

## Reactions of 4-Chloro-5H-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. Copyright © 1996 Elsevier Science Ltd

Cyanothioformamides (1) are an important class of compounds which can be utilized not only as dienophiles for [2 + 4] cyclization reactions<sup>1</sup> but also as starting materials for the synthesis of various compounds such as N-aryldithioxamides,<sup>2</sup> 2-amino-2-cyanothirane,<sup>3</sup> 2-amino-2-cyano-3,5-diaryl-N-aryl-1,3,4-thiadiazole,<sup>3</sup> 2-amino-2-cyano-1,3,5-thioxazoles,<sup>3</sup> N-aroyl-N-arylcyanothioformamides,<sup>3</sup> N-arylcyanoformamidines,<sup>3</sup> 5-imino-4oxazolidinethiones,<sup>4</sup> 5-imino-4-thioxo-2-imidazolidinones,<sup>5</sup> 5-imino-2.4-imidazolidinedithiones,<sup>5</sup> and 4.5diimino-2-thiazolidinethione<sup>5</sup> having appropriated substituents. There have been several methods for the preparation of 1: N-alkyl-<sup>7</sup> and N-arylcyanothioamides<sup>2,6</sup> (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  $N_i$  Additional groups have been mainly achieved by either a nucleophilic displacement of C-sulfonylthioformamide by cyanide<sup>8</sup> or the reaction of sodium cyanodithiaformate with N.N-dialkylamines.<sup>9</sup> Treatment of nitroacetamides with Lawesson's reagent gave N-alkyl- or N.Ndialkylcyanothioformamides depending on the number of alkyl groups on nitrogen atom of the amides.<sup>10</sup> To the best of our knowledge, this is the only known method for providing 1 with both of N-alkyl- and  $N_{N-1}$ 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-5H-1,2,3-dithiazoles (2) with NaBH<sub>3</sub>CN in THF at room temperature.<sup>11</sup>



In connection with our ongoing project for the development of potential utilities of 2 toward the synthesis of new heteroatom compounds,<sup>12</sup> we describe here a novel and effective method for preparing N-alkyl- and N,N-dialkylcyanothioformamides 1 using 4-chloro-5H-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<sub>2</sub>Cl<sub>2</sub> (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<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 80 MHz)  $\delta$  0.90 (t, 3H, *J* = 8.0 Hz, CH<sub>3</sub>), 1.11 - 1.98 (m, 6H, (CH<sub>2</sub>)<sub>3</sub>), 3.60 (t, 2H, *J* = 8.0 Hz, CH<sub>2</sub>), 8.52 (s, 1H, NH). Anal. Calcd for C<sub>7</sub>H<sub>12</sub>N<sub>2</sub>S: 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.

$$S = CI + R^{1}R^{2}NH - R^{1}R^{2}NH = R^{1}R^{2}N + CH_{2}CI_{2}, r. t. = R^{1}R^{2}N - C - CN$$

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

Entry	R <sup>1</sup>	R <sup>2</sup>	Time (h)	Product	Yield * (%)	mp (°C)
1	(CH <sub>3</sub> ) <sub>2</sub> CH	Н	13	1 <b>a</b>	85	56-57 <sup>b</sup> (lit. <sup>14</sup> 55-56)
2	(CH <sub>3</sub> ) <sub>3</sub> C	н	3°	1b	45	89-90 <sup>b</sup>
3	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub>	н	10	1c	48	liquid
4	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	н	10	1d	49	liquid
5	CH <sub>3</sub>	CH <sub>3</sub>	40	1e	27 <sup>d</sup>	59-60 <sup>b</sup> (lit. <sup>9</sup> 60-61)
6	CH <sub>3</sub> CH <sub>2</sub>	CH₃CH₂	3	1f	81	36-38 <sup>b</sup> (lit. <sup>9</sup> 37-38)
7	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>	10	1 <b>g</b>	79	liquid
8	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub>	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub>	3°	1 <b>h</b>	52	liquid
9	CH₂≈CHCH₂	CH <sub>2</sub> =CHCH <sub>2</sub>	10	1i	83	liquid
10	-CH <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> -		4	1j	76	35-36° (lit. <sup>\$</sup> 34-36)
11	-CH2(CH2)3CH2-		3	1 <b>k</b>	92	37-39 <sup>b</sup> (lit. <sup>9</sup> 37-38)
12	-CH2CH2OCH2CH2-		2.5	11	86	117-118 <sup>6</sup> (lit. <sup>9</sup> 118)
13	CH <sub>3</sub> OCH <sub>2</sub> CH <sub>2</sub>	CH <sub>3</sub>	10	1 <b>m</b>	81	liquid
14	(CH <sub>3</sub> ) <sub>2</sub> CH	CH <sub>3</sub>	10	1n	93	48-50 <sup>b</sup>
15	-CH <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> -CH(CH <sub>3</sub> )-		10	10	80	liquid

N-alkyl- and N,N-dialkylcyanothioformamides (1)

<sup>a</sup> Isolated yield. <sup>b</sup> Recrystallized from CHCl<sub>3</sub>+ n-hexane. <sup>c</sup> At reflux. <sup>d</sup> An excess of Me<sub>2</sub>NH HCl (2.4 equiv) and pyridine (2.2 equiv) were employed. <sup>c</sup> Recrystallized from CH<sub>2</sub>Cl<sub>2</sub>+ 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.<sup>8-10</sup>

It has been reported that <sup>1</sup>H NMR spectrum of 1e showed two singlets at 3.34 and 3.55 ppm assignable to two methyl groups,<sup>9</sup> which indicates that 1a exists as a polarized form with double bond character between nitrogen and thione carbon in chloroform.<sup>15</sup> Similarly two identical alkyl groups on nitrogen atom of other N,N-dialkylcyanothioformamides (1f-1i) exhibited different <sup>1</sup>H NMR chemical shifts. In order to assign the magnetically nonequivalent <sup>1</sup>H NMR signals of the identical alkyl groups of 1, compounds 1m, 1n, and 10 which possess two different alkyl groups of 1 were prepared.

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 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<sub>3</sub>, 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 <sup>1</sup>H NMR spectral data.



<sup>13</sup>C NMR (CDCl<sub>3</sub>, 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**.<sup>16</sup> 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<sup>17</sup> than 199.4 ppm of the thione carbon of *N*,*N*-dimethylthioacetamide.<sup>17</sup> <sup>1</sup>H NMR (CDCl<sub>3</sub>, 80 MHz) spectrum of **1o** indicates that **1o** exists as a 1 : 1 mixture of two geometrical isomers.<sup>18</sup> 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 <sup>1</sup>H and <sup>13</sup>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.<sup>12</sup>



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## **References and Notes**

- (a) Friedrich, K.; Zamkanei, M. Tetrahedron Lett. 1977, 25, 2139-2140. (b) Friedrich, K.; Zamkanei, M. Chem. Ber. 1979, 112, 1867-1872. (c) Friedrich, J. D. J. Org. Chem. 1987, 52, 2442-2446.
- 2. Kumelj, B.; Tisler, M. Vestnik Solven. Kemi. drustva, 1958, 5, 69-73 (Chem. Abstr. 1960, 54, 22426f).
- 3. Friedrich, K.; Zamkanei, M. Chem. Ber. 1979, 112, 1873-1878.
- 4. Ketcham, R. Synthesis 1980, 869-870.
- 5. Khattak, I.; Ketcham, R.; Schaumann, E.; Adwidjaja, G. J. Org. Chem. 1985, 50, 3431-3434.
- (a) Grabenko, A. D.; Pel'kis, P. S. Zhur. Obshch. Khim. 1960, 30, 1222-1226 (Chem. Abstr. 1961, 55, 1484f). (b) Olin, J. F. U. S. Pat. 3287102 (1966) (Chem. Abstr. 1967, 66, 55252b).
- (a) Walter, W.; Bode, K.-D. Liebigs Ann. Chem. 1966, 698, 131-144. (b) Walter, W.; Bode, K.-D. Angew. Chem. 1966, 78, 517-532. (c) Cambie, R. C.; Chambers, D.; Rutledge, P. S.; Woodgate, P. D. J. Chem. Soc., Perkin Trans. 1. 1981, 40-51.
- 8. Nilsson, N. H.; Senning, H.; Karlson, S.; Sandstrom, J. Synthesis 1972, 314-316.
- 9. Hansen, P.; Kibbel, H. U. Z. Chem. 1976, 16, 182-183.
- 10. Harris, P. A.; Jackson, A.; Joule, J. A. Tetrahedron Lett. 1989, 30, 3189-3192.
- 11. Lee, H.; Kim, K. Bull. Korean Chem. Soc. 1992, 13, 107-108.
- 12. Lee, H.; Kim, K.; Whang. D.; Kim, K. J. Org. Chem. 1994, 59, 6179-6183.
- 13. Appel, R.; Janssen, H.; Siray, M.; Knoch, F. Chem. Ber. 1985, 118, 1632-1643.
- 14. Kibbel, H. U.; Kuecken, M.; Peters, E.; Weber, H. J. Prakt. Chem. 1981, 323, 41-48.
- (a) Lee, C. M.; Kumler, W. D. J. Org. Chem. 1962, 27, 2052-2054. (b) Hobson, R. F.; Reeves, L. W.; Shaw, K. N. J. Phys. Chem. 1973, 77, 1228-1232. (c) Sandstrom, J. J. Phys. Chem. 1967, 71, 2318-2325.
- 16. <sup>13</sup>C NMR of anti-1n: 19.68 ((CH<sub>3</sub>)<sub>2</sub>C), 32. 90 (CH<sub>3</sub>-N), 58.93 ((CH<sub>3</sub>)<sub>2</sub>CH), 112.03 (C≡N), 162.65 (C=S). <sup>13</sup>C NMR of syn-1n: 17.67 ((CH<sub>3</sub>)<sub>2</sub>C), 36.59 (CH<sub>3</sub>-N), 50.72 ((CH<sub>3</sub>)<sub>2</sub>CH), 112.32 (C≡N), 163.64 (C=S).
- 17. Fresenius, W.; Huber, J. F. K.; Pungor, E.; Rechnitz, G. A.; Simon, W.; West, Th. S. in *Tables of Spectral Data for Structure Determination of Organic Compounds*, 2nd Ed.; Springer-Verlag, 1989; pp. C201 C203.
- <sup>1</sup>H NMR (CDCl<sub>3</sub>, 80 MHz) of anti-10: 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-10: 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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