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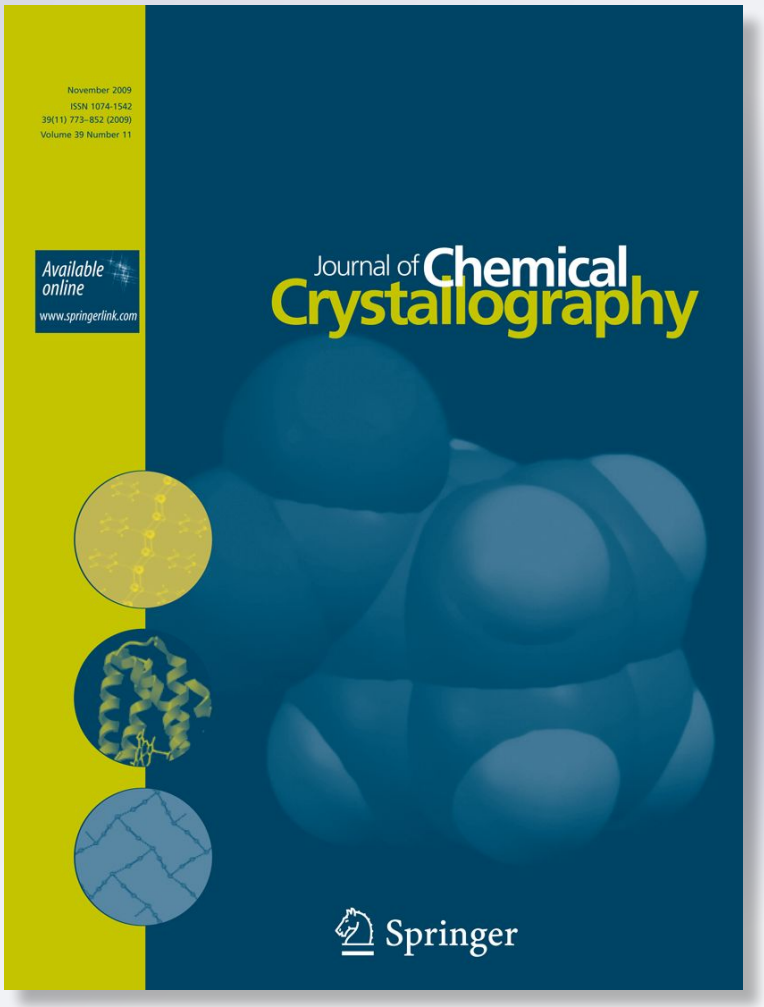

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ORIGINAL PAPER

Synthesis of New Cyano-Quinoline Derivatives by the Baylis–Hillman Reaction

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Abstract Quinoline derivatives represent the major class of heterocycles, and a number of preparations have been known since the late 1800s. The quinoline ring system occurs in various natural products, especially in alkaloids. The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmacological properties. A new quinoline derivative was crystallized from the reaction between acrylonitrile and 2-chloro-3-formyl quinoline derivatives which had themselves been prepared from the Meth Cohn method. The reaction catalyzed by DABCO, gives rise to five new 2-[2-Chloro-quinolin-3-yl)-hydroxy-methyl]-acrylonitrile derivatives. The crystal structure of the 7-Methyoxy-substituted one crystallizes in monoclinic space group C2/c, a = 17.1090 (7) Å, b = 8.3119 (5) Å, c = 19.7949 (6) Å, β = 101.922 (2)°, and its cohesion was assured by O–H···N, O–H···O and C–H···O hydrogen bonds.

Keywords Quinoline derivatives · Baylis–Hillman reaction · Crystal structure · Hydrogen bond · Graph set

Introduction

The quinoline ring system is a common structural component of a wide variety of natural or synthetically prepared products with highly desirable biological activity [1–3]. It is a heterocyclic scaffold of paramount importance to human race. Indeed, quinoline derivatives are some of the oldest compounds which have been utilized for the treatment of a variety of diseases.

The bark of Cinchona plant (also known as Jesuit's or Cardinal's bark) containing quinine was utilized to treat palpitations [4] fevers and tertians since more than 200 years ago. Quinidine, a diastereoisomer of quinine was in the early 20th century acknowledged as the most potent of the antiarrhythmic compounds isolated from the Cinchona plant [5].

Compounds containing quinoline motif are most widely used as antimalarials [6–12], antibacterials [13–17], antifungals [18–20], anti VIH [21, 22] and antitumor agents [23–27]. They have antiseptic, antipyretic and antiperiodic properties [28]. Substituted quinolines play also an important role as receptor antagonists of endothelin [29], 5HT3 [30], NK-3 [31] and leucotriens [32, 33]. Those compounds are used as inhibitors of tyrosine kinase PDGFRTK [34], (H^+/K^+)-ATPase [35], dihydrorotate deshydrogenase [36, 37] and 5-lipoxygenase [38].

Additionally, quinoline derivatives find use in the synthesis of fungicides, virucides, biocides, alkaloids, rubber chemicals and flavoring agents [39, 40]. They are also used as polymers, catalysts, corrosion inhibitors, preservatives, and as solvent for resins and terpenes [41]. Furthermore, these compounds find applications in chemistry of transition-metal catalyst for uniform polymerization and luminescence chemistry [42, 43]. Quinoline derivatives also act as antifoaming agent in refineries [44]. Owing to such significance, the synthesis of substituted quinolines has been a subject of great focus in organic chemistry.

Owing to the interesting biological properties of heterocyclic systems [45–48], this paper aims to describe the

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synthesis and the structure of cyanoquinolines obtained from the Baylis–Hillman derivatives [49]. Those adducts are the result of the Baylis–Hillman reaction of an aldehyde with α, β-unsaturated systems catalyzed by 1,4-diazabicyclo[2]octane (DABCO).

Experimental

Synthesis of Quinoline Derivatives

General Procedure

Baylis–Hillman adducts (**2a–2e**) were prepared from the reaction of 2-chloro-3-formyl quinoline derivatives (**1**), previously obtained from the Meth Cohn procedure [50], and acrylonitrile catalyzed by DABCO (Fig. 1, Table 1). These compounds were obtained according to the literature methods published in the paper of Narender et al. [51].

*Synthesis of 2-[2-Chloro-Quinolin-3-yl)-Hydroxy-Methyl]-Acrylonitrile **2a***

To a stirred solution of 2-chloro-3-Formyl-quinoline (0.5 g; 2.61 mmol) in acrylonitrile (2 ml; 30.40 mmol) was added DABCO (2.61 mmol; 0.292 g) at room temperature and the reaction was allowed to continue for 15 min. The final product was purified via silica gel column chromatography with Petroleum Ether/ethyl acetate (85:15, v/v) as eluent to furnish pure beige crystals in 80 % yield (0.51 g; m.*p* = 116 °C). $R_f = 0.37$ (ethyl acetate/

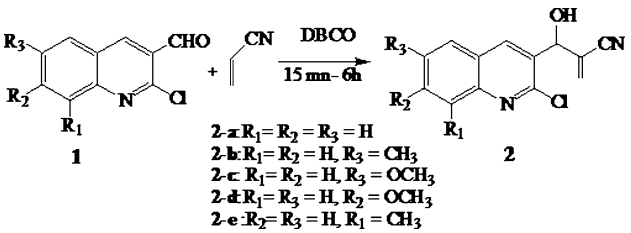

Fig. 1 Synthesis reaction of the compounds **2a–2e**

Table 1 Synthesis of Baylis–Hillman (BH) adducts

Compound	R_1	R_2	R_3	Time (min)	m.p (°C)	Yield[a]
2a	H	H	H	15	115	80
2b	H	H	CH_3	15	148	89
2c	H	H	OCH_3	45	109	71
2d	H	OCH_3	H	360	96	74
2e	CH_3	H	H	15	112	75

[a] Isolated yield of pure product

Petroleum Ether (3/7)). I.R (KBr; *v* cm^{-1}): 3,191(OH), 2,235 (CN), 1613 (C = C). 1H NMR (400 MHz, CDCl3): δ 8.50 (t, 1H, *J* = 1.0 Hz, H–C_3), 8.00 (ddt, 1H, *J* = 8.5, 1.1, 0.7 Hz, H–C_9), 7.86 (ddt, 1H, *J* = 8.1, 1.4, 0.5 Hz, H–C_6), 7.76 (ddd, 1H, *J* = 8.5, 7.0, 1.4 Hz, H–C_8), 7.58 (ddd, 1H, *J* = 8.1, 7.0, 1.2 Hz, H–C_7), 6.15 (d, 1H, *J* = 1.1 Hz, C = $C\underline{H}_2$), 6.11 (d, 1H, *J* = 0.7 Hz, C = $C\underline{H}_2$), 5.85 (dq, 1H, *J* = 4.3, 0.9 Hz, C<u>H</u>OH), 4.13 (d, 1H, *J* = 4.3 Hz, OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.32 ($C_q$uat, C_1), 147.20 (C_{quat}, C_5), 137.56 (<u>C</u>H, C_3), 132.45 (C = <u>C</u>H_2), 131.33 (<u>C</u>H, C_8), 130.95 (C_{quat}, C_2), 128.15 (<u>C</u>H, C_6), 127.85 (<u>C</u>H, C_9), 127.67 (<u>C</u>H, C_7), 127.14 (C_{quat}, C_4), 124.28 (C_{quat}, <u>C</u> = CH_2), 116.39 (C_{quat}, <u>C</u>N), 70.43 (<u>C</u>HOH).

*Synthesis of 2-[(2-Chloro-6-Methyl-Quinolin-3-yl)-Hydroxy-Methyl]-Acrylonitrile **2b***

White single crystals were grown from the mixture of 2-chloro-3-Formyl-6-methyl quinoline (0.5 g; 2.43 mmol), DABCO (0.272 g; 2.43 mmol) and acrylonitrile (1.9 ml; 28.94 mmol). Purification of the resulting product was performed via silica gel column chromatography with the eluent Petroleum Ether/ethyl acetate (85:15, v/v) to obtain finally 0.56 g of the compound **2b** (89 % yield). $R_f = 0.41$ (ethyl acetate/Petroleum Ether (3/7)). m.*p* = 154 °C. I.R (KBr; *v* cm^{-1}): 3,494 (OH), 2,223 (CN), 1,582 (C = C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (t, 1H, *J* = 1.0 Hz, H–C_3), 7.91 (dt, 1H, *J* = 8.6, 0.9 Hz, H–C_9), 7.66–7.62 (m, 1H, H–C_6), 7.59 (dd, 1H, *J* = 8.6, 1.9 Hz, H–C_8), 6.16 (d, 1H, *J* = 1.1 Hz, C = $C\underline{H}_2$), 6.13 (d, 1H, *J* = 0.7 Hz, C = $C\underline{H}_2$), 5.84 (d, 1H, *J* = 3.6 Hz, C<u>H</u>OH), 3.44 (d, 1H, *J* = 4.2 Hz, OH), 2.54 (d, 3H, $C\underline{H}_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.36 (C_{quat}, C_1), 145.95 (C_{quat}, C_5), 137.80 (C_{quat}, C_7), 136.74 (<u>C</u>H, C_3), 133.57 (<u>C</u>H, C_8), 132.32 (C = <u>C</u>H_2), 130.59 (C_{quat}, C_2), 127.69 (<u>C</u>H, C_9), 127.19 (C_{quat}, C_4), 126.97 (<u>C</u>H, C_6), 124.31 (C_{quat}, <u>C</u> = CH_2), 116.34 (C_{quat}, <u>C</u>N), 70.65 (<u>C</u>HOH), 21.61 ($\underline{C}H_3$).

*Synthesis of 2-[(2-Chloro-6-Methyoxy-Quinolin-3-yl)-Hydroxy-Methyl]-Acrylonitrile **2c***

The derivative **2c** was prepared from the reaction of 2-chloro-3-Formyl-6-methoxy quinoline (0.5 g; 2,25 mmol) and acrylonitrile (3 ml; 54 mmol) catalyzed by DABCO (0.252 g; 2.25 mmol). We have obtained 0,44 g (m.*p* = 126 °C; yield = 71 %) of beige single cristals after purification via silica gel column chromatography with the eluent Petroleum Ether/ethyl acetate (85:15, v/v). $R_f = 0.61$ (ethyl acetate). I.R (KBr; *v* cm^{-1}): 3162 (OH), 2144 (CN), 1,623 (C = C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (td, 1H, *J* = 0.8, 0.3 Hz, H–C_3), 7.89 (dt, 1H, *J* = 9.2, 0.5 Hz, H–C_9), 7.40 (dd, 1H, *J* = 9.2, 2.8 Hz, H–C_8), 7.10 (d, 1H, *J* = 2.8 Hz, H–C_6), 6.17

(d, 1H, $J = 1.1$ Hz, C = C$\underline{H}_2$), 6.13 (d, 1H, $J = 0.7$ Hz, C = C$\underline{H}_2$), 5.84 (d, 1H, C$\underline{H}$OH), 3.92 (s, 3H, OC$\underline{H}_3$), 3.61 (d, 1H, $J = 4.1$ Hz, OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.49 (C_{quat}, C_7), 145.56 (C_{quat}, C_1), 143.33 (C_{quat}, C_5), 136.06 (CH, C_3), 132.32 (C = $\underline{C}H_2$), 130.91 (C_{quat}, C_2), 129.35 ($\underline{C}$H, C_9), 128.35 (C_{quat}, C_4), 124.29 (C_{quat}, $\underline{C}$ = CH_2), 124.14 ($\underline{C}$H, C_8), 116.35 (C_{quat}, $\underline{C}$N), 105.40 ($\underline{C}$H, C_6), 70.61 ($\underline{C}$HOH), 55.67 (O$\underline{C}H_3$).

Synthesis of 2-[(2-Chloro-7-Methyoxy-Quinolin-3-yl)-Hydroxy-Methyl]-Acrylonitrile ***2d***

A mixture of 2-chloro-3-Formyl-7-methoxy quinoline (0.5 g; 2.25 mmol), DABCO (0.252 g; 2.25 mmol) and acrylonitrile (5 ml; 90 mmol) has yielded coulorless single crystals of **2d** (0.46 g; 74 %; m. $p = 96$ °C) which have been recristallized from a dichloromethane, ethyle acetate and petroleum ether mixture after being purified via silica gel column chromatography with the eluent Petroleum Ether/ethyl acetate (85:15, v/v). $R_f = 0{,}44$ (ethyl acetate/Petroleum Ether (3/7)). I.R (KBr; ν cm^{-1}): 3,468 (OH), 2,255 (CN), 1,594 (C = C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H, H–C_3), 7.74 (d, 1H, $J = 9.0$ Hz, H–C_6), 7.32 (d, 1H, $J = 2.5$ Hz, H–C_9), 7.23 (dd, 1H, $J = 9.0$, 2.5 Hz, H–C7$_6$), 6.15 (d, 1H, $J = 1.1$ Hz, C = C$\underline{H}_2$), 6.13 (d, 1H, $J = 0.8$ Hz, C = C$\underline{H}_2$), 5.85–5.80 (s, 1H, C$\underline{H}$OH), 3.94 (s, 3H, OC$\underline{H}_3$), 3.63 (d, 1H, $J = 2.8$ Hz, OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.16 (C_{quat}, C_8), 149.32 (C_{quat}, C_1), 148.68 (C_{quat}, C_5), 136.94 ($\underline{C}$H, C_3), 132.07 (C = $\underline{C}H_2$), 129.09 ($\underline{C}$H, C_6), 128.16 (C_{quat}, C_2), 124.46 (C_{quat}, $\underline{C}$ = CH_2), 122.37 (C_{quat}, C_4), 120.85 ($\underline{C}$H, C_7), 116.46 (C_{quat}, $\underline{C}$N), 106.17 ($\underline{C}$H, C_9), 70.55 ($\underline{C}$HOH), 55.71 (O$\underline{C}H_3$).

Synthesis of 2-[(2-Chloro-8-Methyl-Quinolin-3-yl)-Hydroxy-Methyl]-Acrylonitrile ***2e***

To a 2-chloro-3-Formyl-8-methyl quinoline (0.5 g; 243 mmol) and acrylonitrile (1.9 ml; 28.94 mmol) solution was added DABCO (0.252 g; 2.43 mmol). The resulting compound was purified via silica gel column chromatography with the eluent Petroleum Ether/ethyl acetate (85:15, v/v) to give rise to 0.472 g of **2e** white single crystals in 75 % yield (m.$p = 112$ °C). $R_f = 0.43$ (ethyl acetate/petroleum ether (3/7)). I.R (KBr; ν cm^{-1}): 3,170 (OH), 2,226 (CN), 1,617 (C = C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 1H, H–C_3), 7.70 (ddt, 1H, $J = 8.1$, 1.2, 0.7 Hz, H–C_6), 7.60 (ddq, 1H, $J = 7.1$, 3.5, 1.0 Hz, H–C_8), 7.47 (dd, 1H, $J = 8.1$, 7.1 Hz, H–C_7), 6.15 (d, 1H, $J = 1.1$ Hz, C = C$\underline{H}_2$), 6.14 (d, 1H, $J = 0.8$ Hz, C = C$\underline{H}_2$), 5.83 (d, 1H, $J = 3.6$ Hz, C$\underline{H}$OH), 3.06 (d, 1H, $J = 4.3$ Hz, OH), 2.76 (t, 3H, $J = 0.9$ Hz, C$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.22 (C_{quat}, C_1), 146.71 (C_{quat}, C_5), 137.44 ($\underline{C}$H, C_3), 136.46 (C_{quat}, C_9), 132.39 (C = $\underline{C}H_2$), 131.27 ($\underline{C}$H, C_8), 130.19 (C_{quat}, C_2), 127.37 ($\underline{C}$H, C_7), 127.19 (C_{quat}, C_4), 125.99 ($\underline{C}$H, C_6), 124.23 (C_{quat}, $\underline{C}$ = CH_2), 116.36 (C_{quat}, $\underline{C}$N), 70.72 ($\underline{C}$HOH), 17.80 ($\underline{C}H_3$).

X-ray Structure Analysis

Diffraction Data Collection

The structure of **2d** has been determined by single-crystal X-ray diffraction analysis. X-ray diffraction intensities were collected at 170 K using an Oxford Diffraction Xcalibur CCD diffractometer with Mo Kα radiation ($\lambda = 0.71073$ Å), equipped with the required cooling, using ω–θ scan strategy. The complete data collection strategy is summarized in (Table 2).

Data Reduction

The unit cell determination and data reduction were performed using the CrysAlis program suite [52] on the full set of data.

Solution and Refinement

Calculations were carried out using the *WinGX* software package [53]. The crystal structure was solved by direct methods using *SIR2004* [54] and refined by full-matrix least-squares against F^2 using all data (*SHELXL97*) [55].

All non-H atoms were modelled with anisotropic displacement parameters. The H atoms attached to –CH_3 and –OH were located in difference Fourier maps refined as riding atoms (isotropically with a restrained bond distance) with distances constraints of methyle C–H = 0.96 Å and O–H = 0.82 Å [U_{iso}(H) = 1.5 U_{eq}(C,O)]. Except the water and the methylene hydrogen's, which were located from a difference Fourier syntheses and not refined. Aromatic H atoms were positioned geometrically and were allowed to ride on their parent C atoms with C–H = 0.93 Å and U_{iso}(H) = 1.2 U_{eq}(C). Water H atoms (O–Hw = 0.86 Å) were found with the program *CALC*-OH [56] and were refined with fixed bond distances and angles.

Table 2 Experimental details of the data collection

Oxford diffraction Xcalibur diffractometer	2,157 reflections with $I > 2\sigma(I)$
Radiation source: fine-focus sealed	$R_{int} = 0.0412$
Tube graphite	$\theta_{max} = 31.49°$, $\theta_{min} = 3.60°$
ω–θ scans	h = −22 → 24
13,706 measured reflections	k = −12 → 11
4,325 independent reflections	l = −27 → 29

Structure Analysis and Visualization Software

Crystal structure was visualized using *ORTEP3* [57] and *MERCURY* [58]. Analyses were carried out using the program *PLATON* [59], as incorporated in the *WinGX* [53] suite.

Spectroscopic Measurements

Infrared Analysis

The infrared spectrum has been carried out to analyse the chemical bonding and molecular structure of the compound. The FT-IR spectrum of the crystal was recorded in the frequency region from 400 to 4,000 cm^{-1} with a FT-IR NEXUS NICOLET Spectrometer.

^{1}H NMR and ^{13}C NMR Analysis

The ^{1}H and ^{13}CNMR spectra of **2d** were recorded on a Bruker 300 MHz instrument at 23 °C (300 MHz for ^{1}HNMR and 75 MHz for ^{13}CNMR) to confirm the molecular structure.

Results and Discussion

Crystal Structure Analysis

The obtained compound **2d** crystallizes in the centrosymmetric space group C2/c. Its asymmetric unit contains one 2-[(2-Chloro-7-Methyoxy-quinolin-3-yl)-hydroxy-methyl]-acrylonitrile molecule and one water molecule. The molecular structure of the quinoline derivative **2d** and the atom-labeling scheme are shown in (Fig. 2). The crystal and refinement data are given in (Table 3).

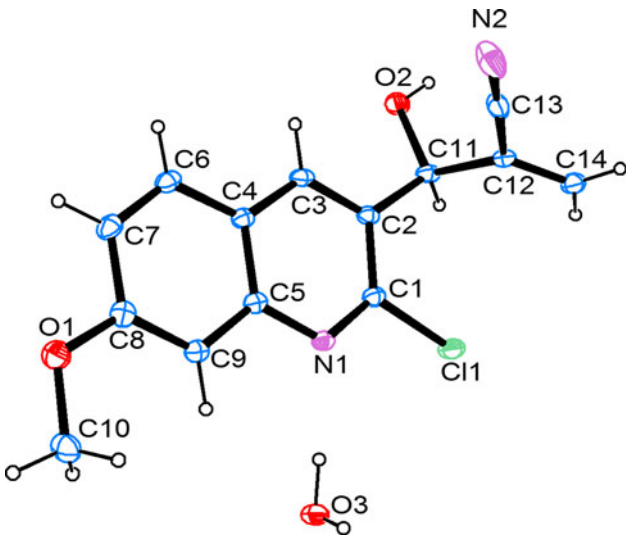

Fig. 2 Ortep3 view of the asymmetric unit. Ellipsoids are drawn at the 30 % probability level, hydrogen atoms are shown as spheres of arbitrary radii

Table 3 Crystal data and structure refinement for 2d

Crystal data	
$C_{14}H_{11}ClN_2O_2{\cdot}H_2O$	F(000) = 1.216
M_r = 292.71	D_x = 1.412 Mg m^{-3}
Monoclinic, C2/c	Mo K_α radiation, λ = 0.71073 Å
a = 17.1091 (7) Å	Cell parameters from 11058 reflections
b = 8.3119 (5) Å	θ = 3.60–31.49°
c = 19.7949 (6) Å	μ = 0.286 mm^{-1}
β = 101.922 (2)°	T = 170 K
V = 2754.3 (2) $Å^3$	Prism, colourless
Z = 8	0.25 × 0.18 × 0.05 mm
Refinement	
Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement
Least-squares matrix: Full	$w = 1/[\sigma^2(F_o^2) + (0.0566P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.0434$	where $p = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.0979$	$(\Delta/\sigma)max = 0.001$
S = 0.859	$\Delta\rho max = 0.367$ e $Å^{-3}$
4325 reflections	$\Delta\rho min = -0.328$ e $Å^{-3}$
182 parameters	
0 restraints	

The quinoline ring (C1–C9/N1) is almost planar, with a maximum deviation of 0.0495(18) Å for C6. The hydroxymethylacrylonitrile moiety lies in the mean plane of the quinoline (C11/C2/C1/N1 = −178.39 (15)°). The methoxy group is in the plane of the quinoline ring (C10/O1/C8/C9 = 1.8 (2)°).

The bond distances within the quinoline portion of the molecule show evidence for significant bond fixation; the N1–C1 bond (1.3081 (19) Å) is thus significantly shorter than N1–C5 (1.3709 (19) Å), while the C2–C3 (1.373 (2) Å), C6–C7 (1.353 (2) Å) and C8–C9 (1.370 (2) Å) bonds are all significantly shorter than the other aromatic C–C bonds. These distances compare well with the results observed in similar 2-chloroquinoline derivatives [60, 61]. Selected bond lengths and angles of the structure are given in Table 4.

The geometry within the 2-[(2-Chloro-7-Methyoxy-quinolin-3-yl)-hydroxy-methyl]-acrylonitrile molecule is usual, the bond lengths and angles are in good agreement with those observed in similar compounds [62, 63]. (2-Chloro-8-methoxyquinolin-3-yl)methanol monohydrate [64] and (2-Chloro-8-methylquinolin-3-yl)methanol [65] have showed similar bond distances and angles.

Table 4 Selected geometric parameters (Å, °)

Bond distances			
Cl1–C1	1.7417 (17)	C9–C8	1.370 (2)
N1–C1	1.3081 (19)	C8–C7	1.407 (2)
N1–C5	1.3709 (19)	O2–C11	1.4067 (18)
C4–C6	1.416 (2)	C14–C12	1.318 (2)
C5–C4	1.420 (2)	C11–C2	1.510 (2)
C6–C7	1.353 (2)	C11–C12	1.517 (2)
C4–C3	1.399 (2)	C12–C13	1.438 (2)
C5–C9	1.402 (2)	C13–N2	1.137 (2)
C2–C3	1.373 (2)	O1–C8	1.355 (2)
C2–C1	1.410 (2)	O1–C10	1.429 (2)
Bond angles			
C6–C7–C8	121.32 (16)	O2–C11–C2	108.64 (13)
C7–C6–C4	120.66 (15)	O2–C11–C12	109.05 (12)
C3–C4–C5	117.88 (14)	C2–C11–C12	111.04 (13)
C3–C4–C9	124.39 (16)	C14–C12–C13	119.97 (16)
C4–C5–C9	120.75 (15)	C14–C12–C11	124.94 (15)
C3–C2–C1	115.29 (15)	C13–C12–C11	114.97 (14)
C3–C2–C11	122.39 (14)	N2–C13–C12	177.6 (2)
C1–C2–C11	122.31 (14)	C8–O1–C10	116.72 (13)
C8–C9–C5	119.64 (15)	N1–C1–C2	126.28 (15)
C2–C3–C4	121.74 (14)	N1–C1–Cl1	114.52 (13)
C9–C8–C7	119.96 (16)	C2–C1–Cl1	119.20 (13)
C1–N1–C5	118.01 (13)	O1–C8–C9	125.41 (15)
N1–C5–C9	118.46 (14)	O1–C8–C7	114.63 (15)
N1–C5–C4	120.78 (14)	C6–C4–C5	117.61 (15)
Torsion angles			
O2–C11–C12–C14	118.11 (18)	C5–C4–C6–C7	−2.0 (2)
C2–C11–C12–C14	−122.22 (17)	C1–C2–C3–C4	−0.9 (2)
O2–C11–C12–C13	−58.03 (18)	C11–C2–C3–C4	178.63 (15)
C2–C11–C12–C13	61.64 (18)	C5–C4–C3–C2	−0.3 (2)
C14–C12–C13–N2	−135 (5)	C6–C4–C3–C2	178.79 (15)
C11–C12–C13–N2	42 (5)	C4–C5–C9–C8	−0.4 (2)
C1–N1–C5–C9	179.01 (14)	C5–N1–C1–C2	−0.1 (2)
C1–N1–C5–C4	−1.3 (2)	C5–N1–C1–Cl1	178.93 (11)
N1–C5–C9–C8	179.30 (14)	C3–C2–C1–N1	1.1 (2)
C4–C6–C7–C8	0.3 (2)	C11–C2–C1–N1	−178.39 (15)
N1–C5–C4–C3	1.5 (2)	C3–C2–C1–Cl1	−177.80 (12)
C9–C5–C4–C3	−178.84 (14)	C11–C2–C1–Cl1	2.7 (2)
N1–C5–C4–C6	−177.71 (14)	C10–O1–C8–C9	1.8 (2)
C6–C5–C4–C9	2.0 (2)	C10–O1–C8–C7	−178.40 (15)
O2–C11–C2–C3	15.2 (2)	C5–C9–C8–O1	−178.49 (16)
C12–C11–C2–C3	−104.75 (16)	C5–C9–C8–C7	−1.3 (2)
O2–C11–C2–C1	−165.34 (14)	C6–C7–C8–O1	−178.43 (15)
C12–C11–C2–C1	74.74 (19)	C9–C8–C7–C6	1.3 (2)
C3–C4–C6–C7	178.95 (16)		

The crystal structure can be described as parallel double sheets in which the quinoline ring systems and water molecules are parallel to the (010) plane (Fig. 3). The same

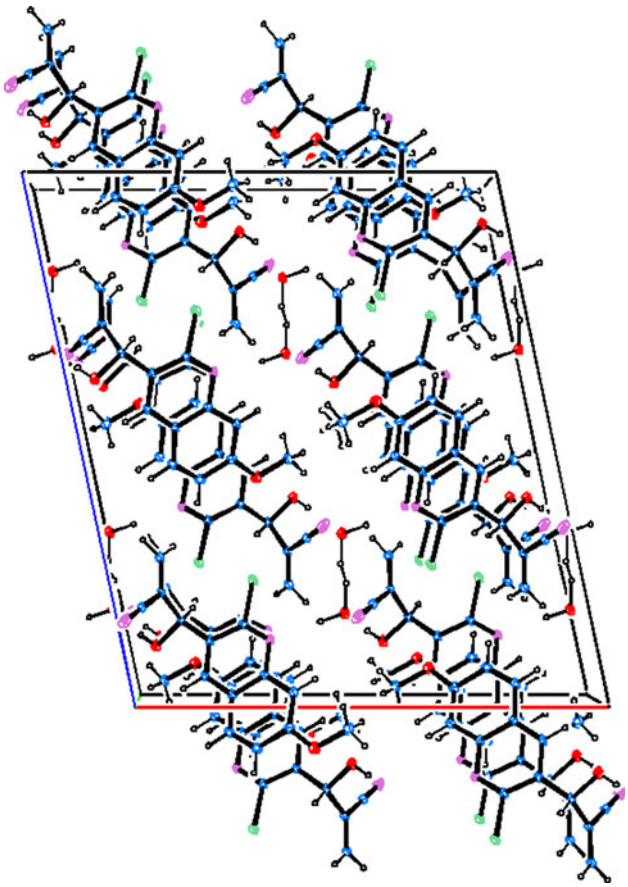

Fig. 3 Ortep 3 projection of the crystal structure on the (ac) plane

arrangement was observed in the structure of 2-Chloro-3-hydroxymethyl-6-methoxyquinoline [66].

The crystal packing is stabilised by a variety of hydrogen bonding interactions (Fig. 4, Table 5). Each water molecule accepts a hydrogen bond from another one and bridges a quinoline system by forming donor interaction with hydroxyl-O2 atom. The aromatic C3 and C10 atoms participate in C–H···O and C–H···N contacts (Table 5).

The compound **2d** present a moderate Ow-H···N bond characteristic of quinoline derivatives, which has been observed in (2-Chloro-8-methoxyquinolin-3-yl)methanol monohydrate [64]. Although the hydroxyl O–H···O hydrogen bond was comparable to those reported in the structure of (2-Chloro-6-methylquinolin-3-yl)methanol [67], (2-Chlorobenzo[h]quinolin-3-yl)methanol [68] and 2-Chloro-3-hydroxymethyl-7,8-dimethylquinoline [69].

The intermolecular connection between 2-[(2-Chloro-7-Methyoxy-quinolin-3-yl)-hydroxy-methyl]-acrylonitrile and water molecules [O2–H2···O3 and O3–H1w···N1] gives rise to binary-level graph set motifs [70] consisting of $C_2^2(8)$ infinite chains running through the a-axis direction (Fig. 5).

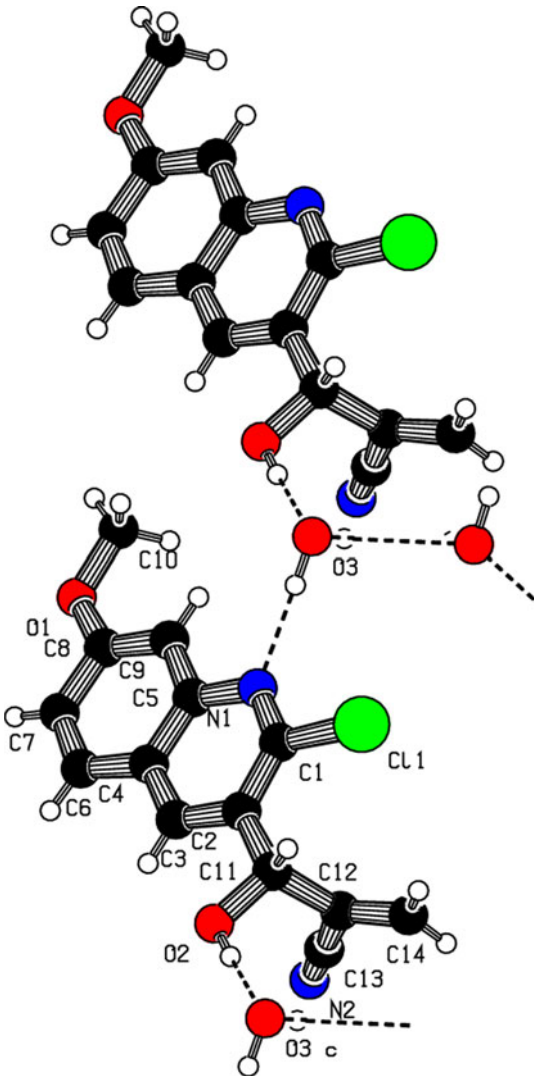

Fig. 4 Strong hydrogen bonding interactions assuring the crystal structure cohesion

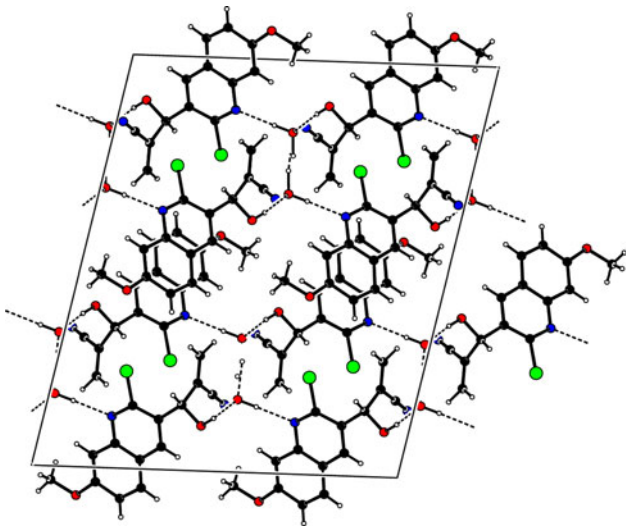

Fig. 5 The (010) projection visualising the infinite chains formed by alternating O–H···O and O–H···N hydrogen bonds

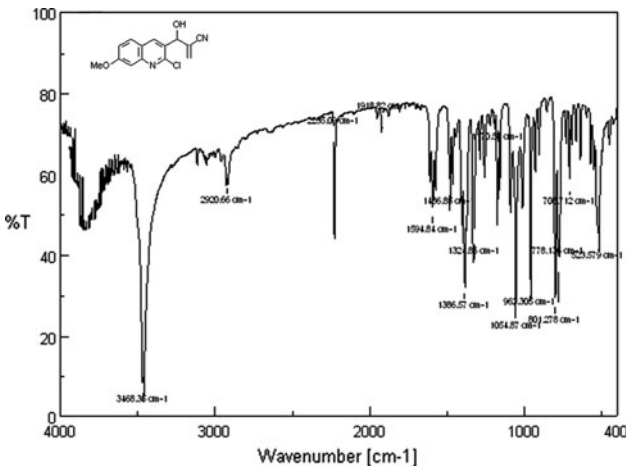

Fig. 6 IR spectrum of the compound 2d

Table 5 Hydrogen bond geometry (A°, °) of the 2d quinoline derivative

D–H···A	D–H	H···A	D···A	D–H···A
O2–H2···O3^{i}	0.82	1.92	2.742 (2)	175
O3–H1w···N1	0.86	2.04	2.878 (2)	164
O3–H2w···O3^{ii}	0.87	2.34	2.9001 (19)	123
C3–H3···O2	0.93	2.38	2.720 (2)	101
C10–H10C···N2^{iii}	0.96	2.51	3.423 (3)	160

Symmetry codes: (i) −1/2 + x, −1/2 + y,z; (ii) 1−x,y,1/2−z; (iii) 1/2−x,3/2−y,−z

Spectroscopic Interpretation

The mid-infrared spectrum of the cyanoquinoline derivative **2d** recorded between 400 and 4,000 cm^{-1} is shown in Fig. 6. The strong peak at 3,468 cm^{-1} at is assigned to the OH stretching vibration. The IR spectrum shows a medium band at 2,255 cm^{-1} assigned to νCN and another vibrational band at 1,594 cm^{-1} attributed to ν(C = C) [71, 72].

The resonance peaks at $\delta = 8.38$ ppm of ^{1}HNMR spectrum is due to the H3–C3 proton while the large singlet peak at $\delta = 5.80$ ppm is assigned to the CH–OH group. The methoxy protons signal at 3.94 ppm is split into a proton singlet and the signal at 6.15 ppm is split into a proton doublet due to the coupling of the two olefinic protons (CH_2).

The ^{13}CNMR spectrum of 2-[(2-Chloro-7-Methyoxy-quinolin-3-yl)-hydroxy-methyl]-acrylonitrile contains a resonance signal at $\delta = 116.46$ ppm due to the nitrile group. The quartet signal at $\delta = 162.16$ ppm is due to the effect of the methoxy group on the C8 carbon. The resonance peak observed as a quartet at $\delta = 149.32$ ppm is assigned to the C1 carbon linked to the chlorine atom.

Supplementary Material

CCDC 812946 contains the supplementary crystallographic data for this paper. These data can beobtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from theCambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +441223 336033.

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