0.0062 mole) was added. The solution was refluxed under nitrogen for 5 days. The pyridine was evaporated and the benzonitrile (b.p. 188 - 192°C) distilled off at reduced pressure (c.a. 10 mm.). The residual oil was fractionally distilled under high vacuum. The final fraction (0.88 g; 56%; b.p. 122°C/0.01 mm.) crystallised on cooling (m.p. 75 - 78°C, lit.[116] 92°C); δ (CCl_4, 100 MHz) 1.2 (s, 9H, t-butyl), 6.6 - 7.5 p.p.m. (m), 6H, aromatic and N-H).

(iv) Methyl Phenyl Ketone Phenylhydrazone. — Methyl phenyl ketone phenylhydrazone (m.p. 104 - 105°C, lit.105°C) was prepared by a method described in the literature.[117] The 100 MHz n.m.r. spectrum in CCl_4 showed the presence of two isomers: δ 2.13 (s, Me), 2.22 (s, Me), 6.6 - 7.8 p.p.m. (m, aromatic and N-H).

The isomeric compositions of the equilibrated mixtures of the alkyl phenyl ketone phenylhydrazones are listed in Table 9.

Preparation of Di-Alkyl Ketone Phenylhydrazones.

(i) Acetone Phenylhydrazone.—— Phenylhydrazine (6 ml.) was thoroughly mixed with acetone (40 ml.), and the solution was left for 5 min. before the excess of acetone was evaporated. The residual oil was fractionally distilled under nitrogen. Pure acetone phenylhydrazone (7.9 g.) (b.p. 94°C/0.3 mm; lit.[101] b.p. 140°C/16 mm.) was collected.

(ii) Butan-2-one Phenylhydrazone.——Butan-2-one phenylhydrazone (b.p. 100°C/1 mm; lit.[101] b.p. 190°C/100 mm.) was prepared by the method described above for acetone phenylhydrazone.

Preparation of Methyl Phenyl Ketone Benzylimine.[111]——

Methyl phenyl ketone benzylimine was prepared by the same method as acetaldehyde benzylimine (see page 116). The product was obtained in 45.5% yield as colourless crystals (m.p. 40 - 43°C, lit.[118] m.p. 40 - 43°C) after recrystallisation from ethanol. The 100 MHz n.m.r. spectrum showed the presence of 2 isomers: δ (CCl_4) 2.18 (s, Me), 2.42 (s,,Me), 4.30 (s, CH_2), 4.60 (s, CH_2), 6.8 - 7.9 p.p.m. (m, aromatic). The isomeric composition of the fresh solution was 98% syn isomer and 2% anti isomer. This changed to 85% syn isomer and 15% anti isomer after 6 days at 20°C. A 250 Hz sweepwidth expansion showed that the methyl singlets of each isomer were coupled to the corresponding methylene singlets by long range coupling (J = 0.8 Hz).

Preparation of Acetaldehyde N-Methyl Phenylhydrazone.——

1-Methyl-1-phenylhydrazine (2 ml.) was slowly added to acetaldehyde (10 ml.) at 0°C. The reaction mixture was left at 20°C for c.a. 15 min. before the excess of acetaldehyde was removed in vacuo. Benzene (c.a. 50 ml.) was added and the solution was decanted from the water which had formed during the condensation. The benzene

was removed *in vacuo* and the residual yellow oil was then distilled (1.86 g; 79%), b.p. 135°C/20 mm., *lit.*[119] b.p. 136°C/25 mm., δ (60 MHz, CCl_4) 1.95 (d, 3H), 3.05 (s, 3H), 6.64 (q, 1H), 6.8 - 7.2 p.p.m. (m, 5H). Only one isomer was apparent.

^{1}H N.M.R. Study of the Condensations of Alkyl Phenyl Ketones with Phenylhydrazine in Pyridine.

The experiments were carried out in the same way as those performed to study the formation of substituted and unsubstituted phenylhydrazones in pyridine (see page 86).

Neither phenyl i-propyl ketone nor t-butyl phenyl ketone formed phenylhydrazones during 24 hours in solution at 20°C. A 10% M solution of phenyl i-propyl ketone in pyridine (5 ml.) and a 12.5% M solution of redistilled phenylhydrazine in pyridine (5 ml.) were mixed and then refluxed overnight, under nitrogen, to give an equilibrated isomer mixture of the phenylhydrazones. The same procedure was used for t-butyl phenyl ketone.

Unreacted ketone was present in each sample of the alkyl phenyl ketone phenylhydrazones examined, (see Table 8) even though a 5 : 4 molar excess of phenylhydrazine over ketone was used.

Determination of the Isomeric Compositions of Equilibrated Solutions of Alkyl Phenyl Ketone Phenylhydrazones.

The phenylhydrazones were prepared as described earlier (see pages 133, 134) and equilibrated by distillation. The 100 Mhz n.m.r. spectra were recorded on 5 - 10% M solutions in CCl_4 under nitrogen and the isomer ratios were determined from integrals on 100 Hz sweep-width expansions of the appropriate absorptions (see Table 9). As the methyl and methylene absorptions of both isomers of ethyl phenyl ketone phenylhydrazone were co-incident in carbon tetrachloride, the spectrum was recorded with benzene as solvent.

After 7 days under nitrogen at 20°C the isomer ratios were constant, but t-butyl phenyl ketone phenylhydrazone was found to have partially decomposed to the ketone (7.5%).

Experiments with Europium 'Shift Reagents'.[46,120]

Early experiments, in which no precautions were taken to dry the reagents and to exclude moisture from the solutions at all times during the experiment, gave changes in chemical shifts that were neither substantial nor reproducable. (Eu $(dpm)_3$, tris (dipivalomethanato) europium (III)[46], was the 'shift reagent' employed in these earlier experiments.) In subsequent experiments Eu $(fod)_3$ (tris (1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octane-dionato) europium III)[46] (34) was employed as the 'shift reagent'.

The Eu $(fod)_3$ was dried (P_2O_5, 0.1 mm., 20°C) for 4 days. A 0.0508 M solution of Eu $(fod)_3$ (0.294 g.) in dry carbon tetrachloride (5 ml.), containing 3% V/V of tetramethylsilane, was prepared in a dry-box (P_2O_5 desiccant). A second Eu $(fod)_3$ solution (0.0530 M) which did not contain tetramethylsilane, was also prepared. Both solutions were stored over molecular sieve (type 4A) in the dry-box.

The induced chemical shifts* were generally measured as follows: each substrate was either distilled or recrystallised and thoroughly dried in vacuo. 0.1 M Solutions of the substrate in one of the Eu $(fod)_3$ solutions described above (0.5 ml.), and also in dry carbon tetrachloride (0.5 ml.) containing 3% V/V tetramethylsilane, were prepared in the dry-box where the solutions were then left for c.a. 30 min. The frequencies of the absorptions were measured from 100 or 250 Hz sweepwidth expansions using a Varian V-4315 frequency counter in conjunction with the 100 MHz n.m.r. spectrometer. *(The term 'induced chemical shift' is used here to refer to the difference between the chemical shift observed for an absorption in the presence of 'shift reagent' and the chemical shift when no 'shift reagent' was present.)

(i) Methyl Phenyl Ketone Phenylhydrazone.—— In the solution without Eu $(fod)_3$, the methyl singlets of the syn and anti isomers were 217.9 and 226.0 Hz respectively downfield from tetramethylsilane. In the 0.0508 M Eu $(fod)_3$ solution only the methyl singlet of the syn isomer, 225.6 Hz downfield from tetramethylsilane, was observed. (The methyl singlet of the anti isomer (3.5%) was probably broadened so much when complexed with the $Eu(fod)_3$ that it was not apparent.) The induced shift for the methyl singlet of the syn isomer was 7.7 Hz.

(ii) Methyl Phenyl Ketone Benzylimine.—— When the experiment was carried out, using the 0.0508 M solution of $Eu(fod)_3$, by the procedure described above, it was difficult to assign the absorptions because the resolution was poor.

A 0.1 M solution of methyl phenyl ketone benzylimine (0.0104 g.) in dry carbon tetrachloride (0.5 ml.) was made up in the dry-box and the 100 MHz n.m.r. spectrum was recorded using an external tetramethylsilane lock. The methyl singlet (2.70 p.p.m.) and the methylene singlet (5.09 p.p.m.) of only one isomer were observed. Two successive dilutions with 0.05 ml. of 0.0530 M $Eu(fod)_3$ solution in carbon tetrachloride (no tetramethylsilane) shifted the methyl and methylene absorptions to 2.90 and 5.19 p.p.m. respectively, and then to 3.09 and 5.35 p.p.m. respectively. After addition of a further 0.1 ml. of $Eu(fod)_3$ solution the resolution was so poor that only the broad methylene singlet was observed at c.a. 5.8 p.p.m., and then at c.a. 6.2 p.p.m. after a total of 0.3 ml. of $Eu(fod)_3$ solution had been added. The methyl absorption was shifted much further downfield (0.39 p.p.m.) by the two 0.05 ml. dilutions with $Eu(fod)_3$ solution than the methylene absorption (0.26 p.p.m.),

suggesting that the methyl group was nearer the sight of complexing with the europium atom[46] than the methylene group. The methyl absorption of methyl phenyl ketone benzylimine had a greater induced chemical shift in a much weaker $Eu(fod)_3$ solution than that of the corresponding phenylhydrazone (see (i)).

(iii) Ethyl Phenyl Ketone Phenylhydrazone. —— The experiment was carried out by the general procedure described above, with tetramethylsilane as internal reference.

In the solution without $Eu(fod)_3$, the methyl triplets of the two isomers were co-incident (123.5 Hz). Two methylene quartets at 263.8 Hz (stronger) and 252.6 Hz (weaker) were present. In the 0.0508 M $Eu(fod)_3$ solution the methyl triplets remained co-incident (129.0 Hz) and only one methylene quartet (272.8 Hz) was observed. This spectrum did not change after 6 hours storage at 20°C. Addition of 0.1 M phenylhydrazone solution (0.5 ml.) failed to separate the absorptions.

The spectrum of a 0.2 M solution of ethyl phenyl ketone phenylhydrazone (0.0224 g.) in dry carbon tetrachloride (0.5 ml.) showed two sets of overlapping, but distinct, methyl triplets and methylene quartets (one for each isomer). After two successive dilutions with 0.0508 M $Eu(fod)_3$ solution in carbon tetrachloride (0.05 ml. each time) the triplets and quartets had shifted to form one broad triplet and one broad quartet. This showed that in the first experiment with ethyl phenyl ketone phenylhydrazone, the methylene absorptions of the most abundant and least abundant isomers had become co-incident, with induced shifts of 9.0 and 20.2 Hz downfield respectively. The methyl absorptions remained co-incident, both having the same induced shift of 5.5 Hz downfield.

(The methylene protons would be expected to be nearer the sight of complexing and correspondingly have larger induced shifts[46].)

(iv) Acetaldehyde Phenylhydrazone.—— The experiment was carried out by the general method described above with an isomer mixture of acetaldehyde phenylhydrazone, a 0.0508 M $Eu(fod)_3$ solution, and with tetramethylsilane as internal reference.

In the solution containing $Eu(fod)_3$ the isomeric composition was approximately the same as that in the solution without $Eu(fod)_3$ (c.a. 60% syn isomer and 40% anti isomer; accurate integrals could not be obtained as the methyl absorptions were broadened when complexed with europium.) In the fresh $Eu(fod)_3$ solution the induced shifts for the methyl doublets of the syn and anti isomers were 108.7 and 278.7 Hz downfield respectively. After 30 min. in the n.m.r. probe the induced shifts for the methyl doublets of the syn and anti isomers had decreased by 19.3 and 42.6 Hz respectively. (The decreases in the induced shifts were probably due to absorption of moisture through the cap of the n.m.r. tube.) The induced shifts continued to decrease, even though the sample was stored in a dry-box.

The experiment was repeated twice. Induced shifts of 260.6 and 258.9 Hz for the methyl doublet of the anti isomer, and 99.4 and 97.8 Hz for the methyl doublet of the syn isomer were observed respectively.

The Ultraviolet Spectra of Alkyl Phenyl Ketone Phenylhydrazones.

The alkyl phenyl ketone phenylhydrazones were freshly prepared and distilled before the ultraviolet spectra in ethanol were recorded. The spectrum of acetone phenylhydrazone in ethanol was also recorded for comparison (see Table 10).

The spectra were first recorded on fresh solutions (0.02 mg./ml. in most cases). Apart from increases in intensity due to evaporation of solvent, no changes in the spectra were noted when the solutions were stored at 20°C for 3 days, or when air was blown through the solutions. This suggested that the alkyl phenyl ketone phenylhydrazones were not readily oxidized in ethanol.

Investigation of the Mechanism of the Oxidative Ring Closure of Adipaldehyde Bisphenylhydrazone.

Preparation of Compounds.

Cyclohexanone Phenylhydrazone. —— Cyclohexanone phenylhydrazone was prepared by the method of O'Connor[122] and recrystallised from aqueous ethanol (m.p. 74 - 75°C, lit.[122] m.p. 74 - 76°C).

Phenylazocyclohexane. —— This compound was prepared by the method of Bellamy and Guthrie.[23] Cyclohexanone phenylhydrazone was reduced to 1-cyclohexyl-2-phenylhydrazine (b.p. 122 - 126°C/0.2 mm., lit.[23] b.p. 111 - 114°C/0.6 mm.) and then oxidized to phenylazocyclohexane (b.p. 83 - 85°C/0.2 mm., lit.[23] b.p. 83 - 87°C/0.6 mm.).

9, 10-Dihydro-9,10-bi-imino-anthracene. —— The 9,10-adduct of anthracene and diethyl azodicarboxylate, (m.p. 130 - 134°C, lit.[123] m.p. 137 - 138°C) was prepared by the method of Diels[123] and then converted to 9,10-dihydro-9,10-bi-imino-anthracene by the method of Corey and Mock.[124] The bi-imine decomposed with evolution of gas at 120 - 130°C and left a solid residue of anthracene. The infra-red spectrum showed an N-H stretch ($\nu_{max.}$ (nujol) 3400 cm.$^{-1}$) and no C = O stretch.

Adipaldehyde Bisphenylhydrazone. —— Undistilled adipaldehyde was prepared by the method of English and Barber[125] and converted to the bisphenylhydrazone by the method of Bellamy, Guthrie and Chittenden.[52] The crude adipaldehyde bisphenylhydrazone (m.p. 135 - 137°C, lit.[52] m.p. 138.5 - 140°C) was recrystallised from aqueous ethanol.

Adipaldehyde Dioxime. —— Undistilled adipaldehyde was prepared by the method of English and Barber[125] converted to adipaldehyde dioxime by a general method[126] for the conversion of water insoluble aldehydes to their oximes. The product (52%, m.p. 175 - 178°C,

lit.[126] m.p. 185 - 186°C) was recrystallised from ethanol: $\nu_{max.}$ (nujol) 3100(b), 1670(m), 1420(m), 1350(m), 1320(m), 1060(m), 920(s) 820(m), 710(m), 700 $cm.^{-1}$ (m).

Adipaldehyde Bismethylhydrazone. —— Adipladehyde bismethylhydrazone, a colourless oil, was prepared in the same way as adipaldehyde bisphenylhydrazone (see above). The product (59%; b.p. 148 - 150°C/ 10 mm.) was purified by fractional distillation: $\nu_{max.}$ (film) 3400(b), 2950(s), 1460(m), 1140 $cm.^{-1}$(m). δ (100 MHz, CCl_4) 1 - 3 (m, CH_2), 2.6 (s, Me), 3.7 (m, NH), 6.2 (t, CH), 6.7 p.p.m. (t, CH). The n.m.r. spectrum showed the presence of more than one isomer. (The ratio of the integrals for the methine triplets was approximately 3 : 1.)

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Potassium Azodicarboxylate. —— This salt was prepared from azoformamide and aqueous potassium hydroxide by the method of Thiele,[127] as interpreted by Bellamy.[128]

trans-1,2-Bisphenylazocyclohexane. —— This compound (m.p. 135 - 136°C, lit.[52] m.p. 135 - 136.5°C) was obtained in 42% yield, after recrystallisation from n-proparol, from oxidation of adipaldehyde bisphenylhydrazone with yellow mercuric oxide, as described by Bellamy, Guthrie and Chittenden.[52] $\nu_{max.}$ (nujol) 1520(w), 1310(w), 1190(m), 1150(m), 1070(w), 1020(m), 920(m), 770(s), 690 $cm.^{-1}$(s).

Manganese Dioxide. —— Manganese dioxide was prepared by the method of Bhatnago and George.[55] The material was dried at 125°C for 24 hours and then allowed to equilibrate with the atmosphere before use.

The Reduction of Phenylazocyclohexane with Di-imide.[129]

Phenylazocyclohexane (1g; 0.0053 mole) was added to a well stirred suspension of potassium azodicarboxylate (5g; 0.026 mole) in dry ether (50 ml.). Glacial acetic acid (3.1g; 0.052 mole) in ether (15 ml.) was slowly added over a 2 hour period, and the mixture was stirred under nitrogen for a further 40 hours.

The solid was filtered off and washed with ether. The washings were combined with the filtrate and the ether solution was washed first with aqueous 5% sodium bicarbonate solution (150 ml.) and then with saturated brine (100 ml.). The solution was dried ($Mg\ SO_4$) and the ether was evaporated to leave a light yellow oil. Comparison of the infra-red spectrum of the product with that of a sample of 1-cyclohexyl-2-phenylhydrazine which was obtained as an intermediate in the preparation of phenylazocyclohexane (see page 143) confirmed that the product was 1-cyclohexyl-2-phenylhydrazine.

$\nu_{max.}$ (film) 3250(b), 2850(s), 1580(s), 1500(m), 1450(m), 1240(m), 740(m), 680 $cm.^{-1}$(m).

The result of this experiment is in agreement with the postulate[54] that di-imide reduces symmetrical multiple bonds.

Attempted Reduction of n-Propionaldehyde Phenylhydrazone with Di-imide.

The experiment was carried out in the same way as the reduction of phenylazocyclohexane with di-imide (see above). The reaction mixture was stirred for 2.5 days after the addition of the glacial acetic acid in ether had been completed. The n-propionaldehyde phenylhydrazone was shown, by comparison of infra-red spectra, to have been recovered from the reaction unaltered. $\nu_{max.}$ (film) 3250(m), 2900(s), 1600(s), 1500(b), 1300(b), 1250(b), 1120 $cm.^{-1}$(b).

The failure of this reduction is in agreement with the specificity of di-imide as a reducing agent[54] i.e. it does not reduce unsymmetrical polar multiple bonds.

Attempted Reductions of Adipaldehyde Bisphenylhydrazone with Di-imide.

(i) With Acetic Acid to generate Di-imide. ——The experiment was carried out in the same way as the two previous di-imide reductions (see above). 10 Molar equivalents of potassium azodicarboxylate were used per mole of adipaldehyde bisphenylhydrazone and the solution was stirred under nitrogen for 16 hours after the addition of the glacial acetic acid solution in ether had been completed. Comparison of infra-red spectra showed that only the starting material, adipaldehyde bisphenylhydrazone, had been isolated from the reaction. $\nu_{max.}$ (nujol) 3200(b), 1600(s), 1540(m), 1500(s), 1420(m), 1300(s), 1260(s), 1160(m), 1100(m), 1060(w), 1040(w), 740(s), 680cm.$^{-1}$(s).

A duplicate experiment gave the same result. It was thought that generation of di-imide had been too rapid to reduce the proposed tautomer (see Discussion, page 45).

(ii) With Triethylamine Hydrochloride to generate Di-imide. —— It was hoped triethylamine hydrochloride would generate di-imide more slowly than glacial acetic acid.

A suspension of adipaldehyde bisphenylhydrazone (1g; 0.0034 mole) in acetonitrile (65 ml.) was added to a mixture of solid potassium azodicarboxylate (3.3 g; 0.017 mole) and triethylamine hydrochloride (4.34g; 0.034 mole). The mixture was stirred, under nitrogen, for 40 hours, during which time the colour changed from bright yellow to white.

The reaction mixture was worked up in the same way as the previous di-imide reductions. Comparison of infra-red spectra showed that only the starting material, adipaldehyde bisphenyl-hydrazone, had been recovered from the reaction.

Reduction of trans-1,2-Bisphenylazocyclohexane with Di-imide.

trans-1,2-Bisphenylazocyclohexane (44) (0.5g; 0.00173 mole) was added to a stirred suspension of potassium azodicarboxylate (3.32 g; 0.0173 mole), in ether (50 ml.) under nitrogen. Glacial acetic acid (2.35g; 0.0346 mole), in ether (15 ml.), was added over a 2 hour period. The mixture was then stirred, under nitrogen, for a further 20 hours.

The solid was filtered off and washed with ether. The washings were combined with the filtrate and the ether solution was first washed with 5% W/V aqueous sodium carbonate solution (200 ml.) and then with saturated brine (100 ml.), and finally dried ($Mg\ SO_4$). The ether was evaporated, leaving a yellow oil. Comparison of infra-red and n.m.r. spectra, showed that the crude product was trans-1,2-bisphenylhydrazocyclohexane (45) (0.32 g. 63%). $\nu_{max.}$ (film) 3310(s), 2920(s), 2860(s), 1600(s), 1510(s), 1460(m), 1390(w), 1310(w), 1260(m), 1120(s), 760(s), 700 cm^{-1}(s) δ (100 MHz, [$^2H_6$] dimethyl sulphoxide) 1.08 (m, 4H, CH_2), 1.52 (m, 2H, CH_2), 1.96 (m, 2H, CH_2), 4.49 (m, 2H, CH), 6.3 - 7.2 (m, 10H, aromatic), 7.4 - 7.8 p.p.m. (m, possibly NH partly deuterated).

The Oxidation of trans-1,2-Bisphenylhydrazocyclohexane with Yellow Mercuric Oxide.

trans-1,2-Bisphenylhydrazocyclohexane (45) (0.2g; 0.00068 mole), obtained from the reduction of trans-1,2-bisphenylazocyclohexane with di-imide (described above), in dry ether (50 ml.) was stirred with yellow mercuric oxide (2g; 0.009 mole), under nitrogen, for 30 hours. The bright yellow suspension darkened in colour during this period.

The dark yellow inorganic solids were removed by filtration through a celite pad and then washed with ether. The washings were combined with the filtrate and the ether was evaporated.

After recrystallisation from petroleum-ether (b.p. 40 - 60°C) the bright yellow crystalline product (m.p. 135 - 136°C) was shown, by comparison of infra-red spectra (see page 145) to be trans-1,2-bisphenylazocyclohexane (66% yield).

Attempted Reductions of Adipaldehyde Bisphenylhydrazone with 9,10-Dihydro-9,10-bi-imino-anthracene.

(i) In Methanol. —— Adipaldehyde bisphenylhydrazone (0.1g; 0.00034 mole) was added to a solution of 9,10-dihydro-9,10-bi-imino-anthracene (46) (0.35g; 0.0017 mole) in dry methanol (25 ml.) and the mixture was refluxed, under nitrogen, for 22 hours. Colourless crystals of anthracene separated out on cooling.

After filtration evaporation of the filtrate left a mixture of red oil and crystalline material. Comparison of infra-red spectra suggested the mixture consisted mainly of adipaldehyde bisphenylhydrazone and anthracene. It was difficult to establish whether or not any trans-1,2-bisphenylhydrazocyclohexane (45), the expected product, was present.

(ii) In Ether. —— It was hoped that di-imide would be generated from 9,10-dihydro-9,10-bi-imino-anthracene more slowly in refluxing ether than in refluxing methanol.

The first experiment was carried out in the same way as the attempted reduction in methanol, and again an inconclusive result was obtained.

A further reduction in ether was attempted on a larger scale (0.67g. of adipaldehyde bisphenylhydrazone). The reaction mixture was refluxed for 4 days. Again only anthracene and adipaldehyde bisphenylhydrazone were recovered.

The Oxidation of 1-Cyclohexyl-2-phenylhydrazine with Hydrogen Perioxide.

1-Cyclohexyl-2-phenylhydrazine (1g; 0.00525 mole), obtained as the intermediate product in the preparation of phenylazocyclohexane, was dissolved in ether (25 ml.). The solution was shaken with 30% (100 vol.) hydrogen perioxide solution (0.87 ml; 50% excess) for 5 hours at 20°C, under nitrogen. The ether solution was separated from the aqueous phase and washed first with 25% aqueous potassium iodide solution (4 x 50 ml.) and then with 1N aqueous sodium thiosulphate solution (2 x 50 ml.). The ether was evaporated after drying ($Mg\ SO_4$). The infra-red spectrum showed that the crude product was phenylazocyclohexane. $\nu_{max.}$ (film) 2850(s), 2800(m), 1480(w), 1450(m), 750(s), 680 $cm.^{-1}$(s).

Attempted Oxidation of Adipaldehyde Bisphenylhydrazone with Hydrogen Peroxide.

The experiment was carried out by the same method described above for the oxidation of 1-cyclohexyl-2-phenylhydrazine with hydrogen peroxide.

Adipaldehyde bisphenylhydrazone (0.24g; 0.000815 mole) was treated with 30% (100 vol.) hydrogen peroxide solution (0.27 ml; 50% excess), in ether (25 ml.). After work-up, only adipaldehyde bisphenylhydrazone was recovered from the reaction.

Attempted Oxidation of the Product Mixture from the Reduction of Adipaldehyde Bisphenylhydrazone with 9,10-Dihydro-9,10 -bi-imino-anthracene.

The crude products from two attempted reductions of adipaldehyde bisphenylhydrazone with 9,10-dihydro-9,10-bi-imino-anthracene (see page 151) were separately treated with 30% (100 vol.) hydrogen peroxide solution as in the oxidation of 1-cyclohexyl-2-phenylhydrazine described above. The molar ratio of hydrogen peroxide to phenylhydrazine was doubled in this case since two phenylhydrazo groups were to be reduced. (In the calculation of the amounts of hydrogen peroxide solution it was assumed that each product mixture consisted entirely of 1,2-bisphenylhydrazocyclohexane.)

No trans-1,2-bisphenylazocyclohexane was isolated from the reactions. In both experiments the products could not be identified from their infra-red spectra.

Attempted Oxidations of Adipaldehyde Dioxime.

(i) With Yellow Mercuric Oxide.—— Adipaldehyde dioxime was treated with yellow mercuric oxide in the same way as adipaldehyde bisphenylhydrazone[52] (see page 145).

Only adipaldehyde dioxime, identified by m.p. and comparison of infra-red spectra (see page 143) was isolated from the reaction mixture.

(ii) With Manganese Dioxide.—— Adipaldehyde dioxime (0.7g; 0.00487 mole) was stirred with manganese dioxide (5 g.) in dry benzene (100 ml.) overnight. The manganese dioxide was removed by filtration through a celite pad and then washed with benzene. No residue remained after the combined benzene solutions had been evaporated. The inorganic residue was washed with boiling ethanol. Only adipaldehyde dioxime (0.25 g.) was obtained after evaporation of the ethanol.

(iii) With Dibenzoyl Peroxide.—— Adipaldehyde dioxime (0.7g; 0.00487 mole) and dibenzoyl peroxide (1.21g; 0.005 mole) were stirred together in dry benzene (100 ml.) under nitrogen. The mixture was refluxed for 40 hours, poured into water (200 ml.), made alkaline to litmus by addition of concentrated sodium hydroxide solution, and then extracted with ether (3 x 200 ml.). The combined extracts were dried ($Mg\ SO_4$) and the ether was evaporated. Only a small quantity of crystalline material was obtained. After recrystallisation from ethanol/light petroleum-ether the yellow compound (6mg; m.p. 307 - 311°C) showed P382 in its mass spectrum. The high molecular weight and m.p. suggested that this compound could be a short chain or cyclic polymer of adipaldehyde dioxime. This possibility was not investigated further.

Only sodium benzoate, identified by comparison of the infra-red spectrum with that of an authentic sample, was obtained on evaporation of water from the aqueous phase.

Attempted Oxidations of Adipaldehyde Bismethylhydrazone.

Adipaldehyde bismethylhydrazone was oxidised, as described above for adipaldehyde dioxime, with both yellow mercuric oxide (at 20°C in this case) and dibenzoyl peroxide.

The products were analysed by dry column chromatography on alumina with benzene as elutent, by G.C. (Apiezon L; 40 - 100°C), and by infra-red and n.m.r. spectroscopy. No 1,2-bismethylazocyclohexane was obtained. A yellow band, which was identified by n.m.r. spectroscopy as impure adipaldehyde bismethylhydrazone was obtained from the alumina chromatography columns in some experiments.

The Reduction of 1,2-Bisphenylazocyclohexane with 9,10-Dihydro-9,10-bi-imino-anthracene.

1,2-Bisphenylazocyclohexane (0.1g; 0.00034 mole) was mixed with 9,10-dihydro-9,10-bi-imino-anthracene (0.573 g; 0.00246 mole) in dry methanol (50 ml.). The mixture was refluxed under nitrogen for 5 days and then cooled to 0°C. The anthracene, which had separated, was filtered off and washed with methanol. The solvent was removed from the combined methanol solutions in vacuo.

The 100 MHz n.m.r. spectrum of a saturated solution of the product mixture in $[^2H_6]$ dimethyl sulphoxide was compared with that of a mixture of anthracene, 1,2-bisphenylhydrazocyclohexane, and adipaldehyde bisphenylhydrazone (50, 40 and 10% molar equivalents respectively) in the same solvent. The spectrum of the product mixture was also compared with the spectra of anthracene, 1,2-bisphenylhydrazocyclohexane and adipaldehyde bisphenylhydrazone in $[^2H_6]$ dimethyl sulphoxide.

The spectra showed that reduction of 1,2-bisphenylazocyclohexane to 1,2-bisphenylhydrazocyclohexane had occured, and that the amount of adipaldehyde bisphenylhydrazone produced, if any, was very small ($< 5\%$).

Oxidation of Adipaldehyde Bisphenylhydrazone with Yellow Mercuric Oxide in Dimethyl Sulphoxide.

Adipaldehyde bisphenylhydrazone (0.5g; 0.0017 mole) was added to a suspension of yellow mercuric oxide (1.11g; 0.005 mole) in dimethyl sulphoxide (70 ml.). The mixture, under nitrogen, was refluxed, with stirring, for 4 hours.

The solid material was removed by filtration through a celite pad and washed with ether. The washings were combined with the filtrate and the solvents were evaporated. The product was then chromatographed on a 20 x 2" dry alumina column with petroleum-ether (b.p. 60 - 80°C) as elutent to remove impurities and dimethyl sulphoxide (b.p. 189°C).

One orange band separated from the origin. This material was extracted into ether, washed with water and then dried ($Mg\ SO_4$). After the solvent had been evaporated an orange crystalline solid was obtained. After recrystallisation from n-propanol this compound was shown, by its melting point (135 - 136°C) and by comparison of infra-red spectra (see page 145) to be trans-1,2-bisphenylazo-cyclohexane (0.08g; 19%, lit.[52] m.p. 135 - 136.5°C).

The oxidative ring closure of adipaldehyde bisphenyl-hydrazone does therefore take place in dimethyl sulphoxide, though it was difficult to recover the product from this solvent. (The yield from carbon tetrachloride was 42%)

Equilibration of Adipaldehyde Bisphenylhydrazone in [$^2H_6$] Dimethyl Sulphoxide.

A 5% M solution of adipaldehyde bisphenylhydrazone (0.0147g.) in degassed [$^2H_6$] dimethyl sulphoxide (1 ml.), containing 3% V/V of tetramethylsilane, was prepared in an n.m.r. tube which was then sealed. The solution was stored at 20°C for 2 days, then heated to 100°C for 10 min., and finally allowed to cool to 20°C before the 100 MHz n.m.r. spectrum was recorded. The spectrum was identical to that of a sample of adipaldehyde bisphenylhydrazone in [$^2H_6$] dimethyl sulphoxide; δ 1.50 (m, 4H, CH_2), 2.25 (m, 4H, CH_2), 6.39 (t, CH), 6.64 (t, CH), 6.7-7.4 (m, 10H, aromatic), 9.02 (s, NH), 9.59 p.p.m. (s, NH). The two CH triplets and two NH singlets (partly deuterated) showed that at least two isomers were present (in the ratio 1:0.2). No 1-phenylazo-2-phenylhydrazocyclohexane (43) was evident. This would have shown methine triplets in the region of 4.5 p.p.m. These broad triplets were present in the spectra of both 1,2-bisphenylhydrazocyclohexane and 1,2-bisphenylazocyclohexane. The sample was heated at 100°C for a further 36 hours after which no change was observed in the n.m.r. spectrum.

The Thermal Stability of 1,2 Bisphenylazo-1,2-diphenylethane and 2,3-Diphenyl-1,4-dibenzaltetrazane.

Preparation of Reagents.

Benzaldehyde Phenylhydrazone. ——Benzaldehyde phenylhydrazone was prepared by the method described by Mann and Saunders.[130] The product (m.p. 155 - 157°C, lit.[130] m.p. 157°C) was recrystallised from ethanol. $\nu_{max.}$ (nujol) 1600(m), 1510(w), 1270(m), 1150(m), 1080(w), 770(m), 700 cm.$^{-1}$(m).

β-Benzil Osazone. ——Benzil osazone (m.p. 234 - 235°C, lit.[131] m.p. 229 - 231.5°C) was prepared by the method described by Mann and Saunders.[131] $\nu_{max.}$ (nujol) 1600(s), 1590(w), 1550(m), 1520(m), 1460(s), 1320(w), 1260(m), 1180(m), 1150(m), 1080(w), 770(s), 700 cm.$^{-1}$(s).

2,3-Diphenyl-1,4-dibenzaltetrazane.

(i) From the Oxidation of Benzaldehyde Phenylhydrazone with Manganese Dioxide. ——This compound was first obtained from the oxidation of benzaldehyde phenylhydrazone with manganese dioxide in refluxing benzene by an adaptation of the method described by Bhatnago and George.[55] (Both biphenyl and 2,4,5-triphenyl-1,2,3-triazole (50) were obtained by following their procedure.)

Benzaldehyde phenylhydrazone (2.5g; 0.0125 mole) was added to a suspension of manganese dioxide (15g. dried at 130° before use)in dry benzene(100 ml.) (see page 51), and the mixture was refluxed, under nitrogen, for 6 hours. The inorganic material was collected in a celite pad and washed with benzene. The washings were combined with the filtrate and the benzene was evaporated. The tarry residue was extracted with boiling petroleum-ether (200 ml., b.p. 60 - 80°C).

The concentrated extract was analysed by T.L.C. on alumina

containing fluorescent indicator (green) with benzene as elutent, and showed 3 spots. Chromatography of the mixture on a 20 x 2" dry alumina column with benzene as elutent separated the mixture into 3 bands. The lowest two bands did not yield crystalline material. The third band (red) was shown by T.L.C. to contain more than one component and was therefore chromatographed further on a 15 x 1.5" dry alumina column with petroleum-ether (b.p. 60 - 80°C) as elutent. The red material from this second column was collected and, after recrystallisation from benzene/ethanol, gave 2,3-diphenyl-1,4-dibenzaltetrazane (0.02g; m.p. 182 - 184°C, lit.[55] m.p. 184 - 185°C). (49): δ (100 MHz, $CDCl_3$) 7.2 - 7.8 (m, 20H, aromatic), 8.1 - 8.22 p.p.m. (m, 2H, CH). $\nu_{max.}$ (film) 3010(w), 2900(m), 1600(s), 1570(w), 1500(s), 1450(w), 1350(b), 1120(w), 750(s), 690 $cm.^{-1}$(s).

(ii) From the Oxidation of Benzaldehyde Phenylhydrazone with Yellow Mercuric Oxide.— Benzaldehyde phenylhydrazone (1g; 0.0051 mole) was added to a suspension of yellow mercuric oxide (3.25g; 0.015 mole) in dry carbon tetrachloride (185 ml.), and the mixture was stirred, under nitrogen, for 24 hours. The solids were collected on a celite pad and washed with carbon tetrachloride. The combined washings and filtrate were evaporated, the residual oil was extracted with petroleum-ether (3 x 100 ml; b.p. 60 - 80°C) and then the combined extracts were concentrated.

The solution was chromatographed on a 20 x 1.5" dry alumina column with petroleum-ether (b.p. 60 - 80°C) as elutent and separated into 3 bands: (i) red (lowest; (ii) pink (middle); (iii) orange (top).

Band (i) gave 2,3-diphenyl-1,4-dibenzaltetrazane (0.03g; m.p. 172 - 175°C, lit.[55] m.p. 184 - 185°C) after one recrystallisation from

benzene/ethanol. The compound was identified by comparison of infra-red spectra (see above).

Band (ii), which was discoloured by 'tailing' from band (i), gave α-benzil osazone (m.p. 206 - 208°C, lit.[60] m.p. 208°C) after recrystallisation from benzene/ethanol: δ (100 MHz, $CDCl_3$) 6.6 - 7.8 p.p.m. (m).

Band (iii) was extracted into ether and the solution was concentrated, to give a yellow compound. After recrystallisation from benzene this was shown, by comparison of infra-red spectra, to be 1,2-bisphenylazo-1,2-diphenylethane m.p. 180 - 182°C (see below).

1,2-Bisphenylazo-1,2-diphenylethane.

(i) From the Oxidation of Benzaldehyde Phenylhydrazone with Manganese Dioxide. ——This compound was obtained by an adaptation of a method described by Bhatnago and George.[55]

Benzaldehyde phenylhydrazone (2g; 0.01 mole) was added to a suspension of dry manganese dioxide (10g.) in dry benzene (100 ml.), and the mixture was stirred, under nitrogen, at 20°C, for 24 hours. The inorganic material was collected in a celite pad and washed with benzene. The combined washings and filtrate were concentrated and then chromatographed on a 25 x 1.5" dry alumina column with benzene as elutent. Three bands were obtained: (i) yellow (lower), (ii) grey (middle), (iii) orange (top).

Band (ii) yielded light yellow 1,2-bisphenylazo-1,2-diphenylethane (m.p. 183 - 184°C, lit.[55] m.p. 184 - 185°C), $\lambda_{max.}$ ($CHCl_3$) 400, 275 nm. (ε 312, 2210) lit.[55] $\lambda_{max.}$ ($CHCl_3$) 400, 268 nm. (ε 394, 2200)).

Band (i) was fractionally crystallised, first from ethanol and then from benzene. A further sample of 1,2-bisphenylazo-1,2-

diphenylethane (m.p. 184 - 186°C) was obtained.

Band (iii) was shown by T.L.C. on alumina, with benzene as elutent, to contain 4 components. Further chromatography on a 25 x 1.5" dry column under the same conditions as for T.L.C. produced 4 bands. Only the lower (yellow) band could be crystallised. After recrystallisation from benzene this material was found to be 1,3,4,6-tetraphenyl-1,2,4,5-tetra-azahexa-2,5-diene (51), m.p. 201 - 202°C, (lit.[55] m.p. 201 - 202°C) $\nu_{max.}$ (nujol) 1600(s), 1560(s), 1500(s) 1280(m), 1250(s), 1370(m), 1330(s), 1080(w), 760(s), 700 $cm.^{-1}$(s).

The lengthy purification procedure resulted in poor recovery of each compound from this experiment (< 0.05g. of each.).

(ii) From the Oxidation of Benzaldehyde Phenylhydrazone with Mercuric Oxide.—— See method (ii) in the preparation of 2,3-diphenyl-1,4-dibenzaltetrazane (page 160).

(iii) From the Oxidation of Benzaldehyde Phenylhydrazone with Dibenzoyl Peroxide.—— 1,2-Bisphenylazo-1,2-diphenylethane was also obtained from the oxidation of benzaldehyde phenylhydrazone with dibenzoyl peroxide (see page 166).

The Thermal Stability of 2,3-Diphenyl-1,4-dibenzaltetrazane.

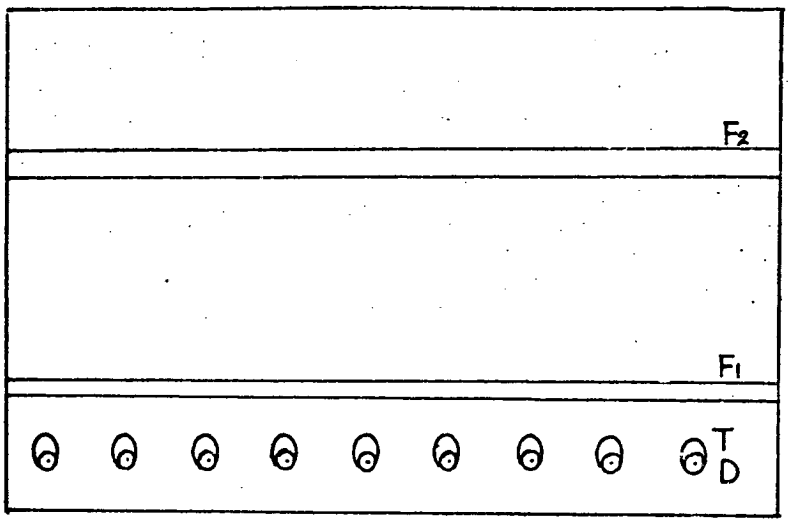
A solution of 2,3-diphenyl-1,4-dibenzaltetrazane (0.02g.) in dry benzene (25 ml.) was refluxed under nitrogen for 24 hours. The solution was analysed by T.L.C. on alumina, containing fluorescent indicator (green), with benzene as elutent. No spot other than those of the tetrazane (dark red) was observed; these disappeared from the T.L.C. plates due to sublimation after c.a. 1 hour.

After evaporation of the benzene in vacuo (c.a. 70°C) the residue was only partially crystalline. (The tetrazane is thermally stable when in boiling benzene under nitrogen but is slightly decomposed when heated in benzene in the presence of air i.e. during evaporation.)

The residue was recrystallised from benzene/ethanol and 2,3 diphenyl-1,4-dibenzaltetrazane (m.p. 180 - 182°C) was recovered. In a further experiment with benzene as solvent no change in the tetrazane had occured after 5 days.

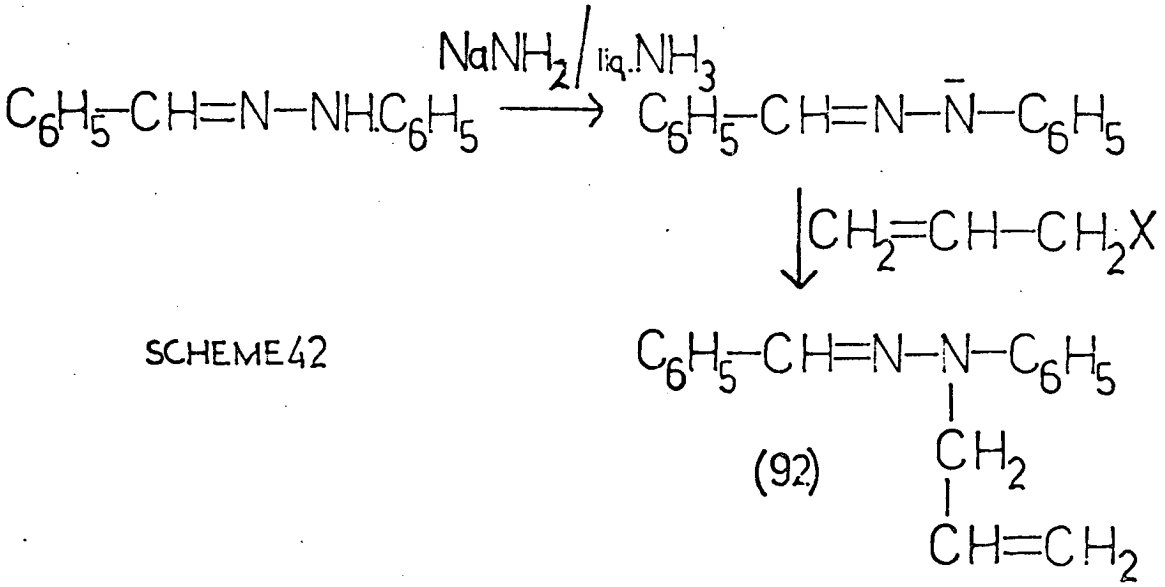
The experiment was repeated with dimethyldigol (b.p. 164°C) as solvent. As the solution was slowly heated the characteristic deep red colour of the 2,3-diphenyl-1,4-dibenzaltetrazane disappeared when the temperature of the oil bath reached 110°C. The solution was allowed to cool and then it was poured into water (50 ml.), extracted with ether (4 x 50 ml.) and dried ($MgSO_4$). The ether was evaporated and the dimethyldigol (b.p. 80°C/10 mm.) was removed by distillation. T.L.C. on alumina containing fluorescent indicator (green) showed that the product mixture consisted of at least three components, none of which was the tetrazane.

The diversity of products suggested decomposition rather than conversion to 1,2-bisphenylazo-1,2-diphenylethane.



(91)

D = 1,2-BISPHENYLAZO-1,2-DIPHENYLETHANE
T = 2,3-DIPHENYL-1,4-DIBENZALTETRAZANE
F1= FLUORESCENT BAND 1
F2= FLUORESCENT BAND 2
SOLVENT IS PETROLEUM-ETHER (b.p. 60-80°C)



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(92)

2,3-Diphenyl-1,4-dibenzaltetrazane (0.1 g.) was dissolved in p-xylene (50 ml; b.p. 138°C). The solution was refluxed under nitrogen for 10 days during which the red colour of the solution lightened considerably. Much of the material appeared to have decomposed and separated from the solution. T.L.C. of the solution on alumina with petroleum-ether (b.p. 60 - 80°C) as elutent showed the presence of a yellow compound with an Rf value similar to that of 1,2-bisphenylazo-1,2-diphenylethane. Dry column chromatography under the same conditions confirmed the presence of a yellow compound but the quantity of this material was insufficient for identification.

This experiment was repeated and the solution was refluxed for 6.5 days. Chromatography again showed the presence of a yellow compound but only the tetrazane was isolated from the dry column.

The Thermal Stability of 1,2-Bisphenylazo-1,2-diphenylethane.

A solution of 1,2-bisphenylazo-1,2-diphenylethane (0.02g.) in dry benzene (25 ml.) was refluxed under nitrogen for 6 hours before the benzene was evaporated.

T.L.C. of the residue on alumina containing fluorescent indicator (green), with petroleum-ether (b.p. 60 - 80°C) as elutent at first showed only a spot for 1,2-bisphenylazo-1,2-diphenylethane. The plate was exposed to the atmosphere for c.a. 1 hour and then examined under a U.V. lamp. A weak luminous spot, Rf $\sim$ 0.5 was then present, as well as the spot for the starting material. (The presence of this weak spot may have been masked earlier by solvent on the plate.)

The remainder of the product mixture was chromatographed on a larger plate (20 x 20") (see 91). Most of the mixture was thought to be 1,2-bisphenylazo-1,2-diphenylethane, and remained at

the origin. A red band, with the same Rf value as 2,3-diphenyl-1,4-dibenzaltetrazane and two bands of colourless (fluorescent) material were also present.

The bands were separately removed from the plate and extracted from the alumina with a mixture of equal volumes of chloroform and ethanol. The 1,2-bisphenylazo-1,2-diphenylethane was isolated as a crystalline solid. The other compounds were not present in sufficient amounts for purification; the fluorescent band nearest the origin had the same Rf value as 2,4,5-triphenyl-1,2,3-triazole (50) (see Discussion, page 51) and may have been formed by oxidation of the diphenylethane. Only a very small quantity of red liquid was recovered from the band that was suspected to be 2,3-diphenyl-1,4-dibenzaltetrazane.

The Oxidation of Benzaldehyde Phenylhydrazone with Dibenzoyl Peroxide.

Benzaldehyde phenylhydrazone (3g; 0.0153 mole) and dibenzoyl peroxide (2g; 0.00827 mole) were dissolved in dry benzene (100 ml.), and the solution was refluxed under nitrogen for 18 hours.

The solution was then poured into water (200 ml.), made alkaline to litmus by the addition of 4 N aqueous sodium hydroxide solution, and extracted with ether (3 x 100 ml.). The combined extracts were washed with water (2 x 100 ml.) and dried ($MgSO_4$). Evaporation of the solvents yielded an orange crystalline material. On recrystallisation from ethanol bright yellow crystals (0.01 g; m.p. 175 - 180°C) were obtained. Comparison of the infra-red spectrum with that of an authentic sample identified the compound as 1,2-bisphenylazo-1,2-diphenylethane (see page 161).

The mother liquor was evaporated and the residual oil was then chromatographed on a 25 x 1" dry alumina column with petroleum-ether (b.p. 60 - 80°C) as elutent. Five coloured bands were observed, with some material remaining at the origin. The material from each band, and also from the origin, was extracted with ether. After the ether had been evaporated from the solutions the total yield of crude organic material was 3.35g. (Only 3 g. of benzaldehyde phenylhydrazone had been reacted.)

An attempt was made to recrystallise the material from each band from ethanol. Bands (i) and (ii) could not be purified and were not identified. Band (iii) gave yellow crystals (30 mg.). This compound was identified, by mixed melting point (m.p. 201 - 202°C) and by comparison of infra-red spectra, as 1,3,4,6-tetraphenyl-1,2,4,5-tetra-azahexa-2,5-diene (51), (see page 162 , paragraph 1).

Band (iv) gave colourless crystals (35 mg; m.p. 178 - 180°C). Band (v) gave bright yellow crystals (100 mg; m.p. 165 - 170°C). The material from the origin gave colourless crystals (30 mg; m.p. 150 - 168°C). Comparison of the infra-red spectra showed that the material from the origin and bands (iv) and (v) had given the same compound; the melting point differences indicating either different isomers or degrees of purity. $\nu_{max.}$ (nujol) 3240(m), 1680(m), 1640(m), 1600(w), 1390(w), 1300(s), 750(w), 720(m), 700 $cm.^{-1}$(s). δ ($CDCl_3$, 100 MHz) 7.1 - 7.9 (m, 15H, aromatic), 9.12 p.p.m. (S, 1H, NH). The n.m.r. sample in $[^2H_1]$ chloroform became purple on standing. This, in combination with spectra, suggested the presence of an N - H group ($\nu_{max.}$ 3240 $cm.^{-1}$). Mass spectrum — P316, 196; accurate mass measurement 316.121816 ($C_{20}H_{16}N_2O_2$ requires 316.121170). The compound was α , β -dibenzoylphenylhydrazine (53) (lit.[63] m.p. 181°C). This compound was also obtained by Edward and Samad[63] from the oxidation of benzaldehyde phenylhydrazone with dibenzoyl peroxide.

Attempted Reduction of β-Benzil Osazone.

β-Benzil osazone (52) (3g; 0.0077 mole) in dry dioxan (20 ml.) was slowly added to a stirred suspension of lithium aluminium hydride (1.166g;0.0208 mole) in dry dioxan (50 ml.) under nitrogen. The mixture was refluxed for 4.5 days during which it changed colour from grey to green, and then to light brown.

The reaction mixture was allowed to cool before water (12 ml.) was cautiously added with stirring to decompose the excess of lithium aluminium hydride. 4N Aqueous sodium hydroxide (12 ml.) was then added. The resulting mixture poured into water (200 ml.). The organic materials were extracted with ether (4 x 100 ml.). The ether solution was washed with saturated brine (2 x 100 ml.) and then dried ($MgSO_4$). The ether and the remaining dioxan were removed *in vacuo* before the product mixture was chromatographed on a 25 x 1.5" dry alumina column with petroleum-ether (b.p. 60 - 80°C) as elutent.

The mixture was separated into 3 bands, all of which gave crystalline material. The yields of crude material were: (i) 0.91g; (ii) 0.66g; (iii) 1.06g.

Band (i) gave a yellow compound (0.17g; m.p. 232 - 233°C) after recrystallisation from benzene/light petroleum-ether. This was shown, by comparison of infra-red spectra, to be β-benzil osazone (*lit.*[131] m.p. 235°C).

Band (ii) gave a yellow compound (0.16 g; m.p. 157 - 158°C) after recrystallisation from ethanol/light petroleum-ether. This was identified as benzaldehyde phenylhydrazone (*lit.*[117] m.p. 158°C) by comparison of infra-red spectra. Benzaldehyde phenylhydrazone (0.18g.) was also obtained from band (iii) after recrystallisation.

The experiment was repeated on the same scale and the crude

product mixture was stirred overnight with a suspension of yellow mercuric oxide (9.9g;0.046 mole) in dry ether (100 ml.) under nitrogen. The insoluble inorganic material was removed by filtration through a celite pad and washed with ether. The washings were combined with the filtrate and dried ($MgSO_4$). The ether was evaporated and the residual orange oil was recrystallised from benzene/light petroleum-ether. Benzaldehyde phenylhydrazone (0.64g; m.p. 153 - 155°C) was collected.

The mother liquor was chromatographed on a 20 x 1.5" dry alumina column with petroleum-ether (b.p. 60 - 80°C) as elutent. Only crude β-benzil osazone (1.24g.) was recovered from the column. This was identified by its melting point and infra-red spectrum after recrystallisation from benzene/light petroleum-ether.

The Reduction of Benzaldehyde Phenylhydrazone followed by Oxidation.

Several reductions of benzaldehyde phenylhydrazone (3g; 0.0153 mole) were attempted with lithium aluminium hydride (1.166g; 0.0208 mole). The experiments were carried out in the same way as the reductions of β-benzil osazone described above but only the starting material was isolated from the reaction mixture.

On one occasion the crude material obtained from the attempted reduction was oxidised with yellow mercuric oxide. The oxidation was carried out in the same way as that already described (see page 160, para. 2), but dry ether was used as solvent instead of carbon tetrachloride.

After chromatography on a 20 x 1" dry alumina column with benzene as elutent only 1,3,4,6-tetraphenyl-1,2,4,5-tetra-azahexa-2,5-diene (51) (0.37g.) was isolated. This compound was identified by mixed m.p. and comparison of infra-red spectra. (see page 162

para. 1).

The reduction was also attempted with sodium metal in tetrahydrofuran by an adaptation of the method of Smith and Ho,[132] but again only the starting material was recovered.

Attempted Rearrangement of Trimethylacetaldehyde Phenylhydrazone.

Preparation of Trimethylacetaldehyde Phenylhydrazone.

Trimethylacetaldehyde (b.p. 72 - 74°C, lit.[133] b.p. 77 - 78°C) was prepared by the method of Campbell[133] and condensed with an equimolar amount of redistilled phenylhydrazine in cold ethanol. The ethanol was evaporated and the solid phenylhydrazone was obtained. No suitable solvent for recrystallisation was found. The phenylhydrazone (b.p. 87 - 91°C/13 mm.) was purified by distillation under nitrogen: δ (100 MHz, CCl_4) 1.02(s, 9H, Me_3 CH), 6.6 - 7.2 p.p.m. (m, 7H, Ph, CH and NH). $\nu_{max.}$ (CCl_4) 3200(w), 2950(s), 1600(s), 1500(s), 1370(m), 1300(m), 1250(m), 1120(s), 1070 $cm.^{-1}$(m).

An earlier attempt to prepare trimethylacetaldehyde by the method of Brown and Subba Rao[134] proved unsuccessful.

An attempt to oxidise neopentyl alcohol to trimethylacetaldehyde by the method of Parikh and Doering[135] with a pyridine-sulphur trioxide complex[136] also proved unsuccessful.

Treatment of Trimethylacetaldehyde Phenylhydrazone with Sulphuric Acid in Methanol.

A solution of sulphuric acid (0.20 ml; S.G.1.84) in 'AnalaR' methanol (4.1 ml.) was added to trimethylacetaldehyde phenylhydrazone (0.180g.). The mixture was sparged with dry nitrogen and shaken until a homogeneous solution had formed.

The solution was stored at 20°C for 118 hours during which the colour changed from red to purple. A solution of sodium bicarbonate (0.65g.) in brine (50 ml.) was added at 0°C under nitrogen followed by ether (50 ml.).

The mixture was shaken and the organic layer was separated and dried ($MgSO_4$).

The n.m.r. and infra-red spectra of the concentrated material showed that no reaction had taken place.

The experiment was repeated using methanol which had been dried and distilled but the same result was obtained.

Treatment of Trimethylacetaldehyde Phenylhydrazone with Concentrated Sulphuric Acid.

Trimethylacetaldehyde phenylhydrazone (200 mg.) was dissolved in concentrated sulphuric acid (5 ml.) and the solution was stored at 20°C, under nitrogen, for 5 days.

The solution was then poured into water (75 ml.), made alkaline to litmus by the addition of solid sodium bicarbonate, and then extracted with ether (3 x 50 ml.). The combined extracts were dried ($MgSO_4$) and the ether was evaporated. Only 15 mg. of straw coloured material was left. The 100 MHz n.m.r. spectrum was very poorly resolved.

The experiment was repeated but again insufficient material for spectroscopy was obtained.

Attempted Protonation of 2-Methyl-2-phenylazopropane.

(i) Preparation of 2-Methyl-2-phenylazopropane. — 2-Methyl-2-phenylazopropane was prepared in 21% yield from t-butyl chloride and phenyldiazonium fluoroborate by the method of Curtin and Ursprung.[84] The compound was purified by chromatography on an alumina column (Activity 1[94]) with petroleum-ether (b.p. 40 - 60°C) as elutent, and then by distillation (b.p. 40 - 45°C/0.05 mm. lit.[84] b.p. 50 - 54°C/0.2mm.).

(ii) Attempted Protonation of 2-Methyl-2-phenylazopropane. — Fluorosulphonic acid (1 ml.) was added to 2-methyl-2-phenylazopropane (80 mg.) in an n.m.r. tube at -78°C, and the mixture was shaken, with occasional cooling until it was homogeneous. The ^1H 100 MHz n.m.r. spectrum was recorded at -65°C with fluorosulphonic acid (chemical shift taken as 10 p.p.m.) as internal reference: δ 0.9 (S, 9H, t-butyl), 6.7 - 7.3 p.p.m. (m, 5H, aromatic). The spectrum was then recorded at 20°C; only the relative chemical shifts changed slightly, and the spectrum had not changed after a further 20 hours at 20°C.

Rearrangement of 1-Phenyl-1-phenylazobut-3-ene.

Preparation of 1-Phenyl-1-phenylazobut-3-ene.

(i) Preparation of Allyl Magnesium Bromide.—— The Grignard reagent was prepared, in dry ether, by the method of Henze, Allan and Leslie.[137] The freshly prepared ether solution was filtered through sintered glass, under dry nitrogen, before use.

(ii) Preparation of 1-Phenyl-1-phenylhydrazobut-3-ene.—— A solution of allyl magnesium bromide (0.1 mole) in dry ether (200 ml.) was refluxed under nitrogen overnight while benzaldehyde phenylhydrazone (6g; 0.0304 mole), which was contained in a Soxhlet extractor, was extracted into the solution.

The reaction mixture was allowed to cool and then poured into water (300 ml.). The aqueous layer was extracted with ether (4 x 100 ml.) and the combined extracts dried ($MgSO_4$). The ether was evaporated and an orange crystalline solid (7.43 g.) was obtained. Comparison of infra-red spectra showed that this material was not benzaldehyde phenylhydrazone. (No ν N - H).

An attempt was made to recrystallise a portion of the product (2 g.) from ethanol but only benzaldehyde phenylhydrazone (0.21g.) was recovered. The product had decomposed in boiling ethanol.

(iii) Oxidation of 1-Phenyl-1-phenylhydrazobut-3-ene with Yellow Mercuric Oxide.——The remainder of the crude product (5.43g.) was dissolved in dry ether (50 ml.) and added to a suspension of yellow mercuric oxide (15g; 0.069 mole) in dry ether (200 ml.). The mixture was stirred for 2 days under nitrogen. The insoluble inorganic material was removed by filtration through a celite pad and washed with ether. The combined washings and filtrate were dried ($MgSO_4$) and then the ether was evaporated. The residual brown oil was chromatographed on a 'wet' alumina column with petroleum-ether

(b.p. 40 - 60°C) as elutent. The material separated into 3 bands: (i) a mobile orange liquid (1.0g.); (ii) a mobile red liquid (0.24g.); (iii) an orange solid (0.99 g.).

Band (iii) was shown, by comparison of infra-red spectra, to be the same as the material before oxidation (1-phenyl-1-phenylhydrazobut-3-ene) and was oxidised again with twice the amount of yellow mercuric oxide/mole equivalent of substrate as was used in the first oxidation. The product mixture was chromatographed in the same manner, and again it separated into 3 bands. Only 1-phenyl-1-phenylhydrazobut-3-ene (0.71g.) was recovered. Band (i) from the first oxidation was distilled to give a bright yellow, viscous liquid (b.p. 118 - 119°C/0.3 mm.) whose spectra data were consistent with it being 1-phenyl-1-phenylazobut-3-ene. δ (60 MHz, CCl_4) 2.85 (m, 2H, CH-$\underline{CH_2}$), 4.6 - 5.2 (m, olefinic $\underline{CH_2}$ and Ph-$\underline{CH}$-N), 5.3 - 6.1 (m, 1H olefinic CH), 7.0 - 7.8 p.p.m. (m, 10H, aromatic). $\nu_{max.}$ (film) 3100(m), 2930(m), 1640(w), 1600(w), 1500(m), 1460(s), 1310(w), 1150(w), 1080(w), 1000(w), 930(s), 770(s), 700 $cm.^{-1}$(s).

Preparation of 1-N-Allyl Benzaldehyde Phenylhydrazone.

A suspension of sodamide (0.025 mole) in liquid ammonia (500 ml.) was prepared by the method of Hauser, Swamer and Adams.[138] Following the method of Kenyon and Hauser[139] the sodamide was used to convert benzaldehyde phenylhydrazone (4.9g; 0.025 mole) to its anion (Scheme 42) which was then reacted with allyl bromide (3.025 g; 0.025 mole). The product, 1-N-allyl benzaldehyde phenylhydrazone (4.32g; 73%) (92) was purified by distillation (b.p. 143 - 144°C/0.1 mm.): δ (60 MHz, CCl_4) 4.4 (broad, s, 2H, -$\underline{CH_2}$-CH = CH_2), 4.9 - 5.4 (m, 2H, -CH_2-CH = $\underline{CH_2}$), 5.5 - 6.2 (m, 1H, CH_2 -$\underline{CH}$ = CH_2), 6.6 - 7.9 p.p.m. (m, 11H, aromatic and $\underline{CH}$ = N). $\nu_{max.}$ (nonane)

1600(s), 1575(m), 1160(s), 960(w), 700 cm.$^{-1}$(s).

The rearrangement of 1-Phenyl-1-phenylazobut-3-ene.

1-Phenyl-1-phenylazobut-3-ene (0.5 g; 0.0021 mole) was dissolved in nonane (50 ml.), and the infra-red spectrum of the initial solution was recorded: $\nu_{max.}$ (nonane) 1650(w), 1610(w), 1030(w), 990(w), 920(s), 770(m), 700(s), 695 cm.$^{-1}$(s). (The absorptions at 1650 and 1610 cm.$^{-1}$ were very weak in the fresh solution.)

The solution was refluxed for 200 hours under nitrogen. Samples were withdrawn at intervals through a spetum and their infra-red spectra were recorded. T.L.C. of the samples were also run on silica gel plates with petroleum-ether (b.p. 60 - 80°C) as elutent. These conditions gave the best separation of 1-phenyl-1-phenylazobut-3-ene.

The absorption at 1610 cm.$^{-1}$ increased in intensity with successive samples while the other absorptions decreased in intensity. After 200 hours only a strong absorbance at 1610 cm.$^{-1}$ and an absorption of medium strength at 700 cm.$^{-1}$ were observed. This was not the spectrum of the expected product, 1-N-allyl benzaldehyde phenylhydrazone (see above).

The spots on the T.L.C. plates darkened in colour with each successive sample, from light yellow to light brown, but they never achieved the characteristic red colour of the spots for 1-N-allyl benzaldehyde phenylhydrazone.

1-Phenyl-1-phenylazobut-3-ene is not stable in refluxing nonane (b.p. 151°C) under nitrogen, but it does not rearrange to 1-N-allyl benzaldehyde phenylhydrazone.

Attempted Preparations of Optically Active Phenylazoalkanes.

Several methods were tried for the preparation of different optically active phenylazoalkanes, but success was only achieved in the case of 2-phenylazobornane (see page 196).

(a) Attempted Resolution of 1-Phenyl-1-phenylhydrazopropane.

Proiophenone phenylhydrazone was reduced to 1-phenyl-1-phenylhydrazopropane (55%; b.p. 140 - 142°C/0.1 mm.) with lithium aluminium hydride in refluxing tetrahydrofuran by the method of Bellamy and Guthrie.[23]

δ(100 MHz, CCl_4) 0.76 (t, 3H, Me), 1.28 - 1.82 (octet, 2H, CH_2), 3.39 (s, 1H, NH), 3.55 (t, 1H, CH), 4.64 (s, 1H, NH), 6.5 - 7.8 p.p.m. (m, 10H, aromatic).

The 1-phenyl-1-phenylhydrazopropane was then oxidised, with yellow mercuric oxide in ether to 1-phenyl-1-phenylazopropane (44%; b.p. 110 - 120°C/0.1mm.) by the method of Bellamy and Guthrie.[23]

δ(60 MHz, CCl_4) 0.72 (t, 3H, Me), 2.1 (octet, 2H, CH_2), 4.5 (t, 1H, CH), 7 - 8.3 p.p.m. (m, 10H, aromatic.).

1-Phenyl-1-phenylhydrazopropane (0.5g; 0.0022 mole) in ethanol (5 ml.) was slowly added, with stirring, to a solution of D-tartaric acid (0.332g; 0.0022 mole) in ethanol (30 ml.), under nitrogen. The mixture was stirred for 30 min. and then left at 20°C overnight.

The solvent was evaporated and the residual viscous oil was recrystallised twice from ethanol. The crystalline material obtained was very dark in colour and appeared to be partially decomposed.

The experiment was also performed with L-(-)-malic acid (0.298g; 0.0022 mole) instead of tartaric acid. Recrystallisations were attempted from ethanol, benzene/ethanol, benzene/tetrahydrofuran,

di-isopropyl ether/water and toluene, but no crystalline product was obtained. The use of 1-phenyl-1-phenylhydrazopropane (1.0g; 0.0044 mole) with L-(-)-malic acid (0.298g; 0.0022 mole) again gave a product which could not be crystallised. The product this time was chromatographed on a 20 x 0.5" dry alumina column with benzene as elutent and a bright yellow band separated, leaving brown impurities at the origin. The yellow band, however, could not be crystallised.

(b) Attempted Reaction of 2-Iodo-octane with Sodium Formylphenylhydrazine. (see Scheme 31 and Discussion, page 60)

(i) Preparation of Formylphenylhydrazine.[140] —— Phenylhydrazine (54g; 0.5 mole) was heated to boiling with 50% aqueous formic acid (184.0g; containing 2.0 mole of formic acid).

When the mixture was allowed to stir overnight colourless crystals (plates) of formylphenylhydrazine separated out. The product (50.45g; 76%) was collected, washed with ether, and then dried *in vacuo* (m.p. 143 - 145°C, lit.[143] m.p.145°C). In subsequent preparations the product was recrystallised from chloroform.

(ii) Preparation of Sodium Formylphenylhydrazine. —— The preparation was first carried out using the method of Freer and Sherman.[74] Reactions which were attempted with the material obtained by their method were unsuccessful (see below). Subsequent preparations were carried out with modifications of their method.

Formylphenylhydrazine was recrystallised from ethanol/chloroform and dried *in vacuo* before use. A solution of sodium ethoxide in ethanol was prepared by dissolving freshly cut sodium metal (10 g.) in dry ethanol (200 ml.).

Formylphenylhydrazine (59g; 0.49 mole) was added to the ethanolic sodium ethoxide. (200 ml; containing 0.455 mole of sodium ethoxide). The mixture was vigorously shaken until the formylphenylhydrazine dissolved to form a red solution, which was then poured into dry ether (1 litre) under nitrogen. The ether solution was shaken until homogenous and then allowed to stand, under nitrogen, for 24 hours to effect complete crystallisation of the sodium formylphenylhydrazine. The product was collected by filtration under nitrogen and then dried in vacuo: $\nu_{max.}$ (nujol) 3100(b), 1650(s), 1590(s), 1020(w), 870(w), 730(m), 680cm.$^{-1}$(m).

(If dry sodium formylphenylhydrazine is allowed to come into contact with air it rapidly decomposes[74] to a mixture of aniline, phenylhydrazine and sodium bicarbonate.)

(iii) Conversion of Octan-2-ol to 2-Iodo-octane.——2-Iodo-octane (82%; b.p. 84 - 85°C, lit.[75] b.p. 87 - 88°C) was prepared from octan-2-ol by the method of Berlak and Gerrard.[75] Octan-2-ol was stirred with phosphorous tri-iodide in carbon disulphide for 36 hours at 20°C.

(iv) Attempted Reaction of 2-Iodo-octane with Sodium Formylphenylhydrazine.——This experiment was adapted from the reaction of ethyl iodide with sodium formylphenylhydrazine as described by Freer and Sherman.[74]

A suspension of sodium formylphenylhydrazine (13.8g; 0.0875 mole) and 2-iodo-octane (21.27g; 0.0945 mole) was placed in a thick walled glass vessel which was placed in an autoclave.

The mixture was flushed with nitrogen for 10 min. and then the temperature was slowly raised to 100°C while the mixture was agitated. (The pressure at 100°C was 6.4 atmospheres.)

The temperature was maintained at 100°C for 3 hours, with agitation, and then allowed to cool to 20°C.

The ether solution was washed with water and the combined washings were extracted with ether. The combined extracts were dried ($MgSO_4$) and the ether was evaporated. The residue, which appeared to be a mixture of colourless crystals and unreacted iodide, was washed with petroleum-ether (b.p. 30 - 40°C) and then recrystallised from ethanol. A yellow solid (3.36g.) was recovered (m.p. 138-140°C). Comparison of infra-red spectra identified the material as formylphenylhydrazine (see above, lit.[140] m.p. 145°C).

(v) Attempted Reaction of Ethyl Iodide with Sodium Formylphenylhydrazine. —— The experiments below were also adapted from the method of Freer and Sherman,[74] who successfully reacted ethyl iodide with sodium formylphenylhydrazine.

Dried sodium formylphenylhydrazine (6g; 0.0381 mole) was rapidly added to a solution of ethyl iodide (6.1g; 0.039 mole) in dry dioxan (150 ml.) and the suspension was refluxed under nitrogen, for 3 hours during which the sodium formylphenylhydrazine appeared to go into solution and a colourless solid separated out. (After c.a. 10 min. reflux the colour of the solution changed from red to orange.)

The reaction mixture was then poured into water (300 ml.) and extracted with ether (4 x 100 ml.). The combined extracts were dried ($MgSO_4$) and the ether and residual dioxan were evaporated. In attempting to prepare a solution of the yellow oil in carbon tetrachloride for n.m.r. spectroscopy a solid precipitated out.

The solid was collected and recrystallised from ethanol. Comparison of the infra-red spectrum of the orange crystals (m.p.

130 - 135°C) with that of an authentic sample of formylphenylhydrazine (see above) identified the product as formylphenylhydrazine (lit.[140] m.p. 145°C).

An attempt was made to generate the sodium formylphenylhydrazine *in situ*. Formylphenylhydrazine (10g; 0.0736 mole) and ethyl iodide (11.52g; 0.074 mole) were added to a suspension of sodium hydride (1.68g; 0.0736 mole) in dry ether which was contained in a thick-walled glass vessel. The vessel was placed in an autoclave and flushed with nitrogen for 10 min. During heating the rubber gasket on the vessel gave way, and the pressure returned to atmospheric. The experiment was repeated three times. The first time the gasket again gave way. When the gasket on the apparatus was modified, the glass reaction vessel shattered during the next two attempts. The experiment was abandoned.

(vi) Determination of the Sodium Content of Sodium Formylphenylhydrazine.——A solution of sodium formylphenylhydrazine (1.58g; sufficient to give 0.1M if pure) in water (100 ml.) was prepared. Aliquots (25 ml.) of this solution were titrated against 0.1158N hydrochloric acid using a pH meter. The 25 ml. aliquots were estimated to be equivalent to 6 ml. of 0.1158N hydrochloric acid.

$$\text{Molarity of base solution} = \frac{6 \times 0.1158}{25}$$

$$= 0.0278\text{M}.$$

Therefore the percentage of sodium in the sodium formylphenylhydrazine was 27.8. (i.e. 27.8% sodium formylphenylhydrazine in the material tested).

The result suggested that the material used as sodium formylphenylhydrazine in the experiments described above was actually

a mixture of sodium formylphenylhydrazine and formylphenylhydrazine itself.

(d) The Attempted Reaction of Ethyl Iodide with Phenyldiazotate.

(i) The Preparation of the Phenyldiazonium Chloride Solution.—— A 15% W/V aqueous solution (50 ml.) of phenyldiazonium chloride (containing 7.5g; 0.0554 mole of $Ph\ N_2^+\ Cl^-$) was prepared by an adaptation of the method described in Vogel.[141]

Redistilled aniline (4.98g; 0.0554 mole) was dissolved in aqueous hydrochloric acid (25 ml; 0.135M). The solution was cooled to 0°C and aniline hydrochloride precipitated. The temperature was maintained at 0 - 5°C while a solution of sodium nitrite (4.14g; 0.06 mole) in water (25 ml.) was slowly added, with stirring, until the reaction mixture gave an immediate blue colouration with potassium iodide-starch paper. The resulting solution was clear and faintly yellow in colour.

(ii) Preparation of Potassium Phenyldiazotate.[142] —— The freshly prepared 15% phenyldiazonium chloride solution (10 ml.) described above was slowly added, with stirring, to a mixture of potassium hydroxide (150 g.) and water (60 ml.) at 5°C.

The temperature was then allowed to increase to 20°C so that all the potassium hydroxide dissolved. The solid material which separated was collected. An attempt was made to recrystallise the product from absolute ethanol but only an oil was obtained. When dry ether (1 litre) was added to the oil a yellow curdy precipitate formed. This was collected and washed with dry ether. Colourless crystals (plates), which reacted in air to form a yellow oil, also separated from the ether solution. The curdy percipitate was again dissolved in absolute ethanol and precipitated by addition of

dry ether. A sample of the precipitate was dissolved in water (1 ml.) and a brown oily layer separated. The aqueous layer was not alkaline to litmus i.e. the precipitate was not potassium hydroxide. The 60 MHz n.m.r. spectrum of the precipitate, in $[^2H_6]$ dimethylsulphoxide, showed only an aromatic multiplet (6.5 - 7.3 p.p.m.) which suggested that the material was potassium phenyldiazotate (0.89g; 50%). A subsequent preparation on the same scale gave a yield of 1.70g; (95%).

(iii) The Attempted Reaction of Potassium Phenyldiazotate with Ethyl Iodide to Form 1-Ethyl-2-phenyldiazotate.[78]

A solution of dry potassium phenyldiazotate (0.89g; 0.0056 mole) in hexamethylphosphoramide (H.M.P.A.) (60 ml.) was mixed with ethyl iodide (0.872g; 0.0056 mole) under nitrogen. The mixture was stirred at 40°C, under nitrogen, for 12 hr. It became dark brown in colour.

The reaction mixture was poured into water (250 ml.) and extracted with ether (3 x 100 ml.). The combined extracts were dried ($MgSO_4$) and the ether was evaporated. The residual dark brown mobile liquid was distilled but only H.M.P.A. (b.p. 60 - 70°C/0.5 mm.), was obtained. The experiment was repeated, but again only H.M.P.A. was collected.

(e) The Attempted Preparation of 2-Methyl-2-phenylazopropane. (Analogous to Scheme 33)

(i) Preparation of Benzene Sulphonyl Hydroxylamine (Piloty's acid). —— Benzene sulphonyl hydroxylamine was prepared by the method of Piloty.[80]

Hydroxylamine hydrochloride (32.5g; 0.465 mole) was dissolved in hot water (11 ml.) and a solution of sodium ethoxide (150 ml. from 10.6g; 0.46 mole of sodium) was slowly added, with

stirring, so that no boiling occurred.

The sodium chloride, which separated, was filtered off and the filtrate was diluted with absolute ethanol (150 ml.). Benzene sulphonyl chloride (25g; 0.141 mole) was slowly added.

When the reaction appeared to be complete, the ethanol was evaporated and the residual colourless solid was recrystallised from hot water and then dried *in vacuo*. Benzene sulphonyl hydroxylamine (10.51g; 43%) (m.p. 125 - 126°C, *lit.*[80] m.p. 126°C) was obtained. Mass spectrum - P173.

(ii) *The preparation of* N-(p-Nitrophenyl Sulphonoxybenzene) Sulphonamide. (see Scheme 33) —— N-(p-Nitrophenyl sulphonoxybenzene) sulphonamide (73) (m.p. 178 - 179°C, *lit.*[81] m.p. 179°C) was prepared by the method of Porter and Marnett[79] and recrystallised from ether. The mass spectrum of the product showed a peak at 342 (Ph SO_2. NH. $SO_2C_6H_4NO_2$ requires 342) with no peak at 358 (Ph SO_2. NH. $OSO_2C_6H_4NO_2$ requires 358). The compound may have lost an atom of oxygen in the spectrometer but subsequent reactions (see below) also suggested that the compound was Ph SO_2.NH.$SO_2C_6H_4NO_2$. The formula reported by Lowoski and Schieffele,[81] on the basis of elemental analysis, was Ph SO_2.NH.$OSO_2C_6H_4NO_2$.

N-(p-Nitrophenyl sulphonoxybenzene) sulphonamide was also prepared by the method of Lowoski and Schieffele,[81] but the yield was low (17%) and the product was impure (m.p. 155 - 165°C, *lit.*[81] m.p. 179°C).

A modification of the method of Porter and Marnett, in which triethylamine was added before the p-nitrobenzene sulphonyl chloride, was also tried. The mass spectrum of the product (m.p. 152 - 158°C, *lit.*[81] m.p. 179°C) suggested it was a mixture consisting mainly of

Ph SO_2.NH.$SO_2C_6H_4NO_2$ (m/e 342) and a little Ph SO_2.NH.O $SO_2C_6H_4NO_2$ (m/e (P-1) 357).

(iii) Attempted Preparation of 2-Methyl-2-phenylazopropane. (see Scheme 33) —— An attempt was first made to prepare the N-phenylsulphamide of 1-phenylethylamine by the method of Porter and Marnett.[79] Only p-nitrobenzene sulphonamide (m.p. 177 - 179°C, lit.[143] m.p. 178°C), identified by n.m.r. spectroscopy and the mass spectrum (P202), was isolated.

In order to discover why the reaction had not worked, what was thought to be the N-phenylsulphamide of 2-amino-2-methylpropane was synthesised and obtained as a brown oil. An attempt was then made to convert this crude product to 2-methyl-2-phenylazopropane by oxidation with sodium hypochlorite in a mixture of 2 N aqueous sodium hydroxide and hexane, as described by Porter and Marnett.

The crude product from the oxidation was chromatographed on a 20 x 1" dry alumina column with petroleum-ether (b.p. 40 - 60°C) as elutent. Only enough bright yellow oil (c.a. 40 mg.) was recovered from the column for characterisation by n.m.r. and mass spectroscopy. δ (60 MHZ, CCl_4) 1.32 (s, 9H, t-butyl), 7.4 - 8.4 p.p.m. (m, 4H, aromatic). The aromatic multiplet was that of an A_2B_2 system, which suggested a para-substituted phenylazo compound. (The spectrum was not that of 2-methyl-2-phenylazopropane (see page 173) the aromatic multiplet of which is not an A_2B_2 system. δ (60 MHz, neat) 1.32 (s, 9H, t-butyl), 7.3 - 7.8 p.p.m. (m, 5H, aromatic).) Mass spectrum - P207, 182, 179. Accurate mass measurement 207.099082 ($C_{10}H_{13}N_3O_2$ requires 207.10070). The compound was thought to be 2-methyl-2-p-nitrophenylazopropane (72).

Reactions to Synthesise a Sample of 2-Methyl-2-p-nitrophenylazopropane by an Unambiguous Route.

(A) Attempted Nitration of 2-Methyl-2-phenylazopropane.

(i) With fuming Nitric Acid.—— This method was an adaptation of that described by Burns et. al.[144] for the nitration of azobenzene.

2-Methyl-2-phenylazopropane (0.40g.) was slowly added, with stirring, to fuming nitric acid (8 ml.; S.G. 1.5) at -10°C. The mixture was stirred for 2 hours at -10°C and then poured onto crushed ice (30 g.). The aqueous solution was neutralised by addition of solid potassium carbonate and black tar separated. The mixture was poured into water (200 ml.) and then extracted with ether (3 x 100 ml.). The combined extracts were dried ($MgSO_4$) and the ether was evaporated. The residual dark brown tar was extracted with ether (50 ml.). The extract was chromatographed on a 24 x 1" dry alumina column with benzene as elutent. No material with an n.m.r. spectrum resembling that of the expected product, 2-methyl-2-p-nitrophenylazopropane, was obtained.

(ii) With Acetyl Nitrite.[145]—— 2-Methyl-2-phenylazopropane (1.62g.; 0.01 mole) was placed in a 5 ml. r.b. flask which was fitted with a small magnetic stirrer, an injection septum and a drying tube ($Ca\ Cl_2$). The 2-methyl-2-phenylazopropane was cooled to 0°C and a mixture of cold acetic anhydride (0.95 ml; 0.01 mole) and concentrated nitric acid (0.42 ml; 0.01 mole) was slowly introduced from a syringe over a period of 1 hour. The reaction mixture became dark brown in colour soon after the addition of the nitrating mixture was begun.

After a further two hours stirring at 0°C the reaction

mixture was quenched by the addition of water (30 ml.), extracted with ether (3 x 50 ml.) and then with aqueous saturated sodium bicarbonate solution (2 x 100 ml.). The combined extracts were dried and the ether was evaporated.

The residue was chromatographed on a 24 x 2" dry alumina column with petroleum-ether (b.p. 60 - 80°C) as elutent. Only the starting material, 2-methyl-2-phenylazopropane (0.47 g.) was recovered from the column.

(B) Attempted Coupling of t-Butyl Zinc Chloride with p-Nitrophenyldiazonium Fluoroborate. This reaction was analogous to that for the preparation of 2-methyl-2-phenylazopropane and was adapted from the method of Curtin and Ursprung.[84] (see page 173).

(i) The Preparation of p-Nitrophenyldiazonium Fluoroborate. This salt was prepared by an adaptation of the method described by Roe.[146]

p-Nitroaniline (34.5g; 0.25 mole) was added to a mixture of concentrated hydrochloric acid (72 ml; 0.75 mole) and water (72 ml.). The mixture was cooled to 0°C and a cold solution of sodium nitrite (17.3g; 0.25 mole) in water (50 ml.) was slowly added, with stirring. The temperature was kept below 0°C by the addition of small pieces of dry ice.

Sodium fluoroborate (37.4g; 0.34 mole) in water (120 ml.) was added to the diazotised solution, with vigorous stirring. The mixture was stirred at 0°C during a further 30 min. The precipitate was filtered off, washed first with cold 5% aqueous sodium fluoroborate solution (25 ml.), then with ice-cold methanol (30 ml.), and finally with ether (5 x 50 ml.). The precipitate was sucked as dry

as possible after each washing and then the product was dried *in vacuo* overnight. The yield of dried product was 56 g. (95%).

(ii) *Attempted Preparation of* 2-Methyl-2-p-nitrophenylazopropane. —— A suspension of t-butyl zinc chloride (1 molar equivalent) in dry ether (290 ml.) was prepared from the reaction of t-butyl magnesium chloride[147] with anhydrous zinc chloride as described by Curtin and Ursprung.[84]

The suspension was slowly added to a suspension of p-nitrophenyldiazonium fluoroborate (35 g; 0.895 molar equivalents) in dry ether (190 ml.) at -10°C, with efficient stirring, under nitrogen. The mixture was stirred for a further 16 hours and then decomposed by the addition of saturated, aqueous ammonium chloride solution (85 ml.). The ether was evaporated and the residual mixture was steam distilled.

The distillate was extracted with ether and the combined extracts were dried ($MgSO_4$). On evaporation of the ether an orange oil was obtained. The oil was chromatographed on a 20 x 1.5" dry alumina column with petroleum-ether (b.p. 40 - 60°C) as elutent and separated into two yellow bands.

One gave crystalline material which was washed with ice-cold ethanol and then dried *in vacuo* (m.p. 78 - 80°C). The 60 MHz n.m.r. spectrum (CCl_4) showed only an A_2B_2 aromatic system. The compound was shown, by comparison of infra-red, n.m.r. and mass spectra with those of an authentic sample, to be 1-chloro-4-nitrobenzene (*lit.*[148] m.p. 83°C).

The n.m.r. spectrum of the material from the other yellow band showed: δ (60 MHz, CCl_4) 1.35, (s, 9H, t-butyl), 1.40 (s, 9H, t-butyl), 7.3 - 7.8 p.p.m. (m, 4H, aromatic). The aromatic

multiplet was that of an A_2B_2 system. Mass spectrum: P218, 161, 133, 85, accurate mass measurement, 218.178079 ($C_{14}H_{22}N_2$ requires 218.178290). The n.m.r. and mass spectra suggested the compound was 2-methyl-2-p-t-butylphenylazopropane. Further evidence of the assigned structure was gained from comparison of the fragmentation pattern in the mass spectrum corresponding to loss of t-butyl (-57) followed by loss of N_2 (-28).

The mother liquor (ether), from which the 1-chloro-4-nitrobenzene had been crystallised, was evaporated. The n.m.r. spectrum of the residue (60 MHz, CCl_4) showed a singlet (1.45 p.p.m.) and an aromatic multiplet (7.3 - 8.4 p.p.m.). Examination of the integration suggested that this might be a mixture of 2-methyl-2-p-nitrophenylazopropane and 1-chloro-4-nitrobenzene.

The mixture was distilled. A little colourless liquid (b.p. 45°C/0.01 mm.) was collected, the n.m.r. spectrum (60 MHz, CCl_4) of which showed only aromatic absorptions (7.2 - 8.3 p.p.m.). The compound was shown, by comparison of n.m.r. and infra-red spectra with those of an authentic sample, to be nitrobenzene.

The residue from the distillation was extracted with ether, the ether was evaporated, and the residue crystallised. This was thought to be a mixture of 2-methyl-2-p-nitrophenylazopropane and 1-chloro-4-nitrobenzene. Mass spectrum; P207, 105 (for NO_2 Ph N = N - But and NO_2 Ph N = N respectively), 159, 157 (for p NO_2 Ph Cl).

An attempt was made to separate the components by reacting the 1-chloro-4-nitrobenzene with piperidine (see below).

(iii) Attempted Separation of 1-Chloro-4-nitrobenzene and 2-Methyl-2-p-nitrophenylazopropane by the Preparation of the Piperidine Derivative of 1-Chloro-4-nitrobenzene.

In a trial experiment the piperidine derivative of pure 1-chloro-4-nitrobenzene was prepared by an adaptation of the method described by Levin and Tamarc.[149]

1-Chloro-4-nitrobenzene (0.03 mole, 4.72 g.) was suspended in absolute ethanol (25 ml.) and piperidine (0.24 mole; 20.82 g.) was added. The mixture was refluxed for 1 hour and then cooled to 0°C. The material which had separated was filtered off, and the mother liquor was treated with water (100 ml.) in order to precipitate the product. This gave 1.9 g. of bright yellow crystals (m.p. 104 - 105°C; from butan-1-ol): δ (60 MHz, CCl_4) 1.73 (m, 6H, CH_2), 3.42 (m, 4H, CH_2), 6.6 - 8.2 p.p.m. (m, 4H, aromatic). The aromatic multiplet was that of an A_2B_2 system. A further quantity of 1-nitro-4-piperidinobenzene was recovered from the butan-1-ol mother liquor. (Total yield 44%)

The material which separated from the reaction mixture before water was added gave a colourless solid (0.43 g; m.p. 247 - 248°C; from ethanol): δ (60 MHz, CCl_4) 1.8 (m, 6H, CH_2), 3.? (m, 4H, CH_2), 9.5 p.p.m. (broad m, 2H, $\overset{+}{N}H_2$); mass spectrum, 85, 36, 38. It was readily soluble in water. The compound was identified as piperidine hydrochloride (lit.[101] m.p. 245°C). (The mass spectrum did not show the parent ion peak for piperidine hydrochloride itself, but 85 corresponds to the molecular weight for piperidine, and 36 and 38 to the molecular weights of H Cl.)

The mixture of 1-chloro-4-nitrobenzene and 2-methyl-2-p-nitrophenylazopropane (0.68 g.) was dissolved in absolute ethanol (15 ml.), and piperidine (3 g; 0.0345 mole) was added. The mixture was refluxed for 1 hour and then the ethanol was evaporated. The residual solid was treated with dilute hydrochloric acid until

just acid to litmus to convert 1-nitro-4-piperidinobenzene to the corresponding hydrochloride. The resulting solution was extracted with ether (3 x 50 ml.); the combined extracts were dried ($MgSO_4$) and then the ether was evaporated. The residue was a mixture of crystalline material and oil. The n.m.r. spectrum (60 MHz, CCl_4) was similar to that of the starting mixture of 1-chloro-4-nitrobenzene and 2-methyl-2-p-nitrophenylazopropane but the intensity of the absorption of the aromatic multiplet was reduced indicating that some 1-chloro-4-nitrobenzene (c.a. 30%) had been removed.

The attempted separation was not totally successful, probably because all of the 1-chloro-4-nitrobenzene did not react with the piperidine or because once the 1-nitro-4-piperidinobenzene had been formed some of it was hydrolysed instead of being converted to the hydochloride by addition of dilute hydrochloric acid.

(C) The Attempted Reaction of t-Butyl Chloride with p-Nitrophenylhydrazine. — p-Nitrophenylhydrazine (5g; 0.0326 mole) was dissolved in pyridine (40 ml.) and a solution of t-butyl chloride (3 g; 0.0326 mole) in pyridine (10 ml.) was added. The dark brown mixture was refluxed overnight. No pyridine hydrochloride crystallised out on cooling.

The pyridine was evaporated and the residue was dried *in vacuo* for 1 hour to remove unreacted t-butyl chloride (b.p. 52°C). The crystalline residue was shown, by comparison of its infra-red and n.m.r. spectra with those of an authentic sample, to be p-nitrophenylhydrazine.

(D) The Attempted Reaction of t-Butyl Iodide with p-Nitrophenylhydrazine. — This reaction was an adaptation of the method for the preparation of t-butylhydrazine, described by

Westphal[150] (see below).

A solution of redistilled t-butyl iodide (6.22 g; 0.0338 mole) in 'AnalaR' methanol (10 ml.) was added to a suspension of p-nitrophenylhydrazine (5 g; 0.0326 mole) in 'AnalaR' methanol (80 ml.). The mixture was refluxed, under nitrogen, for 68 hours. Soon after boiling commenced, all the p-nitrophenylhydrazine dissolved and the solution became deep red in colour.

The methanol was evaporated and the residue was dried in vacuo. The n.m.r. spectrum (60 MHz, MeOH) showed only absorptions in the aromatic region. (The region upfield from 6 p.p.m. was obscured by the absorptions of the solvent.) By comparison of n.m.r. spectra, one A_2B_2 system in the aromatic region was assigned to p-nitrophenylhydrazine. There remained another A_2B_2 system and a singlet in the aromatic region to be accounted for.

The product mixture was chromatographed on a 20 x 1" dry alumina column with benzene as elutent. One yellow band separated from the origin. The material from this band was not soluble enough in carbon tetrachloride for an n.m.r. spectrum to be run. The spectrum in methanol (60 MHz) suggested that this was the compound responsible for the other A_2B_2 system in the mixture described above.

The unknown compound (0.15 g.) was mixed with yellow mercuric oxide (1.5 g.) in dry ether (50 ml.), and the suspension was stirred, under nitrogen, overnight. The inorganic materials were removed by filtration through a celite pad and the residue was washed with ether. The ether was evaporated from the combined washings and filtrate, and the residual orange solid was dried in vacuo. The product was still insoluble in carbon tetrachloride. The 60 MHz n.m.r. spectrum in methanol was the same as that described

above, before the attempted oxidation.

(E) The Attempted Reaction of t-Butylhydrazine with 1-Chloro-4-nitrobenzene.

(i) Preparation of t-Butylhydrazine Hydrochloride.— t-Butylhydrazine hydrochloride was prepared by an adaptation of the method of Westphal.[150]

A suspension of hydrazine hydrate (0.47 mole; 23.85 g.) and t-butyl chloride (0.487 mole; 45 g.) in methanol (50 ml.) was refluxed for 3 days and then allowed to cool. The methanol solution was decanted from the solid hydrazine hydrochloride which had separated. The methanol was evaporated and ether was added to the residue. More hydrazine hydrochloride which separated out was removed by filtration. The ether solution was treated with gaseous HCl until a white floculant precipitate was obtained. The precipitate was collected, recrystallised from methanol/ethyl acetate and dried *in vacuo* to give t-butylhydrazine hydrochloride (0.94g; 1.6%) (m.p. 177 - 178°C, lit.[150] m.p. 202°C) $\nu_{max.}$ (nujol) 3320(m), 3200(w), 1600(m), 1200(w), 1125(m), 1100(m), 960(m), 930(w), 860(w), 730 $cm.^{-1}$(w). (The hydrazine hydrochloride which was isolated did not form a nujol mull readily and no infra-red spectrum could be obtained. After recrystallisation from ethanol the m.p. of 90 - 92°C identified this compound as the monohydrochloride, lit.[148] m.p. 89°C.)

(ii) The Attempted Reaction of t-Butylhydrazine with 1-Chloro-4-nitrobenzene.— t-Butylhydrazine hydrochloride (0.4g; 0.00322 mole) and 1-chloro-4-nitrobenzene (0.507g; 0.00322 mole) were dissolved in 'AnalaR' pyridine (40 ml.), and the solution was refluxed, under nitrogen, for 23 hours. The pyridine was

evaporated, and the residual mixture of yellow oil and colourless solid was dried *in vacuo*. No part of the product mixture was soluble in carbon tetrachloride. The 60 MHz n.m.r. spectrum of the product mixture, in methanol, suggested that it was mainly 1-chloro-4-nitrobenzene (see page 188).

The mixture was dissolved in absolute ethanol (35 ml.) and pyridine (1g.) was added to react with any free hydrochloric acid. The solution was refluxed, under nitrogen, for 12 hr. When the solvent was removed, the product was still insoluble in carbon tetrachloride. The 60 MHz n.m.r. spectrum, in methanol, again indicated the presence of 1-chloro-4-nitrobenzene (see page 188).

The Behaviour of Phenylazobornane and Camphor Phenylhydrazone Under Various Conditions.

Preparation of Compounds.

Camphor Phenylhydrazone.—— Camphor phenylhydrazone was prepared by an adaptation of the general method described in Vogel[151] for the preparation of phenylhydrazones of aldehydes and ketones.

(+)- Camphor (10.50g; 0.0692 mole) in ethanol (50 ml.) was added to a solution of phenylhydrazine hydrochloride (10.0g; 0.0692 mole) and sodium acetate (16 g.) in water (100 ml.). A further 30 ml. of ethanol was added, with shaking, until a clear solution formed. The solution was refluxed, under nitrogen, for 1.5 hours and then allowed to cool. The ethanol was evaporated and the residual mixture of water and oil was extracted with ether (3 x 100 ml.). The extracts were dried ($MgSO_4$), the ether was evaporated and the residual oil was fractionally distilled. The three fractions which were collected boiled over the range of 120 - 132°C/0.1 mm. They were shown, by comparison of infra-red and n.m.r. spectra, to be the same material, camphor phenylhydrazone. (11.55g; 58%): $\nu_{max.}$ (film) 3300(m), 2900(s), 1650(w), 1600(s), 1500(s), 1450(m), 1390(m), 1370(m), 1300(s), 1250(s), 1160(m), 1110(s), 1080(s), 1050(s), 1000 (m), 880(m), 820(w), 740(s), 680 $cm.^{-1}$(s). δ (100 MHz, CCl_4) 0.73 (s, 3H, Me), 0.90 (s, 3H, Me), 1.04 (s, 3H, Me), 0.8 - 2.4 (m, 7H, CH_2 and CH), 6.4 (broad,s, 1H, N-H), 6.5 - 7.3 p.p.m. (m, 5H, aromatic). The phenylhydrazone slowly crystallised on standing. Camphor has δ (100 MHz, CCl_4) 0.77 (s, 3H, Me), 0.80 (s, 3H, Me), 0.90 (s, 3H, Me), 1.15 - 2.35 p.p.m. (m, 7H, CH_2 and CH).

The phenylhydrazone could not be prepared by refluxing an equimolar mixture of redistilled phenylhydrazine and camphor in

ethanol, under nitrogen, overnight. Neither was the phenylhydrazone obtained when an equimolar mixture of redistilled phenylhydrazine and camphor was heated, without solvent, under nitrogen, for 1.5 hours. Only the starting materials were recovered from both these experiments. The latter conditions readily gave the phenylhydrazone of cyclopentanone.

The Preparation of 2-Phenylazobornane.—— During the preparation of this compound difficulty was encountered in separating the phenylazobornane from camphor phenylhydrazone, because of the ease with which the azo compound rearranged to the phenylhydrazone either when the reaction mixture was being worked-up, or chromatographed.

Reduction of camphor phenylhydrazone with lithium aluminium hydride, in tetrahydrofuran, as described below, was found to give phenylazobornane in the highest yield. Oxidation of the intermediate 2-phenylhydrazobornane occurred during work-up, and oxidation with yellow mercuric oxide was not necessary in most cases.

Reductions of camphor phenylhydrazone with lithium aluminium hydride in dioxan, sodium in liquid ammonia, sodium in ethanol, and sodium in amyl alcohol were unsuccessful.

A solution of camphor phenylhydrazone (5 g; 0.016 mole) in dry tetrahydrofuran (40 ml.) was slowly added to a stirred suspension of lithium aluminium hydride (2.48 g; 0.064 mole) in dry tetrahydrofuran (200 ml.). The mixture was refluxed under nitrogen for two weeks.

Water (15 ml.) was cautiously added to destroy the excess of lithium aluminium hydride. This was followed by the addition of 4N aqueous sodium hydroxide solution (200 ml.). The resulting mixture was poured into water (400 ml.), extracted with ether

(4 x 100 ml.), and then dried ($MgSO_4$). A bright yellow oil (1.90 g.) was obtained after the ether had been evaporated.

The product was chromatographed on a 20 x 1.5" wet alumina column, with petroleum-ether (b.p. 60 - 80°C) as elutent. A bright yellow band (1.09 g.) passed rapidly down the column. The n.m.r. spectrum (60 MHz, CCl_4) of this material suggested that some camphor phenylhydrazone was still present.

The material was rechromatographed on a wet silica gel column, with petroleum-ether (b.p. 60 - 80°C) as elutent. The n.m.r. spectrum (60 MHz, CCl_4) of the material that came through the column as a bright yellow band, showed that the amount of camphor phenylhydrazone, relative to phenylazobornane, had increased. (The <u>CH</u> - N=N absorption of the phenylazobornane (3.2 p.p.m.) had decreased in intensity while the NH of the phenylhydrazone (6.4 p.p.m.) had increased in intensity.

The mixture was again chromatographed on a 20 x 0.5" dry alumina column with petroleum-ether (b.p. 40 - 60°C) as elutent. The bright yellow material recovered (0.61 g; 12%) was shown by n.m.r. spectroscopy, to be 2-phenylazobornane: δ (100 MHz, CCl_4) 0.72 (s, 3H, Me), 0.95 (s, 3H, Me), 1.23 (s, 3H, Me), 1.2 - 2.3 (m, 7H, CH_2 and CH), 3.0 - 3.4 (m, 1H, <u>CH</u> - N=N), 7.1 - 7.7 p.p.m. (m, 5H, aromatic). Mass spectrum - P242, 137 (137 corresponds to a loss of 105 i.e. loss of Ph - $\overset{+}{N} \equiv N$ characteristic of phenylazo-alkanes). 2-Phenylazobornane isomerised to camphor phenylhydrazone after 3 days in carbon tetrachloride at 20°C.

In subsequent preparations of 2-phenylazobornane all chromatography was carried out on dry alumina columns.

An attempt was also made to prepare 2-phenylazobornane

by the reductive cleavage[152] of camphor 1-*N*-*p*-tosylphenylhydrazone with lithium hydride.

Crude camphor 1-*N*-*p*-tosylphenylhydrazone was prepared by mixing camphor phenylhydrazone (2 g; 0.00638 mole) and toluene-*p*-sulphonyl chloride (5 g; 0.0262 mole) in pyridine (12 ml.). Courless needles of pyridine hydorchloride began to separate after c.a. 30 min. The reaction mixture was poured into water (50 ml.) after a further 30 min. and a light brown oil separated. The oil was extracted into ether and then the extracts were dried ($MgSO_4$). A viscous brown oil (2.89 g; 93%) was obtained after the ether and pyridine had been evaporated. δ (60 MHz, CCl_4) 0.75 (s, 3H, Me), 0.92 (s, 3H, Me), 1.10 (s, 3H, Me), 1.1 - 2.2 (m, 7H, CH_2 and CH), 2.38 (s, 3H, *p*-Me), 6.4 - 7.2 p.p.m. (m, 9H, aromatic).

Lithium hydride (3 g; 0.378 mole) was added to a solution of crude camphor 1-*N*-*p*-tosylphenylhydrazone (2.89 g; 0.00595 mole) in dry toluene (140 ml.), and the mixture was refluxed overnight under nitrogen. The excess of lithium hydride was filtered off, and the solvent was evaporated from the reaction solution. The residue was taken up in ether, washed with saturated brine (2 x 100 ml.) and dried ($MgSO_4$). The n.m.r. spectrum of the concentrated material showed it was camphor 1-*N*-*p*-tosylphenylhydrazone.

The reductive cleavage with lithium hydride was also unsuccessful when dry dioxan was used as solvent.

In similar experiments with sodium or potassium hydride in dioxan, camphor 1-*N*-*p*-tosylphenylhydrazone was cleaved to camphor phenylhydrazone, and no 2-phenylazobornane was obtained.

Measurement of Optical Rotations.

(i) (+)-Camphor. —— A 1% W/V solution of (+)-camphor (0.05 g.) in dry ethanol was prepared and placed in a clean dry cell (pathlength 1 decimeter). The solution was allowed to equilbrate to 28°C in the cell compartment of a Perkin-Elmer 141 automatic polarimeter for 15 min. before the optical rotation was recorded. Three concordant readings were taken at each wavelength. (see Table 13). The rotations of the solvent and cell were also recorded at each wavelength.

The specific rotations ($[\alpha]^{28}$) and molecular rotations ($[M]^{28}$) at 28°C were calculated using the following formulae:

$$[\alpha]^{28} = \frac{100\,\alpha}{l.\,c}$$

and

$$[M]^{28} = \frac{[\alpha]^{28} \times M.W.}{100}$$

where α was the observed rotation (corrected for solvent and cell contributions)

l was the pathlength of the cell (in decimeters).

c was the concentration of the solution in g./100 ml.

(ii) Camphor Phenylhydrazone.——The optical rotations of a 1% W/V solution of camphor phenylhydrazone in dry methanol were determined, as described above for a solution of camphor in ethanol. The values recorded were found to drift over a four hour period e.g. 546 nm., +0.046 ⟶ +0.007; 578 nm., +0.022 ⟶ -0.012; 589 nm., +0.022 ⟶ -0.004. The solution also darkened in colour on standing overnight. The decrease in optical rotation appeared to be caused by oxidation of the camphor phenylhydrazone.

The absorbance of a 1% W/V solution of camphor phenylhydrazone in methanol ($\lambda_{max.}$ 273 nm., ε 18,400) was not high

enough to absorb all the incident light at any of the wavelengths used for measurement of optical rotation (see measurement of the optical rotation of 2-phenylazobornane).

The optical rotation of a 1% W/V solution of camphor phenylhydrazone in methanol after 2 days was measured and the values did not change over a 2 hour period: λ 589 nm., -0.029°; 578 nm., -0.043°, 546 nm., -0.042°.

A fresh solution was sparged with nitrogen for c.a. 15 min. and then measurements were taken over a six hour period. Air was then blown through the sample for 30 min. and the measurements were again taken. An increase in the values recorded after treatment with air was observed. (This may have been caused by evaporation of solvent but this should have also occured when nitrogen was blown through the sample.) The solution was stored at 20°C for 2 days and the measurements were again taken (see Table 14). Air was blown through the solution for a further 45 min. and again there was an increase in the rotation.

(iii) 2-Phenylazobornane.——An attempt was made to record the optical rotation of a 1% W/V solution of phenylazobornane in dry methanol at various wavelengths, as in the case of camphor described above, but satisfactory readings were not obtained.

2-phenylazobornane has λ max. 410 nm. (ε 145) in the U.V. spectrum. The absorbance of a 1% W/V solution in a cell with 1 cm. pathlength on the longer wavelength side of this λ max., i.e. at 436 nm. was greater than the 95% limit for the polarimeter. The absorbance of a 1% W/V solution in a cell with 1 decimeter pathlength on the shorter wavelength side of this λ max., i.e. at 365 nm., was also greater than the 95% limit of the polarimeter

but was within the limit of the polarimeter using a cell with 1 cm. pathlength. For measurements at 365 and 436 nm. a 1% W/V solution was diluted 5X and a 1 cm. cell was used (see Table 15).

Measurements were made at 546 nm. with a 1 decimeter cell in most kinetic experiments (see later).

^{1}H N.M.R. Study of the Stability of 2-Phenylazobornane in Methanol.

The 60 MHz n.m.r. spectrum of a fresh solution of 2-phenylazobornane in dry methanol was recorded: δ 0.77 (s, 3H, Me), 0.96 (s, 3H, Me), 1.27 (s, 3H, Me), 1.1 - 2.5 (m, 7H, CH and CH_2), 7.2 - 7.8 p.p.m. (m, 5H, aromatic). The CH - N=N absorption was obscured by the solvent.

The 60 MHz spectrum of camphor phenylhydrazone was recorded for comparison: δ 0.77 (s, 3H, Me), 0.98 (s, 3H, Me), 1.13 (s, 3H, Me), 1.2 - 2.4 (m, 7H, CH and CH_2), 6.5 - 7.2 p.p.m. (m, 5H, aromatic).

The spectrum of 2-phenylazobornane was recorded again after 15 min., 40 min., 90 min., and 4 hours, and no change in the spectrum was observed during this period. After 3 days there was a small change in the spectrum; two weak absorptions had appeared at c.a. 6.6 p.p.m. which indicated the presence of a very small amount of camphor phenylhydrazone.

Study of the Base Catalysed Rearrangement of 2-Phenylazobornane in Methanol by Optical Rotation.

A 1% W/V solution of 2-phenylazobornane in dry methanol (5.3 ml.), which had been sparged with dry nitrogen, was placed in a 1 decimeter cell which was thermostated at 45°C. The optical rotations at 546 nm. were recorded at 30 min. intervals over a 2 hour period. The rotation remained fairly constant in the range -1.248° to -1.252°.

A solution of sodium methoxide was prepared by dissolving freshly cut sodium (54 mg.) in dry methanol (0.75 ml.). A 0.25 ml. sample of this solution was thoroughly mixed with the 2-phenylazobornane solution in the cell, and the optical rotations were measured at 45°C. at 5 min. intervals initially and finally at 10 min.

intervals (see Table 16).

The rotation reached +0.029°, the value for a 1% W/V solution of camphor phenylhydrazone (see page 204), after 180 min. and increased to more positive values (+0.095° after 280 min.). After the solution had been stored overnight the rotation had decreased again to +0.014°. This behaviour suggested that more than one reaction had taken place.

The solution was made slightly acid to litmus by the addition of a solution of acetic acid (0.6 ml.) in brine (100 ml.), and then extracted with ether (3 x 50 ml.). The combined extracts were dried ($MgSO_4$), and the ether was evaporated. The n.m.r. spectrum (60 MHz, CCl_4) identified the residual brown oil as camphor phenylhydrazone.

The Stability of Camphor Phenylhydrazone in Methanol Containing Sodium Methoxide.

The optical rotation (+0.035° at 546 nm.) of a 1% W/V solution of camphor phenylhydrazone in dry methanol (5.3 ml.) was recorded at 25°C in a 1 decimeter cell. This value was found to be stable over 40 min.

A solution of sodium methoxide was prepared by dissolving freshly cut sodium (54 mg.) in dry methanol (0.75 ml.). A 0.25 ml. sample of this solution was thoroughly mixed with the camphor phenylhydrazone solution in the cell, and the optical rotations were measured at 15 min. intervals over a 1.5 hour period, the first reading (+0.025°) being taken within 5 min. of addition of the sodium methoxide solution.

The addition of the sodium methoxide solution (0.25 ml.) diluted the camphor phenylhydrazone solution, causing the initial

rotation to decrease from +0.035° to +0.025°. The five subsequent readings, at 30 min. intervals, were all +0.029°.

The results of this experiment suggested that camphor phenylhydrazone in methanol was stable in the presence of sodium methoxide at 25°C.

The U.V. Spectra of 2-Phenylazobornane and Camphor Phenylhydrazone.

The U.V. spectra of solutions of camphor phenylhydrazone and 2-phenylazobornane in dry methanol (both 2 mg./ml.) were recorded in the region 300 - 700 nm: 2-phenylazobornane had λ max. 402 nm. (ε 182); camphor phenylhydrazone had λ max. 402 nm. (ε 11.3).(An earlier sample of 2-phenylazobornane had λ max. 410 n m.)

Air was blown through the solution of camphor phenylhydrazone for 1 hour. The λ max. did not change, but the ε value increased to 16.9, probably because of an increase in the concentration caused by evaporation of solvent.

U.V. Study of the Kinetics of the Rearrangement of 2-Phenylazobornane Catalysed by Sodium Methoxide at 45°C.

Four successive experiments were run, following the procedure described below. Some runs were slightly modified and the modifications are stated under each heading.

Freshly prepared solutions of 2-phenylazobornane and sodium methoxide in dry methanol were used for each experiment.

General Procedure.— A solution of sodium methoxide was prepared by dissolving freshly cut sodium (18 mg.) in dry methanol (0.75 ml.). The sodium methoxide solution (0.125 ml.) and dry methanol (2.65 ml.) were mixed together in two separate U.V. cells. The cells were placed in the U.V. spectrophotometer, thermostated at 45°C, and the base line was recorded over 300 - 700 nm.

One of these solutions was retained as a 'blank' throughout the experiment.

A solution of 2-phenylazobornane in dry methanol (2.65 ml; 2 mg./ml.) was measured into the sample cell and the spectrum was recorded immediately, and then after 30 min. The sodium methoxide solution (0.125 ml.) was mixed with the 2-phenylazobornane solution in the sample cell (t = 0 min.), and the U.V. spectrum was recorded at intervals.

The rate constant for each experiment was calculated from the rate of change of the absorbance of 2-phenylazobornane ($\lambda_{max.}$ 402 nm.) using the relationship:

$$A = x\varepsilon r + (a - x)\varepsilon p = x(\varepsilon r - \varepsilon p) + a\varepsilon p$$

where A = the recorded absorbance (corrected for solvent).

εr = the extinction coefficient of the reactant (2-phenylazobornane, ε 182).

εp = the extinction coefficient of the product (camphor phenylhydrazone, ε 11.3).

x = the concentration of the reactant at time t.

a = the initial concentration of the reactant.

For a first order reaction: $-\frac{dx}{dt} = kx$

Integrating: $\ln x - \ln a = -kt$

$\therefore \quad \ln x/a = -kt$

$$x/a = e^{-kt}$$

$$x = ae^{-kt}$$

$$\therefore A = ae^{-kt}(\varepsilon r - \varepsilon p) + a\varepsilon p.$$

$$A - a\varepsilon p = a(\varepsilon r - \varepsilon p)e^{-kt}$$

$$\frac{A - a\varepsilon p}{a(\varepsilon r - \varepsilon p)} = e^{-kt}$$

$$\therefore \ln \frac{(A - a\varepsilon_p)}{(a(\varepsilon_r - \varepsilon_p))} = -kt$$

and $\ln(A - a\varepsilon_p) - \ln(a(\varepsilon_r - \varepsilon_p)) = -kt.$

—— Equation 2.

(Using x as the concentration of product and working through similar relationships gave the same final equation with opposite sign i.e. $\ln(a(\varepsilon_p - \varepsilon_r)) - \ln(A - a\varepsilon_p) = -kt.$)

This relationship allows for the build-up of absorbance due to the product, camphor phenylhydrazone (λ 402 nm., ε 11.3).

Run 1. —— The U.V. spectra were recorded at intervals over 200 min. (see Table 17A). The sample in the cell was kept at 45°C overnight and then rerun. The U.V. spectrum was recorded again after a further hour. Both these latter spectra showed absorbances with $\lambda_{max.}$ 386 nm., which were more intense than the initial absorbance of the 2-phenylazobornane solution.

Using the value previously obtained for the absorbance of a 2 mg./ml. solution of camphor phenylhydrazone in methanol (A = 0.12 at λ max. 402 nm.) as a ε_p, the values of $\ln(A - a\varepsilon_p)$ were calculated (Table 17A).

A least squares analysis of $\ln(A - a\varepsilon_p)$ v.t was made (see Equation 2). The first point (t = 5 min.) was discarded as it was apparent from the U.V. spectra that the mixing time and dilution on addition of sodium methoxide solution had introduced a large error into the first measurement.

Using the results from Table 17A, from t = 10 min. to t = 200 min. (N, the number of points used, was 14), the values calculated were:

$$k = 0.00165 \pm 0.00009 \text{ min.}^{-1}$$

intercept = +0.02741 $\pm$ 0.0001.

Run 2. —— The only modification to the general procedure was that the 2-phenylazobornane solution in the U.V. cell was sparged with dry nitrogen for 10 min. before its spectrum was recorded. After 20 min. at 45°C, before the sodium methoxide solution was added, the U.V. spectrum of the 2-phenylazobornane solution had not altered.

Spectra were recorded over a period of 150 min. after the addition of the sodium methoxide solution. The first two readings (t = 5 min. and t = 10 min.) were discarded and the results (see Table 17B) were calculated with N = 10, as for Run 1:

$k = 0.00085 \pm 0.0006$ min.$^{-1}$

intercept = 0.22191 $\pm$ 0.0045.

These results do not compare favourably with those from Run 1.

After the sample had been kept in the cell at 45°C overnight the spectrum was rerun. The spectrum was recorded again after another hour. The absorbances were again greater than the initial absorbances of the 2-phenylazobornane solution, and had shifted to λ max. 390 nm. as in Run 1.

Run 3. ——The experiment was carried out in the same way as Run 2. The spectra were recorded over a period of 210 min. and the results (Table 17C) were analysed using the values from t = 10 min. to t = 200 min.:

$k = 0.000276 \pm 0.000758$ min.$^{-1}$

intercept = 0.45112 $\pm$ 0.1652

The errors were large. Graphs of $\ln(A - a \varepsilon p)$ v.t were made for Runs 2 and 3. For both experiments a curve was

obtained which showed that the rate of reaction dropped sharply after c.a. 70 min. The results from Runs 1, 2 and 3 were not consistent.

After the sample had been stored at 45°C overnight the absorbance had again increased and the λ max. had shifted to 390 nm.

Run 4. ——The experiment was carried out in the same way as Run 1. The 2-phenylazobornane solution was not sparged with dry nitrogen. The spectra were recorded over a period of 200 min. and the results (Table 17D) were analysed using the values from t = 5 to t = 200 min. (N = 11).

$k = 0.00658 \pm 0.00336$ min.$^{-1}$

intercept = 0.99892 ± 0.3236

A graph of $\ln(A - a \epsilon p)$ v.t showed that the rate of reaction tailed off sharply after c.a. 100 min. Hence the large errors in k and the intercept.

The results for 10 - 100 min. (N = 7) and 70 - 160 min. (N = 4) were analysed (see Table 17D).

10 - 100 min. (N = 7)	70 - 160 min. (N = 4)
$k = 0.00079 \pm 0.000063$ min.$^{-1}$	0.00048 ± 0.000046 min.$^{-1}$
intercept = 0.23961 ± 0.00336	0.21449 ± 0.00561
error in k = 0.000063 (8%) min.$^{-1}$	0.000046 (9%) min.$^{-1}$

The different rate constants obtained for different times over which the reaction was studied indicated that the reaction was not a simple first order process. It is probable that at least two reactions were taking place.

U.V. Study of the Rearrangement of Phenylazocyclohexane in Methanol Catalysed by Sodium Methoxide at 45°C.

The experiment was carried out in the same way as the U.V. study of the rearrangement of 2-phenylazobornane in methanol catalysed by sodium methoxide at 45°C (see page 204).

A solution of phenylazocyclohexane in methanol (2.65 ml; 2 mg./ml.) was added to 0.125 ml. of a solution of sodium methoxide in methanol (from 18 mg. of sodium in 0.75 ml. of dry methanol). The solution was not sparged with nitrogen.

The initial absorbance was 1.72 ($\lambda_{max.}$ 398 nm.) and this gradually decreased to 0.78 ($\lambda_{max.}$ 390 nm.) after the solution had been kept at 45°C overnight. Dry oxygen was then blown through the solution for 2 hours. The absorbance increased again, probably due to evaporation of solvent, and also shifted to a longer wavelength ($\lambda_{max.}$ 401 nm.). The shift to a longer wavelength was evidence of the formation of cyclohexane phenylazohydroperoxide.[23]

Phenylazocyclohexane did not react in the same way as 2-phenylazobornane under the same conditions after being left overnight (see pages 206 - 208).

Titration of Solutions of Sodium Methoxide Catalyst in Methanol.

The inconsistency in the results obtained from U.V. studies of the kinetics of the rearrangements of 2-phenylazobornane at 45°C in methanol catalysed by sodium methoxide may have been due to variation in the quality of catalyst solution used.

Five solutions of sodium (0.36 g.) in methanol (1.5 ml.) were prepared from two different samples of freshly cut sodium and two different batches of methanol. Each sample was diluted with water (20 ml.) and then titrated against standard aqueous

hydrochloric acid solution (1.008 N) with phenolphthalein as indicator. Titres of 1.35, 1.34, 1.32, 1.45 and 1.35 ml. were obtained. This indicated that the concentration of catalyst solution used in the U.V. kinetic runs was approximately constant. (This method if estimation, however, involved the addition of water and gave the total base concentration, not just methoxide ion concentration.)

Triethylamine was tried as a catalyst but 2-phenylazobornane (2 mg./ml.) was found to be stable for over 1 hour in methanol (2.65 ml.) to which triethylamine (0.4 ml.) had been added.

U.V. Study of the Behaviour of Camphor Phenylhydrazone in Methanol Containing Sodium Methoxide at 45°C.

Run 1.——The baseline for the U.V. spectra was recorded at 45°C in the same way as in the kinetic experiments with 2-phenylazobornane (see page 204). The sample cell was then filled with a solution of camphor phenylhydrazone (2 mg./ml.) in dry methanol (2.65 ml.). A solution of sodium methoxide in methanol was prepared by dissolving freshly cut sodium (18 mg.) in dry methanol (0.75 ml.). A 0.125 ml. sample of this solution was thoroughly mixed with camphor phenylhydrazone solution in the cell, and the U.V. spectrum of this mixture was recorded at 30 min. intervals at 45°C.

The absorbance changed from a weak $\lambda_{max.}$ at 400 nm. (A = 0.19), to a much sharper $\lambda_{max.}$ at 388 nm. (A = 1.31) after 26 hours. The rate of increase in absorbance was initially fast but slowed down greatly after c.a. 2.5 hours. The final solution was yellow in colour.

The methanolic solution from which the aliquot of camphor phenylhydrazone (2 mg./ml.) had been taken, and which did not contain

sodium methoxide, was deep red in colour after storage for 26 hours in a volumetric flask at 20°C. The U.V. spectrum of this residual solution was well off scale at wavelengths shorter than 400 nm., and there was a shoulder (λ 520 nm.; A = 1.09) on the main absorbance. A different reaction (probably oxidation) appeared to have taken place in this solution than that which took place in the U.V. cell at 45°C in the presence of sodium methoxide.

Run 2. — A fresh solution of camphor phenylhydrazone in methanol (? mg./ml.) was prepared. No sodium methoxide was added. The spectrum was recorded immediately, and then after 30 min. and 90 min. at 45°C. No great change in the spectrum was noted up to 90 min., other than a very slight increase in the intensity of absorbance, probably due to evaporation of solvent. The solution was faintly red in colour.

A sample of the same solution, which had been stored under nitrogen in the dark at 20°C in a volumetric flask for 2 hours also showed only a very slight increase in the intensity of absorbance.

Run 3. — Sodium methoxide solution in methanol (2.36 ml.) was added to a solution of camphor phenylhydrazone (50 ml.) in a 100 ml. flask. Both solutions were the same concentration as those used previously. The mixture was heated in a flask, under nitrogen, to 45°C. A sample was withdrawn and stored in the U.V. cell at 45°C for 22 hours. The U.V. spectrum of this sample was off scale at wavelengths shorter than 320 nm., but there was a broad shoulder on this main absorbance at λ 370 nm. (A = 1.62). The solution was yellow.

A sample was withdrawn from the flask after 22 hours. The U.V. spectrum of this sample did not have a sharp absorbance above

300 nm. and showed only a very broad absorbance (A = 0.4) at 370 nm. When this sample was stored in the U.V. cell at 45°C the absorbance rapidly increased towards that of the sample which had been stored in the U.V. cell at 45°C for 22 hours (see above), and became identical to it after 4 hours. This suggested that oxygen was necessary for the reaction to take place. (The U.V. lamp was not left on while samples were thermostated inside the spectrophotometer.)

The remaining solution in the flask was sparged with air and stored in the dark at 45°C. After a further 2 hours another sample was withdrawn from the flask. This sample had to be diluted (x 2) before the U.V. spectrum was on scale. The spectrum was similar to that of the sample that had been stored in the cell for 22 hours (see above) and had a broad shoulder at λ 370 nm.

Both the solution in the cell and in the flask were kept at 45°C for a further 18 hours, after which time the intensity of the shoulders at 370 nm. in the U.V. spectrum of each solution had increased further.

These results confirmed that oxygen was necessary for the reaction of camphor phenylhydrazone in methanol, in the presence of sodium methoxide, to take place.

The methanol was evaporated from the sample in the flask and the residue was extracted with carbon tetrachloride (2 x 5 ml.). The combined extracts were filtered through glass wool to remove sodium methoxide. The solution was concentrated and the 60 MHz n.m.r. spectrum was recorded. The spectrum was similar to that of camphor phenylhydrazone but the resolution was poor and the sample was impure.

The carbon tetrachloride was evaporated and the residue

was dissolved in water (20 ml.) and then extracted with ether (3 x 10 ml.). The combined extracts were dried ($MgSO_4$) and the ether was evaporated. The 60 MHz n.m.r. spectrum of the residue in carbon tetrachloride showed better resolution with aromatic, methylene and methyl absorptions, but did not resemble the spectra of either camphor phenylhydrazone or 2-phenylazobornane.

The carbon tetrachloride was evaporated once more and the residue was analysed by T.L.C. on alumina with petroleum-ether (b.p. 60 - 80°C) as elutent. This showed two spots. The infra-red spectrum (CCl_4) showed a broad band ($\nu_{max.}$ 3300 $cm.^{-1}$) which could either have been an N-H or an O-H stretch, though it was rather low for the latter. The infra-red sample, in CCl_4, turned very dark on storage overnight.

The Hydrolysis of Camphor Phenylhydrazone.

The infra-red spectrum of a solution of camphor phenylhydrazone (0.5 g.) in spectroscopic grade carbon tetrachloride (20 ml.) was recorded. $\nu_{max.}$ (CCl_4) 3450(w), 1240(m), 1170(m), 1150(m), 1120(s), 1092(s), 1080(s), 1010(s), 880(w), 690 $cm.^{-1}$(w). The C = O stretch at 1743 $cm.^{-1}$ was very weak in this spectrum and indicated the presence of some free camphor ($\nu_{max.}$ CCl_4 1743 $cm.^{-1}$).

Water (10 ml.) was added and the mixture was stirred vigorously for 1 hour. The infra-red spectrum of the CCl_4 phase showed that the C = O stretch at 1743 $cm.^{-1}$ had increased in intensity and continued to do so while the mixture was stirred for a further 3 days at 20°C, during which the organic layer became deep red in colour.

The mixture was then extracted with ether (3 x 50 ml.). The combined extracts were dried ($MgSO_4$) and a black tar was

obtained after the ether had been evaporated. The n.m.r. spectrum (60 MHz, CCl_4) showed that the material which had been recovered appeared to be predominantly camphor phenylhydrazone. It was difficult to assign absorptions to camphor in the n.m.r. spectrum due to overlapping absorptions (see page 195).

Measurement of the Oxygen Uptake of Camphor Phenylhydrazone and Related Compounds.

Oxygen absorption was measured in various solvents using a micro-oxygenation apparatus[23] operating at atmospheric pressure. The sample, an amount calculated to give an uptake of about 5 ml. of oxygen, was stored in a glass 'bucket' inside the apparatus which was then flushed with oxygen and allowed to equilibrate. The sample was then allowed to mix with the solvent (10 ml; purified and dried) and the oxygen uptake was recorded. All reactions were carried out at c.a. 17°C under normal lighting conditions.

Camphor Phenylhydrazone in Methanol.

Camphor phenylhydrazone (50 mg.) in methanol (10 ml.) was used. The oxygen uptake began slowly but appeared to speed up after 1 hour. After c.a. 3 hours more oxygen had been taken up than the capacity of the apparatus (5.5 ml.). The experiment was repeated with 25 mg. of camphor phenylhydrazone, but the capacity of the apparatus was again exceeded (after c.a. 20 hr.) showing that more than 2 moles of oxygen per mole of phenylhydrazone was being absorbed. The reaction appeared to have an induction period.

Camphor Phenylhydrazone in Carbon Tetrachloride.

The experiment was carried out using camphor phenylhydrazone (50 mg.) in carbon tetrachloride (10 ml.). Gas appeared to be given off rather than taken up during the first 2 hours and the apparatus

had to be continually adjusted to allow for this. After 2.5 hours, oxygen was suddenly taken up. Within 5 min. the capacity of the apparatus (6-6.5 ml. of gas) was exceeded.

The U.V. spectrum of the solution after dilution to a concentration of 2 mg./ml. was very similar to that of camphor phenylhydrazone ($\lambda_{max.}$ 400 nm.). The 60 MHz n.m.r. spectrum of the concentrated solution was that of camphor phenylhydrazone (see page 195).

The experiment was repeated. Oxygen uptake started very slowly after c.a. 1 hour and then appeared to stop after a further 20 min. After 2.75 hr. the uptake became very fast and the capacity of the apparatus was exceeded in < 2 min. The solution was then yellow. On standing overnight the solution became black in colour.

The infra-red spectrum (CCl_4) suggested that a mixture of camphor and camphor phenylhydrazone was present. There was also evidence for the presence of oxidised phenylhydrazine ($\nu_{max.}$ 3600 $cm.^{-1}$, see page 218).

The solution was concentrated and the 60 MHz n.m.r. spectrum was recorded. This also suggested a mixture of camphor and camphor phenylhydrazone (see page 195).

The percentage of camphor in the mixture was calculated from the intensity of $\nu_{max.}$ C = O (1743 $cm.^{-1}$) by comparison with a solution of camphor in dry carbon tetrachloride (5 mg./ml.).

For the camphor solution ($\nu_{max.}$ C = O 1743 $cm.^{-1}$)

$$E = \log_{.10} \quad Io/I = 1.9345$$

$$\varepsilon = \frac{E \times M.W.}{C \times 1}$$

$$= \frac{1.9345 \times 152}{5 \times 0.1}$$

$= 588$

where E is the absorbance

Ic is the intensity of incident radiation.

I is the intensity of transmitted radiation.

C is the concentration of camphor (in mg./ml.)

l is the pathlength (in cm.)

ε is the molar extinction coefficient.

For the product mixture ($\nu_{max.}$ C = 0 1743 $cm.^{-1}$):

$E = 0.2718$

$$\therefore 588C = \frac{0.2718 \times 152}{0.1}$$

$C = 0.7$ mg./ml.

The original concentration of camphor phenylhydrazone in the solution was 5 mg./ml. The percentage of camphor phenylhydrazone converted to camphor was therefore $0.7/5 \times 1.6^{*} \times 100$ i.e. 22.4%

Camphor Phenylhydrazone in Methanol (Catalysed by Sodium Methoxide).

A solution of sodium methoxide in methanol was prepared by reacting freshly cut sodium (90 mg.) with dry methanol (1.5 ml.). The experiment was carried out using camphor phenylhydrazone (50 mg.) in methanol (10 ml.) to which the sodium methoxide solution (0.47 ml.) had been added. (These amounts gave the same relative concentration of camphor phenylhydrazone to sodium methoxide as had been used in the U.V. kinetic experiments (see page 210).)

Oxygen uptake commenced 5 min. after the camphor phenylhydrazone had been introduced into the methanol/sodium methoxide solution, but progressed very slowly. After 4 hours 6.08 ml. of oxygen had been taken up. Uptake continued but could not be measured as the capacity of the apparatus had been exceeded.

* 1.6 takes into account the difference in the molecular weights of camphor (152) and camphor phenylhdrazone (242).

The use of sodium methoxide as catalyst appeared to eliminate the induction period (see above), though the uptake still occurred slowly at first.

Camphor Phenylhydrazone in Hexane.

The experiment was carried out with the phenylhydrazone (50 mg.) in hexane (10 ml.). Oxygen uptake commenced c.a. 1.5 hours after the phenylhydrazone was introduced into the solvent. Uptake was very slow at first, but after c.a. 2.5 hours the capacity of the apparatus was exceeded by rapid gas uptake.

This behaviour was similar to that of camphor phenylhydrazone in both methanol and carbon tetrachloride (see above).

i-Butyraldehyde Phenylhydrazone in Carbon Tetrachloride.

This experiment was carried out to ensure that the micro-oxygenation apparatus was functioning properly.

The experiment was first run with the phenylhydrazone (50 mg.) in carbon tetrachloride (10 ml.). Oxygen uptake stopped 4 min. after introduction of the phenylhydrazone to the solvent when 3.32 ml. of oxygen had been absorbed. In another experiment 2.52 ml. of oxygen were taken up in 6 min. (i.e. c.a. 0.1m. mole of oxygen per 0.308m. mole of i-butyraldehyde phenylhydrazone).

These results are consistent with the low molar uptake of oxygen by other aldehyde phenylhydrazones in chloroform.[23]

The experiment was repeated with hexane as solvent. Oxygen uptake commenced immediately the sample was introduced into the solvent and was complete after 3 min. when 0.82 molar equivalents of oxygen had been absorbed.

This result was in accordance with others previously reported[23] for aldehyde phenylhydrazones in hexane and showed that

there was no fault in either the apparatus or the method of its operation.

Phenylhydrazine in Carbon Tetrachloride and Methanol.

The experiment was carried out with redistilled phenylhydrazine (12 mg.) in carbon tetrachloride (10 ml.). No oxygen uptake was observed at first. The solution became red in colour after 50 min., but still no uptake was observed. After 1 hour 50 min. there was a very sudden uptake of oxygen which stopped after < 2 min. The capacity of the apparatus was greatly exceeded even though an uptake of two molar equivalents of oxygen per mole of phenylhydrazine had been anticipated. The colour of the final solution was red. The infra-red spectrum of the concentrated solution (CCl_4) showed sharp peaks at 3600 $cm.^{-1}$ and 3580 $cm.^{-1}$ These absorptions were also observed in the infra-red spectrum of the oxidised solution of camphor phenylhydrazone (see page 215) in carbon tetrachloride. Comparison of the 60 MHz n.m.r. spectrum with that of phenylhydrazine indicated that the NH and NH_2 absorptions (4.1 p.p.m.) had gone and the aromatic multiplet had collapsed to 2 singlets.

The experiment was repeated with methanol as solvent. Oxygen uptake started slowly after c.a. 15 min. and then appeared to stop after 1 hour 15 min. when 0.76 molar equivalents of oxygen had been taken up. After a further 12 hr. 1.33 molar equivalents of oxygen had been absorbed. Stirring was continued for a further 34 hours but no more oxygen was absorbed.

Phenylhydrazine in Methanol Catalysed with Sodium Methoxide.

The experiment was carried out in the same way as that described above for phenylhydrazine in methanol, but sodium methoxide solution (0.47 ml. containing 90 mg. sodium per 1.5 ml.

methanol) was added to the methanol (10 ml.) before the phenylhydrazine (12 mg.) was introduced into the solvent.

Oxygen uptake began immediately on introduction of the substrate to the solution but slowed down after 7 min. when 2.66 ml. of oxygen had been absorbed. Uptake continued until, after 4 hours, the capacity of the apparatus had been exceeded, but oxygen was still being absorbed. The colour of the final solution was yellow.

There appeared to be an initial fast uptake of c.a. 1 molar equivalent of oxygen, followed by a period when no gas was absorbed (c.a. 3.5 hours). Uptake then began again, fairly slowly, and accelerated until much more than 2 molar equivalents had been absorbed. This suggested that the sodium methoxide acted as a catalyst in an initial step, during which c.a. 1 molar equivalent of oxygen was taken up. The catalyst also appeared to be responsible for subsequent reaction taking place to a greater extent than in methanol alone (see above).

Phenylhydrazine in Carbon Tetrachloride/Water.

The experiment was carried out in the same way as that already described for phenylhydrazine in carbon tetrachloride except that water (5 ml.) was present.

The solution became orange in colour but after 2 hours only 0.4 ml. of oxygen had been taken up. The solution was stirred overnight, but no further uptake was observed.

Camphor Phenylhydrazone in Carbon Tetrachloride/Water.

The experiment was carried out with camphor phenylhydrazone (50 mg.) in a mixture of carbon tetrachloride (10 ml.) and water (5 ml.).

Oxygen uptake started slowly after c.a. 20 min. and then

appeared to stop after 3 hours when 4.8 ml. had been absorbed. The mixture was stirred for a further 3.5 hours but the gas uptake had ceased.

A sample was withdrawn and the infra-red spectrum recorded. The amount of free camphor in the mixture was calculated to be 35 % from the intensity of the C = O stretch ($\nu_{max.}$ 1743 $cm.^{-1}$ see page 215).

The apparatus was refilled with oxygen and the solution was allowed to stir overnight. The amount of free camphor in the mixture was then found to be 48%. There was, however, no peak at 3600 $cm.^{-1}$, as there was when the experiment was carried out in carbon tetrachloride alone (see page 215). This, together with an uptake of 1.04 molar equivalents of oxygen suggested that the reaction did not take the same course as in carbon tetrachloride alone. There was no sudden uptake of oxygen after c.a. 3 hours in the present experiment.

Phenyldiazonium Fluoroborate in Methanol.

The experiment was carried out with freshly prepared phenyldiazonium fluoroborate (see page 222) (35 mg; 0.230 m.mole) in methanol (10 ml.).

At first gas appeared to be given off and the apparatus had to be continually adjusted to allow for this. No oxygen was taken up within 3 hours. The solution was allowed to stir overnight and 0.65 molar equivalents of oxygen were absorbed. The solution became faintly yellow in colour.

Phenyldiazonium Fluoroborate in Methanol Containing Sodium Methoxide.

The experiment was carried out as described above for phenyldiazonium fluoroborate in methanol but 0.47 ml. of a solution

of sodium methoxide in methanol (90 mg. sodium/1.5 ml. methanol) was added to the solvent before introduction of the phenyldiazonium fluoroborate.

The solution became deep orange in colour immediately on addition of the phenyldiazonium fluoroborate and gas, probably nitrogen, was given off. (This coloration did not occur when the salt was added to the methanol alone.)

After 3.5 hours uptake of oxygen began slowly and appeared to stop after a further 30 min. The solution was left to stir overnight. Only 0.27 molar equivalents of oxygen were absorbed.

The sample was diluted (x 100) to a concentration of 0.035 mg./ml. and the U.V. spectrum was then recorded. $\lambda_{max.}$ 396 nm. (ε 5200). This $\lambda_{max.}$ was at a longer wavelength than those recorded for solutions of camphor phenylhydrazone under similar conditions ($\lambda_{max.}$ 370 nm.) but it may make some contribution to the absorption at this wavelength.

U.V. Study of the Behaviour of Phenyldiazonium Fluoroborate in Methanol Containing Sodium Methoxide.

A solution of phenyldiazonium fluoroborate (12.7 mg; see page 173) in dry methanol (10 ml.) was prepared. (This concentration gave the same molarity as that of the camphor phenylhydrazone solution. (see page 210))

The phenyldiazonium fluoroborate solution (2.65 ml.) was placed in the U.V. cell at 45°C , the sodium methoxide solution (0.125 ml; from 36 mg. sodium in 1.5 ml. methanol) was added. The spectrum was well off scale and remained off scale after oxygen had been bubbled through the solution for 10 min. The solution was therefore diluted (x 50). The absorbance ($\lambda_{max.}$ 396 nm.)

slightly increased in intensity during 3 hours at 45°C, and then remained steady (ε 2,900), even after being kept at 45°C overnight. The intensity of absorbance in this case was much weaker than that obtained in the gas uptake experiment with phenyldiazonium fluoroborate (ε 5,200, see page 220) where the U.V. spectrum was recorded.

It was found that solutions of phenyldiazonium fluoroborate are not stable. After storage for c.a. 2 days at 25°C no strong absorption at 396 nm. appeared after addition of base which caused an orange colouration with fresh solutions.

U.V. Study of the Behaviour of Phenylhydrazine in Methanol Containing Sodium Methoxide.

A solution of sodium methoxide in dry methanol (0.47 ml; from 90 mg. sodium in 1.5 ml. methanol, was diluted with dry methanol (10 ml.). Redistilled phenylhydrazine (12 mg.) was added to this solution, which was then stirred for 10 min., before the U.V. spectrum was recorded. Dry oxygen was blown through the solution for 10 min. and the spectrum was then observed for 18 hours.

There was an increase in the intensity of the broad absorption at 350 - 550 nm. after treatment with oxygen. This increase in intensity diminished, rapidly at first, and, after 18 hrs. the spectrum had almost reverted to that of the solution before treatment with oxygen.

This result contrasts with the results for camphor phenylhydrazone in sodium methoxide/methanol (see pages 210 - 213). After treatment with oxygen the camphor phenylhydrazone solution showed an increase in the intensity of absorption which continued to increase on storage. It is therefore improbable that oxidation of

free phenylhydrazine was responsible for the strong absorption which appeared at 370 nm. with solutions of camphor phenylhydrazone in sodium methoxide/methanol.

A second experiment was carried out as described earlier for phenyldiazonium fluoroborate (page 221), but with redistilled phenylhydrazine (8.9 mg.) in dry methanol (10 ml.).

The phenylhydrazine solution showed no absorbance between 450 and 350 nm. before it was sparged with oxygen for 10 min. It then showed an intense, broad shoulder in this region. This absorbance decreased in intensity, until, after 12 hrs., the spectrum was the same as that obtained from the first experiment (see above).

This result was consisent with that from the first experiment (see above) and showed that oxidation of free phenylhydrazine was not responsible for the strong absorbance ($\lambda_{max.}$ 370 nm.) given by camphor phenylhydrazone in methanol containing sodium methoxide.

U.V. Study of a Mixture of Phenyldiazonium Fluoroborate and Camphor in Methanol Containing Sodium Methoxide.

A solution of phenyldiazonium fluoroborate (0.0127 g; 0.0827 m. mole) and camphor (0.0126 g; 0.0827 m. mole) in dry methanol (10 ml.) was prepared. This solution (2.65 ml.) was placed in a U.V. cell and the spectrum was recorded. Only a very weak shoulder between 550 and 300 nm. was observed.

Sodium methoxide solution (0.125 ml; from 36 mg. sodium in 1.5 ml. methanol) was added and the absorbance was found to be well off scale. The mixture was therefore diluted (50x). The absorbance ($\lambda_{max.}$ 396 nm.) was weaker than that observed in previous experiments with phenyldiazonium fluoroborate (see page 221).

The spectrum did not change after the sample had been stored at 45°C for 1 hour. Addition of a further 0.125 ml. of base solution produced a very slight increase in the intensity at 396 nm. but this did not change during another hour at 45°C. Oxygen was then blown through the sample for 10 min. This resulted in an increase in the intensity at 396 nm. to approximately the same as that in the previous experiment with phenyldiazonium fluoroborate. (ε 2900, see page 222). The sample was kept at 45°C for a further 2 hours. No change occurred in the position or the intensity of the absorbance.

A Japp-Klingemann type of reaction (see Scheme 37) between the phenyldiazonium cation and camphor was not responsible for the absorbances recorded for camphor phenylhydrazone in sodium methoxide/methanol ($\lambda_{max.}$ 370 nm., see page 212).

The N.M.R. Spectra of Di-isopropyl Ketone Phenylhydrazone and Related Compounds.

Preparation of Di-isopropyl Ketone Phenylhydrazone.

Redistilled phenylhydrazine (10.8 g; 9.8 ml.) was added to a solution of di-isopropyl ketone (20 ml.) in dry benzene (50 ml.), and the solution was refluxed for 12 hr., under nitrogen, in an apparatus fitted with a Dean-Stark trap.

The benzene was evaporated and the product was fractionally distilled through a Vigreux column: (i) b.p. 88 - 90°C/0.2 mm. (4.32 g.). (ii) b.p. 90 - 112°C/0.2 mm. (13.30 g.).

Both fractions were shown, by n.m.r. spectroscopy, to be the same compound, di-isopropyl ketone phenylhydrazone (84): δ (60 MHz CCl_4) 1.2 (d, 12H, Me), 2.7 (septet, 2H, CH), 6.4 - 7.4 p.p.m. (m, 6H, aromatic and NH).

Reduction of Di-isopropyl Ketone Phenylhydrazone.

The phenylhydrazone (4 g; 0.0196 mole) was reduced with lithium aluminium hydride in dry tetrahydrofuran by the method of Bellamy and Guthrie.[23] The crude product (3.94 g.) was fractionally distilled: (i) b.p. 50 - 85°C/0.2 mm., (ii) b.p. 85 - 90°C/0.2mm., (iii) b.p. 90 - 92°C/0.2 mm., (iv) b.p. 92°C/0.2 mm.

The n.m.r. spectra (60 MHz, CCl_4) indicated that fractions (i) and (ii) were impure 2,4-dimethyl-3-phenylazopentane (83), formed by oxidation of the intermediate 2,4-dimethyl-3-phenylhydrazopentane during work-up: δ 0.87 (d, 6H, Me), 0.98 (d, 6H, Me), 2.36 (m, 2H, CH), 2.97 (m, 1H, CH), 7.2 - 7.8 p.p.m. (m, 5H, aromatic). The methyl doublets in the spectra of fractions (iii) and (iv) suggested they were both mixtures of 2,4-dimethyl-3-phenylazopentane and either 2,4-dimethyl-3-phenylhydrazopentane or

unchanged di-isopropyl ketone phenylhydrazone or both.

Fractions (i) and (ii) were combined and chromatographed on a 20 x 1" dry alumina column with petroleum-ether (b.p. 60 - 80°C) as elutent and separated into two yellow bands. The light yellow fraction was very impure and was not investigated further. N.m.r. spectroscopy (60 MHz, CCl_4) showed that the other darker yellow band (0.73 g.) was 2,4-dimethyl-3-phenylazopentane. (A small amount of impurity was apparent in the region of 1.7 - 2 p.p.m.) Treatment of this with yellow mercuric oxide in dry ether (see page 145), further chromatography and distillation failed to purify the product further. The product was shown, by n.m.r. spectroscopy, to rearrange to di-isopropyl ketone phenylhydrazone (40%) after 3 days in carbon tetrachloride at 20°C.

In the 100 MHz n.m.r. spectrum of the neat azo-compound the pair of methyl doublets of the i-propyl groups overlapped and appeared as a triplet, as they did in the 60 MHz spectrum (5 - 10% M) with benzene as solvent.

A strong solution of 2,4-dimethyl-3-phenylazopentane c.a. (20% M), in diphenyl ether, was prepared and the 100 MHz n.m.r. spectrum recorded at temperatures varying from 28°C to 180°C. The methyl doublets were separate at 28°C, but began to overlap as the temperature was increased. They did not coalesce or even broaden at 180°C.

2,4-Dimethylpentan-3-ol.

The reduction of the ketone was performed with sodium borohydride in ethanol.[153]

The product was fractionally distilled to give a pure alcohol, b.p. 139 - 140°C (lit.[101] b.p. 139°C): δ (60 MHz, CCl_4) 0.93 (d, 12H

Me), 1.70 (septet, 2H, CH), 2.70 (s, 1H,O-H), 2.95 p.p.m. (t,1H,CH) The 60 MHz n.m.r. spectrum in benzene showed the methyl absorptions of the isopropyl groups as two separate doublets (0.80 and 0.90 p.p.m.).

TABLE 1

^{1}H N.M.R. Study of the Formation and Isomerisation of Phenylhydrazones

R_1R_2C = NNHAr

A. Ar = Ph Solvent = Dioxan

R_1	R_2	time/hr.	syn isomer/%
H	Me	0.5 20 120	58 63 65
Me	Et	0.5 18 168	59 71 72
H	i-Pr	0.5 24 120 168	80 92 89 91
H	Et	1 24 120	73 79 78
Me	CH_2Ph	0.5 18 144	67 84 95

B. Ar = Ph Solvent = Pyridine

R_1	R_2	time/hr.	syn isomer/%
H	Me	0.5 24 120 264	62 66 66 67
Me	Et	0.5 1 5 24 120 144 264	50 54 60 60 66 71 73
Me	CH_2Ph	0.5 24 120 264	67 70 75 85

C. Ar = $C_6H_4NO_2$-p Solvent = Pyridine

R_1	R_2	time/hr.	syn isomer/%
H	Me	0.5	73
		3.75	76
		24	81
		120	80
		264	81
Me	Et	0.5	57
		24	76
		120	86
		264	86
Me	CH_2Ph	0.5	68
		24	77
		120	84
		264	88

D. Ar = C_6H_4Me-p Solvent = Pyridine

R_1	R_2	time/hr.	syn isomer/%
H	Me	0.5	62
		24	62
		120	60
		240	61
Me	Et	0.5	?
		24	?
		120	69
		240	69
Me	CH_2Ph	0.5	70
		24	72
		120	79
		240	81

E. Ar = Ph Solvent = $[^2H_3]$ acetonitrile

R_1	R_2	time/hr.	syn isomer/%
H	Et	0.5	72
		5	70
		24	70
		96	73
		264	72
Me	Et	0.1	83
		2.5	88
		24	90
		96	91
		264	89
Me	CH_2Ph	0.1	73
		0.5	77
		5	83
		24	84
		120	85
		264	86

F. Ar = C_6H_4Cl-p Solvent = $[^2H_3]$ acetonitrile

R_1	R_2	time/hr.	syn isomer/%
H	Et	0.5	72
		5	72
		48	74
		168	72
		264	74
Me	Et	1	93
		7	93
		24	93
		48	94
		120	94
		432	94
Me	CH_2Ph	0.5	62
		1	73
		5	81
		24	84
		120	87
		264	87

G. Ar = C_6H_4Cl-o Solvent = Nitromethane

R_1	R_2	time/hr.	syn isomer/%
H	Et	0.5	75
		20	73
		25	75
		120	75
		264	72
Me	Et	0.5	82
		5	82
		24	83
		120	82
		288	83
Me	CH_2Ph	0.5	87
		5	88
		24	87
		120	88
		264	88

H. Ar = Ph Solvent = Nitromethane

R_1	R_2	time/hr.	syn isomer/%
H	Et	0.5	71
		5	70
		24	72
		120	73
		264	73

TABLE 2

The Isomerisation of anti-Acetaldehyde Phenylhydrazone.

Equation: $\ln (Xe - X) = -t (k_1 + k_{-1}) + \ln Xe$.

X = mole fraction of syn isomer at time t.

Xe = mole fraction of syn isomer at equilibrium.

Run 1

t/min.	X/mole fraction	Xe - X	ln (Xe - X)
0	0.21	0.42	-0.8675
10	0.27	0.36	-1.0217
30	0.382	0.248	-1.3943
45	0.445	0.185	-1.6874
75	0.52	0.110	-2.2073
90	0.525	0.105	-2.2538
105	0.530	0.10	-2.3026
equilibrium	0.63	-	-

Run 2

t/min.	X/mole fraction	Xe - X	ln (Xe - X)
0	0.05	0.53	-0.6349
10	0.07	0.51	-0.6734
30	0.11	0.47	-0.7550
45	0.13	0.45	-0.7985
85	0.23	0.35	-1.0498
115	0.28	0.30	-1.2040
145	0.33	0.25	-1.3863
175	0.36	0.22	-1.5141
270	0.45	0.13	-2.0402
420	0.51	0.07	-2.6593
1415	0.57	0.01	-4.6052
equilibrium	0.58	-	-

TABLE 3

The Isomerisation of anti-Acetaldehyde Phenylhydrazone - Variation of N.

gradient $= -(k_1 + k_{-1})$ intercept = $\ln Xe$

Run 1 Xe = 0.63

N	gradient/min.$^{-1}$	intercept
5	-0.018083 $\pm$0.000259	-0.8570 $\pm$0.0107
7	-0.014637 $\pm$0.001250	-0.9340 $\pm$0.0787

Run 2 Xe = 0.58

N	gradient/min.$^{-1}$	intercept
9	-0.005277 $\pm$0.000092	-0.6043 $\pm$0.0117
10	-0.004974 $\pm$0.000111	-0.6273 $\pm$0.0201
11	-0.002774 $\pm$0.000250	-0.9317 $\pm$0.1152

TABLE 4

The Isomerisation of anti-Acetaldehyde Phenylhydrazone - Variation of Xe

Run 1 N = 5

Xe	gradient/min.$^{-1}$	intercept
0.61	-0.201000 ± 0.000330	-0.8934 ± 0.0137
0.615	-0.019547 ± 0.000291	-0.8846 ± 0.0121
0.62	-0.019028 ± 0.000288	-0.8755 ± 0.0124
0.625	-0.018540 ± 0.000257	-0.8663 ± 0.0107
0.63	-0.018083 ± 0.000259	-0.8570 ± 0.0107
0.635	-0.017645 ± 0.000268	-0.8476 ± 0.0111
0.64	-0.017233 ± 0.000283	-0.8381 ± 0.0117

Run 2 N = 9

Xe	gradient/min.$^{-1}$	intercept
0.57	-0.005489 $\pm$0.000103	-0.6184 $\pm$0.0133
0.58	-0.005276 $\pm$0.000092	-0.6043 $\pm$0.0117
0.59	-0.005080 $\pm$0.000085	-0.5901 $\pm$0.0109
0.60	-0.004901 $\pm$0.000081	-0.5755 $\pm$0.0106
0.61	-0.004735 $\pm$0.000080	-0.5608 $\pm$0.0103
0.615	-0.004656 $\pm$0.000080	-0.5535 $\pm$0.0103
0.62	-0.004581 $\pm$0.000080	-0.5461 $\pm$0.0103
0.63	-0.004438 $\pm$0.000119	-0.5313 $\pm$0.0152

TABLE 5

The Condensation of Acetaldehyde with Phenylhydrazine at Low Temperature.

A. 1,2-Dimethoxyethane.

time/min.	temperature/°C	product/%	Isomeric Composition	
			syn/%	anti/%
0	-40	1	-	-
5	-30	10	-	-
10	-20	28	-	-
15	-10	58	-	-
25	0	73	-	-
30	+10	97	-	-
35	+10	100	65	35
180	+25	100	72	28

B. 2-Methoxyethanol

time/min.	temperature/°C	product/%	Isomeric Composition	
			syn/%	anti/%
8	-60	16	-	-
18	-40	18	-	-
25	-30	24	-	-
30	-30	30	-	-
45	-30	35	-	-
60	-30	37	-	-
90	-30	40	-	-
100	-25	40	66	34
105	-20	41	72	28
110	-20	42	70	30
120	-20	43	69	31
126	-20	44	69	31
130	-20	44	69	31
135	-15	47	69	31
140	-15	48	68	32
145	-15	48	68	32
150	-10	49	69	31
155	-10	54	68	32
160	-10	55	69	31
165	-5	57	64	36
175	-5	62	69	31
180	-5	64	71	29
185	-5	66	69	31
190	0	70	70	30
195	0	72	70	30
200	+20	85	69	31

TABLE 6

The Condensation of Excess Acetaldehyde with Small Amounts of Phenylhydrazine.

vol. Ph NH NH_2 solution added/ml.	syn isomer/%	anti isomer/%	Temperature/°C
0.1	21	79	-40
0.2	43	57	-40
0.3	35	65	-40
0.4	38	62	-40
0.5	58	42	-40
0.5	46[a]	54[a]	-40
0.5	55[b]	45[b]	25

a. Solution stored for 30 min. at -40°C.

b. Solution stored for 1 hr. at 25°C.

TABLE 7

The Condensation of Excess Phenylhydrazine with Small Amounts of Acetaldehyde.

vol. acetaldehyde solution added/ml.	syn isomer/%	anti isomer/%	Temperature/°C
0.1	60	40	10
0.2	51	49	10
0.3	54	46	10
0.4	60	40	10
0.5	55	45	10
0.5	59[a]	41[a]	25

a. Solution stored for 1 hr. at 25°C.

TABLE 8

Condensations of Alkyl Phenyl Ketones with Phenylhydrazine in Pyridine.

R Ph C = N NH Ph

R	time/hr.	Isomeric Composition		free ketone/%
		More Abundant Isomer/%	Less Abundant Isomer/%	
Me	0.5	0	0	100
	24	92	8	67
	120	92	8	34
	264	93	7	17
	528	92	8	9
	792	91	9	7
Et	0.5	0	0	100
	24	84	16	75
	216	88	12	21
	336	88	12	-
i-Pr	after reflux	63	37	21
t-But	after reflux	100	0	52

TABLE 9

Equilibrated Isomeric Compositions for Alkyl Phenyl Ketones.

R Ph C = N NH Ph

R	Solvent	More Abundant Isomer/%
Me	various[a]	100
Me	CCl_4	96
Et	C_6H_6	51
Et	CCl_4[b]	54
i-Pr	CCl_4	82
t-But	CCl_4	>99

a. Reported by Karabatsos and Taller[17]

b. 0.2M solution.

TABLE 10

The Ultraviolet Spectra of Alkyl Phenyl Ketone Phenylhydrazones in Ethanol.

R Ph C = N NH Ph

R	λ max./nm.	ε
Me	233 303 331	12,000 12,200 17,000
Et	235 303 334	13,320 13,460 19,800
i-Pr	260 283	10,500 11,650
t-But.	267	15,600

TABLE 11

The Ultraviolet Spectra of Alkyl Phenyl Ketones in Ethanol*.

R Ph C = O

R	λ max./nm.	ε	Interplanar[a] Angle/°
Me	242	13,200	0
Et	242	13,500	0
i-Pr	242	13,300	0
t-Butyl	242	9,100	34
2-Methylbut-2-yl	239	8,300	38
3-Methylpent-3-yl	238	7,100	43

* Braude and Sondheimer, J. Chem.Soc., 1955, 3754

a. Angle between the plane of the C = O and that of the phenyl group.

TABLE 12

The Chemical Shifts of Alkyl Protons in Some Phenylhydrazones.‡

R_1 R_2 CH = N NH Ph - Chemical Shifts in R_2

R_1	R_2	Solvent	H_α/p.p.m. cis	H_α/p.p.m. trans	H_β (CH_3)/p.p.m. cis	H_β (CH_3)/p.p.m. trans	Most Abundant isomer/%
H	Et	CCl_4	-	2.13	0.98	1.00	-
Me	Et	CCl_4	2.03	2.22	0.97	1.07	-
Ph	Et	CCl_4	2.13	2.13	0.996	0.996	54
H	Et	C_6H_6	1.48	2.05	0.70	0.92	-
Me	Et	C_6H_6	1.67	2.10	0.70	1.03	-
Ph	Et	C_6H_6	2.19	2.56*	0.84	1.18*	51
H	i-Pr	CCl_4	-	2.33	0.95	1.02	-
Me	i-Pr	CCl_4	-	2.45	0.97	1.07	-
Ph	i-Pr	CCl_4	3.14	2.77*	1.30	1.13*	82
H	t-But	CCl_4	-	-	-	-	-
Me	t-But	CCl_4	-	-	-	1.12	-
Ph	t-But	CCl_4	-	-	1.27	1.20*	99

‡ Chemical shifts for compounds in which R_1 is H or Me were reported by Karabatsos and Taller.[17]

* Chemical shift of most abundant isomer.

TABLE 13

Optical Rotations of Camphor in Ethanol.

wavelength/nm.	corrected rotation/°	$[\alpha]^{28}$	$[M]^{28}$
365	3.403	340.3	516
436	1.272	127.2	194
546	0.539	53.9	81.7
578	0.451	45.1	68.5
589	0.428	42.8	65

TABLE 14

Optical Rotations of Camphor Phenylhydrazone in Methanol.

wavelength/nm.	Observed Rotations/°	
	Before treatment with air	After treatment with air
546	-0.008	+0.010
578	-0.023	-0.010
589	-0.024	0.000

TABLE 15

Optical Rotations of 2-Phenylazobornane in Methanol.

wavelength/nm.	pathlength/cm.	concn./%	corrected rotation/°	$[\alpha]^{28}$
365	1	0.2	+0.290	+1450
436	1	0.2	-0.264	-1320
546	10	1	-3.009	-300.9
578	10	1	-2.375	-237.5
589	10	1	-2.211	-221.1

TABLE 16

Base Catalysed Rearrangement of 2 - Phenylazobornane in Methanol Followed by Optical Rotation.

time/min.	observed rotation/°	time/min.	observed rotation/°
0	-1.160	150	-0.013
5	-1.070	160	-0.001
10	-0.980	170	0.016
15	-0.900	180	0.029
20	-0.823	190	0.040
25	-0.755	200	0.050
30	-0.694	210	0.062
35	-0.622	230	0.072
40	-0.570	240	0.080
45	-0.522	250	0.085
50	-0.474	260	0.090
55	-0.430	270	0.090
60	-0.398	280	0.095
70	-0.324		
80	-0.262		
90	-0.203		
100	-0.158		
110	-0.120		
120	-0.090		
130	-0.062		
140	-0.040		

TABLE 17

Base Catalysed Rearrangement of 2- Phenylazobornane in Methanol Followed by U.V. Spectroscopy.

A. Run 1

time/min.	absorbance (A)	A - a εp	ln (A - a εp)
5	1.182	1.062	+0.06015
10	1.155	1.035	+0.03440
15	1.148	1.028	+0.02761
25	1.120	1.000	+0.00000
35	1.090	0.970	-0.03045
45	1.065	0.945	-0.05657
55	1.048	0.928	-0.07472
65	1.030	0.910	-0.09431
80	1.005	0.885	-0.12216
100	0.970	0.856	-0.16251
120	0.948	0.828	-0.18874
140	0.928	0.808	-0.21319
160	0.908	0.788	-0.23825
180	0.890	0.770	-0.26136
200	0.885	0.765	-0.26780

TABLE 17

B. Run 2

time/min.	absorbance (A)	A - aεp	ln (A - aεp)
15	1.368	1.2480	0.22154
20	1.352	1.2320	0.20863
25	1.348	1.2280	0.20538
35	1.330	1.2100	0.19062
45	1.310	1.1900	0.17395
55	1.300	1.1800	0.16551
75	1.284	1.1640	0.15186
95	1.270	1.1500	0.13976
115	1.250	1.1300	0.12221
150	1.230	1.1100	0.10436

C. Run 3

time/min.	absorbance (A)	A - aεp	ln (A - aεp)
5	1.73	1.610	0.47623
10	1.72	1.600	0.47000
20	1.71	1.590	0.46373
30	1.70	1.580	0.45742
50	1.68	1.560	0.44468
70	1.64	1.520	0.41871
90	1.63	1.510	0.41210
120	1.62	1.500	0.40546
150	1.60	1.480	0.39204
190	1.585	1.465	0.38185
210	1.580	1.460	0.37843

D. Run 4

time/min.	absorbance (A)	A - aεp	ln (A - aεp)
5	1.402	1.2820	0.24842
10	1.388	1.2680	0.23744
15	1.380	1.2600	0.23111
25	1.360	1.2400	0.21511
35	1.354	1.2340	0.21026
50	1.355	1.2150	0.19474
70	1.320	1.2000	0.18232
100	1.300	1.1800	0.16551
130	1.280	1.1600	0.14842
160	1.270	1.1500	0.13976
200	1.260	1.1400	0.13102

TABLE 18

Base Catalysed Rearrangement of 2 - Phenylazobornane in Methanol Followed by U.V. Spectroscopy.

Run No.	$k/min.^{-1}$	intercept
1	0.00165 ± 0.00009	0.02741 ± 0.0001
2	0.00085 ± 0.0006	0.22191 ± 0.0045
3	0.000276 ± 0.000758	0.45112 ± 0.1652
4	0.00658 ± 0.00336	0.99892 ± 0.3236

TABLE 19

Sample Concentrations for Investigation of the Basicity of Nitromethane by Infra-red Spectroscopy.

Sample number	Weight of Nitromethane/g.	Concentration of Nitromethane/M	Volume of p-Fluorophenol solution/ml.
1	0.0334	0.01096	2
2	0.0062	0.00203	"
3	0.0092	0.00302	"
4	0.0419	0.01375	"
5	0.0274	0.00897	"
6	-	-	"
7	-	-	1

TABLE 20

Sample Concentrations for Investigation of the Basicity of Acetonitrile by Infra-red Spectroscopy.

Sample number	Weight of Acetonitrile/g.	Concentration of Acetonitrile/M	Volume of p-Fluorophenol solution/ml.
1	0.0181	0.0084	2
2	0.0072	0.0035	"
3	0.0192	0.00938	"
4	0.0159	0.00775	"
5	0.0554	0.0270	"
6	-	-	"
7	-	-	1

TABLE 21

Determination of the Basicity of Acetonitrile by Infra-red Spectroscopy.

Sample number	Transmission/%	B_o^-/M	Absorbance (E)	A/M	K_f/M^{-1}
1	60	0.0084	0.2214	0.00352	24.9
2	58	0.0035	0.2370	0.00380	33.9
3	59	0.00933	0.2294	0.00378	12.4 *
4	59.5	0.00775	0.2263	0.00365	21.2
5	62.5	0.0270	0.2041	0.00329	10.62*
6	56.7	-	0.2478	$A = A^o$	-
7	73.3	-	0.1351	$A = A^o/_2$	-

* Result not used in determination of average K_f .

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