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Full Paper

Synthesis and Crystal Structures of 5-Acetyl-4-(4-methoxyphenyl)-6-methyl-2-(methylsulfanyl)pyridine-3-carbonitrile and 5-Acetyl-2-[(cyanomethyl)sulfanyl]-4-(4-methoxyphenyl)-6-methylpyridine-3-carbonitrile

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Abstract

The first one (**I**) of the two related compounds, $C_{17}H_{16}N_2O_2S$, crystallizes in the monoclinic space group $P2_1/c$ with Z = 4, while the second one (**II**), $C_{18}H_{15}N_3O_2S$, crystallizes in the monoclinic space group *P*-1 with Z = 4. There are two independent molecules in the asymmetric unit of compound (**II**). As expected, the pyridine rings are almost planar (r.m.s. deviation = 0.002 Å). In the molecules **A** and **B** of the compound **II**, the substituents (except methyl and cyano groups) attached to the pyridine ring, are inclined to the different directions. In the crystal of compound **I**, molecules are arranged into the parallel layers to the (001) plane which there exist weak π-π interactions in the *c*-direction. In the crystal of compound **II**, molecules are linked by C—H···O hydrogen bonds, forming infinite C(9) chains along the *b*-axis. Furthermore, C—H···π interactions contribute to the stabilization of molecular packing.

Introduction

Pyridine ring system is very widely distributed in nature, especially in plant kingdom. It is used as a precursor to agrochemicals and pharmaceuticals and is also an important solvent and reagent [1,2]. It plays a key role catalyzing both biological and chemical systems [3]. In the pharmaceutical industry, pyridine forms the nucleus of over 7000 existing drugs [1]. Also, pyridine framework is a key structural fragment of many heterocyclic compounds showing a broad spectrum of pharmacological properties, such as: anti-microbial [4], anti-convulsant [5], anti-viral [6], anti-HlV [7], anti-fungal and anti-mycobacterial activities [8]. In this context, we report the synthesis and crystal structures of the title compounds (**I** and **II**).

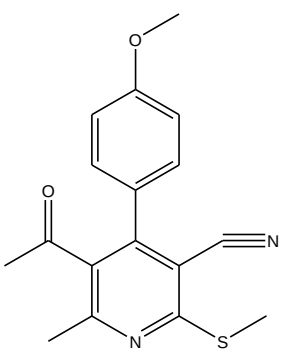
2. Results and discussion

a) Structural commentary

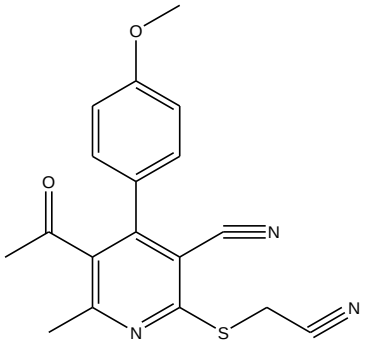
The compounds **I** and **II** are shown in Figs. 1 and 3, respectively. Compound **I** crystallizes in the monoclinic space group $P2_1/c$ with Z = 4, while compound **II** crystallizes in the monoclinic space group *P*-1 with Z = 4. There are two independent molecules in the asymmetric unit of compound **II**. As expected, the pyridine rings are almost planar (r.m.s. deviation = 0.002 Å in (**I**), and for molecules **A** and **B** in (**II**)). The dihedral angle between the planes of the pyridine ring and the benzene ring is 51.47 (8)° in (**I**), and 45.55 (11)° for molecule **A** in (**II**) and 53.59 (12)° for molecule **B** in (**II**). In the molecules **A** and **B** of the compound **II**, the substituents (except methyl and cyano groups) attached to the pyridine ring, are inclined to the different directions (Fig 3). All bond lengths and bond angles in (**I**) and (**II**) are normal and comparable to those observed in similar structures, *v.z.*: 2-benzylamino-4-*p*-tolyl-6,7-dihydro-5H-cyclopenta[*b*]pyridine-3-carbonitrile [9], 2-(2-bromophenyl)-4-(1*H*-indol-3-yl)-6-(2-thienyl)pyridine-3-carbonitrile [10], 3-methyl-1-phenyl-6-propylamino-1*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile [11] and 4,6-diamino-2-(methylsulfanyl)pyridine-3- carbonitrile [12].

b) Supramolecular features

In the crystal (**I**), there is no clasical hydrogen bonds. Molecules are arranged into the parallel layers to the (001) plane which there exist weak π-π interactions in the c-direction (Fig. 2). In the molecule **B** of (**II**), an intramolecular C—H···N and C–H···O interactions close the S(5) and S(6) rings, respectively. Any intramolecular interaction are not observed in the molecule **A**. In the crystal (**II**), molecules are linked by C—H···O hydrogen bonds, forming infinite C(9) chains along the b axis (Fig. 4 and Table 1). Furthermore, C—H···π interactions contribute to the stabilization of molecular packing.



I



II

Table 1 Hydrogen-bond geometry (Å, °) for (II)

Cg4 is a centroid of the C30–C35 benzene ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2B···O1^{i}	0.97	2.33	3.106 (3)	136
C20—H20B···N5	0.97	2.34	2.844 (3)	112
C26—H26C···O3	0.96	2.51	3.066 (3)	117
C29—H29B···Cg4	0.96	2.97	3.711 (3)	135
C36—H36C···Cg4^{ii}	0.96	2.81	3.567 (3)	136

Symmetry codes: (i) *x*, *y*−1, *z*; (ii) −*x*, −*y*+1, −*z*+1.

2. Experimental

a) Synthesis and crystallization

5-Acetyl-4-(4-methoxyphenyl)-6-methyl-2-(methylsulfanyl)pyridine-3-carbonitrile (I): A mixture of equimolar amount of 5-acetyl-3-cyano-4-(4-methoxyphenyl)-6-methylpyridine-2(1*H*)-thione, methyl iodide and sodium acetate trihydrate (0.01 mol) in ethanol (30 mL) was heated under reflux for 2 h. The precipitate that formed after cooling and dilution with water was collected and recrystallized from ethanol as colorless needles of compound **I**. Yield: 93 %, m.p.: 152 ^{o}C; Lit., 153-154 ^{o}C [13]. IR: 2220(CN), 1690 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.0-7.5 (dd, 4H, Ar-H), 3.8 (s, 3H, OCH_3), 2.8 (s, 3H, SCH_3), 2.6 (s, 3H, CH_3), 1.8 (s, 3H, CH_3).

Acetyl-2-[(cyanomethyl)sulfanyl]-4-(4-methoxyphenyl)-6-methylpyridine-3-carbonitrile (II): A mixture of 5-acetyl-3-cyano-4-(4-methoxyphenyl)-6-methyl-pyridine-2(1*H*)-thione (2.98 g; 10 mmol), chloroacetonitrile (0.76 mL, 10 mmol) and sodium acetate trihydrate (1.51 g; 11 mmol) in ethanol (30 mL) was heated under reflux for 1 h. The precipitate that formed after cooling was collected and recrystallized from ethanol to give colorless needles of **II**. Yield: 90 %, m.p.: 163-164 ^{o}C; Lit., 163-164 ^{o}C [14]. IR: 2220 (CN), 2200 (CN), 1690 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ

7.0-7.5 (dd, 4H, Ar-H), 4.2 (s, 2H, SCH_2), 3.8 (s, 3H, OCH_3), 2.6 (s, 3H, CH_3), 1.9 (s, 3H, CH_3).

b) Refinement

All C-bound hydrogen atoms in compound **I** were included in calculated positions with C—H = 0.93 Å (aromatic) or 0.96 Å (methyl) and allowed to ride, with U_{iso}(H) = 1.2 or 1.5U_{eq}(C). In compound **II**, H atoms bound to carbon were positioned geometrically and allowed to ride on their parent atoms with U_{iso} = 1.2 times U_{eq}(C) (C—H = 0.93Å for aromatic and 0.97Å for methylene) and with U_{iso} = 1.5 times U_{eq}(C) (C—H = 0.96Å for methyl). Crystal data, data collection and structure refinement details are summarized in Table 2.

Table 2: Experimental details

	Compound **I**	Compound **II**
Chemical formula	$C_{17}H_{16}N_2O_2S$	$C_{18}H_{15}N_3O_2S$
M_r	312.38	337.39
Crystal system, space group	Monoclinic, $P2_1/c$	Triclinic, P
Temperature (K)	296	296
a, b, c (Å)	11.7197 (7), 15.5468 (11), 8.7451 (6)	9.4807 (6), 9.9039 (6), 19.5898 (12)
α, β, γ (°)	90, 94.538 (5), 90	76.122 (5), 79.746 (5), 79.478 (5)
V (Å^3)	1588.40 (18)	1738.24 (19)
Z	4	4
Radiation type	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.21	0.20
Crystal size (mm)	0.78 × 0.46 × 0.17	0.59 × 0.28 × 0.04
Diffractometer	STOE *IPDS* 2 diffractometer	STOE *IPDS* 2 diffractometer
Absorption correction	Integration X-RED32 (Stoe & Cie, 2002)	Integration X-RED32 (Stoe & Cie, 2002)
T_{min}, T_{max}	0.890, 0.962	0.907, 0.984
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	10232, 3463, 2172	24582, 7851, 4134
R_{int}	0.035	0.081
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.641	0.649
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.039, 0.098, 0.89	0.050, 0.109, 0.92
No. of reflections	3463	7851
No. of parameters	203	438
H-atom treatment	H-atom parameters constrained	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.17, −0.18	0.18, −0.21

c) Computer programs:

SHELXT [16], SHELXL2016/6 [16], ORTEP-3 for Windows [17],, WinGX [17] and PLATON [17].

Conclusion

The compounds **I** and **II** crystallize in the monoclinic space group $P2_1/c$, and in the monoclinic space group *P*-1 with two independent molecules in the asymmetric unit, respectively. In the crystal of compound **I**, molecules are arranged into the parallel layers to the (001) plane which there exist weak π-π interactions in the *c*-direction. In the crystal of compound **II**, molecules are linked by C—H···O hydrogen bonds, forming infinite C(9) chains along the *b*-axis.

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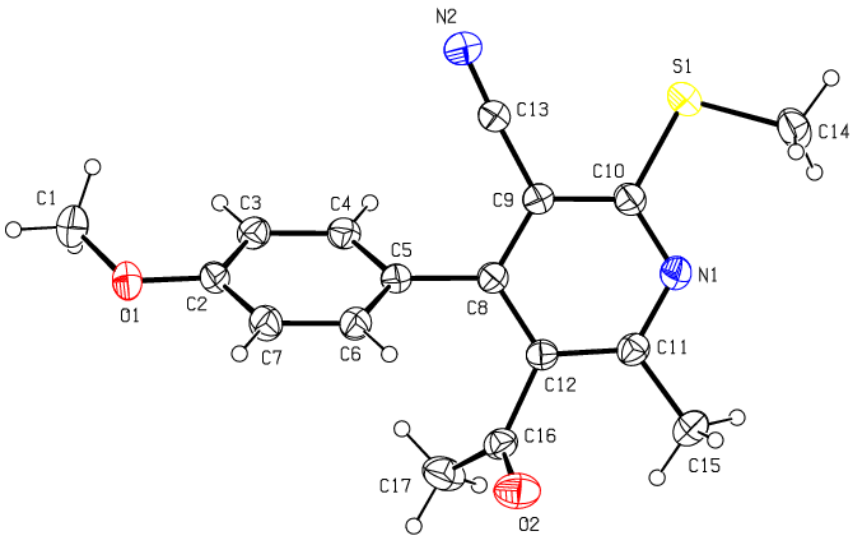

Figure 1 View of the compound **I** with the atom numbering scheme. Displacement ellipsoids for non-H atoms are drawn at the 30% probability level.

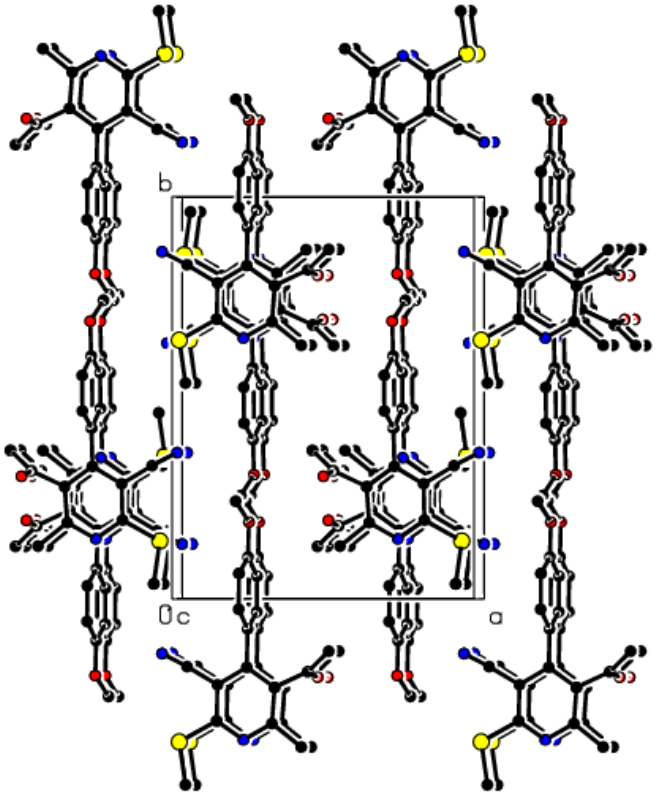

Figure 2 A view along the *c* axis of the crystal packing of the compound I.

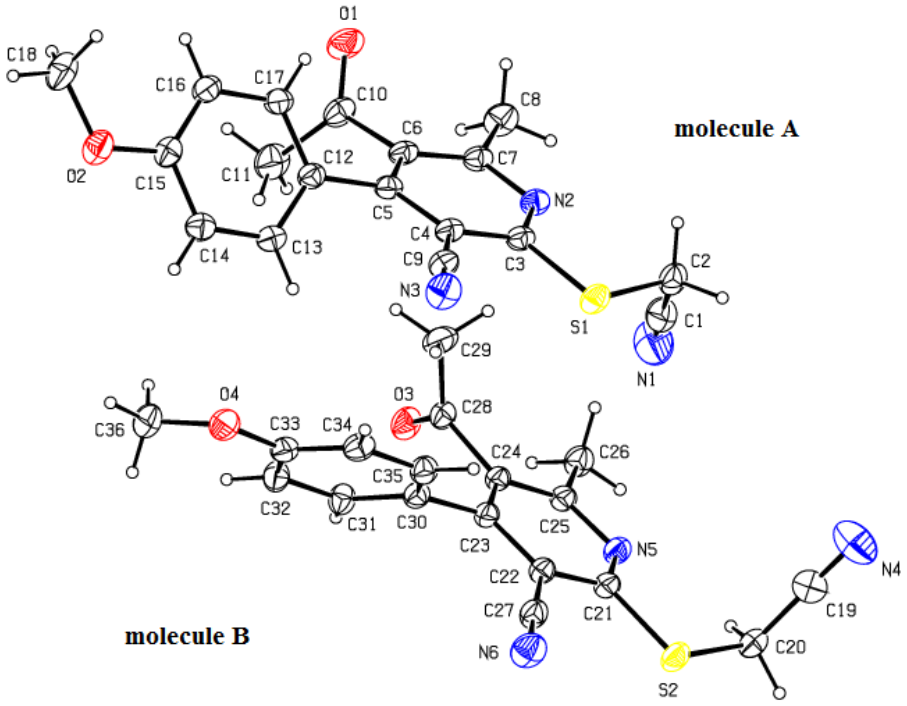

Figure 3 View of the compound **II** with the atom numbering scheme. Displacement ellipsoids for non-H atoms are drawn at the 20% probability level.

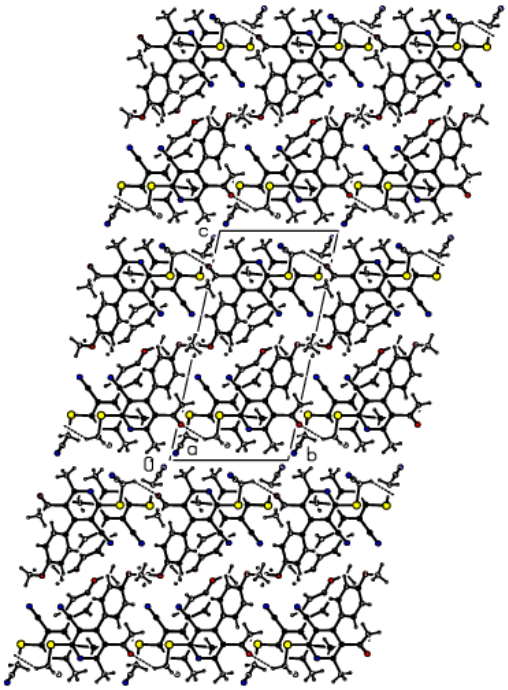

Figure 4 A view along the *a* axis of the crystal packing of the compound **II**.