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Stereochemistry of the Primary Carbon. V. Optically Active Benzyl-*α*-*d* Alcohol[1]

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Benzyl-*α*-*d* alcohol having $[\alpha]^{20}D$ −0.645 ± 0.002° has been prepared by the reduction of benzaldehyde-*d* with optically active isobornyloxymagnesium bromide. The benzaldehyde-*d* was prepared by the Stephens reduction of benzonitrile using stannous chloride and deuterium chloride. Optically active benzyl-*α*-*d* bromide was prepared; the rate of racemization with bromide ion was found to correspond closely to the rate of exchange with radiobromide ion. (−)-Benzyl-*α*-*d* alcohol (−)-bromide, (−)-acetate and (+)-hydrogen phthalate have the same configurations.

The simple benzyl system is unique in that it combines a carbonium ion stability approximately like that of a secondary carbinyl system,[2] with the freedom from steric hindrance effects characteristic of simple primary systems. Hence the stereochemistry of a number of reactions involving intermediates of the carbonium ion type would be particularly interesting for the benzyl system. Furthermore, the benzyl system provides a valuable starting material for the syntheses of other systems. For application to these objects we have synthesized benzyl-*α*-*d* alcohol having a relatively high optical rotation and have demonstrated that the observed optical activity is due to the deutero alcohol and not to an impurity.

The technique adopted was a modification of the method of preparation of optically active 1-butanol-1-*d*, which has been prepared both by the reaction of butyraldehyde with 2-octyloxymagnesium-2-*d* bromide[3] and by the reaction of butyraldehyde-*d* and 2-octyloxymagnesium bromide.[4] The choice of procedures clearly depends on which type of deutero compound is the more readily available.

Benzaldehyde-*d* has been prepared previously by the Rosenmund reduction of benzoyl chloride using deuterium gas.[5] We wished to avoid any catalytic deuteration procedure because of the danger of exchange with other hydrogens. Benzaldehyde-*d* has been prepared with high isotopic purity by the lead tetraacetate oxidation of dideuterohydrobenzoin which was obtained by the reduction of benzil with lithium aluminum deuteride.[6] Because large quantities of benzaldehyde-*d* were required, a less expensive deuterium source was desired. Consequently, the Stephens reduction of benzonitrile was investigated. Using a modification of the procedure of Williams,[7] deuterium chloride (from deuterium oxide and benzoyl chloride)[8] was passed into a mixture of anhydrous ethyl ether and anhydrous stannous chloride until two clear liquid phases formed, the lower of which is an ethereal stannous chloride–deuterium chloride solution. Addition of benzonitrile to this solution followed by hydrolysis in the customary fashion yields benzaldehyde-*d*, which is contaminated by some benzonitrile. Purification by means of the sodium bisulfite addition compound generates pure benzaldehyde-*d* in 27% yield (based on deuterium oxide). Slotta and Kethur[9] have reported that stannous chloride will not dissolve in ethereal hydrogen chloride unless a small amount of water is present. This observation indicates that benzaldehyde-*d* prepared as above is not isotopically pure. The infrared spectrum of benzaldehyde has a characteristic triplet at 3.50, 3.54 and 3.65 μ (C–H stretching). These bands are reported to be absent in isotopically pure benzaldehyde-*d*.[6,10] Our benzaldehyde-*d* contained not only the C–D bands at 4.73, 4.83 and 4.87 μ but also the much less intense triplet at 3.6 μ. Hence our benzaldehyde-*d* is not isotopically pure.

In the partially stereospecific reduction of benzaldehyde-*d* difficulties were anticipated with the use of 2-octanol because of the proximity of the boiling points of the species expected to be present at the end of the reaction. This problem is presumably avoided by the use of 2-butanol but, instead, the successful use of the magnesium bromide salt of isoborneol as a stereospecific reducing agent by Vavon and Antonini[11] prompted its use in our reduction. Isoborneol is readily obtained optically pure and contaminated by only 10% of borneol by the reduction of natural gum camphor with lithium aluminum hydride.[12] The reaction of the magnesium bromide salts of the mixture of isoborneol and borneol with benzaldehyde-*d* was carried out in benzene solution. After precipitation of the magnesium salts and the removal of solvents, the benzyl-*α*-*d* alcohol produced was separated from the bulk of the camphor, borneol and isoborneol present by a unique procedure in which the mixture was refluxed with water using a large coil condenser. The terpenes remained as an adhering solid on the condenser coils, whereas the benzyl-*α*-*d* alcohol remained in the water phase. Final purification was achieved by converting the optically active benzyl-*α*-*d* alcohol to the crystalline hydrogen phthalate and recrystallizing the ester to constant rotation. The amount of pure ester averaged 59% based on benzaldehyde-*d*. Cleavage of the purified hydrogen phthalate with lithium aluminum hydride generated optically active benzyl-*α*-*d* alcohol. Part of the alcohol was reconverted to the hydrogen phthalate, which was recrystallized again and cleaved to yield benzyl-*α*-*d* alcohol of unchanged rotation. These results are summarized in Table

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[1] Part IV, A. Streitwieser, Jr., and W. D. Schaeffer, THIS JOURNAL, **79**, 379 (1957).

[2] A. Streitwieser, Jr., *Chem. Rev.*, **56**, 571 (1956).

[3] A. Streitwieser, Jr., THIS JOURNAL, **75**, 5014 (1953).

[4] A. Streitwieser, Jr., and W. D. Schaeffer, *ibid.*, **78**, 5597 (1956).

[5] A. F. Thompson and N. H. Cromwell, *ibid.*, **61**, 1374 (1939).

[6] K. B. Wiberg, *ibid.*, **76**, 5371 (1954).

[7] J. Williams, *ibid.*, **61**, 2248 (1939).

[8] H. C. Brown and C. Groot, *ibid.*, **64**, 2223 (1942).

[9] K. H. Slotta and R. Kethur, *Ber.*, **71**, 335 (1938).

[10] K. B. Wiberg and R. Stewart, THIS JOURNAL, **77**, 1786 (1955).

[11] G. Vavon and A. Antonini, *Compt. rend.*, **232**, 1120 (1951).

[12] D. S. Noyce and D. B. Denney, THIS JOURNAL, **72**, 5743 (1950).

I. The alcohol from the combined runs 1, 2 and 3 was fractionally distilled under reduced pressure through a spinning band column. The product was collected as 4 fractions, the optical rotations of each of which were identical within experimental error, $[\alpha]^{20}\mathrm{D} - 0.645 \pm 0.002°$. This rotation is so large that in much of the further work the deutero alcohol was diluted with ordinary benzyl alcohol so that larger quantities could be worked with. Benzyl-*α*-*d* alcohol has a band in the C–D stretching region of the infrared centered at 4.67 μ with a shoulder at 4.58 μ.

TABLE I

PREPARATION OF OPTICALLY ACTIVE BENZYL-*α*-*d* ALCOHOL

Run	$[\alpha]^{25-26}\mathrm{D}$ of hydrogen benzyl-*α*-*d* phthalate (*c* 20–25, acetone)	$\alpha^{20-25}\mathrm{D}$ of benzyl-*α*-*d* alcohol (*l* 2)
1	+0.205 ± 0.006°[a]	
2	+ .205 ± .012[a]	−1.355 ± 0.005°[b]
3	+ .202 ± .005[a]	
4	+ .202 ± .004[c]	−1.304 ± .005[d]
5[e]	− .009 ± .008[f]	0.000 ± .005

[a] After crystallization from benzene–cyclohexane to constant rotation. [b] From the combined hydrogen phthalates of runs 1, 2 and 3. [c] Not crystallized to constant rotation. [d] This product was combined with the redistilled foreruns and residues of the fractionation of run 4 and the fractionation of the combined alcohol from runs 1, 2 and 3 giving material having a calculated $\alpha^{25}\mathrm{D}$ −1.321° (*l* 2) and yielding hydrogen phthalate having $[\alpha]^{23}\mathrm{D}$ +0.205 ± 0.005°. Cleavage of this ester with lithium aluminum hydride regenerated benzyl-*α*-*d* alcohol having $\alpha^{20}\mathrm{D}$ −1.321 ± 0.002° (*l* 2). [e] Control run using undeuterated benzaldehyde. [f] After two crystallizations from benzene–cyclohexane. After one crystallization the ester had $[\alpha]^{25}\mathrm{D}$ +0.011 ± 0.006°.

In the original preparation of optically active 1-butanol-1-*d*,[3] the optical activity was definitely associated with the deutero-butyl system by conversion to 1-butyl-1-*d* bromide and by comparing the rate of racemization of the latter by bromide ion with the rate of exchange of *n*-butyl bromide with radiobromide ion. The analogous procedure was adopted in the present work. Two methods were investigated for the preparation of optically active benzyl-*α*-*d* bromide. Corbett and Kenner[13] have reported that (+)-2-octanol was converted by reaction of its *α*-naphthylthiocarbamate with benzhydryl bromide to (−)-2-bromoöctane with a higher rotation than any previously recorded. With suitable modifications in the procedure this method was applied to the benzyl system. (−)-Benzyl-*α*-*d* alcohol was converted to its *α*-naphthylthiocarbamate by adding *α*-naphthyl isothiocyanate to a solution of the alcohol and potassium *t*-butoxide in *t*-butyl alcohol. Treatment of the resulting benzyl-*α*-*d* *α*-naphthylthiocarbamate with benzhydryl bromide in benzene produced (+)-benzyl-*α*-*d* bromide. The latter compound was also prepared by the reaction of (−)-benzyl-*α*-*d* alcohol with phosphorus tribromide. These results are summarized in Table II. Of the several preparations the highest yield of bromide having the highest optical activity relative to the starting alcohol was obtained by the use of equimolar amounts of phosphorus tribromide and the alcohol.

TABLE II

PREPARATION OF OPTICALLY ACTIVE BENZYL-*α*-*d* BROMIDE

Benzyl-*α*-*d* alcohol $\alpha^{20}\mathrm{D}$ (*l* 1)	Reagent	Benzyl-*α*-*d* bromide $\alpha^{20}\mathrm{D}$ (*l* 1)	Yield, %
−0.133 ± 0.002°	[a]	+0.076 ± 0.007°	37
− .103 ± .006	PBr_3[b]	+ .105 ± .005	64
− .660 ± .001	PBr_3[c]	+ .500 ± .003	50

[a] Method of Corbett and Kenner[13] using *α*-naphthyl isothiocyanate and benzhydryl bromide. [b] An equimolar amount was used. [c] An equivalent amount was used.

In order to relate the configuration of benzyl-*α*-*d* bromide to that of benzyl-*α*-*d* alcohol, a portion of the bromide was allowed to react with tetramethylammonium acetate in acetone solution to produce the corresponding benzyl-*α*-*d* acetate. Steigman and Hammett[14] have found that the reaction of optically active *α*-phenylethyl chloride with tetraethylammonium acetate in acetone to produce optically active *α*-phenylethyl acetate shows second-order kinetics and inferred a complete inversion of configuration. Correspondingly, it is reasonable to assume that the reaction of (+)-benzyl-*α*-*d* bromide with tetramethylammonium acetate to produce (−)-benzyl-*α*-*d* acetate also proceeds with inversion. Reaction of (−)-benzyl-*α*-*d* alcohol with acetyl chloride in pyridine also produces (−)-benzyl-*α*-*d* acetate, undoubtedly with retention of configuration because no bond to the asymmetric carbon is broken. Thus benzyl-*α*-*d* bromide, benzyl-*α*-*d* acetate and benzyl-*α*-*d* alcohol of the same sign of rotation have the same configuration; the reaction of benzyl-*α*-*d* alcohol with phosphorus tribromide yields benzyl-*α*-*d* bromide with inversion of configuration. It is interesting to note that, unlike the acetate, hydrogen benzyl-*α*-*d* phthalate of like configuration to the alcohol has the opposite sign of rotation.

Sugden and Willis[15] have measured the second-order rate constant for displacement of benzyl bromide by lithium radiobromide in ethylene glycol diacetate between the temperatures of 5 and 45° at intervals of 10°. This work provided an ideal companion piece to our racemization studies. When optically active benzyl-*α*-*d* bromide from run 3 of Table II was maintained at 33.9° with lithium bromide in ethylene glycol diacetate, the observed rotation fell from an initial value of +0.095° to a final value of 0° within experimental error. Using the equation for the second-order reaction

$$k = \frac{2.303}{2C_{\mathrm{LiBr}}t} \log \frac{\alpha_0}{\alpha_t}$$

in which C_{LiBr} is the concentration of lithium bromide after correction for solvent expansion, the rate constant was calculated by the method of least squares from the data covering up to 75% reaction (two half-lives). After two half-lives the percentage error in the observed rotation became rather large. The experimental results are presented in Fig. 1. The second-order rate constant calculated from the rate of racemization was found to be $9.46 \pm 0.21 \times 10^{-2}$ l. mole^{-1} min.$^{-1}$, in excellent agreement with the value interpolated from Sugden

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(13) W. M. Corbett and J. Kenner, *J. Chem. Soc.*, 3572 (1953).

(14) J. Steigman and L. P. Hammett, THIS JOURNAL, **59**, 2536 (1937).

(15) S. Sugden and J. B. Willis, *J. Chem. Soc.*, 1360 (1951).

and Willis' radiochemical data, 9.36 × 10^{-2} l. mole^{-1} min.^{-1}. This agreement provides substantial evidence that the observed rotations are in fact due to hydrogen–deuterium asymmetry. The present results also represent a further example of the several reactions of alkyl halides with halide ion in which each displacement has been demonstrated to proceed with an inversion of configuration.[3,16]

Experimental

All melting points and boiling points are uncorrected. Optical rotations of the deuterated compounds were taken with a Rudolph precision polarimeter with which readings could be made to the nearest 0.001°. Each rotation recorded for the deuterated compounds is the mean of at least 10 readings for the polarimeter tube containing the optically active compound minus the mean of at least 10 readings for the empty polarimeter tube. The estimated error is given as the standard deviation. Rotations of liquids were taken directly (neat); rotations of solids were taken as the indicated solutions. All rotations were taken using center fill tubes having bores of 3 to 6 mm. The infrared spectra of liquids were taken in a 0.025-mm. cell with a Baird double beam recording infrared spectrometer, model AB2.

Benzaldehyde-*d*.—A typical run was as follows: In a 3-l. three-necked flask equipped with a reflux condenser, mechanical stirrer and gas inlet tube was placed 342 g. (1.8 moles) of anhydrous stannous chloride (prepared by the method of Stephen.[17] Anhydrous stannous chloride prepared by heating stannous chloride dihydrate at 200° for 1 hr. could not be made to dissolve in ether by passing in hydrogen chloride gas). Into the flask was distilled 400 ml. of ethyl ether which had been dried over calcium hydride. Over a period of 4 hr. 4 moles of deuterium chloride gas (prepared from benzoyl chloride and deuterium oxide)[8] were slowly passed into the stirred suspension of stannous chloride and ether. During the last hour it was necessary to stir the reaction mixture rather vigorously in order to prevent the stannous chloride from coagulating at the bottom of the flask. After the mixture had separated into two clear liquid phases the gas inlet tube was replaced by a dropping funnel and 84 g. (0.82 mole) of benzonitrile (Eastman Kodak Co.) was added to the reaction flask. The two-phase solution was stirred vigorously for 1 hr. and was allowed to stand for 24 hr. with intermittent stirring. At the end of this time the reaction mixture had separated into a solid phase and a clear solution. The reaction mixture was then worked up according to the method of Williams.[7] The results of 3 runs are summarized in Table III. A total of 160 g. of crude benzaldehyde-*d* was obtained. After purification by means of the sodium bisulfite addition compound, 102 g. (0.95 mole) of benzaldehyde-*d* was obtained, b.p. 57–58° (7–8 mm.), corresponding to an over-all yield of 27% based on deuterium oxide. The stoichiometry was assumed from the equation

$$C_6H_5CN + 3DCl + SnCl_2 \longrightarrow C_6H_5CDND{\cdot}DCl + SnCl_4$$

TABLE III

PREPARATION OF BENZALDEHYDE-*d*

Reagent (moles)			Ether	Yield of crude benzaldehyde-*d*, %
Benzonitrile	D_2O	$SnCl_2$	(ml.)	(based on D_2O)
0.4	1.4	0.9	1200	33
.95	2.0	1.8	400	53
.8	2.0	1.8	400	42

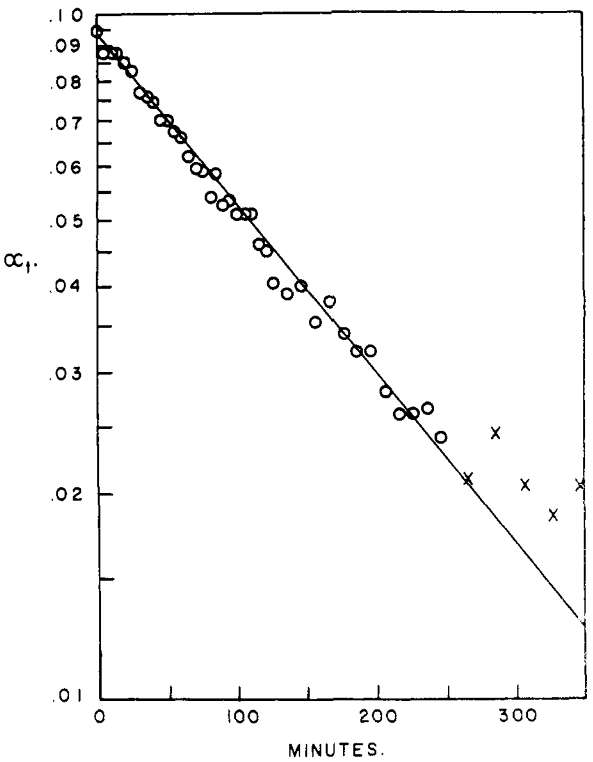

Fig. 1.—Racemization of benzyl-α-*d* bromide by lithium bromide in ethylene glycol diacetate solution at 33.9°. The line drawn has the least squares slope based on points taken during the first two half-lives of reaction (closed circles) and corresponds to a second-order rate constant, 9.46 × 10^{-2} l. mole^{-1} min.^{-1}. The crosses are points taken after 75% reaction and were not used in the calculation of the rate constant.

(+)-Hydrogen Benzyl-α-*d* Phthalate.—To a solution of *n*-propylmagnesium bromide prepared from *n*-propyl bromide and 9.7 g. (0.4 mole) of magnesium in dry ether, maintained at 0°, was added slowly a dry ethereal solution of a mixture of isoborneol and borneol (prepared by the reduction of natural gum camphor with lithium aluminum hydride)[12] until the evolution of gas ceased. About 62 g. (0.4 mole) of the alcohol mixture was added. At the end of the addition a large amount of white precipitate was present. Isobornyloxymagnesium bromide is not soluble in ether.[11] The apparatus was arranged for distillation with a Vigreux column, and 700 ml. of dry benzene was added to the flask. The mixture was distilled until the vapor temperature reached 75° at which time the solution was homogeneous. After cooling to room temperature the flask was again arranged for stirring, and 25 g. (0.23 mole) of benzaldehyde-*d* was added with stirring. After stirring for 3 hr. at room temperature, enough water was added to stop the reaction and form two phases, a clear organic phase and a thick white precipitate. The organic phase was decanted and the precipitated inorganic salts were washed 5 times with small portions of ether. The combined organic phases were dried with anhydrous potassium carbonate. After distillation of the solvent, the liquid residue was added to 500 ml. of water. The aqueous mixture was directly steam distilled to remove the last traces of solvent until white crystalline solids formed on the condenser. The flask was then fitted with a wide bore tube fitted with a large removable coil condenser. When the aqueous mixture was refluxed, white powder formed on the coil condenser. If the white solids did not adhere to the condenser coils the mixture was again directly steam distilled for a short time to remove the last traces of ether and benzene. The coil condenser with the adhering solid was periodically replaced by a clean condenser until solids no longer formed on the condenser. In this manner most of the camphor, borneol and isoborneol was removed while the benzyl-α-*d* alcohol was retained in the water phase. After cooling the aqueous solution to room temperature, 460 g. of potassium carbonate was added to reduce the solubility of benzyl-α-*d* alcohol. The aqueous mixture was then extracted 5 times with ether and the combined ethereal extracts were dried with anhydrous potassium carbonate. Distillation of the solvents left the crude benzyl-α-*d* alcohol as a yellow liquid residue.

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[16] E. D. Hughes, F. Juliusburger, S. Masterman, B. Topley and J. Weiss, *J. Chem. Soc.*, 1525 (1935); E. D. Hughes, F. Juliusburger, A. D. Scott, B. Topley and J. Weiss, *ibid.*, 1173 (1936).

[17] A. J. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., Ltd., London, 1948, p. 193.

To the crude benzyl-*α-d* alcohol was added 45 g. (0.30 mole) of phthalic anhydride. The resulting mixture was maintained at 110° for 14 hr. and was poured into a solution of 0.5 mole of sodium carbonate in 2 l. of water. The aqueous mixture was stirred for 30 min. and was washed once with a small amount of ether to remove any remaining undissolved solid. After acidification to *p*H 2 with concentrated hydrochloric acid, an oily layer formed which solidified to a white crystalline mass on standing. The hydrogen benzyl-*α-d* phthalate was recrystallized from benzene–cyclohexane. The average yield of 4 such runs was 59% based on benzaldehyde-*d*. The rotations of the products of these runs are summarized in Table I.

When this procedure was repeated using benzaldehyde, hydrogen benzyl phthalate was obtained in 58% yield. The properties are summarized in Table I.

(−)-Benzyl-*α-d* Alcohol.—A preliminary experiment in which hydrogen benzyl phthalate was hydrolyzed by indirect steam distillation from a solution of the sodium salt in aqueous 25% sodium hydroxide gave only a 64% yield of benzyl alcohol. As a result cleavage by lithium aluminum hydride was adopted. The combined hydrogen benzyl-*α-d* phthalate from runs 1, 2 and 3 (90 g., 0.35 mole) was reduced in the usual way with 50 g. (1.4 moles) of lithium aluminum hydride. The product was distilled through a 15-inch Vigreux column under reduced pressure and 2 fractions were collected: 1, b.p. 88° (7 mm.), α^{21}_{D} −1.355 ± 0.004° (*l* 2), α^{21}_{5463} −1.671 ± 0.003° (*l* 2); 2, b.p. 87–88° (6–7 mm.), α^{21}_{D} −1.357 ± 0.005° (*l* 2), α^{21}_{5463} −1.666 ± 0.004° (*l* 2). These fractions were combined to yield 30.8 g. (0.28 mole) (83% yield) of benzyl-*α-d* alcohol.

In a similar manner 30 g. (0.12 mole) of hydrogen benzyl-*α-d* phthalate from run 4 gave 4.8 ml. of benzyl-*α-d* alcohol, b.p. 87–89° (7 mm.), having α^{25}_{D} −1.304 ± 0.005° (*l* 2).

The foreruns and residues of the two above distillations were combined and redistilled to give 8.4 ml. of benzyl-*α-d* alcohol, b.p. 87–88° (6 mm.), having α^{25}_{D} −1.330 ± 0.005° (*l* 2). This material and the product from the distillation of run 4 were combined to yield material having a calculated rotation α^{25}_{D} −1.321° (*l* 2). This material, 13.5 g. (0.124 mole), was allowed to react with 20 g. (0.14 mole) of phthalic anhydride to regenerate hydrogen phthalate, 24 g. after crystallization from benzene–cyclohexane (69% yield), $[\alpha]^{23}_{\mathrm{D}}$ +0.205 ± 0.005° (*l* 4, *c* 20, acetone). A further recrystallization from benzene–cyclohexane gave material having $[\alpha]^{23}_{\mathrm{D}}$ + 0.205 ± 0.005° (*l* 4, *c* 20, acetone), $[\alpha]^{23}_{5463}$ +0.255 ± 0.005° (*l* 4, *c* 20, acetone). When this hydrogen phthalate was cleaved as before with lithium aluminum hydride, 7.3 g. (74% yield) of benzyl-*α-d* alcohol was obtained having α^{20}_{D} −2.641 ± 0.004° (*l* 4). No change in rotation was obtained by this further purification sequence.

The hydrogen benzyl phthalate having $[\alpha]^{25}_{\mathrm{D}}$ −0.009 ± 0.008° (*l* 4, *c* 20, acetone), prepared by the same sequence of reactions from ordinary benzaldehyde, was reduced with lithium aluminum hydride and yielded benzyl alcohol having $\alpha^{26.5}_{\mathrm{D}}$ 0.000 ± 0.005° (*l* 2) and the same index of refraction and infrared spectrum as that of freshly fractionated benzyl alcohol.

Fractional Distillation of Benzyl-*α-d* Alcohol.—The benzyl-*α-d* alcohol obtained from runs 1, 2 and 3 was distilled at 7 mm. through a 15-inch spinning band column rated at 13 plates. Four fractions of approximately equal size were taken: 1, b.p. 88.5–90.0°, α^{21}_{D} −2.707 ± 0.004° (*l* 4); 2, b.p. 90.0°, α^{20}_{D} −1.355 ± 0.003° (*l* 2); 3, b.p. 90.0–90.2°, α^{20}_{D} −1.356 ± 0.004° (*l* 2); 4, b.p. 90.2–91.0°, α^{20}_{D} −1.357 ± 0.003° (*l* 2). The infrared spectra of fractions 1 and 3 were identical.

This material had d^{25}_{4} 1.0498 and $n^{20.1}_{\mathrm{D}}$ 1.5381. Freshly fractionated benzyl alcohol had d^{25}_{4} 1.0414 (reported[18] d^{25}_{4} 1.04127) and $n^{20.1}$ 1.5394. Using the formula of McLean and Adams[19] the density of (−)-benzyl-*α-d* alcohol corresponds to 0.87 deuterium atom per molecule.

(+)-Benzyl-*α-d* Bromide from Benzyl-*α-d* *α*-Naphthylthiocarbamate.—To a solution of potassium *t*-butoxide prepared from 2 g. (0.051 mole) of potassium and 45 ml. of *t*-butyl alcohol was added 5 g. (0.046 mole) of benzyl-*α-d* alcohol having α^{20}_{D} −0.265 ± 0.003° (*l* 2) prepared by diluting benzyl-*α-d* alcohol having α^{20}_{D} −2.641 ± 0.004° (*l* 4) with ordinary benzyl alcohol. After stirring for 15 minutes 8.6 g. (0.047 mole) of *α*-naphthyl isothiocyanate (Eastman) was added. The resulting homogeneous dark orange solution was stirred under nitrogen for 3.5 hr. after which 200 ml. of water was added together with enough hydrochloric acid to neutralize the mixture. After removal of the water and *t*-butyl alcohol under reduced pressure, the solid residue was recrystallized twice from ethanol–water to give 10 g. (0.034 mole) (74% yield) of pale yellow crystals of benzyl-*α-d* *α*-naphthylthiocarbamate having m.p. 95–99.5°.

The benzyl-*α-d* *α*-naphthylthiocarbamate was placed in a 250-ml. flask and 9 g. (0.036 mole) of benzhydryl bromide and 150 ml. of dry benzene were added. Fifty ml. of benzene was distilled from the flask to ensure the absence of water. The flask was fitted with a reflux condenser carrying a calcium chloride drying tube and the solution was refluxed for 12 hr. After removing the benzene by distillation the residue was extracted with low boiling petroleum ether. The petroleum ether solution was cooled in a Dry Ice–acetone-bath overnight and was allowed to warm to room temperature. The small amount of precipitated solid remaining was removed by filtration. The petroleum ether was removed by distillation and the liquid residue was distilled under reduced pressure through a 15-inch Vigreux column to give 2.9 g. (0.017 mole) (37% over-all yield) of benzyl-*α-d* bromide, b.p. 76–76.5° (6–7 mm.). The product was redistilled to yield material having α^{20}_{D} +0.076 ± 0.007° (*l* 1) and α^{20}_{5463} + 0.095 ± 0.009° (*l* 1). After heating at 120° for 30 minutes the rotation was found to be unchanged.

When the above synthesis was carried out using benzyl alcohol, benzyl bromide obtained in 42% yield had an infrared spectrum identical with that of freshly fractionated benzyl bromide. The use of phenyl isothiocyanate in this procedure yielded impure benzyl bromide.

An attempt was made to prepare benzyl bromide by the alternative method of Corbett and Kenner[13] by heating a mixture of benzyl *α*-naphthylthiocarbamate with benzhydryl bromide without solvent. There was obtained only a small yield of impure benzyl bromide.

(+)-Benzyl-*α-d* Bromide from Phosphorus Tribromide.—In a 15-ml. centrifuge tube equipped with a reflux condenser topped by a calcium chloride drying tube was placed 2.3 g. (0.021 mole) of benzyl-*α-d* alcohol having α^{20}_{D} −0.103 ± 0.006° (*l* 1), obtained by dilution with benzyl alcohol of benzyl-*α-d* alcohol having α^{20}_{D} −2.641 ± 0.004° (*l* 4). The alcohol was frozen in a Dry Ice–acetone-bath, and 5.7 g. (0.021 mole) of phosphorus tribromide was added. Upon allowing the mixture to warm to room temperature a vigorous exothermic reaction occurred with the evolution of hydrogen bromide. The reaction mixture was warmed for 2 minutes on a steam-cone and was washed successively twice with cold water, twice with 10% aqueous sodium carbonate and once again with water. The resulting organic liquid was diluted with low boiling petroleum ether and was dried with anhydrous sodium sulfate and sodium carbonate. After distillation of the solvent the residue was distilled under reduced pressure to give 2.3 g. (0.013 mole) (64% yield) of benzyl-*α-d* bromide, b.p. 76.5–78° (7 mm.) and having α^{20}_{D} +0.105 ± 0.005° (*l* 1).

When 4.4 g. (0.04 mole) of benzyl-*α-d* alcohol having α^{20}_{D} −2.641 ± 0.004° (*l* 4) was allowed to react with 3.6 g. (0.013 mole) of phosphorus tribromide using the same procedure as the above, with the exception that the reaction mixture was agitated for 1 minute rather than heated for 2 minutes, there was obtained 3.5 g. (0.02 mole, 50% yield) of benzyl-*α-d* bromide, b.p. 78–80° (7–8 mm.), having α^{20}_{D} +1.000 ± 0.006° (*l* 2) and α^{20}_{5463} +1.23 ± 0.01° (*l* 2), d^{25}_{4} 1.439, n^{20}_{D} 1.5756. Freshly fractionated benzyl bromide had d^{25}_{4} 1.430 and n^{20}_{D} 1.5750.

When both procedures were carried out with benzyl alcohol, the product obtained had infrared spectra and indices of refraction identical to that of benzyl bromide which was freshly fractionated.

Reaction of Benzyl-*α-d* Bromide with Tetramethylammonium Acetate.—A mixture of 18.6 g. (0.14 mole) of tetramethylammonium acetate[20] and 100 ml. of acetone was heated to reflux and 3.32 g. (0.019 mole) of benzyl-*α-d* bromide having α^{20}_{D} +0.156 ± 0.005° (*l* 2) and α^{20}_{5463} + 0.207 ± 0.009° (*l* 2) was added. The benzyl-*α-d* bromide was obtained by combining the products of the first two preparations given above. The mixture was refluxed for 4 hr. and was poured into 400 ml. of water. The aqueous mixture was extracted twice with ether and the combined ether

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[18] A. R. Martin and C. M. George, *J. Chem. Soc.*, 1413 (1933).

[19] A. McLean and R. Adams, THIS JOURNAL, **58**, 804 (1936).

[20] H. L. Goering, T. D. Nevitt and E. F. Silversmith, *ibid.*, **77**, 4042 (1955).

extract was dried with anhydrous potassium carbonate. After distillation of the solvent the residue was distilled under reduced pressure to give 2 g. (0.013 mole, 69% yield) of benzyl-α-*d* acetate, b.p. 93–95° (7 mm.) having $\alpha^{20}\mathrm{D}$ $-0.018 \pm 0.004°$, $\alpha^{20}{}_{5463}$ $-0.026 \pm 0.005°$ (l 1). Redistillation gave material having $\alpha^{20}\mathrm{D}$ $-0.014 \pm 0.006°$ and $\alpha^{20}{}_{5463}$ $-0.016 \pm 0.009°$ (l 1).

When benzyl bromide was carried through this procedure, it gave benzyl acetate having an infrared spectrum and index of refraction identical to that of freshly fractionated benzyl acetate.

(−)-Benzyl-α-*d* Acetate.—To a stirred mixture of 4 g. (0.037 mole) of benzyl-α-*d* alcohol having $\alpha^{25}\mathrm{D}$ $-0.860 \pm 0.004°$, $\alpha^{25}{}_{5463}$ $-1.044 \pm 0.007°$ (l 4) (prepared by diluting the product of runs 1, 2 and 3 with ordinary benzyl alcohol), 15 ml. of pentane and 8 g. (0.1 mole) of pyridine maintained in an ice-bath was added 3.9 g. (0.05 mole) of acetyl chloride in 5 ml. of pentane. After stirring at room temperature for 4 hr., the mixture was diluted with pentane, washed with dilute acid and water and dried. Distillation through a small Vigreux column gave 5 g. (0.033 mole, 90% yield) of benzyl-α-*d* acetate, b.p. 99–100° (10–11 mm.), having $\alpha^{25}\mathrm{D}$ $-0.208 \pm 0.004°$, $\alpha^{25}{}_{5463}$ $-0.251 \pm 0.014°$ (l 4).

Ethylene Glycol Diacetate.—Acetic anhydride was added to freshly fractionated commercial ethylene glycol diacetate, and the mixture was refluxed for 2 days. Fractional distillation through a 15-plate Oldershaw column gave ethylene glycol diacetate, b.p. 188.8–190.3°.

Lithium Bromide.—Mallinckrodt N.F. lithium bromide was dried in an oven at 180° for 2 days.

Anal.[21] Calcd. for LiBr: Br, 92.01. Found: Br, 92.00, 91.98.

Kinetics of Racemization of Benzyl-α-*d* Bromide with Lithium Bromide.—A 0.06064 *M* solution of lithium bromide was prepared by making up 0.13170 g. of lithium bromide to a volume of 25 ml. with ethylene glycol diacetate. A 0.78 *M* solution of (+)-benzyl-α-*d* bromide was prepared by diluting 3.34 g. of benzyl-α-*d* bromide having $\alpha^{20}\mathrm{D}$ $+1.000$ (l 2) with ethylene glycol diacetate to a volume of 25 ml. at 20°. After equilibration of each solution in a 35° thermostat overnight the solutions were mixed and were used to fill a 4-dc. jacketed polarimeter tube maintained at 33.9 ± 0.1° by circulating oil from a constant temperature bath. The optical rotation of the solution was measured as a function of time. Each rotation was the average of 2 readings, one taken immediately prior to and the other immediately after the time noted for the observed rotation. The rate was calculated from the data covering 75% completion of reaction by the method of least squares using the usual equation for a second-order rate constant. k_2 was calculated to be $9.46 \pm 0.21 \times 10^{-2}$ l. mole^{-1} min.$^{-1}$. The data are given in Fig. 1. The concentration of lithium bromide was corrected for solvent expansion using the coefficient of expansion of ethylene glycol diacetate determined by Sugden and Willis.[15] From the data of Sugden and Willis[15] the rate constant for exchange of benzyl bromide with lithium radiobromide at 33.9° was calculated to be 9.36×10^{-2} l. mole^{-1} min.$^{-1}$.

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[21] Analysis by the Microanalytical Laboratory, Department of Chemistry, University of California.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BUCKNELL UNIVERSITY]

Intramolecular Substitution Reactions. IX. The Methanolysis of Some N-2-Bromoethylbenzamides[1]

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The kinetics of methanolysis of some N-2-bromoethylbenzamides were studied. It was shown that the kinetics were of first order and that electron-withdrawing groups substituted on the benzene ring decrease the rate of release of bromide ion. The products of solvolysis were N-2-methoxyethylbenzamides and either an oxazolinium bromide or a 2-aminoethylbenzoate hydrobromide. Addition of acetate ion did not affect the rate of methanolysis of N-2-bromoethyl-*p*-chlorobenzamide, although the reaction product was the corresponding oxazoline. The syntheses of a new oxazolinium bromide, a 2-aminoethylbenzoate hydrobromide and two N-2-methoxyethylbenzamides are reported.

In an earlier paper of this series[3] a kinetic study of the reaction of some N-2-bromoethylbenzamides with methoxide ion was described. The kinetics of the reaction was first order with respect to the benzamide and first order with respect to the base and the products were 2-oxazolines. Introduction of electron-withdrawing groups in the aryl system facilitated the formation of 2-oxazolines which indicated that the rate of reaction depends in part on the ease of removal of the hydrogen from the nitrogen. It was also observed that an appreciable displacement of bromine occurred when the N-2-bromoethylbenzamides were dissolved in methanol in the absence of methoxide ion. A kinetic study and product analysis of this solvolysis are presented here.

The rate of solvolysis as measured by the release of bromide ion followed first-order kinetics. In contrast to the reactivity observed in the alkaline methanolysis, substitution of electron-withdrawing groups in the aryl system decreased the reaction rate. In a particularly critical study of the products of methanolysis of N-2-bromoethyl-*p*-chlorobenzamide, it was possible to isolate N-2-methoxyethyl-*p*-chlorobenzamide and in addition either *p*-chlorophenyloxazolinium bromide or 2-aminoethyl-*p*-chlorobenzoate hydrobromide, depending upon the method of working up the reaction mixture.

The methanolysis of N-2-bromoethyl-*p*-chlorobenzamide in the presence of acetate was investigated as well. First-order kinetics were again exhibited, the rate constant being identical with that obtained from the reaction of the benzamide in methanol. The product isolated under these experimental conditions was 2-*p*-chlorophenyl-2-oxazoline.

Experimental

Method of Rate Measurement.—The measurements were carried out analogously to the alkaline methanolysis.[3] The

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[3] H. W. Heine, THIS JOURNAL, **78**, 3708 (1956).