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Nicotinonitrile Derivative from 2-Cyano-3-mercapto-3-methylthioacrylamide

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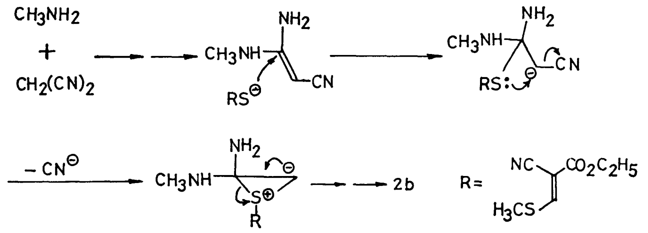
The reaction of 2-cyano-3-mercapto-3-methylthioacrylamide (**1a**) with carbonyl compounds has been reported.[1] This paper deals with the reaction of **1a** with a cyano compound.

It has been found that 2-imino-4-methylthio-6-methylamino-1,2-dihydronicotinonitrile (**3**) can be isolated in 71% yield by the reaction of **1a** with malononitrile and an aqueous solution of methylamine (30%).

The structure of **3** was established on the basis of spectroscopic evidence and the results of elementary analysis. The NMR spectrum (acetone-d_6) showed a broad NH signal at δ 5.80, a singlet peak for one proton of C(5)–H at δ 5.50, a doublet methyl singal at δ 2.85 (J=5 Hz), and a singlet methyl signal at δ 2.43. On addition of deuterium oxide, the NMR peak of NH disappeared and the doublet methyl signal changed to a singlet. This indicates the presence of the $NHCH_3$ group. The NH stretching bands appeared at 3440, 3400, and 3310 cm^{-1}, and a conjugated CN group occurred at 2200 cm^{-1}. The features of the UV spectrum of **3** were similar to those of 2-aminopyridine,[2] but quite different from those of ethyl 3(2-amino-2-methylaminoethenylthio)-2-cyano-3-methylthioacrylate (**2b**) (see Experimental). Compound **3** might better be written in a pyridone type form to accomodate C(5)–H to δ 5.50.

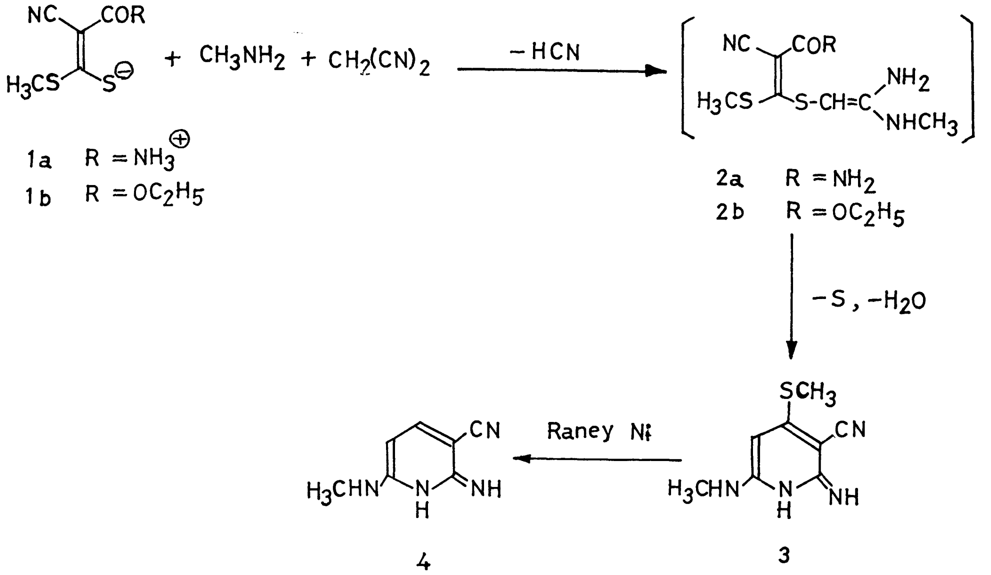
A plausible mechanism for the formation of **3** is illustrated in Scheme 1 by assuming **2a** as an intermediate. Compound **2b**, corresponding to **2a**, could be isolated by the reaction of ethyl 2-cyano-3-mercapto-3-methylthioacrylate with malononitrile and the aqueous solution of methylamine (30%). Formation of **2b** can be accounted for in the following way:



Compound **3** can be formed by the cyclization reaction of **2a**, followed by the loss of an atom of sulfur. A similar desulfuration reaction has been reported on the behavior of a cyclic polysulfide.[3]

Compound **3** was also obtained by refluxing **2b** in alcohol-aqueous ammonia (28%), sulfur being simultaneously eliminated. In the reaction of **1a** with malononitrile and the aqueous solution of methylamine, a small amount of sulfur was detected, while no cyano ion eliminated from malononitrile could be detected by spot test.[4]

Desulfuration of **3** afforded 2-imino-6-methylamino-1,2-dihydronicotinonitrile (**4**). The NMR spectrum (DMSO-d_6) of 4 showed a doublet peak of C(5)–H which caused coupling with that of C(4)–H at δ 5.90



Scheme 1

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[1] M. Yokoyama, This Bulletin, **44**, 1610 (1971).

[2] UV$_{\max}^{99\%EtOH}$ 235 mμ (log ε=3.97), 297 (3.51).

[3] M. S. Raasch, *J. Org. Chem.*, **35**, 3470 (1970).

[4] A dark brown solution containing cuprous sulfate and ammonium sulfide changes to a colorless one by addition of a cyanide ion.

(J=8 Hz), and no peak at δ 2.43 for the methylthio group. Formation of **4** also supports the structure of **3**.

Experimental

Compound **1a** was prepared according to the procedure given in a previous report.[1] The NMR spectra were recorded with a JNM-4H-100 MHz Spectrometer using tetramethylsilane as an internal standard. The IR, UV, and mass spectra were recorded with a Nihon Densi 403G, Hitachi EPS-3T, and Hitachi Double Focus RMU-6E, respectively. Microanalyses were performed at the Institute of Physical and Chemical Research.

Preparation of 2-Imino-4-methylthio-6-methylamino-1,2-dihydronicotinonitrile (3). To a mixture of an aqueous solution of methylamine (30%, 30 m*l*) and **1a** (5 g, 0.03 mol) was gradually added malononitrile (20 g, 0.3 mol) with stirring at room temperature. The reaction mixture immediately started to boil. After 5 min, a colorless crystalline material started to precipitate gradually. After 1 hr, it was filtered, washed with ethanol, and dried. Recrystallization from methanol gave 4 g of colorless needles: yield 71%; mp 223—224°C; $UV_{max}^{99\%EtOH}$ 236.5 mμ (log ε =4.59), 255 (sh, 4.39), 288 (4.10).

Found: C, 49.22; H, 5.14; N, 29.02; S, 16.47%; mol wt, 194 (mass spectrum). Calcd for $C_8H_{10}N_4S$: C, 49.48; H, 5.19; N, 28.85; S, 16.48%; mol wt, 194.19.

A small amount of sulfur was detected from the above filtrate.

Desulfuration of 3. A Raney nickel (Ni: 48%) was activated in the usual way.[5] Compound **3** (3 g, 0.02 mol) was refluxed with the activated Raney nickel (25 g) in ethanol (50 m*l*) for 6 hr. The decolorized reaction mixture was separated from nickel by decantation and centrifugation. The nickel was washed with ethanol and the washings were also centrifuged. The combined alcoholic solution was concentrated to *ca.* 20 m*l* under diminished pressure. The resulting solution was left to stand for 2 weeks. After a small amount of the unreacted **3** was filtered off, the filtrate was allowed to stand for an additional 2 weeks. The second crystalline material (colorless needles) was collected and washed with ethanol: yield 0.1 g; mp 180—181°C; NMR (DMSO-d_6) δ 6.30 (br, 3, NH) δ 5.90 (d, 1, C(4)–H, J=8 Hz) δ 5.50 (d, 1, C(5)–H, J=8 Hz) δ 2.65 (d, 3, CH_3, J=7 Hz); IR (KBr) 3450, 3360, 3130 (s, NH), 2950 (m, CH), 2220 cm^{-1} (s, conj. CN); $UV_{max}^{99\%EtOH}$ 237.5 mμ (logε =4.76), 257 (sh, 4.51), 290 (4.11).

Found: C, 56.69; H, 5.41; N, 37.96%; mol wt, 148 (mass spectrum). Calcd for $C_7H_8N_4$: C, 56.74; H, 5.44; N, 37.82%; mol wt, 148.17.

The NMR absorption of NH disappeared and the doublet methyl signal at δ 2.65 changed to a singlet by addition of deuterium oxide. The structure of the product was thus assigned to 2-imino-6-methylamino-1,2-dihydronicotinonitrile.

*Preparation of Ethyl 3(2-Amino-2-methylaminoethenylthio)-2-cyano-3-methylthioacrylate (**2b**).* To a mixture of **1b** (8 g, 0.046 mol) and the aqueous solution of methylamine (30%, 15 m*l*) was slowly added malononitrile (15 g, 0.15 mol) at room temperature. After 30 min, a colorless crystalline material started to precipitate. After 3 hr, the precipitate was collected and washed with ethanol. Recrystallization from methanol gave 3.6 g of colorless plates: yield 29%; mp 177—178°C; NMR (acetone-d_6) δ 5.58 (d, 1, NH, J=4 Hz) δ 4.08 (q, 2, CH_2, J=8 Hz) δ 3.48 (s, 2, NH_2) δ 3.30 (s, 1, CH) δ 2.60 (d, 3, CH_3, J=4 Hz) δ 1.20 (t, 3, CH_3, J=8 Hz); IR (KBr) 3440, 3420, 3180, 3120 (s, NH_2, NH), 2200 (vs, conj. CN), 1660 cm^{-1} (vs, CO); $UV_{max}^{99\%EtOH}$ 228.5 mμ (logε=4.05), 289 (3.58), 345 (4.38).

Found: C, 43.92; H, 5.63; N, 15.30; S, 23.12%; mol wt, 265 (vapor-pressure osmometer, in acetone). Calcd for $C_{10}H_{15}N_3S_2O_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.44%; mol wt, 273.24.

With the addition of deuterium oxide, the NMR absorptions of NH_2 and NH disappeared and the doublet methyl signal at δ 2.60 changed to a singlet.

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[5] E. C. Horning, "Organic Syntheses," Coll. Vol. III, p. 181 (1967).