Monatsh Chem (2014) 145:993–999
DOI 10.1007/s00706-014-1167-z

ORIGINAL PAPER

Synthesis and further rearrangements of 7-(2-cycloalken-1-yl)-8-quinolinols

Mercedesz Törincsi · Pal Kolonits · Lajos Novak

Received: 11 November 2013 / Accepted: 24 January 2014 / Published online: 8 April 2014

Abstract Rearrangement reaction of 8-(cycloalkenyloxy)quinolines and the acid-catalyzed cyclization of the products were investigated. These reactions afforded insights on interesting new heterocyclic systems. Depending on the size of the cycloalkenyl moiety, we could isolate benzofuro[3,2-*h*]quinoline, methanooxecino[3,2-*h*]quinoline, methanooxonino[3,2-*h*]quinoline, and/or spiro[cycloalkano-1,2′-furo[3,2-*h*]quinoline. The mechanism of the novel rearrangement reactions is also discussed.

Keywords Claisen rearrangement · Cyclization · Furo-quinoline · Oxecino-quinoline · Oxonino-quinoline · Ring constriction

Introduction

8-Hydroxyquinoline, a chelating agent, was a very versatile reagent in various organic reactions [1–8]. It was used as a stabilizer of hydrogen peroxide in rocket fuel oxidizers. The copper-8-quinolate, as well as the heterocyclic compound itself, exhibits antiseptic, growth inhibition, and pesticidal properties [9, 10]. The 8-alkoxyquinolinium salts, especially the lower ethers, also have significant antibacterial activities [11]. 8-Tosylaminoquinoline suppresses macrophage-mediated inflammation by inhibition of the production of NO and PGE [12, 13].

M. Törincsi · P. Kolonits · L. Novak (✉)
Department of Organic Chemistry and Technology, Budapest University of Technology and Economics, Research Group for Alkaloid Chemistry, Hungarian Academy of Sciences, Gellért tér 4, Budapest 1111, Hungary
e-mail: l-novak@mail.bme.hu

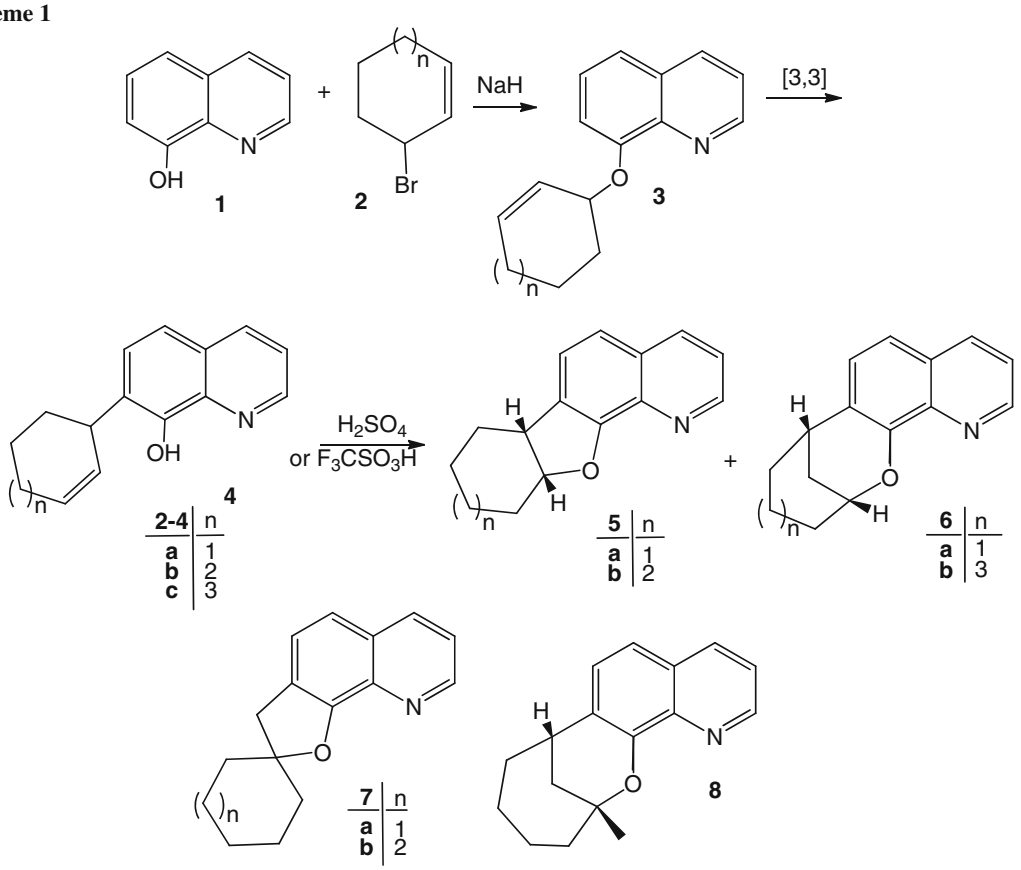
Recently we have developed efficient methods for the preparation of heteroaromatic compounds by Claisen rearrangement and subsequent cyclization [14–17]. With the aim of continuing efforts to synthesize novel heterocyclic compounds, we have examined the preparation of 8-(cycloalkyloxy)quinolines, their sigmatropic rearrangement reactions, and subsequent acid catalyzed cyclizations. We report here the results and the preparation of new tetracyclic compounds.

Results and discussion

8-(Cycloalkyloxy)quinolines **3** (Scheme 1) were prepared from 8-hydroxyquinoline (**1**). Treatment of **1** with sodium hydride afforded the corresponding anion, which was then reacted with 3-bromocycloalk-1-enes **2**. These reactions gave 8-(cycloalkyloxy)quinolines **3** in good to excellent yields. The products were then subjected to thermal-assisted and/or microwave-assisted electrocyclic reaction. The thermal reactions were performed in chlorobenzene at reflux, and the Claisen rearrangement needed 80 h to give compounds **4** in acceptable yield. We obtained essentially the same yield when we kept ethers **3** at 130 °C for 8 h under microwave irradiation.

The acid-catalyzed intramolecular cyclization of compounds **4** was performed with sulfuric acid at 100 °C. Starting with **4a**, the cyclization reaction afforded, besides the expected benzofuro[3,2-*h*]quinoline **5a**, the isomeric methanooxocino[3,2-*h*]quinoline **6a**, in a ratio of 1:2; i.e., the 6-*exo*-trig-like process was favorable [18–20]. The cyclization reaction was significantly faster when we used the more acidic trifluoromethanesulfonic acid ($pK_a = -15$). The reaction took place at r.t. and yielded predominantly compound **6a** (38 %), besides a small amount of compound **5a** (6 %).

Scheme 1



The structure and stereochemistry of the new compounds **5a** and **6a** were established by spectroscopic methods. For instance, an HPLC–MS experiment of compound **6a** showed a molecular ion peak at $m/z = 225$, indicating a molecular formula $C_{15}H_{15}NO$. All proton and carbon signals of this compound were assigned after extensive NMR measurements using COSY, HMQC, and HMBC techniques. ^{1}H and ^{13}C NMR, especially NOE studies, verified the structure and the *cis*-fused arrangement. Namely, the proton spectrum showed the presence of four methylene groups; among them, the one showing up at $\delta = 1.98$ and 2.06 ppm correlated with the methylene at C-13. Furthermore, the two broad singlet peaks (3.15 and 4.99 ppm), one of them originating from an oxymethine proton, could be attributed to the protons at the annelation (C-2 and C-6). The *cis*-annelation was confirmed by NOE correlation. The important NOE interactions of compound **6a** are shown in Fig. 1.

In the analogue cyclization reaction of the homolog **4b** we obtained furo[3,2-*h*]quinoline **5b** and a spiro analog **7a** approximately in equal amounts, in both sulfuric acid-catalyzed and trifluoromethanesulfonic acid-catalyzed processes (yields 39 and 46 %, respectively). The formation of the spiro compound could be the result of a consecutive [1,2]-alkyl migration, [1,2]-H shift, and cyclization (Scheme 2).

Acid-catalyzed intramolecular cyclization of compound **4c** afforded a mixture of three compounds in a ratio of 5:5:1 (yield 56 %). Here, besides the expected methanooxecino [3,2-*h*]quinoline **6b** and the spiro compound **7b**, we also isolated a methyl-substituted compound **8**. The structure of the latter was established by ^{1}H and ^{13}C NMR spectra, and NOE investigation. The ^{1}H NMR spectrum of compound **8** was similar to that of **6b** except the presence of a signal of a methyl group ($\delta = 1.70$ ppm). The carbon signal ($\delta = 31.96$ ppm) also suggested the presence of a methyl group in the molecule. The significant NOE correlation between the methyl protons and the protons at C-14, and the lack of same with the annellation proton at C-7 (3.21 ppm), suggested the *cis*-fused structure (Fig. 1).

A plausible mechanism for the formation of compound **8** is proposed in Scheme 3. On the protonated starting compound **9c,** the [1,2]-alkyl migration took place, which relieved the strain of the cyclooctenyl moiety of the molecule. Deprotonation of the intermediate **12** yielded compound **13**, on which acid-catalyzed intramolecular cyclization afforded compound **8** (the same type of ring constriction reaction was observed earlier during the bromination of *trans*-cyclooctene [21, 22]).

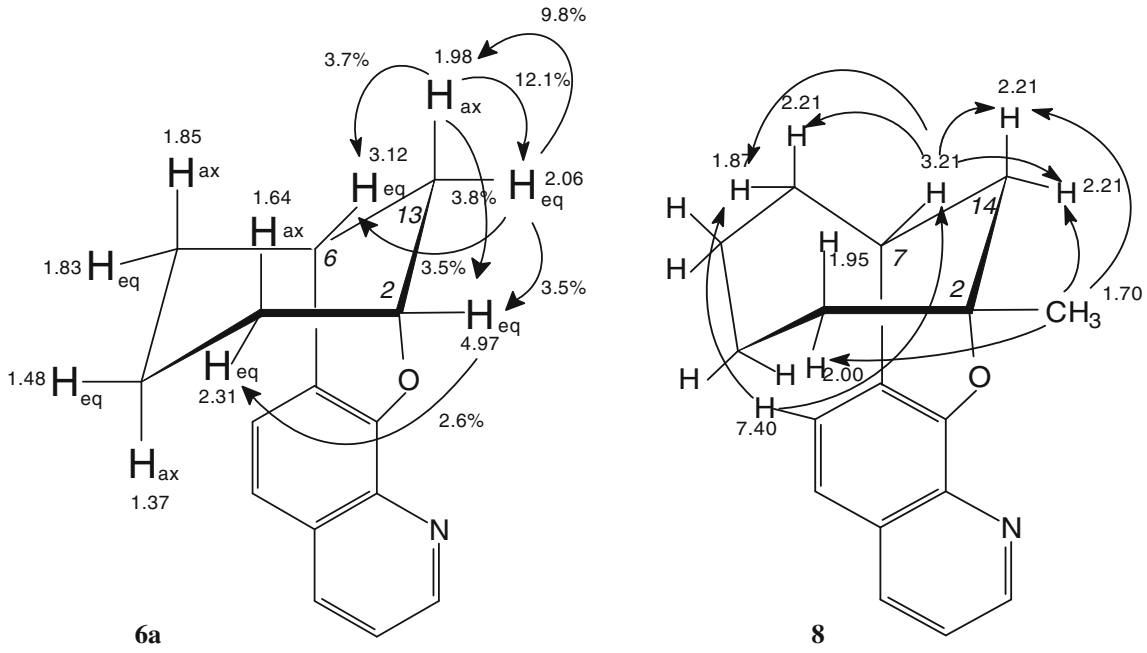
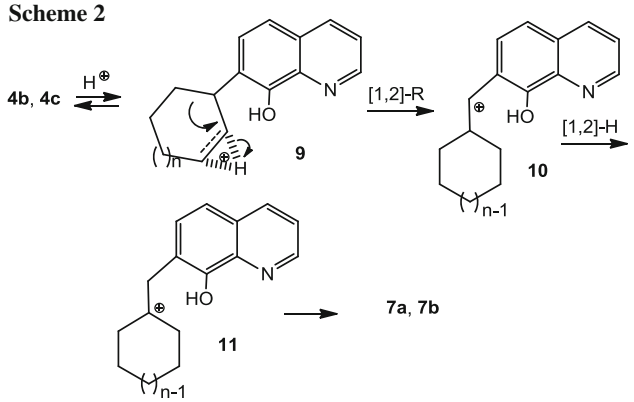


Fig. 1 Selected NOE correlations of compounds **6a** and **8**

Scheme 2



In summary, novel heterocyclic compounds have been prepared from 8-(cycloalkenyloxy)quinolines by thermal rearrangement followed by acid-catalyzed cyclization. The present synthetic schemes would enable access to a variety of furoquinolines, oxocinoquinolines, oxecinoquinolines, and spiro analogues, which would have interesting biological properties.

Experimental

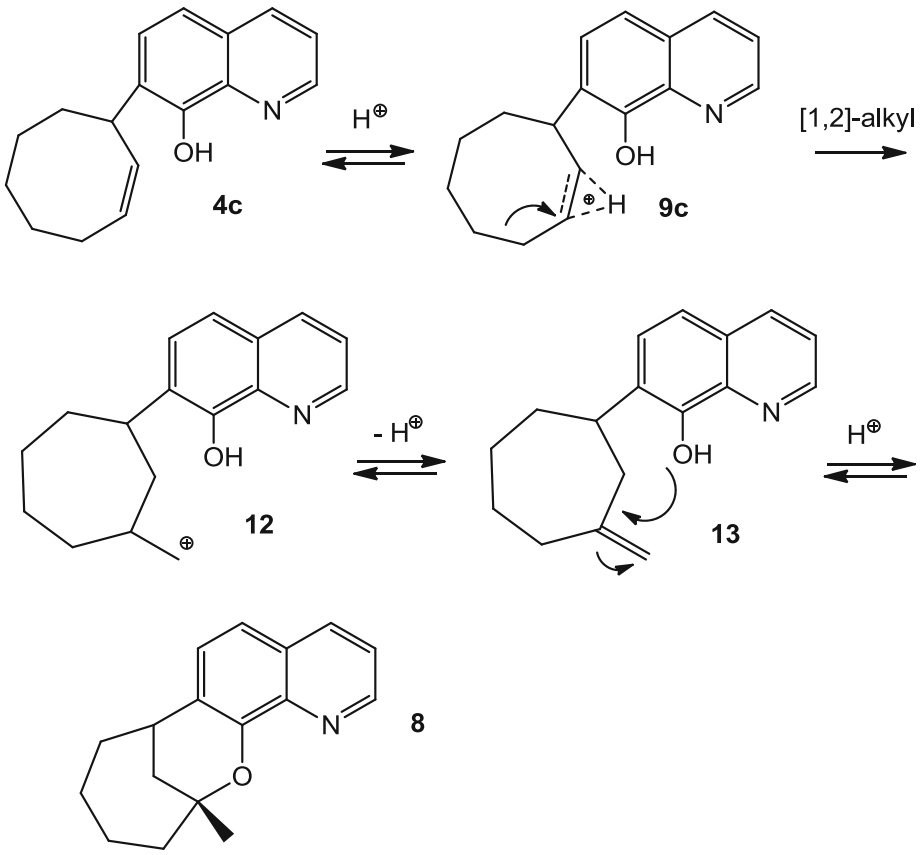
Solvents were used as received from commercial suppliers, and no further attempts were made to purify or dry them. Melting points were determined on a Büchi apparatus. Infrared (IR) spectra were recorded on a Bruker Alpha FT spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker DRX-500 spectrometer operating at 500 and 125 MHz, respectively. All NMR spectra are reported in ppm relative to TMS. MS spectra were conducted on Agilent 6140 quadrupole LC/MS instrument (ESI was +2 kV). Microwave irradiation was carried out using a CEM Explorer microwave reactor equipped with an automatic temperature controller and auto sampler (CEM Corporation, Matthews, NC). Liquid chromatography was conducted on the Agilent LCQ101 LC/MS (column: Gemini 3 μ C18, 50 × 3 mm; solvent H_2O) instrument. Merck precoated silica gel 60 F_{254} plates were used for TLC, and Kieselgel 60 for column chromatography.

Quinolin-8-ol (**1**) was obtained from a commercial source and was of the highest grade available. 3-Bromocyclohex-1-ene (**2a**) [23], 3-bromocyclohept-1-ene (**2b**) [24], and 3-bromocyclooct-1-ene (**2c**) [25] were prepared using their literature procedures.

*General procedure for preparation of 8-(cycloalk-2-enyloxy)quinolines **3***

To a cold-stirred suspension of NaH (12 mmol, 80 % in mineral oil) in 10 cm^3 DME, a solution of 1.0 g quinolin-8-ol (**1**, 6.88 mmol) in 30 cm^3 DME was added dropwise, and the resulting mixture was stirred at 0 °C for 2 h. To this mixture the appropriate bromine **2** (10 mmol) was added dropwise, and stirring was continued at r.t. for 24 h. The reaction mixture was quenched with 100 cm^3 brine and extracted with EtOAc (4 × 50 cm^3). The combined

Scheme 3



organic layers were washed with 1 N NaOH solution and water, and then dried over $MgSO_4$. Evaporation of the solvent under reduced pressure provided a residue which was purified by column chromatography on silica gel using hexane–EtOAc 6:1 as the eluent.

8-(2-Cyclohexen-1-yloxy)quinoline (**3a**, $C_{15}H_{15}NO$)
Yellow oil; yield 56 %; TLC: $R_f = 0.29$ (hexane–EtOAc = 4:1); IR (KBr): $\bar{\nu}$ = 1,650, 1,610, 1,560, 1,500, 1,470, 1,370, 1,310, 1,260, 1,100 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.70$ (m, 1H, $C_{5'}$–H), 1.96 (m, 1H, $C_{5'}$–H), 2.07 (m, 1H, $C_{4'}$–H), 2.10 (m, 2H, $C_{6'}$–H), 2.15 (m, 1H, $C_{4'}$–H), 5.12 (br s, 1H, $C_{1'}$–H), 5.98 (m, 1H, $C_{3'}$–H), 6.02 (d, $J = 11$ Hz, 1H, $C_{2'}$–H), 7.12 (d, $J = 8$ Hz, 1H, C_7–H), 7.36 (d, $J = 8$ Hz, 1H, C_5–H), 7.38 (dd, $J = 8$ Hz, 4 Hz, 1H, C_3–H), 7.42 (t, $J = 8$ Hz, 1H, C_6–H), 8.09 (d, $J = 8$ Hz, 1H, C_4–H), 8.95 (dd, $J = 4$ Hz, 1 Hz, 1H, C_2–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 19.53$ (C-5′), 25.08 (C-4′), 28.17 (C-6′), 72.31 (C-1′), 110.65 (C-7), 119.48 (C-5), 121.31 (C-3), 126.32 (C-2′), 126.45 (C-6), 129.65 (C-4a), 131.99 (C-3′), 135.73 (C-4), 141.04 (C-8a), 149.22 (C-2), 153.69 (C-8) ppm.

8-((Z)-Cyclohept-2-enyloxy)quinoline (**3b**, $C_{16}H_{17}NO$)
Yellow oil; yield 46 %; TLC: $R_f = 0.3$ (hexane–acetone = 5:2); IR (KBr): $\bar{\nu}$ = 1,625, 1,570, 1,510, 1,480, 1,450, 1,380, 1,320, 1,260, 1,100 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.42$ (m, 1H, $C_{5'}$–H), 1.73 (m, 1H, $C_{6'}$–H), 1.80 (m, 1H, $C_{5'}$–H), 2.04 (m, 1H, $C_{7'}$–H), 2.10 (m, 1H, $C_{6'}$–H), 2.19 (m, 1H, $C_{4'}$–H), 2.28 (m, 1H, $C_{4'}$–H), 2.30 (m, 1H, $C_{7'}$–H), 5.18 (m, 1H, $C_{1'}$–H), 5.91 (m, 1H, $C_{3'}$–H), 5.98 (m, 1H, $C_{2'}$–H), 7.03 (d, $J = 8$ Hz, 1H, C_7–H), 7.37 (d, $J = 8$ Hz, 1H, C_5–H), 7.42 (m, 2H, C_3–H and C_6–H), 8.12 (d, $J = 8$ Hz, 1H, C_4–H), 8.97 (d, $J = 3.5$ Hz, 1H, C_8–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 26.47$ (C-5′), 27.94 (C-6′), 28.60 (C-4′), 33.22 (C-7′), 78.60 (C-1′), 110.46 (C-7), 119.37 (C-5), 121.48 (C-3), 126.69 (C-6), 129.68 (C-4a), 130.60 (C-3′), 136.05 (C-2′), 136.15 (C-4), 140.55 (C-8a), 149.20 (C-2), 153.45 (C-8) ppm; MS: *m/z* (%) = 239 (M^+, 100), 145 ($M^+ - C_7H_{10}$, 16).

8-((Z)-2-Cycloocten-2-yloxy)quinoline (**3c**, $C_{17}H_{19}NO$)
Yellow oil; yield 46 %; TLC: $R_f = 0.45$ (hexane–acetone = 5:1); IR (KBr): $\bar{\nu}$ = 1,613, 1,595, 1,497, 1,468, 1,424, 1,374, 1,314, 1,258, 1,180 cm^{-1}; ^1H NMR

($CDCl_3$): $\delta = 1.49$ (m, 1H, $C_{5'}$–H), 1.57 (m, 1H, $C_{6'}$–H), 1.66 (m, 1H, $C_{7'}$–H), 1.71 (m, 1H, $C_{7'}$–H), 1.74 (m, 1H, $C_{6'}$–H), 1.78 (m, 1H, $C_{5'}$–H), 2.03 (m, 1H, $C_{8'}$–H), 2.24 (m, 1H, $C_{4'}$–H), 2.34 (m, 1H, $C_{8'}$–H), 2.37 (m, 1H, $C_{4'}$–H), 5.35 (m, 1H, $C_{1'}$–H), 5.70 (m, 1H, $C_{2'}$–H), 5.80 (m, 1H, $C_{3'}$–H), 7.05 (d, $J = 8$ Hz, 1H, C_7–H), 7.35 (d, $J = 8$ Hz, 1H, C_5–H), 7.41 (m, 1H, C_6–H), 7.43 (m, 1H, C_3–H), 8.13 (d, $J = 8$ Hz, 1H, C_4–H), 8.98 (d, $J = 4$ Hz, 1H, C_2–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 23.49$ (C-7′), 26.27 (C-6′), 26.81 (C-4′), 29.12 (C-5′), 35.82 (C-8′), 76.36 (C-1′), 110.50 (C-7), 119.25 (C-5), 121.38 (C-3), 126.82 (C-6), 129.54 (C-4a), 130.17 (C-3′), 132.95 (C-2′), 136.34 (C-4), 140.15 (C-8a), 149.03 (C-2), 153.88 (C-8) ppm.

General procedures for rearrangement of ethers ***3***

Method A A solution of ether **3** (3 mmol) in 50 cm^3 chlorobenzene was kept at reflux for 80 h. The solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography on silica gel (hexane–EtOAc = 4:1).

Method B Ether **3** (5 mmol) was kept at 130 °C for 8 h under microwave irradiation. After cooling, the reaction mixture was dissolved in a mixture of CH_2Cl_2 and acetone (5:2) and purified by column chromatography (hexane–EtOAc = 4:1).

7-(2-Cyclohexen-1-yl)-8-quinolinol (**4a**, $C_{15}H_{15}NO$)
Greenish crystalline solid; yield: method A 47 %, method B 52 %; m.p.: 97–98 °C; TLC: $R_f = 0.52$ (hexane–EtOAc = 4:1); IR (KBr): $\bar{\nu} = 3{,}320$ (OH), 1,625, 1,505, 1,460, 1,370, 1,340, 1,280, 1,230, 1,090 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.66$ (m, 1H, $C_{6'}$–H), 1.72 (m, 1H, $C_{5'}$–H), 1.77 (m, 1H, $C_{5'}$–H), 2.13 (m, 3H, $C_{4'}$–H and $C_{6'}$–H), 4.12 (m, 1H, $C_{1'}$–H), 5.74 (dd, $J = 8$ Hz, 1.5 Hz, 1H, $C_{2'}$–H), 5.97 (m, 1H, $C_{5'}$–H), 7.28 (d, $J = 8.5$ Hz, 1H, C_5–H), 7.35 (dd, $J = 8.2$ Hz, 4 Hz, 1H, C_3–H), 7.43 (d, $J = 8.5$ Hz, 1H, C_6–H), 8.09 (d, $J = 8.2$ Hz, 1H, C_4–H), 8.46 (br s, 1H, OH), 8.74 (dd, $J = 4$ Hz, 1 Hz, 1H, C_2–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.43$ (C-5′), 25.11 (C-4′), 30.30 (C-6′), 34.86 (C-1′), 117.09 (C-5), 120.97 (C-3), 126.86 (C-4a), 127.77 (C-7), 128.00 (C-6), 128.81 (C-3′), 129.97 (C-2′), 135.89 (C-4), 138.05 (C-8a), 147.73 (C-2), 148.67 (C-8) ppm.

7-((Z)-2-Cyclohepten-1-yl)-8-quinolinol (**4b**, $C_{16}H_{17}NO$)
Light greenish crystals; yield: method A 52 %, method B 52 %; m.p.: 80–84 °C; TLC: $R_f = 0.75$ (hexane–acetone = 5:2); IR (KBr): $\bar{\nu} = 3{,}340$ (OH), 1,640, 1,520, 1,475, 1,405, 1,380, 1,290, 1,240 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.50$ (m, 1H, $C_{5'}$–H), 1.76 (m, 1H, $C_{6'}$–H), 1.83 (m, 1H, $C_{5'}$–H), 1.87 (m, 2H, $C_{7'}$–H), 1.98 (m, 1H, $C_{6'}$–H), 2.31 (m, 2H, $C_{4'}$–H), 4.27 (br s, 1H, $C_{1'}$–H), 5.78 (dd, $J = 11$ Hz, 2.5 Hz, 1H, $C_{2'}$–H), 5.93 (m, 1H, $C_{3'}$–H), 7.39 (d, $J = 8.5$ Hz, 1H, C_5–H), 7.48 (dd, $J = 8$ Hz, 4 Hz, 1H, C_3–H), 7.55 (d, $J = 8.5$ Hz, 1H, C_6–H), 8.28 (d, $J = 8$ Hz, 1H, C_4–H), 8.78 (d, $J = 4$ Hz, 1H, C_2–H), 9.8 (br s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 27.18$ (C-5′), 28.92 (C-4′), 30.38 (C-6′), 34.73 (C-7′), 40.14 (C-1′), 117.82 (C-5), 120.58 (C-3), 127.29 (C-4a), 128.83 (C-6), 132.27 (C-7), 132.30 (C-3′), 135.96 (C-2′), 136.00 (C-8a), 138.46 (C-4), 146.11 (C-2), 147.15 (C-8) ppm.

7-((Z)-2-Cycloocten-1-yl)-8-quinolinol (**4c**, $C_{17}H_{19}NO$)
Greenish crystals; yield: method A 49 %, method B 51 %; m.p.: 107–109 °C; TLC: $R_f = 0.2$ (hexane–EtOAc = 4:1); IR (KBr): $\bar{\nu} = 3{,}340$, 1,505, 1,465, 1,452, 1,405, 1,380, 1,348, 1,300, 1,280, 1,180, 1,040 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.44$ (m, 1H, $C_{5'}$–H), 1.63 (m, 1H, $C_{6'}$–H), 1.71 (m, 2H, $C_{7'}$–H), 1.80 (m, 2H, $C_{5'}$–H and $C_{6'}$–H), 1.83 (m, 2H, $C_{8'}$–H), 2.18 (m, 1H, $C_{4'}$–H), 2.54 (m, 1H, $C_{4'}$–H), 4.45 (m, 1H, $C_{1'}$–H), 5.76 (m, 2H, $C_{2'}$–H and $C_{3'}$H), 7.34 (d, $J = 8.5$ Hz, 1H, C_5–H), 7.39 (dd, $J = 8$ Hz, 4 Hz, 1H, C_3–H), 7.54 (d, $J = 8.5$ Hz, 1H, C_6–H), 8.15 (d, $J = 8$ Hz, 1H, C_4–H), 8.74 (d, $J = 4$ Hz, 1H, C_2–H), 8.8 (br s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 26.26$ (C-7′), 26.47 (C-4′), 26.66 (C-6′), 29.68 (C-5′), 35.99 (C-1′), 36.69 (C-8′), 117.63 (C-5), 120.87 (C-3), 126.86 (C-4a), 127.65 (C-6), 128.63 (C-7), 129.68 (C-3′), 132.73 (C-2′), 136.64 (C-4), 137.53 (C-8a), 147.19 (C-2), 148.24 (C-8) ppm.

General procedures for cyclization of 7-(2-cycloalken-1-yl)-8-quinolinols ***4***

Method A A solution of 1.0 g compound **4** in 0.6 cm^3 sulfuric acid was kept at 100 °C for 1 h. After cooling, the reaction mixture was poured into 10 cm^3 water; the resulting solution was basified with 1 N NaOH solution and extracted with $CHCl_3$ (3×15 cm^3). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography.

Method B A solution of 1.0 g compound **4** in 1 cm^3 trifluoromethanesulfonic acid was stirred at r.t. for 1 h. The reaction mixture was poured in 1 N NaOH solution and extracted with $CHCl_3$ (3×15 cm^3). The combined organic layers were dried over $MgSO_4$; solvent was evaporated in vacuo, and the residue was purified by column chromatography.

cis-6b,7,8,9,10,10a-Hexahydro[1]benzofuro[3,2-h]-quinoline (**5a**, $C_{15}H_{15}NO$) *and cis-3,4,5,6-tetrahydro-2H-2,6-methanooxocino[3,2-h]quinoline* (**6a**, $C_{15}H_{15}NO$)
Compound **5a**: yield: method A 17 %, method B 6 %; light yellow oil; TLC: $R_f = 0.33$ (hexane–EtOAc 4:1); HPLC: $R_t = 3.764$ min; IR (KBr): $\bar{\nu} = 1{,}613$, 1,588, 1,515, 1,450, 1,435, 1,360, 1,348, 1,312, 1,300, 1,260, 1,220, 1,176, 1,137 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.37$ (m, 1H, C_8–H), 1.49 (m, 1H, C_7–H), 1.57 (m, 2H, C_8–H and C_9–H), 1.63

(m, 1H, C_9–H), 1.91 (m, 1H, C_{10}–H), 1.96 (m, 1H, C_7–H), 2.30 (m, 1H, C_{10}–H), 3.37 (m-q, $J = 7$ Hz, 1H, C_{6b}-H), 4.97 (m, 1H, C_{10a}-H), 7.31 (dd, $J = 8$ Hz, 4 Hz, 1H, C_3–H), 7.34 (d, $J = 8$ Hz, 1H, C_5–H), 7.39 (d, $J = 8$ Hz, 1H, C_6–H), 8.11 (d, $J = 8$ Hz, 1H, C_4–H), 8.85 (d, $J = 4$ Hz, 1H, C_2–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.21$ (C-9), 21.97 (C-8), 27.27 (C-10), 28.81 (C-7), 41.48 (C-6b), 84.06 (C-10a), 119.75 (C-5), 120.71 (C-3), 122.63 (C-6), 128.76 (C-4a), 131.63 (C-6a), 136.07 (C-4), 136.27 (C-11b), 149.64 (C-2), 154.75 (C-11a) ppm; MS: *m/z* (%) = 225 (M^+, 100).

Compound **6a**: yield: method A 35 %, method B 38 %; light yellow oil; TLC: $R_f = 0.28$ (hexane–acetone 5:2); HPLC: $R_t = 3.47$ min; IR (KBr): $\bar{\nu} = 1{,}578$, 1,560, 1,500, 1,455, 1,430, 1,380, 1,356, 1,345, 1,326, 1,307, 1,246, 1,210, 1,195, 1,170, 1,111, 1,080, 1,072 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.37$ (m, 1H, C_4–H), 1.48 (m, 1H, C_4–H), 1.64 (m, 1H, C_3–H), 1.83 (m, 1H, C_5–H), 1.85 (m, 1H, C_5–H), 1.98 (m, 1H, C_{13}–H), 2.06 (m, 1H, C_{13}–H), 2.31 (m, 1H, C_3–H), 3.12 (br s, 1H, C_6–H), 4.97 (br s, 1H, C_2–H), 7.17 (d, $J = 8.2$ Hz, 1H, C_7–H), 7.24 (d, $J = 8.2$ Hz, 1H, C_8–H), 7.33 (dd, $J = 8.2$ Hz, 4.2 Hz, 1H, C_{10}–H), 8.05 (dd, $J = 8$ Hz, 1.2 Hz, 1H, C_9–H), 8.90 (dd, $J = 4$ Hz, 1.2 Hz, 1H, C_{11}–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 17.55$ (C-4), 29.60 (C-13), 32.27 (C-6), 32.90 (C-5), 33.55 (C-3), 72.35 (C-2), 118.19 (C-8), 121.14 (C-10), 124.44 (C-6a), 128.15 (C-7), 128.53 (C-8a), 136.19 (C-9), 139.41 (C-12a), 149.43 (C-11), 151.79 (C-12b) ppm; MS: *m/z* (%) = 225 (M^+, 100).

cis-7,8,9,10,11,11a-Hexahydro-6bH-cyclohepta-[4,5]furo[3,2-h]quinolone (**5b**, $C_{16}H_{17}NO$) *and 3′H-spiro[cyclohexane-1,2′-furo[3,2-h]quinolone* (**7a**, $C_{16}H_{17}NO$)

Compound **5b**: yield: method A 19 %, method B 22 %; light yellow oil; TLC: $R_f = 0.2$ (hexane–acetone 4:1); IR (KBr): $\bar{\nu} = 1{,}622$, 1,511, 1,461, 1,440, 1,423, 1,394, 1,368, 1,359, 1,307, 1,244, 1,134, 1,114, 1,077, 1,043, 907 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.45$ (m, 3H, C_8–H, C_9–H, and C_{10}–H), 1.72 (m, 2H, C_8–H and C_9–H), 1.86 (m, 2H, C_7–H and C_{10}–H), 1.94 (m, 1H, C_7–H), 2.10 (m, 1H, C_{11}–H), 2.27 (m, 1H, C_{11}–H), 3.78 (m, t-d, $J = 9.9$ Hz, 3.5 Hz, 1H, C_{6b}-H), 5.25 (m, t-d, $J = 10$ Hz, 4 Hz, 1H, C_{11a}-H), 7.32 (br s, 2H, C_5–H and C_6–H), 7.34 (m, 1H, C_3–H), 8.11 (d, $J = 8.5$ Hz, 1H, C_4–H), 8.85 (d, $J = 4$ Hz, 1H, C_2–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 24.19$ (C-10), 28.62 (C-8), 31.22 (C-9), 31.64 (C-7), 31.81 (C-11), 47.50 (C-6b), 88.50 (C-11a), 119.35 (C-5), 120.79 (C-3), 123.22 (C-6), 128.89 (C-4a), 129.32 (C-6a), 135.46 (C-12b), 136.18 (C-4), 149.40 (C-2), 154.09 (C-12a) ppm; MS: *m/z* (%) = 239 (M^+, 100).

Compound **7a**: yield: method A 20 %, method B 24 %; light yellow oil; TLC: $R_f = 0.5$ (hexane–EtOAc 4:1); IR (KBr): $\bar{\nu} = 1{,}600$, 1,566, 1,508, 1,460, 1,436, 1,361, 1,281, 1,253, 1,214, 1,184, 1,170, 1,078, 1,052, 1,037, 990 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.51$ (m, 4H, C_3–H, C_4–H, and C_5–H), 1.83 (m, 2H, C_2–H and C_6–H), 1.95 (m, 2H, C_3–H and C_5–H), 2.02 (m, 2H, C_2–H and C_6–H), 3.22 (m, 2H, $C_{3'}$–H), 7.32 (d, $J = 8$ Hz, 1H, $C_{5'}$–H), 7.38 (dd, $J = 8$ Hz, 4 Hz, 1H, $C_{7'}$–H), 7.40 (d, $J = 8$ Hz, 1H, $C_{4'}$–H), 8.18 (d, $J = 8$ Hz, 1H, $C_{6'}$–H), 8.91 (d, $J = 4$ Hz, 1H, $C_{8'}$–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 23.12$ (C-3 and C-5), 25.14 (C-4), 37.32 (C-2 and C-6), 41.53 (C-3′), 91.11 (C-1), 119.01 (C-5′), 120.56 (C-7′), 124.57 (C-4′), 125.21 (C-3a), 128.88 (C-5a′), 134.43 (C-9a′), 137.36 (C-6′), 148.67 (C-8′), 153.51 (C-9b′) ppm; MS: *m/z* (%) = 239 (M^+, 100).

3,4,5,6,7,8-Hexahydro-2H-2,8-methanooxecino[3,2-h]-quinolone (**6b**, $C_{17}H_{19}NO$), *3′H-spiro[cycloheptane-1,2′-furo[3,2-h]quinolone* (**7b**, $C_{17}H_{19}NO$), *and 2-methyl-2,3,4,5,6,7-hexahydro-2,7-methanooxonino[3,2-h]-quinolone* (**8**, $C_{17}H_{19}NO$)

Compound **6b**: yield: method B 25 %; light yellow oil; TLC: $R_f = 0.35$ (hexane–acetone 5:2); HPLC: $R_t = 3.824$ min; IR (KBr): $\bar{\nu} = 1{,}502$, 1,451, 1,413, 1,373, 1,259, 1,214, 1,086, 1,017 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.30$ (m, 2H, C_4–H and C_6–H), 1.58 (m, 1H, C_5–H), 1.64 (m, 2H, C_3–H and C_7–H), 1.79 (m, 3H, C_4–H, C_5–H, and C_6–H), 2.13 (m, 1H, C_{15}–H), 2.35 (m, 1H, C_3–H), 2.42 (m, 1H, C_{15}–H), 2.45 (m, 1H, C_7–H), 3.02 (m, 1H, C_8–H), 4.81 (m, 1H, C_2–H), 7.26 (d, $J = 8.5$ Hz, 1H, C_9–H), 7.28 (d, $J = 8.5$ Hz, 1H, C_{10}–H), 7.34 (dd, $J = 8$ Hz, 4 Hz, 1H, C_{12}–H), 8.06 (d, $J = 8$ Hz, 1H, C_{11}–H), 8.90 (d, $J = 4$ Hz, 1H, C_{13}–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 22.46$ (C-6), 23.72 (C-5), 24.59 (C-15), 30.39 (C-8), 30.62 (C-4), 30.86 (C-3), 36.18 (C-7), 74.19 (C-2), 118.08 (C-10), 120.78 (C-12), 125.75 (C-8a), 127.97 (C-9), 128.00 (C-10a), 135.72 (C-11), 140.57 (C-14a), 147.52 (C-14b), 149.07 (C-13) ppm; MS: *m/z* (%) = 253 (100).

Compound **7b**: yield: method A 25 %; light yellow oil; TLC: $R_f = 0.52$ (hexane–acetone 5:2); HPLC: $R_t = 4.174$ min; IR (KBr): $\bar{\nu} = 1{,}511$, 1,462, 1,360, 1,311, 1,278, 1,259, 1,159, 1,080, 1,015 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.52$ (m, 2H, C_3–H and C_6–H), 1.63 (m, 2H, C_4–H and C_5–H), 1.72 (m, 2H, C_4–H and C_5–H), 1.86 (m, 2H, C_3–H and C_6–H), 1.98 (m-dd, 2H, C_2–H and C_7–H), 2.26 (m-dd, 2H, C_2–H and C_7–H), 3.25 (s, 2H, $C_{3'}$–H), 7.29 (d, $J = 8.2$ Hz, 1H, $C_{5'}$–H), 7.32 (dd, $J = 8.2$ Hz, 4.4 Hz, 1H, $C_{4'}$–H), 7.35 (d, $J = 8.2$ Hz, 1H, $C_{7'}$–H), 8.09 (dd, $J = 8.5$ Hz, 1.5 Hz, 1H, $C_{6'}$–H), 8.86 (dd, $J = 4.0$ Hz, 1.5 Hz, 1H, $C_{8'}$–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 22.21$ (C-3 and C-6), 29.18 (C-4 and C-5), 40.73 (C-2 and C-7), 43.29 (C-3′), 94.36 (C-1), 118.93 (C-5′), 120.63 (C-4′), 124.00 (C-7′), 124.12 (C-3a′), 128.82 (C-5a′), 136.01 (C-6′), 136.05 (C-9a′), 149.51 (C-8′), 154.12 (C-9b′) ppm; MS: *m/z* (%) = 253 (100).

Compound **8**: yield: method B 6 %; light yellow oil; TLC: $R_f = 0.29$ (hexane–acetone 5:2); HPLC: $R_t = 3.802$ min; IR (KBr): $\bar{\nu} = 1{,}512$, 1,462, 1,423, 1,394, 1,368, 1,359, 1,308, 1,289, 1,244, 1,134, 1,114, 1,077, 1,043 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.35$ (m, 2H, C_4–H and C_5–H), 1.50 (m, 1H, C_5–H), 1.68 (m, 1H, C_4–H), 1.70 (s, 3H, CH_3), 1.87 (m, 1H, C_6–H), 1.95 (m, 1H, C_3–H), 2.00 (m, 1H, C_3–H), 2.21 (m, 3H, C_6–H and C_{14}–H), 3.21 (m, 1H, C_7–H), 7.35 (d, $J = 8.5$ Hz, 1H, C_9–H), 7.40 (d, $J = 8.5$ Hz, 1H, C_8–H), 7.45 (dd, $J = 8$ Hz, 3 Hz, 1H, C_{11}–H), 8.20 (d, $J = 8.5$ Hz, 1H, C_{10}–H), 9.03 (d, $J = 3$ Hz, 1H, C_{12}–H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 24.04$ (C-5), 26.97 (C-4), 31.96 (CH_3), 33.16 (C-7), 35.30 (C-6), 37.01 (C-14), 42.94 (C-3), 78.72 (C-2), 118.20 (C-9), 120.73 (C-11), 125.59 (C-7a), 128.18 (C-9a), 128.47 (C-8), 137.61 (C-10), 138.00 (C-13a), 148.09 (C-12), 149.02 (C-13b) ppm; MS: m/z (%) = 253 (100).

References

1. Philips JP (1956) Chem Rev 56:271
2. Arias A, Fortuno J, Counselo M, Martin A, Mastrorilli P, Todisco S, Latronico M, Gallo V (2013) Inorg Chem 52:5493
3. Panda BK (2012) J Inorg Chem 2:49
4. Khale AA (2013) J Poly Res 20:1
5. Sosic I, Markovic B, Arenz K, Stefane B, Kos J, Gobec S (2013) J Med Chem 56:521
6. Zhang L, Wen G, Xiu Q, Guo L, Deng J, Zhong C (2012) J Coord Chem 65:1632
7. Alam MM, Shaharyar M, Hamid H, Nazreen S, Haider A, Alam MS (2011) Med Chem 7:663
8. Chen Y, Wang H, Wan L, Bian Y, Yang J (2011) J Org Chem 76:3774
9. Richardson WH, Hodge RL, Glover DW, Pompeo MP, Hayden CG (2005) Composition for wood treatment comprising an injectable aqueous wood preservative slurry having sparingly-soluble biocidal particles and pigments. PCT Int Appl WO 2005115704 A2, Dec 8, 2005. Chem Abstr 144:24100
10. Richardson WH, Hodge RL, Glover DW, Pompeo MP, Hayden CG (2005) Composition, method of making, and treatment of wood with an injectable wood preservative slurry having biocidal particles. PCT Int Appl WO 2005110692 A2, Nov 24, 2005. Chem Abstr 143:479586
11. Foye OW, Marshall RJ (1964) J Pharm Sci 53:1338
12. Byeon JY, Yoo DS, Yu T, Yang Y, Kim JH, Kim E, Jeong D, Rhee MH, Choung ES, Hong S, Cho JY (2012) Acta Pharm Sin 33:1037
13. Jung Y (2013) Pharmazie 68:146
14. Törincsi M, Kolonits P, Palosi E, Novak L (2007) Synthesis 284
15. Törincsi M, Kolonits P, Palosi E, Fekete J, Novak L (2008) Arkivoc 43
16. Törincsi M, Kolonits P, Fekete J, Novak L (2012) Synth Commun 42:3187
17. Kupai K, Banoczi G, Hornyanszky G, Kolonits P, Novak L (2012) Monatsh Chem 143:1663
18. Baldwin JE (1976) J Chem Soc Chem Commun 734
19. Baldwin JE, Thomas RC, Kruse L, Silberman L (1977) J Org Chem 42:3846
20. Baldwin JE, Lusch MJ (1982) Tetrahedron 38:2939
21. Haufe G (1979) Monatsh Chem 110:121
22. Allinger NL, Tushaus LA (1967) Tetrahedron 23:2051
23. Cox RA, Swallow AJ (1958) J Chem Soc 3727
24. Dondas HA, Grigg R, Thibault S (2001) Tetrahedron 57:7035
25. Bond CW, Cresswell AJ, Davies SG, Fletcher AM, Kurasawa W, Lee JA, Roberts PM, Russell AJ, Smith AD, Thomson JE (2009) J Org Chem 74:6735