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MONONITRO- AND DINITROTHIOPHENES

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I. Mononitrothiophene

The introduction of a nitro group into the thiophene nucleus has been a problem fraught with difficulties. Victor Meyer and his co-workers[1] made "countless futile attempts" to nitrate this compound by the usual method. They finally succeeded in accomplishing this[2] by drawing a vigorous stream of air charged with thiophene through red fuming nitric acid. The product was a mixture of mononitro- and dinitrothiophenes and an oily residue. The two nitro compounds could only be extracted and separated by repeated fractional distillation and the yield was admittedly unsatisfactory. The nitration of ethylthiophene by this method failed to produce the mononitro derivative;[3] diethylthiophene yielded a product of unknown composition;[4] while the nitration of thioxene resulted in the formation of a resin.[5] Despite these limitations, for thirty years this remained the only known method for the nitration of thiophene and its homologs.

Following the study of diacetyl-ortho-nitric acid,[6] benzoyl nitrate,[7] and acetyl nitrate,[8] as nitrating agents, Steinkopf and Kirchoff[9] proposed an improved method for the nitration of thiophene. The compound was dissolved in acetic anhydride and treated with a solution of fuming nitric acid in the same solvent, the temperature during nitration being maintained between 0 and 5°. Upon treating the product with ice water, an unstable dark oil and a brown precipitate were formed, from which mononitrothiophene was obtained by distillation with steam. Although it must be admitted that this is a decided improvement over the earlier method, the success of the experiment depends upon painstaking manipulation at a low nitration temperature, and the oily product has been found to undergo rapid decomposition.

A Modified Method of Nitration

The method of nitration proposed in this paper has been given a thorough trial. The process is carried out, almost exclusively, at the room tem-

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[1] Meyer, "Die Thiophengruppe," Braunschweig, **1888**, p. 95.

[2] Meyer and Stadler, *Ber.*, **17**, 2648 (1884).

[3] Bonz, *Ber.*, **18**, 552 (1885).

[4] Muhlert, *Ber.*, **19**, 635 (1886).

[5] Messinger, *Ber.*, **18**, 1639 (1885).

[6] Pictet and Genequand, *Ber.*, **35**, 2526 (1902).

[7] Francis, *Ber.*, **39**, 3801 (1906).

[8] (a) Pictet and Khotinsky, *Ber.*, **40**, 1163 (1907); (b) *Compt. rend.*, **144**, 210 (1907).

[9] (a) Steinkopf and Kirchoff, *Ann.*, **403**, 17, 27 (1914); (b) Steinkopf and Lützkendorf, German patent, 255,394.

perature. The reaction yields a product which is stable under all conditions and the weight of the purified substance is from 80 to 85% of that required by theory. Moreover, the method has been repeatedly employed, with equal success, for the nitration of a derivative of thiophene.

Although solutions containing diacetyl-ortho-nitric acid, or acetyl nitrate, have often been employed with marked success for the nitration of aromatic hydrocarbons or their derivatives,[10] attempts to nitrate thiophene in this Laboratory with these reagents have clearly shown that in order to insure a satisfactory yield it is necessary to observe certain rigid conditions. Pictet and Genequand[11] and, later, Pictet and Khotinsky[12] had made the observation that these reagents may acetylate, oxidize or nitrate, the course of the reaction depending upon circumstances.

With thiophene there is no indication that acetylation occurs when acetic acid or anhydride solutions of these nitrating agents are employed. That oxidation takes place, with the incident rupture of the thiophene ring, cannot be doubted. It has also been demonstrated that in the formation of mononitrothiophene with these solutions, temperature is an important factor. At lower temperatures the reaction, if it takes place at all, is almost exclusively one of nitration; while at elevated temperatures oxidation sets in almost invariably, the course of the reaction being indicated by the evolution of heat and the liberation of nitrogen peroxide. Moreover, at higher temperatures the liberated nitrogen peroxide attacks the thiophene vapor in the nitrating flask, converting it into a tarry product, which has been shown to contain traces of dinitrothiophene by the application of the Meyer-Stadler test.[13] Schaarschmidt's studies[14] show that the nitration of thiophene with nitrogen peroxide yields products which are not easy to purify.

No less than twenty-five nitrations have been carried out in this Laboratory with solutions of nitric acid and thiophene in acetic acid or acetic anhydride. The method that has reduced the side reactions to a minimum is given in outline.

Procedure

(1) Eighty-four g. of thiophene is dissolved in 340 cc. of acetic anhydride and (2) eighty g. of nitric acid (sp. gr. 1.52) is dissolved in 600 cc. of glacial acetic acid.

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[10] (a) Van Romberg, *Rec. trav. chim.*, **7**, 226 (1888); (b) Kunze, *Ber.*, **21**, 3331 (1888); (c) Hirsch, *Ber.*, **22**, 335 (1889); (d) Komppa, *Chem. Zentr.*, **1898**, ii, 1169; (e) Orton, *J. Chem. Soc.*, **81**, 806 (1902); (f) Witt and Utermann, *Ber.*, **39**, 3901 (1906); (g) Arnall, *J. Chem. Soc.*, **125**, 811 (1924); (h) Menke, *Rec. trav. chim.*, **44**, 141 (1925); *C. A.*, **19**, 2191 (1925); (i) *ibid.*, **44**, 269 (1925); *C. A.*, **19**, 2480 (1925); (j) Bacharach, THIS JOURNAL, **49**, 1522 (1927); (k) other examples: Houben, "Die Methoden der organischen Chemie," 2nd ed., Vol. 4, pp. 146–150.

[11] Ref. 6, p. 2526.

[12] Ref. 8a, p. 1163.

[13] Meyer and Stadler, *Ber.*, **17**, 2780 (1884).

[14] Schaarschmidt and co-workers, *Ber.*, **58B**, 499 (1925).

Each solution is divided into two equal parts. One-half of solution (2) is introduced into a large three-necked, round flask, provided with a thermometer, a motor stirrer and a dropping funnel. The flask is cooled to 10°. With moderate stirring one-half of the thiophene solution is introduced, drop by drop, and at such a rate as to prevent the heating of the reaction mixture above the room temperature. A rapid rise of temperature will occur during the addition of the first fraction of the thiophene solution. The temperature is controlled by dipping the nitrating flask into a bath of cold tap water. The use of ice water is not necessary, as cooling with ice will retard the reaction. On the other hand, care should be taken to avoid superheating the reaction mixture. After the addition of the first half of thiophene, the temperature of the reaction mixture is reduced to 10° and the remainder of nitric acid is rapidly introduced into the flask. Nitration is continued by the gradual addition of thiophene. Throughout the nitration the solution should show a permanent light brown color. The appearance of a pink or dark red color indicates oxidation.[15] The product is allowed to remain at the room temperature for two hours. It is then treated with an equal volume of ice water with rapid shaking. Mononitrothiophene will begin to separate out in faint yellow crystals. More crystals will form if the mixture is allowed to remain in the ice chest for at least twenty-four hours. It is filtered cold through a Büchner funnel, washed thoroughly with ice water, pressed and dried in a brown desiccator,[16] charged with sulfuric acid and granules of caustic soda.

The filtrate and the washings contain in solution a quantity of mononitrothiophene. This is recovered by distillation with steam. The acid distillate will consist of white crystals and a solution of the compound. The solid is removed by filtration and washed. The filtrate is extracted with ether, neutralized with a weak solution of sodium carbonate, dried with calcium chloride and subjected to distillation.

If the nitration was carried out in accordance with this outline, the product will be crystalline and faint yellow in color. The color is due to traces of dinitrothiophene and other impurities. Mononitrothiophene has been crystallized by earlier workers from ether, alcohol, benzene and other solvents. As a rule these solvents fail to yield a snow-white product. It has been found in this work that petroleum ether (b. p. 20–40°) possesses decided advantages in that by prolonged boiling it extracts mononitrothiophene but does not readily dissolve the impurities. With petroleum ether snow-white crystals of the compound have been obtained in needles 5 to 8 inches in length.

The method of nitration outlined in this paper has been employed repeatedly by the author. In every instance the yield of the purified product was found to be over 80% of the theoretical quantity.

Discussion

Experiments conducted under varying conditions of concentration and temperature lead to the following generalizations.

1. Glacial acetic acid alone does not induce nitration to any extent at the ordinary temperature. At higher temperatures partial oxidation takes place, a tar is produced and a quantity of unattacked thiophene is recovered.

2. In moderate quantities acetic anhydride alone will induce nitration when the reaction is carried out at 0°. Even at this low temperature ni-

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[15] The tarry product formed as a result of oxidation dissolves in the reaction mixture, imparting to it a pink or a dark red color.

[16] Earlier investigators have noted that the compound is extremely sensitive toward light, ref. 2, p. 2649.

tration is accompanied by oxidation with the formation of an unstable by-product.

3. Under the most favorable conditions the yield is satisfactory and the product free from contamination when thiophene is added to nitric acid. The reverse process does not complete the reaction; if the reaction mixture be heated to complete nitration, the unchanged thiophene is oxidized, heat is evolved and nitrogen peroxide liberated.

II. Dinitrothiophene

The entry of a negative substituent into the thiophene nucleus protects the compound from the oxidizing action of nitric acid, permitting nitration by the ordinary method. By the direct addition of the negatively substituted derivative to fuming nitric acid at low temperatures, nitro compounds have been obtained from β-thiophenic acid,[17] acetothienone,[18] ethyl acetothienone,[19] methyl acetothienone,[20] and from a number of polysubstituted derivatives.[21]

That mononitrothiophene has not been heretofore employed for the large-scale production of the dinitro compound has undoubtedly been due to the difficulty of preparing the former. The only method described in the literature for the preparation of dinitrothiophene is that of Meyer and Stadler.[22] It should be added that although the yield by this process was highly unsatisfactory, the compound had been subjected to a thorough investigation.[23]

The Preparation of Dinitrothiophene

The nitrating mixture proposed for the conversion of thiophene into the mononitro derivative does not react with the latter to produce dinitrothiophene. A reaction carried out with this mixture resulted in the recovery of the nitrothiophene employed. On the other hand, mononitrothiophene is readily nitrated with a mixture of nitric and sulfuric acids to form dinitrothiophene. Although derivatives of thiophene are known to react with sulfuric acid with the greatest ease, sulfonic acids have not been detected in this process of nitration.

Procedure

Thirty-five g. of nitric acid (sp. gr. 1.4) was dissolved in 55 g. of sulfuric acid (sp. gr. 1.82) and the ice-cooled solution was treated with 20 g. of mononitrothiophene in

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[17] Nahnsen, *Ber.*, **17**, 2196 (1884).

[18] Peter, *Ber.*, **17**, 2646 (1884).

[19] Schleicher, *Ber.*, **18**, 3022 (1885).

[20] Demuth, *Ber.*, **18**, 3025 (1885).

[21] (a) Peter, *Ber.*, **18**, 541 (1885); (b) Rosenberg, *Ber.*, **19**, 652 (1886).

[22] Ref. 2, p. 2648.

[23] (a) Meyer and Stadler, *Ber.*, **17**, 2778 (1884); (b) Stadler, *Ber.*, **18**, 530 (1885); (c) Meyer, *Ber.*, **18**, 1328 (1885); (d) Rosenberg, *Ber.*, **18**, 1778 (1885); (e) Gattermann and co-workers, *Ber.*, **18**, 3012 (1885).

gram portions. The first 5 g. of the solid formed an almost colorless solution. Additional quantities produced cloudiness, imparting to the liquid a faint yellow color. When the reaction mixture was brought to room temperature, it separated into two transparent layers—a reddish-yellow upper layer and a faint yellow lower layer. It was heated in a water-bath with continued shaking, the temperature being gradually increased in the course of half an hour from 30 to 85°. The reaction product, consisting of an upper yellow layer and a lower light brown layer, was cooled in an ice-bath for one hour. The white crystals of dinitrothiophene were filtered with suction, digested in ice water and dried. Upon treatment with ice, the filtrate formed an additional quantity of the compound in fine needles. The product was crystallized from ordinary alcohol; yield, over 80% of the theoretical quantity; melting point, 52°.

Anal. Calcd. for $C_4H_2S(NO_2)_2$: S, 18.68. Found: 18.94. *Mol. wt.* Subs., 0.1959: benzene, 21.76; ΔT, 0.256°. Calcd.: 174. Found: 185.

Isomeric Dinitrothiophenes

In their studies of dinitrothiophene, Meyer and his co-workers[24] had found that the compound melting at 52° yields upon distillation with steam an isomer melting at 78°. After searching investigation they concluded that the two isomers were identical in structure. They made the further assertion that by repeated fractional distillation with steam ordinary dinitrothiophene (m. p. 52°) is completely transformed into the isomer melting at 78°.[25,23a,b]

It should be stated that these investigators had based the latter assertion on experiments carried out with only small quantities of the lower melting modification.

An extended study of the behavior of ordinary dinitrothiophene fails to show that the compound melting at 52° can be completely transformed into the isomer melting at 78°.

1. When dinitrothiophene is subjected to prolonged distillation with steam, a dark residue remains in the distillation flask, which was presumably taken by earlier workers as a decomposition product. When an alcoholic solution of this residue is purified with animal charcoal, it yields dinitrothiophene possessing a sharp melting point of 54°. The product is not very volatile with steam and could not be converted into the higher melting modification after repeated distillation with steam.

2. In a study of the vapor pressure curve for dinitrothiophene,[26] a trace of the compound was found to condense in the cooler regions of the isoteniscope at temperatures above 140°. This fraction melted at 76–78°, while the bulk of the compound in the apparatus gave, after crystallization from alcohol, a melting point of 52–54°. If ordinary dinitrothiophene was transformed in the isoteniscope into its isomer at temperatures above 140°, it was natural to assume that prolonged heating would induce fur-

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[24] Ref. 2, p. 2649.

[25] Ref. 1, p. 98.

[26] Results to be published.

ther transformation, converting the lower melting compound into the other modification. The compound melting at 52–54° was therefore transferred into a long combustion tube, closed at the lower end. The tube was submerged in a bath of toluidine and heated at 180°. In a few hours a solid melting at 72–78° condensed in the cooler regions of the tube. Continued heating, for almost one week, failed to produce additional quantities of the higher melting isomer. The residue in the tube when freed from traces of tarry impurities showed a sharp melting point of 54°.

3. Specimens of the two isomers were spread in thin layers in two quartz test-tubes and exposed for one hour, at a distance of ten inches, to the action of ultraviolet irradiation, a Cooper-Hewitt Quartz Uviarc being used for the experiment. The ordinary modification had melted completely at the end of the hour and the isomer had changed into a semi-solid. The two tubes were exposed for another hour at a distance of fifteen inches. A slight decomposition had taken place in each tube. The materials were dissolved in alcohol, treated with animal charcoal and crystallized. No change in melting point was observed in either compound.

Evidently ordinary dinitrothiophene contains a weighable quantity of the isomer melting at 78°, but there is no conclusive evidence of transition from one isomer into the other.

Summary

Solutions containing acetyl nitrate and di-acetyl-ortho-nitric acid will nitrate thiophene and may simultaneously oxidize it, the course of the reaction depending upon concentration and temperature.

When conditions are under proper control, nitration will take place almost exclusively, even at the room temperature, with a satisfactory yield of mononitrothiophene.

With a mixture of nitric and sulfuric acids mononitrothiophene is readily converted into dinitrothiophene.

Studies of the behavior of dinitrothiophene do not confirm the assertion that the ordinarily prepared compound is transformed into a higher melting isomer.

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