Mechanism of Ring Cleavage of Acetylcyclopropanes by Metal–Ammonia Solutions

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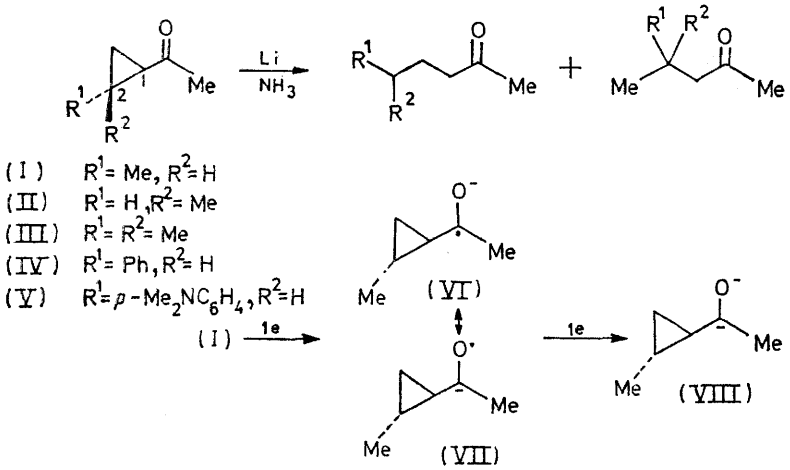
The reduction of acetylcyclopropanes by metal–ammonia solutions involves cleavage of the cyclopropane ring. A mechanism for this process is proposed which accounts for the observations that (i) substituent effects in the cleavage to form the saturated ketone indicate rearrangement of a carbanionic species, (ii) the overall reduction to saturated ketone involves two electrons per molecule, (iii) reductive dimerisation characteristic of a radical species occurs when low concentrations of lithium are employed, and (iv) some starting ketone is always recovered unchanged. The ratio of the two cleavage products formed from 1-acetyl-2,2-dimethylcyclopropane was observed to vary linearly with the lithium concentration. Two possible explanations of this effect are discussed. The preferred direction of cleavage of 2-substituted cyclopropylcarbinyl radicals has been studied. The Nickon–Sinz reaction of *N*-(*trans*-2-methylcyclopropylmethyl)toluene-*p*-sulphonamide gave products which indicate that decomposition of the intermediate alkyldi-imide follows a radical rather than a carbanionic pathway.

During the past ten years a number of groups have published results concerned with the reductive cleavage of cyclopropyl ketones by dissolving metals.[1] While the early work [1a-d] centred mainly on cyclopropyl ketones in which the stereochemical arrangement of the carbonyl group and the α-cyclopropyl bonds was rigidly fixed, the later studies [1d-f] have been focused on conformationally mobile cyclopropyl ketones, *e.g.* acetylcyclopropanes. The results described in the present paper support and extend those in this latter group.



In the conformationally fixed cyclopropyl ketones, the cyclopropyl bond which is preferentially cleaved on treatment with metal–ammonia solutions is the one which is positioned best for overlap with the *p* orbital of the carbonyl carbon,[1a-d] even when electronic factors suggest that the alternative mode of cleavage would produce a more stable intermediate.[1c] By studying the preferred direction of cleavage in appropriately substituted, conformationally 'free' acetylcyclopropanes, it is possible to avoid such stereochemical controlling factors, and to study independently the electronic factors which control the direction of cleavage. Furthermore, it is possible to distinguish between cleavage mechanisms which involve radical and carbanionic species.

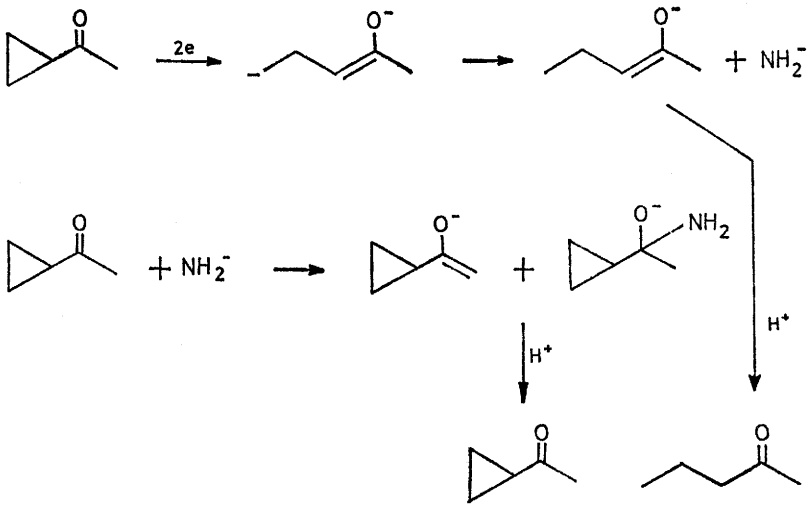
It is generally assumed [1] that the reduction of cyclopropyl ketones occurs by initial addition of one or two electrons to the carbonyl group, followed by cleavage of the cyclopropyl bond in the resulting intermediate species. By studying the preferred direction of cleavage in *trans*-1-acetyl-2-methylcyclopropane (I), it should be apparent whether a radical or a carbanion is involved in the second step, since a radical species, *e.g.* (VI), would be expected to open preferentially towards the 2-methyl group, forming a secondary rather than a primary radical, and a carbanionic species, *e.g.* (VII) or (VIII), would be expected to open preferentially in the other direction, forming a primary rather than a secondary carbanion. Using lithium in ammonia, we observed, in agreement with other workers,[1d,e] that cleavage in (I) occurs predominantly away from the 2-methyl group, indicating that either species (VII) or (VIII), and not (VI), is involved in the cleavage step.

Metal–ammonia reductions are normally performed by dissolving an excess of the metal in ammonia and adding the substrate to the resulting solution. However, it is possible to titrate the metal–ammonia solution with a ketone, using the blue colour of the solution to determine the end-point. The results we have obtained using this technique with lithium–ammonia and

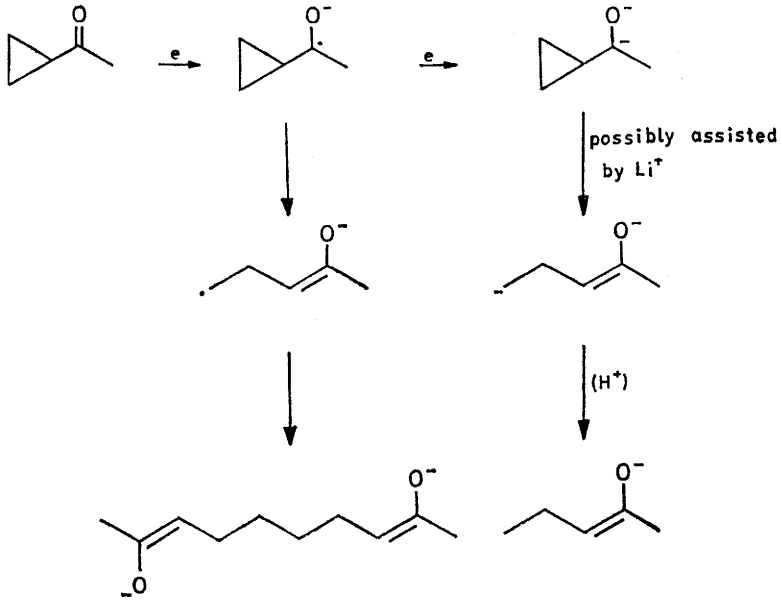
[1] (*a*) T. Norrin, *Acta. Chem. Scand.*, 1965, **19**, 1289; (*b*) W. G. Dauben and E. J. Deviny, *J. Org. Chem.*, 1966, **31**, 3794; (*c*) A. J. Bellamy and G. H. Whitham, *Tetrahedron*, 1968, **24**, 247; (*d*) R. Fraisse-Jullien and C. Frejaville, *Bull. Soc. chim. France*, 1968, 4449; (*e*) W. G. Dauben and R. E. Wolf, *J. Org. Chem.*, 1970, **35**, 374; (*f*) *ibid.*, p. 2361.

a variety of ketones are described in the Experimental section.

Typical acyclic and alicyclic ketones, *viz.* 5-methylhexan-2-one and 2,2,6,6-tetramethylcyclohexanone respectively, gave a 1 : 1 ratio of ketone to lithium at the end-point, indicating the addition of one electron per molecule to form the corresponding radical-anions. A similar result using sodium and acetone in a conductometric titration has recently been reported.[2] For the three acetylcyclopropanes (I)—(III) a 1 : 1 ratio was also observed corresponding to one electron per molecule on average, but subsequent analysis of the volatile products always showed a *ca.* 1 : 1 mixture of the starting ketone and the saturated ketone. Even when acetylcyclopropane was left in the presence of an excess of lithium for 2 h and the excess of lithium was then back-titrated using other unreactive ketones, the ratio of starting ketone to saturated ketone was still *ca.* 1 : 1, with a 1 : 1 ratio for the number of electrons per molecule. We conclude that for each molecule of starting ketone which is converted into the saturated ketone another molecule of starting ketone must be converted into some form which cannot be reduced, and a probable explanation is shown in Scheme 1. (Unchanged starting ketone is also observed among the products in a 'normal' reduction.)



SCHEME 1



SCHEME 2

The conversion of the starting ketone into its enolate ion by the amide ions liberated during the reaction cannot be the only mechanism for protecting the starting ketone since (i) the recovered acetylcyclopropane from a reduction of [$^2H_3$]acetylcyclopropane contained a considerable proportion of molecules which still possessed three deuterium atoms, and (ii) deuterium

[2] R. L. Jones and R. R. Dewald, *Analyt. Chem.*, 1973, **45**, 1753.

exchange of [$^2H_3$]acetylcyclopropane in ammonia containing 5% mol. equiv. of potassium amide showed that the enolate ion of acetylcyclopropane is in equilibrium with the free ketone under these conditions, and could therefore still be reduced. We therefore suggest that part of the recovered acetylcyclopropane arises by addition of amide ion to the carbonyl group. A similar adduct arises in the lithium–ammonia reduction of benzaldehyde to toluene.[3]

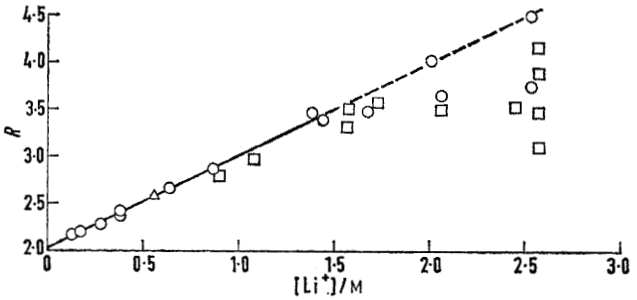
A significant portion of the product in the titration experiments was fairly involatile, and in the case of acetylcyclopropane was a single compound, decane-2,9-dione (*ca.* 40%). In the case of ketones (I) and (III), the amount of involatile product was *ca.* 30 and *ca.* 5% respectively. (These products were not observed under 'normal' reduction conditions.) The formation of these products presumably involves dimerisation after ring cleavage of a radical species (see left half of Scheme 2), but apparently cleavage of this type only leads to dimeric products, since 4-methylpentan-2-one was still the predominant species among the volatile products from ketone (I), *i.e.* the volatile products under these conditions still arise from cleavage of a carbanionic species. The formation of dimeric products will involve one electron per molecule of starting ketone. It therefore follows from the titration results that the formation of monomeric saturated ketone involves *two* electrons per molecule irrespective of how much dimerisation occurs.

In order to account for these observations, *viz.* (i) substituent effects in the cleavage to form saturated ketone indicate rearrangement of a carbanionic species, (ii) the overall reduction to saturated ketone involves 2 electrons per molecule, and (iii) reductive dimerisation characteristic of a radical species occurs in the titration experiments, we propose the reduction mechanism shown in Scheme 2.

In the presence of an excess of reducing metal ('normal' reduction) we expect the addition of two electrons to the carbonyl group to occur before cleavage, but in the presence of a much lower concentration of metal, *e.g.* near the end-point of a titration experiment, the addition of the second electron will be slower, thus giving the radical-anion a chance to rearrange and form dimeric products.

Although reduction of *trans*-1-acetyl-2-methylcyclopropane (I) involves predominant cleavage away from the 2-methyl group, reduction of *cis*-1-acetyl-2-methyl- (II) and 1-acetyl-2,2-dimethyl-cyclopropane (III) using lithium–ammonia involves cleavage predominantly in the other direction, *i.e.* towards C-2. In agreement with other workers,[1d,e] we interpret this change in the preferred direction of cleavage as due not to a change in mechanism, but to the operation of a steric effect between the acetyl group and the *cis*-2-methyl group.

In the case of 1-acetyl-2,2-dimethylcyclopropane (III), we observed a linear relation between the ratio of cleavage products (5-methylhexan-2-one : 4,4-dimethylpentan-2-one) and the concentration of lithium (see Figure). (This was not observed by Dauben and Wolf [1e] who also varied the concentration of lithium.) Up to 1·5M-lithium, the slope was 0·981 l mol^{-1}, intercept 2·03 (correlation coefficient 0·999 for 9 points.) Above this concentration the points were more erratic, probably owing to difficulty in judging whether or not all the lithium had dissolved. The inverse ratio does not of course give a linear relation. Similar behaviour was observed when a low concentration of lithium was used (0·56M) and the lithium ion concentration was increased by the addition of lithium iodide (see Figure), *i.e.* the ratio of



Ratio of products from reductions of 1-acetyl-2,2-dimethylcyclopropane against lithium ion concentration: ○ using lithium alone; □ using lithium–lithium iodide; △ point expected if addition of lithium iodide had no effect *i.e.* 0·56M-lithium used. *R* = 5-Methylhexan-2-one : 4,4-dimethylpentan-2-one

products was increased by an increase in the concentration of lithium ions, demonstrating the importance of lithium ions in the cleavage step of the reduction. This was further established by precipitating most of the lithium ions from the solution by the addition of tetraethylammonium chloride [reaction (1)], lithium chloride

$$Li \xrightarrow{NH_3} Li^+ + e \xrightarrow{Et_4NCl} \downarrow LiCl + Et_4\overset{+}{N} + e \quad (1)$$

being only slightly soluble in ammonia.[4] Reduction under these conditions reduced the product ratio to

Reduction of 1-acetyl-2,2-dimethylcyclopropane in the presence of tetraethylammonium cations

Metal	Quantity of metal (mmol)	Quantity of Et_4NCl (mmol)	Ratio of products *	Ratio of products * without Et_4NCl added
Li	26	27	1·47	2·54
Li	58	60	1·60	3·16
Li	58	60	2·00	3·16
Na	43	45	2·84	2·72
Ba	10·5	22	1·49	1·63
Ba	14·5	30	1·32	1·79
Ba	18	37	1·27	1·84

* 5-methylhexan-2-one : 4,4-dimethylpentan-2-one.

1·47—2·00 (see Table), close to the intercept value in the original graph.

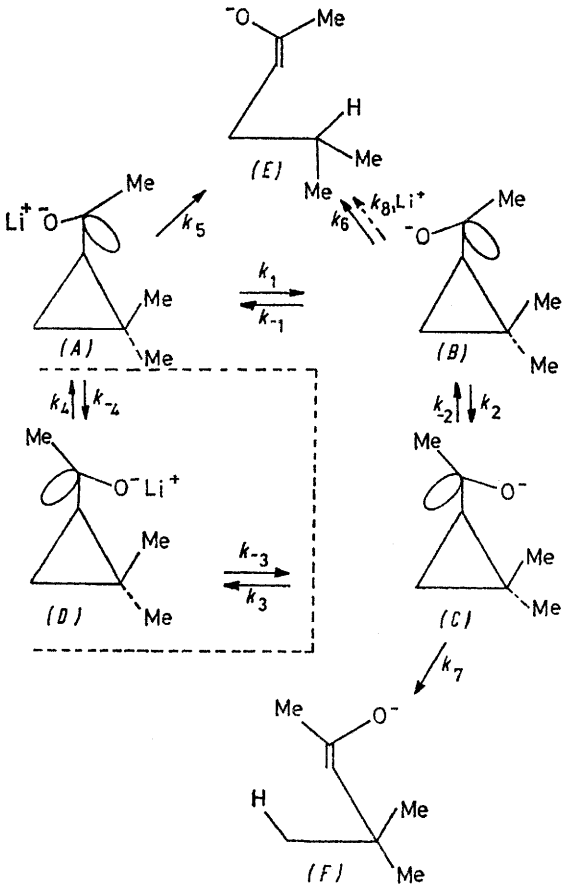
The reduction of ketone (III) with various concentrations of other metals, *i.e.* Na and Ba, did not produce

[3] S. S. Hall, A. P. Bartels, and A. M. Engman, *J. Org. Chem.*, 1972, **37**, 760.

[4] W. C. Johnson and O. F. Krumboltz, *Z. Phys. Chem.* (*Leipzig*), 1933, **A167**, 249.

any change in the product ratio (2·7 and 1·78 respectively). The addition of tetraethylammonium chloride caused a decrease in the product ratio with barium (1·3), but not with sodium (sodium chloride is fairly soluble in ammonia [4]).

In attempting to explain the linear variation of the product ratio from ketone (III) with lithium concentration, we feel it is essential to incorporate the observation made by Dauben and Wolf [1f] that acetylcyclopropanes ring open predominantly from a cisoid conformation to give the *trans*-enolate ion. For ketone



SCHEME 3

(III), 88% of the molecules react *via* this conformation, and this route is equally important for cleavage in both directions, *i.e.* towards C-2 and towards C-3.[1f]

There are two explanations which we wish to present. The first assumes that a significant proportion of the dianion is involved in tight ion-pair formation between the oxygen of the acetyl group and lithium [species (*A*) and (*D*) in Scheme 3]. Since tight ion-pair formation would increase the effective size of the oxygen, and thus the steric interaction with the *cis*-2-methyl group, we feel that species (*D*) would be unimportant. The major product (*E*) would be formed from species (*A*) and (*B*), while the minor product (*F*) would be formed from species (*C*); only cisoid conformations are considered. The relative rates of formation of (*E*) and (*F*) are given by equation (2). We further assume that equilibrium

$$\frac{d[(E)]}{dt} \Big/ \frac{d[(F)]}{dt} = \frac{k_5[(A)] + k_6[(B)]}{k_7[(C)]} \qquad (2)$$

is maintained between species (*A*)—(*C*). Thus equations (3) and (4) are obtained and the ratio of [(*E*)]/[(*F*)] would be a linear function of [Li^+].

$$\frac{d[(E)]}{dt} \Big/ \frac{d[(F)]}{dt} = \frac{\dfrac{k_5 k_{-1}[(B)][Li^+]}{k_1} + k_6[(B)]}{\dfrac{k_7 k_2[(B)]}{k_{-2}}} \qquad (3)$$

$$= \frac{k_5 k_{-1} k_{-2}}{k_7 k_1 k_2}[Li^+] + \frac{k_6 k_{-2}}{k_7 k_2} \qquad (4)$$

However, if this explanation is correct, why does not *cis*-1-acetyl-2-methylcyclopropane (II) also give product ratios which are dependent upon lithium ion concentration? In fact, from this explanation one would expect a stronger dependence upon [Li^+] in this case due to a less demanding electronic effect (secondary *versus* primary carbanion formation instead of tertiary *versus* primary), but this is not observed.

The failure of the first explanation in this respect prompted us to look for a further explanation. This neglects ion-pair formation, and assumes that cleavage towards the more substituted position of ketone (III) (tertiary carbanion formation) is catalysed by lithium ions to some extent, but that cleavage towards C-3 (primary carbanion formation) is not (Scheme 3). We again assume that equilibrium is maintained between species (*B*) and (*C*), with the former predominating due to steric interactions destabilising the latter. k_8 is the rate constant for the Li^+ catalysed conversion of (*B*) to (*E*). The relative rates of formation of (*E*) and (*F*) are given in equations (5)—(7). Again, the ratio of

$$\frac{d[(E)]}{dt} \Big/ \frac{d[(F)]}{dt} = \frac{k_8[(B)][Li^+] + k_6[(B)]}{k_7[(C)]} \qquad (5)$$

$$= \frac{k_8[(B)][Li^+] + k_6[(B)]}{k_7 \dfrac{k_2}{k_{-2}}[(B)]} \qquad (6)$$

$$= \frac{k_8 k_{-2}}{k_7 k_2}[Li^+] + \frac{k_6 k_{-2}}{k_7 k_2} \qquad (7)$$

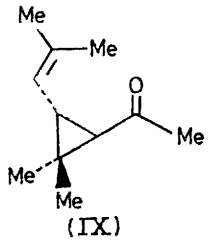
[(*E*)]/[(*F*)] would be a linear function of [Li^+]. For the *cis*-2-methyl derivative (II), the electronic effect would be less demanding (secondary *versus* primary carbanion formation instead of tertiary *versus* primary) and we suggest that participation by lithium ions in forming a secondary carbanion would be unnecessary. Thus, the ratio of products would be equal to $k_6 k_{-2}/k_7 k_2$, *i.e.* independent of [Li^+]. The ratio k_6/k_7 would be slightly larger in this case due to the easier electronic situation, while the ratio k_{-2}/k_2 would be largely unchanged. This second explanation therefore predicts a higher product ratio for ketone (II) than for ketone (III), and this was observed, *viz.* 7·6 *versus* 2·2—4·5.

Reductive cleavage in *trans*-1-acetyl-2-phenylcyclopropane (IV) [1d] and its *p*-dimethylamino-derivative (V)

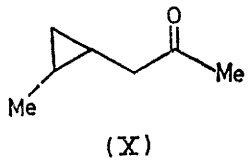
occurs exclusively towards the 2-phenyl group, and therefore a Hammett-type treatment of the product ratios from (IV), (V), and other *para*-substituted 1-acetyl-2-phenylcyclopropanes was not possible.

The reduction of *trans*-1-acetyl-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropane (IX) with lithium–ammonia gave three products. These were all derived by cleavage of the C-1–C-3 cyclopropane bond to give an allylic carbanion, the three products arising from the protonation of the latter. Thus the stabilising influence of the double bond during cleavage outweighs the steric effect encountered in ketone (III) and which would also be present in ketone (IX). The direction of cleavage in ketone (IX) also contrasts markedly with that in 3-methylcar-4-en-2-one;[1c] in this, allylic stabilisation is prevented by the rigid stereochemistry of the molecule.

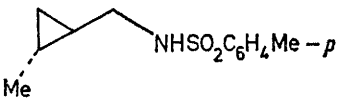
The treatment of benzoylcyclopropane with lithium–ammonia produced very little ring cleavage (<2%). Instead the product mixture was mainly benzylcyclopropane and the starting ketone. The reduction of the carbonyl group to a methylene group under these conditions is typical of a phenyl carbonyl compound.[3]



(IX)



(X)



(XI)

Cleavage of Cyclopropylcarbinyl Radicals.—In order to support the premise that a species such as (VI) would undergo ring cleavage towards the 2-methyl group, we have studied the preferred direction of cleavage of authentic 2-substituted cyclopropylcarbinyl radicals, after the method used by Neckers *et al.*[5] The radicals were generated by heating the ketones (I)—(III) and (IX) in the presence of di-t-butyl peroxide and butan-2-ol (method a), or their corresponding alcohols in the presence of di-t-butyl peroxide alone (method b).

As expected, cleavage in the *trans*-2-methyl derivatives (I) and its alcohol favoured opening towards C-2 by a factor of 4·4—4·7 (method a) and 2·44—3·34 (method b). Neckers *et al.*[5] report factors of 9·3 and 9·2 for *trans*-1-benzoyl-2-methylcyclopropane and the corresponding alcohol respectively. Cleavage favouring opening towards C-2 was even more pronounced for the *cis*-2-methyl (II) and the 2,2-dimethyl derivatives (III) and their alcohols, *viz.* factors of 8·0—9·2 (method a) and 8·05—8·5 (method b) for the *cis*-2-methyl derivatives, and 36—45 (method a) and 18·5—22·9 (method b) for the 2,2-dimethyl derivatives. The cause of the increased selectivity for the *cis*-2-methyl derivatives compared with the *trans*-2-methyl derivatives is a steric effect between the *cis*-2-methyl group and the substituents on the carbinyl carbon which favours cleavage towards C-2, *cf.* lithium–ammonia reduction of ketone (II). The further marked increase in selectivity for the 2,2-dimethyl derivatives is caused by an increased electronic effect favouring cleavage towards C-2 (tertiary *versus* primary radical formation instead of secondary *versus* primary) plus the same steric effect. The original premise is thus well founded.

Using method a, the predominant reaction of ketone (IX) was a thermal rearrangement; <5% of the product mixture was attributable to a radical cleavage. However, these latter products were all formed by C-1–C-3 cyclopropane bond cleavage, allylic stabilisation of the radical being the controlling factor.

Attempted Cleavage of Cyclopropylcarbinyl Carbanions.—In order to support the premise that species such as (VII) or (VIII) would undergo ring cleavage towards C-3, we have attempted to study the cleavage of authentic 2-substituted cyclopropylcarbinyl carbanions. It is significant in this respect that the conjugate base of 1,2,2-trimethylcyclopropanol is reported to undergo cleavage to give predominantly 3,3-dimethylbutan-2-one.[6]

The first attempt involved the treatment of *trans*-1-(2-methylcyclopropyl)propan-2-one (X) with strong base. It was envisaged that base-catalysed abstraction of a proton from the α-methylene group would be followed by ring cleavage to form 5-methylhexan-2-one or heptan-2-one. However, the enolate ion of (X), formed by treating (X) with sodium methoxide in methanol, or sodamide in ammonia, was found to be stable. The anion of benzylcyclopropane is also stable.[7]

In order to generate a less stabilised cyclopropylcarbinyl carbanion, our second approach to this problem involved the synthesis and Nickon–Sinz reaction[8] of *N*-(*trans*-2-methylcyclopropylmethyl)toluene-*p*-sulphonamide (XI). The Nickon–Sinz reaction involves treatment of an *N*-alkyltoluene-*p*-sulphonamide with hydroxylamine-*O*-sulphonic acid in the presence of base, the product being the corresponding alkane. Cram and Bradshaw[8b] concluded from stereochemical studies with chiral alkyl groups, that under the normal conditions employed for the Nickon–Sinz reaction (alkaline aqueous ethanol) an intermediate alkyldi-imide is formed which then undergoes deprotonation and loss of nitrogen to give a carbanion. The final product is formed by protonation of the latter.

Bumgardner *et al.*[9] had already demonstrated that the

[5] D. C. Neckers, A. P. Schaap, and J. Hardy, *J. Amer. Chem. Soc.*, 1966, **88**, 1265.

[6] C. H. DePuy, *Accounts Chem. Res.*, 1968, **1**, 3; J. P. Freeman, and J. H. Plonka, *J. Amer. Chem. Soc.*, 1966, **88**, 3662.

[7] M. J. Perkins and P. Ward, *Chem. Comm.*, 1971, 1134.

[8] (*a*) A. Nickon and A. Sinz, *J. Amer. Chem. Soc.*, 1960, **82**, 753; (*b*) D. J. Cram and J. S. Bradshaw, *ibid.*, 1963, **85**, 1108.

[9] C. L. Bumgardner, K. J. Martin, and J. P. Freeman, *J. Amer. Chem. Soc.*, 1963, **85**, 97.

Nickon–Sinz reaction of *N*-cyclopropylmethyltoluene-*p*-sulphonamide gave but-1-ene, and not methylcyclopropane. If the interpretation made by Cram and Bradshaw [8b] is correct, this indicates that the cyclopropylmethyl carbanion rapidly rearranges to give but-3-enyl carbanion.

With *N*-(*trans*-2-methylcyclopropylmethyl)toluene-*p*-sulphonamide, we found that in aqueous ethanol the major cleavage product was always pent-1-ene, the product which would be expected to predominate in a radical cleavage. Only when water was omitted from the solvent did 3-methylbut-1-ene become the major product. Thus our results suggest that under the normal conditions for the Nickon–Sinz reaction, the decomposition of the alkyldi-imide follows a radical pathway and not a carbanionic one. It may be significant to note that the system studied by Cram and Bradshaw [8b] was 1-methyl-1-phenylpropyldiazene, in which the adjacent phenyl group may have an effect upon the relative rates of radical and base-catalysed decomposition of the di-imide.

Since the volatile reaction product from the Nickon–Sinz reaction was always a complex mixture, containing many more components than the three products expected from (XI), *viz.* *trans*-1,2-dimethylcyclopropane, pent-1-ene, and 3-methylbut-1-ene, we investigated this aspect further. We found that all the ' extra ' products were also formed when *N*-methyltoluene-*p*-sulphonamide was used instead of (XI), therefore they were not derived from the *trans*-2-methylcyclopropylmethyl fragment. We also investigated the possibility that the primary reaction product might be ' hydrogenated ' by di-imide generated from the hydroxylamine-*O*-sulphonic acid.[10] Using 9,10-dihydro-9,10-bi-iminoanthracene as the source of di-imide, we found that pent-1-ene was ' hydrogenated ' 1·17 times faster than 3-methylbut-1-ene. Thus, if di-imide ' hydrogenation ' occurred at all during the Nickon–Sinz procedure, the proportion of pent-1-ene actually measured would be a minimum value, and neither the results nor their interpretation would be significantly affected.

EXPERIMENTAL

trans-1-*Acetyl*-2-*methylcyclopropane*.—A mixture of *trans*-pent-3-en-2-ol [11] (21·5 g, 0·25 mol; from crotonaldehyde and methylmagnesium chloride), anhydrous ether (200 ml) and zinc–copper couple [12] (32·5 g, 0·50 mol) under nitrogen was heated to boiling with vigorous stirring, and methylene iodide (134 g, 0·50 mol) was added slowly. After heating for 4 h, the cooled mixture was hydrolysed with saturated, aqueous ammonium chloride solution, and the product was extracted into ether. The product (16·0 g, 64%), b.p. 80—82° at 80 mmHg, was largely (94%) *trans*-1-(2-methylcyclopropyl)ethanol, the remainder being the starting alcohol. The alcohol, in ether, was oxidised to *trans*-1-acetyl-2-methylcyclopropane with 6N-chromic acid, and was finally purified by preparative g.l.c. (Carbowax; 100°). The spectral data of the product agreed with those reported.[13]

cis-1-*Acetyl*-2-*methylcyclopropane*.—Methylene iodide (5·36 g, 0·02 mol) and iodine (0·01 g) were added to zinc–copper couple [12] (1·63 g, 0·025 mol) in anhydrous ether (100 ml), and the mixture was refluxed under nitrogen for 30 min. After cooling to 25°, *cis*-pent-3-en-2-ol (0·86 g, 0·01 mol; from prop-1-ynylmagnesium bromide and acetaldehyde, followed by catalytic hydrogenation) in ether (10 ml) was added during 20 min, after which the mixture was again refluxed under nitrogen with vigorous stirring during 15 min. The cooled mixture was hydrolysed with saturated, aqueous ammonium chloride solution and the product was extracted into ether. Distillation and preparative g.l.c. (Carbowax; 100°) gave *cis*-1-(2-methylcyclopropyl)ethanol which was dissolved in ether and oxidised with 6N-chromic acid. The crude oxidation product was purified by preparative g.l.c. (Carbowax; 100°) to give *cis*-1-acetyl-2-methylcyclopropane, with spectral data in agreement with those reported.[13]

1-*Acetyl*-2,2-*dimethylcyclopropane*.—This was prepared from trimethylsulphoxonium iodide and mesityl oxide following the procedure of Roberts *et al.*[13]

trans-1-*Acetyl*-2-*phenylcyclopropane* (with J. Dingwall).—This was prepared from trimethylsulphoxonium iodide and 4-phenylbut-3-en-2-one.[14] The *p*-dimethylamino-derivative was prepared in a similar manner using 4-*p*-dimethylaminophenylbut-3-en-2-one.

trans-1-*Acetyl*-2,2-*dimethyl*-3-(2-*methylprop*-1-*enyl*)*cyclopropane*.—Pure ethyl *trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate (ethyl chrysanthemate) was obtained by treating a mixture of the *cis*- and the *trans*-isomers (1 : 2) with boiling ethanolic sodium ethoxide under nitrogen for 7 days.[15] The pure *trans*-ester was converted into the *trans*-methyl ketone with methyl-lithium in ether. The ketone was separated from a small amount of the corresponding tertiary alcohol by dry column chromatography on alumina (activity III; benzene as eluant). It had $\nu_{max.}$ (film) 1693 cm^{-1}, δ (C_6H_6) 5·01 (d, olefinic H), 2·55 (m, 3-H), 1·99 (s, MeCO), 1·72 (d, olefinic Me_2), 1·58 (d, $J_{1,3}$ 5·5 Hz, 1-H), and 1·32 and 1·10 (two s, 2-Me_2), *M* 166 (mass spectrum).

Reduction of Cyclopropyl Ketones with Metal–Ammonia Solutions.—The metal was added to anhydrous liquid ammonia (50 ml; dried by passing the gas through a tube packed with calcium oxide) contained in a graduated, 3-necked flask (100 ml) fitted with a dry-ice condenser, and the resulting blue solution was stirred magnetically for 30 min to ensure complete dissolution of the metal. The ketone (0·50 g), plus, in some experiments, decane (0·15 g) to act as an internal g.l.c. standard, was added slowly, by means of a syringe, directly into the solution. Stirring was continued for 2 h, and then the mixture was quenched by the careful addition of an excess of solid ammonium chloride. Ether (50 ml) was added before the ammonia was allowed to evaporate. After adding water (10 ml) the ether layer was separated and the aqueous layer was extracted with more ether (2 × 25 ml). The combined extracts were dried ($MgSO_4$) and concentrated to *ca.* 5 ml. As the product mixture usually contained a considerable

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quantity of alcohols, the concentrated solution in ether was oxidised with 6N-chromic acid, and then analysed by g.l.c. (Apiezon L; Carbowax). In those experiments in which decane was used as an internal g.l.c. standard, the recovery of material was in most cases >90%.

The reduction of *trans*-1-acetyl-2-methylcyclopropane with lithium gave 4-methylpentan-2-one as the major product, and hexan-2-one, in the ratio 19·3—23·2 : 1, with some starting ketone (10—27%), for lithium concentrations between 0·33 and 1·73M.

The reduction of *cis*-1-acetyl-2-methylcyclopropane with lithium gave hexan-2-one as the major product, and 4-methylpentan-2-one, in the ratio 6·3—9·0 : 1, with some starting ketone (9—19%), for lithium concentrations between 0·17 and 1·79M.

The reduction of 1-acetyl-2,2-dimethylcyclopropane with lithium gave 5-methylhexan-2-one as the major product, and 4,4-dimethylpentan-2-one, with some starting ketone (8—40%). The ratio of products varied with the lithium concentration (see Figure). With other metals the ratio of products was independent of the metal concentration: 2·2—3·5 : 1 for sodium (0·22—1·49M), 1·63—1·86 : 1 for barium (0·10—0·22M).

The reduction of *trans*-1-acetyl-2-phenylcyclopropane with lithium gave one product, 5-phenylpentan-2-one. Similarly, the *p*-dimethylamino-derivative gave only 5-*p*-dimethylaminophenylpentan-2-one.

The reduction of benzoylcyclopropane with lithium gave 58% benzylcyclopropane, the remainder being mainly the starting ketone with a small amount (<2%) of 1-phenylbutan-1-one.

The reduction of *trans*-1-acetyl-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropane with lithium gave a product mixture after chromium trioxide–pyridine oxidation consisting of four components: (*A*) (48%), (*B*) (22%), (*C*) (16%), and (*D*) (14%; starting ketone) (in order of elution on analytical g.l.c.; Carbowax). Preparative g.l.c. (SE 30; 120°) separated the mixture into two fractions, fraction 1 consisting of products (*A*) and (*B*), and fraction 2 consisting of products (*C*) and (*D*). N.m.r. spectral analysis of fraction 1 indicated that it was a mixture of *trans*- and *cis*-4,4,7-trimethyloct-5-en-2-one, δ (CCl_4) 5·63 (m, 5- and 6-H), 2·29 (s, 3-H_2), 2·14 (m, 7-H), 1·98 (s, MeCO), 1·04 (s, 4-Me_2), and 0·95 (d, $J_{7,Me}$ 6 Hz, 7-Me_2). N.m.r. spectral analysis of fraction 2 indicated that product (*C*) was 4,4,7-trimethyloct-6-en-2-one, δ (CCl_4) (*inter alia*) 5·09 (t, 6-H), 2·22 (s, 3-H_2), 2·13 (s, MeCO), and 2·0 (d, 5-H_2).

Reduction of 1-Acetyl-2,2-dimethylcyclopropane with Lithium–Lithium Iodide in Ammonia.—A weighed quantity of anhydrous lithium iodide (dried at 350°) was added to a solution of lithium (0·20 g) in liquid ammonia (50 ml), and the resulting solution was stirred for a further 15 min before the ketone was added. For results, see the Figure.

Reduction of 1-Acetyl-2,2-dimethylcyclopropane in the Presence of Tetraethylammonium Cations.—A slight excess of anhydrous tetraethylammonium chloride was added to a solution of the metal in liquid ammonia in order to precipitate the metal ions as their corresponding chlorides. The resulting mixture was stirred for 10 min before the ketone was added. For results, see Table.

Reduction of Deuteriated Acetylcyclopropane with Lithium in Ammonia.—The reduction of deuteriated acetylcyclopropane (0·25 g; prepared by treatment of the ketone with boiling sodium methoxide–methan[^{2}H]ol for 15 h; it had 73·1% $^2H_3$, 23·8% $^2H_2$, and 3·1% $^2H_1$) using lithium (0·4 g) in ammonia (50 ml) was carried out in the usual manner. The product mixture, without oxidation, was analysed by m.s.–g.l.c.; it contained pentan-2-one, acetylcyclopropane, pentan-2-ol, and 1-cyclopropylethanol. The isotopic composition of the recovered starting ketone was: after 2 h reaction, 53·5% $^2H_3$, 24·9% $^2H_2$, 10·8% $^2H_1$, 10·8% $^2H_0$; after 6 h, 36·5% $^2H_3$, 22·9% $^2H_2$, 13·5% $^2H_1$, 27·1% $^2H_0$. The isotopic composition of the product pentan-2-one was: after 2 h, 65·8% $^2H_3$, 20·3% $^2H_2$, 6·5% $^2H_1$, 7·4% $^2H_0$; after 6 h, 30·7% $^2H_3$, 20·7% $^2H_2$, 19·0% $^2H_1$, 29·6% $^2H_0$. The addition of solid ammonium chloride rapidly in one portion during work-up, instead of the normal slow addition, did not change the isotopic composition of the recovered starting ketone from that already reported for a 2 h reaction.

Treatment of Deuteriated Acetylcyclopropane with Potassium Amide in Ammonia.—The deuteriated ketone (0·25 g; 75·5% $^2H_3$, 21·1% $^2H_2$, 3·3% $^2H_1$) was added dropwise to 5% mol. equiv. of potassium amide in ammonia (50 ml) and the solution was left for 2 h. Solid ammonium chloride and ether (25 ml) were added, and the product was isolated in the usual manner. The recovered acetylcyclopropane had 8·2% $^2H_3$, 19·2% $^2H_2$, 36·2% $^2H_1$, 36·4% $^2H_0$.

Titration of Lithium–Ammonia Solutions with Acetylcyclopropanes.—Lithium (1·73—24·5 mmol) was dissolved in anhydrous liquid ammonia (10 ml) and the ketone was added slowly by injection until the blue colour of the stirred solution was just discharged. The weight of the ketone used was obtained from the difference in weight of the syringe at the beginning and end of the titration. The following results were obtained: 2·74, 5·03, and 24·5 mmol of lithium required 2·84, 4·91, and 26·0 mmol of 5-methylhexan-2-one respectively for neutralisation; 0·58 mmol of lithium required 0·57 mmol of 2,2,6,6-tetramethylcyclohexanone; 5·10, 5·40, 5·48, and 9·95 mmol of lithium required 5·24, 5·34, 5·40, and 9·83 mmol of acetylcyclopropane (the ratios of rearranged to starting ketone were 0·97 and 0·90 respectively in the first and second titrations); 2·14 mmol of lithium required 2·14 mmol of *trans*-1-acetyl-2-methylcyclopropane; 1·73 mmol of lithium required 1·68 mmol of 1-acetyl-2,2-dimethylcyclopropane.

In three experiments, a deficiency of acetylcyclopropane was added to the solution of lithium in ammonia and the reaction was left for 2 h before the remaining lithium was titrated with (i) 5-methylhexan-2-one or (ii) 2,2,6,6-tetramethylcyclohexanone. The results were as follows: to 4·97 mmol of lithium was added 1·91 mmol of acetylcyclopropane; a further 2·90 mmol of 5-methylhexan-2-one was required for neutralisation after 2 h; to 11·15 and 12·88 mmol of lithium was added 9·78 and 10·0 mmol of acetylcyclopropane respectively; a further 0·85 and 1·80 mmol of 2,2,6,6-tetramethylcyclohexanone respectively was required for neutralisation after 2 h; the ratios of rearranged to starting ketone were 1·04 and 1·18 respectively.

The neutralised solution from the titration of all three acetylcyclopropanes was found to contain high molecular weight products as well as the expected volatile products. In the case of acetylcyclopropane itself, the less volatile material (*ca.* 40%) was a single compound, decane-2,9-dione, identified by comparison with an authentic sample (see below). For *trans*-1-acetyl-2-methylcyclopropane, the volatile products, 4-methylpentan-2-one and hexan-2-one, were in the ratio 11·8 : 1, while the less volatile material (*ca.* 30%) had $\nu_{max.}$ (film) 1710 cm^{-1} and an n.m.r. spectrum similar, but not identical, to that of decane-2,9-dione. In

the case of 1-acetyl-2,2-dimethylcyclopropane, only *ca.* 5% of less volatile material was formed.

Decane-2,9-dione.—Hexane-1,8-dicarbonyl chloride (2·11 g, 0·01 mol; from the dicarboxylic acid and thionyl chloride) in benzene was added slowly with stirring to a solution of dimethylcadmium (0·1 mol) in benzene (25 ml), and the mixture was refluxed for 45 min under nitrogen. The mixture was then poured onto ice–sulphuric acid and the product was isolated in the usual manner. It was a crystalline solid, m.p. 60—61° (from pentane) (lit.,[16] 62°), $\nu_{max.}$ (CCl_4) 1710 cm^{-1}, δ ($CDCl_3$) 2·43 (t, 3-H_2 and 8-H_2), 2·15 (s, two MeCO), and 2·0—1·0 (m, 8 aliphatic H), *M* 170 (mass spectrum).

Radical Reactions of Acetylcyclopropanes and 1-Cyclopropylethanols.[5]—(*a*) A mixture of the substituted acetylcyclopropane (1 mmol), butan-2-ol (1·4 g) and di-t-butyl peroxide (0·113, 0·225, and 0·45 g) was heated in a sealed tube for 14 h at 140°. The products were analysed by g.l.c. The recovery of material was usually >90% (decane used as internal g.l.c. standard).

trans-1-*Acetyl-2-methylcyclopropane*. The products were hexan-2-one and 4-methylpentan-2-one in the ratio 4·72, 4·44, and 4·44 : 1 respectively.

cis-1-*Acetyl-2-methylcyclopropane*. The products were hexan-2-one and 4-methylpentan-2-one in the ratio 8·98, 9·20, and 8·04 : 1 respectively.

1-*Acetyl-2,2-dimethylcyclopropane*. The products were 5-methylhexan-2-one and 4,4-dimethylpentan-2-one in the ratio 45, 36, and 41 : 1 respectively.

trans-1-*Acetyl-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropane*. This ketone underwent a thermal rearrangement (140°; 48 h) to give 4-isopropenyl-6-methylhept-5-en-2-one (90%), $\nu_{max.}$ (CCl_4) 1730 cm^{-1}, δ (CCl_4) 4·84 (d, 5-H), 4·62 (t, isopropenyl H_2), 3·52—3·16 (m, 4-H), 2·4 (m, 3-H_2), 2·01 (s, MeCO), and 1·67 (s, 3 vinylic Me), faster than it underwent the radical cleavage (4·5%). The three products formed by the latter reaction all involved C-1–C-3 bond fission.

(*b*) A mixture of the substituted 1-cyclopropylethanol (prepared by lithium aluminium hydride in ether reduction of the corresponding acetylcyclopropane) and di-t-butyl peroxide was heated in a sealed tube for 14 h at 140°. The products were analysed by g.l.c. The recovery of material decreased with increasing amounts of peroxide, but for the lower concentrations of peroxide, it was >90%.

trans-1-(2-*Methylcyclopropyl*)*ethanol*. The products were the same as for the corresponding ketone, in the ratio 3·34, 3·24, and 2·55 : 1 for 0·025, 0·075, and 0·25 g of the peroxide respectively.

cis-1-(2-*Methylcyclopropyl*)*ethanol*. The products were the same as for the corresponding ketone, in the ratio 8·05 and 8·50 : 1 for 0·038 and 0·125 g of the peroxide respectively.

1-(2,2-*Dimethylcyclopropyl*)*ethanol*. The products were the same as for the corresponding ketone, in the ratio 20·9, 22·9, and 18·5 : 1 for 0·05, 0·15, and 0·50 g of the peroxide respectively.

trans-1-(2-*Methylcyclopropyl*)*propan-2-one*.— Hex-4-yn-2-ol (9·8 g, 0·1 mol; from the reaction of methylacetylene with 1,2-epoxypropane in liquid ammonia in the presence of sodamide) in ether (10 ml) was added to a solution of sodium (9·2 g) in anhydrous liquid ammonia (400 ml), and the mixture was stirred for 2 h before the reaction was quenched by the addition of solid ammonium chloride (30 g). Isolation of the product with ether gave pure *trans*-hex-4-en-2-ol (8·8 g), b.p. 66° at 40 mmHg, δ (CCl_4) 5·40 (m, 4- and 5-H), 3·65 (m, 2-H), 3·38br (s, OH), 2·05 (m, 3-H_2), 1·64 (m, vinylic Me), and 1·05 (d, 1-H_3).

trans-Hex-4-en-2-ol (4·0 g, 0·04 mol) and zinc–copper couple (5·24 g, 0·08 mol) in ether (50 ml) were stirred vigorously under nitrogen while methylene iodide (16·08 g, 0·06 mol) was slowly added. The mixture was refluxed for 1 h before it was decomposed by the addition of aqueous ammonium chloride solution. Isolation of the product with ether gave crude *trans*-1-(2-methylcyclopropyl)propan-2-ol (2·95 g), b.p. 70—72° at 30 mmHg, which was purified by preparative g.l.c. (Carbowax; 100°). The purified material had δ (CCl_4) 3·85br (s, OH), 3·74 (m, 2-H), 1·34 (m, 3-H_2), 1·14 (d, 1-H_3), 1·02 (d, Me on cyclopropane), and 0·20 (m, 4 cyclopropyl protons).

The alcohol (2·28 g) in ether (10 ml) was oxidised with 6N-chromic acid, and the isolated product was purified by preparative g.l.c. (Carbowax; 110°). It had $\nu_{max.}$ (film) 1709 cm^{-1}, δ (CCl_4) 2·20 (d, 3-H_2), 2·05 (s, MeCO), 1·05 (d, Me on cyclopropane), and 0·50 (m, 4 cyclopropyl protons), *M* 112 (mass spectrum).

Treatment of trans-1-(2-*Methylcyclopropyl*)*propan-2-one with Base*.—(a) *Sodium methoxide in methanol*. The ketone (0·10 g) in a 10% solution of sodium methoxide in methanol (2·0 ml) was heated in a sealed tube at 80° for 18 h. The isolated material was pure starting ketone.

Similar treatment using methan[^{2}H]ol gave the starting ketone containing 67% $^2H_5$, 27% $^2H_4$, 5% $^2H_3$, 1% $^2H_1$. The absorptions due to CH_2COCH_3 were absent from the n.m.r. spectrum.

(b) *Sodamide in liquid ammonia*. The ketone (0·224 g) was added to a solution of sodamide (0·04 g) in anhydrous ammonia (15 ml) under nitrogen and the mixture was stirred for 8 h. The isolated material was pure starting ketone.

N-(trans-2-*Methylcyclopropylmethyl*)*toluene*-p-*sulphonamide*.—Ethyl 4-chloropentanoate was prepared from γ-valerolactone by the method of Julia *et al.*,[17] and was converted into ethyl 2-methylcyclopropanecarboxylate (*cis* : *trans* 0·25) by the method of Cannon *et al.*[18] The configuration of the major isomer of the cyclised ester was shown to be *trans* by conversion into its corresponding 1-acetyl-2-methylcyclopropane [(i) KOH, (ii) $SOCl_2$, (iii) $CdMe_2$] and comparison of the latter with an authentic sample of *trans*-1-acetyl-2-methylcyclopropane prepared from *trans*-pent-3-en-2-ol [(i) CH_2I_2/Zn–Cu, (ii) CrO_3]. The cyclised ester (*cis–trans*-mixture) was treated with a boiling suspension of sodamide in dioxan under nitrogen for 18 h. The isolated product was recrystallised from methylene chloride–pentane to give pure *trans*-2-methylcyclopropanecarboxamide (20%), m.p. 111° (lit.,[9] m.p. 111—112°). The i.r. spectrum of the amide was in agreement with that reported.[19]

The amide (1·09 g) in ether (5 ml) was added to lithium aluminium hydride (0·4 g) in ether (40 ml) and the mixture was refluxed under nitrogen for 25 h. After the excess of hydride had been destroyed with water the product was

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extracted with ether (3 × 15 ml) and the combined extracts were dried ($MgSO_4$) and concentrated to 1·5 ml. A solution of toluene-*p*-sulphonyl chloride (3 g) in pyridine (6 ml) was added to the ethereal solution of the amine, and the solution was refluxed for 45 min. Isolation of the derivative in the usual manner gave pure N-(trans-2-*methylcyclopropylmethyl*)*toluene*-p-*sulphonamide* (2·1 g, 89%), m.p. 40—41° [from light petroleum (b.p. 60—80°)] (Found: C, 60·4; H, 7·0; N, 6·0%; *M*, 239·0984. $C_{12}H_{17}NO_2S$ requires C, 60·3; H, 7·1; N, 6·0%; *M*, 239·0980), δ ($CDCl_3$) 7·70 and 7·24 (two d, aromatic 4H), 5·63 (t, NH), 2·72 (m, CH_2), 2·40 (s, aromatic Me), 0·93 (d, $J_{Me,H}$ 5 Hz, Me on cyclopropane), 0·5 (m, 2 cyclopropyl protons), and 0·20 (m, 2 cyclopropyl protons).

Reaction of N-(trans-2-*Methylcyclopropylmethyl*)*toluene*-p-*sulphonamide with Hydroxylamine*-O-*sulphonic Acid* (*Nickon–Sinz Reaction* [8,9]).—The sulphonamide (0·6 g, 2·5 mmol) was dissolved in hot, aqueous sodium hydroxide (100 ml) and ethanol (30 ml), and the solution was transferred to a flask fitted with a magnetic stirrer, a vertical reflux condenser, and a take-off condenser. The outlet of the latter passed into carbon tetrachloride (10 ml) at 0°. Hydroxylamine-*O*-sulphonic acid (10 g) was then added in small portions to the stirred solution from a test-tube sidearm connected directly to the flask. Alternatively, the sulphonic acid was added through the reflux condenser, the end of which was kept closed when not being used for the addition. The mixture was heated until ethanol (10 ml) had distilled into the carbon tetrachloride. The carbon tetrachloride–ethanol solution was then analysed by g.l.c. (1,2-bismethoxyethyl adipate–bis-2-ethylhexyl sebacate; 20°). Apart from peaks for the expected products, *trans*-1,2-dimethylcyclopropane, pent-1-ene, and 3-methylbut-1-ene, there was a multitude of other peaks. The latter were also present when the same reaction was performed with *N*-methyltoluene-*p*-sulphonamide, and so were not derived from the *trans*-2-methylcyclopropylmethyl fragment. The ratio pent-1-ene : 3-methylbut-1-ene varied with the concentration of base, and the solvent: (i) 11·5 and 19·0 for 10% NaOH, (ii) 19·0 for 28% NaOH (7·4 and 8·1 for 28% NaOH when the sulphonic acid was added through the reflux condenser), and (iii) 0·48 and 0·27 for a saturated solution of KOEt in ethanol.

Di-imide Reduction of a Mixture of Pent-1-*ene and* 3-*Methylbut*-1-*ene*.—An excess (5×) of 9,10-dihydro-9,10-bi-iminoanthracene (1·7 g) was added to an ethanolic solution (10 ml) of an approximately equimolar mixture of the two alkenes, and the solution was heated at 60° for 14 h. The product solution, analysed by g.l.c., contained pent-1-ene (7·9%), pentane (41·8%), 3-methylbut-1-ene (9·7%), and 2-methylbutane (36·8%).

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