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

ABSORPTION SPECTRA OF SOME POLYPHENYL SEQUENCES[1]

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In a continuation of a study of the chemical, physical, and biological properties of carcinogenic amines and allied compounds, the spectral properties of some polyphenyl sequences were investigated. It is possible that the initiation of cancer comprises reactions at the molecular level involving a 'fit' between some type of aromatic carcinogen and a biological reaction site. This 'fit' would be dependent upon the molecular architecture of the reacting molecules. The authors believe that a clearer understanding of the absorption spectra of the aromatic carcinogens and allied compounds will eventually add to the knowledge of these important compounds.

Many aniline derivatives have been shown to be non-carcinogenic in rats or mice (1, 2) and appear also to be completely devoid of cancer-producing power in human beings (3–6). On the other hand 4-aminobiphenyl derivatives have been shown to be carcinogenic to rats (7–11) and benzidine has been stated to be carcinogenic to man (3, 5, 6).

In the next group of this series, the 4-amino-*p*-terphenyls, carcinogenicity data are apparently lacking. Since *ortho* substitution may be of some importance in carcinogenesis (7), a few *ortho* substituted derivatives of 4-amino-*p*-terphenyl were prepared. The nitration of 4-acetylaminobiphenyl gives the 3-nitro derivative (12). Similarly the nitration of 4-carbethoxyamino-*p*-terphenyl gives the 3-nitro derivative. This is shown by the fact that the derived diamine forms a piaselenole.

p-Dinitrobenzene is known to form complexes with aromatic amines and hydrocarbons. For example, aniline (13) and naphthalene (14) form colored complexes with *p*-dinitrobenzene. 4,4′-Dinitrobiphenyl has also been shown to form colored complexes with 4-aminobiphenyl, benzidine, and other biphenyl derivatives (15). In an analogous manner 4,4″-dinitro-*p*-terphenyl forms brilliantly colored complexes with benzidine, 4,4″-diamino-*p*-terphenyl, and 2,7-diaminofluorene.

The ultraviolet absorption spectra of the analogous benzene, biphenyl, and *p*-terphenyl derivatives in this paper show a striking, regular relationship. In general the spectra speak for themselves, Figs. 1–6.

EXPERIMENTAL[2]

2-Carbethoxyaminonitrobenzene (20), m.p. 56–57°; piaselenole (21), m.p. 75–76°; 3-nitro-4-acetylaminobiphenyl (22), m.p. 132°; 3-nitro-4-aminobiphenyl (22), m.p. 167–168°; and

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[2] Melting points are uncorrected. Analyses are by Peninsular ChemResearch, Inc., Gainesville, Florida.

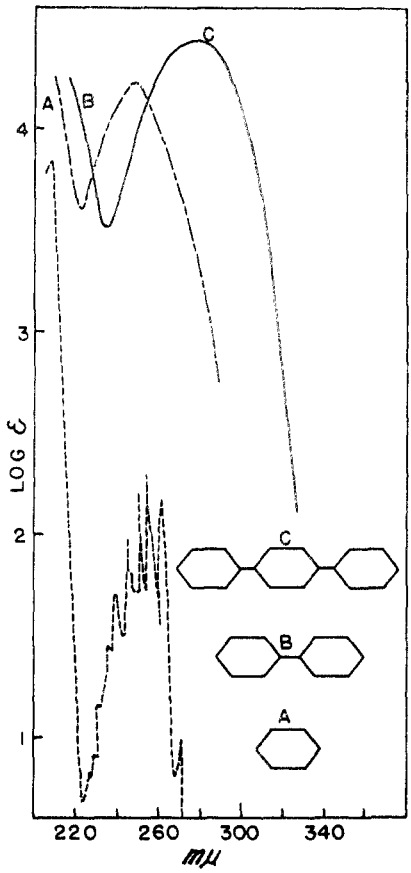

FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA: A, Benzene (16); B, Biphenyl; C, *p*-Terphenyl.

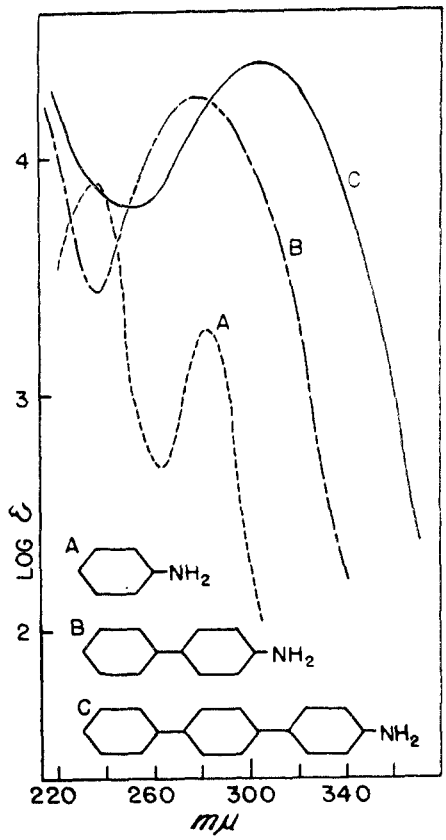

FIG. 2. ULTRAVIOLET ABSORPTION SPECTRA: A, Aniline (17); B, 4-Aminobiphenyl; C, 4-Amino-*p*-terphenyl.

4-amino-*p*-terphenyl (23), m.p. 200°, were each recrystallized from several diverse solvents to a constant sharp melting point which checked closely with literature values.

4,4″-Dinitro-p-terphenyl. The nitration of *p*-terphenyl in acetic acid with fuming nitric acid gave this dinitro compound (23). A preliminary investigation has disclosed that, like *p*-dinitrobenzene and 4,4′-dinitrobiphenyl, the terphenyl analog is a complexing agent. With benzidine, 4,4″-diamino-*p*-terphenyl and 2,7-diaminofluorene were formed yellow-brown needles, m.p. 268–269°, red plates, m.p. 307–309°, and red-brown crystals, m.p. 276–277°, respectively.

4,4″-Diamino-p-terphenyl. A melting point but no details of preparation could be found in the literature (24). A hot solution of 50 g. of hydrated stannous chloride in 80 ml. of concentrated hydrochloric acid was added to a hot solution of 7.0 g. of 4,4″-dinitro-*p*-terphenyl in 150 ml. of Methyl Cellosolve.[3] The mixture was refluxed for 3 hours. Colorless plates replaced the yellow needles. To a stirred suspension of the plates in 50 ml. of Methyl Cellosolve[3] was added concentrated ammonia. Water was added to the hot alkaline mixture to a definite turbidity. The solution was filtered and allowed to cool. The large colorless

[3] Trade name for 2-methoxyethanol.

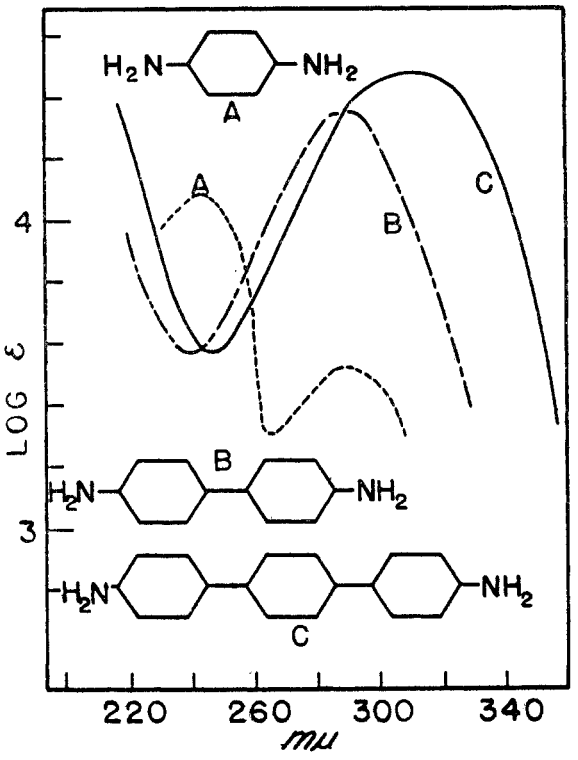

FIG. 3. ULTRAVIOLET ABSORPTION SPECTRA: A, *p*-Phenylenediamine (18); B, Benzidine (17); C, 4,4″-Diamino-*p*-terphenyl.

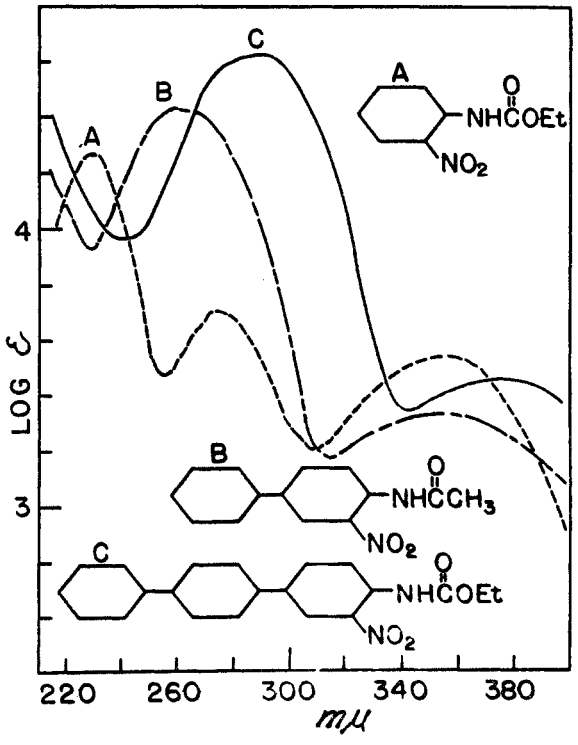

FIG. 4. ULTRAVIOLET ABSORPTION SPECTRA: A, 2-Nitro-1-carbethoxyaminobenzene; B, 3-Nitro-4-acetylaminobiphenyl; C, 3-Nitro-4-carbethoxyamino-*p*-terphenyl.

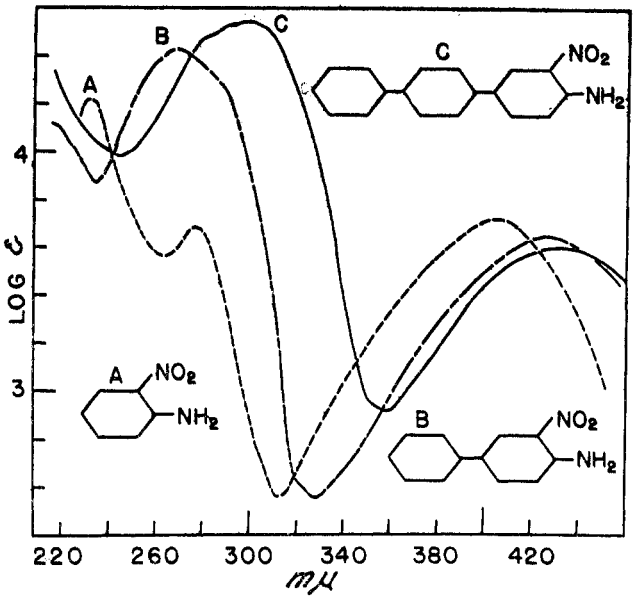

FIG. 5. ULTRAVIOLET ABSORPTION SPECTRA: A, 2-Nitroaniline (19); B, 3-Nitro-4-amino-biphenyl; C, 3-Nitro-4-amino-*p*-terphenyl.

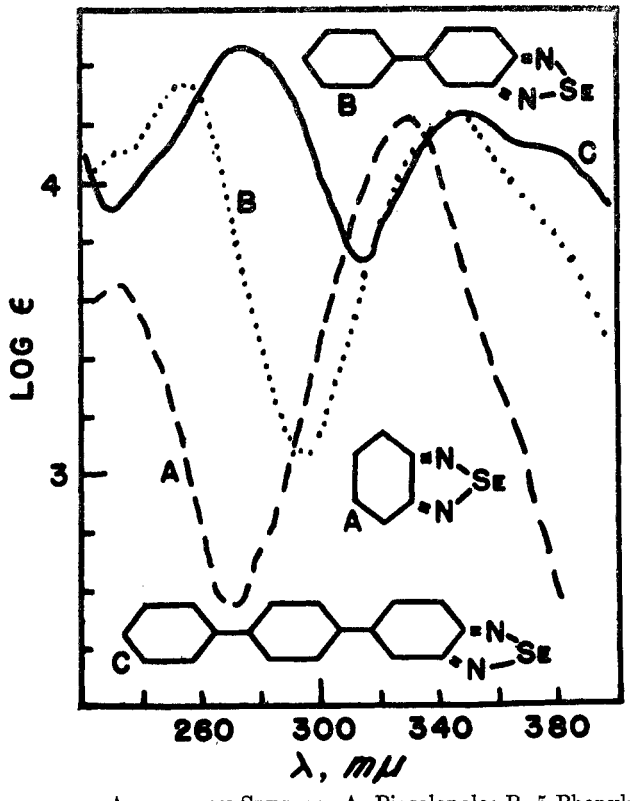

FIG. 6. ULTRAVIOLET ABSORPTION SPECTRA: A, Piaselenole; B, 5-Phenylpiaselenole; C, 5-Xenylpiaselenole.

plates (4.9 g., 91%) were crystallized from xylene, aqueous Methyl Cellosolve, or aqueous acetone to give colorless plates, m.p. 248–249°. Lit. m.p. 236°.

Anal. Calc'd for $C_{18}H_{16}N_2$: C, 83.1; H, 6.15; N, 10.8.
Found: C, 83.0; H, 6.12; N, 10.6.

5-Phenylpiaselenole. Selenium dioxide (0.14 g.) was added to a hot solution of 0.18 g. of 3,4-diaminobiphenyl in 5 ml. of alcohol. Following a half hour's refluxing, excess water was added. Crystallization of the precipitate from hexane gave 0.23 g. (88%) of light yellow plates, m.p. 102°. The compound gave a dark violet color in sulfuric acid.

Anal. Calc'd for $C_{12}H_8N_2Se$: N, 10.8. Found: N, 10.5.

3-Nitro-4-carbethoxyamino-p-terphenyl. The reaction between ethyl chlorocarbonate and 4-amino-*p*-terphenyl in pyridine gave the carbamate which was obtained as a colorless wax-like product from aqueous Methyl Cellosolve.

The nitro derivative was synthesized in an approximately 75% yield by the dropwise addition of 1 ml. of fuming nitric acid (*d.* 1.5) to a stirred suspension of 1.1 g. of 4-carbethoxyamino-*p*-terphenyl in 10 ml. of acetic acid at room temperature. The mixture was allowed to stand at room temperature for 3 hours and then was filtered. Crystallization from methanol gave yellow needles, m.p. 171–172°.

Anal. Calc'd for $C_{21}H_{18}N_2O_4$: C, 69.6; H, 5.0; N, 7.7.
Found: C, 69.7; H, 5.1; N, 7.5.

3-Nitro-4-amino-p-terphenyl. Hydrolysis of 3-nitro-4-carbethoxyamino-*p*-terphenyl in alkaline Methyl Cellosolve solution formed the nitroamine. Crystallization from xylene gave an 85–90% yield of red glistening crystals, m.p. 271–272°.

Anal. Calc'd for $C_{18}H_{14}N_2O_2$: C, 74.5; H, 4.8; N, 9.7.
Found: C, 74.6; H, 4.9; N, 9.6.

3,4-Diamino-p-terphenyl. To 0.29 g. of the finely powdered nitroamino-*p*-terphenyl suspended in 5 ml. of hot Methyl Cellosolve was added a hot solution of 1.4 g. of stannous chloride in 2 ml. of concentrated hydrochloric acid. The mixture was refluxed until it became almost colorless (about 1–2 hours), cooled, and then filtered. Treatment with alkali followed by crystallization from alcohol gave a 50–60% yield of colorless crystals, m.p. 199–200°.

Anal. Calc'd for $C_{18}H_{16}N_2$: N, 10.8. Found: N, 10.6.

5-Xenylpiaselenole. Reaction between 3,4-diamino-*p*-terphenyl and selenium dioxide in alcohol solution gave the piaselenole. Crystallization from alcohol gave an 85–90% yield of faint yellow crystals, m.p. 197–198°.

Anal. Calc'd for $C_{18}H_{12}N_2Se$: N, 8.36. Found: N, 8.40.

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

SUMMARY

Investigation of the absorption spectra of a series of analogous benzene, biphenyl, and *p*-terphenyl derivatives disclosed a strikingly regular relationship. New compounds studied were 4,4″-diamino-*p*-terphenyl, 5-phenylpiaselenole, 3-nitro-4-carbethoxyamino-*p*-terphenyl, 3-nitro-4-amino-*p*-terphenyl, 3,4-diamino-*p*-terphenyl, and 5-xenylpiaselenole.

4,4″-Dinitro-*p*-terphenyl was found to form brilliantly colored complexes with benzidine, 4,4″-diamino-*p*-terphenyl, and 2,7-diaminofluorene.

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