

was determined and found to be indistinguishable from authentic material.

The reactions were followed through 90% reaction, and in most runs eight points were taken per run. In runs that involved calculation of activation enthalpy and entropy, and common ion rate effects, stock solutions were employed to minimize errors from base concentration variation, moisture, carbon dioxide and the like. No corrections were made in concentration changes resulting from solvent expansion.

Data for a typical run (no. 37) are recorded in Table VI.

TABLE VI

RATE OF RACEMIZATION OF 0.0200 SOLUTION OF (+)-1-PHENYLMETHOXYETHANE IN 0.2338 M POTASSIUM *t*-BUTOXIDE-*O*-*d* 0.90 *t*-BUTYL ALCOHOL IN DIMETHYL SULFOXIDE AT 73.80 ± 0.03° (RUN 37)

Time, min.	Prod., g.	n_D^{25}	α_D^{25} , neat, 10.5 dm.	k_a , sec. ⁻¹ , 10 ⁻¹
0	...	1.4880	+43.32°	..
50	0.062	1.4878	21.82	2.29
101	.096	1.4878	12.00	2.12
151	.073	1.4878	5.82	2.21
199	.092	1.4877	3.60	2.08
259	.078	1.4880	1.59	2.13
310	.086	1.4884	0.89	2.09
468	.083	1.4886	.39	2.13
497	.070	1.4882	.074	2.14

Av. 2.15 ± 0.05

Runs 42 and 43 were conducted in a jacketed and thermostated polarimeter tube (25.00 ± 0.02°), utilizing the same techniques described previously.^{3d}

Deuteration of the Aromatic Ring During Hydrogen-Deuterium Exchange Experiment Conducted in *t*-Butyl Alcohol-*O*-*d*.—Under the conditions of runs 1 and 3–5, (potassium *t*-butoxide in *t*-butyl alcohol-*O*-*d* at 205–225°), extensive ring deuteration occurred. This was shown by analysis of the total deuterium content of the product of run 5 by the combustion and falling drop method,²⁰ and analysis of the amount of deuterium in the benzyl position by infrared analysis. The former gave a value of 2.98 atoms of D per molecule, and the latter, 0.57 atom of D per benzyl carbon atom. The difference of 2.4 atoms of D per molecule is presumed due to base-catalyzed hydrogen-deuterium exchange in the aromatic ring. The infrared spectrum of this material (Beckman IR 4 equipped with lithium fluoride optics, spectrum taken on a 0.1-mm. film) revealed the presence of a strong single band at 4.42 μ which was absent in samples of 2-phenylbutane and 2-phenylbutane-2-*d*. Infrared spectra taken on the products of runs 1, 3 and 4 likewise gave the same band. The intensity of this band for each sample was used to estimate the amount of deuterium introduced into the aromatic ring. In making the estimate, Beer's law was presumed to hold, and the product of run 5 was used as standard. The results are as follows: run 1, 1.5 atoms of deuterium per molecule; run 3, 1.3 atoms of deuterium per molecule; run 4, 2.1 atoms of deuterium per molecule. Infrared absorption bands have been observed for both *p*- and *m*-toluene-*d*²³ at 4.44 μ which are absent in toluene itself. There is little doubt that the aromatic ring of 2-phenylbutane undergoes deuteration under these relatively drastic conditions.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, LOS ANGELES, CALIF.]

Electrophilic Substitution at Saturated Carbon. XV. Asymmetric Carbanions, Asymmetric Solvation and d-Orbitals of Sulfur^{1,2}

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The stereochemical course of the base-catalyzed hydrogen-deuterium exchange reaction has been studied through rate comparisons of racemization and exchange of 2-octyl phenyl sulfone and 2-octyl-2-*d* phenyl sulfone in deuterated and non-deuterated solvents. The exchange rates exceeded the racemization rates by factors that ranged from a low of 10 to a high of 1980, depending on the solvent, and in one solvent on the character of the base. In dissociating solvents such as ethylene glycol and dimethyl sulfoxide-methanol mixtures, and in the non-dissociating solvent *t*-butyl alcohol with tetramethylammonium hydroxide as base, the smaller factors and lower degrees of retention of configuration were observed. In *t*-butyl alcohol with potassium *t*-butoxide as base, the larger factors were obtained. These facts coupled with similar experiments carried out previously on other systems indicate that in dissociating solvents, most of the stereospecificity arises from the asymmetry of the carbanion intermediate, and some from asymmetric solvation. In associating solvents, asymmetric solvation plays an important role in the high retention observed for the reaction. The configurational stability of carbanions attached to the sulfone group is attributed to overlap between the d-orbitals of sulfur and the orbital occupied by the two electrons of the anion. Hydrogen-deuterium isotope effects for both the exchange and racemization reactions were measured, and found to vary between extremes of 0.3 and 1.9. These low values are interpreted as evidence that both the exchange and racemization rates are governed by mechanisms that involve kinetically distinguishable, discrete stages in which covalent bonds between carbon and hydrogen, or oxygen and hydrogen are neither made nor broken.

In earlier papers of this series,^{2,4} the stereochemistry and kinetics of the base-catalyzed hydrogen-deuterium exchange reaction at saturated carbon

was studied with two kinds of compounds. Systems in which cyano,^{4c} amido,^{4c} keto,⁵ carboxyl⁶ or ester groups^{4c} are used to acidify the carbon-hydrogen bond fall into one class in the sense that their exchange reactions are devoid of stereospecificity, irrespective of solvent type. This behavior correlates with the fact that all of these systems can (at least in principle) exist in tautomeric forms incapable of optical activity, and these tautomers may intervene as discrete intermediates in the

(1) This work was supported in part by a grant from the National Science Foundation.

(2) Some of these results and the general conclusions were reported in preliminary form: D. J. Cram, W. D. Nielsen and B. Rickborn, *J. Am. Chem. Soc.*, **82**, 6415 (1960).

(3) Drew University, Madison, N. J.; National Science Foundation Senior Postdoctoral Fellow at U.C.L.A., 1960–1961.

(4) D. J. Cram, C. A. Kingsbury and B. Rickborn, *J. Am. Chem. Soc.*, **81**, 5835 (1959); (b) D. J. Cram, B. Rickborn and G. R. Knox, *ibid.*, **82**, 6413 (1960); (c) D. J. Cram, B. Rickborn, C. A. Kingsbury and P. Haberfeld, *ibid.*, **83**, 3678 (1961); (d) D. J. Cram, B. Rickborn and C. A. Kingsbury, *ibid.*, **83**, 3688 (1961).

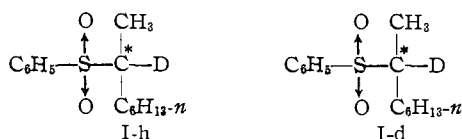
(5) (a) S. K. Hsu, C. K. Ingold and C. L. Wilson, *J. Chem. Soc.*, **78** (1938); (b) C. L. Wilson, *ibid.*, 1550 (1936).

(6) D. J. G. Ives and G. C. Wilks, *ibid.*, 1455 (1938).

hydrogen-deuterium exchange reaction. Systems in which phenyl alone is employed to acidify the carbon-hydrogen bond constitute a second class, whose exchange reactions owe their stereospecificity to asymmetric solvation of otherwise flat carbanions, and whose exchange reactions follow a steric course highly dependent on solvent type.^{4a,4d}

The present investigation was undertaken with the hope of discovering still a third type of system—one which would undergo stereospecific hydrogen-deuterium exchange due to the existence of asymmetric anionic intermediates. At the outset, a compound was sought that would conform to the following specifications. (1) The substance should not exist in tautomeric forms. (2) It should form an anion whose charge would not be delocalized in such a way as to flatten the system. (3) It should undergo the exchange reaction at convenient rates (25–100%) in a series of extreme solvent types. (4) It should be readily preparable in both an optically pure and highly deuterated form.

The 2-octyl phenyl sulfone system (I-h, I-d) was chosen as likely to satisfy these requirements. The



derived carbanion is stabilized by the d-orbitals of sulfur, and it seemed possible that the anion could exist in an asymmetric form.⁷ The base-catalyzed hydrogen deuterium exchange reaction of dimethyl sulfone had been studied previously, and appeared to occur at a convenient rate.⁸ Synthetic routes to both I-h and I-d could be envisioned readily. Additional encouragement was derived from the observation that the anion of optically active 2-methyl-2-benzenesulfonylbutyric acid underwent decarboxylation to give optically active 2-butyl phenyl sulfone.⁹

Starting Materials.—Reduction of 2-octanone with lithium aluminum deuteride gave 2-octanol-2-*d* which was resolved,¹⁰ converted to its tosylate,¹¹ and the tosylate ester was converted to 2-octyl-2-*d* phenyl sulfide.¹² Oxidation of this sulfide with hydrogen peroxide in glacial acetic acid¹³ gave (after crystallization to constant melting point) 2-octyl-2-*d* phenyl sulfone (I-d) with m.p. 44.5–45.0°, $[\alpha]_D^{25} - 12.7^\circ$ (*c* 6, CHCl₃), 0.97 atom of deuterium per molecule. Similar preparation of non-deuterated sulfone (I-h) gave m.p. 44.0–44.5°, $[\alpha]_D - 12.6^\circ$, (*c* 5, CHCl₃). Although these materials analyzed well for carbon and hydrogen,

(7) H. P. Koch and W. E. Moffitt, *Trans. Faraday Soc.*, **47**, 7 (1951).

(8) K. F. Bonhoeffer and J. Hochberg, *Z. physik. Chem.*, **A184**, 419 (1939).

(9) J. E. Taylor and F. H. Verhoek, *J. Am. Chem. Soc.*, **81**, 4537 (1959).

(10) (a) J. Kenyon in "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 418; (b) A. Streitwieser, Jr., *J. Am. Chem. Soc.*, **75**, 5014 (1953).

(11) A. Streitwieser, Jr., and W. D. Schaeffer, *ibid.*, **78**, 5597 (1956).

(12) J. Kenyon, H. Phillips and V. P. Pittman, *J. Chem. Soc.*, 1072 (1935).

(13) F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **79**, 717 (1957).

and did not exhibit a band in the infrared at 1055 cm.⁻¹ characteristic of the sulfoxide group,¹⁴ they were found to be kinetically impure in racemization rates. In 96% dimethyl sulfoxide–4% methanol (by weight) with potassium methoxide as catalyst, in *t*-butyl alcohol with potassium *t*-butoxide as catalyst, and in *t*-butyl alcohol with tetramethylammonium hydroxide as catalyst, the rates were clearly composite. Plots of log α against time gave two, rather than a single straight line. The rate constants calculated from the slopes of these lines differed by factors of from 1.7 to 6.6, depending on the solvent–base system, the two being most easily separable with data obtained in *t*-butyl alcohol–tetramethylammonium hydroxide.

The sulfones were rid of the kinetic impurity in two ways. Two successive reoxidations or chromatography on silicic acid of the impure sulfones gave kinetically pure materials, m.p. 47.5–48°, $[\alpha]_D^{25} - 10.6^\circ$, $[\alpha]_{5461}^{25} - 13.3^\circ$ (*c* 5.4, CHCl₃) for I-h, and m.p. 47.5–48°, $[\alpha]_D^{25} - 14.0^\circ$ (*c* 5, CHCl₃), for I-d (0.97 atom of D per molecule by combustion and falling drop method). With this purification, the melting point rose 3 degrees, and the rotation dropped about 16%, facts that suggest that the original samples contained traces of high-rotating optically active sulfoxides (two possible diastereomers).¹⁵ All of the results reported here were obtained with the purified material.

Survey of Effects of Solvents and Bases on Steric Course of Exchange Reaction.—Table I reports the results of a survey of different media for studying the stereochemistry of the exchange reaction. In each run, either I-h was exchanged with deuterated solvent,¹⁶ or I-d with protonated solvent. The run was interrupted after the material had racemized from 2–48%, and the substrate was isolated and analyzed for deuterium (combustion and falling drop method).¹⁷ The results indicated that in *t*-butyl alcohol–potassium *t*-butoxide, *t*-butyl alcohol–tetramethylammonium hydroxide, ethylene glycol–potassium ethylene glyoxide, methanol–potassium methoxide and dimethyl sulfoxide–methanol–potassium methoxide, exchange occurred at least an order of magnitude faster than racemization. Thus the exchange reaction occurred with net retention of configuration in all media. In other studies of both hydrogen–deuterium^{4a,4d} and carbon–hydrogen¹⁸ exchange, *t*-butyl alcohol–potassium *t*-butoxide had been a retention medium; *t*-butyl alcohol–tetramethylammonium hydroxide and dimethyl sulfoxide–methanol–potassium methoxide were racemization media; and ethylene glycol–potassium ethylene glyoxide and methanol–potassium methoxide were inversion

(14) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 360.

(15) E. J. Corey and E. T. Kaiser, *J. Am. Chem. Soc.*, **83**, 490 (1961), in a preliminary communication of racemization and exchange rates of I-h and I-d in ethanol–water employed material with m.p. 44–45°, $[\alpha]_D^{25} - 13.3^\circ$ (*c* 0.7 to 1.9 in 2:1 ethanol–water). Our kinetically pure material gave m.p. 47.5–48°, $[\alpha]_D^{25} - 13.3^\circ$, $[\alpha]_{5461}^{25} - 14.0^\circ$ (*c* 1.3, 2:1 ethanol–water).

(16) Preparation of *t*-butyl alcohol-0-*d* and ethylene glycol-0-*d* have been reported by D. J. Cram and B. Rickborn, *J. Am. Chem. Soc.*, **83**, 3678 (1961).

(17) Carried out by J. Nemeth, Urbana, Ill.

(18) D. J. Cram and W. D. Nielsen, *J. Am. Chem. Soc.*, **83**, 2174 (1961), and earlier papers.

TABLE I

SURVEY OF EFFECT OF SOLVENT AND BASE ON STEREOCHEMISTRY OF HYDROGEN-DEUTERIUM EXCHANGE REACTION OF 2-OCTYL PHENYL SULFONE^a AND 2-OCTYL-2-*d* PHENYL SULFONE^a

Run	Starting material ^a Isotope type	Concn., <i>M</i>	Solvent	Base Type	Concn., <i>M</i>	Temp., °C.	Tm., hr.	% rac.	% exch. ^b	Net steric course
1	H ^c	0.4	(CH ₃) ₃ COD ^{b,d}	(CH ₃) ₃ COK	0.396	25	0.05	4.5	62	93% ret.
2	D ^{b,e}	.4	(CH ₃) ₃ COH	(CH ₃) ₃ COK +-	.224	25	.70	8.0	96	92% ret.
3	D ^{b,e}	.4	(CH ₃) ₃ COH	(CH ₃) ₄ NOH	.048	25	.80	6	40	85% ret.
4	D ^{b,e}	.4	HOCH ₂ CH ₂ OH	HOCH ₂ CH ₂ OK	.5	75	165	2.2	69	97% ret.
5	H ^c	.4	DOCH ₂ CH ₂ OD ^{b,f}	DOCH ₂ CH ₂ OK	.5	100	2.25	4.5	53	91% ret.
6	D ^{b,e}	.4	CH ₃ OH	CH ₃ OK	.5	100	7.0	48	100	High ret.
7	D ^{b,e}	.4	(CH ₃) ₂ SO-CH ₃ OH ^g	CH ₃ OK	.200	25	1.0	9.8	98	90% ret.

^a Optically pure materials were employed. ^b Analyzed by combustion and falling drop method. ^c M.p. 47.5-48.0°, [α]₅₄₈₀²⁶ -13.3° (*c* 5.37, CHCl₃). ^d 99% O-*d*. ^e 97% C-*d*, m.p. 47.5-48.0°, [α]₅₄₆₁³¹ -14.0° (*c* 5.06, CHCl₃). ^f 99% (O-*d*)₂. ^g 92% (CH₃)₂SO, 8% CH₃OH, by weight.

TABLE II

RACEMIZATION RATES OF 0.375 *M* SOLUTIONS OF 2-OCTYL PHENYL SULFONE (I-h) AND 2-OCTYL-2-*d* PHENYL SULFONE (I-d)

Run ^a	Substrate ^b	Solvent	Base Type	Concn., <i>M</i>	<i>T</i> , °C. ^c	% ret. fol. ^d	<i>k</i> _{obs} ^e , sec. ⁻¹	<i>k</i> ₂ ^f , l. m. ⁻¹ sec. ⁻¹
8	I-d ^e	CH ₃ OH	CH ₃ OK	0.102	100.6	75	7.65 ± 0.48 × 10 ⁻⁶	7.50 ± 0.38 × 10 ⁻⁵
9	I-h	(CH ₃) ₂ SO-CH ₃ OH ^f	CH ₃ OK	.201	25.00	35	5.8 ± .3 × 10 ⁻⁵	2.9 ± .2 × 10 ⁻⁴
10	I-d ^e	(CH ₃) ₂ SO-CH ₃ OH ^f	CH ₃ OK	.200	25.00	34	5.75 ± .29 × 10 ⁻⁵	2.88 ± .15 × 10 ⁻⁴
11	I-d ^e	(CH ₃) ₂ SO-CH ₃ OH ^f	CH ₃ OK	.208	25.00	28	6.19 ± .31 × 10 ⁻⁵	2.97 ± .15 × 10 ⁻⁴
12	I-h	HOCH ₂ CH ₂ OH	HOCH ₂ CH ₂ OK	.0931	100.6	40	3.56 ± .18 × 10 ⁻⁷	3.83 ± .19 × 10 ⁻⁶
13	I-d ^e	HOCH ₂ CH ₂ OH	HOCH ₂ CH ₂ OK	.0964	100.6	40	3.95 ± .20 × 10 ⁻⁷	4.10 ± .20 × 10 ⁻⁶
14	I-h	DOCH ₂ CH ₂ OD ^g	DOCH ₂ CH ₂ OK	.0652	100.6	42	6.74 ± .34 × 10 ⁻⁷	1.03 ± .05 × 10 ⁻⁵
15	I-d ^e	DOCH ₂ CH ₂ OD ^g	DOCH ₂ CH ₂ OK	.0686	100.6	37	8.07 ± .40 × 10 ⁻⁷	1.25 ± .06 × 10 ⁻⁵
16	I-d ^e	(CH ₃) ₄ NOH ^h	(CH ₃) ₄ NOH ^h	.0450	25.00	50	2.59 ± .13 × 10 ⁻⁵	5.76 ± .29 × 10 ⁻⁴
17	I-h	(CH ₃) ₃ COD ⁱ	(CH ₃) ₃ COK	.0460	25.00	50	1.41 ± .06 × 10 ⁻⁶	3.07 ± .13 × 10 ⁻⁵
18	I-d ^e	(CH ₃) ₃ COH	(CH ₃) ₃ COK	.0507	25.00	50	2.12 ± .10 × 10 ⁻⁶	4.18 ± .20 × 10 ⁻⁵
19	I-h	(CH ₃) ₃ COD ⁱ	(CH ₃) ₃ COK	.103	25.00	75	7.50 ± .37 × 10 ⁻⁶	7.28 ± .36 × 10 ⁻⁵
20	I-d ^e	(CH ₃) ₃ COH	(CH ₃) ₃ COK	.098	25.00	50	3.88 ± .20 × 10 ⁻⁶	3.96 ± .20 × 10 ⁻⁵
21	I-h	(CH ₃) ₃ COD ⁱ	(CH ₃) ₃ COK	.167	25.00	37	3.37 ± .17 × 10 ⁻⁵	2.02 ± .10 × 10 ⁻⁴
22	I-d ^e	(CH ₃) ₃ COH	(CH ₃) ₃ COK	.165	25.00	20	1.75 ± .09 × 10 ⁻⁵	1.06 ± .05 × 10 ⁻⁴
23	I-d ^e	(CH ₃) ₃ COH	(CH ₃) ₃ COK	.224	25.00	36	3.69 ± .18 × 10 ⁻⁵	1.65 ± .08 × 10 ⁻⁴
24	I-h	(CH ₃) ₃ COD ⁱ	(CH ₃) ₃ COK	.396	25.00	82	2.35 ± .12 × 10 ⁻⁴	5.93 ± .30 × 10 ⁻⁴
25	I-d ^e	(CH ₃) ₃ COH	(CH ₃) ₃ COK	.367	25.00	72	2.20 ± .11 × 10 ⁻⁴	6.00 ± .30 × 10 ⁻⁴
26	I-d ^{e,f}	(CH ₃) ₃ COH	(CH ₃) ₃ COK	.183	25.00	95	1.91 ± .09 × 10 ⁻⁵	1.04 ± .05 × 10 ⁻⁴
27	I-h ⁱ	(CH ₃) ₃ COD ⁱ	(CH ₃) ₃ COK	.181	25.00	92	3.07 ± .15 × 10 ⁻⁵	1.66 ± .08 × 10 ⁻⁴
28	I-d ^{e,k}	(CH ₃) ₃ COH	(CH ₃) ₄ NOH ^h	.045	25.00	93	8.32 ± .42 × 10 ⁻⁵	1.85 ± .09 × 10 ⁻³
29	I-d ^{e,j}	(CH ₃) ₃ COH	(CH ₃) ₄ NOH ^h	.185	25.00	80	4.34 ± .21 × 10 ⁻⁴	2.35 ± .14 × 10 ⁻³

^a Runs are numbered consecutively from table to table. ^b M.p. 47.5-48.0° for both I-h and I-d; I-h, [α]₅₄₈₀²⁶ -13.3° (*c* 5.4, CHCl₃); I-d, [α]₅₄₆₁³¹ -14.0° (*c* 5.1, CHCl₃), both optically pure. ^c 25.00 ± 0.01°, 100.6 ± 0.1°. ^d % reaction followed kinetically. ^e 0.97 atom of D per molecule, combustion and falling drop method. ^f 92% (CH₃)₂SO, 8% CH₃OH by weight. ^g 1.98 atoms of D per molecule, combustion and falling drop method. ^h Water removed by drying a *t*-butyl alcohol solution of (CH₃)₄NOH·0.27(CH₃)₃N·2.0H₂O with Linde "Molecular Sieves," #4A, 14 by 30 mesh. ⁱ 0.99 atom of D per molecule, combustion and falling drop method. ^j Substrate concentration, 0.185 *M*. ^k Substrate concentration, 0.045 *M*.

media. The present results make it amply clear that carbanions stabilized by the sulfonyl group have different stereochemical capabilities than carbanions stabilized by groups studied previously.

Kinetics of Racemization.—In Table II are reported the results of kinetic runs in which rate constants for racemization of I-h and I-d were determined in the same solvent-base systems employed for the qualitative runs of Table I. The reactions were followed from a minimum of 22 to a maximum of 95% racemization. A minimum of 8 points (usually many more) were taken per run. Those runs conducted at 25° were made in a jacketed and thermostated polarimeter tube, and those carried out at 100.6° involved ampoule technique. Clear pseudo-first-order kinetics were observed in all cases with no trends in rate constants calculated for each point. Probable errors of about

±5% were observed for those runs made in a polarimeter tube, and slightly higher probable errors were observed for those that involved ampoule techniques. No corrections were made for solvent expansion in the higher temperature runs. In representative runs, the reaction mixtures were titrated for base at both the start and finish of a run. No changes of titer were observed.

Previous studies of racemization rates of 2-methyl-3-phenylpropionitrile in methanol, dimethyl sulfoxide-methanol mixtures, and in ethylene glycol demonstrated that the rates were first order in potassium alkoxides at base concentrations and temperatures employed in this study.^{4c} The assumption was made that kinetic order in base in these solvents (dielectric constants, ϵ = 34-49) would not vary from substrate to substrate. Comparison of *k*₂^α (second-order polarimetric rate con-

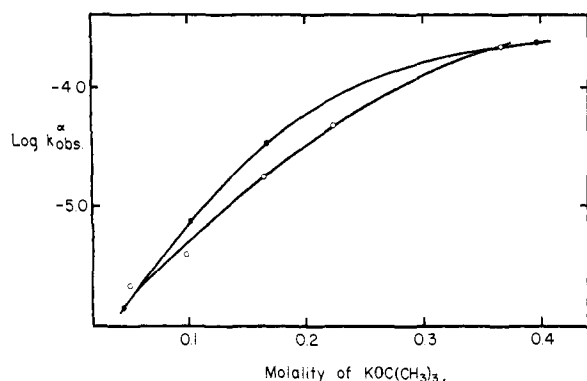


Fig. 1.—Plot of logarithm of observed rates of racemization in *t*-butyl alcohol against concentration of potassium *t*-butoxide: ●, for 2-octyl phenyl sulfone; ○, for 2-octyl-2-*d* phenyl sulfone.

stants) for runs 8 and 10 indicate that substitution of dimethyl sulfoxide for 92% (by weight) of the methanol increased k_2^α by a factor of about 4 in spite of the fact that the temperature was lowered by 75°. Again the rate enhancing character of dimethyl sulfoxide is illustrated.^{4c} The similarity in values of k_2^α for runs 9 and 10, for runs 12 and 13, and for runs 14 and 15 is consistent with the conclusion that exchange is much faster than racemization in both dimethyl sulfoxide-methanol and ethylene glycol. Within each set of runs, the isotopic composition of the solvent was the same, but the isotopic composition of the substrate was different. By the time a few per cent. of the material had racemized, the substrate had essentially the same isotopic composition as the solvent, and hence the values for k_2^α depended only on the isotopic composition of the solvent.

In *t*-butyl alcohol, a solvent of much lower dielectric constant (ϵ 11), the little evidence available^{4d} indicates that racemization rates with other substrates are not first order in potassium *t*-butoxide. Therefore a series of racemization rates were run in *t*-butyl alcohol in which the base concentration was varied (substrate concentration was constant) from about 0.05 to almost 0.4. The calculated over-all second-order rate constant increased with increasing base concentration by a factor of 14 for I-d and 19 for I-h (runs 17-25). Thus the rates in *t*-butyl alcohol exhibited a greater than second-order dependence on the concentration of potassium *t*-butoxide, which suggests that the catalytic species consists of aggregates of ion pairs. In Fig. 1 is plotted base concentration against $\log k_{obs}^\alpha$ for both I-h and I-d.

In all of the runs of Table II, except runs 26-29, the substrate concentration was 0.375 *M*. In runs 26 and 27 carried out in *t*-butyl alcohol-potassium *t*-butoxide, the substrate and base concentrations were both 0.183 ± 0.002 *M*. Comparison of k_2^α for runs 26 and 27 with k_2^α 's estimated for identical base concentrations but with higher substrate concentrations (Fig. 1 was employed) indicates that values for k_2^α changed slightly with substrate concentration. For I-d as substrate, k_2^α decreased by about 15% as substrate concentration was decreased. For I-h, k_2^α decreased by about 35%

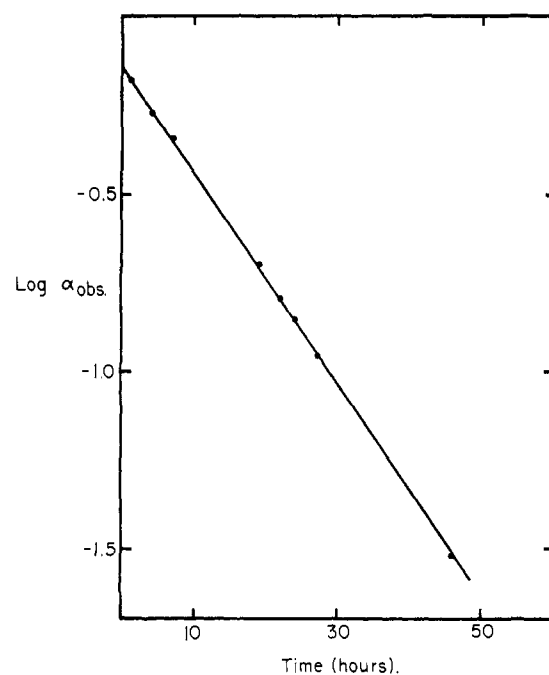


Fig. 2.—Plot of logarithm of observed rotation against time in hours for racemization of 2-octyl-2-*d* phenyl sulfone by potassium *t*-butoxide in *t*-butyl alcohol (run 26).

as the substrate concentration was decreased. Figure 2 is a sample plot of the logarithm of the concentration of unracemized substrate against time.

In runs 16, 28 and 29, tetramethylammonium hydroxide was substituted for potassium *t*-butoxide as base in *t*-butyl alcohol, and in each run I-d was employed as substrate, 0.375 *M* in run 16, 0.045 *M* in run 28 and 0.185 *M* in run 29. Comparison of runs 16 and 18 indicates that substitution of the quaternary ammonium for the potassium base increases the rate of racemization by a factor of 14, whereas a similar comparison of runs 29 and 26 gives a factor of 23.

Kinetics of Exchange.—Table III records the results of kinetic studies of isotope exchange reactions that accompany the racemization reactions described above. The reactions were followed to at least 64% completion in each run, and a minimum of 6 usable points were taken per run. The ampoule technique was employed for runs 30, 32 and 33 (temperature of 100.6°). In the runs conducted at 25.00° (runs 31, 34-42), aliquots of a stock solution were used. For each point, sulfone was isolated, and its deuterium content determined through infrared analysis (see Experimental).

In those runs conducted in methanol, dimethyl sulfoxide-methanol, ethylene glycol and ethylene glycol-*O-d*₂, plots of the logarithm of the concentration of unexchanged starting material against time gave good straight lines with no observable trends (runs 30-33). Probable errors for k_2^α (calculated second-order rate constants for the isotope exchange reaction) in these solvents amounted to about $\pm 5\%$.

In runs 35 and 36 conducted in *t*-butyl alcohol-potassium-*t*-butoxide, the concentrations of sub-

TABLE III
ISOTOPE EXCHANGE RATES OF 0.375 *M* SOLUTIONS OF 2-OCTYL PHENYL SULFONE (I-h) AND 2-OCTYL-2-*d* PHENYL SULFONE (I-d)

Run ^a	Substrate ^b	Solvent	Base		Concn., <i>M</i>	<i>T</i> , °C.	% rct. foll. ^d	Rate type ^e	<i>k</i> _{obs} ^e , sec. ⁻¹	<i>k</i> ₂ ^e , l. m. ⁻¹ sec. ⁻¹
			Type	Type						
30	I-d ^f	CH ₃ OH	CH ₃ OK	CH ₃ OK	0.102	100.6	73	...	7.79 ± 0.39 × 10 ⁻³	7.62 ± 0.38 × 10 ⁻⁴
31	I-d ^f	(CH ₃) ₂ SO-CH ₃ OH ^g	CH ₃ OK	CH ₃ OK	.208	25.00	93	...	6.37 ± .32 × 10 ⁻⁴	3.06 ± .15 × 10 ⁻⁵
32	I-h	DOCH ₂ CH ₂ OD ^h	DOCH ₂ CH ₂ OK	DOCH ₂ CH ₂ OK	.0680	100.6	64	...	1.01 ± .05 × 10 ⁻³	1.49 ± .07 × 10 ⁻⁴
33	I-d ^f	HOCH ₂ CH ₂ OH	HOCH ₂ CH ₂ OK	HOCH ₂ CH ₂ OK	.0918	100.6	68	...	1.14 ± .06 × 10 ⁻³	1.24 ± .06 × 10 ⁻⁴
34	I-d ^f	(CH ₃) ₃ COH	N(CH ₃) ₄ OH ⁱ	(CH ₃) ₃ COK	.0450	25.00	90	...	1.66 ± .09 × 10 ⁻³	3.69 ± .20 × 10 ⁻²
35	I-h ^f	(CH ₃) ₂ COD ^k	(CH ₃) ₂ COK	(CH ₃) ₂ COK	.181	25.00	90	...	3.97 ± .55 × 10 ⁻³	2.15 ± .30 × 10 ⁻²
36	I-d ^{f,i}	(CH ₃) ₃ COH	(CH ₃) ₃ COK	(CH ₃) ₃ COK	.183	25.00	90	...	2.65 ± .34 × 10 ⁻³	1.45 ± .18 × 10 ⁻²
37	I-h	(CH ₃) ₂ COD ^k	(CH ₃) ₂ COK	(CH ₃) ₂ COK	.103	25.00	82	{Fast ^l	2.08 ± .25 × 10 ⁻³	2.02 ± .24 × 10 ⁻²
38	I-d ^f	(CH ₃) ₃ COH	(CH ₃) ₃ COK	(CH ₃) ₃ COK	.098	25.00	89	{Slow	5.48 ± .24 × 10 ⁻⁴	5.32 ± .23 × 10 ⁻³
								{Fast ^m	2.60 ± .10 × 10 ⁻³	2.65 ± .10 × 10 ⁻²
39	I-h	(CH ₃) ₂ COD ^k	(CH ₃) ₂ COK	(CH ₃) ₂ COK	.046	25.00	88	{Slow	6.49 ± .15 × 10 ⁻⁴	6.62 ± .15 × 10 ⁻³
								{Fast ⁿ	1.7 ± .3 × 10 ⁻³	3.7 ± .2 × 10 ⁻²
40	I-d ^f	(CH ₃) ₃ COH	(CH ₃) ₃ COK	(CH ₃) ₃ COK	.0507	25.00	89	{Slow	4.3 ± 1.0 × 10 ⁻⁴	9.3 ± 2.1 × 10 ⁻³
								{Fast ^o	4.2 ± 0.4 × 10 ⁻³	8.3 ± 0.8 × 10 ⁻²
41	I-d ^{f,p}	(CH ₃) ₃ COH	(CH ₃) ₄ NOH ^q	(CH ₃) ₄ NOH ^q	.045	25.00	85	...	4.79 ± .38 × 10 ⁻⁴	9.45 ± .75 × 10 ⁻⁴
								...	2.08 ± .13 × 10 ⁻³	5.95 ± .29 × 10 ⁻²
42	I-d ^{f,i}	(CH ₃) ₃ COH	(CH ₃) ₄ NOH ^q	(CH ₃) ₄ NOH ^q	.185	25.00	90	...	9.47 ± .47 × 10 ⁻³	5.12 ± .26 × 10 ⁻²

^a Runs are numbered consecutively from table to table. ^b M.p. 47.5–48.0° for both I-d and I-h; $[\alpha]_{5461}^{25} - 13.3^\circ$ (*c* 5.4, CHCl₃); I-d, $[\alpha]_{5461}^{31} - 14.0^\circ$ (*c* 5.1, CHCl₃), both optically pure. ^c 25.00 ± 0.01°, 100.6 ± 0.1°. ^d % reaction followed kinetically. ^e In *t*-butyl alcohol, two concurrent pseudo-first-order rates were observed. ^f 0.97 atom of D per molecule, combustion and falling drop method. ^g 92% (CH₃)₂SO-8% CH₃OH, by weight. ^h 1.98 atoms of D per molecule, combustion and falling drop method. ⁱ Footnote *h* in Table II. ^j Substrate concentration, 0.185 *M*. ^k 0.99 atom of D per molecule. ^l 47% of substrate consumed by fast reaction. ^m 38% of substrate consumed by fast reaction. ⁿ 24% of substrate consumed by fast reaction. ^o 8% of substrate consumed by fast reaction. ^p Substrate concentration, 0.045 *M*.

strate and base were approximately equal (0.183 ± 0.002). In these runs, 6 and 8 points were taken, respectively, and plots of the logarithm of the concentration of unexchanged starting material against

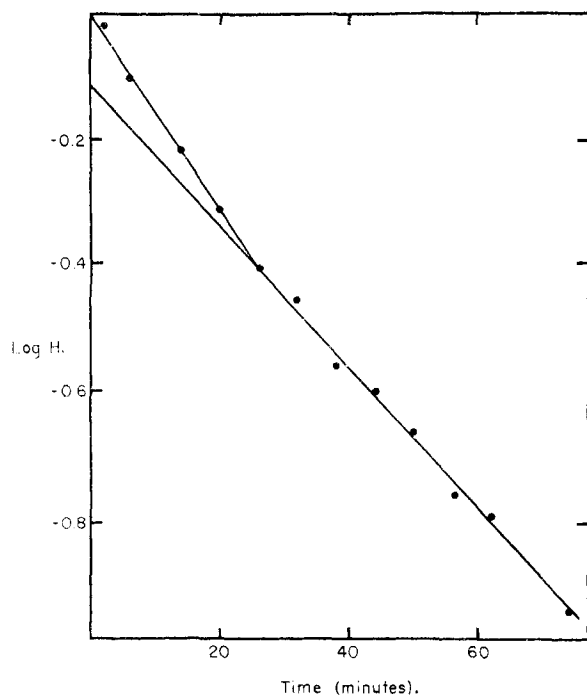


Fig. 3.—Plot of logarithm of concentration of unexchanged α -H against time in potassium *t*-butoxide-catalyzed exchange of 2-octyl phenyl sulfone in *t*-butyl alcohol-O-*d* (run 39).

time gave a single straight line, from which were calculated k_{obs}^e (observed pseudo-first-order rate constant for exchange) and k_2^e . In the other runs in *t*-butyl alcohol that involved potassium *t*-butoxide as base; the substrate concentration exceeded

that of the base by factors of 3.5–8, and the kinetics were more complex. For runs 37–40, plots of the logarithm of the concentration of unexchanged starting material against time gave two straight lines, from which were calculated “fast” and “slow” second-order rate constants (k_2^e). In calculation of the constant for the “fast rate,” correction was made for the contribution made by the concurrent “slow reaction.” In runs 37 and 38, each rate constant was calculated from 4 points. In run 39, the “fast rate” was calculated from 5, and the “slow rate” from 8 points. In run 40, the “fast rate” was calculated from 3 points, and the “slow” from 11 points. The reactions were followed to 82–90% completion, and no trends were observable in the data. The probable error for the rate constants range from a minimum of $\pm 4\%$ to a maximum of $\pm 23\%$. Although in some cases the probable error is rather large, no doubt exists that the rates are composite in these latter runs, and correspond to two reactions, one of which runs its course after from 8–47% of the starting material has been consumed.

In runs 34, 41 and 42 conducted with solutions of I-d in *t*-butyl alcohol, tetramethylammonium hydroxide was employed as base. A single rate was observed for the exchange reaction irrespective of the relative concentrations of base and substrate, and the rate constants were calculated from 10 points in run 34, 6 points in run 41 and from 4 points in run 42, and the reaction was followed in all cases to within 85–90% of completion.

In these exchange reactions, no correction was made for the small change in solvent isotopic composition as the run proceeded. In no case would such a correction have made more than a few per cent. difference in the value of the rate constants. Figure 3 contains a sample plot of the logarithm of unexchanged starting material against time (run 39).

A number of interesting rate relationships are visible in these data. Thus k_2^e for methanol is

TABLE IV
 STEREOCHEMICAL COURSE OF ISOTOPE EXCHANGE REACTION

Runs involved ^a	Substrate ^b	Solvent	Type	Base	Concn., M	T, °C.	$\frac{k_2^e}{k_2^a}$
30 + 8	I-d	CH ₃ OH	CH ₃ OK		0.102	100.6	10
31 + 11	I-d	(CH ₃) ₂ SO-CH ₂ OH	CH ₃ OK		.208	25.00	10
32 + 14	I-h	DOCH ₂ CH ₂ OD	DOCH ₂ CH ₂ OK		.068-0.065	100.6	14.5
33 + 12	I-d	HOCH ₂ CH ₂ OH	HOCH ₂ CH ₂ OK		.092-0.093	100.6	32
34 + 16	I-d	(CH ₃) ₂ COH	(CH ₃) ₂ NOH		.045	25.00	64
41 + 28	I-d	(CH ₃) ₂ COH	(CH ₃) ₂ NOH		.045	25.00	32
42 + 29	I-d	(CH ₃) ₂ COH	(CH ₃) ₂ NOH		.185	25.00	22
35 + 27	I-h	(CH ₃) ₂ COD	(CH ₃) ₂ COK		.181	25.00	129
36 + 26	I-d	(CH ₃) ₂ COH	(CH ₃) ₂ COK		.183	25.00	139
37F + 19	I-h	(CH ₃) ₂ COD	(CH ₃) ₂ COK		.103	25.00	278
37S + 19	I-h	(CH ₃) ₂ COD	(CH ₃) ₂ COK		.103	25.00	73
38F + 20	I-d	(CH ₃) ₂ COH	(CH ₃) ₂ COK		.098	25.00	670
38S + 20	I-d	(CH ₃) ₂ COH	(CH ₃) ₂ COK		.098	25.00	167
39F + 17	I-h	(CH ₃) ₂ COD	(CH ₃) ₂ COK		.046	25.00	1200
39S + 17	I-h	(CH ₃) ₂ COD	(CH ₃) ₂ COK		.046	25.00	303
40F + 18	I-d	(CH ₃) ₂ COH	(CH ₃) ₂ COK		.0507	25.00	1980
40S + 18	I-d	(CH ₃) ₂ COH	(CH ₃) ₂ COK		.0507	25.00	226

^a F stands for "fast reaction," and S for "slow reaction." ^b All substrate concentrations 0.375 M except for runs 41 + 28, in which substrate was 0.045 M, and 42 + 29, 35 + 27 and 36 + 26 in which substrate was 0.185 M.

about 6 times k_2^e for ethylene glycol (runs 30 and 33). In other studies,^{4c} 2-phenylbutyronitrile was found to undergo the exchange reaction three times faster in methanol than in ethylene glycol, whereas with 2-methyl-3-phenylpropionitrile, the rate was 4 times faster in ethylene glycol than in methanol. Thus different substrates possess low degrees of kinetic specificity for media.

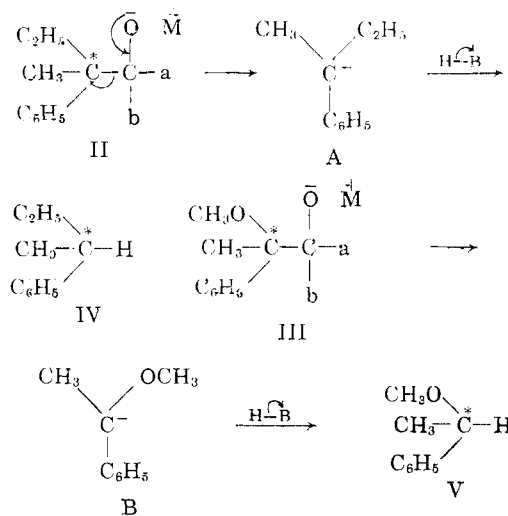
Comparison of runs 30 and 31 again indicates the vast difference between the effect of methanol and dimethyl sulfoxide on rate of the exchange reaction. In other exchange reactions in methanol,^{4c} ΔH^* was found to be 29.3 kcal. per mole, and if this value is used to correct the rate constant of run 30 to 25°, a k_2^e of 3.0×10^{-7} l.m.⁻¹ sec.⁻¹ is estimated. A rate enhancement by a factor of about 4 powers of 10 accompanies the substitution of 92% dimethyl sulfoxide-8% methanol (by weight) for methanol itself in the exchange reaction of sulfone I. An estimated 5 powers of 10 accompanied a similar substitution of solvent in the exchange reaction of 2-methyl-3-phenylpropionitrile.^{4c}

As in the case of the racemization rates, substitution of tetramethylammonium hydroxide for potassium *t*-butoxide in *t*-butyl alcohol resulted in an enhanced rate for the exchange reaction. Comparison of runs 34 and 40S, and of 42 and 36 indicates a rate increase by a factor of 3.5-3.9, which is considerably smaller than the corresponding factors for the racemization rates.

Discussion

Stereochemical Course of the Isotope Exchange Reaction.—In Table IV are listed the ratios of the second-order rate constants for exchange to the corresponding constants for racemization (k_2^e/k_2^a). For all solvents and reaction conditions, the values for the ratios are greater than unity, and range from 10 to 1980. Thus the qualitative observations of Table I that the isotopic exchange reaction occurs with retention of configuration for sulfones I-h and I-d in widely different solvents is borne out by the kinetic data.

These results demonstrate that the carbanion derived from sulfone I possesses a character different from that derived from any of the systems studied previously. The isotopic exchange reaction occurs with net retention in four media which in former studies with anions A or B as intermediates gave either racemic or inverted products. For example, in the base-catalyzed cleavage of systems such as II or III to give IV and V, respectively, methanol and ethylene glycol were found to be

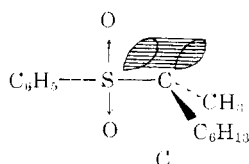


"inversion solvents,"¹⁹ dimethyl sulfoxide a "racemization solvent," and *t*-butyl alcohol with a quaternary ammonium base, a "racemization medium" (*t*-butyl alcohol with metal bases was a "retention solvent"). Likewise, in the base-catalyzed isotopic exchange reaction of IV and V (and their deuterated counterparts), diethylene glycol was found to be an "inversion solvent" and dimethyl sulfoxide a "racemization solvent."^{2,4d,20}

(19) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *J. Am. Chem. Soc.*, **81**, 5774 (1959). This is a summary paper.

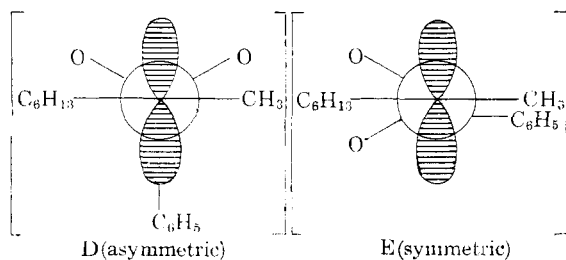
(20) The fact that the exchange reactions of I-h and I-d proceed

The stereospecificity observed in the reactions of II-V was attributed to asymmetric solvation. Clearly the observed retention for sulfone I under conditions that II-V give either racemization or inversion must be associated with phenomena other than asymmetric solvation. It seems likely that the carbanion of system I is itself asymmetric, and that the d-orbitals on sulfur play a role in maintaining the asymmetric character. Two different asymmetric anions can be envisioned. In the first (C),



the sp^3 hybridization at the asymmetric carbon atom is retained, and the normal rate of inversion of this anion is reduced by overlap of the sp^3 -orbital containing the pair of unshared electrons with the empty d-orbitals of sulfur. Such overlap would undoubtedly modify the normal tetrahedral bond angle about carbon somewhat, but not enough to bring the two C_β -carbon atoms, the C_α -carbon atom and the sulfur atom into the same plane. A number of investigators have referred in previous papers to the lack of rigid geometric requirements for d-orbital stabilization of anions.^{7,21} Indeed, even bridgehead^{21b} and cyclopropyl carbanions^{21c} have been found to be greatly stabilized by sulfone groups.

A second possible type of asymmetric carbanion is formulated in D.⁷ In this species, the anion has rehybridized from sp^3 to $sp^2 + p$, and the p-orbital with its unshared pair of electrons is stabilized by overlap with the d-orbitals of sulfur. With this type of hybridization, the symmetry properties of the sulfone anion would depend on the rotomer that was formed. Although D is asymmetric, rotomer E⁷ is not, and equilibration between rotomers would result in loss of asymmetry. If D or a different



asymmetric rotomer was an intermediate in the isotope exchange reactions, the stereospecificity (retention) of the reaction would require that hydrogen (deuterium) be lost and deuterium (hydro-

gen) be acquired from the same side of the molecule before rotation about the carbon-sulfur bond occurred.

gen) be acquired from the same side of the molecule before rotation about the carbon-sulfur bond occurred.

With retention in both *t*-butyl alcohol and ethylene glycol was revealed in a paper given at the Organic Reaction Mechanisms Conference at Princeton, N. J., September, 1959. At that time Dr. H. L. Goering was kind enough to inform me that he and Mr. D. Towns had found that I-d underwent the exchange reaction in methanol at 100°, and that k_2^e/k_2^a was approximately 15. He also revealed his method of analysis.

(21) (a) W. E. Doering and L. K. Levy, *J. Am. Chem. Soc.*, **77**, 511 (1955); (b) W. E. Doering and A. K. Hoffmann, *ibid.*, **77**, 524 (1955); (c) H. E. Zimmerman and B. S. Thyagarajan, *ibid.*, **82**, 2305 (1960); (d) S. Oae and C. C. Price, *ibid.*, **80**, 3425 (1958).

gen) be acquired from the same side of the molecule before rotation about the carbon-sulfur bond occurred.

Of the two general types of asymmetric anions, C provides a simpler explanation for the retention of configuration observed for the isotope exchange reaction. Possibly that portion of the reaction which occurs with racemization involves a rehybridization of C type intermediates to give E type intermediates, or the passage of D type intermediates to E type intermediates.

Although all of the solvent-base systems studied give net retention for the exchange reaction, the stereospecificity of the reaction is very sensitive to the medium. With potassium alkoxides as base, methanol, ethylene glycol and dimethyl sulfoxide give relatively low stereospecificity ($k_2^e/k_2^a = 10$ to 32), whereas *t*-butyl alcohol provides a much more stereospecific reaction ($k_2^e/k_2^a = 73$ to 1980). The more dissociating solvents which gave inversion or racemization for reactions of systems II-V provide lower retention for reactions of sulfone I than does the poorer dissociating solvent, *t*-butyl alcohol, which gave retention for reactions of systems II-V. Furthermore, substitution of a quaternary ammonium base for the potassium *t*-butoxide base in *t*-butyl alcohol as solvent cut the value of k_2^e/k_2^a by a factor of 6.3 at one set of base-substrate concentrations (compare k_2^e/k_2^a for runs 42 + 29 with the ratio for runs 36 and 26), and by a factor of 3.5-31 at a second set of concentrations (ratio for runs 34 + 16 and 40F + 18, or 34 + 16 and 40S + 18). This result recalls the observation that substitution of a quaternary ammonium base for potassium *t*-butoxide in *t*-butyl alcohol destroyed the stereospecificity of reactions of systems such as II and III.

These correlations indicate that asymmetric solvation, which accounts for the stereospecificity in systems II-V, is also playing an important role in the reactions of sulfone I. This role is minimal in dimethyl sulfoxide and methanol ($k_2^e/k_2^a = 10$). It seems to grow slightly more important in ethylene glycol and in *t*-butyl alcohol with the quaternary ammonium base, and likely is mainly responsible for the very high values of k_2^e/k_2^a observed for runs carried out in *t*-butyl alcohol-potassium *t*-butoxide. Possibly the asymmetry of the sulfone anion is responsible for values of k_2^e/k_2^a as high as 10, whereas those parts of the values in excess of 10 are due to asymmetric solvation.

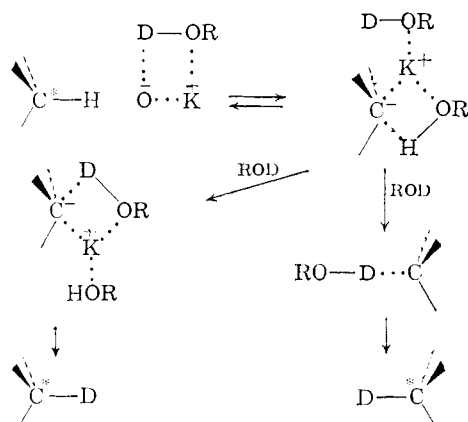
The high stereospecificity associated with asymmetric solvation in *t*-butyl alcohol-potassium *t*-butoxide is attributed to the solvent-orienting ability of intimate ion-pairs (or aggregates), which must be the catalytic species in this medium. In the mechanism formulated in Chart I, the potassium ion coordinates with solvent, and hence deuterated solvent is advantageously oriented on the side of the anion from which a proton has just been removed. The inability of the quaternary ammonium ion to coordinate with solvent destroys the effect, and much of the solvent-orienting ability of the base is lost, although the hydrogen-bonding of anion with solvent is still retained, and this effect probably provides some orientation. Although C type carbanions are envisioned in Chart I, a similar

argument could be based equally well on D type carbanions.

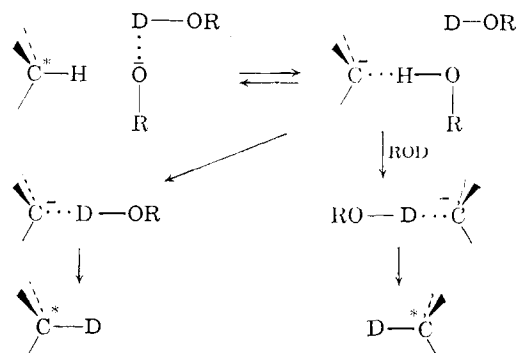
A second role for the potassium ion might be envisioned. Electrostatic attraction between the positive charge of the metal and the negative charge of the anion might inhibit inversion of the anion. Were such an effect dominating, the quaternary ammonium ion should be almost as effective at providing stereospecificity. However, the data indicate that such an effect can play only a subsidiary role.

In ethylene glycol, dissociated anions are the catalytic species,^{3c} and therefore the small amount of stereospecificity that can be attributed to asymmetric solvation would grow out of anion-solvent hydrogen bonding, as is indicated in Chart I. The higher stereospecificity associated with protonated solvent ($k_2^e/k_2^a = 32$ for HOCH₂CH₂OH, and $k_2^e/k_2^a = 14.5$ for DOCH₂CH₂OD) correlates with the fact that the protonated solvent is more acidic, better at hydrogen bonding, and therefore capable of providing more asymmetric solvation. The higher stereospecificity observed for ethylene glycol as compared to methanol is also consistent with the greater acidity of ethylene glycol, and the stronger hydrogen bonds associated with the latter solvent.

CHART I
ASYMMETRIC SOLVATION IN *t*-BUTYL ALCOHOL, R = (CH₃)₃C



ASYMMETRIC SOLVATION IN ETHYLENE GLYCOL, R = OCH₂-CH₂OD



In dimethyl sulfoxide, free anions are the catalytic species, and little asymmetric solvation is expected, since the anions to hydrogen bond must compete with the solvent itself for what little methanol is present.

These results taken together with those obtained from the isotope exchange reactions of 2-phenylbutane (IV) and 1-phenylmethoxyethane (V)^{4d} and cleavage reactions of II and III provide carbanion-solvent systems that can be divided into four classes, according to their symmetry properties (see Table V). Although an asymmetric anion must induce asymmetry in its solvent shell, and asymmetric solvation might induce some asymmetry in an otherwise symmetric species, the dissection of symmetry properties into substrate and environmental components not only has a very real experimental basis, but also helps in recognition and correlation of new experimental observations as they appear.

TABLE V
CARBANION-SOLVENT-BASE SYSTEMS CLASSIFIED
ACCORDING TO THEIR SYMMETRY PROPERTIES

Class	Carbanion	Solvent shell	Examples
I	Symmetric	Symmetric	2-Phenyl-2-butyl anion in either dimethyl sulfoxide-potassium <i>t</i> -butoxide, or <i>t</i> -butyl alcohol - quaternary ammonium hydroxide
II	Symmetric	Asymmetric	2-Phenyl-2-butyl anion in either <i>t</i> -butyl alcohol-potassium <i>t</i> -butoxide, or ethylene glycol-potassium ethylene glycoside
III	Asymmetric	Symmetric	2-Phenylsulfonyl-2-octyl anion in dimethyl sulfoxide - potassium methoxide, or in <i>t</i> -butyl alcohol-tetramethylammonium hydroxide
IV	Asymmetric	Asymmetric	2-Phenylsulfonyl-2-octyl anion in <i>t</i> -butyl alcohol-potassium <i>t</i> -butoxide

Fast and Slow Exchange Reactions in *tert*-Butyl Alcohol.—The racemization of sulfone in *t*-butyl alcohol-potassium *t*-butoxide followed simple pseudo-first-order kinetics over the whole range of the reaction. Some of the exchange reactions were different. Those runs in which substrate concentration exceeded that of base followed kinetics that indicate two competing pseudo-first-order reactions. The data of Table VI provide a rough correlation between the ratios of concentrations of substrate to base, and the amount of substrate consumed by the "fast reaction." The higher the value of the ratio of base to substrate, the larger the amount of substrate that exchanges *via* the "fast reaction." Indeed, the "slow reaction" disappears altogether when this ratio approaches unity. The data also indicate that as the ratio decreases to values in the neighborhood of 0.1, the "fast reaction" accounts for only a small part of the exchange reaction.²²

(22) H. E. Zaugg, B. W. Horrom and S. Borgwardt [*J. Am. Chem. Soc.*, **82**, 2895 (1960)] observed that in the rate of alkylation of sodium malonic esters in benzene, composite kinetics were observed similar to those found in the present investigation.

TABLE VI
CORRELATION BETWEEN RATIO OF BASE TO SUBSTRATE AND AMOUNT OF SUBSTRATE CONSUMED BY FAST EXCHANGE REACTION IN *t*-BUTYL ALCOHOL-POTASSIUM *t*-BUTOXIDE AT 25.0°

Runs involved ^a	Substrate	Concn. KOCH(CH ₃) ₃ / Concn. substrate	Substrate consumed by fast reaction, %
35	I-l	0.98	~100
37	I-h	.28	~ 47
39	I-h	.12	~ 24
36	I-d	.99	~100
38	I-d	.26	~ 38
40	I-d	.13	~ 8

^a Table III.

These data show that substrate is consumed in two independent processes, each of which exhibits pseudo-first-order kinetics. The striking feature is that the rate of the "fast reaction" must be faster than the rate of equilibration between the individual components which contribute to the rate-determining transition states for the two reactions. Had equilibration between all possible states for the base and substrate occurred more rapidly than the "fast reduction," only a single pseudo-first-order rate could have been observed. More extensive investigation is needed before the causes of this phenomenon can be identified.

Isotope Effects in the Isotope Exchange Reaction.—The data of Table VII indicate that in both ethylene glycol and *t*-butyl alcohol, the isotope exchange reaction shows a very small isotope effect on rate. Indeed, k_2^{eH}/k_2^{eD} (ratio of calculated second-order rate constant for exchange of non- and deuterated sulfones) values range between extremes of 0.5 and 1.5. These small values indicate that in neither a good dissociating solvent such as ethylene glycol or an associating solvent such as *t*-butyl alcohol is the observed rate of exchange governed solely by the breaking of the C-H or C-D bond.

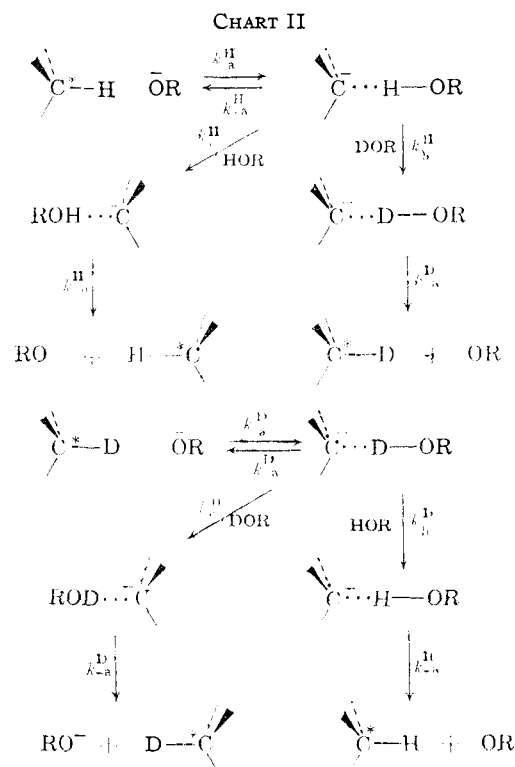
TABLE VII
ISOTOPE EFFECTS IN ISOTOPE EXCHANGE REACTION

Run ^a	Solvent	Base, ^b <i>M</i>	<i>T</i> , °C.	$(\frac{k_2^{eH}}{k_2^{eD}})^c$
32	DOCH ₂ CH ₂ OD	0.068	100.6	1.2
33	HOCH ₂ CH ₂ OH	.092	100.6	
35	(CH ₃) ₂ COD	.181	25.00	1.5
36	(CH ₃) ₂ COH	.183	25.00	
37F	(CH ₃) ₂ COD	.103	25.00	0.8
38F	(CH ₃) ₂ COH	.098	25.00	
37S	(CH ₃) ₂ COD	.103	25.00	0.8
38S	(CH ₃) ₂ COH	.098	25.00	
39F	(CH ₃) ₂ COD	.046	25.00	0.5
40F	(CH ₃) ₂ COH	.051	25.00	
39S	(CH ₃) ₂ COD	.046	25.00	1
40S	(CH ₃) ₂ COH	.051	25.00	

^a Table III. ^b Potassium alkoxide was based employed. ^c K_2^{eH} is k^e for I-h and k_2^{eD} is k_2^e for I-d.

The mechanistic scheme of Chart II provides a ready explanation for the lack of a sizable isotope effect in these exchange reactions. This hypothesis is similar to one developed elsewhere in connection with the observed lack of substantial isotope effect in the base-catalyzed racemization of 1-phenylmethoxyethane in dimethyl sulfoxide.^{4d} Although

this scheme is based on C type carbanions, a similar scheme can be equally well envisioned for D type carbanions.



In this scheme, hydrogen-bonded alkoxide ion, or an ion-pair, or an ion-pair complexed with sulfone and (or) solvent might be the active base, symbolized by $\bar{O}R$. The breaking of the C-H or C-D bond is certainly the slow step in the reaction sequence, and is governed by the rate constants, k_a^H and k_a^D , respectively. The sulfone anion formed is a strong base compared to $\bar{O}R$, and the carbanion is undoubtedly hydrogen bonded to the same molecule of solvent formed in the hydrogen or deuterium transfer to oxygen. Consequently the reverse transfer of the same atom of hydrogen (deuterium) back to carbon (rates governed by k_{-a}^H or k_{-a}^D) might be much faster than the exchange of solvent molecules hydrogen bonded to the carbanion (rate governed by k_b^H or k_b^D). If indeed $k_{-a}^H, k_{-a}^D, k_b^H$ and $k_b^D \gg k_a^H$ and k_a^D , and k_b^H and $k_b^D < k_{-a}^H$ and k_{-a}^D , then the observed rates of exchange are governed by eq. 1 and 2. The resulting isotope effect is

$$k_{obs}^{eH} = (k_a^H/k_{-a}^H) \times k_b^H = K^H k_b^H \quad (1)$$

$$k_{obs}^{eD} = (k_a^D/k_{-a}^D) \times k_b^D = K^D k_b^D \quad (2)$$

expressed by its eq. 3. The term, K^H/K^D is a ratio

$$k_2^{eH}/k_2^{eD} = K^H k_b^H / K^D k_b^D \quad (3)$$

of two equilibrium constants, and value might possibly be somewhat less than unity, since the zero point energy for the stretching vibration of the O-H bond is greater than for the C-H bond. The term k_b^H/k_b^D deals with processes in which no covalent bonds are made or broken, and values close to unity are anticipated.²³

(23) This same argument can be cast in somewhat different terms. The free energies of activation for the exchange reactions depend only on the differences in free energy between the initial states (F_H and F_D)

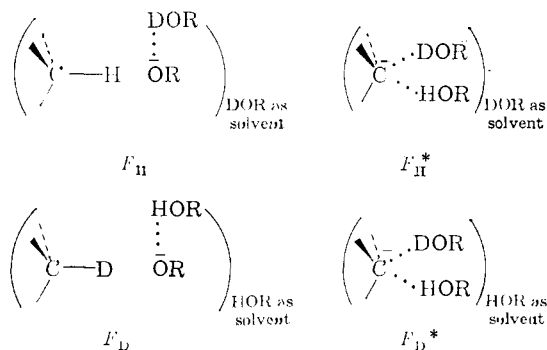
Isotope Effects in the Racemization Reaction.—In Table VIII are found the isotope effects associated with the racemization reaction. The values of $k_2^{\alpha H}/k_2^{\alpha D}$ range from a low of 0.3 to a high of 1.9. Those runs made in the dissociating solvent ethylene glycol, gave values of 0.3–0.4, which are less than unity. In runs 12 and 15 carried out in ethylene glycol the substrate and solvent had the same isotopic composition, and the ratio of rate constants was 0.3. In runs 13 and 14 in which the substrate and solvent initially had different isotopic compositions, the ratio of the rate constants was 0.4. Actually, the latter ratio serves as a check on the former. Since the isotopic exchange reaction was much faster than racemization, solvent and substrate became isotopically homogeneous before racemization could be detected.

TABLE VIII
ISOTOPE EFFECTS IN RACEMIZATION REACTION

Run ^a	Solvent	Base, ^b <i>M</i>	<i>T</i> , °C.	$(k_2^{\alpha H}/k_2^{\alpha D})^c$
12	HOCH ₂ CH ₂ OH	0.0931	100.6	0.3
15	DOCH ₂ CH ₂ OD	.0686	100.6	
13	HOCH ₂ CH ₂ OH	.0964	100.6	0.4
14	DOCH ₂ CH ₂ OD	.0652	100.6	
26 ^d	(CH ₃) ₃ COH	.183	25.00	0.6
27 ^e	(CH ₃) ₃ COD	.181	25.00	
Fig. 1 ^f	(CH ₃) ₃ COH	.055	25.00	1.0
	(CH ₃) ₃ COD	.055	25.00	
Fig. 1 ^f	(CH ₃) ₃ COH	.200	25.00	1.9
	(CH ₃) ₃ COD	.200	25.00	
Fig. 1 ^f	(CH ₃) ₃ COH	.357	25.00	1.0
	(CH ₃) ₃ COD	.357	25.00	

^a Table II. ^b Potassium alkoxide used as base. ^c $k_2^{\alpha H}$ is second-order rate constant for racemization of I-h, and $k_2^{\alpha D}$ that for I-d. ^d Although deuterated substrate was used initially, it was converted to protonated substrate before any substantial amount of racemization had occurred. ^e Although protonated substrate was used initially, it was converted to deuterated substrate before any substantial amount of racemization had occurred. ^f Rates read from Fig. 1 at concentrations indicated.

and the transition states of highest free energy (F_H^* and F_D^*). In both of these transition states, a carbanion is half "hydrogen bonded"



to DOR and half to HOR, and therefore these transition states differ only in the isotopic composition of their solvents. Therefore $F_H^* \cong F_D^*$, and the value of $k_2^{\alpha H}/k_2^{\alpha D}$ would reflect only $F_H - F_D$, which equals the difference in zero point energies between the two starting states. One of these states involves a C–H, a O–D and a $\bar{O} \cdots D$ bond, and the other a C–D, a O–H and a $\bar{O} \cdots H$ bond, and the difference in zero point energy between these states is expected to be too small to produce any sizable isotope effect.

This viewpoint was developed as a result of conversations with Dr. C. A. Bunton, whom the authors wish to thank for his interest.

In *t*-butyl alcohol as solvent, $k_2^{\alpha H}/k_2^{\alpha D}$ ranged from 0.6 to 1.9, depending on the base concentration. In all but runs 26 and 27, the substrate and solvent were isotopically homogeneous. In these two runs, since exchange was so much faster than racemization, the solvent and substrate became isotopically homogeneous before racemization had occurred to any extent.

The mechanistic scheme of Chart II is consistent with the observed lack of sizable isotope effects in the racemization reaction. In all solvents exchange rates were faster than racemization rates, and both processes undoubtedly involved the same primary steps. If k_{-a}^H and $k_{-a}^D > k_b^H$ and k_b^D , then k_{-a}^H and $k_{-a}^D \gg k_{-c}^H$ and k_{-c}^D . Thus eq. 4 and 5 express relationships between $k_{obs}^{\alpha H}$, and $k_{obs}^{\alpha D}$ and the corresponding component rate constants of Chart II for the racemization. The resulting isotope effect for racemization is expressed by eq. 6

$$k_{obs}^{\alpha H} = \frac{k_a^H}{k_{-a}^H} \times 2k_c^H = 2K^H k_e^H \quad (4)$$

$$k_{obs}^{\alpha D} = \frac{k_a^D}{k_{-a}^D} \times 2k_c^D = 2K^D k_e^D \quad (5)$$

which resembles (3) in form, the thermodynamic term, K^H/K^D

$$k_2^{\alpha H}/k_2^{\alpha D} = K^H k_e^H / K^D k_e^D \quad (6)$$

being common to both equations. In eq. 6, the kinetic term k_c^H/k_c^D should be close to unity, since only hydrogen bonds (no covalent bonds) were made or broken in the rate-determining step.²⁴ This same argument could be expressed in terms resembling those of footnote 23.

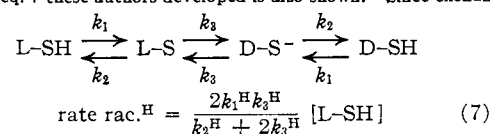
Combinations of eq. 1 and 4 on the one hand, and eq. 2 and 5 on the other produce eq. 9 and 10, which relate the ratios of the measured rate constants for exchange and racemization to the rate constants for exchange of solvent molecules hydrogen bonded to the anion which occur with and without inversion.

$$k_2^{\alpha H}/k_2^{\alpha H} = k_b^H/2k_c^H \quad (9)$$

$$k_2^{\alpha D}/k_2^{\alpha D} = k_b^D/2k_c^D \quad (10)$$

Combination of eq. 9 and 10 gives eq. 11, which in a sense expresses the isotope effect for the stereo-

(24) Corey and Kaiser (ref. 15) in 2:1 ethanol-water reported an isotope effect of 0.97 for racemization of I-h and I-d (80.1°), in each run the solvent and substrate being isotopically homogeneous. No results concerning the isotope effect for the corresponding exchange reactions were reported. The authors explained their lack of isotope effect for racemization on the basis of the kinetic scheme formulated. The rate eq. 7 these authors developed is also shown. Since exchange



was faster than racemization (a factor of 41), $k_2 \gg 2k_1$, and the isotope effect is governed by eq. 8, which contains a thermodynamic and a rate $\text{rac.}^H = \frac{K_H}{K_D} \times \frac{k_3^H}{k_3^D}$ where $K_H = \frac{k_1^H}{k_2^H}$ and $K_D = \frac{k_1^D}{k_2^D}$ (8)

kinetic term. Neither term would involve an appreciable isotope effect. Equation 8 resembles eq. 3 and 6 in form. However, the equilibrium constants have different meanings.

The mechanistic scheme of Corey and Kaiser predicts an ordinary kinetic isotope effect (value of 4–10) for rate exchange^H/rate exchange^D. The fact that isotope effects of only 0.5 to 1.5 were observed for our exchange reactions indicates that the Corey and Kaiser mechanistic scheme cannot apply to our results.

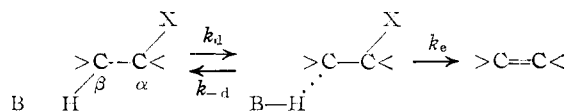
specificity of the reaction. Values for this isotope effect range between 0.4 and 1.3, and are less than unity in all but one case.

$$\frac{k_{2eH}/k_{2eH}}{k_{2eD}/k_{2eD}} = \frac{k_b^H}{k_b^D} \times \frac{k_c^D}{k_c^H} \quad (11)$$

Equations 9 and 10 provide a convenient means of expressing the contributions made to the stereospecificity of the reaction by d-orbital stabilization of the configuration of the anion and by asymmetric solvation. Thus enhancement of the values of k_b^H and k_b^D would be associated with asymmetric solvation, whereas decrease in the values k_c^H and k_c^D would be associated with the ability of the d-orbital on sulfur to depress the rate of inversion of the anion.

The further study of the stereochemistry, kinetics and mechanisms of base-catalyzed hydrogen-deuterium exchange reactions is being vigorously pursued in our laboratories.

Relevance of Results to Other Organic Reactions.—The results obtained in this and previous studies^{3d} raise some doubts concerning the accepted mechanisms for certain other reactions that involve a base-catalyzed breaking of a carbon-hydrogen bond in the rate-determining step. For instance, questions arise concerning the presumed synchronous character of the E_2 reaction, which has been stated to involve loss of both a proton and a leaving group in the same transition state.²⁵ The fact that a base-catalyzed 1,2-elimination reaction follows a *trans*-steric course and is first order in base and in substrate is insufficient evidence for a single transition state for the reaction. If carbanions under many sets of circumstances can hold their configurations, the stereochemical test for the synchronous character of the reaction disappears. Since the E_2 and $E_{1c}B$ ²⁵ mechanisms have the same kinetic characteristics, the kinetic criteria for a single transition state are inapplicable. Even though $k_{-d} \gg k_e$ in the mechanism formulated, isotopic exchange of C_β -H with B-D (deuterated solvent)



might not occur as fast as elimination, and hence lack of observable isotopic exchange at C_β cannot be used as a criterion for the classical E_2 mechanism. About the best criterion for an E_2 mechanism is the presence of a substantial hydrogen-deuterium kinetic isotope effect on the rate of the base-catalyzed elimination reaction.²⁶

An example of a system whose base-catalyzed elimination reaction might proceed through a $E_{1c}B$ mechanism has been studied by Bordwell and Landis.²⁷ Thus, the *threo*- and *erythro*-3-*p*-tolylsulfonyle-2-butyl brosylates were observed to undergo base-catalyzed *trans* elimination reactions. Carbanion intermediates in this system would resemble those of the present study, and would be expected to maintain their configurations.

(25) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 419-467.

(26) Literature pertinent to this discussion is reviewed by V. J. Shiner and M. L. Smith, *J. Am. Chem. Soc.*, **80**, 4095 (1958).

(27) F. G. Bordwell and P. S. Landis, *ibid.*, **79**, 1593 (1957).

Experimental

Starting Materials.—Essentially optically pure 2-octanol,¹⁰ $[\alpha]_{346}^{25} = -11.5^\circ$ (neat, l 1 dm.), was prepared and converted to its tosylate,¹¹ and then to 2-octyl sulfide (68% yield), b.p. 165-168° at 19 mm., $\alpha^{25D} +9.72^\circ$ (neat, l 1 dm.); reported¹² b.p. 178° at 20 mm., $[\alpha]_{17D} +11.31^\circ$ (neat). Reduction of pure 2-octanone with insufficient lithium aluminum deuteride in ether was carried out in the usual way,^{10b} the product was freed of ketone and resolved through its acid phthalate, and converted to optically active 2-octanol-2-*d*, $[\alpha]_{25D} -9.23^\circ$ (neat), reported $[\alpha]_{25D} -9.42^\circ$ (neat). This material was converted through its tosylate to the corresponding sulfide.

In oxidation of 2-octyl phenyl sulfone, the general procedure of Bordwell and Boutan was followed.¹³ To a mixture of 10 g. of (+)-2-octyl phenyl sulfide in 100 ml. of glacial acetic acid was added 20 ml. of 30% hydrogen peroxide. The resulting 2-phase system was warmed until reaction started. The system became hot (reflux) and, after the reaction had subsided, the solution was cooled and diluted with 200 ml. of water. The solid that separated was collected; 8.2 g. (71%), m.p. 42.0-43.5°. Recrystallization of this material from hexane gave m.p. 44.0-44.5°, $[\alpha]_{25D} -12.6^\circ$ (*c* 5, CHCl_3). Additional recrystallizations did not change the melting point. An infrared spectrum of this sample showed two strong bands at 1300 and 1140 cm^{-1} , characteristic of a sulfone group,¹⁴ and no band at 1055 cm^{-1} which is associated with a sulfoxide group. Racemic sulfone, prepared the same way, gave m.p. 28-29°.

Anal. Calcd. for $\text{C}_{11}\text{H}_{20}\text{O}_2\text{S}$: C, 66.10; H, 8.72. Found: C, 65.93; H, 8.83.

Preliminary rate studies on the racemization of the active sulfone were conducted in *t*-butyl alcohol with tetramethylammonium hydroxide as base (conditions of run 16). A plot of $\log \alpha$ against time demonstrated that two simultaneous reactions were occurring. Consequently, the active sulfone was subjected to a second hydrogen peroxide treatment to give material close to kinetic homogeneity, $[\alpha]_{25D} -11.0^\circ$, $[\alpha]_{2546}^{25} -13.3^\circ$, $[\alpha]_{2546}^{25} -26.4^\circ$ (*c* 5.3, CHCl_3). A third oxidation gave kinetically pure sulfone, $[\alpha]_{25D} -10.6^\circ$, $[\alpha]_{2546}^{25} -13.3^\circ$ (*c* 5.4, CHCl_3), $[\alpha]_{25D} -13.3^\circ$ (*c* 1.3, 2:1 ethanol-water), m.p. 47.5-48°.

A sample of the sulfone obtained originally (0.1 g.) was chromatographed on a 2 by 20 cm. column of 2-to-1 silicic acid-Celite with pentane as developer. A total of 34 25-ml. samples of eluent was collected. Sample 7 contained the most weight, and gave sulfone, m.p. 47.5-48.0°, undepressed by admixture with the kinetically pure sulfone prepared by the above procedure.

In a similar manner, (-)-2-octyl-2-*d* phenyl sulfone was prepared (three oxidations) to give from 10.0 g. of sulfide, 7.9 g. (69%) of sulfone, $[\alpha]_{25D} -14.0^\circ$ (*c* 6, CHCl_3), m.p. 47.5-48.0°, 0.97 atom of D per molecule (combustion and falling drop method).¹⁷ This material proved to be kinetically pure under the conditions of run 16.

Solvents.—Purification and drying (Linde "Molecular Sieves," 4A, 14 by 30 mesh) of *t*-butyl alcohol, methanol, dimethyl sulfoxide and ethylene glycol are described in former papers of this series,^{1c,1d} as was the preparation and drying of *t*-butyl alcohol-*O-d*¹⁶ and ethylene glycol-*O-d*.¹⁶ The *t*-butyl alcohol-*O-d* contained 0.99 atom of D per molecule and the ethylene glycol-*O-d* contained 1.98 atoms of D per molecule (combustion and falling drop method).¹⁷ The water content in all solvents was less than the amount detectable with Karl Fischer titration. All solvents before use were flushed with oxygen-free, dry nitrogen.

Preparation of Basic Solutions.—For those runs involving metal alkoxide as base, the basic solutions were prepared by direct addition of clean, dry metal to the alcohol in question under an atmosphere of clean, dry nitrogen. Special precautions had to be taken with methanol and ethylene glycol; the alcohol was cooled to -78°, and the metal was added in very small pieces with very efficient stirring. The solution of tetramethylammonium hydroxide in *t*-butyl alcohol was prepared by dissolving a weighed solid sample of tetramethylammonium hydroxide-0.27(CH_3)₃N·2.0H₂O in *t*-butyl alcohol, and removing the water with Linde Molecular Sieves (4A, 14 by 30 mesh) until the solution was dry to Karl Fischer reagent. Solutions of methanol-potassium methoxide in dimethyl sulfoxide were prepared by adding a solution of potassium methoxide in methanol to dimethyl

sulfoxide. Aliquots of each basic solution were titrated with standard acid.

Preparation of Reaction Solutions.—For those runs conducted at 25.00°, weighed amounts of the appropriate sulfones were placed in a dry, nitrogen-flushed glass stoppered erlenmeyer flask, to which the appropriate basic solution (thermostated) was added. For runs conducted at higher temperatures in methanol, the appropriate basic solution of sulfone was prepared (see above), and appropriate aliquots were introduced carefully into clean, dry ampoules under dry, oxygen-free nitrogen by means of a fast draining automatic pipet. The ampoules were then sealed, and placed in a constant temperature bath. Since sulfone was insoluble in ethylene glycol, the solid sulfone was weighed directly into each ampoule, the solvent was added with the pipet and the vial was sealed; the sulfone dissolved when heated.

Isolation Procedure.—After the desired time, the contents of the ampoule or flask were poured into a 250-ml. separatory funnel (Teflon greaseless stopcock) containing 25 ml. of water and 25 ml. of pure pentane. The flask or ampoule was rinsed with additional pentane. After the mixture was shaken vigorously, the pentane layer was washed twice with 25 ml. of water and dried. The pentane layer was transferred to a 50-ml. pear-shaped flask, and the pentane solution was evaporated with aid of a glass capillary boiling stick. The resulting colorless oil crystallized when allowed to stand. Depending on the measurement to be made, this solid was treated in one of three ways.

If a rotation was desired, the solid was transferred with pure pentane to a preweighed volumetric flask. The pentane was evaporated at 100° and the last traces of solvent removed under vacuum. The flask then was weighed, solvent was added, and the rotation taken in the usual way.

If deuterium analysis by combustion and falling drop method was desired,¹⁷ the solid was dissolved in pure pentane, transferred to a small ampoule, the pentane was evaporated, the last traces were removed under vacuum at 100°, the ampoule was sealed, and submitted for analysis. When samples were removed for analysis, the total sample was first melted and homogenized, and was handled as an oil.

If deuterium analyses by infrared spectroscopic measurements were desired, the solid was transferred from the flask by solution in pentane to weighed screw-cap vials, the pentane was evaporated, and the last traces of pentane evaporated under vacuum at 100°. The vials were weighed again.

Deuterium Analyses by Infrared Spectroscopy.—Preliminary experiments concerning the use of infrared spectroscopy as an analytical tool revealed a band at 918 cm.⁻¹ present in I-d which was absent in I-h. Carbon tetrachloride was chosen as solvent since it was transparent in this region. A concentration of about 15% by weight of pure I-d in a 0.39-mm. cell (sodium chloride) was found to give a full scale deflection of the Beckman IR4 spectrophotometer (sodium chloride optics, and used as a single beam instrument) that was employed.

A series of 6 standard sulfone samples of varying deuterium content were prepared in small screw cap vials by weighing known amounts of I-h and I-d. Carbon tetrachloride was added to the vials (4 microliters per milligram of sulfone with a syringe), and the weight of the added solvent was recorded.

The % transmission at 918 cm.⁻¹ was determined for each of the knowns, and a plot of the absorbance divided by the concentration (by weight) vs. the % of I-d in the mixture was made. This calibration curve was used to determine the deuterium content of each unknown sample. The base line was set before and after each determination through use of the cell-in, cell-out technique. At least two measurements were made on each sample. Since the same cell was used in all measurements, the cell thickness was not included in the calculation of the absorptivity.

Quantitative Stereochemical Picture (Runs 1-7).—Those runs made at 25° were carried out in stoppered flasks, and those made at higher temperatures in ampoules. Rotations were taken on part of the sulfone isolated, and the remainder was submitted for analysis for deuterium (combustion and falling drop method).¹⁷ Rotations were always taken in chloroform, c 5%, $\lambda = 5461 \text{ \AA.}$, in a 1-dm. cell at 25°.

Racemization and Exchange Kinetics (Runs 8-42).—Those runs carried out at 100.6 ± 0.1° involved use of ampoule technique and an oil-bath. One ampoule containing sulfone was prepared for purposes of titrating (with standard acid) for the concentration of base in the run. The ampoules were prepared at 25°, placed in an oil-bath held at 100.6 ± 0.1°, and time 0 was taken 5 minutes after the ampoule was introduced into the bath. One ampoule was not heated, but was retained for rotation or deuterium analysis at time = 0. In those runs in which the racemization and exchange kinetics were measured at the same base concentration ampoules for both runs were prepared at the same time from the same base solution, and made at the same time. At appropriate times, ampoules were withdrawn from the bath, cooled, sulfone isolated (see above) and polarimetric or infrared deuterium analyses performed. Rotations were taken in chloroform, c 5%, $\lambda = 5461 \text{ \AA.}$, in a 1-dm. cell at 25°. All analyses for these runs were performed through use of the infrared technique.

The racemization runs performed at 25.00 ± 0.01° were carried out in a water-jacketed 1-dm. polarimeter tube of about 1.5-ml. capacity. Constant temperature water from a thermostated water-bath was pumped through the jacket. A weighed sample of sulfone was placed in a clean, dry, stoppered flask under dry nitrogen. The flask was thermostated, and thermostated base solution was added. The sulfone dissolved immediately, and the solution was poured into the thermostated polarimeter tube, the tube was stoppered, and the first reading was taken about 1 minute after mixing of the solution. Rotations were taken employing $\lambda = 5461 \text{ \AA.}$ Time was kept with a stop watch which was started when the solutions were mixed.

The exchange kinetics at 25.00° were carried out in a stoppered flask immersed in a constant temperature bath. Aliquots were periodically removed and shaken with a cold mixture of water and pentane. Sulfone for each point was isolated by the procedure shown above.

In all runs, the base concentrations were determined by titration of aliquots of the reaction solutions, after reaction was over. In runs 18-20, 36 and 37, aliquots were titrated before and after the runs had been made, and the base concentration was the same within experimental error. Titrations were made to a phenolphthalein end-point in water.

In exchange run 38, the sulfone recovered from points 2, 4 and 6 gave m.p. 47-48°, and in exchange run 35, the 10th point gave m.p. 47-48°. Mixed melting points of these samples with optically pure sulfone were undepressed. The infrared spectra of these sulfone samples in carbon tetrachloride were superimposable on authentic samples of sulfone, except in the regions where I-h and I-d differed from one another.

Sample Racemization Run (Run 10).—Potassium, 0.57 g., was dissolved in 5 ml. of pure dry methanol at -78° under an oxygen-free, dry, nitrogen atmosphere. A 1.14-ml. aliquot of this solution (weight 1.0264 g.) was introduced into a 25-ml. glass-stoppered, weighed erlenmeyer flask. Purified dimethyl sulfoxide, 8.66 ml., 9.440 g., was added to this solution to give a 92% by weight solution of dimethyl sulfoxide. This solution was thermostated at 25°. In a 2.00-ml. volumetric flask was placed 0.1904 g. of (-)-I-d. The flask was thermostated, and filled to the mark with the base solution (time 0). The solid dissolved immediately, the flask was shaken, the thermostated polarimeter tube was immediately filled, and rotations were taken, the first reading at time = 3 minutes. Twenty points were taken during the first 34% of the reaction. The logarithm of the rotation was plotted against time, and the slope of the line was determined graphically to be $5.75 \pm 0.29 \times 10^{-3} \text{ sec.}^{-1}$. An aliquot of the reaction solution was titrated with standard acid, and the reaction was found to be 0.200 *M*. The second-order rate constant was calculated to be $2.88 \pm 0.15 \times 10^{-4} \text{ l.m}^{-1} \text{ sec.}^{-1}$.

Control Run.—Because of the small amount of trimethylamine present in runs 16, 28, 29, 34, 41 and 42, a control run was made in which a 0.375 *M* solution of trimethylamine in *t*-butyl alcohol was allowed to stand at 25° for 100 hr. The rotations before and after this treatment were identical.