tube was attached. A small crystal of iodine was added, stirring was commenced and the bottom of the reaction vessel was heated lightly to initiate the reaction. It was necessary to moderate the vigorous exothermic reaction by temporary immersion of the flask in an ice-bath. After the spontaneous refluxing had subsided, the reaction was continued for one-half hour by the application of heat after which the reaction mixture was allowed to cool to room temperature. Hydrolysis of the reaction mixture was accomplished by the addition, with vigorous stirring, of 75 ml. of ice-cold 10% sulfuric acid. The non-aqueous layer was separated and combined with a subsequent ether extract of the aqueous portion. The combined solutions were extracted successively with 100 ml. of water, 100 ml. of 10% sodium carbonate solution and 100 ml. of water followed by drying over anhydrous sodium sulfate. After removal of the solvents on a steam-bath, the residue was distilled *in vacuo*. The forerun contained 1.3 g. of ethyl crotonate boiling at 30–40° (80 mm.) and 1.2 g. of 2-thenal, b.p. 58–59° (2 mm.). Following the forerun was the first product which amounted to 6.2 g. (28%) of ethyl α-vinyl-β-hydroxy-β-(2-thienyl)-propionate, boiling at 132–134° (1 mm.), $n^{25}\mathrm{D}$ 1.5270.

Anal. Calcd. for $C_{11}H_{14}O_2S$: C, 58.3; H, 6.2. Found: C, 58.0; H, 6.3.

The second product obtained amounted to 3.6 g. (16%) of ethyl 5-(2-thienyl)-5-hydroxy-2-pentenoate and distilled at 160–161° (1 mm.), $n^{25}\mathrm{D}$ 1.5573.

Anal. Calcd. for $C_{11}H_{14}O_2S$: C, 58.3; H, 6.2. Found: C, 58.6; H, 6.0.

Reformatsky Reaction of 3-Thenal with Ethyl γ-Bromocrotonate.—Following the above described procedure, 5.6 g. (0.05 mole) of 3-thenal, 3.25 g. (0.05 mole) of zinc and 9.7 g. (0.05 mole) of ethyl γ-bromocrotonate were allowed to interact in 50 ml. of dry benzene as a solvent to yield two Reformatsky products. The first amounted to 3.3 g. (29%) of ethyl α-vinyl-β-hydroxy-β-(3-thienyl)-propionate, and had the following physical properties: b.p. 134–135° (1 mm.), $n^{25}\mathrm{D}$ 1.5255.

Anal. Calcd. for $C_{11}H_{14}O_2S$: C, 58.3; H, 6.2. Found: C, 57.8; H, 6.4.

The second product, distilling at 158–160° (1 mm.), amounted to 1.9 g. (17%) of ethyl 5-(3-thienyl)-5-hydroxy-2-pentenoate, $n^{25}\mathrm{D}$ 1.5555.

Anal. Calcd. for $C_{11}H_{14}O_2S$: C, 58.3; H, 6.2. Found: C, 58.3; H, 6.4.

Reformatsky Reaction of 2-Acetylthiophene with Ethyl γ-Bromocrotonate.—Employing the usual procedure, 12.6 g. (0.10 mole) of 2-acetylthiophene, 19.3 g. (0.10 mole) of ethyl γ-bromocrotonate and 6.5 g. (0.10 mole) of zinc dust interacted in 100 ml. of anhydrous benzene. After then carrying out the isolation procedures described above the products were vacuum distilled. The first fraction obtained was 7.1 g. of ethyl crotonate followed by 7.8 g. of 2-acetylthiophene. Following these fractions there was obtained 1.5 g. (7%) of ethyl α-vinyl-β-hydroxy-β-(2-thienyl)-*n*-butyrate boiling at 107–108° (1 mm.), $n^{25}\mathrm{D}$ 1.4959.

Anal. Calcd. for $C_{12}H_{16}O_3S$: C, 59.9; H, 6.7. Found: C, 59.7; H, 6.8.

The next fraction boiling at 155–156° (1 mm.) did not give a correct analysis for the isomeric ester and was refluxed for eight hours in 6% oxalic acid solution to yield 5.8 g. (26%) of ethyl 5-thienyl-5-hydroxy-2,4-hexadienoate boiling at 147–148.5° (1 mm.).

Anal. Calcd. for $C_{12}H_{14}O_2S$: C, 64.8; H, 6.31. Found: C, 64.7; H, 6.5.

4-(2-Thienyl)-4-hydroxy-1-butene.—Into the same apparatus as described above was placed 11.2 g. (0.10 mole) of 2-thenal, 12.1 g. (0.10 mole) of allyl bromide, 6.5 g. (0.10 mole) of zinc, 50 ml. of dry benzene and 50 ml. of anhydrous tetrahydrofuran. The reaction was initiated and carried out in the previously described manner. A quantity of 100 ml. of ice-cold 30% acetic acid being employed to hydrolyze the reaction products. After washing, drying and removal of the solvents, the residue was distilled *in vacuo* to yield 12.0 g. (78%) of a clear colorless liquid boiling at 89–90.5° (1 mm.), $n^{25}\mathrm{D}$ 1.5439.

Anal. Calcd. for $C_8H_{10}OS$: C, 62.3; H, 6.5. Found: C, 62.1; H, 6.9.

1-(2-Thienyl)-3-butyn-1-ol.—The treatment of a solution of 11.2 g. (0.10 mole) of 2-thenal and 11.9 g. (0.10 mole) of propargyl bromide in a mixture of 50 ml. of anhydrous benzene and 50 ml. of dry tetrahydrofuran with 6.5 g. (0.10 mole) of zinc dust according to the preceding procedure yielded 9.1 g. (60%) of the expected product boiling at 84–85° (0.1 mm.), $n^{25}\mathrm{D}$ 1.5220.

Ozonolysis of Ethyl α-Vinyl-β-hydroxy-β-(2-thienyl)-propionate.—Following an already reported procedure,[7] 0.2 g. of the ester was dissolved in 10 ml. of acetic acid and treated with ozone for one hour. The ozonide was decomposed with zinc dust and water and then distilled until 20 ml. of distillate was collected. The distillate was treated with 0.25 g. of dimedone and set aside overnight in the refrigerator. The resulting crystals were filtered off and recrystallized from a methanol–water mixture of equal parts to yield about 0.1 g. of crystalline material which melted sharply at 187°. The melting point was not depressed when the substance was mixed with the product resulting from the interaction of formaldehyde and dimedone.

EAST LANSING, MICHIGAN

[CONTRIBUTION NO. 139 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TENNESSEE]

The Metalation of Phenoxathiin 10-Oxide and 10,10-Dioxide with *n*-Butyllithium

BY DAVID A. SHIRLEY AND ERWIN A. LEHTO

RECEIVED JUNE 7, 1954

In accord with the known activating influence of the sulfone group, and in contrast to phenoxathiin itself which metalates in the 4-position, the metalation of phenoxathiin 10-oxide and phenoxathiin 10,10-dioxide with *n*-butyllithium occurs at the 1-position (adjacent to sulfur).

The sulfone group has a powerful deactivating effect on adjacent rings undergoing electrophilic substitution, but an opposite effect when these rings undergo metalation by alkyllithium reagents. Thus Truce and co-workers[1] have metalated a variety of substituted diphenyl sulfones and have observed metalation *ortho* to the sulfone group under relatively mild conditions and in good yields. Gilman and Esmay[2] have reported the mono- and dimetalation of dibenzothiophene 5,5-dioxide and the metalation (with reduction) of the corresponding sulfoxide, all occurring at the position adjacent to sulfur.

It seemed of interest to examine the metalation of phenoxathiin 10-oxide and -dioxide. Phenoxathiin itself metalates adjacent to the oxygen atom[3] (4-position) and this has been related to the fact that dibenzofuran is metalated exclusively when placed in competition with dibenzothiophene.[3]

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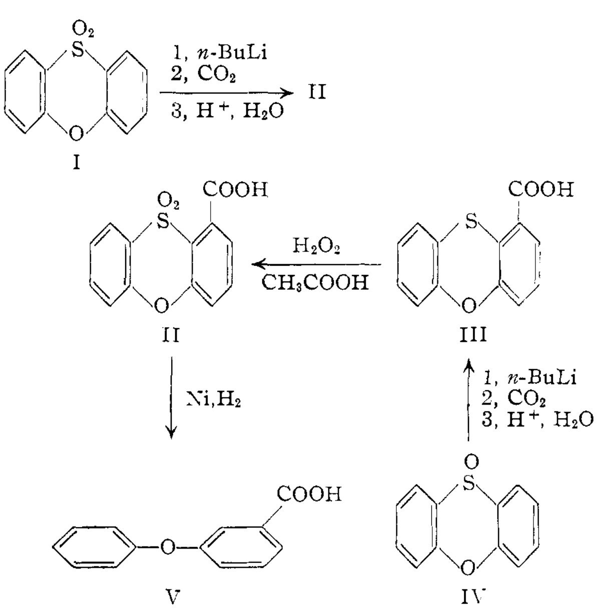
(1) (a) W. E. Truce and M. F. Amos, THIS JOURNAL, **73**, 3013 (1951); (b) W. E. Truce and O. L. Norman, *ibid.*, **75**, 6023 (1953).

(2) (a) H. Gilman and D. L. Esmay, *ibid.*, **74**, 266 (1952); (b) H. Gilman and D. L. Esmay, *ibid.*, **75**, 278 (1953).

(3) H. Gilman, M. W. Van Ess, H. B. Willis and C. G. Stuckwisch, *ibid.*, **62**, 2606 (1940).

In view of this, it seemed that the activating and *ortho*-directing influence of the sulfoxide and sulfone groups might be sufficient to overcome the normal preference for substitution next to oxygen which is shown by phenoxathiin itself. This was found to be the case.

Phenoxathiin 10,10-dioxide (I) was metalated by one equivalent of *n*-butyllithium in the 1-position; subsequent carbonation and acidification gave a 40 to 45% yield of 1-phenoxathiincarboxylic acid 10,10-dioxide (II). Metalation of phenoxathiin 10-oxide (IV) was accompanied by reduction to form 1-phenoxathiincarboxylic acid (III) in about 20% yield. Oxidation of this latter acid to the sulfone, identical with II, proved that the same positions in the ring were involved in both metalations. Degradation of II with Raney nickel according to the method of Mozingo and co-workers[4] gave a 47% yield of *m*-phenoxybenzoic acid (V) identical with a synthetic specimen. The formation of *m*-phenoxybenzoic acid indicated that metalation had taken place in the 1- or 3-position. The metalation acid was shown not to be 3-phenoxathiincarboxylic acid by comparison with an authentic sample.[5]



In view of interest in the hydrazides of heterocyclic carboxylic acids as antitubercular chemotherapeutic agents, we have converted the acids made in this work to the corresponding hydrazides. The compounds are being tested biologically by the Eli Lilly Co. with results to be reported elsewhere.

The view that metalation of dibenzothiophene 5-oxide preceded reduction of the sulfoxide group[2a] was supported by the fact that dibenzothiophene was not metalated at −10° under conditions which allowed metalation of the sulfoxide. Further support for this view is obtained in the present observation that while phenoxathiin metalates in the 4-position, the 1-metalation of the sulfoxide indicates that it, rather than the reduced product, is metalated. This type of evidence was not available in the dibenzothiophene study, since both the sulfoxide and sulfide metalate at the same position.

The fact that phenoxathiin is metalated at a position adjacent to the more electronegative oxygen, until the sulfur is converted to the highly polar sulfoxide or sulfone, can be related to the protolytic character of the attack by butyllithium and to the relative inductive effects of substituents present in the ring.[1,6,7]

Experimental[8,9]

Metalation of Phenoxathiin 10,10-Dioxide.—An ether solution containing 0.10 mole of *n*-butyllithium was added over a half-hour period to a well-stirred suspension of 23.2 g. (0.10 mole) of finely powdered phenoxathiin 10,10-dioxide in 200 ml. of ether. The reaction mixture was cooled in an ice-bath during the addition and for a subsequent two-hour stirring period and an atmosphere of dry nitrogen was maintained over the reactants during these operations. The ice-bath was then removed and stirring continued for one-half hour, after which the mixture was poured into a slurry of ether and crushed excess solid carbon dioxide. After evaporation of the carbon dioxide, 500 ml. of water was added and the aqueous layer separated and acidified with dilute hydrochloric acid. The precipitated solid (21.4 g., m.p. 204–209°) was crystallized once from glacial acetic acid and once from 95% ethanol to yield 12.6 g. (46%) of acid melting at 228–229°.

Other runs under similar conditions gave the product in 40 to 45% yields. Increasing the amount of *n*-butyllithium to 0.15 mole in the above procedure did not increase the amount of metalation acid.

Anal. Calcd. for $C_{13}H_8O_5S$: C, 56.52; H, 2.93; neut. equiv., 276. Found: C, 56.40; H, 3.03; neut. equiv., 279.

Methyl 1-Phenoxathiincarboxylate 10,10-Dioxide.—A suspension of 5.0 g. (0.018 mole) of the acid in ether was treated with a slight excess of diazomethane in ether. The ether was removed by evaporation and the resulting solid recrystallized from water–methanol to yield 4.3 g. (84%) of ester, m.p. 144–145°.

Anal. Calcd. for $C_{14}H_{10}O_5S$: C, 57.92; H, 3.47. Found: C, 57.30; H, 3.62.

The corresponding hydrazide was prepared by heating 2.0 g. of the ester and 2.0 g. of 85% hydrazine hydrate under reflux for 15 minutes. Sufficient ethanol was then added to dissolve the reactants and reflux was continued for two hours. The alcohol was removed by distillation and the residue crystallized from water–ethanol. The yield of hydrazide, m.p. 240°, was 1.4 g. or 70%.

Anal. Calcd. for $C_{13}H_{10}N_2O_4S$: N, 9.65. Found: N, 9.60.

Hydrogenolysis of 1-Phenoxathiincarboxylic Acid 10,10-Dioxide.—Two grams (0.017 mole) of 1-phenoxathiincarboxylic acid 10,10-dioxide in 150 ml. of 75% ethanol–water and 25–30 g. of Raney nickel catalyst were heated under reflux for ten hours. The Raney nickel was prepared in the usual manner[10] except that the final heating was carried out for one hour between 50 and 80°.[4] The nickel was removed by filtration, the filtrate concentrated by evaporation, made alkaline with aqueous sodium hydroxide, and then acidified with hydrochloric acid. The precipitated product (0.73 g. or 47%) was recrystallized from petroleum ether and then several times from aqueous ethanol and aqueous acetic acid to yield white solid acid, m.p. 139–140°.

The amide derivative melted at 121–122°.

The product of the hydrogenolysis was shown to be *m*-phenoxybenzoic acid by preparation of an authentic specimen. *m*-Tolyl phenyl ether, prepared according to the method of Suter and Green,[11] was oxidized with alkaline permanganate to the corresponding acid, m.p. 144–145°

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[4] R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, This Journal, **65**, 1013 (1943).

[5] F. Mauthner, *Ber.*, **39**, 1340 (1906).

[6] J. D. Roberts and D. Y. Curtin, This Journal, **68**, 1658 (1946).

[7] (a) D. Bryce-Smith, *J. Chem. Soc.*, 1079 (1954); (b) E. E. Turner and D. Bryce-Smith, *ibid.*, 861 (1953).

[8] Melting and boiling points are uncorrected.

[9] Analyses are by the Galbraith Microanalytical Laboratories of Knoxville, Tenn.

[10] R. Mozingo, *Organic Syntheses*, **21**, 15 (1941).

[11] C. M. Suter and F. O. Green, This Journal, **59**, 2578 (1937).

(reported[12] 145°); a mixture m.p. with the 139–140° sample from hydrogenolysis melted at 141–143°. The amide of the synthetic acid melted at 122–123° and there was no depression of melting point when mixed with the amide from hydrogenolysis, m.p. 121–122°.

Metalation of Phenoxathiin 10-Oxide.—A solution of 0.32 mole of *n*-butyllithium in ether was added (one-half hour) to a suspension of 21.6 g. (0.10 mole) of phenoxathiin 10-oxide[13] in ether. The mixture was stirred and cooled in a Dry Ice–acetone-bath held at −20° during the addition and for an additional five hours. The bath was removed and stirring continued for an additional hour as the mixture came to room temperature. Carbonation and work-up of the mixture in the usual manner gave 5.4 g. of carboxylic acid melting at 221–222° (crystallized from methanol).

Anal. Calcd. for $C_{13}H_8O_3S$: C, 63.92; H, 3.30; neut. equiv., 244. Found: C, 63.92, 64.03; H, 3.46, 3.37; neut. equiv., 248.

While the analyses indicated the product to be a phenoxathiincarboxylic acid rather than the sulfoxide, further confirmation of this was obtained by treating the acid in glacial acetic acid with zinc dust under conditions which allow reduction of sulfoxides to sulfides.[14] The material was not affected.

The 1-phenoxathiincarboxylic acid (0.5 g.) was oxidized by 30% hydrogen peroxide in glacial acetic acid solution. The yield of product was 0.34 g. (60%) melting at 228–229°. A mixture melting point with 1-phenoxathiincarboxylic acid 10,10-dioxide, m.p. 228–229°, showed no depression.

Methyl 1-Phenoxathiincarboxylate.—The methyl ester was prepared by the diazomethane treatment described earlier. It melted, after crystallization from ethanol, at 95–96°.

Anal. Calcd. for $C_{14}H_{10}O_3S$: C, 65.10; H, 3.90. Found: C, 65.13, 65.17; H, 3.92, 3.92.

The corresponding hydrazide prepared in 89% yield, melted at 197–198°.

Anal. Calcd. for $C_{13}H_{10}H_2O_2S$: N, 10.85. Found: N, 10.81, 10.82.

Synthesis of 3-Phenoxathiincarboxylic Acid.—Four grams (0.016 mole) of 2,2′-dihydroxydiphenyl disulfide[15] and 8.0 g. of 4-chloro-3,5-dinitrobenzoic acid were condensed[5] to give 2.0 g. (22%) of 1-nitro-3-phenoxathiincarboxylic acid, m.p. 260–262°. One gram (0.003 mole) of the nitro compound was reduced with hydrazine and Raney nickel.[16] The resulting amine, m.p. 248–249°, was diazotized and treated with 50% hypophosphorous acid in the usual manner[17] to give 0.2 g. (24% based on the nitro-acid) of 3-phenoxathiincarboxylic acid, m.p. 223–224°; reported[5] m.p. 223°. A mixture melting point between this acid and the sample, m.p. 221–222°, from the metalation of phenoxathiin 10-oxide showed a depression of about 40°.

Methyl 4-Phenoxathiincarboxylate.—Phenoxathiin was metalated with *n*-butyllithium according to the procedure of Gilman and co-workers.[3] The 4-phenoxathiincarboxylic acid obtained was converted in 76% yield to the methyl ester with diazomethane. The ester boiled at 183–187° at 1 mm. pressure.

Anal. Calcd. for $C_{14}H_{10}O_3S$: C, 65.10; H, 3.90. Found: C, 65.12; H, 4.14.

The hydrazide melted at 127–128°.

Anal. Calcd. for $C_{13}H_{10}N_2O_2S$: N, 10.85. Found: N, 10.99.

Hydrazide of 4-Phenoxathiincarboxylic Acid 10,10-Dioxide.—Oxidation of 4-phenoxathiincarboxylic acid with 30% hydrogen peroxide gave the sulfone, m.p. 189–190°; reported[3] m.p. 183–184°. This was esterified with diazomethane to yield the ester, m.p. 123–124°, reported[3] m.p. 124°. The ester was converted to the hydrazide (m.p. 260°) in 57% yield.

Anal. Calcd. for $C_{13}H_{10}N_2O_4S$: N, 9.65. Found: N, 9.67.

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(12) G. Lock and F. H. Kempter, *Monatsh.*, **67**, 24 (1935).

(13) Provided through the courtesy of the Dow Chemical Co.

(14) R. Connor in H. Gilman, editor, "Organic Chemistry—An Advanced Treatise," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 872.

(15) Bios Laboratories, New York.

(16) D. Balcom and A. Furst, THIS JOURNAL, **75**, 4334 (1953).

(17) N. Kornblum in R. Adams, editor, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 262.

KNOXVILLE, TENNESSEE

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ANTIOCH COLLEGE]

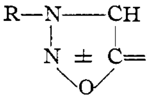
The Preparation of Substituted Hydrazines. I. Alkylhydrazines *via* Alkylsydnones[1]

BY JOSEPH FUGGER, JACK M. TIEN AND I. MOYER HUNSBERGER[2]

RECEIVED SEPTEMBER 25, 1954

The conversion of an alkylamine to an alkylhydrazine *via* the corresponding N-alkylglycine, N-nitroso-N-alkylglycine and N-alkysydnone is shown to constitute an acceptable preparative method in the case of benzylhydrazine, *n*-butylhydrazine and *n*-hexylhydrazine. The infrared spectra of N-benzylsydnone, N-(*n*-butyl)-sydnone and N-(*n*-hexyl)-sydnone are presented.

The sydnones I, a very interesting class of compounds first reported in 1935,[3] were not studied very intensively until 1946 and thereafter.[4] The American literature is virtually devoid of any reference to these unusual compounds, for which no single classical valence-bond formula can be written. The ± symbol is used to indicate the *meso*-ionic nature of the sydnones.[4d,i]



(I)

Sydnones are prepared readily by treatment of an N-substituted-N-nitrosoglycine with acetic anhydride. Alkaline hydrolysis of the sydnone regenerates the nitrosoglycine, whereas hydrolysis in di-

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(1) This work was sponsored by the Air Forces under Contract No. AF 33(038)-22909, Supplemental Agreement Nos. S1 (53-134) and S2 (53-1063).

(2) To whom inquiries regarding this article should be sent.

(3) J. C. Earl and A. W. Mackney, *J. Chem. Soc.*, 899 (1935).

(4) (a) J. C. Earl, *Nature*, **158**, 910 (1946); (b) R. A. Eade and J. C. Earl, *J. Chem. Soc.*, 591 (1946); (c) W. Baker and W. D. Ollis, *Nature*, **158**, 703 (1946); (d) W. Baker, W. D. Ollis, V. D. Poole, J. A. Barltrop, R. A. W. Hill and L. E. Sutton, *ibid.*, **160**, 366 (1947); (e) J. Kenner and K. Mackay, *ibid.*, **158**, 909 (1946); **160**, 465 (1947); (f) J. C. Earl, E. M. W. Leake and R. J. W. LeFevre, *J. Chem. Soc.*, 2269 (1948); (g) R. A. Eade and J. C. Earl, *ibid.*, 2307 (1948); (h) R. A. W. Hill and L. E. Sutton, *J. chim. phys.*, **46**, 244 (1949); *J. Chem. Soc.*, 746 (1949); 1482 (1953); (i) W. Baker, W. D. Ollis and V. D. Poole, *ibid.*, 307 (1949); (j) J. C. Earl, R. J. W. LeFevre and I. R. Wilson, *ibid.*, S103 (1949); (k) W. Baker, W. D. Ollis and V. D. Poole, *ibid.*, 1542 (1950); (l) J. C. Earl, R. J. W. LeFevre, A. G. Pulford and A. Walsh, *ibid.*, 2207 (1951); (m) J. C. Earl, *Chemistry & Industry*, 746, 1284 (1953); (n) D. L. Hammick and A. M. Roe, *ibid.*, 900 (1953); (o) D. L. Hammick, A. M. Roe and D. J. Voaden, *ibid.*, 251 (1954); (p) S. Kruger, *ibid.*, 465 (1954).