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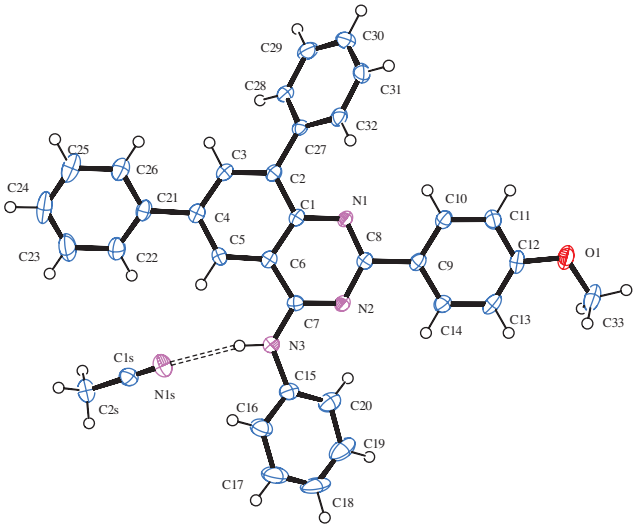
The crystal structure of 2-(4-methoxyphenyl)-6,8-diphenyl-4-(phenylamino)quinazoline — acetonitrile (1/1), $C_{35}H_{28}N_4O$



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Abstract

$C_{35}H_{28}N_4O$, triclinic, $P\bar{1}$ (no. 2), $a = 10.5972(11)$ Å, $b = 11.0497(12)$ Å, $c = 12.0241(12)$ Å, $\alpha = 89.499(4)°$, $\beta = 77.169(4)°$, $\gamma = 79.758(4)°$, $V = 1350.2(2)$ Å^3, $Z = 2$, $R_{gt}(F) = 0.0717$, $wR_{ref}(F^2) = 0.1542$, $T = 173$ K.

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Source of material

A mixture of the previously prepared 2-(4-methoxyphenyl)-6,8-diphenylquinazolin-4(3*H*)-one[1] (0.40 g, 1.06 mmol) and $POCl_3$ (15 mL) was heated at 120 °C for 3 h. The mixture was allowed to cool to room temperature and then quenched with

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Table 1: Data collection and handling.

Crystal:	Yellow needle
	Size 0.36 × 0.10 × 0.08 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.8 cm^{-1}
Diffractometer, scan mode:	Bruker D8 Venture, ω (0.5°)
$2\theta_{max}$, completeness:	51°, >97%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	18764, 4920, 0.040
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 4122
$N(param)_{refined}$:	367
Programs:	SHELX [2], Bruker programs [3], WinGX [4], Platon [5]

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2559(2)	0.5795(2)	0.41878(19)	0.0200(5)
C2	0.3109(2)	0.6347(2)	0.3162(2)	0.0211(5)
C3	0.4333(2)	0.5798(2)	0.2540(2)	0.0239(5)
H3A	0.4709	0.6181	0.1868	0.029*
C4	0.5051(2)	0.4698(2)	0.2851(2)	0.0227(5)
C5	0.4509(2)	0.4170(2)	0.3844(2)	0.0232(5)
H5	0.4976	0.3429	0.4071	0.028*
C6	0.3285(2)	0.4701(2)	0.4525(2)	0.0204(5)
C7	0.2649(2)	0.4201(2)	0.5569(2)	0.0201(5)
C8	0.0879(2)	0.5768(2)	0.5738(2)	0.0209(5)
C9	−0.0450(2)	0.6344(2)	0.6400(2)	0.0228(5)
C10	−0.1210(2)	0.7309(2)	0.5946(2)	0.0251(6)
H10	−0.0873	0.7584	0.5207	0.03*
C11	−0.2437(3)	0.7866(2)	0.6549(2)	0.0285(6)
H11	−0.2937	0.8518	0.6225	0.034*
C12	−0.2940(2)	0.7474(2)	0.7630(2)	0.0276(6)
C13	−0.2212(3)	0.6521(3)	0.8094(2)	0.0303(6)
H13	−0.2554	0.6251	0.8834	0.036*
C14	−0.0974(3)	0.5953(2)	0.7478(2)	0.0266(6)
H14	−0.0484	0.5292	0.78	0.032*
C15	0.2921(2)	0.2555(2)	0.6982(2)	0.0260(6)
C16	0.3383(3)	0.1292(3)	0.6972(3)	0.0368(7)
H16	0.3875	0.0874	0.6282	0.044*
C17	0.3129(3)	0.0647(3)	0.7958(3)	0.0503(9)
H17	0.3439	−0.0215	0.7946	0.06*
C18	0.2429(3)	0.1250(4)	0.8955(3)	0.0540(10)
H18	0.2255	0.0806	0.9635	0.065*

Table 2 (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
C19	0.1976(3)	0.2507(4)	0.8971(3)	0.0487(9)
H19	0.1493	0.2919	0.9668	0.058*
C20	0.2214(3)	0.3179(3)	0.7985(2)	0.0339(7)
H20	0.1901	0.404	0.7999	0.041*
C21	0.6313(2)	0.4085(2)	0.2102(2)	0.0255(6)
C22	0.7232(3)	0.3281(3)	0.2551(3)	0.0342(7)
H22	0.708	0.3173	0.3352	0.041*
C23	0.8365(3)	0.2638(3)	0.1843(3)	0.0491(8)
H23	0.898	0.2089	0.2159	0.059*
C24	0.8600(3)	0.2795(3)	0.0676(3)	0.0519(9)
H24	0.9356	0.2329	0.0186	0.062*
C25	0.7729(3)	0.3635(3)	0.0229(3)	0.0474(8)
H25	0.7907	0.3772	−0.0567	0.057*
C26	0.6599(3)	0.4276(3)	0.0933(2)	0.0355(7)
H26	0.601	0.4853	0.0615	0.043*
C27	0.2408(2)	0.7480(2)	0.27376(19)	0.0208(5)
C28	0.3101(3)	0.8401(2)	0.2293(2)	0.0260(6)
H28	0.4008	0.8315	0.2297	0.031*
C29	0.2481(3)	0.9438(3)	0.1845(2)	0.0354(7)
H29	0.2965	1.0059	0.1544	0.043*
C30	0.1166(3)	0.9577(3)	0.1834(2)	0.0397(7)
H30	0.0744	1.0291	0.1526	0.048*
C31	0.0464(3)	0.8675(3)	0.2270(2)	0.0337(7)
H31	−0.0442	0.8769	0.2261	0.04*
C32	0.1074(2)	0.7634(2)	0.2720(2)	0.0258(6)
H32	0.0582	0.7018	0.3021	0.031*
C33	−0.4688(3)	0.7846(3)	0.9295(2)	0.0446(8)
H33A	−0.474	0.697	0.9352	0.067*
H33B	−0.557	0.834	0.9551	0.067*
H33C	−0.4114	0.8049	0.9776	0.067*
N1	0.13625(19)	0.63455(18)	0.48237(16)	0.0208(4)
N2	0.1464(2)	0.47145(18)	0.61433(16)	0.0223(5)
N3	0.3293(2)	0.3161(2)	0.59496(18)	0.0260(5)
O1	−0.41672(18)	0.81029(19)	0.81495(17)	0.0391(5)
H3	0.406(3)	0.275(3)	0.555(2)	0.032(8)*
C1S	0.7064(3)	0.1106(2)	0.4862(2)	0.0327(6)
C2S	0.8446(3)	0.0641(3)	0.4805(3)	0.0376(7)
H2S1	0.8925	0.1329	0.4733	0.056*
H2S2	0.8805	0.0075	0.4142	0.056*
H2S3	0.8543	0.0203	0.5502	0.056*
N1S	0.5979(3)	0.1485(2)	0.4909(2)	0.0453(7)

a mixture of ice and ammonia. The resulting precipitate was filtered and washed with water followed by ice-cold ethanol. The product was dried in an oven to afford 4-chloro-2-(4-methoxyphenyl)-6,8-diphenylquinazoline. The 4-chloro-2-(4-methoxyphenyl)-6,8-diphenylquinazoline (0.40 g, 0.9 mmol) was in turn reacted with aniline (15 mL) under reflux at 120 °C for 4 h to afford the title compound (0.4 g, 95%), mp. 176–178 °C; ν_{max} (ATR) 754, 804, 831, 1034, 1156, 1213, 1247, 1471, 1504, 1562, 1597, 3436 cm^{-1}; **^{1}H NMR** (500 MHz, DMSO-d_6) 3.81 (s, 3H), 7.03 (d, *J* 8.7Hz, 2H), 7.20 (t, *J* 7.5 Hz, 1H), 7.45–7.56 (m, 8H), 7.80 (d, *J* 8.7 Hz, 2H), 7.96–7.99 (m, 4H), 8.17 (d, *J* 1.8 Hz, 1H), 8.28 (d, *J* 7.5 Hz, 2H), 8.96 (d, *J* 1.8 Hz, 1H), 10.02 (s, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) 55.7, 114.3, 115.0, 120.5, 122.9, 124.2, 127.7, 127.8, 128.2, 128.4, 129.0(2xC), 129.5, 130.0, 131.4, 131.5, 132.6, 137.3, 139.2, 139.6, 139.8, 139.9, 147.9, 158.8, 161.6; *m/z* 480 (MH^+). HRMS (ESI): found: 480.2071. $C_{33}H_{26}N_3O$ requires 480.1998. Crystals were obtained by recrystalization from acetonitrile.

Experimental details

The crystal structure was solved using direct methods [3]. Hydrogen atoms were positioned geometrically and allowed to ride on their respective parent atoms with d(C—H) = 0.95 Å and $U_{iso}(H) = 1.2U_{eq}(C)$.

Discussion

4-Amino–substituted quinazolines constitute an important class of compounds with a wide-ranging applications in the field of medicine and materials [6]. Continued interest in the synthesis of quinazoline derivatives substituted with a primary amino group at the 4-position stems from their importance as selective inhibitors of the epidermal growth factor receptor (EGFR) tyrosine kinase phosphorylation resulting from competitive binding at the ATP site [7]. In pharmaceutical industry, it is not only important to obtain the active ingredients in pure form, but also to have the knowledge of all possible forms of a drug in the solid state, because different forms can influence the physicochemical properties [8]. In this structure, the solvate (acetonitrile) is hydrogen bonded to the N—H group N(3)···N(1S) 3.113(3) Å; <N(3)H(3)N(1S) 167° (*cf*. the figure). In the crystal, the compound adopts the *anti*-orientation (*anti*-5) of the 4-phenylamino group with respect to the quinazoline 5-position to minimize steric interaction with C_{quinaz}-N and N—Ph torsion angles N(2)—C(7)—N(3)—C(15) = −6.2° and C(20)—C(15)—N(3)—C(7) = −31.9°, respectively. Moreover, the anti-arrangement of the *N*-phenyl ring enables hydrogen bonding. The 8-aryl ring, on the other hand, is strongly deformed out of plane of the quinazoline moiety (average torsion angle *ca*. −43°) to avoid steric interaction between its *ortho* hydrogen atoms and quinazoline H-7. The slight twist of the 6-aryl ring from co-planarity minimizes steric interaction with hydrogen atoms on C3 (H-7) and C5 (H-5). The same is true for the 2-aryl moiety.

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