Synthesis and properties of *N*-methylmorpholinium 6-amino-3,5-dicyano-1,4-dihydropyridine-4-spirocyclopentane-2-thiolate

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The reaction of cyclopentylidenecyanothioacetamide with cyanothioacetamide and *N*-methylmorpholine gave *N*-methylmorpholinium 6-amino-3,5-dicyano-1,4-dihydropyridine-4-spirocyclopentane-2-thiolate, which was used in the syntheses of substituted 2-alkylthiodihydropyridines and pyrazolodihydropyridine.

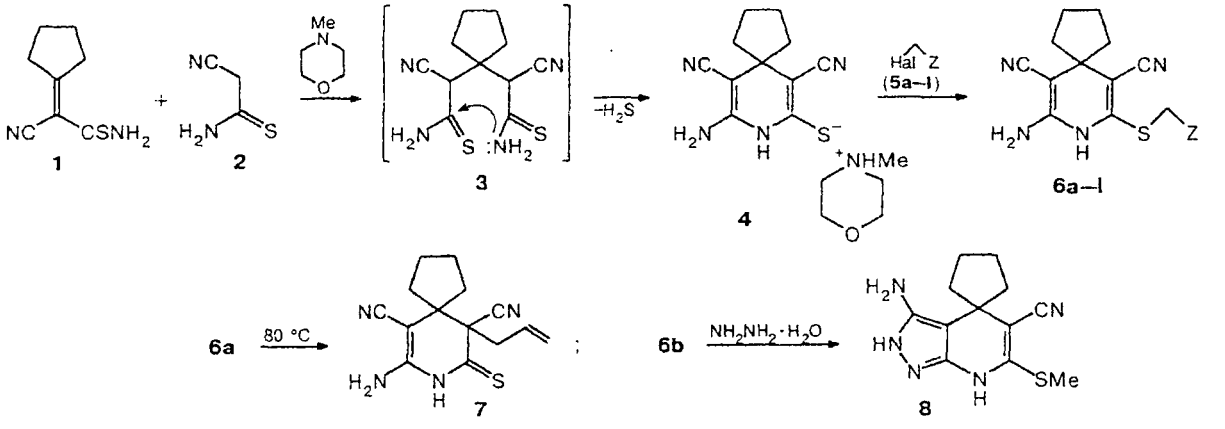
Key words: cyclopentylidenecyanothioacetamide; cyanothioacetamide; dihydropyridines, alkylation, rearrangement.

We have recently shown[1] that cyclohexylidenecyanothioacetamide reacts with cyanothioacetamide in the presence of *N*-methylmorpholine to give *N*-methylmorpholinium 6-amino-3,5-dicyano-1,4-dihydropyridine-4-spirocyclohexane-2-thiolate. In this work, we continue the investigation of the synthesis of chalcogenodihydropyridines and study the reaction of cyclopentylidenecyanothioacetamide (**1**) with cyanothioacetamide (**2**) and *N*-methylmorpholine.

The reaction also occurs as the Michael addition to yield adduct **3**, whose intramolecular cyclocondensation results in salt **4** (Scheme 1). The structure of salt **4** was confirmed by spectroscopic studies (see Experimental) and by its alkylation with alkyl halides **5**. The formation of sulfides **6** (Tables 1 and 2) implies that the negative charge in the molecule of salt **4** is localized on the S atom.

When the substituted 2-allylthiodihydropyridine **6a** is refluxed in benzene, it undergoes [3+3]-sigmatropic rearrangement into compound **7**, whose structure is completely confirmed by IR and ^{1}H NMR spectroscopic data. Thus, the intense absorption band at 2190 cm^{-1} in the IR spectrum of thione **7** can be attributed to the 5-CN group, while the weak absorption band around 2238 cm^{-1}, to the absorption of the nonconjugated cyano group. The ^{1}H NMR spectrum mani-

Scheme 1



5, 6:	a	b	c	d	e	f	g	h	i	j	k	l
Hal:	Br	I	Br	Cl	Cl	Cl	Br	Cl	Br	I	Br	Cl
Z:	$CH=CH_2$	H	4-ClC_6H_4CO	PhNHCO	$CONH_2$	4-BrC_6H_4NHCO	PhCO	COOH	2-MeC_6H_4	Me	Et	Ph

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Table 1. Yields, melting points, and parameters of IR spectra of compounds **6a—l**

Compound	Yield (%)	M.p./°C (A)[a]	ν/cm^{-1} NH, NH_2	C≡N	δ(NH_2), C=O
6a	70	126—128[b]	3360, 3455	2190	1655
6b	73	170—172 (EtOH)	3310, 3450	2190	1645
6c	80	163—165 (EtOH)	3220, 3388, 3425	2190 sh	1654
6d	69	202—203 (Bu^nOH)	3150, 3200, 3295, 3318	2202 sh	1660
6e	92	167—169 (EtOH)	3190, 3370, 3444	2190	1670
6f	88	167—169 (Bu^nOH)	3205, 3350, 3470	2192	1690
6g	70	162—164 (EtOH)	3360, 3448	2180 sh.	1650
6h	66	170—172 (AcOH)	3330, 3455	2188	1670, 1730
6i	85	155—157 (EtOH)	3312, 3474	2185 sh.	1655
6j	69	140—142 (EtOH)	3300, 3482	2205	1650
6k	82	123—125 (EtOH)	3330, 3450	2190	1632
6l	91	160—162 (EtOH)	3300, 3384, 3480	2180, 2192	1630

[a] A is the solvent used for crystalliization. [b] The compound was not recrystallized.

Table 2. ^1H NMR spectral parameters and elemental analysis data for compounds **6a—l**

Compound	δ ^1H NH (s)	NH_2 (s)	$(CH_2)_4$ (m)	SCH_2	Z	Found / Calculated (%) C	H	N	S	Molecular formula
6a	9.18	5.68	1.73	3.62 (d)	5.85 (m, 1 H, CH=); 5.21 (m, 2 H, $=CH_2$)	61.62 / 61.74	6.18 / 5.92	20.66 / 20.57	11.54 / 11.77	$C_{14}H_{16}N_4S$
6b	9.03	5.72	1.72	2.45 (s)	—	58.70 / 58.51	5.64 / 5.73	22.85 / 22.74	12.81 / 13.02	$C_{12}H_{14}N_4S$
6c	9.21	5.68	1.69	4.62 (s)	7.99 (d, 2 H); 7.61 (d, 2 H)	59.14 / 59.29	4.29 / 4.45	14.70 / 14.56	8.42 / 8.33	$C_{19}H_{17}ClN_4OS$
6d	9.46	5.75	1.71	3.85 (s)	10.27 (s, 1 H, NHCO); 7.06—7.57 (m, 5 H, Ph)	62.55 / 62.44	5.02 / 5.24	19.00 / 19.16	8.96 / 8.77	$C_{19}H_{19}N_5OS$
6e	9.78	5.77	1.72	3.63 (s)	7.75 (br.s, 1 H, NH_2); 7.44 (br.s, 1 H, NH_2)	54.07 / 53.96	5.44 / 5.23	24.12 / 24.20	10.83 / 11.08	$C_{13}H_{15}N_5OS$
6f	9.41	5.74	1.71	3.84 (s)	7.52 (s, 4 H, C_6H_4); 10.42 (s, 1 H, NHCO)	51.51 / 51.36	3.87 / 4.08	15.60 / 15.76	7.33 / 7.22	$C_{19}H_{18}BrN_5OS$
6g	9.22	5.64	1.70	4.67 (s)	7.60—7.99 (m, 5 H, Ph)	64.89 / 65.12	4.97 / 5.18	16.16 / 15.99	9.27 / 9.15	$C_{19}H_{18}N_4OS$
6h	9.38	5.69	1.70	3.76 (s)		54.01 / 53.78	4.95 / 4.86	19.12 / 19.30	10.86 / 11.04	$C_{13}H_{14}N_4O_2S$
6i	9.27	5.64	1.61	4.17 (s)	7.14 (m, 4 H, C_6H_4); 2.37 (s, 3 H, CH_3)	67.98 / 67.83	5.75 / 5.99	16.81 / 16.65	9.46 / 9.53	$C_{19}H_{20}N_4S$
6j	9.12	5.67	1.71	2.93 (q)	1.18 (t, 3 H, CH_3)	60.00 / 59.97	6.08 / 6.19	21.73 / 21.52	12.19 / 12.32	$C_{13}H_{16}N_4S$
6k	9.16	5.70	1.73	2.92 (t)	0.97 (t, 3 H, CH_3); 1.55 (m, 2 H, CH_2)	61.12 / 61.28	6.50 / 6.61	20.63 / 20.42	11.75 / 11.69	$C_{14}H_{18}N_4S$
6l	9.27	5.68	1.63	4.20 (s)	7.31 (s, 5 H, Ph)	67.16 / 67.05	5.55 / 5.63	17.50 / 17.38	9.79 / 9.94	$C_{18}H_{18}N_4S$

* The signal is not observed due to deuterium exchange.

fests characteristic signals from protons of the allylic fragment at δ 2.55 (d, 2 H, CH_2), 5.12 (d, 2 H, CH_2=), and 5.75 (m, 1 H, CH=), as well as singlets of the NH and NH_2 protons and a multiplet of the $(CH_2)_4$ protons at δ 11.89, 6.23, and 1.75, respectively.

The attempted synthesis of annelated 3-aminopyrazoles by a popular procedure, *viz.*, by replacement of a methylthio group by a hydrazo group followed by subsequent intramolecular cyclization of the reaction product,[2,3] failed in the case of 6-amino-3,5-dicyano-

2-methylthio-1,4-dihydropyridine-4-spirocyclopentane (**6b**). Instead, imine exchange[4] occurred, which resulted in 3-amino-5-cyano-6-methylthio-2*H*-4,7-dihydropyrazolo[3,4-*b*]pyridine-4-spirocyclopentane (**8**). The structure of the latter corroborated with the spectroscopic data (see Experimental).

Experimental

IR spectra were obtained in Vaseline oil on an IKS-29 spectrometer. ^{1}H NMR spectra were recorded on a Bruker WP-100 SY instrument (100 MHz) in DMSO-d_6 using Me_4Si as the internal standard. The purity of the compounds was monitored by TLC on Silufol UV-254 plates in an acetone—hexane mixture (3 : 5).

***N*-Methylmorpholinium 6-amino-3,5-dicyano-1,4-dihydropyridine-4-spirocyclopentane-2-thiolate (4).** *N*-Methylmorpholine (2 mL, 20 mmol) was added with stirring at 20 °C to a solution of compounds **1** and **2** (10 mmol of each) in dry ethanol (15 mL). After 48 h, the yellow powder that formed was filtered off and washed with dry ethanol and hexane. Yield 2.60 g (78%), m.p. 114—116 °C. Found (%): C, 57.50; H, 6.81; N, 21.22; S, 9.74. $C_{16}H_{23}N_5OS$. Calculated (%): C, 57.63; H, 6.95; N, 21.00; S, 9.62. IR, ν/cm^{-1}: 3395, 3300 (NH, NH_2); 2192 (CN); 1620 ($\delta(NH_2)$). ^{1}H NMR, δ: 7.01 (br.s, 1 H, NH); 5.31 (br.s, 2 H, NH_2); 3.76 (m, 4 H, CH_2OCH_2); 3.11 (m, 4 H, CH_2NCH_2); 2.75 (s, 3 H, CH_3); 1.66 (m, 8 H, $(CH_2)_4$).

6-Amino-3,5-dicyano-2-*Z*-methylthio-1,4-dihydropyridine-4-spirocyclopentanes (6a—l). Halide **5** (10 mmol) was added to a suspension of salt **4** (10 mmol) in ethanol (10 mL), and the mixture was stirred for 4 h and diluted with water (10 mL). The resulting precipitate was washed with water, ethanol, and hexane to give the corresponding compound **6**. Data for the latter are presented in Tables 1 and 2.

3-Allyl-6-amino-3,5-dicyano-3,4-dihydropyridine-4-spirocyclopentane-2(1*H*)-thione (7). A suspension of compound **6a** (10 mmol) in benzene (20 mL) was refluxed for 4 h. The reaction mixture was cooled, and the precipitate was filtered off and washed with hexane. Yield 2.3 g (84%), m.p. 119—121 °C. Found (%): C, 61.90; H, 5.80; N, 20.70; S, 11.60. $C_{14}H_{16}N_4S$. Calculated (%): C, 61.74; H, 5.92; N, 20.57; S, 11.77. IR, ν/cm^{-1}: 3452, 3340, 3220 (NH, NH_2); 2235, 2190 (CN); 1660 ($\delta(NH_2)$). ^{1}H NMR, δ: 11.89 (s, 1 H, NH); 6.23 (s, 2 H, NH_2); 5.75 (m, 1 H, CH=); 5.17 (d, 2 H, CH_2=); 2.55 (d, 2 H, CH_2); 1.75 (m, 8 H, $(CH_2)_4$).

3-Amino-5-cyano-6-methylthio-2*H*-4,7-dihydropyrazolo[3,4-*b*]pyridine-4-spirocyclopentane (8). A suspension of compound **6b** (10 mmol) and hydrazine hydrate (30 mmol) in ethanol (15 mL) was refluxed for 2 h. The reaction mixture was cooled, and the precipitate was filtered off and washed with ethanol and hexane. Yield 1.8 g (69%), m.p. 175—177 °C (from *n*-butanol). Found (%): C, 55.08; H, 5.85; N, 26.94; S, 12.13. $C_{12}H_{15}N_5S$. Calculated (%): C, 55.15; H, 5.79; N, 26.80; S, 12.27. IR, ν/cm^{-1}: 3315—3374 (NH, NH_2); 2195 (CN); 1640 ($\delta(NH_2)$). ^{1}H NMR, δ: 10.74 (br.s, 1 H, N(2)H); 9.49 (br.s, 1 H, N(7)H); 4.55 (s, 2 H, NH_2); 2.45 (s, 3 H, CH_3); 1.82 (m, 8 H, $(CH_2)_4$).

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