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Synthesis of 6*H*-naphtho[2,3-*c*]chromene-7,12-diones via palladium-catalyzed intramolecular cyclization of 2-bromo-3-aryloxymethyl-1,4-naphthoquinones

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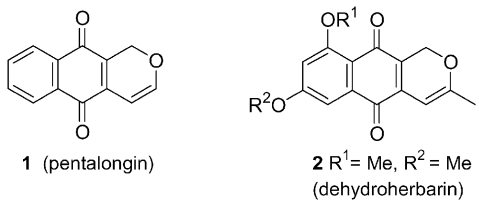
This paper is dedicated to Professor B. Zwanenburg on the occasion of his 70th birthday.

Abstract—6*H*-Naphtho[2,3-*c*]chromene-7,12-diones, to be considered as tetracyclic derivatives of the natural product pentalongin, were conveniently synthesized for the first time via palladium-catalyzed intramolecular cyclization of 2-bromo-3-aryloxymethyl-1,4-naphthoquinones.

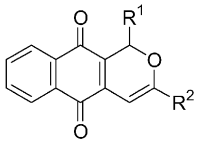
1. Introduction

The diversity of chemical structures of the pyranonaphthoquinone family and their useful biological activities made these compounds attractive targets in synthetic organic chemistry.[1–5] Recently, the synthesis of a particular group of naturally occurring pyranonaphthoquinones, such as pentalongin **1**,[6] dehydroherbarin **2**[7] and several 1,3-disubstituted-3,4-dehydropyranonaphthoquinones **3**[8] were synthesized by us as an effort towards the discovery of new biologically active pyranonaphthoquinone derivatives. Pentalongin is a natural product from the Central-East African medicinal plant *Pentas longifloria*, which is reported in Rwanda and Kenya for the treatment of malaria and skin diseases.[9] Several 3-arylpyranonaphthoquinones **4** were synthesized by Michael addition and intramolecular cyclization of pyridinium ylides with 2-phenoxymethyl-1,4-naphthoquinone[10] and 2-methyl-1,4-naphthoquinone,[11] which were then cyclized by treatment with bromine followed by dehydrobromination with triethylamine. Recently, some 3,4-dehydropyranonapthoquinones were synthesized by a tandem conjugate addition–cyclization between 2-(1-hydroxyalkyl)-1,4-naphthoquinones and enamines or imines.[12]



1 (pentalongin)

2 R^1 = Me, R^2 = Me (dehydroherbarin)



3 R^1 = Me, R^2 = alkyl, aryl
4 R^1 = H, R^2 = aryl

3,4-Dehydropyranonaphthoquinones in which the double bond at C3–C4 is part of an aromatic system have never been synthesized so far. Such derivatives should have a different reactivity because of the change from an enol ether moiety to an *O*-alkyl phenolic unit.

In continuation of our synthetic efforts towards physiologically active pentalongin derivatives, we now report here a convenient synthesis of tetracyclic pentalongin derivatives **1** via palladium-catalyzed intramolecular cyclization of 2-bromo-3-aryloxymethyl-1,4-naphthoquinones.

2. Results and discussion

Based on the retrosynthetic analysis depicted in Scheme 1,

Keywords: pentalongin; palladium-catalyzed intramolecular cyclization; 2-bromo-3-aryloxymethyl-1,4-naphthoquinones.
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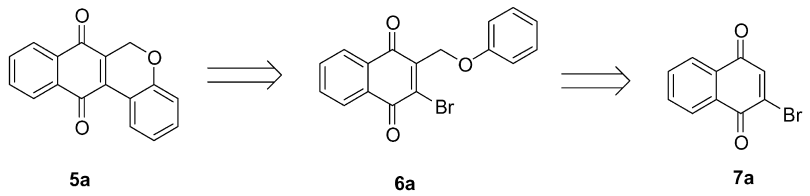
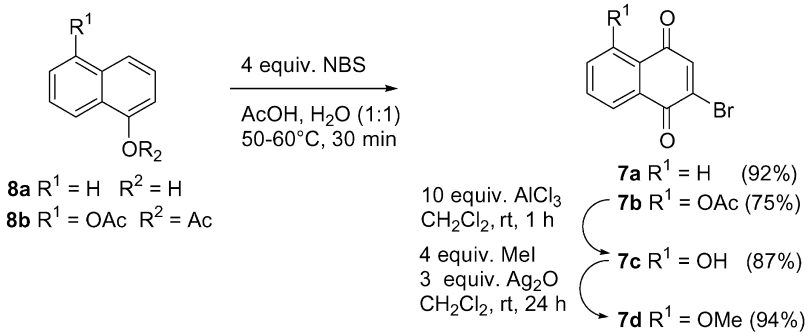


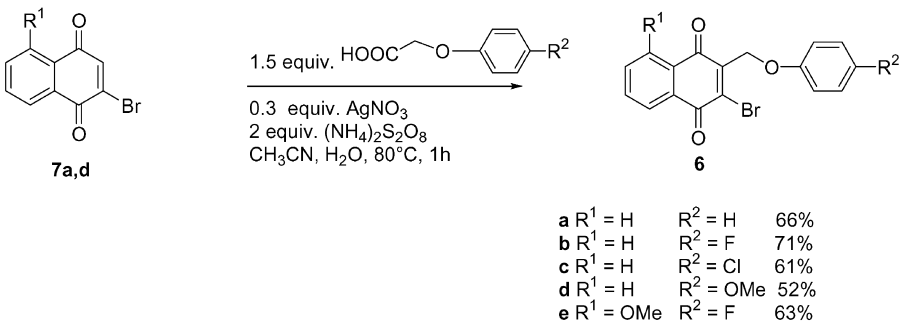
Scheme 1.

the construction of 6*H*-naphtho[2,3-*c*]chromene-7,12-dione skeleton was planned via palladium-catalyzed intramolecular cyclization of 2-bromo-3-phenoxymethyl-1,4-naphthoquinones as key step. Recently, palladium-mediated coupling reactions with quinones have already been mentioned in the literature. Stannylquinones have been cross-coupled with aryl and heteroaryl iodides using a palladium–copper co-catalyzed Stille cross-coupling reaction,[13] while carbazole-1,4-quinone alkaloids were synthesized via a palladium-catalyzed cyclization.[14] Benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione derivatives have been prepared by intramolecular cyclization of 2-chloro-3-phenoxy-1,4-naphthoquinone in the presence of palladium(II) acetate and triphenylphosphine.[15] Therefore, it was of interest to explore further this field of palladium-catalyzed coupling reaction towards the synthesis of new 6*H*-naphtho[2,3-*c*]chromene-7,12-dione derivatives. The starting material, i.e. 2-bromonaphthoquinone **7a**, was prepared from α-naphthol **8a** via oxidation with *N*-bromosuccinimide in aqueous acetic acid in 92% yield.[16] 5-Acetoxy-2-bromo-1,4-naphthoquinone **7b** was synthesized similarly from 1,5-diacetoxynaphthalene **8b** in 75% yield,[16] followed by deacetoxylation by treatment with aluminum(III) chloride in dichloromethane at room temperature to give rise to 2-bromo-5-hydroxy-1,4-napthoquinone **7c**.[17] This bromoquinone **7c** in the presence of silver(I) oxide to afford 2-bromo-5-methoxy-1,4-napthoquinone **7d** (Scheme 2). A radical introduction of a phenoxymethyl substituent using phenoxyacetic acid and silver nitrate in the presence of ammonium persulfate in aqueous acetonitrile at 80°C for 1 h afforded 2-bromo-3-phenoxymethyl-1,4-naphthoquinone **6a** in 66% yield.[10] This protocol was also applied for the synthesis of a series of 2-bromo-3-aryloxymethyl-1,4-naphthoquinones **6b–e** from 2-bromo-1,4-naphthoquinone **7a** and 2-bromo-5-methoxy-1,4-naphthoquinone **7d** in 52–71% yield (Scheme 3).

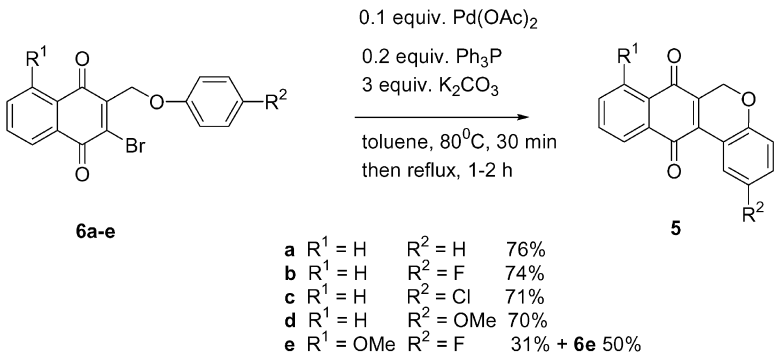
The intramolecular cyclization of 2-bromo-3-aryloxymethyl-1,4-naphthoquinones **6** using a palladium(0)-catalyzed reaction was investigated as a method to achieve the synthesis of tetracyclic pentalongin derivatives **5**. This process can be accomplished using catalytic amounts of palladium(II) by reoxidation of Pd^0 to Pd^{2+}. Examples include the reoxidation of palladium(0) to palladium(II) with cupric acetate[14] or *tert*-butylhydroperoxide.[18] In our first attempts to induce the palladium(0)-catalyzed ring closure of compounds **6a**, several standard conditions for aryl coupling to vinyl bromides using palladium(II) acetate in the presence of triphenylphosphine and tetrakis(triphenylphoshine)palladium(0) as catalyst were applied. The reaction was conducted in toluene at reflux and using



Scheme 2.



Scheme 3.



Scheme 4.

potassium carbonate as a base. The palladium-catalyzed cyclization was investigated in detail resulting in a substantial optimization. Finally, the intramolecular cyclization could be achieved with 10 mol% of palladium(II) acetate in the presence of 20 mol% of triphenylphosphine and 3 equiv. of potassium carbonate in toluene at reflux. Under the above mentioned reaction conditions, 6*H*-naphtho[2,3-*c*]chromene-7,12-dione **5a** was obtained from naphthoquinone **6a** in 76% yield. The investigation of the Pd-catalyzed cyclization of a series of substituted 2-bromo-3-aryloxymethyl-1,4-naphthoquinones **6b–e**, e.g. 2-bromo-3-(4-bromophenyl)methyl-, 2-bromo-3-(4-fluorophenyl)-methyl- and 2-bromo-3-(4-methoxyphenyl)-methyl-1,4-naphthoquinones, showed that the intramolecular cyclization led smoothly to 6*H*-naphtho[2,3-*c*]chromene-7,12-dione derivatives **5b–d** (Scheme 4) in 70–74% yield. However, under the above reaction conditions, 5-fluoro-11-methoxy-6*H*-naphtho[2,3-*c*]chromene-7,12-dione **5e** was obtained in low yield (31%), and the starting material **6e** was recovered in 50% yield. In this case, due to the electron donating effect of the methoxy group, the carbonyl at C-4 of compound **6e** could complex with $Pd(OAc)_2$ so as to result in a decreased reactivity of the oxidative insertion of the Pd(0) catalyst in bromoquinone **6e**.

In conclusion, an efficient intramolecular palladium-catalyzed cyclization of 6*H*-naphtho[2,3-*c*]chromene-7,12-dione derivatives **5a–e** from 2-bromo-3-aryloxymethyl-1,4-naphthoquinones **6a–e** was achieved. This method proved to be useful for the preparation of a variety of analogues of the naturally occuring pyranonapthoquinone pentalongin **1**.

3. Experimental

Melting points were determinated on a Buchi 535 apparatus. ^{1}H NMR spectra (270 MHz) and ^{13}C NMR spectra (67 MHz) were recorded with a Jeol JNM-EX 270 NMR spectrometer. IR spectra were measured with a Perkin–Elmer Model 983 and a Perkin–Elmer Spectrum One spectrophotometer. Mass spectra were recorded with a Varian-MAT 112 mass spectrometer (70 eV).

3.1. 2-Bromo-1,4-naphthoquinone 7a and 5-acetoxy-2-bromo-1,4-naphthoquinone 7b[16]

A solution of 0.005 mol of α-naphthol **8a** or 1,5-diacetoxy-naphthalene **8b** in warm acetic acid (50 mL) was added over a period of 5 min to a solution of *N*-bromosuccinimide (0.02 mol), dissolved in acetic acid (50 mL) and water (100 mL). The resulting solution was stirred at 50–60°C for 30–50 min. Subsequently, water (100 mL) was added and the reaction mixture was extracted with ethyl acetate. The combined extracts were washed with $NaHCO_3$ (5N), dried ($MgSO_4$) and evaporated in vacuo to give the crude product, which was recrystallized from ethanol to afford products **7a** and **7b** in 92 and 75% yield, respectively.

3.1.1. 2-Bromo-1,4-naphthoquinone 7a.[16] Yield 92%, yellow powder, mp 130–132°C (lit.[16] 131–132°C). ^{1}H NMR ($CDCl_3$) δ 8.06–8.19 (2H, m, H-5 and H-8), 7.76–7.82 (2H, m, H-6 and H-7), 7.51 (1H, s, H-3). ^{13}C NMR ($CDCl_3$) δ 182.4 (C=O), 177.8 (C=O), 140.3 (C-3), 140.1 (C_{quat}), 134.5 (C_{quat}), 134.4 and 134.1 (C-6 and C-7), 131.6 (C_{quat}), 127.8 and 126.8 (C-5 and C-8).

3.1.2. 5-Acetoxy-2-bromo-1,4-naphthoquinone 7b.[16] Yield 75%, yellow powder, mp 154–156°C (lit.[16] 154.5–156°C). ^{1}H NMR ($CDCl_3$) δ 8.14 (1H, dd, J=7.9, 1.3 Hz, H-8), 7.77 (1H, t, J=7.9 Hz, H-7), 7.42 (1H, dd, J=7.9, 1.3 Hz, H-6), 7.39 (1H, s, H-3).

3.1.3. 2-Bromo-5-hydroxy-1,4-naphthoquinone 7c.[17] To a cooled (0°C) solution of 5-acetoxy-2-bromo-1,4-naphthoquinone **7a** (3 mmol, 890 mg) in dichloromethane (30 mL) was added portionwise aluminum(III) chloride (30 mmol, 4 g). The reaction mixture was stirred for 1 h at room temperature. Then this mixture was quenched with water (50 mL) and the mixture was extracted with dichloromethane. The extract was washed with water and dried ($MgSO_4$). The solvent was evaporated in vacuo to give the crude product, which was purified by flash chromatography on silica gel to afford 657 mg (87%) of compound **7c** as a yellow powder, mp 131–133°C (lit.[17] 135–136°C). ^{1}H NMR ($CDCl_3$) δ 11.79 (1H, s, OH), 7.72 (1H, dd, J=8.3, 1.3 Hz, H-8), 7.65 (1H, t, J=8.3 Hz, H-7), 7.31 (1H, dd, J=8.3, 1.3 Hz, H-6), 7.19 (1H, s, H-3). ^{13}C NMR ($CDCl_3$) δ 187.8 (C=O), 177.2 (C=O), 161.6 (=C–OH), 147.1 (C_{quat}), 136.5 (C-7), 135.8 (C-8), 131.1 (C_{quat}), 125.5 (C-3), 120.6 (C-6), 114.5 (C_{quat}). IR (KBr): 1675 (C=O), 1633 (C=O), 1590 (C=C), 1432 cm^{-1}. MS *m*/*z* (%): no M^+, 208/210 (26), 173 (100).

3.1.4. 2-Bromo-5-methoxy-1,4-naphthoquinone 7d.[19] To a solution of 2-bromo-5-hydroxy-1,4-naphthoquinone **7c** (2 mmol, 500 mg) in dichlomethane (20 mL) was added

iodomethane (8 mmol, 1.14 g) and silver(I) oxide (4 mmol, 0.93 g). The reaction mixture was stirred for 12 h at room temperature. Then the mixture was filtered over celite, which was washed with little dichloromethane, and the filtrate was evaporated in vacuo to give the crude product. Purification was performed by flash chromatography on silica gel to afford 0.5 g (94%) of 2-bromo-5-methoxy-1,4-naphthoquinone **7d** as a yellow powder, mp 129–130°C (lit.[19] 132–133°C). ^{1}H NMR ($CDCl_3$) δ 7.84 (1H, dd, J=7.6, 1.3 Hz, H-8), 7.69 (1H, d, J=7.6, 8.1 Hz, H-7), 7.41 (1H, s, H-3), 7.35 (1H, dd, J=8.1, 1.3 Hz, H-6), 4.02 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ 181.2 (C=O), 178.1 (C=O), 159.9 (=C–OH), 142.2 (C-7), 136.7 (C_{quat}), 135.1 (C-8), 132.5 (C_{quat}), 120.5 (C-3), 119.1 (C_{quat}), 118.5 (C-6), 56.5 (OMe). IR (KBr): 1675 (C=O), 1645 (C=O), 1580 (C=C), 1432 cm^{-1}. MS *m/z* (%): 266/268 (M^+, 100), 237/239 (16), 187 (37).

3.1.5. 2-Bromo-3-aryloxymethyl-1,4-naphthoquinones 6: general procedure. The synthesis of 2-bromo-3-phenoxymethyl-1,4-naphthoquinone **6a** is representative. A mixture of 2-bromo-1,4-naphthoquinone **7a** (0.02 mol, 4.74 g), phenoxyacetic acid (0.03 mol, 4.56 g) and silver nitrate (0.006 mol, 1.02 g) in acetonitrile (100 mL) was heated at 80°C under N_2.[7] To this mixture was added dropwise over period of 20 min a solution of ammonium persulfate (0.04 mol, 9.12 g) in demineralized water (50 mL) and the reaction mixture was kept at the same temperature for 1 h. Afterwards the reaction mixture was quenched with ice–water and this mixture was cooled in an ice-bath for 2 h. A yellow precipitate was separated by filtration and recrystallized from methanol to afford 4.54 g of 2-bromo-3-phenoxymethyl-1,4-naphthoquinone **6a** (66% yield) as yellow powder, mp 97–99°C. ^{1}H NMR ($CDCl_3$) δ 8.16–8.21 (2H, m, H-5 and H-8), 7.77–7.81 (2H, m, H-6 and H-7), 7.29–7.35 (2H, m, 2×=CH-phenyl), 6.98–7.03 (3H, m, 3×=CH-phenyl), 5.23 (2H, s, CH_2–O). ^{13}C NMR ($CDCl_3$) δ 180.8 (C=O), 177.7 (C=O), 154.5 (=C–O), 144.5 (C_{quat}), 143.2 (C_{quat}), 134.6 and 134.2 (C-6, C-7), 131.4 (C_{quat}), 131.0 (C_{quat}), 129.6 (2×CH-phenyl), 127.7 and 127.4 (C-5, C-8), 121.6 (=CH-phenyl), 115.0 (2×=CH-phenyl), 64.3 (CH_2–O). IR (KBr): 1667 (C=O), 1663 (C=O), 1589 (C=C), 1496, 1286, 1240, 754 cm^{-1}. MS *m/z* (%): no M^+, 265/267 [(M−Ph)$^+$, 6], 279 (7), 236/238 (50), 155/157 (13), 99 (68), 57 (100). Anal. calcd $C_{17}H_{11}BrO_3$: C 59.50%, H 3.23%; found: C 59.58%, H 3.28%.

3.1.6. 2-Bromo-3-(4-fluorophenoxymethyl)-1,4-naphthoquinone 6b. Yield 71%, yellow powder, mp 138–139°C. ^{1}H NMR ($CDCl_3$) δ 8.19–8.25 (2H, m, H-5 and H-8), 7.81–7.87 (2H, m, H-6 and H-7), 6.96–7.07 (4H, m, H-3′, H-6′, H-2′ and H-5′), 5.22 (2H, s, CH_2–O). ^{13}C NMR ($CDCl_3$) δ 180.8 (C=O), 177.6 (C=O), 157.7 (d, J=235.8 Hz, CF), 154.5 (=C–O), 144.1 (C_{quat}), 143.2 (C_{quat}), 134.6 and 134.2 (C-6, C-7), 131.2 (C_{quat}), 130.9 (C_{quat}), 127.7 and 127.3 (C-5, C-8), 116.3 and 116.2 (C-3′, C-5′), 116.0 and 115.7 (C-2′, C-6′), 65.2 (CH_2–O). IR (KBr): 1674 (C=O), 1660 (C=O), 1507, 1458, 1284, 1210, 1025, 770 cm^{-1}. MS *m/z* (%): 362/360 (M^+, 8), 380 (M^+−Br, 12), 268 (14), 210 (10), 84 (100), 81/79 (14). Anal. calcd $C_{17}H_{10}BrFO_3$: C 56.53%, H 2.79%; found: C 56.37%, H 2.91%.

3.1.7. 2-Bromo-3-(4-chlorophenoxymethyl)-1,4-naphthoquinone 6c. Yield 61%, yellow powder, mp 153–154°C. ^{1}H NMR ($CDCl_3$) δ 8.14–8.20 (2H, m, H-5 and H-8), 7.75–7.83 (2H, m, H-6 and H-7), 7.25 (2H, d, J=6.6 Hz, H-2′, H-6′), 6.94 (2H, d, J=6.6 Hz, H-3′ and H-5′), 5.18 (2H, s, CH_2–O). ^{13}C NMR ($CDCl_3$) δ 180.8 (C=O), 177.6 (C=O), 157.0 (=C–O), 144.1 (C_{quat}), 143.4 (Cquat), 134.6 and 134.2 (C-6, C-7), 131.3 (C_{quat}), 131.0 (C_{quat}), 129.4 (C-3′, C-5′), 127.7 and 127.4 (C-5, C-8), 126.6 (C_{quat}), 116.3 (C-2′, C-6′), 64.7 (CH_2–O). IR (KBr): 1671 (C=O), 1667 (C=O), 1490, 1378, 1284, 1226, 1013, 823, 724 cm^{-1}. MS *m/z* (%): 380/378/376 (M^+, 8), 354/352 (34), 252 (12), 175 (10), 155 (15), 81/79 (7), 49 (100). Anal. calcd $C_{17}H_{10}BrClO_3$: C 54.07%, H 2.67%; found: C 54.09%, H 2.69%.

3.1.8. 2-Bromo-3-(4-methoxyphenoxymethyl)-1,4-naphthoquinone 6d. Yield 52%, yellow powder, mp 135–137°C. ^{1}H NMR ($CDCl_3$) δ 8.15–8.21 (2H, m, H-5 and H-8), 7.76–7.81 (2H, m, H-6 and H-7), 6.96 (2H, dd, J=9.2, 2.3 Hz, H-2′ and H-6′), 6.83 (2H, dd, J=9.2, 2.3 Hz, H-3′ and H-5′), 5.17 (2H, s, CH_2–O), 3.77 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ 180.7 (C=O), 177.5 (C=O), 154.5 (=C–O), 152.5 (=C–O), 144.5 (C_{quat}), 142.9 (C_{quat}), 134.4 and 134.0 (C-6, C-7), 131.2 (C_{quat}), 130.8 (C_{quat}), 127.5 and 127.2 (C-5, C-8), 116.2 (C-3′, C-5′), 114.5 (C-2′, C-6′), 65.3 (CH_2–O), 55.5 (O*M*e). IR (KBr): 1674 (C=O), 1653 (C=O), 1507, 1284, 1242, 1096, 1013, 825, 757 cm^{-1}. MS *m/z* (%): no M^+, 293 [(M−Br)$^+$, 2], 279 (7), 200 (10), 88 (11), 84 (100), 81/79 (3), 51(30). Anal. calcd $C_{18}H_{13}BrO_4$: C 57.93%, H 3.51%; found: C 57.81%, H 3.42%.

3.1.9. 2-Bromo-3-(4-fluorophenoxymethyl)-5-methoxy-1,4-naphthoquinone 6e. Yield 63%, yellow powder, mp 122–123°C. ^{1}H NMR ($CDCl_3$) δ 7.86 (1H, dd, J=7.6, 1.0 Hz, H-8), 7.70 (1H, dt, J=7.6, 8.6 Hz, H-7), 7.35 (1H, dd, J=8.6, 1.0 Hz, H-6), 6.94–6.99 (4H, m, H-3′, H-6′, H-2′ and H-5′), 5.16 (2H, s, CH_2–O), 4.02 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ 179.6 (C=O), 178.0 (C=O), 160.1 (C_{quat}), 157.6 (d, J=235.8 Hz, CF), 154.6 (=C–O), 144.6 (C_{quat}), 140.1 (C_{quat}), 135.1 (=CH), 130.0 (C_{quat}), 120.4 (=CH), 118.5 (=CH), 117.9 (C_{quat}), 116.3 (d, J=8.6 Hz, C-3′), 116.0 (C-2′), 115.8 (d, J=8.6 Hz, C-5′), 115.6 (C-6′), 65.3 (CH_2–O), 56.5 (OMe). IR (KBr): 1674 (C=O), 1654 (C=O), 1589, 1491, 1472, 1273, 1263, 1178, 999 cm^{-1}. MS *m/z* (%): no M^+, 311 [(M−Br)$^+$, 9], 297 (9), 218 (10), 97 (100), 81/79 (3). Anal. calcd $C_{18}H_{12}BrFO_4$: C 55.27%, H 3.09%; found: C 55.29%, H 3.17%.

3.1.10. 6*H*-Naphtho[2,3-*c*]chromene-7,12-diones 5: general procedure. The synthesis of 6*H*-naphtho[2,3-*c*]chromene-7,12-dione **5a** is representative. A solution of 2-bromo-3-phenoxymethyl-1,4-naphthoquinones **6a** (1.17 mmol, 60 mg) and palladium(II) acetate (0.12 mmol, 27 mg), triphenylphosphine (0.24 mmol, 64 mg) and potassium carbonate (3.5 mmol, 483 mg) in toluene (10–15 mL) was stirred at 80°C for 30 min. Then this mixture was heated under reflux for 1 h. Afterwards the reaction mixture was poured in water, and extracted with ethyl acetate. The extract was washed with water, dried ($MgSO_4$) and evaporated in vacuo to give the crude product, which was purified by flash chromatography on silica gel (ethyl acetate/hexane 1:4) to afford the pure compound **5a** (76%) as a red

powder, mp 155–156°C. ^{1}H NMR ($CDCl_3$) δ 8.42 (1H, dd, J=8.2, 1.6 Hz, H-1), 8.08–8.18 (2H, m, H-8 and H-11), 7.74–7.80 (2H, m, H-9 and H-10), 7.35 (1H, td, J=8.3, 1.6 Hz, H-3), 7.10 (1H, td, J=8.3, 1.6 Hz, H-2), 6.98 (1H, dd, J=8.3, 0.9 Hz, H-4), 5.16 (2H, s, CH_2–O). ^{13}C NMR ($CDCl_3$) δ 183.3 (C=O), 182.5 (C=O), 156.6 (=C–O), 134.6 (C_{quat}), 134.2 (C_{quat}), 133.9 and 133.7 (C-9, C-10), 132.5 (C-3 and C_{quat}), 131.5 (C_{quat}), 129.9 (C-4), 126.8 and 125.8 (C-8, C-11), 122.3 (C-2), 118.3 (C_{quat}), 116.9 (C-1), 61.9 (CH_2–O). IR (KBr): 1674 (C=O), 1645 (C=O), 1595, 1450, 1382, 1333, 1270, 1111, 963 cm^{-1}. MS *m/z* (%): 262 (M^+, 100), 235 (12), 234 (22), 206 (35), 176 (10), 151 (5), 102 (3). Anal. calcd $C_{17}H_{10}O_3$: C 77.85%, H 3.84%; found: C 77.80%, H 3.96%.

3.1.11. 2-Fluoro-6*H*-naphtho[2,3-*c*]chromene-7,12-dione 5b. Yield 74%, red powder, mp 148–149°C. ^{1}H NMR ($CDCl_3$) δ 8.43 (1H, dd, J=8.9, 2.9 Hz, H-1), 8.09–8.19 (2H, m, H-8 and H-11), 7.76–7.80 (2H, m, H-9 and H-10), 7.06 (1H, m, H-3), 6.94 (1H, dd, J=8.9, 4.9 Hz, H-4), 5.15 (2H, s, CH_2–O). ^{13}C NMR ($CDCl_3$) δ 183.0 (C=O), 182.4 (C=O), 157.6 (d, J=235.8 Hz, CF), 152.5 (=C–O), 135.3 (C_{quat}), 134.1 and 133.9 (C-9, C-10), 133.3 (C_{quat}), 132.4 (C_{quat}), 131.5 (C_{quat}), 126.9 and 125.9 (C-8, C-11), 119.1 (C_{quat}), 119.0 (d, J=22.7 Hz, C-3), 117.8 (d, J=7.3 Hz, C-4), 116.1 (d, J=25.4 Hz, C-1), 62.1 (CH_2–O). IR (KBr): 1668 (C=O), 1650 (C=O), 1592, 1570, 1388, 1334, 1206, 1154, 927 cm^{-1}. MS *m/z* (%): 280 (M^+, 10), 276 (32), 225 (23), 151 (15), 150 (78), 112 (27), 96 (23), 84 (100). Anal. calcd $C_{17}H_9FO_3$: C 72.86%, H 3.24%; found: C 72.98%, H 3.27%.

3.1.12. 2-Chloro-6*H*-naphtho[2,3-*c*]chromene-7,12-dione 5c. Yield 71%, red powder, mp 149–151°C. ^{1}H NMR ($CDCl_3$) δ 8.47 (1H, d, J=2.6 Hz, H-1), 8.08–8.18 (2H, m, H-8 and H-11), 7.76–7.79 (2H, m, H-9 and H-10), 7.30 (1H, dd, J=8.6, 2.6 Hz, H-3), 6.93 (1H, d, J=8.6 Hz, H-4), 5.16 (2H, s, CH_2–O). ^{13}C NMR ($CDCl_3$) δ 182.8 (C=O), 182.3 (C=O), 154.9 (=C–O), 135.0 (C_{quat}), 134.1 and 133.8 (C-9, C-10), 132.3 (C_{quat}), 132.1 (C-3), 131.4 (C_{quat}), 129.4 (C_{quat}), 129.3 (1), 127.3 (C_{qua}t), 126.8 and 125.8 (C-8, C-11), 119.2 (C_{quat}), 118.1 (C-4), 62.1 (CH_2–O). IR (KBr): 1655(C=O), 1650 (C=O), 1591, 1457, 1388, 1334, 1206, 1126, 1093, 927 cm^{-1}. MS *m/z* (%): no M^+, 282 (4), 275 (16), 274 (24), 269 (16), 268 (100), 259 (17), 86 (18), 73 (59). Anal. calcd $C_{17}H_9ClO_3$: C 68.82%, H 3.06%; found: C 68.70%, H 3.12%.

3.1.13. 2-Methoxy-6*H*-naphtho[2,3-*c*]chromene-7,12-dione 5d. Yield 70%, violet powder, mp 135–136°C. ^{1}H NMR ($CDCl_3$) δ 8.09–8.18 (2H, m, H-8 and H-11), 8.03 (1H, dd, J=2.2, 1.1 Hz, H-1), 7.75–7.78 (2H, m, H-9 and H-10), 6.91–6.97 (2H, m, H-3 and H-4), 5.15 (2H, s, CH_2–O), 3.83 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ 183.3 (C=O), 182.4 (C=O), 154.4 (=C–O), 150.6 (=C–O), 134.8 (C_{quat}), 133.9 (C_{quat}), 133.8 and 133.6 (C-9, C-10), 132.4 (C_{quat}), 131.5 (C_{quat}), 126.7 and 125.7 (C-8, C-11), 119.2 (C-3), 118.6 (C_{quat}), 117.4 (C-1), 113.3 (C-4), 61.9 (CH_2–O), 55.6 (OMe). IR (KBr): 1664 (C=O), 1644 (C=O), 1592, 1456, 1485, 1380, 1335, 1250, 1205 cm^{-1}. MS *m/z* (%): no M^+, 275 (15), 274 (28), 181 (10), 162 (12), 150 (36), 130 (66), 108 (23), 86 (100), 84 (46). Anal. calcd $C_{18}H_{12}O_4$: C 73.97%, H 4.14%; found: C 74.09%, H 4.19%.

3.1.14. 2-Fluoro-8-methoxy-6*H*-naphtho[2,3-*c*]chromene-7,12-dione 5e. Yield 31%, red powder, mp 177–178°C (decomp.). ^{1}H NMR ($CDCl_3$) δ 8.20 (1H, dd, J=9.9, 2.9 Hz, H-1), 7.82 (1H, dd, J=7.9, 1.0 Hz, H-9), 7.71 (1H, dd, J=7.9, 7.5 Hz, H-10), 7.32 (1H, dd, J=7.5, 1.0 Hz, H-11), 6.89–6.99 (2H, m, H-3 and H-4), 5.13 (2H, s, CH_2–O), 4.02 (OMe). ^{13}C NMR ($CDCl_3$) δ 183.1 (C=O), 181.7 (C=O), 159.4 (C_{quat}), 157.6 (d, J=235.9 Hz, CF), 152.1 (=C–O), 137.2 (C_{quat}), 135.2 (C-10), 134.7 (C_{quat}), 131.7 (C_{quat}), 119.7 (C-9), 118.8 (C_{quat}), 118.5 (C-8), 117.8 (C-4), 117.8 (d, J=8.0 Hz, C-3), 115.7 (d, J=5.5 Hz, C-1), 62.5 (CH_2–O), 56.3 (OMe). IR (KBr): 1667 (C=O), 1644 (C=O), 1582, 1462, 1270, 1257, 1206, 1016 cm^{-1}. MS *m/z* (%): 310 (M^+, 18), 272 (17), 273 (18), 180 (10), 160 (12), 150 (30), 87 (100). Anal. calcd $C_{18}H_{11}FO_4$: C 69.68%, H 3.57%; found: C 69.71%, H 3.66%.

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