Kurzmitteilungen:

Cleavage Reactions of 4-Thiazolidinone-2-thiones:

Synthesis and Reactions of New 1,2,4-Triazoles and Their Biological Activities

Ringspaltung bei 4-Thiazolidinon-2-thionen: Synthese, Reaktionen und biologische Wirkung neuer 1,2,4-Triazole

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Received April 14, 1989

In the last few years we have been involved in a programme aimed for exploring potential utilities of thiazolidinones in heterocyclic syntheses. During this phase of our research we reported on condensation reactions of thiazolidinones with nucleophiles[1-4]. In conjunction with this work we report here on reactions of thiazolidinones with a nucleophile that leads to ring cleavage.

The reaction of 5-phenylhydrazono-2-thioxo-4-thiazolidinone (**1**) with hydrazine hydrate affords a product $C_9H_9N_5S_2$. Structure **3** was suggested for this product. Its ^{1}H-NMR spectrum showes 9 H, two singlets at δ 13.3 and 13.5 (2 NH) besides a multiplet at δ 6.7-7.4 corresponding to 7 H (5H, arom. + 2H; NH, SH). The formation of **3** is assumed to proceed via the cyclization of 4-(α-phenylhydrazono-mercaptoacetyl)thiosemicarbazide (**2**). The formation of the 4-(1-phenylhydrazono-1-mercaptomethyl)-1,2,4-triazol-4-ine-3-thione (**3**) or tautomers like **3a** via the reaction of **1** with hydrazine hydrate finds parallelism to the formation of 1,2,4-triazoles from reaction of substituted rhodanines with hydrazine hydrate under similar conditions[5-8].

Refluxing of **3** with formaldehyde or benzaldehyde in absol. ethanol gave the new fused thiazolo[4,3-c]triazoles **4a** and **b**. Heating of **3** with acetone gave **4c**. The structures of **4a-c** were deduced from elemental and spectral data.

3 reacted with phenacyl bromide in the presence of triethylamine to give the thiazolo[5,4-c]thiazine **5**.

Treatment of **3** with acetic anhydride affords the diacetyl derivative **6**.

Biological Results

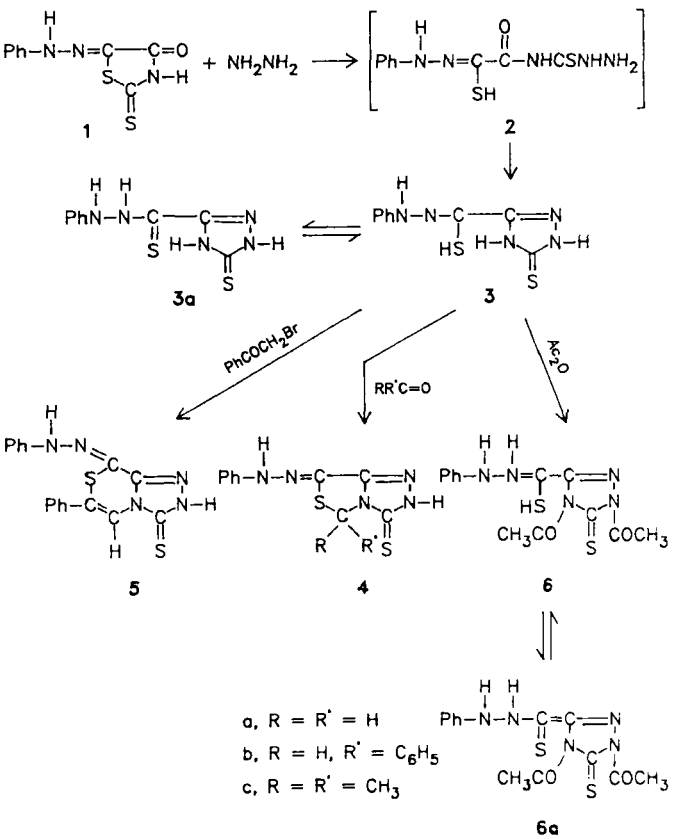
Results of antimicrobial activity tests are shown in Table 1: only **4a** and **5** show slight effect on some organisms.

The authors wish to thank Dr. *Nagwa M. Morsy*, Department of Botany, the same University, for the biological tests.

Table 1: Antimicrobial Activities in vitro

	3	4a	4b	5	6
E. Coli	–	–	–	–	–
B. subtilis	–	–	–	5 mm	–
B. cereus	–	3 mm	–	–	–
Sarcina sp.	–	–	–	5 mm	–
Micrococcus sp.	–	–	–	–	–
Mycobacterium sp.	–	–	–	–	–
Actinomyces sp.	–	–	–	–	–
Saccharomyces sp.	–	–	–	–	–

Inhibition zone around the disc (each disc contains 100 μg).



Experimental Part

Melting points uncorr.- IR spectra: Pye Unicam SP-1100 Spectrophotometer, KBr.- ^{1}H-NMR spectra: Varian EM-390 90 MHz, DMSO-d_6, TMS as intern. standard, chem. shifts δ ppm.- Microanalysis: Microanalytical Center, Cairo University.- **1** was prepared according to lit.[9].

4-(1-Phenylhydrazono-1-mercaptomethyl)-1,2,4-triazol-4-ine-3-thione (**3**)

A mixture of (0.01 mole) 5-phenylhydrazono-2-thioxo-4-thiazolidinone (**1**) and hydrazine hydrate (0.01 mole) was left overnight at room temp.

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Table 2: Data of compounds **3-6**.

Compd	M.p. °C	Yield %	Mol. formula	Mol. Weight	Analysis Calcd./Found C	H	S (%)	^{1}H-NMR (δ ppm)
3a	233-5	70	$C_9H_9N_5S_2$	251.2	43.0	3.61	25.5	two s, 13.3; 13.5 (2H, 2 NH); 6.7-7.4
					42.6	3.40	25.0	(m, 7H, arom. + 2 NH).
4a	226-7	70	$C_{10}H_9N_5S_2$	263.2	45.6	3.45	24.3	5.4-5.6 (s, 2H, CH_2); 13.3 (s, 1H, NH);
					45.2	3.25	23.8	7.2-7.6 (m, 6H, arom. + NH).
4b	235-6	65	$C_{16}H_{13}N_5S_2$	339.3	56.6	3.86	18.8	5.2 (1H, CH); 13.3 (s, 1H, NH); 7.1-7.5
					57.0	3.81	18.6	(m, 11H, arom. + NH).
4c	240-2	75	$C_{12}H_{13}N_5S_2$	291.3	49.5	4.5	21.9	2.2 (s, 6H, 2 CH_3); 13.2 (s, 1H, NH);
					49.5	4.4	21.6	7.2-7.5 (m, 6H, arom. + NH).
5	244-5	65	$C_{17}H_{13}N_5S_2$	351.3	58.1	3.73	18.2	13.6 (s, 1H, NH); 7.0 (s, 1H, CH);
					57.7	3.62	18.0	7.2-7.6 (m, 11H, arom. + NH).
6a	246-7	75	$C_{13}H_{13}N_5O_2S_2$	335.3	46.6	3.91	19.1	2.4 (s, 6H, 2 OCH_3); 7.2-7.6 (m, 7H,
					46.2	3.73	18.9	arom. + 2 NH).

The product was triturated with cold ice-hydrochloric acid. The solid was filtered off and washed two times with H_2O to afford an orange precipitate which crystallized from ethanol as orange crystals (Table 2).

Reaction of **3** *with formaldehyde and benzaldehyde to afford* **4a** *and* **b**

To a solution of **3** (0.01 mole) in absol. ethanol, formaldehyde (40%) or benzaldehyde (0.01 mole) was added. The mixture was refluxed for 2 h then left to cool. The solid was filtered off, washed with ethyl alcohol and crystallized from ethanol/dioxane to afford yellow crystals of **4a** or **b**, respectively (Table 2).

Reaction of **3** *with acetone to afford* **4c**

0.01 Mole **3** were refluxed in acetone (30 ml) for 1 h, then left to cool, filtered off and the solid was crystallized from acetone to give yellow crystals (Table 2).

Reaction of **3** *with Phenacyl bromide to afford* **5**

A solution of equimolar amounts of **3** (0.01 mole) and phenacylbromide in DMF (15 ml) in the presence of a few drops of triethylamine was heated under reflux for 5 h, then left to cool, and filtered off. The solid was purified by crystallization (Table 2).

Acylation of **3** *to afford* **6**

A solution of **3** (0.01 mole) in acetic anhydride (30 ml) was heated for 1 h and then cooled. On dilution with water a crude precipitate was separated. This solid was purified by crystallization from glacial acetic acid (Tables 2).

Methods used in Biological Tests

I. Test Organisms: Differnt strains of bacteria, actinomycetes, and yeast fungi (Table 1).

II. Test Media: A solid nutrient material as described by Wickerham[10].

III. Test for Antimicrobial Activity: Antimicrobial activity was tested by the diffusion plate method[11]. Each pore received about 0.1 ml, equivalent to 100 µg of the test compound.

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