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SYNTHESIS ON THE BASIS

OF 3-CARBOXYMETHYLMERCAPTO-4,5-DIPHENYL-1,2,4-TRIAZOLE

HYDRAZIDE

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3-Carboxymethylmercapto-4,5-diphenyl-1,2,4-triazole hydrazide was synthesized, and some of its chemical properties were studied.

It is known [1, 2] that 1,2,4-triazole-3-thiones react successively with esters of chloro-substituted acids and hydrazine hydrate to give acid hydrazides. Some acid hydrazides of substituted 1,2,4-triazole-3-thiones and their derivatives have potential antitubercular activity [3, 4]. The synthesis of 3-carboxymethylmercapto-4,5-diphenyl-1,2,4-triazole hydrazide (I) is described in the present paper. Some of its chemical properties were studied. Thus hydrazones Vc-e, g were obtained by reaction of I with aldehyde (RCHO), and hydrazo compounds IVa, b were obtained by the action of acid anhydrides [(RCO)₂O] on III.

The reactions of III with isothiocyanates (allyl and phenyl) give acyl thiosemicarbazides (VIc, 1), which form 1,2,4-triazole-5-thione derivatives (VIIc, 1) on refluxing in 2 N sodium hydroxide solution and undergo cyclization to thiazoline derivative VIII on treatment with bromine in carbon tetrachloride.

Condensation of acetoacetic ester with hydrazide III gives IX, which undergoes hydrazinolysis to give starting hydrazide III on heating with a twofold excess of hydrazine hydrate in methanol. Compounds Xc, h-k, which are also obtained by condensation of the products of diazo coupling of acetoacetic esters XIh, i with hydrazide III, are formed by the action of arenediazonium salts on IX (see Table 1).

EXPERIMENTAL

The UV spectra of ethanol solutions of the compounds were recorded with an SF-4 spectrophotometer. Compounds I and VII were obtained by the method in [5], while XI was obtained by the method in [6].

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<u>3-Carbomethoxymethylmercapto-4,5-diphenyl-1,2,4-triazole (II).</u> A 1.26-g (0.005 mole) sample of I was dissolved in an alcohol solution of 0.2 g (0.005 mole) of sodium hydroxide, after which 0.54 g (0.005 mole) of methyl monochloroacetate was added. The mixture was then heated at 50-60° on a water bath for 30 min, after which it was cooled, and the resulting precipitate was removed by filtration and washed with water to give 1.05 g (65%) of a product with mp 116-117° (from ethanol). Uv spectrum: λ_{max} 265 nm (log ϵ 4.20). Found: N 13.0%. C₁₇H₁₅N₃O₂S. Calculated: N 12.9%.

<u>3-Carboxymethylmercapto-4,5-diphenyl-1,2,4-triazole Hydrazide (III).</u> A solution of 3.25 g (0.01 mole) of II and 2 ml of hydrazine hydrate was refluxed in alcohol for 50 min, after which the precipitate was removed by filtration and washed with alcohol to give 2.76 g (85%) of a product with mp 217-218° (from ethanol). UV spectrum: λ_{max} 255 nm (log ε 4.32). Found: N 21.5%. C₁₆H₁₅N₅OS. Calculated: N 21.5%.

<u>3-Carboxymethylmercapto-4,5-diphenyl-1,2,4-triazole Maleylhydrazide (IVb).</u> A suspension of 0.32g (0.001 mole) of III and 0.1 g (0.001 mole) of maleic anhydride was refluxed in dry chloroform for 30 min, after which the solid material was removed by filtration and washed with alcohol. Compound IVa was similarly obtained.

<u>3-Carboxylmethylmercapto-4,5-diphenyl-1,2,4-triazole Benzylidenehydrazide (Va).</u> A mixture of 0.32 g (0.001 mole) of III and 0.1 g (0.001 mole) of benzaldehyde was refluxed in alcohol for 30 min, after which the precipitate was removed by filtration and washed with alcohol. Compounds Vd, e, g and VIc, l were similarly obtained.

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	· · · · · · · · · · · · · · · · · · ·			N, %		UV spectra		6
Com- pound	R	тр , °С	formula	found	calc.	λ _{max}	lgε	Yield
IVa	CO CH-CH COOH	103 104	C.H.N.O.S	16.5	16.5	245. 265	3 81 - 3 00	82
IVb	CO-CH=CH-COOH	189—190	$C_{20}H_{17}N_5O_4S$	16,6	16,5	245; 265; 295;	3,96; 4,08;	83
Vc	C ₆ H ₅ -CH=	237—238	C ₂₃ H ₁₉ N ₅ OS	16,8	16,9	240; 270; 280; 310	3,85; 3,74 4,19; 4,43; 4,50; 3,93	97
Vd	4HO-C ₆ H ₄ —CH=	226-226,5	$C_{23}H_{19}N_5O_2S$	16,4	16,3			80
Ve	$3NO_2C_6H_4$ —CH=	245 - 246	$C_{23}H_{18}N_6O_3S$	18,4	18,3	0.00 000 000		84
Vg	$4(CH_3)_2N-C_6H_4-CH=$	228229	C ₂₅ H ₂₄ N ₆ OS	18,5	18,4	240; 260; 330;	4,21; 4,06;	66
VIc	C6H5-	197—198	$C_{23}H_{20}N_6OS_2$	18,3	18,3	245; 270	4,24; 4,35	98
VII	CH2=CH-CH2	200-201	$C_{20}H_{20}N_6OS_2$	19,9	19,8	-		76
VIIc	C ₆ H ₅ —	226226,5	$C_{23}H_{18}N_6S_2$	18,9	19,0	255	4,38	91
VIII	$CH_2 = CH - CH_2 - CH_2$	207 - 208	$C_{20}H_{18}N_6S_2$	20,8	20,7			72
Xc	C ₆ H ₅	(dec.)	$C_{28}H_{27}N_7O_3S$	17,9	18,1	- -		31
Xh	β-C10H7—	204-206	C ₃₂ H ₂₉ N ₇ O ₃ S	16,7	16,6	240; 270; 415	4,17; 4,09;	42
Xi	4CH ₂ OC ₂ H ₄	290-291	ConHonNzO4S	17.5	17.2		4,77	46
Xi	3HOOC-C ₆ H ₄ -	238 - 240	C ₂₉ H ₂₇ N ₇ O ₅ S	17.0	16,8]		37
		(dec.)				1		
Xk	3HOC ₆ H ₄ —	285287	C ₂₉ H ₂₇ N ₇ O ₄ S	17,5	17,6	240; 270; 420	4,06; 3,85;	49

TABLE 1. Characteristics of the Compounds Obtained

 $\frac{2-[(4,5-\text{Diphenyl-1},2,4-\text{triazol-3-yl})\text{mercaptoacetylhydrazino]-5-bromomethyl-1,3-thiazole Hydrobromide (VIII). A solution of 0.16 g (0.001 mole) of bromine in 10 ml of carbon tetrachloride was added dropwise with cooling and stirring to 0.42 g (0.001 mole) of VII, after which the solid material was removed by filtration and washed with alcohol to give 0.3 g (52%) of a product with mp 220.5-221° (from alcohol). UV spectrum: <math>\lambda_{\text{max}}$ 240, 262 nm (log ε 4.32). Found: N 14.5%. C₂₀H₂₀BrN₆S₂ 'HBr. Calculated: N 14.5%.

<u>3-Carboxymethylmercapto-4,5-diphenyl-1,2,4-triazole Carbethoxyisopropylenehydrazide (IX).</u> A solution of 0.32 g (0.001 mole) of III, 0.13 g (0.001 mole) of acetoacetic ester, and one to two drops of concentrated sulfuric acid in ethanol was refluxed for 20 min, after which it was cooled, and the resulting precipitate was removed by filtration and washed with cold alcohol to give 0.31 g (71%) of a product with mp 164-165° (from ethanol). UV spectrum: λ_{max} 250 nm (log ε 4.30). Found: N 16.1%. C₂₃H₂₃N₅O₃S. Calculated: N 16.0%.

<u>3-(Carboxymethylmercapto-4,5-diphenyl-1,2,4-triazole (1-Carbethoxy-1- β -naphthylhydrazono)isopropylenehydrazide (Xh).</u> A) A solution of 0.14 g (0.001 mole) of β -naphthylamine and 0.8 ml of 17% hydrochloric acid was cooled and diazotized with 0.07 g (0.001 mole) of sodium nitrite in 2 ml of water, after which a solution of 0.32 g (0.001 mole) of IX and 0.6 g of sodium acetate in alcohol was added slowly. The mixture was then stirred for 1.5 h and diluted with water. The resulting oil gradually crystallized. Compounds Xc, i-k were similarly obtained.

B) A solution of 0.001 mole of the product of diazo coupling of acetoacetic ester and β -naphthylamine (XIh), 0.001 mole of III, and one to two drops of concentrated sulfuric acid was stirred for 3 h, after which the product was isolated by the addition of water. Compound XIi was similarly obtained.

No melting-point depression was observed for mixtures of the products obtained by the various methods.

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