Synthesis and redox potentials of methylated vitamin K derivatives

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We report the synthesis of derivatives of vitamin K_3 as well as of vitamins K_1 and K_2 containing a different number of methyl groups in various positions in order to reduce their redox potentials and to change systematically their steric features. The long aliphatic chain of vitamins K_1 and K_2 is simulated by an undecyl chain or a methyl group, respectively. The redox potentials of the first reduction step were measured by cyclic voltammetry in DMF. These compounds are relevant for studies of the structure–function relationship of vitamin K dependent enzymes and the investigation of electron transfer reactions in photosynthetic reaction centers.

Introduction

Among the naturally occurring naphthoquinones, which are widely distributed in microorganisms, plants and mammals, the most important compounds are vitamins of the K group. The basic structure of vitamin K is vitamin K_3 (2-methylnaphtho-1,4-quinone, menadione). In vitamin K_1 (2-methyl-3-phytylnaphtho-1,4-quinone, phylloquinone) and vitamin K_2 (2-methyl-3-(isoprenyl)$_{(7–9)}$naphtho-1,4-quinone, menaquinone) the hydrogen in position 3 is replaced by an aliphatic side chain.

Vitamin K serves as an essential cofactor for the carboxylase that activates the proteins of the blood-clotting cascade.[1] Several artificial vitamin K derivatives have been used for studying the vitamin K dependent carboxylase.[2,3]

Furthermore, the vitamins of the K group are involved as cofactors in various electron transfer reactions. Vitamin K_2 was identified as the primary electron acceptor in reaction centers in a number of photosynthetic bacteria[4–7] and vitamin K_1 was found to be the electron acceptor A_1 in the photosystem I of green plants.[8–10] Electron transfer reactions in biological systems depend strongly on the energetics of the involved cofactors. Hence, the systematic variation of the redox potentials of vitamin K derivatives is of major importance for the investigation of electron transfer reactions in photosynthetic reaction centers.[11–14]

The primary reaction in the bacterial reaction center protein from *Rhodobacter sphaeroides* is the absorption of light by the primary electron donor, D, and the subsequent rapid electron transfer *via* several intermediate acceptors, a bacteriopheophytin, Φ_A, a primary ubiquinone, Q_A, to the secondary ubiquinone, Q_B, forming the final charge separated state $D^+Q_AQ_B^-$. Recently, 2,3,5-trimethylnaphtho-1,4-quinone and 2,3,6,7-tetramethylnaphtho-1,4-quinone have been used to increase the energy level of $D^+Q_A^-Q_B$ relative to the ground state while retaining the native ubiquinone at the Q_B site.[15–17] To increase the free energy gap between the states $D^+Q_A^-Q_B$ and $D^+Q_AQ_B^-$ we synthesized various derivatives of vitamin K_3 as well as of vitamins K_1 and K_2. Their reduction potentials are varied by introducing methyl groups into the ring system. A long aliphatic chain substituent in position 3 is expected to drastically improve the binding affinity of these quinones to the Q_A site as has been found for ubiquinones.[18]

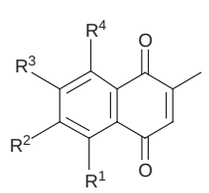
We have determined the redox potentials for the first reduction step of the quinones by cyclic voltammetry in DMF and discuss the influence of electron donating substituents on the *in vitro* redox properties.

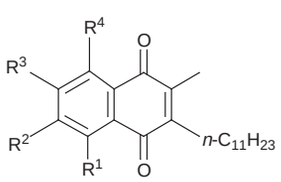
Results and discussion

Synthesis

Depending on the position of the methyl groups in the quinone ring system we chose three ways for the preparation of the naphthoquinone derivatives.

2,3-Dimethylnaphtho-1,4-quinone **3a**, 2,5-dimethylnaphtho-1,4-quinone **1a**, 2,6-dimethylnaphtho-1,4-quinone **1b**,





Vit K_3 $R^1 = R^2 = R^3 = R^4 = H$
1a R^1 = Me, $R^2 = R^3 = R^4 = H$
1b R^2 = Me, $R^1 = R^3 = R^4 = H$
1c R^3 = Me, $R^1 = R^2 = R^4 = H$
1d R^4 = Me, $R^1 = R^2 = R^3 = H$
1e $R^1 = R^4$ = Me, $R^2 = R^3 = H$
1f $R^2 = R^3$ = Me, $R^1 = R^4 = H$
1g $R^1 = R^2 = R^3 = R^4$ = Me

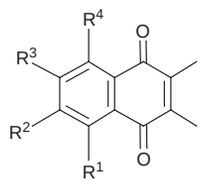
2a R^1 = Me, $R^2 = R^3 = R^4 = H$
2b R^2 = Me, $R^1 = R^3 = R^4 = H$
2c R^3 = Me, $R^1 = R^2 = R^4 = H$
2d R^4 = Me, $R^1 = R^2 = R^3 = H$
2e $R^1 = R^4$ = Me, $R^2 = R^3 = H$
2f $R^2 = R^3$ = Me, $R^1 = R^4 = H$
2g $R^1 = R^2 = R^3 = R^4$ = Me
2h $R^1 = R^2 = R^3 = R^4 = H$

2,7-dimethylnaphtho-1,4-quinone **1c**, 2,8-dimethylnaphtho-1,4-quinone **1d** and 2,3,5-trimethylnaphtho-1,4-quinone **3b** were synthesized from the corresponding naphthalenes (*i.e.* 2,3-dimethylnaphthalene, 1,6-dimethylnaphthalene, 2,6-dimethylnaphthalene, 2,7-dimethylnaphthalene, 1,7-dimethylnaphthalene and 1,6,7-trimethylnaphthalene, respectively), using the chromium trioxide oxidation procedure.[19] 2,3,6-Trimethylnaphtho-1,4-quinone **3c**, 2,5,8-trimethylnaphtho-1,4-quinone **1e**, 2,6,7-trimethylnaphtho-1,4-quinone **1f**, 2,3,5,8-tetramethylnaphtho-1,4-quinone **3d** and 2,3,6,7-tetramethylnaphtho-1,4-quinone **3e** were prepared *via* Diels–Alder additions using 2,3-dimethylbuta-1,3-diene, isoprene or hexa-2,4-diene as the diene and 2-methylbenzo-1,4-quinone or 2,3-dimethylbenzo-1,4-quinone as the dieneophile, followed by dehydrogenation of the adducts with activated MnO_2.[20] For the synthesis of naphthoquinones containing four methyl groups in positions 5,6,7 and 8 (**1g**, **2g**, **3f**), 2,3,4,5-tetramethylthiophene dioxide was prepared to act as the diene reagent.

During the TLC of the Diels–Alder adduct of 2,3,4,5-tetramethylthiophene dioxide and the benzoquinone, a change in the colour of the TLC spot from brown to yellow was observed,

Table 1 Reduction potentials of vitamin K_3 derivatives *vs.* ferrocene/ferrocinium

Quinone	*E*/mV	*E*/mV (calc.)
Vitamin K_3	−1146	−1140
1a	−1218	−1220
1b	−1173	−1180
1c	−1179	−1180
1d	−1224	−1220
1e	−1300	−1300
1f	−1209	−1220
1g	−1391	−1380
Ubiquinone	−1103	—



3a $R^1 = R^2 = R^3 = R^4 = H$
3b $R^1 = Me$, $R^2 = R^3 = R^4 = H$
3c $R^2 = Me$, $R^1 = R^3 = R^4 = H$
3d $R^1 = R^4 = Me$, $R^2 = R^3 = H$
3e $R^2 = R^3 = Me$, $R^1 = R^4 = H$
3f $R^1 = R^2 = R^3 = R^4 = Me$

indicating the formation of a naphthoquinone. Based on this finding, the Diels–Alder adducts were treated with silica to catalyse the loss of SO_2 and the air oxidation to 2,5,6,7,8-pentamethylnaphtho-1,4-quinone **1g** and 2,3,5,6,7,8-hexamethylnaphtho-1,4-quinone **3f**, respectively. For the synthesis of the vitamin $K_{1,2}$ derivatives (**2a**–**2h**) containing an undecyl chain in position 3, we used the radical alkylation of the corresponding vitamin K_3 derivatives with lauric acid (dodecanoic acid) in the presence of $(NH_4)_2S_2O_8$ and $AgNO_3$.[21]

Redox potentials

The redox potentials of methyl substituted vitamin K derivatives were measured by cyclic voltammetry (Tables 1–3). The redox potentials of vitamin K_1, vitamin K_2, 2,3-dimethylnaphtho-1,4-quinone **3a** and 2-methyl-3-undecylnaphtho-1,4-quinone **2h** agree within the accuracy of the method (±15 mV) indicating that the effect of either an alkyl or isoprenyl substituent in position 3 on the reduction potential is very similar. An increasing number of methyl substituents results in a decrease in the reduction potential due to the electron donating effect (+I effect) of alkyl substituents. The reduction potential of the vitamin $K_{1,2}$ derivatives is, in the case of the undecyl substituent, ≈75 mV (see Tables 1 and 2), and in the case of a methyl substituent, ≈85 mV (see Tables 1 and 3) smaller than was found for the corresponding vitamin K_3 analogues since an additional alkyl substituent is present in position 3. For methyl substituents in the aryl ring increments of ≈−80 mV for the positions 5 and 8 (**1a**, **1d**, **1e**, **1g**, **2a**, **2d**, **2e**, **2g**, **3b**, **3d**, **3f**) and ≈−40 mV for the positions 6 and 7 (**1b**, **1c**, **1f**, **1g**, **2b**, **2c**, **2f**, **2g**, **3c**, **3e**, **3f**) were determined. These increments are additive and allow predictions of the reduction potentials of other alkyl substituted naphthoquinones. Column 3 of Tables 1, 2 and 3 refers to the calculated redox potentials using the increments mentioned above and a value of −1140 mV for vitamin K_3.

The *in vitro* reduction potentials cannot be related quantitatively to the *in situ* reduction potentials of the quinone bound at the Q_A site in the bacterial reaction center because these depend subtly on the interactions with the protein environment and the nature of the solvent. However, the effect of methyl substituents is expected to be comparable. Work is in progress to determine the actual *in situ* reduction potentials by correlating the intensity of the delayed fluorescence emitted during the life time of the state $D^+Q_A^-$ to the reduction potentials measured in DMF as described previously.[22]

Table 2 Reduction potentials of vitamin $K_{1,2}$ derivatives containing a long alkyl chain in position 3 *vs.* ferrocene/ferrocinium

Quinone	*E*/mV	*E*/mV (calc.)
2h	−1206	−1215
Vitamin K_2	−1219	−1215
Vitamin K_1	−1197	−1215
2a	−1288	−1295
2b	−1261	−1255
2c	−1255	−1255
2d	−1295	−1295
2e	−1366	−1375
2f	−1294	−1295
2g	−1477	−1455
Ubiquinone	−1103	—

Table 3 Reduction potentials of vitamin $K_{1,2}$ derivatives containing a methyl group in position 3 *vs.* ferrocene/ferrocinium

Quinone	*E*/mV	*E*/mV (calc.)
3a	−1227	−1225
3b	−1297	−1305
3c	−1279	−1265
3d	−1386	−1385
3e	−1280	−1305
3f	−1487	−1465
Ubiquinone	−1103	—

In this work we have reported the synthesis of several vitamin K derivatives covering a wide range of reduction potentials (−43 to −384 mV relative to ubiquinone). Their functional reconstitution to the Q_A site under conditions where ubiquinone is present at Q_B provides a powerful tool to study the coupling between proton transfer and electron transfer reactions in bacterial reaction centers. In addition, this pool of vitamin K derivatives with its systematic variation of the substitution pattern is useful for the investigation of steric properties on the structure–function relationships of vitamin K dependent enzymes.

Experimental

Cyclic voltammetry

Cyclic voltammetry was performed at a platinum working electrode with a platinum counter electrode and silver reference electrode using a potentiostat of local design ($T = 293$ K). The voltammograms were recorded in DMF with 50 mM tetra-*n*-butylammonium tetrafluoroborate as supporting electrolyte at a voltage sweep rate of 20–100 mV s^{-1}. Reduction potentials for the redox couple Q/Q^- were reported against ferrocene as internal standard. Under these conditions ferrocene has a half-reduction potential of +524 mV relative to the saturated calomel electrode.[23]

General methods

Melting points were uncorrected. ^{1}H NMR spectra were recorded on a Bruker WM 250 spectrometer in $CDCl_3$ solution with tetramethylsilane as internal standard. Elemental analyses were performed by the Analytische Abteilung des Chem. Laboratoriums of the Albert-Ludwigs-Universität Freiburg.

Synthesis

Naphthalene oxidation (general procedure).[19] These reactions were performed with slight modifications of the method

described in the literature. CrO_3 (3.0 g, 30 mmol) dissolved in acetic acid (8 ml; 50%) was added dropwise at 10 °C over 1 h to a solution of the naphthalene (6.4 mmol) in acetic acid (25 ml, 90%). The mixture was heated to 50 °C and stirred at this temperature for 45 min. The reaction mixture was diluted with ice–water (25 ml) to precipitate the quinone. The raw product was filtered over a Büchner funnel, washed with 25 ml water, dried *in vacuo* and recrystallized from methanol.

2,3-Dimethylnaphtho-1,4-quinone 3a. Quinone **3a** was synthesized starting from 2,3-dimethylnaphthalene (1.00 g, 6.4 mmol) and gave yellow needles (1.00 g, 84%), mp 88 °C, (lit.,[24] 88–90 °C); δ_H (250 MHz, $CDCl_3$) 2.12 (s, 6 H), 7.58–7.66 (m, 2 H), 7.95–8.08 (m, 2 H).

2,5-Dimethylnaphtho-1,4-quinone 1a. The quinone **1a** was prepared from 1,6-dimethylnaphthalene (1.00 g, 6.4 mmol) as starting material. In this case the general procedure had to be modified as follows. The reaction mixture was extracted three times with diethyl ether, neutralized with saturated $NaHCO_3$ solution and the collected organics were dried over $MgSO_4$. After evaporation of the solvent the remainder was purified by column chromatography with cyclohexane–ethyl acetate (10 : 1) as eluant. Crystallization from methanol gave **1a** (0.25 g, 21%) as yellow needles, mp 93 °C (lit.,[25] 95 °C); δ_H (250 MHz, $CDCl_3$) 2.10 (s, 3 H), 2.68 (s, 3 H), 6.70 (s, 1 H), 7.40–7.55 (m, 2 H), 7.96 (d, 1 H).

2,6-Dimethylnaphtho-1,4-quinone 1b. The starting material for **1b** was 2,6-dimethylnaphthalene (1.00 g, 6.4 mmol). Quinone **1b** formed as yellow needles (0.94 g, 79%), mp 135–136 °C, (lit.,[25] 136–137 °C); δ_H (250 MHz, $CDCl_3$) 2.19 (s, 3 H), 2.49 (s, 3 H), 6.81 (s, 1 H), 7.52 (d, 1 H), 7.85 (s, 1 H), 7.99 (d, 1 H).

2,7-Dimethylnaphtho-1,4-quinone 1c. The quinone **1c** was prepared from 2,7-dimethylnaphthalene (1.00 g, 6.4 mmol) and formed as yellow needles (0.80 g, 67%), mp 111–112 °C (lit.,[25] 114 °C); δ_H (250 MHz, $CDCl_3$) 2.14 (s, 3 H), 2.46 (s, 3 H), 6.75 (s, 1 H), 7.49 (d, 1 H), 7.84 (s, 1 H), 7.91 (d, 1 H).

2,8-Dimethylnaphtho-1,4-quinone 1d. Starting from 1,7-dimethylnaphthalene (1.00 g, 6.4 mmol) **1d** was obtained as yellow needles (0.38 g, 32%), mp 132 °C (lit.,[26] 135 °C); δ_H (250 MHz, $CDCl_3$) 2.10 (s, 3 H), 2.69 (s, 3 H), 6.73 (s, 1 H), 7.40–7.57 (m, 2 H), 7.95 (d, 1 H).

2,3,5-Trimethylnaphtho-1,4-quinone 3b. Quinone **3b** was prepared from 1,6,7-trimethylnaphthalene (0.50 g, 2.9 mmol). Quinone **3b** formed as yellow needles (0.31 g, 54%), mp 126 °C (lit.,[19] 128 °C); δ_H (250 MHz, $CDCl_3$) 2.15 (s, 6 H), 2.74 (s, 3 H), 7.44–7.58 (m, 2 H), 8.01 (d, 1 H).

General procedure for Diels–Alder reactions and subsequent oxidation

The freshly distilled diene (isoprene, hexa-2,4-diene or 2,3-dimethylbuta-1,3-diene; 61 mmol) and the dieneophile (2-methylbenzo-1,4-quinone or 2,3-dimethylbenzo-1,4-quinone; 61 mmol) were dissolved in ethanol (25 ml) and refluxed over night. After cooling with ice the brown precipitate was recrystallized from cyclohexane. The adduct was suspended together with activated MnO_2 (5.0 g, 57 mmol per 1.0 g of the adduct) in petrol ether 60–70 °C (100 ml per 1.0 g of the adduct) and refluxed. After 7 h the hot suspension was filtered off and the remainder washed twice with petrol ether 60–70 °C. The organics were collected and the solvent was evaporated off *in vacuo*. The raw product was recrystallized from ethanol.

2,3,6-Trimethylnaphtho-1,4-quinone 3c. Starting from 2,3-dimethylbenzo-1,4-quinone and isoprene, **3c** formed as yellow needles (6.8 g, 56%), mp 101–102 °C, (lit.,[27] 103 °C); δ_H (250 MHz, $CDCl_3$) 2.09 (s, 6 H), 2.43 (s, 3 H), 7.47 (d, 1 H), 7.81 (s, 1 H), 7.92 (d, 1 H).

2,5,8-Trimethylnaphtho-1,4-quinone 1e. The naphthoquinone **1e** was synthesized from hexa-2,4-diene and 2-methylbenzo-1,4-quinone. Quinone **1e** formed as yellow needles (2.9 g, 24%), mp 104–105 °C ($C_{13}H_{12}O_2$ requires: C, 77.98; H, 6.04. Found: C, 77.92; H, 6.14%); δ_H (250 MHz, $CDCl_3$) 2.08 (s, 3 H), 2.62 (s, 6 H), 6.65 (s, 1 H), 7.31 (s, 2 H).

2,6,7-Trimethylnaphtho-1,4-quinone 1f. Product **1f** was prepared from 2,3-dimethylbuta-1,3-diene and 2-methylbenzo-1,4-quinone and gave yellow needles (6.2 g, 51%), mp 105–106 °C, (lit.,[28] 108 °C); δ_H (250 MHz, $CDCl_3$) 2.12 (s, 3 H), 2.35 (s, 6 H), 6.70 (s, 1 H), 7.76 (s, 1 H), 7.80 (s, 1 H).

2,3,5,8-Tetramethylnaphtho-1,4-quinone 3d. Quinone **3d** was synthesized from hexa-2,4-diene and 2,3-dimethylbenzo-1,4-quinone and formed yellow needles (5.0 g, 39%), mp 122–123 °C ($C_{14}H_{14}O_2$ requires: C, 78.48; H, 6.57. Found: C, 78.34; H, 6.73%); δ_H (250 MHz, $CDCl_3$) 2.05 (s, 6 H), 2.61 (s, 6 H), 7.29 (s, 2 H).

2,3,6,7-Tetramethylnaphtho-1,4-quinone 3e. Oxidation of the Diels–Alder adduct of 2,3-dimethylbuta-1,3-diene and 2,3-dimethylbenzo-1,4-quinone yielded **3e** as yellow needles (7.0 g, 54%), mp 169–170 °C, (lit.,[29] 170 °C); δ_H (250 MHz, $CDCl_3$) 2.09 (s, 6 H), 2.33 (s, 6 H), 7.75 (s, 2 H).

3,4-Bis(chloromethyl)-2,5-dimethylthiophene 4. Refluxing of 2,5-dimethylthiophene (30.0 g, 267 mmol) with trioxane (72.0 g, 801 mmol) in the presence of conc. HCl (100 ml) gave **4** (50.1 g, 90%), mp 73 °C , (lit.,[30] 73 °C); δ_H (250 MHz, $CDCl_3$) 2.41 (s, 6 H), 4.62 (s, 4 H).[31]

2,3,4,5-Tetramethylthiophene 5. The intermediate product **4** (46.0 g, 220 mmol) was subsequently reduced with LiAH (25 g, 660 mmol) in absolute diethyl ether (600 ml) to give **5** (17.3 g, 56%), bp 73–74 °C/33 mbar (lit.,[30] 74–79 °C/20 mbar); δ_H (250 MHz, $CDCl_3$) 1.93 (s, 6 H), 2.20 (s, 6 H).[31]

2,3,4,5-Tetramethylthiophene dioxide 6. Compound **5** (16.3 g, 116 mmol), dissolved in CH_2Cl_2 (35 ml), was added dropwise over an hour at 0 °C to a solution of MCPBA (60.0 g, 348 mmol) in CH_2Cl_2 (450 ml). Stirring was continued for 6 hours at room temperature. The reaction mixture was cooled to −70 °C and filtered off. The filtrate was washed twice with saturated $NaHCO_3$ solution and the solvent was evaporated off. The residue was recrystallized from diethyl ether and gave colourless needles (8.4 g, 42%), mp 116 °C, (lit.,[32] 116–117.5 °C); δ_H (250 MHz, $CDCl_3$) 1.92 (s, 6 H), 2.02 (s, 6 H).

2,5,6,7,8-Pentamethylnaphtho-1,4-quinone 1g. 2-Methylbenzo-1,4-quinone (0.73 g, 6.0 mmol) and **6** (1.03 g, 6.0 mmol) were dissolved in chloroform (30 ml) and refluxed for 24 h. The solvent was removed *in vacuo* and the black precipitate redissolved in diethyl ether. Silica was added and the suspension was allowed to stand at room temperature overnight. The silica adsorbed product was extracted twice with diethyl ether (2 × 50 ml). The collected extracts were washed with H_2O and the solvent was evaporated off. The crude product was purified by column chromatography (silica, cyclohexane–ethyl acetate 10 : 1) and recrystallized from ethanol. Quinone **1g** formed as yellow needles (0.63 g, 46%), mp 107–108 °C ($C_{15}H_{16}O_2$ requires: C, 78.92; H, 7.06. Found: C, 78.72; H, 6.88%); δ_H (250 MHz, $CDCl_3$) 2.04 (s, 3 H), 2.27 (s, 6 H), 2.54 (s, 6 H), 6.56 (s, 1 H).

2,3,5,6,7,8-Hexamethylnaphtho-1,4-quinone 3f. The naphthoquinone **3f** was prepared from 2,3-dimethylbenzo-1,4-quinone

(0.82 g, 6.0 mmol) and **6** (1.03 g, 6.0 mmol) as described for **1g**. Quinone **3f** gave yellow needles (0.78 g, 54%), mp 135–136 °C ($C_{16}H_{18}O_2$ requires: C, 79.31; H, 7.49. Found: C, 79.15; H, 7.56%); δ_H (250 MHz, $CDCl_3$) 2.03 (s, 6 H), 2.28 (s, 6 H) 2.52 (s, 6 H).

Alkylation of 1a–1g (general procedure)

The alkylation was performed with some modifications of a literature method.[33,24] A solution of $(NH_4)S_2O_8$ (2.1 g, 9.1 mmol) in H_2O (20 ml) was added dropwise using a perfusor (5 ml h^{-1}) to a vigorously stirred solution of vitamin K_3 or **1a**–**1g** (3.0 mmol), dodecanoic acid (840 mg, 4.2 mmol) and $AgNO_3$ (720 mg, 4.2 mmol) in a mixture of acetonitrile (60 ml) and water (30 ml). After a further 30 minutes of stirring the reaction was allowed to cool to room temperature. The suspension was extracted three times with diethyl ether. The extract was washed with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$. After evaporation of the solvent the product was recrystallized twice from methanol and if necessary further purified with PTLC using a mixture of cyclohexane and ethyl acetate (5:1) as eluant.

2-Methyl-3-undecylnaphtho-1,4-quinone 2h. The derivative **2h** was prepared from vitamin K_3 (517 mg, 3.0 mmol) and formed yellow needles (595 mg, 61%), mp 86 °C (lit.,[33] 82–83 °C); δ_H (250 MHz, $CDCl_3$) 0.88 (t, 3 H), 1.18–1.54 (m, 18 H), 2.20 (s, 3 H), 2.65 (t, 2 H), 7.66–7.72 (m, 2 H), 8.04–8.12 (m, 2 H).

2,5-Dimethyl-3-undecylnaphtho-1,4-quinone 2a. The alkylation of **1a** (186 mg, 1.0 mmol) yields **2a** (129 mg, 38%) as yellow needles, mp 62–63 °C ($C_{23}H_{32}O_2$ requires: C, 81.13; H, 9.47. Found: C, 80.99; H, 9.53%); δ_H (250 MHz, $CDCl_3$) 0.81 (t, 3 H), 1.13–1.55 (m, 18 H), 2.09 (s, 3 H), 2.55 (t, 2 H), 2.68 (s, 3 H), 7.37–7.50 (m, 2 H), 7.94 (d, 1 H).

2,6-Dimethyl-3-undecylnaphtho-1,4-quinone 2b. The synthesis of **2b** started with **1b** (559 mg, 3.0 mmol). Quinone **2b** (582 mg, 57%) was obtained as yellow needles, mp 77–78 °C ($C_{23}H_{32}O_2$ requires: C, 81.13; H, 9.47. Found: C, 80.96; H, 9.54%); δ_H (250 MHz, $CDCl_3$) 0.85 (t, 3 H), 1.14–1.45 (m, 18 H) 2.16 (s, 3 H), 2.45 (s, 3 H), 2.58 (t, 2 H), 7.48 (d, 1 H), 7.83 (s, 1 H), 7.95 (d, 1 H).

2,7-Dimethyl-3-undecylnaphtho-1,4-quinone 2c. The starting material for **2c** was **1c** (559 mg, 3.0 mmol). Quinone **2c** (623 mg, 61%) formed as yellow needles, mp 52–53 °C ($C_{23}H_{32}O_2$ requires: C, 81.13; H, 9.47. Found: C 80.65; H, 9.36%); δ_H (250 MHz, $CDCl_3$) 0.85 (t, 3 H), 1.13–1.49 (m, 18 H), 2.14 (s, 3 H), 2.44 (s, 3 H), 2.58 (t, 2 H), 7.48 (d, 1 H), 7.85 (s, 1 H), 7.96 (d, 1 H).

2,8-Dimethyl-3-undecylnaphtho-1,4-quinone 2d. The quinone **2d** (204 mg, 41%) resulted from **1d** (279 mg, 1.5 mmol) as yellow needles, mp 72 °C ($C_{23}H_{32}O_2$ requires: C, 81.13; H, 9.47. Found: C 81.06; H, 9.54%); δ_H (250 MHz, $CDCl_3$) 0.82 (t, 3 H), 1.12–1.52 (m, 18 H), 2.10 (s, 3 H), 2.55 (t, 2 H), 2.67 (s, 3 H), 7.38–7.55 (m, 2 H), 7.95 (d, 1 H).

2,5,8-Trimethyl-3-undecylnaphtho-1,4-quinone 2e. Derivative **2e** was synthesized from **1e** (601 mg, 3.0 mmol). Quinone **2e** (425 mg, 40%) crystallized as yellow plates, mp 49–50 °C ($C_{24}H_{34}O_2$ requires: C, 81.31; H, 9.67. Found: C, 80.86; H, 9.79%); δ_H (250 MHz, $CDCl_3$) 0.82 (t, 3 H), 1.12–1.51 (m, 18 H), 2.08 (s, 3 H), 2.53 (t, 2 H), 2.61 (s, 6 H), 7.28 (s, 2 H).

2,6,7-Trimethyl-3-undecylnaphtho-1,4-quinone 2f. The quinone **2f** (457 mg, 43%) was prepared from **1f** (601 mg, 3.0 mmol) and formed as yellow needles, mp 92 °C ($C_{24}H_{34}O_2$ requires: C, 81.31; H, 9.67. Found: C, 81.11; H, 9.87%); δ_H (250 MHz, $CDCl_3$) 0.81 (t, 3 H), 1.11–1.58 (m, 18 H), 2.10 (s, 3 H), 2.28 (s, 6 H), 2.53 (t, 2 H), 7.76 (s, 2 H).

2,5,6,7,8-Pentamethyl-3-undecylnaphtho-1,4-quinone 2g. The alkylation of **1g** (228 mg, 1.0 mmol) yielded **2g** (140 mg, 38%) as yellow needles, mp 72–73 °C ($C_{26}H_{38}O_2$ requires: C, 81.62; H, 10.01. Found: C, 81.31; H, 10.42%); δ_H (250 MHz, $CDCl_3$) 0.82 (t, 3 H), 1.10–1.51 (m, 18 H), 2.02 (s, 3 H), 2.25 (s, 6 H), 2.48 (t, 2 H) 2.50 (s, 6 H).

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