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The crystal structure of 1-((5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-yl)methyl)-1,3-diphenylurea, C₂₄H₂₁ClN₄O

Table 1: Data collection and handling.

Crystal:	Block, clear light colourless
Size:	0.22 × 0.17 × 0.15 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.2 mm ⁻¹
Diffractometer, scan mode:	SuperNova, ω -scans
$\theta_{\max}$, completeness:	26°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	11005, 4348, 0.050
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2365
$N(\text{param})_{\text{refined}}$:	272
Programs:	CrysAlis ^{PRO} [1], SHELX [2]

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Abstract

C₂₄H₂₁ClN₄O, monoclinic, $P2_1/n$ (no. 14), $a = 10.2630(11)$ Å, $b = 17.8954(16)$ Å, $c = 12.3517(14)$ Å, $\beta = 102.510(11)^\circ$, $V = 2214.7(4)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0569$, $wR_{\text{ref}}(F^2) = 0.1617$, $T = 293(2)$ 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

The synthesis pathway of the title compound begins with the reaction of the Vilsmeier-Haack reagent (DMF/POCl₃) and 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazole-3-one. The obtained 1*H*-pyrazole-4-carbaldehyde intermediate and aniline were reacted in ethanol at room temperature, to form the Schiff base derivative that was purified by recrystallization from ethanol. The corresponding secondary amine was obtained by the reduction of corresponding Schiff base using

sodium borohydride. Lastly, the secondary amine was reacted with phenyl isocyanate in CHCl₃ to afford the title compound. Single crystals were obtained by the slow evaporation of acetone/acetonitrile solutions.

Experimental details

All H atoms were positioned geometrically (C–H = 0.93 Å for the aromatic H atoms and C–H = 0.96 Å for the aliphatic H atoms) and were refined as riding, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$.

Discussion

Many pyrazole derivatives have been reported to possess potent anticancer activities *in vitro* and *in vivo*, and much attention was paid to the discovery of Ser/Thr kinases inhibitors based on pyrazole core. In our previous research, [3, 4] we were able to demonstrate that a series of 5-phenyl-1*H*-pyrazole-3-amines and their urea derivatives displayed potent antiproliferative activities against human melanoma cells. In continuation of our earlier studies, and with a view to better understand the SAR around these pyrazole-based anti-melanoma agent, we report the synthesis and crystal structure of a 5-phenyl-1*H*-pyrazole-4-urea derivative.

In title compound, all bond lengths and angles within the *N*-phenylpyrazole core are comparable with those reported for the similar pyrazole derivatives [5–7] (*cf.* the figure). The C6–N1 bond [1.431(3) Å] allows a rotation of the phenyl relative to the pyrazole ring, thus the dihedral angle between the corresponding ring planes is 42.0(4)°.

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
Cl1	0.05912(8)	0.15927(4)	0.02375(7)	0.0717(3)
N1	0.2668(2)	0.07542(12)	0.1289(2)	0.0515(6)
N3	0.1547(2)	0.02605(13)	−0.2413(2)	0.0552(6)
C9	0.2845(3)	−0.01265(15)	0.0147(3)	0.0570(8)
N2	0.3407(2)	0.01360(13)	0.1140(2)	0.0588(7)
N4	0.1926(3)	−0.02079(13)	−0.4069(2)	0.0687(8)
H4	0.219642	0.023875	−0.415376	0.082*
C7	0.1668(3)	0.08574(14)	0.0372(2)	0.0479(7)
C1	0.4306(3)	0.12602(17)	0.2826(3)	0.0676(9)
H1	0.497960	0.111412	0.247452	0.081*
O1	0.0973(2)	−0.09276(11)	−0.2941(2)	0.0760(7)
C8	0.1740(3)	0.03119(15)	−0.0374(2)	0.0502(7)
C12	0.2234(3)	0.09440(14)	−0.2521(2)	0.0479(7)
C6	0.2987(3)	0.11409(14)	0.2327(2)	0.0480(7)
C5	0.1990(3)	0.13585(15)	0.2842(3)	0.0565(8)
H5	0.110108	0.127363	0.250479	0.068*
C21	0.1654(3)	−0.14665(16)	−0.4905(3)	0.0645(9)
H21	0.130661	−0.165319	−0.432397	0.077*
C20	0.2019(3)	−0.07217(15)	−0.4922(3)	0.0554(8)
C3	0.3618(4)	0.18235(17)	0.4375(3)	0.0752(10)
H3	0.383196	0.205338	0.506619	0.090*
C18	0.0838(3)	0.02086(16)	−0.1501(2)	0.0590(8)
H18A	0.041109	−0.027656	−0.152834	0.071*
H18B	0.014388	0.058601	−0.160598	0.071*
C25	0.2504(4)	−0.04602(18)	−0.5795(3)	0.0813(11)
H25	0.275083	0.003906	−0.581157	0.098*
C4	0.2320(4)	0.17067(16)	0.3872(3)	0.0677(9)
H4A	0.164641	0.186054	0.421914	0.081*
C13	0.3599(3)	0.09576(17)	−0.2343(3)	0.0691(9)
H13	0.408814	0.051934	−0.217442	0.083*
C19	0.1460(3)	−0.03329(17)	−0.3131(3)	0.0553(8)
C15	0.3548(5)	0.2271(2)	−0.2636(3)	0.0851(12)
H15	0.399226	0.271868	−0.268100	0.102*
C10	0.3367(4)	−0.08157(18)	−0.0299(3)	0.0853(11)
H10A	0.394578	−0.067639	−0.078094	0.128*
H10B	0.263440	−0.110380	−0.070739	0.128*
H10C	0.385718	−0.110890	0.030449	0.128*
C23	0.2293(4)	−0.1668(2)	−0.6632(3)	0.0852(11)
H23	0.239081	−0.198639	−0.720421	0.102*
C14	0.4243(4)	0.1627(2)	−0.2416(3)	0.0886(12)
H14	0.516748	0.163554	−0.231127	0.106*
C22	0.1813(3)	−0.19270(19)	−0.5763(3)	0.0735(10)
H22	0.158446	−0.242909	−0.574502	0.088*

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
C2	0.4618(4)	0.16000(19)	0.3857(3)	0.0829(11)
H2	0.550682	0.167815	0.420299	0.100*
C24	0.2633(4)	−0.0928(2)	−0.6654(3)	0.0944(13)
H24	0.295076	−0.074003	−0.724992	0.113*
C17	0.1540(4)	0.15958(19)	−0.2742(3)	0.0844(12)
H17	0.061367	0.159319	−0.285994	0.101*
C16	0.2208(5)	0.2259(2)	−0.2791(4)	0.1045(15)
H16	0.172951	0.270244	−0.293158	0.125*

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References

1. Oxford Diffraction Ltd., CrysAlis^{PRO}, Abingdon, Oxfordshire, England, (2006).
2. Sheldrick, G. M.: SHELXT – integrated space-group and crystal-structure determination. *Acta Crystallogr.* **A71** (2015) 3–8.
3. Li, Q. S.; Lu, X. H.; Yang, Y.; Ruan, B. F.; Yao, R. S.; Liao, C. Z.: Discovery and pharmacophore studies of novel pyrazole-based anti-melanoma agents. *Chem. Biodivers.* **12** (2015) 116–132.
4. Dong, J. J.; Li, Q. S.; Wang, S. F.; Li, C. Y.; Zhao, X.; Qiu, H. Y.; Zhao, M. Y.; Zhu, H. L.: Synthesis, biological evaluation and molecular docking of novel 5-phenyl-1*H*-pyrazol derivatives as potential BRAF(V600E) inhibitors. *Org. Biomol. Chem.* **11** (2013) 6328–6337.
5. Buriol, L.; Frizzo, C. P.; Prola, L. D. T.; Moreira, D. N.; Marzari, M. R. B.; Scapin, E.; Zanatta, N.; Bonacorso, H. G.; Martins, M. A. P.: Regioselective reaction of mesoionic 4-trifluoroacetyl-1,3-oxazolium-5-olates and phenylhydrazine: synthesis of trifluoromethyl substituted pyrazole and 1,2,4-triazine derivatives. *Catal. Lett.* **141** (2011) 1130–1135.
6. Beck, J. R.; Wright, F. L.: Synthesis of 1-aryl-5-(trifluoromethyl)-1*H*-pyrazole-4-carboxylic acids and esters. *J. Heterocycl. Chem.* **24** (1987) 739–740.
7. Touzot, A.; Soufyane, M.; Berber, H.; Toupet, L.; Mirand, C.: Synthesis of trifluoromethylated pyrazoles from trifluoromethylenaminones and monosubstituted hydrazines. *J. Fluorine Chem.* **125** (2004) 1299–1304.