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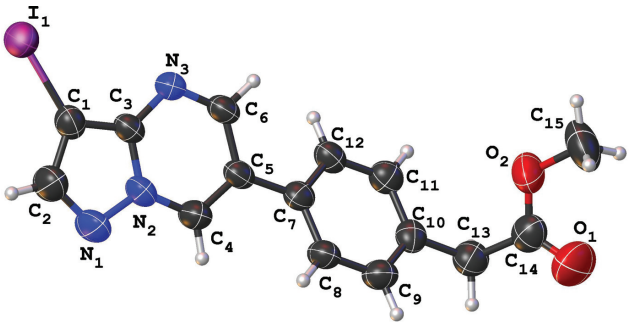
Crystal structure of methyl 2-(4-(3-iodopyrazolo[1, 5-*a*]pyrimidin-6-yl)phenyl)acetate, $C_{15}H_{12}IN_3O_2$



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Abstract

$C_{15}H_{12}IN_3O_2$, triclinic, $P\bar{1}$ (no. 2), $a = 4.511(2)$ Å, $b = 11.891(6)$ Å, $c = 14.557(7)$ Å, $\alpha = 109.709(9)°$, $\beta = 96.971(9)°$, $\gamma = 97.054(9)°$, $V = 718.4(6)$ Å^3, $Z = 2$, $R_{gt}(F) = 0.0449$, $wR_{ref}(F^2) = 0.1052$, $T = 293(2)$ K.

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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 a solution of methyl 2-(4-(pyrazolo[1,5-*a*]pyrimidin-6-yl)phenyl)acetate (1.07 g, 4.0 mmol) in anhydrous dichloromethane (20 mL) was added *N*-iodosuccinimide (0.95 g, 4.2 mmol) while cooled by an ice-water. After addition the mixture was warmed to room temperature naturally and stirred for 20 min. Then the reaction mixture was quenched

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Table 1: Data collection and handling.

Crystal:	Orange block
Size:	0.29 × 0.25 × 0.22 mm
Wavelength:	Mo Kα radiation (0.71073 Å)
μ:	2.24 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	25.0°, 99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	3660, 2512, 0.028
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 1797
$N(param)_{refined}$:	178
Programs:	Bruker [1], SHELX [2, 3], Olex2 [4]

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
I1	1.51074(10)	0.92313(4)	0.77704(3)	0.0673(2)
O1	−0.3231(16)	0.6328(5)	−0.0621(4)	0.123(2)
O2	−0.0358(12)	0.7943(5)	0.0417(3)	0.0865(15)
N1	0.8841(14)	0.6054(5)	0.6021(4)	0.0794(17)
N2	0.8300(12)	0.6828(4)	0.5546(3)	0.0570(12)
N3	0.9939(11)	0.8818(4)	0.5622(3)	0.0503(11)
C1	1.1978(14)	0.7850(5)	0.6763(4)	0.0538(14)
C2	1.1077(17)	0.6686(6)	0.6753(5)	0.0729(19)
H2	1.195792	0.638597	0.721274	0.087*
C3	1.0156(13)	0.7919(5)	0.5972(4)	0.0469(13)
C4	0.6111(14)	0.6588(5)	0.4756(4)	0.0603(16)
H4	0.482292	0.583944	0.448748	0.072*
C5	0.5823(13)	0.7453(5)	0.4363(4)	0.0471(13)
C6	0.7864(13)	0.8562(5)	0.4839(4)	0.0510(14)
H6	0.771551	0.916454	0.457071	0.061*
C7	0.3472(7)	0.7280(3)	0.3508(2)	0.0476(13)
C8	0.2200(8)	0.6122(2)	0.2845(3)	0.0529(14)
H8	0.286246	0.544837	0.293120	0.063*
C9	−0.0063(8)	0.5972(2)	0.2054(2)	0.0579(15)
H9	−0.091475	0.519679	0.161014	0.070*
C10	−0.1054(7)	0.6979(3)	0.1925(2)	0.0495(14)
C11	0.0219(8)	0.8137(3)	0.2588(3)	0.0534(14)
H11	−0.044380	0.881110	0.250160	0.064*
C12	0.2482(8)	0.8288(2)	0.3379(2)	0.0517(14)
H12	0.333343	0.906270	0.382266	0.062*
C13	−0.3502(14)	0.6805(6)	0.1078(4)	0.0631(16)
H13A	−0.485778	0.737453	0.130201	0.076*
H13B	−0.466943	0.599266	0.087190	0.076*
C14	−0.2364(16)	0.6974(6)	0.0202(5)	0.0647(17)

Table 2 (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
C15	0.0847(19)	0.8153(8)	−0.0393(6)	0.107(3)
H15A	0.230316	0.889277	−0.014423	0.160*
H15B	0.181385	0.748928	−0.072003	0.160*
H15C	−0.077200	0.821787	−0.085533	0.160*

by saturated sodium bicarbonate solution and extracted by dichloromethane, and washed with brine. The organic phase was dried by anhydrous sodium sulfate, concentrated and purified by column chromatography over silica gel eluting with a gradient of ethyl acetate/hexane (*v*/*v*, 0–20%) to give the white solid. Yield, 1.45 g, 92%. The title compound was dissolved in ethyl acetate/hexane (*v*/*v*, 1/9), and the solvent was evaporated slowly at room temperature. After three days, colourless crystals were obtained.

Experimental details

Data reduction was carried out using SAINT+ and SADABS [1]. The structure was determined by the intrinsic phasing routines in the SHELXT program [2] and refined in SHELXL [3] by using Olex 2 [4]. All hydrogen atoms were placed in the calculated positions.

Comment

The compounds containing pyrazolo[1,5-*a*]pyrimidine scaffold have rich biological activities, especially this kind of compounds exhibited strong biological effects on AMPK, MET and VEGF in the field of anti-cancer drugs [5, 6]. Therefore, the related derivatives are ideal lead compounds for the development of anti-cancer drugs. In our previous works, we synthesized (methyl 2-(4-(3-bromopyrazolo[1,5-*a*] pyrimidin-6-yl) phenyl)acetate) and hoped to introduce aromatic groups into the position of bromine atom by coupling reaction [7, 8]. But some coupling reactions can not be carried out due to the low reactivity of bromide, so we try to synthesize iodide which exhibits higher reactivity than corresponding bromide to adress this problem. In this work, methyl 2-(4-(3-iodopyrazolo [1,5-*a*]pyrimidin-6-yl)phenyl)acetate was synthesized by a simple halogenation reaction using *N*-iodosuccinimide.

The crystallographically independent molecule of the crystal structure is shown in the figure. The NMR and LC-MS results are consistent with the proposed structure. The bond lengths and angles are in the normal ranges. The subsequent experiments showed that iodide has proper reactivities to introduce diverse aryl functional group into title compounds, which is very important to develop novel anticancer drugs.

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