Vilsmeier-Haack reagent: A facile synthesis of 2-chloro-3-formylquinolines from N-arylacetamides and transformation into different functionalities

Ambika Srivastava & R M Singh*
Department of Chemistry, Banaras Hindu University, Varanasi-221005
E-mail: rmohan@bhu.ac.in

Received 2 August 2004; accepted (revised) 26 July 2005

A simple and regioselective synthesis of 2-chloro-3-formylquinolines through Vilsmeier-Haack cyclisation of N-arylacetamides has been reported. The cyclisation is facilitated by N-arylacetamides bearing electron donating groups at \( m \)-position. However, yields of quinolines having electron donating groups are good in all cases. Further, the nucleophilic substitution reaction of the quinolines is also investigated. Similarly, the formyl group in the quinolines is subjected to further transformation into cyano (CAN-NH\(_3\)) and alkoxy carbonyl (NIS-K\(_2\)CO\(_3\)/alcohols) groups to afford corresponding 3-cyano and 3-alkoxy carbonylquinolines, respectively.

Keywords: Vilsmeier-Haack reagent, 2-chloro-3-formylquinolines, N-arylacetamides

IPC: Int.Cl.7 C 07 D 215/00

The Vilsmeier-Haack reagent has been proved to be a versatile reagent capable of executing a large variety of synthetic transformations\(^1\). It finds application in formylation\(^2\), cyclohalo addition\(^3\), cyclisation\(^4\) and ring annulation\(^5\). Recently, its potentiality was explored in the synthesis of 4-(N,N-dimethylaminomethylene)-2-alkyl/aryl-2-oxazolin-5-ones\(^6\) from N-acyl derivatives of \( \alpha \)-amino acid esters and \( \alpha \)-aminoacetanilides. To develop novel quinoline based fused heterocyclic systems as potential anticancer agents\(^7\), a quinoline nucleus with different substituents at 2- and 3-positions was required which afforded a versatile synthon for further heteroannulations\(^8\).

Results and Discussion

Although many routes have been developed for functionalized quinolines\(^9\), the Vilsmeier\(^10\) approach is found to be among the most efficient for achieving useful transformations and heteroannulations. Thus, in this communication is reported the synthesis of 2-chloro-3-formylquinolines from the reaction N-arylacetamides with Vilsmeier reagent and transformation of the 2-chloro and 3-formyl groups into different functionalities.

The required acetonilide 1a-k was readily prepared from the reaction of corresponding anilines with acetic anhydride in aqueous medium. The Vilsmeier cyclisation of acetonilides 1a-k was carried out by adding POCl\(_3\) to the substrate in DMF at 0-5\(^\circ\)C followed by heating to 90\(^\circ\)C to afford 2-chloro-3-formylquinolines 2a-k in good to moderate yield (Scheme I). The structure of the compound was elucidated from their spectral data (Table I). The reaction condition was optimized by varying the molar proportion of POCl\(_3\) ranging from 3 to 15 moles at temperatures ranging between 80-90\(^\circ\)C with mole equivalent of \( m \)-methoxyacetanilide in DMF. The maximum yield of the product was obtained with 12 moles of POCl\(_3\) at 90\(^\circ\)C (Table II). It was further observed that the electron donating groups at \( m \)-position in acetanilides afforded quinolines not only in a better yield but also with very short reaction time as compared to the \( o \)- and \( p \)-acetanilides (Table III). However, the acetanilide bearing electron withdrawing groups yielded the respective quinoline in poor yield. No quinoline could be obtained from nitroacetanilides. In all cases, only regioselective product was obtained.

The structure of the compounds 2a-k could be matched with their spectral data (Table I). The IR spectra showed a sharp and strong absorption in the range of 1685-1695 cm\(^{-1}\) for the aldehydic group and absorption at around 2730 and 2810 cm\(^{-1}\) for aldehydic proton. The \(^1\)H NMR spectrum of compound 2a shows a singlet at \( \delta \) 10.5 and 8.8 for
SRIVASTAVA et al.: SYNTHESIS OF 2-CHLORO-3-FORMYLQUINOLINES

![Chemical structure and reaction scheme]

Table I — Spectral data of 2-chloro-3-formylquinolines 2a-k

<table>
<thead>
<tr>
<th>Compd</th>
<th>R</th>
<th>(^1)H NMR (CDCl(_3))</th>
<th>(^13)C NMR (CDCl(_3))</th>
<th>MS m/z</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>H</td>
<td>10.5(s, 1H, CH0), 8.8(s, 1H, H-4), 8.1(m, 1H, H-5), 8.0(m, 1H, H-8), 7.9(m, 1H, H-6), 7.7(m, 1H, H-7).</td>
<td>189.12</td>
<td>193(M(^{+}+2)), 191(M(^{+})), 190, 162, 155, 127</td>
</tr>
<tr>
<td>2b</td>
<td>6-Me</td>
<td>10.6(s, 1H, CHO), 8.5(s, 1H, H-4), 8.0(m, 1H, H-8), 7.75(m, 1H, H-7), 7.65(s, 1H, H-5), 2.6(s, 3H, CH(_3)).</td>
<td>189.28</td>
<td>207(M(^{+}+2)), 205(M(^{+})), 176, 141, 115, 89</td>
</tr>
<tr>
<td>2c</td>
<td>7-Me</td>
<td>10.4(s, 1H, CHO), 8.9(s, 1H, H-4), 8.9(s, 1H, H-8), 7.85(d, 1H, H-5), 7.7(m 1H, H-6), 2.6(s, 3H, CH(_3)).</td>
<td>189.59</td>
<td></td>
</tr>
<tr>
<td>2d</td>
<td>8-Me</td>
<td>10.4(s, 1H, CHO), 8.7(s, 1H, H-4), 8.1-7.4 (m, 3H, H-5, H-6 &amp; H-7), 2.8(s, 3H, CH(_3)).</td>
<td>189.51</td>
<td></td>
</tr>
<tr>
<td>2e</td>
<td>8-Et</td>
<td>10.6(s, 1H, CHO), 9.0(s, 1H, H-4), 8.3-7.3 (m, 3H, H-5, H-6 &amp; H-7), 3.4(q, 2H, CH(_2)), 1.5(t, 3H, CH(_3)).</td>
<td>189.25</td>
<td></td>
</tr>
<tr>
<td>2f</td>
<td>6-Ome</td>
<td>10.6(s, 1H, CHO), 9.0(s, 1H, H-4), 8.1(d, 1H, H-8), 7.6(s, 1H, H-7), 7.6(m, 1H, H-5), 4.0(s, 3H, OCH(_3)).</td>
<td>189.26</td>
<td></td>
</tr>
<tr>
<td>2g</td>
<td>7-Ome</td>
<td>10.5(s, 1H, CHO), 8.6(s, 1H, H-4), 7.78(m, 1H, H-5), 7.5(s, 1H, H-8), 7.3 (m, 1H, H-6), 4.0(s, 3H, OCH(_3)).</td>
<td>189.61</td>
<td>223(M(^{+}+2)), 221(M(^{+})), 193, 158, 132, 106.</td>
</tr>
<tr>
<td>2h</td>
<td>8-Ome</td>
<td>10.5(s, 1H, CHO), 8.9 (s, 1H, H-4), 8.0-7.4 (m, 3H, H-5, H-6 &amp; H-7), 3.9 (s, 3H, OCH(_3)).</td>
<td>189.31</td>
<td></td>
</tr>
<tr>
<td>2i</td>
<td>6-Br</td>
<td>10.8(s, 1H, CHO), 8.8 (s, 1H, H-4), 8.4(m, 1H, H-8), 7.6(m, 1H, H-7), 7.6(s, 1H, H-5).</td>
<td>189.38</td>
<td></td>
</tr>
<tr>
<td>2j</td>
<td>7-Cl</td>
<td>10.7(s, 1H, CHO), 8.5(s, 1H, H-4), 7.7 (m, 1H, H-5), 7.5(s, 1H, H-8), 7.2 (m, 1H, H-6).</td>
<td>189.05</td>
<td></td>
</tr>
<tr>
<td>2k</td>
<td>6-Cl</td>
<td>10.8(s, 1H, CHO), 8.6(s, 1H, H-4), 8.1(m, 1H, H-8), 7.7 (m, 1H, H-7) 7.6 (s, 1H, H-5).</td>
<td>189.49</td>
<td></td>
</tr>
</tbody>
</table>
aldehydic and C-4 protons, doublets at δ 8.1 and 8.0 for C-5 and C-8 protons and multiplets at δ 7.9 and 7.7 for C-6 and C-7 protons, respectively. The 13C NMR spectra of these compounds showed a carbonyl carbon peak at around δ 189.

Having obtained chloro and formyl group substituted quinolines the possible transformations of these functionalities could afford the new quinolines (Schemes II and III). Thus, the chloro group in few of the 2-chloro-3-formyl quinolines was investigated with various heteronucleophiles. Of the various reagents available for the replacement of chlorine by sulphur, sodium sulphide in DMF was found to be an efficient reagent affording nucleophilic substitution by sulphur and also providing scope for further reaction and one pot cyclisation. The substitution was achieved in an hour at rt to afford thione 3 in quantitative yield (Scheme II). In no case was disulphide formation observed. Further reaction with alkyl halides in DMF or the reaction of quinolines 2 with Na2S/DMF followed by reaction with alkyl halide in one pot afforded thioethers which are known to have significant fungicidal and bacterial activities. The 1H NMR spectra of compounds 3 show a broad D2O exchangeable signal at around δ 13-14.3 for N-H proton supporting the thione tautomeric structure, a formyl proton peak at around δ 10.0 along with the signals for the other aromatic protons. The strong IR absorption in the range of 1200-1050 cm⁻¹ attributable to C=S group further supports the thione tautomer.

Similarly, the corresponding O-nucleophilic substitution was readily achieved by refluxing quinolines 2 in aqueous acetic acid affording the 2(1H) quinolones 5. However, in contrast to O-alkylation further reaction of 5 with electrophile favored N-alkylation affording compounds 6, while the reaction of 2(1H) quinolines 5 with POCl3 at reflux yielded exclusively the starting quinolines 2 (Scheme II).

### Table III — Yield of m-methoxyacetanilides upon varying the molar proportion of POCl3 from 3 moles to 15 moles

<table>
<thead>
<tr>
<th>DMF</th>
<th>POCl3</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>3</td>
<td>28</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>48</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>89</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>74</td>
</tr>
</tbody>
</table>

### Table III — Physical data of 2-chloro-3-formylquinolines 2a-k

<table>
<thead>
<tr>
<th>Compd</th>
<th>R</th>
<th>Mol. Formula (mol. wt.)</th>
<th>m.p. °C</th>
<th>Yield %</th>
<th>Time (hr at 80-90°C)</th>
<th>Found % (Calcd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>H</td>
<td>C16H15NOCl (191)</td>
<td>149</td>
<td>82</td>
<td>16</td>
<td>3.14 (3.16) 62.72 (62.68) 7.29 (7.31)</td>
</tr>
<tr>
<td>2b</td>
<td>6-Me</td>
<td>C16H16NOCi (205)</td>
<td>123</td>
<td>80</td>
<td>16</td>
<td>3.93 (3.92) 64.28 (64.25) 6.82 (6.81)</td>
</tr>
<tr>
<td>2c</td>
<td>7-Me</td>
<td>C16H15NOCl (205)</td>
<td>146</td>
<td>86</td>
<td>6</td>
<td>3.90 (3.92) 64.23 (64.25) 6.82 (6.81)</td>
</tr>
<tr>
<td>2d</td>
<td>8-Me</td>
<td>C16H15NOCl (205)</td>
<td>137</td>
<td>77</td>
<td>16</td>
<td>3.92 (3.92) 64.25 (64.25) 6.80 (6.81)</td>
</tr>
<tr>
<td>2e</td>
<td>8-Et</td>
<td>C16H16NOCl (219)</td>
<td>98</td>
<td>72</td>
<td>20</td>
<td>4.54 (4.59) 65.59 (65.61) 6.39 (6.38)</td>
</tr>
<tr>
<td>2f</td>
<td>6-OMe</td>
<td>C16H15NOCl (219)</td>
<td>146</td>
<td>62</td>
<td>16</td>
<td>3.59 (3.64) 59.61 (59.61) 6.30 (6.32)</td>
</tr>
<tr>
<td>2g</td>
<td>7-OMe</td>
<td>C16H15NOCl (219)</td>
<td>196</td>
<td>89</td>
<td>4</td>
<td>3.62 (3.64) 59.62 (59.61) 6.29 (6.32)</td>
</tr>
<tr>
<td>2h</td>
<td>8-OMe</td>
<td>C16H15NOCl (221)</td>
<td>190</td>
<td>15</td>
<td>16</td>
<td>3.66 (3.64) 59.65 (59.61) 6.31 (6.32)</td>
</tr>
<tr>
<td>2i</td>
<td>6-Br</td>
<td>C16H15NOClBr (270)</td>
<td>188</td>
<td>35</td>
<td>16</td>
<td>1.81 (1.86) 44.42 (44.40) 5.19 (5.18)</td>
</tr>
<tr>
<td>2j</td>
<td>7-Cl</td>
<td>C16H15NOCl2 (226)</td>
<td>160</td>
<td>28</td>
<td>10</td>
<td>2.25 (2.23) 53.14 (53.13) 6.19 (6.20)</td>
</tr>
<tr>
<td>2k</td>
<td>6-Cl</td>
<td>C16H15NOCl2 (226)</td>
<td>191</td>
<td>36</td>
<td>16</td>
<td>2.23 (2.23) 53.11 (53.13) 6.21 (6.20)</td>
</tr>
</tbody>
</table>
The chlorine atom in quinolines could not be displaced by N-nucleophiles (such as amines) under various conditions. Instead, the reaction of quinolines with N-nucleophiles underwent condensation reaction to afford anils, oximes etc. derivatives of quinolines. However, the reaction of sodium azide with quinolines in the presence of p-toluenesulphonic acid easily displaced the chlorine atom to afford 4-formyltetrazolo[1,5-a]quinolines in good yield instead of the desired 2-azido-3-formylquinoline (Scheme II).

The formyl group in quinolines was also transformed into other functionalities to afford new quinolines (Scheme III) which are equally important synths for the synthesis of fused quinoline systems. Thus, the formyl group in quinolines was converted into a nitrile group in the presence of ceric ammonium nitrate in aqueous NH3 at 0°C in a single step to afford the corresponding 2-chloro-3-
cyanoquinolines 9 in high yield (Scheme III). The formation of compounds 9 was supported spectroscopically by showing the absence of the formyl proton in the 1H NMR spectra and the appearance of characteristic nitrile absorption at 2200 cm\(^{-1}\) in IR spectra. The nature of the new cyanoquinolines 9 was further evaluated chemically from aldoxime derivative 7. The aldoxime 7 on dehydration with thionyl chloride afforded the formyl proton in the 1H NMR spectra and the spectral data as the derivatives 9.

Similarly, the formyl group in a few of the quinolines 2 was oxidized to the ester group. Among the various methods available, the formyl group was oxidized with NIS-K\(_2\)CO\(_3\) in CH\(_2\)OH/C\(_2\)H\(_5\)OH at rt to afford corresponding 2-chloro-3-alkoxybenzoylquinolines 10 in good yield (Scheme III).

In conclusion, we have described a simple and regioselective synthesis of functionalized quinolines through Vilsmeier cyclisation of N-arylacetamides. The cyclisation is facilitated by N-arylacetamides having electron activating groups at \(m\)-position in the aromatic ring. However, satisfactory yields are found in all quinolines bearing electron activating groups. The reaction provides functionalized quinolines which are useful intermediates for further chemical manipulation for the preparation of fused quinoline heterocycles.

**Experimental Section**

Melting points were determined in an open capillary tube with a Buchi melting point apparatus and are uncorrected. Elemental analyses were carried out using Perkin-Elmer 240C CHN-analyzer. IR spectra were recorded on a FT/IR-5300 (JASCO) infrared spectrophotometer. 1H NMR and 13C NMR spectra were run in CDCl\(_3\) at 300 MHz and 75 MHz on a Jeol AL-300 and AL-75 spectrometers (chemical shifts in \(\delta\), ppm relative to TMS as an internal standard). Mass spectra were recorded on a Finnigan MAT 1020B instrument and only the prominent and relevant mass fragments were considered. Reactions were monitored by TLC, using silica gel PF\(_{254+366}\) as an adsorbent and ethyl acetate-hexane in different ratios as eluent. Reagent quality solvents and phosphorous oxychloride were used as such.

**General procedure for the synthesis of 2-chloro-3-formylquinolines 2a-k.** To a solution of 1a-k (5 mmoles) in dry DMF (15 mmoles) at 0-5°C with stirring POCl\(_3\) (60 mmoles) was added dropwise and the mixture stirred at 80-90°C for time ranging between 4-16 hr. The mixture was poured into crushed ice, stirred for 5 min and the resulting solid filtered, washed well with water and dried. The compounds were purified by recrystallisation from either ethyl acetate or acetonitrile.

Spectral and physical data of compounds 2a-k are given in Table I and Table III, respectively.

**Reaction of compounds 2 with sodium sulphide:**

**Formation of 3-formylquinoline-2-thiones 3.** To a solution of 2 (1 mmole) in dry DMF (5 mL), sodium sulphide ((1.5 mmoles, fused flakes) was added and stirred for 1-2 hr at rt. On completion of the reaction (monitored by TLC), the reaction mixture was poured into ice-water (ca. 15 mL) and made acidic with acetic acid. The product was filtered off, washed well with water, dried and was pure enough for further use.

**3-formylquinoline-2(1H)-thione 3a:** Yield 84%, m.p. 285-86°C (dec.) [lit. m.p. 288°C (dec.)]; IR (KBr): 3261, 1687, 1622, 1157 cm\(^{-1}\); 1H NMR (DMSO-d\(_6\)): \(\delta\) 14.0 (s, 1H, NH D\(_2\)O exchangeable), 10.7 (s, 1H, CHO), 8.4 (s, 1H, H-4), 8.0 (d, 1H, H-5), 7.8 (dt, 1H, H-6), 7.6 (d, 1H, H-8), 7.4 (dt, 1H, H-7).

**3-formyl-7-methylquinoline-2(1H)-thione 3b:** Yield 82%, m.p. 254-55°C (dec.); IR (KBr): 3198, 1688, 1618, 1162 cm\(^{-1}\); 1H NMR (DMSO-d\(_6\)): \(\delta\) 14.3 (brs, 1H, NH D\(_2\)O exchangeable), 10.8 (s, 1H, CHO), 9.1 (s, 1H, H-4), 8.2-7.5 (m, 3H, H-5, H-6 & H-8), 2.6 (s, 3H, CH\(_3\)).

**3-formyl-7-methoxyquinoline-2(1H)-thione 3c:** Yield 84%, m.p. 248-49°C (dec.); IR (KBr): 3204, 1691, 1613, 1153 cm\(^{-1}\); 1H NMR (DMSO-d\(_6\)): \(\delta\) 14.4 (br, 1H, NH D\(_2\)O exchangeable), 10.6 (s, 1H, CHO), 8.8 (s, 1H, H-4), 7.9 (m, 1H, H-5), 7.2 (m, 2H, H-6 & H-8), 4.0 (s, 3H, OCH\(_3\)).

**Synthesis of thioethers 4.** To a solution of 2 (1 mmole) in dry DMF (5 mL), sodium sulphide ((1.5 mmoles, fused flakes) was added and stirred for 1-2 hr at rt. On completion of the reaction (monitored by TLC) the corresponding halo compound was added and stirred for another 10-15 min and poured into ice-cooled water. The precipitate obtained was filtered, dried and purified by recrystallisation from ethanol/aq. ethanol/methanol.

**3-Formyl-2-methylthioquinoline 4a:** Yield 93%, m.p. 98°C; IR (KBr): 1687 cm\(^{-1}\); 1H NMR (CDCl\(_3\)): \(\delta\) 10.5 (s, 1H, CHO), 8.6 (s, 1H, H-4), 8.3-7.4 (m, 4H, H-5, H-6, H-7&H-8), 2.8 (s, 3H, SCH\(_3\)).

**3-Formyl-2-benzylthioquinoline 4b:** Yield 96%, m.p. 103-04°C [lit. m.p. 104°C]; IR (KBr): 1688 cm\(^{-1}\); 1H NMR(CDCl\(_3\)): \(\delta\) 10.5 (s, 1H, CHO), 8.6 (s, 1H, H-4), 9.1 (s, 1H, H-2), 8.8 (s, 1H, H-7), 8.0 (d, 1H, H-8), 7.4 (m, 2H, H-5, H-6 & H-8), 6.9 (d, 1H, H-6), 4.0 (s, 3H, OCH\(_3\)).

**3-Formyl-7-methoxyquinoline-2(1H)-thione 3c:** Yield 84%, m.p. 248-49°C (dec.); IR (KBr): 3204, 1691, 1613, 1153 cm\(^{-1}\); 1H NMR (DMSO-d\(_6\)): \(\delta\) 14.4 (br, 1H, NH D\(_2\)O exchangeable), 10.6 (s, 1H, CHO), 8.8 (s, 1H, H-4), 7.9 (m, 1H, H-5), 7.2 (m, 2H, H-6 & H-8), 4.0 (s, 3H, OCH\(_3\)).
3-Formyl-7-methoxy-2-allylthioquinoline 4c: Yield 76%, m.p. 180°C; IR (KBr): 1687 cm⁻¹; 1H NMR (CDCl₃): δ 12.24(br, 1H, NH, D₂O exchangeable), 10.24(s, 1H, CHO), 8.0-7.9 (m, 4H, H-5, H-6, H-7 & H-8), 5.29 (s, 2H, SCH₂), 4.0(s, 3H, CH₃).

3-Formyl-7-methyl-2(1H)-quinolone 5a: Yield 93%, m.p. 303-04°C; IR (KBr): 1687 cm⁻¹; 1H NMR (DMSO-d₆): δ 12.2(br, 1H, NH, D₂O exchangeable), 10.4(s, 1H, CHO), 8.7(s, 1H, H-4), 7.79(d, 1H, H-5), 7.7(s, 1H, H-8), 7.1(d, 1H, H-6), 2.4(s, 3H, OCH₃).

3-Formyl-7-methoxy-2(1H)-quinolone 5b: Yield 83%, m.p. 259°C (dec.); IR (KBr): 1621cm⁻¹; 1H NMR (DMSO-d₆): δ 12.0(s, 1H, CHO), 8.7(s, 1H, H-4), 8.4(d, 1H, H-5), 8.0-7.4 (m, 2H, H-6 & H-8), 6.3(m, 1H, =CH), 5.3(m, 2H, =CH₂), 4.2(d, 2H, CH₂), 4.0(s, 3H, OCH₃).

Synthesis of 3-formyl-2(1H)-quinolones 5.

Method A. A suspension of aldehydes 2 (1 mmole) in 70% acetic acid (10 mL) was heated under reflux for 4-6 hr. The completion of the reaction was checked by TLC. Upon cooling the reaction mixture a solid product precipitated out which was filtered, washed well with water, dried and purified by recrystallisation from DMF.

Method B. A suspension of aldehydes 2 (1 mmole) in dilute dichloroacetic acid (15 mL, 50%) was heated under reflux for 4-6 hr. The solution was diluted with cold water and the solid precipitate so formed was collected by filtration, dried and purified by recrystallisation from DMF.

3-Formyl-2(1H)-quinolone 5c: Yield 98%, m.p. 199°C (dec.); IR (KBr): 1687 cm⁻¹; 1H NMR (DMSO-d₆): δ 12.0(s, 1H, CHO), 8.9 (s, 1H, H-4), 8.6 (d, 1H, H-5), 8.4-7.7 (m, 2H, H-6 & H-8), 5.2 (d, 2H, SCH₂), 4.0 (s, 3H, OCH₃), 2.3 (s, 1H, =CH).

Reaction of quinolones 5 with POCl₃: Formation of 2-chloro-3-formylquinolines 2. To quinolones 5 (1 mmole) POCl₃ (10 mmoles) was added and heated under reflux for 3-4 hr. After completion, the reaction mixture was poured into crushed ice. The resulting precipitate was filtered, washed with water, dried and purified by recrystallisation from ethyl acetate/acetonitrile.

Conversion of compounds 2 into their oxime, hydrazone and anil derivatives 7. To a solution of 2 (1 mmole) in methanol was added with stirring hydroxylamine hydrochloride (1.2 mmoles) and sodium acetate (1.2 mmoles) and stirred at rt for another 20 min whereupon a white precipitate was formed. The reaction mixture was diluted with ice-cooled water and the product was filtered off, dried, and purified by recrystallisation from aqueous ethanol.

2-Chloroquinoline-3-carboxaldoxime 7a: Yield 94%, m.p. 251°C (dec.); IR (KBr): 3482, 1614 cm⁻¹; 1H NMR (DMSO-d₆): δ 12.21(s, 1H, OH, D₂O exchangeable), 9.0(s, 1H, H-4), 8.6(s, 1H, =HC-N), 8.4-7.73(m, 4H, H-5, H-6, H-7& H-8).

2-Chloro-7-methoxyquinoline-3-carboxaldehyde-hydrazone 7e: Yield 86%, m.p. 207°C (dec.); IR (KBr): 3346, 3182, 1623 cm⁻¹; 1H NMR (CDCl₃): δ 13.06(s, 2H, NH₂ D₂O exchangeable), 9.0(s, 1H, =CH).

To a solution of 2 (1 mmole) in ethanol (5 mL) was added with stirring hydrazine hydrate (2 mmoles, 99-100%) and the mixture was refluxed for 15 min. On cooling, the pale yellow crystalline mass of the product which precipitated out was filtered off, washed with cold ethanol and water, dried and purified by recrystallisation from ethanol.

2-Chloro-7-methyliquinoline-3-carboxaldehydehydrazone 7f: Yield 88%, m.p. 198°C (dec.); IR (KBr): 3301, 1693, 1651 cm⁻¹; 1H NMR (CDCl₃): δ 10.5 (s, 1H, CHO), 8.5 (s, 1H, H-4), 7.9-7.6 (m, 4H, H-5, H-6, H-7 & H-8), 5.29 (s, 2H, CH₂), 2.4 (s, 1H, =CH).
To a solution of 2a (1 mmole) in ethanol (5 mL) was added with stirring the amine (1.5 mmole) and a few drops of glacial acetic acid and stirring continued for another 15 min whereupon a yellow solid precipitated out, which was filtered and purified by recrystallisation from ethanol.

2-Chloro-3-p-toulyliminomethylquinoline 7d: Yield 97%, m.p. 124-25°C; IR (KBr): 1636 cm \(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 9.2(s, 1H, H-4), 9.1(s, 1H, -HC=N), 8.33-7.33(m, 8H, H-5, H-6, H-7, H-8 & 4 Ar H's), 1128, 1089, 1057cm \(^{-1}\); 1H NMR (DMSO-\(d_6\)): \(\delta\) 9.1(s, 1H, H-4), 8.8(s, 1H, H-5), 8.1(s, 1H, H-6), 7.75(d, 1H, H-7), 7.65(s, 1H, H-5), 2.66(s, 3H, CH\(_3\)).

Synthesis of tetrazoloquinolines 8. To a solution of 2 (1 mmole) taken in absolute ethanol (5 mL), p-toluenesulphonic acid (1 mmole) and sodium azide (1.5 mmole) were added and the reaction mixture was heated under reflux for time ranging between 2-18hr. After completion of the reaction (monitored by TLC) the reaction mixture was poured into ice-cooled water and the resulting precipitate was filtered, dried and purified by recrystallisation from acetone.

4-Formyltetrazolo[1,5-a]quinoline 8a: Yield 82%, m.p. 245-47°C (dec.); IR (KBr): 1703, 1614, 1128, 1089, 1057cm \(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) 10.6(s, 1H, CHO), 9.2(s, 1H, H-5), 9.28(s, 1H, H-6) 9.8(d, 1H, H-6) 8.6(d, 1H, H-9) 8.4-7.9(m, 1H, H-7 & H-8); Mass: m/z 198(M+), 184, 171, 157, 143.

4-Formyl-8-methyltetrazolo[1,5-a]quinoline 8b: Yield 85%, m.p. 258-59°C (dec.) [lit. m.p. 258°C(dec.)]: IR (KBr): 1700, 1612, 1105, 1079, 1060 cm \(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) 10.5(s, 1H, CHO), 9.1(s, 1H, H-5), 8.5 (m, 2H, H-6 & H-7), 7.8(d, 1H, H-9), 2.6(s, 3H, CH\(_3\)).

4-Formyl-8-methoxytetrazolo[1,5-a]quinoline 8c: Yield 79%, m.p. 236°C (dec); IR (KBr): 1697, 1614, 1110, 1059, 1018 cm \(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) 10.6(s, 1H, CHO), 9.1(s, 1H, H-5), 8.5(d, 1H, H-6), 8.2(d, 1H, H-9), 7.6(d, 1H, H-7), 4.2(s, 3H, OCH\(_3\)).

Conversion into nitrile derivatives 9

Method A. A suspension of aldehydes 2 (1 mmole) in 30%aq. ammonia (3 mL) was stirred for 5 min at rt, resulting in formation of a turbid solution. To this CAN (1 mmole) was added with constant stirring at 0°C. After completion of the reaction (monitored by TLC, indicated by the disappearance of reddish brown colour) in 10-15 min it was extracted with chloroform-ethyl acetate mixture (5:3), dried (anhydrous Na\(_2\)SO\(_4\)), and concentrated under reduced pressure to obtain the solid product which was purified by recrystallisation from ethanol.

Method B. To a solution of oxime of aldehydes 7a (1 mmole) in dry benzene was added 3 mmoles of distilled thionyl chloride and the reaction mixture was refluxed for 30 min. The solvent was removed in vacuo to obtain the solid product which was washed well with water, dried and purified by recrystallisation from ethanol.
1H, H-8), 7.65-7.61(m, 2H, H-5 & H-7), 4.0(s, 3H, OCH3), 2.53(s, 3H, CH3); 13C NMR (CDCl3) δ 165.09(C=O), 52.87(OCH3), 21.57(CH3).

2-Chloro-7-methoxy-3-methoxycarbonylquinoline 10d: Yield 84%, m.p. 118-20°C; IR (KBr): 1728, 1620 cm⁻¹; 1H NMR (CDCl3): 4.0(s, 3H, OCH3), 3.9 (s, 3H, OCH3); 13C NMR (CDCl3): 7.75(d, 1H, H-5), 7.3(s, 1H, H-8), 7.25(d, 1H, H-6), 4.0(s, 3H, OCH3), 3.9 (s, 3H, OCH3); 13C NMR (CDCl3): δ 164.98(C=O), 55.78(OCH3), 52.72 (OCH3).

Acknowledgement
The authors thank the CSIR, New Delhi for financial support.

References
3 (a) Fujisawa T, Lida S & Sato T, Chem Lett 1984, 1173
   (c) Korodi F & Czilai Z, Org Prep Proced, 22, 1990, 579.
   (c) Tom N J & Ruel E M, Synthesis, 9, 2001, 1351.
13 Alsaidi H, Gallo R & Metzer J C R, Acad Sci Ser C 1979, 203
   (b) Bhattacharya B K, J Heterocyclic Chem, 23, 1986, 113
17 (a) Bandgr B P & Makone S S, Synlett, 2003, 262.
   (e) Nair V, Panicker S B, Nair L G, George T G & Augustine A, Synlett, 2 2003, 156.