TABLE I

CHLORAL CONDENSATION PRODUCTS

| | Yield, % | M. p., °C. | Formula | Analyses %C Calcd. | Analyses %C Found | Analyses %H Calcd. | Analyses %H Found |
|---|---|---|---|---|---|---|---|
| | | | Trichloroethanes- | | | | |
| Dicarvacrolyl, monohydrate | 52 | 167.0–167.3 | $C_{22}H_{29}O_3Cl_3$ | 59.00 | 58.94 | 6.53 | 6.66 |
| Dicarvacrolyl, dimethyl ether | 57 | 157–158 | $C_{24}H_{31}O_2Cl_3$ | 62.93 | 63.08 | 6.83 | 6.82 |
| Dithymolyl, dimethyl ether | 52 | 114–115 | $C_{24}H_{31}O_2Cl_3$ | 62.93 | 63.08 | 6.83 | 6.73 |
| Dithymolyl, diethyl ether | 59 | 73.6–74.0 | $C_{26}H_{35}O_2Cl_3$ | 64.26 | 64.44 | 7.26 | 7.41 |
| Dithymolyl, di-*n*-propyl ether | 70 | 83.6–84.1 | $C_{28}H_{39}O_2Cl_3$ | 65.43 | 65.49 | 7.65 | 7.63 |
| Dithymolyl, dimyristyl ether | 55 | 54–55 | $C_{50}H_{83}O_2Cl_3$ | 73.01 | 73.27 | 10.17 | 10.22 |
| Dithymolyl, diacetate | .. | 102.0–102.5 | $C_{26}H_{31}O_4Cl_3$ | 60.77 | 60.60 | 6.08 | 5.93 |
| Dibromodithymolyl | .. | 117–118 | $C_{22}H_{25}O_2Cl_3Br_2$ | 44.96 | 44.74 | 4.29 | 4.50 |
| | | | Dichloroethenes- | | | | |
| Dicarvacrolyl, dimethyl ether | 80 | 117.8–118.3 | $C_{24}H_{30}O_2Cl_2$ | 68.40 | 68.22 | 7.18 | 7.40 |
| Dithymolyl, dimethyl ether | 85 | 103.8–104.5 | $C_{24}H_{30}O_2Cl_2$ | 68.40 | 68.04 | 7.18 | 7.29 |
| Dithymolyl, diethyl ether | 77 | 100–101 | $C_{26}H_{34}O_2Cl_2$ | 69.48 | 69.30 | 7.63 | 7.54 |
| Dithymolyl, di-*n*-propyl ether | 79 | 82.8–83.8 | $C_{28}H_{38}O_2Cl_2$ | 70.43 | 70.13 | 8.02 | 7.93 |

derivatives in the identification of arylalkyl ethers.

Jaeger[6] in his article on the syntheses of dithymolyltrichloroethane and its acetate did not report the melting points. It was found that dithymolyltrichloroethane when recrystallized from absolute ethanol melts at 186° with decomposition, and the acetate at 102.0–102.5°. The free phenol also gives a crystalline dibromo derivative melting at 117–118°.

Table I gives the melting points and analyses of the compounds prepared. All melting points are uncorrected.

## Experimental

**Condensation Methods: Free Phenols and Phenol Ethers.**—Concentrated sulfuric acid, diluted with one third its volume of glacial acetic acid is dropped slowly into a cooled mixture of the phenol and chloral in a two to one molar proportion until a solid or a gummy mass precipitates from the reaction mixture. The mass is washed thoroughly with cold water by decantation and then boiled with a large volume of water for several hours. The phenolic condensation products are recrystallized from 50–50 ethanol–water mixture, and crystallize with one mole of water of crystallization. The condensation products from the phenol ethers are recrystallized from 95% ethanol and contain no solvent of crystallization; yield was 52–80%.

**Dehydrochlorination Methods.**—The phenol ether condensation product (1 to 5 g.) is refluxed for two to six hours with 50 to 100 ml. of 30% ethanolic potassium hydroxide, and the solution poured into water. The ethene precipitates as an orange powder, and is recrystallized twice from 95% ethanol; yield 77–85%.

**Preparation of Thymol Myristyl Ether.**—32.0 g. (0.11 mole) of myristyl bromide, 22.5 g. (0.15 mole) of thymol and 6.0 g. (0.15 mole) of sodium hydroxide were refluxed with 15 ml. of water for ten hours. The water-insoluble layer was then washed and dried for three days over calcium chloride. Distillation gave a fraction boiling at 273–274° at 40 mm.; yield 30.5 g. or 83%.

The physical constants determined for the liquid were $n^{25}D$ 1.4859, $d_{25}$ 0.8888. The molar refraction, calculated 111.2, found 111.5.

*Anal.* Calcd. for $C_{24}H_{42}O$: C, 83.17; H, 12.21. Found: C, 83.17; H, 12.10.

## Summary

The condensation products of chloral with thymol, carvacrol and some of their alkyl ethers, together with the dehydrochlorinated derivatives of these have been prepared.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

# Replacement of Halogen by the Nitro Group in Halogenated Acetothiophenamides

BY HILL M. PRIESTLEY AND CHARLES D. HURD

Nitroso compounds of thiophene are unknown. This statement applies not only to nitrosothiophene but also to N-nitrosoaceto-2-thiophenamide, $C_4H_3S—N(NO)—COCH_3$. Steinkopf[1] attempted to prepare the latter compound but was unable to isolate any definite product.

It was reasoned that by employing 2-acetamido-3,5-dibromothiophene (I) instead of aceto-2-thiophenamide itself, the N-nitroso compound might be the more readily formed. As is known, no difficulty is encountered in the formation of the N-nitroso derivative of aceto-2,4-dibromoanilide. Hence, nitrous fumes, generated from arsenic trioxide and nitric acid, were passed into a solution of 2-acetamido-3,5-dibromothiophene in glacial acetic acid. A yellow compound of melting point 207° was easily isolated. The N-nitroso-N-aryl amides are of low melting point, readily explode, and cannot be kept for more than a few days. The yellow compound obtained possessed none of these properties and hence could not be the

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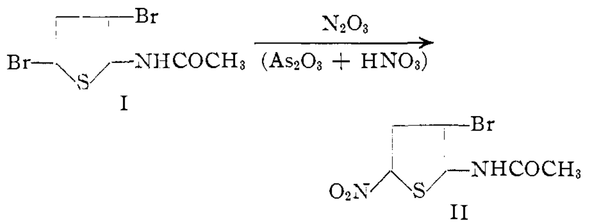
[1] Steinkopf, *Ann.*, **403**, 25 (1914).

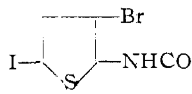
N-nitroso compound in question. What actually happened was that the α-bromine atom in (I) had been replaced by a nitro group


I

II

That a nitro group and not a nitroso group had entered the thiophene ring was demonstrated by nitrating (I) with acetyl nitrate. The same yellow compound of melting point 207° was obtained.

Proof that the α-bromine atom was involved rather than the β was obtained by treating 2-acetamido-5-iodo-3-bromothiophene (III) with acetyl nitrate. The same compound (II), m. p. 207°, was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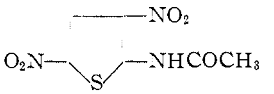

IV

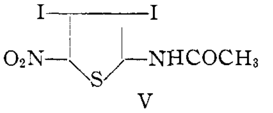
formed, and it was quite free from iodine. The iodo compound (III) was synthesized[2] from (I) by reduction (Al + Hg), mercuration, and iodination.

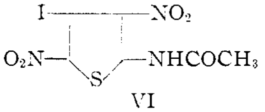
It was also possible to eject the remaining bromine atom in (II) by use of fuming nitric acid or by prolonged exposure to nitrous fumes. This operation yielded 2-acetamido-3,5-dinitrothiophene (IV), a compound melting at 180° previously made[3] by direct nitration of aceto-2-thiophenamide. To obtain (IV) from (I), it is not necessary to isolate (II); instead, if (I) is treated with an excess of acetyl nitrate, followed by fuming nitric acid, the acetamidodinitrothiophene is readily obtained.

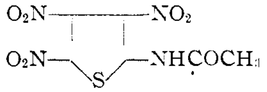
2-Acetamido-3,5-diiodothiophene similarly gives rise to IV, thus showing that the dibromo and diiodo compounds possess the same orientation. The fact that the intermediate 2-acetamido-3-iodo-5-nitrothiophene could not be isolated (analogous to II) reveals the greater reactivity of the β-iodine over the β-bromine. This conclusion is supported also by the contrasting behavior of the two dihalides toward aluminum amalgam. The diiodo compound was converted to aceto-2-thiophenamide in this manner, whereas the dibromo compound yielded 2-acetamido-3-bromothiophene.

The conversion of these halides into 2-acetamido-3,5-dinitrothiophene brings to mind the similar behavior of 5-*p*-nitrophenylazo-3-bromo-2-acetamidothiophene[2] in its reaction with fuming nitric acid.

Stepwise replacements of the iodine atoms in 2-acetamido-3,4,5-triiodothiophene by nitro groups made possible the synthesis of nitrodiiodo (V), dinitroiodo (VI), and trinitro (VII) derivatives

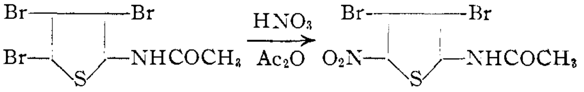

V


VI


VII

of aceto-2-thiophenamide. This synthesis of VII is striking, since the trinitro compound cannot be made by direct nitration.

When 2-acetamido-3,4,5-tribromothiophene was treated with acetyl nitrate, only the α-bromine atom was replaced by the nitro group



## Experimental

**2-Acetamido-3-bromo-5-nitrothiophene** (II).—A. Into a solution of 1.05 g. of crude 2-acetamido-3,5-dibromothiophene in 5 ml. of glacial acetic acid were passed nitrous fumes until the entire mass crystallized. This required about five minutes. The yellow crystals were filtered and washed with a little glacial acetic acid and water. The yield was 0.50 g., m.p. 206° (dec.).

*Anal.* Calcd. for $C_6H_5BrN_2O_3S$: N, 10.57. Found: N, 9.73.

**B.** The acetamidobromonitrothiophene was prepared more conveniently from acetyl nitrate. To 2 ml. of acetic anhydride, cooled with ice, there was added, drop by drop, with stirring, 0.5 ml. of red fuming nitric acid, d. 1.60. This solution was then introduced, all at once, with stirring, into a cooled solution of 2.0 g. of 2-acetamido-3,5-dibromothiophene in 35 g. of glacial acetic acid. Crystallization was completed in about five minutes. The yellow crystals were collected on a filter, washed with water and then with 6 ml. of 50% alcohol. The yield was 1.06 g., m.p. 207° (dec.). A mixture of this substance with the product from part (a) also melted at 207°. The filtrate contained a less pure product, 0.45 g., m.p. 203–205° (dec.).

*Anal.* Calcd. for $C_6H_5BrN_2O_3S$: N, 10.57. Found: N, 9.47.

**C.** The nitration of 2-acetamido-3-bromo-5-iodothiophene, m.p. 159°, was performed by dissolving 0.30 g. of it in 10 g. of glacial acetic acid and adding into this mixture 0.36 ml. of acetyl nitrate solution, prepared as above. After about fifteen minutes, at room temperature, the nitrated compound began to separate. It was filtered off and washed with a little glacial acetic acid, water, and alcohol. The yield was 65 mg., m.p. 207° (dec.). From the filtrate another 35 mg. was recovered, also melting at 207° (dec.). The two fractions were combined and recrystallized from 5 ml. of absolute alcohol, yielding 30 mg., m.p. 207° (dec.). When mixed with the substance of m.p. 207° obtained from (I), the melting point was still 207°. A part of the sample was decomposed with metallic sodium and tested for iodine. No iodine was found.

**2-Acetamido-3,5-dinitrothiophene. From 2-Acetamido-3-bromo-5-nitrothiophene.**—Six 0.10-g. portions of (II) were treated on a porcelain tile with six 0.5-ml. portions of red fuming nitric acid, d. 1.60. After a short lag, a violent reaction took place. The clear solution was poured on ice and the precipitate washed with water and a little alcohol. The yield was 0.18 g. From several

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(2) Hurd and Priestley, This Journal, **69**, 859 (1947).

(3) Steinkopf, *Ann.*, **403**, 25, 40 (1914).

batches there was collected 0.51 g. of crude acetamidodinitrothiophene. This was recrystallized from 40 ml. of absolute alcohol to give light yellow crystals. There was obtained 0.23 g. of IV, m.p. 180°. When mixed with 2-acetamido-3,5-dinitrothiophene, m.p. 180°, prepared according to the directions of Steinkopf,[3] the product still melted at 180°. The low N-value in the analysis need not be considered seriously in view of the satisfactory values for carbon, hydrogen and sulfur, and because of the fact that the micro-Dumas determinations on these nitro compounds tended to give low results.

*Anal.* Calcd. for $C_6H_5N_3O_5S$: C, 30.91; H, 2.18; N, 18.18; S, 13.85; mol. wt., 231. Found: C, 31.25; H, 2.13; N, 16.66; S, 14.15; mol. wt. (Rast), 219.

If nitrous fumes are passed in for a long time into a solution of 2-acetamido-3,5-dibromothiophene in glacial acetic acid, (IV) is also obtained as the final product.

**B. From 2-Acetamido-3,5-diiodothiophene.**—The acetyl nitrate solution was prepared by adding 1 ml. of fuming nitric acid to 2 ml. of acetic anhydride. This mixture was added to a solution of 0.1 g. of 2-acetamido-3,5-diiodothiophene in 5 g. of glacial acetic acid. After thirty seconds, ice was added. The iodine that had separated was removed by sodium bisulfite solution, and the precipitate was washed copiously with water. The material melted at 160–170°, and halogen was present. The substance was then treated with fuming nitric acid on a spot plate. Again iodine was liberated, which again was removed with sodium bisulfite solution. The precipitate was washed with water and alcohol. The melting point was now 180°, and halogen was absent. No melting point depression occurred on mixing it with the material of m.p. 180°, which was made by the nitration of 2-acetamido-3,5-dibromothiophene. It was also possible to prepare the dinitro compound by treatment of the diiodo compound dissolved in ten parts of glacial acetic acid with nitrous anhydride fumes, followed by treatment with fuming nitric acid. The yield of halogen-free substance, m.p. 180°, was 0.10 g. from 0.40 g.

**2-Acetamido-3,4-dibromo-5-nitrothiophene.**—One gram of 2-acetamido-3,4,5-tribromothiophene was dissolved in 50 g. of glacial acetic acid contained in a flask which was heated on an open flame. The solution was cooled to room temperature and treated with a solution of 1 ml. of red fuming nitric acid in 5 ml. of acetic anhydride. After fifteen minutes, the solution was poured into 100 ml. of ice water. The precipitate was separated, washed with water and then with 8 ml. of 50% alcohol. When silver nitrate was added to the nitric acid filtrate, a copious precipitate of silver bromide was obtained. The yield was 0.84 g. (theory, 0.91 g.), m.p. 206° (dec.). It was recrystallized from 35 ml. of absolute alcohol, giving 0.56 g. of yellow crystals melting at 206° (dec.).

*Anal.* Calcd. for $C_6H_4Br_2N_2O_3S$: N, 8.14. Found: 7.84.

**Nitration of 2-Acetamido-3,4,5-triiodothiophene, A. 2-Acetamido-3,4-diiodo-5-nitrothiophene (V).**—In a 500-cc. 3-necked flask, provided with a thermometer and mechanical stirrer, and surrounded with ice, was placed 40 ml. of concentrated nitric acid, d. 1.4. When the temperature of the nitric acid had reached 5°, there was added with vigorous stirring, in the course of five minutes, 8.50 g. of powdered acetamidotriiodothiophene. The mixture was poured into 150 g. of ice water. Free iodine was removed by the addition of sodium bisulfite solution. The solid was filtered, washed with water, then with alcohol, and air dried. The yield was 5.4 g. (75%), m.p. 240°. A small portion, 0.35 g., was recrystallized from 12 ml. of nitrobenzene, washed with 2 ml. of ice-cold nitrobenzene, and then with 10 ml. of absolute alcohol. The yield was 70 mg., m.p. 260° (dec.). These crystals were orange colored.

*Anal.* Calcd. for $C_6H_4I_2N_2O_3S$: N, 6.39; mol. wt., 438. Found: N, 6.24; mol. wt. (Rast), 433, 443.

**B. 2-Acetamido-4-iodo-3,5-dinitrothiophene (VI).**—To 20 ml. of fuming nitric acid in a beaker, surrounded by ice, there was added in small portions 5.4 g. of crude, powdered (V), m. p. 240°, prepared above. Ice was then added, and the free iodine was removed with sodium bisulfite solution. The solid was washed with water and alcohol and air dried. The yield of yellow-orange solid was 3.05 g. (68%), m. p. 194°. A small portion, after recrystallization from a mixture of equal parts of nitrobenzene and absolute alcohol, melted at 195°.

*Anal.* Calcd. for $C_6H_4IN_3O_5S$: N, 11.76; mol. wt., 357. Found: N, 11.00; mol. wt. (Rast), 345.

**C. 2-Acetamido-3,4,5-trinitrothiophene (VII).**—One gram of the monoiodo compound (VI) was dissolved in a cold mixture of 6 ml. of concentrated nitric acid and 9 ml. of concentrated sulfuric acid. After a few minutes a precipitate settled out. The reaction was allowed to continue for thirty minutes. The mixture was decomposed with ice, and the iodine was removed with sodium bisulfite solution. The yield was 0.33 g; the compound exploded in a capillary tube at 140°. Halogen was absent. For purification, the substance was dissolved in 6 ml. of nitromethane, the solution centrifuged, and decanted from carbon. The nitromethane was allowed to evaporate spontaneously to a volume of 2 ml. The light cream colored crystalline solid was filtered off and rinsed with a little 95% alcohol. The yield was 0.15 g., m.p. 140° (explosion).

*Anal.* Calcd. for $C_6H_4N_4O_7S$: C, 26.09; H, 1.46; N, 20.29. Found: C, 25.05; H, 1.53; N, 19.70.

**Acknowledgment.**—Combustion microanalyses for C, H or N were performed by M. M. Ledyard and T. S. Ma. Some of the thiophene used in the last stage of this investigation was generously supplied by Socony-Vacuum Laboratories, Paulsboro, New Jersey.

## Summary

Experiments are described showing replacement of halogen substituents by nitro groups in halogenated derivatives of aceto-2-thiophenamide. Iodo groups are more easily replaced than bromo, and groups in the $\alpha$-position are removed more readily than the $\beta$-substituents. Even 2-acetamido-3,4,5-trinitrothiophene could be synthesized from 2-acetamido-3,4,5-triiodothiophene, whereas this trinitro compound could not be made by direct nitration of aceto-2-thiophenamide.

Evanston, Illinois Received January 23, 1947