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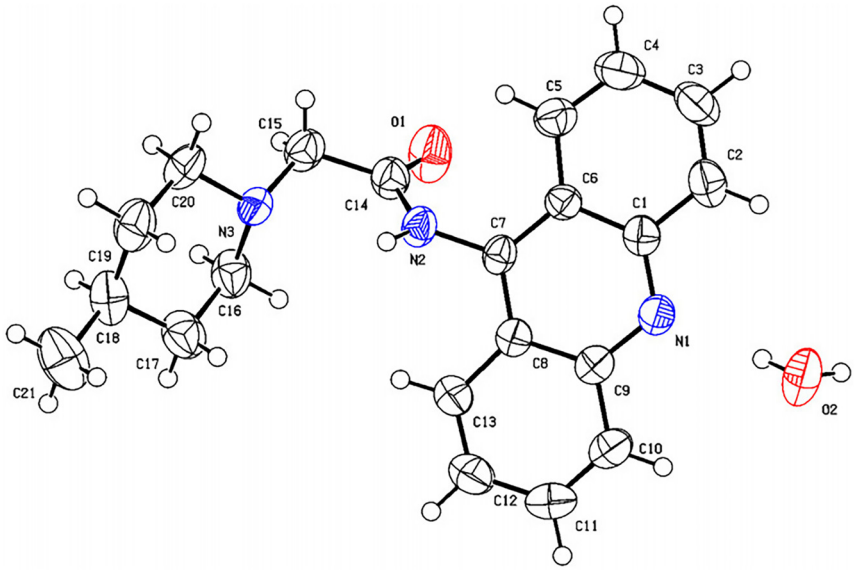
Crystal structure of *N*-(acridin-9-yl)-2-(4-methylpiperidin-1-yl) acetamide monohydrate, $C_{21}H_{25}N_3O_2$



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Abstract

$C_{21}H_{25}N_3O_2$, triclinic, $P\bar{1}$ (no. 2), a = 7.6536(6) Å, b = 11.027(1) Å, c = 12.6899(11) Å, α = 66.863(2)°, β = 80.598(2)°, γ = 71.772(2)°, V = 934.38(14) Å^3, Z = 2, $R_{gt}(F)$ = 0.0679, w$R_{ref}(F^2)$ = 0.1150, T = 296 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.

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1 Source of materials

The mixture of *N*-(9-Acridinyl)-2-chloroacetamide (2.70 g, 10 mmol), 4-methylpiperidine (1.49 g, 15 mmol), K_2CO_3 (2.76 g,

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.22 × 0.20 × 0.18 mm
Wavelength:	MoKα radiation (0.71073 Å)
μ:	0.08 mm^{-1}
Diffractometer, scan mode:	Bruker D8 Quest, Φ and ω,
θ_{max}, completeness:	25.1°, 98 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	18493, 3284, 0.073
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1852
$N(param)_{refined}$:	242
Programs:	SHELX [1, 2]

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.1498 (4)	0.5873 (3)	0.5096 (2)	0.0411 (7)
C2	0.0292 (4)	0.7131 (3)	0.4432 (3)	0.0553 (9)
H2	0.0233	0.7344	0.3650	0.066*
C3	−0.0759 (4)	0.8013 (3)	0.4919 (3)	0.0645 (10)
H3	−0.1553	0.8827	0.4475	0.077*
C4	−0.0673 (4)	0.7719 (3)	0.6092 (3)	0.0640 (9)
H4	−0.1401	0.8346	0.6416	0.077*
C5	0.0449 (4)	0.6541 (3)	0.6758 (3)	0.0514 (8)
H5	0.0484	0.6368	0.7534	0.062*
C6	0.1580 (3)	0.5560 (3)	0.6293 (2)	0.0375 (7)
C7	0.2803 (3)	0.4341 (3)	0.6916 (2)	0.0377 (7)
C8	0.3874 (3)	0.3447 (3)	0.6370 (2)	0.0380 (7)
C9	0.3690 (4)	0.3858 (3)	0.5169 (2)	0.0413 (7)
C10	0.4754 (4)	0.2968 (3)	0.4595 (3)	0.0534 (8)
H10	0.4654	0.3228	0.3811	0.064*
C11	0.5904 (4)	0.1753 (3)	0.5177 (3)	0.0614 (9)
H11	0.6587	0.1178	0.4793	0.074*
C12	0.6080 (4)	0.1348 (3)	0.6360 (3)	0.0620 (9)
H12	0.6875	0.0503	0.6751	0.074*
C13	0.5116 (4)	0.2162 (3)	0.6937 (3)	0.0495 (8)
H13	0.5268	0.1877	0.7718	0.059*
C14	0.1755 (4)	0.3769 (3)	0.8936 (2)	0.0475 (8)
C15	0.2285 (4)	0.3539 (3)	1.0112 (2)	0.0509 (8)
H15A	0.1906	0.4410	1.0219	0.061*
H15B	0.1620	0.2939	1.0689	0.061*
C16	0.4765 (4)	0.1480 (3)	1.0505 (3)	0.0564 (9)
H16A	0.4396	0.1338	0.9876	0.068*
H16B	0.4126	0.1019	1.1202	0.068*
C17	0.6816 (4)	0.0868 (3)	1.0625 (3)	0.0630 (9)
H17A	0.7450	0.1287	0.9909	0.076*
H17B	0.7120	−0.0106	1.0779	0.076*
C18	0.7477 (4)	0.1082 (3)	1.1583 (3)	0.0621 (9)
H18	0.6898	0.0591	1.2308	0.075*
C19	0.6818 (4)	0.2595 (4)	1.1383 (3)	0.0643 (9)
H19A	0.7125	0.2737	1.2030	0.077*
H19B	0.7463	0.3086	1.0704	0.077*
C20	0.4769 (4)	0.3184 (3)	1.1229 (3)	0.0567 (9)
H20A	0.4112	0.2762	1.1933	0.068*
H20B	0.4432	0.4162	1.1068	0.068*
C21	0.9552 (5)	0.0514 (4)	1.1671 (4)	0.0948 (13)
H21A	1.0146	0.0986	1.0970	0.142*
H21B	0.9899	−0.0447	1.1801	0.142*
H21C	0.9921	0.0645	1.2298	0.142*
N1	0.2539 (3)	0.5046 (2)	0.45495 (19)	0.0437 (6)
N2	0.3063 (3)	0.4002 (2)	0.80914 (19)	0.0431 (6)
H2A	0.4127	0.3942	0.8276	0.052*
N3	0.4239 (3)	0.2942 (2)	1.02904 (18)	0.0414 (6)
O1	0.0202 (3)	0.3806 (2)	0.87866 (18)	0.0693 (7)
O2	0.3077 (3)	0.6093 (3)	0.21203 (18)	0.0691 (7)
H2WB	0.219 (4)	0.614 (4)	0.178 (3)	0.104*
H2WA	0.280 (5)	0.574 (4)	0.2824 (17)	0.104*

20 mmol), KI (1.66 g, 10 mmol) and DMF (15 ml) was reacted at 25 °C for 12 h. After the reaction completed (monitored by TLC), extracted with ethyl acetate and water. The organic layer was washed with water, dried over sodium sulfate, and concentrated in vacuo. The crude complex was obtained by preparative TLC separation using petroleum ether/ethyl acetate (3:1, v/v) as the eluent. Yield 75.5 %. The product was dissolved in ethyl acetate and the crystals of the title compound were obtained by slow evaporation at room temperature for 2 days.

2 Experimental details

The structure was solved by Direct Methods and refined with the SHELX [1, 2] crystallographic software package. Hydrogen atoms were placed in their geometrically idealized positions and constrained to ride on their parent atoms. The crystal structure visualization was generated using the OLEX2 software package.

3 Comment

In recent years, antibacterial, anti-tumor and anti-malaria activities of 9-aminoacridine derivatives have been successively discovered [3–7]. Moreover, prior to these findings, 9-aminoacridine [8] amsacridine [9] ethacridine [10] acriflavine [11, 12] had been applied in clinical practice. However, compounds containing acridine moieties generally have lower water solubility and *in vivo* bioavailability [13]. Adding hydrophilic groups is an effective method to increase the solubility of compounds [14–16]. Therefore, we synthesized the title compound by introducing methylpyridine into 9-aminoacridine.

The asymmetric unit contains two molecules of N-(acridin-9-yl)-2-(4-methylpiperidin-1-yl) acetamide and two molecules of water. H(2WA) and H(2WB) of water molecules form hydrogen bonds with N1 and N3. 4-methylpiperidine moieties exist in a chair conformation, which is often the lowest energy state. The bond lengths of C(7)–N(2), C(14)–O(1), C(15)–N(3) are 1.449(3), 1.220(3) and 1.420(3) Å, respectively. The dihedral angles formed by the acridine ring N1–C1–C2–C3–C4–C5–C6–C7–C8–C9–C10–C11–C12–C13 plane, the piperidine group N3–C16–C17–C18–C19–C20 plane and the amide group N2–C14–O2 plane are 45.3° and 64.654°. 3-(difluoromethyl)-1-methyl-*N*-(4,11,11-trimethyl-1,2,3,4-tetrahydro-1,4-methanoacridin-9-yl)-1*H*-pyrazole-4-carboxamide monohydrate (CCDC no. 2153613) has the similar chemical structure to the title compound [17]. There are some differences in the bond length and bond angle of the C–N bond formed by the amino group on the quinoline moieties of the two compounds. The C–N bond lengths of the title compound are 1.420 Å (C7–N2)

and 1.346 Å (N2–C14), and that of 3-(difluoromethyl)-1-methyl-*N*-(4,11,11-trimethyl-1,2,3,4-tetrahydro-1,4-methanoacridin-9-yl)-1*H*-pyrazole-4-carboxamide monohydrate are 1.429 Å (C7–N2) and 1.339Å (N2–C18). The bond angles of the title compound and 3-(difluoromethyl)-1-methyl-*N*-(4,11,11-trimethyl-1,2,3,4-tetrahydro-1,4-methanoacridin-9-yl)-1*H*-pyrazole-4-carboxamide monohydrate are 124.4° (C7–N2–C14) and 121.63° (C7–N2–C18), respectively.

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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