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Crystal structure of 4-chloro-2-methyl-6-(4-(trifluoromethoxy)phenyl)pyrimidine, $C_{12}H_8ClF_3N_2O$

Table 1: Data collection and handling.

Crystal:	Block, colorless
Size:	$0.13 \times 0.13 \times 0.05$ mm
Wavelength:	Cu $K\alpha$ radiation (1.54178 Å)
μ :	2.96 mm^{-1}
Diffractometer, scan mode:	Bruker D8-Venture μS , φ and ω -scans
$2\theta_{\text{max}}$, completeness:	58.9° , >95%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	2940, 1505, 0.070
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 931
$N(\text{param})_{\text{refined}}$:	173
Programs:	Bruker programs [1], SHELX [2], OLEX2 [3], PLATON [4]

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Abstract

$C_{12}H_8ClF_3N_2O$, tetragonal, $I\bar{4}$ (no. 82), $a = 23.280(6)$ Å, $c = 4.7191(15)$ Å, $V = 2557.6(15)$ Å³, $Z = 8$, $R_{\text{gt}} = 0.0700$, $wR_{\text{ref}}(F^2) = 0.1933$, $T = 296(2)$ K.

CCDC no.: 1474902

The asymmetric unit of the title 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

The title compound suitable was obtained from: 4,6-dichloro-2-methylpyrimidine (100 mg, 0.61 mmol) and 4-(trifluoromethoxy)phenylboronic acid (189 mg, 0.92 mmol) in dioxane (2 mL), which were added to a solution of dichlorido-bis(triphenylphosphine)palladium(II) (17 mg, 0.024 mmol) and Cs_2CO_3 2 M (1 mL, 2 mmol). The mixture was stirred at 80 °C for 30 min. in a microwave reactor. The mixture was cooled to room temperature and extracted

with EtOAc, and the organic layer was dried over anhydrous Na_2SO_4 . After filtration, the filtrate was evaporated and purified by chromatography (petroleum ether/EtOAc, 10:1) to give the product as a white solid (71 mg, 40%). Colorless crystals suitable for X-ray analysis were grown in chloroform by slow evaporation of the solvent at room temperature over a period of 24 h.

IR (KBr, cm^{-1}): 1611 ($\text{N}_{\text{sp}2}\text{-C}_{\text{sp}2}$), 1508 ($\text{C}_{\text{sp}2}\text{-Cl}$), 1265 ($\text{C}_{\text{sp}2}\text{-O}$). ^1H NMR (CDCl_3 , 400 MHz) δ 8.08 (d, $J = 8.8$ Hz, 2H, H-7), 7.49 (s, 1H, H-3), 7.32 (d, $J = 8.3$ Hz, 2H, H-6), 2.75 (s, 3H, H-12) ppm. ^{13}C NMR (CDCl_3 , 101 MHz) δ 169.48 (C-1), 164.38 (C-4), 161.92 (C-2), 151.69–151.67 (C-11), 134.33 (C-5), 129.18 (C-7), 124.35–116.64 (C-11), 121.21 (C-6), 114.00 (C-3), 26.08 (C-12) ppm. MS calculated for $C_{12}H_9ClF_3N_2O$ [M + H] 289.04 found 288.80.

Experimental details

H atoms were located in the difference Fourier map, but refined with fixed individual displacement parameters, using a riding model with C–H distances of 0.93 Å (for aromatic rings), 0.96 Å (for CH_3 group) with $U(\text{H})$ values of $1.2U_{\text{eq}}(\text{C})$ for CH in aromatic moiety and $1.5U_{\text{eq}}(\text{C})$ for CH_3 .

Discussion

The pyrimidine nucleus, as well as other nitrogenous heterocyclic systems, have been considered in the design of various compounds with diverse biological properties, especially for the development of new anti-tumor agents [5–8]. Considering this antecedents, several synthetic efforts have

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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} */ <i>U</i> _{eq}
Cl1	0.58916(11)	0.52207(10)	0.2176(7)	0.1145(12)
O1	0.6442(4)	0.8823(3)	0.949(4)	0.181(6)
F1	0.6130(3)	0.9653(3)	1.030(2)	0.166(3)
F2	0.5887(6)	0.9236(4)	0.663(3)	0.215(5)
F3	0.5547(4)	0.8953(4)	1.028(3)	0.186(4)
N1	0.6986(3)	0.6179(3)	0.815(2)	0.094(3)
N2	0.6733(4)	0.5322(3)	0.578(2)	0.093(3)
C1	0.7532(4)	0.5307(5)	0.904(3)	0.119(4)
H1B	0.7858	0.5288	0.7792	0.179*
H1C	0.7408	0.4925	0.9496	0.179*
H1A	0.7639	0.5505	1.0746	0.179*
C2	0.7058(4)	0.5622(4)	0.762(3)	0.096(3)
C3	0.6554(3)	0.6462(4)	0.688(3)	0.086(3)
C4	0.6193(4)	0.6178(4)	0.496(3)	0.088(3)
H4	0.5892	0.6362	0.4043	0.106*
C5	0.6318(4)	0.5604(4)	0.453(3)	0.089(3)
C6	0.6498(4)	0.7085(4)	0.758(3)	0.091(3)
C7	0.6881(4)	0.7342(4)	0.940(3)	0.114(4)
H7	0.7171	0.7125	1.0222	0.136*
C8	0.6841(5)	0.7915(5)	1.000(3)	0.120(4)
H8	0.7094	0.8085	1.1275	0.144*
C9	0.6423(5)	0.8236(4)	0.871(4)	0.125(5)
C10	0.6020(5)	0.7994(4)	0.694(4)	0.128(5)
H10	0.5725	0.8215	0.6178	0.154*
C11	0.6064(4)	0.7413(4)	0.634(3)	0.111(4)
H11	0.5803	0.7242	0.5103	0.133*
C12	0.6041(9)	0.9153(7)	0.928(5)	0.137(5)

been carried out to obtain new 2,4,6-trisubstituted pyrimidine derivatives and later, study their cytotoxic effects in different tumor cell lines. To access a compound such as our here reported, a pivotal step is a carbon-carbon Suzuki coupling, which is obtained from the 4,6-dichloro-2-methylpyrimidine with (4-(trifluoromethoxy)phenyl)boronic acid and dichlorido-bis(triphenylphosphine)palladium(II) as a catalyst.

The dihedral angle formed by the aryl ring with the pyrimidine ring is 3.0(6)°. Bond lengths and angles are all in the expected ranges of a chloro substituted pyrimidine [9]. There are some weak intramolecular C—H···N hydrogen-bonding interactions in the crystal structure. The crystal packing is furthermore stabilized by van der Waals interactions.

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