Electronic Supplementary Material (ESI) for RSC Advances.
This journal is © The Royal Society of Chemistry 2015

Electronic Supplementary Information(ESI)

One-Pot Highly Diastereoselective Synthesis of *anti*,*anti* Vinylic 3-amino-1,2 diols *via* Proline Catalyzed Sequential α-Amination/Benzoyloxyallylation of Aldehydes

*Brij Bhushan Ahuja and Arumugam Sudalai**

Chemical Engineering & Process Development Division, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune-411008 Maharashtra, India. India, Fax: (+) 91-02025902675.

E-mail: a.sudalai@ncl.res.in

Table of Contents

EXPERIMENTAL SECTION

General Description

Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 60–80 °C was used. Melting points are uncorrected. Optical rotations were measured using sodium D line on a JASCO P-2000 polarimeter. Infrared spectra were recorded on Shimadzu FTIR-8400 spectrometer. The wave numbers (n) of recorded IR-signals are quoted in cm−1. ^{1}H and ^{13}C NMR were recorded on Bruker AV-200, AV-400 and AV-500 NMR spectrometers, respectively. HRMS mass spectra were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump. HPLC was performed on Agilent chromatogram with variable wavelength detector. Purification was done using column chromatography (230−400 mesh).

General Experimental Procedure:

General experimental procedure for sequential α-amination/benzoyloxyallylation of Aldehydes:

To a cooled solution of azadicarboxylate (5.0 mmol) and L-proline (10 mol%) in dry CH_3CN (20 mL) at 0 ^{o}C was added aldehydes (**1a-j**, 5 mmol) and the mixture was stirred for 3 h at 0 ^{o}C. This was followed by the addition of zinc powder (7.5 mmol), 3-benzoyloxyallyl bromide (7.5 mmol) and saturated aq. NH_4Cl (20 ml) at -20 ^{o}C for 2 h. The progress of the reaction can be monitored by TLC. After completion of the reaction, it was concentrated in vacuum to remove acetonitrile and the concentrate was extracted with ethyl acetate (3×40 mL). The combined organic layers were washed with brine, dried over anhyd. Na_2SO_4, and concentrated under reduced pressure to give the crude products, which were then purified by flash column chromatography (100-200 mesh) using petroleum ether and ethyl acetate (4:1) as eluents to afford the pure products **2a-j**.

Diisopropyl 1-((2R,3R,4S)-4-(benzoyloxy)-3-hydroxyhex-5-en-2-yl)hydrazine-1,2-dicarboxylate (2a) R' = *i*-Pr:

Yield: 79%; colorless solid; **mp** 110-112 ^{o}C; **IR** ($CHCl_3$): 3303, 2982, 2932, 1708, 1386, 1267, 1105, 753, 712 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.20-1.34 (m, 15H), 4.17 (brs, 1H), 4.38 (brs, 1H), 4.9-5.03 (m, 2H), 5.30-5.48 (m, 3H), 5.98-6.15 (m, 1H), 6.53 (brs, NH), 7.45 (t, *J* = 8.9 Hz, 2H), 7.57 (t, *J* = 6.3 Hz, 1H), 8.09 (d, *J* = 8.9 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 11.0, 21.7, 54.6, 69.6, 69.9, 70.5, 73.9, 118.1, 128.2, 129.6, 132.9, 155.2, 156.5, 165.3; **HRMS (ESI, m/z):** calcd for $C_{21}H_{30}N_2O_7$ $[M+Na]^+$ 445.1945, found 445.1938; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (minor) 20.92 min, (major) 25.13 min, ee 77%]; $[\alpha]^{D}_{25}$ +25.81 (c 3.78, $CHCl_3$).

Di-tert-butyl 1-((2R,3R,4S)-4-(benzoyloxy)-3-hydroxyhex-5-en-2-yl)hydrazine-1,2-dicarboxylate (2a) R' = *t*-Bu:

Yield: 81%; gum; **IR** ($CHCl_3$): 3304, 2983, 1705, 1267, 1106, 749 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.19 (d, *J* = 7.9 Hz, 3H), 1.48 (s, 18H), 4.17 (brs, 1H), 4.31 (brs, 1H), 5.30-5.46 (m, 3H), 5.99-6.16 (m, 1H), 6.31 (brs, NH), 7.44 (t, *J* = 7.9 Hz, 2H), 7.57 (t, *J* = 6.7 Hz, 1H), 8.09 (d, *J* = 7.1 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 10.6, 28.1, 54.5, 73.6, 74.8, 81.9, 118.2, 128.3, 129.7, 133.1, 154.4, 165.3; **HRMS (ESI, m/z):** calcd for $C_{23}H_{34}N_2O_7$ $[M+Na]^+$ 473.2263, found 473.2271. **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (major) 21.18 min and (minor) 28.90 min, ee 78%; $[\alpha]^{D}_{25}$ +56.57 (c 1.84, $CHCl_3$).

Dibenzyl 1-((2R,3R,4S)-4-(benzoyloxy)-3-hydroxyhex-5-en-2-yl)hydrazine-1,2-dicarboxylate (2a) R' = Bn:

Yield: 84%; gum; **IR** ($CHCl_3$): 3303, 2983, 1705, 1368, 1216, 749 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.18 (brs, 3H), 3.97-4.46 (m, 2H), 5.10 (s, 5H), 5.27-5.50 (m, 3H), 5.59 (brs, NH), 7.24 (s, 10H), 7.37 (s, 2H), 7.49 (s, 1H), 8.05 (d, *J* = 7.2 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.2, 55.5, 67.5, 67.8, 73.9, 75.7, 118.1, 127.5, 128, 128.3, 128.4, 129.7, 129.9, 133.1, 135.3, 155.3, 156.7, 169.6; **HRMS (ESI, m/z):** calcd for $C_{29}H_{30}N_2O_7$ $[M+Na]^+$ 541.1951, found 541.1951; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (major) 68.41 min and (minor) 79.74 min, ee 93%]; $[\alpha]^D_{25}$ +120.8 (c 0.9, $CHCl_3$).

Diisopropyl 1-((3R,4R,5S)-5-(benzoyloxy)-4-hydroxyhept-6-en-3-yl)hydrazine-1,2-dicarboxylate (2b):

Yield: 87%; gum; **IR** ($CHCl_3$): 3317, 2982, 1705, 1307, 1237, 741 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.91 (brs, 3H), 1.27 (s, 12H), 1.73 (brs, 2H), 4.13 (brs, 2H), 4.91-5.03 (m, 2H), 5.33-5.54 (m, 3H) 5.99-6.16 (m, 1H), 6.46 (brs, NH), 7.45 (t, *J* = 6.3 Hz, 2H), 7.58 (t, *J* = 6.7 Hz, 1H), 8.1 (s, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 11.2, 18.1, 21.9, 61.1, 70.1, 70.6, 73.6, 75.1, 118.6, 128.3, 129.6, 129.7, 129.9, 133, 155.3, 156, 165.1; **HRMS (ESI, m/z):** calcd for $C_{22}H_{32}N_2O_7$ $[M+Na]^+$ 459.2107, found 459.2091. **HPLC**: Chiracel AS-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (major) 18.49 min and (minor) 28.39 min, ee 91%]; $[\alpha]^D_{25}$ -2.8 (c 2.2, $CHCl_3$).

Diisopropyl 1-((3R,4R,5S)-5-(benzoyloxy)-4-hydroxy-2-methylhept-6-en-3-yl)hydrazine-1,2-dicarboxylate (2c)

Yield: 83%; gum; **IR** ($CHCl_3$): 3306, 2962, 1267, 1105, 754 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.94 (d, *J* = 6.7 Hz, 3H), 1.11 (d, *J* = 3.4 Hz, 3H), 1.23-1.32 (m, 12H), 2.12-2.34 (m, 1H), 4-

4.11 (m, 1H), 4.26 (t, *J* = 4.5 Hz, 1H), 4.86-5.06 (m, 2H), 5.35-5.63 (m, 3H), 6.0-6.17 (m, 1H), 6.88 (brs, NH), 7.43 (t, *J* = 6.9 Hz, 2H), 7.56 (t, *J* = 6.9 Hz, 1H), 8.07 (d, *J* = 4.1 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 19.6, 22, 27.7, 29.6, 63.7, 70.3, 70.8, 71.8, 72.5, 119.4, 128.4, 129.7, 129.8, 130, 133.1, 156, 156.2, 165.3; **HRMS (ESI, m/z):** calcd for $C_{23}H_{34}N_2O_7$ $[M+Na]^+$ 473.2263, found 473.2253; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (major) 16.47 min and (minor) 19.82 min, ee 95%]; $[\alpha]^D_{25}$ +212.69 (c 0.54, $CHCl_3$).

Diisopropyl 1-((4R,5R,6S)-6-(benzoyloxy)-5-hydroxyoct-7-en-4-yl)hydrazine-1,2-dicarboxylate (2d):

Yield: 86%; viscous oil; **IR** ($CHCl_3$): 3316, 2983, 1705, 1267, 1106, 749 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.98 (t, *J* = 6.2 Hz, 3H), 1.28 (s, 12H), 1.6-1.87 (m, 4H), 4.14 (brs, 1H), 4.21 (brs, 1H), 4.92-5.0 (m, 2H), 5.30-5.57 (m, 3H), 5.99-6.16 (m, 1H), 6.69 (brs, NH), 7.44 (t, *J* = 6.8 Hz, 2H), 7.57 (t, *J* = 5.5 Hz, 1H), 8.09 (d, *J* = 5.9 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 13.6, 19.3, 21.7, 26.5, 58.5, 69.8, 70.3, 73.5, 74.9, 118.3, 128.1, 129.5, 132.8, 155.3, 156.7, 165.4; **HRMS (ESI, m/z):** calcd for $C_{23}H_{34}N_2O_7$ $[M+Na]^+$ 473.2258, found 473.2249; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (minor) 27.2 min and (minor) 30.607 min, ee 93%]; $[\alpha]^D_{25}$ +65.68 (c 1.94, $CHCl_3$).

Diisopropyl 1-((3R,4R,5S)-5-(benzoyloxy)-4-hydroxy-1-(methoxymethoxy)hept-6-en-3-yl)hydrazine-1,2-dicarboxylate (2e):

Yield: 87%; gum; **IR** ($CHCl_3$): 3405, 2982, 2938, 1706, 1379, 1231, 1103 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.26 (s, 12H), 2.0 (brs, 2H), 3.24 (s, 3H), 3.54 (brs, 2H), 4.14 (brs, 1H), 4.38 (brs, 1H), 4.49 (s, 2H), 4.87-4.99 (m, 2H), 5.32-5.53 (m, 3H), 6.0-6.17 (m, 1H), 6.87 (brs, NH),

7.44 (t, *J* = 6.9 Hz, 2H), 7.54 (t, *J* = 7.1 Hz, 1H), 8.1 (d, *J* = 6.2 Hz, 2H) **^{13}C NMR** (50 MHz, CDCl3): δ 21.8, 30.6, 54.8, 57.5, 65.2, 69.9, 70.4, 73.6, 74.7, 118.3, 128.2, 129.6, 132.9, 155.4, 165; **HRMS (ESI, m/z):** calcd for $C_{24}H_{36}N_2O_9$ $[M+Na]^+$ 519.2318, found 519.2316; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time :(major) 24.01 min and (minor) 29.12 min, ee 93%]; $[\alpha]^D_{25}$ -6.61 (c 0.66, $CHCl_3$).

Di-tert-butyl 1-((3R,4R,5S)-5-(benzoyloxy)-1-(benzyloxy)-4-hydroxyhept-6-en-3-yl)hydrazine-1,2-dicarboxylate (2f):

Yield: 84%; gum; **IR** ($CHCl_3$): 3364, 2980, 1707, 1269, 1216, 749, 711 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.48 (s, 18H), 2.05 (brs, 2H), 3.61 (brs, 2H), 4.17 (brs, 1H), 4.42 (s, 2H), 4.51 (s, 1H), 5.31-5.54 (m, 3H), 6.02-6.18 (m, 1H), 6.81 (brs, NH), 7.27 (s, 5H), 7.44 (t, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 8.11 (d, *J* = 7.3 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 28.1, 29.6, 57.9, 68.1, 73.1, 73.7, 74.9, 81.1, 81.9, 118.3, 127.5, 128.3, 129.7, 129.8, 130.1, 132.9, 133.1, 137.9, 154.9, 165.2; **HRMS (ESI, m/z):** calcd for $C_{31}H_{42}N_2O_8$ $[M+Na]^+$ 593.2838, found 593.2841; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time : (minor) 22.79 min and (major) 26.14 min, ee 93%]; $[\alpha]^D_{25}$ -5.88 (c 0.76, $CHCl_3$).

Diisopropyl 1-((3S,4R,5R)-3-(benzoyloxy)-4-hydroxynona-1,8-dien-5-yl)hydrazine-1,2-dicarboxylate (2g):

Yield: 82%; gum; **IR** ($CHCl_3$): 3305, 2981, 2923, 1704, 1267, 1105, 754 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.26 (s, 12H), 1.69-2.15 (m, 4H), 4.14 (brs, 1H), 4.22 (brs, 1H), 4.81-5.03 (m, 4H), 5.32-5.48 (m, 3H), 5.65-5.82 (m, 1H), 5.98-6.15 (m, 1H), 6.71 (brs, NH), 7.44 (t, *J* = 7.7 Hz 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 8.09 (d, *J* = 6.7 Hz, 2H), **^{13}C NMR** (50 MHz, $CDCl_3$): δ 22, 29.7,

30.6, 58.5, 70.2, 70.7, 73.8, 74.4, 115.3, 118.7, 128.3, 129.8, 133.1, 137.5, 155.4, 155.8, 165.5; **HRMS (ESI, m/z):** calcd for $C_{24}H_{34}N_2O_7$ $[M+Na]^+$ 485.2264, found 485.2267; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time : (major) 12.530 min and (minor) 15.123 min, ee 95%]; $[\alpha]^D_{25}$ +133.85 (c 0.84, $CHCl_3$).

Di-tert-butyl 1-((2R,3R,4S)-4-(benzoyloxy)-3-hydroxy-1-phenylhex-5-en-2-yl)hydrazine-1,2-dicarboxylate (2h):

Yield: 84%; gum; **IR** ($CHCl_3$): 3323, 2981, 1704, 1267, 1109, 842, 741 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.26-1.48 (m, 18H), 3.05 (brs, 2H), 4.35 (t, *J* = 7.9 Hz, 1H), 4.63 (brs, 1H), 5.32-5.64 (m, 3H), 6.04-6.21 (m, 1H), 7.11-7.26 (m, 5H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.54 (d, *J* = 6.9 Hz 1H,), 8.12 (t, *J* = 6.3 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 28.1, 30.6, 60.5, 74.4, 74.8, 81.6, 82.1, 118.2, 126.4, 128.4, 128.6, 129.7, 130.1, 133, 134.1, 138.7, 154.7, 165.3; **HRMS (ESI, m/z):** calcd for $C_{29}H_{38}N_2O_7$ $[M+Na]^+$ 549.2577, found 549.2579; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (major) 21.64 min and (minor) 32.11 min, ee 97%]; $[\alpha]^D_{25}$ +130.4 (c 0.86, $CHCl_3$).

Di-tert-butyl 1-((2R,3R,4S)-4-(benzoyloxy)-3-hydroxy-1-(4-methoxyphenyl)hex-5-en-2-yl)hydrazine-1,2-dicarboxylate (2i):

Yield: 81%; gum; **IR** (CHCl3): 3364, 2981, 2922, 1708, 1351, 1263, 1105, 833, 711 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.34-1.47 (s, 18H), 2.97 (brs, 2H), 3.74 (s, 3H), 4.26 (brs, 1H), 4.38 (brs, 1H), 5.34 (t, *J* = 8.5 Hz, 1H), 5.45 (dd, *J* = 5.4, 11.6 Hz, 1H), 5.6 (t, *J* = 5.4 Hz, 1H), 6.03-6.15 (m, 1H), 6.36 (brs, NH), 6.75 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.57 (q, *J* = 7.6 Hz, 1H), 8.11 (dd, *J* = 7.1, 12.5 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 28.2, 29.7, 55.1, 59.6, 74.4, 74.8, 81.4, 82.1, 114.1, 118.2, 128.3, 128.4, 129.3, 129.8, 130.1,

133.3, 134.2, 165.1, 165.3, 170.1; **HRMS (ESI, m/z):** calcd for $C_{30}H_{40}N_2O_8$ $[M+H]^+$ 557.2862, found 557.2875; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (major) 26.608 min and (minor) 43.61 min, ee 99%]; $[\alpha]^{D}_{25}$ +288.75 (c 0.4, $CHCl_3$).

Experimental procedure for the preparation of diisopropyl 1-((2R,3R,4S)-4-(benzoyloxy)-3,6-dihydroxyhexan-2-yl)hydrazine-1,2-dicarboxylate (3).

Aminodiol **1a** (0.22 g; 0.5 mmol) was added dropwise to a solution of BH_3.DMS (0.023 mL, 0.025 mmol) in dry THF (10 mL) at room temperature and then mixture was stirred for 3 h. The reaction flask was cooled at 0 °C and NaOH (0.02 g; 0.5 mmol) in ethanol (2 mL) was added to the reaction mixture followed by 30% H_2O_2 (0.06 mL, 0.7 mmol). It was then allowed to stir at rt for 2 h and the product was extracted with ethyl acetate washed with brine, dried over Na_2SO_4 and concentrated in vacuum. Purification by column chromatography over silica gel using petroleum ether and ethyl acetate as eluents (4:1) gave **3** as a colorless oil.

Yield: 75%; colorless oil; **IR** ($CHCl_3$): 3372, 2091, 1706, 1671, 1511, 1363, 711 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.11-1.20 (m, 15H), 1.91-2.15 (m, 2H), 2.67 (brs, OH), 3.39 (brs, OH), 3.52-3.70 (m, 2H), 4.04 (brs, 1H), 4.30 (brs, 1H), 4.84-4.89 (m, 2H), 5.04 (t, *J* = 4.4 Hz, 1H), 7.03 (brs, NH), 7.36 (t, *J* = 7.8 Hz, 2H), 7.49 (t, *J* = 6.8 Hz, 1H), 7.98 (d, *J* = 6.8 Hz, 2H); **^{13}C NMR** (50 MHz, CDCl3): δ 9.9, 21.9, 34.4, 54.5, 58.3, 70.1, 72.4, 73.8, 128.3, 129.7, 133.1, 155.2, 166.4; **HRMS (ESI, m/z):** calcd for $C_{17}H_{25}N_2O_8$ $[M+H]^+$ 441.2237, found 441.2238; $[\alpha]^{D}_{25}$ +32.9 (c 0.21, $CHCl_3$).

Experimental procedure for the preparation of (3S,4R,5R)-5-((tert-butoxycarbonyl)amino)-4-hydroxyhexan-3-yl benzoate (4).

The solution of vicinal amino diol **1c** (1g, 1.9 mmol) in MeOH (20 mL) was treated with Raney Ni (0.5 g, excess) under H_2 atmosphere (80 psig) for 24 h. The reaction mixture was filtered over celite and concentrated to give crude product**,** which was dissolved in CH_2Cl_2 (15 mL) and added NEt_3 (0.26 mL, 1.9 mmol) followed by Boc_2O (0.42 g, 1.9 mmol) and reaction mixture was stirred for 1 h at room temperature. After completion of reaction was quenched with water and extracted with CH_2Cl_2 (3 X 15 mL) and concentrate to give crude product which was purified by flash column chromatography (100-200 mesh) using petroleum ether and ethyl acetate (4:1) as eluents to afford the pure product **4**.

Yield: 89%; gum; **IR** ($CHCl_3$): 3335, 2918, 1734, 1695, 749 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.98 (t, *J* = 7.3 Hz, 3H), 1.17 (d, *J* = 6.8 Hz, 2H), 1.45 (s, 9H), 1.70 (brs, 1H), 1.78-1.85 (m, 1H), 1.93-1.99 (m, 1H), 3.87 (brs, 1H), 4.78-4.83 (m, 1H), 5.09-5.15 (m, 1H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.7 Hz, 1H), 8.05-8.07 (dd, *J* = 1.3, 8.2 Hz, 2H); **^{13}C NMR** (50 MHz, CDCl3): δ 9.6, 15.7, 23.7, 28.4, 48.4, 75.1, 76.2, 79.6, 128.5, 129.7, 133.1, 155.8, 166.3; **HRMS (ESI, m/z):** calcd for $C_{18}H_{27}NO_5$ $[M+Na]^+$ 360.1786, found 360.1792; $[\alpha]^{25}_D$ +29.1 (c 1.0 in $CHCl_3$).

Dibenzyl 1-((2S,3S,4R)-4-(benzoyloxy)-1-(benzyloxy)-3-hydroxyhex-5-en-2-yl)hydrazine-1,2-dicarboxylate (*ent*-2j):

Yield: 85%; gum; **IR** ($CHCl_3$): 3309, 2979, 1706, 1262, 752 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 3.81 (brs, 2H), 4.36 (s, 2H), 4.42 (brs, 1H), 4.57 (brs, 1H), 5.13 (s, 4H), 5.29-5.39 (m, 2H), 5.52 (brs, 1H), 5.94-6.08 (m, 1H), 6.79 (brs, NH), 7.19-7.28 (m, 15H), 7.41 (d, *J* = 7.3 Hz, 2H), 7.52 (s, 1H), 8.06 (d, *J* = 6.8 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 58.6, 67.9, 68.2, 68.7, 73.1, 74.7, 75.6, 118.7, 127.7, 127.8, 128.2, 128.4, 128.4, 128.5, 129.8, 133.1, 135.4, 135.7, 137.5, 155.6, 165.3; **HRMS (ESI, m/z):** calcd for $C_{36}H_{36}N_2O_8$ $[M+H]^+$ 625.255, found

625.2517; **HPLC**: [Chiralpack AD-H, 2-Propanol/n-Hexane = 10/90, flow rate 0.5 mL/min, λ = 220 nm, retention time: (major) 86.00 min and (minor) 93.6 min, ee 93%]; $[\alpha]^{D}_{25}$ +288.75 (c 0.4, $CHCl_3$).

Experimental procedure for the preparation of Benzyl ((4S,5S)-4-((benzyloxy)methyl)-5-((R)-1-hydroxyallyl)-2-oxooxazolidin-3-yl)carbamate (5).

To a solution of vicinal amino diol ***ent*-2j** (2 g, 3.6 mmol) in MeOH (20 ml) at room temperature was added $LiOH.H_2O$ (296 mg, 7.2 mmol) and the reaction mixture was stirred for 3 h. After completion of the reaction, it was diluted with water and the mixture was concentrated in vacuum to remove MeOH and the concentrate was extracted with ethyl acetate (3 × 40 ml). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give crude product, which was then purified by flash column chromatography using petroleum ether: ethyl acetate (2:3) to afford pure oxazolidinone **5.**

Yield: 71%; gum; **IR** (CHCl3): 3368, 2084, 1707, 1675, 1261, 750 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 3.72 (q, *J* = 9.6 Hz, 2H), 4.08 (brs, 1H), 4.33 (s, 1H), 4.48 (t, *J* = 6.9 Hz 1H,), 5.07 (s, 2H), 5.2 (d, *J* = 10.5 Hz, 1H), 5.35 (d, *J* = 17.4 Hz, 1H), 5.84-5.92 (m, 1H), 7.23-7.3 (m, 9H), 7.44 (t, *J* = 9.1 Hz, 1H); **^{13}C NMR** (50 MHz, CDCl3): δ 58.4, 64.5, 67.7, 69.4, 71.1, 73.3, 117.3, 127.5, 127.7, 128, 128.1, 128.2, 128.4, 128.5, 135.2, 135.7, 136.6, 155.5, 156.6; **HRMS (ESI, m/z):** calcd for $C_{22}H_{24}N_2O_6$ $[M+H]^+$ 413.1712, found 413.1792; $[\alpha]^{D}_{25}$ -88.96 (c 4.46, $CHCl_3$).

Experimental procedure for the preparation of benzyl ((4S,5S)-4-((benzyloxy)methyl)-5-((R,E)-1-hydroxypentadec-2-en-1-yl)-2-oxooxazolidin-3-yl)carbamate (6)

To a solution of oxazolidinone **5** (1.3 g, 3.16 mmol) in 20 ml of dry CH_2Cl_2 was added Grubbs^{IInd} generation catalyst (5 mol%, 15 mg) followed by tetradecene (2.1 g, 10.8 mmol) and the resulting mixture was heated at reflux for 6 h. After completion of the reaction, it was concentrated to give the crude product, which was then purified by flash column chromatography (100-200 mesh) using petroleum ether and ethyl acetate (7:3) as eluents to afford the pure product **6**.

Yield: 81%; gum; **IR** (CHCl3): 3368, 2084, 1708, 1671, 1352, 642 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.26 (s, 20 H), 2.03 (q, *J* = 7 Hz, 2H), 2.9 (brs, OH), 3.69-3.79 (m, 2H), 4.09 (brs, 1H), 4.31 (brs, 1H), 4.42 (brs, 1H), 4.51 (q, *J* = 11.6 Hz, 2H), 5.11 (q, *J* = 12.2 Hz, 2H), 5.49 (dd, *J* = 5.8, 9.7 Hz, 1H) 5.78 (m, 1H), 6.89 (brs,NH), 7.25-7.33 (m, 10H); **^{13}C NMR** (50 MHz, CDCl3): δ 14.1, 22.7, 28.9, 29.2, 29.4, 29.5, 29.6, 29.7, 31.9, 32.3, 58.6, 64.5, 67.9, 69.6, 73.6, 77.8, 127.4, 128, 128.2, 128.3, 128.4, 128.5, 128.7, 135.3, 136.3, 155.4, 156.5; **HRMS (ESI, m/z):** calcd for $C_{34}H_{48}N_2O_6$ $[M+Na]^+$ 581.3591, found 581.3573; $[\alpha]^D_{25}$ -232.9 (c 0.34, $CHCl_3$).

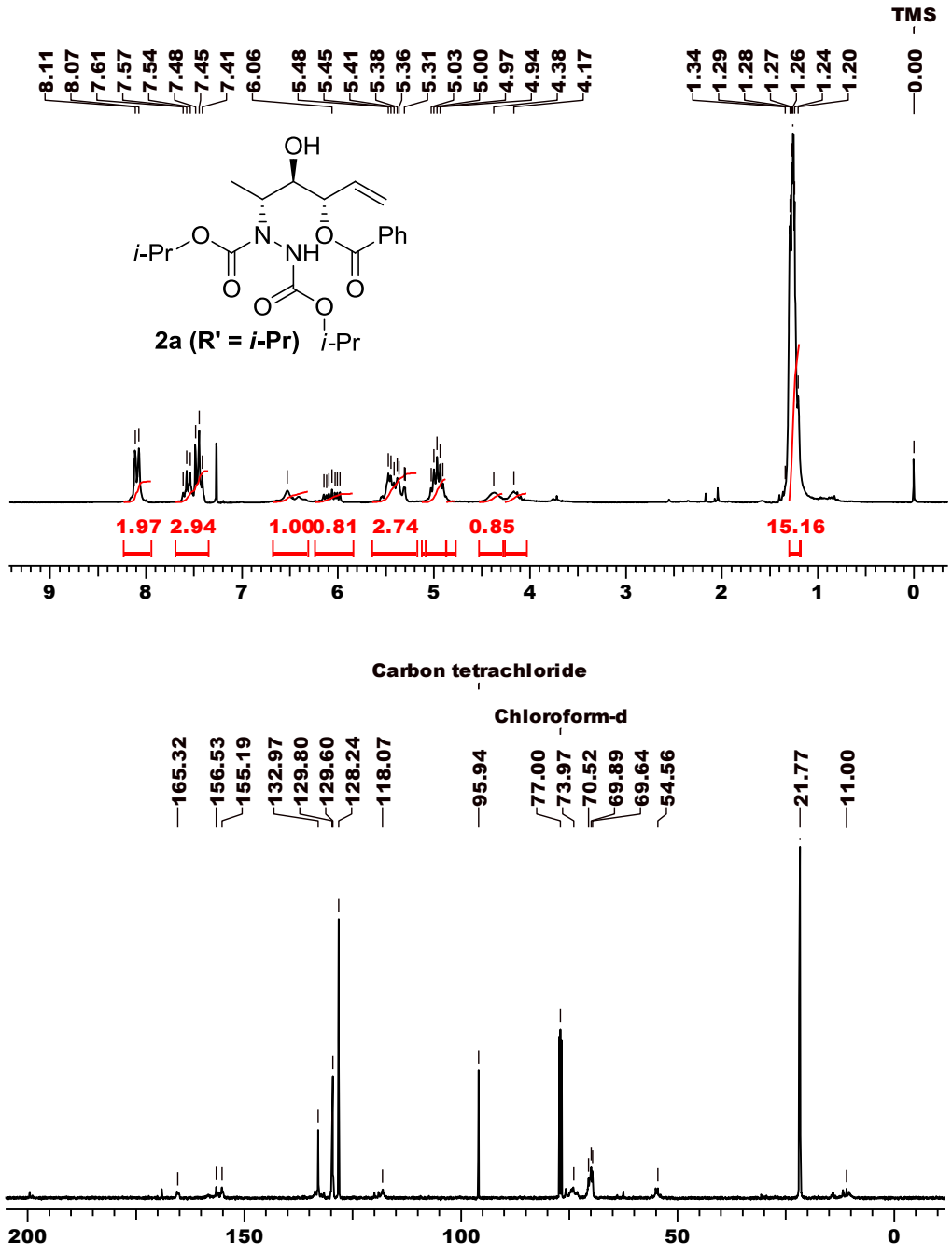
Experimental procedure for the preparation of D-*ribo*-phytosphingosine tetraacetate (7).

A solution of olefin **6** (1 g, 1.7 mmol) in MeOH (20 mL) was treated with Raney Ni (0.5 g, excess) under H_2 atmosphere (80 psig) for 24 h. The reaction mixture was filtered over celite to give crude product**,** in which was added K_2CO_3 (248 mg, 1.8 mmol) and the reaction mixture was stirred for 6 h until consumption of the starting material and methanol was removed in vacuum. H_2O was added to the crude product and extracted with ethyl acetate (3 X 10 mL), dried over Na_2SO_4 and concentrated. The crude material was subsequently acetylated with acetic anhydride (0.72 mL, 7.65 mmol), pyridine (0.62 mL, 7.65 mmol) and DMAP (cat). After

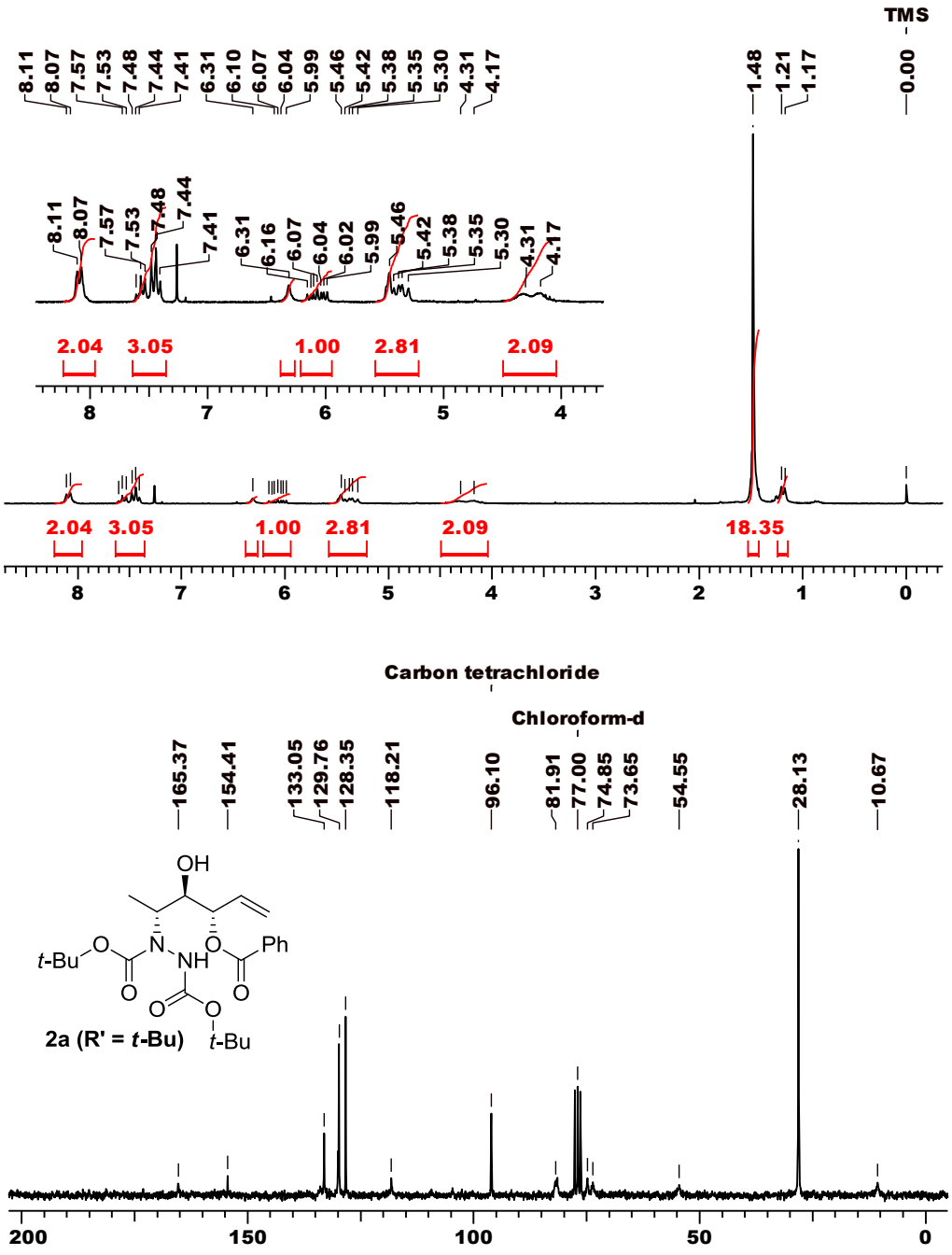
overnight stirring, the solvent was evaporated and the residue was purified on a silica gel column using petroleum ether and ethyl acetate (5 : 1) as eluent to give tetraacetate **7** as a white solid. Spectroscopic data of tetraacetate are in full agreement with those reported in literature.

Yield: 76%; white solid; **mp**: 45-46 ^{o}C; **IR** (CHCl3): 2920, 1734, 1685, 749 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.88 (t, *J* = 7 Hz, 3H), 1.25 (brs, 24 H), 1.6-1.69 (m, 2H), 2.02 (s, 3H), 2.04 (s, 6H), 2.08 (s, 2H), 3.98 (dd, *J* = 2.9, 11.7 Hz, 1H), 4.29 (dd, *J* = 4.7, 11.6, Hz, 1H), 4.42-4.48 (m, 1H), 4.92 (dt, *J* = 3.1, 9.7 Hz, 1H), 5.09 (dd, *J* = 3.1, 8.3 Hz, 1H), 6.01 (d, *J* = 9.3 Hz, NH); **^{13}C NMR** (50 MHz, CDCl3): δ 14.1, 20.7, 20.8, 21.0, 22.7, 23.2, 25.5, 28.1, 29.3, 29.4, 29.5, 29.6, 29.6, 29.6, 29.7, 31.9, 47.6, 62.8, 71.9, 73.0, 169.5, 169.9, 170.7, 171.0; **HRMS (ESI, m/z):** calcd for $C_{26}H_{47}NO_7$ $[M+H]^+$ 486.3431, found 486.3435; $[\alpha]^{D}_{25}$ +20.1 (c 1.0 in $CHCl_3$); {lit. $[\alpha]^{25}_{D}$ +20.9 (c 1.1 in $CHCl_3$)}.

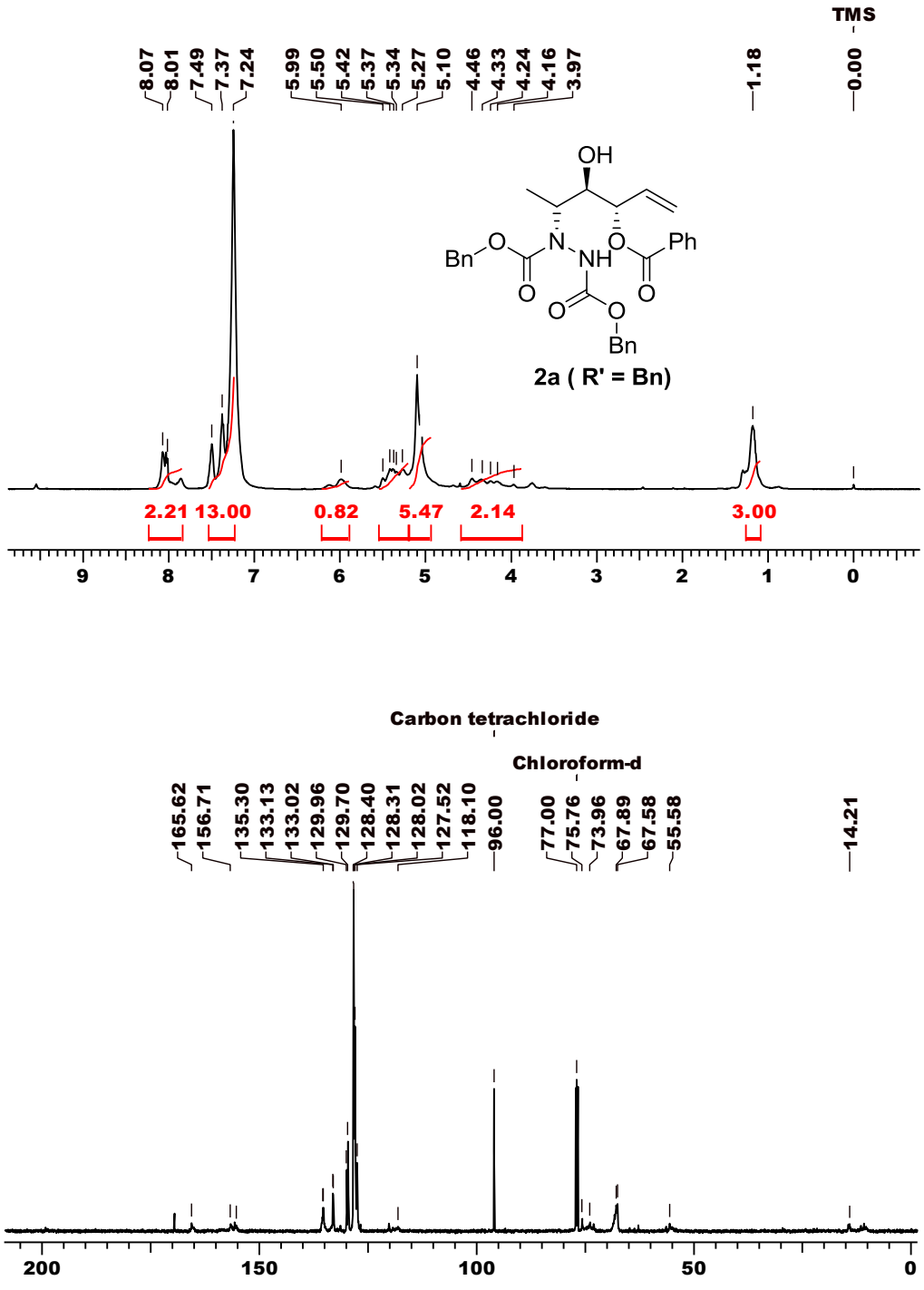
^{1}H and ^{13}C NMR spectra of new compounds



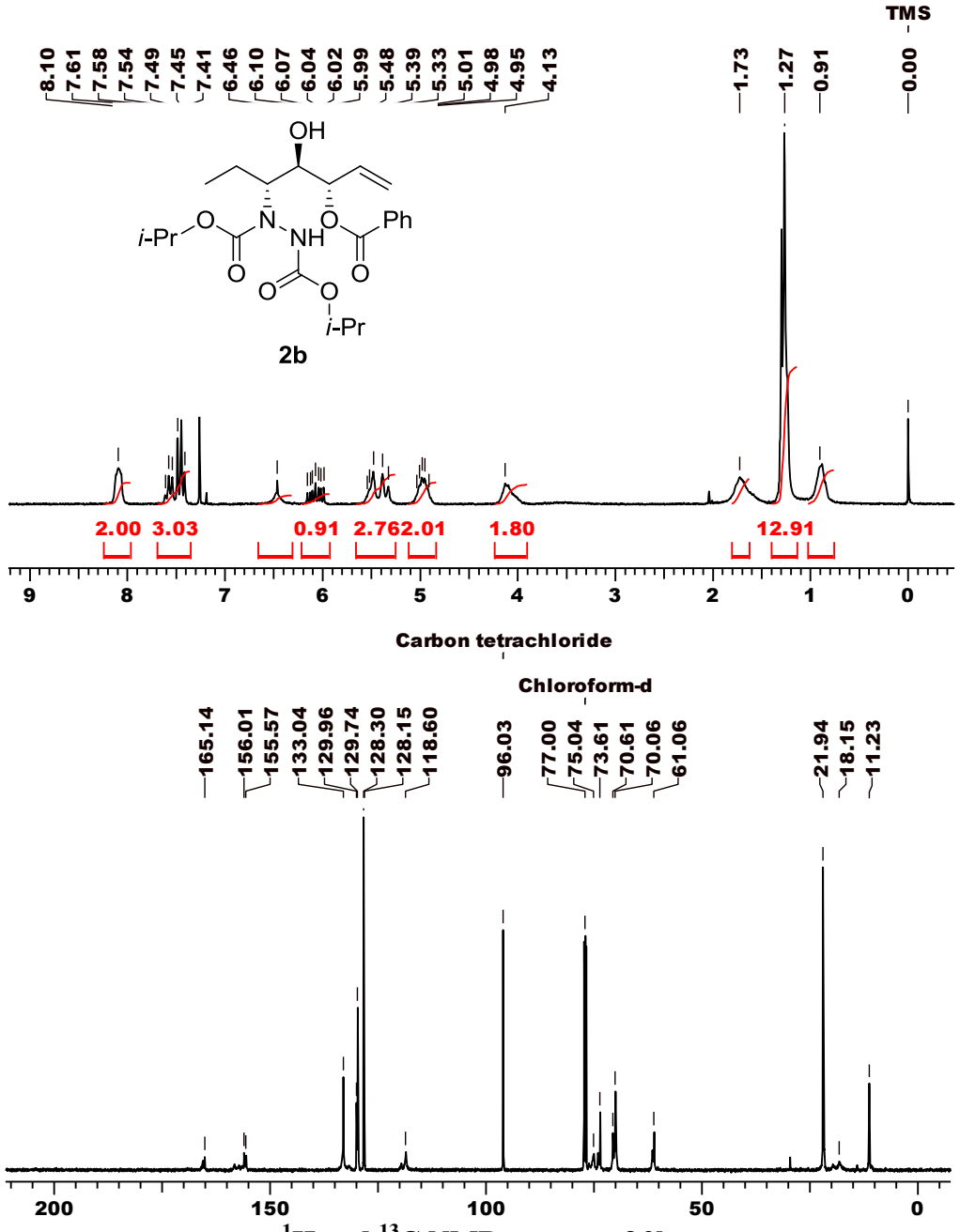
^{1}H and ^{13}C NMR spectra of 2a (R' = *i*-Pr)



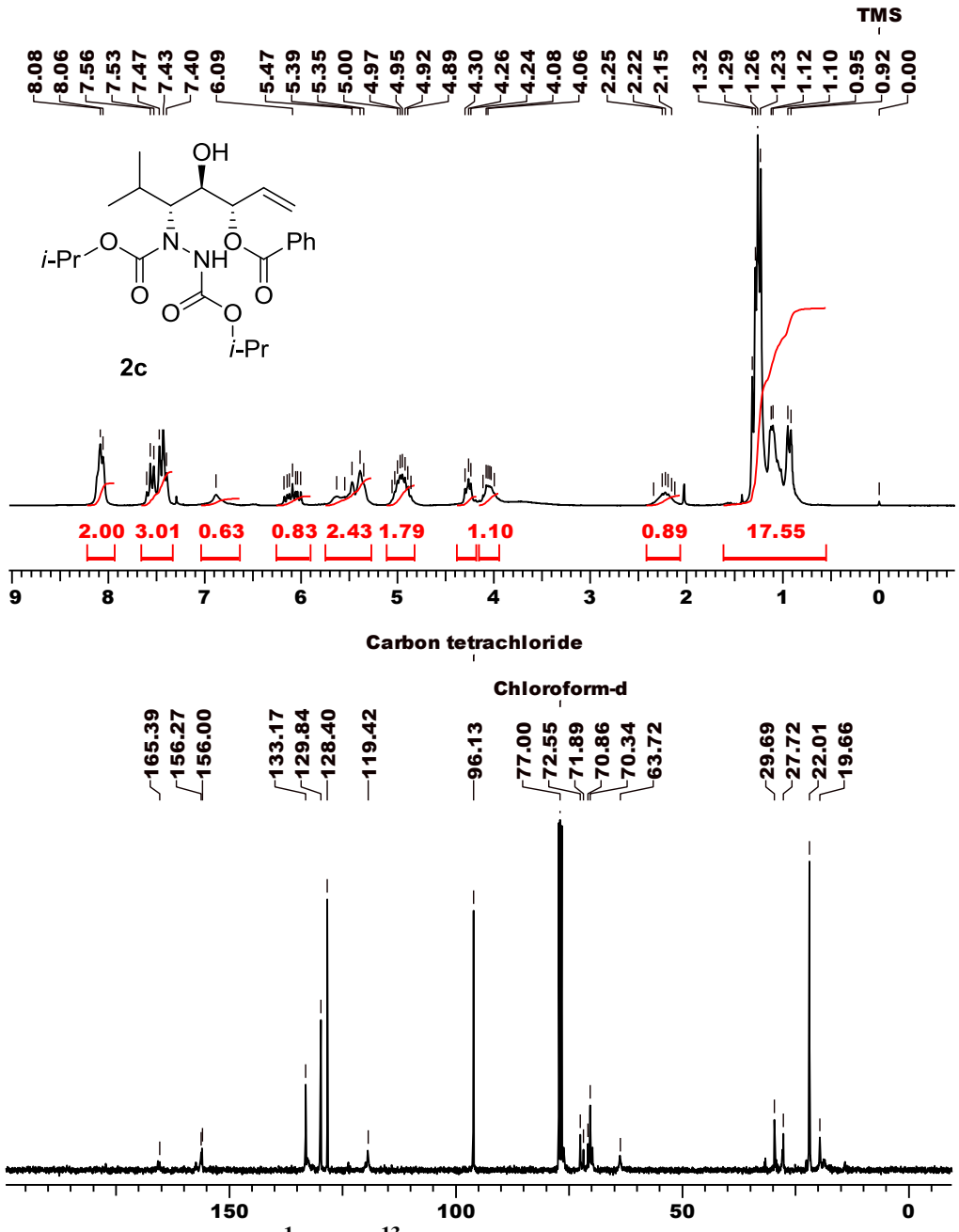
^{1}H and ^{13}C NMR spectra of 2a (R' = *t*-Bu)



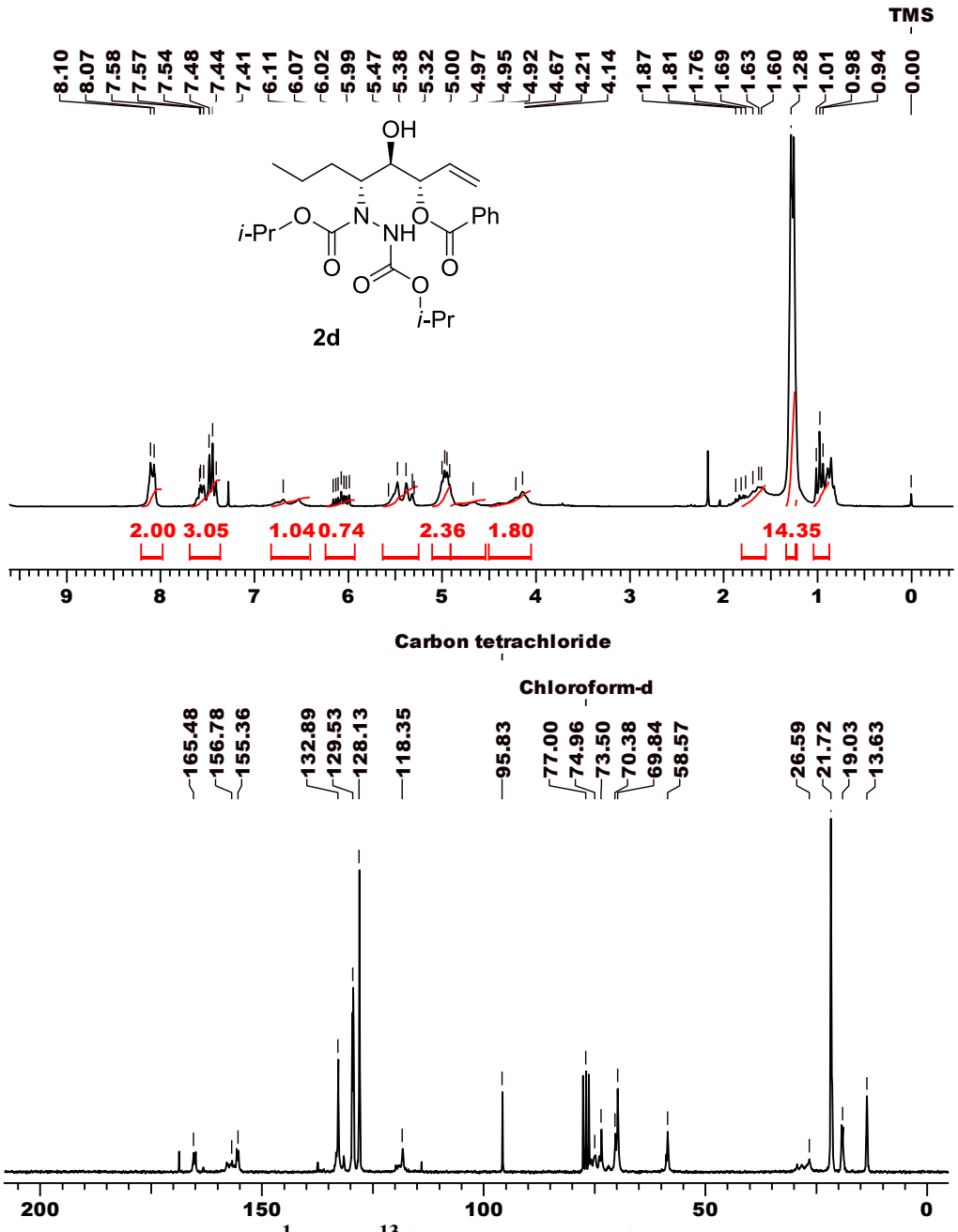
^{1}H and ^{13}C NMR spectra of 2a (R' = Bn)



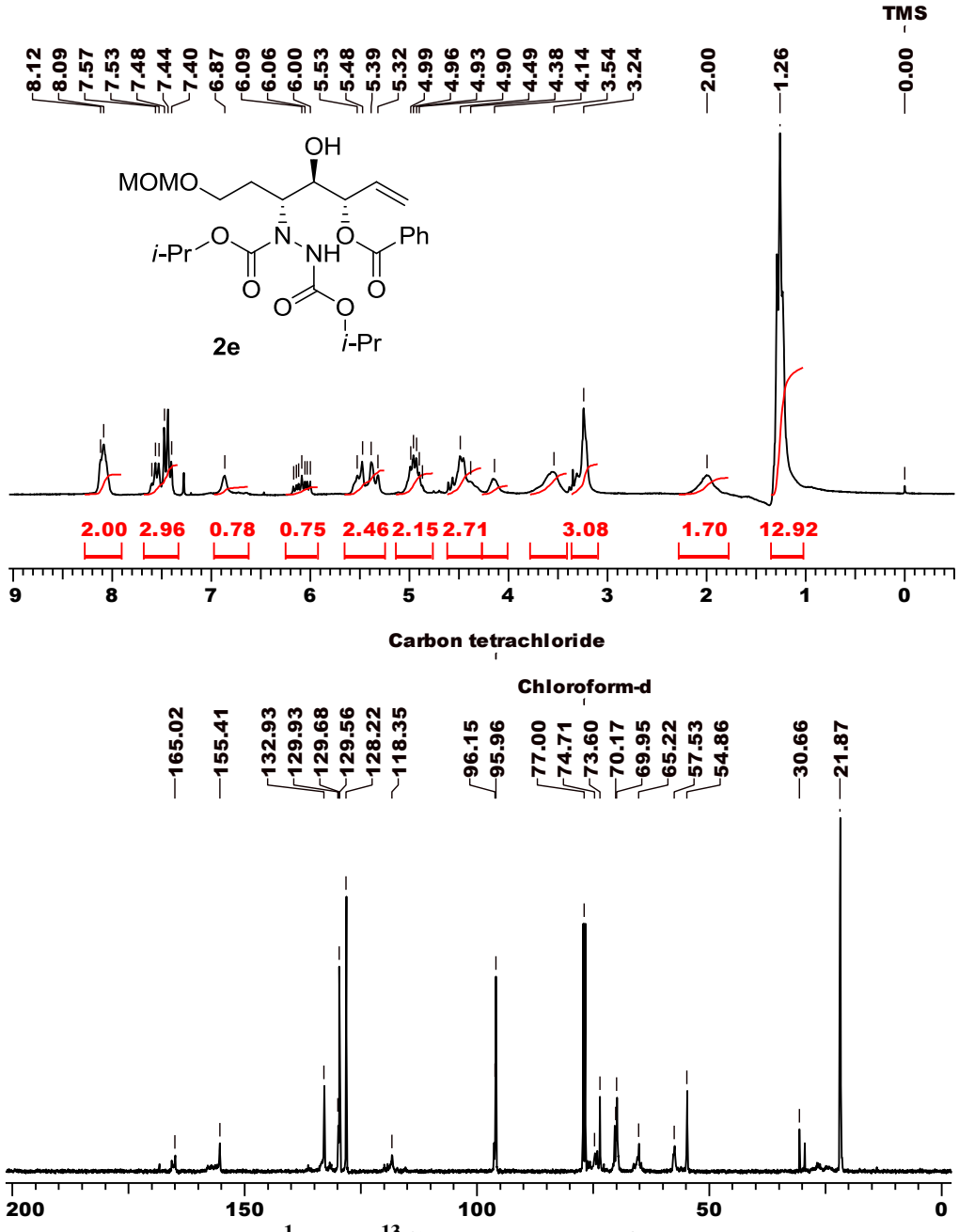
^{1}H and ^{13}C NMR spectra of 2b



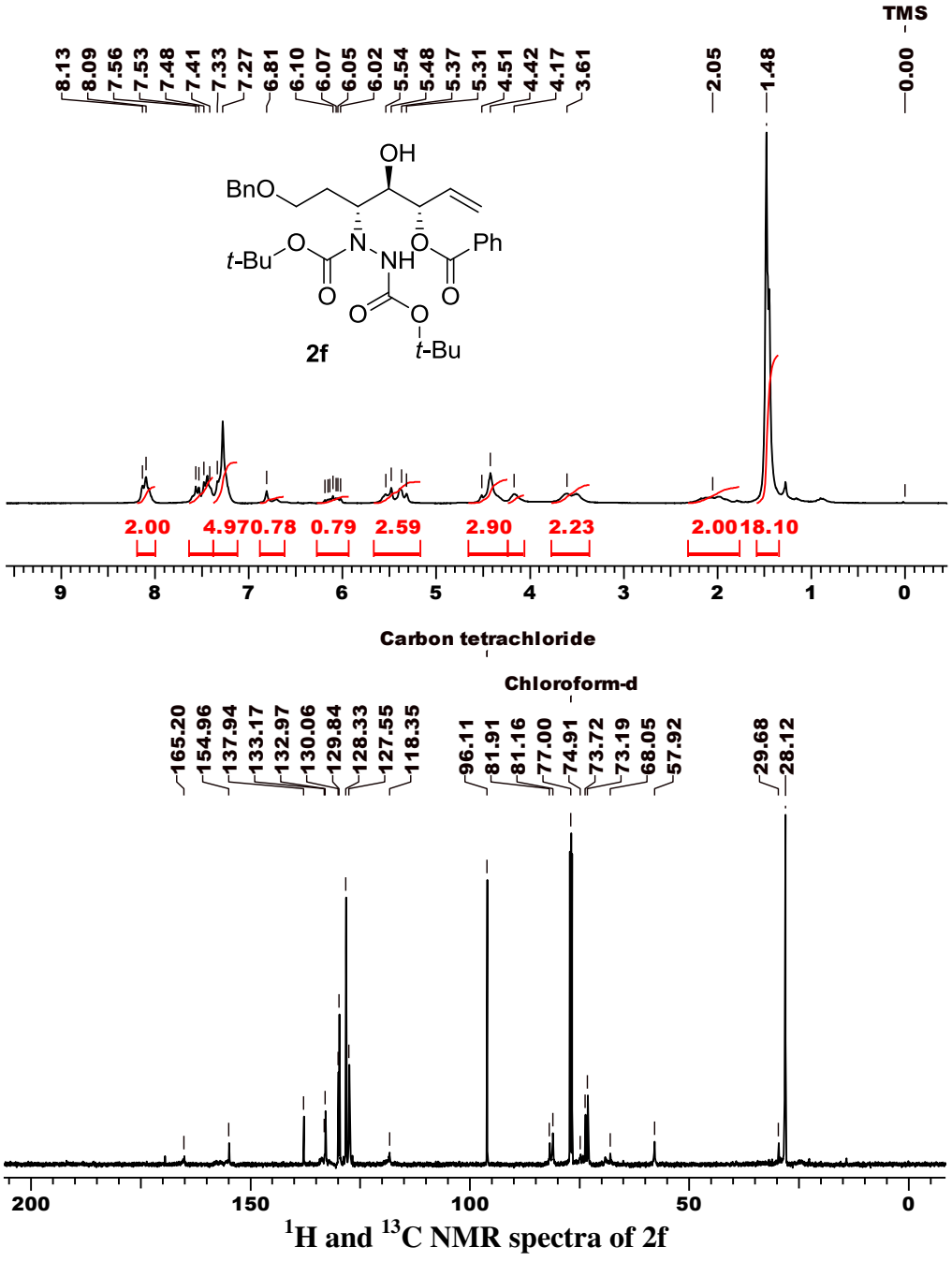
^{1}H and ^{13}C NMR spectra of 2c



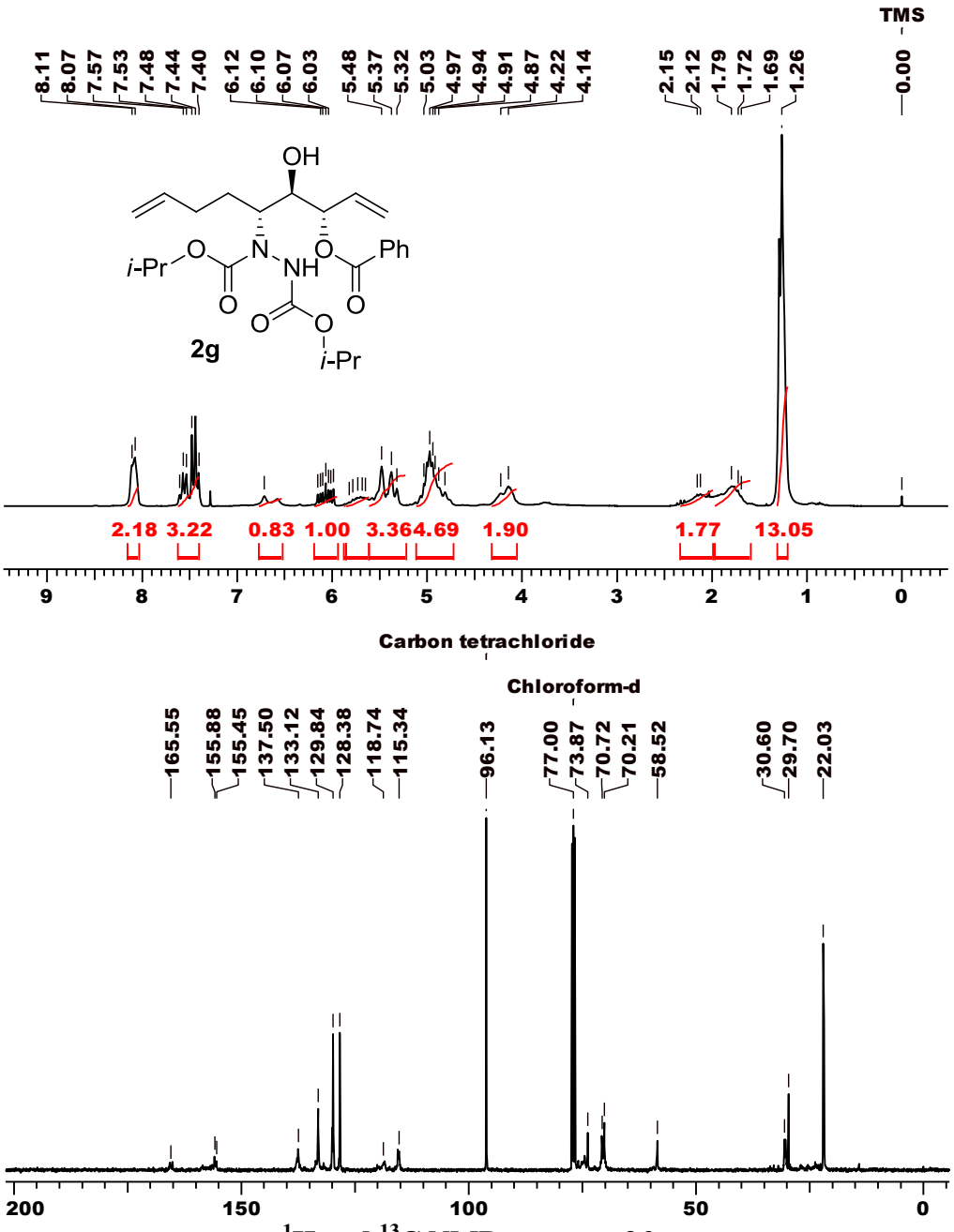
^{1}H and ^{13}C NMR spectra of 2d



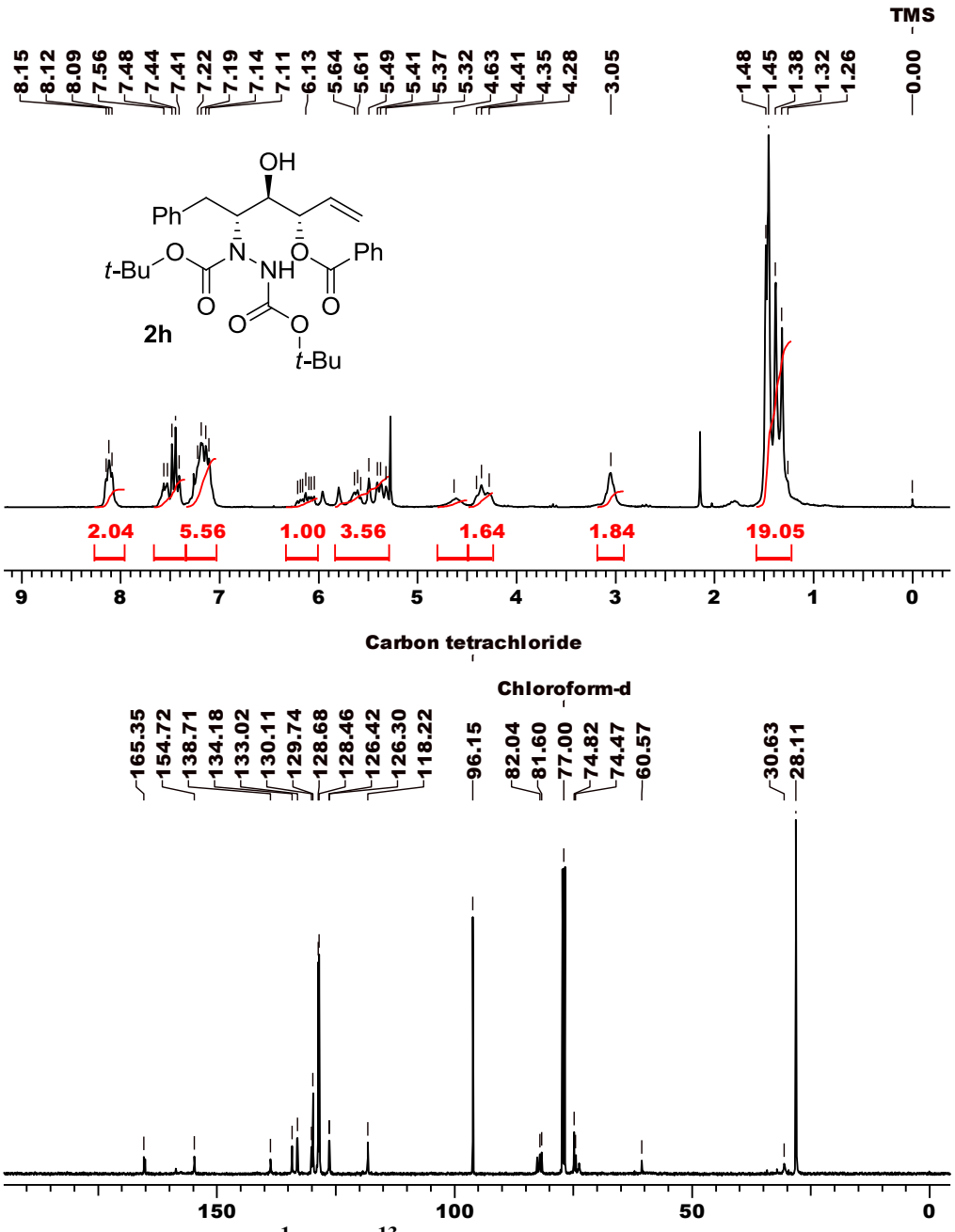
^{1}H and ^{13}C NMR spectra of 2e



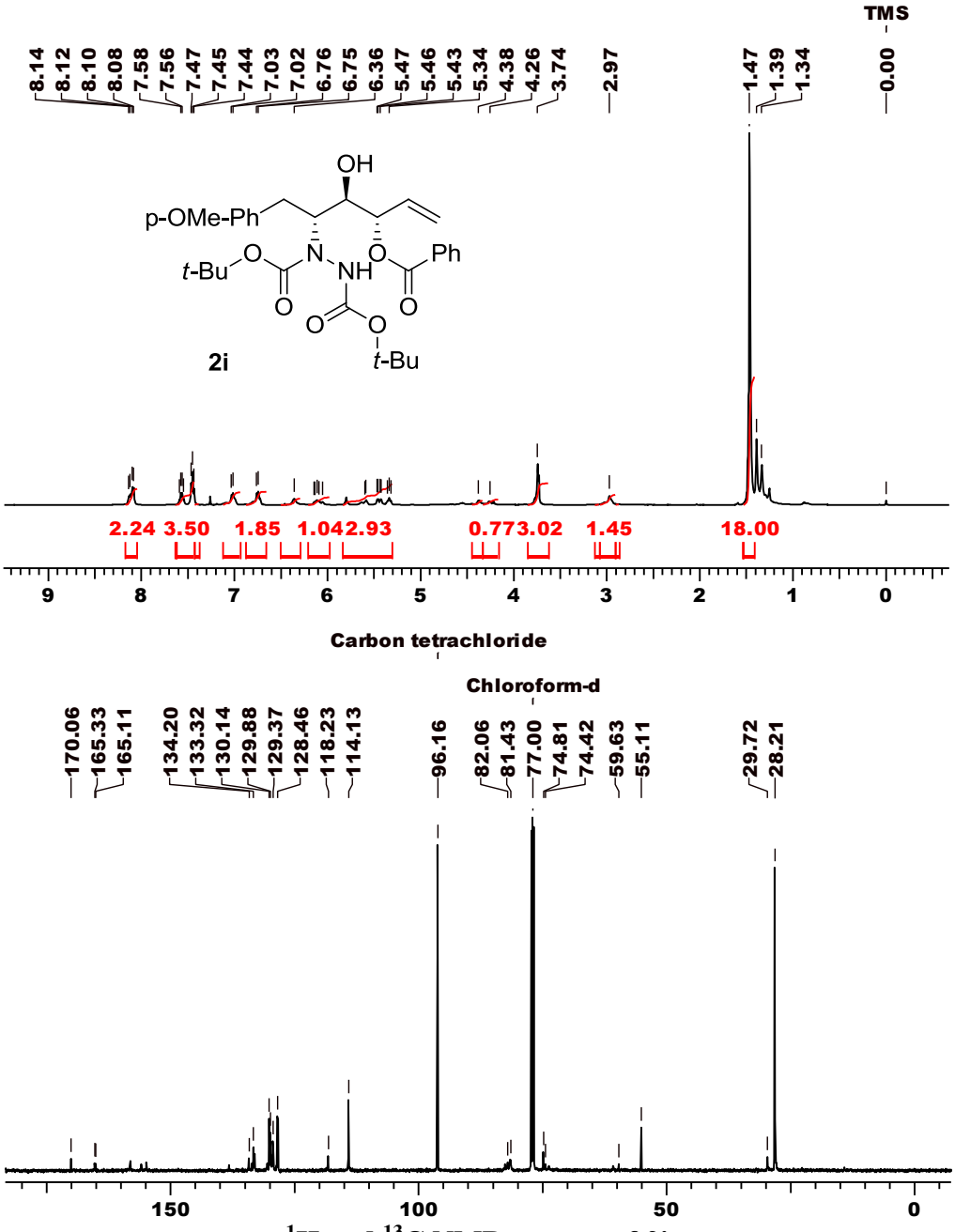
^{1}H and ^{13}C NMR spectra of 2f



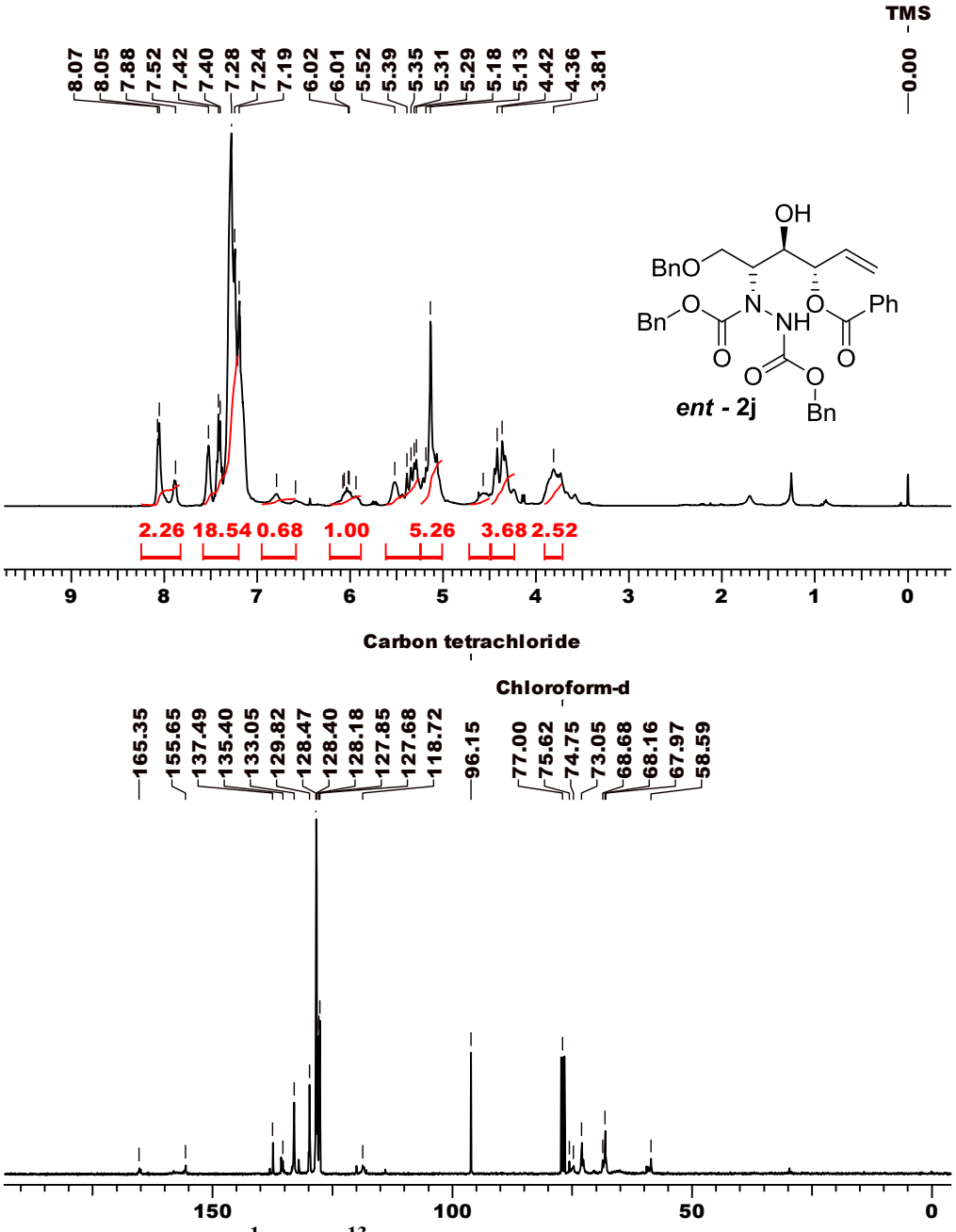
^{1}H and ^{13}C NMR spectra of 2g



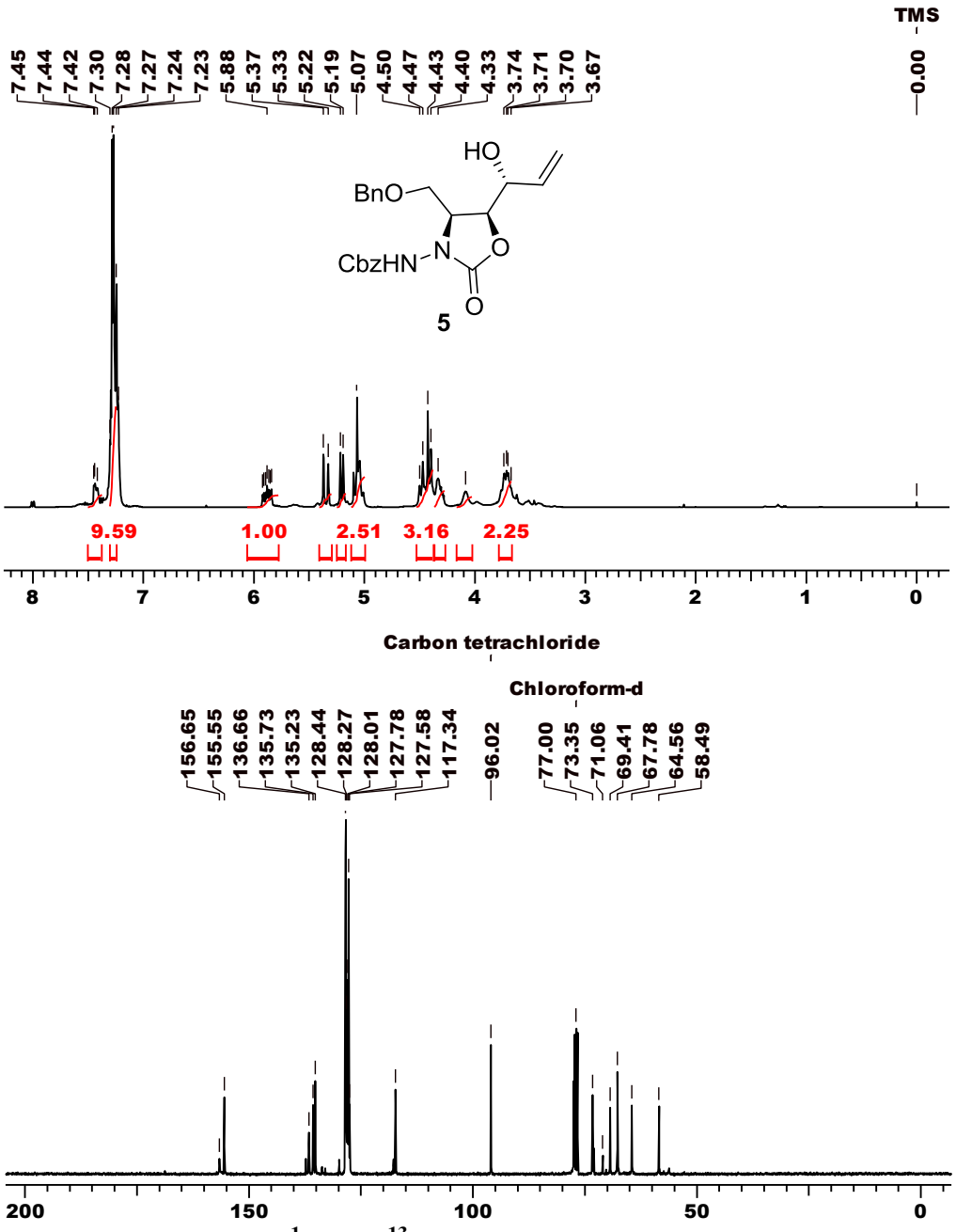
^{1}H and ^{13}C NMR spectra of 2h



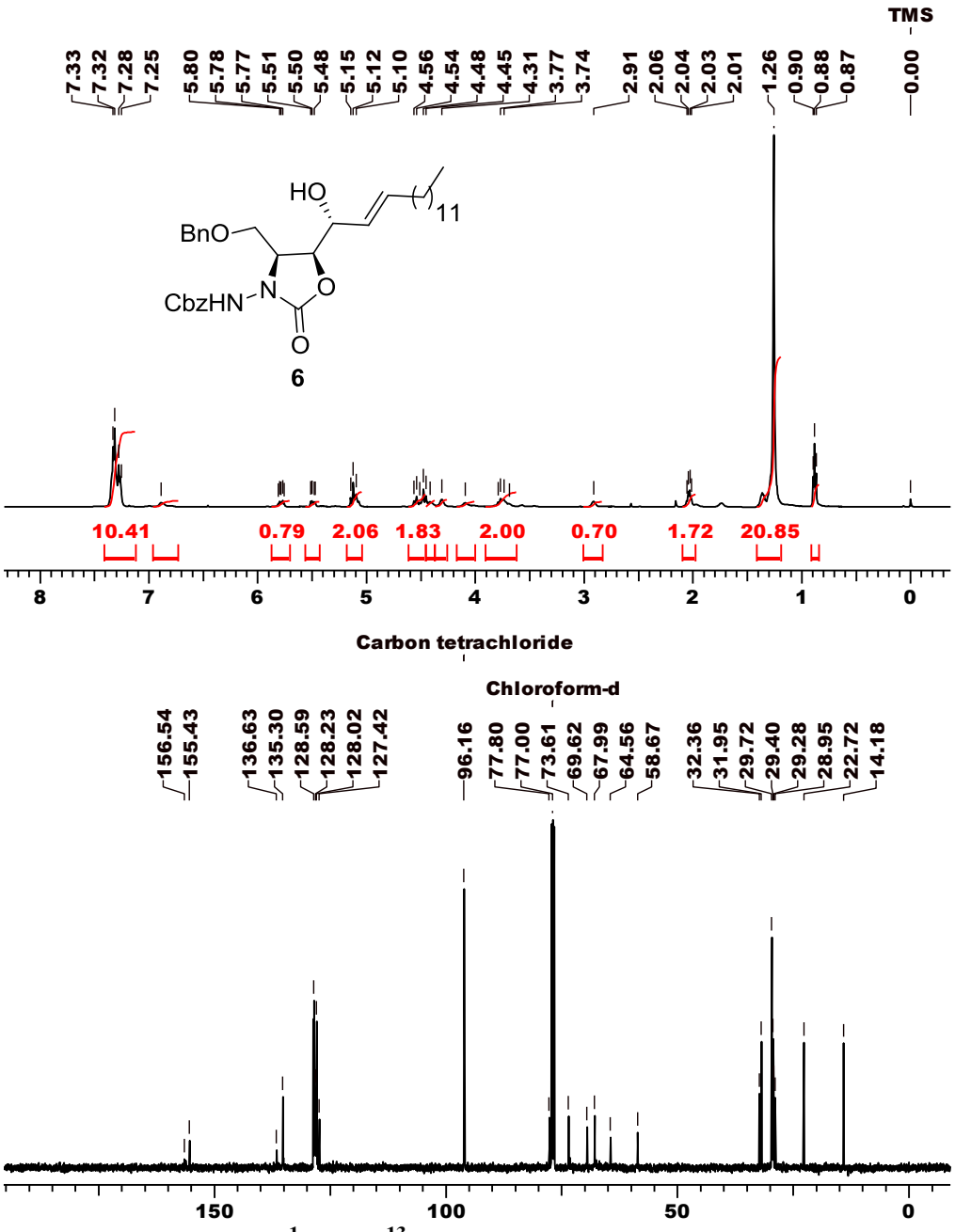
^{1}H and ^{13}C NMR spectra of 2i



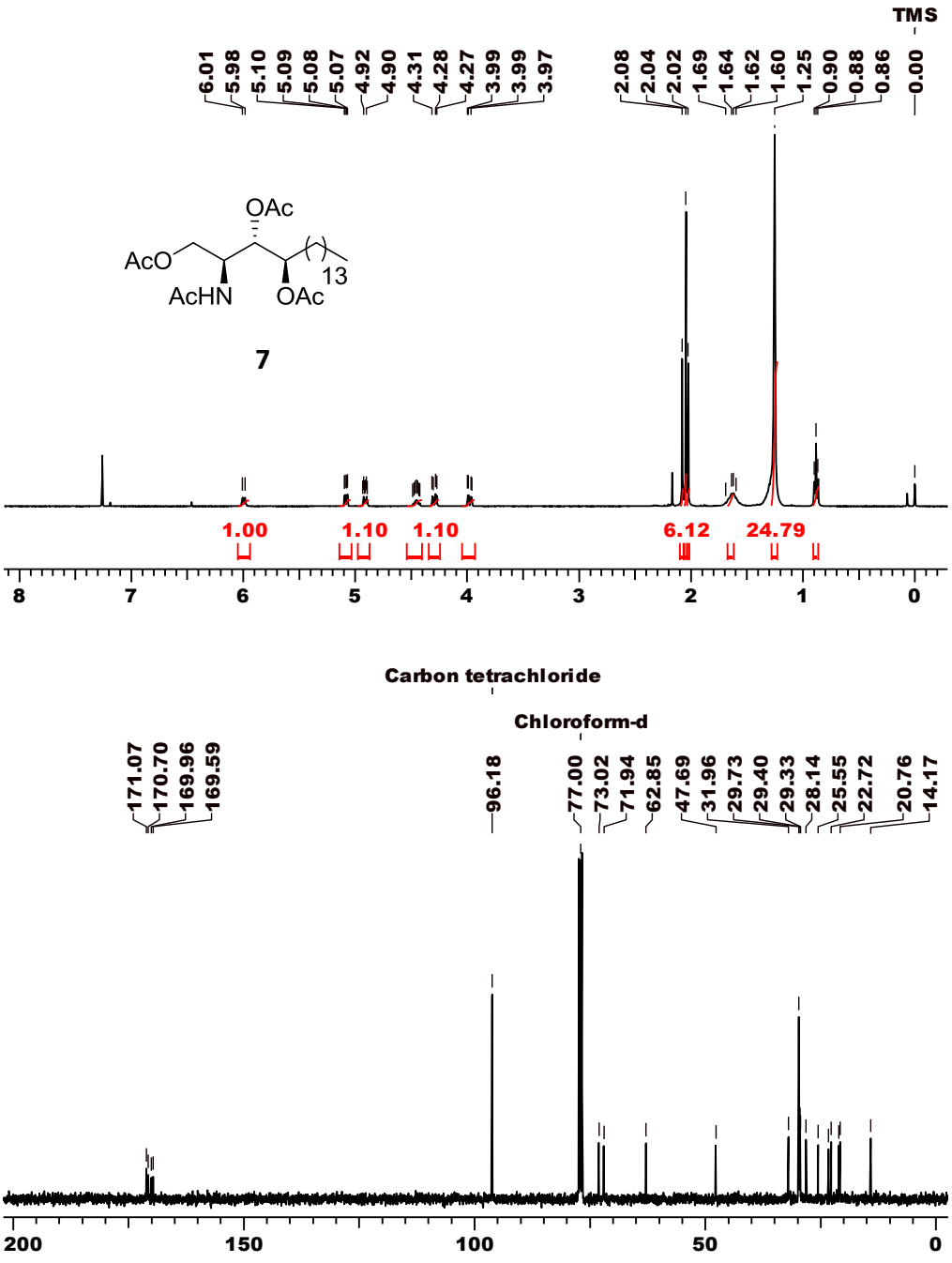
^{1}H and ^{13}C NMR spectra of *ent* – 2j



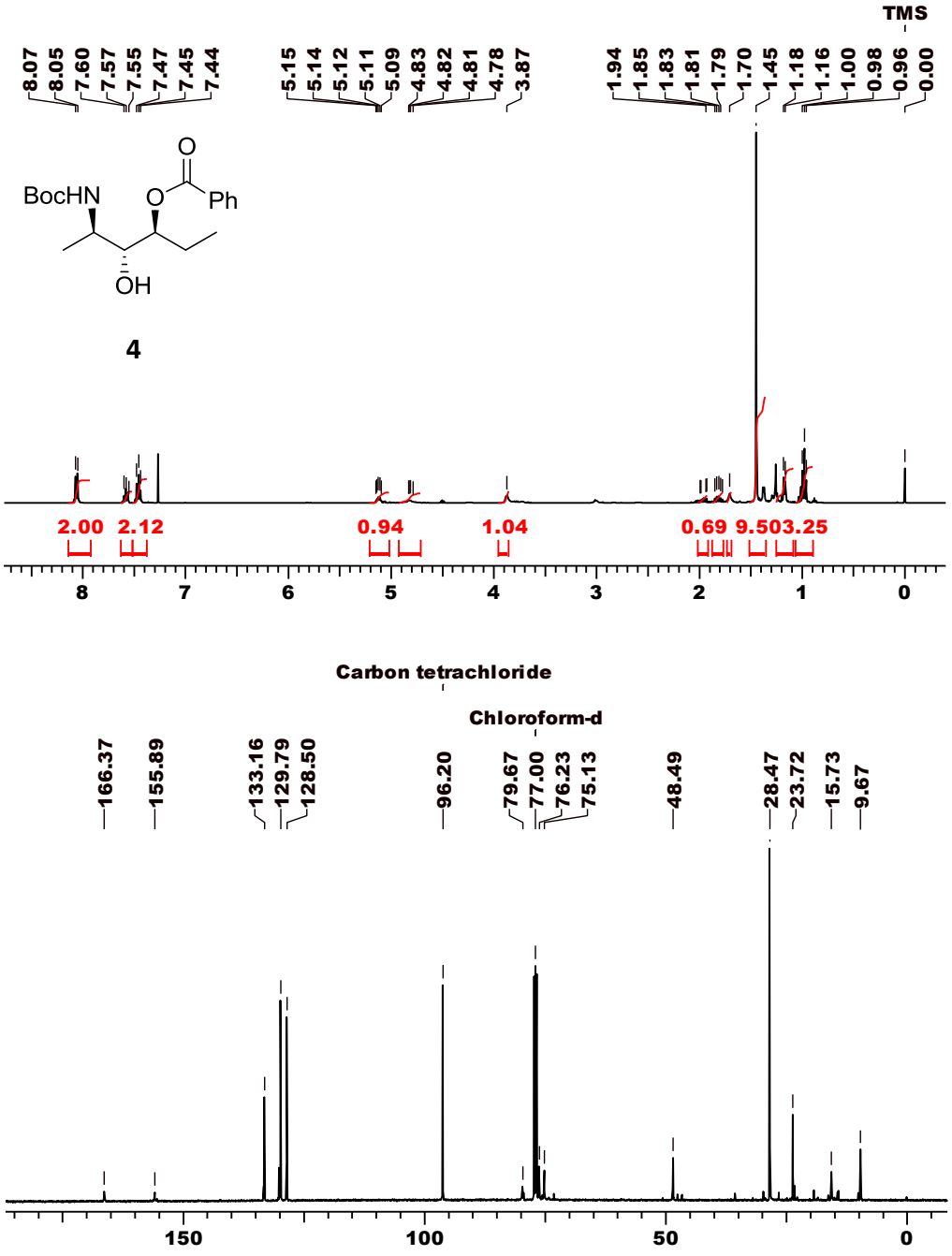
^{1}H and ^{13}C NMR spectra of 5



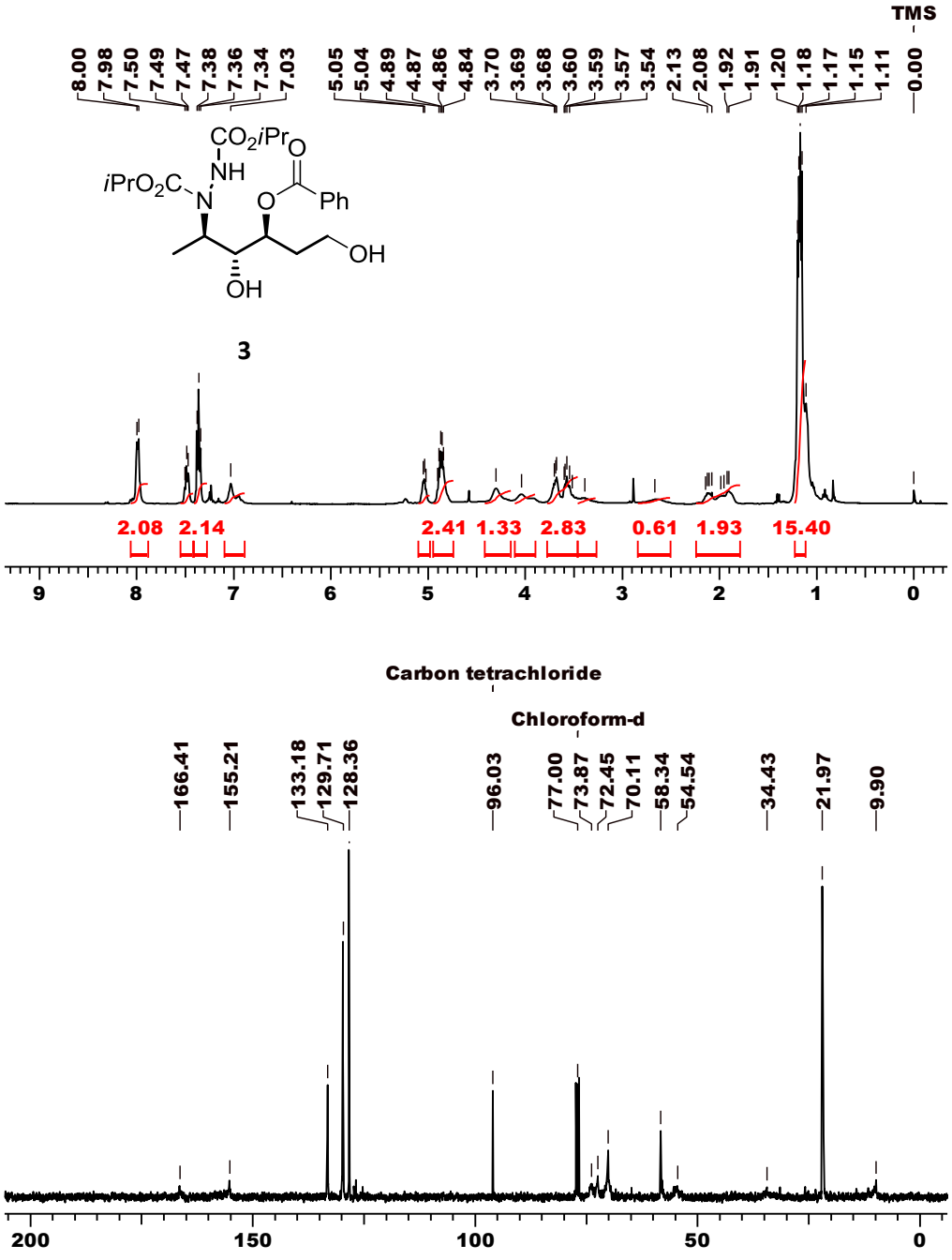
^{1}H and ^{13}C NMR spectra of 6



^{1}H and ^{13}C NMR spectra of 7

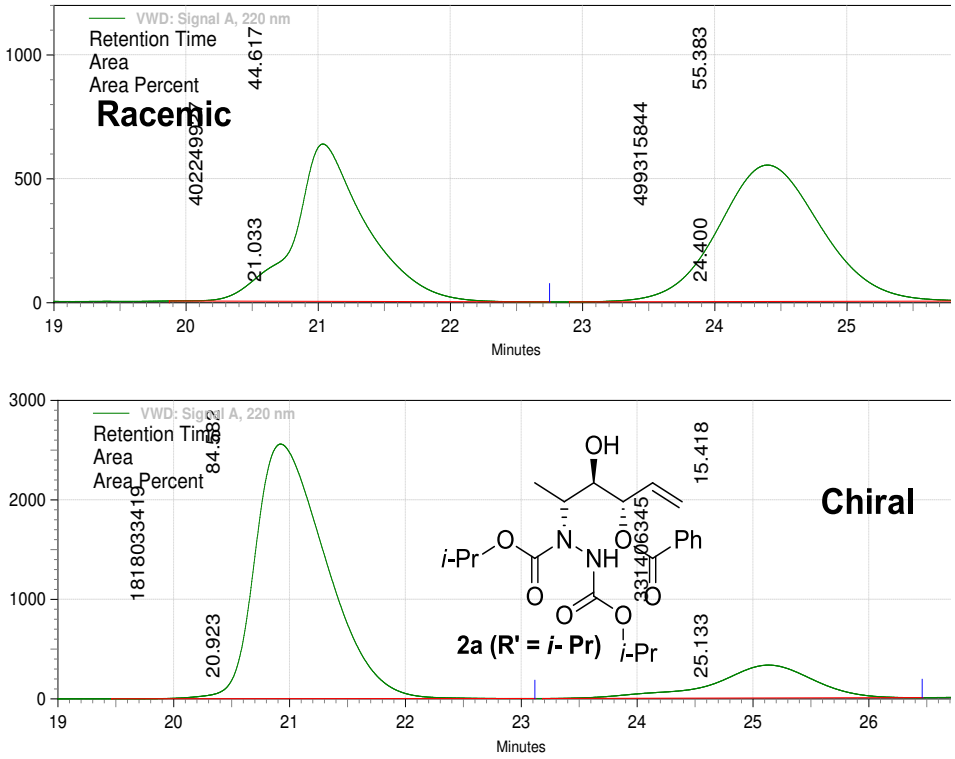


^{1}H and ^{13}C NMR spectra of 4

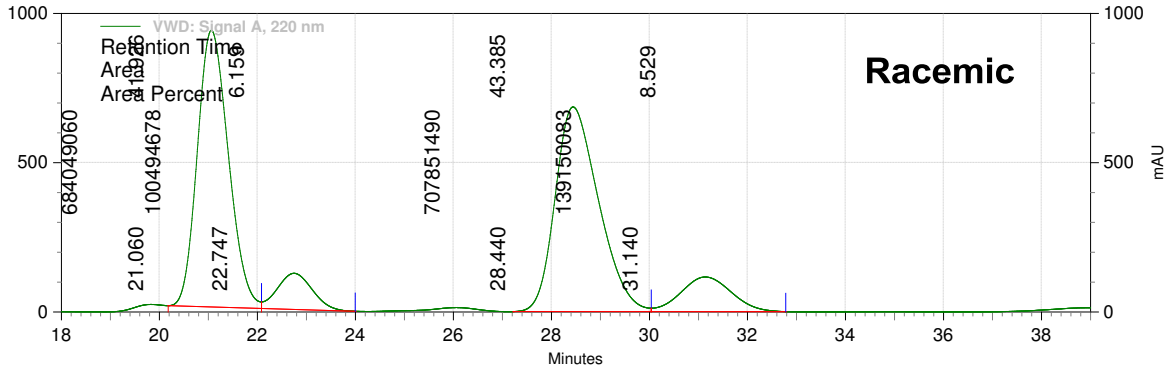


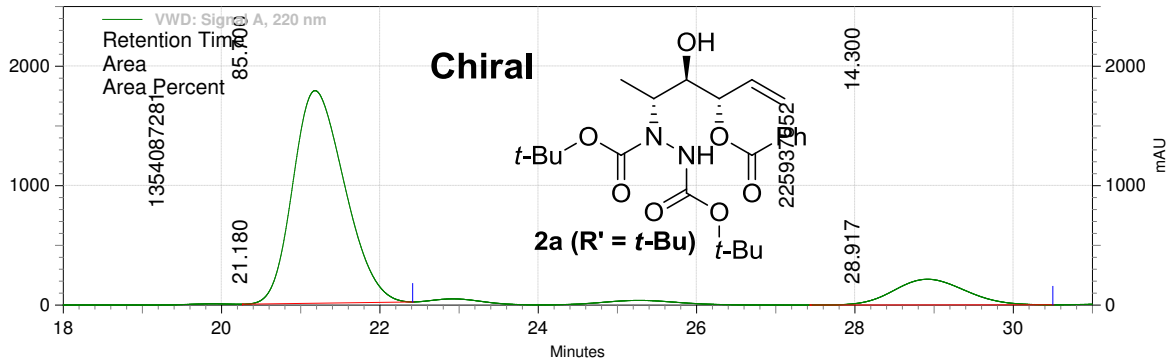
^{1}H and ^{13}C NMR spectra of 3

2. HPLC DATA

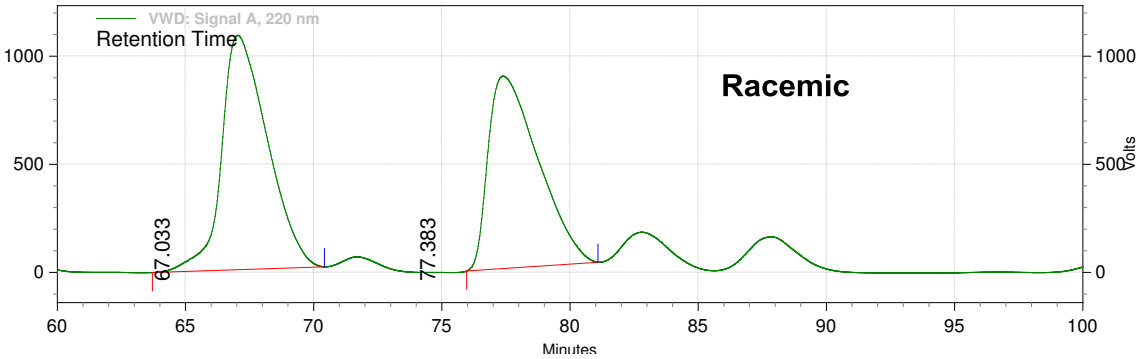


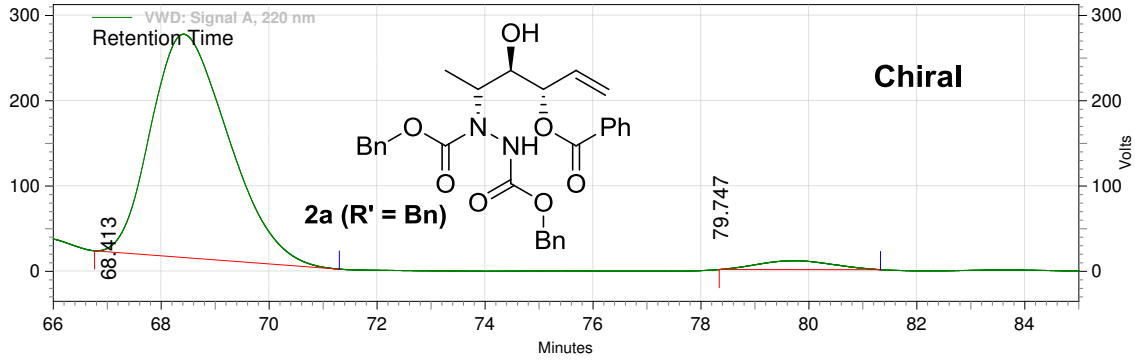
VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
20.923	1818033419	84.58	42920581	88.57
25.133	331406345	15.42	5539913	11.43
Totals				
	2149439764	100.00	48460494	100.00



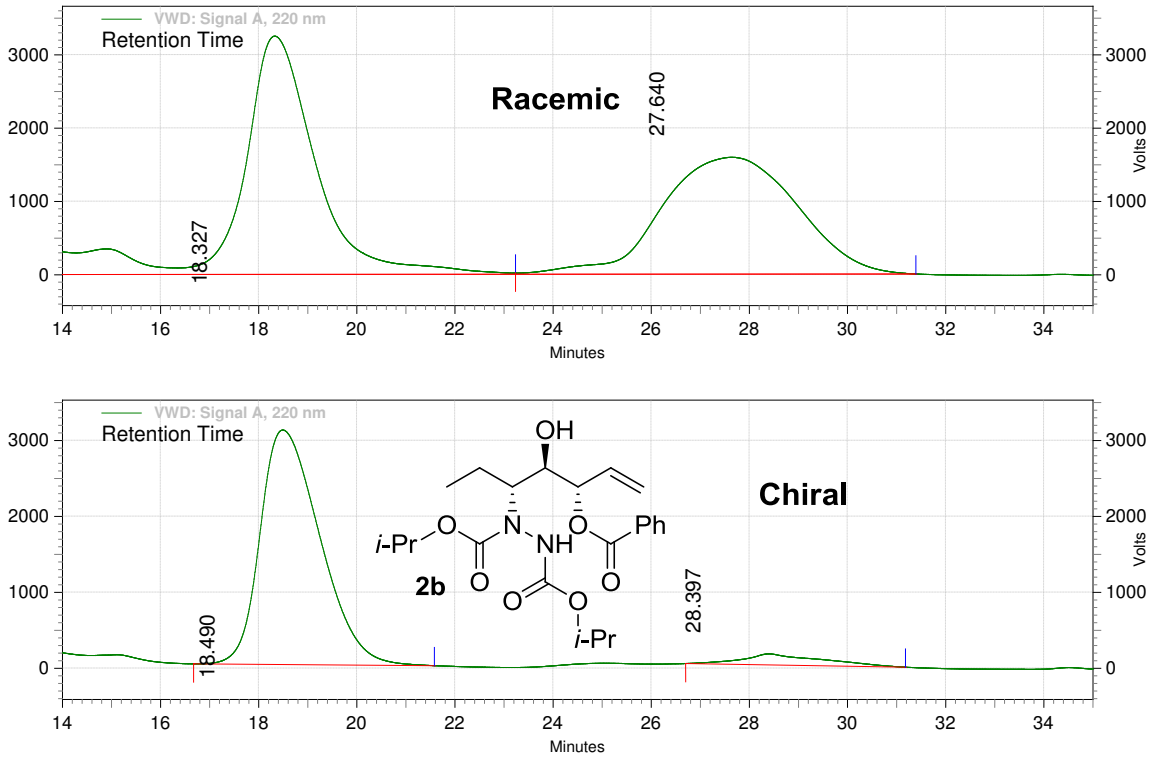


VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
21.180	1354087281	85.70	29871545	89.24
28.917	225937552	14.30	3603280	10.76
Totals				
	1580024833	100.00	33474825	100.00

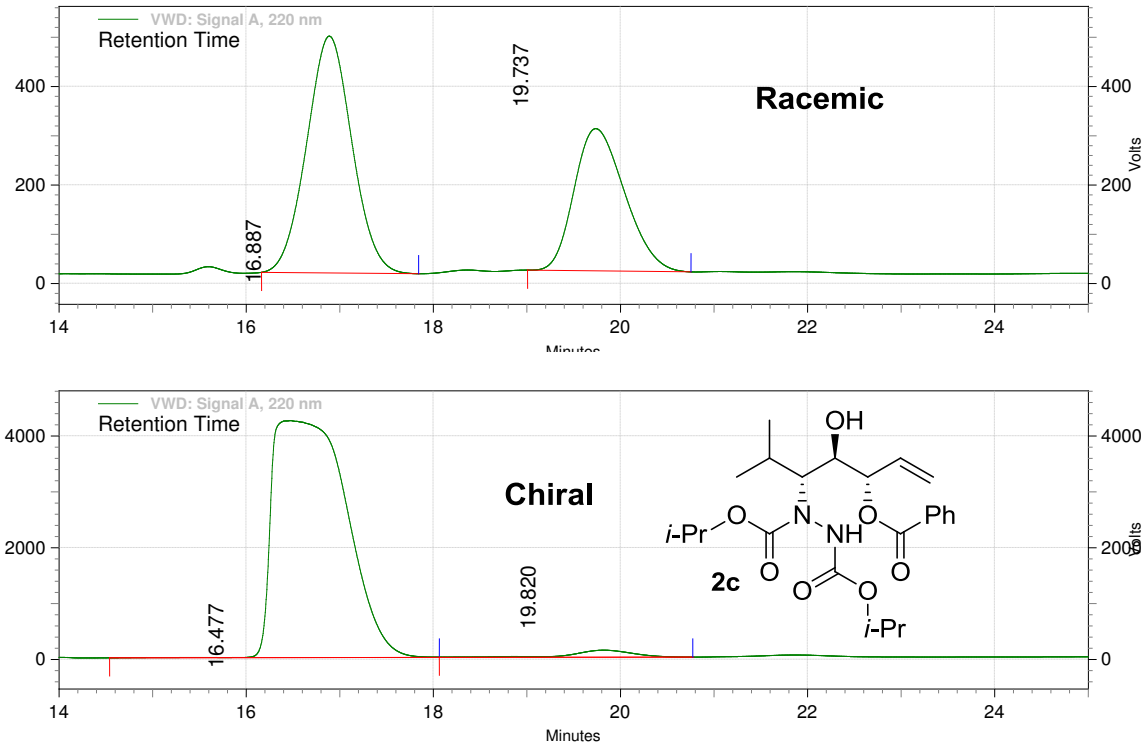




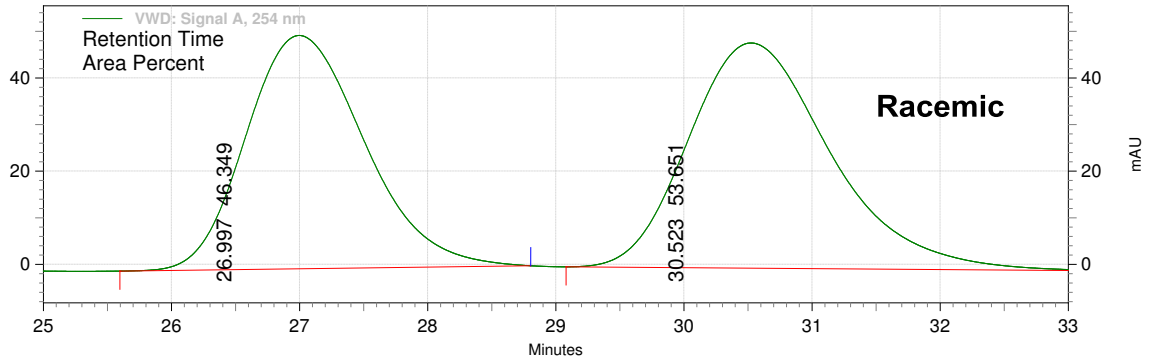
VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
68.413	437872111	96.34	4390683	96.19
79.747	16619017	3.66	174090	3.81
Totals				
	454491128	100.00	4564773	100.00

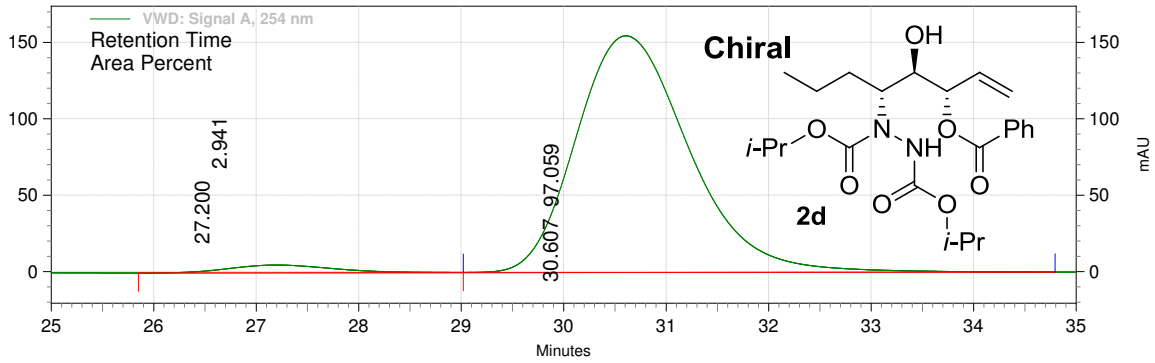


VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
18.490	4377325612	94.10	51823051	95.50
28.397	274385808	5.90	2439513	4.50
Totals				
	4651711420	100.00	54262564	100.00

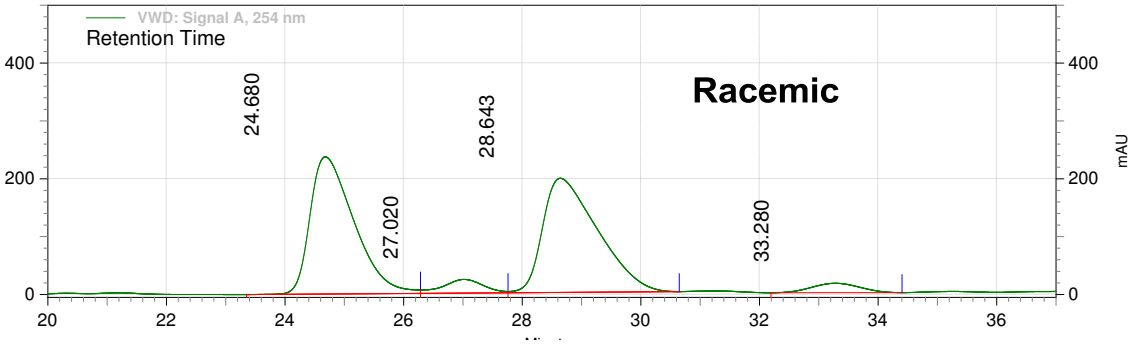


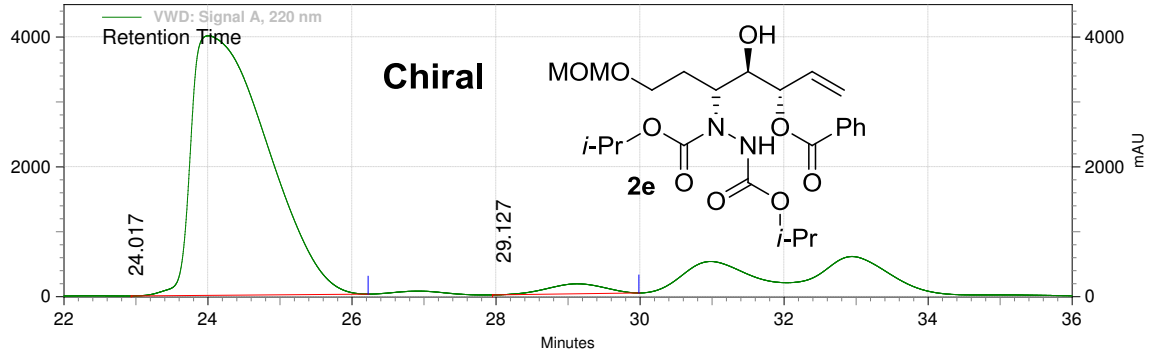
VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
16.477	3927814458	97.64	71167789	97.12
19.820	94731861	2.36	2108664	2.88
Totals				
	4022546319	100.00	73276453	100.00



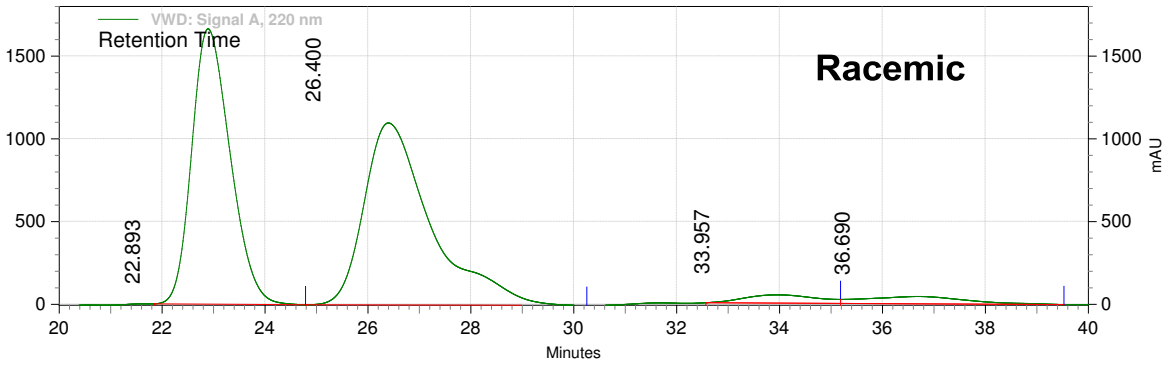


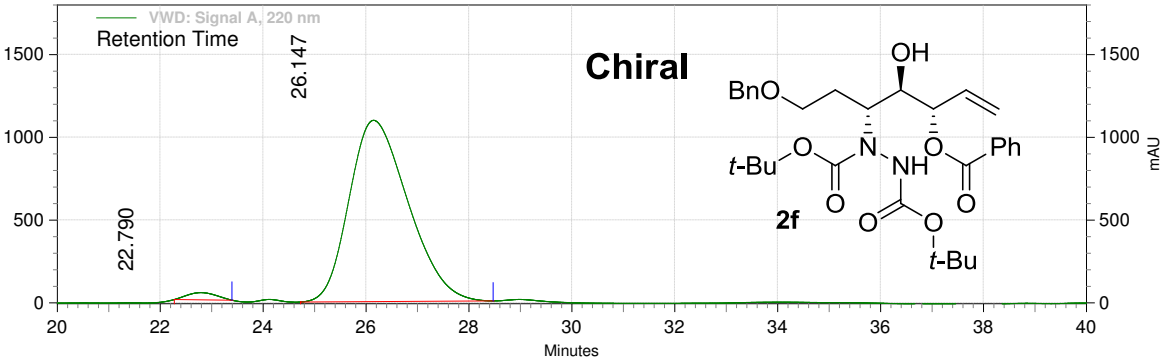
VWD: Signal A, 254 nm Results				
Retention Time	Area	Area %	Height	Height %
27.200	6026001	2.94	85701	3.19
30.607	198857225	97.06	2598245	96.81
Totals				
	204883226	100.00	2683946	100.00



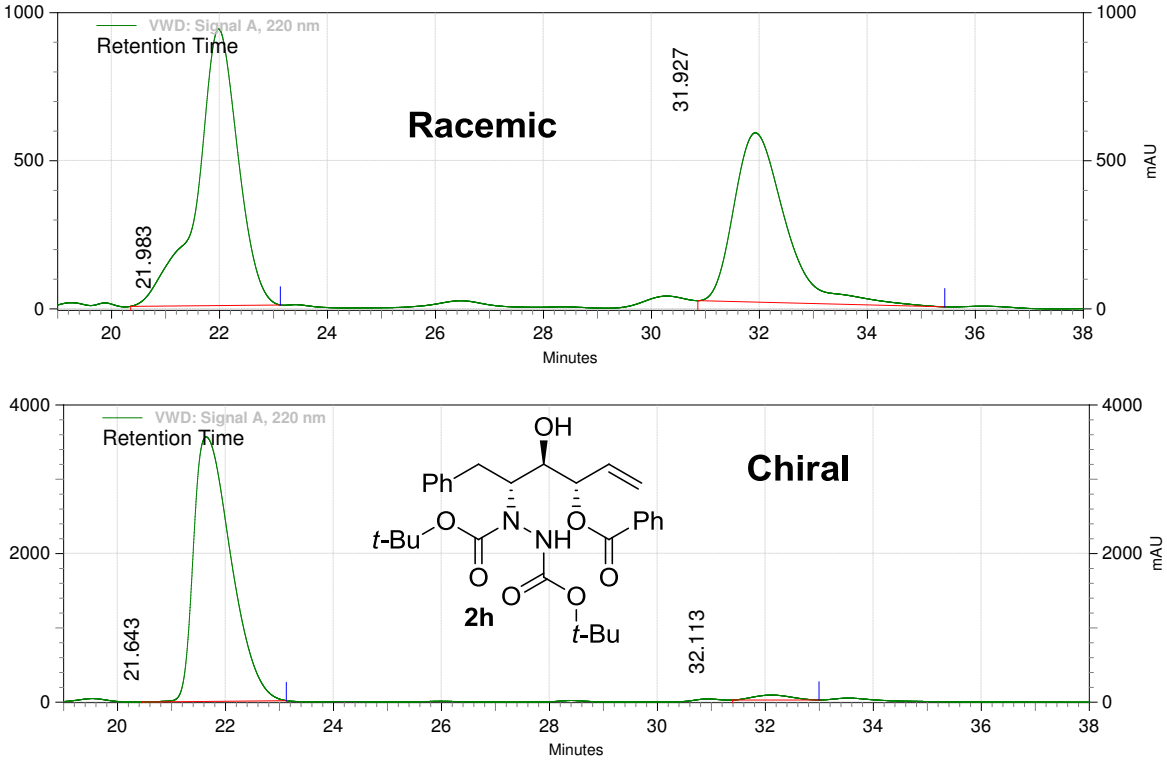


VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
24.017	4883290118	97.22	67088890	96.30
29.127	139847311	2.78	2575790	3.70
Totals				
	5023137429	100.00	69664680	100.00

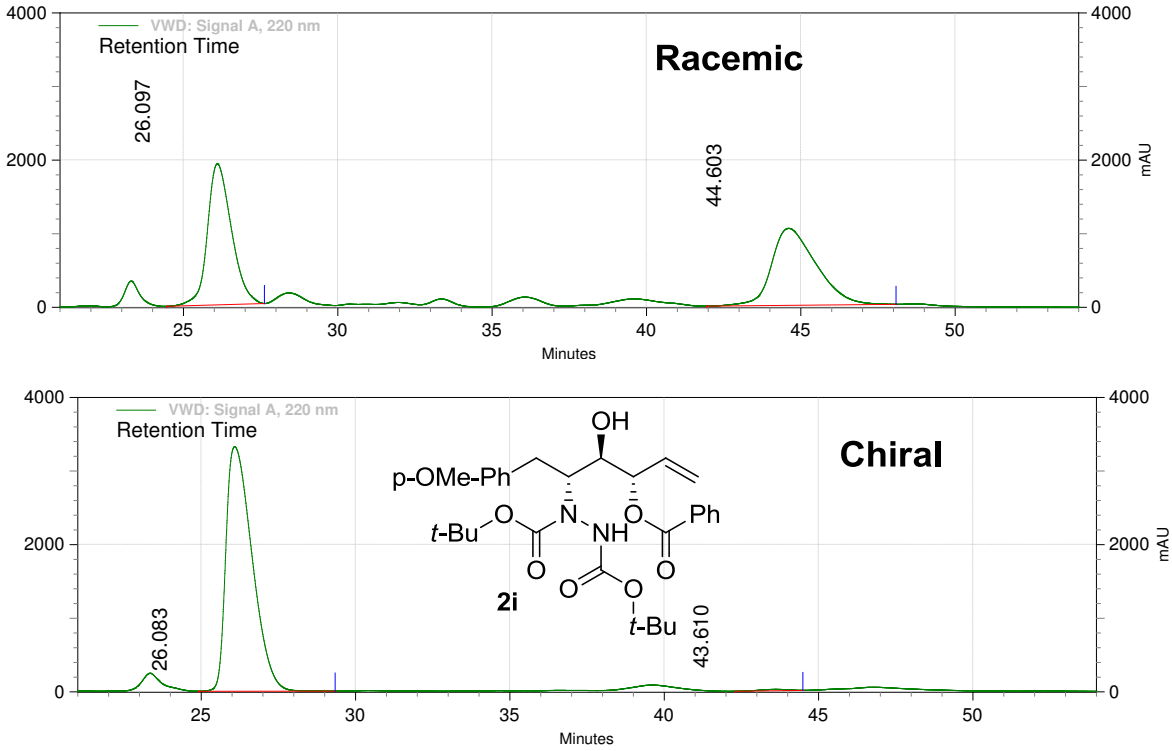




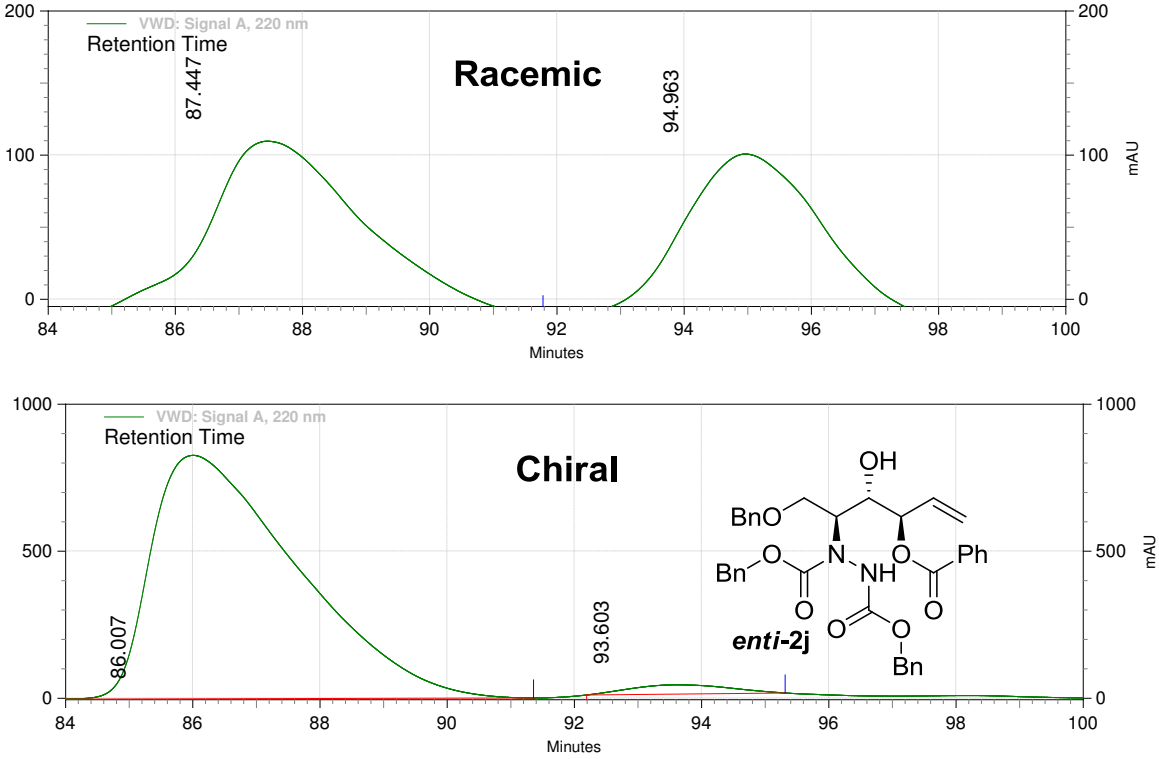
VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
22.790	28750037	1.93	730956	3.83
26.147	1461277993	98.07	18374212	96.17
Totals				
	1490028030	100.00	19105168	100.00



VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
21.643	2864322578	98.15	59702583	98.17
32.113	53898977	1.85	1115457	1.83
Totals				
	2918221555	100.00	60818040	100.00

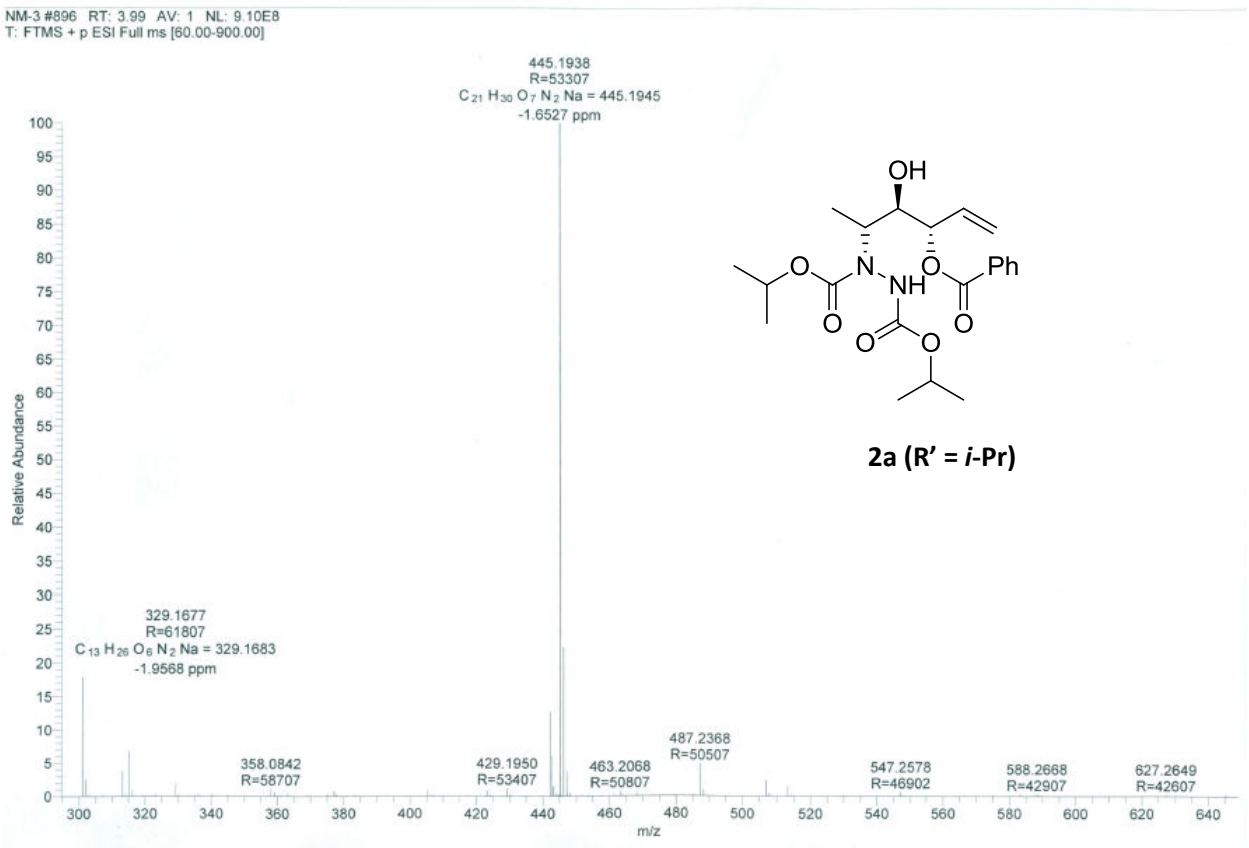


VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
26.083	3280795998	99.43	55728819	99.46
43.610	18850571	0.57	303442	0.54
Totals				
	3299646569	100.00	56032261	100.00

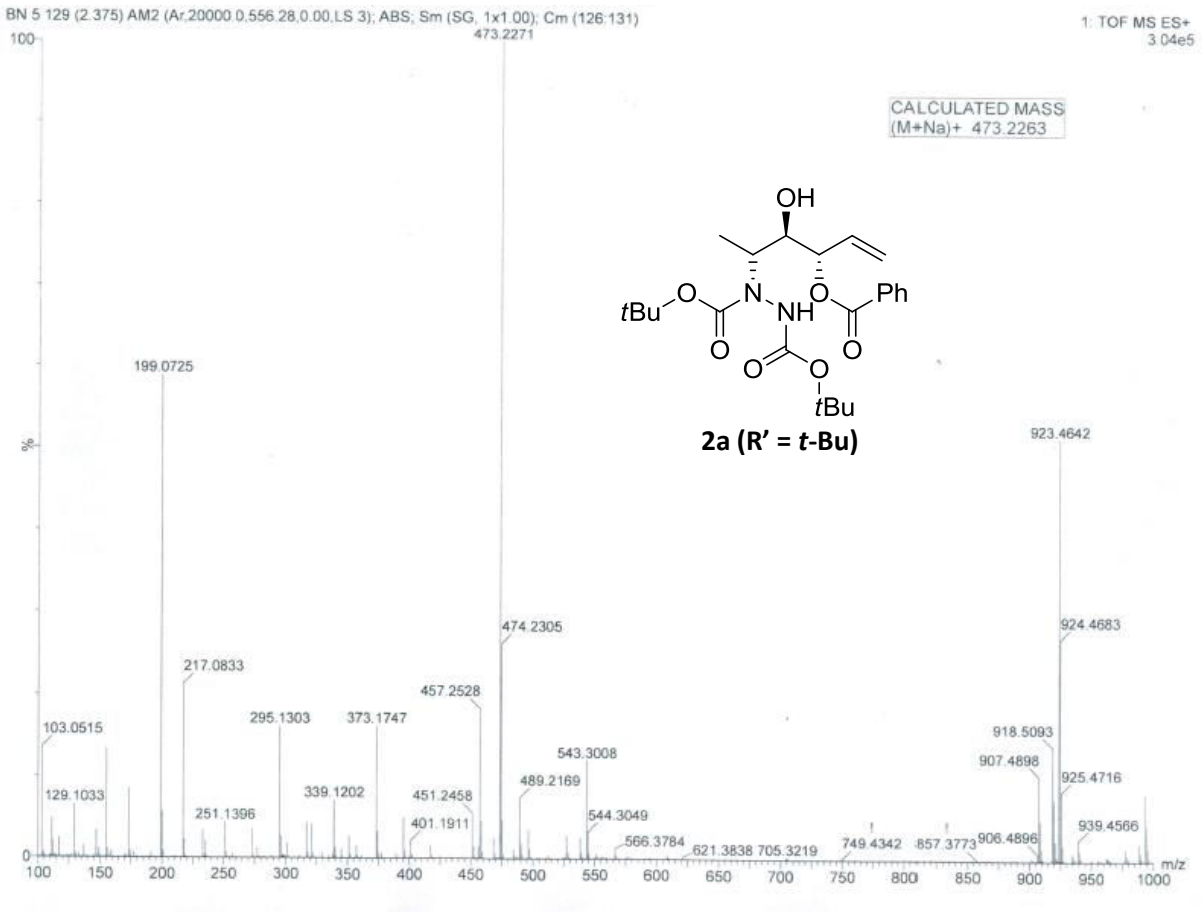


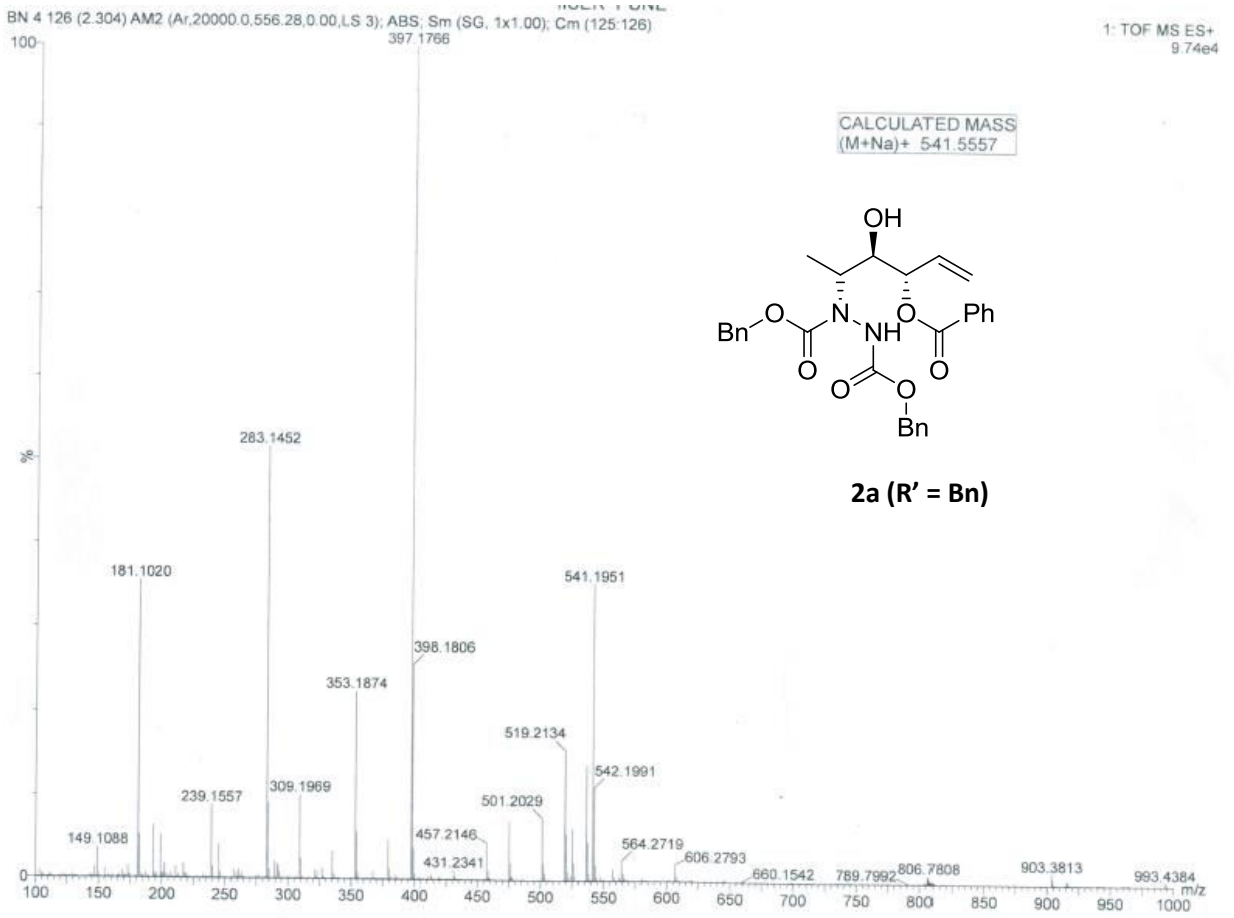
VWD: Signal A, 220 nm Results				
Retention Time	Area	Area %	Height	Height %
86.007	2207902336	97.49	13887984	96.34
93.603	56955538	2.51	527171	3.66
Totals				
	2264857874	100.00	14415155	100.00

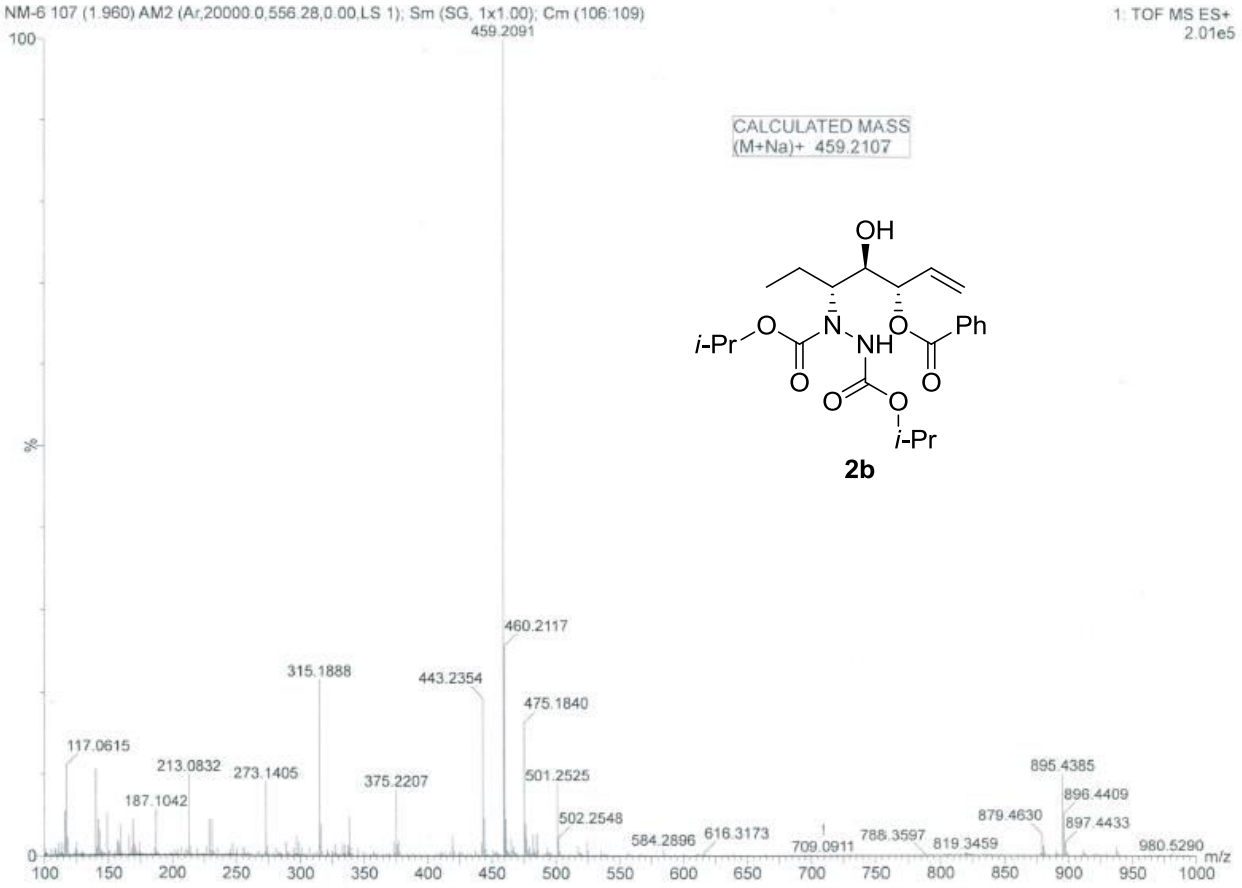
3. HRMS Data

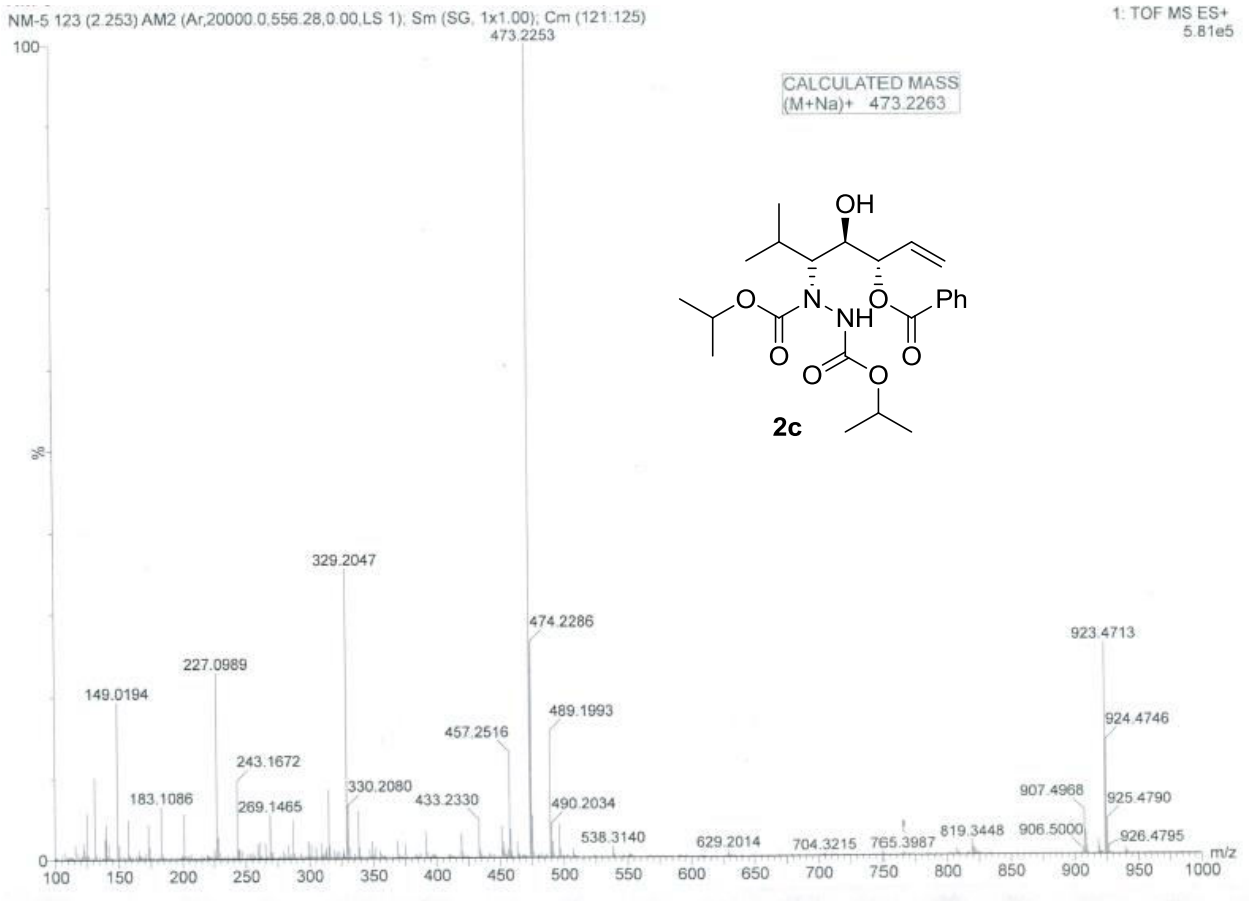


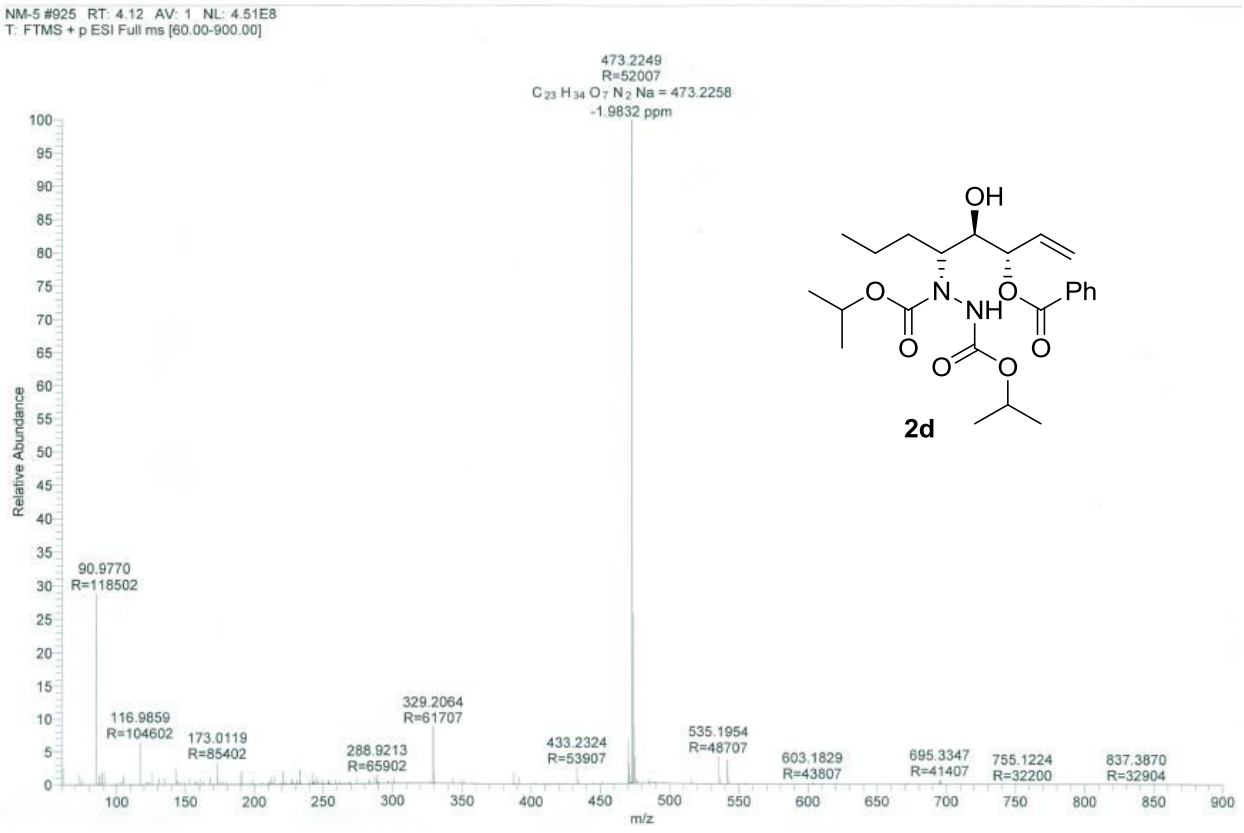
2a (R' = *i*-Pr)

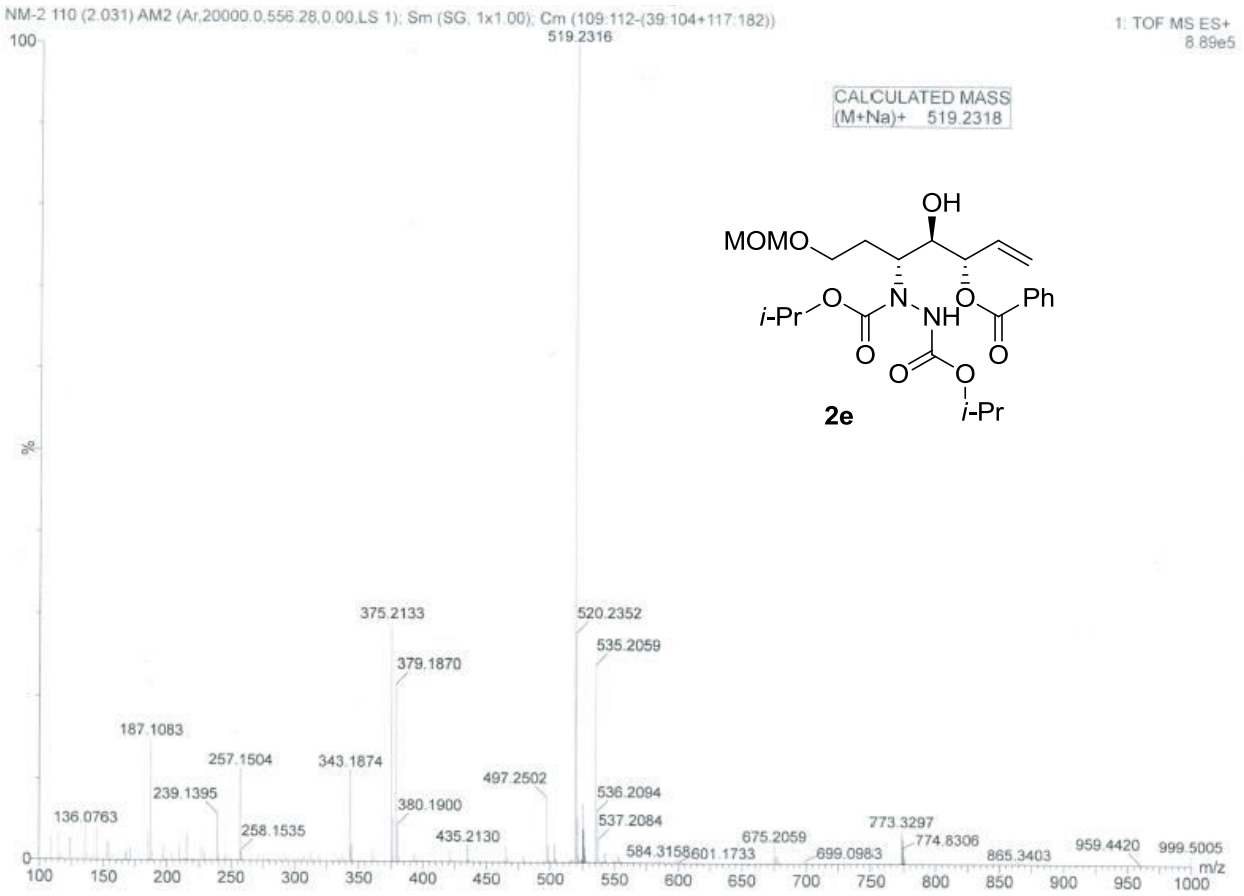

BN 5 129 (2.375) AM2 (Ar,20000 0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (126:131)
1: TOF MS ES+
3.04e5
CALCULATED MASS
(M+Na)+ 473.2263
OH
tBu
O
N
NH
O
Ph
O
O
O
O
tBu
2a (R' = t-Bu)
%
m/z
473.2271
199.0725
923.4642
474.2305
924.4683
217.0833
457.2528
295.1303
373.1747
103.0515
543.3008
918.5093
907.4898
489.2169
925.4716
129.1033
339.1202
451.2458
544.3049
251.1396
401.1911
939.4566
566.3784
621.3838
705.3219
749.4342
857.3773
906.4896

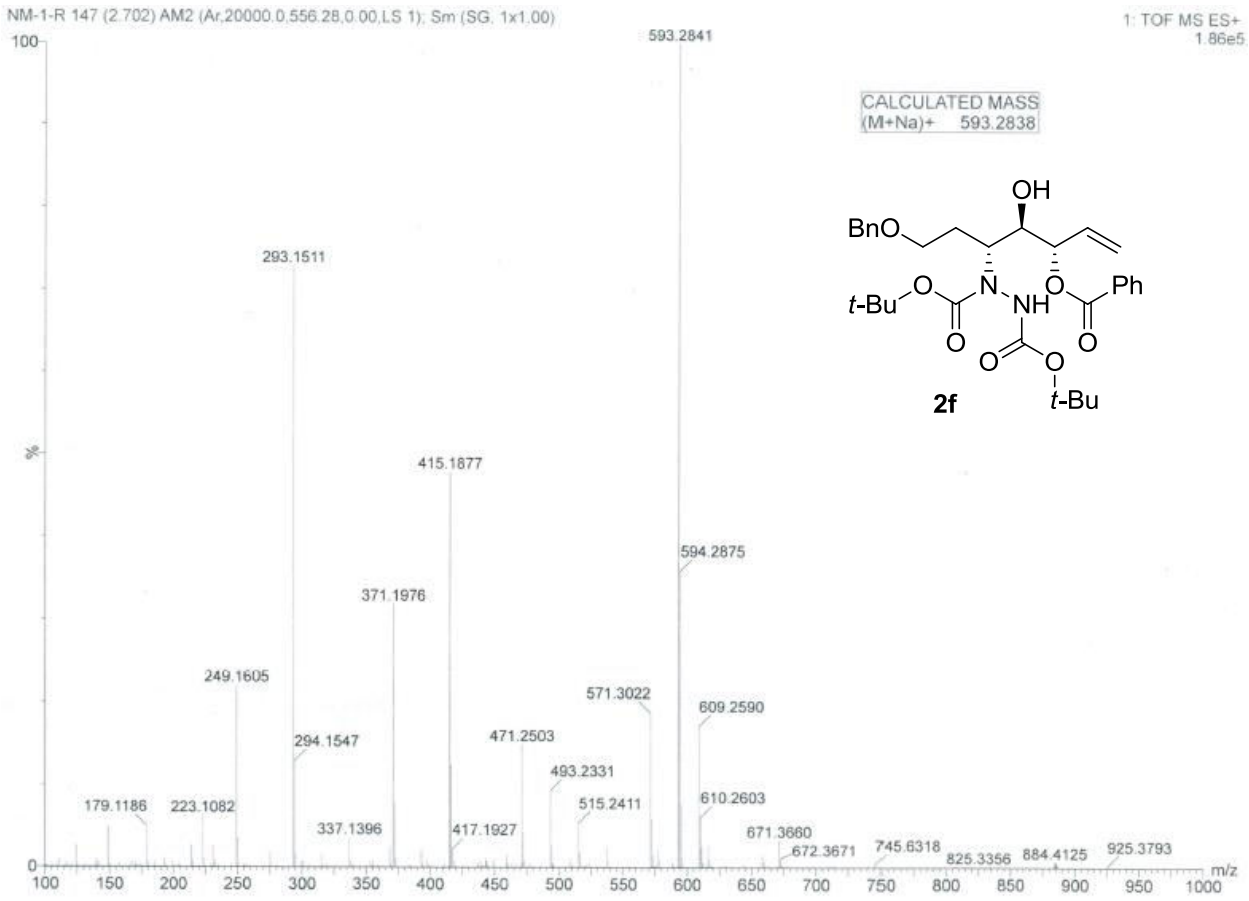

BN 4 126 (2.304) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (125:126)
1: TOF MS ES+
9.74e4
CALCULATED MASS
(M+Na)+ 541.5557
OH
Bn
O
N
NH
O
Ph
O
O
O
O
Bn
2a (R' = Bn)
%
397.1766
283.1452
181.1020
541.1951
398.1806
353.1874
519.2134
542.1991
239.1557
309.1969
501.2029
149.1088
457.2146
564.2719
431.2341
606.2793
660.1542
789.7992
806.7808
903.3813
993.4384
m/z

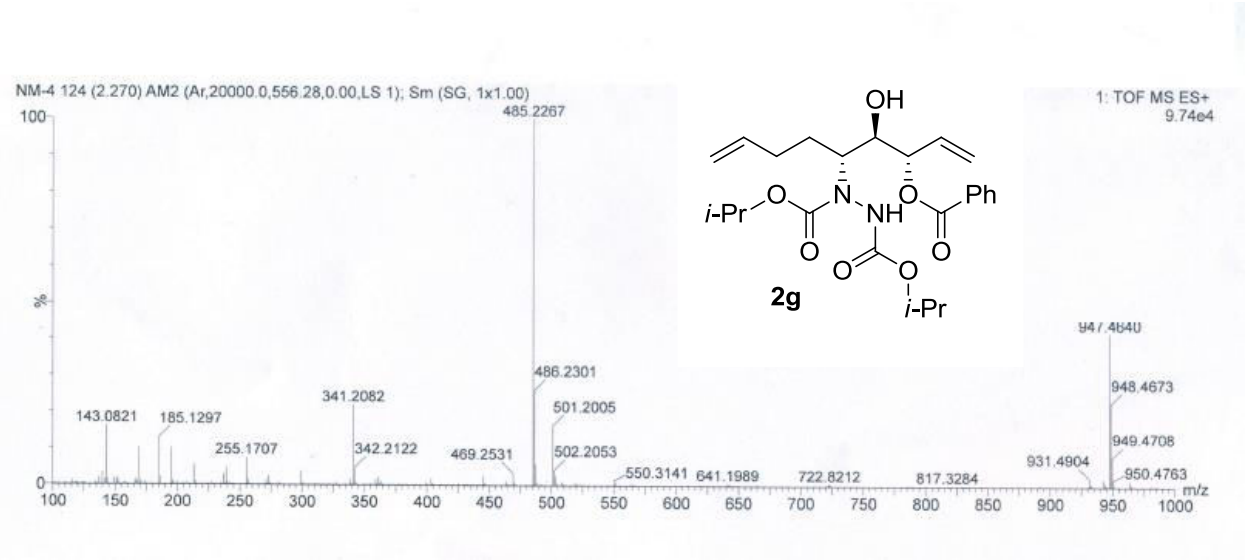

NM-6 107 (1.960) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00); Cm (106:109)
1: TOF MS ES+
2.01e5
459.2091
CALCULATED MASS
(M+Na)+ 459.2107
OH
i-Pr
O
N
NH
O
Ph
O
O
O
O
i-Pr
2b
%
460.2117
315.1888
443.2354
475.1840
117.0615
213.0832
273.1405
375.2207
501.2525
187.1042
502.2548
895.4385
896.4409
879.4630
897.4433
584.2896
616.3173
709.0911
788.3597
819.3459
980.5290
m/z
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
1000

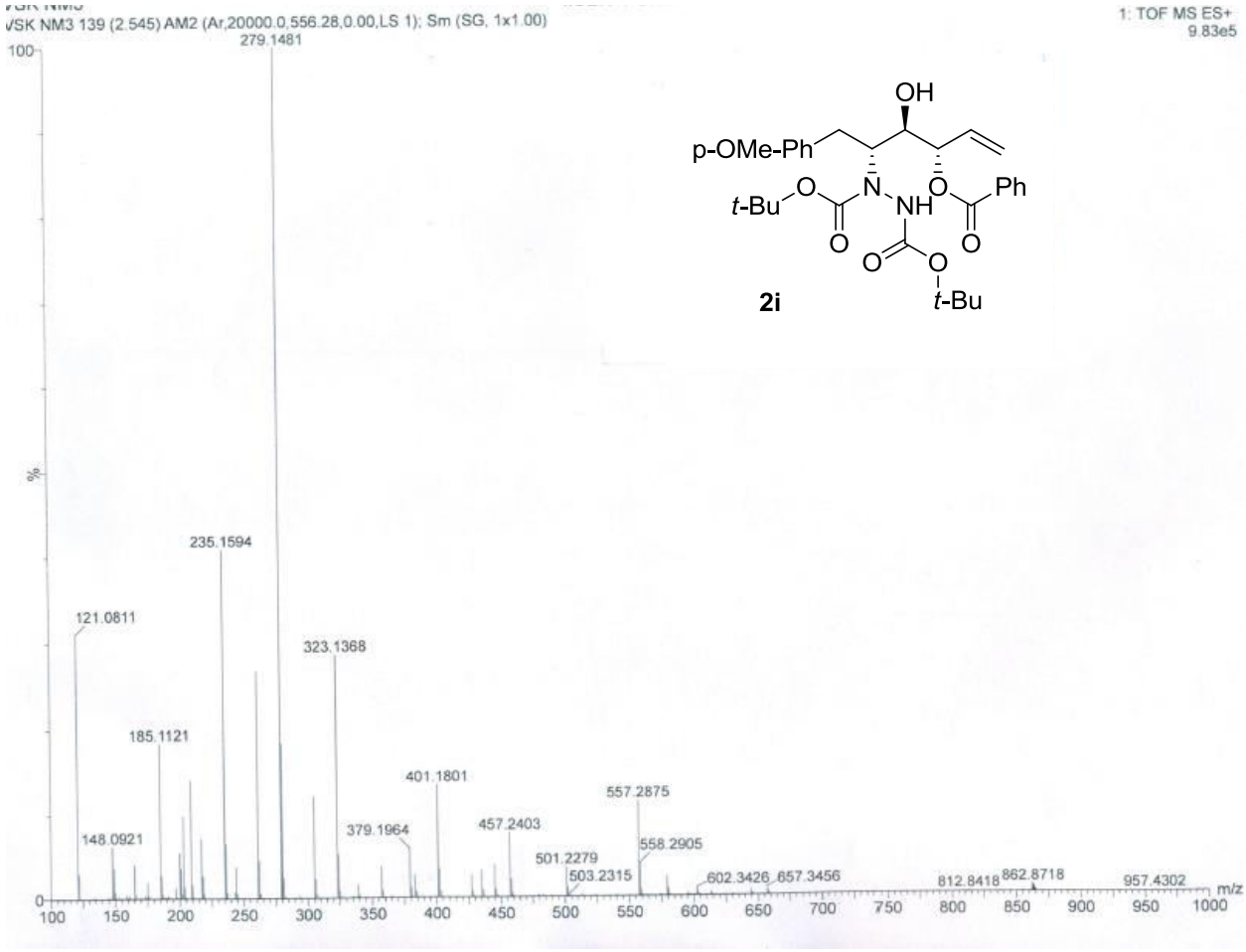

NM-5 123 (2.253) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00); Cm (121:125)
1: TOF MS ES+
5.81e5
CALCULATED MASS
(M+Na)+ 473.2263
2c
%
m/z
473.2253
329.2047
474.2286
227.0989
149.0194
489.1993
457.2516
923.4713
924.4746
243.1672
330.2080
183.1086
269.1465
433.2330
490.2034
907.4968
925.4790
538.3140
629.2014
704.3215
765.3987
819.3448
906.5000
926.4795

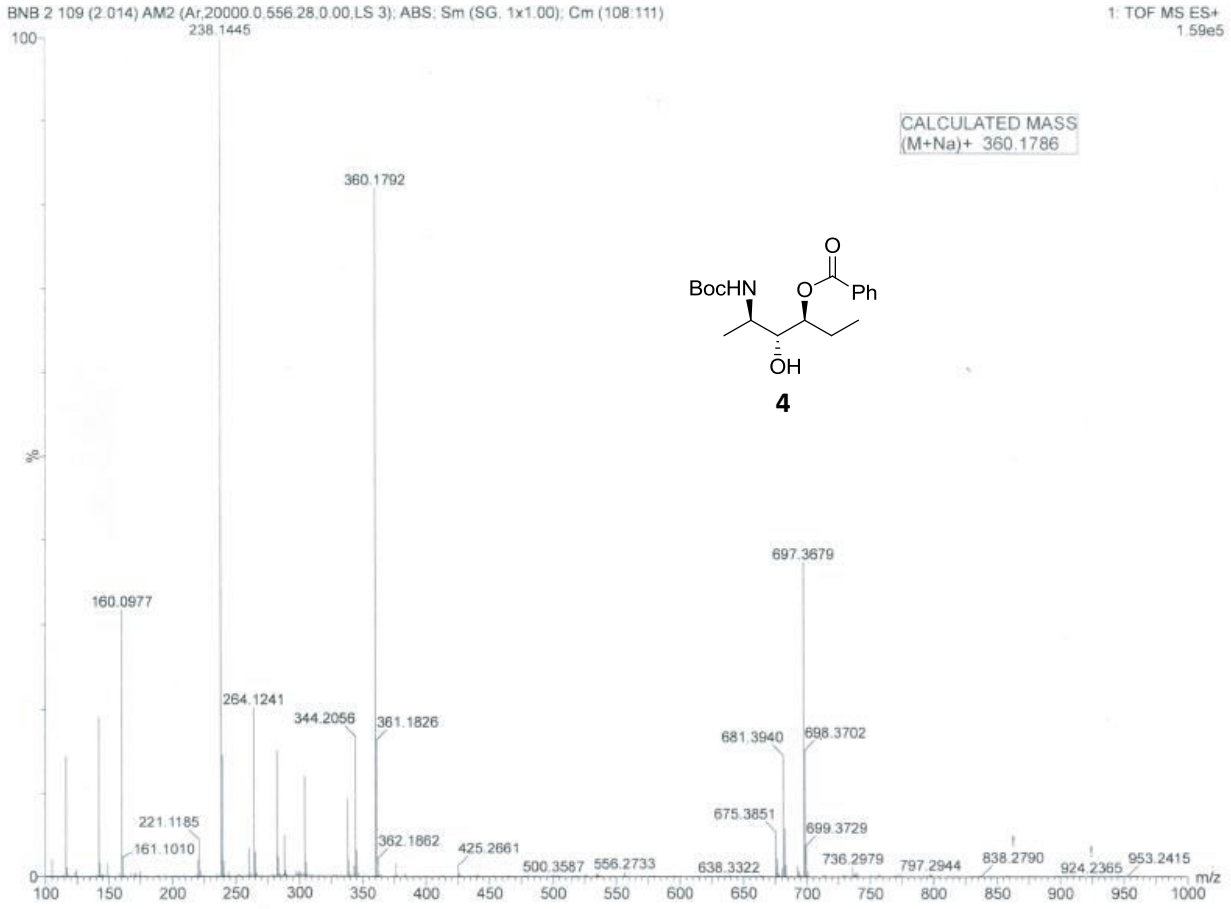

NM-5 #925 RT: 4.12 AV: 1 NL: 4.51E8
T: FTMS + p ESI Full ms [60.00-900.00]
473.2249
R=52007
C23 H34 O7 N2 Na = 473.2258
-1.9832 ppm
Relative Abundance
m/z
90.9770
R=118502
116.9859
R=104602
173.0119
R=85402
288.9213
R=65902
329.2064
R=61707
433.2324
R=53907
535.1954
R=48707
603.1829
R=43807
695.3347
R=41407
755.1224
R=32200
837.3870
R=32904
OH
O
N
NH
O
Ph
O
O
O
O
2d

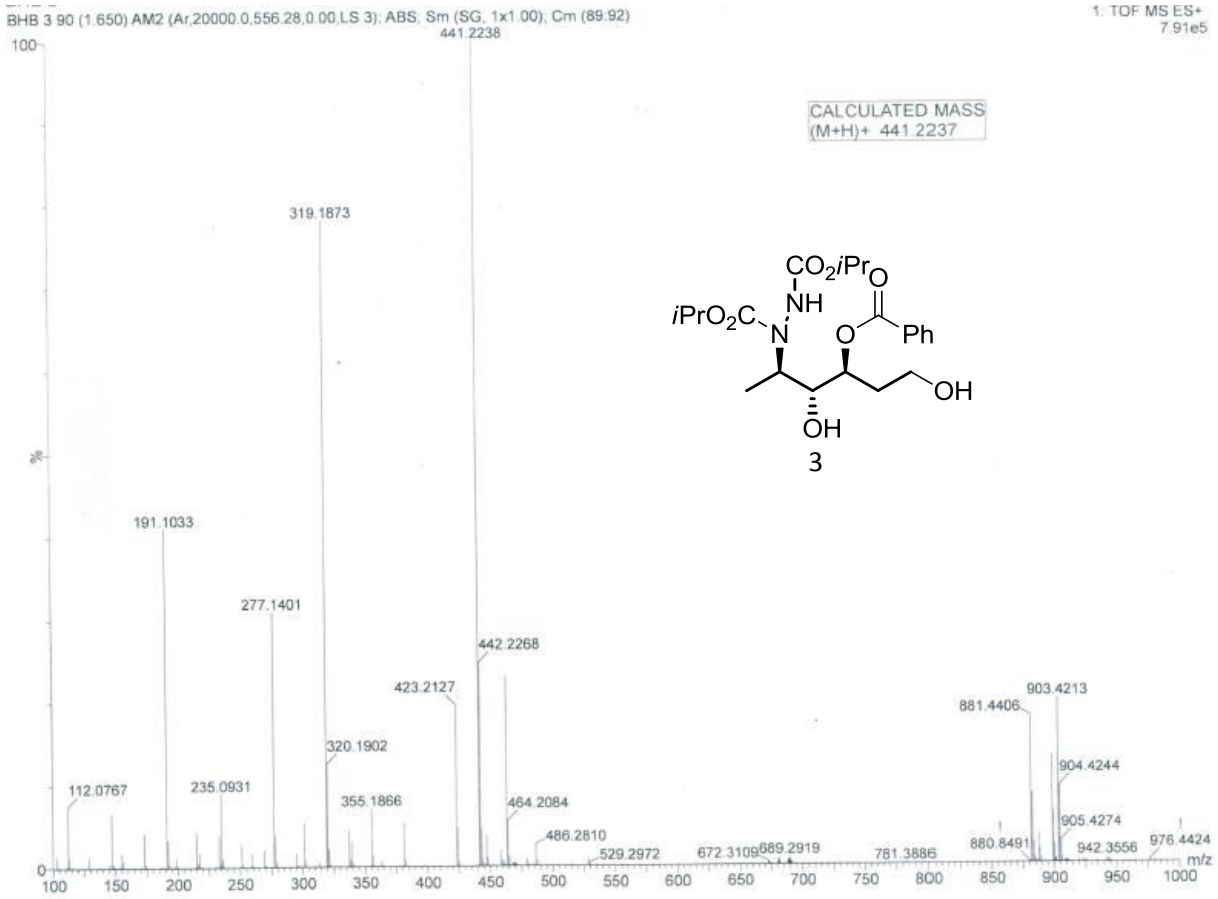

NM-2 110 (2.031) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00); Cm (109:112-(39:104+117:182))
1: TOF MS ES+
8.89e5
519.2316
CALCULATED MASS
(M+Na)+ 519.2318
OH
MOMO
i-Pr
O
N
NH
O
Ph
O
O
O
O
i-Pr
2e
%
100
0
375.2133
520.2352
535.2059
379.1870
187.1083
257.1504
343.1874
497.2502
536.2094
239.1395
380.1900
537.2084
136.0763
258.1535
435.2130
675.2059
773.3297
774.8306
584.3158
601.1733
699.0983
865.3403
959.4420
999.5005
m/z
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000

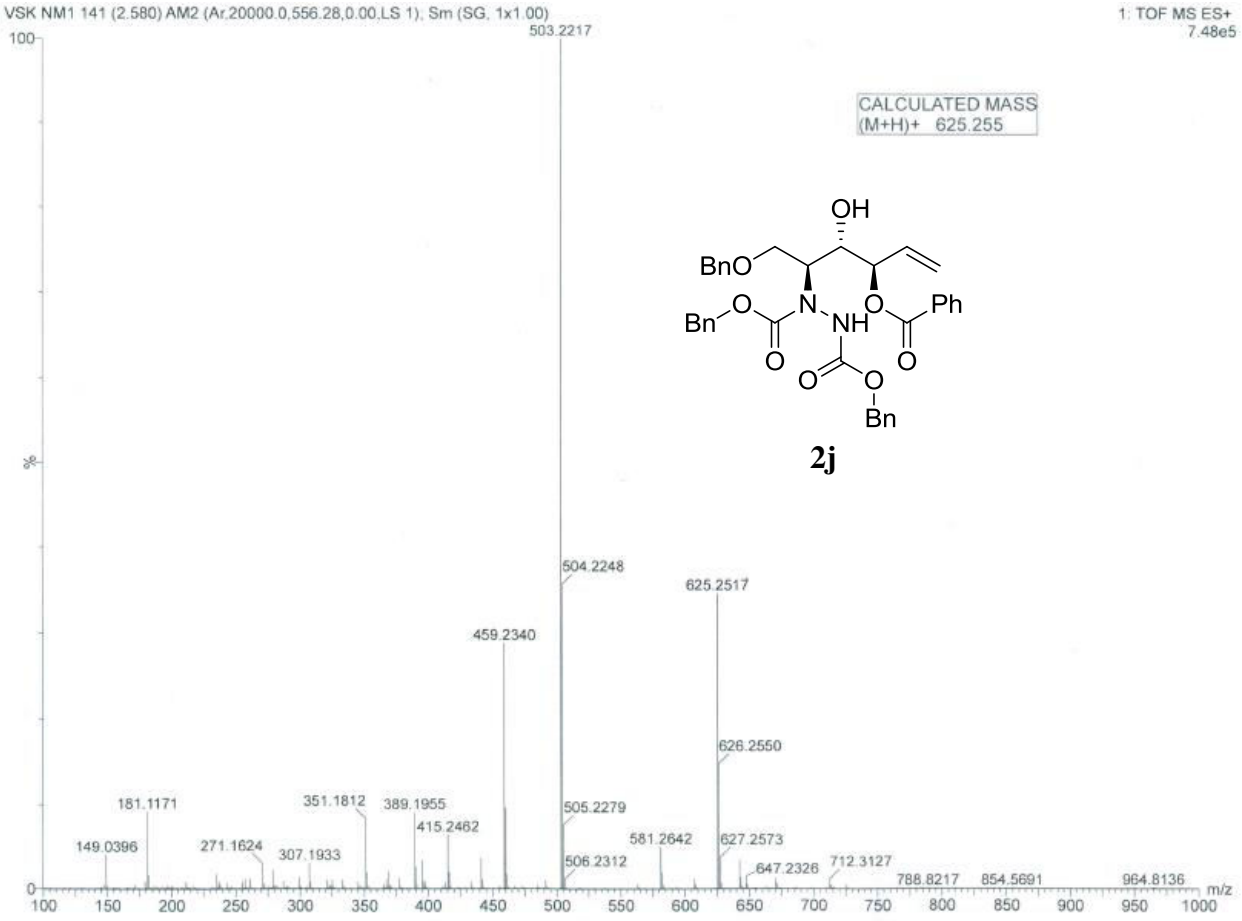

NM-1-R 147 (2.702) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00)
1: TOF MS ES+
1.86e5
100
%
0
593.2841
293.1511
415.1877
594.2875
371.1976
249.1605
571.3022
609.2590
294.1547
471.2503
493.2331
610.2603
179.1186
223.1082
515.2411
337.1396
417.1927
671.3660
672.3671
745.6318
825.3356
884.4125
925.3793
m/z
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
CALCULATED MASS
(M+Na)+ 593.2838
OH
BnO
t-Bu
O
N
NH
O
Ph
O
O
O
O
t-Bu
2f

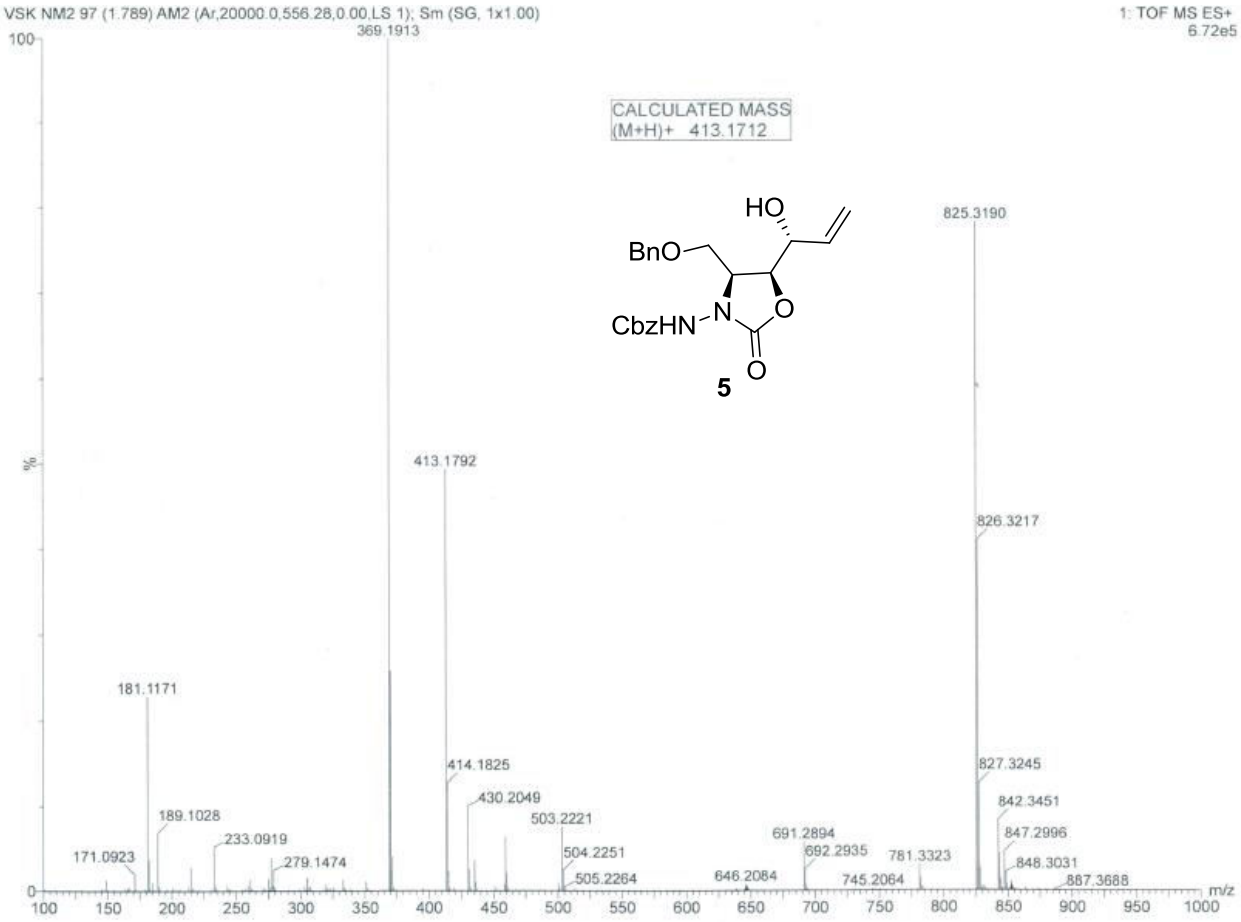

NM-4 124 (2.270) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00)
1: TOF MS ES+
9.74e4
100
%
0
485.2267
486.2301
341.2082
143.0821
185.1297
255.1707
342.2122
469.2531
501.2005
502.2053
550.3141
641.1989
722.8212
817.3284
931.4904
947.4640
948.4673
949.4708
950.4763
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
m/z
OH
i-Pr
O
N
NH
O
Ph
O
O
O
O
i-Pr
2g

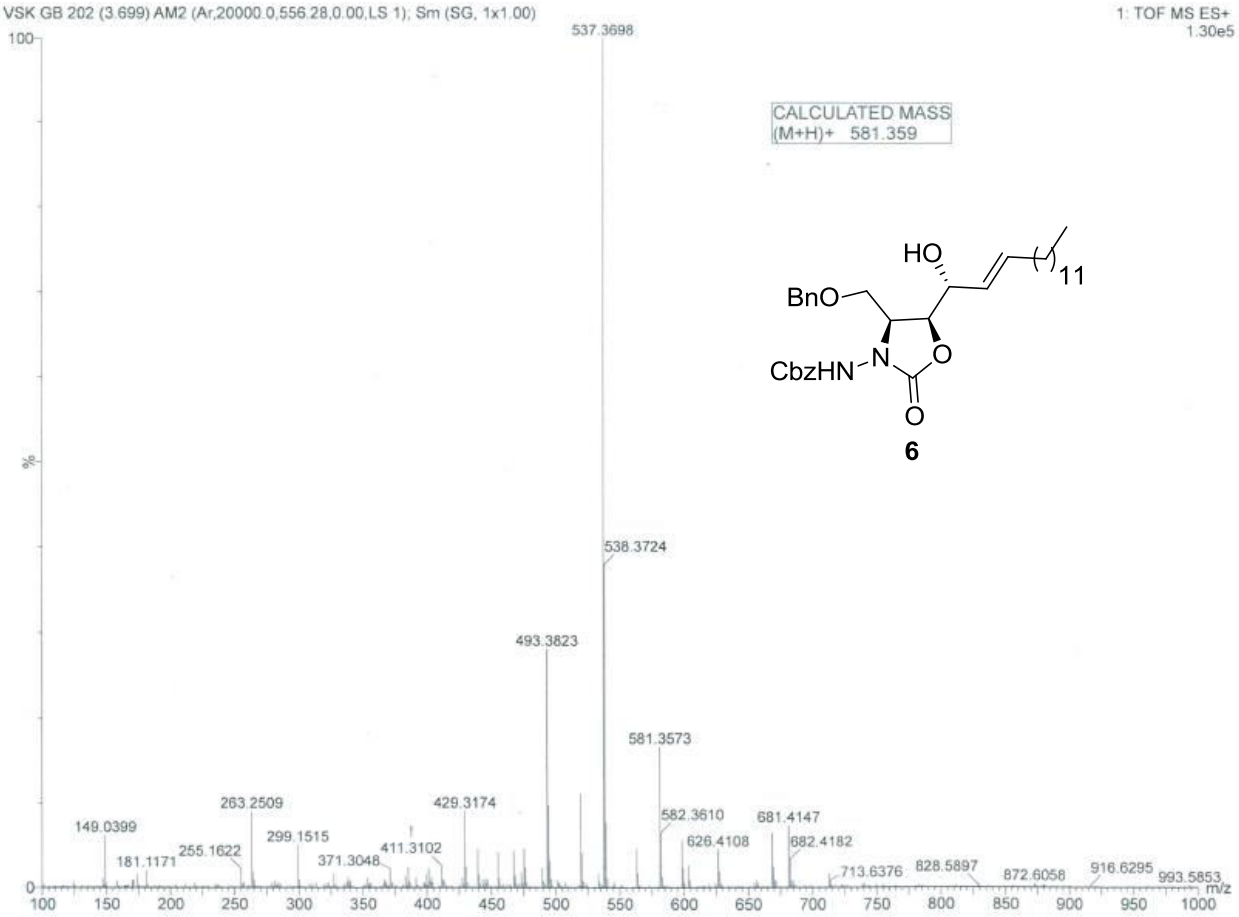

VSK NM3 139 (2.545) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00)
1: TOF MS ES+
9.83e5
279.1481
235.1594
121.0811
323.1368
185.1121
401.1801
557.2875
457.2403
379.1964
148.0921
558.2905
501.2279
503.2315
602.3426
657.3456
812.8418
862.8718
957.4302
m/z
%
OH
p-OMe-Ph
t-Bu
N
NH
Ph
2i
t-Bu

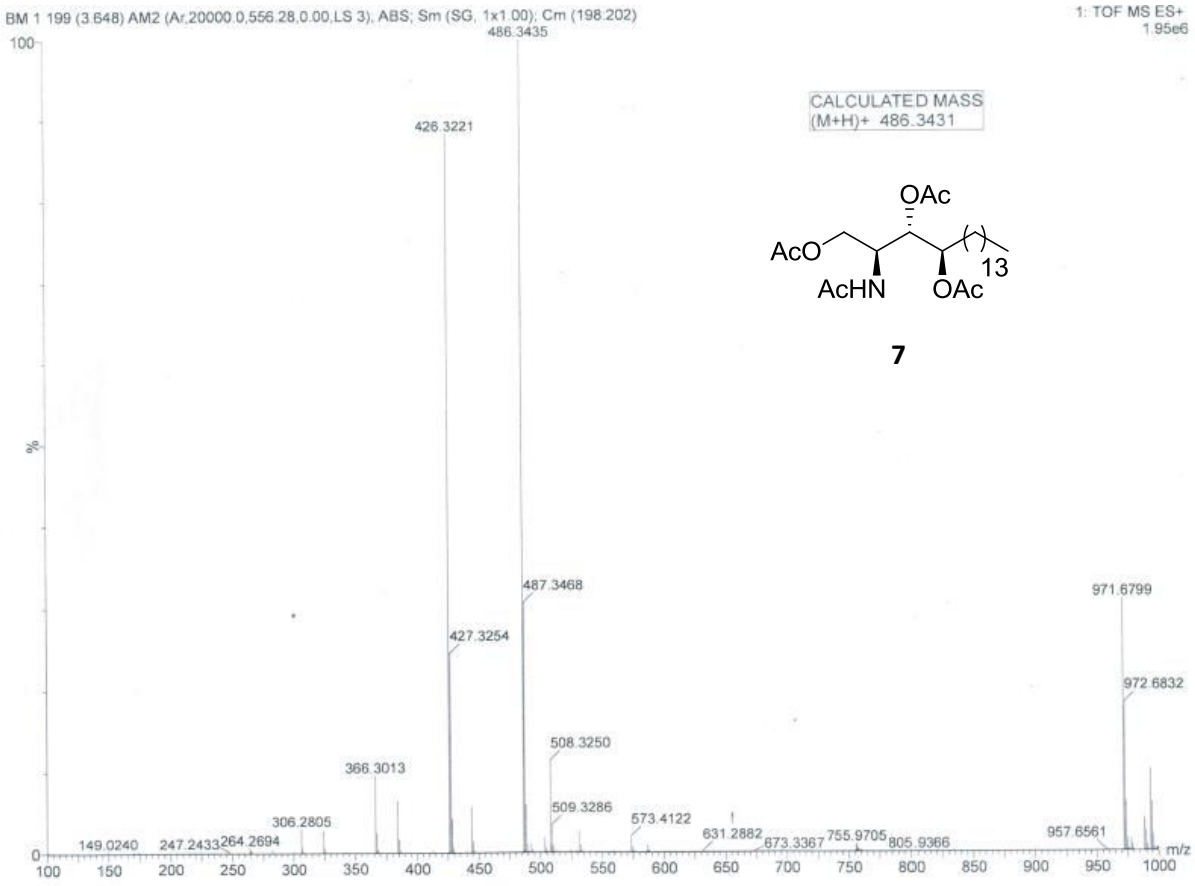

BNB 2 109 (2.014) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (108:111)
1: TOF MS ES+
1.59e5
CALCULATED MASS
(M+Na)+ 360.1786
BocHN
O
Ph
OH
4
%
m/z
238.1445
360.1792
697.3679
160.0977
264.1241
344.2056
361.1826
681.3940
698.3702
675.3851
699.3729
221.1185
161.1010
362.1862
425.2661
500.3587
556.2733
638.3322
736.2979
797.2944
838.2790
924.2365
953.2415

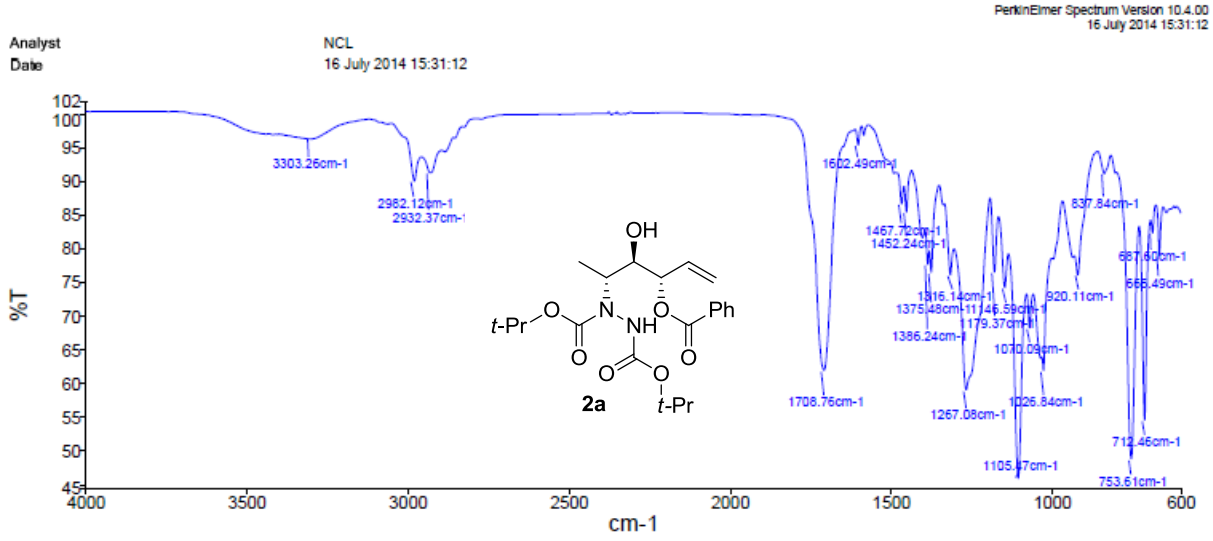

BHB 3 90 (1.650) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (89.92)
1: TOF MS ES+
7.91e5
CALCULATED MASS
(M+H)+ 441.2237
CO2iPr
NH
iPrO2C
N
O
Ph
OH
OH
3
441.2238
319.1873
191.1033
277.1401
442.2268
423.2127
320.1902
112.0767
235.0931
355.1866
464.2084
486.2810
529.2972
672.3109
689.2919
781.3886
881.4406
903.4213
904.4244
905.4274
880.8491
942.3556
976.4424
%
m/z


VSK NM1 141 (2.580) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00)
1: TOF MS ES+
7.48e5
CALCULATED MASS
(M+H)+ 625.255
OH
BnO
Bn
O
N
NH
O
Ph
O
O
O
O
Bn
2j
503.2217
504.2248
625.2517
459.2340
626.2550
181.1171
351.1812
389.1955
505.2279
415.2462
149.0396
271.1624
307.1933
581.2642
627.2573
506.2312
647.2326
712.3127
788.8217
854.5691
964.8136
%
m/z


VSK NM2 97 (1.789) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00)
1: TOF MS ES+
6.72e5
CALCULATED MASS
(M+H)+ 413.1712
HO
BnO
CbzHN
N
O
O
O
5
369.1913
825.3190
413.1792
826.3217
181.1171
414.1825
827.3245
430.2049
842.3451
189.1028
503.2221
691.2894
847.2996
233.0919
692.2935
781.3323
848.3031
171.0923
279.1474
504.2251
505.2264
646.2084
745.2064
887.3688
%
m/z


VSK GB 202 (3.699) AM2 (Ar,20000.0,556.28,0.00,LS 1); Sm (SG, 1x1.00)
1: TOF MS ES+
1.30e5
CALCULATED MASS
(M+H)+ 581.359
HO
11
BnO
CbzHN
N
O
O
6
%
537.3698
538.3724
493.3823
581.3573
263.2509
429.3174
582.3610
681.4147
149.0399
626.4108
682.4182
299.1515
255.1622
411.3102
181.1171
371.3048
713.6376
828.5897
872.6058
916.6295
993.5853
m/z


BM 1 199 (3.648) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (198.202)
1: TOF MS ES+
1.95e6
CALCULATED MASS
(M+H)+ 486.3431
OAc
AcO
AcHN
OAc
13
7
%
m/z
486.3435
426.3221
487.3468
427.3254
971.6799
972.6832
508.3250
366.3013
509.3286
573.4122
306.2805
631.2882
673.3367
755.9705
805.9366
957.6561
149.0240
247.2433
264.2694



Sample Name	Description	Quality Checks
BB1	BB1 By ncl Date Wednesday, July 16 2014	The Quality Checks give rise to a Window Cutoff warning for the sample.