175–176°. A mixed melting point with the picrate of thiophene preamidone I melted at 175–176°.

6-Dimethylamino-4,4-di-(2-thienyl)-5-methyl-3-hexanone.—To an ethylmagnesium bromide–ether solution prepared from 0.88 g. (0.036 mole) of magnesium turnings, 4.4 g. (0.036 mole) of ethyl bromide and 10 ml. of anhydrous ether, 5.4 g. (0.019 mole) of 4-dimethylamino-2,2-di-(2-thienyl)-3-methylbutyronitrile in 10 ml. of dry xylene was added dropwise with stirring. A reaction ensued after which the mixture was heated on the steam-bath for three hours resulting in a gray precipitate. The hot mixture was then poured into 50 ml. of 50% hydrochloric acid. A vigorous reaction resulted causing much of the xylene to distil. Benzene was then added to the mixture and the resulting organic layer was separated. The cold acid solution was made basic with a 20% sodium hydroxide solution and extracted with ether. The ether solution was dried over anhydrous sodium sulfate and the ether then removed by distillation. The resulting precipitate of white needles was filtered and dried. Upon recrystallization from petroleum ether (60–75°), there was obtained 2.9 g. (48%) of 6-dimethylamino-4,4-di-(2-thienyl)-5-methyl-3-hexanone, b.p. 184° (2 mm.). The hydrochloride melted at 195–196°. A mixed melting point with a sample of the hydrochloride of thiophene amidone I melted at 195–196°. A mixed melting point with a sample of the hydrochloride of thiophene amidone II melted at 153–176°.

Acknowledgment.—We are indebted to the Nepera Chemical Company, Inc., for a grant-in-aid of this work.

NEW YORK 58, NEW YORK

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

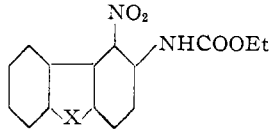
Preparation and Absorption Spectra of Analogous Dibenzothiophene, Dibenzoselenophene and Carbazole Compounds[1]

BY EUGENE SAWICKI

RECEIVED JUNE 11, 1954

The structure of 1,2- and 3,4-disubstituted dibenzoselenophene derivatives is proven by spectral comparison with the known iso-π-electronic dibenzothiophene and carbazole derivatives. Similarly a spectral proof of structure is given for 2-nitro-, 4-nitro-, 2,8-dinitro-, 2-acetyl-, 4-acetyl-, 2,8-diacetyl and 2(?),6-diacetyldibenzoselenophene. The spectra of these compounds, as well as those of 2- and 3-substituted azido and acylamino derivatives of dibenzothiophene, dibenzoselenophene and 9-methylcarbazole, are discussed.

Nitration of 2-carbethoxyaminodibenzothiophene has been shown to give the 1-nitro derivative I,[2] while nitration of the analogous 3-carbethoxyamino-9-methylcarbazole was found to give the 4-nitro derivative II.[3]



I, X = S; II, X = NMe; III, X = Se

The nitration of 2-carbethoxyaminodibenzoselenophene gives a nitro derivative whose spectrum[4] is similar to that of 2-carbethoxyamino-1-nitrodibenzothiophene[2] and 3-carbethoxyamino-4-nitro-9-methylcarbazole.[3] The derived nitroamines of the above compounds are closely similar spectrally, Fig. 1, as are the derived nitroamine hydrochlorides and piaselenoles. On the basis of the similarity of the spectral curves it is concluded that the nitration of 2-carbethoxyaminodibenzoselenophene gives the 1-nitro compound III. From these spectral curves, and additional spectral data in the literature,[2–7] it would seem that analogous dibenzothiophene, dibenzoselenophene and carbazole derivatives have fairly similar absorption spectra. This is of value in proof of structure studies and could be of great value in theoretical molecular spectroscopy work.

(1) This investigation was supported by research grants from the Damon Runyon Memorial Fund and Grant C-1066 from the National Cancer Institute, National Institutes of Health, Public Health Service.

(2) E. Sawicki, *J. Org. Chem.*, **19**, 608 (1954).

(3) E. Sawicki, THIS JOURNAL, **76**, 664 (1954).

(4) The ultraviolet absorption spectra of all compounds in this paper are available from the author.

(5) E. Sawicki and F. E. Ray, THIS JOURNAL, **74**, 4120 (1952).

(6) E. Sawicki and F. E. Ray, *J. Org. Chem.*, **18**, 946 (1953).

(7) E. Sawicki, *ibid.*, **18**, 1492 (1953).

In Fig. 1, the longest wave length band in all three compounds is an *o*-nitroaniline band; in the carbazole derivative the effect of the ring nitrogen is to push this band further into the visible.

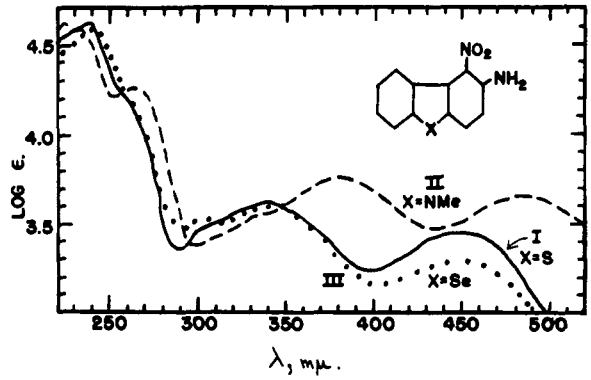


Fig. 1.—I, 2-Amino-1-nitrodibenzothiophene[2] (——); II, 3-amino-4-nitro-9-methylcarbazole[3] (– – –); III, 2-amino-1-nitrodibenzoselenophene (. . . .).

A comparison of the melting points illustrates further the remarkable resemblance among these substances. Compounds I, II and III melt within a range of 189 ± 5°, at 189–190°, 184–185° and 194°, respectively. In the nitroamines derived from I, II and III the melting points have a range of 156 ± 10°, at 165–166°, 145–146° and 154–155°, respectively, while in the piaselenoles derived from I, II and III the melting points have a range of 180 ± 4°; at 176–177°, 180–181° and 184°, respectively.

The nitration of 2-*p*-tosylaminodibenzoselenophene followed by deacylation gave a mixture of nitroamines out of which one main product, m.p. 247–248.5°, was isolated. The absorption spectrum of this derivative is closely similar to the spec-

trum of 2-amino-3-nitrodibenzothiophene,[2] m.p. 246–247°, fairly similar to the spectrum of 3-amino-2-nitrocarbazole, m.p. 233°, Fig. 2 (range in m.p. for these 3-nitroamines is 241 ± 8°) and dissimilar from the spectrum of 2-amino-1-nitrodibenzoselenophene, m.p. 154–155°, Fig. 1. The spectrum of the new nitroamine in strong alcoholic sulfuric acid was also closely similar to the spectra of 3-nitrodibenzothiophene and 2-amino-3-nitrodibenzothiophene sulfate.[2]

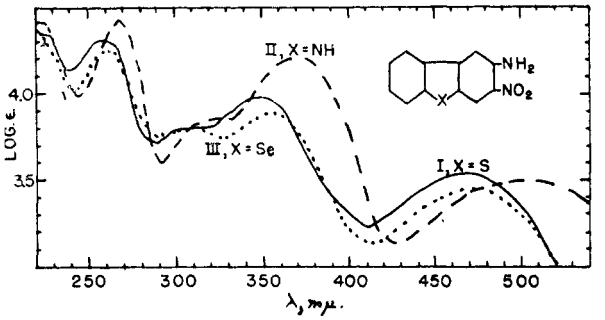


Fig. 2.—I, 2-Amino-3-nitrodibenzothiophene[2] (——); II, 3-amino-2-nitrocarbazole[3] (– – –); III, 2-amino-3-nitrodibenzoselenophene (....).

The 2,3-disubstituted dibenzothiophene and carbazole nitroamines have their *o*-nitroaniline bands at 470 mμ, log ε 3.54, and 500 mμ, log ε 3.50, respectively, while the new nitroamine has a band, which must be an *o*-nitroaniline band at 470 mμ, log ε 3.45. Consequently the new compound is 2-amino-3-nitrodibenzoselenophene.

The nitration of dibenzoselenophene was investigated further. The yield of 2-nitrodibenzoselenophene was doubled over that previously reported.[5] Two main by-products were obtained. One was a mononitro derivative, m.p. 160–161°, which is spectrally similar to 4-nitrodibenzothiophene, m.p. 161°, and 1-nitrocarbazole,[8] Fig. 3. The spectrum of this new nitro derivative is similar also to the spectrum of 3-amino-4-nitrodibenzoselenophene hydrochloride[9] and dissimilar from the spectra of 2-nitrodibenzoselenophene,[5] 3-nitrodibenzothiophene[2] and

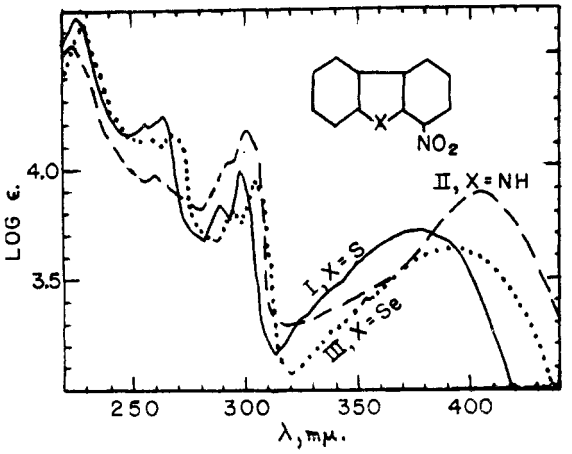


Fig. 3.—I, 4-Nitrodibenzothiophene[7] (——); II, 1-nitrocarbazole[8] (– – –); III, 4-nitrodibenzoselenophene (....).

(8) W. Schroeder, P. Wilcox, K. Trueblood and A. Dekker, *Anal. Chem.*, **23**, 1740 (1951).

2-amino-1-nitrodibenzoselenophene hydrochloride.[4] Just as the spectra of 2-nitrodiphenyl sulfide[10] and 4-nitrodibenzothiophene[7] show *o*-nitrothiophenol bands at wave lengths 368 mμ, log ε 3.65 and 375 mμ, log ε 3.72, respectively, so do 2-nitrodiphenyl selenide[11] and the new nitrodibenzoselenophene have their analogous *o*-nitro bands at wave lengths 386 mμ, log ε 3.62, and 392 mμ, log ε 3.64, respectively. Consequently this new compound must be 4-nitrodibenzoselenophene.

The other by-product was found to be a dinitro derivative (λ_{max} 268, 334–338 and log ε 4.53, 4.15) whose spectrum was almost identical to that of 2,8-dinitrodibenzothiophene (λ_{max} 266, 324–332 and log ε 4.53, 4.10). This dinitro derivative also was synthesized from 2-nitrodibenzoselenophene and from dibenzoselenophene itself. Therefore, the evidence indicates that the dinitro derivative is 2,8-dinitrodibenzoselenophene.

The acetylation of dibenzoselenophene gave at least four products. The acetyldibenzoselenophenes (like the analogous nitrodibenzoselenophenes) were found to pass through alumina when dissolved in benzene–hexane in the order: 4-, 2-, polysubstituted derivatives. The spectra of the acetyldibenzoselenophene, m.p. 143–145° (λ_{max} 223, 242, 264,[12] 298, 362 and log ε 4.46, 4.52, 4.24, 4.01, 3.62, respectively), and 4-acetyldibenzothiophene, m.p. 129–130° (λ_{max} 222, 238, 257, 291, 353 and log ε 4.51, 4.59, 4.29, 4.07, 3.68, respectively), are closely similar, and resemble the spectrum of 4-nitrodibenzothiophene, Fig. 3, fairly closely. The long wave length band of these two compounds must arise mainly from the interaction of the ortho sulfur or selenium atoms with the acetophenone grouping. The two acetyl compounds contain no other groups or combinations of groups that are capable of such low energy electronic oscillations. Therefore, the acetyldibenzoselenophene, m.p. 143–145°, is the 4-derivative. The other acetyl derivative, m.p. 116–117° (λ_{max} 243, 270, 296, 316 and log ε 4.67, 4.30, 4.04, 3.92), has a spectral envelope closely similar to the spectrum of 2-acetyldibenzothiophene, m.p. 111° (λ_{max} 239, 247, 266, 290, 315 and log ε 4.66, 4.60, 4.39, 4.13, 3.82, respectively), so evidently it is 2-acetyldibenzoselenophene. A comparison of the infrared spectra of the 2- and 4-acetyl derivatives of dibenzothiophene and dibenzoselenophene further strengthens the assignments. The 4-acetyl derivatives of dibenzothiophene and dibenzoselenophene are very closely similar spectrally in the infrared and yet differ considerably from the 2-acetyl derivatives which are also spectrally similar to a large extent.

In the acetylation of dibenzoselenophene Buu-Hoi[13] obtained a monoacetyl derivative, m.p. 134°, and a diacetyl derivative, m.p. 213°, both compounds with positions of substitution unknown. As these compounds are difficult to purify it is possible that the lower melting compound is impure

(9) E. Sawicki, *J. Org. Chem.*, **19**, 1163 (1954).

(10) A. Mangini and R. Passerini, *J. Chem. Soc.*, 1168 (1952).

(11) L. Chierici and R. Passerini, *Atti accad. nazl. Lincei, Rend Classe sci. fis., mat. e nat.*, [8] **15**, 69 (1953).

(12) Underlined values are shoulders.

(13) N. Buu-Hoi and H. Hoan, *J. Org. Chem.*, **17**, 643 (1952).

4-acetyldibenzoselenophene, m.p. 143–145°. A diacetyl derivative, m.p. 213–215°, also was obtained in the present work. Its absorption spectrum (λ_{max} 236, 259, 304, 356 and log ϵ 4.48, 4.61, 4.18, 3.80, respectively), was fairly similar to the spectrum of 4-acetyldibenzoselenophene, and dissimilar from the spectrum of 2,8-diacetyldibenzothiophene. The long wave length band at 356 mμ is evidently associated with the *o*-selenoacetophenone group. As the spectrum of the compound resembles the spectrum of 4-acetyldibenzoselenophene so closely with a probable contribution from a 2-acetyl group, the evidence favors the 2(?),6-diacetyldibenzoselenophene structure. The other isolated diacetyl derivative, m.p. 244–245° (λ_{max} 230, 264, 301 and log ϵ 4.20, 4.72, 4.20, respectively), spectrally resembles 2,8-diacetyldibenzothiophene (λ_{max} 227, 260, 296 and log ϵ 4.13, 4.83, 4.24, respectively), has no apparent contribution from a 4-acetyl group, and consequently must be 2,8-diacetyldibenzoselenophene.

The 4-acetyl and 4-nitro derivatives of dibenzothiophene and dibenzoselenophene have absorption spectra that are somewhat similar to the spectra of the parent heterocyclic systems.

Eyster and Gillette[14] have shown in infrared studies that hydrazoic acid has stretching frequencies at 4.67 and 7.88 μ, while methyl azide has its comparable frequencies at 4.67 and 7.72 μ. In a study of the Raman spectra of organic azides the antisymmetric stretching frequency of the azido group is stated to range from 4.61 to 4.8 μ while the symmetrical stretching frequency ranges from 7.45 to 8.50 μ.[15] The infrared spectra of the azides of dibenzothiophene, dibenzoselenophene and carbazole have a very strong band at 4.75 μ and a strong band at 7.75 ± 0.1 μ.[4] These are apparently the stretching frequencies of the azido group. Each of these bands has several moderate to weak bands adjacent to it which may be associated with the azido stretching frequencies.

The ultraviolet absorption spectra of the azido derivatives of dibenzothiophene, dibenzoselenophene and carbazole are very closely similar to the spectra of their analogous acylamino derivatives. From the data it would seem that the azido and acylamino groups interact with the parent heterocyclic systems to approximately the same extent.

Experimental[16]

2-Carbethoxyamino-1-nitrodibenzoselenophene.—To a stirred suspension of 7.65 g. of 2-carbethoxyaminodibenzoselenophene[5] in 120 ml. of glacial acetic acid at room temperature was added 5.3 ml. of nitric acid (d. 1.5). The mixture solidified after standing one hour. Crystallization from heptane gave 7.1 g. (82%) of gleaming, yellow cottony needles, m.p. 194°.

Anal. Calcd. for $C_{15}H_{12}N_2O_4Se$: C, 49.6; H, 3.31; N, 7.7. Found: C, 49.8; H, 3.38; N, 7.6.

2-Amino-1-nitrodibenzoselenophene.—Twelve ml. of aqueous 20% potassium hydroxide was added to a hot solution of 3.6 g. of 2-carbethoxyamino-1-nitrodibenzoselenophene in 50 ml. of alcohol. The mixture was refluxed vigorously for four hours and then poured into excess water. Crystallization from aqueous methanol or a large volume of heptane gave 2.7 g. (93%) of red-orange crystals, m.p. 154–155°.

Anal. Calcd. for $C_{12}H_6N_2O_4Se$: N, 9.6. Found: N, 9.6.

1,2-Diaminodibenzoselenophene.—A solution of the nitroamine in alcohol was reduced by a hydrochloric acid solution of stannous chloride and the diamine was isolated by standard procedure. Crystallization from heptane gave a 55–60% yield of crude, colorless needles, m.p. 75°, which were used to make the piaselenole derivative.

Anal. Calcd. for $C_{12}H_{10}N_2Se$: N, 10.7. Found: N, 10.2.

Selenaphtheno[3,2-e]piaselenole.—Reaction between 1,2-diaminodibenzoselenophene and an equivalent amount of selenium dioxide in hot methanol solution gave the piaselenole in 80–90% yield. Crystallization from a large volume of methanol or from heptane gave gleaming yellow needles, m.p. 184°.

Anal. Calcd. for $C_{12}H_6N_2Se_2$: C, 42.9; H, 1.79; N, 8.33. Found: C, 42.8; H, 1.80; N, 8.23.

2-*p*-Tosylaminodibenzoselenophene.—*p*-Toluenesulfonyl chloride (11.5 g.) was added to a stirred solution of 9.35 g. of 2-aminodibenzoselenophene in 40 ml. of pyridine at 0–10°. The mixture was then refluxed for 5–10 minutes, cooled and added to excess water. Crystallization of the precipitate from aqueous acetic acid or benzene–hexane gave 13.7 g. (90%) of large colorless crystals, m.p. 138–140°.

Anal. Calcd. for $C_{19}H_{15}NO_2SSe$: C, 57.0; H, 3.75. Found: C, 57.1; H, 3.69.

2-Amino-3-nitrodibenzoselenophene.—Nine ml. of fuming nitric acid (d. 1.5) was added dropwise to a suspension of 9.25 g. of 2-*p*-tosylaminodibenzoselenophene in 60 ml. of acetic acid at room temperature. The temperature shot up to 55° but was quickly cooled to 30°. The mixture was allowed to stand 0.5 hour and then filtered.

The crude, dried, nitrated 2-*p*-tosylaminodibenzoselenophene (9.75 g.) was suspended in 90 ml. of concentrated sulfuric acid. After an half-hour of stirring the clear yellow-brown solution was poured upon ice. The dried red precipitate was extracted with boiling xylene. Evaporation of most of the xylene gave black crystals which were crystallized from methyl Cellosolve to give 2.0 g. (30%) of red crystals, m.p. 247–248.5°.

Anal. Calcd. for $C_{12}H_8N_2O_2Se$: C, 49.5; H, 2.75; N, 9.62. Found: C, 49.5; H, 2.75; N, 9.66.

2-Nitrodibenzoselenophene.—Dibenzoselenophene was nitrated by the procedure previously reported.[5] The yield of the 2-nitro compound was doubled (80% yield) with the extra product obtained through chromatography of mother liquor products.

4-Nitrodibenzoselenophene.—The mother liquor from the nitration of dibenzoselenophene and the mother liquor obtained from the crystallization of the crude 2-nitro compound from methanol were poured into excess water. The dried precipitate was dissolved in benzene–hexane (1:1) and chromatographed on alumina with the same solvent. The 4-nitro derivative was eluted first followed by the 2-nitro isomer with the dinitrated products remaining near the top of the column. The crude 4-nitro compound was crystallized several times from methanol to give an 8% yield of golden-yellow needles, m.p. 160–161°.

Anal. Calcd. for $C_{12}H_7NO_2Se$: C, 52.2; H, 2.54; N, 5.07. Found: C, 52.2; H, 2.55; N, 5.00.

2,8-Dinitrodibenzoselenophene.—(a) The dinitrated dibenzoselenophenes were eluted from the column (see preparation of 4-nitrodibenzoselenophene) with acetone. Several crystallizations from xylene gave an approximately 0.1% yield of yellow needles, m.p. 339–342°. (b) To a thick suspension of 2.76 g. of 2-nitrodibenzoselenophene in 100 ml. of acetic acid at 80° was added 9 ml. of fuming nitric acid (d. 1.5). The clear solution was kept at 85–90° until crystals started to come out (about 10–30 minutes). It was then allowed to cool to room temperature and filtered. Crystallization from methyl Cellosolve and then from xylene gave 2.25 g. (70%) of gleaming yellow crystals, m.p. 342–343°. (c) To 2.3 g. of dibenzoselenophene in 20 ml. of acetic acid at 50° was added 10 ml. of fuming nitric acid (d. 1.5). The temperature shot up to 70–80° and the mixture solidified. It was heated at 85° for 15 minutes and

(14) E. Eyster and R. Gillette, *J. Chem. Phys.*, **8**, 369 (1940).

(15) Y. Sheinker and Y. Syrkin, *Izvest. Akad. Nauk. S.S.S.R. Ser. Fiz.*, **14**, 478 (1950); *C. A.*, **45**, 3246 (1951).

(16) All melting points are uncorrected. Analyses are by Peninsular ChemResearch, Inc., Gainesville, Fla.

then allowed to cool. Crystallization from methyl Cellosolve, xylene and then acetic acid gave 1.86 g. (58%) of feathery yellow needles, m.p. 340–342°.

The mixed melting points of (a), (b) and (c) showed these compounds to be identical.

Anal. Calcd. for $C_{12}H_6N_2O_4Se$: C, 44.9; H, 1.87; N, 8.72. Found: C, 44.9; H, 1.84; N, 8.58.

2-Acetyldibenzoselenophene.—*Dibenzoselenophene* was acetylated by Buu-Hoi's directions.[13] The crude oily solid was dissolved in benzene and chromatographed through alumina; the developing solvent was benzene–heptane. The starting product came through first, followed by the monoacetylated compounds. The polyacetylated derivatives had to be eluted from the column with acetone. The middle fraction was dissolved in benzene and chromatographed as before. The 4-acetyl derivative came through first followed by the 2-isomer. Crystallization of the second fraction from methanol gave an approximately 10% yield of colorless needles, m.p. 116–117°.

Anal. Calcd. for $C_{14}H_{10}OSe$: C, 61.5; H, 3.66. Found: C, 61.7; H, 3.73.

4-Acetyldibenzoselenophene.—The crude acetyl derivative obtained from chromatography was crystallized out of methanol to give an approximately 10% yield of colorless crystals, m.p. 143–145°.

Anal. Calcd. for $C_{14}H_{10}OSe$: C, 61.54; H, 3.66. Found: C, 61.5; H, 3.50.

2(?),6-Diacetyldibenzoselenophene.—The polyacetylated fraction obtained through chromatography was fractionally crystallized from benzene. A small amount of colorless needles was obtained, m.p. 213–215°, lit.[13] m.p. 213°

2,8-Diacetyldibenzoselenophene.—Crystallization of the polyacetylated fraction from xylene, alcohol and then nitrobenzene gave a small amount of colorless needles, m.p. 244–245°.

Anal. Calcd. for $C_{16}H_{12}O_2Se$: C, 61.0; H, 3.81. Found: C, 60.9; H, 3.70.

2-Azido-9-methylcarbazole.—The general preparation of the azido compounds, physical properties of which are given in Table I, is essentially as described for the carbazole derivative.

TABLE I

AZIDO DERIVATIVES

Compound	M.p., °C.	Yield, %	Nitrogen, % Calcd.	Found
2-Azidodibenzothiophene	117–118	94	18.7	18.5[a]
3-Azidodibenzothiophene	107–108	90	18.7	18.6
2-Azidodibenzoselenophene	96–97	92	15.4	15.3
3-Azidodibenzoselenophene	85–86	89	15.4	15.4
3-Azido-9-methylcarbazole	81–82	79	25.2	25.1
2-Azido-9-methylcarbazole	109–110	93	25.2	24.9[b]

[a] *Anal.* Calcd. for $C_{12}H_7N_3S$: C, 64.0; H, 3.11. Found: C, 63.9; H, 3.22. [b] *Anal.* Calcd. for $C_{13}H_{10}N_4$: C, 70.3; H, 4.50. Found: C, 70.3; H, 4.58.

To a finely divided stirred suspension of 2.0 g. (0.01 mole) of 2-amino-9-methylcarbazole in 7 ml. of water and 2.5 ml. (0.03 mole) of concentrated hydrochloric acid was added dropwise 0.83 g. (0.012 mole) of sodium nitrite in 5 ml. of water. The mixture was filtered and the filtrate cooled to 0–10°; red needles of the diazonium chloride precipitated out. To this cold stirred mixture a solution of 0.72 g. (0.011 mole) of sodium azide in 7 ml. of water was added dropwise and the foamy mixture allowed to stand for one hour. Filtration and crystallization from aqueous ethanol gave 2.06 g. (93%) of gleaming crystals, m.p. 109–110°.

Ultraviolet Absorption Spectra.—All ultraviolet absorption spectra were determined with a Beckman model DU quartz spectrophotometer in 95% ethanol unless otherwise stated. Infrared absorption spectra were measured with a Perkin-Elmer model 21 infrared spectrophotometer.

Acknowledgment.—The author is indebted to Dr. Francis E. Ray for his encouragement and interest in this work and to Miss Mary Louise Van Natta of the Chemistry Department of the University of Florida for determining the infrared spectra.

GAINESVILLE, FLA.

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, THE ARMOUR LABORATORIES]

Synthesis of Compounds Related to Thymine. I. 5-Mercaptouracil and Some S-Substituted Derivatives

BY THOMAS J. BARDOS, ROSS R. HERR AND TAKASHI ENKOJI

RECEIVED AUGUST 27, 1954

5-Mercaptouracil, 5-uracilyl disulfide and uracil-5-isothiouronium chloride have been synthesized from 5-aminouracil by way of the diazonium salt. These compounds are competitive antagonists of thymine.

Structural analogs of thymine are of biochemical and possibly of chemotherapeutic interest as potential inhibitors (anti-metabolites) of desoxyribonucleic acid synthesis. Several simple analogs are known, including those in which one or both of the oxygens in the thymine molecule are replaced by sulfur (thiothymines),[1,2] or in which the 5-methyl group is replaced by a halogen,[3–5] nitro,[4,6] amino[7] or hydroxyl[8] group.

Most of these compounds inhibit the growth of microörganisms under certain conditions. The inhibitory effect of some, however, can be reversed by metabolites other than thymine (*e.g.*, uracil, folic acid).[9,10] Others, such as 5-bromouracil, can be incorporated into the desoxyribonucleic acids in place of thymine.[11] These latter compounds therefore may act as thymine substitutes rather than inhibitors, depending on the composition of the growth media.[10,11]

In the search for thymine antagonists that would competitively block the utilization of thymine in the presence as well as in the absence of folic acid, and which would not replace thymine as a substitute metabolite, we have synthesized a group

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(2) G. B. Elion and G. H. Hitchings, THIS JOURNAL, **69**, 2138 (1947).

(3) T. B. Johnson, *Am. Chem. J.*, **40**, 27 (1908).

(4) H. L. Wheeler and H. F. Merriam, *ibid.*, **29**, 486 (1903).

(5) T. B. Johnson and C. O. Johns, *J. Biol. Chem.*, **1**, 310 (1906).

(6) H. L. Wheeler and H. S. Bristol, *Am. Chem. J.*, **33**, 441 (1905).

(7) E. Fisher, *Ann.*, **239**, 193 (1887).

(8) R. Behrend, *ibid.*, **229**, 39 (1885).

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(10) G. H. Hitchings, G. B. Elion and E. A. Falco, *J. Biol. Chem.*, **185**, 547 (1950).

(11) F. Weygand, A. Wacker and H. Dellweg, *Z. Naturforsch.*, **7b**, 19 (1952).