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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Relative Rates of Base-Catalyzed Racemization and Deuterium Exchange of Aryl 2-Octyl Sulfones[1]

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The rates of base-catalyzed (sodium methoxide) racemization (k_{rac}) and exchange of deuterium for hydrogen (k_{exc}) of phenyl and *p*-tolyl 2-octyl-2-*d* sulfone in methanol at 100° have been determined. The phenyl sulfone racemizes and exchanges more rapidly than the *p*-tolyl analog. With each sulfone, exchange exceeds racemization—*e.g.*, k_{exc}/k_{rac} is 17 for the phenyl sulfone and 14 for the *p*-tolyl sulfone. Thus exchange occurs for the most part with preservation of optical configuration. This shows that carbanions stabilized by sulfone groups are nonplaner; *i.e.*, enantiomeric sulfones give enantiomeric carbanions.

Recent preliminary reports[3] concerning the relative rates of base-catalyzed racemization and deuterium exchange of optically active 2-octyl-2-*d* phenyl sulfone prompt us to report the results of a similar investigation. Because of work in progress in other laboratories[3,4] we have discontinued our research in this area and report herein results obtained to date which are complementary to those reported in ref. 3.[5] In the present work we determined the pseudo first-order rates of racemization of (−)phenyl and (−)*p*-tolyl 2-octyl sulfone and the rates of racemization and deuterium exchange of the deuterated analogs in methanol containing sodium methoxide.

Our interest in the stereochemical behavior of carbanions stabilized by sulfone functions stems from an investigation of elimination reactions of cyclic β-chloro sulfones.[6] In that work it was suggested that base-promoted *cis*-elimination of *trans*-chloro sulfones to give α,β-unsaturated sulfones may involve a two-step process (removal of the acidic α-hydrogen atom followed by conversion of the intermediate carbanion to product) rather than a concerted process.[7] The primary objective of the present work was to determine if the properties of α-sulfonyl carbanions are consistent with this view.

RESULTS AND DISCUSSION

Optically pure (−)-phenyl and (−)-*p*-tolyl 2-octyl sulfone were prepared from (−)-2-octanol.[8] The alcohol was converted to the *p*-toluenesulfonate derivative,[9] which was reacted with sodium thiophenolate or sodium *p*-thiocresolate to form the desired active aryl 2-octyl sulfide. The sulfide was converted to the corresponding sulfone by oxidation with hydrogen peroxide in glacial acetic acid.[10] The aryl 2-octyl-2-*d* sulfones were prepared in a similar manner from (−)-2-octanol-2-*d*, which was obtained by reduction of 2-octanone with lithium aluminum deuteride.

Kinetic data for the base-catalyzed racemization and exchange of deuterium for hydrogen of phenyl and *p*-tolyl 2-octyl sulfone in methanol at 100° are presented in Table I. Optically pure undeuterated sulfones were used in experiments 1–4 and 6–10. In these experiments the reactions were followed to about 75% completion, and the loss of optical activity was complete. Good pseudo first-order behavior (first order in methoxide ion and sulfone) was observed. The infrared spectra of the racemic products (isolated after ten half-periods) were indistinguishable from those of the optically pure reactants.

Optically pure phenyl and *p*-tolyl 2-octyl-2-*d* sulfone were used in experiments 5 and 11. In these experiments the same reaction solution was used to determine the rates of racemization and deuterium exchange.

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[2] (a) Du Pont Summer Research Fellow, 1959. (b) Du Pont Summer Research Fellow 1957.

[3] (a) E. J. Corey and E. T. Kaiser, *J. Am. Chem. Soc.*, **83**, 490 (1961). (b) D. J. Cram, W. D. Nielsen, and B. Rickborn, *J. Am. Chem. Soc.*, **82**, 6415 (1960).

[4] D. J. Cram, private communication.

[5] The results reported in this paper were obtained prior to the appearance of the communications included in ref. 3.

[6] H. L. Goering, D. I. Relyea, and K. L. Howe, *J. Am. Chem. Soc.*, **79**, 2502 (1957).

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Rate constants for racemization (k_{2rac}) and exchange (k_{2exc}) in Table I are second-order or catalytic constants. Base concentrations[11] were determined periodically and found to decrease only slightly (<5%) during the reactions.[12] The rate constants given in Table I are averages (and average deviations) of from 5 to 7 values determined at appropriately spaced intervals for each experiment.

TABLE I

RACEMIZATION AND DEUTERIUM EXCHANGE OF ARYL 2-OCTYL SULFONES IN METHANOL AT 100°

Exp.	Sulfone, 10 M	NaOCH$_3$, 10^2 M	Temp.	10^5 k_{2rac}, L. Mole^{-1} Sec.$^{-1}$	10^4 k_{2exc}, L. Mole^{-1} Sec.$^{-1}$
		PHENYL 2-OCTYL SULFONE			
1	1.46	4.75	99.72	2.31 ± 0.06	
2	1.34	5.03		2.51 ± 0.10	
3	1.34	6.39		2.64 ± 0.05	
4	1.35	9.34		2.90 ± 0.04	
		PHENYL 2-OCTYL-2-*d* SULFONE			
5	0.43	10.26	99.76	3.17 ± 0.09	5.5 ± 0.3
		p-TOLYL 2-OCTYL SULFONE			
6	1.13	4.08	99.71	1.05 ± 0.06	
7	1.12	7.69		1.19 ± 0.05	
8	1.11	8.16		1.22 ± 0.06	
9	1.26	8.26		1.22 ± 0.02	
10	1.110	12.17	99.72	1.25 ± 0.08	
		p-TOLYL 2-OCTYL-2-*d* SULFONE			
11	1.13	10.36	99.65	1.36 ± 0.07	1.9 ± 0.2

The exchange experiments (experiments 5 and 11) were followed by isolation of the substrate at appropriate intervals and determination of the deuterium content by infrared analysis.[13,14] Deuterium contents determined by this method were in satisfactory agreement with values obtained by combustion.[15] The exchange reaction was also pseudo first order, first order in base and sulfone. In these experiments the ratio of deuterium (originally in the substrate) to exchangeable (hydroxyl) hydrogen in the solvent was low (*ca.* 1/170). Thus at equilibrium the deuterium content of the substrate (and solvent) was negligible, and no correction was required for the reverse reaction.

The results presented in Table I show that in methanol at 100° the base-catalyzed deuterium exchange exceeds racemization by factors of 17 and 14 for (−)-phenyl and (−)-*p*-tolyl 2-octyl-2-*d* sulfone, respectively. The data for the phenyl sulfone are consistent with the qualitative data reported by Cram and co-workers[3b] for the same conditions (in their work they used potassium methoxide instead of sodium methoxide). The present data show that each sulfone the second-order constant for racemization increases slightly with base concentration (*i.e.*, the apparent reaction order with respect to base is slightly larger than unity). Presumably, this is due to a medium (salt) effect. It is noteworthy that the racemization rate constants for the deuterated sulfones (experiments 5 and 11) are the same as would be expected for the undeuterated sulfones under similar conditions. This, of course, has to be the case since k_{exc} is enough larger than k_{rac} that most of the sulfone exchanges prior to racemization. The present data also show that the phenyl sulfone racemizes and exchanges more rapidly than the *p*-tolyl analog as would be expected.

Recently relative rates of racemization and deuterium exchange of optically active phenyl 2-octyl sulfone have been investigated using various solvent–base combinations.[3,4] In most cases the k_{exc}/k_{rac} ratio is higher than the value observed in the present work.[16] For example, in ethanol–water (2:1 vol.) the hydroxide ion-catalyzed exchange is 41 times faster than racemization.[3a] As has been pointed out,[3] the greater rate of exchange than racemization shows that enantiomeric sulfones give rise to enantiomeric (nonplanar[14,17]) carbanions. Possible electronic configurations and interactions for α-sulfonyl carbanions have been discussed.[3]

The rates of base-catalyzed exchange of deuterium for hydrogen of cyclopentyl-1-*d* and cyclohexyl-1-*d* *p*-tolyl sulfone have recently been reported.[13] From these studies it was concluded that carbanion formation cannot be the rate-determining step in *cis* elimination reactions of cyclic *trans*-β-chloro[6] and β-tosyloxy[7] sulfones (hydrogen abstraction to form the anion was estimated to be 10^3 and 10^5 times slower than *cis* elimination).[13] However, this conclusion was based on the assumption that the rate of exchange of deuterium for hydrogen equals the rate of ionization. This now appears to be unlikely. The very fact that sulfones exchange hydrogen with retention of configuration shows that protonation is stereospecific in the sense that there is a preferred or required direction from which the proton donor must approach the nonplanar carbanion. Thus at any instant the configuration of the anion is such that only a fraction of the solvent molecules in the solvation shell are on the required side for partici-

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[11] Reported concentrations are for 25°; the second-order constants (Table I) have not been corrected for thermal expansion of the solvent.

[12] Soft glass ampules were used to minimize destruction of base by reaction with the reaction vessel; see H. L. Goering and H. H. Espy, *J. Am. Chem. Soc.*, **78**, 1454 (1956).

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[14] H. E. Zimmerman and B. S. Thyagarajan, *J. Am. Chem. Soc.*, **82**, 2505 (1960).

[15] Determined by J. Nemeth, Urbana, Ill.

[16] In *t*-butyl alcohol-potassium *t*-butoxide at 25° k_{exc}/k_{rac} = 1980 (ref. 4).

[17] W. E. Doering and K. L. Levy, *J. Am. Chem. Soc.*, **77**, 509 (1955).

pating in the protonation step. It seems reasonable that for each time that exchange occurs the anion may react many times with the solvent molecule produced in the ionization step (from lyate ion and the abstracted hydrogen or deuterium) because this molecule would be expected to occupy a choice site in the solvation shell. Thus exchange may be much slower than the rate of carbanion formation and it seems that the two step (carbanion) mechanism[6] for the *cis* elimination of β-substituted sulfones still has to be considered as a possibility.

TABLE II

RACEMIZATION OF (−)-2-OCTYL PHENYL SULFONE IN METHANOL CONTAINING 0.0639 M $NaOCH_3$ AT 99.72°; EXPERIMENT 3

Time, 10^{-3} Sec.	Rotation[a]	$10^6\ k_{\mathrm{rac}}{}^b$, Sec.$^{-1}$	$10^5\ k_{2\mathrm{rac}}{}^c$, L. Mole^{-1} Sec.$^{-1}$
0	1.623		
147.6	1.269	1.67	2.61
237.6	1.099	1.64	2.57
327.6	0.918	1.74	2.72
500.4	0.688	1.71	2.68
864.0	0.383	1.68	2.62
		1.69 ± 0.03	2.64 ± 0.05

[a] Observed rotation of reaction mixture at 25° in 4-dm. tube. [b] Pseudo first-order constant. [c] Second-order constant.

TABLE III

RATE OF DEUTERIUM EXCHANGE OF (−)-2-OCTYL-2-d PHENYL SULFONE IN METHANOL AT 99.76°; $NaOCH_3$ = 0.1026 (Exp. 5)

Time, 10^{-3} Sec.	Deuterium[a]	$10^5\ k_{\mathrm{exc}}{}^b$, Sec.$^{-1}$	$10^4\ k_{2\mathrm{exc}}{}^c$, L. Mole^{-1} Sec.$^{-1}$
0	1.00		
7.2	0.65	6.08	5.94
16.2	0.41	5.50	5.36
21.6	0.32	5.28	5.14
25.2	0.24	5.75	5.60
28.8	0.17	5.64	6.00
48.6	0.085	5.08	4.94
			5.5 ± 0.3

[a] Atoms of deuterium per molecule. [b] Pseudo first-order constant. [c] Second-order rate constant.

EXPERIMENTAL

Materials. The acid phthalates of 2-octanol and 2-octanol-2-d[18] were resolved in the usual manner.[8] (−)-2-Octyl acid phthalate $[\alpha]^{25}\mathrm{D}$ −48.07° and (−)-2-octyl-2-d acid phthalate $[\alpha]^{25}\mathrm{D}$ −48.12° were converted to the optically active alcohols[8] which in turn were converted to their liquid p-toluenesulfonate derivatives.[9] The latter derivatives were used for preparation of the optically active aryl 2-octyl sulfides which were oxidized[10] to the sulfones.

Preparation of phenyl and p-tolyl 2-octyl sulfones. In a typical preparation of (−)-2-octyl phenyl sulfone, 39 g. of crude 2-octyl p-toluenesulfonate derived from 40.8 g. (0.147 mole) of 2-octyl acid phthalate, m.p. 72.4–73.0° $[\alpha]^{25}\mathrm{D}$ −48.3° (lit.[8] $[\alpha]\mathrm{D}$ −48.4°) was converted to the phenyl sulfide as follows. An alcoholic solution of sodium thiophenolate was prepared by dissolving 5.1 g. (0.22 g.-atom) of clean sodium in 100 ml. of absolute ethanol and adding 24.2 g. (0.22 mole) of freshly distilled thiophenol, b.p. 166°. The p-toluenesulfonate derivative was added to this stirred solution over a period of about 30 min. The mixture was then refluxed and stirred for an additional hour. After cooling, the reaction mixture was diluted with 225 ml. of 5% aqueous sodium hydroxide and extracted with four 50-ml. portions of ether. The combined ether extract was washed with 5% sodium hydroxide, water, and brine. After drying (sodium sulfate) the ether was removed under reduced pressure and 20 g. of residual 2-octyl phenyl sulfide was obtained as a light yellow oil. The sulfide was dissolved in 100 ml. of glacial acetic acid and 75 ml. of 30% hydrogen peroxide was added dropwise over a period of 20 min. The mixture was then heated on a steam bath for 7 hr. during which time three additional 25-ml. portions of hydrogen peroxide were added at about 2-hr. intervals. After cooling, the reaction mixture was diluted with 100 ml. of water and chilled. About 15 g. of product (40.2% based on the acid phthalate) separated and was collected. An additional 2.5 g. was obtained by ether extraction of the mother liquors. After three recrystallizations from petroleum ether, two from 70% ethanol, and a final one from petroleum ether, 8.2 g. of *2-octyl phenyl sulfone*, m.p. 45–46° $[\alpha]^{30}\mathrm{D}$ −13.4° (c 1.7, ethanol) (lit.[3a] m.p. 44–45°, $[\alpha]^{20}\mathrm{D}$ −13.3° (c 1.9; 2:1 ethanol–water). Additional recrystallizations did not affect the physical properties of the product.[19]

(−)-2-Octyl-2-d, phenyl sulfone, m.p. 44.6–45.3°, $[\alpha]^{25}\mathrm{D}$ −13.81° (c 1.6, 95% ethanol) was obtained in 58% yield by the above procedure.

(−)-2-Octyl-2-d p-tolyl sulfone, m.p. 58.5–59.3°, $[\alpha]^{25}\mathrm{D}$ −11.75° (c 2, 95% ethanol) was obtained in 64% yield.

Anal. Calcd. for $C_{15}H_{23}DO_2S$: C, 66.87; H, 9.35. Found: C, 67.08; H, 9.34.

(−)-2-Octyl p-tolyl sulfone had m.p. 58.3–60.3°, $[\alpha]^{30}\mathrm{D}$ −11.6° (c 2.6, ethanol).

Anal. Calcd. for $C_{15}H_{24}O_2S$: C, 67.12; H, 9.01. Found: C, 66.95; H, 8.98.

dl-2-Octyl phenyl sulfone had m.p. 27–27.5°.

Anal. Calcd. for $C_{14}H_{22}O_2S$: C, 66.10; H, 8.72. Found: C, 66.30; H, 8.61.

dl-2-Octyl p-tolyl sulfone had m.p. 42–43°.

Anal. Calcd. for $C_{15}H_{24}O_2S$: C, 67.12; H, 9.01. Found: C, 67.04; H, 8.72.

Kinetic experiments. Solvent for the kinetic studies was prepared by dissolving the desired amount of freshly cut sodium (washed with pure methanol) in freshly distilled anhydrous methanol. The base concentration[11] was determined by titration with standard hydrochloric acid. Reaction mixtures were prepared by dissolving the desired amount of pure sulfone in 50 ml. of the sodium methoxide solution. The reaction mixture was distributed into soft glass ampules[12] (approximately 7-ml. aliquots) which were placed in a thermostat. After temperature equilibration (about 20 min.) the zero-point aliquot was withdrawn and chilled to quench the reaction. Subsequent aliquots were withdrawn at appropriate intervals. The ampules were adjusted to 25°, and the rotations of the aliquots were measured. Titration of the aliquots with standard acid demonstrated that the base concentration decreased only slightly (<5%) during the reaction. Rate constants are not corrected for the slight change in base concentration. The pseudo first-order rate constants were calculated from the rate of loss of optical activity; the rotation of solutions after ten half periods was zero. A typical racemization experiment is summarized in Table II.

In the deuterium exchange experiments (experiments 5 and 11) after the rotations were determined the sulfone was recovered by neutralizing the reaction mixture with 0.05 N hydrochloric acid, diluting with 50 ml. of water and

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(18) A. Streitwieser, *J. Am. Chem. Soc.*, **75**, 5014 (1953).

(19) Samples of acid phthalate varying from 90% to 100% optically pure gave products having the same rotation. Evidently recrystallization of the sulfone completes the resolution.

extracting with one 20-ml. and three 15-ml. portions of ether. The organic extract was washed with water and concentrated to dryness under reduced pressure. The deuterium content was determined by an infrared spectrophotometric method.[13] Weighed samples of recovered sulfone were dissolved in carbon tetrachloride (measured with a micro syringe) and spectra were determined with a Perkin-Elmer, single beam, double pass infrared spectrophotometer Model 112. The same 1.0-mm. sodium chloride cell was used for all of the determinations. Deuterium contents were determined from the intensity of the band near 10.8 μ with the aid of calibration curves[13] constructed from the spectra of synthetic mixtures. To check the method, samples determined to have 0.96, 0.43, and 0 atoms of deuterium per molecule by infrared spectroscopy were analyzed by combustion.[15] The combustion values were 0.967, 0.456, and 0.007. The results of an exchange experiment are shown in Table III.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

Reactions of Alkyl Carboxylic Esters with Mercaptides[1,2]

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A preliminary study of the scope and mechanism of the reaction between carboxylic esters and mercaptides is reported. The reactions were carried out under nitrogen, and in most cases involve attack by mercaptide at the alkyl carbon of the ester; however, with benzyl mercaptide a number of instances of acyl carbon attack were observed, especially where the alkyl carbon was hindered (*e.g.*, *t*-butyl, neopentyl). Since propyl mercaptide does not appear to attack propyl thiolbenzoate, and since the best evidence for effective acyl carbon attack is isolation of a symmetrical dialkyl sulfide formed from an intermediate thiol ester by further mercaptide attacking the alkyl carbon, it is concluded that acyl carbon attack by mercaptide on an ordinary ester is reversible, with the equilibrium favoring the normal ester. Thus when the irreversible formation of dialkyl sulfide is possible, acyl carbon attack as the apparent mode of reaction is observable; otherwise it is not.

The reaction between propyl mercaptide and methyl mesitoate and methyl benzoate has been shown to be a second-order process with an unusually high activation energy.

In connection with other studies in this laboratory it became desirable to investigate the possibility of using the reaction of alkali metal hydrogen sulfides with alkyl acylates as an extension of Kekulé's cleavage of phenyl acylates to phenol and potassium thioacylates.[3] The literature offered conflicting information: thus Wanklyn[4] reported that potassium hydrogen sulfide with ethyl acylates produced "no mercaptans" whereas others[5] have reported that mercaptans are produced. Preliminary work in our hands with sodium hydrogen sulfide and methyl benzoate indicated that the latter claim was correct, and that under all conditions only sodium benzoate (none of the thiol salt) could be produced. This intriguing preference for alkyl attack is in line with Reid's observation that hydrogen sulfide reacts with ethyl benzoate to give mercaptan and normal acid rather than the reverse of the reaction of benzoic acid with ethyl mercaptan which leads to ethyl thiolbenzoate.[6]

Consequently it was decided to see if this preference is general for anions derived from divalent sulfur, and to this end we focused our attention on mercaptides. Apart from the early observation of Seifert[7] that phenyl acylates are cleaved by sodium ethyl mercaptide to the expected ethyl thioacylates and sodium phenylate, all work involving mercaptides with carboxylic esters is of comparatively recent origin. Thus γ-lactones and β-lactones suffer alkyl attack,[8-11] but in one instance a specific β-lactone may experience acyl attack[11] as well. Furthermore, four reports,[12-15] one of which[15] appeared subsequent to initiation of the present work, suggest that alkyl attack by mercaptan or mercaptide may prevail in normal carboxylic esters as well as lactones; but the reported reactions all involve polyfunctional compounds. For example, β-mercaptoethanol diacetate is converted to ethylene sulfide on alkaline hydrolysis.[12] This implies preferential hydrolysis of the

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[1] Abstracted in the main from the Ph.D. dissertation of Jacob Bruce Baumann, University of Michigan, 1961.

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