Enantioselective Polyene Cyclization via Organo-SOMO Catalysis

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Supporting Information

Contents

1 General Information

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] Reagents and solvents for enantioselective polycyclizations were purified prior to use by the following procedures:

- Copper(II) trifluoromethanesulfonate ($Cu(OTf)_2$) was purchased from Acros Organics and purified by dissolution in dry MeCN, filtration in order to remove insoluble residuals, followed by precipitation with Et_2O and crystallization at −18 ºC. The obtained crystalline solid was dried under high vacuum at 150 ºC to give a white powder that was stored and handled in a glove box.
- Sodium trifluoroacetate (NaTFA, Alfa Aesar) was dried under high vacuum at 150 ºC prior to use and stored and handled in a glove box.
- Trifluoroacetic acid (>99%, Reagent Plus®) was purchased from Sigma-Aldrich and used as obtained. All solvents were purified according to the method of Grubbs.[2]
- Isobutyronitrile (*i*-PrCN, Reagent grade, Sigma-Aldrich) and 1,2-Dimethoxyethane (DME, Reagent grade, Sigma-Aldrich) were distilled from CaH_2, degassed following the *freeze-pump-thaw* technique (3 ×) and stored under an argon atmosphere.

Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished using force-flow chromatography on Silicycle silica gel according to the method of Still.[3] Thin-layer chromatography (TLC) was performed on Silicycle 250 μm silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching or Ceric ammonium molybdate stain.

^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III (500 MHz) spectrometer and are internally referenced to residual protio solvent signals (note: $CDCl_3$ referenced at δ 7.26 ppm for ^1H and δ 77.1 ppm for ^{13}C). Data for ^1H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, ddd = doublet of doublet of doublets and m = multiplet), integration, coupling constant (Hz) and assignment. Assignments of ^1H NMR signals were aided by 2D NMR data sets (COSY,

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(1) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford, 1988.

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

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

HSQC, HMBC, and 2D NOESY correlation). Structures with numbering are for NMR assignments and do not necessarily conform with the given chemical name. Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm). IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High Resolution Mass spectra were obtained from the Princeton University mass spectral facility on an Agilent 1200 ESI-TOF instrument. High pressure liquid chromatography (HPLC) was performed on a Hewlett-Packard 1100 Series chromatograph using Daicel Chiralcell chiral columns (25 cm) and guard column (5 cm) as noted for each compound (OD-H, OJ-H, and AS-H columns). Supercritical fluid chromatography (SFC) analyses were obtained from Lotus Separations, LLC, Princeton, NJ. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in 10^{-1} (° cm^2 g^{-1}); concentration (c) is in g/100 mL.

2 General Procedure for Enantioselective Polycyclizations (GP1)

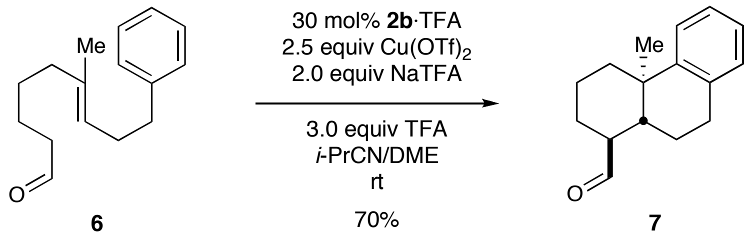
An oven-dried 8-dram vial (10 mL) equipped with a magnetic stir bar was charged with catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv). After sealing with a rubber septum and subsequent evacuation and backfilling with argon (3 ×), the catalyst was dissolved in dry, degassed *i*-PrCN (0.5 mL). A solution of the cyclization precursor (0.200 mmol, 1.00 equiv) in DME (1.0 mL) was added via syringe. Shortly thereafter, the oxidant solution was added dropwise via syringe using a syringe pump within 7 h at room temperature followed by further 17 h of stirring at the same temperature.

The required oxidant solution was freshly prepared as follows: In a glove box, an oven-dried 8-dram vial equipped with a stir bar was charged with $Cu(OTf)_2$ (181 mg, 0.500 mmol, 2.50 equiv) and sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and sealed with a rubber septum. After removal from the glove box, the vial was placed on a magnetic stir plate and connected to an argon inlet. Sequential addition of dry, degassed *i*-PrCN (1.0 mL) and TFA (45 μL, 0.40 mmol, 2.0 equiv) resulted in a blue-green solution upon stirring for 5 min.

At the end of the indicated reaction time, a light-green solution had been formed that was poured onto a mixture of 2M NH_4OH (15 mL) and brine (5 mL), and extracted with Et_2O, EtOAc or $CHCl_3$ (as indicated below, 4 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel using solvent mixtures as specified below afforded the cyclization products in analytically pure form.

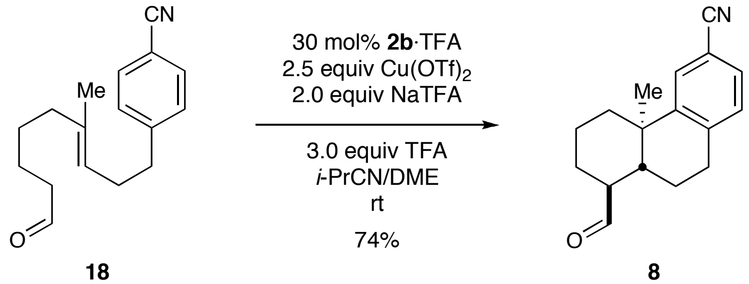
3 Experimental Data for Polycyclization Products

3.1 Bicyclization to Give Aldehyde 7 (Table 2)



According to GP1, aldehyde **6** (46.1 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), Cu(OTf)$_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using Et$_2$O as a solvent and flash chromatography (1.5% EtOAc/hexanes) furnished title compound **7** (32 mg, 70% yield) as a white solid. IR (ATR) ν (cm^{-1}) 3061, 3026, 2924, 2850, 2703, 1722, 1602, 1489, 1445, 1375, 1374, 1260, 1236, 1089, 1074, 1044, 973, 905, 869, 800, 758, 726, 699. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.55 (d, *J* = 4.5 Hz, C**H**O, 1H), 7.30 (dd, *J* = 7.8, 1.0 Hz, Ar**H**, 1H), 7.16 (br dd, *J* = 2 × 7.1 Hz, Ar**H**, 1H), 7.12 (ddd, *J* = 2 × 7.2, 1.4 Hz, Ar**H**, 1H), 7.08 (br d, *J* = 7.3 Hz, Ar**H**, 1H), 2.93 (ddd, *J* = 17.5, 10.5, 7.5 Hz, $\mathrm{CH_A}\mathbf{H_B}$, 1H), 2.87 (ddd, *J* = 17.5, 6.9, 2.5 Hz, $\mathbf{CH_A}\mathrm{H_B}$, 1H), 2.38 (dddd, *J* = 2 × 11.8, 2 × 4.2 Hz, C**H**CHO, 1H), 2.32 (br d, *J* = 13.0 Hz, $\mathrm{ArCH_A}\mathbf{H_B}$, 1H), 1.89-1.77 (m, $\mathbf{CH_2}$, C**H**, 3H), 1.77-1.64 (m, $\mathrm{CH_A}\mathbf{H_B}$, $\mathbf{CH_2}$, 3H), 1.51-1.37 (m, $\mathrm{ArC}\mathbf{H_A}\mathrm{H_B}$, $\mathbf{CH_A}\mathrm{H_B}$, 2H), 1.13 (s, $\mathbf{CH_3}$, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 205.4, 147.0, 135.0, 129.4, 125.82, 125.80, 124.6, 51.3, 41.5, 37.1, 36.4, 29.0, 26.4, 23.0, 22.8, 20.6. HRMS (ESI$^+$) exact mass calcd for $C_{16}H_{21}O$ [M+H]$^+$ requires *m/z* 229.1587, found *m/z* 229.1588. The enantiomeric excess was determined by HPLC (Chiracel OD-H, 2% *i*-PrOH/hexanes, flow rate 1.0 mL/min, λ = 214 nm); t_r = 14.3 (major) and 18.8 (minor) min. $[\alpha]_D^{23}$ = –58.0 (c = 0.68, CHCl$_3$, 87% ee).

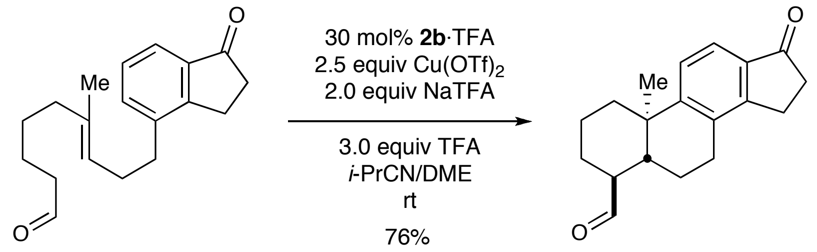
3.2 Bicyclization to Give Aldehyde 8 (Table 2)



18 **8**

According to GP1, aldehyde **18** (46.1 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), $Cu(OTf)_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using Et_2O as a solvent and flash chromatography (8% EtOAc/hexanes) furnished title compound **8** (36 mg, 74% yield) as a white solid. IR (ATR) ν (cm^{-1}) 2929, 2854, 2713, 2223, 1716, 1605, 1560, 1491, 1444, 1407, 1378, 1276, 1172, 1076, 1042, 918, 891, 878, 843, 818, 750, 732. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.57 (d, *J* = 3.7 Hz, C**H**O, 1H), 7.57 (s, Ar**H**, 1H), 7.39 (d, *J* = 7.9 Hz, Ar**H**, 1H), 7.16 (d, *J* = 7.8 Hz, Ar**H**, 1H), 3.00-2.86 (m, C$\mathbf{H_2}$, 2H), 2.43-2.35 (m, C**H**CHO, 1H), 2.30-2.23 (m, $ArCH_A\mathbf{H_B}$, 1H), 1.93-1.64 (m, C**H**, 2 × C$\mathbf{H_2}$, $CH_A\mathbf{H_B}$, 6H), 1.50-1.33 (m, $ArC\mathbf{H_A}H_B$, $C\mathbf{H_A}H_B$, 2H), 1.11 (s, C$\mathbf{H_3}$, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.6, 148.3, 141.1, 130.3, 129.1, 128.9, 119.6, 109.6, 51.1, 40.8, 36.9, 36.5, 29.1, 26.3, 22.7, 22.3, 20.5. HRMS (ESI$^+$) exact mass calcd for $C_{17}H_{20}NO$ $[M+H]^+$ requires *m/z* 254.1539, found *m/z* 254.1537. The enantiomeric excess was determined by HPLC (Chiracel OD-H, 10% *i*-PrOH/hexanes, flow rate 1.0 mL/min, λ = 214 nm); t_r = 11.7 (major) and 14.3 (minor) min. $[\alpha]_D^{23}$ = −86.3 (c = 0.82, $CHCl_3$, 88% ee).

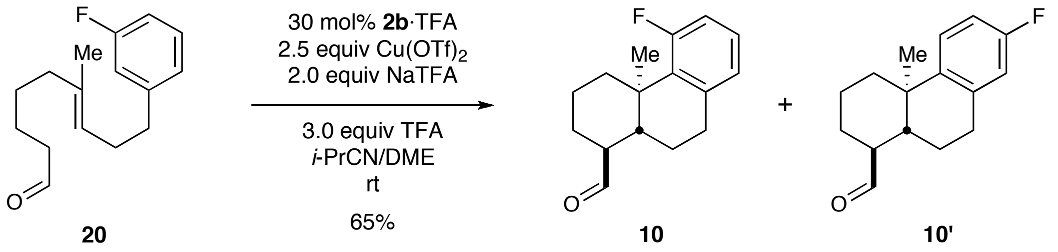
3.3 Bicyclization to Give Aldehyde 9 (Table 2)



19 **9**

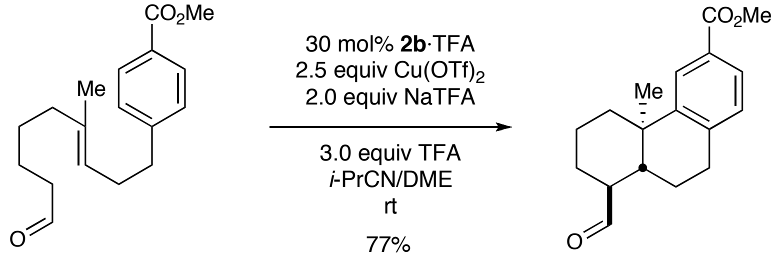
According to GP1, aldehyde **19** (56.9 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), Cu(OTf)$_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv) for 12 h (7 h syringe pump addition + 5 h additional stirring). Aqueous work-up using Et$_2$O as a solvent and flash chromatography (20% EtOAc/hexanes) furnished title compound **9** (43 mg, 76% yield) as a white solid. IR (ATR) ν (cm^{-1}) 3378, 3035, 2924, 2850, 2691, 1722, 1700, 1592, 1466, 1443, 1418, 1400, 1375, 1351, 1289, 1270, 1250, 1209, 1192, 1145, 1095, 1059, 1044, 973, 922, 822, 753, 734, 712, 694, 643, 612. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.59 (d, *J* = 3.4 Hz, C**H**O, 1H), 7.58 (d, *J* = 8.0 Hz, Ar**H**, 1H), 7.38 (d, *J* = 8.1 Hz, Ar**H**, 1H), 3.00-2.64 (m, 3 × C**H**$_2$, 6H), 2.48-2.31 (m, C**H**CHO, ArCH$_A$**H**$_B$, 2H), 1.93-1.69 (m, C**H**, 2 × C**H**$_2$, CH$_A$**H**$_B$, 6H), 1.51-1.35 (m, ArC**H**$_A$H$_B$, C**H**$_A$H$_B$, 2H), 1.16 (s, C**H**$_3$, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 207.3, 204.9, 155.1, 153.7, 134.7, 132.9, 124.4, 120.9, 51.1, 41.0, 37.14, 37.09, 36.5, 26.3, 25.4, 24.7, 22.6, 22.2, 20.6. HRMS (ESI$^+$) exact mass calcd for $C_{19}H_{23}O_2$ [M+H]$^+$ requires *m*/*z* 283.1691, found *m*/*z* 283.1693. The enantiomeric excess was determined by HPLC (Chiracel OJ-H, 10% *i*-PrOH/hexanes, flow rate 1.0 mL/min, λ = 214 nm); t_r = 23.3 (minor) and 27.5 (major) min. $[\alpha]_D^{25}$ = –65.6 (c = 0.84, CHCl$_3$, 85% ee).

3.4 Bicyclization to Give Aldehyde 10 (Table 2)



According to GP1, aldehyde **20** (46.7 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), $Cu(OTf)_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using Et_2O as a solvent and flash chromatography (1.5% EtOAc/hexanes) furnished title compound **10** (32 mg, 65% yield, 4:1 mixture of **10**:**10’**) as a colorless oil. Clean **10** (19 mg, 39% yield) could be obtained after a second flash column chromatography. IR (ATR) ν (cm^{-1}) 2933, 2867, 2709, 1722, 1703, 1613, 1588, 1572, 1494, 1449, 1377, 1349, 1293, 1233, 1139, 1057, 1020, 966, 941, 908, 865, 832, 812, 779, 731, 691. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (d, J = 4.5 Hz, C**H**O, 1H), 7.08 (ddd, J = 7.8, $J_{H,F}$ = 5.3 Hz, Ar**H**, 1H), 6.85 (d, J = 7.5 Hz, Ar**H**, 1H), 6.81 (dd, $J_{H,F}$ = 13.1, J = 8.0 Hz, Ar**H**, 1H), 2.93 (ddd, J = 17.6, 11.7, 7.4 Hz, $CH_A\mathbf{H_B}$, 1H), 2.84-2.76 (m, $C\mathbf{H_A}H_B$, $ArCH_A\mathbf{H_B}$, 2H), 2.47 (dddd, J = 2 × 12.0, 2 × 4.2 Hz, C**H**CHO, 1H), 1.88-1.70 (m, C**H**, $CH_A\mathbf{H_B}$, $C\mathbf{H_2}$, 4H), 1.60-1.55 (m, $C\mathbf{H_2}$, 2H), 1.48-1.38 (m, $ArC\mathbf{H_A}H_B$, $C\mathbf{H_A}H_B$, 2H), 1.26 (s, $C\mathbf{H_3}$, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.2, 162.1 (d, $J_{C,F}$ = 248 Hz), 138.6 (d, $J_{C,F}$ = 5.2 Hz), 133.4 (d, $J_{C,F}$ = 11 Hz), 126.9 (d, $J_{C,F}$ = 9.9 Hz), 125.3 (d, $J_{C,F}$ = 2.8 Hz), 113.8 (d, $J_{C,F}$ = 25 Hz), 50.5, 43.6, 37.2 (d, $J_{C,F}$ = 3.2 Hz), 35.7 (d, $J_{C,F}$ = 12 Hz), 30.8 (d, $J_{C,F}$ = 2.4 Hz), 26.5 (d, $J_{C,F}$ = 1.3 Hz), 22.7, 20.5, 19.0 (d, $J_{C,F}$ = 1.0 Hz). HRMS (ESI$^+$) exact mass calcd for $C_{16}H_{20}OF$ $[M+H]^+$ requires m/z 247.1493, found m/z 247.1494. The enantiomeric excess was determined by HPLC (Chiracel OD-H, 2% i-PrOH/hexanes, flow rate 1.0 mL/min, λ = 214 nm); t_r = 7.92 (major) and 9.23 (minor) min. $[\alpha]_D^{23}$ = –83.5 (c = 0.52, $CHCl_3$, 90% ee).

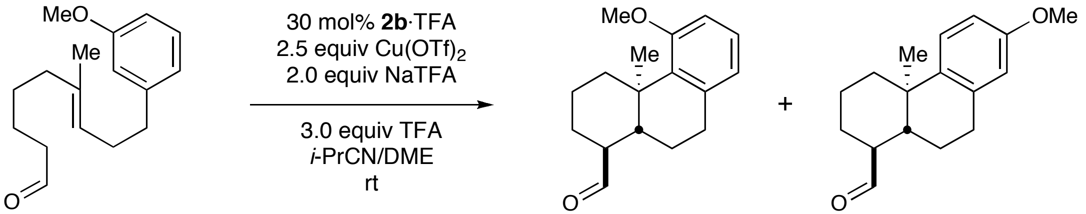
3.5 Bicyclization to Give Aldehyde 11 (Table 2)



21 **11**

According to GP1, aldehyde **21** (57.7 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), $Cu(OTf)_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using Et_2O as a solvent and flash chromatography (8% EtOAc/hexanes) furnished title compound **11** (44 mg, 77% yield) as a white solid. IR (ATR) ν (cm^{-1}) 2932, 2863, 2707, 1717, 1703, 1606, 1568, 1496, 1435, 1405, 1377, 1332, 1291, 1262, 1225, 1188, 1144, 1109, 1069, 972, 904, 880, 860, 802, 762. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.57 (d, *J* = 3.9 Hz, C**H**O, 1H), 7.99 (s, Ar**H**, 1H), 7.77 (d, *J* = 7.9 Hz, Ar**H**, 1H), 7.13 (d, *J* = 7.9 Hz, Ar**H**, 1H), 3.90 (s, $CO_2\mathbf{CH_3}$, 3H), 3.00-2.88 (m, $C\mathbf{H_2}$, 2H), 2.45-2.34 (m, C**H**CHO, $ArCH_A\mathbf{H_B}$, 2H), 1.92-1.66 (m, $C\mathbf{H_2}$, $CH_A\mathbf{H_B}$, C**H**, $C\mathbf{H_2}$ 6H), 1.51-1.35 (m, $ArC\mathbf{H_A}H_B$, $C\mathbf{H_A}H_B$, 2H), 1.13 (s, $\mathbf{CH_3}$, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0, 167.4, 147.2, 140.8, 129.5, 127.6, 126.8, 126.1, 52.0, 51.2, 41.1, 37.0, 36.4, 29.1, 26.3, 22.64, 22.56, 20.5. HRMS (ESI$^+$) exact mass calcd for $C_{18}H_{23}O_3$ $[M+H]^+$ requires *m/z* 287.1640, found *m/z* 287.1640. The enantiomeric excess was determined by HPLC (Chiracel AS-H, 10% *i*-PrOH/hexanes, flow rate 1.0 mL/min, λ = 230 nm); t_r = 16.3 (major) and 22.1 (minor) min. $[\alpha]_D^{23}$ = –62.3 (c = 1.2, $CHCl_3$, 87% ee).

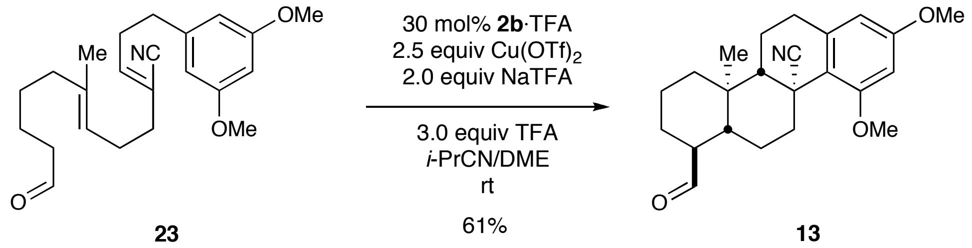
3.6 Bicyclization to Give Aldehyde 12 (Table 2)



22 **12** **12'**

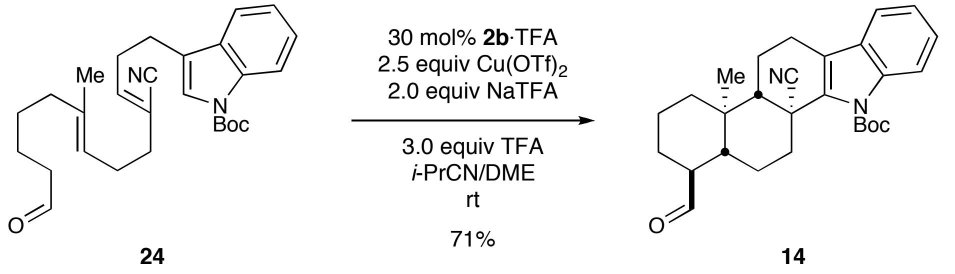
According to GP1, aldehyde **22** (52.1 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), Cu(OTf)$_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using Et$_2$O as a solvent and flash chromatography (5% EtOAc/hexanes) furnished title compound **12** (39 mg, 75% yield, 2:1 mixture of **12**:**12'**) as a colorless oil. Clean **12** (white solid, 15 mg, 29% yield) and **12'** (colorless oil, 8.0 mg, 15% yield) could be obtained after a second flash column chromatography. Analytical data for **12**: IR (ATR) ν (cm^{-1}) 3407, 3056, 3008, 2982, 2925, 2863, 2834, 2735, 1722, 1596, 1574, 1462, 1454, 1434, 1372, 1355, 1347, 1329, 1295, 1274, 1246, 1194, 1129, 1113, 1075, 1059, 1038, 1013, 974, 950, 913, 883, 863, 830, 802, 773, 693, 669. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.54 (d, *J* = 4.6 Hz, C**H**O, 1H), 7.99 (dd, *J* = 2 × 7.9 Hz Ar**H**, 1H), 7.10 (d, *J* = 7.4 Hz, 2 × Ar**H**, 2H), 3.80 (s, OC**H$_3$**, 3H), 3.15 (br d, *J* = 13.3 Hz, ArCH$_A$**H$_B$**, 1H), 2.94 (ddd, *J* = 16.8, 12.6, 6.4 Hz, CH$_A$**H$_B$**, 1H), 2.78 (dd, *J* = 17.0, 5.1 Hz, C**H$_A$**H$_B$, 1H), 2.48 (dddd, *J* = 2 × 15.7, 2 × 3.9 Hz, C**H**CHO, 1H), 1.82 (ddd, *J* = 2 × 12.0 Hz, C**H**, 1H), 1.78-1.70 (m, C**H$_2$**, CH$_A$**H$_B$**, 3H), 1.66-1.56 (m, CH$_A$**H$_B$**, 1H), 1.53-1.37 (m, C**H$_A$**H$_B$, C**H$_A$**H$_B$, 2H), 1.28-1.19 (m, ArC**H$_A$**H$_B$, 1H), 1.26 (s, C**H$_3$**, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 205.7, 158.9, 137.8, 134.6, 126.5, 122.4, 109.2, 55.1, 50.8, 44.6, 37.9, 34.9, 31.6, 26.6, 22.8, 20.7, 17.6. HRMS (ESI$^+$) exact mass calcd for C$_{17}$H$_{23}$O$_2$ [M+H]$^+$ requires *m/z* 259.1692, found *m/z* 259.1693. The enantiomeric excess was determined by HPLC (Chiracel OD-H, 2% *i*-PrOH/hexanes, flow rate 1.0 mL/min, λ = 230 nm); t_r = 8.1 (minor) and 21.5 (major) min. $[\alpha]_D^{23}$ = –70.8 (c = 0.53, CHCl$_3$, 88% ee). Analytical data for **12'**: ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.55 (d, *J* = 4.3 Hz, C**H**O, 1H), 7.20 (d, *J* = 8.6 Hz, Ar**H**, 1H), 7.33 (dd, *J* = 8.5, 2.1 Hz, Ar**H**, 1H), 6.60 (s, Ar**H**, 1H), 3.77 (s, OC**H$_3$**, 3H), 2.94-2.82 (m, C**H$_2$**, 2H), 2.36 (dddd, *J* = 2 × 11.8, 2 × 3.9 Hz, C**H**CHO, 1H), 2.28 (br d, *J* = 12.9 Hz, ArCH$_A$**H$_B$**, 1H), 1.88-1.63 (m, C**H$_2$**, CH$_A$**H$_B$**, C**H**, C**H$_2$**, 6H), 1.48-1.35 (m, ArC**H$_A$**H$_B$, C**H$_A$**H$_B$, 2H), 1.10 (s, C**H$_3$**, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 205.5, 157.4, 139.5, 136.4, 125.7, 113.6, 112.0, 55.2, 51.2, 41.7, 37.3, 35.8, 29.3, 26.4, 23.0, 22.8, 20.6. The enantiomeric excess was determined by HPLC (Chiracel AS-H, 2% *i*-PrOH/hexanes, flow rate 1.0 mL/min, λ = 230 nm); t_r = 21.2 (major) and 52.9 (minor) min.

3.7 Tricyclization to Give Aldehyde 13 (Table 2)



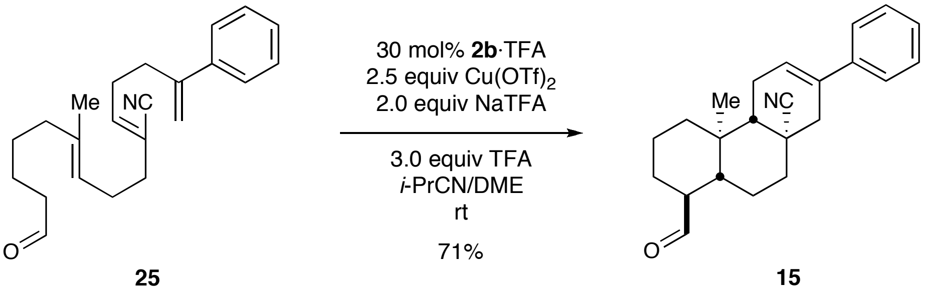
According to GP1, aldehyde **23** (73.9 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), Cu(OTf)$_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using EtOAc as a solvent and flash chromatography (15% EtOAc/hexanes) furnished title compound **13** (45 mg, 61% yield) as a white solid. IR (ATR) ν (cm^{-1}) 2933, 2872, 2844, 2695, 2223, 1724, 1614, 1577, 1474, 1461, 1445, 1424, 1355, 1345, 1317, 1303, 1264, 1246, 1219, 1202, 1189, 1158, 1124, 1107, 1083, 1047, 1034, 988, 956, 876, 856, 830, 800, 749, 735, 669, 637. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.54 (d, *J* = 4.2 Hz, C**H**O, 1H), 6.32 (d, *J* = 2.4 Hz, Ar**H**, 1H), 6.23 (d, *J* = 2.4 Hz, Ar**H**, 1H), 3.83 (s, OC**H$_3$**, 3H), 3.78 (s, OC**H$_3$**, 3H), 3.58 (ddd, *J* = 13.7, 2 × 3.3 Hz, ArCH$_A$**H$_B$**, 1H), 2.86 (m, C**H$_2$**, 2H), 2.33 (dddd, *J* = 2 × 12.0, 2 × 3.9 Hz, C**H**CHO, 1H), 2.02 (br d, *J* = 12.0 Hz, CH$_A$**H$_B$**, 1H), 1.93 (br d, *J* = 12.8 Hz, CH$_A$**H$_B$**, 1H), 1.82-1.62 (m, C**H$_2$**, 2 × CH$_A$**H$_B$**, C**H$_A$**H$_B$, 5H), 1.57-1.52 (m, C**H$_A$**H$_B$, 1H), 1.46-1.26 (m, 2 × C**H**, C**H$_A$**H$_B$, ArC**H$_A$**H$_B$, 4H), 1.17 (s, C**H$_3$**, 3H), 0.96 (ddd, *J* = 2 × 12.3, 2 × 6.3 Hz, C**H$_A$**H$_B$, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 205.3, 160.1, 159.8, 139.6, 123.3, 119.2, 105.1, 97.7, 55.6, 55.3, 55.0, 49.9, 46.8, 39.6, 37.7, 37.1, 35.2, 32.8, 26.4, 23.9, 20.2, 19.7, 12.8. HRMS (ESI$^+$) exact mass calcd for $C_{23}H_{30}NO_3$ [M+H]$^+$ requires *m*/*z* 368.2221, found *m*/*z* 368.2222. The enantiomeric excess was determined by HPLC (Chiracel OD-H, 20% *i*-PrOH/hexanes, flow rate 1.0 mL/min, λ = 214 nm); t_r = 10.8 (major) and 14.1 (minor) min. $[\alpha]_D^{25}$ = +81.3 (c = 0.77, CHCl$_3$, 91% ee).

3.8 Tricyclization to Give Aldehyde 14 (Table 2)



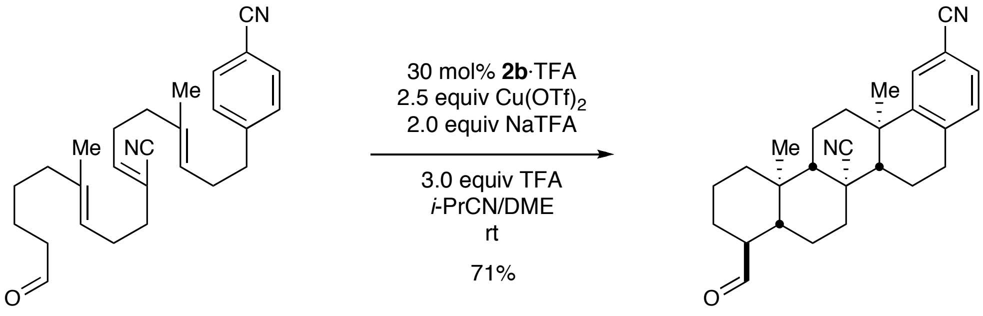
According to GP1, aldehyde **24** (89.7 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), Cu(OTf)$_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using EtOAc as a solvent and flash chromatography (10% EtOAc/hexanes) furnished title compound **14** (63 mg, 71% yield as a white solid. IR (ATR) ν (cm^{-1}) 2974, 2930, 2868, 2711, 2229, 1723, 1603, 1476, 1452, 1394, 1369, 1355, 1310, 1253, 1237, 1214, 1153, 1136, 1119, 1092, 1024, 1010, 976, 937, 911, 846, 829, 746. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.54 (d, *J* = 4.0 Hz, C**H**O, 1H), 7.98 (d, *J* = 8.4 Hz, Ar**H**, 1H), 7.44 (d, *J* = 7.5 Hz, Ar**H**, 1H), 7.33 (ddd, *J* = 2 × 8.4, 1.2 Hz, Ar**H**, 1H), 7.25 (dd, *J* = 2 × 7.5 Hz, Ar**H**, 1H), 3.16 (ddd, *J* = 13.2, 2 × 3.1 Hz, ArCH$_\mathrm{A}\mathbf{H_B}$, 1H), 2.91 (dd, *J* = 16.8, 4.4 Hz, CH$_\mathrm{A}\mathbf{H_B}$, 1H), 2.66 (ddd, *J* = 16.8, 11.9, 6.2 Hz, C$\mathbf{H_A}$H$_\mathrm{B}$, 1H), 2.37 (dddd, *J* = 2 × 11.8, 2 × 3.8 Hz, C**H**CHO, 1H), 2.21 (dd, *J* = 14.0, 6.2 Hz, CH$_\mathrm{A}\mathbf{H_B}$, 1H), 2.05-1.94 (m, C$\mathbf{H_A}$H$_\mathrm{B}$, CH$_\mathrm{A}\mathbf{H_B}$, 2H), 1.85-1.64 (m, 2 × CH$_\mathrm{A}\mathbf{H_B}$, C$\mathbf{H_2}$, 4H), 1.70 (s, C(C$\mathbf{H_3}$)$_3$, 9H), 1.63-1.58 (m, C$\mathbf{H_A}$H$_\mathrm{B}$, 1H), 1.54-1.18 (m, ArC$\mathbf{H_A}$H$_\mathrm{B}$, 2 × C**H**, C$\mathbf{H_A}$H$_\mathrm{B}$, 4H), 1.24 (s, C$\mathbf{H_3}$, 3H), 1.00-0.91 (m, C$\mathbf{H_A}$H$_\mathrm{B}$, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 205.0, 150.6, 137.3, 134.3, 128.3, 125.4, 122.9, 121.9, 120.9, 118.7, 115.4, 85.1, 56.9, 49.8, 47.0, 40.0, 37.7, 37.2, 33.6, 28.3, 26.4, 23.2, 22.8, 19.7, 19.6, 12.9. HRMS (ESI$^+$) exact mass calcd for $C_{28}H_{34}N_2O_3Na$ [M+Na]$^+$ requires *m/z* 469.2462, found *m/z* 469.2462. The enantiomeric excess was determined by HPLC (Chiracel OD-H, 10% *i*-PrOH/hexanes, flow rate 0.80 mL/min, λ = 230 nm); t_r = 12.5 (major) and 14.5 (minor) min. $[\alpha]_D^{24}$ = +59.7 (c = 0.69, CHCl$_3$, 92% ee).

3.9 Tricyclization to Give Aldehyde 15 (Table 2)



According to GP1, aldehyde **25** (67.1 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), $Cu(OTf)_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using EtOAc as a solvent and flash chromatography (10% EtOAc/hexanes) furnished title compound **15** (36 mg, 54% yield). IR (ATR) ν (cm^{-1}) 3035, 2929, 2855, 2706, 2230, 1720, 1646, 1598, 1577, 1497, 1470, 1446, 1431, 1393, 1365, 1346, 1277, 1243, 1192, 1159, 1138, 1077, 1047, 1023, 1004, 988, 914, 848, 834, 752, 695, 676. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (d, *J* = 3.9 Hz, C**H**O, 1H), 7.36-7.30 (m, Ar**H**, 4H), 7.27-7.23 (m, Ar**H**, 1H), 6.20-6.17 (m, $\mathbf{CH_{vin}}$, 1H), 2.84 (d, *J* = 16.7 Hz, $CH_A\mathbf{H_B}$, 1H), 2.53-2.27 (m, $\mathbf{CH_A}H_B$, $\mathbf{CH_2}$, C**H**CHO, $CH_A\mathbf{H_B}$, 5H), 1.85-1.77 (m, $CH_A\mathbf{H_B}$, $CH_A\mathbf{H_B}$, 2H), 1.74-1.41 (m, 2 × $\mathbf{CH_2}$, $\mathbf{CH_A}H_B$, 2 × C**H**, 7H), 1.36-1.23 (m, $\mathbf{CH_A}H_B$, 1H), 1.14, (s, $\mathbf{CH_3}$, 3H), 0.98 (ddd, *J* = 2 × 13.0, 4.1 Hz, $\mathbf{CH_A}H_B$, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.9, 140.7, 132.7, 128.5, 127.3, 125.2, 124.2, 123.9, 50.2, 49.4, 45.9, 42.8, 38.0, 37.9, 36.11, 36.05, 26.4, 24.1, 23.1, 19.6, 12.4. HRMS (ESI^+) exact mass calcd for $C_{23}H_{28}NO$ $[M+H]^+$ requires *m*/*z* 334.2165, found *m*/*z* 334.2164. The enantiomeric excess was determined by HPLC (Chiracel OD-H, 10% *i*-PrOH/hexanes, flow rate 1.0 mL/min, λ = 214 nm); t_r = 22.3 (major) and 31.0 (minor) min. $[\alpha]_D^{25}$ = –48.6 (c = 0.75, $CHCl_3$, 85% ee).

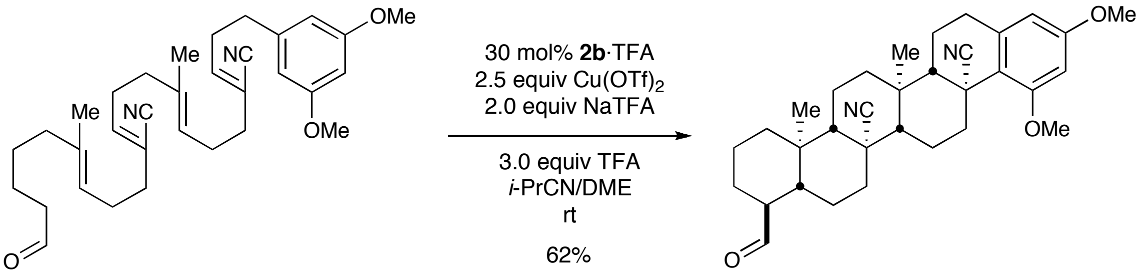
3.10 Tetracyclization to Give Aldehyde 5 (Scheme 2)



1 **5**

According to GP1, aldehyde **1** (80.5 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), $Cu(OTf)_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using $CHCl_3$ as a solvent and flash chromatography (10% EtOAc/20% $CHCl_3$/70% hexanes) furnished title compound **5** (45 mg, 56% yield). IR (ATR) ν (cm^{-1}) 2923, 2858, 2731, 2224, 1719, 1606, 1560, 1505, 1492, 1445, 1405, 1377, 1290, 1248, 1203, 1179, 1164, 1065, 1046, 1032, 1021, 938, 913, 844, 824, 728. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.53 (d, *J* = 4.0 Hz, C**H**O, 1H), 7.52 (d, *J* = 1.3 Hz, Ar**H**, 1H), 7.39 (dd, *J* = 7.9, 1.5 Hz, Ar**H**, 1H), 7.15 (d, *J* = 7.9 Hz, Ar**H**, 1H), 3.09 (ddd, *J* = 18.4, 8.0, 2.1 Hz, $CH_A\mathbf{H_B}$, 1H), 2.93 (ddd, *J* = 18.1, 2 × 8.9 Hz, $C\mathbf{H_A}H_B$, 1H), 2.45 (ddd, *J* = 12.9, 2 × 3.2 Hz, $CH_A\mathbf{H_B}$, 1H), 2.40 (ddd, *J* = 13.3, 2 × 3.3 Hz, $ArCH_A\mathbf{H_B}$, 1H), 2.34 (dddd, *J* = 2 × 12.0, 2 × 3.9 Hz, C**H**CHO, 1H), 2.11-1.93 (m, $C\mathbf{H_2}$, $CH_A\mathbf{H_B}$, 3H), 1.88 (br d, *J* = 12.8 Hz, $CH_A\mathbf{H_B}$, 1H), 1.83-1.44 (m, $CH_A\mathbf{H_B}$, 2 × $C\mathbf{H_2}$, 2 × $C\mathbf{H_A}H_B$, C**H**, 8H), 1.39 (s, $C\mathbf{H_3}$, 3H), 1.38-1.23 (m, $ArC\mathbf{H_A}H_B$, $C\mathbf{H_A}H_B$, C**H**, 3H), 1.16 (s, $C\mathbf{H_3}$, 3H), 1.07-1.01 (m, C**H**, 1H), 0.93-0.84 (m, $C\mathbf{H_A}H_B$, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0, 149.4, 140.5, 129.9, 129.3, 128.1, 123.8, 119.5, 109.7, 56.4, 50.9, 49.9, 46.2, 40.1, 38.6, 38.0, 37.8, 37.4, 36.7, 28.6, 26.5, 23.8, 22.9, 19.7, 19.6, 18.2, 12.7. HRMS (ESI^+) exact mass calcd for $C_{27}H_{33}N_2O$ $[M+H]^+$ requires *m/z* 401.2587, found *m/z* 401.2583. The enantiomeric excess was determined by SFC (Chiracel AD-H, 60% EtOH w/0.1% DEA/CO_2, 100 bar, flow rate 2.5 mL/min, λ = 220 nm); t_r = 2.64 (major) and 3.64 (minor) min. $[\alpha]_D^{24}$ = −26.1 (c = 0.68, $CHCl_3$, 92% ee).

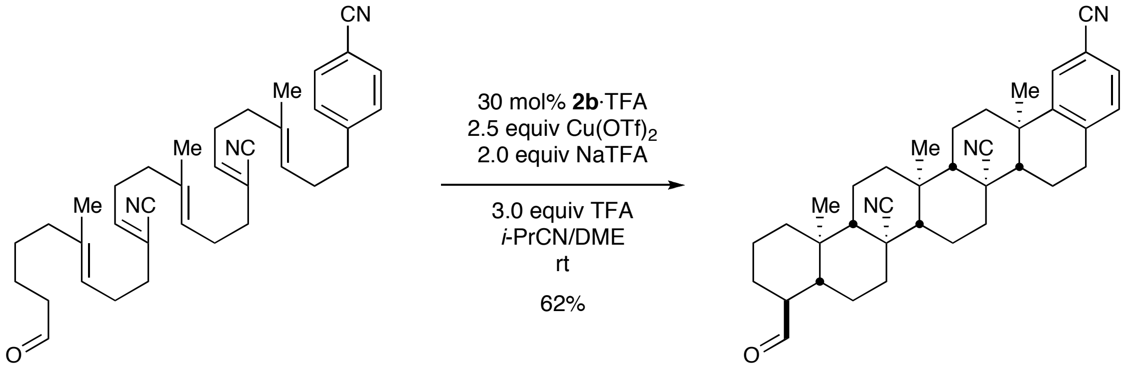
3.11 Pentacyclization to Give Aldehyde 16 (Scheme 2)



26 **16**

According to GP1, aldehyde **26** (103 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), Cu(OTf)$_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using CHCl$_3$ as a solvent and flash chromatography (15% EtOAc/30% CHCl$_3$/55% hexanes) furnished title compound **16** (66 mg, 62% yield). IR (ATR) ν (cm^{-1}) 2952, 2928, 2865, 2846, 2229, 1717, 1607, 1589, 1447, 1381, 1358, 1349, 1336, 1308, 1281, 1206, 1195, 1165, 1144, 1104, 1075, 1062, 1038, 1016, 979, 965, 947, 930, 864, 843, 817, 696, 672, 627. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.53 (d, *J* = 3.8 Hz, C**H**O, 1H), 6.32 (d, *J* = 2.1 Hz, Ar**H**, 1H), 6.22 (d, *J* = 1.9 Hz, Ar**H**, 1H), 3.84 (s, $\mathrm{OC}\mathbf{H_3}$, 3H), 3.77 (s, $\mathrm{OC}\mathbf{H_3}$, 3H), 3.70 (br d, *J* = 13.9 Hz, $\mathrm{ArCH_A}\mathbf{H_B}$, 1H), 2.91-2.74 (m, $\mathrm{C}\mathbf{H_2}$, 2H), 2.38-2.27 (m, C**H**, $\mathrm{CH_A}\mathbf{H_B}$, 2H), 2.06 (br d, *J* = 13.0 Hz, $\mathrm{CH_A}\mathbf{H_B}$, 1H), 2.03-1.94 (m, $\mathrm{C}\mathbf{H_2}$, 2H), 1.91-1.50 (m, 4 × $\mathrm{C}\mathbf{H_2}$, 2 × $\mathrm{CH_A}\mathbf{H_B}$, 10H), 1.45 (s, $\mathrm{C}\mathbf{H_3}$, 3H), 1.37-1.08 (m, 3 × C**H**, $\mathrm{ArC}\mathbf{H_A}\mathrm{H_B}$, 2 × $\mathrm{C}\mathbf{H_A}\mathrm{H_B}$, 6H), 1.13 (s, $\mathrm{C}\mathbf{H_3}$, 3H), 1.04-0.95 (m, C**H**, $\mathrm{C}\mathbf{H_A}\mathrm{H_B}$, 2H), 0.84 (ddd, *J* = 2 × 12.3, 4.2 Hz, $\mathrm{C}\mathbf{H_A}\mathrm{H_B}$, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 205.1, 160.1, 159.8, 139.4, 123.5, 122.8, 119.2, 105.1, 97.7, 57.1, 56.9, 56.6, 55.6, 55.3, 49.9, 46.3, 39.7, 39.1, 38.6, 38.5, 37.7, 37.6, 36.7, 35.8, 32.7, 26.5, 22.9, 20.0, 19.8, 19.7, 18.8, 15.1, 12.6. HRMS (ESI$^+$) exact mass calcd for $C_{33}H_{42}N_2O_3Na$ $[M+Na]^+$ requires *m/z* 537.3088, found *m/z* 537.3085. The enantiomeric excess was determined by SFC (Chiralpak IA, 40% EtOH/CO$_2$, 100 bar, flow rate 3.0 mL/min, λ = 220 nm); t_r = 3.42 (major) and 5.13 (minor) min. $[\alpha]_D^{24}$ = +44.6 (c = 0.62, CHCl$_3$, 93% ee).

3.12 Hexacyclization to Give Aldehyde 17 (Table 2)



27 **17**

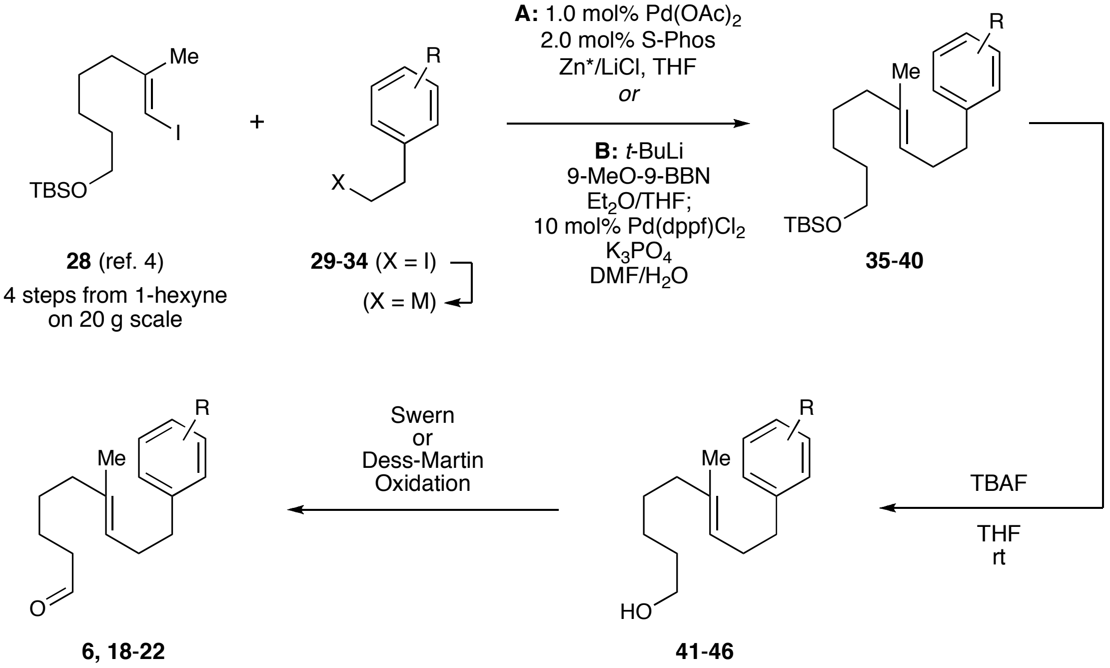
According to GP1, aldehyde **27** (107 mg, 0.200 mmol, 1.00 equiv) was subjected to catalyst catalyst **2b**·TFA (24.6 mg, 0.0600 mmol, 0.300 equiv), $Cu(OTf)_2$ (181 mg, 0.500 mmol, 2.50 equiv), sodium trifluoroacetate (54.4 mg, 0.400 mmol, 2.00 equiv), and TFA (45 μL, 0.40 mmol, 2.0 equiv). Aqueous work-up using $CHCl_3$ as a solvent and flash chromatography (20% EtOAc/30% $CHCl_3$/50% hexanes) furnished title compound **17** (66 mg, 62% yield). IR (ATR) ν (cm^{-1}) 2926, 2855, 2715, 2226, 1729, 1607, 1564, 1492, 1447, 1380, 1257, 1165, 1060, 1037, 1021, 965, 937, 889, 847, 826, 754, 626. ^1H NMR (500 MHz, $CDCl_3$) δ 9.54 (d, *J* = 3.6 Hz, C**H**O, 1H), 7.51 (s, Ar**H**, 1H), 7.39 (d, *J* = 7.7 Hz, Ar**H**, 1H), 7.16 (d, *J* = 7.7 Hz, Ar**H**, 1H), 3.10 (dd, *J* = 16.9, 9.0 Hz, $CH_A\mathbf{H_B}$, 1H), 2.93 (ddd, *J* = 18.3, 2 × 9.2 Hz, $C\mathbf{H_A}H_B$, 1H), 2.54 (br d, *J* = 13.4 Hz, $CH_A\mathbf{H_B}$, 1H), 2.45 (br d, *J* = 12.7 Hz, $CH_A\mathbf{H_B}$, 1H), 2.39-2.25 (m, C**H**CHO, $ArCH_A\mathbf{H_B}$, 2H), 2.12-1.74 (m, $C\mathbf{H_2}$, 5 × $CH_A\mathbf{H_B}$, $C\mathbf{H_A}H_B$, 8H), 1.74-1.15 (m, 3 × $C\mathbf{H_2}$, 3 × $C\mathbf{H_A}H_B$, $ArC\mathbf{H_A}H_B$, 2 × C**H**, 12H), 1.44 (s, $C\mathbf{H_3}$, 3H), 1.39 (s, $C\mathbf{H_3}$, 3H), 1.12 (s, $C\mathbf{H_3}$, 3H), 1.05-0.80 (m, 3 × $C\mathbf{H_A}H_B$, 3 × C**H**, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0, 149.3, 140.5, 129.9, 129.3, 128.1, 123.4, 123.2, 119.5, 109.8, 57.9, 56.9 (2 × **C**H), 51.1, 49.9, 46.3, 39.6, 39.5, 38.7, 38.5, 38.22, 38.21, 37.9, 37.72, 37.68, 36.7, 28.6, 26.5, 23.7, 22.9, 19.8, 19.3, 18.9, 18.8, 18.3, 14.8, 12.6. HRMS (ESI^+) exact mass calcd for $C_{37}H_{46}N_3O$ $[M+H]^+$ requires *m*/*z* 548.3635, found *m*/*z* 548.3627. The determination of the enantiomeric excess was unsuccessful under a variety of HPLC and SFC conditions due to extremely low solubility of **17** in common solvents. $[\alpha]_D^{24}$ = −25.3 (c = 0.68, $CHCl_3$).

4 Preparation of Cyclization Precursors

4.1 General Strategy toward Bicyclization Precursors

All bicyclization substrates were prepared by palladium-catalyzed cross-coupling of vinyl iodide **28**[4] with alkyl metal intermediates derived from homobenzylic iodides following either Knochel's Negishi coupling protocol (**A**)[5] or a *B*-alkyl Suzuki coupling (**B**)[6] (Scheme S1). Known vinyl iodide **28**[4] was prepared in a scalable four-step sequence starting from hexyne consisting of (i) hydroxymethylation,[7] (ii) alkyne isomerization,[8] (iii) silyl protection,[4] and (iv) carboalumination/iodination.[9] Deprotection and oxidation completed substrate synthesis of **6**, **18-22** for organo-SOMO bicyclizations.

Scheme S1. Synthetic Access to Bicyclization Substrates.



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(5) a) Manolikakes, G.; Schade, M. A.; Muñoz Hernandez, C.; Mayr, H.; Knochel, P. *Org. Lett.* **2008**, *10*, 2765. b) Krasovskiy, A.; Malakhov, V.; Gavrushin, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 6040.

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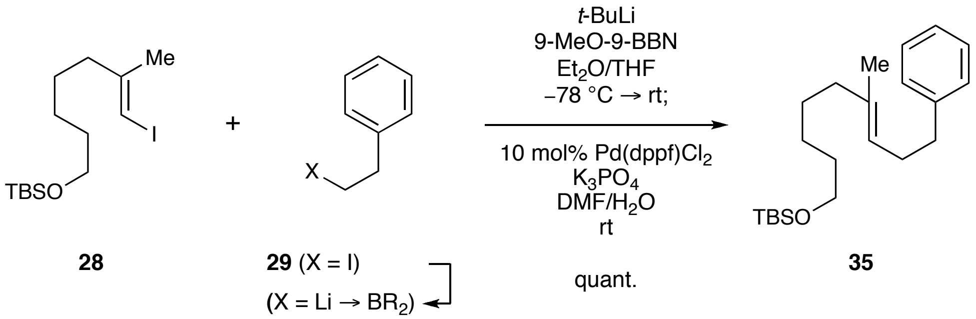
4.2 Preparation of Aldehyde 6

4.2.1 (*E*)-*tert*-Butyldimethyl(6-methyl-9-phenylnon-6-enyloxy)silane (**35**)

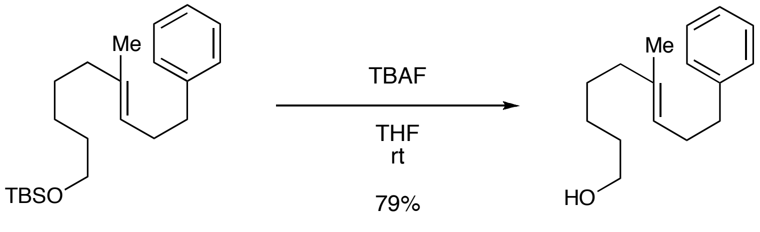


t-BuLi (14.6 mL of a 1.7M solution in pentane, 24.0 mmol, 3.30 equiv) was rapidly added to a solution of alkyl iodide **29** (2.20 mL, 3.42 g, 11.3 mmol, 1.50 equiv) in Et_2O (40 mL) at –78 °C. After strirring for 3 min, 9-methoxy-9-borabicyclononane (25.8 mL of a 1.0M solution in hexanes, 25.8 mmol, 3.45 equiv) was added in one portion followed by THF (40 mL). The solution was stirred for 10 min at –78 °C and then allowed to warm to room temperature for 1.5 h. To this mixture, aqueous 3M K_3PO_4 (12.5 mL, 37.5 mmol, 5.00 equiv), vinyl iodide **28** (2.74 g, 7.50 mmol, 1.00 equiv) in DMF (40 mL), and $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ (612 mg, 0.750 mmol, 0.100 equiv) were added sequentially, and the resultant dark solution was stirred for 5 h. Upon addition of water (100 mL), the reaction mixture was extracted with Et_2O (3 × 75 mL). The combined organic layers were washed with water (2 × 30 mL) and brine (30 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude mixture by flash chromatography (1% EtOAc/hexanes) furnished title compound **35** (2.60 g, quant. yield, approx. 90% purity). Remaining impurities were separated after the following deprotection step.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.24 (m, Ar**H**, 2H), 7.21-7.15 (m, Ar**H**, 3H), 5.18 (t, *J* = 7.3 Hz, $\mathbf{CH_{vin}}$, 1H), 3.60 (t, *J* = 7.6 Hz, $\mathbf{CH_2}$OSi, 2H), 2.64 (t, *J* = 7.6 Hz, Ar$\mathbf{CH_2}$, 2H), 2.30 (dt, *J* = 2 × 7.8 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 1.97 (t, *J* = 7.4 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.54 (s, $\mathbf{CH_3}$, 3H), 1.52 (tt, *J* = 2 × 7.7 Hz, $\mathbf{CH_2}CH_2O$, 2H), 1.52 (tt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}(CH_2)_3O$, 2H), 1.27 (tt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}(CH_2)_2O$, 2H), 0.90 (s, $SiC(\mathbf{CH_3})_3$, 9H), 0.05 (s, $Si(\mathbf{CH_3})_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$)

δ 142.4, 136.0, 128.5, 128.2, 125.6, 123.5, 63.3, 39.7, 36.2, 32.8, 30.0, 27.7, 26.0, 25.4, 18.4, 15.9, –5.2.

4.2.2 (*E*)-6-Methyl-9-phenylnon-6-en-1-ol (**41**)

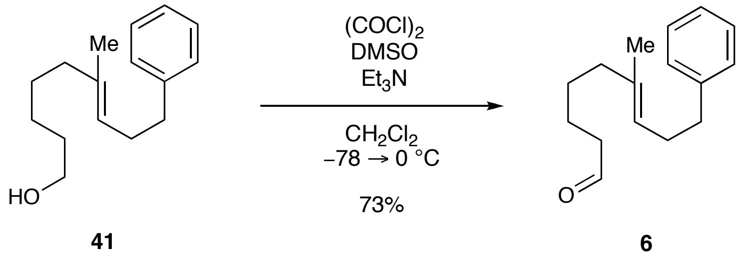


35 **41**

TBAF (9.0 mL of a 1.0M solution in THF, 9.0 mmol, 1.20 equiv) was added slowly to a solution of silyl ether **35** (2.60 g, 7.50 mmol, 1.00 equiv) in THF (40 mL) at room temperature. After stirring had been continued for 6 h, water (50 mL) and sat. NH_4Cl (30 mL) were added and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **41** (1.36 g, 79% yield over two steps) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3320, 3062, 3026, 2929, 2856, 1666, 1603, 1495, 1453, 1381, 1152, 1073, 1052, 1030, 956, 885, 843, 745, 695. ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.24 (m, Ar**H**, 2H), 7.20-7.15 (m, Ar**H**, 3H), 5.17 (t, *J* = 7.0 Hz, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 3.63 (t, *J* = 6.7 Hz, C$\mathbf{H_2}$OH, 2H), 2.63 (t, *J* = 7.6 Hz, ArC$\mathbf{H_2}$, 2H), 2.30 (dt, *J* = 2 × 7.5 Hz, C$\mathbf{H_2}$CH_{vin}, 2H), 1.97 (t, *J* = 7.5 Hz, C$\mathbf{H_2}$(CH_3)C=C, 2H), 1.56 (tt, *J* = 2 × 7.3 Hz, C$\mathbf{H_2}$$CH_2$OH, 2H), 1.53 (s, C$\mathbf{H_3}$, 3H), 1.40 (tt, *J* = 2 × 7.3 Hz, C$\mathbf{H_2}$(CH_2)$_3$O, 2H), 1.29 (tt, *J* = 2 × 7.1 Hz, C$\mathbf{H_2}$(CH_2)$_2$O, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 135.9, 128.5, 128.3, 125.7, 123.7, 63.1, 39.6, 36.2, 32.8, 30.0, 27.7, 25.4, 15.9. HRMS (ESI^+) exact mass calcd for $C_{16}H_{25}O$ $[M+H]^+$ requires *m/z* 233.1900, found *m/z* 233.1896.

4.2.3 (*E*)-6-Methyl-9-phenylnon-6-en-1-al (**6**)

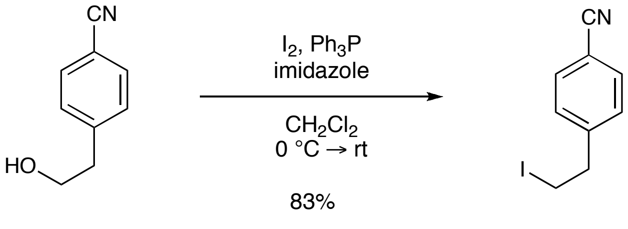


Oxalyl chloride (0.48 mL, 0.70 g, 5.50 mmol, 1.10 equiv) was dissolved in CH_2Cl_2 (50 mL) and cooled to –78 °C. DMSO (0.85 mL, 0.94 g, 12.0 mmol, 2.40 equiv) was added dropwise and the resultant solution stirred for 10 min. Subsequently, a solution of alcohol **41** (1.15 g, 5.00 mmol, 1.00 equiv) in CH_2Cl_2 (5 mL) was added slowly and stirring was continued for 10 min at –78 °C. Upon addition of Et_3N (3.30 mL, 2.42 g, 24.0 mmol, 4.80 equiv), the reaction mixture was allowed to warm to 0 °C within 1 h. After addition of water (50 mL) and aqueous 2M HCl (20 mL), the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (10% EtOAc/hexanes) furnished title compound **6** (841 mg, 73% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3061, 3026, 2930, 2857, 2717, 1723, 1603, 1495, 1453, 1409, 1386, 1242, 1158, 1107, 1078, 1030, 1002, 844, 746, 698. ^1H NMR (500 MHz, $CDCl_3$) δ 9.76, (t, *J* = 1.7 Hz, C**H**O, 1H), 7.30-7.24 (m, Ar**H**, 2H), 7.21-7.15 (m, Ar**H**, 3H), 5.18 (t, *J* = 7.0 Hz, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 2.64 (t, *J* = 7.5 Hz, ArC$\mathbf{H_2}$, 2H), 2.41 (td, *J* = 7.4, 1.7 Hz, C$\mathbf{H_2}$CHO, 2H), 2.31 (dt, *J* = 2 × 7.5 Hz, C$\mathbf{H_2}$$CH_{vin}$, 2H), 1.99 (t, *J* = 7.5 Hz, C$\mathbf{H_2}$(CH_3)C=C, 2H), 1.57 (tt, *J* = 2 × 7.5 Hz, C$\mathbf{H_2}$$CH_2$CHO, 2H), 1.53 (s, C$\mathbf{H_3}$, 3H), 1.41 (tt, *J* = 2 × 7.5 Hz, C$\mathbf{H_2}$$(CH_2)_2$CHO, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.0, 142.4, 135.9, 128.5, 128.3, 125.8, 124.1, 43.9, 39.3, 36.1, 29.9, 27.3, 21.6, 15.8. HRMS (ESI^+) exact mass calcd for $C_{16}H_{23}O$ $[M+H]^+$ requires *m/z* 231.1743, found *m/z* 231.1744.

4.3 Preparation of Aldehyde 18

4.3.1 4-(2-Iodoethyl)benzonitrile (**30**)



30

Iodine (25.9 g, 102 mmol, 1.50 equiv) was added to a solution of Ph_3P (26.8 g, 102 mmol, 1.50 equiv) in CH_2Cl_2 (300 mL) at 0 °C and stirred for 10 min. Upon addition of imidazole (11.6 g, 170 mmol, 2.50 equiv) and further 10 min of stirring, a solution of 2-(4-cyanophenyl)ethanol[10] (10.0 g, 68.0 mmol, 1.00 equiv) in CH_2Cl_2 (40 mL) was added via syringe followed by stirring for 1 h at room temperature. The reaction mixture was washed with aqueous Na_2SO_3 (2 × 100 mL) and the aqueous layer extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residual was treated with PE/Et_2O (1:1, 300 mL) to precipitate Ph_3PO. Filtration, removal of the volatiles *in vacuo*, and purification by flash chromatography (5% EtOAc/hexanes) furnished iodide **30** (14.5 g, 83% yield) as a yellowish solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 8.1 Hz, Ar**H**, 2H), 7.31 (d, J = 8.0 Hz, Ar**H**, 2H), 3.36 (t, J = 7.5 Hz, $\mathbf{CH_2}$, 2H), 1.78 (t, J = 8.0 Hz, $\mathbf{CH_2}$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.7, 132.6, 129.3, 118.9, 111.0, 39.9, 3.9. HRMS (ESI$^+$) exact mass calcd for $[M+H]^+$ (C_9H_9IN) requires *m/z* 257.9776, found *m/z* 257.9774.

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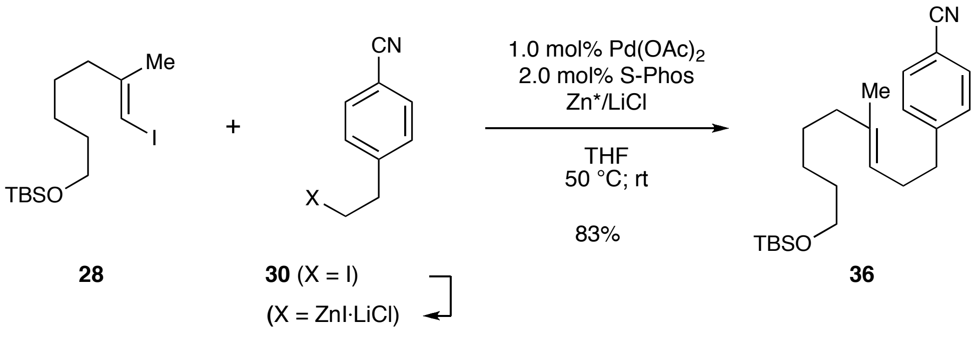
(10) Prepared from 2-(4-aminophenyl)ethanol: Wagner, G.; Vieweg, H. *Pharmazie* **1982**, *37*, 13.

4.3.2 (*E*)-4-(9-(*tert*-Butyldimethylsilyloxy)-4-methylnon-3-enyl)benzonitrile (**36**)

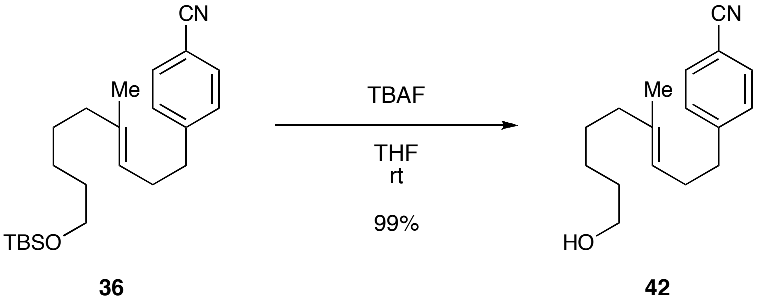


Anhydrous LiCl (636 mg, 15.0 mmol, 1.25 equiv) was placed in an argon-flushed 25-mL Schlenk flask and dried for 30 min at 150-180 °C under high vacuum (<1 torr) with slow stirring. Upon addition of zinc powder (325 mesh, 1.47 g, 22.5 mmol, 1.88 equiv) heating under high vacuum was continued for 30 min. After cooling to room temperature and backfilling with argon, the mixture was suspended with THF (10 mL). Subsequently, the zinc powder was activated by sequential addition of 1,2-dibromoethane (65 μL, 140 mg, 0.75 mmol, 0.060 equiv), TMSCl (3 drops), and iodine (15 drops of a 1M solution in THF); each addition followed by gentle heating to reflux with a heat gun. A solution of iodide **30** (3.86 g, 15.0 mmol, 1.25 equiv) in THF (10 mL) was added portionwise at room temperature and followed by heating of the reaction mixture to 50 °C for 4 h. The thus generated solution of homobenzylic iodide was allowed to cool to room temperature and separated via syringe from remaining zinc powder.

In a separate 50-mL Schlenk flask, $Pd(OAc)_2$ (26.9 mg, 0.120 mmol, 0.0100 equiv) and S-Phos (98.5 mg, 0.240 mmol, 0.0200 equiv) was dissolved in THF (3.0 mL) and a solution of vinyl iodide **28** (4.42 g, 12.0 mmol, 1.00 equiv) in THF (3.0 mL) was added. The previously prepared solution of homobenzylic zinc reagent was quickly added via syringe leading to an exothermic reaction. Further stirring at room temperature for 3 h was followed by aqueous work-up with sat. NH_4Cl (50 mL) and extraction with EtOAc (4 × 30 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (5% EtOAc/hexanes) furnished title compound **36** (3.70 g, 83% yield) as a yellowish oil.

IR (ATR) ν (cm^{-1}) 2929, 2856, 2228, 1668, 1608, 1504, 1471, 1462, 1413, 1386, 1360, 1254, 1176, 1096, 1020, 1006, 938, 917, 829, 774, 710, 661. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.8 Hz, Ar**H**, 2H), 7.28 (d, *J* = 8.0 Hz, Ar**H**, 2H), 5.11 (t, *J* = 6.7 Hz, $\mathbf{CH_{vin}}$, 1H), 3.59 (t, *J* = 6.5 Hz, $\mathbf{CH_2}$OSi, 2H), 2.69 (t, *J* = 7.5 Hz, Ar$\mathbf{CH_2}$, 2H), 2.31 (dt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 1.95 (t, *J* = 7.4 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.51 (tt, *J* = 2 × 6.8 Hz, $\mathbf{CH_2}CH_2OSi$, 2H), 1.49 (s, $\mathbf{CH_3}$, 3H), 1.36 (tt, *J* = 2 × 7.6 Hz, $\mathbf{CH_2}(CH_2)_3OSi$, 2H), 1.27 (tt, *J* = 2 × 7.6 Hz, $\mathbf{CH_2}(CH_2)_2OSi$, 2H), 0.89 (s, $SiC(\mathbf{CH_3})_3$, 9H), 0.05 (s, $Si(\mathbf{CH_3})_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 137.0, 132.1, 129.4, 122.5, 119.3, 109.6, 63.3, 39.7, 36.3, 32.8, 29.4, 27.8, 26.1, 25.5, 18.5, 15.9, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{23}H_{38}NOSi$ $[M+H]^+$ requires *m/z* 372.2717, found *m/z* 372.2720.

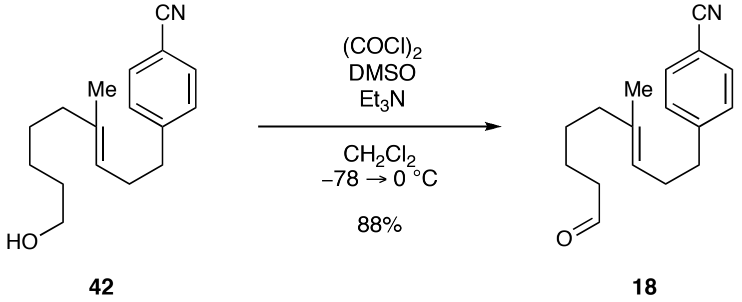
4.3.3 (*E*)-4-(9-Hydroxy-4-methylnon-3-enyl)benzonitrile (**42**)



TBAF (12.0 mL of a 1.0M solution in THF, 12.0 mmol, 1.20 equiv) was added slowly to a solution of silyl ether **36** (3.70 g, 10.0 mmol, 1.00 equiv) in THF (60 mL) at room temperature. After stirring had been continued for 6 h, water (60 mL) and sat. NH_4Cl (40 mL) were added and the aqueous layer was extracted with EtOAc (3 × 60 mL). The combined organic layers were washed with brine (40 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **42** (2.58 g, 99% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3381, 2930, 2857, 2227, 1665, 1607, 1504, 1451, 1413, 1383, 1176, 1149, 1107, 1050, 1020, 954, 822, 753, 666. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.2 Hz, Ar**H**, 2H), 7.27 (d, *J* = 9.3 Hz, Ar**H**, 2H), 5.10 (t, *J* = 7.1 Hz, $\mathbf{CH_{vin}}$, 1H), 3.63 (t, *J* = 6.7 Hz, $\mathbf{CH_2}$OH, 2H), 2.69 (t, *J* = 7.5 Hz, Ar**CH$_2$**, 2H), 2.30 (dt, *J* = 2 × 7.5 Hz, **CH$_2$**CH$_{vin}$, 2H), 1.96 (t, *J* = 7.3 Hz, **CH$_2$**(CH$_3$)C=C, 2H), 1.56 (tt, *J* = 2 × 7.0 Hz, **CH$_2$**CH$_2$OH, 2H), 1.49 (s, **CH$_3$**, 3H), 1.38 (tt, *J* = 2 × 7.8 Hz, **CH$_2$**(CH$_2$)$_3$OH, 2H), 1.33-1.26 (m, **CH$_2$**(CH$_2$)$_2$OH, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 148.1, 136.8, 132.1, 129.4, 122.6, 119.3, 109.5, 63.1, 39.6, 36.3, 32.7, 29.3, 27.7, 25.4, 15.9. HRMS (ESI$^+$) exact mass calcd for $C_{17}H_{24}NO$ [M+H]$^+$ requires *m/z* 258.1852, found *m/z* 258.1855.

4.3.4 (*E*)-4-(4-Methyl-9-oxonon-3-enyl)benzonitrile (**18**)

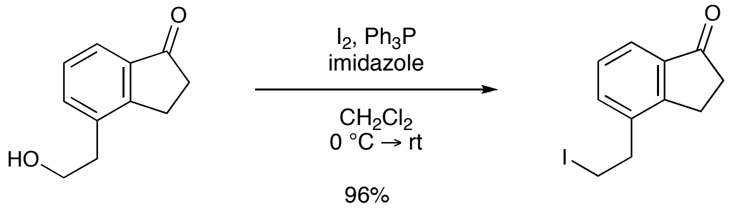


Oxalyl chloride (0.97 mL, 1.40 g, 11.0 mmol, 1.10 equiv) was dissolved in CH$_2$Cl$_2$ (80 mL) and cooled to –78 °C. DMSO (1.70 mL, 1.88 g, 24.0 mmol, 2.40 equiv) was added dropwise and the resultant solution stirred for 10 min. Subsequently, a solution of alcohol **42** (2.58 g, 10.0 mmol, 1.00 equiv) in CH$_2$Cl$_2$ (10 mL) was added slowly and stirring was continued for 10 min at –78 °C. Upon addition of Et$_3$N (6.70 mL, 4.86 g, 48.0 mmol, 4.80 equiv), the reaction mixture was allowed to warm to 0 °C within 1 h. After addition of water (100 mL) and aqueous 2M HCl (40 mL), the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine (50 mL), dried (MgSO$_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **18** (2.25 g, 88% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2931, 2859, 2718, 2226, 1721, 1607, 1504, 1448, 1412, 1387, 1291, 1176, 1108, 1020, 823, 744, 693. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.76 (t, *J* = 1.6 Hz, C**HO**, 1H), 7.56 (d, *J* = 8.3 Hz, Ar**H**, 2H), 7.27 (d, *J* = 8.3 Hz, Ar**H**, 2H), 5.11 (t, *J* = 6.6 Hz, **CH$_{vin}$**, 1H), 2.69 (t, *J* = 7.5 Hz, Ar**CH$_2$**, 2H), 2.42 (td, *J* = 7.3, 1.6 Hz, **CH$_2$**CHO, 2H), 2.30 (dt, *J* = 2 × 7.4 Hz, **CH$_2$**CH$_{vin}$, 2H), 1.97 (t, *J* = 7.5 Hz, C**H**$_2$(CH$_3$)C=C, 2H), 1.55 (tt, *J* = 2 × 7.8 Hz, C**H**$_2$CH$_2$CHO, 2H), 1.49 (s, C**H**$_3$, 3H), 1.38 (tt, *J* = 2 × 7.2 Hz, C**H**$_2$(CH$_2$)$_2$CHO, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 202.9, 148.0, 136.2, 132.1, 129.4, 123.0, 119.3, 109.6, 43.8, 39.3, 36.2, 29.3, 27.2, 21.6, 15.8. HRMS (ESI$^+$) exact mass calcd for $C_{17}H_{22}NO$ [M+H]$^+$ requires *m*/*z* 256.1696, found *m*/*z* 256.1696.

4.4 Preparation of Aldehyde 19

4.4.1 4-(2-Iodoethyl)-2,3-dihydro-1*H*-inden-1-one (**31**)



31

Iodine (2.82 g, 11.1 mmol, 1.50 equiv) was added to a solution of Ph$_3$P (2.91 g, 11.1 mmol, 1.50 equiv) in CH$_2$Cl$_2$ (40 mL) at 0 °C and stirred for 10 min. Upon addition of imidazole (1.26 g, 18.5 mmol, 2.50 equiv) and further 10 min of stirring, a solution of 4-(2-hydroxyethyl)-2,3-dihydro-1*H*-inden-1-one[11] (1.30 g, 7.40 mmol, 1.00 equiv) in CH$_2$Cl$_2$ (5.0 mL) was added via syringe followed by stirring for 1 h at room temperature. The reaction mixture was washed with aqueous Na$_2$SO$_3$ (2 × 20 mL) and the aqueous layer extracted with CH$_2$Cl$_2$ (2 × 20 mL). The combined organic layers were dried (MgSO$_4$) and concentrated *in vacuo*. Purification by flash chromatography (10% EtOAc/hexanes) furnished iodide **31** (2.03 g, 96% yield) as a yellowish solid.

IR (ATR) ν (cm^{-1}) 3028, 2956, 2917, 2850, 2780, 1696, 1598, 1585, 1473, 1448, 1433, 1397, 1332, 1275, 1257, 1230, 1180, 1168, 1154, 1115, 1048, 990, 976, 933, 841, 818, 783, 741, 715, 650, 613. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.70 (d, *J* = 7.5 Hz, Ar**H**, 1H), 7.45 (d, *J* = 7.1 Hz, Ar**H**, 1H), 7.38 (dd, *J* = 2 × 7.5 Hz, Ar**H**, 1H), 3.39 (t, *J* = 7.4 Hz, C**H**$_2$, 2H), 3.28 (t, *J* = 7.4 Hz, C**H**$_2$,

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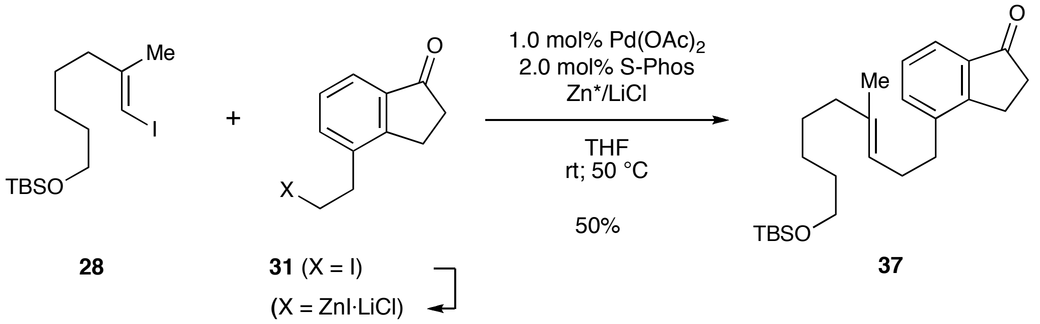
[11] Nakada, Y.; Ohno, S.; Yoshimoto, M.; Yura, Y. *Agric. Biol. Chem.* **1978**, *42*, 1365.

2H), 3.13-3.08 (m, C**H**$_2$, 2H), 2.76-2.71 (m, C**H**$_2$, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 207.0, 153.4, 138.4, 137.5, 134.3, 128.0, 122.6, 36.14, 36.10, 24.4, 3.4. HRMS (ESI$^+$) exact mass calcd for $C_{11}H_{12}IO$ [M+H]$^+$ requires *m/z* 286.9927, found *m/z* 286.9926.

4.4.2 (*E*)-4-(9-(*tert*-Butyldimethylsilyloxy)-4-methylnon-3-enyl)-2,3-dihydro-1*H*-inden-1-one (**37**)

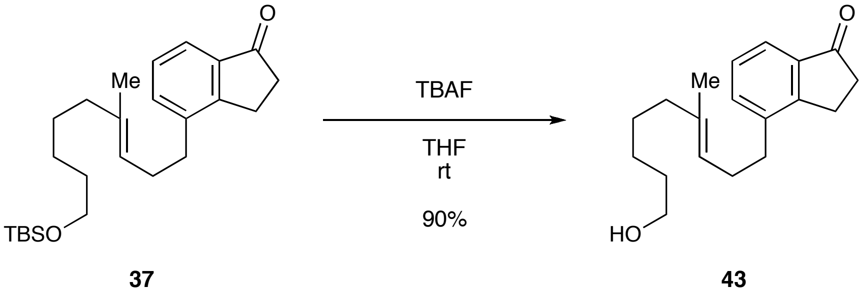


Anhydrous LiCl (297 mg, 7.00 mmol, 1.25 equiv) was placed in an argon-flushed 25-mL Schlenk flask and dried for 30 min at 150-180 °C under high vacuum (<1 torr) with slow stirring. Upon addition of zinc powder (325 mesh, 686 mg, 10.5 mmol, 1.88 equiv) heating under high vacuum was continued for 30 min. After cooling to room temperature and backfilling with argon, the mixture was suspended with THF (5.0 mL). Subsequently, the zinc powder was activated by sequential addition of 1,2-dibromoethane (30 μL, 66 mg, 0.35 mmol, 0.060 equiv), TMSCl (2 drops), and iodine (7 drops of a 1M solution in THF); each addition followed by gentle heating to reflux with a heat gun. A solution of iodide **31** (2.03 g, 7.00 mmol, 1.25 equiv) in THF (5.0 mL) was added portionwise at room temperature and stirring continued for 3.5 h. The thus generated solution of homobenzylic iodide was separated via syringe from remaining zinc powder.

In a separate 25-mL Schlenk flask, Pd(OAc)$_2$ (15.7 mg, 0.0700 mmol, 0.0100 equiv) and S-Phos (57.4 mg, 0.140 mmol, 0.0200 equiv) was dissolved in THF (5.0 mL) and a solution of vinyl iodide **28** (2.06 g g, 5.60 mmol, 1.00 equiv) in THF (3.0 mL) was added. The previously prepared solution of homobenzylic zinc reagent was quickly added via syringe leading to an exothermic reaction. Further stirring at 50 °C for 3 h was followed by aqueous work-up with sat. NH$_4$Cl (30 mL) and extraction with EtOAc (4 x 20 mL). The combined organic layers were washed with brine (20 mL), dried (MgSO$_4$), and concentrated *in vacuo*. Purification by flash chromatography (3%→10% EtOAc/hexanes) furnished title compound **37** (1.12 g, 50% yield) as a yellowish oil.

IR (ATR) ν (cm^{-1}) 2927, 2855, 1713, 1604, 1588, 1471, 1462, 1435, 1405, 1386, 1360, 1332, 1270, 1250, 1153, 1096, 1046, 1005, 982, 938, 911, 833, 773, 708, 679, 660. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.5 Hz, Ar**H**, 1H), 7.42 (d, *J* = 7.9 Hz, Ar**H**, 1H), 7.33 (dd, *J* = 2 × 7.5 Hz, Ar**H**, 1H), 5.18 (t, *J* = 7.1 Hz, $C\mathbf{H}_{\mathbf{vin}}$, 1H), 3.60 (t, *J* = 6.6 Hz, $C\mathbf{H_2}OSi$, 2H), 3.13-3.04 (m, $C\mathbf{H_2}$, 2H), 2.74-2.65 (m, $C\mathbf{H_2}$, $ArC\mathbf{H_2}CH_2CH_{vin}$, 4H), 2.32 (dt, *J* = 2 × 7.4 Hz, $C\mathbf{H_2}CH_{vin}$, 2H), 1.96 (t, *J* = 7.4 Hz, $C\mathbf{H_2}(CH_3)C{=}C$, 2H), 1.55-1.46 (m, $C\mathbf{H_2}CH_2OSi$, 2H), 1.51 (s, $C\mathbf{H_3}$, 3H), 1.37 (tt, *J* = 2 × 7.6 Hz, $C\mathbf{H_2}(CH_2)_3OSi$, 2H), 1.27 (tt, *J* = 2 × 7.4 Hz, $C\mathbf{H_2}(CH_2)_2OSi$, 2H), 0.89 (s, $SiC(C\mathbf{H_3})_3$, 9H), 0.04 (s, $Si(C\mathbf{H_3})_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 153.8, 140.2, 137.0. 136.8, 134.4, 127.6, 122.9, 121.4, 63.3, 39.7, 36.3, 32.8, 32.1, 28.3, 27.8, 26.1, 25.6, 24.5, 18.5, 15.9, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{25}H_{41}O_2Si$ [M+H]$^+$ requires *m/z* 401.2870, found *m/z* 401.2868.

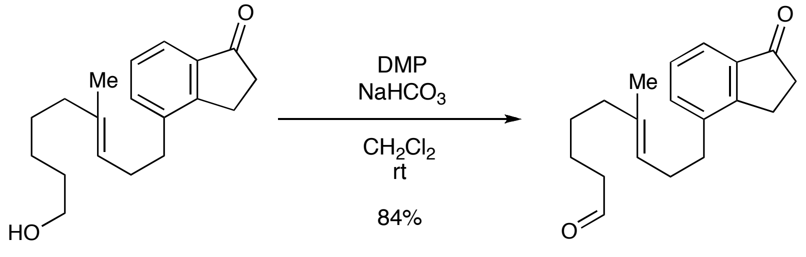
4.4.3 (*E*)-4-(9-Hydroxy-4-methylnon-3-enyl)-2,3-dihydro-1*H*-inden-1-one (**43**)



TBAF (3.4 mL of a 1.0M solution in THF, 3.4 mmol, 1.2 equiv) was added slowly to a solution of silyl ether **37** (1.12 g, 2.80 mmol, 1.00 equiv) in THF (30 mL) at room temperature. After stirring had been continued for 1.5 h, water (20 mL) and sat. NH_4Cl (10 mL) were added and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (35% EtOAc/hexanes) furnished the title compound **43** (725 mg, 90% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3410, 2927, 2856, 1706, 1602, 1588, 1480, 1434, 1403, 1382, 1333, 1271, 1252, 1154, 1048, 819, 781, 729, 707, 638, 610. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.63 (d, *J* = 7.6 Hz, Ar**H**, 1H), 7.43 (d, *J* = 7.3 Hz, Ar**H**, 1H), 7.31 (dd, *J* = 2 × 7.5 Hz, Ar**H**, 1H), 5.18 (t, *J* = 7.1 Hz, $\mathbf{CH_{vin}}$, 1H), 3.63 (td, *J* = 6.5, 4.9 Hz, $\mathbf{CH_2}$OH, 2H), 3.12-3.04 (m, $\mathbf{CH_2}$, 2H), 2.75-2.66 (m, $\mathbf{CH_2}$, Ar$\mathbf{CH_2}$CH$_2$CH$_{vin}$, 4H), 2.33 (dt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}$CH$_{vin}$, 2H), 1.97 (t, *J* = 7.3 Hz, $\mathbf{CH_2}$(CH$_3$)C=C, 2H), 1.56 (tt, *J* = 2 × 6.9 Hz, $\mathbf{CH_2}$CH$_2$OH, 2H), 1.51 (s, $\mathbf{CH_3}$, 3H), 1.39 (tt, *J* = 2 × 7.1 Hz, $\mathbf{CH_2}$(CH$_2$)$_3$OH, 2H), 1.29 (tt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}$(CH$_2$)$_2$OH, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 207.7, 153.8, 140.1, 137.0. 136.6, 134.4, 127.6, 122.9, 121.3, 63.0, 39.6, 36.2, 32.7, 32.0, 28.3, 27.7, 25.4, 24.5, 15.9. HRMS (ESI$^+$) exact mass calcd for $C_{19}H_{27}O_2$ [M+H]$^+$ requires *m*/*z* 287.2006, found *m*/*z* 287.2005.

4.4.4 (*E*)-6-Methyl-9-(1-oxo-2,3-dihydro-1*H*-inden-4-yl)non-6-enal (**19**)



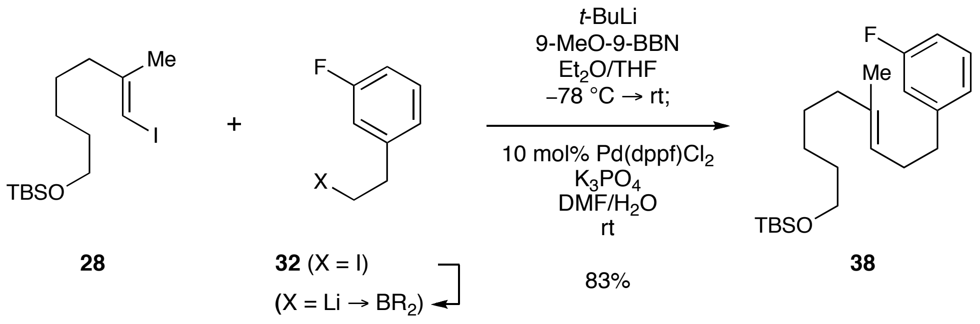
43 **19**

To a solution of alcohol **43** (710 mg, 2.48 mmol, 1.00 equiv) in CH$_2$Cl$_2$ (25 mL) and solid NaHCO$_3$ (1.04 g, 12.4 mmol, 5.00 equiv) was added Dess-Martin periodinane (1.58 g, 3.72 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na$_2$CO$_3$ (20 mL) and aqueous Na$_2$S$_2$O$_3$ (10 mL) was followed by extraction with CH$_2$Cl$_2$ (4 × 15 mL). The combined organic layers were washed with brine (15 mL), dried (MgSO$_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **19** (591 mg, 84% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2927, 2858, 2722, 1706, 1602, 1588, 1480, 1434, 1405, 1386, 1333, 1270, 1156, 1107, 1047, 984, 819, 782, 755, 707, 639, 608. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.77 (br s, C**H**O, 1H), 7.62 (d, *J* = 7.5 Hz, Ar**H**, 1H), 7.42 (d, *J* = 7.4 Hz, Ar**H**, 1H), 7.32 (dd, *J* = 2 × 7.5 Hz, Ar**H**, 1H), 5.19 (t, *J* = 7.1 Hz, $\mathbf{CH_{vin}}$, 1H), 3.12-3.03 (m, $\mathbf{CH_2}$, 2H), 2.74-2.65 (m, $\mathbf{CH_2}$, Ar$\mathbf{CH_2}$CH$_2$CH$_{vin}$, 4H), 2.43 (t, *J* = 7.3 Hz, $\mathbf{CH_2}$CHO, 2H), 2.33 (dt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}$CH$_{vin}$, 2H), 1.99 (t, *J* = 7.5 Hz, $\mathbf{CH_2}$(CH$_3$)C=C, 2H), 1.57 (tt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}$CH$_2$CHO, 2H), 1.51 (s, $\mathbf{CH_3}$, 3H), 1.40 (tt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}$(CH$_2$)$_2$CHO, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 207.6, 202.9, 153.8, 140.1, 137.0. 136.0, 134.4, 127.6, 123.4, 121.4, 43.8, 39.3, 36.2, 32.0, 28.3, 27.3, 24.5, 21.6, 15.8. HRMS (ESI$^+$) exact mass calcd for $C_{19}H_{24}O_2Na$ [M+Na]$^+$ requires *m/z* 307.1669, found *m/z* 307. 1672.

4.5 Preparation of Aldehyde 20

4.5.1 (*E*)-*tert*-Butyl(9-(3-fluorophenyl)-6-methylnon-6-enyloxy)dimethylsilane (**38**)



t-BuLi (12.9 mL of a 1.7M solution in pentane, 22.0 mmol, 3.30 equiv) was rapidly added to a solution of alkyl iodide **32**[12] (2.50 g, 10.0 mmol, 1.50 equiv) in Et$_2$O (40 mL) at –78 °C. After strirring for 3 min, 9-methoxy-9-borabicyclononane (23.0 mL of a 1.0M solution in hexanes, 23.0 mmol, 3.45 equiv) was added in one portion followed by THF (40 mL). The solution was stirred for 10 min at –78 °C and then allowed to warm to room temperature for 1.5 h. To this mixture, aqueous 3M K$_3$PO$_4$ (11.0 mL, 33.4 mmol, 5.0 equiv), vinyl iodide **28** (2.50 g, 6.67 mmol, 1.00 equiv) in DMF (40 mL), and Pd(dppf)Cl$_2$·CH$_2$Cl$_2$ (545 mg, 0.670 mmol, 0.100 equiv) were added sequentially, and the resultant dark solution was stirred for 5 h. Upon addition of water (100 mL), the reaction mixture was extracted with Et$_2$O (3 × 75 mL). The combined organic

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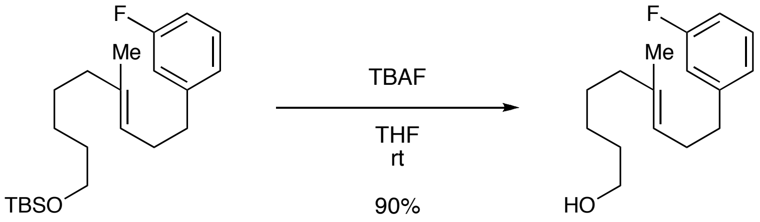
(12) Avery, M. A.; Alvim-Gaston, M.; Vroman, J. A.; Wu, B.; Ager, A.; Peters, W.; Robinson, B. L.; Charman, W. *J. Med. Chem.* **2002**, *45*, 4321.

layers were washed with water (2 × 30 mL) and brine (30 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude mixture by flash chromatography (2% EtOAc/hexanes) furnished title compound **38** (2.02 g, 83% yield, approx. 90% purity). The obtained silyl ether was directly subjected to the following deprotection step.

4.5.2 (*E*)-9-(3-Fluorophenyl)-6-methylnon-6-en-1-ol (**44**)

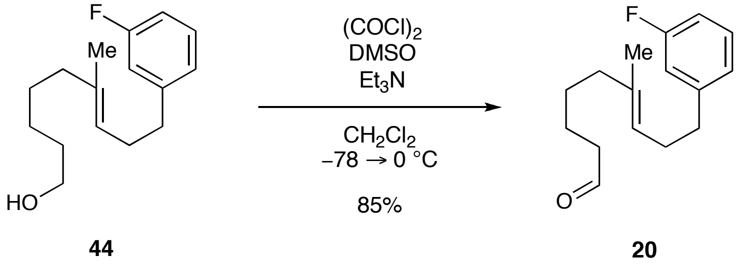


38 **44**

TBAF (6.6 mL of a 1.0M solution in THF, 6.6 mmol, 1.2 equiv) was added slowly to a solution of silyl ether **38** (2.02 g, 5.54 mmol, 1.00 equiv) in THF (50 mL) at room temperature. After stirring had been continued for 1.5 h, water (40 mL) and sat. NH_4Cl (20 mL) were added and the aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with brine (40 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **44** (1.15 g, 90% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3334, 2930, 2857, 1615, 1588, 1487, 1448, 1382, 1254, 1138, 1072, 1051, 1012, 962, 938, 886, 863, 780, 742, 690. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (ddd, *J* = 2 × 7.4 Hz, $J_{H,F}$ = 7.4 Hz, Ar**H**, 1H), 6.96 (d, *J* = 7.5 Hz, Ar**H**, 1H), 6.92-6.83 (m, Ar**H**, 2H), 5.14 (t, *J* = 7.0 Hz, $\mathbf{CH_{vin}}$, 1H), 3.64 (t, *J* = 6.7 Hz, $\mathbf{CH_2}$OH, 2H), 2.63 (t, *J* = 7.5 Hz, Ar$\mathbf{CH_2}$, 2H), 2.29 (dt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 1.97 (t, *J* = 7.4 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.56 (tt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}CH_2OH$, 2H), 1.52 (s, $\mathbf{CH_3}$, 3H), 1.39 (tt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}(CH_2)_3OH$, 2H), 1.34-1.24 (m, $\mathbf{CH_2}(CH_2)_2OH$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9 ($J_{C,F}$ = 245 Hz), 145.0 ($J_{C,F}$ = 7.1 Hz), 136.3, 129. 6 ($J_{C,F}$ = 8.3 Hz), 124.2 ($J_{C,F}$ = 2.6 Hz), 123.2, 115.4 ($J_{C,F}$ = 21 Hz), 112.6 ($J_{C,F}$ = 21 Hz), 63.4, 39.6, 35.9, 32.7, 29.6, 27.7, 25.3, 15.9. HRMS (ESI$^+$) exact mass calcd for $C_{16}H_{24}OF$ $[M+H]^+$ requires *m/z* 251.1806, found *m/z* 251.1806.

4.5.3 (*E*)-9-(3-Fluorophenyl)-6-methylnon-6-en-1-al (**20**)

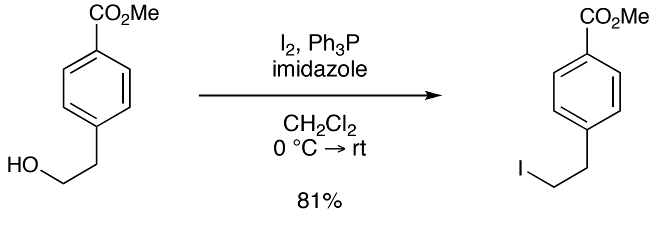


Oxalyl chloride (0.48 mL, 685 mg, 5.40 mmol, 1.10 equiv) was dissolved in CH_2Cl_2 (50 mL) and cooled to −78 °C. DMSO (0.84 mL, 922 mg, 11.8 mmol, 2.40 equiv) was added dropwise and the resultant solution stirred for 10 min. Subsequently, a solution of alcohol **44** (2.58 g, 10.0 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) was added slowly and stirring was continued for 10 min at −78 °C. Upon addition of Et_3N (3.30 mL, 2.38 g, 23.6 mmol, 4.80 equiv), the reaction mixture was allowed to warm to 0 °C within 1 h. After addition of water (50 mL) and aqueous 2M HCl (20 mL), the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (5% EtOAc/hexanes) furnished title compound **20** (1.03 g, 85% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2931, 2858, 2718, 1721, 1615, 1588, 1487, 1448, 1410, 1386, 1253, 1138, 1106, 1078, 1005, 964, 937, 889, 864, 781, 742, 717, 690. ^1H NMR (500 MHz, $CDCl_3$) δ 9.76 (br s, C**H**O, 1H), 7.23 (ddd, *J* = 2 × 7.2 Hz, $J_{H,F}$ = 7.2 Hz, Ar**H**, 1H), 6.96 (d, *J* = 7.6 Hz, Ar**H**, 1H), 6.91-6.84 (m, Ar**H**, 2H), 5.15 (t, *J* = 6.9 Hz, C$\mathbf{H_{vin}}$, 1H), 2.64 (t, *J* = 7.5 Hz, C$\mathbf{H_2}$CHO, 2H), 2.41 (t, *J* = 7.3 Hz, ArC$\mathbf{H_2}$, 2H), 2.30 (dt, *J* = 2 × 7.4 Hz, C$\mathbf{H_2}$CH_{vin}, 2H), 1.99 (t, *J* = 7.4 Hz, C$\mathbf{H_2}$(CH_3)C=C, 2H), 1.57 (tt, *J* = 2 × 7.4 Hz, C$\mathbf{H_2}$CH_2CHO, 2H), 1.52 (s, C$\mathbf{H_3}$, 3H), 1.41 (tt, *J* = 2 × 7.2 Hz, C$\mathbf{H_2}$(CH_2)$_2$CHO, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.9, 162.9 ($J_{C,F}$ = 246 Hz), 145.0 ($J_{C,F}$ = 7.1 Hz), 135.7, 129.7 ($J_{C,F}$ = 8.4 Hz), 124.2 ($J_{C,F}$ = 2.6 Hz), 123.7, 115.3 ($J_{C,F}$ = 21 Hz), 112.6 ($J_{C,F}$ = 21 Hz), 43.8, 39.3, 35.8 ($J_{C,F}$ = 1.5 Hz), 29.6, 27.3, 21.6, 15.8. HRMS (ESI^+) exact mass calcd for $C_{16}H_{22}OF$ $[M+H]^+$ requires *m/z* 249.1649 found *m/z* 249.1646.

4.6 Preparation of Aldehyde 21

4.6.1 Methyl 4-(2-iodoethyl)benzoate (**33**)



33

Iodine (6.14 g, 24.2 mmol, 1.50 equiv) was added to a solution of Ph_3P (6.35 g, 24.2 mmol, 1.50 equiv) in CH_2Cl_2 (100 mL) at 0 °C and stirred for 10 min. Upon addition of imidazole (2.74 g, 40.3 mmol, 2.50 equiv) and further 10 min of stirring, a solution of methyl 4-(2-hydroxyethyl)benzoate[13] (2.90 g, 16.1 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) was added via syringe followed by stirring for 1 h at room temperature. The reaction mixture was washed with aqueous Na_2SO_3 (2 × 40 mL) and the aqueous layer extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residual was treated with PE/Et_2O (1:1, 300 mL) to precipitate Ph_3PO. Filtration, concentration *in vacuo*, and purification by flash chromatography (5% EtOAc/hexanes) furnished iodide **33** (3.79 g, 81% yield) as a yellowish solid.

IR (ATR) ν (cm^{-1}) 3067, 3032, 2956, 1718, 1677, 1606, 1572, 1505, 1445, 1431, 1411, 1365, 1304, 1273, 1188, 1174, 1162, 1107, 1013, 961, 861, 833, 812, 762, 733, 703, 647, 635. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 7.4 Hz, Ar**H**, 2H), 7.28 (d, J = 7.4 Hz, Ar**H**, 2H), 3.92 (s, $CO_2\mathbf{CH_3}$, 3H), 3.37 (t, J = 7.6 Hz, $\mathbf{CH_2}$, 2H), 3.24 (t, J = 7.6 Hz, $\mathbf{CH_2}$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 145.7, 130.1, 128.5, 128.1, 52.2, 40.1, 4.7. HRMS (ESI$^+$) exact mass calcd for $C_{10}H_{12}IO_2$ $[M+H]^+$ requires *m/z* 290.9877, found *m/z* 290.9874.

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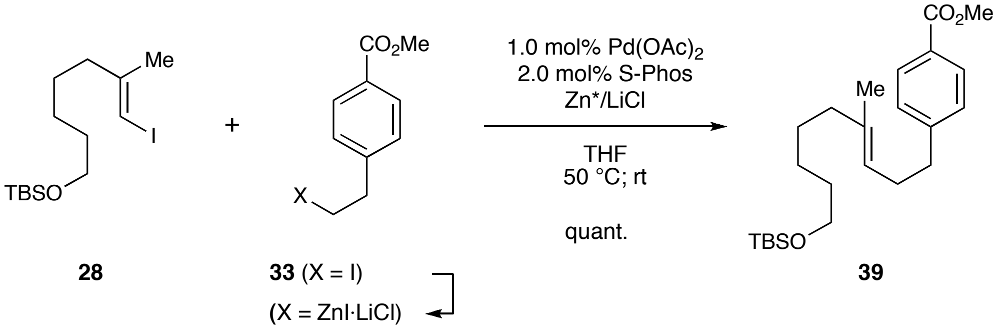
[13] Tietze, L. F.; Goerlach, A.; Beller, M. *Liebigs Ann. Chem.* **1988**, 559.

4.6.2 (*E*)-Methyl 4-(9-(*tert*-butyldimethylsilyloxy)-4-methylnon-3-enyl)benzoate (**39**)

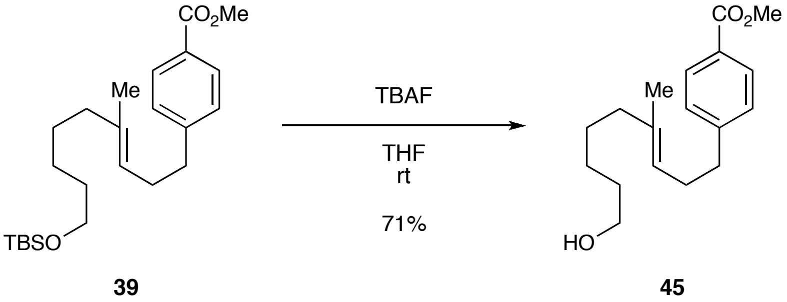


Anhydrous LiCl (530 mg, 12.5 mmol, 1.25 equiv) was placed in an argon-flushed 25-mL Schlenk flask and dried for 30 min at 150-180 °C under high vacuum (<1 torr) with slow stirring. Upon addition of zinc powder (325 mesh, 1.23 g, 18.8 mmol, 1.88 equiv) heating under high vacuum was continued for 30 min. After cooling to room temperature and backfilling with argon, the mixture was suspended with THF (10 mL). Subsequently, the zinc powder was activated by sequential addition of 1,2-dibromoethane (54 μL, 118 mg, 0.63 mmol, 0.063 equiv), TMSCl (3 drops), and iodine (12 drops of a 1M solution in THF); each addition followed by gentle heating to reflux with a heat gun. A solution of iodide **33** (3.63 g, 12.5 mmol, 1.25 equiv) in THF (5.0 mL) was added portionwise at room temperature and stirring was continued for 4 h at 50 °C. The solution of homobenzylic zinc iodide and was allowed to cool to room temperature and separated via syringe from remaining zinc powder.

In a separate 50-mL Schlenk flask $Pd(OAc)_2$ (22.5 mg, 0.100 mmol, 0.0100 equiv) and S-Phos (82.1 mg, 0.200 mmol, 0.0200 equiv) was dissolved in THF (5.0 mL) and a solution of vinyl iodide **28** (3.68 g g, 10.0 mmol, 1.00 equiv) in THF (3.0 mL) was added. The previously prepared solution of homobenzylic zinc reagent was quickly added via syringe leading to an exothermic reaction. Further stirring at room temperature for 3 h was followed by aqueous work-up with sat. NH_4Cl (50 mL) and extraction with EtOAc (4 × 30 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (5% EtOAc/hexanes) furnished title compound **39** (4.09 g, quant. yield, 90% purity) as a yellowish oil.

IR (ATR) ν (cm^{-1}) 2929, 2856, 1723, 1610, 1574, 1462, 1434, 1386, 1360, 1309, 1275, 1254, 1191, 1178, 1099, 1020, 1006, 971, 938, 912, 832, 813, 773, 703, 661. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.3 Hz, Ar**H**, 2H), 7.26 (d, *J* = 8.0 Hz, Ar**H**, 2H), 5.14 (t, *J* = 6.8 Hz, $\mathbf{CH_{vin}}$, 1H), 3.91 (s, $CO_2\mathbf{CH_3}$, 3H), 3.60 (t, *J* = 6.3 Hz, $\mathbf{CH_2}$OSi, 2H), 2.68 (t, *J* = 7.6 Hz, Ar$\mathbf{CH_2}$, 2H), 2.31 (dt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 1.95 (t, *J* = 7.4 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.55-1.46 (m, 2H, $\mathbf{CH_2}CH_2OSi$, 2H), 1.51 (s, $\mathbf{CH_3}$, 3H), 1.37 (tt, *J* = 2 × 7.2 Hz, $\mathbf{CH_2}(CH_2)_3OSi$, 2H), 1.30-1.22 (m, $\mathbf{CH_2}(CH_2)_2OSi$, 2H), 0.89 (s, $SiC(\mathbf{CH_3})_3$, 9H), 0.05 (s, $Si(\mathbf{CH_3})_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 148.0, 136.6, 129. 6, 128.6, 127.7, 122.9, 63.4, 52.1, 39.7, 36.2, 32.8, 29.6, 27.8, 26.1, 25.5, 18.5, 15.9, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{24}H_{41}O_3Si$ $[M+H]^+$ requires *m*/*z* 405.2820, found *m*/*z* 405.2819.

4.6.3 (*E*)-Methyl 4-(9-hydroxy-4-methylnon-3-enyl)benzoate (**45**)

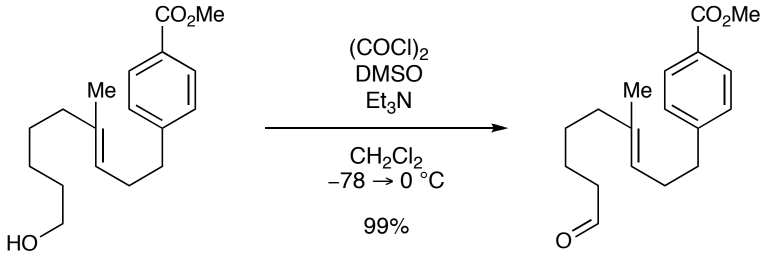


TBAF (11.0 mL of a 1.0M solution in THF, 11.0 mmol, 1.10 equiv) was added slowly to a solution of silyl ether **39** (4.09 g, 10.0 mmol, 1.00 equiv) in THF (90 mL) at room temperature. After stirring had been continued for 6 h, water (60 mL) and sat. NH_4Cl (40 mL) were added and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (40 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **45** (2.06 g, 71% yield over two steps) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3410, 2930, 2857, 1720, 1610, 1574, 1510, 1435, 1414, 1382, 1309, 1275, 1178, 1108, 1048, 1019, 966, 853, 832, 763, 704. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.3 Hz, Ar**H**, 2H), 7.23 (d, *J* = 8.3 Hz, Ar**H**, 2H), 5.12 (t, *J* = 7.1 Hz, $\mathbf{CH_{vin}}$, 1H), 3.89 (s, $CO_2\mathbf{CH_3}$, 3H), 3.61 (t, *J* = 6.7 Hz, $\mathbf{CH_2}$OH, 2H), 2.68 (t, *J* = 7.5 Hz, Ar$\mathbf{CH_2}$, 2H), 2.30 (dt, *J* = 2 × 7.4 Hz,

C$\mathbf{H_2}$CH_{vin}, 2H), 1.95 (t, *J* = 7.3 Hz, **C$\mathbf{H_2}$**(CH_3)C=C, 2H), 1.58-1.51 (m, 2H, **C$\mathbf{H_2}$**CH_2OH, 2H), 1.49 (s, **C$\mathbf{H_3}$**, 3H), 1.37 (tt, *J* = 2 × 7.2 Hz, **C$\mathbf{H_2}$**$(CH_2)_3OH$, 2H), 1.32-1.23 (m, **C$\mathbf{H_2}$**$(CH_2)_2OH$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 148.0, 136.6, 129. 6, 128.6, 127.6, 123.0, 63.0, 52.0, 39.6, 36.1, 32.7, 29.5, 27.7, 25.3, 15.9. HRMS (ESI$^+$) exact mass calcd for $C_{18}H_{26}O_3Na$ [M+Na]$^+$ requires *m/z* 313.1774, found *m/z* 313.1772.

4.6.4 (*E*)-Methyl 4-(4-methyl-9-oxonon-3-enyl)benzoate (**21**)



45 **21**

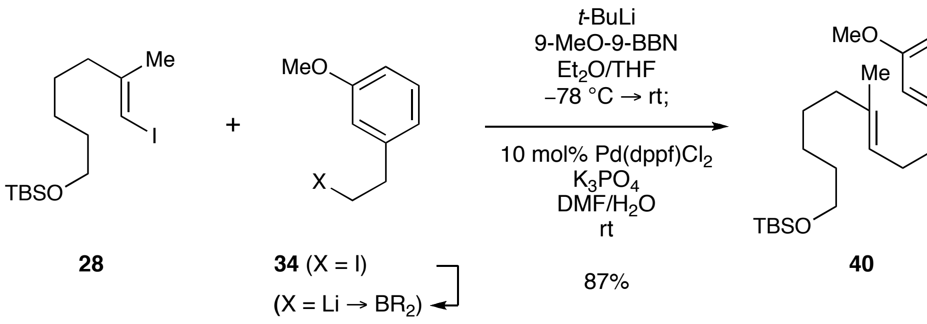
Oxalyl chloride (0.62 mL, 899 mg, 7.08 mmol, 1.10 equiv) was dissolved in CH_2Cl_2 (65 mL) and cooled to −78 °C. DMSO (1.10 mL, 1.21 g, 15.5 mmol, 2.40 equiv) was added dropwise and the resultant solution stirred for 10 min. Subsequently, a solution of alcohol **45** (1.87 g, 6.44 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) was added slowly and stirring was continued for 10 min at −78 °C. Upon addition of Et_3N (4.30 mL, 3.13 g, 30.9 mmol, 4.80 equiv), the reaction mixture was allowed to warm to 0 °C within 1 h. After addition of water (70 mL) and aqueous 2M HCl (30 mL), the aqueous layer was extracted with EtOAc (3 × 60 mL). The combined organic layers were washed with brine (40 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (5% EtOAc/hexanes) furnished the title compound **20** (1.47 g, 99% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2933, 2858, 2717, 1717, 1609, 1574, 1510, 1434, 1413, 1387, 1309, 1274, 1178, 1107, 1020, 966, 853, 831, 762, 704. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75, (br s, C**H**O), 7.94 (d, *J* = 7.5 Hz, Ar**H**, 2H), 7.25 (d, *J* = 7.6 Hz, Ar**H**, 2H), 5.14 (t, *J* = 7.0 Hz, **C$\mathbf{H_{vin}}$**, 1H), 3.90 (s, CO_2**C$\mathbf{H_3}$**, 3H), 2.69 (t, *J* = 7.5 Hz, ArC**$\mathbf{H_2}$**, 2H), 2.41 (t, *J* = 7.3 Hz, **C$\mathbf{H_2}$**CHO, 2H), 2.31 (dt, *J* = 2 × 7.4 Hz, **C$\mathbf{H_2}$**CH_{vin}, 2H), 1.97 (t, *J* = 7.4 Hz, **C$\mathbf{H_2}$**(CH_3)C=C, 2H), 1.55 (tt, *J* = 2 × 7.5

Hz, $\mathbf{CH_2}CH_2CHO$, 2H), 1.50 (s, $\mathbf{CH_3}$, 3H), 1.39 (tt, $J = 2 \times 7.6$ Hz, $\mathbf{CH_2}(CH_2)_2CHO$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.0, 167.3, 147.9, 135.8, 129.6, 128.6, 127.7, 123.5, 52.1, 43.8, 39.3, 36.1, 29.5, 27.3, 21.6, 15.8. HRMS (ESI^+) exact mass calcd for $C_{18}H_{24}O_3Na$ $[M+Na]^+$ requires *m/z* 311.1618, found *m/z* 311.1617.

4.7 Preparation of Aldehyde 22

4.7.1 (*E*)-*tert*-Butyl(9-(3-methoxyphenyl)-6-methylnon-6-enyloxy)dimethylsilane (**40**)



t-BuLi (41.2 mL of a 1.6M solution in pentane, 66.0 mmol, 4.40 equiv) was rapidly added to a solution of alkyl iodide **34**[14] (7.86 g, 30.0 mmol, 2.00 equiv) in Et_2O (115 mL) at –78 °C. After strirring for 3 min, 9-methoxy-9-borabicyclononane (69.0 mL of a 1.0M solution in hexanes, 69.0 mmol, 4.60 equiv) was added in one portion followed by THF (75 mL). The solution was stirred for 10 min at –78 °C and then allowed to warm to room temperature for 1.5 h. To this mixture, aqueous 3M K_3PO_4 (25.0 mL mL, 75.0 mmol, 5.0 equiv), vinyl iodide **28** (5.52 g, 15.0 mmol, 1.00 equiv) in DMF (100 mL), and $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ (1.22 g, 1.50 mmol, 0.100 equiv) were added sequentially, and the resultant dark solution was stirred for 5 h. Upon addition of water (200 mL), the reaction mixture was extracted with Et_2O (3 × 150 mL). The combined organic layers were washed with water (2 × 60 mL) and brine (60 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude mixture by flash chromatography (2% EtOAc/hexanes) furnished the title compound **40** (4.91 g, 87% yield, approx. 90% purity). Remaining impurities were separated after the following deprotection step.

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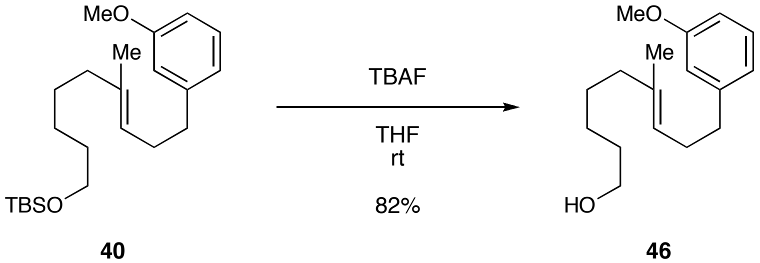
(14) Lanni, T. B., Jr; Greene, K. L.; Kolz, C. N.; Para, K. S.; Visnick, M.; Mobley, J. L.; Dudley, D. T.; Baginski, T. J.; Liimatta, M. B. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 756.

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.20 (dd, *J* = 2 × 7.0 Hz, Ar**H**, 1H), 6.80 (d, *J* = 7.2 Hz, Ar**H**, 1H), 6.77-6.69 (m, Ar**H**, 2H), 5.18 (t, *J* = 6.4 Hz, $\mathbf{CH_{vin}}$, 1H), 3.80 (s, $\mathrm{OC}\mathbf{H_3}$, 3H), 3.60 (t, *J* = 6.6 Hz, $\mathbf{CH_2}$OSi, 2H), 2.61 (t, *J* = 6.6 Hz, Ar$\mathbf{CH_2}$, 2H), 2.30 (dt, *J* = 2 × 7.3 Hz, $\mathbf{CH_2}\mathrm{CH_{vin}}$, 2H), 1.97 (t, *J* = 7.1 Hz, $\mathbf{CH_2}\mathrm{(CH_3)C{=}C}$, 2H), 1.55 (s, $\mathbf{CH_3}$, 3H), 1.55-1.48 (m, 2H, $\mathbf{CH_2}\mathrm{CH_2OSi}$, 2H), 1.42-1.34 (m, $\mathbf{CH_2}\mathrm{(CH_2)_3OSi}$, 2H), 1.31-1.22 (m, $\mathbf{CH_2}\mathrm{(CH_2)_2OSi}$, 2H), 0.90 (s, $\mathrm{SiC(C}\mathbf{H_3}\mathrm{)_3}$, 9H), 0.05 (s, $\mathrm{Si(CH_3)_2}$, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.6, 144.2, 136.1, 129.2, 123.5, 121.0, 114.3, 111.0, 63.4, 55.2, 39.7, 36.3, 32.9, 29.9, 27.8, 26.1, 25.5, 18.5, 16.0, –5.2.

4.7.2 (*E*)-9-(3-Methoxyphenyl)-6-methylnon-6-en-1-ol (**46**)

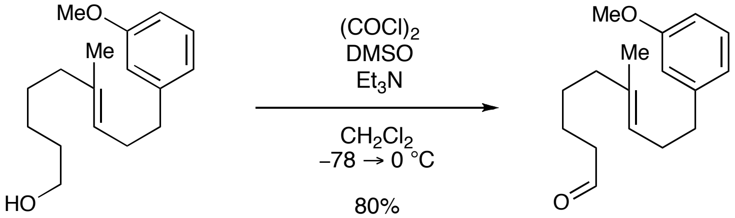


40 **46**

TBAF (15.7 mL of a 1.0M solution in THF, 15.7 mmol, 1.20 equiv) was added slowly to a solution of silyl ether **40** (4.91 g, 13.1 mmol, 1.00 equiv) in THF (120 mL) at room temperature. After stirring had been continued for 6 h, water (100 mL) and sat. NH$_4$Cl (60 mL) were added and the aqueous layer was extracted with EtOAc (3 × 80 mL). The combined organic layers were washed with brine (50 mL), dried (MgSO$_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **46** (2.82 g, 82% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3336, 2929, 2856, 1601, 1584, 1487, 1453, 1436, 1413, 1370, 1325, 1291, 1259, 1163, 1151, 1108, 1045, 872, 848, 775, 735, 676, 643. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.20 (dd, *J* = 2 × 7.7 Hz, Ar**H**, 1H), 6.80 (d, *J* = 7.8 Hz, Ar**H**, 1H), 6.77-6.70 (m, Ar**H**, 2H), 5.17 (t, *J* = 7.1 Hz, $\mathbf{CH_{vin}}$, 1H), 3.80 (s, $\mathrm{OC}\mathbf{H_3}$, 3H), 3.64 (t, *J* = 6.5 Hz, $\mathbf{CH_2}$OH, 2H), 2.62 (t, *J* = 7.4 Hz, Ar$\mathbf{CH_2}$, 2H), 2.30 (dt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}\mathrm{CH_{vin}}$, 2H), 1.98 (t, *J* = 7.4 Hz, $\mathbf{CH_2}\mathrm{(CH_3)C{=}C}$, 2H), 1.60-1.52 (m, 2H, $\mathbf{CH_2}\mathrm{CH_2OH}$, 2H), 1.55 (s, $\mathbf{CH_3}$, 3H), 1.40 (tt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}\mathrm{(CH_2)_3OH}$, 2H), 1.34-1.26 (m, $\mathbf{CH_2}\mathrm{(CH_2)_2OH}$, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.6, 144.1, 135.9, 129.2, 123.7, 121.0, 114.4, 110.9, 63.1, 55.2, 39.6, 36.2, 32.8, 29.8, 27.7, 25.4, 15.9. HRMS (ESI$^+$) exact mass calcd for $C_{17}H_{27}O_2$ [M+H]$^+$ requires *m/z* 263.2006, found *m/z* 263.2003.

4.7.3 (*E*)-9-(3-Methoxyphenyl)-6-methylnon-6-enal (**22**)



46 **22**

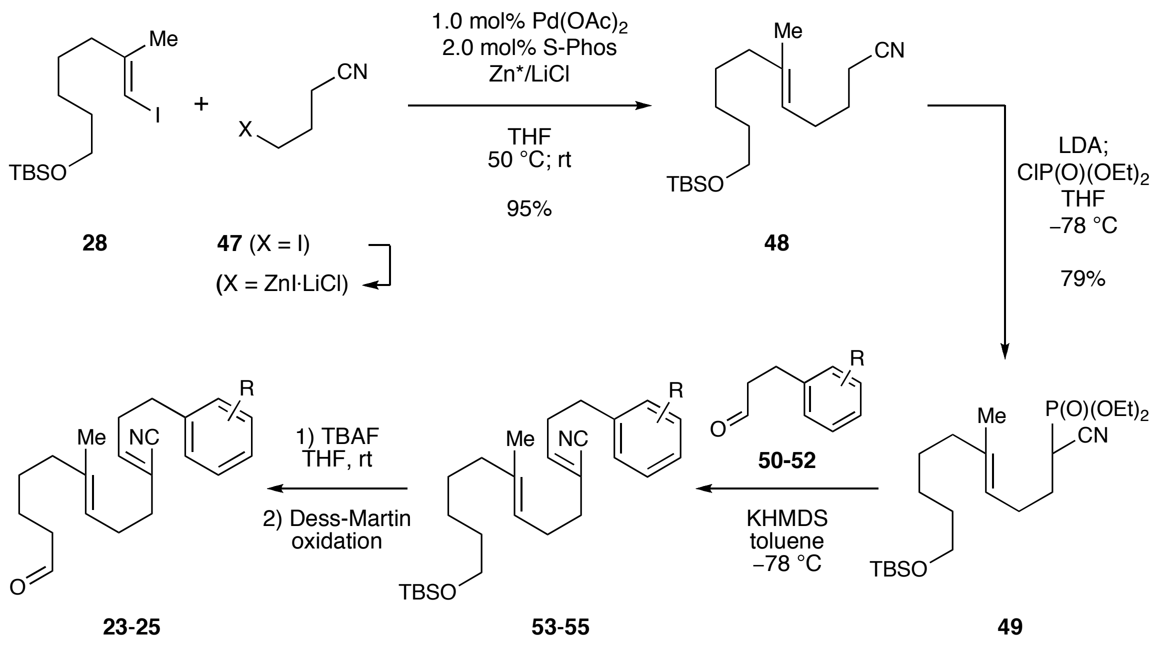
Oxalyl chloride (0.34 mL, 490 mg, 3.86 mmol, 1.10 equiv) was dissolved in CH_2Cl_2 (30 mL) and cooled to –78 °C. DMSO (0.60 mL, 658 g, 8.42 mmol, 2.40 equiv) was added dropwise and the resultant solution stirred for 10 min. Subsequently, a solution of alcohol **46** (920 g, 3.51 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) was added slowly and stirring was continued for 10 min at –78 °C. Upon addition of Et_3N (2.34 mL, 1.70 g, 16.8 mmol, 4.80 equiv) the reaction mixture was allowed to warm to 0 °C within 1 h. After addition of water (50 mL) and aqueous 2M HCl (20 mL), the aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (5% EtOAc/hexanes) furnished title compound **22** (731 mg, 80% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2933, 2857, 2835, 2718, 1722, 1601, 1583, 1487, 1453, 1437, 1386, 1313, 1259, 1164, 1151, 1106, 1082, 1043, 995, 960, 872, 850, 777, 736, 716, 644. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75, (br s, C**H**O, 1H), 7.20 (dd, *J* = 2 × 7.7 Hz, Ar**H**, 1H), 6.59 (d, *J* = 7.5 Hz, Ar**H**, 1H), 6.75 (s, Ar**H**, 1H), 6.74 (d, *J* = 7.8 Hz, Ar**H**, 1H), 5.18 (t, *J* = 6.7 Hz, C**H**$_{\text{vin}}$, 1H), 3.80 (s, OC**H$_3$**, 3H), 2.61 (t, *J* = 8.1 Hz, ArC**H$_2$**, 2H), 2.42 (t, *J* = 7.3 Hz, C**H$_2$**CHO, 2H), 2.30 (dt, *J* = 2 × 7.6 Hz, C**H$_2$**CH$_{\text{vin}}$, 2H), 1.99 (t, *J* = 7.4 Hz, C**H$_2$**(CH_3)C=C, 2H), 1.57 (tt, *J* = 2 × 7.4 Hz, C**H$_2$**CH_2CHO, 2H), 1.54 (s, C**H$_3$**, 3H), 1.41 (tt, *J* = 2 × 7.8 Hz, C**H$_2$**(CH_2)$_2$CHO, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 159.5, 144.0, 135.3, 129.2, 124.1, 121.0, 114.3, 110.9, 55.2, 43.8, 39.3, 36.2, 29.8, 27.3, 21.6, 15.8. HRMS (ESI$^+$) exact mass calcd for $C_{17}H_{25}O_2$ [M+H]$^+$ requires *m/z* 261.1849, found *m/z* 261.1847.

4.8 General Strategy toward Tricyclization Precursors

All tricyclization substrates were available following the synthetic sequence outlined in Scheme S2. The synthesis included sp^2-sp^3 cross-coupling[5] of vinyl iodide **28**[4] and the organozinc reagent derived from alkyl iodide **47** followed by phosphorylation of nitrile **48** to give cyanophosphonate **49**.[15] A Horner-Wadsworth-Emmons coupling[16] furnished intermediates **53**-**55** in good diastereoselectivities (typically 6:1 *Z*/*E*). Finally, deprotection and oxidation delivered the desired aldehydes **23**-**25**.

Scheme S2. Synthetic Access to Tricyclization Substrates.



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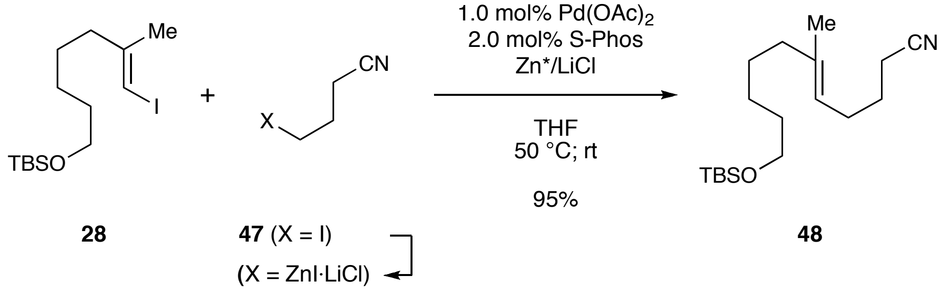
(15) Procedure adapted from: Iorga, B.; Ricard, L.; Savignac, P. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3311.

(16) Procedure adapted from: Zoretic, P. A.; Zhang, Y.; Fang, H.; Ribeiro, A. A.; Dubay, G. *J. Org. Chem.* **1998**, *63*, 1162.

4.9 Synthesis of Phosphonate 49

4.9.1 (*E*)-11-(*tert*-Butyldimethylsilyloxy)-6-methylundec-5-enenitrile (**48**)



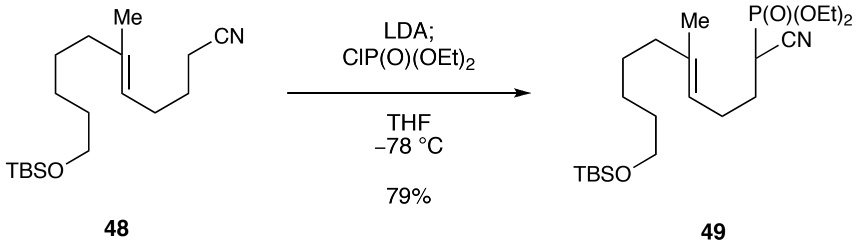
28 **47** (X = I) (X = ZnI·LiCl) **48**

Anhydrous LiCl (636 mg, 15.0 mmol, 1.25 equiv) was placed in an argon-flushed 25-mL Schlenk flask and dried for 30 min at 150-180 °C under high vacuum (<1 torr) with slow stirring. Upon addition of zinc powder (325 mesh, 1.47 g, 22.5 mmol, 1.88 equiv) heating under high vacuum was continued for another 30 min. After cooling to room temperature and backfilling with argon, the mixture was suspended with THF (10 mL). Subsequently, the zinc powder was activated by sequential addition of 1,2-dibromoethane (64 μL, 141 mg, 0.75 mmol, 0.05 equiv), TMSCl (3 drops), and iodine (15 drops of a 1M solution in THF); each addition followed by gentle heating to reflux with a heat gun. Portionwise addition of alkyl iodide **47** (3.86 g, 15.0 mmol, 1.25 equiv) at room temperature and subsequent stirring at for 4 h at 50 °C furnished a solution of alkyl zinc iodide that was allowed to cool to room temperature and separated via syringe from remaining zinc powder.

In a separate 50-mL Schlenk flask Pd(OAc)$_2$ (26.9 mg, 0.120 mmol, 0.0100 equiv) and S-Phos (98.5 mg, 0.240 mmol, 0.0200 equiv) was dissolved in THF (10 mL) and a solution of vinyl iodide **28** (4.42 g, 12.0 mmol, 1.00 equiv) in THF (4.0 mL) was added. The previously prepared solution of alkyl zinc reagent was quickly added via syringe leading to an exothermic reaction. Further stirring at room temperature for 3 h was followed by aqueous work-up with sat. NH$_4$Cl (50 mL) and extraction with EtOAc (4 × 30 mL). The combined organic layers were washed with brine (30 mL), dried (MgSO$_4$), and concentrated under reduced pressure. Purification by flash chromatography (3% EtOAc/hexanes) furnished title compound **48** (3.53 g, 95% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2929, 2856, 2248, 1668, 1471, 1462, 1386, 1360, 1253, 1097, 1006, 978, 938, 911, 829, 813, 773, 712, 679, 661. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.05 (t, *J* = 7.0 Hz, $\mathbf{CH}_{\mathbf{vin}}$, 1H), 3.60 (t, *J* = 6.6 Hz, $\mathbf{CH_2}OSi$, 2H), 2.31 (t, *J* = 7.2 Hz, $\mathbf{CH_2}CN$, 2H), 2.15 (dt, *J* = 2 × 7.2 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 1.98 (t, *J* = 7.4 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.70 (tt, *J* = 2 × 7.2 Hz, $\mathbf{CH_2}CH_2CN$, 2H), 1.61 (s, $\mathbf{CH_3}$, 3H), 1.52 (tt, *J* = 7.5 Hz, $\mathbf{CH_2}CH_2OSi$, 2H), 1.40 (tt, *J* = 7.5 Hz, $\mathbf{CH_2}(CH_2)_3OSi$, 2H), 1.28 (tt, *J* = 7.5 Hz, $\mathbf{CH_2}(CH_2)_2OSi$, 2H), 0.89 (s, $SiC(\mathbf{CH}_3)_3$, 9H), 0.04 (s, $Si(\mathbf{CH}_3)_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 121.6, 120.0, 63.3, 39.8, 32.8, 27.8, 26.7, 26.1, 25.62, 25.56, 18.5, 16.5, 16.1, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{18}H_{36}NOSi$ $[M+H]^+$ requires *m*/*z* 310.2561, found *m*/*z* 310.2562.

4.9.2 (*E*)-Diethyl 10-(*tert*-butyldimethylsilyloxy)-1-cyano-5-methyldec-4-enylphosphonate (**49**)



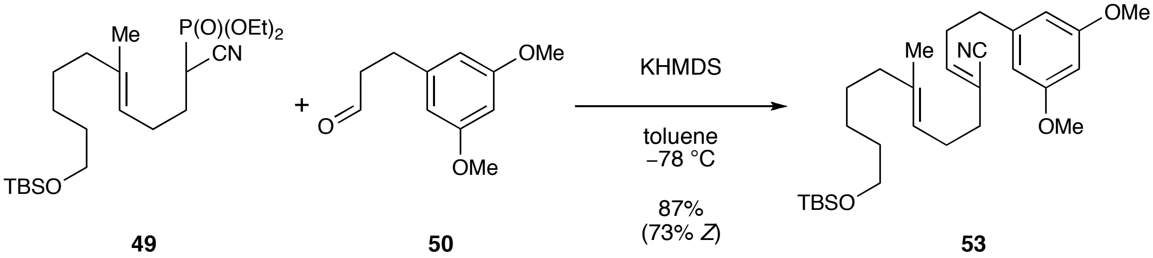
48 **49**

To a solution of *i*-Pr_2NH (2.82 mL, 2.13 g, 21.0 mmol, 2.15 equiv) in THF (32 mL) was added *n*-BuLi (8.6 mL of a 2.4M solution in hexanes, 20.6 mmol, 2.10 equiv) at –78 °C. After stirring at 0 °C for 30 min, the reaction mixture was cooled again to –78 °C and a solution of nitrile **48** (3.03 g, 9.79 mmol, 1.00 equiv) in THF (8 mL) was added and stirred for further 30 min at this temperature. Subsequently, diethyl chlorophosphate (1.48 mL, 1.77 g, 10.3 mmol, 1.05 equiv) was added dropwise to give a bright yellow solution. After 2 h stirring at –78 °C the reaction mixture was poured onto sat. NH_4Cl (40 mL) and water (40 mL) and the aqeous layer was extracted with EtOAc (4 × 30 mL). Washing of the combined organic phases with brine (50 mL), drying over $MgSO_4$ and evaporation under reduced pressure furnished the crude phosphonate that was purified by flash chromatography (30% EtOAc/hexanes) to give the title compound **49** (3.45 g, 79% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2930, 2857, 2242, 1472, 1462, 1444, 1389, 1369, 1361, 1255, 1163, 1097, 1048, 1016, 971, 903, 833, 813, 774, 754, 712, 680, 663. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.04 (t, J = 6.9 Hz, **C**$\mathbf{H}_{\mathbf{vin}}$, 1H), 4.29-4.17 (m, P(OC**H**$_2$CH$_3$)$_2$, 4H), 3.59 (t, J = 6.6 Hz, C**H**$_2$OSi, 2H), 2.92 (ddd, $J_{C,P}$ = 23.2 Hz, J = 8.8, 6.5 Hz, PC**H**CN, 1H), 2.27 (m, C**H**$_2$CH$_{vin}$, 2H), 1.98 (t, J = 7.4 Hz, C**H**$_2$(CH$_3$)C=C, 2H), 1.92 (tt, J = 2 × 7.6 Hz, C**H**$_2$CHCN, 2H), 1.63 (s, C**H**$_3$, 3H), 1.51 (tt, J = 6.8 Hz, C**H**$_2$CH$_2$OSi, 2H), 1.43-1.33 (m, P(OCH$_2$C**H**$_3$)$_2$, C**H**$_2$(CH$_2$)$_3$OSi, 8H), 1.32-1.23 (m, C**H**$_2$(CH$_2$)$_2$OSi, 2H), 0.89 (s, SiC(C**H**$_3$)$_3$, 9H), 0.04 (s, Si(C**H**$_3$)$_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 120.8, 116.5 (d, $J_{C,P}$ = 9.3 Hz), 64.1 (d, $J_{C,P}$ = 7.0 Hz), 63.8 (d, $J_{C,P}$ = 6.8 Hz), 63.3, 39.8, 32.8, 29.3 (d, $J_{C,P}$ = 144 Hz), 27.8, 27.1 (d, $J_{C,P}$ = 4.0 Hz), 26.0, 25.9 (d, $J_{C,P}$ = 13 Hz), 25.6, 18.5, 16.5 (d, $J_{C,P}$ = 3.8 Hz), 16.4 (d, $J_{C,P}$ = 3.8 Hz), 16.2, –5.2. ^{31}P NMR (202 MHz, $CDCl_3$) δ 18.4. HRMS (ESI$^+$) exact mass calcd for $C_{22}H_{45}NO_4PSi$ [M+H]$^+$ requires *m/z* 446.2850, found *m/z* 446.2863.

4.10 Synthesis of Aldehyde 23

4.10.1 Preparation of Diene **53**



To a solution of phosphonate **49** (1.34 g, 3.00 mmol, 1.00 equiv) in toluene (40 mL) at –78 °C was added dropwise a solution of KHMDS (598 mg, 3.00 mmol, 1.00 equiv) in toluene (6.0 mL). After stirring had been continued for 1 h, a solution of aldehyde **50**[17] (583 mg, 3.00 mmol, 1.00 equiv) in toluene (6.0 mL) was added dropwise via syringe. The reaction mixture was stirred for 2 h at –78 °C, subsequently poured onto sat. NH_4Cl (50 mL), and extracted with EtOAc (4 × 25 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (4% EtOAc/hexanes) afforded title

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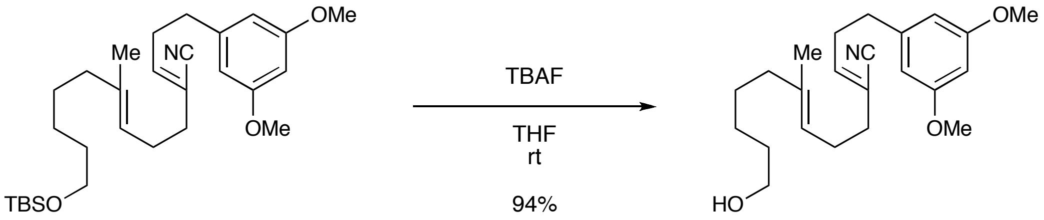
(17) Nikas, S. P.; Thakur, G. A.; Makriyannis, A. *Synth. Commun.* **2002**, *32*, 1751.

compound **53** (1.06 g, 73% , >20:1 *Z*/*E*) along with the separable diastereomer (210 mg, 14%, 1:3 *Z*/*E*) as viscous oils.

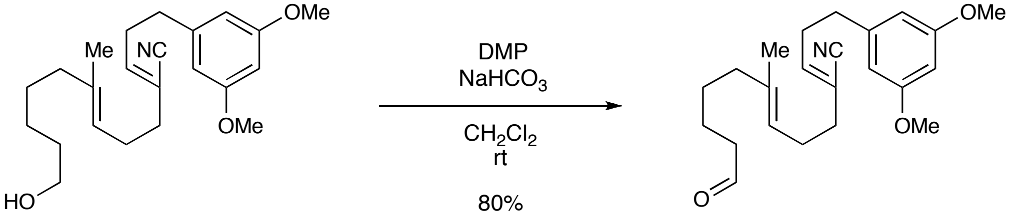
IR (ATR) ν (cm^{-1}) 2929, 2856, 2214, 1596, 1461, 1429, 1386, 1350, 1312, 1293, 1254, 1205, 1150, 1096, 1059, 1006, 938, 924, 831, 774, 692, 661. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.37-6.29 (m, Ar**H**, 3H), 6.12 (t, *J* = 7.1 Hz, NCC=C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.01 (t, *J* = 7.0 Hz, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 3.79 (s, OC$\mathbf{H}_3$, 6H), 3.59 (t, *J* = 6.6 Hz, C$\mathbf{H}_2$OSi, 2H), 2.72-2.62 (m, 2 × C$\mathbf{H}_2$, 4H), 2.24-2.12 (m, 2 × C$\mathbf{H}_2$, 4H), 1.95 (t, *J* = 7.2 Hz, C$\mathbf{H}_2$, 2H), 1.58 (s, C$\mathbf{H}_3$, 3H), 1.51 (tt, *J* = 7.5 Hz, C$\mathbf{H}_2$$CH_2$OSi, 2H), 1.41-1.33 (m, C$\mathbf{H}_2$$(CH_2)_3$OSi, 2H), 1.31-1.22 (m, C$\mathbf{H}_2$$(CH_2)_2$OSi, 2H), 0.89 (s, SiC(C$\mathbf{H}_3$)$_3$, 9H), 0.04 (s, Si(C$\mathbf{H}_3$)$_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 146.5, 142.7, 137.4, 121.7, 117.7, 115.1, 106.4, 98.2, 63.3, 55.4, 39.7, 35.1, 34.5, 32.83, 32.76, 27.8, 26.7, 26.1, 25.5, 18.5, 16.1, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{29}H_{47}NO_3SiNa$ [M+Na]$^+$ requires *m*/*z* 508.3217, found *m*/*z* 508.3216.

4.10.3 Preparation of Aldehyde **23**



TBAF (2.10 mL of a 1.0M solution in THF, 2.10 mmol, 1.10 equiv) was added slowly to a solution of silyl ether **53** (930 mg, 1.91 mmol, 1.00 equiv) in THF (20 mL) at room temperature. After stirring had been continued for 2 h, water (20 mL) and sat. NH_4Cl (20 mL) were added and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (30% EtOAc/hexanes) furnished the free alcohol (668 mg, 94% yield, 9:1 *Z*/*E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3416, 2931, 2857, 2214, 1595, 1460, 1428, 1349, 1312, 1293, 1260, 1204, 1148, 1056, 938, 924, 830, 754, 693, 667. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.39-6.28 (m, Ar**H**, 3H), 6.12 (t, *J* = 7.1 Hz, NCC=**CH**$_{\text{vin}}$, 1H), 5.01 (t, *J* = 7.0 Hz, **CH**$_{\text{vin}}$, 1H), 3.79 (s, OC**H**$_3$, 6H), 3.63 (t, *J* = 8.6 Hz, **CH$_2$**OH, 2H), 2.73-2.61 (m, 2 × **CH$_2$**, 4H), 2.23-2.15 (m, 2 × **CH$_2$**, 4H), 1.96 (t, *J* = 7.2 Hz, **CH$_2$**, 2H), 1.59 (s, **CH$_3$**, 3H), 1.59-1.53 (m, **CH$_2$**CH$_2$OH, 2H), 1.42-1.35 (m, **CH$_2$**(CH$_2$)$_3$OH, 2H), 1.34-1.27 (m, **CH$_2$**(CH$_2$)$_2$OH, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 160.9, 146.7, 142.7, 137.2, 121.8, 117.7, 115.1, 106.4, 98.2, 63.0, 55.4, 39.6, 35.1, 34.4, 32.72, 32.71, 27.7, 26.7, 25.4, 16.0. HRMS (ESI$^+$) exact mass calcd for $C_{23}H_{33}NO_3Na$ [M+Na]$^+$ requires *m/z* 394.2351, found *m/z* 394.2353.



23

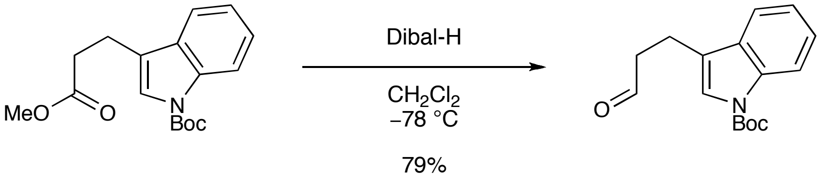
To a solution of the alcohol (598 mg, 1.61 mmol, 1.00 equiv) prepared in the previous step in CH$_2$Cl$_2$ (16 mL) and solid NaHCO$_3$ (676 mg, 8.05 mmol, 5.00 equiv) was added Dess-Martin periodinane (1.02 g, 2.41 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na$_2$CO$_3$ (20 mL) and aqueous Na$_2$S$_2$O$_3$ (10 mL) was followed by extraction with CH$_2$Cl$_2$ (4 × 15 mL). The combined organic layers were washed with brine (15 mL), dried (MgSO$_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (15% EtOAc/hexanes) furnished title compound **23** (477 mg, 80% yield, 13:1 *Z*/*E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2935, 2859, 2839, 2718, 1721, 1594, 1459, 1429, 1387, 1349, 1316, 1293, 1260, 1204, 1148, 1057, 1016, 924, 830, 754, 693. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.77 (br s, C**H**O, 1H), 6.40-6.29 (m, Ar**H**, 3H), 6.12 (t, *J* = 7.0 Hz, NCC=**CH**$_{\text{vin}}$, 1H), 5.02 (br s, **CH**$_{\text{vin}}$, 1H), 3.78 (s, OC**H$_3$**, 6H), 2.72-2.62 (m, 2 × **CH$_2$**, 4H), 2.43 (br t, *J* = 7.2 Hz, **CH$_2$**CHO, 2H), 2.24-2.14 (m, 2 × **CH$_2$**, 4H), 1.98 (t, *J* = 7.5 Hz, **CH$_2$**, 2H), 1.64-1.52 (m, **CH$_2$**CH$_2$CHO, 2H), 1.58 (s, **CH$_3$**, 3H), 1.45-1.36 (m, **CH$_2$**(CH$_2$)$_2$CHO, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 202.9, 160.9, 146.7, 142.7, 122.3, 117.7, 115.1, 106.4, 98.2, 55.4, 43.8, 39.3, 35.0, 34.4, 32.7, 27.3, 26.6, 21.6, 16.0.

HRMS (ESI^+) exact mass calcd for $C_{23}H_{31}NO_3Na$ $[M+Na]^+$ requires *m/z* 392.2196, found *m/z* 392.2197.

4.11 Synthesis of Aldehyde 24

4.11.1 *tert*-Butyl 3-(3-oxopropyl)-1*H*-indole-1-carboxylate (**51**)



51

To a solution of *tert*-butyl 3-(3-methoxy-3-oxopropyl)-1*H*-indole-1-carboxylate[18] (2.12 g, 7.00 mmol, 1.00 equiv) in CH_2Cl_2 (70 mL) at −78 °C was added Dibal-H (7.4 mL of a 1.0M solution in hexanes, 7.4 mmol, 1.05 equiv). After stirring at this temperature had been continued for 1 h the reaction mixture was poured onto ice, diluted with 2M HCl until pH 3-4 was reached and extracted with CH_2Cl_2 (4 × 30 mL). The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo*, and purified by flash chromatography (10% EtOAc/hexanes) to afford title compound **51** (1.51 g, 79%) as a colorless oil that solidified upon standing.

IR (ATR) ν (cm^{-1}) 3115, 3057, 2991, 2933, 2973, 2891, 2862, 2755, 1913, 1807, 1715, 1607, 1566, 1475, 1455, 1434, 1410, 1396, 1364, 1347, 1307, 1282, 1268, 1256, 1218, 1154, 1085, 1065, 1051, 1013, 944, 900, 857, 837, 808, 793, 767, 757, 745, 686, 662. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (t, *J* = 1.2 Hz, C**H**O, 1H), 8.12 (br s, Ar**H**, 1H), 7.52 (d, *J* = 7.7 Hz, Ar**H**, 1H), 7.37 (br s, Ar**H**, 1H), 7.33 (ddd, *J* = 2 × 7.7, 1.0 Hz, Ar**H**, 1H), 7.25 (ddd, *J* = 2 × 7.7, 1.0 Hz, Ar**H**, 1H), 3.04 (t, *J* = 7.6 Hz, C$\mathbf{H_2}$, 2H), 2.88 (t, *J* = 7.6 Hz, C$\mathbf{H_2}$, 2H), 1.66 (s, OC(C$\mathbf{H_3}$)$_3$, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.8, 149.8, 136.2, 130.2, 124.6, 122.7, 122.5, 119.2, 118.8, 115.4, 83.6, 43.2, 28.3, 17.5. HRMS (ESI^+) exact mass calcd for $[M+Na]^+$ ($C_{16}H_{19}NO_3Na$) requires *m/z* 296.1257, found *m/z* 296.1257.

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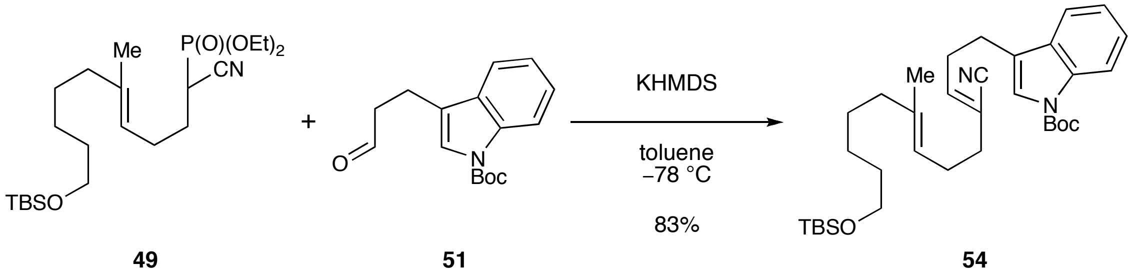
(18) Micuch, P.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 1567.

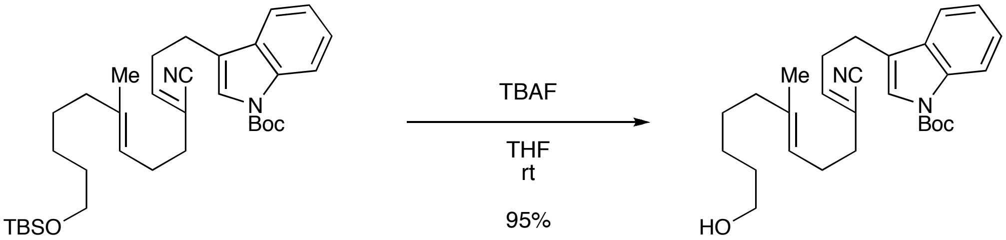
4.11.2 Preparation of Diene **54**



To a solution of phosphonate **49** (1.12 g, 2.50 mmol, 1.00 equiv) in toluene (30 mL) at −78 °C was added dropwise a solution of KHMDS (499 mg, 2.50 mmol, 1.00 equiv) in toluene (5.0 mL). After stirring had been continued for 1 h, a solution of aldehyde **51** (752 mg, 2.50 mmol, 1.00 equiv) in toluene (5.0 mL) was added dropwise via syringe. The reaction mixture was stirred for 2 h at −78 °C, subsequently poured onto sat. NH_4Cl (50 mL), and extracted with EtOAc (4 × 25 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (3%→5% EtOAc/hexanes) afforded title compound **54** (1.17 g, 83%, >20:1 *Z*/*E*) as a viscous oil.

IR (ATR) ν (cm^{-1}) 2929, 2856, 2214, 1731, 1610, 1472, 1453, 1370, 1339, 1308, 1252, 1225, 1156, 1084, 1040, 1018, 937, 833, 813, 767, 744, 661. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (br s, Ar**H**, 1H), 7.52 (d, *J* = 7.7 Hz, Ar**H**, 1H), 7.40 (br s, Ar**H**, 1H), 7.33 (dd, *J* = 2 × 7.4 Hz, Ar**H**, 1H), 7.25 (dd, *J* = 2 × 7.2 Hz, Ar**H**, 1H), 6.20 (t, *J* = 7.4 Hz, NCC=$\mathbf{CH}_{\mathbf{vin}}$, 1H), 5.03 (br s, $\mathbf{CH}_{\mathbf{vin}}$, 1H), 3.59 (t, *J* = 6.6 Hz, $\mathbf{CH_2}$OSi, 2H), 2.88-2.72 (m, 2 × $\mathbf{CH_2}$, 4H), 2.25-2.15 (m, 2 × $\mathbf{CH_2}$, 4H), 1.94 (t, *J* = 7.4 Hz, $\mathbf{CH_2}$, 2H), 1.67 (s, OC($\mathbf{CH_3}$)$_3$, 9H), 1.58 (s, $\mathbf{CH_3}$, 3H), 1.53-1.45 (m, $\mathbf{CH_2}$$CH_2$OSi, 2H), 1.36 (tt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}$$(CH_2)_3$OSi, 2H), 1.30-1.21 (m, $\mathbf{CH_2}$$(CH_2)_2$OSi, 2H), 0.88 (s, SiC($\mathbf{CH_3}$)$_3$, 9H), 0.04 (s, Si($\mathbf{CH_3}$)$_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.8, 146.7, 137.4, 135.6, 130.4, 124.5, 122.7, 122.5, 121.7, 119.3, 118.9, 117.7, 115.4, 115.3, 83.6, 63.3, 39.7, 34.5, 32.8, 31.1, 28.3, 27.8, 26.6, 26.1, 25.5, 24.2, 18.5, 16.1, −5.2. HRMS (ESI$^+$) exact mass calcd for $C_{34}H_{53}N_2O_3Si$ $[M+H]^+$ requires *m*/*z* 565.3820, found *m*/*z* 565.3817.

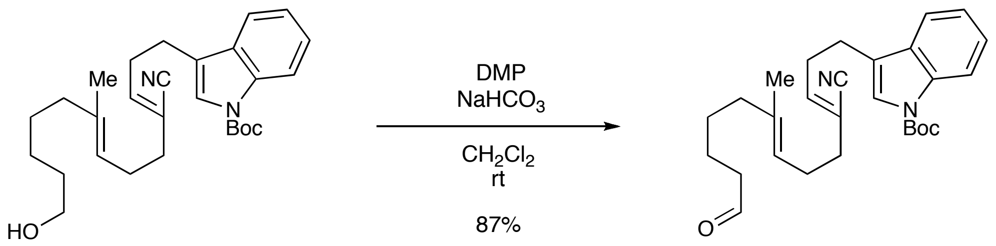
4.11.3 Synthesis of Aldehyde **24**



54

TBAF (2.20 mL of a 1.0M solution in THF, 2.20 mmol, 1.10 equiv) was added slowly to a solution of silyl ether **54** (1.11 g, 1.97 mmol, 1.00 equiv) in THF (18 mL) at room temperature. After stirring had been continued for 2 h, water (20 mL) and sat. NH_4Cl (20 mL) were added and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (30% EtOAc/hexanes) furnished the free alcohol (845 mg, 95% yield, 8:1 *Z*/*E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3433, 2978, 2932, 2857, 2215, 1729, 1609, 1475, 1452, 1369, 1338, 1308, 1254, 1224, 1154, 1083, 1017, 855, 745, 666. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (br s, Ar**H**, 1H), 7.53 (d, *J* = 7.8 Hz, Ar**H**, 1H), 7.40, (br s, Ar**H**, 1H), 7.33 (dd, *J* = 2 × 7.7 Hz, Ar**H**, 1H), 7.26 (dd, *J* = 2 × 7.4 Hz, Ar**H**, 1H), 6.20 (t, *J* = 7.2 Hz, NCC=C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.03 (br s, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 3.62 (t, *J* = 6.6 Hz, C$\mathbf{H_2}$OH, 2H), 2.86-2.72 (m, 2 × C$\mathbf{H_2}$, 4H), 2.25-2.16 (m, 2 × C$\mathbf{H_2}$, 4H), 1.95 (t, *J* = 7.3 Hz, C$\mathbf{H_2}$, 2H), 1.67 (s, OC(C$\mathbf{H_3}$)$_3$, 9H), 1.58 (s, C$\mathbf{H_3}$, 3H), 1.54 (tt, *J* = 2 × 7.0 Hz, C$\mathbf{H_2}$$CH_2$OH, 2H), 1.38 (tt, *J* = 2 × 7.2 Hz, C$\mathbf{H_2}$(CH_2)$_3$OH, 2H), 1.30-1.24 (m, C$\mathbf{H_2}$(CH_2)$_2$OH, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.8, 146.7, 137.4, 135.6, 130.4, 124.5, 122.7, 122.5, 121.8, 119.2, 118.8, 117.7, 115.3, 115.2, 83.6, 63.0, 39.6, 34.4, 32.7, 31.0, 28.2, 27.6, 26.6, 25.3, 24.1, 16.1. HRMS (ESI$^+$) exact mass calcd for $C_{28}H_{38}N_2O_3Na$ [M+Na]$^+$ requires *m*/*z* 473.2775, found *m*/*z* 473.2771.



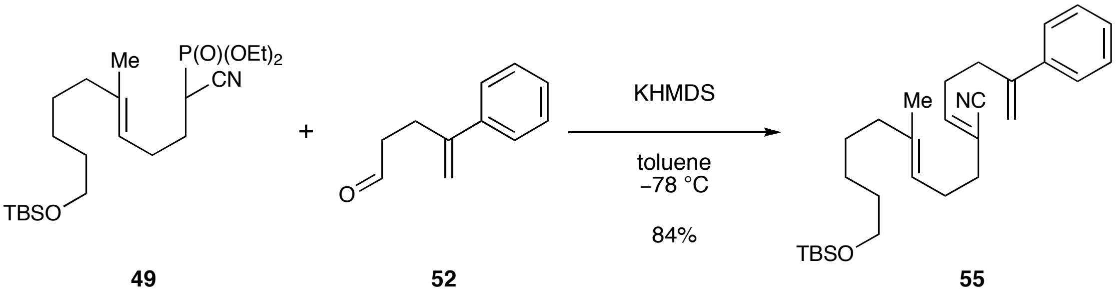
24

To a solution of the alcohol (800 mg, 1.77 mmol, 1.00 equiv) prepared in the previous step in CH_2Cl_2 (18 mL) and solid $NaHCO_3$ (743 mg, 8.85 mmol, 5.00 equiv) was added Dess-Martin periodinane (1.13 g, 2.66 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na_2CO_3 (20 mL) and aqueous $Na_2S_2O_3$ (10 mL) was followed by extraction with CH_2Cl_2 (4 × 15 mL). The combined organic layers were washed with brine (15 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (15% EtOAc/hexanes) furnished title compound **24** (691 mg, 87% yield, 8:1 *Z*/*E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2978, 2933, 2861, 2214, 1726, 1608, 1477, 1452, 1369, 1339, 1308, 1252, 1225, 1154, 1083, 1044, 1017, 938, 854, 766, 745. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (s, C**H**O, 1H), 8.14 (br s, Ar**H**, 1H), 7.53 (d, *J* = 7.7 Hz, Ar**H**, 1H), 7.40, (br s, Ar**H**, 1H), 7.33 (dd, *J* = 2 × 7.7 Hz, Ar**H**, 1H), 7.26 (dd, *J* = 2 × 7.3 Hz, Ar**H**, 1H), 6.21 (t, *J* = 7.2 Hz, NCC=$\mathbf{CH}_{\mathbf{vin}}$, 1H), 5.03 (br s, $\mathbf{CH}_{\mathbf{vin}}$, 1H), 2.86-2.72 (m, 2 × $\mathbf{CH_2}$, 4H), 2.40 (t, *J* = 7.3 Hz, $\mathbf{CH_2}$CHO, 2H), 2.25-2.13 (m, 2 × $\mathbf{CH_2}$, 4H), 1.96 (t, *J* = 7.3 Hz, $\mathbf{CH_2}$, 2H), 1.67 (s, OC($\mathbf{CH_3}$)$_3$, 9H), 1.60-1.51 (m, $\mathbf{CH_2}$$CH_2$CHO, 2H), 1.58 (s, $\mathbf{CH_3}$, 3H), 1.38 (tt, *J* = 2 × 6.9 Hz, $\mathbf{CH_2}$(CH_2)$_2$CHO, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.9, 149.8, 146.8, 136.7, 135.5, 130.4, 124.5, 122.5, 122.2, 121.5, 119.2, 118.9, 117.7, 115.4, 115.2, 83.6, 43.8, 39.3, 34.4, 31.1, 28.3, 27.3, 26.6, 24.1, 21.6, 16.0. HRMS (ESI$^+$) exact mass calcd for $C_{28}H_{36}N_2O_3Na$ $[M+Na]^+$ requires *m*/*z* 471.2618, found *m*/*z* 471.2617.

4.12 Synthesis of Aldehyde 25

4.12.1 Preparation of Diene **55**



To a solution of phosphonate **49** (1.34 g, 3.00 mmol, 1.00 equiv) in toluene (40 mL) at −78 °C was added dropwise a solution of KHMDS (598 mg, 3.00 mmol, 1.00 equiv) in toluene (6.0 mL). After stirring had been continued for 1 h, a solution of aldehyde **52**[19] (481 mg, 3.00 mmol, 1.00 equiv) in toluene (6.0 mL) was added dropwise via syringe. The reaction mixture was stirred for 2 h at −78 °C, subsequently poured onto sat. NH_4Cl (50 mL), and extracted with EtOAc (4 × 25 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (2.5% EtOAc/hexanes) afforded title compound **55** (1.14 g, 84%, 7:1 *Z*/*E*) as a viscous oil.

IR (ATR) ν (cm^{-1}) 2929, 2855, 2214, 1627, 1600, 1574, 1494, 1471, 1461, 1443, 1386, 1360, 1297, 1252, 1096, 1028, 1005, 938, 897, 833, 774, 702, 660. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.31 (m, Ar**H**, 4H), 7.31-7.26 (m, Ar**H**, 1H), 6.12 (t, *J* = 7.5 Hz, NCC=$\mathbf{CH_{vin}}$, 1H), 5.33 (br s, C=$CH_A\mathbf{H_B}$, 1H), 5.09 (br s, C=$\mathbf{CH_A}H_B$, 1H), 5.03 (br s, $\mathbf{CH_{vin}}$, 1H), 3.59 (t, *J* = 6.6 Hz, $\mathbf{CH_2}$OH, 2H), 2.68-2.58 (m, $\mathbf{CH_2}$, 2H), 2.54-2.47 (m, $\mathbf{CH_2}$, 2H), 2.23-2.13 (m, 2 × $\mathbf{CH_2}$, 4H), 1.96 (t, *J* = 7.7 Hz, $\mathbf{CH_2}$, 2H), 1.59 (s, $\mathbf{CH_3}$, 3H), 1.51 (tt, *J* = 2 × 7.2 Hz, $\mathbf{CH_2}CH_2$OSi, 2H), 1.38 (tt, *J* = 2 × 7.2 Hz, $\mathbf{CH_2}(CH_2)_3$OSi, 2H), 1.31-1.22 (m, $\mathbf{CH_2}(CH_2)_2$OSi, 2H), 0.89 (s, $SiC(\mathbf{CH_3})_3$, 9H), 0.05 (s, $Si(\mathbf{CH_3})_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.82, 146.80, 140.6, 137.3, 128.5, 127.7, 126.2, 121.7, 117.7, 114.8, 113.4, 63.3, 39.7, 34.5, 34.3, 32.8, 30.1, 27.8, 26.6, 26.1, 25.5,

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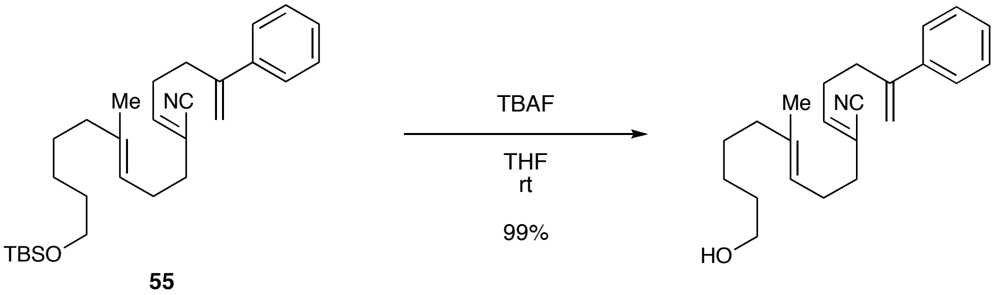
[19] Tokuyasu, T.; Kunikawa, S.; McCullough, K. J.; Masuyama, A.; Nojima, M. *J. Org. Chem.* **2005**, *70*, 251.

18.5, 16.1, –5.2. HRMS (ESI$^+$) exact mass calcd for $[M+H]^+$ ($C_{29}H_{46}NOSi$) requires *m*/*z* 452.3343, found *m*/*z* 452.3335.

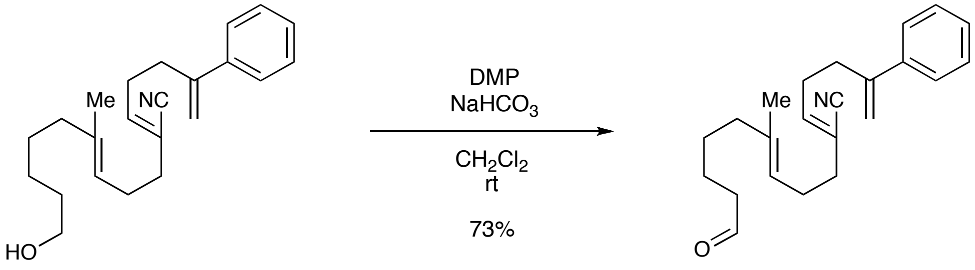
4.12.2 Synthesis of Aldehyde **25**



55

TBAF (2.00 mL of a 1.0M solution in THF, 2.00 mmol, 1.10 equiv) was added slowly to a solution of silyl ether **55** (817 mg, 1.81 mmol, 1.00 equiv) in THF (16 mL) at room temperature. After stirring had been continued for 2 h, water (20 mL) and sat. NH_4Cl (20 mL) were added and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished the free alcohol (604 mg, 99% yield, 7:1 *Z*/*E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3383, 2930, 2856, 2214, 1627, 1599, 1574, 1494, 1442, 1383, 1296, 1241, 1156, 1071, 1049, 1028, 896, 777, 703. ^1H NMR (500 MHz, $CDCl_3$) δ 7.42-7.31 (m, Ar**H**, 4H), 7.31-7.26 (m, Ar**H**, 1H), 6.12 (t, *J* = 7.5 Hz, NCC=$\mathbf{CH}_{\mathbf{vin}}$, 1H), 5.33 (br s, C=$CH_A\mathbf{H}_\mathbf{B}$, 1H), 5.09 (br s, C=$\mathbf{CH}_\mathbf{A}H_B$, 1H), 5.04 (br s, $\mathbf{CH}_{\mathbf{vin}}$, 1H), 3.63 (t, *J* = 6.5 Hz, $\mathbf{CH_2}$OH, 2H), 2.68-2.58 (m, $\mathbf{CH_2}$, 2H), 2.54-2.47 (m, $\mathbf{CH_2}$, 2H), 2.22-2.10 (m, 2 × $\mathbf{CH_2}$, 4H), 2.01-1.92 (m, $\mathbf{CH_2}$, 2H), 1.59 (s, $\mathbf{CH_3}$, 3H), 1.56 (tt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}CH_2OH$, 2H), 1.44-1.35 (m, $\mathbf{CH_2}(CH_2)_3OH$, 2H), 1.34-1.26 (m, $\mathbf{CH_2}(CH_2)_2OH$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0, 146.8, 140.6, 137.2, 128.5, 127.7, 126.2, 121.9, 117.7, 114,8, 113.4, 63.0, 39.6, 34.4, 34.2, 32.7, 30.1, 27.7, 26.6, 25.4, 16.1. HRMS (ESI$^+$) exact mass calcd for $C_{23}H_{31}NONa$ $[M+Na]^+$ requires *m*/*z* 360.2298, found *m*/*z* 360.2298.



25

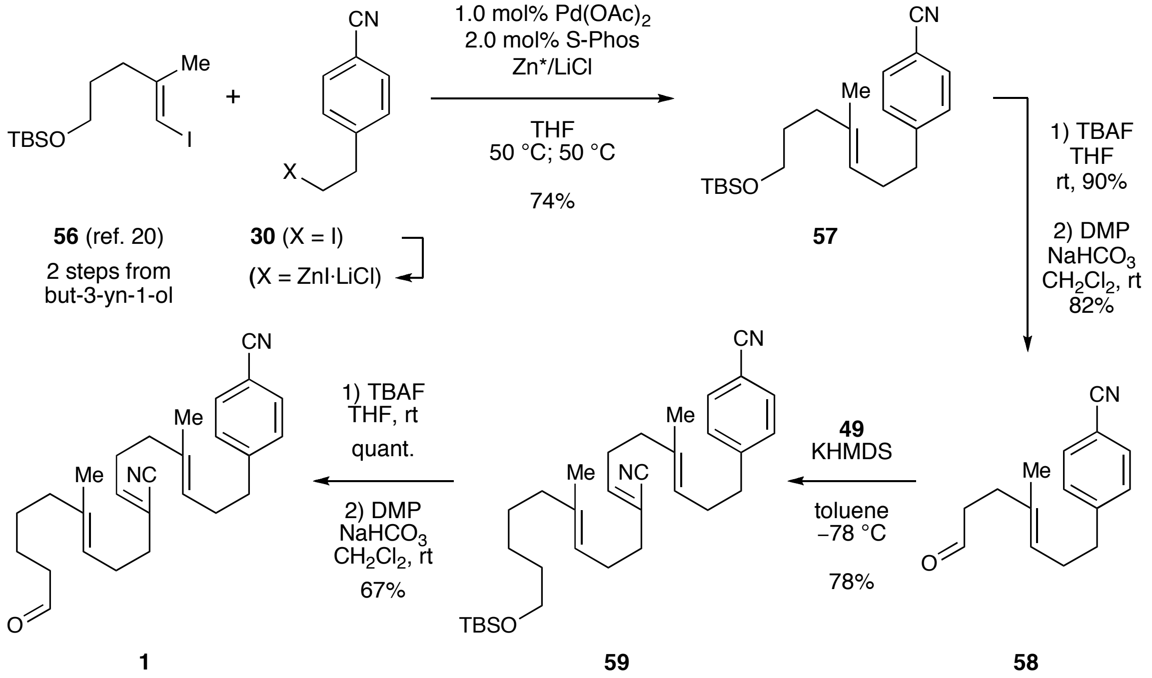
To a solution of the alcohol (630 mg, 1.80 mmol, 1.00 equiv) prepared in the previous step in CH_2Cl_2 (18 mL) and solid $NaHCO_3$ (756 mg, 9.00 mmol, 5.00 equiv) was added Dess-Martin periodinane (1.15 g, 2.70 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na_2CO_3 (20 mL) and aqueous $Na_2S_2O_3$ (10 mL) was followed by extraction with CH_2Cl_2 (4 × 15 mL). The combined organic layers were washed with brine (15 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (8% EtOAc/hexanes) furnished the title compound **25** (442 mg, 73% yield, 7:1 *Z*/*E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3083, 2933, 2858, 2719, 2214, 1722, 1627, 1599, 1574, 1495, 1443, 1410, 1387, 1298, 1242, 1158, 1073, 1027, 897, 778, 703. ^1H NMR (500 MHz, $CDCl_3$) δ 9.76 (br s, C**H**O, 1H), 7.42-7.31 (m, Ar**H**, 4H), 7.31-7.26 (m, Ar**H**, 1H), 6.12 (t, J = 7.4 Hz, NCC=C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.33 (br s, C=$CH_A\mathbf{H}_\mathbf{B}$, 1H), 5.09 (br s, C=$C\mathbf{H}_\mathbf{A}H_B$, 1H), 5.07 (br s, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 2.68-2.59 (m, C$\mathbf{H}_\mathbf{2}$, 2H), 2.55-2.47 (m, C$\mathbf{H}_\mathbf{2}$, 2H), 2.45-2.38 (m, C$\mathbf{H}_\mathbf{2}$, 2H), 2.25-2.27 (m, 2 × C$\mathbf{H}_\mathbf{2}$, 4H), 2.03-1.93 (m, C$\mathbf{H}_\mathbf{2}$, 2H), 1.63-1.52 (m, C$\mathbf{H}_\mathbf{2}$$CH_2CHO$, 2H), 1.59 (s, C$\mathbf{H}_\mathbf{3}$, 3H), 1.41 (tt, J = 7.3 Hz, C$\mathbf{H}_\mathbf{2}$$(CH_2)_2CHO$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.9, 146.9, 146.8, 140.6, 136.6, 128.5, 127.7, 126.2, 122.3, 117.6, 114.8, 113.4, 43.8, 39.3, 34.4, 34.2, 30.1, 27.3, 26.6, 21.6, 16.0. HRMS (ESI^+) exact mass calcd for $C_{23}H_{29}NONa$ $[M+Na]^+$ requires m/z 358.2141, found m/z 358.2140.

4.13 Synthesis of Tetracyclization Precursor 1

Tetracyclization precursor **1** was prepared in a convergent assembly of fragment **58** and phosphonate **49** (*cf* section 4.9) employing a Horner-Wadsworth-Emmons coupling[16]; deprotection and oxidation completed the synthesis of aldehyde **1** (Scheme S3). Aldehyde **58** was prepared from **56** (prepared in two steps from but-4-yn-1-ol)[20] by cross-coupling with homobenzylic zinc reagent derived from **30** (*cf* section 4.3.1) and a deprotection/oxidation sequence.

Scheme S3. Synthetic Access to Tetracyclization Substrate **1**.



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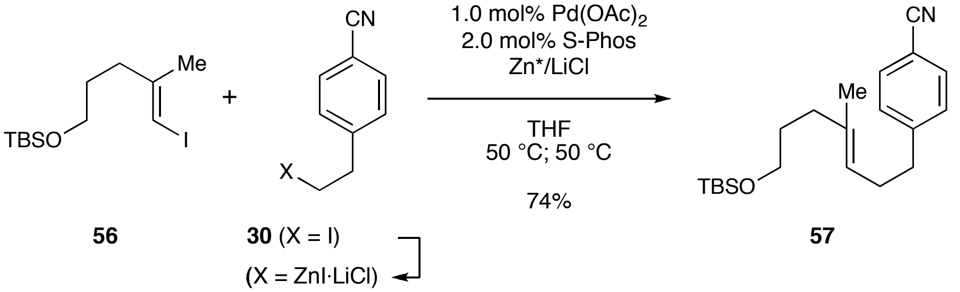
(20) Kujat, C.; Bock, M.; Kirschning, M. *Synlett* **2006**, 419.

4.13.1 Synthesis of Intermediate **57**

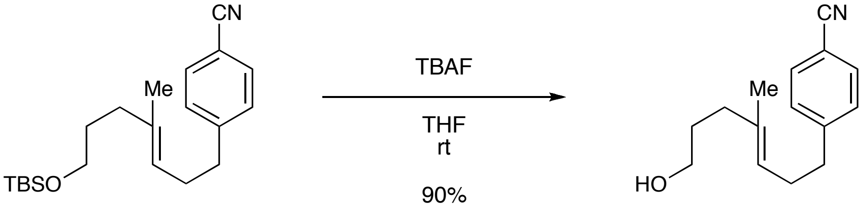


Anhydrous LiCl (530 mg, 12.5 mmol, 1.25 equiv) was placed in an argon-flushed 25-mL Schlenk flask and dried for 30 min at 150-180 °C under high vacuum (<1 torr) with slow stirring. Upon addition of zinc powder (325 mesh, 1.23 g, 18.8 mmol, 1.88 equiv) heating under high vacuum was continued for 30 min. After cooling to room temperature and backfilling with argon, the mixture was suspended with THF (7.5 mL). Subsequently, the zinc powder was activated by sequential addition of 1,2-dibromoethane (54 µL, 117 mg, 0.63 mmol, 0.063 equiv), TMSCl (3 drops), and iodine (12 drops of a 1M solution in THF); each addition followed by gentle heating to reflux with a heat gun. Portionwise addition of a solution of alkyl iodide **30** (3.21 g, 12.5 mmol, 1.25 equiv) in THF (5.0 mL) at room temperature and subsequent stirring at for 4 h at 50 °C furnished a solution of homobenzylic zinc iodide that was allowed to cool to room temperature and separated via syringe from remaining zinc powder.

In a separate 50-mL Schlenk flask Pd(OAc)$_2$ (22.5 mg, 0.100 mmol, 0.0100 equiv) and S-Phos (82.1 mg, 0.200 mmol, 0.0200 equiv) was dissolved in THF (5.0 mL) and a solution of vinyl iodide **56** (3.40 g, 10.0 mmol, 1.00 equiv) in THF (5.0 mL) was added. The previously prepared solution of homobenzylic zinc reagent was quickly added via syringe leading to an exothermic reaction. Further stirring at 50 °C for 3 h was followed by aqueous work-up with sat. NH$_4$Cl (50 mL) and extraction with EtOAc (4 × 30 mL). The combined organic layers were washed with brine (30 mL), dried (MgSO$_4$), and concentrated under reduced pressure. Purification by flash chromatography (3% EtOAc/hexanes) furnished title compound **57** (2.54 g, 74% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2929, 2856, 2227, 1608, 1504, 1471, 1462, 1413, 1387, 1360, 1253, 1176, 1095, 1020, 1005, 952, 832, 774, 712, 662. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.9 Hz, Ar**H**, 2H), 7.28 (d, *J* = 8.0 Hz, Ar**H**, 2H), 5.13 (t, *J* = 7.1 Hz, $\mathbf{CH_{vin}}$, 1H), 3.56 (t, *J* = 6.6 Hz, $\mathbf{CH_2}$OSi, 2H), 2.69 (t, *J* = 7.6 Hz, Ar$\mathbf{CH_2}$, 2H), 2.30 (dt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 1.99 (t, *J* = 7.4 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.61-1.54 (m, $\mathbf{CH_2}CH_2OSi$, 2H), 1.51 (s, $\mathbf{CH_3}$, 3H), 0.89 (s, $SiC(\mathbf{CH_3})_3$, 9H), 0.05 (s, $Si(\mathbf{CH_3})_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 136.5, 132.1, 129.4, 122.6, 119.3, 109.6, 62.9, 36.3, 35.8, 31.2, 29.4, 26.0, 18.4, 16.1, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{21}H_{33}NOSiNa$ [M+Na]$^+$ requires *m*/*z* 366.2224, found *m*/*z* 366.2223.

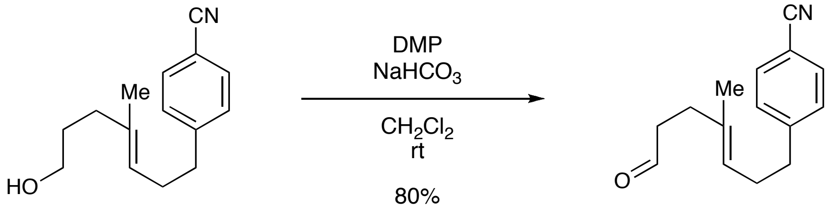
4.13.2 Synthesis of Aldehyde **58**



57

TBAF (8.90 mL of a 1.0M solution in THF, 8.90 mmol, 1.20 equiv) was added slowly to a solution of silyl ether **57** (2.54 g, 7.40 mmol, 1.00 equiv) in THF (60 mL) at room temperature. After stirring had been continued for 2 h, water (50 mL) and sat. NH_4Cl (50 mL) were added and the aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with brine (40 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (30% EtOAc/hexanes) furnished the free alcohol (1.54 g, 90% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3360, 2935, 2861, 2227, 1666, 1607, 1504, 1446, 1413, 1383, 1176, 1055, 1020, 919, 822. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.2 Hz, Ar**H**, 2H), 7.27 (d, *J* = 8.4 Hz, Ar**H**, 2H), 5.16 (t, *J* = 7.1 Hz, $\mathbf{CH_{vin}}$, 1H), 3.60 (t, *J* = 6.4 Hz, $\mathbf{CH_2}$OH, 2H), 2.69 (t, *J* = 7.5 Hz, Ar$\mathbf{CH_2}$, 2H), 2.31 (dt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 2.04 (t, *J* = 7.9 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.63 (tt, *J* = 2 × 6.5 Hz, $\mathbf{CH_2}CH_2OH$, 2H), 1.52 (s, $\mathbf{CH_3}$, 3H), 1.35 (br s, O**H**, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 136.4, 132.1, 129.4, 123.0, 119.3, 109.6, 62.7, 36.2, 35.9, 30.8, 29.3, 15.9. HRMS (ESI$^+$) exact mass calcd for $C_{15}H_{19}NONa$ $[M+Na]^+$ requires *m/z* 252.1359, found *m/z* 252.1358.

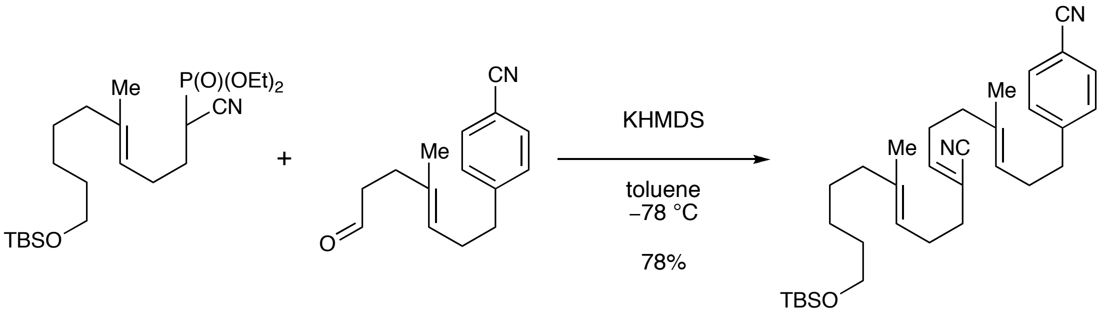


58

To a solution of the alcohol (1.35 g, 5.89 mmol, 1.00 equiv) prepared in the previous step in CH_2Cl_2 (60 mL) and solid $NaHCO_3$ (2.47 g, 29.5 mmol, 5.00 equiv) was added Dess-Martin periodinane (3.75 g, 8.83 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na_2CO_3 (60 mL) and aqueous $Na_2S_2O_3$ (20 mL) was followed by extraction with CH_2Cl_2 (4 × 40 mL). The combined organic layers were washed with brine (40 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (15% EtOAc/hexanes) furnished title compound **58** (1.07 g, 80% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2919, 2858, 2794, 2226, 1720, 1607, 1504, 1443, 1412, 1387, 1176, 1060, 1001, 826. ^1H NMR (500 MHz, $CDCl_3$) δ 9.74 (t, *J* = 1.8 Hz, C**H**O, 1H), 7.56 (d, *J* = 8.3 Hz, Ar**H**, 2H), 7.26 (d, *J* = 8.1 Hz, Ar**H**, 2H), 5.15 (t, *J* = 7.1 Hz, $C\mathbf{H}_{\mathbf{vin}}$, 1H), 2.69 (t, *J* = 7.5 Hz, $ArC\mathbf{H_2}$, 2H), 2.50 (td, *J* = 7.3, 1.7 Hz, $C\mathbf{H_2}CHO$, 2H), 2.35-2.26 (m, $C\mathbf{H_2}CH_{vin}$, $C\mathbf{H_2}(CH_3)C{=}C$, 4H), 1.52 (s, $C\mathbf{H_3}$, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 147.7, 134.4, 132.2, 129.4, 123.7, 119.3, 109.7, 42.1, 36.1, 31.8, 29.3, 16.1. HRMS (ESI$^+$) exact mass calcd for $C_{15}H_{17}NONa$ $[M+Na]^+$ requires *m/z* 250.1202, found *m/z* 250.1201.

4.13.3 Synthesis of Intermediate **59**

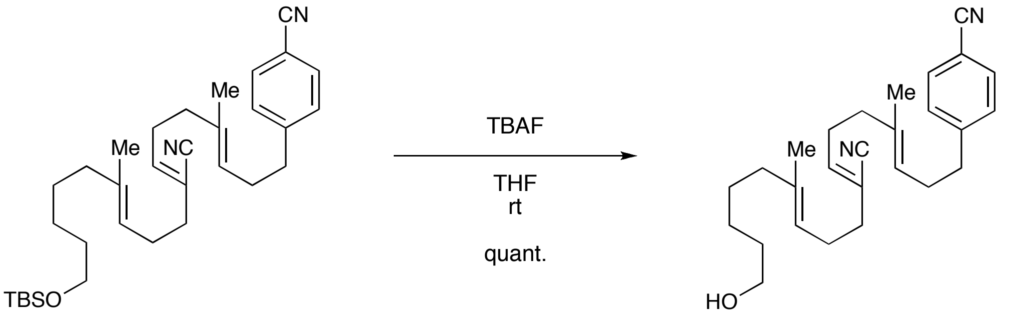


49 **58** **59**

To a solution of phosphonate **49** (1.12 g, 2.50 mmol, 1.00 equiv) in toluene (30 mL) at −78 °C was added dropwise a solution of KHMDS (499 mg, 2.50 mmol, 1.00 equiv) in toluene (5.0 mL). After stirring had been continued for 1 h, a solution of aldehyde **58** (568 mg, 2.50 mmol, 1.00 equiv) in toluene (5.0 mL) was added dropwise via syringe. The reaction mixture was stirred for 2 h at −78 °C, subsequently poured onto sat. NH_4Cl (40 mL), and extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with brine (25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (10% EtOAc/hexanes) afforded title compound **59** (1.01 g, 78%, 10:1 *Z*/*E*) as a viscous oil.

IR (ATR) ν (cm^{-1}) 2929, 2856, 2227, 1739, 1608, 1505, 1471, 1462, 1445, 1413, 1386, 1360, 1249, 1176, 1096, 1046, 1006, 938, 833, 774, 710, 662. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.2 Hz, Ar**H**, 2H), 7.28 (d, *J* = 8.2 Hz, Ar**H**, 2H), 6.05 (t, *J* = 7.6 Hz, NCC=$\mathbf{CH_{vin}}$, 1H), 5.15 (t, *J* = 7.1 Hz, $\mathbf{CH_{vin}}$, 1H), 5.04 (br s, $\mathbf{CH_{vin}}$, 1H), 3.59 (t, *J* = 6.3 Hz, $\mathbf{CH_2}$OSi, 2H), 2.69 (t, *J* = 7.5 Hz, Ar$\mathbf{CH_2}$, 2H), 2.42 (dt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 2.31 (dt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 2.26-2.15 (m, 2 × $\mathbf{CH_2}$, 4H), 2.07 (t, *J* = 7.6 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.96 (t, *J* = 7.5 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.60 (s, $\mathbf{CH_3}$, 3H), 1.54 (s, $\mathbf{CH_3}$, 3H), 1.54-1.45 (m, $\mathbf{CH_2}CH_2OSi$, 2H), 1.38 (tt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}(CH_2)_3OSi$, 2H), 1.31-1.23 (m, $\mathbf{CH_2}(CH_2)_2OSi$, 2H), 0.88 (s, $SiC(\mathbf{CH_3})_3$, 9H), 0.04 (s, $Si(\mathbf{CH_3})_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.3, 137.4, 135.0, 132.2, 129.3, 123.9, 121.7, 119.2, 117.8, 114.6, 109.7, 63.3, 39.7, 38.4, 36.1, 34.5, 32.8, 30.0, 29.3, 27.8, 26.7, 26.0, 25.5, 18.5, 16.1, 16.0, −5.2. HRMS (ESI$^+$) exact mass calcd for $C_{33}H_{50}N_2OSiNa$ $[M+Na]^+$ requires *m/z* 541.3585, found *m/z* 541.3581.

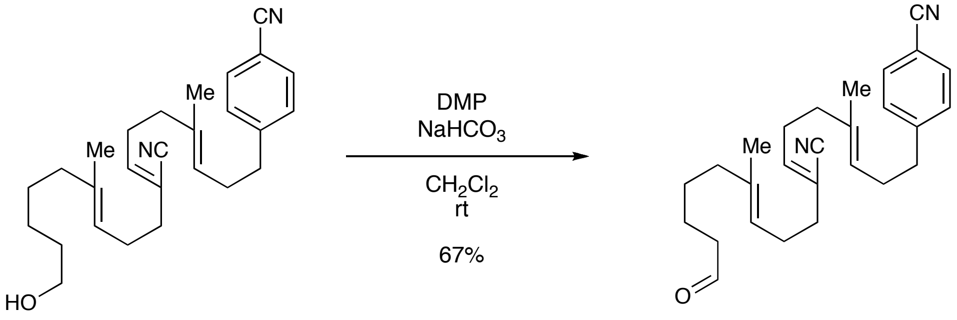
4.13.4 Synthesis of Aldehyde **1**



59

TBAF (2.6 mL of a 1.0M solution in THF, 2.6 mmol, 1.10 equiv) was added slowly to a solution of silyl ether **59** (1.23 g, 2.39 mmol, 1.00 equiv) in THF (22 mL) at room temperature. After stirring had been continued for 1.5 h, water (20 mL) and sat. NH_4Cl (20 mL) were added and the aqueous layer was extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (30% EtOAc/hexanes) furnished the free alcohol (967 mg, quant. yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3332, 2928, 2856, 2227, 1607, 1504, 1438, 1384, 1218, 1176, 1048, 824, 754, 678. ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J = 8.2 Hz, Ar**H**, 2H), 7.28 (d, J = 8.2 Hz, Ar**H**, 2H), 6.07 (t, J = 7.6 Hz, NCC=C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.15 (t, J = 7.1 Hz, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.05 (br s, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 3.64 (t, J = 6.6 Hz, C$\mathbf{H_2}$OH, 2H), 2.70 (t, J = 7.9 Hz, ArC$\mathbf{H_2}$, 2H), 2.42 (dt, J = 2 × 7.5 Hz, C$\mathbf{H_2}$CH$_{vin}$, 2H), 2.32 (dt, J = 2 × 7.4 Hz, C$\mathbf{H_2}$CH$_{vin}$, 2H), 2.26-2.15 (m, 2 × C$\mathbf{H_2}$, 4H), 2.07 (t, J = 7.6 Hz, C$\mathbf{H_2}$(CH$_3$)C=C, 2H), 1.98 (t, J = 7.5 Hz, C$\mathbf{H_2}$(CH$_3$)C=C, 2H), 1.62-1.52 (m, C$\mathbf{H_2}$CH$_2$OH, 2H), 1.59 (s, C$\mathbf{H_3}$, 3H), 1.54 (s, C$\mathbf{H_3}$, 3H), 1.44-1.37 (m, C$\mathbf{H_2}$(CH$_2$)$_3$OH, 2H), 1.35-1.28 (m, C$\mathbf{H_2}$(CH$_2$)$_2$OH, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.4, 137.2, 135.0, 132.2, 129.4, 124.0, 121.9, 119.2, 117.8, 114.6, 109.7, 63.0, 39.6, 38.4, 36.1, 34.4, 32.7, 30.0, 29.3, 27.7, 26.7, 25.4, 16.1, 16.0. HRMS (ESI$^+$) exact mass calcd for $C_{27}H_{36}N_2ONa$ $[M+Na]^+$ requires *m/z* 427.2720, found *m/z* 427.2718.



1

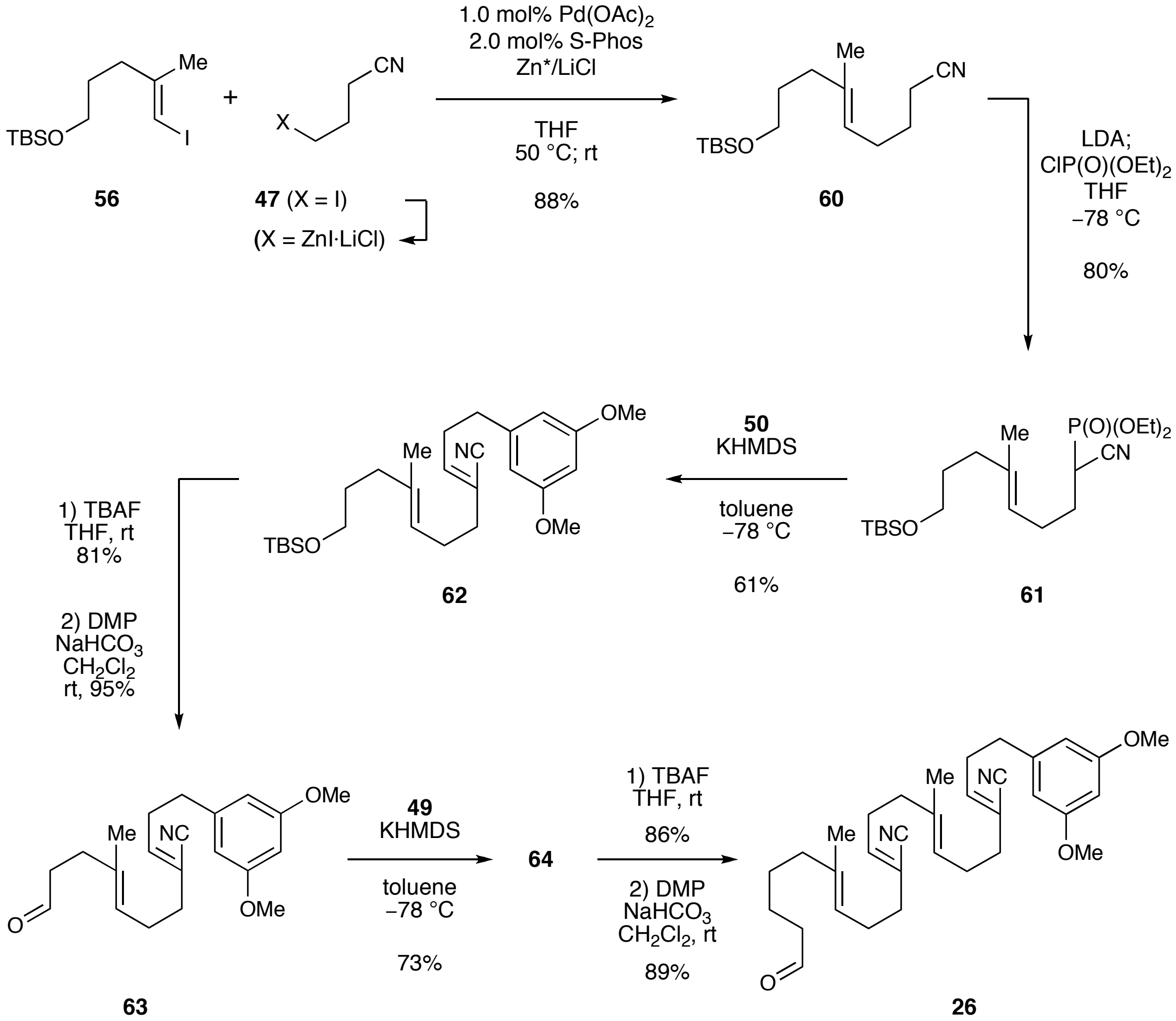
To a solution of the alcohol (967 mg, 2.39 mmol, 1.00 equiv) prepared in the previous step in CH_2Cl_2 (25 mL) and solid $NaHCO_3$ (1.01 g, 12.0 mmol, 5.00 equiv) was added Dess-Martin periodinane (1.75 g, 4.12 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na_2CO_3 (20 mL) and aqueous $Na_2S_2O_3$ (10 mL) was followed by extraction with CH_2Cl_2 (4 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (15% EtOAc/hexanes) furnished title compound **1** (602 mg, 67% yield, 92% *E,Z,E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2925, 2856, 2230, 2212, 1638, 1667, 1606, 1504, 1448, 1384, 1316, 1177, 1155, 1135, 1078, 1054, 1035, 1013, 854, 819, 752, 678. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.7 Hz, C**H**O, 1H), 7.57 (d, *J* = 7.7 Hz, Ar**H**, 2H), 7.28 (d, *J* = 8.3 Hz, Ar**H**, 2H), 6.06 (t, *J* = 7.6 Hz, NCC=$\mathbf{CH_{vin}}$, 1H), 5.14 (t, *J* = 7.0 Hz, $\mathbf{CH_{vin}}$, 1H), 5.05 (br s, $\mathbf{CH_{vin}}$, 1H), 2.70 (t, *J* = 7.9 Hz, Ar$\mathbf{CH_2}$, 2H), 2.47-2.37 (m, $\mathbf{CH_2}$CHO, $\mathbf{CH_2}CH_{vin}$, 4H), 2.31 (dt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 2.27-2.16 (m, 2 × $\mathbf{CH_2}$, 4H), 2.07 (t, *J* = 7.5 Hz, $\mathbf{CH_2}(CH_3)C=C$, 2H), 1.99 (t, *J* = 7.5 Hz, $\mathbf{CH_2}(CH_3)C=C$, 2H), 1.62-1.54 (m, $\mathbf{CH_2}CH_2CHO$, 2H), 1.59 (s, $\mathbf{CH_3}$, 3H), 1.54 (s, $\mathbf{CH_3}$, 3H), 1.45-1.37 (m, $\mathbf{CH_2}(CH_2)_2CHO$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.8, 147.8, 147.4, 136.6, 135.0, 132.2, 129.3, 124.0, 122.3, 119.2, 117.8, 114.6, 109.7, 43.8, 39.3, 38.4, 36.1, 34.4, 30.0, 29.3, 27.3, 26.7, 21.6, 16.02, 15.98. HRMS (ESI$^+$) exact mass calcd for $C_{27}H_{34}N_2ONa$ $[M+Na]^+$ requires *m*/*z* 425.2563, found *m*/*z* 425.2557.

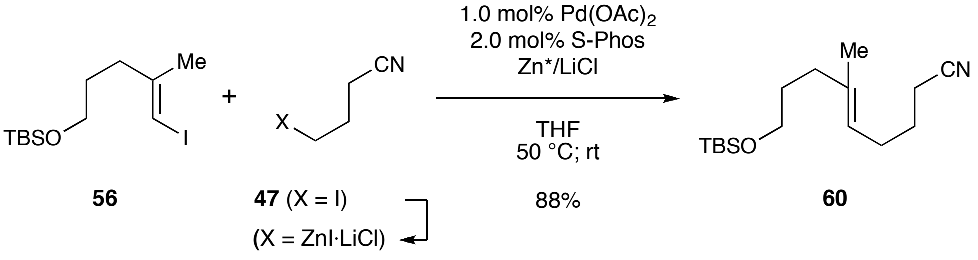
4.14 Synthesis of Pentacyclization Precursor 26

Pentacyclization substrate **26** was synthesized following a similar sequence than previously utilized to make tri- and tetracyclization precursors available (Scheme S4). Negishi cross-coupling[5] (**56**[20] → **60**), phosphonylation[15] (**60** → **61**), and two Horner-Wadsworth-Emmons coupling[16] stages (**61** → **62** and **63** → **64**) were used to assemble the polyunsaturated carbon skeleton.

Scheme S4. Synthesis of Pentacyclization Substrate **26**.



4.14.1 Synthesis of Intermediate **60**



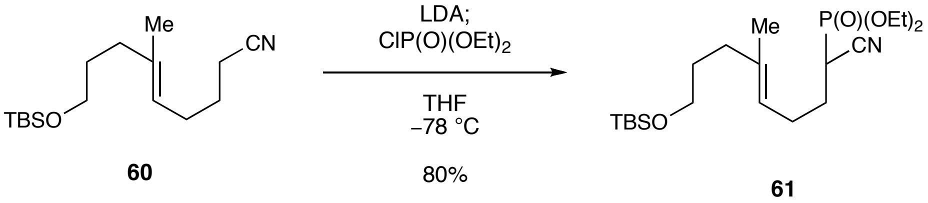
Anhydrous LiCl (636 mg, 15.0 mmol, 1.25 equiv) was placed in an argon-flushed 25-mL Schlenk flask and dried for 30 min at 150-180 °C under high vacuum (<1 torr) with slow stirring. Upon addition of zinc powder (325 mesh, 1.47 g, 22.5 mmol, 1.88 equiv) heating under high vacuum was continued for 30 min. After cooling to room temperature and backfilling with argon, the mixture was suspended with THF (15 mL). Subsequently, the zinc powder was activated by sequential addition of 1,2-dibromoethane (64 μL, 141 mg, 0.75 mmol, 0.05 equiv), TMSCl (3 drops), and iodine (15 drops of a 1M solution in THF); each addition followed by gentle heating to reflux with a heat gun. Portionwise addition of alkyl iodide **47** (3.86 g, 15.0 mmol, 1.25 equiv) at room temperature and subsequent stirring at for 4 h at 50 °C furnished a solution of alkyl zinc iodide that was allowed to cool to room temperature and separated via syringe from remaining zinc powder.

In a separate 50-mL Schlenk flask Pd(OAc)$_2$ (26.9 mg, 0.120 mmol, 0.0100 equiv) and S-Phos (98.5 mg, 0.240 mmol, 0.0200 equiv) was dissolved in THF (10 mL) and a solution of vinyl iodide **56** (4.42 g, 12.0 mmol, 1.00 equiv) in THF (4.0 mL) was added. The previously prepared solution of alkyl zinc reagent was quickly added via syringe leading to an exothermic reaction. Further stirring at room temperature for 3 h was followed by aqueous work-up with sat. NH$_4$Cl (50 mL) and extraction with EtOAc (4 × 30 mL). The combined organic layers were washed with brine (30 mL), dried (MgSO$_4$), and concentrated under reduced pressure. Purification by flash chromatography (5% EtOAc/hexanes) furnished title compound **60** (3.56 g, 88% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2929, 2895, 2856, 2248, 1471, 1462, 1386, 1360, 1252, 1187, 1095, 1006, 950, 833, 813, 773, 713, 661. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.07 (t, J = 7.2 Hz, **CH**$_{\mathbf{vin}}$, 1H), 3.58

(t, *J* = 6.5 Hz, **CH$_2$**OSi, 2H), 2.32 (t, *J* = 7.1 Hz, **CH$_2$**CN, 2H), 2.16 (dt, *J* = 2 × 7.2 Hz, **CH$_2$**CH$_{vin}$, 2H), 2.03 (t, *J* = 7.4 Hz, **CH$_2$**(CH$_3$)C=C, 2H), 1.71 (tt, *J* = 2 × 7.1 Hz, **CH$_2$**CH$_2$CN, 2H), 1.66-1.56 (m, **CH$_2$**CH$_2$OSi, 2H), 1.62 (s, **CH$_3$**, 3H), 0.89 (s, SiC(**CH$_3$**)$_3$, 9H), 0.04 (s, Si(**CH$_3$**)$_2$, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 137.6, 121.8, 120.0, 62.8, 35.9, 31.2, 26.7, 26.0, 25.6, 18.4, 16.5, 16.2, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{16}H_{32}NOSi$ [M+H]$^+$ requires *m/z* 282.2248, found *m/z* 282.2253.

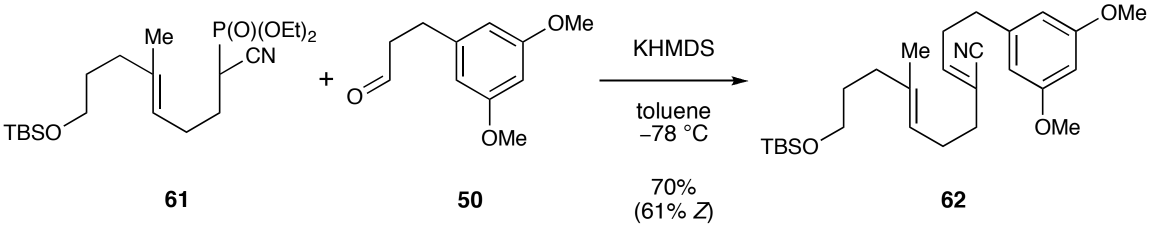
4.14.2 Synthesis of Phosphonate **61**



To a solution of *i*-Pr$_2$NH (3.04 mL, 2.30 g, 22.7 mmol, 2.20 equiv) in THF (35 mL) was added *n*-BuLi (8.6 mL of a 2.5M solution in hexanes, 21.6 mmol, 2.10 equiv) at –78 °C. After stirring at 0 °C for 30 min, the reaction mixture was cooled again to –78 °C and a solution of nitrile **60** (2.90 g, 10.3 mmol, 1.00 equiv) in THF (5 mL) was added and stirred for further 30 min at this temperature. Subsequently, diethyl chlorophosphate (1.48 mL, 1.78 g, 10.3 mmol, 1.05 equiv) was added dropwise to give a bright yellow solution. After 2 h stirring at –78 °C the reaction mixture was poured onto sat. NH$_4$Cl (40 mL) and water (40 mL) and the aqueous layer was extracted with EtOAc (4 x 30 mL). Washing of the combined organic phases with brine (50 mL), drying over MgSO$_4$ and evaporation under reduced pressure furnished the crude phosphonate that was purified by flash chromatography (30% EtOAc/hexanes) to give the title compound **61** (3.44 g, 80% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2930, 2857, 2242, 1472, 1463, 1445, 1389, 1255, 1163, 1096, 1048, 1016, 962, 903, 833, 813, 773, 714, 662. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.06 (t, *J* = 7.0 Hz, **CH$_{vin}$**, 1H), 4.29-4.18 (m, P(O**CH$_2$**CH$_3$)$_2$, 4H), 3.58 (t, *J* = 6.6 Hz, **CH$_2$**OSi, 2H), 2.93 (ddd, $J_{C,P}$ = 23.3 Hz, *J* = 8.8, 6.5 Hz, PC**H**CN, 1H), 2.38-2.19 (m, **CH$_2$**CH$_{vin}$, 2H), 2.03 (t, *J* = 7.9 Hz, **CH$_2$**(CH$_3$)C=C, 2H), 1.92 (tt, J = 2 × 7.6 Hz, $\mathbf{CH_2}$CHCN, 2H), 1.65 (s, $\mathbf{CH_3}$, 3H), 1.65-1.55 (m, $\mathbf{CH_2}$CH$_2$OSi, 2H), 1.38 (t, J = 7.1 Hz, P(OCH$_2$$\mathbf{CH_3}$)$_2$, 6H), 0.89 (s, SiC($\mathbf{CH_3}$)$_3$, 9H), 0.04 (s, Si($\mathbf{CH_3}$)$_2$, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 138.6, 121.0, 116.5 (d, $J_{C,P}$ = 9.3 Hz), 64.1 (d, $J_{C,P}$ = 7.0 Hz), 63.8 (d, $J_{C,P}$ = 6.9 Hz), 62.8, 35.9, 31.2, 29.3 (d, $J_{C,P}$ = 144 Hz), 27.1 (d, $J_{C,P}$ = 4.1 Hz), 26.0, 25.9, 18.4, 16.51 (d, $J_{C,P}$ = 3.8 Hz), 16.47 (d, $J_{C,P}$ = 3.9 Hz), 16.3, –5.2. ^{31}P NMR (202 MHz, CDCl$_3$) δ 18.4. HRMS (ESI$^+$) exact mass calcd for $C_{20}H_{41}NO_4PSi$ [M+H]$^+$ requires *m/z* 418.2537, found *m/z* 418.2537.

4.14.3 Synthesis of Diene **62**

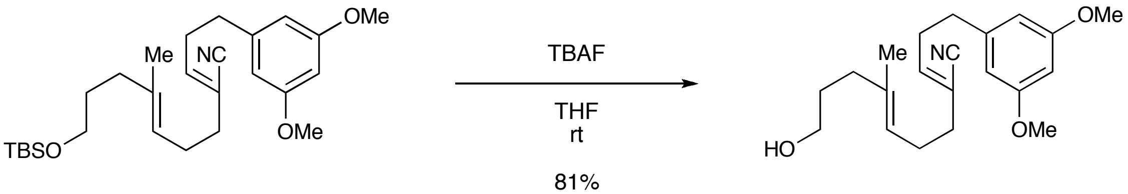


61 **50** **62**

To a solution of phosphonate **61** (2.23 g, 5.34 mmol, 1.00 equiv) in toluene (90 mL) at –78 °C was added dropwise a solution of KHMDS (1.08 g, 5.34 mmol, 1.00 equiv) in toluene (10 mL). After stirring had been continued for 1 h, a solution of aldehyde **50**[17] (876 mg, 5.34 mmol, 1.00 equiv) in toluene (10 mL) was added dropwise via syringe. The reaction mixture was stirred for 2 h at –78 °C, subsequently poured onto sat. NH$_4$Cl (80 mL), and extracted with EtOAc (4 × 40 mL). The combined organic layers were washed with brine (40 mL), dried (MgSO$_4$) and concentrated *in vacuo*. Purification by flash chromatography (4% EtOAc/hexanes) afforded title compound **62** (1.48 g, 61%, >20:1 *Z*/*E*) and its diastereomer (227 mg, 9% yield, 1:3 *Z*/*E*) as viscous oils.

IR (ATR) ν (cm^{-1}) 2929, 2856, 2214, 1595, 1461, 1429, 1386, 1350, 1316, 1293, 1253, 1204, 1150, 1095, 1066, 1006, 939, 925, 831, 774, 693, 661. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.38-6.28 (m, Ar**H**, 3H), 6.12 (t, J = 6.8 Hz, NCC=$\mathbf{CH_{vin}}$, 1H), 5.04 (br s, $\mathbf{CH_{vin}}$, 1H), 3.79 (s, OC$\mathbf{H_3}$, 6H), 3.58 (t, J = 6.5 Hz, $\mathbf{CH_2}$OSi, 2H), 2.74-2.61 (m, 2 × $\mathbf{CH_2}$, 4H), 2.21-2.15 (m, 2 × $\mathbf{CH_2}$, 4H), 2.00 (t, J = 7.4 Hz, $\mathbf{CH_2}$, 2H), 1.65-1.54 (m, $\mathbf{CH_2}$CH$_2$OSi, 2H), 1.60 (s, $\mathbf{CH_3}$, 3H), 0.89 (s, SiC($\mathbf{CH_3}$)$_3$, 9H), 0.04 (s, Si(C**H**$_3$)$_2$, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 160.9, 146.6, 142.7, 136.9, 121.8, 117.7, 115.1, 106.4, 98.2, 62.9, 55.4, 35.8, 35.1, 34.5, 32.8, 31.2, 26.7, 26.0, 18.4, 16.2, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{27}H_{43}NO_3SiNa$ [M+Na]$^+$ requires *m/z* 480.2904, found *m/z* 480.2902.

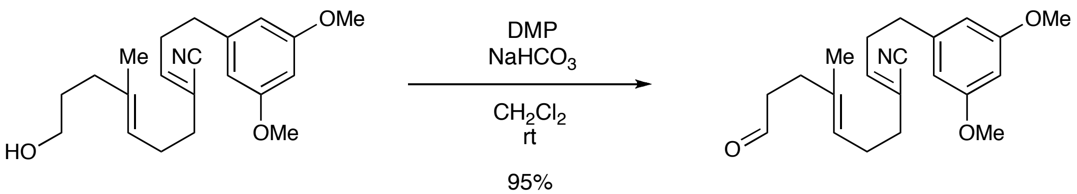
4.14.4 Synthesis of Aldehyde **63**



62

TBAF (3.5 mL of a 1.0M solution in THF, 3.5 mmol, 1.10 equiv) was added slowly to a solution of silyl ether **62** (1.47 g, 3.20 mmol, 1.00 equiv) in THF (30 mL) at room temperature. After stirring had been continued for 1.5 h, water (30 mL) and sat. NH$_4$Cl (30 mL) were added and the aqueous layer was extracted with EtOAc (4 × 25 mL). The combined organic layers were washed with brine (30 mL), dried (MgSO$_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (30% EtOAc/hexanes) furnished the free alcohol (889 mg, 81% yield) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3446, 2937, 2840, 2214, 1594, 1459, 1428, 1384, 1349, 1313, 1293, 1204, 1148, 1056, 1014, 923, 830, 693. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.36-6.29 (m, Ar**H**, 3H), 6.12 (t, *J* = 6.9 Hz, NCC=C**H**$_{\text{vin}}$, 1H), 5.06 (br s, C**H**$_{\text{vin}}$, 1H), 3.79 (s, OC**H**$_3$, 6H), 3.62 (td, *J* = 2 × 5.8 Hz, C**H**$_2$OH, 2H), 2.74-2.62 (m, 2 × C**H**$_2$, 4H), 2.25-2.15 (m, 2 × C**H**$_2$, 4H), 2.05 (t, *J* = 6.7 Hz, C**H**$_2$, 2H), 1.69-1.54 (m, C**H**$_2$CH$_2$OH, 2H), 1.61 (s, C**H**$_3$, 3H), 1.43 (br s, O**H**). ^{13}C NMR (125 MHz, CDCl$_3$) δ 160.9, 146.8, 142.6, 136.8, 122.3, 117.7, 115.0, 106.5, 98.2, 62.7, 55.4, 35.8, 35.0, 34.4, 32.7, 30.7, 26.6, 16.1. HRMS (ESI$^+$) exact mass calcd for $C_{21}H_{29}NO_3Na$ [M+Na]$^+$ requires *m/z* 366.2040, found *m/z* 366.2039.

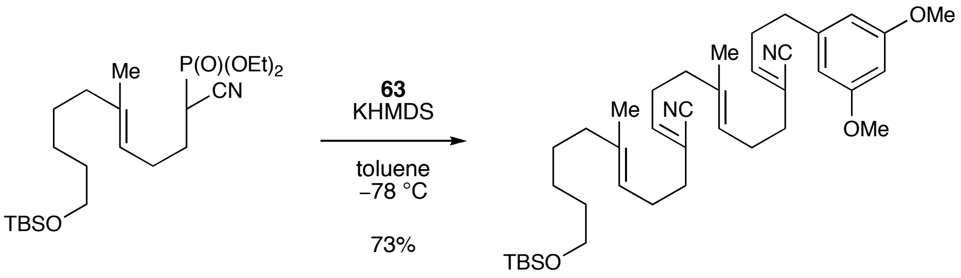


63

To a solution of the alcohol (859 mg, 2.50 mmol, 1.00 equiv) prepared in the previous step in CH_2Cl_2 (25 mL) and solid $NaHCO_3$ (1.05 g, 12.5 mmol, 5.00 equiv) was added Dess-Martin periodinane (1.59 g, 3.75 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na_2CO_3 (25 mL) and aqueous $Na_2S_2O_3$ (10 mL) was followed by extraction with CH_2Cl_2 (4 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **63** (811 mg, 95% yield, >20:1 *Z*:*E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2937, 2839, 2722, 2213, 1721, 1594, 1459, 1429, 1388, 1349, 1312, 1293, 1261, 1204, 1148, 1057, 1015, 993, 924, 831, 693. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (br s, C**H**O, 1H), 6.37-6.28 (m, Ar**H**, 3H), 6.12 (t, *J* = 6.9 Hz, NCC=C$\mathbf{H_{vin}}$, 1H), 4.99 (br s, C$\mathbf{H_{vin}}$, 1H), 3.79 (s, OC$\mathbf{H_3}$, 6H), 2.73-2.63 (m, 2 × C$\mathbf{H_2}$, 4H), 2.51 (t, *J* = 7.4 Hz, C$\mathbf{H_2}$CHO, 2H), 2.31 (t, *J* = 7.5 Hz, C$\mathbf{H_2}$$CH_2$CHO, 2H), 2.17-2.08 (m, 2 × C$\mathbf{H_2}$, 4H), 1.62 (s, C$\mathbf{H_3}$, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 160.9, 146.9, 142.6, 135.2, 122.9, 117.6, 114.9, 106.4, 98.2, 55.3, 42.0, 35.0, 34.2, 32.6, 31.7, 26.6, 16.3. HRMS (ESI$^+$) exact mass calcd for $C_{21}H_{28}NO_3$ $[M+H]^+$ requires *m/z* 342.2064, found *m/z* 342.2064.

4.14.5 Synthesis of Tetraene **64**

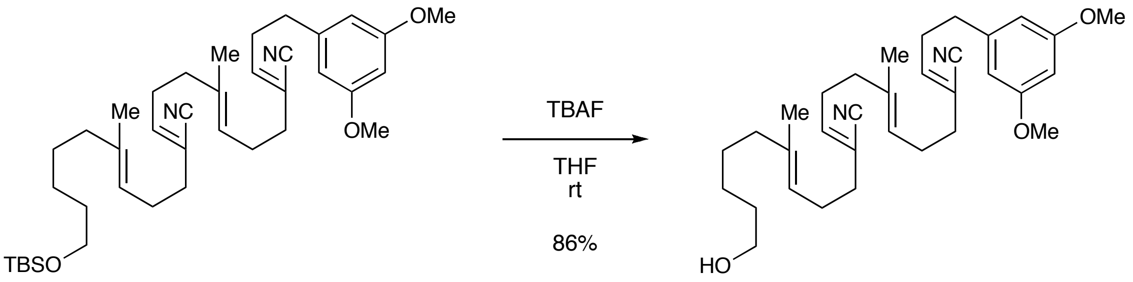


49 **64**

To a solution of phosphonate **49** (987 mg, 2.21 mmol, 1.00 equiv) in toluene (30 mL) at −78 °C was added dropwise a solution of KHMDS (441 mg, 2.21 mmol, 1.00 equiv) in toluene (3.0 mL). After stirring had been continued for 1 h, a solution of aldehyde **63** (755 mg, 2.21 mmol, 1.00 equiv) in toluene (3.0 mL) was added dropwise via syringe. The reaction mixture was stirred for 2 h at −78 °C, subsequently poured onto sat. NH_4Cl (40 mL), and extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (5%→10% EtOAc/hexanes) afforded title compound **64** (1.02 g, 73%, >95% *E,Z,E,Z*) as a viscous oil.

IR (ATR) ν (cm^{-1}) 2929, 2856, 2214, 1596, 1461, 1429, 1386, 1350, 1293, 1254, 1204, 1150, 1096, 1066, 1006, 938, 924, 832, 774, 693, 660. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.38-6.29 (m, Ar**H**, 3H), 6.14 (t, *J* = 6.5 Hz, NCC=C$\mathbf{H}_{\mathbf{vin}}$, 1H), 6.08 (t, *J* = 7.5 Hz, NCC=C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.11-4.98 (m, 2 × C$\mathbf{H}_{\mathbf{vin}}$, 2H), 3.79 (s, OC$\mathbf{H_3}$, 6H), 3.59 (t, *J* = 6.6 Hz, C$\mathbf{H_2}$OSi, 2H), 2.73-2.62 (m, 2 × C$\mathbf{H_2}$, 4H), 2.43 (dt, *J* = 2 × 7.4 Hz, NCC=CH$_{vin}$C$\mathbf{H_2}$, 2H), 2.25-2.15 (m, 4 × C$\mathbf{H_2}$, 8H), 2.06 (t, *J* = 7.5 Hz, C$\mathbf{H_2}$, 2H), 1.96 (t, *J* = 7.5 Hz, C$\mathbf{H_2}$, 2H), 1.62 (s, C$\mathbf{H_3}$, 3H), 1.59 (s, C$\mathbf{H_3}$, 3H), 1.51 (tt, *J* = 2 × 7.2 Hz, C$\mathbf{H_2}$CH$_2$OSi, 2H), 1.38 (tt, *J* = 2 × 7.4 Hz, C$\mathbf{H_2}$(CH$_2$)$_3$OSi, 2H), 1.27 (tt, *J* = 2 × 7.5 Hz, C$\mathbf{H_2}$(CH$_2$)$_2$OSi, 2H), 0.89 (s, SiC(C$\mathbf{H_3}$)$_3$, 9H), 0.04 (s, Si(C$\mathbf{H_3}$)$_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 147.3, 146.8, 142.6, 137.3, 135.5, 123.2, 121.7, 117.8, 117.6, 115.0, 114.6, 106.4, 98.2, 63.3, 55.4, 39.7, 38.3, 35.0, 34.5, 34.3, 32.8, 32.7, 30.0, 27.8, 26.7 (2 × **C**H$_2$), 26.1, 25.5, 18.5, 16.11, 16.09, −5.2. HRMS (ESI$^+$) exact mass calcd for $C_{39}H_{60}N_2O_3SiNa$ $[M+Na]^+$ requires *m/z* 655.4265, found *m/z* 655.4260.

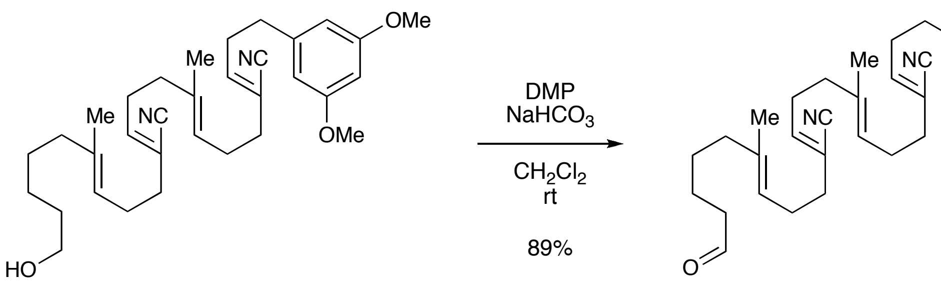
4.14.6 Synthesis of Aldehyde **26**



64

TBAF (1.72 mL of a 1.0M solution in THF, 1.72 mmol, 1.10 equiv) was added slowly to a solution of silyl ether **64** (984 mg, 1.56 mmol, 1.00 equiv) in THF (15 mL) at room temperature. After stirring had been continued for 1.5 h, water (15 mL) and sat. NH_4Cl (15 mL) were added and the aqueous layer was extracted with EtOAc (4 × 15 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (40% EtOAc/hexanes) furnished the free alcohol (692 mg, 86% yield, >95% *E,Z,E,Z*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3525, 2930, 2856, 2214, 1736, 1595, 1459, 1429, 1384, 1350, 1313, 1293, 1242, 1204, 1149, 1057, 924, 830, 730, 693, 655. ^1H NMR (500 MHz, $CDCl_3$) δ 6.37-6.27 (m, Ar**H**, 3H), 6.14 (t, J = 6.8 Hz, NCC=$\mathbf{CH_{vin}}$, 1H), 6.09 (t, J = 7.4 Hz, NCC=$\mathbf{CH_{vin}}$, 1H), 5.11-4.99 (m, 2 × $\mathbf{CH_{vin}}$, 2H), 3.78 (s, O$\mathbf{CH_3}$, 6H), 3.63 (td, J = 2 × 5.0 Hz, $\mathbf{CH_2}$OH, 2H), 2.73-2.63 (m, 2 × $\mathbf{CH_2}$, 4H), 2.43 (dt, J = 2 × 7.4 Hz, NCC=$CH_{vin}\mathbf{CH_2}$, 2H), 2.24-2.14 (m, 4 × $\mathbf{CH_2}$, 8H), 2.07 (t, J = 7.4 Hz, $\mathbf{CH_2}$, 2H), 1.97 (t, J = 7.5 Hz, $\mathbf{CH_2}$, 2H), 1.62 (s, $\mathbf{CH_3}$, 3H), 1.59 (s, $\mathbf{CH_3}$, 3H), 1.56 (tt, J = 2 × 7.2 Hz, $\mathbf{CH_2}CH_2OH$, 2H), 1.40 (tt, J = 2 × 7.6 Hz, $\mathbf{CH_2}(CH_2)_3OH$, 2H), 1.31 (tt, J = 2 × 7.5 Hz, $\mathbf{CH_2}(CH_2)_2OH$, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 147.4, 146.8, 142.6, 137.2, 135.4, 123.2, 121.9, 117.8, 117.6, 115.0, 114.5, 106.4, 98.2, 63.0, 55.3, 39.6, 38.3, 35.0, 34.4, 34.3, 32.7 (2 × $\mathbf{C}H_2$), 29.9, 27.7, 26.7 (2 × $\mathbf{C}H_2$), 25.4, 16.07, 16.05. HRMS (ESI$^+$) exact mass calcd for $C_{33}H_{46}N_2O_3SiNa$ $[M+Na]^+$ requires m/z 541.3401, found m/z 541.3401.



26

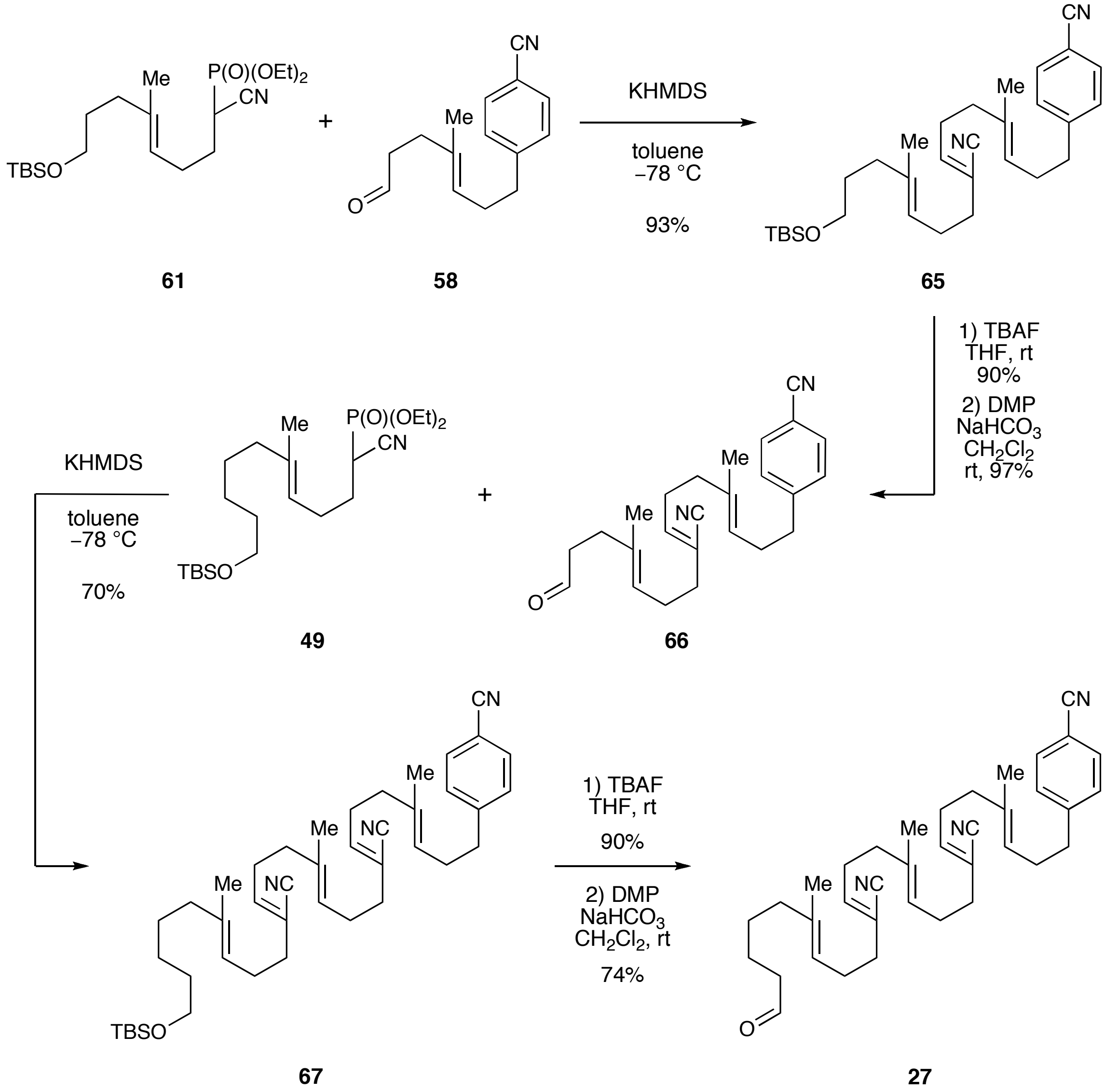
To a solution of the alcohol (609 mg, 1.17 mmol, 1.00 equiv) prepared in the previous step in CH_2Cl_2 (15 mL) and solid $NaHCO_3$ (491 mg, 5.85 mmol, 5.00 equiv) was added Dess-Martin periodinane (491 mg, 1.76 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na_2CO_3 (15 mL) and aqueous $Na_2S_2O_3$ (5 mL) was followed by extraction with CH_2Cl_2 (4 × 15 mL). The combined organic layers were washed with brine (15 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **26** (541 mg, 89% yield, >95% *E,Z,E,Z*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2935, 2859, 2723, 2213, 1722, 1595, 1458, 1429, 1386, 1350, 1315, 1293, 1240, 1204, 1149, 1058, 924, 831, 754, 694, 666. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (br s, C**H**O, 1H), 6.36-6.29 (m, Ar**H**, 3H), 6.14 (t, *J* = 6.7 Hz, NCC=C**H**$_{\mathbf{vin}}$, 1H), 6.09 (t, *J* = 7.4 Hz, NCC=C**H**$_{\mathbf{vin}}$, 1H), 5.13-5.00 (m, 2 × C**H**$_{\mathbf{vin}}$, 2H), 3.78 (s, OC**H**$_{\mathbf{3}}$, 6H), 2.74-2.63 (m, 2 × C**H**$_{\mathbf{2}}$, 4H), 2.46-2.38 (m, 2 × C**H**$_{\mathbf{2}}$, 4H), 2.25-2.15 (m, 4 × C**H**$_{\mathbf{2}}$, 8H), 2.07 (t, *J* = 7.5 Hz, C**H**$_{\mathbf{2}}$, 2H), 1.99 (t, *J* = 7.5 Hz, 2H), 1.64-1.53 (m, C**H**$_{\mathbf{2}}$CHO, 2H), 1.61 (s, C**H**$_{\mathbf{3}}$, 3H), 1.59 (s, C**H**$_{\mathbf{3}}$, 3H), 1.41 (tt, *J* = 2 × 7.6 Hz, C**H**$_{\mathbf{2}}$$CH_2$CHO, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.9, 160.9, 147.4, 146.8, 142.6, 136.6, 135.4, 123.2, 122.3, 117.8, 117.6, 115.0, 114.5, 106.4, 98.2, 55.4, 43.8, 39.3, 38.3, 35.0, 34.4, 34.3, 32.7, 30.0, 27.3, 26.7 (2 × **C**H_2), 21.6, 16.1, 16.0. HRMS (ESI$^+$) exact mass calcd for $C_{33}H_{45}N_2O_3$ $[M+H]^+$ requires *m/z* 517.3425, found *m/z* 517.3425.

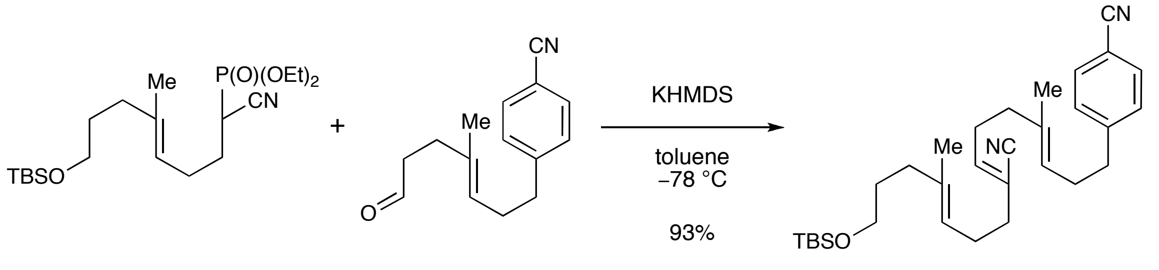
4.15 Synthesis of Hexacyclization Precursor 27

Hexacylization precursor **27** was prepared following a similar sequence as outlined above: Terminating unit **58** (*cf* section 4.13) was coupled with fragment **61** (*cf* section 4.14) to give triene **65** (Scheme S5). Upon deprotection and oxidation, and second Horner-Wadsworth-Emmons coupling[16] with phosphonate **49** (*cf* section 4.9) completed the assembly of the carbocyclic skeleton leading to silyl ether **67** that was further elaborated to give the desired aldehyde **27**.

Scheme S5. Synthesis of Hexacyclization Substrate **27**.



4.15.1 Synthesis of Triene **65**

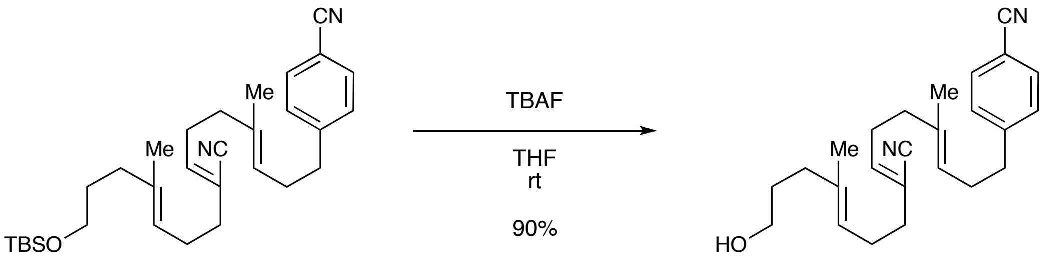


61 **58** **65**

To a solution of phosphonate **61** (1.13 g, 2.71 mmol, 1.00 equiv) in toluene (36 mL) at −78 °C was added dropwise a solution of KHMDS (541 mg, 2.71 mmol, 1.00 equiv) in toluene (6.0 mL). After stirring had been continued for 1 h, a solution of aldehyde **58** (615 mg, 2.71 mmol, 1.00 equiv) in toluene (6.0 mL) was added dropwise via syringe. The reaction mixture was stirred for 2 h at −78 °C, subsequently poured onto sat. NH_4Cl (50 mL), and extracted with EtOAc (4 × 25 mL). The combined organic layers were washed with brine (25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (5%→10% EtOAc/hexanes) afforded title compound **65** (1.24 g, 93%, 15:1 *Z*/*E*) as a viscous oil.

IR (ATR) ν (cm^{-1}) 2928, 2856, 2227, 1608, 1505, 1471, 1444, 1413, 1386, 1360, 1252, 1177, 1095, 1021, 1006, 953, 833, 774, 756, 665. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.2 Hz, Ar**H**, 2H), 7.28 (d, *J* = 8.2 Hz, Ar**H**, 2H), 6.07 (t, *J* = 7.5 Hz, NCC=C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.15 (t, *J* = 7.1 Hz, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.06 (br s, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 3.58 (t, *J* = 6.5 Hz, C$\mathbf{H}_2$OSi, 2H), 2.70 (t, *J* = 7.9 Hz, ArC$\mathbf{H}_2$, 2H), 2.42 (dt, *J* = 2 × 7.5 Hz, C$\mathbf{H}_2$CH$_{vin}$, 2H), 2.32 (dt, *J* = 2 × 7.4 Hz, C$\mathbf{H}_2$CH$_{vin}$, 2H), 2.27-2.16 (m, 2 × C$\mathbf{H}_2$, 4H), 2.07 (t, *J* = 7.6 Hz, C$\mathbf{H}_2$(CH$_3$)C=C, 2H), 2.01 (t, *J* = 7.5 Hz, C$\mathbf{H}_2$(CH$_3$)C=C, 2H), 1.64-1.56 (m, C$\mathbf{H}_2$CH$_2$OSi, 2H), 1.61 (s, C$\mathbf{H}_3$, 3H), 1.55 (s, C$\mathbf{H}_3$, 3H), 0.89 (s, SiC(C$\mathbf{H}_3$)$_3$, 9H), 0.04 (s, Si(C$\mathbf{H}_3$)$_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.3, 136.9, 135.0, 132.2, 129.3, 124.0, 121.9, 119.2, 117.8, 114.6, 109.7, 62.9, 38.4, 36.1, 35.9, 34.4, 31.2, 30.0, 29.3, 26.7, 26.0, 18.4, 16.2, 16.0, −5.2. HRMS (ESI$^+$) exact mass calcd for $C_{31}H_{46}N_2OSiNa$ [M+Na]$^+$ requires *m*/*z* 513.3272, found *m*/*z* 513.3270.

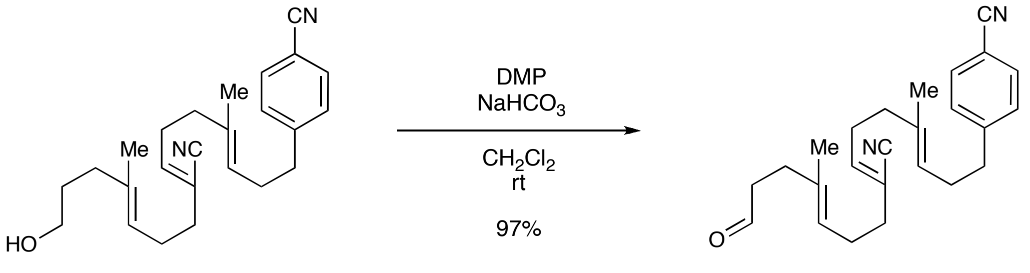
4.15.2 Synthesis of Aldehyde **66**



65

TBAF (2.80 mL of a 1.0M solution in THF, 2.80 mmol, 1.10 equiv) was added slowly to a solution of silyl ether **65** (1.24 g, 2.53 mmol, 1.00 equiv) in THF (23 mL) at room temperature. After stirring had been continued for 1.5 h, water (20 mL) and sat. NH_4Cl (20 mL) were added and the aqueous layer was extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (30% EtOAc/hexanes) furnished the free alcohol (857 mg, 90% yield, 91% *E,Z,E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3434, 2935, 2859, 2227, 1666, 1607, 1504, 1444, 1414, 1385, 1176, 1056, 1020, 824, 754, 666. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.2 Hz, Ar**H**, 2H), 7.27 (d, *J* = 8.3 Hz, Ar**H**, 2H), 6.05 (t, *J* = 7.5 Hz, NCC=$\mathbf{CH_{vin}}$, 1H), 5.13 (t, *J* = 6.7 Hz, $\mathbf{CH_{vin}}$, 1H), 5.09 (br s, $\mathbf{CH_{vin}}$, 1H), 3.60 (t, *J* = 6.9 Hz, $\mathbf{CH_2}$OH, 2H), 2.68 (t, *J* = 7.8 Hz, Ar$\mathbf{CH_2}$, 2H), 2.40 (dt, *J* = 2 × 7.6 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 2.30 (dt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 2.24-2.12 (m, 2 × $\mathbf{CH_2}$, 4H), 2.10-2.01 (m, 2 × $\mathbf{CH_2}(CH_3)C=C$, 4H), 1.69-1.61 (m, $\mathbf{CH_2}CH_2OH$, 2H), 1.61 (s, $\mathbf{CH_3}$, 3H), 1.53 (s, $\mathbf{CH_3}$, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.5, 136.7, 135.0, 132.1, 129.3, 123.9, 122.3, 119.2, 117.7, 114.5, 109.6, 62.6, 38.3, 36.1, 35.9, 34.4, 30.7, 29.9, 29.3, 26.7, 16.1, 15.9. HRMS (ESI$^+$) exact mass calcd for $C_{25}H_{32}N_2ONa$ $[M+Na]^+$ requires *m/z* 399.2407, found *m/z* 399.2407.

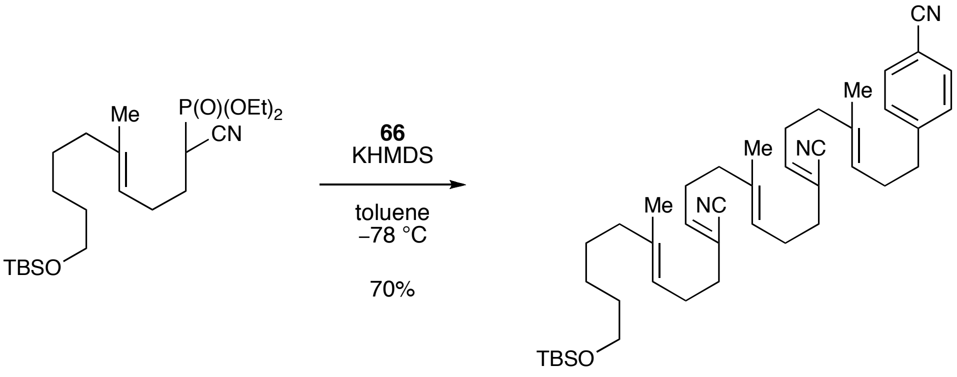


66

To a solution of the alcohol (1.13 g, 3.00 mmol, 1.00 equiv) prepared in the previous step in CH_2Cl_2 (30 mL) and solid $NaHCO_3$ (1.26 g, 15.0 mmol, 5.00 equiv) was added Dess-Martin periodinane (1.91 g, 4.50 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na_2CO_3 (30 mL) and aqueous $Na_2S_2O_3$ (10 mL) was followed by extraction with CH_2Cl_2 (4 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (30% EtOAc/hexanes) furnished title compound **66** (1.09 g, 97% yield, 91% *E,Z,E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2922, 2857, 2227, 1721, 1607, 1504, 1444, 1413, 1386, 1224, 1177, 1092, 1020, 825, 752, 666. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.74 (t, *J* = 1.7 Hz, C**H**O, 1H), 7.56 (d, *J* = 8.2 Hz, Ar**H**, 2H), 7.27 (d, *J* = 8.2 Hz, Ar**H**, 2H), 6.05 (t, *J* = 7.5 Hz, NCC=$\mathbf{CH_{vin}}$, 1H), 5.14 (t, *J* = 6.5 Hz, $\mathbf{CH_{vin}}$, 1H), 5.08 (br s, $\mathbf{CH_{vin}}$, 1H), 2.69 (t, *J* = 7.4 Hz, Ar$\mathbf{CH_2}$, 2H), 2.52 (td, *J* = 7.3, 1.8 Hz, $\mathbf{CH_2}$CHO, 2H), 2.41 (dt, *J* = 2 × 7.4 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 2.36-2.27 (m, 2 × $\mathbf{CH_2}$, 4H), 2.25-2.14 (m, 2 × $\mathbf{CH_2}(CH_3)$C=C, 4H), 2.06 (t, *J* = 7.5 Hz, $\mathbf{CH_2}CH_2$CHO, 2H), 1.62 (s, $\mathbf{CH_3}$, 3H), 1.53 (s, $\mathbf{CH_3}$, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 147.8, 147.6, 135.1, 134.9, 132.1, 129.3, 123.9, 123.0, 119.2, 117.7, 114.5, 109.6, 42.0, 38.3, 36.1, 34.2, 31.7, 29.9, 29.3, 26.6, 16.3, 15.9. HRMS (ESI$^+$) exact mass calcd for $C_{25}H_{30}N_2ONa$ $[M+Na]^+$ requires *m/z* 397.2250, found *m/z* 397.22251.

4.15.3 Synthesis of Pentaene **67**

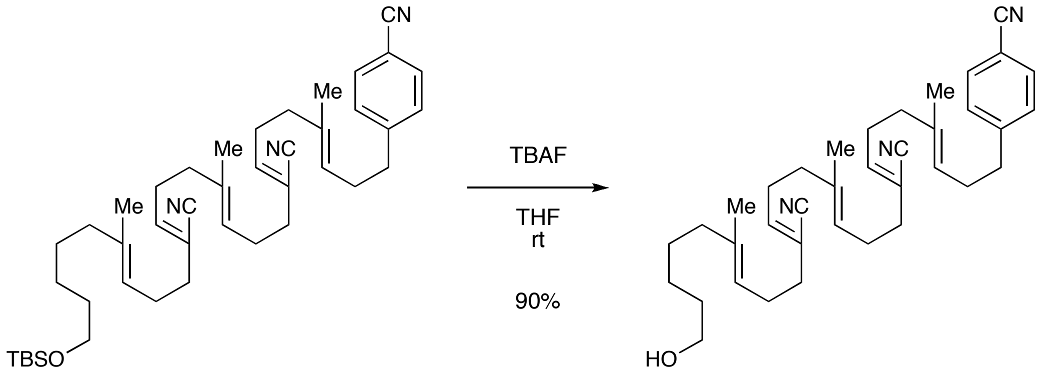


49 **67**

To a solution of phosphonate **49** (978 mg, 2.19 mmol, 1.00 equiv) in toluene (30 mL) at −78 °C was added dropwise a solution of KHMDS (437 mg, 2.19 mmol, 1.00 equiv) in toluene (5.0 mL). After stirring had been continued for 1 h, a solution of aldehyde **66** (820 mg, 2.19 mmol, 1.00 equiv) in toluene (5.0 mL) was added dropwise via syringe. The reaction mixture was stirred for 2 h at −78 °C, subsequently poured onto sat. NH_4Cl (50 mL), and extracted with EtOAc (4 × 25 mL). The combined organic layers were washed with brine (25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (5%→10% EtOAc/hexanes) afforded the title compound **67** (1.03 g, 70%, 91% *E,Z,E,Z,E*) as a viscous oil.

IR (ATR) ν (cm^{-1}) 2928, 2856, 2227, 2214, 1608, 1504, 1440, 1386, 1360, 1253, 1176, 1096, 1006, 938, 833, 774, 661. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.1 Hz, Ar**H**, 2H), 7.28 (d, *J* = 8.2 Hz, Ar**H**, 2H), 6.13-6.05 (m, 2 × NCC=$\mathbf{CH_{vin}}$, 2H), 5.15 (t, *J* = 6.7 Hz, $\mathbf{CH_{vin}}$, 1H), 5.09 (br s, $\mathbf{CH_{vin}}$, 1H), 5.04 (br s, $\mathbf{CH_{vin}}$, 1H), 3.59 (t, *J* = 6.6 Hz, $\mathbf{CH_2}$OSi, 2H), 2.70 (t, *J* = 7.5 Hz, Ar$\mathbf{CH_2}$, 2H), 2.48-2.38 (m, 2 × $\mathbf{CH_2}CH_{vin}$, 4H), 2.32 (dt, *J* = 2 × 7.3 Hz, $\mathbf{CH_2}CH_{vin}$, 2H), 2.27-2.15 (m, 4 × $\mathbf{CH_2}$, 8H), 2.14-2.03 (m, 2 × $\mathbf{CH_2}(CH_3)C{=}C$, 4H), 1.96 (t, *J* = 7.5 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.65 (s, $\mathbf{CH_3}$, 3H), 1.59 (s, $\mathbf{CH_3}$, 3H), 1.54 (s, $\mathbf{CH_3}$, 3H), 1.54-1.46 (m, $\mathbf{CH_2}CH_2OSi$, 2H), 1.38 (tt, *J* = 2 × 7.5 Hz, $\mathbf{CH_2}(CH_2)_3OSi$, 2H), 1.31-1.22 (m, $\mathbf{CH_2}(CH_2)_2OSi$, 2H), 0.89 (s, $SiC(\mathbf{CH_3})_3$, 9H), 0.04 (s, $Si(\mathbf{CH_3})_2$, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.5, 147.3, 137.4, 135.5, 135.0, 132.2, 129.3, 124.0, 123.2, 121.7, 119.2, 117.8, 117.7, 114.6, 114.5, 109.7, 63.3, 39.7, 38.4, 38.3, 36.1, 34.5, 34.3, 32.8, 30.02, 30.01, 29.3, 27.8, 26.8, 26.7, 26.0, 25.5, 18.5, 16.2, 16.1, 16.0, –5.2. HRMS (ESI$^+$) exact mass calcd for $C_{43}H_{63}N_3OSiNa$ $[M+Na]^+$ requires *m*/*z* 688.4633, found *m*/*z* 688.4629.

4.15.4 Synthesis of Aldehyde **27**

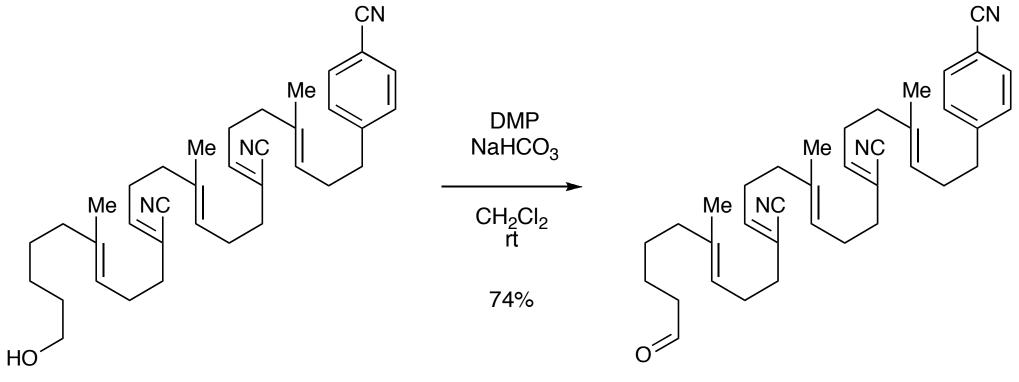


67

TBAF (1.60 mL of a 1.0M solution in THF, 1.60 mmol, 1.14 equiv) was added slowly to a solution of silyl ether **67** (932 mg, 1.40 mmol, 1.00 equiv) in THF (13 mL) at room temperature.

After stirring had been continued for 1.5 h, water (20 mL) and sat. NH_4Cl (20 mL) were added and the aqueous layer was extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (30% EtOAc/hexanes) furnished the free alcohol (857 mg, 90% yield, 88% *E,Z,E,Z,E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 3518, 2925, 2856, 2230, 2212, 1667, 1638, 1606, 1504, 1448, 1384, 1316, 1177, 1135, 1078, 1054, 1035, 1013, 854, 819, 752, 678. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.2 Hz, Ar**H**, 2H), 7.28 (d, *J* = 8.2 Hz, Ar**H**, 2H), 6.14-6.05 (m, 2 × NCC=$\mathbf{CH_{vin}}$, 2H), 5.15 (t, *J* = 6.2 Hz, $\mathbf{CH_{vin}}$, 1H), 5.09 (br s, $\mathbf{CH_{vin}}$, 1H), 5.04 (br s, $\mathbf{CH_{vin}}$, 1H), 3.63 (t, *J* = 6.4 Hz, $\mathbf{CH_2}$OH, 2H), 2.70 (t, *J* = 7.7 Hz, Ar$\mathbf{CH_2}$, 2H), 2.48-2.37 (m, 2 × $\mathbf{CH_2}CH_{vin}$, 4H), 2.36-2.28 (m, $\mathbf{CH_2}CH_{vin}$, 2H), 2.27-2.15 (m, 4 × $\mathbf{CH_2}$, 8H), 2.13-2.04 (m, 2 × $\mathbf{CH_2}(CH_3)C{=}C$, 4H), 1.98 (t, *J* = 7.2 Hz, $\mathbf{CH_2}(CH_3)C{=}C$, 2H), 1.63 (s, $\mathbf{CH_3}$, 3H), 1.61-1.52 (m, $\mathbf{CH_2}CH_2OH$, 2H), 1.59 (s, $\mathbf{CH_3}$, 3H), 1.54 (s, $\mathbf{CH_3}$, 3H), 1.44-1.28 (m, $\mathbf{CH_2}(CH_2)_3OH$, $\mathbf{CH_2}(CH_2)_2OH$, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.5, 147.4, 137.2, 135.5, 135.0, 132.2, 129.4, 124.0, 123.2, 121.9, 119.2, 117.8, 117.7, 114.6, 114.5, 109.7, 63.0, 39.6, 38.4, 38.3, 36.1, 34.4, 34.3, 32.8, 30.02, 29.99, 29.3, 27.7, 26.8, 26.7, 25.4, 16.2, 16.1, 16.0. HRMS (ESI$^+$) exact mass calcd for $C_{37}H_{49}N_3ONa$ [M+Na]$^+$ requires *m/z* 574.3768, found *m/z* 574.3764.



27

To a solution of the alcohol (660 mg, 1.23 mmol, 1.00 equiv) prepared in the previous step in CH_2Cl_2 (12 mL) and solid $NaHCO_3$ (517 mg, 6.15 mmol, 5.00 equiv) was added Dess-Martin periodinane (781 mg, 1.84 mmol, 1.50 equiv) and water (1 drop). The resultant mixture was stirred for 20 min at room temperature. Addition of sat. Na_2CO_3 (20 mL) and aqueous $Na_2S_2O_3$ (5 mL) was followed by extraction with CH_2Cl_2 (4 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished title compound **27** (485 mg, 74% yield, 88% *E,Z,E,Z,E*) as a colorless oil.

IR (ATR) ν (cm^{-1}) 2930, 2857, 2721, 1722, 1607, 1504, 1444, 1413, 1385, 1239, 1176, 1091, 1020, 826, 754, 666. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (s, C**H**O, 1H), 7.57 (d, *J* = 8.0 Hz, Ar**H**, 2H), 7.28 (d, *J* = 7.8 Hz, Ar**H**, 2H), 6.14-6.04 (m, 2 × NCC=C$\mathbf{H}_{\mathbf{vin}}$, 2H), 5.14 (t, *J* = 6.7 Hz, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.09 (br s, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 5.05 (br s, C$\mathbf{H}_{\mathbf{vin}}$, 1H), 2.69 (t, *J* = 7.7 Hz, ArC$\mathbf{H_2}$, 2H), 2.48-2.37 (m, C$\mathbf{H_2}$CHO, 2 × C$\mathbf{H_2}$CH_{vin}, 6H), 2.36-2.27 (m, C$\mathbf{H_2}$CH_{vin}, 2H), 2.25-2.14 (m, 4 × C$\mathbf{H_2}$, 8H), 2.12-2.03 (m, 2 × C$\mathbf{H_2}$(CH_3)C=C, 4H), 1.98 (t, *J* = 7.5 Hz, C$\mathbf{H_2}$(CH_3)C=C, 2H), 1.63 (s, C$\mathbf{H_3}$, 3H), 1.61-1.53 (m, C$\mathbf{H_2}$$CH_2$CHO, 2H), 1.59 (s, C$\mathbf{H_3}$, 3H), 1.52 (s, C$\mathbf{H_3}$, 3H), 1.44-1.36 (m, C$\mathbf{H_2}$($CH_2$)$_2$CHO, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.8, 147.8, 147.5, 147.4, 136.6, 135.4, 135.0, 132.1, 129.3, 123.9, 123.2, 122.3, 119.2, 117.74, 117.69, 114.6, 114.5, 109.6, 43.8, 39.3, 38.3 (2 × **C**H_2), 36.1, 34.4, 34.3, 29.99, 29.98, 29.3, 27.3, 26.8, 26.7, 21.6, 16.1, 16.00, 15.96. HRMS (ESI$^+$) exact mass calcd for $C_{37}H_{47}N_3ONa$ $[M+Na]^+$ requires *m/z* 572.3611, found *m/z* 572.3605.

5 X-ray Crystallographic Proof of Stereochemistry

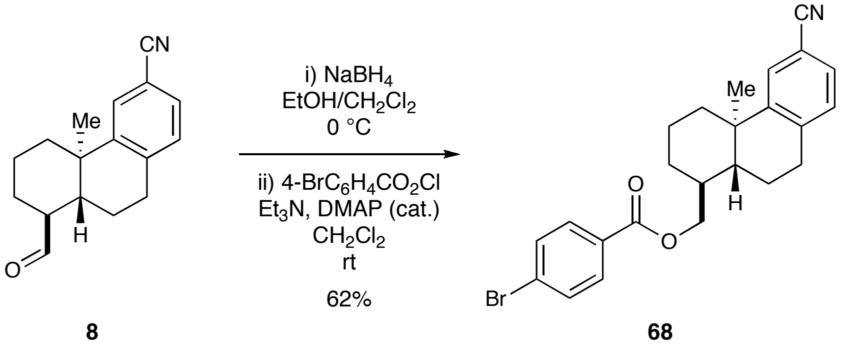
The absolute configuration of tricyclic aldehyde **8** was determined after derivatization to incorporate a heavy atom. X-ray crystallographic analysis of derivative **68** secured absolute and relative stereochemistry based on anomalous dispersion (see Section 5.3.2 for the crystallographic report). The absolute stereochemistry of all other polycyclic aldehydes was assigned accordingly. Additionally, crystallographic analyses of suitable single crystals of tricyclic **8** and tetracyclic **13** secured the assigned product structures (see Section 5.3.1 & 5.3.3).

5.1 X-ray Crystallographic Proof of Aldehyde 8

Single crystals of **8** suitable for X-ray crystallographic analysis were obtained by a single recrystallization at room temperature using hexanes/$CHCl_3$ as a solvent by slow evaporation. X-ray crystallographic analysis was conducted at the X-ray diffraction facility of the Department of Chemistry at the University of Pennsylvania, Philadephia/PA. See Section 5.3.1 for the crystallographic report.

5.2 Chemical Derivatization of Aldehyde 8

5.2.1 Synthesis of 4-Bromobenzoate **68**



To a solution of the aldehyde **8** (68.2 mg, 0.267 mmol, 1.00 equiv) in CH_2Cl_2 (3.0 mL) at 0 ºC was added a solution of $NaBH_4$ (50.6 mg, 1.34 mmol, 5.00 equiv) in EtOH (2.0 mL). The resultant mixture was allowed to warm to room temperature and stirred for 2 h. Careful addition of water (5 mL) and aq. HCl (10 mL) was followed by extraction with CH_2Cl_2 (4 × 5 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (20% EtOAc/hexanes) furnished the alcohol intermediate (62 mg, 90% yield) which was directly subjected to the following step.

To a solution of the alcohol intermediate (62 mg, 0.24 mmol, 1.00 equiv) in CH_2Cl_2 (5.0 mL) and DMAP (2.9 mg, 0.024 mmol, 0.10 equiv) at room temprature was added Et_3N (50 μL, 0.36 mmol, 1.50 equiv) followed by 4-bromobenzoyl chloride. The resultant solution was stirred for 2 h at room temperature. Addition of water (15 mL) was followed by extraction with CH_2Cl_2 (4 × 5 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (10% EtOAc/hexanes) furnished title the bromobenzoate **68** (73 mg, 69% yield).

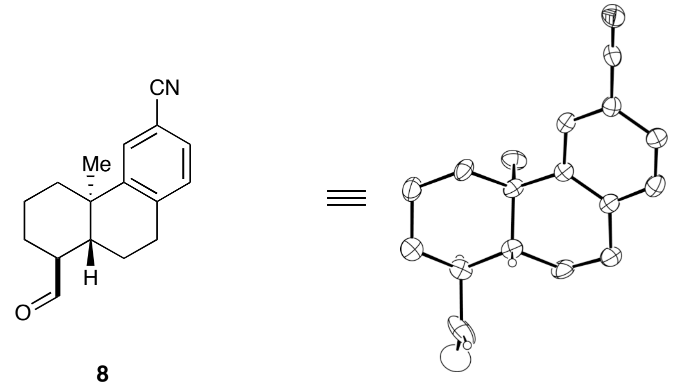
Single crystals of **68** suitable for X-ray crystallographic analysis were obtained by a single recrystallization at room temperature using hexanes/$CHCl_3$ as a solvent by slow evaporation. X-ray crystallographic analysis was conducted at the X-ray diffraction facility of the Department of Chemistry at University of Pennsylvania, Philadephia/PA. See Section 5.3.2 for the crystallographic report.

IR (ATR) ν (cm^{-1}) 3069, 2921, 2856, 2222, 1922, 1714, 1591, 1485, 1462, 1440, 1429, 1398, 1378, 1361, 1332, 1272, 1239, 1172, 1135, 1119, 1103, 1069, 1012, 961, 942, 921, 884, 857, 845, 815, 753, 711, 681, 623. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.3 Hz, Ar**H**, 2H), 7.60 (s, Ar**H**, 1H), 7.59 (d, J = 8.6 Hz, Ar**H**, 2H), 7.38 (d, J = 7.5 Hz, Ar**H**, 1H), 7.15 (d, J = 7.7 Hz, Ar**H**, 1H), 4.44-4.36 (m, $OCH_A\mathbf{H_B}$, 1H), 4.34-4.26 (m, $O\mathbf{CH_A}H_B$, 1H), 3.00-2.81 (m, $Ar\mathbf{CH_2}$, 2H), 2.27 (d, J = 12.6 Hz, $CH_A\mathbf{H_B}$, 1H), 2.09-1.99 (m, $CH_A\mathbf{H_B}$, 1H), 1.99-1.37 (m, 2 × $CH_A\mathbf{H_B}$, 3 × $C\mathbf{H_A}H_B$, 2 × C**H**, 7H), 1.36-1.22 (m, $C\mathbf{H_A}H_B$, 1H), 1.14 (s, $C\mathbf{H_3}$, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 149.0, 141.2, 131.9, 131.1, 130.0, 129.2, 128.9, 128.2 (2 ×), 119.7, 109.5, 68.1, 43.7, 37.6, 37.4, 36.6, 30.3, 29.4, 22.5, 21.4, 20.8. HRMS (ESI$^+$) exact mass calcd for $C_{24}H_{25}BrNO_2$ $[M+H]^+$ requires m/z 438.1063, found m/z 438.1061. $[\alpha]_D^{24}$ = –64.4 (c = 0.82, $CHCl_3$).

5.3 X-ray Crystallographic Reports

5.3.1 Aldehyde **8**

X-ray Structure Determination of Compound 99119



8

Compound 99119, $C_{17}H_{19}NO$, crystallizes in the monoclinic space group $P2_1$ (systematic absences 0k0: k=odd) with a=7.7406(6)Å, b=25.5147(18)Å, c=14.5225(11)Å, β=91.630(3)°, V=2867.0(4)$Å^3$, Z=8, and d_{calc}=1.174 g/cm^3 . X-ray intensity data were collected on a Rigaku Mercury CCD area detector employing graphite-monochromated Mo-Kα radiation (λ=0.71073 Å) at a temperature of 143(1)K. Preliminary indexing was performed from a series of twelve 0.5° rotation images with exposures of 30 seconds. A total of 1060 rotation images were collected with a crystal to detector distance of 50 mm, a 2θ swing angle of -14°, rotation widths of 0.5° and exposures of 30 seconds:

scan no.	scan type	ω	χ	ϕ
1	ϕ	10.0	20.0	225.0 — 525.0
2	ϕ	0.0	-60.0	110.0 — 140.0
3	ϕ	0.0	-30.0	280.0 — 480.0

Rotation images were processed using CrystalClear[21], producing a listing of unaveraged F^2 and

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(21) CrystalClear: Rigaku Corporation, 1999.

$\sigma(F^2)$ values which were then passed to the CrystalStructure[22] program package for further processing and structure solution on a Dell Pentium 4 computer. It became apparent during data collection that the crystal was twinned; there were a number of “double spots”. Two twin components were found by the twinsolve module of CrystalClear; the two components were related by a rotation of 180° about the 1 0 0 reciprocal direction. A total of 33406 reflections were measured over the ranges $2.63 \leq \theta \leq 25.12°$, $-8 \leq h \leq 9$, $-30 \leq k \leq 30$, $-17 \leq l \leq 17$. The intensity data were corrected for Lorentz and polarization effects and for absorption using REQAB[23] (minimum and maximum transmission 0.9224, 1.0000).

The structure was solved by direct methods (SIR97[24]). The asymmetric unit consists of four molecules. Refinement was by full-matrix least squares based on F^2 using SHELXL-97.[25] All reflections were used during refinement. The weighting scheme used was $w=1/[\sigma^2(F_o^2)+(0.0763P)^2 + 3.5526P]$ where $P = (F_o^2 + 2F_c^2)/3$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using a riding model. Refinement converged to R1=0.0838 and wR2=0.1914 for 24705 observed reflections for which $F > 4\sigma(F)$ and R1=0.1200 and wR2=0.2158 and GOF =1.143 for all 33406 unique, non-zero reflections and 692 variables.[26] The maximum Δ/σ in the final cycle of least squares was 0.001 and the two most prominent peaks in the final difference Fourier were +0.345 and -0.341 e/Å^3. The twinning parameter refined to a value of 0.3835(7).

Table 1. lists cell information, data collection parameters, and refinement data. Final positional and equivalent isotropic thermal parameters are given in Tables 2. and 3. Anisotropic thermal

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(22) CrystalStructure: Crystal Structure Analysis Package, Rigaku Corp. Rigaku/MSC, 2002.

(23) REQAB4: Jacobsen R. A. **1994**, private communication.

(24) SIR97: Altomare, A.; Burla M.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A.; Polidori G.; Spagna, R. *J. Appl. Cryst.* **1999**, *32*, 115.

(25) SHELXL-97: Sheldrick, G.M. *Acta Cryst.* **2008**, *A64*, 112.

(26) $R1 = S||F_o| - |F_c|| / S\,|F_o|$
$wR2 = [Sw(F_o^2 - F_c^2)^2/Sw(F_o^2)^2]^{½}$
$GOF = [Sw(F_o^2 - F_c^2)^2/(n - p)]^{½}$
where n = the number of reflections and p = the number of parameters refined.

parameters are in Table 4. Tables 5. and 6. list bond distances and bond angles. Figure 1. is an ORTEP[27] representation of the molecule with 30% probability thermal ellipsoids displayed.

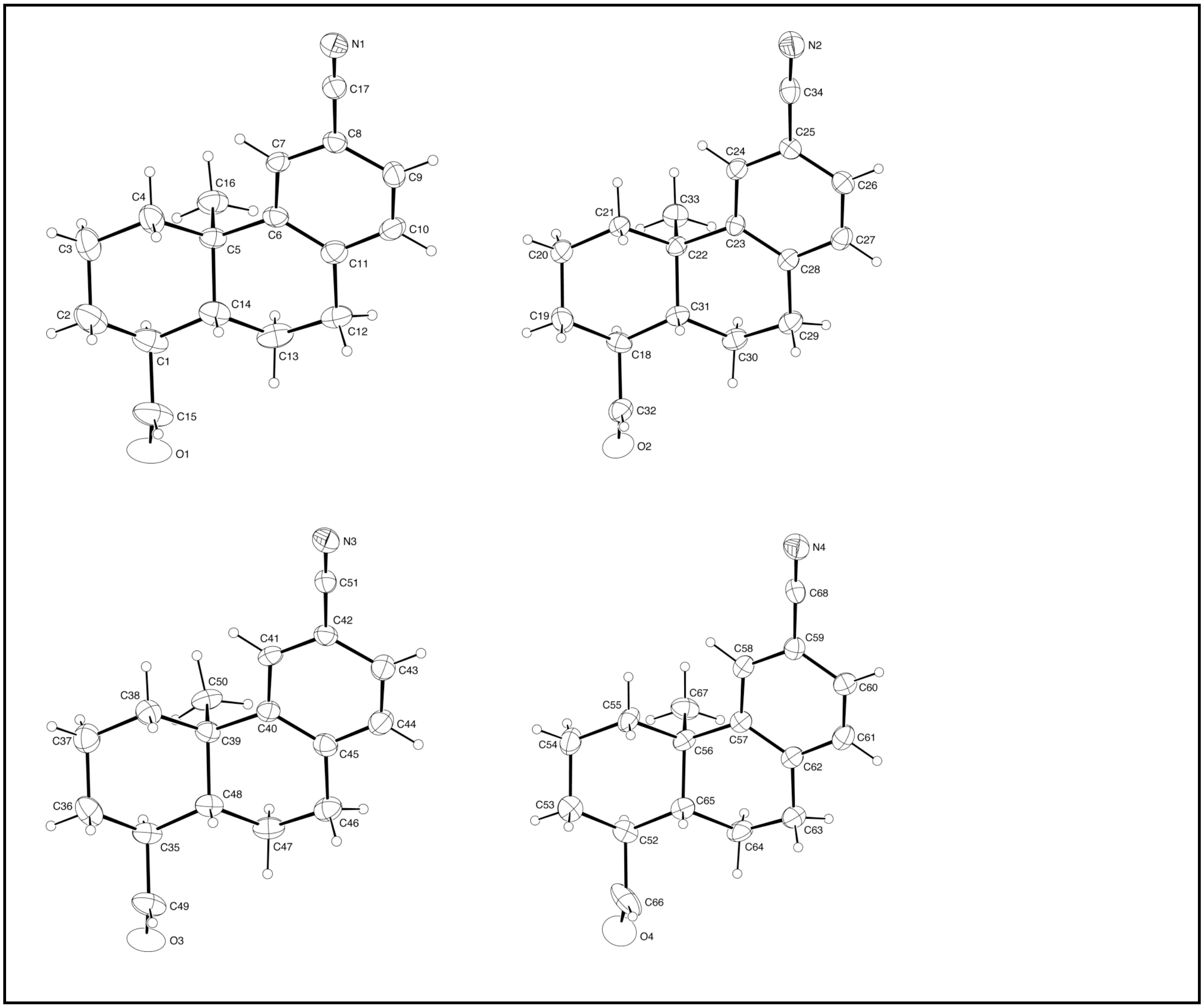

Figure 1. ORTEP drawing of the four molecules in the asymmetric unit with 30% probability thermal ellipsoids.

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(27) "ORTEP-II: A Fortran Thermal Ellipsoid Plot Program for Crystal Structure Illustrations". Johnson, C. K. (1976) ORNL-5138.

Table 1. Summary of Structure Determination of Compound 99119

Empirical formula	$C_{17}H_{19}NO$
Formula weight	253.33
Temperature	143(1) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P\ 2_1$
Cell constants:	
a	7.7406(6) Å
b	25.5147(18) Å
c	14.5225(11) Å
β	91.630(3)°
Volume	2867.0(4) $Å^3$
Z	8
Density (calculated)	1.174 Mg/m^3
Absorption coefficient	0.072 mm^{-1}
F(000)	1088
Crystal size	0.32 x 0.12 x 0.10 mm^3
Theta range for data collection	2.63 to 25.12°
Index ranges	$-8 \leq h \leq 9$, $-30 \leq k \leq 30$, $-17 \leq l \leq 17$
Reflections collected	33406
Independent reflections	33406 [R(int) = 0.0000]
Completeness to theta = 25.12°	92.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.9224
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	33406 / 1 / 692
Goodness-of-fit on F^2	1.143
Final R indices [I>2sigma(I)]	R1 = 0.0838, wR2 = 0.1914
R indices (all data)	R1 = 0.1200, wR2 = 0.2158
Extinction coefficient	0.0154(6)
Largest diff. peak and hole	0.345 and -0.341 $e.Å^{-3}$

Table 2. Refined Positional Parameters for Compound 99119

Atom	x	y	z	U_{eq}, Å^2
C1	-0.1178(6)	0.79483(18)	0.7846(4)	0.0632(14)
C2	-0.2852(6)	0.7915(2)	0.8375(4)	0.0752(16)
C3	-0.2528(5)	0.7936(2)	0.9419(4)	0.0680(15)
C4	-0.1244(5)	0.75076(18)	0.9726(4)	0.0568(13)
C5	0.0506(5)	0.75494(16)	0.9230(3)	0.0413(10)
C6	0.1687(5)	0.70881(16)	0.9496(3)	0.0422(11)
C7	0.1628(4)	0.68413(16)	1.0357(3)	0.0402(11)
C8	0.2734(5)	0.64372(16)	1.0604(3)	0.0428(11)
C9	0.4017(5)	0.62746(18)	1.0009(4)	0.0538(13)
C10	0.4092(5)	0.65106(18)	0.9157(3)	0.0519(12)
C11	0.2921(5)	0.69041(17)	0.8872(3)	0.0465(12)
C12	0.2961(5)	0.70867(19)	0.7882(3)	0.0560(13)
C13	0.1821(6)	0.75466(19)	0.7648(3)	0.0642(14)
C14	0.0143(5)	0.75264(17)	0.8176(3)	0.0498(11)
C15	-0.1604(7)	0.7860(2)	0.6834(4)	0.0823(18)
C16	0.1480(5)	0.80461(17)	0.9526(3)	0.0585(13)
C17	0.2560(5)	0.61739(18)	1.1487(4)	0.0492(12)
N1	0.2399(4)	0.59524(16)	1.2165(3)	0.0600(11)
O1	-0.1401(5)	0.81662(15)	0.6218(3)	0.0956(13)
C18	0.6550(4)	0.43702(17)	0.8205(3)	0.0454(11)
C19	0.7256(5)	0.42929(18)	0.9191(3)	0.0536(12)
C20	0.5822(5)	0.41838(18)	0.9860(3)	0.0537(12)
C21	0.4388(4)	0.45906(16)	0.9808(3)	0.0440(11)
C22	0.3605(4)	0.46453(14)	0.8822(3)	0.0354(10)
C23	0.2263(4)	0.50886(15)	0.8751(3)	0.0350(10)
C24	0.1185(4)	0.51863(15)	0.9491(3)	0.0404(10)
C25	-0.0073(4)	0.55766(15)	0.9438(3)	0.0371(10)
C26	-0.0299(4)	0.58806(17)	0.8647(3)	0.0450(11)
C27	0.0775(5)	0.57867(16)	0.7915(3)	0.0448(11)
C28	0.2046(4)	0.53989(15)	0.7961(3)	0.0380(10)
C29	0.3216(5)	0.53448(17)	0.7141(3)	0.0493(11)
C30	0.4386(5)	0.48665(17)	0.7168(3)	0.0473(11)
C31	0.5069(4)	0.47736(16)	0.8158(3)	0.0393(10)
C32	0.8001(5)	0.45493(19)	0.7620(3)	0.0517(12)
C33	0.2639(5)	0.41347(16)	0.8564(3)	0.0498(12)
C34	-0.1149(5)	0.56715(17)	1.0229(3)	0.0475(11)
N2	-0.2042(4)	0.57517(16)	1.0825(3)	0.0644(11)
O2	0.8596(4)	0.43253(13)	0.6975(2)	0.0716(10)
C35	1.0678(5)	0.44747(17)	0.2940(3)	0.0498(12)
C36	1.2380(5)	0.4536(2)	0.3507(4)	0.0660(15)
C37	1.2075(5)	0.4509(2)	0.4553(4)	0.0642(14)
C38	1.0724(5)	0.49112(17)	0.4829(3)	0.0499(12)
C39	0.8989(5)	0.48572(16)	0.4304(3)	0.0424(11)
C40	0.7745(5)	0.52954(16)	0.4526(3)	0.0408(10)
C41	0.7779(5)	0.55373(16)	0.5402(3)	0.0432(11)
C42	0.6617(5)	0.59230(16)	0.5628(3)	0.0417(11)
C43	0.5305(5)	0.60797(18)	0.5001(4)	0.0533(13)
C44	0.5271(5)	0.58424(18)	0.4131(3)	0.0547(13)
C45	0.6476(5)	0.54722(17)	0.3887(3)	0.0441(11)
C46	0.6441(5)	0.52952(19)	0.2892(3)	0.0536(12)

C47	0.7608(5)	0.48382(18)	0.2679(3)	0.0543(12)
C48	0.9318(5)	0.48817(17)	0.3249(3)	0.0472(11)
C49	1.1091(6)	0.45660(19)	0.1948(4)	0.0627(14)
C50	0.8108(5)	0.43385(16)	0.4561(3)	0.0534(12)
C51	0.6778(5)	0.61997(17)	0.6511(4)	0.0451(11)
N3	0.6912(4)	0.64265(16)	0.7185(3)	0.0596(11)
O3	1.0882(4)	0.42526(13)	0.1334(3)	0.0737(10)
C52	0.2656(5)	0.80128(17)	0.3154(3)	0.0476(12)
C53	0.1946(5)	0.80192(17)	0.4135(3)	0.0536(12)
C54	0.3365(5)	0.80998(19)	0.4867(3)	0.0604(13)
C55	0.4831(5)	0.76880(17)	0.4777(3)	0.0515(12)
C56	0.5615(5)	0.77015(15)	0.3804(3)	0.0427(11)
C57	0.6970(5)	0.72745(15)	0.3713(3)	0.0393(10)
C58	0.8082(5)	0.71495(16)	0.4463(3)	0.0430(11)
C59	0.9341(5)	0.67637(16)	0.4399(3)	0.0429(11)
C60	0.9555(5)	0.64948(16)	0.3572(3)	0.0453(11)
C61	0.8495(5)	0.66264(16)	0.2822(3)	0.0504(12)
C62	0.7202(5)	0.70090(16)	0.2872(3)	0.0409(11)
C63	0.6070(5)	0.71131(18)	0.2031(3)	0.0564(13)
C64	0.4875(5)	0.75784(19)	0.2109(3)	0.0549(12)
C65	0.4141(5)	0.76131(16)	0.3082(3)	0.0448(11)
C66	0.1179(6)	0.7827(3)	0.2484(4)	0.090(2)
C67	0.6548(5)	0.82288(16)	0.3683(3)	0.0560(13)
C68	1.0462(5)	0.66420(17)	0.5194(4)	0.0462(11)
N4	1.1335(4)	0.65455(16)	0.5814(3)	0.0626(11)
O4	0.0540(5)	0.80957(19)	0.1948(3)	0.1080(15)

$U_{eq}={}^{1}/_{3}[U_{11}(aa^{*})^{2}+U_{22}(bb^{*})^{2}+U_{33}(cc^{*})^{2}+2U_{12}aa^{*}bb^{*}\cos\gamma+2U_{13}aa^{*}cc^{*}\cos\beta+2U_{23}bb^{*}cc^{*}\cos\alpha]$

Table 3. Positional Parameters for Hydrogens in Compound 99119

Atom	x	y	z	U_{iso}, Å^2
H1	-0.0668	0.8297	0.7930	0.084
H2a	-0.3443	0.7591	0.8215	0.100
H2b	-0.3601	0.8204	0.8190	0.100
H3a	-0.3611	0.7887	0.9728	0.090
H3b	-0.2070	0.8277	0.9591	0.090
H4a	-0.1752	0.7167	0.9599	0.076
H4b	-0.1032	0.7534	1.0386	0.076
H7	0.0818	0.6953	1.0775	0.053
H9	0.4800	0.6014	1.0183	0.072
H10	0.4944	0.6406	0.8758	0.069
H12a	0.4142	0.7178	0.7744	0.074
H12b	0.2624	0.6796	0.7486	0.074
H13a	0.1553	0.7547	0.6991	0.085
H13b	0.2432	0.7869	0.7798	0.085
H14	-0.0387	0.7185	0.8045	0.066
H15	-0.2071	0.7535	0.6673	0.109
H16a	0.1598	0.8055	1.0186	0.088
H16b	0.0848	0.8349	0.9314	0.088
H16c	0.2605	0.8046	0.9265	0.088
H18	0.6117	0.4034	0.7969	0.060
H19a	0.8063	0.4002	0.9204	0.071
H19b	0.7879	0.4605	0.9387	0.071
H20a	0.5334	0.3841	0.9728	0.071
H20b	0.6312	0.4176	1.0482	0.071
H21a	0.4846	0.4927	1.0009	0.058
H21b	0.3485	0.4491	1.0223	0.058
H24	0.1312	0.4988	1.0026	0.054
H26	-0.1146	0.6139	0.8609	0.060
H27	0.0645	0.5987	0.7382	0.060
H29a	0.2500	0.5331	0.6583	0.066
H29b	0.3932	0.5656	0.7107	0.066
H30a	0.5347	0.4920	0.6765	0.063
H30b	0.3745	0.4561	0.6953	0.063
H31	0.5569	0.5107	0.8368	0.052
H32	0.8497	0.4871	0.7774	0.069
H33a	0.1765	0.4068	0.9005	0.075
H33b	0.3443	0.3848	0.8564	0.075
H33c	0.2108	0.4170	0.7961	0.075
H35	1.0224	0.4119	0.3016	0.066
H36a	1.2905	0.4870	0.3362	0.088
H36b	1.3175	0.4261	0.3339	0.088
H37a	1.1686	0.4160	0.4713	0.085
H37b	1.3153	0.4576	0.4889	0.085
H38a	1.1178	0.5260	0.4725	0.066
H38b	1.0530	0.4876	0.5483	0.066
H41	0.8611	0.5433	0.5839	0.057
H43	0.4492	0.6331	0.5156	0.071
H44	0.4410	0.5937	0.3704	0.073
H46a	0.5264	0.5200	0.2716	0.071
H46b	0.6765	0.5590	0.2511	0.071

H47a	0.7849	0.4836	0.2028	0.072
H47b	0.7032	0.4512	0.2826	0.072
H48	0.9797	0.5229	0.3125	0.063
H49	1.1546	0.4891	0.1796	0.083
H50a	0.8140	0.4299	0.5219	0.080
H50b	0.8706	0.4051	0.4286	0.080
H50c	0.6928	0.4342	0.4338	0.080
H52	0.3050	0.8363	0.2981	0.063
H53a	0.1102	0.8298	0.4179	0.071
H53b	0.1362	0.7690	0.4248	0.071
H54a	0.2877	0.8072	0.5473	0.080
H54b	0.3845	0.8449	0.4807	0.080
H55a	0.4373	0.7341	0.4892	0.069
H55b	0.5733	0.7758	0.5238	0.069
H58	0.7973	0.7329	0.5015	0.057
H60	1.0388	0.6234	0.3525	0.060
H61	0.8646	0.6454	0.2266	0.067
H63a	0.5377	0.6803	0.1902	0.075
H63b	0.6804	0.7168	0.1509	0.075
H64a	0.3931	0.7546	0.1659	0.073
H64b	0.5502	0.7897	0.1977	0.073
H65	0.3646	0.7269	0.3213	0.060
H66	0.0801	0.7482	0.2522	0.120
H67a	0.7429	0.8267	0.4157	0.084
H67b	0.5731	0.8510	0.3726	0.084
H67c	0.7067	0.8238	0.3091	0.084

Table 4. Refined Thermal Parameters (U's) for Compound 99119

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.097(4)	0.036(3)	0.055(4)	0.000(3)	-0.028(3)	-0.009(3)
C2	0.080(4)	0.066(4)	0.077(5)	-0.004(3)	-0.031(3)	0.000(3)
C3	0.058(3)	0.061(3)	0.085(5)	0.003(3)	-0.006(3)	0.016(2)
C4	0.054(3)	0.051(3)	0.064(4)	0.000(3)	-0.006(2)	0.008(2)
C5	0.053(2)	0.035(3)	0.035(3)	-0.006(2)	-0.0077(19)	-0.005(2)
C6	0.043(2)	0.049(3)	0.034(3)	-0.004(2)	-0.0050(19)	-0.010(2)
C7	0.042(2)	0.043(3)	0.035(3)	-0.012(2)	-0.0020(19)	-0.004(2)
C8	0.047(2)	0.041(3)	0.039(3)	-0.007(2)	-0.008(2)	0.004(2)
C9	0.041(2)	0.059(3)	0.061(4)	-0.018(3)	-0.008(2)	0.009(2)
C10	0.057(3)	0.060(3)	0.039(3)	-0.011(3)	0.005(2)	-0.001(2)
C11	0.049(3)	0.045(3)	0.045(3)	-0.010(2)	-0.002(2)	-0.009(2)
C12	0.069(3)	0.064(4)	0.035(3)	-0.003(3)	0.004(2)	-0.011(2)
C13	0.096(4)	0.054(3)	0.043(3)	-0.003(3)	0.004(3)	-0.021(3)
C14	0.069(3)	0.031(2)	0.048(3)	-0.001(2)	-0.012(2)	-0.011(2)
C15	0.136(5)	0.050(3)	0.059(5)	-0.009(3)	-0.041(4)	0.010(3)
C16	0.081(3)	0.046(3)	0.048(3)	-0.008(3)	-0.009(2)	-0.004(2)
C17	0.049(3)	0.050(3)	0.048(4)	-0.010(3)	-0.008(2)	0.008(2)
N1	0.066(2)	0.067(3)	0.047(3)	0.008(2)	-0.004(2)	0.009(2)
O1	0.169(4)	0.064(3)	0.052(3)	0.005(2)	-0.030(2)	-0.002(2)
C18	0.040(2)	0.053(3)	0.043(3)	-0.009(2)	0.009(2)	-0.001(2)
C19	0.045(2)	0.049(3)	0.066(4)	0.005(3)	-0.003(2)	0.004(2)
C20	0.054(3)	0.067(3)	0.041(3)	0.009(3)	0.007(2)	0.010(2)
C21	0.046(2)	0.047(3)	0.040(3)	0.009(2)	0.0083(19)	0.007(2)
C22	0.042(2)	0.033(2)	0.032(3)	0.000(2)	0.0051(18)	0.0012(19)
C23	0.040(2)	0.034(2)	0.031(3)	-0.001(2)	-0.0006(18)	0.0013(18)
C24	0.045(2)	0.044(3)	0.033(3)	0.002(2)	-0.0011(19)	-0.002(2)
C25	0.039(2)	0.040(3)	0.032(3)	-0.009(2)	0.0010(18)	0.0005(19)
C26	0.039(2)	0.045(3)	0.051(3)	-0.003(2)	-0.002(2)	-0.0022(19)
C27	0.050(2)	0.040(3)	0.044(3)	0.007(2)	-0.004(2)	-0.008(2)
C28	0.044(2)	0.036(3)	0.034(3)	-0.001(2)	-0.0020(19)	-0.0052(19)
C29	0.056(3)	0.054(3)	0.038(3)	0.002(2)	0.001(2)	-0.005(2)
C30	0.056(2)	0.052(3)	0.034(3)	-0.003(2)	0.007(2)	-0.004(2)
C31	0.045(2)	0.037(3)	0.036(3)	-0.004(2)	0.0035(18)	-0.0064(19)
C32	0.058(3)	0.058(3)	0.039(3)	0.003(3)	0.002(2)	0.000(2)
C33	0.052(2)	0.044(3)	0.053(3)	-0.003(2)	0.005(2)	-0.005(2)
C34	0.051(3)	0.049(3)	0.042(3)	-0.004(2)	-0.010(2)	0.009(2)
N2	0.064(2)	0.082(3)	0.047(3)	-0.007(2)	0.006(2)	0.018(2)
O2	0.085(2)	0.075(2)	0.056(3)	-0.001(2)	0.0221(19)	0.0005(18)
C35	0.074(3)	0.041(3)	0.035(3)	0.000(2)	0.014(2)	-0.002(2)
C36	0.062(3)	0.061(3)	0.077(4)	-0.006(3)	0.018(3)	0.007(2)
C37	0.064(3)	0.066(4)	0.063(4)	-0.003(3)	-0.001(2)	0.009(2)
C38	0.054(3)	0.047(3)	0.048(3)	-0.009(2)	0.002(2)	0.001(2)
C39	0.050(2)	0.038(3)	0.039(3)	-0.002(2)	0.007(2)	-0.001(2)
C40	0.042(2)	0.041(3)	0.040(3)	0.010(2)	0.006(2)	-0.0048(19)
C41	0.051(2)	0.048(3)	0.031(3)	0.012(2)	0.0009(19)	-0.001(2)
C42	0.045(2)	0.043(3)	0.037(3)	0.004(2)	0.007(2)	0.003(2)
C43	0.047(3)	0.057(3)	0.055(4)	0.007(3)	0.001(2)	0.003(2)
C44	0.051(3)	0.066(3)	0.047(4)	0.009(3)	-0.004(2)	-0.003(2)
C45	0.041(2)	0.049(3)	0.043(3)	-0.002(2)	0.004(2)	-0.007(2)
C46	0.055(3)	0.062(3)	0.044(3)	0.001(3)	-0.005(2)	-0.011(2)

C47	0.074(3)	0.052(3)	0.037(3)	-0.004(2)	0.003(2)	-0.014(2)
C48	0.065(3)	0.037(3)	0.041(3)	-0.001(2)	0.010(2)	-0.004(2)
C49	0.093(4)	0.041(3)	0.055(4)	-0.001(3)	0.028(3)	-0.004(3)
C50	0.081(3)	0.045(3)	0.034(3)	0.005(2)	0.001(2)	-0.007(2)
C51	0.042(2)	0.049(3)	0.045(3)	0.004(3)	0.004(2)	0.008(2)
N3	0.065(2)	0.067(3)	0.048(3)	-0.009(2)	0.007(2)	0.008(2)
O3	0.122(3)	0.051(2)	0.050(3)	-0.011(2)	0.025(2)	-0.0060(19)
C52	0.044(2)	0.042(3)	0.056(3)	0.009(2)	-0.006(2)	-0.003(2)
C53	0.059(3)	0.042(3)	0.060(4)	0.006(2)	0.001(2)	0.001(2)
C54	0.069(3)	0.061(3)	0.052(4)	-0.008(3)	0.005(2)	0.019(2)
C55	0.071(3)	0.050(3)	0.033(3)	-0.003(2)	-0.003(2)	0.017(2)
C56	0.054(2)	0.039(3)	0.035(3)	-0.001(2)	-0.0029(19)	0.000(2)
C57	0.045(2)	0.036(2)	0.037(3)	0.003(2)	0.0035(19)	-0.0054(19)
C58	0.050(2)	0.039(3)	0.041(3)	-0.004(2)	0.004(2)	0.000(2)
C59	0.046(2)	0.039(3)	0.043(3)	-0.001(2)	0.005(2)	-0.002(2)
C60	0.050(2)	0.040(3)	0.046(3)	0.000(2)	-0.001(2)	-0.0028(19)
C61	0.059(3)	0.048(3)	0.045(3)	-0.005(2)	0.013(2)	-0.007(2)
C62	0.047(2)	0.039(3)	0.036(3)	0.002(2)	0.0035(19)	-0.012(2)
C63	0.053(3)	0.072(3)	0.044(3)	-0.009(3)	0.001(2)	-0.006(2)
C64	0.061(3)	0.074(3)	0.029(3)	0.003(3)	-0.006(2)	-0.003(2)
C65	0.052(2)	0.041(3)	0.041(3)	0.002(2)	0.0006(19)	-0.007(2)
C66	0.047(3)	0.120(5)	0.102(6)	0.056(4)	0.007(3)	0.033(3)
C67	0.053(3)	0.045(3)	0.069(4)	0.003(3)	-0.015(2)	0.001(2)
C68	0.041(3)	0.048(3)	0.051(4)	0.001(2)	0.008(2)	0.008(2)
N4	0.063(2)	0.071(3)	0.053(3)	0.007(2)	-0.006(2)	0.018(2)
O4	0.089(3)	0.144(4)	0.091(4)	0.003(3)	-0.009(2)	0.011(3)

The form of the anisotropic displacement parameter is: $\exp[-2\pi^2(a^{*2}U_{11}h^2+b^{*2}U_{22}k^2+c^{*2}U_{33}l^2+2b^*c^*U_{23}kl+2a^*c^*U_{13}hl+2a^*b^*U_{12}hk)]$

Table 5. Bond Distances in Compound 99119, Å

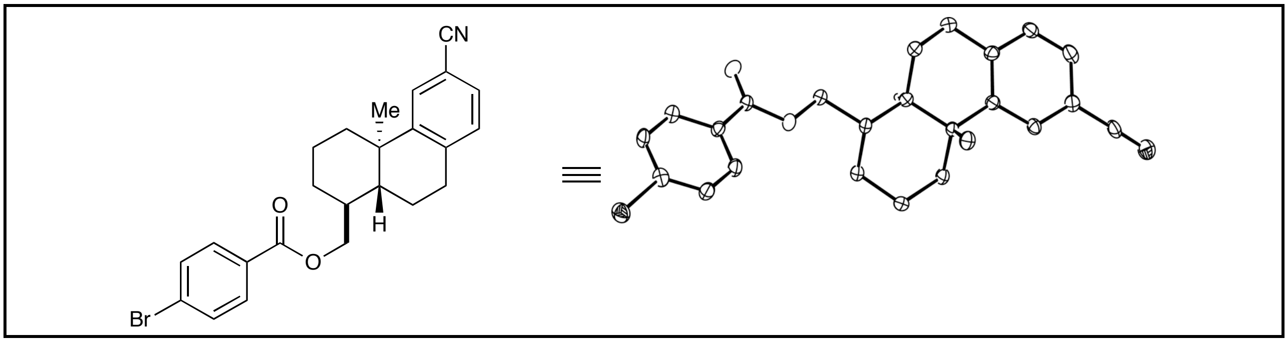
C1-C15	1.514(7)	C1-C2	1.527(7)	C1-C14	1.551(6)
C2-C3	1.530(7)	C3-C4	1.535(6)	C4-C5	1.556(6)
C5-C16	1.530(5)	C5-C6	1.533(6)	C5-C14	1.549(6)
C6-C7	1.401(6)	C6-C11	1.415(6)	C7-C8	1.382(5)
C8-C9	1.398(6)	C8-C17	1.457(7)	C9-C10	1.378(6)
C10-C11	1.407(6)	C11-C12	1.512(6)	C12-C13	1.502(6)
C13-C14	1.529(6)	C15-O1	1.202(6)	C17-N1	1.146(6)
C18-C32	1.499(5)	C18-C19	1.531(6)	C18-C31	1.541(5)
C19-C20	1.521(5)	C20-C21	1.520(5)	C21-C22	1.546(5)
C22-C23	1.537(5)	C22-C33	1.543(5)	C22-C31	1.543(5)
C23-C28	1.400(5)	C23-C24	1.402(5)	C24-C25	1.394(5)
C25-C26	1.394(6)	C25-C34	1.458(6)	C26-C27	1.389(5)
C27-C28	1.396(5)	C28-C29	1.523(5)	C29-C30	1.519(6)
C30-C31	1.536(5)	C32-O2	1.200(5)	C34-N2	1.141(5)
C35-C49	1.503(6)	C35-C36	1.541(6)	C35-C48	1.554(6)
C36-C37	1.544(6)	C37-C38	1.528(6)	C38-C39	1.531(5)
C39-C40	1.516(5)	C39-C50	1.540(6)	C39-C48	1.562(6)
C40-C45	1.406(6)	C40-C41	1.414(6)	C41-C42	1.379(5)
C42-C43	1.403(5)	C42-C51	1.465(7)	C43-C44	1.400(6)
C44-C45	1.380(6)	C45-C46	1.514(6)	C46-C47	1.512(6)
C47-C48	1.545(5)	C49-O3	1.206(5)	C51-N3	1.139(5)
C52-C53	1.542(6)	C52-C65	1.543(6)	C52-C66	1.554(7)
C53-C54	1.522(6)	C54-C55	1.554(5)	C55-C56	1.555(6)
C56-C57	1.521(5)	C56-C67	1.539(5)	C56-C65	1.544(5)
C57-C58	1.406(5)	C57-C62	1.412(5)	C58-C59	1.390(5)
C59-C60	1.397(6)	C59-C68	1.458(6)	C60-C61	1.386(6)
C61-C62	1.401(5)	C62-C63	1.507(6)	C63-C64	1.511(6)
C64-C65	1.540(6)	C66-O4	1.140(6)	C68-N4	1.138(5)

Table 6. Bond Angles in Compound 99119, °

C15-C1-C2	108.4(4)	C15-C1-C14	108.7(4)	C2-C1-C14	111.6(4)
C1-C2-C3	112.2(4)	C2-C3-C4	110.5(4)	C3-C4-C5	112.5(4)
C16-C5-C6	106.2(3)	C16-C5-C14	112.6(4)	C6-C5-C14	108.1(3)
C16-C5-C4	110.8(4)	C6-C5-C4	110.6(3)	C14-C5-C4	108.6(3)
C7-C6-C11	117.5(4)	C7-C6-C5	122.4(4)	C11-C6-C5	120.1(4)
C8-C7-C6	122.1(4)	C7-C8-C9	120.4(4)	C7-C8-C17	120.0(4)
C9-C8-C17	119.5(4)	C10-C9-C8	118.3(4)	C9-C10-C11	122.2(4)
C10-C11-C6	119.3(4)	C10-C11-C12	118.0(4)	C6-C11-C12	122.6(4)
C13-C12-C11	115.4(4)	C12-C13-C14	111.2(4)	C13-C14-C5	111.2(3)
C13-C14-C1	112.6(4)	C5-C14-C1	112.2(4)	O1-C15-C1	126.6(5)
N1-C17-C8	177.7(5)	C32-C18-C19	108.4(3)	C32-C18-C31	109.9(4)
C19-C18-C31	111.9(3)	C20-C19-C18	111.9(3)	C21-C20-C19	112.9(4)
C20-C21-C22	112.0(3)	C23-C22-C33	106.4(3)	C23-C22-C31	108.0(3)
C33-C22-C31	112.8(3)	C23-C22-C21	112.0(3)	C33-C22-C21	108.9(3)
C31-C22-C21	108.8(3)	C28-C23-C24	117.9(3)	C28-C23-C22	122.4(3)
C24-C23-C22	119.7(4)	C25-C24-C23	121.0(4)	C24-C25-C26	121.0(4)
C24-C25-C34	119.3(4)	C26-C25-C34	119.7(4)	C27-C26-C25	118.1(4)
C26-C27-C28	121.5(4)	C27-C28-C23	120.5(4)	C27-C28-C29	117.4(4)
C23-C28-C29	122.0(3)	C30-C29-C28	114.8(4)	C29-C30-C31	109.7(3)
C30-C31-C18	112.4(3)	C30-C31-C22	112.2(3)	C18-C31-C22	112.9(3)
O2-C32-C18	127.4(4)	N2-C34-C25	177.4(5)	C49-C35-C36	107.1(4)
C49-C35-C48	109.7(4)	C36-C35-C48	110.7(4)	C35-C36-C37	111.6(4)
C38-C37-C36	110.6(4)	C37-C38-C39	114.0(4)	C40-C39-C38	112.4(3)
C40-C39-C50	107.1(3)	C38-C39-C50	110.2(3)	C40-C39-C48	107.5(3)
C38-C39-C48	108.6(3)	C50-C39-C48	111.0(4)	C45-C40-C41	116.7(4)
C45-C40-C39	122.2(4)	C41-C40-C39	121.2(4)	C42-C41-C40	122.0(4)
C41-C42-C43	120.9(4)	C41-C42-C51	120.8(4)	C43-C42-C51	118.2(4)
C44-C43-C42	117.2(4)	C45-C44-C43	122.1(4)	C44-C45-C40	121.0(4)
C44-C45-C46	117.1(4)	C40-C45-C46	121.8(4)	C47-C46-C45	115.5(4)
C46-C47-C48	110.1(4)	C47-C48-C35	112.0(4)	C47-C48-C39	111.1(3)
C35-C48-C39	112.8(3)	O3-C49-C35	125.4(5)	N3-C51-C42	178.2(5)
C53-C52-C65	110.8(3)	C53-C52-C66	107.8(3)	C65-C52-C66	107.0(4)
C54-C53-C52	112.2(3)	C53-C54-C55	111.4(4)	C54-C55-C56	111.5(3)
C57-C56-C67	106.8(3)	C57-C56-C65	109.5(3)	C67-C56-C65	113.0(3)
C57-C56-C55	110.6(3)	C67-C56-C55	108.6(4)	C65-C56-C55	108.3(3)
C58-C57-C62	118.1(4)	C58-C57-C56	120.2(4)	C62-C57-C56	121.6(4)
C59-C58-C57	121.6(4)	C58-C59-C60	120.4(4)	C58-C59-C68	120.0(4)
C60-C59-C68	119.6(4)	C61-C60-C59	118.3(4)	C60-C61-C62	122.4(4)
C61-C62-C57	119.2(4)	C61-C62-C63	118.7(4)	C57-C62-C63	122.1(4)
C62-C63-C64	114.9(4)	C63-C64-C65	110.9(4)	C64-C65-C52	113.3(4)
C64-C65-C56	110.3(3)	C52-C65-C56	113.3(4)	O4-C66-C52	122.7(6)
N4-C68-C59	179.8(5)				

5.3.2 4-Bromobenzoate **68**

X-ray Structure Determination of Compound 99118



Compound 99118, $C_{24}H_{24}NO_2Br$, crystallizes in the triclinic space group P1 with a=8.5337(9)Å, b=10.3702(6)Å, c=13.3899(12)Å, α=69.135(8)°, β=82.489(10)°, γ=67.433(8)°, V=1022.44(15)Å^3, Z=2, and d_{calc}=1.424 g/cm^3 . X-ray intensity data were collected on a Rigaku Mercury CCD area detector employing graphite-monochromated Mo-Kα radiation (λ=0.71073 Å) at a temperature of 143(1)K. Preliminary indexing was performed from a series of twelve 0.5° rotation images with exposures of 30 seconds. A total of 1060 rotation images were collected with a crystal to detector distance of 35 mm, a 2θ swing angle of -12°, rotation widths of 0.5° and exposures of 30 seconds:

scan no.	scan type	ω	χ	ϕ
1	ϕ	10.0	20.0	157.5 — 367.5
2	ω	-20.0 — +20.0	-90.0	225.0
3	ω	-20.0 — +20.0	-90.0	0.0
4	ω	-20.0 — +20.0	-90.0	135.0
5	ω	-20.0 — +20.0	-90.0	45.0
6	ω	-20.0 — +20.0	-90.0	90.0
7	ω	-20.0 — +20.0	-90.0	180.0
8	ω	-20.0 — +20.0	-90.0	270.0
9	ω	-20.0 — +20.0	-90.0	315.0

Rotation images were processed using CrystalClear[28], producing a listing of unaveraged F^2 and

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(28) CrystalClear: Rigaku Corporation, 1999.

$\sigma(F^2)$ values which were then passed to the CrystalStructure[29] program package for further processing and structure solution on a Dell Pentium 4 computer. A total of 13602 reflections were measured over the ranges $2.58 \leq \theta \leq 25.00°$, $-10 \leq h \leq 10$, $-12 \leq k \leq 12$, $-14 \leq l \leq 15$ yielding 5922 unique reflections (Rint = 0.0275). The intensity data were corrected for Lorentz and polarization effects and for absorption using REQAB[30] (minimum and maximum transmission 0.7944, 1.0000).

The structure was solved by direct methods (SIR97[31]). The asymmetric unit consists of two molecules of the title compound. Refinement was by full-matrix least squares based on F^2 using SHELXL-97.[32] All reflections were used during refinement. The weighting scheme used was $w=1/[\sigma^2(F_o^2)+ (0.0552P)^2 + 0.0833P]$ where $P = (F_o^2 + 2F_c^2)/3$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using a riding model. Refinement converged to R1=0.0408 and wR2=0.0986 for 5465 observed reflections for which $F > 4\sigma(F)$ and R1=0.0441 and wR2=0.1036 and GOF =1.096 for all 5922 unique, non-zero reflections and 509 variables.[33] The maximum Δ/σ in the final cycle of least squares was 4.439 and the two most prominent peaks in the final difference Fourier were +0.451 and -0.658 e/Å^3. The Flack absolute structure parameter refined to a value of 0.000(9), thus corroborating the assigned stereochemistry.

Table 1. lists cell information, data collection parameters, and refinement data. Final positional and equivalent isotropic thermal parameters are given in Tables 2. and 3. Anisotropic thermal parameters are in Table 4. Tables 5. and 6. list bond distances and bond angles. Figures 1. and 2. are ORTEP[34] representations of the molecule with 30% probability thermal ellipsoids displayed.

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(29) CrystalStructure: Crystal Structure Analysis Package, Rigaku Corp. Rigaku/MSC, 2002.

(30) REQAB4: Jacobsen, R. A., 1994, private communication.

(31) SIR97: Altomare, A.; Burla, M.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A.; Polidori, G.; Spagna R. *J. Appl. Cryst.* **1999**, *32*, 115.

(32) SHELXL-97: Sheldrick, G.M. *Acta Cryst.* **2008**, *A64*, 112.

(33) $R1 = \Sigma||F_o| - |F_c|| / \Sigma |F_o|$

$wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{½}$

$GOF = [\Sigma w(F_o^2 - F_c^2)^2/(n - p)]^{½}$

where n = the number of reflections and p = the number of parameters refined.

(34) "ORTEP-II: A Fortran Thermal Ellipsoid Plot Program for Crystal Structure Illustrations". Johnson, C. K. (1976) ORNL-5138.

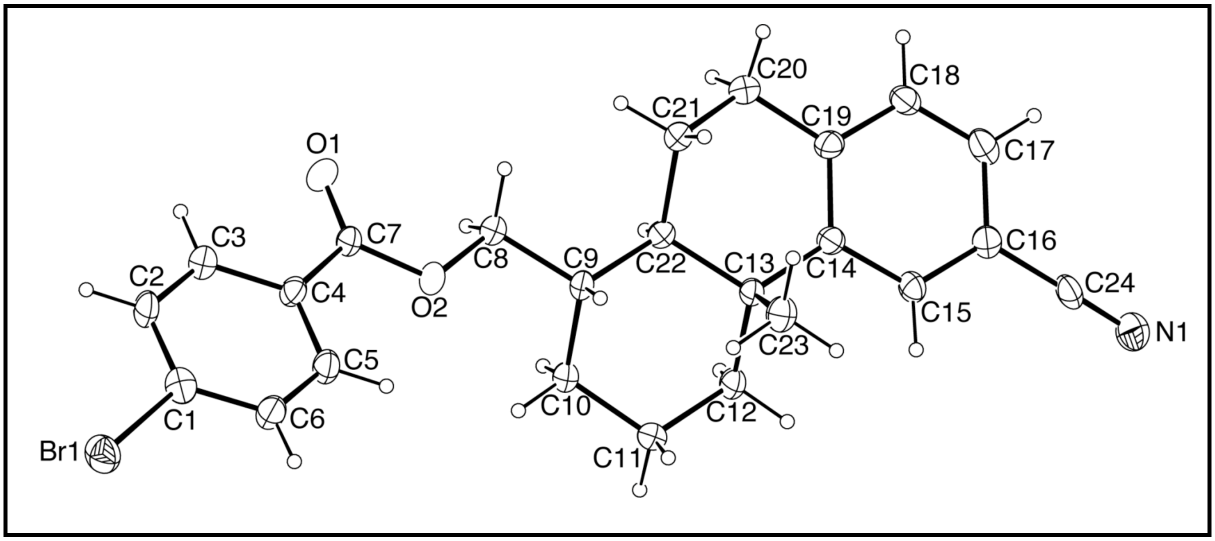


Figure 1. ORTEP drawing of molecule no. 1 of the asymmetric unit with 30% probability thermal ellipsoids.

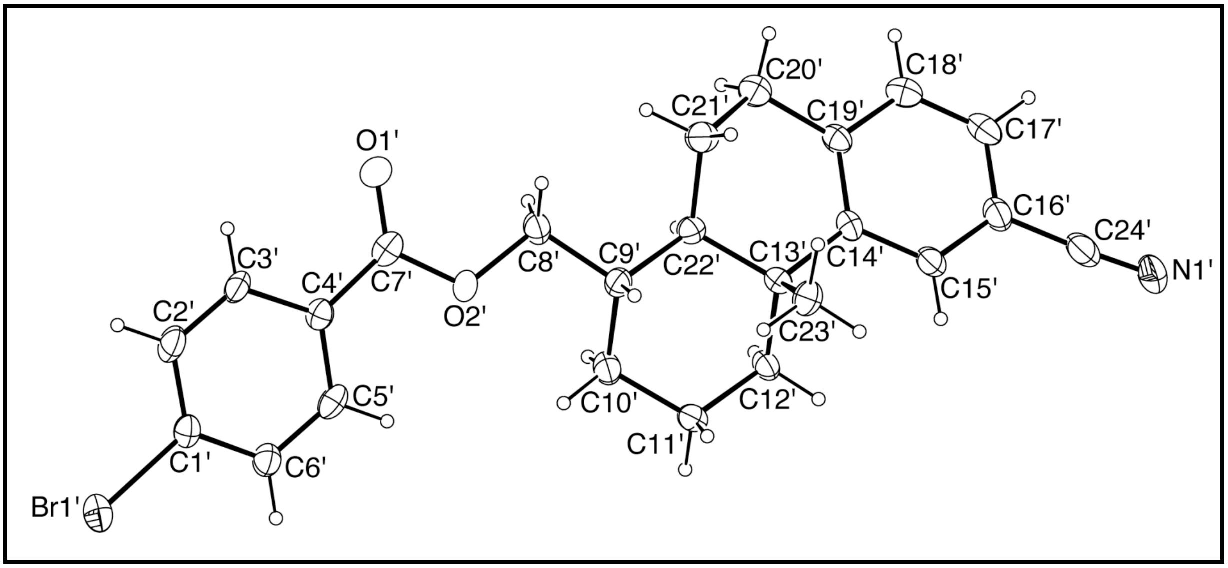


Figure 2. ORTEP drawing of molecule no. 2 of the asymmetric unit with 30% probability thermal ellipsoids.

Table 1. Summary of Structure Determination of Compound 99118

Empirical formula	$C_{24}H_{24}NO_2Br$
Formula weight	438.35
Temperature	143(1) K
Wavelength	0.71073 Å
Crystal system	triclinic
Space group	P1
Cell constants:	
a	8.5337(9) Å
b	10.3702(6) Å
c	13.3899(12) Å
α	69.135(8)°
β	82.489(10)°
γ	67.433(8)°
Volume	1022.44(15) $Å^3$
Z	2
Density (calculated)	1.424 Mg/m^3
Absorption coefficient	2.030 mm^{-1}
F(000)	452
Crystal size	0.28 x 0.15 x 0.12 mm^3
Theta range for data collection	2.58 to 25.00°
Index ranges	$-10 \le h \le 10, -12 \le k \le 12, -14 \le l \le 15$
Reflections collected	13602
Independent reflections	5922 [R(int) = 0.0275]
Completeness to theta = 25.00°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.7944
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5922 / 3 / 509
Goodness-of-fit on F^2	1.096
Final R indices [I>2sigma(I)]	R1 = 0.0408, wR2 = 0.0986
R indices (all data)	R1 = 0.0441, wR2 = 0.1036
Absolute structure parameter	0.000(9)
Largest diff. peak and hole	0.451 and -0.658 e.$Å^{-3}$

Table 2. Refined Positional Parameters for Compound 99118

Atom	x	y	z	U_{eq}, Å^2
C1	0.1669(7)	1.2157(7)	0.4766(4)	0.0396(14)
C2	0.0215(7)	1.2331(7)	0.5399(5)	0.0430(14)
C3	-0.0077(7)	1.1084(7)	0.6071(5)	0.0415(13)
C4	0.1060(6)	0.9667(7)	0.6127(5)	0.0342(13)
C5	0.2474(7)	0.9535(6)	0.5465(5)	0.0385(13)
C6	0.2762(7)	1.0767(7)	0.4782(5)	0.0414(14)
C7	0.0713(6)	0.8376(6)	0.6898(5)	0.0342(12)
C8	0.1648(6)	0.5774(7)	0.7590(5)	0.0424(14)
C9	0.3198(6)	0.4468(6)	0.7484(4)	0.0308(12)
C10	0.4749(5)	0.4406(5)	0.7980(4)	0.0358(10)
C11	0.6362(5)	0.3118(5)	0.7904(4)	0.0385(10)
C12	0.6083(6)	0.1652(6)	0.8329(4)	0.0343(12)
C13	0.4551(6)	0.1695(6)	0.7791(4)	0.0289(11)
C14	0.4293(6)	0.0228(6)	0.8252(4)	0.0302(11)
C15	0.5683(6)	-0.1098(6)	0.8380(4)	0.0340(11)
C16	0.5494(6)	-0.2459(6)	0.8774(4)	0.0354(11)
C17	0.3870(7)	-0.2533(7)	0.9019(4)	0.0420(13)
C18	0.2500(6)	-0.1241(7)	0.8877(5)	0.0355(12)
C19	0.2674(6)	0.0120(6)	0.8513(4)	0.0344(12)
C20	0.1120(6)	0.1495(6)	0.8397(5)	0.0471(14)
C21	0.1340(5)	0.2917(5)	0.7670(4)	0.0391(10)
C22	0.2959(6)	0.2977(6)	0.7976(4)	0.0330(12)
C23	0.4937(7)	0.1940(7)	0.6591(4)	0.0392(13)
C24	0.6959(6)	-0.3831(5)	0.8954(4)	0.0394(11)
N1	0.8118(6)	-0.4905(5)	0.9123(4)	0.0542(11)
O1	-0.0520(5)	0.8468(5)	0.7461(4)	0.0502(11)
O2	0.1939(4)	0.7088(4)	0.6914(3)	0.0400(9)
Br1	0.21570(5)	1.38402(4)	0.39049(4)	0.05183(17)
C1'	0.8109(7)	-0.2135(7)	0.5083(5)	0.0371(13)
C2'	0.9432(7)	-0.2281(7)	0.4357(5)	0.0484(16)
C3'	0.9713(7)	-0.1047(7)	0.3699(5)	0.0426(14)
C4'	0.8696(7)	0.0363(7)	0.3742(5)	0.0350(13)
C5'	0.7389(7)	0.0470(7)	0.4480(5)	0.0423(14)
C6'	0.7103(7)	-0.0769(7)	0.5159(5)	0.0420(14)
C7'	0.9098(7)	0.1656(7)	0.3031(5)	0.0386(14)
C8'	0.8189(7)	0.4304(6)	0.2451(5)	0.0402(13)
C9'	0.6589(6)	0.5600(6)	0.2509(4)	0.0354(13)
C10'	0.5834(6)	0.5374(5)	0.3640(4)	0.0426(11)
C11'	0.4272(6)	0.6751(5)	0.3655(4)	0.0438(12)
C12'	0.4629(7)	0.8172(6)	0.3224(4)	0.0365(12)
C13'	0.5346(6)	0.8408(6)	0.2077(4)	0.0329(12)
C14'	0.5818(7)	0.9813(6)	0.1698(4)	0.0340(12)
C15'	0.4582(7)	1.1169(6)	0.1712(4)	0.0435(14)
C16'	0.4925(7)	1.2458(6)	0.1343(4)	0.0453(14)
C17'	0.6528(7)	1.2434(7)	0.0962(4)	0.0471(14)
C18'	0.7756(8)	1.1102(9)	0.0933(5)	0.0450(14)
C19'	0.7410(7)	0.9796(6)	0.1273(4)	0.0368(12)
C20'	0.8767(7)	0.8434(7)	0.1105(5)	0.0557(16)
C21'	0.8038(6)	0.7301(6)	0.1127(4)	0.0480(12)
C22'	0.6992(6)	0.7023(6)	0.2126(4)	0.0349(12)

C23'	0.4021(7)	0.8669(6)	0.1287(4)	0.0424(13)
C24'	0.3621(8)	1.3871(7)	0.1297(4)	0.0612(16)
N1'	0.2618(8)	1.5021(6)	0.1210(5)	0.093(2)
O1'	1.0376(5)	0.1592(5)	0.2510(3)	0.0486(11)
O2'	0.7868(4)	0.2940(4)	0.3050(3)	0.0382(9)
Br1'	0.76426(5)	-0.38251(4)	0.59919(3)	0.05068(17)

$U_{eq}={}^{1}/_{3}[U_{11}(aa^*)^2+U_{22}(bb^*)^2+U_{33}(cc^*)^2+2U_{12}aa^*bb^*\cos\gamma+2U_{13}aa^*cc^*\cos\beta+2U_{23}bb^*cc^*\cos\alpha]$

Table 3. Positional Parameters for Hydrogens in Compound 99118

Atom	x	y	z	U_{iso}, Å^2
H2	-0.0543	1.3271	0.5367	0.057
H3	-0.1044	1.1189	0.6493	0.055
H5	0.3233	0.8599	0.5488	0.051
H6	0.3694	1.0665	0.4330	0.055
H8a	0.0631	0.5742	0.7365	0.056
H8b	0.1511	0.5750	0.8326	0.056
H9	0.3417	0.4634	0.6720	0.041
H10a	0.4523	0.4316	0.8726	0.048
H10b	0.4935	0.5329	0.7621	0.048
H11a	0.6716	0.3301	0.7164	0.051
H11b	0.7263	0.3058	0.8311	0.051
H12a	0.5897	0.1401	0.9093	0.046
H12b	0.7100	0.0880	0.8210	0.046
H15	0.6759	-0.1064	0.8197	0.045
H17	0.3731	-0.3442	0.9273	0.056
H18	0.1422	-0.1282	0.9031	0.047
H20a	0.0792	0.1578	0.9099	0.063
H20b	0.0199	0.1387	0.8120	0.063
H21a	0.0373	0.3764	0.7739	0.052
H21b	0.1401	0.2955	0.6932	0.052
H22	0.2900	0.2776	0.8750	0.044
H23a	0.5935	0.1138	0.6514	0.059
H23b	0.5123	0.2857	0.6265	0.059
H23c	0.3993	0.1978	0.6247	0.059
H2'	1.0116	-0.3210	0.4322	0.064
H3'	1.0596	-0.1140	0.3210	0.057
H5'	0.6693	0.1397	0.4514	0.056
H6'	0.6243	-0.0687	0.5662	0.056
H8'1	0.8451	0.4361	0.1713	0.053
H8'2	0.9143	0.4321	0.2761	0.053
H9'	0.5737	0.5718	0.2025	0.047
H10a'	0.5509	0.4513	0.3865	0.057
H10b'	0.6682	0.5197	0.4139	0.057
H11a'	0.3373	0.6839	0.3231	0.058
H11b'	0.3870	0.6617	0.4383	0.058
H12a'	0.5440	0.8134	0.3688	0.049
H12b'	0.3589	0.9003	0.3220	0.049
H15'	0.3509	1.1201	0.1976	0.058
H17'	0.6772	1.3294	0.0731	0.063
H18'	0.8833	1.1075	0.0681	0.060
H20a'	0.9625	0.7989	0.1661	0.074
H20b'	0.9311	0.8723	0.0423	0.074
H21a'	0.7333	0.7670	0.0499	0.064
H21b'	0.8949	0.6386	0.1124	0.064
H22'	0.7684	0.6921	0.2699	0.046
H23a'	0.3738	0.7801	0.1474	0.064
H23b'	0.4476	0.8871	0.0577	0.064
H23c'	0.3020	0.9499	0.1314	0.064

Table 4. Refined Thermal Parameters (U's) for Compound 99118

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.048(3)	0.035(4)	0.034(3)	-0.009(3)	-0.007(3)	-0.013(3)
C2	0.043(3)	0.023(3)	0.057(3)	-0.015(3)	-0.005(3)	-0.003(2)
C3	0.039(3)	0.034(3)	0.052(3)	-0.019(3)	0.001(2)	-0.009(2)
C4	0.027(2)	0.030(3)	0.044(3)	-0.016(3)	-0.007(2)	-0.002(2)
C5	0.039(3)	0.027(3)	0.045(3)	-0.013(3)	-0.002(3)	-0.006(3)
C6	0.036(3)	0.037(4)	0.048(3)	-0.019(3)	0.001(3)	-0.007(3)
C7	0.030(3)	0.023(3)	0.047(3)	-0.012(3)	-0.004(2)	-0.005(2)
C8	0.029(2)	0.030(3)	0.069(4)	-0.022(3)	0.000(3)	-0.007(2)
C9	0.029(2)	0.025(3)	0.038(3)	-0.015(3)	0.000(2)	-0.006(2)
C10	0.031(2)	0.027(2)	0.050(3)	-0.016(2)	-0.0020(19)	-0.0071(18)
C11	0.029(2)	0.033(2)	0.056(3)	-0.017(2)	0.001(2)	-0.0132(19)
C12	0.032(2)	0.024(3)	0.042(3)	-0.010(2)	-0.005(2)	-0.005(2)
C13	0.026(2)	0.023(3)	0.037(3)	-0.012(2)	-0.004(2)	-0.006(2)
C14	0.030(2)	0.034(3)	0.031(2)	-0.015(2)	0.005(2)	-0.013(2)
C15	0.038(2)	0.024(2)	0.038(2)	-0.008(2)	0.004(2)	-0.014(2)
C16	0.040(2)	0.032(3)	0.034(2)	-0.012(2)	0.003(2)	-0.014(2)
C17	0.057(3)	0.041(3)	0.041(3)	-0.020(3)	0.009(3)	-0.028(3)
C18	0.038(3)	0.042(3)	0.037(2)	-0.019(2)	0.007(2)	-0.022(3)
C19	0.028(2)	0.040(3)	0.040(3)	-0.020(2)	-0.001(2)	-0.011(2)
C20	0.031(2)	0.042(3)	0.074(4)	-0.026(3)	0.008(3)	-0.015(2)
C21	0.029(2)	0.036(3)	0.056(3)	-0.022(2)	-0.002(2)	-0.0082(18)
C22	0.026(2)	0.028(3)	0.044(3)	-0.013(2)	-0.004(2)	-0.006(2)
C23	0.045(3)	0.034(3)	0.034(3)	-0.011(3)	0.001(2)	-0.011(2)
C24	0.051(3)	0.028(3)	0.046(3)	-0.013(2)	0.005(2)	-0.022(2)
N1	0.055(3)	0.035(3)	0.068(3)	-0.011(2)	0.003(2)	-0.017(2)
O1	0.0331(19)	0.036(3)	0.075(3)	-0.021(2)	0.011(2)	-0.0074(18)
O2	0.0350(18)	0.024(2)	0.056(2)	-0.015(2)	0.0005(18)	-0.0048(16)
Br1	0.0560(3)	0.0376(4)	0.0567(3)	-0.0069(3)	-0.0074(3)	-0.0173(3)
C1'	0.036(3)	0.030(3)	0.045(3)	-0.014(3)	-0.006(2)	-0.009(3)
C2'	0.043(3)	0.033(4)	0.067(4)	-0.024(3)	0.000(3)	-0.005(3)
C3'	0.033(3)	0.030(3)	0.059(3)	-0.019(3)	0.004(3)	-0.003(2)
C4'	0.035(3)	0.033(3)	0.040(3)	-0.016(3)	-0.003(2)	-0.011(2)
C5'	0.039(3)	0.040(4)	0.047(3)	-0.026(3)	-0.001(3)	-0.003(3)
C6'	0.043(3)	0.034(4)	0.046(3)	-0.015(3)	0.000(3)	-0.010(3)
C7'	0.033(3)	0.042(4)	0.048(3)	-0.026(3)	-0.007(3)	-0.009(3)
C8'	0.040(3)	0.030(3)	0.048(3)	-0.007(3)	-0.005(2)	-0.014(2)
C9'	0.031(2)	0.031(3)	0.046(3)	-0.014(3)	0.000(2)	-0.012(2)
C10'	0.046(2)	0.032(3)	0.045(3)	-0.008(2)	-0.002(2)	-0.014(2)
C11'	0.047(3)	0.036(3)	0.047(3)	-0.013(2)	0.015(2)	-0.020(2)
C12'	0.048(3)	0.028(3)	0.034(3)	-0.009(2)	0.005(2)	-0.018(2)
C13'	0.036(3)	0.032(3)	0.028(3)	-0.006(2)	0.003(2)	-0.014(2)
C14'	0.042(3)	0.028(3)	0.032(2)	-0.007(2)	-0.002(2)	-0.015(2)
C15'	0.055(3)	0.035(3)	0.037(3)	-0.008(2)	0.010(2)	-0.020(2)
C16'	0.062(3)	0.032(3)	0.040(3)	-0.010(2)	0.005(3)	-0.019(3)
C17'	0.065(3)	0.047(4)	0.035(3)	-0.009(3)	0.008(3)	-0.034(3)
C18'	0.048(3)	0.054(4)	0.041(3)	-0.017(3)	0.006(2)	-0.029(3)
C19'	0.043(3)	0.035(3)	0.038(3)	-0.011(2)	0.003(2)	-0.021(2)
C20'	0.047(3)	0.044(3)	0.074(4)	-0.016(3)	0.013(3)	-0.022(3)
C21'	0.047(3)	0.047(3)	0.053(3)	-0.020(3)	0.011(2)	-0.021(2)
C22'	0.036(3)	0.034(3)	0.035(3)	-0.013(2)	0.004(2)	-0.013(2)

C23'	0.042(3)	0.039(3)	0.046(3)	-0.018(3)	-0.006(2)	-0.009(2)
C24'	0.083(4)	0.045(4)	0.050(3)	-0.007(3)	0.020(3)	-0.031(3)
N1'	0.109(5)	0.032(3)	0.104(5)	-0.010(3)	0.047(4)	-0.018(3)
O1'	0.037(2)	0.044(3)	0.060(3)	-0.018(2)	0.0087(19)	-0.0120(19)
O2'	0.0346(18)	0.025(2)	0.050(2)	-0.0125(19)	0.0000(17)	-0.0061(16)
Br1'	0.0597(3)	0.0350(3)	0.0520(3)	-0.0094(3)	-0.0046(3)	-0.0148(3)

The form of the anisotropic displacement parameter is: $\exp[-2\pi^2(a^{*2}U_{11}h^2+b^{*2}U_{22}k^2+c^{*2}U_{33}l^2+2b^*c^*U_{23}kl+2a^*c^*U_{13}hl+2a^*b^*U_{12}hk)]$

Table 5. Bond Distances in Compound 99118, Å

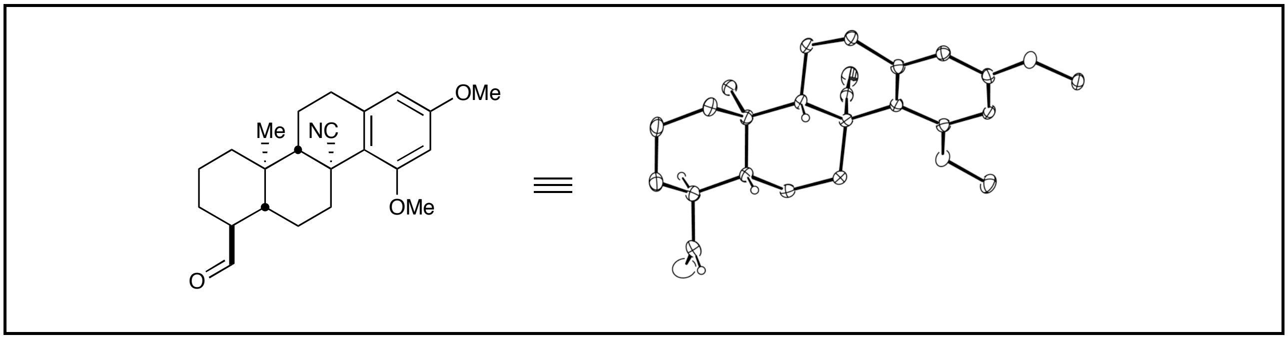
C1-C6	1.378(8)	C1-C2	1.398(7)	C1-Br1	1.884(6)
C2-C3	1.380(9)	C3-C4	1.397(8)	C4-C5	1.393(7)
C4-C7	1.479(8)	C5-C6	1.371(9)	C7-O1	1.205(6)
C7-O2	1.339(6)	C8-O2	1.436(7)	C8-C9	1.522(7)
C9-C10	1.527(7)	C9-C22	1.532(7)	C10-C11	1.529(5)
C11-C12	1.523(7)	C12-C13	1.553(7)	C13-C14	1.515(7)
C13-C23	1.545(7)	C13-C22	1.561(7)	C14-C15	1.400(7)
C14-C19	1.417(6)	C15-C16	1.386(7)	C16-C17	1.406(7)
C16-C24	1.454(7)	C17-C18	1.368(9)	C18-C19	1.380(9)
C19-C20	1.503(7)	C20-C21	1.517(7)	C21-C22	1.521(6)
C24-N1	1.142(6)	C1'-C6'	1.378(8)	C1'-C2'	1.389(8)
C1'-Br1'	1.898(6)	C2'-C3'	1.360(9)	C3'-C4'	1.403(8)
C4'-C5'	1.388(7)	C4'-C7'	1.476(8)	C5'-C6'	1.373(9)
C7'-O1'	1.208(6)	C7'-O2'	1.349(7)	C8'-O2'	1.466(6)
C8'-C9'	1.521(8)	C9'-C22'	1.538(7)	C9'-C10'	1.540(6)
C10'-C11'	1.539(6)	C11'-C12'	1.514(7)	C12'-C13'	1.547(6)
C13'-C23'	1.531(8)	C13'-C14'	1.553(7)	C13'-C22'	1.565(7)
C14'-C19'	1.398(7)	C14'-C15'	1.402(8)	C15'-C16'	1.382(8)
C16'-C17'	1.390(7)	C16'-C24'	1.446(8)	C17'-C18'	1.388(10)
C18'-C19'	1.400(9)	C19'-C20'	1.513(8)	C20'-C21'	1.517(7)
C21'-C22'	1.510(6)	C24'-N1'	1.146(7)		

Table 6. Bond Angles in Compound 99118, °

C6-C1-C2	120.7(6)	C6-C1-Br1	119.9(4)	C2-C1-Br1	119.5(4)
C3-C2-C1	118.9(5)	C2-C3-C4	120.9(5)	C5-C4-C3	118.7(6)
C5-C4-C7	123.1(5)	C3-C4-C7	118.3(5)	C6-C5-C4	120.9(5)
C5-C6-C1	119.9(5)	O1-C7-O2	123.7(5)	O1-C7-C4	124.0(5)
O2-C7-C4	112.4(4)	O2-C8-C9	106.5(4)	C8-C9-C10	110.0(4)
C8-C9-C22	113.5(4)	C10-C9-C22	110.0(4)	C9-C10-C11	113.1(4)
C12-C11-C10	111.5(3)	C11-C12-C13	112.9(4)	C14-C13-C23	106.6(4)
C14-C13-C12	111.2(4)	C23-C13-C12	108.7(4)	C14-C13-C22	111.0(4)
C23-C13-C22	112.3(5)	C12-C13-C22	107.1(4)	C15-C14-C19	117.0(5)
C15-C14-C13	119.8(4)	C19-C14-C13	123.0(5)	C16-C15-C14	121.6(4)
C15-C16-C17	120.1(5)	C15-C16-C24	121.0(4)	C17-C16-C24	118.9(5)
C18-C17-C16	118.7(5)	C17-C18-C19	121.8(5)	C18-C19-C14	120.7(5)
C18-C19-C20	119.1(4)	C14-C19-C20	120.2(5)	C19-C20-C21	114.5(4)
C20-C21-C22	109.4(4)	C21-C22-C9	116.4(4)	C21-C22-C13	110.9(4)
C9-C22-C13	111.1(4)	N1-C24-C16	178.0(6)	C7-O2-C8	116.0(4)
C6'-C1'-C2'	121.1(6)	C6'-C1'-Br1'	118.5(4)	C2'-C1'-Br1'	120.3(4)
C3'-C2'-C1'	119.1(5)	C2'-C3'-C4'	121.2(5)	C5'-C4'-C3'	118.2(6)
C5'-C4'-C7'	123.0(5)	C3'-C4'-C7'	118.7(5)	C6'-C5'-C4'	121.2(5)
C5'-C6'-C1'	119.1(5)	O1'-C7'-O2'	123.4(6)	O1'-C7'-C4'	125.1(5)
O2'-C7'-C4'	111.5(5)	O2'-C8'-C9'	107.3(4)	C8'-C9'-C22'	109.2(4)
C8'-C9'-C10'	113.0(5)	C22'-C9'-C10'	109.5(4)	C11'-C10'-C9'	110.3(4)
C12'-C11'-C10'	113.2(4)	C11'-C12'-C13'	111.2(4)	C23'-C13'-C12'	111.2(4)
C23'-C13'-C14'	107.0(5)	C12'-C13'-C14'	109.5(4)	C23'-C13'-C22'	112.9(4)
C12'-C13'-C22'	107.2(4)	C14'-C13'-C22'	109.0(4)	C19'-C14'-C15'	118.4(5)
C19'-C14'-C13'	122.1(5)	C15'-C14'-C13'	119.4(5)	C16'-C15'-C14'	121.4(5)
C15'-C16'-C17'	120.4(5)	C15'-C16'-C24'	121.4(5)	C17'-C16'-C24'	118.2(5)
C18'-C17'-C16'	118.8(6)	C17'-C18'-C19'	121.4(5)	C14'-C19'-C18'	119.6(5)
C14'-C19'-C20'	122.7(5)	C18'-C19'-C20'	117.6(5)	C19'-C20'-C21'	111.7(4)
C22'-C21'-C20'	108.6(4)	C21'-C22'-C9'	117.9(4)	C21'-C22'-C13'	111.5(4)
C9'-C22'-C13'	110.9(4)	N1'-C24'-C16'	176.5(6)	C7'-O2'-C8'	116.7(4)

5.3.3 Aldehyde **13**

X-ray Structure Determination of Compound 99127



Compound 99127, $C_{23}H_{31}NO_3$, crystallizes in the monoclinic space group C2 (systematic absences hkl: h+k=odd) with a=13.0078(3)Å, b=6.8941(2)Å, c=21.3275(6)Å, β=91.374(2)°, V=1912.04(9)Å^3, Z=4, and d_{calc}=1.284 g/cm^3 . X-ray intensity data were collected on a Bruker APEXII CCD area detector employing graphite-monochromated Cu-Kα radiation (λ=1.54178 Å) at a temperature of 153(1)K. Preliminary indexing was performed from a series of thirty-six 0.5° rotation frames with exposures of 30 seconds. A total of 2348 frames were collected with a crystal to detector distance of 37.628 mm, rotation widths of 0.5° and exposures of 30 seconds:

scan type	2θ	ω	φ	χ	frames
φ	92.00	88.66	-2.53	-26.26	690
φ	87.00	76.65	-115.66	62.65	311
ω	32.00	26.05	-74.74	-33.72	197
φ	92.00	132.53	-9.61	-22.49	739
ω	92.00	-12.19	-42.47	90.29	153
ω	-58.00	-149.11	-256.72	19.46	202
ω	-43.00	-35.31	-224.99	-80.21	131
ω	92.00	-163.69	-93.53	-93.68	82

Rotation frames were integrated using SAINT[35], producing a listing of unaveraged F^2 and

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[35] Bruker (2009) SAINT. Bruker AXS Inc., Madison, Wisconsin, USA.

$\sigma(F^2)$ values which were then passed to the SHELXTL[36] program package for further processing and structure solution on a Dell Pentium 4 computer. A total of 5967 reflections were measured over the ranges $4.15 \leq \theta \leq 64.37°$, $-13 \leq h \leq 15$, $-8 \leq k \leq 7$, $-22 \leq l \leq 24$ yielding 2871 unique reflections (Rint = 0.0382). The intensity data were corrected for Lorentz and polarization effects and for absorption using SADABS[37] (minimum and maximum transmission 0.787, 1.000).

The structure was solved by direct methods (SHELXS-97[38]). Refinement was by full-matrix least squares based on F^2 using SHELXL-97.[39] All reflections were used during refinement. The weighting scheme used was $w=1/[\sigma^2(F_o^2) + (0.0691P)^2 + 0.0000P]$ where $P = (F_o^2 + 2F_c^2)/3$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using a riding model. Refinement converged to R1=0.0389 and wR2=0.0957 for 2478 observed reflections for which $F > 4\sigma(F)$ and R1=0.0528 and wR2=0.1215 and GOF =1.143 for all 2871 unique, non-zero reflections and 257 variables.[40] The maximum Δ/σ in the final cycle of least squares was 0.000 and the two most prominent peaks in the final difference Fourier were +0.323 and -0.450 e/Å^3.

Table 1. lists cell information, data collection parameters, and refinement data. Final positional and equivalent isotropic thermal parameters are given in Tables 2. and 3. Anisotropic thermal parameters are in Table 4. Tables 5. and 6. list bond distances and bond angles. Figure 1. is an ORTEP[41] representation of the molecule with 30% probability thermal ellipsoids displayed.

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(36) Bruker (2009) SHELXTL. Bruker AXS Inc., Madison, Wisconsin, USA.

(37) Sheldrick, G.M. (2007) SADABS. University of Göttingen, Germany.

(38) Sheldrick, G.M. *Acta Cryst.* **2008**, *A64*,112.

(39) Sheldrick, G.M. *Acta Cryst.* **2008**, *A64*,112.

(40) $R1 = \Sigma||F_o| - |F_c|| / \Sigma |F_o|$

$wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{½}$

$GOF = [\Sigma w(F_o^2 - F_c^2)^2/(n - p)]^{½}$

where n = the number of reflections and p = the number of parameters refined.

(41) "ORTEP-II: A Fortran Thermal Ellipsoid Plot Program for Crystal Structure Illustrations". Johnson, C. K. (1976) ORNL-5138.

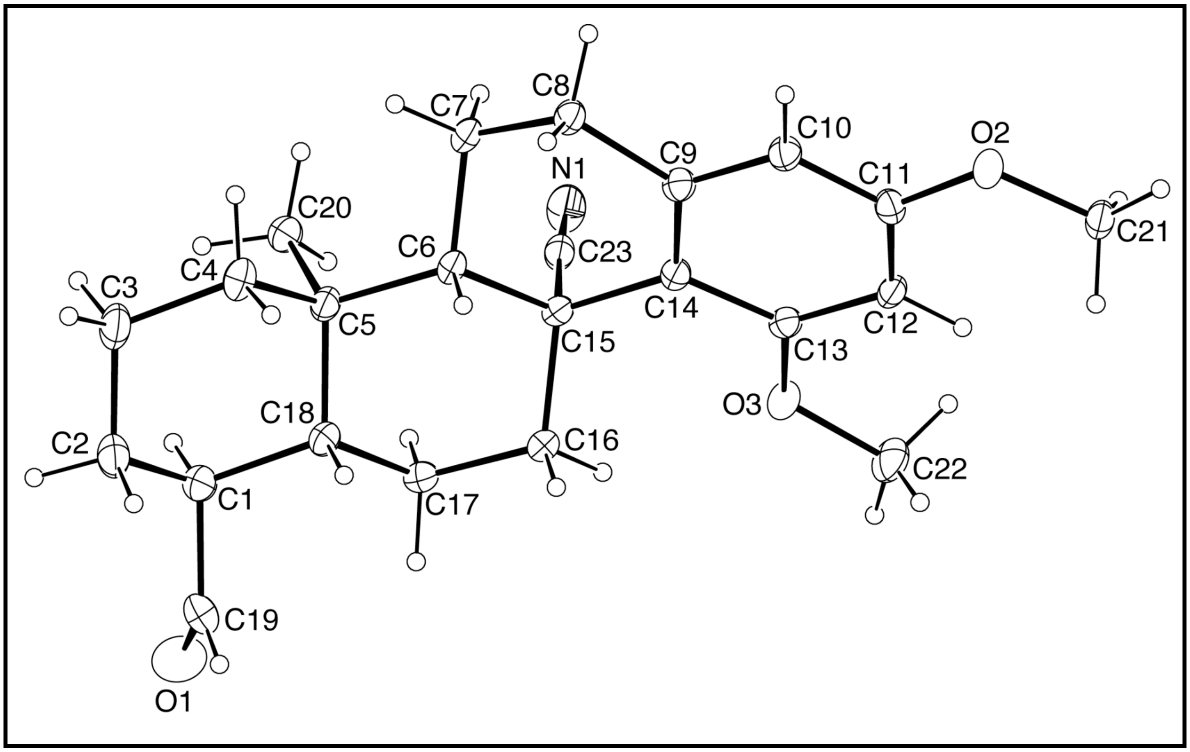

Figure 1. ORTEP drawing of the title compound with 30% probability thermal ellipsoids.

Table 1. Summary of Structure Determination of Compound 99127

Empirical formula	$C_{23}H_{31}NO_3$
Formula weight	369.49
Temperature	153(1) K
Wavelength	1.54178 Å
Crystal system	monoclinic
Space group	C2
Cell constants:	
a	13.0078(3) Å
b	6.8941(2) Å
c	21.3275(6) Å
β	91.374(2)°
Volume	1912.04(9) Å^3
Z	4
Density (calculated)	1.284 Mg/m^3
Absorption coefficient	0.664 mm^{-1}
F(000)	800
Crystal size	0.48 x 0.08 x 0.005 mm^3
Theta range for data collection	4.15 to 64.37°
Index ranges	$-13 \le h \le 15$, $-8 \le k \le 7$, $-22 \le l \le 24$
Reflections collected	5967
Independent reflections	2871 [R(int) = 0.0382]
Completeness to theta = 64.37°	96.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.787
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2871 / 1 / 257
Goodness-of-fit on F^2	1.143
Final R indices [I>2sigma(I)]	R1 = 0.0389, wR2 = 0.0957
R indices (all data)	R1 = 0.0528, wR2 = 0.1215
Absolute structure parameter	0.0(3)
Largest diff. peak and hole	0.323 and -0.450 e.Å^{-3}

Table 2. Refined Positional Parameters for Compound 99127

Atom	x	y	z	U_{eq}, Å^2
C1	0.2497(2)	0.7868(4)	0.92022(14)	0.0368(7)
C2	0.1531(3)	0.8916(5)	0.94142(15)	0.0442(8)
C3	0.0554(2)	0.7850(5)	0.92201(15)	0.0390(7)
C4	0.0521(2)	0.7290(5)	0.85280(14)	0.0337(7)
C5	0.1483(2)	0.6180(4)	0.83196(13)	0.0257(6)
C6	0.14177(18)	0.5956(4)	0.75942(13)	0.0223(6)
C7	0.0524(2)	0.4704(4)	0.73550(13)	0.0275(6)
C8	0.02802(18)	0.5226(5)	0.66836(13)	0.0292(6)
C9	0.12224(18)	0.5322(4)	0.62809(13)	0.0251(6)
C10	0.10570(19)	0.5358(4)	0.56350(13)	0.0272(6)
C11	0.18614(19)	0.5380(4)	0.52271(12)	0.0249(5)
C12	0.28643(18)	0.5310(4)	0.54605(12)	0.0245(6)
C13	0.30340(17)	0.5253(4)	0.61104(12)	0.0231(5)
C14	0.22286(17)	0.5331(4)	0.65406(12)	0.0217(5)
C15	0.24224(17)	0.5310(4)	0.72599(12)	0.0218(5)
C16	0.33204(19)	0.6627(4)	0.74975(13)	0.0271(6)
C17	0.3403(2)	0.6695(4)	0.82111(13)	0.0313(6)
C18	0.2423(2)	0.7467(4)	0.84912(13)	0.0276(6)
C19	0.3430(3)	0.9070(6)	0.93617(16)	0.0525(10)
C20	0.1523(2)	0.4203(4)	0.86506(13)	0.0316(7)
C21	0.24179(19)	0.5394(4)	0.41634(13)	0.0289(6)
C22	0.4861(2)	0.5134(6)	0.59557(15)	0.0395(7)
C23	0.2703(2)	0.3269(4)	0.74124(13)	0.0268(6)
N1	0.2947(2)	0.1691(4)	0.75049(13)	0.0400(6)
O1	0.4176(4)	0.8472(9)	0.9693(3)	0.0788(18)
O1'	0.3371(5)	1.0886(10)	0.9378(4)	0.081(2)
O2	0.16023(12)	0.5427(3)	0.46039(9)	0.0304(5)
O3	0.40055(13)	0.5051(3)	0.63624(9)	0.0305(5)

$U_{eq}={}^{1}/_{3}[U_{11}(aa^*)^2+U_{22}(bb^*)^2+U_{33}(cc^*)^2+2U_{12}aa^*bb^*\cos\gamma+2U_{13}aa^*cc^*\cos\beta+2U_{23}bb^*cc^*\cos\alpha]$

Table 3. Positional Parameters for Hydrogens in Compound 99127

Atom	x	y	z	U_{iso}, Å^2
H1	0.2553	0.6627	0.9425	0.049
H2a	0.1558	0.9048	0.9867	0.059
H2b	0.1515	1.0209	0.9235	0.059
H3a	-0.0034	0.8667	0.9306	0.052
H3b	0.0496	0.6684	0.9472	0.052
H4a	0.0448	0.8458	0.8278	0.045
H4b	-0.0081	0.6490	0.8445	0.045
H6	0.1270	0.7261	0.7434	0.030
H7a	0.0708	0.3343	0.7385	0.037
H7b	-0.0074	0.4924	0.7609	0.037
H8a	-0.0062	0.6476	0.6672	0.039
H8b	-0.0193	0.4273	0.6507	0.039
H10	0.0386	0.5367	0.5474	0.036
H12	0.3414	0.5302	0.5190	0.033
H16a	0.3961	0.6144	0.7334	0.036
H16b	0.3215	0.7931	0.7338	0.036
H17a	0.3538	0.5401	0.8371	0.042
H17b	0.3975	0.7520	0.8338	0.042
H18	0.2293	0.8725	0.8291	0.037
H19	0.3458	1.0329	0.9206	0.070
H19'	0.4056	0.8464	0.9449	0.070
H20a	0.1410	0.4377	0.9090	0.047
H20b	0.2185	0.3621	0.8594	0.047
H20c	0.0998	0.3373	0.8474	0.047
H21a	0.2877	0.6458	0.4247	0.043
H21b	0.2134	0.5508	0.3745	0.043
H21c	0.2788	0.4194	0.4203	0.043
H22a	0.4825	0.4068	0.5666	0.059
H22b	0.5489	0.5055	0.6200	0.059
H22c	0.4844	0.6334	0.5727	0.059

Table 4. Refined Thermal Parameters (U's) for Compound 99127

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0472(17)	0.0382(18)	0.0250(16)	-0.0003(14)	0.0050(13)	-0.0143(14)
C2	0.060(2)	0.0422(17)	0.0310(18)	-0.0084(16)	0.0167(14)	-0.0092(16)
C3	0.0451(17)	0.0427(18)	0.0300(17)	-0.0027(15)	0.0152(13)	0.0021(14)
C4	0.0321(14)	0.0391(17)	0.0304(17)	0.0009(14)	0.0097(12)	0.0038(12)
C5	0.0274(14)	0.0270(14)	0.0229(15)	0.0015(12)	0.0061(11)	-0.0015(11)
C6	0.0224(12)	0.0226(12)	0.0222(15)	0.0028(11)	0.0061(10)	0.0016(10)
C7	0.0236(13)	0.0336(16)	0.0258(15)	0.0009(12)	0.0078(10)	-0.0028(11)
C8	0.0227(12)	0.0396(15)	0.0254(14)	-0.0025(14)	0.0046(10)	-0.0028(13)
C9	0.0226(12)	0.0243(12)	0.0284(15)	-0.0021(13)	0.0038(10)	0.0019(12)
C10	0.0224(12)	0.0344(14)	0.0250(14)	-0.0009(14)	0.0006(10)	0.0000(12)
C11	0.0313(13)	0.0225(12)	0.0211(14)	-0.0014(13)	0.0024(10)	0.0014(12)
C12	0.0253(12)	0.0224(12)	0.0264(15)	-0.0003(12)	0.0105(10)	-0.0019(11)
C13	0.0213(12)	0.0208(12)	0.0275(15)	-0.0008(12)	0.0031(10)	0.0002(11)
C14	0.0247(12)	0.0172(11)	0.0234(14)	0.0003(12)	0.0048(10)	0.0016(11)
C15	0.0203(11)	0.0204(11)	0.0250(14)	0.0013(13)	0.0031(10)	-0.0005(11)
C16	0.0256(14)	0.0299(14)	0.0260(15)	-0.0017(12)	0.0054(11)	-0.0060(11)
C17	0.0275(14)	0.0389(15)	0.0276(16)	-0.0022(14)	0.0021(11)	-0.0113(13)
C18	0.0333(14)	0.0270(13)	0.0228(15)	0.0029(12)	0.0053(11)	-0.0055(11)
C19	0.059(2)	0.071(3)	0.0281(19)	-0.0174(19)	0.0059(16)	-0.025(2)
C20	0.0388(16)	0.0310(14)	0.0250(16)	0.0037(13)	0.0030(12)	-0.0067(12)
C21	0.0316(13)	0.0323(14)	0.0232(14)	0.0002(14)	0.0090(10)	0.0005(13)
C22	0.0222(13)	0.0590(19)	0.0376(18)	0.0001(17)	0.0082(11)	0.0027(15)
C23	0.0293(14)	0.0283(15)	0.0230(15)	-0.0006(12)	0.0064(11)	-0.0005(11)
N1	0.0529(16)	0.0284(13)	0.0393(16)	0.0039(12)	0.0117(12)	0.0079(12)
O1	0.062(3)	0.117(5)	0.057(3)	-0.001(3)	-0.006(3)	-0.040(3)
O1'	0.067(4)	0.058(4)	0.119(7)	-0.024(4)	0.002(4)	-0.030(3)
O2	0.0278(9)	0.0414(11)	0.0221(10)	0.0006(10)	0.0049(7)	0.0002(9)
O3	0.0198(8)	0.0434(11)	0.0287(10)	-0.0003(9)	0.0058(7)	0.0018(8)

The form of the anisotropic displacement parameter is: $\exp[-2\pi^2(a^{*2}U_{11}h^2+b^{*2}U_{22}k^2+c^{*2}U_{33}l^2+2b^*c^*U_{23}kl+2a^*c^*U_{13}hl+2a^*b^*U_{12}hk)]$

Table 5. Bond Distances in Compound 99127, Å

C1-C19	1.502(5)	C1-C2	1.527(4)	C1-C18	1.542(4)
C2-C3	1.517(5)	C3-C4	1.525(4)	C4-C5	1.541(4)
C5-C20	1.536(4)	C5-C18	1.547(4)	C5-C6	1.555(4)
C6-C7	1.526(4)	C6-C15	1.568(3)	C7-C8	1.503(4)
C8-C9	1.515(4)	C9-C10	1.389(4)	C9-C14	1.409(3)
C10-C11	1.377(4)	C11-O2	1.364(3)	C11-C12	1.386(3)
C12-C13	1.399(4)	C13-O3	1.368(3)	C13-C14	1.410(4)
C14-C15	1.549(4)	C15-C23	1.488(4)	C15-C16	1.555(3)
C16-C17	1.524(4)	C17-C18	1.516(4)	C19-O1'	1.254(8)
C19-O1	1.256(7)	C21-O2	1.434(3)	C22-O3	1.428(3)
C23-N1	1.148(4)				

Table 6. Bond Angles in Compound 99127, °

C19-C1-C2	109.8(3)	C19-C1-C18	110.6(2)	C2-C1-C18	110.1(2)
C3-C2-C1	112.3(3)	C2-C3-C4	113.0(3)	C3-C4-C5	113.6(3)
C20-C5-C4	109.1(2)	C20-C5-C18	112.5(2)	C4-C5-C18	106.9(2)
C20-C5-C6	111.7(2)	C4-C5-C6	108.1(2)	C18-C5-C6	108.4(2)
C7-C6-C5	114.3(2)	C7-C6-C15	108.9(2)	C5-C6-C15	117.02(19)
C8-C7-C6	108.9(2)	C7-C8-C9	113.3(2)	C10-C9-C14	120.7(2)
C10-C9-C8	117.1(2)	C14-C9-C8	122.3(2)	C11-C10-C9	121.7(2)
O2-C11-C10	116.3(2)	O2-C11-C12	124.0(2)	C10-C11-C12	119.7(2)
C11-C12-C13	118.8(2)	O3-C13-C12	121.0(2)	O3-C13-C14	116.2(2)
C12-C13-C14	122.8(2)	C9-C14-C13	116.2(2)	C9-C14-C15	121.1(2)
C13-C14-C15	122.6(2)	C23-C15-C14	105.0(2)	C23-C15-C16	107.6(2)
C14-C15-C16	114.9(2)	C23-C15-C6	111.8(2)	C14-C15-C6	109.27(18)
C16-C15-C6	108.3(2)	C17-C16-C15	112.2(2)	C18-C17-C16	111.4(2)
C17-C18-C1	114.7(2)	C17-C18-C5	111.9(2)	C1-C18-C5	111.4(2)
O1'-C19-O1	111.1(5)	O1'-C19-C1	120.4(5)	O1-C19-C1	123.7(4)
N1-C23-C15	176.8(3)	C11-O2-C21	117.95(19)	C13-O3-C22	118.9(2)

Enantioselective Polyene Cyclization via Organo-SOMO Catalysis

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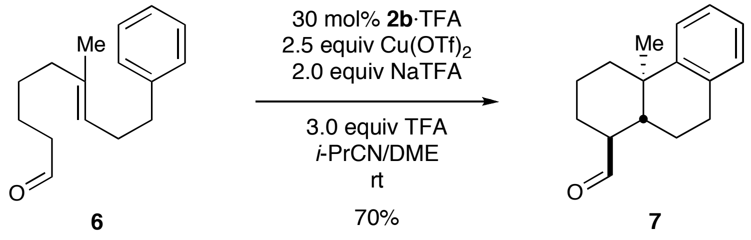
Supporting Information II

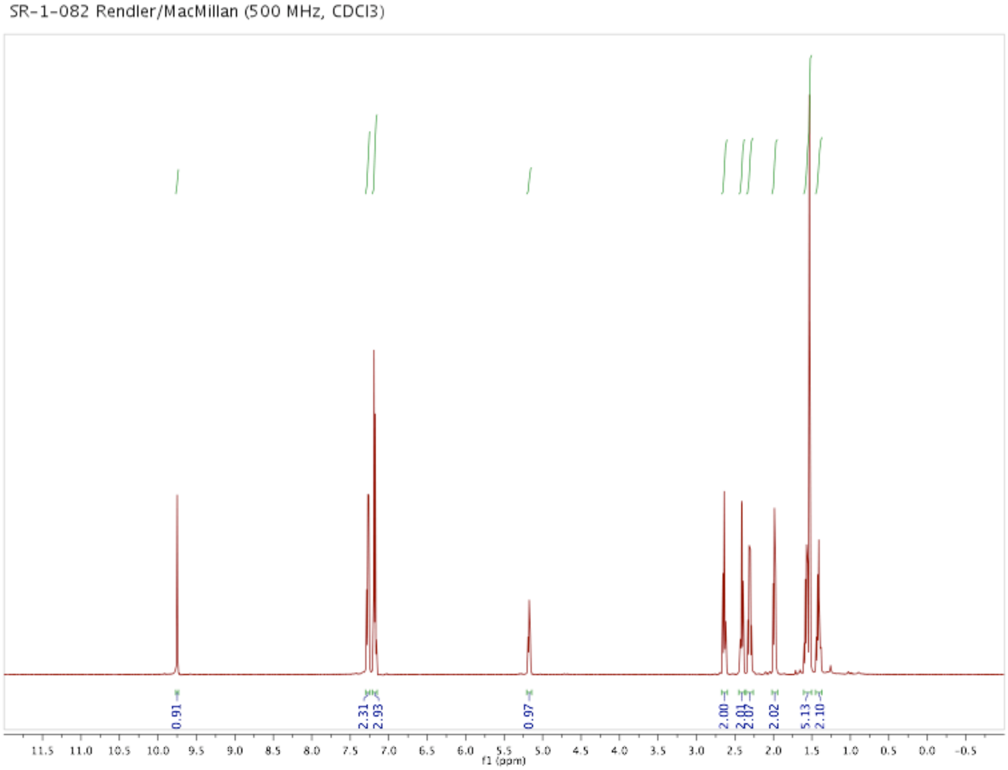
Contents

1 Copies of ^{1}H and ^{13}C NMR Spectra of Cyclization Products and Their Respective Precursors

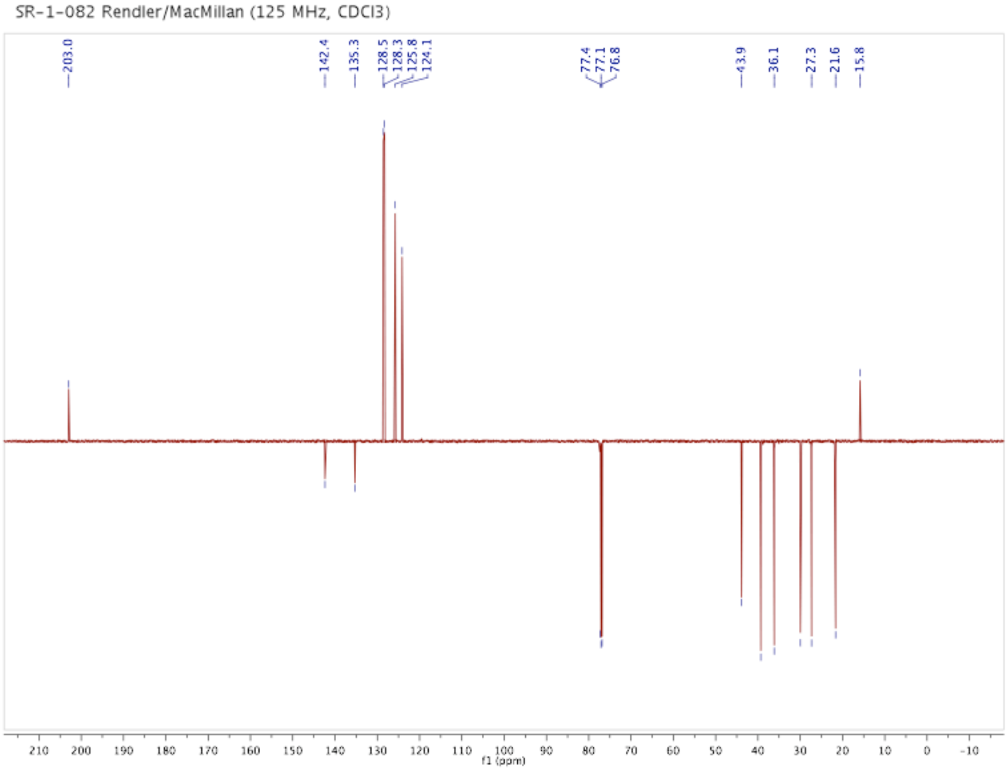
1.1 Bicyclization to give aldehyde **7** (**6** → **7**, Table 2)



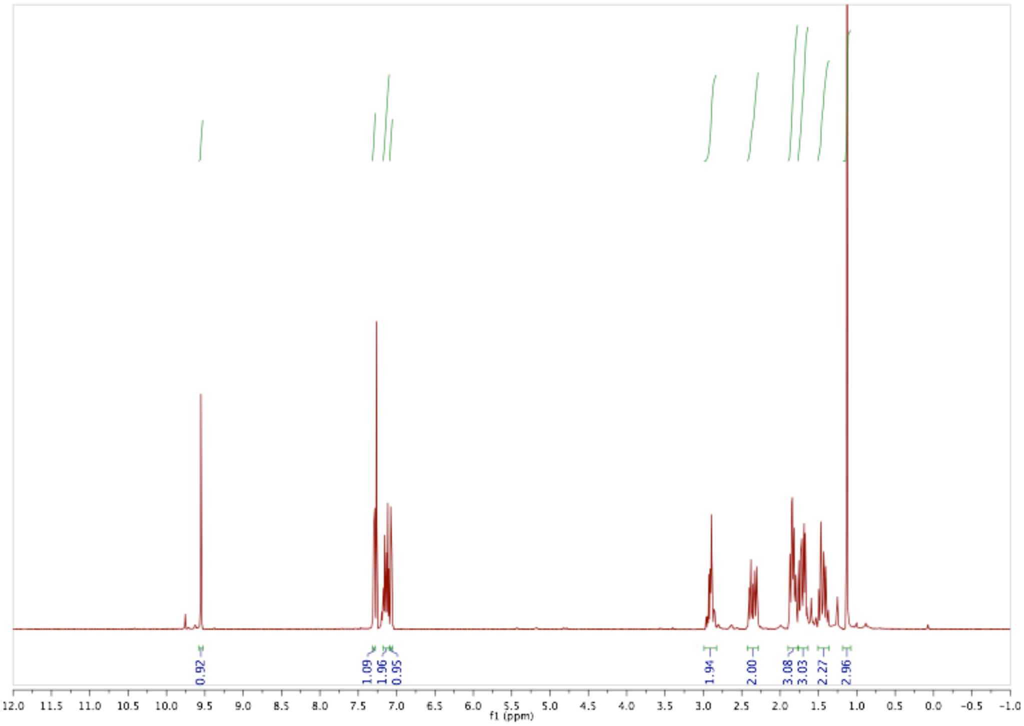
6 (^{1}H NMR, 500 MHz, CDCl$_3$)



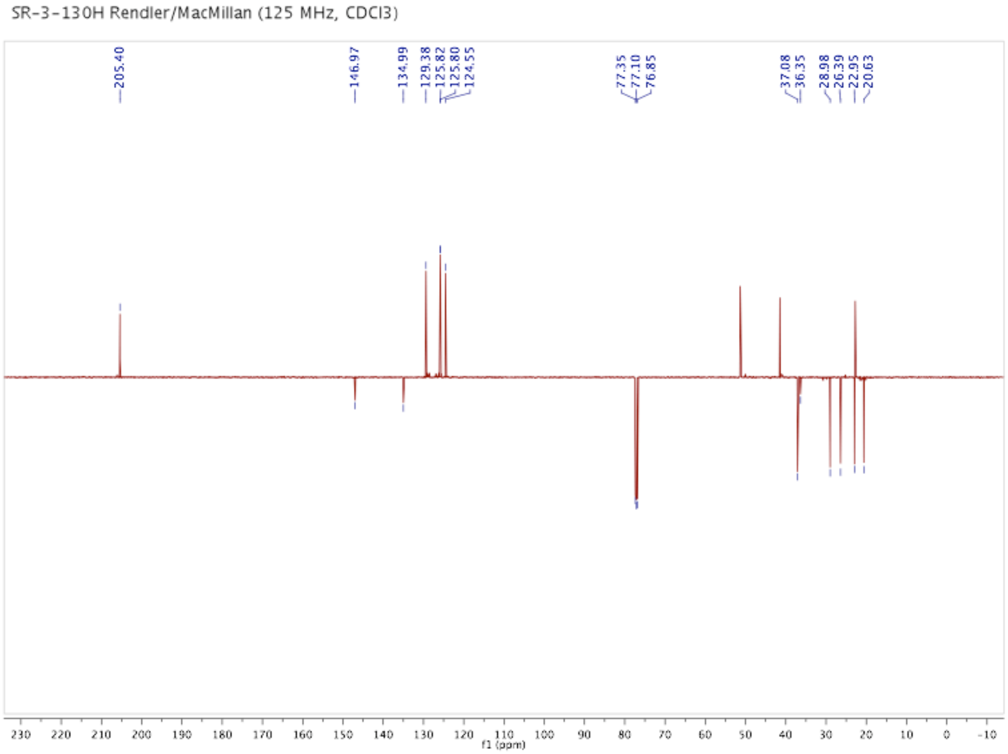
6 (^{13}C NMR, 125 MHz, CDCl$_3$)



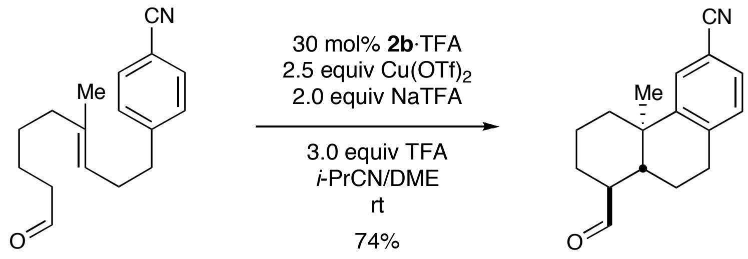
7 (^{1}H NMR, 500 MHz, CDCl$_3$)



7 (^{13}C NMR, 125 MHz, CDCl$_3$)

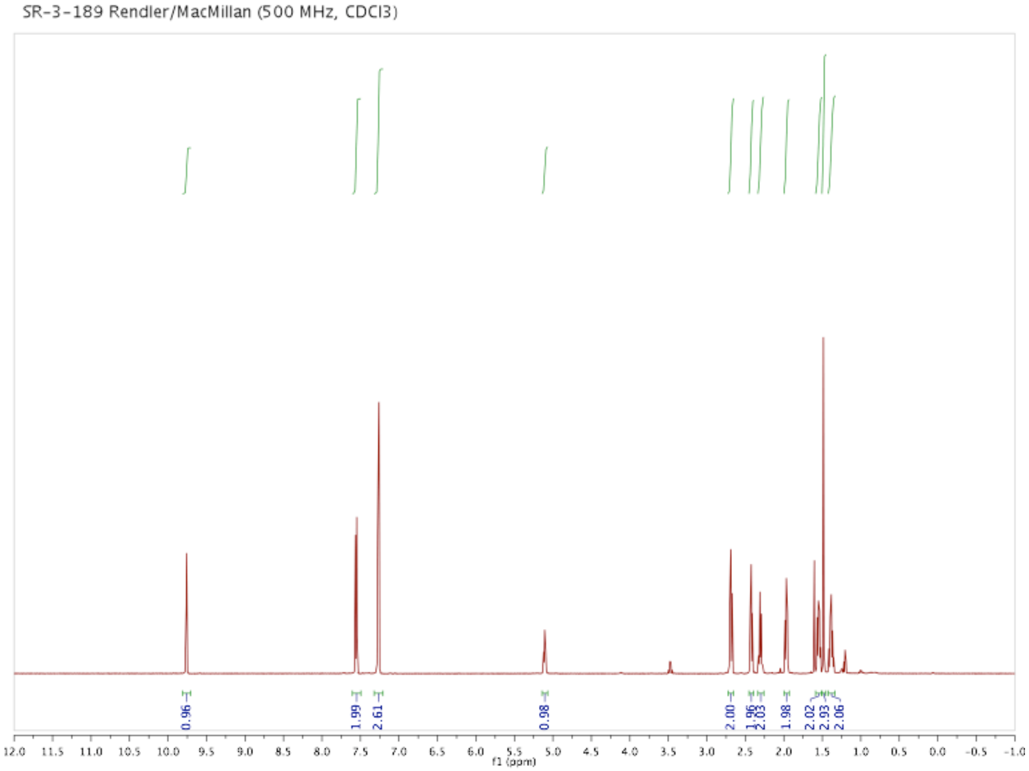


1.2 Bicyclization to give aldehyde **8** (**18** → **8**, Table 2)

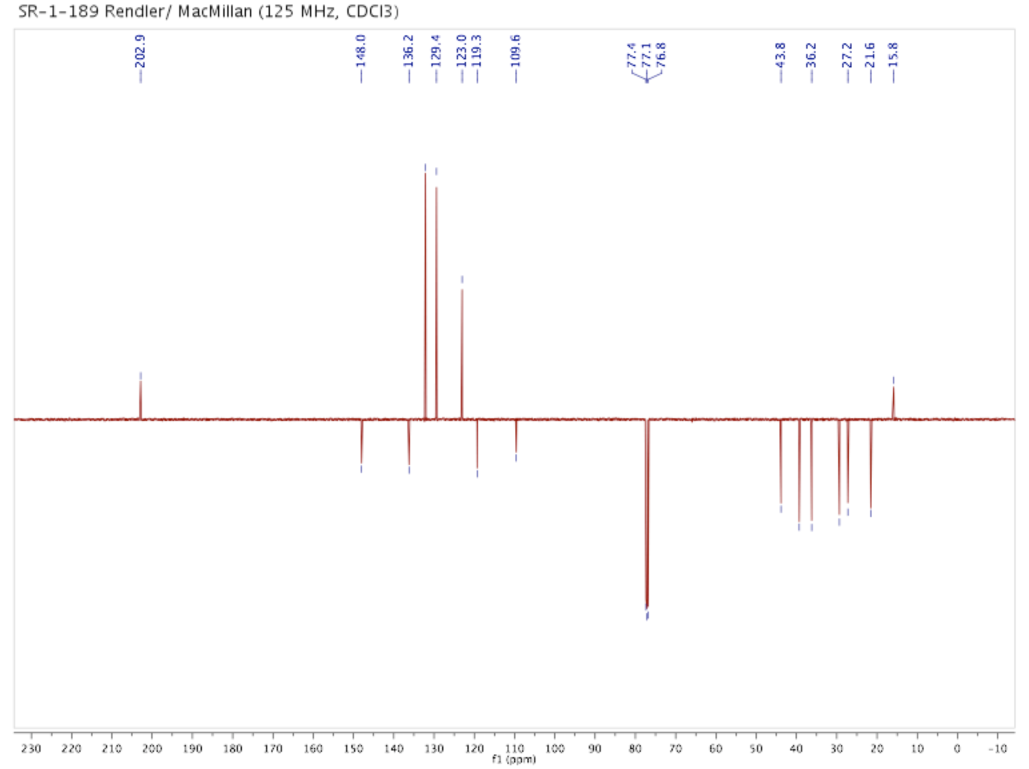


18 **8**

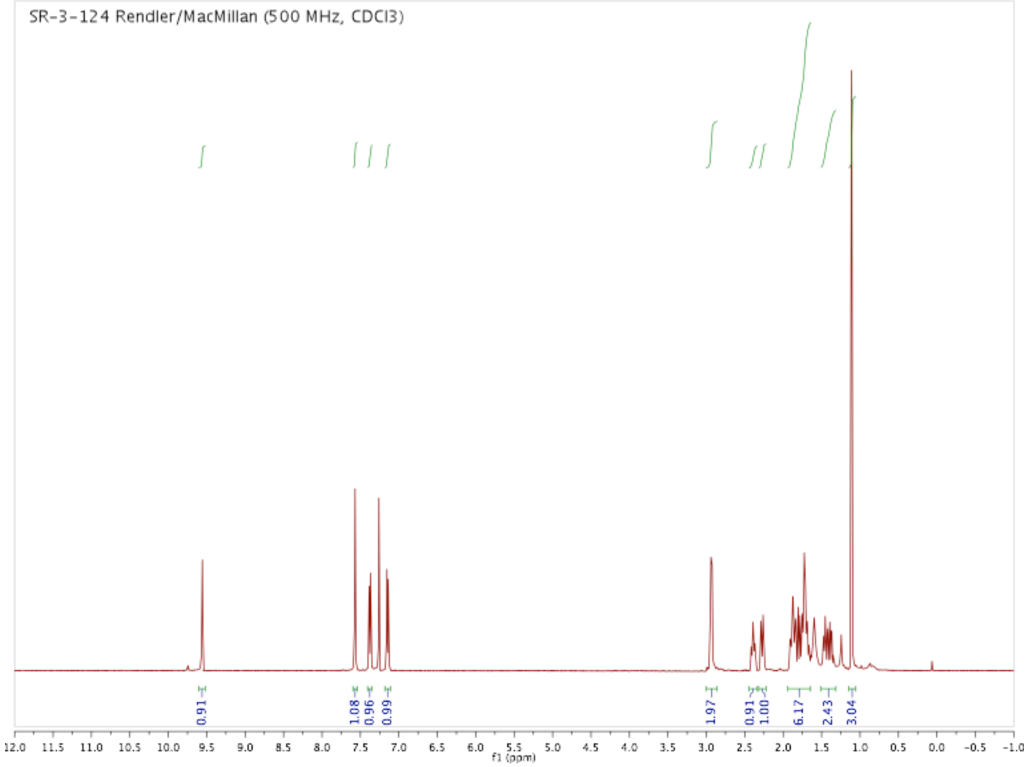
18 (^{1}H NMR, 500 MHz, CDCl$_3$)



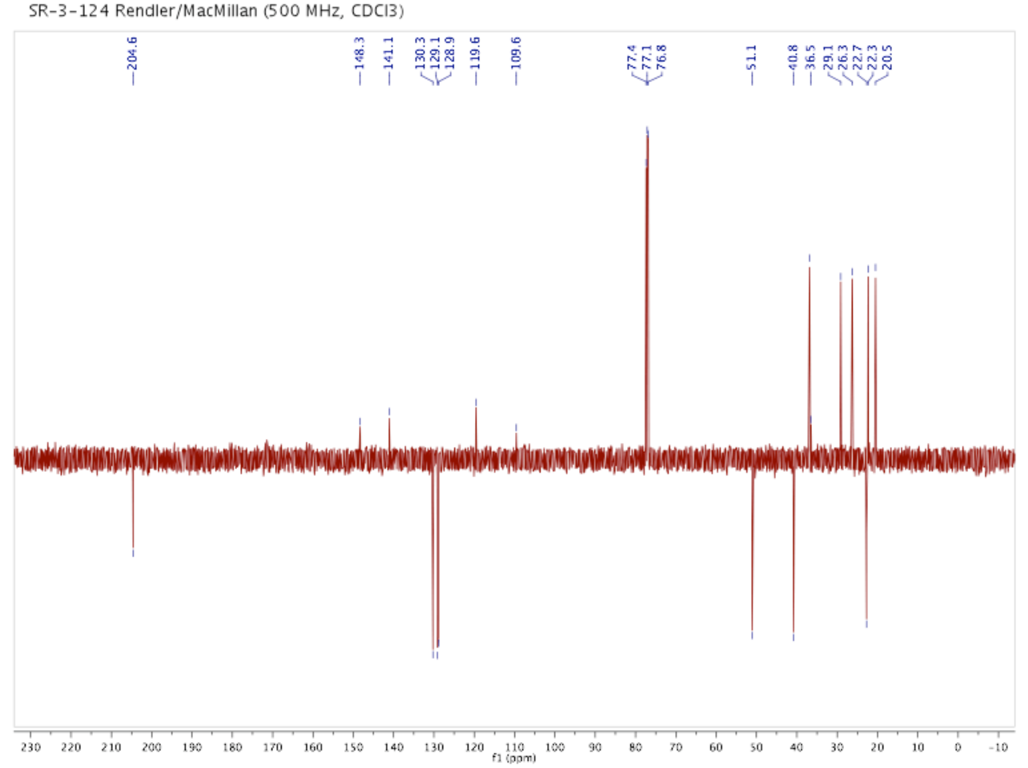
18 (^{13}C NMR, 125 MHz, CDCl$_3$)



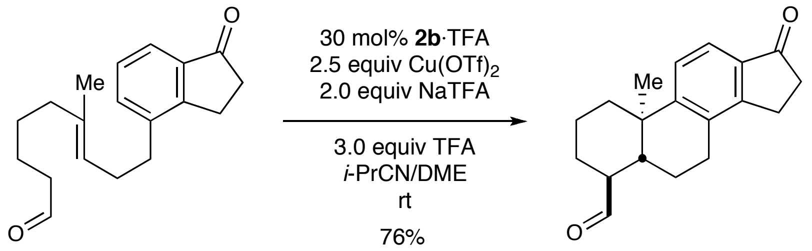
8 (^{1}H NMR, 500 MHz, $CDCl_3$)



8 (^{13}C NMR, 125 MHz, $CDCl_3$)



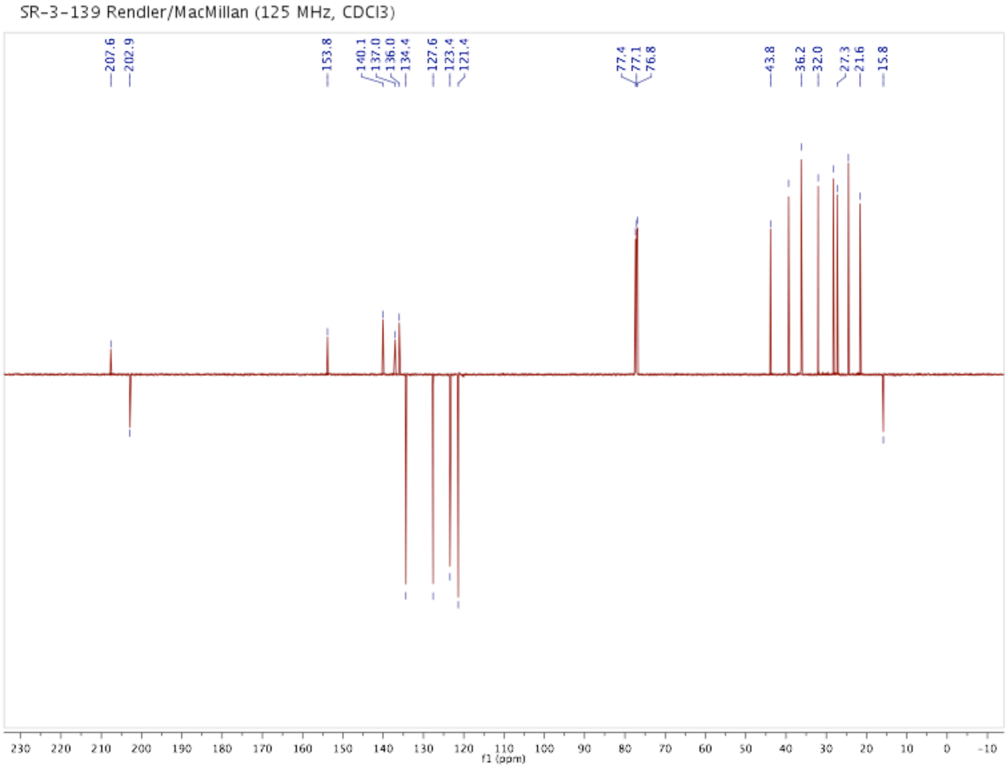
1.3 Bicyclization to give aldehyde **9** (**19** → **9**, Table 2)



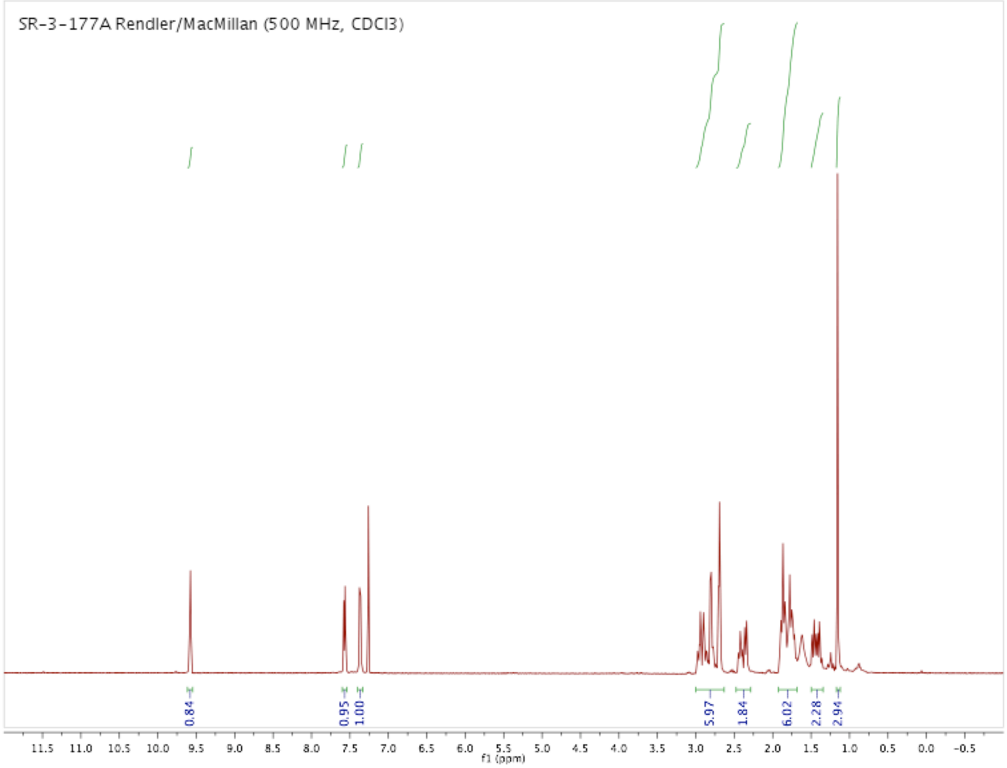
19 **9**

19 (^{1}H NMR, 500 MHz, CDCl$_3$)

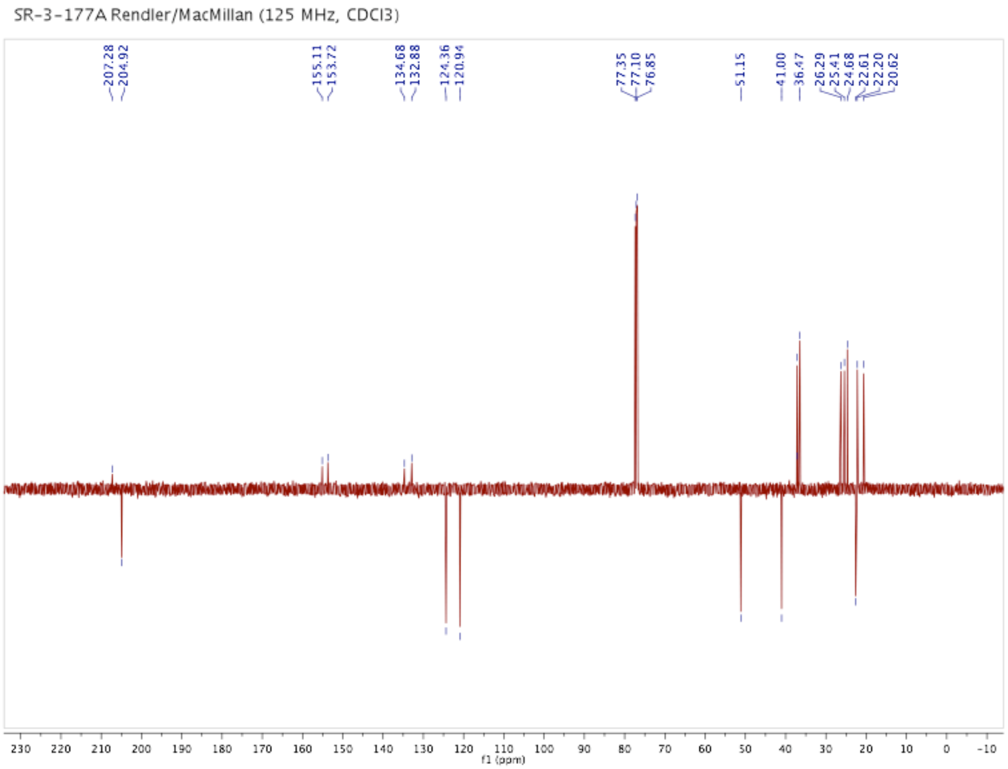
19 (^{13}C NMR, 125 MHz, $CDCl_3$)



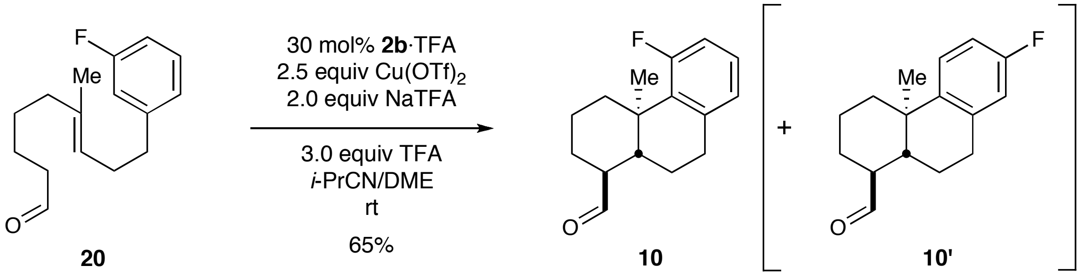
9 (^{1}H NMR, 500 MHz, $CDCl_3$)



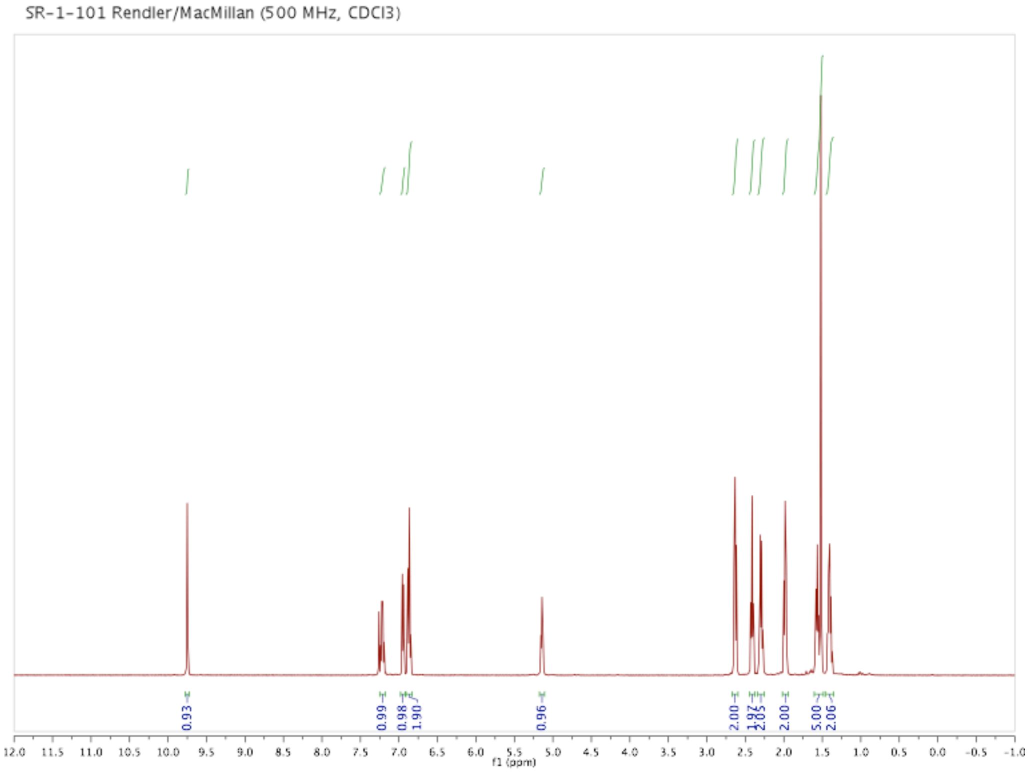
9 (^{13}C NMR, 125 MHz, CDCl$_3$)



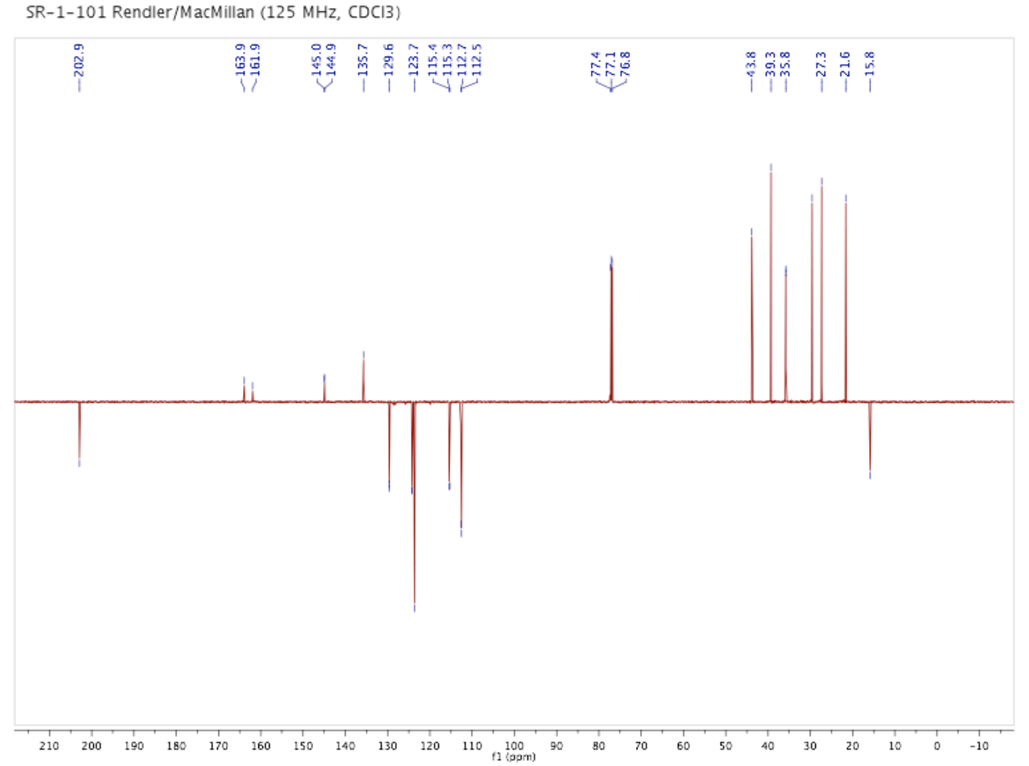
1.4 Bicyclization to give aldehyde **10** (**20** → **10**, Table 2)



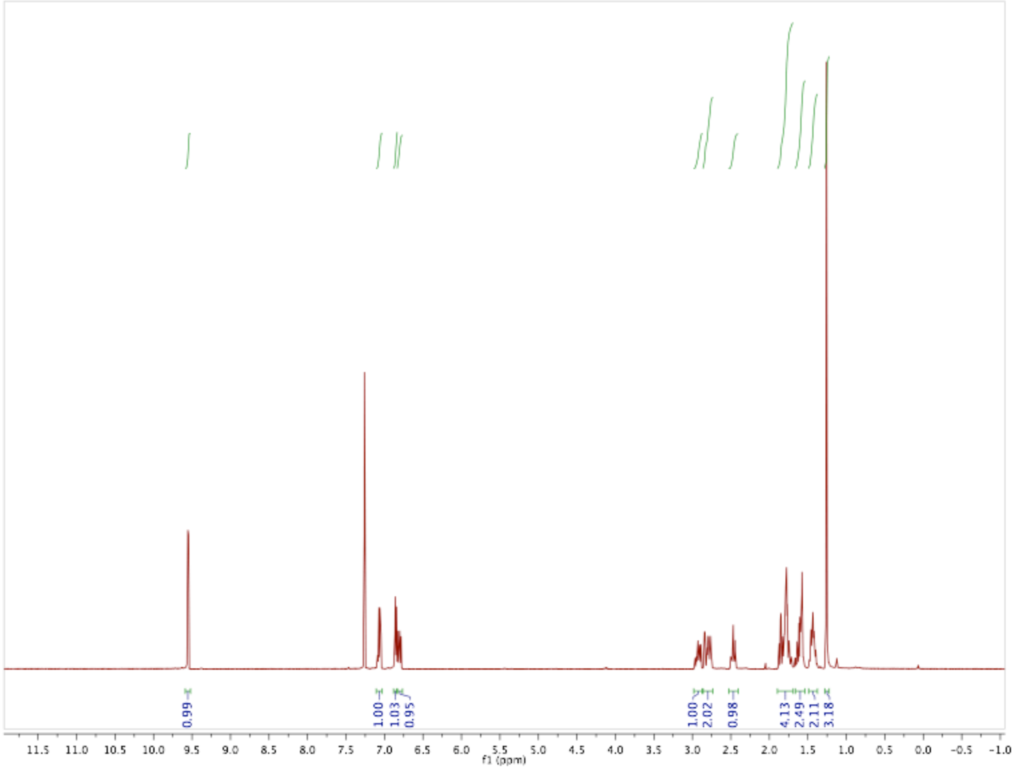
20 (^{1}H NMR, 500 MHz, CDCl$_3$)



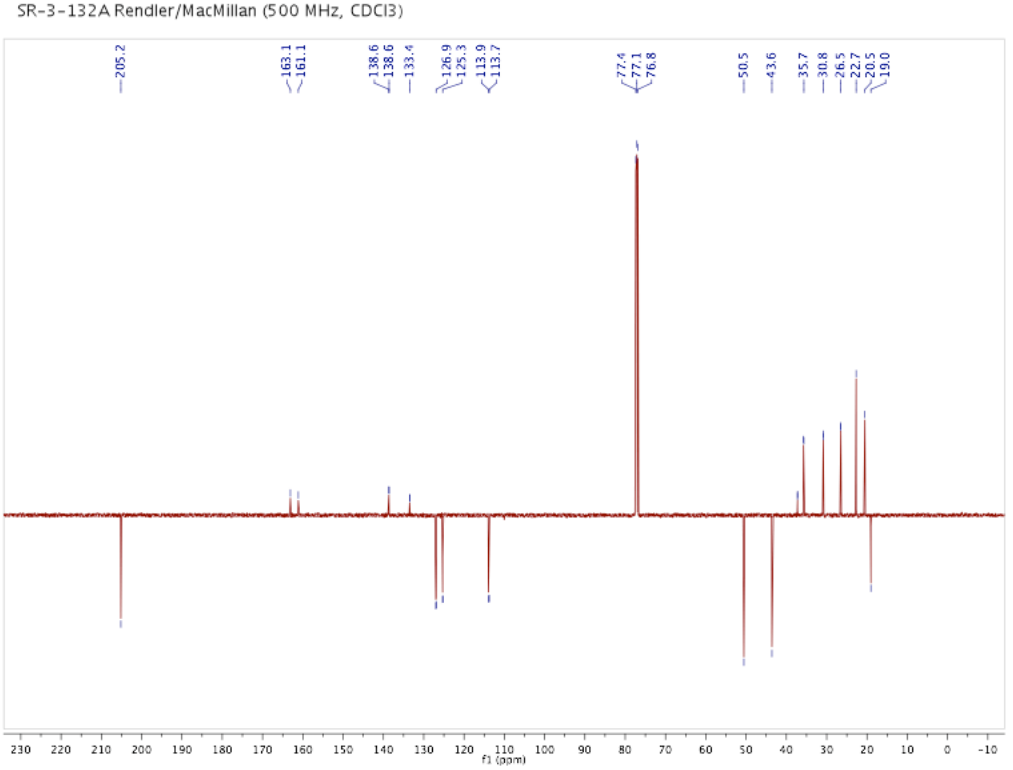
20 (^{13}C NMR, 125 MHz, CDCl$_3$)



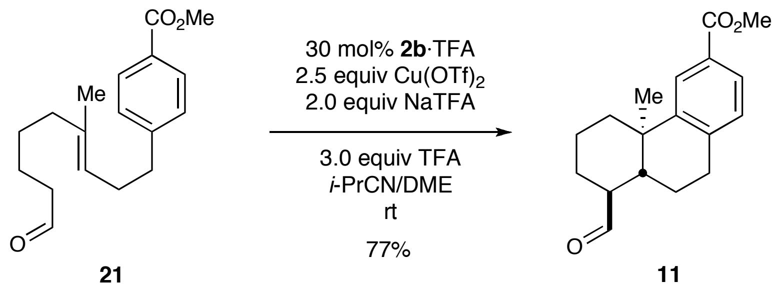
10 (^{1}H NMR, 500 MHz, CDCl$_3$)



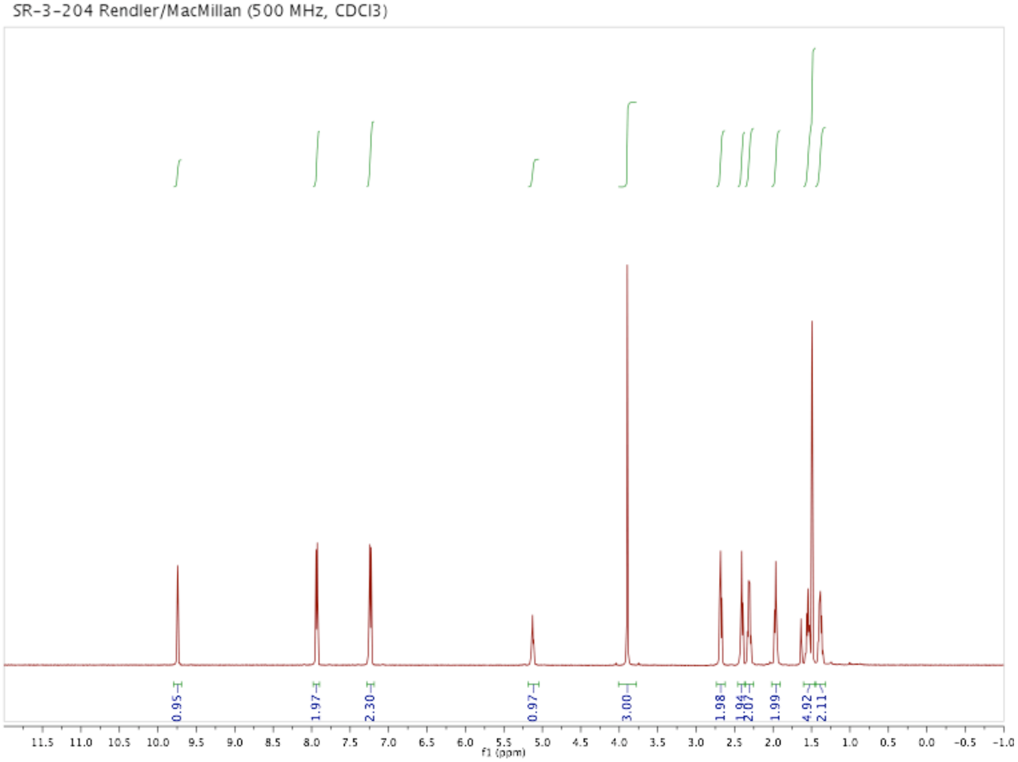
10 (^{13}C NMR, 125 MHz, CDCl$_3$)



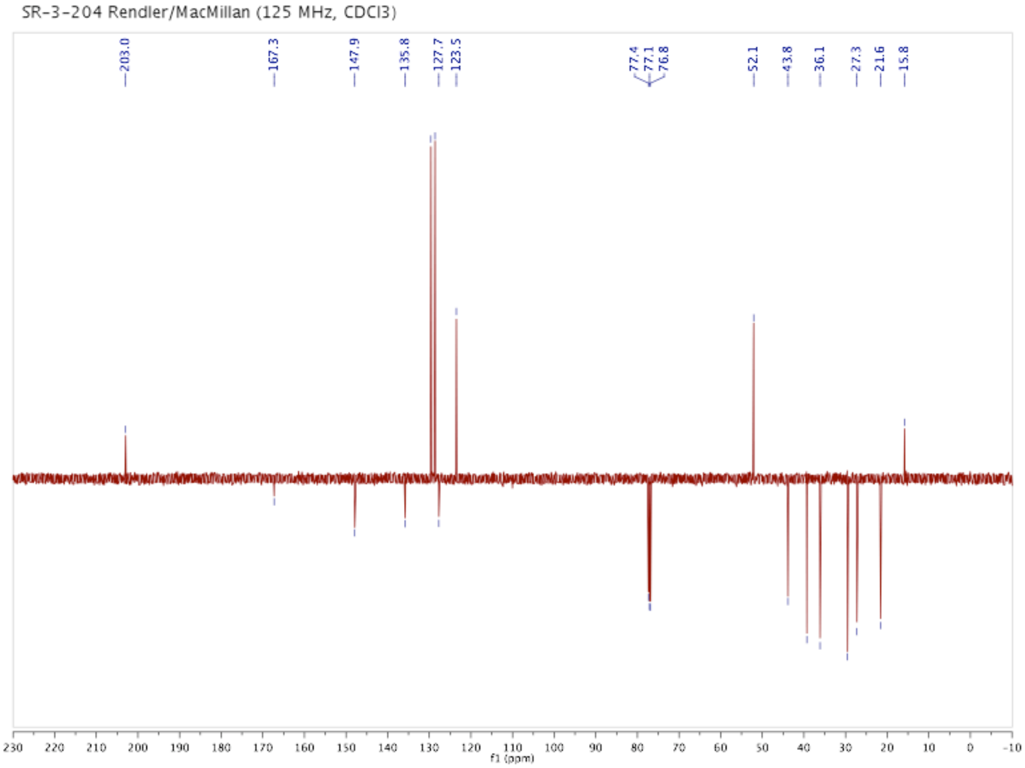
1.5 Bicyclization to give aldehyde **11** (**21** → **11**, Table 2)



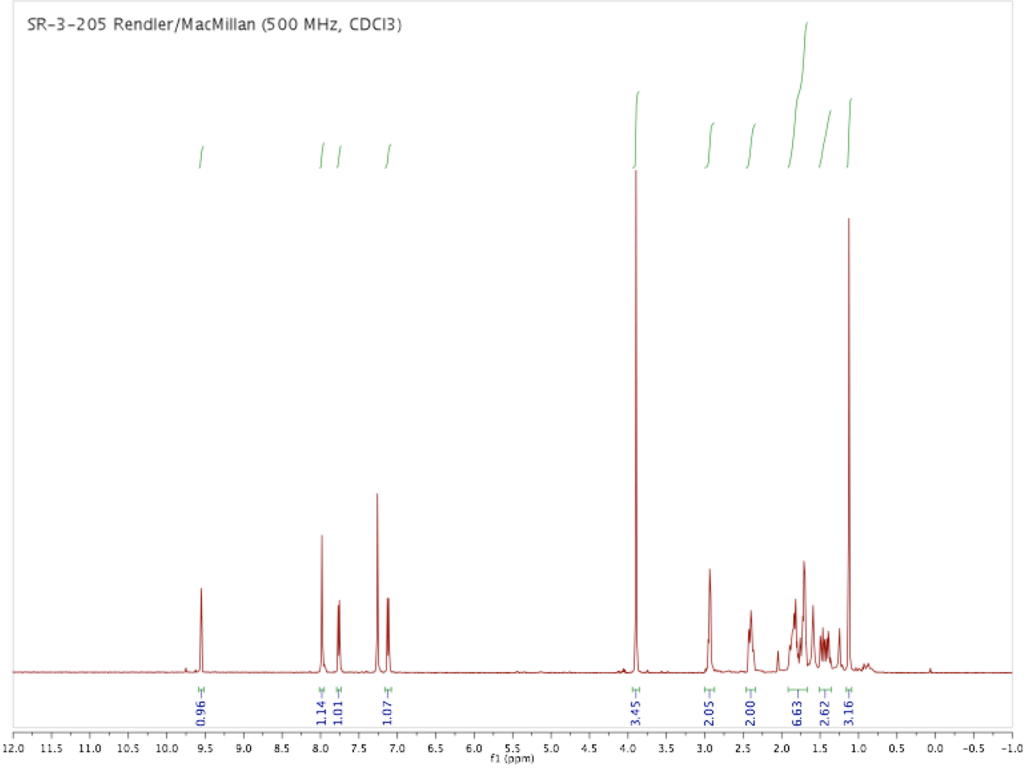
21 (^{1}H NMR, 500 MHz, $CDCl_3$)



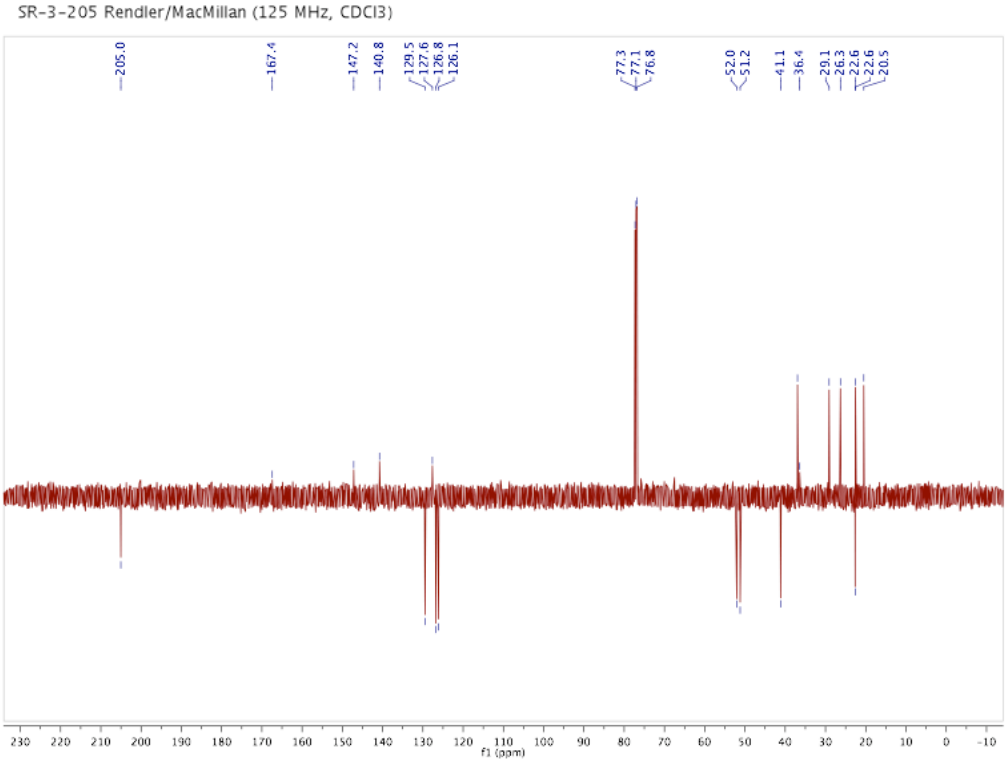
21 (^{13}C NMR, 125 MHz, CDCl$_3$)



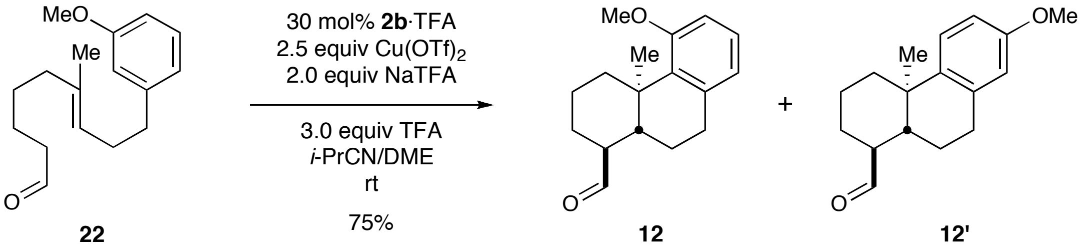
11 (^{1}H NMR, 500 MHz, CDCl$_3$)



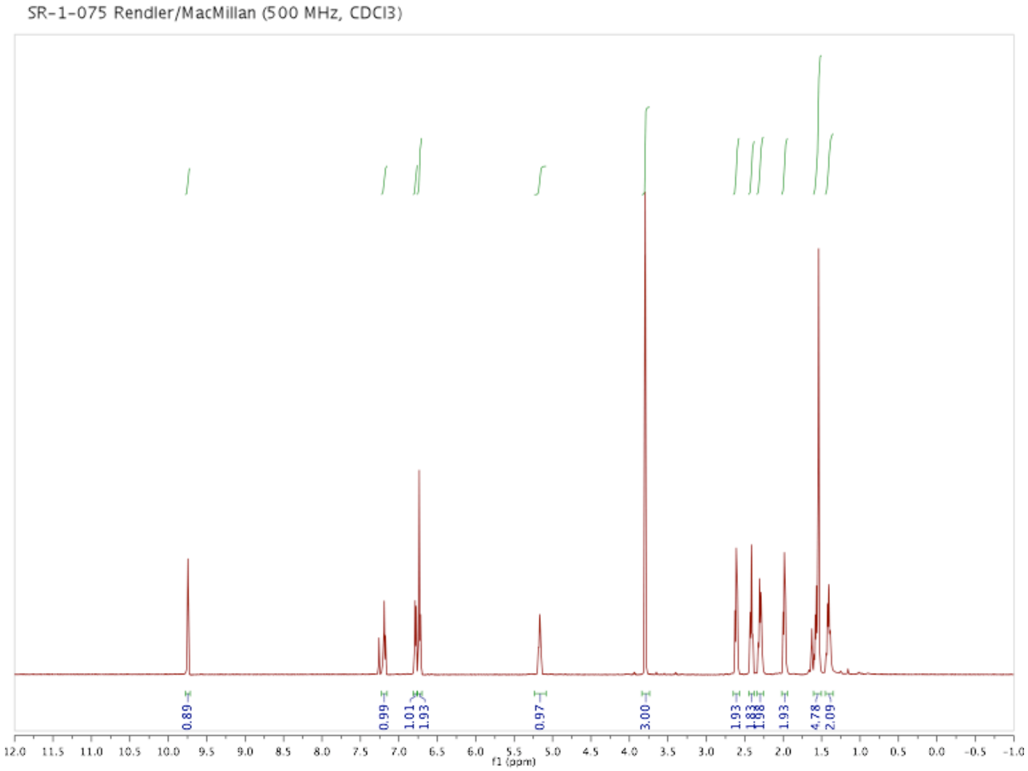
11 (^{13}C NMR, 125 MHz, CDCl$_3$)



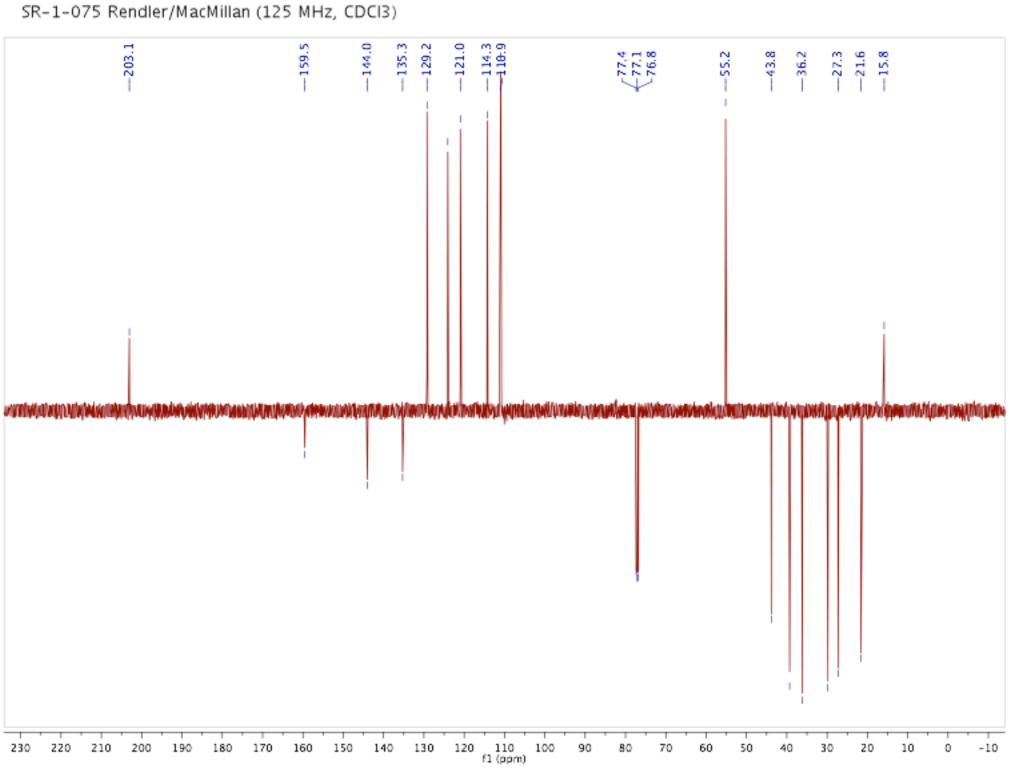
1.6 Bicyclization to give aldehyde **12** (**22** → **12**, Table 2)



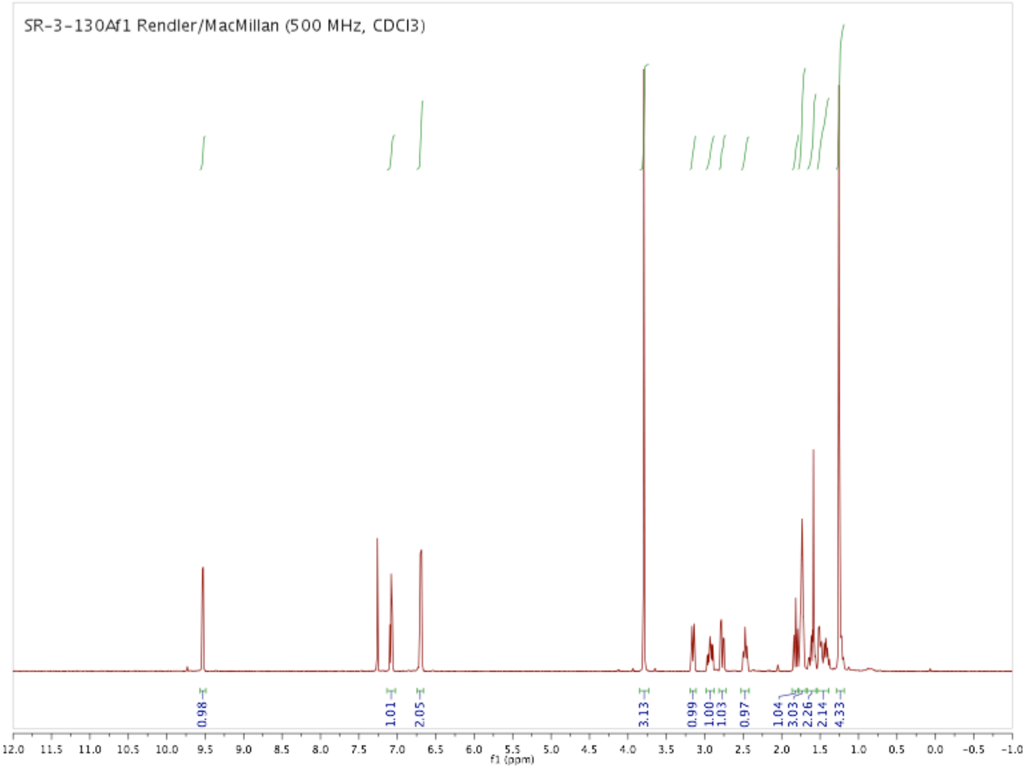
22 (^{1}H NMR, 500 MHz, CDCl$_3$)



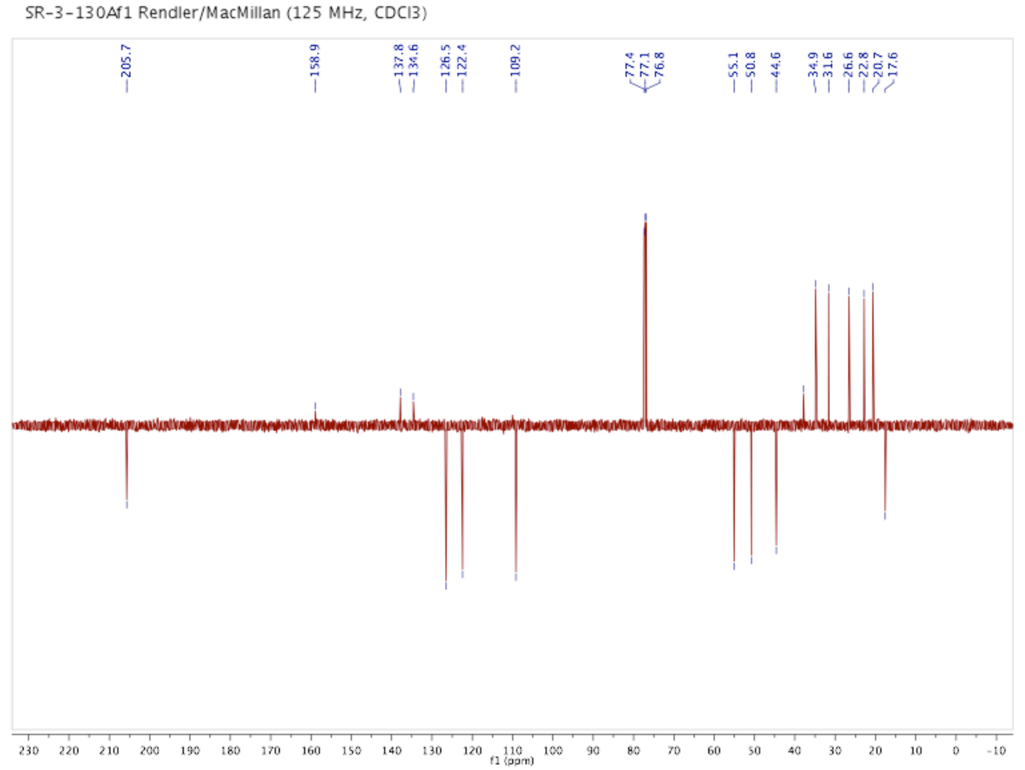
22 (^{13}C NMR, 125 MHz, CDCl$_3$)



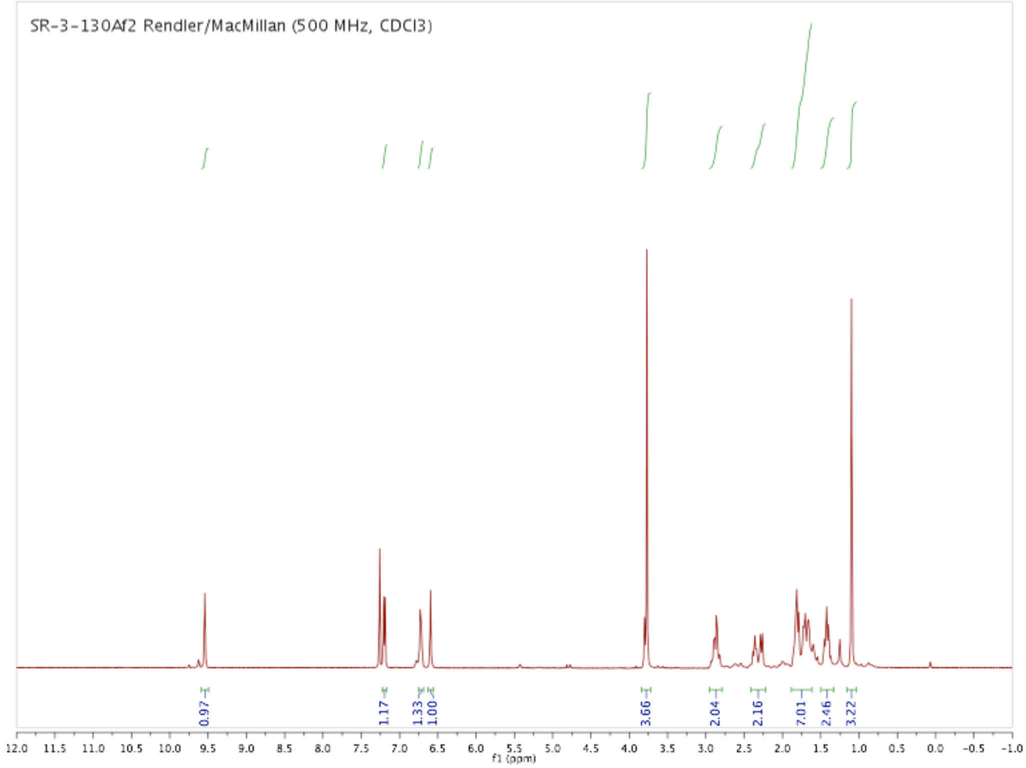
12 (^{1}H NMR, 500 MHz, $CDCl_3$)



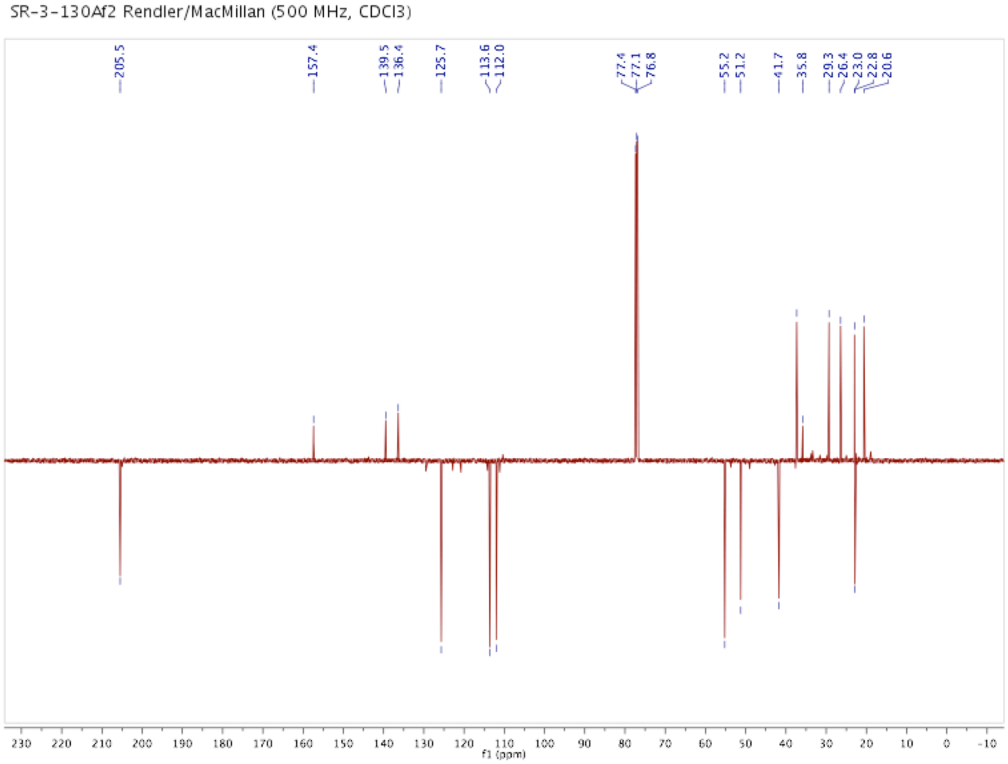
12 (^{13}C NMR, 125 MHz, $CDCl_3$)



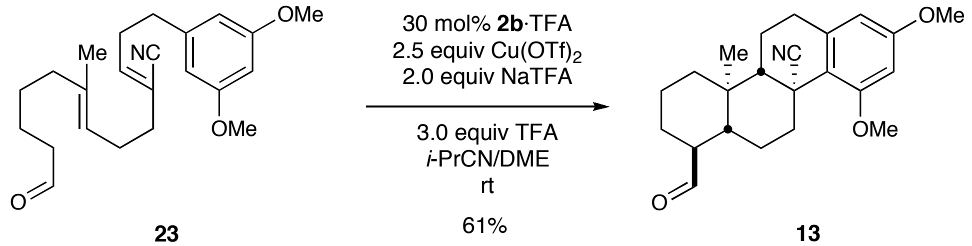
12’ (^{1}H NMR, 500 MHz, CDCl$_3$)



12’ (^{13}C NMR, 125 MHz, CDCl$_3$)

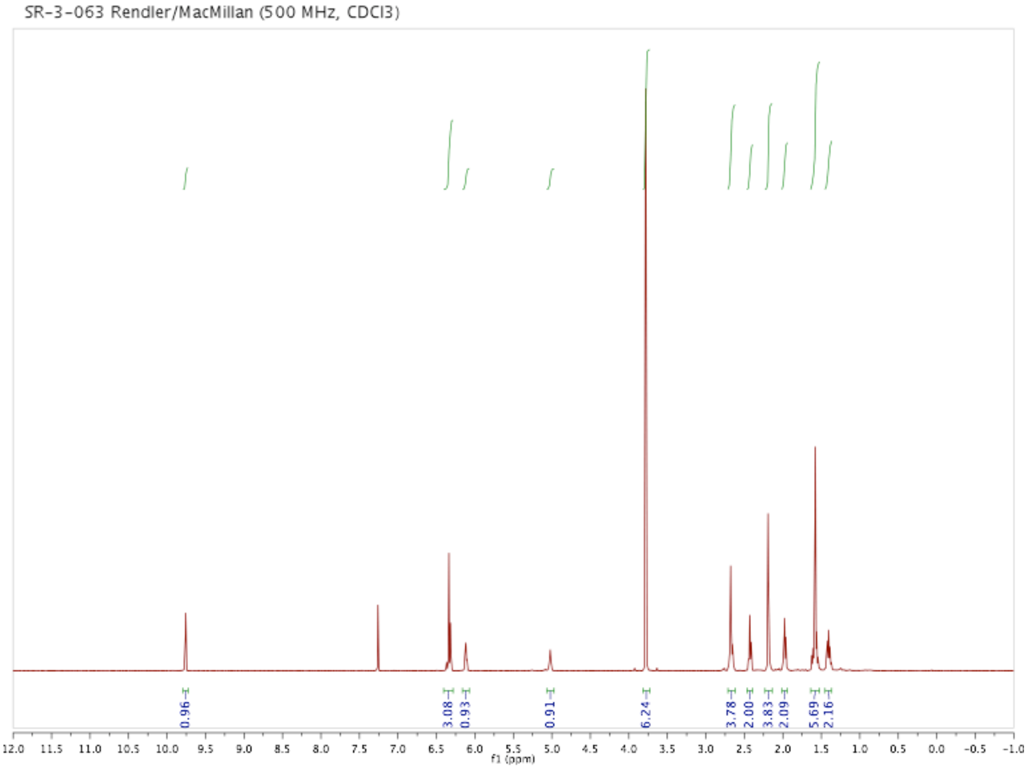


1.7 Tricyclization to give aldehyde **13** (**23** → **13**, Table 2)

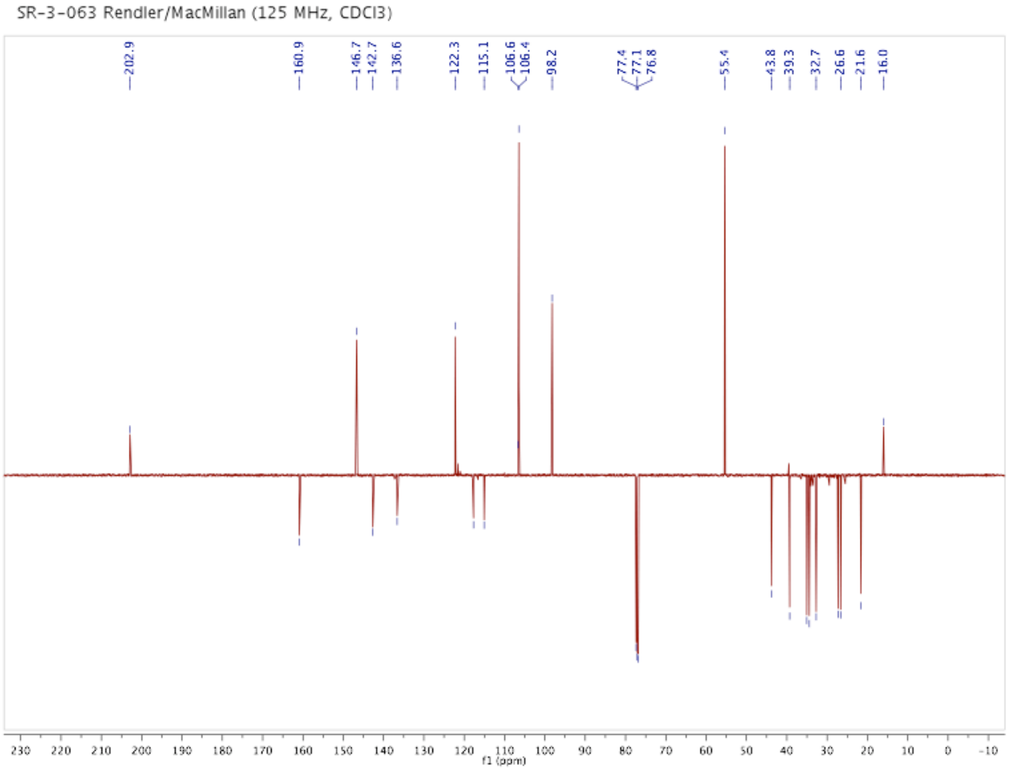


23 **13**

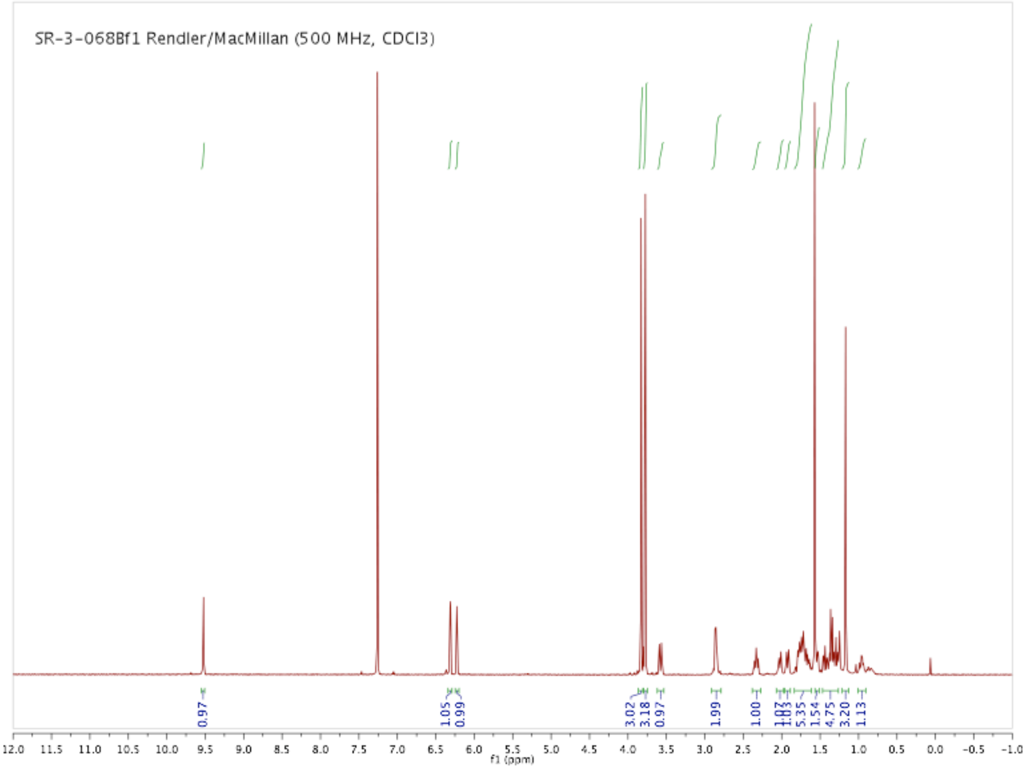
23 (^{1}H NMR, 500 MHz, $CDCl_3$)



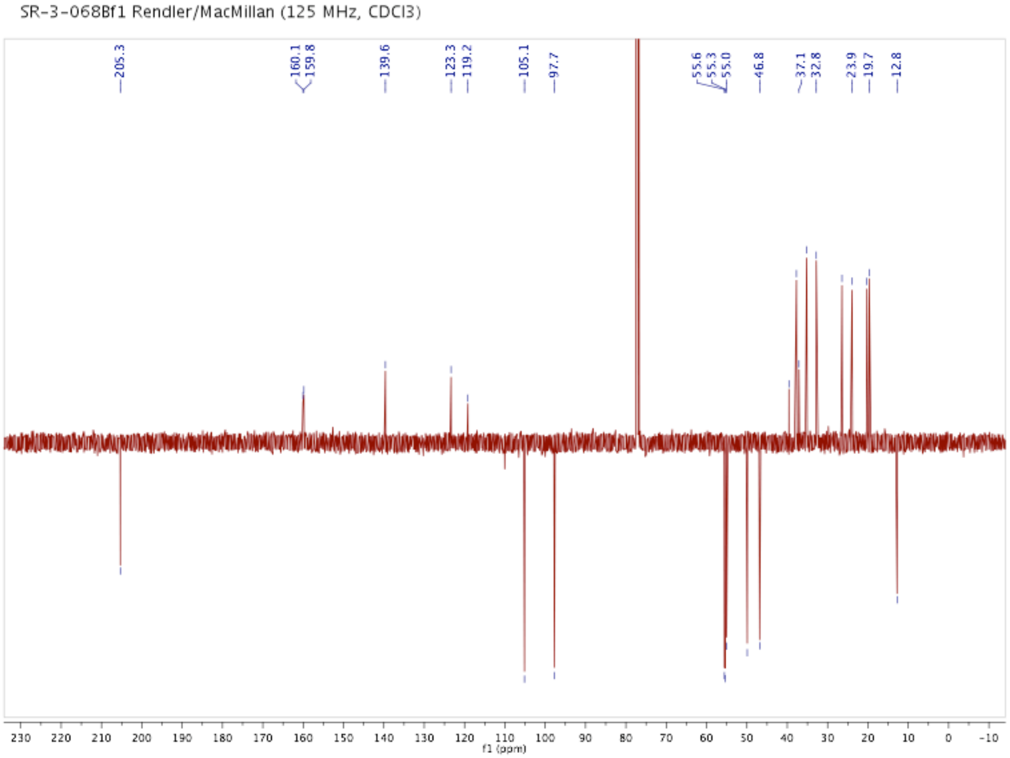
23 (^{13}C NMR, 125 MHz, CDCl$_3$)



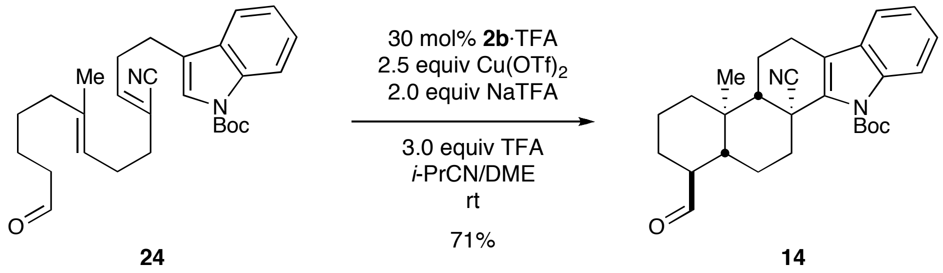
13 (^{1}H NMR, 500 MHz, CDCl$_3$)



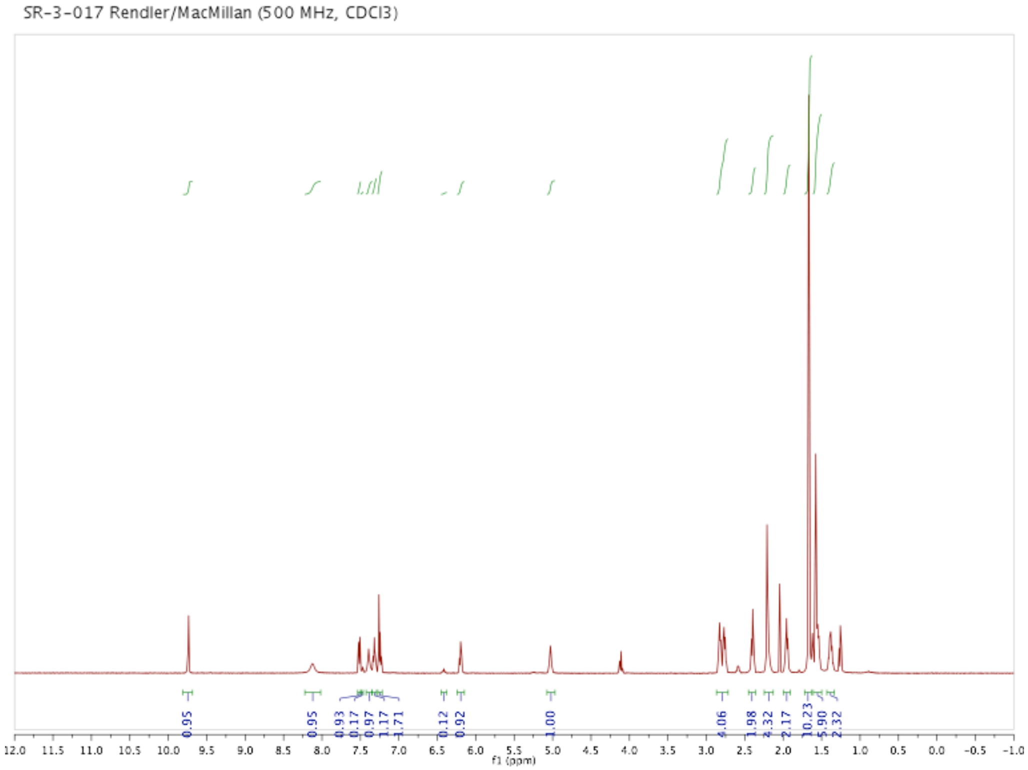
13 (^{13}C NMR, 125 MHz, CDCl$_3$)



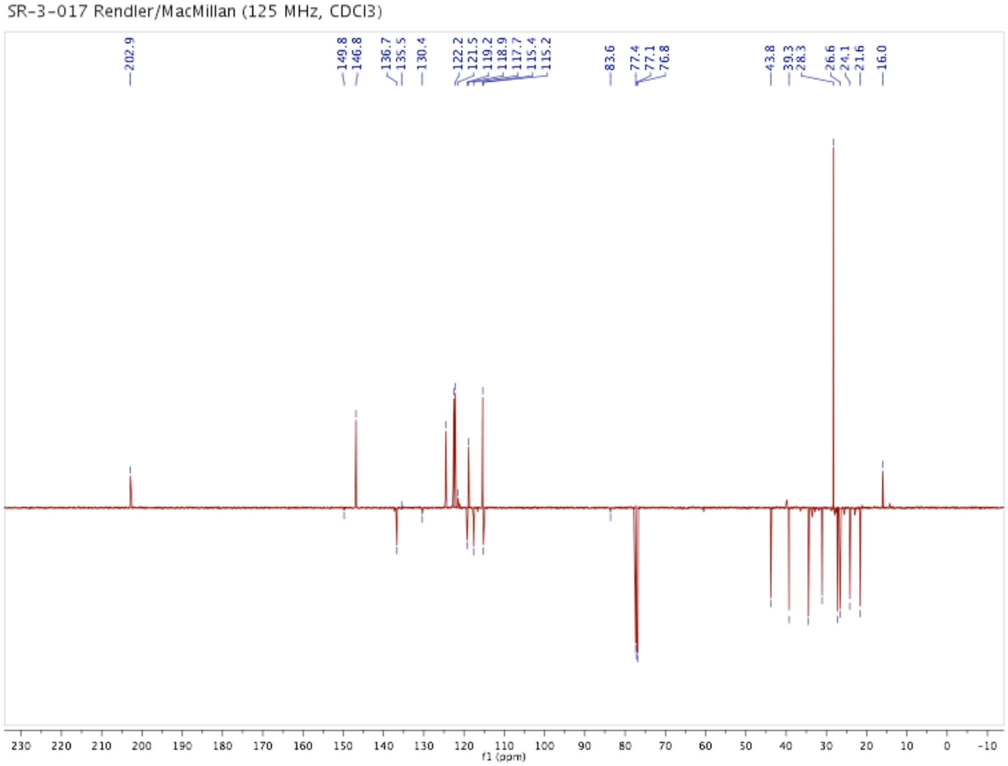
1.8 Trcyclization to give aldehyde **14** (**24** → **14**, Table 2)



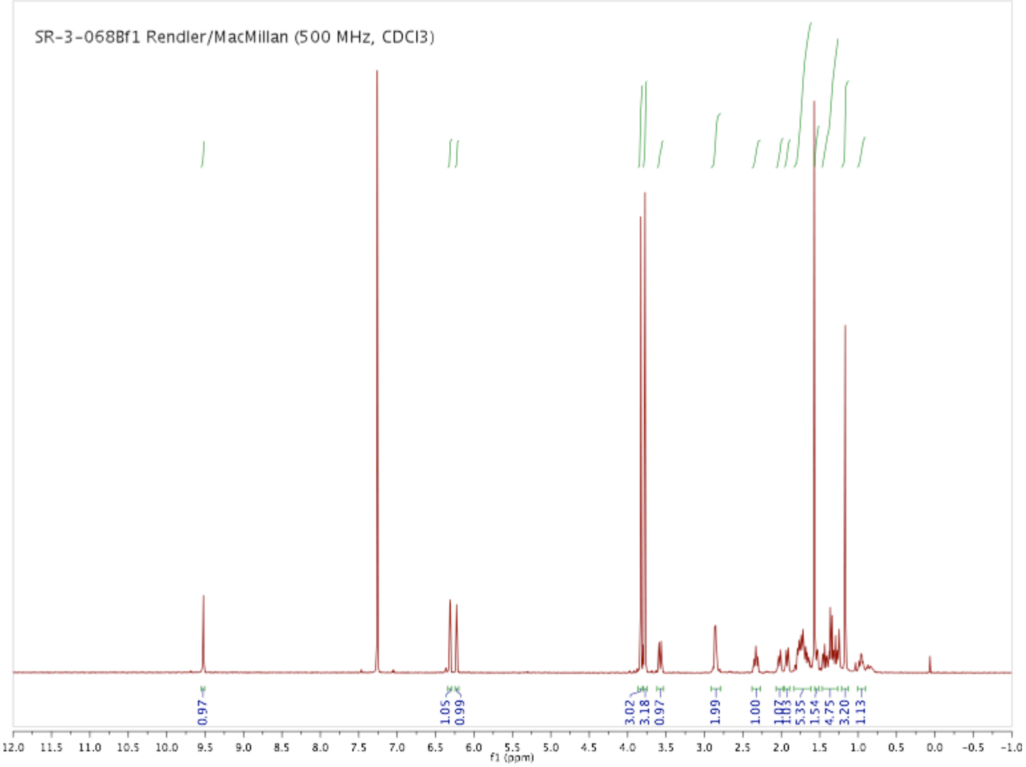
24 (^{1}H NMR, 500 MHz, $CDCl_3$)



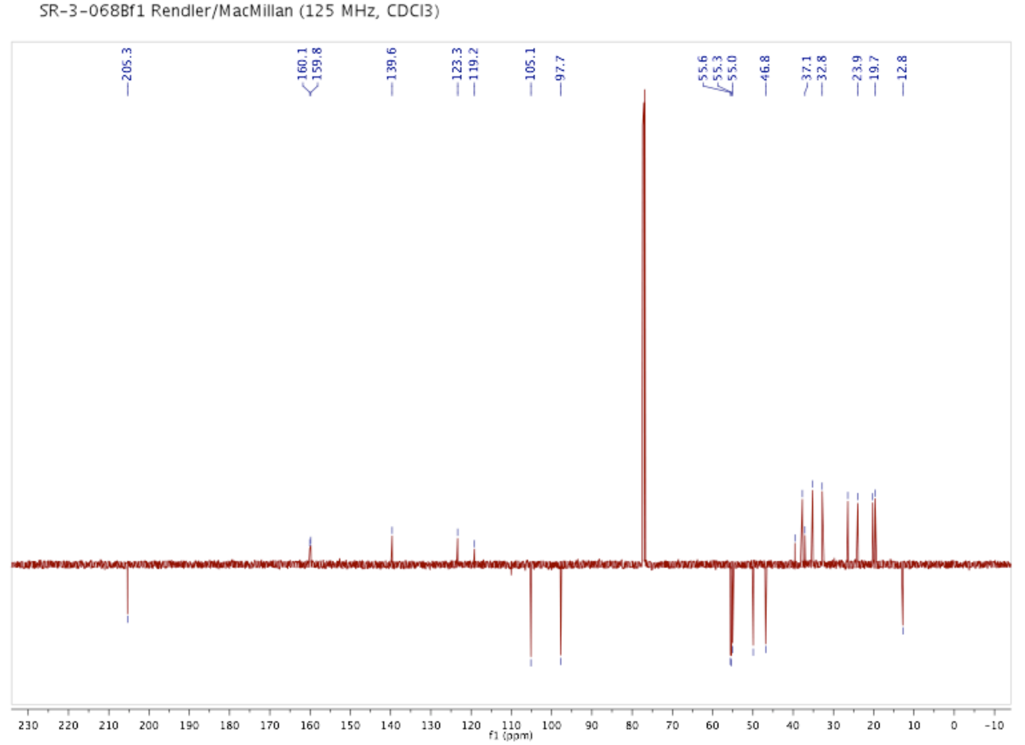
24 (^{13}C NMR, 125 MHz, $CDCl_3$)



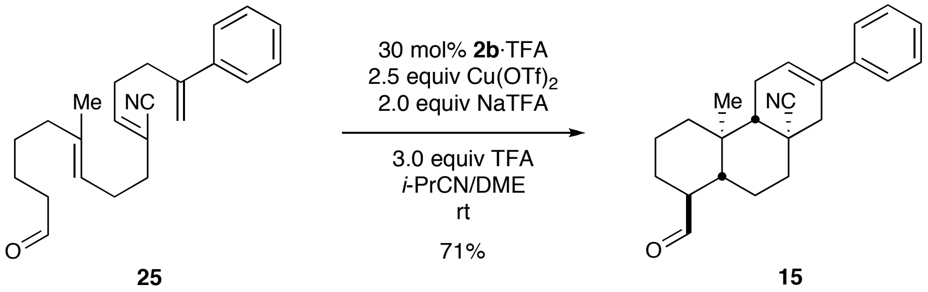
14 (^{1}H NMR, 500 MHz, CDCl$_3$)



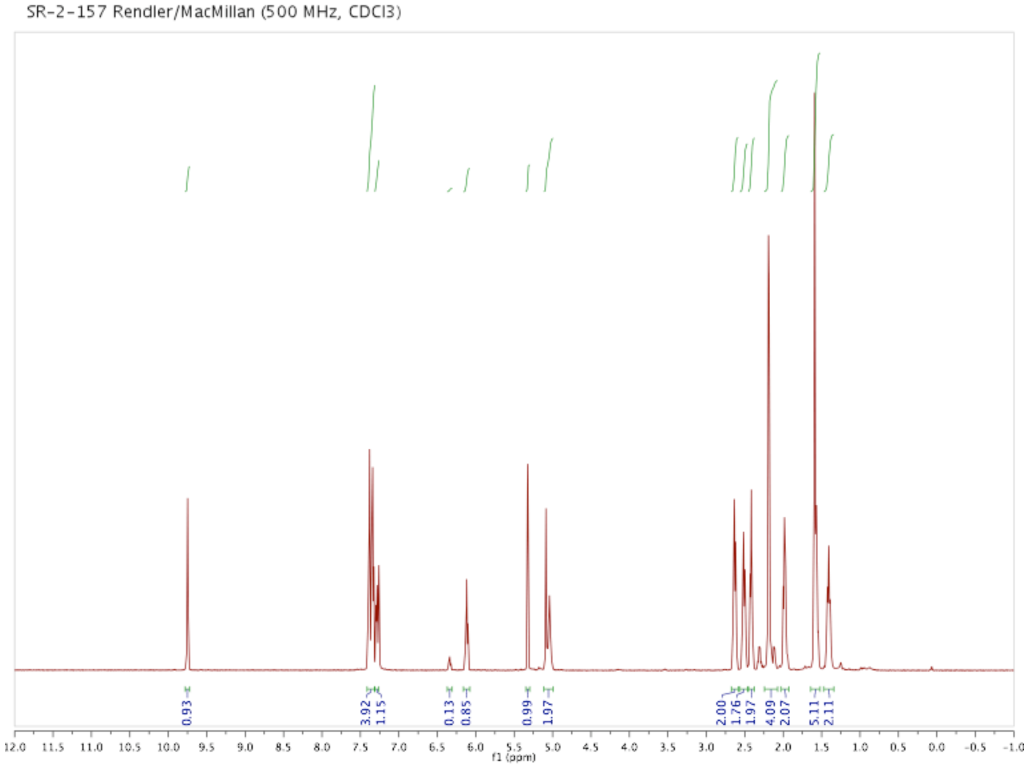
14 (^{13}C NMR, 125 MHz, CDCl$_3$)



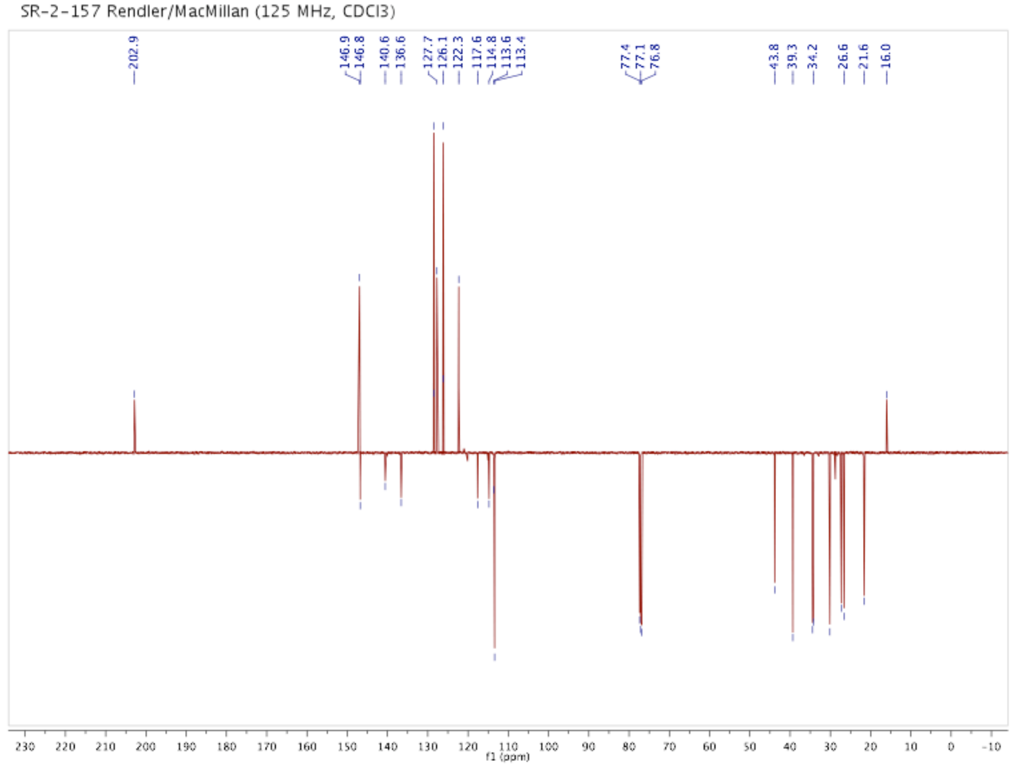
1.9 Bicyclization to give aldehyde **15** (**25** → **15**, Table 2)



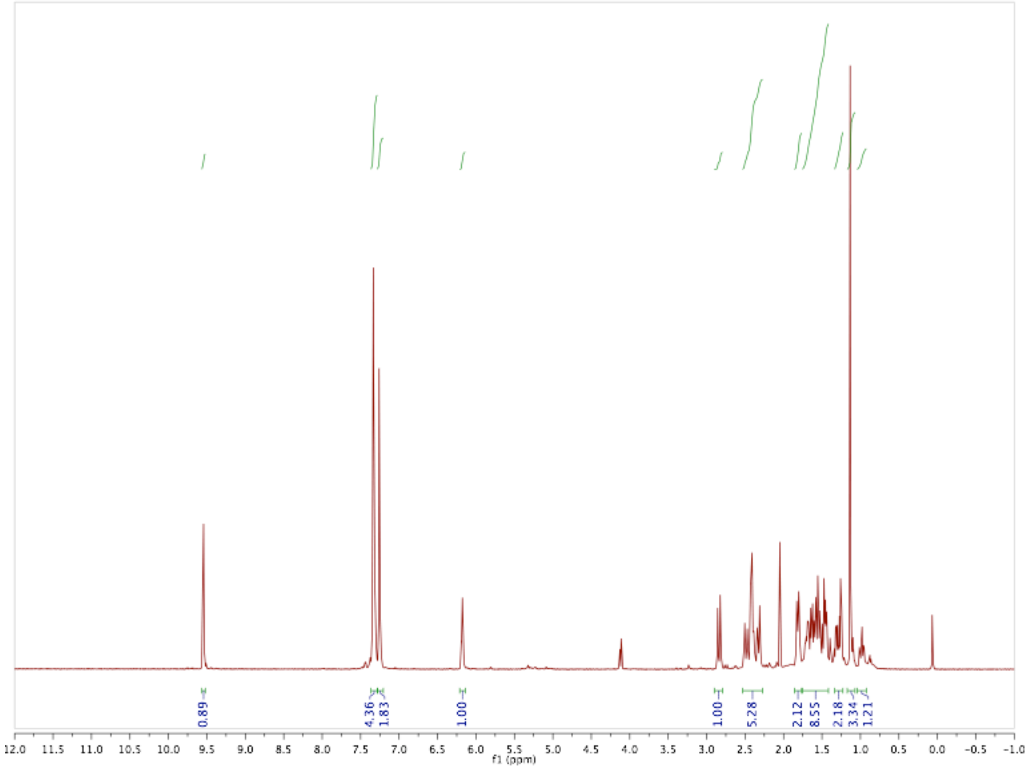
25 (^{1}H NMR, 500 MHz, CDCl$_3$)



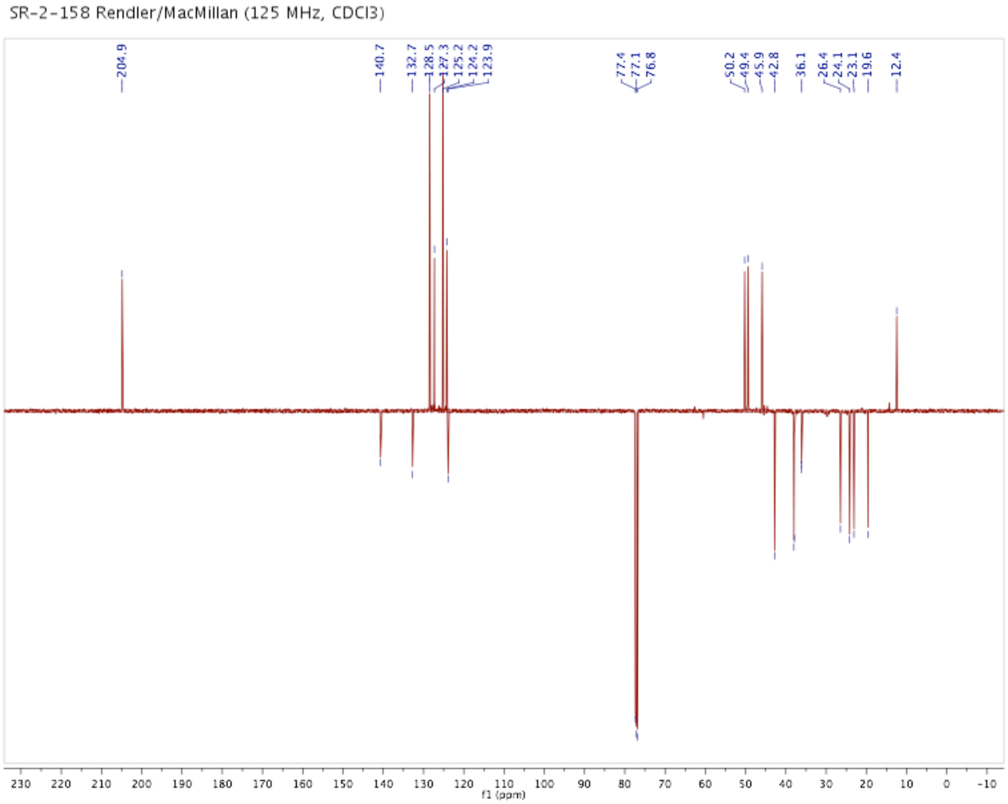
25 (^{13}C NMR, 125 MHz, $CDCl_3$)



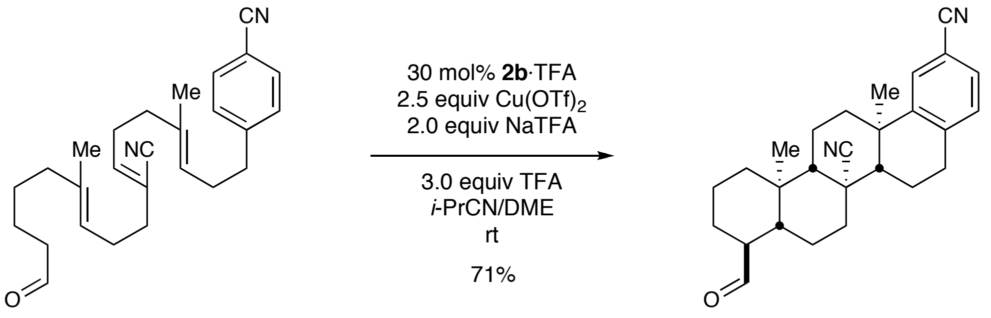
15 (^{1}H NMR, 500 MHz, $CDCl_3$)



15 (^{13}C NMR, 125 MHz, $CDCl_3$)



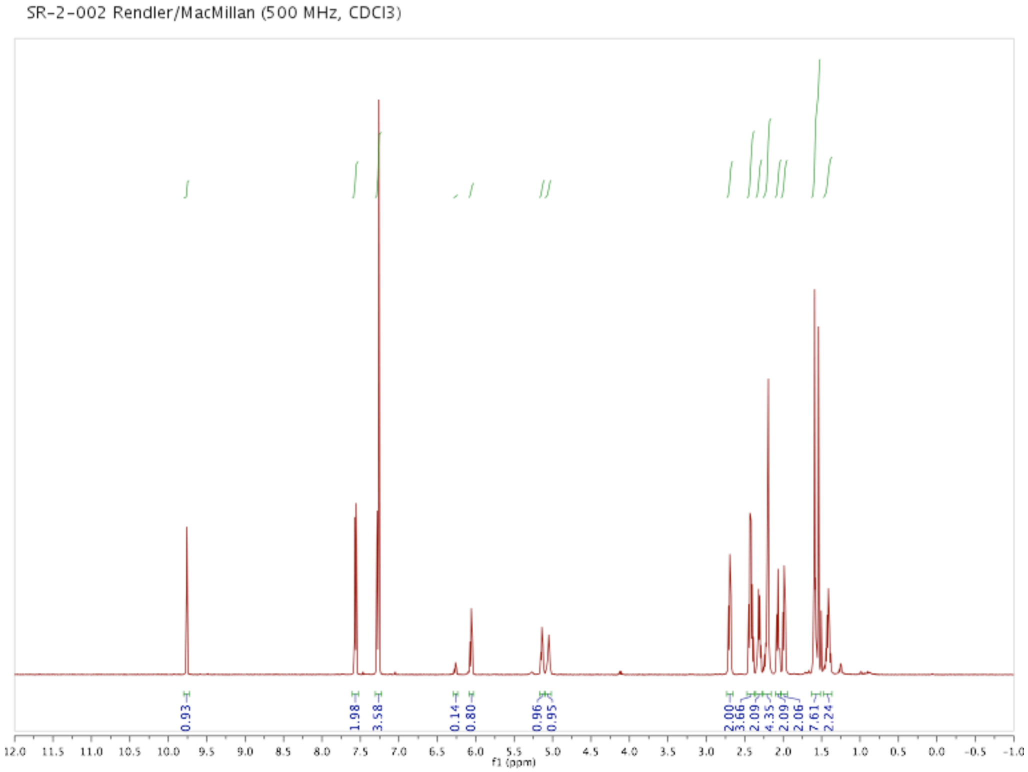
1.10 Tetracyclization to give aldehyde **5** (**1** → **5**, Scheme 2)



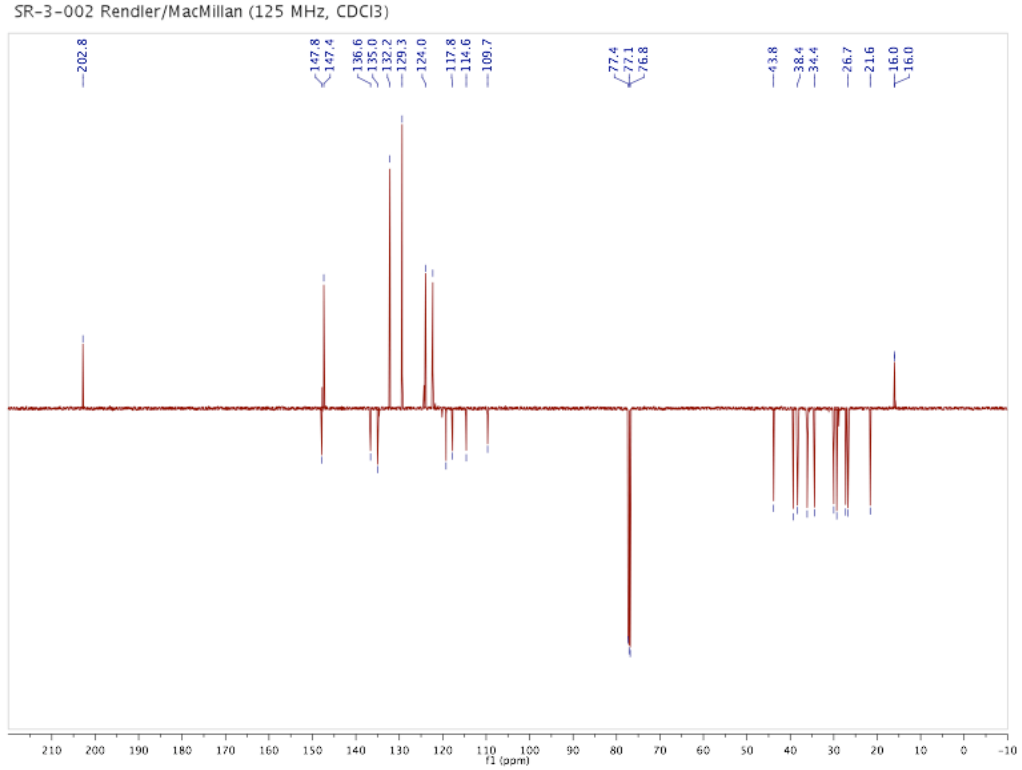
1

5

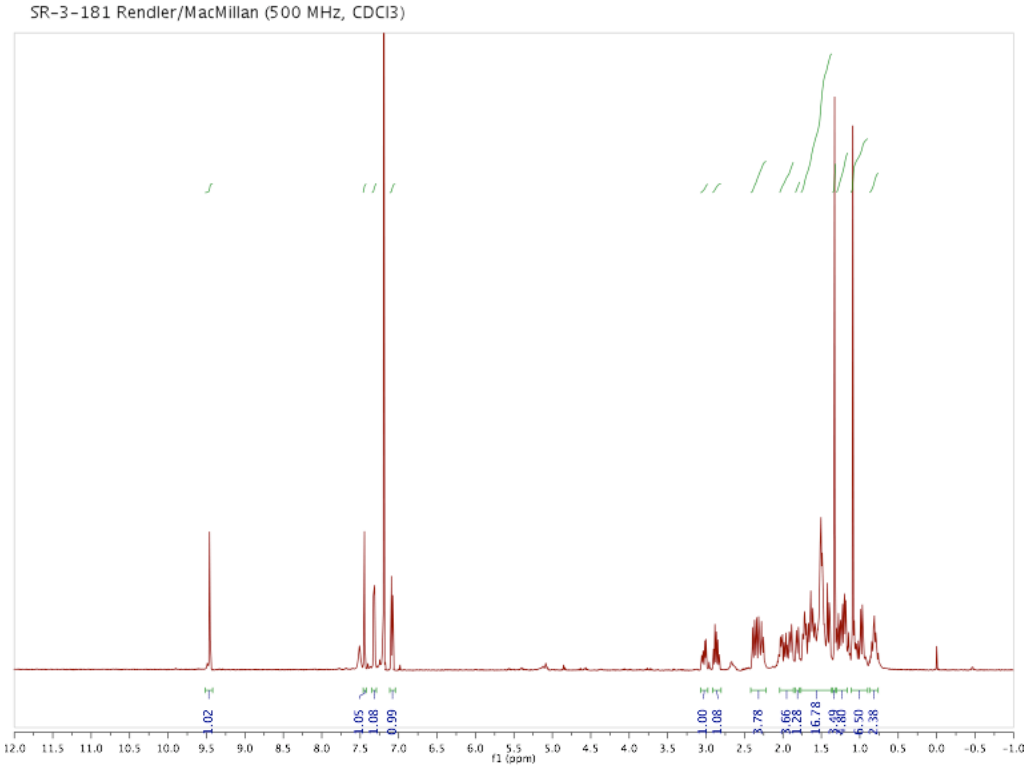
1 (^{1}H NMR, 500 MHz, CDCl$_3$)



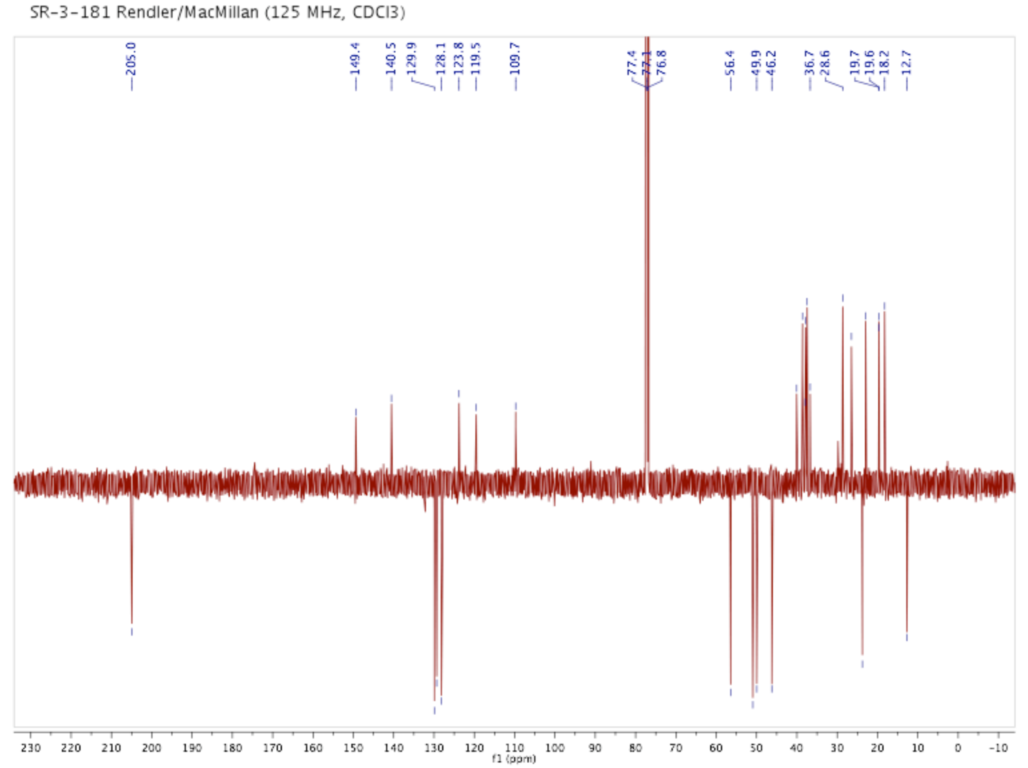
1 (^{13}C NMR, 125 MHz, CDCl$_3$)



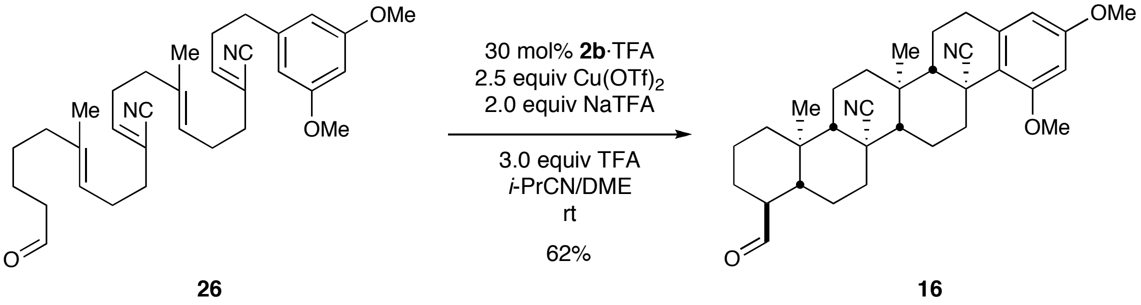
5 (^{1}H NMR, 500 MHz, $CDCl_3$)



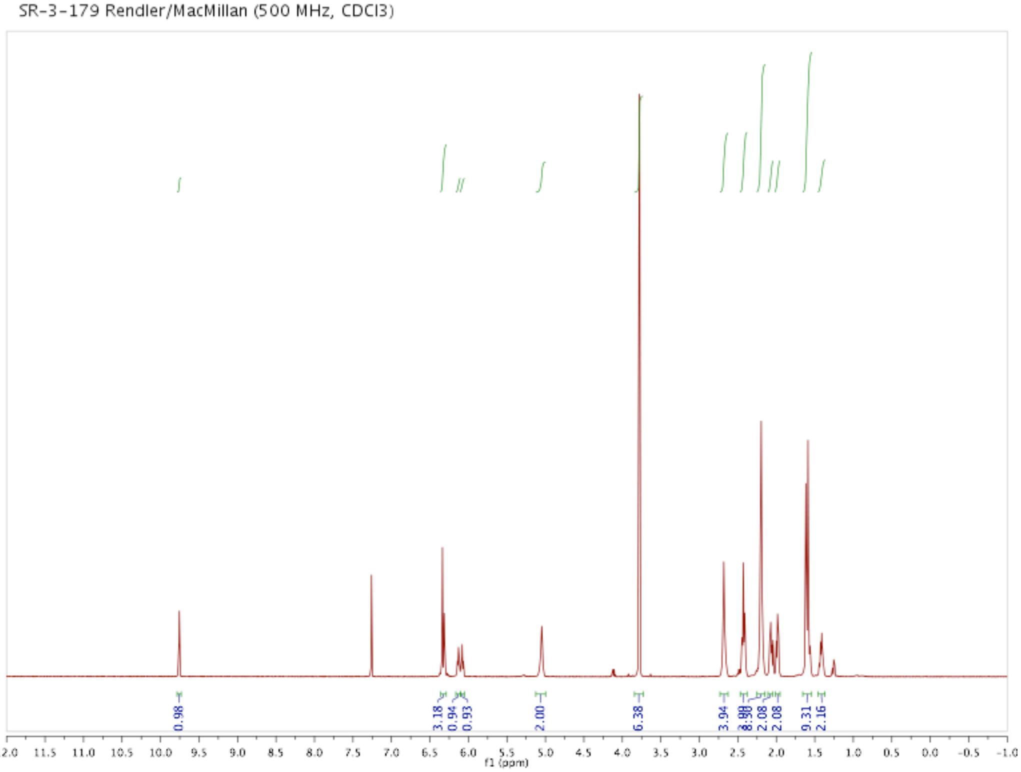
5 (^{13}C NMR, 125 MHz, $CDCl_3$)



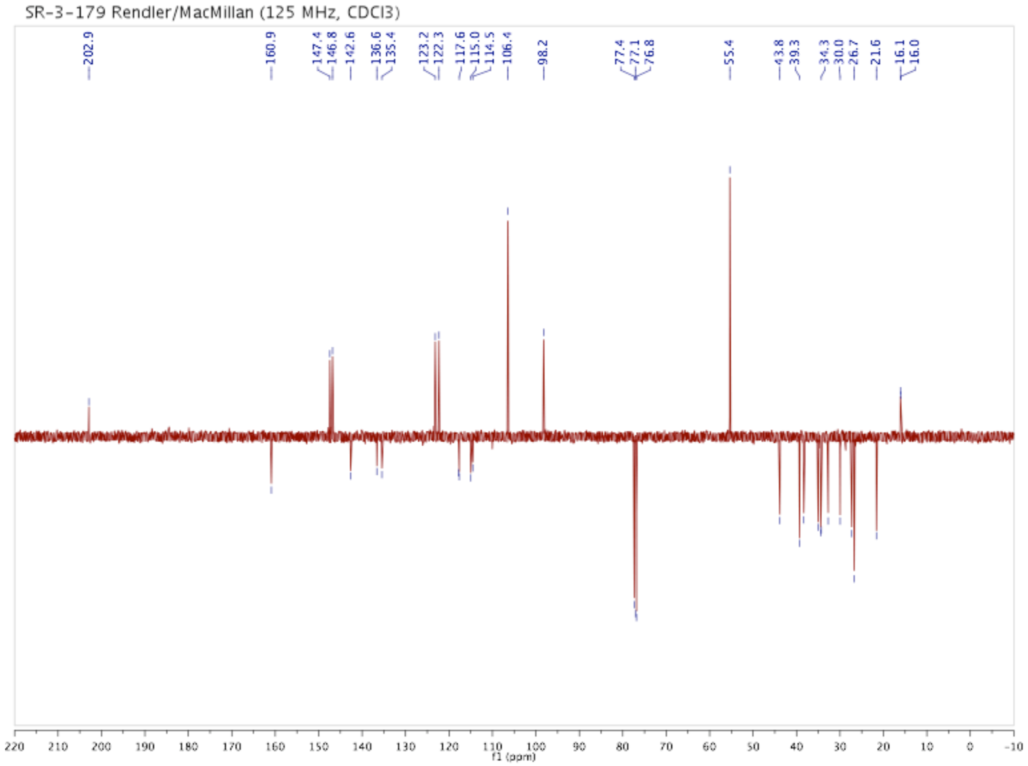
1.11 Pentacyclization to give aldehyde **16** (**26** → **16**, Scheme 2)



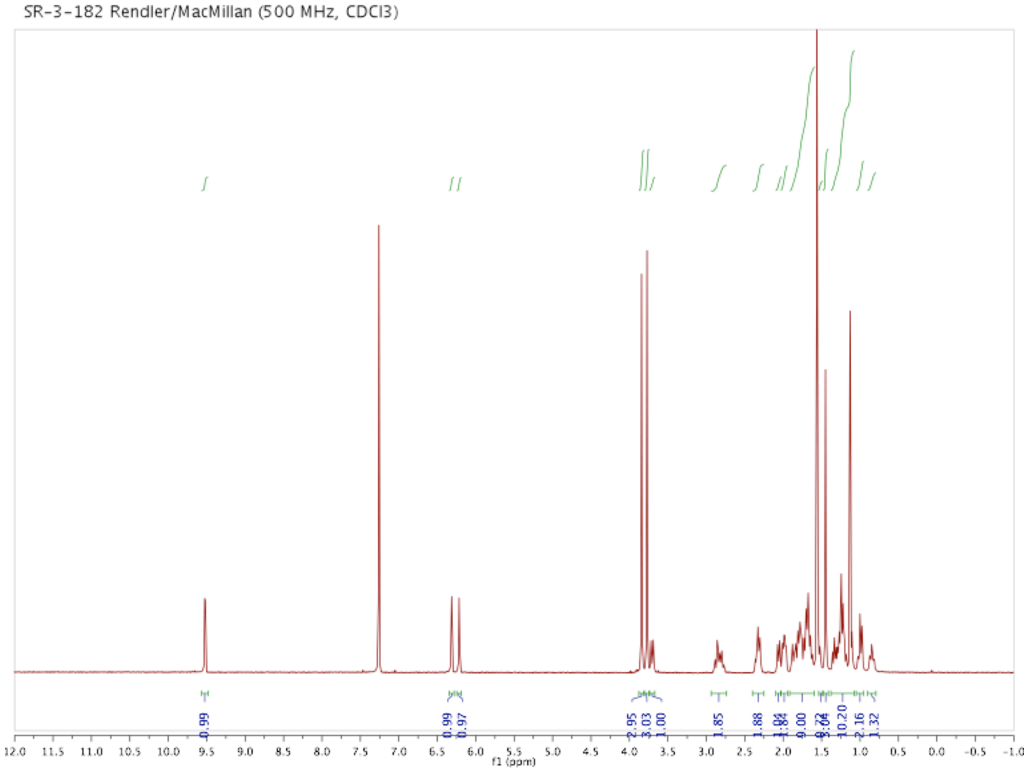
26 (^{1}H NMR, 500 MHz, CDCl$_3$)



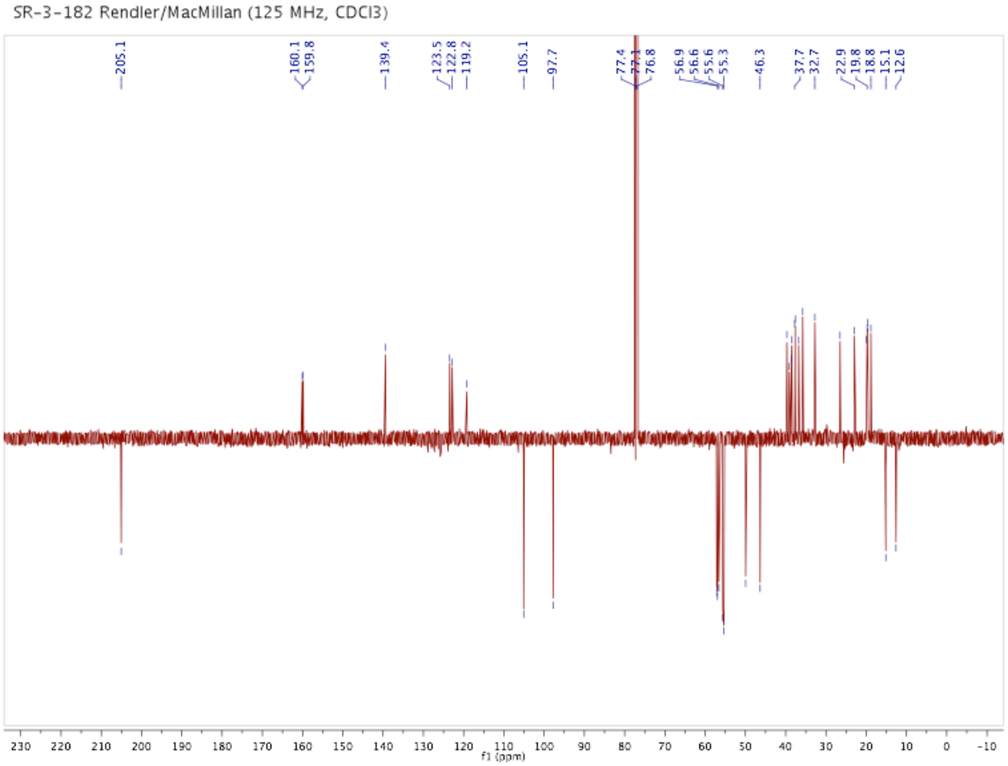
26 (^{13}C NMR, 125 MHz, CDCl$_3$)



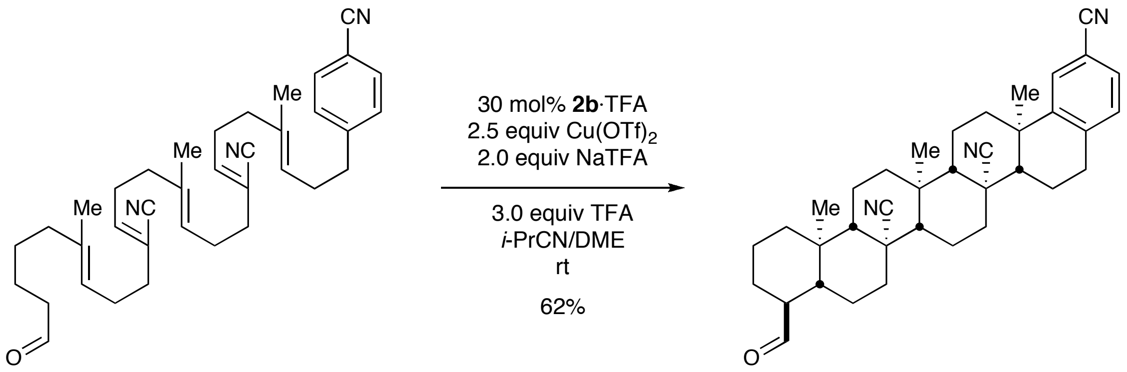
16 (^{1}H NMR, 500 MHz, CDCl$_3$)



16 (^{13}C NMR, 125 MHz, CDCl$_3$)

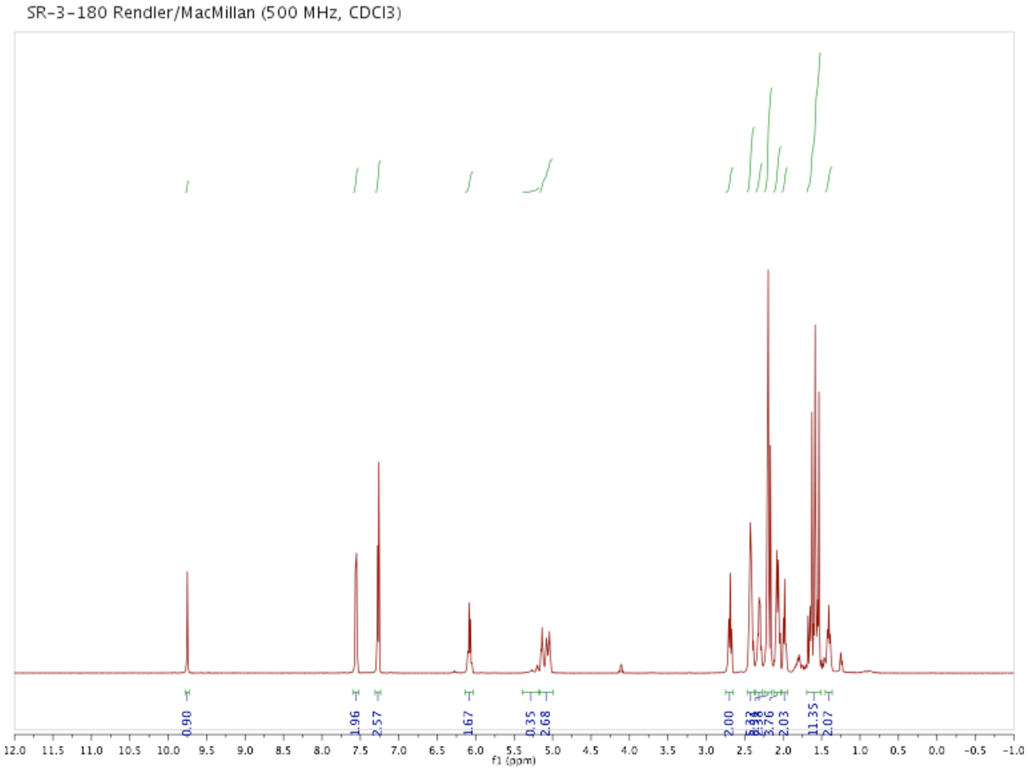


1.12 Hexacyclization to give aldehyde **17** (**27** → **17**, Scheme 2)

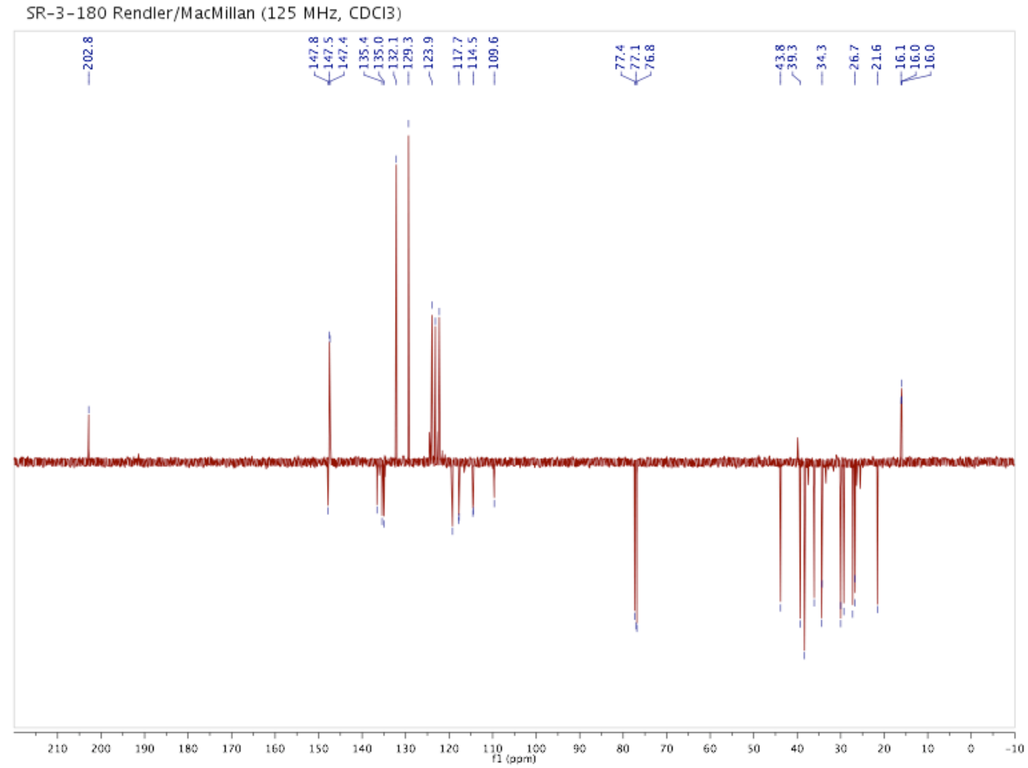


27 **17**

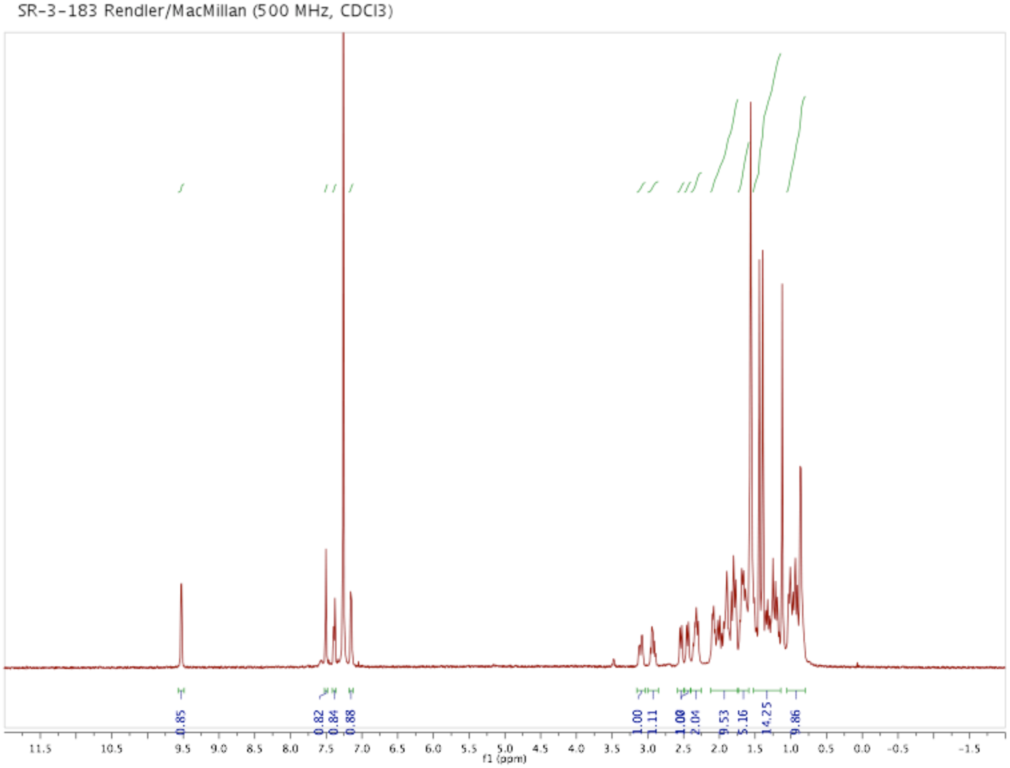
27 (^{1}H NMR, 500 MHz, CDCl$_3$)



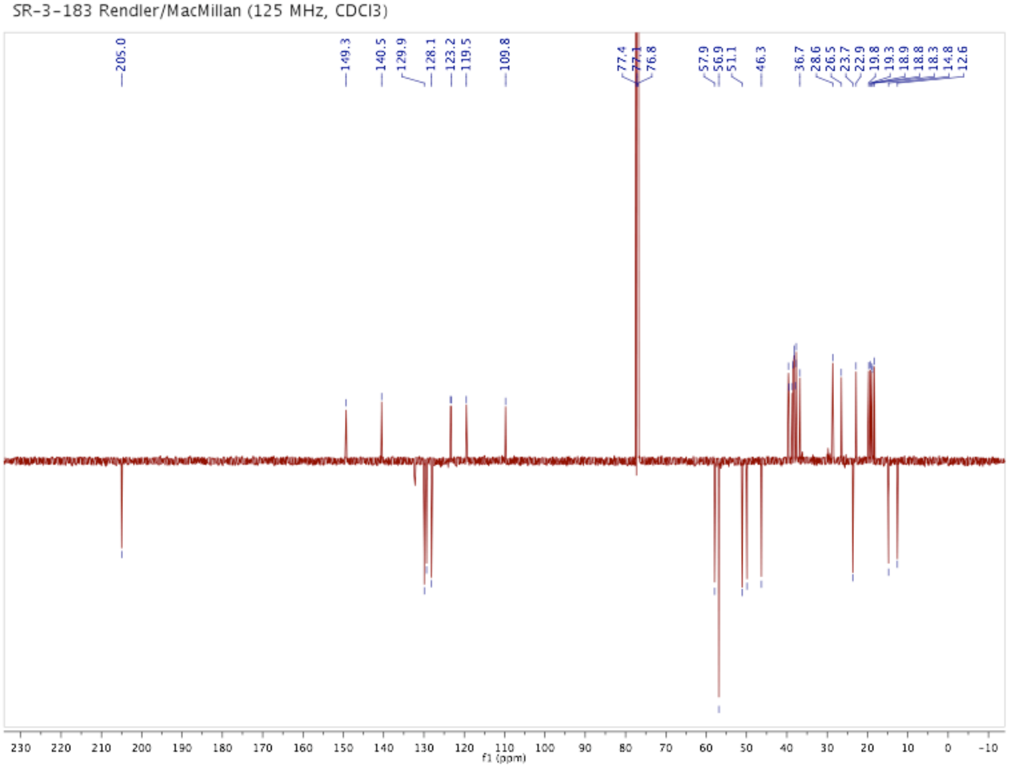
27 (^{13}C NMR, 125 MHz, CDCl$_3$)



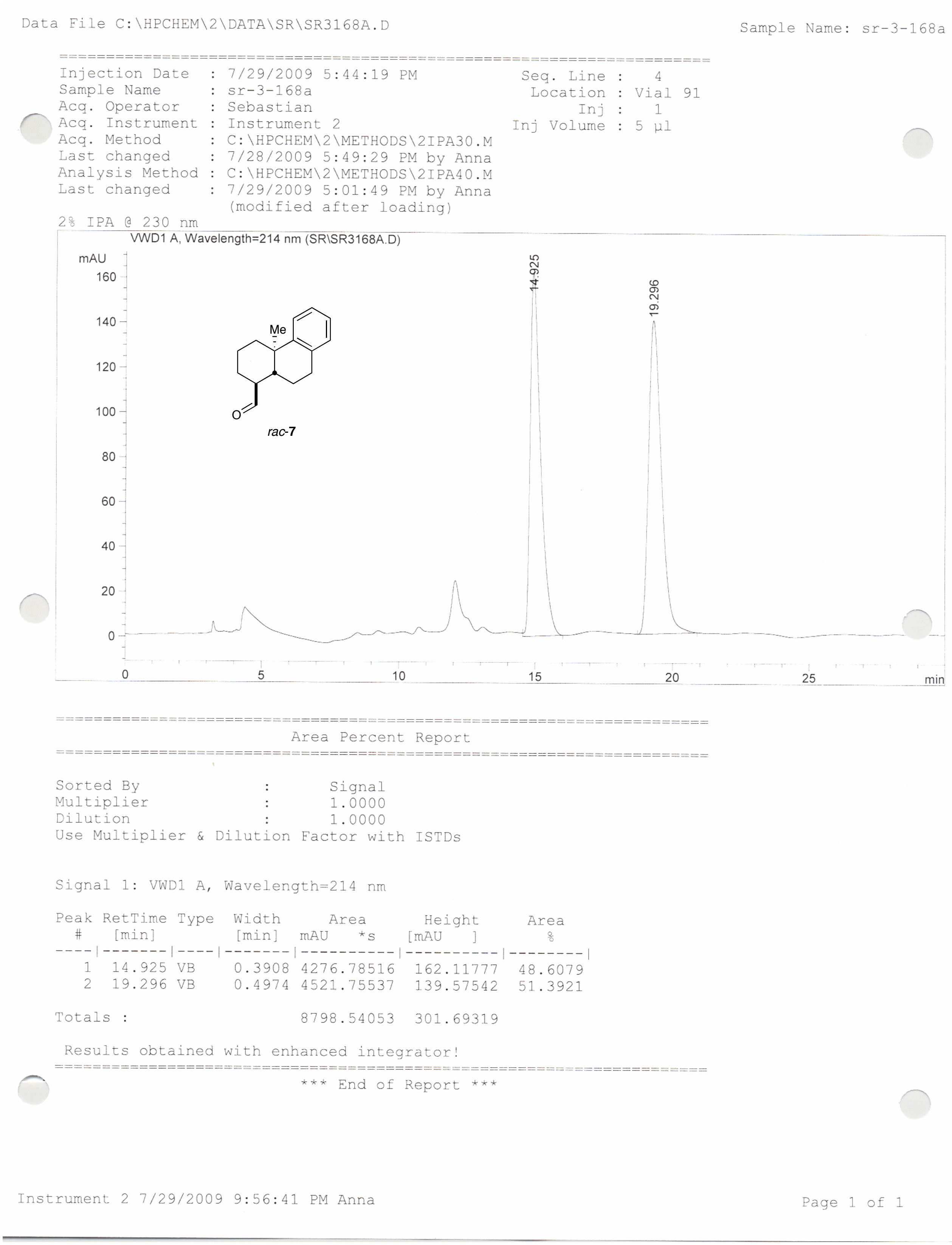
17 (^{1}H NMR, 500 MHz, $CDCl_3$)



17 (^{13}C NMR, 125 MHz, $CDCl_3$)



2 Copies of HPLC Traces of Products 5, 7-16



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Data File C:\HPCHEM\2\DATA\SR\SR3168A.D                         Sample Name: sr-3-168a

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    Sample Name     : sr-3-168a                          Location : Vial 91
    Acq. Operator   : Sebastian                               Inj :   1
    Acq. Instrument : Instrument 2                     Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\2IPA30.M
    Last changed    : 7/28/2009 5:49:29 PM by Anna
    Analysis Method : C:\HPCHEM\2\METHODS\2IPA40.M
    Last changed    : 7/29/2009 5:01:49 PM by Anna
                      (modified after loading)
    2% IPA @ 230 nm
```

```
    ===================================================================
                             Area Percent Report
    ===================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=214 nm

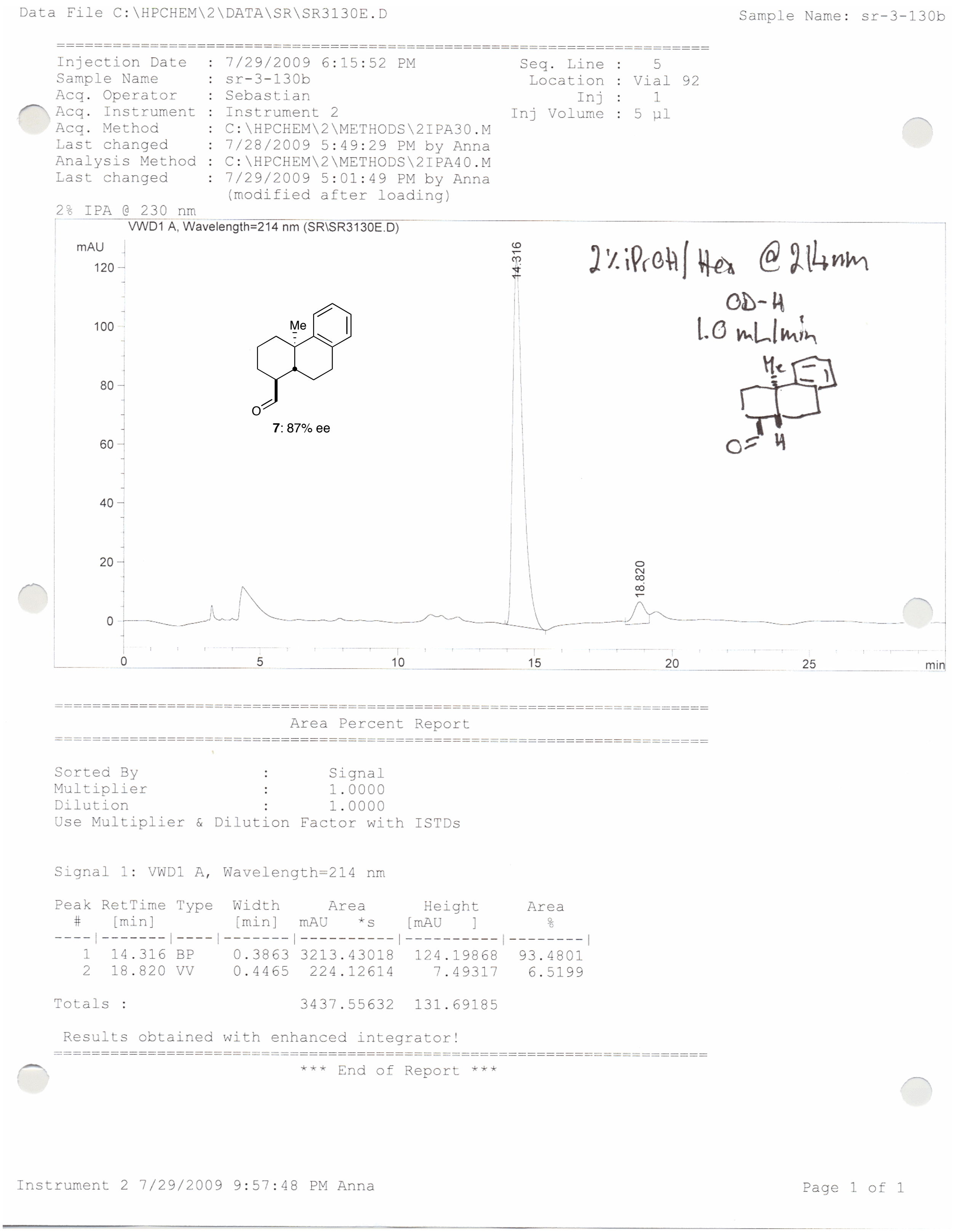
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  14.925 VB    0.3908 4276.78516  162.11777  48.6079
       2  19.296 VB    0.4974 4521.75537  139.57542  51.3921

    Totals :                  8798.54053  301.69319

     Results obtained with enhanced integrator!
    ===================================================================
                             *** End of Report ***



 Instrument 2 7/29/2009 9:56:41 PM Anna                              Page 1 of 1
```



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Data File C:\HPCHEM\2\DATA\SR\SR3130E.D                              Sample Name: sr-3-130b

    =====================================================================
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    Sample Name     : sr-3-130b                       Location : Vial 92
    Acq. Operator   : Sebastian                            Inj :   1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\2IPA30.M
    Last changed    : 7/28/2009 5:49:29 PM by Anna
    Analysis Method : C:\HPCHEM\2\METHODS\2IPA40.M
    Last changed    : 7/29/2009 5:01:49 PM by Anna
                      (modified after loading)
    2% IPA @ 230 nm
```

7: 87% ee

2% iPrOH/Hex @ 214nm

OD-H

1.0 mL/min

```
    =====================================================================
                             Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs

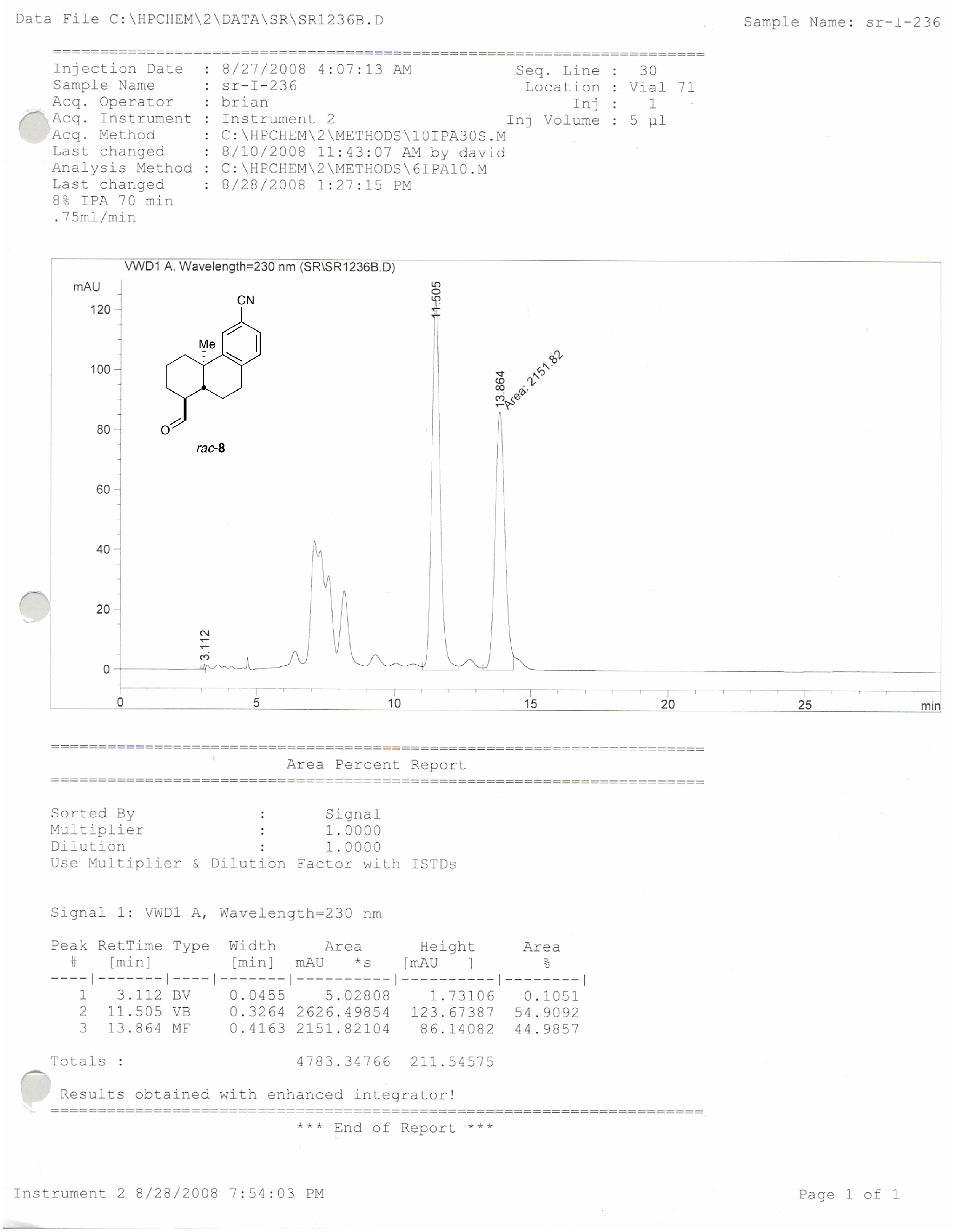

    Signal 1: VWD1 A, Wavelength=214 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU    *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  14.316 BP    0.3863 3213.43018  124.19868 93.4801
       2  18.820 VV    0.4465  224.12614    7.49317  6.5199

    Totals :                  3437.55632  131.69185

     Results obtained with enhanced integrator!
    =====================================================================
                              *** End of Report ***


Instrument 2 7/29/2009 9:57:48 PM Anna                                   Page 1 of 1
```



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Data File C:\HPCHEM\2\DATA\SR\SR1236B.D                              Sample Name: sr-I-236

    =====================================================================
    Injection Date  : 8/27/2008 4:07:13 AM           Seq. Line :  30
    Sample Name     : sr-I-236                        Location : Vial 71
    Acq. Operator   : brian                                Inj :   1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\10IPA30S.M
    Last changed    : 8/10/2008 11:43:07 AM by david
    Analysis Method : C:\HPCHEM\2\METHODS\6IPA10.M
    Last changed    : 8/28/2008 1:27:15 PM
    8% IPA 70 min
    .75ml/min
```

```
    =====================================================================
                             Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=230 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1   3.112 BV    0.0455    5.02808    1.73106   0.1051
       2  11.505 VB    0.3264 2626.49854  123.67387  54.9092
       3  13.864 MF    0.4163 2151.82104   86.14082  44.9857

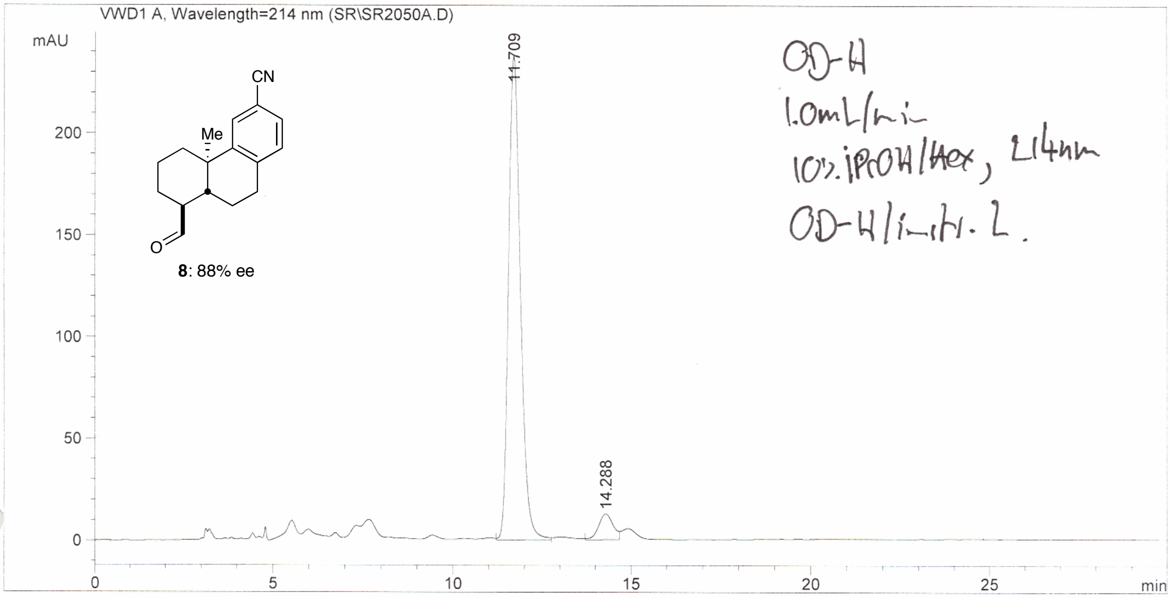
    Totals :                  4783.34766  211.54575

     Results obtained with enhanced integrator!
    =====================================================================
                              *** End of Report ***

Instrument 2 8/28/2008 7:54:03 PM                                     Page 1 of 1
```

```
Data File C:\HPCHEM\2\DATA\SR\SR2050A.D                                  Sample Name: sr-II-050a

    =====================================================================
    Injection Date  : 11/3/2008 9:41:29 AM           Seq. Line :    4
    Sample Name     : sr-II-050a                      Location : Vial 31
    Acq. Operator   : Sebastian                            Inj :    1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\10IPA30S.M
    Last changed    : 11/3/2008 8:48:26 AM by jongrock
    Analysis Method : C:\HPCHEM\2\METHODS\5IPA40S.M
    Last changed    : 11/3/2008 8:50:41 AM by jongrock
    5% IPA @ 214 nm
```



8: 88% ee

OD-H
1.0mL/min
10% iPrOH/Hex, 214nm
OD-H/init. 2.

```
    =====================================================================
                           Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs

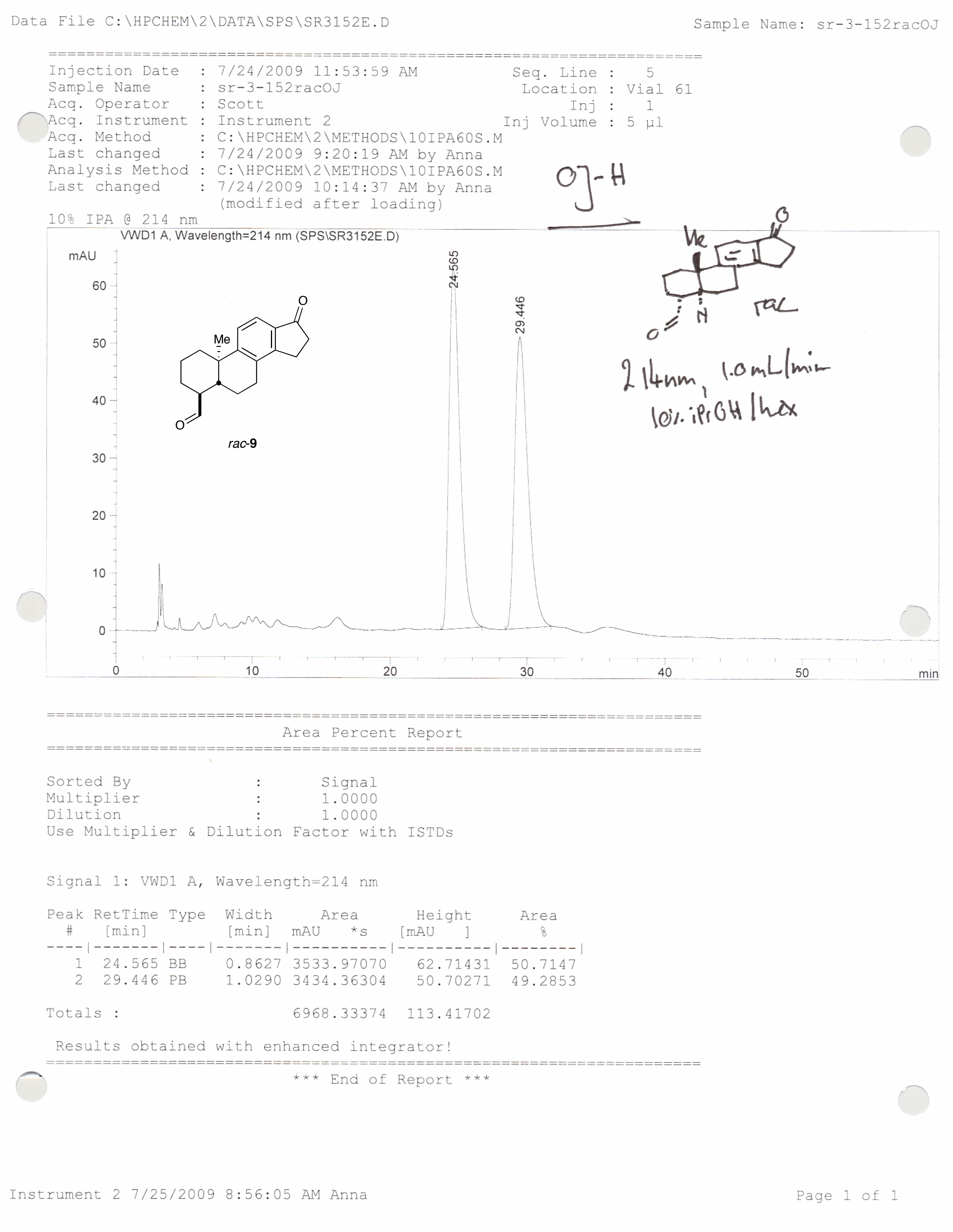

    Signal 1: VWD1 A, Wavelength=214 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  11.709 VB    0.3608 5534.14063  237.38855  93.9081
       2  14.288 VV    0.4276  359.00363   12.69063   6.0919

    Totals :                  5893.14426  250.07918

     Results obtained with enhanced integrator!
    =====================================================================
                           *** End of Report ***
```

```
Instrument 2 11/3/2008 11:29:48 AM jongrock                          Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SPS\SR3152E.D                        Sample Name: sr-3-152racOJ

    =====================================================================
    Injection Date  : 7/24/2009 11:53:59 AM          Seq. Line :    5
    Sample Name     : sr-3-152racOJ                   Location : Vial 61
    Acq. Operator   : Scott                                Inj :    1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\10IPA60S.M
    Last changed    : 7/24/2009 9:20:19 AM by Anna
    Analysis Method : C:\HPCHEM\2\METHODS\10IPA60S.M
    Last changed    : 7/24/2009 10:14:37 AM by Anna
                      (modified after loading)
    10% IPA @ 214 nm
```

OJ-H

214nm, 1.0mL/min
10% iPrOH/hex

```
    =====================================================================
                         Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=214 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU    *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  24.565 BB    0.8627 3533.97070   62.71431  50.7147
       2  29.446 PB    1.0290 3434.36304   50.70271  49.2853

    Totals :                  6968.33374  113.41702

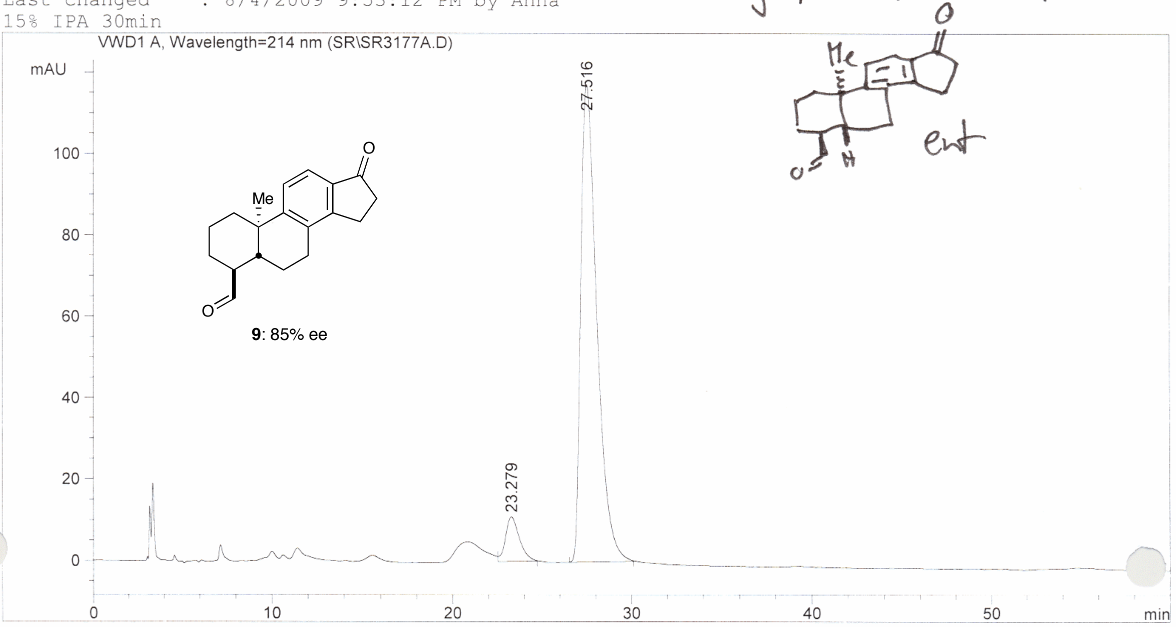
     Results obtained with enhanced integrator!
    =====================================================================
                              *** End of Report ***


Instrument 2 7/25/2009 8:56:05 AM Anna                               Page 1 of 1
```

```
Data File C:\HPCHEM\2\DATA\SR\SR3177A.D                              Sample Name: sr-3-177aOJ

    =====================================================================
    Injection Date  : 8/5/2009 11:21:34 AM           Seq. Line :    4
    Sample Name     : sr-3-177aOJ                     Location : Vial 64
    Acq. Operator   : Sebastian                            Inj :    1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\10IPA60S.M
    Last changed    : 7/24/2009 9:20:19 AM by Anna
    Analysis Method : C:\HPCHEM\2\METHODS\SCOTT2.M
    Last changed    : 8/4/2009 9:53:12 PM by Anna
    15% IPA 30min
```

OJ-H, 214nm, 1.0mL/min, 15%iPrOH/hex



9: 85% ee

```
    =====================================================================
                            Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=214 nm

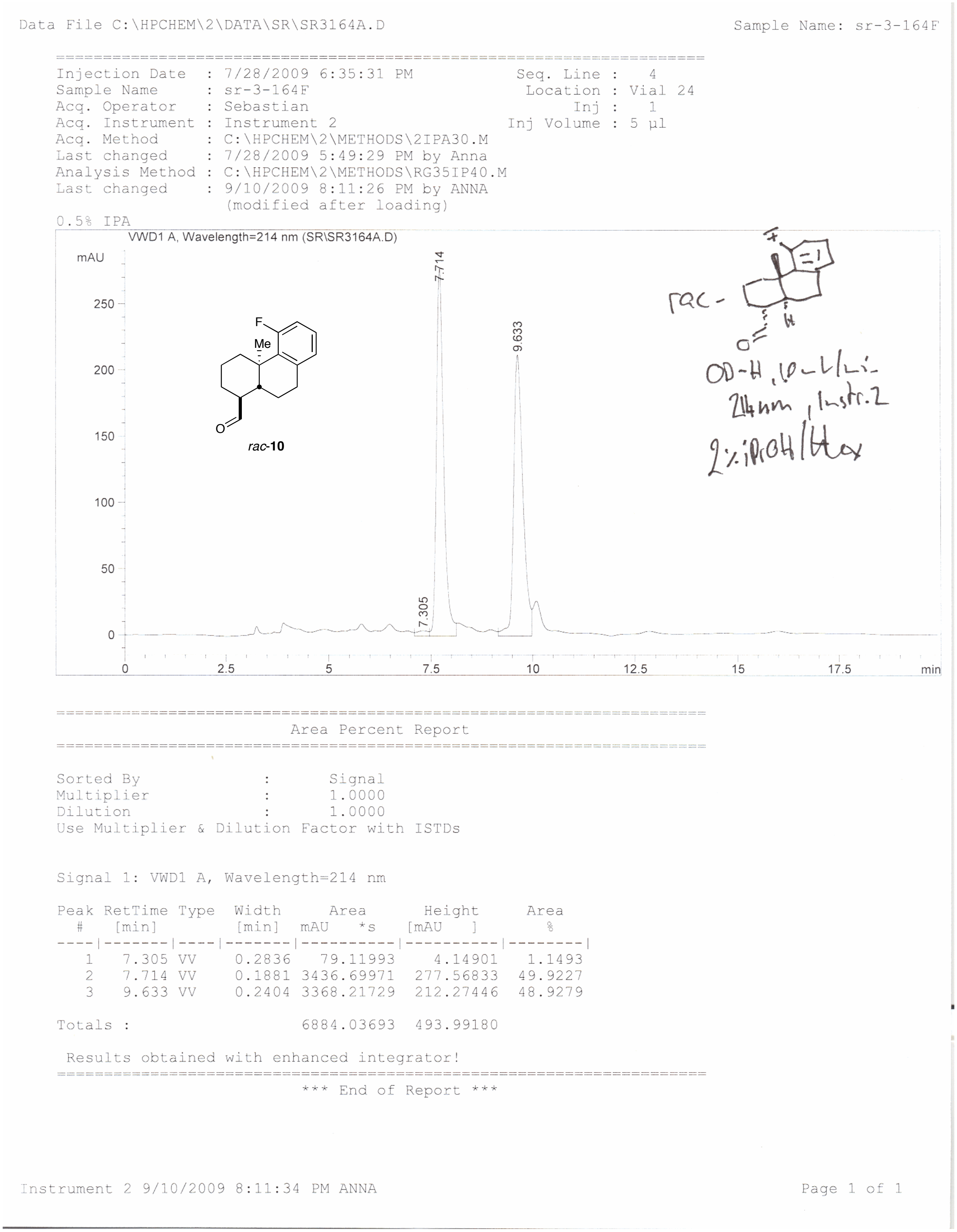
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  23.279 VB    0.7967  590.89819   10.95492   7.4566
       2  27.516 PB    0.9591 7333.64893  117.36439  92.5434

    Totals :                  7924.54712  128.31931

     Results obtained with enhanced integrator!
    =====================================================================
                              *** End of Report ***
```

85%ee

```
Instrument 2 8/5/2009 1:14:18 PM mark                                    Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR3164A.D                                  Sample Name: sr-3-164F

    =====================================================================
    Injection Date  : 7/28/2009 6:35:31 PM           Seq. Line :    4
    Sample Name     : sr-3-164F                       Location : Vial 24
    Acq. Operator   : Sebastian                            Inj :    1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\2IPA30.M
    Last changed    : 7/28/2009 5:49:29 PM by Anna
    Analysis Method : C:\HPCHEM\2\METHODS\RG35IP40.M
    Last changed    : 9/10/2009 8:11:26 PM by ANNA
                      (modified after loading)
    0.5% IPA
```

OD-H, 1.0 mL/min
214 nm, Instr. 2
2% iPrOH/Hex

```
    =====================================================================
                         Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs

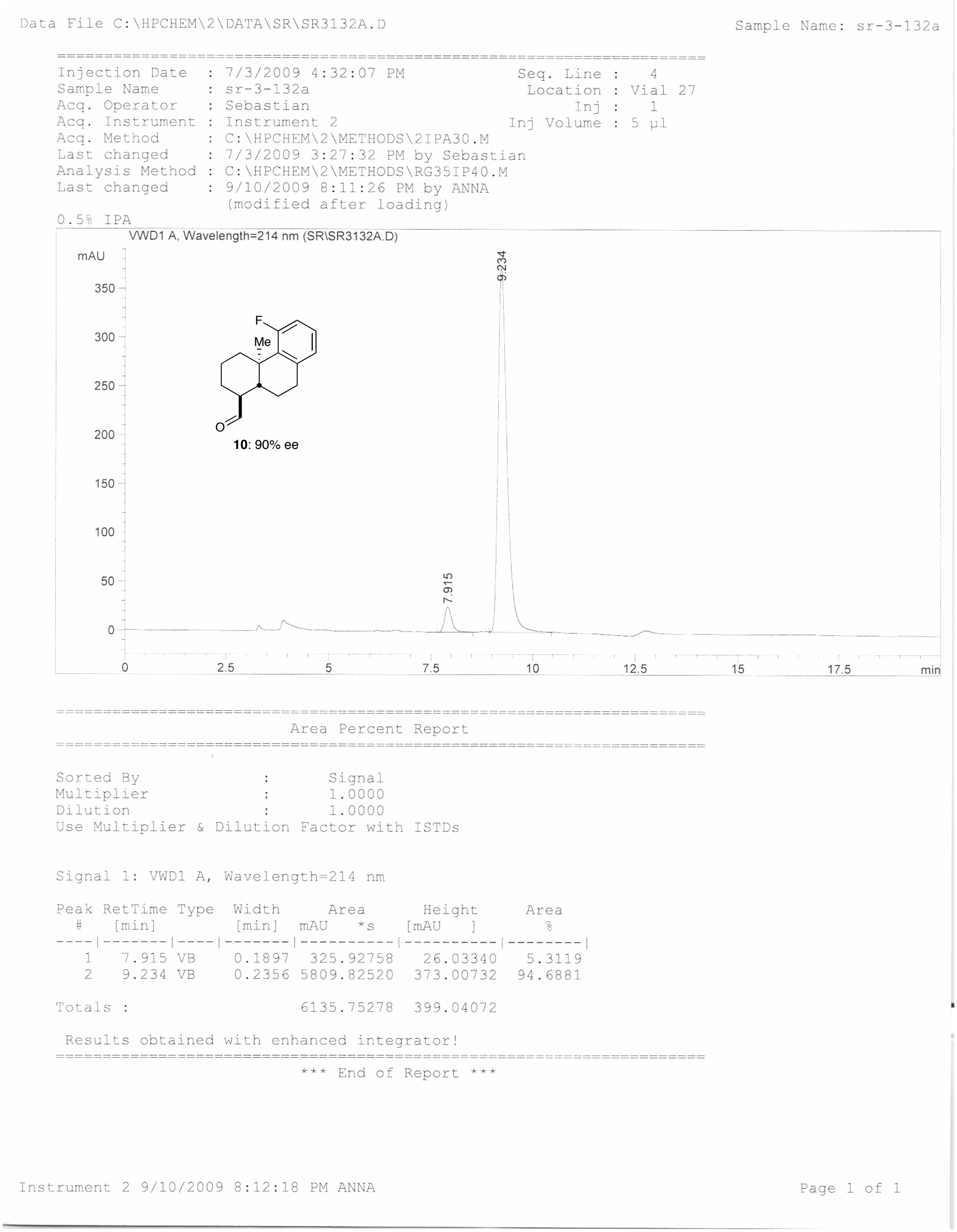

    Signal 1: VWD1 A, Wavelength=214 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1   7.305 VV    0.2836   79.11993    4.14901   1.1493
       2   7.714 VV    0.1881 3436.69971  277.56833  49.9227
       3   9.633 VV    0.2404 3368.21729  212.27446  48.9279

    Totals :                  6884.03693  493.99180

     Results obtained with enhanced integrator!
    =====================================================================
                         *** End of Report ***


Instrument 2 9/10/2009 8:11:34 PM ANNA                                Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR3132A.D                          Sample Name: sr-3-132a

    =====================================================================
    Injection Date  : 7/3/2009 4:32:07 PM             Seq. Line :   4
    Sample Name     : sr-3-132a                        Location : Vial 27
    Acq. Operator   : Sebastian                             Inj :   1
    Acq. Instrument : Instrument 2                   Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\2IPA30.M
    Last changed    : 7/3/2009 3:27:32 PM by Sebastian
    Analysis Method : C:\HPCHEM\2\METHODS\RG35IP40.M
    Last changed    : 9/10/2009 8:11:26 PM by ANNA
                      (modified after loading)
    0.5% IPA
```

```
    =====================================================================
                           Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=214 nm

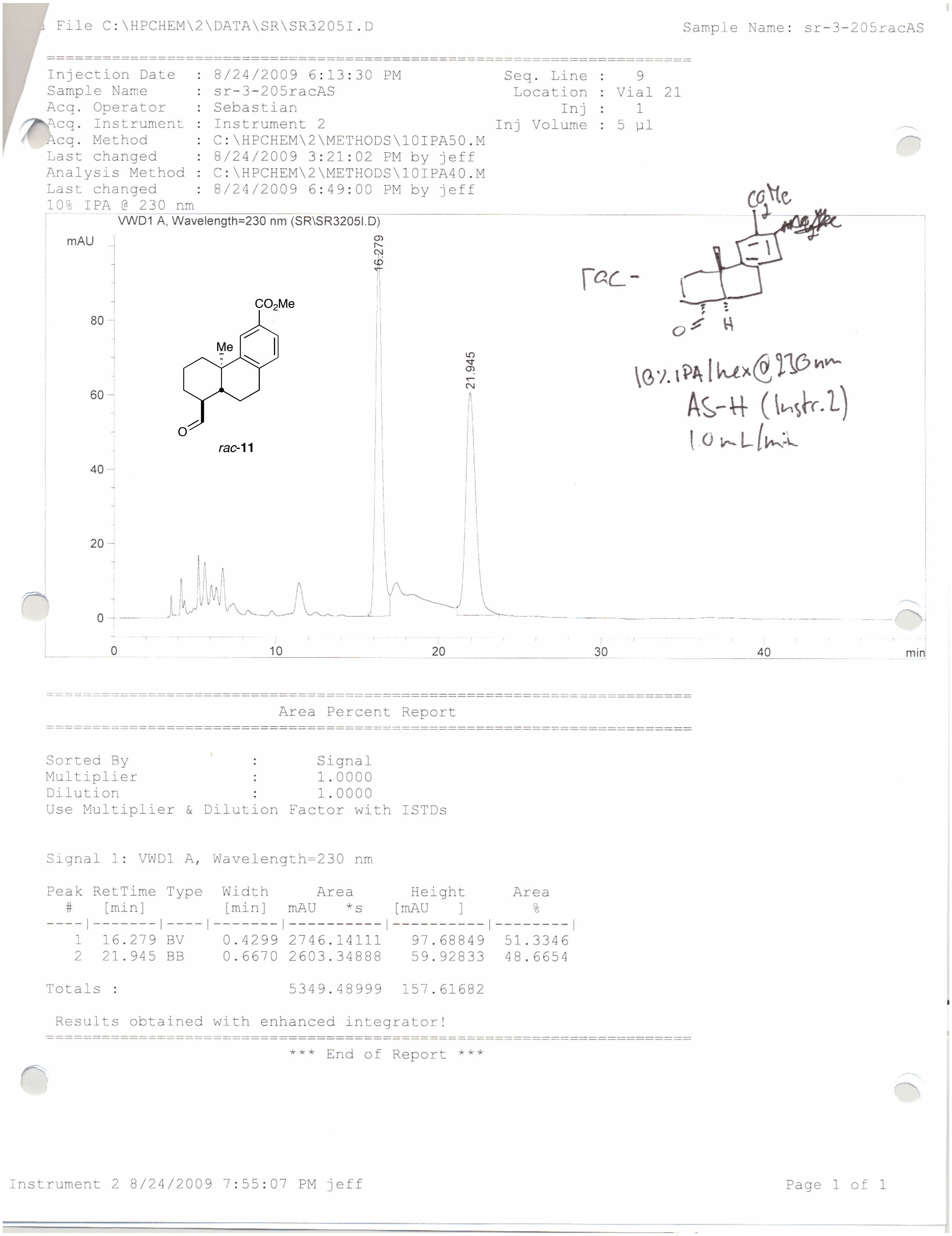
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU    *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1   7.915 VB    0.1897  325.92758   26.03340   5.3119
       2   9.234 VB    0.2356 5809.82520  373.00732  94.6881

    Totals :                  6135.75278  399.04072

     Results obtained with enhanced integrator!
    =====================================================================
                             *** End of Report ***



Instrument 2 9/10/2009 8:12:18 PM ANNA                                  Page 1 of 1
```



```
a File C:\HPCHEM\2\DATA\SR\SR3205I.D                                Sample Name: sr-3-205racAS

=====================================================================
Injection Date  : 8/24/2009 6:13:30 PM           Seq. Line :   9
Sample Name     : sr-3-205racAS                    Location : Vial 21
Acq. Operator   : Sebastian                             Inj :   1
Acq. Instrument : Instrument 2                    Inj Volume : 5 µl
Acq. Method     : C:\HPCHEM\2\METHODS\10IPA50.M
Last changed    : 8/24/2009 3:21:02 PM by jeff
Analysis Method : C:\HPCHEM\2\METHODS\10IPA40.M
Last changed    : 8/24/2009 6:49:00 PM by jeff
10% IPA @ 230 nm
```

rac-

CO_2Me

H

10% IPA/hex@230nm
AS-H (Instr.2)
1.0mL/min

```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

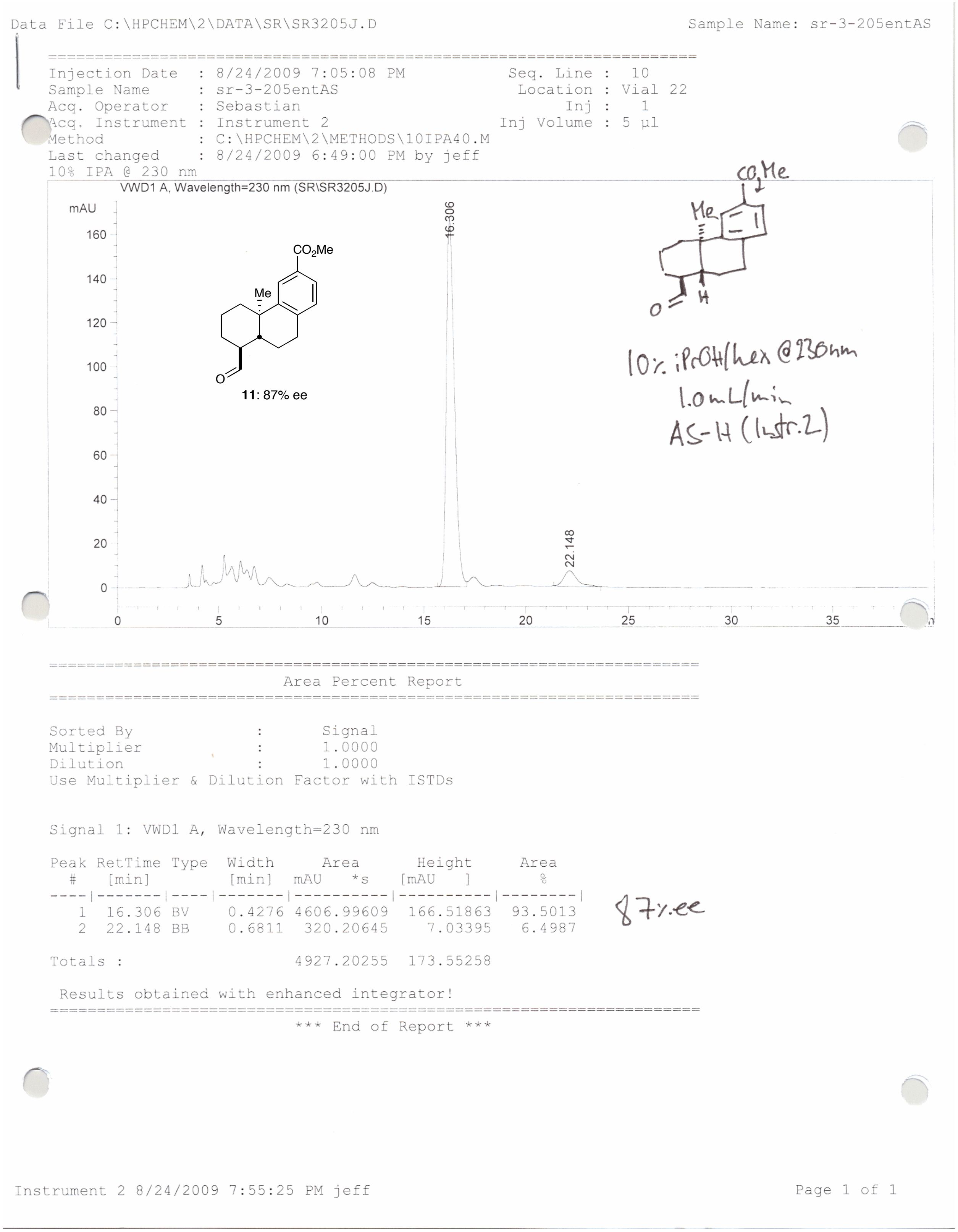

Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  16.279 BV    0.4299 2746.14111   97.68849  51.3346
   2  21.945 BB    0.6670 2603.34888   59.92833  48.6654

Totals :                  5349.48999  157.61682

 Results obtained with enhanced integrator!
=====================================================================
                          *** End of Report ***


Instrument 2 8/24/2009 7:55:07 PM jeff                             Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR3205J.D                        Sample Name: sr-3-205entAS

    =================================================================
    Injection Date  : 8/24/2009 7:05:08 PM           Seq. Line :  10
    Sample Name     : sr-3-205entAS                   Location : Vial 22
    Acq. Operator   : Sebastian                            Inj :   1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Method          : C:\HPCHEM\2\METHODS\10IPA40.M
    Last changed    : 8/24/2009 6:49:00 PM by jeff
    10% IPA @ 230 nm
```

11: 87% ee

CO_2Me

10% iPrOH/hex @ 230nm
1.0mL/min
AS-H (Instr.2)

```
    =================================================================
                          Area Percent Report
    =================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=230 nm

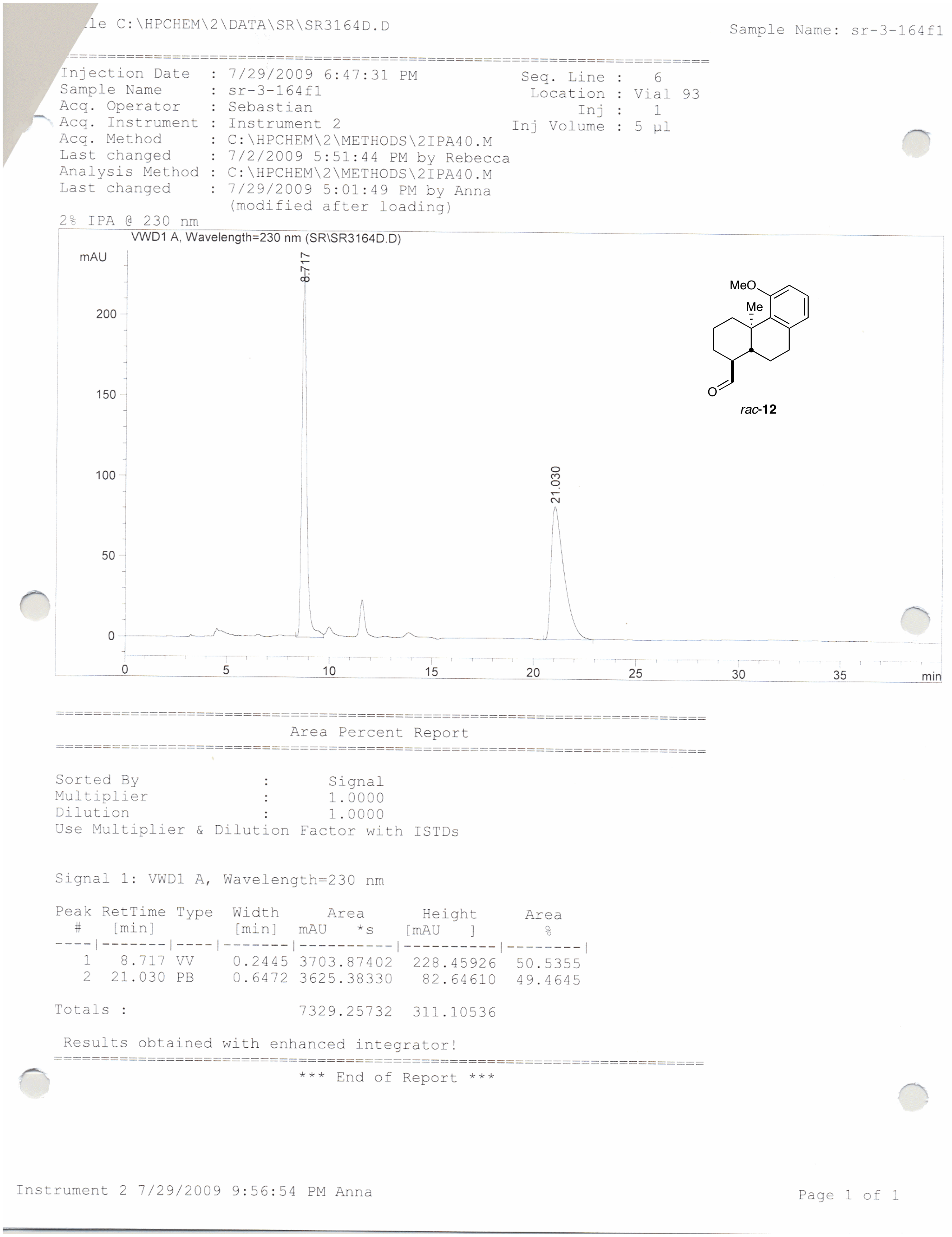
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU    *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  16.306 BV    0.4276 4606.99609  166.51863  93.5013
       2  22.148 BB    0.6811  320.20645    7.03395   6.4987

    Totals :                  4927.20255  173.55258

     Results obtained with enhanced integrator!
    =================================================================
                             *** End of Report ***
```

87% ee

```
Instrument 2 8/24/2009 7:55:25 PM jeff                              Page 1 of 1
```



```
le C:\HPCHEM\2\DATA\SR\SR3164D.D                              Sample Name: sr-3-164f1
=====================================================================
Injection Date  : 7/29/2009 6:47:31 PM            Seq. Line :   6
Sample Name     : sr-3-164f1                       Location : Vial 93
Acq. Operator   : Sebastian                             Inj :   1
Acq. Instrument : Instrument 2                   Inj Volume : 5 µl
Acq. Method     : C:\HPCHEM\2\METHODS\2IPA40.M
Last changed    : 7/2/2009 5:51:44 PM by Rebecca
Analysis Method : C:\HPCHEM\2\METHODS\2IPA40.M
Last changed    : 7/29/2009 5:01:49 PM by Anna
                  (modified after loading)
2% IPA @ 230 nm
```

```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

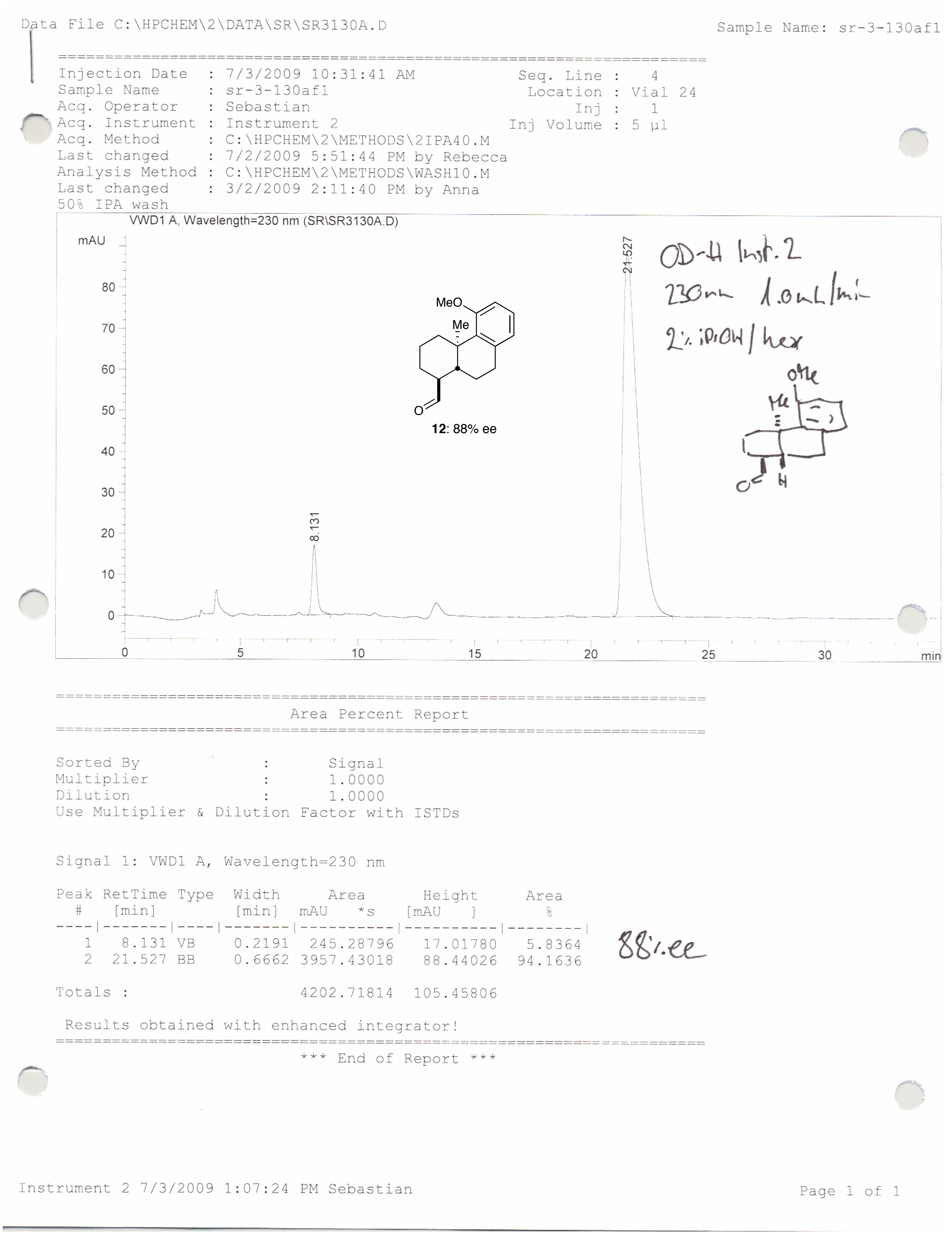

Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]     %
----|-------|----|-------|----------|----------|--------|
   1   8.717 VV    0.2445 3703.87402  228.45926 50.5355
   2  21.030 PB    0.6472 3625.38330   82.64610 49.4645

Totals :                  7329.25732  311.10536

 Results obtained with enhanced integrator!
=====================================================================
                          *** End of Report ***
```

```
Instrument 2 7/29/2009 9:56:54 PM Anna                        Page 1 of 1
```



12: 88% ee

OD-H Inst. 2
230nm 1.0mL/min
2% iPrOH/hex

```
Data File C:\HPCHEM\2\DATA\SR\SR3130A.D                          Sample Name: sr-3-130af1

    ====================================================================
    Injection Date  : 7/3/2009 10:31:41 AM           Seq. Line :    4
    Sample Name     : sr-3-130af1                     Location : Vial 24
    Acq. Operator   : Sebastian                            Inj :    1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\2IPA40.M
    Last changed    : 7/2/2009 5:51:44 PM by Rebecca
    Analysis Method : C:\HPCHEM\2\METHODS\WASH10.M
    Last changed    : 3/2/2009 2:11:40 PM by Anna
    50% IPA wash

    ====================================================================
                             Area Percent Report
    ====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=230 nm

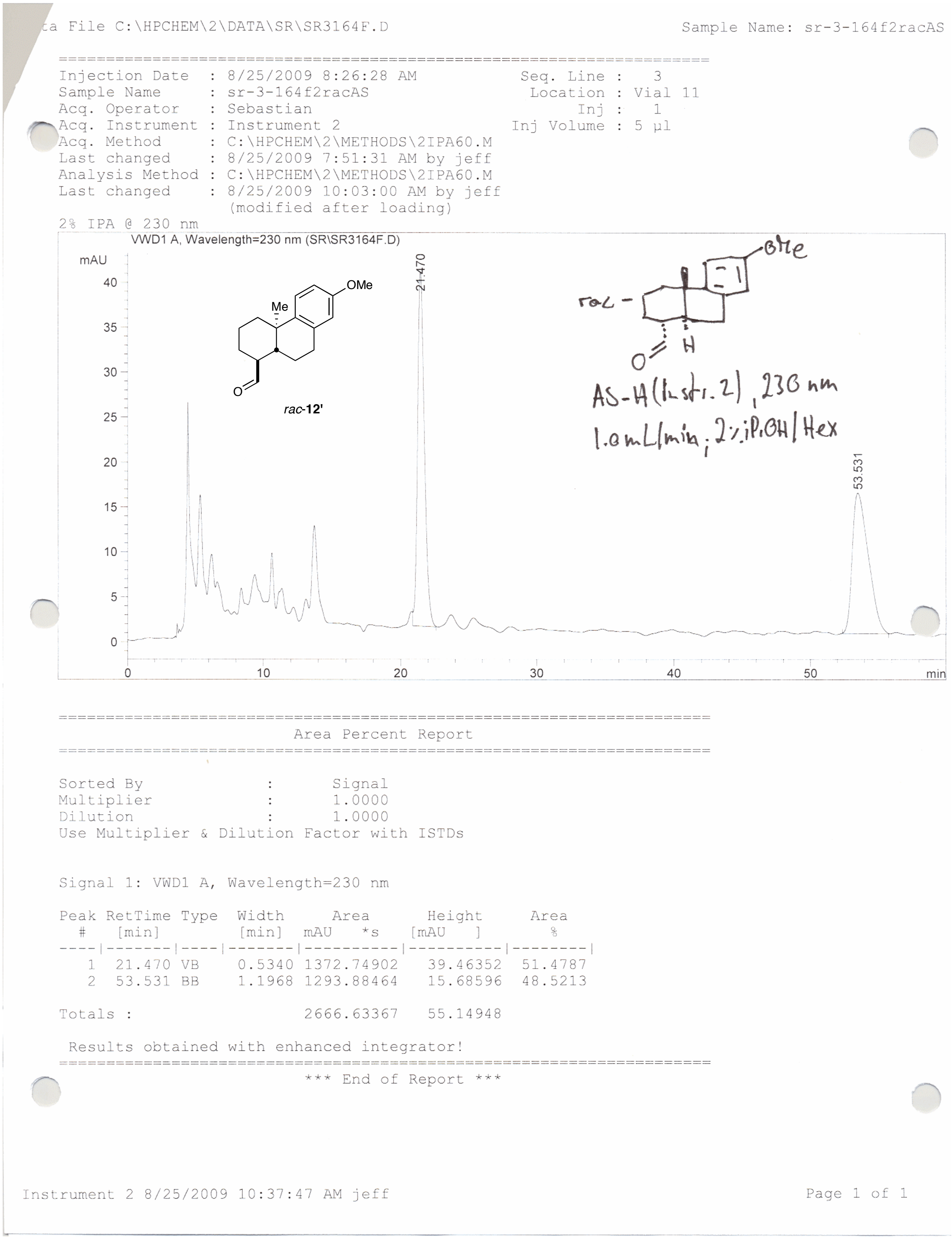
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1   8.131 VB    0.2191  245.28796   17.01780   5.8364
       2  21.527 BB    0.6662 3957.43018   88.44026  94.1636

    Totals :                  4202.71814  105.45806

     Results obtained with enhanced integrator!
    ====================================================================
                             *** End of Report ***


Instrument 2 7/3/2009 1:07:24 PM Sebastian                         Page 1 of 1
```

88% ee



```
ta File C:\HPCHEM\2\DATA\SR\SR3164F.D                            Sample Name: sr-3-164f2racAS

    =====================================================================
    Injection Date  : 8/25/2009 8:26:28 AM          Seq. Line :    3
    Sample Name     : sr-3-164f2racAS                Location : Vial 11
    Acq. Operator   : Sebastian                           Inj :    1
    Acq. Instrument : Instrument 2                 Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\2IPA60.M
    Last changed    : 8/25/2009 7:51:31 AM by jeff
    Analysis Method : C:\HPCHEM\2\METHODS\2IPA60.M
    Last changed    : 8/25/2009 10:03:00 AM by jeff
                      (modified after loading)
    2% IPA @ 230 nm
```

AS-H (Instr. 2), 230 nm
1.0 mL/min; 2% iPrOH/Hex

```
    =====================================================================
                             Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=230 nm

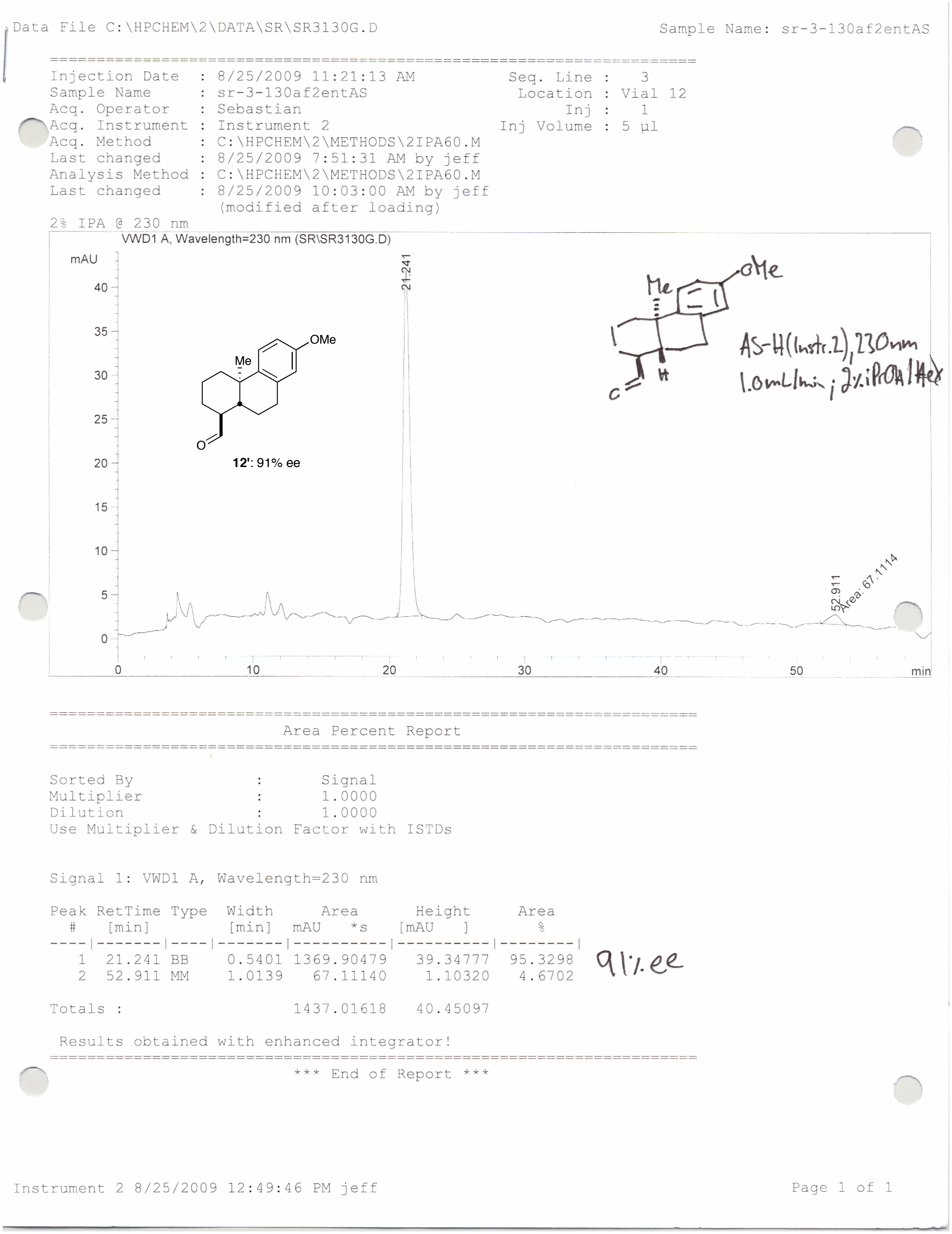
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  21.470 VB    0.5340 1372.74902   39.46352  51.4787
       2  53.531 BB    1.1968 1293.88464   15.68596  48.5213

    Totals :                  2666.63367   55.14948

     Results obtained with enhanced integrator!
    =====================================================================
                             *** End of Report ***



Instrument 2 8/25/2009 10:37:47 AM jeff                                    Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR3130G.D                          Sample Name: sr-3-130af2entAS

    =====================================================================
    Injection Date  : 8/25/2009 11:21:13 AM          Seq. Line :    3
    Sample Name     : sr-3-130af2entAS                Location : Vial 12
    Acq. Operator   : Sebastian                            Inj :    1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\2IPA60.M
    Last changed    : 8/25/2009 7:51:31 AM by jeff
    Analysis Method : C:\HPCHEM\2\METHODS\2IPA60.M
    Last changed    : 8/25/2009 10:03:00 AM by jeff
                      (modified after loading)
    2% IPA @ 230 nm
```

12': 91% ee

AS-H(Instr.2), 230nm
1.0mL/min; 2% iPrOH/Hex

```
    =====================================================================
                             Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=230 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]     %
    ----|-------|----|-------|----------|----------|--------|
       1  21.241 BB    0.5401 1369.90479   39.34777  95.3298
       2  52.911 MM    1.0139   67.11140    1.10320   4.6702

    Totals :                  1437.01618   40.45097

     Results obtained with enhanced integrator!
    =====================================================================
                             *** End of Report ***



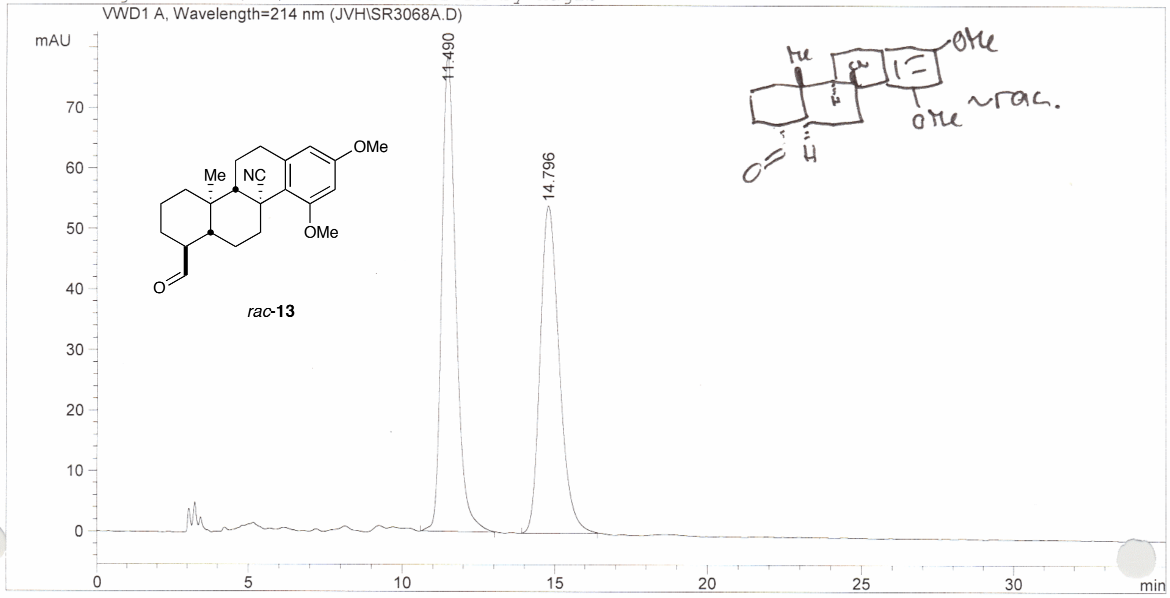
Instrument 2 8/25/2009 12:49:46 PM jeff                                      Page 1 of 1
```

91% ee

```
Data File C:\HPCHEM\2\DATA\JVH\SR3068A.D                        Sample Name: sr-3-068racOD

    ======================================================================
    Injection Date  : 5/15/2009 12:27:53 PM          Seq. Line :  14
    Sample Name     : sr-3-068racOD                   Location : Vial 25
    Acq. Operator   : Jeff                                 Inj :  1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\20IPA40.M
    Last changed    : 4/8/2009 9:27:41 AM by nagib
    Analysis Method : C:\HPCHEM\2\METHODS\05IPA60W.M
    Last changed    : 5/12/2009 11:08:01 PM by nagib
```

Instr. 2, OD-H, 1.0mL/min, 214nm



rac-**13**

```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=214 nm

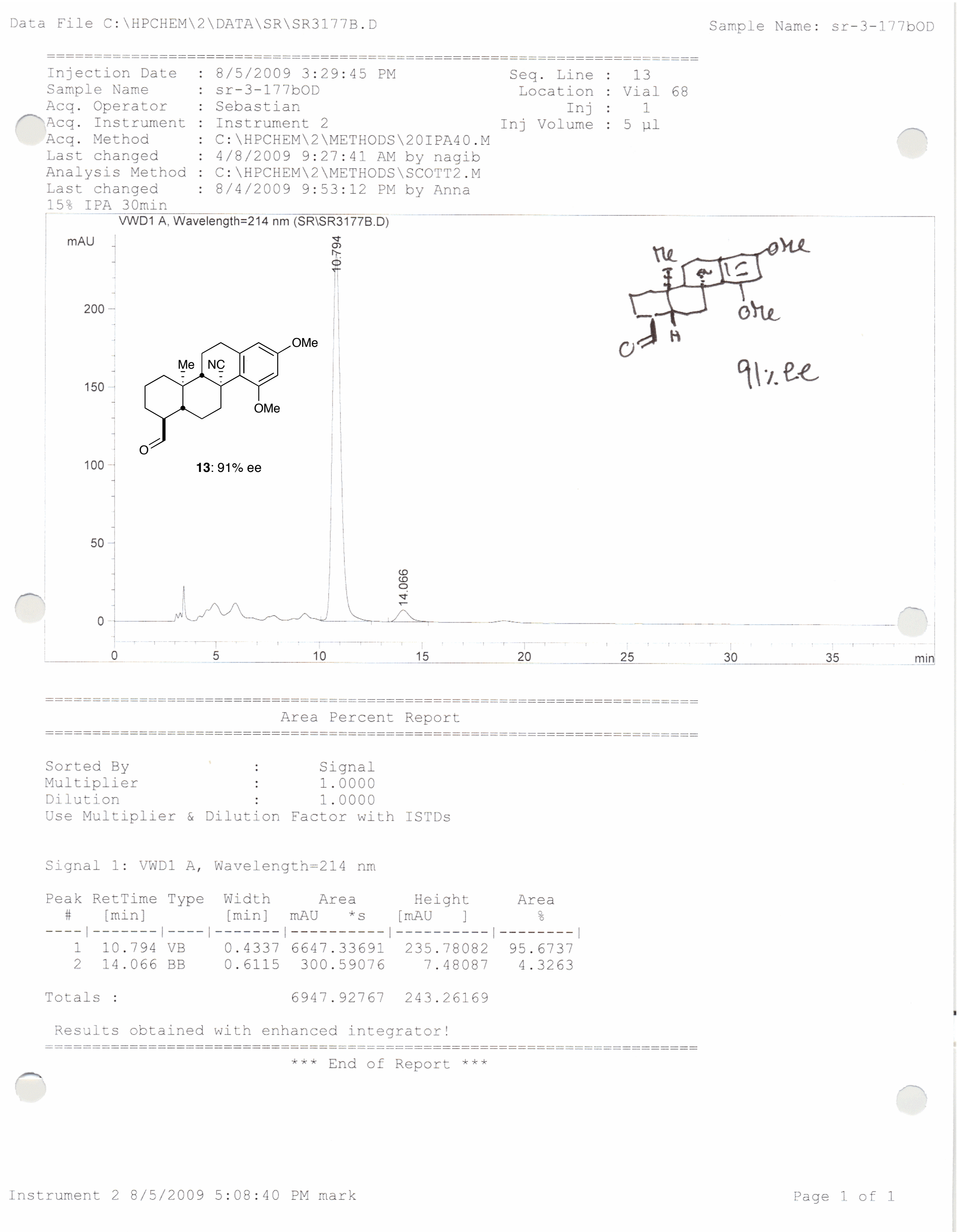
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  11.490 PB    0.4939 2531.44849   78.55261  51.6623
       2  14.796 BB    0.6796 2368.54785   54.10532  48.3377

    Totals :                  4899.99634  132.65793

     Results obtained with enhanced integrator!
    ======================================================================
                             *** End of Report ***



Instrument 2 5/15/2009 3:39:04 PM nagib                                   Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR3177B.D                                  Sample Name: sr-3-177bOD

    ======================================================================
    Injection Date   : 8/5/2009 3:29:45 PM             Seq. Line :  13
    Sample Name      : sr-3-177bOD                      Location : Vial 68
    Acq. Operator    : Sebastian                             Inj :   1
    Acq. Instrument  : Instrument 2                   Inj Volume : 5 µl
    Acq. Method      : C:\HPCHEM\2\METHODS\20IPA40.M
    Last changed     : 4/8/2009 9:27:41 AM by nagib
    Analysis Method  : C:\HPCHEM\2\METHODS\SCOTT2.M
    Last changed     : 8/4/2009 9:53:12 PM by Anna
    15% IPA 30min
```

13: 91% ee

```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=214 nm

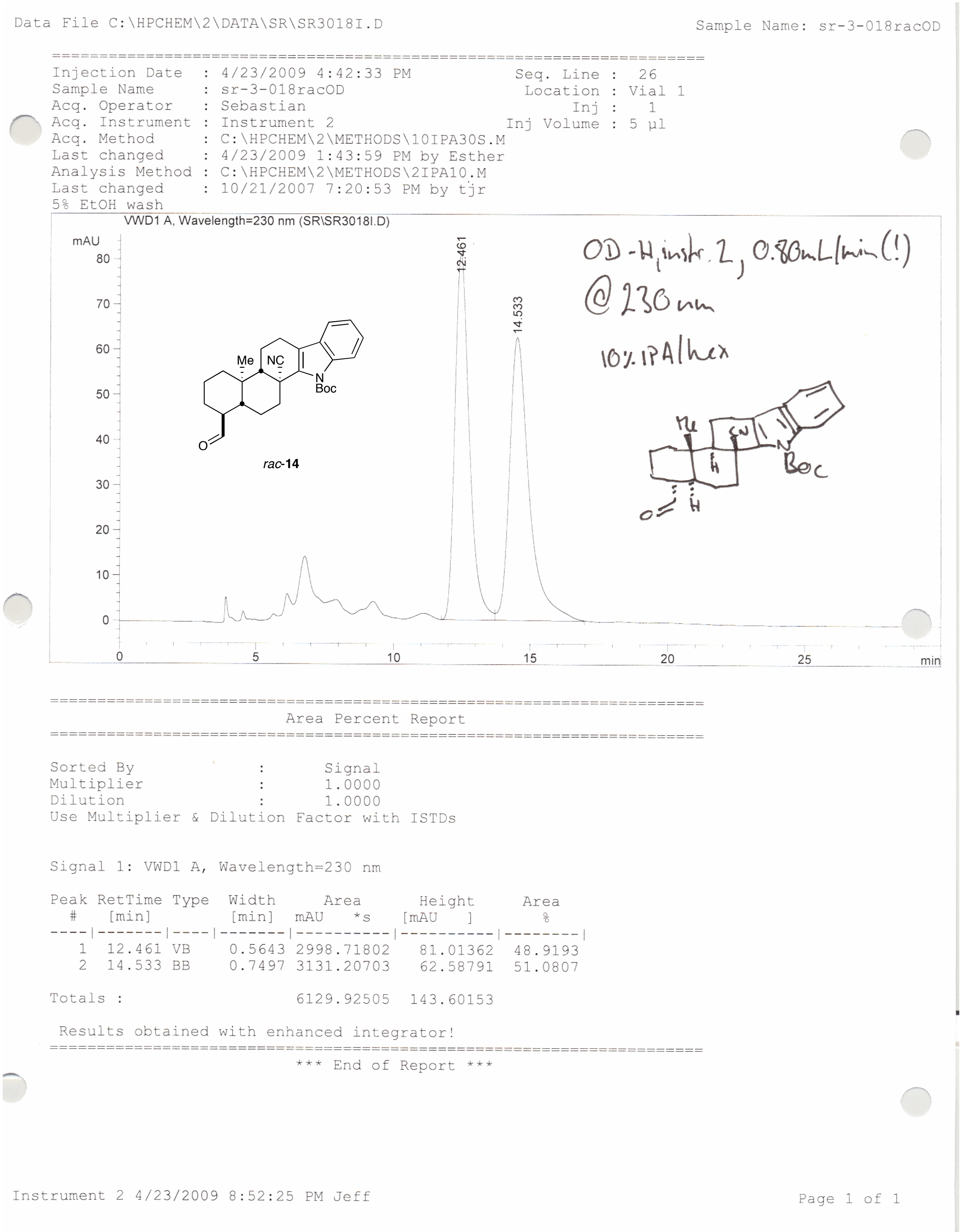
    Peak RetTime Type  Width      Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  10.794 VB    0.4337 6647.33691  235.78082  95.6737
       2  14.066 BB    0.6115  300.59076    7.48087   4.3263

    Totals :                  6947.92767  243.26169

     Results obtained with enhanced integrator!
    ======================================================================
                              *** End of Report ***



Instrument 2 8/5/2009 5:08:40 PM mark                                      Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR3018I.D                        Sample Name: sr-3-018racOD

    ======================================================================
    Injection Date  : 4/23/2009 4:42:33 PM           Seq. Line :  26
    Sample Name     : sr-3-018racOD                   Location : Vial 1
    Acq. Operator   : Sebastian                            Inj :   1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\10IPA30S.M
    Last changed    : 4/23/2009 1:43:59 PM by Esther
    Analysis Method : C:\HPCHEM\2\METHODS\2IPA10.M
    Last changed    : 10/21/2007 7:20:53 PM by tjr
    5% EtOH wash
```

rac-**14**

OD-H, instr. 2, 0.80 mL/min (!)
@ 230 nm
10% IPA/hex

```
    ======================================================================
                             Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs

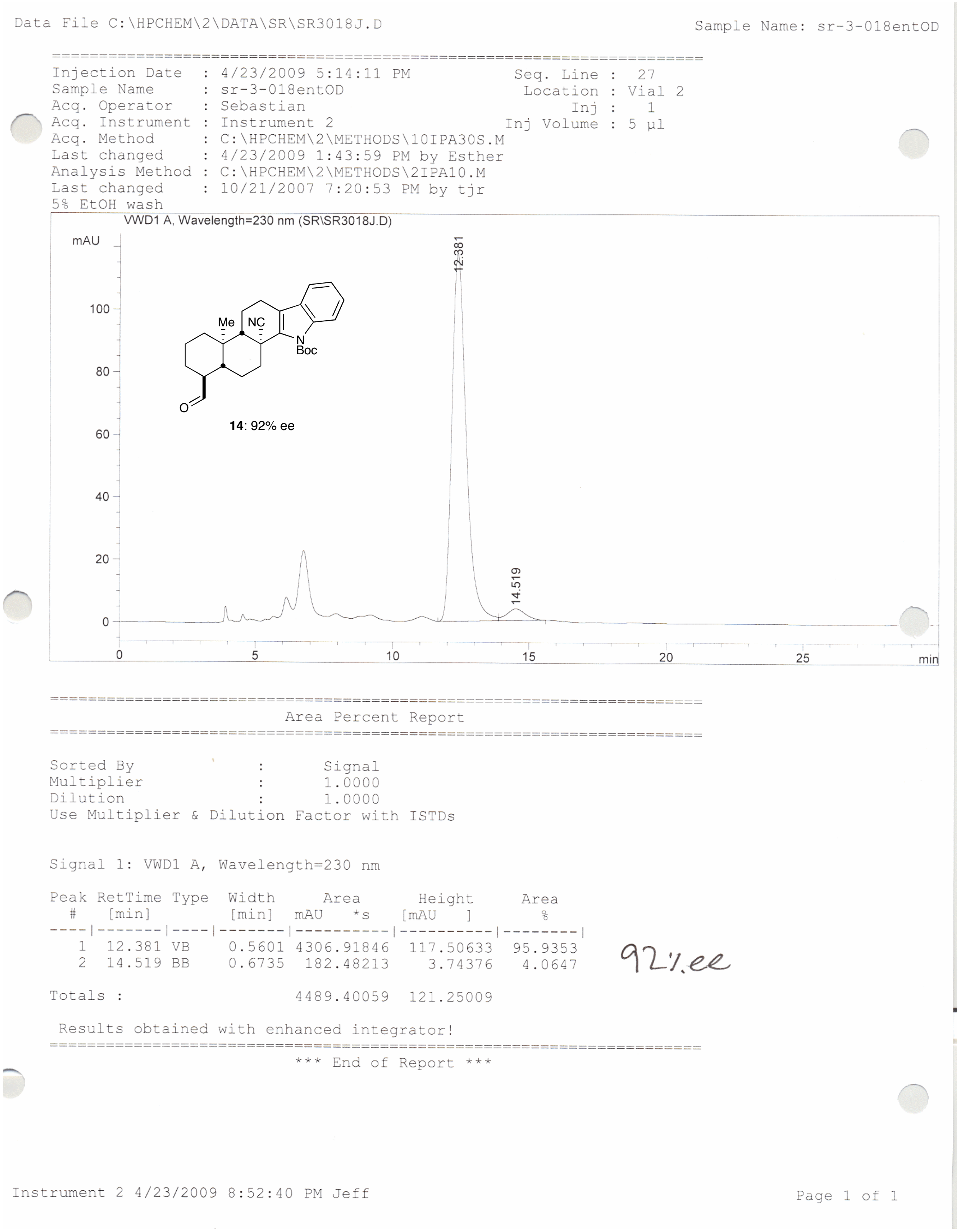

    Signal 1: VWD1 A, Wavelength=230 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  12.461 VB    0.5643 2998.71802   81.01362  48.9193
       2  14.533 BB    0.7497 3131.20703   62.58791  51.0807

    Totals :                  6129.92505  143.60153

     Results obtained with enhanced integrator!
    ======================================================================
                             *** End of Report ***


Instrument 2 4/23/2009 8:52:25 PM Jeff                          Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR3018J.D                    Sample Name: sr-3-018entOD

    ===================================================================
    Injection Date  : 4/23/2009 5:14:11 PM          Seq. Line :  27
    Sample Name     : sr-3-018entOD                  Location : Vial 2
    Acq. Operator   : Sebastian                           Inj :   1
    Acq. Instrument : Instrument 2                 Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\10IPA30S.M
    Last changed    : 4/23/2009 1:43:59 PM by Esther
    Analysis Method : C:\HPCHEM\2\METHODS\2IPA10.M
    Last changed    : 10/21/2007 7:20:53 PM by tjr
    5% EtOH wash
```

14: 92% ee

```
    ===================================================================
                         Area Percent Report
    ===================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=230 nm

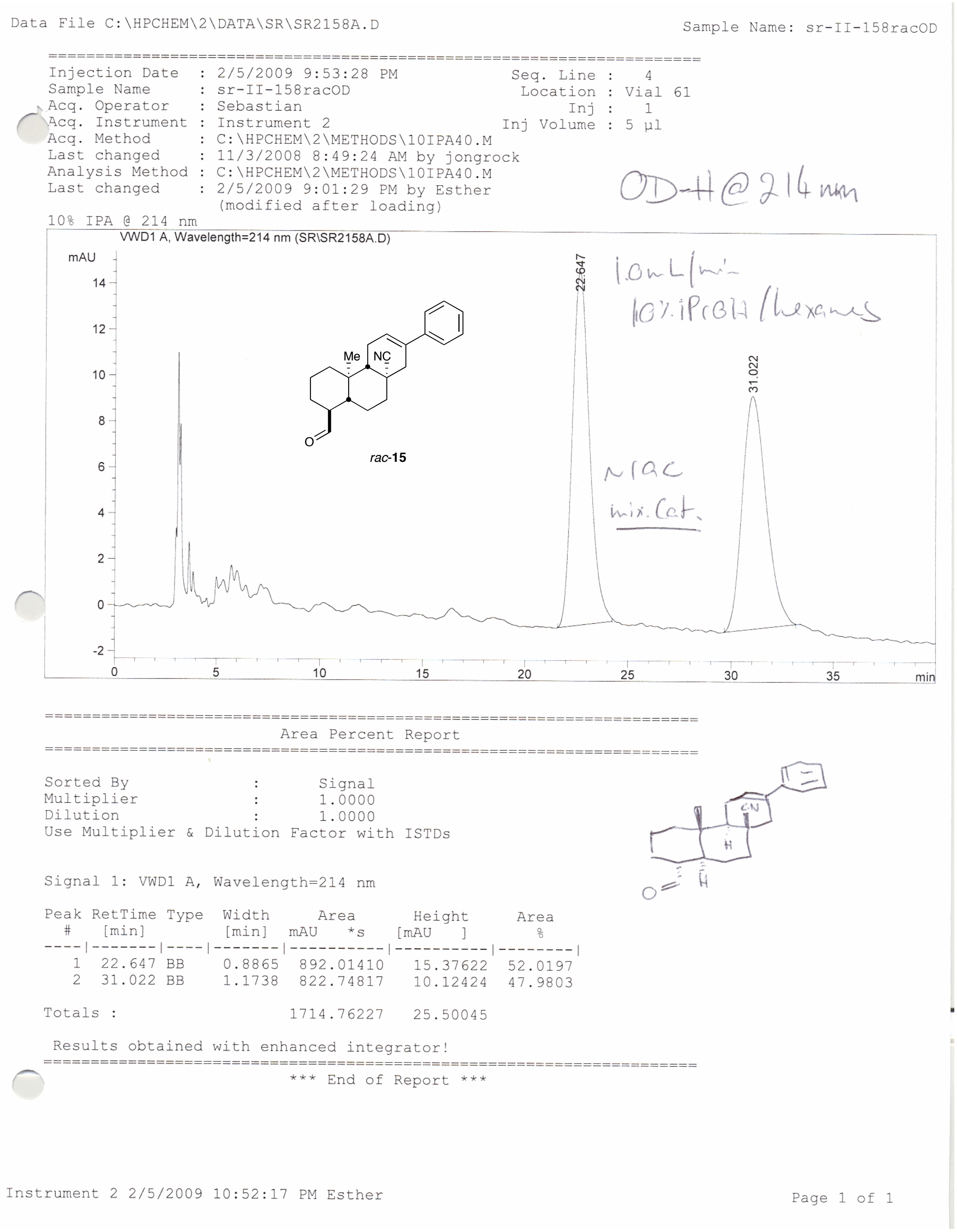
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  12.381 VB    0.5601 4306.91846  117.50633  95.9353
       2  14.519 BB    0.6735  182.48213    3.74376   4.0647

    Totals :                  4489.40059  121.25009

     Results obtained with enhanced integrator!
    ===================================================================
                         *** End of Report ***
```

92%.ee

```
Instrument 2 4/23/2009 8:52:40 PM Jeff                               Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR2158A.D                      Sample Name: sr-II-158racOD

    =====================================================================
    Injection Date  : 2/5/2009 9:53:28 PM            Seq. Line :    4
    Sample Name     : sr-II-158racOD                  Location : Vial 61
    Acq. Operator   : Sebastian                            Inj :    1
    Acq. Instrument : Instrument 2                  Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\10IPA40.M
    Last changed    : 11/3/2008 8:49:24 AM by jongrock
    Analysis Method : C:\HPCHEM\2\METHODS\10IPA40.M
    Last changed    : 2/5/2009 9:01:29 PM by Esther
                      (modified after loading)
    10% IPA @ 214 nm
```

OD-H @ 214 nm

1.0mL/min

10% iPrOH/hexanes

rac-**15**

rac

mix. Cat.

```
    =====================================================================
                             Area Percent Report
    =====================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs

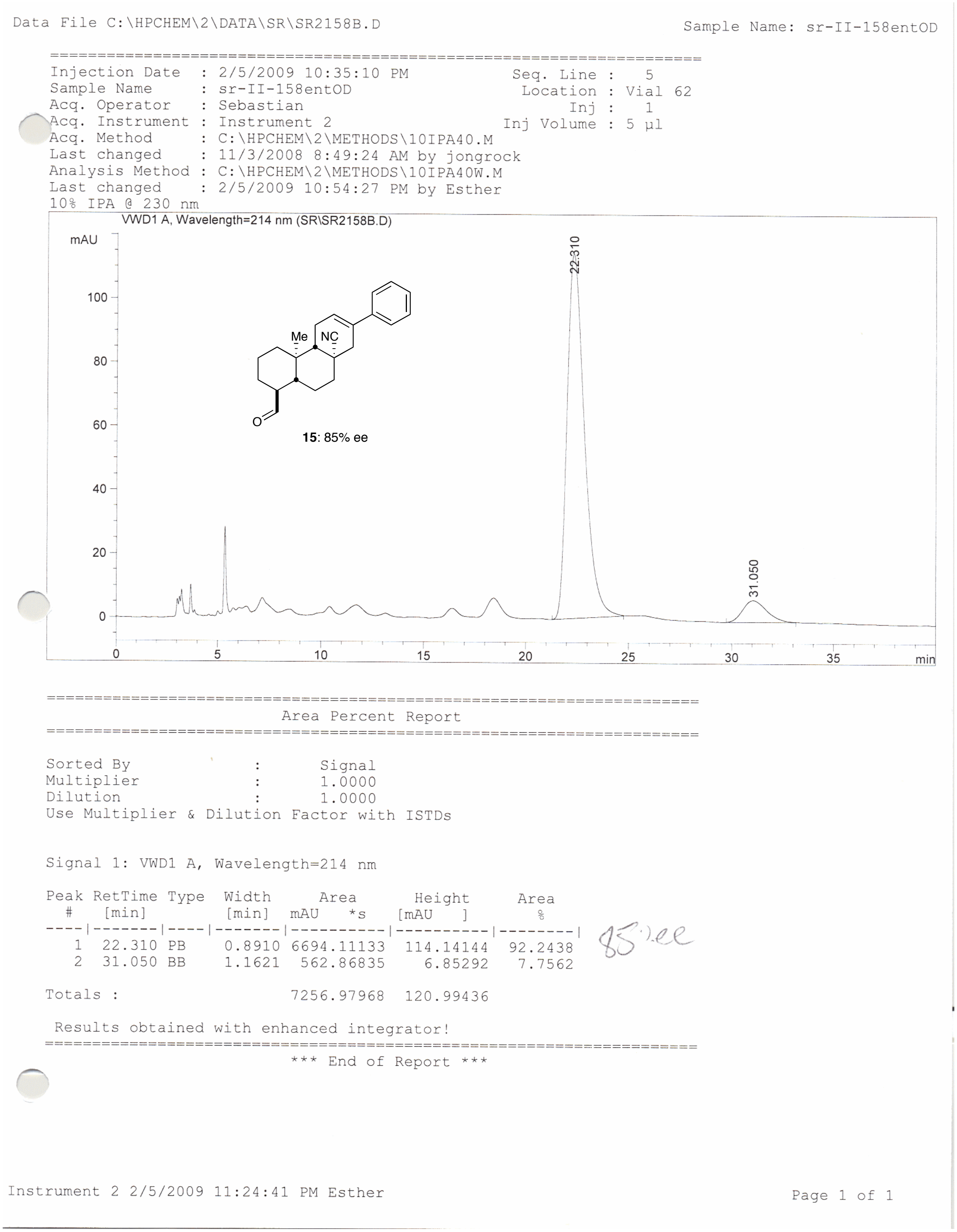

    Signal 1: VWD1 A, Wavelength=214 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  22.647 BB    0.8865  892.01410   15.37622  52.0197
       2  31.022 BB    1.1738  822.74817   10.12424  47.9803

    Totals :                  1714.76227   25.50045

     Results obtained with enhanced integrator!
    =====================================================================
                             *** End of Report ***


Instrument 2 2/5/2009 10:52:17 PM Esther                           Page 1 of 1
```



```
Data File C:\HPCHEM\2\DATA\SR\SR2158B.D                     Sample Name: sr-II-158entOD

    =================================================================
    Injection Date  : 2/5/2009 10:35:10 PM          Seq. Line :    5
    Sample Name     : sr-II-158entOD                 Location : Vial 62
    Acq. Operator   : Sebastian                           Inj :    1
    Acq. Instrument : Instrument 2                 Inj Volume : 5 µl
    Acq. Method     : C:\HPCHEM\2\METHODS\10IPA40.M
    Last changed    : 11/3/2008 8:49:24 AM by jongrock
    Analysis Method : C:\HPCHEM\2\METHODS\10IPA40W.M
    Last changed    : 2/5/2009 10:54:27 PM by Esther
    10% IPA @ 230 nm

    =================================================================
                         Area Percent Report
    =================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=214 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  22.310 PB    0.8910 6694.11133  114.14144  92.2438
       2  31.050 BB    1.1621  562.86835    6.85292   7.7562

    Totals :                  7256.97968  120.99436

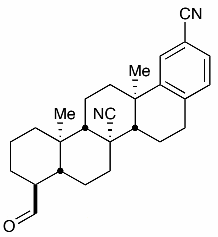
     Results obtained with enhanced integrator!
    =================================================================
                         *** End of Report ***


Instrument 2 2/5/2009 11:24:41 PM Esther                          Page 1 of 1
```

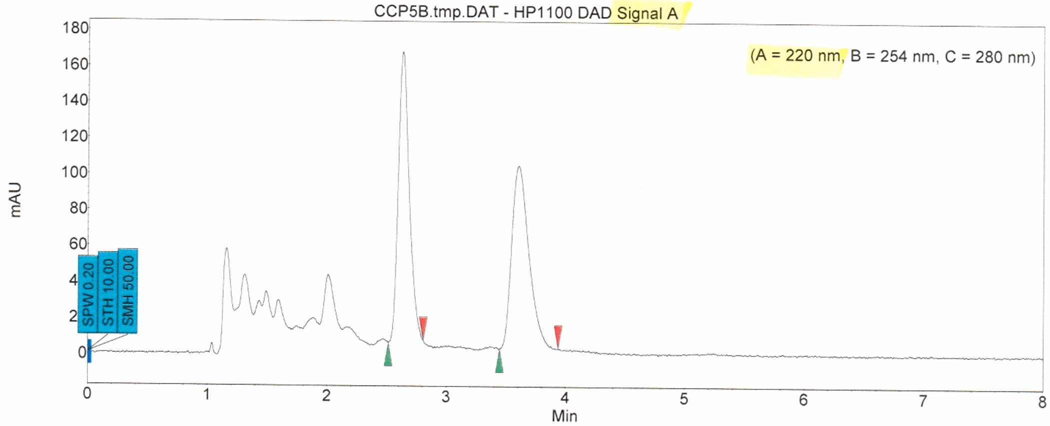
85%ee

Filename: SR-3-181 RAC file#5

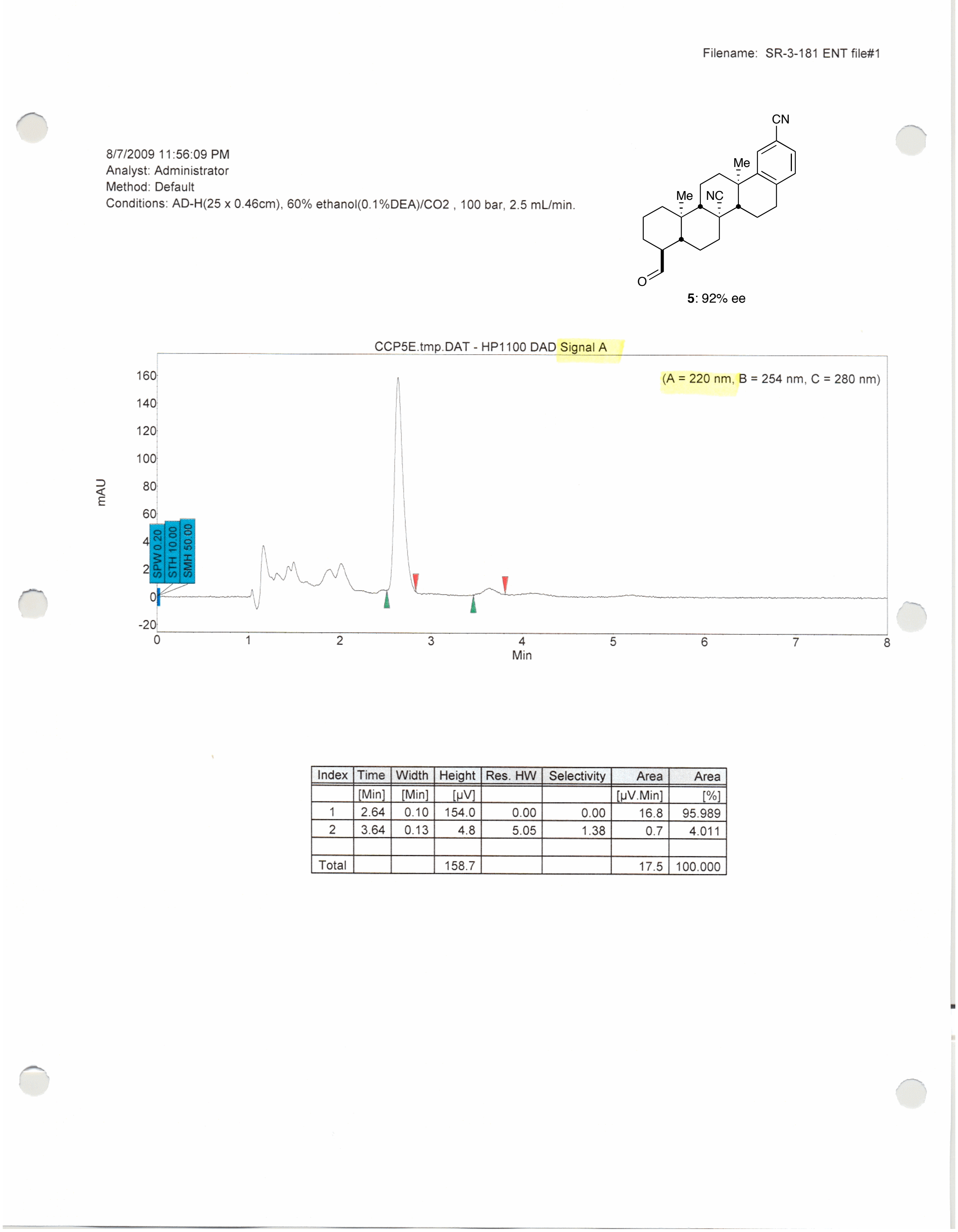
8/8/2009 12:14:10 AM
Analyst: Administrator
Method: Default
Conditions: AD-H(25 x 0.46cm), 60% ethanol(0.1%DEA)/CO2 , 100 bar, 2.5 mL/min.



rac-**5**



Index	Time	Width	Height	Res. HW	Selectivity	Area	Area
	[Min]	[Min]	[µV]			[µV.Min]	[%]
2	2.63	0.10	160.8	0.00	0.00	17.1	50.291
1	3.60	0.15	101.3	4.58	1.37	16.9	49.709
Total			262.1			34.1	100.000



Filename: SR-3-181 ENT file#1

8/7/2009 11:56:09 PM
Analyst: Administrator
Method: Default
Conditions: AD-H(25 x 0.46cm), 60% ethanol(0.1%DEA)/CO2 , 100 bar, 2.5 mL/min.

5: 92% ee

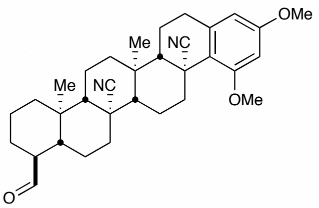
CCP5E.tmp.DAT - HP1100 DAD Signal A

(A = 220 nm, B = 254 nm, C = 280 nm)

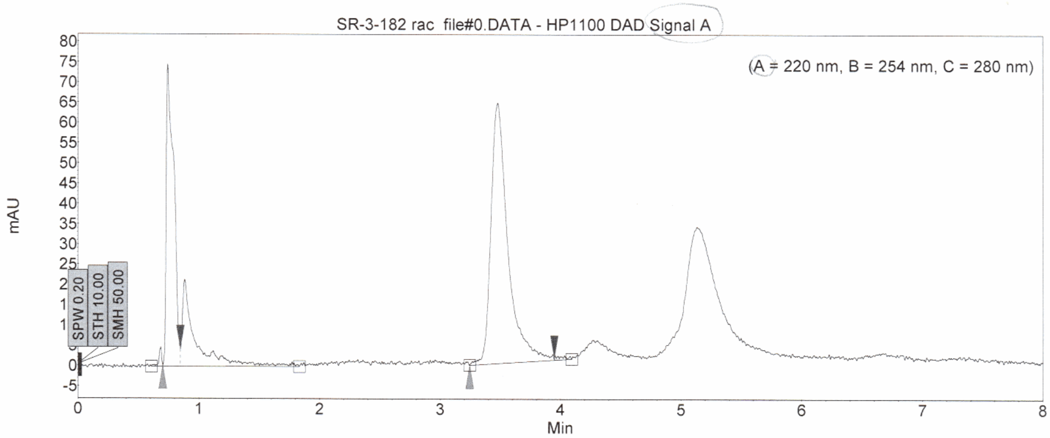
Index	Time	Width	Height	Res. HW	Selectivity	Area	Area
	[Min]	[Min]	[µV]			[µV.Min]	[%]
1	2.64	0.10	154.0	0.00	0.00	16.8	95.989
2	3.64	0.13	4.8	5.05	1.38	0.7	4.011
Total			158.7			17.5	100.000

Filename: SR-3-182 rac file#0

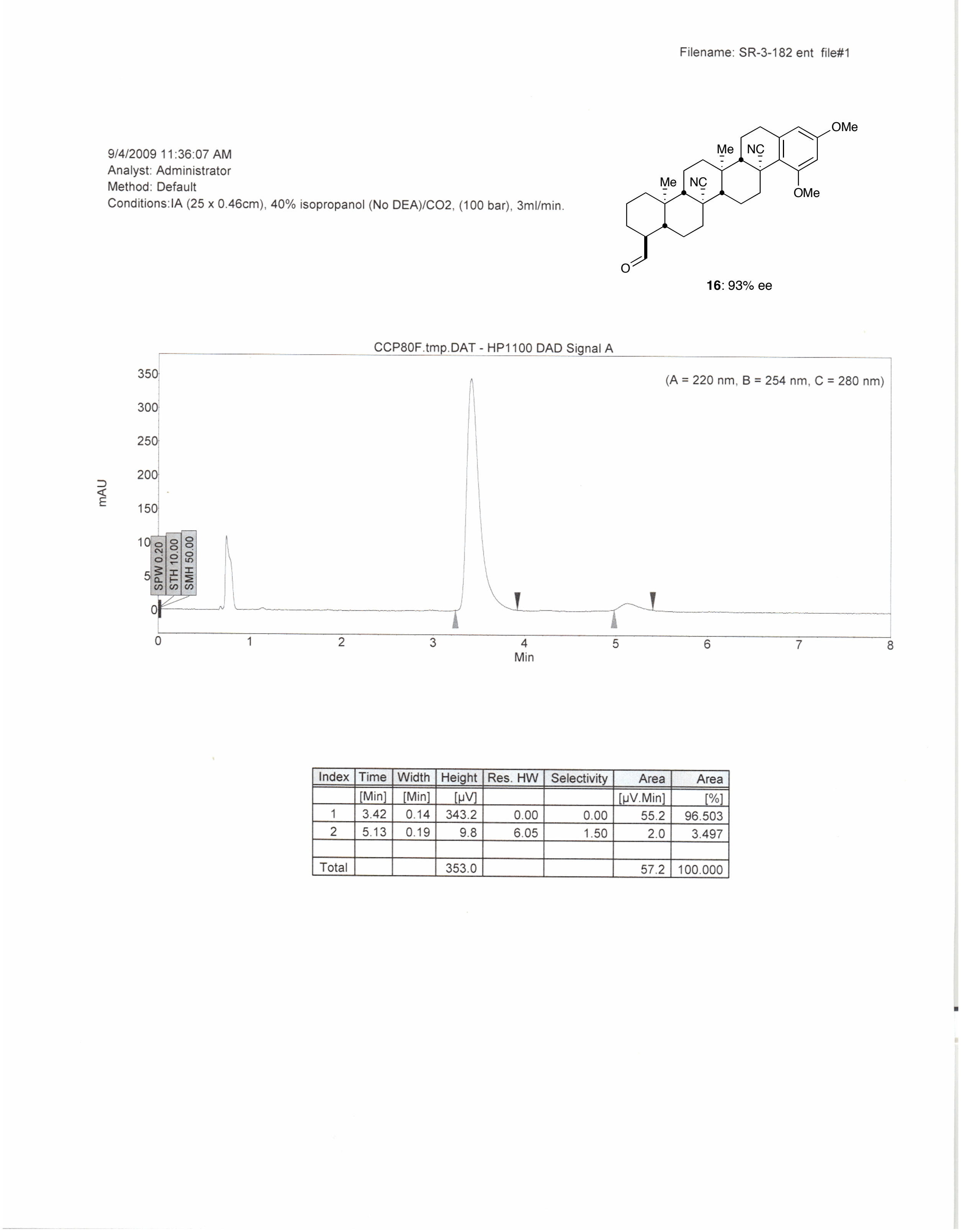
9/4/2009 11:17:35 AM
Analyst: Administrator
Method: Default
Conditions:IA (25 x 0.46cm), 40% isopropanol (No DEA)/CO2, (100 bar), 3ml/min.



rac-**16**



Index	Time	Width	Height	Res. HW	Selectivity	Area	Area
	[Min]	[Min]	[µV]			[µV.Min]	[%]
1	0.74	0.08	74.6	0.00	0.00	5.4	33.792
2	3.48	0.14	64.3	15.06	4.69	10.5	66.208
Total			138.8			15.9	100.000



Filename: SR-3-182 ent file#1

9/4/2009 11:36:07 AM
Analyst: Administrator
Method: Default
Conditions:IA (25 x 0.46cm), 40% isopropanol (No DEA)/CO2, (100 bar), 3ml/min.

16: 93% ee

CCP80F.tmp.DAT - HP1100 DAD Signal A

(A = 220 nm, B = 254 nm, C = 280 nm)

Index	Time	Width	Height	Res. HW	Selectivity	Area	Area
	[Min]	[Min]	[µV]			[µV.Min]	[%]
1	3.42	0.14	343.2	0.00	0.00	55.2	96.503
2	5.13	0.19	9.8	6.05	1.50	2.0	3.497
Total			353.0			57.2	100.000