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SYNTHESIS OF METHYL-SUBSTITUTED THIAZOLE BASES WITH A CONDENSED FURAN, THIOPHENE, OR SELENOPHENE RING

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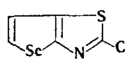
Methyl-substituted heterocyclic bases with a furan, thiophene, or selenophene ring condensed with a thiazole ring were synthesized by heating the appropriate o-bromo acetamido derivatives with phosphorus pentasulfide or by oxidation of thioacyl compounds with potassium ferricyanide in alkaline media.

Methyl-substituted thieno- and benzothienothiazoles have been previously synthesized [1-5]. Polymethine dyes of various types have been obtained from the quaternary salts of bases of this type, and their color has been studied [6-8]. It seemed of interest to obtain dyes based on derivatives of heterocyclic bases containing a selenophene or furan ring condensed with the thiazole ring and to study their spectral and photographic properties.

In the present communication we describe the synthesis of methyl-substituted selenopheno-, benzofuro-, and benzoselenopheno[2,3-d]thiazoles (I-III).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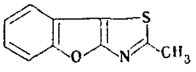
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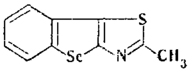
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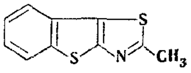
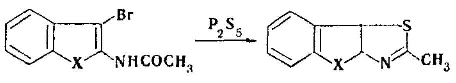

IV

2-Methylselenopheno[2,3-d]thiazole (I) was synthesized by acetylation of 2-aminoselenophene by the action of phosphorus pentasulfide on the acetamido derivative and subsequent oxidation of 2-thioacetamidoselenophene with potassium ferricyanide in alkaline media. 2-Methylbenzofuro[2,3-d]thiazole (II) and 2-methylbenzofuro[2,3-d]thiazole (IV), which was previously obtained by a different method [3], were synthesized similarly from the corresponding amino derivatives of benzofuran and benzothiophene. Base II was also synthesized by bromination of 2-acetamidobenzofuran and by heating phosphorus pentasulfide with 2-acetamido-3-bromobenzofuran (V, X=O).


V II, III

II X=O; III X=Se; V X=O, Se

2-Methylbenzoselenopheno[2,3-d]thiazole (III) was similarly obtained from 2-acetamido-3-bromoselenophene (V, X=Se).

It should be noted that II is not formed in the reduction of 2,2'-dinitro-3,3'-benzofuryl disulfide under various conditions because of facile opening of the furan ring in this case to give an intermediate amino deriva-

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tive. The 2-hydroxycoumarain ester of iminothioacetic acid was obtained instead of the expected II in the reaction of 3-bromo-2-coumaranone with thioacetamide.

EXPERIMENTAL

The UV spectra of the compounds were recorded with an SF-4 spectrophotometer. The IR spectra were recorded with a UR-10 spectrometer. The PMR spectrum of II in $CDCl_3$ was recorded with a Varian T-60 spectrometer.

2-Acetamidoselenophene. The double tin salt of 2-aminoselenophene hydrochloride was obtained by reduction of 17.5 g (0.1 mole) of 2-nitroselenophene [9] with 90 g of stannous chloride in 230 ml of concentrated hydrochloric acid for 2.5-3 h at 43-45 deg C; workup gave the product in 50% yield. A mixture of 13.6 g (0.12 mole) of acetic anhydride and 20 ml of ether was added dropwise to a suspension of 25 g (0.04 mole) of the double salt in 60 ml of water at 0-5 deg C, after which a solution of 26 g of sodium hydroxide in 60 ml of water was added dropwise, and the mixture was stirred at 0-5 deg C for 30 min. The ether was then removed in vacuo, and the solid material was removed by filtration and washed with water to give 3.8 g (51.3%) of colorless prisms (from benzene) with mp 134-135 deg C. Found: C 38.4; H 3.6; N 7.4%. C_6H_7NOSe. Calculated: C 38.3; H 3.7; N 7.5%.

2-Thioacetamidoselenophene. This compound was obtained by the action of 8.5 g (0.038 mole) of phosphorus pentasulfide on 18.7 g (0.1 mole) of 2-acetamidoselenophene in anhydrous pyridine at 85-95 deg C for 30 min by the method in [10]. Workup gave 5.7 g (28%) of light-yellow prisms (from alcohol) with mp 121-122 deg. Found: C 35.5; H 3.4; S 15.6%. C_6H_7NSSe. Calculated: C 35.3; H 3.45; S 15.7%.

2-Methylselenopheno[2,3-d]thiazole (I). This compound was synthesized by oxidation of 2-thioacetamidoselenophene by the method in [1]. Workup gave 0.64 g (9.2%) of a light-yellow oil with bp 107-110 deg (7 mm). Found: C 35.65; H 2.4; N 6.9%. C_6H_5NSSe. Calculated: C 35.6; H 2.5; N 7.0%.

o-Hydroxyphenylacetic Acid Lactone (2-Coumaranone). A 2.4-g sample of concentrated hydrochloric acid was added to a solution of 3.74 g (0.02 mole) of benzofuran-2-carboxylic acid azide [11] in 20 ml of glacial acetic acid, and the mixture was refluxed gently for 15-30 min. It was then vacuum evaporated, and the residue (an oil) was treated with ether. The ether extract was dried with sodium sulfate, and the ether was removed by distillation. The residue was fractionated, and the fraction with bp 247-255 deg C was collected to give 1.7 g (65%) of product, which solidified to give rhombic needles with mp 48°C (49°C) (mp 47-48 deg C [12, 13]).

3-Bromo-2-coumaranone. A solution of 5 g (0.02 mole) of dioxane dibromide in 20 ml of ether was added with stirring to a solution of 2.7 g (0.02 mole) of 2-coumaranone in 15 ml of ether (the reaction was initiated by UV light). After the ether solution became colorless, it was washed with water and dried with sodium sulfate. The ether was removed by vacuum distillation, and the residue was treated with water. The solid material was removed by filtration, washed, and air dried to give 3.8 g (88%) of a product with mp 87-88 deg C. Recrystallization from petroleum ether gave colorless needles with mp 95-96 deg C. UV spectrum (in alcohol), λ_{max} (log ε): 278 nm (4.34). IR spectrum (Nujol): 2950 and 2880 (ν_{C-H} and ν_{CH_2}); 1813 cm^{-1} ($\nu_{C=O}$).

2-Hydroxy-3-coumaranyl Iminothioacetate Hydrobromide. A 2.14-g (0.01 mole) sample of 3-bromo-2-coumaranone was added to a solution of 0.8 g (0.0106 mole) of thioacetamide in 3.0 ml of anhydrous ethanol, and the mixture was refluxed for 3 h. The alcohol was then removed by vacuum distillation, and the residue was treated with anhydrous benzene. The resulting precipitate was removed by filtration and washed with benzene and ether to give 1.35 g (47%) of colorless crystals (from alcohol) with mp > 300 deg C. UV spectrum (in alcohol), λ_{max} (log ε): 322 (4.95) and 247 nm (4.93). IR spectrum (KBr): 2600-2900 cm^{-1} (ν_{OH}). Found: Br 27.6; S 11.1%. $C_{10}H_9NO_2S \cdot HBr$. Calculated: Br 27.7; S 11.1%.

2-Acetamidobenzofuran. A solution of isocyanate, prepared by heating 37.4 g (0.2 mole) of benzofuran-2-carboxylic acid azide in 200 ml of anhydrous xylene at 120-125 deg C for 1 h in a stream of nitrogen, was added with stirring to a solution of methylmagnesium iodide, obtained from 28.4 g (0.2 mole) of methyl iodide and 4.6 g (0.2 g-atom) of magnesium in 300 ml of anhydrous ether at 0-5 deg in a stream of nitrogen, after which the mixture was stirred with cooling for 1 h. A solution of 20 g of ammonium chloride in 100 ml of water was then added with cooling, and the reaction product was extracted with benzene. The benzene solution was washed with water, dried, and evaporated. The residue was chromatographed on neutral ammonium oxide in benzene to give 15 g (43%) of a product with mp 121-123 deg C. Recrystallization from benzene gave colorless plates with mp 129-130 deg C. IR spectrum (KBr): 3440-3480 (ν_{NH}); 3075 (ν_{C-H}); 1615, 1253, and 1109 cm^{-1} (characteristic ring bands). Found: C 68.4; H 5.1; N 7.8%. $C_{10}H_9NO_2$. Calculated: C 68.5; H 5.1; N 8.0%.

2-Acetamido-3-bromobenzofuran. A solution of 16 g (0.1 mole) of bromine in 100 ml of ether was added at 10-15 deg C to a solution of 17.5 g (0.1 mole) of 2-acetamidobenzofuran in 400 ml of chloroform, and the mixture was stirred at room temperature for 1 h. It was then vacuum evaporated, and the residue was chromatographed on neutral aluminum oxide in benzene to give 19.3 g (76%) of colorless prisms (from benzene) with mp 134-135 deg C. Found: C 47.0; H 3.1; Br 31.3%. $C_{10}H_8BrNO_2$. Calculated: C 47.2; H 3.1; Br 31.5%.

2-Thioacetamidobenzofuran. A 2-g sample of phosphorus pentasulfide was added in the course of 15-20 min to a refluxing solution of 4.05 g (0.023 mole) of 2-acetamidobenzofuran in 130 ml of anhydrous benzene, after which the mixture was refluxed with stirring for 2 h. The benzene layer was then decanted, and the residue was treated with 130 ml of boiling benzene. The combined benzene solutions were extracted with 4% sodium hydroxide solution, and the alkaline solution was filtered. The filtrate was cooled with ice water and acidified with dilute (1 : 1) hydrochloric acid, and the precipitate was removed by filtration, washed with water, and dried to give 1.6 g (36%) of a product with mp 88-89 deg C. Recrystallization from alcohol gave light-yellow prisms with mp 94-95 deg C. Found: C 62.6; H 4.6; N 7.1%. $C_{10}H_9NOS$. Calculated: C 62.8; H 4.7; N 7.3%.

2-Methylbenzofuro[2,3-d]thiazole (II). A) This compound was obtained by heating 3.8 g (0.015 mole) of 2-acetamido-3-bromobenzofuran and 2.5 g of phosphorus pentasulfide at 130-140 deg C [5] for 5 min. Workup gave colorless needles (from petroleum ether) with mp 51-52 deg C in 8.6% yield. PMR spectrum ($CDCl_3$), δ: 2.75 (s, CH_3) and 7.1 ~ 7.5 ppm (m, aromatic protons). Found: C 63.2; H 3.7; N 7.4; S 16.9%. $C_{10}H_7NOS$. Calculated: C 63.5; H 3.7; N 7.4; S 16.9%.

B) This compound was also obtained by the addition of a solution of 7.65 g (0.04 mole) of 2-thioacetamidobenzofuran in 100 ml of 5% sodium hydroxide solution to 270 ml of 10% potassium ferricyanide solution at 0-5 deg C (see [3]). Workup gave colorless needles (from petroleum ether) with mp 51-52 deg C in 35% yield.

2-Acetamidobenzo[b]selenophene. This compound was obtained by acetylation of 10 g of the double tin salt of 2-aminobenzoselenophene hydrochloride by the method in [14]. Workup gave 3.3 g of light-brown plates (from benzene) with mp 201-202 deg C. Found: C 50.5; H 3.9; N 5.8%. $C_{10}H_9NOSe$. Calculated: C 50.4; H 4.0; N 5.9%.

2-Bromo-3-acetamidobenzo[b]selenophene. This compound was obtained in 86% yield by the action of bromine on 2-acetamidobenzo[b]selenophene in chloroform by the method in [15, 16]. Found: C 37.7; H 2.4; Br 25.3; N 4.3%. $C_{10}H_7BrNOSe$. Calculated: C 37.9; H 2.5; Br 25.0; N 4.4%.

2-Methylbenzoselenopheno[2,3-d]thiazole (III). A method similar to the method used to prepare I was employed to obtain this compound from 3.17 g (0.01 mole) of 2-acetamido-3-bromobenzoselenophene and 3 g of phosphorus pentasulfide; the mixture was heated at 140-145 deg C for 20-30 min. Workup gave colorless plates (from petroleum ether) with mp 73-74 deg C (mp 73-74 deg C [17]) in 14% yield. UV spectrum (in alcohol), λ_{max} (log ε): 256 (4.12) and 300 nm (4.04). Found: C 47.5; H 2.9; N 5.5; S 12.6%. $C_{10}H_7NSSe$. Calculated: C 47.6; H 2.8; N 5.55; S 12.7%.

2-Acetamidobenzo[b]thiophene. This compound was synthesized by acetylation of the double tin salt of 2-aminobenzo[b]thiophene hydrochloride. Workup gave colorless plates (from benzene) with mp 222-223 deg C. Found: N 7.3%. $C_{10}H_9NOS$. Calculated: N 7.3%. IR spectrum (KBr): 3300 (ν_{NH}), 1670 (amide C = O), and 1510 cm^{-1} (amide CONH). PMR spectrum: 7.1-7.8 (benzene ring protons), 6.90 (3-H), and 1.45 ppm (CH_3).

2-Thioacetamidobenzo[b]thiophene. A 10.0-g sample of phosphorus pentasulfide was added with stirring to a refluxing solution of 19.1 g (0.1 mole) of 2-acetamidobenzo[b]thiophene in 900 ml of anhydrous benzene, after which the mixture was refluxed with stirring for 1.5 h. The benzene layer was decanted, and the residue was treated with 500 ml of boiling benzene. The benzene solutions were combined and vacuum evaporated to half their original volume. The concentrate was extracted with 4% sodium hydroxide solution, and the alkaline extract was cooled with ice water and acidified with dilute (1 : 1) hydrochloric acid. The resulting precipitate was removed by filtration, washed with water, and dried to give 12.9 g (62%) of a product with mp 152-154 deg C. Recrystallization from 50% alcohol gave light-yellow prisms with mp 159-160 deg C. Found: C 58.0; H 4.2; S 30.8%. $C_{10}H_9NS_2$. Calculated: C 58.0; H 4.3; S 30.9%.

2-Methylbenzothieno[2,3-d]thiazole. This compound was synthesized by oxidation of 2-thioacetamidobenzothiophene under the conditions in [3, 18]. Workup gave colorless crystals (from alcohol) with mp 85-86 deg C in 78% yield.

2,2'-Dinitro-3,3'-dibenzofuryl Disulfide. A solution of 3.2 g of sodium disulfide in 15 ml of 70% ethanol was added to a solution of 4.86 g of 2-nitro-3-bromobenzofuran [19] in 50 ml of anhydrous ethanol, and the mixture was refluxed for 4-5 h. It was then cooled, and the precipitate was removed by filtration, washed with ethanol, and air dried to give 3.5 g (90%) of a product with mp 189-191 deg C. Recrystallization from alcohol gave light-yellow needles with mp 207-209 deg C. UV spectrum, λ_{max} (log ε): 330 nm (in alcohol) (4.81). Found: C 49.4; N 7.1; S 16.4%. $C_{16}H_8N_2O_6S_2$. Calculated: C 49.5; N 7.2; S 16.5%.

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