Xia Mi, Zheng Zhong, Jing Yang and Jingyu Zhang*

Crystal structure of 2-(3-methoxyphenyl)-3-((phenylsulfonyl)methyl)imidazo[1,2-*a*]pyridine, $C_{21}H_{18}N_2O_3S$

<https://doi.org/10.1515/ncrs-2019-0228>

Received March 27, 2019; accepted May 6, 2019; available online May 24, 2019

Abstract

$C_{21}H_{18}N_2O_3S$, monoclinic, $P2_1/n$ (no. 14), $a = 12.1263(2)$ Å, $b = 11.6913(3)$ Å, $c = 12.7643(3)$ Å, $\beta = 92.340(2)^\circ$, $V = 1808.11(7)$ Å³, $Z = 4$, $R_{gt}(F) = 0.0433$, $wR_{ref}(F^2) = 0.1310$, $T = 293(2)$ K.

CCDC no.: 1903606

The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

*Corresponding author: Jingyu Zhang, Henan University of Chinese Medicine, Zhengzhou 450046, P.R. China, e-mail: jyzhang2004@126.com

Xia Mi, Zheng Zhong and Jing Yang: Henan University of Chinese Medicine, Zhengzhou 450046, P.R. China

Table 1: Data collection and handling.

Crystal:	Yellow prism
Size:	$0.17 \times 0.15 \times 0.10$ mm
Wavelength:	Cu $K\alpha$ radiation (1.54184 Å)
μ :	1.80 mm^{-1}
Diffractometer, scan mode:	Xcalibur, ω
$\theta_{\max}$, completeness:	67.1° , >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	7020, 3225, 0.022
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2681
$N(\text{param})_{\text{refined}}$:	245
Programs:	CrysAlis ^{PRO} [1], Olex2 [2], SHELX [3, 4]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.39922(19)	0.3377(2)	0.57198(18)	0.0500(5)
H1	0.3254	0.3167	0.5748	0.060*
C2	0.4614(2)	0.2997(2)	0.49385(19)	0.0591(6)
H2	0.4301	0.2514	0.4430	0.071*
C3	0.5731(2)	0.3321(2)	0.48789(19)	0.0608(6)
H3	0.6143	0.3057	0.4330	0.073*
C4	0.6202(2)	0.4012(2)	0.56117(19)	0.0575(6)
H4	0.6939	0.4222	0.5572	0.069*
C5	0.55702(17)	0.4416(2)	0.64449(17)	0.0483(5)
C6	0.4041(16)	0.4604(18)	0.73441(16)	0.0406(4)
C7	0.4905(16)	0.5242(18)	0.77896(16)	0.0422(5)
C8	0.49568(17)	0.59562(18)	0.87408(16)	0.0432(5)
C9	0.40303(17)	0.63507(19)	0.92349(17)	0.0447(5)
H9	0.3332	0.6171	0.8955	0.054*
C10	0.41298(18)	0.70109(19)	1.01428(16)	0.0464(5)
C11	0.51688(19)	0.7320(2)	1.05471(18)	0.0517(5)
H11	0.5244	0.7763	1.1151	0.062*
C12	0.60844(19)	0.6957(2)	1.00385(19)	0.0570(6)
H12	0.6781	0.7177	1.0297	0.068*
C13	0.59978(17)	0.6279(2)	0.91581(19)	0.0507(5)
H13	0.6632	0.6033	0.8839	0.061*
C14	0.28950(16)	0.43723(18)	0.76508(17)	0.0422(4)
H14A	0.2844	0.4495	0.8399	0.051*
H14B	0.2714	0.3579	0.7504	0.051*
C15	0.06321(16)	0.49374(18)	0.74764(16)	0.0412(4)
C16	−0.00322(19)	0.4119(2)	0.6991(2)	0.0570(6)
H16	0.0201	0.3729	0.6405	0.068*

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
C17	−0.1048(2)	0.3890(2)	0.7392(2)	0.0643(7)
H17	−0.1498	0.3330	0.7080	0.077*
C18	−0.1405(2)	0.4481(2)	0.8248(2)	0.0598(6)
H18	−0.2098	0.4331	0.8502	0.072*
C19	−0.0744(2)	0.5286(3)	0.8723(2)	0.0648(7)
H19	−0.0985	0.5681	0.9303	0.078*
C20	0.0285(2)	0.5519(2)	0.83453(19)	0.0569(6)
H20	0.0739	0.6063	0.8674	0.068*
C21	0.3211(2)	0.8103(3)	1.1426(2)	0.0741(8)
H21A	0.3625	0.8769	1.1244	0.111*
H21B	0.3568	0.7731	1.2018	0.111*
H21C	0.2479	0.8326	1.1599	0.111*
N1	0.44709(14)	0.40809(15)	0.64738(13)	0.0427(4)
N2	0.58354(14)	0.51097(18)	0.72348(15)	0.0497(4)
O1	0.18869(13)	0.49651(18)	0.58682(13)	0.0597(5)
O2	0.21728(13)	0.64503(14)	0.72286(15)	0.0580(4)
O3	0.31537(13)	0.73337(16)	1.05579(13)	0.0586(4)
S1	0.19151(4)	0.52834(4)	0.69546(4)	0.04319(18)

Source of material

The title compound was prepared by the reaction of 2-(3-methoxyphenyl)imidazo[1,2-*a*]pyridine (0.2 mmol) and bromomethyl phenyl sulfone (0.4 mmol) in the presence of 2 mol% Ir(ppy)₃ as catalyst, K₂HPO₄ (0.4 mmol) as base, MeCN (1 mL) as solvent. The reaction was performed under N₂ atmosphere at 25 °C for 12 h and a 26 W CFL irradiation. The solvents were removed under reduced pressure and the residue was purified by chromatography to give the target product. The compound was crystallized by slow evaporation from a mixture solution of CH₂Cl₂ and hexane at room temperature.

Experimental details

Hydrogen atoms were placed in their geometrically idealized positions and constrained to ride on their parent atoms.

Comment

Imidazo[1,2-*a*]pyridine shows diverse bioactivity such as antiviral, antiulcer, antifungal, antibacterial, *etc.*, which make it very useful for pharmacological purposes [5]. For example, several marketed drugs such as Necopidem and Saripidem contain imidazo[1,2-*a*]pyridine unit [6]. Imidazo[1,2-*a*]pyridines are also important in material science because of their capabilities to exhibit excited-state intramolecular proton transfer [7, 8]. The benzenesulfonyl methyl group (CH₂SO₂Ph) could be easily unmasked to reveal a methyl group by reduction reactions [9], providing easy access to

methyated compounds which are interesting for biological applications.

The single-crystal structure of the title compound was determined by X-ray crystallography and is shown (*cf.* the figure). All bond lengths are in normal ranges [10]. The imidazo[1,2-*a*]pyridine ring system in the structure is planar. The torsion angle of C6–C7–C8–C9 is −17.1(3)° which shows the 2-phenyl moiety is not coplanar to the imidazo[1,2-*a*]pyridine moiety.

Acknowledgements: We gratefully acknowledge support by the National Natural Science Foundation of China (No. 21602046) and the Doctor's Scientific Research Foundation of Henan University of Chinese Medicine (No. BSJJ2016–12).

Funding: Science and Technology Research Projects of Henan Province (No. 162102310462).

References

- Agilent Technologies: CrysAlis^{Pro} Software System. Agilent Technologies UK Ltd, Oxford, UK (2017).
- Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H.: OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* **42** (2009) 339–341.
- Sheldrick, G. M.: A short history of SHELX. *Acta Crystallogr. A* **64** (2008) 112–122.
- Sheldrick, G. M.: Crystal structure refinement with SHELXL. *Acta Crystallogr. C* **71** (2015) 3–8.
- Koubachi, J.; Kazzouli, S. E.; Bousmina, M.; Guillaumet, G.: Functionalization of imidazo[1,2-*a*]pyridines by means of metal-catalyzed cross-coupling reactions. *Eur. J. Org. Chem.* **2014** (2014) 5119–5138.
- Jain, A. N.: Ligand-based structural hypotheses for virtual screening. *J. Med. Chem.* **47** (2004) 947–961.
- Takizawa, S.; Nishida, J.; Yamashita, Y.; Tsuzuki, T.; Tokito, S.: Phosphorescence color tunable iridium complexes with ligands of 2-phenylimidazo[1,2-*a*]pyridine derivatives. *Mol. Cryst. Liq. Cryst.* **455** (2006) 381–385.
- Pi, C.; Cui, X.; Liu, X.; Guo, M.; Zhang, H.; Wu, Y.: Synthesis of ferrocene derivatives with planar chirality *via* palladium-catalyzed enantioselective C–H bond activation. *Org. Lett.* **16** (2014) 5164–5167.
- Gui, J.; Zhou, Q.; Pan, C. M.; Yabe, Y.; Burns, A. C.; Collins, M. R.; Ornelas, M. A.; Ishihara, Y.; Baran, P. S.: C–H Methylation of heteroarenes inspired by radical SAM methyl transferase. *J. Am. Chem. Soc.* **136** (2014) 4853–4856.
- Lu, S.; Zhu, X.; Li, K.; Guo, Y. J.; Wang, M. D.; Zhao, X. M.; Hao, X. Q.; Song, M. P.: Reactivity of *p*-toluenesulfonylmethyl isocyanide: iron-involved C–H tosylmethylation of imidazopyridines in nontoxic media. *J. Org. Chem.* **81** (2016) 8370–8377.