A Method for the Rapid Synthesis of Highly Functionalized 2-Hydroxy-1-Naphthoates. Syntheses of the Naphthoic Acid Components of Neocarzinostatin Chromophore and N1999A2

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Experimental Section:

General Procedures. All reactions were performed in oven- or flame-dried round bottomed or modified Schlenk flasks fitted with rubber septa under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Where necessary (so noted), solutions were deoxygenated by alternative freeze (liquid nitrogen)/evacuation/thaw cycles ($\geq$ three iterations). Organic solutions were concentrated by rotary evaporation (house vacuum, $\sim$ 25 Torr) at 23–30 °C. Flash column chromatography was performed as described by Still et al.,¹ employing silica gel (60-Å pore size, 230–400 mesh, Merck KGA; or 60-Å pore size, 32–63 μ m, standard grade, Sorbent Technologies). Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with silica gel (0.25 mm, 60-Å pore size, 230–400 mesh, Merck KGA) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV) and/or exposure to ceric ammonium molybdate solution (CAM) or an acidic solution of *p*-anisaldehyde (anisaldehyde) followed by brief heating on a hot plate ($\sim$ 200 °C, 10–15 s).

Materials. Commercial reagents and solvents were used as received unless mentioned otherwise. Dichloromethane, ether, tetrahydrofuran, *N,N*-dimethylformamide and toluene were purified by the method of Pangborn et al.² The molarity of solutions of *n*-butyllithium and *t*-butyllithium was determined by titration against a standard solution of 2-butanol in tetrahydrofuran using triphenylmethane as an indicator (average of three determinations).³

(1) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.

(3) Duhamel, L.; Palquevent, J.-C. *J. Org. Chem.* **1979**, *44*, 3404-3405.

Instrumentation. Proton nuclear magnetic resonance (^1H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) were recorded with Varian Unity/Inova 600 (600 MHz), Varian Unity/ Inova 500 (500 MHz/125 MHz), or Varian Mercury 400 (400 MHz/100 MHz) NMR spectrometers. Chemical shifts for protons are reported in parts per million scale (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvents (CHCl_3 : δ 7.26). Chemical shifts for carbon are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl_3 : δ 77.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constant in Hz, and assignment. Infrared (IR) spectra were obtained using a Perkin-Elmer 1600 FT-IR spectrophotometer referenced to a polystyrene standard. High resolution mass spectra were obtained at the Harvard University Mass Spectrometry Facilities.

List of Abbreviations

AcOH	acetic acid
$\text{CF}_3\text{CH}_2\text{OH}$	trifluoroethanol
CH_2Cl_2	dichloromethane
Cl_3CCCl_3	hexachloroethane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DMF	<i>N,N</i> -dimethylformamide
<i>E</i>	<i>Ger.</i> , entgegen
equiv	equivalent
ESI	electrospray ionization
FTIR	Fourier transform infrared spectroscopy
g	gram
HRMS	high resolution mass spectrometry
Hz	hertz
<i>J</i>	coupling constant

LiOH	lithium hydroxide
M	Molarity
mg	milligram
mL	milliliter
μL	microliter
mmol	millimole
$\text{Mn}(\text{OAc})_3$	manganese (III) acetate
mol	mole
NaH	sodium hydride
NBS	<i>N</i> -bromosuccinimide
<i>n</i> -BuLi	normal butyllithium
NMR	nuclear magnetic resonance
ppm	parts per million
THF	tetrahydrofuran
TIPS	triisopropylsilyl
<i>Z</i>	<i>Ger.</i> , zusammen

(2,2-Dimethyl-6-oxo-6H-[1,3]dioxin-4-ylmethyl)-phosphonic acid diphenyl ester (6).

Diphenyl phosphite (Aldrich, 85%, containing 15% phenol, 9.09 g, 38.8 mmol, 3.5 equiv) was added dropwise via syringe over 10 min to an ice-cooled solution of potassium *tert*-butoxide (4.36 g, 38.8 mmol, 3.5 equiv) in DMF (50 mL). The resulting solution was allowed to stir at 0 °C for 15 min. A solution of 6-chloromethyl-2,2-dimethyl-4*H*-1,3-dioxin-4-one (1.96 g, 11.1 mmol, 1 equiv)⁴ in DMF (10.0 mL) was then added via cannula over 2 min. After stirring for 1 h at 0 °C, the deep purple reaction mixture was allowed to warm to 23 °C. After 9 h at 23 °C, concentrated aqueous hydrochloric acid solution was added dropwise until the solution turned colorless (~ 3 mL). The resulting mixture was partitioned between water (300 mL) and a 1:1 mixture of ethyl acetate and hexanes (300 mL). The aqueous layer was separated and extracted with a 1:1 mixture of ethyl acetate and hexanes (300 mL). The organic extracts were combined and dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (50% ether–hexanes, grading to 67% ether–hexanes) to afford phosphonate **6** as a white solid, mp 75–77 °C (2.52 g, 61%).

¹H NMR (500 MHz, CDCl₃) δ: 7.35 (t, J=8.0 Hz, 4H, C(3')-**H**), 7.23–7.17 (m, 2H, C(4')-**H**; 4H, C(2')-**H**), 5.50 (d, J=4.0 Hz, 1H, C(5)-**H**), 3.15 (d, J=22.5 Hz, 2H, C(7)-**H**), 1.69 (s, 6H, C(2)-(CH₃)₂)

¹³C NMR (100 MHz, CDCl₃) δ: 161.7, 161.6, 160.20, 160.18, 149.8, 149.7, 129.9, 125.6, 120.3, 120.2, 107.4, 97.0, 96.9, 33.0, 31.6, 24.8

⁴ Boeckman, R. K.; Perni, R. B.; Macdonald, J. E.; Thomas, A. J. *Organic Syntheses*, **1988**, 66, 194–202.

HRMS (ESI⁺): m/z calcd for (C₁₉H₁₉O₆P+NH₄)⁺ 392.1263, found: 392.1255

FTIR (cm⁻¹): 3500, 3099, 3067, 2995, 2923, 1728, 1634, 1590, 1488, 1376, 1274, 1187, 935

Neocarzinostatin Chromophore Naphthoic Acid (1, 4 steps)

(Z)-Olefin 7. DBU (359 μ L, 365 mg, 2.40 mmol, 2.0 equiv) was added dropwise via syringe over 2 min to a stirring solution of phosphonate **6** (629 mg, 1.68 mmol, 1.4 equiv) in tetrahydrofuran (5 mL) at 23 $^{\circ}$ C. The reaction mixture was allowed to stir at 23 $^{\circ}$ C for 20 min. A solution of 4-methoxy-2-methylbenzaldehyde (**5**) (181 μ L, 200 mg, 1.20 mmol, 1 equiv) in tetrahydrofuran (5 mL) was added dropwise via cannula. The resulting mixture was allowed to stir at 23 $^{\circ}$ C for 18.5 h. Saturated aqueous ammonium chloride solution (20 mL) was added, and the resulting biphasic mixture was concentrated in vacuo to remove tetrahydrofuran. The aqueous residue was extracted with ether (3 $\times$ 20 mL). The organic extracts were combined and dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (50% ether–hexanes) to give (Z)-olefin **7** as a yellow oil (298 mg, 82 %).

^1H NMR (400 MHz, CDCl_3) δ : 7.11 (d, $J=8.4$ Hz, 1H, C(6')-**H**), 6.92 (d, $J=12.0$ Hz, 1H, C(8)-**H**), 6.70 (d, $J=2.4$ Hz, 1H, C(3')-**H**), 6.66 (dd, $J_1=2.4$ Hz, $J_2=8.4$ Hz, C(5')-**H**), 5.93 (d, $J=12.0$ Hz, 1H, C(7)-**H**), 5.25 (s, 1H, C(5)-**H**), 3.78 (s, 3H, C(4')- OCH_3), 2.23 (s, 3H, C(2')- CH_3), 1.51 (s, 6H, C(2)-(CH $_3$) $_2$)

^{13}C NMR (100 MHz, CDCl_3) δ : 163.9, 161.7, 159.6, 139.6, 137.4, 130.2, 127.9, 121.2, 114.8, 110.5, 105.9, 95.3, 55.1, 24.7, 20.1

HRMS (ESI⁺):

m/z calcd for (C₁₆H₁₈O₄+H)⁺ 275.1283, found 275.1280

FTIR (cm⁻¹):

3087, 2995, 2944, 2841, 1723, 1631, 1605, 1564, 1497, 1462, 1390, 1375, 1333, 1271, 1251, 1205, 1164, 1113, 1041, 1015, 903, 831

Trifluoroethyl 2-hydroxy-1-naphthoic acid ester 8. Sodium hydride (60% dispersion in mineral oil, 51.4 mg, 2.14 mmol, 6.0 equiv) was added to a stirring solution of trifluoroethanol (260 μ L, 357 mg, 3.57 mmol, 10.0 equiv) in tetrahydrofuran (5 mL) at 23 °C. The reaction mixture was allowed to stir at 23 °C for 20 min. A solution of (Z)-olefin **7** (98.0 mg, 0.357 mmol, 1 equiv) in tetrahydrofuran (5 mL) was added via cannula. After stirring for 30 min at 23 °C, the resulting mixture was concentrated in vacuo. The residue was taken up in acetic acid (4 mL). Manganese (III) acetate dihydrate (192 mg, 0.714 mmol, 2.0 equiv) was added. After stirring for 20 h at 23 °C, the reaction mixture was diluted with water (20 mL). The resulting biphasic mixture was extracted with ethyl acetate (3 $\times$ 25 mL). The organic extracts were combined and washed with saturated aqueous sodium bicarbonate solution (2 $\times$ 25 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (50% ether–hexanes) to give trifluoroethyl 2-hydroxy-1-naphthoic acid ester **8** as a white solid (104 mg, 93%).

^1H NMR (500 MHz, CDCl_3) δ : 11.78 (s, 1H, C(2)-OH), 8.06 (d, $J=9.5$ Hz, 1H, C(4)-H), 7.97 (d, $J=2.5$ Hz, 1H, C(8)-H), 7.03 (d, $J=9.0$ Hz, 1H, C(3)-H), 6.90 (d, $J=1.0$ Hz, 1H, C(6)-H), 4.84 (q, $J=8.5$ Hz, 2H, C(1)-C(O)OCH₂CF₃), 3.89 (s, 3H, C(7)-OCH₃), 2.61 (s, 3H, C(5)-CH₃)

^{13}C NMR (100 MHz, CDCl_3) δ : 170.9, 165.3, 159.9, 137.1, 134.0, 133.6, 123.2 (q, $J=275$ Hz), 123.0, 117.3, 115.8, 103.3, 103.0, 61.4 (q, $J=36.6$ Hz), 54.9, 19.9

HRMS (ESI⁻): m/z calcd for (C₁₅H₁₃F₃O₄-H)⁻ 313.0688, found 313.0694

FTIR (cm⁻¹): 2976, 1672, 1652, 1614, 1415, 1369, 1318, 1276, 1175, 1166, 1039, 959, 846

NCS chromophore naphthoic acid (1). Lithium hydroxide monohydrate (54.5 mg, 1.30 mmol, 20.0 equiv) was added to a stirring solution of trifluoroethyl 2-hydroxy-1-naphthoic acid ester **8** (20.5 mg, 0.65 mmol, 1 equiv) in tetrahydrofuran (4.0 mL) and water (2.0 mL). The resulting biphasic mixture was allowed to stir at 40 °C for 19 h. Water (10 mL) was added, the biphasic mixture was cooled to 0 °C, and 1N aqueous hydrochloric acid solution was added carefully to an end point of pH~1.0 (~ 1.5 mL). The product was extracted with ethyl acetate (3 × 15 mL). The organic extracts were combined and washed with brine (2 × 10 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated to afford NCS chromophore naphthoic acid (**1**) as a white solid (15.0 mg, 100%).

^1H NMR (500 MHz, CDCl_3) δ : 12.02 (s, br, 1H, C(2)-OH), 8.23 (d, $J=2.0$ Hz, 1H, C(8)-H), 8.11 (d, $J=9.5$ Hz, 1H, C(4)-H), 7.06 (d, $J=9.5$ Hz, 1H, C(3)-H), 6.93 (d, $J=1.0$ Hz, 1H, C(6)-H), 3.95 (s, 3H, C(7)-OCH₃), 2.65 (s, 3H, C(5)-CH₃)

^{13}C NMR (100 MHz, CDCl_3) δ : 175.9, 165.9, 159.9, 137.1, 134.7, 133.9, 123.1, 116.5, 116.0, 104.2, 103.1, 55.2, 20.0

HRMS (ESI^+): m/z calcd for $(\text{C}_{10}\text{H}_{12}\text{O}_4+\text{H})^+$ 233.0814, found 233.0811

FTIR (cm^{-1}): 2930, 2829, 2705, 2627, 2548, 1634, 1620, 1589, 1449, 1415, 1286, 1247, 1219, 1101, 1073, 1017, 848

N1999A2 Naphthoic Acid in Protected Form (12, 8 steps)

2-Chloro-3-methoxybenzyl alcohol. A solution of *n*-butyllithium in hexanes (2.5 M, 19.3 mL, 48.3 mmol, 3.0 equiv) was added via syringe over 10 min to a solution of 3-methoxybenzyl alcohol (2.00 mL, 16.1 mmol, 1 equiv) in toluene (70 mL) at 23 °C. After 1 h at 23 °C, a solution of hexachloroethane (7.62 g, 32.2 mmol, 2.0 equiv) in toluene (20 mL) was added via cannula. Upon completed addition, the reaction mixture was allowed to stir at 23 °C for 10 min. Saturated aqueous sodium bicarbonate solution (100 mL) was added, and the resulting biphasic mixture was partitioned between ether (150 mL) and water (100 mL). The organic layer was separated and washed with brine (100 mL). The washed organic solution was dried over sodium sulfate. The dried solution was filtered and filtrate was concentrated. The residue was purified by flash column chromatography (40% ethyl acetate–hexanes) to afford 2-chloro-3-methoxybenzyl alcohol as a white solid, mp 104–106 °C (1.83 g, 66%).

¹H NMR (400 MHz, CDCl₃) δ: 7.26 (dd, *J*₁=8.4 Hz, *J*₂=7.6 Hz, 1 H, C(5)-**H**), 7.10 (dd, *J*₁=7.6 Hz, *J*₂=0.8 Hz, 1H, C(6)-**H**), 6.90 (d, br, *J*=8.4 Hz, 1H, C(4)-**H**), 4.79 (d, *J*=6.4 Hz, 2H, C(1)-CH₂OH), 3.91 (s, 3H, C(3)-OCH₃), 2.02 (t, *J*=6.4 Hz, 1H, C(1)-CH₂OH)

¹³C NMR (100 MHz, CDCl₃) δ: 155.0, 139.7, 127.4, 120.8, 120.4, 111.1, 63.0, 56.2

HRMS (EI⁺): *m/z* calcd for (C₈H₉ClO₂)⁺ 172.0291, found 172.0283

FTIR (cm⁻¹): 3281, 3188, 2976, 2941, 2842, 1597, 1578, 1478, 1361, 1298, 1284, 1049, 766

6-Bromo-2-chloro-3-methoxybenzyl alcohol. N-Bromosuccinimide (recrystallized from water prior to use, 5.41 g, 30.4 mmol, 1.05 equiv) was added to a solution of 2-chloro-3-methoxybenzyl alcohol (5.00 g, 29.0 mmol, 1 equiv) in dimethylformamide (25 mL). After stirring at 23 °C in the dark for 56 h, the reaction mixture was partitioned between water (600 mL) and ether (300 mL). The aqueous layer was separated and extracted with ether (2 × 300 mL). The organic layers were combined and washed with an aqueous solution of sodium hydroxide (1N, 2 × 100 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was recrystallized (ethyl acetate–hexanes) to afford 6-bromo-2-chloro-3-methoxybenzyl alcohol as a white solid, mp 92–93 °C (6.70 g, 92%).

¹H NMR (500 MHz, CDCl₃) δ: 7.44 (d, J=9.0 Hz, 1H, Ar-**H**), 6.78 (d, J=8.5 Hz, 1H, Ar-**H**), 4.97 (d, J=7.0 Hz, 2H, C(1)-CH₂OH), 3.88 (s, 3H, C(2)-OCH₃), 2.25 (t, J=7.0 Hz, 1H, C(1)-CH₂OH)

¹³C NMR (100 MHz, CDCl₃) δ: 154.9, 138.0, 131.4, 124.3, 115.7, 112.7, 63.0, 56.5

HRMS (EI⁺): *m/z* calcd for (C₈H₈BrClO₂)⁺ 249.9396, found 249.9402

FTIR (cm⁻¹): 3390, 2941, 2899, 2834, 1567, 1462, 1434, 1289, 1274, 1069, 1013, 917, 802

6-Bromo-2-chloro-3-methoxybenzyl alcohol triisopropylsilyl ether. Triisopropylsilyl chloride (8.34 mL, 39.0 mmol, 2.0 equiv) was added via syringe over 2 min to a solution of 6-bromo-2-chloro-3-methoxybenzyl alcohol (4.90 g, 19.5 mmol, 1 equiv) and imidazole (4.69 g, 78.0 mmol, 4.0 equiv) in dimethylformamide (40 mL) at 23 °C. The resulting solution was stirred at 23 °C for 3 h, then was diluted with ether (200 mL). The diluted product mixture was washed with water (2 × 100 mL) and the combined aqueous layers were extracted with ether (2 × 200 mL). The organic layers were combined and dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (5% ether–hexanes) to afford the triisopropylsilyl ether as a white solid (7.63 g, 96%).

¹H NMR (500 MHz, CDCl₃) δ: 7.44 (d, J=9.0 Hz, 1H, Ar-**H**), 6.76 (d, J=9.0 Hz, 1H, Ar-**H**), 5.05 (s, 2H, C(1)-CH₂OTIPS), 3.89 (s, 3H, C(3)-OCH₃), 1.17 (m, 3H, C(1)-CH₂OSi(CH(CH₃)₂)₃), 1.11 (d, J=2.0 Hz, 18H, C(1)-CH₂OSi(CH(CH₃)₂)₃)

¹³C NMR (100 MHz, CDCl₃) δ: 154.7, 138.4, 131.2, 124.8, 116.3, 112.3, 63.7, 56.4, 18.0, 12.2

HRMS (Cl^+): m/z calcd for $(\text{C}_{17}\text{H}_{28}\text{BrClO}_2\text{Si}+\text{NH}_4)^+$ 424.1074, found 424.1069

FTIR (cm^{-1}): 2941, 2864, 1567, 1462, 1433, 1280, 1073

Aldehyde 9. A solution of *tert*-butyllithium in pentanes (1.78 M, 26.4 mL, 47.0 mmol, 3.0 equiv) was added via syringe over 25 min to a deoxygenated solution of the triisopropylsilyl ether (6.39 g, 15.7 mmol, 1 equiv) in tetrahydrofuran (400 mL) at $-96\text{ }^\circ\text{C}$ (liquid N_2 /ethanol cooling bath). The resulting yellow solution was stirred at $-96\text{ }^\circ\text{C}$ for 5 min. Dimethylformamide (3.64 mL, 47.0 mmol, 3.0 equiv) was added, causing the reaction mixture to turn colorless. After 10 min at $-96\text{ }^\circ\text{C}$, the cooling bath was removed and the reaction mixture was allowed to warm to $23\text{ }^\circ\text{C}$ over approximately 1 h. Saturated aqueous ammonium chloride solution (300 mL) was added, and tetrahydrofuran was removed in vacuo. The aqueous residue was extracted with ether ($3 \times 200\text{ mL}$). The combined organic layers were dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (20% ether–hexanes) to afford aldehyde **9** as a colorless oil (5.03 g, 90%).

^1H NMR (500 MHz, CDCl_3) δ : 10.41 (s, 1H, C(1)-C(O)**H**), 7.90 (d, $J=9.0\text{ Hz}$, 1H, C(6)-**H**), 6.96 (d, $J=9.0\text{ Hz}$, 1H, C(5)-**H**), 5.31 (s, 2H, C(2)-**CH**₂OTIPS), 3.97 (s, 3H, C(4)-O**CH**₃), 1.15 (m, 3H, C(2)-**CH**₂OSi(**CH**(**CH**₃)₂)₃), 1.04 (d, $J=7.5\text{ Hz}$, 18H, C(2)-**CH**₂OSi(**CH**(**CH**₃)₂)₃)

^{13}C NMR (100 MHz, CDCl_3) δ : 190.6, 158.8, 142.1, 129.4, 128.6, 122.1, 110.4, 59.0, 56.5, 17.9, 11.9

HRMS (ESI^+): m/z calcd for $(\text{C}_{18}\text{H}_{29}\text{ClO}_3\text{Si}+\text{H})^+$ 357.1653, found 357.1645

FTIR (cm^{-1}): 2943, 2866, 1686, 1586, 1282, 1061

(Z)-Olefin 10. DBU (1.27 mL, 8.46 mmol, 2.0 equiv) was added dropwise via syringe over 2 min to a solution of phosphonate **6** (1.74 g, 4.65 mmol, 1.1 equiv) in tetrahydrofuran (16 mL) at 0 °C. After stirring for 10 min at 0 °C, the resulting mixture was cooled to −78 °C. A solution of aldehyde **9** (1.51 g, 4.23 mmol, 1 equiv) in tetrahydrofuran (16 mL) was added over 2 min via cannula. The resulting mixture was allowed to warm to 0 °C and was stirred at 0 °C for 15 h. Saturated aqueous ammonium chloride solution (60 mL) and water (10 mL) were added, and the resulting biphasic mixture was extracted with ether (4 × 75 mL). The organic layers were combined and dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (50% ether–hexanes) to afford the (Z)-olefin **10** as a white solid (1.51 g, 74%).

^1H NMR (500 MHz, CDCl_3) δ : 7.20 (d, $J=12.0$ Hz, 1H, C(8)-H), 7.12 (d, $J=8.5$ Hz, 1H, C(6')-H), 6.81 (d, $J=8.0$ Hz, 1H, C(5')-H), 5.97 (d, $J=12.0$

Hz, 1H, C(7)-**H**), 5.27 (s, 1H, C(5)-**H**), 4.93 (s, 2H, C(2')-CH₂OTIPS), 3.91 (s, 3H, C(4')-OCH₃), 1.49 (s, 6H, C(2)-(CH₃)₂), 1.14 (m, 3H, C(2)-CH₂OSi(CH(CH₃)₂)₃), 1.06 (d, J=7.5 Hz, 18H, C(2)-CH₂OSi(CH(CH₃)₂)₃)

¹³C NMR (100 MHz, CDCl₃) δ: 163.7, 161.7, 154.9, 139.5, 137.4, 130.1, 128.5, 122.3, 121.5, 109.8, 106.0, 95.9, 61.0, 56.3, 24.8, 18.0, 12.0

HRMS (ESI⁺): *m/z* calcd for (C₂₅H₃₇ClO₅Si+H)⁺ 481.2177, found 481.2174

FTIR (cm⁻¹): 2942, 2863, 1733, 1718, 1560, 1275, 1060

Trifluoroethyl 2-hydroxy-1-naphthoic acid ester 11. Sodium hydride (60% dispersion in mineral oil, 27.0 mg, 1.13 mmol, 4.3 equiv) was added to a solution of trifluoroethanol (150 μ L, 2.06 mmol, 7.9 equiv) in tetrahydrofuran (1.5 mL). The resulting mixture was stirred at 23 °C for 20 min. (Z)-Olefin **10** (125 mg, 0.260 mmol, 1 equiv) was added, and the resulting yellow solution was stirred at 23 °C for 1 h. The reaction mixture was concentrated in vacuo, and the residue was taken up in acetic acid (3.0 mL). Manganese (III) acetate dihydrate (139 mg, 0.520 mmol, 2.0 equiv) was added. After stirring for 2 h at 40 °C, the resulting mixture was partitioned between water (20 mL) and ethyl acetate (25 mL). The aqueous layer was separated and extracted further with ethyl acetate (2 $\times$ 25 mL). The organic layers were combined and washed with saturated aqueous sodium bicarbonate solution (2 $\times$ 25 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (14% ether–hexanes) to

give trifluoroethyl 2-hydroxy-1-naphthoic acid ester **11** as a yellow solid (125 mg, 93% over 2 steps).

^1H NMR (500 MHz, CDCl_3) δ : 11.83 (s, 1H, C(2)-OH), 8.47 (d, $J=9.0$ Hz, 1H, C(4)-H), 8.17 (s, 1H, C(8)-H), 7.10 (d, $J=9.5$ Hz, 1H, C(3)-H), 5.36 (s, 2H, C(5)-CH₂OTIPS), 4.85 (q, $J=7.0$ Hz, 2H, C(1)-C(O)OCH₂CF₃), 3.99 (s, 3H, C(7)-OCH₃), 1.18 (m, 3H, C(5)-CH₂OSi(CH(CH₃)₂)₃), 1.06 (d, $J=7.0$ Hz, 18H, C(5)-CH₂OSi(CH(CH₃)₂)₃)

^{13}C NMR (100 MHz, CDCl_3) δ : 170.5, 165.5, 154.8, 136.1, 135.4, 132.1, 123.5, 123.2 (q, $J=275$ Hz), 121.3, 117.1, 105.6, 102.9, 61.6 (q, $J=36.6$ Hz), 60.3, 56.0, 18.0, 12.1

HRMS (ESI^-): m/z calcd for $(\text{C}_{24}\text{H}_{32}\text{ClF}_3\text{O}_5\text{Si-H})^-$ 519.1582, found 519.1599

FTIR (cm^{-1}): 2943, 2867, 1658, 1610, 1592, 1464, 1418, 1315, 1281, 1201, 1175, 1110, 1050

2-Hydroxy-1-naphthoic acid 12. Lithium hydroxide monohydrate (302 mg, 7.20 mmol, 30 equiv) was added to a solution of trifluoroethyl 2-hydroxy-1-naphthoic acid ester **11** (125 mg,

0.240 mmol, 1 equiv) in tetrahydrofuran (8 mL) and water (4 mL). The resulting biphasic mixture was allowed to stir at 40 °C for 18 h. Water (10 mL) was added, the biphasic mixture was cooled to 0 °C, and 2N aqueous hydrochloric acid solution was carefully added to an end point of pH~1.0 (~ 3.5 mL). The product was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (2 × 12 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated to give crude acid **12** as a white solid (105 mg, 100%).

^1H NMR (500 MHz, CDCl_3) δ :	12.08 (s, br, 1H, C(2)-OH), 8.49 (d, $J=10.0$ Hz, 1H, C(4)-H), 8.41 (s, 1H, C(8)-H), 7.11 (d, $J=9.5$ Hz, 1H, C(3)-H), 5.38 (s, 2H, C(5)-CH ₂ OTIPS), 4.05 (s, 3H, C(7)-OCH ₃), 1.19 (m, 3H, C(5)-CH ₂ OSi(CH(CH ₃) ₂) ₃), 1.07 (d, $J=7.0$ Hz, 18H, C(5)-CH ₂ OSi(CH(CH ₃) ₂) ₃)
^{13}C NMR (100 MHz, CDCl_3) δ :	176.4, 166.0, 154.7, 135.9, 135.7, 132.8, 123.6, 121.3, 117.2, 106.0, 102.8, 60.3, 56.2, 18.0, 12.0
HRMS (ESI ⁻):	m/z calcd for $(\text{C}_{22}\text{H}_{31}\text{ClO}_5\text{Si}-\text{H})^-$ 437.1551, found 437.1554
FTIR (cm^{-1}):	2940, 2865, 1631, 1441, 1421, 1283, 1251, 1234, 1216, 1116, 1064, 1014, 882

Table 1, Entry 1 (3 steps)

(Z)-Olefin 15. DBU (323 μ L, 329 mg, 2.16 mmol, 2.0 equiv) was added dropwise via syringe over 2 min to a stirring solution of phosphonate **6** (566 mg, 1.51 mmol 1.4 equiv) in tetrahydrofuran (6 mL) at 0 °C. The reaction mixture was allowed to stir at 0 °C for 20 min. A solution of 2-bromobenzaldehyde (200 mg, 1.08 mmol, 1 equiv) in tetrahydrofuran (5 mL) was added dropwise via cannula. The reaction mixture was allowed to stir at 0 °C for 18 h. Saturated aqueous ammonium chloride solution (20 mL) was added, and the resulting biphasic mixture was concentrated in vacuo to remove tetrahydrofuran. The aqueous residue was extracted with ether (3 $\times$ 30 mL). The organic extracts were combined and washed with brine (2 $\times$ 20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (33% ether–hexanes) to give (Z)-olefin **15** as a colorless oil (324 mg, 97 %).

^1H NMR (500 MHz, CDCl_3) δ : 7.58 (d, $J=8.0$ Hz, 1H, C(3')-**H**), 7.27 (d, $J=4.0$ Hz, 2H, C(5',6')-**H**), 7.18 (m, $J_1=4.0$ Hz, $J_2=8.0$ Hz, 1H, C(4')-**H**), 6.92 (d, $J=9.6$ Hz, 1H, C(8)-**H**), 6.09 (d, $J=8.0$ Hz, 1H, C(7)-**H**), 5.33 (s, 1H, C(5)-**H**), 1.46 (s, 6H, C(2)-(CH₃)₂)

^{13}C NMR (100 MHz, CDCl_3) δ : 163.0, 161.5, 138.9, 137.1, 132.0, 130.5, 129.5, 126.4, 123.0, 122.5, 106.2, 96.5, 24.6

HRMS (ESI⁺): m/z calcd for (C₁₄H₁₂BrO₃+H)⁺ 309.0126, found 309.0125

FTIR (cm⁻¹):

2997, 2942, 1732, 1643, 1596, 1577, 1468, 1433, 1391,
1376, 1329, 1274, 1253, 1203, 1018, 964, 905, 822, 744

Trifluoroethyl 2-hydroxy-1-naphthoic ester 16. Sodium hydride (60% dispersion in mineral oil, 40.3 mg, 1.68 mmol, 6.0 equiv) was added to a stirring solution of trifluoroethanol (245 μ L, 336 mg, 3.36 mmol, 10.0 equiv) in tetrahydrofuran (2 mL) at 23 °C. The reaction mixture was allowed to stir at 23 °C for 20 min. A solution of (Z)-olefin **15** (86.5 mg, 0.280 mmol, 1 equiv) in tetrahydrofuran (2 mL) was added via cannula. The resulting mixture was allowed to stir at 23 °C for 45 min and was then concentrated in vacuo. The residue was taken up in acetic acid (2 mL). Manganese (III) acetate dihydrate (150 mg, 0.560 mmol, 2.0 equiv) was added. After stirring for 17 h at 23 °C, the resulting mixture was partitioned between water (25 mL) and ethyl acetate (25 mL). The aqueous layer was separated and extracted further with ethyl acetate (2 $\times$ 25 mL). The organic extracts were combined and washed with saturated aqueous sodium bicarbonate solution (2 $\times$ 15 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (33% ether–hexanes) to give trifluoroethyl 2-hydroxy-1-naphthoic acid ester **16** as a white solid (78.2 mg, 80%).

¹H NMR (500 MHz, CDCl₃) δ : 11.69 (s, 1H, C(2)-OH), 8.63 (dd, $J_1=1.0$ Hz, $J_2=9.0$ Hz, 1H, C(8)-H), 8.48 (d, $J=9.0$ Hz, 1H, C(4)-H), 7.70 (dd, $J_1=1.0$ Hz, $J_2=7.5$ Hz, 1H, C(6)-H), 7.40 (dd, $J_1=7.5$ Hz, $J_2=9.0$

Hz, C(7)-**H**), 7.27 (d, J=9.5 Hz, 1H, C(3)-**H**), 4.87 (q, J=8.0 Hz, 2H, C(1)-C(O)O**C**H₂CF₃)

¹³C NMR (100 MHz, CDCl₃) δ: 170.1, 165.1, 136.7, 133.2, 129.2, 128.5, 127.0, 124.8, 124.1, 122.9 (q, J=275 Hz), 120.5, 103.7, 61.3 (q, J=36.7 Hz), 127.1, 127.0

HRMS (ESI⁻): *m/z* calcd for (C₁₃H₈BrF₃O₃-H)⁻ 346.9531, found 346.9529

FTIR (cm⁻¹): 3426, 1656, 1578, 1463, 1446, 1411, 1321, 1281, 1237, 1171, 1143, 1097, 1060, 1002, 966, 830, 807, 751, 737, 705

Table 1, Entry 2 (3 steps)

(Z)-Olefin 17. DBU (360 μ L, 365 mg, 2.4 mmol, 2.0 equiv) was added dropwise via syringe over 1 min to a stirring solution of phosphonate **6** (631 mg, 1.68 mmol 1.4 equiv) in tetrahydrofuran (5 mL) at 23 $^{\circ}$ C. After stirring for 20 min at 23 $^{\circ}$ C, the reaction mixture was cooled to 0 $^{\circ}$ C. A solution of 2,4-dimethoxybenzaldehyde (200 mg, 1.20 mmol, 1 equiv) in tetrahydrofuran (5 mL) was added dropwise via cannula. The resulting mixture was allowed to stir at 0 $^{\circ}$ C for 18 h. Saturated aqueous ammonium chloride solution (20 mL) was added, and the resulting biphasic mixture was concentrated in vacuo to remove tetrahydrofuran. The aqueous residue was extracted with ethyl acetate (3 $\times$ 30 mL). The organic extracts were combined and washed with brine (2 $\times$ 20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (50% ethyl acetate–hexanes) to give (Z)-olefin **17** as a bright yellow solid (269 mg, 77%).

^1H NMR (500 MHz, CDCl_3) δ : 7.26 (d, $J=8.5$ Hz, 1H, C(6')-**H**), 6.93 (d, $J=12.5$ Hz, 1H, C(8)-**H**), 6.43–6.41 (m, 2H, C(3',5')-**H**), 5.84 (d, $J=12.5$ Hz, 1H, C(7)-**H**), 5.33 (s, 1H, C(5)-**H**), 3.81 (s, 3H, $-\text{OCH}_3$), 3.80 (s, 3H, $-\text{OCH}_3$), 1.58 (s, 6H, C(2)-(CH₃)₂)

^{13}C NMR (100 MHz, CDCl_3) δ : 164.3, 161.9, 161.7, 158.3, 135.8, 131.6, 119.5, 117.3, 105.9, 103.9, 97.6, 94.9, 55.4, 55.3, 24.8

HRMS (ESI⁺):

m/z calcd for (C₁₆H₁₈O₅+H)⁺ 291.1232, found 291.1231

FTIR (cm⁻¹):

2998, 2942, 2839, 1720, 1607, 1570, 1390, 1295, 1271, 1209, 1017, 830

Trifluoroethyl 2-hydroxy-1-naphthoic acid ester 18. Sodium hydride (60% dispersion in mineral oil, 98.8 mg, 4.11 mmol, 6.0 equiv) was added to a stirring solution of trifluoroethanol (500 μ L, 686 mg, 6.86 mmol, 10.0 equiv) in tetrahydrofuran (5 mL) at 23 °C. The resulting mixture was allowed to stir at 23 °C for 20 min. A solution of (Z)-olefin **17** (199 mg, 0.686 mmol, 1 equiv) in tetrahydrofuran (5 mL) was added via cannula. After stirring for 45 min at 23 °C, the resulting mixture was concentrated in vacuo. The residue was taken up in acetic acid (3 mL). Manganese (III) acetate dihydrate (368mg, 1.37 mmol, 2.0 equiv) was added. After stirring for 17 h at 23 °C, the reaction mixture was partitioned between with water (30 mL) and ethyl acetate (25 mL). The aqueous layer was separated and extracted further with ethyl acetate (2 $\times$ 25 mL). The organic extracts were combined and washed with saturated aqueous sodium bicarbonate solution (2 $\times$ 20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (20% ethyl acetate–hexanes) to give trifluoroethyl 2-hydroxy-1-naphthoic acid ester **18** as a white solid (205 mg, 91 % over two steps).

¹H NMR (500 MHz, CDCl₃) δ :

11.85 (s, 1H, C(2)-OH), 8.35 (d, J=9.0 Hz, 1H, C(4)-H), 7.69 (d, J=2.0 Hz, 1H, C(8)-H), 6.96 (d, J=9.5 Hz, 1H,

C(3)-**H**), 6.42 (d, $J = 2.5$ Hz, 1H, C(6)-**H**), 4.83 (q, $J = 8.5$ Hz, 2H, C(1)-C(O)OCH₂CF₃), 3.94 (s, 3H, -OCH₃), 3.90 (s, 3H, -OCH₃)

¹³C NMR (100 MHz, CDCl₃) δ : 171.0, 166.3, 161.3, 157.1, 134.2, 131.8, 123.2 (q, $J = 275$ Hz), 116.1, 115.1, 102.8, 97.2, 95.9, 61.4 (q, $J = 36.4$ Hz), 55.6, 55.2

HRMS (ESI⁺): m/z calcd for (C₁₅H₁₃F₃O₅+H)⁺ 331.0793, found 331.0790

FTIR (cm⁻¹): 2959, 2912, 2850, 1658, 1598, 1452, 1436, 1404, 1344, 1312, 1252, 1155, 1053, 955, 826, 777, 625

Table 1, Entry 3 (3 steps)

(Z)-Olefin 19. DBU (395 μ L, 401.9 mg, 2.64 mmol, 2.0 equiv) was added dropwise via syringe over 1 min to a stirring solution of phosphonate **6** (692 mg, 1.85 mmol, 1.4 equiv) in tetrahydrofuran (5 mL) at 23 °C. After stirring for 20 min at 23 °C, the reaction mixture was cooled to 0 °C. A solution of 2-nitrobenzaldehyde (200 mg, 1.08 mmol, 1 equiv) in tetrahydrofuran (5 mL) was added dropwise via cannula. The reaction mixture was allowed to stir at 0 °C for 30 min. Saturated aqueous ammonium chloride solution (20 mL) was added, and the resulting biphasic mixture was concentrated in vacuo to remove tetrahydrofuran. The aqueous residue was extracted with ethyl acetate (3 $\times$ 30 mL). The organic extracts were combined and washed with brine (2 $\times$ 20 mL). The washed solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (66% ether–hexanes) to give (Z)-olefin **19** as a yellow oil (309 mg, 84%).

¹H NMR (500 MHz, CDCl₃) δ: 8.08 (dd, J₁=1.5 Hz, J₂=8.5 Hz, 1H, C(3')-**H**), 7.57 (dt, J₁=1.5 Hz, J₂=8.0 Hz, 1H, C(5')-**H**), 7.47 (dt, J₁=1.0 Hz, J₂=7.8 Hz, 1H, C(4')-**H**), 7.29 (d, J=7.5 Hz, 1H, C(6')-**H**), 7.20 (d, J=12.0 Hz, 1H, C(8)-**H**), 6.10 (d, J=12.0 Hz, 1H, C(7)-**H**), 5.28 (s, 1 H, C(5)-**H**), 1.27 (s, 6H, C(2)-(CH₃)₂)

^{13}C NMR (100 MHz, CDCl_3) δ : 162.4, 161.0, 147.0, 136.2, 133.0, 132.6, 130.8, 128.6, 124.0, 122.3, 106.0, 96.7, 24.2

HRMS (ESI^+): m/z calcd for $(\text{C}_{14}\text{H}_{13}\text{NO}_5+\text{H})^+$ 276.0872, found 276.0885

FTIR (cm^{-1}): 3092, 2997, 2943, 2859, 1721, 1645, 1612, 1580, 1523, 1391, 1376, 1345, 1274, 1202, 1018, 905, 823, 719

Trifluoroethyl 2-hydroxy-1-naphthoic acid ester 20. Sodium hydride (60% dispersion in mineral oil, 16.9 mg, 0.706 mmol, 6.0 equiv) was added to a stirring solution of trifluoroethanol (85.7 μL , 118 mg, 1.12 mmol, 10.0 equiv) in tetrahydrofuran (3 mL). The reaction mixture was allowed to stir at 23 $^{\circ}\text{C}$ for 20 min. A solution of (*Z*)-olefin **19** (32.4 mg, 0.117 mmol, 1 equiv) in tetrahydrofuran (3 mL) was added via cannula at 23 $^{\circ}\text{C}$. After stirring for 45 min at 23 $^{\circ}\text{C}$, the reaction mixture was concentrated in vacuo. The residue was taken up with acetic acid (3 mL). Manganese (III) acetate dihydrate (62.7 mg, 0.234 mmol, 2.0 equiv) was added. After stirring for 2 h at 40 $^{\circ}\text{C}$, the reaction mixture was partitioned between water (20 mL) and ethyl acetate (25 mL). The aqueous layer was separated and further extracted ethyl acetate (2×25 mL). The organic extracts were combined and washed with saturated aqueous sodium bicarbonate solution (2×20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (33% ether–hexanes) to give trifluoroethyl 2-hydroxy-1-naphthoic acid ester **20** as a white solid (34.8 mg, 94% over two steps).

^1H NMR (500 MHz, CDCl_3) δ : 11.71 (s, 1H, C(2)-OH), 8.94 (d, $J=9.0$ Hz, 1H, C(8)-H), 8.54 (d, $J=9.5$ Hz, 1H, C(4)-H), 7.99 (dd, $J_1=1.0$ Hz, $J_2=8.0$ Hz, 1H, C(6)-H), 7.66 (dt, $J_1=8.0$ Hz, $J_2=9.0$ Hz, 1H, C(7)-H), 7.39 (d, $J=9.5$ Hz, 1H, C(3)-H), 4.91 (q, $J=8.5$ Hz, 2H, C(1)-C(O)OCH₂CF₃)

^{13}C NMR (100 MHz, CDCl_3) δ : 169.8, 165.1, 148.2, 132.8, 131.6, 130.3, 127.4, 122.8 (q, $J=276$ Hz), 122.5, 121.0, 120.4, 104.0, 61.5 (q, $J=36.8$ Hz)

HRMS (ESI⁻): m/z calcd for (C₁₃H₈F₃NO₃-H)⁻ 314.0276, found 314.0279

FTIR (cm⁻¹): 3021, 2361, 1662, 1524, 1343, 1284, 1213, 1155, 984, 961, 820

Table 1, Entry 4 (3 steps)

(Z)-Olefin 21. DBU (281 μ L, 287 mg, 1.88 mmol, 2.0 equiv) was added dropwise via syringe over 1 min to a stirring solution of phosphonate **6** (494 mg, 1.32 mmol, 1.4 equiv) in tetrahydrofuran (5 mL) at 23 $^{\circ}$ C. After stirring for 20 min at 23 $^{\circ}$ C, the reaction mixture was cooled to 0 $^{\circ}$ C. A solution of 2-benzyloxybenzaldehyde (200 mg, 0.942 mmol, 1 equiv) in tetrahydrofuran (5.0 mL) was added and the resulting mixture was allowed to stir at 0 $^{\circ}$ C for 1 h. Saturated aqueous ammonium chloride solution (20 mL) was added, and the resulting biphasic mixture was concentrated in vacuo to remove tetrahydrofuran. The aqueous residue was extracted with ethyl acetate (3 $\times$ 30 mL). The combined organic extracts were washed with brine (2 $\times$ 20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (33% ether–hexanes) to give a (Z)/(E) mixture of olefin **21** (317 mg, 83%), which was used in the next reaction without further purification.

Trifluoroethyl-2-hydroxy-1-naphthoic acid ester 22. Sodium hydride (60% dispersion in mineral oil, 136 mg, 5.66 mmol, 6.0 equiv) was added to a stirring solution of trifluoroethanol (687 μ L, 943 mg, 9.43 mmol, 10.0 equiv) in tetrahydrofuran (5 mL) at 23 $^{\circ}$ C. The reaction mixture was allowed to stir at 23 $^{\circ}$ C for 20 min. A (Z)/(E) mixture of olefin **21** (317 mg, 0.943 mmol, 1 equiv, ~10:1 Z:E, from the experiment above) in tetrahydrofuran (5 mL) was added via cannula. After stirring for 1 h at 23 $^{\circ}$ C, the reaction mixture was concentrated in vacuo. The

residue was taken up in acetic acid (4 mL). Manganese (III) acetate dihydrate (506 mg, 1.89 mmol, 2.0 equiv) was added. After stirring for 1 h at 40 °C, the reaction mixture was partitioned between with water (20 mL) and ethyl acetate (30 mL). The aqueous layer was separated and extracted further with ethyl acetate (2 × 30 mL). The organic extracts were combined and washed with saturated aqueous sodium bicarbonate solution (2 × 20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (33% ethyl acetate–hexanes) to give trifluoroethyl 2-hydroxy-1-naphthoic acid ester **22** as a white solid (266 mg, 75 % over 3 steps).

^1H NMR (500 MHz, CDCl_3) δ : 11.76 (s, 1H, C(2)-OH), 8.57 (d, $J=9.5$ Hz, 1H, C(4)-H), 8.25 (d, $J=9.0$ Hz, 1H, C(8)-H), 7.52-7.48 (m, 2H, C(2')-H), 7.50(t, $J=8.5$ Hz, 1H, C(7)-H), 7.38 (t, $J=7.5$ Hz, 1H, C(4')-H), 7.44 (t, $J=8.0$ Hz, 2H, C(3')-H), 7.14 (d, $J=9.5$ Hz, 1H, C(3)-H), 6.86 (d, $J=8.0$ Hz, 1H, C(6)-H), 5.22 (s, 2H, C(5)-OCH₂Ph), 4.87 (q, $J=8.5$ Hz, 2H, C(1)-C(O)OCH₂CF₃)

^{13}C NMR (100 MHz, CDCl_3) δ : 170.7, 165.4, 155.1, 136.7, 132.9, 131.9, 129.4, 128.6, 128.1, 127.4, 123.0 (q, $J=275$ Hz), 120.6, 118.0, 117.6, 104.3, 103.3, 70.3, 61.1 (q, $J=36.7$ Hz)

HRMS (ESI⁺): m/z calcd for $(\text{C}_{20}\text{H}_{15}\text{F}_3\text{O}_4+\text{H})^+$ 377.1000, found 377.1007

FTIR (cm^{-1}): 3068, 3033, 2974, 2904, 2857, 1660, 1620, 1602, 1427,
1394, 1330, 1253, 1222, 1183, 1163, 1087, 1055, 986, 956,
909, 810, 792, 766, 744, 700, 662

Table 1, Entry 5 (4 steps)

Aldehyde 23. Triisopropylsilyl chloride (527 μ L, 474 mg, 2.46 mmol, 1.5 equiv) was added to a stirring solution of 3-hydroxybenzaldehyde (200 mg, 1.64 mmol, 1 equiv) and imidazole (295 mg, 4.91 mmol, 3.0 equiv) in dimethylformamide (3 mL) at 23 $^{\circ}$ C. After stirring for 19 h at 23 $^{\circ}$ C, the reaction mixture was diluted with ether (50 mL). The diluted product mixture was washed with water (2×50 mL). The combined aqueous layers were extracted with ethyl acetate (3×20 mL). The organic extracts were combined and washed with brine (2×25 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (10% ether–hexanes) to give aldehyde **23** as a colorless oil (398 mg, 87 %).

^1H NMR (400 MHz, CDCl_3) δ :	9.95 (s, 1H, C(1)-C(O) H), 7.45 (dt, $J_1=1.2$ Hz, $J_2=7.6$ Hz, 1H, C(6)- H), 7.39 (t, $J=7.6$ Hz, 1H, C(5)- H), 7.36 (m, 1H, C(4)- H), 7.14 (ddd, $J_1=0.8$ Hz, $J_2=2.4$ Hz, $J_3=8.1$ Hz, 1H, C(2)- H) 1.28 (m, 3H, C(3)-OSi(CH (CH_3) $_2$) $_3$), 1.10 (d, $J=7.6$ Hz, 18H, C(3)-OSi(CH (CH_3) $_2$) $_3$)
^{13}C NMR (100 MHz, CDCl_3) δ :	192.1, 156.8, 137.9, 130.0, 126.3, 123.3, 119.6, 17.8, 12.6
HRMS (ESI^+):	m/z calcd for $(\text{C}_{16}\text{H}_{26}\text{O}_2\text{Si}+\text{H})^+$ 279.1780, found 279.1778
FTIR (cm^{-1}):	3396, 2946, 2868, 2724, 1704, 1598, 1584, 1484, 1458, 1446, 1387, 1311, 1280, 1250, 1167, 1140, 1074, 1003, 982, 968, 883, 830, 790, 686

(Z)-Olefin 24. DBU (228 μ L, 232 mg, 1.52 mmol, 2.0 equiv) was added dropwise via syringe over 1 min to a stirring solution of phosphonate **6** (399 mg, 1.07 mmol, 1.4 equiv) in tetrahydrofuran (5 mL) at 23 $^{\circ}$ C. After stirring for 20 min at 23 $^{\circ}$ C, the reaction mixture was cooled to 0 $^{\circ}$ C. A solution of aldehyde **23** (212 mg, 0.761 mmol, 1 equiv) in tetrahydrofuran (5.0 mL) was added. The resulting mixture was allowed to stir at 0 $^{\circ}$ C for 30 min. Saturated aqueous ammonium chloride solution (30 mL) was added, and the resulting biphasic mixture was concentrated in vacuo to remove tetrahydrofuran. The aqueous residue was extracted with ethyl acetate (3 $\times$ 30 mL). The combined organic extracts were washed with brine (2 $\times$ 20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (33% ether–hexanes) to provide a 6.7:1 (*Z*)/(*E*) mixture of olefin **24** (277 mg, 90%), which was used without further purification in the next reaction.

Trifluoroethyl 2-hydroxy-1-naphthoic acid ester 25. Sodium hydride (60% dispersion in mineral oil, 53.7 mg, 5.66 mmol, 6.0 equiv) was added to a stirring solution of trifluoroethanol (271 μ L, 373 mg, 3.73 mmol, 10.0 equiv) in tetrahydrofuran (5 mL) at 23 $^{\circ}$ C. The reaction mixture was allowed to stir at 23 $^{\circ}$ C for 20 min. A (*Z*)/(*E*) mixture of olefin **24** (150 mg, 0.373 mmol, 1 equiv, $\sim$ *Z*:*E* 6:1, from the experiment above) in tetrahydrofuran (5 mL) was added via cannula. After stirring for 30 min at 23 $^{\circ}$ C, the reaction mixture was concentrated in vacuo. The residue was taken up in acetic acid (4 mL). Manganese (III) acetate dihydrate (200 mg, 0.747 mmol, 2.0 equiv) was added. After stirring for 1 h at 40 $^{\circ}$ C, the reaction mixture was partitioned

between water (20 mL) and ethyl acetate (30 mL). The aqueous layer was separated and extracted further with ethyl acetate (2 × 30 mL). The organic extracts were combined and washed with saturated aqueous sodium bicarbonate solution (2 × 20 mL). The washed organic solution was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography (10% ether–hexanes) to give trifluoroethyl 2-hydroxy-1-naphthoic acid ester **25** as a clear colorless oil (111 mg, 61 % over 3 steps).

^1H NMR (500 MHz, CDCl_3) δ : 11.62 (s, 1H, C(2)-OH), 8.54 (d, $J=9.5$ Hz, 1H, C(8)-H), 7.80 (d, $J=9.5$ Hz, 1H, C(4)-H), 7.23 (dd, $J_1=2.5$ Hz, $J_2=9.5$ Hz, 1H, C(7)-H), 7.18 (d, $J=2.5$ Hz, 1H, C(5)-H), 7.13 (d, $J=9.0$ Hz, 1H, C(3)-H), 4.87 (q, $J=8.5$ Hz, 2H, C(1)-C(O)OCH₂CF₃), 1.31 (m, 3H, C(6)-OSi(CH₃)₃), 1.13 (d, $J=7.5$ Hz, 18H, C(6)-OSi(CH₃)₃)

^{13}C NMR (100 MHz, CDCl_3) δ : 170.6, 163.9, 152.4, 136.9, 130.1, 126.4, 126.2, 124.1, 123.0 (q, $J=276$ Hz), 119.4, 116.6, 103.4, 61.0 (q, $J=37.2$ Hz), 17.9, 12.7

HRMS (CI^+): m/z calcd for $(\text{C}_{22}\text{H}_{29}\text{F}_3\text{O}_4\text{Si}+\text{NH}_4)^+$ 443.1866, found 443.1872

FTIR (cm^{-1}): 3046, 2944, 2872, 1661, 1624, 1603, 1579, 1519, 1464, 1402, 1352, 1326, 1283, 1208, 1254, 1208, 1166, 1134, 1067, 988, 971, 882, 843, 828, 797, 758, 686, 651