EFFECT OF DEUTERIUM SUBSTITUTION ON SOLVOLYSIS RATES OF (METHYLCYCLO-PROPYL)-CARBINYL DERIVATIVES

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The ionization hypothesis, and the introduction of a general mechanism known as the S_N1 reaction, was without doubt one of the most important developments in theoretical organic chemistry. The pioneering work of Ingold and (the late) Hughes stimulated an extensive investigation of solvolytic displacement reactions and the development of more and more refined methods for the study of reaction mechanisms.

One of the latest addenda to the set of tools used for this purpose was the application of isotopes. Although ^{14}C was, at the beginning, one of the most widely used isotopes in organic chemistry, more recently the light isotopes, particularly deuterium and tritium, have gained in importance.

In connection with kinetic studies isotopic substitution proved to be of great help in the investigation of the rate-determining step in unimolecular displacement reactions, and for the elucidation of the structure of short-lived ionic intermediates.

In the limiting case of displacement reactions the influence of an internal nucleophile—the neighbouring group—has been the subject of extensive studies. Systematic investigation of unusual reactivities in systems with neighbouring group participation produced the hypothesis of resonance-stabilized transition states, and led to the idea of "non-classical" ions[1]. Such ionic species have been proposed as relatively stable intermediates in a number of cases where rate enhancements and/or skeletal rearrangements were observed (*Figure 1*).

In all these structures the transition state stabilization is explained by a charge delocalization due to partial overlapping of the empty p-orbital at the reaction centre with the neighbouring carbon–carbon bond.

The relative importance of non-classical intermediates recently became the subject of considerable controversy[2]. The number of non-classical structures that has been proposed has multiplied fantastically in recent years, and a critical re-examination of the basic concept is certainly justified.

Brown expressed the opinion[2] that essentially in every case where non-classical structures have been suggested, strained initial states were involved. This raises the question as to what extent the observed rate accelerations are due to non-classical resonance, and how much to raised initial state free energy.

The cyclopropylcarbinyl system is one of the numerous examples where high reactivities have been attributed to non-classical stabilization of the transition state. The cationic reactions of this system have been thoroughly

studied by Roberts and co-workers[3] and the hypothesis was advanced that these reactions can be best explained by means of non-classical intermediates. The symmetrical tricyclobutonium ion structure (I) first proposed

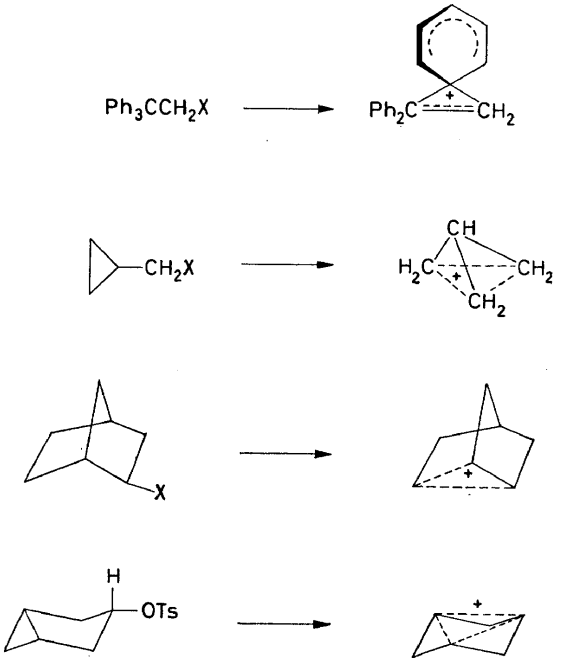
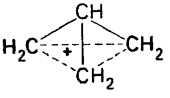
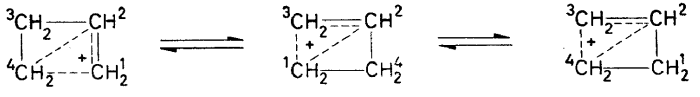


Figure 1

was later replaced by the non-symmetrical bicyclobutonium structures (IIa–IIc).



(I)



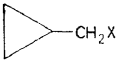
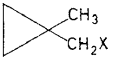
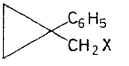
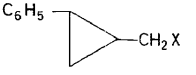
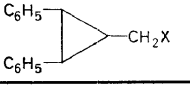
(IIa) (IIb) (IIc)

One of the important arguments in favour of (II) was the reported observation[3] that (1-methylcyclopropyl)-carbinyl chloride was about 50 times more reactive than cyclopropylcarbinyl chloride. However, the peculiar behaviour of this system is still not fully understood. The introduction of a phenyl group in the 2-position has only a small effect on the

reaction rate[4], and the same is the case if phenyl groups are attached to positions 3 and 4 in the cyclopropyl ring[5, 6] (*Table 1*).

We became interested in this problem some years ago, and the idea was to find out if the introduction of deuterium at certain positions in cyclopropylcarbinyl derivatives could yield more information about the structure

Table 1. Relative solvolytic reactivities of some cyclopropylcarbinyl derivatives

Compound	*Relative rates*
	1·00
	50[a]
	1·3[b]
	0·62 (*cis*)[c] 2·19 (*trans*)[c]
	0·34[d]

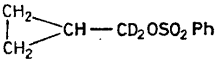
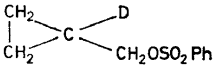
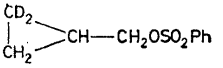
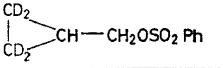
[a] Chlorides in "50% ethanol" at 50° (ref. 3).
[b] Benzenesulphonates in acetic acid at 20° (ref. 4).
[c] β-Naphthalenesulphonates in "90% dioxan" at 25° (ref. 5).
[d] Tosylates in absolute ethanol at 30° (ref. 6).

of the intermediate cation formed in the rate-determining step. Unfortunately, the measurements of the solvolysis rates of deuterated compounds listed in *Table 2* provided no clear evidence of the structure of the transition state[7]. At this stage the only conclusion which could be reached was that a symmetrical cation of structure (I) is certainly not involved, and that only a small dispersion of positive charge occurs in the rate-determining step at the ring methylene carbon atoms.

In view of the experimental evidence presented so far, it was of considerable interest to investigate the influence of deuterium substitution in the methyl groups of methyl substituted cyclopropylcarbinyl derivatives on the solvolytic reactivity. If in these reactions an intermediate resembling (II) is formed, the solvolysis of (1-methyl-d_3-cyclopropyl)-carbinyl derivatives can be considered as analogous to that of *beta* deuterium labelled

compounds, and a secondary kinetic isotope effect would be expected. On the other hand, the introduction of *gem* methyl and methyl-d_3 groups in position 3 should have only a small effect on the solvolysis rate (*Figure 2*).

Table 2. Isotope effects in the acetolysis of deuterium-labelled cyclopropylcarbinyl benzenesulphonates

Compound	k_H/k_D
	1·29
	1·15
	0·97
	0·99

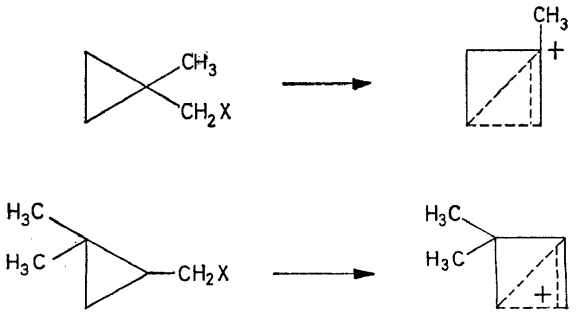
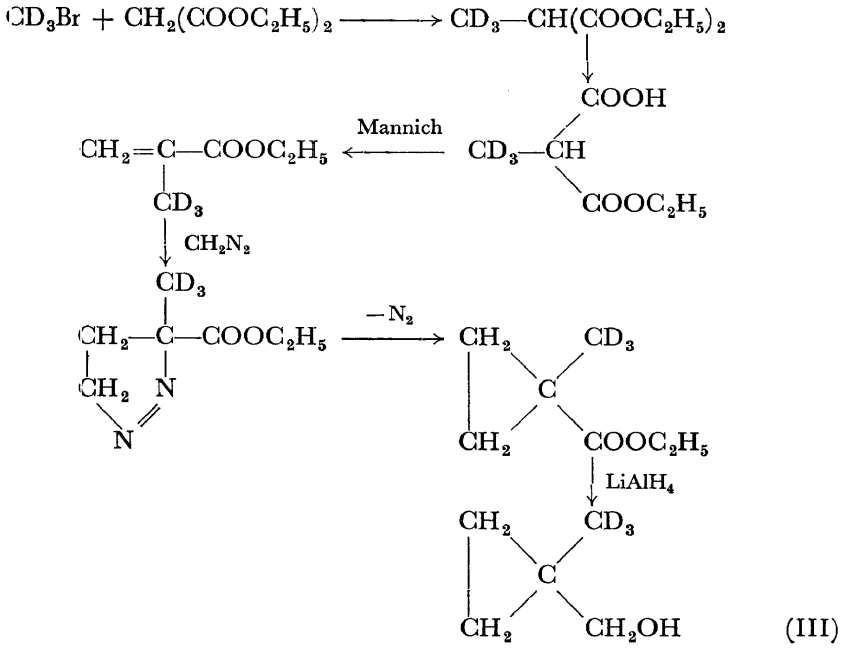


Figure 2

SYNTHETIC PROCEDURES

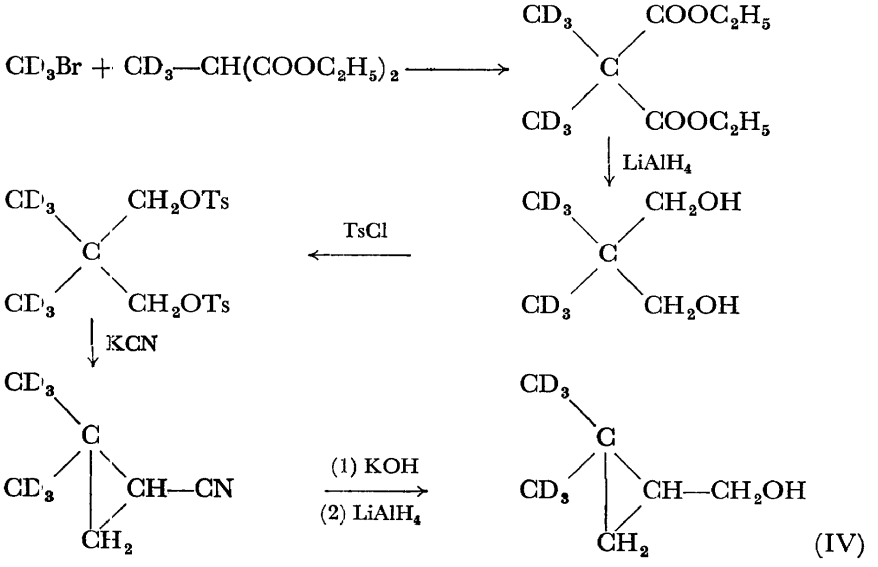
The carbinols (III) and (IV) were synthesized according to the following schemes.

Scheme 1



(III)

Scheme 2



(IV)

1-Methylcyclobutanol was prepared by hydrochloric acid isomerization of (1-methylcyclopropyl)-carbinol.

The methanesulphonates listed in *Table 3* were prepared by esterification of the alcohols with methanesulphonyl chloride in the presence of pyridine. They are viscous oils which decompose upon standing at room temperature. Their purity was in all cases better than 99 per cent as estimated from the neutralization equivalent. The i.r. spectra were in agreement with the proposed structure.

Table 3. Solvolysis rates of cyclopropylcarbinyl methanesulphonate and related methyl and methyl-d_3 substituted compounds at 20° in 96% ethanol

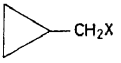
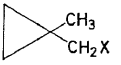
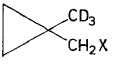
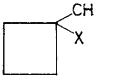
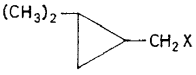
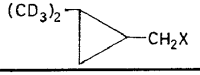
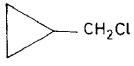
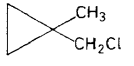
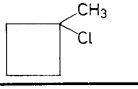
Compound	k ($sec^{-1} \times 10^4$)	*Relative rates*
	0·61	1·00
	2·88	4·72
	2·86	4·70
	4·53	7·42
	58·2	96
	59·2	97

Table 4. Solvolysis rates in "50% ethanol" of cyclopropylcarbinyl chloride and related methyl substituted derivatives[a]

Compound	$t°$	k ($sec^{-1} \times 10^4$)		*Relative rates*	
	30		(0·14)[b]	1	(1)
	50	1·70	(1·25)[b]	1	(1)
	30	1·76	(6·90)[c]		(49)
	50	12·08		7	
	30	1·02	(0·72)[c]	4	(5·2)
	50		(6·17)[c]		(4·9)

[a] Values given in brackets refer to published data.
[b] J. D. Roberts and R. H. Mazur. *J. Am. Chem. Soc.* **73**, 2509 (1951).
[c] E. F. Cox, M. C. Caserio, M. S. Silver, and J. D. Roberts. *J. Am. Chem. Soc.* **83**, 2719 (1961).

As reference compounds the chlorides listed in *Table 4* were also prepared using the procedure of Young *et al.*[8] Purification was achieved by gas–liquid chromatography and checked by determination of the neutralization equivalent, n.m.r. and i.r. spectra. The deuterium content of labelled compounds was determined from the n.m.r. spectra and was at least 95 per cent of the theoretical values.

RESULTS AND DISCUSSION

The kinetic measurements were performed in a thermostated cell using an automatic recording titrator (Radiometer, Copenhagen, Type SBR 2/SBU 1).

The solvolysis of all compounds with the exception of (1-methylcyclopropyl)-carbinyl derivatives followed first-order kinetics. The reaction of the 1-methyl derivatives was accompanied by an internal rearrangement to the corresponding cyclobutyl derivative (*Figure 3*), and the instant rate constant was calculated according to the procedure of Young *et al.*[9].

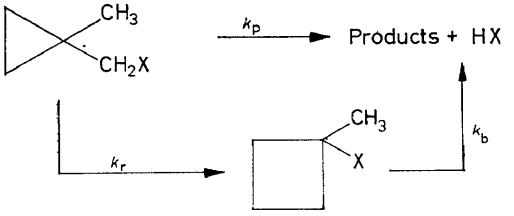


Figure 3

The results of the kinetic measurements are summarized in *Tables 3* and *4*.

Perhaps the most salient feature of our results is the clear disparity between the expected data and those obtained. The effect of deuterium substitution in the methyl groups had no influence on the reaction rate. In the case of (1-methyl-d_3-cyclopropyl)-carbinyl methanesulphonate this cannot be rationalized on the basis of a non-classical intermediate of structure (II). We were also unable to confirm the reported data[3] whereby the introduction of a methyl group in the 2 position causes a 50-fold rate acceleration. The relative rate ratio was only 1 : 5 (for methanesulphonates) and 1 : 7 (for chlorides) respectively. This observation weakens one of the arguments in favour of (II).

The introduction of two *gem* methyl groups in the 3 position of the cyclopropane ring resulted in a hundred-fold increase of the reactivity. This result can be accommodated only by assuming a pronounced increase of the initial state free energy. If this were not the case, two methyl groups being approximately as effective in stabilizing a carbonium ion as one phenyl group, the reactivity of the dimethyl derivative should be the same as of the corresponding phenyl derivative and not much different from the unsubstituted methanesulphonate.

Although further experimental evidence is needed for this and other systems before a conclusion can be reached regarding the relative importance

of non-classical intermediates, our results re-open the question of how to formulate the structure of the first formed intermediate in solvolytic reactions of cyclopropylcarbinyl derivatives.

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S. Winstein, A. H. Lewin, and K. C. Panda. *J. Am. Chem. Soc.* **85**, 2324 (1963).
[3] E. F. Cox, M. C. Caserio, M. S. Silver, and J. D. Roberts. *J. Am. Chem. Soc.* **83**, 2719 (1961) and previous papers.
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[8] S. H. Sharman, F. F. Caserio, R. F. Nystrom, J. C. Leak, and W. G. Young. *J. Am. Chem. Soc.* **80**, 5965 (1958).
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