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Synthesis of [1,2,3]Thiadiazolo[5,4-*d*]pyrimidines

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Treatment of 4,6-dimethyl-*v*-triazolo[4,5-*d*]pyrimidine-5,7(4H,6H)-dione (I) with phosphorus pentasulfide in pyridine afforded 5,7-dimethyl[1,2,3]thiadiazolo[5,4-*d*]pyrimidine-4(5H)-one-6(7H)-thione (II) through the *v*-triazole-thiadiazole rearrangement. The reaction of (II) with thionyl chloride gave 5,7-dimethyl[1,2,3]thiadiazolo[5,4-*d*]-pyrimidine-4,6(5H,7H)-dione (III).

Keywords——4,6-dimethyl-*v*-triazolo[4,5-*d*]pyrimidine-5,7(4H,6H)-dione; phosphorus pentasulfide-pyridine; *v*-triazole-thiadiazole rearrangement; 5,7-dimethyl[1,2,3]-thiadiazolo[5,4-*d*]pyrimidine-4(5H)-one-6(7H)-thione; thionyl chloride; 5,7-dimethyl-[1,2,3]thiadiazolo[5,4-*d*]pyrimidine-4,6(5H,7H)-dione

A recent paper[2] from our laboratory described a facile synthesis of [1,2,3]thiadiazolo-[4,5-*d*]pyrimidine derivatives, a new class of heterocyclic ring system, by the reaction of 6-hydrazinouracils with thionyl chloride. During the course of study on the thermal and photochemical reactions of this ring system,[3] it became desirable to synthesize 5,7-dimethyl-[1,2,3]thiadiazolo[5,4-*d*]pyrimidine-4(5H)-one-6(7H)-thione (II) and 5,7-dimethyl[1,2,3]thiadiazolo[5,4-*d*]pyrimidine-4,6(5H,7H)-dione (III), which are isomeric with [1,2,3]thiadiazolo-[4,5-*d*]pyrimidines.

Refluxing of 4,6-dimethyl-*v*-triazolo[4,5-*d*]pyrimidine-5,7(4H,6H)-dione (I)[4] with an excess of phosphorus pentasulfide in pyridine for 5 hr afforded II in a moderate yield. The structure of II was ascertained by the following evidences. The characteristic secondary amino absorption band at 3100 cm^{-1} of I was disappeared and a new carbonyl absorption band came out at 1700 cm^{-1} in the infrared (IR) spectrum (Nujol). The mass spectrum revealed a parent ion at *m/e* 214 and the elemental analysis indicated good agreement with the proposed structure.

The conversion of I into II is best explained by assuming the initial formation of the 5,7-dithione intermediate (A), *v*-triazole-thiadiazole rearrangement of (A) to (B), followed by hydrolysis of the imino group to II (Chart 1). The rearrangement of this type has previously been documented.[5a–d]

Replacement of the sulfur of II by oxygen to give III was simply carried out in a high yield by refluxing of II in excess thionyl chloride for 30 min.[6] The formation of III was indicated by the satisfactory elemental analysis and spectral data. Namely, the mass spectrum showed a parent ion at *m/e* 198 and the IR spectrum (Nujol) revealed two carbonyl

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6) Replacement of a sulfur by oxygen with thionyl chloride has recently been reported in certain isothiazolo-[3,4-*d*]pyrimidine: Y. Furukawa, O. Miyashita, and S. Shima, *Chem. Pharm. Bull.* (Tokyo), 24, 970 (1976).

absorption bands at 1685 and 1720 cm^{-1}. Moreover, the nuclear magnetic resonance (NMR) spectrum (DMSO-d_6) showed singlets at δ 3.33 (N^5-CH_3) and δ 3.56 (N^7-CH_3).

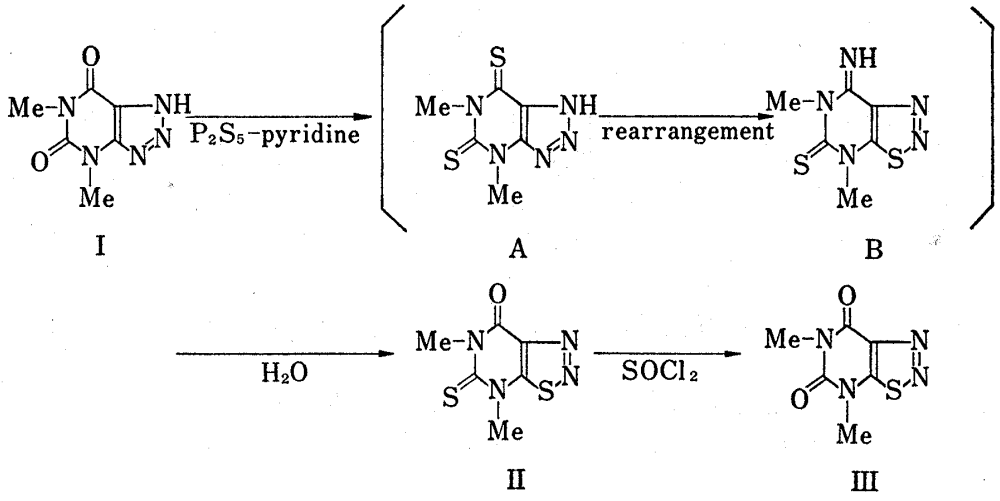

Chart 1

Experimental[7]

5,7-Dimethyl[1,2,3]thiadiazolo[5,4-*d*]pyrimidine-4(5H)-one-6(7H)-thione (II)——A mixture of 4,6-dimethyl-*v*-triazolo[4,5-*d*]pyrimidine-5,7(4H,6H)-dione (I)[4] (7.5 g, 0.04 mol) and phosphorus pentasulfide (26.5 g, 0.12 mol) in pyridine (100 ml) was refluxed for 5 hr. The reaction mixture was evaporated *in vacuo* and the residue was treated with hot water (50 ml). After cooling, the precipitates were collected and recrystallized from ethyl acetate to give 4.8 g (55%) of pure product (II) as pale yellow scales, mp 209—210° (dec.). IR ν_{max}^{Nujol} cm^{-1}: 1700 (C=O). *Anal.* Calcd. for $C_6H_6N_4OS_2$: C, 33.63; H, 2.83; N, 26.15. Found: C, 33.77; H, 2.89; N, 26.42.

5,7-Dimethyl[1,2,3]thiadiazolo[5,4-*d*]pyrimidine-4,6(5H,7H)-dione (III)——A mixture of II (3.57 g, 0.017 mol) and thionyl chloride (20 ml) was refluxed for 30 min. The reaction mixture was evaporated *in vacuo* and the residue was triturated with 5% aqueous ammonia to give a solid. Recrystallization from ethanol gave 3.2 g (94%) of pure product (III) as colorless needles, mp 164—165°. IR ν_{max}^{Nujol} cm^{-1}: 1685 (C=O), 1720 (C=O). NMR (DMSO-d_6) δ: 3.33 (3H, s, N^5–CH_3), 3.56 (3H, s, N^7–CH_3). UV λ_{max}^{EtOH} nm (log ε): 230 (shoulder) (3.94), 275 (3.92). *Anal.* Calcd. for $C_6H_6N_4O_2S$: C, 36.35; H, 3.06; N, 28.27. Found: C, 36.18; H, 3.06; N, 28.38.

7) Melting points were taken on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were recorded on a Japan Spectroscopic Co., Ltd. spectrophotometer, Model IR-E from samples mulled in Nujol. NMR spectrum was determined at 60 MHz with a Varian T-60 spectrometer using tetramethylsilane as the internal reference. Ultraviolet (UV) spectrum was recorded on a Hitachi 124 spectrophotometer.