Total Synthesis of Angucyclines 14,[1] Biomimetic Synthesis of the Racemic Angucyclinones of the Aquayamycin and WP 3688-2 Types

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Supporting Information

For general methods and instrumentation see ref. [2].

General Procedure I: Alkylation of benzyl bromides with silyl enol ethers. To a solution of naphthyl bromide (1 mmol) and tetrabutylammonium iodide (TBAI, 0.3 mmol) in THF (10 mL) was added at −78 °C under argon the silyl enol ether (2.2 mmol) and then in one portion [n-Bu4N][Ph3SnF2][3] (1.2 mmol). The cooling bath was removed after 15 min and the mixture was stirred for the time indicated for the individual compounds at 20 °C (TLC monitoring). If the conversion was incomplete, another portion of [n-Bu4N][Ph3SnF2] (0.6 mmol) was added at −78 °C. The solution was then filtered through a short silica gel column (5 g, CH2Cl2) and the solvent was removed under reduced pressure.

General Procedure II: Formation of silyl enol ethers from ketones. A solution of the ketone (4 mmol) in CH2Cl2 (10 mL) was treated at 0 °C with triethyl amine (12 mmol) and TBDMS-triflate (4.6 mmol). The solution was then stirred for 1 h (TLC monitoring) under argon. The reaction was quenched by addition of saturated aqueous NaHCO3 solution (20 mL), the phases were separated, and the aqueous phase extracted with CH2Cl2 (2 x 20 mL). The combined organic phases were washed with brine (20 mL), dried (MgSO4), filtered and the solvent removed under reduced pressure.

General Procedure III: Addition of electrophiles to lithiated naphthalenes. To a solution of the naphthyl bromides (3 mmol) in THF (20 mL) was added at −78 °C under argon a solution of n-BuLi in hexane (3.3 mmol). After 15 min of stirring at −78 °C, the electrophiles (3.6 mmol) were added [solid electrophiles in THF (2 mL) solution]. After a further 30 min at −78 °C, the reaction was quenched by addition of Et2O (20 mL) and saturated NH4Cl
solution (20 mL). The phases were separated, the aqueous phase extracted with Et₂O (3 x 20 mL) and the combined organic phases washed with water (20 mL) and brine (20 mL). The solutions were dried (MgSO₄), filtered, and the solvent removed under reduced pressure.

**General Procedure IV: NBS bromination of benzylic positions.** A solution of the methyl naphthalene (5 mmol), NBS (5.1 mmol) and AIBN (20 mg) was refluxed in CCl₄ (20 mL) for the times indicated individually. After cooling of the mixture, the succinimide was filtered off, the solvent removed under reduced pressure, and the residue purified by column chromatography on silica gel.

**General Procedure V: Acidic cleavage of TBDMS enol ethers.** A solution of the functionalized silyl enol ethers (crude products from electrophilic addition) was vigorously stirred in a mixture of CH₂Cl₂ and 2 N HCl (4:1, 125 ml, TLC monitoring) at 20 °C. The phases were separated, the organic phase was washed with aqueous NaHCO₃ solution (30 mL), water (30 mL) and brine (30 mL), dried (MgSO₄), filtered, and the solvent removed under reduced pressure.

**General Procedure VI: Coupling of diketones using samarium diiodide.** A 0.1 M SmI₂ solution in THF was prepared according to a literature procedure. This solution of SmI₂ in THF (10 ml, 1 mmol) was treated under argon at the temperatures and times indicated individually with a solution of the diketone (0.4 mmol) in THF (2 mL) (TLC monitoring). After conversion of the starting material, the reaction was quenched by addition of saturated NH₄Cl solution (10 mL). Et₂O (20 mL) was added, the phases separated, and the aqueous phase extracted twice with Et₂O (20 mL). The combined organic phases were washed with water (20 mL) and brine (20 mL), dried (MgSO₄), filtered, and the solvent removed under reduced pressure.

**4-(3-Bromo-1,4-dimethoxynaphthalen-2-yl)-butan-2-one (9):** The dibromide 7[5] (2.41 g, 6.7 mmol) was reacted with acetone silyl enol ether 8 (1.68 g, 14.7 mmol) and stirred for 21 h at 22 °C as described in the general procedure I to yield ketone 9 (2.06 g, 91 %), m. p. 114 °C as a white solid. ¹H NMR (200 MHz, CDCl₃): δ = 2.21 (s, 3 H, 1-H), 2.70–2.81 (m, 2 H, 3-H), 3.20–3.28 (m, 2 H, 4-H), 3.91 (s, 3 H, OCH₃), 3.97 (s, 3 H, OCH₃), 7.51–7.59 (m, 2 H, 6'-H, 7'-H), 8.01–8.11 (m, 2 H, 5'-H, 8'-H); ¹³C NMR (50 MHz, CDCl₃): δ = 25.12 (t, C-4), 30.24 (q, C-1), 43.73 (t, C-3), 61.77/62.94 (2 x q, 2 x OCH₃), 116.57 (s, C-3'), 122.95 (2 d, C-5', C-8'), 126.96/127.14 (2 x d, C-6', C-7'), 128.26/128.41/130.31 (3 x s, C-2', C-4a', C-8a'), 149.86/151.12 (2 x s, C-1', C-4a'), 208.29 (s, C-2); UV (methanol): λ max (lg ε) = 212 nm (4.22), 236 (4.18), 326 (3.72); MS (EI, 80 eV): m/z (%) = 337/335 (27) [M⁺], 256 (100) [M⁺–Br], 213 (2) [M⁺–Br–CH₃CO], 199 (20) [M⁺–Br–CH₃COCH₂], 182 (6) [M⁺–Br–CH₂CO–CH₃O], 43 (42) [CH₃CO⁺]; IR (KBr): ν = 2930 (CH), 1713 (C=O), 1450,
1351, 1170, 1077 (cm⁻¹); HRMS C₁₆H₁₇BrO₃: calcd 336.0361 (⁷⁹Br); found 336.0362 (⁷⁹Br); elemental analysis (%) calcd C₁₆H₁₇BrO₃ (337.21): C 57.14, H 5.10; found C 57.02, H 5.06.

\[\text{1-[2-(3-Bromo-1,4-dimethoxynaphthalen-2-yl)-ethyl-vinyloxy]-tert-butyldimethylsilane (10).}\] The ketone 9 (1.35 g, 4 mmol) was converted to the silyl ether 19 according to the general procedure II. The crude mixture was purified by flash chromatography on silica gel (60 g, PE/EE 9:1 plus 0.5 % Et₃N) to afford the oily silyl ether 10 (1.73 g, 96 %) containing ca. 25 % of the regioisomeric olefin (NMR). \(^1\)H NMR (200 MHz, CDCl₃): \(\delta = 0.23\) (s, 6 H, SiCH₃), 0.99 [s, 9 H, C(CH₃)₃], 2.31–2.39 (m, 2 H, 4-H), 3.13–3.22 (m, 2 H, 3-H), 3.93 (s, 3 H, OCH₃), 3.98 (s, 3 H, OCH₃), 4.15 (d, \(J_{\text{gem}} = 16.2\) Hz, 2 H, 1-H), 7.49–7.58 (m, 2 H, 6'-H, 7'-H), 8.02–8.11 (m, 2 H, 5'-H, 8'-H); \(^{13}\)C NMR (50 MHz, CDCl₃): \(\delta = -4.21\) (q, SiCH₃), 18.53 [s, C(CH₃)₃], 26.16 [q, C(CH₃)₃], 29.26 (t, C-4), 37.20 (t, C-3) 61.73/63.00 (2 x q, 2 x OCH₃), 90.30 (t, C-1), 117.01 (s, C-3'), 122.95/123.02 (2 x d, C-5', C-8'), 126.76/126.95 (2 x d, C-6', C-7'), 128.28/131.35 (3 x s, C-2', C-4'a, C-8'a), 150.48/151.07 (2 x s, C-1', C-4'), 159.61 (s, C-2).

Regioisomer: [3-(3-Bromo-1,4-dimethoxynaphthalen-2-yl)-1-methylpropenyl]oxygenyl-tert-butyldimethylsilane. \(^1\)H NMR (200 MHz, CDCl₃): \(\delta = 0.25\) (s, 6 H, SiCH₃), 1.05 [s, 9 H, C(CH₃)₃], 1.79 (s, 3 H, 1-H), 3.76 (d, \(J = 6.2\) Hz, 2 H, 4-H), 4.51 (t, \(J = 6.2\) Hz, 1 H, 3-H), 7.49–7.58 (m, 2 H, 6'-H, 7'-H), 8.02–8.11 (m, 2 H, 5'-H, 8'-H).

Data for 4:1 mixture of olefins: UV (methanol): \(\lambda_{\text{max}} (\log \varepsilon) = 223\) nm (4.10), 248 (4.25), 322 (3.85); MS (EI, 80 eV); \(m/z\) (%) = 450/452 (2) \([\text{M}^+\]), 392/394 (33) \([\text{M}^+ - \text{C(CH₃)₃}]\), 377/379 (32) \([\text{M}^+ - \text{C(CH₃)₃} - 2\text{xCH₃}]\), 362/364 (31) \([\text{M}^+ - \text{C(CH₃)₃} - 3\text{xCH₃}]\), 336/334 (3) \([\text{M}^+ - \text{C(CH₃)₃} - 2\text{xCH₃} - \text{Si}]\) 313 (17) \([\text{M}^+ - \text{C(CH₃)₃} - \text{Br}]\), 73 (100) \([\text{CH₃COCH₂CH₂}^+ + 2\text{H}^+]\); IR (KBr): \(\tilde{\nu} = 2924\) (CH), 2851 (CH), 1667 (CH₂=CH₂), 1569, 1540, 1356 (cm⁻¹); HRMS C₂₂H₃₁BrO₃Si: calcd 450.1226 (⁷⁹Br); found 450.1236 (⁷⁹Br); elemental analysis (%) calcd C₂₂H₃₁BrO₃Si (451.48) C 58.65, H 6.94; found C 58.53, H 6.84.

4-(3-Acetyl-1,4-dimethoxynaphthalen-2-yl]-butan-2-one (11). The TBDMS-protected brominated naphthalene 10 (1.64 g, 3.6 mmol) was reacted as described in the general procedure III with the acetic acid anhydride (0.378 ml, 4.0 mmol). The crude product was desilylated according to general procedure V and purified by chromatography on silica gel (100 g, PE/EE 6:1) to afford the diketone 11 (530 mg, 49 %) as a faint yellow oil. \(^1\)H NMR (200 MHz, CDCl₃): \(\delta = 2.16\) (s, 3 H, 1-H), 2.66 (s, 3 H, 2''-H), 2.72–2.93 (m, 4 H, 3-H, 4-H), 3.89 (s, 3 H, OCH₃), 3.91 (s, 3 H, OCH₃), 7.48–7.61 (m, 2 H, 6'-H, 7'-H), 8.02–8.10 (m, 2 H, 5'-H, 8'-H); \(^{13}\)C NMR (50 MHz, CDCl₃): \(\delta = 22.23\) (t, C-4), 30.19 (q, C-1), 33.27 (q, C-2'), 45.20 (t, C-3), 62.62/64.12 (2 x q, 2 x OCH₃), 122.87/122.99 (2 x d, C-5', C-8'), 126.58 (s, C-2'/C-3'), 126.71/127.65 (2 x d, C-6', C-7'), 127.94/129.49 (2 x s, C-4'a, C-8'a), 133.50 (s, C-2'/C-3'), 149.56 (t, C-4'), 150.48/151.07 (2 x s, C-1', C-4'), 205.90 (s, C-1''), 208.39 (s, C-2); UV (methanol): \(\lambda_{\text{max}} (\log \varepsilon) = 220\) nm (4.03), 232 (4.17), 312 (3.77); MS (EI, 80 eV); \(m/z\) (%) = 300 (13)}
[M⁺], 299 (72) [M⁺−H], 282 (7) [M⁺−CO], 256 (24) [M⁺−CH₃CO−H], 239 (86) [M⁺−CO−CH₃CO], 226 (35) [M⁺−CH₃CO−CH₃O], 200 (14) [M⁺−CH₃CO−CH₃COCH₂], 43 (100) [CH₃CO⁺]; IR (KBr): ʋ = 2939 (CH), 2841 (CH), 1713 (C=O), 1708 (C=O), 1408, 1356, 1082 (cm⁻¹); HRMS C₁₈H₂₀O₄: calcd 300.1362; found 300.1351.

4-[3-(2-Benzoyloxypropionyl)-1,4-dimethoxynaphthalen-2-yl]-butan-2-one (12). The TBDMS-protected brominated naphthalene 10 (1.90 g, 4.2 mmol) was reacted as described in the general procedure III with the anhydride 15 (1.51 g, 4.4 mmol). The crude product was desilylated according to general procedure V and purified by chromatography on silica gel (100 g, PE/EE 6:1) to afford the diketone 12 (800 mg, 45 %) as a faint yellow oil and the corresponding debrominated ketone (490 mg, 45 %). ¹H NMR (300 MHz, CDCl₃): δ = 1.44 (d, J = 7.0 Hz, 3 H, 3''-H) 2.11 (s, 3 H, 1-H), 2.65−3.05 (m, 4 H, 3-H, 4-H), 3.84 (s, OCH₃), 3.89 (s, OCH₃), 3.84−3.94 (q, overlapping, 1 H, 2''-H), AB-signal (Δδ = 0.08, δₐ = 4.66, δₐ = 4.58, Jₐb = 11.6 Hz, 2 H, OCH₂Ph), 7.22 (s, Ph-H), 7.46−7.60 (m, 2 H, 6'-H, 7'-H), 8.04−8.08 (m, 2 H, 5'-H, 8'-H); ¹³C NMR (75 MHz, CDCl₃): δ = 16.62 (q, C-3''), 22.21 (t, C-4), 29.50 (q, C-1), 44.58 (t, C-3), 61.70/63.61 (2 x q, 2 x OCH₃), 71.89 (t, OCH₂Ph), 80.53 (d, C-2''), 122.34 (2 d, C-5', C-8'), 126.07 (d, C-6'/C-7'), 126.44 (s, C-2/C-3'), 127.11 (d + s, C-6/C-7', C-2'/C-3'), 127.45/127.53/128.08 (3 x d, Ph-CH), 129.24/130.88 (2 x s, C-4'a, C-8'a), 137.71 (s, Ph-C), 149.26/150.64 (2 x s, C-1', C-4'), 207.45/207.61 (2 x s, C-1'', C-2); UV (methanol): λₘₐₓ (lg ε) = 214 nm (4.16), 226 (4.14), 234 (4.20), 312 (3.84); MS (EI, 70 eV): m/z (%) = 420 (10) [M⁺], 285 (72) [M⁺−H−CH₃CO−C₇H₇], 163 (22) [COCH(CH₃)OC₇H₇⁺], 91 (100) [C₇H₇⁺], 43 (54) [CH₃CO⁺]; IR (KBr): ʋ = 2934 (CH), 2851 (CH), 1719 (C=O), 1708 (C=O), 1455, 1274 (cm⁻¹); HRMS C₂₆H₂₈O₅: calcd 420.1937; found 420.1938.

1-[1,4-Dimethoxy-3-(3-oxobutyl)-naphthalen-2-yl]-2-methylpropenone (13). The TBDMS-protected brominated naphthalene 10 (1.73 g, 3.8 mmol) was reacted as described in general procedure III with methacrylic acid anhydride (0.71 g, 4.6 mmol). The crude product was desilylated according to general procedure V and purified by chromatography on silica gel (100 g, PE/EE 6:1) to afford the diketone 13 (475 mg, 39 %) as a faint yellow oil. The corresponding debrominated ketone was isolated in ca. 50 % yield. ¹H NMR (200 MHz, CDCl₃): δ = 2.08 (s, 3 H, 4-H), 2.13 (s, 3 H, 4''-H), 2.77 (br s, 4 H, 1''-H, 2''-H), 3.84 (s, 3 H, OCH₃), 3.91 (s, 3 H, OCH₃), 5.63 (s, 1 H, 3-H), 6.00 (s, 1 H, 3-H), 7.47−7.60 (m, 2 H, 6'-H, 7'-H), 8.02−8.08 (m, 2 H, 5'-H, 8'-H); ¹³C NMR (50 MHz, CDCl₃): δ = 17.11 (q, C-4), 22.27 (t, C-1''), 30.14 (q, C-4''), 44.98 (t, C-2'') 62.67/63.94 (2 x q, 2 x OCH₃), 122.87/123.04 (2 x d, C-5', C-8'), 126.60/127.39 (2 x d, C-6', C-7'), 127.50/127.80/129.50/131.20 (4 x s, C-2', C-3', C-4'a, C-8'a), 130.67 (t, C-3), 146.20 (s, C-2), 149.47/150.90 (2 x s, C-1', C-4'), 199.58 (s, C-1), 208.21 (s, C-3''); UV (methanol): λₘₐₓ (lg ε) = 225 nm (3.87), 266 (4.07), 328 (3.75); MS (EI, 80 eV): m/z (%) = 326 (2) [M⁺], 325 (17) [M⁺−H], 267 (26) [M⁺−CH₃CO−CH₃], 252 (100) [M⁺−CH₃CO−CH₃O], 240 (15) [M⁺−CH₃CO−CH₃CH=CH₂], 224 (4)
[M⁺–CH₃CO–CH₃O–CO], 43 (30) [CH₃CO⁺⁺]; IR (KBr): \( \tilde{\nu} = 2929 \text{ (CH)}, 2836 \text{ (CH), 1713 (C=O)}, 1656 \text{ (C=O), 1589 (CH₂=CH₂), 1455, 1351, 1077 (cm}^{-1}) \); HRMS C₂₀H₂₂O₄ calcd 326.1518, found 326.1509.

1-[1,4-Dimethoxy-3-(3-oxobutyl)-naphthalen-2-yl]-propane-1,2-dione (14). The TBDMS-protected brominated naphthalene 10 (1.67 g, 3.7 mmol) was reacted as described in the general procedure III with pyruvic acid chloride (0.44 g, 4.1 mmol). The crude product was desilylated according to general procedure V and purified by chromatography on silica gel (100 g, PE/EE 6:1) to afford the triketone 14 (156 mg, 13 %) as a faint yellow oil and the corresponding debrominated naphthalene (573 mg, 60 %). ¹H NMR (200 MHz, CDCl₃): \( \delta = 2.15 \text{ (s, 3 H, 4''-H), 2.54 (s, 3 H, 3-H), 2.73–2.86 (m, 2 H, 1''-H), 3.01–3.09 (m, 2 H, 2''-H), 3.88 (s, 3 H, OCH₃), 3.92 (s, 3 H, OCH₃), 7.49–7.67 (m, 2 H, 6'-H, 7'-H), 8.02–8.10 (m, 2 H, 5'-H, 8'-H); ^{13}C NMR (50 MHz, CDCl₃): \delta = 21.53 \text{ (t, C-1''), 24.65 (t, C-2''), 34.07 (q, C-3), 45.07 (t, C-4''), 62.62/63.98 (2 x q, 2 x OCH₃), 123.36/123.44 (2 x d, C-5', C-8'), 126.29/129.25/131.49 (3 x s, C-2', C-3', C-4'a/C-8'a), 126.85 (s + d, C-4'a/C-8'a, and C-6/C-7'), 128.96 (d, C-6/C-7'), 151.52/154.50 (2 x s, C-1', C-4'), 196.41/198.91 (2 x s, C-1, C-2), 208.26 (s, C-3''); UV (methanol): λ_max (lg ε) = 227 nm (4.15), 265 (3.99), 324 (3.57); MS (EI, 70 eV): m/z (%) = 328 (7) [M⁺], 300 (8) [M⁺–CO], 285 (50) [M⁺–CH₂CO], 241 (24) [M⁺–CH₃CO–CO₂], 43 (100) [CH₃CO⁺⁺]; IR (KBr): \( \tilde{\nu} = 2934 \text{ (CH), 2836 (CH), 1713 (C=O), 1656 (C=O), 1589 (CH₂=CH₂), 1455, 1351, 1077 (cm}^{-1}) \); HRMS C₂₀H₂₂O₄ calcd 328.1311; found 328.1308; elemental analysis (%) calcd C₂₀H₂₂O₄ (328.36): C 69.48, H 6.14; found C 69.12, H 5.87.

2-Benzyl oxypropionic acid anhydride (15): A solution of 2-benzyloxypropionic acid[6] (2.95 g, 16.4 mmol) in CH₂Cl₂ (10 mL) was treated at 20 °C with a solution of DCC (1.69 g, 8.2 mmol) in CH₂Cl₂ (2 mL) and the mixture was stirred for 15 h. The suspension was filtered, the solvent removed under reduced pressure, and the residue purified by bulb to bulb distillation to yield the anhydride 15 (2.09 g, 74 %, 170 °C/0.5 mbar) as a colorless liquid. ¹H NMR (200 MHz, CDCl₃): \( \delta = 1.50 \text{ (d, J = 6.7 Hz, 3 H, CH₃), 4.09 (q, J = 6.7 Hz, OCH)}, AB-signal (\Delta \delta = 0.25, \delta_A = 4.73, \delta_B = 4.48, J_{AB} = 11.5 Hz, 2 H, OCH₂Ph), 7.34 (br s, 5 H, Ph-H); ^{13}C NMR (50 MHz, CDCl₃): \delta = 18.54 (q, CH₃), 72.66 (t, OCH₂Ph), 74.56 (d, OCH₂Ph), 128.40/128.50/128.97 (3 x d, Ph-CH), 137.50 (s, Ph-C) 169.40 (s, COO); UV (methanol): \( \lambda_{max} \text{ (lg ε) = 230 (4.49), 285 (3.74), 328 (3.31); MS (EI, 70 eV); m/z (%): 316 (10) [M⁺⁺], 229 (9) [M⁺ – C(OCH₂CH₂O)CH₃], 214 (3) [M⁺ – C(OCH₂CH₂O)CH₃ – CH₃], 199 (4), 171 (4), 143 (3), 128 (3), 115 (5) [CO(OCH₂CH₂O)CH₃⁺], 87 (100) [C(OCH₂CH₂O)CH₃⁺]; IR (CH₂Cl₂): \( \tilde{\nu} = 2939 \text{ (CH), 2895 (CH), 1712 (Keton-CO), 1532 cm}^{-1}; \) elemental analysis (%) calcd for C₁₈H₂₀O₅ (316.35) C 68.34, H 6.37; found C 68.34, H 6.49.
2-Methyl-[1,3]dioxolan-2-carboxylic acid anhydride (17) A solution of 2-methyl-[1,3]dioxolan-2-carboxylic acid[7] (3.00 g, 22.5 mmol) in CH₂Cl₂ (10 mL) was treated at 22 °C with a solution of DCC (2.25 g, 11.3 mmol) in CH₂Cl₂ (3 mL) as described for 15 to afford the anhydride 17 (2.34 g, 84 %) as a colorless liquid. ¹H NMR (200 MHz, CDCl₃): δ = 1.65 (s, 6 H, 3-H), 4.14 (s, 8 H, OCH₂CH₂O); ¹³C NMR (50 MHz, CDCl₃): δ = 21.98 (q, C-3), 66.36 (t, OCH₂CH₂O), 105.58 (s, C-2), 165.50 (s, C-1).

(1,4-Dimethoxy-3-methylnaphthalen-2-yl)-(2-methyl-[1,3]dioxolan-2-yl)-methanone (18). Bromonaphthalene 16[8] (4.78 g, 17 mmol) was reacted with the anhydride 17 (4.65 g, 18.9 mmol) as described in the general procedure III. The residue was purified by column chromatography on silica gel (150 g, PE/EE 9:1) to afford 18 (4.11 g, 70 %) as a yellow oil. ¹H NMR (200 MHz, CDCl₃): δ = 1.66 (s, 3 H, 3-H), 2.33 (s, 3 H, 2'-CH₃), 3.77−4.00 (m, 4 H, OCH₂CH₂O), 3.86 (s, 3 H, OCH₃), 3.87 (s, 3 H, OCH₃), 7.50−7.63 (m, 2 H, 6'-H, 7'-H), 8.07−8.15 (m, 2 H, 5'-H, 8'-H); ¹³C NMR (50 MHz, CDCl₃): δ = 13.40 (q, 2'-CH₃), 21.71 (q, C-3), 61.82/63.96 (2 x q, 2 x OCH₃), 66.39 (t, OCH₂CH₂O), 108.68 (t, OCH₂CH₂O), 108.68 (s, C-2), 122.80/122.98 (2 x d, C-5', C-8'), 123.81 (s, C-2'), 126.31/127.47 (2 x d, C-6', C-7'), 127.16/129.68/131.13 (3 x s, C-3', C-4a', C-8a'), 149.59/150.74 (2 x s, C-1', C-4'), 205.28 (s, C-1).

(3-Bromomethyl-1,4-dimethoxynaphthalen-2-yl)-(2-methyl-[1,3]dioxolan-2-yl)-methanone (19). The methylnaphthalene 18 (2.9 g, 9.2 mmol) was brominated with NBS as described in the general procedure IV (1 h reflux). The crude product was purified by flash chromatography on silica gel (100 g, PE/EE 9:1) to afford the bromide 19 (3.01 g, 83 %, m. p. 89 °C) as a white solid. ¹H NMR (200 MHz, CDCl₃): δ = 1.70 (s, 3 H, 3-H), 3.89 (s, 3 H, OCH₃), 3.87−4.00 (m, 4 H, OCH₂CH₂O), 4.10 (s, 3 H, OCH₃), 4.75 (s, 2 H, CH₂Br), 7.53−7.62 (m, 2 H, 6'-H, 7'-H), 8.06−8.14 (m, 2 H, 5'-H, 8'-H); ¹³C NMR (50 MHz, CDCl₃): δ = 21.81 (q, C-3), 25.13 (t, CH₂Br), 63.13/64.15 (2 x q, 2 x OCH₃), 66.39 (t, OCH₂CH₂O), 108.54 (s, C-2), 123.38/123.59 (2 x d, C-5', C-8'), 124.47 (s, C-2'/C-3'), 127.85/128.02 (2 x d, C-6', C-7'), 129.00 (s, C-2'/C-3'), 129.42/129.69 (2 x s, C-4'a, C-8'a), 150.54/152.45 (2 x s, C-1', C-4'), 203.93 (s, C-1); UV (methanol): λ_max (lg ε) = 225 nm (4.05), 262 (4.32), 330 (3.75); MS (EI, 70 eV); m/z (%) = 396/394 (<1) [M⁺], 315 (2) [M⁺−Br], 307/309 (1) [M⁺−C(OCH₂CH₂O)CH₃], 243 (5), 228 (5), 213 (15), 199 (5), 87 (100) [C(OCH₂CH₂O)CH₃⁺]; IR (KBr): v̄ = 2939 (CH), 1714 (C=O), 1358, 1200, 1103, 1038, 989 (cm⁻¹); HRMS C₁₈H₁₉BrO₅: calc'd 394.0416 (79Br); found 394.0413 (79Br). elemental analysis (%) calc'd for C₁₈H₁₀BrO₅ (395.25): C 54.82, H 4.86; found C 54.70, H 4.78.

4-[1,4-Dimethoxy-3-(2-methyl-[1,3]dioxolan-2-carbonyl)-napthalen-2-yl]butan-2-one (20). The bromide 19 (1.98 g, 5 mmol) was reacted with the silyl enol ether 8 (1.43 g, 11 mmol) as described in the general procedure I. The crude product was purified by chromatography on silica gel (75 g, PE/EE 2:1) to afford the diketone 20 (915 mg, 49 %, m.
p. 82 °C) as a white solid. \(^1\)H NMR (200 MHz, CDCl\(_3\)): \(\delta = 1.66\) (s, 3 H, 3''-H), 2.18 (s, 3 H, 1-H), 2.76–2.96 (m, 4 H, 3-H, 4-H), 3.84–4.03 (m, 4 H, OCH\(_2\)CH\(_2\)O), 3.88 (s, 3 H, OCH\(_3\)), 3.93 (s, 3 H, OCH\(_3\)), 7.53–7.60 (m, 2 H, 6'-H, 7'-H), 8.06–8.11 (m, 2 H, 5'-H, 8'-H); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)): \(\delta = 21.74\) (q, C-3''), 22.83 (t, C-4), 30.20 (q, C-1), 44.94 (t, C-3), 62.68/63.99 (2 x q, 2 x OCH\(_3\)), 66.30 (t, OCH\(_2\)CH\(_2\)O), 108.59 (s, C-2''), 122.87/123.09 (2 x d, C-5', C-8'), 126.58 (d, C-6'/C-7'), 127.36 (s, C-2'/C-3'), 127.57 (d + s, C-6'/C-7' and C-2'/C-3'), 129.68/130.78 (2 x s, C-4'a', C-8'a'), 149.77/151.03 (2 x s, C-1', C-4'), 205.20 (s, C-1''), 208.37 (s, C-2); UV (methanol): \(\lambda_{\text{max}}\) (lg \(\varepsilon\)) = 224 nm (4.07), 246 (4.30), 332 (3.82); MS (EI, 70 eV); \(m/z\) (%): 372 (7) [M\(^+\)], 285 (3) [M\(^+\) C(OCH\(_2\)CH\(_2\)O)CH\(_3\)], 213 (3), 128 (3), 87 (100) [C(OCH\(_2\)CH\(_2\)O)CH\(_3\)]\(^+\); IR (KBr): \(\nu = 2983\) (CH), 2935 (CH), 1716 (C=O), 1354, 1203, 1036 (cm\(^{-1}\)); HRMS C\(_{21}\)H\(_{24}\)O\(_6\): calcd 372.1573; found 372.1581; elemental analysis (%) calcd for C\(_{21}\)H\(_{24}\)O\(_6\) (372.42): C 67.71, H 6.50; found C 67.58, H 6.42.

9,10-Dimethoxy-1,2-dimethyl-1,2,3,4-tetrahydroanthracen-1,2-diol (21). The diketone 11 (82 mg, 0.27 mmol) was treated with samarium(II) iodide at 0 °C for 30 min as described in the general procedure VI. The crude mixture (9 products by TLC) was purified by preparative TLC chromatography on silica gel (1 mm, PE/EE 1:1) to afford the diol 21 (22 mg, 27 %) as a single isomer. The same reaction with activated magnesium\(^9\) gave 21 (15 mg, 21 %) as 1:1 mixture of isomers (1H NMR).

Data for the single isomer 21: \(^1\)H NMR (200 MHz, CDCl\(_3\)): \(\delta = 1.28\) (s, 3 H, 2'-H), 1.66 (s, 3 H, 1'-H), 1.78–2.21 (m, 2 H, 3-H), 2.53 (br s, 1 H, OH), 2.89–3.24 (m, 2 H, 4-H), 3.88 (s, 3 H, OCH\(_3\)), 4.09 (s, 3 H, OCH\(_3\)), 5.30 (s, 1 H, OH), 7.44–7.53 (m, 2 H, 6-H, 7-H), 7.94–8.07 (m, 2 H, 5-H, 8-H); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)): \(\delta = 21.98\) (t, C-4), 23.47 (q, C-2'), 27.34 (q, C-3), 31.17 (t, C-3), 61.12/64.04 (2 x q, 2 x OCH\(_3\)), 74.31 (s, C-2), 77.73 (s, C-1), 122.52 (2 x d, C-5, C-8), 125.95/126.41 (2 x d, C-6, C-7), 125.42/127.58/128.22/134.00 (4 x s, C-4a, C-8a, C-9a, C-10a), 150.06/150.39 (2 x s, C-9, C-10); UV (methanol): \(\lambda_{\text{max}}\) (lg \(\varepsilon\)) = 213 nm (4.02), 226 (4.18), 260 (4.13), 321 (3.87); MS (EI, 70 eV): \(m/z\) (%) = 302 (66) [M\(^+\)], 284 (11) [M\(^+\)-H\(_2\)O], 231 (100) [M\(^+\)-CH\(_3\)CO–CO], 43 (92) [CH\(_3\)CO\(^+\)]; IR (KBr): \(\nu = 3436\) (OH), 2929 (CH), 2836 (CH), 1584, 1450, 1015 (cm\(^{-1}\)); HRMS C\(_{18}\)H\(_{24}\)O\(_4\): calcd 302.15179; found 302.15017; elemental analysis (%) calcd for C\(_{18}\)H\(_{24}\)O\(_4\) (302.37): C 71.49, H 7.34; found C 70.73, H 7.01.

8-Hydroxy-7-(2-hydroxyethoxy)-5,11-dimethoxy-7,8-dimethyl-7,8,9,10-tetrahydrocyclohept[a]naphthalen-6-one (22). The diketone 20 (152 mg, 0.41 mmol) was treated with samarium(II) iodide at –78 °C for 30 min as described in the general procedure VI. The crude mixture was purified by column chromatography on silica gel (10 g, CH\(_2\)Cl\(_2\)/MeOH 95:5) to afford the oily diol 22 (129 mg, 84 %) as a single isomer in addition to starting material 20 (10 mg, 7 %). \(^1\)H NMR (200 MHz, [D\(_6\)]-DMSO, 100 °C): \(\delta = 1.24\) (s, 3 H, 8-CH\(_3\)), 1.37 (s, 3 H, 7-CH\(_3\)), 1.83 (ddd, \(J = 14.1\) Hz, \(J = 9.8\) Hz, \(J = 1.4\) Hz, 1 H, 9-H/10-H), 2.22 (m, 1 H, 9-
H/10-H), 2.67 (m, 1 H, 9-H/10-H), 3.14 (m, 1 H, 9-H/10-H), 3.27 (m, 2 H, CH₂OH),
3.34–3.57 (m, 2 H, CH₂OC), 3.87 (s, 3 H, OCH₃), 3.95 (s, 3 H, OCH₃), 4.11 (br s, 1 H, 8-
OH), 7.53–7.66 (m, 2 H, 2-H, 3-H), 8.04–8.11 (m, 2 H, 1-H, 4-H); ¹³C NMR (50 MHz,
CDCl₃): δ = 16.79 (q, 7-CH₃), 20.50 (t, C-10), 26.01 (q, 8-CH₃), 38.16 (t, C-9), 62.56 (t,
CH₂OH), 62.92 (q, OCH₃), 66.75 (t, CH₂OC), 77.20 (s, C-8), 88.39 (s, C-7),
123.09/123.16 (2 x d, C-1, C-4), 126.41/127.97 (2 x s, C-5a, C-10a), 126.59/127.63 (2 x d, C-
2, C-3), 130.06/132.30 (2 x s, C-4a, C-11a), 149.07 (s, C-5 and C-11), 206.92 (s, C-6); UV
(methanol): λₘₐₓ (lg ε) = 215 nm (4.20), 236 (4.16), 270 (4.32), 328 (3.90); MS (CI, NH₃):
m/z (%) = 375 (4) [M+H+], 374 (19) [M+], 359 (23) [M+–CH₃], 312 (100) [M+–OCH₂CH₂O],
297 (14) [M⁺–CH₂–OCH₂–CH₃]; IR (KBr): ~ ν (cm⁻¹) = 3405 (OH), 2934 (CH), 2846 (CH),
1713 (C=O), 1584, 1351, 1274, 1046 (cm⁻¹); HRMS calcd 374.1729; found 374.1735;
elemental analysis (%) calcd for C₂₁H₂₆O₆ (374.43): C 67.35, H 7.00; found C 66.92, H 6.87.

4-{3-[2-(2-Hydroxyethoxy)-propionyl]-1,4-dimethoxynaphthalen-2-yl}-butan-2-one (23).
A solution of 22 (60 mg, 0.16 mmol) in d⁶-DMSO (0.5 mL) was heated at 100 °C for 15 h in
an NMR tube. The products were recovered by dilution with ethyl acetate and washed with
water (3 x 2 mL). The products were separated by preparative TLC on silica gel (1 mm,
CH₂Cl₂/MeOH 95:5) to yield the starting material 22 (33 mg, 55 %) and the oily less polar
retro aldol product 23 (16 mg, 27 %). ¹H NMR (200 MHz, CDCl₃): δ = 1.40 (d, J = 7.0 Hz, 3
H, 3''-H), 2.16 (s, 3 H, 1-H), 2.56–3.08 (m, 4 H, 3-H, 4-H), 3.60–3.82 (m, 5 H,
OCH₂CH₂OH), 3.88 (s, OCH₃), 3.91 (s, 3 H, OCH₃), 4.68 (q, J = 7.0 Hz, 1 H, 2''-H),
7.51–7.63 (m, 2 H, 6'-H, 7'-H), 8.04–8.08 (m, 2 H, 5'-H, 8'-H); ¹³C NMR (50 MHz, CDCl₃): δ
= 17.43 (q, C-3''), 22.80 (t, C-4), 30.18 (q, C-1), 45.26 (t, C-3), 62.31 (t, CH₂OH), 62.62 (q,
OCH₃), 64.30 (q, OCH₃), 72.12 (t, CH₂OCH), 82.17 (d, C-2''), 122.87/123.01 (2 x d, C-5',
C-8'), 126.86/127.90 (2 x d, C-6', C-7'), 127.47/127.67/129.94/130.91 (4 x s, C-2', C-3', C-4a',
C-8a'), 149.94/150.43 (2 x s, C-1', C-4'), 208.22/208.35 (2 x s, C-1'', C-2).

8-Hydroxy-5,11-dimethoxy-7,8-dimethyl-7,8,9,10-tetrahydrocyclohepta[b]naphthalen-6-
one (24). The diketone 12 (84 mg, 0.2 mmol) was treated with samarium diiodide at −15 °C
for 3 h as described in the general procedure VI. The product was purified by preparative TLC
on silica gel (1 mm, CH₂Cl₂/MeOH 98:2) to afford the faint yellow oily
cycloheptannaphthalene 24 (27 mg, 43 %) as a single isomer. ¹H NMR (200 MHz, CDCl₃, T =
40 °C): δ = 0.98 (d, J = 6.9 Hz, 3 H, 1'-H), 1.38 (s, 3 H, 2'-H), 1.86–1.98 (m, 2 H, 7-H, 9-H),
2.82–2.98 (m, 2 H, 9-H, 10-H), 3.23–3.41 (m, 2 H, 10-H), 3.69 (s, 1 H, OH), 3.88 (s, 3 H,
OCH₃), 4.03 (s, 3 H, OCH₃), 7.54–7.66 (m, 2 H, 2-H, 3-H), 8.08–8.23 (m, 2 H, 1-H, 4-H); ¹³C
NMR (50 MHz, CDCl₃): δ = 12.09 (q, C-1'), 21.53 (t, C-10), 30.12 (t, C-9), ~ 35 (q, C-2'),
58.61 (d, C-7), 62.66/65.31 (2 x q, 2 OCH₃), 74.40 (s, C-8), 122.98/123.65/126.54/127.79 (4 x
d, C-1, C-2, C-3, C-4), 126.98/128.24/129.89/~ 132 (4 x s, C-4a, C-5a, C-10a, C-11a), 149.40
(t, s, C-5, C-11), 206.70 (s, C-6); UV (methanol): λₘₐₓ (lg ε) = 218 nm (4.03), 236 (4.21),
cis- and trans-1-(1,2-Dihydroxy-9,10-dimethoxy-2-methyl-1,2,3,4-tetrahydroanthracen-1-yl)-ethanone (cis-25) (trans-26). The diketone 14 (70 mg, 0.21 mmol) was treated with samarium diiodide at –78 °C for 30 min as described in the general procedure VI. The products were purified by preparative TLC on Al₂O₃ (neutral, 1mm, CH₂Cl₂) to afford the cis-diol 25 (25 mg) from the polar fraction as a colorless oil and the trans-diol 26 (39 mg) from the less polar fraction as white crystals, m. p. 110 °C in a combined yield of 91 %.

Data for 25: ¹H NMR (300 MHz, CDCl₃):  δ = 1.31 (s, 3 H, 2'-CH₃), 1.89–1.98 (m, 1 H, 3'-H), 2.27 (s, 3 H, 2-H), 2.98–3.08 (m, 2 H, 3'-H/4'-H), 3.21–3.31 (m, 1 H, 4'-H), 3.86 (s, 3 H, OCH₃), 3.93 (s, 3 H, OCH₃), 7.44–7.57 (m, 2 H, 6'-H, 7'-H), 7.99 (d, J = 7.4 Hz, 1 H, 5'-H/8'-H), 8.07 (d, J = 8.2 Hz, 1 H, 5'-H/8'-H); ¹³C NMR (75 MHz, CDCl₃):  δ = 20.89 (t, C-4'), 23.73 (q, C-2), 27.00 (q, 2'-CH₃), 32.87 (t, C-3'), 60.70/62.70 (2 x q, 2 x OCH₃), 71.26 (s, C-2'), 81.59 (s, C-1'), 122.00/122.32/125.36/126.50 (4 x d, C-5', C-6', C-7', C-8'), 122.75/126.23/126.91/128.36 (4 x s, C-4'a, C-8'a, C-9'a, C-10'a), 124.38/151.04 (2 x s, C-9', C-10'), 208.65 (s, C-1); UV (methanol):  λ max (lg ε) = 217 nm (4.17), 235 (4.30), 260 (3.95), 326 (3.68); IR (KBr): ~  ν (cm⁻¹) = 3436 (OH), 2929 (CH), 2847 (CH), 1703 (C=O), 1584, 1459, 1357, 767; (cm–¹); elemental analysis (%) calcd for C₁₉H₂₂O₅ (330.38): C 69.06, H 6.72; found for 25: C 68.24, H 6.46; found for 26: C 69.43 H 6.87.

Data for 26: ¹H NMR (300 MHz, CDCl₃):  δ = 1.25 (s, 3 H, 2'-CH₃), 1.78–1.85 (m, 2 H, 3'-H), 2.31 (s, 3 H, 2-H), 3.09–3.16 (m, 2 H, 4'-H), 3.76 (s, 3 H, OCH₃), 3.92 (s, 3 H, OCH₃), 5.00 (s, 1 H, OH), 7.43–7.55 (m, 2 H, 6'-H, 7'-H), 7.99 (d, J = 8.3 Hz, 1 H, 5'-H/8'-H), 8.05 (d, J = 8.4 Hz, 1 H, 5'-H/8'-H); ¹³C NMR (75 MHz, CDCl₃):  δ = 19.72 (t, C-4'), 24.00 (q, C-2), 27.89 (q, 2'-CH₃), 31.75 (t, C-3'), 60.84/62.71 (2 x q, 2 x OCH₃), 73.21 (s, C-2'), 79.43 (s, C-1'), 122.16/122.61/125.52/126.65 (4 x d, C-5', C-6', C-7', C-8'), 125.89/127.33/127.93/128.62 (4 x s, C-4'a, C-8'a, C-9'a, C-10'a), 149.63/151.00 (2 x s, C-9', C-10'), 210.39 (s, C-1); UV (methanol):  λ max (lg ε) = 215 nm (4.12), 232 (4.24), 262 (3.98), 328 (3.70); IR (KBr):  ν = 3462 (OH), 2934 (CH), 2841 (CH), 1688 (C=O), 1357, 1052 (cm–¹); MS (EI, 70 eV):  m/z (%) = 330 (14) [M⁺], 287 (93) [M⁺–CH₂CO], 269 (77) [M⁺–CH₃CO–H₂O], 241 (100) [M⁺–H₂CO–H₂O–CO], 43 (42) [CH₂CO⁺]; HRMS C₁₉H₂₂O₅: calcd 330.1467; found 330.1483.

1-(1,4-Dimethoxy-3-methylnaphthalen-2-yl)-2-methylpropenone (27). The brominated naphthalene 16 (1.12 g, 4 mmol) was reacted with methacrylic acid anhydride (0.68 g, 4.4 mmol) as described in the general procedure III. The residue was purified by column
chromatography on silica (80 g, PE/EE 9:1) to afford the acylated naphthalene 27 (0.61 g, 57 %), mp 94-95 °C, as a white solid. $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 2.10 (s, 3 H, 4-H), 2.24 (s, 3 H, Ar-CH$_3$), 3.86 (s, 3 H, OCH$_3$), 3.88 (s, 3 H, OCH$_3$), 5.62 (s, 1 H, 3-H), 5.98 (s, 1 H, 3-H), 7.46–7.58 (m, 2 H, 6'-H, 7'-H), 8.02–8.11 (m, 2 H, 5'-H, 8'-H), $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ = 13.01 (q, Ar-CH$_3$), 17.05 (q, C-4), 61.89/63.99 (2 x q, 2 x OCH$_3$), 122.78/122.90/126.34/127.30 (4 x d, C-5', C-6', C-7', C-8'), 123.93/127.42/129.52/131.70 (4 x s, C-2', C-3', C-4'a, C-8'a), 130.53 (t, C-3), 145.87 (s, C-2), 149.24/150.58 (2 x s, C-1', C-4'), 199.88 (s, C-1); UV (methanol): $\lambda$$_{\text{max}}$ (lg $\varepsilon$) = 230 nm (4.30), 246 (4.22), 317 (3.92); MS (EI, 70 eV): m/z (%) = 270 (100) [M$^+$], 255 (25) [M$^+$–CH$_3$], 240 (16) [M$^+$–CH$_2$O], 229 (18) [M$^+$–C$_3$H$_5$], 227 (20) [M$^+$–CH$_3$–CO], 223 (18), 195 (17), 171 (10), 115 (16); IR (KBr): v (cm$^{-1}$) = 2932 (CH), 2838 (CH), 1656 (C=O), 1354, 1078, 1011 (cm$^{-1}$); HRMS C$_{17}$H$_{18}$O$_3$: calcd 270.1256, found 270.1251; elemental analysis (%) calcd for C$_{17}$H$_{18}$O$_3$ (270.33): C 75.52, H, 6.72; found C 75.70, H 6.78.

1-(3-Bromomethyl-1,4-dimethoxynaphthalen-2-yl)-2-methylpropenone (28). The methylnaphthalene 27 (1.43 g, 5.3 mmol) was brominated with NBS as described in the general procedure IV. The crude product was purified by column chromatography on silica gel (100 g, PE/EE 9:1) to afford the bromide 28 (0.80 g, 43 %) as a yellow oil. $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 2.13 (s, 3 H, 2-CH$_3$), 3.84 (s, 3 H, OCH$_3$), 4.07 (s, 3 H, OCH$_3$), 4.68 (s, 2 H, CH$_2$Br), 5.78 (s, 1 H, 3-H), 6.04 (s, 1 H, 3-H), 7.56–7.63 (m, 2 H, 6'-H, 7'-H), 8.05–8.14 (m, 2 H, 5'-H, 8'-H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ = 17.36 (q, CH$_3$), 24.76 (t, CH$_2$Br), 63.13/63.96 (2 x q, 2 x OCH$_3$), 123.29/123.57/127.92 (4 x d, C-5', C-6', C-7', C-8'), 124.76/129.13/129.51/130.00 (4 x s, C-2', C-3', C-4'a, C-8'a), 131.04 (t, C-3), 145.73 (s, C-2), 150.18/152.09 (2 x s, C-1', C-4'), 198.51 (s, C-1); UV (methanol): $\lambda$$_{\text{max}}$ (lg $\varepsilon$) = 228 nm (4.27), 247 (4.15), 320 (4.00); MS (EI, 70 eV): m/z ($\%$) = 348/350 (48) [M$^+$], 307/309 (5) [M$^+$–C$_3$H$_5$], 100 (100) [M$^+$–Br], 255 (15) [M$^+$–CH$_2$Br], 241 (42) [M$^+$–Br–CO], 239 (20) [M$^+$–Br–CH$_2$O], 226 (21) [M$^+$–Br–CO–CH$_3$], 211 (25) [M$^+$–Br–CO–CH$_2$O], 210 (25) [M$^+$–Br–CO–CH$_2$O–H]; IR (KBr): v (cm$^{-1}$) = 2939 (CH), 2845 (CH), 1649 (C=O), 1582, 1360, 1065; HRMS C$_{17}$H$_{17}$BrO$_3$: calcd 348.0361 ($^{79}$Br); found 348.0351 ($^{79}$Br).

4,9-Dimethoxy-2-methyl-2-[4-(2-methyl-[1,3]dioxolan-2-yl)-3-oxobutyl]-2,3-dihydro- cyclopenta[b]naphthalen-1-one (30). The bromide 28 (560 mg, 1.6 mmol) was reacted with silyl enol ether 29$^{[1]}$ (0.76 g, 3.5 mmol) according to the general procedure I. The crude product was purified by chromatography on silica gel (70 g, PE/EE 4:1) to afford 30 (80 mg, 12 %) as a faint yellow oil. $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 1.28 (s, 3 H, 2-CH$_3$), 1.36 (s, 3 H, 1'-H), 1.89–1.98 (m, 2 H, 6'-H), 2.48–2.56 (m, 5'-H), 2.71 (s, 2 H, 3'-H), AB-signal ($\Delta$\delta = 0.13, $\delta_A = 3.19$, $\delta_B = 3.06$, $J_{AB} = 17.2$ Hz, 2 H, 3'-H), 3.89 (br s, 4 H, OCH$_2$CH$_2$O), 3.99 (s, 3 H, OCH$_3$), 4.17 (s, 3 H, OCH$_3$), 4.17 (s, 3 H, OCH$_3$), 7.48–7.69 (m, 2 H, 6-H, 7-H), 8.12 (d, $J = 8.1$ Hz, 1 H, 5-H/8-H), 8.37 (d, $J = 8.4$ Hz, 1 H, 5-H/8-H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ = 24.40 (q, 2-
CH3), 24.86 (q, C-1'), 32.37 (t, C-6'), 37.34 (t, C-3), 39.96 (t, C-5'), 49.27 (s, C-2), 52.05 (t, C-3'), 61.45/63.64 (2 x q, 2 x OCH3), 64.97 (t, OCH2CH2O), 108.25 (s, C-2'), 122.13/125.26/126.41/129.40 (4 x d, C-5, C-6, C-7, C-8), 122.94/129.16/133.09/134.56 (4 x s, C-3a, C-4a, C-8a, C-9a), 148.18/153.00 (2 x s, C-4, C-9), 207.43 (s, C-4'), 208.17 (s, C-1); UV (methanol): \( \lambda_{\text{max}} \) (lg \( \varepsilon \)) = 218 nm (4.20), 243 (4.13), 267 (3.80), 328 (3.20); MS (EI, 70 eV): \( m/z \) (%) = 412 (12) [M+], 397 (1) [M+−CH3], 311 (2) [M+−CH3C(OCH2CH2O)CH2], 296 (2) [M+−CH3C(OCH2CH2O)CH2−CH3], 129 (18), 87 (73) [CH3C(OCH2CH2O)+], 43 (100) [CH3CO+]; IR (KBr): ~\( \nu \) = 2935 (CH), 2888 (CH), 1709 (C=O), 1682 (C=O), 1621, 1357, 1047 (cm–1); HRMS C24H28O6: calcd 412.1886; found 412.1907.

1-(1,4-Dimethoxy-3-methylnaphthalen-2-yl)-propane-1,2-dione (31). Naphthalene 16 (562 mg, 2 mmol) was treated with pyruvic acid chloride (256 mg, 2.4 mmol) as described in the general procedure III. The crude product was purified by column chromatography on silica gel (30 g, PE/EE 9:1) to afford the dione 31 (114 mg, 21 %, m. p. 89 °C) as a yellow solid. \( ^1H \) NMR (200 MHz, CDCl3): \( \delta = 2.43 \) (s, 3 H, Ar-CH3), 2.53 (s, 3 H, 3-H), 3.87 (2 x s, 6 H, 2 x OCH3), 7.46−7.61 (m, 2 H, 6'-H, 7'-H), 8.02 (dd, 1 H, \( ^3J = 7.5 \) Hz, \( ^4J = 1.0 \) Hz, 5'-H/8'-H), 8.10 (dd, 1 H, \( ^3J = 8.4 \) Hz, \( ^4J = 1.0 \) Hz, 5'-H/8'-H); \( ^13C \) NMR (50 MHz, CDCl3): \( \delta = 13.11 \) (q, Ar-CH3), 24.73 (q, C-3), 61.90/64.05 (2 x q, 2 x OCH3), 122.76/125.81/126.19/131.61 (4 x s, C-2', C-3', C-4'a, C-8'a), 123.22/123.34/126.57/128.91 (4 x d, C-5', C-6', C-7', C-8'), 151.37/154.40 (2 x s, C-1', C-4'), 196.40/199.17 (2 x s, C-1, C-2); UV (methanol): \( \lambda_{\text{max}} \) (lg \( \varepsilon \)) = 226 nm (4.20), 248 (4.11), 322 (3.82); MS (EI, 70 eV): \( m/z \) (%) = 272 (8) [M+], 229 (100) [M+−CH3CO], 214 (19) [M+−CH3−CH2CO], 43 (18) [CH3CO+]; IR (KBr): ~\( \nu \) = 2944 (CH), 2841 (CH), 1713 (C=O), 1693 (C=O), 1346, 1067 (cm–1); HRMS C16H16O4: calcd 272.1049, found 272.1051; elemental analysis (%) calcd for C16H16O4 (272.30): C 70.56, H 5.93; found C 70.38, H 5.82.

1-(3-Bromomethyl-1,4-dimethoxynaphthalen-2-yl)-propane-1,2-dione (32). Methylnaphthalene 31 (230 mg, 0.85 mmol) was brominated with NBS according to the general procedure IV (1 h). The crude product was purified by column chromatography on silica gel (30 g, PE/EE 9:1) to yield the bromide 32 (201 mg, 67 %, m. p. 98 °C) as a yellow solid. \( ^1H \) NMR (200 MHz, CDCl3): \( \delta = 2.55 \) (s, 3 H, 3-H), 3.88 (s, 3 H, OCH3), 4.05 (s, 3 H, OCH3), 4.99 (s, 2 H, CH2Br), 7.56−7.71 (m, 2 H, 6'-H, 7'-H), 8.05 (dd, \( ^3J = 8.1 \) Hz, \( ^4J = 1.7 \) Hz, 5'-H/8'-H), 8.13 (dd, \( ^3J = 8.5 \) Hz, \( ^4J = 1.7 \) Hz, 5'-H/8'-H); \( ^13C \) NMR (50 MHz, CDCl3): \( \delta = 24.08 \) (t, CH2Br), 24.91 (q, C-3), 63.10/64.34 (2 x q, 2 x OCH3), 123.72/124.01 (2 x d, C-5', C-8'), 124.58/126.26/131.35 (3 x s, C-2', C-3', C-4'a/C-8'a), 128.14 (d + s, C-6'/C-7', C-4'a/C-8'a), 129.47 (d, C-6'/C-7'), 152.25/155.30 (2 x s, C-1', C-4'), 195.60/197.94 (2 x s, C-1, C-2); UV (methanol): \( \lambda_{\text{max}} \) (lg \( \varepsilon \)) = 226 nm (4.15), 246 (4.04), 320 (3.86); MS (EI, 70 eV): \( m/z \) (%) = 352/350 (9) [M+], 309/307 (100) [M+−CH3], 271 (17) [M+−Br], 229 (30) [M+−CH3CO−Br], 213 (69) [M+−CH3CO−CH2Br], 43 (18) [CH3CO+]; IR (KBr): \( \tilde{\nu} \) (cm–1)
= 2939 (CH), 2836 (CH), 1713 (C=O), 1682 (C=O), 1351, 1046 (cm⁻¹); HRMS C_{16}H_{15}BrO_{4}: calcd 350.0154 (^{79}\text{Br}); found 350.0155 (^{79}\text{Br}); elemental analysis (%) calcd for C_{16}H_{15}BrO_{4} (351.20): C 54.85, H 4.32; found C 54.96, H 4.40.

5,10-Dimethoxy-3-methyl-3-(2-oxopropyl)-1H-benzo[g]isochromen-4-one (33). The bromide 32 (201 mg, 0.57 mmol) was reacted with the silyl enol ether 8 (163 mg, 1.25 mmol) as described in the general procedure I. The crude product was purified by column chromatography on silica gel (20 g, PE/EE 5:1) to afford the isochromene derivative 33 (46 mg, 25 %) as a faint yellow oil. \(^1\text{H NMR}\) (200 MHz, CDCl\(_3\)): \(\delta = 1.54\) (s, 3 H, 3-CH\(_3\)), 2.18 (s, 3 H, 3'-H), AB-signal (\(\Delta\delta = 0.41, \delta_{A} = 3.44, \delta_{B} = 3.03, J_{AB} = 16.6\) Hz, 2 H, 3'-H), 3.95 (s, 3 H, OCH\(_3\)), 4.10 (s, 3 H, OCH\(_3\)), AB-signal (\(\Delta\delta = 0.12, \delta_{A} = 5.20, \delta_{B} = 5.08, J_{AB} = 15.9\) Hz, 2 H, 1-H), 7.65–7.73 (m, 2 H, 7-H, 8-H), 8.08 (d, \(J = 7.9\) Hz, 1 H, 6-H/9-H), 8.42 (d, \(J = 8.6\) Hz, 1 H, 6-H/9-H); \(^{13}\text{C NMR}\) (50 MHz, CDCl\(_3\)): \(\delta = 20.95\) (q, 3-CH\(_3\)), 31.22 (q, C-1'), 31.22 (q, C-1'), 53.76 (t, C-3'), 58.52 (t, C-3'), 62.16/63.27 (2 x q, 2 x OCH\(_3\)), 80.39 (s, C-3), 122.13/125.37/126.84/129.67 (4 x d, C-6, C-7, C-8, C-9), 127.39/129.56/131.76/136.62 (4 x s, C-4a, C-5a, C-9a, C-10a), 146.42/156.14 (2 x s, C-5, C-10), 197.03 (s, C-4), 205.53 (s, C-2'); UV (methanol): \(\lambda_{\text{max}} (\text{lg} \varepsilon) = 216\) nm (4.32), 240 (4.22), 270 (3.99), 336 (3.62); MS (EI, 70 eV): \(m/z\) (%) = 328 (20) [M\(^{+}\)], 285 (16) [M\(^{+}\)−CH\(_3\)CO], 270 (22) [M\(^{+}\)−CH\(_3\)CO−CH\(_3\)], 213 (100) [M\(^{+}\)−CH\(_3\)−CH\(_3\)COCH\(_2\)−CH\(_2\)O], 43 (36) [CH\(_3\)CO\(^{+}\)]; IR (KBr): \(\tilde{\nu} = 2939\) (CH), 2846 (CH), 1713 (C=O), 1687 (C=O), 1610, 1351, 1056 (cm⁻¹); HRMS C\(_{19}\)H\(_{20}\)O\(_5\): calcd 328.1311; found 328.1295.