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A practical procedure for multisubstituted β-naphthols and their derivatives

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Abstract—A number of multisubstituted β-naphthols were efficiently prepared by intramolecular aldol condensation of readily available substituted benzyaldehydes, whose substituents were introduced easily by a selective alkylation on the benzylic position of the substrates.

1. Introduction

The multisubstituted naphthalenes and naphthols have attracted much attention on account of their usefulness as bioactive agents, where the substitution patterns may play an important role in the biological activities,[1] as well as their potential as intermediates in structural and synthetic chemistry.[2] The most important step in the synthetic pathways to construct these molecules is the introduction of suitable substitution groups into the naphthalene skeleton, which is often not easily achieved by those conventional electrophilic aromatic substitutions, especially owing to the problems associated with regiochemical control. The various substitutions of naphthalene-based complex structure are usually introduced at the stage of starting material.[3] Therefore, the development of efficient synthetic strategies and methods is a very important issue today in the synthesis of multisubstituted naphthalenes and naphthols.

In the course of our synthetic study toward the natural product chlorofusin,[4] we found that the key intermediate **8a** was very susceptible to cyclization in the presence of base to furnish β-naphthol **9a**. It gave us an idea to check the generality of this transformation and its potential applications in the synthesis of multisubstituted naphthalene-based structures. Herein we describe our recent results on the synthetic investigation of highly substituted β-naphthols utilizing the above mentioned aldol condensation of benzyaldehydes. The newly developed synthetic procedure for α-substituted β-naphthols allows to establish diverse substituents easily in the α-position. These naphthols would be very useful in the synthesis of many naturally occurring products. For example, naphthol **9a** could be modified and applied in the synthesis of quinonoid compounds, which acted as potential intermediates in the synthesis of biologically important naphthoquinones[5] and heterocycles[6] (Fig. 1).

2. Results and discussion

The presented procedure was started from aldehyde **1**, which could be easily prepared by a known method.[7] Dithioacetal **4** was synthesized by condensation of benzyl chloride **2** with lithium salt of 1,3-dithane **3**. At this stage, the dithiane and dimethylacetal protecting groups allowed **4** to expose to severe basic reaction conditions, such as metallation in the 4-position of the benzene ring to introduce

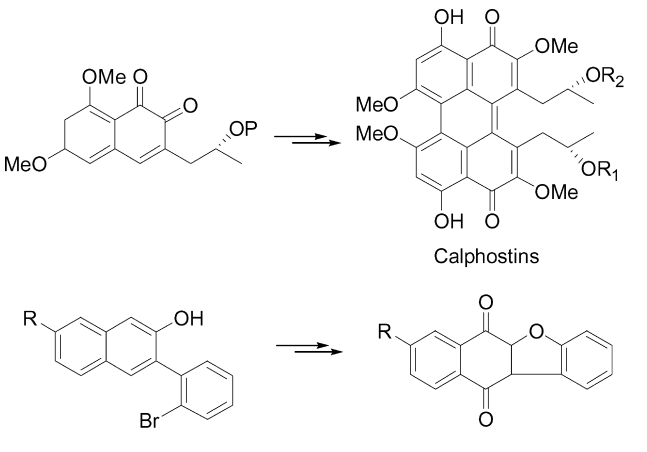

Figure 1. Examples of naturally occurring naphthoquinones and their multisubstituted naphthol-based synthetic intermediates.

Keywords: β-naphthols; benzyaldehyde; benzylic position.
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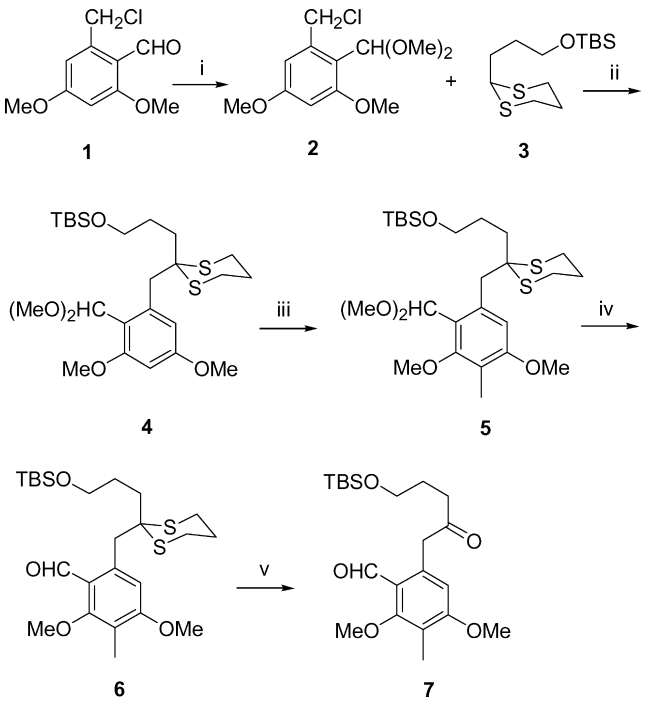
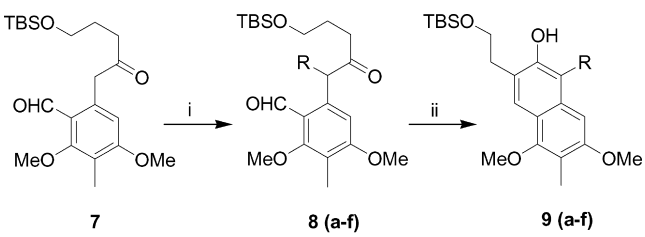


Scheme 1. *Reagents and conditions*: (i) $CH(OMe)_3$, *p*-TsOH, MeOH, 50°C, 87%; (ii) *n*-BuLi, THF, −78 to −20°C, **3**, 42%; (iii) *n*-BuLi, THF, MeI, −78 to −10°C, 75%; (iv) Acetone, *p*-TsOH (cat), 94%; (v) $Hg(OAc)_2$, CH_3CN/H_2O, 83%.

an alkyl group, affording alkylated product **5**. The subsequent facile removal of the acetal (with *p*-TsOH) and dithiane (with $Hg(OAc)_2$) both in high yields makes this synthetic route to precursor **7** very simple and efficient (Scheme 1).

With the intermediate **7** in hand, a selective alkylation on the benzylic position with various alkyl halides was performed by using *n*-Bu_4NOH as the base, affording **8**(**b**–**f**) in desirable yields. Other bases, such as tetrapropylammonium hydroxide, had also been investigated, but most



Scheme 2. *Reagents and conditions*: (i) RX, CH_2Cl_2, *n*-Bu_4NOH (10%), 40°C; (ii) MeOH, aq NaOH, rt.

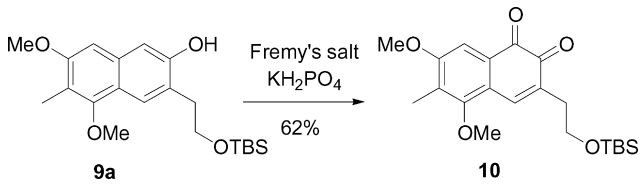
Table 1. The results of alkylation of **7** and intramolecular aldol condensation of **8**

Entry	Alkyl halide (RX)	Yield (%)[a]	
		Product **8**	Product **9**
1	R=H (**7**=**8a**)		**9a**/86
2	MeI	**8b**/74	**9b**/77
3	EtI	**8c**/78	**9c**/72
4	Allyl bromide	**8d**/87	**9d**/40
5	BnBr	**8e**/85	**9e**/67
6	PMBBr	**8f**/92	**9f**/65

[a] Isolated yields.

of them made the reaction more complicated. Finally, an intramolecular aldol condensation of **8**(**a**–**f**) with sodium hydroxide, and dehydration in situ provided the corresponding α-substituted β-naphthols **9**(**a**–**f**) in moderate to good yields (Scheme 2 and Table 1).

As an application, the multisubstituted naphthols could be easily converted to the corresponding naphthoquinones by various oxidative conditions. Thus, **9a** (it was slightly unstable when exposed to air) could be converted into *o*-naphthoquinone **10** in 62% yield by treatment with Fremy's salt[8] in THF (Scheme 3).



Scheme 3.

3. Conclusion

In summary, we have developed an efficient way to the synthetically important intermediate **7**, which allows us to introduce a variety of substitutents on the benzylic position by a convenient alkylation reaction. A subsequent intramolecular aldol condensation of intermediates **8**(**a**–**f**) leads to α-substituted β-naphthols that contain a variety of substituents at its α-position.

4. Experimental

4.1. General

^1H NMR spectra were recorded on a Varian 300 MHz spectrometer for solution in $CDCl_3$ with TMS as internal standards. IR spectra were recorded on an FT-IR instrument. MPs were obtained with a Yanagimoto micro melting point apparatus and are uncorrected. Mass spectra were recorded with a HP-5989 instrument and HRMS were measured by a Finnigan MA^+ mass spectrometer. Flash column chromatography was performed on silica gel (10–40 μm) using a mixture of petroleum ether and ethyl acetate as the eluent.

4.1.1. 1-Chloromethyl-2-dimethoxymethyl-3,5-dimethoxybenzene (2). To a solution of **1**[7] (195 mg, 1 mmol) and *p*-TsOH (8 mg, cat) in anhydrous methanol (5 mL) was added $CH(OMe)_3$ (0.6 mL, 5.5 mmol). After being stirred at 45°C for 2 h, Et_3N (1 mL) was added and most of the solvent was removed under reduced pressure. The residue was partitioned between water and ethyl ether. The organic phase was separated and washed with brine, dried over Na_2SO_4 and evaporated. The crude white solid product was dried and used directly without further purification (206 mg, 87%). ^1H NMR (300 MHz, $CDCl_3$): δ 6.70 (d, *J*=2.4 Hz, 1H), 6.40 (d, *J*=2.4 Hz, 1H), 5.72 (s, 1H), 4.96 (s, 2H), 3.82 (s, 3H), 3.80 (s, 3H), 3.40 (s, 6H) ppm.

4.1.2. *tert*-Butyl-(3-[1,3]dithian-2-ylpropoxy)dimethylsilane (3). To a solution of 3-[1,3]dithian-2-ylpropan-1-ol[9]

(40.72 g, 228 mmol), imidazole (25 g, 365 mmol) in DMF (50 mL) was added dropwise a solution of TBSCl (45 g, 297 mmol) in DMF (80 mL). The reaction mixture was stirred at 0°C for 1 h and then at room temperature for another 1 h. The reaction was quenched by aqueous NH_4Cl solution (150 mL), extracted with EtOAc (3×150 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, concentrated and purified by chromatography to afford product as a colorless oil (64.2 g, 96%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.00 (t, J=6.6 Hz, 1H), 3.60 (t, J=6.0 Hz, 2H), 2.82–2.78 (m, 4H), 2.10–1.60 (m, 6H), 0.82 (s, 9H), 0.00 (s, 6H) ppm. IR (neat, cm^{-1}): 2953, 2858, 1256, 1105, 837, 776. EIMS (*m*/*z*): 291 $(M-1)^+$.

4.1.3. *tert*-Butyl-{3-[2-(2-dimethoxymethyl-3,5-dimethoxybenzyl)-[1,3]dithian-2-yl]propoxy}dimethylsilane (4). A solution of the dithiane **3** (3.81 g, 13.05 mmol) in THF (20 mL) at −78°C was treated with 1.6 M *n*-BuLi in hexane (10 mL, 16.0 mmol). The resulting reaction solution was stirred at −40°C for 3 h and then at −30°C for 1.5 h. To the solution cooled at −78°C was added benzyl chloride **2** (2.83 g, 10.9 mmol) in THF (25 mL) slowly and the reaction mixture was warmed to room temperature overnight. The reaction was quenched with brine and the aqueous phase was extracted with ethyl acetate. The combined organic extracts were dried over Na_2SO_4 and evaporated, the residue was purified by chromatography to afford the crude product **4** as a yellow oil (2.33 g, 42%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18 (d, J=2.4 Hz, 1H), 6.38 (d, J=2.4 Hz, 1H), 5.72 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.60 (s, 2H), 3.58 (t, J=6.3 Hz, 2H), 3.40 (s, 6H), 2.94–2.90 (m, 4H), 2.00–1.60 (m, 6H), 0.90 (s, 9H), 0.01 (s, 6H) ppm. EIMS (*m*/*z*): 485 $(M-31)^+$.

4.1.4. *tert*-Butyl-{3-[2-(2-dimethoxymethyl-3,5-dimethoxy-4-methylbenzyl)-[1,3]dithian-2-yl]propoxy}-dimethylsilane (5). A solution of crude **4** (16.57 g, 32.0 mmol) in THF (100 mL) at −78°C was treated with 1.6 M *n*-BuLi (34.0 mL, 54.6 mmol). The mixture was stirred at −20°C for 5 h and then at −10°C for 0.5 h. MeI (6.0 mL, 96 mmol) was added dropwise, and the mixture was stirred at room temperature overnight. The reaction was quenched with aqueous brine and extracted with acetyl acetate. The combined extracts were dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography and recrystallized from hexane and ethyl acetate to give **5** as a white solid (12.8 g, 75%). Mp: 81–82°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18 (s, 1H), 5.58 (s, 1H), 3.80 (s, 3H), 3.68 (s, 3H), 3.60 (s, 2H), 3.58 (t, J=6.3 Hz, 2H), 3.40 (s, 6H), 3.00–2.80 (m, 4H), 2.12 (s, 3H), 2.08–1.62 (m, 6H), 0.87 (s, 9H), 0.00 (s, 6H) ppm. IR (KBr, cm^{-1}): 2925, 2884, 1606, 1577, 1446, 1124, 1067, 848, 774. ESIMS (*m*/*z*): 553 $(M+Na)^+$. Anal. calcd for $C_{26}H_{46}O_5S_2Si$: C, 58.83; H, 8.73. Found: C, 58.87; H, 8.60.

4.1.5. 6-{2-[3-(*tert*-Butyldimethylsilyloxy)propyl]-[1,3]dithian-2-ylmethyl}-2,4-dimethoxy-3-methylbenzaldehyde (6). A solution of **5** (83 mg, 0.16 mmol) in acetone (2 mL) was treated with *p*-TsOH (cat) at room temperature for 5 min. The reaction was quenched with aqueous Na_2CO_3 solution and the organic solvent was removed under reduced pressure. The resulting mixture was extracted with ethyl acetate. The combined extracts were washed with water and brine, dried over Na_2SO_4, evaporated and purified by chromatography to give **6** as a colorless oil (61 mg, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.40 (s, 1H), 6.80 (s, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.70 (s, 2H), 3.60 (t, J=6.0 Hz, 2H), 2.90–2.70 (m, 4H), 2.16 (s, 3H), 1.95–1.70 (m, 6H), 0.80 (s, 9H), 0.09 (s, 6H) ppm. EIMS (*m*/*z*): 469 $(M-15)^+$. IR (liquid film, cm^{-1}): 2954, 2931, 2857, 1682, 1598, 1568, 1464, 1383, 1292, 1257, 1129, 837, 777. Anal. calcd for $C_{24}H_{40}O_4S_2Si$: C, 59.46; H, 8.32. Found: C, 59.50; H, 8.63.

4.1.6. 6-[5-(*tert*-Butyldimethylsilyloxy)-2-oxopentyl]-2,4-dimethoxy-3-methylbenzaldehyde (7). To a solution of **6** (218 mg, 0.45 mmol) in CH_3CN (8 mL) and H_2O (2 mL) was added $Hg(OAc)_2$ (359 mg, 1.13 mmol). After a while, the resulting solution became homogenous and a white slurry appeared. After being stirred at room temperature for 1 h, the mixture was filtered through celite and washed with CH_2Cl_2. The organic layer was separated and washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography to give **7** as a yellow oil (147 mg, 83%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.20 (s, 1H), 6.40 (s, 1H), 4.00 (s, 2H), 3.80 (s, 3H), 3.75 (s, 3H), 3.60 (t, J=6.0 Hz, 2H), 2.65 (t, J=7.5 Hz, 2H), 2.10 (s, 3H), 1.80–1.70 (m, 2H), 0.85 (s, 9H), 0.00 (s, 6H) ppm. IR (liquid film, cm^{-1}): 2955, 2931, 1720, 1677, 1600, 1569, 1465, 1131, 837. EIMS (*m*/*z*): 337 $(M-57)^+$. Anal. calcd for $C_{21}H_{34}O_5Si$: C, 63.92; H, 8.68. Found: C, 64.29; H, 8.88.

4.2. General procedure for the preparation of 8(b–f)

A solution of **7** (0.3 mmol) in CH_2Cl_2 (10 mL) was treated with tetrabutylammonium hydroxide (10% in H_2O) and RX (2.0 equiv.) at 40°C and the reaction process was monitored by TLC. Upon completion, saturated NH_4Cl aqueous solution was added. The mixture was extracted with EtOAc (3×15 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography to afford **8**(**b**–**f**).

4.2.1. 6-[5-(*tert*-Butyldimethylsilyloxy)-1-methyl-2-oxopentyl]-2,4-dimethoxy-3-methylbenzaldehyde (8b). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.40 (s, 1H), 6.48 (s, 1H), 5.15 (q, J=7.2 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.55 (t, J=6.0 Hz, 2H), 2.50 (t, J=7.2 Hz, 2H), 2.10 (s, 3H), 1.75–1.65 (m, 2H), 1.35 (d, J=7.2 Hz, 3H), 0.80 (s, 9H), 0.00 (s, 6H) ppm. IR (liquid film, cm^{-1}): 2955, 2932, 1714, 1680, 1597, 1567, 1464, 1131, 837. EIMS (*m*/*z*): 351 $(M-57)^+$. HRMS calcd for $C_{22}H_{36}O_5SiNa$ $(M+Na)^+$ calcd: 431.2230, found: 431.2224.

4.2.2. 6-[5-(*tert*-Butyldimethylsilyloxy)-1-ethyl-2-oxopentyl]-2,4-dimethoxy-3-methylbenzaldehyde (8c). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.50 (s, 1H), 6.50 (s, 1H), 5.25 (t, J=7.2 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.55 (t, J=6.3 Hz, 2H), 2.50 (t, J=7.2 Hz, 2H), 2.20 (s, 3H), 2.15–2.00 (m, 1H), 1.75–1.60 (m, 3H), 0.75 (s, 9H), 0.90–0.70 (q, 3H, superimposed on 0.75), 0.00 (s, 6H) ppm. IR (liquid film, cm^{-1}): 2957, 2932, 1712, 1682, 1597, 1567, 1464, 1129, 837. EIMS (*m*/*z*): 365 $(M-57)^+$. HRMS calcd for $C_{23}H_{38}O_5SiNa$ $(M+Na)^+$ calcd: 445.2386, found: 445.2381.

4.2.3. 6-[1-Allyl-5-(*tert*-butyldimethylsilyloxy)-2-oxopentyl]-2,4-dimethoxy-3-methylbenzaldehyde (8d). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.40 (s, 1H), 6.50 (s, 1H), 5.75–5.60 (m, 1H), 4.40 (t, J=7.2 Hz, 1H), 5.00–4.85 (m, 2H), 3.80 (s, 3H), 3.75 (s, 3H), 3.50 (t, J=6.0 Hz, 2H), 2.80–2.70 (m, 1H), 2.50 (t, J=7.5 Hz, 2H), 2.40–2.30 (m, 1H), 2.10 (s, 3H), 1.75–1.65 (m, 2H), 0.75 (s, 9H), −0.05 (s, 6H) ppm. IR (liquid film, cm^{-1}): 2955, 2931, 1714, 1681, 1597, 1567, 1464, 1129, 837, 777. EIMS (*m*/*z*): 377 $(M-57)^+$. Anal. calcd for $C_{24}H_{38}O_5Si$: C, 66.32; H, 8.81. Found: C, 66.20; H, 8.53.

4.2.4. 6-[1-Benzyl-5-(*tert*-butyldimethylsilyloxy)-2-oxopentyl]-2,4-dimethoxy-3-methylbenzaldehyde (8e). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.30 (s, 1H), 7.20–7.10 (m, 5H), 6.55 (s, 1H), 5.70 (t, J=7.2 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.45 (t, J=6.3 Hz, 2H), 3.30 (dd, J=8.1 Hz, 13.2 Hz, 1H), 2.70 (dd, J=6.3 Hz, 13.2 Hz, 1H), 2.50–2.25 (m, 2H), 2.10 (s, 3H), 1.65–1.55 (m, 2H), 0.80 (S, 9H), −0.10 (s, 6H) ppm. IR (liquid film, cm^{-1}): 2955, 2931, 1714, 1679, 1596, 1567, 1464, 1129, 837, 777. EIMS (*m*/*z*): 427 $(M-57)^+$. Anal. calcd for $C_{28}H_{40}O_5Si$: C, 69.38; H, 8.32. Found: C, 69.05; H, 8.77.

4.2.5. 6-[5-(*tert*-Butyldimethylsilyloxy)-1-(4-methoxybenzyl)-2-oxopentyl]-2,4-dimethoxy-3-methylbenzaldehyde (8f). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.40 (s, 1H), 7.10 (d, J=8.7 Hz, 2H), 6.80 (d, J=5.4 Hz, 1H), 6.60 (s, 3H), 5.65 (t, J=5.4 Hz, 1H), 3.95 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H), 3.50 (t, J=6.3 Hz, 2H), 3.40 (dd, J=8.1 Hz, 14.1 Hz, 1H), 2.85 (dd, J=6.6, 14.1 Hz, 1H), 2.55–2.30 (m, 2H), 2.20 (s, 3H), 1.75–1.60 (m, 2H), 0.80 (s, 9H), 0.00 (s, 6H) ppm. IR (liquid film, cm^{-1}): 2955, 2931, 1713, 1679, 1596, 1566, 1464, 1149, 1128, 836, 777. EIMS (*m*/*z*): 514 $(M)^+$. Anal. calcd for $C_{29}H_{42}O_6Si$: C, 67.67; H, 8.22. Found: C, 67.77; H, 8.48.

4.3. General procedure for the preparation of 9(a–f)

To a solution of **8** (0.2 mmol) in CH_3OH (5 mL) was added aqueous NaOH solution (6N, 0.1 mL). The reaction mixture was stirred at room temperature for 15 min. Most of the solvent was removed under reduced pressure and the residue was diluted with ethyl acetate, washed with aqueous NH_4Cl solution. The organic phase was dried over Na_2SO_4 and evaporated. The residue was purified by column chromatography to give **9**(**a**–**f**).

4.3.1. 3-[2-(*tert*-Butyldimethylsilyloxy)-ethyl]-5,7-dimethoxy-6-methylnaphthalen-2-ol (9a). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.45 (s, 1H), 7.70 (s, 1H), 7.20 (s, 1H), 6.75 (s, 1H), 4.00 (t, J=5.1 Hz, 2H), 3.90 (s, 3H), 3.85 (s, 3H), 3.05 (t, J=5.1 Hz, 2H), 2.30 (s, 3H), 0.90 (s, 9H), 0.10 (s, 6H) ppm. IR (liquid film, cm^{-1}): 3277 (br), 2954, 2932, 1641, 1576, 1464, 1396, 1256, 1144, 1110, 838, 782. EIMS (*m*/*z*): 376 $(M)^+$, 319 $(M-57)^+$. Anal. calcd for $C_{21}H_{32}O_4Si$: C, 66.98; H, 8.56. Found: C, 66.79; H, 8.37.

4.3.2. 3-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-5,7-dimethoxy-1,6-dimethylnaphthalen-2-ol (9b). Mp: 115–117°C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.30 (s, 1H), 7.50 (s, 1H), 6.85 (s, 1H), 3.95 (t, J=4.8 Hz, 2H), 3.90 (s, 3H), 3.80 (s, 3H), 3.00 (t, J=5.4 Hz, 2H), 2.45 (s, 3H), 2.20 (s, 3H), 0.85 (s, 9H), 0.00 (s, 6H) ppm. IR (KBr, cm^{-1}): 3260 (br), 2955, 2933, 1635, 1580, 1497, 1465, 1259, 1112, 826, 779. EIMS (*m*/*z*): 390 $(M)^+$. Anal. calcd for $C_{22}H_{34}O_4Si$: C, 67.65; H, 8.77. Found: C, 67.57; H, 8.86.

4.3.3. 3-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-1-ethyl-5,7-dime thoxy-6-methylnaphthalen-2-ol (9c). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.30 (s, 1H), 7.60 (s, 1H), 7.00 (s, 1H), 4.00 (t, J=5.1 Hz, 2H), 3.95 (s, 3H), 3.85 (s, 3H), 3.10–3.00 (m, 4H), 2.30 (s, 3H), 1.25 (t, J=4.5 Hz, 3H), 0.90 (s, 9H), 0.10 (s, 6H) ppm. IR (liquid film, cm^{-1}): 3280 (br), 2956, 2932, 1633, 1580, 1465, 1387, 1253, 1115, 827. EIMS (*m*/*z*): 404 $(M)^+$. HRMS calcd for $C_{23}H_{36}O_4SiNa$ $(M+Na)^+$ calcd: 427.2281, found: 427.2275.

4.3.4. 1-Allyl-3-[2-(*tert*-butyldimethylsilyloxy)ethyl]-5,7-dimethoxy-6-methylnaphthalen-2-ol (9d). White solid, Mp: 75–78°C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.40 (s, 1H), 7.60 (s, 1H), 6.95 (s, 1H), 6.10–5.95 (m, 1H), 5.10–5.00 (m, 2H), 4.00 (t, J=5.1 Hz, 2H), 3.90 (s, 3H), 3.85 (s, 3H), 3.80 (d, J=0.6 Hz, 2H), 3.08 (t, J=5.1 Hz, 2H), 2.25 (s, 3H), 0.90 (s, 9H), 0.08 (s, 6H) ppm. IR (KBr, cm^{-1}): 3268 (br), 2954, 2932, 1635, 1579, 1465, 1387, 1259, 1116, 826, 734. EIMS (*m*/*z*): 416 $(M)^+$.

4.3.5. 1-Benzyl-3-[2-(*tert*-butyldimethylsilyloxy)ethyl]-5,7-dimethoxy-6-methylnaphthalen-2-ol (9e). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.45 (s, 1H), 7.60 (s, 1H), 7.25–7.00 (m, 5H), 6.85 (s, 1H), 4.40 (s, 2H), 3.95 (t, J=4.8 Hz, 2H), 3.80 (s, 3H), 3.70 (s, 3H), 3.05 (t, J=5.1 Hz, 2H), 2.20 (s, 3H), 0.80 (s, 9H), 0.00 (s, 6H) ppm. IR (liquid film, cm^{-1}): 3259 (br), 2953, 2931, 1633, 1579, 1460, 1388, 1257, 1110, 836. EIMS (*m*/*z*): 466 $(M)^+$. Anal. calcd for $C_{28}H_{38}O_4Si$: C, 72.06; H, 8.21. Found: C, 72.48; H, 8.46.

4.3.6. 3-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-5,7-dimethoxy1-(4-methoxybenzyl)-6-methylnaphthalen-2-ol (9f). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.45 (s, 1H), 7.70 (s, 1H), 7.20 (d, J=8.4 Hz, 2H), 6.95 (s, 1H), 6.75 (d, J=8.4 Hz, 2H), 4.40 (s, 2H), 4.00 (t, J=5.0 Hz, 2H), 3.90 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H), 3.10 (t, J=5.1 Hz, 2H), 0.90 (s, 9H), 0.05 (s, 6H) ppm. IR (liquid film, cm^{-1}): 3258 (br), 2953, 2933, 1633, 1581, 1511, 1465, 1387, 1248, 1141, 1110, 839, 784. EIMS (*m*/*z*): 496 $(M)^+$. Anal. calcd for $C_{29}H_{40}O_5Si$: C, 70.12; H, 8.12. Found: C, 69.94; H, 8.38.

4.3.7. 3-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-5,7-dimethoxy-6-methyl-[1,2]naphthoquinone (10). To an aqueous solution of Fremy's salt (90 mg, 0.34 mmol) in 0.4N K_2HPO_4 (2.0 mL) was added a solution of phenol **9a** (42 mg, 0.11 mmol) in THF (3.0 mL). The resulting mixture was stirred at room temperature for 2 days (monitored by TLC, additional Fremy's salt was added if necessary). The mixture was extracted with ethyl acetate and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, evaporated and purified by chromatography to afford **10** as a reddish oil (17 mg, 62%) with material recovered (**9a**, 10 mg, 24%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.60 (s, 1H), 7.38 (s, 1H), 3.92 (s, 3H), 3.80 (s, 3H), 3.80 (t, J=6.0 Hz, 2H), 2.62 (t, J=6.0 Hz, 2H), 2.20 (s, 3H), 0.90 (s, 9H), 0.05 (s, 6H) ppm. IR (liquid film, cm^{-1}): 2956, 2920, 1663, 1584, 1465, 1319, 1258, 1143, 1101, 836, 778. ESIMS (*m*/*z*): 391 $(M+1)^+$. HRMS calcd

for $C_{21}H_{30}O_5SiNa$ $(M+Na)^+$ calcd: 413.1760, found: 413.1770.

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