Reactions with 5-Arylmethylene-2-phenylhydrazono-4-thiazolidinones A Novel Synthesis of Thiazolo[2,3-c]triazine Derivatives

Sanaa O. Abd Allah*, Sherif M. Fahmy, and Hamed A. Ead

Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt

Z. Naturforsch. **39b**, 390–392 (1984); received June 7, 1983

Alkylation, Alkylcyclization, Cyanoethylation, Acetylation

The 5-arylmethylene derivatives of 2-phenylhydrazono-4-thiazolidinone (**1**) reacted with phenacyl bromide and with ethyl bromoacetate to yield the thiazolo[2,3-c]triazine derivatives (**3**) and (**4**). The reaction of **1** with carbon disulphide in alkaline solution afforded the bis(N^1 -2-phenylhydrazono-4-thiazolidinone)thiocarbonyl derivatives (**6**). Cyanoethylation of **1** afforded the N^1 - β -cyanoethylphenylhydrazono derivatives (**7**).

In extension of our program directed for the development of new simple routes for the synthesis of fused thiazolo-triazoles [1, 2] we have investigated the reaction of 5-arylmethylene-2-phenylhydrazono-4-thiazolidinones [3] (**1a**) and (**1b**) with phenacyl bromide and with ethyl bromoacetate aiming to obtain new thiazolo-triazines of probable biological activities.

Thus, subjecting **1a** or **1b** to the action of phenacyl bromide in dimethylformamide effected alkylation on the exocyclic N^1 -phenylhydrazono moiety to give the N^1 -phenacylphenylhydrazono derivatives **2a** and **2b**, respectively. The structure assigned for **2** was inferred from analytical and IR data; besides, ethanolhydrochloric acid hydrolysis of **2a** afforded 5-phenylmethylene-2,4-thiazolidinedione [4]. On the other hand, when the reaction between **1a** or **1b** and phenacyl bromide was carried out in refluxing ethanol containing few drops of triethylamine the thiazolo[2,3-c]-1,2,4-triazine derivative **3a** or **3b** was obtained. The structure of **3a** or **3b** was assigned based on elemental and IR data; besides its synthesis via another route, by refluxing compound **2a** and/or **2b** in ethanol containing catalytic amounts of triethylamine.

When equimolecular amounts of **1a** or **1b** and ethyl bromoacetate were allowed to react in dimethylformamide the thiazolo[2,3-c]-1,2,4-triazinone derivative **4a** or **4b** was obtained. The structure of **4** was assigned based on elemental and IR data; besides ethanolhydrochloric acid hydrolysis of **4a** to afford 5-phenylmethylene-2,4-thiazolidinedione [4]. The

reaction of an ethanolic solution of **1a** or **1b** with carbon disulphide in alkaline medium was carried out aiming to obtain the thiazolo-triazolthione derivative **5**, but instead, the bis(N^1 -2-phenylhydrazono-4-thiazolidinone) thiocarbonyl derivative **6a** or **6b** was obtained. The structure of **6** was infer-

* Reprint requests to Dr. S. Abd Allah.
0340-5087/84/0300-0390/\$ 01.00/0

red from analytical and IR data; besides the hydrolysis of **6a** to afford 5-phenylmethylene-2,4-thiazolidinedione.

The reaction of **1** with acrylonitrile was also investigated. Thus, treatment of **1a** or **1b** with excess amount of acrylonitrile in aqueous pyridine afforded a 1:1 adduct as inferred from analytical data. Two structures **7** and **8** were considered for the adduct as they both agreed with the ^1H NMR and IR data. Structure **8** was ruled out based on the ethanol-hydrochloric acid hydrolysis of the adducts to afford the corresponding 5-arylmethylene-2,4-thiazolidinedione.

The reaction of **1a** or **1b** with acetic anhydride afforded the 2- N^1 -acetylphenylhydrazono-4-thiazolidinone derivative **9a** or **9b** as established from analytical and IR data. Besides, an authentic sample for **9a** was obtained *via* the reaction between N^1 -acetylphenylhydrazine hydrochloride [5] and 5-phenylmethylene-2-thioxo-4-thiazolidinone [6].

Experimental

All melting points are uncorrected. IR spectra were obtained as a KBr disc with a Py-Unicam SP 1100 spectrophotometer. ^1H NMR spectra were ob-

tained on a Varian A-60 spectrometer in DMSO-d_6 , using TMS as internal standard and chemical shift are expressed as δ ppm.

5-Arylmethylene-2- N^1 -phenacylphenylhydrazono-4-thiazolidinones **2a** and **2b**.

To a solution of each of **1a** or **1b** (0.01 mol) in 20 ml of dimethylformamide was added an equimolecular amount of phenacyl bromide. The reaction mixture was heated on a water bath for 30 min and then allowed to cool. The solid product obtained on dilution with water was filtered off and crystallised from ethanol. The yellow coloured products **2a** and **2b** are listed in Table I. The IR spectrum of **2a** showed absorption at 3300 cm^{-1} (NH), 1710 cm^{-1} (phenacyl CO) and 1680 cm^{-1} (ring CO).

Thiazolo[2,3-*c*]-1,2,4-triazine derivatives **3a** and **3b**.

A solution of equimolecular amounts (0.01 mol) of each of **1a** or **1b** and phenacyl bromide in 100 ml of ethanol containing few drops of triethylamine was heated under reflux for 5 h and then allowed to cool. The solid product so obtained was filtered off and crystallised from ethanol. The yellow coloured products **3a** and **3b** are listed in Table I. The IR spectrum of **3a** showed absorption at 1690 cm^{-1} (ring CO) and 1620 cm^{-1} (C=N).

Compound	m.p. (°C)	Yield (%)	Formula (mol.wt.)	Analysis C	H	Calcd/Found N	S
2a	165	55	$\text{C}_{24}\text{H}_{19}\text{N}_3\text{O}_2\text{S}$	69.72	4.63	10.16	7.74
			413.4	69.63	4.61	10.11	7.70
2b	176	50	$\text{C}_{25}\text{H}_{21}\text{N}_3\text{O}_3\text{S}$	67.71	4.77	9.48	7.21
			443.4	67.83	4.72	9.50	7.17
3a	185	60	$\text{C}_{24}\text{H}_{17}\text{N}_3\text{OS}$	72.90	4.33	10.63	8.09
			395.4	73.01	4.29	10.83	8.11
3b	198	60	$\text{C}_{25}\text{H}_{19}\text{N}_3\text{O}_2\text{S}$	70.58	4.50	9.88	7.52
			425.4	70.65	4.50	9.80	7.60
4a	215	70	$\text{C}_{18}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$	64.47	3.91	12.53	9.54
			335.3	64.80	3.90	12.71	9.61
4b	244	75	$\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}_3\text{S}$	62.46	4.14	11.50	8.76
			365.3	62.66	4.09	11.62	8.91
6a	190	60	$\text{C}_{33}\text{H}_{24}\text{N}_6\text{O}_2\text{S}_3$	62.65	3.82	13.29	15.17
			632.6	62.54	3.85	13.09	15.33
6b	222	62	$\text{C}_{35}\text{H}_{28}\text{N}_6\text{O}_4\text{S}_3$	60.69	4.05	12.14	13.87
			692.0	60.81	4.00	12.00	14.01
7a	176	80	$\text{C}_{19}\text{H}_{16}\text{N}_4\text{OS}$	65.51	4.63	16.08	9.18
			348.3	65.55	4.55	16.30	8.99
7b	190	80	$\text{C}_{20}\text{H}_{18}\text{N}_4\text{O}_2\text{S}$	63.48	4.80	14.81	8.45
			378.4	63.49	4.91	14.93	8.60
9a	185	55	$\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}_2\text{S}$	64.09	4.48	12.46	9.48
			337.3	64.10	4.51	12.60	9.41
9b	188	50	$\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}_3\text{S}$	62.12	4.66	11.44	8.71
			367.3	61.91	4.70	11.70	8.50

Table I. Analytical data for compounds **2–9**.

Cyclization of **2a** or **2b** to afford **3a** or **3b**.

A solution of **2a** or **2b** (1.0 g) in 50 ml of ethanol containing few drops of triethylamine was refluxed for 5 h then allowed to cool. The solid product so obtained was filtered off and crystallised from ethanol to afford **3a** or **3b** respectively (m.p. and mixed m.p.).

Thiazolo[2,3-*c*]-1,2,4-triazinone derivatives **4a** and **4b**.

A solution of **1a** or **1b** (0.01 mol) in 30 ml of dimethylformamide was treated with an equimolecular amount of ethyl bromoacetate. The reaction mixture was heated on a water bath for 4 h then allowed to cool and diluted with water. The solid product so obtained was filtered off and crystallised from ethanol-acetone mixture. Compounds **4a** and **4b** are orange coloured and listed in Table I. The IR spectrum of **4a** showed absorption at 1730 and 1680 cm^{-1} (CO) and 1620 cm^{-1} (C=N). The ^1H NMR spectrum of **4a** showed signals at 7.8–6.8 (m, 11 H, 2 Ph and vinylic proton) and 3.9 (s, 2 H, $\text{CO}-\text{CH}_2$).

Bis(5-arylmethylene-2-phenylhydrazono-4-thiazolidinone)thiocarbonyl derivatives **6a** and **6b**.

To a 100 ml solution of ethanolic potassium hydroxide (0.1 M) was added 0.01 mol of **1a** or **1b** and 10 ml of carbon disulphide. The reaction mixture was refluxed for 8 h then allowed to cool. The solid product obtained after treatment with acetic acid was collected by filtration and crystallised from ethanol. Compounds **6a** and **6b** are orange coloured and are listed in Table I. The IR spectrum of **6a** showed absorption at 3300 cm^{-1} (NH) and 1680 cm^{-1} (ring CO).

5-Arylmethylene-2-*N*¹- β -cyanoethylphenylhydrazono-4-thiazolidinones **7a** and **7b**.

To a solution of each of **1a** or **1b** (0.01 mol) in aqueous pyridine (30 ml pyridine and 10 ml water) was added excess of acrylonitrile and the reaction

mixture was refluxed for 5 h. The solid product obtained after evaporation of pyridine was filtered off and crystallised from ethanol. Compounds **7a** and **7b** are yellow coloured and are listed in Table I. The IR spectrum of **7a** showed absorption at 3200 cm^{-1} (NH), 2220 cm^{-1} (C $\equiv$ N) and 1680 cm^{-1} (ring CO). The ^1H NMR spectrum of **7a** showed signals at 9.2 (s, 1 H, NH), 7.8 (s, 1 H, $\text{Ph}-\text{CH}=\text{C}$), 7.6–6.8 (m, 10 H, 2 Ph), 3.2 (t, 2 H, $\text{CH}_2-\text{CH}_2\text{CN}$) and 2.9 (t, 2 H, $\text{CH}_2-\text{CH}_2-\text{CN}$).

5-Arylmethylene-2-*N*¹-acetylphenylhydrazono-4-thiazolidinones **9a** and **9b**.

A suspension of **1a** or **1b** (2.0 g) in acetic anhydride (30 ml) was heated on a water bath for 15 min. The reaction mixture was poured in water and the solid so obtained was filtered off. Compounds **9a** and **9b** formed yellow crystals from ethanol and are listed in Table I. The IR spectrum of **9a** showed absorption at 3180 cm^{-1} (NH), broad absorption at 1690 cm^{-1} (amide and ring CO).

5-Phenylmethylene-2-*N*¹-acetylphenylhydrazono-4-thiazolidinone **9a**.

An equimolecular amount (0.01 mol) of *N*¹-acetylphenylhydrazine hydrochloride and 5-phenylmethylene-2-thioxo-4-thiazolidinone in 50 ml of ethanol containing anhydrous sodium acetate (1.0 g) was refluxed for 5 h. The reaction mixture was allowed to cool, the solid so obtained was filtered off, washed with water and crystallised from ethanol to afford **9a** (m.p. and mixed m.p.).

Action of ethanolic-hydrochloric acid mixture on **2a**, **4a**, **6a** and **7a**.

A solution of each of **2a**, **4a**, **6a** or **7a** (1.0 g) in a mixture of ethanol (20 ml) and hydrochloric acid (4 ml) was refluxed for 2 h then allowed to cool and diluted with water. The solid product so obtained was crystallised from ethanol, m.p. 225°, proved to be identical (m.p. and mixed m.p.) with 5-phenylmethylene-2,4-thiazolidinedione.

- [1] N. A. Kassab, S. O. Abd Allah, and H. A. Ead, Z. Naturforsch. **31b**, 380 (1976).
- [2] N. A. Kassab, S. O. Abd Allah, and H. A. Ead, Z. Naturforsch. **31b**, 853 (1976).
- [3] H. Taniyama and T. Yusa, J. Pharm. Soc. Jpn. **75**, 5 (1955).

- [4] D. Libermann, J. Himbert, and L. Hengl, Bull. Soc. Chim. Fr. **1948**, 1120.
- [5] H. Yamamoto, J. Org. Chem. **32**, 3693 (1967).
- [6] A. Mackie and A. L. Misra, J. Chem. Soc. **1954**, 3919.