SYNTHESIS OF 6-SUBSTITUTED IMIDAZO[4,5-*c*]PYRAZOLE-5-THIONES

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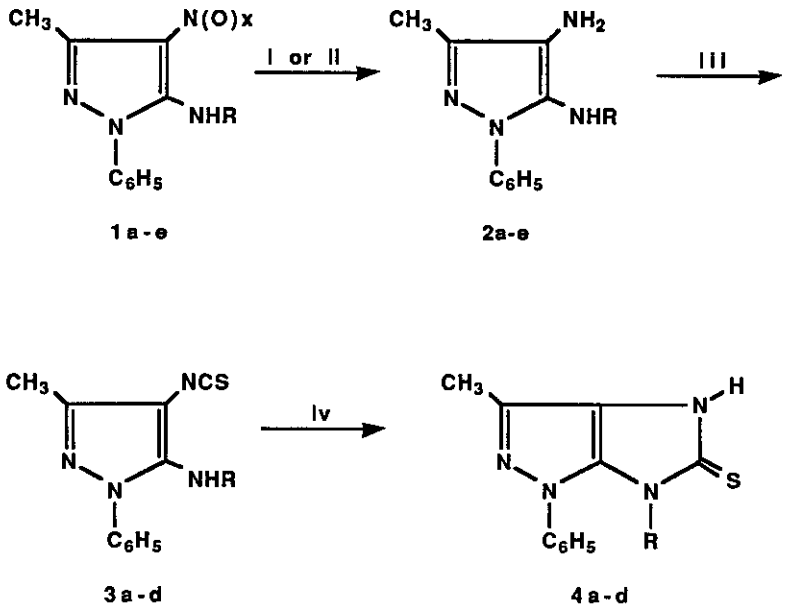
Abstract- Treatment of diaminopyrazole derivatives (**2**) with thiophosgene afforded selectively the isothiocyanatopyrazoles (**3**). Heating of **3** in pyridine gave the imidazo[4,5-*c*]pyrazole-5-thiones (**4**).

There is a paucity on the literature[1-7] concerning the synthesis and biological activity of imidazo[4,5-*c*]pyrazoles. Apart from a few patents that are claimed to provide particular derivatives employed as photographic couplers, the synthetic approaches up to now available are restricted to the following: a) the Curtius rearrangement followed by cyclization of 4-carbonylazido-5-aminopyrazoles,[1] b) the cyclization of 4-nitro-5-benzylaminopyrazoles,[2] c) the reaction of 4,5-diaminopyrazoles with carbon disulfide[3] or with 2-methoxybenzoic acid[4] and d) the cycloaddition of diazomethane onto 5-nitroimidazoles.[5] The only pharmacological evaluation of this class of compounds was made by Barraclough *et al.*[4] which reported that some imidazo[4,5-*c*]pyrazoles are inotropic agents more potent than the reference sulmazole. In previous researches in this area,[6] we proved that the intramolecular cyclodehydration of 5-alkylamino-4-nitrosopyrazoles constitutes an efficient method for the synthesis of 5-substituted imidazo[4,5-*c*]pyrazoles. By applying the above procedure, we have prepared a series of homologues which in tests for biological evaluation showed interesting properties as CNS depressants.[7] In order to better evaluate the structural requirements for activity, a procedure for the regioselective functionalization of position 6 became the target of our synthetic efforts. The present paper describes a general route to imidazo[4,5-*c*]pyrazole-5-thiones in which the nitrogen atom in position 6 can be selectively linked to acyl, aryl and acylamino groups.

The key intermediates to the target products were the isothiocyanates (**3**) (see Scheme). The intermediates (**3a-c**) were prepared from the corresponding nitrosopyrazolylamines (**1a-c**), which were reduced with hydrazine hydrate in the presence of palladized charcoal to the diamines (**2a-c**). These compounds were

isolated as colorless crystalline solids, quite stable if stored at 4°C *in vacuo* over phosphorus pentoxide. The successive treatment of **2a-c** with thiophosgene afforded the isothiocyanates (**3a-c**) as the lone reaction products; the selectivity of the thiophosgene attack is due to the higher nucleophilicity of the pyrazole 4-amino group in comparison with that in position 5.[8]

Scheme



For compounds (1):

	x	R
a	1	H
b	1	COC_6H_5
c	1	$CH_2C_6H_5$
d	2	$NHCOC_6H_5$
e	2	NH_2

For compounds (2-4):

	R
a	H
b	COC_6H_5
c	$CH_2C_6H_5$
d	$NHCOC_6H_5$
e	NH_2

For x=1: I, 5% C/Pd, N_2H_4; for x=2: II, 5% C/Pd, H_2, 50 psi; III, $CSCl_2$; IV, Reflux, pyridine.

The isothiocyanate (**3d**) was obtained starting from nitropyrazolylhydrazine (**1e**), prepared according to the literature method.[9] Compound (**1e**) was acylated with benzoyl chloride to the hydrazide (**1d**) which was hydrogenated in the presence of palladized charcoal to give the *N*-(4-amino-5-pyrazolyl)-*N'*-benzoylhydrazine (**2d**). Since **2d** was unstable during the usual work-up for isolation, it was directly reacted with thiophosgene

to give selectively the isothiocyanate (**3d**). Finally, when **1e** was submitted to catalytic reduction and then treated with thiophosgene under the same conditions followed for the synthesis of **3d,** the reaction product was the 4-isothiocyanato-3-methyl-1-phenyl-*1H*-pyrazol-5-ylamine (**3a**), identical to the product obtained from the reaction of **2a** with thiophosgene.

The intramolecular cyclization of all isothiocyanates (**3a-d**) was performed by heating under reflux in pyridine; the yields of the target imidazo[4,5-c]pyrazole-5-thiones (**4a-d**) ranged from good to quantitative. The proposed structures were supported by analytical and spectral data. A particular attention was paid to the product (**4d**), given that its nmr spectra could not exclude the structure of pyrazolo[4,3-*e*][1,2,4]triazine-5-thione deriving from a hypothetical alternative cyclization of **3d**. For the definitive assignment, a single-crystal X-ray analysis was performed on a sample of **4d** recrystallized from methanol-hexane. It is worthwhile noting that the melting point of our product (**4a**) resulted quite different from that reported by other authors,[3] who claimed to have obtained the same compound by reacting **2a** with carbon disulfide: anyway the structure proposed by these authors was not supported by spectral data.

EXPERIMENTAL

Melting points were determined with a Büchi capillary apparatus and are uncorrected. The ir spectra were recorded from potassium bromide discs on a Perkin-Elmer 299B spectrophotometer. The ^{1}H nmr and ^{13}C nmr spectra were recorded on a Bruker AC 200 spectrometer. Chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane as internal standard. Column chromatography was performed using Merck silica gel (70-230 mesh); for flash chromatography technique silica gel (230-400 mesh) was employed. Compounds (**1c**), (**1e**) and (**2b**) were prepared according to the reported procedures.[6,9,10]

Procedure for the synthesis of diamines (2a,c).

99% Hydrazine hydrate (0.98 ml, 20 mmol) and 5% palladized charcoal (0.30 g) were added to a solution of each nitrosopyrazolylamine (**1a,c**) (4 mmol) in methanol (50 ml). After heating under reflux for 5 min, the catalyst was removed and the filtrate was evaporated to dryness *in vacuo*. The resulting solid was purified by flash chromatography or by recrystallization from the indicated solvent.

3-Methyl-1-phenyl-*1H*-pyrazol-4,5-yldiamine (2a).

Colorless crystals, yield 89%, mp 120.5-121.5°C (ligroin) (lit.,[3] 119-121°C); ir (KBr): 3350-3100 (br), 1650, 1600, 1500 cm^{-1}; ^{1}H nmr (DMSO-d_6) δ: 2.02 (s, 3H, Me), 3.19 (br s, 2H, NH_2), 4.57 (br s, 2H, NH_2), 7.18-7.63 (m, 5H, Ph).

4-Amino-3-methyl-1-phenyl-*1H*-pyrazol-5-ylbenzylamine (2c).

Colorless crystals from flash chromatography (eluent: 8:2 ethyl acetate/petroleum ether); yield 78%, mp 82-83°C (ethyl acetate/petroleum ether); ir (KBr): 3400, 3320, 1610, 1510 cm^{-1}; ^{1}H nmr (DMSO-d_6) δ: 2.04 (s, 3H, Me), 3.42 (br s, 2H, NH_2), 3.87 (d, J=6.8 Hz, 2H, CH_2), 4.87 (t, J=6.8 Hz, 1H, NH), 7.20-7.72 (m, 10H, 2Ph). Anal. Calcd for $C_{17}H_{18}N_4$: C, 73.35; H, 6.52; N, 20.13. Found: C, 73.60; H, 6.47; N, 20.28.

Procedure for the synthesis of isothiocyanates (3a-c)

Thiophosgene (0.23 ml, 3 mmol) was added dropwise to a suspension or solution of **2a-c** (3 mmol) in water (15 ml). After 2 h stirring at room temperature, the white precipitate was collected, washed with water and dissolved in ethyl acetate. After drying over anhydrous magnesium sulfate, the solvent was removed to give a solid which was recrystallized from the indicated solvent.

4-Isothiocyanato-3-methyl-1-phenyl-*1H*-pyrazol-5-ylamine (3a).

Pale yellow crystals, yield 86%, mp 163-164°C (ethyl acetate/petroleum ether); ir (KBr): 3410, 3290, 3100 (br), 2150, 1640, 1600, 1530, 1500 cm^{-1}; ^1H nmr (DMSO-d_6) δ: 2.14 (s, 3H, Me), 6.10 (br s, 2H, NH_2), 7.34-7.50 (m, 5H, Ph). Anal. Calcd for $C_{11}H_{10}N_4S$: C, 57.37; H, 4.38; N, 24.33, S, 13.92. Found: C, 57.22; H, 4.42; N, 24.21, S, 13.80.

***N*-(4-Isothiocyanato-3-methyl-1-phenyl-*1H*-pyrazol-5-yl)benzamide (3b).**

Colorless crystals, yield 94%, mp 165-166°C (ethyl acetate/petroleum ether); ir (KBr): 3200 (br), 2100, 1650, 1590, 1500 cm^{-1}; ^1H nmr (DMSO-d_6) δ: 2.31 (s, 3H, Me), 7.48-7.91 (m, 10H, 2Ph), 10.72 (br s, 1H, NH). Anal. Calcd for $C_{18}H_{14}N_4OS$: C, 64.65; H, 4.22; N, 16.75, S, 9.59. Found: C, 64.60; H, 4.32; N, 16.64, S, 9.48.

4-Isothiocyanato-3-methyl-1-phenyl-*1H*-pyrazol-5-ylbenzylamine (3c).

Colorless crystals, yield 84%, mp 66-67°C (methanol/water); ir (KBr): 3250, 2100, 1600, 1540, 1500 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.26 (s, 3H, Me), 4.15 (br t, 1H, NH), 4.43 (d, J=7.0 Hz, 2H, CH_2), 7.27-7.42 (m, 10H, 2Ph). Anal. Calcd for $C_{18}H_{16}N_4S$: C, 67.48; H, 5.03; N, 17.49, S, 10.01. Found: C, 67.60; H, 5.12; N, 17.64, S, 9.88.

Synthesis of *N*-(3-methyl-4-nitro-1-phenyl-*1H*-pyrazol-5-yl)-*N'*-benzoylhydrazine (1d).

A solution of benzoyl chloride (0.35 ml, 3 mmol) in ethyl acetate (20 ml) was added dropwise to a mixture of **1e** (0.70 g, 3 mmol) in ethyl acetate (120 ml) and sodium hydrogen carbonate (0.25 g, 3 mmol) in water (25 ml). After 1 h stirring at room temperature the organic phase was washed with water and then dried over anhydrous magnesium sulfate. The solvent was evaporated to leave a crude white product which was recrystallized from toluene. Yield 0.89 g, 88%, mp 169-171°C; ir (KBr): 3350, 3220 (br), 1680, 1600, 1530 cm^{-1}; ^1H nmr (DMSO-d_6) δ: 2.42 (s, 3H, Me), 7.13-7.43 (m, 10H, 2Ph), 9.40 (br s, 1H, NH), 10.35 (br s, 1H, NH). Anal. Calcd for $C_{17}H_{15}N_5O_3$: C, 60.53; H, 4.48; N, 20.76. Found: C, 60.70; H, 4.47; N, 20.68.

Synthesis of *N*-(4-isothiocyanato-3-methyl-1-phenyl-*1H*-pyrazol-5-yl)-*N'*-benzoylhydrazine (3d).

N-(3-Methyl-4-nitro-1-phenyl-*1H*-pyrazol-5-yl)-*N'*-benzoylhydrazine (**1d**) (1.01 g, 3 mmol) in methanol (11 ml) was hydrogenated under 50 psi in the presence of 5% Pd/C (0.23 g) for 5 h . The mixture was rapidly filtered through Celite and the solvent evaporated. The crude product was suspended in water (15 ml) and thiophosgene (0.23 ml, 3 mmol) was added dropwise to the suspension. After 2 h stirring at room temperature, the white precipitate was collected, washed with water and dissolved in ethyl acetate. After drying over anhydrous magnesium sulfate, the solvent was removed to give a solid which was recrystallized from the indicated solvent.

Pale yellow crystals, yield 75%, mp 189°C (ethyl acetate/petroleum ether); ir (KBr): 3210, 2100, 1650, 1550 cm^{-1}; ^1H nmr (DMSO-d_6) δ: 2.18 (s, 3H, Me), 7.35-7.90 (m, 10H, 2Ph), 8.58 (br s, 1H, NH), 10.70 (br s,

1H, NH). Anal. Calcd for $C_{18}H_{15}N_5OS$: C, 61.88; H, 4.33; N, 20.04, S, 9.18. Found: C, 61.70; H, 4.37; N, 20.08, S, 9.10.

Reduction and treatment with thiophosgene of 1e.

A solution of 3-methyl-4-nitro-1-phenyl-*1H*-pyrazol-5-ylhydrazine (**1e**) (0.70 g, 3 mmol) in methanol (50 ml) was hydrogenated for 1 h and treated with thiophosgene (0.23 ml, 3 mmol) under the same conditions followed for the synthesis of **3d**.

Pale yellow crystals, yield 52%, mp 163-164°C (ethyl acetate/petroleum ether). The product was identical to compound (**3a**) obtained from the reaction of **2a** with thiophosgene.

Procedure for the synthesis of imidazo[4,5-*c*]pyrazole-5-thiones (4a-d).

A solution of each 4-isothiocyanatopyrazole(**3**)(1 mmol) in pyridine (35 ml) was heated under reflux until the intramolecular cyclicization was completed (1 h for **3a** and **3c**, 3 h for **3d** and 6 h for **3b**). The solvent was removed under reduced pressure to give a solid which was purified by flash chromatography or by recrystallization from the indicated solvent.

3-Methyl-1-phenylimidazo[4,5-*c*]pyrazole-5-thione (4a).

Colorless crystals, yield 95% , mp 233°C (ethyl acetate/petroleum ether); ir (KBr): 3100 (br), 1590, 1510, 1480 cm^{-1}; ^1H nmr (DMSO-d_6) δ: 2.26 (s, 3H, Me), 7.23-7.75 (m, 5H, Ph), 12.47 (br s, 1H, NH), 13.39 (br s, 1H, NH); ^{13}C nmr (DMSO-d_6) δ: 11.74 (q, J=128.4 Hz, Me), 117.14 (d, J=163.1 Hz, Ph), 120.17 (s, C-3a), 125.16 (d, J=162.7 Hz, Ph), 129.39 (d, J=162.5 Hz, Ph), 130.21 (s, C-3), 135.33 (s, C-6a), 137.87 (s, Ph), 169.01 (CS). Anal. Calcd for $C_{11}H_{10}N_4S$: C, 57.37; H, 4.38; N, 24.33, S, 13.92. Found: C, 57.30; H, 4.42; N, 24.18, S, 13.84.

6-Benzoyl-3-methyl-1-phenylimidazo[4,5-*c*]pyrazole-5-thione (4b).

Colorless crystals from column chromatography (eluent: 8:2 ethyl acetate/petroleum ether); yield 62%, mp 243-244°C (ethyl acetate/petroleum ether); ir (KBr): 3450 (br), 3250 (br), 1700, 1640, 1550 cm^{-1}; ^1H nmr (DMSO-d_6) δ: 2.12 (s, 3H, Me), 7.31-7.85 (m, 10H, 2Ph), 10.40 (br s, 1H, NH). Anal. Calcd for $C_{18}H_{14}N_4OS$: C, 64.65; H, 4.22; N, 16.75, S, 9.59. Found: C, 64.55; H, 4.29; N, 16.54, S, 9.38.

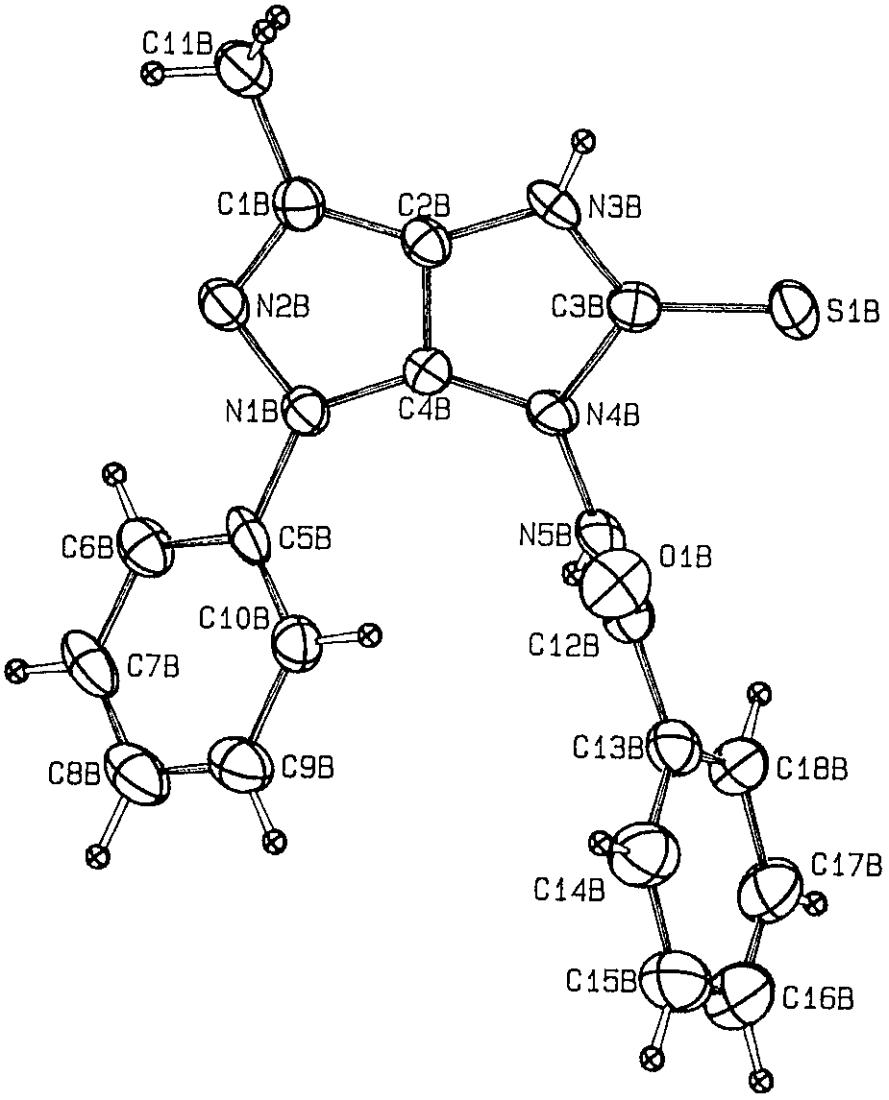
6-Benzyl-3-methyl-1-phenylimidazo[4,5-*c*]pyrazole-5-thione (4c).

Colorless crystals, yield 89% , mp 201-202°C (ethyl acetate/petroleum ether); ir (KBr): 3100 (br), 1610, 1580, 1520, 1480 cm^{-1}; ^1H nmr (DMSO-d_6) δ: 2.26 (s, 3H, Me), 5.36 (s, 2H, CH_2), 6.66-7.41 (m, 10H, 2Ph), 12.61 (br s, 1H, NH). Anal. Calcd for $C_{18}H_{16}N_4S$: C, 67.48; H, 5.03; N, 17.49, S, 10.01. Found: C, 67.30; H, 5.12; N, 17.48, S, 9.88.

6-Benzamido-3-methyl-1-phenylimidazo[4,5-*c*]pyrazole-5-thione (4d).

Pale yellow crystals from flash chromatography (eluent: 3:7 ethyl acetate/petroleum ether); yield 77%, mp 206-207°C (ethyl acetate/petroleum ether); ir (KBr): 3450 (br), 3000 (br), 1700, 1600, 1470 cm^{-1}; ^1H nmr (DMSO-d_6) δ: 2.32 (s, 3H, Me), 7.22-7.85 (m, 10H, 2Ph), 11.93 (br s, 1H, NH), 13.05 (br s, 1H, NH); ^{13}C nmr (DMSO-d_6) δ: 11.58 (q, J=128.0 Hz, Me), 117.15 (s, C-3a), 121.01 (d, J=163.1 Hz, Ph), 126.76 (d, J=162.3 Hz, Ph), 127.49 (d, J=162.5 Hz, Ph), 128.67 (d, J=163.4 Hz, Ph), 129.10 (d, J=161.2 Hz, Ph), 130.98 (s, C-3), 131.02 (s, Ph), 132.62 (d, J=162.8 Hz, Ph), 134.98 (s, C-6a), 137.22 (s, Ph), 165.61 (s, CONH), 170.64 (s, CS). Anal. Calcd for $C_{18}H_{15}N_5OS$: C, 61.88; H, 4.33; N, 20.04, S, 9.18. Found: C, 61.74; H, 4.42; N, 19.88, S, 9.04.

X-Ray Crystallographic Analysis



An ORTEP[14] view of molecule displaying the termal ellipsoids at 30% probability

Table 1. Final fractional atomic coordinates

Atom	x	y	z
S (1A)	0.16048 (6)	0.1328 (2)	0
O (1A)	0.2924 (2)	0.3665 (6)	0.0738 (2)
N (1A)	0.3650 (2)	0.2679 (6)	- 0.1089 (2)
N (2A)	0.3599 (2)	0.3188 (6)	- 0.1687 (2)
N (3A)	0.2101 (2)	0.2508 (6)	- 0.1049 (2)
N (4A)	0.2775 (2)	0.1890 (6)	- 0.0348 (2)
N (5A)	0.3009 (2)	0.1082 (6)	0.0162 (2)
C (1A)	0.2998 (2)	0.3260 (2)	- 0.1827 (2)
C (2A)	0.2680 (2)	0.2832 (7)	- 0.1295 (2)
C (3A)	0.2156 (2)	0.1912 (8)	- 0.0488 (2)
C (4A)	0.3090 (2)	0.2482 (7)	- 0.0859 (3)
C (5A)	0.4235 (2)	0.2572 (7)	- 0.0812 (3)
C (6A)	0.4720 (2)	0.1906 (8)	- 0.1141 (3)
C (7A)	0.5289 (2)	0.1828 (9)	- 0.0867 (3)
C (8A)	0.5355 (2)	0.2391 (9)	- 0.0287 (3)
C (9A)	0.4875 (3)	0.3048 (9)	0.0037 (3)
C (10A)	0.4295 (2)	0.3166 (8)	- 0.0217 (3)
C (11A)	0.2771 (3)	0.3716 (10)	- 0.2441 (3)
C (12A)	0.3046 (2)	0.2039 (9)	0.0699 (3)
C (13A)	0.3264 (2)	0.0794 (9)	0.1201 (3)
C (14A)	0.3653 (3)	0.1554 (11)	0.1637 (3)
C (15A)	0.3884 (3)	0.0378 (13)	0.2098 (3)
C (16A)	0.3725 (4)	- 0.1484 (14)	0.2091 (3)
C (17A)	0.3336 (4)	- 0.2167 (13)	0.1681 (3)
C (18A)	0.3111 (3)	- 0.1043 (10)	0.1229 (3)
H (3A)	0.181 (2)	0.288 (6)	- 0.127 (2)
H (5A)	0.317 (1)	0.012 (4)	0.011 (1)
S (1B)	0.08812 (6)	0.4051 (2)	- 0.17571 (8)
O (1B)	- 0.0360 (2)	0.0940 (6)	- 0.2343 (2)
N (1B)	- 0.1157 (2)	0.2419 (6)	- 0.0684 (2)
N (2B)	- 0.1105 (2)	0.1919 (7)	- 0.0077 (2)
N (3B)	0.0386 (2)	0.2864 (6)	- 0.0702 (2)
N (4B)	- 0.0292 (2)	0.3322 (6)	- 0.1413 (2)
N (5B)	- 0.0521 (2)	0.3843 (6)	- 0.1969 (27
C (1B)	- 0.0511 (2)	0.1943 (8)	0.0048 (3)
C (2B)	- 0.0179 (2)	0.2428 (7)	- 0.0458 (2)
C (3B)	0.0333 (2)	0.3404 (8)	- 0.1286 (2)
C (4B)	- 0.0591 (2)	0.2701 (7)	- 0.0909 (2)
C (5B)	- 0.1753 (2)	0.2388 (8)	- 0.0952 (3)
C (6B)	- 0.2249 (2)	0.2999 (9)	- 0.0625 (3)
C (7B)	- 0.2811 (2)	0.2883 (9)	- 0.0877 (3)
C (8B)	- 0.2892 (3)	0.2239 (9)	- 0.1454 (3)
C (9B)	- 0.2398 (3)	0.1640 (8)	- 0.1784 (3)
C (10B)	- 0.1825 (2)	0.1702 (8)	- 0.1529 (2)
C (11B)	- 0.0290 (3)	0.1572 (11)	0.0674 (3)
C (12B)	- 0.0542 (2)	0.2504 (8)	- 0.2416 (2)
C (13B)	- 0.0822 (2)	0.3217 (9)	- 0.2986 (3)
C (14B)	- 0.1144 (3)	0.1957 (10)	- 0.3330 (3)
C (15B)	- 0.1456 (3)	0.2594 (14)	- 0.3846 (3)
C (16B)	- 0.1422 (3)	0.4406 (14)	- 0.4011 (3)
C (17B)	- 0.1094 (3)	0.5614 (12)	- 0.3679 (3)
C (18B)	- 0.0793 (3)	0.5082 (11)	- 0.3160 (3)
H (3B)	0.071 (2)	0.255 (5)	- 0.059 (2)
H (5B)	- 0.081 (2)	0.466 (7)	- 0.198 (2)

Table 2. Bond distances (Å) with esds in parentheses

Molecule A		Molecule B	
S(1A)-C(3A)	1.673 (5)	S(1B)-C(3B)	1.657 (5)
O(1A)-C(12A)	1.199 (8)	O(1B)-C(12B)	1.201 (7)
N(1A)-N(2A)	1.376 (6)	N(1B)-N(2B)	1.394 (6)
N(1A)-C(4A)	1.336 (6)	N(1B)-C(4B)	1.352 (6)
N(1A)-C(5A)	1.423 (7)	N(1B)-C(5B)	1.435 (6)
N(2A)-C(1A)	1.354 (6)	N(2B)-C(1B)	1.331 (6)
N(3A)-C(2A)	1.400 (6)	N(3B)-C(2B)	1.387 (6)
N(3A)-C(3A)	1.318 (6)	N(3B)-C(3B)	1.353 (6)
N(3A)-H(3A)	0.85 (4)	N(3B)-H(3B)	0.78 (4)
N(4A)-N(5A)	1.368 (6)	N(4B)-N(5B)	1.380 (6)
N(4A)-C(3A)	1.392 (6)	N(4B)-C(3B)	1.400 (6)
N(4A)-C(4A)	1.391 (8)	N(4B)-C(4B)	1.368 (6)
N(5A)-C(12A)	1.374 (8)	N(5B)-C(12B)	1.379 (7)
N(5A)-H(5A)	0.78 (3)	N(5B)-H(5B)	0.86 (5)
C(1A)-C(2A)	1.402 (6)	C(1B)-C(2B)	1.380 (8)
C(1A)-C(11A)	1.483 (8)	C(1B-C(11B)	1.491 (9)
C(2A)-C(4A)	1.342 (7)	C(2B)-C(4B)	1.360 (6)
C(5A)-C(6A)	1.374 (7)	C(5B)-C(6B)	1.377 (8)
C(5A)-C(10A)	1.389 (9)	C(5B)-C(10B)	1.377 (8)
C(6A)-C(7A)	1.388 (7)	C (6B)-C(7B)	1.355 (7)
C(7A)-C(8A)	1.352 (9)	C(7B)-C(8B)	1.369 (9)
C(8A)-C(9A)	1.357 (8)	C(8B)-C(9B)	1.375 (9)
C(9A)-C(10A)	1.393 (8)	C(9B)-C(10B)	1.378 (8)
C(12A)-C(13A)	1.502 (9)	C(12B)-C(13B)	1.492 (8)
C(13A)-C(14A)	1.398 (9)	C(13B)-C(14B)	1.376 (9)
C(13A)-C(18A)	1.360 (9)	C(13B)-C(18B)	1.392 (10)
C(14A)-C(15A)	1.416 (11)	C(14B)-C(15B)	1.407 (10)
C(15A)-C(16A)	1.379 (13)	C(15B)-C(16B)	1.351 (14)
C(16A)-C(17A)	1.338 (11)	C(16B)-C(17B)	1.344 (11)
C(17A)-C(18A)	1.375 (11)	C(17B)-C(18B)	1.378 (10)

Crystal data for 4d. $C_{18}H_{15}N_5OS$, M= 349.42, orthorhombic, space group: *Pca2 1* (No. 29), a = 21.923(3), b = 7.167(2), c = 22.117(2) Å, V= 3475(1) Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centered reflections, λ =0.71069 Å), Z = 8, (two molecule in the asymmetric unit), D_X = 1.33 g/cm^{-3}, μ(Mo$K\alpha$)= 1.92 cm^{-1}, T = 295 K, crystal dimensions: 0.19 x 0.19 x 0.45 mm.

Data collection, analysis and refinement. A Enraf-Nonius CAD-4 diffractometer was used, with graphite-monochromated Mo$K\alpha$ radiation and $\omega/2\theta$ scan technique. 3877 unique reflections measured ($2 \leq \theta \leq 27°$), giving 1935 with $I \geq 3\sigma$ (I). Solution by direct methods (SIR88)[11] and Fourier synthesis. Hydrogen atoms of the amino groups found in difference-Fourier maps. Two-blocks matrix least-squares refinement. The weighting scheme $w=4Fo^2/[\sigma^2(Fo^2) + (0.03Fo^2)^2]$ gave satisfactory agreement analysis. Goodness of fit= 1.45. Final R = 0.044 and Rw = 0.048. All calculations were performed by the MolEN[12] and PARST[13] programs.

Table 3. Bond angles (°) with esds in parentheses

Molecule A		Molecule B	
C(4A)-N(1A)-C(5A)	131.2 (5)	C(4B)-N(1B)-C(5B)	133.3 (5)
N(2A)-N(1A)-C(5A)	120.1 (4)	N(2B)-N(1B)-C(5B)	117.9 (4)
N(2A)-N(1A)-C(4A)	108.6 (4)	N(2B)-N(1B)-C(4B)	108.5 (4)
N(1A)-N(2A)-C(1A)	108.0 (4)	N(1B)-N(2B)-C(1B)	106.1 (4)
C(2A)-N(3A)-C(3A)	109.7 (4)	C(2B)-N(3B)-C(3B)	111.1 (4)
C(3A)-N(4A)-C(4A)	107.4 (4)	C(3B)-N(4B)-C(4B)	108.6 (4)
N(5A)-N(4A)-C(4A)	127.8 (4)	N(5B)-N(4B)-C(4B)	129.8 (4)
N(5A)-N(4A)-C(3A)	123.6 (4)	N(5B)-N(4B)-C(3B)	121.6 (4)
N(4A)-N(5A)-C(12A)	121.6 (4)	N(4B)-N(5B)-C(12B)	117.6 (4)
N(2A)-C(1A)-C(11A)	123.0 (4)	N(2B)-C(1B)-C(11B)	120.6 (4)
N(2A)-C(1A)-C(2A)	106.5 (4)	N(2B)-C(1B)-C(2B)	110.5 (4)
C(2A)-C(1A)-C(11A)	130.6 (4)	C(2B)-C(1B)-C(11B)	128.8 (5)
N(3A)-C(2A)-C(1A)	144.4 (4)	N(3B)-C(2B)-C(1B)	147.5 (5)
C(1A)-C(2A)-C(4A)	108.1 (4)	C(1B)-C(2B)-C(4B)	106.3 (4)
N(3A)-C(2A)-C(4A)	107.3 (4)	N(3B)-C(2B)-C(4B)	106.0 (4)
N(3A)-C(3A)-N(4A)	107.6 (4)	N(3B)-C(3B)-N(4B)	105.3 (4)
S(1A)-C(3A)-N(4A)	123.9 (4)	S(1B)-C(3B)-N(4B)	126.6 (4)
S(1A)-C(3A)-N(3A)	128.5 (4)	S(1B)-C(3B)-N(3B)	128.2 (4)
N(4A)-C(4A)-C(2A)	108.0 (4)	N(4B)-C(4B)-C(2B)	109.0 (4)
N(1A)-C(4A)-C(2A)	108.8 (4)	N(1B)-C(4B)-C(2B)	108.6 (4)
N(1A)-C(4A)-N(4A)	142.9 (5)	N(1B)-C(4B)-N(4B)	142.0 (4)
N(1A)-C(5A)-C(10A)	118.5 (4)	N(1B)-C(5B)-C(10B)	119.5 (4)
N (1A)-C(5A)-C(6A)	119.2 (5)	N(1B)-C(5B)-C(6B)	119.8 (5)
C(6A)-C(5A)-C(10A)	122.3 (4)	C(6B)-C(5B)-C(10B)	120.6 (4)
C(5A)-C(6A)-C(7A)	118.6 (6)	C(5B)-C(6B)-C(7B)	118.8 (6)
C(6A)-C(7A)-C(8A)	119.9 (5)	C(6B)-C(7B)-C(8B)	121.5 (5)
C(7A)-C(8A)-C(9A)	121.4 (5)	C(7B)-C(8B)-C(9B)	119.9 (6)
C(8A)-C(9A)-C(10A)	121.1 (6)	C(8B)-C(9B)-C(10B)	119.4 (6)
C(5A)-C(10A)-C(9A)	116.7 (5)	C(5B)-C(10B)-C(9B)	119.7 (5)
O(1A)-C(12A)-N(5A)	122.3 (6)	O(1B)-C(12B)-N(5B)	122.8 (5)
N(5A)-C(12A)-C(13A)	111.2 (5)	N(5B)-C(12B)-C(13B)	112.4 (5)
O(1A)-C(12A)-C(13A)	126.5 (6)	O(1B)-C(12B)-C(13B)	124.7 (5)
C(12A)-C(13A)-C(18A)	122.0 (5)	C(12B)-C(13B)-C(18B)	122.9 (5)
C(12A)-C(13A)-C(14A)	118.2 (6)	C(12B)-C(13B)-C(14B)	117.0 (6)
C(14A)-C(13A)-C(18A)	119.8 (6)	C(14B)-C(13B)-C(18B)	120.0 (6)
C(13A)-C(14A)-C(15A)	118.9 (7)	C(13B)-C(14B)-C(15B)	119.0 (7)
C(14A)-C(15A)-C(16A)	118.5 (6)	C(14B)-C(15B)-C(16B)	120.3 (6)
C(15A)-C(16A)-C(17A)	121.5 (8)	C(15B)-C(16B)-C(17B)	120.1 (7)
C(16A)-C(17A)-C(18A)	120.5 (8)	C(16B)-C(17B)-C(18B)	122.2 (7)
C(13A)-C(18A)-C(17A)	120.8 (6)	C(13B)-C(18B)-C(17B)	118.3 (7)

Table 4. Bond distances (Å) and angles (°) for inter- and intramolecular hydrogen bonds with esd in parentheses

	D---A[a]	H---A	Angle	Sym.Op.[b]
N(3A)-H(3A)---S(1B)	3.290 (5)	2.45 (4)	171 (4)	0
N(3B)-H(3B)---S(1A)	3.281 (5)	2.51 (4)	166 (4)	0
N(5A)-H(5A)---N(2B)	2.946 (6)	2.20 (3)	160 (2)	I
N(5B)-H(5B)---N(2A)	2.939 (6)	2.12 (5)	159 (4)	II

[a] D=donor; A=acceptor.

[b] Symmetry Operations: (0) x,y,z; (I) x+1/2,-y,z; (II) x-1/2,1-y,z.

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