

Synthesis of β -Alkylimino α -Cyano Dithiocarboxylic Acids, 3-Alkyl-1,3-thiazine-2,6-dithiones, and Related Compounds

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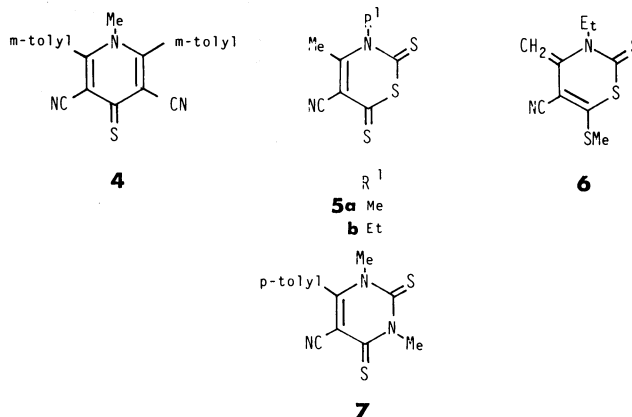
Synopsis. The title compounds **2** and **5** were synthesized by the reaction of β -alkylimino nitriles with carbon disulfide.

β -Alkylimino dithiocarboxylic acids have been reported to be unstable except 2-(alkylimino)cyclopentanecarbodithioic acids.¹⁾ No stable acyclic β -alkylimino dithiocarboxylic acids²⁾ and 2- and 4-(dithiocarboxymethylene)dihydropyridines³⁾ at room temperature are known. We have previously reported the first examples of stable acyclic imino dithiocarboxylic acids, α -cyano β -imino dithiocarboxylic acids.⁴⁾ 2-(Alkylimino)cyclopentanecarbodithioic acids have been prepared by the reaction of 2-iminocyclopentanecarbodithioic acid and alkylamines.⁵⁾ This method, however, could not be applied to the synthesis of β -alkylimino α -cyano dithiocarboxylic acids from the imino cyano dithiocarboxylic acids.

Our present finding is that β -alkylimino nitriles⁶⁾ react with carbon disulfide in the presence of a base to give β -alkylimino dithiocarboxylic acids (**2**). In some cases, 3-alkyl-2H-1,3-thiazine-2,6(3H)-dithiones (**5**) were produced.

Compounds **2a–g** were obtained as major product when β -alkylimino nitriles (**1a–g**) were treated with carbon disulfide in the presence of sodium 1,1-dimethylpropoxide in benzene. In some cases, the imino acids were accompanied by a small amount of 4-cyano-3H-1,2-dithiole-3-thiones (**3a–c**). 3-Methylimino-3-(*m*-tolyl)propanenitrile gave 3,5-dicyano-2,6-di(*m*-tolyl)-1-methyl-4(1H)-pyridinethione (**4**) in addition to compounds **2e** and **3b**. We have reported that the same type of *N*-unsubstituted 4(1H)-pyridinethiones are synthesized by the reaction of 5-cyano-2H-1,3-thiazine-2,6(3H)-dithiones with β -imino nitriles.⁷⁾

When these reactions were performed in *N,N*-dimethylformamide, 3H-1,2-dithiole-3-thiones (**3a–c**) were formed as a major product instead of the β -alkylimino dithiocarboxylic acids (**2c–g**). Furthermore, 3-(alkylimino)butanenitriles (**1a–b**) produced 3-alkyl-5-cyano-4-methyl-2H-1,3-thiazine-2,6(3H)-dithiones (**5a–b**) in addition to **2**. In the ¹³C NMR spectrum of compound **5b** in dimethyl-*d*₆ sulfoxide, two quartets at δ 11.86 and 23.62 ppm were observed. Compound **5b** was easily methylated with



BLOCK 1

methyl iodide to form 5-cyano-3,4-dihydro-3-ethyl-4-methylene-6-methylthio-2H-1,3-thiazine-2-thione (**6**). In the ¹H NMR spectrum of compound **6**, a pair of doublets appeared at δ 4.98 and 5.17 ppm suggesting the existence of a terminal methylene. From these facts, an alternative structure; 4-alkylimino-3-cyanothiane-2,6-dithiones for compounds **5** was eliminated.

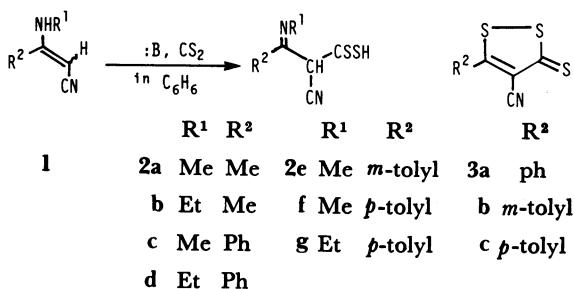
Occasionally, 1,3-dimethyl-5-cyano-4-(*p*-tolyl)-2,6(1H, 3H)-pyrimidinedithione (**7**) was obtained in very low yield besides compounds **2f** and **3c**.

Experimental

Measurements. NMR spectra were recorded with a Jeol JNM-GX-270 spectrometer. Infrared spectra were measured on Nippon Bunko IR-A-302 spectrophotometer. Mass spectra were determined with a Hitachi LKB-9000 mass spectrometer. Electronic spectra were measured with a Hitachi 557 Double Wavelength Double Beam Spectrophotometer.

2-Cyano-3-(methylimino)butanedithioic Acid (2a). A mixture of 3-(methylimino)butanenitrile (0.80 g, 8.32 mmol), sodium 1,1-dimethylpropoxide (1.40 g, 12.7 mmol), carbon disulfide (1.00 g, 13.1 mmol), and dry benzene (20 ml) was shaken at room temperature for 3 h. Water (40 ml) was added to the mixture and the aqueous layer was washed with ether. Ether (100 ml) and 2M-hydrochloric acid (10 ml (1 M=1 mol dm⁻³)) were added to the aqueous layer and extracted several times with ether. A small quantity of methanol containing piperidine was added to the combined ethereal extracts. Resulting solid was collected, dissolved in hydrochloric acid in acetone (ca. 0.5 M, 30 ml), and to this was added water. The yellow crystals separated were recrystallized. ν_{\max} (KBr) 2850 s, 2510 s, 2200 s, 1630 vs, 1500 s, and 1270 s cm⁻¹; δ (CD₃COCD₃) 13.62 vb (s, 1H, NH or SH), 5.95 (s, 1H, NH or SH), 3.25 (d, 1.5H, *J*=3.1 Hz, NHCH₃), 3.23 (d, 1.5H, *J*=3.1 Hz, NHCH₃), and 2.48 ppm (s, 3H, CH₃). (Found: C, 42.01; H, 4.73; N, 16.20; S, 37.07. C₆H₈N₂S₂ requires C, 41.79; H, 4.68; N, 16.25; S, 37.22%). Other β -alkylimino dithiocarboxylic acids (**2b–g**) were prepared in the same way.

4-Cyano-5-aryl-3H-1,2-dithiole-3-thiones (3a–c). A mixture of 3-alkylimino-3-arylpropanenitrile (5 mmol), carbon disulfide (12 mmol), and *N,N*-dimethylformamide (5 ml) was added dropwise to a mixture of sodium 1,1-dimethylpropoxide (15 mmol) and *N,N*-dimethylformamide (15 ml) at 0°C.



Scheme 1.

TABLE 1. YIELDS AND PHYSICAL PROPERTIES OF 2-7

Compound	Yield	Mp	UV (EtOH) nm (log ϵ)
	%	$\theta_m/^\circ\text{C}$	
2a	39	73-75 ^{a)}	243 (4.12), 303 (3.83), 368 (4.35)
2b	50	117-118 ^{a)}	244 (4.12), 304 (3.72), 369 (4.35)
2c	51	131-132 ^{a)}	243 (4.06), 309 (3.72), 373 (4.34)
2d	44	110 ^{a)}	243 (4.09), 309 (3.79), 373 (4.36)
2e	45	111-112 ^{a)}	238 (4.13), 370 (4.40)
2f	42	132-133 ^{a)}	241 (4.12), 373 (4.40)
2g	42	106-110 ^{a)}	241 (4.10), 373 (4.38)
3a	38, ^{b)} 44 ^{c)}	178 ^{d)}	223 (4.10), 292 (4.23), 312 (4.12), 430 (3.88)
3b	53	183 ^{d)}	226 (4.11), 293 (4.20), 318 (4.12), 433 (3.94)
3c	24, ^{e)} 49 ^{f)}	210.5 ^{d)}	230 (4.13), 293 (4.16), 329 (4.20), 433 (3.93)
4	6	280 ^{g)}	263 (4.20), ^{h)} 350 (4.36) ^{h)}
5a	49	151-152 ^{a)}	308 (4.38), 417 (3.64) These λ_{max} 's shifted to 268 (3.98) and 305 (4.46) in 2 h.
5b	47	161 ^{a)}	310 (3.84), 417 (3.78) These λ_{max} 's shifted to 268 (3.84) and 308 (4.48) in 2 h.
6	85	93.5 ^{a)}	293 (4.44)
7	9	232.5 ^{d)}	293 (4.58), 303 (3.95)

a) Recrystallized from acetone-water. b) Yield from 1c. c) Yield from 1d. d) Recrystallized from ethanol. e) Yield from 1f. f) Yield from 1g. g) Recrystallized from *N,N*-dimethylformamide-water. h) Dioxane used as solvent. All compounds gave satisfactory IR and elemental analyses data.

The mixture was kept standing at room temperature for 4 h. Water was added to the mixture and the solid which separated was collected.

3,5-Dicyano-2,6-di(*m*-tolyl)-1-methylpyridine-4(1H)-thione (4). A mixture of 3-methylimino-3-(*m*-tolyl)propanenitrile (2.00 g, 11.6 mmol), sodium 1,1-dimethylpropoxide (2.00 g, 18.2 mmol), carbon disulfide (1.40 g, 18.4 mmol), and benzene (50 ml) was mechanically shaken at room temperature for 3 h and water (50 ml) was added to this. The solids from both layers were collected and recrystallized. ν_{max} (KBr) 2240 w, 1575 vs, 1480 m, 1260 s, and 1080 m cm^{-1} ; δ (DMSO-*d*₆) 7.42 (m, 8H, C₆H₄), 2.99 (s, 3H, NCH₃), and 2.40 ppm (s, 6H, C₆H₄CH₃); m/z 355 (M⁺, 98%), 354 (M⁺-1, 100%), and 340 (M⁺-CH₃, 48%). (Found: C, 74.40; H, 4.62; N, 11.86; S, 9.17. C₂₂H₁₇N₃S requires C, 74.35; H, 4.62; N, 11.86; S, 9.02%).

5-Cyano-3,4-dimethyl-2H-1,3-thiazine-2,6(3H)-dithione (5a). To a mixture of 3-(methylimino)butanenitrile (2.00 g, 20.8 mmol), sodium 1,1-dimethylpropoxide (6.88 g, 62.4 mmol), and *N,N*-dimethyl formamide (20 ml), was added dropwise carbon disulfide (4.75 g, 62.4 mmol) at -15°C and the mixture was kept standing at -20°C for 40 h. Ether (150 ml) and 1M-hydrochloric acid (30 ml) were added to the reaction mixture. The brown crystals insoluble in both layers were collected. ν_{max} (KBr) 2230 m, 1535 s, 1420 s, 1365 s, 1265 s, 1225 s, and 1085 s cm^{-1} ; δ (C₅D₅N) 3.88 (s, 3H, NCH₃) and 2.75 ppm (s, 3H, CH₃). (Found: C, 39.01; H, 3.03; N, 13.00; S, 44.91. C₇H₆N₂S₃ requires C, 39.22; H, 2.82; N, 13.07; S, 44.91%).

5-Cyano-3-ethyl-4-methyl-2H-1,3-thiazine-2,6(3H)-dithione (5b) was Prepared Similarly. ν_{max} (KBr) 2980 w, 2900 w, 2220 m, 1530 s, 1525 s, 1405 s, 1300 s, 1240 s, 1200 s, and 1100 s cm^{-1} ; ¹H NMR δ (DMSO-*d*₆) 4.60 (q, 2H, *J*=6.6 Hz, NCH₂CH₃), 2.80 (s, 3H, CH₃), and 1.35 ppm (t, 3H, *J*=6.6 Hz, NCH₂CH₃); ¹³C NMR (DMSO-*d*₆) 201.70 (s), 191.96 (t, *J*=6.1 Hz), 158.62 (s), 114.91 (s), 110.96 (s), 47.98 (t, *J*=143.4 Hz), 23.63 (q, *J*=131.2 Hz), and 11.86 ppm (q, *J*=128.2 Hz); m/z 228 (M⁺, 100%), 195 (M⁺-SH, 13%), 141 (M⁺-C₂H₅NCS, 4%), and 70 (CH₃C≡N⁺-C₂H₅, 33%). (Found: C, 42.28; H, 3.38; N, 12.39; S, 42.38. C₈H₈N₂S₃ requires C, 42.08; H, 3.53; N, 12.27; S, 42.12%).

5-Cyano-3,4-dihydro-3-ethyl-4-methylene-6-methylthio-2H-1,3-thiazine-2-thione (6). Triethylammonium salt of 5b was methylated by treating with methyl iodide in methanol. Water was added to this mixture and resulting solids were collected. ν_{max} (KBr) 2980 w, 2950 w, 2220 m, 1600 s, 1530 m, 1460 m, 1420 m, 1390 s, and 1375 s cm^{-1} ; δ (CDCl₃) 5.17 (d, 1H, *J*=3.7 Hz, =CH₂), 4.98 (d, 1H, *J*=3.7 Hz, =CH₂), 4.48 (q, 2H, *J*=7.1 Hz, NCH₂CH₃), 2.56 (s, 3H, SCH₃), and 1.38 ppm (t, 3H, *J*=7.1 Hz, NCH₂CH₃); m/z 242 (M⁺, 100%), 213 (M⁺-C₂H₅, 82%), 195 (M⁺-SCH₃, 32%), 155 (M⁺-C₂H₅NCS, 26%), and 108 (CH₂=C=C(CN)C≡S⁺, 31%). (Found: C, 44.87; H, 4.38; N, 11.72; S, 39.48. C₉H₁₀N₂S₃ requires C, 44.59; H, 4.16; N, 11.56; S, 39.69%).

1,3-Dimethyl-5-cyano-4-(*p*-tolyl)-2,4(1H,3H)-pyrimidinedithione (7). This compound was isolated on recrystallization of 3c from the filtrate. ν_{max} (KBr) 2890 w, 2220 m, 1600 w, 1560 s, 1505 s, 1460 s, 1420 m, 1405 s, 1330 s, 1305 s, and 1275 s cm^{-1} ; m/z 287 (M⁺, 100%) and 132 (C₇H₇C≡N⁺-CH₃, 24%). (Found: C, 58.66; H, 4.51; N, 14.33; S, 22.10. C₁₄H₁₃N₃S₂ requires C, 58.50; H, 4.59; N, 14.62; S, 22.32%).

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