Short and efficient method for the preparation of furo[3,2-f] quinoline

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Dedicated to Professor Csaba Szántay on his 80th birthday

Abstract
Furo[3,2-f]quinolines 5 were prepared by reacting the sodium salt of quinolin-6-ol and allyl bromides 2. The allyl aryl ethers 3 formed were then thermally rearranged under standard or microwave conditions. Acid-catalyzed cyclization of the products 4 afforded the title compounds.

Keywords: Furo[3,2-f]quinoline, allyl aryl ethers, Claisen rearrangement, ring closure, sonochemical conditions, pyrano[3,2-f]quinoline

Introduction

Furo[3,2-f]quinolines have not received much attention. Only three papers have so far been published dealing with the preparation of this ring system. B. B. Dey and T. R. Seshadri prepared the furoquinoline skeleton by the thermal decomposition of a quinolinopyrone derivative.1 R. Royer et al.2 described the synthesis of substituted furo[3,2-f]quinolines by the rearrangement of allylaryl ether followed by cyclization. Later on, M. Natsume et al.3 isolated the furoquinoline as by-product of their duocarmycin SA's synthesis.

Recently we have developed an effective method for the preparation of furo[2,3-f]isoquinolines by aromatic Claisen rearrangement and subsequent cyclization.4 Following these synthetic efforts toward the preparation of novel heterocyclic compounds which might be useful intermediates for the development of molecules of pharmaceutical or biological interest, we planned the elaboration of new synthesis generally applicable for the preparation of furo[3,2-f]quinolines. We present here a method for the preparation of furoquinolines 5a-c and their cycloalkano analogues 5d,e.
Results and Discussion

Ethers of quinolin-6-ol 3a-d were synthesized by reaction of the sodium salt of quinolinol (1) with the appropriate alkyl bromide 2a-d in good to acceptable yields (Scheme 1, Table 1, entries 1-4).

Scheme 1. Reagent and conditions: (a) NaH, DME, r.t.; (b) microwave oven, 175°C; or chlorobenzene, reflux; (c) H$_2$SO$_4$, 100°C.
The allyl ether 3a was subjected to thermal [3,3] rearrangement in a microwave oven to afford 4a. Acid-catalyzed intramolecular cyclization of the latter afforded the known furan[3,2]quinoline 5a\(^2\) (entries 5 and 10).

Starting with compound 3b, the microwave assisted rearrangement gave two products 4b and 4c (entry 6). Compound 4b was formed in the normal Claisen rearrangement. The unexpected product took its origin from consecutive rearrangement reactions (Scheme 2). Namely, [3,3]-sigmatropic rearrangement of ether 3b yielded intermediate 4c which then underwent a homo[1,5]-H shift to afford compound 6. Further [1,5]-H migration on this intermediate led to the formation of 4c.\(^7\)

Table 1. Compounds prepared by the rearrangement of 3a-d and subsequent cyclization

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>R(^1)</th>
<th>R(^2)</th>
<th>R(^3)</th>
<th>R(^4)</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield(^a) (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>3a</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>-</td>
<td>r.t.</td>
<td>24</td>
<td>69</td>
</tr>
<tr>
<td>2</td>
<td>2b</td>
<td>3b</td>
<td>Me</td>
<td>Me</td>
<td>H</td>
<td>-</td>
<td>r.t.</td>
<td>24</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>2c</td>
<td>3c</td>
<td>H</td>
<td>(CH(_2))(_3)</td>
<td>-</td>
<td>r.t.</td>
<td>24</td>
<td>46</td>
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<tr>
<td>4</td>
<td>2d</td>
<td>3d</td>
<td>H</td>
<td>(CH(_2))(_4)</td>
<td>-</td>
<td>r.t.</td>
<td>24</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3a</td>
<td>4a</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>175 (^b)</td>
<td>8</td>
<td>49.5</td>
</tr>
<tr>
<td>6</td>
<td>3b</td>
<td>4b</td>
<td>Me</td>
<td>Me</td>
<td>H</td>
<td>H</td>
<td>175 (^b)</td>
<td>10</td>
<td>44</td>
</tr>
<tr>
<td>7</td>
<td>3b</td>
<td>4c</td>
<td>Me</td>
<td>H</td>
<td>H</td>
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<td>12</td>
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<td>8</td>
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<tr>
<td>9</td>
<td>3c</td>
<td>4e</td>
<td>H</td>
<td>(CH(_2))(_3)</td>
<td>H</td>
<td>132 (^c)</td>
<td>100</td>
<td>70</td>
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<tr>
<td>10</td>
<td>4a</td>
<td>5a</td>
<td>H</td>
<td>H</td>
<td>H</td>
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<td>35</td>
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<tr>
<td>11</td>
<td>4b</td>
<td>5b</td>
<td>Me</td>
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<td>H</td>
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<td>54</td>
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<tr>
<td>14</td>
<td>4d</td>
<td>5d</td>
<td>H</td>
<td>(CH(_2))(_3)</td>
<td>H</td>
<td>100</td>
<td>1.5</td>
<td>75</td>
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<tr>
<td>15</td>
<td>4e</td>
<td>5e</td>
<td>H</td>
<td>(CH(_2))(_4)</td>
<td>H</td>
<td>100</td>
<td>1.5</td>
<td>74</td>
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</table>

\(^a\)Isolated and unoptimized yields; \(^b\)in microwave oven; \(^c\)in chlorobenzene.

Having the above result, we tried to synthesize compounds 3b and 4b with a phase transfer catalyzed reaction. Interestingly, the quaternary ammonium salt catalyzed reaction of quinolin-6-ol 1 with prenyl bromide (2b) afforded three compounds (entry 7). Besides the expected ether 3b, compounds 7 and 8 were isolated as major products. The formation of these new compounds is probably the result of direct aromatic electrophilic substitutions.
Acid-catalyzed intramolecular cyclization of 4b gave furoquinoline 5b in moderate yield. Likewise, compound 4c yielded 5c by acid (H2SO4 or HClO4) promoted ring closure (entries 11 and 12).

Treatment of the dimethylallyl derivative 7 with sulfuric acid provided pyrano [3,2-f]quinoline derivative 9 (entry 13).

Due to their sensitivity at the temperature of the microwave oven, compounds 3c and 3d were submitted to thermal rearrangement in boiling chlorobenzene. This protocol was especially effective for the preparation of 4d, but a moderate result was obtained for the synthesis of 4e (entries 8 and 9). Acid-catalyzed cyclization of 4d and 4e yielded 5d and 5e (respectively), as an approximately 4:1 mixture of trans and cis stereoisomers (entries 14 and 15). Small amounts of these mixtures were separated by preparative HPLC and the stereochemistry of isomers was established by 1H and 13C NMR studies. For example, in the cis-fused isomer of 5d we saw a NOE interaction between the 7a proton and 11a proton (4.82 and 3.45, respectively). This interaction was absent in the spectrum of the corresponding trans-isomer. For 5e, on the bases of γ-effect in chemical shift between C8 and C12 in the spectrum the cis-isomer was identified. This correlation is in concord with our earlier findings in the series of furo[2,3-f]isoquinolines.4

In summary, we have developed a general and efficient method for the preparation of [3,2-f]quinoline derivatives 5a-e from quinolin-6-ol (1) and allyl bromides 2a-d. This process involves the thermal rearrangement of ethers 3a-d, followed by acid-catalyzed intramolecular cyclization of the products 4a-e. This synthesis using the readily available starting compounds seems to provide a powerful methodology for the construction of furo-condensed quinoline derivatives.

**Experimental Section**

**General Procedures.** Solvents were used as received from commercial vendors and no further attempts were made to purify or dry them. Mps were determined on a Büchi apparatus and are uncorrected. 1H and 13C NMR spectra were obtained on a Bruker DRX-500 spectrometer. All NMR spectra are reported in ppm relative to TMS. IR spectra were measured on a Specord 2000
spectrometer. Merck precoated silica gel 60 F254 plates were used for TLC and Kieselgel 60 for column chromatography. Solvent were mixed on a v/v basis. HPLC chromatographic analyses and separation were performed with a Waters 600 equipped with a photodiode array detector 990. Stationary phase for compound 5e was Supelcosil™ SPLC-18-DB, 250x10 mm, eluens MeOH/H2O/H3PO4 4:6:0.05. For compound 5d stationary phase was Waters Symmetry C18, 150x3.9 mm. For the separation of isomers of 5f we worked on Supelcosil™ PLC-18 column, 250x21.2 mm, eluens MeOH/3% tartaric acid solution/H3PO4 4:6:0.02. Microwave accelerated reactions were conducted in an CEM Focused Microwave™ Synthesis System (CEM Corporation, Metthews, NC,USA).

3-Bromocyclohex-1-ene (2c) and 3-bromocyclohept-1-ene (2d) were prepared by literature procedures.

**Preparation of ethers 3. General procedure**

To a cold stirred suspension of NaN3 (24 mmol, 63.7% in mineral oil) in DME (10 mL) a solution of quinolin-6-ol (I: 2.23 g, 15.4 mmol) in DME (200 mL) was added dropwise and the resultant mixture was stirred at 0 °C for 1.5 h. To this mixture the appropriate bromide (2: 23 mmol) was then added and stirring was continued at r.t. for 24 h. The reaction mixture was quenched with sat. aq. NaCl (400 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with 1N NaOH solution and H2O and then dried over MgSO4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (CH2Cl2 – acetone 4:1).

**6-Allyloxyquinoline (3a).** Yield: 69%; brown oil; Rf = 0.77 (CH2Cl2 – acetone 2:1). 1H NMR (CDCl3): δ = 4.66 (d, J = 5.4 Hz, 2H, CH2), 5.34 (dd, J = 10.6 and 1.1 Hz, 1H, =CH), 5.47 (dd, J = 17.2 and 1.2 Hz, 1H, =CH), 7.08 (d, J = 2.7 Hz, 1H, C5-H), 7.34 (dd, J = 8.2 and 1.2 Hz, 1H, C3-H), 7.40 (dd, J = 9.1 and 2.7 Hz, 1H, C7-H), 7.99 (d, J = 9.1 Hz, 1H, C8-H), 8.02 (m, 1H, C4-H), 8.77 (dd, J = 4.2 and 1.6 Hz, 1H, C2-H).

**6-(3-Methylbut-2-en-1-yloxy)quinoline (3b).** Yield: 83%; brown oil; Rf = 0.77 (CH2Cl2 – acetone 2:1). 1H NMR (CDCl3): δ = 1.78 (s, 3H, CH3), 1.82 (s, 3H, CH3), 4.62 (d, J = 6.6 Hz, 2H, CH2), 5.56 (t, J = 6.6 Hz, 1H, C2'-H), 7.08 (d, J = 2.5 Hz, 1H, C5-H), 7.34 (dd, J = 8.2 and 4.2 Hz, 1H, C3-H), 7.39 (dd, J = 9.2 and 2.5 Hz, 1H, C7-H), 8.01 (d, J = 9.6 Hz, 1H, C8-H), 8.03 (d, J = 9.8 Hz, 1H, C4-H).

**6-(Cyclohex-2-en-1-yloxy)quinoline (3c).** Yield: 46%; yellow solid mp 65-69 °C; Rf = 0.28 (hexane – EtOAc 4:1). 1H NMR (CDCl3): δ = 1.78 (m, 1H, C5'-H), 1.87 (m, 1H, C5'-H), 1.95 (m, 1H, C6'-H), 2.03 (m, 1H, C6'-H), 2.06 (m, 1H, C4'-H), 2.17 (m, 1H, C4'-H), 4.95 (m, 1H, C1'-H), 8.02 (m, 1H, C4-H), 8.77 (dd, J = 4.2 and 1.6 Hz, 1H, C2-H).

**6-(3-Methylbut-2-en-1-yloxy)quinoline (3b).** Yield: 83%; brown oil; Rf = 0.77 (CH2Cl2 – acetone 2:1). 1H NMR (CDCl3): δ = 1.78 (s, 3H, CH3), 1.82 (s, 3H, CH3), 4.62 (d, J = 6.6 Hz, 2H, CH2), 5.56 (t, J = 6.6 Hz, 1H, C2'-H), 7.08 (d, J = 2.5 Hz, 1H, C5-H), 7.34 (dd, J = 8.2 and 4.2 Hz, 1H, C3-H), 7.39 (dd, J = 9.2 and 2.5 Hz, 1H, C7-H), 8.01 (d, J = 9.6 Hz, 1H, C8-H), 8.03 (d, J = 9.8 Hz, 1H, C4-H).

**6-(3-Methylbut-2-en-1-yloxy)quinoline (3b).** Yield: 83%; brown oil; Rf = 0.77 (CH2Cl2 – acetone 2:1). 1H NMR (CDCl3): δ = 1.78 (s, 3H, CH3), 1.82 (s, 3H, CH3), 4.62 (d, J = 6.6 Hz, 2H, CH2), 5.56 (t, J = 6.6 Hz, 1H, C2'-H), 7.08 (d, J = 2.5 Hz, 1H, C5-H), 7.34 (dd, J = 8.2 and 4.2 Hz, 1H, C3-H), 7.39 (dd, J = 9.2 and 2.5 Hz, 1H, C7-H), 8.01 (d, J = 9.6 Hz, 1H, C8-H), 8.03 (d, J = 9.8 Hz, 1H, C4-H).

**6-(Cyclohex-2-en-1-yloxy)quinoline (3c).** Yield: 46%; yellow solid mp 65-69 °C; Rf = 0.28 (hexane – EtOAc 4:1). 1H NMR (CDCl3): δ = 1.78 (m, 1H, C5'-H), 1.87 (m, 1H, C5'-H), 1.95 (m, 1H, C6'-H), 2.03 (m, 1H, C6'-H), 2.06 (m, 1H, C4'-H), 2.17 (m, 1H, C4'-H), 4.95 (m, 1H, C1'-H), 8.02 (m, 1H, C4-H), 8.77 (dd, J = 4.2 and 1.6 Hz, 1H, C2-H).
5.94 (m, 1H, C2'-H), 6.02 (m, 1H, C3'-H), 7.12 (d, \( J = 2.6 \) Hz, 1H, C5-H), 7.33 (dd, \( J = 8.3 \) and 4.3 Hz, 1H, C7-H), 7.38 (dd, \( J = 9.2 \) and 2.6 Hz, 1H, C7-H), 8.01 (d, \( J = 9.2 \) Hz, 1H, C8-H), 8.03 (d, \( J = 9.2 \) Hz, 1H, C4-H), 8.75 (dd, \( J = 4.3 \) and 1 Hz, 1H, C2-H). 13C NMR (CDCl3): \( \delta = 19.11 \) (C-5'), 25.19 (C-4'), 28.25 (C-6'), 71.13 (C-1'), 107.26 (C-5), 121.08 (C-3), 123.14 (C-7), 125.55 (C-2'), 129.11 (C-4a), 130.59 (C-8), 132.39 (C-3'), 134.60 (C-4), 143.83 (C-8a), 147.45 (C-2'), 155.61 (C-6).


6-(Cyclohept-2-en-1-yloxy)quinoline (3d). Yield: 38%; brown oil; \( R_f = 0.71 \) (CH2Cl2 – acetone 2:1). 1H NMR (CDCl3): \( \delta = 1.45 \) (m, 1H, C5'-H), 1.72 (m, 1H, C6'-H), 1.76 (m, 1H, C5'-H), 1.83 (m, 1H, C7'-H), 2.07 (m, 1H, C6'-H), 2.10 (m, 1H, C7'-H), 2.20 (m, 1H, C4'-H), 2.27 (m, 1H, C4'-H), 5.02 (m, 1H, C1'-H), 5.84 (m, 1H, C2'-H), 5.92 (m, 1H, C3'-H), 7.01 (d, \( J = 2.5 \) Hz, 1H, C5-H), 7.32 (dd, \( J = 8.3 \) and 4.2 Hz, 1H, C3-H), 7.37 (dd, \( J = 9.2 \) and 2.5 Hz, 1H, C7-H), 8.00 (d, \( J = 9.0 \) Hz, 1H, C8-H), 8.02 (d, \( J = 9.2 \) and 2.5 Hz, 1H, C7-H), 8.00 (d, \( J = 9.0 \) Hz, 1H, C8-H), 8.02 (d, \( J = 7.0 \) Hz, 1H, C4-H), 8.75 (d, \( J = 3.8 \) Hz, 1H, C2-H). 13C NMR (CDCl3): \( \delta = 26.48 \) (C-5'), 27.49 (C-6'), 28.58 (C-4'), 77.65 (C-1'), 107.44 (C-5), 121.25 (C-3), 123.18 (C-7), 129.30 (C-4a), 130.85 (C-8), 131.44 (C-3'), 134.84 (C-4), 135.16 (C-2'), 144.17 (C-8a), 147.76 (C-2), 155.73 (C-6). Anal. Calcd for C16H17NO: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.02; H, 7.12; N, 6.01.

5-Allylquinolin-6-ol (4a) 3\( a \) (1.2 g, 6.4 mmol) was heated at 175 °C for 8 h in a microwave oven. After cooling, the light brown solid was treated with CH2Cl2 and the precipitated crystals were collected by filtration. Yield: 0.59 g (49.5%); mp 158-162 °C [lit., 2 155°C]; \( R_f = 0.44 \) (CH2Cl2 – acetone 2:1). 1H NMR (CDCl3): \( \delta = 3.73 \) (d, \( J = 5.7 \) Hz, 2H, CH2), 4.93 (m, 2H, =CH), 5.95 (m, 1H, HC=), 7.41 (dd, \( J = 9 \) and 4 Hz, 1H, C5-H), 7.42 (d, \( J = 9 \) Hz, 1H, C7-H), 7.78 (d, \( J = 9 \) Hz, 1H, C8-H), 8.26 (d, \( J = 8.5 \) Hz, 1H, C4-H), 8.66 (d, \( J = 3 \) Hz, 1H, C2-H), 9.88 (s, 1H, OH). 13C NMR (CDCl3): \( \delta = 28.46 \) (CH2), 115.16 (=C), 116.80 (C-5), 121.20 (C-3), 121.49 (C-7), 128.23 (C-4a), 128.75 (C-8), 131.33 (C-4), 136.79 (C=), 143.56 (C-C-8a), 146.72 (C-2), 152.59 (C-6).

5-(2-Methylbut-3-en-2-yl)quinolin-6-ol (4b) and 5-(3-methylbut-3-en-2-yl)quinolin-6-ol (4c) 3\( b \) (1.0 g, 4.7 mmol) was heated at 175 °C for 10 h in a microwave oven. After cooling, the reaction mixture was dissolved in a mixture of CH2Cl2 – acetone (5:2) and purified by column chromatography to yield 0.44 g of 4b (44%) and 0.12 g of 4c (12%).

Compound 4b. Brown crystalline solid; mp 132-136 °C; \( R_f = 0.18 \) (CHCl3 – acetone 10:1). 1H NMR (CDCl3): \( \delta = 1.80 \) (s, 6H, 2 CH3), 5.20 (m, 2H, =CH), 6.44 (m, 1H, HC=), 7.28 (m, 2H, C3-H and C7-H), 7.84 (d, \( J = 9 \) Hz, 1H, C5-H), 8.67 (d, \( J = 3.7 \) Hz, 1H, C2-H), 8.79 (d, \( J = 8.9 \) Hz, 1H, C4-H). 13C NMR (CDCl3): \( \delta = 29.84 \) (2 CH3), 42.65 (C-2'), 110.95 (C-4'), 119.13 (C-3), 123.23 (C-5), 124.33 (C-7), 128.89 (C-4a), 129.28 (C-8), 135.36 (C-4'), 144.61 (C-8a), 145.59 (C-2'), 151.22 (C-3'), 153.33 (C-6). Anal. Calcd for C14H15NO: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.60; H, 7.17; N, 6.35.

Compound 4c. Light brown crystals; mp 172-176 °C; \( R_f = 0.26 \) (CHCl3 – acetone 10:1). 1H NMR (CDCl3): \( \delta = 1.55 \) (d, \( J = 6.2 \) Hz, 3H, CH3), 1.71 (s, 3H, CH3), 4.32 (q, \( J = 6.5 \) Hz, 1H, C2-H), 5.22 (d, \( J = 0.9 \) Hz, 1H, C4-H), 5.29 (s, 1H, C4-H), 7.34 (d, \( J = 9.1 \) Hz, 1H, C7-H), 7.37 (dd,
\( J = 8.7 \) and \( 4.2 \) Hz, \( 1H, C_3-H \), \( 7.89 \) (d, \( J = 9.1 \) Hz, \( 1H, C_8-H \)), \( 8.47 \) (d, \( J = 8.6 \) Hz, \( 1H, C_4-H \)), \( 8.74 \) (dd, \( J = 4.2 \) and \( 1.2 \) Hz, \( 1H, C_2-H \)). \(^{13}C\) NMR (CDCl\(_3\)): \( \delta = 17.34 \) (C-1'), \( 22.77 \) (CH\(_3\)), \( 37.48 \) (C-2'), \( 111.43 \) (C-5), \( 120.81 \) (C-3), \( 122.86 \) (C-7), \( 128.37 \) (C-4a), \( 129.08 \) (C-8), \( 131.35 \) (C-4), \( 144.09 \) (C-8a), \( 146.53 \) (C-2), \( 150.06 \) (C-3'), \( 153.36 \) (C-6). Anal. Calcd for C\(_{14}H_{15}NO\): C, 78.84; H, 7.09; N, 6.57. Found: C, 78.66; H, 6.92; N, 6.38.

5-(3-Methylbut-2-en-1-yl)quinolin-6-ol (7) and 5,5-bis(3-methylbut-2-en-1-yl)quinolin-6(5H)-one (8)

To a stirred mixture of 1 (1.0 g, 6.9 mmol), KOH (24.4 mL 12.5% solution), and triethylbenzylammonium chloride (0.73 g, 4 mmol) in toluene (70 mL) was added 2b (1.87 g, 12.6 mmol), and stirring was continued at r.t. for 16 h. The reaction mixture was extracted with EtOAc (3 x 50 mL), the combined extracts were washed with sat. aq NaCl, and dried over MgSO\(_4\). Evaporation of the solvent under reduced pressure provided a mixture of three compounds which was separated by column chromatography on silica gel (CHCl\(_3\) – acetone 10:1) to give 3b (0.25 g, 16.8%), 7 (0.38 g, 26.2%), and 8 (0.47 g, 32.4%).

**Compound 7.** Brown crystals; mp 154-158 °C (EtOH - H\(_2\)O 3:2); \( R_f = 0.21 \) (CHCl\(_3\) – acetone 10:1). IR (KBr): 3450 (s, OH) cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\)): \( \delta = 1.69 \) (s, \( 3H, CH_3 \)), 1.88 (s, \( 3H, CH_3 \)), 3.76 (d, \( J = 6 \) Hz, \( 2H, C_1'-H \)), 3.83 (br s, 1H, OH), 5.19 (t, \( J = 6.5 \) Hz, 1H, C-2'H), 7.36 (t, \( J = 6.5 \) Hz, 1H, C-3'H), 7.38 (d, \( J = 9 \) Hz, 1H, C-7'H), 7.80 (d, \( J = 9 \) Hz, 1H, C-8'H), 8.27 (d, \( J = 9 \) Hz, 1H, C-4'H), 8.63 (d, \( J = 5 \) Hz, 1H, C-2'H). \(^{13}C\) NMR (CDCl\(_3\)): \( \delta = 17.82 \) (CH\(_3\)), 23.67 (C-1'-H), 25.38 (CH\(_3\)), 119.64 (C-5), 120.63 (C-3), 121.79 (C-7), 122.65 (C-2'), 127.16 (C-8), 128.62 (C-4a), 131.98 (C-3'), 132.42 (C-4), 134.14 (C-8a), 145.88 (C-2), 152.12 (C-6). Anal. Calcd for C\(_{14}H_{15}NO\): C, 78.84; H, 7.09; N, 6.57. Found: C, 78.60; H, 6.87; N, 6.33.

**Compound 8.** Brown oil; \( R_f = 0.82 \) (CHCl\(_3\) – acetone 10:1). IR (film): 1680 (s, CO) cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\)): \( \delta = 1.43 \) (s, \( 6H, 2 CH_3 \)), 1.47 (s, \( 6H, 2 CH_3 \)), 2.49 (dd, \( J = 14 \) and 7 Hz, \( 2H, C_1'-H \)), 2.88 (dd, \( J = 14 \) and 7 Hz, 2H, C-1'-H), 4.58 (t, \( J = 7 \) Hz, \( 2H, C_2'-H \)), 6.36 (d, \( J = 10 \) Hz, 1H, C-7'H), 7.29 (dd, \( J = 7 \) and 7.5 Hz, 1H, C-3'H), 7.57 (d, \( J = 10 \) Hz, \( 1H, C_8-H \)), 7.69 (d, \( J = 8 \) Hz, \( 1H, C_4-H \)), 8.56 (d, \( J = 5 \) Hz, 1H, C-2'H). \(^{13}C\) NMR (CDCl\(_3\)): \( \delta = 17.82 \) (CH\(_3\)), 23.67 (C-1'H), 25.38 (CH\(_3\)), 119.64 (C-5), 120.63 (C-3), 121.79 (C-7), 122.65 (C-2'), 127.16 (C-8), 128.62 (C-4a), 131.98 (C-3'), 132.42 (C-4), 143.14 (C-8a), 145.88 (C-2), 152.12 (C-6). Anal. Calcd for C\(_{19}H_{23}NO\): C, 81.10; H, 8.24; N, 4.98. Found: C, 80.82; H, 7.95; N, 4.69.

5-(Cyclohex-2-en-1-yl)quinolin-6-ol (4d)

A solution of 3c (1.0 g, 4.4 mmol) in chlorobenzene (45 mL) was stirred under reflux for 100 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (CH\(_2\)Cl\(_2\) – acetone 10:1) to yield 4d (0.7 g, 70%) as colorless crystals. Mp 148-152°C. \( R_f = 0.27 \) (CHCl\(_3\) – acetone 10:1).

IR (KBr): 3400 (s, OH) cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\)): \( \delta = 1.84 \) (m, \( 1H, C_5'-H \)), 1.97 (m, \( 2H, C_5'-H \) and \( C_6'-H \)), 2.05 (m, \( 1H, C_6'-H \)), 2.20 (m, \( 1H, C_4'-H \)), 2.29 (m, \( 1H, C_4'-H \)), 4.51 (m, \( 1H, C_1'-H \)), 5.82 (m, \( 1H, C_2'-H \)), 5.88 (m, \( 1H, C_3'-H \)), 7.34 (dd, \( J = 8.5 \) and 4.0 Hz, \( 1H, C_3-H \)), 7.42 (d, \( J = 9.0 \) Hz, \( 1H, C_7-H \)), 7.80 (d, \( J = 9.0 \) Hz, \( 1H, C_8-H \)), 8.65 (d, \( J = 8.5 \) Hz, \( 1H, C_4-H \)), 8.66 (d, \( J = 4.0 \) Hz, \( 1H, C_2-H \)), 8.8 (br. s, 1H, OH). \(^{13}C\) NMR (CDCl\(_3\)): \( \delta = 24.12 \) (C-5'), 25.57 (C-4'), 29.8 (C-6'9, 34.99
(C-1’), 121.07 (C-3), 122.19 (C-7), 123.46 (C-5), 127.71 (C-3’), 129.25 (C-4a), 130.29 (C-8), 133.00 (C-4), 133.02 (C-2’), 145.85 (C-4a), 147.59 (C-2), 153.18 (C-6). Anal. Calcd for C_{15}H_{15}NO: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.22; H, 6.95; N, 6.01.

5-(Cyclohept-2-en-1-yl)quinolin-6-ol (4e)

A solution of 3d (0.5 g, 2.1 mmol) in chlorobenzene (20 mL) was stirred under reflux for 100 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$ – acetone 10:1) to yield 4e (0.2 g, 38%) as colorless crystals. Mp 85-90°C. R$_f$ = 0.42 (CH$_2$Cl$_2$ – acetone 4:1). IR (KBr): 3420 (s, OH) cm$^{-1}$.

1H NMR (CDCl$_3$): δ = 1.50 (m, 1H, C 5'-H), 1.75 (m, 1H, C 6'-H), 1.88 (m, 1H, C 7'-H), 1.93 (m, 1H, C 5'-H), 2.08 (m, 1H, C 6'-H), 2.11 (m, 1H, C 7'-H), 2.27 (m, 1H, C 4'-H), 2.41 (m, 1H, C 4'-H), 4.62 (m, 1H, C1'-H), 5.95 (m, 2 H, C 2'-H and C 3'-H), 7.34 (d, $J = 9.0$ Hz, 1H, C 7-H), 7.36 (dd, $J = 9.0$ and 4.2 Hz, 1H, C 3-H), 7.74 (d, $J = 9.0$ Hz, 1H, C 8-H), 8.56 (d, $J = 8.4$ Hz, 1H, C 4-H), 8.70 (dd, $J = 4.2$ Hz, 1H, C 2-H), 11.7 (br. s, 1H, OH). 13C NMR (CDCl$_3$): δ = 27.59 (C-5'), 29.58 (C-4'), 31.24 (C-6'), 34.86 (C-7'), 38.36 (C-1'), 120.23 (C-3), 122.73 (C-7), 125.48 (C-5), 127.36 (C-8), 128.14 (C-4a), 131.65 (C-3'), 133.90 (C-4), 136.82 (C-2'), 143.14 (C-8a), 145.48 (C-2), 152.65 (C-6). Anal. Calcd for C$_{16}$H$_{17}$NO: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.12; H, 7.32; N, 6.03.

Furo[3,2-f]quinolines (5a-e). General procedure

A mixture of 4 (2.5 mmol) and concd H$_2$SO$_4$ (0.25 g, 5.3 mmol) was heated in a water bath for 1.5 h. After cooling, the reaction mixture was poured onto ice (10g), basified with 1N NaOH (15 ml) and extracted with CHCl$_3$ (3 x 15 mL). The combined organic layers were washed with H$_2$O, dried over MgSO$_4$ and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (using CH$_2$Cl$_2$ – acetone 5:1 as eluent).

1,2-Dihydro-2-methylfuro[3,2-f]quinoline (5a). Yield: 35%; brown oil, [lit.,$^2$ 26.5°C], R$_f$ = 0.87 (CH$_2$Cl$_2$ – acetone 2:1). 1H NMR (CDCl$_3$): δ = 1.56 (d, $J = 6.3$ Hz, 3H, CH$_3$), 3.07 (dd, $J = 15.2$ and 7.5 Hz, 1H, C 1-H), 3.60 (dd, $J = 15.2$ and 9.3 Hz, 1H, C 1-H), 5.17 (m, 1H, C 2-H), 7.29 (d, $J = 8.4$ and 4.1 Hz, 1H, C 8-H), 7.90 (d, $J = 8.3$ Hz, 1H, C 9-H), 7.93 (d, $J = 9.0$ Hz, 1H, C 5-H), 8.74 (d, $J = 2.9$ Hz, 1H, C 7-H). 13C NMR (CDCl$_3$): δ = 22.09 (CH$_3$), 35.56 (C-1), 80.88 (C-2), 115.39 (C-4), 118.20 (C-9b), 121.31 (C-8), 126.02 (C-9a), 130.33 (C-5), 130.88 (C-9), 144.54 (C-5a), 147.16 (C-7), 157.20 (C-3a).

1,2-Dihydro-1,1,2-trimethylfuro[3,2-f]quinoline (5b). Yield: 42.2%; light yellow oil; R$_f$ = 0.44 (CHCl$_3$ – acetone 10:1). 1H NMR (CDCl$_3$): δ = 1.32 (s, 3H, C 1-CH$_3$), 1.46 (d, $J = 6.6$ Hz, 3H, C 2-CH$_3$), 1.62 (s, 3H, C 1-CH$_3$), 4.53 (q, $J = 6.6$ Hz, 1H, C 2-H), 7.29 (d, $J = 8.9$ Hz, 1H, C 4-H), 7.33 (dd, $J = 8.5$ and 4.0 Hz, 1H, C 5-H), 7.93 (d, $J = 8.9$ Hz, 1H, C 9-H), 8.29 (d, $J = 8.5$ Hz, 1H, C 6-H), 8.73 (d, $J = 3.0$ Hz, 1H, C 7-H). 13C NMR (CDCl$_3$): δ = 13.89 (CH$_3$), 22.07 (CH$_3$), 26.56 (CH$_3$), 45.31 (C-1), 89.45 (C-2), 115.77 (C-4), 120.97 (C-8), 125.68 (C-9a), 126.89 (C-9b), 129.77 (C-9), 130.60 (C-5), 145.15 (C-5a), 146.88 (C-7), 156.10 (C-3a). Anal. Calcd for C$_{14}$H$_{15}$NO: C, 78.84; H, 7.09; N, 6.57. Found: C, 79.07; H, 6.92; N, 6.33.
1,2-Dihydro-1,2,2-trimethylfuro[3,2-f]quinoline (5c). Yield: 40%; light yellow oil; \( R_f = 0.59 \) (CHCl₃ – acetone 10:1). \(^1\)H NMR (CDCl₃): \( \delta = 1.31 \) (d, \( J = 7.1 \) Hz, 3H, C₁-CH₃), 1.44 (s, 3H, C₂-CH₃), 1.53 (s, 3H, C₂-CH₃), 3.44 (q, \( J = 7.1 \) Hz, 1H, C₅-H), 7.27 (d, \( J = 8.9 \) Hz, 1H, C₄-H), 7.34 (dd, \( J = 8.4 \) and 4.1 Hz, 1H, C₈-H), 7.93 (d, \( J = 8.9 \) Hz, 1H, C₅-H), 8.04 (d, \( J = 8.4 \) Hz, 1H, C₉-H), 8.73 (d, \( J = 3.3 \) Hz, 1H, C₇-H). \(^{13}\)C NMR (CDCl₃): \( \delta = 16.37 \) (C₁-CH₃), 22.41 (C₂-CH₃), 28.52 (C₂-CH₃), 44.66 (C-1), 90.23 (C-2), 115.96 (C-4), 121.13 (C-8), 123.90 (C-9b), 126.05 (C-9a), 130.36 (C-9), 130.44 (C-5), 144.80 (C-5a), 146.91 (C-7), 155.32 (C-3a). Anal. Calcd for C₁₄H₁₅NO: C, 78.84; H, 7.09; N, 6.57. Found: C, 79.01; H, 6.92; N, 6.30.

2,3-Dihydro-3,3-dimethyl-1H-pyrano[3,2-f]quinoline (9). Yield: 54%; brown oil; \( R_f = 0.66 \) (CHCl₃ – acetone 10:1). \(^1\)H NMR (CDCl₃): \( \delta = 1.39 \) (s, 6H, 2 CH₃), 1.95 (m, 2H, C₂-H), 3.00 (m, 2H, C₁-H), 7.25 (d, \( J = 9.6 \) Hz, 1H, C₅-H), 7.40 (m, 1H, C₉-H), 7.91 (d, \( J = 9.0 \) Hz, 1H, C₆-H), 8.19 (d, \( J = 8.2 \) Hz, 1H, C₁₀-H), 8.74 (m, 1H, C₈-H). \(^{13}\)C NMR (CDCl₃): \( \delta = 18.84 \) (C-1), 26.48 (CH₃), 32.23 (C-2), 74.53 (C-3), 112.08 (C₁₀b), 120.88 (C₉), 123.80 (C-5), 128.12 (C₁₀a), 128.45 (C-6), 130.77 (C₁₀), 143.51 (C-6a), 146.38 (C-8), 151.75 (C-4a).

7a,8,9,10,11,11a-Hexahydrobenzofuro[3,2-f]quinoline (5d). Yield: 75%; yellow oil; \( R_f = 0.72 \) (CH₂Cl₂ – acetone 2:1). cis-Isomer. \( t_R = 15.72 \) min. \(^1\)H NMR (CDCl₃): \( \delta = 1.25 \) (m, 1H, C₁₁-H), 1.32 (m, 1H, C₁₀-H), 1.57 (m, 1H, C₁-H), 1.67 (m, 1H, C₁₀-H), 1.86 (m, 1H, C₈-H), 2.12 (m, 1H, C₁₁-H), 2.35 (m, 1H, C₈-H), 3.45 (m, 1H, C₁₁a-H), 4.82 (m, 1H, C₇a-H), 7.32 (dd, \( J = 8.5 \) and 4.2 Hz, 1H, C₂-H), 7.34 (d, \( J = 9 \) Hz, 1H, C₂-H), 7.93 (d, \( J = 9 \) Hz, 1H, C₂-H), 7.99 (d, \( J = 8.2 \) Hz, 1H, C₁-H), 8.73 (d, \( J = 3 \) Hz, 1H, C₃-H). \(^{13}\)C NMR (CDCl₃): \( \delta = 20.18 \) (C-9), 22.37 (C₁₀), 27.24 (C₈), 29.19 (C₁₁), 39.59 (C₁₁a), 84.00 (C₇a), 115.85 (C₁₁b), 121.20 (C₁₁c), 125.35 (C₁₁e), 126.48 (C₁₁b), 129.89 (C₅), 130.88 (C₁), 144.66 (C₄a), 147.19 (C₃), 156.93 (C₆a). Anal. Calcd for C₁₅H₁₅NO: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.25; H, 6.98; N, 6.00.

trans-Isomer. \( t_R = 13.37 \) min. \(^1\)H NMR (CDCl₃): \( \delta = 1.32 \) (m, 1H, C₉-H), 1.50 (m, 1H, C₉-H), 1.67 (m, 1H, C₈-H), 1.88 (m, 2H, C₁₀-H), 2.03 (m, 2H, C₁₁-H), 2.15 (m, 1H, C₈-H), 3.62 (br. s, 1H, C₁₁a-H), 4.68 (br. s, 1H, C₇a-H), 7.30 (d, \( J = 9.1 \) Hz, 1H, C₆-H), 7.34 (dd, \( J = 8.5 \) and 4.0 Hz, 1H, C₂-H), 7.32 (d, \( J = 9.0 \) Hz, 1H, C₂-H), 7.93 (d, \( J = 9 \) Hz, 1H, C₂-H), 7.99 (d, \( J = 8.2 \) Hz, 1H, C₁-H), 8.73 (d, \( J = 3 \) Hz, 1H, C₃-H). \(^{13}\)C NMR (CDCl₃): \( \delta = 23.67 \) (C₉), 26.33 (C₁₁a), 29.20 (C₁₁), 31.06 (C₁₀), 33.79 (C₈), 70.84 (C₇a), 116.83 (C₁₁b), 120.94 (C₁₁c), 121.67 (C₆), 126.92 (C₁₁e), 129.56 (C₁), 144.22 (C₄a), 146.83 (C₃), 153.90 (C₆a). Anal. Calcd for C₁₅H₁₅NO: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.17; H, 6.99; N, 5.98.

7a,8,9,10,11,11a-Hexahydrobenzofuro[3,2-f]quinoline (5d). Yield: 75%; yellow oil; \( R_f = 0.72 \) (CH₂Cl₂ – acetone 2:1). cis-Isomer. \( t_R = 7.78 \) min. \(^1\)H NMR (CDCl₃): \( \delta = 1.45 \) (m, 1H, C₉-H), 1.50 (m, 2H, C₁₀-H and C₁₁-H), 1.71 (m, 1H, C₁₀-H), 1.75 (m, 1H, C₁₁-H), 1.89 (m, 2H, C₉-H and C₁₂-H), 1.94 (m, 1H, C₁₂-H), 2.08 (m, 1H, C₈-H), 2.27 (m, 1H, C₈-H), 3.87 (m, 1H, C₁₂a-H), 5.14 (m, 1H, C₇a-H), 7.27 (d, \( J = 8.0 \) Hz, 1H, C₂-H), 7.32 (dd, \( J = 8.5 \) and 4.2 Hz, 1H, C₂-H), 7.92 (d, \( J = 8.0 \) Hz, 1H, C₅-H), 8.03 (d, \( J = 8.3 \) Hz, 1H, C₁-H), 8.72 (dd, \( J = 3.7 \) and 1.0 Hz, 1H, C₃-H). \(^{13}\)C NMR (CDCl₃): \( \delta = 23.67 \) (C₉), 28.84 (C₁₁), 30.01 (C₁₂), 31.21 (C₁₀), 31.45 (C₈), 46.47 (C₁₂a), 88.19 (C₇a), 115.23 (C₆), 121.12 (C₂), 122.59 (C₅), 125.69 (C₁₂b), 130.32 (C₁), 130.67 (C₅), 144.89
trans-Isomer. $t_R = 7.08$ min. $^1$H NMR (CDCl$_3$): $\delta$ = 1.34 (m, 1H, C$_{11}$-H), 1.48 (m, 1H, C$_9$-H), 1.57 (m, 1H, C$_{11}$-H), 1.93 (m, 1H, C$_8$-H), 2.10 (m, 3H, C$_8$-H, C$_{10}$-H and C$_{12}$-H), 2.36 (m, 1H, C$_{10}$-H), 3.68 (br. s, 1H, C$_{12a}$-H), 4.82 (br. s, 1H, C$_{7a}$-H), 7.24 (d, $J$ = 9.2 Hz, 1H, C$_6$-H), 7.36 (dd, $J$ = 8.5 and 4.2 Hz, 1H, C$_2$-H), 7.86 (d, $J$ = 9.2 Hz, 1H, C$_5$-H), 8.17 (d, $J$ = 8.5 Hz, 1H, C$_1$-H), 8.73 (d, $J$ = 3.3 Hz, 1H, C$_3$-H). $^{13}$C NMR (CDCl$_3$): $\delta$ = 23.77 (C-9), 25.67 (C-11), 27.50 (C$_{12a}$), 28.43 (C-10), 34.63 (C-12), 36.89 (C-8), 73.03 (C-7a), 117.05 (C-12b), 120.78 (C-2), 122.64 (C-6), 127.14 (C-12c), 129.20 (C-5), 130.30 (C-1), 144.61 (C-4a), 146.71 (C-3), 151.84 (C-6a). Anal. Calcd for C$_{16}$H$_{17}$NO: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.10; H, 7.38; N, 6.04.

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References and Notes

