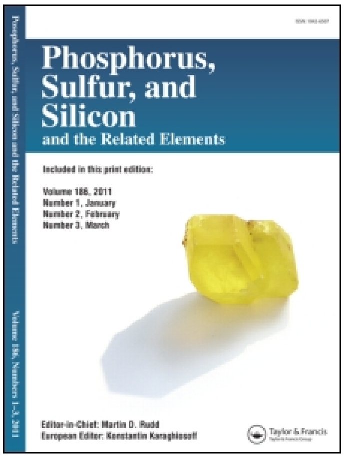


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS AND REACTIONS OF NOVELPYRAZOLO[1,5-c][1,3]THIAZINE-7-THIONES

Mohaed Gaber Marei[a]; Moneim El-ghanam[a]
[a] Chemistry Department, Faculty of Science, Alexandria University, Alexandria, Egypt

To cite this Article Marei, Mohaed Gaber and El-ghanam, Moneim(1995) 'SYNTHESIS AND REACTIONS OF NOVELPYRAZOLO[1,5-c][1,3]THIAZINE-7-THIONES', Phosphorus, Sulfur, and Silicon and the Related Elements, 107: 1, 1 — 5

To link to this Article: DOI: 10.1080/10426509508027914

URL: http://dx.doi.org/10.1080/10426509508027914

Phosphorus, Sulfur, and Silicon, 1995, Vol. 107, pp. 1-5
Reprints available directly from the publisher
Photocopying permitted by license only

SYNTHESIS AND REACTIONS OF NOVEL PYRAZOLO[1,5-c][1,3]THIAZINE-7-THIONES

MOHAMED GABER MAREI* and MONEIM EL-GHANAM
Chemistry Department, Faculty of Science, Alexandria University,
Ibrahimia, P.O. Box 426, Alexandria 21321, Egypt

(Received November 16, 1994; in final form April 28, 1995)

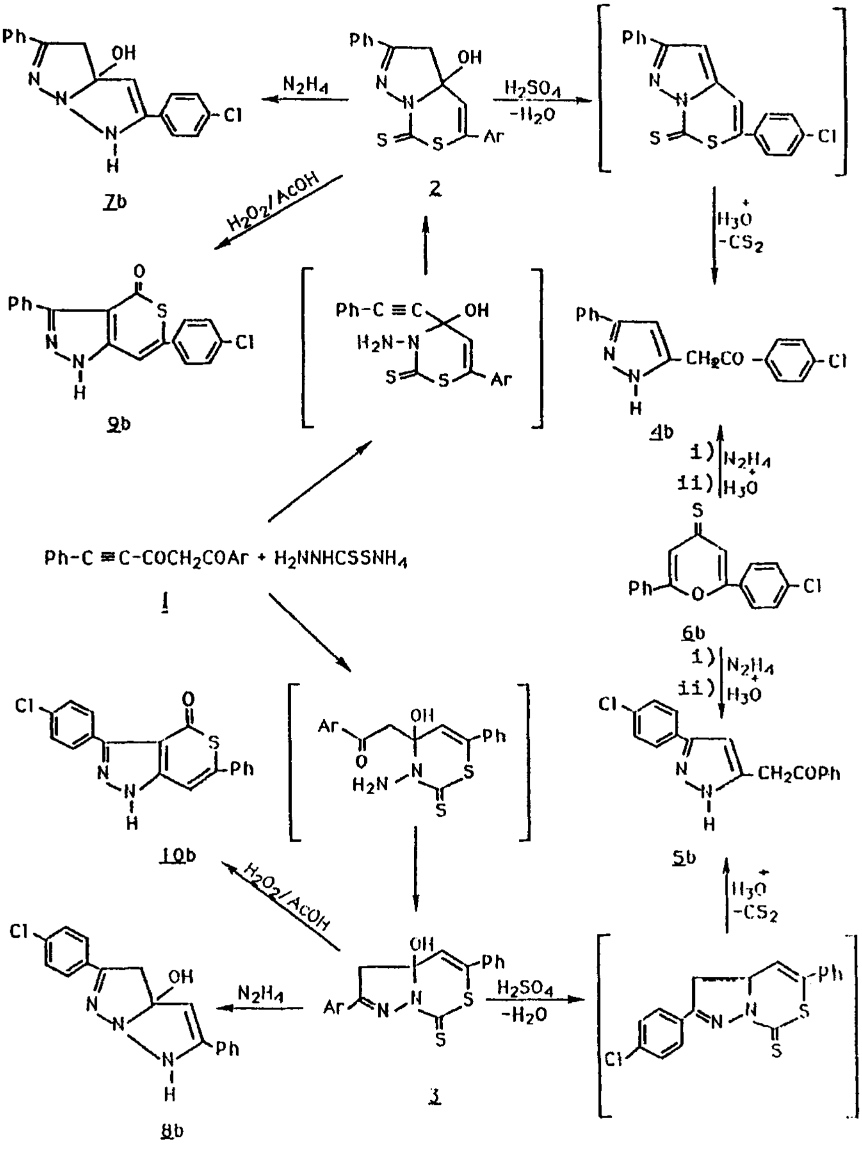
The reaction of 1,5-diaryl-4-pentyne-1,3-diones with S-ammonium hydrazinecarbodithiolate led to the formation of a new ring system, the pyrazolo[1,5-c][1,3]thiazines, which were converted into the corresponding pyrazoles. These pyrazolothiazines gave with hydrazine hydrate the respective pyrazolo[1,5-b]pyrazoles. With hydrogen peroxide in glacial acetic acid, pyrazolo[4,3-c]thiopyran-4-ones were formed. The latter reactions furnish a new series of pyrazolo[1,5-b]pyrazoles and a new heterocyclic system, pyrazolo[4,3-c]thiopyrans.

Key words: Acetylenic β-diketones, pyrazolothiazinethiones, pyrazolopyrazoles and pyrazolothiopyran-4-ones, synthesis and structure elucidation.

There are four classes of pyrazolo[1,3]thiazines are present in the literature, [3,4-d],[1-5] [4,3-d],[6,7] [5,1-b][8] and [5,4-d],[9] but the pyrazolo[1,5-c][1,3]thiazine nucleus is unknown. Some of these pyrazolothiazines showed herbicidal,[10] antibacterial[10] and fungicidal activities.[9,10] Moreover, they have been used as gluconeogenesis and passive cutaneous anaphylaxis inhibition.[3] Very limited methods are reported for the synthesis of pyrazolo[1,3]thiazines. They are generally prepared from pyrazole[1-5,8,9] or 1,3-thiazine derivatives.[6,7] In the present investigation, "One-pot" construction of the novel pyrazolo[1,5-c][1,3]thiazines from acyclic precursors, in the first instance, is developed.

Treatment of 1,5-diaryl-4-pentyne-1,3-diones[11,12] (**1a–e**) with S-ammonium hydrazinecarbodithiolate in refluxing ethanol afforded a mixture of 5-aryl-2-phenyl-(**2a–e**)- and 2-aryl-5-phenyl-(**3b–e**)-3′-hydroxy-3H-pyrazolo[1,5-c][1,3]thiazine-7-thiones. The reaction can be assumed to proceed by the intermediate formation of the acetylenic thiazines and aracyl-1,3-thiazines, which are susceptible to cyclization to the corresponding **2** and **3** under the reaction conditions, respectively (Scheme I). It is worth mentioning that the reaction of hydrazinecarbodithiolate with acetylenic β-diketones was never reported to the best of our knowledge. Thus, the above reaction repairs this gap, in the first instance.

The structure of the pyrazolothiazines was confirmed from their analytical and spectral data. The IR spectra of **2a–e** and **3b–e** showed the pyrazole C=N band in the region 1580–1594 cm^{-1} as well as a thiocarbonyl and OH absorptions in the ranges 1070–1095 and 3322–3429 cm^{-1}, respectively. Their NMR spectra (Table I) exhibited two singlets at δ 4.10–4.52 and 6.08–6.80 for the methylene and H-4 protons, respectively. Moreover, an exchangeable signal for the OH proton was observed at δ 8.26–9.60. Further support of the structure of the pyrazolothiazines was obtained from their mass spectra (cf. Experimental). The compounds studied **2b,d** and **3b** gave a weak molecular ion peak. A major fragmentation route is the



Ar : a = C_6H_5, b = p-Cl-C_6H_4, c = p-Br-C_6H_4, d = p-CH_3-C_6H_4, e = p-$CH_3OC_6H_4$.

SCHEME I

elimination of water giving the (M-H_2O) as a very intense or base peak. The detection of the pyrazolyne species characterizes their spectra (cf. Experimental).

In addition, the structures of pyrazolothiazines were confirmed by the conversion of **2b** and **3b** into the corresponding 3(5)-phenyl-5(3)-*p*-chlorophenacylpyrazole(**4b**) and 3(5)-*p*-chlorophenyl-5(3)-phenacylpyrazole(**5b**) with sulfuric acid in refluxing ethanol, respectively. The formation of **4** and **5** was suggested in Scheme I. These pyrazoles were found to be completely identical (m.p., IR, NMR and mass spectra)

TABLE I

Analytical and NMR data of pyrazolothiazines and their reaction products

Compd.	m.p. (°C)	Yield (%)	Molecular Formula	% Found/Required					NMR,DMSO-d$_6$ (δ/ppm)*
				C	H	N	S	X	
2a	189	46	$C_{18}H_{14}N_2OS_2$	63.7	3.9	8.1	18.6		4.22 (s, CH_2), 6.16 (s, H-4), 7.34 (m, Ar-H), 8.62 (s,OH)
				(63.9	4.1	8.3	18.9	)	
2b	238	38	$C_{18}H_{13}ClN_2OS_2$	57.8	3.7	7.2	17.4	9.8	4.16 (s, CH_2), 6.08 (s, H-4), 7.28 (m, Ar-H), 8.46 (s, OH)
				(58.0	3.5	7.5	17.2	9.5)	
2c	195	51	$C_{18}H_{13}BrN_2OS_2$	51.6	2.8	6.4	15.2	18.9	4.10 (s, CH_2), 6.18 (s, H-4), 7.32 (m, Ar-H), 8.66 (s, OH)
				(51.8	3.1	6.7	15.4	19.2)	
2d	208	49	$C_{19}H_{16}N_2OS_2$	64.6	4.6	8.2	18.0		4.26 (s, CH_2), 6.24 (s, H-4), 6.82 (m, Ar-H), 8.92 (s,OH), 2.34 (s, CH_3)
				(64.8	4.6	8.0	18.2	)	
2e	221	52	$C_{19}H_{16}N_2O_2S_2$	62.2	4.1	7.8	17.2		4.32 (s, CH_2), 6.32 (s, H-4), 7.68 (m, Ar-H), 9.42 (s,OH), 3.84 (s, OCH_3)
				(62.0	4.4	7.6	17.4	)	
3b	225	42	$C_{18}H_{13}ClN_2OS_2$	57.7	3.3	7.8	17.3	9.6	4.28 (s, CH_2), 6.52 (s, H-4), 7.36 (m, Ar-H), 8.62 (s, OH)
				(58.0	3.5	7.5	17.2	9.5)	
3c	182	32	$C_{18}H_{13}BrN_2OS_2$	51.6	3.3	6.9	15.1	19.0	4.52 (s, CH_2), 6.60 (s, H-4), 7.42 (m, Ar-H), 8.26 (s, OH)
				(51.8	3.1	6.7	15.4	19.2)	
3d	145	31	$C_{19}H_{16}N_2OS_2$	64.6	4.8	8.2	17.9		4.42 (s, CH_2), 6.80 (s, H-4), 7.36 (m,Ar-H), 8.88 (s, OH), 2.30 (s, CH_3)
				(64.8	4.6	8.0	18.2	)	
3e	178	22	$C_{19}H_{16}N_2O_2S_2$	61.8	4.3	7.3	17.1		4.36 (s, CH_2), 6.58 (s, H-4), 8.16 (m, Ar-H), 9.60 (s,OH), 3.82 (s, OCH_3)
				(62.0	4.4	7.6	17.4	)	
7b	172	66	$C_{17}H_{14}ClN_3O$	65.2	4.8	13.3		11.6	4.26 (s, CH_2), 6.34 (s, H-3), 7.42 (m, Ar-H), 9.42 (s, OH), 11.88 (s,NH)
				(65.5	4.5	13.5		11.4)	
8b	178	62	$C_{17}H_{14}ClN_3O$	65.8	4.2	13.6		11.1	4.64 (s, CH_2), 6.16 (s, H-3), 7.32 (m, Ar-H), 8.88 (s, OH), 11.20 (s,NH)
				(65.5	4.5	13.5		11.4)	
9b	195	66	$C_{18}H_{11}ClN_2OS$	63.8	3.6	8.5	9.2	10.3	7.42 (m, Ar-H + H-7), 11.20 (s, NH)
				(63.8	3.3	8.3	9.5	10.5)	
10b	168	72	$C_{18}H_{11}ClN_2OS$	63.6	3.6	8.1	9.8	10.2	7.36 (m, Ar-H + H-7), 11.62 (s, NH)
				(63.8	3.3	8.3	9.5	10.5)	

s: Singlet. m: Multiplet. All NH and OH signals were exchangeable with deuterium oxide.

with authentic samples prepared from 4H-pyran-4-thiones **6b** and hydrazine hydrate.[13,14]

The chemistry of pyrazolothiazines generally has been little explored. In the present study, the reaction of **2b** or **3b** with hydrazine hydrate in ethanol afforded

2-*p*-chlorophenyl-5-phenyl-(**7b**)- and 5-*p*-chlorophenyl-2-phenyl-(**8b**)-3′-hydroxy-1H,4H-pyrazolo[1,5-b]pyrazoles, respectively. However, the reaction of **2b** and **3b** with hydrogen peroxide in glacial acetic acid gave 6-*p*-chlorophenyl-3-phenyl-(**9b**)- and 3-*p*-chlorophenyl-6-phenyl-(**10b**)-1H-pyrazolo[4,3-c]thiopyran-4-ones, respectively.

The structures of compounds **7b**–**10b** were fully confirmed by their spectral (IR, NMR) and analytical data (cf. Experimental and Table I). From the above examples, it is apparent that the reaction of pyrazolothiazines with hydrazine hydrate provides a new and useful route to a new series of pyrazolo[1,5-b]pyrazole derivatives. Some of the pyrazolo[1,5-b]pyrazoles are used as photo magenta couplers and provide excellent color reproduction.[15] In addition, their reaction with hydrogen peroxide led to the formation of a new heterocyclic system, the pyrazolo-[4,3-c]thiopyans which have not been reported previously.

EXPERIMENTAL

Melting points were determined on a Kofler Block and are uncorrected. Microanalyses were performed by the Microanalysis Unit, Cairo University, Cairo. IR spectra were measured with a Unicam SP 1025 spectrophotometer for potassium bromide pellets. The NMR spectra were recorded on a Varian EM-390 90 MHz spectrometer with TMS as internal standard. Mass spectra were recorded on an AEI MS 30 spectrometer. For TLC, Merck Kiesegel 60-F254 precoated plastic plates were used.

5-Aryl-2-phenyl-(**2a**–**e**)- *and 2-aryl-5-phenyl-*(**3b**–**e**)*-3′-hydroxy-3H-pyrazolo[1,5-c][1,3]thiazine-7-thiones (Table I)*: A solution of **1a**–**e**[11,12] (0.0020 mol) in ethanol (23 mL) was refluxed with S-ammonium hydrazinecarbodithiolate (0.0021 mol) in water (1 mL) for 20–23 h. The yellow precipitate was subjected to fractional crystallization from benzene, the pyrazolothiazine **2a**–**e** separated first, and from mother liquors, the isomeric **3b**–**e** was obtained as yellow needles. MS: m/z (relative abundance) for **2b**: M^+ 374, 372 (3, 11), 356, 354 (20, 77), 280, 278 (6, 22), 279, 277 (9, 26), 243 (15), 141 (18), 138, 136 (32, 100), 113, 111 (12, 32), 103 (16), 77 (18); **2d**: M^+ 352 (6), 334 (82), 258 (18), 141 (18), 116 (100), 91 (42), 77 (14); **3b**: M^+ 374, 372 (2, 8), 356, 354 (18, 66), 280, 278 (8, 20), 279, 277 (5, 18), 243 (16), 139, 137 (6, 20), 177, 175 (11, 32), 102 (32), 111 (16), 77 (100).

5(3)-p-Chlorophenacyl-3(5)-phenyl-(**4b**)- *and 3(5)-p-chlorophenyl-5(3)-phenacyl-*(**5b**)*pyrazoles*: A solution of **2b** or **3b** (0.0018 mol) in ethanol (20 mL) was refluxed with concentrated sulfuric acid (1 mL) for 4–6 h. After concentration and cooling, **4b** or **5b** separated out and then crystallized from ethanol as needles. The pyrazole **4b** and **5b** were found to be completely identical (m.p. mixed m.p., IR and NMR spectra) with authentic samples prepared from 2-*p*-chlorophenyl-6-phenyl-4H-pyran-4-thione **6b** and 99% hydrazine hydrate in ethanol as described earlier.[13,14]

2-p-Chlorophenyl-5-phenyl-(**7b**)- *and 5-p-chlorophenyl-2-phenyl-*(**8b**)*-3′-hydroxy-1H,4H-pyrazolo[1,5-b]pyrazoles (Table I)*: A solution of **2b** or **3b** (0.0022 mol) in 95% ethanol (15 mL) was refluxed with 99% hydrazine hydrate (1 mL; 0.0199 mol) for 6–9 h. After removal of most of the solvent and dilution with water, the separated pyrazolopyrazole **7b** or **8b** was crystallized from ethanol as needles. IR, Δ_{max} (cm^{-1}): 1584–1596 (C=N, pyrazole ring), 3230–3336 (NH), 3426–3486 (OH).

6-p-Chlorophenyl-3-phenyl-(**9b**)- *and 3-p-chlorophenyl-6-phenyl-*(**10b**)*-1H-pyrazolo[4,3-c]thiopyran-4-ones (Table I)*: A mixture of **2b** or **3b** (0.0018 mol), 30% hydrogen peroxide (3 mL) in glacial acetic acid (20 mL) was heated on a boiling water bath for 6–8 h. After removal of most of the solvent under reduced pressure, the separated solid **9b** or **10b** was crystallized from ethanol as needles. IR, Δ_{max} (cm^{-1}): 1582–1590 (C=N), pyrazole ring), 1678–1692 (C=O), 3268–3356 (NH).

REFERENCES

1. T. Eisenaecher, R. Pech and R. Boehm, *J. Prakt. Chem.*, **333**, 437 (1991).
2. R. Boehm, R. Pech, D. Lohmann and T. Eisenaecher, Ger. (East) DD 290,657 (Cl.CO7D513/04), 06 Jun 1991, Appl. 336,230 22 Dec 1989; *Chem. Abstr.*, **115**, 208006g (1991).
3. G. Auzzi, L. Cecchi, A. Costanzo, V. L. Pecori and F. Bruni, *Farmaco, Ed. Sci.*, **33**, 799 (1978).

4. M. H. Elnagdi, S. M. Fahmy, E. M. Zayed and M. A. M. Ilias, Z. *Naturforsch.*, **31B,** 795 (1976).
5. P. Papini and G. Auzzi, *Gazz. Chem. Ital.*, **96,** 125,430 (1966).
6. D.-B. Renee, D. Danil, P. J. Pauli, R. J. Claude, Q. Herve and K. Alexander, *Sulfur Lett.*, **3,** 51 (1985).
7. G. A. Mironova, E. N. Kirillova, V. N. Kuklin, N. A. Smorygo and B. A. Ivin, *Khim Geterotsikl. Soedin.*, 1328 (1984); *Chem. Abstr.*, **102,** 149205c (1985).
8. K. Peseke and C. Vogel, Ger. (East) DD 157,803 (Cl.CO7D513/04), 08 Dec 1982, Appl. 219,771 20 Mar 1980; *Chem. Abstr.*, **99,** 22114m (1983).
9. B. Dwivedi, N. Tiwari and Nizamuddin, *J. Indian Chem. Soc.*, **68,** 515 (1991).
10. N. Tiwari, B. Dwiredi, R. Ali and Nizamuddin, *J. Indian Chem. Soc.*, **67,** 521 (1990).
11. I. E. El-Kholy, M. G. Marei and M. M. Kishrikey, *J. Heterocycl. Chem.*, **16,** 737 (1979).
12. I. E. El-Kholy, M. M. Mishrikey and M. G. Marei, *J. Heterocycl. Chem.*, **19,** 1421 (1982).
13. M. G. Marei, *Alex. J. Pharm. Sci.*, **6,** 41 (1992).
14. M. G. Marei and M. M. Mishrikey, *Phosphorus, Sulfur, and Silicon*, **73,** 229 (1992).
15. T. Kawagishi and N. Koyaka, Jpn. Kokai Tokkyo Koho JP 60,140,241 (Cl.GO3C7/38), 25 Jul 1985, Appl. 83/250,345, 27 Dec 1983; *Chem. Abstr.*, **104,** 12999m (1986).