

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, LOS ANGELES 24, CALIF.]

Electrophilic Substitution at Saturated Carbon. XIV. Asymmetric Solvation of Carbanions in Stereospecific Hydrogen-Deuterium Exchange Reactions^{1,2}

BY DONALD J. CRAM, CHARLES A. KINGSBURY AND BRUCE RICKBORN

RECEIVED FEBRUARY 27, 1961

The stereochemical course of the base-catalyzed hydrogen-deuterium reaction at saturated carbon has been investigated in *t*-butyl alcohol, in diethylene glycol and in dimethyl sulfoxide as solvent. Substrates were 2-phenylbutane, 2-phenylbutane-2-*d*, 1-phenylmethoxyethane and 1-phenylmethoxyethane-1-*d*. In *t*-butyl alcohol the exchange proceeded with as high as 97% net retention of configuration, in dimethyl sulfoxide with 100% racemization, and in diethylene glycol probably with small amounts of net inversion. The stereospecificity of these reactions is interpreted in terms of asymmetric solvation of a carbanion, itself symmetrical due to delocalization of charge into the benzene ring. Kinetics of the racemization reaction were studied in dimethyl sulfoxide and in *t*-butyl alcohol. The values of the rate constants with potassium *t*-butoxide as catalyst differed by a factor of 6 powers of 10 in the two solvents, the rate being slower in the hydroxylic (hydrogen bonding) solvent. Substitution of sodium for potassium *t*-butoxide made only small differences in *t*-butyl alcohol, but in dimethyl sulfoxide the value of the rate constant was depressed by a factor of 100 when the sodium base was used. The racemization was found to be approximately half order in potassium *t*-butoxide when run in dimethyl sulfoxide as solvent, and the rate was markedly depressed by addition of potassium iodide.

Although a number of previous studies have been made of the stereochemistry of the hydrogen-deuterium exchange reaction at saturated carbon,³ the systems always contained carbanion-stabilizing substituents capable of producing the tautomer of the starting material in the protonation of the intermediate carbanion. Such acidifying groups as the carbonyl,^{3a} carboxyl,^{3b} amide,^{3d} cyano^{3d} and ester^{3d} have been used in systems for the study of this reaction, and exchange has always proceeded with complete racemization. The present study was inspired by the observation that carbanions produced in the S_N1 reaction with carbon as leaving group were found to give optically active products by virtue of asymmetric solvation of the intermediate

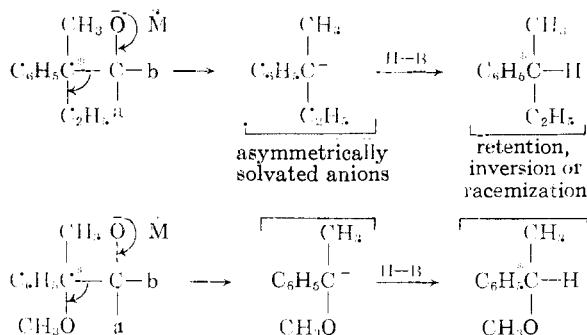
In the present investigation, 2-phenylbutane (I-h), 2-phenylbutane-2-*d* (I-d), 1-phenylmethoxyethane (II-h) and 1-phenylmethoxyethane-1-*d* (II-d) were selected for study, particularly since on treatment with base these systems produce the same anions observed when carbon was used as leaving group (see formulations).



As a result of the previous investigations, *t*-butyl alcohol, diethylene glycol and dimethyl sulfoxide were chosen as the solvents most likely to reveal extremes of steric course for the exchange reaction, and to accentuate the similarities and differences between carbon and hydrogen as leaving group in the electrophilic substitution reaction.

Results

Starting Materials.—Optically active 2-phenylbutane and 2-phenylbutane-2-*d* were available from other studies.⁶ It was established earlier⁶ that the maximum rotations of the deuterated and non-deuterated material were essentially equal ($\alpha^{25}_{\text{D}} \pm 24.0^\circ$, *l* 1 dm., neat, for the former and $\alpha^{25}_{\text{D}} \pm 24.3^\circ$, *l* 1 dm., neat, for the latter). Non-deuterated 1-phenylmethoxyethane was also prepared in an earlier investigation.⁵ Reduction of acetophenone with lithium aluminum deuteride gave 1-phenylethanol-1-*d* containing 0.97 atom of deuterium per molecule. Resolution of the substance by the same method used for the non-deuterated compound gave optically pure material with a rotation of $\alpha^{25}_{\text{D}} - 44.1^\circ$, *l* 1 dm., neat, as compared to $\alpha^{25}_{\text{D}} - 44.2^\circ$, *l* 1 dm., neat, for undeuterated alcohol.⁵ Conversion of the deuterated alcohol to 1-phenylmethoxyethane-1-*d* gave material containing 0.97 atom of deuterium per molecule, $\alpha^{25}_{\text{D}} - 120.0^\circ$, *l* 1 dm., neat, compared to $\alpha^{25}_{\text{D}} - 120.2^\circ$, *l* 1 dm., neat, for the undeuterated compound.⁵ Thus substitution of deuterium for hydrogen at the benzyl position of these three compounds has little effect on their maximum rotations. Calculations in this paper are



anion.⁴ The reactions formulated were found to proceed with as high as 96% net retention⁵ in *t*-butyl alcohol, 63% net inversion⁶ in ethylene glycol, and total racemization in dimethyl sulfoxide.⁴

(1) Some of the results of this paper appeared in preliminary form: (a) D. J. Cram, C. A. Kingsbury and B. Rickborn, *J. Am. Chem. Soc.*, **81**, 5835 (1959); (b) D. J. Cram, W. D. Nielsen and B. Rickborn, *ibid.*, **82**, 6415 (1960); (c) D. J. Cram, B. Rickborn and G. R. Knox, *ibid.*, **82**, 6412 (1960).

(2) The authors wish to thank the National Science Foundation for a grant which supported this work.

(3) (a) C. L. Wilson, *J. Chem. Soc.*, 1550 (1936); (b) S. K. Hsu, C. K. Ingold and C. L. Wilson, *ibid.*, 78 (1938); (c) D. J. G. Ives and G. C. Wilkes, *ibid.*, 1455 (1938); (d) D. J. Cram, B. Rickborn, C. A. Kingsbury and P. Haberfeld, *J. Am. Chem. Soc.*, **83**, 3678 (1961).

(4) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *ibid.*, **81**, 5774 (1959), and previous papers.

(5) D. J. Cram, K. R. Kopecky, F. Hauck and A. Langemann, *ibid.*, **81**, 5754 (1959).

(6) D. J. Cram and B. Rickborn, *ibid.*, **83**, 2178 (1961).

TABLE I
 STEREOCHEMICAL COURSE OF BASE-CATALYZED HYDROGEN-DEUTERIUM EXCHANGE REACTIONS

Run	Substrate Nature	Concn., N	Solvent	Base concn., N ^b	T, °C.	Tm., hr.	% benzyl ex- change	% rac.	Steric course ^a
1	2-Phenylbutane ^e	0.41	(CH ₃) ₂ COD ^d	0.41	215	75	37	4.2	89% ret.
2	2-Phenylbutane-2-d ^e	.26	(CH ₃) ₂ COH	.38	225	69	73	9.5	87% ret.
3	2-Phenylbutane	.09	(CH ₃) ₂ COD ^d	.40	210	75	41	10	76% ret.
4	2-Phenylbutane	.15	(CH ₃) ₂ COD ^d	.38	225	148	55	12.5	77% ret.
5	2-Phenylbutane	.26	(CH ₃) ₂ COD ^d	.38	225	69	57	30.6	46% ret.
6	2-Phenylbutane-2-d ^e	.07	(HOCH ₂ CH ₂) ₂ O	.40	260	229	9	10.5	~ 6% inv.
7	2-Phenylbutane-2-d ^f	.02	(HOCH ₂ CH ₂) ₂ O	.40	260	229	10	11.0	~11% inv.
8	2-Phenylbutane-2-d ^g	.19	(HOCH ₂ CH ₂) ₂ O	.36	260	140	13	19.6	51% inv.
9	1-Phenylmethoxyethane-1-d ^h	.097	(CH ₃) ₂ COH	.49	220	10	16	1.1	94% ret.
10	1-Phenylmethoxyethane-1-d ^h	.088	(CH ₃) ₂ COH	.55	220	10	13	1.6	88% ret.
11	1-Phenylmethoxyethane ⁱ	.113	(CH ₃) ₂ COD ^d	.33	220	26	51	9.6	80% ret.
12	1-Phenylmethoxyethane-1-d ^h	.077	(CH ₃) ₂ COH	.55	230	24	47	21	55% ret.
13	1-Phenylmethoxyethane-1-d ^h	.086	(CH ₃) ₂ COH	.24 ^j	248	9	11	2.7	75% ret.
14	1-Phenylmethoxyethane-1-d ^h	.12	(HOCH ₂ CH ₂) ₂ O	.40	260	240	4	6.6	~60% inv.
15	1-Phenylmethoxyethane-1-d ^h	.19	(CH ₃) ₂ SO ^k	.26 ^l	85	14	31	31	100% rac.

^a In calculation of steric course, no account is taken of lack of isotopic purity of the solvent, nor of optical instability of the product once formed. ^b Potassium alkoxide derived from solvent unless noted otherwise. ^c $\alpha^{25}\text{D} = -17.6^\circ$ (l 1 dm., neat), 72.5% optically pure based on $\alpha^{25}\text{D} \pm 24.3^\circ$ for optically pure 2-phenylbutane. ^d 97% O-d by combustion and falling drop analysis. ^e 87% optically pure, 81% α -D. ^f 87% optically pure, 87% α -D. ^g 90% optically pure, 82% α -D. ^h Optically pure, $\alpha^{25}\text{D} = -120.0^\circ$, 97% α -D. ⁱ Optically pure, $\alpha^{25}\text{D} = -120.2^\circ$. ^j Lithium *t*-butoxide as base. ^k Solution contained *t*-butyl alcohol, concentration 2 *M*. ^l Potassium *t*-butoxide as base.

based on $\alpha^{25}\text{D} \pm 24.3^\circ$ (l 1 dm., neat) for both I-h and I-d, and on $\alpha^{25}\text{D} \pm 120^\circ$ (l 1 dm., neat) for II-h and II-d.

Exchange Reactions.—Table I reports the results of the investigation of the stereochemical course of the exchange reactions. In runs 1 and 3–5, optically active 2-phenylbutane was racemized from 4 to 30.6% by potassium *t*-butoxide in *t*-butyl alcohol-O-d (0.97 atom of deuterium per mole). The substrate was then recovered, and the amount of deuterium incorporated into the benzyl position measured by infrared analysis (see Experimental). In run 2, optically active 2-phenylbutane-2-d was similarly racemized in ordinary *t*-butyl alcohol. In runs 9–13 similar experiments were carried out in the same solvent systems with either II-h or II-d. In these experiments, hydrogen-deuterium exchange at the benzyl position occurred much faster than racemization, and therefore with net retention of configuration. The extent of retention was calculated through use of 1. This equation takes no account of the fact that exchanged product, once formed, itself underwent subsequent racemization, so the values of % net retention are minimal.

% net retention =

$$\frac{\% \text{ benzyl exchange} - \% \text{ racemization}}{\% \text{ benzyl exchange}} \times 100\% \quad (1)$$

In Fig. 1 is plotted the percentage racemization vs. percentage calculated net retention for I-h and I-d, and for II-h and II-d. The data for these plots were obtained under somewhat differing conditions of temperature and concentration, involved isotope transfers in opposite directions, and probably involved isotope effects for both the bond breaking and making processes. These variables are probably responsible for the scatter of points in the plots. In spite of the non-ideal character of the data, extrapolation of the lines to 0% racemization should give some idea as to what the net steric course would have been had the exchanged product

maintained its optical integrity. For 2-phenylbutane and its deuterated counterpart, the extrapolated value is 97% net retention, and for 1-phenylmethoxyethane and its deuterated counterpart, 95% net retention. Substitution of lithium for potassium *t*-butoxide in run 13 resulted in no gross stereochemical change.

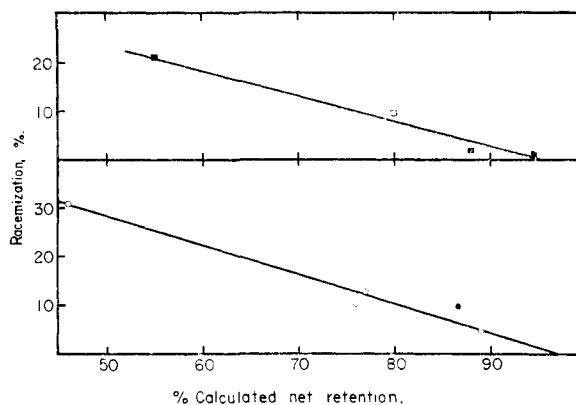


Fig. 1.—Plot of % racemization against % calculated net retention for hydrogen-deuterium exchange: upper curve: ■, 1-phenylmethoxyethane-1-d in *t*-butyl alcohol; □, 1-phenylmethoxyethane in *t*-butyl alcohol-O-d; lower curve: ●, 2-phenylbutane-2-d in *t*-butyl alcohol; ○, 2-phenylbutane in *t*-butyl alcohol-O-d.

Runs 6–8 and 14 were carried out in diethylene glycol. Racemization occurred in this solvent only at a temperature (260°) where the base was neutralized by the glass. Therefore the racemization could be carried out to only a minor extent. In runs 7, 8 and 14, the percentage racemization exceeded the percentage exchange by small amounts that were within experimental error. The difference in values in run 8 was 6.6%, which is outside of probable errors in the analyses. Therefore the reaction has the appearance of having occurred with

TABLE II
RATES OF RACEMIZATION AND EXCHANGE FOR CALCULATION OF STEREOCHEMICAL COURSE AND ISOTOPE EFFECTS IN DIMETHYL SULFOXIDE-POTASSIUM *t*-BUTOXIDE

Run ^a	Substrate Nature	Concn., <i>N</i>	<i>t</i> -BuOH concn., <i>N</i>	Base concn., <i>N</i>	<i>T</i> , °C.	<i>k</i> _α , sec. ⁻¹	<i>k</i> _e , sec. ⁻¹
16	2-Phenylbutane ^b	0.239	1.35	0.312	83.88	3.21 ± 0.02 × 10 ⁻⁶
17	2-Phenylbutane-2- <i>d</i> ^c	.248	1.35	.310	83.99	1.46 ± .03 × 10 ^{-6d}	0.89 ± 0.03 × 10 ^{-6e}
18	2-Phenylbutane-2- <i>d</i> ^c	.214	0.145	.1605	80.29	1.79 ± .06 × 10 ⁻⁴
19	1-Phenylmethoxyethane ^e	.214	.145	.1605	80.29	4.00 ± .07 × 10 ⁻⁴
20	1-Phenylmethoxyethane-1- <i>d</i> ^f	.216	.145	.1605	80.29	2.45 ± .05 × 10 ⁻⁴
21	1-Phenylmethoxyethane	.167	1.35	.210	81.38	5.66 ± .22 × 10 ⁻⁶
22	1-Phenylmethoxyethane-1- <i>d</i> ^e	.160	1.35	.210	81.38	3.22 ± .18 × 10 ⁻⁶	2.84 ± 0.12 × 10 ^{-6g}

^a Runs are numbered consecutively from table to table. ^b 72.5% optically pure. ^c 81% deuterated, 87% optically pure. ^d When corrected for protium impurity, value becomes 1.05 ± 0.03 × 10⁻⁶. ^e Optically pure. ^f Optically pure, 0.97 atom of deuterium per molecule.

about 50% net inversion (calculated from eq. 2),

$$\% \text{ net inversion} = \frac{\% \text{ racemization} - \% \text{ benzyl exchange}}{\% \text{ benzyl exchange}} \times 100\% \quad (2)$$

The conclusion that exchange actually occurred with net inversion must be made with reservations, particularly since the starting material I-*d* was only 81% deuterated, and the calculation is based on the assumption that I-*h* and I-*d* racemize at the same rates.⁷ Any racemization that occurred by a competing radical reaction would be accompanied by an equal amount of exchange as was demonstrated in an earlier study in which the 2-phenyl-2-butyl radical was generated in a basic solution of diethylene glycol.⁸ In any case, the data make it abundantly clear that ethylene glycol gives an entirely different steric result from that of *t*-butyl alcohol.

In run 15, 1-phenylmethoxyethane-1-*d* was examined in a 2 *M* solution of *t*-butyl alcohol in dimethyl sulfoxide at 85°. In this experiment the racemization and exchange rates appeared identical, since the percentage of exchange and of racemization were equal to one another. In the next section, kinetic data are presented that indicate that both I-*d* and II-*d* racemize and exchange at about the same rates in dimethyl sulfoxide which is 1.34 *N* in *t*-butyl alcohol.

Kinetics and Isotope Effects.—Table II records the pseudo-first-order rate constants of racemization (*k*_α) for I-*h*, I-*d*, II-*h* and II-*d*, and of exchange (*k*_e) for I-*d* and II-*d* in potassium *t*-butoxide solutions of dimethyl sulfoxide containing small amounts of *t*-butyl alcohol. Runs 19–22 provide data with which the kinetic isotope effect for racemization of 1-phenylmethoxyethane can be calculated. Since II-*d* was 97% deuterated in the benzyl position, no correction of *k*_α in runs 20 and 22 is necessary. A value of *k*_{α^H}/*k*_{α^D} = 1.62 is obtained with runs 19 and 20 where the base was 0.1605 *N* and *t*-butyl alcohol 0.145 *N*, and a value of 1.76 is found in runs 21 and 22 in which the base concentration was 0.210 *M* and the *t*-butyl alcohol

(7) In the next section an isotope effect of about *k*_H/*k*_D = 2.7 is calculated for racemization of I-*h* and I-*d* in dimethyl sulfoxide which was 1.35 *M* in *t*-butyl alcohol at 81°. Because of the small size of this isotope effect, and the expected decrease in *k*_H/*k*_D with increased temperature, it is unlikely that *k*_H/*k*_D for racemization in diethylene glycol is much greater than unity at 260°.

(8) D. J. Cram, A. Langemann, W. Lwowski and K. R. Kopecky, *J. Am. Chem. Soc.*, **81**, 5760 (1959).

was 1.35 *M*. These values of the isotope effect are within the experimental error of one another, although the absolute values of *k*_α for the runs at the two concentrations of *t*-butyl alcohol varied by a factor of almost 2 powers of 10.

Calculation of *k*_{α^H}/*k*_{α^D} for runs 16 and 17 involves corrections of *k*_{α^D} for run 17 since the 2-phenylbutane-2-*d* was only 81% deuterated. With the corrected rate constant (1.05 ± 0.03 × 10⁻⁶), *k*_{α^H}/*k*_{α^D} = 3.0.

Potential ambiguity arises in connection with the values of *k*_e for runs 17 and 22, since as the reaction proceeds, the 1.35 *N* *t*-butyl alcohol present becomes diluted with *t*-butyl alcohol-*O-d*. Such an effect would require a correction of *k*_e to slightly higher values. This correction was not made since it is highly probable that under conditions drastic enough to cause 2-phenylbutane to undergo the exchange reaction, dimethyl sulfoxide should itself exchange hydrogen for deuterium even more rapidly and thus the accumulation of *t*-butyl alcohol-*O-d* should be negligible.

Comparison of *k*_α with *k*_e in run 22 gives values just outside of probable error of one another, and the same is true when the corrected value of *k*_α is compared with *k*_e for run 17. The differences are too small to conclude that exchange occurred with small net inversion in this solvent, and the balance of evidence fosters the conclusion that the hydrogen-deuterium exchange reaction occurs with racemization in dimethyl sulfoxide as solvent.

TABLE III
KINETIC ORDER FOR RACEMIZATION BY POTASSIUM *t*-BUTOXIDE^a OF 0.20 *M* SOLUTIONS OF 1-PHENYLMETHOXYETHANE IN DIMETHYL SULFOXIDE AT 80.10^b

Run ^c	Base concn., <i>M</i>	<i>k</i> _α , sec. ⁻¹	<i>k</i> _{3/2} , l. ^{1/2} m. ^{-1/2} sec.	<i>k</i> ₂ , l. m. ⁻¹ sec. ⁻¹
23	0.0537	3.16 ± 0.19 × 10 ⁻⁴	1.37 × 10 ⁻³	5.87 × 10 ⁻³
24	.0597	3.46 ± .09 × 10 ⁻⁴	1.42 × 10 ⁻³	5.78 × 10 ⁻³
25	.0779	3.61 ± .16 × 10 ⁻⁴	1.29 × 10 ⁻³	4.63 × 10 ⁻³
26 ^d	.1049	4.36 ± .16 × 10 ⁻⁴	1.36 × 10 ⁻³	4.16 × 10 ⁻³
27	.1635	5.46 ± .23 × 10 ⁻⁴	1.33 × 10 ⁻³	3.34 × 10 ⁻³
28 ^e	.2338	6.06 ± .14 × 10 ⁻⁴	1.25 × 10 ⁻³	2.58 × 10 ⁻³
29	.4525	5.83 ± .13 × 10 ⁻⁴	0.87 × 10 ⁻³	1.29 × 10 ⁻³
30 ^f	.0537	1.05 ± .06 × 10 ⁻⁴	4.53 × 10 ⁻⁴	1.96 × 10 ⁻³
31 ^g	.0537	1.41 ± .03 × 10 ⁻⁵	6.08 × 10 ⁻⁵	2.62 × 10 ⁻⁴

^a KOC(CH₃)₃·0.90HOC(CH₃)₃. ^b ±0.03°. ^c Runs are numbered consecutively from table to table. ^d Rate constants extrapolated from data of runs 32 and 33. ^e Rate constants extrapolated from data of runs 36 and 37. ^f Solution was 0.0804 *M* in potassium iodide. ^g Solution was 0.4925 *M* in potassium iodide.

TABLE IV
RACEMIZATION OF 0.18 M^a SOLUTIONS OF 1-PHENYLMETHOXYETHANE IN DIMETHYL SULFOXIDE, ACTIVATION PARAMETERS AND EFFECT OF BASE TYPE

Run ^b	Nature	Base Concn., <i>N</i>	<i>T</i> , °C.	<i>k</i> _α , sec. ⁻¹	<i>k</i> _{3/2} , 1.1/2 m. ^{-1/2} sec. ⁻¹	ΔH^* , kcal. M. ⁻¹	ΔS^* , e.u.
32	KOC(CH ₃) ₃ ^c	0.1049	48.70	9.86 ± 0.37 × 10 ⁻⁶	3.04 × 10 ⁻⁵	22.2 ± 0.7	-10.3 ± 2.2
33	KOC(CH ₃) ₃ ^c	.1049	75.08	1.99 ± .06 × 10 ⁻⁴	6.14 × 10 ⁻⁴		
34	NaOC(CH ₃) ₃ ^d	.1521	75.10	2.20 ± .09 × 10 ⁻⁶	5.64 × 10 ⁻⁶	23.7 ± 0.7	-6.0 ± 1.8
35	KOC(CH ₃) ₃ ^c	.2336	45.43	8.18 ± .24 × 10 ⁻⁶	1.69 × 10 ⁻⁵		
36	KOC(CH ₃) ₃ ^c	.2338	45.43	9.28 ± .69 × 10 ⁻⁶	1.92 × 10 ⁻⁵	23.7 ± 0.7	-6.0 ± 1.8
37	KOC(CH ₃) ₃ ^c	.2338	73.80	2.15 ± .05 × 10 ⁻⁴	4.45 × 10 ⁻⁴		
38	NaOC(CH ₃) ₃ ^d	.2278	73.60	1.62 ± .06 × 10 ⁻⁶	3.40 × 10 ⁻⁶		

^a ±0.03 M. ^b Runs are numbered consecutively from table to table. ^c KOC(CH₃)₃·0.90(CH₃)₃COH. ^d NaOC(CH₃)₃·0.32(CH₃)₃COH.

TABLE V
RACEMIZATION OF 0.18 M SOLUTIONS OF 1-PHENYLMETHOXYETHANE IN *t*-BUTYL ALCOHOL, AND DIMETHYL SULFOXIDE-*t*-BUTYL ALCOHOL

Run ^a	Solvent	Base Type	Concn., <i>M</i>	<i>T</i> , °C.	<i>k</i> _α , sec. ⁻¹	<i>k</i> _{3/2} , 1.1/2 m. ^{-1/2} sec. ⁻¹	<i>k</i> ₂ , 1. m. ⁻¹ sec. ⁻¹
39	(CH ₃) ₂ COH	(CH ₃) ₃ COK	0.4700	173	7.61 ± 0.14 × 10 ⁻⁷		1.62 × 10 ⁻⁶
40	(CH ₃) ₂ COH	(CH ₃) ₃ CONa	.3928	173	4.46 ± 0.12 × 10 ⁻⁷		1.14 × 10 ⁻⁶
41 ^b	(CH ₃) ₂ SO	(CH ₃) ₃ COK ^c	.1049	173	0.288	0.885	2.75
42	(CH ₃) ₂ SO	(CH ₃) ₃ COK ^d	.0208	25.00	9.08 ± 0.45 × 10 ⁻⁷	6.28 × 10 ⁻⁶	4.36 × 10 ⁻⁵
43	(CH ₃) ₂ SO	(CH ₃) ₃ COK ^d	.1590	25.00	3.65 × 0.08 × 10 ⁻⁶	9.12 × 10 ⁻⁷	2.30 × 10 ⁻⁵
44 ^b	(CH ₃) ₂ SO	(CH ₃) ₃ COK ^c	.1049	25.00	5.41 × 10 ⁻⁷	1.65 × 10 ⁻⁶	5.17 × 10 ⁻⁶

^a Runs numbered consecutively from table to table. ^b Run was calculated by extrapolating from runs 32 and 33. ^c (CH₃)₃COK·0.90(CH₃)₃COH. ^d (CH₃)₃COK·0.05(CH₃)₃COH.

Comparison of *k*_α for runs 18 and 19 indicates that 1-phenylmethoxyethane racemizes about 2.2 times as fast as 2-phenylbutane in dimethyl sulfide.

Effect of Base Character and Concentration on Rates of Racemization.—Table III summarizes rate data that pertain to the kinetic order in base for racemization of 1-phenylmethoxyethane in potassium *t*-butoxide [KOC(CH₃)₃·0.90 HOCH(CH₃)₃] solutions of dimethyl sulfoxide at 80.1°. Over molar concentrations of base ranging from 0.05 to 0.23, the rates approximated half order in base (runs 23–28), as is indicated in Fig. 2. At 0.45 M concentration of base *k*_{3/2} decreased to a value lower than *k*_{3/2} calculated for 0.23 M base (compare runs 28 and 29).

Runs 23, 30 and 31 were conducted under identical conditions except that potassium iodide was added to the medium in the two latter runs. With a concentration of 0.08 M potassium iodide, the pseudo-first-order rate constant decreased by a factor of 3, and with a concentration of 0.49, a decrease by a factor of about 22 was observed.

Data for calculation of activation parameters for racemization of 1-phenylmethoxyethane in dimethyl sulfoxide are found in Table IV. Values of ΔH^* and ΔS^* were calculated for two different concentrations of the base, KOC(CH₃)₃·0.90 HOCH(CH₃)₃. For both ΔH^* and ΔS^* the values obtained at the two concentrations (0.105 and 0.233 M) are just outside of probable error. The entropy was calculated through use of *k*_{3/2}.

In runs 34 and 38, NaOC(CH₃)₃·0.32 (CH₃)₃COH was substituted for KOC(CH₃)₃·0.90 (CH₃)₃COH. The data clearly indicate that had runs 33 and 34 (and likewise runs 37 and 38) been carried out at identical base concentrations, *k*_{α^K}/*k*_{α^{Na}} > 100 for both sets of runs. It should be noted that the amount of *t*-butyl alcohol complexed with the

potassium *t*-butoxide used was almost 3 times that complexed with the sodium *t*-butoxide.

Table V contains data which allow rough comparisons to be made between *t*-butyl alcohol and dimethyl sulfoxide as solvents for the racemization of 1-phenyl-methoxyethane. Before reasonable rates

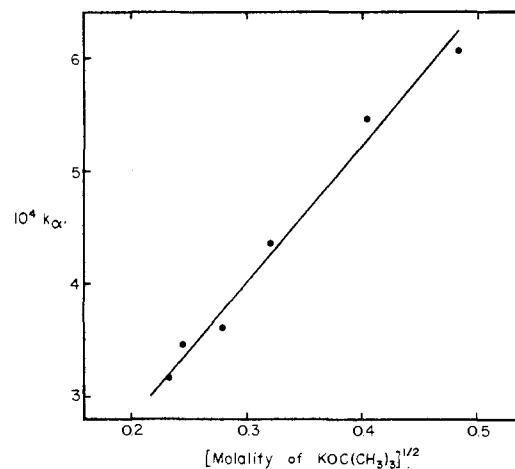


Fig. 2.—Plot of observed polarimetric rate constant (*k*_α) against square root of base concentration for the potassium *t*-butoxide-catalyzed racemization of 1-phenylmethoxyethane in dimethyl sulfoxide at 80.1°.

of racemization could be observed in *t*-butyl alcohol as solvent, the temperature had to be raised to 173°. Only a small difference is visible in the rates of the reaction catalyzed by sodium and potassium *t*-butoxide (compare runs 39 and 40). Extrapolation of the rates obtained at lower temperatures in dimethyl sulfoxide (Table IV) to 173° gives a rate constant which is over 6 powers of 10 greater than the rate constants obtained in *t*-butyl alcohol.

Runs 42 and 43 made at 25° were carried out to determine whether the rates in dimethyl sulfoxide were sensitive to the amount of *t*-butyl alcohol complexed with the potassium *t*-butoxide employed. In these two runs, carefully sublimed potassium *t*-butoxide was used which contained only 0.05 mole of *t*-butyl alcohol. In run 44, the data of Table IV were extrapolated to 25° for comparison of runs in which the amount of alcohol complexed with base was varied.

In runs 42 and 43, the base was varied from 0.0208 to 0.1590 *M*, and lack of integral or half-order dependence of rate on base concentration is apparent in the lack of constancy of either $k_{1/2}$ or k_2 . Thus the order in base seems to lie between half and one, being closer to the former. This result differs from that observed when almost equal molar amounts of *t*-butyl alcohol and potassium *t*-butoxide were present (Table III), and the rates were about half order in base.

The values of the rate constants of runs 42–44 indicate that an increase in rate by a factor of about 4.5 accompanies a nineteen-fold decrease in *t*-butyl alcohol concentration in the medium from 0.094 to 0.005 *M* at 25°. A larger effect of *t*-butyl alcohol concentration is visible in the data of runs 19 and 21 of Table II. Had these runs been carried out at identical temperatures and base concentrations, an increase in rate by a factor of over 100 would have been observed for a decrease of *t*-butyl alcohol concentration from 1.35 to 0.145 *M* (a decrease by a factor of about 9.3).

Discussion

Stereochemistry of the Hydrogen–Deuterium Exchange Reaction.—The data of Tables I and II clearly demonstrate that the exchange reactions occur in the systems under study with high retention (~95% net) in *t*-butyl alcohol, with racemization in dimethyl sulfoxide, and probably with low net inversion in diethylene glycol.⁹ Thus the same pattern of dependence of steric course on solvent is observed when the 2-phenyl-2-butyl and 1-phenyl-1-methoxy-1-ethyl anions are generated either by proton (or deuterium) abstraction by base, or by base-catalyzed carbon–carbon bond cleavages.⁴ Similar factors appear to play a role in the mechanisms of these two sets of general reactions.

In the base-catalyzed hydrogen–deuterium exchange reactions, carbanions undoubtedly intervene as discrete intermediates. The deep red color of 2-phenyl-2-butylpotassium in dry ether¹⁰ indicates that negative charge is highly delocalized in the 2-phenyl-2-butyl anion. Further evidence for delocalization is found in the fact that treatment of an ether solution of 2-phenyl-2-propylpotassium with deuterium chloride resulted in deuteration of about a quarter of the base in the *p*-position.¹¹ With weaker acids such as water, α -deuteration/*p*-deuteration = 7500.¹¹ These facts strongly support a flat structure for benzyl anions, and a flat species is incapable of asymmetry. This argument

(9) A. Streitwieser, Jr., D. E. Van Sickle and L. Reif, *J. Am. Chem. Soc.*, **82**, 1513 (1960), reported that optically active ethylbenzene- α -*d* undergoes lithium cyclohexylamide catalyzed deuterium–hydrogen exchange reactions in cyclohexylamine as solvent with 83% net retention.

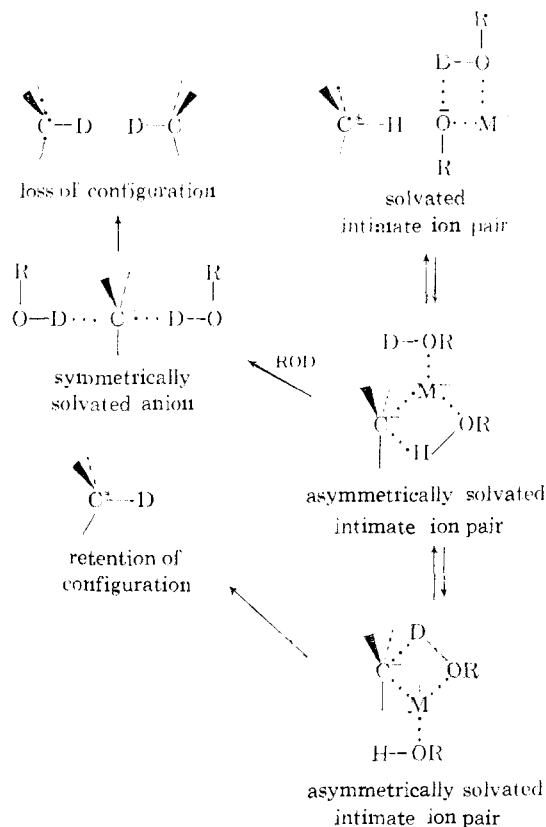
(10) D. J. Cram and J. D. Knight, *ibid.*, **74**, 5835 (1952).

coupled with the observed importance of solvent in determining the stereochemistry of the exchange reaction leads to the conclusion that the stereospecificity of the reaction is due to asymmetric solvation of an otherwise symmetrical intermediate.¹²

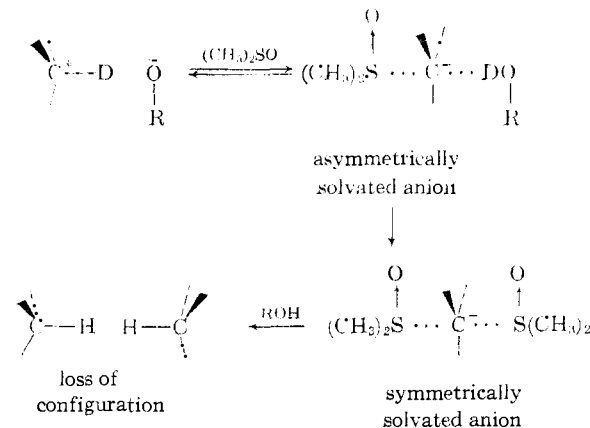
Chart I summarizes the mechanisms considered most likely for the three varieties of stereochemical results. In the retention mechanism, the active catalytic species are heavily solvated metal alkoxide intimate ion-pairs, and the carbanion–metal cation intimate ion pair produced is heavily solvated on

CHART I

Retention mechanism:



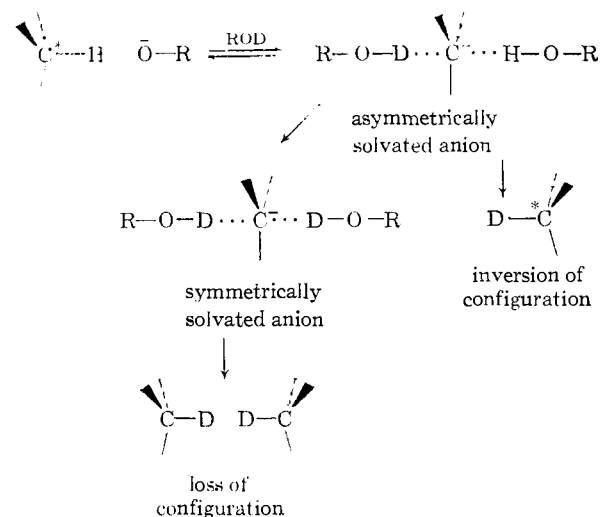
Racemization mechanism:



(11) G. A. Russell, *ibid.*, **81**, 2017 (1959).

(12) Small deviations from planarity induced by asymmetric solvation probably exist.

Inversion mechanism:

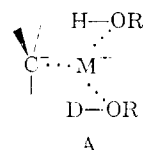


the front side with deuteron donors because of the solvent-orienting power of the metal cation. Thus deuterium capture from the front is the favored reaction path. Some carbanions are long enough lived to pass into a symmetrical environment, and these give racemic product.¹³

In dimethyl sulfoxide a racemization mechanism must apply. Either an alkoxide anion or an ion pair could be the active species, depending on their activities and the dissociation constant of the metal alkoxide. In either case, the anion is solvated by dimethyl sulfoxide. The carbanion produced is relatively long lived due to the low concentration of proton donors in the solvent; it passes into a symmetrical environment, and protonation eventually occurs from either side of the symmetrically solvated anion with equal probability.

In the inversion mechanism, a dissociated anion is the catalytic species, and its attack on the proton attached to carbon is aided by solvation of the incipient carbanion by deuteron donors on the side re-

(13) In the formulation of the asymmetrically solvated ion pair in the retention mechanism of Chart I, certain alternatives are possible. Conceivably a non-hydrogen bonded species such as A might apply to a solvent-base system which gave retention, which was poor at hydrogen-bonding, and which provided a high kinetic isotope effect for the exchange reaction (*e.g.*, the cyclohexylamine-cyclohexylamide system of Streitwieser, *et al.*, ref. 9). Unfortunately the kinetic isotope effect

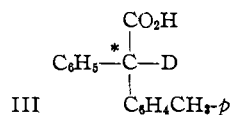


for the exchange reaction in *t*-butyl alcohol-potassium *t*-butoxide could not be measured because of the high temperature involved. However, this solvent-base system when applied to 2-octyl phenyl sulfone [D. J. Cram, D. A. Scott and W. D. Nielsen, *J. Am. Chem. Soc.*, **83**, 3696 (1961)] gave isotope effects for the exchange reaction that ranged between 0.5 and 1.5. Isotope effects this low in value are inconsistent with an intermediate such as A dominating the reaction mechanism, since such an intermediate makes no provision for the pre-equilibrium required to explain a low isotope effect (see next section).

The fact that cyclohexylamine is a retention solvent in the exchange reaction (ref. 9) is not surprising since in the cleavage reactions studied previously [D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, *J. Am. Chem. Soc.*, **81**, 5740 (1959)], *N*-methylaniline was observed to be a retention solvent.

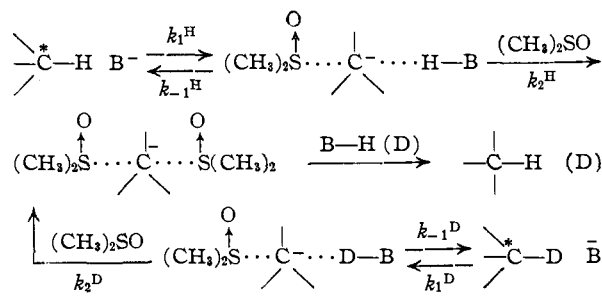
note from the leaving proton. The resulting carbanion is solvated at the front by a proton donor and at the back by a deuteron donor. Proton recapture gives back starting material whereas deuteron capture produces inverted product. Longer lived carbanions pass into a symmetrical environment, and give racemic product.¹⁴

Isotope Effect in the Racemization Reaction.—A wide range of kinetic isotope effects associated with base-catalyzed carbanion formation have been observed in the past.^{16,9} The smallest (of which the authors are aware) is $k_{\text{H}}/k_{\text{D}} = 2.7$,¹⁶ for the fluoride ion-catalyzed bromination of 2-carbethoxycyclopentanone-2-*d* in deuterium oxide (anion formation is rate limiting). The largest is 12 for the deuterium-hydrogen exchange reaction of ethylbenzene-2-*d* catalyzed by lithium cyclohexylamide in cyclohexylamine.⁹ Most of the observed values for $k_{\text{H}}/k_{\text{D}}$ lie between 5 and 6. Ives and Wilkes^{3c} observed a value of 4.6 for the racemization and exchange of III catalyzed by hydroxide ion in water at 100°, and this system is perhaps more similar to those of this study than most of the others. Had the reaction been carried out at a lower temperature, the isotope effect would undoubtedly have been greater than 5.



In the present investigation, very low values for $k_{\text{H}}/k_{\text{D}}$ have been observed in the dimethyl sulfoxide-*t*-butyl alcohol-potassium *t*-butoxide system at about 80°. For I-h and I-d, $k_{\alpha^{\text{H}}}/k_{\alpha^{\text{D}}} = 3.0$, and for II-h and II-d, $k_{\alpha^{\text{H}}}/k_{\alpha^{\text{D}}} = 1.66$ to 1.76. Although these values apply to the racemization reactions, the fact that the rates of exchange and racemization were essentially the same for the deuterated derivatives indicates that the racemization rate measured the exchange rate of hydrogen for hydrogen in the case of the non-deuterated compounds.

A plausible explanation for the low values is that the exchange reaction involves a pre-equilibrium of a special nature. In the reactions formulated, k_1^{H} and k_1^{D} are



(14) The concept of asymmetric solvation of ions has been applied to explain the stereospecificity of many nucleophilic solvolytic reactions in which carbonium ions intervene as intermediates [for a review, see A. Streitwieser, Jr., *Chem. Revs.*, **56**, 631 (1956)].

(15) (a) K. B. Wiberg, *ibid.*, **55**, 713 (1955); (b) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p. 183.

(16) R. P. Bell, J. A. Fendley and J. R. Hulett, *Proc. Roy. Soc. A*, **235**, 453 (1956).

presumed to be $\ll k_{-1}^H, k_{-1}^D, k_2^H, k_2^D$. If the reactions are non-stereospecific, then equations 1 and 2 relate the rate constants for racemization (exchange) with the rate constants of the formulation. Combination of (1) and (2) provides (3).

$$k_{\alpha}^H = k_1^H k_2^H / (k_{-1}^H + k_2^H) \quad (1)$$

$$k_{\alpha}^D = k_1^D k_2^D / (k_{-1}^D + k_2^D) \quad (2)$$

If $k_2^H \gg k_{-1}^H$ and $k_2^D \gg k_{-1}^D$, then (3) becomes (4)

$$\frac{k_{\alpha}^H}{k_{\alpha}^D} = \frac{k_1^H k_2^H (k_{-1}^D + k_2^D)}{k_1^D k_2^D (k_{-1}^H + k_2^H)} \quad (3)$$

$$k_{\alpha}^H / k_{\alpha}^D = k_1^H / k_1^D \quad (4)$$

and the ordinary kinetic isotope effect for dissociation of the carbon-hydrogen bond would be measured by racemization rates. However, if $k_{-1}^H \gg k_2^H$ and $k_{-1}^D \gg k_2^D$, then (3) becomes (5).

$$\frac{k_{\alpha}^H}{k_{\alpha}^D} = \frac{k_1^H}{k_{-1}^H} \times \frac{k_{-1}^D}{k_1^D} \times \frac{k_2^H}{k_2^D} = \frac{K^H}{K^D} \times \frac{k_2^H}{k_2^D} \quad (5)$$

In this case, the observed isotope effect for racemization (exchange) is the product of a thermodynamic and a kinetic term. The value of K^H/K^D is expected to be close to unity, and possibly less than one.¹⁷ The value of k_2^H/k_2^D is also expected to be not far from unity, since no covalent bonds (only hydrogen bonds) are being made or broken in this solvation exchange reaction. Thus $k_{\alpha}^H/k_{\alpha}^D$ is expected to be much lower valued when the "back reaction" described by k_{-1}^H or k_{-1}^D becomes important. In fact, a whole spectrum of values for $k_{\alpha}^H/k_{\alpha}^D$ can be envisioned, ranging from a little less than unity to over 10, depending primarily on the values of k_{-1}^H/k_2^H and k_{-1}^D/k_2^D . The concept of the "back reaction" could be equally well used to explain low isotope effects in exchange reactions in hydroxylic solvents.

Nature of the Catalytic Species.—In a solvent of such low dielectric constant as *t*-butyl alcohol ($\epsilon = 11$ at 19°), potassium *t*-butoxide undoubtedly exists as ion pairs, or even as aggregates of ion pairs, heavily solvated by *t*-butyl alcohol.¹⁸ Potassium is a little more active than sodium *t*-butoxide in *t*-butyl alcohol (runs 39 and 40 Table V, and runs of ref. 3d) as a racemization catalyst. Furthermore, substitution of lithium for potassium *t*-butoxide in *t*-butyl alcohol made no gross difference in the stereochemical course of the deuterium-hydrogen exchange reaction (run 13 of Table I). In these respects, the exchange reactions appear similar to the cleavage reactions of earlier studies.¹⁹

Although evidence for complete dissociation of potassium, sodium and lithium methoxide in dimethyl sulfoxide was obtained,^{3d} the less than first-order dependence on concentration of potassium *t*-butoxide for the racemization of II-h in the same solvent suggests incomplete dissociation for the tertiary base. The half-order dependence obtained

(17) The zero point energy for the stretching vibration of the O-H bond is greater than for the C-H bond, and this consideration alone would predict $K^H/K^D < 1$. The above kinetic scheme and the data of this paper were presented in a colloquium at Harvard University, October, 1959.

(18) Alcohol of solvation is so firmly held that rapid sublimation of potassium *t*-butoxide-*t*-butyl alcohol solvate gives base that still contains as much as 0.7 mole of solvate.

(19) D. J. Cram, F. Hauck, K. R. Kopecky and W. D. Nielsen, *J. Am. Chem. Soc.*, **81**, 5707 (1959).

with $(\text{CH}_3)_3\text{COK} \cdot 0.9(\text{CH}_3)_3\text{COH}$ is consistent with the following hypothesis. In eq. 6 for the dissociation of potassium *t*-butoxide, if $K \ll 1$ and the catalytic activity of *t*-butoxide anion is much greater than that of associated material, then eq. 7 would be the governing rate law.

$$K = \frac{[\text{M}^+][-\text{OC}(\text{CH}_3)_3]}{[\text{MOC}(\text{CH}_3)_3]} \quad (6)$$

$$-\frac{d(*\text{C}-\text{H})}{dt} = k_{3/2} [*C-\text{H}][\text{MOC}(\text{CH}_3)_3]^{1/2} = \frac{k_{3/2}}{K^{1/2}} [*C-\text{H}][-\text{OC}(\text{CH}_3)_3] \quad (7)$$

The substantial decrease in rate observed upon addition of a common ion salt (potassium iodide) is consistent with this hypothesis (compare runs 23, 30 and 31). The dissociation constant for potassium iodide is probably greater than that for potassium *t*-butoxide, and the rate depression would be due to the common ion (K^+) mass law depression of the concentration of *t*-butoxide anion in the equilibrium governed by eq. 6.

The fact that sodium *t*-butoxide is about 100 times less reactive than potassium *t*-butoxide is also consistent with these views. The value of K is probably lower valued for sodium than for potassium *t*-butoxide, and $K^{1/2}$ appears in the denominator in the second part of eq. 7. Data of other investigators²⁰ indicate that the solubility of potassium, sodium and lithium chlorides in dimethyl sulfoxide drops off markedly in that order. Also interesting is the fact that the dielectric constant of the solvent drops from about $\epsilon = 49$ to $\epsilon = 38$ in going from 20 to 80°.

The above hypothesis is probably an oversimplification. The fact that the rate of racemization showed somewhat higher than half-order dependence on base when the amount of *t*-butyl alcohol was decreased to almost zero (runs 42 and 43) indicates that the alcohol even at low concentrations plays an important role. Clearly much further work is needed before the exact nature of the catalytic species in dimethyl sulfoxide can be ascertained.

Effect of Solvent on Catalytic Activity of Potassium *t*-Butoxide.—Solutions of potassium *t*-butoxide in dimethyl sulfoxide have catalytic activity in the racemization reaction between 6 and 7 powers of 10 greater than is observed for the same base in *t*-butyl alcohol (runs 39-41). Had exchange rates been compared, and had the potassium *t*-butoxide been completely free of *t*-butyl alcohol, a factor of about 10^5 probably would have been observed. These observations correlate with those made previously^{3d} with respect to the behavior of potassium methoxide in methanol and dimethyl sulfoxide. Here a factor of about 10^9 was estimated for the difference in rates for racemization (and exchange) of 2-methyl-3-phenylpropionitrile. Since the rate of racemization of this substrate was also determined in *t*-butyl alcohol, it can be estimated that the rate of exchange catalyzed by potassium methoxide in methanol is approximately $1/10^{12}$ as fast as the rate catalyzed by potassium *t*-butoxide in dimethyl sulfoxide.

(20) H. L. Schlafer and W. Schaffernicht, *Angew. Chem.*, **72**, 618 (1960).

As in the previous investigation,^{3d} the difference in activity of the alkoxide anion in the two solvents is attributed to hydrogen bonding present in the hydroxylic solvents and absent in dimethyl sulfoxide. Others have noted²⁰ from conductivity experiments with potassium chloride and potassium picrate in dimethyl sulfoxide that the potassium ion is highly solvated, but that the anions are relatively little solvated. Thus the intrinsic activity of the *t*-butoxide anion should be more fully realized in dimethyl sulfoxide as solvent.

Experimental

Starting Materials.—Optically active (+)-2-phenylbutane ($\alpha^{25D} + 23.5^\circ$, *l* 1 dm., neat, n^{25D} 1.4881) was prepared as previously described from optically pure (-)-3-phenylbutanoic acid.²¹ Other material ($\alpha^{25D} - 17.6^\circ$, *l* 1 dm., neat, n^{25D} 1.4880) was also available which was obtained as product of the cleavage reactions.⁴ Similarly, the three different samples of optically active 2-phenylbutane-2-*d* used in this investigation were prepared by cleavage of optically pure (+)-2,3-diphenyl-3-methyl-2-pentanol in *t*-butyl alcohol-*O-d* (0.97 atom of D per molecule) with potassium *t*-butoxide at 130°.⁶ These samples possessed the properties: $\alpha^{25D} + 21.1^\circ$, *l* 1 dm., neat, 87% optically pure, 81% α -*d* by infrared analysis (see below); $\alpha^{25D} + 21.2^\circ$, *l* 1 dm., neat, 87% optically pure, 81% α -*d* by infrared analysis; $\alpha^{25D} + 21.8^\circ$, *l* 1 dm., neat, 90% optically pure, 82% α -*d* by infrared analysis, and contained 0.82 atom of D per molecule (combustion and falling drop method). The concentrations of base in these cleavage reactions were identical, and the only difference was the substrate concentration.⁶ The fact that the two methods of deuterium analysis gave the same results indicates the absence of deuterium in other parts of the molecule (e.g., in the benzene ring), and it is safe to conclude that the same applies to all three samples. The fact that the leaving group does not supply protons directly to the carbanion, and that the protons and deuterons come from solvent in both retention and inversion solvents⁶ indicates that the active and racemic 2-phenylbutane in these samples should be equally deuterated.

Optically pure 1-methoxyphenylethane, prepared as described previously,⁵ had $\alpha^{25D} - 120.0^\circ$, *l* 1 dm., neat, n^{25D} 1.4882. Deuterated material was produced as follows. Acetophenone was carefully distilled, and reduced in carefully dried ether with about 0.20 mole of lithium aluminum deuteride (acetophenone = 1 mole). Excess acetophenone was not removed from the isolated alcohol, but the whole mixture was converted directly to the acid phthalate, and the neutral and acidic materials were separated at this stage. The acid phthalate was resolved,⁸ and converted to 1-phenylethanol-1-*d*, $\alpha^{25D} - 44.1^\circ$, *l* 1 dm., neat, 0.97 atom of deuterium per molecule (combustion and falling drop method).²² Conversion of this material to its methyl ether⁵ gave material $\alpha^{25D} - 120.0^\circ$, *l* 1 dm., neat, 0.97 atom of deuterium per molecule (combustion and falling drop method).

Infrared Analyses of Benzyl-Deuterium.—Analysis of deuterium in the α -position of 2-phenylbutane was carried out by exactly the same method described previously⁶ making use of the C-D stretching band at 4.71 μ . In all cases, unknowns were compared with standard mixtures. The estimated absolute error in all cases was less than 1%. Two separate samples of 2-phenylbutane-2-*d* were analyzed by infrared and by combustion and the falling drop method.²² In no case did the two methods disagree by more than 1%.

The same method was used for infrared analysis of 1-phenylmethoxyethane except that the C-D stretch appeared at 4.725 μ . A plot of % α -*d* vs. optical density was linear from 10-90% 1-phenylmethoxyethane-1-*d* in 1-phenylmethoxyethane-1-*h*. Deviations from Beer's law were observed from 0-10 and 90-100% 1-phenylmethoxyethane-1-*d*. As little as 2% deuterated material could be detected easily. To ensure reproducibility, it was necessary for every analysis to run undeuterated material to obtain the base line, then the unknown, then a 1-phenylmethoxyethane-1-*d* standard,

and finally undeuterated material again to recheck the base line. A Beckman IR-4 spectrophotometer equipped with lithium fluoride optics and a sodium chloride cell of 0.2 mm. thickness was employed. All measurements were made in the same cell, neat. Three separate samples of 1-phenylmethoxyethane-1-*d* were analyzed by this method and then checked by combustion and the falling drop method.²² The largest difference was 1%.

Exchange Reactions.—Preparation of *t*-butyl alcohol-*O-d* (97% *O-d* by combustion and falling drop method)²² has been described previously.⁶ The other solvents were purified, dried and stored under dry pure nitrogen as previously reported.^{3d} The runs of Table I were all carried out in clean, flamed out heavy-walled Pyrex sealed tubes that were never filled more than 60% full, to allow for solvent expansion. Before runs were made, the solvent was flushed with dry nitrogen in the reaction tube. In all cases except when dimethyl sulfoxide was solvent, clean, weighed samples of metal were added directly to the reaction tube containing solvent under dry, pure nitrogen. After reaction was complete, the hydrogen was flushed from the tube with pure dry nitrogen, a weighed sample of substrate was introduced, the tube cooled in Dry Ice, evacuated and sealed. In run 15 with dimethyl sulfoxide as solvent, potassium *t*-butoxide, 0.90 *t*-butyl alcohol^{3d} and enough more *t*-butyl alcohol were added to the dimethyl sulfoxide to make the solution 2 *M* in the *t*-butyl alcohol. The tubes were heated in Woods metal-baths, and were immersed only to the level of the liquid inside of the tube, so that the solution refluxed in those cases where *t*-butyl alcohol was solvent. The tubes were opened at Dry Ice temperatures, and no pressure had developed in the tubes except for runs 6-8 and 14 when diethylene glycol was used as solvent. In these runs tremendous pressure developed, and the tubes had to be opened with great care. The base was quite well preserved except in the runs conducted in diethylene glycol, where the base was completely destroyed by the glass.

The content of each tube was shaken with an equal mixture of pure pentane and water, the water was extracted with two additional portions of pentane, and the combined pentane layers were washed four times with water, dried, evaporated through a packed column, and the residue was distilled at 50 mm. in a micro-still. The resulting material was submitted to deuterium analyses and polarimetric measurements. In representative cases, indices of refraction and infrared spectra of the products were taken, and found to match those of authentic material. Between 0.20 and 0.40 g. of substrate were employed in runs 1-15, and between 60-80% of the starting material was recovered in each run. In runs 6-8 and 14 carried out in ethylene glycol, the product before distillation was passed through a small chromatograph column of alumina with pure pentane as the eluent. In these runs, recovery of starting material was lower (50-70%).

Kinetic Runs.—All kinetic runs except 42-44 were made with the ampoule technique described in detail elsewhere.^{3d} The contents of each ampoule were isolated and subjected to polarimetric and in runs 17 and 22 infrared analysis for the amount of deuterium in the α -position. The purification of solvents, preparation of base and basic solutions and cleaning of ampoules has appeared elsewhere.^{3d} The procedure used for runs involving dimethyl sulfoxide is as follows: All equipment was heated under vacuum and allowed to cool in a dry nitrogen atmosphere. The base in question was weighed rapidly under dry conditions and added to 70 ml. of pure dry dimethyl sulfoxide under dry pure nitrogen. The solution was warmed to promote solution. In order to ensure homogeneity it was frequently necessary to transfer the stock solution to a second flask in a dry nitrogen atmosphere by means of a pipet with a glass wool filter in its end. To the stock solution was added 1.7 g. of 1-phenylmethoxyethane, and the solution was shaken. A sample of the kinetic solution was withdrawn and titrated for base in an aqueous solution (potentiometric titration). The rate tubes were filled through use of a fast draining pipet with 3.8 ml. of the reaction mixture. A stream of nitrogen was passed over the stock solution during this time. The tubes were sealed and placed in a temperature bath, constant to ± 0.03 in all runs except 39 and 40, where the temperature was $173.0 \pm 0.3^\circ$. Each ampoule was quenched by cooling and adding water. The substrate was isolated as in the previous section, and distilled at 130° at 200 mm. in a micro still. In representative cases, the total infrared spectrum of the product

(21) (a) D. J. Cram, *J. Am. Chem. Soc.*, **74**, 2137 (1952); (b) **74**, 5518 (1952).

(22) Carried out by Dr. Joseph Nemeth, Urbana, Ill.

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-0.90 *t*-BUTYL ALCOHOL IN DIMETHYL SULFOXIDE AT $73.80 \pm 0.03^\circ$ (RUN 37)

Time, min.	Prod., g.	n_D^{20}	α_D^{20} , neat, / 0.5 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	0.80	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 ($25.00 \pm 0.02^\circ$), 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.

(23) J. Turkevich, H. A. McKenzie, L. Friedman and R. Spurr, *J. Am. Chem. Soc.*, **71**, 4045 (1949).

[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}

BY DONALD J. CRAM, DONALD A. SCOTT³ AND W. DAVID NIELSEN

RECEIVED FEBRUARY 27, 1961

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).