[CONTRIBUTION FROM THE "RUDJER BOŠKOVIĆ" INSTITUTE, ZAGREB, YUGOSLAVIA]

# Secondary Hydrogen Isotopes Effects. IV. Solvolysis Rates of Specifically Deuterium Labeled Cyclopropylmethyl Benzenesulfonates[1]

BY STANKO BORČIĆ, MARIJA NIKOLETIĆ AND DIONIS E. SUNKO

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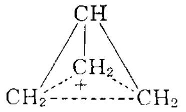
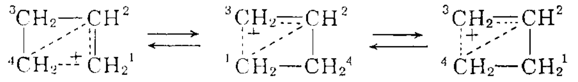
The synthesis of cyclopropylmethyl-1,1-$d_2$, -2-$d$, -3,3-$d_2$ and -3,3,4,4-$d_4$ benzenesulfonates is described. Acetolysis and ethanolysis rates were measured and it was found that the first two compounds solvolyze more slowly and the last two more rapidly than the undeuterated analogs. It was also found that the isotope effects are more pronounced in ethanolysis and that the rate increase per atom deuterium is larger with the dideuteriated than with the tetradeuteriated compound. The results are discussed in terms of rehybridization, hyperconjugation and induction and are found to be consistent with the solvolysis mechanism postulating the participation of the neighboring cyclopropyl group in the rate-determining step with the formation of a "bicyclobutonium" ion.

In the solvolysis reactions of cyclopropylmethyl derivatives a pronounced rate enhancement has been observed.[2-4] In an attempt to correlate the unusual solvolytic reactivity with the extensive rearrangements which take place in SN1 type reactions of cyclopropylmethyl derivatives,[5] various mechanisms have been proposed all of them involving the participation of the neighboring cyclopropyl group in the rate-determining step. Much attention has been given to the possible structure of the resulting non-classical carbonium ion intermediate. Thus, Bergstrom and Siegel[4] proposed a symmetrical "tricyclobutonium" ion structure (I). Roberts, *et al.*,[3,6,7] have shown that the formation of an equilibrating mixture of "bicyclobutonium" ions (IIa-c) account better for the experimental observations.



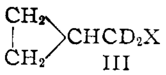
I



IIa IIb IIc

Some implications of a mechanism involving intermediates like I or II are: (1) If the transition state of the reaction resembles I then all methylene carbon atoms become equivalent in the intermediate. (2) If IIa is formed in the rate-determining process, then a partial positive charge is generated on carbon atoms 1, 2 and 4 with the consequence that carbon atoms 3 and 4 loose their equivalency.

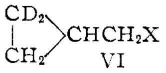
The purpose of this work was to investigate if such changes on different carbon atoms could be depicted by the measurement of the secondary deuterium kinetic isotope effect.[8-10] Therefore, compounds IIIb–VIb were prepared and their solvolysis rates determined. By this experiment it was hoped to achieve a deeper insight into the structure of the intermediate formed after the transition state and to gain some additional knowledge about the secondary hydrogen isotopes effects.[11]



III

IV

V



VI

a, X = OH; b, X = $O_3S$-Ph

## Synthetic Procedures

Cyclopropylcarbinol (IIIa) was obtained by lithium aluminum deuteride reduction of the corresponding carboxylic acid. The carbinols IVa, Va and VIa were prepared according to the following schemes.

Scheme 1

$$\begin{tikzcd}
 & \mathrm{ClCH_2CH_2COOCH_3} \arrow[r, "\mathrm{LiAlD_4 + AlCl_3}"] & \mathrm{ClCH_2CH_2CD_2OH} \arrow[d, "\mathrm{1,\ PBr_3}"', "\mathrm{2,\ KCN}"] \\
 & \mathrm{IVa} & \mathrm{ClCH_2CH_2CD_2CN} \arrow[l, "\mathrm{1,\ NaOD + D_2O}"', "\mathrm{2,\ LiAlH_4}"]
\end{tikzcd}$$

Scheme 2

$$\begin{tikzcd}
\mathrm{CH_3OOC{-}C{\equiv}C{-}COOCH_3} \arrow[r, "\mathrm{D_2 + Pt}"] & \mathrm{CH_3OOCCD_2CD_2COOCH_3} \arrow[d, "\mathrm{1,\ H^+ + H_2O}"', "\mathrm{2,\ CH_3OH}\ \mathrm{3,\ AgNO_3}"] \\
\mathrm{ClCD_2CD_2COOCH_3} \arrow[d, "\mathrm{1,\ LiAlH_4 + AlCl_3}"', "\mathrm{2,\ PBr_3}\ \mathrm{3,\ KCN}"] & \mathrm{AgOOCCD_2CD_2COOCH_3} \arrow[l, "\mathrm{Cl_2}"'] \\
\mathrm{ClCD_2CD_2CH_2CN} \arrow[r, "\mathrm{1,\ KOH + H_2O}", "\mathrm{2,\ LiAlH_4}"'] & \mathrm{Va}
\end{tikzcd}$$

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[1] Presented in part at the First Yugoslav Congress of Pure and Applied Chemistry, Zagreb, June, 1960; paper III of this series, S. Borčić, V. Belanić-Lipovac and D. E. Sunko, *Croat. Chem. Acta*, **33**, 35 (1961).

(2) J. D. Roberts and R. H. Mazur, *J. Am. Chem. Soc.*, **73**, 2509 (1951).

(3) M. C. Caserio, W. H. Graham and J. D. Roberts, *Tetrahedron*, **11**, 171 (1960).

(4) C. G. Bergstrom and S. Siegel, *J. Am. Chem. Soc.*, **74**, 145 (1952).

(5) For references see A. Streitwieser, Jr., *Chem. Revs.*, **56**, 710 (1956).

(6) R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 4390 (1959).

(7) E. F. Cox, M. C. Caserio, M. S. Silver and J. D. Roberts, *ibid.*, **83**, 2719 (1961).

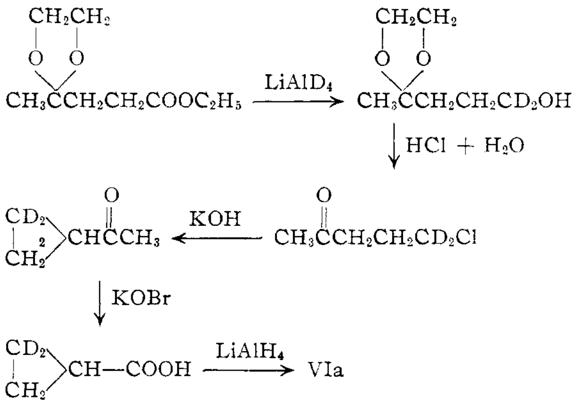
(8) W. H. Saunders, Jr., S. Ašperger and D. H. Edison, *ibid.*, **80**, 2421 (1958).

(9) A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey and S. Suzuki, *ibid.*, **80**, 2326 (1958).

(10) K. Mislow, S. Borčić and V. Prelog, *Helv. Chim. Acta*, **40**, 2477 (1957).

(11) For preliminary communications see (a) S. Borčić, M. Nikoletić and D. E. Sunko, *Chemistry & Industry*, 527 (1960); (b) S. Borčić and D. E. Sunko, *J. Am. Chem. Soc.*, **83**, 2777 (1961).

Scheme 3



## Results

The benzenesulfonates were subjected to acetolysis and ethanolysis and the reaction rates measured titrimetrically. The results are summarized in Tables I and II. A rate decrease was observed with the compounds labeled with deuterium in the α- or β-positions (IIIb and IVb) while the deuteriation of the ring methylene carbon atoms caused a rate increase (Vb and VIb).[12] The isotope effect per atom D was calculated in all cases and is given in Table III.

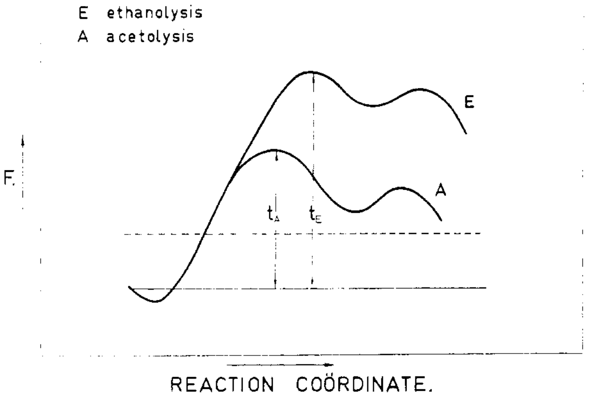


Fig. 1.—Free energy curves for the acetolysis and ethanolysis of cyclopropylmethyl benzenesulfonates.

Based on the statistical analysis of the results (see Experimental) the following conclusions have been reached: (1) The rate decrease with IIIb is larger in ethanolysis than in acetolysis (92% confidence). (2) The rate increase with Vb and VIb is more pronounced in ethanolysis than in acetolysis (95, resp. 97.5% confidence). (3) In the ethanolysis the isotope effect per atom D is larger with VIb than with Vb (99.5% confidence).

In the acetolysis reaction a large difference of the "infinity titers" at 100 and at 20.0° was observed in all cases. This could be due to the presence of relatively unreactive rearranged benzenesulfonates in the starting material and/or to the formation of such species during the reaction. The purities of the starting materials were therefore checked by ethanolysis where a rearrangement to less reactive benzenesulfonates during the reaction does not occur.[4] Thus, an "internal return" rearrangement during the acetolysis reaction could clearly be established. This concurrent reaction accounts for about one-third of all the products. Experimental observations concerning this rearrangement and a discussion of the results are given elsewhere.[13]

## Discussion

Although at the present the theory of secondary deuterium isotope effects is still quite fluid, there is a prevailing agreement that they are mainly due to three causes; *i.e.* (1) rehybridization,[9] (2) hyperconjugation[14,15] of the carbon–hydrogen carbon–deuterium bonds, respectively, and (3) the electron-releasing inductive effect of deuterium.[16,17] Some of these factors may act jointly either in the same or in the opposite direction and it is sometimes difficult or impossible to establish their relative importance. Here lies the main difficulty in interpreting any results based upon the measurement of the secondary deuterium isotope effect.

According to Streitwieser, *et al.*,[9] the rate retardation which occurs in solvolysis reactions when hydrogen on the reactive carbon is replaced by deuterium is due to vibrational changes associated with the $sp^3$–$sp^2$ rehybridization of the carbon–hydrogen (deuterium) bonding orbitals in the rate-determining process. The isotope effect occurring in the solvolyses of IIIb can be ascribed to such a rehybridization. If the magnitude of the rate depression can be considered as indicative of the amount of corresponding rehybridization in the transition state, then the larger isotope effect in ethanolysis than in acetolysis can be well understood. The transition state in the acetolysis as the faster reaction will resemble more the starting material than in the slower ethanolysis, as shown diagrammatically in Fig. 1.[18] Thus, the carbon–deuterium bonding orbitals will be nearer to $sp^3$-hybrids in the transition state of the former than of the latter reaction.[19,20]

The isotope effect observed in the acetolysis of IVb could be analogous to those observed in many cases when hydrogen on the carbon atom β to the leaving group is replaced by deuterium.[21–23] These

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[12] It was reported[11] that no isotope effect occurs in the solvolysis of Vb. However, this first set of measurements (Table I, result 6, Table II, result 7) was found to be inadequate because of the large error, especially as the results had to be compared with the more accurate measurements of the $k_H/k_D$ values with VIb. Therefore, Vb was resynthesized and its ethanolysis rate constant determined more precisely. An isotope effect of 6.3% was found to occur. This result is in the ±2*s* range of the first set of measurements.

[13] S. Borčić and D. E. Sunko, *Croat. Chem. Acta*, **33**, 77 (1961).

[14] V. J. Shiner, Jr., *Tetrahedron*, **5**, 243 (1959).

[15] E. S. Lewis, *ibid.*, **5**, 143 (1959).

[16] E. A. Halevi, *Intern. J. Appl. Radiation and Isotopes*, **7**, 192 (1960).

[17] L. S. Bartell, *Tetrahedron Letters*, **6**, 13 (1960).

[18] Recently, L. S. Bartell, *J. Am. Chem. Soc.*, **83**, 3567 (1961), has pointed out that secondary α- and β-deuterium isotope effects may partly be due to the relief of non-bonded repulsions during the formation of the carbonium ion intermediate. If this were the case, the rate retardation in the ethanolysis of IIIb, for reasons similar to those given above, would also be expected to be more pronounced than in acetolysis. The isotope effect in the acetolysis of IVb could possibly also be partly ascribed to steric repulsions.

[19] A. Streitwieser, Jr., *Chem. Revs.*, **56**, 638 (1956).

[20] G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

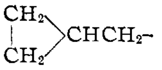
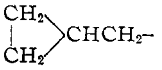
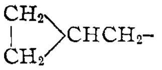
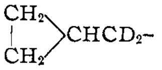
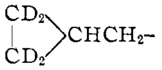
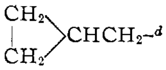
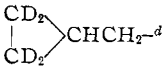
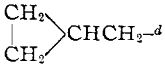
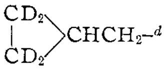
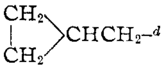
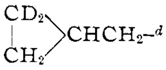
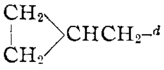
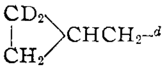
[21] E. S. Lewis and C. E. Boozer, *ibid.*, **76**, 791(1954).

[22] V. J. Shiner, Jr., *ibid.*, **75**, 2925 (1953).

[23] N. Ilakovac and S. Ašperger, *Chemistry & Industry*, 1191 (1960).

TABLE I

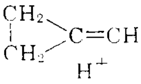
ETHANOLYSIS RATES OF DEUTERIATED CYCLOPROPYLMETHYL BENZENESULFONATES AT 20.0°

| Result | $RO_3SPh$ R = | Atoms D/molecule | Concn.,[a] mole/l. | $k \times 10^5$, sec.$^{-1}$ [b] | $k_H/k_D$ [b] |
|---|---|---|---|---|---|
| 1 |  | .. | 0.042 | 6.165 ± 0.030[c] | |
| 2 |  | .. | .038 | 6.325 ± .035[c] | |
| 3 |  | .. | .028 | 5.955 ± 0.30[c] | |
| 4 | | | Av. | 6.148 ± .108 | |
| 5 |  | 1.88 | .042 | 4.341 ± .036[c] | 1.416 ± 0.046 |
| 6 |  | 3.70 | .037 | 6.256 ± .029[c] | 0.983 ± 0.034 |
| 7 |  | .. | .034 | 5.806 ± .017 | .9383 ± 0.0054 |
| 8 |  | 3.70 | .032 | 6.188 ± .028 | .9385 ± .0046[e] |
| 9 |  | .. | .033 | 5.854 ± .025 | .9355 ± .0075 |
| 10 |  | 3.70 | .032 | 6.258 ± .038 | .9356 ± .0051[e] |
| 11 | | | | | .9371 ± .0034[f] |
| 12 |  | .. | .025 | 5.729 ± .010 | .9555 ± .0022 |
| 13 |  | 1.76 | .024 | 5.996 ± .009 | .9556 ± .0023[e] |
| 14 |  | .. | .032 | 5.802 ± .011 | .9579 ± .0028 |
| 15 |  | 1.76 | .032 | 6.057 ± .014 | .9579 ± .0026[e] |
| 16 | | | | | .9568 ± .0017[g] |

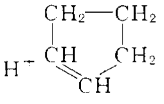
[a] Concentration of pure cyclopropylmethyl benzenesulfonate. [b] Uncertainties are standard errors. [c] At 20.1°. [d] Simultaneous measurement of $k_H$ and $k_D$. [e] Calculated by pairing the corresponding instant $k_H$ and $k_D$ values. [f] Mean of the $k_H/k_D$ values 8 and 10. [g] Mean of the $k_H/k_D$ values 13 and 15.

rate depressions have been attributed to hyperconjugative carbon–hydrogen (deuterium) bond weakening in the transition state of the reaction.[14,15]

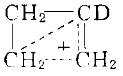
Shiner[14] has investigated the influence of substituents on the magnitude of the β-deuterium isotope effect and has shown that it is possible "to attribute the substituent influences on the isotope effect as being due to their stabilizing influences on the hyperconjugating resonance contributing forms." It is therefore possible to assume that the magnitude of the β-deuterium isotope effect will be determined by the amount of contribution of hyperconjugating structures to the intermediate formed after the transition state. In this respect one can expect that structure VII would contribute much less effectively to its mesomeric carbonium ion than, *e.g.*, structure VIII. Nevertheless, the isotope effect observed in the acetolysis of β-deuteriated cyclopentyl *p*-toluenesulfonate is about the same (per atom deuterium) as with IVb.[7] Consequently, hyperconjugation alone does not seem to explain the relatively large rate retardation observed in the acetolysis of IVb and at least a part of the isotope effect could be due to rehybridization.[18] Thus, the acetolysis rate of IVb indicates that the transition state of the reaction may be represented by IX.



VII



VIII



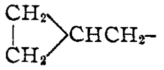
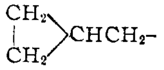
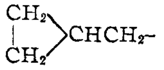
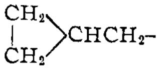
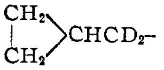
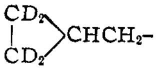
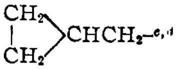
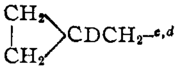
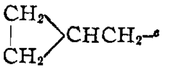
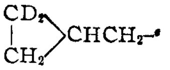
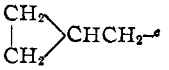
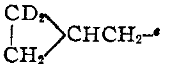
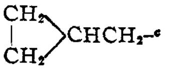
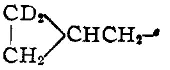
IX

The rate enhancement in the solvolyses of Vb and VIb could be due to the electron-releasing inductive effect of deuterium. Considering the proposed reaction mechanisms, deuterium induction can influence the rate in either one of the two following ways: (1) If the transition state of the solvolysis resembles a classical cyclopropylmethyl carbonium ion, then the rate increase observed with Vb and VIb can be explained by a looser bond to the leaving group in the reactant. In this case, the effect of deuterium induction would be in the destabilizing of the *ground state*.

(2) Deuterium in Vb and VIb induces a negative charge on the methylene carbon atoms in the ring. Thus, if a non-classical carbonium ion is formed in

TABLE II

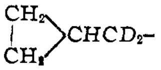
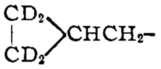
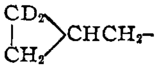
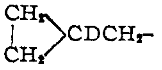
ACETOLYSIS RATES OF DEUTERIATED CYCLOPROPYLMETHYL BENZENESULFONATES AT 20.0°

| Result | $RO_3SPh$ R = | Atoms D/molecule | Concn.,[a] mole/l. | $k \times 10^4$, sec.$^{-1}$[b] | $k_H/k_D$[b] |
|---|---|---|---|---|---|
| 1 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$ | .. | 0.037 | 2.179 ± 0.023 | |
| 2 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$ | .. | .039 | 2.157 ± .030 | |
| 3 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$ | .. | .038 | 2.170 ± .016 | |
| 4 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$ | .. | .042 | 2.240 ± .012 | |
| 5 | | | Av. | 2.187 ± .019 | |
| 6 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCD_2-$ | 1.88 | .037 | 1.688 ± .009 | 1.296 ± 0.024 |
| 7 |  $\begin{matrix}CD_2\\ \vert\\ CD_2\end{matrix}\!>CHCH_2-$ | 3.70 | .033 | 2.220 ± .033 | 0.985 ± .019 |
| 8 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$[c,d] | .. | .028 | 2.451 ± .035 | 1.164 ± .020 |
| 9 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CDCH_2-$[c,d] | 0.88 | .023 | 2.106 ± .029 | 1.149 ± .015[e] |
| 10 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$[c] | .. | .048 | 2.179 ± .005 | .9633 ± 0.0057 |
| 11 |  $\begin{matrix}CD_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$[c] | 1.76 | .048 | 2.262 ± .012 | .9666 ± .0049[e] |
| 12 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$[c] | .. | .045 | 2.186 ± .009 | .09698 ± .0093 |
| 13 |  $\begin{matrix}CD_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$[c] | 1.76 | .045 | 2.254 ± .019 | .9701 ± .0058[e] |
| 14 |  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$[c] | .. | .045 | 2.205 ± .011 | .9888 ± .0059 |
| 15 |  $\begin{matrix}CD_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$[c] | 1.76 | .045 | 2.230 ± .008 | .9885 ± .0068[e] |
| 16 | | | | | .9751 ± .0068[f] |

[a] Concentration of pure cyclopropylmethyl benzenesulfonate. [b] Uncertainties are standard errors. [c] Simultaneous measurement of $k_H$ and $k_D$. [d] At 20.06°. Calculated by pairing the corresponding instant $k_H$ and $k_D$ values. [f] Mean of the $k_H/k_D$ values 11, 13 and 15.

TABLE III

ISOTOPE EFFECTS IN THE SOLVOLYSIS OF DEUTERIATED CYCLOPROPYLMETHYL BENZENESULFONATES IN PER CENT.

| $RO_3SPh$ R = | Ethanolysis | | Acetolysis | |
|---|---|---|---|---|
| | $(k_H/k_D - 1) \times 100$[a] | Per atom D[a,b] | $(k_H/k_D - 1) \times 100$[a] | Per atom D[a,b] |
|  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CHCD_2-$ | +41.6 ± 4.6 | +22.13 ± 2.72 | +29.6 ± 2.4 | +15.74 ± 1.52 |
|  $\begin{matrix}CD_2\\ \vert\\ CD_2\end{matrix}\!>CHCH_2-$ | −6.29 ± 0.34 | −1.70 ± 0.13 | −1.5 ± 1.9 | −0.41 ± 0.58 |
|  $\begin{matrix}CD_2\\ \vert\\ CH_2\end{matrix}\!>CHCH_2-$ | −4.32 ± 0.17 | −2.45 ± 0.17 | −2.49 ± 0.68 | −1.42 ± 0.40 |
|  $\begin{matrix}CH_2\\ \vert\\ CH_2\end{matrix}\!>CDCH_2-$ | | | +14.9 ± 1.5 | +16.93 ± 1.96 |

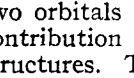
[a] Uncertainties are standard errors. [b] The largest possible error in the deuterium analysis is taken into account.

the rate-determining process, deuteriation would facilitate the participation of the neighboring cyclopropyl group by increasing its ability to accommodate the developing positive charge. Therefore, the effect of deuterium induction would be in stabilizing the *transition state* of the reaction.

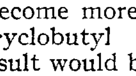
If the first interpretation is correct, then the rate increase should be larger for the faster reaction, *i.e.*, for the acetolysis, as the higher ground state energy level of the deuteriated species would favor more the reaction with a lower activation energy (Fig. 1).

If, however, participation is important in the rate-determining step, then one can expect that the acceleration due to deuterium induction will be more pronounced for the reaction in which the transition state resembles more a non-classical carbonium ion intermediate, *i.e.*, for the slower ethanolysis. This hypothesis is an extension of Hammond's postulate.[19,20] The transition state for the faster acetolysis, $t_A$ (Fig. 1), is structurally nearer to the starting material and the participation of the cyclopropyl group in reaching this stage is less important. Any change which will facilitate participation will affect less the reaction in which it is less pronounced. Therefore, the significantly smaller isotope effect observed in the acetolysis of Vb and VIb, when compared with the ethanolysis, may be considered as indicative for the *formation of a non-classical carbonium ion in the rate-determining step of these reactions*. The same conclusion can be reached even if the observed rate accelerations were not due to the $+$I effect of deuterium but to some other cause (*e.g.*, rehybridization). However, it has to be pointed out that the internal return reaction observed in the acetolysis could cause deuterium scrambling in the starting material[3] and in this way complicate the evaluation of the observed kinetic isotope effect.

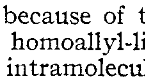
If the isotope effects in the solvolysis of Vb and VIb are to be ascribed to induction only, then these effects are obviously not additive. The values per atom D in the ethanolysis are significantly smaller with Vb that with VIb (Table III). An alternative explanation of this difference is that the observed rate increases are not due to induction only and that the two ring methylene carbon atoms are not equivalent in the transition state of the solvolysis.[11b] From all proposed reaction mechanisms such non-equivalency is implicit only in a bicyclobutonium ion like transition state. If the first formed intermediate in the solvolysis of Vb resembles X, then a rehybridization of the carbon–deuterium bonds has to be considered. Theoretical studies[24] have shown that the carbon–hydrogen bonding orbitals in cyclopropane are properly regarded as hybridized between $sp^3$ and $sp^2$. Thus, in the formation of X two deuterium bonding orbitals will become more $sp^2$ owing to the positive charge generated on carbon atom 4, while the other two orbitals will become more $sp^3$ because of the contribution of cyclobutyl and homoallyl-like structures. The result would be an intramolecular compensation of the isotope effects due to rehybridization[7,11b] and the rate enhancement observed would arise more or less from induction only.



X



XIa



XIb

With VIb the formation of two different bicyclobutonium ions is possible, *i.e.*, XIa and XIb. These two species do not necessarily represent equivalent energy levels and the formation of one could be faster than that of the other. To decide which one of the two possible carbonium ion intermediates represents the transition state of the reaction path with the lowest free energy of activation, one has to consider (1) the electron-releasing inductive effect of deuterium which would favor the formation of XIb, and (2) that owing to the unsymmetrical labeling of VIb the rehybridization of the carbon–deuterium bonding orbitals toward either more or less p-character is possible. More *p*-character would result in a rate increase and favor the formation of XIa.

From the above-mentioned arguments it can be deduced that, assuming a bicyclobutonium ion like transition state, the rehybridization of carbon–deuterium bonding orbitals and the $+$I effect of deuterium will affect in an opposite way the solvolysis rate of VIb. If the formation of XIb requires the least activation energy, then the rate increase caused by induction is diminished by an unfavorable rehybridization. Alternatively, if the rate increase is due to rehybridization associated with the formation of XIb, the favorable influence of the $+$I effect of deuterium on the reaction rate is lost. The magnitude of the isotope effect will depend on the relative importance of these two factors. If rehybridization has a prevailing importance in favoring participation, one can expect that the isotope effect per atom D in the solvolysis of VIb will exceed that of Vb, and this is actually the case.

It is evident that the present state of our knowledge of the theory of secondary hydrogen isotope effects does not enable a clear interpretation of our results. However, they seem to be consistent with the reaction mechanism which postulates neighboring group participation through the formation of bicyclobutonium ions.

## Experimental[25]

**Cyclopropylcarbinol-1,1-$d_2$.**—Cyclopropanecarboxylic acid (2.0 g.) was reduced in anhydrous ether with 1.05 equivalents of lithium aluminum deuteride. The reaction mixture was decomposed with 1.1 equivalents of water, the precipitate centrifuged off, washed once with ether and again centrifuged. Ether was distilled from the combined extracts and the residue fractionated; yield 1.2 g., b.p. 123° (760 mm.). The product contained a small amount of ether as the sole impurity.

**The dinitrobenzoate**, m.p. 101°, contained 1.88 atoms of deuterium per molecule.

**Dimethyl Succinate-$d_4$.**[26]—Dimethyl acetylenedicarboxylate (100 g.) was deuteriated in portions of 4 to 10 g. over Adams catalyst in anhydrous tetrahydrofuran, or without solvent; yield of the pure product, 95 g., b.p. 94–96° (24 mm.).

**Succinic Anhydride-$d_4$.**[26]—Deuteriated dimethyl succinate (93 g.) was refluxed for 24 hr. with 940 ml. of water and 1 ml. of concentrated nitric acid. After neutralization of the mineral acid with a solution of sodium carbonate, water was evaporated from the reaction mixture and the residual succinic acid dried *in vacuo*. Then, 137 ml. of acetyl chloride was added and the mixture refluxed for 3 hr. Upon filtration and cooling the product crystallizes in long needles, which are filtered off, washed twice with 50 ml. of anhydrous ether and dried *in vacuo*. The product, 53.3 g., m.p. 121°, contained 3.78 atoms of deuterium per molecule.

**Methyl Succinate-2,2,3,3-$d_4$.**—Anhydrous methanol (25.4 ml.) was added to the deuteriated succinic anhydride (52.3 g.) and the mixture refluxed until solution was complete. After refluxing for an additional 20 min., methanol was evaporated *in vacuo*, the residue crushed to a powder and dried *in vacuo* (66.2 g., m.p. 47–55°).

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[24] C. A. Coulson and W. Moffitt, *Phil. Mag.*, **40**, 1 (1949).

[25] All melting points are corrected and all boiling points are uncorrected. The purity of the volatile compounds was checked by vapor phase chromatography. Deuterium analyses were accomplished by the falling drop method.

[26] A. McLean and R. Adams, *J. Am. Chem. Soc.*, **58**, 804 (1936).

**Methyl 3-Chloropropionate-2,2,3,3-$d_4$.**—Methyl succinate-$d_4$ (46.4 g.) was dissolved in 300 ml. of ethanol and neutralized with a solution of sodium hydroxide in 80% aqueous ethanol (160 ml.). A solution of silver nitrate (63 g.) in 50 ml. of water was then added with stirring. The precipitate was filtered off, washed with 500 ml. of aqueous ethanol (80%) and 500 ml. of ether, dried, crushed to a powder and dried again *in vacuo*. The silver salt (72.5 g.) was suspended in 200 ml. of anhydrous carbon tetrachloride and a solution of dry chlorine (23.3 g.) in 200 ml. of anhydrous carbon tetrachloride was added dropwise during 3 hr. with stirring and exclusion of moisture. The stirring was continued until the development of carbon dioxide ceased. The precipitate was then filtered off, the solvent removed from the filtrate by distillation and the residue fractionated. The fraction boiling at 74–108° (70 mm.) was collected. The product (13.0 g.) contained some carbon tetrachloride and other impurities which were not identified.

**3-Chloropropanol-2,2,3,3-$d_4$.**—The crude chloroester (12.6 g.) was reduced with lithium aluminum hydride at −75° according to the procedure of Nystrom[27] (normal-addition). The product (6.9 g.) contained several unidentified impurities.

**1-Bromo-3-chloropropane-2,2,3,3-$d_4$** was prepared from the above carbinol and phosphorus tribromide as described for the undeuteriated material.[28] From 6.9 g. of starting material, 4.3. g. of pure chlorobromide, b.p. 145–148° (750 mm.), was obtained.

**4-Chlorobutyronitrile-3,3,4,4-$d_4$**[29] was prepared from 4.3 g. of deuteriated chlorobromide; yield of the pure product 1.7 g., b.p. 95–100° (30 mm.).

**Cyclopropanecarboxylic Acid-3,3,4,4-$d_4$.**[30]—The cyclization of 1.7 g. of deuteriated chlorobutyronitrile and hydrolysis of the product yielded 0.98 g. of pure deuteriated cyclopropanecarboxylic acid, b.p. 117–119° (75 mm.).

**Cyclopropylcarbinol-3,3,4,4-$d_4$.**—The reduction of cyclopropanecarboxylic acid-$d_4$ with lithium aluminum hydride was carried out as described for the preparation of cyclopropylcarbinol-1,1-$d_2$. From 0.98 g. of the acid 0.57 g. of the product, b.p. 124° (750 mm.), was obtained which contained a small amount of ether as the sole impurity.

**The dinitrobenzoate**, m.p. 100–101°, contained 3.70 atoms of deuterium per molecule.

**3-Chloropropanol-1,1-$d_2$.**[27]—Methyl 3-chloropropionate (12.3 g.) was reduced at −75° with a solution of lithium aluminum deuteride (4.2 g.) and aluminum chloride (13.4 g.) in anhydrous ether; yield of the pure product, b.p. 65° (10 mm.), was 7.2 g.

**4-Chlorobutyronitrile-2,2-$d_2$.**—3-Chloropropanol-$d_2$ (6.8 g.) treated with phosphorus tribromide[28] yielded 9.5 g. of the corresponding chlorobromide, b.p. 145–148° (750 mm.), which with potassium cyanide[29] gave 2.45 g. of the nitrile, b.p. 96–98° (30 mm.).

**Cyclopropylcarbinol-2-*d*.**—Deuterium oxide (5 ml.) was covered in a quartz tube with 20 ml. of anhydrous ether and 1.85 g. of sodium added in small pieces. After standing overnight an additional 1 ml. of deuterium oxyde was added, the ether decanted and the aqueous solution evaporated to dryness. The residue was dried *in vacuo* by heating over a free flame. 4-Chlorobutyronitrile-2,2-$d_2$ (1.0 g.) was then cyclized and the product hydrolyzed with deuteriated reagents[30,31] to cyclopropanecarboxylic acid-2-*d*. The acid was not isolated but its ethereal solution directly reduced with lithium aluminum hydride as described previously. The yield of the carbinol, b.p. 125° (750 mm.), was 0.3 g.

**The dinitrobenzoate**, m.p. 101°, contained 0.88 atom of deuterium per molecule.

**1-Hydroxy-4-pentanone-1,1-$d_2$ Ethylene Ketal.**—A solution of ethyl levulinate ethylene ketal[32] (37.6 g.) in 300 ml. of anhydrous ether was added under stirring to a solution 4.2 g. of lithium aluminum deuteride in 350 ml. of anhydrous ether, the reaction mixture refluxed for 1 hr. and stirred overnight. The complex was decomposed with 16 ml. of water, the ether decanted, the precipitate washed with ether and filtered off. After removal of ether from the combined filtrates, 32.6 g. of the crude product was obtained.

**1-Chloro-4-pentanone-1,1-$d_2$.**—The crude deuteriated ketal carbinol (32.6 g.) was poured into 35 ml. of water and 30 ml. of concentrated hydrochloric acid and the mixture heated up rapidly until distillation begins. The heating was continued with occasional addition of water until no more oily material distilled over. The distillate was extracted three times with ether, the extracts dried with calcium chloride and the solvent removed over a column. Thus, 16.4 g. of the crude ketone was obtained.

**Methyl Cyclopropyl-2,2-$d_2$ Ketone.**[33]—The cyclization of 16.4 g. of the crude chloropentanone-$d_2$ gave after distillation 8.1 g. of the pure product, b.p. 110–112° (750 mm.), $n^{22}\text{D}$ 1.4232.

**Cyclopropanecarboxylic Acid-3,3-$d_2$.**[34]—The oxidation of the ketone (7.5 g.) with a solution of sodium hypobromide yielded after distillation 5.0 g. of the pure product, b.p. 94–97° (24 mm.), $n^{23}\text{D}$ 1.4263.

**Cyclopropylcarbinol-3,3-$d_2$.**—The reduction with lithium aluminum hydride of the corresponding carboxylic acid-$d_2$ (4.4 g.), carried out as described previously, yielded 3.0 g. of the pure product, b.p. 122–123° (750 mm.), $n^{23}\text{D}$ 1.4283.

**The dinitrobenzoate**, m.p. 100°, contained 1.76 atoms of deuterium per molecule.

**The benzenesulfonates** were prepared according to the published procedure.[4] The purities, calculated from "infinity" titers of the ethanolyses at 20.0°, ranged from 85–95%.

**Rate measurements** were accomplished by the usual techniques. The titrating solutions were for the acetolyses, 0.03 *N* sodium acetate in acetic acid and, for the ethanolyses, 0.03 *N* sodium hydroxide in anhydrous ethanol. The indicators used were brom phenol blue and methyl red, respectively.

**Calculation of Errors and Significance Tests. Ethanolysis.**—The differences between the rate constants 1, 2 and 3 (Table I) are significant and are most probably due to small temperature variations between the runs. These values were considered as 3 independent measurements and their mean ($k_\text{H}$ no. 4) with its standard error calculated accordingly. Thus, $k_\text{H}$ no. 4 has 2 degrees of freedom. It was assumed that the distribution of $k_\text{D}$ nos. 5 and 6 was the same as that of $k_\text{D}$ nos. 1–3. Thus, in the calculation of the corresponding $k_\text{H}/k_\text{D}$ values the standard error was estimated by taking the standard deviation of $k_\text{H}$ no. 4 as the uncertainty of $k_\text{D}$. $k_\text{H}/k_\text{D}$ values nos. 5 and 6 have therefore 2 degrees of freedom. The measurement of $k_\text{H}$ and $k_\text{D}$ nos. 7 and 8, resp., 9 and 10 were performed simultaneously. Thus, it is believed that the systematic errors were largely avoided. This is shown by the small difference between $k_\text{H}/k_\text{D}$ values nos. 8 and 10, which turns out to be not significant. The standard error of the mean ($k_\text{H}/k_\text{D}$ no. 11) was calculated from the standard errors of $k_\text{H}/k_\text{D}$ nos. 8 and 10. The result no. 11 has 13 degrees of freedom. In the same way the result no. 16 was calculated from the $k_\text{H}/k_\text{D}$ values nos. 13 and 15. The result no. 16 has 21 degrees of freedom.

In the calculation of the percentage isotope effect per atom deuterium (Table III) the largest possible error in the determination of deuterium (about 5%) was combined with the standard errors of $k_\text{H}/k_\text{D}$ values nos. 5, 11 and 16.

*t*-Test for the hypothesis that the isotope effect per atom deuterium is the same for Vb and VIb gives $t = 3.50$, with 34 degrees of freedom, $P < 0.5\%$.

**Acetolysis.**—The calculation of errors for $k_\text{H}/k_\text{D}$ values nos. 6 and 7 was analogous to that of the corresponding values in the ethanolysis. $k_\text{H}/k_\text{D}$ values 6 and 7 have 3 degrees of freedom. Owing to the fast rate of acetolysis, it is difficult to avoid systematic errors in the determination of the $k_\text{H}/k_\text{D}$ values even if the rate measurements are carried out simultaneously. This is shown by the differences between the $k_\text{H}/k_\text{D}$ values nos. 11, 13 and 15 which are significant. The refore,the latter values were considered as 3 independent measurements and their mean ($k_\text{H}/k_\text{D}$ no. 16) calculated accordingly. The result no. 16 has thus 2 degrees of freedom.

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[27] R. F. Nystrom, *J. Am. Chem. Soc.*, **81**, 610 (1959).

[28] J. B. Cloke, R. J. Anderson, J. Lachmann and G. E. Smith, *ibid.*, **53**, 2794 (1931).

[29] "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 156.

[30] "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 221.

[31] A sample of cyclopropanecarboxylic acid prepared with the aid of "light" reagents contained only 0.3 atom of deuterium per molecule.

[32] M. Kühn, *J. prakt. Chem.*, **156**, 103 (1940).

[33] G. W. Cannon, R. C. Ellis and J. R. Leal, *Org. Syntheses*, **31**, 74 (1951).

[34] G. H. Jeffery and A. I. Vogel, *J. Chem. Soc.*, 1805 (1948); L. I. Smith and S. McKenzie, *J. Org. Chem.*, **15**, 74 (1950).

The percentage isotope effect per atom deuterium (Table III) was calculated as for ethanolysis.

*t*-Test for the hypothesis that the isotope effect for IIIb is the same in acetolysis and in ethanolysis gives $t = 2.31$, with 5 degrees of freedom, $P = 8\%$.

*t*-Test for the hypothesis that the isotope effect per atom deuterium for Vb is the same in acetolysis and ethanolysis gives $t = 2.17$, with 16 degrees of freedom, $P < 5\%$.

*t*-Test for the hypothesis that the isotope effect for VIb is the same in acetolysis and ethanolysis gives $t = 2.61$, with 23 degrees of freedom, $P < 2.5\%$.

In the same way it was found that the isotope effect per atom deuterium in acetolysis was not significantly different with Vb than with VIb.

**Acknowledgment.**—We are indebted to Professor K. Mislow of the New York University for the very helpful discussions leading to the conception of this work. The help of Dr. K. Ilakovac in the statistical evaluation of the results is gratefully acknowledged. Thanks are also due to Mrs. J. Zake and Mr. T. Magjer for performing the deuterium analyses.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY, LAFAYETTE, IND.]

# The Cleavage of Sulfides and Sulfones by Alkali Metals in Liquid Amines. II. The Cleavage of Sulfides by Lithium in Methylamine[1,2]

BY WILLIAM E. TRUCE AND JEROME J. BREITER

RECEIVED SEPTEMBER 25, 1961

The direction of cleavage has been determined for a series of unsymmetrical dialkyl sulfides and alkyl-aryl sulfides. The results obtained are explained on the basis of a gradation of mechanism.

Earlier, it was reported[1] that sulfides and sulfones were cleaved in good yields to the hydrocarbon and mercaptan or sulfinic acid by sodium in liquid ammonia or lithium in methylamine. Another recent report[3] has shown that sulfides can also be cleaved by the use of calcium hexammine.

In the latter report, the authors state that their results can be explained on the basis of a reaction scheme involving either a one- or a two-electron transfer. In the case of ether cleavage with sodium in ammonia[4] the results are best explained on the basis of a two-electron transfer,[5] whereas in the case of the cleavage of tetraalkylammonium halides by sodium in ammonia,[6] the authors suggest a gradation of mechanism involving both a one- and a two-electron transfer. They propose that *t*-butyl, isopropyl and *sec*-butyl groups cleave as radicals, while ethyl and higher primary alkyl groups cleave as carbanions.

In this work, a series of unsymmetrical dialkyl and alkylaryl sulfides were prepared and treated with lithium in methylamine to determine the direction of preferred cleavage. Cleavage of alkyl-aryl sulfides produced exclusively the aromatic thiol and aliphatic hydrocarbon regardless of the amount of branching in the alkyl chain. In the dialkyl series, the preference for cleavage is *t*-alkyl > *sec*-alkyl ≈ *n*-alkyl. The compounds prepared and the results of their cleavages are presented in Table I of the Experimental part.

The preferred direction of cleavage of groups from sulfides by lithium in methylamine does not correspond in a simple way to the order expected for either radical cleavage (one-electron transfer) or carbanion cleavage (two-electron transfer). The stability of carbanions is given as CH$_3$ > Et *n*- Bu > *i*-Pr, *sec*-Bu > *t*-Bu,[7] while the stability of alkyl free radicals is the reverse of that given for carbanions, with methyl being the least stable and *t*-butyl the most stable.[8] Reductive cleavage also involves the formation of thiolates as well as hydrocarbons, so differences in stability of thiolates could affect the preferred direction of cleavage; the more basic the thiolate, the less readily it might be expected to be formed by reductive cleavage. This factor cannot account for the large preference of *t*-alkyl cleavage over *n*-alkyl cleavage since all of the thiolates formed in the alkyl series have about the same basicity.[9] However, the fact that aromatic thiols are about 10$^4$ times more acidic than aliphatic thiols[9] may be an important factor in the cleavage of alkyl-aryl sulfides

Steric factors would not be expected to play an important role in determining the direction of cleavage since models show no steric compression in the starting sulfides.

In the dialkyl series, it is postulated that the *t*-butyl group cleaves as a free radical under these conditions and that some other factor than stability of radicals or carbanions is involved in the cleavage of the less highly branched alkyl groups. The cleavage procedure used would seem to favor the formation of radicals as intermediates since the metal is added to a solution of the sulfide and is, therefore, never in excess. These results correspond closely to those observed by Grovenstein.[6]

In the alkyl-aryl series, it is postulated that the alkyl groups may cleave as free radicals although, as mentioned above, the basicity of the thiols may be an important factor in determining the direction of cleavage. This reaction path is suggested by the

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(1) Paper I, W. E. Truce, D. P. Tate and D. N. Burdge, *J. Am. Chem. Soc.*, **82**, 2872 (1960).

(2) Taken from the Ph.D. Thesis of J. J. B.

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