determination indicated that the conversion was practically quantitative.

**3,4,5-Triethylisoxazole.**—4-Ethyl-3,5-heptanedione dioxime (100 g.) and 3 *N* sulfuric acid (200 cc.) were refluxed for four hours. The layers of the reaction mixture were separated and the oil layer was washed with a little water. It weighed 84 g. This was distilled under vacuum yielding 80.5 g. of product, 98% of the theoretical. The hydroxylamine content of the water layer and washings was determined by Raschig's method. It was found to be 17.8 g., which is the theoretical amount. The hydroxylamine was further identified by conversion to acetoxime. Triethylisoxazole is a colorless liquid; b. p. (761) 215.3 ± 0.2°, $d^{20}_{20}$ 0.9363, $n^{20}_{D}$ 1.45803.

*Anal.* Calcd. for $C_9H_{15}NO$: N, 9.15. Found: N, 9.17.

Triethylisoxazole was also prepared by dissolving 4-ethyl-3,5-heptanedione dioxime in dilute sodium hydroxide solution and steam distilling. The product separated from the distillate.

**3,4,5-Tri-*n*-propylisoxazole.**—5-*n*-Propyl-4,6-nonanedione dioxime (45.2 g.) and 2 *N* sulfuric acid (270 cc.) were refluxed for six hours. The layers of the reaction mixture were separated and the oil layer was washed with a little water. The oil layer weighed 40 g. This was vacuum distilled, yielding 36 g. or 96% of the theoretical. The aqueous layer and washings were combined and analyzed for hydroxylamine; yield, 6.3 g., or 96% of the theoretical. Tripropylisoxazole is a water white liquid, b. p. 255.5 ± 0.2°, $d^{20}_{20}$ 0.9128, $n^{20}_{D}$ 1.46088.

## Summary

1. 3-Methyl-2,4-pentanedione dioxime, 4-ethyl-3,5-heptanedione dioxime and 5-*n*-propyl-4,6-nonanedione dioxime have been prepared from nitroethane, 1-nitropropane and 1-nitrobutane, respectively.

2. The dioximes named above were converted to the corresponding trialkylisoxazoles and hydroxylamine.

3. A mechanism for the conversion of primary nitroparaffins to isoxazoles has been proposed.

TERRE HAUTE, INDIANA RECEIVED JULY 12, 1940

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

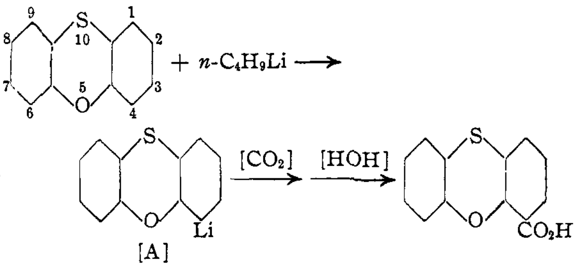
# The Metalation of Phenoxathiin

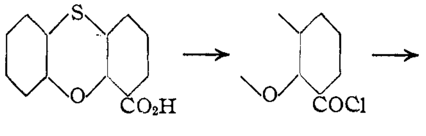
BY HENRY GILMAN, MARIAN W. VAN ESS, H. B. WILLIS AND C. G. STUCKWISCH

The initial purpose of this study was to investigate the possibility of synthesizing dibenzofuran derivatives from phenoxathiin compounds by the removal of sulfur.

**Metalation.**—Carbonation of the *n*-butyllithium metalation product of phenoxathiin gave an acid which melted at 168–169°. Decarboxylation of this acid to phenoxathiin showed that there was no cleavage of the oxygen or sulfur bridge. Suter and co-workers[1a] had previously prepared 2-phenoxathiincarboxylic acid, and found it to melt at 260–262°; and Mauthner's[2] 3-phenoxathiincarboxylic acid melts at 223°. Accordingly, the acid obtained by metalation must have the carboxyl group in either the 1- or 4-position. By analogy with earlier extensive studies[3] one might have predicted that metalation would have involved the 1- or 4-position. However, because anomalous orientations in metalations have been noted with sulfides,[4] all four possible positions might have been involved originally On the assumption that metalation probably took place in the 4-position, two different ring-closures were tried for the synthesis of 4-phenoxathiincarboxylic acid. These were unsuccessful, and are described in the Experimental Part.

The acid was shown to be 4-phenoxathiincarboxylic acid by an indirect procedure involving comparison with the chlorophenoxathiins. Inasmuch as three of the four possible chlorophenoxathiins were known, and among them 4-chlorophenoxathiin, we converted our acid to a chloro derivative by the following sequence of reactions





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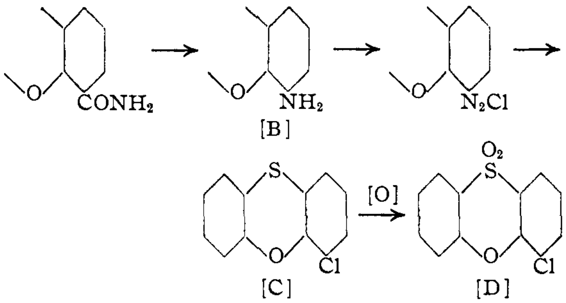
(1) (a) Suter, McKenzie and Maxwell, THIS JOURNAL, **58**, 717 (1936); (b) Suter and Maxwell, "Organic Syntheses," Vol. 18, 1938, p. 64.

(2) Mauthner, *Ber.*, **39**, 1340 (1906).

(3) Gilman and Bebb, THIS JOURNAL, **61**, 109 (1939).

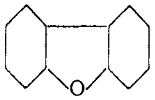
(4) Gilman and Jacoby, *J. Org. Chem.*, **3**, 108 (1938); Gilman, Jacoby and Pacevitz, *ibid.*, **3**, 120 (1938); Gilman and Webb, THIS JOURNAL, **62**, 987 (1940).

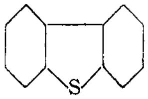


The chloro compound [C], an oil, was oxidized to a dioxide [D] melting at 148–149°, and Professor C. M. Suter kindly showed that a sample was identical (mixed m. p.) with an authentic specimen of his 4-chlorophenoxathiin 10-dioxide.[5] Incidentally, the 4-aminophenoxathiin [B] also was prepared directly from the 4-phenoxathiinyllithium [A] by reaction with α-methylhydroxylamine in general accordance with a procedure described by Sheverdina and Kocheskov.[6]

Another approach to establishing the structure of the metalation product involved the conversion of 4-methylphenoxathiin 10-dioxide to the corresponding acid by oxidation. The unsuccessful attempt at oxidation recalls the inordinate resistance to oxidation of a methyl derivative[7] of a related heterocycle, dibenzofuran.

**Relative Rates of Metalation of Compounds Having Oxygen and Sulfur Bridges.**—The preferential metalation in the position ortho to oxygen rather than ortho to sulfur in the symmetrical phenoxathiin, suggested a comparison of the relative rates of metalation of dibenzofuran and dibenzothiophene.





In conformity with the results of metalation observed with phenoxathiin, it was found that dibenzofuran was metalated more rapidly than dibenzothiophene. This was established by three different procedures. First, in a competitive reaction, a mixture of dibenzofuran and dibenzothiophene was metalated by *n*-butyllithium. Second, preformed 4-dibenzothienyllithium metalated dibenzofuran, whereas preformed 4-dibenzofuryllithium did not metalate dibenzothiophene. Third, separate metalations showed dibenzofuran to be metalated more readily.

**Halogen–Metal Interconversion with 2-Bromophenoxathiin.**—Metalation, or hydrogen–metal interconversion, is particularly useful for the introduction of a miscellany of substituents in positions otherwise inaccessible by other nuclear-substitution reactions. The metalation of phenoxathiin in the 4-position, which is otherwise inaccessible by direct nuclear substitution reactions, is a new case in point. Halogen–metal interconversion reactions are also of synthetic value in the preparation of reactive organometallic compounds from bromides and iodides which are highly resistant to reaction with lithium or magnesium leading to the formation of the corresponding organolithium compounds or Grignard reagents. Only after several attempts were Suter and co-workers[1a] successful in obtaining a Grignard reagent from 2-bromophenoxathiin, and the yield of 2-phenoxathiincarboxylic acid in the successful preparation was but 8%. We have found that a fifteen-minute period of reaction between 2-bromophenoxathiin and *n*-butyllithium in ether gives sufficient 2-phenoxathiinyllithium to yield 63.7% of pure 2-phenoxathiincarboxylic acid on carbonation.

$$\mathrm{RBr} + n\text{-}\mathrm{C_4H_9Li} \longrightarrow$$
$$n\text{-}\mathrm{C_4H_9Br} + \mathrm{RLi} \xrightarrow{[\mathrm{CO_2}]} \xrightarrow{[\mathrm{HOH}]} \mathrm{RCO_2H}$$

The organolithium compounds can, if necessary, be converted readily and completely to the corresponding Grignard reagents by means of magnesium bromide or iodide in ether solution[8]: $\mathrm{RLi} + \mathrm{MgX_2} \longrightarrow \mathrm{RMgX} + \mathrm{LiX}$.

**Attempted Conversion of Phenoxathiin to Dibenzofuran.**—Ferrario[9] reported that a good yield of dibenzofuran was obtained by heating phenoxathiin with copper at 250°. Suter and coworkers[1a] were unable to obtain such a result, even with freshly reduced copper bronze and a higher temperature (285–290°). We, likewise, had no success in converting phenoxathiin to dibenzofuran in a series of experiments involving various metals and temperatures.

## Experimental Part

The phenoxathiin was prepared in accordance with the Suter[1a,b] modification of the method of the diphenyl ether

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[5] Suter and Green, THIS JOURNAL, **59**, 2578 (1937).

[6] Sheverdina and Kocheskov, *J. Gen. Chem.* (U. S. S. R.), **8**, 1825 (1938).

[7] See Gilman, Van Ess and Hayes, THIS JOURNAL, **61**, 643 (1939), for a series of unsuccessful attempts to oxidize 2-bromo-4-methyldibenzofuran. Another recent illustration is the high resistance to oxidation of the methyl group in a methylcarbazole: Dunlap and Tucker, *J. Chem. Soc.*, 1945 (1939).

[8] Gilman and Swiss, THIS JOURNAL, **62**, 1847 (1940). See, also, p. 459 in Gilman "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938.

[9] Ferrario, *Bull. soc. chim.*, [4] **9**, 536 (1911).

synthesis of Ferrario[9] and Ackermann.[10] The yields reported were checked.

**Metalation of Phenoxathiin.**—Twelve grams (0.06 mole) of phenoxathiin was refluxed for twenty-four hours with an equimolecular quantity of *n*-butyllithium in ether solution in a manner identical with that used in the metalation of dibenzofuran.[3] The resulting solution was poured in jets on solid carbon dioxide, and the ether and carbon dioxide allowed to evaporate. The residue was extracted with four 200-cc. portions of hot water. The final extraction gave only a small portion of acid upon acidification. The water extracts were combined after acidification, and filtered. The precipitate, after washing with water, weighed 7.8 g. (53% yield) and melted between 157–160°. Three recrystallizations from glacial acetic acid raised the melting point to 168–169°. In another preparation, the yield of crude acid was 9 g. or 61%.

*Anal.* Calcd. for $C_{13}H_8OS$: S, 13.12; neut. equiv., 244. Found: S, 13.21 and 13.07; neut. equiv., 246.

One-tenth gram of the acid was decarboxylated by heating with 0.5 g. of copper bronze in 2.5 cc. of quinoline at 200° for thirty minutes. The yield of phenoxathiin (mixed melting point) after sulfuric acid washing and steam distillation was 0.05 g.

**4-Phenoxathiincarboxylic Acid 10-Dioxide.**—A solution of 2 g. (0.008 mole) of 4-phenoxathiincarboxylic acid in 30 cc. of glacial acetic acid was oxidized by heating with 30% hydrogen peroxide. Crystallization from 50% ethanol yielded 1.6 g. or 58% of 4-phenoxathiincarboxylic acid 10-dioxide melting at 183–184°.

*Anal.* Calcd. for $C_{13}H_8O_5S$: neut. equiv., 256. Found: neut. equiv., 261.

**Methyl 4-Phenoxathiincarboxylate 10-Dioxide.**—This ester was prepared from the corresponding acid by means of diazomethane, and melted at 124° after recrystallization from dilute methanol.

*Anal.* Calcd. for $C_{14}H_{10}O_5S$: $OCH_3$, 10.7. Found: $OCH_3$, 10.5.

**4-Phenoxathiincarboxylic Acid Amide.**—4-Phenoxathiincarboxylic acid chloride was prepared by refluxing 15.4 g. (0.0642 mole) of the 4-acid for forty-five minutes with an excess of thionyl chloride. After removing the excess thionyl chloride by distillation, the residual crude acid chloride was poured into concd. ammonium hydroxide to give 14 g. or 91% of crude amide melting at 173–175°. Crystallization from ethanol yielded 7 g. or 46% of amide melting at 185–186°. The melting point was unchanged after recrystallization from glacial acetic acid. There was also isolated 1.5 g. or 9.7% of unchanged acid.

*Anal.* Calcd. for $C_{13}H_9O_2NS$: N, 5.74. Found: N, 5.63.

**4-Aminophenoxathiin Hydrochloride.**—This compound was prepared in essential accordance with a procedure[11] for the preparation of 4-aminodibenzofuran by the Hofmann reaction. A solution of 7.2 g. (0.036 mole) of bromine and 10.8 g. (0.272 mole) of sodium hydroxide in 60 cc. of water was added to a suspension of 4 g. (0.016 mole) of 4-phenoxathiincarboxylic acid amide in 30 cc. of dioxane and 20 cc. of 10% sodium carbonate. The solution was heated on the water-bath for six hours, then cooled and extracted with ether. The crude amine hydrochloride was precipitated by passing hydrogen chloride into the dried ether extract. The amine hydrochloride was then dissolved in water, the solution made alkaline with ammonium hydroxide and again extracted with ether. A second precipitation by hydrogen chloride of the dried ether extract gave the pure 4-aminophenoxathiin hydrochloride which melted at 223–225° with decomposition. The yield was 1.4 g. or 34%.

*Anal.* Calcd. for $C_{12}H_9ONClS$: N, 5.06. Found: N, 5.17.

**4-Chlorophenoxathiin 10-Dioxide.**—A solution of 0.5 g. (0.002 mole) of 4-aminophenoxathiin hydrochloride in 50 cc. of water containing 2 cc. of concd. hydrochloric acid was cooled in an ice-bath and vigorously stirred while a solution of 0.14 g. (0.002 mole) of sodium nitrite was added. The solution was kept at 0° while a solution of 0.0025 mole of freshly prepared cuprous chloride in 1 cc. of concd. hydrochloric acid was added. The solution was allowed to come gradually to room temperature and then steam-distilled. The oily product which collected was extracted with ether, then the ether was evaporated and glacial acetic acid was added. The solution was heated on the steam-bath and oxidized with excess 30% hydrogen peroxide. The acetic acid was neutralized with potassium hydroxide solution and the 4-chlorophenoxathiin 10-dioxide was filtered off. The crude yield was 0.08 g. or 17.1% and melted at 144–145°. Recrystallization from alcohol raised the melting point to 148–149°. The identity of this compound was established by a mixed melting point with an authentic specimen (m. p. 148–149°) prepared by ring closure.

**Reaction of 4-Phenoxathiinyllithium with α-Methylhydroxylamine.**—A solution of *n*-butyllithium, prepared from 134 g. (1 mole) of *n*-butyl bromide in 150 cc. of ether and 17.5 g. (2.5 g. atoms) of lithium metal in 500 cc. of ether, was added to 84 g. (0.42 mole) of phenoxathiin.[1] This solution was stirred and heated at reflux temperature for twenty hours. At the end of this period an aliquot was withdrawn and titrated to determine the approximate content of organometallic compounds. Since the solution was found to be approximately 0.68 molar in organolithium compounds, 9.9 g. (0.21 mole) of α-methylhydroxylamine in 60 cc. of ether was added slowly with constant stirring while the solution was cooled in a salt–ice-bath. A color test[12] taken two hours after the addition of the α-methylhydroxylamine was negative.

The solution became brown during the addition of the amine solution and a flocculent precipitate settled out. Refluxing was continued for several hours to make certain that the reaction was completed. The solution was cooled in an ice–salt-bath and very carefully hydrolyzed by the very slow addition of 200 cc. of ice water, with vigorous stirring. The ether layer was separated and the aqueous solution extracted twice with 50-cc. portions of ether. The combined ether extracts were dried and then dry hydrogen chloride gas was passed in to precipitate the amine hydrochloride. When the ether was saturated with hydrogen chloride, the amine hydrochloride was filtered off and suspended in a liter of dilute ammonium hydroxide

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(10) Ackermann, German Patent 234,743.

(11) Studies by Jack Swiss.

(12) Gilman and Schulze, THIS JOURNAL, **47**, 2002 (1925).

solution. Since the amine is an oil, it was extracted with ether and again precipitated as the hydrochloride. The yield of 4-aminophenoxathiin hydrochloride was 36.5 g. (70.6% based on the α-methylhydroxylamine). It sintered at 217° and melted at 222–224° with decomposition.

Several attempts to recrystallize the hydrochloride from water gave only oils even from 6 *N* hydrochloric acid. Accordingly the free amine was precipitated from an alkaline aqueous solution, extracted with ether and vacuum distilled; boiling point, 209° (5 mm.). The yield of light yellow amine was 21 g. (59%). This liquid amine was dissolved in 400 cc. of ether and again precipitated as the hydrochloride. The product was creamy white and melted at 223–224° with decomposition.

In addition there was recovered from the original ether solution 57 g. of phenoxathiin.

**2-Bromophenoxathiin.**—A solution of 10 g. (0.05 mole) of phenoxathiin in 50 cc. of carbon tetrachloride was brominated in accordance with the procedure of Suter.[13] The yield of 2-bromophenoxathiin was 10 g. or 88.3%, melting at 58–59°.

**Halogen–Metal Interconversion with 2-Bromophenoxathiin.**—A solution of *n*-butyllithium prepared from 9.65 g. (0.072 mole) of *n*-butyl bromide in 25 cc. of ether and 2.1 g. (0.3 g. atom) of lithium in 25 cc. of ether was added to 5 g. (0.018 mole) of 2-bromophenoxathiin in 50 cc. of benzene. The solution was stirred and refluxed for fifteen minutes and then carbonated with solid carbon dioxide. The yield of crude acid was 5.92 g. (89.3%), melting in the range 240–250°. The crude acid was decolorized with Norit, and recrystallized twice from ethanol. The yield of purified product was 2.3 g. (52.3%), melting between 260–265°. In a second experiment the yield of crude acid was 77%, and of pure acid 63.7%.

The ethyl ester was prepared from the acid chloride and ethanol and a mixed melting point showed no depression with an authentic sample.[13]

**Attempted Oxidation of 4-Methylphenoxathiin 10-Dioxide.**—A suspension of 0.3 g. of 4-methylphenoxathiin 10-dioxide[14] in a solution of 10 g. of potassium permanganate and 5 g. of potassium hydroxide in 50 cc. of water was heated just below reflux temperature (to retard bumping) for forty-eight hours. The mixture was cooled, acidified and the excess oxidizing agent removed with sodium bisulfite. This solution was extracted with ether several times but the only product isolated was the original starting material.

**Competitive Metalation of Dibenzofuran and Dibenzothiophene.**—A solution of 0.066 mole of *n*-butyllithium in 200 cc. of ether was refluxed with equivalent quantities of dibenzofuran (13.9 g., 0.066 mole) and dibenzothiophene (14.9 g., 0.066 mole) for six hours. The mixture was then carbonated by solid carbon dioxide, and the acidic material obtained subsequent to alkali extraction and acidification gave no sodium fusion test for sulfur and melted between 198–202°. Recrystallization from dilute ethanol gave a melting point of 208–209°. This acid showed no depression in a mixed melting point determination with an authentic specimen of 4-dibenzofurancarboxylic acid. The acid was then converted to the methyl ester (m. p. 92–93°), and this ester was shown to be identical with an authentic specimen of methyl 4-dibenzofurancarboxylate. The yield of acid was 39%.

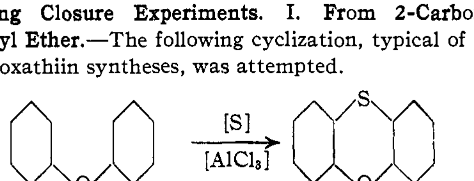
In another experiment, using 0.177 mole of *n*-butyllithium in 300 cc. of ether, and a twelve-hour period of refluxing, the same series of operations and identifications were carried out. The yield of 4-dibenzofurancarboxylic acid was 35%.

In a third experiment, using 0.083 mole of *n*-butyllithium in 200 cc. of ether and a two-hour period of refluxing, the acidic material gave a weak sulfur test. To facilitate isolation of any possible small quantity of 4-dibenzothiophenecarboxylic acid, the acid mixture (in glacial acetic acid) was treated with sodium dichromate and sulfuric acid to convert any 4-dibenzothiophenecarboxylic acid to 4-dibenzothiophenecarboxylic acid 5-dioxide. The small quantity of solid remaining after extracting the mixture with ether to remove 4-dibenzofurancarboxylic acid, was just sufficient to identify (mixed m. p.) as methyl 4-dibenzothiophenecarboxylate 5-dioxide subsequent to methylation by diazomethane. The yield of 4-dibenzofurancarboxylic acid was 45%.

**Metalation of Dibenzofuran by 4-Dibenzothienyllithium.**—A solution of 0.096 mole of *n*-butyllithium in 200 cc. of ether was refluxed for twenty hours with a slight excess of dibenzothiophene. Ten cc. aliquots were then withdrawn, carbonated and acidified. The absence of any odor of *n*-valeric acid established that no appreciable quantity of *n*-butyllithium was left. Then 0.096 mole of dibenzofuran was added and the mixture was refluxed for six hours. The mixture of acids resulting after carbonation melted in the range 180–220°. This mixture was then oxidized by dichromate, and the resulting acids separated by ether extraction in accordance with the procedure mentioned previously. The basic yields were 20% of 4-dibenzofurancarboxylic acid and 79.4% of 4-dibenzothiophenecarboxylic acid. All acidic products were identified both by comparison with authentic acids (mixed m. p.), and by converting the acids to their methyl esters and again using the method of mixed melting points with authentic specimens.

In a corresponding manner and under duplicated conditions, 4-dibenzofuryllithium and dibenzothiophene were refluxed for six hours, carbonated, and then examined for any 4-dibenzothiophenecarboxylic acid. There was no test for sulfur, and the only acid isolated was 4-dibenzofurancarboxylic acid.

**Ring Closure Experiments. I. From 2-Carboxydiphenyl Ether.**—The following cyclization, typical of some phenoxathiin syntheses, was attempted.



The 2-carboxydiphenyl ether was prepared by the metalation of diphenyl ether with *n*-butyllithium.[3,15] Five and thirty-five hundredths grams (0.025 mole) of 2-carboxydiphenyl ether was heated with 0.6 g. (0.02 mole) of sulfur and 1.33 g. (0.01 mole) of aluminum chloride between the

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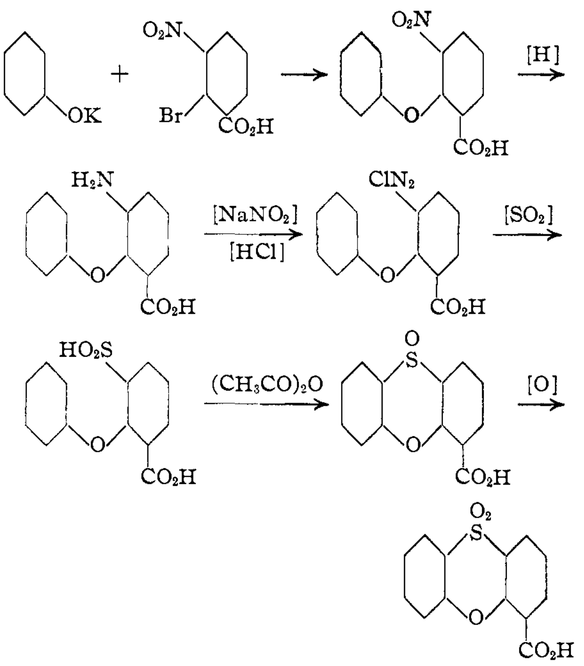
(13) Kindly provided by Professor C. M. Suter.

(14) Prepared from 4-methylphenoxathiin.[13]

(15) Recent studies have shown that ethyl- and propyl-lithium are also effective metalating agents.

temperature range of 120–140° for four hours. No hydrogen sulfide was formed.

**II. From 2-Phenoxy-3-carboxybenzenesulfinic Acid.**—The following ring closure was attempted, but the replacement of the diazonium group by the sulfinic acid radical was unsuccessful.



2-Bromo-3-nitrobenzoic acid, prepared in accordance with the directions of Culhane,[16] was converted to its potassium salt by dissolving in the theoretical quantity of saturated methyl alcoholic potassium hydroxide solution and then diluting with ether. Of this salt, 7.1 g. (0.025 mole), was heated with 2.44 g. (0.026 mole) of phenol, and 1.4 g. (0.025 mole) of potassium hydroxide dissolved in a few cc. of methanol. The temperature was gradually increased to 170°, and held at that point for two hours. The solid product was parted between ether and water, and the water layer acidified. The crude acid was recrystallized from water to a constant melting point of 153–153.5°. *Neut. equiv.* Calcd., 259. Found, 264.

The nitro group was reduced by passing hydrogen chloride into an ether solution of 3.35 g. (0.013 mole) of 2-nitro-6-carboxydiphenyl ether and 8.76 g. of stannous chloride hydrate in 50 cc. of ether at 0° until the solution was saturated. The crystalline amine hydrochloride was filtered off and dried; yield, 2.9 g. The free amine was formed by adding a slight excess of ammonium hydroxide, and then a few drops of acetic acid.

The attempted replacement of the amino group by the sulfinic acid radical was based on a procedure by Gattermann.[17] The moist amine was dissolved in a solution of 3 g. of concd. sulfuric acid in 10 cc. of water, and diazotized at 0° by adding sodium nitrite solution. Sulfur dioxide was passed into the stirred diazonium solution at 0°, until 3 g. of the gas had been absorbed. Two grams of copper bronze was then added, and the mixture allowed to stand a few hours. The precipitate was removed and extracted with boiling water. Cooling of this extract deposited a very small quantity of a gum which has not been purified.

**Attempted Conversion of Phenoxathiin to Dibenzofuran.**—Phenoxathiin in one-gram lots was heated with 1.5 equivalents of silver powder, powdered iron, mercury, zinc dust, and a catalytic copper[18] at 280–290° for two hours. No trace of dibenzofuran was detected in any of these trials, and the phenoxathiin was recovered unchanged in each case. In a second series of experiments, the same quantities of the reactants were sealed in small tubes and heated at 345° for four and one-half hours. The metals used in this series were the same as those previously listed, except that mercury was omitted. Again no trace of dibenzofuran was found, and the phenoxathiin was recovered.

**Metalation with Phenylcalcium Iodide.**—A filtered solution of phenylcalcium iodide, prepared from 6 g. (0.15 g. atom) of calcium turnings and 20.4 g. (0.1 mole) of iodobenzene in 30 cc. of ether, was added to a solution of 16 g, (0.08 mole) of phenoxathiin in 100 cc. of ether. The resultant solution was refluxed for twenty-four hours and carbonated in the usual manner. Extraction of the product with dilute sodium hydroxide and subsequent acidification gave a purple tar, which on crystallization from dilute ethanol yielded 0.68 g. of almost black material melting between 190–217°. Two recrystallizations from 50% acetic acid gave a deep yellow crystalline compound melting at 260–262°. This is the melting point reported for 2-phenoxathiincarboxylic acid; however, a mixed melting point determination with an authentic specimen[14] showed a depression.

The apparently anomalous orientation in metalation recalls the striking case of dibenzothiophene which when metalated by phenylcalcium iodide gave on carbonation 3-dibenzothiophenecarboxylic acid,[4] in contrast to the formation of the isomeric 4-acid when a series of RLi compounds was used in the metalation.

## Summary

The following general results were obtained incidental to a study on the preparation of difficultly accessible dibenzofurans from phenoxathiins. (1) Phenoxathiin is metalated in the 4-position, a position otherwise unavailable by direct nuclear substitution reactions. (2) 2-Bromophenoxathiin undergoes a prompt halogen–metal interconversion with *n*-butyllithium to give a very good yield of 2-phenoxathiinyllithium. The bromine is uncommonly resistant to reaction with magnesium to form the corresponding Grignard reagent. The RMgBr compound is now readily available by the following reaction: $RLi + MgBr_2 \longrightarrow RMgBr + LiBr$. (3) In conformity with the greater orienting effect of oxygen over sulfur in the symmetrical phenoxathiin, competitive and other reactions show that di-

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[16] Culhane, "Organic Syntheses," Vol. 7, 1927, p. 12.

[17] Gattermann, *Ber.*, **32**, 1137 (1899).

[18] Piccard, *Helv. Chim. Acta*, **5**, 147 (1922).

benzofuran is metalated more readily than dibenzothiophene. (4) Contrary to earlier work, but in agreement with Suter's experiments, phenoxathiin was not converted to dibenzofuran by heating with some metals.

AMES, IOWA RECEIVED JUNE 13, 1940

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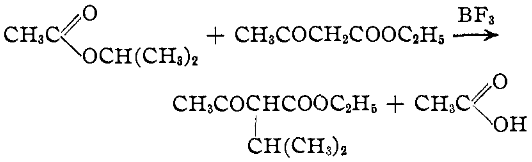
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DUKE UNIVERSITY]

# Condensations. XIV.[1] The Alkylation of Ethyl Acetoacetate with Isopropyl Acetate in the Presence of Boron Trifluoride[2]

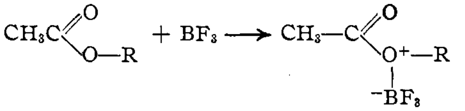
BY DAVID S. BRESLOW AND CHARLES R. HAUSER

It is well known that aliphatic esters generally alkylate rather than acylate in the Friedel–Crafts reaction. In this paper it is shown that isopropyl acetate likewise alkylates the reactive methylenic compound, ethyl acetoacetate, in the presence of boron trifluoride. The reaction may be represented as follows.

(I) 

$$CH_3C(=O)OCH(CH_3)_2 + CH_3COCH_2COOC_2H_5 \xrightarrow{BF_3} CH_3COCH(CH(CH_3)_2)COOC_2H_5 + CH_3C(=O)OH$$

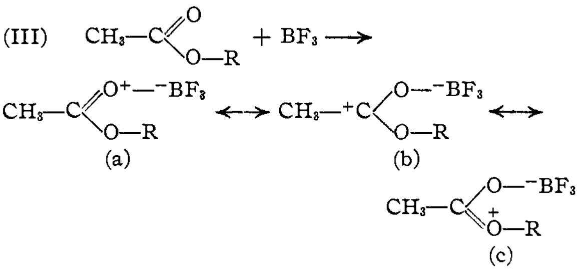
In this condensation as well as in the corresponding Friedel–Crafts reaction it is considered that the ester is activated[3] by the boron trifluoride. The mechanism of this activation may involve an attack of the reagent on either the alcohol oxygen or the carbonyl oxygen. As pointed out by Price,[4] an attack of the boron trifluoride on the alcohol oxygen of the ester would give a complex which would be analogous to that obtained from an alcohol or ether, thus

(II) 

$$CH_3C(=O)O{-}R + BF_3 \longrightarrow CH_3{-}C(=O)O^{+}({-}R)({}^{-}BF_3)$$

The positive charge on the oxygen atom should facilitate the release of R as a carbonium ion, which is considered to be the "active" electron-accepting component[3] in the alkylation.

An attack of the boron trifluoride on the carbonyl oxygen may also lead to the intermediate formation of R as a carbonium ion. The boron trifluoride-ester complex that would result from such an attack may be represented in several resonance forms, thus[5]



$$\text{(III)}\quad CH_3{-}C(=O)O{-}R + BF_3 \longrightarrow \underset{\text{(a)}}{CH_3{-}C(=O^{+}{-}{}^{-}BF_3)O{-}R} \longleftrightarrow \underset{\text{(b)}}{CH_3{-}{}^{+}C(O{-}{}^{-}BF_3)O{-}R} \longleftrightarrow \underset{\text{(c)}}{CH_3{-}C(O{-}{}^{-}BF_3)=O^{+}{-}R}$$

Similar to the complex formed in (II), the resonance form (c) with the positive charge on the oxygen should lead to the formation of R as a carbonium ion ("active" intermediate). It seems possible that because of the strongly electron-attracting nature of boron trifluoride, resonance form (c) may contribute to a large extent to the structure of the coördination complex; or the complex may acquire the structure of resonance form (c) as it approaches the electron-donating component in the condensation.

Recently it has been shown[6] that, although esters apparently only alkylate in the Friedel–Crafts reaction at room temperature, at least certain esters both alkylate and acylate at higher temperatures. An attempt to effect the acylation of ethyl acetoacetate with isopropyl acetate by means of boron trifluoride at relatively high temperatures, however, has been unsuccessful.

It should be pointed out that the mechanism of activation of esters by boron trifluoride (or aluminum chloride) represented above in (III) may lead to an "active" acylating intermediate as well as an "active" alkylating intermediate.

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(1) For paper XIII of this series see THIS JOURNAL, **62**, 2457 (1940).

(2) This investigation was supported by a grant from the Duke University Research Council.

(3) See Hauser and Breslow, THIS JOURNAL, **62**, 2389 (1940).

(4) Price and Ciskowski, *ibid.*, **60**, 2499 (1938).

(5) The double-headed arrow is used to illustrate resonance forms. See especially Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940.

(6) Norris and Sturgis, THIS JOURNAL, **61**, 1413 (1939); Norris and Arthur, *ibid.*, **62**, 874 (1940); Kursanov and Zel'vin, *J. Gen. Chem.* (U. S. S. R.), **9**, 2173 (1939).