using a Beckman Century SS-1 pH meter (*4*). The end point and the HNP were determined graphically. All runs were carried out in duplicate, with a precision of ±5 mV.

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Preparation of (+)- and (−)-2,3-Dibromo-1-propanols

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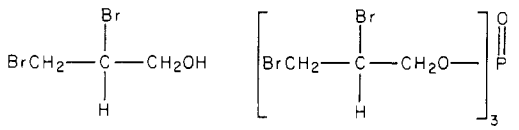
The enantiomers of 2,3-dibromo-1-propanol were obtained by diazotization of the diastereomeric *d*-tartrate salts of 2,3-dibromopropylamine. The products of the reaction contained approximately 13% of the secondary alcohol 1,3-dibromo-2-propanol which was separated by either column chromatography on silica gel or preparative GLC to obtain the primary alcohols (+)-2,3-dibromo-1-propanol ($[\alpha]^{26}_D$ +13.8°) and (−)-2,3-dibromo-1-propanol ($[\alpha]^{24}_D$ −12.8°). NMR and EI mass spectra of the primary and secondary dibromopropanols clearly distinguished the structural isomers from one another. The optical isomers will be used to examine possible stereoselective differences in mutagenic potency, since 2,3-dibromo-1-propanol is a mutagenic metabolite of the potent mutagen and carcinogen tris(2,3-dibromopropyl) phosphate.

2,3-Dibromo-1-propanol (**1**) is a mutagenic metabolite of the



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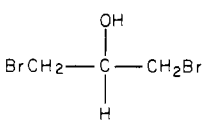

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potent mutagen, carcinogen, and nephrotoxin tris(2,3-dibromopropyl) phosphate (**2**) (*1*–*4*). Both the alcohol and the ester are oxidized by microsomal cytochrome P-450 to reactive metabolites that apparently bind covalently to tissue macromolecules (DNA, RNA, and protein) (*5*), causing reactions that eventually damage the cell. Because oxidations by cytochrome P-450 are often stereoselective, we were interested in determining the influence of stereochemistry on the toxic properties of 2,3-dibromo-1-propanol and its phosphate ester. Herein we describe the synthesis and purification of the optical isomers of **1**.

Enantiomeric 2,3-dibromo-1-propanols were obtained by the diazotization of the diastereomeric *d*-tartrate salts of 2,3-dibromopropylamine. The products of the diazotization reaction invariably contained about 13% of the secondary alcohol 1,3-dibromo-2-propanol (**3**). Failure to recognize this side-reaction rearrangement by early investigators may account in part for the lower specific rotation values reported for the dextrorotary isomer ranging from 6.5° (*6*) to 7.27° (*7*, *8*) compared to $[\alpha]^{26}_D$ = +13.8° for our purified product. In the 7.27° case there is another possible complicating factor. The bromination of allylamine was carried out on the hydrochloride instead of the hydrobromide salt. A mixture of dibromo and chlorobromo products is formed in this reaction (personal observation).

A similar question is raised regarding the report by Dix and Bresson (*9*) of the synthesis of 2,3-dibromopropylamine hydrochloride by the bromination of allylamine in hydrochloric acid solution. Mass-spectrometric analysis, in our laboratory, of products obtained by the reaction conditions described by Dix and Bresson showed approximately an equimolar mixture of chlorobromo and dibromo products.

Experimental Section

General Methods. Capillary melting points were determined on a Thomas-Hoover apparatus and are uncorrected. NMR spectra were recorded on a Varian EM 360A spectrometer and are expressed in parts per million from Me_4Si as internal standard. Specific rotations were determined with a Jasco DIP-4 digital polarimeter using a 1-dm, 10-mL cell. GLC analyses were performed on a Hewlett-Packard 5840A gas chromatograph using a 6 ft × 2 mm glass column packed with 3% SE-30 on 100–120 mesh Gas Chrom Q at 150 °C oven temperature. Preparative GLC separation was performed on a Varian Aerograph Model 920 using a 20 ft × $^3/_8$ in. stainless-steel column packed with 3% SE-30 on 60–80 mesh Gas Chrom Q, at 130 °C. Mass spectra were recorded on a VG MicroMass 707OH double-focusing instrument. Samples of compounds were introduced by using a direct insertion probe and EI spectra were recorded at a nominal resolution of 1000 (10% valley) using an accelerating voltage of 4 kV, an electron energy of 70 eV, and a trap current of 100 μA. Source temperature was 200 °C.

Materials. *d*-Tartaric acid was "Baker Analyzed" reagent grade. Allylamine was obtained from Aldrich Chemical Co. Silica gel 0.05–0.2 mm was from E. Merck, Germany, and neutral aluminum oxide (Activity I) was from M. Woelm, Germany. Benzene and hexane were distilled prior to use for chromatography.

***2,3-Dibromopropylamine Hydrobromide* (4).** Concentrated HBr (280 mL, 2.4 mol) was added with stirring to a cooled solution of allylamine (2 mol) in 150 mL of H_2O at such a rate that the temperature did not exceed 20 °C. Bromine (320 g, 2 mol) was then added at such a rate that the temperature remained between 15 and 20 °C. A white precipitate developed when less than half of the bromine was added. Bromine addition was continued until yellow color persisted and about 1

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g of bromine remained. Filtration yielded 469 g of colorless crystalline product, mp 168–172 °C. Evaporation of the filtrate gave 60 g of additional product. Recrystallization from methanol gave mp 170–172.5 °C (lit. (*6*) 164 °C).

Resolution. All procedures in the formation of the *d*-tartrate salts were performed at ice temperatures. To a stirred cold mixture of **4** (29.8 g, 0.1 mol) in 180 mL of H_2O and 125 mL of ether was added a cold solution of NaOH (4.4 g, 0.11 mol) in 40 mL of H_2O. After separation of the ether layer, the aqueous layer was extracted with three portions of cold ether (100-mL total). The combined ether solution was washed once with cold H_2O and added to a cold solution of *d*-tartaric acid (15.1 g of 99.7%, 0.1 mol) in 175 mL of methanol. Filtration of the resulting precipitate yielded 32.4 g of colorless crystalline material, $[\alpha]^{22}_D$ +10.7° (*c* 1.0, H_2O). The material was recrystallized from methanol (temperature below 60 °C): first crop (room temperature), 13 g, $[\alpha]^{22}_D$ −2.5°; second crop (0 °C), 4 g, $[\alpha]^{22}_D$ +9°; third crop (solvent reduction), 12 g, $[\alpha]^{22}_D$ +24°.

Several recrystallizations of the levorotary first-crop material from methanol (temperature < 60 °C) gave the (−) *d*-tartrate salt of mono-2,3-dibromopropylamine [**(−)-5**], $[\alpha]^{24}_D$ −12.8° (*c* 0.939, H_2O).

Several recrystallizations of the third-crop material (dextrorotary) from H_2O (temperature < 60 °C) gave the (+) *d*-tartrate salt of mono-2,3-dibromopropylamine [**(+)-5**], $[\alpha]^{24}_D$ +34.8° (*c* 0.939, H_2O) (lit. (*6*) $[\alpha]_D$ 31°).

(+)-2,3-Dibromo-1-propanol **[(+)-1].** To a cold solution of the (+) *d*-tartrate salt **(+)-5** (5.5 g, 0.015 mol) in 40 mL of H_2O containing 0.77 g of H_2SO_4 was added with stirring a solution of $NaNO_2$ (1.25 g of 97%, 0.0175 mol) in 10 mL of H_2O over a period of 6 min. Stirring of the cold mixture was continued for 30 min and the mixture was then allowed to stand at room temperature overnight. Usual workup, after adding 0.5 g of urea, gave 2.4 g of light yellow liquid, $[\alpha]^{22}_D$ +12.6° (*c* 1.253, MeOH). Comparison of the NMR spectrum with that of reference 2,3-dibromo-1-propanol showed an extraneous doublet (J = 6 Hz) at δ 3.6, indicative of contamination with some 1,3-dibromo-2-propanol. GLC analysis showed 87% of the major primary alcohol and 13% of the secondary.

Chromatographic separation was performed on dry packed columns of silica gel or neutral aluminum oxide (deactivated with 8% H_2O) using mixtures of hexane, benzene, and ether. The secondary alcohol eluted first on the silica gel while the primary was first on the aluminum oxide. There was considerable retention on aluminum oxide which varied with degree of deactivation. Fractions were analyzed by NMR or GLC. Distillation of combined best fractions from several runs (0.395 g), using a micro cold finger apparatus, at 3 mm (oil bath temperature gradually raised to 90 °C) gave 0.301 g of colorless liquid (99.5% primary alcohol by GLC), $[\alpha]^{26}_D$ +13.8° (*c* 1.004, MeOH).

(−)-2,3-Dibromo-1-propanol **[(−)-1].** The levorotary enantiomer was obtained from the (−) *d*-tartrate salt **(−)-5** by the procedure described above for the dextrorotary enantiomer. Distillation of 0.36 g of combined chromatography fractions yielded 0.19 g of colorless liquid (98.8% primary alcohol by GLC), $[\alpha]^{29}_D$ −12.6° (*c* 1.076, MeOH).

Separation of the primary and secondary alcohols was also accomplished by preparative GLC. The compounds so obtained were analyzed by mass spectrometry. Both 2,3-dibromo-1-propanol and 1,3-dibromo-2-propanol gave low-intensity (~2% of height of the base peak) molecular ions at *m/z* 216, 218, and 220 in an approximate ratio of 1:2:1 corresponding to the abundance of the various bromine isotopes. Corresponding low-intensity ion fragments due to loss of the hydroxyl radical were observed at *m/z* 199, 201, and 203. The spectra for the two structural isomers differed markedly in the intensities of other fragment ions. Whereas 2,3-dibromo-1-propanol produced intense (80–90% of the height of the base peak) fragment ions from the loss of a bromine radical and HBr, 1,3-dibromo-2-propanol produced weakly intense ions at *m/z* 136, 137, 138, and 139 (17–20% of the height of the base peak). Furthermore, the base peaks for the primary alcohol were at *m/z* 106 and 108, corresponding to the loss of HBr plus H_2CO, whereas the base peaks for the secondary alcohol were at *m/z* 123 and 125, corresponding to the loss of the bromomethylene radical.

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Preparation of New *N*-[α-(Benzylidenamino)benzyl]benzamides and *N*,*N*′-Benzylidenebis(benzamides)

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Several benzylamines were oxidized with buffered potassium permanganate to give complex iminobenzamides. These products were then aroylated with acid chlorides to give bis(benzamides).

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In connection with the earlier work concerning the novel oxidation of benzylamines to give complex iminobenzamides (*1–3*), several new examples of the reaction are now reported (Table I). These iminobenzamides, and others, were transformed into complex bis(benzamides) by treatment with a variety of aromatic acid chlorides (Table II).

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