The following control in tetrahydroquinoline was performed. Potassium metal, 0.193 g. (0.00484 mole), was dissolved in 4 ml. of tetrahydroquinoline and mixed with 0.647 g. of (+)-I, $\alpha^{25}D$ +12.1° (l 1 dm., neat), and the resulting mixture was refluxed for 24 hours. The product isolated by the usual method contained olefin, $n^{25}D$ 1.4889. This material was rid of olefin by treatment with 2,4-dinitrobenzenesulfenyl chloride,[15] and 0.30 g. of totally racemic I was obtained, $n^{25}D$ 1.4879.

In a control run in N-methylaniline, the potassium was omitted. A solution of 0.35 g. of (+)-I, $n^{25}D$ 1.4878, $\alpha^{25}D$ +16.3° (l 1 dm., neat) and 6 ml. of dry N-methylaniline was heated to 200° for 20 hours. The starting material was recovered in 77% yield, $n^{25}D$ 1.4878, $\alpha^{25}D$ +16.29° (l 1 dm., neat).

Reaction of 2-Phenyl-2-butylpotassium with 2-Butanone.—To 600 ml. of ether under dry nitrogen was added 16 ml. of sodium-potassium alloy. Methyl 2-phenylbutyl ether[13] (26.8 g.) was added and the mixture was stirred at room temperature under nitrogen for 18 hours. The mixture was filtered under dry nitrogen, and 2-butanone (7.4 g.) was added to the filtrate until the red color had just disappeared. The ether solution was washed with water, dried, and the ether was removed. The residue was fractionally distilled to give 10 fractions. Fractions 1–5 contained some 2-butanone. Fractions 6–9, 15.2 g., b.p. 75–77° (27 mm.), $n^{25}D$ 1.4876–1.4878, was 2-phenylbutane (74% yield).

Anal. Calcd. for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 89.60; H, 10.40.

The pot residue was crystallized from pentane to give 0.50 g. white needles, m.p. 169–170°.

Anal. Calcd. for $C_{20}H_{26}$: C, 90.16; H, 9.84. Found: C, 90.15; H, 9.74. The structure of this compound was not elucidated.

LOS ANGELES 24, CALIF.

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

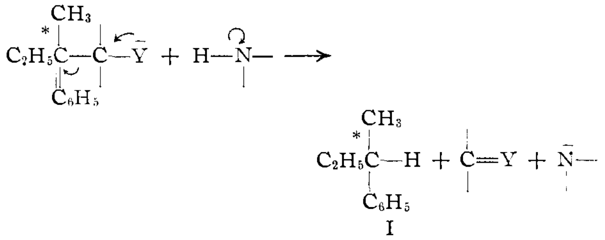
Electrophilic Substitution at Saturated Carbon. II. Retention and Inversion Reaction Paths[1]

BY DONALD J. CRAM, ALBERT LANGEMANN AND FRED HAUCK

RECEIVED JANUARY 2, 1959

The effect of solvent on the stereochemistry of electrophilic substitution at saturated carbon has been investigated. In the base-catalyzed cleavage reactions of (−)-3,4-dimethyl-4-phenyl-3-hexanol, (−)-2,3-dimethyl-3-phenyl-2-pentanol, (+)-2,3-diphenyl-3-methyl-2-pentanol, (+)-3-methyl-3-phenyl-2-pentanol and (+)-1,2-diphenyl-2-methyl-1-butanol, 2-phenylbutane is produced as the result of solvent (as an electrophile) donating a proton to negative carbon. Fourteen different solvents have been examined, and the optical purity of the 2-phenylbutane produced ranges from 96% (retention of configuration) to 51% (inversion of configuration). The steric courses of the reactions are relatively insensitive to variations in the leaving group, acidity and concentration of the nucleophile, and are controlled largely by the nature of the solvent. Solvents of low dielectric constant tend to give retention whereas solvents of high dielectric constant give inversion of configuration.

In paper I of this series[2] (which summarizes the relevant literature), eleven systems were subjected to base-catalyzed (anionic) cleavage reactions in secondary amines as solvents to give 2-phenylbutane as product. The reaction was found to occur in each case with predominant retention of configuration at C-2 of 2-phenylbutane.

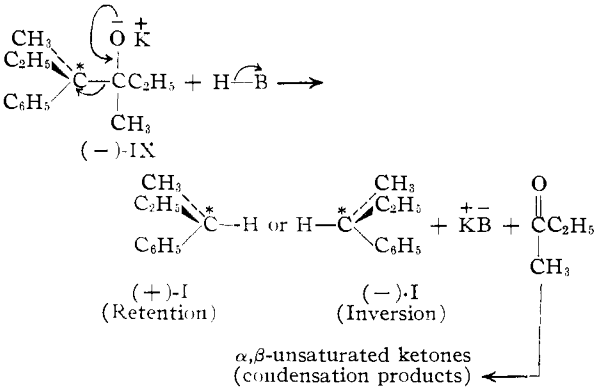


I

The present paper reports the results of a survey of sixteen solvents to assess their effect on the steric course of the cleavage of five systems of the type formulated. The relative configuration of starting materials and products have been established elsewhere.[3,4]

Results

Table II[5] records the conditions for and the results of cleavages of system IX, which is a mixture of diastereomers[6] configurationally homogeneous at the carbon atom which undergoes substitution. The 2-phenylbutane (I) produced was characterized by its refractive index in all cases, which constant is very sensitive to olefinic and other contaminants, and serves as a good criterion of purity. In representative cases, the infrared spectrum of this hydrocarbon was also compared with that of authentic I,[7] and in all cases the spectra were superimpossible. In a number of reactions carried out in tertiary alcohols or ethers as solvents, mixtures of α,β-unsaturated ketones were isolated which are presumably condensation products of 2-butanone produced in the cleavage reaction. In some of the runs in primary and secondary alcohols, these α,β-



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[1] This work was sponsored by the Office of Ordnance Research, U. S. Army.

[2] D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, THIS JOURNAL, **81**, 5740 (1959).

[3] D. J. Cram and J. Allinger, *ibid.*, **76**, 4516 (1954).

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

[5] Tables, compounds and runs are numbered consecutively throughout the first six papers of this series.

[6] D. J. Cram and J. D. Knight, THIS JOURNAL, **74**, 5835 (1952).

[7] D. J. Cram, *ibid.*, **74**, 2149 (1952).

TABLE II: EFFECT OF SOLVENT ON CLEAVAGE REACTIONS OF (−)-3,4-DIMETHYL-4-PHENYL-3-HEXANOL (−)-IX[a]

Run	Molality st. mat.	Solvent	Base		Temp., °C.	Time, hr.	2-Phenylbutane				Predom. steric course	Remarks[d]
			Nature	Molality			Yld., %	$\alpha^{23-26}\text{D}$[b]	$n^{25}\text{D}$	% opt. purity[c]		
16	0.81	C_6H_6	KO–*t*Bu	0.80	82	24	41	+22.5°	1.4878	93	Ret.	Ketonic mat. isol.
17	.88	$(CH_3)_3COH$	KOH	.88	150	20	76	+22.6	1.4878	93	Ret.	Sealed tube
18	.88	$(CH_3)_3COH$	KO–*t*Bu	.87	83	24	41	+21.7	1.4878	89	Ret.	Open flask + N_2
19	.88	$CH_3CHOHC_2H_5$	KO–*s*Bu	.87	206	24	61	+20.6	1.4878	85	Ret.	Sealed tube
20	.88	$CH_3(CH_2)_3OH$	KO–*n*Bu	.87	206	24	54	+17.3	1.4877	72	Ret.	Sealed tube
21	1.43	C_2H_5OH	KOC_2H_5	1.42	203	12	91	+14.66	1.4878	60	Ret.	Sealed tube
22	0.093	$CH_3(OCH_2CH_2)_4OCH_3$[e]	$KO(CH_2CH_2O)_2CH_3$	0.12	210	24	77	+14.53	1.4877	60	Ret.	Sealed tube
23	1.08	$H_2NCH_2CH_2NH_2$	$KNHCH_2CH_2NH_2$	1.07	121	24	57	+ 4.55	1.4878	19	Ret.	Open flask + N_2[f]
24	2.03	CH_3OH	$KOCH_3$	2.01	210	27	79	+ 2.79	1.4876	11	Ret.	Sealed tube
25	1.22	$O(CH_2CH_2OH)_2$	KOH	2.44	200	21	71	− 5.62	1.4878	23	Inv.	Open flask + N_2
26	1.22	$O(CH_2CH_2OH)_2$ + 31% C_2H_5OH	KOH	1.22	160[g]	24	9	− 5.80	1.4877	24	Inv.	Open flask, reflux[h]
27	0.61	$O(CH_2CH_2OH)_2$	KOH	0.61	237	24	61	− 6.70	1.4877	28	Inv.	Open flask + N_2
28	1.22	$O(CH_2CH_2OH)_2$ + 31% H_2O	KOH	1.22	160[g]	24	26	− 7.60	1.4876	31	Inv.	Open flask, reflux[i]
29	1.22	$HOCH_2CH_2OH$	KOH	2.08	190	22	6	−11.71	1.4876	48	Inv.	Open flask, heterog.
30	0.10	$HOCH_2CH_2OH$	$KOCH_2CH_2OH$	0.10	150	24	4	−11.72	1.4886	48	Inv.	Open flask, homogen.
31	1.17	$HOCH_2CH_2OH$ + 20% H_2O	KOH	3.32	230	24	10	−11.92	1.4878	49	Inv.	Sealed tube, heterog.[i]
32	0.70	$HOCH_2CHOHCH_2OH$	$KOCH_2CHOHCH_2OH$	0.70	230	36	38	−12.16	1.4877	50	Inv.	Open flask, heterog.
33	1.04	$HOCH_2CH_2OH$	$KOCH_2CH_2OH$	1.03	212	24	42	−12.43	1.4878	51	Inv.	Open flask, heterog.

[a] Mixture of diastereomers, optically pure at C-4; $[\alpha]^{25}\text{D}$ −11.2° (*c* 11 in benzene), ref. 6. [b] *l* 1 dm., neat. [c] Based on $\alpha^{25}\text{D}$ ±24.3° (*l* 1 dm., neat) for 2-phenylbutane. [d] Homogeneous unless otherwise specified. [e] Contained 5% $CH_3(OCH_2CH_2)_2OH$ by volume. [f] Control run with optically active 2-phenylbutane under the same conditions gave 4% racemization. [g] Bath temperature, solution at reflux. [h] 60% starting material recovered, $n^{25}\text{D}$ 1.5204, $[\alpha]^{25}\text{D}$ −11.8° (*c* 11 in benzene). [i] 40% starting material recovered, $n^{25}\text{D}$ 1.5202, $[\alpha]^{25}\text{D}$ −11.3° (*c* 8 in benzene).

TABLE III: RESULTS OF CLEAVAGE REACTIONS OF SYSTEMS VI, VII, VIII AND X

Run	Starting material		Solvent	Base		Temp., °C.	Time, hr.	2-Phenylbutane				Predom. steric course	Remarks
	Compound	Molality		Nature	Molality			Yld., %	$\alpha^{23-26}\text{D}$[a]	$n^{25}\text{D}$	% opt. purity[b]		
34	(−)-X	0.100	$O(CH_2CH_2)_2O$	$KOC(CH_3)_3$	0.090	150	49	85	+23.0°	1.4877	95	Ret.	Sealed tube
35	(−)-X	.52	$(CH_3)_3COH$	$KOC(CH_3)_3$	.57	150	44	78	+21.8	1.4876	90	Ret.	Sealed tube
36	(−)-X	.096	$CH_3(OCH_2CH_2)_4OCH_3$[c]	$KO(CH_2CH_2O)_2CH_3$	.12	202	24	79	+13.02	1.4875	54	Ret.	Open flask + N_2
37	(−) X	.102	$CH_3(OCH_2CH_2)_2OH$	$KO(CH_2CH_2O)_2CH_3$	.12	202	24	83	+ 3.93	1.4875	16	Ret.	Open flask + N_2
38	(−)-X	.100	$HOCH_2CH_2OH$	$KOCH_2CH_2OH$	.135	210	55	33	−12.56	1.4876	52	Inv.	Open flask + N_2[d]
39	(+)-VIII	.105	$O(CH_2CH_2)_2NH$[e]	$KOC(CH_3)_3$	.105	124	14	92	+21.5	1.4878	89	Ret.	Reflux
40	(+)-VIII	.087	$O(CH_2CH_2)_2O$[f]	KOH	.107	150	60	36	+21.4	1.4808	88	Ret.	Sealed tube
41	(+)-VIII	.082	$(CH_3)_3COH$	$KOC(CH_3)_3$	.10	102	48	64	+20.4	1.4878	84	Ret.	Reflux
42	(+)-VIII	.20	CH_3OH	$KOCH_3$	.40	180	72	30	−10.2	1.4878	42	Inv.	Sealed tube
43	(+)-VIII	.095	$O(CH_2CH_2OH)_2$	$KO(CH_2CH_2O)_2H$	.13	180	50	68	−13.13	1.4876	54	Inv.	Open flask + N_2
44	(+)-VII	1.22	$O(CH_2CH_2OH)_2$	KOH	1.83	210	48	7	+ 7.00	1.4915	29	Inv.	Open flask + N_2
45	(+)-VI	0.108	$O(CH_2CH_2)_2O$	$KOC(CH_3)_3$	0.12	150	48	85	+20.0	1.4876	83	Ret.	Sealed tube
46	(+)-VI	0.085	$CH_3(OCH_2CH_2)_4OCH_3$[g]	$KO(CH_2CH_2O)_2CH_3$	0.14	190	27	85	+ 1.80	1.4864	7	Ret.	Open flask + N_2
47	(+)-VI	1.22	$O(CH_2CH_2OH)_2$	$KO(CH_2CH_2O)_2H$	1.22	250	24	61	− 9.24	1.4876	38	Inv.	Open flask + N_2
48	(+)-VI	1.22	$HOCH_2CH_2OH$	$KOCH_2CH_2OH$	1.16	240	36	71	− 9.98	1.4882	41	Inv.	Sealed tube
49	(+)-VI	0.10	$O(CH_2CH_2OH)_2$	$KO(CH_2CH_2O)_2H$	0.10	210	42	22	−11.94	1.4876	49	Inv.	50% alc. recovd. $n^{25}\text{D}$ 1.5702

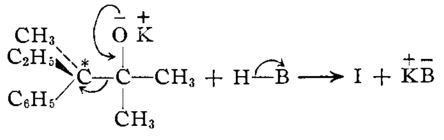
[a] *l* 1 dm., neat. [b] Based on $\alpha^{25}\text{D}$ ±24.3°. (*l* 1 dm., neat) for optically pure 2-phenylbutane. [c] Contained 5% by volume of $CH_3(OCH_2CH_2)_2OH$. [d] 38% recovery of alcohol $n^{25}\text{D}$ 1.5198, $\alpha^{24}\text{D}$ −2.19° (*l* 1 dm., neat); starting material was $\alpha^{27}\text{D}$ −2.03° (*l* 1 dm., neat). [e] Contained 2% $(CH_3)_3COH$. [f] Contained 1% water. [g] Contained 7% by volume of $CH_3(OCH_2CH_2)_2OH$.

unsaturated ketones appeared to have been reduced to their corresponding alcohols.

Attempts were made to cleave (−)-IX in water, nitrobenzene and formamide, but starting material was recovered unchanged in each case. The insolubility of IX in water accounts for its failure to cleave, whereas in the other two cases the base was destroyed by solvent faster than cleavage occurred.

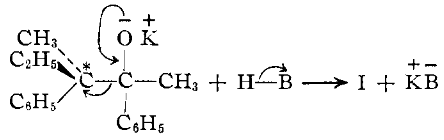
Alcohols (−)-X, (+)-VIII, (+)-VII and (+)-VI were all prepared from optically pure 2-methyl-2-phenylbutanoic acid by procedures that have been previously reported.[4] These systems were cleaved in enough solvents to determine whether they were similar in their behavior to IX, which was examined more thoroughly. The results are recorded in Table III.

Control experiments (see Experimental) established that 2-phenylbutane (I) is optically stable under the conditions of most of these experiments. An exception is run 23 (Table II). In a control experiment, optically active I racemized 4% under the conditions of run 23. System (−)-X failed to cleave in tri-*n*-butylamine and di-*n*-amylamine at temperatures of 225 and 210°, respectively. Apparently these bases are not strong enough to cause reaction.



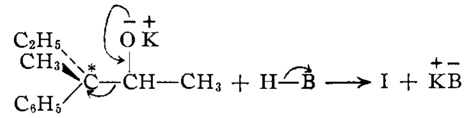
Potassium salt of (−)-X

+ Ketone condensation products



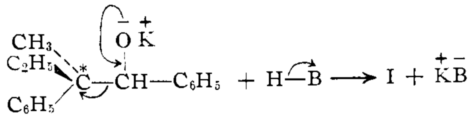
Potassium salt of (+)-VIII

+ $CH_3COC_6H_5$



Potassium salt of (+)-VII

+ Aldehyde condensation products

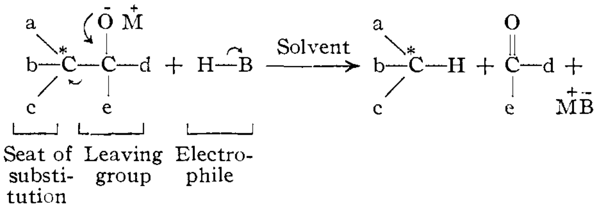


Potassium salt of (+)-VI

+ Aldehyde condensation and disproportion products

Discussion

Evidence is provided in a later paper[8] of this series that homolytic does not compete with heterolytic cleavage in systems VI-X. Since these reactions are base catalyzed, a species such as an alkoxide is undoubtedly undergoing fragmentation, and the general mechanistic class can be defined by the expression formulated. Thus the reaction whose stereochemistry is under observation is that of electrophilic substitution at saturated carbon.



Correlation between Stereochemical Outcome of Electrophilic Substitution and the Dielectric Constant of the Solvent.—The results of Table II indicate that the solvent-electrophile plays a dominant role in controlling the stereochemistry of the electrophilic substitution reaction. In the cleavage of IX in 14 different solvents, the *stereospecificity of the reaction ranges from 93% predominating retention to 51% predominating inversion of configuration.* These results demonstrate that at least two mechanisms are operative; one which occurs with retention and one with inversion of configuration. A third mechanism, one which is stereochemically indiscriminate and leads to racemic product, might also be involved. In no single reaction was a single mechanistic path followed. The task at hand is to identify and describe these mechanisms, and to correlate the structural and environmental factors which control them. In this paper a preliminary correlation of this sort will be made, but detailed discussions of mechanism are reserved for papers V[9a] and VI[9b] of this series.

The solvents employed for cleavage of IX (Table II) differ from one another in many respects. They vary in basicity, acidity, in dielectric constant, in their ionizing and dissociating power, and in the number of proton-donating groups which they contain per unit volume of solvent. Of these properties, the dielectric constant (which to a limited extent also provides a measure of ionizing and dissociating power) correlates best with the stereochemical results. This fact is illustrated by the data of Table IV. This correlation is by necessity crude, since the dielectric constants change with temperature, and the reactions whose results are quoted in Table IV were not run at the same temperature. Nevertheless, when the values of k_{ret}/k_{inv} are arranged in decreasing order, this order is almost the same as the order of increasing dielectric constant. The expression of the stereochemical result in terms of k_{ret}/k_{inv} allows a continuous scale to be constructed which permits the relative rates of the two stereospecific processes to be compared, at least in a primitive sense. The values of k_{ret}/k_{inv} vary by a factor of 84, while the values of the dielectric constant (ϵ) vary between 2 and 46.

The existence of this correlation suggests that some undissociated species such as A gives rise to product with predominantly retained configuration,

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

(9) (a) D. J. Cram, F. Hauck, K. R. Kopecky and W. D. Nielsen, *ibid.*, **81**, 5767 (1959); (b) D. J. Cram, J. L. Mateos, F. Hauck, H. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *ibid.*, **81**, 5774 (1959).

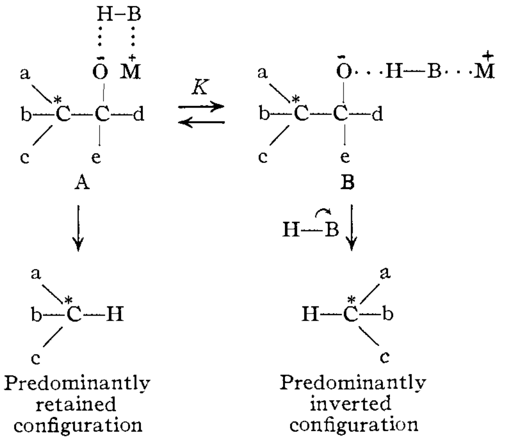
TABLE IV

CORRELATION BETWEEN STEREOCHEMICAL COURSE OF CLEAVAGE REACTIONS OF (−)-3,4-DIMETHYL-4-PHENYL-3-HEXANOL ((−)-IX) AND DIELECTRIC CONSTANT OF THE SOLVENT SYSTEM

Run[a]	Solvent	k_{ret}/k_{inv}	°C.	Normality of electrophiles in medium
16	C_6H_6	28	2^{20}	1
11[b]	$CH_3NHC_6H_5$	17	6^{20}	9
18	$(CH_3)_3COH$	17	11^{19}	13
19	$CH_3CHOHC_2H_5$	12	19^{20}	13
20	$CH_3(CH_2)_3OH$	6	18^{25}	13
21	C_2H_5OH	4	27^{20}	22
23	$H_2NCH_2CH_2NH_2$	1.5	16^{18}	66
24	CH_3OH	1.2	34^{18}	31
27	$O(CH_2CH_2OH)_2$	0.56	35^{20}	18
30	$HOCH_2CH_2OH$	0.35	35^{20}	32
32	$HOCH_2CHOHCH_2OH$	0.33	46^{20}	33

[a] See Table II for experimental details. [b] Table I, paper I of this series.

while a partially or wholly dissociated species such as B forms product with a predominantly inverted configuration. The equilibrium constant, K, would be very sensitive to the dissociating power of the solvent, which in turn correlates with the dielectric constant.



Since the reaction of either A or B involves a proton donor (H–B), the question arises as to whether there is any correlation between the concentration of proton-donating functional groups in the solvents of Table IV, and the ratios of k_{ret}/k_{inv}. In the last column of this table, the *normalities* of the proton-donating functional groups of the media are listed.

Except for ethylenediamine, which is a very weak acid, there exists a crude correlation between the values of k_{ret}/k_{inv}, and the concentration of electrophiles in the medium. The inversion mechanism appears to be favored by a high concentration of H–B, whereas the retention mechanism dominates in media with a low concentration of H–B.

Most of the solvents which give inversion contain the bifunctional units $-OCH_2CH_2OH$. This structural feature undoubtedly enhances the dissociating power of the solvent toward metal salts, since two coördination sites are available to metal cations on each solvent molecule. That such a structural feature is not controlling is shown by the results of runs 22, 36, 37 and 46, in which the electrophile contained this part structure, and yet the reactions went with from 7 to 60% predominant retention of configuration. That inversion of configuration can occur in a solvent without this structure unit is demonstrated by run 42 conducted in methanol. The reaction occurred with 42% predominating inversion.

Effect of Leaving Group on the Steric Course of Electrophilic Substitution.—Although much less data were obtained for systems VI, VII, VIII and X than for IX, the results of Table III indicate that the steric course of the reactions of all five systems shows the same kind of sensitivity to medium effects. System X cleaved in various solvents to give values of k_{ret}/k_{inv} that varied between 38 and 0.28, or by a factor of 135. System VIII gave values that range between 17 and 0.23 (factor of 74), whereas the values obtained for the two cleavages of VII that have been reported thus far (runs 8 and 44) are 3 and 0.56. For VI, the extreme values of k_{ret}/k_{inv} are 10 and 0.33 (factor of 33). Although the nature of the leaving groups of these systems was different enough to make the reactivities of the substances vary a great deal, all of the systems show the same sort of sensitivity toward the medium with respect to the stereochemical course of their reactions. If with each of the five alcohols, the runs are arranged in order of decreasing values of k_{ret}/k_{inv}, the order of solvents which results is the same for each starting material.

Systems that contain an even wider range of types of leaving groups cleave to give product with predominating retention of configuration in N-methylaniline, although the stereospecificity of the reactions could not be accurately measured[2] in many of the systems.

The correlations between the steric course of these reactions and the nature of the solvent are visible in spite of the fact that the other conditions for the runs were far from constant. The temperatures ranged from 72 to 237°, the concentrations of the starting materials varied from 0.1 to 2 molar, the concentrations of the basic catalyst varied from 0.1 to 2 molar, and the pK_a's of the electrophile varied from 16 to an estimated 30.[10] Although these variables play some role in controlling the stereochemical course of the electrophilic substitution reaction, the present data indicate that medium effects dominate.

Experimental

Purification of Solvents.—All solvents used in the cleavage reactions were purified through distillation from sodium metal or the alkoxide formed from sodium and the alcohol. The pentane employed for extraction and chromatography was distilled through a 50-plate (bubble) column, and was free of olefin. Dioxane was purified by the method of Fieser.[11]

Cleavage Reactions.—In the cleavage reactions, the reaction solvent was first saturated with dry nitrogen. The metal was freshly cut under clean mineral oil, cleaned and weighed under dry pentane. The metal was added to the

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[10] This value is estimated for the pK_a of N-methylaniline from the table of pK_a values for various substances listed by W. K. McEwen, THIS JOURNAL, **58**, 1124 (1936).

[11] L. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1941, p. 369.

reaction solvent under nitrogen, and dissolved with the aid of heat where necessary. When potassium was dissolved in diethylene glycol, the mixture had to be swirled to prevent local heating. Potassium could not be dissolved directly in ethylene glycol without explosion. Dry potassium *t*-butoxide was first prepared, added to ethylene glycol, and the *t*-butyl alcohol was distilled from the mixture along with some of the ethylene glycol. When potassium was dissolved in methanol or ethanol, the mixtures were cooled with Dry Ice to control the reactions.

The reactions carried out below or at the boiling point of the reaction medium were run in open systems under a nitrogen atmosphere. Runs made above the boiling points of the medium and at 150° or below were carried out in heavy-walled pressure bottles (100-ml. capacity). Above this temperature, heavy-walled sealed tubes were used. Wood metal-baths heated electrically were employed. The isolation procedure is illustrated as follows:

Run 37.—In 10 ml. of nitrogen-saturated monomethyl ether of ethylene glycol was dissolved 0.254 g. (6.50 mmoles) of freshly cut oil-free potassium. When solution was complete, 1.087 g. (5.64 mmoles) of (–)-2,3-dimethyl-3-phenyl-2-pentanol was added in enough additional solvent to give a total volume of 55 ml. The mixture was maintained in a bath at 202° for 24 hours under a slight nitrogen pressure acting through a spiral condenser. The mixture was cooled, diluted with 2 volumes of water, and extracted 3 times with pentane. The combined extracts were washed 3 times with water, dried, evaporated to a small volume through a two-foot Vigreux column, and the residue was adsorbed on 70 g. of activity I alumina.[12] The desired product (2-phenylbutane) was eluted with pentane, and the solvent was evaporated through a two-foot Vigreux column to an oil. This material was twice distilled through a micro-Claisen still at 40 mm. pressure to give 0.628 g. (83%) of 2-phenylbutane, $n^{25}\text{D}$ 1.4875, $\alpha^{26}\text{D}$ +3.93° (l 1 dm., neat). This material possessed an infrared spectrum superimposable on that of authentic 2-phenylbutane.

The product of runs 16, 18, 19, 20 and 33 also possessed infrared spectra identical to that of authentic 2-phenylbutane. From the chromatogram of the product from run 16 was eluted with ether a colorless liquid (0.316 g. from 1.0 g. of starting [(–)-IX], $\alpha^{25}\text{D}$ –7.17 (l 1 dm., neat)). The infrared spectrum of this material showed the presence of starting material and ketones (1650 cm.$^{-1}$ in infrared and $\lambda_{\max}$ 242 mμ in ultraviolet spectra). When treated with 2,4-dinitrophenylhydrazine in ethanol and hydrochloric acid, 30 mg. of a red derivative was isolated, m.p. 125–129°. This material was not characterized further, but seemed to be a mixture of derivatives of unsaturated ketones (infrared and ultraviolet spectra).

Optically pure starting material was isolated from runs 31, 32, 33, 38 and 49. Acetophenone, characterized as its 2,4-dinitrophenylhydrazone, was isolated from run 40.

Control Runs.—As a control on runs which involved potassium glycoxide as base and 2-phenylbutane as product, the following run was made. A 1 *M* solution of potassium diethylene glycoxide in diethylene glycol was prepared, and 50 ml. of this solution was refluxed at 244° for 24 hours with 0.300 g. of 2-phenylbutane, $n^{25}\text{D}$ 1.4878, $\alpha^{26}\text{D}$ –12.4° (l 1 dm., neat). Starting material (0.210 g.) was recovered in the usual way, $n^{25}\text{D}$ 1.4876, $\alpha^{25}\text{D}$ –12.4° (l 1 dm., neat).

As a control for those runs in which potassium *t*-butoxide was employed and 2-phenylbutane was product, the following experiment was carried out. To a 0.8 molar solution of potassium *t*-butoxide in *t*-butyl alcohol (10 ml.) was added 0.35 g. of 2-phenylbutane, $n^{25}\text{D}$ 1.4878, $\alpha^{25}\text{D}$ +16.30° (l 1 dm., neat). The solution was sealed in a heavy-walled tube and heated to 200° for 20 hours. Recovery of 2-phenylbutane in the usual way gave 0.25 g. of material, $n^{25}\text{D}$ 1.4878, $\alpha^{25}\text{D}$ +15.49° (l 1 dm., neat). In this treatment, 2-phenylbutane was 5% racemized. All of the runs of Table I that involve potassium *t*-butoxide as base were run at temperatures of 150° or less, and at lower base concentrations.

As a control for run 23, under the condition of the experiment, optically active 2-phenylbutane was found to racemize 4%. A procedure similar to those reported above was employed.

LOS ANGELES 24, CALIF.

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[12] H. Brockmann and H. Schodder, *Ber.*, **74B**, 73 (1941).

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

Electrophilic Substitution at Saturated Carbon. III. Effect of Solvent Composition on Reaction Path[1]

BY DONALD J. CRAM, KARL R. KOPECKY, FRED HAUCK AND ALBERT LANGEMANN

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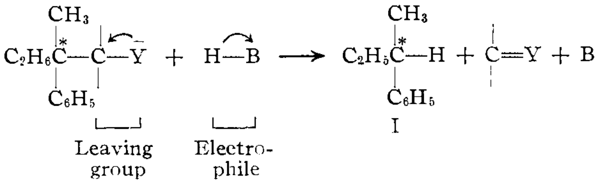
The stereochemistry of the base-catalyzed cleavage reactions of three tertiary alcohols (VIII, IX and XIV) and two ketones (V and XV) have been studied. In dioxane with about 5% diethylene or ethylene glycol as a proton source (electrophile), the three alcohols cleave to give *electrophilic substitution at saturated carbon which occurs with from 69 to 95% predominating retention of configuration. In diethylene glycol, these alcohols cleave with from 41 to 58% predominating inversion.* In all three systems, as the amount of glycol in dioxane is increased, the steric course undergoes a smooth transition from predominant retention to predominant inversion of configuration. In cleavages of the three tertiary alcohols in dioxane with 1% *t*-butyl alcohol as the proton source, electrophilic substitution occurs with from 84 to 96% predominating retention of configuration. Ketones V and XV cleave in dioxane with 1% *t*-butyl alcohol as proton source with 74 and 61% predominating retention, respectively, and in diethylene glycol with 38 and 17% predominating inversion, respectively. The stereospecificity of the reactions of XIV in dioxane and of VIII in diethylene glycol were found to decrease with increasing temperature. In the intermediate solvent, methanol, alcohol IX gave product with 25% predominating inversion at 180°, and with 9% predominating inversion at 210°.

The previous papers[2] in this series report the results of a survey of cleavage reactions and of solvent–electrophile systems suitable for determining the stereochemistry and mechanism of electrophilic substitution at saturated carbon. Eleven compounds which correspond to the general structure formulated (the leaving group, C–Y, was varied) were found to cleave to give 2-phenylbutane (I). The steric courses of the reactions were found to correlate with the dielectric constants and with the concentration of proton donors in the medium.



$$\text{C}_2\text{H}_6\overset{*}{\text{C}}(\text{CH}_3)(\text{C}_6\text{H}_5)\text{—C—Y} + \text{H—B} \longrightarrow \text{C}_2\text{H}_5\overset{*}{\text{C}}(\text{CH}_3)(\text{C}_6\text{H}_5)\text{—H} + \text{C=Y} + \text{B}$$

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[1] This work was sponsored by the Office of Ordnance Research, U. S. Army.

[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).