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DEUTERIUM ISOTOPE EFFECTS FOR MIGRATING AND NON-MIGRATING GROUPS IN THE WAGNER-MEERWEIN REARRANGEMENT. AN EXPERIMENTAL DISSECTION OF THE γ-DEUTERIUM RATE EFFECTS IN THE SOLVOLYSIS OF NEOPENTYL-TYPE ESTERS

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Some controversy still surrounds the question of whether or not the methyl group rearrangement in the solvolysis of neopentyl sulfonates occurs during ("participation") or after ionization.[1,2,3] We here report results which we believe settle the issue by reconciling in favor of participation the major remaining evidence which has been used against it.

Schubert and Henson[2] found that CH_3 groups migrate 1.20–1.30 times more rapidly than CD_3 in intramolecular competition. Despite this, they found only a small normal isotope rate effect in the acetolysis of neopentyl-γ-d_9 2,4-dinitrobenzenesulfonate and therefore concluded that methyl migration occurred after the rate-determining step. On the other hand, Ando and coworkers[4] have argued that the moderate-sized α-^{14}C effect (1.05), which they observed in the acetolysis of neopentyl-α-^{14}C p-nitrobenzenesulfonate, indicated, by analogy with similar effects in S_N2 reactions, methyl group participation. The low α-deuterium effects (~1.12) in several solvolyses of neopentyl-α-d_2 trifluoromethanesulfonate ("triflate") have also been interpreted as indicating participation.[1] These results, together with inverse isotope rate effects observed for non-migrating groups in isobutyl[1,5] and neophyl[6] sulfonate ester solvolyses, indicate that the low isotope rate effects observed for solvolysis of neopentyl-γ-d_9 sulfonates arise from nearly cancelling effects exerted by the migrating and non-migrating groups.[1] This possibility was considered by Schubert and Henson but rejected because they did not expect sufficiently large inverse effects for the non-migrating groups.

We have determined α-, β-, and γ-deuterium rate effects for solvolysis of cyclohexylcarbinyl triflate (**I**)[7] and α- and γ-deuterium rate effects for solvolysis of 1-methylcyclohexylcarbinyl triflate (**III**).[8] These compounds were synthesized by standard methods. The key intermediate was the methyl ester of cyclohexane carboxylic acid. The β-deuterium was introduced by converting the methyl ester to the carbanion with lithium diisopropylamide followed by addition of deuterium oxide. The γ-CD_3 compound was made by treating the ester carbanion with deuteromethyl iodide. The α-d_2 alcohols were made by lithium aluminum deuteride reduction of the corresponding methyl esters. The γ-d_4 compounds were made by exchange of cyclohexanone, conversion to methylene-cyclohexane-d_4, cyclohexyl-d_4 carbinol, cyclohexyl-d_4 carboxylic acid, etc. The 60 M Hz ^{1}H nmr spectra of all compounds were consistent with their assigned structures as were the 33.77 M Hz ^{2}H nmr spectra of the alcohol precursors of the triflate esters. The deuterium incorporation, determined by mass spectral analysis, was >95% for cyclohexanone-d_4 and CD_3I, and 82% for 1-methylcyclohexane-d_1 carboxylic acid.

Table. Solvolysis Rates[a] and Isotope Effects at 25°C

Compound	**I**, Cyclohexyl Carbinyl Trifluoromethanesulfonate	**III**, 1-Methylcyclohexyl Carbinyl Trifluoromethanesulfonate	
Solvent[b]	97T	97T	80E
k_H, sec^{-1}	11.60×10^{-5}	57.5×10^{-5}	17.67×10^{-5}
$\left(k_H/k_{\alpha\text{-}\underline{d}_2}\right)^{1/2}$	1.122	1.130	1.120
$k_H/k_{\beta\text{-}\underline{d}}$	1.98	c	c
$k_H/k_{\gamma\text{-}\underline{d}_4}$[d]	0.984	e	0.963
$k_H/k_{\gamma\text{-}\underline{d}_3}$[f]	c	1.073	1.057

[a]Rates were measured using the precise conductometric method described earlier.[10] [b]97T and 70T refer to 97 and 70 wt. % 2,2,2-trifluoroethanol in water, respectively, while 80E refers to 80 vol. % ethanol in water. [c]Not applicable. [d]Deuterium in the ring methylene groups attached to the β-carbon. [e]Not determined. [f]Deuterium in the β-methyl group attached to the β-carbon.

The isotope effects for the trifluoroethanolysis of **I**, given in the Table, are very close to those observed for isobutyl triflate in the same solvent.[1] The large β-$\underline{d}$ effect (1.98), the intermediate α-$\underline{d}$ effect (1.122), and the inverse γ-$\underline{d}_4$ effect (0.984) are all consistent only with hydrogen participation.[1,6,9] ^2H nmr of the reaction mixture from the solvolysis of **I**-β-$\underline{d}$ showed that the products were derived principally after β-deuterium migration: 24.4% 1-methyl-$\underline{d}$-cyclohexyl alcohol and trifluoroethyl ether (δ 1.2), 72.7% 1-methyl-$\underline{d}$-cyclohexene (δ 1.6), and 2.9% cycloheptene-1-$\underline{d}$ (δ 5.3).

In both 97T and 80E, the α-$\underline{d}$ effects for **III**-α-$\underline{d}_2$ (1.12–1.13 per D) are the same as those observed for neopentyl sulfonates[1] and indicate participation.[9] The ^2H nmr spectrum of the product reaction mixture from the solvolysis of **III**-α-$\underline{d}_2$ in 80E indicates that methyl migration occurred to the extent of 58% (34% 1-ethyl-α-$\underline{d}_2$-cyclohexyl alcohol and ethyl ether, δ 1.5; 15.9% ethylidene-α-$\underline{d}$-cyclohexene, δ 4.8; 8.7% 1-ethyl-α-$\underline{d}_2$-cyclohexene, δ 1.93) and ring expansion to the extent of 42% (27.9% 1-methyl-cycloheptyl-2,2-$\underline{d}_2$ alcohol and ethyl ether, δ 1.73; 5.2% 1-methylcycloheptene-2-$\underline{d}$, δ 5.5; 8.1% 1-methylcycloheptene-7,7-$\underline{d}_2$, δ 2.1). Very similar results are obtained from the analysis of the ^2H nmr spectrum of the reaction-mixture product from the solvolysis of **III**-γ-$\underline{d}_3$ in 80E and 97T. This dominance of migration of methyl over methylene groups is also reflected in the normal methyl-$\underline{d}_3$ isotope effect on the solvolysis rates, 1.057 in 80E and 1.073 in 97T, which also clearly indicate participation. The methylene-$\underline{d}_4$ isotope effect is inverse, 0.963, clearly indicative of the dominant non-migrating role of the

methylene groups. The product of these two γ-d effects (1.057 x 0.963) is 1.018, close to the value of 1.03 observed for the γ-d_9 rate effect for the neopentyl ester.[1,3]

If we assume that the characteristic migrating and non-migrating isotope effects are the same for CD_3 and CD_2 groups in **III**, equations can be derived to sort out the intrinsic migrating and non-migrating group effects which are mixed to produce the experimentally observed rate effects. Thus,

$$\left(\frac{k_H}{k_{\gamma\text{-}d_3}}\right)_{obs} = 1.057 = \frac{R_H^D R_D^H}{\left(0.58\, R_D^H + 0.42\, R_H^D\right)}$$

where R_H^D is the isotope effect (k_H/k_D) for the part of the reaction in which only the methyl-d_3 group migrates, and R_D^H is the isotope effect for the part of the reaction involving ring expansion.

Similarly,

$$\left(\frac{k_H}{k_{\gamma\text{-}d_4}}\right)_{obs} = 0.963 = \frac{\left(R_D^H\right)^2 R_H^D}{\left(0.58\, R_H^D + 0.42\, R_D^H\right)}$$

where the isotope effects for the methylene groups are assumed to be numerically the same as the corresponding ones for the methyl group. Solving the two equations for the two unknowns, the non-migrating isotope effect, R_D^H, is 0.942 and the migrating one, R_H^D, is 1.160. The product $(0.942)^2$ x 1.160 is 1.029, which is equal to the experimental value for the isotope effect in solvolysis of the neopentyl-γ-d_9 ester.[1,3] The ratio R_H^D/R_D^H, or 1.23 is the calculated intramolecular isotope effect for CH_3 vs. CD_3 migration; this is well within the range of 1.20 to 1.30 found by Schubert and Henson.[3] If there were about a 4% error in the determination of the product ratio, and the yield of methyl migration product were 56 rather than 58% (and the yield of ring expansion product 44 rather than 42%), the calculated values of R_D^H, 0.936, and R_H^D, 1.176, and the derived values $\left(R_D^H\right)^2 R_H^D$, 1.030, and of R_H^D/R_D^H, 1.26, are not significantly different. Also, if it be assumed that the isotope effects per D, rather than per group, were constant so that the methylene isotope effects were equal to the 2/3rds power of the methyl effects, the calculated values for $R_{CD_3}^{CH_3}$, 0.927, $R_{CH_3}^{CD_3}$, 1.177, $\left(R_{CD_3}^{CH_3}\right)^2 R_{CH_3}^{CD_3}$, 1.011, and $R_{CH_3}^{CD_3}/R_{CD_3}^{CH_3}$, 1.270, are still the same, within the range of allowed experimental error.

These results clearly indicate that the non-migrating isotope effect, R_D^H, is significantly more inverse for methyl participation than it is for hydrogen participation (~0.99 per CD_3 group) or phenyl participation in neophyl sulfonates (~0.97–0.99 per CD_3 group).[6] Experiments designed to further our understanding of these differences are currently being carried out.

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