ACTION OF PHOSPHORUS PENTASULFIDE ON 5-ACETAMIDOTHIOHYDANTOINS AND 4-BROMO-5-ACETAMIDOPYRAZOLES

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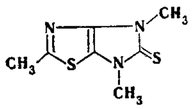
New condensed systems – (5,4-thiazolo)imidazoline-2-thione and pyrazolo[5,4-d]thiazoles –are formed by reaction of phosphorus pentasulfide with 5-acetamidothiohydantoins and 4-bromo-5-acetamido derivatives of pyrazole.

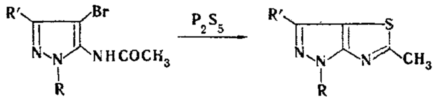
Thiazoles condensed with pyrimidine [1], thionaphthene [2], thiazolinethione [3], and pyrazole [4] rings were synthesized by reaction of phosphorus pentasulfide with α-acylaminocarbonyl derivatives of heterocyclic compounds.

In the present paper it is shown in the case of 1,3-dimethyl-5-acetamidothiohydantoin that this reaction gives a representative of yet another condensed system – (5,4-thiazolo)imidazoline-2-thione (I).



I

It was of interest to extend the action of phosphorus pentasulfide also to 1-bromo-2-acetamido-substituted heterocyclic compounds. As a result of this reaction with pyrazoles II, derivatives of the previously undescribed pyrazolo[5,4-d]thiazole condensed system (III) are formed.



II a, b

III a, b

II-III a $R=C_6H_5$, $R'=CH_3$; II-III b $R=C_4H_9$, $R'=C_6H_5$

Bases I and III are quite soluble in most organic solvents, slightly soluble in petroleum ether, insoluble in water, and readily form picrates and quaternary salts.

EXPERIMENTAL

1,3-Dimethyl-5-nitrosothiohydantoin. A 2.8-g sample of $NaNO_2$ was added with stirring to a solution of 2.88 g (0.02 mole) of 1,3-dimethylthiohydantoin in 20 ml of CH_3COOH. After 3 h, another 2.8 g of $NaNO_2$ was added, and the next day the resulting white-yellow precipitate was removed by filtration and washed with water to give 3 g (88%) of a product with mp 205° (from 35% ethanol). Found: N 24.2; S 18.3%. $C_5H_7N_3O_2S$. Calculated: N 24.4; S 18.5%.

1,3-Dimethyl-5-acetamidothiohydantoin. A thoroughly ground mixture of 3.4 g (0.02 mole) of 1,3-dimethyl-5-nitrosothiohydantoin and 6.5 g (0.1 mole) of zinc dust was added in small portions to 60 ml of CH_3COOH and 30 ml of acetic anhydride heated to 60°, and the mixture was held at this temperature for 2 h.

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The hot solution was filtered, and the filtrate was diluted with 15 ml of water and evaporated to dryness in vacuo. Another 15 ml of water was added, and the mixture was again evaporated. The residue was crystallized from alcohol to give 2 g (50%) of colorless prisms with mp 168°. The product was soluble in benzene, alcohol, and ether. Found: N 20.6; S 15.7%. $C_7H_{10}N_3O_2S$. Calculated: N 20.8; S 15.9%.

1-Phenyl-3-methyl-5-aminopyrazole. This compound was synthesized by heating diacetonitrile with phenylhydrazine in hydrochloric acid by the method in [5].

1-Phenyl-3-methyl-5-acetamidopyrazole. This compound was obtained by acetylation of 1-phenyl-3-methyl-5-aminopyrazole by the method in [6].

1-Butyl-3-phenyl-5-aminopyrazole. A mixture of 1.44 g (1 mmole) of ω-cyanoacetophenone and 1.26 g (2 mmole) of butylhydrazine in 10 ml of ethanol was refluxed for 9 h, after which the ethanol and excess butylhydrazine were removed by vacuum distillation, and the residual oil was crystallized by trituration with 10 ml of petroleum ether to give 1.8 g (81%) of colorless needles with mp 81-82° [from benzene–petroleum ether (2 : 1)]. Found: N 19.4%. $C_{13}H_{17}N_3$. Calculated N 19.5%.

1-Butyl-3-phenyl-5-acetamidopyrazole. A mixture of 2.15 g (1 mmole) of 1-butyl-3-phenyl-5-aminopyrazole and 6.12 g (6 mmole) of acetic anhydride was heated at 100° for 45 min. It was then diluted with three volumes of water, and the contents were evaporated to dryness. This operation was repeated twice. The resulting viscous oil crystallized on trituration with 10 ml of cold water to give 2.5 g (97%) of a product with mp 90-91° (from 50% ethanol). Found: N 16.2%. $C_{15}H_{19}N_3O$. Calculated: N 16.3%.

1-Phenyl-3-methyl-4-bromo-5-acetamidopyrazole (IIa). A solution of 3.7 g (23 mmole) of bromine in 6 ml of CH_3COOH was added with stirring to a solution of 4.2 g (20 mmole) of 1-phenyl-3-methyl-5-acetamidopyrazole in 5 ml of 50% CH_3COOH, after which 20 ml of water and 50 ml of 25% sodium carbonate solution were added. The crystalline product was removed by filtration, washed with water, and recrystallized from benzene to give 5.2 g (90%) of a product with mp 162-163°. Found: Br 27.2; N 14.2%. $C_{12}H_{12}BrN_3O$. Calculated: Br 27.2; N 14.2%.

1-Butyl-3-phenyl-4-bromo-5-acetamidopyrazole (IIb). A solution of 2.2 g (13 mmole) of bromine in 2 ml of CH_3COOH was added to a solution of 2.6 g (10 mmole) of 1-butyl-3-phenyl-5-acetamidopyrazole in 15 ml of CH_3COOH. After 2 h, 200 ml of water and 20 ml of 25% sodium carbonate solution were added, and the resulting precipitate was removed by filtration, washed with water, and dried to give 2.8 g (82%) of a product with mp 109-110° (from benzene). Found: Br 23.6; N 12.6%. $C_{15}H_{18}BrN_3O$. Calculated: Br 23.5; N 12.5%.

1,3-Dimethyl-4,5-(2-methyl-5,4-thiazolo)imidazoline-2-thione (I). A finely ground mixture of 2 g (10 mmole) of 1,3-dimethyl-5-acetamidothiohydantoin and 2.2 g of phosphorus pentasulfide was heated in 10 ml of dry toluene and 110° for 30 min. The toluene was decanted, 60 ml of toluene was added, and the mixture was refluxed again for 30 min. This operation was repeated twice. The toluene was removed by vacuum distillation, and the residue was triturated with 15 ml of 5% NaOH. The solid was removed by filtration, washed with water, and dried to give 0.85 g (33%) of a product with mp 150°. Found: N 21.3; S 32.1%. $C_7H_9N_3S_2$. Calculated: N 21.1; S 32.2%. The methosulfate was obtained from equimolecular amounts of I and dimethyl sulfate in benzene and had mp 140°. Found: N 13.0; S 29.3. $C_9H_{15}N_3O_4S_3$. Calculated: N 12.9; S 29.6%.

2,6-Dimethyl-4-phenylpyrazolo[5,4-d]thiazole (IIIa). A finely ground mixture of 2.95 g (10 mmole) of IIa and 3 g (14 mmole) of phosphorus pentasulfide was heated at 145-150° until hydrogen sulfide and hydrogen bromide evolution ceased (1 h), after which 20 ml of water and 5 ml of 25% NaOH were added, and the mixture was steam distilled to give 1.2 g (52%) of a product with mp 90-91° (from petroleum ether). Found: N 18.3; S 13.9%. $C_{12}H_{11}N_3S$. Calculated: N 18.3; S 14.0%. The picrate had mp 96-97° (from ethanol). Found: N 18.4%. $C_{12}H_{11}N_3S \cdot (NO_2)_3C_6H_2OH$. Calculated: N 18.3%.

1,2,6-Trimethyl-4-phenylpyrazolo[5,4-d]thiazolium Perchlorate. An equimolecular mixture of IIIa and dimethyl sulfate (0.5 mmole of each) was heated at 130° for 3 h, after which it was triturated with 1 ml of water, heated with activated charcoal, and filtered. Sodium perchlorate (1 g) was added to the filtrate, and the resulting precipitate was removed by filtration, washed successively with 1 ml of water, 0.5 ml of alcohol, and 2 ml of ether, and dried to give 0.15 g (86%) of a product with mp 179-180° (from ethanol). Found: Cl 9.9; N 12.5; S 8.5%. $C_{14}H_{16}ClN_3O_4S$. Calculated: Cl 9.9; N 12.4; S 8.6%.

2-Methyl-4-butyl-6-phenylpyrazolo[5,4-d]thiazole (IIIb). A finely ground mixture of 1.68 g (5 mmole) of pyrazole IIb and 1.5 g (7 mmole) of phosphorus pentasulfide was heated at 120° for 2 h, after which the melt was triturated with 20 ml of water and made slightly alkaline with 10% NaOH. The liberated oil was extracted with benzene and chromatographed on Al_2O_3. The benzene was removed by distillation, and the residue was crystallized from petroleum ether to give 0.5 g (38%) of a product with mp 82-83°. Found: N 15.6; S 11.7%. $C_{15}H_{17}N_3S$. Calculated: N 15.5; S 11.8%. The picrate had mp 100-101° (from ethanol). Found: N 16.7%. $C_{15}H_{17}N_3S \cdot (NO_2)_3C_6H_2OH$. Calculated: N 16.7%.

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