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Synthesis, Structure and Tuberculostatic Activity of N′-(Amino-pyridyl-methylene)-hydrazinecarbodithioic Acid Methyl Esters

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The methods of preparation of the title esters from imidates or amidrazones are described, and structures of the compounds are elucidated on the basis of ^{1}H, ^{13}C-NMR, 2D-NMR spectra and X-ray diffraction method. Tuberculotic activity was also studied.

Key words: amidrazones, hydrazinecarbodithioic acid esters, tuberculostatics, configuration, tautomers, NMR spectra, X-ray structure

Amidrazones are known to undergo various addition and addition-cyclization reactions [1–4]. However, their N^1-carbodithioates remained relatively little investigated. *Sandoz* patents described synthesis from imidates and reported high antimicrobial activity of these type of amidrazone derivatives containing five-membered heterocyclic systems [5,6], but no structure details have been discussed so far.

In the course of our studies of potential tuberculostatic agents, we have already prepared derivatives of pyrazinecarboxamidrazone [7]. Extending our investigations we report in this paper the synthesis of pyridinecarboxamidrazone dithioic acid methyl esters and attempts to determine their tautomerism and configuration.

RESULTS AND DISCUSSION

As outlined in Scheme 1, pyridine-carbonitriles **1a–c** were converted into imidates **2a–c** by acid-promoted reaction, followed by alkalization. Crude imidates **2a–c** were then treated with methyl dithiocarbazate in similar manner as described previously [5,6] to afford S-esters **3a–c**. Attempts to obtain compounds **3a–c** directly from

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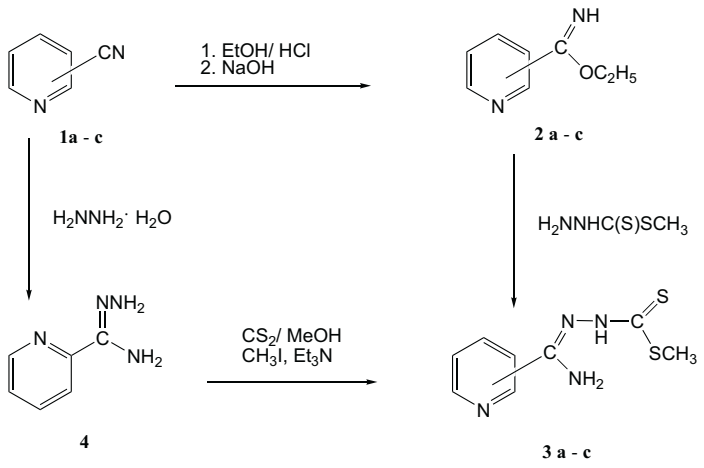
dithiocarbazate addition to nitriles were unsuccessful. Alternative route *via* amidrazone **4** could be used in case of compound **3a**. The synthesis preceeded easily on stirring equimolar amounts of amidrazone **4**, carbon disulphide and methyl iodide in the presence of triethylamine in alcohol.

The newly synthesized S-esters **3a–c** were characterized by IR, MS and NMR spectra. The IR spectra show the absorption bands of δ N–H (partially overlapped by ν C=N) at 1600–1680 cm^{-1}. The mass spectra show parent ions peaks at *m/e* 226 and the main fragmentation includes the loss of SCH_3 with ion peak at *m/e* 179; the peak at *m/e* 105 corresponds to $[C_5H_4NCNH]^+$, which after loss of hydrogen cyanide gives peak at *m/e* 78.

In NMR spectra of **3a** each proton and each carbon gave two signals (see Experimental Section). The isomers ratio was determined from their relative integral values in the ^1H spectrum (in acetone-d_6, ambient temperature) as 5:4. ^1H-NMR spectra recorded in $CDCl_3$ and DMSO-d_6 contained two sets of signals as well (similar ratio). Additional proof for dynamic isomerization in solution is the ROESY (*R*otating Frame *O*verhauser *E*nhancement *S*pectroscop*Y*) spectrum, which exhibits chemical exchange cross peaks of protons of both isomers.

To find out the origin of the observed isomerization of compound **3a**, three types of interconversion should be considered 1) tautomerism, 2) configuration changes around C=N bond and 3) conformations. Tautomerism of related compounds, such as amidines [8,9], amidrazones [10–12], dithiocarbazoic acids [13–15] has been described. There are several possible tautomeric forms of this system – nonpolar (A – D) and dipolar (E, F) (Fig. 1). For the discrimination between the tautomers the ^1H-^{15}N 2D-NMR spectra (HSQC – *H*eteronuclear *S*ingle *Q*uantum *C*oherence and HMBC – *H*eteronuclear *M*ultiple *B*ond *C*oherence) are of great value. Analysis of HSQC spec-

Scheme 1



trum of compound **3a** reveals that the signal of N(3) atom in the amidrazone moiety is coupled with two protons (of both isomers) with $^{1}J_{NH}$ = 95 Hz and 90–92 Hz, respectively, nitrogen atom (of both isomers) from hydrazone system is coupled with one proton with $^{1}J_{NH}$ *ca*. 98 Hz. Whereas pyridine nitrogen atom shows no $^{1}J_{NH}$ couplings and its chemical shift value (–80 ppm) is typical for nonprotonated form [16]. Therefore, only tautomers A and E may be consistent with these data.

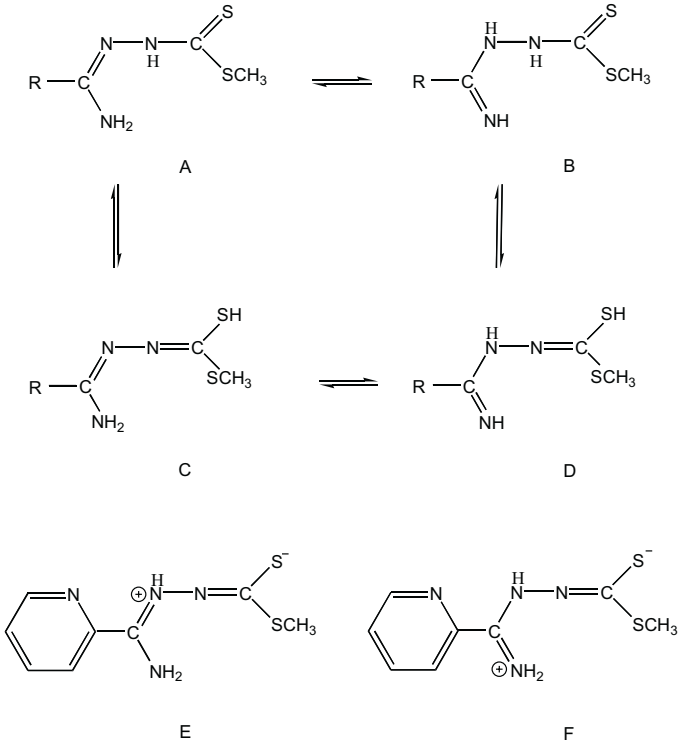
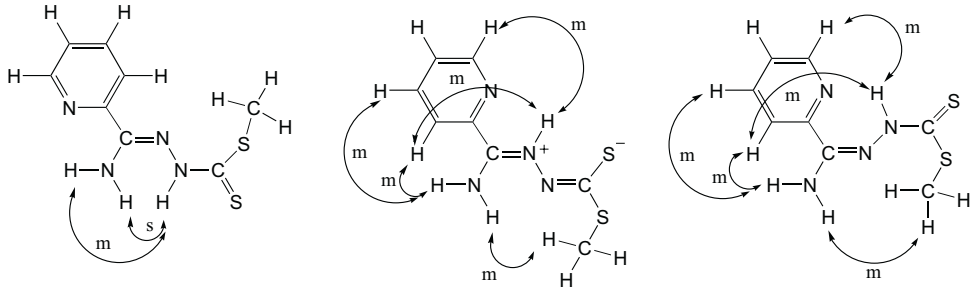


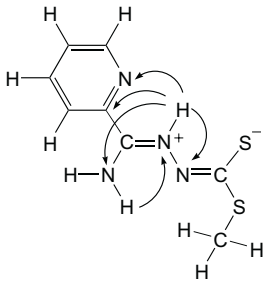
Figure 1. Possible tautomeric forms of compound **3a**.

Configuration and conformation around C=N bond is clearly assigned by the NOE in spectrum in case of the predominant (at ambient temperature) isomer as nonpolar *Z* form (Fig. 2). Detected NOEs for the second isomer do not allow unambiguous determination of geometry – *Z* (dipolar) or *E* (nonpolar). Although structure *Z* (dipolar) seems to be more plausible, particularly corroborated by the pattern of long–range proton-carbon correlations in ^{1}H-^{13}C HMBC spectrum, which shows correlation between hydrazone NH proton and C(2) carbon of pyridine ring; as well as in ^{1}H-^{15}N HMBC spectrum – correlation of hydrazone NH proton with amide (NH_2) and pyridine nitrogens (Fig. 3). Similar mixture of isomers in solutions is observed in case of 3-pyridine derivative **3b**. Its ^{1}H-NMR spectrum (DMSO-d_6, ambient temperature) shows two sets of signals (ratio 10:3).



Z (nonpolar) *Z* (dipolar) *E* (nonpolar)

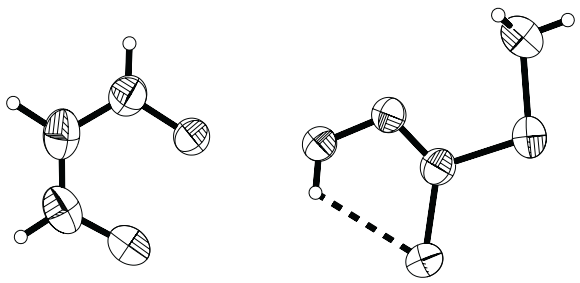
Figure 2. NOE-s determined in the ^{1}H-NMR spectrum of S-ester **3a**.



Z (dipolar)

Figure 3. Multibond ^{1}H-^{13}C and ^{1}H-^{15}N correlations in HMBC spectra of compound **3a**.

In order to establish which of these forms is present in the crystalline phase, indicating usually dominant form in a solution, X-ray analysis of compound **3a** was undertaken. Results of this analysis revealed that, surprisingly, in the crystal state the compound exists as the dipolar form *Z* with strong *intra*molecular hydrogen bond between hydrazone group as a donor and pyridine nitrogen as an acceptor (Fig. 4).

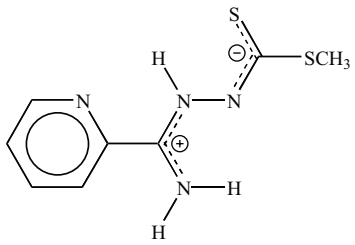


As all hydrogen atoms in crystal structure of **3a** were univocally located on respective Fourier map and refined, so there is no doubt, that only two dipolar tautomeric forms (*E* and *F* in Scheme 2) with two H atoms at N(5) and one at N(3) have to be considered. The same dipolar form with a very similar geometry has been observed in the crystals of (1-methyl-2-pyrrolidinylidene)-hydrazinecarbodithioic acid methyl ester [17]. The main difference concerns N(3)–C(4)–N(5) fragment, which shows a positive charge localized at N(5) (*F* form in Fig. 1), while in this study the charge is spread over the whole amidine fragment as seen from respective C(4)–N bond lengths, being 1.306(2) and 1.317(2) Å (Table 3), respectively. It indicates dipolar form intermediate between *E* and *F* (Fig. 1) in the crystal state. The length of a single C(sp^2)–NH_2 bond (in amines) is about 1.33 Å [18] and of a double C(sp^2)=N bond it is 1.280 Å in a N–N=C$(SMe)_2$ group [19]. Similar π electrons delocalization has been observed for anionic fragment S(1)–C(1)–N(2) (Scheme 2) as a single C–SMe bond in thioethers has a length of about 1.75 Å and a double C=S bond (in organic sulphides) of about 1.67 Å [18], while in this study the length of C–S^- bond is 1.710(2) Å.

Present X-ray study of **3a** has also confirmed *Z* configuration around C(4)–N(3) bond, which allows three *intra*molecular hydrogen bonds, stabilizing the conformation observed and preserving planarity of the molecule, as seen clearly from respective torsion angles (Table 3).

Microbiological activity: The new compounds **3a–c** were screened *in vitro* for their tuberculostatic activity using the BACTEC 460 radiometric system [20]. 2-Pyridine derivative **3a** exhibited the highest bacteriostatic activity against *Mycobacterium tuberculosis* (H_{37}Rv strain) with MIC (minimum inhibitory concentration) 3.13 μg/mL (rifampicin – used as the standard – MIC = 0.125 μg/mL), but proved to be not active against *Myc. avium*. Derivatives **3b** and **3c** showed no significant tuberculostatic activity at concentration 12.5 μg/mL.

Scheme 2



EXPERIMENTAL

Melting points are uncorrected. The mass spectra were recorded on a LKB 9000 spectrometer, IR spectra – on a Specord 75 IR spectrophotometer. Proton-NMR spectra were obtained using a Varian Gemini 200 or Varian Unity Plus 500 spectrometers; carbon- and 2D-NMR spectra were recorded on Varian Unity Plus 500; proton and carbon chemical shifts are reported in ppm referenced to TMS, nitrogen chemical shifts referenced to nitromethane. Results of elemental analyses were within ± 0.3% of the theoretical values. Imidates **2a–c** [21], methyl dithiocarbazate [22] and pyridine-2-carboxamidrazone (**4)** [23] were prepared by the literature methods.

General procedure for the reaction of methyl dithiocarbazate with imidates 2a–c: To a stirred solution of appropriated imidate **2** (15 g, 0.10 mol) in MeOH (10 mL) solution of methyl dithiocarbazate (12 g, 0.10 mol) in MeOH (100 mL) was added. The mixture was stirred for 1 h, then cooled. The precipitated yellow solid was separated by filtration and purified by recrystallization from MeOH or EtOH.

N′-(Amino-2-pyridyl-methylene)-hydrazinecarbodithioic acid methyl ester **(3a)** 14.4 g (64%), $C_8H_{10}N_4S_2$, 226.32, m.p. 146–148°C (dec.) (EtOH); UV (CCl_4) λ_{max} 350 nm (ε 26800); IR (KBr) ν 3350, 3120–2700, 1664, 1623, 1583, 1516, 1443, 1303, 1072, 960. ^{1}H-NMR (acetone-d_6, 500 MHz) δ 2.58 (s, 3H, CH_3), 7.00 (br.s, 2H, NH_2), 7.53 (ddd, H-5pyr., J = 7.8, 4.9, 1.1 Hz), 7.95 (td, H-4pyr., J = 7.8,1.5 Hz), 8.27 (m, H-3pyr.), 8.63 (br.d, H-6pyr., J = 4.4 Hz), 10.90 (br.s, 1H, NH); 2.46 (s, 1H, CH_3), 7.77 (dd, H-5pyr, J = 7.8, 5.3Hz), 8.02 (br.s, 1H, NH), 8.18 (td, H-4pyr., J = 7.8, 1.5 Hz), 8.27 (m, H-3pyr.), 8.56 (br.s, 1H, NH), 8.85 (br.d, H-6pyr., J = 4.4 Hz), 12.88 (br.s, 1H, NH); ratio of isomers 5:4. ^{13}C-NMR (acetone-d_6, 125 MHz) 17.31 (S<u>C</u>H$_3$), 121.38 (C-3pyr.), 125.83 (C-5pyr.), 137.66 (C-4pyr.), 144.98 (N-C=N), 149.02 (C-6pyr.), 150.35 (C-2pyr.), 197.59 (S-C=S); 15.55 (S<u>C</u>H$_3$), 122.52 (C-3pyr.), 128.37 (C-5pyr.), 139.12 (C-4pyr.), 144.14 (C-2pyr.), 149.24 (N-C=N), 150.89 (C-6pyr.), 186.39 (S-C=S).

^{15}N chemical shifts (from HSQC and HMBC spectra, acetone-d_6, temperature –98°C): –313 (NH_2), –198 (NH), –150 (=N-), –80 (Npyr.); –293 (NH_2), –209 (NH), –125 (=N-), –80 (Npyr.). MS (EI) *m/e* (%) 226 (9, M^+), 209 (12), 179 (88), 178 (53), 121 (15), 105 (100), 79 (52), 78 (72), 52 (28), 51 (33), 48 (35), 47 (45), 45 (22).

N′-(Amino-3-pyridyl-methylene)-hydrazinecarbodithioic acid methyl ester (**3b**) 18.0 g (80%), $C_8H_{10}N_4S_2$, 226.32, m.p. 161–162°C (MeOH); IR (KBr) ν 3376, 3024, 1640, 1563, 1403, 1344, 992. ^{1}H-NMR (DMSO-d_6, 200 MHz) δ 2.47 (s, 3H, CH_3), 7.23 (br.s, 2H, NH_2), 7.47 (ddd, H-5pyr, J = 8.0, 4.8, 0.7 Hz), 8.15 (dt, H-4pyr., J = 8.0, 2.2 Hz) 8.64 (dd, H-6pyr., J = 4.8, 1.6 Hz), 9.00 (br.d, H-2pyr., J = 2.2 Hz), 12.02 (br.s, 1H, NH); 2.44 (s, 3H, CH_3), 7.66 (dd, H-5pyr., J = 7.9, 4.8 Hz), 8.20 (m, H-4pyr.), 8.54 (br.s, 1H, NH), 8.87 (dd, H-6pyr, J = 4.8, 1.6 Hz), 8.97 (br.d, H-2pyr, J = 2.3 Hz), 9.30 (br.s, 1H, NH), 11.46 (br.s, 1H, NH); ratio of isomers 10:3. MS (EI) *m/e* (%) 226 (5, M^+), 210 (8), 209 (100), 180 (6), 179 (63), 178 (76), 122 (17), 121 (12), 120 (9), 119 (12), 105 (44), 104 (15), 94 (12), 78 (45), 77 (7), 48 (45), 47 (73), 46 (20).

N′-(Amino-4-pyridyl-methylene)-hydrazinecarbodithioic acid methyl ester (**3c**) 13.5 g (60%), $C_8H_{10}N_4S_2$, 226.32, m.p. 163–165°C (dec.) (MeOH), IR (KBr) ν 3312, 3136, 2912, 1680, 1508, 1416, 1328, 1080, 960. ^{1}H-NMR (DMSO-d_6, 200 MHz) δ 2.48 (s, 3H, CH_3), 7.25 (br.s, 2H, NH_2), 7.77 (dd, 2Hpyr., J = 4.7, 1.6 Hz), 8.66 (dd, 2Hpyr., J = 4.7, 1.6 Hz), 12.05 (br.s, 1H, NH); signals of second isomer are partially obscured, ratio estimated > 8. ^{13}C-NMR (DMSO-d_6, 125 MHz) 17.41, 121.23, 141.58, 145.08, 150.67, 196.39. MS (EI) *m/e* (%) 226 (4, M^+), 210 (10), 209 (100), 180 (5), 179 (34), 178 (49), 136 (5), 122 (17), 121 (10), 120 (8), 119 (11), 105 (30), 105 (30), 104 (16), 78 (38), 77 (9), 50 (11), 48 (43), 47 (61), 46 (27), 45 (32), 44 (26), 43 (13).

Preparation of N'-(amino-2-pyridyl-methylene)-hydrazinecarbodithioic acid methyl ester (3a) from pyridine-2-carboxamidrazone (4): To a stirred solution of pyridine-2-carboxamidrazone (**4**) (1.36 g, 10 mmol) in MeOH (10 mL) triethylamine (1.39 mL, 10 mmol) and, on cooling (ice-water bath) carbon disulphide (0.60 mL, 10 mmol) were added, then methyl iodide (0.62 mL, 10 mmol) was added dropwise. The mixture was stirred for 30 min. at room temperature. After cooling precipitate formed was separated by filtration, washed with cooled MeOH, recrystallized from EtOH to give 0.95 g (42%) of **3a**.

X-ray crystallography (3a): Crystals suitable for X-ray diffraction studies were obtained by slow evaporation of a chloroform solution. X-ray data were collected on KM4 diffractometer at room temperature with copper radiation. The data were not corrected for absorption. The structure was solved by direct method [24] and refined by full-matrix least-squares [25]. Hydrogen atoms were located from difference

Fourier maps due to possible tautomerism and presence of the pyridine ring. They were refined freely with isotropic temperature factors.

Other details of data collection and refinement are summarized in Table 1, while Table 2 lists atomic coordinates.

Table 1. Crystal data and refinement details for crystal structure **3a**.

Chemical formula	$C_8H_{10}N_4S_2$
Molecular weight	226.34
Crystal size [mm]	0.14 × 0.24 × 0.28
Space group	P-1 (triclinic)
a, *b*, *c* [Å]	7.976(2), 8.067(2), 9.011(2)
α, β, γ [°]	80.21(3), 74.64(3), 73.81(3)
V [Å^3]	534.0(2)
D_{cal} [g /cm^{-3}]	1.408 ($Z = 2$)
F(000)	236
μ [mm^{-1}]	4.3
Scan width [°]	1.0 + 0.38 tgθ
Radiation [λ, Å]	Cu (1.54178)
θ_{max} [°]	80.3
Range of hkl	–9/10, –1/9, –11/11
Intensity decay	1.042
No. of measured reflections	2486
No. of independent reflections	2229
No. of observed (2σ) reflections	1933
No. of reflections used in the refinement	2229
No. of refined parameters	167
Weighting scheme, $w =$ where $P = (F_o^2 + 2F_c^2)/3$	$1/\sigma^2(F_o^2) + (0.1016P)^2 + 0.0642P$
R, R_w, S	0.0536, 0.1350, 1.04
$(\Delta/\rho)_{max,\ min}$ [e/Å^{-3}]	0.32, –0.78

Table 2. Final atomic coordinates (×10^4 and ×10^3 for H atom) and equivalent isotropic (isotropic for H) displacement parameters (Å^2 ×10^3) in the crystal structure of **3a**. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor attached to N atoms*.

Atom	x	y	z	U_{eq}
S(1)	–0.56614(7)	–0.31591(6)	0.69137(6)	0.0571(2)
S(2)	–0.21545(6)	–0.33272(7)	0.47552(6)	0.0563(2)
N(2)	–0.3766(2)	–0.0724(2)	0.64012(18)	0.0477(4)
N(3)	–0.5157(2)	0.0006(2)	0.75620(19)	0.0483(5)
N(5)	–0.4207(2)	0.2504(2)	0.7106(2)	0.0542(6)
N(42)	–0.8071(3)	0.1293(3)	0.9654(2)	0.0611(6)
C(1)	–0.3932(2)	–0.2187(2)	0.6106(2)	0.0465(5)
C(2)	–0.0655(4)	–0.1919(4)	0.4150(4)	0.0704(9)
C(4)	–0.5337(2)	0.1572(2)	0.7888(2)	0.0454(5)
C(41)	–0.6817(2)	0.2202(2)	0.9202(2)	0.0466(5)
C(43)	–0.9439(4)	0.1814(4)	1.0839(3)	0.0695(8)
C(44)	–0.9596(3)	0.3200(3)	–1.1611(2)	0.0658(7)

Table 2 (continuation)

C(45)	–0.8297(4)	0.4095(4)	1.1151(3)	0.0650(8)
C(46)	–0.6872(3)	0.3607(3)	0.9915(2)	0.0543(6)
H(N3)	–0.593(4)	–0.062(4)	0.805(3)	0.079(8)
H′(N5)	–0.364(4)	0.212(4)	0.634(3)	0.071(8)
H(C2)	–0.030(4)	–0.164(4)	0.498(4)	0.087(10)
H′(C2)	0.026(6)	–0.247(6)	0.349(5)	0.122(14)
H″(C2)	–0.110(5)	–0.089(6)	0.382(4)	0.113(14)
H(C43)	–1.037(4)	0.116(4)	1.114(3)	0.082(8)
H(C44)	–1.055(4)	0.349(4)	1.240(4)	0.079(8)
H(C45)	–0.832(4)	0.512(4)	1.167(4)	0.088(9)
H(C46)	–0.595(4)	0.418(4)	0.958(3)	0.070(7)
H(N5)	–0.455(3)	0.367(4)	0.716(3)	0.064(7)

Table 3. Selected geometric parameters for crystal structure of **3a**. Distances are in Å and angles in degrees.

	3a	Similar compound [17]
C(1)–S	1.7101(18)	1.709(4)
C(1)–SCH_3	1.7541(18)	1.750(4)
C(1)–N(2)	1.301(2)	1.229(5)
N(2)–N(3)	1.379(2)	1.392(5)
N(3)–C(4)	1.306(2)	1.342(6)
C(4)–N(5)	1.317(2)	1.286(5)
C(4)–Pyr	1.478(2)	
S(1)–C(1)–N(2)–N(3)	3.2(2)	0.1(5)
C(1)–N(2)–N(3)–C(4)	–171.61(17)	178.1(4)
N(2)–N(3)–C(4)–N(5)	0.8(3)	
N(3)–C(4)–C(41)–N(42)	–16.3(2)	179.3(4)
H(N3).....N(42)	2.32(4)	
H(N3).....S(1)	2.38(4)	
H(N5).....N(2)	2.32(4)	

Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC, 12 Union Road, Cambridge CB2, 1E2, UK). The deposited structure number for **3a** is 161852.

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REFERENCES

1. Zelenin K.N., Solod O.V. and Khrustalev V.A., *Khim. Geterotsikl. Soedin*., (7), 867, (1989) and references cited therein.
2. Kubota S., Koida Y., Kosaka T. and Kirino O., *Chem. Pharm. Bull*., **18**, 1696 (1970).
3. Doyle K.M. and Kurzer F., *Tetrahedron*, **32**, 2343 (1976).

4. Strzemecka L., *Polish J. Chem*., **64**, 157 (1990).
5. Nesvadba H. and Reinshagen H. (Sandoz-Patent-G.m.b.H.), German Pat. 26 28 974 (1977); *C.A*. **87**, P23274 (1977).
6. Nesvadba H. and Reinshagen H., (Sandoz A.-G.), Swiss Pat. 597, 208 (1978); *C.A*. **89**, P43395n (1978).
7. Foks H. and Orlewska C., *Acta Polon. Pharm. – Drug Research*, **49**, 47 (1992).
8. Oszczapowicz J., in *The Chemistry of Amidines and Imidates*, Ed. S. Patai and Z. Rappoport, Wiley, NY, 1991, p. 662.
9. Clement B. and Kämpchen T., *Chem. Ber.*, **119**, 1101 (1986).
10. Smith R.F., Johnson D.S., Hyde C.L., Rosenthal T.C. and Bates A.C., *J. Org. Chem*., **36**, 1155 (1971).
11. Smith R.F., Johnson D.S., Abgott R.A. and Madden M.J., *ibid*., **38**, 1344 (1973).
12. Oszczapowicz J., in *The Chemistry of Amidines and Imidates*, Eds. S. Patai and Z. Rappoport, Wiley, NY, 1991, pp. 671–672.
13. Anthoni U., Dahl B.M., Larsen Ch. and Nielsen P.H., *Acta Chem. Scand*., **23**, 1061 (1969).
14. Anthoni U., Dahl B.M., Larsen Ch. and Nielsen P.H., *ibid*., **24**, 959 (1970).
15. Anthoni U., *ibid*., **20**, 2742 (1966).
16. Berger S., Braun S. and Kalinowski H.-O., *NMR-Spectroscopie von Nichtmetallen*, vol 2, ^{15}*N-NMR-Spectroscopie*, Georg Thieme Verlag, Stuttgard, 1992, p. 43.
17. Radics U., Liebscher J., Ziemer B. and Rybakov V., *Chem. Ber.*, **125**, 1389 (1992).
18. Allen F.H., Davies J.E., Galloy J.J., Johnson O., Kennard O., Macrae C.F., Mitchel E.M., Smith J.M. and Watson D.G. (eds.), acc.: W.A. Warren, C*ambridge Crystallographic Database System, ver. 5.19. J. Chem. Inf. Comput. Sci.,* **31**, 187 (1991).
19. Główka M.L., Martynowski D., Olczak A., Kozłowska K., Ołubek Z., Orlewska C. and Foks H. *Polish J. Chem.,* **73**, 845 (1999).
20. The microbiological tests were performed at the NIAID [*National Institute of Allergy and Infectious Diseases; Southern Research Institute* (TAACF)], USA.
21. Libman D.D. and Slack R., *J. Chem. Soc*., 2253 (1956).
22. Audrieth L.F., Scott E.S. and Kippur P.S., *J. Org. Chem*., **19**, 740 (1954).
23. Case F.H., *J. Org. Chem*., **30**, 931 (1965).
24. Sheldrick G.M., *SHELXTL/PC, User Manual*. Simens Analytical Instrument. An Integrated System for Solving, Refining and Displaying Crystal Structures from Diffraction Data, Siemens Analytical X-Ray Instruments, Inc. Medison, Wisconsin, USA (1990).
25. Sheldrick G.M., *SHELXL97. Program for Refinement of Crystal Structures*. University of Göttingen, Germany (1997).