[Chem. Pharm. Bull. 18(8)1696—1698(1970)]

UDC 547.789.07 : 547.334.1.04 : 546.265.1.04

Studies on the Synthesis of 1,3,4-Thiadiazole Derivatives. II.[1] Synthesis of 1,3,4-Thiadiazoline-5-thiones from Amidrazones and Carbon Disulfide

Seiju Kubota, Yoshiyuki Koida, Takayuki Kosaka and Osamu Kirino

Faculty of Pharmaceutical Sciences, University of Tokushima[2]

(Received March 10, 1970)

It has been reported that potassium 3-thiobenzoyldithiocarbazate (II), which was prepared from thiobenzhydrazide and carbon disulfide, was cyclized to 2-phenyl-1,3,4-thiadiazoline-5-thione (I) with potassium hydroxide in ethanol.[3,4] The thione (I) was also prepared by cyclization of potassium 3-benzoyldithiocarbazate (III), which was obtained from benzhydrazide, potassium hydroxide and carbon disulfide, with cold concentrated sulfuric acid.[3]

Recently, Dornow and Fischer[5] reported that the reaction of benzhydrazoxime (IV) with carbon disulfide gave I.

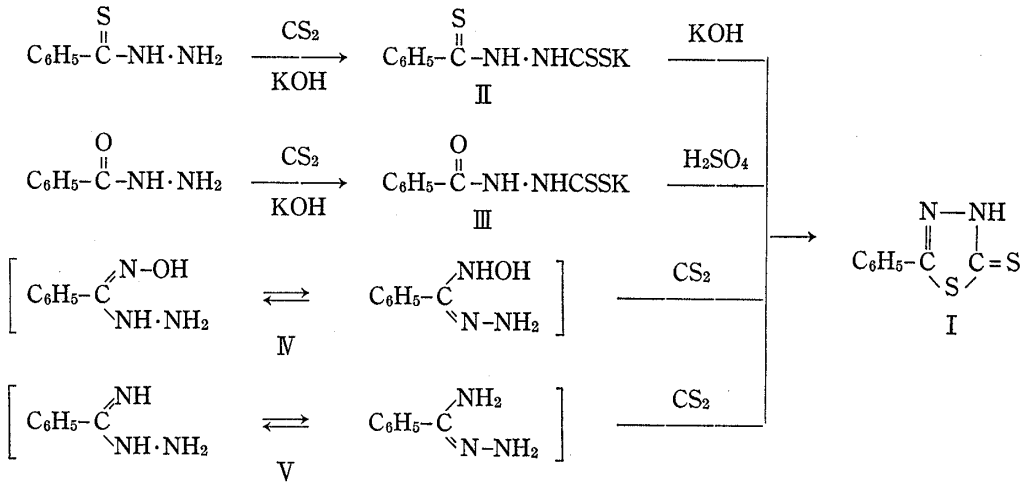


Chart 1

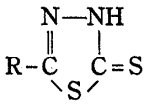
In view of these facts, we examined the reaction of benzamidrazone (V), which has a similar structure to thiobenzhydrazide or benzhydrazide, with carbon disulfide. In contrast with benzhydrazide or thiobenzhydrazide, benzamidrazone afforded I directly in the reaction with carbon disulfide in ethanol at room temperature without any condensing agent.

Application of this procedure was extended to the other aromatic and heterocyclic amidrazones and a number of 1,3,4-thiadiazoline-5-thiones were obtained in excellent yields (Table I).

The starting picolinic and quinaldic acid amidrazones were prepared by direct action of hydrazine hydrate on the corresponding nitriles by the method of Case.[6] The same procedure was

1) Part I: S. Kubota, T. Okitsu and Y. Koida, *Yakugaku Zasshi*, **90**, 841 (1970).
2) Location: *Shomachi, Tokushima.*
3) M. Baron and C. Wilson, *J. Org. Chem.*, **23**, 1021 (1958).
4) R.W. Young and K.H. Wood, *J. Am. Chem. Soc.*, **77**, 400 (1955).
5) A. Dornow and K. Fischer, *Chem. Ber.*, **99**, 72 (1966).
6) F.H. Case, *J. Org. Chem.*, **30**, 931 (1965).

Table I. 2-Substituted-1,3,4-thiadiazoline-5-thiones



	R	Yield (%)	mp (°C)
I	phenyl	82	217—219
VI	α-napthyl	76	213—214
VII	2-pyridyl	80	245—246
VIII	3-pyridyl	73	266—267[a]
IX	4-pyridyl	90	279—280
X	2-quinolyl	95	300
XII	1-isoquinolyl	86	257—259

a) literature mp 219—221° (ref. 3)

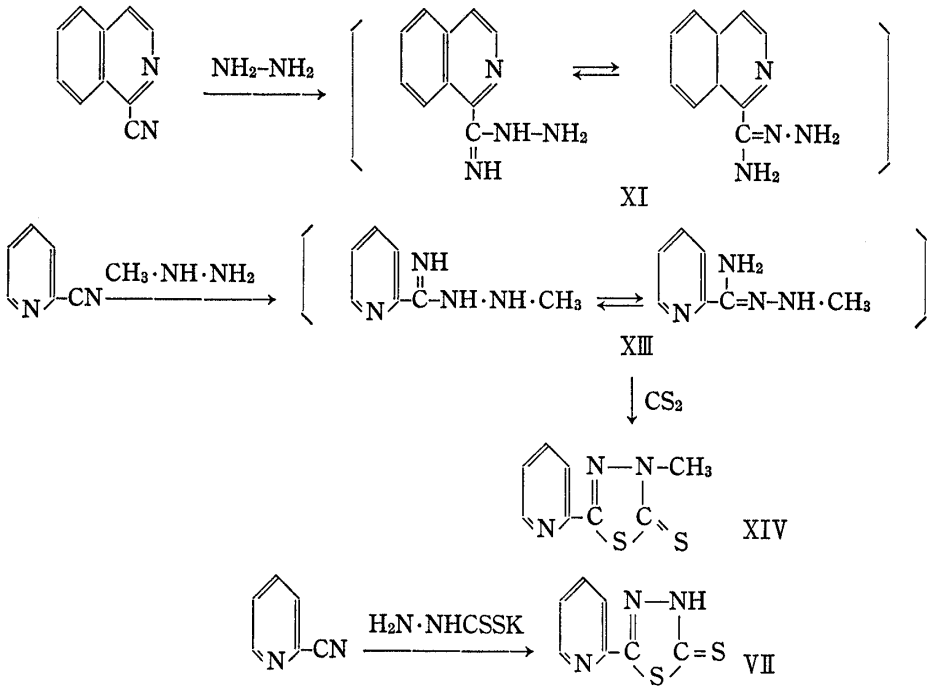


Chart 2

also applied to 1-isoquinolinecarbonitrile yielding isoquinaldic acid amidrazone (XI). Similar reaction of 2-cyanopyridine with methylhydrazine gave N^1-methyl picolinic acid amidrazone (XIII), which was cyclized to 2-(2-pyridyl)-4-methyl-1,3,4-thiadiazoline-5-thione (XIV) with carbon disulfide.

Further investigation revealed that the reaction of 2-cyanopyridine with potassium dithiocabazate also afforded 2-(2-pyridyl)-1,3,4-thiadiazoline-5-thione (VII) at room temperature.

Experimental[7]

2-Substituted-1,3,4-thiadiazoline-5-thiones——General Procedure: To a solution of 0.01 mole amidrazone in 10 ml of EtOH, 0.02 mole of CS_2 was added and the mixture was stirred at room temperature for 2 hr cooling, the crystalline product was collected by filtration. Recrystallization from appropriate solvents After gave the corresponding 2-substituted-1,3,4-thiadiazoline-5-thiones.

7) All melting points were uncorrected.

2-Phenyl-1,3,4-thiadiazoline-5-thione (I)——Recrystallized from isopropanol to give colorless needles. *Anal.* Calcd. for $C_8H_6N_2S_2$: C, 49.46; H, 3.11; N, 14.42. Found: C, 49.52; H, 2.71; N, 14.12.

2-α-Napthyl-1,3,4-thiadiazoline-5-thione (VI)——Recrystallized from isopropanol to give yellow needles. *Anal.* Calcd. for $C_{12}H_8N_2S_2$: C, 58.99; H, 3.30; N, 11.46. Found: C, 59.05; H, 3.48; N, 11.74.

2-(2-Pyridyl)-1,3,4-thiadiazoline-5-thione (VII)——Recrystallized from ethanol to give yellow needles. *Anal.* Calcd. for $C_7H_5N_3S_2$: C, 43.06; H, 2.58; N, 21.52. Found: C, 43.17; H, 2.73; N, 21.35.

2-(3-Pyridyl)-1,3,4-thiadiazoline-5-thione (VIII)——Recrystallized from 50% ethanol to give yellow crystals. *Anal.* Calcd. for $C_7H_5N_3S_2$: C, 43.06; H, 2.58; N, 21.52. Found: C, 42.71; H, 2.73; N, 21.87.

2-(4-Pyridyl)-1,3,4-thiadiazoline-5-thione (IX)——Recrystallized from methanol to give yellow needles. *Anal.* Calcd. for $C_7H_5N_3S_2$: C, 43.06; H, 2.58; N, 21.52. Found: C, 43.43; H, 2.71; N, 21.24.

2-(2-Quinolyl)-1,3,4-thiadiazoline-5-thione (X)——Purified by dissolving in alkali and reprecipitating with acid to give yellow crystals. *Anal.* Calcd. for $C_{11}H_7N_3S_2$: C, 53.86; H, 2.88; N, 17.13. Found: C, 53.83; H, 2.92; N, 16.81.

Isoquinaldic Acid Amidrazone (XI)——To a solution of 3 g of 1-isoquinolinecarbonitrile in 30 ml of methanol, 9 ml of anhydrous hydrazine was added and allowed to stand for 4 days at room temperature. The reaction mixture was extracted with chloroform. The chloroform layer was washed with water, dried over Na_2SO_4 and evaporated *in vacuo*. The residue was recrystallized from isopropyl ether to give 3.3 g (91.0%) of colorless crystals. mp 88—89°. Mass Spectrum *m/e*: 286 (M^+). *Anal.* Calcd. for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41; N, 30.09. Found: C, 65.16; H, 5.41; N, 30.46.

2-(1-Isoquinolyl)-1,3,4-thiadiazoline-5-thione (XII)——Recrystallized from ethanol to give yellow needles. *Anal.* Calcd. for $C_{11}H_7N_3S_2$: C, 53.86; H, 2.88; N, 17.13. Found: C, 53.85; H, 2.95; N, 17.42.

N^1-Methyl Picolinic Acid Amidrazone (XIII)——To a solution of 5 g of 2-cyanopyridine in 10 ml of methanol, 6 g of methylhydrazine was added and stirred at room temperature for 2 days. After methanol had been removed *in vacuo*, the residue was recrystallized from benzene to give 4.9 g (68%) of yellow prisms, mp 106—108°. *Anal.* Calcd. for $C_7H_{10}N_4$: C, 55.98; H, 6.71; N, 37.31. Found: C, 56.28; H, 6.82; N, 37.79.

2-(2-Pyridyl)-4-methyl-1,3,4-thiadiazoline-5-thione (XIV)——To a solution of 0.5 g of N^1-methyl picolinic acid amidrazone in 4 ml of ethanol, 0.5 g of carbon disulfide was added and the mixture was stirred at room temperature for 2 hr. The precipitated crystals were collected by filtration and recrystallized from methanol to give 0.34 g (49%) of colorless crystals, mp 139—141°. *Anal.* Calcd. for $C_8H_7N_3S_2$: C, 45.91; H, 3.37; N, 20.08. Found: C, 46.13; H, 3.31; N, 20.05.

Reaction of 2-Cyanopyridine with Potassium Dithiocarbazate——2-Cyanopyridine (1 g) and potassium dithiocarbazate (4 g) were dissolved in 16 ml of methanol. The resulting mixture was stirred at room temperature for 20 hr. After methanol had been removed *in vacuo*, the appeared precipitate was removed by filtration. The mother liquor was acidified with 10% HCl, and the precipitated solid was collected by filtration. Recrystallization from ethanol gave 0.53 g (33.5%) of yellow needles (VII), mp 245—246°.

Acknowledgement The authors are grateful to Mrs. F. Shimizu of this Faculty for elemental analysis.