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SECONDARY HYDROGEN ISOTOPE EFFECTS—IX

SOLVOLYSIS RATES OF METHYL AND METHYL-d_3 SUBSTITUTED CYCLOPROPYLCARBINYL AND CYCLOBUTYL DERIVATIVES[1]

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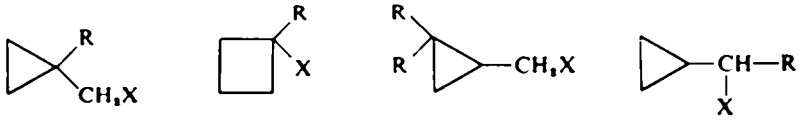
Abstract—Methyl and methyl-d_3 substituted cyclopropylcarbinyl and cyclobutyl derivatives (I–IV) were prepared and their solvolysis rates measured. It was found that methyl substitution on the ring in cyclopropylcarbinyl derivatives (I, III) produces small but significantly larger rate enhancements than an analogous phenyl substitution. Methyl deuteration has no significant effect on the solvolysis rates. Methyl substitution at the carbinyl position (IV) accelerates the solvolysis rate by a factor of $2 \cdot 10^9$ to $4 \cdot 10^9$ which is less than usually observed (10^4–10^6). 1-Methyl-d_3-cyclobutyl methanesulfonate (IIb–D) and 1-cyclopropylethyl-2-d_3 chloride (IVc–D) display upon solvolysis in 96% ethanol only one fourth ($k_H/k_D = 1{\cdot}09$) resp. one half ($k_H/k_D \cdot 1{\cdot}19$) of the kinetic secondary β-deuterium isotope effect usually observed for a CD_3-group (1·30–1·40). The results are discussed in terms of transition states and carbonium ion intermediates related to bicyclobutonium ions (V). The reduced magnitude of the secondary deuterium isotope effects is correlated with small methyl- and phenyl-substitution rate effects. The hypothesis is advanced that secondary β-deuterium isotope effects might be a criterion for charge delocalization such as occurs in the formation of non-classical carbonium ions.

INTRODUCTION

IN A previous paper[3] the solvolysis rates of specifically deuterated cyclopropylcarbinyl derivatives was reported. In order to obtain additional information about the mechanism of these processes, the solvolytic reactivities of a series of methyl and methyl-d_3 substituted cyclopropylcarbinyl and cyclobutyl derivatives I–IV (X = OMs and Cl) was investigated. The results of the present investigation are discussed in terms of cationic



I-H I-D II-H II-D III-H III-D IV-H IV-D

R = Me R = CD_3 R = Me R = CD_3 R = Me R = CD_3 R = Me R = CD_3

a, X = −OH
b, X = $-OSO_2Me$
c, X = −Cl

[1] For a preliminary communication see *Proc. Nat'l. Acad. Sci., U.S.* **52**, 893 (1964). Reported in part at the Symposium on *Isotope Mass Effects in Chemistry and Biology* Vienna, Austria, December (1963). See *Pure and Appl. Chem.* **8**, 441 (1964). The preceding paper of this series, K. L. Servis, O. Gjurović-Deletis, S. Borčić, and D. E. Sunko, *Croat. Chem. Acta* **37**, 191 (1965).

[2] Taken in part from the Ph. D. Thesis of Mrs. M. N., Zagreb University (1963).

[3] S. Borčić, M. Nikoletić and D. E. Sunko, *J. Amer. Chem. Soc.* **84**, 1615 (1962).

intermediates and transition states cognate to V. In view of the recent questioning of the existence of non-classical carbonium ions in general[4-6] and of bicyclobutonium ions in particular,[4] it seems appropriate before reporting and discussing the results of the present investigation to mention the experimental data obtained by other authors that are salient to this particular problem.[7]

Solvolysis reactions of either cyclopropylcarbinyl, cyclobutyl[8] or homoallyl derivatives[9] are accelerated and yield, regardless of the starting material, the same product mixtures consisting of about the same amounts of cyclopropylcarbinyl and cyclobutyl compounds with a small amount of homoallyl compounds.

If the release of steric strain is invoked as the cause of the extremely high solvolytic reactivity of cyclopropylcarbinyl derivatives,[4] then a separate explanation is needed for rate enhancement and product distributions observed in solvolyses of cyclobutyl and homoallyl derivatives. Moreover, the large proportion of cyclopropylcarbinyl products formed in competition with less strained cyclobutyl and homoallyl products rules out the release of steric strain as a driving force in solvolysis of these compounds.[9]

A mechanistic interpretation postulating an equilibrating set of classical cyclopropylcarbinyl, cyclobutyl and homoallyl cations as intermediates in these reactions,[4] implicitly assumes a similar high stability of all these three ions. In order to make such a mechanism plausible, a separate explanation for the stability of each of the three ions must be given. As long as this has not been done, every mechanistic explanation must postulate the same highly stabilized intermediate common to reactions of cyclopropylcarbinyl, cyclobutyl and homoallyl derivatives. From this intermediate, by principle of microscopic reversibility, all observed products must arise. At present the best description of such an intermediate appears to be the bicyclobutonium ion V, proposed by Roberts *et al.*[10] In fact, an equilibrating mixture of three such ions must be assumed in order to accommodate all available experimental data.[10] The apparent resemblance of the latter to three equilibrating classical ions[4] is, in our opinion, purely formal and of no further consequence.

V

[4] H. C. Brown, *The Transition State*. Special Publ. No. 16, Chemical Society, London (1962).

[5] [a] H. C. Brown and F. J. Chloupek, *J. Amer. Chem. Soc.* **85**, 2322 (1963); H. C. Brown and H. M. Bell, *Ibid.* **85**, 2324 (1963); H. C. Brown, F. J. Chloupek and Min-Hon Rei, *Ibid.* **86**, 1247, 1248, 1246 (1964); H. C. Brown and H. M. Bell, *Ibid.* **86**, 5006, 5007 (1964); [b] H. C. Brown and H. M. Bell, *Ibid.* **86**, 5003 (1964); H. C. Brown and Min-Hon Rei, *Ibid.* **86**, 5004, 5008 (1964); [c] W. Hückel, *J. Prakt. Chem.* **28**, 27 (1965), H. C. Brown, K. J. Morgan and F. J. Chloupek, *J. Amer. Chem. Soc.* **87**, 2137 (1965).

[6] E. J. Corey and Hisashi Uda, *J. Amer. Chem. Soc.* **85**, 1788 (1963).

[7] For a general review see R. Breslow *Molecular Rearrangements* (Edited by P. deMayo) Interscience, New York (1963).

[8] J. D. Roberts and R. H. Mazur, *J. Amer. Chem. Soc.* **73**, 2509 (1951).

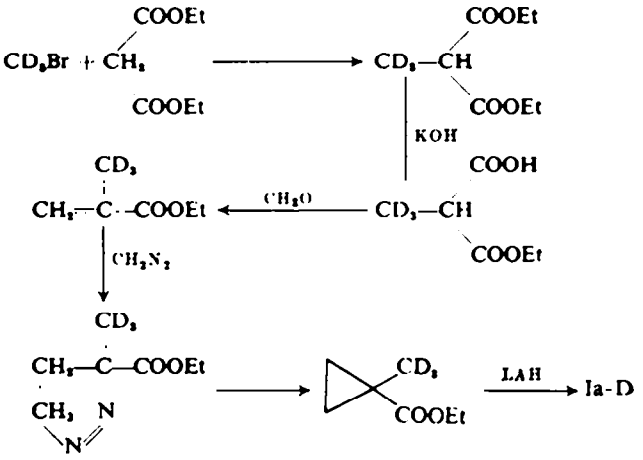
[9] K. L. Servis and J. D. Roberts, *J. Amer. Chem. Soc.* **86**, 3773 (1964).

[10] R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver and J. D. Roberts, *J. Amer. Chem. Soc.* **81**, 4390 (1959); E. Renk and J. D. Roberts, *Ibid.* **83**, 878 (1961); M. C. Caserio, W. H. Graham and J. D. Roberts, *Tetrahedron* **11**, 171 (1960).

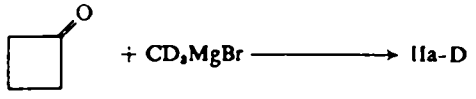
RESULTS

The carbinols Ia-D–IVa-D were prepared according to schemes 1–4.

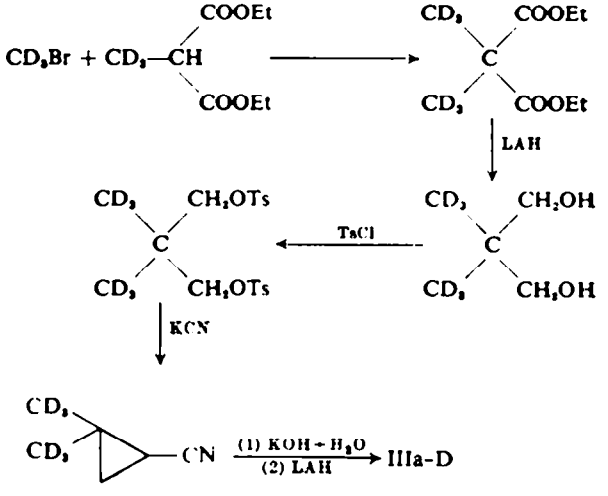
Scheme 1



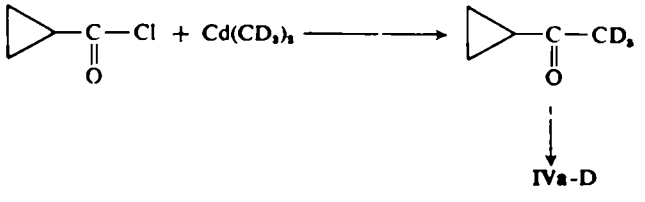
Scheme 2



Scheme 3



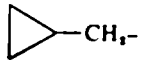
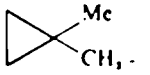
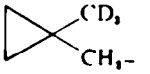
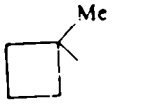
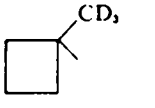
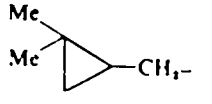
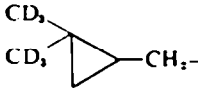
Scheme 4



From the carbinols, methanesulfonates Ib, IIb, IIIb and chlorides Ic-H, IIc and IVc were prepared. The solvolysis rates of these derivatives were followed by continuous automatic titration of the liberated acid by means of a pH-stat. In the calculation of the average rate constant and uncertainty limits, every individual rate constant calculated from 20–30 points on the titration curve, was taken as one measurement. The results, given in Tables 1 and 2, represent an average of 3–8 measurements with different samples.

All reactions were first order up to 85–90% completion except for solvolyses of (1-methylcyclopropyl)carbinyl mesylates and chlorides. For the former derivatives

TABLE 1. SOLVOLYSIS RATES OF SOME METHANESULFONATES IN 96% ETHANOL AT 20·0°[a]

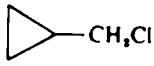
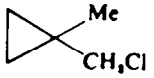
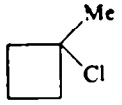
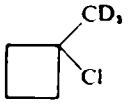
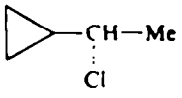
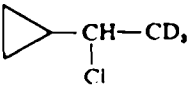
R—OSO$_2$Me R =	$k \cdot 10^4$(sec^{-1})	k_H/k_D
	0·610 ± 0·008	
	2·883 ± 0·025[b]	1·007 ± 0·009
	2·863 ± 0·011[b]	
	4·32 ± 0·10[c] 4·53 ± 0·008	1·068 ± 0·045
	4·24 ± 0·19[c]	
	58·2 ± 0·18	0·983 ± 0·005
	59·2 ± 0·23	

[a] Uncertainties are standard errors.

[b] Calculated from the initial slope of the titration curves, see text.

[c] Calculated from the last portion (after 95% reaction) of the titration curve in the reaction of the corresponding (1-methylcyclopropyl)carbinyl mesylate, see text.

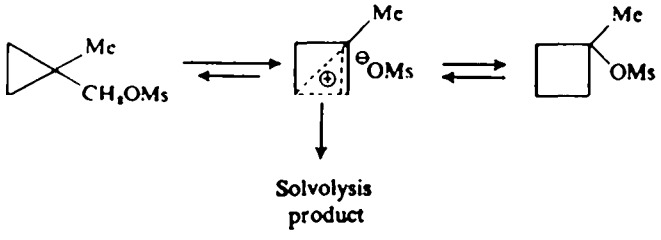
TABLE 2. SOLVOLYSIS RATES OF SOME CHLORIDES[a]

Compound	Reaction conditions	$k \cdot 10^4$(sec^{-1})	k_H/k_D
	50% EtOH, 50·0°	1·25[b]	
	50% EtOH, 50·0°	12·08[c]	
	50% EtOH, 50·0°	8·313 ± 0·05	1·092 ± 0·007
	50% EtOH, 50·0°	7·610 ± 0·03	
	50% EtOH, 20·0° 96% EtOH, 40·0°	520 ± 50 26·32 ± 0·08	1·178 ± 0·005
	96% EtOH, 40·0°	22·35 ± 0·10	

[a] Uncertainties are standard errors.
[b] See Ref. 8.
[c] Calculated from the initial slope of the titration curves, see text.

the specific rate showed an upward drift, for the latter a downward drift as the reactions proceeded. In both cases it was observed that the last 5% of the reacting mesylate or chloride solvolysed according to a strictly first order law with a rate constant identical to that of the corresponding 1-methylcyclobutyl derivative. From analogies[3,10] it was therefore concluded that a concurrent internal rearrangement occurs during solvolysis (Scheme 5). The solvolysis rate constants of Ib and Ic were therefore calculated graphically by measuring the initial slopes of the titration curves.

Scheme 5

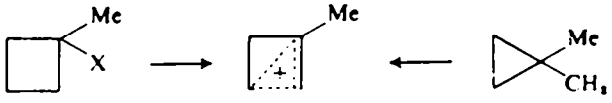


DISCUSSION

Substituent effects

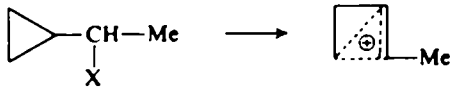
In solvolysis of compounds which give charge localized carbonium ions, methyl substitution at the reaction center produces a rate enhancement of the order of 10^4–$10^{6.5}$[b] (e.g. the solvolysis of 1-methylcyclopentyl chloride is ~28·000 times faster than that of cyclopentyl chloride[11]).

The fact that a much smaller methyl group rate effect was observed in solvolysis of 1-methylcyclobutyl chloride *vs.* cyclobutyl chloride (130:1) was considered by Roberts[11] as consistent with the formation of the bicylobutonium ion. Assuming that the reactivity of cyclobutyl derivatives is enhanced due to charge delocalization, the cationic intermediate VI (and the transition state) can only be stabilized by a methyl group to that extent by which stabilization through charge delocalization is reduced. A balance of both factors therefore accounts for the observed small methyl group rate effect in II.



II VI I

In an analogous manner it is possible to rationalize the comparatively small rate enhancement observed in solvolysis of 1-cyclopropylethyl chloride relative to cyclopropylcarbinyl chloride (Table 3).



IV VII

However, based on the assumption that the positive charge in V is fairly evenly distributed over carbon atoms 1, 2 and 3, it was predicted[11] that methyl substitution on ring position 1 (I) should result in an appreciable enhancement of solvolytic reactivity of cyclopropylcarbinyl compounds "since the greater contribution of the cyclobutyl structure in intermediate VI relative to V constitutes a greater driving force for the reaction".[11] By an extension of this reasoning, methyl substitution on ring position 2 (III) should predictably also result in a large rate acceleration. Moreover, the rate effect of a methyl group at the carbinyl position (IV) should presumably be smaller than at the ring position 1 (I) because the larger contribution of the more strained and secondary cyclopropylcarbinyl structure in intermediate VII relative to V constitutes less of driving force than the greater contribution of the less strained and tertiary cyclobutyl structure in intermediate VI relative to V.

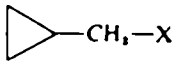
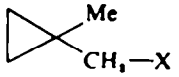
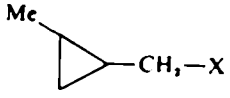
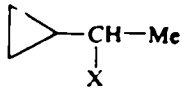
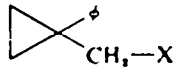
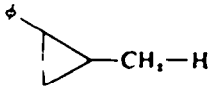
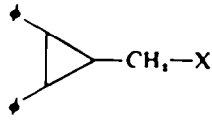
In fact all these predictions are contradicted by experiment,[12,13] as seen from Table 3. Although relatively small, the largest acceleration is found to be produced

[11] E. F. Cox, M. C. Caserio, M. S. Silver and J. D. Roberts, *J. Amer. Chem. Soc.* **83**, 2719 (1961).

[12] The large rate constant reported in Ref. 11 for the solvolysis of (1-methylcyclopropyl)carbinyl chloride ($k = 6{\cdot}9 \cdot 10^{-5}$ sec^{-1} in 50% EtOH at 30°) could not be reproduced.

[13] D. D. Roberts, *J. Org. Chem.* **29**, 294 (1964).

TABLE 3. RELATIVE SOLVOLYSIS RATES

Compound	X = Cl 50% EtoH	X = OSO_2Me 96% EtOH
	1[a]	1
	9·7	4·7
	20·2[b,c]	9·8[c]
	4160	2020[c]
	1·3[d]	
	0·64 (*cis*)[e] 2·20 (*trans*)[e]	
	0·3[f]	

[a] Ref. 8.

[b] Calculated, ignoring the stereochemistry of the methyl substituent, as the square root of the effect produced by *gem*-dimethyl group.

[c] Calculated using the data obtained with (1-methylcyclopropyl) carbinyl derivatives.

[d] Benzenesulfonates in anhydl. EtOH. J. W. Wilt and D. D. Roberts, *J. Org. Chem.* **27**, 3430 (1962).

[e] Naphthalenesulfonates in 90% dioxan. R. A. Sneen, K. M. Lewandowsky, I. A. I. Taha and B. R. Smith, *J. Amer. Chem. Soc.* **83**, 4843 (1961).

[f] *trans,trans*-compound benzenesulfonate and tosylate ($k_{ROTs}/k_{ROSO_2PH} = 0·6$) in anhydl. EtOH. R. Breslow, J. Lockhart and A. Small, *J. Amer. Chem. Soc.* **84**, 2793 (1962).

through the methyl group at the carbinyl position (IV), the smallest at the ring position 1(I) and intermediate at the ring position 2(III).[14]

Therefore, we must conclude that the predictions based upon concepts derived from studies of substituent rate effects in classical system, fail when applied to cyclopropylcarbinyl system. The use of "classical" criteria should certainly be applied with great caution when dealing with "non-classical" systems.[5b,6]

An even more dramatic example of this is provided by studies of phenyl group substituent effects.

If methyl substitution on the ring produces only small rate enhancement in solvolysis of cyclopropylcarbinyl compounds, the effect of an analogous phenyl substitution is practically nil or even inverse (Table 3). Thus a *gem*-dimethyl group at ring position 2 produces a 100-fold rate enhancement while the effect of one phenyl group at the same position is only 0·6–2·2 (Table 3). This shows clearly that the empirical rule that a phenyl group stabilizes a carbonium ion about as well as two methyl groups[15] does not apply here. Obviously, with respect to substituent rate effects, the ring position cannot be considered as analogous to the reaction center in solvolysis proceeding through classical carbonium ions.[14]

An explanation of the observed phenyl group effects inevitably necessitates some speculations and the following rationale can be suggested.

The usual favorable effect of a phenyl substituent on solvolysis reactions is due to combination of two factors, a rate retarding, electron withdrawing inductive effect and a rate enhancing effect due to conjugative stabilization of the incipient positive charge. Usually, the latter factor heavily outweighs the former and an overall large rate acceleration is observed. However, in solvolyses of (phenylcyclopropyl)carbinyl derivatives, the geometry of the transition state (leading to intermediates cognate to V) may not be favorable for the full operation of the conjugative effect. The very small rate changes therefore result from the cancellation of the conjugative effect by the stereoelectronically independent inductive effect.

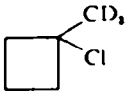
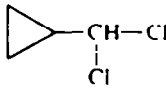
Analogous reasoning applies to methyl substituent rate effects. A methyl substituent acts through inductive and hyperconjugative electron release—both factors favorable to solvolysis rate. In the cases under discussion, if conjugation with a phenyl group fails to stabilize the transition state relative to ground state to any appreciable degree, much less stabilization can be expected through hyperconjugation with a methyl group.

Therefore, the small but significant rate enhancements observed in solvolysis of

[14] K. L. Servis and J. D. Roberts, *J. Amer. Chem. Soc.* **87**, 1331 (1965) report solvolysis rates of several methyl substituted homoallyl tosylates. The relative rate enhancements correspond to those observed with cyclopropylcarbinyl compounds substituted at the analogous carbon atoms. These authors have explained their results in terms of differences in structure between the solvolysis transition state (homoallylic ion-like) and the intermediate (bicyclobutonium ion). In our opinion a similar interpretation may also be valid for solvolyses of cyclopropylcarbinyl derivatives. A homoallylic ion and a bicyclobutonium ion are related and one can imagine structures intermediate between these two extremes that may serve as models for transition states in solvolyses of cyclopropylcarbinyl derivatives as in accordance with Hammond's postulate. It should also be pointed out that although the bicyclobutonium ion seems to be a good representation of the intermediate formed in solvolysis of unsubstituted cyclopropylcarbinyl derivatives, this may not be the case for some substituted derivatives (such as e.g. IIIb and c or tricyclopropyl carbinyl benzoate).

[15] A. Streitwieser, Jr., *Solvolytic Displacement Reactions* p. 43. McGraw-Hill, New York (1962).

TABLE 4. KINETIC ISOTOPE EFFECTS IN SOME UNIMOLECULAR SOLVOLYSES OF β-DEUTERATED COMPOUNDS

Compound	Reaction conditions	k_H/k_D	k_H/k_D per atom D (corrected)
	50% EtOH, 50°	1·09[a]	1·029
$CD_3C(Me_2)_2$ Cl	60% EtOH, 25°	1·33[b]	1·100
$(CD_3)_2C\,CH_3$ Cl	60% EtOH, 25°	1·71[b]	1·102
$(CD_3)_2C—Cl$	60% EtOH, 25°	2·33[b]	1·103
t-Bu—CH_2—C(Me)(Cl)—CD_3	80% EtOH, 25°	1·40[c]	1·139
t-Bu—CD_2—$C(Me)_2$ Cl	80% EtOH, 25°	1·08[c,d]	1·046
$EtCD_2CH—CD_3$ OTs	HCOOH, 24·9°	1·73[e]	1·136
	96% EtOH, 40°	1·18[e]	1·057

[a] This work

[b] V. J. Shiner, Jr., B. L. Murr and G. Heineman, *J. Amer. Chem. Soc.* **85**, 2413 (1963).

[c] Ref. 18.

[d] Here, the conformation of the transition state should be unfavorable to hyperconjugative electron release from the CD bonds because of steric requirements. See Ref. 18.

[e] E. S. Lewis and C. E. Boozer, *J. Amer. Chem. Soc.* **76**, 791 (1954). Several cases of smaller kinetic isotope effects in solvolyses of secondary β-deuterated compounds have been reported. However, the reduced isotope effect in such reactions is probably only a reflection of the non-limiting character of the reaction mechanism. Thus, the above compound displays an isotope effect (k_H/k_D) of only 1·40 in the reaction with 80% ethanol.

I and III can be ascribed to the inductive effect of methyl groups in the absence of the usual hyperconjugative stabilization of the incipient positive charge in the transition state.

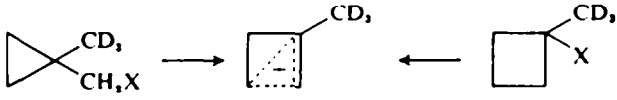
Some evidence for such a conclusion is found in the results obtained with methyl-d_3 substituted derivatives.

Isotope effects

In a skillfully planned and conducted series of experiments Shiner and collaborators provided strong evidence for the hyperconjugative origin of secondary kinetic β-deuterium isotope effects.[16] In addition recent work of this group clearly establishes the conformational dependence of this effect.[17,18]

If the solvolysis of I-D proceeds via a transition state of structure VI-D a certain amount of positive charge should be located on the carbon atom adjacent to the CD_3 group. The same should be the case for the solvolysis of III-D.

The fact that no kinetic isotope effect could be observed in solvolysis of either III-D or I-D is consistent with the conclusion reached on basis of substituent effects; namely that, in these cases the hyperconjugative electron release from the CD_3 group is negligible.



I-D VI-D II-D

A strong indication that the charge delocalization in the nonclassical intermediate V reduces the hyperconjugative electron release from a methyl substituent is provided by the observation that *the* 1-*methyl-d_3-cyclobutyl chloride* (IIc-D) *and methyl-d_3 cyclopropylcarbinyl chloride* (IVc-D) *display only one-fourth and one-half, respectively, of the usual kinetic isotope effect upon solvolysis.* Both compounds bear deuterium at the carbon β to the leaving group. The usual rate retardation in solvolysis of similarly β-deuterated compounds amount to 10–15% per atom deuterium. (Table 4.)

However, instead of an expected isotope effect of 30–40% compounds IIc-D and IVc-D display a rate retardation of only 9% and 18% respectively. On the basis of these results we suggest the possibility of using secondary β-deuterium effect as a criterion for neighboring group participation.

EXPERIMENTAL[19]

Diethyl methyl-d_3-malonate (VIII).[20] The reaction of diethyl malonate (48 g, 0·3 mole) with Na (6·9 g, 0·33 mole) and methyl-d_3-bromide[21] (31 g, 0·316 mole) gave 39 g (73%) of the product, b.p.

[16] For a recent review see E. A. Halevi, *Secondary Isotope Effects in Progress in Physical Organic Chemistry* Vol. 1. Wiley, New York (1963).

[17] V. J. Shiner, Jr. and J. S. Humphrey, Jr., *J. Amer. Chem. Soc.* **85**, 2416 (1963).

[18] V. J. Shiner and J. G. Jewett, *J. Amer. Chem. Soc.* **86**, 945 (1964).

[19] The purity of volatile products was checked by VPC. IR spectra: Perkin–Elmer 221 grating spectrometer; NMR spectra: Varian A-60 instrument. If not stated otherwise, the prep of deuterated materials was performed in the same manner as described in the literature for the undeuterated compound.

[20] *Organic Syntheses* Coll. Vol. II; p. 279, Wiley, New York (1948).

[21] M. Nikoletić, *Croat. Chem. Acta* **36**, 43 (1964).

82·5–84·5°/11 mm. The product contained 9% of unreacted diethyl malonate and traces of diethyl dimethyl-d_6-malonate.

Ethyl methyl-d_3-malonate (IX).[33] Compound VIII (37 g) was partially saponified with KOH in abs EtOH. After work up and distillation the yield of the product was 23·4 g (75%), b.p. 138–139°/16 mm, n_D^{20} 1·4165.

Ethyl 2-methyl-d_3-acrylate (X).[33] Compound IX (23·4 g) with Et_2NH (11·5 g) and HCHO (17 g of 36% soln) yielded after distillation 14 g (76%) of the pure product.

Ethyl (1-methyl-d_3-cyclopropane)carboxylate (XI).[34] The reaction of X (14 g) with diazomethane (from 18 g nitrosomethylurea) gave the corresponding pyrazoline in 90% yield. The crude, distilled, pyrolysis product (11·3 g) was subjected to ozonolysis in CH_2Cl_2 (30 ml) soln at −75°. The cyclopropane product and the solvent were then separated from the ozonide by flash distillation at 10^{-4} mm and 20°. After removing CH_2Cl_2 over a column, the residue was distilled *in vacuo* yielding XI (6·35 g, 57·8%) b.p. 132–136°/746 mm. The product contained 10% of CH_2Cl_2.

(1-Methyl-d_3-cyclopropyl)carbinol (Ia-D).[34] The reaction of XI (6·35 g) with LAH (2·0 g) and subsequent hydrolysis of the reaction mixture with 1·5 equivs water yielded after usual work up and fractional distillation 2·5 g (58%) of the product, b.p. 124–126°/744 mm. According to UPC and NMR spectra, the product was pure Ia-D containing more than 95% of the theoretical amount of deuterium.

Diethyl dimethyl-d_6-malonate (XII). Diethyl methyl-d_3-malonate (36·5 g) in benzene (1·1 l.) was added to a soln of EtONa (from 4·9 g Na) in anhyd EtOH (100 ml). EtOH was then removed through azeotropic distillation and methyl-d_3 bromide (26 g) introduced into the reaction mixture at room temp and under stirring. After stirring overnight, the reaction was completed by refluxing for 1 hr. After cooling, aqueous AcOH was added, the benzene layer separated, washed with water and dried over $MgSO_4$. Benzene was evaporated and the residue fractionated *in vacuo*. The yield of the pure product, b.p. 83–84°/12 mm, was 32·6 g (81·5%).

2,2-*Dimethyl-d_6*-1,3-*propanediol* (XIII). The reduction of XII (32·6 g) with LAH (11·0 g) carried out in the usual manner gave after distillation 15·9 g (86%) of pure XIII, b.p. 110–112°.

2,2-*Dimethyl-d_6*-1,3-*propanediol ditosylate* (XIV).[35] The reaction of XIII (15·9 g) with tosyl chloride (82·5 g) in dry pyridine gave quantitatively XIV (60 g), m.p. 118–120°.

(2,2-Dimethyl-d_6-cyclopropane)nitrile (XV).[35] The reaction of XIV (53 g) with KCN (24·8 g) in ethylene glycol gave 7·8 g (61%) of pure XV, b.p. 152–154°.

(2,2-Dimethyl-d_6-cyclopropane)carboxylic acid (XVI).[36] Hydrolysis of XV (7 g) with KOH (11 g) in water (35 ml) gave 6·8 g (82%) pure XVI, b.p. 97°/13 mm.

(2,2-Dimethyl-d_6-cyclopropyl)carbinol (IIIa-D). The reduction of XVI (6·5 g) with LAH (2·3 g) in the usual manner yielded 5·3 g (92·5%) IIIa-D, b.p. 55°/14 mm. According to VPC, IR and NMR spectra the product was pure IIIa-D containing more than 95% of the theoretical amount of deuterium.

1-*Methyl-d_3-cyclobutanol* (IIa-D).[34] The reaction of cyclobutanone (5 g) with methyl-d_3 magnesium bromide (from 9·8 g methyl-d_3 bromide and 2·53 g Mg) in ether (50 ml) and subsequent hydrolysis yielded 5·3 g (87%) of the pure product, b.p. 116–120°. According to VPC, IR and NMR spectra the product was pure IIa-D and contained more than 95% of the theoretical amount of deuterium.

Cyclopropyl methyl-d_3 ketone (XVII). This product was prepared by the published procedure for the preparation of methyl cyclobutyl ketone.[37] The reaction of dimethyl-d_6 cadmium (prepared from 2·72 g Mg, 13·0 g of methyl-d_3 bromide and 10·2 g $CaCl_2$ in 60 ml ether) with cyclopropanecarboxylic acid chloride (8·2 g) and hydrolysis of the reaction product with 10 ml heavy water yielded, after work up and distillation, 4·5 g (65·5%) XVII, b.p. 108–112°, $n_D^{20.6}$ 1·4218.

1-*Cyclopropylethanol-2-d_3* (IVa-D). The reduction of XVII (4·5 g) with LAH (0·8 g) carried out in the usual way yielded 3·6 g (72%) of the product, n_D^{19} 1·4235. According to VPC, IR and NMR spectra the product was pure IVa-D containing more than 95% of the theoretical amount of deuterium.

Methanesulfonates. The general procedure for the preparation of the mesylates is illustrated on

[33] H. Aebli and C. A. Grob, *Helv. Chim. Acta* **40**, 2185 (1957).
[34] C. Mannich and K. Ritsert, *Ber. Dtsch. Chim. bis.* **57**, 1116 (1924).
[35] S. Siegel and C. G. Bergstrom, *J. Amer. Chem. Soc.* **72**, 3815 (1950).
[36] E. R. Nelson, M. Maienthal, L. A. Lane and A. A. Benderly, *J. Amer. Chem. Soc.* **79**, 3467 (1957).
[37] D. Semenow, E. Cox and J. D. Roberts, *J. Amer. Chem. Soc.* **78**, 3221 (1956).
[37] R. Pinson, Jr. and S. L. Friess, *J. Amer. Chem. Soc.* **72**, 5333 (1950).

the following example. To a stirred solution of the carbinol (1·0 g, 0·0116 mole) in CH_2Cl_2 (1 ml) and anhydrous pyridine (1·6 ml) at 0° was added during 2 hr methanesulfonyl chloride (1·3 g, 0·0116 mole) in CH_2Cl_2 (1 ml). After stirring the mixture for additional 2 hr at 0°, 2 ml of cold CH_2Cl_2 was added and the soln washed 3 times with 4 ml ice water, 4 ml 2% Na_2CO_3aq (at 0°) and again with 4 ml ice water. After drying over K_2CO_3 the solvent was evaporated *in vacuo* at 0°.

According to IR and NMR spectra and titration equivs, all mesylates were free from isomeric compounds and contained 2–4% of unesterified carbinol and traces of pyridine as the only impurities.

(1-Methylcyclopropyl)carbinyl chloride. To a stirred soln of (1-methylcyclopropyl)carbinol (6·0 g, 0·07 mole)in tri-n-butylamine (13·0 g, 0·07 mole) and di-n-butyl ether (9·2 g) at −10° $SOCl_2$ (8·32 g, 0·07 mole) was added during 4 hr. The mixture was stirred for an additional 0·5 hr at −5° and 1 hr at 0–10°. Low boiling materials were then flash-distilled at and 10^{-4} mm, washed with a cold, 10% Na_2CO_3aq, and dried overnight with Na_2CO_3. Fractional distillation yielded 5 g (68·5%) of product, b.p. 86–95°, containing 53% (1-methylcyclopropyl)chloride and 44% of 1-methylcyclobutyl chloride. The separation of the chlorides was accomplished through preparative VPC on a Perkin Elmer 154 fractometer with a 3 m. 3/8" polyethyleneglycol column at 80° (carrier gas H at 240 ml/min). After distillation each chloride was pure and free from the other isomer, as shown by IR and NMR spectra.

1-Methyl-d_3-cyclobutyl chloride. The reaction of 1-methyl-d_3-cyclobutanol (3 g) with $SOCl_2$ carried out as described for (1-methylcyclopropyl)carbinol gave, after purification through preparative VPC and distillation, 2·3 g (64%) pure 1-methyl-d_3-cyclobutyl chloride.

1-Cycolpropylethyl chloride-2-d_2.[28] The reaction of 1-cyclopropylethanol-2-d_2 (1·26 g) with PCl_5 (2·90 g) in pentane (15 ml) yielded 0·76 g (50%) pure chloride.

Kinetic measurements. Solvolysis rates were followed by potentiometric titration of the liberated acid using an automatic recording pH-stat (Radiometer, Kopenhagen, Type TTT-1). Approximately 12 ml of solvent and 50 mg samples were used for each determination.

[28] M. Hanack und H. Eggensperger, *Liebigs. Ann.* 663, 31 (1963). In this Ref. 27·5 g (0·1 mole PCl_5) should read 20·8 g (0·1 mole) PCl_5.