

Experimental

In a typical experiment, 2.10 g. (0.055 mole) of lithium aluminum hydride was suspended in 150 ml. of absolute ether in a 500 ml. 3-necked flask equipped with a dropping funnel and reflux condenser. The mixture was refluxed for several hours in order to dissolve the lithium aluminum hydride. Then 9.8 g. (0.050 mole) of benzenephosphonyl dichloride⁵ in 40 ml. of absolute ether was added dropwise over a three-hour period. A white precipitate formed on the addition of each drop. The contents of the flask were stirred by means of a magnetic stirrer. The repulsive and penetrating odor of phenylphosphine could be noted from the beginning of the reaction. Stirring was continued for an hour after the addition was complete. The reaction mixture was then filtered with nitrogen pressure through a coarse line filter into a distilling flask. The ether was removed and the oily residue distilled in an atmosphere of nitrogen. The yield of phenylphosphine b.p.⁶ 154–157°, was 3.0 g. (55%). In air this material ignites spontaneously at its b.p. and at room temperature gradually changes to white crystalline benzenephosphonic acid. *Anal.* Calcd. for C₆H₅PO₂H₂: neut. equiv., 142.1. Found: neut. equiv., 140.7.

Reduction with lithium borohydride was performed under similar conditions. Tetrahydrofuran⁷ was used as the solvent, and the reaction mixture was refluxed for several hours after the addition of the phosphonyl dichloride. After the solvent was removed, a white solid was obtained together with the oily phosphine. The presence of this solid made the distillation of the phenylphosphine more difficult than when lithium aluminum hydride was used.

Because of the persistent and offensive odor of phenylphosphine, considerable difficulty was encountered in cleaning the apparatus at the conclusion of the experiment. The residual phenylphosphine was best destroyed by adding dilute hydrogen peroxide before disassembling the apparatus and then washing with a slow stream of water for 24 hours or longer.

(5) Kindly furnished by the Victor Chemical Works.

(6) Previously reported b.p. 160–161°, *cf.* ref. 3 and 4.

(7) Kindly furnished by the E. I. du Pont de Nemours and Company.

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Arylcycloalkylamines. III. 2-(3,4-Dimethoxyphenyl)-cyclopropylamine¹

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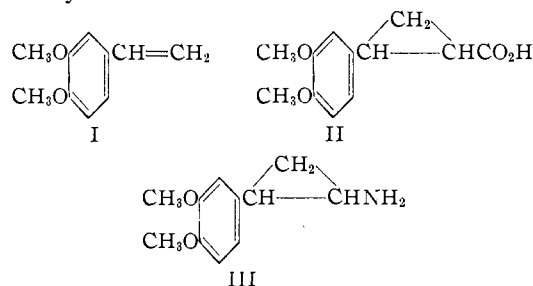
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In view of the observation that substitution of the 3-position by a methyl group enhances the antispasmodic effect of 1-benzylisoquinoline derivatives,² we wished to prepare 1-(3,4-dimethoxybenzyl)-3,4-cyclopropano-3,4-dihydro-6,7-dimethoxyisoquinoline. Although we were unable to effect a Bischler-Napieralski ring closure of N-[2-(3,4-dimethoxyphenyl)-cyclopropyl]-homoveratramide, we are reporting the preparation of this compound from 2-(3,4-dimethoxyphenyl)-cyclopropylamine (III) and homoveratryl chloride.

For the synthesis of III, 3,4-dimethoxystyrene³ (I) was condensed with ethyl diazoacetate, and the resulting mixture of ethyl 2-(3,4-dimethoxyphenyl)-cyclopropanecarboxylates was hydrolyzed to two

stereoisomeric 2-(3,4-dimethoxyphenyl)-cyclopropanecarboxylic acids (II). One of them could be converted to the other one by distilling its chloride and hydrolyzing the latter. The more abundant of the two acids could be degraded to the amine III by the Curtius method, either from the acid chloride and sodium azide, or from the ester by way of the hydrazide, azide and urethan.

Considerable difficulties were encountered in the preparation of the starting material, 3,4-dimethoxystyrene (I), and we were unable to reproduce consistently the procedure described by Frank, *et al.*³ In decomposing the Grignard complex from veratraldehyde and methylmagnesium iodide, extreme caution had to be exercised not to use strongly acidic conditions, or else a polymer of the styrene was formed exclusively.⁴ Furthermore, distillation of 1-(3,4-dimethoxyphenyl)-ethanol under reduced pressure gave mainly the styrene (I) by spontaneous dehydration.



Experimental⁵

2-(3,4-Dimethoxyphenyl)-cyclopropanecarboxylic Acid.—A cold mixture of 51.2 g. (0.312 mole) of 3,4-dimethoxystyrene³ and 62.5 g. (0.55 mole) of ethyl diazoacetate began to evolve nitrogen when it was warmed gradually to 50°. At 110° the exothermic reaction became self-sustaining and had to be retarded by cooling as the temperature rose to 150°. The mixture was then heated at 135–140° for another three hours, and the dark red material was fractionated. The main fractions distilled as thick yellow oils at 175° (*n*_D²⁰ 1.5307) and 192–200° (*n*_D²⁵ 1.5270) under 8.5 mm. but were combined (50 g., 63%) and hydrolyzed by refluxing with a solution of 47 g. of potassium hydroxide in 50 ml. of 85% ethanol for five hours. The alcohol was removed, the residue was acidified with 80 ml. of concentrated hydrochloric acid, and the precipitated mixture of carboxylic acids was allowed to crystallize in the refrigerator. The filtered crude material was dissolved in 3 l. of boiling water which, upon cooling, deposited 23.5 g. (29%) of colorless crystals; recrystallization rendered a sample melting at 105–105.5°.

Anal. Calcd. for C₁₂H₁₄O₄: C, 64.85; H, 6.35. Found: C, 64.77; H, 6.06.

When the mother liquors of the acid of m.p. 105° were evaporated further, a brown solid separated out from which by repeated crystallizations from water, yellowish crystals of m.p. 107–109.5° were obtained.

Anal. Calcd. for C₁₂H₁₄O₄: C, 64.85; H, 6.35. Found: C, 65.10; H, 6.12.

A mixture melting point of the two stereoisomers lay at 79–82°.

2-(3,4-Dimethoxyphenyl)-cyclopropanecarboxylhydrazide.—The acid of m.p. 105° was methylated with diazomethane in a 1:1 mixture of ether and methanol and the solvents were removed. The oily methyl ester (1.9 g.) was refluxed with a solution of 10 ml. of 100% hydrazine hydrate in 4 ml. of ethanol for five hours, and excess solvent and reagent

(1) (a) I. A. Burger and W. L. Yost, *THIS JOURNAL*, **70**, 2198 (1948); (b) II, A. Burger, C. R. Walter, Jr., W. B. Bennet and L. B. Turnbull, *Science*, **112**, 2907 (1950).

(2) H. Kreitmair, *Arch. exper. Pathol. Pharmacol.*, **164**, 509 (1932).

(3) R. L. Frank, C. E. Adams, R. E. Allen, R. Gander and P. V. Smith, *THIS JOURNAL*, **68**, 1365 (1946).

(4) This observation has been confirmed in a private communication from Dr. R. L. Frank, Edwal Laboratories, Inc., Ringwood, Illinois.

(5) All melting points are corrected. Microanalyses by Clark Microanalytical Laboratory, Urbana, Illinois.

was distilled off. The solid colorless hydrazide thus obtained was filtered, washed with water, and recrystallized from slightly dilute ethanol. The yield was 1.5 g. (75%), m.p. 142–144°.

Anal. Calcd. for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.83. Found: C, 60.79; H, 6.79.

2-(3,4-Dimethoxyphenyl)-cyclopropylmethylurethan.—

The hydrazide just described (1.5 g.), dissolved in 100 ml. of 5% hydrochloric acid, was diazotized at 0° with 9 ml. of 5% sodium nitrite solution. The azide separated as an oil; it was extracted into toluene, and dried over sodium sulfate at 0°. Fifty milliliters of methanol was added, the solution was refluxed for five hours, and the solvents were removed under reduced pressure. The remaining oily urethan solidified on treatment with one drop of methanol. The yield of colorless crystals melting at 118–119.5° was 0.7 g. (46%).

Anal. Calcd. for $C_{13}H_{17}NO_4$: C, 62.13; H, 6.82. Found: C, 62.60, 62.62; H, 6.84, 6.60.

2-(3,4-Dimethoxyphenyl)-cyclopropylamine. (a)—2-(3,4-Dimethoxyphenyl)-cyclopropyl methylurethan (0.5 g.) was refluxed for 30 hours with 25 ml. of a saturated methanolic barium hydroxide solution, barium carbonate was filtered and the solvent evaporated under reduced pressure. The white residue was extracted with benzene, and the benzene was removed, yielding 0.2 g. of the amine. The compound was purified by sublimation and was identical with the amine obtained by procedure (b).

(b)—To a solution of 10 g. of 2-(3,4-dimethoxyphenyl)-cyclopropanecarboxylic acid (m.p. 105°) in 250 ml. of dry benzene was added 10 ml. of thionyl chloride, and the mixture was allowed to stand for three days at about 26°. Excess thionyl chloride and benzene was removed under reduced pressure at 55–60°, and dry xylene was added and stripped off to remove the last traces of thionyl chloride. A sample of the dark acid chloride was hydrolyzed with boiling water. The acid⁶ thus obtained melted, after purification, at 103.5–105.5°.

The crude acid chloride was dropped into a stirred suspension of 15 g. of pulverized sodium azide in 50 ml. of xylene over a period of four minutes. Nitrogen evolution (78% conversion) ceased after 11 hours of refluxing. Most of the xylene was distilled off under reduced pressure, and the dark-red isocyanate was hydrolyzed by stirring with 75 ml. of 35% hydrochloric acid at 55–60° for three hours. The solution was concentrated under reduced pressure and neutralized with 10% sodium hydroxide solution. The amine was extracted with ether, dried, and the solvent was distilled off. The oily residue (2.2 g.) (25%) solidified on standing. Purification was achieved by distillation (b.p. 140–150° (1.6 mm.)), and sublimation of the solidified distillate (m.p. 63–64°) at 0.1 mm. The colorless sublimate melted at 68–70°.

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.86; H, 8.25; N, 7.28.

3,4-Dimethoxyphenylacetothiomorpholide.—Using the Schwenk and Bloch⁷ modification of the Willgerodt reaction, a mixture of 37 g. of acetoveratrone, 10.3 g. of sulfur and 28.2 g. of morpholine was refluxed for 13 hours and poured onto ice. The oily thiomorpholide (37.5 g.) was extracted with benzene and crystallized on treatment with ether. After several recrystallizations from ethanol, the initially low-melting pale yellow product had m.p. 153–155°.

Anal. Calcd. for $C_{14}H_{17}NO_3S$: N, 4.98. Found: N, 5.05.

The thiomorpholide was hydrolyzed by refluxing with 10% potassium hydroxide solution for 10 hours. The solution was cleared with charcoal, acidified, and homoveratric acid (71% yield) was obtained. After two recrystallizations from benzene-petroleum ether it melted at 93–97°. Homoveratryl chloride was formed in 84% yield from the acid and thionyl chloride in benzene solution. It boiled at 145–149° (2 mm.).

N-[2-(3,4-Dimethoxyphenyl)-cyclopropyl]-homoveratramide.—A solution of 4.2 g. of homoveratryl chloride in 50 ml. of anhydrous ether was dropped slowly into a stirred solution

of 2.5 g. of 2-(3,4-dimethoxyphenyl)-cyclopropylamine in 50 ml. of dry ether. The white precipitate which appeared immediately was filtered, washed with ice-water, and recrystallized from ethanol or benzene-isoöctane. The colorless crystals weighed 1.3 g. (27%), m.p. 115–117°.

Anal. Calcd. for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.79. Found: C, 68.02; H, 6.82.

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Recovery of Mellitic Acid from its Salts by Electrolysis

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The recovery in good yields of a non-volatile, water-soluble, organic acid, such as mellitic, from solutions of its salts, constitutes a difficult problem. Previous workers have resorted to double decomposition of barium, lead or silver salts with the appropriate acid.¹ Acidification with a mineral acid, followed by evaporation to dryness and soxhlet extraction of the solid, salt-organic acid mixture, is unsatisfactory due to acid salt formation and hence incomplete metathesis.^{2,3} Liquid-liquid phase extraction of an acidified salt solution with an immiscible organic solvent is slow because of unfavorable distribution coefficients. Methyl ethyl ketone has been found one of the most satisfactory solvents for this purpose. The usefulness of electrolytic decomposition of aqueous salt solutions for the recovery of the water-soluble, organic acids from the oxidation of coal has been previously reported.³

In the present investigation a study has been made of the electrical efficiency and material yields in the electrolytic decomposition of aqueous solutions of the potassium and the ammonium salts of mellitic acid.

Experimental

Materials.—The mellitic acid was prepared by the oxidation of carbon black.⁴ The ammonium salt of the acid was made as follows: Fifty grams of the crude acid was dissolved in 250 ml. of warm water, insoluble material filtered out, the filtrate cooled, poured into a liter of concentrated ammonium hydroxide, the mixture cooled to 0° and maintained at that temperature for an hour. The needle-like, crystalline precipitate of ammonium mellitate was filtered off on a buchner funnel, sucked dry and washed with a small amount of cold, concentrated ammonium hydroxide. The greater part of the ammonium hydroxide was removed by drying in a crystallizing dish on a steam-bath for about 30 minutes and the balance in vacuum over concentrated sulfuric acid at room temperature. The ammonium salt prepared by this procedure had the following approximate composition⁵ $C_6(COONH_4)_6 \cdot 6H_2O$, molecular weight 552.3. The yield of salt was about 90% of the theoretical. The theoretical yield of mellitic acid from a gram-mole of this salt is 342.1 g. or 61.9% by weight.

The potassium acid salt was prepared by adding to a warm, aqueous solution of the free acid, prepared as above, 4 N potassium hydroxide until alkaline to litmus and then acidifying with glacial acetic acid. After standing for 12 hours the crystalline precipitate of the potassium acid salt

(1) W. Treibs, *Ges. Abhandl. Kenntnis Kohle*, **5**, 585 (1920).

(2) W. A. Bone, L. Hortou, S. G. Ward, *Proc. Roy. Soc. (London)*, **A127**, 489 (1930).

(3) B. Juettner, R. C. Smith, H. C. Howard, *This Journal*, **59**, 237 (1937).

(4) B. Juettner, *ibid.*, **59**, 1472 (1937).

(5) *Ibid.*, **59**, 208 (1937).

(6) Strong decomposition occurred when the acid chloride was distilled in another run, and only a few drops of an oil, b.p. 165° (7 mm.) were obtained. Hydrolysis of this distillate gave the stereoisomeric acid of m.p. 107–108°.

(7) E. Schwenk and E. Bloch, *This Journal*, **64**, 3051 (1942).