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SYNTHESIS OF 4-ALKYL-6-AMINO-3,5-DICYANO-2(1H)-PYRIDINETHIONES

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Condensation of aliphatic aldehydes with cyanothioacetamide has given 4-alkyl-6-amino-3,5-dicyano-2(1H)-pyridinethiones, which have also been synthesized by recyclization of 4-alkyl-2,6-diamino-4H-thiopyrans. Substituted 2-alkylthiopyridines and thieno[2,3-b]pyridines have been prepared from the pyridinethiones. 2,6-Diamino-4-isopropyl-3,5-dicyano-4H-thiopyran and 6-amino-4-isobutyl-2-methylthio-3,5-dicyanopyridine have been studied by x-ray crystallography.

We have previously reported the synthesis of 4-alkyl-6-amino-3,5-dicyano-2(1H)-pyridinethiones by recyclization of 4-alkyl-2,6-diamino-3,5-dicyano-4H-thiopyrans [1]. Bearing in mind the practical importance of alkyl substituted 3-cyanopyridine-2-chalcogenones as synthons for preparing antiviral [2], cardiovascular [3-5], and anti-AIDS [6-7] preparations, we have developed a novel method for their synthesis and have studied some of their properties.

It was found that condensation of aliphatic aldehydes Ia-c with cyanothioacetamide (II) at a molar ratio of 1:2 and in the presence of N-methylmorpholine gives substituted acrylonitriles III which can further undergo a Michael addition with a second molecule of the CH-acid II.

The formed adducts IV then cyclocondense to 4-alkyl-6-amino-3,5-dicyano-2(1H)-thiones (Va,b) (method A) in 63-82% yield which is significantly higher than for the known method B [1]. We have also simplified the synthesis of the thiopyrans VIa-c. By means of the developed method we have prepared the previously unknown selenopyrans VId,e. It was found that VI are formed at room temperature by reaction of aldehydes Ia-c, malononitrile, and cyanochalcogenoacetamides II in ethanol in the presence of a catalytic amount of N-methylmorpholine or morpholine in 68-92% yield.

The spectral characteristics of V, VI confirm their structure (see Experimental section).

To confirm the proposed scheme for the studied reactions and to prove the structure of VI, we examined 2,6-diamino-4-isopropyl-3,5-dicyano-4H-thiopyran (VIa) by x-ray analysis. The general view of the molecule is given in Fig. 1 and the bond lengths and valence angles in Tables 3 and 4.

In this molecule the thiopyran heterocycle has a boat conformation. Atoms S_1 and C_4 deviate from the plane defined by atoms C_2, C_3, C_5, and C_6 by −0.394 and −0.464 Å respectively (planarity occurring within an accuracy of ± 0.005 Å). The folding of the ring along the lines $C_2\cdots C_6$, $C_3\cdots C_5$, and $S_1\cdots C_4$ being 20.7, 147.5, and 143.7°. We have previously shown [8] that the same heterocycle conformation (folding of 23.3, 36.5, and 141.6°) occurs in 2,6-diamino-4-phenyl-3,5-dicyano-4H-thiopyran (VII) and in the 4H-selenopyran VIII [9] which is an isoelectronic analog of the latter.

The observed disordering of the isopropyl substituent is probably due to its relatively free rotation around the $C_4...C_9$ bond. This leads to a marked twist of the ring (see above) and to a separation of the atoms of the fragment discussed from the remaining atoms. A similar structure for the heterocycle in VII and VIII also probably allows rotation of the phenyl ring (see [8, 9]). At the same time, in 2-amino-4-isopropyl-6-methyl-3,5-dicyano-4H-pyran (IX), flattening of the heterocycle leads to the formation of induced, intramolecular, nonvalent contacts which preclude rotation of the isopropyl substituent relative to the ring [10].

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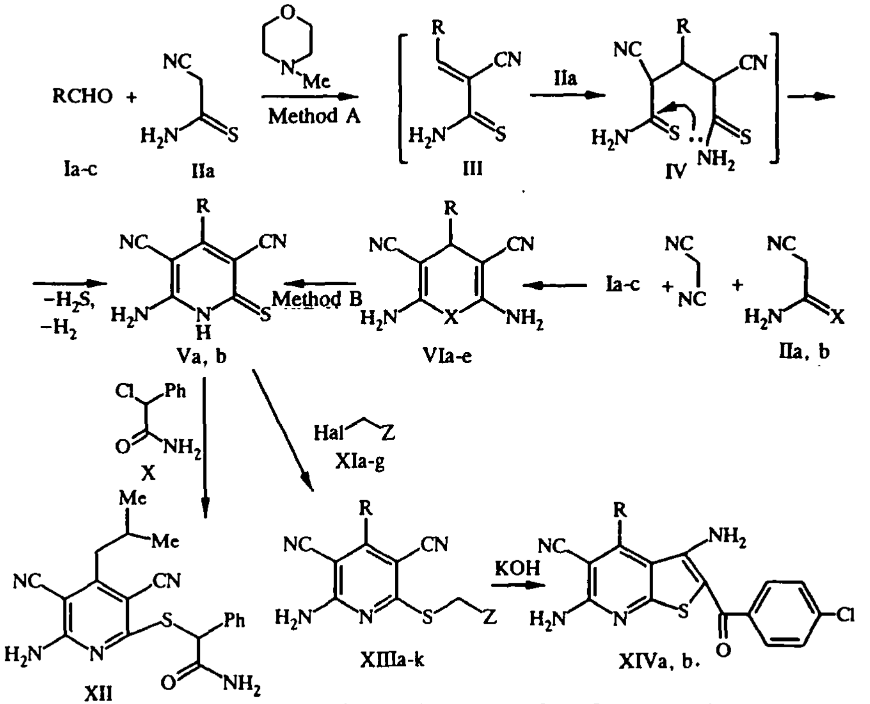

I, V, XIV a R = $CH(CH_3)_2$, b R = $CH_2CH(CH_3)_2$, c R = $(CH_2)_2CH_3$; II a X = S, b X = Se;
VI a R = $CH(CH_3)_2$, X = S, b R = $(CH_2)_2CH_3$, X = S, c R = $CH_2CH(CH_3)_2$, X = S,
d R = $CH_2CH(CH_3)_2$, X = Se, e R = $CH(CH_3)_2$, X = Se; XI a Z = 4-ClC_6H_4CO, b Z = CH_3OCO,
c Z = 4-PhC_6H_4CO, d Z = H, e Z = CH_3, f Z = 3,4-$Cl_2C_6H_3CO$, g Z = coumarin-3-yl-carbonyl,
XIII a Z = 4-ClC_6H_4CO, R = $CH_2CH(CH_3)_2$, b Z = 4-ClC_6H_4CO, R = $CH(CH_3)_2$, c Z = CH_3OCO,
R = $CH_2CH(CH_3)_2$, d Z = 4-PhC_6H_4CO, R = $CH_2CH(CH_3)_2$, e Z = H, R = $CH_2CH(CH_3)_2$, f Z = CH_3,
R = $CH(CH_3)_2$, g Z = H, R = $CH(CH_3)_2$, h Z = CH_3OCO, R = $CH(CH_3)_2$, i Z = 4-PhC_6H_4CO,
R = $CH(CH_3)_2$, j Z = 3,4-$Cl_2C_6H_3CO$, R = $CH(CH_3)_2$, k Z = coumarin-3-yl-carbonyl,
R = $CH(CH_3)_2$; XIa,c,f,g Hal = Br; XIbHal = Cl; XId,e Hal = I

The similarity of the parameters for the unit cells of VIa with VII and VIII was also noted. Thus, the existence of two conformers in the VIa crystal can be explained by packing effects as in the case of VII and VIII.

The bond lengths and valence angles in the investigated molecule VIa agree with those determined in VII and VIII and with standard values [11].

In the crystal, intermolecular hydrogen bonds $N_1-H_{12}\cdots N_3$ (−0.5 + x, −0.5 − y, −0.5 + z) [$N_1\cdots N_3$ 3.010(4), N_1-H_{12} 0.84(3), $H_{12}\cdots N_3$ 2.18(3) Å, angle $N_1-H_{12}\cdots N_3$ 172(3)°], $N_4-H_{42}\cdots N_2$ (0.5 + x, −0.5 − y, 0.5 + z) [$N_4\cdots N_2$ 3.187(4), N_4-H_{42} 0.96(3), $H_{42}\cdots N_2$ 2.24(3) Å, angle $N_4-H_{42}\cdots N_2$ 169(3)°] assemble the molecule VIa in infinite chains aligned along (101) (Fig. 2).

Pyridinethiones V treated with halides X and XIa-g in basic medium give sulfides XII, XIIIa-k which can undergo a Thorpe-Ziegler reaction to give the corresponding thieno[2,3-b]pyridines XIVa,b.

The structures for XII, XIIIa-k, and XIVa,b fully agree with investigated spectral data (see Experimental section and Tables 1 and 2).

In order uniquely to prove the recyclization course of the thiopyrans VI and to determine the regioselectivity of alkylation of its products we have studied 6-amino-4-isobutyl-2-methylthio-3,5-dicyanopyridine (XIIIe) by x-ray analysis. A general view of the molecule is given in Fig. 3 and bond lengths and angles in Tables 5 and 6.

The molecule studied has a regular structure [11]. The orientation of the alkyl substituent relative to the heterocycle is identified by the torsional angles: $C_{13}S_1C_2N_1$ −7.4, $C_3C_4C_9C_{10}$ 102.6, $C_4C_9C_{10}C_{11}$ 169.7, and $C_4C_9C_{10}C_{12}$ −66.8°. The presence of the induced, intramolecular, steric, non-valence contact $C_7\cdots C_{10}$ of 3.342(4) Å (doubled van der Waal radius of the atom 3.40 Å [12]) precludes possible rotation of the isobutyl fragment around the $C_9\cdots C_{10}$ bond.

In the crystal, intramolecular hydrogen bonds $N_1-H_{21}\cdots N_4$ (−0.5 − x, 0.5 + y, 0.5 − z) [$N_1\cdots N_4$ 3.089(4), N_1-H_{21} 0.79(3), $H_{21}\cdots N_4$ 2.31(3) Å, angle $N_1-H_{21}\cdots N_4$ 172(3)°] and $N_1-H_{22}\cdots N_3$ (−0.5 − x, 1.5 − y, −z) [$N_1\cdots N_3$ 3.150(4), N_1-H_{22} 0.88(3), $H_{22}\cdots N_3$ 2.30(3) Å, angle $N_1-H_{22}\cdots N_3$ 163(3)°] assemble the molecule of XIIIe in bc sheets (Fig. 4).

TABLE 1. Parameters for Compounds XII, XIIIa-k

Compound	Empirical formula	Found, %/ Calculated, % C	H	N	S	mp, °C (solvent for crystallization)	Yield, %
XII	$C_{19}H_{19}N_5OS$	62,19 62,44	5,05 5,24	19,30 19,16	8,91 8,77	248...250 (n-butanol)	68
XIIIa	$C_{19}H_{17}ClN_4OS$	59,15 59,29	4,22 4,45	14,68 14,56	8,48 8,33	206...208 (AcOH)	80
XIIIb	$C_{18}H_{15}ClN_4OS$	58,39 58,30	3,90 4,08	14,95 15,11	8,78 8,65	119...121 (AcOH)	85
XIIIc	$C_{14}H_{16}N_4O_2S$	55,40 55,25	5,48 5,30	18,25 18,41	10,37 10,53	123...125 (AcOH)	79
XIIId	$C_{25}H_{22}N_4OS$	70,55 70,40	5,11 5,20	13,28 13,14	7,36 7,52	226...228 (DMF)	73
XIIIe	$C_{12}H_{14}N_4S$	58,70 58,51	5,81 5,73	22,54 22,74	12,95 13,02	149...151 (ethanol)	75
XIIIf	$C_{12}H_{14}N_4S$	58,40 58,51	5,61 5,73	22,89 22,74	13,10 13,02	236...238 (ethanol)	79
XIIIg	$C_{11}H_{12}N_4S$	56,92 56,87	5,38 5,21	23,99 24,12	13,71 13,80	198...200 (ethanol)	80
XIIIh	$C_{13}H_{14}N_4O_2S$	53,87 53,78	4,91 4,86	19,19 19,30	10,85 11,04	131...133 (acetonitrile)	71
XIIIi	$C_{24}H_{20}N_4OS$	70,01 69,88	5,11 4,89	13,29 13,58	7,55 7,77	207...209 (n-butanol)	83
XIIIj	$C_{18}H_{14}Cl_2N_4OS$	53,50 53,34	3,20 3,48	14,04 13,82	7,80 7,91	208...210 (n-butanol)	71
XIIIk	$C_{21}H_{16}N_4O_3S$	62,42 62,36	4,15 3,99	13,69 13,85	7,80 7,93	215...217 (n-butanol)	68

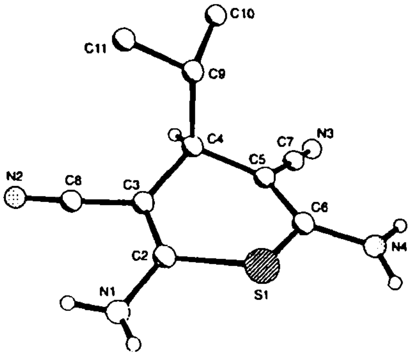

Fig. 1. General view of one of the conformers of the VIa molecule.

EXPERIMENTAL

IR spectra were recorded on an IRS-29 instrument as Vaseline oils. PMR spectra were taken on a Bruker WP-100SY (100 MHz) instrument using DMSO-D_6 solvent and TMS standard.

Crystals of VIa ($C_{10}H_{12}N_4S$) are monoclinic, at 20°C: a = 11.954(3), b = 6.744(2), c = 14.172(5) Å, β = 99.23(2)°, V = 1128(1) Å^3, d_{calc} = 1.298 g/cm^3, Z = 4, space group $P2_{1/n}$. Unit cell parameters and intensities of 1976 independent reflections were measured on a Siemens P3/PC four circle automatic diffractometer (λMoKα, graphite monochromator, $\theta/2\theta$-scanning to θ_{max} = 27°). The structure was solved by a direct method, revealing all non-hydrogen atoms and refined by a full matrix, least squares method in the anisotropic approximation for nonhydrogen atoms for 1507 reflections with $I > 3\sigma$ (I). Atoms C_{10} and C_{11} were disordered in two positions. The ratio of the populations for C_{10}, C_{11} and $C_{10'}$, $C_{11'}$ according to the least squares refinement was 0.50 and 0.50 respectively. All of the hydrogen atoms (except those connected to atoms C_9, C_{10}, $C_{10'}$, C_{11}, $C_{11'}$) were directly revealed in Fourier synthesis and refined isotropically. Final difference factors were R = 0.042 and R_w = 0.042 (S = 0.724). All calculations were carried out using the SHELXTL PLUS program [13] (PC version). Atomic coordinates are given in Table 7.

TABLE 2. IR and PMR Spectral Data for Compounds XII, XIIIa-k

Compound	IR spectrum, ν, cm^{-1}			PMR spectrum, δ, ppm
	$C\equiv N$	NH_2	$C=O$	
XII	2215 sh	3195, 3330, 3410, 3454	—	7,90 (2H, br. s, NH_2); 7,50 (2H, br. s, $CONH_2$); 7,31 (5H, m, Ph); 5,55 (1H, s, SCH); 2,53 (2H, d, CH_2); 1,93 (1H, m, CH); 0,91 (6H, d, $2CH_3$)
XIIIa	2202	3210, 3366	1700	8,08 d and 7,65 d (each 2H, C_6H_4); 7,82 (2H, br. s, NH_2); 4,93 (2H, s, SCH_2); 2,63 (2H, d, CH_2); 2,01 (1H, m, CH); 0,97 (6H, m, $2CH_3$)
XIIIb	2220	3275, 3480	1680	7,80 (2H, s, NH_2); 8,08 d and 7,55 d (each 2H, C_6H_4); 4,92 (2H, s, SCH_2); 3,26 (1H, m, CH); 1,40 (6H, d, $2CH_3$)
XIIIc	2218	3190, 3295, 3394	1730	7,81 (2H, br. s, NH_2); 4,19 (2H, s, SCH_2); 3,71 (3H, s, OCH_3); 2,66 (2H, d, CH_2); 2,04 (1H, m, CH); 0,99 (6H, d, $2CH_3$)
XIIId	2218 sh	3300, 3393, 3430	1705	8,15 d and 7,50 d (4H, C_6H_4); 7,90 (5H, m, Ph); 7,82 (2H, br. s, NH_2); 4,99 (2H, s, SCH_2); 2,59 (2H, d, CH_2); 2,01 (1H, m, CH); 0,96 (6H, d, $2CH_3$)
XIIIe	2180	3322, 3380	—	7,91 (2H, br. s, NH_2); 2,62 (2H, d, CH_2); 2,53 (3H, s, SCH_3); 1,97 (1H, m, CH); 0,94 (6H, d, $2CH_3$)
XIIIf	2225 sh	3224, 3317, 3392	—	7,80 (2H, s, NH_2); 3,17 (2H, q, SCH_2); 3,30 (1H, m, CH); 1,42 (6H, d, $(CH_3)_2$); 1,30 (3H, t, CH_3)
XIIIg	2215	3165, 3248, 3390	—	7,88 (2H, s, NH_2); 2,54 (3H, s, SCH_3); 3,26 (1H, m, CH); 1,40 (6H, d, $(CH_3)_2$)
XIIIh	2218 sh	3240, 3335, 3433	1742	7,89 (2H, s, NH_2); 4,14 (2H, s, SCH_2); 3,67 (3H, s, OCH_3); 3,26 (1H, m, CH); 1,38 (6H, d, $(CH_3)_2$)
XIIIi	2220	3240, 3330, 3432	1695	7,80 (2H, s, NH_2); 5,00 (2H, s, SCH_2); 3,28 (1H, m, CH); 1,39 (6H, d, $(CH_3)_2$); 8,15 d and 7,38 d (each 2H, C_6H_4); 7,48 (5H, m, C_6H_5)
XIIIj	2217 sh	3233, 3330, 3418	1690	7,74 (2H, s, NH_2); 8,24 (1H, d, C_6H_3); 8,01 (1H, d, C_6H_3); 7,83 (1H, s, C_6H_3); 4,91 (2H, s, SCH_2); 3,30 (1H, m, CH); 1,40 (6H, d, $(CH_3)_2$)
XIIIk	2224	3320, 3418	1694	7,77 (2H, s, NH_2); 4,74 (2H, s, SCH_2); 3,26 (1H, m, CH); 1,39 (6H, d, $(CH_3)_2$); 8,74 (1H, s, CH); 8,00 (2H, m, H_{arom}); 7,48 (2H, m, H_{arom})

TABLE 3. Bond Lengths in VIa

Bond	Å	Bond	Å
$S_{(1)}$—$C_{(2)}$	1,770(3)	$C_{(4)}$—$C_{(5)}$	1,518(4)
$S_{(1)}$—$C_{(6)}$	1,763(3)	$C_{(4)}$—$C_{(9)}$	1,551(6)
$N_{(1)}$—$C_{(2)}$	1,352(4)	$C_{(5)}$—$C_{(6)}$	1,345(4)
$N_{(2)}$—$C_{(8)}$	1,149(4)	$C_{(5)}$—$C_{(7)}$	1,416(4)
$N_{(3)}$—$C_{(7)}$	1,139(4)	$C_{(9)}$—$C_{(10)}$	1,71(1)
$N_{(4)}$—$C_{(6)}$	1,362(4)	$C_{(9)}$—$C_{(10')}$	1,53(1)
$C_{(2)}$—$C_{(3)}$	1,349(4)	$C_{(9)}$—$C_{(11)}$	1,39(1)
$C_{(3)}$—$C_{(4)}$	1,510(4)	$C_{(9)}$—$C_{(11')}$	1,33(1)
$C_{(3)}$—$C_{(8)}$	1,417(4)		

Crystals of XIIIe are monoclinic, at 20°C: a = 7.651(3), b = 17.122(5), c = 20.687(6) Å, β = 97.80(2)°, V = 2685(3) Å^3, d_{calc} = 1.219 g/cm^3, Z = 8, space group C2/c. Unit cell parameters and intensities of 3584 independent reflections were measured on a Siemens P3/PC four circle automatic diffractometer (λMoKα, graphite monochromator, $\theta/2\theta$ scanning to θ_{max} = 28°). The structure was solved by a direct method revealing all nonhydrogen atoms and refined by a full matrix least squares method in the anisotropic approximation for nonhydrogen atoms for 2021 reflections with $I > 3\sigma(I)$. All of the hydrogen atoms were directly revealed in Fourier synthesis and refined isotropically. Final difference factor values were R = 0.051 and R_w = 0.051. All calculations were carried out using the SHELXTL PLUS program [13] (PC version). Atomic coordinates are given in Table 8.

4-Alkyl-6-amino-3,5-dicyanopyridine-2(1H)-thiones (Va,b). A. A mixture of aldehyde I (10 mmole), cyanothioacetamide II (20 mmole), and N-methylmorpholine (15 mmole) in ethanol (20 ml) was stirred for 4 h at 20°C. The reaction

TABLE 4. Valence Angles ω (deg.) in VIa

Angle	ω	Angle	ω
$C_{(2)}—S_{(1)}—C_{(6)}$	101,8(1)	$C_{(6)}—C_{(5)}—C_{(7)}$	118,8(3)
$S_{(1)}—C_{(2)}—N_{(1)}$	112,4(2)	$S_{(1)}—C_{(6)}—N_{(4)}$	112,8(2)
$S_{(1)}—C_{(2)}—C_{(3)}$	120,9(2)	$S_{(1)}—C_{(6)}—C_{(5)}$	121,0(2)
$N_{(1)}—C_{(2)}—C_{(3)}$	126,7(3)	$N_{(4)}—C_{(6)}—C_{(5)}$	126,2(3)
$C_{(2)}—C_{(3)}—C_{(4)}$	123,8(2)	$N_{(3)}—C_{(7)}—C_{(5)}$	177,1(3)
$C_{(2)}—C_{(3)}—C_{(8)}$	120,0(2)	$N_{(2)}—C_{(8)}—C_{(3)}$	176,3(3)
$C_{(4)}—C_{(3)}—C_{(8)}$	116,2(2)	$C_{(4)}—C_{(9)}—C_{(10)}$	101,6(7)
$C_{(3)}—C_{(4)}—C_{(5)}$	110,4(2)	$C_{(4)}—C_{(9)}—C_{(10')}$	112,7(8)
$C_{(3)}—C_{(4)}—C_{(9)}$	112,6(3)	$C_{(4)}—C_{(9)}—C_{(11)}$	118,3(5)
$C_{(5)}—C_{(4)}—C_{(9)}$	113,2(3)	$C_{(4)}—C_{(9)}—C_{(11')}$	121,6(6)
$C_{(4)}—C_{(5)}—C_{(6)}$	123,9(2)	$C_{(10)}—C_{(9)}—C_{(11)}$	103,3(9)
$C_{(4)}—C_{(5)}—C_{(7)}$	117,3(3)	$C_{(10')}—C_{(9)}—C_{(11')}$	97,3(7)

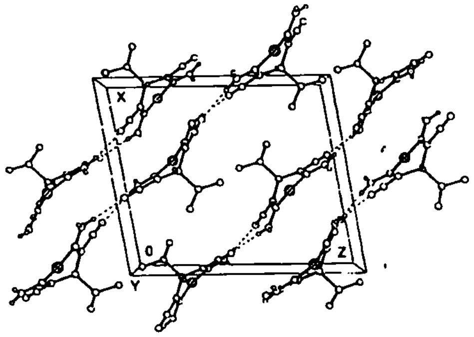

Fig. 2. Crystallographic bc projection of VIa. Broken lines indicate NH···N intermolecular hydrogen bonds.

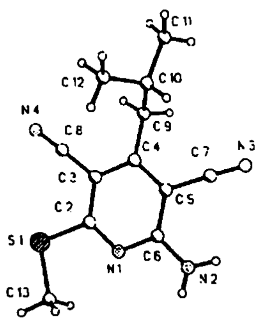

Fig. 3. General view of XIIIe.

mixture was diluted with hydrochloric acid (10%) to pH 3 and the precipitate was separated and washed with ethanol and hexane. Compounds Va,b obtained had similar IR and PMR spectra to those described before [1].

Compound Va: yield 1.53 g (70%). mp 241-243°C (AcOH).

Compound Vb: Yield 1.9 g (82%). mp 215-218°C (AcOH).

B. N-Methylmorpholine (10 mmole) was added to a suspension of thiopyran VI (10 mmole) in ethanol (20 ml) and the mixture refluxed for 2 h. After cooling, the product was diluted with hydrochloric acid (10%) to pH 3. The precipitate was separated and washed with ethanol and hexane. Va,b were obtained similar in mp and PMR data to those synthesized by method A. Yield of thione Va 1.37 g (63%); Vb 1.6 g (69%).

4-Alkyl-2,6-diamino-3,5-dicyano-4H-thiopyrans (VIa-c) and Selenopyrans (VId,e). A mixture of aldehyde I (10 mmole), malononitrile (10 mmole), amide II (10 mmole, in the case of IIb under argon and in absolute ethanol), and N-methyl-

TABLE 5. Bond Lengths d (Å) in XIIIe

Bond	Å	Bond	Å
$S_{(1)}$—$C_{(2)}$	1,758(3)	$C_{(3)}$—$C_{(8)}$	1,436(4)
$S_{(1)}$—$C_{(13)}$	1,791(4)	$C_{(4)}$—$C_{(5)}$	1,395(4)
$N_{(1)}$—$C_{(2)}$	1,320(3)	$C_{(4)}$—$C_{(9)}$	1,506(4)
$N_{(1)}$—$C_{(6)}$	1,350(3)	$C_{(5)}$—$C_{(6)}$	1,417(4)
$N_{(2)}$—$C_{(6)}$	1,336(4)	$C_{(5)}$—$C_{(7)}$	1,436(4)
$N_{(3)}$—$C_{(7)}$	1,137(4)	$C_{(9)}$—$C_{(10)}$	1,524(4)
$N_{(4)}$—$C_{(8)}$	1,143(4)	$C_{(10)}$—$C_{(11)}$	1,523(6)
$C_{(2)}$—$C_{(3)}$	1,415(4)	$C_{(10)}$—$C_{(12)}$	1,494(5)
$C_{(3)}$—$C_{(4)}$	1,394(4)		

TABLE 6. Valence Angles ω (deg) in XIIIe

Angle	ω	Angle	ω
$C_{(2)}$—$S_{(1)}$—$C_{(13)}$	101,4(2)	$C_{(4)}$—$C_{(5)}$—$C_{(7)}$	120,8(2)
$C_{(2)}$—$N_{(1)}$—$C_{(6)}$	118,0(2)	$C_{(6)}$—$C_{(5)}$—$C_{(7)}$	118,6(2)
$S_{(1)}$—$C_{(2)}$—$N_{(1)}$	118,2(2)	$N_{(1)}$—$C_{(6)}$—$N_{(2)}$	116,1(2)
$S_{(1)}$—$C_{(2)}$—$C_{(3)}$	117,8(2)	$N_{(1)}$—$C_{(6)}$—$C_{(5)}$	121,5(2)
$N_{(1)}$—$C_{(2)}$—$C_{(3)}$	124,0(2)	$N_{(2)}$—$C_{(6)}$—$C_{(5)}$	122,4(3)
$C_{(2)}$—$C_{(3)}$—$C_{(4)}$	118,9(2)	$N_{(3)}$—$C_{(7)}$—$C_{(5)}$	177,9(3)
$C_{(2)}$—$C_{(3)}$—$C_{(8)}$	119,8(2)	$N_{(4)}$—$C_{(8)}$—$C_{(3)}$	178,5(3)
$C_{(4)}$—$C_{(3)}$—$C_{(8)}$	121,2(2)	$C_{(4)}$—$C_{(9)}$—$C_{(10)}$	114,0(3)
$C_{(3)}$—$C_{(4)}$—$C_{(5)}$	116,9(2)	$C_{(9)}$—$C_{(10)}$—$C_{(11)}$	110,5(3)
$C_{(3)}$—$C_{(4)}$—$C_{(9)}$	122,5(2)	$C_{(9)}$—$C_{(10)}$—$C_{(12)}$	111,5(3)
$C_{(5)}$—$C_{(4)}$—$C_{(9)}$	120,6(2)	$C_{(11)}$—$C_{(10)}$—$C_{(12)}$	110,7(3)
$C_{(4)}$—$C_{(5)}$—$C_{(6)}$	120,5(2)		

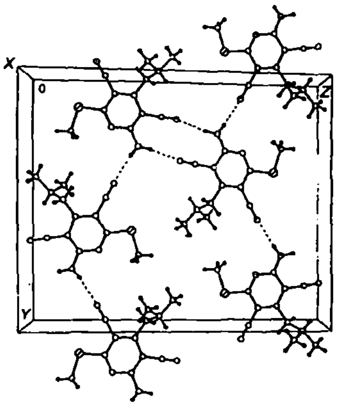

Fig. 4. Crystallographic bc projection of XIIIe. Broken lines indicate NH···N intermolecular bonds.

morpholine (0.1 ml) in ethanol (20 ml) was stirred for 3 h at 20°C. The precipitate was filtered and washed with ethanol and hexane. Compounds VIa-c were identical in IR and PMR spectra to those described earlier [1].

Compound VIa: yield 1.87 g (85%), mp 203-205°C (ethanol).

Compound VIb: yield 2.02 g (92%), mp 156-158°C (ethanol).

Compound VIc: yield 2.06 g (88%), mp 191-193°C (ethanol).

Compound VId: yield 2.0 g (71%), mp 168-170°C (ethanol). IR spectrum: 2177 sh ($C\equiv N$), 3222, 3323, 3416 cm^{-1} (NH_2). PMR spectrum: 6.87 (4H, s, $2NH_2$); 2.96 (1H, t, 4-H); 1.62 (1H, m, CH); 1.40 (2H, t, CH_2); 0.91 ppm (6H, d, $2CH_3$). Found, %: C 47.21; H 4.85; N 20.14; Se 27.80. $C_{11}H_{14}N_4Se$. Calculated, %: C 46.98; H 5.02; N 19.92, Se 28.08.

TABLE 7. Coordinates ($\times 10^4$) for the Atoms in VIa

Atom	x	y	z
$S_{(1)}$	4211(1)	1688(1)	7354(1)
$N_{(1)}$	2351(3)	765(5)	6214(2)
$N_{(2)}$	2309(2)	-4582(4)	5731(2)
$N_{(3)}$	6011(3)	-4053(5)	9420(2)
$N_{(4)}$	5464(3)	1169(4)	9022(2)
$C_{(2)}$	3322(3)	-60(4)	6667(2)
$C_{(3)}$	3631(2)	-1979(4)	6634(2)
$C_{(4)}$	4774(3)	-2765(5)	7089(2)
$C_{(5)}$	5152(2)	-1781(4)	8051(2)
$C_{(6)}$	5010(2)	158(4)	8220(2)
$C_{(7)}$	5648(3)	-3009(5)	8815(2)
$C_{(8)}$	2880(2)	-3373(4)	6123(2)
$C_{(9)}$	5672(4)	-2636(10)	6414(3)
$C_{(10)}$	6600(11)	-4455(17)	6865(13)
$C_{(10')}$	6842(11)	-3356(20)	6888(14)
$C_{(11)}$	5353(8)	-3192(21)	5463(7)
$C_{(11')}$	5999(7)	-903(19)	6100(6)
$H_{(11)}$	224(3)	198(5)	621(2)
$H_{(12)}$	200(3)	18(5)	574(2)
$H_{(41)}$	524(3)	231(5)	913(2)
$H_{(42)}$	596(3)	53(5)	953(2)
$H_{(4)}$	470(2)	-412(5)	721(2)

TABLE 8. Coordinates ($\times 10^4$, for H = $\times 10^3$) for the Atoms in XIIIe

Atom	x	y	z
$S_{(1)}$	2239(1)	6216(1)	3371(1)
$N_{(1)}$	2408(3)	7006(1)	2280(1)
$N_{(2)}$	2454(5)	7790(2)	1391(1)
$N_{(3)}$	3320(4)	6629(2)	65(1)
$N_{(4)}$	2829(4)	4287(2)	2796(1)
$C_{(2)}$	2481(4)	6302(2)	2541(1)
$C_{(3)}$	2734(4)	5608(2)	2193(1)
$C_{(4)}$	2976(4)	5662(2)	1539(1)
$C_{(5)}$	2871(4)	6405(2)	1261(1)
$C_{(6)}$	2585(4)	7070(2)	1641(1)
$C_{(7)}$	3137(4)	6518(2)	593(1)
$C_{(8)}$	2786(4)	4868(2)	2522(1)
$C_{(9)}$	3324(4)	4957(2)	1140(1)
$C_{(10)}$	1724(4)	4679(2)	678(1)
$C_{(11)}$	2263(7)	4066(3)	209(2)
$C_{(12)}$	318(6)	4368(2)	1044(2)
$C_{(13)}$	2247(7)	7220(2)	3615(2)
$H_{(21)}$	232(5)	815(2)	162(2)
$H_{(22)}$	245(5)	789(2)	98(2)
$H_{(91)}$	430(4)	508(2)	89(1)
$H_{(92)}$	383(4)	451(2)	142(1)
$H_{(10)}$	127(4)	512(2)	44(1)
$H_{(111)}$	120(5)	386(2)	-7(2)
$H_{(112)}$	297(6)	362(2)	40(2)
$H_{(113)}$	313(6)	426(2)	-2(2)
$H_{(121)}$	-86(5)	421(2)	75(2)
$H_{(122)}$	-21(5)	478(2)	131(2)
$H_{(123)}$	75(5)	391(2)	131(2)
$H_{(131)}$	123(5)	750(2)	338(2)
$H_{(132)}$	341(6)	744(2)	358(2)
$H_{(133)}$	194(6)	723(3)	405(2)

Compound VIe: yield 1.82 g (68%), mp 169-171°C (ethanol). IR spectrum: 2185 ($C{\equiv}N$), 1627 (δNH_2), 3300, 3398, 3443 cm^{-1} (νNH_2). PMR spectrum: 6.87 (4H, s, $2NH_2$); 2.58 (1H, d, 4-H); 1.89 (1H, m, CH), 0.90 ppm (6H, d, $2CH_3$). Found, %: C 45.14; H 4.34; N 21.15; Se 29.37. $C_{10}H_{12}N_4Se$. Calculated, %: C 44.95; H 4.53; N 20.97; Se 29.55.

4-Alkyl-2-alkylthio-6-amino-3,5-dicyanopyridines (XII, XIIIa-k). Aqueous KOH solution (10%, 5.6 ml, 10 mmole) was added with stirring to a suspension of thione V (10 mmole) in DMF (10 ml) and the corresponding halide X or XI (10 mmole) was added after 1 min. The mixture was stirred for 3 h, diluted with water (10 ml), and the separated precipitate washed successively with water, ethanol, and hexane. Parameters for the compounds obtained XII, XIIIa-k are given in Tables 1 and 2.

3,6-Diamino-4-R-2-(4′-chlorobenzoyl)-5-cyanothieno[2,3-b]pyridines (XIVa,b). Aqueous KOH solution (10%, 5.6 ml, 10 mmole) was added to a suspension of the corresponding substituted pyridine XIII (10 mmole) in DMF (15 ml) and the product stirred for 4 h. The precipitate was separated and washed with water, ethanol, and hexane.

Compound XIVa: yield 2.89 g (78%), mp 247-249°C (n-butanol). IR spectrum: 3330, 3472 (νNH_2), 1635 (δNH_2), 2218 cm^{-1} ($C\equiv N$). PMR spectrum: 8.42 (2H, s, 6-NH_2); 7.62 (4H, q, C_6H_4); 7.46 (2H, s, 3-NH_2); 3.90 (1H, m, CH); 1.49 ppm (6H, d, $2CH_3$). Found, %: C 58.48; H 4.19; N 14.92; S 8.48. $C_{18}H_{15}ClN_4OS$. Calculated, %: C 58.30; H 4.08; N 15.11; S 8.65.

Compound XIVb: yield 2.7 g (70%), mp 255-257°C (AcOH). IR spectrum: 2220 ($C\equiv N$), 1710 ($C=O$), 3284, 3422 cm^{-1} (NH_2). PMR spectrum: 8.15 (2H, br s, 6-NH_2); 7.71 and 7.55 d (each 2H, C_6H_4); 7.50 (2H, br s, 3-NH_2); 3.07 (2H, d, CH_2); 2.04 (1H, m, CH); 0.96 ppm (6H, d, $2CH_3$). Found, %: C 59.10; H 4.18; N 14.71; S 8.42. $C_{19}H_{17}ClN_4OS$. Calculated, %: C 59.29; H 4.45; N 14.56; S 8.33.

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