The Ring Cleavage of Acetylcyclopropanes by Metal-Ammonia Solutions.

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CONTENTS.

SUMMARY.

The reduction of acetylcyclopropanes with metal-ammonia solutions has been investigated. By studying the preferred direction of ring-opening of acetylcyclopropanes substituted in the 2-position of the cyclopropane ring, it has been shown that both steric and electronic factors are important in deciding the products of rearrangement. The reductive cleavage of conjugated cyclopropyl ketones with metals in liquid ammonia is, overall, a two electron reduction. Rearrangement could, theoretically, occur *via* (a), a radical-anion species, after the addition of one electron to the carbonyl group, or (b), a dianion species, generated by the addition of two electrons to the carbonyl group. In the absence of any steric effect, ring-opening has been shown to occur predominantly such that the cyclopropane bond cleaved is the one which gives rise to the more thermodynamically stable carbanion intermediate (least substituted β carbon atom).

A polarographic study of various conjugated cyclopropyl ketones in liquid ammonia was undertaken to try and differentiate between the mechanism involving (a), a radical-anion intermediate in which the negative charge was associated with carbon and not, as is more usually considered, with oxygen, and (b), a dianion intermediate. Although waves, corresponding to the polarographic reduction, in liquid ammonia, of the ketones studied, were observed, no information was obtained to enable a differentiation of the two mechanisms to be made.

The existence of a salt effect in the reductive rearrangement of 1-acetyl-2,2-dimethylcyclopropane, with lithium in liquid ammonia, has been shown, and a mechanism to explain the observed ratio of rearranged products has been proposed.

The radical-induced rearrangement of acetylcyclopropanes, substituted in the 2-position of the cyclopropane ring, has also been shown to be dependent on both steric and electronic factors. In the absence of any steric effect, ring-opening occurs such that the cyclopropane bond cleaved gives rise to the more thermodynamically stable intermediate, from considerations of relative radical stability.

All attempts to rearrange acetylcyclopropanes through authentic carbanion intermediates failed.

The importance of transition state conformations in the reduction of conjugated cyclopropyl ketones has been discussed.

INTRODUCTION.

Preparation of Cyclopropyl Compounds.

Because of the difficulty experienced in synthesising some cyclopropylcarbonyl compounds used in this work, it is relevant to give a brief summary of the synthetically important routes to this type of compound.

There are three important routes to α-cyclopropyl ketones:

1) Cyclisation of chains of three carbon atoms, the first or third of which is adjacent to a carbonyl, or potential carbonyl centre. Of this type are the cyclisation of γ-substituted ketones and in particular the intramolecular alkylation of γ-halogenoketones and related compounds in basic media,[1] the reaction of α,β-unsaturated ketones with ylides such as dimethyloxosulfonium methylide,[2] and the reaction of epoxides with ylides.[3]

2) Addition of a methylene, or substituted methylene group, onto the olefinic double bond of an α,β-unsaturated carbonyl, or potential carbonyl compound.[4]

3) Addition of an acetonyl (CH_3COCH-), or potential acetonyl group, to an olefin.[5]

Other, less general, methods are the ring contraction of 1,2-epoxycyclobutane derivatives[6] and 2-bromocyclobutanone derivatives,[7] the dehalogenation of α,α-bis(bromomethyl)cycloalkanones,[8] and the reaction of α-halocarbonyl compounds with dimethyloxosulfonium methylide.[9]

The photosensitised decomposition of aliphatic α-diazoketones in the presence of olefins,[10] and the acid-catalysed, thermal rearrangement of allenic tosylates[11] have also been used to prepare cyclopropylcarbonyl compounds.

Considerations such as the availability of starting materials, variation of substitution in the product, configuration of the product,

and yield make the three most important methods, from a synthetic viewpoint, the reaction of α,β -unsaturated ketones with ylides, the addition of a methylene group, or substituted methylene group, onto the olefinic double bond of an α,β -unsaturated carbonyl, or potential carbonyl compound, and the addition of an acetonyl group to an olefin. Of these three methods, the second, in the form of the Simmons-Smith reaction[12-14] of unsaturated compounds with the organo-zinc compound prepared from methylene iodide and zinc-copper couple in ether,[15] has widest application. Methylenation occurs with olefins,[12,14] and α,β -unsaturated alcohols,[12,13,16-20] amines,[19] esters,[13,21,22] ethers,[13,17,20,22] and ketones.[18,23] The reaction is stereospecific[17] and so specific geometric isomers can be prepared.

Methylenation, using the Simmons-Smith reaction, of β,γ - and γ,δ -unsaturated compounds[18,19,24] is the only general method for preparing directly products in which the cyclopropane group is other than α to a functional group.

Reductive Ring-Opening of Conjugated Cyclopropyl Ketones.

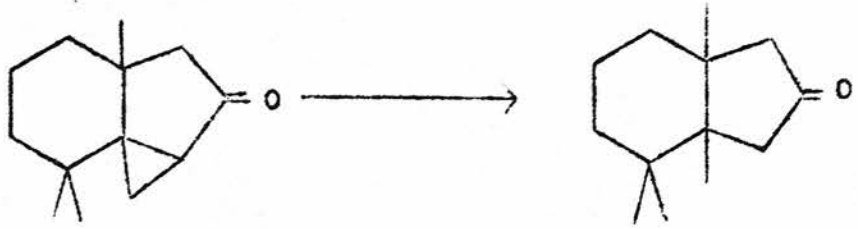
The reduction of organic compounds by metals dissolved in liquid ammonia is a well-established technique.[25,26] When conjugated cyclopropyl ketones are reduced by metals in liquid ammonia,[27] they undergo reductive cleavage of the cyclopropane ring. The reduction of this function when contained in a fused bicyclic system has been shown[28,29] to proceed with a highly stereospecific opening of the cyclopropane ring, the steric course of which appears to be determined by the stereochemistry of the starting material. Examination of molecular models shows that the cyclopropane bond which is cleaved is the one possessing maximum orbital overlap with the π -orbital of the carbonyl group.

This stereoselective, reductive cleavage is illustrated with the reduction of (+)-carone (1), which gives only

(-)- carvomenthone (2) on treatment with lithium in liquid ammonia.[28,29]

(1) (2)

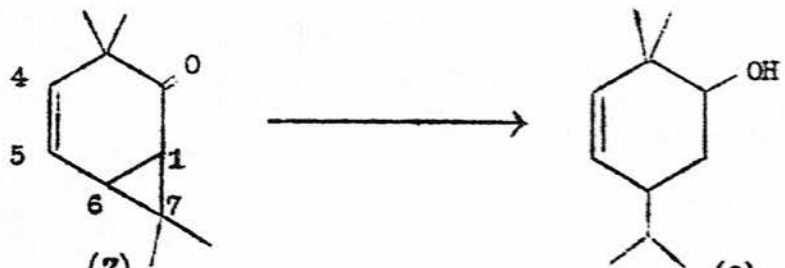
Only the $C_{(1)}$-$C_{(7)}$ bond, which from models appears to have good overlap with the π-orbital of the carbonyl group is cleaved. None of the product which would be formed by cleavage of the $C_{(1)}$-$C_{(6)}$ bond is observed. Similarly, the cyclopropyl ketone (3) gives only one product, (4),[30] and (-)- sabinaketone (5) gives only (R)-(+)-3- methyl-3-isopropyl- - cyclopentanone (6).[28]



(3) (4)

(5) (6)

Orbital overlap considerations also appear to control the direction of ring-cleavage in the reduction of 3- methylcar-4- en-2- one (7) with sodium in ethanol.[31] A priori, $C_{(1)}$-$C_{(6)}$ bond cleavage might be expected to be energetically favourable here, owing to the formation of an intermediate allyl radical or anion, but only $C_{(1)}$-$C_{(7)}$ bond cleavage, to give product (8), is observed.



(7) (8)

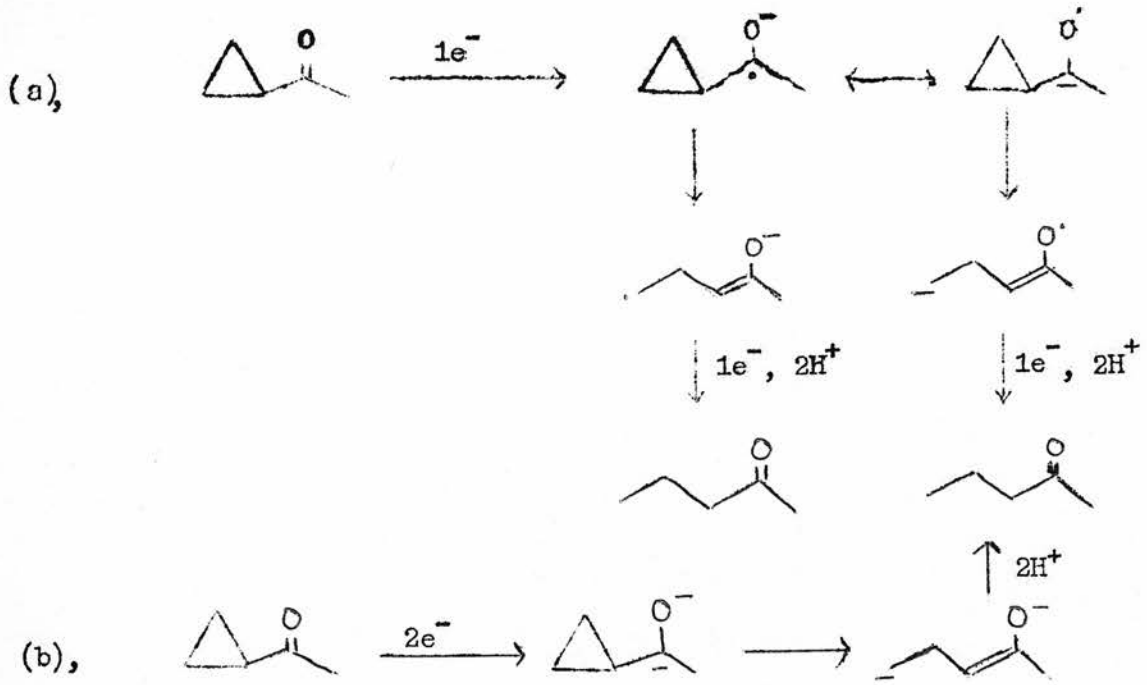
Examination of models indicates that the C(1)-C(7) bond is better placed to overlap with a π-orbital of the carbonyl group than the C(1)-C(6) bond, considerable distortion of the molecule being necessary to give overlap in the latter case. Models also suggest that further distortion would be necessary to allow a radical or anion produced at $C_{(6)}$ to overlap with the C(4)-C(5) double bond.

In the above examples, it is obvious which of the two cyclopropane bonds concerned overlaps best with the π-orbital of the carbonyl group, but in some cases it is difficult to decide which bond gives the best orbital overlap. This situation is illustrated in the reductive cleavage of (+)-pericyclocamphanone (9) which gives only (+) - camphor (10).[28]

(9) (10)

A priori, one would expect the C(3)-C(4) and C(3)-C(5) bonding orbitals to overlap equally well with the π-orbitals of the carbonyl group, However, Norin postulated that the interaction between the geminal methyl group and the hydrogens on C(6) caused a slight distortion increasing the C(3)-C(5) bond overlap, thus explaining the observed single product.

The reductive cleavage of conjugated cyclopropyl ketones with metals in liquid ammonia is, overall, a two electron reduction. Rearrangement could occur through (a), a radical-anion species, after the addition of one electron to the carbonyl group, or (b), a dianion species, generated by the addition of two electrons to the carbonyl group. It can be seen that rearrangement of



electrons in the bond cleavage step of the reduction leads to either an alkyl radical or a carbanion intermediate.

Because of the differing stabilities of primary, secondary, and tertiary carbanions and radicals, it should be possible to differentiate between a mechanism involving an alkyl radical intermediate and a mechanism involving a carbanion intermediate. It is known that the stability of a radical increases with increasing substitution[32a] and that the stability of a carbanion decreases with increasing substitution.[32b] Therefore, when electronic factors alone decide the direction of cleavage, cleavage of an unsymmetrically substituted cyclopropane ring should give rise preferentially to that product which is derived from the most substituted radical intermediate for an alkyl radical mechanism, and to that product which is derived from the least substituted carbanion intermediate if rearrangement occurs through a carbanion mechanism.

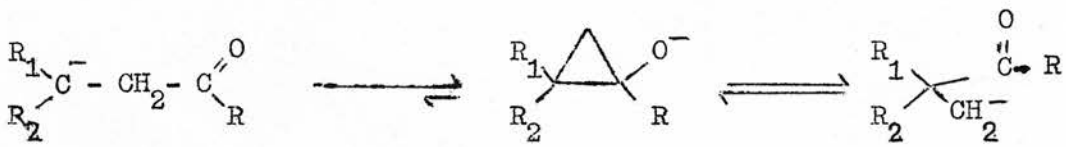
The assumption that the relative stabilities of the intermediates should influence the direction of ring-opening when electronic factors alone are controlling has

been confirmed for rearrangement through both radical and carbanion intermediates.

Neckers, Schaap, and Hardy[33] have shown that the radical rearrangement of trans-2-methylcyclopropyl phenyl ketone (11), with di-t-butyl peroxide in butan-2-ol, gives the two possible rearranged products, butyl phenyl ketone (12), and isobutyl phenyl ketone (13), in the ratio of 9:1. The rearrangement is predominantly in the direction favouring the more stable secondary radical intermediate.

(11) (12) (13)

In the hydrolysis of 3-acetoxy-Δ'-pyrazolines, Freeman and Plonka[34] have shown the existence of an intermediate cyclopropyl homoenolate ion (14), formed from a secondary carbanion, which rearranges in the direction favouring the more stable primary carbanion product.

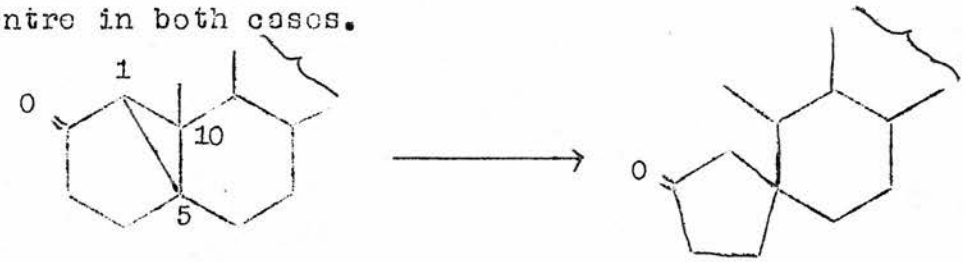


(14)

However, in fused bicyclic systems, the very high stereospecificity of the reduction, which has already been explained in terms of orbital overlap, indicates that stereochemical factors control the direction of ring opening. Consideration of the actual direction of ring opening obtained confirms that the controlling factors are not electronic.

In the reduction of (-) - sabinaketone (5),[28] the observed single product, 3-isopropyl-3-methylcyclopentanone

(6) is formed from C(1)-C(6) bond cleavage *via* an intermediate in which C(6) is a primary centre. C(1)-C(5) bond cleavage, giving an intermediate in which C(5) became a tertiary centre, would give 4-isopropylcyclohexanone which is not observed. In the reduction of (+) - carone (1),[28,29] the product obtained (-) - carvomenthone (2) is formed by C(1)-C(7) bond cleavage *via* an intermediate in which C(7) is a tertiary centre. C(1)-C(6) bond cleavage, giving an intermediate in which C(6) became a secondary centre, would give 3,3-dimethyl-7-methylcycloheptanone, which is not observed. Finally, in the reduction of lumicholestenone (15), to 1(10→5α) - abeocholestan-2-one (16),[29] no competition is observed between C(1)-C(10) bond cleavage and C(1)-C(5) cleavage although ring opening gives rise to a tertiary centre in both cases.

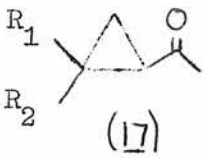


(15) (16)

It is seen that in the first example rearrangement occurs *via* the least substituted intermediate, in the second *via* the most substituted intermediate, and in the last *via* one of two similarly substituted intermediates, thus confirming that electronic factors are not decisive in directing ring opening in this type of system.

It is obvious, therefore, that before the electronic factors influencing the direction of ring-opening can be evaluated, the steric factors must be eliminated. It is necessary, therefore, to study the reductive opening of conjugated cyclopropyl ketones in which both bonds of the cyclopropane ring are free to overlap with the π-orbital of the carbonyl group, thus eliminating any steric effect.

For this reason, the reduction of conjugated ketones of the general type (17) was studied. In this system there is free rotation of the acetyl group allowing overlap with either cyclopropyl bond.

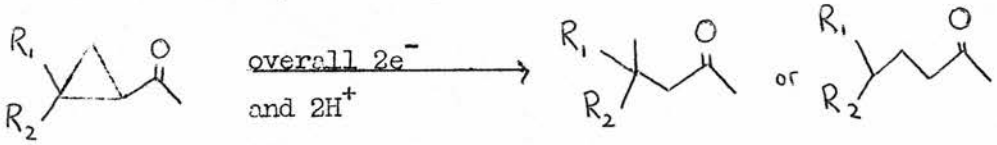


(17)

(R_1, R_2, =H, Me; Me, H; or Me, Me.)

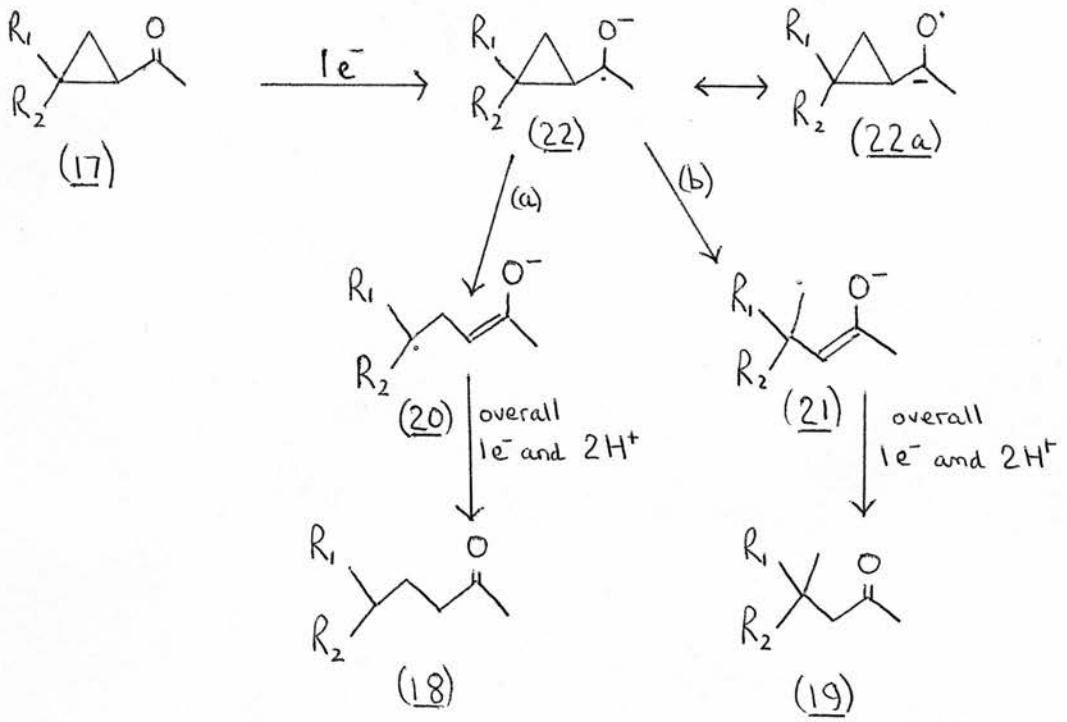
The basic premise to the present work is that by placing substituents at the 2-position of acetylcyclopropane, and studying the preferred direction of ring-opening, it should be possible to deduce whether the rearrangement occurs through a radical or an anion species.

In principle, cleavage is possible in two directions.



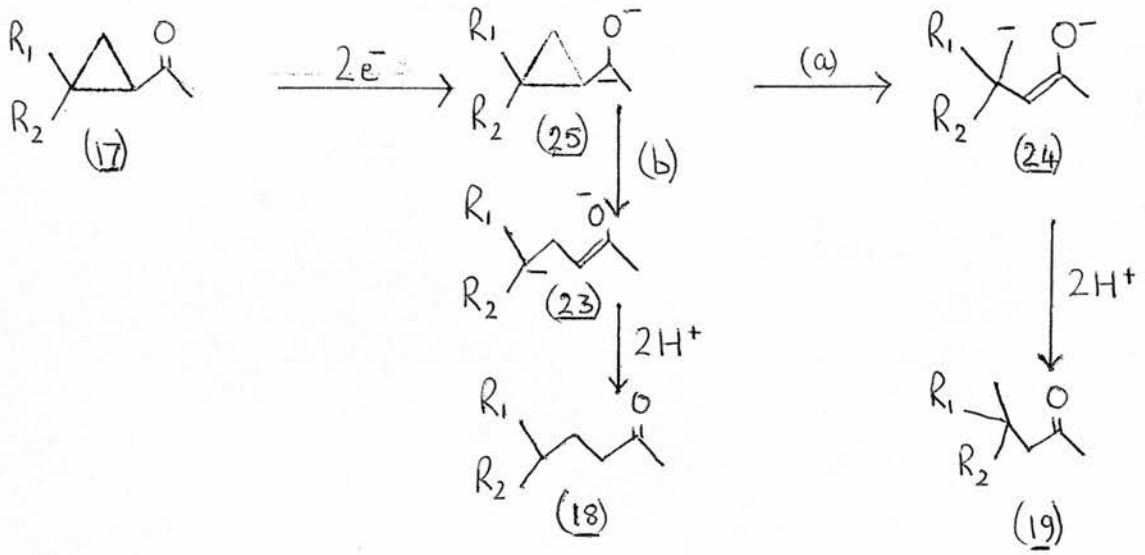
However, the favoured direction of opening should be controlled by the type of species involved, i.e. radical or anion.

For a radical-anion process, ketone (17) could give rise to two products, (18) and (19), through two radical-anion intermediates, (20) and (21) respectively.



Assuming that equal overlap of both cyclopropane bonds with the π-orbital of the carbonyl is possible and that the energy of the transition state reflects the stability of the open-chain species being formed, product (18) would be expected to predominate, since the intermediate secondary or tertiary radical (20) would be more stable than the primary radical (21).[32a] Rearrangement of (22a), the alternative form of the radical-anion (22), i.e. two electrons on carbon and the odd electron on oxygen, is considered unlikely, since it has been shown that the major contributor to the resonance hybrid of the radical anion has two electrons on oxygen and the odd electron on carbon.[35,36]

For a dianion process, ketone (17) could give rise to two products, again (18) and (19), via the two carbanion intermediates, (23) and (24) respectively.



Using the same assumptions made in the above discussion of the radical-anion mechanism, product (19) would now be expected to predominate since the intermediate primary carbanion (24) would be more stable than the secondary or tertiary carbanion (25).[32b]

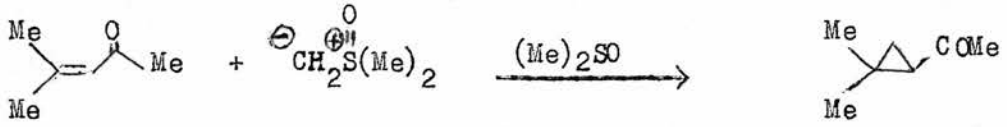
It has been shown that cyclopropyl ketones undergo reductive cleavage with metals in ammonia by a mechanism

similar to that found for enones.[27] In the latter case, alkylation[37] and deuteration[38] studies have shown that, during reduction, the β carbon atom behaves as a carbanion. The assumption, therefore, that ring-opening of cyclopropyl ketones occurs *via* a carbanion intermediate is logical, and is generally favoured.[29,39,40] However, in the reduction of α,β -unsaturated carbonyl compounds, both by metals, and electrolytically, Wiemann[41] has shown the existance of radical-anions, formed on the surface of the metal or at the cathode during the reduction process. Furthermore, in the polarographic reduction of carbonyl compounds at high pH, Schmid and Heilbronner[35] have viewed the mechanism of reduction as the addition of one electron to the carbonyl group. The assumption that ring-opening of cyclopropyl ketones occurs *via* a radical-anion mechanism is therefore equally reasonable. Surprisingly, only one group of workers[31] considers that the ring-opening of cyclopropyl ketones might proceed by a radical-anion mechanism.

DISCUSSION

1-Acetyl-2,2-dimethylcyclopropane (26)

1-Acetyl-2,2-dimethylcyclopropane was prepared by the method of Roberts et al[42] using the Corey-Chaykovsky reaction[43] of dimethyloxosulfonium methylide, in dimethyl sulfoxide, with mesityl oxide (27).



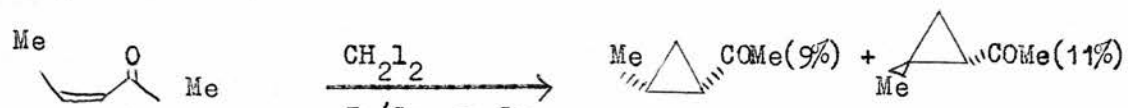
(27) (26)

The spectral data (ir and nmr) of the product, purified by preparative vpc, are given in the experimental section and were in agreement with literature values.[42]

cis-1-Acetyl-2-methylcyclopropane (28)

Great difficulty was experienced in the preparation of this essential product and many different approaches were tried before a successful synthesis was found.

Roberts et al[42] have described the preparation of a mixture of cis-1-acetyl-2-methylcyclopropane (28) and trans-1-acetyl-2-methylcyclopropane (29) in the Simmons-Smith reaction of cis-pent-3-en-2-one (30) with the organo-zinc compound prepared from zinc/copper couple and methylene iodide in zinc.



(30) (28) (29)

In their preparation of cis-pent-3-en-2-one, it was reported that if iodine was added to refluxing trans-pent-3-en-2-one, an equilibrium mixture of the cis and trans isomers was formed, and, since the cis

isomer had a lower b.p. (98-101°)than the trans isomer (b.p. 120-122°), it was possible to distil out the cis isomer using a very efficient distillation apparatus.

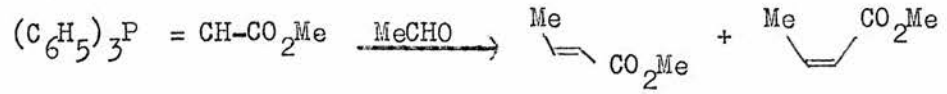
Accordingly, trans-pent-3-en-2-one was prepared using the Wittig reaction of acetylmethylenetriphenylphosphorane and acetaldehyde in methylene chloride. It has been reported[44] that this method gives trans-pent-3-on-2-one in a very high state of purity. The product was obtained by distillation (b.p. 120-122°, lit.,[45] b.p., 124°) and contained less than 0.5% impurity (vpc; Apiezon L, 55°). The spectral data (ir and nmr) of the product, given in the experimental section, confirmed the assigned structure.

However, the attempted distillation of cis-pent-3-en-2-one from a refluxing, equilibrium mixture of cis and trans isomers, using a Buchi spinning band distillation apparatus with a very high reflux/take-off ratio, gave only trans-pent-3-on-2-one and water, as an azeotropic mixture (b.p., 99°). A slight modification of technique, suggested by a private communication from Professor Roberts, was that the water formed in the equilibration was removed by distillation and fresh iodine was added. Again, however, only the trans isomer was obtained.

This approach to the synthesis of cis-pent-3-en-2-one was, therefore, abandoned. It has since been reported[46] that cis-pent-3-en-2-one has b.p., 130°; this was confirmed by oxidation of an authentic sample of cis-pent-3-en-2-ol (experimental section, p. 77) to give a product with b.p., 131-133°.

House et al[47] report obtaining both the cis and trans isomers of methyl crotonate (31), in the ratio of 38:62, from carbomethoxy-

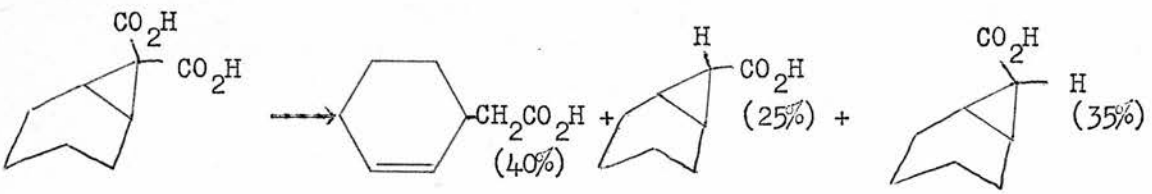
methylenetriphenylphosphorane (32) and acetaldehyde using methanol as the solvent.



(32) (31a) (31b)

The preparation of trans-pent-3-en-2-one was, therefore, repeated using acetylmethylenetriphenylphosphorane (0.90 m mole) and acetaldehyde (4.3 m mole) in methanol (4 ml.). Only the trans isomer was obtained, however. It has since been found, in this laboratory, that some subsequent preparations of trans-pent-3-en-2-one, using the method given on p.72 , gave as much as 11% of a product identified as cis-pent-3-en-2-one (nmr, ir, and ms) although in the preparation given on p. 72 , no cis isomer was obtained. No explanation for this can be offered.

The decarboxylation of bicyclo [4.1.0] heptane-7,7-dicarboxylic acid (33) to give exo- and endo- bicyclo [4.1.0] heptane-7-carboxylic acid (34, and 35) and cyclohex-2-enylacetic acid (36) suggested that it [48]



(33) (36) (34) (35)

might be possible to prepare cis-2-methylcyclopropylcarboxylic acid (37) by decarboxylation of 2-methylcyclopropanedicarboxylic acid (38). The required

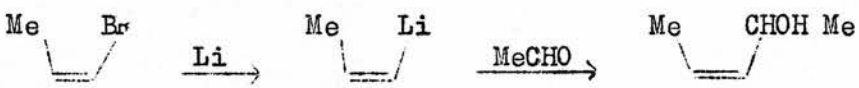
(38) (37)

acetylcyclopropane could then be prepared by treatment of the cis-acid chloride with dimethylcadmium.[49]

However, no product was obtained from the reaction of 1,2-dibromopropane (39) and the sodium salt of ethylcyano-acetate (40) using the method of Perkin and Carpenter,[50] and so 1-carbo-ethoxy-1-cyano-2-methylcyclopropane (41), the chosen precursor to (38) could not be obtained.

(39) (40) (41)

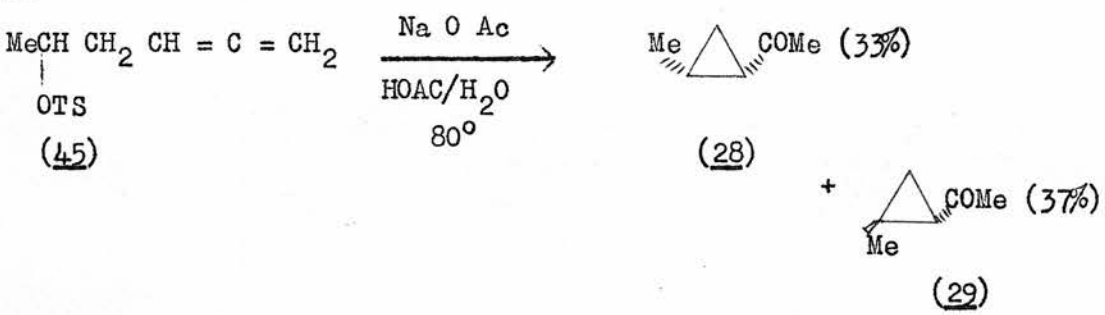
It has been reported[51] that the reaction of cis-1-bromoprop-1-ene (42) with lithium in ether gives cis-prop-1-enyl-lithium (43), and that the configuration of the propenyl lithium is retained in the subsequent reaction with acetaldehyde, to give cis-pent-3-en-2-ol (44).



(42) (43) (44)

All attempts to synthesise cis-prop-1-enyl-lithium, however, failed due, it is thought, to an impurity in the bromide used.

Bertrand and Santelli[11] have reported the production of a mixture of cis- and trans-1-acetyl-2-methylcyclopropane (28, and 29) from the acid-catalysed solvolysis of hexa-4,5-dien-2-yl toluene-p-sulphonate (45),



(45) (28) (29)

which is prepared from hex-4-en-1-yn-3-ol by a three-stage synthesis.[11,52,53]

However, the attempted preparation of hex-4-en-1-yn-3-ol from crotonaldehyde and sodium acetylide, in liquid ammonia,[54] resulted in an explosion when the product was being distilled and so this route to cis-1-acetyl-2-methylcyclopropane was abandoned.

cis-1-Acetyl-2-methylcyclopropane was finally obtained by oxidation of cis-1-(2-methylcyclopropyl)ethanol, prepared from cis-pent-3-en-2-ol by a modified Simmons-Smith reaction. The procedure of Raphael,[55] for the preparation of ∝-acetylenic carbinols was used to prepare pent-3-yn-2-ol from prop-1-yn-1-yl magnesium bromide and acetaldehyde. Hydrogenation of pent-3-yn-2-ol over a modified Lindlar's palladium catalyst gave a product, the spectral data of which were in full agreement with the structure of cis-pent-3-en-2-ol.

The Simmons-Smith reaction on cis-pent-3-en-2-ol was first tried using the method given on p.[75] of the experimental section, which was used successfully in the preparation of trans-1-(2-methylcyclopropyl) ethanol from trans-pent-3-en-2-ol. Three different experiments, using the conditions given, gave (1), recovered cis-pent-3-en-2-ol, (2), a crude product which contained more than twenty components of roughly equal amounts (vpc), none of which had a retention time of the order expected for the product (i.e. a retention time similar to the trans isomer), and (3), a mixture of three unknown iodo-compounds.

However, the Simmons-Smith procedure as described by Dauben and Berezin[17] was found to give the desired product (purified by preparative vpc; 43% yield overall) when a very short reaction time and a very large ratio of solvent to reactant was used. The spectral data (nmr and ir) of the product, given in the experimental section, were as expected for

cis-1-(2-methylcyclopropyl) ethanol.

Oxidation of an ethereal solution of this alcohol with chromic acid (6N), gave cis-1-acetyl-2-methycyclopropane which had spectral data (ir and nmr) identical with literature values.[42] The mass spectrum of the ketone was as expected.

trans-1-Acetyl-2-methylcyclopropane (29)

It was originally intended that both the cis and the trans isomers of 1-acetyl-2-methylcyclopropane would be prepared at the same time from cis-pent-3-en-2-one, see p. 13, but the difficulty experienced in the preparation of cis-pent-3-en-2-one precluded this.

Since α,β-unsaturated alcohols are reported to give much better yields than α,β-unsaturated ketones in the Simmons-Smith reaction,[18] it was decided to prepare trans-1-acetyl-2-methylcyclopropane by oxidation of the product obtained from the Simmons-Smith reaction of trans-pent-3-en-2-ol.

trans-Pent-3-en-2-ol, prepared from crotonaldehyde and methylmagnesium chloride, was reacted with the organo-zinc compound from methylene iodide and zinc/copper couple, generated *in situ* using the modification of the Simmons-Smith procedure described by Perraud and Arnaud.[19] The spectral data of the vpc pure product are given in the experimental section, and were in agreement with the published values[56] for trans-1-(2-methylcyclopropyl) ethanol. Oxidation of this material (6N chromic acid) gave a product which had the expected spectral data (ir, nmr, and ms) for trans-1-acetyl-2-methylcyclopropane.

^{1}H Nuclear Magnetic Resonance Spectra

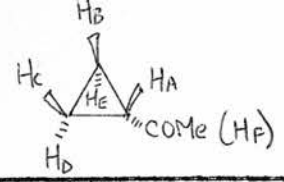
The ^{1}H nuclear magnetic resonance spectra of acetylcyclopropane, cis- and trans-1-acetyl-2-methylcyclopropane, and 1-acetyl-2,2-dimethylcyclopropane were obtained at 100 MHz in carbon tetrachloride

as solvent, with tetramethylsilane as lock, and in benzene as solvent and lock. The chemical shifts of most of the protons were found to be different with benzene as the solvent. This is to be expected since it is known[57] that the carbonyl group forms a loose π-type complex with benzene, and that this complex has a sufficient life-time to enable the π-electrons of the benzene ring to affect the chemical shifts of protons close to the carbonyl group.

The data from the spectra of all four compounds are given in the experimental section but since there are few published values for chemical shifts of protons in this type of compound, the chemical shift data are summarised below in tabular form. For ease of identification, protons are labelled HA, HB, etc., as shown at the head of the Table. Only HC and/or HD of the cyclopropane ring may be substituted by a methyl group; for example, in the spectrum of trans-1-acetyl-2-methylcyclopropane HC would represent the three protons of a methyl group.

As expected, the chemical shifts of those protons on the same side of the cyclopropane ring as the acetyl group were most affected when the spectrum was obtained in benzene.

Coupling constants (if any) and integration of peaks in the spectra, spin-decoupling, and deuteration provided the evidence for the proton assignations given in the Table.



Proton	Chemical Shift (δ scale)			
	Acetylcyclo-propane	trans-1-Acetyl-2-methyl-cyclopropane	cis-1-Acetyl-2-methyl-cyclopropane	1-Acetyl-2,2-Dimethyl-cyclopropane
HA(CCl_4)	1.88 (m,1H)	1.53 (m,1H)	1.98 (m,1H)	1.78 (d of d, 1H)
(C_6H_6)	1.68 (m,1H)	1.50 (m,1H)	1.72 (m,1H)	1.62 (m, 2H)
HB(CCl_4)	0.80 (m,4H)	0.60 (m,1H)	0.96 (m,2H)	0.71 (d of d, 1H)
(C_6H_6)	0.70 (m,2H)	0.60 (m,1H)	1.00 (m,1H)	0.74 (d of d, 1H)
HC(CCl_4)	0.80 (m,4H)	1.13 (d,3H)	0.96 (m,2H)	1.17 (s, 3H)
(C_6H_6)	0.70 (m,2H)	1.02 (d,3H)	0.85 (m,1H)	1.12 (s, 3H)
HD(CCl_4)	0.80 (m,4H)	1.20 (m,2H)	1.01 (d,3H)	1.05 (s, 3H)
(C_6H_6)	1.10 (m,2H)	1.50 (m,2H)	1.23 (d,3H)	1.32 (s, 3H)
HE(CCl_4)	0.80 (m,4H)	1.20 (m,2H)	1.30 (m,1H)	1.11 (m, 1H)
(C_6H_6)	1.10 (m,2H)	1.50 (m,2H)	1.23 (m,1H)	1.62 (m, 2H)
HF(CCl_4)	2.15 (s,3H)	2.13 (s,3H)	2.15 (s,3H)	2.14 (s, 3H)
(C_6H_6)	2.04 (s,3H)	2.06 (s,3H)	2.08 (s,3H)	2.10 (s, 3H)

Mass Spectra

At low ionisation potentials ($\lesssim$20 eV), the fragmentation patterns of acetylcyclopropane, trans- and cis-1-acetyl-2-methylcyclopropane, and 1-acetyl-2,2-dimethylcyclopropane were identical, each spectrum showing only four mass peaks, the molecular formula of which were obtained by accurate mass measurement. In all cases, the parent ion was formed from the parent acetylcyclopropane by loss of one electron, and the base peak was at m/e = 43 (C_2H_3O, the acetylium ion)[58], formed by loss of a cyclopropyl radical from the parent ion. The two other peaks had m/e = (p - 15), and (p - 43), respectively. The first peak was shown by accurate mass measurement to be due to loss of a methyl radical from the parent ion. Comparison with the mass spectrum of 1-acetyl-2,2-dimethylcyclopropane in which all three hydrogen atoms of the acetyl group were replaced by deuterium showed that the methyl radical lost came exclusively from the acetyl group. The peak at m/e = (p - 43) was shown by accurate mass measurement to correspond to the cation formed by loss of an acetyl radical.

1-Acetyl-2,2-diethylcyclopropane (46)

The attempted route to this product was from 4-ethylhex-3-en-2-one (47) using either the Corey-Chaykovsky reaction[43] as described on p. 72 for the preparation of 1-acetyl-2,2-dimethylcyclopropane, or the Simmons-Smith reaction.[14,17]

(47) (46)

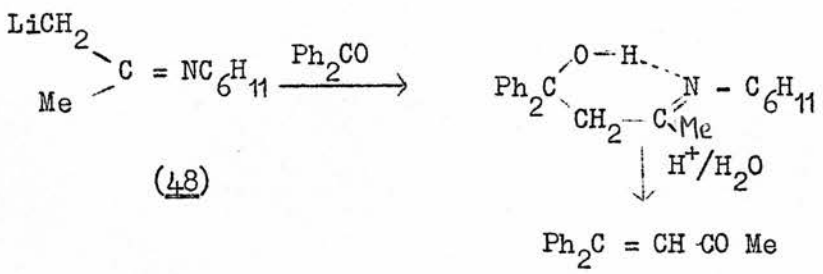
trans-pent-3-en-2-one had already been prepared using the Wittig reaction[44] of acetylmethylenetriphenylphosphorane and acetaldehyde and

so it was thought that reaction of the same ylide with pentan-3-one would give the required 4-ethylhex-3-en-2-one. However, using the conditions described, only unchanged starting material was obtained.

Ruchardt, Eichler, and Panse[59] report that carbonyl compounds can be made to react with stabilised ylides such as acetylmethylenetriphenylphosphorane if the reaction is carried out in the presence of benzoic acid and a large excess of carbonyl compound.

However, boiling a solution of the ylide, pentan-3-one, and benzoic acid in benzene for 48 hours, again gave only unchanged pentan-3-one.

Wittig and Suchanek[60] have reported that the reaction of the lithium derivative of the Schiff's base isopropylidenecyclohexylamine (48), with benzophenone, a directed aldol condensation, gives 1,1-diphenylbut-1-en-3-one (49).



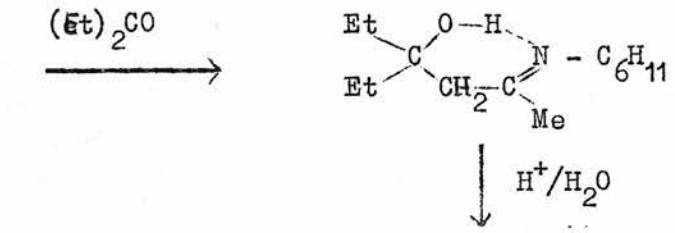
(48)

$Ph_2C = CH\text{-}CO\ Me$

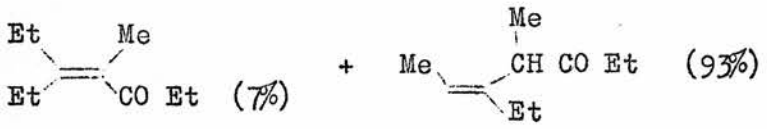
(49)

The directed aldol condensation using (48) and pentan-3-one gave a mixture of three products in almost equal amounts and with very similar vpc retention times. Examination of the ir spectrum showed the presence of a large olefinic absorption (1620 cm^{-1}), and a conjugated (1685 cm^{-1}) and unconjugated (1710 cm^{-1}) carbonyl absorption. At low eV, the mass spectrum showed only peaks at m/e = 126 (p), 111 (p - 15), 97 (p - 29), and 43, almost as expected; the major peaks, at low eV in the mass spectrum, being expected to correspond to a parent ion at m/e = 126,

loss of a methyl radical from the parent ion, at m/e = 111, loss of an ethyl radical from the parent ion, at m/e = 97, and the acetylium ion at m/e = 43. The presence of a peak at m/e = 83, corresponding to the loss of an acetyl radical from the parent ion, was considered possible but was not, in fact, observed. It seems likely, therefore, that the product was a mixture of 4-ethylhex-3-en-2-one (47), and cis- and trans-4-ethylhex-4-en-2-one (50, and 51), since Faulk and Fry[61] found



that a large amount of the unconjugated isomer could be formed in the preparation of unsaturated ketones. For example, in the preparation of 5-ethyl-4-methylhept-4-en-3-one (52), 93% of the unconjugated isomer, 5-ethyl-4-methylhept-5-en-3-one (53) was formed with only 7% of the expected product (52).



The isomeric mixture of products (47), (50), and (51) could not be separated by distillation, preparative vpc, or thin layer chromatography.

It was thought that reaction of this product mixture with dimethyloxosulfonium methylide might give a product mixture from which 1-acetyl-2,2-diethylcyclopropane could be isolated. Accordingly, the mixture of the three isomers of 4-ethylhexen-2-one in dimethylformamide was reacted with dimethyloxosulfonium methylide in anhydrous dimethylformamide using the method of Landor and Punja.[62] After the usual work-up procedure, and distillation, a mixture of three new products was obtained, which was only partially resolved by vpc. This mixture could not be separated by preparative vpc, column or thin-layer chromatography.

The Reduction of Substituted Acetylcyclopropane with Metals in Liquid Ammonia

During the period since this work was commenced, results have been published[39,40] duplicating in part some of the work discussed below, and where appropriate, comparisons are drawn with relevant results.

The results of the reductions of 1-acetyl-2,2-dimethylcyclopropane, and cis- and trans-1-acetyl-2-methylcyclopropane with metals in liquid ammonia are shown in Tables 1-10 in the Appendix.

Two methods of reduction were employed; method A, in which the reducing metal was added to a solution of ketone in liquid ammonia, and method B, in which ketone was added, by syringe through a septum cap, to a solution of the reducing metal in liquid ammonia.

Tables 1 and 2 show the results of several reductions on 1-acetyl-2,2-dimethylcyclopropane with lithium in liquid ammonia, using methods A and B respectively. Using method A, the ratio of the rearranged products, 5-methylhexan-2-one (54), and 4,4-dimethylpentan-2-one (55), was virtually independent (±5%) of the amount of lithium added, but

using method B, the ratio of rearranged products varied with the concentration of lithium used in the reduction.

Since the aim of the reduction experiments was to differentiate between the possible mechanisms for the reduction of acetylcyclopropanes by dissolving metals in liquid ammonia, the significance of the differences observed using the two reduction methods are discussed in detail later.

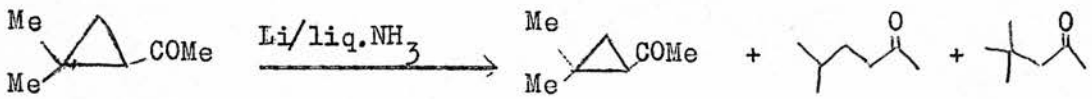
It will be seen that method B was used in all reduction experiments apart from those the results of which are shown in Table 1. There are two reasons for this. Firstly, the experiments shown in Tables 3-8 were carried out primarily to investigate the reasons for the variation in ratio of rearranged product using method B, and secondly method B was preferred to method A because of the practical difficulty of keeping the reduction mixture anhydrous and minimising loss of volatile material using method A.

Before vpc analysis of the product mixture from a reduction, any alcohols present were converted to the corresponding ketones by oxidation with 6N chromic acid. Postulated mechanisms for the formation of alcohols are presented later.

Decane was added as an internal vpc standard in most reductions. In a control experiment, a mixture of decane (0.10 g), 5-methylhexan-2-one (54) (0.25g), and 4,4-dimethylpentan-2-one (55) (0.25 g) was analysed by vpc (peak integration) and then added to liquid ammonia (50 ml.). The mixture was stirred for 2 hours and then solid ammonium chloride was added in the usual work-up procedure. After evaporation of the ammonia and concentration of the ether extract, vpc analysis (peak integration) gave an unchanged ratio of decane : (54) : (55).

The ratio also remained unchanged after treatment of a portion of the ether extract with 6N chromic acid. The results of the control experiment indicated that if decane was added at the start of each reduction, it could be used as an internal vpc standard to estimate the yield of recovered material in the reduction experiments.

In the reduction of 1-acetyl-2,2-dimethylcyclopropane (26), the only three products observed on vpc analysis of the oxidised product mixture were 1-acetyl-2,2-dimethylcyclopropane, 5-methylhexan-2-one (54), and 4,4-dimethylpentan-2-one (55).



(26) (26) (54) (55)

Dauben and Wolf,[40] who have made a similar study, occasionally observed 2-methyl-1-hexen-5-one , as well as the three products shown above, on vpc analysis of the oxidised product mixture from the reduction of ketone (26) with lithium in liquid ammonia. They assumed that the extra product was produced thermally, possibly by rearrangement on the vpc column used (20% XF - 1150 Cyanosilicone, 150°), and not by lithium/liquid ammonia reduction.

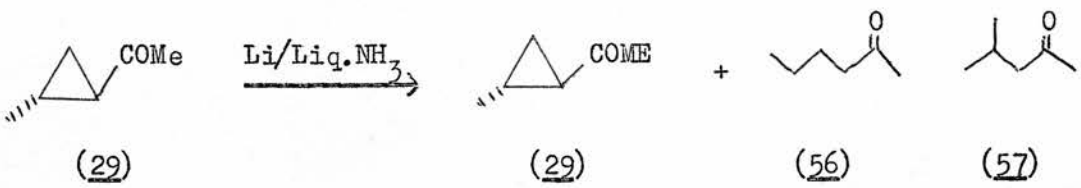
The extra product was never observed in the present work, even at the maximum vpc temperatures used (120°, Carbowax; 180° Apiezon).

Tables 1 and 2 show that in the reduction of ketone (26), the favoured product of rearrangement was ketone (54), the ratio of (54)/(55) varying from 2.05 to 4.50. The decane integral in these tables shows an average recovery of material, of 90%.

For the same reduction, Dauben and Wolf[40] found random values for the ratio of (54)/(55) in the range 2.5 - 3.4, and Fraisse-Jullien and Fréjaville,[39] another group studying this system, found a ratio of 1.5, results quantitatively in agreement with those shown in Tables 1 and 2, although the methods of reduction were slightly different. Dauben and Wolf, however, obtained a minimum loss of material of 16%, with an average loss of 35%. Cyclo-octane was used as an internal vpc standard and was added after work-up of the reduction mixture. Preferential loss of standard was noted when cyclo-octane was added at the start of the reaction but no explanation for this was offered. Fraisse-Jullien and Fréjaville did not give any information about product loss during reduction.

The yield of rearranged product from the reductions varied from 57 to 98% of the total product recovered. That there was no relationship between the yield and the ratio of rearranged product can be seen from Table 1. The product ratio remained essentially the same although the percentage of rearranged product varied from 79 to 97% of the total obtained.

The results of several reduction of trans-1-acetyl-2-methylcyclopropane (29) with lithium in liquid ammonia, using method B, are shown in Table 9. The three products observed on vpc analysis of the oxidised product mixture were trans-1-acetyl-2-methylcyclopropane, hexan-2-one (56), and 4-methylpentan-2-one (57), as expected.



(29) (29) (56) (57)

The favoured product of rearrangement was ketone (57), the ratio of (56)/(57) ranging from 0.0518 to 0.0431, in a random manner.

Dauben and Wolf observed the same three products in the reduction of ketone (29), and found values of 0.068 and 0.027 for the ratio of (56)/(57), no reason for this large variation being offered. Fraisse-Jullien and Frejaville, however, observed only one product, ketone (57), in the reduction of ketone (29).

The results of several reductions of cis-1-acetyl-2-methylcyclopropane (28) with lithium in liquid ammonia, are shown in Table 10. Owing to shortage of material, the weight of ketone (28) used in each reduction (0.25 g.) was lessthan the weight of ketones (26) and (29) used (0.50 g.). However, in a control reduction on ketone (26), using 0.300 g. of lithium, the same ratio of rearranged products was obtained with 0.25 g. as with 0.50 g. of starting material.

The three products observed on vpc analysis of the oxidised product mixture were cis-1-acetyl-2-methylcyclopropane (28), hexan-2-one (56), and 4-methylpentan-2-one (57), as expected.

(28) (28) (56) (57)

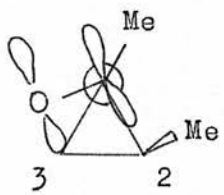
The favoured product of rearrangement was ketone (56), the ratio of (56)/(57) ranging from 6.3 to 9.0 randomly.

Dauben and Wolf observed the same three products in the reduction of ketone (28), and found values of 13 and 22 for the ratio of (56)/(57) no reason for the variation being given.

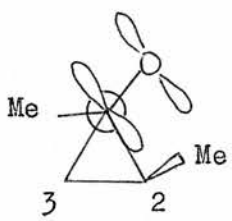
As has been discussed in the Introduction, the direction of ring-opening observed in the reduction of conjugated cyclopropyl ketones is influenced both by steric and electronic factors. The basic premise to the present work was that by placing alkyl substituents at the 2-position of acetylcyclopropane, and studying the preferred direction of ring-opening, it would be possible to deduce whether the rearrangement occurred through a radical or an anion species, since it was assumed that both bonds of the cyclopropane ring in this type of system would be free to overlap with the π-orbital of the carbonyl group, thus eliminating any steric effect.

This last assumption was shown to be false by comparing the results of the reductions of ketones (28) and (29) which should give the same rearranged products, in the same ratio, if free rotation about the cyclopropane-carbonyl bond can occur. The ratio of the rearranged products in the reduction of ketone (29) was in fact reversed in the reduction of ketone (28).

Examination of molecular models showed that in cis-1-acetyl-2-methylcyclopropane (28) the cis-methyl group exerts a steric effect such that the $C_{(1)}$-$C_{(2)}$ cyclopropane bond has better overlap with the carbonyl π-system than the $C_{(1)}$-$C_{(3)}$ bond, but that in trans-1-acetyl-2-



(28)

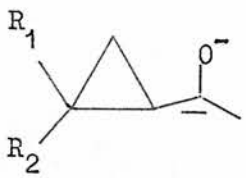


(28)

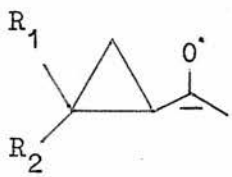
methylcyclopropane (29), no such steric effect is present. The observed ratios of rearranged products can, therefore, be explained as follows: with ketone (29), where there is no steric effect, the favoured product of rearrangement is decided by the relative thermodynamic stability of the intermediates generated, but with ketone (28), the tendency to form the thermodynamically most stable intermediate is outweighed by the steric effect, giving a reversal in the ratio of rearranged products.

In ketone (29), where thermodynamic considerations alone control the direction of ring-opening, the favoured product of rearrangement is ketone (57). As a consequence of the arguments advanced in the Introduction, rearrangement must occur, therefore, via a mechanism involving an anion intermediate (formation of a primary carbanion rather than a secondary carbanion).

Two mechanisms for this type of rearrangement were advanced in the Introduction, one involving an initial dianion of the general type (25), and one involving a radical-anion of the general type (22a). Rearrangement of the



(25)



(22a)

radical-anion species (22a) was considered unlikely, but was not entirely excluded. By reference to the Introduction, it can be seen that rearrangement through the dianion (25) necessitates ring-opening

after the addition of two electrons, but that ring-opening can occur after the addition of only one electron if rearrangement proceeds via the radical-anion (22a). It was hoped that it might be possible to differentiate between these two mechanisms by a polarographic study of acetylcyclopropane (58) and the substituted acetylcyclopropanes (26), (28), and (29). The results of that investigation are presented later.

The observed ratio of rearranged products from the reduction of ketone (28) has been explained by the steric effect of the cis-methyl group. This steric effect should be the same in 1-acetyl-2,2-dimethylcyclopropane (26), and, in fact, the observed ratio of products does favour the product arising from the thermodynamically least stable intermediate. However, in the latter case, the ratio lies in the range of 2.05 - 4.50 against a range of 6.3 to 9.0 for the rearranged product from the reduction of (28).

The difference between the two systems arises because the preferred direction of ring-opening is influenced by both electronic and steric factors. The tendency to form a primary carbanion rather than a tertiary carbanion from ketone (26) is stronger than the tendency to form a primary carbanion rather than a secondary carbanion from ketone (28). If, therefore, the magnitude of the steric effect is the same for both ketones, the ratio of products from ketone (26) should be closer to that expected on stability grounds than the ratio of products from ketone (28), i.e. (54)/(55) < (56)/(57). In the absence of any steric effect (55) and (57) would be expected to be the major products c.f. trans-1-acetyl-2-methylcyclopropane.

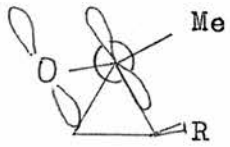
Since the ratio of rearranged products from ketones (26) and (28) was very sensitive to steric effects, several reductions were

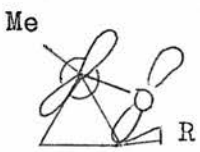
carried out using different reducing metals to see if the ratio was influenced by the size of the reducing metal.

The results of several reductions of ketone (26) using barium and sodium as the reducing metal are shown in Tables 4 and 5 respectively. With barium as the reducing metal, the ratio of rearranged ketones (54)/(55) ranged from 1.63 to 1.87, and with sodium, from 2.22 to 2.93. In one experiment using sodium, a value of 3.50 for the ratio of (54)/(55) was observed but since proferential loss of the standard was observed in that reduction, the result may well be anomolous. In fact, in three of the twelve reductions carried out with sodium, some loss of the standard was observed. However, at no other time was loss of the internal vpc standard suspected.

Dauben and Wolf[40] have reported results of the reduction of ketone (26) with sodium, calcium, and potassium. Using sodium, they found the ratio of (54)/(55) was 3.5, and with calcium and potassium was 2.8 and 3.2 respectively. Their reported value of 3.5 for the ratio of (54)/(55), using sodium, was certainly higher than the range for this ratio given above, but was the result of only one reported reduction.

There is, therefore, only a small difference in the ratio of rearranged products observed when different reducing metals are used, suggesting that the conformation of the transition state changes little with different metals. The reducing metal with the smallest atomic size, lithium, must, therefore, be large enough to fix the preferred conformation since it has been shown that the ground-state[63,64] and transition state conformations[65] in the metal-ammonia reductions of cyclopropyl methyl ketones are predominantly cisoid.





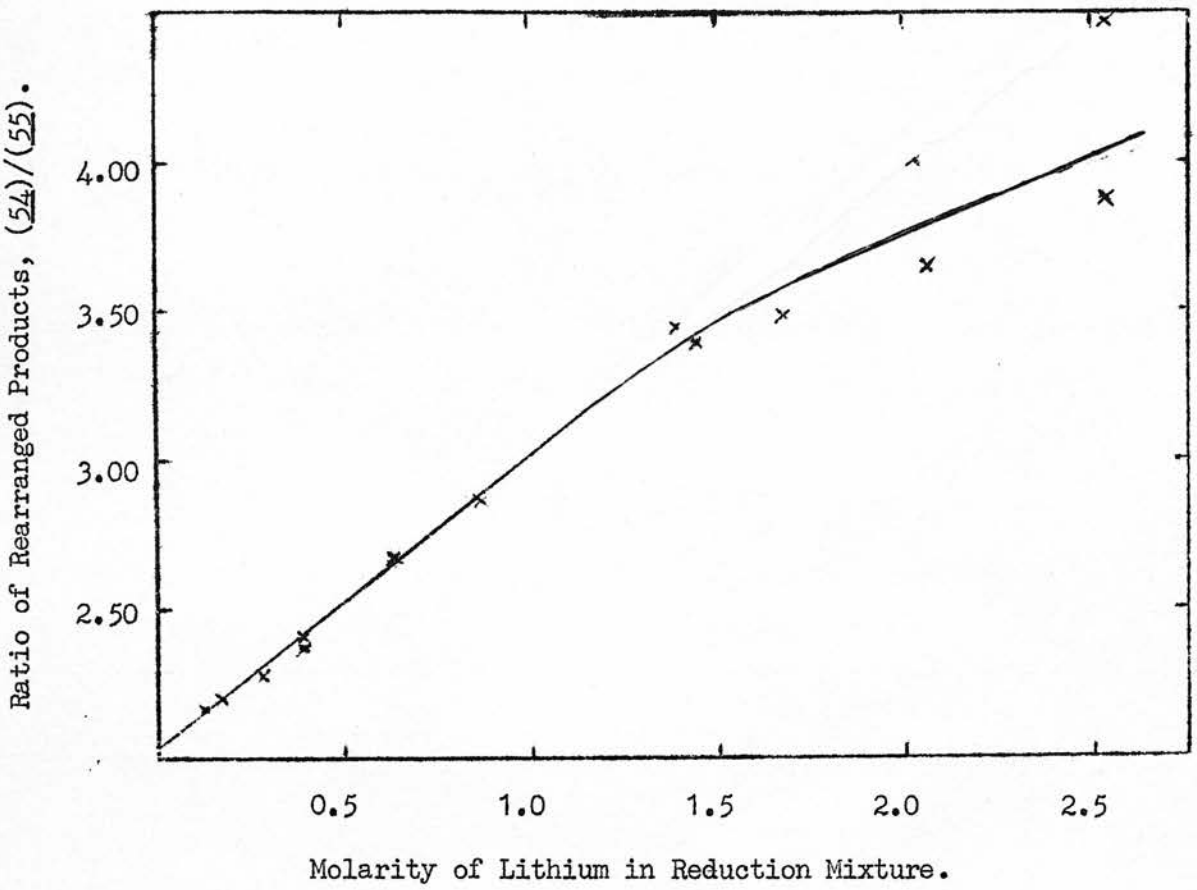
The data in Table 2 shows that there is a direct correlation between the ratio of (54)/(55) observed and the concentration of lithium used in the reduction of ketone (26). A graph of the ratio of the rearranged products against the molarity of the lithium solution used in the reduction is shown below. The straight line part of the curve obtained had a slope of 0.981 litres moles^{-1} and an intercept of 2.03, with a correlation coefficient of 0.9994 (regression analysis, nine points).

The variation of the ratio of (54)/(55) with concentration of lithium was shown to be caused by a salt effect. Table 7 shows the results of several reductions of ketone (26) with a constant weight of lithium metal (0.20 g.) but with varying weights of lithium iodide added. As expected for a salt effect, the ratio varied with total molarity of lithium ion although the weight of lithium metal used was constant.

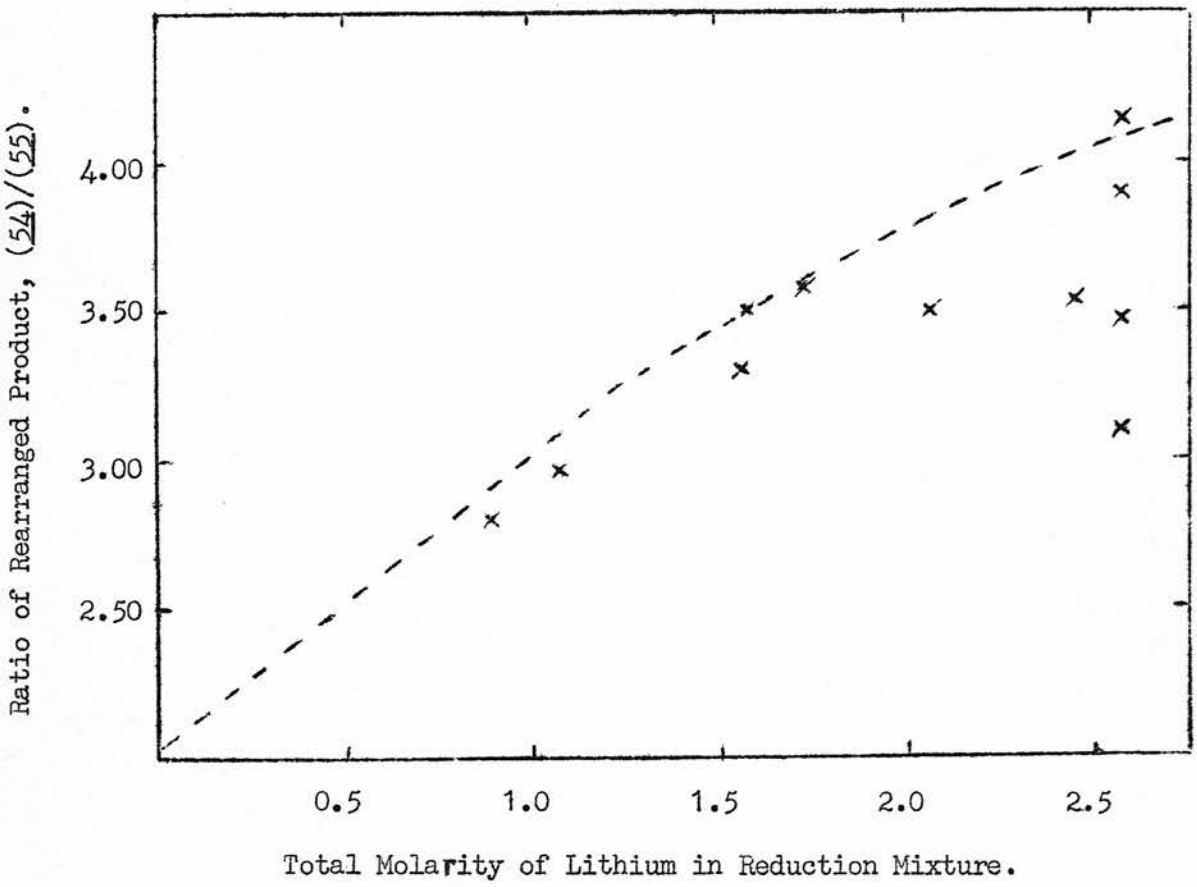
A graph of the ratio of (54)/(55) against total molarity of lithium is shown below, the dotted line showing the curve obtained using lithium metal alone. Excellent correlation was obtained.

Table 8 shows the results of several similar reductions with mixtures of lithium and lithium iodide but using varying weights of lithium metal. Again there is a correlation between the ratio of (54)/(55) and the total molarity of lithium. The two reductions using the smallest weight (0.050 g.) of lithium metal were exceptional

Ratio of rarranged products, (54)/(55), from the reduction of 1-acetyl-2,2-dimethylcyclopropane with lithium in liquid ammonia, plotted against molarity of lithium in the reduction mixture.



Ratio of rearranged products, (54)/(55), from reduction of 1-acetyl-2,2-dimethylcyclopropane with lithium / lithium iodide mixtures in liquid ammonia, plotted against total molarity of lithium in the reduction mixture.



in that the recovery of starting material was very much higher than usual (50 and 67% respectively).

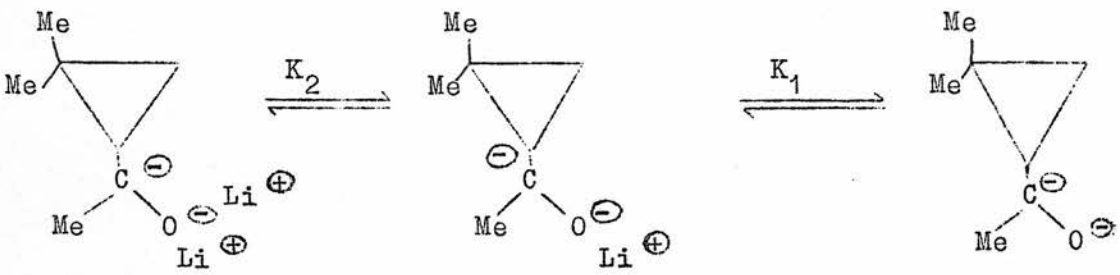
The above data is consistent with a salt effect in the reduction of ketone (26) with lithium in liquid ammonia, using method B. It was of interest, therefore, to carry out some reductions using a cation which was too large to give any salt effect due to intimate contact with the anion, the tetra-ethylammonium cation. Solutions of metals in liquid ammonia were made up as usual, using method B, and then anhydrous tetra-ethylammonium chloride was added. When barium was used as the reducing metal, the barium cations were precipitated as insoluble barium chloride leaving only tetra-ethylammonium cations in solution. The results of three reductions using barium and tetra-ethylammonium chloride are shown in Table 6. The ratio of rearranged products, (54)/(55), ranged from 1.27 to 1.49 compared with values of 1.63 to 1.86 for reductions using barium metal alone. Also shown in the Table are the results of three reductions using lithium and tetra-ethyl-ammonium chloride. The ratio of (54)/(55) in this case ranged from 1.47 to 2.00. It is thought that the values of the ratio of rearranged products were slightly higher in this system because of the slight solubility of lithium chloride in liquid ammonia (0.54 g./100 g.NH_3, - 34°)[65] allowing a small salt effect to be exerted. However, the values for the ratio using lithium and tetra-ethylammonium chloride were still lower than those observed using lithium metal alone.

The value of the ratio obtained using sodium and tetra-ethylammonium chloride (2.84) was in the same range as that obtained using sodium alone (2.22 to 2.93) presumably because sodium chloride is fairly soluble in liquid ammonia, (4.0 g./100 g. NH_3).[66]

It is surprising that a straight line was obtained when the ratio of (54)/(55) was plotted against the molarity of lithium used in the reduction of ketone (26) with lithium. The competition between the two possible routes of bond cleavage must be directly dependent upon the concentration of lithium ions, since virtually the same curve was obtained using lithium metal and lithium iodide as was obtained using lithium metal alone.

This can, however, be rationalised by assuming that the anion formed in the reduction process forms ion pairs with lithium and examining the relative rates of cleavage of the different ion pairs possible.

If it is assumed that the anionic species is formed by the addition of two electrons before the bond cleavage step, two possible ion-paired species, (60) and (61), can be envisaged. There will be an equilibrium between the ion-pair (60) and the ion-triplet (61), and also between the ion-pair (60) and a free dianion (59). The equilibrium constant between the free dianion (59) and the ion-pair (60) is

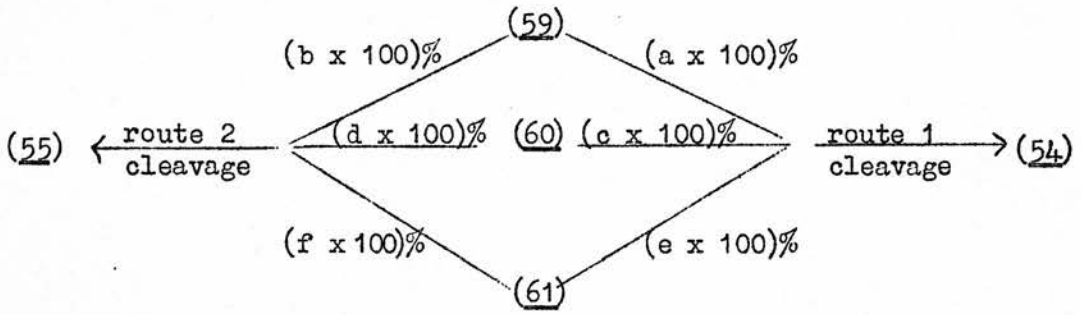


(61) (60) (59)

assumed to be K_1, and between the ion-pair (60) and the ion-triplet (61), K_2.

Product (54) arises from cleavage of the $C_{(1)}$- $C_{(2)}$ cyclopropane bond (route 1 cleavage) and product (55) from cleavage of the $C_{(1)}$ - $C_{(3)}$ cyclopropane bond (route 2 cleavage).

We assumed that when the dianion (59) undergoes rearrangement, a fraction a follows route 1 cleavage and a fraction b follows route 2 rearrangement. Similarly, when the ion-pair (60) undergoes rearrangement, fractions c and d follow routes 1 and 2 cleavage respectively, and when the ion-triplet (61) rearranges, fractions e and f follow routes 1 and 2 cleavage respectively. The relative rates of rearrangement of (59), (60), and (61) are k_1, k_2, and k_3 respectively. It then follows that the observed ratio



of (54)/(55) is equal to:

$$\frac{\frac{a}{a+b} \cdot k_1 [(59)] + \frac{c}{c+d} \cdot k_2 [(60)] + \frac{e}{e+f} \cdot k_3 [(61)]}{\frac{b}{a+b} k_1 [(59)] + \frac{d}{c+d} k_2 [(60)] + \frac{f}{e+f} k_3 [(61)]}$$

Since (a+b) = 1, (c+d) = 1, and (e+f) = 1, this ratio is equal to:

$$\frac{a k_1 [(59)] + c k_2 [(60)] + e k_3 [(61)]}{b k_1 [(59)] + d k_2 [(60)] + f k_3 [(61)]}$$

$$K_1 = \frac{[(59)]\,[Li^+]}{[(60)]} \quad \text{, and } K_2 = \frac{[(60)]\,[Li^+]}{[(61)]}$$

$\therefore$ Ratio of (54)/(55) =

$$\frac{ak_1K_1\,[(60)]/[Li^+] + ck_2\,[(60)] + ek_3\,[(60)]\,[Li^+]\,/\,K_2}{bk_1K_1\,[(60)]/[Li^+] + dk_2\,[(60)] + fk_3\,[(60)]\,[Li^+]\,/\,K_2}$$

$$= \frac{ak_1K_1K_2 + ck_2K_2\,[Li^+] + ek_3\,[Li^+]^2}{bk_1K_1K_2 + dk_2K_2\,[Li^+] + fk_3\,[Li^+]^2}$$

For $[Li^+]$ large,

$$\text{Ratio} = \frac{ck_2K_2 + ek_3\,[Li^+]}{dk_2K_2 + fk_3\,[Li^+]}$$

The straight line obtained by plotting the ratio of (54)/(55) against molarity of lithium has been shown to have a gradient of 0.981 lm^{-1}, and zero intercept of 2.031. Therefore at extrapolated zero concentration of lithium

$$2.031 = \frac{ck_2K_2}{dk_2K_2} = \frac{c}{d}$$

$\therefore$ c = 0.67, and d = 0.33 $\left\{ \text{Since } (c + d) = 1 \right\}$

It is apparent from molecular models, that steric interaction between the carbonyl group and a cis-substituent on the cyclopropane ring would cause route 1 cleavage of the $C_{(1)} - C_{(2)}$ cyclopropane bond to be

favoured. It is also obvious from the models that increasing the effective bulk of the oxygen anion by ion-pair formation would also cause route 1 cleavage of the $C_{(1)} - C_{(2)}$ bond to be favoured. Hence we would expect that the ratio $\frac{a}{b} < \frac{c}{d} < \frac{e}{f}$.

Assuming that e $\sim$ 1, and f $\sim$ 0, since the steric effect of two lithium atoms in the ion-triplet (61) should make route 2 cleavage much less favourable than in the rearrangement of the ion-pair (60),

$$\text{the gradient, } 0.981 \sim \frac{ek_3}{dk_2K_2}$$

$$\therefore \frac{k_3}{k_2K_1} \sim 0.981 \times 0.33$$

The equilibrium constant between the free carbonion (59), and the ion-pair (60), K_1 would be of the order[67] of 1×10^{-4}, and so

$$\frac{k_3}{k_2} \sim 3 \times 10^{-5}.$$

The variation of product ratio with molarity of lithium used for the reduction of ketone (26) can be rationalised by the above theory. However, no variation of product ratio with molarity was observed with any other metal presumably because they have a lower tendency for ion-pair formation due to their larger size.

No variation was observed using ketone (28), although the steric effect of the cis-methyl group might be thought to be the same. This is presumably due to the delicate balance between the steric and the electronic factors influencing the preferred direction of ring-opening

of ketones (26) and (28). In the transition state for cleavage of ketone (28), there is a smaller electronic effect arising from the competition between the stability of a primary and a secondary carbanion intermediate, as opposed to a primary and a tertiary carbanion intermediate from ketone (26), making the steric effect much more predominant.

As mentioned earlier, no variation in the ratio of (54)/(55) with the number of moles of lithium used was observed using method A for the reduction. The reason for this is thought to be that using method A, where lithium metal was added to a solution of ketone (26) in liquid ammonia, the reduction reaction occurred faster than the dissolution of lithium metal. Thus ketone (26) was effectively being reduced by a constant concentration of lithium, and so no variation in the ratio of ring-opened products occurred.

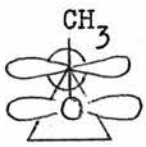
The proposed reduction scheme for acetylcyclopropanes with metals in liquid ammonia does not allow for alcohol formation. It is thought, in fact, that alcohols are produced, not in the reduction itself, but during the work-up procedure. A typical reduction of ketone (26) with lithium in liquid ammonia, using method B, gave 45% of the total product as alcohols. In a control reduction, in which the work-up was performed by adding, in one portion, a very large excess of solid ammonium chloride, with vigorous stirring, the percentage of the total product isolated as alcohols dropped to 8%. It is thought that the normal work-up procedure, in which solid ammonium chloride is added slowly to the reduction mixture, results in protonation of the product enolates to give the product ketones in the presence of electrons, which can further reduce the product ketones to alcohols. The

percentage of the total product isolated as alcohols was much lower in the control reduction because ammonium chloride was added so quickly in the work-up procedure that protonation of the product enolates occurred in the presence of a very much smaller concentration of electrons.

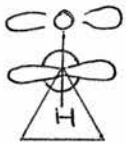
Transition-State Conformations in the Reduction of Substituted Acetylcyclopropanes with Metals in Liquid Ammonia

The importance of transition-state conformations in the reduction of various conjugated acetylcyclopropanes with metals in liquid ammonia is well established.[28,29,39,40] In conjugated cyclopropyl ketones in which the stereochemistry is fixed, ring-opening occurs by cleavage of that cyclopropane bond which has the better orbital overlap with the π-system of the carbonyl group. In acyclic conjugated acetylcyclopropanes, such as ketones (26) and (28), in which steric interactions between the cis-methyl group and the carbonyl group prevent free rotation about the cyclopropane-carbonyl bond, the conformation of the transition state is affected such that the preferred product of rearrangement is that arising from the apparently less thermodynamically stable carbanion intermediate. In acyclic conjugated acetylcyclopropanes, such as ketone (29), in which free rotation about the cyclopropane-carbonyl bond is possible, no conformational preference is observed and all conformations are of equal probability, so that the preferred product of rearrangement is controlled solely by the thermodynamic stability of the anion species.

Electron diffraction[64] and nmr spectral[63] measurements indicate that unsubstituted acetylcyclopropane (58) exists predominantly as the bisected cisoid conformer A in the ground state, whereas cyclopropylcarboxaldehyde (62) exists mainly as the bisected transoid conformer B.[68]

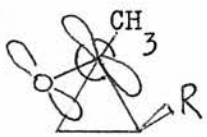


A

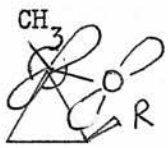


B

The bisected conformers A and B represent the situation where both bonds of the cyclopropane ring have equal overlap with the carbonyl π cloud. However, because of the high bond-breaking selectivity of the reductive process it is more important to consider the *gauche* conformers C, D, E, and F shown below.

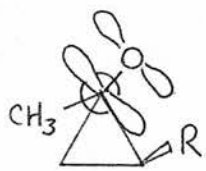


C



D

(R = H,Me)



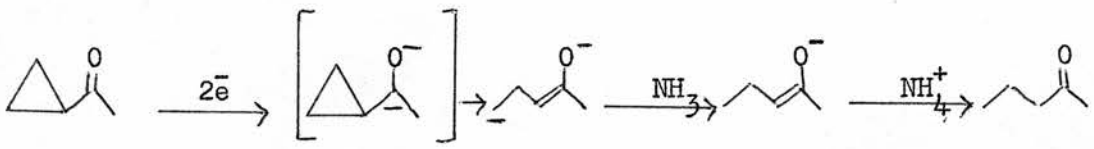
E

F

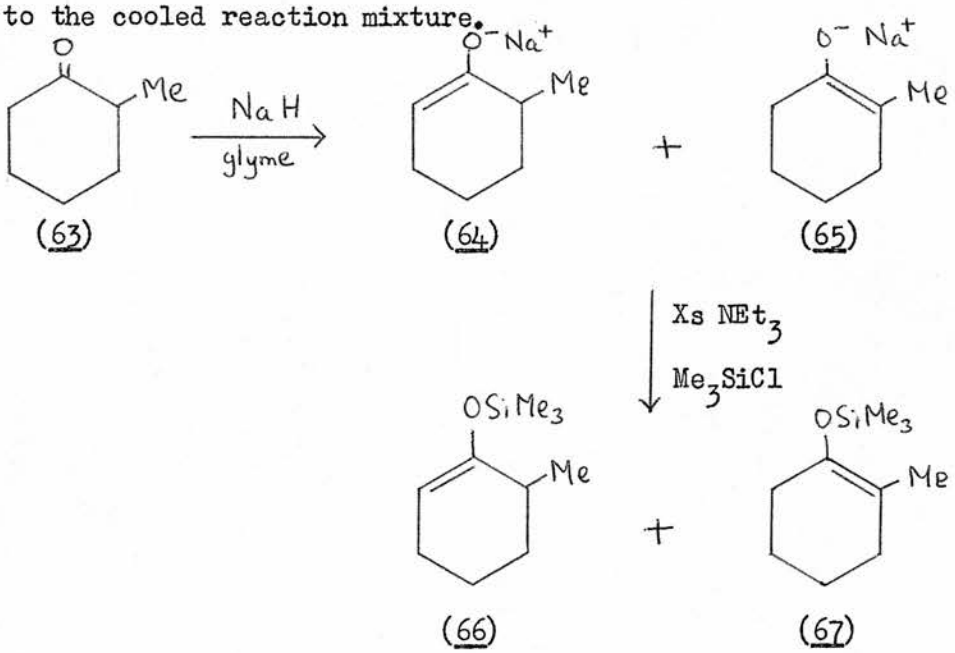
In the absence of any steric effect, i.e. R = H, conformers C and D have equal probability, and conformers E and F have equal probability, and thermodynamic considerations control the reductive process. However, as has been discussed previously, when a cis-substituent is present, i.e. R = Me, rototation of the carbonyl group is restricted and conformers D and F would be expected to be of much higher energy than conformers C and E, owing to the unfavourable interaction of the cis-substituent and the carbonyl oxygen. The cisoid conformer C and the transoid conformer E would be preferred, and ring cleavage would occur preferentially at the $C_{(1)}$-$C_{(2)}$ bond in agreement with orbital overlap considerations.

It has been reported[63,64] that ground-state conformations of acetylcyclopropanes are predominantly cisoid and so it was of interest to see if there was any conformational change between the ground-state and the transition-state conformer populations during the reductive process.

As has been described in the Introduction, the reduction of an acetylcyclopropane with lithium in liquid ammonia can be viewed as an overall two-electron process giving a carbanion-enolate intermediate. The carbanion generated will be sufficiently basic (pKa > 50)[26] to abstract a proton from ammonia (pKa ~ 34),[26] but the resulting enolate ion is not basic enough (pKa ~ 16)[26] to abstract a proton from ammonia, and will remain in the reduction mixture until a proton source, e.g. ammonium chloride, is added.



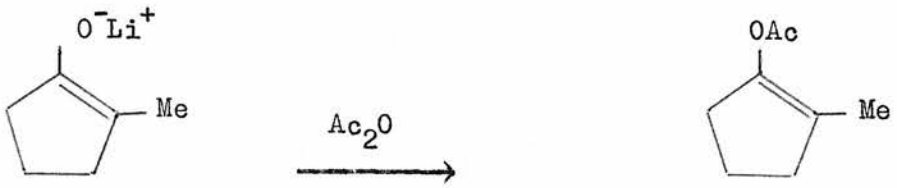
Stork and Hudrlik[69] have reported that enolates produced in a structure-specific manner can be isolated as the corresponding trialkylsilylenol ethers, and that the structures of the trimethylsilyl enol ethers isolated corresponded accurately to those of the enolates in a given mixture . They found, for example, that when 2-methylcyclohexanone (63) was treated with sodium hydride in refluxing glyme, the two sodium enolates produced, (64) and (65), were isolated as the corresponding trimethylsilyl enol ethers (66) and (67), in the ratio of 27:73, by adding a 50% excess of triethylamine and trimethylchlorosilane to the cooled reaction mixture.



It was also reported[69] that trimethylsilyl enol ethers were rapidly hydrolysed by water, but that the corresponding t-butyldimethylsilyl enol ethers, prepared similarly from t-butyldimethylchlorosilane and the metal enolates, were hydrolytically much more stable.

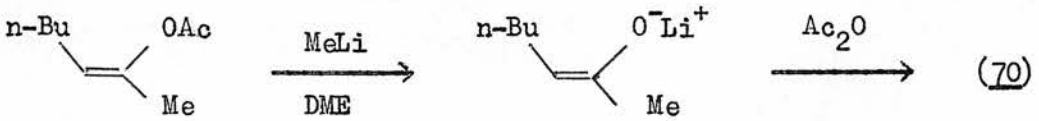
The trapping of enolate anions, under both kinetic and equilibrating conditions, as the corresponding enol acetates has undergone extensive investigation.[70,71] House and Trost, for example,

found[71] that the lithium enolate (68) could be rapidly converted to the corresponding enol acetate (69) merely by quenching a solution of the enolate with excess acetic anhydride.

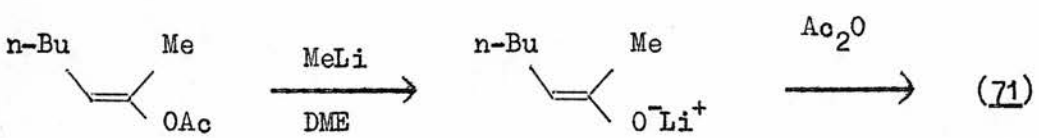


(68) (69)

House and Trost[71] have also demonstrated that lithium enolates are particularly resistant to isomeric equilibration during trapping with acetic anhydride. Each of the stereo isomeric, acyclic enol acetates (70) and (71) could be converted to the corresponding lithium enolate (72) or (73), by treatment with methyl-lithium in 1,2-dimethoxyethane, and then converted back to the starting enol acetate, by treatment with acetic anhydride, without loss of either structural or stereochemical integrity.



(70) (72)

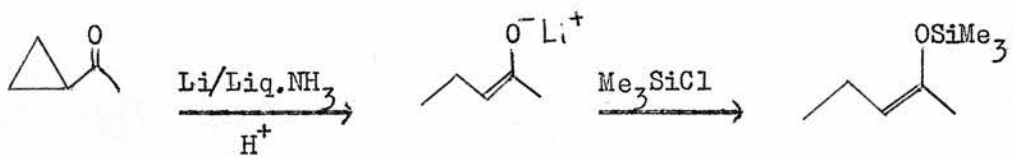


(71) (73)

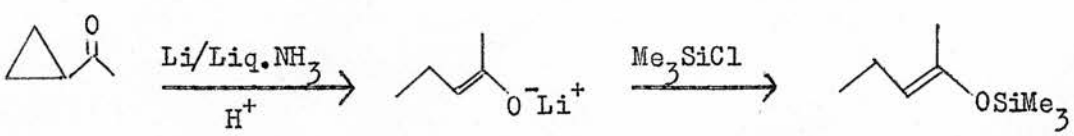
In fact, solutions of each of the enolate anions (72) and (73) could be heated to 73° for 40 minutes without detecting interconversion

of the two anions. In general, House and Trost found[71] that solutions of lithium enolate anions in 1,2-dimethoxyethane did not interconvert over periods of several hours at room temperature. These results indicate that the activation energy for interconversion of lithium enolate anions must be substantial (> 20 Kcal/mole).[72]

It was originally hoped that the lithium enolates formed in the reduction of acetylcyclopropanes with lithium/liquid ammonia could be trapped as the silyl enol ethers by adding hexamethyldisilazane to the reduction mixture. However, the work of House and Trost suggested that it would be possible to remove the ammonia from the reduction mixture and replace it by 1,2 dimethoxyethane without affecting the lithium enolates, and thus the enolates could be trapped as the trimethylsilyl enol ethers, using trimethylchlorosilane and triethylamine, or the hydrolytically more stable t-butyldimethylsilyl enol ethers, using t-butyldimethylchlorosilane and triethylamine, as described by Stork and Hudrlik.[69] If no equilibration of the lithium occurs, as suggested by the previous work, the geometry of the silyl enol ethers thus formed will be related to the original conformations of the acetylcyclopropane at the time of ring-opening as shown below.



cisoid — trans-enol ether



transoid — cis-enol ether

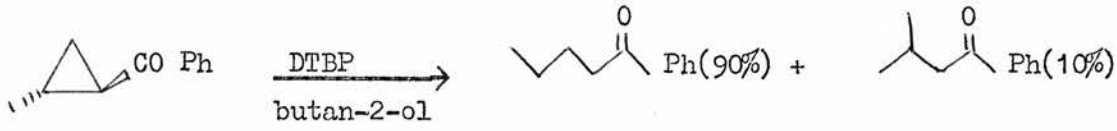
Additional evidence that little interconversion of the lithium enolates occurs was furnished by carrying out a lithium/liquid ammonia reduction, using method B, on acetylcyclopropane in which all three H atoms of the acetyl group had been replaced by deuterium. The distribution of deuterium in the starting acetylcyclopropane was d_2, 2.90%; and d_3, 97.10%, and in the product pentan-2-one was d_1, 0.4%; d_2, 6.8%; and d_3, 92.8%. In a control experiment, no loss of deuterium was noted when a sample of deuterated 1-acetyl-2,2-dimethylcyclopropane was stirred for 2 hours in anhydrous liquid ammonia and then worked-up in the usual manner.

Unfortunately, owing to shortage of time, the trapping experiments could not be completed. However, it is of interest to note that Dauben and Wolf[65] have since reported the results of similar experiments in which they trapped the intermediate enolate anions as the corresponding enol acetates. Their results showed the preference for a cisoid geometry in the transition state of the lithium/liquid ammonia reduction of acetylcyclopropanes, and thus a similarity between the transition-state and ground-state conformational populations.

Radical Rearrangement of Substituted Acetylcyclopropanes

Neckers, Schaap and Hardy[33] have shown that the radical rearrangement of trans-2-methylcyclopropyl phenyl ketone (11), with di-t-butyl peroxide in butan-2-ol, gives the two possible rearranged products, butyl phenyl ketone (12) and isobutyl phenyl ketone (13), in the ratio of 9:1. The rearrangement is predominantly in the direction favouring the more stable radical intermediate (secondary

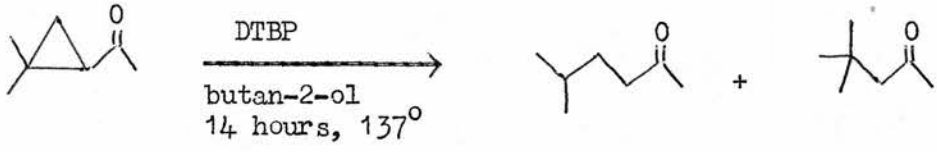
radical more stable than a primary radical).



(11) (12) (13)

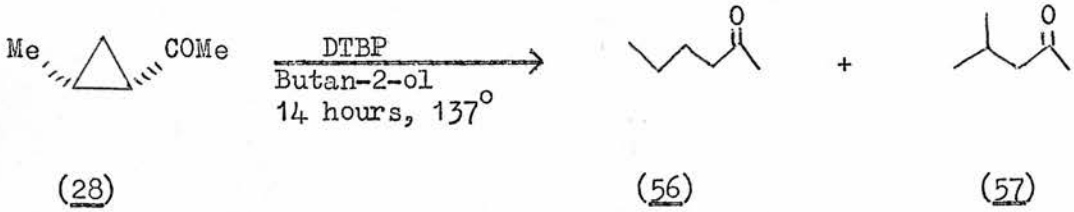
The results of similar radical rearrangements on 1-acetyl-2,2-dimethylcyclopropane (26), trans-1-acetyl-2-methylcyclopropane (29), and cis-1-acetyl-2-methylcyclopropane (28) are shown in Tables 11, 12 and 13 in the Appendix.

Ketone (26) gave 5-methylhexan-2-one (54), and 4,4-dimethylpentan-2-one (55) as expected, in the average ratio of 41:1.

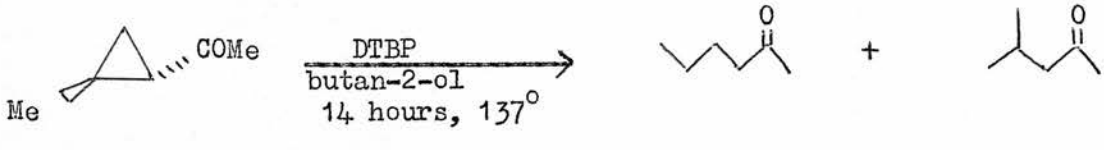


(26) (54) (55)

The rearranged products from ketones (28) and (29) were, as expected, hexan-2-one (56), and 4-methylpentan-2-one (57), in the average ratio of 8.7:1, from ketone (28), and 4.5:1, from ketone (29).



(28) (56) (57)



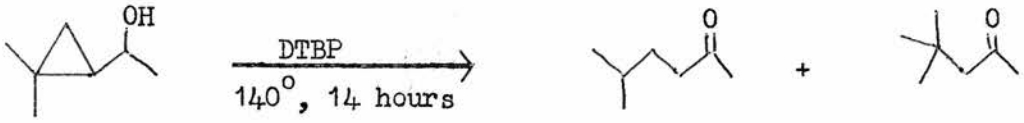
(29) (56) (57)

The rearrangement in all three cases is predominantly in the direction favouring the more stable radical intermediate. Although ketones (28) and (29) gave the same rearranged products, the ratio of the rearranged products was not the same. A priori, the ratio of the ring-opened products in both cases might be thought to be influenced solely by the competition between the thermodynamic stability of a secondary as opposed to a primary radical intermediate. However, the results suggest that the cis-methyl group of ketone (28) exerts a steric effect such that the radical intermediate leading to product (56) is favoured both by steric and thermodynamic considerations, and that no such steric effect is present in the rearrangement of ketone (29).

In ketone (26), the preferred direction of ring-opening is influenced, not considering any possible steric effect of the cis-methyl group, by the competition between the relative thermodynamic stability of a tertiary as opposed to a primary radical intermediate. It would be expected, then, that the ratio of ring-opened products would reflect this, and that cleavage of the $C_{(1)}$-$C_{(2)}$ bond of the cyclopropane ring, rather than the $C_{(1)}$-$C_{(3)}$ bond, would be more preferred in ketone (26), than ketones (28) and (29). This is, in fact, found to be the case.

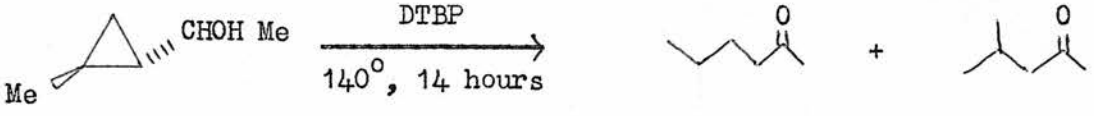
Rearrangements with di-t-butyl peroxide have also been carried out on the alcohols corresponding to ketones (26), (28), and (29). In these cases, butan-2-ol was not required as a source of hydrogen atoms. The results of the rearrangements are shown in Tables 14, 15, and 16.

1-(2,2-dimethylcyclopropyl) ethanol (74) gave 5-methylhexan-2-one (54), and 4,4-dimethylpentan-2-one (55), as expected, in the average ratio of 21:1.

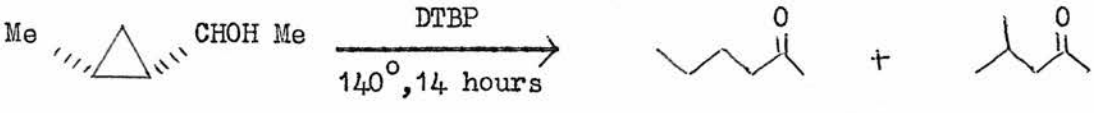


(74) (54) (55)

trans-1-(2-Methylcyclopropyl) ethanol (75) gave hexan-2-one (56) and 4-methylpentan-2-one (57), as expected, in the average ratio of 3.0:1, and cis-1-(2-methylcyclopropyl) ethanol (76) gave the same two products of rearrangement in the ratio of 8.3:1.



(75) (56) (57)



(76) (56) (57)

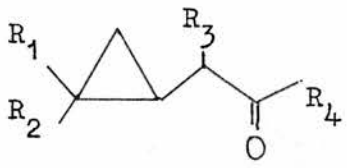
The results for the ratio of rearranged products are higher for the ketones than the corresponding alcohols. However, the same trends are observed in the results for the rearrangement of the alcohols as were discussed for the ketones.

The radical rearrangements, then, can be explained in terms of the relative thermodynamic stability of the intermediates involved

and the lithium/ammonia reductions can be explained also by the relative thermodynamic stability of the intermediates involved but with a major contribution from the steric effect of a cis-methyl substituent when present.

Attempted Ring-Opening of Substituted Cyclopropanes via a Carbanion Intermediate

Since the lithium/ammonia reductions of acetylcyclopropanes has been shown to proceed via a mechanism involving a carbanion intermediate, it was of interest to synthesise compounds of the general type (77), in which it might be possible to generate a



R_1 = H, or Me
R_2 = H, or Me
R_3 = H, or Me
R_4 = Me, or Ph

carbanion on the carbon α to the cyclopropane ring, and study the preferred direction, if any, of ring-opening.

Since the substituted acetylcyclopropanes (26), (28) and (29) had already been synthesised, the first attempts to synthesise a ketone of the general type (77) used acetylcyclopropane (58) as starting material.

Wittig and Knauss,[73] and Levine,[74] have described the reaction of carbonyl compounds, e.g. (78), with methoxymethylenetriphenylphosphoran (79) to give the enol ether, 80, which can then be hydrolysed to an aldehyde (81).

$$R_1R_2C = O + Ph_3P = CHOCH_3 \longrightarrow R_1R_2C = CHOCH_3 + Ph_3PO$$

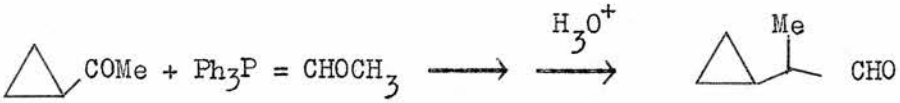
(78) (79) (80)

$$\downarrow H_3O^+$$

$$R_1R_2CHCHO + CH_3OH$$

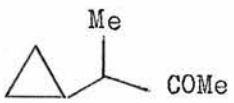
(81)

It can be seen that reaction of acetylcyclopropane (58) with (79) will give, after hydrolysis , 2-cyclopropylpropionaldehyde (82), which, by conversion to the acid, and then the



(58) (79) (82)

acid chloride, followed by treatment with dimethylcadmium, would give the desired 3-cyclopropylbutan-2-one (83)



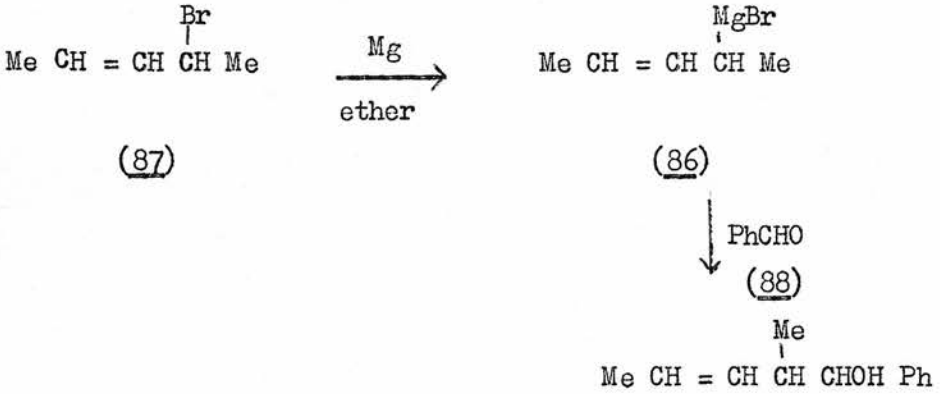
(83)

Unfortunately, however, no volatile product was isolated from the reaction of 79 with acetylcyclopropane (58).

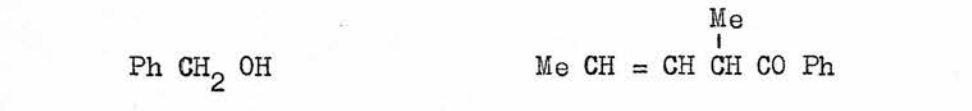
In a second attempted synthesis of a ketone of the general type (77), 2-methyl-1-phenylpent-3-en-1-ol (84) was reacted with the organo-zinc compound from methylene iodide and zinc/copper couple[15] using the procedure of Perraud and Arnaud.[19] The expected product, 2-(2-methylcycloproplyl)-1-phenylpropan-1-ol (85), however, was not obtained.

(84) (85)

The alcohol (84) was prepared by the reaction of the Grignard magnesium compound (86) of 2- bromopent-3-ene (87), with benzaldehyde (88). The benzaldehyde was added slowly,



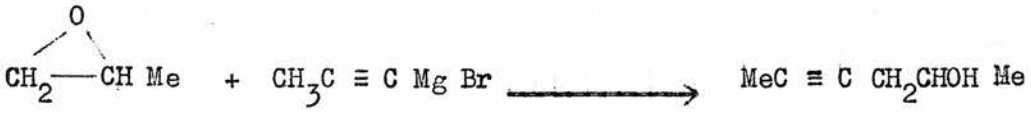
in a solution of ether, over 5 hours, to an excess of an ethereal solution of the Grignard reagent (86), since in the first attempted preparation of the alcohol (84), in which excess benzaldehyde had been added, a Grignard transfer reaction took place between the intermediate magnesium complex of the product alcohol (84), and unreacted benzaldehyde (88), and so the products obtained were benzyl alcohol (89) and the corresponding ketone (90) of 2-methyl-1-phenylpent-3-en-1-ol (84). Benzyl alcohol (89) was



(89) (90)

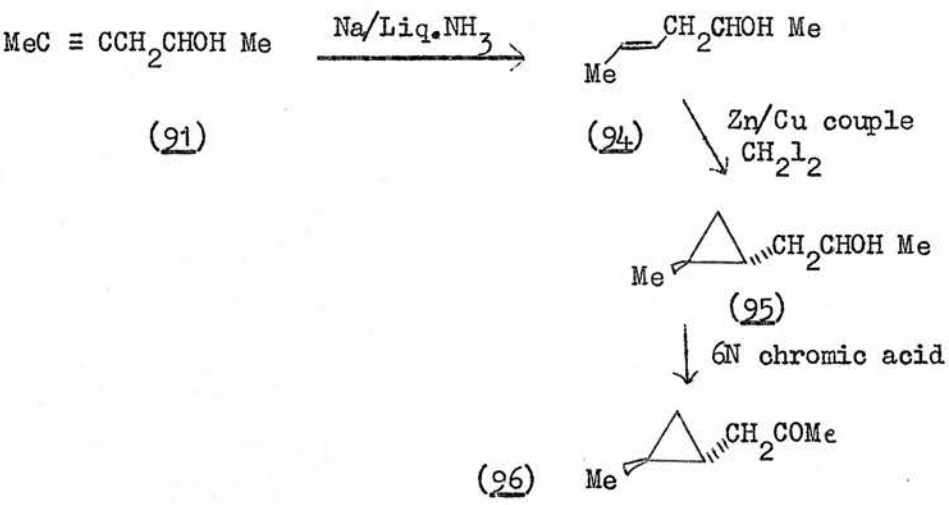
identified by comparison with an authentic sample, and the structure of ketone (90) was assigned on the basis of its ir spectrum and its mass spectrum. The ir spectrum showed a very strong absorption at 1684 cm^{-1} characteristic of a conjugated carbonyl compound, and the mass spectrum at low eV showed a parent ion at m/e = 174, and only two other peaks at m/e = 105, and 69, as expected for ketone (90).

The third attempted synthesis of a ketone of the general type (77) met with success. Hex-4-yn-2-ol (91) was prepared by the reaction of 1,2-epoxypropane (92) with the Grignand compound (93) of methylacetylene. Product (91) was



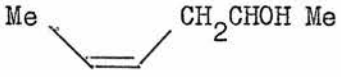
(92) (93) (91)

also prepared by the reaction of the sodium salt of methylacetylene with 1,2-epoxypropane (92). Reduction of the acetylenic alcohol (91) with sodium in liquid ammonia gave trans-hex-4-en-2-ol (94), from which trans-1-(2-methylcyclopropyl) propan-2-ol (95) was prepared using the Simmons-Smith reaction as modified by Perraud and Arnaud.[19] Oxidation of (95) (6N chromic acid) gave the required trans-1-(2-methylcyclopropyl) propan-2-one (96).



(91) (94) (95) (96)

Catalytic reduction of hex-4-yn-2-ol (91) over a Lindlar's palladium catalyst[75] gave cis-hex-4-en-2-ol (97). Since it proved impossible, however, to rearrange ketone (96), as is described below, the synthesis of the cis-isomer (98) from the cis-alcohol (97) was not carried farther.



(97)

(98)

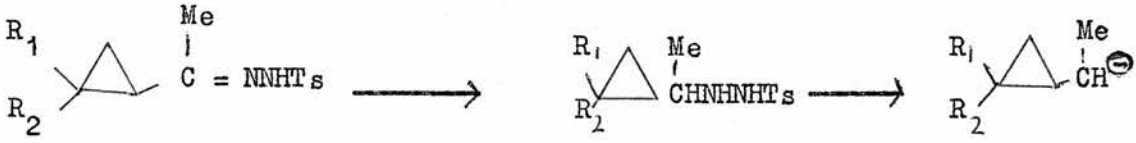
Treatment of trans-1-(2-methylcyclopropyl) propan-2-one (96), with a 5% solution of sodium methoxide in methanol for 24 hours at room temperature, and with a 10% solution of sodium methoxide in methanol for 18 hours at 80°, gave unchanged starting ketone (96).

Treatment of ketone (96) with half the molar amount of sodamide in liquid ammonia for 8 hours, followed by the normal work-up procedure gave unchanged starting ketone (96).

Since under the enolising conditions used, no rearrangement of ketone (96) occurred, it was thought that there might not be any enolisation taking place in the d rection of the cyclopropane ring. This was shown not to be the case by treating ketone (96) with a 10% solution of sodium methoxide in methanol-$[^2H_1]$ during 12 hours. Calculation of the relative isotope abundance of the product from the mass spectrum showed that the total deuterium exchange was 92.4% of five replaceable hydrogens, and that 66.75% of the product contained five deuterium atoms.

The failure of trans-1-(2-methycyclopropyl) propan-2-one (96) to rearrange prompted a different approach to the generation of a carbanion α to a cyclopropane ring.

It was thought that if the p-toluenesulphonylhydrazones (99) of ketones (26), (28), (29), and (58) were reduced to the corresponding hydrazines (100), treatment with base would produce an anion of the general type (101), which might then rearrange.



(99) (100) (101)

(R_1 = H, or Me)

(R_2 = H, or Me)

The p-toluenesulphonylhydrazone (99, $R_1 = R_2$ = Me) of 1-acetyl-2,2-dimethylcyclopropane (26) was prepared from ketone (26) and p-toluenesulphonylhydrazide (102) in the usual manner[76] and identified by its ir, nmr, and mass spectrum. The attempted reductions of the hydrazone to the corresponding hydrazine were carried out on the p-toluenesulphonylhydrazone (103) of hexan-2-one (56) since the latter is more readily available than ketone (26).

(102) (56) (103)

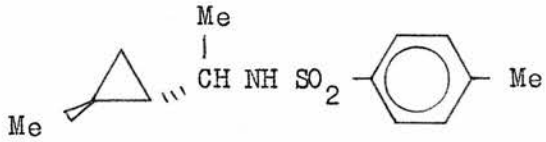
The attempted reduction of the hydrazone (103) with lithium cyanoborohydride,[77] and sodium borohydride gave unchanged (103).

Reduction of (103) with lithium aluminium hydride gave an unidentified product which did not have the required spectral

characteristics for the hydrazine. As n-hexane was identified (vpc) in the ether from the reaction product, it is suggested that the intermediate aluminium complex in the reduction was undergoing rearrangement.

Unchanged (103) was obtained from the attempted catalytic reduction of (103) with palladium on charcoal, Raney nickel, platinum on charcoal, Adam's platinum catalyst in ethanol, in acetic acid, in ethanol saturated with anhydrous hydrogen chloride, and in acetic anhydride.

The final approach to the generation of a carbanion ∝ to a cyclopropane ring was the treatment of N-1-(trans-2-methylcyclopropyl) ethyl-p-toluenesulphonamide (104) with hydroxylamine-O-sulphonic acid (105), the Nickon-Sinz reaction.[78]

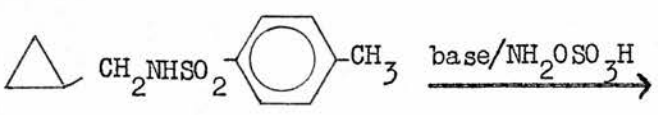


(104)

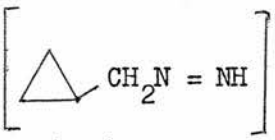
NH_2OSO_3H

(105)

Bumgardner, Martin, and Freeman[79] have described the reaction of N-cyclopropylmethyl-p-toluenesulphonamide (106) with hydroxylamine-O-sulphonic acid (105) and base to give an intermediate (107) which rearranges through a carbanion intermediate to give but-1-ene (108). A similar



(106)

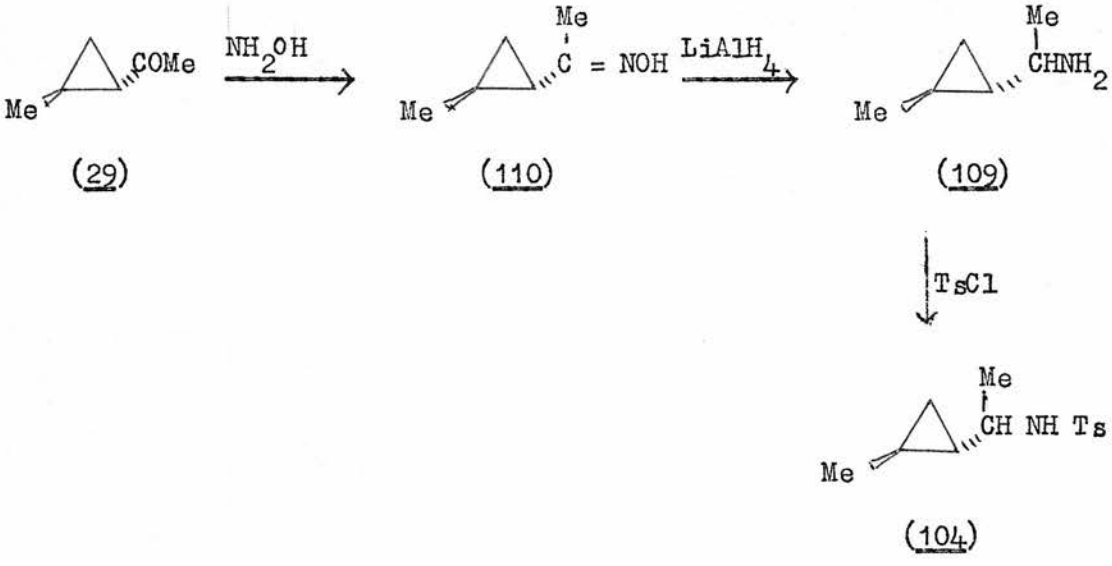


(107)

$CH_2 = CH\ CH_2CH_3$

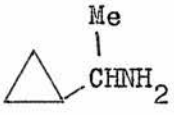
(108)

reaction, using the conditions given by Bumgardner, Martin and Freeman, between products (104) and (105), however, gave no volatile products. The reaction was repeated using a reaction time twice as long but again no product was observed. N-1-(trans-2-methylcyclopropyl) ethyl-p-toluenesulphonamide (104) was prepared from 2- (trans-2-methylcyclopropyl) ethylamine (109) and p-toluenesulphonyl chloride using the usual conditions.[80] The amine (109) was prepared from trans-1-acetyl-2-methylcyclopropane (29) by conversion to the oxime (110) followed by reduction with lithium



(29) (110) (109) (104)

aluminium hydride in ether as described by Roberts et al,[81] for the preparation of 1-cyclopropylethylamine (111).



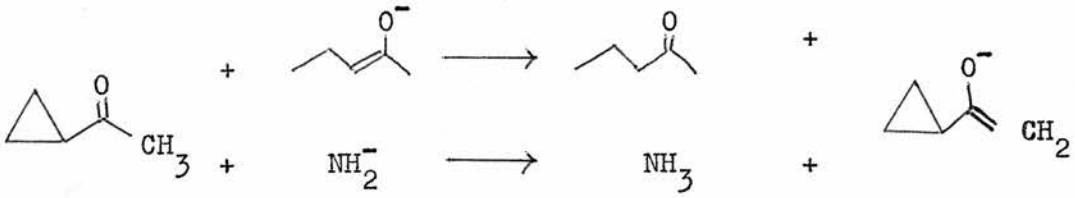
(111)

It therefore proved impossible to carry out authentic carbanion rearrangements and so it was not possible to compare the rearrangement occurring in the reduction of acetylcyclopropanes with lithium/liquid ammonia and that of authentic radical reactions with the rearrangement occurring in authentic carbanion reactions. Since the lack of ring-opening of cyclopropylmethyl carbanions stabilised in some way, e.g. by a carbonyl or by a phenyl group, is well documented,[82] it is perhaps not surprising that it proved impossible to observe rearrangement through a cyclopropylmethyl carbanion in the present work.

Titration of Lithium/Liquid Ammonia Solutions with Various Ketones

A series of titrations of lithium/liquid ammonia solutions was carried out with various ketones. When the solutions were titrated with an acyclic enolisable ketone such as 5-methylhexan-2-one (54), the mole ratio of lithium to (54) was, as expected, almost unity. However, when solutions of lithium/liquid ammonia were titrated with acetylcyclopropanes, the results were very surprising. Using ketones (26), (29), and (58), the mole ratio of lithium to ketone was very nearly unity and not, as expected, 2:1. One suggested reason for this was that not all the ketone was reduced in the titration. It is thought that unchanged starting material is obtained in the reduction of acetylcyclopropanes with lithium in liquid/ammonia because the rearranged lithium enolate, or the amide ion, NH_2^-, produced in the reduction (see p. 44) can abstract a proton from starting material to give an unreactive enolate ion which does not use up any

lithium. Therefore, if the ratio



of rearranged product: starting ketone is unity and the reduction process requires two electrons, the overall mole ratio of lithium used: ketone will be unity. However, in those titrations in which the ratio of rearranged product/starting ketone was measured, the ratio varied from 0.44 to 4, while the mole ratio of lithium/ketone was always virtually unity. The same results were obtained when an excess of lithium was used and the excess lithium was back-titrated with either an enolisable or a non-enolisable ketone. In control titrations, the non-enolisable ketone 2,2,6,6-tetramethylcyclohexanone (112) gave a mole ratio of lithium: (112) of unity, as expected, but the non-enolisable ketone 2,2,4,4-tetramethylpentan-3-one (113) gave a mole ratio of lithium: (113) of almost 3:1, and so could not be used in the back-titrations.

The surprising nature of the results of the titrations of solutions of lithium in liquid ammonia with the acetylcyclopropanes (26),(29), and (58) cannot be adequately explained at present.

Polarography in Liquid Ammonia

The use of the dropping mercury electrode in liquid ammonia is well documented. Murtazaev[83] has measured electrocapillary curves of salts in liquid ammonia and Pleskov and Monosson[84] have measured the potential of the electrocapillary maximum in a 0.1N solution of

ammonium nitrate in liquid ammonia. In the determination of the standard electrode potentials of the alkali metals in liquid ammonia, dropping amalgam electrodes were used by Pleskov,[85] and Pleskov and Monosson.[86]

The polarographic half-wave potentials, and diffusion currents, of alkali metal ions,[87] and alkaline earth metal ions,[88] in liquid ammonia have been measured. Laitinen and Shoemaker[89] have studied the polarography of thallium (I), copper (II), and ammonium ions, and of molecular oxygen, in liquid ammonia. The behaviour of the mercury pool anode[90] and of the electron electrode[91] has also been systematically investigated.

Since it was known that the dropping mercury electrode would function in liquid ammonia, a polarographic study of the reduction of substituted acetylcyclopropanes in liquid ammonia was undertaken in the hope that more information on the reduction of this type of compound with solutions of lithium in liquid ammonia could be obtained.

The apparatus and the experimental procedure used are described fully in the Experimental section. The results obtained are presented below.

Laitinen and Shoemaker[90] have found that the potential of the mercury pool anode is independent of the concentration of nitrate, chloride, iodide, or ammonium ions in solution, and that the concentration of mercuric ion is the only potential determining factor. They also found that the small amount of mercuric ion formed at the anode during the recording of three polarograms was sufficient to

stabilise the anode potential so that the mercury pool anode could be used as the reference electrode with a potential 0.32 v. more positive than the standard lead - 0.1N lead nitrate electrode.[87] For this reason, the mercury pool anode was used as the reference electrode in the present work.

Typical polarograms are shown in Figures 1, 2, and 3 below.

Figure 1.- Polarograms in liquid ammonia: curve I, sodium iodide (2.13×10^{-4} M) in saturated tetrabutylammonium iodide solution; curve II, hexan-2-one (3.6×10^{-4} M) in saturated tetrabutylammonium iodide solution; curve III, saturated tetrabutylammonium iodide solution (57×10^{-4} M).

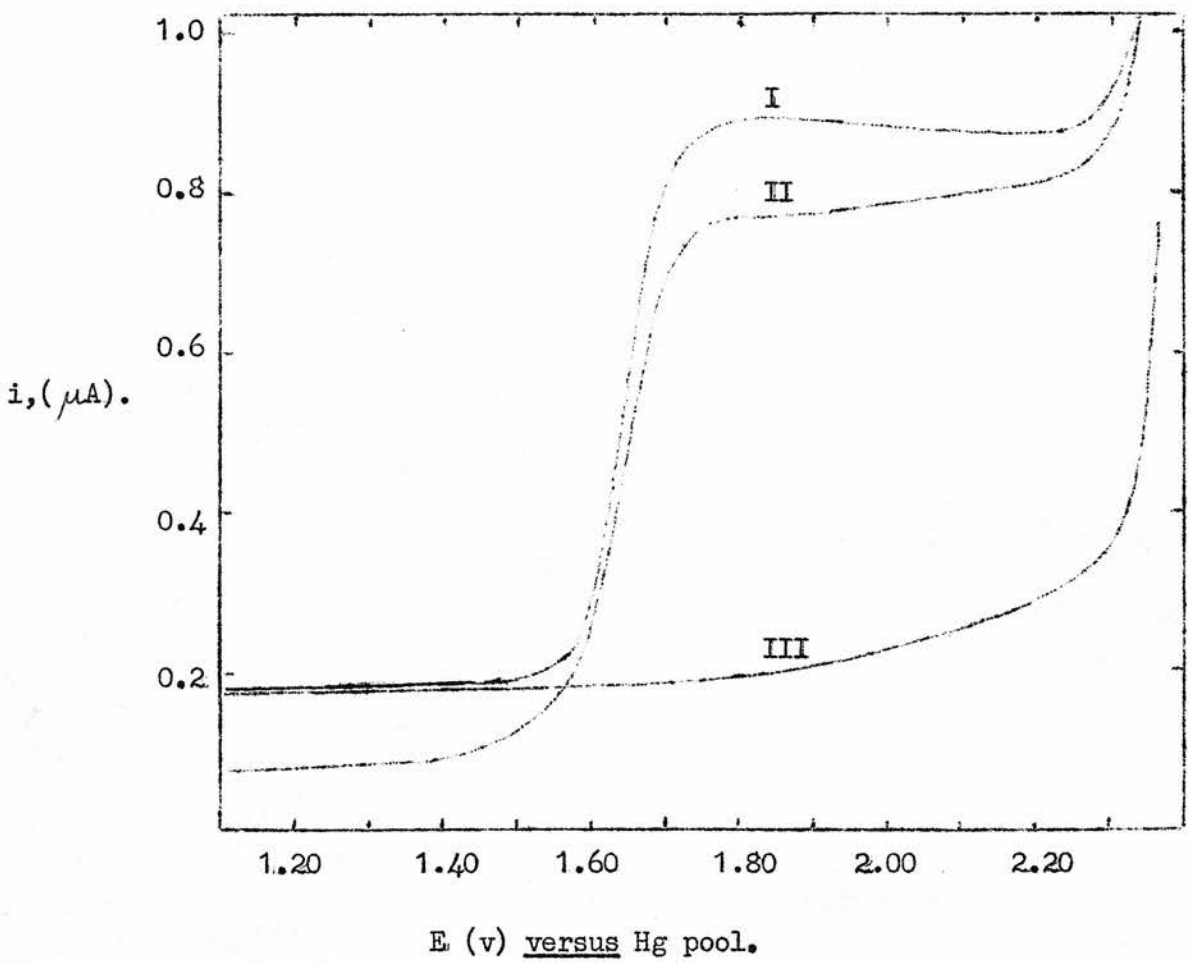


Figure 2.- Polarograms in saturated solutions of tetrabutylammonium iodide in liquid ammonia: curve I, 1-acetyl-2,2-dimethylcyclopropane (2.7×10^{-4} M); curve II, acetylcyclopropane (1.90×10^{-4} M).

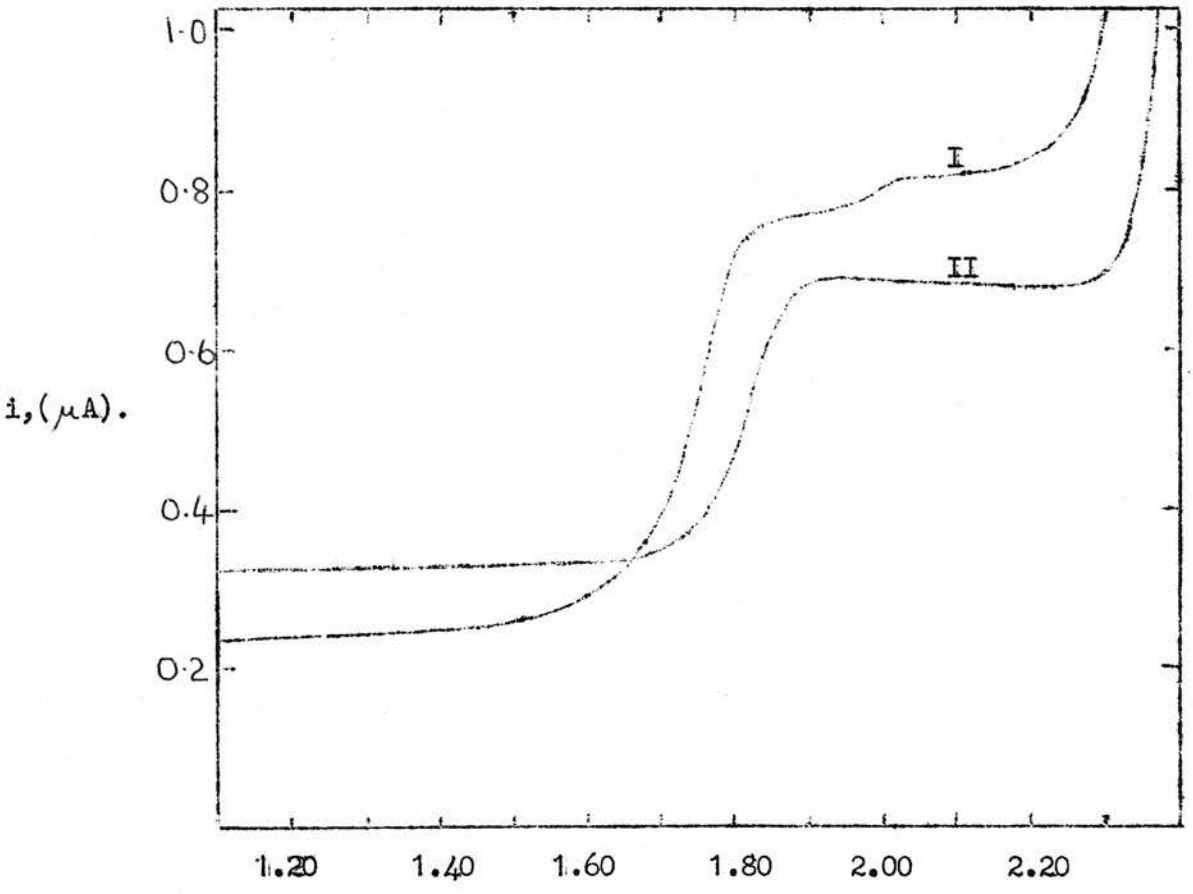
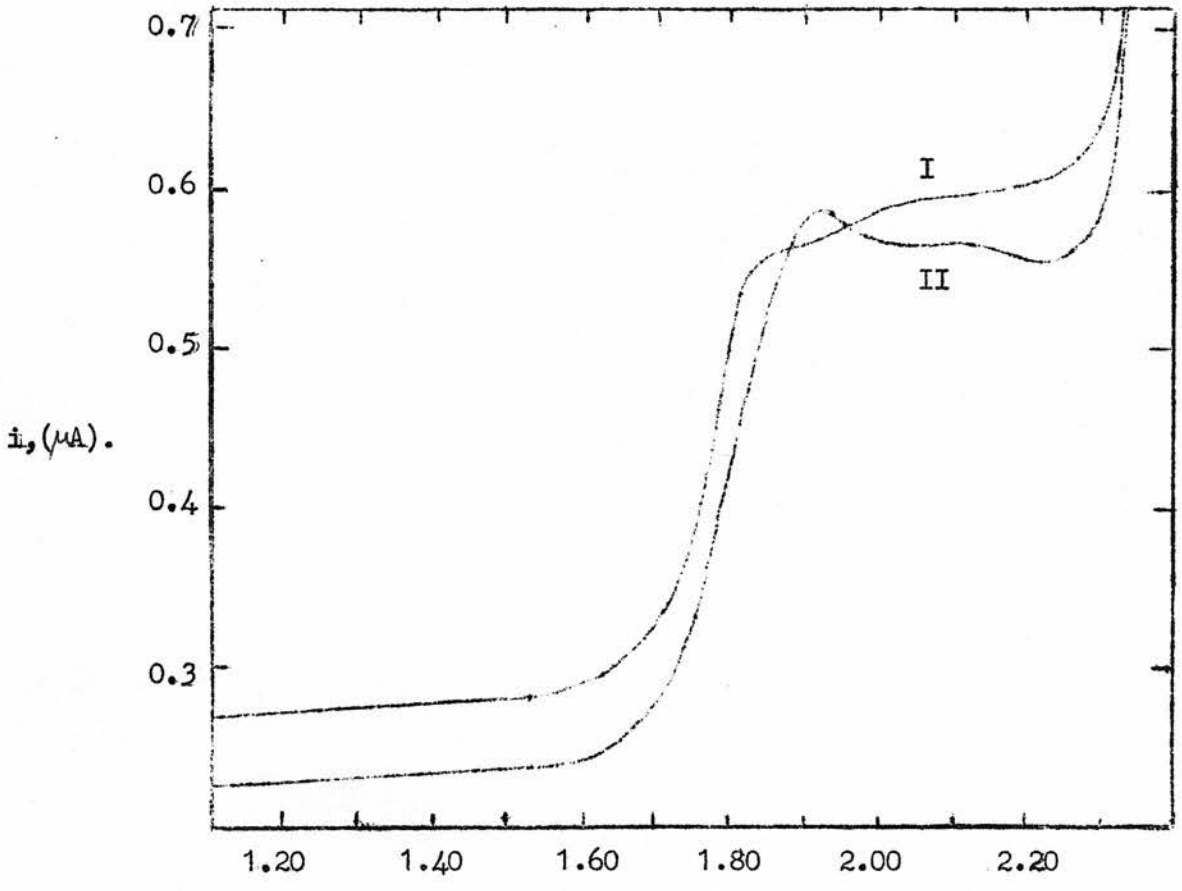


Figure 3.- Polarograms in saturated solutions of tetrabutylammonium iodide in liquid ammonia: curve I, trans-1-acetyl-2-methylcyclopropane (2.2×10^{-4} M); curve II, cis-1-acetyl-2-methylcyclopropane (2.20×10^{-4} M).



Laitinen and Nyman[87] have obtained detailed polarograms of sodium iodide in saturated tetrabutylammonium iodide. They found the half-wave potential for the reduction of the sodium ion in a solution of liquid ammonia to be -1.31 volts with reference to the standard lead/ 0.1N lead nitrate electrode. The calculated half-wave potential

for this reduction, with reference to the same standard electrode, was -1.30 volts. In the present work, the observed value in this reduction, with reference to the standard lead / 0.1N lead nitrate electrode, was -1.33 volts (-1.65 volts with reference to the mercury pool electrode).

Laitinen and Nyman also compared the observed diffusion current of sodium ions, as measured in liquid ammonia at -36°, with the theoretical current calculated from the Ilkovic equation[92]

$i_d = 605\ n\ C\ D^{\frac{1}{2}}\ m^{\frac{2}{3}}\ t^{\frac{1}{6}}$ which relates the diffusion current i_d (μA) of an ion to n, the number of faradays of electricity required per mole of electrode reaction, to its concentration C (m.moles litre^{-1}), to its ionic diffusion coefficient D (cm.^{2} sec.$^{-1}$), and to the capillary characteristics m (mg.sec.$^{-1}$) and t (sec.). The ionic diffusion coefficient D was evaluated using the expression[93]

$D = R\ T\lambda^\circ / zF^2$, where R is 8.317 volt-coulombs-degree^{-1}, T is the absolute temperature, λ° is the equivalent conductance of the ion at infinite dilution (ohm^{-1}-cm.^{2}-equiv.$^{-1}$), z is the charge of the ion, and F is 96,500 coulombs. The remaining terms in the Ilkovic equation are experimental quantities which are easily obtained.

The table below shows the data necessary for, and the results of, such calculations. The value taken for the equivalent conductance at infinite dilution was that used by Laitinen and Nyman.[87] For comparison, the table also shows the calculated and observed diffusion currents obtained by Laitinen and Nyman. The capillary characteristics, m, and t, were measured, in the present work, at a potential of -1.80 volts with reference to the mercury pool electrode, the potential at which the diffusion current was measured.

Diffusion Current of Sodium Ions in Liquid Ammonia, at -35.5°.

	Λ_0 $ohm^{-1} cm.^2 equiv.^{-1}$	D X 10^5 $cm.^2 sec.^{-2}$	$m^{\frac{2}{3}} t^{\frac{1}{6}}$ $mg.^{\frac{2}{3}} sec.^{-\frac{1}{2}}$	C m.moles $litre^{-1}$	i_d (calc.) μA	i_d (obs.) μA	% Diff.
Present Work	135	2.86	0.919	0.213	0.633	0.688	9
Literature[87]	135	2.86	1.256	1.04	4.23	4.84	14

As can be seen from the table above, better agreement with the Ilkovic equation was obtained in the present work than in the original work by Laitinen and Nyman. This is presumably due to more complete supression of the migration current being obtained in the present work, in which the molar ratio of indifferent electrolyte to reducible ion was approximately 27:1, as opposed to approximately 6:1 in the original work.

The table below shows the half-wave potentials of various cyclopropyl ketones, and hexan-2-one, measured in liquid ammonia at -35.5°, with reference to the mercury pool electrode. The values of $E_{\frac{1}{2}}$ given with reference to the standard lead / 0.1N lead nitrate electrode were obtained by assuming that the potential of the mercury pool electrode was 0.32 volts more positive than the lead electrode. It was shown that the observed waves did not arise from impurities in the supporting electrolyte by recording a polarogram of saturated tetrabutylammonium iodide in liquid ammonia (see Fig.1). No impurity waves were observed.

$E_{\frac{1}{2}}$ of Various Ketones in Liquid Ammonia, at -35.5, versus Mercury Pool Electrode and versus Lead / 0.1N Lead Nitrate Electrode.

Ketone	$E_{\frac{1}{2}}$ (volts) versus Hg pool	versus Pb/0.1N $Pb(NO_3)_2$
Hexan-2-one	-1.65	-1.33
Acetylcyclopropane	-1.80	-1.48
cis-1-Acetyl-2-methylcyclopropane	-1.79	-1.47
trans-1-Acetyl-2-methylcyclopropane	-1.76	-1.44
1-Acetyl-2,2-dimethylcyclopropane	-1.74	-1.41

The table below gives a comparison of the diffusion currents obtained, in liquid ammonia at -35.5°, with the above ketones.

Diffusion Current of Various Ketones in Liquid Ammonia, at -35.5°.

Ketone	Concentration m.moles litre^{-1}	i_d (μA)
Hexan-2-one	0.36	0.65
Acetylcyclopropane	0.19	0.34
cis-1-Acetyl-2-methylcyclopropane	0.22	0.34
trans-1-Acetyl-2-methylcyclopropane	0.22	0.27
1-Acetyl-2,2-dimethylcyclopropane	0.27	0.48

No information about the reduction of ketones in liquid ammonia could be found in the literature. However, the reduction of carbonyl compounds in aqueous media appears to give a one-electron wave.[94] Therefore, if it is assumed that hexan-2-one gives a one-electron wave in liquid ammonia, and that the cyclopropyl ketones (26), (28), (29),

and (58) have a diffusion coefficient similar to that of hexan-2-one, the polarographic wave observed with each cyclopropyl ketone corresponds to a one-electron reduction.

This unfortunately does not help to explain the mechanism of the reduction of conjugated cyclopropyl ketones in liquid ammonia since, if addition of a second electron to the reduced species occurred at a potential more negative than the potential at which electron dissolution from the mercury drop occurred, approximately -1.90 volts with reference to the standard lead / 0.1N lead nitrate electrode[91], no wave for that second reduction step would be observed. Consideration must also be given to the possibility that the reduction wave given by hexan-2-one in liquid ammonia does not correspond to a one-electron addition, but to a two-electron addition.

A controlled potential electrolysis of acetylcyclopropane in liquid ammonia was therefore undertaken to try and obtain information about the type of species involved in the polarographic reduction of carbonyl compounds, and in particular cyclopropylcarbonyl compounds, in liquid ammonia. If the observed polarographic waves given by the ketones examined correspond to addition of only one electron, one would expect to observe only pinacol formation in the controlled potential electrolysis, but, if the observed waves correspond to addition of two electrons, one might expect rearrangement of the acetylcyclopropane to occur during the electrolysis.

The apparatus and the experimental procedure used are described in the Experimental section. Anhydrous calcium nitrate was used as the supporting electrolyte since it was the most soluble (76g. / 100g. NH_3, -41°)[95] reasonably inert salt available at the time. Unfortunately, $E_{\frac{1}{2}}$ for the polarographic wave observed with acetylcyclopropane was -1.80 volts,

relative to the mercury pool electrode, and for calcium ion was -1.96 volts, relative to the mercury pool electrode.[88] This meant that only a very small range of applied potential was available within which to carry out the electrolysis.

Three separate electrolysis experiments gave, (1), acetylcyclopropane (58) and the product from rearrangement, pentan-2-one, in the ratio of 19:1, when the electrolysis was carried out at -1.74 volts, relative to the mercury pool electrode, (2), an unknown polymeric material when the electrolysis was carried out at -1.80 volts, relative to the mercury pool electrode, and (3), 75% recovery of a mixture of acetylcyclopropane and rearranged pentan-2-one in the ratio of 1.5:1, when the electrolysis was carried out at -1.69 volts, relative to the mercury pool electrode.

Because it proved impossible to keep the applied potential within the narrow limits required, reduction of the supporting electrolyte occurred during the electrolysis, and it is thought that this is the explanation for the ambiguity of the results obtained. However, the technique is sufficiently promising to justify repitition when a more inert supporting electrolyte is found.

EXPERIMENTAL

The infared spectra were recorded on Unicam SP200 and Perkin-Elmer 237 Spectrophotometers, and the suffixes to the infrared bands quoted are abbreviated weak (w), medium (m), strong (s), very strong (vs), and broad absorption (b).

^{1}H Nuclear magnetic resonance spectra were run on a Perkin-Elmer R.10 spectrometer (60 MHz) at 33°, or a Varian Associates H.A. 100 spectrometer (100 MHz) at 28°. Samples were run as solutions (5-10%) in carbon tetrachloride, deuterochloroform, or benzene, with tetramethylsilane as the internal reference, or as solutions (5-10%) with benzene as the solvent and the internal reference, using the δ value of 7.37 for the benzene absorption to convert the measurements to the δ scale. In the tabulation of nmr data the following abbreviations are used : singlet (s), doublet (d), doublet of doublets (d of d), triplet (t), quartet (q), and multiplet (m).

Analysis figures were obtained using a Perkin-Elmer 240 elemental analyser.

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

Melting points are uncorrected.

Analytical scale vpc was carried out on a Perkin-Elmer F11 instrument, equipped with a flame ionisation detector using a 50m. stainless steel capillary column, coated with either Apiezon L or Carbowax.

Integration of peaks on vpc traces was achieved using a Gas Chromatography Digital Integrator Type IE. 165.

Preparative scale vpc was performed on a Wilkens Instrument and Research Inc. Aerograph Autoprep instrument, model A-700, using either 10% AgBF4-20% Carbowax 20M on Chromosorb P(45-60M) (10ft. x 0.375 in.), 15% Carbowax 20M on Chromosorb S(10ft. x 0.375in.), or 30% SE-30 on Chromosorb W(20ft. x o.375in.) as the column packing. The carrier gas was helium (200 ml./min.), and the injector, detector, and collector temperatures were 120°, 150°, and 120° respectively.

Preparation of 1-Acetyl-2,2-dimethylcyclopropane.[42] Dried, recrystallised trimethyloxosulfonium iodide[96] (39.0g., 0.175 moles) was stirred into dry dimethyl sulfoxide (130ml.) A nitrogen atmosphere was maintained as sodium hydride (4.2g., 0.175 moles) was added slowly, the temperature being kept below 40° with an ice-bath. Mesityl oxide (16.7g., 0.170 moles) was added slowly over a period of 15 minutes, and again the ice-bath was used to moderate the temperature of the mixture.

Stirring was continued for 3 hours and, after a further 12 hours, the mixture was poured onto ice (150g.). Pentane (50ml.) was added, and, after separation, the aqueous portions were extracted with pentane (2x100ml.). The combined pentane extracts were washed with water (3x100ml.), and brine (100ml.). The extract was finally dried ($MgSO_4$) and the pentane was distilled off at atmospheric pressure.

Vacuum distillation of the residue gave 1-acetyl-2,2-dimethylcyclopropane (8.37g., 44% yield; b.p. 55-56°/45mm.) which contained less than 1% impurity (vpc; Apiezon L, 85°, and Carbowax, 60°).

The spectral data (ir and nmr) were in agreement with literature values[42] : ir (film), 1690 cm^{-1} (vs); nmr (CCl_4), δ 0.71 (d of d,1H,J= 4.0 and 8.0Hz,$H_{(3)}$ trans to acetyl), 1.11 (m,1H,$H_{(3)}$ cis to acetyl), 1.05 (s,3H, methyl cis to acetyl), 1.17 (s,3H, methyl trans to acetyl), 1.78 (d of d,1H,J=5.5 and 8.0Hz,$H_{(1)}$), and 2.14 (s,3H, acetyl). The mass spectrum was as expected : p=112, and at low eV the only peaks in the spectrum were at m/e=112 ($C_7H_{12}O$), 97 (C_6H_9O), 69 (C_5H_9), and 43 (C_2H_3O). The molecular formulae of the ions in the spectrum were obtained by accurate mass measurement.

Preparation of trans-Pent-3-en-2-one.[44] A solution of triphenylphosphine (10.0g.) and freshly distilled chloroacetone (3.25g.) in chloroform (30ml.) was refluxed for 45 minutes. The solution was filtered into anhydrous ether (300ml.), and the precipitated acetonyltriphenylphosphonium chloride was filtered off, and dried *in vacuo*. The yield was 11.0g.; m.p.231-236°, (lit.[97], 11.2g.,m.p. 234-237°).

Acetonyltriphenylphosphonium chloride (11.0g.) was shaken with an excess of 10% aqueous sodium carbonate for 8 hours, and the

acetylmethylenetriphenylphosphorane formed was filtered off and dried. The yield was 10.2g.; m.p. 198-201°, (lit.[97], 199-202°).

Acetylmethylenetriphenylphosphorane (10.2g.) in methylene chloride (30ml.) was treated with freshly distilled acetaldehyde (2.8g.) in methylene chloride (50ml.). After refluxing for 6 hours and then standing at 20° for 6 hours, the solvent was distilled off through a 50 cm. column packed with Fenske helices, and the residue was diluted with pentane (30ml.). The precipitated, crystalline triphenylphosphine oxide was filtered off and washed, until colourless, with pentane. The organic filtrates were combined and the solvent was distilled through the packed column.

Distillation of the residue through a 25 cm. Vigreux column yielded trans-pent-3-en-2-one (2.10g.; b.p. 120-122°, lit.[45], b.p.124°) which contained less than 0.5% impurity (vpc; Apiezon L,55°).

The spectral data confirmed the assigned structure : ir (film), 1672 (vs), 1630 (s), and 973 cm^{-1} (s); nmr (CCl_4), δ 1.96 (d of d, 3H, J=1.3 and 6.5 Hz, $CH_3C=C$), 2.08 (s,3H, acetyl), 6.00 (m,1H, consisting of a doublet, J=15.9 Hz, each peak of which was split into a quartet J=1.3Hz, $H_{(3)}$), and 6.90 (m,1H, consisting of a doublet, J=15.9Hz, each peak of which was split into a quartet J=6.5Hz, $H_{(4)}$).

The preparation when repeated using acetylmethylenetriphenylphosphorane (215.6g) and acetaldehyde (58g.) gave trans-pent-3-en-2-one (46.2g.).

Attempted Isomerisation of trans-Pent-3-en-2-one to cis-Pent-3-en-2-one- Roberts et al.[42] reported that if iodine was added to refluxing trans-pent-3-en-2-one, an equilibrium mixture of the cis-and trans-isomers was formed and, since the cis- isomer had a lower b.p. (98-101°) than the trans- isomer (120-122°), it was possible to distil out the cis- isomer using a very efficient distillation apparatus.

trans-Pent-3-en-2-one (20g.) to which a crystal of iodine had been added was heated under fast total reflux on a spinning-band distillation apparatus. Total reflux was continued for 4 hr. to allow a build-up of the cis- isomer at the head of the column. After this time, the temperature at the head of the column was 99°.

Distillation of product was then commenced, using a very high reflux/take-off ratio, so that the equilibrium on the column was disturbed as little as possible. This gave distillate (15g.), which was very wet, (3g. water), and a black and tarry residue (5g.).

Vpc (Apiezon L, 55°, and Carbowax, 60°) of the wet distillate, and ir (film) of the dried distillate, showed it to be trans-pent-3-en-2-one.

The attempted equilibration was repeated. The water formed was removed by distillation and fresh iodine was added. After total reflux for 8 hr. the temperature at the distillation head was 118°, and very slow distillation gave only trans-isomer. (vpc,ir). No product with b.p. 98-101° was obtained.

Preparation of trans-Pent-3-en-2-ol.[98]- Dry, freshly distilled, crotonaldehyde (71g.) in anhydrous ether (150ml.) was added dropwise to an ice-cold, vigorously stirred solution of methylmagnesium chloride in anhydrous ether (850ml.), prepared from magnesium (30.5g.) and methyl chloride. The reaction mixture was allowed to stand at room temperature for 1 hr., and was then decomposed cautiously with saturated, aqueous ammonium chloride solution (218ml.) forming a dense off-white precipitate. After the mixture had stood for 1 hr., the ether solution was decanted off and the precipitate was washed by decantation with ether (4x150ml.). The combined ether solutions were dried ($MgSO_4$), and the solvent was removed by distillation.

Distillation of the residue through a 30 cm. Vigreux column gave trans-pent-3-en-2-ol (75g.,86%; b.p. 119-121°, lit[46] 121.5°) which contained less than 0.5% impurity (vpc; Apiezon L, 55°, and Carbowax, 60°). The spectral data confirmed the structure of the product: ir (film), 3360 (b,s), 1675 (w), and 970 cm^{-1} (s), identical with the literature spectrum[46]; nmr (CCl_4), δ 1.14 (d,3H J=6.5Hz, methyl α to C-OH), 1.64 (d of d,3H, J=1.0 and 5.0Hz, $CH_3C{=}C$), 4.00 (s,1H, which disappeared on shaking with D_2O,OH), 4.10 (m,1H,$H_{(2)}$), and 5.46 (m,2H,$H_{(3)}$ and $H_{(4)}$).

Preparation of trans-1-(2-methylcyclopropyl) ethanol.- The Simmons-Smith procedure[12-14] as modified by Perraud and Arnaud[19] was employed using trans-pent-3-en-2-ol.

A mixture of trans-pent-3-en-2-ol (21.5g.,0.25 mole), anhydrous ether (200ml.) and Zn/Cu couple[15] (32.5g.,0.50 moles) under nitrogen was warmed to reflux with vigorous stirring, and methylene iodide (134g.,0.50 moles) was added slowly. The reaction mixture was refluxed for 4 hours, and then hydrolysed with saturated, aqueous ammonium chloride solution. The solid residue was broken up, filtered off, and then washed with ether (4x50ml.). The combined filtrates were dried ($MgSO_4$), and distilled to give product (16.0g., 64%; b.p. 30-82°/80mm.) which was shown by vpc (Carbowax, 65°) to contain 6% of unchanged trans-pent-3-en-2-ol.

Preparative vpc (Carbowax, 100°) of the crude cyclopropylcarbinol gave material which contained less than 0.5% impurity (Vpc; Apiezon L, 65°). The spectral data of this material agreed with the published values.[56]

Preparation of trans-1-Acetyl-2-methylcyclopropane.- An ice-cold solution of trans-1-(2-methylcyclopropyl)-ethanol (0.50g.,0.005 moles) in ether (10ml.) was treated dropwise with 6N chromic acid (2.00ml.). After stirring for 2 hr., vpc examination (Carbowax, 60°) indicated that some unchanged carbinol remained. After the addition of a further 2.00 ml. of 6N chromic acid, the reaction mixture was stirred for a further 2 hr. when vpc examination (Carbowax 60°) showed the complete oxidation of all starting carbinol. The aqueous layer was separated off and washed with ether (2x10ml.). The combined ether extracts were washed with water (5ml.), saturated, aqueous sodium bicarbonate solution (5ml.), and water (5ml.), and then dried ($MgSO_4$). Evaporation of the ether gave the crude product (0.45g.) which contained 6% of an impurity shown to be trans-pent-3-en-2-one by comparative vpc (Apiezon L, 55°, and Carbowax, 60°).

Preparative vpc (Carbowax, 100°) gave trans-1-acetyl-2-methyl-cyclopropane which was shown to contain less than 0.5% impurity by

analytical vpc (Apiezon L, 55°), and which had spectral properties almost identical to the published values[42]: ir (film), 1690 (vs), and 1322 cm^{-1} (m); nmr (CCl_4), δ 0.60 (m,1H,H(3) trans to acetyl), 1.10-1.30 (m,2H,H(2) and H(3) cis to acetyl), 1.13 (d,3H, J=5.0 Hz, methyl at C(2)), 1.53 (m,1H,H(1)) and 2.13 (s,3H, acetyl). The mass spectrum was as expected: p=98, and at low eV the only peaks in the spectrum were at m/e=98 ($C_6H_{10}O$), 83 (C_5H_9O), 55 (C_4H_7), and 43 (C_2H_3O), the molecular formulae of the ions being determined by accurate mass measurement.

The oxidation was repeated on a larger scale, using 15.0g. of trans-1-(2-methylcyclopropyl) ethanol and 120 ml. of 6N chromic acid, to give, after preparative vpc (Carbowax, 100°), trans-1-acetyl-2-methylcyclopropane (12.1g.) which contained less than 1% impurity (vpc; Apiezon L, 55°).

Preparation of Pent-3-yn-2-ol.- The procedure of Raphael[55] for the preparation of α-acetylenic carbinols was followed.

Methylacetylene (80g., 2 moles) was bubbled into a stirred solution of ethylmagnesium bromide (2 moles) in anhydrous ether (1600ml.), in a flask fitted with a dry-ice condenser. After the addition was complete, stirring was continued for 5 hr., during which time the propynylmagnesium bromide separated out as a dark oil, heavier than ether. Freshly distilled acetaldehyde (88g., 2 moles) in anhydrous ether (2000ml.) was added slowly and the resulting solution was stirred vigorously for a further 12 hr. The magnesium salt was decomposed with saturated aqueous ammonium chloride solution and the product was extracted with ether (2x1000 ml.).

The combined extracts were then dried ($MgSO_4$), and distilled to give pent-3-yn-2-ol (102g., b.p. 73°/50mm., lit.[46], 82°/80mm.) which was shown by vpc (Apiezon L, 65°) to contain less than 0.5% impurity: ir (film), 3380 (b,vs), and 2260 cm^{-1} (w); nmr (CCl_4), δ 1.34 (d,3H, J= 6.7 Hz, methyl α to CHOH), 1.79 (d,3H, J=2.2Hz, $CH_3C{\equiv}C$), 3.92 (s,1H, which disappeared on shaking with D_2O, OH), and 4.38 (m,1H, quartet of quartets superimposed to give 13 lines, J=2.2 and 6.7Hz $C{\equiv}CCH$).

Preparation of cis-Pent-3-en-2-ol,- Lindlar's palladium catalyst was prepared as described in Organic Syntheses.[75]

Pent-3-yn-2-ol (0.84g.,0.01 moles) was added to the catalyst (0.10g.) which had been prehydrogenated in pentane/ether (1:1; 40ml.) and to which had been added freshly distilled quinoline (1.0ml.). No uptake of hydrogen was observed.

When the procedure was repeated on fresh material, in the absense of quinoline, a very slow uptake of hydrogen was observed. A trial hydrogenation of phenyl acetylene, as described in Organic Syntheses,[75] in the presence of quinoline, gave a satisfactory rate of hydrogenation.

A fresh sample of Lindlar's palladium catalyst was prepared using 60% of the stated amount of lead acetate as the catalyst inhibitor. This was found to give satisfactory results on pent-3-yn-2-ol when used without quinoline.

Pent-3-yn-2-ol (0.84g.,0.01 moles) was hydrogenated over prehydrogenated, modified catalyst (0.10g.) in pentane/ether (1:1; 40ml.). Uptake of hydrogen ceased after 25 min. when the theoretical volume had been absorbed. The catalyst was removed by filtration through a Celite pad and the solvent was distilled off at atmospheric pressure.

Vpc (Apiezon L, 65°) of the product (0.82g.) showed only one peak, of shorter retention time than the starting material. The ir spectrum of this material, which was quite different from that of pent-3-yn-2-ol and trans-pent-3-en-2-ol, was identical to the published spectrum of cis-pent-3-en-2-ol:[46] ir (film), 3300 (b,s,) 1658 (w), and 733 cm^{-1} (m); nmr (CCl_4), δ 1.15 (d,3H, J=6.2 Hz, methyl α to CHOH), 1.64 (d of d,3H J=0.9 and 4.0 Hz, $CH_3C{=}C$), 2.88 (s,1H, which disappeared on shaking with D_2O,OH), 4.54 (m,1H,H(2)), and 5.37 (m,2H,H(3) and H(4)).

The hydrogenation was repeated on a larger scale using pent-3-yn-2-ol (84g., 1.0 mole) and catalyst (10.0g.) in pentane/ether (1:1; 1000ml.). Uptake of 1 mole of hydrogen required 5 hours. Isolation of the product gave pure cis-pent-3-en-2-ol (76.0g.; b.p. 69°/50 mm., lit.[46] b.p. 65.5°/75 mm.).

Preparation of cis-1-(2-Methylcyclopropyl) ethanol.[19] - The Simmons-Smith procedure, as modified by Perraud and Arnaud, did not give the desired product with cis-pent-3-en-2-ol. Instead, three different experiments gave (1), recovered starting material, (2), a crude product which contained more than twenty components of roughly equal amounts (vpc), none of which had a retention time of the order expected for the product, and (3), a mixture of three unknown iodo-compounds.

The Simmons-Smith procedure as described by Dauben and Berezin[17] was found to give the desired product if a very short reaction time and a large volume of solvent was used.

Methylene iodide (5.36g., 0.02 moles) and iodine (0.01g.) were added to Zn/Cu couple[15] (1.63g., 0.025 moles) in anhydrous ether (100ml.) and the mixture was refluxed for 30 minutes under nitrogen. Heating was discontinued and cis-pent-3-en-2-ol (0.86g., 0.01 mole) in anhydrous ether (10ml.) was added during 20 minutes. The mixture was refluxed, under nitrogen, for 15 minutes with vigorous stirring followed by cautious addition of an excess of saturated, aqueous ammonium chloride solution. The residue was broken up, filtered off, and washed with ether (2x50ml.). The combined ethereal filtrates were washed with water (25ml.), dilute aqueous hydrochloric acid (5%; 2x25ml.), water (25ml.), and saturated, aqueous sodium bicarbonate solution (25ml.), and then dried ($MgSO_4$).

Vpc (Apiezon L, 75°) of the crude reaction product showed one peak (~ 10%) in the region expected for the product with about twenty other peaks of much longer retention time.

Distillation of the crude product (1.50g.), after the solvent had been removed, gave the following fractions,

I, b.p. 130 -140 ° (0.21g.),

II, b.p. 140 -142° (0.39g.),

and III, b.p. 120°/ 20mm. (0.34g.).

Vpc (Apiezon L, 75°) of the fractions showed predominantly one peak (80% in I, 85% in II, and 65% in III), with a number of impurities with much longer retention time. The nmr spectral data

of the purest fraction (NT), while showing several impurity peaks, was identical to the published spectrum for cis-1-(2-methylcyclopropyl) ethanol.[56]

The preparation was repeated on a larger scale (20x) and the crude product was purified, by preparative vpc (Carbowax, 100°), giving cis-1-(2-methylcyclopropyl) ethanol (8.6g.,43°/o) which was shown by analytical vpc (Apiezon L, 75°, Carbowax, 80°) to be 98°/o pure: ir (film), 3350 (b,vs), and 3060 cm^{-1} (w); nmr (CCl_4), δ 0.07 (m,1H, cyclopropyl H), 0.60-0.85 (m,3H, cyclopropyl H's), 1.03 (d,3H, J=3.0Hz, methyl at $C_{(2)}$), 1.22 (d,3H, J=6.0Hz, methyl α to CHOH), 3.27 (m,1H,$H_{(2)}$), and 3.42 (s,1H, which disappeared on shaking with D_2O,OH); nmr (C_6H_6), 0.22 (m,1H, cyclopropyl H), 0.74-0.96 (m,3H, cyclopropyl H's), 1.12 (d,3H, J=3.0Hz,methyl at $C_{(2)}$), 1.49 (d, 3H, J=6.0Hz,methyl to CHOH), 3.26 (1H, which was partially resolved into a doublet, J=3.2Hz, and which disappeared on shaking with D_2O, OH), and 3.50 (m,1H,$H_{(2)}$).

Preparation of cis-1-Acetyl-2-methylcyclopropane.- cis-1-(2-Methylcyclopropyl) ethanol (5.0g., 0.05mole) in ether (25ml.) was oxidised with 6N chromic acid (20ml.). The work-up procedure employed in the preparation of trans-1-acetyl-2-methylcyclopropane, p. 75, gave crude material (6.3g.) which was purified by preparative vpc (Carbowax, 100°) to give cis-1-acetyl-2-methylcyclopropane (4.2g., 86°/o), containing less than 1°/o impurity (vpc; Apiezon L, 70°, Carbowax, 65°).

The ir and nmr spectral data for this compound were as expected and agreed with published values[42]: ir (film), 1690 cm^{-1} (vs); nmr CCl_4), δ 0.96 (m,2H,$H_{(2)}$ and $H_{(3)}$ trans to acetyl), 1.01 (d,3H, J= 5.8Hz, methyl at $C_{(2)}$), 1.30 (m,1H,H(3) cis to acetyl), 1.98 (m,1,$H_{(1)}$), and 2.15 (s,3H, acetyl); nmr (C_6H_6), 0.85 (m,1H,H(2)), 1.00(m,1H, H(3) trans to acetyl group), 1.23 (d,3H, J=1.8Hz, methyl at C(2)), 1.46 (m,1H,H(3) cis to acetyl), 1.72 (m,1H,$H_{(1)}$ α to acetyl group), and 2.08 (s,3H, acetyl).

The mass spectrum showed a cracking pattern identical to that of trans-1-acetyl-2-methylcyclopropane : p=98, and at low eV the

only peaks in the spectrum were at m/e=98 ($C_6H_{10}O$), 83 (C_5H_7O), 55 (C_4H_7), and 43 (C_2H_3O). The formulae of the ions were obtained from accurate mass measurement.

Preparation of 4-Ethylhex-3-en-2-one. (a) By the Wittig Reaction - The method first tried was that used in the preparation of trans-pent-3-en-2-one, p. 72.

A solution of acetylmethylenetriphenylphosphorane (100g.) and pentan-3-one (34.4g., 0.40 moles) in methylene chloride (450ml.) was refluxed for 12 hr. under nitrogen. The solvent was distilled off and the residue diluted with pentane (250ml.) to give a white chrystalline precipitate which was filtered off. The organic filtrate was concentrated and distilled to give a product (33.0g.; b.p. 99-102°) identified as pentan-3-one (b.p., ir spectrum, and vpc; Apiezon L, 75°, Carbowax, 85°). The unchanged acetylmethylene-triphenylphosphorane, which was precipitated with pentane, was recrystallised from methylene chloride to give pure material (95g.; m.p. 198-201°, lit.,[97] 199-202°).

The attempted preparation was repeated using the conditions of Ruchardt, Eichler and Panse[59] for the reaction of stabilised ylides with carbonyl compounds.

A solution of acetylmethylenetriphenylphosphorane (95g.), a large excess of pentan-3-one (172g., 2.0 moles), and benzoic acid (12g.), in anhydrous, redistilled benzene, was refluxed for 48 hours under nitrogen. The same work-up procedure as above gave unchanged pentan-3-one as the only product.

(b). By a Directed Aldol Condensation (Wittig and Suchanek[69]).- Concentrated hydrochloric acid (0.75g.) was added to a mixture of acetone (72.5g., 1.25 mole) and cyclohexylamine (123.75g., 1.25 moles), and, after shaking for a few seconds, was set aside for 12 hr. Several pellets of sodium hydroxide were then added and, after 8 hours, the aqueous layer was separated. The organic layer was dried over phos-

-phorus pentoxide and distilled under nitrogen. The fraction b.p. 75-6°/20mm. was collected and redistilled under nitrogen to give N-isopropylidenecyclohexylamine (120g., 69%, b.p. 79°/24mm., lit.,[99] 180·6°/760 mm.) as a colourless liquid. The product was stored over phosphorus pentoxide under nitrogen. Vpc (Apiezon L, 150°) showed only one peak and ir examination showed the expected absorption at 1663 cm^{-1} (s).

A solution of methyl-lithium in anhydrous ether (600ml.) was prepared by the method of Gilman,[100] from lithium sand[101] (15.2g., 2.20 moles) and methyl iodide (142g., 1.0 mole), and was shown to be 1.40M (by the Gilman test[102]).

Pure di-isopropylamine (76.8g., 0.76 moles) in anhydrous ether (400ml.) was added dropwise to 500 ml. of a stirred ethereal solution of methyl-lithium (1.40M; 0.70 mole) under nitrogen. When the evolution of methane ceased and the reaction mixture had stopped boiling, freshly distilled N-isopropylidenecyclohexylamine (97.3g., 0.70 mole) was added at 0°. The reaction mixture was then cooled to -70°, when the metal derivative of the Schiff's base crystallised out, and pentan-3-one (60.2g., 0.70 mole) was added. The reaction mixture was allowed to warm up to room temperature and left for 48 hours.

Aqueous oxalic acid solution (0.8M, 4000ml.) was added and the product was steam-distilled. The ethereal solution of product was then dried ($MgSO_4$) and fractionally distilled to give two fractions, I, b.p. 98-102°, (19.0g.), identified as pentan-3-one by comparative vpc (Apiezon L, 85°), b.p., and ir spectrum, and II, b.p. 92-94°/80mm., (40g.; 45.5%).

Vpc (Apiezon L, 75°, (Carbowax, 85°) of fraction II showed 3 peaks in roughly equal amounts and of almost identical retention time. Examination of the ir spectrum ((film), 1710 (s), 1685 (s), and 1620 cm^{-1} (s)), showed the presence of a large olefinic absorption and conjugated and unconjugated carbonyl absorptions, At low eV, the mass spectrum showed only peaks at m/e=126,111,97, and 43.

Faulk and Fry[61] found that, in the preparation of 5-ethyl-4-methylhept-4-en-3-one, 93% of the unconjugated isomer, 5-ethyl-4-methyhept-5-en-3-one, was formed and only 7% of the expected conjugated isomer.

The product obtained was probably, therefore, a mixture of 4-ethylhex-3-en-2-one and cis and trans-4-ethylhex-4-en-2-one.

The product mixture could not be separated by either preparative vpc (Carbowax or SE-30) or thin layer chromatography (alumina or silica).

Attempted Preparation of 1-Acetyl-2,2-diethylcyclopropane.- The procedure of Landor and Punja was used.[62]

To a suspension of sodium hydride (2.4g., 0.10 mole) in anhydrous dimethylformamide (200ml.) was added, in one portion, powdered trimethylsulfoxonium iodide (22.1g., 0.104 mole).[96] An exothermic reaction occurred with vigorous evolution of hydrogen. After stirring for 15 minutes, the mixture of isomers of 4-ethylhexen-2-one (12.6g., 0.10 mole) in dimethylformamide (50ml.) was added. The reaction mixture was stirred overnight under nitrogen, poured into hydrochloric acid / ice-water (200ml.; 3%) and extracted with pentane (3x200 ml.). The combined pentane extracts were washed with water (100ml.), dried ($MgSO_4$), and the pentane removed by distillation.

Distillation of the residue gave material (12.6g., 96°/69mm.) which was a mixture of three products, partially resolved by vpc (Apiezon L, 60°, Carbowax, 50°). The mixture could not be separated by preparative vpc (Carbowax, SE-30), or column or thin layer chromatography (silica gel or alumina). The nmr spectrum of the product mixture was very complex and showed a large number of lines between δ 0.62 and 2.50, and a small multiplet at δ 5.30 in the region expected for olefinic protons.

Preparation of 4,4-Dimethylpentan-2-one.- 4,4-Dimethylpentan-2-one was prepared from methylmagnesium iodide and mesityl oxide, using the procedure described by Asinger and Gentz[103] for the abnormal Grignard addition of methylmagnesium iodide to $\alpha\beta$-unsaturated carbonyl compounds, and purified by preparative vpc (SE-30, 120°):ir (film), 1712 (vs), 1366 (s), and 1220 cm^{-1} (s); nmr (CCl_4), δ 1.00 (s, 9H, Me_3C), 2.03 (s, 3H, acetyl), and 2.23 (s, 2H, CH_2CO).

Preparation of 4,4-Dimethylpentan-2-ol.- Reduction of 4,4-dimethylpentan-2-one (1.14g., 0.01 moles), with lithium aluminium hydride (0.13g., 0.003 moles) in ether (10ml.), gave 4,4-dimethylpentan-2-ol (0.94g.), after purification by preparative vpc (SE-30, 120°).

Oxidation of this product, with 6N chromic acid in ether, gave back 4,4-dimethylpentan-2-one, identified by comparative vpc (Apiezon L, 75°, Carbowax, 60°).

Preparation of 1-(2,2-Dimethylcyclopropyl) ethanol.- Reduction of 1-acetyl-2,2-dimethylcyclopropane (4.48g., 0.04 moles), with lithium aluminium hydride (0.475g., 0.0125 moles) in ether (20ml.), gave the product (39.2g.; 86%; b.p. 70-72°/48mm.), which showed two partially resolved peaks on vpc (Apiezon L, 50°, Carbowax 50°) with retention time longer than that of 1-acetyl-2,2-dimethylcyclopropane: ir (film), 3410 (s), and 3080 cm^{-1} (w).

The product alcohol was shown to be a mixture of the two possible diastereoisomers by oxidation with 6N chromic acid in ether. 1-Acetyl-2,2-dimethylcyclopropane, identified by its ir spectrum and by comparative vpc (Apiezon L, 85°, Carbowax, 65°), was the only product.

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Lithium in Liquid Ammonia. Method A. - Anhydrous ammonia (25ml.), dried by passing through calcium oxide, was condensed into a graduated, 100ml., 3-necked, R.B. flask, fitted with a Dry-Ice condenser, and protected from atmospheric moisture by a drying tube filled with calcium oxide.

1-Acetyl-2,2-dimethylcyclopropane (0.25g.) was added, followed by lithium (0.110g.) in one portion. Magnetic stirring of the blue solution obtained was continued for 2 hours, and then the reduction mixture was decomposed by the cautious addition of an excess of solid ammonium chloride. Ether (50ml.) was added, and the ammonia was allowed to evaporate. Water (10ml.) was added to dissolve the solid salts left in the flask, the ether layer was separated, and the aqueous layer was extracted with ether (2x25ml.). The combined ether layers were washed with water (10ml.), dilute hydrochloric acid (5%, 10ml.), and saturated sodium bicarbonate solution (10ml.). The dried solution ($MgSO_4$) was concentrated to approximately 2ml. by distilling off most of the ether through a column packed with Fenske helices.

The product showed six peaks on vpc examination (Apiezon L, 65°, Carbowax, 60°). These were identified as 1-acetyl-2,2-dimethylcyclopropane, 4,4-dimethylpentan-2-one, 5-methylhexan-2-one, and their corresponding alcohols by comparative vpc (Apiezon L, 65°, Carbowax, 60°). The preparation of authentic samples of 1-(2,2-dimethylcyclopropyl) ethanol, 4,4-dimethylpentan-2-one, and 4,4-dimethylpentan-2-ol was described on pages 83 and 83 respectively, and authentic samples of 5-methylhexan-2-one and 5-methylhexan-2-ol were obtained from Koch-Light Co.

Oxidation of the reduction product in ether (5ml.), with 6N chromic acid, gave a product mixture showing only three peaks on vpc examination (Apiezon L, 65°, Carbowax 60°). These were identified as 1-acetyl-2,2-dimethylcyclopropane (26),4,4-dimethylpentan-2-one (55), and 5-methylhexan-2-one (54) by comparative vpc (Apiezon L, 65°, Carbowax, 60°). The three were separated by preparative vpc (Carbowax, 100°) and their structure confirmed by comparison of the ir spectrum of each with that of authentic samples. Peak integration on several vpc analyses of the oxidised product gave a product distribution which was uncorrected for the different molar sensitivity of the products to the detector.

Table 1 shows the results of several reductions using the procedure

described in the above representative reduction. The actual weights of lithium and 1-acetyl-2,2-dimethylcyclopropane used, and the volume of liquid ammonia in which the reduction was performed, are shown in the Table. Product distributions were corrected for molar sensitivity (obtained by peak integration on vpc analyses of several accurately weighed mixtures of the three products.) and normalised to 100%. Product ratios were calculated from this corrected product distribution

In some reductions, a vpc internal standard, decane, was added with 1-acetyl-2,2-dimethylcyclopropane. The ratios of starting material to decane, and total product to decane (all corrected for molar sensitivity), are shown in the Table as the 'decane integral', 'before reduction', and 'after reduction'.

Method B. - Lithium (0.110g.) was added to anhydrous liquid ammonia (50ml.) in a graduated, 100ml., 3-necked, R.B. flask fitted with a Dry-Ice condenser, as in method A, and the resulting blue solution was stirred magnetically for 30 minutes to ensure complete dissolution of the lithium. One arm of the flask carried a screw-cap adaptor, fitted with a serum cap, and through this a mixture of 1-acetyl-2,2-dimethylcyclopropane (0.50g.) and decane (0.15g.) was slowly added, by means of a syringe, directly into the ammonia solution. Stirring was continued for 2 hours, and then the reduction mixture was decomposed by the careful addition of an excess of solid ammonium chloride. Ether (50ml.) was added and the ammonia was allowed to evaporate. Water (10ml.) was added, the ether layer was separated, and the aqueous layer was extracted with ether (2x25ml.). The combined extracts were dried ($MgSO_4$) and concentrated to about 2ml. by distilling off the ether through a column packed with Fenske helices.

Comparative vpc examination (Apiezon L, 65°, Carbowax, 60°) of this material showed decane and the same six products observed using method A.

The reduction product mixture in ether (5ml.), was oxidised with 6N chromic acid. Vpc examination (Apiezon L, 65°, Carbowax 60°) of the oxidised product showed it to be a mixture of decane and the same

three ketones obtained using method A. Peak integration on several vpc analyses of this product gave the product distribution.

Table 2 shows the results of several reductions using the conditions described above. All integrations were corrected for molar sensitivity. The 'decane integral', 'before reduction', refers to the ratio of starting material to decane, and 'after reduction', to the ratio of total product to decane.

Table 3 shows the results of two reductions on 1-acetyl-2,2-dimethylcyclopropane (0.50g.), using the method as above, but carried out in 500ml. liquid ammonia.

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Barium in Liquid Ammonia.- Table 4 shows the results of several reductions of 1-acetyl-2,2-dimethylcyclopropane with barium in liquid ammonia, using the conditions described in method B, page 85 for the reduction of this ketone with lithium in liquid ammonia.

All reductions were carried out in 50ml. liquid ammonia on a mixture of ketone (0.50g.) and decane (0.15g.). All integrations were corrected for molar sensitivity.

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Sodium in Liquid Ammonia.- Table 5 shows the results of the reduction of 1-acetyl-2,2-dimethylcyclopropane (0.50g.) with sodium in liquid ammonia (50ml.), using method B, page 85 In those cases in which decane was not added with the cyclopropyl ketone, no entry was shown in that column of the table for the 'decane integral'.

Reduction of 1-Acetyl-2,2-dimethylcyclopropane in the Presence of Tetra-ethylammonium Cations.- Solutions of metals in liquid ammonia (50ml.) were made up as in method B, page 85 and then a slight excess of tetra-ethylammonium chloride was added to precipitate the metal as its chloride. The resulting solution was stirred for ten minutes and then 1-acetyl-2,2-dimethylcyclopropane (0.50g.) was added as before. The same work-up procedure as described in

method B was followed.

The results of these reductions are shown in Table 6.

Tetra-ethylammonium chloride was obtained from B.D.H. and dried, in vacuo, over P_2O_5, before use.

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Lithium/Lithium Iodide Mixtures in Liquid Ammonia. - A weighed quantity of lithium iodide was added to a solution of lithium (0.20g.) in liquid ammonia, made up as in method B, page 85, and the resulting solution was stirred for a further 15 minutes, before adding 1-acetyl-2,2-dimethylcyclopropane (0.50g.). The same work-up procedure as used in method B was followed.

Table 7 shows the results of reductions using lithium (0.20g.) and varying amounts of lithium iodide.

Table 8 shows the results of reductions using other quantities of lithium metal, with lithium iodide.

Lithium iodide was obtained, as the trihydrate, from B.D.H. and was dried at 350° before use.

Reductions of trans-1-Acetyl-2-methylcyclopropane with Lithium in Liquid Ammonia. - The results of several reductions, using method B, p. 85, on trans-1-acetyl-2-methylcyclopropane (0.50g.), in liquid ammonia (50ml.), are shown in Table 9. All product distributions and ratios were corrected for molar sensitivity, and decane (0.15g.) was used as a vpc internal standard.

The reduction product was shown to be a mixture of decane, trans-1-acetyl-2-methylcyclopropane, 4-methylpentan-2-one, hexan-2-one and their corresponding alcohols by comparative vpc (Carbowax, 60°). Authentic samples of 4-methylpentan-2-one, 4-methylpentan-2-ol, hexan-2-one, and hexan-2-ol were obtained from Koch-Light Co., and trans-1-(2-methylcyclopropyl) ethanol was prepared as described on page

Oxidation of this reduction product mixture gave a mixture which showed only three peaks, apart from decane, on vpc examination. These were identified as trans-1-acetyl-2-methylcyclopropane (29),

hexan-2-one (56), and 4-methylpentan-2-one (57) by comparative vpc (Apiezon L, 65°, Carbowax, 60°). The three products were separated by preparative vpc (Carbowax, 85°) and their identity confirmed by comparison of the ir spectrum of each with that of authentic samples.

Reduction of cis-1-Acetyl-2-methylcyclopropane with Lithium in Liquid Ammonia. - The results of reductions, using method B, page 85 on cis-1-acetyl-2-methylcyclopropane (0.25g.) in liquid ammonia (50ml.) are shown in Table 10. All product distributions and ratios were corrected for molar sensitivity, and decane (0.15g.) was used as a vpc internal standard.

The products, after oxidation, were identified as cis-1-acetyl-2-methylcyclopropane (28), hexan-2-one (56), and 4-methylpentan-2-one (57) by comparative vpc (Carbowax, 60°).

Reaction of Substituted Acetylcyclopropanes with Di-t-butyl Peroxide and Butan-2-ol. - A mixture of the substituted acetylcyclopropane (0.001 mole), butan-2-ol (1.40g.), and di-t-butyl peroxide was heated in a sealed, thick-walled, Pyrex tube for 14 hours at 137°. The product was analysed directly by vpc and all product distributions were corrected for detector sensitivity.

Table 11 shows the results of three reactions on 1-acetyl-2,2-dimethylcyclopropane (0.112g., 0.001 mole), using 0.113g., 0.225g., and 0.450g. respectively of di-t-butyl peroxide. The reaction product was shown to be a mixture of 1-acetyl-2,2-dimethylcyclopropane, 4,4-dimethylpentan-2-one, and 5-methylhexan-2-one (vpc; Apiezon L, 80°, and Carbowax, 40°).

Table 12 shows the results of three reactions on trans-1-acetyl-2-methylcyclopropane (0.098g., 0.001 mole), using 0.113g., 0.225g., and 0.450g. respectively of di-t-butyl peroxide. The reaction product was shown to be a mixture of trans-1-acetyl-2-methycyclopropane,4-methylpentan-2-one, and hexan-2-one (vpc; Apiezon L, 80°, and Carbowax, 40°).

Table 13 shows the results of three reactions on cis-1-acetyl-2-methylcyclopropane (0.098g., 0.001 mole), using 0.113g., 0.225g., and 0.450g. respectively of di-t-butyl peroxide. The reaction product was shown to be a mixture of cis-1-acetyl-2-methylcyclopropane, 4-methylpentan-2-one, and hexan-2-one (vpc; Apiezon L, 80°, and Carbowax, 40°).

Rearrangement of Substituted 1-(Cyclopropyl) ethanols with Di-t-butyl Peroxide. - A mixture of the substituted 1-(cyclopropyl) ethanol, and di-t-butyl peroxide, with decane as an internal vpc standard, was heated in a sealed, thick-walled, Pyrex tube for 14 hours at 140°. The product was analysed directly by vpc and all product distributions were corrected for detector sensitivity.

Table 14 shows the results of three reactions on 1-(2,2-dimethylcyclopropyl) ethanol (0.50g.), using 0.05g., 0.15g., and 0.50g. respectively of di-t-butyl peroxide. The reaction product was shown to be a mixture of 1-(2,2-dimethylcyclopropyl) ethanol, 4,4-dimethylpentan-2-one, and 5-methylhexan-2-one (vpc; Carbowax, 60°).

1-(2,2-Dimethylcyclopropyl) ethanol was prepared as a mixture of the two possible diastereo-isomers and was used as such. The ratio of the diastereoisomers was unchanged in the unreacted material in the above reactions.

Table 15 shows the results of three reactions on trans-1-(2-methylcyclopropyl) ethanol (0.25g.), using 0.025g., 0.075g., and 0.250g. respectively of di-t-butyl peroxide. The reaction product was shown to be a mixture of trans-1-(2-methylcyclopropyl) ethanol 4-methylpentan-2-one, and hexan-2-one (vpc; Carbowax, 60°).

Table 16 shows the results of three reactions on cis-1-(2-methylcyclopropyl) ethanol (0.125g.), using 0.013g., 0.038g., and 0.125g. respectively of di-t-butyl peroxide. The reaction product was shown to be a mixture of cis-1-(2-methylcyclopropyl) ethanol, 4-methylpentan-2-one, and hexan-2-one (vpc; Carbowax, 60°).

Reaction of trans-1-Acetyl-2-methylcyclopropane with Sodium in Dioxan.- 1-Acetyl-2-methylcyclopropane (0.098g., 0.001 mole) in redistilled, purified dioxan (1ml.), and sodium ((a), 0.024g., and (b), 0.048g.) was heated for 14 hours, at 135°, in a sealed, thick-walled, Pyrex tube with decane (0.10g.) as an internal vpc standard.

Dilute hydrochloric acid (2ml.) was added cautiously and the hydrolysed product was extracted with ether. Vpc examination of the ether extract of both reaction products showed that trans-1-acetyl-2-methylcyclopropane, 4-methylpentan-2-one, and hexan-2-one accounted for less than 20% of the starting material. The vpc retention time of dioxan was such that the product distribution could not be determined. The vpc examination showed many unidentified products of long retention time.

Attempted Preparation of 2-Cyclopropylpropionaldehyde.- The procedure used was that of Wittig and Knauss,[73] and Levine,[74] for the addition of methoxymethylenetriphenylphosphorane to carbonyl compounds.

A solution of sodium ethoxide (0.02 moles) in anhydrous ethanol (10ml.) was added to a mixture of acetylcyclopropane (0.02 moles, 1.68g.), and methoxymethyltriphenylphosphonium chloride[104] (6.84g., 0.02 moles) in anhydrous ethanol (50ml.). The solution was stirred with heating, under nitrogen, during 12 hours.

A small portion (1ml.) of the reaction mixture was shaken for 8 hours with saturated aqueous, sodium bisulphite solution (1ml.). The resulting precipitate was decomposed with aqueous potassium carbonate solution, and the solution obtained was saturated with sodium chloride and extracted with ether. Vpc examination (Apiezon L, 40°, and 100°) of the ether extract showed no volatile product.

A small portion (2ml.) of the reaction mixture was heated under reflux, for 10 minutes, with dilute hydrochloric acid (1ml.), and then saturated with sodium chloride and extracted with ether. Vpc examination (Carbowax, 60°) of the ether extract showed only ethanol and acetylcyclopropane.

Preparation of 2-Methyl-1-phenylpent-3-en-1-ol. - (a) 2-Bromopent-3-ene (0.20 moles, 30g.), prepared from pent-3-en-2-ol,[105] was added with stirring to magnesium turnings (0.60 moles, 14.6g.), in anhydrous ether (200ml.), during 10 hours. Redistilled benzaldehyde (0.15 moles, 15.9) in ether (50ml.) was added slowly, the resulting solution was stirred for a further 1 hour, and then the reaction mixture was cautiously hydrolysed with saturated, aqueous ammonium chloride solution.

The product was extracted with ether (3x150ml.), and, after drying ($MgSO_4$), the ether was removed by rotary evaporation. Infared examination of this crude product showed a large absorption at 1699 cm^{-1} attributed to unreacted benzaldehyde.

The crude product was redissolved in ether (100ml.) and shaken with saturated, aqueous sodium bisulphite solution to remove benzaldehyde as the bisuphite addition compound. The filtered ether solution was then washed with water (2x50ml.), aqueous sodium bicarbonate solution (50ml.), and water (2x50ml.), dried ($MgSO_4$), and concentrated by rotary evaporation.

Infrared examination of this product showed no absorption at 1699 cm^{-1}, but a broad, hydroxyl absorption at 3330 cm^{-1}, and an absorption at 1684 cm^{-1} characteristic of a conjugated carbonyl.

Distillation gave the product (10.1g.; b.p. 61-62°/0.03mm.; ir (film), 3330 (b,vs), and 1684 cm^{-1} (vs)) which showed two peaks on vpc analysis (Apiezon L, 170°). The two components were separated and purified by preparative vpc (Carbo ax, 140°).

The product with the shortest retention time (Apiezon L, 170°) was identical with benzyl alcohol (ir spectrum, nmr spectrum, mass spectrum, and vpc).

Analytical vpc examination (Apiezon L, 170°) of the second product showed that preparative vpc purification (Carbowax, 140°) had caused some rearrangement (15%) to another isomeric product of slightly longer retention time. The product mixture had the following spectral data : ir (film),1684 (vs), and 1648 cm^{-1} (s); mass spectrum, p=174,- at low eV, the only other peaks in the spectrum were at m/e=105 and 69.

(b) The Grignard magnesium compound of 2-bromopent-3-ene (0.2 moles, 30g.) was prepared as described in the previous preparation. The solution was filtered through a glass-wool plug, under nitrogen, and shown, by titration, to contain 0.113 moles of Grignard reagent.

Benzaldehyde (0.100 moles, 10.6g.) in ether (100ml.) was added slowly, over 5 hours, to the vigorously stirred solution of Grignard reagent. After standing for 1 hour, the reaction mixture was cautiously hydrolysed with an excess of saturated, aqueous ammonium chloride solution. The ether extract was washed with water (2x50ml.), dried ($MgSO_4$), and then concentrated by rotary evaporation.

Distillation gave a product (17.1g.; b.p. 60-63°/0.03mm.) which was shown by vpc (Apiezon L, 170°) to contain 10% of an impurity which had the same retention time as the main product ketone isolated in the previous preparation.

Redistillation gave 2-methyl-1-phenylpent-3-en-1-ol as a colourless liquid (16.2g.; b.p. 61-62°/0.03mm.) containing 5% of a single impurity (vpc; Apiezon L, 170°) : ir (film), 3400 cm^{-1} (b,s), and a small absorption at 1684 cm^{-1} (attributed to a conjugated-ketone impurity); nmr (CCl_4), δ 0.85 (pair of d,3H J=6.5Hz, CH_3CH), 0.90 (m,1H,H(2)), 1.40 and 1.60 (two t, 3H, J=6.0Hz and 2.0Hz, $CH_2C{=}C$), 2.60 (s,1H,OH), 4.2(m,1H,H(1)), 5.30 (broad m,2H,H(3) and H(4)), and 7.10 (broad s,5H, phenyl); mass spectrum, p=176,- at low eV, the major peaks in the spectrum were at m/e=107 and 69.

Attempted Preparation of 2-(2-Methylcyclopropyl)-1-phenylpropan-1-ol.- (a) Freshly distilled 2-methyl-1-phenylpent-3-en-1-ol (0.01 moles, 1.76g.) and Zn/Cu couple[15] (0.02 moles, 1.30g.) in ether (25ml.), under nitrogen, were warmed to reflux with vigorous stirring. Methylene iodide (0.02 moles, 5.36g.) was added slowly and, after refluxing for 6 hours, the reaction mixture was cautiously decomposed with an excess of dilute, aqueous hydrochloric acid, followed by extraction with ether (3x25ml.).

The ether extract was washed with water (20ml.), and saturated, aqueous sodium bicarbonate solution (20ml.), dried ($MgSO_4$), and

concentrated by rotary evaporation to give the crude product (3.05g.) identified as a mixture of starting material and methylene iodide (vpc, infrared and mass spectra).

(b) The reaction was repeated using 2-methyl-1-phenylpent-3-en-1-ol (0.02 moles, 3.52g.), Zn/Cu couple (0.08 moles, 5.2g.), and methylene iodide (0.04 moles, 10.72g.) in ether (25ml.).

Vpc examination (Apiezon L, 170°) of the crude material obtained after a reaction time of 48 hours showed twenty peaks.

Distillation gave a fraction (2.20g.; b.p. 80-88°/0.05mm.) which showed fifteen different peaks on vpc examination (Apiezon L, 170°). The major component (15%) of this mixture had a retention time identical with that of 2-methyl-1-phenylpent-3-en-1-ol. The mass spectrum of this mixture, at low eV, showed a large peak at m/e=176, and only a small peak at m/e=190.

Preparation of Hex-4-yn-2-ol.- (a) Methylacetylene (1 mole, 40g.) was bubbled into a solution of ethylmagnesium bromide in ether (400ml.), under nitrogen, contained in a flask fitted with a Dry-Ice condenser. After the addition of methyacetylene was complete, stirring was continued for 5 hours, during which time the Grignard reagent separated out as a dark oil, heavier than ether. The Dry-Ice condenser was replaced by a water condenser, 1,2-epoxypropane (1 mole, 58g.) in ether (50ml.) was added slowly and the mixture was stirred vigorously for 18 hours.

The reaction mixture was hydrolysed with saturated, aqueous ammonium chloride solution and extracted with ether (2x200ml.). The ethereal extract was dried ($MgSO_4$), concentrated, and distilled to give a mixture (51g.; b.p. 64-68°/28mm.) of two products (vpc; Apiezon L, 70°). Distillation on a Buchi spinning band distillation apparatus gave the following product fractions:

I (27g.; b.p. 71-74°/60mm.), which was pure by vpc (Apiezon L, 70°) and was identified as 1-bromopropan-2-ol : ir (film), 3380 (b,vs), and 670 cm^{-1} (s); nmr (CCl_4), δ 1.28 (d,3H, J=6.3Hz, methyl),

3.40 (two overlapping doublets, 2H, J=5.0 and 6.0Hz, methylene), 3.67 (s,1H, which disappeared on shaking with D_2O,OH), and 3.92 (m,1H,CH); mass spectrum, p=140 and 138,- at low eV, the other main peaks in the spectrum were at m/e=125,123,82,80,59 and 45.

II (10g.; b.p. 75-85°/60mm.), which was shown by vpc (Apiezon L, 70°) to be a mixture of 1-bromopropan-2-ol and hex-4-yn-2-ol.

III (12.5g.; b.p. 85-86°/60mm.), which was pure by vpc (Apiezon L, 70°) and had the spectral properties expected for hex-4-yn-2-ol : ir (film), 3350 cm^{-1} (b,vs); nmr (CCl_4), δ 1.18 (d,3H, J= 6.3Hz, methyl), 1.76 (t, 3H, J=2.6Hz, $CH_3C{\equiv}C$), 2.20 (m,2H, methylene), 3.68 (s,1H, which disappeared on shaking with D_2O,OH), and 3.89 (m,1H,$H_{(2)}$); mass spectrum : p=98 (low intensity) with base peak at m/e=83.

(b) A suspension of sodamide in liquid ammonia (150ml.) was prepared from sodium[106] (5.75g.) in a flask fitted with a Dry-Ice condenser and a gas-inlet tube. Methylacetylene was bubbled through the vigorously stirred reaction mixture for 2 hours, and then 1,2-epoxypropane (0.33 moles, 18g.) was added during 1 hour. The flow of methylacetylene was continued for a further 2 hours.

After stirring for 24 hours, the reaction mixture was decomposed by the addition of solid ammonium chloride. Ether (100ml.) was added and the ammonia was allowed to evaporate. Sufficient dilute, aqueous hydrochloric acid was added to dissolve the solid residue and the resulting solution was extracted with ether (2x100ml.). The ethereal extract was washed with saturated, aqueous sodium bicarbonate solution (50ml.), and water (50ml.), and then dried ($MgSO_4$).

Distillation gave the product (14.2g.; 88-90°/78mm.) which was shown by vpc (Apiezon L, 70°) to contain less than 0.5% impurity, and which had ir, nmr, and mass spectra identical to those of the hex-4-yn-2-ol prepared above.

Preparation of trans-Hex-4-en-2-ol.- Hex-4-yn-2-ol (0.1 moles, 9.8g.) in anhydrous ether (10ml.) was added to a solution of sodium (9.2g.) in anhydrous liquid ammonia (400ml.), in a flask fitted with a Dry-Ice condenser protected from atmospheric moisture by a drying-tube filled with calcium oxide.

After stirring for 2 hours, the reaction mixture was decomposed by the addition of solid ammonium chloride (30g.), and the ammonia was allowed to evaporate. The residual salt was extracted with ether (3x50ml.). The ethereal extract was washed with dilute, aqueous hydrochloric acid (2x25ml.), saturated, aqueous, sodium bicarbonate solution (25ml.), and water (25ml.), and then dried ($MgSO_4$), and concentrated by rotary evaporation.

Distillation gave the product (8.8g.; b.p. 66°/40mm.) which was pure by vpc analysis (Apiezon L, 70°). The spectral properties were as expected for the required product : ir (film), similar, but not identical, to that of hex-4-yn-2-ol; nmr (CCl_4), δ 1.05 (d, 3H, J=15.8 Hz, methyl), 1.64 (m, consisting of a doublet, J=12.0Hz, further split into two triplets, J=3.0Hz, 3H, $CH_3C{\equiv}C$), 2.05 (m, 2H, methylene), 3.38 (broad s, 1H, which disappeared on shaking with D_2O, OH), 3.65 (m, 1H, $H_{(2)}$), and 5.40 (m, 2H, $H_{(4)}$ and $H_{(5)}$).

Preparation of cis-Hex-4-en-2-ol.- Hex-4-yn-2-ol (4.9g.) was shaken in a hydrogen atmosphere with prehydrogenated Lindlar's palladium catalyst (0.50g.) in pentane/ether (1:1; 50ml.) until the uptake of hydrogen ceased. The uptake of hydrogen (95% of theoretical) required 8 hours.

After the catalyst had been removed by filtration through a Celite pad, the product was obtained by distillation (3.95g.; b.p. 71°/53mm.). This was shown to be largely the cis-alcohol, contaminated by trans-hex-4-en-2-ol (7%) and hex-4-yn-2-ol (5%) by comparative vpc examination (Apiexon L, 70°); nmr (CCl_4), δ 1.14 (d, 3H, J=15.7Hz, methyl), 1.66 (m, 3H, $CH_3C{\equiv}C$), 2.10 (m, 2H, methylene), 2.95 (broad s, 1H, which disappeared on shaking with D_2O, OH), 3.70 (m, 1H, $H_{(2)}$), and 5.45 (m, 2H, $H_{(4)}$ and $H_{(5)}$). The nmr spectrum also contained small peaks corresponding to protons in trans-hex-4-en-2-ol and hex-4-yn-2-ol.

Preparation of trans-1-(2-methylcyclopropyl) propan-2-ol. - trans-Hex-4-en-2-ol (0.04 moles, 4.00g.), and Zn/Cu couple (0.08 moles, 5.24g.) in ether (50ml.) were stirred vigorously, under nitrogen, while methylene iodide (0.06 moles, 16.08g.) was added slowly. After refluxing for 1 hour, the reaction mixture was decomposed by the addition of an excess of aqueous ammonium chloride solution and extracted with ether (2x50ml.). The combined extracts were washed with dilute, aqueous hydrochloric acid (50ml.), saturated, aqueous, sodium bicarbonate solution (25ml.), and water (25ml.), and dried ($MgSO_4$).

Distillation gave the product (2.95g.; b.p. 70-72°/30mm.) which was 92% pure (vpc; Apiezon L, 70°).

Purification by preparative vpc (Carbowax, 100°) of this crude product gave material which showed no impurity on analytical vpc examination (Apiezon L, 70°).

The spectral properties of the purified material were as expected for trans-1-(2-methylcyclopropyl) propan-2-ol : ir (film), 3380 cm^{-1} (b,s); nmr (CCl_4), δ 0.20 (m, 4 cyclopropyl protons), 1.02 (d,3H, J=4.8Hz, methyl attached to cyclopropane), 1.14 (d,3H, J=6.0Hz, methyl α to CHOH), 1.34 (m,2H, methylene), 3.74 (m,1H,CH), and 3.85 (broad s,1H, which disappeared on shaking with D_2O,OH); mass spectrum, p=114.

Preparation of trans-1-(2-methylcyclopropyl) propan-2-one. - trans-1-(2-Methylcyclopropyl) propan-2-ol (0.02 moles, 2.28g.) in ether (10ml.) was stirred at room temperature with 6N chromic acid (10.0ml.) until vpc examination (Apiezon L, 70°) showed no starting material remained. The separated ether layer and combined ether extracts (2x15ml.) were washed with saturated, aqueous, sodium bicarbonate solution (15ml.), and water (15ml.), and dried ($MgSO_4$).

Distillation gave the product (1.76g.; b.p. 57°/35mm.) which showed less than 10% impurity on vpc examination (Apiezon L, 70°).

Purification by preparative vpc (Carbowax, 110°) gave trans-1-(2-methylcyclopropyl) propan-2-one (1.24g.) which showed no impurity on analytical vpc examination (Apiezon L, 70°). The spectral properties were in agreement with the proposed structure: ir (film), 1709 cm^{-1}(vs); nmr (CCl_4); δ 0.50 (m, 4 cyclopropyl protons), 1.05 (d, 3H, J= 5.6Hz, methyl attached to cyclopropane), 2.05 (s, 3H, acetyl), and 2.20 (d, 2H,

J = 6.6Hz, methylene) ; mass spectrum, p= 112, and main peaks at m/e = 97, 69, 58, 55, 43, and 41.

Treatment of trans-1-(2-Methylcyclopropyl)propan-2-one with Sodium Methoxide in Methanol.- (a) trans-1-(2-Methylcyclopropyl)propan-2-one (0.10g.) was added to a 5% solution of sodium methoxide in methanol (2.0ml.) and the resulting solution was allowed to stand for 24 hours. Vpc examination (Apiezon L,70°, and Carbowax,60°) showed only starting material.

The solution was diluted with water (5ml.) and extracted with pentane (3x5ml.). The extract was washed with water (2x2ml.) and dried over calcium chloride for 6 hours. The infrared spectrum of the product obtained after removal of the pentane was identical to that of trans-1-(2-methylcyclopropyl)propan-2-one.

(b) A solution of trans-1-(2-methylcyclopropyl)propan-2-one (0.10g.) in a 10% solution of sodium methoxide in methanol (2.0ml.) was heated in a sealed, thick-walled, Pyrex tube for 18 hours at 80°. The product, isolated as above, had ir and nmr spectra, and vpc retention time (Apiezon L, Carbowax, 60°) identical to those of the starting material.

Deuteration of trans-1-(2-Methylcyclopropyl)propan-2-one with Sodium Methoxide in Methanol-$[^2H_1]$.- trans-1-(2-Methylcyclopropyl)propan-2-one (0.002 moles, 0.224g.) was treated with a 10% solution of sodium methoxide in methanol-$[^2H_1]$ (3.42g.) during 12 hours. The reaction mixture was extracted with sodium-dried n-pentane (3x5ml.), and the ethereal extract was dried over anhydrous calcium chloride.

Preparative vpc (100°, Carbowax column which had been treated with hexamethyldisilazane immediately prior to use) gave the product (0.198g.) which showed no impurities on vpc examination (Apiezon L, 70°, Carbowax, 60°). The spectral properties of the product showed that deuteration had occurred: ir(film), 2200 cm^{-1}(w); nmr(CCl_4), δ 0.60 (m, 4 cyclopropyl protons), and 1.40 (d, 3H, J=5.6Hz, methyl at $C_{(2)}$). Calculation of the relative isotope abundance from the mass spectrum showed that the total deuterium exchange was 92.4% of five replaceable hydrogens

(theoretical, 95%). The distibution of deuterium was calculated to be : Do, 0%; D1, 0.08%; D_2, 0.77%; D_3, 4.95%; D_4, 27.43%; D_5, 66.75%.

Treatment of trans-1-(2-Methylcyclopropyl) propan-2-one with Sodamide in Liquid Ammonia. - trans-1-(2-Methylcyclopropyl) propan-2-one (0.002 moles, 0.224g.) was added to a solution of sodamide (0.001 moles, 0.039g.) in anhydrous ammonia (15ml.),[106] under nitrogen. The reaction mixture was stirred for 8 hours.

Solid ammonium chloride (0.005 moles, 0.27g.) was added and the ammonia allowed to evaporate. The residual salt was dissolved in water (1.0ml.) and extracted with ether (2x10ml.). The ethereal extract was washed with dilute, aqueous hydrochloric acid (5ml.), and saturated, aqueous sodium bicarbonate solution (2ml.), and dried ($MgSO_4$).

Vpc examination (Apiezon L, 70°, Carbowax, 60°) showed only trans-1-(2-methylcyclopropyl) propan-2-one. The infrared spectrum of the product was identical to that of the starting material.

Preparation of the p-Toluenesulphonylhydrazone[76] of Hexan-2-one-Hexan-2-one (0.50g.) was added to p-toluenesulphonylhydrazide (0.93g.) dissolved in a minimum of hot ethanol containing one drop of concentrated hydrochloric acid. The mixture was warmed for a few minutes and left to cool. On dilution with water (10ml.) an oil was obtained which solidified on scratching. The crude product was recrystallised from aqueous ethanol (50%) and dried over phosphorus pentoxide to give the pure product as white needles (1.28g., 96%; m.p. 73-75°): ir (nujol), 3240 (s) and 1640 cm^{-1} (m); nmr ($CDCl_3$), δ 0.80 (distorted triplet, 3H, Me), 1.00 - 1.50 (m,4H, CH_2CH_2), 1.72 (s,3H, MeC=N), 1.86 (s,1H, NH), 2.16 (t,2H,CH_2, J=7.2Hz), 2.39 (s,3H, p-Me), 7.27 (d, 2 aromatic

protons, J=8.0Hz), and 7.82 (d,2 aromatic protons, J=8.0Hz); mass spectrum, p=268 (low intensity) with base peak at m/e= 113 (Found : C,57.97; H,7.21; N, 10.47. $C_{13}H_{20}NO_2S$ requires C, 58.20; H, 7.46; N, 10.45%).

Preparation of the p-Toluenesulphonylhydrazone of 1-Acetyl-2,2-dimethylcyclopropane. - The product was obtained from 1-acetyl-2,2-dimethylcyclopropane (0.56g.) and p-toluenesulphonylhydrazide (0.93g.), as described for hexan-2-one, as white needles (1.34g., 96%; m.p. 116-118°) : ir (nujol), 3240 (s) and 1635 cm^{-1} (m); nmr ($CDCl_3$), δ 0.50 (m, 1 cyclopropyl proton), 0.56 (s,3H,Me), 1.02 (m,1 cyclopropyl proton), 1.08 (s,3H,Me), 1.20 (s,1H,NH), 1.28 (m, 1 cyclopropyl proton), 1.82 (s,3H,MeC=N), 2.40 (s,3H, p-Me), 7.26 (d, farther split without resolution, 2 aromatic protons, J=8.2Hz), and 7.80 (d, further split without resolution, 2 aromatic protons, J=8.2Hz); mass spectrum, p=280 (low intensity) with base peak at m/e=125.

Attempted Reduction of the p-Toluenesulphonylhydrazone of Hexan-2-one with Lithium Cyanoborohydride. - (a) Lithium cyanoborohydride monodioxanate[77] (0.06g.) was added to the hydrazone (0.10g.) in methanol (1ml.). After leaving at room temperature for 24 hours, the reaction mixture was diluted with water (4ml.) and extracted with ether (3x4ml.). The combined extracts were washed with water (4ml.), and dried ($MgSO_4$), and concentrated. Infrared examination of the crude product showed it to be unchanged starting material. (b) Hexan-2-one (0.05g.) was added to p-toluenesulphonylhydrazide (0.093g.) dissolved in methanol (1.0ml.). Anhydrous hydrochloric acid was added to bring the pH of the solution to 5.5 and then lithium cyanoborohydride monodioxanate (0.07g.) was added.[77] After leaving at room temperature for 24 hours, the reaction mixture was diluted with water

(2.5ml.) and extracted with ether (3x4ml.). The combined extracts were washed with water (2x2.5ml.), dried ($MgSO_4$), and concentrated. Infrared examination of the crude product showed it to be the p-toluenesulphonylhydrazone of hexan-2-one.

Attempted Reduction of the p-Toluenesulphonylhydrazone of Hexan-2-one with Sodium Borohydride. - Sodium borohydride (0.25g.) was added to the hydrazone (0.33g.) in methanol (8ml.) at 0°. After the initial evolution of gas had ceased, the reaction mixture was left under nitrogen for one hour at room temperature. The reaction mixture was diluted with water (10ml.), and extracted with ether (3x10ml.). The combined ether extracts were washed with water (2x5ml.) and concentrated by rotary evaporation. The product obtained was dried over phosphorus pentoxide to give a pale yellow solid (0.23g.). Infrared examination of the product showed it to be unchanged starting material.

The combined aqueous residues were washed with chloroform (3x10ml.). Evaporation of the chloroform extracts gave no residue.

Reduction of the p-Toluenesulphonylhydrazone of Hexan-2-one with Lithium Aluminium Hydride. - The hydrazone (0.10g.) in ether (1.0ml.) was added to a suspension of lithium aluminium hydride (0.043g.) in ether (5ml.), under nitrogen. After stirring for 24 hours, the reaction mixture was filtered and the solid residue was washed with ether (10ml.). The combined ethereal filtrates were treated with a little water and the white solid which separated out was filtered off. The filtrate was concentrated on the rotary evaporator to give a mobile oil. The ir spectrum of the product was less complex than that of the starting material and showed a very broad absorption at 3400 cm^{-1} and no absorption at

1640 cm^{-1}. However, the product obtained did not have the ir spectral characteristics of the expected substituted hydrazide, i.e. an ir spectrum very similar to that of the hydrazone with two sharp absorptions between 3200 and 3400 cm^{-1}.

The reduction was repeated adding a solution of the hydrazone (0.34g.) in ether (2.5ml.) to a suspension of lithium aluminium hydride (0.095g.) in ether (10ml.), under nitrogen. After stirring for 1 hour, the reaction mixture was worked up as before. The ethereal extract was concentrated on a rotary evaporator to give a white solid (0.05g.). The ir spectrum of the product was again less complex than that of the starting material and showed a very broad absorption at 3400 cm^{-1}.

The residues from the filtrations were treated with water and extracted with methanol (10ml.), followed by ether (10ml.). The combined extracts were concentrated by rotary evaporation, to give, after drying, a white solid (0.18g.). The ir spectrum of this product was also less complex than that of the starting material and showed a very broad absorption at 3400 cm^{-1}. None of the products obtained in either reduction had identical ir spectra.

The ether which was removed from the reaction product by rotary evaporation was shown by vpc examination (Apiezon L, 45°; Carbowax, 50°) to contain a small amount of a product which was not present in the solvent ether and which had the same vpc characteristics as commercial n-hexane.

Attempted Catalytic Reduction of the p-Toluenesulphonyl-hydrazone of Hexan-2-one. A. With Palladium on Charcoal.-

B. With Raney Nickel. -

C. With Platinum on Charcoal. -

D. With Adam's Platinum Catalyst in Ethanol. -

E. With Adam's Platinum Catalyst in Acetic Acid. -

F. With Adam's Platinum Catalyst in Ethanol Saturated with Anhydrous Hydrogen Chloride. -

G. With Adam's Platinum Catalyst in Acetic Anhydride. -

All the attempted reductions were unsuccessful.

Preparation of N-1-(trans-2-Methylcyclopropyl) ethyl-p-toluenesulphonamide. - Aqueous sodium hydroxide solution (40ml; 10%) and trans-1-acetyl-2-methylcyclopropane (4.0g.) were added to hydroxylamine hydrochloride (10g.) dissolved in water (40ml.).[107] The mixture was heated under reflux for 15 minutes, then cooled, acidified with dilute hydrochloric acid, and extracted with ether (3x100ml.). The ethereal solution was dried ($MgSO_4$) and concentrated to a volume of approximately 100ml.

The ethereal solution of the oxime was added to a suspension of lithium aluminium hydride (7.00g.) in ether, under nitrogen.[81] The reaction mixture was stirred for 1 hour, and was then treated cautiously with water. The dense white solid which separated out was filtered off and washed several times with ether. The combined ethereal filtrates were concentrated on the rotary evaporator to give a pale yellow oil (1.90g.).

The product was treated during 12 hours with p-toluenesulphonyl chloride (4.5g.) in redistilled pyridine (40ml.).[80] The reaction mixture was poured into water (25ml.) and the product was extracted with ether (50ml.). Removal of the ether by distillation gave N-1-(trans-2-methylcyclopropyl) ethyl-p-toluenesulphonamide as a thick yellow oil (2.5g.) : ir (nujol), 3300 (s), and 1600 cm^{-1} (s); nmr (CCl_4), δ 1.00 (m, 4 cyclopropyl protons), 1.20 (d,3H, J=6.5 Hz, cyclopropyl methyl), 1.54 (d,3H, J=5.5Hz, methyl), 1.60-1.85 (m,1H,CH), 2.40 (s,3H, aromatic methyl), 7.24 (d, 2 aromatic protons, J=8.0Hz), and 7.68 (d, 2 aromatic protons, J=8.0Hz).

The spectral data of the product were very similar to those of N-cyclohexyl-p-toluenesulphonamide, prepared from cyclohexylamine using the method above : ir (nujol), 3300 (s), and 1600 cm^{-1} (s); nmr (CCl_4), δ 2.40 (s,3H, aromatic methyl), 7.20 (d, 2 aromatic protons, J=8.0Hz), and 7.74 (d, 2 aromatic protons, J=8.0Hz).

Thin layer chromatography (silica, or alumina, in chloroform) separated the cyclopropyl derivative into two components, one of which (10%) was immobile. The other component was shown to have an Rf value almost identical to that of N-cyclohexyl-p-toluenesulphonamide.

Treatment of N-1-(trans-2-Methylcyclopropyl) ethyl-p-toluenesulphonamide with Hydroxylamine-O-sulphonic Acid. - 78,79
The p-toluenesulphonamide (1.0g.) was dissolved in a hot solution of sodium hydroxide (11.0g.) in water (80ml.) and ethanol (20ml.), contained in a R.B. flask set up for distillation. A gas trap, cooled in liquid nitrogen, was connected to the exit of the condenser. Solid hydroxylamine-O-sulphonic acid (20 equivalents, 8.9g.) was added in 0.5g. portions during 20 minutes, and the resulting mixture was then distilled slowly for 1 hour. No product was observed on vpc examination (Apiezon L; Carbowax) of the carbon tetrachloride extract of the aqueous distillate. The contents of the gas trap were extracted with carbon tetrachloride. Again no product was observed on vpc (Apiezon L; Carbowax) and infrared examination of the extract.

The reaction was repeated using the same quantities of reactants. The reaction mixture was refluxed for 2 hours before distillation. Again, no volatile product was detected.

Titration of Lithium in Liquid Ammonia. A. With 5-Methylhexan-2-one. - Lithium (0.034g., 5.03 m.moles)

was dissolved in anhydrous liquid ammonia (10ml.) in a 3-necked, R.B. flask fitted with a Dry-Ice condenser and protected from atmospheric moisture by a calcium oxide drying-tube. 5-Methylhexan-2-one was added slowly by injection until the blue colour of the stirred solution was just discharged. The weight of ketone required was 0.560g. (4.91 m.mole).

In three further reductions, 2.74 m.moles (0.019g.), 5.03 m.moles (0.034g.), and 24.5 m.moles (0.170g.) of lithium in liquid ammonia (10ml.), required 2.84 m.moles (0.324g.), 4.91 m.moles (0.560g.), and 26.0 m.moles (2.96g). of 5-methylhexan-2-one respectively to discharge the blue colour of the liquid ammonia solution.

In several titrations of lithium in anhydrous liquid ammonia, the reaction mixture was allowed to stand for periods ranging from 1 minute to 1 hour after titration before solid ammonium chloride was added. In all the titrations, the mole ratio of lithium to 5-methylhexan-2-one was almost unity, but the ratio of 5-methylhexan-2-one to 5-methylhexan-2-ol varied randomly from 1:1 to 1:2.

B. With 1-Acetyl-2,2-dimethylcyclopropane. - Using the procedure described in A, 1.73 m.moles (0.0125g.) of lithium in liquid ammonia (10ml.) required 1.68 m.moles (0.188g.) of the ketone.

C. With trans-1-Acetyl-2-methylcyclopropane. - 2.14 M.moles (0.0148g.) of lithium required 2.14 m.moles (0.210g.) of the ketone. After the blue colour had been discharged, an excess of solid ammonium chloride was added, and the reduction product was isolated and oxidised with 6N chromic acid in the usual manner. The ratio of total rearranged product to unchanged starting material was 0.44: 1.

D. With Acetylcyclopropane. - In two reductions, 9.95 m.moles (0.069g.), and 5.48 m.moles (0.038g.) of lithium required 9.83 m.moles (0.825g.), and 5.40 m.moles (0.454g.) respectively of the ketone.

In two further reductions in which the product was examined by vpc (Apiezon L and Carbowax), 5.10 m.moles (0.0354g.), and 5.40 m.moles (0.375g.) of lithium required 5.24 m.moles (0.440g.), and 5.35 m.moles (0.450g.) respectively of acetylcyclopropane, and the corresponding ratios of rearranged product to unchanged acetylcyclopropane were 0.97: 1, and 0.90:1 respectively.

In another experiment, an excess of lithium was back-titrated with 5-methylhexan-2-one. Acetylcyclopropane (0.160g., 1.91 m.moles) was added to lithium (0.0345g., 4.97 m.moles) in anhydrous liquid ammonia (10ml.) and the resulting solution was stirred for 2 hours before the excess of lithium was back-titrated with 5-methylhexan-2-one (0.330g., 2.90 m.moles). The ratio of rearranged product to unrearranged product was 4.0:1.

In two further reductions, an excess of lithium was back-titrated with 2,2,6,6-tetramethylcyclohexanone (see E). Acetylcyclopropane (9.78 m.moles, 0.8206g., and 10.0 m.moles, 0.8717g.) was added to lithium (11.15 m.moles, 0.0774g., and 12.88 m.moles, 0.0892g. respectively) in anhydrous liquid ammonia (10ml.). The resulting solutions were stirred for 2 hours before the excess of lithium was back-titrated with 0.85 m.moles (0.013g.), and 1.80 m.moles (0.278g.) respectively of 2,2,6,6-tetramethylcyclohexanone. The ratios of rearranged product to recovered acetylcyclopropane were 1.04:1, and 1.18:1 respectively.

E. With Non-Enolisable Ketones. - 2,2,4,4- Tetramethylpentan-3-one was prepared by the method of Bartlett and Schneider,[108] from sodium, t-butyl chloride, and methyl

pivalate. Preparative vpc (Carbowax, 100°) gave pure 2,2,4,4-tetramethylpentan-3-one : ir (film), 1684 cm^{-1} (vs); nmr (CCl_4), δ 1.21 (s). In two titrations, 1.80 m.moles and 2.15 m.moles of lithium required 0.61 m.moles and 0.74 m.moles respectively of 2,2,4,4-tetramethylpentan-3-one.

2,2,6,6-Tetramethylcyclohexanone was prepared by refluxing a suspension of sodium hydride in a solution of methyl iodide and 2,2-dimethylcyclohexanone in dioxan. Preparative vpc (Carbowax, 120°) gave pure 2,2,6,6-tetramethylcyclohexanone : ir (film), 1695 cm^{-1} (vs); nmr (CCl_4), δ 1.06 (s, 12 protons from 4 methyl groups), and 1.69 (m, 6 cyclohexyl protons). Titration of a solution of lithium (0.578 m.moles, 0.0040g.) in liquid ammonia (10ml.) required 0.570 m.moles (0.0878g.) of 2,2,6,6- tetramethylcyclohexanone.

Deuteration of 1-Acetyl-2,2-dimethylcyclopropane. - 1-Acetyl-2,2-dimethylcyclopropane (1.12g., 0.01 moles) was stirred for 12 hours, in a stoppered flask, with 5.14 ml. of a solution containing 0.0644g. of sodium hydroxide-d, in 100 ml. of water-d_2. The reaction mixture was extracted with anhydrous ether (3x5ml.), and the product was obtained by distilling ether from the dried, combined extracts.

Repetition of the above procedure gave material which was purified by preparative vpc (100°; Carbowax column, which had been treated with hexamethyldisilazane immediately prior to use) to give product (0.95g.) which had the following spectral properties; ir (film), 2260 cm^{-1} (w); nmr (CCl_4), δ 0.71 (d of d,1H, J=4.0 and 8.0 Hz, $H_{(3)}$ trans to acetyl),1.11 (m,1H, $H_{(3)}$ cis to acetyl), 1.05 (s,3H, methyl cis to acetyl), 1.17 (s,3H, methyl trans to acetyl), and 1.78 (d of d, 1H, J=5.5 and 8.0Hz, $H_{(1)}$). The mass spectrum showed that the deuterium exchange was 99.0% of three replaceable hydrogens. The distribution of

of deuterium was calculated to be d_2, 2.90%; and d_3, 97.10%.

Deuteration of Acetylcyclopropane. - Acetylcyclopropane (0.98g., 0.01 moles) was deuterated using the same procedure as above. The mass spectrum showed that the total deuterium exchange was 98.8% of three replaceable hydrogens. The distribution of deuterium was calculated to be d_2, 3.5%; and d_3, 96.5%.

Treatment of Deuterated 1-Acetyl-2,2-dimethylcyclopropane with Liquid Ammonia. - Deuterated 1-Acetyl-2,2-dimethylcyclopropane (0.10g.) was stirred for 2 hours in anhydrous liquid ammonia (10ml.). Solid ammonium chloride (1g.) was added, followed by anhydrous ether (10ml.). After the ammonia had evaporated, the filtered solution was concentrated and then purified by preparative vpc (100°; Carbowax column, which had been treated with hexamethyldisilazane immediately prior to use) to give vpc pure product (0.08g.). The mass spectrum of this product showed the deuterium distribution to be d_2, 2.9%; and d_3, 97.1%.

Reduction of Deuterated Acetylcyclopropane with Lithium in Liquid Ammonia. - Deuterated acetylcyclopropane (0.50g.) was added to a solution of lithium (0.20g.) in liquid ammonia (50ml.) in the usual manner. The solution was stirred for 2 hours and an excess of solid ammonium chloride was added quickly, followed by 'sodium-dried' ether (20ml.). After the ammonia had evaporated, the ether was separated and the residues were washed with anhydrous ether (10ml.). The combined ether extracts were concentrated to a volume of approximately 2 ml. The reduction product was shown by vpc (Carbowax, 50°) to be a mixture containing acetylcyclopropane (28%) and pentan-2-one

(70%) with 2% of the corresponding alcohols. Purification of the product by preparative vpc (100°; Carbowax column, which had been treated with hexamethyldisilazane immediately prior to use) gave vpc pure acetylcyclopropane and pentan-2-one.

The mass spectrum of the recovered acetylcyclopropane showed that the distribution of deuterium was d_0, 0.4%; d_1, 7.7%; and d_2, 91.9%. The distribution of deuterium in the pentan-2-one was d_1; 0.4%; d_2, 6.8%; and d_3, 92.8%.

Polarography in Liquid Ammonia. - The electrolysis cell which was used in this investigation is shown in Figure 4, p. 109 The cell was graduated so that the volume it contained could be measured directly. A platinum wire was sealed through the bottom of the cell so that the mercury pool could be used as the non-polarisable electrode. The dropping mercury electrode was positioned so that when the cell contained 15 ml. of mercury and 50 ml. of liquid ammonia solution the whole of the capillary was immersed.

Anhydrous, oxygen-free ammonia was prepared using the drying system of Laitinen and Nyman,[87] shown in Figure 5, p. 109 but because of the volatility of the ketones being studied, the actual drying procedure differed from that of Laitinen and Nyman. Tubes B and B^1 each contained a small piece of sodium metal (1g.) in order to remove oxygen and water from the ammonia. With tap E closed, the system was evacuated through tap C, and, after cooling tube B in a Dry-Ice/ethanol bath, gaseous ammonia was allowed to enter the system through tap D. When approximately 80 ml. had been collected, the ammonia was distilled from tube B to B^1. The cell was then flushed with anhydrous, oxygen-free nitrogen, the ketone to be electrolysed and the indifferent electrolyte (0.106g.) were added and the cell was again flushed with nitrogen. After that part of the drying system

Figure 4.- Electrolysis cell for polarography in liquid ammonia.

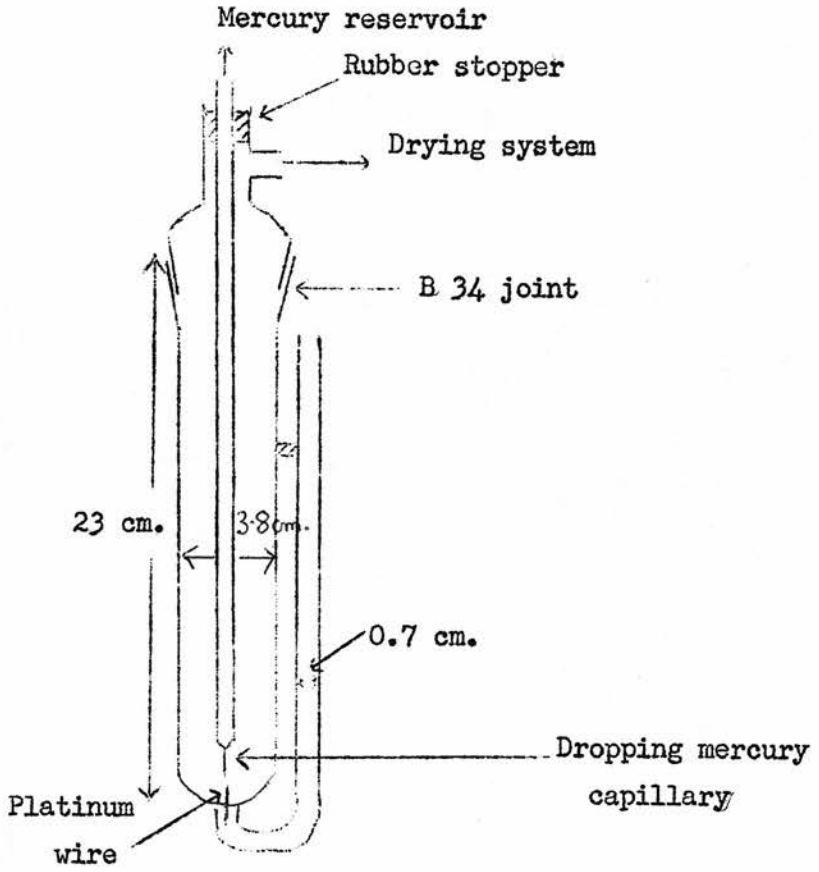
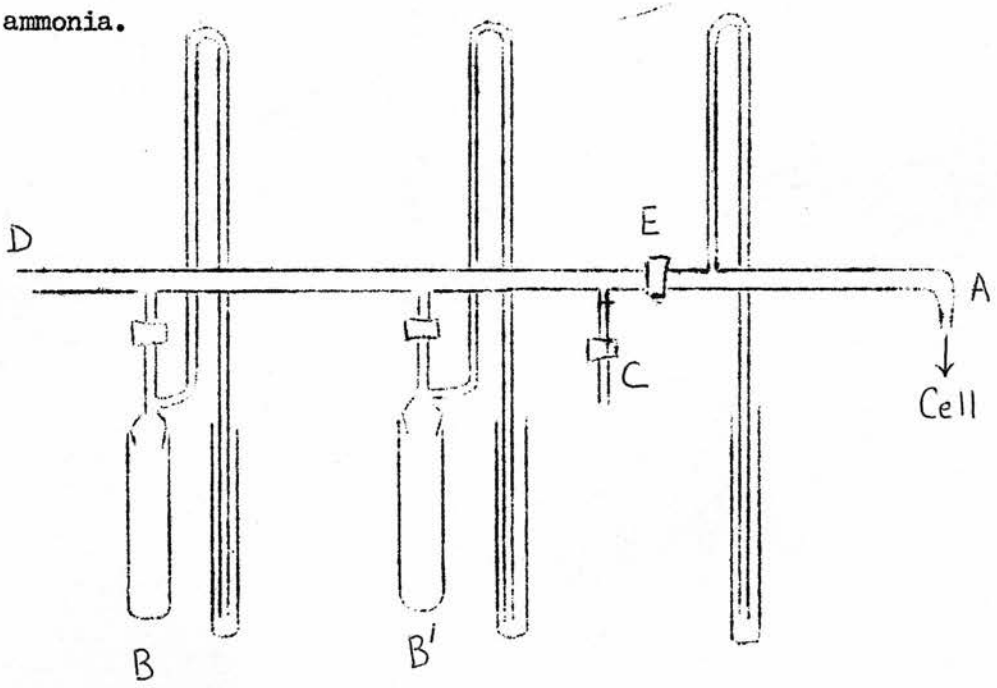


Figure 5.- Drying system for the preparation of anhydrous, oxygen-free liquid ammonia.



between A and E had been flushed with nitrogen, the cell was connected at A as shown, cooled in a Dry-Ice/ethanol bath, and then evacuated through tap C. Ammonia was distilled into the graduated cell until the desired volume (50ml. at -35.5°) had been collected. Tap E was then closed and the cell was allowed to stand for 1 hour in a slush bath of 1,2-dichloro-ethane (m.p., -35.5°) to ensure that the indifferent electrolyte had reached solubility equilibrium.

The indifferent electrolyte, tetrabutylammonium iodide, was obtained from B.D.H. and was dried at 110°, in vacuo, prior to use. Because of the low solubility of tetrabutylammonium iodide in liquid ammonia (0.106g./50 ml., at -36°, 0.0057M ± 5%)[87], all polarograms were measured using a saturated solution of the salt.

The current flowing at a given potential of the dropping mercury electrode was measured using a simple spot-galvanometer. This instrument was calibrated by inserting a known resistance in place of the electrolysis cell and applying a known potential. The potential of the dropping mercury electrode relative to the mercury pool was set with a manual polarograph. Polarograms were run successively until the observed half-wave potential was constant (generally three runs were sufficient) before a final polarogram was recorded.

Controlled Potential Electrolysis in Liquid Ammonia. - The cell shown in Figure 6, p.114 was used for all the experiments in this investigation. A platinum wire was sealed through the bottom of both parts of the cell to provide electrical contact with the cell. A sintered glass disc prevented mixing of the solutions in the two compartments and a stop-cock at the top of the cell allowed equilibration of pressure between both parts. The cathode compartment

was fitted with a sealed-in dropping mercury electrode (reference electrode) and a stirrer to keep the surface of the mercury pool cathode clean.

The cell was set up as shown in the diagram, with the side-arm of each compartment filled with mercury to provide an electrical contact with the platinum wire at the base of each compartment. Mercury (15ml.) was placed in the anode compartment, and sufficient mercury was put into the cathode compartment to leave a gap of about 0.5 cm. between the surface of the resulting mercury pool and the tip of the fixed, dropping mercury electrode. Any mercury remaining on the sides of the cell was removed.

The supporting electrolyte, anhydrous calcium nitrate (49.2g.), prepared from the AnalaR tetrahydrate by drying at 170°,[109] in vacuo, was put in a pressure-equalising dropping-funnel fitted with a Dry-Ice condenser and protected from atmospheric moisture by a calcium oxide drying-tube. Anhydrous ammonia, prepared as on p.108 was passed into the graduated funnel until 150 ml. of solution had been prepared. The dropping funnel and Dry-Ice condenser were then connected to the electrolysis cell so that the prepared ammonia solution could be run directly into the anode compartment.

After a weighed quantity of the ketone to be electrolysed had been introduced into the cathode compartment, the cell was flushed with anhydrous nitrogen and then surrounded by a slush bath of 1,2-dichloro-ethane (m.p., -35.5°). After several minutes, the prepared solution of anhydrous calcium nitrate in liquid ammonia was added to the anode compartment. The cathode compartment filled through the sintered glass disc. The cell was then left for 15 minutes to reach temperature equilibrium with the slush bath. The pressure-equalising funnel and Dry-Ice condenser were removed and replaced by a mercury safety-valve.

Stirring was commenced and current was passed using the circuit shown in Figure 7, p. 114 the potential of the cathode relative to the dropping mercury reference electrode being maintained constant using the decade resistance box.

To isolate the product after electrolysis, benzene (25ml.) was added to the anode and cathode compartments of the cell and the ammonia was evaporated. The combined residues were dissolved in water and extracted with benzene (25ml.). The product could then be examined by analytical vpc or isolated by concentration of the benzene extract.

The results of three experiments with acetylcyclopropane are shown below.

a) Acetylcyclopropane (0.210g.) was electrolysed for 20 hours, as described above, the voltage of the mercury pool cathode being kept at approximately -1.74 volts relative to the reference electrode. The initial current passing through the cell was 37 mA, while the final current was 12 mA.

Vpc examination (Carbowax, and Apiezon L) of the benzene extract showed only acetylcyclopropane and pentan-2-one (5%). Evaporation of the extract gave no residue.

b) Acetylcyclopropane (0.300g.), with decane (0.200g.) as an internal vpc standard, was electrolysed for 32 hours. The voltage of the cathode was maintained at -1.80 volts, and the initial and final current through the cell was 30 mA and 24 mA respectively.

Vpc examination (Carbowax, and Apiezon L) of the benzene extract showed that 20% of the starting acetylcyclopropane was recovered unchanged along with some product pentan-2-one. The ratio of recovered acetylcyclopropane to pentan-2-one was 5:1.

Evaporation of the extract gave a brown residue which showed no hydroxyl absorption in the infrared. The nmr spectrum showed a large absorption at δ 7.26 with smaller,

broad absorptions at δ 0.08, 1.20, and 1.60. Thin-layer chromatography of this residue showed no mobile fractions.

c) Acetylcyclopropane (0.100g.), with decane (0.100g.) as an internal vpc standard, was electrolysed for 24 hours. The voltage of the cathode was maintained at -1.69 volts, and the initial and final current through the cell was 18 and 5 mA respectively.

Vpc examination of the benzene extract showed that 45% of the starting acetylcyclopropane was recovered unchanged along with product pentan-2-one. The ratio of recovered acetylcyclopropane to pentan-2-one was 3:2.

Evaporation of the extract gave no residue.

Figure 6.- Cell used for controlled potential electrolysis in liquid ammonia.

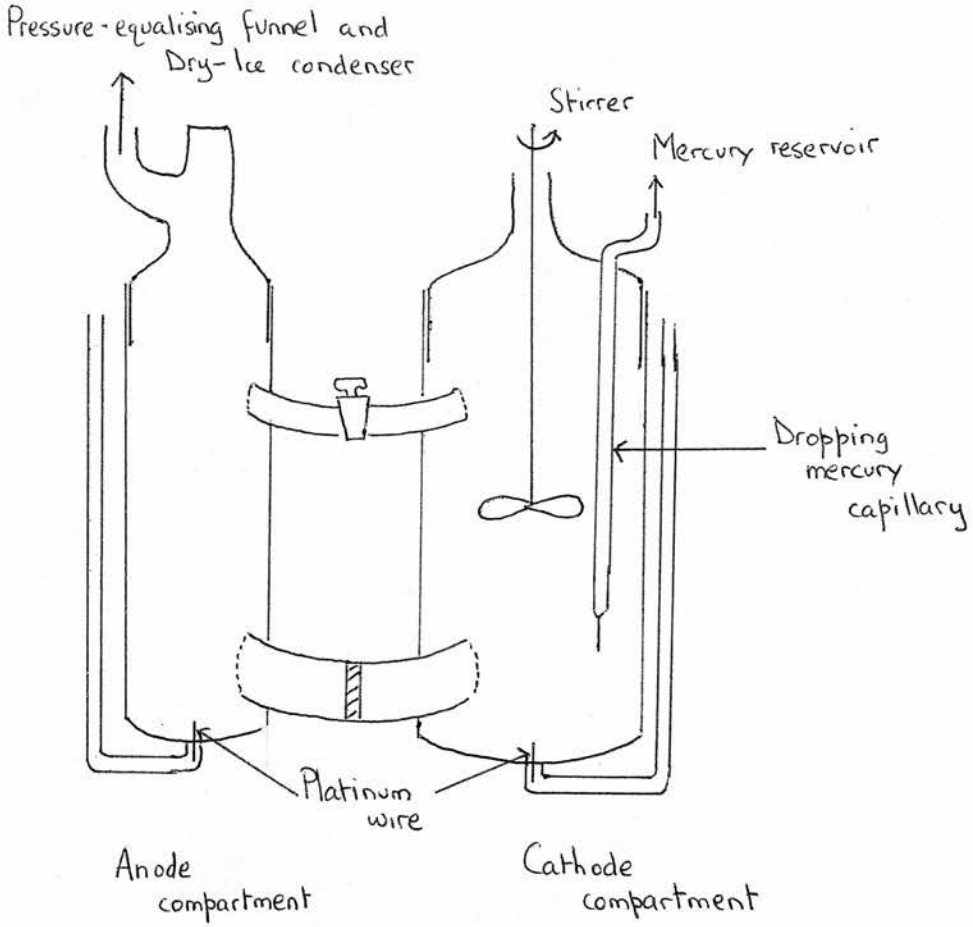
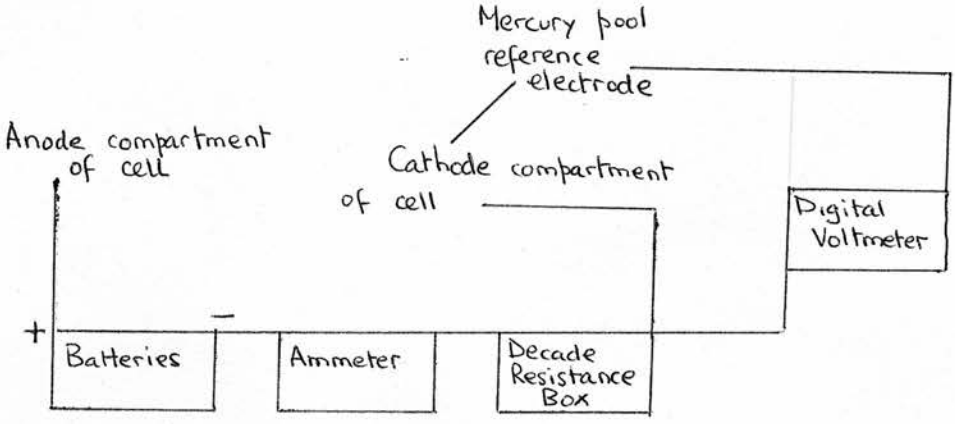


Figure 7.- Electrical circuit used for controlled potential experiments in liquid ammonia.



APPENDIX.

Table 1

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Lithium in Liquid Ammonia -(Method A).

Wt. of Li(g)	Wt. of (26)	Vol of Liq. NH_3 (ml.)	%(26)	%(55)	%(54)	Decane Integral		(54)/(55)	(55)/(54)
						Before Reduction	After Reduction		
0.11 (0.0158 moles)	0.25 (0.00223 moles)	25	14.6	26.4	59.0			2.24	0.447
0.11	0.25	25	12.2	27.8	60.0			2.16	0.463
0.11	0.25	25	21.0	25.8	53.2	2.478:1	1.820:1	2.05	0.488
0.22 (0.0317 moles)	0.25	25	3.3	30.1	66.6			2.22	0.451
0.66 (0.0952 moles)	0.50 (0.00446 moles)	50	4.2	30.6	65.2	2.280:1	2.150:1	2.14	0.467

Table 2

Reduction of 1-Acetyl-2,2-dimethycyclopropane with Lithium in Liquid Ammonia - (Method B).

Wt. Li(g.)	Molarity of Li	%(26)	%(55)	%(54)	Decane Integral		(54)/(55)	(55)/(54)
					Before Reduction	After Reduction		
0.045	0.130	1.9	31.1	67.0	2.924:1	2.865:1	2.17	0.461
0.060	0.173	40.4	18.9	40.7	3.232:1	2.890:1	2.20	0.455
0.096	0.277	11.3	27.1	61.6	2.375:1	2.042:1	2.28	0.438
0.132	0.381	12.2	26.0	61.8	3.500:1	3.403:1	2.41	0.415
0.133	0.383	13.0	25.8	61.2	-	-	2.37	0.422
0.222	0.639	13.6	23.5	62.9	3.320:1	3.150:1	2.67	0.375
0.300	0.864	13.7	22.4	63.9	-	-	2.87	0.348
0.482	1.388	8.1	20.6	71.3	3.090:1	2.523:1	3.46	0.289
0.500	1.442	43.2	13.0	43.8	-	-	3.39	0.295
0.582	1.677	28.2	16.1	55.7	-	-	3.48	0.288
0.705	2.012	16.4	16.6	67.0	3.115:1	3.000:1	4.02	0.249
0.715	2.061	17.6	17.7	64.7	-	-	3.65	0.274
0.880	2.537	28.0	13.1	58.9	2.775:1	2.430:1	4.49	0.223
0.880	2.537	22.2	16.4	61.4	-	-	3.75	0.267

Table 3

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Lithium in Liquid Ammonia (500ml.)-(Method B).

Wt. Li(g.)	Molarity of Li	% (26)	% (55)	% (54)	Decane Integral		(54)/(55)	(55)/(54)
					Before Reduction	After Reduction		
0.05	0.0144	39.7	27.6	32.7	3.03:1	2.93:1	1.200	0.834
0.05	0.0144	37.2	27.7	35.1	3.13:1	3.01:1	1.260	0.794

Table 4

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Barium in Liquid Ammonia - (Method B).

Wt. of Ba(g.)	Molarity of Ba	% (26)	% (55)	% (54)	Decane Integral		(54)/(55)	(55)/(54)
					Before Reduction	After Reduction		
1.40	0.102	57.1	16.2	26.7	3.29:1	3.18:1	1.633	0.612
1.55	0.113	32.2	24.2	43.6	2.50:1	2.28:1	1.800	0.555
2.02	0.147	33.8	23.8	42.4	3.38:1	3.19:1	1.794	0.557
2.50	0.182	21.8	27.4	50.8	3.05:1	2.89:1	1.856	0.539
2.50	0.182	33.2	23.7	43.1	3.61:1	3.30:1	1.830	0.546
3.00	0.219	27.8	25.9	46.3	3.20:1	2.89:1	1.770	0.565

Table 5

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Sodium in Liquid Ammonia-(Method B).

Wt. of Na(g)	Molarity of Na	%(26)	%(55)	%(54)	Decane Integral		(54)/(55)	(55)/(54)
					Before Reduction	After Reduction		
0.25	0.217	33.4	18.9	47.7	1.81:1	2.46:1	2.52	0.397
0.35	0.303	7.1	20.6	72.3	3.44:1	3.92:1	3.50	0.286
0.40	0.346	12.1	25.4	62.5	3.61:1	2.98:1	2.46	0.416
0.50	0.433	11.0	25.2	63.8	2.20:1	2.26:1	2.54	0.394
0.67	0.580	7.8	28.7	63.5	-	-	2.22	0.449
0.68	0.589	9.3	23.7	67.0	3.38:1	2.51:1	2.83	0.354
0.80	0.693	6.9	26.7	66.4	-	-	2.48	0.403
1.00	0.866	14.5	23.0	62.5	2.10:1	1.86:1	2.72	0.368
1.05	0.909	5.1	25.5	69.4	1.73:1	1.69:1	2.72	0.368
1.10	0.952	5.7	24.8	69.5	-	-	2.80	0.358
1.45	1.256	7.4	23.6	69.0	2.26:1	1.78:1	2.93	0.342
1.72	1.490	17.2	39.7	43.1	4.62:1	3.66:1	2.52	0.397

Table 6

Reduction of 1-Acetyl-2,2-dimethylcyclopropane in the Presence of Tetraethylammonium Cations.

Metal	Wt. of Metal (g.)	Wt. of Et4NCl (g.)	%(26)	%(55)	%(54)	Decane Integral		(54)/(55)	(54)/(55) Value for Reduction Without Et4NCl
						Before Reduction	After Reduction		
Ba	1.45	3.60	46.8	21.2	32.0	2.36:1	2.19:1	1.49	1.63
Ba	2.00	4.90	31.9	29.4	38.7	2.81:1	2.54:1	1.32	1.79
Ba	2.50	6.10	90.4	4.2	5.4	3.15:1	3.08:1	1.27	1.84
Li	0.40	10.00	39.4	23.3	37.3	—	—	1.60	3.16
Li	0.40	10.00	76.5	7.8	15.6	—	—	2.00	3.16
Li	0.18	4.50	40.7	24.0	35.3	3.05:1	2.71:1	1.47	2.54
Na	1.00	7.40	33.4	17.3	49.3	2.86:1	2.37:1	2.84	2.72

Table 7

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Lithium/Lithium Iodide Mixtures in Liquid Ammonia.

Wt. of Lithium Metal (g.)	Wt. of LiI (g.)	Molarity Li+(total)	%(26)	%(55)	%(54)	Decane Integral		(54)/(55)	(55)/(54)	(54)/(55) for Lithium Metal
						Before Reduction	After Reduction			
0.20	2.12	0.893	23.1	20.2	56.7			2.80	0.357	2.58
0.20	3.30	1.075	38.4	15.5	46.1	3.29:1	3.14:1	2.97	0.337	2.58
0.20	6.65	1.567	36.5	14.7	48.8			3.31	0.320	2.58
0.20	6.70	1.576	17.8	18.2	64.0	3.04:1	2.89:1	3.51	0.285	2.58
0.20	7.72	1.729	40.1	13.1	46.8	3.64:1	3.36:1	3.58	0.279	2.58
0.20	9.94	2.061	37.7	13.8	48.5			3.50	0.286	2.58
0.20	12.55	2.450	36.8	13.9	49.3			3.54	0.282	2.58
0.20	13.39	2.576	10.1	21.9	68.0	2.81:1	2.69:1	3.10	0.322	2.58
0.20	13.39	2.576	15.5	18.9	65.6			3.48	0.288	2.58
0.20	13.39	2.576	12.6	17.9	69.5	2.91:1	2.57:1	3.89	0.257	2.58
0.20	13.39	2.576	4.6	19.3	76.1	1.81:1	1.70:1	4.16	0.240	2.58

Table 8

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Lithium / Lithium Iodide Mixtures in Liquid Ammonia.

Wt. of Lithium Metal (g.)	Wt. of LiI (g.)	Molarity Li^+ (total)	%(26)	%(55)	%(54)	Decane Integral		(54)/(55)	(55)/(54)	(54)/(55) for Lithium Metal
						Before Reduction	After Reduction			
0.050	1.93	0.433	49.7	16.4	33.9			2.07	0.483	2.17
0.050	3.86	0.720	66.6	10.3	23.1	2.56:1	2.47:1	2.23	0.449	2.17
0.100	6.70	1.288	36.1	15.2	48.7	3.32:1	3.23:1	3.21	0.312	2.30
0.240	4.00	1.292	5.6	22.2	72.2	1.88:1	2.21:1	3.25	0.308	2.70
0.150	7.90	1.609	5.5	23.3	71.2	2.44:1	2.19:1	3.07	0.326	2.44
0.348	0.66	1.101	3.8	23.1	73.1	2.10:1	2.02:1	3.18	0.314	3.00

Table 9

Reduction of trans-1-Acetyl-2-methylcyclopropane with Lithium in Liquid Ammonia - (Method B).

Wt. of Li (g.)	Molarity of Li	%(29)	%(56)	%(57)	Decane Integral		(57)/(56)	(56)/(57)
					Before Reduction	After Reduction		
0.113	0.326	27.1	3.1	69.8	1.70:1	1.67:1	22.5	0.0445
0.211	0.618	10.6	3.9	85.5	2.55:1	2.80:1	21.9	0.0457
0.313	0.889	14.4	4.2	81.4	1.84:1	2.02:1	19.3	0.0518
0.315	0.909	10.1	3.7	86.2	2.32:1	2.34:1	23.2	0.0431
0.473	1.372	10.3	4.0	85.7	1.97:1	2.14:1	21.6	0.0463
0.600	1.730	9.7	3.7	86.6	2.06:1	1.87:1	23.2	0.0431

Table 10

Reduction of cis-1-Acetyl-2-methylcyclopropane (0.25g.) with Lithium in Liquid Ammonia - (Method B).

Wt. of Li (g.)	Molarity of Li	%(28)	%(56)	%(57)	Decane Integral		(56)/(57)	(57)/(56)
					Before Reduction	After Reduction		
0.060	0.173	19.3	69.7	11.0	3.08:1	2.83:1	6.32	0.158
0.160	0.461	8.7	81.9	9.4	3.42:1	3.27:1	8.80	0.114
0.230	0.664	15.4	73.6	11.0	3.08:1	2.81:1	6.72	0.149
0.300	0.866	9.9	81.1	8.9	3.42:1	3.24:1	9.02	0.111
0.400	1.153	8.4	81.8	9.8	3.42:1	3.20:1	8.35	0.120
0.600	1.730	11.5	77.0	11.5	3.42:1	2.46:1	6.69	0.150
0.620	1.788	13.5	76.0	10.5	3.08:1	2.49:1	7.24	0.138

Table 11

Reaction of 1-Acetyl-2,2-dimethylcyclopropane with Di-t-butyl Peroxide and Butan-2-ol.

Wt. of DTBP (g.)	% (26)	% (55)	% (54)	(54)/(55)	(55)/(54)
0.113	72.8	0.7	26.5	45	0.022
0.225	62.3	1.0	36.7	36	0.028
0.450	53.9	1.1	45.0	41	0.024

Table 12

Reaction of trans-1-Acetyl-2-methylcyclopropane with Di-t-butyl Peroxide and Butan-2-ol.

Wt. of DTBP (g.)	% (29)	% (56)	% (57)	Decane Integral		(57)/(56)	(56)/(57)
				Before Reaction	After Reaction		
0.113	86.7	11.0	2.3	0.687:1	0.653:1	0.212	4.72
0.225	74.6	20.8	4.7	0.687:1	0.615:1	0.225	4.44
0.450	76.5	19.1	4.3	0.687:1	0.600:1	0.225	4.44

Table 13

Reaction of cis-1-Acetyl-2-methylcyclopropane with Di-t-butyl Peroxide and Butan-2-ol.

Wt. of DTBP (g.)	% (28)	% (56)	% (57)	Decane Integral		(57)/(56)	(56)/(57)
				Before Reaction	After Reaction		
0.113	89.5	9.5	1.0	2.08:1	1.84:1	0.111	8.98
0.225	83.6	14.8	1.6	2.08:1	1.78:1	0.109	9.20
0.450	81.5	16.5	2.0	2.08:1	1.71:1	0.124	8.04

Table 14

Reaction of 1-(2,2-dimethylcyclopropyl) ethanol (0.50g.) with Di-t-butyl Peroxide.

Wt. of DTBP (g.)	% (74)	% (55)	% (54)	Decane Integral		(54)/(55)	(55)/(54)
				Before Reaction	After Reaction		
0.05	90.5	0.4	9.1	0.845:1	0.798:1	20.9	0.0478
0.15	85.6	0.6	13.8	0.845:1	0.759:1	22.9	0.0436
0.50	75.2	1.3	23.5	0.845:1	0.705:1	18.5	0.0540

Table 15

Reaction of trans-1-(2-methylcyclopropyl) ethanol (0.25g.) with Di-t-butyl Peroxide.

Wt. of DTBP (g.)	% (75)	% (56)	% (57)	Decane Integral		(57)/(56)	(56)/(57)
				Before Reaction	After Reaction		
0.025	62.2	29.1	8.7	2.84:1	2.44:1	0.299	3.34
0.075	41.3	45.0	13.7	2.84:1	1.91:1	0.308	3.24
0.250	8.7	65.7	25.6	2.84:1	1.26:1	0.391	2.55

Table 16

Reaction of cis-1-(2-methylcyclopropyl) ethanol (0.125g.) with Di-t-butyl Peroxide.

Wt. of DTBP (g.)	% (76)	% (56)	% (57)	Decane Integral		(57)/(56)	(56)/(57)
				Before Reaction	After Reaction		
0.013	100	-	-	3.84:1	3.75:1	-	-
0.038	87.5	11.1	1.4	3.84:1	3.62:1	0.124	8.05
0.125	84.5	13.9	1.6	3.84:1	3.58:1	0.118	8.50

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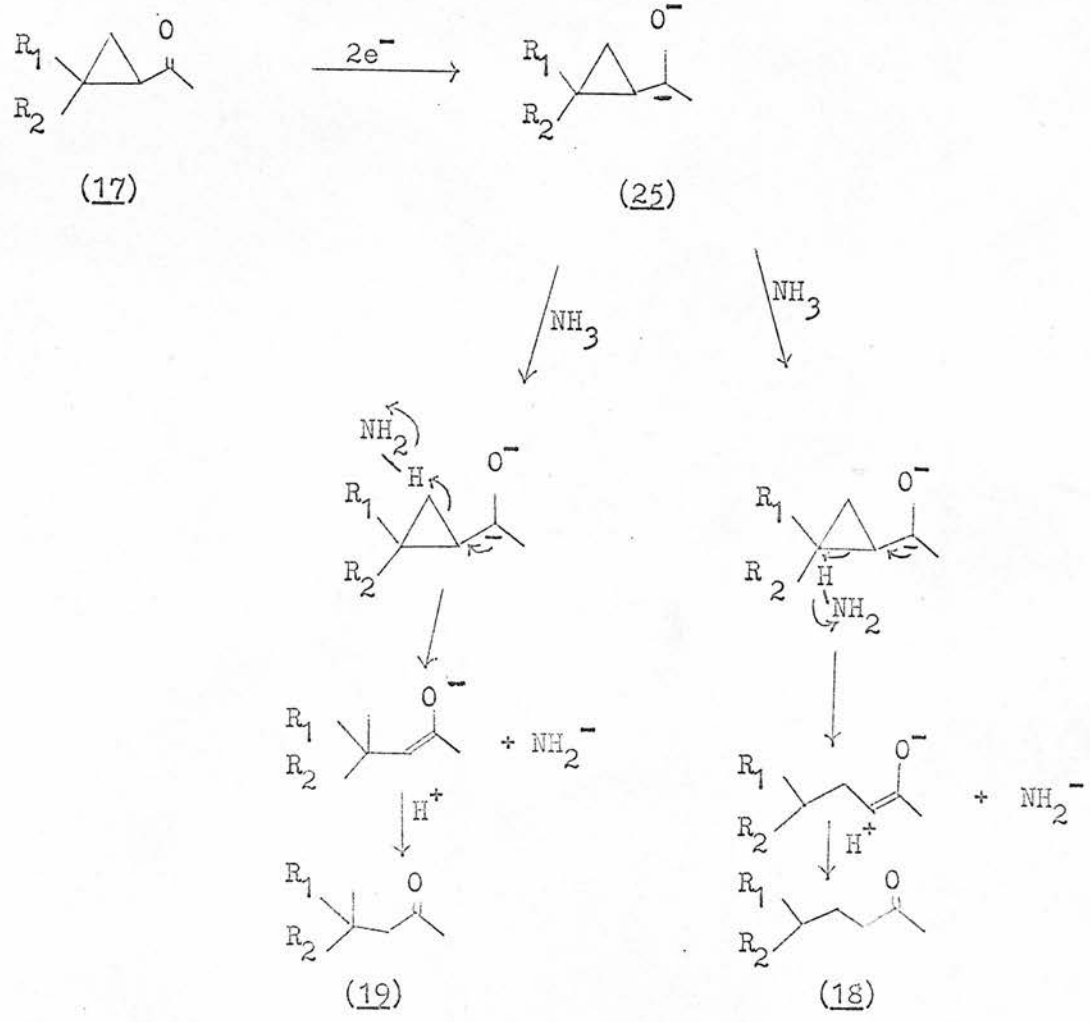
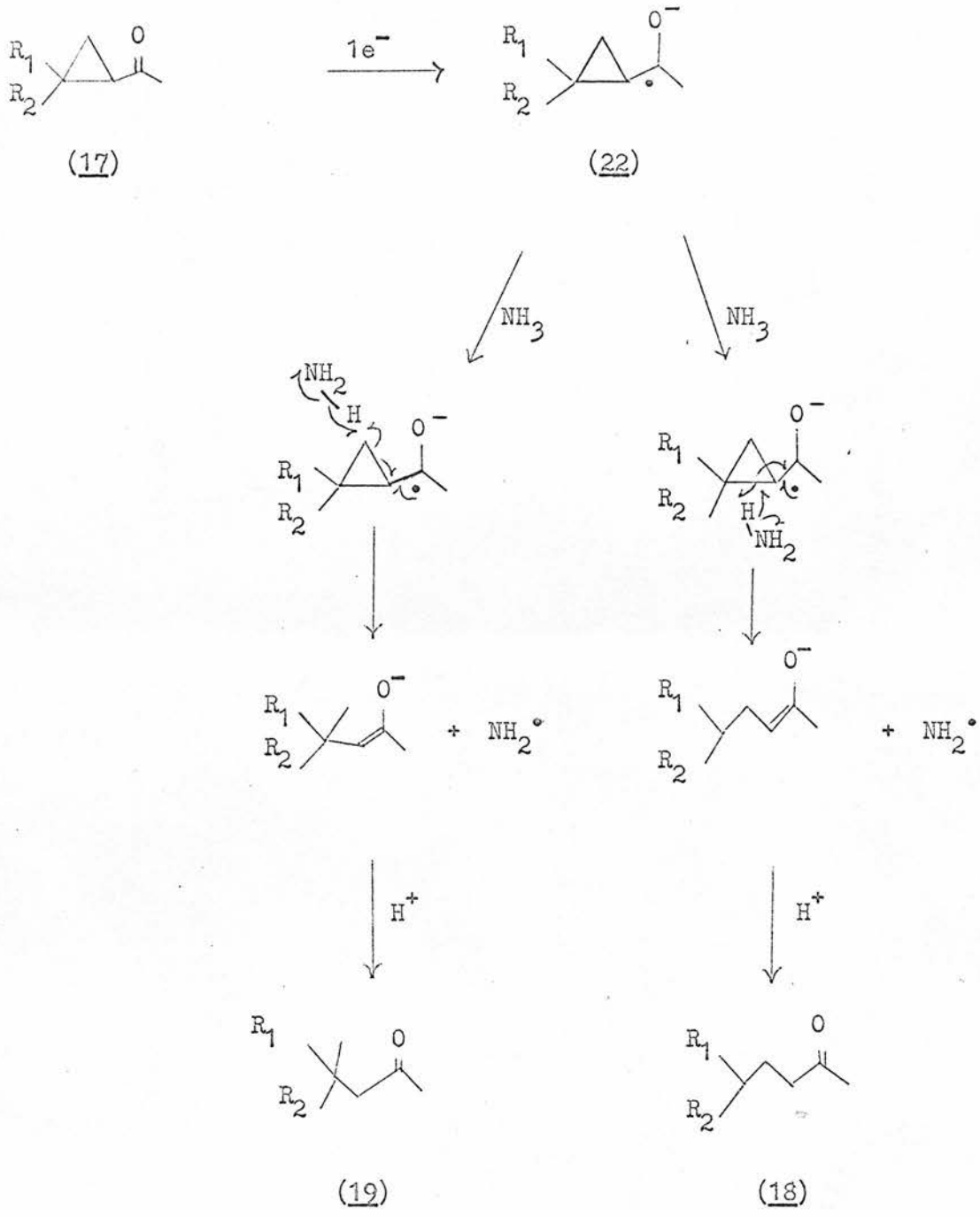
APPENDIX

The reductive cleavage of conjugated cyclopropyl ketones with metals in liquid ammonia is, overall, a two electron reduction. In the present work, it was assumed that rearrangement could, theoretically, occur via (a), a radical-anion species, after the addition of one electron to the carbonyl group, or (b), a dianion species, generated by the addition of two electrons to the carbonyl group (see p.7). It was assumed that rearrangement and protonation in the reduction were separate steps and that the radical-anion intermediates of general type (20) and (21), and the carbanion intermediates of general type (23) and (24), were discrete reaction intermediates. However, it has since been pointed out[111] that rearrangement and addition of hydrogen could occur concomitantly.

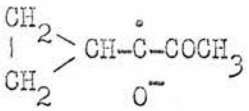
After the addition of two electrons to a conjugated ketone of the general type (17), rearrangement could be viewed as



and, after the addition of one electron to a conjugated ketone of the general type (17), rearrangement could be viewed as

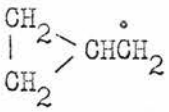


E.S.R. evidence indicates that in the semidione (114), prepared[112] by spontaneous disproportionation of methyl cyclopropyl acyloin in dimethylsulphoxide solution containing potassium t-butoxide,



(114)

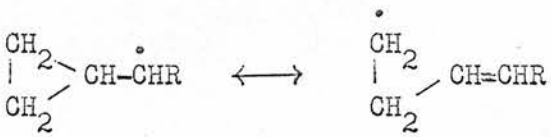
in cyclopropylcarbinyl radicals[113] such as product (115),



(115)

and in free-radicals from alkylcyclopropanes[114], there is some odd-electron density on the β hydrogen atom of the cyclopropane ring.

This can be interpretated as meaning that there is some resonance between the cyclopropyl and open-chain form of these radicals.



Concomitant rearrangement and hydrogen addition in the reduction of ketone (17) would lead to the production of amino radicals, and hence hydrazine. The presence of small amounts of hydrazine in the reaction product from the titration of a solution of lithium in liquid ammonia was demonstrated after this work was completed.

If concomitant rearrangement and hydrogen addition occurred in the reduction of substituted acetylcyclopropanes, the products observed

might not be those expected on grounds of radical or carbanion stability alone because of the possibility of a steric effect between substituents on the cyclopropane ring and the ammonia molecule which is taking part in the reduction.

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