distillation of solvent. After removal of the volatile material the residue was dissolved in 5.5 l. of water, washed with ether, filtered, and acidified to *p*H 2, whereupon the product separated, 262 g. (96.5%), m.p. 207–211°. On recrystallization (9 parts methyl ethyl ketone) there was obtained 217 g. (83%), m.p. 217–218°.

Sodium(2-lauroyl)indandione-1,3 (Compound 32). Method C. To a suspension of 54 g. (1 mole) of sodium methoxide in 1200 ml. of benzene was added 198 g. (1 mole) of methyl undecyl ketone and 194 g. (1 mole) of dimethyl phthalate; the mixture was heated under reflux for 24 hr. with stirring. The benzene was removed, the residue suspended in a mixture of 1500 ml. of water and 200 ml. of ether, and while vigorously stirred, acidified with hydrochloric acid to *p*H 3. On extraction of the ethereal phase with 2.5 l. of 2% sodium hydroxide, the sparingly soluble sodium enolate precipitated, was separated, dried (100°), and recrystallized (methylal) to give 93.1 g. (25.9%), m.p. 208–209°.

A suspension of 30 g. (0.084 mole) of the above product in 250 ml. of water and 250 ml. of ether was acidified to *p*H 3 with hydrochloric acid. The ethereal layer was dried (magnesium sulfate), the ether removed, and the residue on recrystallization (methanol) gave 24.8 g., (88%) of 2-lauroylindandione-1,3, m.p. 45–46° (compound 29).

N-Methylglucamine salt of 2-lauroylindandione-1,3, (Compound 30). The mixture of 8 g. (0.024 mole) of 2-lauroylindandione-1,3 and 4.76 g. (0.024 mole) of *N*-methylglucamine in 15 ml. of methanol dissolved after 60 min. heating on the steam bath. The methanol was removed and the residue recrystallized (isopropyl alcohol) to give 6.5 g. (51%) of product, m.p. 90–94°.

2-(Cyclopropylketo)indandione-1,3 (Compound 22). Method D. A solution of 5.75 g. (0.25 mole) of sodium in methanol was prepared and the methanol removed. Benzene (150 ml.) was added and residual methanol removed by azeotropic distillation. After addition of 21 g. (0.25 mole) of methyl cyclopropyl ketone and 48.5 g. (0.25 mole) of dimethyl phthalate in 125 ml. of benzene, the reaction mixture was heated under reflux for 6 hr. with stirring. After steam distillation, the nonvolatile residue was diluted with one l. of water, filtered, and the product precipitated by acidification with hydrochloric acid to *p*H 3. Recrystallization (acetone-water) gave 16 g. (30%) of product, m.p. 132–134°.

Acknowledgment. The authors wish to thank Dr. G. Ungar and his staff for the pharmacological screening of the compounds, M. Blitz and R. Levinton for the antibacterial results, and D. Farkas for the ultraviolet absorption data.

YONKERS 1, N. Y.

[CONTRIBUTION FROM PLASTICS LABORATORY AND RESEARCH CENTER, MINNEAPOLIS-HONEYWELL REGULATOR CO.]

Reaction of Aniline with 3-Phenoxy-1,2-epoxypropane

LEMONT B. KIER[1] AND RAYMOND B. PENLAND[2]

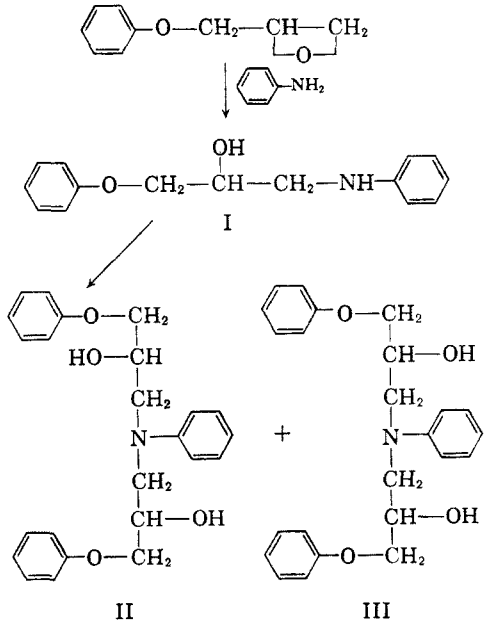
Received December 21, 1959

The products from the reaction of aniline and 3-phenoxy-1,2-epoxypropane have been characterized. One compound was shown to be a secondary amine and the other two to be the *dl* and *meso* forms of a tertiary amine. The structures were proved by independent synthesis.

In order to study the reaction between polyfunctional epoxides and polyfunctional aromatic amines in the formation of resins, a study was made of the model reaction between 3-phenoxy-1,2-epoxypropane and aniline. Fourneau[3] reported one compound from this reaction to which he assigned the structure I; however he reported no evidence for his assignment.

From the direct reaction of 3-phenoxy-1,2-epoxypropane and aniline, the authors have obtained three crystalline products, I, II, and III. Compound I proved to be a secondary amine, while II and III, not previously reported, were higher molecular weight tertiary amines. By the reaction of I with a second mole of 3-phenoxy-1,2-epoxypropane, II and III were formed, indicating that the original model reaction involved two steps.

The infrared spectrum of I indicated it to be a secondary aminoalcohol in conformance with Fourneau's assignment, and the spectra of II and III, which were identical, indicated that they were tertiary aminoalcohols, hence must be related as the *dl* and *meso* forms. The structures of I,



I

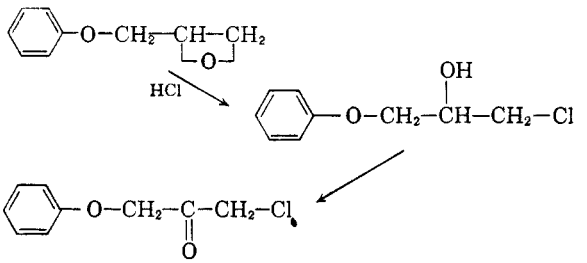
II III

(1) Present address: College of Pharmacy, University of Florida, Gainesville, Fla.

(2) Present address: U. S. Borax Research, Anaheim, Calif.

(3) E. Fourneau, *J. Pharm. Chem.*, 1, 99 (1910).

II, and III were proven by an independent synthesis[4,5] using 3-phenoxy-2-hydroxypropyl chloride IV prepared by the reaction of 3-phenoxy-1,2-epoxypropane and hydrochloric acid. Proof of the structure of IV was made by oxidation to the haloketone V which was identified by its infrared spectrum.



The reaction of IV with aniline gave a product which proved to be identical with I. This product was treated with additional IV to give two compounds which were found to be identical with II and III. Attempts to resolve either II or III to prove which one was the *dl* were unsuccessful. A quantity of the (+) form of I was prepared by separation of the diastereoisomers formed with *d*-camphor sulphonic acid. This (+) I was treated with 3-phenoxy-1,2-epoxypropane to give two tertiary aminoalcohols, one of which was optically active. The optically active product must be a resolved form of II which is the *dl* form.

EXPERIMENTAL

Model reaction of aniline and 3-phenoxy-1,2-epoxypropane. Aniline (6.2 g., 0.067 mole) was treated with 3-phenoxy-1,2-epoxypropane (10 g., 0.067 mole) at 95° in an oven for 16 hr. The product was a dark resinous material which eventually crystallized. The crude product was fractionally crystallized from methanol-water yielding three products: I, 4.0 g., m.p. 56–57°, yield 25%; II, 3.0 g., m.p. 87–88°, III, 3.0 g., m.p. 96–97°, yields for both 23% based on 3-phenoxy-1,2-epoxypropane.

3-Phenoxy-1-anilino-propan-2-ol (I). The material for analysis was recrystallized from methanol-water four times, giving needles, m.p. 56–57°.

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.04; H, 7.04; N, 5.76; Mol. wt., 243. Found: C, 74.22; H, 6.98; N, 5.70; Mol. wt., 250 (Rast camphor).

The infrared spectrum (potassium bromide pellet) had a band at 7.75 μ (*sec*-amine C—N).

A *picrate* of I was prepared and recrystallized from ethanol as yellow plates, m.p. 127–129°.

Anal. Calcd. for $C_{21}H_{20}N_4O_9$: C, 53.39; H, 4.27; N, 11.86. Found: C, 53.53; H, 4.30; N, 11.68.

dl-N,N-Di(3-phenoxy-2-hydroxypropyl) aniline (II). The material was recrystallized several times from methanol-water to give needles, m.p. 87–88°.

Anal. Calcd. for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56, Mol. wt., 394. Found: C, 73.53; H, 6.70; N, 3.68; Mol. wt., 412 (Rast camphor).

The infrared spectrum had a band at 7.40 μ (*tert*-amine C—N).

A *picrate* of II was prepared and recrystallized from ethanol as yellow needles, m.p. 125–127°.

Anal. Calcd. for $C_{30}H_{30}N_4O_{11}$: C, 57.87; H, 4.86; N, 9.00. Found: C, 57.76; H, 4.80; N, 8.83.

meso-N,N-Di(3-phenoxy-2-hydroxypropyl) aniline (III). This material was isolated from the final mother liquor and recrystallized four times from methanol-water as transparent plates, m.p. 96–97°.

Anal. Calcd. for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56; Mol. wt., 394. Found: C, 73.10; H, 6.72; N, 3.62; Mol. wt., 406 (Rast camphor).

The infrared spectrum showed a band at 7.40 μ (*tert*-amine C—N).

A *picrate* derivative of III was recrystallized from ethanol as yellow needles m.p. 137–139°.

Anal. Calcd. for $C_{30}H_{30}N_4O_{11}$: C, 57.87; H, 4.86; N, 9.00. Found: C, 57.83; H, 4.91; N, 8.87.

Reaction of I *with 3-phenoxy-1,2-epoxypropane.* Compound I (6.85 g., 0.028 mole) and 3-phenoxy-1,2-epoxypropane (4.05 g., 0.027 mole) were allowed to react at 120° in an oven overnight. The resinous solid was recrystallized to give 4.7 g., 43% yield, of a compound, m.p. 96–97° and 4.7 g., 43% yield of a compound, m.p. 87–88°. Both of these compounds gave no depression in mixed melting point with their respective products II and III from the model reaction.

3-Phenoxy-2-hydroxypropyl chloride. Hydrochlorination of 3-phenoxy-1,2-epoxypropane to the corresponding chlorohydrin, 3-phenoxy-2-hydroxypropyl chloride IV, was accomplished with dry hydrogen chloride.[6,7] The conversion was almost quantitative, b.p. 136–137° (8 mm.), n_D^{24} 1.5410, d_4^{24} 1.210. Literature values[8]: b.p. 125–126° (2 mm.), n_D^{25} 1.540, d_4^{25} 1.209; and[9] b.p. 153–155° (12.5 mm.), n_D^{25} 1.542, $d_4^{23.5}$ 1.210.

Anal. Calcd. for $C_9H_{11}ClO_2$: C, 57.90; H, 5.94; Cl, 18.00. Found: C, 58.03; H, 6.11; Cl, 18.75.

Oxidation of IV *to ketone.* To prove the secondary hydroxyl of IV, it was oxidized with chromium trioxide in sulfuric acid[10] to give the corresponding ketone V, b.p. 145–146° (12 mm.). The infrared spectrum had a strong band at 5.73 μ (α-halo ketone). The absence of a band at 3.45–3.70 μ (aldehyde C—H) indicated that the 3-phenoxy-1-hydroxy-2-chloropropane isomer was not formed.

Anal. Calcd. for $C_9H_9ClO_2$: C, 58.65; H, 4.92; Cl, 19.23. Found: C, 58.48; H, 5.11, Cl, 18.95.

Independent synthesis of I. Aniline (42 g., 0.45 mole) was treated with IV (37.4 g., 0.2 mole) at 125° for 7 hr. The amines were dissolved in dilute acid, washed, then rendered alkaline to recover them. The aniline was removed by distillation and the residue recrystallized from methanol-water to give 18 g. (37% yield based on IV) of product, m.p. 56–57°. A mixed melting point with I gave no depression. A comparison of the infrared spectra of the two compounds indicated that they were identical.

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.04; H, 7.04; N, 5.76; Mol. wt., 243. Found: C, 73.92; H, 6.79; N, 5.94: Mol. wt., 237 (Rast camphor).

Independent synthesis of II *and* III. Compound I (48.5 g., 0.2 mole) was refluxed with IV (18.7 g., 0.1 mole) in 50 ml. of xylene at 120° for 10 hr. The reaction mixture was recrystallized from methanol-water to give 7 g. product identical with II (30% yield) and 7 g. of product identical with III (30% yield).

Anal. of product identical with II. Calcd. for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56. Found: C, 72.94; H, 6.65; N, 3.59.

(4) R. T. E. Schenck, and S. Karzerman, *J. Am. Chem. Soc.*, **75**, 1636 (1953).

(5) F. G. Ponomareau, *Zhur. Obshchei Khim.*, **23**, 1638 (1953).

(6) M. Dalfe, *J. Chem. Soc.*, 1861 (1950).

(7) O. J. Stephanson, *J. Chem. Soc.*, 1571 (1954).

(8) A. Fairbourne, *J. Chem. Soc.*, 1965 (1932).

(9) E. Levas, *Compt. rend.*, **222**, 555 (1946).

(10) J. B. Conant, and O. R. Quayle, *Org. Syntheses*, Coll. Vol. I, 206 (1932).

Anal. of product identical with III. Calcd. same as above. Found: C, 73.06; H, 6.95; N, 3.52.

Both of these compounds, as well as their picrates gave no depression in melting point when compared with the corresponding compounds from the model reaction. The infrared spectra of the corresponding products were identical.

d-Camphor sulfonate of I. *d*-Camphor sulfonic acid (23.2 g., 0.1 mole) was dissolved in ethyl acetate containing I (24.3 g., 0.1 mole). From the solution, 20 g., (42% yield) of white crystalline material formed, m.p. 154.5–155.5°.

Anal. Calcd. for $C_{25}H_{33}NO_6S$: C, 63.16; H, 6.99; N, 2.95; S, 6.74. Found: C, 63.15; H, 7.13: N, 3.03; S, 6.73.

The diastereoisomer was not isolated since only one active form of I was needed.

(+) I. The *d*-camphor sulfonate salt (8 g., 0.017 mole) was dissolved in 200 ml. of benzene and refluxed with stirring with 100 ml. of 5% sodium hydroxide for 2 hr. The benzene was washed with water and concentrated to dryness. The residue was taken up in naphtha and refrigerated. Several crops of amorphous material formed totalling 2.6 g., (63.5% yield). After several recrystallizations from methanol-water a white crystalline material formed, m.p. 62–63.5°, $[\alpha]_D^{25}$ + 17.16° (*c*, 2.25 methanol).

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.04; H, 7.04; N, 5.76. Found: C, 74.10; H, 6.89; N, 5.81.

Reaction of (+) I with 3-phenoxy-1,2-epoxypropane. The active I (2.6 g., 0.0107 mole) was treated with 3-phenoxy-1,2-epoxypropane as before. Two products were isolated. The first, m.p. 96–97°, gave no mixed melting point depression with III and was optically inactive. The second compound, m.p. 84.5–85.5°, $[\alpha]_D^{25}$ +23.5° (*c*, 3.45 methanol) gave a marked mixed melting point depression with II.

Anal. of compound m.p. 84.5–85.5°. Calcd. for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56. Found: C, 73.08; H, 6.90; N, 3.76.

Acknowledgment. We are grateful to L. L. Bolstad and P. A. Joyner for their assistance with this work.

MINNEAPOLIS, MINN.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN CO.]

Some Reactions of Mannich Bases Derived from α-Phenoxyacetophenone and α-Phenoxypropiophenone

JOHN B. WRIGHT

Received April 6, 1960

Mannich bases (I) derived from α-phenoxyacetophenone on treatment with polyphosphoric acid were converted in good yields to 2-dialkylaminomethyl-3-phenylbenzofurans (II). The carbinols (III), obtained by catalytic hydrogenation or by treatment of the Mannich bases with Grignard reagents, on treatment with polyphosphoric acid in a similar manner gave the corresponding dihydrobenzofurans (IV). The carbinols were also acylated (V) and several converted to urethanes (VI) by conventional procedures. Attempted acylation of one of the carbinols, namely 1,1-diphenyl-2-phenoxy-2-methyl-3-dimethylaminopropanol (III. R_2 = C_6H_5, R_1 = CH_3, R = CH_3) gave in good yield a nitrogen-free product which was identified as 1,1-diphenyl-2-phenoxypropene (VIII). Heating under reflux with dimethylaniline was found to be a convenient method for converting the Mannich bases (I) to α-phenoxyacrylophenones (VII).

Mannich bases (I) derived from α-phenoxyacetophenone and α-phenoxypropiophenone are prepared readily in good yield.[1,2] They are readily hydrogenated under catalytic conditions to the corresponding carbinols (III. R_2 = H).[1,3] We wish to report now on some further reactions of these compounds.

Reaction of the Mannich bases (I) with polyphosphoric acid, according to the method used by Davies and Middleton[4,5] to prepare phenylbenzofuran from α-phenoxyacetophenone, gave in good yield the corresponding 2-dialkylaminomethyl-3-phenylbenzofurans (II). These compounds, isolated as the *hydrochlorides*, are listed in Table I.

Reaction of the Mannich bases (I) with Grignard reagents gave the corresponding tertiary carbinols (III). These compounds are listed in Table II. In those cases where reaction with the Grignard reagent produced a new asymmetric carbon atom a mixture of diastereoisomers was produced and some difficulty was experienced in separating the two isomers. Treatment of several of the carbinols (III) with polyphosphoric acid in the manner described above gave the corresponding 3-phenyl-2-dialkylaminodihydrobenzofurans (IV, Table III). In the preparation of these compounds a simple dehydration of the carbinols (III. where R_1 = H) to give an isomeric substituted styrene is also possible; however, the dihydrobenzofuran structure is assigned on the basis of the ultraviolet absorption data obtained for these compounds.

The carbinols (III) when treated with acetic anhydride or propionic anhydride in the presence of pyridine gave the corresponding acylated compounds (V). Treatment of the carbinols with phenyl chlorocarbonate followed by cleavage of the resulting product with liquid ammonia gave the

---

(1) J. B. Wright and E. H. Lincoln, *J. Am. Chem. Soc.*, 74, 6301 (1952).

(2) U. S. Patent 2,655,542.

(3) U. S. Patent 2,695,919.

(4) W. Davies and S. Middleton, *Current Trends in Heterocyclic Chemistry*, Academic Press, Inc., New York, N.Y., 1958, p. 58.

(5) W. Davies and S. Middleton, *J. Chem. Soc.*, 822 (1958).