

potassium. When the potassium had reacted, the excess *t*-butyl alcohol was evaporated and the resulting white solid was dried in the tube under vacuum overnight. A nitrogen atmosphere was again provided and 25.0 ml. of dimethyl carbonate added followed by 1.25 g. (0.005 mole) of alcohol I. The tube was sealed in the usual manner and then immersed in a Wood metal-bath at 180° for 72 hours. At the end of the reaction, a crystalline solid was observed at the bottom of the tube. When opened at -78°, a gas was evolved.

The basic solution was extracted with pentane. Examination of the aqueous layer revealed the absence of any acid. The pentane concentrate was chromatographed on 100 g. of Activity I alumina, and the first two 100-ml. fractions contained 2-phenylbutane, weight 0.160 g. (24%), n_D^{20} 1.4877, α_D^{20} - 18.08° (neat, 1 dm.), 74% net retention. The developer was changed to pentane-ether (one-to-one), and six fractions of eluant were collected. After removal of the solvent from the combined six fractions, the oily residue was saponified with 10% sodium hydroxide and the resulting acid purified. Sublimation of this solid acid gave 0.062 g. of impure benzoic acid, m.p. 112-118°. Recrystallization of the sublimate from water produced white crystals, m.p. 121-122°, undepressed by admixture with an authentic sample. When 2-phenylbutane was subjected to the same reaction conditions, no ester was formed.

Control Runs.—Previously,^{2b} 2-phenylbutane was found not to racemize when heated at 240° for 24 hours in a 1 *M* solution of potassium diethylene glycolide in diethylene glycol. This result serves as a control for runs 1-5 conducted at 170-200° with primary alkoxide catalysts. As a control for runs 6 and 7 (conditions for the latter run were the more drastic, since dimethyl sulfoxide enhances the activity of the base), 2-phenylbutane (α_D^{25} + 3.48°, neat, 1 dm.) was submitted to the conditions of run 7. Recovered material was not racemized (α_D^{25} + 3.45°, neat, 1 dm.). As a control for runs 8 and 9, 2-phenylbutane (α_D^{25} + 23.50° neat, 1 dm.) was submitted to the conditions of run 9 except that potassium was substituted for lithium. Recovered material was 88% racemized (α_D^{25} + 2.82° neat, 1 dm.). Previously,^{2b} 2-phenylbutane was found to racemize only 5% when heated for 20 hours in an 0.8 *M* solution of potassium *t*-butoxide at 200°. Extensive unpublished work has established that potassium alkoxides racemize 2-phenylbutane at rates either faster than or equal to the rates for lithium alkoxides. Clearly no racemization could have occurred in runs 10 or 21. As a control for runs 11-13, 2-phenylbutane (α_D^{25} + 6.90°, neat, 1 dm.) was found to racemize only 17% when submitted to the conditions of run 13. As a control for runs 14-20, 2-phenylbutane (α_D^{25} + 5.82°, neat, 1 dm.) was submitted to the conditions of run 20, and the recovered material was only 3% racemized (α_D^{25} + 5.64°, neat, 1 dm.).

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

Electrophilic Substitution at Saturated Carbon. IX. Stereochemistry at Secondary Carbon¹

BY DONALD J. CRAM AND BRUCE RICKBORN

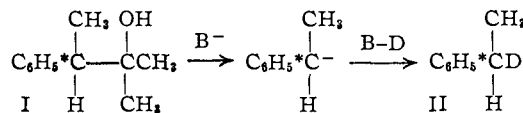
RECEIVED OCTOBER 4, 1960

Optically active phenylethane-1-*d* was produced by the base-catalyzed cleavage of (-)-2-methyl-3-phenyl-2-butanol in *t*-butyl alcohol-*O-d* and ethylene glycol-*O,O'-d*, whose preparation is described. The reaction proceeded with about 75% predominating retention in the tertiary alcohol and 50% predominating inversion in the glycol. Cleavage of (+)-2,3-diphenyl-3-methyl-2-pentanol in *t*-butyl alcohol-*O-d* gave 2-phenylbutane-2-*d* with 87% predominating retention, and over 80% deuterium in the α -position. The same system in ethylene glycol-*O,O'-d* gave 2-phenylbutane-2-*d* with 65% predominating inversion and 91% deuterium in the α -position. These results indicate that solvent serves as proton or deuterium donor in these reactions, and that electrophilic substitution at secondary and tertiary benzyl systems involve similar stereochemical paths.

The change of reaction site from tertiary to secondary to primary carbon is a logical and time-honored approach to the study of stereochemistry and reaction mechanism of substitution at saturated carbon. When the reaction in question involves a carbanion rather than a carbonium ion as intermediate, the problem of leaving group and electrophile is more troublesome than the corresponding problem of leaving group and nucleophile in nucleophilic substitution. In contrast to the long list of nucleophiles, only a few electrophiles are available, the best of which are proton donors. Although hydroxylic solvents react with tertiary carbanions to produce optically active products,² reactions with secondary carbanions lead to products incapable of optical activity, irrespective of stereochemical course. However, deuterium donors can in principle react with asymmetric secondary carbanions to give asymmetric products, as is illustrated by the system chosen for the present study.

(1) This work was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of this fund.

(2) D. J. Cram, J. Allinger and A. Langemann, *Chemistry & Industry*, 919 (1955).

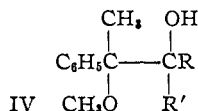
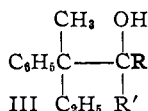


The advantages of this system are manifold: (1) The base-catalyzed cleavage of systems such as III and IV have been studied in detail, and provide a basis for comparison of the behavior of secondary and tertiary carbanions.³ (2) Reaction product II is the simplest secondary benzyl system capable of optical activity, and has been shown to possess a small but measurable rotation.⁴ (3) The absolute configuration of II has been demonstrated,⁵ and that of I is established by its synthesis from

(3) (a) D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, *J. Am. Chem. Soc.*, **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); (f) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *ibid.*, **81**, 5774 (1959).

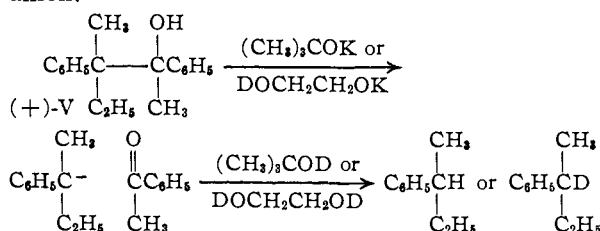
(4) E. L. Ellel, *ibid.*, **71**, 3970 (1949).

(5) These configurational correlations are summarized by J. A. Mills and W. Klyne in "Progress in Stereochemistry," edited by J. Klyne, Butterworths Scientific Publications, London, 1954, p. 187.

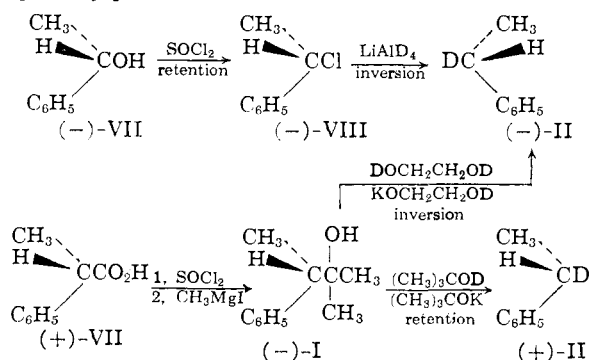


optically active materials of known configuration. (4) A preliminary study of a number of alcohols whose cleavage could in principle lead to ethylbenzene revealed that Compound I was the easiest to prepare and gave the desired product most free of contaminants.

Use of this reaction (I \rightarrow II) for the study of electrophilic substitution depends on the absence of a mechanism in which acetone as a leaving group donates a proton directly to the 1-phenylethyl anion. Such a process would produce undeuterated ethylbenzene incapable of optical activity. As an independent probe of this possibility, (+)-2,3-diphenyl-3-methyl-2-pentanol ((+)-V) was cleaved in *t*-butyl alcohol-*O-d* and in ethylene glycol-*O-O'-d*₂ to see if the deuterated solvent or the undeuterated acetophenone produced served as a source of electrophiles for the 2-phenyl-2-butyl anion.



Configurations and Rotations of Starting Materials and Products.—The absolute configurations of (–)-1-phenylethanol ((–)-VI) and (+)-2-phenylpropanoic acid ((+)-VII) as previously determined⁶ are formulated, and provide the foundation for knowledge of the configurations of I and II. Since optically pure (+)-2-phenylpropanoic acid was converted to (–)-2-methyl-3-phenyl-2-butanol without involvement of the asymmetric carbon atom, the absolute configuration and magnitude of rotation of the latter compound in an optically pure state is established.



Proof that (–)-1-phenylethanol is converted with predominant retention to (–)-1-chlorophenylethane, (–)-VIII, with thionyl chloride has been summarized elsewhere.⁷ Since lithium aluminum

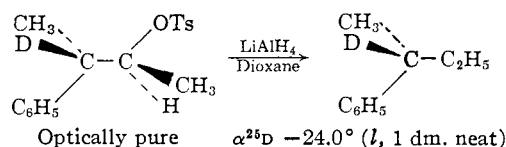
(6) (a) P. A. Levene and P. G. Stevens, *J. Biol. Chem.*, **89**, 471 (1930); (b) H. I. Bernstein and F. C. Whitmore, *J. Am. Chem. Soc.*, **61**, 1324 (1939).

(7) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 114.

deuteride reduction of optically active secondary halides has been demonstrated to proceed with predominant inversion,⁸ the configurations of (–)-II and (–)-VIII become interrelated, and the absolute configuration of phenylethane-1-*d* becomes clear.

Unfortunately, the rotation of optically pure phenylethane-1-*d* is obscured by lack of knowledge of the rotation of optically pure 1-chlorophenylethane. Only maximum and minimum values have been established [$\alpha^{25}\text{D}$ 118 \pm 8° (*l*, 1 dm., neat)].⁹ The average of these values was used to calculate a probable maximum rotation of $\alpha^{25}\text{D}$ 0.63 \pm 0.05° (*l*, 1 dm., neat) for phenylethane-1-*d*.¹⁰ The actual conversion of 1-chlorophenylethane to phenylethane had been carried out⁴ with halide of known but not maximum rotation. The uncertainty in the above calculated value for the rotation of optically pure phenylethane-1-*d* is magnified by the possibility that the conversion of (–)-1-chlorophenylethane to (–)-phenylethane-1-*d* was accompanied by a small amount of racemization, as was the similar reduction of 2-methanesulfonylbutane.⁸ However, this minor ambiguity in no way vitiates the conclusions reached in the next section.

The relative configurations of (+)-2,3-diphenyl-3-methyl-2-pentanol ((+)-V) and of 2-phenylbutane have been established previously.^{3a} Although the rotation of optically pure 2-phenylbutane has been previously determined, the rotation of optically pure 2-phenylbutane-2-*d* was needed for the current study. This compound was prepared¹¹ by reduction with lithium aluminum hydride of the tosylate of optically pure *D-erythro*-3-phenyl-2-butanol-3-*d*.¹² Reduction of the undeuterated but optically pure *erythro*-tosylate was shown in an earlier investigation to lead to



optically pure 2-phenylbutane.¹³ A similar reduction of the optically pure *threo*-tosylate was found¹³ to proceed with 10% racemization due to 5% rearrangement of the phenyl from C-2 to C-3 during the reduction. This rearrangement involved a symmetrical phenonium ion as intermediate and led to racemic product. A similar rearrangement in the *erythro* series would have gone undetected since rearranged and unrearranged 2-phenylbutane would have had the same configuration.¹³

In the reduction of the tosylate of *D-erythro*-3-phenyl-2-butanol-3-*d*, any rearrangement would lead to optically pure 2-phenylbutane-3-*d*. That

(8) G. K. Helmkamp and B. Rickborn, *J. Org. Chem.*, **22**, 479 (1957).

(9) R. L. Burwell, A. D. Shields and H. Hart, *J. Am. Chem. Soc.*, **76**, 908 (1954).

(10) A. Streitwieser, J. R. Wolfe and W. D. Schaeffer, *Tetrahedron*, **6**, 338 (1959).

(11) The authors wish to thank Dr. J. Tadanier for this part of the investigation.

(12) D. J. Cram and J. Tadanier, *J. Am. Chem. Soc.*, **81**, 2737 (1959).

(13) D. J. Cram, *ibid.*, **74**, 2149 (1952).

TABLE I
RESULTS OF CLEAVAGE REACTIONS OF 2-METHYL-3-PHENYL-2-BUTANOL (I) TO ETHYLBENZENE (II)

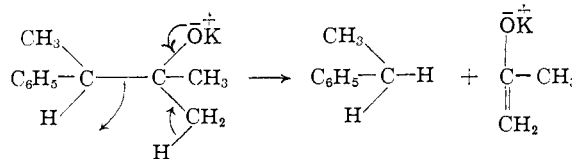
Run	Substrate concn., <i>M</i>	Solvent	Base Nature	Base Concen., <i>M</i>	Temp., °C.	Time, hr.	Yield, %	$\alpha^{25}\text{D}$ heat	Steric course
1	0.07	O(CH ₂ CH ₂) ₂ O	KOC(CH ₃) ₃	0.16	150	18	60
2	.15	(CH ₃) ₃ COH	KOC(CH ₃) ₃	.20	135	42	Trace
3	.18	(CH ₃) ₃ COH	KOC(CH ₃) ₃	.30	150	74	18
4	.15	HOCH ₂ CH ₂ OH	KOCH ₂ CH ₂ OH	.20	200	18	0
5	.16	HOCH ₂ CH ₂ OH	KOCH ₂ CH ₂ OH	.15	240	84	10
6	.43	(CH ₃) ₃ COD ^a	KOC(CH ₃) ₃	.53	160	120	68	+0.44 ± 0.02 ^{ob}	75 ± 9% ret. ^{c,d}
7	.60	DOCH ₂ CH ₂ OD ^e	KOCH ₂ CH ₂ OD	.30	250	151	35	-0.31 ± 0.01 ^{of}	51 ± 5% inv. ^e

^a Contained 0.97 atom of D per mole (combustion analysis). ^b *l* = 1 dm. Based on value of $\alpha^{25}\text{D}$ 0.63 ± 0.05° (1 dm., neat) for optically pure 1-phenylethane-1-*d*. The steric course was calculated after correcting the observed rotation for: (1) the optical purity of starting material (98% optically pure); (2) incompletely deuterated solvent. The results were not corrected for solvent-deuterium dilution due to acetone product exchange with solvent or to ring deuteration. ^d Combustion analysis of ethylbenzene indicated 1.08 atoms of D per molecule. Infrared spectrum showed some aromatic C-D stretch (4.5 μ); value is corrected for 3% contamination of ethylbenzene with pentane, as shown by vapor phase chromatographic analysis. ^e Contained 1.95 atoms of D per molecule (combustion analysis).

rearrangement occurred to only a slight extent was shown as follows. The alcohol used for preparation of the tosylate contained 0.94 atom of deuterium per molecule in the 3-position, and the 2-phenylbutane product contained 0.94 atom of deuterium per molecule. The n.m.r. spectrum of this deuterated product was compared with that of ordinary 2-phenylbutane, and the absorption due to the tertiary benzyl hydrogen in the latter sample was very weak in the deuterated sample. From a comparison of the areas under the two curves, it is clear that the deuterated sample contained not less than 0.80 atom of deuterium at C-2. Thus, the reduction of the tosylate could not have involved more than 14% phenyl migration. The rotation of this optically pure deuterated 2-phenylbutane was found to be $\alpha^{25}\text{D}$ -24.0° (*l* 1 dm., neat) as compared to undeuterated material which has a rotation, $\alpha^{25}\text{D}$ -24.3° (*l* 1 dm., neat).¹⁴

Source of Electrophile in Cleavage Reactions.—Table I records the results of base-catalyzed cleavage of 2-methyl-3-phenyl-2-butanol to ethylbenzene. Runs 1-5 were made in non-deuterated solvent to determine the conditions needed for the reaction, whereas runs 6 and 7 were carried out in *t*-butyl alcohol-*O-d* (97% deuterated) and in ethylene glycol-*O,O'-d*₂ (98% deuterated), respectively. The 75 ± 9% predominating retention observed with the tertiary alcohol (run 6) and 51 ± 5% predominating inversion with glycol (run 7) set lower limits on the amount of deuterium which solvent donated to the benzyl position during the course of the reaction. The acetone produced or its condensation products as well as the starting alcohol undoubtedly diluted the deuterated solvent with protonated solvent which lowered the purity of the deuterated *t*-butyl alcohol-*O-d* to an average of about 85% throughout run 6, and of the deuterated ethylene glycol to an average of about 95% throughout run 7. These values were calculated from the molar concentrations of substrate and solvent at the beginning of the reaction, and of acetone after one half-life (the reasonable assumption was made that hydrogen-deuterium exchange between acetone and solvent occurred faster than the cleavage reaction). Clearly the leaving group (acetone) could have provided protons to the benzyl

carbon atom in only minor amounts if at all in these reactions. Thus either single or multistage processes that contain the essentials of the reaction formulated account for little if any of the observed product.



The results of cleavage of (+)-2,3-diphenyl-3-methyl-2-pentanol in deuterated solvents (Table II) point to a similar conclusion. Runs 8 (solvent (CH₃)₃COH) and 9 (solvent (CH₃)₃COD) gave the same steric result (~87% retention). The 2-phenylbutane produced was 87% deuterated in the 2-position in run 9, and only 81% in run 10. Only the concentration of the substrate was varied in these two runs, and the product of lower deuterium content was associated with the higher concentration of substrate. Thus the deuterated *t*-butyl alcohol is diluted with ordinary alcohol, both by addition of the protonated substrate, and by rapid exchange with the α -hydrogens of the acetophenone (or its condensation products) produced as the reaction proceeds. It is estimated that at half reaction, the solvent was 7% (CH₃)₃COH in run 9, and 13% (CH₃)₃COH in run 10. Clearly acetophenone as a leaving group was not the immediate source of electrophiles in the production of 2-phenylbutane-2-*d* since deuterium could come only from the solvent.

A similar situation was encountered when ethylene glycol and its deuterated counterpart were employed in runs 13 and 14. Both cleavage reactions gave essentially equivalent stereochemical results (64 ± 1%), and ethylene glycol-*O,O'-d*₂ gave 2-phenylbutane 91% deuterated in the 2-position. The time-average deuterium content of the solvent was calculated to be 97%. The approximately 6% excess non-deuterated 2-phenylbutane may be due to protium dilution of solvent by base-catalyzed and reversible exchange of O-D and C-H by an oxidation-reduction process involving acetophenone and solvent (Oppenauer-Meerwein-Ponndorf reactions). In any case, not

(14) D. J. Cram, *J. Am. Chem. Soc.*, **74**, 2137 (1952).

TABLE II
 CLEAVAGE OF OPTICALLY PURE (+)-2,3-DIPHENYL-3-METHYL-2-PENTANOL ((+)-V)

Run	Solvent	Subst. concn., M	Base		Temp., °C.	Time, hr.	% yld.	α^{25D} ^a	Predom. steric course ^b	% α -d
			Nature	Concn., M						
8	(CH ₃) ₃ COH	0.20	KOC(CH ₃) ₃	0.20	130	68	70	+20.99°	87% ret.	..
9	(CH ₃) ₃ COD ^c	.21	KOC(CH ₃) ₃	.20	130	60	81	+21.17	88% ret.	87 ^d
10	(CH ₃) ₃ COD ^c	.39	KOC(CH ₃) ₃	.20	130	48	91	+21.09	88% ret.	81 ^e
11	HOCH ₂ CH ₂ OH	.16	NaOCH ₂ CH ₂ OH	.12	185	79	61	-15.32	63% inv.	..
12	DOCH ₂ CH ₂ OD ^f	.16	NaOCH ₂ CH ₂ OD	.12	185	79	63	-15.76	65% inv.	91 ^d

^a $l = 1$ dm., neat. ^b Based on values of $\alpha^{25D} \pm 24.3^\circ$ for optically pure 2-phenylbutane-2-d, and $\alpha^{25D} \pm 24.0^\circ$ for optically pure 2-phenylbutane-2-d ($l = 1$ dm., neat). ^c Contained 0.97 atom of D per mole (combustion analysis). ^d Analyzed by infrared analysis of benzyl C-D band at 4.71 μ ; no ring deuteration occurs at the temperatures of these reactions. ^e This same value was obtained by both infrared (see *d*) and combustion analysis. ^f Contained 1.95 atoms of D per molecule (combustion analysis).

more than 6% of product could have been formed by direct proton abstraction from the acetophenone leaving group by the 2-phenyl-2-butyl anion.

In both *t*-butyl alcohol and ethylene glycol, the same stereochemical result was observed in deuterated and non-deuterated solvent. In the former solvent retention competed with racemization, and in the latter, inversion competed with racemization. *These results could have been obtained only if the three kinds of stereochemical processes possessed the same kinetic isotope effect. This fact provides strong evidence for carbanion intermediates for all three processes. Had any of the three stereochemical processes involved a mechanism in which the carbon-carbon bond was broken and a carbon-hydrogen bond was made in the same transition state, the above result would be highly improbable.*

Comparison of Electrophilic Substitution at Secondary and Tertiary Carbon.—A remarkable similarity between the steric courses of electrophilic substitution at secondary and tertiary benzyl carbon is visible in the data of Table III. In the tertiary alcohol, both systems gave high retention, and in the glycol they gave about the same amount of inversion. Somewhat more strenuous reaction conditions were required for cleavage when R = H than when R = C₂H₅, a fact which probably reflects the release of more internal strain in the cleavage of the system with R = C₂H₅. On electronic grounds, the system with R = H might be expected to cleave with more ease, since both inductive effects and a lower degree of steric inhibition of resonance should combine to make the 1-phenylethyl anion more stable than the 2-phenyl-2-butyl anion.

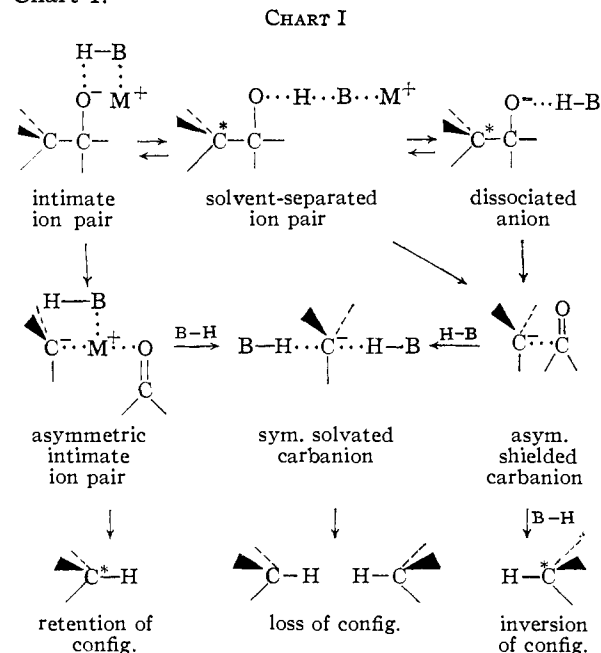
The general mechanism involving asymmetrically enveloped carbanions as discrete intermediates^{3f} would appear to apply to the cleavage of 2-methyl-3-phenyl-2-butanol. The multistage character of this mechanism is in harmony with the insensitivity of the steric course of the reaction to the degree of ramification at the seat of substitution. Partitioning between various reaction paths of a high energy, symmetrical carbanion in an asymmetric environment of proton donors, leaving group and metal cation should be little subject to steric effects. Although secondary and tertiary benzyl anions probably differ somewhat in stability, if their protonations are very fast and exothermic, their stereochemical fates should be quite similar. The similarity between the result of substitution at secondary and tertiary carbon supports a mech-

 TABLE III
 COMPARISON BETWEEN SUBSTITUTION AT SECONDARY AND TERTIARY CARBON

Run	R	Solvent	Temp., °C.	Time, hr.	% yld.	Predom. steric course
$\text{CH}_3-\overset{\text{R}}{\underset{\text{C}_6\text{H}_5}{\text{C}}}-\overset{\text{O}^+\text{K}}{\underset{\text{CH}_3}{\text{C}}}-\text{CH}_3 \xrightarrow{\text{B-H(D)}} \text{CH}_3-\overset{\text{R}}{\underset{\text{C}_6\text{H}_5}{\text{C}}}-\text{H(D)} + \overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3$						
35 ^a	C ₂ H ₅	(CH ₃) ₃ COH	150	44	78	90% ret.
6	H	(CH ₃) ₃ COD	160	55	33	71 ± 9% ret.
38 ^a	C ₂ H ₅	HOCH ₂ CH ₂ OH	210	120	68	52% inv.
7	H	DOCH ₂ CH ₂ OD	250	150	35	51 ± 5% inv.

^a Data taken from Table III of ref. 3b.

anism whose rate-limiting transition states involves little if any direct involvement of proton donors with either the front or back of the incipient carbanion. The mechanistic scheme most compatible with the variety of facts is summarized in Chart I.



Experimental

(-)-2-Methyl-3-phenyl-2-butanol (I).—Resolution of 2-phenylpropanoic acid was accomplished by slightly modifying the procedure of Arcus and Kenyon.¹⁵ The acid

(15) C. L. Arcus and J. Kenyon, *J. Chem. Soc.*, 916 (1939).

(424 g. or 2.82 moles) and strychnine (945 g. or 2.82 moles) formed a very difficultly soluble salt which was dissolved first in chloroform in order to get it into the recrystallization solvent, 80% aqueous ethanol. Seven recrystallizations and subsequent decomposition of the salt gave 53.5 g. of (+)-2-phenylpropanoic acid, $\alpha^{25D} + 99.1^\circ$ (l 1 dm., neat), b.p. 116–117° at 2.2 mm. A rotation of $\alpha^{25D} + 98.8^\circ$ (l 1 dm., neat) has been previously reported for this acid.¹⁶ Its rotation varies inversely with temperature, 0.74% per degree in the neighborhood of 25°.

This acid (12.0 g.) was converted to its acid chloride¹⁶ (12.8 g.) with thionyl chloride in the usual way, b.p. 78–80° at 5 mm. The acid chloride (12.8 g. or 0.076 mole) was added to a stirred ether solution of 0.30 mole of methylmagnesium iodide in ether. Excess Grignard reagent was decomposed at 0° with ammonium chloride, and the usual isolation procedure gave 9.6 g. (77%) of the desired (-)-I, b.p. 75–77° at 2 mm., $\alpha^{25D} - 20.40^\circ$ (1 dm., neat). The alcohol solidified on standing, m.p. 43–44°, $[\alpha]^{25D} - 16.5^\circ$ (c 1.6, CHCl₃).

Anal. Calcd. for C₁₁H₁₆O: C, 80.44; H, 9.84. Found: C, 80.31; H, 10.05.

That no racemization occurred in any of the above steps was demonstrated by repeating the procedure several times with partially active acid as starting material. Different times were used in the thionyl chloride treatment of the acid, and the acid chloride was sometimes distilled and sometimes not before the next step. In one case the methyl ester of the acid was substituted for the acid chloride. In all preparations the ratios of the rotations of starting material and product were the same.

t-Butyl Alcohol-*O-d*.—Pure *t*-butyl alcohol, 176 g., was treated with six successive 37-g. portions of D₂O (>99.5% D). After each addition of D₂O the azeotrope (*ca.* 20% D₂O by weight) was fractionally distilled from the mixture, and the residue retained for further exchange work. The final azeotrope, 205 g., was treated with 35 g. (0.84 mole) of calcium hydride (very vigorous reaction), and the resulting slurry was refluxed for 3 hr. The alcohol was then distilled, b.p. 81.1–81.2° (uncor.), wt. 130 g. This material solidified when allowed to stand, and analyzed by the combustion and falling drop method¹⁷ for 0.97 atom of D per molecule.

In a second preparation, the final azeotrope (382 g.) was dried with 184 g. of calcium oxide (reagent grade material purified by heating in a muffle furnace at 1150°F. for 2 days, then stored in an evacuated desiccator over phosphorus pentoxide). After the first fairly vigorous initial reaction had subsided, the mixture was refluxed for 18 hr., distilled, and the distillate was again refluxed for 24 hr. with a fresh 100 g. of calcium oxide and redistilled to give 272 g. of *t*-butyl alcohol-*O-d*, b.p. 81.2° (uncor.), 90% yield. The n.m.r. absorption indicated this sample contained 0.98 atom per molecule.

Ethylene Glycol-*O,O'-d*₂.—Ethylene carbonate (100 g. or 1.14 moles) was mixed with 100 g. (5.0 moles) of D₂O (>99.5% D) and 1.0 g. of anhydrous potassium carbonate, and heated at 100°. Shortly after solution was complete, a steady evolution of carbon dioxide began, and continued for several hours. After 16 hours, the excess water (76 g.) was distilled at atmospheric pressure and retained for future use. The residue was cooled and distilled, b.p. 77–78° (3.3 mm.), wt. 68 g. This material was again distilled from 1 g. of clean sodium metal, and analyzed by the combustion and falling drop method¹⁷ for 1.95 atoms of D per molecule.

Use of mole-to-mole ratio of D₂O to carbonate in this reaction results in formation of polyethylene glycols.

Cleavage of (-)-2-Methyl-3-phenyl-2-butanol.—The apparatus and conditions for these reactions were essentially those reported for previous cleavage reactions carried out in sealed tubes.⁸ Because of the lower boiling point of ethylbenzene as compared to 2-phenylbutane, considerable care had to be taken in separating the pentane from the ethylbenzene. A long Vigreux column was employed. Last traces of pentane could not be removed from ethylbenzene by distillation through a short path still. In run 6, the final product was shown to contain 3% pentane by vapor phase chromatographic analysis. Comparisons with known

mixtures were employed in this analysis. Cleavage in ethylene glycol-*O,O'-d*₂ presented an additional problem, for at the temperature necessary for a reaction (run 7), the starting material dehydrated somewhat. After the usual extraction, wash, alumina chromatography and short path distillation, the product was found to have a rotation of $\alpha^{25D} + 0.80^\circ$ (1 dm., neat), due to contamination with optically active olefin. The entire sample (*ca.* 200 mg.) was subjected to vapor phase chromatography on a 4-foot column packed with 30% didecyl phthalate supported on Chromosorb W, and operated at 10 p.s.i. at 100° with helium as carrier gas. Retention times and approximate quantities of material present were: pentane, 2–4 min., 2–3%; ethylbenzene, 20–36 min., major constituent; olefin 106–132 min., 3–5% (two peaks of nearly equal intensity, not completely resolved, presumably a mixture of 2-methyl-3-phenyl-1-butene and 2-methyl-3-phenyl-2-butene). The condensed ethylbenzene was redistilled to separate it from traces of didecyl phthalate which had been washed from the column. Mechanical losses of product in these operations amounted to about 40%.

(-)- and Racemic-2-Phenylbutane-2-*d*.—Resolution of racemic *erythro*-3-phenyl-2-butanol-3-*d* (prepared in connection with a previous investigation)¹² was accomplished by the method previously reported for its undeuterated counterpart.¹⁸ The acid 3-nitrophthalate after resolution through its cinchonidine salt gave material, m.p. 139–140°, $[\alpha]^{25D} + 34.4^\circ$ (c 3% ethanol), literature¹⁸ (for undeuterated material), m.p. 144–145°, $[\alpha]^{25D} + 34.2^\circ$. Hydrolysis of this material gave (+)-*D-erythro*-3-phenyl-2-butanol-3-*d*, n^{25D} 1.5154, $\alpha^{25D} + 0.19 \pm 0.04^\circ$ (l 1 dm., neat), 0.94 atom of D per molecule (combustion and falling drop method).¹⁷ The sign of rotation of this stereomer is opposite to the sign of the rotation of the undeuterated stereomer, which was found to be $\alpha^{25D} - 0.65^\circ$ (l 1 dm., neat).¹⁸ This observation is not surprising in view of the low magnitude of each rotation. The deuterated alcohol was converted to the tosylate which was reduced with lithium aluminum hydride by the method used for its nondeuterated counterpart, except that dioxane was substituted for ether in the procedure.¹³ Olefin was removed as previously,¹³ and the 2-phenylbutane-2-*d* produced had the following properties: n^{25D} 1.4876, $\alpha^{25D} - 24.0^\circ$ (l 1 dm., neat), 0.94 atom of D per molecule (combustion analysis and falling drop method).¹⁷

For purposes of preparing a larger amount of racemic 2-phenylbutane-2-*d* for use as a standard in infrared analysis, the following procedure served.¹⁹ A reaction vessel with an upper and lower chamber separated by a fritted disk and fitted with dropping funnel (upper chamber) and gas and vacuum outlets (both chambers) was thoroughly dried in a stream of dry nitrogen. Fresh anhydrous ether (Molecular Sieves), 375 ml., and 12.5 ml. of sodium-potassium alloy was placed in the upper chamber under nitrogen. This mixture was supported on the fritted disk by a slight positive pressure of dry nitrogen in the lower chamber. Purified 2-methoxy-2-phenylbutane, 17.5 g., was added with stirring over a period of 30 min., and after 45 more min. the deep red solution was allowed to filter through the disk by nitrogen pressure adjustments. To the clear solution of potassium-2-phenyl-2-butyl was added cautiously a solution of 3 ml. of D₂O (>99.5% D) in 1 l. of dry ether. The reaction mixture was washed with water, dried, evaporated through a Vigreux column, and the residue was passed through 600 g. of basic alumina (ignited at 500° for 15 minutes for activation) with purified pentane as developer. The column filtrate was evaporated through a Vigreux column, and the residue was distilled twice through a short path still, wt. 9.5 g., n^{25D} 1.4876, 0.91 atom of D per molecule (combustion and falling drop method).¹⁷

Infrared Analysis for 2-Phenylbutane-2-*d*.—Deuterium in the benzyl position of 2-phenylbutane was determined with a Beckman IR-4 spectrophotometer equipped with lithium fluoride optics and a sodium chloride cell of 0.1 mm. thickness. All measurements were made in the same cell, neat. The C-D stretching band at 4.71 μ was found to obey Beer's law exactly from 0 to 91% D (8 points). The racemic deuterated material described in the last section

(16) F. A. Abd Elhafez and D. J. Cram, *J. Am. Chem. Soc.*, **74**, 5848 (1952).

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

(18) D. J. Cram, *J. Am. Chem. Soc.*, **74**, 2129 (1952).

(19) The authors are indebted to Dr. Charles Kingsbury for this preparation.

was used for preparation of the standard solutions. As little as 1% deuterated material could be detected, although the relative error at very low deuterium concentration was larger than that at higher concentrations, where the estimated absolute error was $\pm 1\%$. To ensure reproducibility, for every analysis, it was necessary to run undeuterated 2-phenylbutane to obtain the base line, then the unknown, then a 2-phenylbutane-2-*d* standard, and finally the undeuterated material again to recheck the base line. The general method was checked against the combustion analy-

sis-falling drop method with the product of run 10 (Table II). Both methods gave exactly the same value.

Cleavages of (+)-2,3-Diphenyl-3-methyl-2-pentanol.—The starting material was prepared as before^{3a} from (–)-1,2-diphenyl-2-methyl-1-butanone which had $\alpha^{27D} - 68.91^\circ$, l 1 dm., neat. The alcohol employed had $\alpha^{27D} + 17.5^\circ$ (*c.*, 71 in benzene). The cleavages were carried out in sealed tubes under nitrogen, and in solvents flushed with nitrogen. The runs were made and the products isolated and analyzed by the methods described in ref. 3.

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

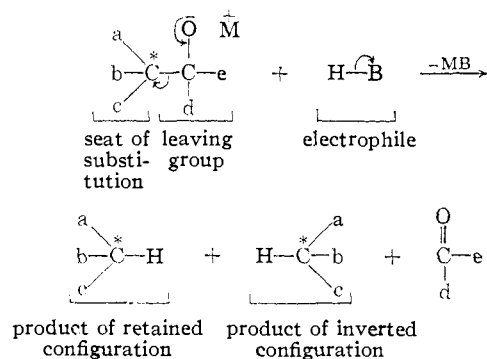
Electrophilic Substitution at Saturated Carbon. X. Steric Course in Systems that Contain an Internal Electrophile¹

BY DONALD J. CRAM, LYLE K. GASTON² AND HERB. JÄGER

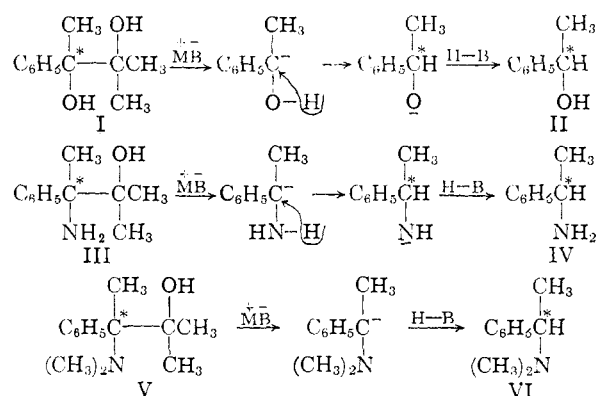
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Three systems have been prepared in an optically pure state, and submitted to the base-catalyzed cleavage reaction in which acetone served as leaving group, and proton-donors as electrophiles in an S_N1 reaction. Thus (+)-2-methyl-3-phenyl-2,3-butanediol produced optically active 1-phenylethanol; (–)-3-amino-2-methyl-3-phenyl-2-butanol gave active 1-phenylethylamine, and (–)-3-dimethylamino-2-methyl-3-phenyl-2-butanol gave active 1-dimethylaminophenylethane. The configurations of starting materials and products were established by independent means. The first two systems produced carbanions which contained an internal proton source (hydroxyl or amino group), whereas the last did not. The steric courses of the reactions varied between extremes of 98% net retention and 34% net inversion, depending on the availability of internal protons, the solvent, the cation of the base and the temperature. The results are interpreted by a mechanistic scheme in which intermediate carbanions in asymmetric environments partition between products of retained and inverted configurations, depending on the detailed structure of the solvent-leaving group envelope.

The use of reactions of the type formulated for the study of the steric course and mechanism of electrophilic substitution at saturated carbon has been described in the first set of papers of this series.³ The steric course of the reaction was found to vary between extremes of 99% net retention to 100% racemization to 64% net inversion as solvent, substituents, cations of the base and temperature were changed. In all systems, a, b and c were alkyl, phenyl, hydrogen or methoxyl groups,



three systems formulated, two of which (I and III) are capable of producing carbanions which could in principle go to product by internal proton transfer. The third (V) contains no internal proton source, and provides a basis of comparison for the other two.



none of which could act as a proton source for the carbanion intermediate involved in the reaction. This paper involves a study of the cleavage of the

Configurations of Starting Materials and Products.—Conclusions drawn about the steric course of these cleavage reactions are directly dependent on prior knowledge of the relative configurations and maximum rotations of starting materials and products. The absolute configurations and maximum rotations of atrolactic acid and 1-phenylethanol have been previously established and reviewed.⁴ Since (+)-I was prepared directly from 97% optically pure (+)-atrolactic acid without involvement of the asymmetric center, the relative configurations and maximum rotations of I and II become known.

(1) This work was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of this Fund.

(2) Dow Chemical predoctoral fellow, 1956–1957.

(3) (a) D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, *J. Am. Chem. Soc.*, **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); (f) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *ibid.*, **81**, 5774 (1959).

(4) D. J. Cram and K. R. Kopecky, *ibid.*, **81**, 2748 (1959).