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A New Synthetic Route to Aliphatic and Alicyclic Nitriles via Homolytic Desulfurization of α-(Dithiocarbamoylthio) Nitriles

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Synopsis. Chloroacetonitrile was transformed into aliphatic and alicyclic nitriles through (dimethyldithiocarbamoylthio)acetonitrile. The key steps in the synthetic route consisted of mono- and dialkylation via sulfur-stabilized carbanion and homolytic desulfurization using tributyltin hydride.

Recently, synthetic applications of homolytic processes by use of organotin hydrides have been intensively exploited in synthetic methodology.[1] One of the fundamental value of organotin hydrides lies in the selective reduction of carbon-sulfur bond via radical intermediates.[2] With regard to reductive desulfurization, several methods using reagents such as Raney nickel,[3] alkali metal in ammonia solution,[4] copper(II) chloride-zinc chloride-lithium aluminium hydride,[5] hydrazine,[6] and nickel boride[7] have been reported. Although these procedures are effective for the purpose of complete desulfurization, they lack the selectivity for the reduction of one carbon-sulful bond in polyfunctional-sulfur compounds.[8] In comparison with such procedures, the homolytic desulfurization using organotin hydrides enables an effective and a chemoselective reduction of sulfur containing moiety. On the other hand, the technique for carbon-carbon bond formation via sulfur-stabilized carbanion has been utilized for syntheses of various nitrile compounds, in which organosulfur derivatives are employed as the useful intermediates.[9] The combination of this technique and the homolytic desulfurization has the possibility to provide a convenient process for the preparation of nitriles. In this report, we wish to present a new synthetic route to aliphatic and alicyclic nitriles from chloroacetonitrile, which is derived from the strategy involving alkylation via sulfur-stabilized carbanion and reductive desulfurization via the homolytic process by use of tributyltin hydride (Bu_3SnH).

Results and Discussion

The choice of organosulfur intermediate was (dimethyldithiocarbamoylthio)acetonitrile (**1**), since the carbanion derived from **1** has been shown to possess suitable stability and reactivity towards electrophiles in the preceeding paper.[10] In addition, dithiocarbamoyl moiety is preferable to alkylthio one in view of facility of the desulfurization using organotin hydrides.[11]

The intermediate **1** was readily prepared by the reaction of chloroacetonitrile with sodium dimethyldithiocarbamate. The alkylation of **1** using alkyl halides with tetrabutylammonium iodide ($Bu_4N^+I^-$) in alkaline aqueous medium gave various α-cyano dithioesters **2** and **3**.[10] The reductive desulfurization using

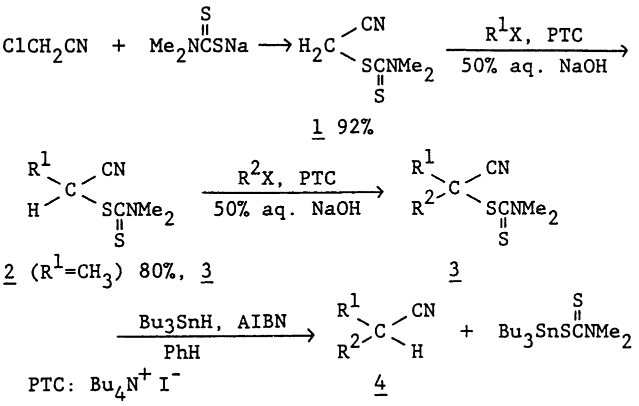
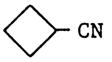
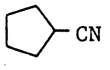
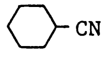


Table 1. Preparation of α-Cyano Dithioesters **3** and Nitriles **4**

Entry	α-Cyano dithioester **3**			Nitrile **4**, Yield/%	
	R^1	R^2	Yield/%		
a	$PhCH_2$	H	79	$PhCH_2CH_2CN$	95
b	$PhCH=CHCH_2$	H	45	$PhCH=CHCH_2CH_2CN$	82
c	$PhCH_2$	CH_3	85	$PhCH_2CH(CH_3)CN$	88
d	$PhCH=CHCH_2$	CH_3	40	$PhCH=CHCH_2CH(CH_3)CN$	90
e	$PhCH_2$	$PhCH_2$	65	$(PhCH_2)_2CHCN$	71
f	$—(CH_2)_3—$		93		71
g	$—(CH_2)_4—$		81		85
h	$—(CH_2)_5—$		90		93

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† Deceased February 27, 1985.

Bu_3SnH was performed under the usual conditions. Thus, a solution of **3**, Bu_3SnH, and a catalytic amount of azobisisobutyronitrile (AIBN) in dry benzene was refluxed under a nitrogen atmosphere for 5—6 h. The results of these reactions are listed in Table 1.

The process employing appropriate 1, ω-dibromoalkanes enabled the preparations of various carbocyclic cyanides such as cyclohexyl (**4f**), cyclopentyl (**4g**), and cyclobutyl cyanide (**4h**). The potential utility of the homolytic desulfurization was demonstrated by the preparations of functionalized nitriles **4b** and **4d**, which contained unsaturated carbon-carbon bond. Those results demonstrated that both primary and secondary cyanides could be prepared in high yields by the process starting from simple nitrile compound. The effectiveness of this procedure for desulfurization may be explained by the favorable influence of cyano group, which stabilizes the carbon-centered radical generated at the α-position.

Experimental

Preparation of α-Cyano Dithioesters 2 and 3. The α-cyano dithioesters **2**, **3a**, **3c**, and **3e—h** were prepared by the procedure reported before.10) In the same manner, **3b** and **3d** were prepared as follows: 2-dimethyldithiocarbamoylthio-5-phenyl-4-pentenonitrile (**3b**). The mixture of (dimethyldithiocarbamoylthio)acetonitrile (**1**) (0.56 g, 3.5 mmol), cinnamyl bromide (0.45 g, 2.3 mmol) and tetrabutylammonium iodide (0.08 g) in benzene (5 ml) and 50% aqueous sodium hydroxide solution (10 ml) was stirred vigorously at room temperature. After 17 h, the mixture was diluted with water and extracted with ether. The ethereal extracts were dried over sodium sulfate and then evaporated. The residue was chromatographed on alumina with hexane and dichloromethane as eluant. The pure **3b** was obtained as viscous oil (0.30 g, 45%), IR (neat) 3040, 2920, 2240 (νC≡N), 1490, 1375, 1245 970, 745 cm^{-1}; ^1H NMR $\delta=2.86$ (t, 1H, $J=6.0$ Hz), 3.28, 3.49 (ss, 6H), 5.23 (t, 1H, $J=7.0$ Hz), 5.99—6.86 (m, 2H), 7.35 (s, 5H). Found: C, 60.50; H, 5.73; N, 10.19; S, 23.39%. Calcd for $C_{14}H_{16}N_2S_2$: C, 60.84; H, 5.83; N, 10.19; S, 23.20%.

2-Methyl-2-dimethyldithiocarbamoylthio-5-phenyl-4-pentenonitrile (3d). Colorless prisms (methanol), mp 124—127 °C. IR (KBr) 3040, 2930, 2240 (νC≡N), 1490, 1380, 1250, 970, 750 cm^{-1}; ^1H NMR $\delta=1.87$ (s, 3H), 2.75—3.62 (m, 8H), 5.85—6.85 (m, 2H), 7.38 (s, 5H). Found: C, 62.35; H, 6.19; N, 9.41; S, 21.8%. Calcd for $C_{15}H_{18}N_2S_2$: C, 62.04; H, 6.24; N, 9.64; S, 22.1%.

Reductive Desulfurization of α-Cyano Dithioesters (3). The solution of **3a** (0.76 g, 3.3 mmol), Bu_3SnH (0.96 g, 3.3 mmol), and AIBN (0.03 g, 5.5 mol%) in benzene (4 ml) was stirred at 80 °C for 5 h. The resulting solution was concentrated by a rotary evaporator and then distilled with a Kugelrohr apparatus to give hydrocinnamonitrile (**4a**) (0.18 g, 91%): bp 164—166 °C/6 mmHg (1 mmHg≈133.322Pa) (Kugelrohr). In the same manner, the nitriles **4b—h** were obtained in the yields shown in Table 1 and identified by comparison of spectral data with those of authentic samples.12)

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