[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF XAVIER UNIVERSITY]

Nitration of Phenoxathiin and Some New Amino Derivatives[1]

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Through the use of the Friedel–Crafts reaction and Beckmann rearrangement, new routes to 2-aminophenoxathiin and 2,8-diaminophenoxathiin have been developed. 2-Nitrophenoxathiin-10-dioxide and 2,8-dinitrophenoxathiin-10-dioxide have been produced by nitration of phenoxathiin, phenoxathiin-10-oxide or phenoxathiin-10-dioxide. Subsequent reduction of the nitro compounds makes available 2-aminophenoxathiin-10-dioxide and 2,8-diaminophenoxathiin-10-dioxide. Thus, several important amino derivatives may now be prepared as a result of direct nuclear substitution reactions thereby eliminating the use of tedious ring closure procedures.

In connection with a study of the pharmacological properties of some derivatives of phenoxathiin structurally related to *p,p'*-diaminodiphenyl sulfone, it was necessary to prepare some new nitro and amino substituted phenoxathiins. Since it seemed more desirable to start with the parent heterocycle rather than to use the tedious method of ring closure, it was of interest to examine direct nuclear substitution as a route to the preparation of the desired compounds.

The only aminophenoxathiin that has been prepared as a result of a direct nuclear substitution reaction is the 4-amine[5] although a number of studies[6–9] have reported the preparation of both nitro and aminophenoxathiins by ring closure methods.

Phenoxathiin reacts in the expected manner with acetyl chloride and aluminum chloride to give either 2-acetylphenoxathiin[8,10,11] or 2,8-diacetylphenoxathiin.[12] Through the oximes of these acetyl derivatives, methods have now been developed for the preparation of 2-amino- and 2,8-diaminophenoxathiin. Thus, when the oxime of 2-acetylphenoxathiin is subjected to a Beckmann rearrangement with phosphorus pentachloride, the expected 2-acetaminophenoxathiin is produced. Hydrolysis of this crude acetamino compound gives 2-aminophenoxathiin (m.p. 93–95° after repeated recrystallization) in 75% yield. Irie[8] has reported the melting point of 2-aminophenoxathiin as 98°. His compound was prepared by reduction of 2-nitrophenoxathiin which was the end product of a series of reactions involving ring closure.

Acetylation of 2-aminophenoxathiin (82% yield) followed by oxidation with hydrogen peroxide in glacial acetic acid gives 2-acetaminophenoxathiin-10-dioxide (70% yield). When 2-acetaminophenoxathiin is treated with sodium hypochlorite a mixture of 2-acetaminophenoxathiin-10-oxide and 2-acetaminophenoxathiin-10-dioxide results. Such a mixture was unexpected since this oxidative method is admirably suited for the oxidation of other closely related sulfur heterocyclic acetamino compounds to the corresponding acetamino dioxides.[13]

2,8-Diaminophenoxathiin is prepared in 75% yields by a Beckmann rearrangement of 2,8-diacetylphenoxathiin dioxime followed by hydrolysis of the crude diacetamino compound. Subsequent acetylation (88% yield) and hydrogen peroxide oxidation gives 2,8-diacetaminophenoxathiin-10-dioxide (61% yield). The melting point (118°) previously reported for 2,8-diaminophenoxathiin, prepared by ring closure reactions, does not agree with that determined in this work (171–173°). However, a mixed melting point between the 2,8-diacetaminophenoxathiin-10-dioxide prepared from this diamine and another specimen, prepared by oxidation, nitration, reduction and acetylation, was not depressed. In addition, Todd[14] in some independent studies on 2,8-diaminophenoxathiin, prepared by Hoffman reaction from 2,8-dicarboxamidophenoxathiin, obtained a melting point (166–168°) in essential agreement with that reported here.

In an attempt to prepare 2-nitrophenoxathiin, a solution of phenoxathiin in glacial acetic acid was treated with fuming nitric acid at 30°. There was isolated only phenoxathiin-10-oxide (91% yield) (m.p. 154–156°). An authentic specimen of this material was prepared in 81% yield by treating phenoxathiin in glacial acetic acid with chlorine followed by hydrolysis of the resulting 10,10-dichlorophenoxathiin with water. A mixed melting point between the two samples was not depressed. Such a proof was considered advisable since phenoxathiin-10-oxide melts higher than the 10-dioxide and it was necessary to make certain that the material obtained by the attempted nitration reaction was not just a higher melting sample of 10-dioxide.

An examination of the reaction of other nitrating mixtures upon phenoxathiin showed that neither 2-nitrophenoxathiin nor the corresponding 2-nitrophenoxathiin-10-dioxide could be produced directly from phenoxathiin. It was found possible however, to prepare 2,8-dinitrophenoxathiin-10-dioxide by treatment of phenoxathiin in glacial acetic acid with a large excess of fuming nitric acid and concentrated sulfuric acid.

2-Nitrophenoxathiin-10-dioxide may be prepared either by nitration of phenoxathiin-10-oxide with a mixture of fuming nitric acid and concentrated sul-

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(3) Taken in part from the M.S. Thesis of A.J.B.

(4) Taken in part from the B.S. Thesis of D.J.B.

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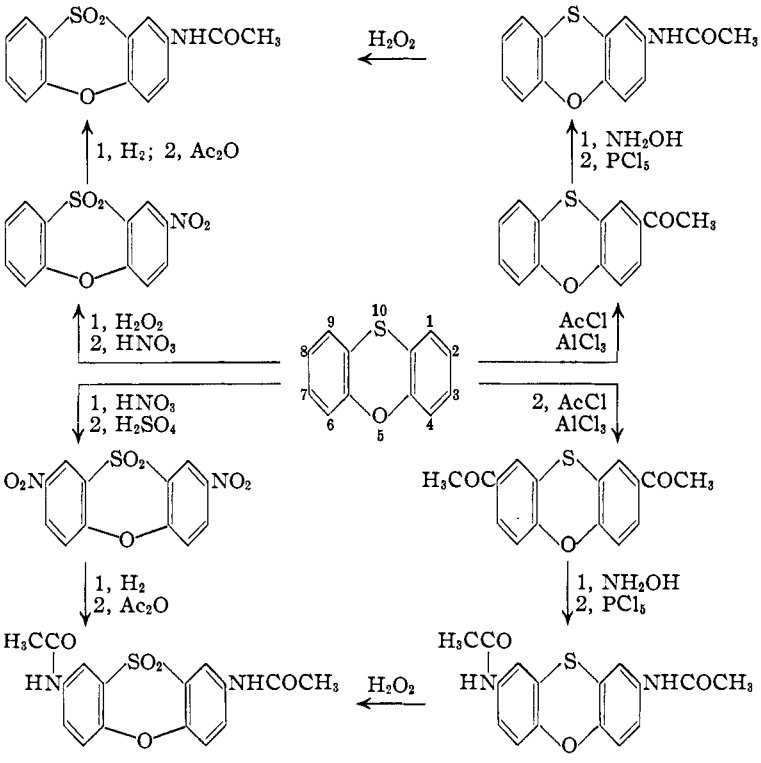
(13) H. Gilman and J. F. Nobis, THIS JOURNAL, **71**, 274 (1949).

(14) Private communication from Dr. David Todd, Amherst University.

furic acid (30% yield) or by treating phenoxathiin-10-dioxide with fuming nitric in glacial acetic acid (43% yield). The melting point of this nitro dioxide (194–195°) is somewhat lower than the melting point of the 2-nitrophenoxathiin-10-dioxide prepared by ring closure[8] (204–205°). Additional proof of structure of this compound was obtained by reduction to 2-aminophenoxathiin-10-dioxide (63% yield) followed by acetylation to 2-acetaminophenoxathiin-10-dioxide (90% yield). A mixed melting point with the 2-acetaminophenoxathiin-10-dioxide prepared as described above, from 2-acetylphenoxathiin oxime, was not depressed.

2,8-Dinitrophenoxathiin-10-dioxide may be prepared, as mentioned earlier, directly from phenoxathiin (30% yield) but is best prepared by treatment of phenoxathiin-10-dioxide in concentrated sulfuric acid with fuming nitric acid (41% yield). The structure of this dinitro compound was proved by reduction to 2,8-diaminophenoxathiin-10-dioxide (81% yield) with subsequent acetylation to 2,8-diacetaminophenoxathiin-10-dioxide (61% yield). Mixed melting points of either the diamino dioxide or the diacetamino dioxide with the corresponding compounds prepared from the 2,8-diacetylphenoxathiin dioxime were not depressed. Also, 2,8-dinitrophenoxathiin-10-dioxide and 2,8-diaminophenoxathiin-10-dioxide have been previously prepared by ring closure reactions[8] and the melting points recorded are the same as those included here. The various reactions required for the structure proof of the compounds described in this paper may be shown as



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Experimental

2-Acetylphenoxathiin.—All attempts to duplicate the yields previously reported[10,11] in the preparation of 2-acetylphenoxathiin were unsuccessful. The best yields were obtained when 80 g. (0.6 mole) of anhydrous aluminum chloride was added in small portions over a period of five hours to a mechanically stirred mixture consisting of 80 g. (0.4 mole) of phenoxathiin and 34 g. (0.44 mole) of acetyl chloride in 400 cc. of dry carbon disulfide. The reaction mixture was kept at 30° during the addition of the aluminum chloride. When the addition was complete, the temperature was raised to reflux for three hours. The crude acetyl compound was isolated in the usual manner and purified by distillation (b.p. range, 82–110° (5 mm.)). After several recrystallizations from methanol there was obtained 25 g. (25.8%) of 2-acetylphenoxathiin melting at 117.5–118°. The melting point previously reported[10,11] was 111–112°.

2-Acetylphenoxathiin Oxime.—Twenty-four grams (0.1 mole) of 2-acetylphenoxathiin and 18.75 g. (0.27 mole) of hydroxylamine hydrochloride were dissolved in a mixture of 60 ml. of absolute ethanol and 90 ml. of dry pyridine. The reaction mixture was refluxed for three hours with mechanical stirring. Half of the solvent mixture was then removed by distillation, and, after cooling, the remainder of the retion mixture was poured into water. There was obtained 24.4 g. (99.3%) of crude product melting at 154–157°. Recrystallization of a small amount of the material raised the melting point to 158–159.5°. No experimental conditions were given in a previous report of this compound[10] and the melting point was reported as 142–144°.

Anal. Calcd. for $C_{14}H_{11}O_2NS$: S, 12.42. Found: S, 12.31.

2-Aminophenoxathiin.—To a solution of 29.2 g. (0.113 mole) of 2-acetylphenoxathiin oxime in 450 ml. of dry benzene at 40° was added with stirring 29.2 g. (0.14 mole) of phosphorus pentachloride over a period of 45 minutes. When the reaction was complete, the mixture was poured into water, the suspension neutralized with sodium carbonate and the benzene removed by steam distillation. The remaining crude acetamino compound was refluxed for 3.5 hours with 20% hydrochloric acid. After hot filtration and several extractions of the insoluble residue with hot water, there was obtained by neutralization with ammonium hydroxide, 18.2 g. (75%) of 2-aminophenoxathiin melting at 91–93°. Repeated crystallization of a small sample from dilute ethanol and a variety of other solvents raised the melting point to 93–95°.

Anal. Calcd. for $C_{12}H_9ONS$: S, 14.9. Found: S, 14.5.

2-Acetaminophenoxathiin.—To 5.0 g. (0.023 mole) of 2-aminophenoxathiin in 20 ml. of dry benzene was added 2.48 g. (0.024 mole) of acetic anhydride. The resulting mixture was refluxed for 3.5 hours and allowed to stand overnight. Some of the solvent was removed, the solution cooled and the tan precipitate removed by filtration. This material was recrystallized from 20 ml. of 2:1 ethanol–water. There was obtained 4.9 g. (81.9%) of 2-acetaminophenoxathiin melting at 129–130°.

Anal. Calcd. for $C_{14}H_{11}O_2NS$: S, 12.46. Found: S, 12.25.

2-Acetaminophenoxathiin-10-oxide.—One gram (0.004 mole) of 2-acetaminophenoxathiin in 30 ml. of glacial acetic acid was treated with 10 ml. of sodium hypochlorite in the same manner as reported[13] for the preparation of 2,8-diacetaminodibenzothiophene-5-dioxide. The crude product melted at 215–225°. After three successive treatments with an amount of ethanol insufficient for solution of all of this material, the residue melted at 234–235°. Recrystallization from benzene did not change the melting point. A mixed melting point with 2-acetaminophenoxathiin-10-dioxide melted at 230–240°.

Anal. Calcd. for $C_{14}H_{11}O_3NS$: S, 11.72. Found: S, 11.75.

2-Acetaminophenoxathiin-10-dioxide. (A) From **2-Acetaminophenoxathiin.**—A mixture of 1 g. (0.004 mole) of 2-acetaminophenoxathiin and 2 ml. of 30% hydrogen peroxide in 10 ml. of glacial acetic acid was refluxed for four hours. At the end of two hours an additional 1 ml. of peroxide was added. At the end of the reflux period the reaction mixture containing suspended solid was cooled and filtered. There was obtained 0.7 g. of 2-acetaminophenoxathiin-10-dioxide melting at 280–282°. Dilution of the filtrate and recrystallization of the crude product from ethanol gave an additional 0.1 g. of dioxide thus raising the total yield to 70% (0.8 g.).

(B) From **2-Aminophenoxathiin-10-dioxide.**—A mixture of 62.8 g. (0.24 mole) of 2-aminophenoxathiin-10-dioxide, 250 ml. of dry benzene and 94.4 ml. (1.0 mole) of acetic anhydride was refluxed for 15 minutes. On cooling there was obtained 65.8 g. (90% yield) of the acetamino compound melting at 275–277°. Recrystallization from ethanol raised the melting point to 279.5–281°. A mixed melting point with the material prepared above by hydrogen peroxide oxidation was not depressed.

Anal. Calcd. for $C_{14}H_{11}O_4NS$: S, 11.09. Found: S, 11.03.

Phenoxathiin-10-oxide.—This compound has been previously prepared by a controlled oxidation of phenoxathiin with hydrogen peroxide.[15,16] However, since the reported melting point was higher than that determined for the dioxide an alternate preparation was devised in order to check this melting point.

In a method similar to that used for the preparation of dibenzothiophene-5-dioxide,[17] 15 g. (0.075 mole) of phenoxathiin in 150 ml. of glacial acetic acid was treated with 6 g. of chlorine. The reaction mixture containing an orange precipitate was poured onto ice and stirred for 15 minutes to complete the hydrolysis of the 10-dichlorophenoxathiin. There was obtained 13 g. (81%) of phenoxathiin-10-oxide melting at 154–156° after recrystallization from benzene. This melting point is in agreement with that reported by Drew.[15] It should be noted that this method may be used for the preparation of other substituted phenoxathiin-10-oxides.

2-Nitrophenoxathiin-10-dioxide. (A) From **Phenoxathiin-10-dioxide.**—Eighty grams (0.34 mole) of phenoxathiin-10-dioxide[15,16] was dissolved in 300 ml. of glacial acetic acid in a one-liter three-necked flask fitted with a reflux condenser and mechanical stirrer. Through a dropping funnel fitted loosely to the top of the condenser was added 240 ml. (5.75 mole) of fuming nitric acid (sp. gr. 1.5) over a 30-minute period. When the addition of the acid was complete the reaction mixture was allowed to stir at reflux for an additional two hours. At the end of this time the flask was placed in a refrigerator and allowed to stand overnight. There was obtained 55 g. of product melting at 179–185°. Recrystallization from acetone gave 43.5 (43%) of the desired 2-nitrophenoxathiin-10-dioxide melting at 192–194°. The melting point previously reported for this compound as prepared by ring closure was 205–206°. Repeated recrystallization from a variety of solvents failed to raise the melting point of our product above 194°. However, in other experiments it was noted that if the mononitro and dinitro compounds are obtained as a mixture from dinitration reactions, the impure mixture melts above 200° over a range.

Anal. Calcd. for $C_{12}H_7O_5NS$: S, 11.55. Found: S, 11.40.

(B) From **Phenoxathiin-10-oxide.**—A mixture of 15 g. (0.07 mole) of phenoxathiin-10-oxide, 50 ml. of glacial acetic acid, 30 ml. of fuming nitric acid and 20 ml. of concd. sulfuric acid was heated at 100–110° for 45 minutes. The yellow crystals that formed on cooling were removed and recrystallized from glacial acetic acid. There was obtained 5.5 g. (30%) of 2-nitrophenoxathiin-10-dioxide melting at 187–188°.

Treatment of phenoxathiin-10-oxide in glacial acetic acid with fuming nitric acid at temperatures ranging from 5 to 110° gave only unreacted starting material.

Attempted direct nitration of phenoxathiin in glacial acetic acid with fuming nitric acid over the range of 5–110° gave a 91% yield of phenoxathiin-10-oxide (mixed m.p.).

2-Aminophenoxathiin-10-dioxide.—To a suspension of 4 g. (0.015 mole) of 2-nitrophenoxathiin-10-dioxide in 200 ml. of methanol containing 30 ml. of concentrated hydrochloric acid was added 10 g. (0.15 mole) of zinc dust in small portions. The temperature gradually rose during the addition and was held at 60–70° until all of the insoluble nitro compound had disappeared. The reaction mixture was made basic with ammonium hydroxide after cooling and the crude amine extracted from the precipitate with 30 ml. of acetone. After removal of the acetone, the amine was purified by recrystallization from methanol. There was obtained 2 g. (62%) of product melting at 164–165°.

An alternate procedure involves the stannous chloride reduction of 2-nitrophenoxathiin-10-dioxide. Thus, a mixture of 45 g. (0.16 mole) of 2-nitrophenoxathiin-10-dioxide, 148 g. (0.66 mole) of stannous chloride dihydrate and 500 ml. of glacial acetic acid that had been previously saturated with dry hydrogen chloride was held at 110° for four hours. After cooling, the reaction mixture was made basic with sodium hydroxide and the crude amine extracted from the precipitate with hot methanol. The amine was purified by three recrystallizations from 50:50 methanol–water and one recrystallization from 50:50 acetone–water. There was obtained 24 g. (60%) of product melting at 163–164.5°.

Anal. Calcd. for $C_{12}H_9O_3NS$: S, 12.95. Found: S, 12.70.

2-Aminophenoxathiin-10-dioxide also was prepared by treatment of 2-acetaminophenoxathiin-10-dioxide, made by oxidation of 2-acetaminophenoxathiin, with dilute hydrochloric acid. A mixed melting point with the material prepared by reduction of the nitro compound showed no depression.

2,8-Diacetylphenoxathiin.—Three hundred grams (2.3 moles) of anhydrous aluminum chloride was added in portions over a three-hour period to a well-stirred mixture of 150 g. (0.75 mole) of phenoxathiin, 194 g. (2.45 moles) of acetyl chloride and 1250 ml. of dry carbon disulfide. When the addition was complete the reaction mixture was refluxed for three hours. The aluminum chloride complex was then decomposed by the addition of ice and hydrochloric acid. The crude product was purified by extraction of the 2-acetyl impurity with hot acetone. The remaining material was recrystallized from dioxane to give 113 g. (53%) of 2,8-diacetylphenoxathiin melting at 184–186°. The melting point previously reported for this material was 175°.[12]

Anal. Calcd. for $C_{16}H_{12}O_3S$: S, 11.28. Found: S, 10.95.

2,8-Diacetylphenoxathiin Dioxime.—Fifteen grams (0.05 mole) of 2,8-diacetylphenoxathiin and 14.5 g. (0.2 mole) of hydroxylamine hydrochloride were dissolved in 60 ml. of pyridine and 225 ml. of absolute ethanol, and the mixture refluxed for 2.5 hours. After standing overnight there was obtained 14.2 g. of insoluble material. Dilution of the filtrate with water gave an additional 4.7 g. of product. Purification was accomplished by treatment of the material with hot ethanol followed by hot filtration. The insoluble material melted at 220–221° and amounted to 15.8 g. (95%).

Anal. Calcd. for $C_{16}H_{14}O_3N_2S$: S, 10.20. Found: S, 10.05.

2,8-Diaminophenoxathiin.—This compound was prepared by the same method used for preparation of the 2-aminophenoxathiin. Thus, 15.8 g. (0.05 mole) of 2,8-diacetylphenoxathiin dioxime in 350 ml. of dry benzene treated with 33.3 g. (0.16 mole) of phosphorus pentachloride at 40° gave 9 g. (75%) of product melting at 171–173°. The product had been purified by recrystallization from dilute methanol.

Anal. Calcd. for $C_{12}H_{10}ON_2S$: S, 13.90. Found: S, 13.95.

2,8-Diacetaminophenoxathiin.—Two grams (0.009 mole) of 2,8-diaminophenoxathiin in 20 ml. of dry benzene was refluxed for three hours with 2 ml. of acetic anhydride. Hot filtration of the residue followed by recrystallization from dilute ethanol gave 2.4 g. (88%) of product melting at 253–254°.

Anal. Calcd. for $C_{16}H_{14}O_3N_2S$: S, 10.20. Found: S, 10.11.

2,8-Diacetaminophenoxathiin-10-dioxide. (A) From **2,8-Diacetaminophenoxathiin.**—A suspension of 3.3 g. (0.1 mole) of 2,8-diacetaminophenoxathiin in 30 ml. of glacial acetic acid was treated with 6.6 ml. of 30% hydrogen per-

(15) H. D. K. Drew, *J. Chem. Soc.*, 511 (1928).

(16) H. Gilman and D. L. Esmay, THIS JOURNAL, **74**, 2021 (1952).

(17) R. K. Brown, R. G. Christiansen and R. B. Sandin, *ibid.*, **70**, 1749 (1948).

oxide at 90° for 2.5 hours. The impure material obtained after cooling and filtering was extracted with hot dioxane. The insoluble material melted at 349–353° and amounted to 2.2 g. (61%).

(B) From **2,8-Diaminophenoxathiin-10-dioxide**.—To 1.25 g. (0.005 mole) of 2,8-diaminophenoxathiin-10-dioxide in 10 ml. of dry benzene was added 1.25 g. (0.012 mole) of acetic anhydride. The resulting mixture was refluxed for three hours and filtered hot. The white crystals of 2,8-diacetaminophenoxathiin-10-dioxide that were obtained melted at 328–333°. The yield was 1.2 g. or 61%. Recrystallization from dioxane, acetone and glacial acetic acid raised the melting point to 338–341°. A mixed melting point with the material prepared by method (A) melted at 345–350°.

Anal. Calcd. for $C_{16}H_{14}O_4N_2S$: S, 9.32. Found: S, 9.17.

2,8-Dinitrophenoxathiin-10-dioxide.—To 10 g. (0.05 mole) of phenoxathiin were added 50 ml. of glacial acetic acid, 20 ml. of concentrated sulfuric acid and 30 ml. of fuming nitric acid. The reaction mixture was refluxed for 3.5 hours, cooled and poured into water. The crude yellow product was purified by extracting the mononitro compound with hot acetone. The insoluble residue amounted to 4.8 g. (30%) and melted at 283–286°.

Anal. Calcd. for $C_{12}H_6O_7N_2S$: S, 10.25. Found: S, 10.20.

Nitration of 20 g. (0.086 mole) of phenoxathiin-10-dioxide in 80 ml. of concd. sulfuric acid by the addition of 30 ml. of fuming nitric acid over a period of 15 minutes gave 11 g. (41%) of 2,8-dinitrophenoxathiin-10-dioxide melting at 277–280°.

2,8-Diaminophenoxathiin-10-dioxide.—To a mixture of 17 g. (0.052 mole) of 2,8-dinitrophenoxathiin-10-dioxide, 200 ml. of ethanol and 225 ml. of concd. hydrochloric acid was added 80 g. of zinc dust in portions over a period of 1.5 hours. After refluxing for two hours an additional 50 ml. of hydrochloric acid and 25 g. of zinc dust were added. Refluxing was continued for one hour and the reaction mixture allowed to stand overnight. The insoluble product was removed by filtration, suspended in water and neutralized with sodium hydroxide. The desired diamine was removed by solution in hot acetone and the acetone extracts evaporated nearly to dryness. There was obtained 9.7 g. (81%) of 2,8-diaminophenoxathiin-10-dioxide melting at 244–247.5°.

Anal. Calcd. for $C_{12}H_{10}O_3N_2S$: S, 12.20. Found: S, 12.05.

CINCINNATI, OHIO

[CONTRIBUTION FROM THE LABORATORY OF CHEMISTRY OF NATURAL PRODUCTS, NATIONAL HEART INSTITUTE, NATIONAL INSTITUTES OF HEALTH, U. S. PUBLIC HEALTH SERVICE, FEDERAL SECURITY AGENCY]

Synthesis of 3',4'-Dimethoxyphenylindanones and Tetralones

BY GORDON N. WALKER

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Both stereoisomers of 2-methyl-3-(3',4'-dimethoxyphenyl)-5,6-dimethoxy-1-indanone have been synthesized, the first by reduction of the corresponding indenone and the second by cyclization of the required acid. The polyphosphoric acid cyclization of β-carbethoxy-γ,γ-di-(3,4-dimethoxyphenyl)-butyric acid to 3-carbethoxy-4-(3',4'-dimethoxyphenyl)-6,7-dimethoxy-1-tetralone is described, and evidence is presented favoring a *trans* configuration for this product.

An earlier report[1] established the fact that simple benzylsuccinic acids and acid esters cyclize exclusively to tetralone derivatives in the presence of polyphosphoric acid. This reaction has now been extended (Chart II) to include substituted benzhydryl succinic acid esters, as IX, as a means of preparing compounds having a ring system such as that which occurs in the tumor-damaging compound, podophyllotoxin. At the same time, the related indanone, VI, was studied (Chart I) in an attempt to clarify questions of isomerism. The ketone, I, was employed as starting material in each case, for the sake of simplicity, since ring closures of compounds in the symmetrical tetramethoxydiphenylmethane series are not subject to the difficulty that two structural isomers can be formed.

A Stobbe reaction of I with ethyl succinate furnished an acid ester, VII, in high yield when potassium *t*-butoxide was used as the condensing agent. The product, VII, was hydrogenated in acetic acid at 80° in the presence of a palladium catalyst. Cyclization of the reduced material, IX, in polyphosphoric acid at 100° afforded a crystalline carbethoxytetralone, X, the only product which could be isolated from this reaction. Present evidence indicates that X was the *trans* isomer with respect to the 3-carbethoxy group and the 4-(3',4'-dimethoxyphenyl) group. Alkaline hydrolysis of X led to a ketoacid, XI. Inversion of the carboxy function did not occur under these conditions since material identical with X was obtained when XI was esterified in ethanol. Catalytic hydrogenolysis of the tetralone, X, gave the corresponding tetralin derivative, XII. Saponification of XII in turn yielded an acid, XIII, which was dehydrogenated at 255° in the presence of 5% palladium–charcoal. This aromatization established the fact that X, XI, XII and XIII were compounds of the tetralin rather than of the indane, series. No dehydrogenation was observed at a lower temperature (175°), although 2-carboxy-6,7-dimethoxytetralin loses hydrogen readily at 175° in the presence of the same catalyst.[1] A possible explanation for the difficulty experienced in aromatizing XIII is that the hydrogen atoms at positions 3- and 4- in the latter are disposed *trans* to one another.

The indanone, VI, was synthesized by two different methods, first by hydrogenation of indenone III, which led to a glassy ketone, VIa, and secondly by polyphosphoric acid cyclization of the acid V, which led to a crystalline ketone, VIb. The properties of V and VIb indicated that they were the same compounds, acid and ketone, respectively, obtained by Müller and Gal[2] by different methods. The two ketones, VIa and VIb, were very probably stereoisomers, *cis* and *trans*, respectively. Evidence in favor of this conclusion was furnished by

(1) E. C. Horning and G. N. Walker, THIS JOURNAL, **74**, 5147 (1952).

(2) A. Müller and E. Gal, *Ber.*, **77**, 343 (1944).