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Synthesis and Properties of an ω,ω'-Appended Eighteen Carbon Chains Hypericin Derivative

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Summary. An ω,ω'-appended eighteen carbon chains hypercin derivative (**2**) was synthesized starting from emodin. The overall yield of the seven step synthesis was 12%. The ^1H and ^{13}C NMR, absorption, and emission spectroscopic properties were measured; **2** can be dissolved even in apolar solvents and polyethylene.

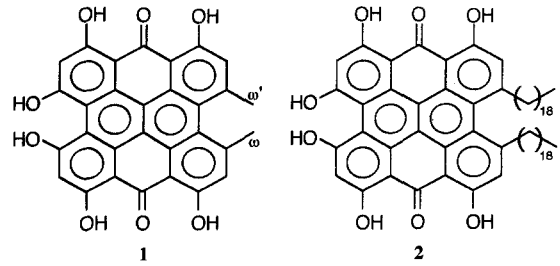
Keywords. Hypericin derivative; Synthesis; NMR spectroscopy; Absorption spectra; Fluoresence.

Synthese und Eigenschaften eines mit C_{18}-Ketten ω,ω'-substituierten Hypericinderivats

Zusammenfassung. Ein in den Positionen ω,ω' mit zwei C_{18}-Ketten substituiertes Derivat des Hypericins (**2**) wurde ausgehend von Emodin synthetisiert. Die Gesamtausbeute der siebenstufigen Synthese betrug 12%. Die ^1H- und ^{13}C-NMR, absorptions- und emissionsspektroskopischen Eigenschaften wurden gemessen; **2** kann sogar in apolaren Lösungsmitteln und Polyethylen gelöst werden.

Introduction

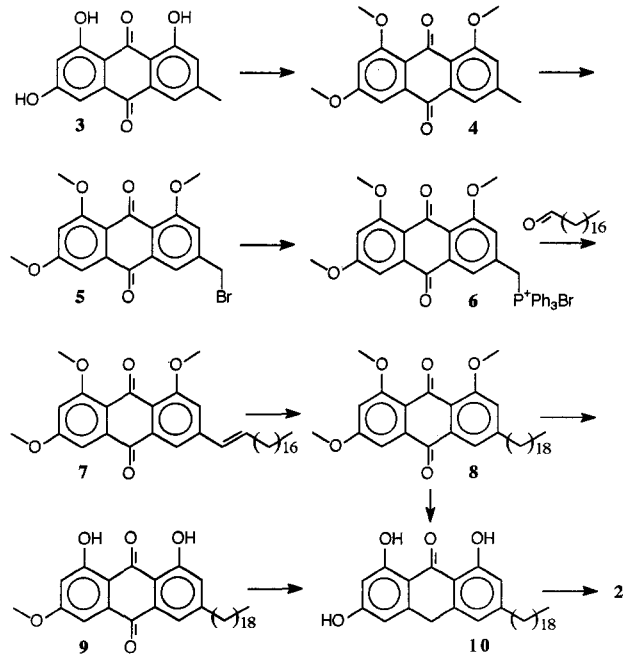
The limited solubility of hypericin (**1**) in common solvents constitutes a main obstacle to studies of its chemistry and its physiological and physical properties. Recently, the synthesis of ω,ω'-appended hypericin derivatives has been reported [1]. The appending residues were either long chain alkyloxy groups or *oligo*-hydroxyethyl and *oligo*-oxaalkanyl chains. Although this derivatization rendered the compounds more soluble in apolar and polar solvents, the alkoxy derivatives refrained from being incorporated into polymers. This polymer solubility is of interest with respect to embedding and orienting the hypericin chromophore for polarized absorption spectroscopy [2]. Therefore, it appeared to be interesting to synthesize a true ω,ω'-homologized hypericin derivative with sufficiently long alkyl chains to achieve its solubility in apolar solvents like polyethylene. The ω,ω'-eighteen carbon homologue of hypericin **2** seemed to be the most appropriate target molecule. Thus, a convenient synthesis of this compound was devised and will be described in this paper together with its properties.



1 2

Results and Discussion

For a synthesis of **2**, a retrosynthetic approach clearly favoured the dimerization of an anthrone type precursor attached to a nineteen carbon atom chain instead of a methyl group. This strategy was mainly enforced by the observation that the methyl groups of **1** refrained from derivatization reactions [1]. It should be mentioned that the ω,ω'-appended derivatives described recently have also been prepared along this path [1].



The *Wittig* strategy [3, 4] was chosen for the chain elongation sequence. For this key step, two substrate-reagent situations were encountered. The first one involves an emodin aldehyde reacting with a long chain phosphonium salt reagent; the other one combines an emodin derived phosphonium salt reagent with a long chain aldehyde. Given the results of orienting experiments, the latter alternative was chosen as the most convenient one.

Since **3** itself and also its tri-O-acetyl derivative [1] were not stable under the envisaged chain elongation reaction conditions, O-methyl groups were thought to

be the most appropriate to protect **3**. The tri-O-methyl protected emodin derivative **4** was easily obtained in 96% yield from **3** by methylation with dimethyl sulfate under basic conditions. Compound **4** was then brominated by means of N-bromosuccinimide to yield 70% of the bromomethyl derivatives **5**. Compounds **4** and **5** have been obtained earlier [5]; however, the yields could be improved and their characterization was expanded. The latter was converted into the emodin derived phosphonium salt **6** with 90% yield. The ylid derived from **6** by solid transfer catalysis [6] using 18-crown-6 as the catalyst was then reacted with octadecanal to produce stereoselectively the alkene **7** in 90% yield. Its (*E*)-configuration could be derived from its ^1H coupling constant of $J_{AB} = 16$ Hz [7]. Catalytic hydrogenation of **7** afforded 82% of **8**. The anthraquinone **8** was partially demethylated upon reaction with HBr which resulted in 97% yield of the anthraquinone derivative **9**. Its complete demethylation and reduction to the anthrone derivative **10** could be achieved in 95% yield by means of HI. However, it turned out that **10** could also be produced in a single step reaction with a yield of 94% under similar conditions starting from **8**. Finally, the dimerization of **10** to afford **2** in 29% yield was achieved using a two step methodology [1, 8], which involved oxidative phenol coupling using Fe(III), followed by photochemical ring closure.

The consititutions of **2** and its synthesis precursors were evident from their spectroscopic properties. The ^1H and ^{13}C NMR spectra of **2** were found to be similar to those of **1** and other appended hypericin derivatives [1]. Moreover, the absorption spectra and emission data in a series of solvents also proved to be comparable to these derivatives [1]. The alkyl appended derivative **2** could be monomolecularly dispersed in Triton X-100 micelles as judged from the absorption and emission spectra [9]. From the low emission quantum yields and the absorption spectroscopic band shapes of **2** dispersed in N-cetyl-N,N,N-trimethylammonium bromide and sodium dodecyl sulfate micellar systems it was deduced that homoassociates of **2** predominated as was also the case for buffer solutions. It turned out that **2** could be dissolved in apolar solvents like *n*-heptane. In this solutions it was present as a homoassociated species according to the absorption spectrum which was found to be similar to those obtained for **1** in protic polar solvents [9]. Moreover, **2** was found to be even soluble in polyethylene in concentrations high enough to allow spectroscopic measurements. The results of this study involving absorption measurements on stretched polyethylene foils colored with **2** will be presented in a forthcoming paper together with the results of a thorough semiempirical quantum mechanical investigation of the fundamental hydroxy-phenanthroperylendione chromophores.

Experimental

Melting points were measured by means of a Kofler hot stage microscope (Reichert, Vienna). ^1H, ^{13}C, IR, UV/Vis, fluorescence, and mass spectra were recorded using Bruker AC 200 and WM 360, Biorad FT-IR 45, Hitachi U-3210, F-4010, and MAT-95 instruments. Rhodamine B served as the standard for quantum yield determinations ($\Phi_f = 0.69$), and "*für Fluoreszenz*" grade (Merck) solvents were used. Octadecanal was prepared according to Ref. [4], and emodin (**3**) was isolated from Buckthorn bark (*Cortex frangulae*) as described earlier [10].

1,3,4,6,8,13-Hexahydroxy-10,11-bis-nonadecyl-phenanthro[1,10,9,8-o,p,q,r,a]perylene-7,14-dione (**2**; $C_{66}H_{88}O_8$)

A mixture of 92 mg anthrone **10** (0.18 mmol), 112 mg pyridine N-oxide (1.3 mmol), 96 µl piperidine, and 12 mg $FeSO_4 \cdot 7H_2O$ dissolved in 1 ml pyridine was stirred in the dark for 2 h at 110 °C, cooled to room temperature, and quenched with a solution of 1.5 ml conc. HCl in 15 ml H_2O. After standing for 1 h, the precipitate was isolated by centrifugation and washed once with water. The precipitate was suspended in 300 ml acetone and irradiated with 500 W photo flood lamp for 3 h. The resulting suspension was filtered and the raspberry colored solution was evaporated. Preparative silica thin layer chromatography of the residue using a mixture of chloroform/methanol = 5/1 as the eluent gave 26 mg (29%) **2**; m.p.: not up to 350 °C. ^{1}H NMR ($CDCl_3$/*DMSO*-d_6 = 5/1, *TMS*, δ, 360 MHz): 18.44 (bs, OH3 + OH4), 14.84 (s, OH1 + OH6), 14.27 (s, OH8 + OH13), 7.35 (s, ar-H9 + ar-H12), 6.73 (s, ar-H2 + Ar-H5), 3.3 (overlap with water signal, 2ar–CH_2), 1.4–0.85 (bm, 2$(CH_2)_{17}CH_3$) ppm; ^{1}H NMR ($CDCl_3/CD_3OD$ = 5/1, *TMS*, δ, 360 MHz): 7.38 (s, ar-H9 + ar-H12), 6.84 (s, ar-H2 and ar-H5), 3.3 (overlap with CD_3OD peaks), 1.4–0.85 (bm, 2$(CH_2)_{17}CH_3$) ppm; ^{1}H NMR (Acetone-d_6, *TMS*, δ, 200 MHz): 18.80 (bs, OH3 + OH4), 14.83 (s, OH1 + OH6), 14.28 (s, OH8 + OH13), 7.41 (s, ar-H9 + ar-H12), 6.63 (s, ar-H2 + ar-H5), 3.47 (m, 2ar–CH_2), 1.4–0.85 (bm, 2$(CH_2)_{17}CH_3$) ppm; ^{13}C NMR ($CDCl_3$/*DMSO*-d_6 = 5/1, *TMS*, δ, 90 MHz): 184.2 (C=O-7, 14), 174.5 (C-3,4), 168.4 (C-1,6), 162.2 (C-8,13), 148.6 (C-10,11), 127.6 (C-3a,3b), 126.1 (C-6b,14b), 122.0 (C-6c,13c), 120.2 (C-10a,10b), 119.6 (C-7b,13b), 117.4 (C-9,12), 108.9 (C-6a,14a), 105.9 (C-2,5), 102.7 (C-7a,13a), 36.3 (2ar–CH_2), 32.6, 31.6, 29.4, 29.2, 29.1, 28.6, 28.4, 22.4 (8 CH_2 signals were observed instead of 2 × 17 CH_2 due to signal overlap), 14.01 (2CH_3) ppm; IR (KBr): 3422 (ν_{OH}), 2953 (ν_{CH3}), 2918, 2850 (s, ν_{CH} of aliphatic chain), 1591 ($\nu_{C=O\cdots HO}$), 1556, 1461, 1421 ($\nu_{C=Car}$), 1248, 1182, 1116, 844, 799, 720 (CH_2) cm^{-1}; UV/Vis (ethanol; 9.10^{-6} mol/l): λ = 592 (42120), 549 (20780), 511 (8580), 474 (12720), 447 (11540), 389 (10820), 329 (28740), 287 (38080) nm (ε); UV/Vis (methanol; 9.10^{-6} mol/l): λ = 590 (29100), 547 (13690), 509 (7270), 474 (10970), 339 (23330), 287 (29960) nm (ε); UV/Vis (acetone; 9.10^{-6} mol/l): λ = 597 (41350), 553 (19011), 514 (6660), 480 (9560), 453 (8310), 386 (9030), 334 (23670) nm (ε); UV/Vis (*DMSO*; 9.10^{-6} mol/l): λ = 601 (41240), 556 (18780), 517 (6390), 482 (9890), 454 (8520), 389 (8330), 334 (23140), 279 (56110) nm (ε); UV/vis (*THF*; 10^{-5} mol/l): λ = 585 (26470), 543 (14090), 508 (5570), 455 (14850), 430 (10490), 330 (22040), 283 (32880) nm (ε); UV/Vis (*THF*; $5.2.10^{-5}$ mol/l): λ = 597 (30280), 553 (15540), 515 (5820), 479 (8540), 452 (7590), 387 (7650), 334 (20670), 288 (26470) nm (ε); UV/Vis ($CHCl_3$; $4.7.10^{-6}$ mol/l): λ = 585 (27120), 543 (14790), 508 (5380), 456 (17230), 432 (11490), 329 (22230), 320 (22020), 283 (34540) nm (ε); UV/Vis (Triton X-100 1% in phosphate buffer, *pH* = 7, 0.01 *M*; 5.10^{-6} mol/l): λ = 597 (44820), 553 (21480), 515 (8700), 478 (13600), 447 (12760), 392 (12400), 331 (31360), 293 (39380) nm (ε); UV/Vis (CTAB 1% in phosphate buffer, *pH* = 7, 0.01 *M*; 5.10^{-6} mol/l): λ = 587 (7740), 545 (12700), 518 (7660), 446 (11860), 463 (11940), 331 (23920) nm (ε); UV/Vis (*n*-heptane; 10^{-5} mol/l): λ = 596 (2340), 553 (2690), 481 (2700) nm (ε); UV/Vis (polyethylene foil saturated with **2**): λ = 600 (0.101), 556 (0.080), 515 (0.062), 469 (0.09), 403 (0.065), 336 (0.152), 294 (0.151) nm (abs.); fluorescence (ethanol, λ_{ex} = 550 nm): λ_{em} = 598 (1), 646 (0.29), 700 (0.05) nm (rel. int.); Φ_f = 0.62; fluorescence (methanol, λ_{ex} = 550 nm): λ_{em} = 598 (1), 645 (0.29) nm (rel. int.); Φ_f = 0.59; fluorescence (acetone, λ_{ex} = 550 nm); λ_{em} = 604 (1), 653 (0.26) nm (rel. int.); Φ_f = 0.61; fluorescence (*DMSO*, λ_{ex} = 550 nm): λ_{em} = 607 (1), 656 (0.25) nm (rel. int.); Φ_f = 0.60; fluorescence (*THF*, λ_{ex} = 550 nm): λ_{em} = 607 (1), 656 (0.24) nm (rel. int.); Φ_f = 0.58; fluorescence ($CHCl_3$, λ_{ex} = 550 nm): λ_{em} = 593 (1), 638 (0.33) nm (rel. int.); Φ_f = 0.80; fluorescence (Triton X-100 1% in phosphate buffer, *pH* = 7, 0.01 *M*; λ_{ex} = 550 nm): λ_{em} = 604 (1), 653 (0.24) nm (rel. int.); Φ_f = 0.59; fluorescence (CTAB 1% in phosphate buffer, *pH* = 7, 0.01 *M*; λ_{ex} = 550 nm): λ_{em} = 602 (1), 650 (0.27) nm (rel. int.); Φ_f = 0.03; fluorescence (SDS 1% in phosphate buffer, *pH* = 7, 0.01 *M*; λ_{ex} = 550 nm): λ_{em} = 599 (1), 648 (0.27) nm (rel. int.); Φ_f = 0.04; fluorescence (phosphate buffer, *pH* = 7, 0.01 *M*; λ_{ex} = 550 nm): λ_{em} = 601 (1), 651 (0.5) nm (rel. int.); Φ_f = 0.003; MS (FAB pos/Noba, scan from 500 to 1300): *m/z* (%) = 1010.52 ($M + H^+$; 97), 1009.52 (M^+, 100), 992.38 (18), 936.92 (9), 870.13 (9), 763.27 (12), 754.28 (17), 742.16 (58), 613.64 (19), 559.94 (22), 545.91 (31), 513.81 (40), 501.83 (75).

1,3,8-Trimethoxy-6-methyl-anthraquinone (**4**; $C_{18}H_{16}O_5$)

To a stirred suspension of 1.05 g emodin (**3**; 3.89 mmol) and 10.6 g anhydrous K_2CO_3 (76.8 mmol) in 90 ml dry acetone, 15.5 g dimethyl sulfate (123 mmol) were added dropwise. The mixture was sitrred at room temperature for 30 min and then heated under reflux for 15 h, cooled to room temperature, and diluted with 100 ml H_2O. After stirring for further 15 min, the mixture was extracted with 300 ml $CHCl_3$, washed with water, dried with Na_2SO_4, and evaporated. Crystallization from ethanol gave 1.1 g (96%) **4**; m.p.: 230–232 °C (Ref. [5]: 225 °C). ^{1}H NMR ($CDCl_3$, δ, 200 MHz): 7.62 (s, ar-H5), 7.30 (d, $J = 2.3$ Hz, ar-H4), 7.07 (s, ar-H7), 6.75 (d, $J = 2.3$ Hz, ar-H2), 3.97 (s, OCH_3), 3.95 (s, OCH_3) 3.93 (s, OCH_3), 2.45 (s, ar–CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 50 MHz): 184.3 (C=O), 181.7 (C=O), 163.9 (C_{ar}), 161.7 (C_{ar}), 159.7 (C_{ar}), 144.6 (C_{ar}), 136.4 (C_{ar}), 134.4 (C_{ar}), 121.5 (C_{ar}), 119.5 (CH_{ar}), 118.9 (CH_{ar}) 118.4 (C_{ar}), 105.2 (CH_{ar}), 101.8 (CH_{ar}), 56.4 ($2OCH_3$), 55.8 (OCH_3), 22.1 (CH_3) ppm; IR (KBr): $\nu = 2944$ (ν_{CH} of CH_3–Ar), 2842 (ν_{CH} of CH_3O–ar), 1660 ($\nu_{C=O}$), 1599, 1564, 1461, 1435 ($\nu_{C=Car}$), 1317, 1242, 1164, 1130, 1021, 947, 871, 756, 620, 556 cm^{-1}; UV (ethanol; 2.10^{-5} mol/l): $\lambda = 401$ (7200), 277 (26400), 222 (41700) nm (ε).

6-Bromomethyl-1,3,8-trimethoxy-anthraquinone (**5**; $C_{18}H_{15}BrO_5$)

A mixture of 822 mg **4** (2.64 mmol), 565 mg N-bromosuccinimide (3.15 mmol), 24 mg benzoyl peroxide, and 80 ml CCl_4 was refluxed for 46 h. After cooling to room temperature, the yellow solid was filtered, washed with CCl_4, hot H_2O, and dried. Crystallization from benzene gave 970 mg (70%) of the bromo methyl compound **12**; m.p.: 234–236 °C (Ref. [5]: 233.5–234 °C). ^{1}H NMR ($CDCl_3$, δ, 200 MHz): 7.83 (d, $J = 1.4$ Hz, ar-H5), 7.32 (m, ar-H4,7), 6.78 (d, $J = 2.2$ Hz, ar-H2), 4.52 (s, ar–CH_2–Br), 4.02 (s, OCH_3), 3.97 (s, OCH_3), 3.96 (s, OCH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 50 MHz): 183.6 (C=O), 181.3 (C=O), 163.9 (Car), 161.7 (C_{ar}) 160.0 (C_{ar}), 143.4 (C_{ar}), 136.2 (C_{ar}), 135.0 (C_{ar}), 123.6 (C_{ar}), 119.1 (CH_{ar}), 118.4 (CH_{ar}), 118.2 (C_{ar}), 105.3 (CH_{ar}), 56.6 (OCH_3), 56.4 (OCH_3), 55.9 (OCH_3), 31.8 (CH_2–Br) ppm; UV (ethanol; 2.10^{-5} mol/l): $\lambda = 401$ (9400), 278 (29700), 224 (43600) nm (ε).

1,6,8-Trimethoxy-anthraquinon-3-yl-methyl-triphenylphosphonium bromide (**6**; $C_{36}H_{30}BrO_5P$)

A solution of 470 mg **5** (1.2 mmol) and 413 mg triphenylphosphine (1.58 mmol) in 40 ml anhydrous benzene was refluxed for 32 h. The yellow triphenylphosphonium salt was filtered off and washed with benzene and dry ether. Column chromatography of the crude product on silica using first a mixture of $CHCl_3$/methanol = 20/1 as eluent and then $CHCl_3$/methanol = 2/1 gave 705 mg (90%) of **6**; m.p.: 220 °C (decomp). ^{1}H NMR ($CDCl_3$, δ, 200 MHz): 8.02 (m, ar-H4), 7.89–7.61 (m, P^+Ph_3), 7.18 (d, $J = 2.2$ Hz, ar-H5), 7.06 (m, ar-H2), 6.73 (d, $J = 2.2$ Hz, ar-H7), 5.67 (d, $J = 15$ Hz, CH_2–P^+Ph_3), 3.93 (s, OCH_3), 3.91 (s, OCH_3), 3.83 (s, OCH_3) ppm; IR (KBr): $\nu = 3055$, 3008 (ν_{CHar}), 2845 (ν_{CH} of CH_3O–ar), 2789 (ν_{CH} of ar–CH_2–P^+Ph_3), 1666 ($\nu_{C=O}$), 1596, 1567, 1460, 1437 (ν_{CCar}), 1329, 1247, 1198, 1155, 1111, 1015, 961, 890, 753, 691, 516 cm^{-1}; UV (ethanol; 2.10^{-5} mol/l): $\lambda = 397$ (5900), 276 (19800), 221 (47200) nm (ε).

(E)-6-Nonadec-1-enyl-1,3,8-trimethoxy-anthraquinone (**7**; $C_{36}H_{50}O_5$)

A mixture of 138 mg **6** (0.21 mmol), 60 mg K_2CO_3 (0.42 mmol), and 40 mg 18-Crown-6 in 4 ml dry CH_2Cl_2 was refluxed for 15 min. To this refluxing dark blue ylide solution, 567 mg octadecanal (2.1 mmol) dissolved in 4 ml CH_2Cl_2 were added in 3 portions spaced by 40 min time intervals. During this time, the color changed from blue back to yellow. After refluxing for an additional 30 min, the reaction mixture was cooled to room temperature, diluted with benzene, and filtered to remove K_2CO_3. The filtrate was washed with saturated NaCl solution, dried with Na_2SO_4, and evaporated. Column chromatography in silica using first a mixture of petrol ether/ethyl acetate = 7/3 as eluent to recover the excess amount of unreacted octadecanal and then a mixture of chloroform/ethyl acetate = 1/1 gave 108 mg (90%) **7**; m.p.: 128–130 °C. ^{1}H NMR ($CDCl_3$, δ, 360 MHz): 7.82 (d, $J = 1.2$ Hz, ar-H5), 7.33

(d, $J = 2.2$ Hz, ar-H4), 7.18 (d, $J = 1.2$ Hz, ar-H7), 6.76 (d, $J = 2.2$ Hz, ar-H2), 6.46 (m, ar–CH=CH–CH_2, AB part of ABX_2, collapsed to an AB system upon irradiation at $\delta = 2.25$, $J_{AB} = 16$ Hz, $\Delta\nu = 14$ Hz, 1′-H 6.49 and 2′-H 6.42 ppm), 4.0 (s, OCH_3), 3.96 (s, OCH_3), 3.95 (s, OCH_3), 2.25 (m, CH=CH–CH_2), 1.5 (m, CH=CHCH$_2$CH$_2$), 1.25 (bs, $(CH_2)_{14}$), 0.87 (t, $J = 6.3$ Hz, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 90 MHz): 184.3 (C=O), 181.5 (C=O), 163.6 (C_{ar}), 161.7 (C_{ar}), 160.0 (C_{ar}), 143.3 (C_{ar}), 136.4 (C_{ar}), 135.9 (ar–CH=CH), 134.7 (C_{ar}), 128.5 (Ar–CH=CH), 122.0 (C_{ar}), 118.5 (C_{ar}), 116.4 (CH_{ar}), 115.3 (CH_{ar}), 105.3 (CH_{ar}), 101.9 (CH_{ar}), 56.4 (2OCH_3 overlap), 55.8 (OCH_3), 33.1 (9CH=CH–CH_2), 31.9, 29.66, 29.48, 29.32, 29.25, 28.99, 22.9 (7 CH_2 signals were observed instead of 15 CH_2 due to signal overlap), 14.1 (CH_3) ppm; IR (KBr); 2920, 2850 (strong, ν_{CH} of alifatic chain), 1662 ($\nu_{C=O}$), 1598, 1565, 1453, 1423 ($\nu_{C=C}$), 1323, 1250, 1162, 1134, 1023, 968, 947, 878, 754, 723 (CH_2), 628, 574 cm^{-1}; UV (ethanol; 2.10^{-6} mol/l): $\lambda = 403$ (8200), 280 (30700), 224 (41900) nm (ε).

6-Nonadecyl-1,3,8-trimethoxy-anthraquinone (**8**; $C_{36}H_{52}O_5$)

A suspension of 115 mg **7** (0.2 mmol) and 50 mg 10% Pd/C in 40 ml ethyl acetate was hydrogenated at room temperature and atmospheric pressure for 6 h. The catalyst was filtered off and washed with 30 ml ethyl acetate. The combined organic solutions were evaporated, and the residue was chromatographed on a dry silica column using a mixture of chloroform/ethyl acetate = 9/1 as eluent gave 94 mg (82%) of **8**; m.p.: 119–120 °C. ^{1}H NMR ($CDCl_3$, δ, 200 MHz): 7.65 (d, $J = 1.4$ Hz, ar-H5), 7.32 (d, $J = 2.4$ Hz, ar-H-4), 7.08 (d, $J = 1.4$ Hz, ar-H7), 6.76 (d, $J = 2.4$ Hz, ar-H2), 3.98 (s, OCH_3), 3.95 (s, OCH_3), 3.94 (s, OCH_3), 2,7 (t, $J = 7.6$ Hz, ar–CH_2), 1.66 (m, ar–CH_2–CH_2), 1.24 (bm, $(CH_2)_{16}$), 0.87 (t, $J = 6.6$ Hz, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 90 MHz): 184.4 (C=O), 181.8 (C=O), 163.7 (C_{ar}), 161.8 (C_{ar}), 159.8 (C_{ar}), 149.6 (C_{ar}) 136.5 (C_{ar}), 134.5 (C_{ar}), 121.7 (C_{ar}), 118.90 (CH_{ar}), 118.43 (C_{ar}), 118.41 (CH_{ar}), 105.2 (CH_{ar}), 101.9 (CH_{ar}), 56.49 (OCH_3), 56.45 (OCH_3), 55.8 (OCH_3), 36.4 (ar–CH_2), 31.9, 30.9, 29.7, 29.67, 29.57, 29.46, 29.37, 29.29, 22.7 (9 CH_2 signals were observed instead of 17 CH_2 due to signal overlap), 14.1 (CH_3) ppm; IR (KBr): $\nu = 2918$, 2848 (s, ν_{CH} of aliphatic chain), 1665 ($\nu_{C=O}$), 1598, 1567, 1464, 1431, ($\nu_{C=Car}$), 1355, 1321, 1249, 1203, 1168, 1126, 1016, 948, 870, 754, 722 (CH_2) cm^{-1}; UV ($CHCl_3$; 2.10^{-6} mol/l): $\lambda = 404$ (5800), 275 (14100) nm (ε).

6-Nonadecyl-1,8-dihydroxy-3-methoxy-anthraquinone (**9**; $C_{34}H_{48}O_5$)

A suspension of 94 mg **8** (0.167 mmol) in 18 ml glacial acetic acid was heated until it became homogeneous. To this solution, 6 ml of HBr (48% aq, 54 mmol) was added in one portion. The mixture was heated to reflux (130 °C) for 2 h, cooled to room temperature, shaken with 50 ml H_2O, and then extracted with three 50 ml portions of $CHCl_3$. The organic phase was washed with saturated NaCl solution, dried with Na_2SO_4, and evaporated. Column chromatography on silica with $CHCl_3$/ethyl acetate (9/1) gave 86 mg (97%) **9**; m.p.: 124–125 °C. ^{1}H NMR ($CDCl_3$, δ, 200 MHz): 12.33 (s, OH1 or OH8), 12.13 (s, OH8 or OH1), 7.64 (d, $J = 1.1$ Hz, ar-H5), 7.38 (d, $J = 2.7$ Hz, ar-H4), 7.08 (d, $J = 1.1$ Hz, ar-H7), 6.69 (d, $J = 2.7$ Hz, ar-H2), 3.94 (s, OCH_3-6), 2.68 (t, $J = 7.6$ Hz, ar–CH_2), 1.66 (m, ar–CH_2–CH_2), 1.25 (bs, $(CH_2)_{16}$), 0.87 (t, $J = 6.4$ Hz, CH_3) ppm; ^{13}C NMR ($CDCl_3$, δ, 50 MHz): 190.8 (C=O), 182.1 (C=O), 166.50 (C_{ar}), 165.2 (C_{ar}), 165.2 (C_{ar}), 153.4 (C_{ar}), 135.3 (C_{ar}), 133.3 (C_{ar}), 123.9 (CH_{ar}), 120.7 (CH_{ar}), 113.8 (C_{ar}), 110.2 (C_{ar}), 108.2 (CH_{ar}), 106.7 (CH_{ar}), 56.1 (OCH_3), 36.3 (ar–CH_2), 31.9, 30.5, 29.69, 29.5, 29.36, 29.18, 22.7 (7 CH_2-signals were observed instead of 17 CH_2 due to signal overlap), 14.1 (CH_3) ppm; UV ($CHCl_3$; 2.10^{-5} mol/l): $\lambda = 439$ (10600), 287 (16900), 267 (18100) nm (ε).

6-Nonadecyl-1,3,8-trihydroxy-10H-anthracene-9-one (**10**; $C_{33}H_{48}O_4$)

Method 1. A suspension of 100 mg **9** (0.186 mmol) in 10 ml glacial acetic acid was heated until it became homogeneous. To this solution, 4 ml of HI (57% aq, 30 mmol) was added. The mixture was heated to reflux (130 °C) for 1.75 h, cooled to room temperature, and poured into 100 ml of an ice and H_2O mixture. The precipitate formed was centrifugated, washed with H_2O, and dried under vacuum at 60 °C

to yield 90 mg (95%) **10**; m.p.: 139–140 °C. ^{1}H NMR ($CDCl_3$/*DMSO*-d_6 = 5/1; *TMS*, δ, 200 MHz): 12.5 (s, OH1), 12.35 (s, OH8), 10.2 (bs, OH3), 6.69 (s, ar-H), 6.64 (s, ar-H), 6.39 (s, ar-H), 6.28 (d, J = 1.9 Hz, ar-H), 4.22 (s, CH_2-10), 2.5 (overlap with *DMSO* peaks, ar–CH_2), 1.64 (m, ar–CH_2–$\mathbf{CH_2}$), 1.26 (bs $(CH_2)_{16}$), 0.87 (t, J = 6.5 Hz, CH_3) ppm; ^{1}H NMR ($CDCl_3$/CH_3OD = 5/1; *TMS*, δ, 200 MHz): 6.71 (s, ar-H), 6.69 (s, ar-H), 6.39 (s, ar-H), 6.29 (d, J = 2.1 Hz, ar-H), 4.24 (s, CH_2-10), 2.60 (t, J = 7.5 Hz, ar–CH_2–R), 1.64 (m, ar–CH_2–$\mathbf{CH_2}$), 1.26 (bs, $(CH_2)_{16}$), 0.88 (t, J = 6.5 Hz, CH_3) ppm; ^{13}C NMR ($CDCl_3$/*DMSO*-d_6 = 5/1; *TMS*, δ, 50 MHz): 190.9 (C=O), 164.6 (Car), 164.3 (Car), 161.8 (Car), 151.2 (Car), 143.5 (Car), 140.6 (C_{ar}), 118.4 (CH_{ar}), 114.3 (CH_{ar}), 112.9 (C_{ar}), 108.4 (C_{ar}), 106.7 (CH_{ar}), 101.0 (CH_{ar}), 35.6 (ar–CH_2–R), 32.2 (CH_2-10), 31.2, 30.0, 28.94, 28.80, 28.72, 28.60, 28.54, 22.0 (8 CH_2 signals were observed instead of 17 CH_2 due to signal overlap), 13.49 (CH_3) ppm; HC-COSY ($CDCl_3$/*DMSO*-d_6 = 5/1; TMS, δ, 200 MHz): CH_2-10 at 4.22 correlated with CH_2-10 at 32.24 ppm; IR (KBr): 3469 (ν_{OH}), 2954 (ν_{CH} of CH_2-10), 2918, 2850 (strong, ν_{CH} of aliphatic chain), 1634 ($\nu_{C=O}$), 1595, 1502, 1473 ($\nu_{C=Car}$), 1384, 1289, 1256, 1164, 1059, 803, 744, 722 (CH_2) cm^{-1}; UV (ethanol; 2.10^{-5} mol/l): λ = 358 (14400), 305 (7200), 271 (10800), 260 (10200), 220 (25200) nm (ε).

Method 2. The procedure and the molar ratios of the educts were the same as those given under method 1. However, **8** was used instead of **9**, and the reaction time was extended to 2.5 h. This resulted in a yield of 9.4% of **10**.

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