

came a bright green, which soon faded to a greenish-brown. The products were isolated as in other cases. The hydrocarbon fraction from the chromatograph column readily distilled to give 0.48 g. (55% yield) of 2-cyclohexylbutane<sup>3a</sup> heavily contaminated with olefin,  $n_D^{25}$  1.4503. After olefin was removed,<sup>3b,3c</sup> the product weighed 0.095 g.,  $n_D^{25}$  1.4440,  $\alpha_D^{25}$  0.00° (1 dm., neat).

Elution of the chromatograph column with 1-to-1 ether-pentane gave an oil which was treated with 2,4-dinitrophenylhydrazine reagent to give orange crystals. Two recrystal-

izations of this material from ethanol gave 0.09 g. of the 2,4-dinitrophenylhydrazone of benzophenone, m.p. 237–239°, undepressed by admixture with an authentic sample. A second hydrazone of a higher molecular weight ketone was also isolated, but was not identified.

Elution of the chromatograph column with ether gave 0.25 g. (25% yield) of benzhydrol, m.p. 64–65°, undepressed by admixture with an authentic sample.

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

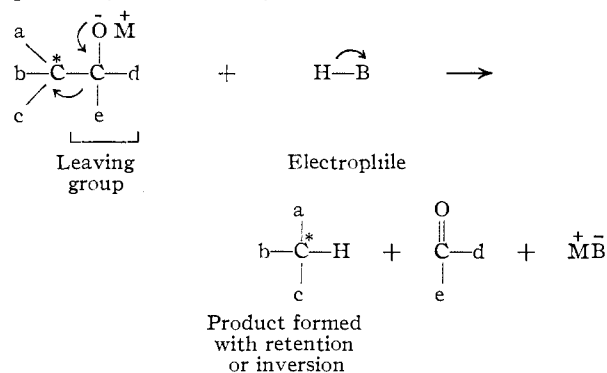
## Electrophilic Substitution at Saturated Carbon. V. Starting States and Intermediates

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The effect of variation of the configuration of the leaving group in electrophilic substitution at saturated carbon has been investigated. In base-catalyzed cleavage reactions of optically pure *threo*- and *erythro*-1,2-diphenyl-2-methyl-1-butanol to give 2-phenylbutane, the degree of stereospecificity was essentially the same for both diastereomers in both dioxane (about 94% predominating retention) and diethylene glycol (48% predominating inversion of configuration). The steric course of electrophilic substitution in the cleavage of optically pure diastereomers of 2,3-diphenyl-3-methoxy-2-butanol to give 1-methoxy-1-phenylethane in the above solvents was also shown to be independent of the *configuration of the leaving group*. This result indicates that intermediates common to both diastereomers intervene in both the retention and inversion mechanisms. Other support for this conclusion is found in the following facts. (1) In retention solvents, the steric course of electrophilic substitution is independent of the acidity of the electrophile over a range of about 14  $pK_a$  units. (2) In retention solvents, the steric course of the reaction is insensitive to the concentration of electrophile over concentrations that differ by a factor of 130. (3) In extreme retention and extreme inversion solvents, the steric course of the reaction depends only secondarily on the structure of the leaving group. The effect of both the nature and concentration of metal cation on the steric course of electrophilic substitution has been studied in four systems. The steric course of the reaction was independent of the concentration of the metal cation in all solvents studied. Lithium salts underwent cleavage reactions slower than potassium salts in all types of solvents. In extreme retention solvents, lithium salts gave higher retention than potassium salts. In extreme inversion solvents, with some leaving groups, both kinds of salts gave the same results. With other leaving groups, potassium salts gave higher inversion than lithium. In intermediate solvents, lithium salts gave higher inversion than potassium salts. In intermediate solvents, the systems with the least basic leaving groups gave the least retention and the highest inversion. These results provide evidence for two species in equilibrium with each other, both of which undergo electrophilic substitution. In non-dissociating solvents, intimate ion pairs cleave to give product of retained configuration. In dissociating solvents, solvent-separated ion-pairs give product of inverted configuration.

The base-catalyzed cleavage of a number of systems which conform to the general scheme indicated has been studied, and the results have been reported in previous papers of this study.<sup>2</sup> In the course of these reactions, electrophilic substitution occurs at the asymmetric carbon of the starting material, the steric course of which seems to be primarily controlled by the dissociating power of the



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(2) (a) D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, *THIS JOURNAL*, **81**, 5740 (1959); (b) D. J. Cram, A. Langemann and F. Hauck, *ibid.*, **81**, 5750 (1959); (c) D. J. Cram, K. R. Kopecky, F. Hauck and A. Langemann, *ibid.*, **81**, 5754 (1959); (d) D. J. Cram, A. Langemann, W. Lwowski and K. R. Kopecky, *ibid.*, **81**, 5760 (1959). Tables, compounds and runs are numbered consecutively throughout the first six papers of this series.

solvent. Variation of the substituents (d and e) attached to the leaving group, and of the acidity and concentration of the electrophile (HB) were examined (the latter only in retention solvents), and were found to play only a secondary role in determining the steric course of the reaction.

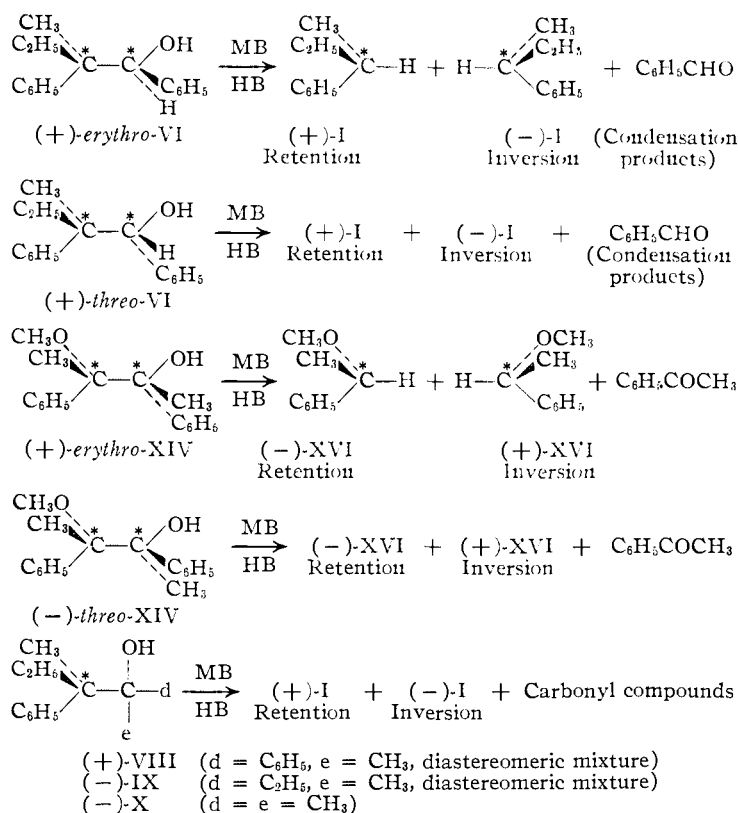
The present study is concerned with the effects of changes in *configuration and basicity of the leaving group*, and changes in the character and concentration of the metal cation upon the steric course of the electrophilic substitution reaction.

The absolute configurations of all starting materials and products in the reactions studied have been reported in other papers, as have the rotations of optically pure materials.<sup>3</sup> Only optically pure starting materials were employed in these investigations.

### Results

Table X records the results of cleavages of optically pure diastereomers of VI and XIV in dioxane with potassium *t*-butoxide as base (runs 108, 109, 112, 113), the former in ethylene glycol with potassium ethylene glycoxide as base (runs 110 and 111), and the latter in diethylene glycol with potassium diethylene glycoxide as base (runs 114 and 115). System VI is a secondary alcohol, and in runs 110 and 111, a possibility exists that some equilibration

(3) See ref. 2c for a summary of references and for data that demonstrate the relative configurations of starting materials and products. Rotations of optically pure starting materials are found in reference 2b.



between diastereomers occurred in a reaction that competed with cleavage. A control run conducted at 200° with *erythro*-VI in diethylene glycol (0.78 *M* in potassium hydroxide) indicated that cleavage occurs much faster than equilibration of diastereomers. Although cleavage occurred to give 51% optically pure 2-phenylbutane (inversion), starting material (35%) was recovered from the reaction mixture unchanged. Similarly in run 109, starting material (70%) was recovered with unaltered configuration. System XIV is a tertiary alcohol, so the diastereomers could not be interconverted by an oxidation-reduction sequence. The absence of radical-dimer in the product, the high stereospecificity of the reactions (runs 108–111), and the absence of a green color during the reaction indicates<sup>2d</sup> that no homolytic cleavage occurred in these runs. The recovery of unaltered starting material from some of these and from previous runs in either the same or similar systems coupled with the above facts indicates that the starting materials in runs 108–115 maintained their configurational integrity throughout the reactions. These results clearly demonstrate that within experimental error ( $\pm 1\%$ ) both diastereomers give the same balance of products irrespective of solvent.

Table XI reports the results of cleavages in which the effect of the metal cation on the steric course was assessed. Three metals (lithium, sodium and potassium) were employed and four different systems (VIII, IX, X and XIV) were cleaved. A variety of solvents (dioxane, *t*-butyl alcohol, methyl diethylene glycol, diethylene glycol and ethylene glycol) and their conjugate bases were employed.

The effect of the concentration of metal cations on the steric course of electrophilic substitution was investigated with systems VIII, IX and X, and Table XII records the results.

All of the runs reported in this paper were homogeneous.

## Discussion

**Intermediates in Electrophilic Substitution at Saturated Carbon.**—A body of evidence has accumulated that the retention, inversion and racemization mechanisms for the reactions under observation all involve discrete intermediates.

The data of Table X demonstrate that the balance between the two steric courses of electrophilic substitution is independent of the configuration of the leaving group. Thus in dioxane, both *threo*- and *erythro*-VI gave 81–82% retention of configuration in their cleavage reactions. Similarly, *threo*- and *erythro*-XIV in the same solvent gave  $94 \pm 1\%$  retention. In contrast, *threo*- and *erythro*-VI in ethylene glycol gave 41–42% inversion, and *threo*- and *erythro*-XIV in diethylene glycol gave 48–49% inversion. Since the starting materials in these sets of runs are diastereomeric, the transition

states in which the carbon-carbon bond is broken are diastereomeric, and therefore both the ground and transition states are of different energies. If either or both the inverted or retained product arose by a mechanism in which a carbon-carbon bond was broken and a carbon-hydrogen bond was made in a single transition state (*concerted process*), only a high order of fortuity could provide the results of Table X.

For similar reasons, it is also unlikely that two concerted mechanisms compete with one another in these reactions. On the other hand, when two distinctly different starting materials give the same ratio of products under a variety of different conditions, it is highly probable that the reactions possess a common intermediate.<sup>4</sup>

Three additional and independent lines of evidence support the thesis that neither the retention or inversion mechanisms involve transition states in which are coupled the carbon-carbon bond breaking and carbon-hydrogen bond making processes.

(1) *The steric course of electrophilic substitution is independent of the acidity of the electrophile over a range of about 14 pK<sub>a</sub> units in retention solvents.*<sup>2a,2c</sup> An example of the lack of effect is found in entry 2 of Table VII (paper III<sup>2c</sup>), runs 67 and 9. Thus system VIII in dioxane with 1% diethylene glycol gave 91% retention, in pure *t*-butyl alcohol 95% retention, and in pure aniline 90% retention. Other examples are found in references 2a and 2b. Neither of the two mechanistic pathways that combine to

(4) This same type of argument for a common intermediate has been applied before, both with respect to open carbonium ions [C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 354] and phenonium ions [D. J. Cram, THIS JOURNAL, 71, 3863, 3875 (1949)].

TABLE X: EFFECT OF CONFIGURATION OF LEAVING GROUP ON STERIC COURSE OF ELECTROPHILIC SUBSTITUTION

Run	Starting material		Solvent	Base		Temp., °C.	Time, hr.	Product				Predom. steric course	
	Comp.	Concn., M		Nature	Concn., M			Nature	Yld., %	$n_D^{25}$	$\alpha_D^{25}$		% opt. purity <sup>b</sup>
108	(+)-erythro-VI	0.11	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	KOtBu	0.12	150	48	(+)-I	85	1.4876 <sup>e</sup>	+ 19.9°	82	Ret.
109	(+)-threo-VI	0.08	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	KOtBu	0.10	150	48	(+)-I	88	1.4876 <sup>e</sup>	+ 19.7	81	Ret.
110	(+)-erythro-VI	1.22	HOCH <sub>2</sub> CH <sub>2</sub> OH	KOCH <sub>2</sub> CH <sub>2</sub> OH	1.22	244	24	(-)-I	83	1.4876 <sup>e</sup>	- 10.3	42	Inv.
111	(+)-threo-VI	1.22	HOCH <sub>2</sub> CH <sub>2</sub> OH	KOCH <sub>2</sub> CH <sub>2</sub> OH	1.22	244	24	(-)-I	78	1.4876 <sup>e</sup>	- 10.0	41	Inv.
112	(+)-erythro XIV	0.09	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	KOtBu	0.10	100	44	(-)-XVI	56	1.4884 <sup>c</sup>	-114	95	Ret.
113	(-)-threo-XIV	.08	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	KOtBu	.16	100	30	(-)-XVI	74	1.4897 <sup>c,d</sup>	-110	93	Ret.
114	(+)-erythro-XIV	.11	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	KO(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> H	.09	170	70	(+)-XVI	6	1.4893 <sup>c,d</sup>	+ 58	48	Inv.
115	(-)-threo-XIV	.08	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	KO(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> H	.08	170	88	(+)-XVI	24	1.4888 <sup>c,d</sup>	+ 59	49	Inv.

<sup>a</sup> *l* 1 dm., neat. <sup>b</sup> Based on  $\alpha_D^{25} \pm 120.2^\circ$  (*l* 1 dm., neat) for optically pure 1-methoxy-1-phenylethane (ref. 2b), and  $\alpha_D^{25} \pm 24.3^\circ$  for 2-phenylbutane. <sup>c</sup>  $n_D^{25}$  1.4882 for pure XVI (ref. 2b). <sup>d</sup> Olefin not removed with KMnO<sub>4</sub>. <sup>e</sup>  $n_D^{25}$  1.4878 for pure I (ref. 2a).

TABLE XI: EFFECT OF METAL CATION ON STERIC COURSE OF ELECTROPHILIC SUBSTITUTION

Run	Starting material		Solvent	Base		Temp., °C.	Time, br.	Product				Predom. steric course		
	No.	M <sup>+</sup>		Concn., M	Anion			Nature	Yld., %	$n_D^{25}$	$\alpha_D^{25}$		% opt. purity <sup>c</sup>	
116	(+)-VIII <sup>d</sup>	Li <sup>+</sup>	0.09	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	0.11	$\bar{O}C(CH_3)_3$	125	49	(+)-I	43	1.4876	+23.0°	95	Ret.
117	(+)-VIII <sup>d</sup>	Na <sup>+</sup>	.08	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	.11	$\bar{O}C(CH_3)_3$	125	48	(+)-I	91	1.4872	+23.6	97	Ret.
118	(+)-VIII <sup>d</sup>	K <sup>+</sup>	.09	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	.13	$\bar{O}C(CH_3)_3$	125	26	(+)-I	80	1.4877	+23.2	96	Ret.
119	(+)-VIII <sup>d</sup>	K <sup>+</sup>	.08	(CH <sub>3</sub> ) <sub>3</sub> COH	.09	$\bar{O}C(CH_3)_3$	102	48	(+)-I	64	1.4878	+20.4	84	Ret.
120	(+)-VIII <sup>d</sup>	Li <sup>+</sup>	.08	(CH <sub>3</sub> ) <sub>3</sub> COH	.14	$\bar{O}C(CH_3)_3$	102	48	(+)-I	0	....	....	..	..
121	(+)-VIII <sup>d</sup>	Li <sup>+</sup>	.08	(CH <sub>3</sub> ) <sub>3</sub> COH	.12	$\bar{O}C(CH_3)_3$	102	48	(+)-I	0	....	....	..	..
122	(-)-IX <sup>d</sup>	Li <sup>+</sup>	.88	(CH <sub>3</sub> ) <sub>3</sub> COH	.88	$\bar{O}C(CH_3)_3$	150	24	(+)-I	62	1.4877	+23.9	98	Ret.
123	(-)-IX <sup>d</sup>	K <sup>+</sup>	.88	(CH <sub>3</sub> ) <sub>3</sub> COH	.88	$\bar{O}C(CH_3)_3$	150	20	(+)-I	76	1.4878	+22.6	93	Ret.
124	(-)-X	Li <sup>+</sup>	.11	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	.12	$\bar{O}C(CH_3)_3$	150	57	(+)-I	58	1.4878	+24.1	99	Ret.
125	(-)-X	K <sup>+</sup>	.10	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	.09	$\bar{O}C(CH_3)_3$	150	49	(+)-I	85	1.4876	+23.0	95	Ret.
126	(+)-XIV <sup>d</sup>	Li <sup>+</sup>	.09	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	.32	$\bar{O}C(CH_3)_3$	150	94	(-)-XVI	20	1.4880	-104	86	Ret.
127	(+)-XIV <sup>d</sup>	K <sup>+</sup>	.09	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	.16	$\bar{O}C(CH_3)_3$	150	20	(-)-XVI	25	1.4881	-92.8	77	Ret.
128	(+)-XIV <sup>d</sup>	Na <sup>+</sup>	.09	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	.12	$\bar{O}C(CH_3)_3$	125	35	(-)-XVI	57	1.4885	-103	86	Ret.
129	(+)-XIV <sup>d</sup>	K <sup>+</sup>	.11	O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	.18	$\bar{O}C(CH_3)_3$	125	24	(-)-XVI	27	1.4887	-101	84	Ret.
130	(+)-VIII <sup>d</sup>	Li <sup>+</sup>	.08	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	.12	$\bar{O}(CH_2CH_2O)_2H$	180	48	(-)-I	61	1.4876	-13.3	55	Inv.
131	(+)-VIII <sup>d</sup>	Na <sup>+</sup>	.08	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	.12	$\bar{O}(CH_2CH_2O)_2H$	180	48	(-)-I	28 <sup>e</sup>	1.4877	-11.9	49	Inv.
132	(+)-VIII <sup>d</sup>	K <sup>+</sup>	.08	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	.12	$\bar{O}(CH_2CH_2O)_2H$	180	48	(-)-I	68	1.4877	-13.4	55	Inv.
133	(-)-IX <sup>d</sup>	Li <sup>+</sup>	1.04	HOCH <sub>2</sub> CH <sub>2</sub> OH	1.07	$\bar{O}CH_2CH_2OH$	200	36	(-)-I	28	1.4880	-12.2	50	Inv.
134	(-)-IX <sup>d</sup>	K <sup>+</sup>	1.04	HOCH <sub>2</sub> CH <sub>2</sub> OH	1.04	$\bar{O}CH_2CH_2OH$	200	24	(-)-I	52	1.4878	-11.7	48	Inv.
135	(-)-X	Li <sup>+</sup>	0.10	HOCH <sub>2</sub> CH <sub>2</sub> OH	0.10	$\bar{O}CH_2CH_2OH$	210	96	(-)-I	3	1.4881	- 6.56	27	Inv.
136	(-)-X	K <sup>+</sup>	.10	HOCH <sub>2</sub> CH <sub>2</sub> OH	.13	$\bar{O}CH_2CH_2OH$	210	55	(-)-I	33	1.4876	-12.6	52	Inv.
137	(-)-X	Li <sup>+</sup>	.10	HO(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> CH <sub>3</sub>	.08	$\bar{O}(CH_2CH_2O)_2CH_3$	210	24	(+)-I	9	1.4880	+ 1.24	5	Ret.
138	(-)-X	K <sup>+</sup>	.10	HO(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> CH <sub>3</sub>	.11	$\bar{O}(CH_2CH_2O)_2CH_3$	202	24	(+)-I	83	1.4875	+ 3.93	16	Ret.
139	(+)-XIV <sup>d</sup>	Li <sup>+</sup>	.18	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	.32	$\bar{O}(CH_2CH_2O)_2H$	180	126	(+)-XVI	16	1.4887	+46.0	38	Inv.
140	(+)-XIV <sup>d</sup>	K <sup>+</sup>	.08	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	.08	$\bar{O}(CH_2CH_2O)_2H$	180	88	(+)-XVI	24	1.4888	+59.0	49	Inv.
141	(+)-VIII	Li <sup>+</sup>	.20	CH <sub>3</sub> OH	.4	$\bar{O}CH_3$	180	96	(-)-I	34	1.4878	-13.6	56	Inv.
142	(+)-VIII	K <sup>+</sup>	.20	CH <sub>3</sub> OH	.4	$\bar{O}CH_3$	180	72	(-)-I	30	1.4878	-10.2	42	Inv.
143	(-)-IX	Li <sup>+</sup>	.20	CH <sub>3</sub> OH	.4	$\bar{O}CH_3$	180	96	(-)-I	6	1.4875	- 9.74	40	Inv.
144	(-)-IX	K <sup>+</sup>	.20	CH <sub>3</sub> OH	.4	$\bar{O}CH_3$	180	96	(-)-I	28	1.4876	- 6.18	25	Inv.

<sup>a</sup> Pure XVI has  $n_D^{25}$  1.4882 and pure I,  $n_D^{25}$  1.4878. <sup>b</sup> Neat, *l* 1 dm. <sup>c</sup> Optically pure XVI has  $\alpha_D^{25} \pm 120.2^\circ$  (*l* 1 dm., neat) and optically pure I has  $\alpha_D^{25} \pm 24.3^\circ$  (*l* 1 dm., neat). Mixture of optically pure diastereomers, configurationally homogeneous at the substituting carbon atom. <sup>e</sup> Yield was low due to mechanical difficulties.

TABLE XII  
 EFFECT OF CATION CONCENTRATION ON STERIC COURSE OF ELECTROPHILIC SUBSTITUTION AT SATURATED CARBON

Run	Starting mater.		Solvent	Base		Temp., °C.	Time, hr.	2-Phenylbutane			Predom. steric course	
	Comp.	Concn., M		Nature	Concn., M			Yld., %	$n_D^{25}$	$\alpha_D^{25}$ <sup>a</sup>		% opt. purity <sup>b</sup>
145	(+)-VIII	0.08	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	LiO(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> H	0.12	180	48	61	1.4876	-13.22°	55	Inv.
146	(+)-VIII	.16	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	LiO(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> H	.24	180	7	57	1.4878	-13.42	55	Inv.
147	(-)-X	.10	HOCH <sub>2</sub> CH <sub>2</sub> OH	KOCH <sub>2</sub> CH <sub>2</sub> OH	.57	210	85	69	1.4873	-12.54	50	Inv.
148	(-)-X	.10	HOCH <sub>2</sub> CH <sub>2</sub> OH <sup>c</sup>	KOCH <sub>2</sub> CH <sub>2</sub> OH	.50	210	85	66	1.4878	-12.5	50	Inv.
149	(-)-X	.10	CH <sub>3</sub> (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> OH	KO(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> CH <sub>3</sub>	.12	202	24	83	1.4875	+ 3.93	16	Ret.
150	(-)-X	.10	CH <sub>3</sub> (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> OH	KO(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> CH <sub>3</sub>	2.1	210	36	90	1.4876	+ 2.41	10	Ret.
151	(+)-VIII	.20	CH <sub>3</sub> OH	KOCH <sub>3</sub>	0.05	180	129	25	1.4875	-11.12	46	Inv.
152	(+)-VIII	.20	CH <sub>3</sub> OH	KOCH <sub>3</sub>	.20	180	76	34	1.4878	-11.00	45	Inv.
153	(+)-VIII	.20	CH <sub>3</sub> OH	KOCH <sub>3</sub>	.50	180	84	30	1.4877	-10.28	42	Inv.
154	(+)-VIII	.20	CH <sub>3</sub> OH	KOCH <sub>3</sub>	2.00	180	48	5	1.4878	- 9.70	40	Inv.
144	(-)-IX	.20	CH <sub>3</sub> OH	KOCH <sub>3</sub>	0.40	180	96	28	1.4878	- 6.81	25	Inv.
155	(-)-IX	.20	CH <sub>3</sub> OH	KOCH <sub>3</sub>	2.00	180	96	4	....	- 5.98	25	Inv.

<sup>a</sup>  $l$  1 dm., neat. <sup>b</sup> Optically pure 2-phenylbutane has  $\alpha_D^{25} \pm 24.3^\circ$  ( $l$  1 dm., neat). <sup>c</sup> Solution was 1 M in added potassium chloride.

give the above values could have been concerted. Otherwise a wide variety of results would have been obtained.

(2) *The steric course of electrophilic substitution is insensitive to the concentration of the electrophile over a concentration range of from 0.1 to 13 N in retention solvents.* A representative sample of data is found in runs 34 and 35 (Table III, paper II<sup>2b</sup>), with system X as the substrate. In the former run, a 0.1 M solution of *t*-butyl alcohol in dioxane gave 95% retention, whereas pure *t*-butyl alcohol (13 M) gave 90% retention. Other examples are found in reference 2c. Clearly X was partitioning between two reactions paths, neither of which could have been bimolecular. Otherwise the ratio of products would have varied widely with the electrophile concentration.

(3) *Although the rates of the reactions in the extreme retention and inversion solvents vary over a wide range as the nature of the leaving group changes, the stereochemical result depends only secondarily on the leaving group* (see Table XIII).

TABLE XIII

EFFECT OF LEAVING GROUP ON STERIC COURSE OF REACTION IN EXTREME RETENTION AND INVERSION SOLVENTS

$\begin{array}{c} \text{CH}_3 \text{---} \text{C}^+ \text{---} \text{C}^{\ominus} \text{---} \text{d} \\   \quad   \\ \text{C}_2\text{H}_5 \quad \text{C}_6\text{H}_5 \\ \text{Leaving group} \end{array}$		$\xrightarrow{\text{H-B}} \begin{array}{c} \text{CH}_3 \\   \\ \text{C}_2\text{H}_5 \text{---} \text{C}^+ \text{---} \text{C}^{\ominus} \text{---} \text{H} \\   \\ \text{C}_6\text{H}_5 \end{array}$		
Solvent-electrophile	d	e	Steric result	Run
Dioxane as solvent, (CH <sub>3</sub> ) <sub>3</sub> COH as electrophile	CH <sub>3</sub>	CH <sub>3</sub>	95% R <sup>a</sup>	125
	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	96% R <sup>a</sup>	68
	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	96% R <sup>a</sup>	118
	H	C <sub>6</sub> H <sub>5</sub>	82% R <sup>a</sup>	108
Ethylene or diethylene glycol as solvent and electrophile	C <sub>6</sub> H <sub>5</sub>	OC(CH <sub>3</sub> ) <sub>3</sub>	74% R <sup>a</sup>	70
	CH <sub>3</sub>	CH <sub>3</sub>	52% I <sup>b</sup>	136
	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	48% I <sup>b</sup>	134
	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	55% I <sup>b</sup>	132
	H	C <sub>6</sub> H <sub>5</sub>	42% I <sup>b</sup>	110
	C <sub>6</sub> H <sub>5</sub>	O(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> H	38% I <sup>b</sup>	71

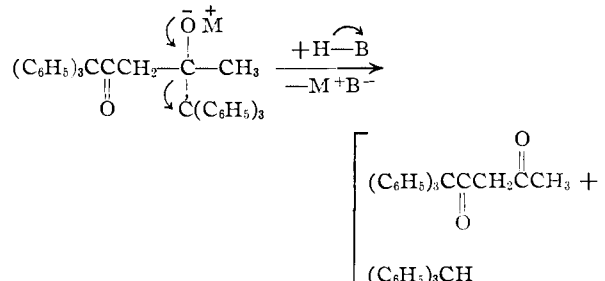
<sup>a</sup> Net retention. <sup>b</sup> Net inversion.

If in either retention or inversion solvents the carbon-carbon bond was broken and the carbon-hydrogen bond was made in the same transition

state, a much wider range of steric results would be expected as the leaving group was varied.

These results taken together provide strong evidence that in the production of retained, inverted or racemic material, the carbon-carbon bond is broken in one transition state and the carbon-hydrogen bond is made in a second. Discrete, high energy intermediates must intervene in all three reaction sequences. Since the reaction under study involves electrophilic substitution, these intermediates must be carbanions, or ion-pairs in which carbanions are one of the members. A discussion of the character and fate of these intermediates is reserved for paper VI of this series.<sup>5</sup>

**Effect of the Nature of Metal Cation on the Steric Course of Electrophilic Substitution.**—The data of Table XI indicate that the metal cation plays a minor but nevertheless detectable role in controlling the stereochemical course of electrophilic substitution at saturated carbon, and has a definite effect on the rate of cleavage of the carbon-carbon bond. In runs 120 and 121 in which lithium was the cation and *t*-butyl alcohol was solvent, (+)-VIII failed to cleave under conditions (temperature was 102°) in which the system cleaved with potassium as cation (run 119) to give a 64% yield of 2-phenylbutane. In other runs in which the effects of lithium and potassium were compared, the reaction involving the former metal was slower. This effect of the metal cation on the rate of cleavage reactions has been observed by others,<sup>6</sup> who found that K > Na > Li in cleavage of the system formulated.<sup>7</sup>

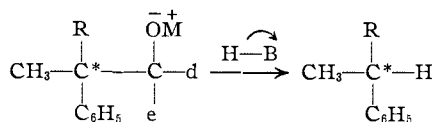


(5) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, THIS JOURNAL, **81**, 5774 (1959).

(6) H. D. Zook, T. L. Greene and D. F. Smith, Abstracts of Papers Presented before American Chemical Society, San Francisco, Calif., Meeting, April, 1958, p. 12-N.

(7) Lithium salts have in many cases been demonstrated to be less reactive in a variety of reactions than potassium or sodium salts: (a)

TABLE XIV  
EFFECT OF METAL CATION ON STERIC COURSE OF REACTION IN EXTREME RETENTION AND INVERSION SOLVENTS



Solvent	Electrophile	R	d	e	Steric result		Run nos. <sup>a</sup>
					Li	K	
O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	(CH <sub>3</sub> ) <sub>3</sub> COH	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	99% R <sup>b</sup>	95% R <sup>b</sup>	124, 125
(CH <sub>3</sub> ) <sub>3</sub> COH	(CH <sub>3</sub> ) <sub>3</sub> COH	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	98% R <sup>b</sup>	93% R <sup>b</sup>	122, 123
O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	(CH <sub>3</sub> ) <sub>3</sub> COH	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	95% R <sup>b</sup>	96% R <sup>b</sup>	116, 118
O(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	(CH <sub>3</sub> ) <sub>3</sub> COH	CH <sub>3</sub> O	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	86% R <sup>b</sup>	77% R <sup>b</sup>	126, 127
O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	55% I <sup>c</sup>	55% I <sup>c</sup>	130, 132
HOCH <sub>2</sub> CH <sub>2</sub> OH	HOCH <sub>2</sub> CH <sub>2</sub> OH	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	50% I <sup>c</sup>	48% I <sup>c</sup>	133, 134
HOCH <sub>2</sub> CH <sub>2</sub> OH	HOCH <sub>2</sub> CH <sub>2</sub> OH	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	27% I <sup>c</sup>	52% I <sup>c</sup>	135, 136
O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	O(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub>	CH <sub>3</sub> O	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	38% I <sup>c</sup>	49% I <sup>c</sup>	139, 140

<sup>a</sup> Runs all taken from Table XI. <sup>b</sup> Net retention. <sup>c</sup> Net inversion.

Lithium salts gave somewhat higher retention in the extreme retention solvents than did potassium or sodium salts, which provided about the same results. In extreme inversion solvents, lithium and potassium salts of VIII and IX gave the same results, but the lithium salt gave lower inversion than the potassium with systems X and XIV. The pertinent results are summarized in Table XIV.

**Structures of the Species that Undergo Cleavage.** The first problem in developing a mechanistic scheme is associated with the structures of the species that undergo cleavage. In the reaction medium, a series of equilibria exist which are outlined in Chart I. Because of the usually rapid rates at which acid-base and salt dissociation reactions occur, it is reasonable to assume that these equilibria are established much more rapidly than any cleavage reaction occurs. This scheme includes three species which might undergo cleavage, A, B and C. The first of these is an intimate ion-pair<sup>8</sup> (A), the second is a solvent-separated ion-pair<sup>8</sup> (B), and the third is the dissociated anion (C). Species A is presumed to cleave to give predominantly product of retained configuration, B and C to give predominantly product of inverted configuration.

The concentration of M<sup>+</sup> is probably constant throughout most of the runs for the following reasons: (1) The basic catalyst, ROM is not consumed in the reaction. (2) The position of the equilibrium governed by K<sub>2</sub> must lie far on the left, since ROH as solvent is at much higher concentration than the starting alcohol, and (or) because the starting alcohol is a weaker acid than ROH. (3) As a result, very little of the metal can be accounted for in the form of A at any particular time.<sup>9</sup>

D. Y. Curtin, R. J. Crawford and M. Wilhelm, *THIS JOURNAL*, **80**, 1391 (1958); (b) G. Wittig and W. Benz, *Ber.*, **91**, 873 (1958); (c) G. Wittig and E. Stahnecker, *Ann.*, **605**, 69 (1957); (d) D. Y. Curtin and S. Leskowitz, *THIS JOURNAL*, **73**, 2630 (1951); (e) W. Doering, G. Cortes and L. Knox, *ibid.*, **69**, 1705 (1947); (f) O. L. Brady and J. Jakobovits, *J. Chem. Soc.*, 767 (1950); (g) E. Pfeil, *Ber.*, **84**, 229 (1951); (h) E. Pfeil and G. Schroth, *ibid.*, **85**, 293 (1952); (i) E. Pfeil, G. Geissler, W. Jacquemin and F. Lomker, *ibid.*, **89**, 1210 (1956).

(8) The nomenclature of S. Winstein is adopted here [see e.g., S. Winstein and G. C. Robinson, *THIS JOURNAL*, **80**, 169 (1958)].

(9) Exceptions to these generalizations would be runs carried out in which amine salts were catalysts, or possibly reactions carried out in dioxane with small amounts of potassium *t*-butoxide as catalyst. Even in the latter case, M<sup>+</sup> would not be expected to vary widely during a run if K<sub>1</sub> and KK' had about the same values.

Under the above conditions, the relative amounts of D and E produced are governed by expression 1.<sup>10</sup>

$$\frac{D}{E} = \frac{k_a[M^+]}{k_bK[M^+] + k_cKK'} \quad (1)$$

Equation 1 reduces to either equation 2 or 3 with certain sets of relative values of k<sub>b</sub>, k<sub>c</sub>, K, K' and [M<sup>+</sup>]. If k<sub>b</sub>K[M<sup>+</sup>] >> k<sub>c</sub>KK', then equation 2 governs the value of D/E. If k<sub>c</sub>KK' >> k<sub>b</sub>K[M<sup>+</sup>], then equation 3 applies.

$$\frac{D}{E} = \frac{k_a}{k_bK} \quad (2)$$

$$\frac{D}{E} = \frac{k_a[M^+]}{k_cKK'} \quad (3)$$

Since [M<sup>+</sup>] appears in equations 1 and 3 but not in 2, the presence or absence of a common ion effect on the steric course of the cleavage reaction differentiates between the applicability of equation 1 or 3 on the one hand or equation 2 on the other to the mechanism under study.

CHART I

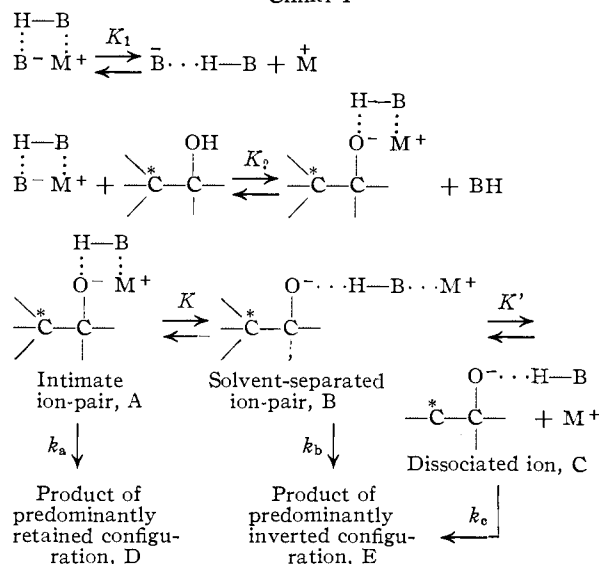


Table XII reports the results of attempts to alter the stereochemical course of the reaction by

(10) The authors wish to thank Professor W. G. McMillan for valuable help in developing this equation.

varying the concentration of  $[M^+]$  in the medium. Three different systems (VIII, IX and X), four different solvents (diethylene glycol, ethylene glycol, methylethylene glycol and methanol), and two different metals (lithium and potassium), were employed. The most extensive experiments were carried out in methanol, in which the concentration of potassium methoxide was varied by a factor of 40 (runs 151-154). The steric result varied between the extremes of 46 and 40% net inversion of configuration. If equation 3 applied, it is estimated that the steric course should have varied between 46% net inversion to from 10 to 54% net retention as the concentration of potassium methoxide was increased.<sup>11</sup> These and other results of Table XII demonstrate the absence of a common ion effect on the stereochemistry of these reactions in the solvent systems at hand. Thus equations 1 and 3 cannot apply to the reaction mechanisms involved. On the other hand, equation 2 is consistent with the lack of common ion effect.

A rationalization of these results is as follows. It is reasonable to suppose that in all solvents,  $k_c > k_b \gg k_a$ , since the closer positive and negative charges are to one another, the higher become the electrostatic forces that must be overcome in the transition states in question. The terms in equation 1 that vary the most with the character of the solvent are probably  $K$ ,  $K'$  and  $[M^+]$ . In extremely poor dissociating solvents such as *t*-butyl alcohol or dioxane, the values of  $K$  would be so small that only intimate ion pairs (A) would cleave.<sup>12</sup> In the best dissociating solvents used in this study (e.g., ethylene glycol),  $K > K'$ , and both constants are probably much less than unity. The values of  $[M^+]$  are controlled by the initial concentration of the basic catalyst employed and by  $K_1$ . The best dissociating solvents are primary alcohols, and the basic catalysts in these solvents are metal alkoxides of primary alcohols. The systems that undergo cleavage are metal alkoxides of tertiary alcohols, and therefore  $K_1 > KK'$ , and  $[M^+] > K'$ . Thus the concentration of solvent-separated ion pairs is much higher than that of dissociated anions, and in effect only the former undergo the cleavage reaction. In solvents of intermediate dissociating power such as methanol, both intimate and solvent-separated ion-pairs cleave to give results between those of the extreme retention and inversion solvents.

It is likely that with less basic groups in solvents of high dissociating power, dissociated anions would become the reacting species, and common ion effects would be observed.

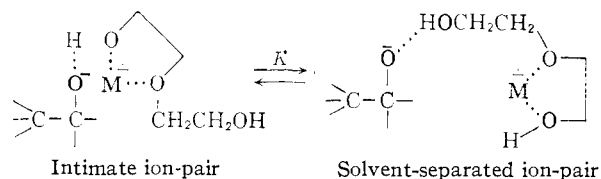
The mechanism embodied in equation 2 and Chart I provides explanations for the following facts. (1) *In extreme retention and inversion sol-*

(11) In the calculation involved in this estimate, A was presumed to cleave to give 90% retention and 10% racemization, whereas C was assumed to give 55% inversion and 45% racemization. If the value of the dissociation constant for potassium methoxide in methanol is large,  $[M^+]$  varied by a maximum factor of 40 between runs 151 and 154. If the dissociation constant was very small,  $[M^+]$  varied by a minimum of 6.6.

(12) The intimate ion pairs are probably somewhat polymerized in solvents such as dioxane, but monomer, dimer, etc., are all presumed to cleave to give about the same steric result, and thus no account need be taken of such species.

*vents, the potassium and lithium salts of the two alcohols, VIII and IX, give almost the same steric results (see Table XIV). These two alcohols are tertiary alcohols, and in this interpretation, only A reacted in the extreme retention and only B reacted in the extreme inversion solvents. The small differences between lithium and potassium salts in the extreme retention solvents is associated with the proximity of the ions in the intimate ion-pair. The lack of difference in extreme inversion solvents is attributed to the fact that in B, solvent intervenes between the two ions.<sup>13</sup>*

(2) *Although methanol and diethylene glycol have similar dielectric constants, the former is an intermediate and the latter is an extreme inversion solvent. The three basic oxygen atoms in diethylene glycol increase its solvating power for metal cations, and thus  $K$  for ethylene glycol is larger than for methanol.*



(3) *Lithium salts cleave more slowly than potassium salts in both retention and inversion solvents. The small ionic radius and lack of shielding of the positive charge of lithium makes the oxygen-lithium bond stronger than that between potassium and oxygen. As a result, both  $k_a$  and  $K$  of equation 2 are lower in value for lithium than for potassium. However, since charge is much more separated in B than A, the values for  $k_b$  are much closer together for potassium and lithium salts. Thus in retention solvents, the rates of cleavage of lithium salts are low because of the low values of  $k_a$ . In extreme inversion solvents, the rates of cleavage of lithium salts are low because of the low value of  $K$ . Since  $k_b \gg k_a$ , only B cleaves in these solvents, even though its concentration is very low.*

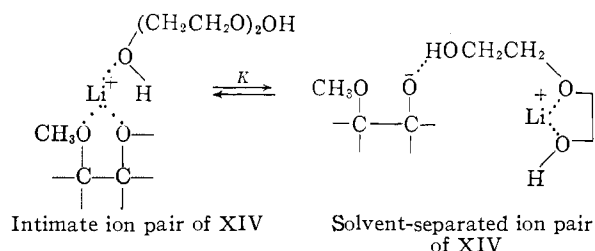
(4) *In the intermediate solvent, methanol, the lithium salts of VIII and IX both give about 15% higher inversion than the potassium salts (runs 141-144 of Table XI). In this solvent, with the potassium salts, the value of  $k_a/k_bK$  (equation 2) is not low enough to completely channel the reaction through B as the cleaving species. With the lithium salts, both  $k_a$  and  $K$  decrease in value, but the former more than the latter. As a result, the value of  $k_a/k_bK$  for the lithium salt is lower than that for the potassium salt, and more of B cleaves with the lithium than with the potassium salt.*

(5) *The lithium salt of XIV gave 11% lower inversion in diethylene glycol than the potassium salt (runs 139 and 140). The presence of two coordination sites in XIV allows it to compete more favorably with glycols for the metal cation, particularly for the small lithium ion.<sup>14</sup> As a result, the value of  $K$  for XIV is lower than that for systems VIII*

(13) This point is discussed further in paper VI of this series, ref. 5.

(14) G. A. Guter and G. S. Hammond, *THIS JOURNAL*, **78**, 5166 (1956), have separated lithium from sodium and potassium ions by utilizing the small size of the lithium ion and its consequent ability to chelate with dipivaloylmethane.

and IX, particularly for lithium salts. The transition state for cleavage of the intimate ion pair of XIV would be somewhat stabilized by the presence in the molecule of the second basic oxygen, and the value of  $k_a/k_b$  would accordingly not be depressed so much by the increased stability of the intimate ion pair. As a result of these effects, a small amount of intimate ion pair of XIV cleaves at the expense of the solvent-separated ion pair, and the amount of inverted product decreases.



(6) The lithium salt of X gave 25% lower inversion in ethylene glycol than the potassium salt (runs 135 and 136). In this system, the interplay of  $K$ ,  $K_a$  and  $K_b$  is such that A cleaves to a small extent in competition with B, and lowers the stereospecificity accordingly. The fact that the two salts of VIII and IX give the same results in glycols but different results with X (see Table XIV) indicates the delicate balance between the values of  $K$ ,  $k_a$  and  $k_b$ . The difference between X and the other two systems correlates with the lower bulk of the leaving group of X. Thus the steric repulsions in the intimate ion-pair (A) are less for X, the concentration of A is higher, the value of  $K$  lower, and the overall value of  $k_a/Kk_b$  higher than in the other two systems.

(7) In intermediate solvents such as dimethyltetraethylene glycol and methanol, retention decreases and inversion increases as the basic character of the anion of the leaving group decreases (see Table XV). Both the intimate and solvent-separated ion-pairs cleave in these intermediate solvents, and as  $K$  (equation 2) increases in value, retention decreases and inversion increases. The less basic the leaving group, the higher the value of  $K$ . Steric effects probably also play some role, but not a dominant one in these solvents.

**Possible Asymmetric Induction in Electrophilic Substitution at Saturated Carbon.**—The following experiment was conducted to determine if the electrophilic substitution reaction was subject to asymmetric induction. Racemic IX was cleaved in optically pure (+)-2-octanol as solvent with its potassium salt as base to give a 69% yield of 2-phenylbutane. This material gave  $\alpha^{25D} 0.00 \pm 0.02^\circ$  ( $l$  1 dm., neat), which indicates that no asymmetric induction was involved in the donation of a proton by 2-octanol to the ethylmethylphenyl carbanion. This result demonstrates that the ratio  $k_{ret}/k_{inv}$  was the same for the two enantiomers of IX in the optically active solvent. The value of this ratio has previously been shown to be rather insensitive to the acidity of the proton donor,<sup>2b,2c</sup> which is consistent with the postulate that the value is controlled only by the relative rates of capture of a proton from the front and back sides of a high en-

ergy carbanion or ion pair. In principle, in the run in (+)-2-octanol, the transition states leading to 2-phenylbutane were diastereomeric, and therefore, of different energy. However, it would have been surprising indeed if any appreciable amount of asymmetric induction were observed for two reasons. (1) The activation energies for proton capture by the ethylmethylphenyl carbanion must be very low, and therefore, the process would be expected to be sterically indiscriminate.

TABLE XV  
VARIATION OF STERIC RESULT WITH CHANGES IN BASICITY OF LEAVING GROUP IN INTERMEDIATE SOLVENTS

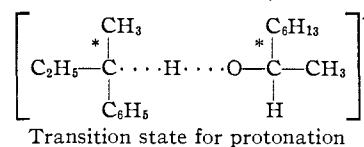
$\bar{\text{O}}$	$\bar{\text{O}}$	$\bar{\text{O}}$	$\bar{\text{O}}$
$\text{RCC}_2\text{H}_5$	$\text{RCCH}_3$	$\text{RCC}_6\text{H}_5$	$\text{RCC}_6\text{H}_5$
$\text{CH}_3$	$\text{CH}_3$	$\text{CH}_3$	$\text{H}$
IX	X	VIII	VI
Decreasing basicity $\rightarrow$			

Solvent, electrophile base	Comp.	Steric result	Run
CH <sub>3</sub> O(CH <sub>2</sub> CH <sub>2</sub> O) <sub>4</sub> CH <sub>3</sub> , 5% CH <sub>3</sub> (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> OH, K salt	IX	60% R <sup>a</sup>	22
	X	54% R <sup>a</sup>	36
	VI	7% R <sup>a</sup>	46
CH <sub>3</sub> OH, CH <sub>3</sub> OK	IX	25% I <sup>b</sup>	144
	VIII	42% I <sup>b</sup>	142
CH <sub>3</sub> OH, CH <sub>3</sub> OLi	IX	40% I <sup>b</sup>	143
	VIII	56% I <sup>b</sup>	141

<sup>a</sup> Net retention. <sup>b</sup> Net inversion.

(2) The two asymmetric centers in the transition states would be separated by hydrogen and oxygen atoms, and the steric differences between diastereomeric transition states would be expected to be very small.

In an independent experiment, 2-phenyl-2-butylpotassium was protonated with (–)-2-octanol. Completely racemic 2-phenylbutane was produced ( $\alpha^{25D} 0.00 \pm 0.02^\circ$ ,  $l$  1 dm., neat).



## Experimental

**Starting Materials.**—The preparation of optically pure (+)-*erythro*-2,3-diphenyl-3-methoxy-2-butanol (XIV) and (–)-*threo*-XIV, and the determination of their configurations has been described previously.<sup>2b</sup> The properties of the material used in this investigation are: (+)-*erythro*-XIV,  $[\alpha]^{25D} +11.9^\circ$  (chloroform,  $c$  5); (–)-*threo*-XIV,  $[\alpha]^{25D} -9.07^\circ$  (chloroform,  $c$  5). The preparation and configurations of (+)-*erythro*- and (+)-*threo*-1,2-diphenyl-2-methyl-1-butanol (VI) were previously demonstrated.<sup>15,20</sup> The properties of the material used here are: (+)-*erythro*-VI,  $[\alpha]^{25D} +1.85^\circ$  (benzene,  $c$  9) and (+)-*threo*-VI,  $[\alpha]^{25D} +59.5^\circ$  (benzene,  $c$  11). Other starting materials employed have the properties: (–)-3,4-dimethyl-4-phenyl-3-hexanol [(–)-IX],<sup>2a</sup> a mixture of optically pure diastereomers,  $[\alpha]^{25D} -11.20^\circ$  (benzene,  $c$  11), 80% *threo*-isomer, 20% *erythro*-isomer; (–)-2,3-dimethyl-3-phenyl-2-pentanol,<sup>2a</sup> (–)-X,  $\alpha^{25D} -2.03^\circ$  ( $l$  1 dm., neat); (+)-2,3-diphenyl-3-methyl-2-pentanol, (+)-VIII, mixture of optically pure diastereomers,<sup>2a</sup>  $[\alpha]^{25D} +17.5^\circ$  (benzene,  $c$  71).

**Solvents.**—The dioxane, diethylene glycol, ethylene glycol and *t*-butyl alcohol were all purified by distillation from dissolved potassium metal.

(15) D. J. Cram and J. Allinger, *THIS JOURNAL*, **76**, 4516 (1954).

**Cleavage Reactions.**—All of the runs were conducted in solvent which was first saturated with nitrogen. Runs 108–129, 141–144 and 151–155 were conducted in closed systems under nitrogen, either in sealed tubes or pressure bottles. The other runs were carried out in flasks with reflux condensers under nitrogen. All runs were homogeneous. In those runs involving lithium, the metal was dissolved directly in the alcohol for preparation of the base. The same was true for potassium and lithium when *t*-butoxide or diethylene glycoxide was the base. Potassium or sodium metal could not be dissolved directly in ethylene glycol without danger of explosion and therefore potassium and sodium ethylene glycoxide was prepared from the corresponding *t*-butoxide as described earlier.<sup>2b,2c</sup> The reactions were run in a Wood metal-bath heated electrically. The products were isolated as described in previous investigations.<sup>2b,2c</sup> In representative runs the 1-methoxy-1-phenylethane or 2-phenylbutane products were demonstrated to have infrared spectra identical with those of authentic samples of these compounds.

Cleavage of (–)-V in (+)-2-octanol provides a typical procedure (other examples are found in papers II<sup>2b</sup> and III<sup>2c</sup> of this series). A solution of 0.96 *M* potassium alkoxide was prepared by dissolving 0.188 g. of potassium metal in a nitrogen-saturated solution of 5 ml. of optically pure (+)-2-octanol,<sup>16</sup>  $[\alpha]^{25}_D +48.1^\circ$  (*c* 5, ethanol). To the resulting solution was added 1.0 g. of racemic V, and the solution was

(16) A. W. Ingersoll in "Organic Reactions," John Wiley and Sons, Inc., New York, 1944, p. 402.

heated in a sealed tube at 150° for 16 hours. The reaction mixture was then chromatographed on 200 g. of alumina in pure pentane, and the 2-phenylbutane was eluted with pentane. Pentane was evaporated through a Vigreux column, and the residual 2-phenylbutane was twice distilled through a micro still at 25 mm. to give 0.43 g. of product,  $n^{25}_D$  1.4878,  $\alpha^{25}_D$  0.00 ± 0.02°.

In the other runs, solvent was washed from the reaction mixture in the isolation procedure by shaking the reaction mixture with pentane and water before chromatography.

**Control Runs.**—The products (I and XVI) of electrophilic substitution in these experiments were demonstrated to be optically stable under the conditions of their formation by control experiments reported in papers II and III of this series.<sup>2b,2c</sup> In runs 109, 120, 121, 135, 137 and 139, optically pure starting materials were recovered.

**Protonation of 2-Phenyl-2-butylpotassium with (–)-2-Octanol.**—A solution (30 ml.) of 2-phenyl-2-butylpotassium in ether was prepared by the action of sodium-potassium alloy on 3 g. of racemic 2-methoxy-2-phenylbutane.<sup>2a</sup> This material was protonated by addition of 1.0 g. of optically pure (–)-2-octanol,  $[\alpha]^{25}_D -48.3^\circ$  (*c* 5, ethanol).<sup>5</sup> The resulting mixture was shaken with water, dried, and evaporated to an oil. This material was dissolved in pure pentane, passed through 50 g. of alumina, and the 2-phenylbutane was isolated in the usual way to give 1.9 g. of material,  $n^{25}_D$  1.4878,  $\alpha^{25}_D$  0.00 ± 0.02°.

LOS ANGELES 24, CALIF.

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

## Electrophilic Substitution at Saturated Carbon. VI. Stereochemical Capabilities of Carbanions<sup>1</sup>

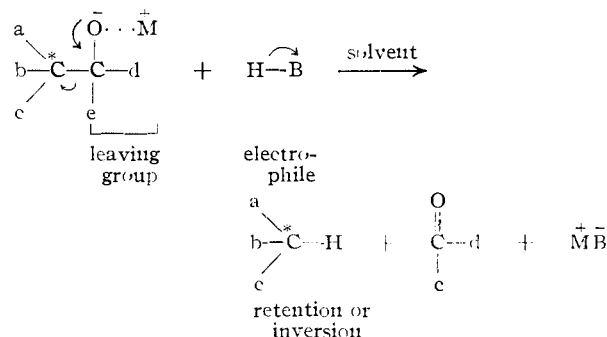
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Evidence is presented that in base-catalyzed reverse condensation reactions, carbanions or ion pairs involving carbanions intervene which capture protons from neighboring molecules, either before or after their solvent envelope becomes symmetric. Depending chiefly on the character of the medium, this electrophilic substitution at saturated carbon can occur with either predominating retention, predominating inversion or complete racemization. In solvents of low dissociating power (*e.g.*, *t*-butyl alcohol) and with metal alkoxides as bases, high retention of configuration is observed. This result is attributed to a favorable orientation of proton donors, which coordinate with the metal cation of an intimate ion-pair which undergoes cleavage. This species reacts to give a very reactive, carbanion-metal-cation intimate ion pair which is favorably solvated from the side of the leaving group by proton donors. Retention of configuration is observed because of the proximity of a very strong base and acidic hydroxyl or amino groups. In similar solvents with quaternary ammonium hydroxides as bases, complete racemization is observed since the carbanion survives long enough to pass into a symmetrical environment. In solvents of high dissociating power which are not proton donors (*e.g.*, dimethyl sulfoxide), the carbanion is long enough lived to become symmetrically solvated, and electrophilic substitution gives racemic product. In solvents of high dissociating power which are good proton donors (*e.g.*, diethylene glycol), a solvent-separated ion pair undergoes cleavage. The carbanion produced is protonated more rapidly from the side remote from the leaving group because of the shielding effect of that group. In diethylene glycol, metal and quaternary ammonium salts give the same result. The behavior of carbanions and carbonium ions is compared.

In the five previous papers of this series,<sup>3</sup> the steric course of electrophilic substitution at saturated carbon has been examined in a number of systems which are generally represented below. The substituents of both the asymmetric carbon (a, b and c) and of the leaving group (d and e) have been varied, as well as the characters of the metal

cation, the electrophile, and the solvent. With various combinations of the above factors, the reactions were found to give product that ranged from 99% retention to 60% inversion of configuration.



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(2) Rockefeller Postdoctoral Fellow at U.C.L.A., 1957–1958.

(3) (a) D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, *THIS JOURNAL*, **81**, 5740 (1959); (b) D. J. Cram, A. Langemann and F. Hauck, *ibid.*, **81**, 5750 (1959); (c) D. J. Cram, K. R. Kopecky, F. Hauck and A. Langemann, *ibid.*, **81**, 5754 (1959); (d) D. J. Cram, A. Langemann, W. Lwowski and K. R. Kopecky, *ibid.*, **81**, 5760 (1959); (e) D. J. Cram, F. Hauck, K. R. Kopecky and W. D. Nielsen, *ibid.*, **81**, 5767 (1959). Tables, compounds and runs are numbered consecutively throughout the first six papers of this series.