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o-(2-Thenoyl)-benzoic Acids and Thiophanthraquinones

BY VIKTOR WEINMAYR

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o-(2-Thenoyl)-benzoic acids substituted in the benzene nucleus and in the thiophene nucleus were prepared. The condensation of 2-thienylmagnesium bromide with phthalic anhydrides unsymmetrically substituted with chlorine or nitro groups gave in every case the expected two isomeric *o*-(2-thenoyl)-benzoic acids. The condensations of carbomethoxynitrobenzoyl chlorides with thiophene by the Friedel–Crafts method proceeded with rearrangements leading to *o*-(2-thenoyl)-benzoic acids not normally expected. The constitution of the mononitro- and monochloro-2-(2-thenoyl)-benzoic acids was established. Properties of thiophanthraquinone which differ from those of anthraquinone are reported.

Few condensations of thiophenes with phthalic anhydrides have been reported in the literature.[1]

In this paper we will present a study of the condensation of phthalic anhydride with thiophene, chloro- and methylthiophenes, the condensation of nitrophthalic anhydrides and halogenated phthalic anhydrides with thiophene, and the preparation and some properties of thiophanthraquinones from some of the *o*-(2-thenoyl)-benzoic acids.

The Friedel–Crafts method proved entirely satisfactory for the condensation of phthalic anhydride with thiophene, 2-chlorothiophene, 2-methyl- and 3-methylthiophene.

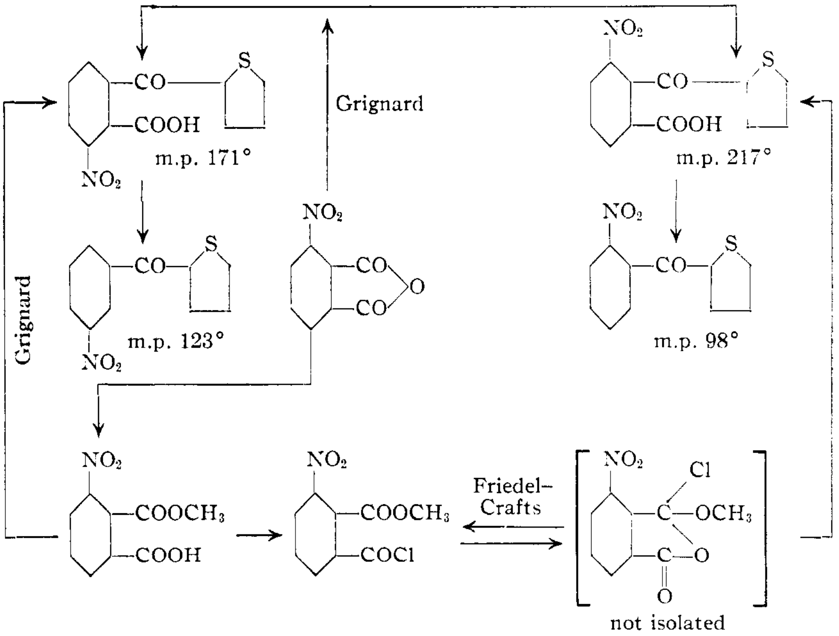
Steinkopf[2] had proved the constitution of the *o*-(2-thenoyl)-benzoic acid through a synthesis from 2-thienyl-2-tolyl ketone. This constitution was confirmed when the identical *o*-(2-thenoyl)-benzoic acid was obtained from phthalic anhydride and 2-bromothiophene by the Grignard method.

The Friedel–Crafts reaction was not satisfactory in general for the condensation of thiophene with chlorophthalic anhydrides or with nitrophthalic anhydrides. In these cases the Grignard reaction using 2-thienylmagnesium bromide gave excellent results. Whenever unsymmetrically substituted phthalic anhydrides were used, two isomeric *o*-(2-thenoyl)-benzoic acids were obtained. They could be separated because of the great differences in solubility in organic solvents. They were even more readily separated by acidifying the salt solutions of the mixtures of the isomers first with acetic acid, then with hydrochloric acid.

The constitution of the four possible mononitro-2-(2-thenoyl)-benzoic acids was at first thought to have been established by comparing the acids obtained by the Grignard method from nitrophthalic anhydrides and 2-bromothiophene with those obtained in excellent yields by the Friedel–Crafts method from carbomethoxynitrobenzoyl chlorides and thiophene. A very recent publication[3] cast serious doubt on the constitution we had arrived at, and caused us to reinvestigate the constitution of the nitro-2-(2-thenoyl)-benzoic acids by decarboxylating them to the corresponding nitrophenyl-(2-thienyl) ketones. It was found that the constitution previously assigned to them[4] was in error.

It is believed that a rearrangement of the carbomethoxynitrobenzoyl chlorides had taken place under the influence of the Friedel–Crafts catalyst. The rearrangement of *sym*-*o*-phthalyl chloride to the *unsym*-*o*-phthalyl chloride has been reported in the literature.[5] The course of the reaction is illustrated by the formulation of the condensation of 3-nitrophthalic anhydride. From the same 2-carbomethoxy-3-nitrobenzoyl chloride both isomeric nitro-2-(2-thenoyl)-benzoic acids could be obtained, the 3-nitro-2-(2-thenoyl)-benzoic acid by the Friedel–Crafts method in a practically quantitative yield, and the 6-nitro-2-(2-thenoyl)-benzoic acid by the Grignard method in a low yield.

A similar rearrangement occurred when starting with 2-carbomethoxy-5-nitrobenzoic acid as obtained from 4-nitrophthalic anhydride.



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[1] W. Steinkopf, "Die Chemie des Thiophens," Verlag von Theodor Steinkopf, Dresden, 1941, pp. 71, 187.

[2] W. Steinkopf, *Ann.*, **407**, 94 (1914).

[3] R. Goncalves and E. V. Brown, *J. Org. Chem.*, **17**, 698 (1952), and R. Goncalves, M. R. Kegelman and E. V. Brown, *ibid.*, **17**, 705 (1952).

[4] H. R. Lee and V. Weinmayr, U. S. Patent 2,513,573 (1950).

[5] E. Ott, *Ann.*, **392**, 245 (1910).

The constitution of the four monochloro-2-(2-thenoyl)-benzoic acids obtained from the monochlorophthalic anhydrides and 2-bromothiophene by the Grignard method was determined by reducing the 3- and 4-nitro-2-(2-thenoyl)-benzoic acids to the amino-2-(2-thenoyl)-benzoic acids and converting them to the chloro-2-(2-thenoyl)-benzoic acids by the Sandmeyer method.

The *o*-(2-thenoyl)-benzoic acids unsubstituted in the benzene nucleus were readily closed to the corresponding thiophanthraquinones.[6]

The reactions involved in the closure of the *o*-(2-thenoyl)-benzoic acids substituted in the benzene nucleus with an amino group, a nitro group, or one chlorine atom will be reported in a separate paper.[7]

A few reactions observed on some of the compounds prepared should be reported.

Thiophanthraquinone had a lower oxidation-reduction potential than anthraquinone and was easier to reduce. In contrast to anthraquinone, which requires sodium hydrosulfite for reduction, thiophanthraquinone could be converted to an alkali soluble leuco compound (vatted) when heated in a solution of sodium sulfide (green colored vat).

In contrast to anthraquinone, thiophanthraquinone was destroyed to a considerable extent with chromic acid or potassium permanganate in acetic acid. It also behaved differently from anthraquinone under certain reduction conditions. Thus the analytical method of determining the purity of anthraquinone with $TiCl_3$ which is based on its reduction to anthrone was not applicable to thiophanthraquinone. Upon catalytic reduction with hydrogen under pressure, using reduced nickel catalyst thiophanthraquinone was reduced to leuco thiophanthraquinone while anthraquinone was reduced to anthrone under similar conditions.[8]

Thiophanthraquinone reacted with carbon tetrachloride under pressure and in the presence of a catalyst to give, after hydrolysis, thiophanthraquinone-2-carboxylic acid, m.p. 293–294°. Benzanthrone, but not anthraquinone, gave a carboxylic acid under similar conditions.[9] This thiophanthraquinone-2-carboxylic acid was identical with the thiophanthraquinone-2-carboxylic acid obtained when 2-methylthiophanthraquinone was oxidized.

The *o*-(2-thenoyl)-benzoic acid as well as the thiophanthraquinone reacted with mercuric acetate to give triacetoxy mercury compounds. Anthraquinone did not react under similar conditions.

Although thiophene was reported to be considerably more reactive than benzene in some Friedel–Crafts reactions so that condensations could be carried out using benzene as the solvent,[10] benzene could not be used satisfactorily as a solvent for condensations with phthalic anhydride.

It has been reported that toluene reacts more readily with phthalic anhydride in the Friedel–Crafts reaction than does benzene.[11] This was not the case with either the 2-methylthiophene or the 3-methylthiophene. In both cases the lowest temperature at which a condensation occurred was considerably above the temperature at which thiophene condensed.

Experimental

***o*-(2-Thenoyl)-benzoic Acid by the Grignard Method.**—The condensation was carried out in a flask which had been thoroughly dried immediatly before use and was constantly swept with a slow stream of dry nitrogen during the condensation. Magnesium metal turnings (9 g., Grignard grade) and a crystal of iodine were agitated in anhydrous ether (400 cc.). A few cc. of a solution of 2-bromothiophene (42 g.) in ether (100 cc.) was added and the charge was heated until the reaction started. As soon as the reaction proceeded vigorously without requiring external heating the rest of the 2-bromothiophene solution was added during about one hour while the charge was kept at a strong reflux. Depending upon the size of the charge more or less external cooling was required to prevent the reaction from getting out of control. Refluxing was continued for about one hour after all of the 2-bromothiophene had been charged. Then the reaction mass was cooled to about 20°.

Phthalic anhydride (45 g.) was suspended in benzene (1000 cc.) at 40°, and vigorously agitated. The Grignard solution was added through a dropping funnel in about five minutes, allowing the temperature to rise to 56°. A white precipitate was formed instantly. Refluxing was continued for about 90 minutes, then cold water (750 cc.), and a few grams of magnesium oxide were added and the charge was agitated at room temperature overnight. Excess magnesium oxide was filtered off and the slightly alkaline water layer was separated from the benzene layer and was acidified with acetic acid. Crude *o*-(2-thenoyl)-benzoic acid (42 g., 60% yield) was precipitated, m.p. 141–142°. Crystallized from toluene (5 parts) it melted at 145° and was identical with the *o*-(2-thenoyl)-benzoic acid formed by the Friedel–Crafts method.

Anal. Calcd. for $C_{12}H_8O_3S$: S, 13.79. Found: S, 13.82.

***o*-(2-Thenoyl)-benzoic Acid by the Friedel–Crafts Method.**—A solution of anhydrous aluminum chloride (587 g.) and phthalic anhydride (296 g.) in dry nitrobenzene (1200 g.) was prepared at 50° and thiophene (168 g.) was added uniformly over a period of two hours while maintaining the reaction temperature at 40–45°. One hour later the reaction temperature was raised to 50–55° and held there one hour after which time the hydrochloric acid evolution had practically stopped. The dark red colored reaction mass was poured into cold water (11 liters) and the nitrobenzene layer was washed nearly acid free. The crude *o*-(2-thenoyl)-benzoic acid obtained after steam distilling off the nitrobenzene was washed acid free and dissolved at 90° in water (3 liters) containing an excess of sodium carbonate. The filtered solution was carefully acidified with hydrochloric acid; yield 345 g. of crude *o*-(2-thenoyl)-benzoic acid (74.4%). Upon crystallization from toluene (245 g. of keto acid in 1500 g. of toluene) it was obtained pure, m.p. 145° (yield 218 g., 66.2% from thiophene).

Anal. Calcd. for $C_{12}H_8O_3S$: S, 13.79; acid number, 241.5. Found: S, 13.81; acid number, 233.9.

By extraction with magnesium oxide a further quantity of *o*-(2-thenoyl)-benzoic acid was separated from the tarry residue of crystallization. The magnesium oxide and toluene insoluble residue was again dissolved in dilute sodium hydroxide and was precipitated with acetic acid as a dark brown product, m.p. about 250°. Based on the sulfur content of 21.34% it appeared to be a condensation product of phthalic anhydride with polymerized thiophene.

***o*-(2-Thenoyl)-benzoic acid methyl ester** was obtained when a solution of *o*-(2-thenoyl)-benzoic acid in absolute methanol was heated to 160° in a bomb. It was crystallized from benzene and petroleum ether, m.p. 63-64°.

Anal. Calcd. for $C_{13}H_{10}O_3S$: C, 63.4; H, 4.07; S, 13.0. Found: C, 63.26; H, 3.97; S, 12.96.

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(6) In analogy to anthraquinone for which the parent compound is anthracene we propose to call the diketo compound derived from thiophanthrene: thiophanthraquinone.

(7) H. E. Schroeder and V. Weinmayr, THIS JOURNAL, **74**, 4357 (1952).

(8) J. v. Braun and O. Bayer, *Ber.*, **58**, 2667 (1925).

(9) J. M. Tinker and V. Weinmayr, U. S. Patent 1,990,807; *C. A.*, **29**, 2179 (1935).

(10) G. Stadnikoff and I. Goldfarb, *Ber.*, **61**, 2341 (1928).

(11) O. Halla, *Monatsh.*, **32**, 638 (1911).

The substituted *o*-(2-thenoyl)-benzoic acids of Table I were obtained in a similar manner.

TABLE I

(2-Thenoyl)-benzoic acid	M.p., °C.	Yield, %	Reaction temp., °C.	Formula	Analyses, % Calcd. Sulfur	Analyses, % Found Sulfur
o-(5-Cl-	130[a]	61	75–80	$C_{12}H_7ClO_3S$	S 12.00	S 12.25
					Cl 13.32	Cl 13.15
o-(4-Me-	135[b]	78	79–85	$C_{13}H_{10}O_3S$	13.00	13.06
o-(5-Me-	133[b]	86	78–85	$C_{13}H_{10}O_3S$	13.00	13.16

[a] From high boiling (120°) petroleum ether. [b] From benzene. A mixed m.p. between the two *o*-(methyl-2-thenoyl)-benzoic acids showed a strong depression.

Triacetoxy Mercury-2-(2-thenoyl)-benzoic Acid.—*o*-(2-Thenoyl)-benzoic acid (10 g., 0.043 mole) and mercuric acetate (82 g., 0.26 mole) were heated for 12 hours in boiling glacial acetic acid (175 cc.). A precipitate was formed (8.7 g.) which was insoluble in dilute aqueous sodium carbonate or ammonia, and contained some metallic mercury. The acetic acid filtrate was diluted to 1500 cc. with water and a triacetoxy mercury-2-(2-thenoyl)-benzoic acid (20 g.) was obtained.

Anal. Calcd. for $C_{18}H_{14}O_9SHg_3$: Hg, 59.5; S, 3.17. Found: Hg, 59.1; S, 3.5.

Thiophanthraquinone.—A solution of anhydrous aluminum chloride (13.3 g.) and *o*-(2-thenoyl)-benzoic acid (10 g.) in nitrobenzene (65 cc.) was heated to 120° for 18 hours. After dilution with water and steam distillation to remove the nitrobenzene crude thiophanthraquinone (8.42 g., 91.6% yield), m.p. 220–228° was obtained. After distillation at atmospheric pressure and crystallization from chlorobenzene (36 cc.) it melted at 229–230°.

Anal. Calcd. for $C_{12}H_6O_2S$: S, 14.95. Found: S, 14.93.

The substituted thiophanthraquinones of Table II were obtained in a similar manner from the corresponding *o*-(-2-thenoyl)-benzoic acids.

TABLE II

Compound, thiophanthraquinone	M.p., °C.	Yield, %	Reaction Temp., °C.	Reaction Time, hours	Formula	Analyses, % Calculated Cl	Analyses, % Calculated S	Analyses, % Found Cl	Analyses, % Found S
2-Chloro-	179[a]	86	130	24	$C_{12}H_5ClO_2S$	14.3	12.88	14.33	12.94
3-Methyl-	180[a]	35	120	18	$C_{13}H_8O_2S$		14.04		13.95
2-Methyl-	250[b]	38	135	20	$C_{13}H_8O_2S$		14.04		14.00
5,8-Dichloro-	228[c]	20[d]	100	6	$C_{12}H_4Cl_2O_2S$	25.03	11.30	24.86	11.32
3,4,5,6-Tetrachloro-	203[c]	75	130	20	$C_{12}H_2Cl_4O_2S$	40.63		40.63	

[a] From high boiling (120°) petroleum ether. [b] From benzene and petroleum ether after vatting with alkaline sodium hydrosulfite. [c] From acetic acid. [d] The crude product was chromatographed on alumina.

Thiophanthraquinone from Thiophene without Isolation of the *o*-(2-Thenoyl)-benzoic Acid.—The condensation to *o*-(2-thenoyl)-benzoic acid was carried out as described above, using 460 g. of nitrobenzene, 208 g. of aluminum chloride, 104.7 g. of phthalic anhydride and 59.4 g. of thiophene mixed with 170 g. of nitrobenzene. When the condensation was complete at 55°, 1130 g. of nitrobenzene and 188 g. of aluminum chloride were added, the temperature was raised to 120° in four hours and held at 120–125° for about 18 hours. The reaction mass was then poured into water (4 liters) and ice (700 g.), containing 96% sulfuric acid (140 g.). The solvent layer was washed nearly acid-free and the nitrobenzene was removed with steam. The crude, crystalline thiophanthraquinone was filtered, heated to 40–45° in a solution of sodium hydroxide (125 g.) and sodium hydrosulfite (150 g.) in water (2800 g.) and precipitated from the clear red filtrate by blowing it with air or adding sodium *m*-nitrobenzenesulfonate (about 130 g.). Thiophanthraquinone (100 g.), m.p. 225–228°, was obtained (66% based on thiophene).

Thiophanthraquinone, Purification by Vatting with Sodium Sulfide.—Thiophanthraquinone (48 g.) was added to a solution of crystallized sodium sulfide (130 g.) and sodium hydroxide (4 g.) in water (2 liters). At 50° the reaction mass began to turn green and a deep green solution resulted at 90°. Upon oxidation with air pure thiophanthraquinone was obtained.

Thiophanthraquinone-2-carboxylic Acid from Thiophanthraquinone and Carbon Tetrachloride.—Thiophanthraquinone (125 g.), copper bronze (1 g.) and carbon tetrachloride (600 cc.) were heated in an autoclave to 200° for 10 hours. The charge was then cooled, the solvent distilled off and the residue refluxed in 4% aqueous sodium hydroxide (1000 cc.) for 24 hours. A brown, caustic-insoluble residue (125 g.) was filtered off. The dark brown filtrate was acidified, the precipitate was filtered, redissolved with magnesium oxide (8 g.) in water (4 liters) and precipitated again with hydrochloric acid. Thiophanthraquinone - 2 - carboxylic acid (6.7 g.), m.p. 280–282°, was obtained. After crystallization from chlorobenzene (1 g. in 125 cc.) it formed pale yellow needles, m.p. 293–294°. It was identical with the carboxylic acid obtained when 2-methylthiophanthraquinone was oxidized. It formed a deep red vat with alkaline sodium hydrosulfite.

Anal. Calcd. for $C_{13}H_6O_4S$: S, 12.4. Found: S, 12.24.

Thiophanthraquinone-2-carboxylic Acid from 2-Methylthiophanthraquinone.—2-Methylthiophanthraquinone (4.1 g.) was dissolved in boiling glacial acetic acid (50 cc.), a solution of chromic acid (12 g.) in 50% acetic acid (24 cc.) was added at the boil (108–112°), in one hour, and refluxing was continued four hours longer. The reaction mass was diluted with water (150 cc.), the precipitate was filtered and extracted with dilute sodium carbonate (300 cc.). Upon acidification crude thiophanthraquinone-2-carboxylic acid (0.5 g.) was obtained m.p. 288–290°, crystallized from chlorobenzene, m.p. 293–294°. It was identical with the compound obtained from thiophanthraquinone and carbon tetrachloride.

Triacetoxy Mercury - thiophanthraquinone.—Thiophanthraquinone (5 g.) and mercuric acetate (30 g.) were heated in boiling glacial acetic acid (150 cc.) for 12 hours. At 80° a clear solution was formed but shortly after the temperature had reached 120° a crystalline product began to precipitate. The pale yellow compound was filtered, slurried in acetic acid and filtered again, washed with water and dried at 95°. The compound thus obtained (20 g.) analyzed as a triacetoxy mercury-thiophanthraquinone (no m.p.). Anthraquinone did not give a mercury compound under identical conditions.

Anal. Calcd. for $C_{18}H_{12}O_8SHg_3$: S, 3.23; Hg, 60.8. Found: S, 3.1; Hg, 61.1.

3-Nitro-2-(2-thenoyl)-benzoic Acid and 6-Nitro-2-(2-thenoyl)-benzoic Acid.—The Grignard reagent was prepared from 2-bromothiophene (84 g.), magnesium metal (14 g.) and ether (350 g.); it was poured at 40–50° into a suspension of 3-nitrophthalic anhydride (97 g.) in benzene (1500 cc.), and the reaction mass was agitated at 50° for two hours. Crude, crystalline 3-nitro-2-(2-thenoyl)-benzoic acid (42 g., 30.6%), m.p. 212–213°, was obtained when the magnesium salt solution of the mixed keto acids was acidified with acetic acid. Crystallized from nitrobenzene (1 g. in 4 cc.) it melted at 216–217°. The solubility in chlorobenzene was low, requiring about 600 cc. of boiling solvent per g. of product.

Anal. Calcd. for $C_{12}H_7NO_5S$: N, 5.05; S, 11.55. Found: N, 5.14; S, 11.73.

The acetic acid filtrate was made strongly acid with hydrochloric acid and the crude 6-nitro-2-(2-thenoyl)-benzoic acid (27 g., 19.5% yield), m.p. 164–166°, was precipitated. Crystallized from chlorobenzene (1 g. in 15 cc.) it melted at 170°.

Anal. Calcd. for $C_{12}H_7NO_5S$: N, 5.05; S, 11.55. Found: N, 5.10; S, 11.63.

When both keto acids were precipitated together from their magnesium salt solutions with hydrochloric acid the mixture melted from 180–210°. The isomers could be separated by crystallizations, but not nearly as well as by first fractionally precipitating with acetic and hydrochloric acid.

TABLE III

R-Phthalic anhydride used, R	R-2-(2-Thenoyl)-benzoic acid obtained R	M.p., °C.	Yield, %	Formula	Analyses, % Calculated Cl	N	S	Found Cl	N	S
4-Nitro	5-Nitro[a]	190[b]	22	$C_{12}H_7NO_5S$		5.05	11.55		5.16	11.34
	4-Nitro[c]	147[d]	33	$C_{12}H_7NO_5S$		5.05	11.55		4.95	11.44
3-Chloro	3-Chloro[a]	239[d]	30	$C_{12}H_7ClO_3S$	13.32		12.01	13.50		11.94
	6-Chloro[e]	129[d]	35	$C_{12}H_7ClO_3S$	13.32		12.01	13.10		11.99
4-Chloro	4-Chloro[a]	226[b]	47	$C_{12}H_7ClO_3S$	13.32		12.01	13.06		12.00
	5-Chloro[c]	155[d]	14	$C_{12}H_7ClO_3S$	13.32		12.01	13.21		11.95
4-Bromo	x-Bromo[a]	226[a]	42	$C_{12}H_7BrO_3S$	25.72[h]		10.08	25.98[h]		10.20
	y-Bromo[c]	146[c]	8	$C_{12}H_7BrO_3S$	25.72[h]			25.90[h]		
3,4-Dichloro	x,x-Dichloro[f]	203[d]	17	$C_{12}H_6Cl_2O_3S$	23.58		10.63	23.70		10.60
	y,y-Dichloro[c]	167[d]	41	$C_{12}H_6Cl_2O_3S$	23.58		10.63	23.70		10.70
3,6-Dichloro	3,6-Dichloro[a]	146[g]	75	$C_{12}H_6Cl_2O_3S$	23.58		10.63	23.80		10.53
3,4,5,6-Tetrachloro	3,4,5,6-Tetrachloro[f]	207[d]	86	$C_{12}H_4Cl_4O_3S$	38.4		8.65	38.7		8.70

[a] By acidifying with acetic acid. This isomer was also obtained from thiophene, 4-nitrophthalic anhydride and aluminum chloride at 60°. [b] From nitrobenzene. [c] From the acetic acid filtrate with hydrochloric acid. [d] From chlorobenzene. [e] From toluene and high boiling (120°) petroleum ether. [f] The magnesium salt was poorly soluble in water. [g] From benzene. [h] Bromine.

The substituted *o*-(2-thenoyl)-benzoic acids of Table III were obtained in a similar manner from the correspondingly substituted phthalic anhydrides and 2-bromothiophene.

Decarboxylation of the Nitro-2-(2-thenoyl)-benzoic Acids.—3-Nitro-2-(2-thenoyl)-benzoic acid (3 g.), m.p. 217°, copper oxide (3 g.) and copper chromite (3 g.) were heated to the boil in freshly distilled quinoline (20 g.) until the gas evolution had stopped (20 minutes). The reaction mass was filtered and poured into 15% hydrochloric acid (200 cc.). *o*-Nitrophenyl-(2-thienyl) ketone (2.87 g.), m.p. 94–95°, precipitated. Upon crystallization from methanol it melted at 99–99.5°.

Anal. Calcd. for $C_{11}H_7NO_3S$: N, 6.01; S, 13.73. Found: N, 5.93; S, 13.42.

The same ketone was obtained in a lower yield when 3-nitro-2-(2-thenoyl)-benzoic acid was mixed with calcium carbonate and copper powder and dry distilled.

m-Nitrophenyl-(2-thienyl) ketone, m.p. 123°, was obtained when 6-nitro-2-(2-thenoyl)-benzoic acid, m.p. 171°, was decarboxylated. *p*-Nitrophenyl-(2-thienyl) ketone, m.p. 171°, resulted upon the decarboxylation of 5-nitro-2-(2-thenoyl)-benzoic acid, m.p. 190°. 4-Nitro-2-(2-thenoyl)-benzoic acid, m.p. 150°, was decarboxylated to *m*-nitrophenyl-(2-thienyl) ketone.

2-Carbomethoxy-3-nitrobenzoic Acid.—3-Nitrophthalic anhydride (300 g.) was refluxed in absolute methanol (2500 g.) for 16 hours. Thereafter methanol (2000 g.) was distilled off while water (1000 g.) was added simultaneously. The crystalline slurry was cooled to 20°, the precipitate was filtered, washed with water (400 cc.) and dried at 75°. 2-Carbomethoxy-3-nitrobenzoic acid, m.p. 152–156°, was obtained in an 83% yield.[12]

3-Nitro-2-(2-thenoyl)-benzoic Acid from 2-Carbomethoxy-3-nitrobenzoic Acid.—2-Carbomethoxy-3-nitrobenzoic acid (113 g.) suspended in benzene was converted to 2-carbomethoxy-3-nitrobenzoyl chloride with phosphorus pentachloride (115 g.) at 50–65°. The resulting solution was cooled to below 10° and stannic chloride (149 g.) was added without exceeding 15°. A solution of thiophene (48 g.) in dry benzene (180 g.) was added at 10–15° in one hour. Thirty minutes later the reaction mass was poured into ice and steamed free of benzene and unreacted thiophene. The crude 3-nitro-2-(2-thenoyl)-benzoic acid methyl ester which separated in pellets upon cooling was filtered and then hydrolyzed at room temperature by slurrying it in a solution of sodium hydroxide (50 g.) in 50% ethanol (1000 cc.). The alcoholic solution was diluted with water to 3000 cc., clarified, and acidified.

3-Nitro-2-(2-thenoyl)-benzoic acid (115 g., 83% of theory) was obtained melting at 217–218°.

Anal. Calcd. for $C_{12}H_7NO_5S$: N, 5.05; S, 11.55. Found: N, 5.12; S, 11.41.

Upon decarboxylation *o*-nitrophenyl-(2-thienyl) ketone, m.p. 99°, was obtained.

6-Nitro-2-(2-thenoyl)-benzoic Acid from 2-Carbomethoxy-3-nitrobenzoyl Chloride (by the Grignard Method).—A Grignard solution was prepared from 2-bromothiophene (16 g.) and magnesium (2.7 g.) in ether (100 cc.). This solution was poured at 45–50° into a solution of 2-carbomethoxy-3-nitrobenzoyl chloride (29 g.) in benzene (300 cc.). The charge was agitated at 50° for one hour and then decomposed with water. The ether was removed with steam, and the tarry condensation product was filtered off. When the filtrate was acidified some 2-carbomethoxy-3-nitrobenzoic acid (7 g.) was recovered (m.p. 151°, no mixed m.p. depression).

The tarry condensation product was hydrolyzed with alcoholic caustic at room temperature. The solution was clarified and acidified with hydrochloric acid (acetic acid formed no precipitate). 6-Nitro-2-(2-thenoyl)-benzoic acid (7 g.) was obtained. Upon decarboxylation it gave *m*-nitrophenyl-(2-thienyl) ketone, m.p. 123°.

3-Amino-2-(2-thenoyl)-benzoic Acid.—3-Nitro-2-(2-thenoyl)-benzoic acid (14 g.), reduced nickel catalyst (4 g.) and thiophene free benzene (300 cc.) were heated in a shaker bomb to 100° under a pressure of 500–600 lb. of hydrogen until the hydrogen absorption had stopped. The catalyst was removed by filtration and the filtrate was evaporated to dryness on the steam-bath (yield 14.5 g.). The product thus obtained was extracted with chlorobenzene. Crude 3-amino-2-(2-thenoyl)-benzoic acid (8.18 g.) was obtained, m.p. 179–180°. Crystallizations from chlorobenzene (1 g. in 25 cc.) did not further change the m.p. The compound was soluble in dilute hydrochloric acid and dilute caustic.

Anal. Calcd. for $C_{12}H_9NO_3S$: N, 5.67; S, 12.96. Found: N, 5.64; S, 12.80.

The same compound was obtained when the 3-nitro-2-(2-thenoyl)-benzoic acid was reduced with ferrous sulfate as follows: Ammonia (320 cc. of 28% strength) was added to a boiling solution of ferrous sulfate crystals (200 g.) in water (1200 cc.). 3-Nitro-2-(2-thenoyl)-benzoic acid (20 g.) was dissolved in 28% ammonia (200 cc.) and this solution was added to the ferrous hydroxide slurry at 85–90° in 15 minutes. After boiling for a few minutes the charge was filtered and the filtrate was evaporated to dryness on a steam-bath (yield 118 g.). This crude product was slurried in ethanol (1000 cc.) and filtered from the inorganic salts. If evaporated to dryness a sticky material was obtained which changed to a crystalline product only very slowly. However, if the alcoholic solution was concentrated to about 200 cc. and then diluted with an equal part of water and again concentrated to 200 cc. a crystalline 3-amino-2-(2-thenoyl)-benzoic acid (8.3 g., 46.6% yield) was obtained at once, m.p. 177–180°.

The same compound was also obtained when the 3-nitro-2-(2-thenoyl)-benzoic acid was reduced in water with iron filings at 75°.

5-Nitro-2-(2-thenoyl)-benzoic Acid from 2-Carbomethoxy-5-nitrobenzoic Acid.—A solution of 2-carbomethoxy-5-nitrobenzoic acid (22.5 g.)[13] in thionyl chloride (30 cc.) was refluxed for 30 minutes, then the excess thionyl chloride was distilled off under vacuum. The residual 2-carbomethoxy-

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[12] A. McKenzie, *J. Chem. Soc.*, **79**, 1140 (1901).

[13] R. Wegscheider, *Monatsh.*, **21**, 805 (1900).

5-nitrobenzoyl chloride was dissolved in benzene (200 cc.), and stannic chloride (29 g.) was added at 0–5° in one hour. The temperature of the charge was raised to 20° in four hours and agitation at 20–25° was continued for 18 hours. The reaction mass was then poured into dilute hydrochloric acid and steam distilled to remove the benzene. The filtered and washed solid residue was stirred at 20–25° for 24 hours in a solution of sodium hydroxide (5 g.) in 33% ethanol (100 cc.). The insoluble residue was filtered off and the crude 5-nitro-2-(2-thenoyl)-benzoic acid was precipitated from the filtrate with hydrochloric acid (17 g., yield 61.3%), m.p. about 170°. When crystallized from chlorobenzene it melted at 189–190° and was identical with the 5-nitro-2-(2-thenoyl)-benzoic acid obtained by the Grignard reaction.

Anal. Calcd. for $C_{12}H_7NO_5S$: N, 5.05; S, 11.55. Found: N, 5.27; S, 11.34.

4-Amino-2-(2-thenoyl)-benzoic Acid.—A solution of 4-nitro-*o*-(2-thenoyl)-benzoic acid (14 g.) in thiophene-free benzene (200 cc.) was hydrogenated at 100° and 600 lb. of hydrogen pressure, using reduced nickel as the catalyst. The crude product obtained upon evaporation of the filtered reduction mass was extracted with chlorobenzene and crystallized from the same solvent. 4-Amino-2-(2-thenoyl)-benzoic acid (2.5 g.) was obtained, m.p. 218–219°.

Anal. Calcd. for $C_{12}H_9NO_3S$: N, 5.67; S, 12.95. Found: N, 5.64; S, 12.71.

3-Chloro-2-(2-thenoyl)-benzoic Acid from 3-Amino-2-(2-thenoyl)-benzoic Acid.—3-Amino-2-(2-thenoyl)-benzoic acid (2.8 g.) was dissolved in water (10 cc.) and the minimum amount of sodium hydroxide necessary to dissolve it was added. The solution was poured on ice (20 g.) and concd. hydrochloric acid (20 cc.), and was diazotized with 21 cc. of a 0.54 *N* sodium nitrite solution. The diazotized mass formed a thick white crystalline slurry. It was poured into a solution of cuprous chloride (3 g.) in concd. hydrochloric acid (25 cc.) at 25–29°. The flocculent precipitate changed to a crystalline form when the charge was heated to 100°. It was filtered, washed, dissolved in dilute sodium hydroxide, clarified and reprecipitated with hydrochloric acid. 3-Chloro-2-(2-thenoyl)-benzoic acid (2.4 g., 80% yield) was obtained, m.p. 236–238°. Crystallized from chlorobenzene it melted at 238°. It was identical with the 3-chloro-2-(2-thenoyl)-benzoic acid obtained by the Grignard reaction.

Anal. Calcd. for $C_{12}H_7ClO_3S$: Cl, 13.23. Found: Cl, 13.21.

It was observed that it was necessary to carry out the reaction in highly concentrated acid and in small dilutions. Otherwise low melting products were obtained from which the pure 3-chloro-2-(2-thenoyl)-benzoic acid could be isolated only with difficulty.

4-Chloro-2-(2-thenoyl)-benzoic Acid from 4-Amino-2-(2-thenoyl)-benzoic Acid.—4-Amino-2-(2-thenoyl)-benzoic acid (1 g.) was dissolved in dilute sodium hydroxide (5 cc.) and poured into concd. hydrochloric acid (10 cc.) and ice (10 g.). It was diazotized with 7.5 cc. of 0.54 *N* sodium nitrite solution (the diazonium salt remained in solution) and was then poured into a solution of cuprous chloride (1 g.) in concd. hydrochloric acid (10 cc.) at 20–30° in about 30 minutes. Heating to 100° changed the amorphous precipitate to a crystalline form. 4-Chloro-2-(2-thenoyl)-benzoic acid (1 g., 93% yield), m.p. 215–220° was obtained. Crystallized from chlorobenzene it melted at 225–226° and was identical with the 4-chloro-2-(2-thenoyl)-benzoic acid obtained by the Grignard reaction.

WILMINGTON, DELAWARE

[CONTRIBUTION NO. 110 FROM JACKSON LABORATORY, E. I. DU PONT DE NEMOURS AND CO.]

The Synthesis of Thiophanthraquinones from Thenoyl and Thenylbenzoic Acids

BY H. E. SCHROEDER AND V. WEINMAYR

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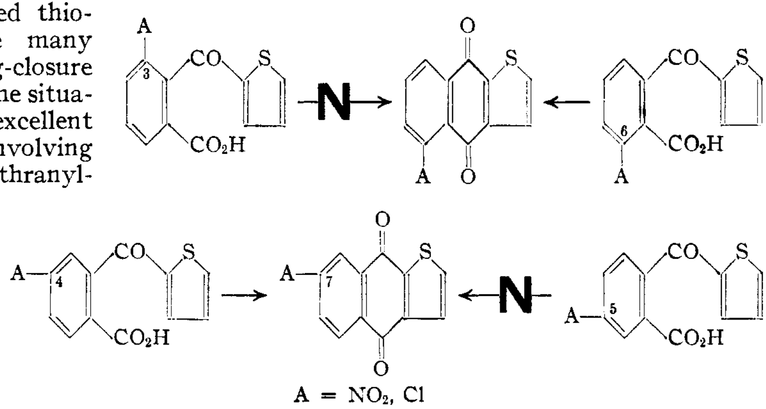
The structures of the thiophanthraquinones substituted in the benzene ring by amino, chloro and nitro groups have been established beyond doubt. Ring-closure of the chloro- and nitro-thenoylbenzoic acids proceeds normally when the substituent is meta to the thenoyl group but with rearrangement when in any ortho or para position. Conversely the amines cyclize normally when ortho or para but rearrange when meta to the thenoyl group.

The normal procedures for ring-closure of benzene substituted 2-(2-thenoyl)-benzoic acids,[1] did not give expected isomeric substituted thiophanthraquinones. Since there are many known cases of rearrangement on ring-closure of substituted *benzoyl*benzoic acids,[2,3] the situation has been clarified by use of the excellent method of Fieser and Hershberg, involving cyclization of benzylbenzoic acids to anthranylacetates,[4] followed by oxidation to the quinones. Synthetic routes have been developed for the preparation of the pure isomers, particularly those which are inaccessible by ring-closure of 2-(2-thenoyl)-benzoic acids because of rearrangements, *i.e.*, 8- and 6-chlorothiophanthraquinones, and 6- and 5-aminothiophanthraquinones. These have shown that when nitro or chloro groups are in a meta position with respect to the thenoyl group the thenoyl benzoic acids cyclize normally but when either ortho or para they cyclize only with rearrangement



Conversely, in the case of the aminothenoylbenzoic acids, the amino derivatives ortho and para to the thenoyl group cyclize normally while the meta derivatives rearrange as shown.

These rearrangements are independent of the condensing agent, *e.g.*, sulfuric acid, hydrogen fluoride, aluminum chloride, etc. yield the same isomer.

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[1] V. Weinmayr, THIS JOURNAL, **74**, 4353 (1952).

[2] M. Hazaski, *J. Chem. Soc.*, 1520, 1524 (1930).

[3] R. B. Sandin and L. F. Fieser, THIS JOURNAL, **62**, 3098 (1940).

[4] L. F. Fieser and E. B. Hershberg, *ibid.*, **59**, 1028 (1937); **60**, 1893 (1938).