Chemistry of Heterocyclic Compounds, Vol. 34, No. 6, 1998

DERIVATIVES OF CONDENSED THIENOPYRIMIDINES. 11.* SYNTHESIS OF 2,4-DITHIOXOPYRANO(THIOPYRANO)-[4′,3′:4,5]THIENO[2,3-*d*]PYRIMIDINES

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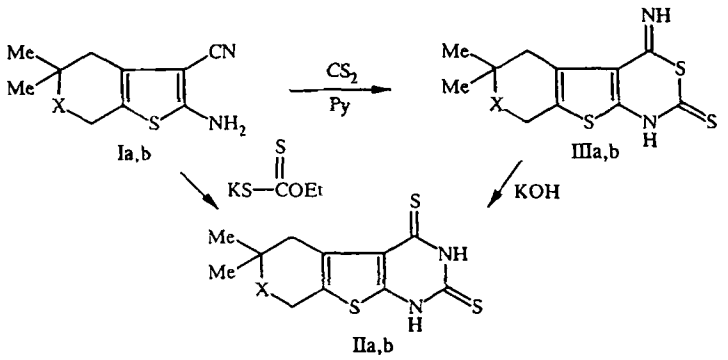
Methods for the synthesis of 2,4-dithioxo-6,6-dimethyl-5,6-dihydro-8H-pyrano(thiopyrano)[4′,3′:4,5]thieno[2,3-d]pyrimidines have been developed.

During recent years there has been a systematic study of the derivatives of condensed thieno[2,3-*d*]pyrimidines [2, 3] but 2,4-dithieno[2,3-*d*]pyrimidines have been insufficiently investigated. In this connection we have carried out the development of real and potential methods for the synthesis of new condensed derivatives of 2,4-dithioxopyrano(thiopyrano)thieno-pyrimidines and have studied their biological activity.



Ia, IIa, IIIa X = O; Ib, IIb, IIIb X = S

4-Imino-6,6-dimethyl-2-thioxo-5,6-dihydro-8H-pyrano(thiopyrano)[4′,3′:4,5]thieno-1,3-thiazines (IIa, b) have been obtained by the reaction 2-amino-5,5-dimethyl-3-cyano-4,5-dihydro-7H-thieno[2,3-*c*]pyran(thiopyran) (Ia, b) [4] with carbon disulfide in boiling pyridine (method A). The Dimroth rearrangement occurred when they were boiled in aqueous potassium hydroxide to give 6,6-dimethyl-2,4-dithioxo-5,6-dihydro-8H-pyrano(thiopyrano)[4′,5′:4,5]thieno[2,3-*d*]pyrimidines (IIIa, b). Compounds IIIa, b were also synthesized by the reaction of 2-amino-3-cyanopyran(thiopyran) with potassium xanthate (method B). Even though the reaction consisted of a single stage, the yields of the desired products were higher than the method involving the Dimroth rearrangement.

*For Communication 10 see [1].

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 0009-3122/98/3406-0700$20.00

EXPERIMENTAL

IR Spectra of were recorded in Vaseline oil with a UR-20 spectrophotometer, ^{1}H NMR spectra were recorded with a Varian T-60 spectrometer, and mass spectra with an MX-1303 instrument with an ionizing current of 70 eV. TLC was carried out on Silufol UV-254 strips developed with iodine vapor.

4-Imino-6,6-dimethyl-2-thioxo-5,6-dihydro-8H-pyrano[4',3':4,5]thieno[3,2-*e*]-1,3-thiazine (IIa). A mixture of thienopyran (Ia) [4] (2.1 g, 0.01 mole) and carbon disulfide (7.6 g, 0.1 mole) in absolute pyridine (15 ml) was boiled for 10 h. The precipitated crystals were filtered off and washed with ethanol to give the thiazine IIa (2.8 g, 97%), mp 278-279°C (dimethylformamide), R_f 0.62 (1:1 pyridine–methanol). IR Spectrum: 1430 (C=S), 1620 (C=N), 3140 cm^{-1} (NH). Mass spectrum, *m/z* (I_{rel}, %): 284 (M^+) (100), 269 (20), 255 (30), 250 (15), 241 (10), 226 (40), 168 (10). Found, %: C 46.61, H 4.21, N 10.02, S 33.75. Calculated for $C_{11}H_{12}N_2OS_3$, %: C 46.44, H 4.32, N 9.88, S 33.90.

4-Imino-6,6-dimethyl-2-thioxo-5,6-dihydro-8H-thiopyrano[4',3':4,5]thieno[3,2-*e*]-1,3-thiazine (IIb). Thiazine IIb was obtained by the same method from a mixture of thienopyran Ib (2.26 g, 0.01 mole) [2] and carbon disulfide (7.6 g, 0.1 molee). Yield 2.8 g (92%), mp ~300°C (decomp.)(pyridine), R_f 0.57 (1:1 pyridine–methanol). IR Spectrum: 1435 (C=S), 1630 (C=N), 3200 cm^{-1} (NH). Mass spectrum, *m/z* (I_{rel}, %): 300 (M^+) (98), 284 (54), 267 (48), 257 (100), 226 (51), 168 (29), 76 (45). Found, %: C 44.12, H 4.52, N 9.74, S 42.72. Calculated for $C_{11}H_{12}NS_4$, %: C 44.30, H 4.20, N 9.38, S 42.75.

6,6-Dimethyl-2,4-dithioxo-5,6-dihydro-8H-pyrano[4',3':4,5]thieno[2,3-*d*]pyrimidine (IIIa). A. A mixture of thiazine IIa (2.84 g, 0.01 mole) and potassium hydroxide (1.7 g, 0.03 mole) in water (50 ml) was boiled with stirring for 2 h. The reaction mixture was filtered after cooling and then acidified with hydrochloric acid. The precipitated crystals were filtered off, washed with water, and dried to give pyrimidine IIIa (2.3 g, 80%). mp 259-260°C (ethanol), R_f 0.55 (3:1 ether–ethyl acetate). IR Spectrum: 1445 (C=S), 3135 cm^{-1} (NH). ^{1}H NMR Spectrum (pyridine-D_5): 12.33 (2H, br. s, 1-NH, 3-NH), 4.70 (2H, s, 8-CH_2), 3.36 (2H, s, 5-CH_2), 1.33 ppm (6H, s, 6-$(CH_3)_2$). Found, %: C 46.5, H 4.2, N 9.7, S 33.9. Calculated for $C_{11}H_{12}N_2OS_3$, %: C 46.4, H 4.3, N 9.9, S 33.7.

B. A mixture of thienopyran Ia (2.1 g, 0.01 mole), potassium xanthate (2.9 g, 0.02 mole), and absolute pyridine (20 ml) were boiled with stirring for 15 h. The crystals were filtered off after cooling, washed with water, and recrystallized from ethanol to give compound IIIa (1.0 g, 35%).

6,6-Dimethyl-2,4-dithioxo-5,6-dihydro-8H-thiopyrano[4',3':4,5]thieno[2,3-*d*]pyrimidine(IIIb).A.Pyrimidine(IIIb) was obtained by method A from a mixture of thiazine IIb (3.0 g, 0.01 mole) and potassium hydroxide (1.7 g, 0.03 mole). Yield 2.5 g (83%), mp 285-287°C (ethanol), R_f 0.56 (1:2:1 acetone–chloroform–hexane). ^{1}H NMR Spectrum (DMSO-D_6): 13.0 (2H, br. s, 1-NH, 3-NH), 3.70 (2H, s, 8-CH_2), 3.23 (2H, s, 5-CH_2), 1.27 ppm (6H, s, 6-$(CH_3)_2$). Found, %: C 44.13, H 4.08, N 8.91, S 42.85. Calculated for $C_{11}H_{12}N_2S_4$, %: C 43.90, H 4.22, N 9.38, S 42.70.

B. Pyrimidine IIIb (1.1 g, 36%) was obtained by method B from a mixture of thienopyran Ib (2.26 g, 0.01 mole) and potassium xanthate (2.9 g, 0.02 mole).

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