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REACTION OF 6-OXO-, THIOXO-2,3-DIMETHYLTHIENO[2,3-d]PYRIMIDIN-4-ONES WITH ELECTROPHILIC REAGENTS

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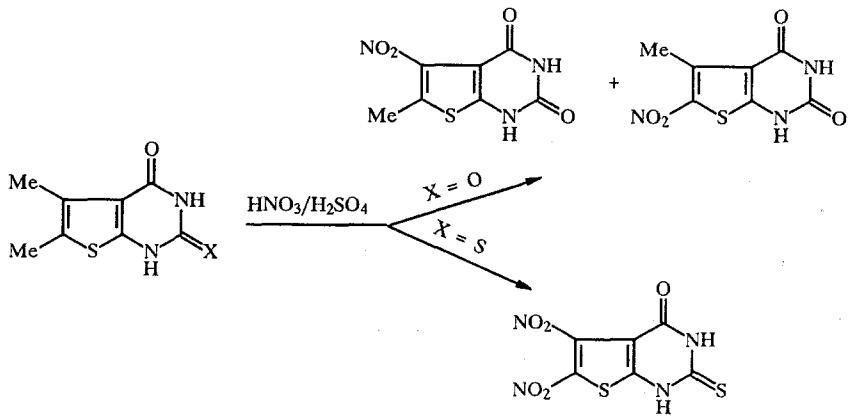
The reaction of 6-oxo-, thioxo-2,3-dimethylthieno[2,3-d]pyrimidin-4-ones with electrophilic agents was studied. It was shown that during nitration these compounds undergo electrophilic unco-substitution forming 3-nitro- and 2-nitro-6-oxo- and 2,3-dinitro-6-thioxothieno[2,3-d]pyrimidin-4-ones, respectively; the reaction of these compounds with bromine proceeds in other directions.

Electrophilic unco-substitution reactions have been fairly well studied for derivatives of benzene, diphenyl ethers, and other compounds with respect to nitration, sulfonation and bromination [1-4]. The investigation of lesser known unco-substitution reactions of heterocyclic compounds having various hetero atoms and condensed with other hetero-rings and the clarification of the characteristics of the substitution are of considerable theoretical interest. The present work is devoted to the investigation of 6-oxo-, thioxothieno[2,3-d]pyrimidin-4-ones with certain electrophilic reagents and to the clarification of the influence of the nature of the substituent at the 6-position on the reactivity and direction of the substitution reaction of the methyl group (or methyl groups). The nitration was carried out using a nitrating mixture and the bromination using molecular bromine in acetic acid.

During treatment of 2,3-dimethylthieno[2,3-d]pyrimidine-4,6-dione with a doubled quantity of the nitrating mixture, a mixture of 3-nitro-2-methyl and 3-methyl-2-nitrothieno[2,3-d]pyrimidine-4,6-diones is formed in a 1:1 ratio.



On using a 1:1 ratio of the reagents a mixture of the isomers in a 1:8 ratio is obtained — the difference can be attributed to the different nucleophilicity of the C_2 and C_3 carbon atoms. Increase in the amount of the nitric acid used does not lead to the formation of the dinitro product. The action of the nitrating mixture on 2,3-dimethyl-6-thioxothieno[2,3-d]pyrimidin-4-one gave 2,3-dinitro-6-thioxothieno[2,3-d]pyrimidin-4-one.

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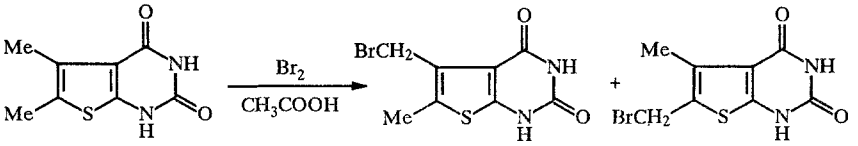
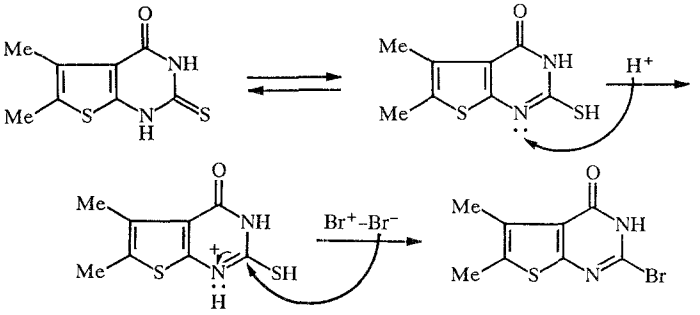
The bromination of 2,3-dimethylthienopyrimidinedione does not give unco-substitution products — a mixture of 3-bromomethyl-2-methyl- and 3-methyl-2-bromomethyl[2,3-d]pyrimidine-4,6-diones is formed in a ratio of 7.5:1, i.e., the bromination proceeds at both methyl groups in the side chain.



It has been assumed previously [5] that this type of substitution reaction, in particular nitration, proceeds in two stages: the formation of intermediate products substituted in the side chain and further splitting of the methyl group. It could be assumed that in the present case, on using a stronger electrophile, i.e., during nitration, the reaction is accompanied by the water, and dried. The isomers were separated by fractional crystallization from hexane. Yield, 3.01 g (40%) of 3-nitro-2-methylthieno[2,3-d]pyrimidine-4,6-dione, mp 310-312°C; R_f 0.69 (chloroform–methanol, 15:1). Mass spectrum m/z (I, %): M^+ 227 (100), 199 (30), 184 (54), 181 (10), 138 (90). PMR spectrum: 235 ppm (3H, s, 2-CH_3); and 3.2 g (41%) of 3-methyl-2-nitrothieno[2,3-d]pyrimidine-4,6-dione, mp 328-330°C; R_f 0.73 (chloroform–methanol, 15:1). Mass spectrum: M^+ 227. PMR spectrum: 245 ppm (3H, s, 3-CH_3).



2,3-Dinitro-6-thioxothieno[2,3-d]pyrimidin-4-one ($C_6H_2N_4O_5S_2$). A 1 g portion (0.004 mole) of 6-thioxo-2,3-dimethylthieno[2,3-d]pyrimidin-4-one was dissolved in 5 ml of concentrated sulfuric acid and a mixture of 0.5 ml (0.008 mole) of fuming nitric acid and 2 ml of sulfuric acid was added. The reaction mixture was allowed to stand with stirring for 2 days, then was diluted with water, and the precipitate that separated out was filtered off, washed with water, and dried. Yield, 0.5 g (40%) of a compound, mp 350°C (alcohol), R_f 0.37 (chloroform–methanol, 9:1). Mass spectrum m/z (I, %): M^+ 274 (100), 244 (40), 231 (50), 214 (20).

2-Bromomethyl-3-methyl and 3-Bromomethyl-2-methylthieno[2,3-d]pyrimidine-4,6-diones ($C_8H_7BrN_2O_2S$). A 1 ml portion (0.01 mole) of bromine dissolved in 10 ml of acetic acid was added to a solution of 1.0 g (0.005 mole) of 2,3-dimethylthieno[2,3-d]pyrimidine-4,6-dione in 30 ml of acetic acid. The reaction mixture was allowed to stand for 2 days. It was then diluted with water, the precipitate that separated out was filtered off, washed with hot water, and dried. The mixture of the isomers was separated by fractional crystallization from benzene. Yield, 0.3 g (42%) of 3-bromomethyl-2-methylthieno[2,3-d]pyrimidine-4,6-dione, mp 280-290°C (alcohol); R_f 0.30 (chloroform–methanol, 9:1). Mass spectrum m/z (I, %): M^+ 276/274 (100), 261/254 (30), 248/246 (10), 233/232 (80), 218/216 (70), 180 (50). PMR spectrum: 2.07 (3H, s, 2′-CH_3); 5.32 ppm (2H, s, 3-CH_2); and 0.2 g (38%) of 3-methyl-2-bromomethylthieno[2,3-d]pyrimidine-4,6-dione, mp 278-280°C (alcohol), R_f 0.37 g (chloroform–methanol, 9:1). Mass spectrum: M^+ 276/274. PMR spectrum: 2.17 (3H, s, 3′-CH_3); 4.27 ppm (2H, s, 2-CH_2).

6-Bromo-2,3-dimethylthieno[2,3-d]pyrimidin-4-one ($C_8H_7BrN_2OS$). A 2 ml portion (0.02 mole) of bromine dissolved in 15 ml of acetic acid was added to a solution of 2.12 g (0.01 mole) of 6-thioxo-2,3-dimethylthieno[2,3-d]pyrimidin-4-one in 50 ml of acetic acid. The reaction mixture was allowed to stand for 2 days. It was then diluted with water, the precipitate that separated out was filtered off, washed with hot water, recrystallized from alcohol, and dried. Yield 1.65 g (63%) of 6-bromo-2,3-dimethylthieno[2,3-d]pyrimidin-4-one, mp 268-269°C (alcohol); R_f 0.55 (chloroform–methanol, 9:1). Mass spectrum m/z (I, %): M^+ 260/258 (100), 245/243 (10), 230/228 (15), 179 (70), 178 (10). PMR spectrum: 2.10 ppm (6H, s).

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