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Crystal structure of 2-chloro-3-(isopentylamino) naphthalene-1,4-dione, $C_{15}H_{16}ClNO_2$

Table 1: Data collection and handling.

Crystal:	Red needle
Wavelength:	Size $0.47 \times 0.12 \times 0.11$ mm Mo $K\alpha$ radiation ($0.71073 \text{ \AA}$)
μ :	0.27 mm^{-1}
Diffraction, scan mode:	φ and ω
$\theta_{\max}$, completeness:	27.5° , >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	14672, 3219, 0.057
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2\sigma(I_{\text{obs}})$, 2111
$N(\text{param})_{\text{refined}}$:	178
Programs:	Bruker [1], SHELX [2, 3]

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Abstract

$C_{15}H_{16}ClNO_2$, triclinic, $P\bar{1}$ (no. 2), $a = 7.4339(12) \text{ \AA}$, $b = 8.2564(14) \text{ \AA}$, $c = 12.184(2) \text{ \AA}$, $\alpha = 108.804(6)^\circ$, $\beta = 93.672(5)^\circ$, $\gamma = 94.373(6)^\circ$, $V = 702.8(2) \text{ \AA}^3$, $Z = 2$, $R_{\text{gt}}(F) = 0.0650$, $wR_{\text{ref}}(F^2) = 0.1974$, $T = 273 \text{ K}$.

CCDC no.: 2103275

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.

Source of material

The educts 2,3-dichloro-1,4-naphthoquinone (dichlone, 0.22 mmol) and NaHCO_3 (0.44 mmol) were mixed uniformly

and moved to a 100 ml double necked round bottom flask. Isoamylamine (0.22 mmol, diluted with 40 mL of anhydrous methanol) was added to above mixed solid to start reaction with magnetic stirring at 0°C in anhydrous environment. The products were monitored by TLC using petroleum ether ($60\text{--}90^\circ \text{C}$ boiling range)/acetic ether (5:1 v/v) as developing phase. After 24 h, the reacting mixture was concentrated by a rotary evaporator at 60°C to give a crude solid, which was subsequently extracted by chloroform to achieve a clear red solution after filtration. Finally, red colored crystals were obtained from this solution by room temperature volatilization. The melting point was determined as $377\text{--}378 \text{ K}$ using a XT-4 melting point instrument (Beijing Taike Instrument Co., Ltd, China). NMR spectra were recorded using a DRX-500 spectrometer (Bruker, Germany). HRAPCI-MS: $[M]^-$ found 277.08725; $C_{15}H_{16}O_2NCl$ $[M]^-$ requires 277.08641. ^1H -NMR (500 MHz, CDCl_3) δ : [p.p.m.] 8.10–8.11 (1H, d, $J = 7.7 \text{ Hz}$, H-6), 7.97–7.99 (1H, d, $J = 7.7 \text{ Hz}$, H-9), 7.66–7.70 (1H, td, $J = 7.6, 1.0 \text{ Hz}$, H-7), 7.56–7.59 (1H, td, $J = 7.6, 1.0 \text{ Hz}$, H-8), 3.81–3.85 (2H, m, H-11), 1.63–1.74 (1H, m, H-13), 1.53–1.57 (2H, m, H-12), 0.91–0.95 (6H, d, $J = 6.6 \text{ Hz}$, H-14 and 15). ^{13}C -NMR and DEPT 135 (125 MHz, CDCl_3) δ : [p.p.m.] 180.5 (qC, C-1), 176.8 (qC, C-4), 144.2 (qC, C-3), 134.9 (CH, C-7), 132.8 (qC, C-10), 132.4 (CH, C-8), 129.7 (qC, C-5), 126.8 (CH, C-6), 126.8 (CH, C-9), 43.3 (CH_2 , C-11), 39.9 (CH_2 , C-12), 25.8 (CH, C-13), 22.5 (CH_2 , C-14 and 15). ^1H was assigned to ^{13}C by HSQC correlations. In the HMBC spectrum, the correlations of H-9 with C-1, 7; H-7 with C-5; H-6 with C-4, 8; H-11 with C-3, 12, 13; H-12 with C-11, 13, 14, 15; H-13 with C-12, 14, 15; H-14, 15 with C-12, 13 were observed.

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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}
C1	0.2951 (3)	0.2482 (3)	0.9100 (2)	0.0498 (6)
C2	0.4437 (3)	0.3022 (3)	0.85496 (19)	0.0438 (6)
C3	0.6218 (3)	0.3226 (3)	0.89986 (18)	0.0407 (5)
C4	0.6629 (3)	0.2939 (3)	1.0150 (2)	0.0452 (6)
C5	0.5144 (3)	0.2296 (3)	1.0696 (2)	0.0458 (6)
C6	0.5497 (4)	0.1871 (3)	1.1697 (2)	0.0588 (7)
H6	0.6681	0.2009	1.2034	0.071 [*]
C7	0.4107 (5)	0.1247 (4)	1.2195 (2)	0.0668 (8)
H7	0.4355	0.0952	1.2860	0.080 [*]
C8	0.2352 (4)	0.1062 (3)	1.1705 (3)	0.0663 (8)
H8	0.1415	0.0636	1.2038	0.080 [*]
C9	0.1975 (4)	0.1506 (3)	1.0722 (2)	0.0570 (7)
H9	0.0781	0.1406	1.0409	0.068 [*]
C10	0.3365 (3)	0.2101 (3)	1.0195 (2)	0.0450 (6)
C11	0.8048 (3)	0.4157 (3)	0.7568 (2)	0.0500 (6)
H11A	0.9129	0.4966	0.7747	0.060 [*]
H11B	0.7037	0.4747	0.7403	0.060 [*]
C12	0.8273 (4)	0.2676 (3)	0.6491 (2)	0.0546 (6)
H12A	0.7180	0.1881	0.6293	0.066 [*]
H12B	0.9267	0.2067	0.6656	0.066 [*]
C13	0.8649 (4)	0.3257 (4)	0.5453 (2)	0.0663 (8)
H13	0.9667	0.4161	0.5710	0.080 [*]
C14	0.7050 (6)	0.4038 (5)	0.5061 (3)	0.0935 (11)
H14A	0.5996	0.3217	0.4868	0.140 [*]
H14B	0.7317	0.4344	0.4388	0.140 [*]
H14C	0.6825	0.5048	0.5677	0.140 [*]
C15	0.9208 (7)	0.1841 (6)	0.4459 (3)	0.1187 (17)
H15A	0.9412	0.2256	0.3823	0.178 [*]
H15B	0.8267	0.0901	0.4215	0.178 [*]
H15C	1.0304	0.1455	0.4702	0.178 [*]
Cl1	0.37878 (9)	0.32735 (10)	0.72237 (5)	0.0664 (3)
N1	0.7733 (3)	0.3660 (3)	0.85855 (18)	0.0520 (6)
O1	0.1372 (2)	0.2296 (3)	0.86772 (18)	0.0747 (6)
O2	0.8179 (2)	0.3235 (3)	1.05979 (15)	0.0646 (5)
H16	0.860 (4)	0.359 (4)	0.899 (3)	0.061 (8) [*]

^{*}The H atoms were placed in idealized positions and treated as riding on their parent atoms, with $d(C-H) = (0.96) \text{ \AA}$ (methyl), $U_{iso}(H) = 1.5 U_{eq}(C)$, $d(C-H) = (0.97) \text{ \AA}$ (methylene), $U_{iso}(H) = 1.2 U_{eq}(C)$, $d(C-H) = (0.98) \text{ \AA}$ (methine), $U_{iso}(H) = 1.2 U_{eq}(C)$, $d(C-H) = (0.93) \text{ \AA}$ (aromatic), $U_{iso}(H) = 1.2 U_{eq}(C)$, and $d(N-H) = (0.80(3)) \text{ \AA}$ (secondary amine), $U_{iso}(H) = 1.2 U_{eq}(N)$.

Experimental details

H atoms bonded to C and N atoms were positioned geometrically with $d(N-H) = 0.80 \text{ \AA}$, $d(C-H) = 0.93 \text{ \AA}$ (aromatic CH), $0.98 \text{ \AA}$ (methenyl CH), $0.97 \text{ \AA}$ (methylene CH₂) or $0.96 \text{ \AA}$ (methyl CH₃), and treated as riding atoms. For all H atoms, isotropic displacement parameters were assigned as $U_{iso}(H) = 1.2 U_{eq}(N, C)$.

Comment

Side chain homologated derivatives of 2-chloro-3-(*n*-alkylamino)-1,4-naphthoquinone (such as 2-(*n*-butylamino)-3-chloronaphthalene-1,4-dione) manifested various biological activities, which included anti-inflammatory/antiallergic activity (inhibitory effect on the release of β -glucuronidase and lysozyme from neutrophils) [4], antiproliferative/anticancer activity [5, 6], aromatase inhibitory activity (for anti-breast-cancer use) [7], antifungal activity [8] and so on. The drug 2-isopentylamino-1,4-naphthoquinone, with hydrogen substitution instead of chlorine at 2-position of the title compound, displayed full protection in a rodent pharmacoresistant seizure model with limited rotarod motor toxicity and favorable pharmacokinetic properties [9]. In the course of our research, the title compound was synthesized for anticancer investigation, in which its interactions with Caspase-3 and Topoisomerase-II α/β will be tested, so it is necessary to study the single-crystal structure.

According to the absence of 2-carbon signal in its ¹³C-NMR spectrum, which may be caused by neighboring Cl or N atom, it is extremely necessary to determine the title structure through single-crystal diffraction experiments. Otherwise, the literature merely reports its ¹H NMR, but not ¹³C-NMR [10]. The title crystal structure is only built up by the C₁₅H₁₆ClNO₂ molecules, in which all values of the geometric parameters are normal. The crystal packing is stabilized by intermolecular hydrogen bonds: N1—H16O $\cdots$ O2 ($d(N1-H16O\cdots O2) = 2.591 \text{ \AA}$; $\angle N1-H16O\cdots O2 = 118.02^\circ$). N1—H16O $\cdots$ O1 ($d(N1-H16O\cdots O1) = 3.017 \text{ \AA}$; $\angle N1-H16O\cdots O1 = 135.98^\circ$).

By similar molecular scaffold searching, eight crystals with 2-Cl replaced by fatty amines were found, among which, six were *n*-alkyl amine (methyl, ethyl, propyl, butyl, hexyl and octyl amine) substituted products, the other two were dimethylamine alkyl amine substitutions (2-chloro-3-(3-di-methyl-amino-propyl-amino)-1,4-naphthoquinone [11] and the corresponding hydrochloride [12, 13]). The title compound, 2-Cl replaced by *gem*-dimethyl-amine, was somewhat similar in spatial structure to those substituted by dimethylamine amine.

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