Asian Journal of Chemistry; Vol. 27, No. 2 (2015), 435-440

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2015.16938

Synthesis and Crystal Structure of Novel 9-Styrylquinoline Substituted Acridines as Potential Inhibitors of Bacteria

JIA-JUAN QI[1,2], SHU-AN LI[2,*], ZHEN-MING ZHANG[1,2], TING WANG[1,2], HONG-BO ZHAO[1,2], XUAN WANG[1,2] and FU-JUN YIN[2]

[1]School of Chemical Engineering and Technology, China University of Mining and Technology, Xuzhou 221116, P.R. China
[2]Jiangsu Province R&D Institute of Marine Resources, Huaihai Institute of Technology, Lianyungang 222005, P.R. China

*Corresponding author: E-mail: li_shu_an@163.com; qjj581@163.com

Received: 27 December 2013; *Accepted*: 19 June 2014; *Published online*: 10 January 2015; AJC-16591

Novel compounds of 1,8-dioxodecahydroacridines were designed as potential inhibitors of bacteria and prepared *via* the multi-component reaction of styrylquinoline aldehydes, dimedone and ammonium acetate in high yield under mild condition. The structure of products has been characterized by X-ray crystal structural analyses, ^{1}H NMR, IR, LC-MC and elemental analysis. The preliminary biological screening shows that target product display a certain degree of activity against the vibrio harveyi at 100 μg mL^{-1}.

Keywords: 1,8-Dioxodecahydroacridines, Antibacterial activities, Quinolines moiety, Three component reactions.

INTRODUCTION

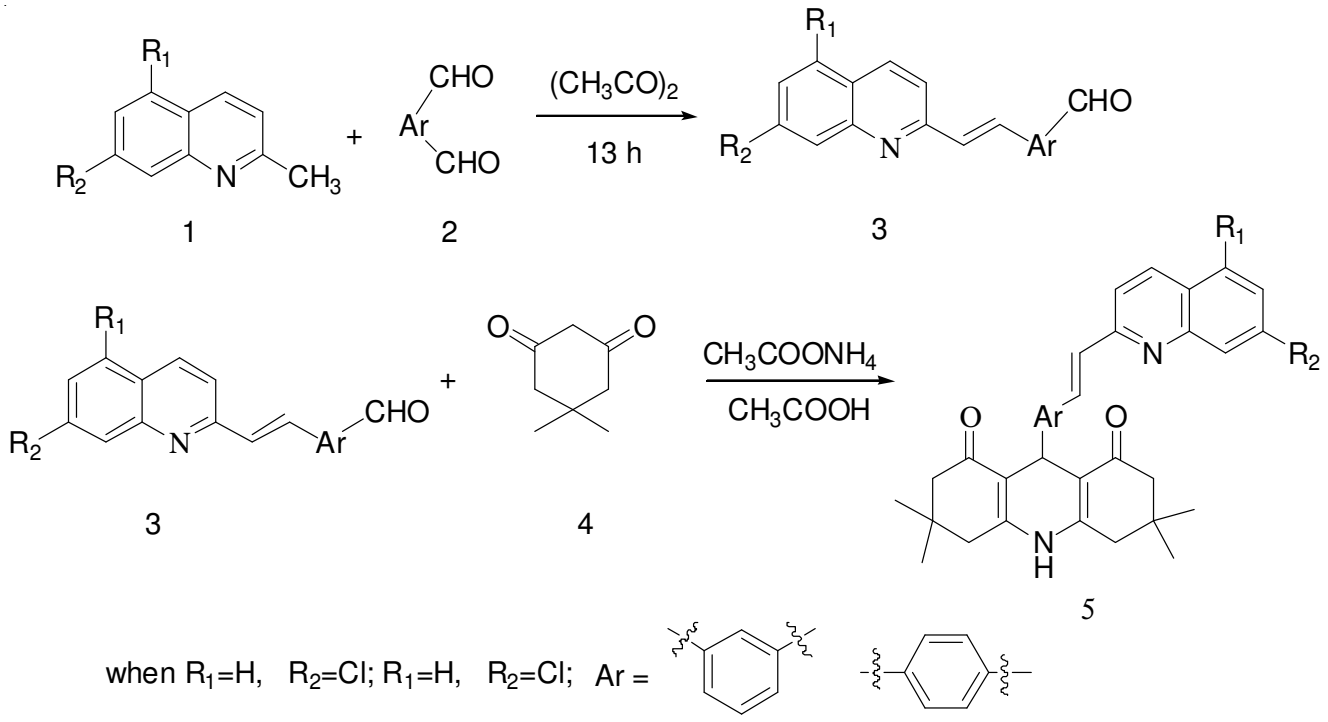
The acridine derivatives in addition to their optical properties, for example, laser dyes[1,3], fluorescent probes[4,5], occupy a prominent place in medicinal chemistry[6-8] due to their diverse pharmacological properties such as anticancer[9], antitumor[10], antioxidant[11], antihypertensive[11], treatment of Alzheimer's disease[12] and diabetes[13], anti-atherosclerotic and vasodilator[14] activities. The synthetic arylpolyhydroacridine acting as model compounds for treatment of diseases have also attracted much attention. Hence a series of 1,8-dioxodecahydroacridines is generally synthesized by using a multi-component reaction of dimedone, aldehydes and different anilines or ammonium acetate in the presence of catalysts. However, much effort to design synthetic arylpolyhydroacridine has focused primarily on simple aldehyde as reactants such as derivatizatives of benzaldehyde[15-19], furaldehyde[20], pyridine carboxaldehyde and low-aliphatic aldehyde[14]. Few aromatic aldehydes bearing quinoline moiety have been reported. Furthermore, quinoline compounds have been clinically used as antibacterial[21], antimalarial[22], antifungal[23], and antineoplastics[24] as well as fluorescence[25,26].

Based on the styrylquinoline derivatives having strong antifungal activity[27,28] and treatment of asthma[29-32], we designed and synthesized a novel 9(10H)-acridone derivatives *via* a one-pot three component reaction of dimedone, ammonium acetate and styrylquinoline aldehydes, which prepared from condensation of 7(5)-chloroquinaldine and aromatic dialdehydes, as shown in **Scheme-I**.

EXPERIMENTAL

Unless specified otherwise, all reagents and solvents used were of analytical grade. 7-Chloroquinaldine and 5-chloroquinaldine used for the synthesis were obtained from Zhejiang sunshine Chemical Co., Ltd. and also used as received without any further purification or treatment. Deionized water was used throughout the reactions and in all solutions. Simultaneous synthesizing and finishing processes were done by means of a mechanical stirrer. Melting points were determined on SGWX-4 melting point apparatus and uncorrected. Elemental analyses for C, H and N were performed with a PE 2400-II CHN elemental analyzer. IR spectra were recorded with a Brucker TENSOR 37 using KBr pellets in the frequency range 4000-400 cm^{-1}. ^{1}H-Nuclear magnetic resonance (NMR) spectra were determined in $CDCl_3$ on a Bruker-400 MHz ARX400. Chemical shifts (δ) were reported in parts per million (ppm) relative to tetramethylsilane, TMS as the internal reference. Mass spectra (electrospray ionization, ESI) were recorded on a Micromass Quanto LC-MC/MS spectrophotometer.

General procedure: Synthesis of compound 3: A mixture of 7-chloroquinaldine (0.1 mol) and isophthaladehyde (0.1 mol) in Ac_2O (20 mL), *n*-heptane (40 mL) and methylbenzene (20 mL) was heated to and maintained at reflux for 13 h, then the batch was cooled to and held at 90 °C for 2 h, collded to 80 °C over 3 h. The precipitated yellow solid 3-[2-(7-chloro-2-quinolinyl)ethenyl]-benzaldehyde (**3a**) was collected by filtration and the filter cake was washed with 15 °C *n*-heptane/methylbenzene (1/1). The crude product was purified by



Scheme-I

recrystallization from methylbenzene to give **3a**. **3b-3d** with the structure shown in Table-1 prepared as described previously. The spectral data are given below.

3-[2-(7-Chloro-2-quinolinyl)ethenyl]-benzaldehyde (3a): LC-MC (*m/z*):294.3 (M + 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.08 (s, 1H, CHO), 8.16 (s, 1H), 8.14-8.12 (d, *J* = 8.0 Hz, 1H), 8.03 (s, 1H), 7.91-7.89 (d, *J* = 8.0 Hz, 1H), 7.85-7.83 (d, *J* = 8.0 Hz, 1H), 7.75-7.73 (d, *J* = 8.4 Hz, 1H), 7.66-7.64 (d, *J* = 8.4 Hz, 1H), 7.59-7.57 (d, *J* = 8.0 Hz, 1H), 7.48-7.44 (t, $J_1 = J_2$ = 8.0 Hz, 1H), 7.39-7.37 (d, *J* = 8.0 Hz, 1H), 7.35-7.34 (d, *J* = 8.0 Hz, 1H); IR (KBr, ν_{max}, cm^{-1}): 3426, 3106, 2920, 2850, 1689, 1572, 1496, 1397, 869, 851, 758 and 688.

4-[2-(7-Chloro-2-quinolinyl)ethenyl]-benzaldehyde (3b): LC-MC (*m/z*):294.3 (M + 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.03 (s, 1H, CHO), 8.16 (s, 1H), 8.14-8.12 (d, *J* = 8.0 Hz, 1H), 7.93-7.91 (d, *J* = 8.0 Hz, 2H), 7.81-7.79 (d, *J* = 8.0 Hz, 1H), 7.75-7.73 (d, *J* = 8.0 Hz, 1H), 7.65-7.63 (d, *J* = 8.0 Hz, 2H), 7.59-7.57 (d, *J* = 8.0 Hz, 1H), 7.49-7.47 (d, *J* = 8.0 Hz, 1H), 7.26-7.24 (d, *J* = 8.0 Hz, 1H). IR (KBr, ν_{max}, cm^{-1}): 3426, 3086, 2868, 2850, 1690, 1601, 1494, 1397, 837 and 654.

3-[2-(5-Chloro-2-quinolinyl)ethenyl]-benzaldehyde (3c): LC-MC (*m/z*):294.3 (M + 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ :10.08 (s, 1H, CHO), 8.60-8.58 (d, *J* = 8.0 Hz, 1H), 8.15 (s, 1H), 8.05-8.03 (d, *J* = 8.0 Hz, 1H), 7.92-7.90 (d, *J* = 8.0 Hz, 1H), 7.86-7.84 (d, *J* = 8 Hz, 2H), 7.76-7.74 (d, *J* = 8.0 Hz, 1H), 7.66-7.62 (t, $J_1 = J_2$ = 8.0 Hz,1H), 7.61-7.57 (t, $J_1 = J_2$ = 8.0 Hz,1H), 7.51-7.49 (d, *J* = 8.0 Hz, 1H), 7.26-7.24 (d, *J* = 8.0 Hz, 1H). IR (KBr, ν_{max}, cm^{-1}):3442, 2920, 2850, 1696, 1588, 1497, 1396, 959, 808 and 753.

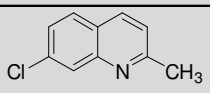
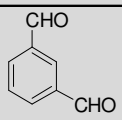
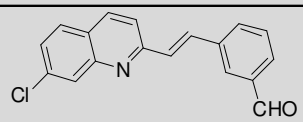
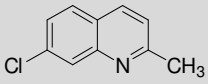
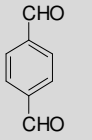
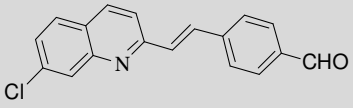
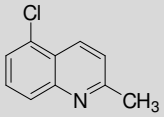
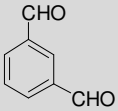
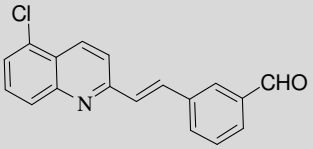
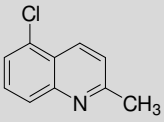
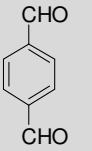
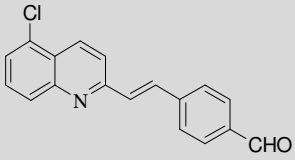
4-[2-(5-Chloro-2-quinolinyl)ethenyl]-benzaldehyde (3d): LC-MC (*m/z*):294.3 (M + 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ:10.04 (s, 1H, CHO), 8.62-8.60 (d, *J* = 8.0 Hz, 1H), 8.05-8.03 (d, *J* = 8.0 Hz, 1H), 7.94-7.92 (d, *J* = 8.0 Hz, 2H), 7.82-7.80 (d, *J* = 8 Hz, 2H), 7.68-7.64 (t, $J_1 = J_2$ = 8.0 Hz, 1H), 7.62-7.60 (d, *J* = 8.0 Hz, 1H), 7.58-7.56 (d, *J* = 8.0 Hz, 2H), 7.26-7.24 (d, *J* = 8.0 Hz, 1H). IR (cm^{-1}): 3440, 2922, 2851, 1696, 1601, 1498, 1397 and 811.

General procedure: Synthesis of compound 5: To a solution of an aromatic aldehyde **3** (1 mmol), 5,5-dimethyl-1,3- cyclohex-anedione (2 mmol) in AcOH (10 mL) in a round-bottom flask, ammonium acetate (7 mmol)) was added. The mixture was stirred at 80-90 °C (Table-2) and the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into 100 mL of ice water and the yellow solid was precipitated. Then, The soild was filtered off and wash with water. For further purification, the crude products were recrystallized from hot ethanol. **5a** and **5b,** respectively was dissolved in 20 mL solvent of ethanol and deionized water and left to stand at room temperature for several days, pale yellow diamond crystals of **5a** and pale yellow block crystals of **5b** were obtained.The spectral data are given below.

9-[3-{2-(7-Chloroquinolin-2-yl)vinyl}phenyl]-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (5a): LC-MC (*m/z*): 537.23 (M + 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12(s, 1H), 8.10-8.08 (d, *J* = 8.0 Hz, 1H), 7.73-7.71 (d, *J* = 8.0 Hz, 1H), 7.67-7.66 (d, *J* = 4.0 Hz, 1H), 7.64-7.63 (d, *J* = 4.0 Hz, 1H), 7.61-7.59 (d, *J* = 8.0 Hz, 1H), 7.53-7.51 (d, *J* = 8.0 Hz, 1H), 7.46-7.44 (d, *J* = 8.0 Hz, 1H), 7.40 (s, 1H), 7.37-7.33 (t, $J_1 = J_2$ = 8.0 Hz,1H), 7.24-7.22 (d, *J* = 8.0 Hz, 1H), 5.13 (s, 1H), 2.36-2.32 (d, *J* = 16 Hz, 2H), 2.23-2.19 (d, *J* = 16 Hz, 2H), 1.77 (s, 4H), 1.23 (s, 6H), 1.12 (s, 6H); IR (KBr, ν_{max}, cm^{-1}): 3415, 3178, 3056, 2947, 1656, 1601, 1498, 1397, 1225, 965, 811, 762 and 712.

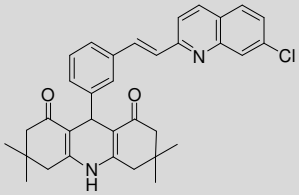
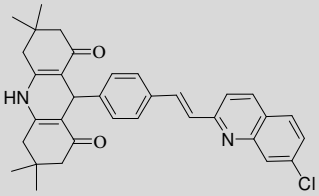
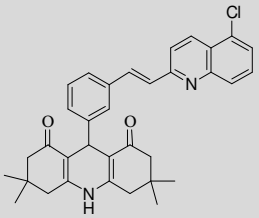
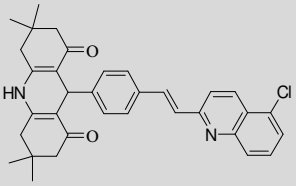
9-[4-{2-(7-Chloroquinolin-2-yl)vinyl}phenyl]-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (5b): LC-MC (*m/z*):537.23 (M + 1); ^{1}H NMR (400 MHz,

TABLE-1
SYNTHESIS OF STYRYLQUINOLINE ALDEHYDE UNDER REFLUX CONDITIONS

Entry	1	2	Product	Reaction time (h)	Yields[a] (%)	m.p. (°C)
1			 (3a)	13	65	147-150 °C lit[33]: 146-150
2			 (3b)	11	60	188-190
3			 (3c)	15	52	147-148
4			 (3d)	12	56	152-154

[a]Isolated yield

TABLE-2
SYNTHESIS OF 1,8-DIOXO-DECAHYDROACRIDINE DERIVATIVES 5a-5d IN THE PRESENCE OF AMMONIUM ACETATE IN ACETIC ACID

Entry	3	Product	Reaction time (h)	Yields[a] (%)	m.p. (°C)
1	3a	 (5a)	1.5	92	190-191
2	3b	 (5b)	2	88	306-307
3	3c	 (5c)	1	80	336-337
4	3d	 (5d)	2	84	328-330

[a] Isolated yield

$CDCl_3$) δ 8.11-8.09 (d, *J* = 8.0 Hz, 1H), 8.07 (s, 1H), 7.74-7.72 (d, *J* = 8.0 Hz, 1H), 7.68-7.66 (d, *J* = 8.0 Hz, 1H), 7.62-7.60 (d, *J* = 8.0 Hz, 1H), 7.51-7.49 (d, *J* = 8.0 Hz, 2H), 7.47-7.45 (d, *J* = 8.0 Hz, 1H), 7.44-7.42 (d, *J* = 8.0 Hz, 2H), 7.32-7.30 (d, *J* = 8.0 Hz, 1H), 5.15 (s, 1H), 2.38-2.34 (d, *J* = 16 Hz, 2H), 2.24-2.20 (d, *J* = 16 Hz, 2H), 1.71 (s, 4H), 1.09 (s, 6H), 0.98 (s, 6H); IR (KBr, ν_{max}, cm^{-1}): 3415, 3168, 2958, 2871, 1611, 1495, 1397, 1366, 1224, 968 and 838.

9-[3-{2-(5-Chloroquinolin-2-yl)vinyl}phenyl]-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (5c): LC-MC (*m/z*):537.23 (M + 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62-8.60 (d, *J* = 8.0 Hz, 1H), 8.14-8.12 (d, *J* = 8.0 Hz, 1H), 7.83-7.81(d, *J* = 8.0 Hz, 1H), 7.70-7.68 (d, *J* = 8.0 Hz, 2H), 7.64-7.60 (t, $J_1 = J_2$ = 8.0 Hz, 1H), 7.54 (s, 1H), 7.45-7.43 (d, *J* = 8.0 Hz, 1H), 7.39-7.37 (d, *J* = 8.0 Hz, 1H), 7.33-7.29 (t, $J_1 = J_2$ = 8.0 Hz, 1H), 7.27-7.25 (d, *J* = 8.0 Hz, 1H), 5.15 (s, 1H), 2.29-2.25 (d, *J* = 16 Hz, 2H), 2.21-2.17 (d, *J* = 16 Hz, 2H), 1.73 (s, 4H), 1.12 (s, 6H), 1.00 (s, 6H); IR (KBr, ν_{max}, cm^{-1}): 3415, 3177, 3062, 2959, 1644, 1607, 1490, 1394, 1366, 1222, 959, 812, 756 and 702.

9-[4-{2-(5-Chloroquinolin-2-yl)vinyl}phenyl]-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (5d) LC-MC (*m/z*):537.23 (M + 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52-8.50 (d, *J* = 8.0 Hz, 1H), 7.97-7.95 (d, *J* = 8.0 Hz, 1H), 7.77-7.75 (d, *J* = 8.0 Hz, 1H), 7.63-7.61 (d, *J* = 8.0 Hz, 1H), 7.59-7.55 (t, $J_1 = J_2$ = 8.0 Hz,1H), 7.52-7.50 (d, *J* = 8.0 Hz, 2H), 7.44-7.42 (d, *J* = 8.0 Hz, 2H), 7.30-7.28 (d, *J* = 8.0 Hz, 2H), 5.15 (s, 1H), 2.38-2.34 (d, *J* = 16 Hz, 2H), 2.24-2.20 (d, *J* = 16 Hz, 2H), 1.75 (s, 4H), 1.08 (s, 6H), 0.97 (s, 6H); IR (KBr, ν_{max}, cm^{-1}): 3417, 2957, 2930, 2871, 1630, 1488, 1367, 1224, 1143, 962 and 809.

Crystal structure determination: A single crystal of the **5b** (0.12 mm × 0.15 mm × 0.20 mm), respectively were selected and mounted on a glass fiber. All measurements were made on a Bruker Smart 1000 diffractometer with a graphite-monochromated MoK_α radiation (λ = 0.71073 Å). All data were collected at 296(2) K using the ω-2θ scan mode and corrected for Lorenz-polarization effects. A total of 8316 reflections in the range of 1.09 to 25.25° (-10 ≤ h ≤ 11, -10 ≤ k ≤ 11, -21 ≤ l ≤ 22) and 5693 unique ones (R_{int} = 0.0188) were collected. The empirical absorption corrections by SADABS were carried out.

Structure was solved by direct methods: The non-hydrogen atoms were refined with anisotropic thermal parameters. The final cycle of full-matrix least-squares refinement was based on 5693 observed reflections and 383 variable parameters to give the final R = 0.0794 and wR = 0.2196 (I > 2σ(I)). [w = $1/[\sigma^2(Fo^2) + (0.1000P)^2 + 1.0193P$, where $P = (Fo^2 + 2Fc^2)/3$)]. All calculations were performed with SHELX-97 crystallographic software package[34]. The crystal data and refinement details for the compound are listed in Table-3 (CCDC: 965808). Further details of **5a** can be obtained from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ by quoting the number CCDC 965807; e-mail: deposit@ccdc.cam.ac.uk.

Antibacterial activities: The preliminary evaluation of antibacterial activities of all compounds against *Vibrio harveyi* was caried out according to the published procedures[35]. The tested results are summarized in Table-4. The preliminary biological screening shows that all compounds display a certain degree of activity against the *Vibrio harveyi* at 100 μg mL^{-1}.

RESULTS AND DISCUSSION

The results of the reaction time and yields of the styrylquinoline aldehyde procedure are shown in Table-1. Three-component condensation of dimedone, aldehydes and ammonium acetate in the presence of acetic acid led to hexahydroacridine-1,8-diones. In each case, we obtained the corresponding products after 1-2 h in good to excellent yields (Table-2). The facts have been proved that the products can be obtained under the condition of in the absence of catalyst and has a good yield.

The styrylquinoline aldehyde **3a-3d** and the acridine derivatives **5a-5d** were obtained as high melting crystalline solids in good yields (Tables 1 and 2) and the structures were confirmed by elemental analyses, mass spectra as well as IR

TABLE-3
CRYSTALLOGRAPHIC DATA FOR COMPOUND **5b**

Empirical formula	$C_{34}H_{33}Cl_1N_2O_2$	Crystal color	Yellow
Fw	573.11	D_c (g cm^{-3})	1.214
Crystal system	Ticlinic	μ (mm^{-1})	0.162
Space group	P-1	Crystal dimension / mm	0.12 × 0.15 × 0.20
a/Å	9.2056(15)	θ range/(°)	1.09-25.25
b/Å	9.8039(16)	F(000)	614
c/Å	18.779(3)	Goodness of fit	0.162
α(°)	93.167(2)	Reflections collected	8316
β(°)	90.845(2)	Independent reflns. (R_{int})	5693
γ(°)	109.098(2)	Obsd. Reflns. (I > 2σ(I))	3372
V (Å)	1598.1(5)	Parameters refined	383
Z	1	R, wR (I > 2σ(I))	0.0794, 0.2196
Temperature (K)	296(2)	R, wR (all reflections)	0.1242, 0.2400

TABLE-4
CELL CONCENTRATION DETERMINED BY TURBIDIMETRIC METHOD

	1[a]	1[b]	3a	3b	3c	3d	5a	5b	5c	5d
OD	0.257	0.215	0.176	0.184	0.153	0.173	0.009	0.011	0.005	0.027

1[a] 7-Chloroquinaldine; 1[b] 5-chloroquinaldine; OD 600 nm

and NMR spectroscopy. The spectra are in good agreement with the proposed molecular structures. In the IR spectrum of **3a-3d** strong absorption bands at 2850 and 1690 cm^{-1} were due to CHO groups. In the IR spectrum of **5a-5d** the absorption bands for N-H at 3415 cm^{-1} appeared. It is worth mentioning that these compounds **3a-3d** showed in their ^1H NMR spectra signals for CHO at higher d values than those expected for typical aldehyde group. In the ^1H NMR spectrum of compounds **5a-5d**, two single peaks of four methyls at 1.10 and 1.00 ppm were appeared due to the steric effect of compounds.

The crystal structure analysis was carried out to understand the packing and/or hydrogen bonding patterns in crystal of this molecule and results are summarized in the following section. As shown in Fig. 1(a), the crystal cell is consisted of one molecule the title compound and one molecule the ethanol. It was shown that there were some strong indicated supramolecular interaction between ethanol molecules and carbonyl oxygen (C = O) and Nitrogen-hydrogen. Since only two supramolecular interactions (N2-H2A…O4 = 2.844(4) Å and O4-H4…O1 = 2.715(4) Å) were present between hydrogen and oxygen, hence it gave very short network as shown in Fig. 1(b). However, the crystal cell of **5b** is consisted of one molecule the title compound and three molecule of the water as shown in Fig. 2(a). It was shown that there were some strong indicated supramolecular interaction between water molecules and carbonyl oxygen (C = O) and Nitrogen-hydrogen. The four supramolecular interactions (O3W-H3A…O2#2 = 2.941(6) Å, O1W-H1A…N1 = 3.137(10) Å, O2W-H2A…O3W = 2.693(7) Å and O2W-H2B…O1#1 = 2.734 Å) were present between hydrogen and oxygen, hence it gave very short network as shown in Fig. 2(b). These supramolecular interactions were within the range of van der Waals radii.

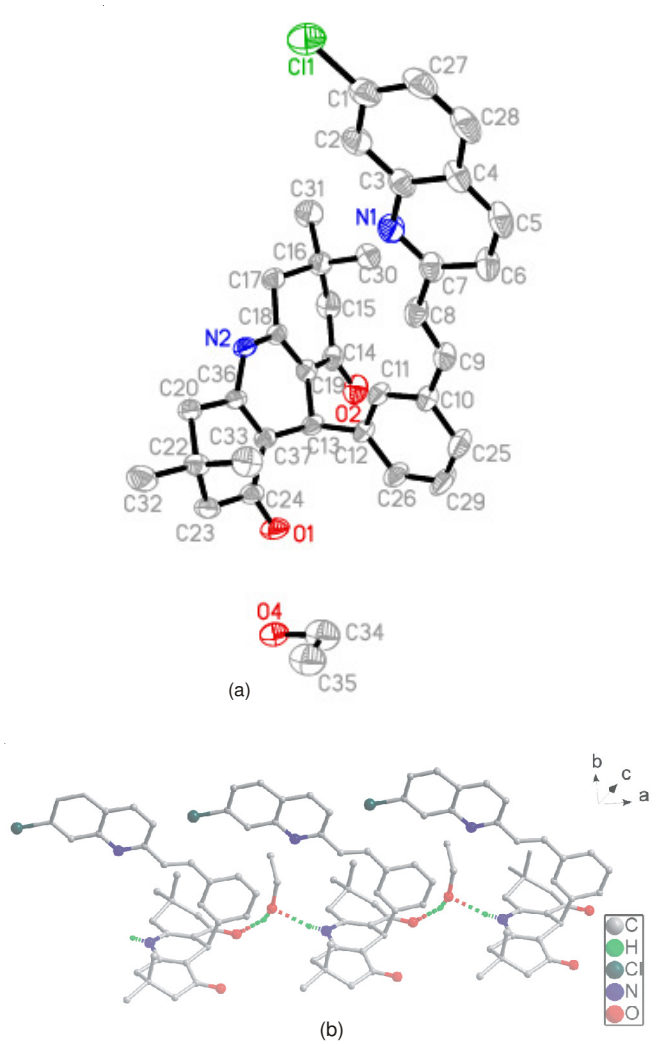


Fig. 1. (a) X-ray image of compound **5a**. Hydrogen atoms are omitted for clarity. (b) The supramolecular interactions between hydrogen and oxygen in compound **5a**

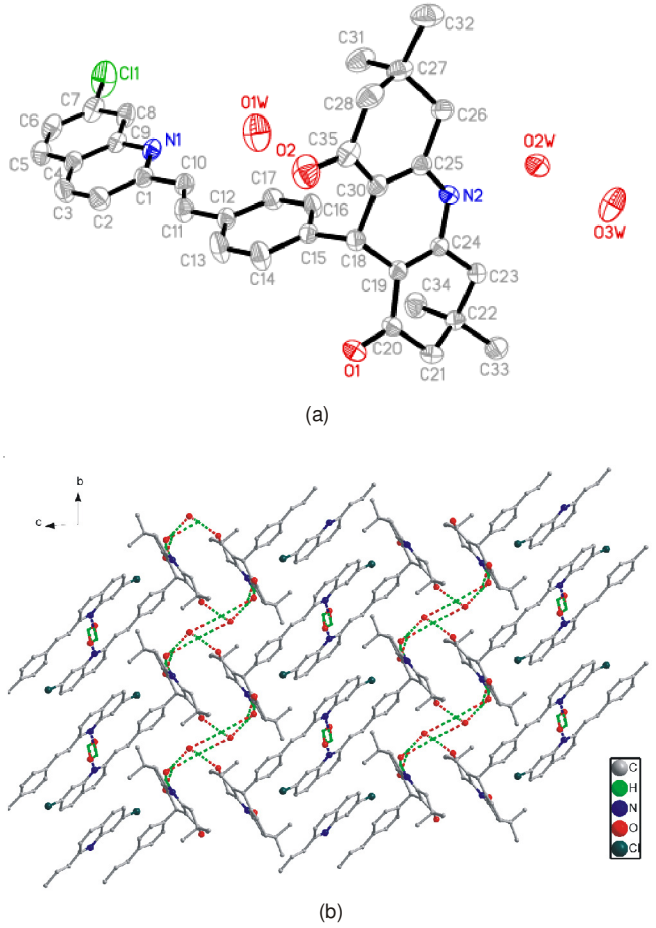


Fig. 2 (a) X-ray image of compound **5b**. Hydrogen atoms are omitted for clarity. (b) The supramolecular interactions between hydrogen and oxygen in compound **5a**

Antibacterial screening indicates that all compounds display good growth inhibition against *Vibrio harveyi*. Moreover, high growth inhibition percentage at 100 μg mL^{-1} was observed *in vitro* in case of **5a** and **5c**. Furthermore, it seems that the antibacterial activity of **5a-5d** showed stronger inhibition ratios against *Vibrio harveyi* than that of **3a-3d**, 7-chloroquinaldine and 5-chloroquinaldine.

REFERENCES

1. P. Shanmugasundaram, K.J. Prabahar and V.T. Ramakrishnan, *J. Heterocycl. Chem.*, **30**, 1003 (1993).
2. P. Shanmugasundaram, P. Murugan, V.T. Ramakrishnan, N. Srividya and P. Ramamurthy, *Heteroatom Chem.*, **7**, 17 (1996).
3. P. Murugan, P. Shanmugasundaram, V.T. Ramakrishnan, N. Srividya, B. Venkatachalapathy, P. Ramamurthy, K. Gunasekaran and D. Velmurugan, *J. Chem. Soc., Perkin Trans. II*, 999 (1998).

4. P. Ilich, P.K. Mishra, S. Macura and T.P. Burghardt, *Spectrochim. Acta A*, **52**, 1323 (1996).
5. T.P. Burghardt and K. Ajtai, *Biophys. Chem*., **60**, 119 (1996).
6. V. Gekeler, R. Boer, W. Ise, K.H. Sanders, C. Schachtele and J. Beck, *Biochem. Biophys. Res. Commun*., **206**, 119 (1995).
7. R.G. Bretzel, C.C. Bollen, E. Maeser and K.F. Federlin, *Am. J. Kidney Dis*., **21**, 53 (1993).
8. V. Klusa, *Drugs Future*, **20**, 135 (1995).
9. J. Avruch, N.C. Birnberg, J. Kyriakis, H. Liu and Q. Weng, Xanthene Compounds for Cancer Chemotherapy, WO 2004044219 A2 (2004).
10. A. Nakhi, P. Srinivas, M.S. Rahman, R. Kishore, G.P.K. Seerapu, K. Lalith Kumar, D. Haldar, M.V.B. Rao and M. Pal, *Bioorg. Med. Chem. Lett*., **23**, 1828 (2013).
11. X.-M. Yu, F. Ramiandrasoa, L. Guetzoyan, B. Pradines, E. Quintino, D. Gadelle, P. Forterre, T. Cresteil, J.-P. Mahy and S. Pethe, *ChemMedChem*, **7**, 587 (2012).
12. X.H. Yang, P.H. Zhang, L.H. Hu, M. Zhang, C.-G. Liu, H.-J. Liu and Y.-H. Zhou, *Ind. Crops Prod*., **38**, 14 (2012).
13. R. Boer and V. Gekeler, *Drugs Future*, **20**, 499 (1995).
14. S. Chandrasekhar, Y. Srinivasa Rao, L. Sreelakshmi, B. Mahipal and C. Raji Reddy, *Synthesis*, 1737 (2008).
15. X.S. Wang, D.S. Shi, S.H. Wang and S.J. Tu, *J. Org. Chem*., **23**, 1291 (2003).
16. X.S. Wang, D.S. Shi, Y.F. Zhang and S.J. Tu, *J. Org. Chem*., **24**, 430 (2004).
17. M. Dabiri, M. Baghbanzadeh and E. Arzroomchilar, *Catal. Commun*., **9**, 939 (2008).
18. X.S. Wang, M.M. Zhang, H. Jiang, D.-Q. Shi, S.-J. Tu, X.-Y. Wei and Z.-M. Zong, *Synthesis*, 4187 (2006).
19. T.S. Jin, J.S. Zhang, T.T. Guo, A.-Q. Wang and T.-S. Li, *Synthesis*, 2001 (2004).
20. N. Martín, M. Quinteiro, C. Seoane, J.L. Soto, A. Mora, M. Suárez, E. Ochoa, A. Morales and J.R.D. Bosque, *Heterocycl. Chem.*, **32**, 235 (1995).
21. R. Wise, J.M. Andrews and L.J. Edwards, *Antimicrob. Agents Chemother*., **23**, 559 (1983).
22. T.J. Egan, D.C. Ross and P.A. Adams, *FEBS Lett*., **352**, 54 (1994).
23. S.A. Jenekhe, L. Lu and M.M. Alam, *Macromolecules*, **34**, 7315 (2001).
24. B.S. Reddy and A. Rivenson, *Cancer Res*., **53**, 3914 (1993).
25. R. Musiol, J. Jampilek, V. Buchta, L. Silva, H. Niedbala, B. Podeszwa, A. Palka, K. Majerz-Maniecka, B. Oleksyn and J. Polanski, *Bioorg. Med. Chem*., **14**, 3592 (2006).
26. C.J. Frederickson, E.J. Kasarskis, D. Ringo and R.E. Frederickson, *J. Neurosci. Methods*, **20**, 91 (1987).
27. R. Musiol, J. Jampilek, K. Kralova, D.R. Richardson, D. Kalinowski, B. Podeszwa, J. Finster, H. Niedbala, A. Palka and J. Polanski, *Bioorg. Med. Chem*., **15**, 1280 (2007).
28. R. Musiol, J. Jampilek, V. Buchta, L. Silva, H. Niedbala, B. Podeszwa, A. Palka, K. Majerz-Maniecka, B. Oleksyn and J. Polanski, *Bioorg. Med. Chem*., **14**, 3592 (2006).
29. A. Merschaert, P. Boquel, J.P. Van Hoeck, H. Gorissen, A. Borghese, B. Bonnier, A. Mockel and F. Napora, *Org. Process Res. Dev*., **10**, 776 (2006).
30. Z.-M. Zhang, S.-A. Li, L.-P. Wang, Q. Dong and J.K. Liang, *Chinese J. Pharmaceuticals*, **41**, 92 (2010).
31. H.T. Hsien and M.H. David, Process for 3-(2-(7-chloro-2-quinolinyl)-ethenyl)benzaldehyde, US Patent 5869673 (1999).
32. D.M. Hobbs, P. Schubert and H.H. Tung, *Ind. Eng. Chem. Res*., **36**, 5302 (1997).
33. J. Gilmore and A. Todd, N-Benzyl-indoles, Processes for their Preparation and Pharmaceutical Compositions Containing them: European Patent, 469833; *Chem. Abstr*., **116**, 214508 (1992).
34. G.M. Sheldrick, SHELX-97, Program for the Solution and Refinement of Crystal Structures, University of Göttingen, Germany (1997).
35. X. Wang, B.F. Chu, C.L. Wang *et al*., *Clin. Stomatol*., **20**, 662 (2004).