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Synthesis of 2-alkoxymethyl-3-trifluoromethyl-1,4-naphthoquinones

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Abstract—2-Alkoxymethyl-3-trifluoromethyl-1,4-naphthoquinones were conveniently synthesized in two steps by treatment of 2-substituted-3-bromo-1,4-dimethoxynaphthalene with CF_3COONa/CuI and subsequent dealkylative oxidation by treatment with cerium(IV) ammonium nitrate.

1. Introduction

The trifluoromethyl group (CF_3) is an important structural moiety in diverse classes of bioactive organic molecules.[1,2] The C–F bond in fluorinated compounds results in an increased stability and lipophilicity. Because fluorine is the most electronegative element and the van der Waals radius of fluorine is close to that of hydrogen,[3,4] the introduction of the CF_3 group into organic molecules often changes their physical, chemical and physiological properties in a dramatic way, without the introduction of extra steric demand.[5,6] There are many compounds containing the CF_3-moiety that have been used in agrochemicals,[7] pharmaceuticals,[1,2] polymers and the dye industry.[8] For this reason, many efforts were made to introduce the trifluoromethyl group into different types of organic molecules.[3,4,9] Concerning the quinone system, there are few literature references reported on the use of trifluoromethyl-substituted benzoquinones as redox system[10] and as synthon for organic synthesis.[11,12] Very recently, 3-bromo- or 3-chloro-2-substituted naphthoquinones have been reported having interesting biological activities, including antiplatelet, antiinflammatory, antiallergic activities and inhibitor of human cytomegalovirus protease.[13–15] It would therefore be of interest to have access to the hitherto unknown trifluoromethylated alkoxymethylbenzoquinones **7** because such compounds could exert interesting physiological properties. Accordingly, the synthesis of 2-substituted-3-trifluoromethyl-1,4-naphthoquinones is reported here as an effort towards the discovery of new biologically active naphthoquinones.

Keywords: trifluoromethylnaphthoquinones; alkoxymethylnaphthoquinones.

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2. Results and discussion

The synthesis of a series of benzyloxymethyl-, 2-arylethyloxymethyl- and allyloxymethylnaphthalenes **5** bearing an additional bromo substituent at the 3-position is outlined in Scheme 1. Reductive methylation of 2-methyl-1,4-naphthoquinone **1** with tin(II) chloride and HCl (12 M) with ethanol as solvent at room temperature for 30 min, followed by alkylation with dimethylsulfate in acetone in the presence of potassium carbonate gave 1,4-dimethoxynaphthalene **2** in 83% yield.[16] The bromination of compound **2** with *N*-bromosuccinimide in carbon tetrachloride in the presence of benzoyl peroxide as initiator under reflux for two hours gave 2-bromo-3-bromomethyl-1,4-dimethoxynaphthalene **3** in 80% yield.[17] The alkylation of dibromonaphthalene **3** was carried out with sodium alkoxides in tetrahydrofuran to afford compounds **5** in 90–95% yield.[18] Allylic and benzylic alcohols **4** were deprotonated by treatment with NaH in THF at 40°C for 30 min, after which the alkoxides were treated with dibromonaphthalene **3** in the same solvent at 40°C for 2 h to give 2-bromo-3-alkoxymethyl-1,4-dimethoxynaphthalenes **5** (Scheme 1).

The directed introduction of the CF_3 group in an electron-rich environment is an important item in organic chemistry. However, it is very difficult to generate the CF_3-cation chemically, due to the high electronegativity of the trifluoromethyl group. Recently, the introduction of the CF_3 group on an aromatic ring via the trifluoromethyl anion was performed by substitution of halogens using (trifluoromethyl)copper. This short-lived intermediate may be produced either from gaseous CF_3I (using an autoclave) and copper,[19] or more conveniently from CF_3COONa/CuI by decarboxylation.[10]

The replacement of the bromine with the CF_3 group in the

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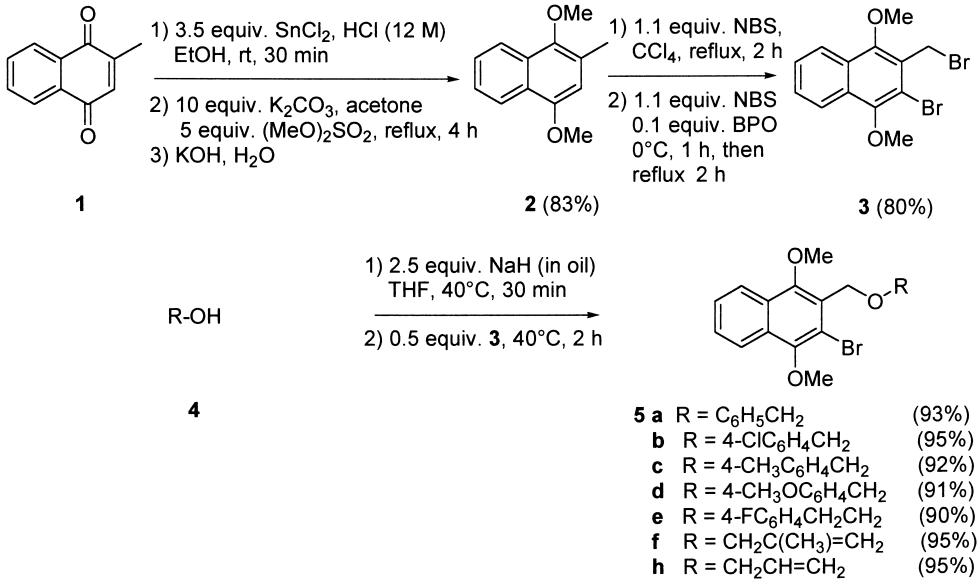
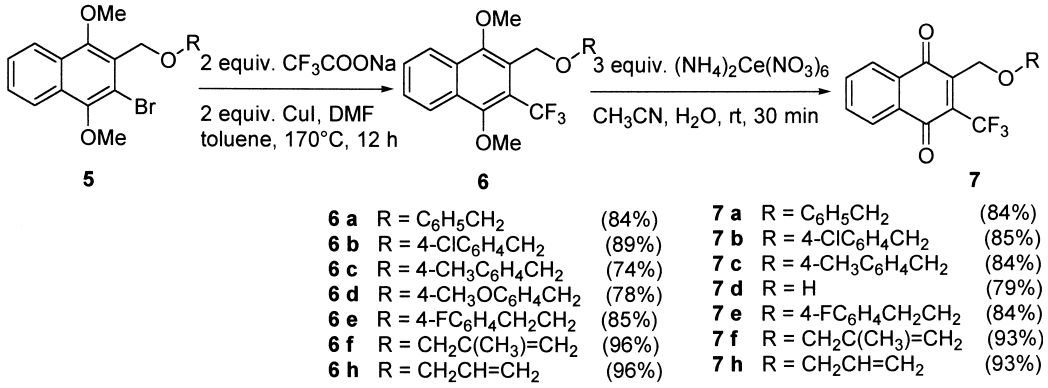
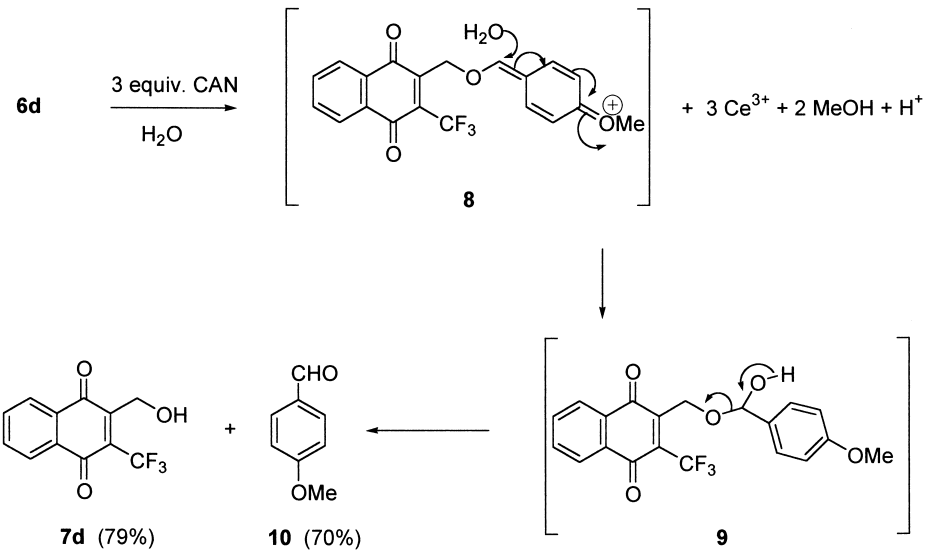


Scheme 1.



Scheme 2.



Scheme 3.

aromatic ring of compounds **5a**–**h** is described in Scheme 2.[10] Heating of 3-substituted-2-bromo-1,4-dimethoxynaphthalenes **5** with CF_3COONa, CuI in DMF and toluene (2:1) at 170°C for 12 h gave trifluoromethylnaphthalenes **6a**–**h** in 74–96% yield. The structure of these compounds was confirmed mainly on the basis of their ^{13}C NMR spectra. In the ^{13}C NMR spectra ($CDCl_3$), the CF_3-carbon in all of the trifluoromethylated compounds appeared as a quartet at about 124 ppm with a J_{C-F} of about 274–278 Hz and a J_{C-C-F} of about 30 Hz for the α-carbon at position **3**, bearing the CF_3 substituent.

The oxidation of 2-alkoxymethyl-1,4-dimethoxy-3-(trifluoromethyl)naphthalenes **6** by treatment with 2 equiv. of cerium(IV) ammonium nitrate (CAN) in acetonitrile and water at room temperature for 30 min afforded the corresponding 2-allyloxy-, 2-(4-fluorophenyl)ethoxy- and 2-benzyloxy-3-trifluoromethyl-1,4-naphthoquinones **7a**–**h**. Although the electron-withdrawing property of the CF_3 group in compounds **6a**–**h** was very strong, the dealkylative oxidation reaction proceeded smoothly with CAN transfering two electrons of the substrates to Ce^{4+} to give products **7a**–**h** in excellent yield (79–93%). In the ^{13}C NMR spectra ($CDCl_3$) of the trifluoromethylated compounds **7**, the CF_3 carbon also appeared as a quartet at about 121–127 ppm with J_{C-F} of about 274–278 Hz. However, in the case of compound **6d**, containing the electron-donating *para*-methoxy substituent, an easy transfer of electrons from the benzyl group to Ce^{4+} occurred, resulting in the formation of the intermediate **8**. This intermediate **8** underwent attack of water to give hemi-acetal **9**, which was then decomposed to give 2-hydroxymethyl-3-trifluoromethyl-1,4-naphthoquinone **7d** and 4-methoxybenzaldehyde **10**. The mechanism of the reaction is outlined in Scheme 3.

In conclusion, the introduction of the CF_3 group into functionalized naphthoquinones was performed by reaction of bromonaphthalenes with CF_3COONa/CuI through decarboxylation to 2-substituted-3-trifluoromethyl-1,4-dimethoxynaphthalenes **5a**–**h**. The latter were conveniently demethylated by oxidation with CAN to give 2-substituted-3-trifluoromethyl-1,4-naphthoquinones **7a**–**h** in excellent isolated yields.

3. Experimental

3.1. General

Melting points were determined on a Büchi 535 apparatus. ^1H NMR spectra (270 MHz) and ^{13}C NMR spectra (67 MHz) were recorded with a Jeol JNM-EX 270 NMR spectrometer. IR spectra were measured with a Perkin Elmer Model 983 spectrophotometer. Mass spectra were recorded with a Varian-MAT 112 mass spectrometer (70 eV).

3.1.1. 1,4-Dimethoxy-2-methylnaphthalene 2.[16] To a solution of 2-methylnaphthoquinone **1** (5.16 g, 0.03 mol) in absolute ethanol (100 mL) was added dropwise over a period of 30 min, a solution of tin(II) chloride (19.95 g, 0.1 mol) in 12 M HCl (20 mL). The reaction mixture was stirred for 30 min, then ethanol was evaporated in vacuo and the residue was poured into water. The hydroquinone precipitate was filtered and dissolved in acetone (150 mL). The solution was dried ($MgSO_4$), after which potassium carbonate (44.4 g, 0.32 mol) and dimethyl sulfate (20.1 g, 0.16 mol) was added. Then the reaction mixture was refluxed for 4 h, and afterwards filtered. The filtrate was evaporated in vacuo, the residue was dissolved in ether (200 mL) and aqueous 20% KOH (100 mL). The mixture was stirred vigorously for 1 h, the organic layer was separated and dried ($MgSO_4$). The solvent was evaporated in vacuo to give naphthalene **2** (5.0 g, 83% yield, white solid) which was not purified further (purity >96%) and was used as such for the next step. ^1H NMR ($CDCl_3$) δ: 8.02–8.11 (2H, m, H-5, H-8), 7.37–7.52 (2H, m, H-6, H-7), 6.57 (1H, s, H-3), 3.93 (3H, s, OMe), 3.84 (3H, s, OMe), 2.43 (3H, s, Me). ^{13}C NMR ($CDCl_3$) δ: 151.5 (C-1), 147.0 (C-4), 128.7 (Cquat), 125.6 (Cquat), 125.2 (Cquat), 126.4 and 124.5 (C-6 and C-7), 122.2 and 121.5 (C-5 and C-8), 106.8 (C-3), 61.1 (OMe), 55.5 (OMe), 16.2 (CH3). IR (NaCl): 1595, 1460, 1355, 1265, 1220, 1120, 955, 770 cm^{-1}; MS, *m/z* (%): 202 (M^+, 56), 187 (100), 159 (82).

3.1.2. 2-Bromo-3-(2-bromomethyl)-1,4-dimethoxynaphthalene 3. To a solution of 1,4-dimethoxy-2-methylnaphthalene **2** (13 g, 0.064 mol) in CCl_4 (200 mL) was added *N*-bromosuccinimide (NBS) (11.45 g, 0.064 mol). The reaction mixture was refluxed for 2 h, then it was cooled to 0°C. To this mixture was added NBS (11.45 g, 0.064 mol) and benzoyl peroxide (1.41 g, 0.006 mol) and the reaction mixture was refluxed for 2 h. After cooling of the reaction mixture to room temperature, succinimide was filtered off. The filtrate was washed with aqueous $Na_2S_2O_5$, 2 M NaOH, after which the filtrate was dried ($MgSO_4$). The solvent was evaporated in vacuo to give crude product (20.0 g), which was crystallized from methanol to give **3** (16.0 g, 80% yield), white powder, mp 83–85°C (lit.[17] mp 88°C). ^1H NMR ($CDCl_3$) δ: 8.05–8.11 (2H, m, H-5, H-8), 7.52–7.59 (2H, m, H-6, H-7), 4.92 (2H, s, C*H*$_2$–Br), 4.07 (3H, s, OMe), 3.98 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 152.2 (C-1), 150.6 (C-4), 130.1 (Cquat), 129.3 (Cquat), 128.5 (Cquat), 127.8 (C-7), 127.7 (Cquat), 127.0 (C-6), 123.1 (C-5), 122.7 (C-8), 62.8 (OMe), 61.4 (OMe), 28.9 (CH_2–Br). IR (KBr): 1565, 1451, 1349, 1261, 1079, 1004, 957, 714 cm^{-1}; MS, *m/z* (%): 362/360/358 (M^+, 16), 281/279 (44), 279 (38), 200 (46), 185 (59), 174 (100), 159 (82).

3.1.3. 2-(4-Benzyloxymethyl)-3-bromo-1,4-dimethoxynaphthalene 5a. The preparation of compound **5a** is representative of all other analogous compounds. A solution of benzyl alcohol **4a** (180 mg, 1.16 mmol) in dry THF (10 mL) was added to a stirred suspension of NaH (166 mg, 4.15 mmol, 60% dispersion in mineral oil, oil included in the mixture) at room temperature and this mixture was stirred for 45 min.[18] Then 2-bromo-3-(2-bromomethyl)-1,4-naphthalene **3** (300 mg, 0.83 mmol) was added. The reaction mixture was kept at 45°C for 2 h. Then, the reaction mixture was treated with water and extracted with CH_2Cl_2 (three times). The combined extracts were washed with water and dried ($MgSO_4$). The solvent was evaporated in vacuo to give the crude product (350 mg), which was purified by flash chromatography on a SiO_2 column (hexane/ethyl acetate 9:1) to give pure product **5a** (330 mg, 93% yield), white powder, mp 72–73°C (hexane/ethyl acetate

9:1). ^{1}H NMR ($CDCl_3$) δ: 7.93–7.91 (2H, m, H-5, H-8), 7.30–7.39 (2H, m, H-6, H-7), 7.22–7.28 (2H, m, H-2′, H-6′), 7.12–7.19 (3H, m, H-3′, H-4′ and H-5′), 4.72 (2H, s, OCH_2), 4.55 (2H, s, OCH_2–C_6H_5), 3.82 (3H, s, OMe), 3.80 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 152.6 (C-1), 150.0 (C-4), 138.0 (Cquat), 129.1 (Cquat), 128.3 (Cquat), 128.1 (C-5′, C-3′), 128.0 (C-6′, C-2′), 127.7 (Cquat), 127.5 (C-6), 127.2 (C-7), 126.5 (C-4′), 122.9 (C-8), 122.3 (C-5), 116.4 (Cquat), 73.0 (OCH_2–C_6H_5), 66.6 (OCH_2), 63.7 (OMe), 61.1 (OMe). IR (KBr): 1578, 1454, 1359, 1005, 748 cm^{-1}; MS, *m/z* (%): 388/386 (M^+, 43), 203 (38), 202 (67), 201 (100); Anal. $C_{20}H_{19}BrO_3$: calcd C 62.03%, H 4.95%; Found: C 62.23%, H 5.06%.

3.1.4. 3-Bromo-2-(4-chlorobenzyloxymethyl)-1,4-dimethoxynaphthalene 5b. Yield: 95%, white powder, mp 97–98°C (hexane). ^{1}H NMR ($CDCl_3$) δ: 8.08–8.12 (2H, m, H-5, H-8), 7.54–7.57 (2H, m, H-6, H-7), 7.33 (4H, m, H-2′, H-6′, H-3′ and H-5′), 4.85 (2H, s, OCH_2), 4.65 (2H, s, OCH_2–C_6H_4), 3.98 (3H, s, OMe), 3.95 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 152.7 (C-1), 150.2 (C-4), 136.7 (Cquat), 133.4 (Cquat), 129.4 (C-3′, C-5′), 129.2 (Cquat), 128.4 (C-2′, C-6′), 127.8 (Cquat), 127.4 (C-7), 126.7 (C-6), 126.3 (Cquat), 123.0 (C-8), 122.5 (C-5), 116.3 (Cquat), 72.1 (OCH_2–C_6H_4), 66.7 (OCH_2), 63.9 (OMe), 61.3 (OMe). IR (KBr): 1579, 1451, 1353, 1084, 1006, 754 cm^{-1}; MS, *m/z* (%): 424/422/420 (M^+, 24), 201(81), 186 (16), 125 (46), 97 (29), 85 (56), 57 (100); Anal. $C_{20}H_{18}BrClO_3$: calcd C 56.96%, H 4.30%; Found: C 57.12%, H 4.41%.

3.1.5. 3-Bromo-2-(4-methylbenzyloxymethyl)-1,4-dimethoxynaphthalene 5c. Yield: 92%, white powder, mp 67–69°C (hexane). ^{1}H NMR ($CDCl_3$) δ: 8.06–8.10 (2H, m, H-5, H-8), 7.51–7.54 (2H, m, H-6, H-7), 7.32 (2H, d, *J*=8.1 Hz, H-2′ and H-6′), 7.14 (2H, d, *J*=8.1 Hz, H-3′, H-5′), 4.83 (2H, s, OCH_2), 4.65 (2H, s, OCH_2–C_6H_4), 3.96 (3H, s, OMe), 3.94 (3H, s, OMe), 2.33 (3H, s, Me). ^{13}C NMR ($CDCl_3$) δ: 152.7 (C-1), 150.2 (C-4), 137.4 (Cquat), 135.1 (Cquat), 129.2 (Cquat), 129.0 (C-3′, C-5′), 128.3 (C-2′, C-6′), 127.9 (Cquat), 127.3 (C-7), 126.8 (Cquat), 126.6 (C-6), 123.0 (C-8), 122.5 (C-5), 116.5 (Cquat), 73.0 (OCH_2–C_6H_4), 66.6 (OCH_2), 63.9 (OMe), 61.3(OMe), 21.2 (Me). IR (KBr): 1574, 1441, 1407, 1360, 1075, 1006, 810, 753 cm^{-1}; MS, *m/z* (%): 402/400 (M^+, 21), 252 (12), 202 (16), 201 (100); Anal. $C_{21}H_{21}BrO_3$: calcd C 62.85%, H 5.27%; Found: C 62.95%, H 5.15%.

3.1.6. 3-Bromo-2-(4-methoxybenzyloxymethyl)-1,4-dimethoxynaphthalene 5d. Yield: 91%, white powder, mp 70–72°C (hexane). ^{1}H NMR ($CDCl_3$) δ: 8.07–8.10 (2H, m, H-5, H-8), 7.52–7.55 (2H, m, H-6, H-7), 7.35 (2H, d, *J*=8.6 Hz, H-2′ and H-6′), 6.88 (2H, d, *J*=8.6 Hz, H-3′, H-5′), 4.82 (2H, s, OCH_2), 4.63 (2H, s, OCH_2–C_6H_4), 3.97 (3H, s, OMe), 3.94 (3H, s, OMe), 3.79 (3H, s, C_6H_4–O*Me*). ^{13}C NMR ($CDCl_3$) δ: 159.3 (C-4′), 152.7 (C-1), 150.2 (C-4), 132.0 (Cquat), 130.4 (Cquat), 129.8 (C-3′, C-5′), 129.2 (Cquat), 127.9 (Cquat), 127.3 (C-7), 126.7 (C-6), 123.0 (C-8), 122.5 (C-5), 116.5 (Cquat), 113.8 (C-2′, C-6′), 72.8 (OCH_2–C_6H_4), 66.5 (O*C*H), 63.9 (OMe), 61.5 (OMe), 55.3 (C_6H_4–O*Me*). IR (KBr): 1613, 1518, 1453, 1358, 1259, 1083, 810, 750 cm^{-1}; MS, *m/z* (%): 418/416 (M^+, 25), 252 (10), 202 (16), 201 (100), 149 (11), 121 (40), 99 (36), 57 (42); Anal. $C_{21}H_{21}BrO_4$: calcd C 60.44%, H 5.07%; Found: C 60.28%, H 5.13%.

3.1.7. 3-Bromo-2-(4-fluorophenylethoxymethyl)-1,4-dimethoxynaphthalene 5e. Yield: 90%, white powder, mp 62–63°C (hexane). ^{1}H NMR ($CDCl_3$) δ: 8.11–8.19 (2H, m, H-5, H-8), 7.60–7.65 (2H, m, H-6, H-7), 7.16–7.25 (2H, m, H-2′ and H-6′), 6.91–6.97 (2H, m, H-3′ and H-5′), 4.79 (2H, s, OCH_2), 4.00 (3H, s, OMe), 3.89 (3H, s, OMe), 3.77 (2H, m, OCH_2CH_2), 2.90 (2H, m, OCH_2CH_2). ^{13}C NMR ($CDCl_3$) δ: 161.0 (d, *J*=245 Hz, CF), 153.2 (C-1), 153.1 (C-4), 152.8 (Cquat), 134.7. (Cquat), 134.6 (Cquat), 130.3 (C-3′), 130.2 (C-5′), 129.1 (Cquat), 128.5 and 127.5 (C-7, C-6), 124.4 (Cquat), 123.6 and 123.0 (C-5, C-8), 115.1 and 114.8 (C-2′, C-6′), 71.8 (CH_2–*C*H_2–O), 64.3 (OMe), 64.2 (OMe), 63.9 (O*C*H_2), 35.4 (*C*H_2–CH_2–O). IR (KBr): 1584, 1513, 1455, 1366, 1220, 1164, 1094, 1009, 829, 759 cm^{-1}; MS, *m/z* (%): 420/418 (M^+, 5), 411/409 (24), 403/401 (16), 381/379 (100), 356/358 (64), 341/343 (30), 313 (19), 281 (19), 200 (29), 185 (15), 170 (23); Anal. $C_{21}H_{20}BrFO_3$: calcd C 62.16%, H 4.81%; Found: C 61.92%, H 4.55%.

3.1.8. 3-Bromo-2-(methylallyloxymethyl)-1,4-dimethoxynaphthalene 5f. Yield: 95%, colorless oil. ^{1}H NMR ($CDCl_3$) δ: 8.06–8.12 (2H, m, H-5, H-8), 7.49–7.55 (2H, m, H-6, H-7), 5.07 (1H, broad s, C=CH_2), 4.94 (1H, broad s, C=CH_2), 4.79 (2H, s, OCH_2), 4.07 (2H, s, OCH_2–C_3H_5), 3.98 (3H, s, OMe), 3.96 (3H, s, OMe), 1.82 (3H, s, Me). ^{13}C NMR ($CDCl_3$) δ: 152.8 (C-1), 150.2 (C-4), 142.3 (*C*=CH_2), 129.2 (Cquat), 127.9 (Cquat), 127.3 (C-7), 126.8 (Cquat), 126.7 (C-6), 123.0 (C-8), 122.5 (C-5), 116.5 (Cquat), 112.9 (C=*C*H_2), 75.2 (OCH_2–C_3H_5), 66.6 (OCH_2), 64.0 (OMe), 61.3 (OMe), 19.78 (Me). IR (NaCl): 1568, 1449, 1356, 1260, 1085, 1030, 1007, 966, 759, 748 cm^{-1}; MS, *m/z* (%): 352/350 (M^+, 17), 265 (12), 251 (10), 201 (30), 201 (54), 141 (30), 77 (49), 71 (48), 57 (100); Anal. $C_{17}H_{19}BrO_3$: calcd C 58.13%, H 5.47%; Found: C 57.99%, H 5.39%.

3.1.9. 2-(Allyloxymethyl)-3-bromo-1,4-dimethoxynaphthalene 5h. Yield: 95%, colorless oil. ^{1}H NMR ($CDCl_3$) δ: 8.07–8.13 (2H, m, H-5, H-8), 7.52–7.57 (2H, m, H-6, H-7), 6.03 (1H, m, C*H*=CH_2), 5.20–5.41 (2H, m, C=CH_2), 4.83 (2H, s, CH_2–O), 4.18 (2H, dt, *J*=5.9, 1.3 Hz, OCH_2–C_3H_5), 3.99 (3H, s, OMe), 3.97 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 152.8 (C-1), 150.2 (C-4), 134.8 (*C*H=CH_2), 129.2 (Cquat), 127.9 (Cquat), 127.3 (C-7), 126.7 (C-6), 123.0 (C-8), 122.5 (C-5), 117.5 (C=*C*H_2), 116.5 (Cquat), 72.0 (OCH_2–CH=CH_2), 66.6 (OCH_2), 64.0 (OMe), 61.3 (OMe); one quaternary carbon was not visible due to overlap. IR (NaCl): 1570 (CH=CH_2), 1455, 1400, 1360 1260, 1085, 1030, 1007, 966, 775, 760 cm^{-1}; MS, *m/z* (%): 336/338 (M^+, 26), 201 (100), 185 (40), 141 (30), 77 (49); Anal. $C_{16}H_{17}BrO_3$: calcd C 56.99%, H 5.08%; Found: C 56.82%, H 5.06%.

3.1.10. 2-(Benzyloxymethyl)-3-trifluoromethyl-1,4-dimethoxynaphthalene 6a. The synthesis of compound **6a** is representative of all other preparation of compounds **6**. A mixture of 2-(benzyloxymethyl)-3-bromo-1,4-dimethoxynaphthalene **5a** (1.0 g, 2.584 mmol), CF_3COONa (701 mg, 5.16 mmol) and CuI (975 mg, 5.16 mmol) was dissolved in a mixture of DMF (10 mL) and toluene (5 mL).[10] The

reaction mixture was heated at 170°C for 12 h under N_2. Then the mixture was dissolved in CH_2Cl_2 (100 mL), after which it was filtered. The filtrate was washed with HCl (12 M) and $NaHCO_3$ (5%) and dried ($MgSO_4$). The solvent was evaporated in vacuo to give the crude product, which was purified by flash chromatography on a SiO_2 column with hexane/ethyl acetate (9:1) to give product **6a** (760 mg, 84% yield), colorless oil. ^{1}H NMR ($CDCl_3$) δ: 8.06–8.18 (2H, m, H-5, H-8), 7.57–7.63 (2H, m, H-6, H-7), 7.28–7.50 (5H, m, H-2′, H-3′, H-4′, H-5′ and H-6′), 4.84 (2H, s, OCH_2), 4.65 (2H, s, OCH_2–C_6H_5), 3.98 (3H, s, OMe), 3.94 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 153.1 (C-1), 152.5 (C-4), 138.5 (Cquat), 137.9 (Cquat), 130.4 (Cquat), 129.7 (Cquat), 128.55 and 128.46 (C-6 and C-7), 128.3 and 128.2 (C-2′, C-6′ and C-3′, C-5′), 127.7 (C-4′), 124.2 (q, J=276 Hz, CF_3), 123.7 (C-8), 123.1 (C-5), 122.5 (q, J=29.4 Hz, C–CF_3), 73.4 (OCH$_2$–C_6H_5), 66.9 (OCH$_2$), 64.0 (OMe), 63.8 (OMe). IR (NaCl): 1618, 1590, 1450, 1358, 1293, 1160, 1117, 966, 775 cm^{-1}; MS, *m*/*z* (%): 376 (M^+, 5), 271 (10), 270 (71), 256 (23), 255 (93), 241 (17), 227 (12), 159 (22), 92 (20), 91 (96), 71 (58), 57 (100); Anal. $C_{21}H_{19}F_3O_3$: calcd C 67.20%, H 5.09%; Found: C 67.20%, H 5.18%.

3.1.11. 2-(4-Chlorobenzyloxymethyl)-3-trifluoromethyl-1,4-dimethoxynaphthalene 6b. Yield: 89%, white powder, mp 67–68°C (hexane). ^{1}H NMR ($CDCl_3$) δ: 8.11–8.18 (2H, m, H-5, H-8), 7.58–7.64 (2H, m, H-6, H-7), 7.30 (4H, m, H-3′, H-2′, H-6′ and H-5′), 4.84 (2H, s, OCH_2), 4.59 (2H, s, OCH_2–C_6H_4), 3.98 (3H, s, OMe), 3.94 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 153.2 (C-1), 152.9 (C-4), 136.6 (Cquat), 133.4 (Cquat), 130.3 (Cquat), 129.4 (C-3′, C-5′), 129.2 (Cquat), 128.6 (C-7), 128.4 (C-2′, C-6′), 127.5 (C-6), 123.8 (Cquat), 124.5 (q, J=278 Hz, CF_3), 123.7 (C-8), 123.0 (C-5), 118.8 (q, J=29.8 Hz, C–CF_3), 72.4 (OCH$_2$–C_6H_4), 64.0 (OCH$_2$), 63.9 (OMe), 63.7 (OMe). IR (KBr): 1617, 1422, 1362, 1293, 1164, 1012 cm^{-1}; MS, *m*/*z* (%): 410 (M^+, 41), 270 (49), 269 (13), 256 (16), 255 (87), 240 (50), 239 (18), 201 (27), 200 (34), 127 (46), 125 (100); Anal. $C_{21}H_{18}ClF_3O_3$: calcd C 61.40%, H 4.42%; Found: C 61.59%, H 4.49%.

3.1.12. 2-(4-Methylbenzyloxymethyl)-3-trifluoromethyl-1,4-dimethoxynaphthalene 6c. Yield: 74%, white powder, mp 63–64°C (hexane). ^{1}H NMR ($CDCl_3$) δ: 8.11–8.18 (2H, m, H-5, H-8), 7.58–7.63 (2H, m, H-6, H-7), 7.24 (2H, d, J=11.9 Hz, H-2′ and H-6′), 7.15 (2H, d, J=11.9 Hz, H-3′, H-5′), 4.82 (2H, s, OCH_2), 4.61 (2H, s, OCH_2–C_6H_4), 3.98 (3H, s, OMe), 3.94 (3H, s, OMe), 2.33 (3H, s, Me). ^{13}C NMR ($CDCl_3$) δ: 153.2 (C-1), 152.9 (C-4), 137.3 (Cquat), 135.0 (Cquat), 130.4 (Cquat), 129.2 (Cquat), 129.0 (C-3′, C-5′), 128.5 (C-7), 128.3 (C-2′, C-6′), 128.0 (Cquat), 127.4 (C-6), 125.5 (q, J=277 Hz, CF_3), 123.7 (C-8), 123.0 (C-5), 120.9 (q, J=29.4 Hz, C–CF_3), 73.3 (OCH$_2$–C_6H_4), 64.0 (OCH$_2$), 63.8 (2×OMe), 21.2 (Me). IR (KBr): 1617, 1457, 1420, 1360, 1295, 1163, 1118, 1015, 781 cm^{-1}; MS, *m*/*z* (%): 390 (M^+, 38), 255 (59), 240 (25), 202 (24), 200 (19), 156 (8), 135 (10), 91 (28), 85 (24), 77 (25), 71 (39), 57 (100); Anal. $C_{22}H_{21}F_3O_3$: calcd C 67.68%, H 5.42%; Found: C 67.48%, H 5.62%.

3.1.13. 2-(4-Methoxybenzyloxymethyl)-3-trifluoromethyl-1,4-dimethoxynaphthalene 6d. Yield: 78%, colorless oil. ^{1}H NMR ($CDCl_3$) δ: 8.11–8.18 (2H, m, H-5, H-8), 7.53–7.64 (2H, m, H-6, H-7), 7.32 (2H, dd, J_1=8.9 Hz, J_2=2.0 Hz, H-2′, H-6′), 6.87 (2H, dd, J_1=8.9 Hz, J_2=2.0 Hz, H-3′, H-5′), 4.82 (2H, d, J=1.6 Hz, OCH_2), 4.58 (2H, s, OCH_2–C_6H_4), 3.99 (3H, s, OMe), 3.94 (3H, s, OMe), 3.79 (3H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 159.3 (C-4′), 153.9 (C-1), 152.5 (C-4), 132.0 (Cquat), 130.4 (Cquat), 130.3 (Cquat), 129.7 (C-3′, C-5′), 128.5 (C-7), 127.4 (C-6), 123.7 (C-8), 123.1 (q, J=278 Hz, CF_3), 123.0 (C-5), 122.9 (q, J=29.3 Hz, C–CF_3), 113.8 (C-2′, C-6′), 73.0 (OCH$_2$–C_6H_4), 64.0 (OCH$_2$), 63.8 (OMe), 63.7 (OMe), 55.3 (OMe). IR (NaCl): 1609, 1583, 1509, 1441, 1358, 1294, 1160, 1019 cm^{-1}; MS, *m*/*z* (%): 406 (M^+, 15), 270 (37), 255 (39), 256 (16), 240 (27), 122 (21), 121 (100); Anal. $C_{22}H_{21}F_3O_4$: calcd C 65.02%, H 5.21%; Found: C 65.23%, H 5.09%.

3.1.14. 2-(4-Fluorophenylethoxymethyl)-3-trifluoromethyl-1,4-dimethoxynaphthalene 6e. Yield: 85%, white powder, mp 110–111°C (hexane). ^{1}H NMR ($CDCl_3$) δ: 8.11–8.19 (2H, m, H-5, H-8), 7.59–7.65 (2H, m, H-6, H-7), 7.15–7.25 (2H, m, C-2′ and H-6′), 6.90–6.97 (2H, m, C-3′ and H-5′), 4.79 (2H, s, OCH_2), 3.99 (3H, s, OMe), 3.88 (3H, s, OMe), 3.77 (2H, m, OCH_2CH$_2$), 2.92 (2H, m, OCH$_2$CH_2). ^{13}C NMR ($CDCl_3$) δ: 161.5 (d, J=247 Hz, CF), 153.9 (C-1), 152.8 (C-4), 134.7 (Cquat), 134.6 (Cquat), 130.3 (C-3′), 130.2 (C-5′), 129.2 (Cquat), 128.6 (C-7), 127.5 (C-6), 124.1 (Cquat), 124.0 (q, J=278 Hz, CF_3), 123.7 (C-8), 123.0 (C-5), 118.5 (q, J=29.6 Hz, C–CF_3), 115.1 (C-2′), 114.8 (C-6′), 71.8 (OCH$_2$CH$_2$–C_6H_4), 64.3 (OMe), 64.0 (OMe) 63.8 (OCH_2), 35.8 (OCH$_2$$CH_2$$C_6H_4$). IR (KBr): 1586, 1504, 1423, 1365, 1296, 1221, 1143, 1097, 1003 cm^{-1}; MS, *m*/*z* (%): no M^+, 379 (62), 268 (18), 267 (100), 239 (10), 200 (70), 185 (12), 200 (70), 186 (12), 123 (19); Anal. $C_{22}H_{20}F_4O_3$: calcd C 64.70%, H 4.94%; Found: C 64.55%, H 4.68%.

3.1.15. 2-(2-Methylallyloxymethyl)-3-trifluoromethyl-1,4-dimethoxynaphthalene 6f. Yield: 96%, colorless oil. ^{1}H NMR ($CDCl_3$) δ: 8.09–8.16 (2H, m, H-5, H-8), 7.53–7.58 (2H, m, H-6, H-7), 5.03 (1H, s, C=CH_2), 4.90 (1H, s, C=CH_2), 4.76 (2H, s, OCH_2), 4.02 (2H, s, OCH_2–C_3H_5), 3.96 (6H, s, OMe), 1.79 (3H, s, Me). ^{13}C NMR ($CDCl_3$) δ: 153.1 (C-1), 152.9 (C-4), 142.1 (C=CH$_2$), 130.3 (Cquat), 128.8 (Cquat), 128.4 (C-7), 128.0 (Cquat), 127.3 (C-6), 123.5 (C-8), 122.9 (C-5), 122.4 (q, J=278 Hz, CF_3), 119.2 (q, J=29.2 Hz, C–CF_3), 112.6 (C=CH$_2$), 75.3 (OCH$_2$–C_3H_5), 63.7 (OCH$_2$), 63.6 (2–OMe), 19.5 (Me). IR (NaCl): 1617, 1588, 1451, 1417, 1358, 1294, 1117, 966, 777 cm^{-1}; MS, *m*/*z* (%): 340 (M^+, 45), 284 (10), 270 (43), 269 (28), 202 (41), 200 (47), 196 (23), 136 (23), 134 (20), 99 (40), 91 (96), 77 (48), 57 (100); Anal. $C_{18}H_{19}F_3O_3$: calcd C 63.52%, H 5.63%; Found: C 63.46%, H 5.68%.

3.1.16. 2-(Allyloxymethyl)-3-trifluoromethyl-1,4-dimethoxynaphthalene 6h. Yield: 96%, colorless oil. ^{1}H NMR ($CDCl_3$) δ: 8.13–8.20 (2H, m, H-5, H-8), 7.57–7.67 (2H, m, H-6, H-7), 5.93–5.99 (1H, m, CH=CH$_2$), 5.33 (1H, dd, J_1=17 Hz, J_2=4.6 Hz, CH=CH_a), 5.20 (1H, dd, J_1=9.6 Hz, J_2=4.6 Hz, CH=CH_b), 4.80 (2H, d, J=1.6 Hz, OCH_2), 4.13 (2H, dt, J_1=6.9 Hz, J_2=2.3 Hz, OCH_2), 4.00 (3H, s, OMe), 3.99 (OMe). ^{13}C NMR ($CDCl_3$) δ: 153.1 (C-1), 153.0 (C-4), 134.8 (CH=CH$_2$), 130.4 (Cquat),

129.3 (Cquat), 128.6 (C-7), 127.5 (C-6), 124.2 (Cquat), 123.7 (C-8), 123.0 (C-5), 124.5 (q, J=279 Hz, CF_3), 119.1 (q, J=36 Hz, C–CF_3), 117.4 (CH=CH_2), 72.1 (OCH_2CH=CH_2), 64.0 (OCH_2), 63.9 (OMe), 63.7 (OMe). IR (NaCl): 1617, 1584, 1496, 1451, 1416, 1358, 1158, 1118, 967 cm^{-1}; MS, m/z (%): 326 (M^+, 100), 270 (37), 269 (32), 266 (23), 255 (80), 240 (30), 200 (70), 127 (22), 113 (21), 71 (59); Anal. $C_{17}H_{17}F_3O_3$: calcd C 62.57%, H 5.25%; Found: C 62.46%, H 5.20%.

3.1.17. 2-(Benzyloxymethyl)-3-trifluoromethyl-1,4-naphthoquinone 7a. The synthesis of compound **7a** is representative of all other preparation of compounds **7**. To a solution of 2-(4-benzyloxymethyl)-3-trifluoromethyl-1,4-dimethoxynaphthalene **6a** (635 mg, 1.69 mmol) in a mixture of water (10 mL) and acetonitrile (10 mL) was added cerium ammonium nitrate (2.8 g, 5 mmol). The reaction was stirred for 15 min at room temperature, then it was treated with water and extracted with ether. The combined extracts were washed with water, brine, dried ($MgSO_4$). The solvent was evaporated in vacuo to give the crude product, which was purified by flash chromatography on a SiO_2 column with hexane/ethyl acetate (9:1) to give compound **7a** (490 mg, 84% yield), yellow oil. ^{1}H NMR ($CDCl_3$) δ: 8.05–8.09 (2H, m, H-5, H-8), 7.74–7.77 (2H, m, H-6, H-7), 7.22–7.35 (5H, m, H-2′, H-6′, H-3′, H-4′ and H-5′), 4.71 (2H, s, OCH_2), 4.70 (2H, s, OCH_2–C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 183.1 (C-1), 180.4 (C-4), 137.4 (Cquat), 134.7 (C-7), 134.4 (C-6), 131.2 (q, J=31.2 Hz, C–CF_3), 131.1 (Cquat), 128.5 (Cquat), 128.4 (C-3′, C-5′), 128.1 (C-2′, C-6′), 128.0 (C-4′), 127.4 (q, J=278 Hz, CF_3), 126.8 (C-8), 126.6 (C-5), 126.2 (C quat), 74.2 (OCH_2–C_6H_5), 61.4 (OCH_2). IR (NaBr): 1672 (C=O), 1624 C=O), 1591, 1340, 1283, 1179, 1146, 1075, 727 cm^{-1}; MS, m/z (%): 346 (M^+, 5), 271 (10), 270 (71), 256 (23), 255 (93), 241 (17), 227 (12), 159 (22), 92 (20), 91 (96), 71 (58), 57 (100); Anal. $C_{19}H_{13}F_3O_3$: calcd C 65.90%, H 3.78%; Found: C 65.98%, H 3.68%.

3.1.18. 2-(4-Chlorobenzyloxymethyl)-3-trifluoromethyl-1,4-naphthoquinone 7b. Yield: 85%, yellow powder, mp 67–68°C (hexane). ^{1}H NMR ($CDCl_3$) δ: 8.08–8.13 (2H, m, H-5, H-8), 7.77–7.86 (2H, m, H-6, H-7), 7.27 (4H, m, H-3′, H-4′, H-6′ and H-5′), 4.72 (2H, s, OCH_2), 4.59 (2H, s, OCH_2–C_6H_4). ^{13}C NMR ($CDCl_3$) δ: 183.1 (C-1), 180.4 (C-4), 145.2 (Cquat), 135.9 (Cquat), 134.9(Cquat), 134.8 (C-7), 134.5 (C-6), 133.8 (Cquat), 130.1 (Cquat), 129.3 (C-3′, C-5′), 129.2 (q, J=31.5 Hz, C–CF_3), 128.6 (C-2′, C-6′), 126.9 (C-8), 126.7 (C-5), 125.4 (d, J=279 Hz, CF_3), 73.3 (OCH_2–C_6H_4), 61.5 (OCH_2). IR (KBr): 1673 (C=O), 1650 (C=O), 1591, 1284, 1181, 1150, 1087, 809, 725 cm^{-1}; MS, m/z (%): no M^+, 256 ($M-C_7H_5Cl^+$, 3), 255 (15), 194 (10), 192 (25), 174 (41), 105 (30), 91 (29), 86 (43), 49 (100); Anal. $C_{19}H_{12}ClF_3O_3$: calcd C 59.94%, H 3.18%; Found: C 59.65%, H 3.28%.

3.1.19. 2-(4-Methylbenzyloxymethyl)-3-trifluoromethyl-1,4-naphthoquinone 7c. Yield: 84%, yellow powder, mp 68–69°C (hexane/ethyl acetate 85:15). ^{1}H NMR ($CDCl_3$) δ: 8.00–8.04 (2H, m, H-5, H-8), 7.70–7.73 (2H, m, H-6, H-7), 7.16 (2H, d, J=8.1 Hz, H-2′ and H-6′), 7.03 (2H, d, J=8.1 Hz, H-3′ and H-5′), 4.66 (2H, s, CH_2), 4.55 (2H, s, OCH_2–C_6H_4), 2.22 (3H, s, Me). ^{13}C NMR ($CDCl_3$) δ: 183.0 (C-1), 180.3 (C-4), 145.8 (Cquat), 137.7 (Cquat), 134.6 (C-7), 134.3 (C-6), 131.5 (Cquat), 131.0 (Cquat), 129.1 (q, J=31 Hz, C–CF_3), 129.0 (C-3′, C-5′), 128.3 (C-2′, C-6′), 128.1 (Cquat), 126.7 (C-8), 126.5 (C-5), 124.6 (d, J=279 Hz, CF_3), 74.0 (OCH_2–C_6H_4), 61.3 (OCH_2), 21.0 (3H, s, Me). IR (KBr): 1673 (C=O), 1669 (C=O), 1593, 1350, 1288, 1213, 1141, 801, 728 cm^{-1}; MS, m/z (%): no M^+ 341 [$(M-F)^+$, 1], 203 (34), 202 (63), 156 (29), 121 (26), 105 (20), 91 (84), 44 (100); Anal. $C_{20}H_{15}F_3O_3$: calcd C 66.67%, H 4.20%; Found: C 66.55%, H 4.38%.

3.1.20. 2-(1-Hydroxymethyl)-3-trifluoromethyl-1,4-naphthoquinone 7d. Yield: 79%, yellow powder, mp 91–93°C. ^{1}H NMR ($CDCl_3$) δ: 8.06–8.14 (2H, m, H-5, H-8), 7.71–7.84 (2H, m, H-6, H-7), 4.86 (2H, s broad, CH_2OH). ^{13}C NMR ($CDCl_3$) δ: 183.6 (C-1), 180.4 (C-4), 147.4 (Cquat), 135.1 (C-7), 134.5 (C-6), 134.4 (q, J=5 Hz, C-2), 127.5 (q, J=30 Hz, C–CF_3), 127.1 (Cquat), 126.8 (C-5), 126.7 (C-8), 123.9 (q, J=280 Hz, CF_3), 61.8 (CH_2OH). IR (KBr): 3500 (OH), 1675 (C=O), 1667 (C=O), 1588, 1458, 1281, 1186, 1142 cm^{-1}; MS, m/z (%): 256 (M^+, 6), 236 (36), 216 (18), 202 (14), 151 (11), 149 (26), 141 (11), 84 (64), 57 (100); Anal. $C_{12}H_7F_3O_3$: calcd C 56.26%, H 2.75%; Found: C 56.15%, H 2.68%.

3.1.21. 2-(4-Fluorophenylethoxymethyl)-3-trifluoromethyl-1,4-naphthoquinone 7e. Yield: 84%, yellow oil. ^{1}H NMR ($CDCl_3$) δ: 8.07–8.15 (2H, m, H-5, H-8), 7.72–7.77 (2H, m, H-6, H-7), 7.12–7.17 (2H, m, H-6′, H-2′), 6.85–6.91 (2H, m, H-3′ and H-5′), 4.68 (2H, s, OCH_2), 3.75 (2H, m, OCH_2CH_2–C_6H_4), 2.84 (2H, m, OCH_2CH_2–C_6H_4). ^{13}C NMR ($CDCl_3$) δ: 183.1 (C-1), 180.5 (C-4), 161 (d, J=244 Hz, CF), 145.0 (Cquat), 135.0 (Cquat), 134.7 (C-7), 134.4 (C-6), 134.2 (Cquat), 134.1 (Cquat), 130.3 (C-5), 130.2 (C-8) 128.9 (q, J=29.6 Hz, C–CF_3), 127.5 (q, J=279 Hz, CF_3), 126.8 (C-3′), 126.6 (C-5′), 115.4 (C-2′), 114.8 (C-6′), 72.6 (OCH_2CH_2), 61.8 (OCH_2), 35.3 (OCH_2CH_2). IR (NaCl): 1676 (C=O), 1594 (C=O), 1510, 1345, 1286, 1221, 1180, 1149, 1101 cm^{-1}; MS, m/z: 378 (M^+, 3), 280 (8), 256 (32), 240 (12), 239 (61), 228 (10), 219 (13), 123 (66), 122 (100); Anal. $C_{20}H_{14}F_4O_3$: calcd C 63.50%, H 3.73%; Found: C 63.69%, H 3.68%.

3.1.22. 2-(2-Methylallyloxymethyl)-3-trifluoromethyl-1,4-naphthoquinone 7f. Yield: 93%, yellow oil. ^{1}H NMR ($CDCl_3$) δ: 8.05–8.09 (2H, m, H-5, H-8), 7.76–7.79 (2H, m, H-6, H-7), 4.99 (1H, s, C=CH_2), 4.92 (1H, s, C=CH_2), 4.63 (2H, d, J=1.6 Hz, OCH_2), 4.00 (2H, s, OCH_2–C_3H_5), 1.75 (3H, s, Me). ^{13}C NMR ($CDCl_3$) δ: 183.0 (C-1), 180.3 (C-4), 145.3 (Cquat), 141.5 (C=CH_2), 134.6 (C-7), 134.4 (q, J=29.4 Hz, C–CF_3), 134.3 (C-6), 131.5 (Cquat), 130.9 (Cquat), 126.7 (C-8), 126.5 (C-5), 123.8 (q, J=278 Hz, CF_3), 113.3 (C=CH_2), 75.9 (OCH_2–C_3H_5), 60.8 (OCH_2), 19.2 (Me). IR (NaCl): 1673 (C=O), 1669 (C=O), 1592 (C=C), 1343, 1284, 1181, 1151 cm^{-1}; MS, m/z (%): 310 (M^+, 2), 269 (10), 256 (13), 255 (65), 241 (34), 240 (100), 239 (23), 220 (47), 212 (50), 151 (67), 76 (44), 55 (87); Anal. $C_{16}H_{13}F_3O_3$: calcd C 61.94%, H 4.22%; Found: C 61.75%, H 4.28%.

3.1.23. 2-(2-Allyloxymethyl)-3-trifluoromethyl-1,4-naphthoquinone 7h. Yield: 93%, yellow oil. ^{1}H NMR ($CDCl_3$) δ: 8.10–8.17 (2H, m, H-5, H-8), 7.62–7.84 (2H, m, H-6,

H-7), 5.85–5.99 (1H, m, C*H*=CH_2), 2.19–2.29 (2H, m, CH=CH_2), 4.68 (2H, d, J=1.6 Hz, OCH_2), 4.11 (2H, dt, J_1=2.9 Hz, J_2=1.0 Hz, OCH_2CH=CH_2). ^{13}C NMR ($CDCl_3$) δ: 183.1 (C-1), 180.5 (C-4), 145.5 (Cquat), 134.8 (C-7), 134.5 (C-6), 134.1 (*C*H=CH_2), 131.6 (Cquat), 131.0 (Cquat), 129.5 (q, J=31 Hz, *C*–CF_3), 126.8 (C-8), 126.6 (C-5), 119.9 (q, J=278 Hz, CF_3), 118.0 (C=*C*H_2), 72.9 (O*C*H_2CH=CH_2), 61.0 (O*C*H_2). IR (NaCl): 1674 (C=O), 1669 (C=O), 1591 (C=C), 1341, 1284, 1181, 1151 cm^{-1}; MS, *m*/*z* (%): 296 (M^+, 4), 292 (4), 256 (8), 255 (60), 240 (22), 221 (15), 207 (25), 151(45), 41 (100); Anal. $C_{15}H_{11}F_3O_3$: calcd C 60.82%, H 3.74%; Found: C 60.61%, H 3.88%.

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References

1. Welch, J. T. *Tetrahedron* **1987**, *43*, 3123–3197.
2. Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; Wiley: New York, 1991.
3. Yang, J. J.; Kirchmeier, R. L.; Shreeve, J. M. *J. Org. Chem.* **1998**, *63*, 2600–2656.
4. McClinton, M. A.; McClinton, D. A. *Tetrahedron* **1992**, *48*, 6555–6666.
5. Lin, P.; Jiang, J. *Tetrahedron* **2000**, *56*, 3635–3671.
6. Banks, R. E.; Smart, B. E.; Tatlow, J. C. *Organofluorine Chemistry, Principles and Commercial Application*; Plenum: New York, 1994.
7. Yoshika, H.; Nakayama, C.; Matsuo, N. *J. Synth. Chem. Jpn* **1984**, *42*, 809.
8. Reynolds, D. W.; Cassidi, P. E.; Johnson, C. G.; Gameron, M. L. *J. Org. Chem.* **1990**, *55*, 4448–4454.
9. Zang, X.; Qing, F. L.; Yang, Y.; Yu, J.; Fu, X. K. *Tetrahedron Lett.* **2000**, *41*, 2953–2955.
10. Hünig, S.; Bau, R.; Kemmer, M.; Meixner, H.; Metzenthin, T.; Peters, K.; Sinzger, K.; Gulbis, J. *Eur. J. Org. Chem.* **1998**, 335–348.
11. Blazejewski, J. C.; Dorme, R.; Wakselman, C. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1861–1864.
12. Blazejewski, J. C.; Dorme, R.; Wakselman, C. *Synthesis* **1985**, 1120–1121.
13. Peter, E.; Cooper, D.; Allen, G.; Slater, M. J. *Bioorg. Med. Chem.* **1999**, *9*, 2863–2866.
14. Lien, J. C.; Huang, L. J.; Wang, J. P.; Teng, C. M.; Lee, K. H.; Kuo, S. C. *Bioorg. Med. Chem.* **1997**, *12*, 2111–2120.
15. Huang, L. J.; Chang, F. C.; Lee, K. H.; Wang, J. P.; Teng, C. M.; Kuo, S. C. *Bioorg. Med. Chem.* **1998**, *6*, 2261–2269.
16. Ansbacher, S.; Fernholz, E.; Dolliver, M. A. *J. Am. Chem. Soc.* **1940**, *62*, 155–158.
17. Syper, L.; Mlochowski, J.; Kloc, K. *Tetrahedron* **1983**, *39*, 781–792.
18. Cutler, H. G.; Majetich, G.; Tian, X.; Spearing, P. *J. Agric. Food Chem.* **1997**, *45*, 1422–1429.
19. Ramanchandran, V.; Davidson, R. I.; Maloney, J. R. (Ethyl Corporation) US 4,590,010, 1986; *Chem. Abstr.*, **1986**, *105*, P78690f.