[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

Stereospecificity in the Rearrangement of Amino Alcohols. III. The Configurations of "α"- and "β"-1-*p*-Chlorophenyl-1,2-diphenyl-2-aminoethanol[1]

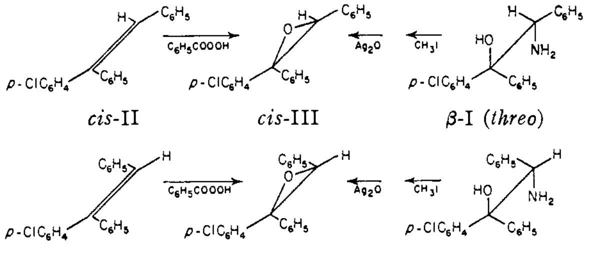
BY DAVID Y. CURTIN, ELBERT E. HARRIS AND PETER I. POLLAK

On the basis of its rearrangement with nitrous acid the "α"-racemate of 1-*p*-chlorophenyl-1,2-diphenyl-2-aminoethanol had been tentatively assigned the *erythro*-configuration and the "β"-racemate, the *threo*-. This assignment is now confirmed by the conversion with methyl iodide and silver oxide of the "α"-racemate to *trans*-1-*p*-chlorophenyl-1,2-diphenylethylene oxide and the "β"-racemate to the *cis*-oxide. These oxides are prepared (and their configurations assigned) by the oxidation with perbenzoic acid of *trans*- and *cis*-1-*p*-chlorophenyl-1,2-diphenylethylene, respectively.

In the previous paper of this series[2] the two racemates of 1-*p*-chlorophenyl-1,2-diphenyl-2-aminoethanol (*dl*-α- and *dl*-β-I)[3] were described. The two racemates were rearranged with nitrous acid and found to give two different products. On the basis of an interpretation of the stereospecificity observed in this reaction, *dl*-α-I was tentatively assigned the *erythro*-configuration and *dl*-β-I, the *threo*-. In order to support our explanation of the stereospecificity of these rearrangements it was desirable to establish the configurations of α-I and β-I by an independent route.

Since *cis*- and *trans*-1-*p*-chlorophenyl-1,2-diphenylethylene (*cis*- and *trans*-II) have been prepared and their stereochemistry determined[4] they provided the starting point for this work. *cis*-II, on oxidation with perbenzoic acid, gave a single racemic oxide, *dl*-*cis*-1-*p*-chlorophenyl-1,2-diphenylethylene oxide (*dl*-*cis*-III) while *trans*-II, on similar oxidation, gave only *dl*-*trans*-III. Perbenzoic acid oxidations of other olefins have been shown to lead to retention of configuration at the double bond.[5] The configurations of *cis*- and *trans*-III have therefore been assigned on the basis of the perbenzoic acid oxidations.

The configurations of α- and β-I were related to those of *cis*- and *trans*-III in the following manner. When *dl*-α-I was converted to the quaternary ammonium salt with methyl iodide and then treated with silver oxide it was converted to an oxide shown to be identical with *dl*-*trans*-III. Similar treatment changed *dl*-β-I to *dl*-*cis*-III. This conversion of a quaternary ammonium alcohol to an oxide has been shown in other cases to proceed with inversion of configuration at the N-containing carbon.[6] If the reactions of α- and β-I are accepted as proceeding with an analogous steric course then *dl*-α-I has the *erythro*-configuration and *dl*-β-I, the *threo*-, in agreement with the configurational assignment based on the nitrous acid reaction. These reactions are illustrated below for one enantiomorph of each racemic pair.



cis-II *cis*-III β-I (*threo*)

trans-II *trans*-III α-I (*erythro*)

Experimental[7]

***dl*-*cis*-1-*p*-Chlorophenyl-1,2-diphenylethylene Oxide** (*dl*-*cis*-III).—*cis*-1-*p*-Chlorophenyl-1,2-diphenylethylene[4] (0.40 g., 0.00137 mole) was allowed to stand at room temperature for 23 hours in 1.8 cc. of chloroform containing 0.0014 mole of perbenzoic acid as shown by iodometric titration.[8] At the end of this time the solution no longer gave a color with potassium iodide solution. After extraction with 5% sodium bicarbonate solution and water, the chloroform was removed at reduced pressure, yielding 0.73 g. (88%) of white crystals, m.p. 67–74°. Two recrystallizations from ethanol gave 0.23 g. (55%) of long white needles, m.p. 87–88°. The analysis was carried out on a sample of the compound prepared from *dl*-β-I below.

Anal. Calcd. for $C_{20}H_{15}OCl$: C, 78.3; H, 4.9; Cl, 11.6. Found: C, 78.2; H, 5.1; Cl, 11.4.

***dl*-*trans*-1-*p*-Chlorophenyl-1,2-diphenylethylene Oxide** (*dl*-*trans*-III).—*trans*-1-*p*-Chlorophenyl-1,2-diphenylethylene[4] (0.50 g., 0.00172 mole) was oxidized with a solution of 0.00185 mole of perbenzoic acid in 2.4 cc. of chloroform at room temperature. After 52 hours the reaction was not yet complete. It was run for a total of 70 hours at the end of which time a test for perbenzoic acid as above was negative. The oxide (*dl*-*trans*-III) was isolated as above (yield, 0.43 g., 81%, m.p. 87–98°). Two recrystallizations from ethanol gave small white prisms, m.p. 101–102°. The analysis was carried out on a sample prepared from *dl*-α-I below.

Anal. Calcd. for $C_{20}H_{15}OCl$: C, 78.3; H, 4.9; Cl, 11.6. Found: C, 78.4; H, 5.1; Cl, 11.1.

Conversion of *dl*-α-1-*p*-chlorophenyl-1,2-diphenyl-2-aminoethanol (*dl*-α-I) **to *dl*-*trans*-III.**—The aminoalcohol (*dl*-α-I) (2.0 g., 0.0062 mole) was converted to the quaternary ammonium iodide by the method used by Rabe and Hallensleben for the 1,2-diphenylethanolamines.[9] Their method of stirring the quaternary ammonium salt with silver oxide was found less satisfactory than decomposition of the salt by passing it through a column packed with freshly precipitated silver oxide (10 cm. high, 3 cm. in diameter). The brown column slowly became white with considerable evolution of heat (the temperature rose to about 40°). Evaporation of the resulting solution gave *dl*-*trans*-III (1.5 g., 75% yield) which after recrystallization from ethanol melted at 102–103°. A mixed m.p. with *trans*-III above was not depressed.

Conversion of *dl*-β-1-*p*-Chlorophenyl-1,2-diphenyl-2-aminoethanol (*dl*-β-I) **to *dl*-*cis*-III.**—The aminoalcohol (*dl*-

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(1) Taken in part from the Ph.D. thesis submitted to Columbia University by Peter I. Pollak. Presented at the 118th Meeting of the American Chemical Society, September, 1950.

(2) D. Y. Curtin and P. I. Pollak, THIS JOURNAL, **73**, 992 (1951).

(3) The designations "α" and "β" have been used with compounds of this type to refer to the method of synthesis rather than to configuration. Thus, the α-racemate is that prepared from α-aminobenzyl-phenyl ketone and *p*-chlorophenylmagnesium bromide while the β-racemate is that prepared from α-amino-*p*-chlorobenzyl phenyl ketone and phenylmagnesium bromide.

(4) D. Y. Curtin and E. E. Harris, THIS JOURNAL, **73**, 2716 (1951).

(5) F. Kayser, *Compt. rend.*, **196**, 1127 (1933); D. Swern, THIS JOURNAL, **70**, 1235 (1948).

(6) See S. Winstein and R. B. Henderson, "Heterocyclic Compounds," R. C. Elderfield, Editor, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 13.

(7) All melting points are corrected. The elemental analyses were carried out by the Clark Microanalytical Laboratories, Urbana, Illinois.

(8) "Organic Syntheses," Collected Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 431.

(9) P. Rabe and J. Hallensleben, *Ber.*, **43**, 884 (1910).

β-I) (2.0 g., 0.0062 mole) was treated in the same manner as *dl*-α-I above. The yield of crude *dl*-*cis*-III was 1.6 g. (85%) which after recrystallization from ethanol melted at 86–87°. A mixed m.p. with *dl*-*cis*-III prepared above showed no depression.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF GEORGIA]

The Action of Silver Picrate on Alkyl Halides

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The synthesis of alkyl picryl ethers by the method of Stenhouse and Muller has been studied and extended to the preparation of seven alkyl picryl ethers. Isopropyl and *n*-butyl picryl ethers have been prepared for the first time. The effect of the nature of the alkyl group on these reactions has been studied. Silver picrate has been found to dehydrohalogenate alkyl iodides under mild conditions and the production of picric acid in these reactions has been explained. The method of Bird for the synthesis of these compounds has been re-examined.

The production of ethyl picryl ether from silver picrate and ethyl iodide was first reported by Stenhouse and Muller.[2] These authors observed that picric acid was the major product of this reaction unless large excesses of ethyl iodide were used. Picric acid was the main product also when ethyl alcohol was present as a solvent. The method was applied by Holleman[3] to the preparation of methyl picryl ether from methyl iodide, and by Meisenheimer[4] to the preparation of isobutyl picryl ether.

Bird[5] has claimed the preparation of the methyl, ethyl, phenyl and benzyl ethers by the reaction of organic halides with a solution of silver picrate in diethylene glycol monoethyl ether.

These reactions have been investigated. The method of Stenhouse and Muller[2] has been extended to cover the preparation of the methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl and isoamyl ethers. Attempts to prepare the *n*-amyl compound failed. The method of Bird was found to yield picric acid in all the cases examined other than the preparation of ethyl picryl ether.

It has been found that silver picrate does not react with methyl, ethyl, *n*-propyl, *n*-butyl, *n*-amyl and isoamyl bromides when refluxed on the water-bath. The silver picrate was recovered unchanged.

The production of picric acid was observed in these reactions by Stenhouse and Muller.[2] This product is obtained in the presence of alcohol or benzene as solvents. The picric acid was shown not to result from hydrolysis by running the reactions under anhydrous conditions. When the reaction was carried out in a closed system and the gaseous products were swept through a solution of bromine in ligroin, the bromine was rapidly decolorized. That the alkyl radical was probably lost as the unsaturated hydrocarbon was shown in the case of *t*-butyl bromide by isolating 2-methyl-1,2-dibromopropane from the ligroin solution after decolorization. Silver picrate dehydrohalogenates the primary alkyl iodides examined above methyl at reflux temperatures. This reaction does not appear to have been reported and accounts for the production of picric acid frequently observed in these reactions. The three secondary iodides investigated gave picric acid at temperatures of 0° and higher. Isopropyl iodide gave the ether when the temperature was lowered to −60°. 2-Butyl and 3-pentyl iodides gave no reaction at −60°. *t*-Butyl bromide gave picric acid at all temperatures investigated (−60 to 72°).

In the course of this study two new alkyl picryl ethers, isopropyl picryl ether and *n*-butyl picryl ether, were prepared. The isopropyl compound appears to be the only picryl ether known with a secondary alkyl group. It has an unexpectedly high melting point and is resistant to hydrolysis in water or dilute hydrochloric acid.

The yields of the crude compound in these reactions varied from 30 to 80% based on silver picrate, and were somewhat variable. Practically all of the unreacted halide may be recovered and the yields based on halide are comparable if allowance is made for the recovered halide. The losses on recrystallization of the lower melting compounds are rather high. In most cases recrystallization is unnecessary.

Experimental[6]

Materials.—The alkyl halides used in this study were prepared by standard methods and dried over calcium chloride.

Bird's[5] directions for the preparation of silver picrate solutions call for the addition of the stoichiometric amount of picric acid to a suspension of "silver hydroxide" in diethylene glycol monoethyl ether, and heating the solution at 80° until the mixture gives a neutral reaction. We were unable to obtain neutral reactions from these solutions even with large excesses of "silver hydroxide." The following technique was employed in this study. "Silver hydroxide" was prepared by the slow addition of sodium hydroxide (24 g., 0.60 mole) dissolved in water (500 ml.) to silver nitrate (100 g., 0.56 mole) dissolved in water (500 ml.). The precipitated "silver hydroxide" was washed by decantation, filtered and transferred to a liter beaker containing diethylene glycol monoethyl ether (345 g., 350 ml.). Air dried picric acid (130 g., 0.56 mole) was added with stirring and the mixture was heated on an oil-bath at 90–95° for 45 minutes. The viscous solution was filtered with suction through an asbestos mat to remove a small quantity of unreacted "silver hydroxide." Dried "silver hydroxide" or commercial silver oxide with added water will not dissolve under these conditions.

Silver picrate[7] was prepared by diluting 300 ml. of the

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[1] Richmond Fellow 1949–1950. Part of this material is from a thesis submitted by D. J. Massey in partial fulfillment of the requirements for the degree of Master of Science in Chemistry.

[2] J. Stenhouse and H. Muller, *Ann.*, **141**, 80 (1867).

[3] A. F. Holleman, *Rec. trav. chim.*, **22**, 263 (1903).

[4] J. Meisenheimer, *Ann.*, **323**, 242 (1902).

[5] J. C. Bird and A. Barol, *J. Am. Pharm. Assoc.*, **23**, 996 (1934); J. C. Bird, U. S. Patent 2,165,111 (1937).

[6] All melting points are corrected. Other temperatures are uncorrected.

[7] Silver picrate is sensitive to heat and shock and has been employed as a detonator. The precautions appropriate to the preparation and handling of highly explosive compounds should be observed at all times.