Studies on Heteroaromaticity. XVIII.[1] Reaction of Aromatic Hydroxamoyl Chlorides with Methyl Dithiocarbazinate

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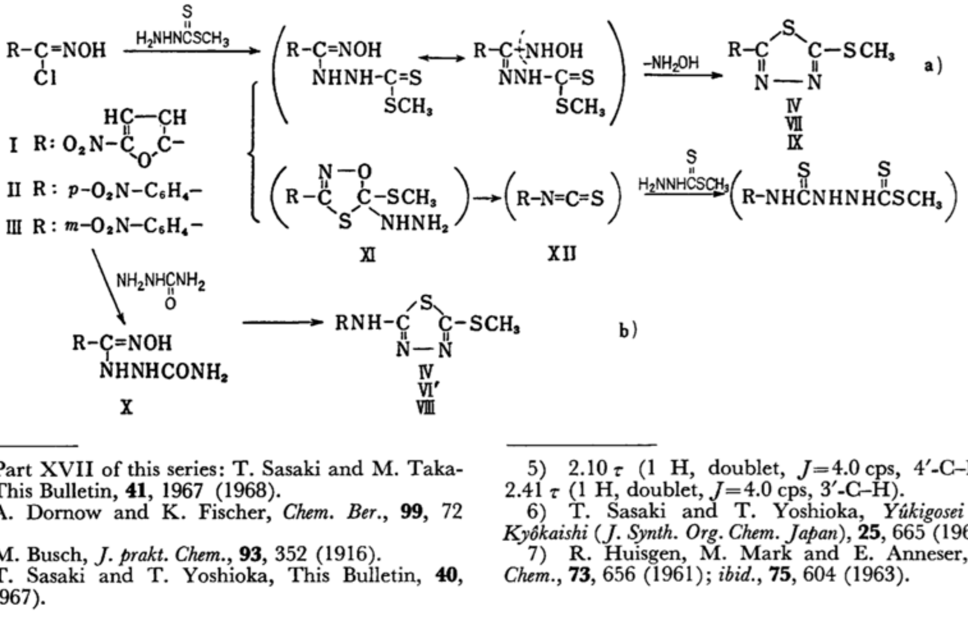
Dornow and Fischer[2] have reported interesting reactions of aromatic hydroxamoyl chlorides with methyl dithiocarbazinate to give 2-substituted amino-5-methylmercapto-1,3,4-thiadiazoles; for example, 2-anilino-5-methylmercapto-1,3,4-thiadiazole, mp 126°C,[3] was obtained in 48% yield, from phenylhydroxamoyl chloride.

Since this kind of reactions is obviously involved in the thermal 1,3-dipolar cycloaddition reactions,[1,4] we attempted the similar reactions with 5-nitro-2-furyl- (I), *p*-nitrophenyl- (II), and *m*-nitrophenylhydroxamoyl chloride (III) and we wish to report on some interesting results.

I was refluxed in ethanol with two equivalent amounts of methyl dithiocarbazinate to afford a product in 50% yield, the structure of which was, however, characterized from the elemental analysis and the NMR measurement as 2-(5′-nitro-2′-furyl)-5-methylmercapto-1,3,4-thiadiazole, IV, instead of the expected 2-substituted amino-1,3,4-thiadiazole, IV′. The NMR spectrum of IV in DMSO-d_6 manifested a chemical shift at 7.14 τ (singlet, 3 H, $-SC\underline{H}_3$) besides those due to nitrofuran ring protons.[5] Similar treatment of II afforded, however, a mixture of VI and VII in 45 and 27% yields respectively. The structural elucidation of both compounds was done from their elemental analyses and NMR sepctra and VI was confirmed to be 2-(*p*-nitroanilino)-5-methylmercapto-1,3,4-thiadiazole and VII, to be 2-(*p*-nitrophenyl)-5-methylmercapto-1,3,4-thiadiazole. Similarly, a mixture of the corresponding *m*-nitro compounds, VIII and IX, was obtained from III in 45 and 20% yields respectively. Treatment of I with two equivalent amounts of thiosemicarbazide under the similar reaction conditions resulted in the formation of intractable tars only, but when semicarbazide was used in place of thiosemicarbazide, normal substitution reaction had occurred between a chlorine atom of I and an amino group of semicarbazide affording X in 50% yield; the similar substitution has been observed in the reaction of I with some amino- and hydrazino compounds.[6]

About the mechanism of the formation of IV from I, VI and VII from II, and VIII and IX from III, we would propose here two competitive reactions, a) and b): in a), simple substitution reaction, followed by elimination of hydroxylamine afforded IV, VII and IX respectively; on the contrary, in b), thermal 1,3-dipolar cycloaddition might take place at first between hydroxamoyl chloride and carbon-sulfur double bond as shown in the usual nitrile oxide reactions[7] and this assumption seems to be reasonable from our previous findings on the parallel



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[1] Part XVII of this series: T. Sasaki and M. Takahashi, This Bulletin, **41**, 1967 (1968).

[2] A. Dornow and K. Fischer, *Chem. Ber.*, **99**, 72 (1966).

[3] M. Busch, *J. prakt. Chem.*, **93**, 352 (1916).

[4] T. Sasaki and T. Yoshioka, This Bulletin, **40**, 2604 (1967).

[5] 2.10 τ (1 H, doublet, J=4.0 cps, 4′-C–H) and 2.41 τ (1 H, doublet, J=4.0 cps, 3′-C–H).

[6] T. Sasaki and T. Yoshioka, *Yûkigosei Kagaku Kyôkaishi* (*J. Synth. Org. Chem. Japan*), **25**, 665 (1967).

[7] R. Huisgen, M. Mark and E. Anneser, *Angew. Chem.*, **73**, 656 (1961); *ibid.*, **75**, 604 (1963).

reactivity between thermal 1,3-dipolar cycloaddition of hydroxamoyl chloride and the corresponding nitrile oxide cycloaddition.[1,4] As is suggested by Huisgen,[7] the intermediate thioisocyanate XII, produced by decomposition of the adduct XI *via* route b), seems to react with an equivalent amount of methyl dithiocarbazinate to give VI and VIII, which is the known procedure for preparing 2-anilino-5-methylmercapto-1,3,4-thiadiazole.[3] Other examples of the thermal 1,3-dipolar cycloaddition of hydroxamoyl chlorides with compounds possessing carbon-sulfur double bond are under investigation. The reason why phenylhydroxamoyl chloride affords exclusively 2-substituted amino compound through b)[2] and 1, giving 2-substituted IV through a), while the corresponding *p*- (II), and *m*-nitrophenylhydroxamoyl chloride (III) gave a mixture of the products through a) and b) at the same time, is uncertain at the present stage.

Experimental

Reaction of 5-Nitro-2-furylhydroxamoyl Chloride (I). A solution of 0.95 g (5 mmol) of I[1] and 1.15 g (11 mmol) of methyl dithiocarbazinate[8] in 40 m*l* of ethanol was refluxed for 12 hr. After removal of ethanol, the residue was digested with 20 m*l* of a ethanol-water mixture (1:1). The resulting crystals were collected and recrystallized from ethanol to give 0.6 g of IV as yellow crystals, mp 180—181°C. UV λ_{max}^{EtOH} mμ (ε); 356 (14500), 282 (6300).

Found: C, 34.02; H, 1.76; N, 16.92%. Calcd for $C_7H_6O_3N_4S_2$: C, 34.58; H, 2.07; N, 17.28%.

Reaction of *p*-Nitrophenylhydroxamoyl Chloride (II). A solution of 0.6 g (3 mmol) of II[1] and 0.75 g (6 mmol) of methyl dithiocarbazinate[8] in 20 m*l* of ethanol was refluxed for 10 hr. The resulting crystals were collected after cooling and extracted with hot chloroform. The insoluble part was recrystallized several times from pyridine-ethanol to afford 0.36 g of yellow needles, VI, mp 270—271°C. IR (KBr) cm^{-1}; 3310, 3250 νNH). UV λ_{max}^{EtOH} mμ (ε); 354 (22800). NMR (DMSO-d_6) τ; 6.5 (broad, 1 H, –N$\underline{H}$–), 7.25 (singlet, 3 H, –SC$\underline{H}_3$).

Found: C, 41.13; H, 2.74; N, 20.57%. Calcd for $C_9H_8O_2N_4S_2$: C, 40.62; H, 3.01; N, 20.89%.

From the chloroform solution, 0.2 g of VII as colorless plates, mp 222—223°C, were obtained after removing chloroform, followed by recrystallization from benzene-ethanol. IR (KBr) cm^{-1}; no νNH. UV λ_{max}^{EtOH} mμ (ε); 335 (16300), 254 (8500). NMR (DMSO-d_6) τ; 7.14 (singlet, 3 H, –SC$\underline{H}_3$).

Found: C, 42.13; H, 2.46; N, 16.72%. Calcd for $C_9H_7O_2N_3S_2$: C, 42.68; H, 2.74; N, 16.59%.

Reaction of *m*-Nitrophenylhydroxamoyl Chloride (III). Similar treatment of III[1] and work-up as above afforded VIII as yellow crystals, mp 234—236°C, in 45% and IX as colorless crystals, mp 172—173°C, in 20% yield.

VIII: IR (KBr) cm^{-1}; 3310, 3260 (νNH). UV λ_{max}^{EtOH} mμ (ε); 350 (2600, shoulder), 300 (24200), 245 (13400). NMR (DMSO-d_6)τ; 6.5 (broad, 1 H, –N$\underline{H}$–) 7.25 (singlet, 3 H, –SCH$_3$).

Found: C, 40.43; H, 2.64; N, 20.59%. Calcd for $C_9H_8O_2N_4S_2$: C, 40.62; H, 3.01; N, 20.89%.

IX: IR (KBr) cm^{-1}; no νNH. UV $\lambda_{max}^{CHCl_3}$ mμ (ε); 306 (16600), 273 (12000). NMR (DMSO-d_6) τ; 7.15 (singlet, 3 H, –SC$\underline{H}_3$).

Found: C, 42.68; H, 2.51; N, 16.21%. Calcd for $C_9H_7O_2N_3S_2$: C, 42.68; H, 2.78; N, 16. 59%.

Reaction of I with Semicarbazide. A solution of 0.93 g (5 mmol) of I[1] and 0.75 g (10 mmol) of semicarbazide in 10 m*l* of ethanol was refluxed for 1 hr. The resulting crystals were collected after cooling, washed with a small amount of water and recrystallized from water-ethanol-DMF to afford 0.5 g (44%) of X as pale yellow crystals, mp 195—197°C (decomp). IR (KBr) cm^{-1}; 3500, 3250 (νNH), 1660 (νCO).

Found: C, 31.00; H, 2.84; N, 29.94%. Calcd for $C_6H_7O_5N_5$: C, 31.45; H, 3.08; N, 30.56%.

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8) F. Audrieth, F. S. Scott and P. S. Kippur, *J. Org. Chem.*, **19**, 733 (1954).