Toshio Itahara

Institute of Chemistry, College of Liberal Arts, Kagoshima University, Korimoto, Kagoshima 890, Japan

Received October 15, 1996

Treatment of 2,4-dithiouracil with dihaloalkanes under a basic condition gave three types of thiapyrimidinophanes, whose structures were confirmed by their nmr and mass spectral data.

J. Heterocyclic Chem., **34**, 687 (1997).

Cyclophanes are of interest in connection with synthetic recepters in molecular recognition [1]. Pyrimidinophanes are regarded as being a sort of metacyclophanes containing pyrimidine bases, and the compounds **1**, **2**, and **3** as pyrimidinophanes are known [2-9]. We also reported the facile preparation of the pyrimidinophanes from uracils and dihaloalkanes (X-R-X): Chart 1-A [9]. Furthermore, we reported the reaction of 2-thiouracils with dihalogenated compounds [10]. As part of the investigation of the synthesis of pyrimidinophanes from uracils, the reaction of 2,4-dithiouracil with dihaloalkanes was studied, although the treatment of 6-methyl-2,4-dithiouracil with α,ω-dibromoalkanes (n = 4-6) had been reported [11]. This paper describes a preparation of three thiapyrimidinophanes **4**, **5**, and **6** by the reaction of 2,4-dithiouracil with dihaloalkanes: Chart 1-B. Products **4**, **5**, and **6** are interesting compounds because of the greater aromaticity of the pyrimidine ring, compared with **1**, **2**, and **3**.

Chart 1

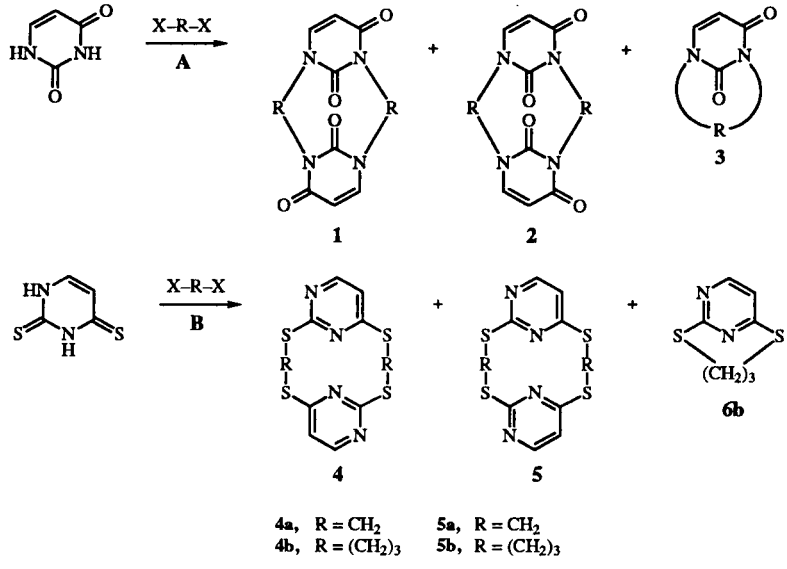

Table 1

Spectral Data of Thiapyrimidinophanes

mp °C	^{1}H nmr ($CDCl_3$) δ Pyrimidine	^{1}H nmr ($CDCl_3$) δ Polymethylene chain	^{13}C nmr ($CDCl_3$) δ Pyrimidine	^{13}C nmr ($CDCl_3$) δ Polymethylene	MS:m/z (relative intensity)
4a [a]	8.12 (d, 2H, J = 4.2 Hz),	7.09 (d, 2H, J = 14.5 Hz)	169.0, 167.3,	29.3	312
265-268	6.85 (d, 2H, J = 4.2 Hz),	4.24 (d, 2H, J = 14.5 Hz)	155.3, 115.1		(M$^+$, 100)
5a [b]	8.13 (d, 2H, J = 4.2 Hz),	7.27 (d, 2H, J = 14.5 Hz)	169.6, 166.5,	31.5	
	6.82 (d, 2H, J = 4.2 Hz),	4.35 (d, 2H, J = 14.5 Hz)	155.4, 115.9,	26.9	
4b [b]	8.09 (d, 2H, J = 4.2 Hz),	3.38 (t, 4H, J = 8.0 Hz)	171.3, 169.2,	32.5	
	6.82 (d, 2H, J = 4.2 Hz),	3.32 (t, 4H, J = 8.0 Hz)	154.7, 114.6,	28.9	
		2.30-2.15 (m, 4H)		26.8	
5b [c]	8.10 (d, 2H, J = 4.2 Hz),	3.37 (t, 4H, J = 8.0 Hz)	171.3, 169.2,	32.7	368
207-210	6.82 (d, 2H, J = 4.2 Hz),	3.32 (t, 4H, J = 8.0 Hz)	154.8, 114.5,	32.3	(M$^+$, 100)
		2.31-2.12 (m, 4H)		29.0, 26.7	
6b [d]	7.50 (d, 1H, J = 6.0 Hz),	4.63 (t, 2H, J = 5.5 Hz)	186.5, 161.4,	49.0	184
146-147	7.24 (d, 1H, J = 6.0 Hz),	3.24 (t, 2H, J = 6.4 Hz)	145.9, 125.7,	28.5	(M$^+$, 100)
		2.37 (tt, 2H, J = 5.5 and 6.4 Hz)		23.2	

[a] Found: C, 38.53; H, 2.47; N, 17.90. *Anal.* Calcd. for $C_{10}H_8N_4S_4$: C, 38.44; H, 2.58; N, 17.93. [b] The compounds **5a** and **4b** were not isolated as pure compounds. [c] Found: C, 45.88; H, 4.20; N, 15.04. *Anal.* Calcd. for $C_{14}H_{16}N_4S_4$: C, 45.62; H, 4.38; N, 15.20. [d] Found: C, 45.55; H, 4.24. *Anal.* Calcd. for $C_7H_8N_2S_2$: C, 45.62; H, 4.38.

Treatment of 2,4-dithiouracil with diiodomethane or dibromomethane in the presence of sodium hydride in *N,N*-dimethylformamide (DMF) gave a mixture of the thiapyrimidinophanes **4a** and **5a**, however, it was not an easy matter to isolate both compounds in the pure state. Separation of the mixture by hplc resulted in the isolation of **4a**, but attempts to isolate **5a** by hplc were unsuccessful. Under similar conditions, the reaction of 2,4-dithiouracil with 1,3-diiodopropane gave **6b** and a mixture of **4b** and **5b**, and the further separation of the mixture by hplc resulted in the isolation of **5b**.

The spectral data of **4a,b**, **5a,b** and **6b** are summarized in Table 1. As can be seen from Table 1, **4** and **5** showed similar ^{1}H nmr spectra. On the other hand, we reported the structural elucidation of **1** and **2** on the basis of the ^{13}C nmr spectral data [9]. The structures of **4a,b** and **5a,b** were differentiated on the basis of the numbers of peaks on the ^{13}C nmr spectra, *e.g.*, the numbers of the peaks of the methylene and trimethylene chains of **4a** and **4b** were one and three, respectively, while those of **5a** and **5b** were two and four, respectively. However, this method may not be effective for the structural elucidation of **4** and **5** when the carbon numbers of the polymethylene chains are even numbers. The structure of **6b** was distinguishable from **4b** and **5b** on the basis of mass spectral data.

EXPERIMENTAL

The melting points were determined on a Yanagimoto micro melting-point apparatus and are uncorrected. The ^{1}H nmr spectra (400 MHz) and ^{13}C nmr spectra (100 MHz) were obtained with a JEOL GSX400 spectrometer. Mass spectra were obtained with a JEOL JMS-D300 spectrometer. The elemental analyses were performed by the Analytical Center of Kyoto University.

Thiapyrimidinophanes **4-6** from 2,4-Dithiouracil.

Into a solution of 2,4-dithiouracil (10 mmoles) in DMF (100 ml), sodium hydride (20 mmoles) and diiodomethane (10 mmoles) was added. The resulting mixture was stirred at room temperature for 24 hours. The reaction mixture was evaporated to give a residue which was chromatographed on silica gel. By monitoring at 254 nm, elution of ethyl acetate gave a mixture of **4a** and **5a** (*ca.* 1:1) in 56% yield. Separation of the mixture by hplc (Tosoh CCPMprep, flow rate: 2.0 ml/minute) with Tosoh TSKgel Silica-60 column (10 μm, 21.5 mm ID x 300 mm, elution: a mixture of chloroform and methanol) resulted in the isolation of **4a** as a pure compound, however **5a** was obtained as a mixture of **5a** and **4a** (*ca.* 85:15 by ^{1}H nmr). Under similar conditions, the treatment of **3** with dibromomethane instead of diiodomethane also gave a mixture of **4a** and **5a** (*ca.* 1:1) in 47% yield.

Treatment of 2,4-dithiouracil (10 mmoles) with 1,3-diiodopropane (10 mmoles) in the presence of sodium hydride (20 mmoles) in DMF (100 ml) gave **6b** (8%) and a mixture of **4b** and **5b** (*ca.* 1:1) in 32% yield. Further separation of the mixture by the hplc (elution: a mixture of chloroform and methanol) resulted in the isolation of **5b**, however **4b** was obtained as a mixture of **4b** and **5b** (*ca.* 4:1 by ^{1}H nmr). The spectral data are summarized in Table 1.

REFERENCES AND NOTES

[1] F. Diederich, Cyclophanes, Monographs in Supermolecular Chemistry, The Royal Society of Chemistry, 1994.

[2] M. M. Htay and O. Meth-Cohn, *Tetrahedron Letters*, 79 (1976).

[3] Y. S. Shvetsov, A. N. Shirshov, and V. S. Reznik, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 1103 (1976); *Chem. Abstr.*, **85**, 108609z (1976).

[4] R. Golankiewicz and B. Skalski, *Pol. J. Chem.*, **52**, 1365 (1978); *Chem. Abstr.*, **90**, 22963b (1979).

[5] H. Koroniak, B. Skalski, and K. Golankiewicz, *Biochem. Biophys. Res. Commun.*, **91**, 375 (1979).

[6] T. Kinoshita, S. Odawara, K. Fukumura, and S. Furukawa, *J. Heterocyclic Chem.*, **22**, 1573 (1985).

[7] T. Kinoshita, H. Tanaka, and S. Furukawa, *Chem. Pharm. Bull.*, **34**, 1809 (1986).

[8] A. F. Cichy, R. Saibaba, H. El Subbagh, R. Panzica, and E. Abushanab, *J. Org. Chem.*, **56**, 4653 (1991).

[9] T. Itahara, *Bull. Chem. Soc. Japan*, **69**, 3239 (1996).

[10] T. Itahara, *Chem. Letters*, 1099 (1996).

[11] A. S. Mikhailov, N. G. Pashkurov, and V. S. Reznik, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 930 (1982); *Chem. Abstr.*, **97**, 23766w (1982).