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SYNTHESIS OF NOVEL 1-HYDROXYQUINOLONES WITH HIGH ANTI-TOXOPLASMA ACTIVITY

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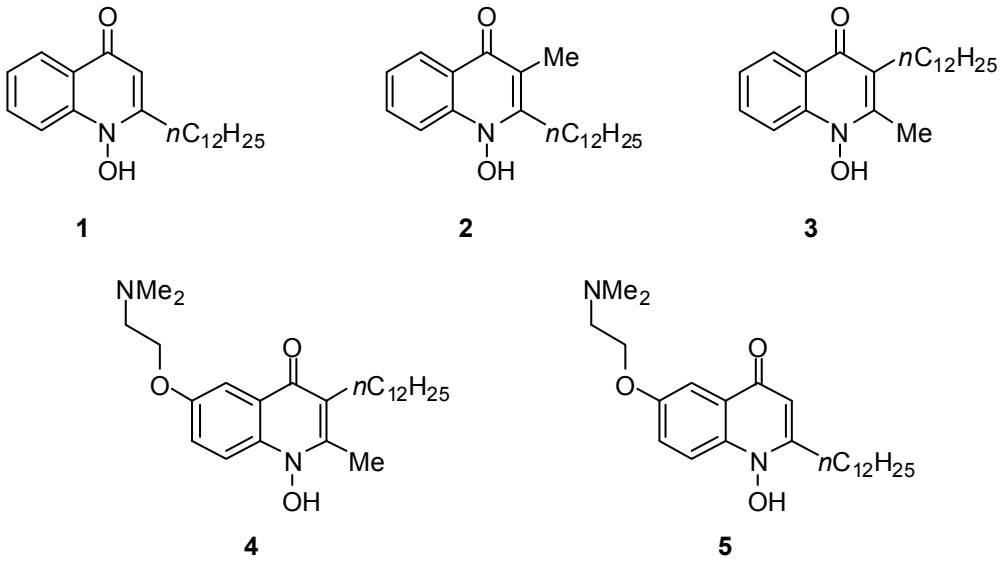
Abstract – All for the treatment of malaria and toxoplasmosis the novel hydroxyquinolones **2**–**5** were prepared by reaction of aniline and hydroxyaniline, respectively and the β-ketoesters **10a-c**. As products the quinolones **8** and **15**, respectively were obtained. Benzylation, oxidation and hydrogenation then led to the desired substances. Compound **2** has a similar anti-malaria activity as the approved drug Atovaquone.

INTRODUCTION

The 1-hydroxyquinolone HDQ (**1**) containing a dodecyl side chain at C-2 shows a strong inhibitory activity against parasite replication of *Toxoplasma gondi* and *Plasmodium falciparum* in tissue culture.[1] These widespred humanes pathogens cause toxoplasmosis and malaria, respectively. The mode of action of **1** seems to be an inhibition of ubiquinol binding enzymes. Recently, it has been shown that HDQ (**1**) is a high affinity inhibitor for the *T. gondi* alternative NADH dehydrogenase (TgNDH2-I).[2] In this species **1** causes a rapid loss of the mitochondrial membrane potential followed by the decrease of ATP concentration, whereas in *P. falciparum* the *de novo* synthesis of pyrimidin is affected. Here we describe the synthesis of the 1-hydroxyquinolones **2-5** (Scheme 1), of which the new compound **2** is up to ten times more active than HDQ in cell culture[3] and almost match the activity of the approved antimalaria drug Atovaquone.[4] Moreover, compound **2** as well as compound **3** caused a significant reduction of inflammatory foci in mice.

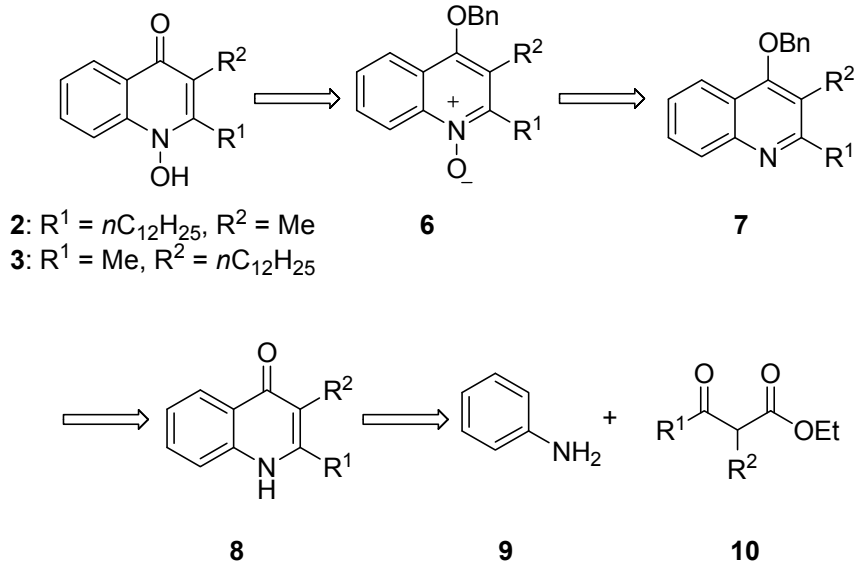
This paper is dedicated to Prof. Dr. Albert Eschenmoser on the occasion of his 85th birthday.



Scheme 1. Structures of HDQ (**1**) and 1-hydroxyquinolone **2**-**5**.

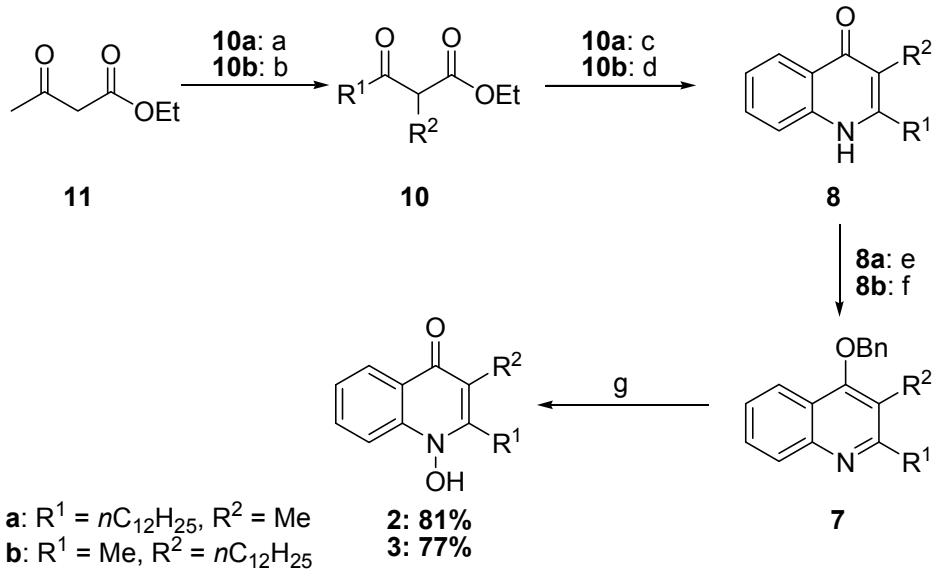
The hydroxyquinolone **2** contains an extra methyl group at C-3 in comparison to HDQ, whereas in **3** the two alkyl groups at C-2 and C-3 are exchanged.[5] Compounds **4** and **5** have an additional dimethylaminoethoxy group, which was introduced to improve their water solubility. However, these substances show a much lower activity against *P. gondi* compared with **2** and **3**. This could be traced back to a reduced penetration of these compounds through the cell wall of the parasites.

RESULTS AND DISCUSSION



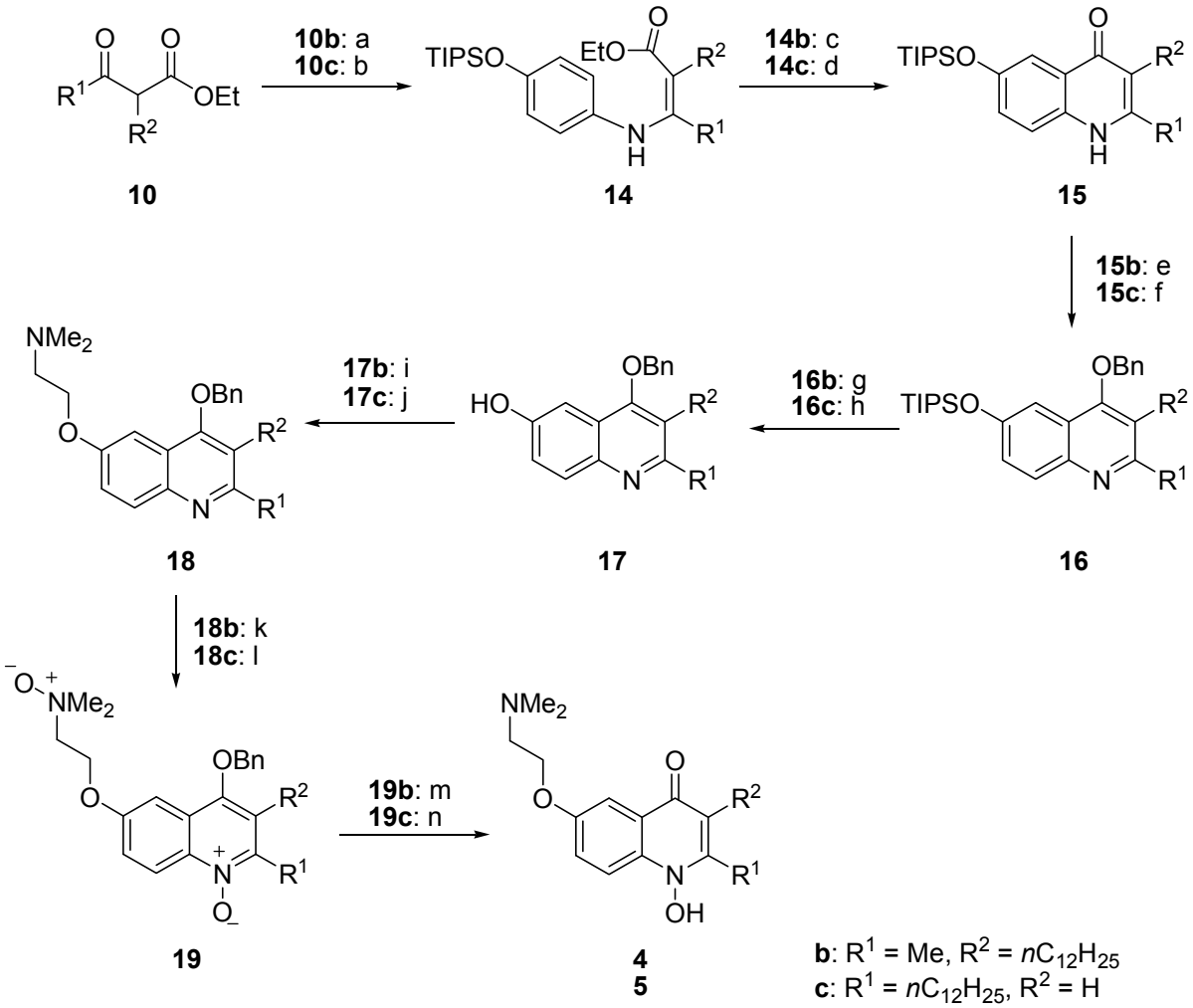
Scheme 2. Retrosynthetic analysis of 1-hydroxyquinolones **2** and **3**.

Several syntheses of hydroxyquinolones are known[6] and the most common follows the retrosynthetic analysis shown in Scheme 2, where the hydroxyl group is introduced as one of the last steps by oxidation of the nitrogen atom in the quinoline **7**. Thus, compounds **2** and **3** lead via **6** to the quinoline **7**, which is accessible via **8** by a Conrad-Limpach cyclization[7] using aniline (**9**) and substituted acetoacetates (**10**). According to this scheme, **2** and **3** could be obtained from aniline and ethyl acetoacetate (**11**) in four steps (Scheme 3). For the synthesis of **2** and **3**, ethyl acetoacetate was transformed into the esters **10a** and **10b**, respectively using known procedures.[8] The following Conrad-Limpach cyclizations were carried out in a two-step fashion[7,9]: treatment of aniline and **10a** as well as **10b** under the given conditions (Scheme 3) led to the corresponding enamines, which on reflux in diphenyl ether at 260 °C gave the quinolones **8a** and **8b**, respectively in moderate yield. It followed the formation of the corresponding enolates with LDA in DMSO,[10] which were benzylated using benzyl bromide to give the protected quinolines **7a** and **7b** in 80% and 78% yield, respectively. Interestingly, employing LDA in THF as solvent followed by an alkylation with benzyl bromide or TIPSCl or TIPSOTf[11] failed completely. For the following oxidation we used *m*CPBA in dichloromethane and the removal of the benzyl protecting group by hydrogenolysis to give the desired 1-hydroxyquinolones **2** and **3**, respectively was achieved under mild conditions with Pd/C under a hydrogen atmosphere in ethanol at ambient pressure.



Scheme 3. Synthesis of 1-hydroxyquinolone **2** and **3**; (a) 1) LDA, THF, –78 °C, 1 h, 1-bromoundecane, rt, 1.5h; 2) NaH, THF, 0 °C, 15 min, MeI, rt, 16 h, 42% from **11**; (b) NaOEt, 1-bromododecane, EtOH, 80 °C, 6 h, 65%; (c) 1) aniline, *p*-TsOH, benzene, Dean-Stark apparatus, 80 °C, 42 h; 2) Ph_2O, 260 °C, 1 h, 25% from **10a**; (d) 1) aniline, AcOH, MS 3 Å, EtOH, 70 °C, 44 h; 2) Ph_2O, 260 °C, 1 h, 38% from **10b**; (e) LDA, DMSO, rt, 1 h, BnBr, rt, 40 min, 80%; (f) LDA, DMSO, rt, 1 h, BnBr, rt, 25 min, 78%; (g) 1) *m*CPBA, CH_2Cl_2, rt, 1 h; 2) Pd/C, H_2, EtOH, rt, 30 min.

One of the problems in the application of the hydroxyquinolones for treatment is their low water solubility; we therefore prepared analogues containing a *N*,*N*-dimethylaminoethoxy group at C-6. The synthesis of the desired hydroxyquinolones **4** and **5** was carried out in a smilar way as described for **2** and **3** in 8 steps with an all over yield of 31% for **4** and 25% for **5** (scheme 4).



Scheme 4. Synthesis of 1-hydroxyquinolone **4** and **5**; (a) **13**, AcOH, MS 3 Å, EtOH, 75 °C, 42 h, 68%; (b) **13**, AcOH, MS 3 Å, EtOH, 75 °C, 44 h, 89%; (c) Ph_2O, 260 °C, 1 h, 82%; (d) Ph_2O, 260 °C, 1 h, 79%; (e) LDA, DMSO, rt, 1 h, BnBr, rt, 2 h, 88%; (f) LDA, DMSO, rt, 1.25 h, BnBr, rt, 45 min, 71%; (g) TBAF, THF, 0 °C, 1 h, rt, 2 h, 98%; (h) TBAF, THF, 0 °C, 1 h, rt, 3.5 h, 90%; (i) NaH, DMF, rt, 1 h, $Me_2NCH_2CH_2Cl{\cdot}HCl$, 100 °C, 2 h, 95%; (j) NaH, DMF, rt, 1 h, $Me_2NCH_2CH_2Cl{\cdot}HCl$, 100 °C, 2 h, 98%; (k) *m*CPBA, CH_2Cl_2, rt, 1.5 h, 80%; (l) *m*CPBA, CH_2Cl_2, rt, 1.5 h, 84%; (m) Pd/C, H_2, EtOH, rt, 1.5 h, 89%; (n) Pd/C, H_2, EtOH, rt, 1.3 h, 73%.

As starting material 4-hydroxyaniline (**12**) was used instead of aniline (**9**). The free hydroxyl group was protected as TIPS-ether to give 4-triisopropylsilyloxyaniline (**13**).[12] For the Conrad-Limpach cyclization,

13 was treated with **10b** and **10c**, respectively in the presence of acetic acid to give the corresponding enamines **14b** and **14c** which were then cyclized as described for **2** and **3** at 260 °C to give the quinolones **15b** and **15c** in reasonable yields of 82% and 79% yield, respectively. Benzylation using LDA and benzyl bromide in DMSO led to the benzyl protected compounds **16b** and **16c** in 88% and 71% yields respectively. After removal of the TIPS group with TBAF, the free hydroxyl group in the quinolines **17b** and **17c** was deprotonated with sodium hydride and treated with 2-dimethylaminoethyl chloride hydrochloride in DMF to introduce the *N*,*N*-dimethylaminoethoxy group at C-6 position.[13] In the following oxidation of the obtained compounds **18b** and **18c** using *m*CPBA in dichloromethane both nitrogen atoms in the substrates were oxidized to afford the *N*,*N'*-dioxides **19b** and **19c**. As the last step hydrogenation using Pd/C as catalyst in ethanol led to a reduction of the *N*-oxide of the dimethylaminoethoxy group at the C-6 position and concurrently to a hydrogenolysis of the benzyl group to give the desired 1-hydroxyquinolones **4** and **5**. Under the employed conditions, a reduction of second *N*-oxide in the molecule was not observed. For the biological tests of the inhibition activity against parasite replication compounds **2**-**5** were twice recrystallized from ethanol/acetone for a high purity.

CONCLUSION

Hydroxyquinolone **1** is known as a potent inhibitor of toxoplasmosis and malaria. We have prepared novel hydroxyquinolones containing different side chains at different positions, which have an up to ten times increased biological activity with compound **2** nearly matching the potency of the known antimalaria drug Atovaquone (IC_{50} values: HDQ = 4.2 ± 1.5 nM, **2** = 0.4 ± 0.1 nM, **3** = 0.8 ± 0.1 nM). In contrast, compounds **4** and **5** containing a tertiary amino functionality to improve their water solubility by formation of a salt show a reduced activity probably due to a decreased penetration through the cell wall of the parasites.

EXPERIMENTAL

General: All reactions were performed in flame-dried glassware under an atmosphere of argon and the reactants were introduced by syringe. Solvents were dried and purified purified according to the method defined by Perrin and Armarego.[14] Commercial reagents were used without further purification. Thin-layer chromatography (TLC) was carried out on precoated Alugram SIL G/UV_{254} (0.25 mm) plates from Macherey–Nagel & Co. Column chromatography was carried out on silica gel 60 from Merck with particle size 0.063–0.200 mm for normal pressure and 0.040–0.063 mm for flash chromatography. Melting points were recorded on a Mettler FP61 and are uncorrected. IR spectra were determined on a Bruker Vektor 22 (KBr pellets or films), UV/Vis spectra on a Perkin–Elmer Lambda 2 (MeCN), and mass spectra on a Finnigan MAT 95 (for EI-MS, EI-HRMS, DCI) and a Bruker Daltronik Apex IV (for

ESI-HRMS). ^{1}H-NMR spectra were recorded either on a Varian Mercury 300, Unity 300 or Inova 600 spectrometer. ^{13}C-NMR spectra were recorded at 75, 125 or 150 MHz. Spectra were taken at room temperature in deuterated solvents as indicated using the solvent peak or TMS as internal standard.

Synthesis of 2-dodecyl-1-hydroxy-3-methyl-4-quinolone (2)

Ethyl 3-oxopentadecanoate (10c): To a solution of LDA, prepared from *i*-Pr_2NH (24.7 mL, 0.175 mol) and *n*-BuLi (72.8 mL, 0.182 mol; 2.5 M in hexanes), in dry THF (150 mL) at –78 °C was added ethyl acetoacetate (9.11 g, 70.0 mmol) and the suspension was stirred at –78 °C for 1 h. Afterwards 1-bromoundecane (1.20 mL, 70.0 mmol) was added at 0 °C and the solution was stirred at room temperature for 1.5 h. The solution was neutralized with 2 M hydrochloric acid and extracted with Et_2O (3 × 120 mL). The combined organic extracts were washed with brine (2 × 270 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 20:1) provided **10c** (9.80 g, 49%) as a yellowish solid. $\boldsymbol{R}_\mathbf{f}$ = 0.37 (pentane/EtOAc, 20:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3 H, 15-H_3), 1.22–1.38 (m, 21 H, 6-H_2 to 14-H_2, OCH_2CH_3), 1.52–1.64 (m, 2 H, 5-H_2), 2.54 (t, J = 7.2 Hz, 2 H, 4-H_2), 3.42 (s, 2 H, 2-H_2), 4.19 (q, J = 7.2 Hz, 2 H, OCH_2CH_3) ppm. **^{13}C-NMR** (125 MHz, $CDCl_3$): δ = 14.08 (C-15, OCH_2CH_3), 22.66 (C-14), 23.46 (C-5), 29.01, 29.32, 29.33, 29.42, 29.56, 29.60, 29.62 (C-6 to C-12), 31.89 (C-13), 43.03 (C-4), 49.30 (C-2), 61.30 (OCH_2CH_3), 167.2 (C-1), 202.9 (C-3) ppm. **IR** (KBr): $\tilde{\nu}$ = 2917, 2850, 1742, 1710, 1468, 1411, 1367, 1329, 1272, 1166, 1095, 1033, 717, 651 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 221.5 (2.661), 246.0 nm (2.714). **MS** (70 eV, EI): *m*/*z* (%) = 284.4 (7) $[M]^+$, 197.3 (7) $[M–CH_2COOEt+H]^+$, 130.1 (100) $[M–n\text{-}C_{11}H_{23}+H]^+$. HRMS (ESI): calcd. for $C_{17}H_{32}O_3 + H^+$ 285.2424; found 285.2424.

Ethyl 2-methyl-3-oxopentadecanoate (10a): Sodium hydride (1.56 g, 38.8 mmol, 60% in mineral oil) was added slowly to a solution of **10c** (10.0 g, 35.3 mmol) in THF (35 mL) at 0 °C. After stirring for 15 min at 0 °C iodomethane (6.01 g, 42.3 mmol) was added and the solution was stirred at room temperature for 16 h. The reaction was quenched by addition of H_2O (10 mL), the layers were separated and the aqueous layer was extracted with EtOAc (4 × 30 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 20:1) provided **10a** (8.95 g, 85%) as a yellow oil. $\boldsymbol{R}_\mathbf{f}$ = 0.41 (pentane/EtOAc, 20:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3 H, 15-H_3), 1.18–1.38 (m, 24 H, 6-H_2 to 14-H_2, OCH_2CH_3, 2-CH_3), 1.52–1.63 (m, 2 H, 5-H_2), 2.40–2.62 (dt, J = 12.0, 7.2 Hz, 2 H, 4-H_2), 3.50 (q, J = 7.2 Hz, 1 H, 2-H), 4.19 (q, J = 7.2 Hz, 2 H, OCH_2CH_3) ppm. **^{13}C-NMR** (125 MHz, $CDCl_3$): δ = 12.74 (2-CH_3), 14.05, 14.07 (C-15, OCH_2CH_3), 22.65 (C-14), 23.53 (C-5), 29.06,

29.30, 29.35, 29.43, 29.56, 29.59, 29.61 (C-6 to C-12), 31.88 (C-13), 41.33 (C-4), 52.85 (C-2), 61.22 (O*C*H_2CH$_3$), 170.6 (C-1), 205.9 (C-3) ppm. **IR** (film): $\tilde{\nu}$ = 2925, 2854, 1745, 1717, 1464, 1376, 1324, 1242, 1192, 1118, 860 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 258.0 nm (2.754). **MS** (ESI): *m*/*z* (%) = 299.2 (78) $[M+H]^+$, 321.2 (100) $[M+Na]^+$, 619.5 (80) $[2M+Na]^+$. HRMS (ESI): calcd. for $C_{18}H_{34}O_3 + H^+$ 299.2580; found 299.2582.

2-Dodecyl-3-methyl-4-quinolone (8a): Ester **10a** (8.10 g, 27.1 mmol) and *p*-toluenesulfonic acid (0.6 g) were added to a solution of aniline (4.04 g, 43.4 mmol) in benzene (450 mL) using a Dean-Stark apparatus. After stirring for 42 h at 80 °C the precipitate was separated by filtration through celite, which was rinsed with EtOH (300 mL), the filtrate was then concentrated under reduced pressure. The brown liquid residue was added dropwise to refluxing diphenyl ether (70 g) and the formed EtOH was removed by distillation. After stirring for 1 h at 260 °C and cooling to room temperature, diphenyl ether was evaporated under reduced pressure (20 mbar, 80 °C), *n*-pentane (80 mL) was added and the formed solid separated by filtration and recrystallized from EtOH/acetone to give **8a** (2.18 g, 25%) as a yellow solid. $\boldsymbol{R_f}$ = 0.29 (CH_2Cl_2/MeOH, 95:5); **m.p.** 173 °C. **^{1}H-NMR** (600 MHz, DMSO-d_6, 35 °C): δ = 0.88 (t, J = 7.2 Hz, 3 H, 12′-H_3), 1.20–1.40 (m, 18 H, 3′-H_2 to 11′-H_2), 1.63 (m, 2 H, 2′-H_2), 1.98 (s, 3 H, 3-CH_3), 2.66 (t, J = 7.8 Hz, 2 H, 1′-H_2), 7.22 (t, J = 8.4 Hz, 1 H, 6-H), 7.48 (d, J = 8.4 Hz, 1 H, 8-H), 7.57 (t, J = 8.4 Hz, 1 H, 7-H), 8.04 (d, J = 8.4 Hz, 1 H, 5-H), 11.26 (s_{br}, 1 H, NH) ppm. **IR** (KBr): $\tilde{\nu}$ = 3060, 2919, 2850, 1638, 1607, 1592, 1555, 1501, 1394, 1358, 1258, 1190, 999, 861, 754, 693, 604, 572, 539, 434 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 213.0 (4.400), 239.5 (4.490), 322.0 (4.056), 334.5 nm (4.066). **MS** (ESI): *m*/*z* (%) = 328.2 (100) $[M+H]^+$, 655.5 (7) $[2M+H]^+$. HRMS (ESI): calcd. for $C_{22}H_{33}NO + H^+$ 328.2634; found 328.2636.

4-Benzyloxy-2-dodecyl-3-methylquinoline (7a): To a solution of LDA, prepared from *i*-Pr_2NH (0.65 mL, 4.6 mmol) and *n*-BuLi (2.0 mL, 5.0 mmol; 2.5 M in hexanes), in dry THF (7 mL) at room temperature was added a suspension of **8a** (1.5 g, 4.6 mmol) in DMSO (160 mL) and the solution was stirred at room temperature for 1 h. Afterwards benzyl bromide (1.1 mL, 9.2 mmol) was added and the solution was stirred at room temperature for 40 min. The reaction was quenched by addition of brine (450 mL) and the mixture extracted with EtOAc (3 × 340 mL). The combined organic extracts were washed with brine (3 × 400 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 10:1) provided **7a** (1.50 g, 80%) as a yellow solid. $\boldsymbol{R_f}$ = 0.41 (pentane/EtOAc, 8:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 7.2 Hz, 3 H, 12′-H_3), 1.20–1.52 (m, 18 H, 3′-H_2 to 11′-H_2), 1.75 (m, 2 H, 2′-H_2), 2.37 (s, 3 H, 3-CH_3), 2.96 (t, 2 H, J = 7.8 Hz, 1′-H_2), 5.03 (s, 2 H, -CH_2Ph), 7.35–7.54 (m, 6 H, 6-H, 5 × Ph-H), 7.98 (dd, J = 2 × 8.4 Hz,

1 H, 7-H), 7.98 (m, 2 H, 5-H, 8-H) ppm. **^{13}C-NMR** (125 MHz, $CDCl_3$): δ = 11.93 (3-*C*H_3), 14.09 (C-12′), 22.67 (C-11′), 29.03, 29.33, 29.55, 29.59, 29.63, 29.64, 29.66, 29.88, 31.90, 37.10 (C-1′ to C-10′), 75.95 (-*C*H_2Ph), 121.2, 122.4 (C-3, C-4a), 121.6 (C-5), 125.4 (C-6), 127.9 (2 × Ph-C_o), 128.3, 128.5, 128.9 (C-7, C-8, Ph-C_p), 128.6 (2 × Ph-C_m), 136.7 (Ph-C_i), 147.9 (C-8a), 159.5, 164.3 (C-2, C-4) ppm. **IR** (KBr): $\tilde{\nu}$ = 3060, 2914, 2847, 1618, 1600, 1558, 1491, 1468, 1454, 1393, 1353, 1216, 1170, 1105, 1072, 1026, 1005, 965, 913, 752, 735, 707, 694, 616 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 225.0 (4.656), 274.0 (3.639), 303.0 (3.349), 316.5 nm (3.360). **MS** (70 eV, EI): *m*/*z* (%) = 417.5 (4) $[M]^+$, 263.3 (63) $[M–n\text{-}C_{11}H_{23}+H]^+$, 91.1 (100) $[CH_2Ph]^+$. HRMS (ESI): calcd. for $C_{29}H_{39}NO + H^+$ 418.3104; found 418.3104.

2-Dodecyl-1-hydroxy-3-methyl-4-quinolone (2): A solution of *m*-chloroperbenzoic acid (0.990 g, 4.03 mmol, 70%) in CH_2Cl_2 (105 mL) was added to a solution of **7a** (1.40 g, 3.35 mmol) in CH_2Cl_2 (220 mL). After stirring for 1 h at room temperature, the solution was washed with saturated aq. $NaHCO_3$ (2 × 310 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in EtOH (270 mL), Pd/C (10%, 100 mg) was added, and after applying an H_2 atmosphere (1 bar), the solution was stirred at room temperature for 30 min. After filtration through celite, which was thoroughly rinsed with EtOH (270 mL), the filtrate was concentrated under reduced pressure and the residue recrystallised from EtOH/acetone to give **2** (0.93 g, 81%) as a colorless solid. $\boldsymbol{R_f}$ = 0.31 (CH_2Cl_2/MeOH, 95:5). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.2 Hz, 3 H, 12′-H_3), 1.17–1.43 (m, 18 H, 3′-H_2 to 11′-H_2), 1.59 (m, 2 H, 2′-H_2), 2.02 (s, 3 H, 3-CH_3), 2.86 (t, *J* = 7.8 Hz, 2 H, 1′-H_2), 6.98 (dd, *J* = 2 × 8.4 Hz, 1 H, 6-H), 7.28 (dd, *J* = 2 × 8.4 Hz, 1 H, 7-H), 7.78 (d, *J* = 8.4 Hz, 1 H, 8-H), 7.97 (d, *J* = 8.4 Hz, 1 H, 5-H), 10.86 (s_{br}, 1 H, OH) ppm. **^{13}C-NMR** (125 MHz, $CDCl_3$): δ = 11.46 (3-*C*H_3), 14.10 (C-12′), 22.68 (C-11′), 27.50, 29.00, 29.29, 29.35, 29.58, 29.64, 29.67, 29.89 (C-1′ to C-9′), 31.92 (C-10′), 114.5 (C-3), 115.5 (C-8), 122.8 (C-4a), 123.7 (C-6), 124.6 (C-5), 131.0 (C-7), 139.0 (C-8a), 153.5 (C-2), 172.2 (C-4) ppm. **IR** (KBr): $\tilde{\nu}$ = 2921, 2850, 1587, 1397, 1339, 1014, 755, 479, 435 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 214.5 (4.373), 249.5 (4.353), 336.5 (3.889), 347.0 nm (3.889). **MS** (ESI): *m*/*z* (%) = 344.2 (100) $[M+H]^+$, 687.5 (38) $[2M+H]^+$, 1030.7 (13) $[3M+H]^+$. HRMS (ESI): calcd. for $C_{22}H_{33}NO_2 + H^+$ 344.2584; found 344.2584.

Synthesis of 3-dodecyl-1-hydroxy-2-methyl-4-quinolone (3)

Ethyl 2-dodecylacetoacetate (10b): Sodium (2.87 g, 0.125 mol) was added to EtOH (50 mL) and the suspension was stirred for 30 min at room temperature. Afterwards ethyl acetoacetate (14.9 g, 0.115 mol) and 1-bromododecane (26.0 g, 0.104 mol) were added dropwise. After stirring at 80 °C for 6 h the solution was concentrated under reduced pressure, ice-water (180 mL) was added, the layers were

separated and the aqueous layer was extracted with Et_2O (20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/Et_2O, 4:1) provided **10b** (20.3 g, 65%) as a colorless oil. $\boldsymbol{R_f}$ = 0.49 (pentane/Et_2O, 4:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3 H, 14-H_3), 1.18–1.36 (m, 23 H, 4-H_2 to 13-H_2, OCH_2CH_3), 1.85 (m, 2 H, 3-H_2), 2.22 (s, 3 H, 2-$COCH_3$), 3.40 (t, J = 7.8 Hz, 1 H, 2-H), 4.19 (q, J = 7.2 Hz, 2 H, OCH_2CH_3) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 14.08 (C-14, OCH_2CH_3), 22.66, 27.37, 28.19, 29.29, 29.31, 29.49, 29.57, 29.60, 29.61, 31.88 (C-3 to C-13), 28.67 (2-$COCH_3$), 59.94 (C-2), 61.23 (OCH_2CH_3), 169.9 (C-1), 203.4 (2-$COCH_3$) ppm. **IR** (film): $\tilde{\nu}$ = 2925, 2854, 1743, 1718, 1466, 1358, 1242, 1150, 1026 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 256.0 nm (2.941). **MS** (70 eV, EI): m/z (%) = 298.4 (3) $[M]^+$, 256.3 (42) $[M–CH_3CO+H]^+$, 130.1 (100) $[M–n\text{-}C_{12}H_{25}+H]^+$, 43.1 (27) $[CH_3CO]^+$. HRMS (ESI): calcd. for $C_{18}H_{34}O_3 + H^+$ 299.2580; found 299.2580.

3-Dodecyl-2-methyl-4-quinolone (8b): Ester **10b** (10.0 g, 33.5 mmol), molecular sieves 3 Å (6.62 g) and acetic acid (0.29 mL) were added to a solution of aniline (5.00 g, 53.7 mmol) in EtOH (200 mL). After stirring for 44 h at 70 °C the precipitate was separated by filtration through celite, which was thoroughly rinsed with EtOH (200 mL), and the filtrate was concentrated under reduced pressure. The brown liquid residue was added dropwise to refluxing diphenyl ether (150 g) and the formed EtOH was removed by distillation. After stirring for 1 h at 260 °C and cooling to room temperature, diphenyl ether was evaporated under reduced pressure (20 mbar, 80 °C), *n*-pentane (150 mL) was added and the formed solid was separated by filtration and recrystallized from EtOH/acetone to give **8b** (4.16 g, 38%) as a colorless solid. $\boldsymbol{R_f}$ = 0.31 (CH_2Cl_2/MeOH, 95:5). **^{1}H-NMR** (300 MHz, CD_3OD): δ = 0.88 (t, J = 7.2 Hz, 3 H, 12′-H_3), 1.20–1.43 (m, 18 H, 3′-H_2 to 11′-H_2), 1.50 (m, 2 H, 2′-H_2), 2.50 (s, 3 H, 2-CH_3), 2.64 (t, J = 7.8 Hz, 2 H, 1′-H_2), 7.32 (dd, J = 2 × 8.4 Hz, 1 H, 6-H), 7.48 (d, J = 8.4 Hz, 1 H, 8-H), 7.61 (dd, J =2 × 8.4 Hz, 1 H, 7-H), 8.20 (d, J = 8.4 Hz, 1 H, 5-H) ppm. **^{13}C-NMR** (125 MHz, CD_3OD): δ = 14.42 (C-12′), 18.08 (2-CH_3); 23.73 (C-11′), 26.39, 30.11, 30.46, 30.73, 30.76, 30.77, 30.97, 33.07 (C-1′ to C-10′), 118.5 (C-8), 121.7 (C-4a), 124.4 (C-6), 124.9 (C-2), 126.2 (C-5), 132.5 (C-7), 140.5 (C-8a), 149.1 (C-3), 178.8 (C-4) ppm. **IR** (KBr): $\tilde{\nu}$ = 2919, 2849, 1639, 1606, 1592, 1555, 1500, 1358, 1255, 1023, 753, 721, 698, 601, 569, 448 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 213.0 (4.414), 240.0 (4.461), 245.5 (4.451), 322.5 (4.033), 335.0 nm (4.033). **MS** (ESI): m/z (%) = 328.2 (100) $[M+H]^+$, 655.5 (16) $[2M+H]^+$. HRMS (ESI): calcd. for $C_{22}H_{33}NO + H^+$ 328.2634; found 328.2635.

4-Benzyloxy-3-dodecyl-2-methylquinoline (7b): To a solution of LDA, prepared from *i*-Pr_2NH (0.43 mL, 3.1 mmol) and *n*-BuLi (1.3 mL, 3.4 mmol; 2.5 M in hexanes), in dry THF (2 mL) at room temperature was added a suspension of **8b** (1.0 g, 3.1 mmol) in DMSO (100 mL) and the solution was

stirred at room temperature for 1 h. Afterwards benzyl bromide (0.72 mL, 6.1 mmol) was added and the solution was stirred at room temperature for 25 min. The reaction was quenched by addition of brine (300 mL) and the mixture extracted with EtOAc (3 × 200 mL). The combined organic extracts were washed with brine (3 × 200 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 4:1) provided **7b** (1.01 g, 78%) as a yellow oil. R_f = 0.50 (pentane/EtOAc, 3:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 7.2 Hz, 3 H, 12′-H_3), 1.20–1.43 (m, 18 H, 3′-H_2 to 11′-H_2), 1.55 (m, 2 H, 2′-H_2), 2.70–2.80 (m, 5 H, 2-CH_3, 1′-H_2), 5.08 (s, 2 H, -CH_2Ph), 7.33–7.64 (m, 7 H, 6-H, 7-H, 5 × Ph-H), 7.98 (d, J = 8.4 Hz, 2 H, 5-H, 8-H) ppm. **^{13}C-NMR** (125 MHz, $CDCl_3$): δ = 14.19 (C-12′), 22.76 (C-11′), 23.67 (2-CH$_3$), 26.85, 29.42, 29.46, 29.67, 29.72, 29.73, 29.99, 30.08, 31.99 (C-1′ to C-10′), 76.68 (-CH$_2$Ph), 121.9 (C-5), 122.7 (C-3), 125.5 (C-6), 126.8 (C-4a), 127.6 (2 × Ph-C$_o$), 128.3, 128.7, 128.8, (C-7, C-8, Ph-C$_p$), 128.7 (2 × Ph-C$_m$), 137.0 (Ph-C$_i$), 148.0 (C-8a), 159.7, 160.5 (C-2, C-4) ppm. **IR** (film): $\tilde{\nu}$ = 2924, 2853, 1592, 1562, 1493, 1455, 1402, 1363, 1346, 1208, 1122, 1106, 1059, 1004, 765, 733, 696 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 226.0 (4.757), 273.5 (3.738), 303.0 (3.441), 316.5 nm (3.459). **MS** (ESI): m/z (%) = 418.3 (100) $[M+H]^+$. HRMS (ESI): calcd. for $C_{29}H_{39}NO + H^+$ 418.3104; found 418.3102.

3-Dodecyl-1-hydroxy-2-methyl-4-quinolone (3): A solution of *m*-chloroperbenzoic acid (1.57 g, 6.37 mmol, 70%) in CH_2Cl_2 (160 mL) was added to a solution of **7b** (2.22 g, 5.31 mmol) in CH_2Cl_2 (320 mL). After stirring for 1 h at room temperature the solution was washed with saturated aq. $NaHCO_3$ (2 × 500 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in EtOH (400 mL), Pd/C (10%, 100 mg) was added, and after applying an H_2 atmosphere (1 bar), the solution was stirred at room temperature for 30 min. After filtration through celite, which was thoroughly rinsed with EtOH (400 mL), the filtrate was concentrated under reduced pressure and the residue recrystallised from EtOH/acetone to give **3** (1.40 g, 77%) as a colorless solid. R_f = 0.32 (CH_2Cl_2/MeOH, 95:5); **m.p.** 145 °C. **^{1}H-NMR** (300 MHz, DMSO-d_6): δ = 0.88 (t, J = 7.2 Hz, 3 H, 12′-H_3), 1.15–1.45 (m, 20 H, 2′-H_2 to 11′-H_2), 2.48 (s, 3 H, 2-CH_3), 2.55 (t, J = 7.8 Hz, 2 H, 1′-H_2), 7.26 (dd, J = 2 × 8.4 Hz, 1 H, 6-H), 7.62 (dd, J = 2 × 8.4 Hz, 1 H, 7-H), 7.78 (d, J = 8.4 Hz, 1 H, 8-H), 8.14 (d, J = 8.4 Hz, 1 H, 5-H), 11.38 (s_{br}, 1 H, OH) ppm. **^{13}C-NMR** (125 MHz, DMSO-d_6): δ = 13.67 (C-12′), 14.20 (2-CH$_3$), 21.92 (C-11′), 25.43, 28.54, 28.70, 28.86, 28.89, 28.91, 29.10, 31.14 (C-1′ to C-10′), 114.0 (C-8), 115.7 (C-3), 122.2 (C-6), 123.0 (C-4a), 125.0 (C-5), 130.9 (C-7), 139.3 (C-8a), 146.8 (C-2), 173.2 (C-4) ppm. **IR** (KBr): $\tilde{\nu}$ = 2921, 2850, 2432, 1591, 1467, 1418, 1347, 1109, 1081, 986, 754, 708, 636, 487, 443 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 214.5 (4.499), 251.0 (4.421), 337.5 (3.930), 348.5 nm (3.948). **MS** (ESI): m/z (%) = 344.2 (100) $[M+H]^+$, 687.5 (7) $[2M+H]^+$. HRMS (ESI): calcd. for $C_{22}H_{33}NO_2 + H^+$ 344.2584; found 344.2585.

Synthesis of 6-[2-(dimethylamino)ethoxy]-3-dodecyl-1-hydroxy-2-methyl-4-quinolone (4)

4-Triisopropylsilyloxyaniline (13): Triisopropylsilyl chloride (11.6 g, 60.0 mmol) was added to a suspension of 4-hydroxyaniline (4.37 g, 40.0 mmol) and imidazole (4.08 g, 60.0 mmol) in CH_2Cl_2 (100 mL). After stirring for 26 h at room temperature water (180 mL) was added, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 310 mL). The combined organic layers were washed with brine (150 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 4:1, 1% NEt_3) provided **13** (10.7 g, 100%) as a yellow oil. R_f = 0.20 (pentane/EtOAc, 6:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 1.08 (d, J = 6.6 Hz, 18 H, $CH(CH_3)_2$), 1.13–1.30 (m, 3 H, $CH(CH_3)_2$), 3.26 (s_{br}, 2 H, NH_2), 6.56 (d, J = 8.4 Hz, 2 H, 2-H, 6-H), 6.70 (d, J = 8.4 Hz, 2 H, 3-H, 5-H) ppm. **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 12.53 ($CH(CH_3)_2$), 17.88 ($CH(CH_3)_2$), 116.2 (C-2, C-6), 120.3 (C-3, C-5), 139.9 (C-1), 148.6 (C-4) ppm. **IR** (film): $\tilde{\nu}$ = 3348, 2944, 2866, 1611, 1509, 1463, 1250, 1071, 997, 921, 883, 829, 686 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 197.0 (4.496), 241.5 (3.989), 306.5 nm (3.339). **MS** (70 eV, EI): m/z (%) = 265.3 (100) $[M]^+$, 222.3 (85) $[M–C_3H_7+H]^+$. HRMS (ESI): calcd. for $C_{15}H_{27}NOSi + H^+$ 266.1934; found 266.1934.

Ethyl 2-dodecyl-3-[4-(triisopropylsilyloxy)phenylamino]-2-butenoate (14b): Ester **10b** (7.32 g, 24.5 mmol), molecular sieves 3 Å (6.50 g) and acetic acid (0.30 mL) were added to a solution of **13** (10.4 g, 39.3 mmol) in EtOH (150 mL). After stirring for 42 h at 75 °C the precipitate was separated by filtration through celite, which was thoroughly rinsed with EtOH (150 mL), and the filtrate was concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 20:1) provided **14b** (9.05 g, 68%) as a brown oil. R_f = 0.51 (pentane/EtOAc, 20:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.6 Hz, 3 H, 14-H_3), 1.09 (d, J = 6.6 Hz, 18 H, $CH(CH_3)_2$), 1.14–1.40 (m, 26 H, 4-H_2 to 13-H_2, $CH(CH_3)_2$, OCH_2CH_3), 1.91 (s, 3 H, 2′-H_3), 2.22 (t, J = 7.2 Hz, 2 H, 3-H_2), 4.14 (q, J = 6.6 Hz, 2 H, OCH_2CH_3), 6.78 (d, J = 8.4 Hz, 2 H, 2′′-H, 6′′-H), 6.88 (d, J = 8.4 Hz, 2 H, 3′′-H, 5′′-H), 10.76 (s_{br}, 1 H, NH) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 12.57 ($CH(CH_3)_2$), 14.11, 14.57 (OCH_2CH_3, C-14), 16.34 (C-2′), 17.86 ($CH(CH_3)_2$), 22.68 (C-13), 27.27, 29.35, 29.55, 29.63, 29.65, 29.69, 30.54, 31.91 (C-3 to C-12), 58.83 (OCH_2CH_3), 95.80 (C-2), 120.0 (C-2′′, C-6′′), 126.6 (C-3′′, C-5′′), 133.3 (C-1′′), 153.3, 156.7 (C-1′, C-4′′), 171.0 (C-1) ppm. **IR** (film): $\tilde{\nu}$ = 2925, 2854, 1648, 1603, 1509, 1464, 1245, 1164, 1119, 1013, 914, 883, 788, 683 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 223.0 (3.671), 312.5 nm (4.056). **MS** (ESI): m/z (%) = 546.4 (100) $[M+H]^+$, 1091.8 (29) $[2M+H]^+$. HRMS (ESI): calcd. for $C_{33}H_{59}NO_3Si + H^+$ 546.4337; found 546.4335.

3-Dodecyl-2-methyl-6-triisopropylsilyloxy-4-quinolone (15b): Ester **14b** (8.82 g, 16.2 mmol) was

added dropwise to refluxing diphenyl ether (100 g) and the formed EtOH was removed by distillation. After stirring for 1 h at 260 °C and cooling to room temperature, diphenyl ether was evaporated under reduced pressure (20 mbar, 80 °C) to afford the crude product which was absorbed on silica gel. Elution with CH_2Cl_2 (2.5 L) allowed to remove the remaining diphenyl ether and afterwards elution with EtOAc (1 L) provided the product, which was recrystallised from EtOH/acetone to give **15b** (6.65 g, 82%) as colorless needles. $\boldsymbol{R}_\mathbf{f}$ = 0.62 (CH_2Cl_2/MeOH, 95:5). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 7.2 Hz, 3 H, 12′-H_3), 0.98 (d, J = 7.2 Hz, 18 H, CH(CH_3)$_2$), 1.07–1.38 (m, 21 H, 3′-H_2 to 11′-H_2, CH(CH$_3$)$_2$), 1.52 (m, 2 H, 2′-H_2), 2.49 (s, 3 H, 2-CH_3), 2.68 (t, J = 7.2 Hz, 2 H, 1′-H_2), 7.08 (dd, J = 9.0, 2.4 Hz, 1 H, 7-H), 7.56 (d, J = 9.0 Hz, 1 H, 8-H), 7.76 (d, J = 2.4 Hz, 1 H, 5-H), 12.18 (s_{br}, 1 H, NH) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 12.56 (*C*H(CH$_3$)$_2$), 14.10 (C-12′), 17.82 (CH(*C*H$_3$)$_2$), 18.19 (2-*C*H$_3$), 22.68, 25.86, 29.36, 29.66, 29.70, 30.09, 31.92 (C-1′ to C-11′), 112.5 (C-8), 125.5 (C-7), 119.5, 125.1, 134.6 (C-2, C-4a, C-5, C-8a), 146.4, 152.0 (C-3, C-6), 176.3 (C-4) ppm. **IR** (KBr): $\tilde{\nu}$ = 2923, 2853, 1588, 1547, 1491, 1431, 1365, 1263, 1157, 969, 883, 827, 689, 587 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 217.0 (4.344), 246.0 (4.549), 288.0 (3.472), 300.5 (3.484), 335.5 (3.961), 349.0 nm (3.937). **MS** (ESI): *m*/*z* (%) = 500.3 (100) [M+H]$^+$, 999.7 (53) [2M+H]$^+$, 1499.1 (19) [3M+H]$^+$. HRMS (ESI): calcd. for $C_{31}H_{53}NO_2Si + H^+$ 500.3918; found 500.3918.

4-Benzyloxy-3-dodecyl-2-methyl-6-(triisopropylsilyloxy)quinoline (16b): To a solution of LDA, prepared from *i*-Pr$_2$NH (0.71 mL, 5.0 mmol) and *n*-BuLi (2.2 mL, 5.5 mmol; 2.5 M in hexanes), in dry THF (3.5 mL) at room temperature was added a suspension of **15b** (2.5 g, 5.0 mmol) in DMSO (165 mL) and the solution was stirred at room temperature for 1 h. Afterwards benzyl bromide (1.2 mL, 10 mmol) was added and the solution was stirred at room temperature for 2 h. The reaction was quenched by addition of brine (450 mL) and the mixture extracted with EtOAc (3 × 300 mL). The combined organic extracts were washed with brine (2 × 250 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 12:1) provided **16b** (2.6 g, 88%) as a yellow oil. $\boldsymbol{R}_\mathbf{f}$ = 0.37 (pentane/EtOAc, 10:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.6 Hz, 3 H, 12′-H_3), 1.08 (d, J = 7.2 Hz, 18 H, CH(CH_3)$_2$), 1.17–1.48 (m, 21 H, 3′-H_2 to 11′-H_2, CH(CH$_3$)$_2$), 1.58 (m, 2 H, 2′-H_2), 2.70 (s, 3 H, 2-CH_3), 2.77 (t, J = 7.8 Hz, 2 H, 1′-H_2), 5.05 (s, 2 H, -CH_2Ph), 7.25 (dd, J = 9.0, 2.4 Hz, 1 H, 7-H), 7.34 (d, J = 2.4 Hz, 1 H, 5-H), 7.36–7.56 (m, 5 H, 5 × Ph-H), 7.87 (d, J = 9.0 Hz, 1 H, 8-H) ppm. **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 12.63 (*C*H(CH$_3$)$_2$), 14.11 (C-12′), 17.88 (CH(*C*H$_3$)$_2$), 22.67 (C-11′), 23.29 (2-*C*H$_3$), 26.83, 29.33, 29.38, 29.59, 29.63, 29.64, 29.65, 29.97, 30.08, 31.90 (C-1′ to C-10′), 76.02 (-*C*H$_2$Ph), 108.2 (C-5), 123.3 (C-3), 124.6 (C-7), 126.7 (C-4a), 127.3 (2 × Ph-C$_o$), 128.6 (2 × Ph-C$_m$), 128.1, 130.1 (C-8, Ph-C$_p$), 136.9, 144.0 (C-8a, Ph-C$_i$), 153.6, 157.7, 158.5 (C-2, C-4, C-6) ppm. **IR** (film): $\tilde{\nu}$ = 2924, 2865, 1619, 1593, 1492, 1463, 1388, 1364,

1346, 1267, 1233, 1206, 1121, 1058, 997, 947, 882, 835, 732, 692 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 234.5 (4.751), 269.5 (3.653), 279.0 (3.664), 318.0 (3.484), 330.5 (3.559), 358.0 nm (2.385). **MS** (ESI): *m*/*z* (%) = 590.4 (100) $[M+H]^+$. HRMS (ESI): calcd. for $C_{38}H_{59}NO_2Si + H^+$ 590.4387; found 590.4387.

4-Benzyloxy-3-dodecyl-2-methylquinolin-6-ol (17b): TBAF·3 H_2O (2.12 g, 6.71 mmol) was added to a solution of **16b** (1.98 g, 3.36 mmol) in THF (25 mL) at 0 °C. After stirring at 0 °C for 1 h and at room temperature for 2 h the solution was concentrated under reduced pressure. Purification of the residue by flash chromatography (CH_2Cl_2/MeOH, 97:3) provided **17b** (1.43 g, 98%) as a pale-yellow solid. $\boldsymbol{R_f}$ = 0.38 (CH_2Cl_2/MeOH, 95:5). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.6 Hz, 3 H, 12′-H_3), 1.12–1.41 (m, 18 H, 3′-H_2 to 11′-H_2), 1.49 (m, 2 H, 2′-H_2), 2.60–2.78 (m, 5 H, 2-CH_3, 1′-H_2), 4.97 (s, 2 H, -CH_2Ph), 7.19 (dd, *J* = 9.0, 2.4 Hz, 1 H, 7-H), 7.26–7.39 (m, 5 H, 5 × Ph-H), 7.42 (d, *J* = 2.4 Hz, 1 H, 5-H), 7.83 (d, *J* = 9.0 Hz, 1 H, 8-H) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 14.12 (C-12′), 21.94 (2-*C*H_3), 22.68 (C-11'), 26.66, 29.34, 29.59, 29.64, 29.91, 30.04, 31.90 (C-1′ to C-10′), 76.02 (-*C*H_2Ph), 104.0, (C-5), 121.7 (C-7), 124.2, 127.2 (C-3, C-4a), 127.5 (2 × Ph-C_o), 128.2, 128.7 (C-8, Ph-C_p), 128.5 (2 × Ph-C_m), 136.6, 142.0 (C-8a, Ph-C_i), 155.6, 156.5, 159.2 (C-2, C-4, C-6) ppm. **IR** (KBr): $\tilde{\nu}$ = 2956, 2922, 2851, 2555, 1873, 1620, 1592, 1517, 1469, 1393, 1357, 1267, 1241, 1207, 1123, 1084, 1057, 1015, 973, 909, 860, 846, 827, 747, 719, 698, 617, 541, 484 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 200.5 (4.324), 232.5 (4.702), 282.5 (3.668), 335.0 nm (3.653). **MS** (ESI): *m*/*z* (%) = 434.3 (100) $[M+H]^+$. HRMS (ESI): calcd. for $C_{29}H_{39}NO_2 + H^+$ 434.3053; found 434.3053.

4-Benzyloxy-6-[2-(dimethylamino)ethoxy]-3-dodecyl-2-methylquinoline (18b): Sodium hydride (0.302 g, 7.56 mmol, 60% in mineral oil) was added slowly to a solution of **17b** (1.43 g, 3.29 mmol) in DMF (25 mL) at 0 °C. After stirring for 1 h at room temperature, the solution was cooled to 0 °C, 2-dimethylaminoethyl chloride hydrochloride (0.497 g, 3.45 mmol) was added and the suspension was stirred at 100 °C for 2 h. After cooling to room temperature the reaction was quenched by addition of H_2O (25 mL) and the mixture extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with H_2O (2 × 100 mL) and brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (CH_2Cl_2/MeOH, 96:4) provided **18b** (0.916 g, 95%) as an orange oil. $\boldsymbol{R_f}$ = 0.15 (CH_2Cl_2/MeOH, 98:2, 0.5% NEt_3). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.6 Hz, 3 H, 12′′-H_3), 1.18–1.44 (m, 18 H, 3′′-H_2 to 11′′-H_2), 1.55 (m, 2 H, 2′′-H_2), 2.33 (s, 6 H, N(CH_3)$_2$), 2.68 (s, 3 H, 2′-CH_3), 2.70–2.80 (m, 4 H, 1′′-H_2, 1-H_2), 4.01 (t, *J* = 6.0 Hz, 2 H, 2-H_2), 5.04 (s, 2 H, -CH_2Ph), 7.17 (d, *J* = 2.4 Hz, 1 H, 5′-H), 7.27 (dd, *J* = 9.0, 2.4 Hz, 1 H, 7′-H), 7.32–7.52 (m, 5 H, 5 × Ph-H), 7.86 (d, *J* = 9.0 Hz, 1 H, 8′-H) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 14.10 (C-12′′), 22.66 (C-11′′), 23.26 (2′-*C*H_3), 26.84, 29.32, 29.37, 29.57, 29.61, 29.63, 29.90, 30.00, 31.89 (C-1′′ to C-10′′),

45.85 (N(*C*H$_3$)$_2$), 58.16 (C-1), 66.05 (C-2), 76.18 (-*C*H$_2$Ph), 100.6 (C-5′), 121.5 (C-7′), 123.2, 126.8 (C-3′, C-4a′), 127.5 (2 × Ph-C$_o$), 128.2, 130.1 (C-8, Ph-C$_p$), 128.6 (2 × Ph-C$_m$), 137.1, 143.9 (C-8a′, Ph-C$_i$), 156.3, 157.5, 158.9 (C-2′, C-4′, C-6′) ppm. **IR** (film): $\tilde{\nu}$ = 2924, 2853, 2770, 1622, 1593, 1495, 1456, 1349, 1269, 1226, 1121, 1030, 832, 734, 697 cm^{-1}. **UV** (CH$_3$CN): λ_{max} (lg ε) = 233.5 (4.787), 257.5 (3.672), 267.0 (3.714), 276.0 (3.704), 318.5 (3.591), 331.5 (3.673), 357.5 nm (2.260). **MS** (ESI): *m*/*z* (%) = 505.3 (100) [M+H]$^+$, 1009.7 (29) [2M+H]$^+$. HRMS (ESI): calcd. for C$_{33}$H$_{48}$N$_2$O$_2$ + H$^+$ 505.3788; found 505.3787.

4-Benzyloxy-6-[2-(dimethylamino)ethoxy]-3-dodecyl-2-methylquinoline *N*,*N*'-dioxide (19b): A solution of *m*-chloroperbenzoic acid (1.85 g, 7.52 mmol, 70%) in CH$_2$Cl$_2$ (160 mL) was added to a solution of **18b** (1.58 g, 3.13 mmol) in CH$_2$Cl$_2$ (160 mL). After stirring for 1.5 h at room temperature the solution was washed with saturated aq. NaHCO$_3$ (2 × 320 mL), dried over Na$_2$SO$_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (MeOH) provided **19b** (1.42 g, 80%) as a yellowish solid. R_f = 0.18 (MeOH). **^{1}H-NMR** (300 MHz, CDCl$_3$): δ = 0.85 (t, *J* = 6.6 Hz, 3 H, 12′′-H$_3$), 1.15–1.40 (m, 18 H, 3′′-H$_2$ to 11′′-H$_2$), 1.52 (m, 2 H, 2′′-H$_2$), 2.67 (s, 3 H, 2′-C*H*$_3$), 2.73 (t, *J* = 8.4 Hz, 2 H, 1′′-H$_2$), 3.28 (s, 6 H, N(C*H*$_3$)$_2$), 3.62 (t, *J* = 4.2 Hz, 2 H, 1-H$_2$), 4.57 (t, *J* = 4.2 Hz, 2 H, 2-H$_2$), 5.04 (s, 2 H, -C*H*$_2$Ph), 7.20–7.50 (m, 7 H, 5′-H, 7′-H, 5 × Ph-H), 8.65 (d, *J* = 9.6 Hz, 1 H, 8′-H) ppm. **^{13}C-NMR** (125 MHz, CDCl$_3$): δ = 14.08 (C-12′′), 15.17 (2′-*C*H$_3$), 22.65, 27.29, 29.29, 29.30, 29.53, 29.59, 29.61, 29.72, 29.87, 31.88 (C-1′′ to C-11′′), 60.35 (N(*C*H$_3$)$_2$), 62.34 (C-2), 69.86 (C-1), 77.10 (-*C*H$_2$Ph), 101.9 (C-5′), 121.4, 122.3 (C-7′, C-8′), 125.0 (C-3′), 127.8 (2 × Ph-C$_o$), 128.6 (Ph-C$_p$), 128.8 (2 × Ph-C$_m$), 128.9 (C-4a′), 136.4, 136.8 (Ph-C$_i$, C-8a′), 145.7 (C-2′), 149.8 (C-4′), 156.8 (C-6′) ppm. **IR** (KBr): $\tilde{\nu}$ = 2919, 1621, 1573, 1454, 1324, 1237, 1123, 959, 697 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 243.5 (4.676), 323.0 nm (3.903). **MS** (ESI): *m*/*z* (%) = 537.37 (100) [M+H]$^+$, 1073.73 (43) [2M+H]$^+$. HRMS (ESI): calcd. for C$_{33}$H$_{48}$N$_2$O$_4$ + H$^+$ 537.3683; found 537.3687.

6-[2-(Dimethylamino)ethoxy]-3-dodecyl-1-hydroxy-2-methyl-4-quinolone (4): Pd/C (10%, 130 mg) was added to a solution of **19b** (0.994 g, 1.85 mmol) in EtOH (150 mL). After applying an H$_2$ atmosphere (1 bar), the solution was stirred at room temperature for 1.5 h. After filtration through celite, which was thoroughly rinsed with EtOH (200 mL), the filtrate was concentrated under reduced pressure and the residue recrystallised from EtOH/acetone to give **4** (0.708 g, 89%) as a colorless solid. R_f = 0.42 (MeOH); **m.p.** 144 °C. **^{1}H-NMR** (300 MHz, CDCl$_3$): δ = 0.85 (t, *J* = 6.6 Hz, 3 H, 12′-H$_3$), 1.10–1.40 (m, 20 H, 2′-H$_2$ to 11′-H$_2$), 2.32 (s, 6 H, N(C*H*$_3$)$_2$), 2.42 (s, 3 H, 2-C*H*$_3$), 2.55 (t, *J* = 8.4 Hz, 2 H, 1′-H$_2$), 2.72 (t, *J* = 4.2 Hz, 2 H, 2′′-H$_2$), 3.92 (t, *J* = 4.2 Hz, 2 H, 1′′-H$_2$), 6.90 (d, *J* = 9.0 Hz, 1 H, 7-H), 7.44 (d, *J* = 1.8 Hz, 1 H, 5-H), 8.65 (d, *J* = 9.0 Hz, 1 H, 8-H), 10.8 (s$_{br}$, 1 H, 1-O*H*) ppm. **^{13}C-NMR**

(125 MHz, $CDCl_3$): δ = 14.07 (C-12′), 14.62 (2-*C*H_3), 22.64 (C-11′), 26.53 (C-1′), 29.33, 29.63, 29.70, 29.94 (C-2′ to C-9′), 31.88 (C-10′), 45.50 (N(*C*H_3)$_2$), 57.86 (C-2′′), 65.39 (C-1′′), 104.4 (C-5), 117.4 (C-8), 119.7 (C-3), 122.3 (C-7), 124.6 (C-4a), 134.8 (C-8a), 147.5 (C-2), 155.1 (C-6), 170.1 (C-4) ppm. **IR** (KBr): $\tilde{\nu}$ = 2921, 2850, 1540, 1467, 1035 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 202.0 (4.125), 221.0 (4.457), 242.5 (4.363), 261.5 (4.355), 270.5 (4.220), 347.0 (3.873), 357.5 nm (3.872). **MS** (ESI): *m*/*z* (%) = 431.33 (100) $[M+H]^+$, 861.64 (100) $[2M+H]^+$. HRMS (ESI): calcd. for $C_{26}H_{42}N_2O_3 + H^+$ 431.3269; found 431.3268.

Synthesis of 6-[2-(dimethylamino)ethoxy]-2-dodecyl-1-hydroxy-4-quinolone (5)

Ethyl 3-[4-(triisopropylsilyloxy)phenylamino]-2-pentadecenoate (14c): Ester **10c** (7.11 g, 25.0 mmol), molecular sieves 3 Å (5.00 g) and acetic acid (0.30 mL) were added to a solution of **13** (10.6 g, 40.0 mmol) in EtOH (150 mL). After stirring for 44 h at 75 °C the precipitate was separated by filtration through celite, which was thoroughly rinsed with EtOH (150 mL), and the filtrate was concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 20:1) provided **14c** (11.9 g, 89%) as a brown oil. $\boldsymbol{R}_\mathbf{f}$ = 0.46 (pentane/EtOAc, 20:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.6 Hz, 3 H, 15-H_3), 1.09 (d, *J* = 6.6 Hz, 18 H, CH(C*H*$_3$)$_2$), 1.12–1.43 (m, 26 H, 5-H_2 to 14-H_2, C*H*(CH$_3$)$_2$, OCH$_2$C*H*$_3$), 2.17 (t, *J* = 7.2 Hz, 2 H, 4-H_2), 4.14 (q, *J* = 6.6 Hz, 2 H, OC*H*$_2$CH$_3$), 4.65 (s, 1 H, 2-H), 6.83 (d, *J* = 8.4 Hz, 2 H, 2′-H, 6′-H), 6.95 (d, *J* = 8.4 Hz, 2 H, 3′-H, 5′-H), 10.09 (s_{br}, 1 H, NH) ppm. **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 12.58 (*C*H(CH$_3$)$_2$), 14.10, 14.61 (OCH$_2$*C*H$_3$, C-15), 17.85 (CH(*C*H$_3$)$_2$), 22.68 (C-14), 27.98, 29.15, 29.18, 29.33, 29.40, 29.55, 29.61, 29.63, 31.90, 32.30 (C-4 to C-13), 58.60 (O*C*H$_2$CH$_3$), 83.64 (C-2), 120.2 (C-2′, C-6′), 127.2 (C-3′, C-5′), 132.3 (C-1′), 154.0 (C-4′), 164.6 (C-3), 170.7 (C-1) ppm. **IR** (film): $\tilde{\nu}$ = 3246, 2926, 2866, 1655, 1611, 1511, 1465, 1384, 1255, 1159, 1096, 1049, 1013, 996, 913, 883, 845, 788, 685 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 294.5 nm (4.369). **MS** (ESI): *m*/*z* (%) = 532.4 (100) $[M+H]^+$. HRMS (ESI): calcd. for $C_{32}H_{57}NO_3Si + H^+$ 532.4180; found 532.4178.

2-Dodecyl-6-triisopropylsilyloxy-4-quinolone (15c): Ester **14c** (11.5 g, 21.6 mmol) was added dropwise to refluxing diphenyl ether (110 g) and the formed EtOH was removed by distillation. After stirring for 1 h at 260 °C and cooling to room temperature, diphenyl ether was evaporated under reduced pressure (20 mbar, 80 °C) to afford the crude product which was absorbed on silica gel. Elution with CH_2Cl_2 (3.5 L) allowed to remove the remaining diphenyl ether and afterwards elution with EtOAc (1.5 L) provided the product, which was recrystallised from EtOH/acetone to give **15c** (8.31 g, 79%) as colorless needles. $\boldsymbol{R}_\mathbf{f}$ = 0.34 (CH_2Cl_2/MeOH, 95:5). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.6 Hz, 3 H,

12′-H_3), 0.99 (d, J = 7.2 Hz, 18 H, CH(CH_3)$_2$), 1.08–1.34 (m, 21 H, 3′-H_2 to 11′-H_2, CH(CH$_3$)$_2$), 1.70 (m, 2 H, 2′-H_2), 2.66 (t, J = 7.2 Hz, 2 H, 1′-H_2), 6.18 (s, 1 H, 3-H), 7.14 (dd, J = 9.0, 2.4 Hz, 1 H, 7-H), 7.68–7.75 (m, 2 H, 5-H, 8-H), 12.81 (s_{br}, 1 H, NH) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 12.59 (*C*H(CH$_3$)$_2$), 14.09 (C-12′), 17.83 (CH(*C*H$_3$)$_2$), 22.67 (C-11′), 29.15, 29.32, 29.35, 29.40, 29.55, 29.64, 29.67, 31.90, 34.24 (C-1′ to C-10′), 107.0 (C-3), 112.4 (C-8), 120.1 (C-5), 126.0 (C-4a), 126.1 (C-7), 135.6 (C-8a), 152.4, 154.4 (C-2, C-6), 178.0 (C-4) ppm. **IR** (KBr): $\tilde{\nu}$ = 3061, 2922, 2850, 1637, 1589, 1546, 1495, 1371, 1301, 1263, 1222, 1174, 1135, 1080, 995, 961, 882, 842, 809, 685, 621, 579, 509 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 215.5 (4.373), 242.0 (4.599), 284.0 (3.600), 295.5 (3.596), 330.0 (3.946), 342.5 nm (3.902). **MS** (ESI): *m*/*z* (%) = 486.3 (100) [M+H]$^+$, 971.7 (86) [2M+H]$^+$, 1457.1 (19) [3M+H]$^+$. HRMS (ESI): calcd. for $C_{30}H_{51}NO_2Si$ + H^+ 486.3761; found 486.3763.

4-Benzyloxy-2-dodecyl-6-(triisopropylsilyloxy)quinoline (16c): To a solution of LDA, prepared from *i*-Pr$_2$NH (0.44 mL, 3.1 mmol) and *n*-BuLi (1.4 mL, 3.4 mmol; 2.5 M in hexanes), in dry THF (2 mL) at room temperature was added a suspension of **15c** (1.5 g, 3.1 mmol) in DMSO (100 mL) and the solution was stirred at room temperature for 1.25 h. Afterwards benzyl bromide (0.73 mL, 6.2 mmol) was added and the solution was stirred at room temperature for 45 min. The reaction was quenched by addition of brine (300 mL) and the mixture extracted with EtOAc (3 × 200 mL). The combined organic extracts were washed with brine (3 × 200 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 15:1 → 8:1) provided **16c** (1.3 g, 71%) as a yellow oil. R_f = 0.42 (pentane/EtOAc, 10:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.6 Hz, 3 H, 12′-H_3), 1.12 (d, J = 7.2 Hz, 18 H, CH(CH_3)$_2$), 1.20–1.44 (m, 21 H, 3′-H_2 to 11′-H_2, CH(CH$_3$)$_2$), 1.76 (m, 2 H, 2′-H_2), 2.86 (t, J = 7.2 Hz, 2 H, 1′-H_2), 5.27 (s, 2 H, -CH_2Ph), 6.65 (s, 1 H, 3-H), 7.29 (dd, J = 9.0, 2.4 Hz, 1 H, 7-H), 7.35–7.52 (m, 5 H, 5 × Ph-H), 7.60 (d, J = 2.4 Hz, 1 H, 5-H), 7.86 (d, J = 9.0 Hz, 1 H, 8-H) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 12.62 (*C*H(CH$_3$)$_2$), 14.12 (C-12′), 17.93 (CH(*C*H$_3$)$_2$), 22.68 (C-11′), 29.36, 29.57, 29.61, 29.64, 29.65, 29.67, 30.24, 31.91, 39.80 (C-1′ to C-10′), 69.75 (-*C*H$_2$Ph), 100.9 (C-3), 108.5 (C-5), 120.8 (C-4a), 125.1 (C-7), 127.0 (2 × Ph-C$_o$), 128.1, 129.6 (C-8, Ph-C$_p$), 128.6 (2 × Ph-C$_m$), 136.2, 144.6 (C-8a, Ph-C$_i$), 153.1 (C-6), 160.3, 161.7 (C-2, C-4) ppm. **IR** (film): $\tilde{\nu}$ = 3066, 2924, 2865, 1598, 1564, 1498, 1470, 1404, 1357, 1266, 1216, 1179, 1095, 996, 959, 882, 837, 801, 734, 693 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 235.0 (4.792), 269.5 (3.746), 277.5 (3.829), 287.0 (3.734), 317.0 (3.526), 328.5 nm (3.548). **MS** (ESI): *m*/*z* (%) = 576.4 (100) [M+H]$^+$. HRMS (ESI): calcd. for $C_{37}H_{57}NO_2Si$ + H^+ 576.4231; found 576.4233.

4-Benzyloxy-2-dodecylquinolin-6-ol (17c): TBAF·3 H_2O (2.16 g, 6.84 mmol) was added to a solution of **16c** (1.97 g, 3.42 mmol) in THF (20 mL) at 0 °C. After stirring at 0 °C for 1 h and at room temperature

for 3.5 h the solution was concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/EtOAc, 4:1) provided **17c** (1.30 g, 90%) as a colorless solid. R_f = 0.22 (pentane/EtOAc, 4:1). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 6.6 Hz, 3 H, 12′-H_3), 1.05–1.35 (m, 18 H, 3′-H_2 to 11′-H_2), 1.68 (m, 2 H, 2′-H_2), 2.86 (t, J = 7.8 Hz, 2 H, 1′-H_2), 5.23 (s, 2 H, -CH_2Ph), 6.63 (s, 1 H, 3-H), 7.18 (dd, J = 9.0, 2.4 Hz, 1 H, 7-H), 7.28–7.48 (m, 5 H, 5 × Ph-H), 7.62 (d, J = 2.4 Hz, 1 H, 5-H), 7.71 (d, J = 9.0 Hz, 1 H, 8-H), 12.08 (s_{br}, 1 H, OH) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 14.12 (C-12′), 22.67 (C-11′), 29.32, 29.36, 29.41, 29.46, 29.60, 30.32, 31.90, 38.50 (C-1′ to C-10′), 69.95 (-CH$_2$Ph), 100.9, 104.6 (C-3, C-5), 121.6 (C-4a), 122.1 (C-7), 127.1 (2 × Ph-C_o), 127.8, 128.1 (C-8, Ph-C_p), 128.6 (2 × Ph-C_m), 135.8, 142.2 (C-8a, Ph-C_i), 155.4, 160.7, 161.0 (C-2, C-4, C-6) ppm. **IR** (KBr): $\tilde{\nu}$ = 2921, 2850, 1620, 1591, 1531, 1466, 1390, 1351, 1323, 1268, 1220, 1184, 1163, 1096, 998, 834, 738, 696, 630, 604, 560, 472 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 234.0 (4.730), 277.5 (3.806), 287.0 (3.709), 322.5 (3.604), 332.5 nm (4.618). **MS** (ESI): m/z (%) = 420.2 (100) $[M+H]^+$. HRMS (ESI): calcd. for $C_{28}H_{37}NO_2 + H^+$ 420.2897; found 420.2897.

4-Benzyloxy-6-[2-(dimethylamino)ethoxy]-2-dodecylquinoline (18c): Sodium hydride (0.109 g, 2.74 mmol, 60% in mineral oil) was added slowly to a solution of **17c** (0.499 g, 1.19 mmol) in DMF (6 mL) at 0 °C. After stirring for 1 h at room temperature the solution was cooled to 0 °C, 2-dimethylaminoethyl chloride hydrochloride (0.180 g, 1.25 mmol) was added and the suspension was stirred at 100 °C for 2 h. After cooling to room temperature the reaction was quenched by addition of H_2O (10 mL) and the mixture extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with H_2O (2 × 50 mL) and brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (CH_2Cl_2/MeOH, 30:1, 1% NEt_3) provided **18c** (0.572 g, 98%) as a colorless solid. R_f = 0.30 (CH_2Cl_2/MeOH, 30:1, 1% NEt_3). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.6 Hz, 3 H, 12′′-H_3), 1.18–1.42 (m, 18 H, 3′′-H_2 to 11′′-H_2), 1.77 (m, 2 H, 2′′-H_2), 2.38 (s, 6 H, N(CH_3)$_2$), 2.79 (t, J = 6.0 Hz, 2 H, 1-H_2), 2.86 (t, J = 7.8 Hz, 2 H, 1′′-H_2), 4.18 (t, J = 6.0 Hz, 2 H, 2-H_2), 5.27 (s, 2 H, -CH_2Ph), 6.67 (s, 1 H, 3′-H), 7.30–7.53 (m, 7 H, 5′-H, 7′-H, 5 × Ph-H), 7.89 (d, J = 9.0 Hz, 1 H, 8′-H) ppm. **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 14.08 (C-12′′), 22.63 (C-11′′), 29.31, 29.51, 29.60, 29.62, 30.15, 31.86, 39.65 (C-1′′ to C-10′′), 45.84 (N(CH$_3$)$_2$), 58.17 (C-1), 66.12 (C-2), 70.05 (-CH$_2$Ph), 100.8, 101.1 (C-3′, C-5′), 120.5 (C-4a′), 121.9 (C-7′), 127.4 (2 × Ph-C_o), 128.2, 129.7 (C-8′, Ph-C_p), 128.6 (2 × Ph-C_m), 135.9, 144.6 (C-8a′, Ph-C_i), 155.9, 160.3, 161.5 (C-2′, C-4′, C-6′) ppm. **IR** (KBr): $\tilde{\nu}$ = 2920, 2850, 2769, 1598, 1568, 1503, 1468, 1359, 1266, 1222, 1077, 1032, 991, 838, 732, 697 cm^{-1}. **UV** (CH_3CN): λ_{max} (lg ε) = 235.0 (4.737), 273.5 (3.801), 317.5 (3.484), 330.0 nm (3.528). **MS** (ESI): m/z (%) = 491.3 (28) $[M+H]^+$, 401.3 (100) $[M–CH_2Ph+H]^+$. HRMS (ESI):

calcd. for $C_{32}H_{46}N_2O_2 + H^+$ 491.3632; found 491.3631.

4-Benzyloxy-6-[2-(dimethylamino)ethoxy]-2-dodecylquinoline *N,N'*-dioxide (19c): A solution of *m*-chloroperbenzoic acid (1.15 g, 4.68 mmol, 70%) in CH_2Cl_2 (100 mL) was added to a solution of **18c** (0.957 g, 1.95 mmol) in CH_2Cl_2 (100 mL). After stirring for 1.5 h at room temperature the solution was washed with saturated aq. $NaHCO_3$ (2 × 180 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (MeOH) provided **19c** (0.857 g, 84%) as a colorless solid. R_f = 0.17 (MeOH). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 6.6 Hz, 3 H, 12′′-H_3), 1.20–1.50 (m, 18 H, 3′′-H_2 to 11′′-H_2), 1.78 (m, 2 H, 2′′-H_2), 3.08 (t, J = 8.4 Hz, 2 H, 1′′-H_2), 3.34 (s, 6 H, N(CH_3)$_2$), 3.72 (t, J = 4.2 Hz, 2 H, 1-H_2), 4.72 (t, J = 4.2 Hz, 2 H, 2-H_2), 5.27 (s, 2 H, -CH_2Ph), 6.65 (s, 1 H, 3′-H), 7.30–7.50 (m, 6 H, 7′-H, 5 × Ph-H), 7.57 (d, J = 2.4 Hz, 1 H, 5′-H), 8.70 (d, J = 9.6 Hz, 1 H, 8′-H) ppm. **^{13}C-NMR** (125 MHz, $CDCl_3$): δ = 14.08 (C-12′′), 22.65, 26.37, 29.32, 29.43, 29.53, 29.57, 29.61, 29.64, 31.83, 31.89 (C-1′′ to C-11′′), 60.32 (N(*C*H_3)$_2$), 62.55 (C-2), 69.98 (C-1), 70.91 (-*C*H_2Ph), 102.1, 102.5 (C-5′, C-3′), 122.0, 122.2 (C-7′, C-8′), 122.7 (C-4a′), 127.6 (2 × Ph-C$_o$), 128.7 (Ph-C$_p$), 128.9 (2 × Ph-C$_m$), 135.2, 137.5 (Ph-C$_i$, C-8a′), 148.0, 151.6 (C-2′, C-4′), 156.5 (C-6′) ppm. **IR** (KBr): $\tilde{\nu}$ = 2921, 1576, 1471, 1202, 729 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 201.0 (4.263), 233.0 (4.622), 264.5 (4.060), 320.5 nm (3.832). **MS** (ESI): *m*/*z* (%) = 523.35 (100) $[M+H]^+$, 1045.70 (23) $[2M+H]^+$. HRMS (ESI): calcd. for $C_{32}H_{46}N_2O_4 + H^+$ 523.3530; found 523.3533.

6-[2-(Dimethylamino)ethoxy]-2-dodecyl-1-hydroxy-4-quinolone (5): Pd/C (10%, 115 mg) was added to a solution of **19c** (0.857 g, 1.64 mmol) in EtOH (130 mL). After applying an H_2 atmosphere (1 bar), the solution was stirred at room temperature for 1.3 h. After filtration through celite, which was thoroughly rinsed with EtOH (150 mL), the filtrate was concentrated under reduced pressure and the residue recrystallised from EtOH/acetone to give **5** (0.499 g, 73%) as a colorless solid. R_f = 0.42 (MeOH); **m.p.** 152 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 6.6 Hz, 3 H, 12′-H_3), 1.08–1.30 (m, 18 H, 3′-H_2 to 11′-H_2), 1.47 (m, 2 H, 2′-H_2), 2.34 (s, 6 H, N(CH_3)$_2$), 2.55 (m, 2 H, 1′-H_2), 2.77 (t, J = 4.2 Hz, 2 H, 2′′-H_2), 4.13 (t, J = 4.2 Hz, 2 H, 1′′-H_2), 6.21 (s, 1 H, 3-H), 7.20 (dd, J = 9.0, 1.8 Hz, 1 H, 7-H), 7.56 (d, J = 1.8 Hz, 1 H, 5-H), 7.98 (d, J = 9.0 Hz, 1 H, 8-H), 11.9 (s_{br}, 1 H, 1-O*H*) ppm. **^{13}C-NMR** (125 MHz, $CDCl_3$): δ = 14.07 (C-12′), 22.64 (C-11′), 27.43 (C-2′), 29.32, 29.34, 29.48, 29.59, 29.64, 29.69 (C-3′ to C-9′), 31.32 (C-1′), 31.89 (C-10′), 45.68 (N(*C*H_3)$_2$), 58.03 (C-2′′), 66.04 (C-1′′), 103.9 (C-5), 105.2 (C-3), 118.5 (C-8), 123.7 (C-7), 124.9 (C-4a), 136.0 (C-8a), 152.9 (C-2), 156.2 (C-6), 168.6 (C-4) ppm. **IR** (KBr): $\tilde{\nu}$ = 2922, 2854, 1467, 1234, 1028 cm^{-1}. **UV** (MeOH): λ_{max} (lg ε) = 222.5 (4.557), 259.0 (4.206), 270.0 (4.240), 352.5 nm (3.893). **MS** (ESI): *m*/*z* (%) = 417.31 (22) $[M+H]^+$, 833.61 (100) $[2M+H]^+$, 1249.92 (8) $[3M+H]^+$. HRMS (ESI): calcd. for $C_{25}H_{40}N_2O_3 + H^+$ 417.3112; found 417.3111.

$C_{25}H_{40}N_2O_3$ (416.60): calcd. C 72.08 H 9.68; found C 71.87 H 9.90.

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