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Crystal structure of 4-(1-phenylimidazo[1,5-*a*]pyridin-3-yl)benzoic acid (C₂₀H₁₄N₂O₂)

Table 1: Data collection and handling.

Crystal:	Yellow needle
Size:	0.27 × 0.16 × 0.11 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.09 mm ⁻¹
Diffractometer, scan mode:	Bruker SMART APEX-II, φ and ω
$\theta_{\max}$, completeness:	26.0°, 98%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	9187, 2897, 0.018
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2410
$N(\text{param})_{\text{refined}}$:	219
Programs:	Bruker [1], SHELX [2, 3], Mercury [4]

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Abstract

C₂₀H₁₄N₂O₂, monoclinic, *C*2/*c* (no. 15), $a = 17.8410(5)$ Å, $b = 15.3081(4)$ Å, $c = 11.3881(3)$ Å, $\beta = 104.280(1)^\circ$, $V = 3014.12(14)$ Å³, $Z = 8$, $R_{\text{gt}}(F) = 0.0364$, $wR_{\text{ref}}(F^2) = 0.0997$, $T = 100(2)$ K.

CCDC no.: 1940906

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.

Source of material

To anhydrous ethanol solution (10 mL) of 2-benzoylpyridine (1 mmol, 0.183 g) was added anhydrous ethanol solution (15 mL) of 4-(aminomethyl)benzoic acid (1 mmol, 0.151 g) in the presence of few drops of concentrated hydrochloric acid as a catalyst and refluxed at 80 °C for 48 h using a modified procedure from literature [5, 6]. The resulting off-

white solid was isolated by filtration and washed three times with small amounts of ethanol and the white solid was then recrystallized from a solution of ethanol to give a needle crystals. Yield: (55.74%, 0.175 g), m.p.: 186–187 °C; ¹H-NMR: (400 MHz, CD₃OD) δ ppm = 8.60 (1H, d), 8.37 (2H, d, $J = 8.70$ Hz), 8.10 (3H, m), 7.89 (2H, m), 7.67 (2H, m), 7.59 (1H, m), 7.40 (1H, m), 7.26 (1H, m), 4.89 (2H, s); ¹³C-NMR: (400 MHz, CD₃OD) δ ppm = 168.24, 135.27, 131.95, 131.03, 130.90, 130.77, 130.68, 129.15, 128.82, 128.14, 127.63, 126.57, 126.45, 123.75, 120.19, 120.10. MS (ESI): m/z Calc. for [C₂₀H₁₄N₂O₂]: 314.34; found [M⁺]: 315 (100%), 316 (24%).

Experimental details

The structure was solved by the direct method using the SHELXS [2] program and refined. The visual crystal structure information was performed using Mercury [4] system software. The C–H and O–H distances were restrained to 0.950 Å and 0.84 Å, respectively with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ and $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{O})$. The carboxylate hydrogen was found to be disordered over two positions.

Comment

Heterocyclic compounds possessing both the imidazole and pyridines moieties are of great importance as ligands in inorganic synthesis [7]. The title compound is known to be present in the structures of some biologically active compounds, thus giving it some importance. The compound has a great potential to be applied in other fields such as material science [8], organic synthesis [9], in lighting and photovoltaic technologies [8], and in pharmaceutical science where imidazole[1,5-*a*]pyridines moiety has been shown to be active

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

Atom	x	y	z	<i>U</i> _{iso} ^a / <i>U</i> _{eq}
O1	0.45803(6)	0.58344(6)	0.89839(9)	0.0332(2)
H1 ^a	0.485522	0.571311	0.967603	0.050*
O2	0.45394(6)	0.43778(6)	0.88330(10)	0.0336(3)
H2 ^a	0.479068	0.442588	0.955813	0.050*
N1	0.20104(7)	0.46362(7)	0.31121(11)	0.0273(3)
N2	0.22653(6)	0.60197(7)	0.27783(11)	0.0261(3)
C1	0.08324(8)	0.34730(8)	0.17026(15)	0.0323(3)
H1A	0.089667	0.344332	0.255496	0.039*
C2	0.04545(8)	0.28042(9)	0.09727(16)	0.0383(4)
H2A	0.025986	0.232030	0.132816	0.046*
C3	0.03580(8)	0.28345(10)	−0.02699(16)	0.0398(4)
H3	0.010928	0.236780	−0.076569	0.048*
C4	0.06266(8)	0.35498(10)	−0.07829(15)	0.0389(4)
H4	0.055527	0.357907	−0.163668	0.047*
C5	0.09999(8)	0.42253(9)	−0.00583(14)	0.0333(3)
H5	0.117576	0.471745	−0.042280	0.040*
C6	0.11203(7)	0.41922(8)	0.11944(13)	0.0274(3)
C7	0.15896(8)	0.48505(8)	0.19842(13)	0.0266(3)
C8	0.17283(8)	0.57220(8)	0.17395(13)	0.0270(3)
C9	0.14577(8)	0.63081(9)	0.07735(14)	0.0317(3)
H9	0.106713	0.613206	0.008572	0.038*
C10	0.17598(8)	0.71284(9)	0.08326(15)	0.0357(4)
H10	0.157382	0.752973	0.019050	0.043*
C11	0.23537(8)	0.73849(9)	0.18550(14)	0.0333(3)
H11	0.258019	0.794774	0.187020	0.040*
C12	0.25989(8)	0.68422(8)	0.28002(14)	0.0294(3)
H12	0.299695	0.701931	0.347744	0.035*
C13	0.24128(8)	0.53362(8)	0.35861(13)	0.0261(3)
C14	0.29179(8)	0.53397(8)	0.48083(13)	0.0264(3)
C15	0.32061(8)	0.45291(8)	0.52923(13)	0.0285(3)
H15	0.308096	0.401752	0.481162	0.034*
C16	0.36645(8)	0.44626(8)	0.64448(13)	0.0285(3)
H16	0.385193	0.390681	0.675557	0.034*
C17	0.38587(7)	0.52053(8)	0.71677(13)	0.0267(3)
C18	0.35693(8)	0.60152(8)	0.66987(13)	0.0288(3)
H18	0.369701	0.652565	0.718102	0.035*
C19	0.31004(8)	0.60802(8)	0.55434(13)	0.0291(3)
H19	0.289904	0.663335	0.524293	0.035*
C20	0.43548(8)	0.51214(8)	0.83985(13)	0.0276(3)

^aOccupancy: 0.5.

against HIV protease [10], as a cardiotonic agent [11] and also as an anti-tumour agent [12] among others. They are also known to be used as precursors for synthesis of *N*-heterocyclic carbenes [13], as ligands in coordination chemistry [14] and as pH-probes [15]. A number of methods have been used in the preparation of an imidazole[1,5-*a*]pyridine. One is the Vilsmeier-type cyclization reaction along with the variant methods [16, 17]. Other methods involve the usage of organometallic catalysts [18] or an oxidant [19] and also the one-pot condensation reactions of amines and aldehydes [20, 21]. In an attempt to synthesize a Schiff base using the one-pot condensation reaction using 4-(aminomethyl)benzoic acid

and 2-benzoylpyridine, imidazole[1,5-*a*]pyridine moiety was isolated as a product in agreement with Wang et al. [20] and Volpi et al. [21].

The asymmetric unit of the title compound contains one molecule defined by a benzoic acid moiety, an imidazole [1,5-*a*]pyridine moiety with an attached phenyl ring, all non coplanar. The dihedral angles between the imidazole[1,5-*a*] pyridine moiety, the benzoic acid moiety, and the phenyl ring moiety are 27.3 and 29.9(9)°, respectively. The N_{pyridinyl}–C_{benzoic acid}, C_{benzoic acid}–N_{imidazole} and the N_{imidazole}–C_{phenyl} are similar to those of reported analogues [14, 21–24]. In the crystal, two molecules are centrosymmetrically connected through intermolecular O–H...Oⁱ hydrogen bonds (symmetry code: (i) = 1 – *x*, 1 – *y*, 2 – *z*). The centrosymmetric dimers are further connected through C_{gpyridine}...C_{gbenzoic acid} interaction and the distance between them is 3.9676(8) Å (symmetry code: (i) = *x*, 1 – *y*, –1/2 – *z*).

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References

1. Bruker. APEXII. Bruker AXS Inc, Madison, WI, USA (2009).
2. Sheldrick, G. M.: A short history of SHELX. *Acta Crystallogr. A* **64** (2008) 112–122.
3. Sheldrick, G. M.: Crystal structure refinement with SHELXL. *Acta Crystallogr. C* **71** (2015) 3–8.
4. Macrae, C. F.; Bruno, I. J.; Chisholm, J. A.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Rodriguez-Monge, L.; Taylor, R.; van de Streek, J.; Wood, P. A.: Mercury CSD 2.0 – new features for the visualization and investigation of crystal structures. *J. Appl. Crystallogr.* **41** (2008) 466–470.
5. Abdel-Monem, Y. K.; Abouel-Enein, S. A.; El-Seady, S. M.: Synthesis, characterization and molecular modeling of some transition metal complexes of Schiff base derived from 5-aminouracil and 2-benzoyl pyridine. *J. Mol. Struct.* **1152** (2018) 115–127.
6. Njogu, E. M.; Omondi, B.; Nyamori, V. O.: Silver(I)-pyridinyl Schiff base complexes: synthesis, characterization and antimicrobial studies. *J. Mol. Struct.* **1135** (2017) 118–128.
7. Anitha, P.; Manikandan, R.; Prakash, G.; Pachiyappan, B.; Viswanathamurthi, P.; Malecki, J. G.: Ruthenium(II) 8-quinolinolates: synthesis, characterization, crystal structure and catalysis in the synthesis of 2-oxazolines. *J. Organomet. Chem.* **791** (2015) 266–273.
8. Tavasli, M.; Moore, T. N.; Zheng, Y.; Bryce, M. R.; Fox, M. A.; Griffiths, G. C.; Jankus, V.; Al-Attar, H. A.; Monkman, A. P.: Colour tuning from green to red by substituent effects in phosphorescent tris-cyclometalated iridium(III) complexes of carbazole-based ligands: synthetic, photophysical,

- computational and high efficiency OLED studies. *J. Mater. Chem.* **22** (2012) 6419–6428.
9. Alcarazo, M.; Roseblade, S. J.; Cowley, A. R.; Fernández, R.; Brown, J. M.; Lassaletta, J. M.: Imidazo[1,5-*a*]pyridine: a versatile architecture for stable *N*-heterocyclic carbenes. *J. Am. Chem. Soc.* **127** (2005) 3290–3291.
 10. Ganguly, S.; Vithlani, V.; Kesharwani, A.; Kuhu, R.; Baskar, L.; Mitramazumder, P.; Sharon, A.; Dev, A.: Synthesis, antibacterial and potential anti-HIV activity of some novel imidazole analogs. *Acta Pharm.* **61** (2011) 187–201.
 11. Kwong, H. C.; Chidan Kumar, C. S.; Mah, S. H.; Mah, Y. L.; Chia, T. S.; Quah, C. K.; Lim, G. K.; Chandraru, S.: Crystal correlation of heterocyclic imidazo[1,2-*a*]pyridine analogues and their anticholinesterase potential evaluation. *Sci Rep.* **9** (2019) 926.
 12. Nassar, I. F.; Atta-Allah, S. R.; Elgazwy, A. S.: A convenient synthesis and molecular modeling study of novel pyrazolo[3,4-*d*]pyrimidine and pyrazole derivatives as anti-tumor agents. *J. Enzyme Inhib. Med. Chem.* **30** (2015) 396–405.
 13. Herrmann, W. A.; Köcher, C.; Gooßen, L. J.; Artus, G. R. J.: Heterocyclic carbenes: a high-yielding synthesis of novel, functionalized *N*-heterocyclic carbenes in liquid ammonia. *Chem. Eur. J.* **2** (1996) 1627–1636.
 14. Ardizzoia, G. A.; Brenna, S.; Durini, S.; Therrien, B.: Synthesis and characterization of luminescent zinc(II) complexes with a *N,N*-bidentate 1-pyridylimidazo[1,5-*a*]pyridine ligand. *Polyhedron* **90** (2015) 214–220.
 15. Hutt, J. T.; Jo, J.; Olsz, A.; Chen, C.-H.; Lee, D.; Aron, Z. D.: Fluorescence switching of imidazo[1,5-*a*]pyridinium ions: pH-sensors with dual emission pathways. *Org. Lett.* **14** (2012) 3162–3165.
 16. Huang, C.; Giokaris, A.; Gevorgyan, V.: Palladium-catalyzed highly regioselective C-3 arylation of imidazo[1,5-*a*]pyridine. *Chem. Lett.* **40** (2011) 1053–1054.
 17. Wang, H.; Xu, W.; Xin, L.; Liu, W.; Wang, Z.; Xu, K.: Synthesis of 1,3-disubstituted imidazo[1,5-*a*]pyridines from amino acids via catalytic decarboxylative intramolecular cyclization. *J. Org. Chem.* **81** (2016) 3681–3687.
 18. Li, Y.; Chao, A.; Fleming, F. F.: Isonitrile alkylations: a rapid route to imidazo[1,5-*a*]pyridines. *Chem. Commun.* **52** (2016) 2111–2113.
 19. Chen, L.; Zhu, H.; Wang, J.; Lui, H.: One-pot NBS-promoted synthesis of imidazoles and thiazoles from ethylarenes in water. *Molecules* **24** (2019) 893–905.
 20. Wang, J.; Mason, R.; VanDerveer, D.; Feng, K.; Bu, X. R.: Convenient preparation of a novel class of imidazo[1,5-*a*]pyridines: decisive role by ammonium acetate in chemoselectivity. *J. Org. Chem.* **68** (2003) 5415–5418.
 21. Volpi, G.; Garino, C.; Priola, E.; Diana, E.; Gobetto, R.; Buscaino, R.; Viscardi, G.; Barolo, C.: Facile synthesis of novel blue light and large Stoke shift emitting tetradentate polyazines based on imidazo[1,5-*a*] pyridine. *Dyes Pigments* **143** (2017) 284–290.
 22. Sheng, H.; Hu, Y.; Zhou, Y.; Fan, S.; Cao, Y.; Zhao, X.; Yang, W.: A highly selective ESIPT-based fluorescent probe with a large Stokes shift for the turn-on detection of cysteine and its application in living cells. *Dyes Pigments* **160** (2019) 48–57.
 23. Volpi, G.; Garino, C.; Conterosito, E.; Barolo, C.; Gobetto, R.; Viscardi, G.: Facile synthesis of novel blue light and large Stoke shift emitting tetradentate polyazines based on imidazo[1,5-*a*]pyridine. *Dyes Pigments* **128** (2016) 96–100.
 24. Volpi, G.; Magistris, C.; Garino, C.: FLUO-SPICES: natural aldehydes extraction and one-pot reaction to prepare and characterize new interesting fluorophores. *Educ. Chem. Eng.* **24** (2018) 1–6.