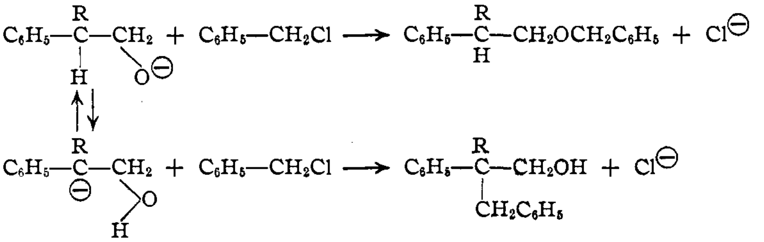
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Preparation and Attempted Racemization of Optically Active 2,4-Diphenylbutanol

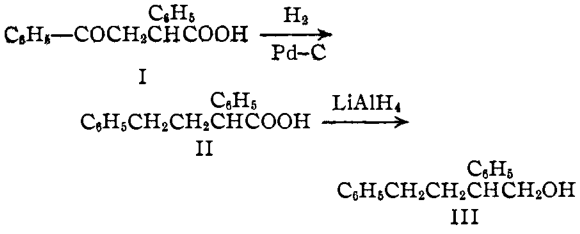
BY ROBERT H. BAKER AND SIDNEY H. JENKINS, JR.

Recently it has been shown that the reaction of sodium 2-phenylethoxide with benzyl chloride in toluene produces not only the ether but also a surprising quantity of the carbon-alkylation product, 2-benzyl-2,4-diphenylpropanol.[1] Among the possible modes of formation of this unusual product is one involving successive alkylations of the carbanion tautomers of the phenethylate and substituted phenethylate ions. These reactions, where R is first H and then benzyl, would be



$$\mathrm{C_6H_5{-}\overset{R}{\underset{H}{C}}{-}CH_2O^{\ominus} + C_6H_5{-}CH_2Cl \longrightarrow C_6H_5{-}\overset{R}{\underset{H}{C}}{-}CH_2OCH_2C_6H_5 + Cl^{\ominus}}$$
$$\updownarrow$$
$$\mathrm{C_6H_5{-}\overset{R}{\underset{\ominus}{C}}{-}CH_2OH + C_6H_5{-}CH_2Cl \longrightarrow C_6H_5{-}\overset{R}{\underset{CH_2C_6H_5}{C}}{-}CH_2OH + Cl^{\ominus}}$$

Although the existence of such carbanions seemed highly improbable, the possibility was easily brought to test by attempting the racemization of a suitable optically active alcohol. For this purpose the enantiomorphic forms of 2,4-diphenylbutanol were synthesized and heated at 100° with sodium in toluene. No racemization was observed and thus the possibility of the tautomeric anion is eliminated. This result might have been anticipated from those of Doering and Aschner[2] on 2-methylbutanol but it was felt that the acid-strengthening phenyl group on the 2-carbon atom would increase the probability of C-anion formation.



$$\underset{\mathrm{I}}{\mathrm{C_6H_5{-}COCH_2\overset{C_6H_5}{C}HCOOH}} \xrightarrow[\mathrm{Pd{-}C}]{\mathrm{H_2}} \underset{\mathrm{II}}{\mathrm{C_6H_5CH_2CH_2\overset{C_6H_5}{C}HCOOH}} \xrightarrow{\mathrm{LiAlH_4}} \underset{\mathrm{III}}{\mathrm{C_6H_5CH_2CH_2\overset{C_6H_5}{C}HCH_2OH}}$$

In a less critical test sodium 2-phenylethoxide in toluene was treated with carbon dioxide. Critical examination of the alkali-soluble hydrolysis product revealed the presence of a trace of benzoic acid, but no tropic acid could be isolated.

2,4-Diphenylbutanol was chosen for the racemization studies because it was needed in another problem and an easy synthesis was indicated. 2-Phenyl-3-benzoylpropanoic acid was resolved and the active forms were reduced catalytically to the 2,4-diphenylbutanoic acids.[3] These acids were then reduced with lithium aluminum hydride to the 2,4-diphenylbutanols, Table I. The ratios of the rotations of the (+) and (−) isomers is sufficiently constant to suggest that little or no racemization accompanies the reductions. Some attempts were made to resolve 2,4-diphenylbutanoic acid but the results were not promising.

TABLE I

REDUCTION OF ACTIVE ACIDS

2-Phenyl-3-benzoylpropanoic acid Mmoles reduced	2-Phenyl-3-benzoylpropanoic acid $[\alpha]^{27}D$	2,4-Diphenylbutanoic acid Yield, %	2,4-Diphenylbutanoic acid $[\alpha]^{27}D$	2,4-Diphenylbutanoic acid Concn. in EtOH	2,4-Diphenylbutanoic acid Mmoles reduced	2,4-Diphenylbutanol Yield, %	2,4-Diphenylbutanol $n^{25}D$	2,4-Diphenylbutanol $[\alpha]^{27}D$	2,4-Diphenylbutanol Concn. in EtOH
49	+136	84	+55	0.84	40	96	1.5673	+24	2.60
20	−111	75	−41	1.03					
30	−111	90	−43	1.13	40	77	1.5675	−15	1.74

TABLE II

α-NAPHTHYLCARBAMATES AND 3,5-DINITROBENZOATES OF 2,4-DIPHENYLBUTANOL

Cmpd. $[\alpha]^{27}D$ of alcohol	Formula	M. p., °C.	$[\alpha]^{27}D$	Conc.	Solvent	Analyses, %[a] Carbon Calcd.	Analyses, %[a] Carbon Found	Analyses, %[a] Hydrogen Calcd.	Analyses, %[a] Hydrogen Found
ANC +24	$C_{27}H_{25}NO_2$	106–107[b]	+12	0.67	EtOH	81.90	81.91	6.38	6.56
ANC −15		106–106.5	−10	.60	EtOH		81.65		6.48
DNB +24	$C_{23}H_{20}N_2O_6$	97–98.2	− 5.5	.55	EtOAc	65.71	65.67	4.81	5.04
DNB −15		97–97.5	+21[c]	.52	EtOAc		65.76		4.80

[a] Microanalyses by Margaret Hines. [b] Mr. Martin Knell of these laboratories reports the m. p. of the racemic material is 102–103°. [c] The optical purity of this compound may have been increased by its extensive crystallization preparatory to analysis.

Solid derivatives of the alcohols are presented

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(1) Baker, THIS JOURNAL, **70**, 3857 (1948).

(2) Doering and Aschner, *ibid.*, **71**, 838 (1949).

(3) Baker and Jenkins, *ibid.*, **68**, 2102 (1946).

in Table II. It is observed that the dinitrobenzoates have signs of rotation opposite to the alcohols from which they are derived.

Experimental

Resolution of 2-Phenyl-3-benzoylpropanoic Acid.—A solution of the acid, 50.8 g. (0.2 mole) in 1 l. of ethyl acetate was mixed with 64.8 g. (0.2 mole) of (–) quinine in 1 l. of ethyl acetate and the mixture was allowed to crystallize at 8° overnight.[4] The first crop of crystals was alternately crystallized from methanol and ethyl acetate and decomposed by sodium hydroxide to produce the acid which was crystallized from ether, $[\alpha]^{27}_{D}$ +136° (*c*, 1.03 in ethyl acetate). This acid was 86% optically pure as judged by Hann and Lapworth's values.[4]

The ethyl acetate-soluble salt gave 13 g. (51%) of acid, $[\alpha]^{27}_{D}$ –111° (*c*, 1.40 in ethyl acetate).

(+) and (–)2,4-Diphenylbutanoic Acids.—The keto acid, I, was reduced over palladium-charcoal in glacial acetic acid containing perchloric acid as previously described for the racemic acid.[3] The acids were crystallized once from 60-70° petroleum ether to give the results shown in Table I.

(+) and (–)2,4-Diphenylbutanols.—The active diphenylbutanoic acids were reduced in ethyl ether by lithium aluminum hydride following the directions of Nystrom and Brown.[5] After the addition of the acid the mixture was refluxed for one-half hour and then hydrolyzed with 10% hydrochloric acid. The alcohols were distilled, b. p. 178–180° (1 mm.).[6] Rotations and yields are summarized in Table I.

The α-Naphthylcarbamates and 3,5-dinitrobenzoates of the active alcohols were crystallized from petroleum ether and ethanol, respectively. Their constants are presented in Table II.

Attempted Racemizations of 2,4-Diphenylbutanols.—The procedure and essentially the apparatus which Doering and Aschner[2] had shown to be capable of excluding the effects of oxidants were used. The freshly prepared alcohols, 2 millimoles, were added to equivalent amounts of powdered sodium under toluene and allowed to react until hydrogen evolution had ceased. The suspension was then heated at 100° for a time and the alcohol recovered by washing the toluene with acid, then water, and distilling finally *in vacuo*. The specific rotations of the alcohols at comparable temperatures and concentrations before and after heating for specified times were

–15.1°	5 hr.	–14.6°
–14.6	8 hr.	–13.3
+24.3	8 hr.	+24.1

Summary

Optically active forms of 2,4-diphenylbutanoic acid and 2,4-diphenylbutanol have been prepared by convenient methods. The latter compound is not racemized by heating of its sodium derivative at 100° for eight hours.

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[4] These are more specific directions than those of Hann and Lapworth, *J. Chem. Soc.*, **85**, 1355 (1904).

[5] Nystrom and Brown, THIS JOURNAL, **69**, 2548 (1947).

[6] Marion, *Canadian J. Res.*, **16B**, 213 (1938), gives 174–180° at 1 mm. for the racemic alcohol.

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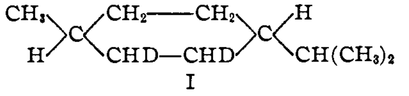
The Reduction of Optically Active Phenylmethylcarbinyl Chloride with Lithium Aluminum Deuteride[1]

BY ERNEST L. ELIEL

Recently Alexander and Pinkus[1a] showed that the reduction of optically active *trans*-2-menthene gives rise to *active* 2,3-dideutero-*trans*-menthane (I) thus demonstrating that a compound of type R_1R_2CHD is capable of rotating the plane of polarized light.



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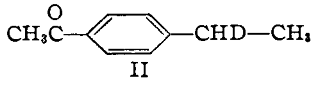

II

Compound I has four asymmetric centers (not all of which, however, necessarily contribute towards its rotation[1a]) and it seemed desirable to investigate again the possibility of optical activity in the case of a compound having only one carbon atom of the R_1R_2CHD-type. Such a compound is α-deuteroethylbenzene, C_6H_5-$CHDCH_3$. This hydrocarbon was expected to be accessible by the reduction of phenylmethylcarbinyl chloride, $C_6H_5CHClCH_3$, with lithium aluminum deuteride–lithium deuteride according to a method recently described[2] for reductions of alkyl halides to alkanes. The fact that primary halides are reduced more easily by lithium aluminum hydride than secondary, while tertiary ones are not reduced at all,[2,3] might lead one to believe that the reaction is of the nucleophilic displacement (S_N2) type and that the reduction of optically active α-phenethyl chloride with lithium aluminum deuteride might proceed with Walden inversion and give rise to an active product. Walden inversion has been demonstrated for the reduction of epoxides with lithium aluminum hydride.[3]

The reduction of (–)-α-chloroethylbenzene with lithium aluminum deuteride–lithium deuteride in tetrahydrofuran yielded about 80% of the theoretical amount of α-deuteroethylbenzene which was free of chlorine-containing impurities

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[1] Presented before the Organic Division of the American Chemical Society at Atlantic City, N. J., September 20, 1949.

[1a] Alexander and Pinkus, THIS JOURNAL, **71**, 1786 (1949). This publication reviews earlier unsuccessful attempts to synthesize optically active compounds of the R_1R_2CHD type. The present author is indebted to Dr. Elliot R. Alexander for information regarding the results of his investigation several months in advance of publication.

[2] Johnson, Blizzard and Carhart, *ibid.*, **70**, 3644 (1948).

[3] Trevoy and Brown, *ibid.*, **71**, 1675 (1949). At the time this paper appeared, the present investigation was almost complete.