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Reactions of 4-Chloro-5*H*-1,2,3-dithiazol-5-thione with Primary and Secondary Alkylamines : Novel Method for Preparing *N*-Alkyl- and *N,N*-Dialkylcyanothioformamides

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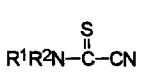
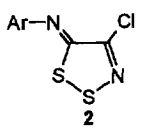
***Abstract**: Treatment of 4-chloro-5H-1,2,3-dithiazol-5-thione with primary and secondary alkylamines in CH_2Cl_2 at room temperature afforded N-alkyl- and N,N-dialkylcyanothioformamides, respectively.*

Cyanothioformamides (**1**) are an important class of compounds which can be utilized not only as dienophiles for [2 + 4] cyclization reactions[1] but also as starting materials for the synthesis of various compounds such as *N*-aryldithioxamides,[2] 2-amino-2-cyanothirane,[3] 2-amino-2-cyano-3,5-diaryl-*N*-aryl-1,3,4-thiadiazole,[3] 2-amino-2-cyano-1,3,5-thioxazoles,[3] *N*-aroyl-*N*-arylcyanothioformamides,[3] *N*-arylcyanoformamidines,[3] 5-imino-4-oxazolidinethiones,[4] 5-imino-4-thioxo-2-imidazolidinones,[5] 5-imino-2,4-imidazolidinedithiones,[5] and 4,5-diimino-2-thiazolidinethione[5] having appropriated substituents. There have been several methods for the preparation of **1**: *N*-alkyl-[7] and *N*-arylcyanothioamides[2,6] (**1**, R^1 = H, R^2 = alkyl and aryl groups) have been exclusively prepared by the reactions of alkyl- and arylisothiocyanates with cyanides, respectively. On the other hand, synthesis of **1** with *N,N*-dialkyl groups have been mainly achieved by either a nucleophilic displacement of C-sulfonylthioformamide by cyanide[8] or the reaction of sodium cyanodithiaformate with *N,N*-dialkylamines.[9] Treatment of nitroacetamides with Lawesson's reagent gave *N*-alkyl- or *N,N*-dialkylcyanothioformamides depending on the number of alkyl groups on nitrogen atom of the amides.[10] To the best of our knowledge, this is the only known method for providing **1** with both of *N*-alkyl- and *N,N*-dialkyl groups. Recently we reported a new facile synthetic method for *N*-arylcyanothioformamide which involved *in situ* treatment of hydrochloride salts of 5-(*N*-arylimino)-4-chloro-5*H*-1,2,3-dithiazoles (**2**) with $NaBH_3CN$ in THF at room temperature.[11]



1

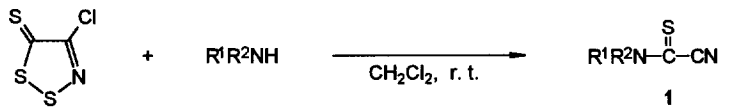


2

In connection with our ongoing project for the development of potential utilities of **2** toward the synthesis of new heteroatom compounds,[12] we describe here a novel and effective method for preparing *N*-alkyl- and *N,N*-dialkylcyanothioformamides **1** using 4-chloro-5*H*-1,2,3-dithazol-5-thione (**3**)[13] with a variety of alkylamine.

Yields of the *N*-alkyl products are much higher than those of *N,N*-dialkyl products. These results are summarized in Table 1.

A typical procedure: To a solution of **3** (90 mg, 0.583 mmol) in CH_2Cl_2 (30 mL) was added pentylamine (131 mg, 1.50 mmol). The mixture was stirred for 10 h at room temperature. After removal of the solvent, the residue was chromatographed on silica-gel (70 - 230 mesh, 1.5 x 15 cm) column. Elution with *n*-hexane gave a small amount of sulfur and unreacted **3**. Further elution with chloroform gave *N*-pentylcyanothioformamide (**1c**) (44 mg, 48 %); IR (neat) 3272 (NH), 2928, 2224 (C≡N, very weak), 1520, 1450, 1402, 1301, 1154, 1091, and 730 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 0.90 (t, 3H, J = 8.0 Hz, CH_3), 1.11 - 1.98 (m, 6H, $(CH_2)_3$), 3.60 (t, 2H, J = 8.0 Hz, CH_2), 8.52 (s, 1H, NH). *Anal.* Calcd for $C_7H_{12}N_2S$: C, 53.81; H, 7.74; N, 17.93; S, 20.52. Found: C, 53.73; H, 7.72; N, 17.91; S, 20.64.



3 **1**

Table 1. Reaction of 4-chloro-5*H*-1,2,3-dithazol-5-thione (**3**) with amines to give *N*-alkyl- and *N,N*-dialkylcyanothioformamides (**1**)

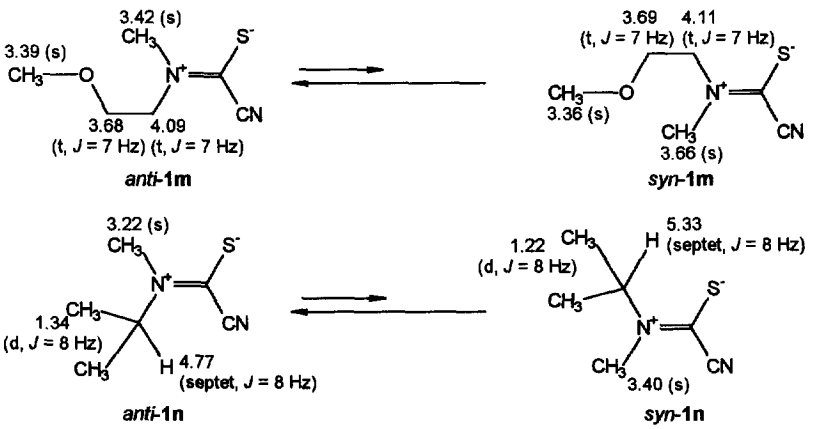
Entry	R^1	R^2	Time (h)	Product	Yield [a] (%)	mp (°C)
1	$(CH_3)_2CH$	H	13	**1a**	85	56-57[b] (lit.[14] 55-56)
2	$(CH_3)_3C$	H	3[c]	**1b**	45	89-90[b]
3	$CH_3(CH_2)_3CH_2$	H	10	**1c**	48	liquid
4	$C_6H_5CH_2$	H	10	**1d**	49	liquid
5	CH_3	CH_3	40	**1e**	27[d]	59-60[b] (lit.[9] 60-61)
6	CH_3CH_2	CH_3CH_2	3	**1f**	81	36-38[b] (lit.[9] 37-38)
7	$CH_3CH_2CH_2$	$CH_3CH_2CH_2$	10	**1g**	79	liquid
8	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	3[c]	**1h**	52	liquid
9	CH_2=$CHCH_2$	CH_2=$CHCH_2$	10	**1i**	83	liquid
10	-$CH_2(CH_2)_2CH_2$-		4	**1j**	76	35-36[e] (lit.[8] 34-36)
11	-$CH_2(CH_2)_3CH_2$-		3	**1k**	92	37-39[b] (lit.[9] 37-38)
12	-$CH_2CH_2OCH_2CH_2$-		2.5	**1l**	86	117-118[b] (lit.[9] 118)
13	$CH_3OCH_2CH_2$	CH_3	10	**1m**	81	liquid
14	$(CH_3)_2CH$	CH_3	10	**1n**	93	48-50[b]
15	-$CH_2(CH_2)_3$-$CH(CH_3)$-		10	**1o**	80	liquid

[a] Isolated yield. [b] Recrystallized from $CHCl_3$ + *n*-hexane. [c] At reflux. [d] An excess of Me_2NH HCl (2.4 equiv) and pyridine (2.2 equiv) were employed. [e] Recrystallized from CH_2Cl_2 + *n*-hexane.

The structures of **1** were determined on the basis of the spectroscopic and mass spectral data, and elemental analyses, along with comparing mps with those in the literatures.[8-10]

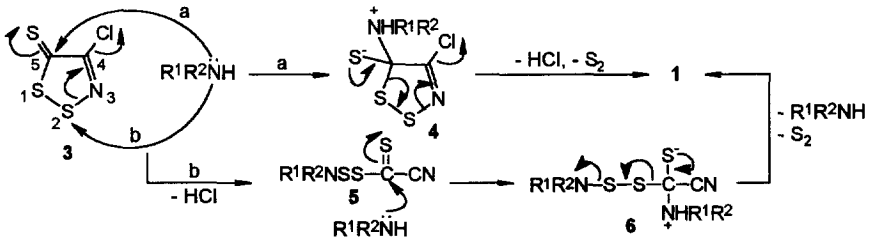
It has been reported that ^{1}H NMR spectrum of **1e** showed two singlets at 3.34 and 3.55 ppm assignable to two methyl groups,[9] which indicates that **1a** exists as a polarized form with double bond character between nitrogen and thione carbon in chloroform.[15] Similarly two identical alkyl groups on nitrogen atom of other *N,N*-dialkylcyanothioformamides (**1f-1i**) exhibited different ^{1}H NMR chemical shifts. In order to assign the magnetically nonequivalent ^{1}H NMR signals of the identical alkyl groups of **1**, compounds **1m**, **1n**, and **1o** which possess two different alkyl groups of **1** were prepared.

^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **1m** showed clearly an equilibrium mixture (3 : 2) of two geometrical isomers, *anti*-**1m** and *syn*-**1m**. Similarly, a clean spectrum ($CDCl_3$, 200 MHz) was shown in the case of **1n** with a 2 : 1 equilibrium mixture of two isomers, *anti*-**1n** and *syn*-**1n**. In addition, 2 : 1 ratio of the intensities shown by a pair of the corresponding signals are in good agreement with the results obtained from ^{1}H NMR spectral data.



^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of **1n** showing ten signals at 17.67, 19.68, 32.90, 36.59, 50.72, 58.93, 112.03, 112.32, 162.03, and 163.64 ppm supports that the compound **1n** exists an equilibrium mixture of *anti*- and *syn*-**1n**.[16] It is noteworthy that the chemical shifts, 162.03 and 163.64 ppm assignable to the polarized thione carbon rather than the thione carbon of nonpolar form **1n** are closer to 163.4 ppm assignable to the imino carbon of *N*-isopropyl-2-propanonimine[17] than 199.4 ppm of the thione carbon of *N,N*-dimethylthioacetamide.[17] ^{1}H NMR ($CDCl_3$, 80 MHz) spectrum of **1o** indicates that **1o** exists as a 1 : 1 mixture of two geometrical isomers.[18] We propose that *anti*-**1m** and *anti*-**1n** predominate in chloroform than the corresponding *syn* isomers which are likely to have more steric repulsion between bulkier 2-methoxyethyl and isopropyl groups than methyl group, and an electron-rich sulfur atom. Based on this assumption are assigned ^{1}H and ^{13}C NMR signals of **1m**, **1n**, and **1o** as shown. By the same token, 3.34 and 3.55 ppm shown by **1a** are assigned to methyl proton signals of *anti*- and *syn*-**1a**, respectively.

The formation of **1** can be rationalized by a nucleophilic attack of alkylamine at C-5 to give an intermediate **4**, which loses HCl and S_2 to yield **1**. Alternatively, a nucleophilic attack of alkylamine at S-2 concomitant with the displacement of chlorine atom can lead to an intermediate **5**, which is attacked by the second molecule of alkylamine to give **1** via an intermediate **6**. Both mechanisms are proposed for the reactions of **2** with alkylamines.[12]



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16. ^{13}C NMR of *anti*-**1n**: 19.68 ($(CH_3)_2C$), 32. 90 (CH_3-N), 58.93 ($(CH_3)_2CH$), 112.03 (C≡N), 162.65 (C=S). ^{13}C NMR of *syn*-**1n**: 17.67 ($(CH_3)_2C$), 36.59 (CH_3-N), 50.72 ($(CH_3)_2CH$), 112.32 (C≡N), 163.64 (C=S).
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18. ^{1}H NMR ($CDCl_3$, 80 MHz) of *anti*-**1o**: 1.28 (d, 3H, J = 8.0 Hz), 1.50-2.03 (m, 6H), 3.40-3.60 (m, 2H), 5.58 (m, 1H). *syn*-**1o**: 1.36 (d, 3H, J = 8.0 Hz), 1.50-2.03 (m, 6H), 3.40-3.60 (m, 2H), 5.10 (m, 1H).

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