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Crystal structure of methyl 2-(4-(pyrazolo[1,5-*a*]pyrimidin-6-yl)phenyl)acetate, C₁₅H₁₃N₃O₂

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Abstract

C₁₅H₁₃N₃O₂, triclinic, $P\bar{1}$ (no. 2), $a = 4.6502(18)$ Å, $b = 11.937(3)$ Å, $c = 13.1822(19)$ Å, $\alpha = 115.26(4)^\circ$, $\beta = 94.81(5)^\circ$, $\gamma = 96.49(5)^\circ$, $V = 650.4(4)$ Å³, $Z = 2$, $R_{\text{gt}}(F) = 0.0762$, $wR_{\text{ref}}(F^2) = 0.1794$, $T = 296(2)$ K.

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The crystal structure is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Source of material

A suspension of 6-bromopyrazolo[1,5-*a*]pyrimidine (396 mg, 2 mmol), methyl 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetate (552 mg, 2 mmol), potassium carbonate (414 mg, 3 mmol) and tetrakis(triphenylphosphine) palladium (211 mg, 0.2 mmol) in dioxane (5 mL) and water (1 mL) was sealed, degassed by nitrogen and heated under

Table 1: Data collection and handling.

Crystal:	Colourless
Size:	0.28 × 0.25 × 0.21 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.09 mm ^{−1}
Diffractometer, scan mode:	SuperNova, φ and ω
θ_{max} , completeness:	25.0°, 99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	3225, 2261, 0.046
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 993
$N(\text{param})_{\text{refined}}$:	181
Programs:	CrysAlis ^{PRO} [1], Olex2 [2], SHELX [3]

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.5390(7)	0.1469(3)	−0.1336(3)	0.0596(10)
O2	0.7261(9)	−0.0100(3)	−0.1211(3)	0.0934(14)
N1	−0.1024(10)	0.6792(4)	0.5519(4)	0.0642(12)
N2	0.0355(8)	0.6778(3)	0.4638(3)	0.0460(10)
N3	0.1338(10)	0.7950(4)	0.3600(4)	0.0616(12)
C1	−0.2031(11)	0.7896(5)	0.5885(4)	0.0623(15)
H1A	−0.305936	0.818184	0.649841	0.075*
C2	−0.1412(11)	0.8560(4)	0.5279(4)	0.0590(14)
H2A	−0.190943	0.933395	0.539520	0.071*
C3	0.0139(11)	0.7812(4)	0.4443(4)	0.0490(13)
C4	0.2762(11)	0.7030(4)	0.2969(4)	0.0587(14)
H4A	0.357454	0.711280	0.237830	0.070*
C5	0.3135(10)	0.5941(4)	0.3122(4)	0.0429(11)
C6	0.1825(10)	0.5849(4)	0.3977(4)	0.0488(13)
H6A	0.192296	0.515144	0.411541	0.059*
C7	0.4705(10)	0.4969(4)	0.2400(4)	0.0397(11)
C8	0.5866(11)	0.5032(4)	0.1494(4)	0.0552(14)
H8A	0.565289	0.571320	0.134184	0.066*
C9	0.7386(10)	0.4088(4)	0.0782(4)	0.0549(13)
H9A	0.816233	0.417095	0.018477	0.066*
C10	0.7711(10)	0.3065(4)	0.0968(4)	0.0460(12)
C11	0.6616(11)	0.3000(4)	0.1896(4)	0.0568(14)
H11A	0.685333	0.232334	0.205252	0.068*
C12	0.5155(11)	0.3944(4)	0.2601(4)	0.0558(14)
H12A	0.447019	0.388152	0.322112	0.067*
C13	0.9187(10)	0.2019(4)	0.0182(4)	0.0572(14)
H13A	1.074829	0.238814	−0.007988	0.069*
H13B	1.007457	0.162990	0.061494	0.069*
C14	0.7181(11)	0.1002(5)	−0.0845(4)	0.0520(13)
C15	0.3461(12)	0.0569(4)	−0.2352(4)	0.0673(16)
H15A	0.226183	0.100510	−0.263780	0.101*
H15B	0.460872	0.011239	−0.291673	0.101*
H15C	0.223614	−0.000651	−0.217492	0.101*

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microwave irradiation at 80 °C for 30 min. The reaction mixture was diluted with ethyl acetate (10 mL) and washed with water and brine. The organic phase was dried over and concentrated, which was after that purified by column chromatography over silica gel eluting with a gradient of ethyl acetate/hexane (v/v, 0–20%) to afford the white solid. Yield, 402 mg, 75%. The title compound was dissolved in ethyl acetate, and the solvent was evaporated slowly at room temperature. After one week, colourless crystals were obtained.

Experimental details

Single crystal X-ray data for the title compound was collected on a SuperNova four-circle diffractometer using graphite monochromated MoK α (0.71073 Å) radiation at 296(2) °C [1]. All hydrogen atoms were placed in calculated positions and all the non-hydrogen atoms were refined anisotropically.

Comment

The pyrazolo[1,5-*a*]pyrimidine core is an important aromatic fused heterocycle widely present in synthetic drugs and related intermediates [4]. Especially in recent years, many studies focused on the synthesis of pyrazolo[1,5-*a*]pyrimidine derivatives for the development of novel anticancer drugs, since these derivatives exhibit diverse biological characteristics while linked with different substituents [5, 6]. In this work, we report on the synthesis of methyl 2-(4-(pyrazolo[1,5-*a*]pyrimidin-6-yl)phenyl)acetate by a simple Suzuki-Miyaura cross-coupling reaction with a high yield, which is a key intermediate for the synthesis of various types of pyrazolo[1,5-*a*]pyrimidine derivatives with high anticancer potentiality. The crystallographically independent molecule of the crystal structure is shown in the figure. The NMR results are consistent with the proposed structure. The bond lengths and angles are in the normal ranges [7]. In conclusion, we

have synthesized methyl 2-(4-(pyrazolo[1,5-*a*]pyrimidin-6-yl)phenyl)acetate as a key intermediate of anticancer drugs by a Suzuki-Miyaura cross-coupling reaction, which can be readily used to synthesize a diverse range of compounds for high throughput screening in medicinal chemistry.

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