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Secondary Deuterium Isotope Effects in Some S_N1 and E_2 Reactions*

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An α-deuterium isotope effect k_H/k_D of 17% was found in the E_2 reaction of 2-phenylethyl-1,1-d_2 bromide with sodium ethoxide in ethanol. This supports the Streitwieser change-of-hybridization theory and the associated explanation of the absence of such effects in S_N2 reactions as being due to the proximity of the incoming group.

The magnitude of the β- and α-deuterium isotope effects in the S_N1 and E_2 reactions of some alkylsulphonium salts were determined and compared with the isotope effects of the corresponding alkyl-halides. An explanation for these differences is given.

Secondary deuterium isotope effects in reactions involving carbonium ion transition states have been studied by several authors[1]. The retardation of deuterium substitution at β-carbons is mainly attributed to a hyperconjugative weakening of C-H or C-D bonds on the β-carbon atoms. The retardation when deuterium is linked to α-carbon atom is explained in terms of the reduction in the force constant for the bending of the C-H bond in the sp^2-bonded activated complex[2]. Substitution of deuterium for hydrogen on the β-carbon atoms of alkyl-halides was found to retard the rates of S_N1 and E_1-type reactions by factors of about 10—30% per deuterium atom[3,4]. α-secondary deuterium isotope effects are of the similar magnitude ($k_H/k_D \sim 1.10—1.20$). In S_N2 reactions with nucleophilic reagents $k_H/k_D > 1$ was not observed and it was suggested[5] that the α-deuterium isotope effect be used as a criterion for distinguishing the mechanism involved. An inverse isotope effect ($k_H/k_D < 1$) has been observed in solvolyses of some trideuteromethyl compounds which seem to undergo S_N2 displacement reactions, having k_H/k_D values from 0.87 to 1.00. It was also shown that the magnitude of the isotope effect correlates rather well with relative proximities of entering and leaving groups and that the stiffening of out-of-plane vibrations may account for the direction of the observed isotope effect[6].

In the present investigation the magnitude of the β- and α-deuterium isotope effects in the S_N1 and E_2 reactions of some alkylsulphonium salts were determined and compared with the isotope effects of the corresponding alkyl-halides. In both cases it was found that the isotope effects of alkylsulphonium salts were much smaller than those of the corresponding alkyl-halides.

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An α-deuterium isotope effect of 17% in the E_2 reaction of 2-phenylethyl-1,1-d_2 bromide with sodium ethoxide in ethanol was found which is interesting since an α-deuterium isotope effect in a bimolecular elimination (E_2) has not been reported as yet.

β-DEUTERIUM ISOTOPE EFFECTS IN THE S_N1 REACTIONS

2,2-Dideutero-1,1-di(trideuteromethyl)propyl-dimethyl-sulphonium iodide (II) was prepared and the rate of solvolysis in aqueous solution was measured and compared with that of the non-deuterated sulphonium salt (I). An isotope effect of 25% (3.3% per deuterium atom) was observed (Table I). This is a much smaller isotope effect than Shiner found in the solvolysis of 2,2-dideutero-1,1-di (trideuteromethyl)propyl-chloride[3]. In 80% aqueous ethanol at 25°C Shiner found k_H/k_D to be 2.35, *i. e.* 135%.

The kinetics and mechanism of the solvolysis of the ion (I) were previously studied in aqueous ethanol containing 20 and 40% water respectively and it was shown that water content influenced only slightly the proportion of olefin formation, and that the reaction followed a unimolecular mechanism[7].

TABLE I

Rates of the S_N1 hydrolysis of 0.05 M 2,2-dideutero-1,1-di-(trideuteromethyl) propyl-dimethylsulphonium iodide in aqueous solution at 59.75°C

Compound	Atoms D/ Molecule	k x 10^4 sec.$^{-1}$	k_H/k_D
(I) $CH_3CH_2C(CH_3)_2S(CH_3)_2I$	none	$1.381^a \pm 0.014^c$	1.25
(II) $CH_3CD_2C(CD_3)_2S(CH_3)_2I$	7.57	$1.107^b \pm 0.012^c$	

a Mean of: 1.344; 1.370, 1.372, 1.393 and 1.425.
b Mean of: 1.098, 1.089, 1.099 and 1.142
c Standard error of the mean

α-DEUTERIUM ISOTOPE EFFECTS IN THE E_2 REACTIONS

The elimination reactions of 2-phenylethyl bromide and the correspoding dimethylsulphonium ion with the base show second-order kinetics[8]. The second-order kinetics is consistent not only with bimolecular elimination E_2 but also with unimolecular elimination in the conjugate base (E_1cB). Skell and Hauser[9] have shown how in the reaction of 2-phenylethyl bromide with ethoxide ion these two mechanisms can be distinguished by an isotopic test. The E_1cB mechanism would involve the prior production of the conjugate base, a carbanion, and the unimolecular loss of bromide ion from the latter. In this case the formation of the carbanion must be reversible. Skell and Hauser conducted the reaction in ethanol-O-d and they found that the unreacted bromide does not accumulate deuterium. This was taken as an evidence that hydrogen and bromine are lost simultaneously.

The mechanism of the second-order elimination reaction of 2-phenylethyl-dimethylsulphonium ion with hydroxide ion in aqueous solution was studied by ^{34}S kinetic isotope effect[10]. It was found that the ^{34}S isotope effect is only

0.15%, as compared with the isotope effect of 1.8% predicted for the complete cleavage of the C-S bond in the rate-determining step. Evidently in this E_2 reaction the β C-H bond is stretched considerably more than the C-S bond in the transition state. It still seems rather unlikely that a carbanion of appreciable stability is involved.

2-Phenylethyl-dimethylsulphonium-1,1-d_2 bromide was prepared and the rate of elimination in aqueous alkali at 79.55° was followed by potentiometric titration. The rate was found almost equal to that of the non-deuterated sulphonium salt (Table II).

TABLE II

Rates of the E_2 reaction of 0.05 *M* 2-*phenylethyl-dimethylsulphonium*-1,1-d_2 *bromide with* 0.05 M *NaOH in aqueous solution at* 79.55°*C*.

Compound	Atoms D/ Molecule	$k \times 10^4$ $sec.^{-1}$ $mole^{-1}$ l	k_H/k_D
$C_6H_5CH_2CH_2S(CH_3)_2Br$	none	9.54^a	1.015
$C_6H_5CH_2CD_2S(CH_3)_2Br$	1.91	9.40^b	

a Mean of: 9.35, 9.46 and 9.80*
b Mean of: 9.03, 9.36 and 9.80*
* Both higher values of the rate constants were obtained with 0.1 *M* NaOH

It was also found that approximately 3/4 of the original quantity of deuterium exchanged prior to the reaction at the same temperature (80°C) and in more concentrated solutions which had to be used in order to obtain enough deuterium oxide in the solution for the analysis. In the first experiment 2*M* 2-phenylethyl-dimethylsulphonium-1,1-d_2 bromide and 2.5 *M* sodium hydroxide in aqueous solution were allowed to react at 80°C for 24 hours. (It was calculated that under the conditions described 99% completion of the reaction should take place in about 55 minutes.) The water was separated from styrene by distillation through a short Vigreux column, shaken with ether, the ether layer was separated and ether distilled off. A few drops of the water were *burned* in a furnace for further purification and again condensed in a dry ice-aceton trap. Additional purification in the vacuum line was carried out as required by the *falling drop* method[11] which was used for deuterium analyses. In the second experiment 5*M* sodium hydroxide was used and the reaction mixture was left at 80°C for 38 hours, all other procedures being the same as in the first experiment. The third experiment differred from the second only in that that the extraction with ether was left out. It was found that 74.1% (average of 73.6, 76.4 and 72.3%) of deuterium in the sulphonium salt exchanged prior to the reaction. The reaction conditions of the kinetic measurements shown in Table II were not the same, but it seems that if there had been an appreciable α-deuterium isotope effect it would have been still noticeable.

The rate of the reaction of 2-phenylethyl-1,1-d_2 bromide with sodium ethoxide in absolute ethanol was followed by measuring the extinction of styrene at 248 mμ using Hilger H 700 quartz spectrophotometer and 10 mm cells. In the definite reaction times 1 ml of the reaction solution was withdrawn and diluted with absolute ethanol so that the concentration of styrene was about 5×10^{-5} *M*. At 248 mμ the molar extinction coefficient of styrene amounted to 1.35×10^{4} mole^{-1} cm^{-1} l. It was established that other components in the solution show no observable absorption at these dilutions. The results of the kinetic measurements are listed in Table III. An α-deuterium isotope effect of 17% was observed .

TABLE III

Rates of the E_2 *reaction of* 0.025 M 2-*phenylethyl*-1,1-d_2 *bromide with* 0.019 M *sodium ethoxide in absolute ethanol at* 59.8°C.

Compound	Atoms D/ Molecule	$k \times 10^2$ sec.$^{-1}$ mole^{-1} l	k_H/k_D
$C_6H_5CH_2CH_2Br$	none	1.015[a] ± 0.008[c]	1.17
$C_6H_5CH_2CD_2Br$	1.90	0.867[b] ± 0.010[c]	

a Mean of: 1.018, 1.048, 0.985, 1.006, 1.017 and 1.015

b Mean of: 0.891, 0.877, 0.844 and 0.877

c Standard error of the mean

The α-isotope effect in the E_2 reactions studied was again larger for a halide than for a sulphonium ion, as it had been the case with the β-isotope effect in the S_N1 reactions described above.

DISCUSSION

The differences in the deuterium isotope effects between halides and sulphonium salts are most probably due to the same reason as the old established difference in bimolecular eliminations between alkyl halides and alkyl sulphonium or ammonium ions governed by Saytzeff and Hofmann rules. A larger electron transfer from carbon to halogen is needed to give the transition state than in C-S heterolysis. Thus there should be more unsaturation in the transition state and the α-carbon should be closer to sp^2 hybridization.

The solvation difference needed to heterolyse the initially non-ionic C-halide bond and the CS^+ bond must be appreciable. The solvation change is much smaller in the heterolysis of CS^+, where the total ionic change remains the same.

The α-isotope effect observed in an E_2 reaction supports the Streitwieser change-of-hybridization theory[2] and the associated explanation of the absence of such effects in S_N2 reactions as being due to the proximity of the incoming group[6]. Such an interpretation of the α-isotope effect explains also the possibility of the existence of this effect in an E_2 reaction where the out-of-plane C-H bending motion is not hindered because of the distance of the site of attack by base.

EXPERIMENTAL

2-Phenylethyl-1,1-d_2 *bromide*

The compound was prepared by reduction of ethyl-phenylacetate with lithium aluminium deuteride (Metal Hydrides, Inc. U. S. A., 97% deuterium) and the reaction mixture worked up as described by Amundsen and Nelson[12]. 2-Phenylethanol 1,1-d_2, b. p. 110°C, 20 mm, was obtained in 87% yield. Bromination with PBr_3[13] gave 2-prenylethyl-1,1-d_2 bromide, b. p. 105°C, 18 mm, in 92% yield. The undeuterated bromide distilled at 107°C, 21 mm. The content of deuterium, determined by the *falling drop* method[11] amounted to 1.90 atoms of deuterium per molecule.

Anal. C_8H_9Br (185.076) calc'd: C 51.92; H 4.90%
found: C 51.49; H 4.52%.

Taking into account the degree of deuteration the average molecular weight was calculated to be 186.989.

Anal. $C_8H_7D_2Br$ (186.989) calc'd: C 51.39%
found: C 52.07%

($H_2O + D_2O$) per 100 g of $C_8H_7D_2Br$ containing 1.90 atoms of deuterium per molecule calc'd: 44.38 g found: 45.93 g
If all water collected is considered to be H_2O than calc'd: H 4.97% found: H 5.14%

*2-Phenylethyl-dimethylsulphonium-1,1-*d$_2$ *bromide*

Methyl 2-phenylethyl-1,1-d_2 sulphide was prepared from 2-phenylethyl-1,1-d_2 bromide (new batch) by the procedure of Fehnel and Carmack[14]. Equimolar quantities of this compound and methyl bromide were mixed in nitromethane. After recrystallization from ethanol-ether the product was obtained in 50% yield. Undeuterated and deuterated sulphonium salts were prepared in the same way. The undeuterated product *decomposed* at about 135.5°C, which agreed fully with our previous measurements[10]. The deuterated sulphonium salts *decomposed* at about 133.5°C (after several recrystallizations).

Anal. $C_{10}H_{15}SBr$ (247.20) calc'd: C 48.58; H 6.12; Br 32.33%
found: C 48.72; H 6.28; Br 32.27%

The deuterium analysis showed that the molecule contained 1.91 atoms of deuterium per molecule. Taking this into account the average molecular weight was calculated to be 249.1.

Anal. $C_{10}H_{13}D_2SBr$ (249.1) calc'd: Br 32.08%
found: Br 31.67%

2,2-Dideutero-1,1-di(trideuteromethyl)propyl-dimethylsulphonium iodide

2,2-dideutero-1,1-di(trideuteromethyl)-propanol was prepared by Shiner's procedure[3]. (Deuterated aceton, containing about 5.9 atoms of deuterium per molecule, needed in the preparation, was obtained from Tracerlab. Inc., Mass., U. S. A.) The alcohol was converted to iodide using Bauer's procedure[15]. The sulphonium salt was prepared by the procedure of Cooper *et al.*[16].

Deuterium analysis showed that the molecule of the sulphonium salt contained 7.57 atoms of deuterium.

Anal $C_7H_{17}SI$ (260.19) calc'd.: I 48.77%
found: I 48.4 %

Taking into account the degree of deuteration the average molecular weight of the deuterated sulphonium salt amounted 267.80.

Anal. $C_7H_9D_8SI$ (267.80) calc'd: I 47.39%
found: I 47.35%

Deuterium analyses. — The *falling drop* method[11] was used. Duplicate analyses usually agreed to within 1%.

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IZVOD

Sekundarni deuterijski izotopski efekti kod nekih S_N1 i E_2 reakcija

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U E_2 reakciji između 2-feniletil-1,1-d_2 bromida i natrijeva etilata u etilnom alkoholu nađen je α-sekundarni deuterijski izotopski efekt k_H/k_D od 17%. Ta činjenica govori u prilog Streitwieser-ove teorije o promjeni hibridizacije sp^3 u sp^2 kao uzroka α-deuterijskoga izotopskog efekta. Prema toj teoriji α-deuterijski izotopski efekt nije moguć kod S_N2 reakcija zbog blizine reaktanta α-ugljiku u prijelaznom stanju. Međutim, izvršena mjerenja pokazuju, da je taj efekt moguć u E_2 reakcijama, jer zbog udaljenosti mjesta atake od α-ugljika može u E_2 reakcijama doći do promjene hibridizacije, pa tako i do izotopskog efekta. α-sekundarni deuterijski izotopski efekt nije bio do sada zapažen.

Određena je veličina β i α-sekundarnoga deuterijskog izotopskog efekta u S_N1 i E_2 reakcijama nekih alkil-sulfonijskih soli i odgovarajućih alkil-halogenida. Nađeno je da su izotopski efekti znatno manji kod alkil-sulfonijskih soli nego kod odgovarajućih alkil-halogenida. Dano je tumačenje za ove razlike i povučena je usporedba sa Saytzeffovim i Hofmanovim pravilom.

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