[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CINCINNATI AND THE CANCER RESEARCH LABORATORY OF THE UNIVERSITY OF FLORIDA]

PREPARATION AND ABSORPTION SPECTRA OF 3,4-DISUBSTITUTED DIBENZOTHIOPHENE DERIVATIVES[1]

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In the course of an investigation into the physical and chemical properties of carcinogenic amines, the nitration of the carcinogenic (1) 3-acetylaminodibenzothiophene (AAD) was studied. Nitration of dibenzothiophene takes place in the 2-position (2). Consequently one could expect nitration of AAD to also take place in the same position but such is not the case.

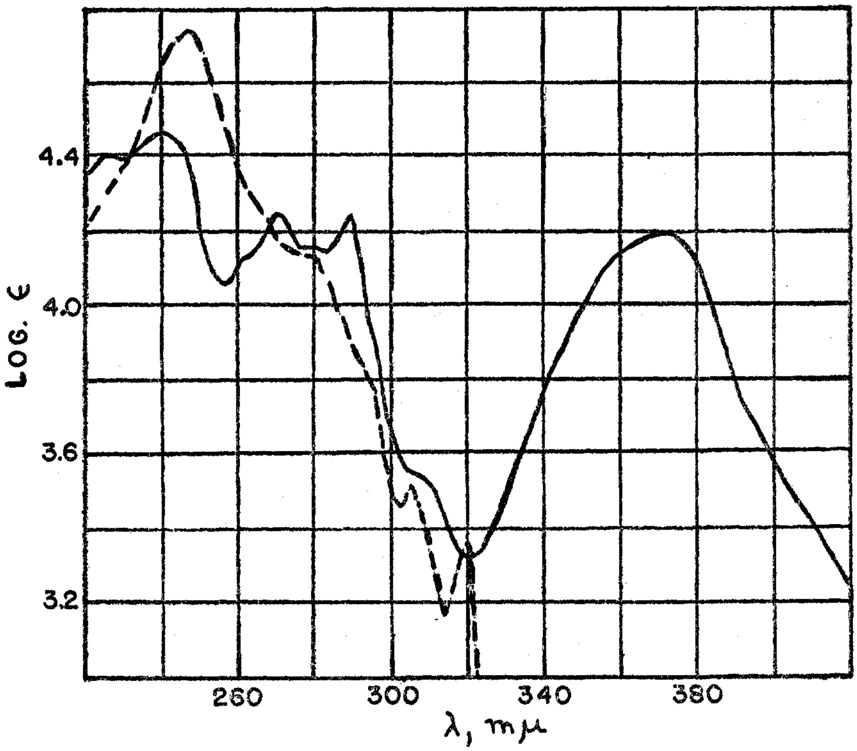

FIG. 1. 2-METHYL-*1H*-THIANAPHTHENO[2,3-*e*]BENZIMIDAZOLE (- - -) AND THIANAPHTHENO[2,3-*e*]PIASELENOLE (————) IN 95% ETHANOL

The deacetylation and reduction of nitro AAD forms a diamine which reacts with selenium dioxide and with benzil. The product formed from the diamine and selenium dioxide gives a qualitative test for selenium, a wine-red color with con-

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centrated sulfuric acid, and a typical high intensity low energy piaselenole band (3) (in this case λ_{max} 372 mμ and shoulder at 400 mμ, Fig. 1). It is evident that a piaselenole has been formed. The diamine and benzil give a high-melting compound which dissolves in sulfuric acid to a dark violet color. Consequently this new compound is a quinoxaline derivative. The reduction of nitro-3-aminodibenzothiophene in acetic acid forms a high-melting compound which does not give a violet color reaction with benzenesulfonyl chloride and pyridine (4). This shows the absence of a free amino group in the molecule. Therefore the derivative must be an imidazole, the absorption spectra of which is shown in Fig. 1. This is substantiated by the nitrogen analysis. On the basis of these facts the nitro group in nitro AAD is either in the 2- or 4-position.

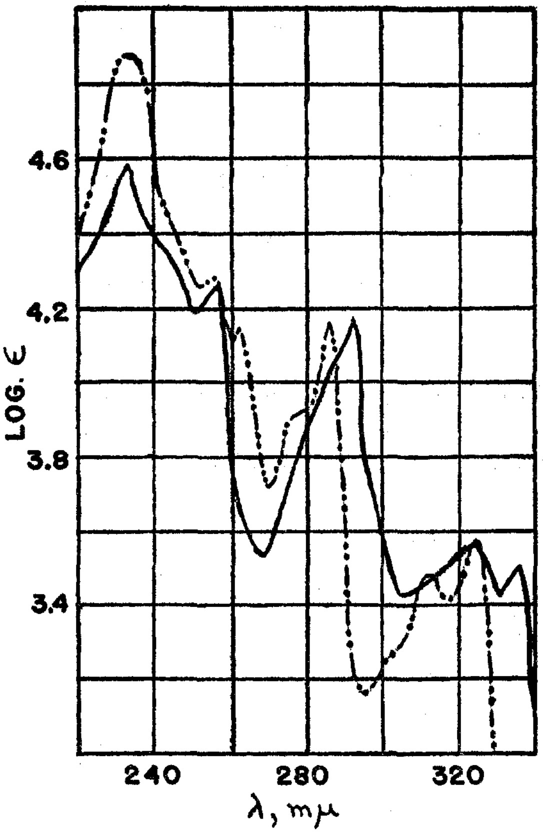


FIG. 2. CARBAZOLE (8) (————) AND DIBENZOTHIOPHENE (- •• - ••) IN 95% ETHANOL

Deamination of nitro-3-aminodibenzothiophene gave a nitro compound, m.p. 161°, which apparently was different from 2-nitrodibenzothiophene, m.p. 186–187°. On this basis one could say that nitration of AAD took place in the 4-position. To substantiate this, spectral studies were undertaken.

In previous papers (5, 6) the structures of new compounds were proven through

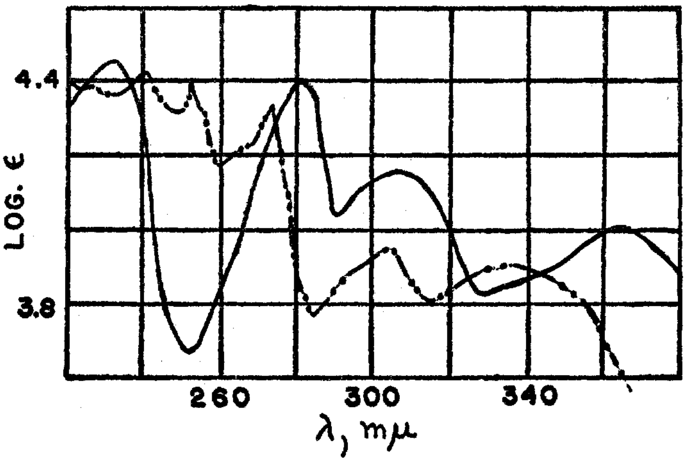


FIG. 3. 3-NITROCARBAZOLE (8) (———) AND 2-NITRODIBENZOTHIOPHENE (- •• - ••) IN 95% ETHANOL

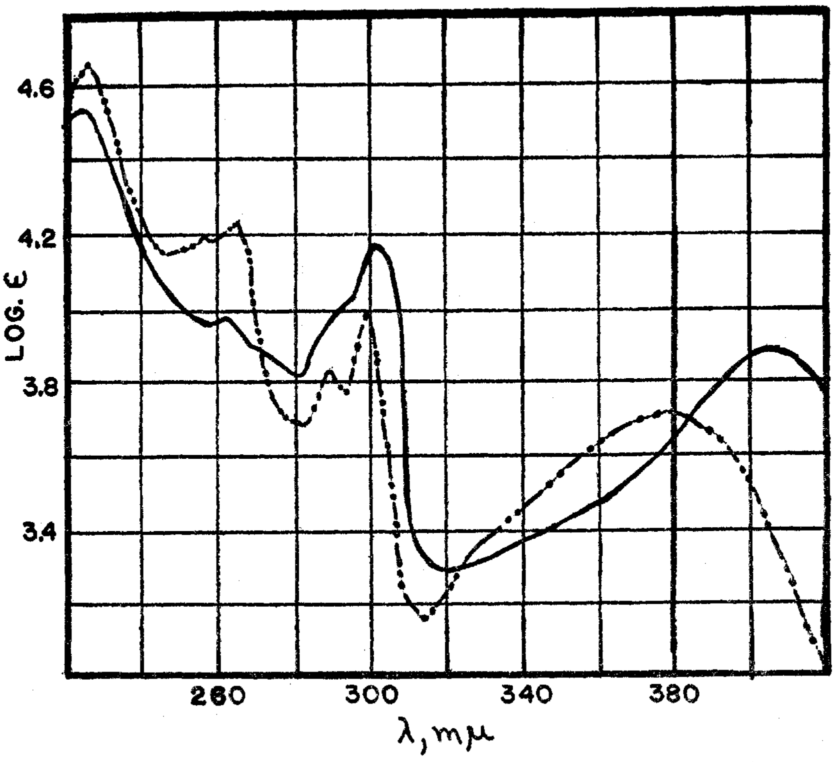


FIG. 4. 1-NITROCARBAZOLE (8) (———) AND 4-NITRODIBENZOTHIOPHENE (- •• - ••) IN 95% ETHANOL

the principle that analogous derivatives of iso-*pi*-electronic molecules are also iso-*pi*-electronic, and consequently spectrally similar. By iso-*pi*-electronic molecules is meant compounds containing the same number of *pi*-electrons, with approximately the same geometrical arrangement and bound about equally tightly, in a planar conjugated system (7). Under these conditions the two compounds are spectrally similar.

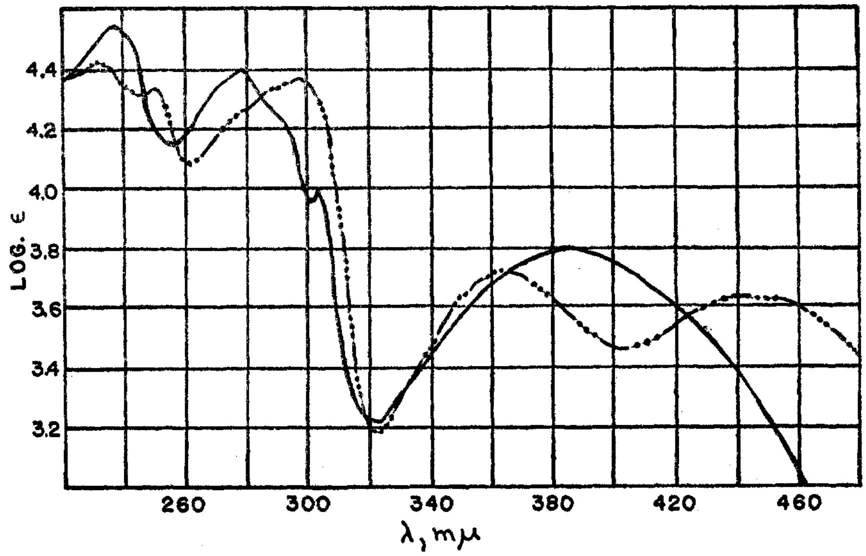
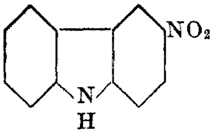
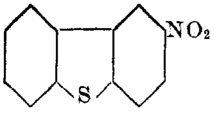


Fig. 5. 3-Amino-4-nitrodibenzothiophene (- ••• - •••) and 3-acetylamino-4-nitrodibenzothiophene (————) in 95% Ethanol

Carbazole (8) and dibenzothiophene are iso-*pi*-electronic and so are spectrally similar, Fig. 2. Consequently it is not surprising that 3-nitrocarbazole (I) and 2-nitrodibenzothiophene (II) are spectrally similar, Fig. 3.

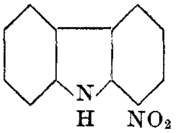


I

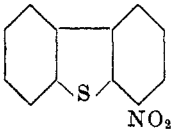


II

As the new nitrodibenzothiophene is spectrally similar to 1-nitrocarbazole (III), Fig. 4, and has an entirely different spectra from 3-nitrocarbazole, Fig. 3, this new compound must be 4-nitrodibenzothiophene (IV).



III



IV

On the basis of these facts it is concluded that the nitration of 3-acetylaminodibenzothiophene takes place in the 4-position.

The absorption spectra of 3-amino-4-nitrodibenzothiophene and its acetyl derivative are shown in Fig. 5. In the nitroamine the band in the visible end of the spectrum is a low energy band which has consistently been found in the spectra of *o*-nitroaromatic amines (3). Protonization of the nitroamine destroys this band. For example, 3-amino-4-nitrodibenzothiophene in 50% alcoholic 16 *N* sulfuric acid has a spectra similar to that of 4-nitrodibenzothiophene, Fig. 6.

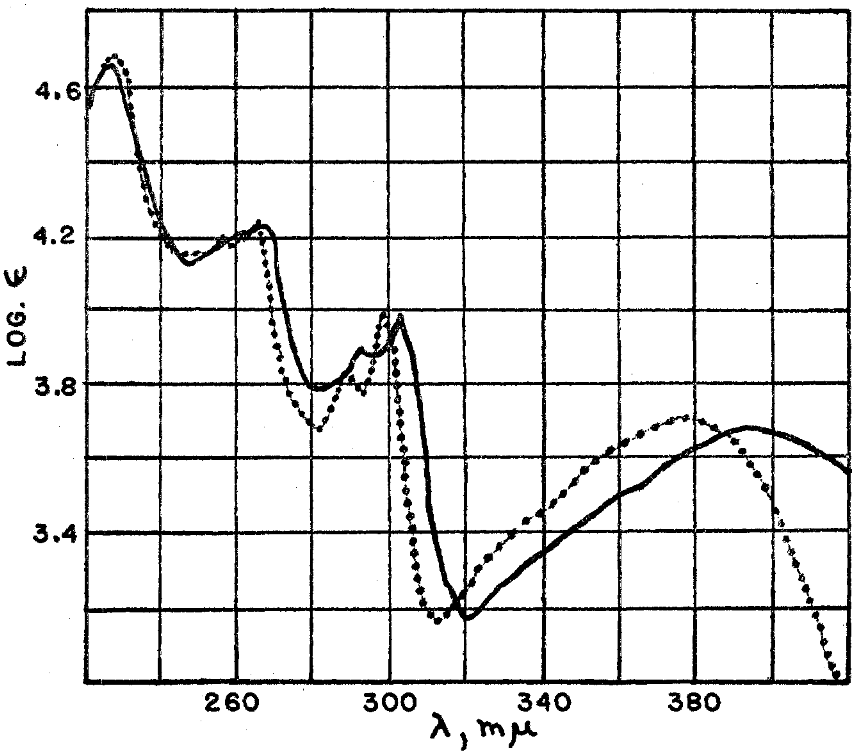


Fig. 6. 3-Amino-4-nitrodibenzothiophene in 50% Alcoholic 16 *N* Sulfuric Acid (————) and 4-Nitrodibenzothiophene in 95% Alcohol (••••••)

EXPERIMENTAL[3]

Ultraviolet absorption spectra. All spectra were determined with a Beckman Model DU quartz spectrophotometer in 95% ethanol.

n-Propyl N-(3-dibenzothienyl)carbamate. To a solution of 20 g. (0.1 mole) of 3-dibenzothiophenamine (9) in 200 ml. of ice-cold pyridine, 14.7 g. (0.12 mole) of *n*-propyl chlorocarbonate was added dropwise while stirring. The solution was stirred an additional 15

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[3] Melting points are not corrected. Analyses are by the Rowland Chemical Laboratories, 1330 Talleyrand Ave., Jacksonville, Fla.

minutes at ice-water temperature and then poured into 2 liters of ice-cold 10% aqueous sulfuric acid. The mixture was allowed to stand until the yellow oil had solidified. The product was filtered, washed with water, and dried. Crystallization from heptane gave 24 g. (84%) of colorless crystals, m.p. 103–104°.

Anal. Calc'd for $C_{16}H_{15}NO_2S$: N, 4.91. Found: N, 5.02.

n-Propyl N-(4-nitro-3-dibenzothienyl)carbamate. Fuming nitric acid (4.5 ml., 0.095 mole) was added dropwise to a stirred solution of 5.85 g. (0.021 mole) of *n*-propyl-N-3-dibenzothienyl carbamate in 150 ml. of acetic acid at room temperature. A thick yellow-orange precipitate was formed. The mixture was stirred an additional half hour and then filtered. Crystallization from heptane gave 3.2 g. (47% of clumps of orange-yellow needles, m.p. 188–189°.

Anal. Calc'd for $C_{16}H_{14}N_2O_4S$: N, 8.48. Found: N, 8.38.

3-Acetylamino-4-nitrodibenzothiophene. (*a*). 3-Acetylaminodibenzothiophene (12 g., 0.05 mole) was dissolved in 90 ml. of hot glacial acetic acid and cooled quickly. Then 8 g. (0.127 mole) of fuming nitric acid (*d.* 1.5) was added dropwise (½ hr.) at room temperature to the stirred solution. The yellow pasty mixture was allowed to stand an additional half hour. The yellow product was collected and washed thoroughly with water. Crystallization from aqueous Methyl Cellosolve[4] gave 11 g. (77%) of yellow crystals, m.p. 247–248.5°.

(*b*). To a suspension of 0.05 g. of 3-amino-4-nitrodibenzothiophene in 2 ml. of acetic anhydride was added a drop of concentrated sulfuric acid. The solution was stirred for 15 minutes and 5 ml. of water was added. The precipitate was crystallized from aqueous Methyl Cellosolve to give 0.04 g. (70%) of yellow crystals, m.p. 254–255°. A mixture melting point with the product, m.p. 247–248.5°, gave a melting point of 247–254°.

Anal. Calc'd for $C_{14}H_{10}N_2O_3S$: N, 9.79. Found: N, 9.57.

3-Amino-4-nitrodibenzothiophene. (*a*). Concentrated hydrochloric acid (35 ml.) was added to a suspension of 7 g. of 3-acetylamino-4-nitrodibenzothiophene in 100 ml. of Methyl Cellosolve. The yellow pasty mixture was refluxed (about 2 hours) to a clear red color. The nitroamine was precipitated by the addition of 200 ml. of water. Crystallization from chlorobenzene gave 5.0 g. (84%) of bright red crystals, m.p. 245–246.5°.

(*b*). To a hot solution of 1.8 g. of *n*-propyl N-(4-nitro-3-dibenzothienyl)carbamate in 60 ml. of Methyl Cellosolve was added 30 ml. of 15% aqueous sodium hydroxide. The mixture was refluxed for one hour and then poured into 300 ml. of water. Crystallization of the red precipitate from chlorobenzene gave 1.2 g. (90%) of bright red crystals, m.p. 248–249°. The mixture melting point with the nitroamine from 3-acetylamino-4-nitrodibenzothiophene melted at 247.5–249°.

Anal. Calc'd for $C_{12}H_8N_2O_2S$: C, 59.0; H, 3.28; N, 11.5.
Found: C, 59.3; H, 3.25; N, 11.2.

4-Nitrodibenzothiophene. 3-Amino-4-nitrodibenzothiophene (4 g.) was dissolved in 60 ml. of Methyl Cellosolve and 120 ml. of ethanol. Following the addition of 32 ml. of concentrated sulfuric acid, a saturated solution containing 10 g. of sodium nitrite was gradually added to the hot solution. The mixture was refluxed for one hour and was poured into 800 ml. of water. The yellow precipitate was crystallized from aqueous Methyl Cellosolve, acetic acid, benzene, and finally alcohol to give a small amount of yellow needles, m.p. 161°.

Anal. Calc'd for $C_{12}H_7NO_2S$: N, 6.11. Found: N, 6.27.

2-Methyl-1H-thianaphtheno[2,3-e]benzimidazole. A solution of 9.0 g. of dihydrated stannous chloride in 10 ml. of concentrated hydrochloric acid was added to a hot suspension of 2.44 g. of 3-amino-4-nitrodibenzothiophene in 20 ml. of acetic acid. The mixture turned dark, then became clear and in a few minutes a thick mush of needles was formed. After one hour of standing, the crystals were filtered, suspended in water and made alkaline with dilute sodium hydroxide solution. Crystallization from methanol gave 2.0 g. (84%) of colorless needles, m.p. 247–248°.

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[4] Trade name for 2-methoxyethanol.

Anal. Calc'd for $C_{14}H_{10}N_2S$: N, 11.8. Found: N, 12.1.

3,4-Diaminodibenzothiophene. A solution of 2.0 g. of hydrated stannous chloride in 5 ml. of concentrated hydrochloric acid was added to a hot solution of 0.5 g. of 3-amino-4-nitrodibenzothiophene in 10 ml. of Methyl Cellosolve. The mixture was allowed to stand for several hours. The collected precipitate was treated with excess aqueous sodium hydroxide and was filtered. Crystallization from heptane gave 0.26 g. (60%) of colorless needles, m.p. 147–148°.

Anal. Calc'd for $C_{12}H_{10}N_2S$: N, 13.1. Found: N, 12.9.

Thianaphtheno[2,3-e]piaselenole. To a stirred solution of 0.08 g. of 3,4-diaminodibenzothiophene in 4 ml. of hot ethanol was added 0.05 g. of selenium dioxide. A yellow precipitate was immediately formed. The mixture was refluxed for 15 minutes, cooled, and then thoroughly washed with water. Crystallization from aqueous Methyl Cellosolve gave 0.1 g. (93%) of yellow needles, m.p. 218–219°. The compound dissolved in concentrated sulfuric acid to give an intense wine red color.

Anal. Calc'd for $C_{12}H_8N_2SSe$: N, 9.69. Found: N, 9.55.

2,3-Diphenylthianaphtheno[2,3-f]quinoxaline. A solution of 1.2 g. of 3,4-diaminodibenzothiophene and 1.2 g. of benzil in 3 ml. of 95% ethanol was refluxed for one hour. Crystals started to appear after 15 minutes of heating. The hot solution was filtered and the yellow crystals were refluxed with 3 ml. of ethanol and were filtered hot. The crystals were rinsed with methanol. One gram (45%) of yellow crystals, m.p. 277–278°, was obtained. The quinoxaline dissolved in concentrated sulfuric acid to give an intense violet color.

Anal. Calc'd for $C_{26}H_{16}N_2S$: N, 7.22. Found: N, 7.40.

SUMMARY

1. Chemical and spectrophotometric evidence has been presented to show that the nitration of 3-acetylaminodibenzothiophene takes place in the 4-position.

2. Several new derivatives of 3,4-diaminodibenzothiophene have been prepared.

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REFERENCES

(1) MILLER, MILLER, SANDIN, AND BROWN, *Cancer Research*, **9**, 504 (1949).
(2) GILMAN AND NOBIS, *J. Am. Chem. Soc.*, **71**, 274 (1949).
(3) Unpublished research.
(4) SAWICKI, *Chemist Analyst*, **42**, 8 (1953).
(5) SAWICKI AND RAY, *J. Am. Chem. Soc.*, **74**, 4120 (1952).
(6) SAWICKI AND RAY, *J. Org. Chem.*, **18**, 946 (1953).
(7) PLATT, *J. Chem. Phys.*, **19**, 101 (1951).
(8) SCHROEDER, WILCOX, TRUEBLOOD, AND DEKKER, *Anal. Chem.*, **23**, 1740 (1951).
(9) BROWN, CHRISTIANSEN, AND SANDIN, *J. Am. Chem. Soc.*, **70**, 1748 (1948).