[CONTRIBUTION FROM THE CANCER RESEARCH LABORATORY OF THE UNIVERSITY OF FLORIDA]

SYNTHESIS AND ABSORPTION SPECTRA OF 3,4-DISUBSTITUTED DIBENZOSELENOPHENE DERIVATIVES[1]

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Received January 22, 1954

A fairly large number of aromatic chemicals are known to cause cancer in animals (1). Some of these compounds are known to cause cancer in humans, for example, 2-naphthylamine and benzidine (2–4). It is only reasonable to believe that cancer may be primarily a problem at the molecular level. For this reason the molecular architecture of the aromatic carcinogens is worthy of investigation. In this respect an understanding of the absorption spectra of the aromatic carcinogens and allied compounds may eventually shed some light on the molecular architecture and relationships of these compounds.

In previous papers on the chemistry of dibenzoselenophene (5, 6), the remarkable spectral similarity of analogous monosubstituted dibenzothiophene and dibenzoselenophene derivatives was shown. In this paper the same striking spectral similarity is shown between analogous disubstituted dibenzothiophene and dibenzoselenophene compounds.

The nitration of the carcinogenic (7) 3-acetylaminodibenzothiophene has been shown to take place in the 4-position (8). The nitration of 3-acetylaminodibenzoselenophene gives a new nitro compound whose derivatives are very closely similar spectrally to the analogous dibenzothiophene compounds, Figs. 1–4. On the basis of these curves the new nitro compound is 4-nitro-3-acetylaminodibenzoselenophene.

In his thought-provoking paper on "Isoconjugate Spectra and Variconjugate Sequences" Platt has pointed out a gradual spectral transition in the biphenyl → fluorene → carbazole → dibenzothiophene → phenanthrene series (9). It has been shown that dibenzothiophene and dibenzoselenophene are almost spectrally identical in the ultraviolet (5). So it is not surprising that the spectra of dibenzoselenophene and phenanthrene show many points of resemblance, Fig. 5. The major differences in going from phenanthrene to dibenzoselenophene are the loss in fine structure and the increase in intensity of the low intensity bands at 320 mμ. This is evidently due to the hetero atom, for substitution of a N for a CH group in a large group of polynuclear hydrocarbons causes the same phenomena (10). Similarly the lowest energy bands of aromatic compounds are more intense with hetero group substitutents than with alkyl or olefinic groups. For example, the high wave length bands of fluorobenzene, phenol, thiophenol, and aniline are more intense than the corresponding bands of toluene or styrene; the high wave length bands of benzofuran, indole, and thianaphthene are more intense than corresponding bands of indene and naphthalene (9).

It is generally agreed that one to three main groups of bands are usually

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[1] This investigation was supported by research grant C-1308 from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

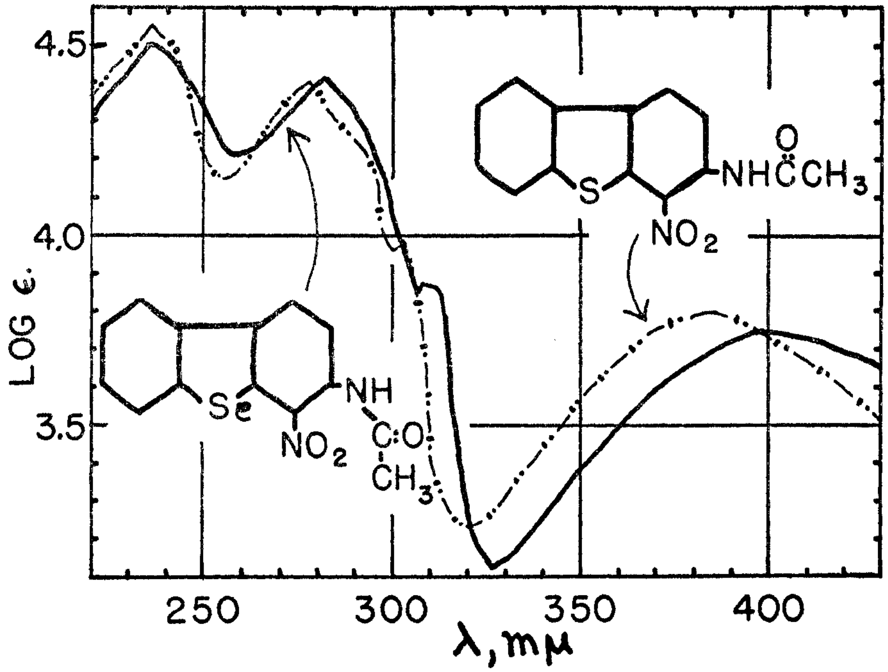

FIG. 1. 3-ACETYLAMINO-4-NITRODIBENZOSELENOPHENE (————) AND 3-ACETYLAMINO-4-NITRODIBENZOTHIOPHENE (—••—) in 95% ethanol.

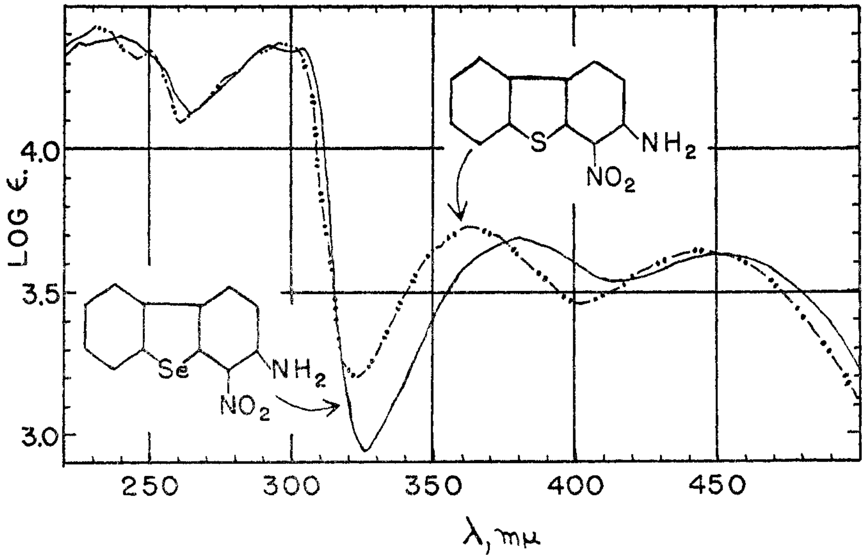

FIG. 2. 3-AMINO-4-NITRODIBENZOSELENOPHENE (————) AND 3-AMINO-4-NITRODIBENZOTHIOPHENE (—••—) in 95% ethanol.

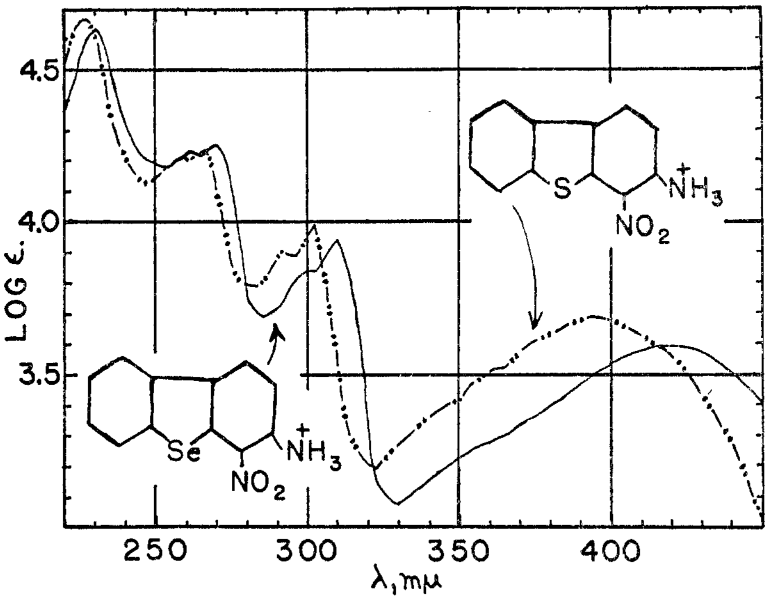

Fig. 3. 3-Amino-4-nitrodibenzoselenophene (————) and 3-Amino-4-nitrodibenzothiophene (—••—) in alcoholic 50% sulfuric acid.

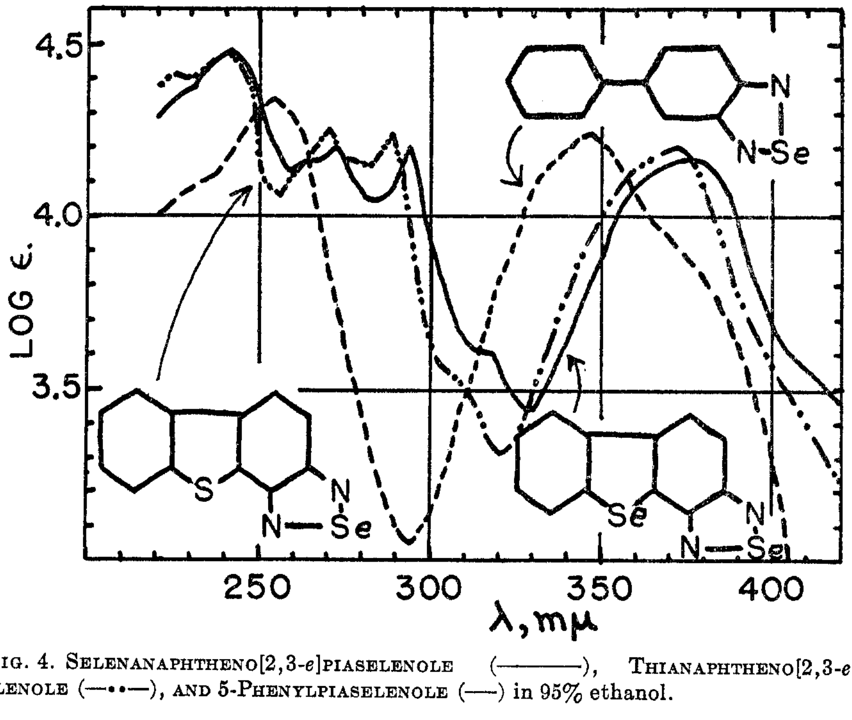

Fig. 4. Selenanaphtheno[2,3-*e*]piaselenole (————), Thianaphtheno[2,3-*e*]piaselenole (—••—), and 5-Phenylpiaselenole (——) in 95% ethanol.

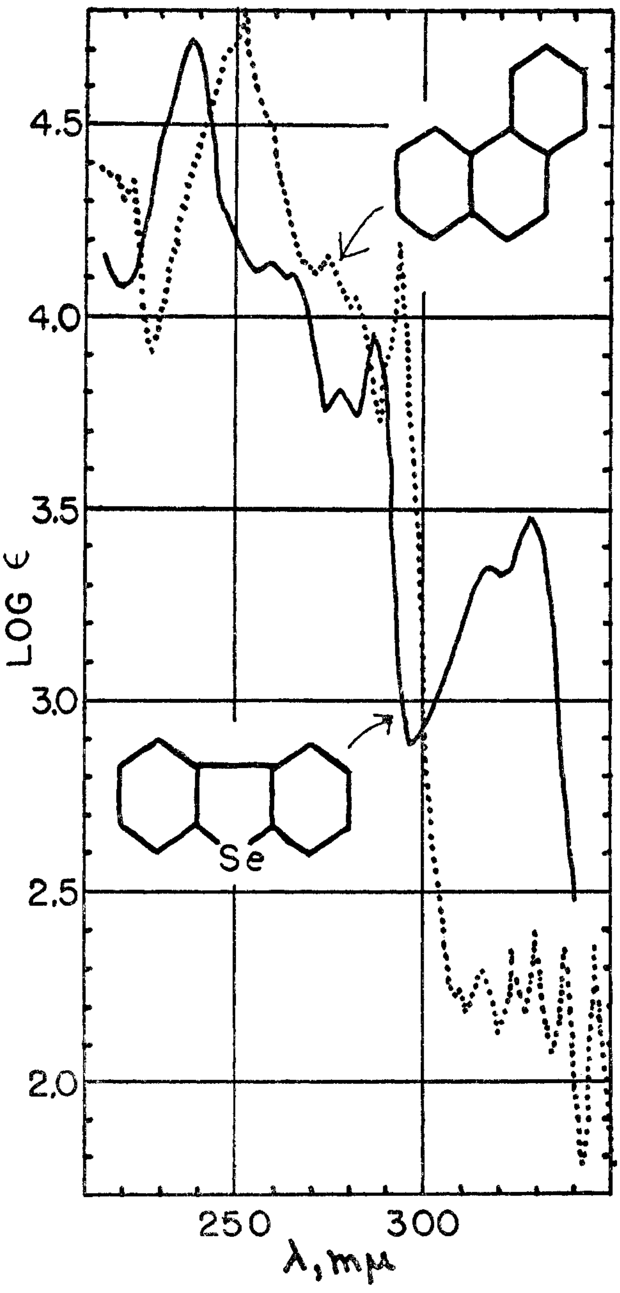

Fig. 5. Dibenzoselenophene (———) in 95% ethanol and Phenanthrene (•••••) in cyclohexane.

found in the spectra of aromatic hydrocarbons in the ultraviolet and visible absorption spectra (approx. 200–800 mμ) (9–11). Badger (10) has named these bands group-III, group-II, and group-I bands; Clar (11) has called them the α-, *para*-, and β-bands; Platt (9) has named them ^{1}Lb, ^{1}La, and ^{1}Bb bands. Benzene has its intense Band I (β- or ^{1}Bb band) in the vacuum ultraviolet at 179 mμ (12), its moderately intense Band II (*para*- or ^{1}La band) at 203.5 mμ, and a Band III (α- or ^{1}Lb band) of low intensity near 254 mμ (13). Phenanthrene has its analogous bands at aproximately 252 mμ, 294 mμ, and 310–350 mμ, respectively (10). On the basis of these relationships the tentative assignment of the dibenzoselenophene bands is as follows: The intense band at 238 mμ is Band I, the moderately intense band system at 287 mμ is Band II, and the two bands of low intensity at 317 mμ and 328 mμ are Band III.

The II band in phenanthrene can be further subdivided into the main II band at 294 mμ and a II′ band system at approximately 280 mμ. In dibenzoselenophene the II′ band consists of bands at 259 mμ and 265 mμ.

As dibenzothiophene, dibenzoselenophene, and carbazole, as well as their analogous derivatives, are spectrally similar (5, 6, 8, 14, 15), the band assignments for dibenzoselenophene should also apply to the iso-*pi*-electronic dibenzothiophene and carbazole. In the derivatives of the above three parent compounds these band systems, as well as other types of bands, can also be found. In Fig. 6 comparison of *o*-nitrodiphenyl sulfide (16) and 3-nitro-4-aminobiphenyl with 3-amino-4-nitrodibenzothiophene suggests strongly that the bands of the latter compound at 362 mμ and 446 mμ are due mainly to the *o*-nitrothiophenol and *o*-nitroaniline groups, respectively. This is reasonable, for the spectrum of *o*-nitrodiphenyl sulfide is closely similar to that of S-methyl-*o*-nitrothiophenol (16) while the spectra of all *o*-nitro aromatic amines studied

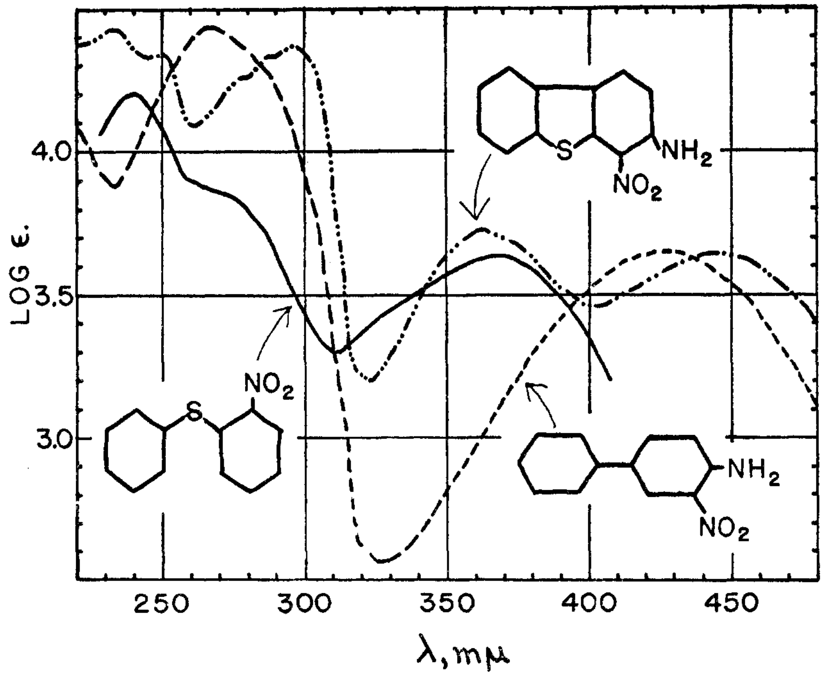

Fig. 6. 2-Nitrodiphenyl sulfide (16) (————), 3-Amino-4-nitrodibenzothiophene (-•••-), and 3-Nitro-4-aminobiphenyl (——) in 95% ethanol.

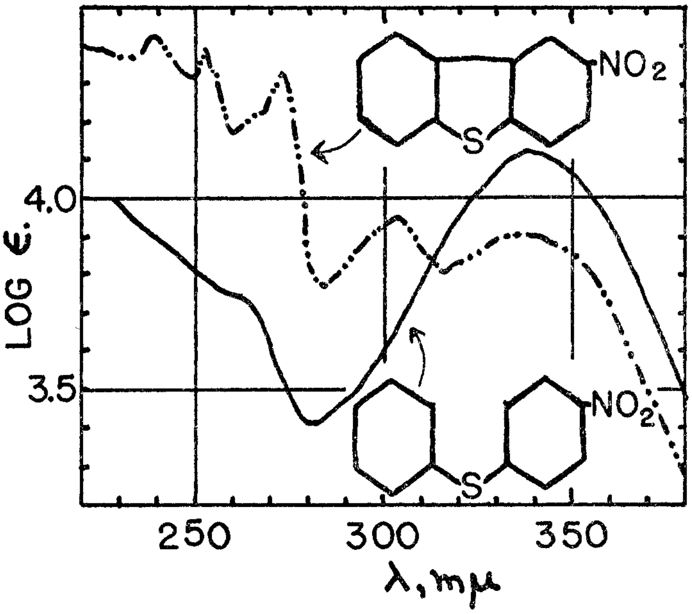

Fig. 7. 4-Nitrodiphenyl sulfide (16) (———) and 2-Nitrodibenzothiophene (—••—) in 95% ethanol.

by the author (8, 14, 15) exhibit a broad low intensity band in the visible spectra. Consequently the bands of 3-amino-4-nitrodibenzoselenophene, Fig. 2, at 380 mμ and 451 mμ are probably due mainly to the *o*-nitrophenylselenol and *o*-nitroaniline groups, respectively. If these conclusions, as applied to *o*-nitroaniline and *o*-nitrothiophenol bands, are valid, then the same relationship should be found in the analogous *p*-nitro bands. In Fig. 7 comparison of the spectra of 4-nitrodiphenyl sulfide (16) and 2-nitrodibenzothiophene (5) show that these compounds have their *p*-nitrothiophenol bands at 337 mμ and 334–337 mμ, respectively. Comparison of the spectrum of 3-nitro-9-methylcarbazole (15) with *p*-nitroaniline (17) shows the former with a band at 372 mμ, log ε 4.04 and the latter with a band at 371–372 mμ, log ε 4.18. These are, apparently, *p*-nitroaniline bands. Thus, the assignment of the nitro bands is borne out by the facts.

In Fig. 4 comparison of the low energy bands of thianaphtheno[2,3-*e*]piaselenole and selenanaphtheno[2,3-*e*]piaselenole with 5-phenylpiaselenole (14) indicates that the thianaphtheno band at 372 mμ, log ε 4.20 with a shoulder at approximately 410 mμ, the selenanaphtheno band at 375 mμ with a shoulder at about 410 mμ, and the phenylpiaselenole band at 346 mμ, log ε 4.24 with a shoulder at 372 mμ are evidently due to the piaselenole part of the molecule. This type of band system has been found in the spectra of other types of piaselenoles studied by the author (8, 14, 15).

On the basis of the spectroscopic work cited in this paper on dibenzothiophene, dibenzoselenophene, and carbazole derivatives, the proof of structure of many new dibenzothiophene, dibenzoselenophene, carbazole, and (probably) phenanthrene derivatives is now possible. For example, a large series of new dibenzoselenophene compounds (18) and a few carbazole derivatives (19) of uncertain structure have been recently synthesized. Through a determination of the spectra of several of the key derivatives it would now be fairly simple to prove their structure.

In future papers the assignment of bands as given here will be perfected, broadened, and used as a stepping stone to delve further into the field of molecular spectroscopy.

EXPERIMENTAL[2]

3-Acetylamino-4-nitrodibenzoselenophene. 3-Acetylaminodibenzoselenophene (6) (2.88 g., 0.01 mole) was dissolved in 18 ml. of hot acetic acid and cooled quickly. Then 1.2 ml. of fuming nitric acid (*d.* 1.5) was added dropwise at room temperature to the stirred solution. The yellow pasty mixture was allowed to stand a half hour, filtered, and crystallized from Methyl Cellosolve[3] to give 2.33 g. (70%) of bright orange needles, m.p. 254.5–255.5°.

Anal. Calc'd for $C_{14}H_{10}N_2O_3Se$: C, 50.5; H, 3.00; N, 8.41.
Found: C, 50.5; H, 3.00; N, 8.40.

3-Amino-4-nitrodibenzoselenophene. To a refluxing mixture of 3.4 g. of 3-acetylamino-4-nitrodibenzoselenophene in 50 ml. of Methyl Cellosolve was added 18 ml. of concentrated hydrochloric acid over 3 hours. Excess water was added to the mixture. The precipitate was crystallized from xylene to give 2.6 g. (90%) of red needles, m.p. 253–254°.

Anal. Calc'd for $C_{12}H_8N_2O_2Se$: C, 49.5; H, 2.75; N, 9.62.
Found: C, 49.5; H, 2.73; N, 9.62.

3,4-Diaminodibenzoselenophene. 3-Amino-4-nitrodibenzoselenophene in Methyl Cellosolve solution was reduced with a hydrochloric acid solution of stannous chloride by a standard procedure. Crystallization from heptane gave a 40–50% yield of yellowish crystals, m.p. 155–157°.

Anal. Calc'd for $C_{12}H_{10}N_2Se$: N, 10.7. Found: N, 10.3.

Selenanaphtheno[2,3-e]piaselenole. Reaction between 3,4-diaminodibenzoselenophene and an equivalent amount of selenium dioxide in hot Methyl Cellosolve solution gave the piaselenole in 80–90% yield. Crystallization from heptane gave yellow cottony crystals, m.p. 203–204°.

Anal. Calc'd for $C_{12}H_6N_2Se_2$: C, 42.9; H, 1.79; N, 8.33.
Found: C, 43.1; H, 1.68; N, 8.25.

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

SUMMARY

1. Spectrophotometric evidence has been presented to show that the nitration of 3-acetylaminodibenzoselenophene takes place in the 4-position.

2. 3-Acetylamino-4-nitrodibenzoselenophene, 3-amino-4-nitrodibenzoselenophene, 3,4-diaminodibenzoselenophene, and selenaphtheno[2,3-*e*]piaselenole have been prepared.

3. Many of the bands in dibenzothiophene and dibenzoselenophene derivatives have been assigned.

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[2] Melting points are not corrected. Analyses are by Rowland Chemical Laboratories, Jacksonville, Fla.

[3] 2-Methoxyethanol.

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