(6) A. Nechvatal, *Advan. Free Radical Chem.*, **4**, 175 (1972).
(7) L. Ramberg and A. Mellander, *Ark. Kemi, Mineral. Geol.*, **11B**, No. 31 (1934); L. Ramberg and I. Hedlund, *ibid.*, **11B**, No. 41 (1934). When bromine was not in excess the reaction was found to display a component for bromine in the rate expression.[8]
(8) See R. P. Bell and B. G. Cox, *J. Chem. Soc. B*, 652 (1971), for a recent discussion.
(9) See also J. E. Taylor and F. H. Verhoek, *J. Amer. Chem. Soc.*, **81**, 4537 (1959). The authors observed a base-catalyzed decarboxylation of (−)-$PhSO_2C(Me)(Et)CO_2H$ to (+)-$PhSO_2CH(Me)Et$. Their conclusion that formation of an optically active decarboxylation product ruled out the presence of a carbanion intermediate has been invalidated, however, by later work.[10]
(10) E. J. Corey and T. H. Lowry, *Tetrahedron Lett.*, **No. 13**, 808 (1965).
(11) For precedents see F. G. Bordwell and B. M. Pitt, *J. Amer. Chem. Soc.*, **77**, 572 (1955); D. L. Tuleen and T. B. Stephens, *J. Org. Chem.*, **34**, 31 (1969).
(12) Decarboxylation of sulfonium salts of the type $[R_2SCH_2CO_2H]^+X^-$ is known to occur readily in refluxing acetone.[13]
(13) D. M. Burness, *J. Org. Chem.*, **24**, 849 (1959).

Facilitation of Deuterium Exchange in a Sulfone by a γ-Halogen Atom in a Ramberg-Bäcklund Reaction

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Received December 10, 1973

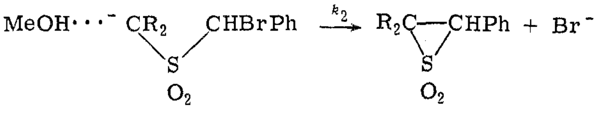
Observation of deuterium exchange occurring during 1,3-dehydrobromination of $Me_2CHSO_2CHBrPh$ in NaOMe-MeOD and of a low k^H/k^D isotope effect (1.2) for 1,3-dehydrobromination in 40% aqueous dioxane shows that this reaction is occurring by a two-stage, carbanion mechanism, rather than a one-stage, concerted mechanism. Deuterium exchange at the methine position of $Me_2CHSO_2CHClPh$ was found to be over 1000 times as rapid as that in the parent sulfone, $Me_2CHSO_2CH_2Ph$. It is postulated that the chlorine atom accelerates exchange not only by an inductive effect but also by facilitating solvent exchange at the initially formed singly solvated carbanion.

In a previous paper we reported some surprising differences for the effect of methyl substitution on deuterium exchange α to a sulfonyl group *vs.* removal of a similarly situated proton in a Ramberg-Bäcklund reaction. Each substitution of a methyl group in the series $PhCH_2SO_2CH_3$ (1), $PhCH_2SO_2CH_2Me$ (2), $PhCH_2SO_2CHMe_2$ (3) caused a decrease in methoxide-catalyzed deuterium exchange rate of about 100-fold.[1] The rate-limiting step in such exchanges has been shown by Cram to be the rate of solvent exchange between the initially solvated carbanion and bulk solvent (k_s).[2]

$$\begin{tikzcd} MeO^- + HCR_2SO_2CH_2Ph \arrow[r, shift left, "k_1"] & MeOH\cdots{}^-CR_2SO_2CH_2Ph \arrow[l, shift left, "k_{-1}"] \arrow[d, "k_s", "MeOD"'] \\ MeO^- + DCR_2SO_2CH_2Ph & MeOD\cdots{}^-CR_2SO_2CH_2Ph \arrow[l, "k_{-1}"'] \end{tikzcd}$$

Methyl substitution probably decreases k_1 by an inductive effect, and may also decrease k_s. Since k_{-1} (internal return) is extremely fast—perhaps even faster than a diffusion-controlled rate—it will be affected to a much lesser extent. Let us assume that the 10^4 rate decrease from 1 to 3 results from a tenfold decrease in k_1 and also in k_s for each methyl substitution. An overall decrease in rate of ~100-fold would then be expected in analogous Ramberg-Bäcklund reactions in the series $PhCHBrSO_2CH_3$ (4), $PhCHBrSO_2CH_2Me$ (5), $PhCHBrSO_2CHMe_2$ (6), since a tenfold retardation in k_1 should be observed on each methyl substitution.

$$MeO^- + \underset{\substack{\mathbf{4,\ 5,\ 6}\\ (R\ =\ H\ or\ Me)}}{HCR_2SO_2CHBrPh} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}$$



Instead, the overall rate is affected but little by methyl substitution, the relative rates for **4**:**5**:**6** being (1.0):1.7:0.62.[1] One way to account for these results is to assume that competition between k_2 and k_{-1} has decreased the relative amount of internal return.[1] Another possibility is that there is a change in mechanism along the series; for example, the reaction of 4 (R = R = H) might occur in two stages, as indicated by the equations, whereas the reaction of 6 (R = R = Me) might occur in one stage (concerted mechanism). Additional experiments have now been carried out in an attempt to choose between these two possibilities.

Ordinarily, because of internal return, one observes low or even inverse k^H/k^D isotope effects for exchange of protons α to sulfonyl groups.[2] On the other hand, in a concerted reaction one might expect to observe a sizable k^H/k^D isotope effect. The isotope effect for 6 was therefore examined. Since the two-stage Ramberg-Bäcklund reaction is known to have a large k^{Br}/k^{Cl} leaving-group effect,[3] it was also of interest to examine the behavior of the chloro analog of 6, $PhCHClSO_2CHMe_2$ (7).

Results

The desired α-bromobenzyl isopropyl sulfone and its deuterated analog were obtained by methods reported in the literature. The rates of hydroxide- or methoxide-initiated dehydrobromination were measured spectrophotometrically in 40% aqueous dioxane and methanol solutions, respectively (Table I).

The k^H/k^D of 1.0 in methanol indicated that prior exchange was occurring, and this was supported by quenching experiments. In an experiment run with 6 at 25° in methanol-*O-d* the starting material was 37% deuterated at the methine position after the reaction was only 18% complete. Some exchange at the methine position occurred also in 40% aqueous dioxane, but the amount was not sufficient to affect the rate data, as may be judged by the high correlation coefficients obtained from a least-squares plot in the rate calculations ($r = 0.9992$ for the deuterium compound and 0.9999 for the hydrogen compound). We believe, therefore, that the k^H/k^D of 1.2 at 50° is reasonably accurate; at 25° one would expect the ratio to increase slightly.

Table I
Spectrophotometric Rate Constants for the Reaction of $PhCDBrSO_2CD(CH_3)_2$ and $PhCHBrSO_2CH(CH_3)_2$ with Sodium Hydroxide in 40% Dioxane–Water and with Sodium Methoxide in Methanol at 50°

Compd	[NaOH]	k_2, l. mol^{-1} sec^{-1}	k^H/k^D
H	0.252	$3.56 \pm 0.02 \times 10^{-3}$	1.21
D	0.252	$2.94 \pm 0.05 \times 10^{-3}$	
H	0.252	$3.58 \pm 0.01 \times 10^{-3}$ [a]	1.18
D	0.252	$3.03 \pm 0.05 \times 10^{-3}$ [a]	
H	0.1155	3.53[b]	

Compd	[NaOMe]	k_2, l. mol^{-1} sec^{-1}	k^H/k^D
D	0.261	$4.17 \pm 0.08 \times 10^{-4}$	
D	0.261	$3.82 \pm 0.09 \times 10^{-4}$	
H	0.261	$4.33 \pm 0.08 \times 10^{-4}$	1.0
H	0.261	$4.17 \pm 0.08 \times 10^{-4}$	

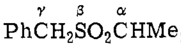
[a] Calculated by the infinity method. All others are calculated by the Guggenheim method. [b] Single run; this indicates that the reaction is second order in hydroxide ion.

The relatively slow rate of release of halide ion from α-chlorobenzyl isopropyl sulfone (7) allowed a direct measurement of the rate of exchange of the methine hydrogen in D_2O-dioxane by quenching experiments. The results are summarized in Table II.

Discussion

The observation of 37% exchange at the Me_2CH proton of $Me_2CHSO_2CHBrPh$ (6) with NaOMe in MeOD at 18% reaction together with a k^H/k^D isotope effect of 1.0 (Table I) shows that $k_s > k_2$ and that 6 is reacting by a two-stage, carbanion mechanism and not by a one-stage, concerted mechanism. In 40% aqueous dioxane no exchange was observable. This does not mean, however, that a change to a concerted mechanism has occurred. A more reasonable interpretation would be that now k_2 has become larger than k_s. The low k^H/k^D isotope effect (1.2) is consistent with a two-stage mechanism with extensive internal return ($k_{-1} \gg k_2$). This interpretation is strongly supported by the kinetic data for the chloro analog, $Me_2CHSO_2CHClPh$ (7). Now k_2 would be expected to be slower by a factor of at least 100,[3] and k_s should be larger than k_2. This is what is observed (Table II). It is amusing to note that if one looks only at the relative rates of reaction with NaOMe in MeOD of $Me_2CHSO_2CHBrPh$ (Ramberg–Bäcklund) and $Me_2CHSO_2CH_2Ph$ (exchange of the methine proton), which are 560:(1.0), and at the failure of exchange in $Me_2CHSO_2CHBrPh$ to occur during reaction in 40% aqueous dioxane, one could make a strong case for a concerted reaction. It is only by a careful examination of additional aspects that the two-stage mechanism is revealed.[4]

The most surprising result of the present investigation was the greater than 1000-fold increase in exchange rate on substitution of a chlorine atom for a hydrogen atom in the γ position of 3 (Table II). An effect of comparable size


$$\overset{\gamma}{PhCH_2}\overset{\beta}{SO_2}\overset{\alpha}{CH}Me_2$$

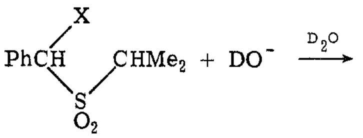
3

is also apparently operative for γ-bromine atom substitution. This acceleration is remarkable when one considers that chlorine substitution at the α position of $PhSO_2CH_3$ causes only a slightly larger effect.[6] Also, the result contrasts sharply with that in ketones where an α-chlorine atom has been reported to cause an 800-fold acceleration in exchange rate for acetone,[7] whereas a γ-chlorine atom causes only about a tenfold increase for $PhCHClCOCHMe_2$ vs. $PhCH_2COCHMe_2$.[8] Our previous estimate of a fivefold increase in the exchange rate due to the inductive effect of a γ-bromine (or γ-chlorine) atom[1] can be raised to ca. tenfold, since the transmission of electronic effects "through" an SO_2 group appears to be more efficient than "through" a methylene group.[9] Nevertheless, a factor of ca. 100 remains to be accounted for. It seems likely that an increase in the rate of exchange of external solvent with the initially formed solvated carbanion (k_s) is responsible for the unexpected increase in rate of exchange. A pictorial representation is shown.[11]

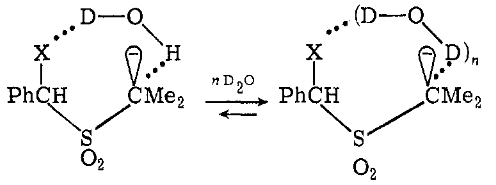
Table II
Effect of an α-Chlorine Atom on the Deuteroxide-Catalyzed Exchange of the α′-Hydrogen Atom in 40% Dioxane–D_2O at 50°

Compd	[NaOD]	k_2, l. mol sec	k_{rel}
$PhCH(Cl)SO_2CH(CH_3)_2$ (7)	0.0355	$(7.19 \pm 0.02) \times 10^{-3}$ [a]	1035
$PhCH_2SO_2CH(CH_3)_2$ (3)	0.518	$(6.94 \pm 0.4) \times 10^{-6}$ [a,b]	(1.0)

[a] Average of two runs. [b] M. D. Wolfinger reports 7.21×10^{-6} (single run): Ph.D. Dissertation, Northwestern University, 1968, p 78.



6 or 7



8 9

For bromide 6 the exchange data show that deuterium exchange rate and intramolecular displacement rate are competitive. In contrast, for $PhCHBrSO_2CH_3$ deuterium exchange at methyl is much faster than intramolecular displacement. In view of the strong accelerating effect of the γ-halogen atom on the exchange rate, it seems likely that this rate may remain relatively constant on methyl substitution in the series $PhCHBrSO_2CH_3$, $PhCHBrSO_2CH_2Me$, $PhCHBrSO_2CHMe_2$, in sharp contrast to the 10^4 retardation observed in the parent series (hydrogen replaces bromine). If k_s does remain constant, then the rate of intramolecular displacement (k_2) along the series must increase progressively in order for the change $k_s \gg k_2$ to $k_s \cong k_2$ with methyl substitution to be observed. The constancy in the rate of Ramberg–Bäcklund reaction along this series must then be due to a balance of effects. Methyl substitution decreases k_1 and thereby decreases the equilibrium concentration of carbanion, but this effect is offset by an increase in the rate of k_2.[12]

Experimental Section

Deuterium Exchange Kinetics. Hydrogen–deuterium exchange rates were measured by integration of the remaining proton signal in the pmr spectrum. A typical procedure is as follows. The sulfone (600 mg) was dissolved in 10 ml of purified dioxane (thermostatted to 50.04 ± 0.02°) and added to 15 ml of D_2O, 0.0527 M in NaOD (thermostatted). Aliquots (5 ml) were withdrawn at appropriate intervals and quenched with 0.15 M HNO_3

(20 ml). The suspension was extracted with carbon tetrachloride (2 × 10 ml) and the carbon tetrachloride layers were washed with water and dried. Solvent was removed by rotary evaporation. Residual dioxane was removed by pumping on the samples (0.1 mm, 48 hr). Samples were dissolved in 500 μl of $CDCl_3$ and the exchangeable hydrogen was integrated. The aromatic protons were used as an internal standard. Four integrations of the proton and standard were performed in each case. Rate constants were determined by plotting the natural logarithm of the remaining proton against time, using a least-squares method. Second-order rate constants were determined by dividing the first-order rate constants by the base strength.

The validity of the integration method was checked by preparation of a calibration curve for α-chlorobenzyl isopropyl sulfone. Mixtures of 0, 25, 50, and 75 deuterated material were prepared by mixing together appropriate weights of undeuterated and fully deuterated (at the site of exchange) substrate. These mixtures were then dissolved in 500 μl of chloroform-*d* and integrated in a manner identical with that used in the rate determinations. The per cent of deuterium in the sample (by weight) was plotted against the per cent of deuterium in the sample by integration to give a straight line ($r = 0.997$) of slope 1.06 ± 0.05.

Acknowledgment. We are grateful to the National Science Foundation (GP-29539X) for support of this investigation.

Registry No.—**3**, 34009-00-2; **7**, 51392-16-6; $PhCDBrSO_2CD(CH_3)_2$, 51392-17-7; $PhCHBrSO_2CH(CH_3)_2$, 35500-99-3.

References and Notes

(1) F. G. Bordwell and M. D. Wolfinger, *J. Amer. Chem. Soc.*, **93**, 6303 (1971). J. R. Jones (private communication) has found relative rates of about $(1.0):10^2:10^4$ in the rates of tritium exchange in NaOMe–MeOH for the series $p\text{-}ClC_6H_4SO_2CHMe_2$, $p\text{-}ClC_6H_4SO_2CH_2Me$, $p\text{-}ClC_6H_4SO_2CH_3$. Experimental details are given in the Ph.D. Dissertation of Mark D. Wolfinger, Northwestern University, 1968.

(2) D. J. Cram, D. A. Scott, and W. D. Nielsen, *J. Amer. Chem. Soc.*, **83**, 3696 (1961).

(3) (a) F. G. Bordwell and J. M. Williams, Jr., *J. Amer. Chem. Soc.*, **90**, 435 (1968); (b) see F. G. Bordwell and M. D. Wolfinger, *J. Org. Chem.*, **39**, 2521 (1974), for additional examples.

(4) We have commented elsewhere on the rarity of the one-stage mechanism for 1,3-eliminations.[5]

(5) (a) F. G. Bordwell, *Accounts Chem. Res.*, **3**, 281 (1970); (b) F. G. Bordwell and B. B. Jarvis, *J. Amer. Chem. Soc.*, **95**, 3585 (1973). See also F. G. Bordwell and E. Doomes, *J. Org. Chem.*, **39**, 2531 (1974).

(6) D. A. Schexnayder, Ph.D. Dissertation, Northwestern University, 1968, observed *ca.* a 1400-fold increase in the rate of exchange of $PhSO_2CH_2Cl$ *vs.* $PhSO_2CH_3$ in NaOMe–MeOD at 25°.

(7) R. P. Bell and A. Lidwell, *Proc. Roy. Soc., Ser. A*, **176**, 88 (1950).

(8) F. G. Bordwell and J. Almy, *J. Org. Chem.*, **38**, 575 (1973).

(9) The ρ for $ArSO_2CH_2CO_2H$ is 0.253,[10] as compared to 0.237 for $ArCH_2CH_2CO_2H$.[10] (Our earlier estimate was based on a transmission coefficient of 2.8 for SO_2.)

(10) D. J. Pasto, D. McMillan, and T. Murphy, *J. Org. Chem.*, **30**, 2688 (1965).

(11) An alternative possibility, which we believe to be less likely, is facilitation of ionization and solvent exchange at the methine position by a 1,3 proton shift of the type $Ph\bar{C}ClSO_2CHMe_2 \rightarrow PhCHClSO_2\bar{C}Me_2$.

(12) See ref 3b for additional data on the effects of methyl substitution on the rate of Ramberg–Bäcklund reactions.

Solvent and Substituent Effects in the Ramberg–Bäcklund Reaction

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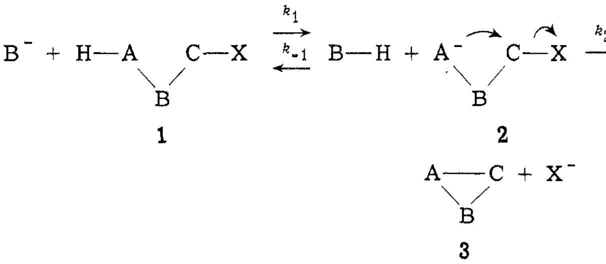
Received December 13, 1973

The effects of increasing the proportion of nonaqueous solvent on the rate of reaction of $PhCHBrSO_2CH_2Ph$ with lyate ion in mixtures of water with 1,2-dimethoxyethane, dioxane, ethanol, or methanol have been found to be remarkably similar to those observed earlier under similar conditions with ethylene chlorohydrin. Deuterium exchange studies indicate that with $ArCH_2SO_2CH_2X$ (**4**) and $ArCHXSO_2CH_3$ (**5**), as well as with $ArCHXSO_2CH_2Ar$ (**6**), equilibrium concentrations of α′ carbanions are formed prior to halide loss. The overall ρ values for alkene formation from **4**, **5**, and **6** range from +1.29 to +3.43. Analysis shows that ρ for halide ion loss is negative for **4** and slightly positive for **5** and **6**. Methyl substitution at the α position of **4** or the α′ position of **5** causes surprisingly little change in the overall rate of alkene formation. The k^{Br}/k^{Cl} leaving group effects for **4**, **5**, and **6** in 40% aqueous dioxane ranged from 169 to 207. All of these observations are shown to be consistent with a mechanism wherein equilibrium concentrations of α′ carbanions are formed in the first step and these carbanions participate in a nucleophilic displacement in a second, rate-limiting step.

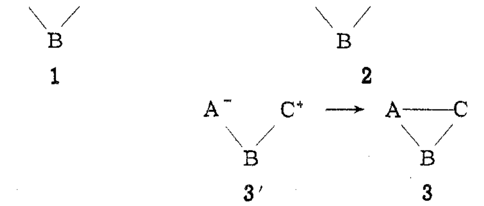
A variety of stepwise mechanisms can be visualized for base-promoted 1,3-elimination of H-X from a system H-A-B-C-X with consequent formation of a three-membered ring.[2] In the most common mechanism (1), deprotonation by a base, B^-, generates an anion (2) from which X^- is eliminated by an intramolecular nucleophilic displacement initiated by atom A. (Either k_1 or k_2 can be rate limiting, depending on the system.)



(1)

Numerous examples are known where A is O, N, C, S, P, etc., and B and C are carbon atoms.[3,4]

The presence of a negative charge in 2 would be expected to enhance greatly the tendency for X to ionize without direct participation by the nucleophilic atom A^-. If one or more groups capable of stabilizing a carbonium ion, such as Ar, R, or RO, are present on the atom holding X, it would not be surprising, then, to find that the mechanism has changed to one where a dipolar ion intermediate (3′) is produced in the second step (mechanism 2).



(2)

Examples where the evidence indicates that a type 2 mechanism obtains, at least in some instances, include (a) α-lactone formation by solvolysis of $ArCHXCO_2H$ in