Supporting Information

Photolabile Protection of Alcohols, Phenols, and Carboxylic Acids with 3-Hydroxy-2-Naphthalenemethanol.

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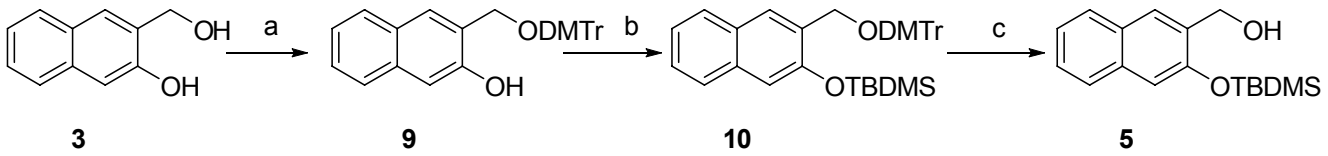
General Experimental Methods. All organic solvents were dried and freshly distilled before use. Flash chromatography was performed using 40-63 μm silica gel. Melting points are uncorrected. All NMR spectra were recorded in $CDCl_3$ and referenced to TMS unless otherwise noted. Solutions were prepared using HPLC grade water, methanol, and acetonitrile. Photolyses of $3*10^{-4}$ - $1*10^{-3}$ M solutions of compounds **1a-g** were conducted using mini-Rayonet photochemical reactor equipped with 8 fluorescent UV lamps (4W, 254 nm or 300 nm, at ambient temperatures) or using an immersion type reactor equipped with a 450W medium-pressure mercury lamp (at 25.0 ± 0.5 ^{0}C). Reaction mixtures after photolysis were analyzed by HPLC using pure substrates as references. Quantum efficiencies of photochemical reactions were measured by ferrioxalate actinometry.[1] The laser flash photolytic experiments were conducted using the fourth harmonic (266 nm) from the Brilliant B Nd:YAG laser as an excitation source and LKS.60 nanosecond kinetic spectrometer (by Applied PhotoPhysics).

Preparation of 3-tert-butyldimethylsilyloxy-2-naphthalenemethanol (**5**)

Scheme S1



3 **9** **10** **5**

Reagents and conditions: (a) DMTrCl / Pyridine; (b) TBDMSCl / Imidazole/ DMF/ DMAP; (c) $Ce(OTf)_4$ / aq. acetonitrile.

4,4'-Dimethoxytrityl (3-tert-butyldimethylsilyloxy-2-naphthalenyl)methyl ether (**10**): 570 mg (1.68 mmol) of 4,4'-dimethoxytrityl chloride and 42 mg (0.34 mmol) of DMAP were added to a solution of **3** (300 mg, 1.72 mmol) in dry pyridine (5.1 mL). The reaction mixture was stirred at r.t. overnight and pyridine was removed under vacuum. The residue was dissolved in dichloromethane, washed with brine, dried over sodium sulfate. Solvent was removed and 4,4'-dimethoxytrityl (3-hydroxy-2-naphthalenyl)methyl ether (**9**) was used in the next step without further purification.

257 mg (3.78 mmol) of imidazole, 42 mg (0.34 mmol) of DMAP and 516 mg (3.44 mmol) of TBDMS chloride were added to a solution of **9** in dry DMF (9 mL). The reaction mixture was stirred at r.t. overnight, poured into saturated solution of sodium bicarbonate (200 mL), and extracted with ethyl acetate. Combined organic layers were washed with brine, dried over sodium sulfate, and solvent was removed in vacuum. The residue was purified by chromatography (ethyl acetate / hexanes : 1/4) to give 764 mg of **10** as a white solid (82% over two steps). M.p. 139 - 141ºC. ^{1}H NMR (300 MHz): 8.30 (s, 1H), 7.91 (m, 1H), 7.66 (m, 1H), 7.56 (dt, *J* = 6.96,1.5 Hz, 2H), 7.49-7.16 (m, 9H), 7.04 (s, 1H), 6.84 (dt, *J* = 9.03, 3.03 Hz, 4H), 4.30 (d, *J* = 1.14 Hz, 2H), 3.78 (s, 6H), 0.82 (s, 9H), 0.13 (s, 6H); ^{13}C

NMR (75 MHz): 158.5, 151.1, 145.2, 136.5, 133.3, 132.0, 130.0, 129.3, 128.2, 127.9, 127.8, 126.8, 126.2, 125.7, 125.6, 123.7, 113.2, 112.7, 96.2, 86.7, 62.2, 55.2, 25.7, 18.1, -4.4. MS *m/z* 590 (M+, 2), 305 (5), 304 (30), 303 (100), 273 (7), 229 (9), 227 (5), 215 (10), 195 (7), 165 (5), 152 (6), 141 (5). FW calc. for $C_{38}H_{42}O_4Si$: 590.2852, EI-HRMS found: 590.2847.

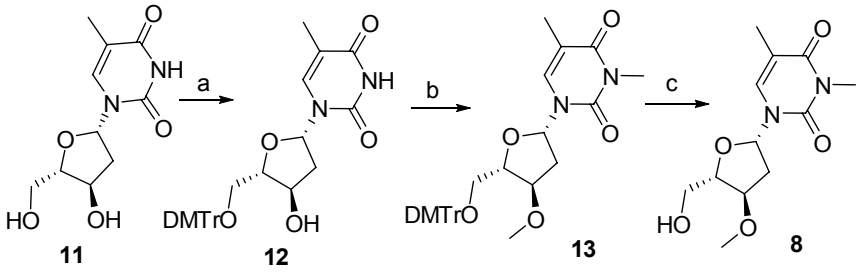
3-tert-butyldimethylsilyloxy-2-naphthalenemethanol (**5**): Cerium (IV) triflate (40 mg, 0.053 mmol) was added to a stirred solution of **10** (200 mg, 0.34 mmol) in wet acetonitrile (4 mL). Reaction mixture was stirred at r.t. for 3 h, poured into saturated solution of sodium bicarbonate (100 mL), and extracted with ethyl acetate. Combined organic layers were washed with brine, dried over sodium sulfate, and solvent removed under vacuum. Chromatographic purification (chloroform) of the residue gave 83 mg (85%) of **5** as a yellowish oil. ^{1}H NMR (300 MHz): 7.79 (m, 2H), 7.71 (d, *J* = 7.53 Hz, 1H), 7.45 (m, 1H), 7.37 (m, 1H), 7.17 (s,1H), 4.86 (s, 2H), 2.21 (br. s 1H), 1.09 (s, 9H), 0.37 (s, 6H); ^{13}C NMR (75 MHZ): 151.8, 134.0, 132.8, 129.1, 127.6, 127.4, 126.3, 126.1, 124.0, 113.3, 62.4, 25.8, 18.2, -4.2; MS *m/z*: 288 (M+, 5), 233 (7), 232 (27), 231 (100), 229 (6), 215 (17), 214 (18), 213 (80), 212 (5), 210 (18), 199 (6), 198 (7), 197 (8), 185 (26), 157 (8), 156 (6), 155 (19), 153 (6), 152 (7), 141 (9), 139 (5),129 (6), 128 (20), 127 (10), 115 (5). FW calc. for $C_{17}H_{24}O_2Si$ 288.1546, EI-HRMS found 288.1541.

(3-tert-Butyldimethylsilyloxy-2-naphthalenyl)methyl Bromide (**7**)*.* *Method A:* Triphenylphosphine (195 mg, 0.74 mmol) was added to a stirred solution of **5** (200 mg, 0.69 mmol) in dry THF (2mL) at r.t., followed by slow addition of carbon tetrabromide (256 mg, 0.74 mmol) after 5 min. The reaction mixture was stirred at r.t. for 2 h. Solids were removed by filtration, dried under vacuum, and purified by chromatography (3% ethyl acetate in hexanes) to afford 165 mg (67%) of **7** as a white solid.

Method B: 0.5 equivalent of PBr_3 was added dropwise to the solution of **5** (500 mg, 1.73 mmol) in anhydrous ether (3mL). The resultant solution was stirred for 3 h at r.t., poured in to 50 mL of saturated sodium bicarbonate solution. The resulting suspension was extracted with ethyl ether, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by chromatography (3% ethyl acetate in hexanes) to yield 490 mg (80%) of **7**. M. p. 57-59ºC. ^{1}H NMR (300 MHz): 7.86 (s, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 8.28 Hz, 1H), 7.45 (s, 1H), 7.36 (s, 1H), 7.18 (s, 1H), 4.71 (s, 2H), 1.15 (s, 9H), 0.41 (s, 6H); ^{13}C NMR (75MHz): 151.7, 134.7, 130.6, 129.9, 128.8, 127.6, 126.7, 126.3, 125.5, 124.1, 113.4, 29.6, 25.9, 18.4, -4.1; MS *m/z*: 352 (M+ + 2, 4), 350 (M+, 4), 297 (9), 296 (43), 295 (100), 294 (44), 293 (92), 279 (13), 277 (11), 272 (8), 271 (20), 216 (10), 215 (51), 214 (16), 213 (24), 211 (11), 205 (12), 199 (38), 197 (12), 185 (19), 155 (23), 153 (15), 152 (13), 141 (25), 140 (10), 139 (24). FW calc. for $C_{17}H_{23}OSi$ 350.0702, EI-HRMS found 350.0710.

***Synthesis of 3'-O-3-dimethylthymidine** (**8**).*

Scheme S2



Reagents and conditions: (a) 4,4'-dimethoxytrityl chloride / pyridine; (b) NaH / THF; Me_2SO_4; (c) *p*-TosOH / CH_2Cl_2

5'-*O*-(4,4'-Dimethoxytrityl)thymidine (**12**)[2]: 4,4'-Dimethoxytrityl chloride (2.85 g, 8.45 mmol) and DMPA (100 mg) were added to the solution of thymidine (**11**, 1.00 g, 7.04 mmol) in freshly distilled pyridine (17 mL). Reaction mixture was stirred overnight at r.t., pyridine removed under vacuum; residue was redissolved in ethyl acetate, washed with brine, and dried under sodium sulfate. Solvent was removed under reduced pressure and residue was purified by chromatography (50% ethyl acetate in hexanes) to give 1.80 g (80%) of **12** as a colorless oil. H^1 NMR (400 MHz): 9.45 (br s, 1H), 7.63 (s, 1H), 7.38-7.40 (d, 1H, 7.2 Hz), 7.15-7.27 (m, 5H), 6.81-6.83 (d, 4H, 9.2Hz), 6.43-6.47 (m, 1H) 4.57 (m, 1H), 4.09-4.10 (m, 1H), 3.76 (s, 6H), 3.43-3.46 (m, 1H), 3.33-3.36 (m, 1H), 2.67 (br s, 1H), 2.43-2.47 (m, 1H), 2.29-2.34 (m, 1H), 1.42 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 12.1, 42.0, 55.5, 63.4, 72.7, 81.7, 85.1, 86.6, 87.1, 96.4, 111.2, 113.4, 113.5, 127.3,127.4, 128.1, 128.2, 128.4, 129.4, 130.3, 135.6, 135.7, 136.1, 139.8, 144.6, 147.6, 151.0, 158.8, 158.9, 158.9, 164.4; DIP-MS *m/z*: 544 (M+), 303 (100), 304, 288, 273, 227, 195, 152, 117, 81, 55.

3'-*O*-3-dimethylthymidine (**8**): **12** (1.00 g, 1.84 mmol) was added to a suspension of NaH (180 mg, 7.36 mmol, 4 eq.) in dry THF (25 mL) at 0°C, stirred for 30 min, and dimethyl sulfate (0.7 mL, 7.36 mmol, 4 eq.) was added dropwise. Reaction mixture was allowed to warm to r.t., stirred for 3 h, and quenched by addition of water (5 mL). Organic layer was diluted with ethyl acetate (100 mL), separated, washed with brine, dried over sodium sulfate, and solvent was removed under reduced pressure to produce ca 1.2 g of crude **5'-*O*-(4,4'-dimethoxytrityl)-3'-*O*-3-dimethylthymidine** (**13**). H^1 NMR (400 MHz, $CDCl_3$): 7.62 (s, 1H), 7.39-7.41 (d, 1H, 7.6 Hz), 7.23-7.31 (m, 5H), 6.80-6.83 (d, 4H, 8.8Hz), 6.37-6.33 (m, 1H), 4.09-4.11 (m, 1H), 4.05-4.07 (m, 1H), 3.75 (s, 6H), 3.48-3.52 (m, 2H), 3.32 (s, 1H), 3.29 (s, 1H), 2.45-2.50 (m, 1H), 2.18-2.30 (m, 1H), 1.49 (s, 3H). DIP-MS *m/z*: 572 (M+), 303 (base peak), 304, 288, 253, 227, 195, 165, 140, 81, 45.

p-Toluenesulfonic acid (433 mg, 2.52 mmol, 1.2 eq.) was added to a solution crude **13** (1.20 g, 2.10 mmol) in CH_2Cl_2 (15 mL), and stirred for 1.5 h. The reaction mixture was diluted with ethyl acetate

(100 mL), washed with saturated sodium bicarbonate solution, brine, dried over sodium sulfate, and solvent removed under reduced pressure. The residue was purified by column chromatography (50% of ethyl acetate in hexanes) to yield 410 mg of **13** (82%) as a colorless oil. H^1 NMR (400 MHz): 7.49 (s, 1H), 6.07-6.11 (m, 1H), 4.0-4.03 (m, 2H), 3.82-3.86 (m, 1H), 3.69-3.73 (m, 1H), 3.51 (br s, 1H), 3.26 (s, 1H), 3.23 (s, 1H), 2.29-2.34 (m, 1H), 2.14-2.21 (m, 1H), 1.84 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 13.3, 27.9, 37.3, 56.3, 62.2, 81.9, 85.9, 87.0, 96.2, 109.7, 135.0, 151.1, 163.9; GC-MS *m/z*: 270 (M+), 141, 140, 122 112, 99, 87 (base peak), 71, 69, 59, 43; FW calc. for $C_{12}H_{18}N_2O_5$ 270.1216, EI-HRMS found 270.1202.

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[1] Murov, S.L.; Carmichael, I.; Hug, G.L. in: Handbook of Photochemistry, Marcel Dekker: New York, 1993, p.299.

[2] Bleasdale, C.; Ellwood, S. B.; Golding, B. T. *J. Chem. Soc. Perkin Trans. 1* **1990**, 803