[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Nitrothienols and Halogenated Nitrothiophenes

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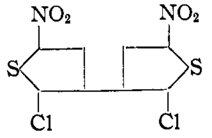
Experiments are reported describing the nitration of 2-chlorothiophene, 5-chloro-2-acetothienone, methyl 5-chloro-2-thenoate and 5-chloro-2-thiophenesulfonyl chloride. The activating effect of the nitro group on the nuclear halogen atom was demonstrated by reactions of hydrolysis, alcoholysis and ammonolysis. 3,5-Dinitro-2-chlorothiophene is much more reactive than 2,4-dinitrochlorobenzene. 3,5-Dinitrothienol and 3-nitro-5-acetyl-2-thienol were prepared by treatment of the corresponding chlorides with sodium formate. They were colorless, unstable solids giving colored, stable sodium salts. Ionization constants were of the order of 10^{-2} and 10^{-3}. Diazomethane converted these thienols into their methyl ethers. Several amines and ethers related to these nitrothiophenes were synthesized.

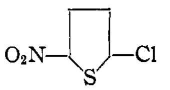
In an earlier communication[2] we discussed the chemistry of 2-thienol, pointing out the inapplicability of most methods of synthesis which are general for phenols. One of the seemingly inapplicable methods was hydrolysis of chlorothiophene. In contrast, in the present work, we expected that nitrothienols could be prepared from nitrochlorothiophenes by metathetic reactions because of the labilizing effect of the nitro group on the halogen. The present paper reports experiments which were carried out in the development of this idea.

Nitration of 2-chlorothiophene with a mixture of nitric acid and acetic anhydride yielded 5-nitro-2-chlorothiophene (I). This compound melted at room temperature and was quite soluble. A small amount of insoluble, high-melting, yellow by-product was isolated. Analysis was satisfactory for a bis-(nitrochlorothienyl), probably bis-(5-nitro-2-chloro-3-thienyl)

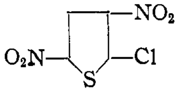


This was insoluble even in benzene, thus preventing the benzene cryoscopic method for molecular weight determination.

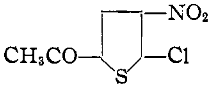
Continued nitration of I with nitric and sulfuric acids gave rise to 3,5-dinitro-2-chlorothiophene (II). The second nitrating mixture was effective also in the conversion of 5-chloro-2-acetothienone and methyl 5-chloro-2-thenoate into 4-nitro-5-chloro-2-acetothienone (III) and methyl 4-nitro-5-chloro-2-thenoate (IV), respectively. Fuming nitric acid caused the nitration of 5-chloro-2-thiophenesulfonyl chloride. The 4-nitro derivative (V) thus produced was readily hydrolyzed by superheated steam in good yields into 3-nitro-2-chlorothiophene (VI). VI was prepared also from IV by hydrolysis and decarboxylation, but with greater difficulty than from V. Conversion of VI into II by nitration proved its structure.



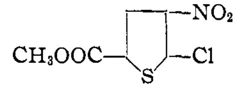
I



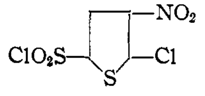
II



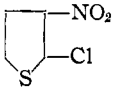
III



IV



V



VI

These compounds are structurally related to 2,4-dinitrochlorobenzene (VII), which is known to possess a reactive chlorine atom. Hence the above compounds were treated with methanolic potassium hydroxide at 27° for varying lengths of time to determine the relative lability of halogen as judged by formation of chloride ion. Results are shown in Table I. Also included are 3-nitro-2,5-dichlorothiophene (VIII), 3,4-dinitro-2,5-dichlorothiophene (IX) and 2-nitro-3-bromothiophene (X), all previously known compounds.

TABLE I

ALCOHOLYSIS OF THE NITRO HALO COMPOUNDS

Compound	Base	Duration, min.	Cl or Br removal, %
VII	A	15	23
I	B	480	66
II	A	1	100
III	A	15	83
IV	A	15	61
VI	B	480	34
VIII[b]	A	15	18
VIII	B	480	100[a]
IX	A	1	100[a]
X	B	480	28

A, 3 moles excess of 0.013 *N* base. B, 4 moles excess of 0.067 *N* base. [a] Basis of both Cl atoms. [b] Furnished by The Texas Company, b.p. 90° (2 mm.).

Since dinitrochlorothiophene (II) was much more reactive than dinitrochlorobenzene (VII), one must conclude that the lability of halogen in the thiophene series is much greater than in the benzene series. Among individual members, the 5-nitro-2-chlorothiophene (I) is somewhat more reactive than the 3-nitro-2-chloro isomer (VI). This result compares with the observation[3] that *p*-nitrochlorobenzene undergoes hydrolysis or alcoholysis appreciably faster than the ortho isomer. It is interesting to note that X is about as reactive as VI, showing that an adjacent nitro group activates the halogen atom whether it is on the 2- or 3-position.

In reaction with piperidine, VI is much more reactive than I, thus reversing the order shown

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[1] The Texas Company Fellow, 1946–1948.

[2] C. D. Hurd and K. L. Kreuz, THIS JOURNAL, **72**, 5543 (1950).

[3] W. Davies and E. S. Wood, *J. Chem. Soc.*, 1122 (1928).

toward alcoholic potassium hydroxide. Again this follows the behavior found in the benzene series, wherein *o*-nitrochlorobenzene is much more reactive[4] toward piperidine than the para isomer.

The Thienols.—One might surmise from the above reactivities that the introduction of the hydroxy group into the thiophene ring should be a simple matter. It became evident at once, however, that the conventional approach was inapplicable, namely, alkaline hydrolysis. In aqueous solvents over a considerable range of temperature and alkali concentration the products obtained on acidification were not the desired thienols but were resinous materials, accompanied often by hydrogen sulfide and sometimes by oxides of nitrogen.

Hydrolysis in bicarbonate solution occurred at a convenient rate only with II, the most reactive halide. The sodium 3,5-dinitrothienoxide thus obtained could be changed into dinitrothienol in low yield, together with resinous material.

Satisfactory indirect hydrolysis of II and III was accomplished by use of sodium formate in refluxing methanol, followed by acidification. These steps apparently took place (let TCl represent II)

$$\mathrm{TCl} \xrightarrow{\mathrm{HCOONa}} \mathrm{TOCHO} \xrightarrow[\mathrm{HCOONa}]{\mathrm{CH_3OH}}$$

$$\mathrm{HCOOCH_3} + \mathrm{TONa} \xrightarrow{\mathrm{HCl}} \mathrm{TOH}$$

The process was clean-cut and free from side reactions.

The less reactive halides could not be hydrolyzed satisfactorily in this manner. With VI, halogen removal was very slow; extended refluxing with an excess of sodium formate yielded the methyl ether of the thienol. With IX, the initial step (formation of 2 Cl^-) proceeded almost as rapidly as with II, but the products were resinous.

The thienols which were obtained were colorless crystalline substances, characterized by their instability and high acidity. They deteriorated with evolution of nitrogen oxides and formation of dark resins, but could be stored at −20° for a day.

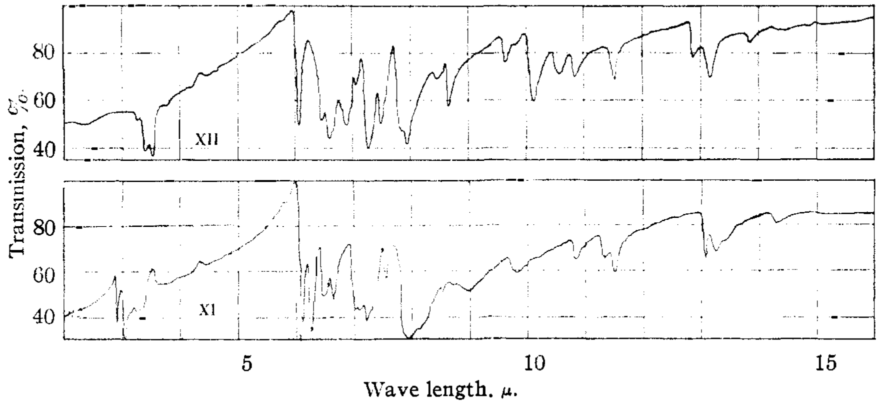
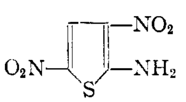


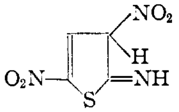
Fig. 1.—Infrared absorption spectra of XI and XII.

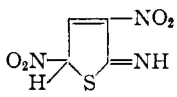
The nitrothienols dissolved easily in ether or water to yield fairly stable, intensely yellow solutions. Like picric acid, small amounts of these compounds produced intense yellow stains on the skin. The sodium salt of II was red, whereas that of III was yellow, and both were stable at 100°. The ionization constants of II and III were 3 × 10^{-2} and 5 × 10^{-3}, respectively. Both II and III reacted readily with diazomethane to yield the corresponding methyl ethers.

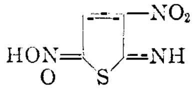
Good yields of the methyl or ethyl ethers from III and VI were obtained by use of alcoholic potassium hydroxide, but to obtain ethers from II it was expedient to operate under conditions which allowed only partial conversion of the reactant. The phenyl ethers from all three were readily prepared by reaction with solid sodium phenoxide. These ethers were colorless solids, melting without decomposition.

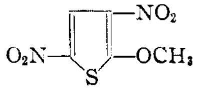
Amino derivatives in the thiophene series, while not unknown, are not numerous. These chlorides (II, III), by their reactivity toward ammonia and amines, provided an opportunity to synthesize several new substituted thienylamines. These were yellow crystalline compounds which gave deeply colored solutions even on high dilution. Sharp color changes were noticed on changing the *p*H of these solutions, showing possible utility of these compounds as indicators.


XI


XIa


XIb


XIc


XII

The fine structure of these amines is still an open question, but it is reasonable to consider keto as well as enol forms, just as with thienol.[2] Tautomeric forms for dinitrothienylamine (XI) would include XIa, b, c. The *aci*-nitro form, XIc, should react with bases and indeed these nitro amines are soluble in sodium hydroxide solution.

To secure additional evidence on this point, infrared and ultraviolet absorption spectra were obtained on the amine XI and the analogous ether XII, which is incapable of tautomerism. For the infrared determinations the solid sample was mulled in Nujol and was run *versus* Nujol. A sodium chloride prism was used in the infrared spectrophotometer. The doublet in the region of 3μ (Fig. 1) might be assigned to the $-NH_2$ group, since aniline shows bands at 2.90, 2.97μ. The peak at 6.28μ might be assigned to the C=N group in view of the fact that structures containing the S—C=N

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(4) A. Brewin and E. E. Turner, *J. Chem. Soc.*, 332 (1928).

sequence of atoms have been reported[5] to absorb in the region 6.0–6.3μ.

The ultraviolet spectrum of XII shows two peaks at 246 and 300 mμ. The analogous curve for XI shows these two peaks moved to regions of considerably longer wavelengths, 332 and 376 mμ, respectively. This result would be expected if XIc was present to any considerable extent, because of its extended conjugate unsaturation. The spectral evidence is not conclusive but does lend support to the contention that both keto and enol forms of the amine are present.

Experimental

2-Chlorothiophene, b.p. 126–127°, and 2,5-dichlorothiophene, b.p. 161–162°, were generously supplied by The Texas Company. Analyses were performed by J. Anderson, M. Ledyard, P. Craig and N. Mold.

2-Chloro-5-nitrothiophene.—To a protected, chilled (to −10°), stirred mixture of 37 g. of 2-chlorothiophene and 100 ml. of acetic anhydride was added dropwise a mixture of 50 g. of nitric acid (d. 1.50) and 100 ml. of acetic anhydride. The mixture was maintained at −10° for 15 hours, then was poured on ice and water and kept at −10° for two days.

The solid product was taken up in petroleum hexane, the solution filtered from 1 g. of yellow, insoluble crystals (m.p. 211–213°) and evaporated to incipient crystallization; yield 34 g. (67%), of long colorless needles, m.p. 5–15°. Two crystallizations from hexane yielded crystals melting at 25°; b.p. 85–90° (5 mm.). This product possessed a sweet aromatic odor.

Anal. Calcd. for $C_4H_2ClNO_2S$: N, 8.56. Found: N, 7.96.

Bis-(5-nitro-2-chloro-3-thienyl).—The crystals of m.p. 211–213° were insoluble not only in hexane but also in cold benzene.

Anal. Calcd. for $C_8H_2Cl_2N_2O_4S_2$: Cl, 21.8; N, 8.61; S, 19.7. Found: Cl, 21.6, 22.1; N, 8.46; S, 19.5, 19.7.

2-Chloro-3,5-dinitrothiophene.—Twenty-nine grams of 2-chloro-5-nitrothiophene (m.p. 5–15°) was added with stirring during 30 minutes to a mixture of 150 g. each of nitric acid (d. 1.50) and sulfuric acid (d. 1.84) at 0–5°. A heavy yellow slurry developed. After ten minutes more stirring the mixture was processed by pouring on ice, separating the yellow solid and crystallizing it from methanol. The glistening leaflets obtained were colorless to yellow, m.p. 121–122°; yield 30 g. (81%).

Anal. Calcd. for $C_4HClN_2O_4S$: N, 13.4. Found: N, 13.1.

2-Chloro-2-acetothienone.—This compound has been synthesized[6] from 2-chlorothiophene, acetyl chloride and aluminum chloride. We confirmed this synthesis. Also we demonstrated that the ketone could be prepared readily by diluting the reagents in 2–3 vol. of benzene and substituting stannic chloride for the aluminum chloride.

4-Nitro-5-chloro-2-acetothienone.—To 48 g. of the chloroacetothienone was added the nitric–sulfuric mixture (26.5 g. of nitric, 30 ml. of sulfuric) at 0–5° during 30 minutes. The mixture was poured into ice and the resulting solid (55 g.) was separated, washed with water and crystallized from ethanol; m.p. 85–87°.

Anal. Calcd. for $C_6H_4ClNO_3S$: N, 6.81. Found: N, 6.99.

Methyl 4-Nitro-5-chloro-2-thenoate.—5-Chloro-2-thenoic acid of m.p. 140° has been made[5] by the hypochlorite oxidation of 5-chloro-2-acetothienone. The same acid, of m.p. 146–147°, was prepared[7] by chlorination of 2-thenoic acid. We prepared the acid in 91% yield by the first method. Its melting point was 151–152° after crystallization from aqueous alcohol. The acid was esterified with methanol to form the methyl ester, b.p. 95–97° (7 mm.), m.p. 16.5–18°.

To a solution of 18 g. of methyl 5-chloro-2-thenoate in 60 ml. of sulfuric acid (d. 1.84) maintained at 0–5° was added dropwise with stirring 7.7 g. of nitric acid (d. 1.42) in 10 ml. of sulfuric acid. The mixture was poured on ice and the pink solid product was decolorized in hot methanol with Norit, then was crystallized from hexane; m.p. 83–84°; yield 16 g.

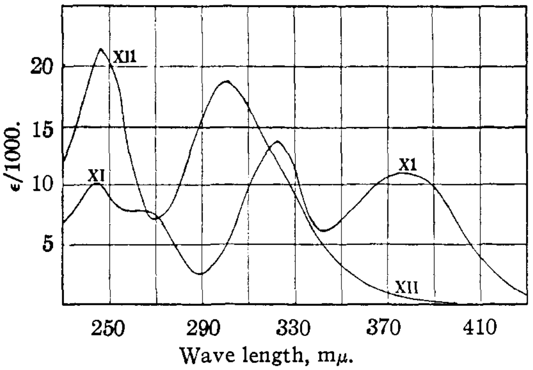

Fig. 2.—Ultraviolet absorption spectra of XI and XII.

Anal. Calcd. for $C_6H_4ClNO_4S$: N, 6.33. Found: N, 6.30.

4-Nitro-5-chloro-2-thenoic Acid.—A mixture of 8 g. of the above ester, 80 g. of water and 40 ml. of sulfuric acid was refluxed for four hours. An odor of hydrogen sulfide was apparent. Some oily ester phase remained. The hot clear solution was decanted into ice-water and unreacted ester was retreated as above. There was obtained 7.6 g. of colorless solid. It was recrystallized first from water, then from benzene; m.p. 156.5–157.5°.

Anal. Calcd. for $C_5H_4ClNO_4S$: neut. equiv., 208. Found: neut. equiv., 208.

4-Nitro-5-chloro-2-thiophenesulfonyl Chloride.—5-Chloro-2-thiophenesulfonyl chloride, m.p. 26–28°, was prepared by the method of Steinkopf and Köhler.[8] Twenty grams of it was added in small portions with swirling to 80 ml. of nitric acid (d. 1.50), the temperature being maintained at 30°. The resulting solution was kept at 40–45° for 2 hours, then was poured on ice. The solid which separated (21.7 g.) appeared as flat, stocky needles after recrystallization from hexane. The first crop (19.5 g., m.p. 51.5–52.5°) was not changed by further recrystallization. The second crop of 1.8 g. melted at 48–52°.

Anal. Calcd. for $C_4HCl_2NO_4S_2$: N, 5.34. Found: N, 5.23.

2-Chloro-3-nitrothiophene. First Method.—4-Nitro-5-chloro-2-thenoic acid (0.88 g.) was refluxed with 6 g. of mercuric oxide and 50 ml. of acetic acid for 12 hours. The product was diluted with two volumes of ice-water and the precipitated colorless mercury derivative was collected; weight 2.1 g. This solid was added to 50 ml. of dilute (1:5) hydrochloric acid and the contents of the flask were steam distilled. The solid product was taken up in ether and recrystallized from hexane; the colorless needles, weight 0.35 g., melted at 49.5–50.5°. The odor of the pure product was faint, reminiscent of nitrobenzene. The compound showed no change on storing at room temperature.

Anal. Calcd. for $C_4H_2ClNO_2S$: N, 8.50. Found: N, 8.31.

Second Method.—Refluxing 19.5 g. of 4-nitro-5-chloro-2-thiophenesulfonyl chloride for 2 hours with 75 g. of water resulted in a yellow solution of the sulfonic acid. This was dropped slowly into a flask containing boiling (150–160°) dilute sulfuric acid through which a current of steam was passing. The solid condensate (12.3 g.) was taken up in ether, then was crystallized from petroleum hexane; yield 10.6 g., m.p. 49.4–50.5°. A mixed melting point with that of the first method showed no depression.

Nitration of a 0.25-g. sample with nitric and sulfuric acids at 5° gave rise to 0.23 g. of 2-chloro-3,5-dinitrothiophene, m.p. 121–122°.

3-Bromothiophene.—The procedure described below is modified somewhat from Steinkopf's directions.[9] His yield

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[5] H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl, "Infrared Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, N. Y., 1949, p. 210.

[6] L. Gattermann and M. Roemer, *Ber.*, **19**, 688 (1886).

[7] W. Steinkopf, H. Jacob and H. Penz, *Ann.*, **512**, 136 (1934).

[8] W. Steinkopf and W. Köhler, *ibid.*, **532**, 250 (1937).

[9] W. Steinkopf, *ibid.*, **543**, 128 (1940); W. Steinkopf, "Die Chemie des Thiophens," T. Steinkopff, Dresden, 1941, p. 51.

was 56%, $n^{20}\text{D}$ 1.5861, whereas ours was 78%, $n^{20}\text{D}$ 1.5902.

2,3-Dibromothiophene, b.p. 99–100° (20 mm.), was prepared[8] from 4,5-dibromo-2-thenoic acid. A Grignard solution was prepared by adding to 26.2 g. of magnesium a solution of 81 g. of 2,3-dibromothiophene and 81 g. of ethyl bromide in 500 ml. of ether. Reaction was initiated with a crystal of iodine. Addition was completed in 45 minutes. Refluxing was maintained for 1.5–2 hours. After hydrolysis with ice and dilute hydrochloric acid (hydrogen sulfide detected), the ether was removed and the residue was steam distilled. The distillate was taken up in ether, dried over sodium sulfate, the solvent removed and the residue distilled. There was obtained 42.2 g. (78%) of 3-bromothiophene, distilling almost entirely at 79–80° under 60 mm. On redistillation the material was found to have an odor unlike that of 2-bromothiophene; b.p. 158.5–159° (cor.), $n^{20}\text{D}$ 1.5902.

2-Nitro-3-bromothiophene.—This compound, m.p. 80–81.5°, was obtained by nitration[7] of 3-bromothiophene.

Halogen Lability in Alcoholysis.—To obtain the findings reported in Table I, a sample (0.01 to 0.05 g.) of the halogen compound was dissolved in methanol, and a measured volume (1 or 5 ml.) of 0.20 methanolic potassium hydroxide was pipetted in, the total volume being 15 ml. The flask was kept at 27–28° for the time listed, then the solution was poured into 20 ml. of 5% nitric acid. A given excess of 0.01 *N* silver nitrate was introduced by pipet, 0.5 ml. of nitrobenzene added and the flask was shaken vigorously for one minute. A saturated solution of ferric alum (5 ml.) was then added, and the solution back-titrated with 0.01 *N* potassium thiocyanate.

Reactions of I and VI with Piperidine.—To a solution of 0.0325 g. of 2-chloro-3-nitrothiophene (VI) in 10 ml. of benzene was added 5 ml. of 0.8 *M* piperidine in the same solvent. After standing at 27–28° for one hour, needles of piperidine hydrochloride had formed. After 3 hours elapsed time the sample was extracted with three 25-ml. portions of water. The aqueous extract was acidified and analyzed for chloride content as described above, with 20 ml. of 0.01 *N* silver nitrate. Back-titration required less than 0.2 ml. of 0.01 *N* thiocyanate. Hydrolysis was, therefore, complete.

The above experiment was repeated, using 0.0327 g. of 2-chloro-5-nitrothiophene (I). There was no precipitate in 18 hours, but the solution darkened. The sample was then heated. After refluxing for 3.5 hours crystals of the hydrochloride had formed. After 5 hours the sample was acidified, decolorized with Norit, and analyzed as above for chloride content. Back-titration required about 0.5 ml. of thiocyanate. Thus hydrolysis was essentially complete.

Hydrolysis of 2-Chloro-3,5-dinitrothiophene.—To 5 g. of 2-chloro-3,5-dinitrothiophene was added a solution of 10 g. of sodium bicarbonate in 400 g. of water. After 5 hours of heating on the steam-bath, chloride analysis on the resulting clear aqueous solution showed complete halogen removal. The final product was an amber-colored solution with approximately one-half gram of sediment. This halogen-free solid was practically insoluble in ether or alcohol, but could be recrystallized from benzene or acetic acid to yield light yellow needles, m.p. 204–206°. Analysis showed 13.5% nitrogen.

The aqueous phase was acidified with dilute sulfuric acid, saturated with salt, and extracted with ether. The ether solution was treated with Norit and most of the ether removed. Addition of hexane and cooling caused separation of colorless crystals (*ca.* 0.5 g.), which began to darken at once. On rapid heating, the product decomposed with gas evolution at 45–47°. On standing for a few minutes the crystalline structure degenerated to a dark resinous mass.

No crystalline materials could be obtained when 2-chloro-3,5-dinitrothiophene was acted upon by sodium hydroxide in water, alcohol–water or dioxane–water, either at reflux or at room temperature. Acidification of the black or dark red solutions caused the evolution of hydrogen sulfide or oxides of nitrogen. Processing of the products yielded only resins and amorphous materials.

3,5-Dinitrothienol.—Anhydrous sodium formate (4.09 g.) and 6.27 g. of 2-chloro-3,5-dinitrothiophene were dissolved in 200 ml. of anhydrous methanol. After refluxing for one hour, chloride analysis on an aliquot sample indicated 70% hydrolysis. After 22 hours, refluxing was discontinued and the product evaporated to dryness. The 9.5 g. of red solid remaining was washed with ether to remove a very small amount of a liquid having an ester-like odor.

A portion of the above crude sodium salt on recrystallization from methanol yielded deep red-violet crystals. The substance was stable at 100°. It burned explosively on a copper wire without imparting any green color to the flame. It was easily soluble in water, moderately so in methanol, and insoluble in ether or benzene. In aqueous solution it gave no precipitate with potassium chloride, calcium chloride or silver nitrate, but a bulky yellow precipitate formed on the addition of barium hydroxide. This latter solid decomposed at the temperature of the steam-bath.

Two grams of the crude sodium salt was treated with cold dilute hydrochloric acid, and the resulting solution extracted with ether after saturating with salt. The dried (magnesium sulfate) ether solution was evaporated under vacuum, leaving yellow crystals of the free thienol. This material began to decompose within 5–10 minutes at 25°, but could be stored overnight at −20° without appreciable change. On rapid heating it decomposed violently at 50–52°. It burned explosively on a copper wire, without giving a green flame.

The compound was easily soluble in ether and in water, giving intensely yellow solutions. Addition of excess alkali, ammonia or bromine water discharged the yellow color.

A solution of 0.185 g. of the thienol in 11 ml. of water showed a *p*H value (*p*H meter) of 1.40. This value is not exact, since some decomposition probably occurred during drying and weighing of the sample. For the same reason a satisfactory neutral equivalent could not be obtained, although on electrometric titration the compound behaved as a typical strong acid. The red sodium salt could be obtained by evaporation of the neutralized solution.

Approximately 0.2 g. of the thienol was dissolved in 50 ml. of ether and an ethereal solution of diazomethane (prepared from 4 g. of N-nitrosomethylurea) was added. Evolution of nitrogen occurred, and upon each addition a transient cloudiness was observed. When addition was complete, the ether was removed under vacuum, leaving a crystalline residue. After recrystallization from methanol, the product melted at 137–139°. A mixed melting point with an authentic sample of methyl 3,5-dinitrothienyl ether (see below) gave no depression. When one gram of the original crude sodium salt was acidified, and the resulting ether solution of the thienol treated directly with diazomethane as above, there was obtained 0.35 g. of the methyl ether, which corresponds to a yield of 55%, based on the 2-chloro-3,5-dinitrothiophene originally taken.

3-Nitro-5-acetyl-2-thienol.—A solution of 0.17 g. of 4-nitro-5-chloro-2-acetothienone and 4.09 g. of anhydrous sodium formate in 250 ml. of anhydrous methanol was heated under reflux. After 24 and 48 hours the extent of hydrolysis was shown by chloride analysis to be 50 and 75%, respectively. At the end of this time the solvent was removed, leaving a yellow solid (8 g.) which was extracted (Soxhlet) with ether. The ether-soluble material (0.5 g.) consisted of unchanged starting material, m.p. 85–87°. The crude yellow sodium salt which remained was stable at 100°. It dissolved readily in water.

A 3-g. portion of this salt was acidified with cold dilute hydrochloric acid, and the resulting solution extracted with ether after saturating with salt. Removal of ether gave 1 g. of a yellow solid, which on freezing out of methylene chloride, after treatment with Norit, gave colorless microcrystals, which decomposed at 65°. The free thienol thus obtained gave a negative Beilstein test. It gradually darkened and lost its crystalline appearance on standing an hour or two, but at −10° it could be stored for several days.

The thienol was readily soluble in ether or in water. Its yellow aqueous solution was immediately decolorized by bromine water. A solution of 0.0193 g. of the thienol in 10 g. of water showed a *p*H value (*p*H meter) of 2.25. In an electrometric titration against alkali, it behaved as a typical strong acid.

Anal. Calcd. for $C_6H_5NO_4S$: neut. equiv., 187. Found: neut. equiv., 184.

Treatment of 0.5 g. of the thienol with diazomethane (from 2 g. of N-nitrosomethylurea) in ether solution gave, after removal of solvent and recrystallization from methanol, yellow cottony needles, m.p. 155–157°, identical with methyl 3-nitro-5-acetyl-2-thienyl ether (see below).

Reaction of Other Halides with Sodium Formate.—When a solution of 4.25 g. of 2,5-dichloro-3,4-dinitrothiophene and 4.75 g. of anhydrous sodium formate in 230 ml. of anhydrous methanol was refluxed for 3.5 hours, hydrolysis of both halogens was complete, as shown by chloride analysis. Evaporation of solvent from the dark cloudy solution yielded only resinous materials.

When the same procedure was carried out using 6 g. of 2-chloro-5-nitrothiophene, the resulting solution rapidly became very dark, and an amorphous suspension formed. After 18 hours analysis for chloride showed less than 10% halogen removal.

When a solution of 1.63 g. of 2-chloro-3-nitrothiophene and 1.36 g. of anhydrous sodium formate in 100 ml. of absolute methanol was refluxed for 1, 2 and 4 days, the extent of halogen removal was 5, 13 and 25%, respectively. The solution very gradually assumed an amber color during this time. An additional 1.36 g. of sodium formate was added, and refluxing was continued until the tenth day, when halogen removal was 63%. The now red amber solution on evaporation yielded a solid residue which, after recrystallization from methanol, gave 0.5 g. of brown needles, m.p. 90–98°. Further recrystallization raised the melting point to 97–99°. A mixed melting point with an authentic sample of methyl 3-nitro-2-thienyl ether showed no depression.

2-Methoxy-3,5-dinitrothiophene.—To a solution of 10 g. of 2-chloro-3,5-dinitrothiophene in 500 ml. of methanol was added gradually during 12 hours a solution of 2.7 g. (1 equiv.) of potassium hydroxide in 40 g. of water. After standing for six days at 20°, the deep red solution was diluted to 1.5 liters with water, precipitating a yellow-brown amorphous solid. Extraction with ether and evaporation of the dried extract yielded 6 g. of a brown powder. Recrystallization from methanol gave 1.1 g. of a crystalline solid which, on further recrystallization from ethanol, was obtained as almost colorless glistening leaflets, m.p. 138–139°. This halogen-free product was soluble in common organic solvents. It dissolved in concentrated hydrochloric acid giving a yellow solution.

Anal. Calcd. for $C_5H_4N_2O_5S$: H, 1.98; C, 29.41. Found: H, 1.89; C, 29.81.

When the above procedure was repeated using 200 ml. of methanol as the solvent at reflux or at room temperature, no crystalline product could be isolated. Acidification of the deep red solutions after 15 minutes gave much hydrogen sulfide, and resins or amorphous solids.

2-Ethoxy-3,5-dinitrothiophene.—To a solution of 1 g. of 2-chloro-3,5-dinitrothiophene in 50 ml. of absolute ethanol was added 1 g. of sodium bicarbonate. On refluxing, a red color developed in the solution. After seven hours the solution was filtered and evaporated to dryness under vacuum. From the residual red-brown solid there was extracted with ligroin (b.p. 30–60°) 0.13 g. of a powder which on recrystallization from carbon tetrachloride yielded approximately 0.1 g. of light yellow, stocky needles, m.p. 94–95°.

Anal. Calcd. for $C_6H_6N_2O_5S$: H, 2.77; C, 33.03. Found: H, 2.90; C, 32.90.

No crystalline product was obtained when the above halide was acted on by an equivalent of sodium methoxide in ethanol for 15 minutes at reflux temperature or at 25°. Acidification yielded only hydrogen sulfide, amorphous materials and resins.

2-Phenoxy-3,5-dinitrothiophene.—To 0.5 g. of powdered 2-chloro-3,5-dinitrothiophene in a mortar was added, in small portions and with intimate mixing, 0.32 g. of solid potassium phenoxide. A transient red color appeared with each addition. The final yellow solid was recrystallized from methanol, yielding 0.5 g. (80%) of large yellow plates. A single further recrystallization from methanol gave a product of constant melting point, 151.5–152.5°. The compound was difficultly soluble in methanol or ethanol, but dissolved readily in benzene. With concentrated hydrochloric acid, it showed no apparent coloration or solution.

Anal. Calcd. for $C_{10}H_6N_2O_5S$: N, 10.52. Found: N, 10.07.

4-Nitro-5-methoxy-2-acetothienone.—To a solution of 4.1 g. of 4-nitro-5-chloro-2-acetothienone in 50 ml. of methanol was added at reflux a solution of 1.2 g. of potassium hydroxide in 1.2 g. of water. After ten minutes the red reaction product was diluted with water, acidified, and collected; yield 3.3 g. (80%); m.p. 145–155°. A recrystallization from methanol yielded colorless, cottony needles, m.p. 158–159°.

Anal. Calcd. for $C_7H_7NO_4S$: N, 6.97. Found: N, 6.74.

4-Nitro-5-ethoxy-2-acetothienone.—One gram of 4-nitro-5-chloro-2-acetothienone was dissolved in 100 ml. of ethanol, and to this solution was added 0.56 g. of potassium hydroxide in 0.5 g. of water. After standing at 20° for 1.5 hours the red opaque solution was warmed on the steam-bath for 15 minutes. The solution was cooled, acidified, filtered from amorphous sediment, diluted to thrice its volume with water, and allowed to stand at 0°. The solid which separated (0.5 g., 50%) was recrystallized from methanol; m.p. 125–126°.

Anal. Calcd. for $C_8H_9NO_4S$: N, 6.51. Found: N, 6.95.

4-Nitro-5-phenoxy-2-acetothienone.—An intimate mixture of 1.05 g. of 4-nitro-5-chloro-2-acetothienone and 0.70 g. of potassium phenoxide was heated on the steam-bath (one-half hour) until it lost its original pink color and pasty texture. The tan solid was extracted with benzene, and the benzene evaporated. Recrystallization of the residue from methanol gave 0.9 g. (70%) of colorless cotton-like needles, m.p. 120–122°. Further recrystallization from ethanol raised the melting point to a constant value of 122–123°.

Anal. Calcd. for $C_{11}H_9NO_4S$: N, 5.33. Found: N, 5.14.

3-Nitro-2-methoxythiophene.—On refluxing a mixture of 0.50 g. of 2-chloro-3-nitrothiophene with 35 ml. of 0.2 *N* methanolic potassium hydroxide for one-half hour, a red solution gradually developed. The cooled product was acidified and brought to 0°. The yellow solid which formed was recrystallized from methanol, and finally from hexane, to give 0.35 g. of fine needles, m.p. 98.5–99.0°.

Anal. Calcd. for $C_5H_5NO_3S$: N, 8.80. Found: N, 9.02.

3-Nitro-2-ethoxythiophene.—Sodium (0.14 g.) was dissolved in absolute ethanol (20 ml.) after which 2-chloro-3-nitrothiophene (0.82 g.) was added. The solution was heated on the steam-bath for 10 minutes, cooled, and acidified to produce 0.75 g. of leaflets, m.p. 93–96°. Recrystallization from hexane gave broad spears, m.p. 96.5–97.5°.

Anal. Calcd. for $C_6H_7NO_3S$: N, 8.09. Found: N, 8.09.

3-Nitro-2-phenoxythiophene.—A mixture of 0.41 g. of 2-chloro-3-nitrothiophene and an equivalent of potassium phenoxide was maintained at 100° for 1.5 hours. The product was extracted with benzene, and the resulting yellow solid was recrystallized from alcohol. The yield of colorless needles, m.p. 89.5–90.5°, was 0.35 g.

Anal. Calcd. for $C_{10}H_7NO_3S$: N, 6.33. Found: N, 5.93.

N-(3,5-Dinitro-2-thienyl)-aniline.—To 0.50 g. of 2-chloro-3,5-dinitrothiophene in 20 ml. of methanol was added 0.50 g. of aniline. Crystals (0.7 g.) formed immediately at room temperature. Recrystallization from ethanol yielded orange-yellow plates, m.p. 162–163°. The halogen-free product was readily soluble in acetone but sparingly so in cold methanol or hot water, to give violet-colored solutions, which retained their color on high dilution with water. Addition of acid caused a sharp color change (violet to yellow) at *p*H 7.0, while addition of base gave a change of violet to colorless at *p*H 12.0. These color changes were reversible.

Anal. Calcd. for $C_{10}H_7N_3O_4S$: N, 15.84. Found: N, 15.81.

N-(3,5-Dinitro-2-thienyl)-*p*-toluidine.—The above procedure was followed with 0.50 g. of 2-chloro-3,5-dinitrothiophene and 0.56 g. of *p*-toluidine as reactants. The product was crystallized from ethanol yielding 0.70 g. of orange-yellow plates, m.p. 146–147°.

Anal. Calcd. for $C_{11}H_9N_3O_4S$: N, 15.05. Found: N, 14.71.

N-(3,5-Dinitrothienyl)-*p*-nitroaniline.—Similarly, 0.50 g. of 2-chloro-3,5-dinitrothiophene and 1.4 g. of *p*-nitroaniline were placed in reaction. A refluxing period of 15 minutes was required for separation of 0.8 g. of opalescent violet crystals; m.p. 210° (dec.), after washing with hot methanol.

Anal. Calcd. for $C_{10}H_6N_4O_6S$: N, 18.06. Found: N, 18.15.

3-Nitro-5-acetyl-2-thienylamine.—A solution of 1.0 g. of 4-nitro-5-chloro-2-acetothienone and 3.5 ml. of concentrated ammonium hydroxide in 25 ml. of methanol was heated at 60° for one hour. Cooling to 0° gave 0.8 g. of dark needles. Recrystallization from methanol, after treatment with charcoal, yielded bright yellow needles, m.p. 225–227° (sublimes with slight decomposition). This halogen-free product was practically insoluble in ether or benzene. Mineral acids also failed to dissolve it, but it gave a reddish-colored solution with 5% potassium hydroxide.

Anal. Calcd. for $C_6H_6N_2O_3S$: N, 15.05. Found: N, 15.06.

N-(3-Nitro-5-acetyl-2-thienyl)-aniline.—To a warm solution of 0.2 g. of 4-nitro-5-chloro-2-acetothienone in 10 ml. of methanol was added 1 g. of aniline. Within a few minutes a mass of crystals formed (0.2 g.). Recrystallization from methanol gave orange needles, m.p. 138.5–139.5°, free from halogen.

Anal. Calcd. for $C_{12}H_{10}N_2O_3S$: N, 10.68. Found: N, 11.11.

N-(3-Nitro-5-acetyl-2-thienyl)-butylamine.—The above procedure was repeated using butylamine in place of aniline. No solid product separated after 30 minutes. Acidification and dilution with water gave a yellow solid, very soluble in methanol. Recrystallization from hexane yielded fine yellow needles, m.p. 96.5–97.5°, which contained no halogen.

Anal. Calcd. for $C_{10}H_{14}N_2O_3S$: N, 11.56. Found: N, 11.46.

EVANSTON, ILLINOIS

[COMMUNICATION NO. 1455 FROM THE KODAK RESEARCH LABORATORIES]

The Reaction of Quinone and Sulfite. I. Intermediates[1]

BY JAMES E. LUVALLE

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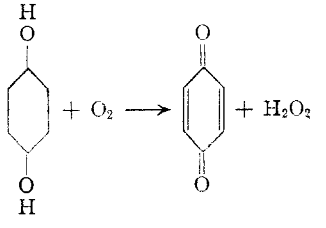
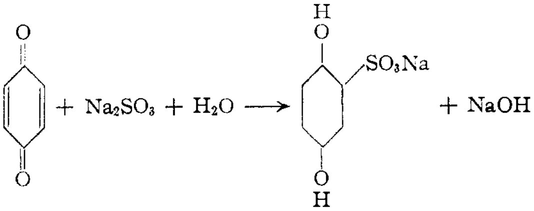
The reactions of quinone and sulfite, quinhydrone and sulfite, and quinone monosulfonate and sulfite have been investigated over the *p*H range 1 to 12. Below *p*H 4 the products of the reaction between quinone and sulfite or quinhydrone and sulfite are hydroquinone, sulfate and hydroquinone monosulfonate; between *p*H 4 and 7.5 the product is hydroquinone monosulfonate. Below *p*H 8.5 the quinhydrone acts as though only quinone were present. Above *p*H 7.5 a greenish-blue intermediate appears in the reaction of quinone and sulfite; this intermediate increases in stability with increase in *p*H, whereas above this *p*H the greenish-blue intermediate does not appear in the reaction of quinhydrone and sulfite. Over the whole *p*H range in the reaction of quinone and sulfite, a transient orange intermediate is apparently the first step in the reaction. The reaction of quinone monosulfonate and sulfite parallels the reaction of quinone and sulfite in part, *i.e.*, at low *p*H values the reaction is a simple oxidation–reduction reaction, between *p*H 2.7 and 7.0 it goes through a transition range, and above *p*H 7 the product is virtually all quinone disulfonate. In the transition range a yellow intermediate, probably a semiquinone, appears. Quinone also forms a greenish-blue intermediate with cysteine and glutathione and a very transient greenish complex with *l*-ascorbic acid. The greenish-blue intermediates bleach in the light and are regenerated by shaking in air.

Introduction

The reaction of quinone and sulfite is the first of a series of some very rapid reactions of photographic interest which are now being studied in these Laboratories. Although the use of sulfite as a preservative in photographic developers was first mentioned in 1882,[2] the mechanism of the sulfite action has not been adequately explained. The data for the autoxidation of hydroquinone in an alkaline medium and in the presence of excess sulfite have been explained by the reaction scheme[3]



(1)



(2)

$$H_2O_2 + Na_2SO_3 \longrightarrow Na_2SO_4 + H_2O \qquad (3)$$

It was reasoned by analogy that quinone was formed in the developing solution, and thence removed by the sulfite, with formation of hydroquinone monosulfonate.

When quinone and sulfite react in air[4a–4c] or under hydrogen[4b] in an alkaline medium, an unstable green (or greenish-blue) compound is formed which, upon standing, fades to bright yellow[4a,c] or red brown.[4b] Shaking in air restores the color.[4a–4c] A trace of bisulfite or hydroquinone, added before the sodium sulfite, is reported[4a] to prevent formation of the colored intermediate. Hydroquinone monosulfonate is also found,[4b,c] and reduction of the alkalinity increases the yield of the monosulfonate.[4c] The theoretical yield of the monosulfonate is obtained from the reaction in a buffer alcohol–water solution between *p*H 4.5 and 5.0.[4d]

Experimental

All inorganic chemicals were General Chemical Reagent Grade. Ordinary distilled water was used. Unless otherwise stated, *p*H measurements were made with a Beckman Model G laboratory *p*H meter. The visual spectra were recorded on a General Electric Recording Spectrophotometer and the ultraviolet spectra with a Beckman Model DU spectrophotometer. On recording the visual spectra, the wave length drive was driven manually to permit recording of a complete curve in one minute. The solutions were prepared by discharging from hypodermic syringes, sulfite always preceding quinone, into a beaker containing an aliquot of buffer. The reaction mixture was immediately transferred to a cuvette and placed in the spectrophotometer, elapsed time from mixing to start of recording being not more than 30 seconds. Two absorption curves were recorded consecutively, the cuvette was removed, the solution

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[1] Presented before the Division of Biological Chemistry at the Philadelphia Meeting of the American Chemical Society, April, 1950.

[2] H. B. Berkely, *Phot. News*, **26**, 41 (1882).

[3] (a) J. Pinnow, *Z. wiss. Phot.*, **11**, 289 (1913); *ibid.*, **13**. 44 (1914); *ibid.*, **27**, 344 (1930); *ibid.*, **37**, 76 (1938); (b) E. Lehmann and E. Tausch, *Phot. Korr.*, **71**, 17 (1935); (c) T. H. James and A. Weissberger, THIS JOURNAL, **61**, 442 (1939).

[4] (a) R. Luther and A. J. Leubner, *J. prakt. Chem.*, **85**, 233 (1912); (b) J. Pinnow, *ibid.*, **89**, 536 (1914); (c) J. W. Dodgson, *J. Chem. Soc.*, **105**, 2435 (1914); (d) G. H. Chase, W. T. Hanson, Jr., and R. M. Evans, private communication.