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 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**.

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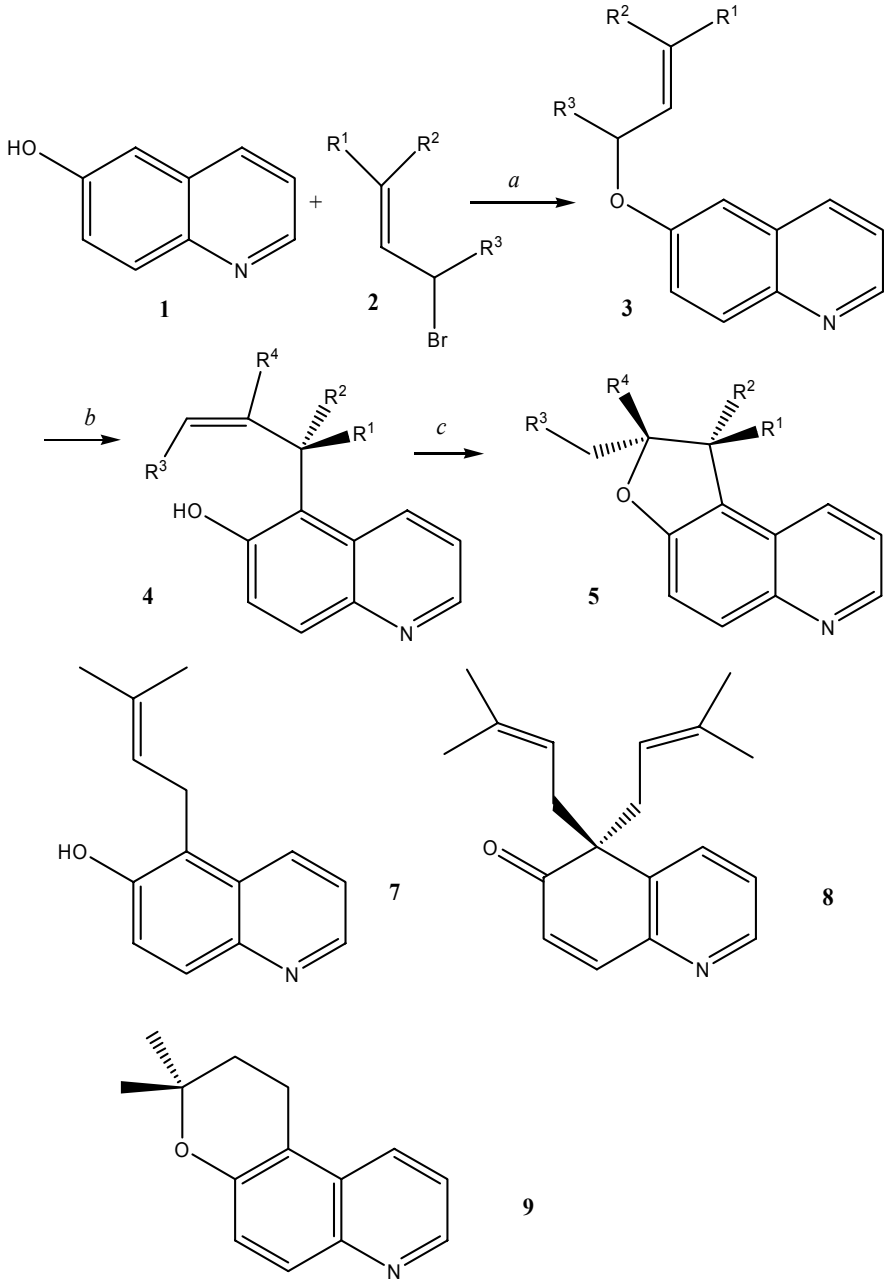
Results and Discussion

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_2SO_4, 100°C.

The allyl ether **3a** was subjected to thermal [3,3] rearrangement in a microwave oven to afford **4a**.[5] Acid-catalyzed intramolecular cyclization of the latter afforded the known furo[3,2]quinoline **5a**[2] (entries 5 and 10).

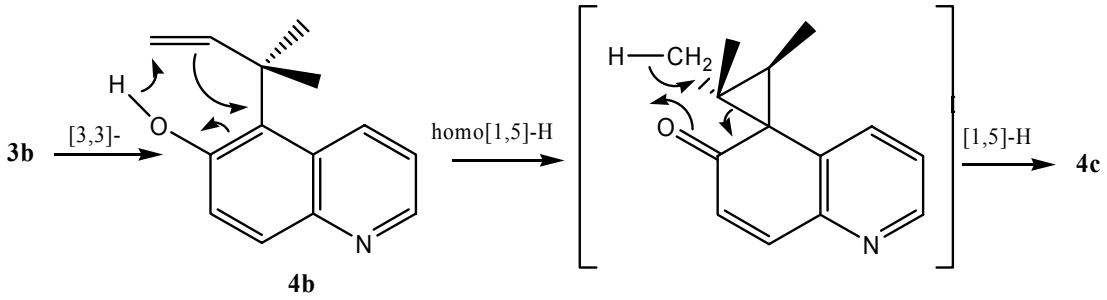
Starting with compound **3b**, the microwave assisted rearrangement gave two products **4b** and **4c** (entry 6). Compound **4b** was formed in the normal Claisen rearrangement.[6] The unexpected product took its origin from consecutive rearrangement reactions (Scheme 2). Namely, [3,3]-sigmatropic rearrangement 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

Entry	Substrate	Product	R^1	R^2	R^3	R^4	Temp (^oC)	Time (h)	Yield[a] (%)
1	**2a**	**3a**	H	H	H	-	r.t.	24	69
2	**2b**	**3b**	Me	Me	H	-	r.t.	24	83
3	**2c**	**3c**	H	$(CH_2)_3$		-	r.t.	24	46
4	**2d**	**3d**	H	$(CH_2)_4$		-	r.t.	24	38
5	**3a**	**4a**	H	H	H	H	175 [b]	8	49.5
6	**3b**	**4b**	Me	Me	H	H	175 [b]	10	44
		4c	Me	H	H	Me			12
7	**2b**	**3b**	Me	Me	H	H	r.t.	16	16.8
		7	H	H	Me	Me			26.2
		8	-	-	-	-			32.4
8	**3c**	**4e**	H	$(CH_2)_3$		H	132 [c]	100	70
9	**3d**	**4f**	H	$(CH_2)_4$		H	132 [c]	100	38
10	**4a**	**5a**	H	H	H	Me	100	1.5	35
11	**4b**	**5b**	Me	Me	H	H	100	1	42.2
12	**4c**	**5c**	Me	H	Me	H	100	1	40
13	**7**	**9**	-	-	-	-	100	1	54
14	**4d**	**5d**	H	$(CH_2)_3$		H	100	1.5	75
15	**4e**	**5e**	H	$(CH_2)_4$		H	100	1.5	74

[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.



Scheme 2

Acid-catalyzed intramolecular cyclization of **4b** gave furoquinoline **5b** in moderate yield. Likewise, compound **4c** yielded **5c** by acid (H_2SO_4 or $HClO_4$) 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 ^{1}H and ^{13}C 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 C_8 and C_{12} 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. ^{1}H and ^{13}C 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 F_{254} 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/H_2O/H_3PO_4 4:6:0.05. For compound **5d** stationary phase was Waters Symmetry C_{18}, 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/H_3PO_4 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**)[8] and 3-bromocyclohept-1-ene (**2d**)[9] were prepared by literature procedures.

Preparation of ethers 3. General procedure

To a cold stirred suspension of NaH (24 mmol, 63.7% in mineral oil) in DME (10 mL) a solution of quinolin-6-ol (**1**: 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 H_2O and then dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (CH_2Cl_2 – acetone 4:1).

6-Allyloxyquinoline (3a). Yield: 69%; brown oil; R_f = 0.77 (CH_2Cl_2 – acetone 2:1). ^{1}H NMR ($CDCl_3$): δ= 4.66 (d, *J*= 5.4 Hz, 2H, CH_2), 5.34 (dd, *J*= 10.6 and 1.1 Hz, 1H, =CH), 5.47 (dd, *J*= 17.2 and 1.2 Hz, 1H, =CH), 6.12 (m, 1H, =CH), 7.08 (d, *J*= 2.7 Hz, 1H, C_5-H), 7.34 (dd, *J*= 8.2 and 1.2 Hz, 1H, C_3-H), 7.40 (dd, *J*= 9.1 and 2.7 Hz, 1H, C_7-H), 7.99 (d, *J*= 9.1 Hz, 1H, C_8-H), 8.02 (m, 1H, C_4-H), 8.77 (dd, *J*= 4.2 and 1.6 Hz, 1H, C_2-H).

^{13}C NMR ($CDCl_3$): δ= 69.07 (C-2'), 106.38 (C-5), 118.04 (C-4'), 121.37 (C-3), 122.51 (C-6), 129.25 (C-4a), 130.94 (C-7), 132.84 (C-3'), 134.81 (C-4), 144.48 (C-7a), 148.06 (C-2), 156.67 (C-6).

6-(3-Methylbut-2-en-1-yloxy)quinoline (3b). Yield: 83%; brown oil; R_f = 0.56 ($CHCl_3$ – acetone 10:1). ^{1}H NMR ($CDCl_3$): δ= 1.78 (s, 3H, CH_3), 1.82 (s, 3H, CH_3), 4.62 (d, *J*= 6.6 Hz, 2H, CH_2), 5.56 (t, *J*= 6.6 Hz, 1H, $C_{2'}$-H), 7.08 (d, *J*= 2.5 Hz, 1H, C_5-H), 7.34 (dd, *J*= 8.2 and 4.2 Hz, 1H, C_3-H), 7.39 (dd, *J*= 9.2 and 2.5 Hz, 1H, C_7-H), 8.01 (d, *J*= 9.6 Hz, 1H, C_8-H), 8.03 (d, *J*= 9.8 Hz, 1H, C_4-H). ^{13}C NMR ($CDCl_3$): δ= 18.21 (CH_3), 25.69 (CH_3), 64.90 (C-1'), 105.74 (C-5), 118.86 (C-2'), 120.93 (C-3), 122.41 (C-7), 128.93 (C-4a), 130.28 (C-8), 134.52 (C-4), 138.29 (C-3'), 143.75 (C-8a), 147.25 (C-2), 156.54 (C-6). Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.57; H, 7.12; N, 6.32.

6-(Cyclohex-2-en-1-yloxy)quinoline (3c). Yield: 46%; yellow solid mp 65-69 °C; R_f = 0.28 (hexane – EtOAc 4:1). ^{1}H NMR ($CDCl_3$): δ= 1.78 (m, 1H, $C_{5'}$-H), 1.87 (m, 1H, $C_{5'}$-H), 1.95 (m, 1H, $C_{6'}$-H), 2.03 (m, 1H, $C_{6'}$-H), 2.06 (m, 1H, $C_{4'}$-H), 2.17 (m, 1H, $C_{4'}$-H), 4.95 (m, 1H, $C_{1'}$-H),

5.94 (m, 1H, $C_{2'}$-H), 6.02 (m, 1H, $C_{3'}$-H), 7.12 (d, *J*= 2.6 Hz, 1H, C_5-H), 7.33 (dd, *J*= 8.3 and 4.3 Hz, 1H, C_3-H), 7.38 (dd, *J*= 9.2 and 2.6 Hz, 1H, C_7-H), 8.01 (d, *J*= 9.2 Hz, 1H, C_8-H), 8.03 (d, *J*= 9.2 Hz, 1H, C_4-H), 8.75 (dd, *J*= 4.3 and 1 Hz, 1H, C_2-H). ^{13}C NMR ($CDCl_3$): δ= 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). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.71; H, 6.53; N, 6.34.

6-(Cyclohept-2-en-1-yloxy)quinoline (3d). Yield: 38%;brown oil ; R_f = 0.71 (CH_2Cl_2 – acetone 2:1). ^{1}H NMR ($CDCl_3$): δ= 1.45 (m, 1H, $C_{5'}$-H), 1.72 (m, 1H, $C_{6'}$-H), 1.76 (m, 1H, $C_{5'}$-H), 1.83 (m, 1H, $C_{7'}$-H), 2.07 (m, 1H, $C_{6'}$-H), 2.10 (m, 1H, $C_{7'}$-H), 2.20 (m, 1H, $C_{4'}$-H), 2.27 (m, 1H, $C_{4'}$-H), 5.02 (m, 1H, $C_{1'}$-H), 5.84 (m, 1H, $C_{2'}$-H), 5.92 (m, 1H, $C_{3'}$-H), 7.01 (d, *J*= 2.5 Hz, 1H, C_5-H), 7.32 (dd, *J*= 8.3 and 4.2 Hz, 1H, C_3-H), 7.37 (dd, *J*= 9.2 and 2.5 Hz, 1H, C_7-H), 8.00 (d, *J*= 9.0 Hz, 1H, C_8-H), 8.02 (d, *J*= 7.0 Hz, 1H, C_4-H), 8.75 (d, *J*= 3.8 Hz, 1H, C_2-H). ^{13}C NMR ($CDCl_3$): δ=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 $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85.Found: C, 80.02; H, 7.12; N, 6.01.

5-Allylquinolin-6-ol (4a)

3a (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 CH_2Cl_2 and the precipitated crystalls were collected by filtration. Yield: 0.59 g (49.5%); mp 158-162 °C [lit.,[2] 155°C] ; R_f = 0.44 (CH_2Cl_2 – acetone 2:1).

^{1}H NMR ($CDCl_3$): δ= 3.73 (d, *J*= 5.7 Hz, 2H, CH_2), 4.93 (m, 2H, =CH), 5.95 (m, 1H, HC=), 7.41 (dd, *J*= 9 and 4 Hz, 1H, C_3-H), 7.42 (d, *J*= 9 Hz, 1H, C_7-H), 7.78 (d, *J*= 9 Hz, 1H, C_8-H), 8.26 (d, *J*= 8.5 Hz, 1H, C_4-H), 8.66 (d, *J*= 3 Hz, 1H, C_2-H), 9.88 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ= 28.46 (CH_2), 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)

3b (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 CH_2Cl_2 – 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 ($CHCl_3$ – acetone 10:1). ^{1}H NMR ($CDCl_3$): δ= 1.80 (s, 6H, 2 CH_3), 5.20 (m, 2H, =CH), 6.44 (m, 1H, HC=), 7.28 (m, 2H, C_3-H and C_7-H), 7.84 (d, *J*= 9 Hz, 1H, C_8-H), 8.67 (d, *J*= 3.7 Hz, 1H, C_2-H), 8.79 (d, *J*= 8.9 Hz, 1H, C_4-H). ^{13}C NMR ($CDCl_3$): δ= 29.84 (2 CH_3), 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 $C_{14}H_{15}NO$: 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 ($CHCl_3$ – acetone 10:1). ^{1}H NMR ($CDCl_3$): δ= 1.55 (d, *J*= 6.2 Hz, 3H, CH_3), 1.71 (s, 3H, CH_3), 4.32 (q, *J*= 6.5 Hz, 1H, $C_{2'}$-H), 5.22 (d, *J*= 0.9 Hz, 1H, $C_{4'}$-H), 5.29 (s, 1H, $C_{4'}$-H), 7.34 (d, *J*= 9.1 Hz, 1H, C_7-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 ($CDCl_3$): δ= 17.34 (C-1'), 22.77 (CH_3), 37.48 (C-2'), 111.43 (C-4'), 120.67 (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(5*H*)-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_2O 3:2); R_f = 0.21 ($CHCl_3$ – acetone 10:1). IR (KBr): 3450 (s, OH) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ= 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 ($CDCl_3$): δ= 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 $C_{14}H_{15}NO$: 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 ($CDCl_3$): δ= 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 ($CDCl_3$): δ= 17.83 (CH_3), 25.58 (CH_3), 56.02 (C-5), 117.84 (C-2'), 123.19 (C-3), 129.81 (C-7), 134.24 (C-4), 134.90 (C-3'), 140.18 (C-4a), 145.97 (C-8), 147.98 (C-2), 149.85 (C-8a), 202.69 (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_2Cl_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 ($CDCl_3$): δ= 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 ($CDCl_3$): δ= 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-8a), 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_2Cl_2 – acetone 10:1) to yield **4e** (0.2 g, 38%) as colorless crystals. Mp 85-90°C. R_f= 0.42 (CH_2Cl_2 – acetone 4:1). IR (KBr): 3420 (s, OH) cm^{-1}.

^{1}H 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, $C_{1'}$-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). ^{13}C 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_2SO_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_2O, dried over $MgSO_4$ and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (using CH_2Cl_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_2Cl_2 – acetone 2:1). ^{1}H 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*= 9 Hz, 1H, C_4-H), 7.35 (dd, *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 Hz, 1H, C_5-H), 8.74 (d, *J*= 2.9, 1H, C_7-H). ^{13}C 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). ^{1}H 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_8-H), 7.93 (d, *J*= 8.9 Hz, 1H, C_5-H), 8.29 (d, *J*= 8.5 Hz, 1H, C_9-H), 8.73 (d, *J*= 3.0 Hz, 1H, C_7-H). ^{13}C 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 ($CHCl_3$ – acetone 10:1). ^{1}H NMR ($CDCl_3$): δ= 1.31 (d, *J*= 7.1 Hz, 3H, C_1-CH_3), 1.44 (s, 3H, C_2-CH_3), 1.53 (s, 3H, C_2-CH_3), 3.44 (q, *J*= 7.1 Hz, 1H, C_1-H), 7.27 (d, *J*= 8.9 Hz, 1H, C_4-H), 7.34 (dd, *J*= 8.4 and4.1 Hz, 1H, C_8-H), 7.93 (d, *J*= 8.9 Hz, 1H, C_5-H), 8.04 (d, *J*= 8.4 Hz, 1H, C_9-H), 8.73 (d, *J*= 3.3 Hz, 1H, C_7-H). ^{13}C NMR ($CDCl_3$): δ= 16.37 (C_1-CH_3), 22.41 (C_2-CH_3), 28.52 (C_2-CH_3), 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 $C_{14}H_{15}NO$: 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 ($CHCl_3$ – acetone 10:1). ^{1}H NMR ($CDCl_3$): δ= 1.39 (s, 6H, 2 CH_3), 1.95 (m, 2H, C_2-H), 3.00 (m, 2H, C_1-H), 7.25 (d, *J*= 9.6 Hz, 1H, C_5-H), 7.40 (m, 1H, C_9-H), 7.91 (d, *J*= 9.0 Hz, 1H, C_6-H), 8.19 (d, *J*= 8.2 Hz, 1H, C_{10}-H), 8.74 (m, 1H, C_8-H). ^{13}C NMR ($CDCl_3$): δ= 18.84 (C-1), 26.48 (CH_3), 32.23 (C-2), 74.53 (C-3), 112.08 (C-10b), 120.88 (C-9), 123.80 (C-5), 128.12 (C-10a), 128.45 (C-6), 130.77 (C-10), 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 (CH_2Cl_2 – acetone 2:1). **cis-Isomer.** t_R= 15.72 min. ^{1}H NMR ($CDCl_3$): δ= 1.25 (m, 1H, C_{11}-H), 1.32 (m, 1H, C_{10}-H), 1.57 (m, 1H, C_9-H), 1.67 (m, 1H, C_{10}-H), 1.86 (m, 1H, C_8-H), 2.12 (m, 1H, C_{11}-H), 2.35 (m, 1H, C_8-H), 3.45 (m, 1H, C_{11a}-H), 4.82 (m, 1H, C_{7a}-H), 7.32 (dd, *J*= 8.5 and 4.2 Hz, 1H, C_2-H), 7.34 (d, *J*= 9 Hz, 1H, C_6-H), 7.93 (d, *J*= 9 Hz, 1H, C_5-H), 7.99 (d, *J*= 8.2 Hz, 1H, C_1-H), 8.73 (d, *J*= 3 Hz, 1H, C_3-H). ^{13}C NMR ($CDCl_3$): δ= 20.18 (C-9), 22.37 (C-10), 27.24 (C-8), 29.19 (C-11), 39.59 (C-11a), 84.00 (C-7a), 115.85 (C-6), 121.20 (C-2), 125.35 (C-11c), 126.48 (C-11b), 129.89 (C-5), 130.88 (C-1), 144.66 (C-4a), 147.19 (C-3), 156.93 (C-6a).
Anal. Calcd for $C_{15}H_{15}NO$: 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 ($CDCl_3$): δ= 1.32 (m, 1H, C_9-H), 1.50 (m, 1H, C_9-H), 1.67 (m, 1H, C_8-H), 1.88 (m, 2H, C_{10}-H), 2.03 (m, 2H, C_{11}-H), 2.15 (m, 1H, C_8-H), 3.62 (br. s, 1H, C_{11a}-H), 4.68 (br. s, 1H, C_{7a}-H), 7.30 (d, *J*= 9.1 Hz, 1H, C_6-H), 7.34 ((dd, *J*= 8.5 and 4.0 Hz, 1H, C_2-H), 7.88 (d, *J*= 9.1 Hz, 1H, C_5-H), 8.15 (d, *J*= 8.5 Hz, 1H, C_1-H), 8.72 (d, *J*= 3 Hz, 1H, C_3-H). ^{13}C NMR ($CDCl_3$): δ= 17.86 (C-9), 26.33 (C-11a), 29.20 (C-11), 31.06 (C-10), 33.79 (C-8), 70.84 (C-7a), 116.83 (C-11b), 120.94 (C-2), 121.67 (C-6), 126.92 (C-11c), 128.97 (C-5), 129.56 (C-1), 144.22 (C-4a), 146.83 (C-3), 153.90 (C-6a). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.17; H, 6.99; N, 5.98.

8,9,10,11,12,12a-hexahydro-7a*H*-cycloheptafuro[3,2-*f*]quinoline (5e)

Yield: 74%; R_f= 0.71 (CH_2Cl_2 – acetone 4:1).

cis-Isomer. t_R= 7.78 min. ^{1}H NMR ($CDCl_3$): δ= 1.45 (m, 1H, C_9-H), 1.50 (m, 2H, C_{10}-H and C_{11}-H), 1.71 (m, 1H, C_{11}-H), 1.75 (m, 1H, C_{10}-H), 1.89 (m, 2H, C_9-H and C_{12}-H), 1.94 (m, 1H, C_{12}-H), 2.08 (m, 1H, C_8-H), 2.27 (m, 1H, C_8-H), 3.87 (m, 1H, C_{12a}-H), 5.14 (m, 1H, C_{7a}-H), 7.27 (d, *J*= 8.0 Hz, 1H, C_6-H), 7.32 (dd, *J*= 8.5 and 4.2 Hz, 1H, C_2-H), 7.92 (d, *J*= 8.0 Hz, 1H, C_5-H), 8.03 (d, *J*= 8.3 Hz, 1H, C_1-H), 8.72 (dd, *J*= 3.7 and 1.0 Hz, 1H, C_3-H). ^{13}C NMR ($CDCl_3$): δ= 23.67 (C-9), 28.84 (C-11), 30.01 (C-12), 31.21 (C-10), 31.45 (C-8), 46.47 (C-12a), 88.19 (C-7a), 115.23 (C-6), 121.12 (C-2), 122.59 (C-5), 125.69 (C-12b), 130.32 (C-1), 130.67 (C-5), 144.89

(C-4a), 146.95 (C-3), 156.63 (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.

trans-Isomer. t_R= 7.08 min. ^{1}H NMR ($CDCl_3$): δ= 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 ($CDCl_3$): δ= 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, 80.06; H, 7.28; N, 6.07.

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