Chemistry

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1962

SovietRxiv

Abstract

Full Text

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2′-AMINO-5,5-DIMETHYLCYCLOHEXANONE-1-(2,3 : 4′,5′)-THIAZOLE (I)

Haloketones with thiourea form aminothiazole derivatives (1-7). There are no data in the literature on the interaction of 2-halo-1,3-diketones. In the search for new physiologically active substances in the thiazole series (8-11), we carried out the reactions of 2-halo-5,5-dimethylcyclohexanedione-1,3 (2-halodimedone) with thiourea. The best yields of 2′-amino-5,5-dimethylcyclohexanone-1-(2,3 : 4′,5′)-thiazole (I) were obtained in ethyl alcohol solution:

$$\text{2-halo-5,5-dimethylcyclohexanedione-1,3} + \mathrm{H_2NCSNH_2} \longrightarrow \text{(I)} + \mathrm{HX} + \mathrm{H_2O},$$
$$X = \mathrm{Cl, Br, J}$$

It proved that the reaction with thiourea proceeds especially readily when dimedone and a free halogen (chlorine, bromine, iodine) (12-15) are used—and yellow crystals of aminothiazole (I) are formed in 70% yield. Aminothiazole gives salts with acids, soluble in water; it is soluble in alkalis, but potassium or sodium derivatives could not be isolated in pure form. On acidification of alkaline solutions, unchanged aminothiazole (I) precipitates. On interaction with acid anhydrides, (I) readily gives N-acylaminothiazole (II).

(II)

IIa $R = \mathrm{CH_3CO}$

b $R = \mathrm{CH_3CH_2CO}$

v $R = \mathrm{NO_2}$

g $R = \mathrm{Br},\ \mathrm{H} = \mathrm{Br}$

On nitration of aminothiazole (I) with concentrated nitric acid in a solution of concentrated sulfuric acid, N-nitroaminothiazole (IIv) was obtained.

On bromination with dioxane dibromide in dioxane solution, aminothiazole (I) readily replaces the hydrogen atoms of the amino group and forms N,N-dibromoaminothiazole (IIg). The latter, on boiling with water and on dissolution in alkalis, eliminates bromine atoms, displaces iodine from an acidic solution

Structural formula of compound (III)

Figure 1: Structural formula of compound (III)

of potassium iodide, and in its properties resembles haloamines. Diazotization of aminothiazole (I) could be achieved only in 85% orthophosphoric acid solution. The diazonium salt readily enters into coupling reactions with phenols and aromatic amines. On coupling the diazonium salt of aminothiazole (I) with phenol, dark-red crystals of 2′-azo-[5,5-dime-

···thylcyclohexanone-1-(2,3 : 4′,5′)-thiazol-*p*-oxybenzene ·(III). Other azo-coupling products will be reported separately.

Analogously to dimedone and its above-mentioned derivatives, other 1,3-diketones also react with thiourea, which opens up broad possibilities for obtaining derivatives of 2-aminothiazoles.

Experimental Part

2′-Amino-5,5-dimethylcyclohexanone-1-(2,3 : 4′,5′)-thiazole (I). a) 7 g of 2-bromodimedone (16) and 4.7 g of thiourea in 100 ml of ethyl alcohol are boiled in a round-bottom flask with a reflux condenser for 1.5–2 hours. The ethyl alcohol is distilled off (~50 ml). After cooling, the residue in the flask is neutralized with ammonia to pH ~8 and diluted with water. The yellow crystals (I) that separate are recrystallized from dilute ethyl alcohol, giving 5.4 g (84%) of pure product (I). M.p. 207°. Found, %: N 14.32. $C_9H_{12}ON_2S$. Calculated, %: 14.33.

The reaction with 2-chlorodimedone proceeds analogously.

b) 4.2 g of dimedone, 4.6 g of thiourea, 3.5 g of iodine, and 50 ml of ethyl alcohol are boiled in a flask with a reflux condenser for 5 hours, and the solution is treated as indicated above. Yield 4.1 g (70%). M.p. 207°. On admixture with aminothiazole (I) obtained from 2-bromodimedone, it gives no depression of the melting point. Aminothiazole (I) is soluble in methyl and ethyl alcohols, glacial acetic acid, acetone, and alkalis; insoluble in water, benzene, toluene, ether, chloroform, and carbon tetrachloride. Found, %: N 14.18. $C_9H_{12}ON_2S$. Calculated, %: N 14.33.

Salts of 2′-amino-5,5-dimethylcyclohexanone-1-(2,3 : 4′,5′)-thiazole. **Hydrochloride** was obtained by passing dry hydrogen chloride into a suspension of 1 g of aminothiazole (I) in anhydrous diethyl ether. It crystallizes from dilute ethyl alcohol in the form of white crystals. M.p. 225° (decomp.). Readily soluble in ethyl alcohol and dioxane, less soluble in water. Insoluble in benzene, toluene, ether, and carbon tetrachloride. Found, %: N 11.86. $C_9H_{13}ON_2SCl$. Calculated, %: N 12.03.

Picrate is formed on mixing alcoholic solutions of 1 g of aminothiazole (I) and

1.1 g of picric acid. It is recrystallized from ethyl alcohol, giving 1.4 g (70%) of bright-yellow crystals. M.p. 235° (decomp.). The picrate is readily soluble in water, ethyl alcohol, and dioxane. Insoluble in benzene, ether, and carbon tetrachloride. Found, %: N 17.24. $C_{15}H_{15}O_8N_5S$. Calculated, %: N 17.03.

N-Acetyl-2′-amino-5,5-dimethylcyclohexanone-1-(2,3 : 4′,5′)-thiazole (IIa). On boiling 0.5 g of aminothiazole (I) in 5 ml of acetic anhydride for 30 min, the N-acetyl derivative (IIa) is formed. The latter is isolated by diluting the reaction mass with water and alkalinizing with ammonia to pH ~8. The pale-yellow crystals are recrystallized from ethyl alcohol, giving 0.4 g (68%) of pure product (IIa). M.p. 219°. Found, %: N 12.00. $C_{11}H_{14}O_2N_2S$. Calculated, %: N 11.75.

N-Propionylaminothiazole (IIb) was obtained analogously. M.p. 212°. Found, %: N 11.9. $C_{12}H_{16}O_2N_2S$. Calculated, %: 11.10.

N-Nitro-2′-amino-5,5-dimethylcyclohexanone-1-(2,3 : 4′,5′)-thiazole (IIc). To a solution of 1 g of aminothia-

of (I) in 2 ml of conc. sulfuric acid, 2 ml of conc. nitric acid is added, the mixture is kept at this temperature for 1 hour and poured onto ice. The separated yellowish crystals are recrystallized from ethyl alcohol. Yield 0.8 g (75%) of pink crystals. M.p. 201° (decomp.). Soluble in alkalis, mineral acids, ethyl and methyl alcohols, and dioxane. Found, %: N 17.09. $C_9H_{10}O_3N_3S$. Calculated, %: N 17.42.

N,N-Dibromo-2′-amino-5,5-dimethylcyclohexanone-1-(2,3 : 4′,5′)-thiazole (II). To 1 g of aminothiazole (I), dissolved in 10 ml of dioxane, 1.3 g of dioxane dibromide is added while boiling for 15 min. The solution loses its yellow color, and a precipitate of the dibromo derivative (II) is formed. It is recrystallized from ethyl alcohol, giving 1.2 g (66%) of the dibromo derivative as colorless crystals. M.p. 225–226° (decomp.). Product (II) is readily soluble in ethyl alcohol and glacial acetic acid, sparingly soluble in dioxane and ether, and insoluble in toluene, benzene, and carbon tetrachloride. On boiling with water it liberates bromine in the form of hypobromous acid (the aqueous solution displaces iodine from potassium iodide).

	Found, %:	N 7.70; Br 45.09
$C_9H_{10}ON_2SBr_2$.	Calculated, %:	N 7.91; Br 45.14

2′-Azo-[5,5-dimethylcyclohexanone-1-(2,3 : 4′,5′)-thiazol]-*p*-oxybenzene (III). 1 g of aminothiazole (I) is diazotized in 10 ml of 85% phosphoric acid with 0.35 g of sodium nitrite, and 0.94 g of phenol, dissolved in 2 ml of methyl alcohol, is added. The red solution is diluted with water and the precipitate is crystallized from ethyl alcohol. 1.2 g (80%) of the azo product (III) is obtained as shiny red crystals. The product is insoluble in acids, but readily soluble in alkalis with a violet coloration. It is readily soluble in ethanol, methanol, glacial acetic acid, and dioxane, and insoluble in benzene, toluene, and carbon

tetrachloride. M.p. 245° (decomp.). Found, %: N 14.26. $C_{15}H_{13}O_2N_3S$. Calculated, %: N 14.04.

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Received
8 II 1962

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Note: Figure translations are in progress. See original paper for figures.

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