Arabian Journal of Chemistry (2011) **xxx**, xxx–xxx

King Saud University

**Arabian Journal of Chemistry**

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

# Synthesis and characterization of new 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones and 3-(4-styryl)isoxazolo[4,5-*c*]quinolin-4(5*H*)-one derivatives

**S. Sarveswari *, V. Vijayakumar**

*Organic Chemistry Division, School of Advanced Sciences, VIT University, Vellore 632014, India*

Received 24 February 2011; accepted 10 September 2011

**KEYWORDS**

Synthesis of 4-hydroxy-3-(3-arylacryloyl)quinolin-2(1*H*)-ones;
3-(4,5-Dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones;
3-(4-Styryl)isoxazolo[4,5-*c*]quinolin-4(5*H*)-ones

**Abstract** The 4-hydroxy-3-(3-arylacryloyl)quinolin-2(1*H*)-ones were synthesized from 3-acetyl-4-hydroxyquinolin-2(1*H*)-one by microwave assisted synthesis, which in turn converted into their corresponding 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones and 3-(4-styryl)isoxazolo[4,5-*c*]quinolin-4(5*H*)-one derivatives.



## 1. Introduction

The quinolones known for their anti-microbial activities, based on their improved activities have been classified into four generations (Hooper et al., 2000). First-generation agents, are used less often today, with moderate gram-negative activity and minimal systemic distribution. Second-generation quinolones have expanded gram-negative activity and atypical pathogen coverage, but limited gram-positive activity. These agents are most active against aerobic gram-negative *bacilli*. Ciprofloxacin remains the most active quinolone against *Pseudomonas aeruginosa* (Hooper, 2000). Third-generation quinolones retain expanded gram-negative and atypical intracellular activity but have improved gram-positive coverage. Finally, fourth-generation agents improve gram-positive coverage, maintain gram-negative coverage, and gain anaerobic coverage. Marginal susceptibility and acquired resistance limit the usefulness of second-generation quinolones in the treatment of staphylococcal, streptococcal, and enterococcal infections (Oliphant et al., 2002). Clinafloxacin an investigational fluoroquinolone has the most potent in vitro anaerobic activity (Oliphant Applebaum, 1999). Several isoxazoline derivatives reported to show anti-inflammatory activity and imidazolyl isoxazoline derivatives show (Basappa et al., 2004) inhibitory activity

* Corresponding author. Tel.: +91 0416 2202535.
E-mail address: ssarveswari@vit.ac.in (S. Sarveswari).



Peer review under responsibility of King Saud University.
doi:10.1016/j.arabjc.2011.09.020

Production and hosting by Elsevier

against venom $PLA_2$ and reduced oedema inducing activity in mice. Andronati et al., 2004) reported that isoxazoline derivatives exhibit high activity in vitro bioassays on inhibiting platelet aggregation and was a potent anti-platelet agent for intravenous injection (Olson et al., 1999; Batt et al., 2000; Stilz et al., 1996). Isoxazole derivatives were reported as an important class of bioactive molecules, which exhibit significant activities such as antifungal (Desai et al., 2008) Aβ precursor protein (Rajeshwar et al., 2008) protein tyrosine phosphatase 1B inhibitors (Sung et al., 2003), antiviral (Lee et al., 2009), antihelmintics (Hansen and Stronge, 1977), anti-inflammatory (Adhikari et al., 2009), anticonvulsant (Balalaie et al., 2000), insecticidal (Kai et al., 2000), antitubercular (Kachhadia et al., 2004), immunomodulatory (Marcin et al., 2005) and hypolipemics (Nagar and Shan, 2003). The methylene-bis-isoxazoles reported to show 100% efficiency against PMA stimulated neutrophils (Mazzei et al., 2003). A series of structural optimizations led to improved efficacy and excellent functional receptor selectivity for PPARδ (Srinivas et al., 2010). The isoxazoles represent a series of agonists which display a scaffold that lies outside the typical PPAR agonist motif (Epple et al., 2006). The 3-pyrazolyl-4,5-dicarbethoxy isoxazoles exhibited the maximum Antinociceptive activity (Karthikeyan et al., 2009). Based on the above literature's importance here in we report some new quinolinyl isoxazoline and isoxazole derivatives (Scheme 1).

## 2. Experimental

All the melting points reported were recorded in open capillaries and uncorrected. IR spectra of all the compounds were recorded on AVATAR330 FT-IR Spectrometer. $^1$H NMR spectra were recorded on Bruker AMX 300. Chemicals for the synthesis were from Sigma Aldrich Co, St Louis, USA, and SD fine chemicals Pvt. Ltd., Boisar, India.

### *2.1. General procedure for the synthesis of 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1H)-ones. Method A*

A mixture of 4-hydroxy-3-(3-arylacryloyl) quinolin-2(1*H*)-one **1a–f** (0.3 M) and hydroxylamine hydrochloride (1 M) in glacial acetic acid was refluxed for 9 h. The reaction was monitored with TLC after the completion of the reaction, the reaction mixture concentrated and cooled. The solid formed was filtered, washed with petroleum ether and ethylacetate. The product was purified by column chromatography using 4:1 mixture of chloroform and methanol. Structural assignments of the products were made on the basis of spectral data.

### *2.2. General procedure for the synthesis of 3-(4-substituted styryl)isoxazolo[4,5-c]quinolin-4(5H)-ones Method B*

A mixture 3-arylacryloyl-4-hydroxyquinolin-2(1*H*)-ones (0.3 M) and hydroxylamine hydrochloride (1 M) in glacial acetic acid was refluxed for 18–20 h. The reaction was monitored with TLC after the completion of the reaction, the reaction mixture was concentrated and cooled. The solid obtained was filtered, washed with petroleum ether and ethylacetate. The product was recrystallized from glacial acetic acid. All the compounds were characterised by IR, $^1$H NMR and Mass spectral data and the Physical data of the synthesized compounds (**2a–2f** and **3a–3f**) are given in (Tables 1 and 2). The data are given in results and discussion.

## 3. Results and discussion

4-Hydroxy-3-(3-arylacryloyl)quinolin-2(1*H*)-ones (**1a–f**) were synthesized from 3-acetyl-4-hydroxy-quinolin-2(1*H*)-one by the literature method (Sarveswari and Raja, 2006). The 4-hydroxy-3-(3-arylacryloyl)quinolin-2(1*H*)-ones in turn were converted into 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones (**2a–f**) and 3-(4-substituted styryl) isoxazolo[4,5-*c*]quinolin-4(*5H*)-ones (**3a–f**). The initial attempt of conversion of 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones from (**1a–f**) by refluxing with hydroxylamine hydrochloride failed in methanol, ethanol or benzene solvent. Where as the same reaction in glacial acetic acid resulted in the formation of two products. The mixture was purified through column chromatography using 4:1 mixture of chloroform and methanol. The spectral characterisation of products revealed the formation of **2a–f** and **3a–f**. Since the isoxazole (**3a–f**) formation could not be controlled to get only isoxazolines (**2a–f**), we increased the reaction duration to 19–20 h. The increased reaction duration resulted in isoxazoles as the major products and the minor products could not be isolated. We observed that both the isoxazole and isoxazoline derivatives are not stable in water, so the aqueous work up results in decomposition of the products.

All the compounds were characterized through IR, $^1$H NMR and mass spectral studies. The compound **2a** has been taken as the representative example and its proton chemical shift assignment, IR and mass spectral interpretations are discussed. Three doublet of doublets in aliphatic region of spectrum at $\delta$ 2.83 ppm (1H, dd, $J_{AM}$ = 16 Hz and $J_{AX}$ = 11 Hz), $\delta$ 3.50 ppm (1H, dd, $J_{AM}$ = 16 Hz and $J_{MX}$ = 3.3 Hz), $\delta$ 5.52 ppm (1H, dd, $J_{MX}$ = 3.3 Hz and $J_{AX}$ = 11 Hz) confirm the formation of isoxazoline ring. H-7 and H-6 protons of quinolone ring appear as two triplets at $\delta$ 7.41 ppm (7.3 Hz), $\delta$ 7.17 ppm (7.3 Hz) and H-5 and H-8 appear as two doublets at $\delta$ 7.82 ppm (7.8 Hz) and $\delta$ 7.23 ppm (8.1 Hz) respectively. The summary of the above chemical shift assignments is given in Fig. 1 The molecular ion peak at 307.1 in ESI mass spectrum confirms the formation of the product.

**Table 1** Physical data of compounds (**2a–2f** and **3a–3f**) obtained in 9 h reflux.

| S. No. | Ar | M.p (°C) | Yield (%) |
|---|---|---|---|
| **2a** | Phenyl | 320–321 | 76 |
| **2b** | 4-Methoxyphenyl | 235–237 | 83 |
| **2c** | 3,4-Dimethoxy phenyl | 252–253 | 81 |
| **2d** | 4-Chlorophenyl | 248–250 | 58 |
| **2e** | 2,4-Chlorophenyl | 234–236 | 60 |
| **2f** | 3-Nitrophenyl | 230–233 | 50 |
| **3a** | Phenyl | 340–342 | 18 |
| **3b** | 4-Methoxyphenyl | 328–330 | 12 |
| **3c** | 3,4-Dimethoxy phenyl | 336–338 | 14 |
| **3d** | 4-Chlorophenyl | 228–230 | 24 |
| **3e** | 2,4-Chlorophenyl | 320–322 | 28 |
| **3f** | 3-Nitrophenyl | 332–333 | 30 |

Please cite this article in press as: Sarveswari, S., Vijayakumar, V. Synthesis and characterization of new 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones and 3-(4-styryl)isoxazolo[4,5-*c*]quinolin-4(5*H*)-one derivatives. Arabian Journal of Chemistry (2011), doi:10.1016/j.arabjc.2011.09.020

**Table 2** Physical data of compounds **3a**–**3f** obtained in 19–20 h reflux.

| S. No. | Ar | M.p (°C) | Yield (%) |
|---|---|---|---|
| **3a** | Phenyl | 340–342 | 72 |
| **3b** | 4-Methoxyphenyl | 328–330 | 70 |
| **3c** | 3,4-Dimethoxy phenyl | 336–338 | 76 |
| **3d** | 4-Chlorophenyl | 228–230 | 78 |
| **3e** | 2,4-Chlorophenyl | 320–322 | 81 |
| **3f** | 3-Nitrophenyl | 332–333 | 80 |

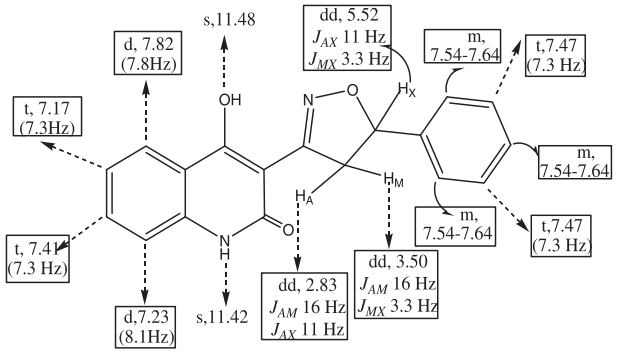



**Figure 1** Summary of Proton chemical shift values ($\delta$) in ppm of 3-(4,5-dihydro-5-phenyl) isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-one (**2a**).

The compound **3d** has been taken as the representative example for isoxazole derivatives and its proton chemical shift assignment, IR and mass spectral interpretations are discussed. In proton NMR spectrum of compound **3d**, the four quinolone ring protons appear as two triplets viz $\delta$ 7.35 ppm ($J$ = 7.5 Hz) for H-6, $\delta$ 7.59 ppm ($J$ = 7.3 Hz) for H-7 and two doublets viz $\delta$ 7.94 ppm ($J$ = 7.7 Hz) for H-5 and 7.50 ppm ($J$ = 7.9 Hz) for H-8 protons. The styryl protons give two characteristic doublets with coupling constant 16.5 Hz. A peak at $\delta$ 7.41 ppm is due to styryl proton attached with 4-chlorophenyl substituent and $\delta$ 7.84 ppm is due to styryl proton attached with isoxazolo quinoline ring system. The downfield shift of styryl proton at $\delta$ 7.84 ppm compared to $\delta$ 7.41 ppm is due to its attachment with the highly electron withdrawing isoxazolo quinoline ring system. The four protons of 4-chlorophenyl substituents appear as doublets at 7.85 ppm ($J$ = 8.3 Hz) and 7.52 ppm ($J$ = 8.3 Hz) each of two proton intensity. The summary of the above chemical shift assignment is given in Fig. 2. The proton chemical shift values of other compounds in these series have been assigned and given below.

### *3.1. 3-(4,5-Dihydro-5-phenyl)isoxazol-3-yl)-4-hydroxy quinolin-2(1H)-one (**2a**)*

IR (KBr): 3300 (NH), 1653 (C═O), 1602 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 2.83 (dd, 1H, $J$ = 16.0 Hz, 11.0 Hz), 3.50 (dd, 1H, $J$ = 16.0 Hz, 3.3 Hz), 5.52 (dd,1H, $J$ = 11.0 Hz, 3.3 Hz), 7.82 (d, 1H, $J$ = 7.8 Hz), 7.17 (t, 1H, $J$ = 7.3 Hz), 7.41 (t, 1H, $J$ = 7.3 Hz), 7.23 (d, 1H, $J$ = 8.1 Hz), 7.54–7.64 (m, 3H), 7.47 (t, 2H, $J$ = 7.3 Hz), 11.42 (s, NH), 11.48 (s, OH); ESI–MS: 307.1 $[M+1]^+$.

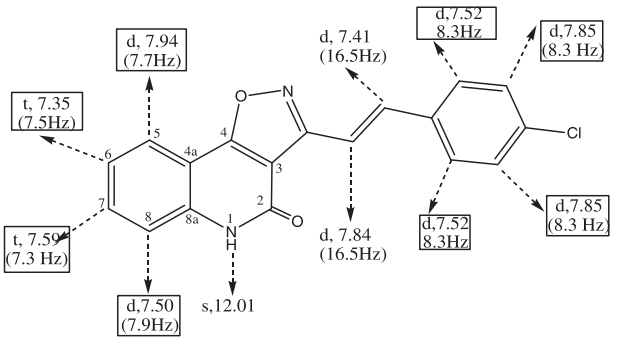
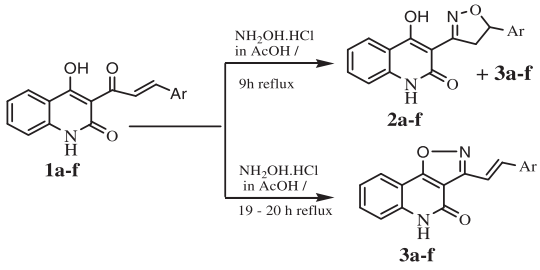



**Figure 2** Summary of proton chemical shift values ($\delta$) in ppm of 3-(4-chlorostyryl) isoxazolo[4,5-c]quinolin-4(5*H*)-one (**3d**).




**Scheme 1** Synthesis of 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones and 3-(4-substituted styryl)isoxazolo[4,5-*c*]quinolin-4(5*H*)-ones.

### *3.2. 3-(4,5-Dihydro-5-(4-methoxyphenyl)isoxazol-3-yl)-4-hydroxyquinolin-2(1H)-one (**2b**)*

IR (KBr): 3440 (NH), 1658 (C═O), 1606 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 3.74 (s, 3H, $OCH_3$), 3.66 (dd, 1H, $J$ = 18.3 Hz, 8.3 Hz), 4.09 (dd,1H, $J$ = 18.3, 10.7), 5.66 (t, 1H, $J$ = 9.32 Hz), 7.95 (d, 1H, $J$ = 7.8 Hz), 7.25 (t, 1H, $J$ = 7.6 Hz), 7.61 (t, 1H, $J$ = 7.2 Hz), 7.32 (d, 1H, $J$ = 8.4 Hz), 6.97 (d, 2H, $J$ = 8.6 Hz), 7.37 (d, 2H, $J$ = 8.5 Hz), 11.67 (s, NH), 12.02 (s, –OH); ESI–MS: 337 $[M+1]^+$.

### *3.3. 3-(4,5-Dihydro-5-(3,4-dimethoxyphenyl))isoxazol-3-yl)-4-hydroxyquinolin-2(1H)-one (**2c**)*

IR (KBr): 3444 (NH), 1666 (C═O), 1605 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 3.74 (s, 3H, $OCH_3$), 3.76 (s, 3H, $OCH_3$), 3.82 (dd, 1H, $J$ = 11.5 Hz, 7.7 Hz), 4.01 (dd, 1H, $J$ = 18.2 Hz, 10.7 Hz), 5.61 (t, 1H, $J$ = 9.9 Hz), 8.06 (d, 1H, $J$ = 7.7 Hz), 7.23 (t, 1H, $J$ = 7.9 Hz), 7.58 (t, 1H, $J$ = 7.1 Hz), 7.30 (d, 1H, $J$ = 8.1 Hz), 6.95 (s, 2H), 7.02 (d, 1H, $J$ = 8.2 Hz), 11.64 (s, NH), 12.29 (s, OH); ESI–MS: 367 $[M+1]^+$.

### *3.4. 3-(4,5-Dihydro-5-(4-chlorophenyl)isoxazol-3-yl)-4-hydroxyquinolin-2(1H)-one (**2d**)*

IR (KBr) cm$^{-1}$: 3436 (NH), 1675 (C═O), 1603 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 3.72 (dd, 1H, $J$ = 11.3 Hz, 7.7 Hz], 3.98 (dd, 1H, $J$ = 17.4 Hz, 10.7 Hz), 5.51 (t, 1H, $J$ = 9.8 Hz), 7.86 (d, 1H, $J$ = 7.8 Hz); 7.37

Please cite this article in press as: Sarveswari, S., Vijayakumar, V. Synthesis and characterization of new 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones and 3-(4-styryl)isoxazolo[4,5-*c*]quinolin-4(5*H*)-one derivatives. Arabian Journal of Chemistry (2011), doi:10.1016/j.arabjc.2011.09.020

(t, 1H, $J$ = 7.8 Hz); 7.57 (t, 1H, $J$ = 7.3 Hz), 7.53 (d, 1H, $J$ = 7.9 Hz), 7.54 (d, 2H, $J$ = 8.1 Hz), 7.83 (d, 2H, $J$ = 8.1 Hz), 11.78 (s, NH), 13.29 (s, OH); ESI–MS: 340 $[M]^+$.

### 3.5. 3-(4,5-Dihydro-5-(2,4-dichlorophenyl)isoxazol-3-yl)-4-hydroxyquinolin-2(1H)-one (**2e**)

IR (KBr) $cm^{-1}$: 3434 (NH), 1659 (C═O), 1607 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 4.12 (dd, 2H, $J$ = 19.2 Hz, 2.0 Hz), 3.7 (m, 2H) 5.62 (dd, $J$ = 4.6 Hz, 12.0 Hz) , 7.90–8.00 (m, 1H), 7.18–7.67 (m, 6H), 11.24 (bs, NH), 13.74 (s, OH); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ (ppm) 158.90, 150.05, 143.5, 137.86, 133.89, 131.81, 131.29, 129.55, 129.13, 128.47, 127.95, 127.22, 122.02, 121.71, 115.96, 31.29, 26.90; ES-MS: $m/z$ 378.1 $[M+4]^+$.

### 3.6. 3-(4,5-Dihydro-5-(3-nitrophenyl))isoxazol-3-yl)-4-hydroxyquinolin-2(1H)-one (**2f**)

IR (KBr) $cm^{-1}$: 3425 (NH), 1659 (C═O), 1607 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 4.04 (t, 2H, $J$ = 12.4 Hz), 4.99 (t, 1H, $J$ = 12.4 Hz), 8.27 (s, 1H), 8.14 (d, 1H, $J$ = 7.6 Hz), 7.91–7.88 (m, 3H), 7.67 (t, 1H, $J$ = 7.9 Hz), 7.51 (t, 1H, $J$ = 7.3 Hz); 7.24 (d, 1H, $J$ = 8.1 Hz), 7.16 (t, 1H, $J$ = 7.1 Hz), 11.36 (bs, NH), 14.14 (bs, OH). ES–MS: $m/z$ 352 $[M+1]^+$.

### 3.7. 3-(Styryl)isoxazolo[4,5-c]quinolin-4(5H)-one (**3a**)

$^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 8.38 (d, 1H, $J$ = 16.2 Hz), 7.29 (d, 1H, $J$ = 16.2 Hz), 7.80 (d, 1H, $J$ = 7.7 Hz), 7.15 (t, 1H, $J$ = 7.2 Hz), 7.42 (t, 1H, $J$ = 7.2 Hz), 7.23 (d, 1H, $J$ = 8.1 Hz), 7.56–7.66 (m, 3H), 7.46 (t, 2H, $J$ = 7.4 Hz), 12.11 (s, NH); ESI–MS: 289.1 $[M+1]^+$.

### 3.8. 3-(4-Methoxystyryl)isoxazolo[4,5-c]quinolin-4(5H)-one (**3b**)

$^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 3.75 (s, 3H, $OCH_3$), 8.38 (d, 1H, $J$ = 16.4 Hz), 7.29 (d, 1H, $J$ = 16.4 Hz) 8.08 (d,1H, $J$ = 7.6 Hz), 7.72 (t, 1H, $J$ = 7.8 Hz), 7.27 (t, 1H, $J$ = 8.5 Hz), 7.54 (d, 1H, $J$ = 8.1 Hz), 7.34 (d, 1H, $J$ = 8.2 Hz), 6.84 (d, 1H, $J$ = 8.2 Hz) . ESI–MS: 318.1 $[M+1]^+$.

### 3.9. 3-(3,4-Dimethoxystyryl)isoxazolo[4,5-c]quinolin-4(5H)-one (**3c**)

$^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 3.72 (s, 3H, $OCH_3$), 3.75 (s, 3H, $OCH_3$), 8.34 (d, 1H, $J$ = 16.6 Hz), 7.27 (d, 1H, $J$ = 16.6 Hz), 8.06 (d, 1H, $J$ = 7.8 Hz), 7.70 (t, 1H, $J$ = 7.5 Hz), 7.20 (t, 1H, $J$ = 8.6 Hz) 7.52 (d, 1H, $J$ = 8.1 Hz) 6.88 (s,1H), 7.01–7.02 (m, 2H); ESI–MS: 348.1 $[M+1]^+$.

### 3.10. 3-(4-Chlorostyryl)isoxazolo[4,5-c]quinolin-4(5H)-one (**3d**)

IR (KBr): 3425 (NH), 1685 (C═O), 1631 (C═C), 1605 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 7.84 (d, 1H, $J$ = 16.5 Hz), 7.41 (d, 1H, $J$ = 16.5 Hz), 7.94 (d, 1H, $J$ = 7.7 Hz); 7.35 (t, 1H, $J$ = 7.5 Hz); 7.59 (t, 1H, $J$ = 7.3 Hz), 7.50 (d, 1H, $J$ = 7.9 Hz), 7.52 (d, 2H, $J$ = 8.3 Hz), 7.85 (d, 2H, $J$ = 8.3 Hz), 12.01 (s, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ (ppm) 161. 41, 156.75, 152.59, 137.38, 134.24, 133.80, 130.29, 130.08, 129.46, 128.93, 116.16, 113.93, 109.59; ESI–MS: 323 $[M]^+$.

### 3.11. 3-(2,4-Dichlorostyryl)isoxazolo[4,5-c]quinolin-4(5H)-one (**3e**)

IR (KBr): 3440 (NH), 1690 (C═O), 1632 (C═C), 1602 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 8.00 (d, 1H, $J$ = 16.0 Hz), 7.52 (d, 1H, $J$ = 16.0 Hz), 8.15 (d, 1H, $J$ = 8.5 Hz); 7.35 (t, 1H, $J$ = 7.5 Hz), 7.59 (t, 1H, $J$ = 8.0 Hz); 7.50 (d, 1H, $J$ = 7.9 Hz), 7.49-7.51 (m, 2H), 7.77 (d, 1H), 12.04 (s, NH); ESI–MS: 357 $[M]^+$.

### 3.12. 3-(3-Nitrostyryl)isoxazolo[4,5-c]quinolin-4(5H)-one (**3f**)

IR (KBr): 3425 (NH), 1665 (C═O), 1628 (C═C), 1600 (C═N); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) 8.03 (d, 1H, $J$ = 16.4 Hz), 7.65 (d, 1H, $J$ = 16.4 Hz), 8.33 (d, 1H, $J$ = 7.8 Hz), 7.38 (t, 1H, $J$ = 7.5 Hz), 7.61 (t, 1H, $J$ = 8.0 Hz); 7.52 (d, 1H, $J$ = 8.3 Hz), 7.76 (t, 1H, $J$ = 7.9 Hz), 7.96 (d, 1H, $J$ = 7.7 Hz), 8.32 (d, 1H, $J$ = 7.8 Hz), 8.67 (s, 1H), 12.06 (s, NH); ESI–MS: 334 $[M]^+$.

## 4. Conclusion

Synthesis of 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones and 3-(4-substituted styryl)isoxazolo[4,5-*c*]quinolin-4(*5H*)-ones were effected from the corresponding 4-hydroxy-3-(3-arylacryloyl) quinolin-2(1*H*)-ones (**1a–f**). The compounds **2a–f** were found to form in lower yields since the reaction involves the formation of **3a–f** also. The presence of electron releasing groups favours the formation of **2a–f** in higher yields where as the presence of electron withdrawing groups favours the formation of **3d–f** with the reaction conditions adapted in method A. But the method B results in 3-(4-styryl) isoxazolo[4,5-*c*] quinolin-4(*5H*)-ones as the major product, from the obtained yield we can conclude that the presence of electron withdrawing groups favours the formation of **3a–f**, Since the styryl double bond is stabilized by the presence of electron withdrawing groups and is unavailable for cyclization.

## Acknowledgments

The authors are thankful to the NMR Research centre, IISc, Bengaluru, IIT-Madras and VIT-TBI for providing NMR, Mass and IR spectral facilities respectively.

## References

Adhikari, T.K., Vasudeva, A., Girisha, M., 2009. Indian J. Chem. 48B, 430–437.
Andronati, S.A., Karaseva, T.L., Krysko, A.A., 2004. Curr. Med. Chem. 11 (9), 1183–1211.
Balalaie, S., Sharifi, A., Ahangarian, B., 2000. Indian J. Heterocycl. Chem. 10 (2), 149–150.
Basappa, S.K.M., Nanjundaswamy, S., Mahendra, M., Prasad, J.S., Vishwanath, B.S., Rangappa, K.S., 2004. Bioorg. Med. Chem. Lett. 14 (14), 3679–3681.

Please cite this article in press as: Sarveswari, S., Vijayakumar, V. Synthesis and characterization of new 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones and 3-(4-styryl)isoxazolo[4,5-*c*]quinolin-4(5*H*)-one derivatives. Arabian Journal of Chemistry (2011), doi:10.1016/j.arabjc.2011.09.020

Batt, D.G., Houghton, G.C., Daneker, W.F., Jadhav, P.K., 2000. J. Org. Chem. 65 (23), 8100–8104.
Desai, J.T., Desai, C.K., Desai, K.R., 2008. J. Iran Chem. Soc. 5, 67–73.
Epple, R., Russo, R., Azimioara, M., Cow, C., Xie, Y., Wang, X., Wityak, J., Karanewsky, D., Gerken, A., Iskandar, M., Saez, E., Martin Seidel, H., Tian, S.S., 2006. Bioorg. Med. Chem. Lett. 16, 4376–4380.
Hansen, J.F., Stronge, S.A., 1977. J. Heterocycl. Chem. 14, 1289.
Hooper, D.C., 2000. Clin. Infect. Dis. 30 (2), 243–254.
Hooper, D., Mandell, G.L., Bennett, J.E., Dolin, R, Mandell, Douglas, Bennett's., 2000. 5th Ed, Churchill Livingstone, Philadelphia, 404-406.
Kachhadia, V.V., Patel, M.R., Joshi, H.S., 2004. J. Sci. I. R. Iran 15, 47–57.
Kai, H., Ichiba, T., Tomida, M., Nakai, H., Morita, K., 2000. J. Pest. Sci. 25, 267–269.
Karthikeyan, K., Veenus Seelan, T., Lalitha, K.G., Perumal, P.T., 2009. Bioorg. Med. Chem. Lett. 19, 3370–3373.
Lee, Y.S., Park, S.M., Kim, B.H., 2009. Bioorg. Med. Chem. Lett. 19, 1126–1128.
Marcin, M., Michal, Z., Ewa, D.S., Stanislaw, R., 2005. Cell. Mol. Biol. Lett. 10, 613–623.
Mazzei, M., Nieddu, E., Melloni, E., Minafr, 2003. Il Farmaco 58, 121–127.
Nagar, N.R., Shan, V.H., 2003. Indian J. Heterocycl. Chem. 13, 173–175.
Oliphant Applebaum, P.C., 1999. Drugs 58 (suppl 2), 60–64.
Oliphant, C.M., Pharm, D., Green, G.M., 2002. Am. Family Phys. 65 (3), 455–464.
Olson, R.E., Sielecki, T.M., Wityak, J., Pinto, D.J., Batt, D.G., Frietze, W.E., Liu, J., Tobin, A.E., Orwat, M.J., Di Meo, S.V., Houghton, G.C., Lanka, G.K., Mousa, S.A., Racanelli, A.L., Hausner, E.A., Kapil, R.P., Rabel, S.R., Thoolen, M.J., Reilly, T.M., Anderson, P.S., Wexler, R.R., 1999. J. Med. Chem. 42 (7), 1178–1192.
Rajeshwar, N., Marcus, P., Stefanie, L., Karlheinz, B., Sabine, K., Thomas, D., Sascha, W., Eckhard, M., Boris, S., 2008. Chem. Med. Chem. 3 (1), 165–172.
Sarveswari, S., Raja, T.K., 2006. Indian J. Heterocycl. Chem. 16, 171–174.
Srinivas, A., Nagaraj, A., Sanjeeva Reddy, C., 2010. Eur J. Med. Chem. 45, 2353–2358.
Stilz, H.U., Jablonka, B., Just, M., Knolle, J., Paulus, E.F., Zoller, G., 1996. J. Med. Chem. 39 (11), 2118–2122.
Sung, Y.C., Jin, H.A., Jae, D.H., Seung, K.K., Ji, Y.B., Sang, S.H., Eun, Y.S., Sung, S.K., Kwang, R.K., Hyae, G.C., Joong, K.C., 2003. Bull. Kor. Chem. Soc. 24, 1455.

Please cite this article in press as: Sarveswari, S., Vijayakumar, V. Synthesis and characterization of new 3-(4,5-dihydro-5-aryl)isoxazol-3-yl)-4-hydroxyquinolin-2(1*H*)-ones and 3-(4-styryl)isoxazolo[4,5-*c*]quinolin-4(5*H*)-one derivatives. Arabian Journal of Chemistry (2011), doi:10.1016/j.arabjc.2011.09.020