Supporting Information

for

A unified approach to the important protein kinase inhibitor balanol and a proposed analogue

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Experimental details and characterization data for the prepared compounds are included. Copies of ^{1}H and ^{13}C NMR spectra of all new compounds are also provided. Data for comparison of 30 and 1 with reported data are also presented

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Experimental

General

Optical rotations were recorded in spectroscopic grade chloroform on a Jasco DIP-370 polarimeter, $[\alpha]_D$ values are recorded in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded on a Perkin-Elmer Spectrum-1 spectrophotometer purchased through a DST-FIST grant. Proton and carbon NMR spectra were recorded on a Bruker DRX-300 spectrometer. Chemical shifts are recorded relative to residual solvent or TMS as standard. Mass spectra were recorded on a JEOL-JMS 600 instrument from I. I. C. B., Kolkata or IACS, Kolkata. Petroleum ether refers to the fraction boiling in the range 60–80 °C. Silica gel (60–120 mesh) for column chromatography was purchased from Spectrochem, India.

2-(1,3-Dioxan-2-yl)-6-(methoxymethoxy)benzaldehyde (9):

n-BuLi (5.5 mL, 2 M in hexane) was added dropwise to a stirred solution of 2-(3-(methoxymethoxy)phenyl)-1,3-dioxane [1] (2.24 g, 10 mmol) in cyclohexane (15 mL) at room temperature and stirring was continued for 15 min. Then DMF (2.25 mL, 30 mmol) was slowly added to this reaction mixture and stirred for another 30 min. It was then quenched by slow addition of brine (20 mL) and extracted with ethyl acetate (2 × 50 mL). The combined organic extract was washed successively with water (2 × 50 mL) and brine (50 mL), and then dried (Na_2SO_4). It was filtered and the filtrate was concentrated in vacuo to leave a crude mass which on chromatographic purification over silica gel using a mixture of petroleum ether/ethyl acetate (95:5) as eluent provided compound **9** as a pale yellow solid (1.63 g, 65%). mp 58-60 °C. IR (KBr): 2930, 1694, 1598, 1590 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.63 (s, 1H), 7.54-7.50 (m, 2H), 7.27-7.21 (m, 1H), 6.26 (s, 1H), 5.27 (s, 2H), 4.23 (dd, *J* = 1.6, 5.2 Hz, 2H), 4.06 (dt, *J* = 12, 1.6 Hz, 2H), 3.49 (s, 3H), 2.25-2.20 (m, 1H), 1.47-1.43 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.0, 159.8, 139.9, 134.7, 122.9, 119.9, 115.6, 97.8, 94.7, 67.6, 56.4, 25.8; HRMS (TOF MS ES+): *m/z* calcd for $C_{13}H_{16}NaO_5$ (M^++Na): 275.0895. Found: 275.0893.

(2-(1,3-Dioxan-2-yl)-6-(methoxymethoxy)phenyl)(2,6-bis(benzyloxy)-4-((*tert*-butyldiphenylsilyloxy)methyl)phenyl)methanol (10):

n-BuLi (0.7 mL, 2 M in hexane) was added dropwise to a stirred solution of **8** (0.955 g, 1.5 mmol) in THF (10 mL) at −78 °C, and stirring was continued for 5 min. A solution of the aldehyde **9** (250 mg, 1 mmol) in THF (5 mL) was then added dropwise to the reaction mixture at −78 °C. It was allowed to

come to room temperature over 2 h and then cooled to 0 °C before being quenched with saturated aqueous NH_4Cl (5 mL). It was extracted with ethyl acetate (2 × 50 mL) and the combined organic extract was washed successively with water (50 mL) and brine (50 mL). It was then dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo to leave a crude mass which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) as eluent to provide compound **10** as a colourless viscous liquid (0.6 g, 75%). IR (KBr): 3469, 2928, cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 1.2 Hz, 4H), 7.43-7.41 (m, 3H), 7.4-7.34 (m, 4H), 7.32-7.23 (m, 6H), 7.21-7.7.12 (m, 4H), 6.98 (d, *J* = 12 Hz, 1H), 6.70 (d, *J* = 7.6 Hz, 1H), 6.56 (s, 2H), 6.11 (s, 1H), 5.23 (d, *J* = 8 Hz, 1H), 4.99 (s, 4H), 4.8 (dd, *J* = 10.8, 6.8 Hz, 2H), 4.63 (s, 2H), 4.13-4.08 (m, 2H), 3.98-3.82 (m, 1H), 3.69 (t, *J* = 12 Hz, 1H), 2.92 (s, 3H), 1.32-1.28 (m, 1H), 2.18-2.09 (m, 1H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 154.7, 141.4, 138.2, 136.9, 135.5, 133.4, 130.5, 129.7, 128.5, 127.7, 127.5, 127.2, 119.5, 118.6, 114.6, 103.7, 99.1, 93.7, 70.5, 67.3, 67.2, 66.7, 65.3, 55.4, 26.8, 25.7, 19.3. MS (TOF MS ES+): *m/z* (%) = 834 (M^++Na, 100).

(2-(1,3-Dioxan-2-yl)-6-(methoxymethoxy)phenyl)(2,6-bis(benzyloxy)-4-((*tert*-butyldiphenylsilyloxy)methyl)phenyl)methanone (11):

A solution of the benzylic alcohol **10** (0.81 g, 1 mmol) in CH_3CN (15 mL) was stirred for 15 min in the presence of molecular sieves (4 Å, 2 g). 4-Methylmorpholine *N*-oxide (0.175 g, 1.5 mmol) and tetrapropylammonium perruthenate (17.5 mg, 0.05 mmol) were then sequentially added and the resulting mixture was stirred for 18 h at room temperature. It was then diluted with ethyl acetate, filtered through Celite, concentrated in vacuo and the residual mass was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) to provide compound **11** as a colourless viscous liquid (0.645 g, 80%). IR (KBr): 2930, 2865, 1674, 1606, 1589 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 6.8 Hz, 4H), 7.43 (dt, *J* = 6.4, 0.8 Hz, 3H), 7.35 (m, 5H), 7.25-7.21 (m, 6H), 7.11-7.10 (m, 4H), 6.98 (d, *J* = 8 Hz, 1H), 6.55 (s, 2H), 5.61 (s, 1H), 4.96 (s, 4H), 4.73 (s, 2H), 4.66 (s, 2H), 4.08 (dd, *J* = 11.2, 4.4 Hz, 2H), 3.74 (t, *J* = 12 Hz, 2H), 2.95 (s, 3H), 2.1-2.14 (m, 1H), 1.31-1.24 (m, 1H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.7, 157.8, 154.2, 145.5, 138.2, 136.7, 135.5, 133.2, 132.1, 130.2, 129.8, 128.4, 127.8, 127.5, 126.9, 119.9, 119.8, 115.2, 102.8, 99.5, 94.1, 70.0, 67.3, 65.3, 55.5, 26.8, 25.7, 19.3. HRMS (TOF MS ES+): *m/z* calcd for $C_{50}H_{53}O_8Si(M^+$+H): 809.3501. Found: 809.3505 (M^++H).

2-(2,6-Bis(benzyloxy)-4-((*tert*-butyldiphenylsilyloxy)methyl)benzoyl)-3-(methoxymethoxy)benzaldehyde (12):

p-Toluenesulfonic acid (25 mg) was added to a solution of the benzophenone **11** (0.81 g, 1 mmol) in acetone/water (20 mL, 9:1) and the resulting solution was refluxed gently for 4 h. It was allowed to come to room temperature, concentrated in vacuo and then diluted with ethyl acetate (200 mL). The ethyl acetate extract was washed successively with water (100 mL) and brine (100 mL), and then dried (Na_2SO_4). It was filtered and the filtrate was concentrated in vacuo to leave a crude mass which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) as eluent to provide compound **12** as a colourless viscous liquid (0.67 g, 89%). IR (KBr): 2932, 2859, 1693, 1672, 1584 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 9.95 (s, 1H), 7.63 (d, *J* = 6.8 Hz, 4H), 7.46-7.43 (m, 3H), 7.38-7.35 (m, 5H), 7.25-7.19 (m, 7H), 7.11-7.08 (m, 4H), 6.61 (s, 2H), 4.93 (s, 4H), 4.81 (s, 2H), 4.70 (s, 2H), 3.00 (s, 3H), 1.08 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.0, 191.3, 157.7, 154.6, 146.2, 136.5, 136.2, 136.1, 135.5, 133.2, 130.5, 129.9, 128.5, 127.9, 127.8, 127.2, 120.9, 119.5, 119.2, 102.7, 94.2, 70.4, 65.3, 55.8, 26.9, 19.3. MS (TOF MS ES+): *m/z* (%) = 774 (M^++Na, 100).

General procedure of the $NaClO_2$-oxidation of an aldehyde to a carboxylic acid:

Aq. NaH_2PO_4 (1.5 mL, 1 M), 1-methylcyclohexene (120 µL, 1 mmol) and $NaClO_2$ (181 mg, 2 mmol) were sequentially added to a solution of the aldehyde (0.5 mmol) in THF-*t*-BuOH-water (5 mL, 4:4:1), and the resulting mixture was stirred for 6–8 h at room temperature before being treated with aqueous $KHSO_4$ (5 mL, 0.5 M). The resulting reaction mixture was concentrated in vacuo and then extracted with ethyl acetate (2 × 50 mL). The combined organic extract was washed successively with water (50 mL), saturated aqueous sodium sulfite (10 mL) and brine (50 mL). It was then dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo to leave a crude mass which was purified by chromatography over silica gel to produce the corresponding pure carboxylic acid.

2-(2,6-Bis(benzyloxy)-4-((*tert*-butyldiphenylsilyloxy)methyl)benzoyl)-3-(methoxymethoxy)benzoic acid (13):

Yield: 82%. IR (KBr): 3403, 1767, 1696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) : δ 8.43 (s), 7.63 (dd, *J* = 7.6, 1.2 Hz), 7.46-7.35 (m), 7.22-7.21 (m), 7.08-7.06 (m), 6.80-6.78 (m), 6.55 (brs), 5.23 (brs), 5.16 (d, *J* = 6.4 Hz), 5.50 (d, *J* = 6.4 Hz), 4.92 (br s), 4.71-4.69 (overlapping singlets), 3.17(s), 1.07 (s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.8, 170.7, 169.1, 159.1, 156.9, 154.1, 151.1, 146.6, 144.2, 139.7, 136.4, 135.5,

135.2, 133.2, 130.7, 129.9, 129.1, 129.0, 129.9, 129.1, 129.0, 128.7, 128.5, 128.3, 127.8, 127.6, 127.3, 123.7, 119.4, 118.9, 117.8, 112.0, 105.6, 104.5, 104.1, 102.9, 94.5, 93.8, 72.7, 70.7, 70.5, 65.3, 65.0, 55.9, 55.8, 29.7, 26.8, 19.3. HRMS (TOF MS ES+): *m/z* calcd for $C_{47}H_{46}NaO_8Si$ (M^+ + Na) : 789.2860. Found: 789.2858. [spectral data revealed the presence of an equilibrium between ketocarboxilic acid and its hemiketal form and hence counting of protons is not included. This has also been observed [2] by Nicolaou et al.].

3,5-Bis(benzyloxy)-4-(2-(benzyloxy)-6-benzyloxycarbonyl)benzoic acid (7):

Yield: 87%. IR (KBr): 3441, 1718, 1698, 1652, 1583 cm^{-1}. mp 158-160 °C [Lit. [2] mp 158-160 °C]; ^1H NMR (400 MHz, $CDCl_3$): δ 7.33-7.0 (m, 16H), 7.14 (t, *J* = 7.2 Hz, 2H), 7.08-7.07 (m, 4H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 2H), 5.14 (s, 2H), 4.80 (s, 4H), 4.72 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7, 171.0, 167.6, 157.9, 156.5, 136.1, 135.8, 135.6, 133.1, 131.7, 131.6, 130.9, 128.4, 128.3, 128.0, 127.7, 127.2, 124.7, 122.1, 115.2, 107.2, 70.6, 70.4, 67.2.

2-(2,6-Bis(benzyloxy)-4-(hydroxymethyl)benzoyl)-3-hydroxybenzoic acid (14):

Hydrochloric acid (12 N, 0.2 mL) was added to a solution of the carboxylic acid **13** (380 mg, 0.5 mmol) in methanol (6 mL) and the resulting mixture was stirred at 50 °C for 2 h. It was then concentrated in vacuo, diluted with water (25 mL) and extracted with ethyl acetate (2 × 25 mL). The combined organic extract was successively washed with saturated sodium bicarbonate (2 × 25 mL), water (25 mL) and brine (25 mL). It was then dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo to leave a crude solid which was purified over silica gel using a mixture of petroleum ether/ethyl acetate/methanol (50:48:2) to provide compound **14** as a colourless solid (200 mg, 83%). mp 210-212 °C. IR (KBr): 3488, 2865, 1692, 1625, 1610, 1576 cm_{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 10.04 (s, 1H), 7.28-7.24 (m, 7H), 7.20-7.18 (m, 4H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.89 (dd, *J* = 8, 0.4 Hz, 1H), 6.72 (s, 2H), 5.36 (brs, 1H), 4.98 (s, 4H), 4.48 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 193.1, 169.4, 158.3, 156.7, 147.8, 137.4, 134.8, 131.3, 128.6, 128.5, 127.8, 127.3, 120.0, 119.4, 118.5, 103.8, 70.1, 63.2. Anal. Calcd for $C_{29}H_{24}O_7$: C, 71.89; H, 4.99. Found: C, 71.62; H, 5.27.

Benzyl 3-(benzyloxy)-2-(2,6-bis(benzyloxy)-4 (hydroxymethyl)benzoyl) benzoate (15):

Potassium carbonate (175 mg, 1.25 mmol) was added to a stirred solution of **14** (0.242 g, 0.5 mmol) and benzyl bromide (125 µL, 1.05 mmol) in *N*,*N*-dimethylformamide (10 mL) and the resulting solution was stirred for 24 h at room temperature. The reaction mixture was then poured into water (50 mL) and extracted with ethyl acetate (2 × 25 mL). The combined organic extract was successively washed with water (2 × 25 mL) and brine (25 mL). It was then dried (Na_2SO_4), filtered and concentrated in vacuo to leave a crude solid which was purified over silica gel using a mixture of petroleum ether/ethyl acetate (6:4) to provide the *O*-benzylated compound **15** as a colourless solid (0.26 g, 78%). mp 138-140 °C [Lit. [2] mp 138.5-139.5 °C]; IR (KBr): 3293, 1697, 1656, 1614, 1535 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.22-7.21 (m, 5H), 7.20-7.15 (m, 9H), 7.13-7.12 (m, 2H), 7.09-7.06 (m, 4H), 6.97 (d, *J* = 7.2 Hz, 2H), 6.89 (d, *J* = 8 Hz, 1H), 6.50 (s, 2H), 5.12 (s, 2H), 4.77 (s, 6H), 4.60 (d, *J* = 3.2 Hz, 2H) 1.89 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.4, 167.0, 159.0, 155.8, 147.0, 136.6, 136.3, 136.0, 134.4, 131.5, 129.6, 128.3, 128.2, 128.1, 127.9, 127.6, 127.5, 127.2, 127.1, 122.2, 118.3, 115.6, 103.4, 70.5, 70.4, 66.8, 64.6. HRMS (TOF MS ES+): *m/z* calcd for $C_{43}H_{36}NaO_7$: 687.2359 (M^++Na): Found : 687.2357.

Benzyl 3-(benzyloxy)-2-(2,6-bis(benzyloxy)-4-formylbenzoyl)benzoate (16):

A solution of the alcohol **15** (332 mg, 0.5 mmol) in dichloromethane (10 mL) was stirred with MnO_2 (435 mg, 5 mmol) for 12 h. It was then filtered through Celite and the filtrate was concentrated in vacuo to leave a crude mass which was purified over silica gel using a mixture of petroleum ether/ethyl acetate (3:1) as eluent to provide the aldehyde **16** as a colourless solid (300 mg, 91%). mp 110-112 °C [Lit. [2] mp 110-112 °C]; IR (KBr): 1721, 1695, 1670, 1579 cm^{-1} .^1H NMR (400 MHz, $CDCl_3$): δ 9.81 (s, 1H), 7.3 (t, *J* = 8 Hz, 1H), 7.26-7.21 (m, 13H), 7.11-7.06 (m, 6H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.90 (s, 2H), 6.83 (d, *J* = 7.6 Hz, 2H), 5.14 (s, 2H), 5.81 (s, 4H), 4.70 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.5, 191.4, 167.6, 158.3, 156.7, 138.2, 136.0, 135.8, 135.5, 133.4, 131.3, 131.1, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.1, 125.3, 122.0, 115.1, 106.5, 70.6, 70.4, 67.2. MS (TOF MS ES+): *m/z* (%) = 685 (M^++Na, 100).

(*R*)-*tert*-Butyl 4-((allylamino)methyl)-2,2-dimethyloxazolidine-3-carboxylate (18):

A solution of Garner's aldehyde **17** (1.15 g, 5 mmol) in tetrahydrofuran (15 mL) was stirred at room temperature with allyl amine (410 µL, 5.5 mmol) and $MgSO_4$ (2.65 g, 22 mmol) under nitrogen for

12 h. Then it was cooled to 0 °C and $NaBH_4$ (0.208 g, 5.5 mmol) was added in portions under nitrogen atmosphere. The reaction mixture was allowed to come to room temperature and stirred for 12 h. It was then quenched by adding of 5% NH_4Cl solution at 0 °C. It was diluted with water (50 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layer was washed successively with water (2 × 50 mL) and brine (50 mL). It was then dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo to leave a pale yellow liquid which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (93:7) as eluent to give the product **18** as a colourless liquid (1.28 g, 94%). $[\alpha]_D^{25} = +15.8$ (*c* 1.56, $CHCl_3$). IR (KBr): 3438, 1700 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$) : δ 5.77-5.69 (m, 1H), 5.02 (d, *J* =17.2 Hz, 1H), 4.94 (br m, 1H), 3.79 (s, 2H), 3.68 (br s, 1H), 3.12-3.11 (m, 2H), 2.76-2.65 (m, 1H), 2.50-2.48 (m, 1H), 1.48-1.33 (overlapping singlets, 15H). ^{13}C NMR (100MHz, $CDCl_3$): δ 152.4 (151.7), 136.8, 115.8, 93.3 (93.7), 80.1 (79.6), 66.3, 57.4 (57.1), 52.3 (52.2), 51.0 (50.9), 28.4, 27.5 (26.7), 24.3 (23.0).

(*R*)-*tert*-Butyl 4-((allyl(benzyloxycarbonyl)amino)methyl)-2,2-dimethyloxazolidine-3-carboxylate (19):

Water (0.5 mL) and benzyl chloroformate (0.78 mL, 5.5 mmol) were added sequentially at room temperature to a stirred solution of the amine **18** (1.35 g, 5 mmol) and sodium bicarbonate (1.26 g, 15 mmol) in ethyl acetate (20 mL), and the resulting reaction mixture was stirred overnight. It was quenched by dropwise addition of pyridine (350 µL, 4.3 mmol) and then stirred for 10 min before being diluted with ethyl acetate (50 mL). The combined organic layer was washed successively with 1 N HCl (50 mL), water (50 mL), brine (50 mL) and then dried over Na_2SO_4. It was filtered and the filtrate was concentrated under reduced pressure to leave a pale yellow liquid which was purified by chromatography over silica gel with petroleum ether/ethyl acetate (93:7) as eluent to give the product **19** as a colourless liquid (1.8 g, 95 %). $[\alpha]_D^{25} = +5$ (*c* 1.75, $CHCl_3$). IR(neat): 1697, 1645, 1398, 1233, 1075,769 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$): δ 7.38-7.35 (m,5H), 5.79 (br s, 1H), 5.16 (m, 4H), 4.11-4.01 (m, 5H), 3.95-3.87 (m, 1H), 3.65-3.26 (m, 1H), 1.6-1.48 (overlapping siglets,15H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9 (156.5), 151.5 (152.1), 136.4, 133.0, 127.7 (128.3), 127.2, 126.7, 116.5 (117.0), 93.3 (94.0), 79.8 (80.0), 67.1, 65.1 (65.7), 55.7 (55.9), 49.8 (50.0), 47.4 (48.0), 28.2, 26.8 (27.4), 22.9 (24.2). HRMS (TOF MS ES+): *m/z* calcd for $C_{22}H_{32}N_2NaO_5$ 427.2209 (M^++Na): Found: 427.2208.

(*R*)-benzyl allyl(2-((*tert*-butoxycarbonyl)amino)-3-hydroxypropyl)carbamate (20)

Hydrochloric acid (1.25 mL, 5%) was added dropwise while stirring to an ice-cooled solution of compound **19** (0.5 g, 1.24 mmol) in methanol (10 mL) and stirring was continued for 1 h at 0 °C, and then at room temperature for 5 h. The reaction mixture was quenched with saturated sodium bicarbonate solution and then extracted with ethyl acetate (2 x 25 mL). The combined organic extract was washed successively with water (10 mL), brine (10 mL) and then dried (Na_2SO_4). It was filtered and the filtrate was concentrated under reduced pressure to leave a crude product which on chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (4:1) afforded the product **20** as a colourless viscous liquid (405 mg, 90%). $[\alpha]_D^{25} =$ - 8 (*c* 3.00, $CHCl_3$). IR (neat): 3435, 1702, 1693, 1391, 1248, 1169, 1063 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.25 (m, 5H), 5.79-5.72 (m, 1H), 5.17-5.14 (m, 4H), 3.97 (dd, *J* = 14, 5 Hz, 1H), 3.80 (dd, *J* = 16, 5.5 Hz, 1H), 3.68-3.62 (m, 1H), 3.59-3.56 (m, 3H), 3.50-3.47 (m, 1H), 3.13(dd, *J* = 14, 5 Hz, 1H), 1.68 (br s, 1H), 1.42 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6, 155.6, 136.1, 132.8, 128.4, 128.0, 127.6, 117.2, 79.3, 67.6, 64.8, 61.4, 50.1, 46.6, 28.2; MS (TOF MS ES+): *m/z* (%) = 387 (M^+ + Na, 100).

***tert*-Butyl (2*R*,3*R*)-1-(*N*-benzyloxycarbonyl(allyl)amino)-3-hydroxypent-4-en-2-ylcarbamate (22) and *tert*-butyl (2*R*,3*S*)-1-(*N*-benzyloxycarbonyl(allyl)amino)-3-hydroxypent-4-en-2-ylcarbamate (23):**

A solution of DMSO (310 µL, 4.2 mmol) in CH_2Cl_2 (2 mL) was added dropwise to a stirred solution of oxalyl chloride (155 µL, 1.8 mmol) in CH_2Cl_2 (3 mL) at −78 °C. It was then stirred for 20 min at the same temperature. A solution of the alcohol **20** (0.55 g, 1.5 mmol) in CH_2Cl_2 (5 mL) was then added dropwise to the reaction mixture. It was then warmed to −25 °C and stirred at this temperature for 35 min followed by dropwise addition of diiospropylethylamine (1.8 mL, 10.5 mmol). Stirring was continued at the same temperature for another 10 min. The reaction mixture was cooled back to −78 °C and diluted with THF (20 mL). Then vinylmagnesium bromide (6 mL, 1 M solution in THF) was added dropwise to the reaction mixture. The reaction mixture was allowed to warm to −40 °C and stirred at this temperature for 2 h. Then the reaction mixture was allowed to come to room temperature and stirred for 8 h before being quenched by slow addition of saturated aq NH_4Cl (10 mL) at 0 °C. It was extracted with ethyl acetate (2 × 25 mL) and the combined organic extract was washed successively with HCl (1 N, 2 × 20 mL), H_2O (2 × 20ml) and brine (20 mL). After drying (Na_2SO_4), it was filtered and the filtrate was concentrated in vacuo to leave a pale yellow crude product which on chromatographic purification over silica gel using a mixture of petroleum

ether/ethyl acetate (85:15) as eluent provided sequentially the diastereomeric alcohols **22** and **23** as colorless liquids in a combined yield of 64%.

Compound 22: Yield: 0.255 mg (43.5%). $[\alpha]_D^{25} = -8$ (*c* 1.5, $CHCl_3$). IR (neat): 3416, 1687 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$) : δ 7.36-7.34 (m, 5H), 5.85-5.74 (m, 2H), 5.37 (d, *J* = 16 Hz, 1H), 5.21-5.15 (m, 5H), 4.94 (d, *J* = 8 Hz, 1H), 4.16-3.98 (br m, 3H), 3.89-3.62 (br m, 3H), 3.14(dd, *J* = 13.6, 4.8 Hz, 1H), 1.45-1.41 (s, 9H). ^{13}C NMR (100MHz, $CDCl_3$): δ 157.9, 156.0, 136.7, 136.2, 132.8, 128.6, 128.2, 127.8, 117.6, 116.0, 79.4, 69.4, 67.9, 52.5, 50.3, 47.7, 28.3 (27.9). HRMS (TOF MS ES+) *m/z* calcd for $C_{21}H_{30}N_2NaO_5$ (M^++Na): 413.2052. Found. 413.2051.

Compound 23: Yield: 0.12 g (20.5%). $[\alpha]_D^{25} = +9$ (*c* 2.0, $CHCl_3$). IR (KBr): 3437, 2977, 2930, 1698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.33 (m, 5H), 5.88-5.73 (m, 2H), 5.30 (d, *J* = 17 Hz, 1H), 5.16-5.10 (m, 7H), 4.14 (br s, 1H), 3.94-3.78 (m, 3H), 3.56-3.52 (m, 1H), 3.33-3.30 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 156.3, 137.0, 136.3, 133.0, 128.5, 128.1, 127.8, 117.2, 115.7, 79.7, 73.8, 67.6, 54.0, 50.0, 46.0, 28.3. HRMS (TOF MS ES+) *m/z* calcd for $C_{21}H_{30}N_2NaO_5$ (M^++Na): 413.2052. Found. 413.2054.

Mitsunobu inversion of 23 to 22:

4-Nitrobenzoic acid (167 mg, 1 mol), PPh_3 (262 mg, 1 mmol) and diethylazodicarboxylate (157.5 µL, 1 mmol) were sequentially added to a solution of **23** (195 mg, 0.5 mmol) in anhydrous THF (10 mL) at 0 °C. Then the reaction mixture was allowed to come to room temperature and stirred for 24 h. Then it was diluted with ethyl acetate (25 mL) and washed successively with saturated aqueous $NaHCO_3$ and then with water (20 mL) and brine (20 mL). It was then dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo to leave a crude product which was used without further purification for the next step. A solution of this crude product in methanol/water (10 mL, 9:1) was stirred with K_2CO_3 (350 mg, excess) for 4 h. Then the reaction mixture was filtered and concentrated in vacuo, diluted with ethyl acetate (25 mL), washed with water (20 mL) and brine (20 mL), and then dried (Na_2SO_4), filtered and concentrated in vacuo to provide a crude liquid which was purified by column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) to produce compound **22** as colourless liquid (140 mg, 72%).

(3*R*,4*R*)-5-(*N*-Benzyloxycarbonyl(allyl)amino)-4-(*tert*-butoxycarbonylamino)pent-1-en-3-yl acetate (24):

Acetic anhydride (71 µL, 0.75 mmol) and DMAP (0.01 g) were added to a stirred solution of the alcohol **22** (195 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) at room temperature under nitrogen and the reaction mixture was stirred for 12 h before being poured into ice-cooled water (20 mL). The resulting mixture was stirred for 30 min and then extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with H_2O (2 × 25 mL) followed by brine (25 mL). It was dried over Na_2SO_4, filtered and the filtrate was concentrated in vacuo to leave a crude product which was purified by column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (9:1) to produce compound **24** as a colourless liquid (182 mg, 84%). $[\alpha]_D^{25} = -15$ (*c* 2.0, $CHCl_3$). IR (neat): 3352, 1745, 1712, 1644, 1502, 1367, 1235, 1166, 1025, 770, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39-7.36 (m, 5H), 5.84-5.73 (m, 2H), 5.31-5.14 (m, 7H), 4.91 (d, *J* = 9.6 Hz, 1H), 4.17-4.06 (m, 2H), 3.82-3.78 (m, 1H), 3.57-3.51 (m, 1H), 3.38-3.24 (m, 1H), 2.13(1.89) (s, 3H), 1.46 (1.42) (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5 (170.3), 157.3, 155.8 (155.5), 136.5(136.2), 133.2, 133.1(132.7), (128.6) 128.5, 128.3 (128.0), 127.7, 118.3 (118.1), 117.1 (117.6), 79.5 (79.9), 73.6 (73.5), 67.4 (67.7), 51.0(50.5), 49.3 (49.7), 45.4 (44.7), 35.4, 28.3, 21.0 (20.8). MS (TOF MS ES+): *m/z* (%) = 455 (M^++Na, 100). Anal. Calcd for $C_{23}H_{32}N_2O_6$: C, 63.87; H, 7.46; N, 6.48. Found: C, 64.09; H, 7.65; N, 6.61.

(3*R*,4*R*,*Z*)-Benzyl 4-acetoxy-3-(*tert*-butoxycarbonylamino)-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (26):

Catalyst **25** (0.011 g, 0.0125 mmol) was added to a stirred solution of the diene **24** (110 mg, 0.24 mmol) in dry and degassed CH_2Cl_2 (25 mL) under argon and the homogeneous mixture was gently refluxed for 12 h. It was then concentrated in vacuo to leave a crude product which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) to produce compound **26** as colourless viscous liquid (95 mg, 89 %); $[\alpha]_D^{25} =$ **-12** (*c* 2.0, $CHCl_3$). IR(KBr): 3350, 1738, 1713, 1699, 1504,1367, 1240, 1167, 1037, 771 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$) : δ 7.39-7.33 (m,5H), 5.74-5.48 (m, 3H), 5.24-5.12 (m, 2H), 4.79 (d, *J* = 9.2, 1H), 4.59-4.46 (m, 1H), 4.25-4.11 (m, 1H), 3.89-3.65 (m, 2H), 3.51 (dd, *J* = 15, 7.2, 1H), 2.06-2.02 (m,3H), 1.43-1.38 (singlets, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4 (170.3), 156.5 (155.5), 155.3 (154.9), 136.1, 129.4, 129.0, 128.5(128.4), 128.1, 127.7 (127.2), 79.2 (79.4), 72.9 (72.0), 67.6, 53.6 (52.8), 49.9 (49.0), 48.3 (47.9), 28.2, 20.7 (20.8). HRMS (TOF MS ES+): calcd for $C_{21}H_{28}N_2NaO_6$ (M^+ + Na): 427.1845. Found: 427.1848.

(3*R*,4*R*,*Z*)-Benzyl 3-(*tert*-butoxycarbonylamino)-4-hydroxy-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (27):

K_2CO_3 (345 mg, 2.5 mmol) was added to a stirred solution of **26** (100 mg, 0.25 mmol) in MeOH (2 mL) and the resulting mixture was stirred for 4 h at room temperature. Then the reaction mixture was filtered, concentrated in vacuo and extracted with ethyl acetate (2 × 25 mL). The ethyl acetate extract was washed with water (2 × 25 mL) and brine (25 mL), and dried (Na_2SO_4). It was filtered and the filtrate was concentrated in vacuo to leave a crude product which on chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (5:1) provided the product **27** as a colourless viscous liquid (80 mg, 89%); $[\alpha]_D^{25} =$ - 20.0 (*c* 2.0, $CHCl_3$). IR (neat): 3410, 1694 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$) : δ 7.37-7.35 (m, 5H), 6.35 (br s, 1H), 5.69 (d, *J* = 8 Hz, 1H), 5.41 (d, *J* = 11 Hz, 1H), 5.21-5.12 (m, 2H), 4.58-4.54 (m, 2H), 4.17-4.11 (m,1H), 3.92-3.91 (m, 1H), 3.82 (d, *J* = 15 Hz, 1H), 3.67-3.62 (m, 1H), 3.50 (dd, *J* = 15, 6 Hz, 1H), 1.45-1.40 (s, 9H); ^{13}C NMR (400MHz, $CDCl_3$) : δ 157.9, 157.0, 136.1, 134.2 (133.5), (128.8) 128.6, (128.5) 128.4, (128.3) 127.8, 124.4, 80.3, 73.8, (68.0) 67.8, 58.1 (56.7), 49.2, 48.7 (48.4), 28.4; HRMS (TOF MS ES+): *m/z* calcd for $C_{19}H_{26}N_2NaO_5$ (M^++Na): 385.1740. Found: 385.1755.

(3*R*,4*R*,*Z*)-Benzyl 3-amino-4-hydroxy-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (28):

An ice-cooled solution of TFA (1 mL, excess) in CH_2Cl_2 (1 mL) was added to the alcohol **27** (70 mg, 0.2 mmol) at 0 °C. The reaction mixture was allowed to come to room temperature and stirred for another 1 h. Then the reaction mixture was concentrated in vacuo, basified by slow addition of saturated aqueous sodium bicarbonate (10 mL), and extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed successively with water (2 × 25 mL) and brine (25 mL), dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo to provide a crude mass. It was then purified by chromatography over silica gel using a mixture of chloroform/methanol (95:5) to provide the product **28** as colourless liquid (39 mg, 76 %). $[\alpha]_D^{25} =$ - 12.8 (*c* 1.3, $CHCl_3$). IR(KBr): 3357, 3290,1683 cm^{-1}.^{1}H NMR (400MHz, $CDCl_3$) : δ 7.37-7.35 (m, 5H), 5.77-5.71 (m, 2H), 5.20-5.11 (m, 2H), 4.16-4.10 (m, 1H), 3.99 (t, *J* = 13 Hz, 1H), 3.85-3.80 (m, 2H), 3.47-3.37 (m, 1H), 2.89-2.85 (m, 1H), 2.55 (br s, 3H). ^{13}C NMR (400MHz, $CDCl_3$): δ 156.1 (155.6), 136.5, 135.2 (134.7), (128.6) 128.5, (128.2) 128.1, 127.7, (126.7) 126.3, 73.1 (72.6), (67.5) 67.4, 55.6 (55.3), 53.3 (52.9), (46.7) 46.5. HRMS (TOF MS ES+): *m/z* calcd for $C_{14}H_{19}N_2O_3$ (M^++H): 263.1396. Found: 263.1395.

(3*R*,4*R*,*Z*)-Benzyl 3-(4-(benzyloxy)benzamido)-4-hydroxy-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (29):

A suspension of the amino alcohol **28** (33 mg, 0.125 mmol), *p*-benzyloxybenzoic acid (28 mg, 0.125 mmol) and EDC·HCl (29 mg, 0.125 mmol) in CH_2Cl_2 (2.5 mL) was treated with DMAP (8 mg, 0.06 mmol) at room temperature under nitrogen and the resulting solution was stirred for 24 h. It was then quenched with water (5 mL) and extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extract was washed successively with water (2 × 20 mL) and brine (20 mL), and dried (Na_2SO_4). It was filtered and the filtrate was concentrated in vacuo to provide a crude mass which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate/methanol (60:40:1) as eluent to provide compound **29** as a gummy liquid (51 mg, 84%). $[\alpha]_D^{25} =$ - 45.2 (*c* 1.67, $CHCl_3$). IR (KBr): 3391, 1720, 1661 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$) : δ 8.67 (d, *J* = 5.6 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.45-7.35 (m, 11H), 7.03 (d, *J* = 8.8 Hz, 2H), 5.74 (d, *J* = 12 Hz, 1H), 5.43-5.41 (m, 1H), 5.21 (s, 2H), 5.13 (s,2H), 4.66-4.61 (m,2H), 4.30 (dd, *J* = 12.0, 5.8 Hz, 1H), 4.0-3.92 (m, 1H), 3.71 (d, *J* = 18 Hz, 1H), 3.62 (dd, *J* = 15.2, 5.6 Hz, 1H). ^{13}C NMR (400MHz, $CDCl_3$): δ 168.8, 161.7, 157.7, 136.4, 136.0, 134.6, 129.2, 128.7, 128.6, 128.4, 128.2, 127.9, 127.5, 125.6, 123.9, 114.7, 74.6, 70.1, 68.1, 59.4, 48.8 48.5. MS (TOF MS ES+): *m/z* (%) = 495 (M^+ +Na, 100).

(3*R*,4*R*)-Benzyl 3-(4-(benzyloxy)benzamido)-4-hydroxyazepane-1-carboxylate (30):

A solution of the olefin **29** (25 mg, 0.022 mmol) in ethyl acetate (2 mL) was stirred vigorously in the presence of Pd/C (5%, 5 mg) at room temperature under hydrogen for 30 min. It was then filtered through Celite, washed with ethyl acetate (5 mL) and the combined filtrate was concentrated in vacuo to provide a crude product which on column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (60:40) as eluent produced compound **30** as a colourless solid (16 mg, 66%). mp 120-122 °C [Lit. [2] mp: 123 ^{0}C]. $[\alpha]_D$: - 72.0 (*c* 2.0, $CHCl_3$). [Lit. [2] $[\alpha]_D$: - 73.0 (*c* 1.0, $CHCl_3$).]. IR (KBr): 3442, 1502, 1367, 1235, 1166, 1025, 770,699 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.72 (d, *J* = 5.4 Hz, 1H), 7.81 (d, *J* = 8.8 Hz, 2H), 7.44-7.29 (m, 10H), 7.02 (d, *J* = 8.8 Hz, 2H), 5.43 (br s, 1H), 5.20 (ABq, *J* = 12.3 Hz, 2H), 5.13 (s, 2H), 4.20 (dd, J = 14.2, 3.75 Hz, 2H), 4.16 (d, J = 15.8 Hz, 1H), 4.10-4.06 (m, 1H), 3.76 (dd, J = 8.9, 6.5 Hz, 1H), 3.34 (dd, *J* = 5.1, 15.3 Hz, 1H), 2.79 (dt, J = 13.6, 3.4 Hz, 1H), 1.97-1.93 (m, 1H), 1.90-1.81 (m, 2H), 1.70-1.67 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.5, 161.6, 157.7, 136.4, 136.2, 129.1, 128.6, 128.4, 128.2, 128.1, 127.7, 127.4, 125.7, 114.7, 79.5, 70.0, 67.8, 60.7, 50.4, 50.2, 32.7, 27.2.MS (TOF MS ES^+): *m/z* (%) = 513 (M^++K, 100).

(3*S*,4*S*,*Z*)-Benzyl 3-(4-(benzyloxy)benzamido)-4-(3,5-bis(benzyloxy)-4-(2-(benzyloxy)-6-(benzyloxy-carbonyl)benzoyl)benzoyloxy)-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (31):

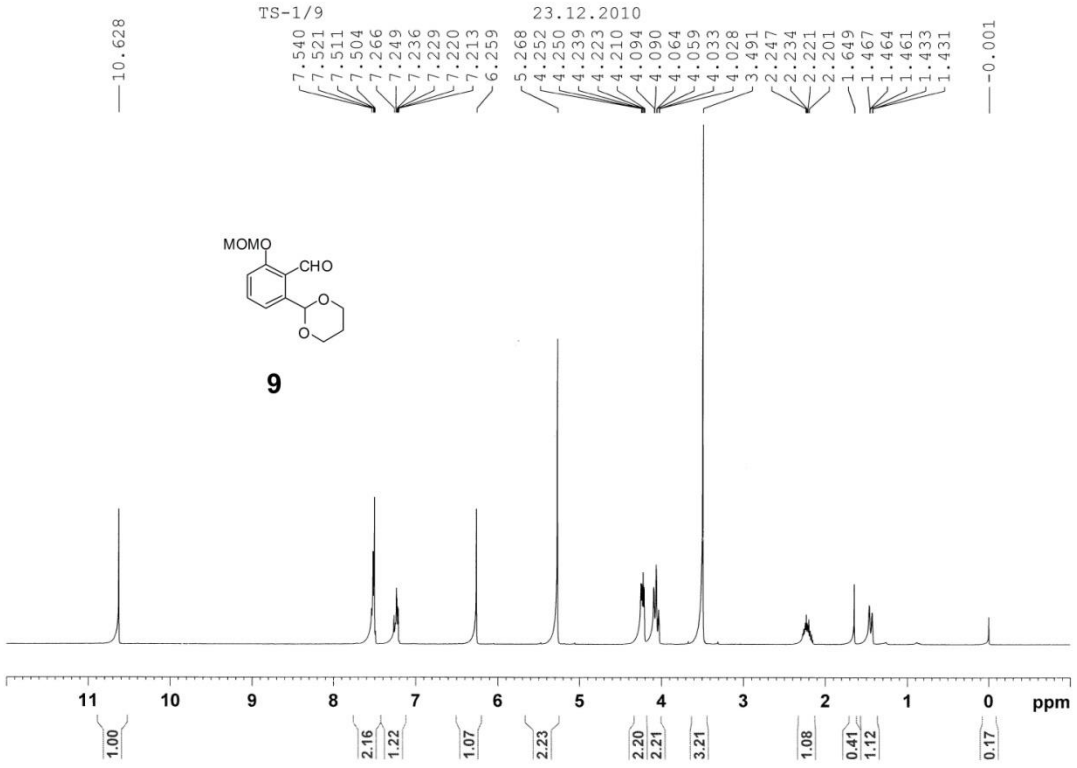
A mixture of the amido alcohol **29** (25 mg, 0.05 mmol), acid **7** (35 mg, 0.05 mmol) and 2-chloro-1-methylpyridinium iodide (16.5 mg, 0.065 mmol) in CH_2Cl_2 (2.5 mL) was treated with Et_3N (15 µL, 0.1 mmol) at room temperature under nitrogen and stirred for 30 min. Then DMAP (3 mg, 0.025 mmol) was added and the resulting mixture was stirred for another 1 h at room temperature. It was then filtered through a pad of silica, concentrated in vacuo to produce a crude mass which on chromatographic purification over silica gel using a mixture of petroleum ether/ethyl acetate (7:3) as eluent provided the compound **31** (41 mg, 73%). $[\alpha]_D^{25} =$ - 66.1 (*c* 1.1, $CHCl_3$). IR(KBr): 3351,2924, 1728, 1660 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$) : δ 7.86 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.45-7.35 (m, 12H), 7.30-7.28 (m, 4H), 7.25-7.24 (m, 3H), 7.21-7.71 (m, 14H), 7.11-7.10 (m, 6H), 7.06-7.02 (m, 2H), 6.92-6.89 (m, 2H), 6.83-6.82 (m, 2H), 5.80-5.73 (m, 2H), 5.67-5.64 (m, 1H), 5.36-5.33 (m, 1H), 5.26-5.23 (m, 1H), 5.10-5.07 (m, 3H), 5.04-5.03 (m, 3H), 4.9-4.79 (m, 6H), 4.68 (s, 2H), 4.07-4.03 (m, 1H), 3.77 (d, *J* = 16.4 Hz, 1H), 3.68 (dd, *J* = 15, 6.8 Hz, 1H). ^{13}C NMR (400MHz, $CDCl_3$) : δ 191.7, 167.33, (166.1) 165.9, 161.4, 158.1 (158.0), 157.4 (156.2), 136.4 (136.0), 135.8, 132.6 (132.4), 130.5 (130.4), 129.6, 128.9, 128.7 (128.6), 128.5, 128.9, 127.7 (128.6), 128.5, 128.4, 128.3, 128.2, 128.18, 128.0, 127.9, 127.7, 127.5, 127.4, 127.3, 127.0, 126.6, 126.1, 123.7, 122.0, 115.4, 114.7, 107.1, 75.1, 70.5, 70.0, 68.2, 67.0, 52.8, 50.0, 49.1. HRMS (TOF MS ES+): *m/z* calcd for $C_{71}H_{60}N_2O_{12}Na$ (M^++ Na): 1155.4044. Found: 1155.4070. [The compound exhibited extensive rotamerism and hence the number of proton and carbon signals exceeds. This has also been observed [3] by Nicolaou et al.]

Balanol (1):

To a solution of protected balanol **31** (20 mg, 0.018 mmol) in formic acid (5 mL) was added palladium black (50 mg) and the reaction mixture was allowed to stir vigorously for 18 h. The reaction mixture was then filtered through a pad of silica gel and the filtrate was concentrate under vacuo to provide a crude mass which on repeated purification by preparative TLC following Nicolaou's protocol provided (−)-balanol (**1**) as yellowish amorphous powder (4 mg, 41%). $[\alpha]_D^{25} =$ −106.0 (*c* 0.10 MeOH) [Lit. [3] $[\alpha]_D^{25} =$ − 111.0 (*c* 0.10 MeOH)] [Lit. [4] $[\alpha]_D^{25} =$ − 107.0 (*c* 0.252 MeOH)] . ^{1}H NMR (500MHz, CD_3OD+ D_2O) : 7.58 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.18 (t, *J* = 9.0 Hz, 1H), 6.82 (s, 2H), 6.71 (d, *J* = 7.6 Hz, 2H), 5.39 (m, 1H), 4.47 (m, 1H), 3.52-2.92 (m, 4H), 2.19-2.02 (m, 4H).MS (TOF MS ES^+): *m/z* = 573.4 (M^++Na).

(3*R*,4*S*)-Benzyl 3-(4-(benzyloxy)benzamido)-4-(3,5-bis(benzyloxy)-4-(2-(benzyloxy)-6-(benzyloxy-carbonyl)benzoyl)benzoyloxy)-5,6-dihydroxyazepane-1-carboxylate (32):

N-Methylmorpholine *N*-oxide (3.5 mg, 0.03 mmol) and OsO_4 (32.5 µL, 1% aq solution) were sequentially added to a solution of **31** (28 mg, 0.025 mmol) in acetone/water (1:1) and the resulting mixture was stirred at room temperature for 12 h before being quenched by addition of saturated aqueous sodium bisulfite (0.1 mL). The resulting mixture was concentrated in vacuo and then diluted with water (10 mL). It was extracted with ethyl acetate (2 × 15 mL) and the combined organic extract was washed successively with water (2 × 20 mL) and brine (20 mL) and dried (Na_2SO_4). After filtration, the filtrate was concentrated in vacuo to provide a crude mass which was roughly purified by chromatography over flash silica using a mixture of petroleum ether/ethyl acetate (1:1) as eluent to provide a mixture (81:19) of isomers **31** as a viscous liquid (20 mg, 68%). IR (KBr): 3436, 1719, 1667, 1605, 1580, 1498 cm^{-1}.^{1}H NMR (400MHz, $CDCl_3$) : δ 7.81 (d, *J*=8.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.41-7.32 (m, 11H), 7.23-7.19 (m, 16H), 7.12-7.02 (m, 9H), 6.90-6.87 (m, 3H), 6.82 (d, *J*=7.2 Hz, 2H), 5.30-5.22 (m, 2H), 5.16-5.08 (m, 4H), 5.00-5.08 (m, 2H), 5.00 (s, 1H), 4.97-4.88 (m, 1H), 4.86-4.79 (m, 3H), 4.75 (d, *J*=2.8 Hz, 1H), 4.71-4.64 (m, 2H), 4.35 (br s, 1H), 4.19 (dd, *J*=14.4, 6 Hz, 1H), 4.04 (d, *J*=15 Hz, 2H), 3.67 (dd, *J* = 15, 6.4 Hz, 1H). ^{13}C NMR (100MHz,$CDCl_3$): δ 191.7, 171.2, 167.2, 166.6, 166.0, 161.4, 158.1, 157.6, 156.2, 137.6, 136.4, 136.3, 135.9, 135.8, 135.3, 132.5, 130.4, 130.1, 128.9, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.5, 127.5, 127.4, 127.3, 127.2, 126.9, 126.3, 123.6, 122.0, 115.5, 114.9, 114.7, 107.1, 78.7, 75.1, 70.5, 70.4, 70.0, 68.4, 68.2, 67.0, 60.4, 52.0, 50.0, 49.9. HRMS (TOF MS ES+): *m/z* calcd for $C_{71}H_{62}N_2NaO_{14}$ (M^++ Na): 1189.4099. Found: 1189.4105.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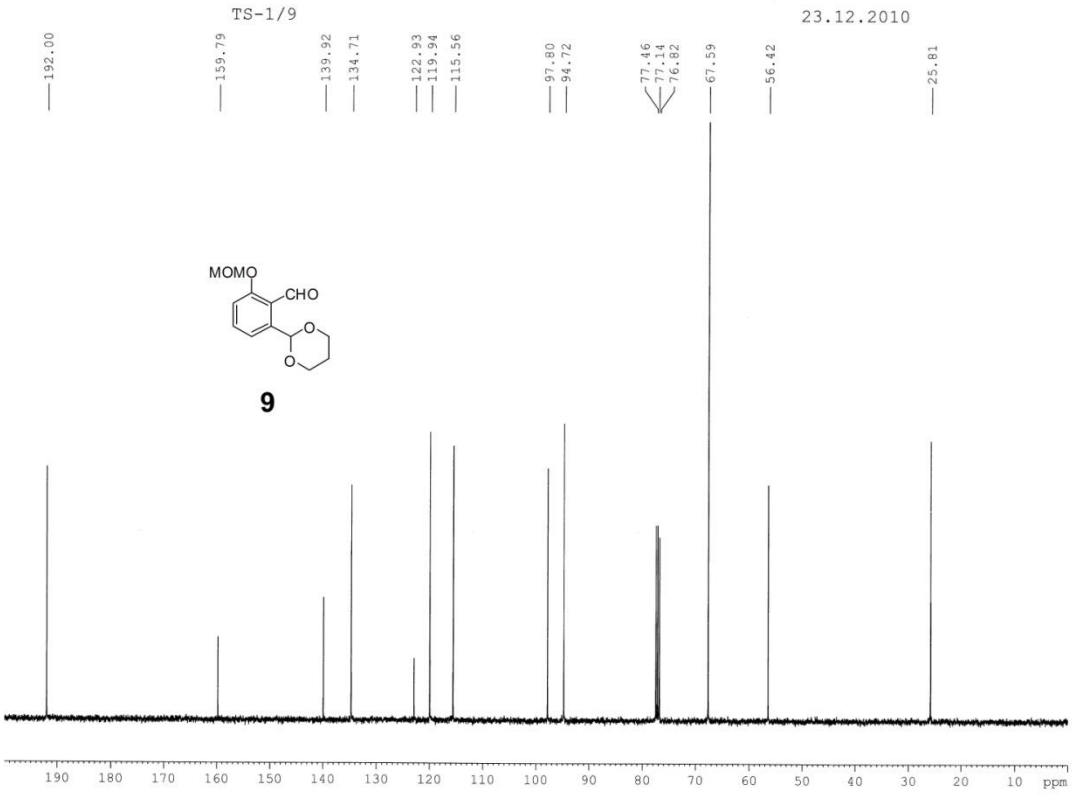
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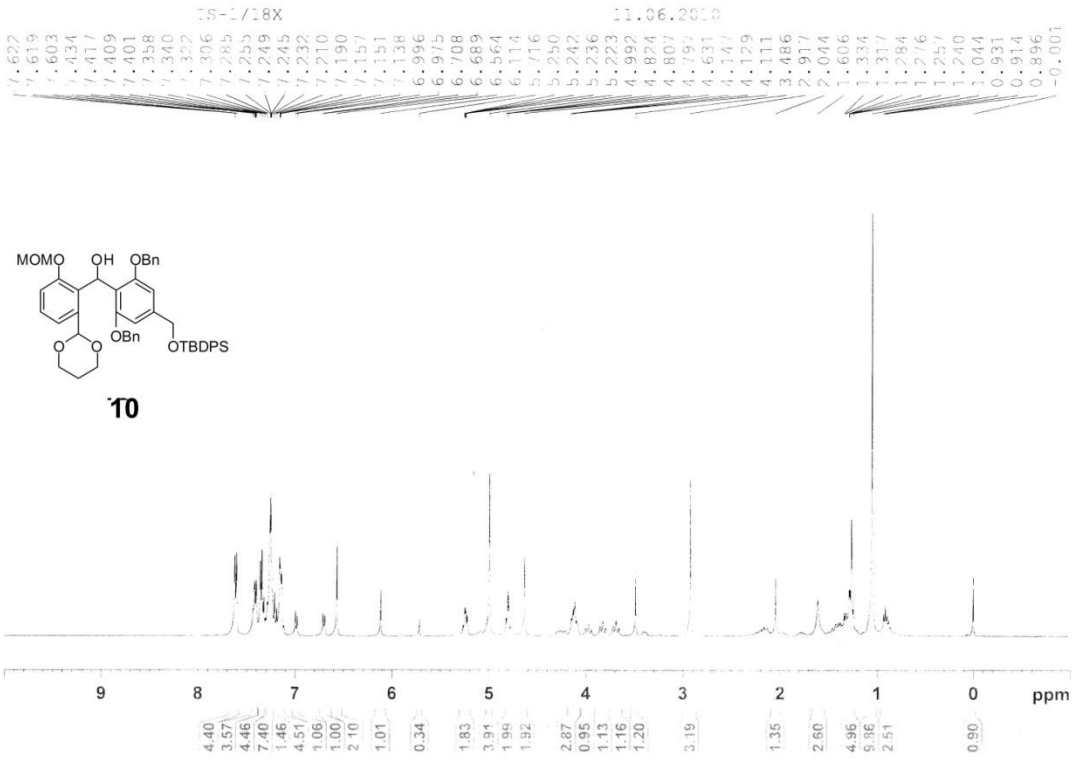
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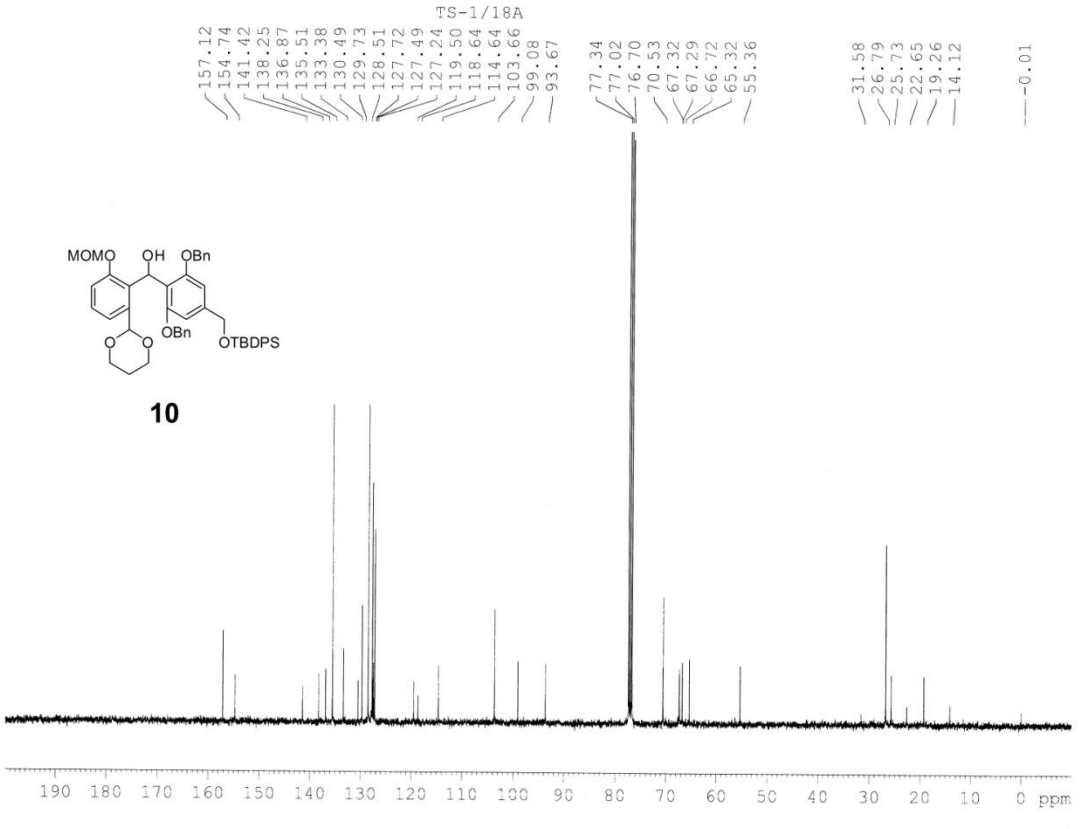
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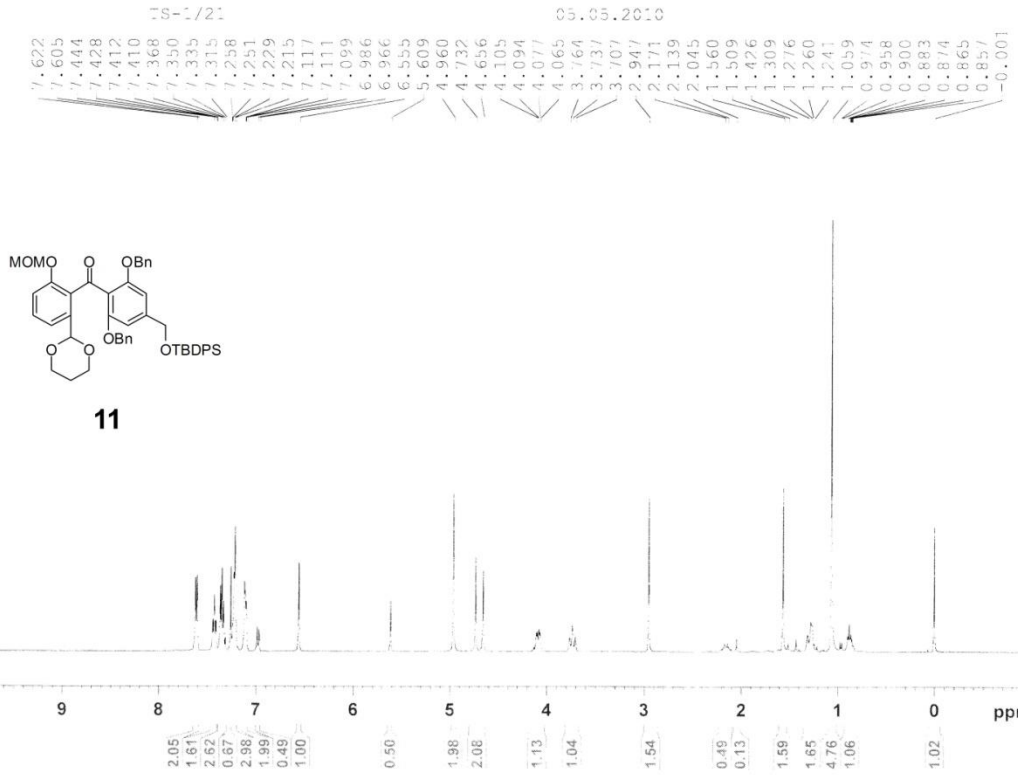
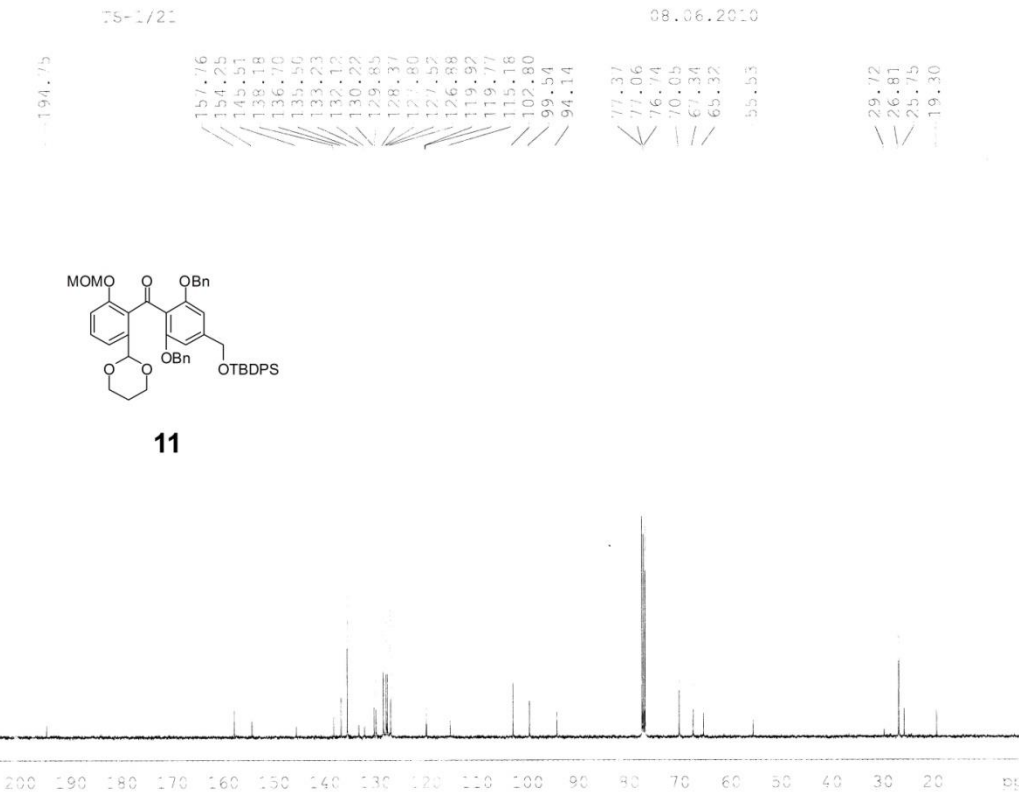
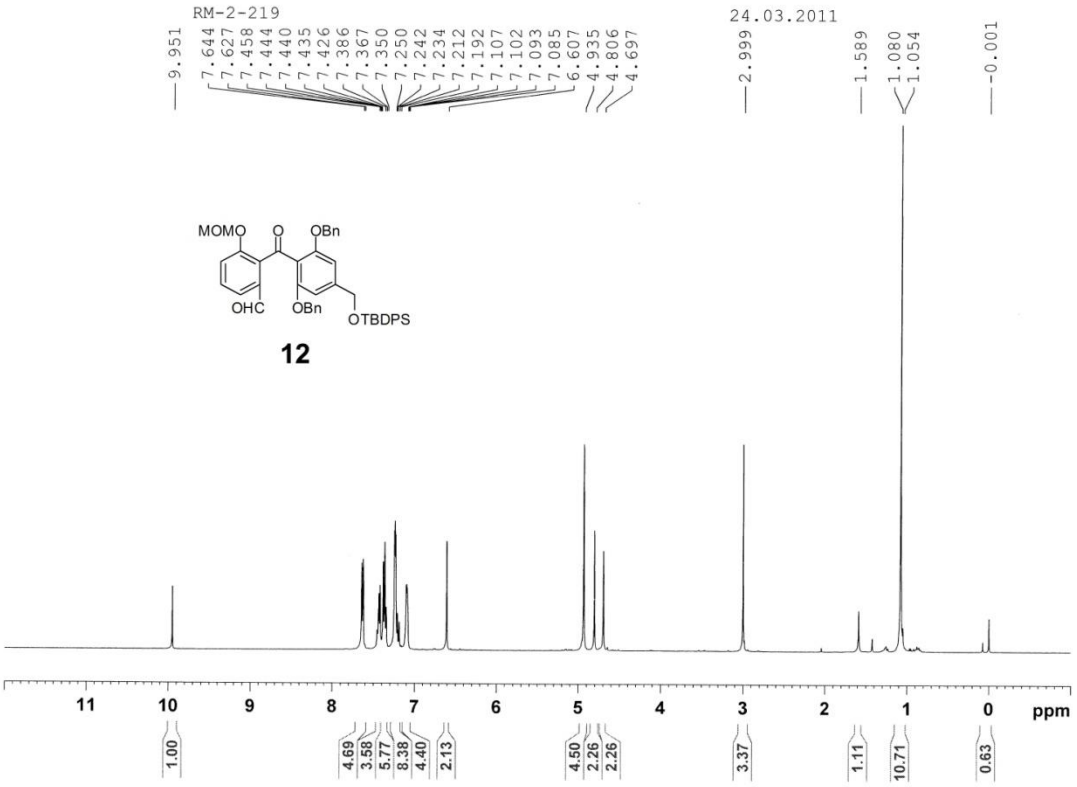
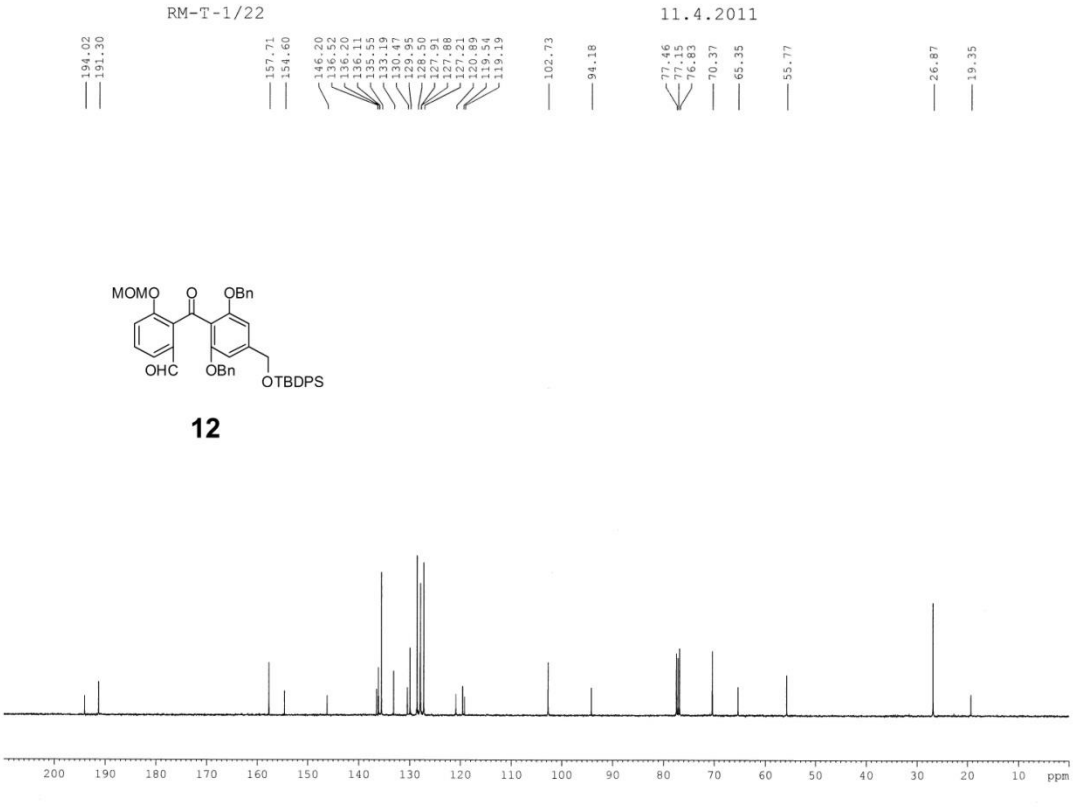

TS-1/21
05.05.2010
MOMO
OBn
OBn
OTBDPS
ppm

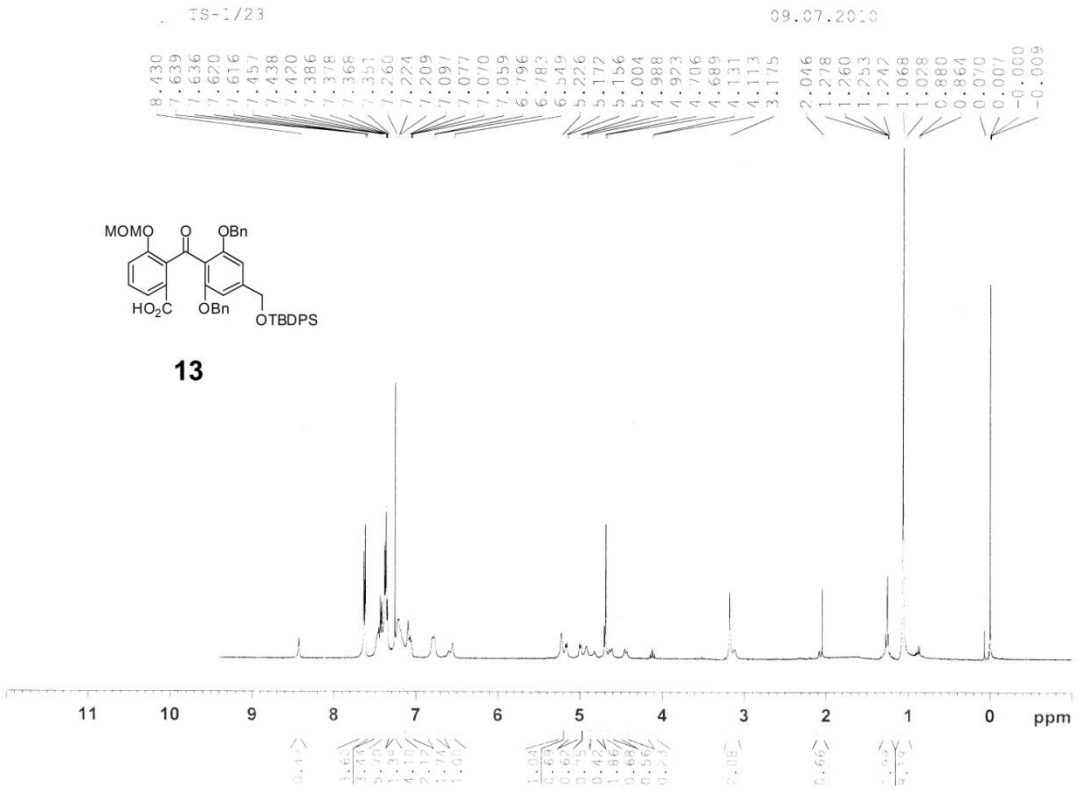
11

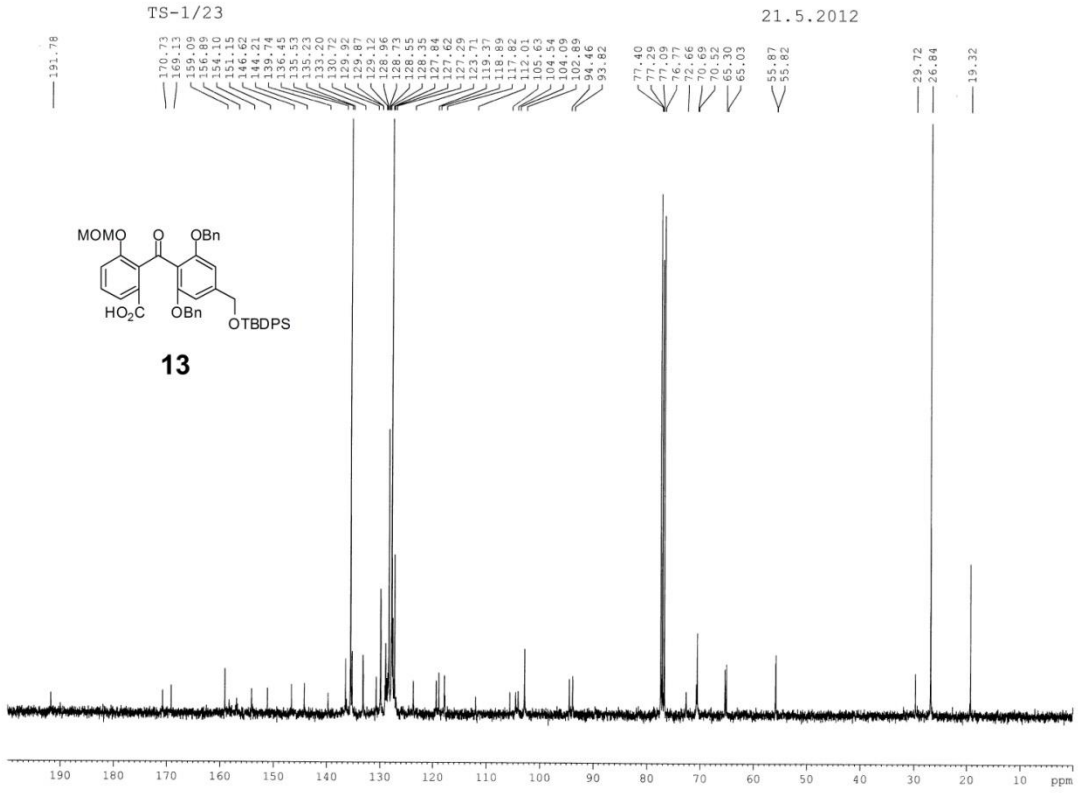

TS-1/21
08.06.2010
MOMO
OBn
OBn
OTBDPS
ppm

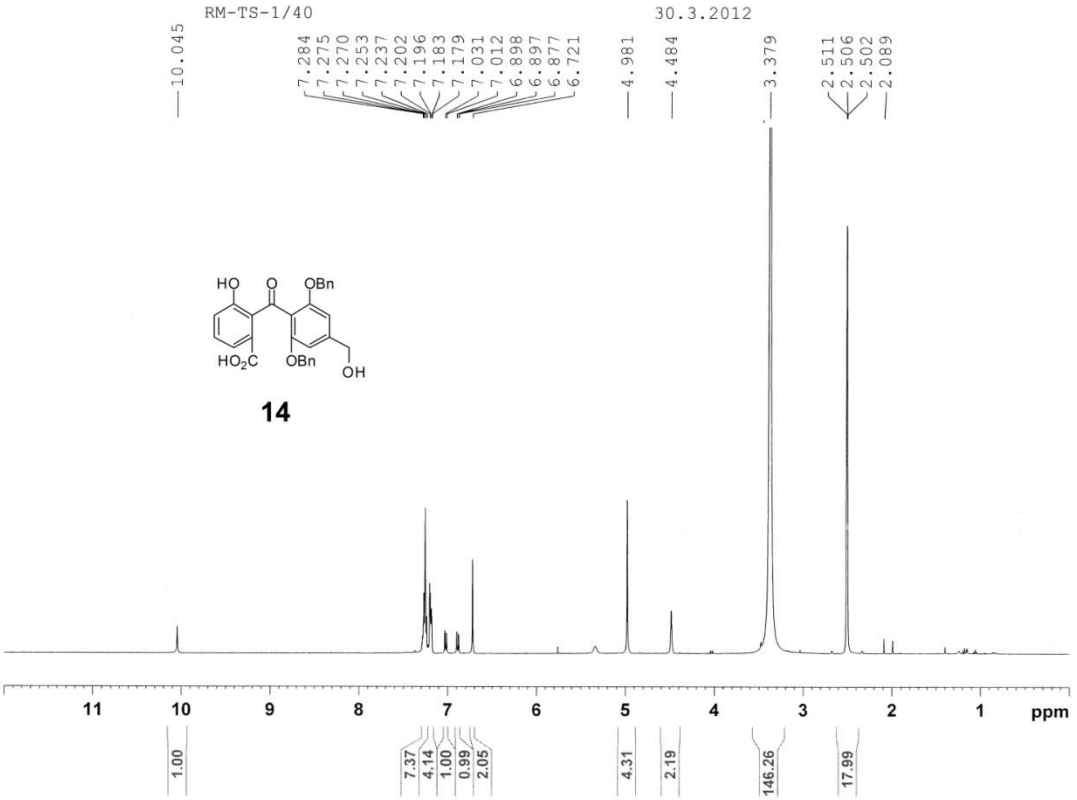
11

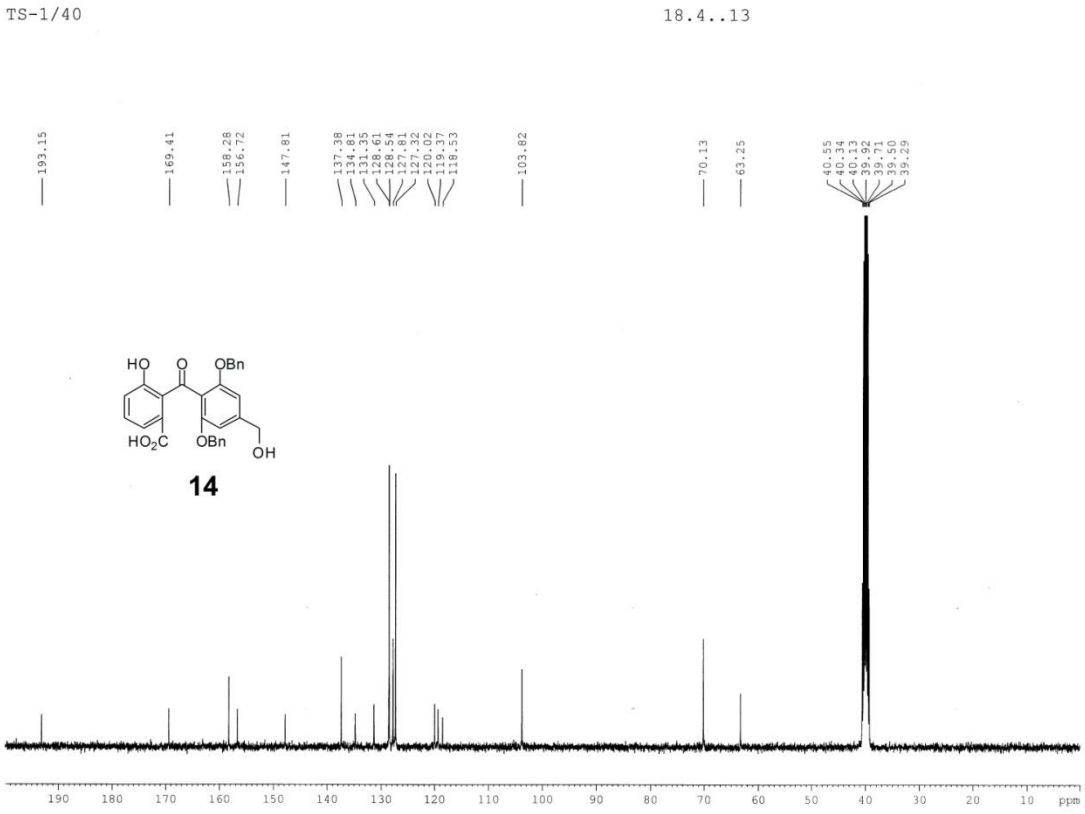

RM-2-219
24.03.2011
9.951
7.644
7.627
7.458
7.444
7.440
7.435
7.426
7.386
7.367
7.350
7.250
7.242
7.234
7.212
7.192
7.107
7.102
7.093
7.085
6.607
4.935
4.806
4.697
2.999
1.589
1.080
1.054
-0.001
MOMO
O
OBn
OHC
OBn
OTBDPS
12
ppm
1.00
4.69
3.58
5.77
8.38
4.40
2.13
4.50
2.26
2.26
3.37
1.11
10.71
0.63

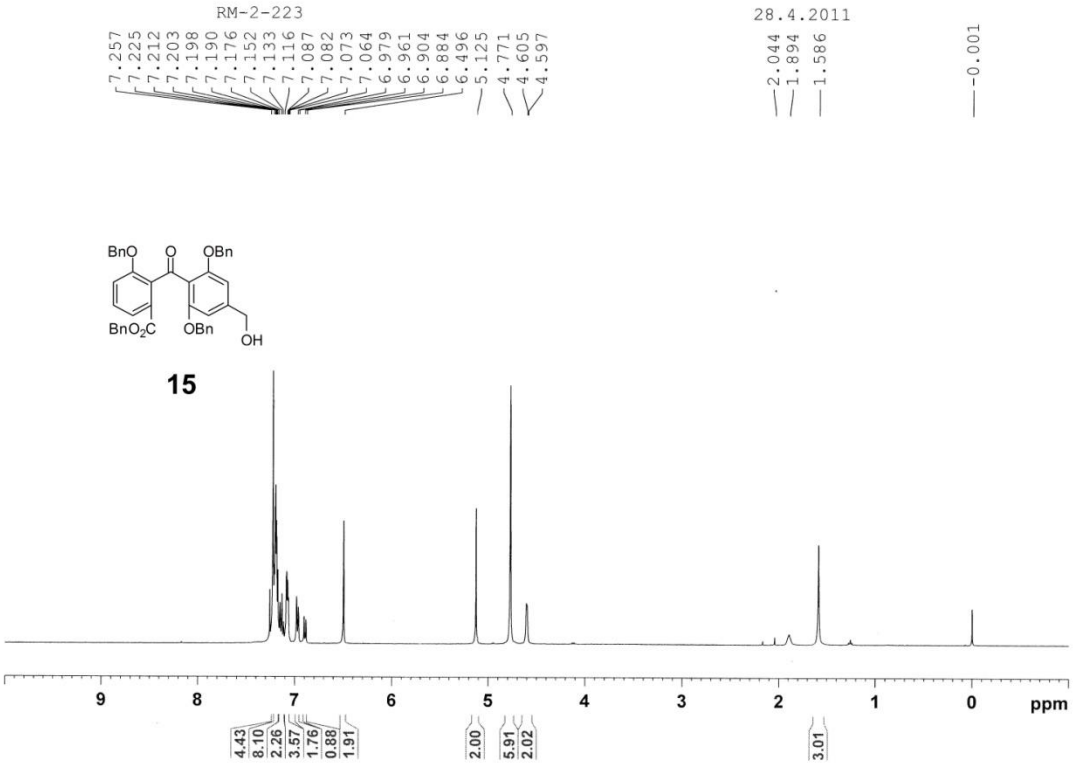

RM-T-1/22
11.4.2011
194.02
191.30
157.71
154.60
146.20
136.52
136.20
136.11
135.55
133.19
130.47
129.46
128.50
127.91
127.88
127.21
120.89
119.54
119.19
102.73
94.18
77.46
77.15
76.83
70.37
65.35
55.77
26.87
19.35
MOMO
O
OBn
OHC
OBn
OTBDPS
12
ppm

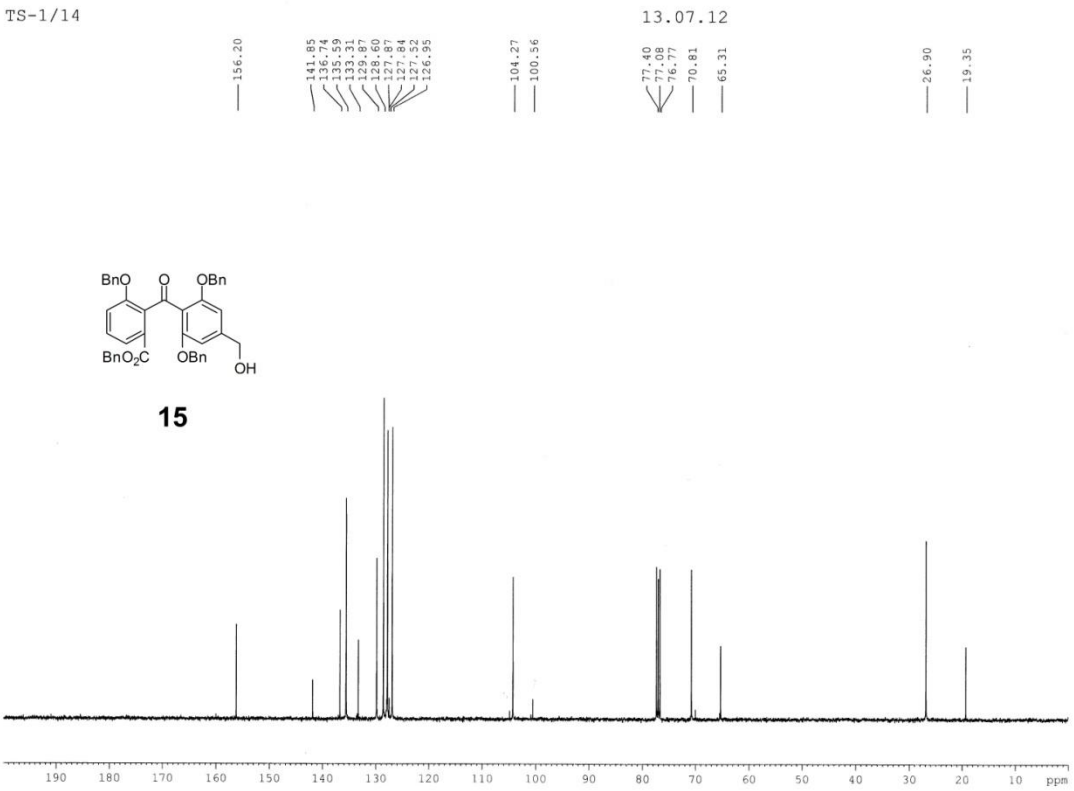

TS-1/23
09.07.2010
MOMO
OBn
HO2C
OBn
OTBDPS
13
ppm

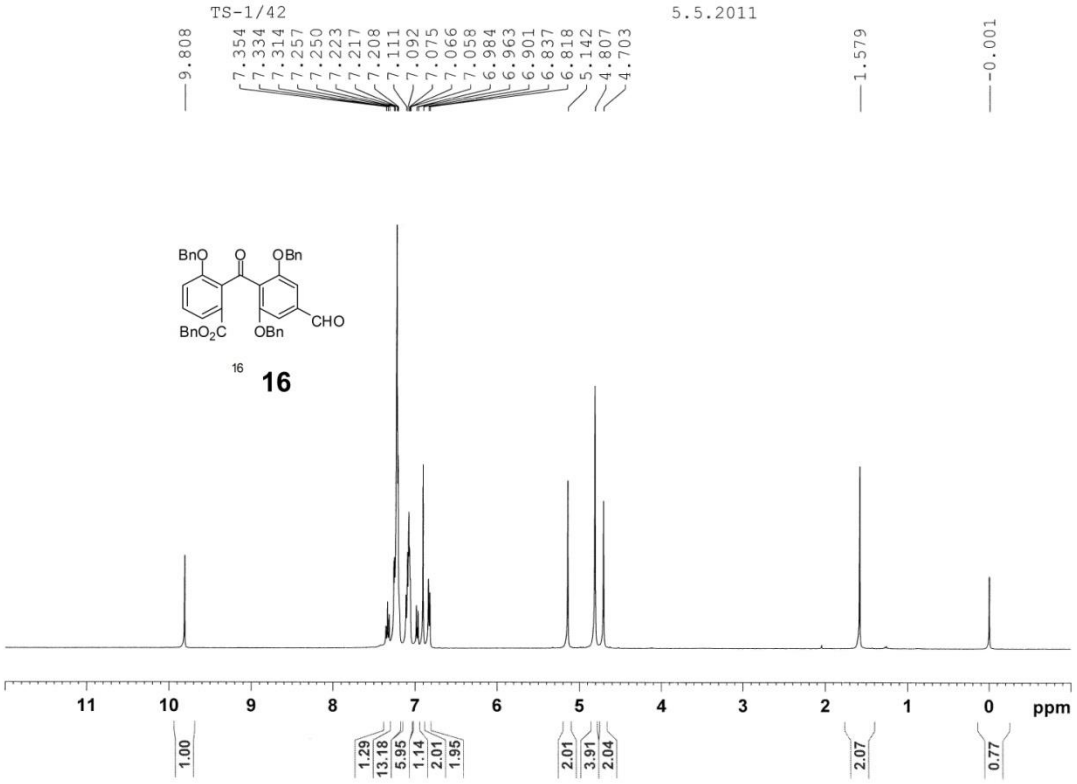

TS-1/23
21.5.2012
MOMO
OBn
HO2C
OBn
OTBDPS
13
ppm

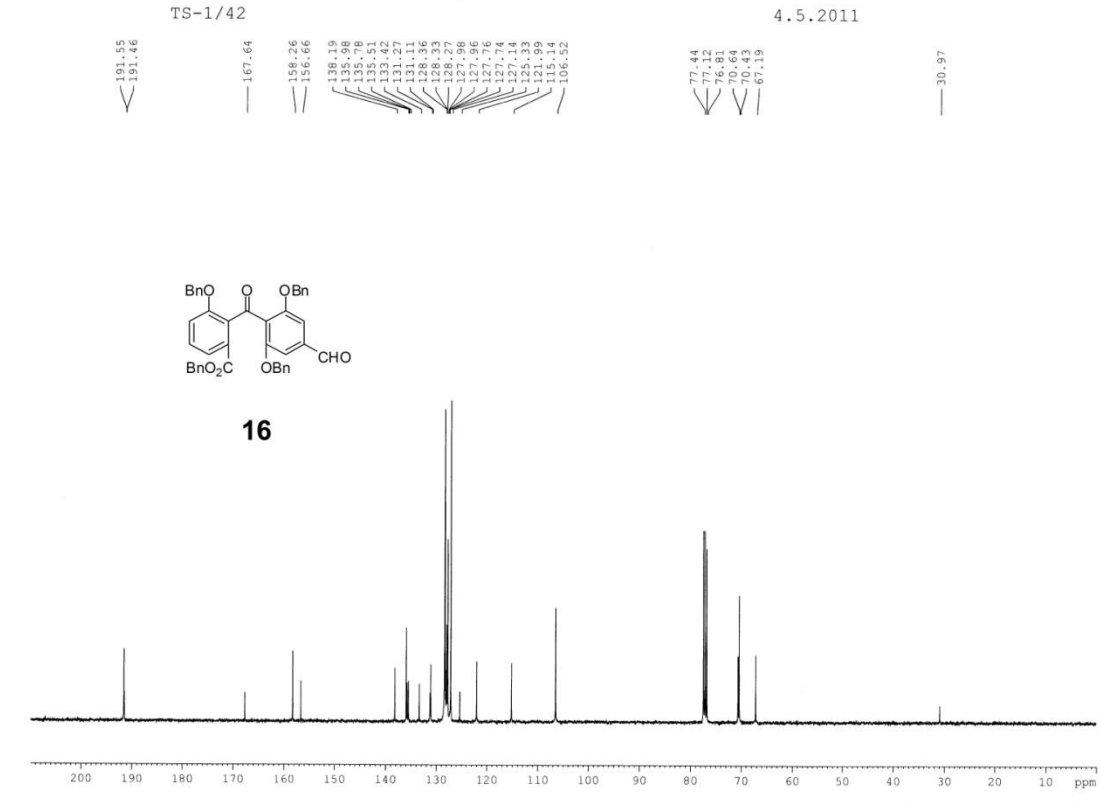

RM-TS-1/40
30.3.2012
10.045
7.284
7.275
7.270
7.253
7.237
7.202
7.196
7.183
7.179
7.031
7.012
6.898
6.897
6.877
6.721
4.981
4.484
3.379
2.511
2.506
2.502
2.089
HO
O
OBn
HO2C
OBn
OH
14
11
10
9
8
7
6
5
4
3
2
1
ppm
1.00
7.37
4.14
1.00
0.99
2.05
4.31
2.19
146.26
17.99

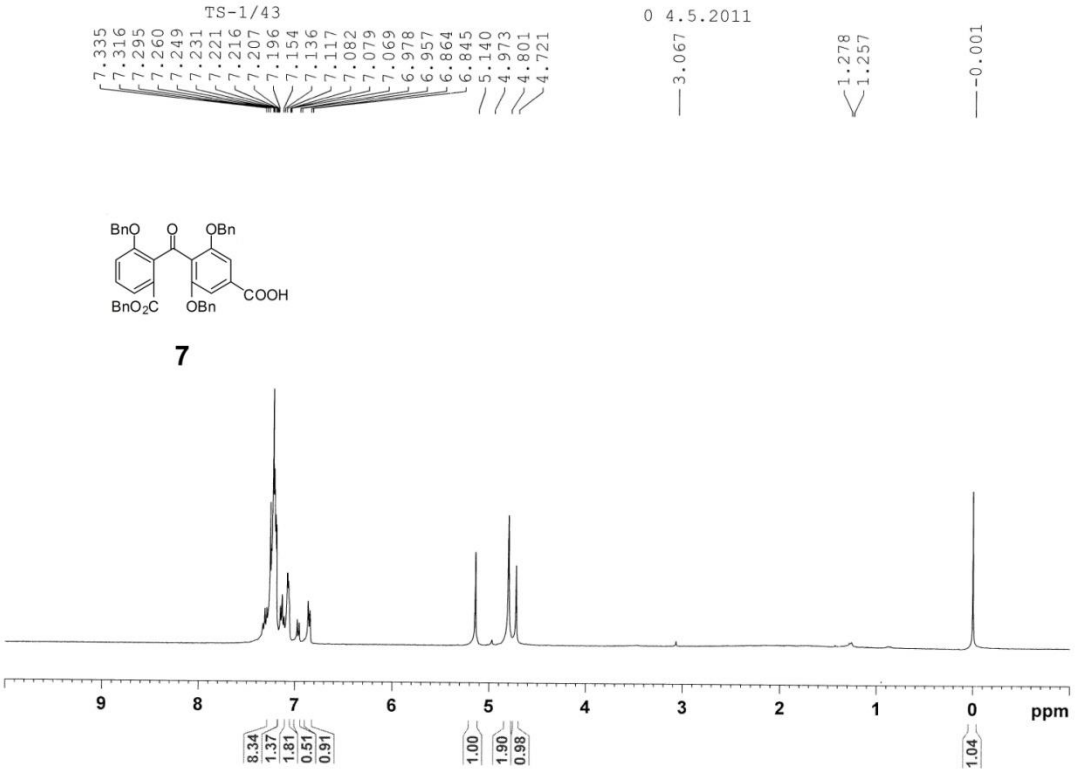

TS-1/40
18.4..13
193.15
169.41
158.28
156.72
147.81
137.38
134.81
131.35
128.61
128.54
127.81
127.32
120.02
119.37
118.53
103.82
70.13
63.25
40.55
40.34
40.13
39.92
39.71
39.50
39.29
HO
O
OBn
HO2C
OBn
OH
14
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

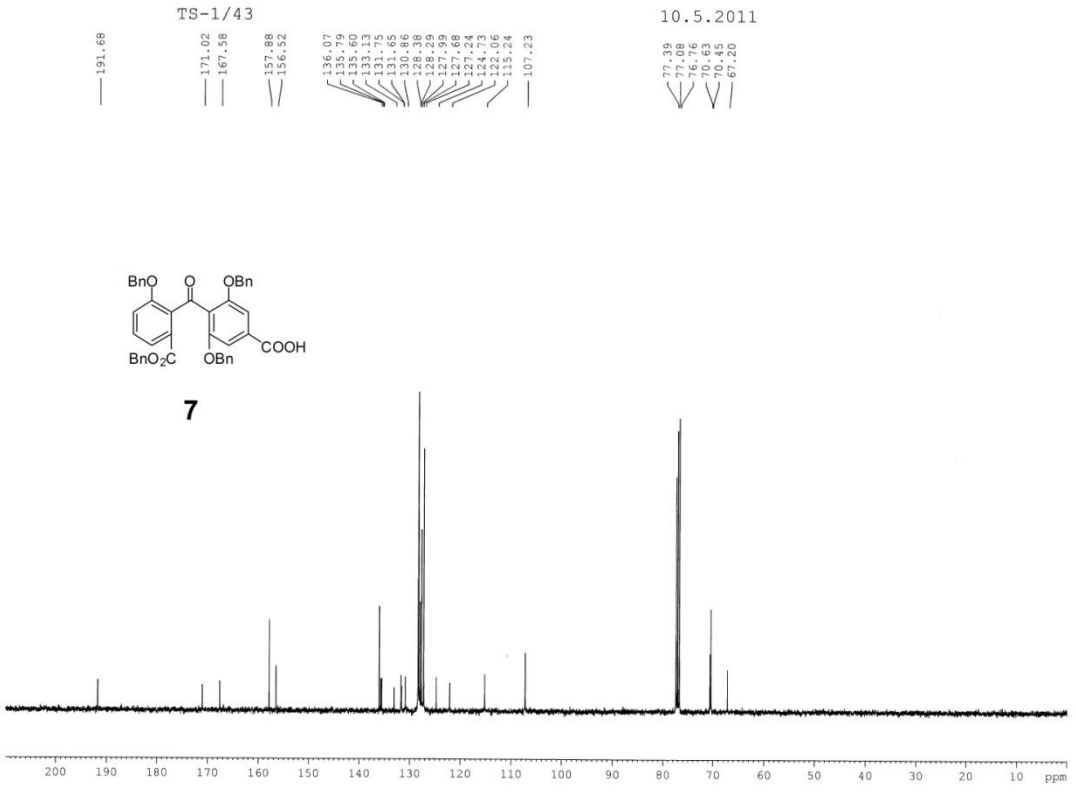

RM-2-223
28.4.2011
7.257
7.225
7.212
7.203
7.198
7.190
7.176
7.152
7.133
7.116
7.087
7.082
7.073
7.064
6.979
6.961
6.904
6.884
6.496
5.125
4.771
4.605
4.597
2.044
1.894
1.586
0.001
BnO
O
OBn
BnO2C
OBn
OH
15
9
8
7
6
5
4
3
2
1
0
ppm
4.43
8.10
2.26
3.57
1.76
0.88
1.91
2.00
5.91
2.02
3.01

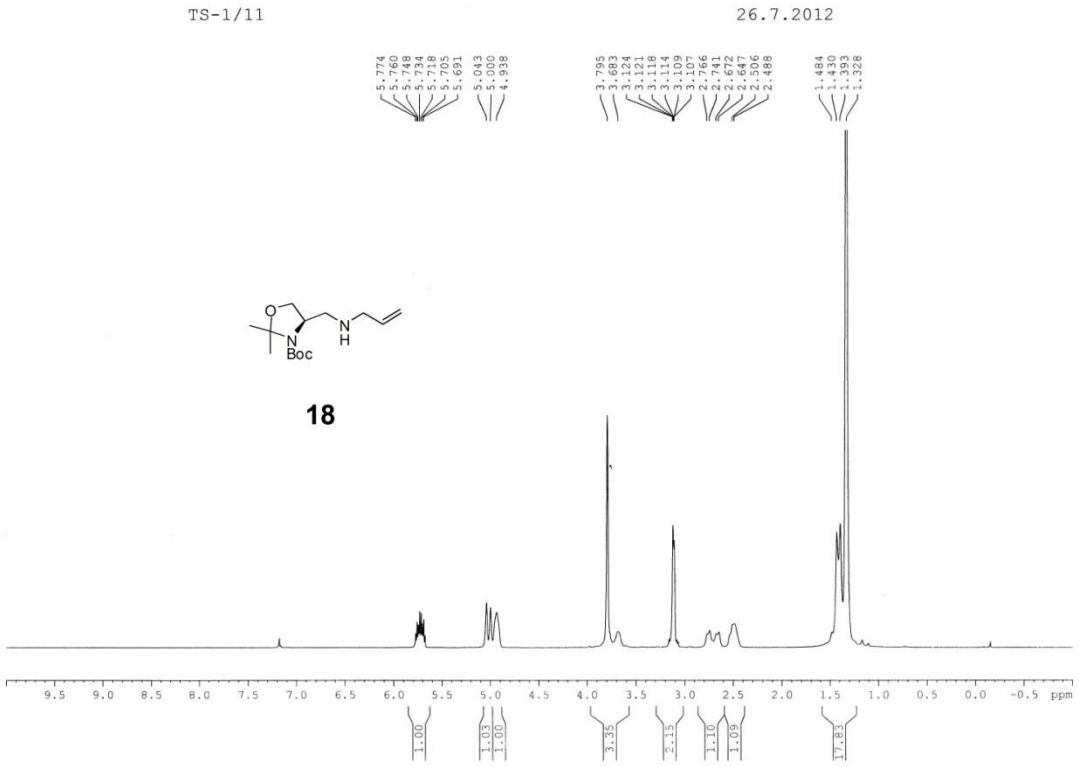

TS-1/14
13.07.12
156.20
141.85
136.74
135.59
133.31
129.87
128.60
127.87
127.84
127.52
126.95
104.27
100.56
77.40
77.08
76.77
70.81
65.31
26.90
19.35
BnO
O
OBn
BnO2C
OBn
OH
15
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

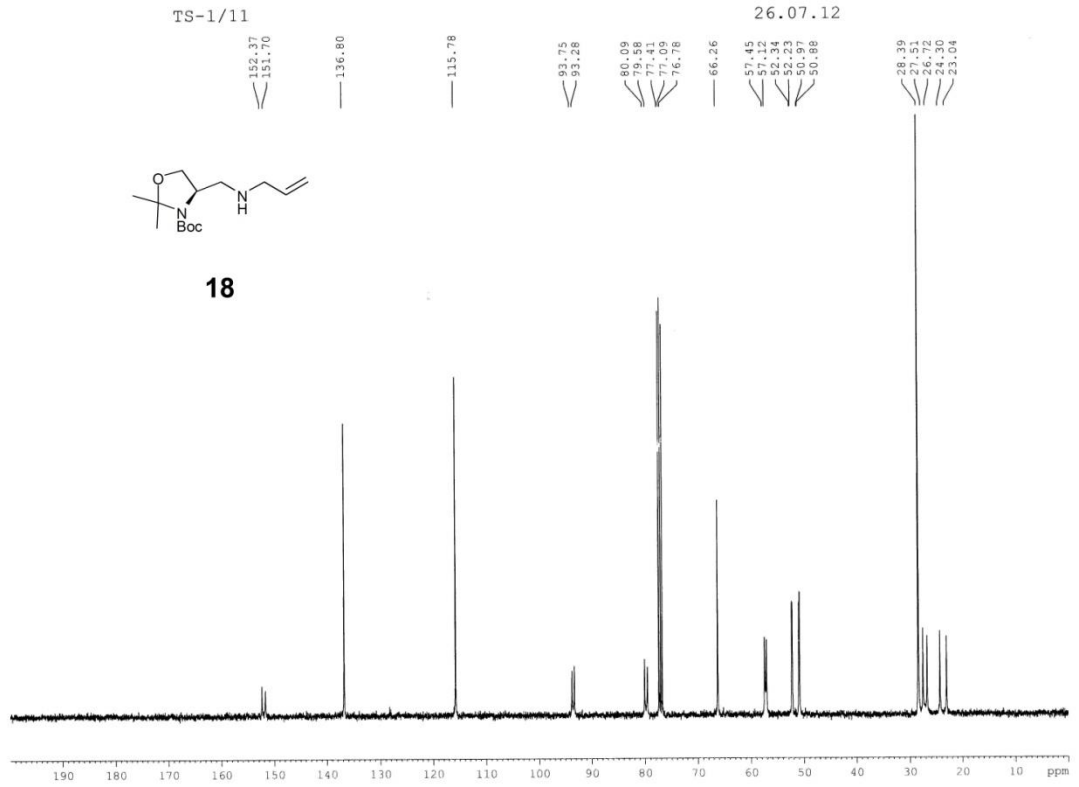

TS-1/42
5.5.2011
9.808
7.354
7.334
7.314
7.257
7.250
7.223
7.217
7.208
7.111
7.092
7.075
7.066
7.058
6.984
6.963
6.901
6.837
6.818
5.142
4.807
4.703
1.579
0.001
BnO
O
OBn
CHO
BnO2C
OBn
16
16
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.29
13.18
5.95
1.14
2.01
1.95
2.01
3.91
2.04
2.07
0.77

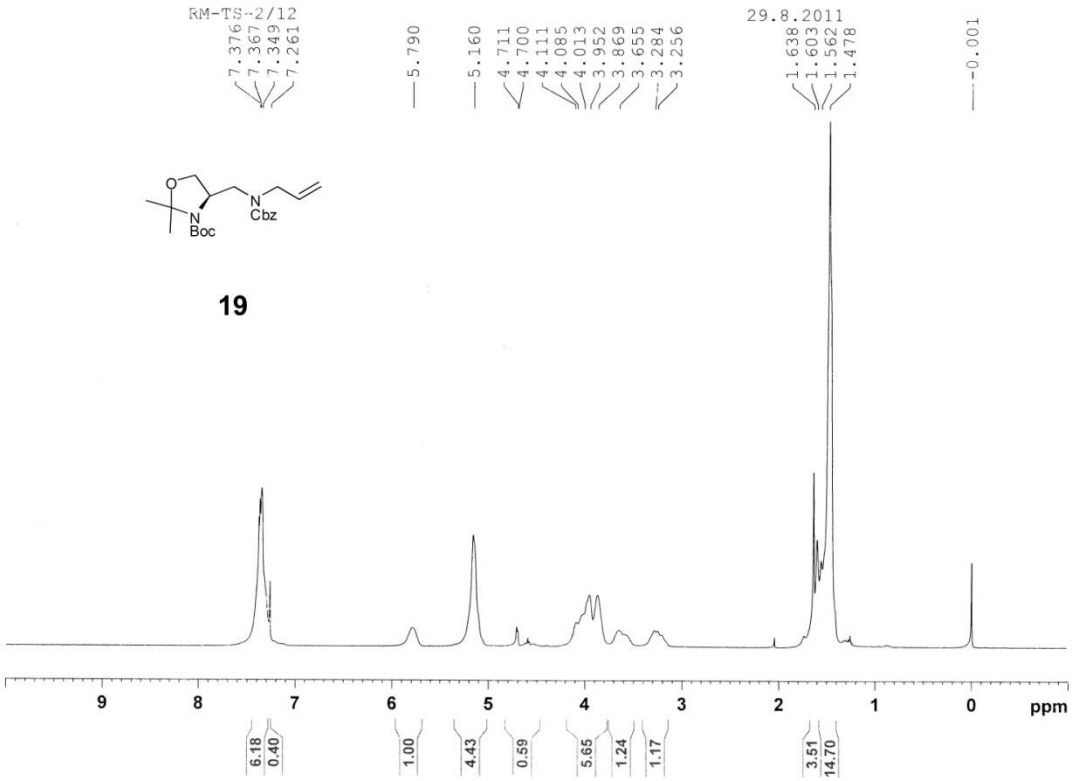

TS-1/42
4.5.2011
191.55
191.46
167.64
158.26
156.66
138.19
135.98
135.78
135.51
133.42
131.27
131.11
128.56
128.33
128.27
127.98
127.96
127.76
127.74
127.14
125.33
121.99
115.14
106.52
77.44
77.12
76.81
70.64
70.43
67.19
30.97
BnO
O
OBn
CHO
BnO2C
OBn
16
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


TS-1/43
0 4.5.2011
7.335
7.316
7.295
7.260
7.249
7.231
7.221
7.216
7.207
7.196
7.154
7.136
7.117
7.082
7.079
7.069
6.978
6.957
6.864
6.845
5.140
4.973
4.801
4.721
3.067
1.278
1.257
0.001
BnO
O
OBn
COOH
BnO2C
OBn
7
9
8
7
6
5
4
3
2
1
0
ppm
8.34
1.37
1.81
0.51
0.91
1.00
1.90
0.98
1.04

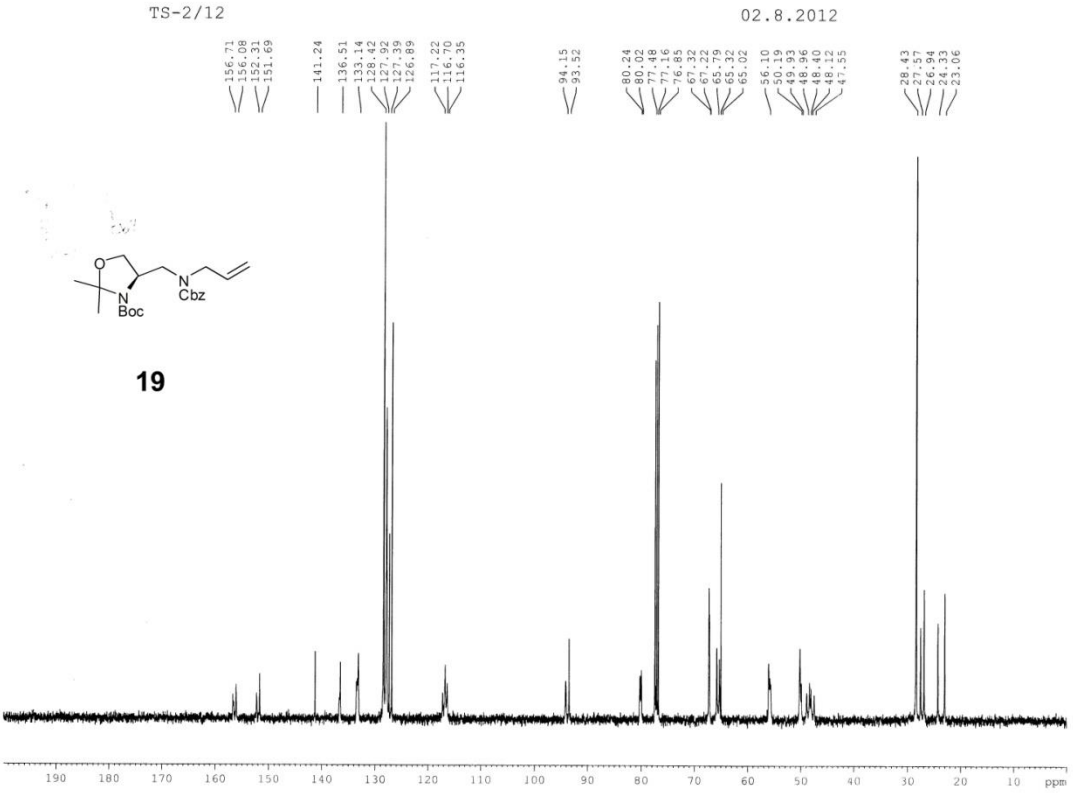

TS-1/43
10.5.2011
191.68
171.02
167.58
157.88
156.52
136.07
135.79
135.60
133.13
131.75
131.65
130.86
128.38
128.29
127.99
127.68
127.24
124.73
122.06
115.24
107.23
77.39
77.08
76.76
70.43
70.15
67.20
BnO
O
OBn
COOH
BnO2C
OBn
7
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


TS-1/11
26.7.2012
5.774
5.760
5.748
5.734
5.718
5.705
5.691
5.043
5.000
4.938
3.795
3.683
3.124
3.121
3.118
3.114
3.109
3.107
2.766
2.741
2.672
2.647
2.506
2.488
1.484
1.430
1.393
1.328
Boc
18
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
1.00
1.03
1.00
3.35
2.15
1.10
1.09
17.83


TS-1/11
26.07.12
152.37
151.70
136.80
115.78
93.75
93.28
80.09
79.58
77.41
77.09
76.78
66.26
57.45
57.12
52.34
52.23
50.97
50.88
28.39
27.51
26.72
24.30
23.04
Boc
18
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


RM-TS-2/12
29.8.2011
7.376
7.367
7.349
7.261
5.790
5.160
4.711
4.700
4.111
4.085
4.013
3.952
3.869
3.655
3.284
3.256
1.638
1.603
1.562
1.478
-0.001
Boc
N
Cbz
9
8
7
6
5
4
3
2
1
0
ppm
6.18
0.40
1.00
4.43
0.59
5.65
1.24
1.17
3.51
14.70

19


TS-2/12
02.8.2012
156.71
156.08
152.31
151.69
141.24
136.51
133.14
128.42
127.92
127.89
126.89
117.22
116.70
116.35
94.15
93.52
80.24
80.02
77.48
77.16
76.85
67.32
67.22
65.79
65.32
65.02
56.10
50.19
49.93
48.96
48.60
48.12
47.55
28.43
27.57
26.94
24.33
23.06
Boc
N
Cbz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

19

SKC-SPR-4-4 IN CDCl3

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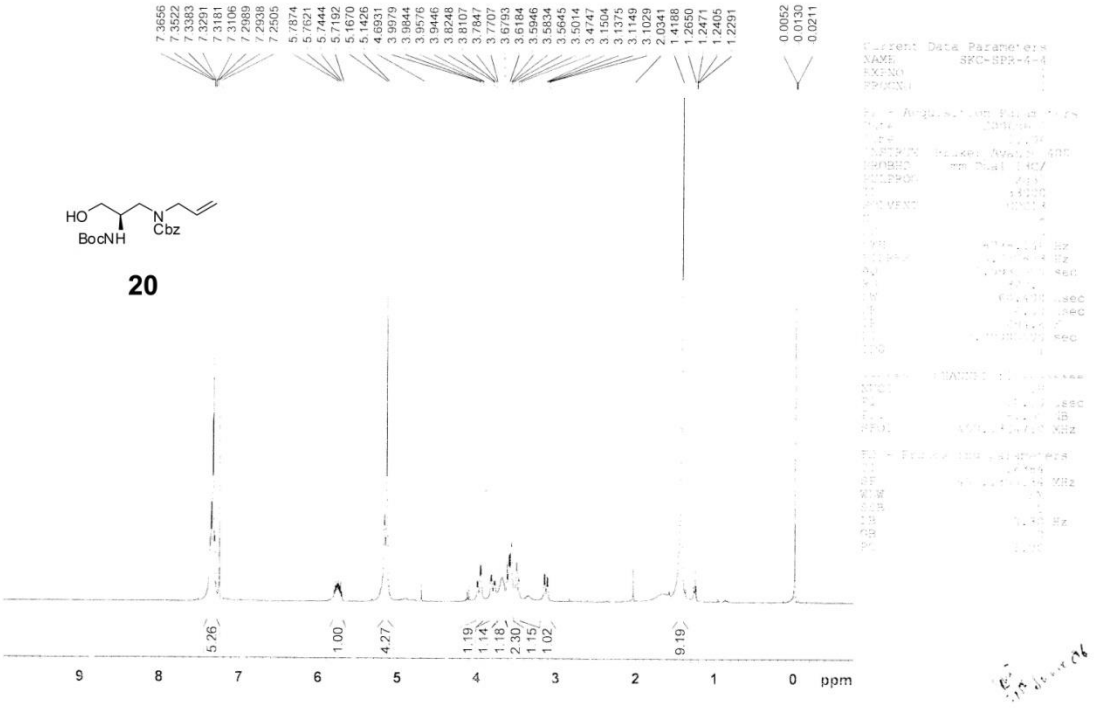
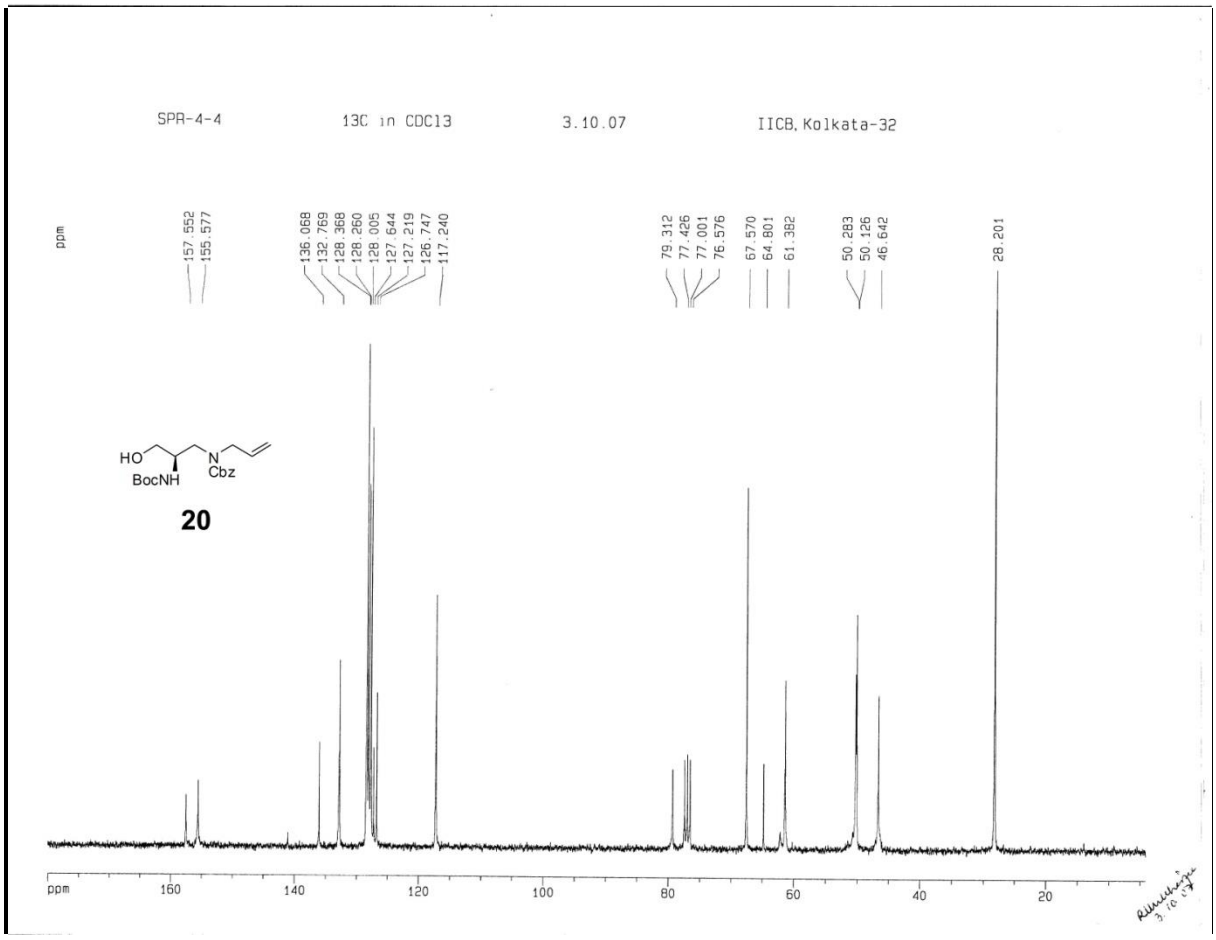
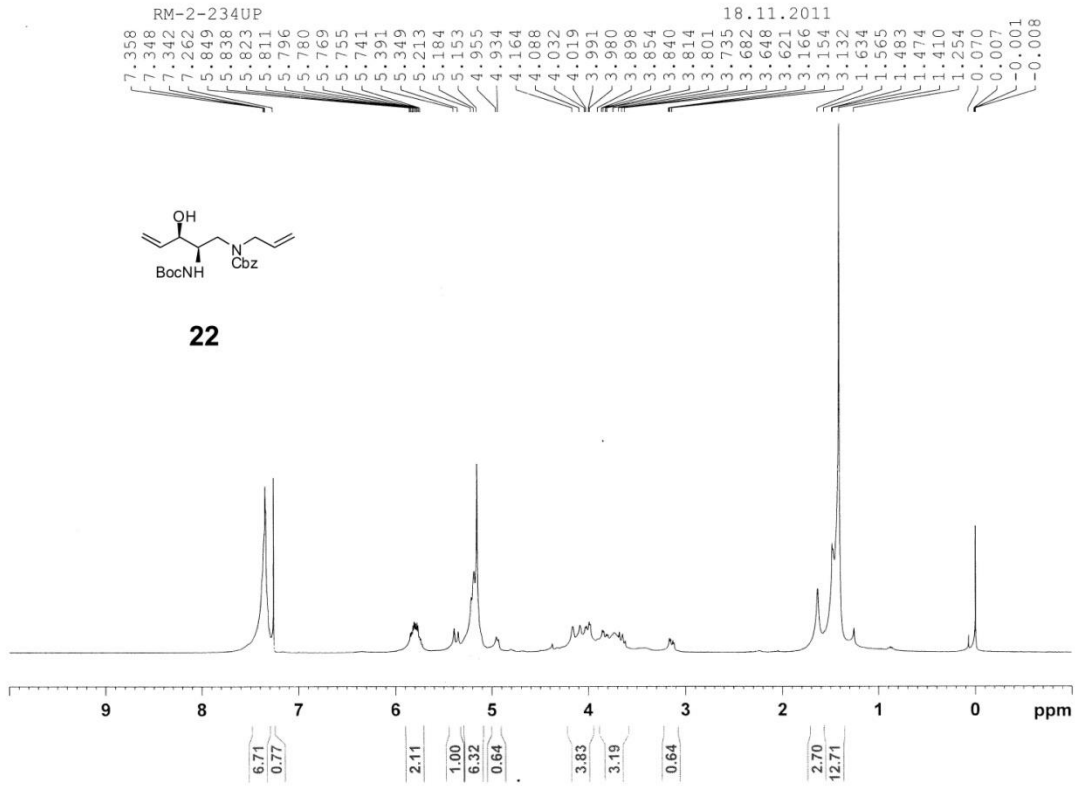
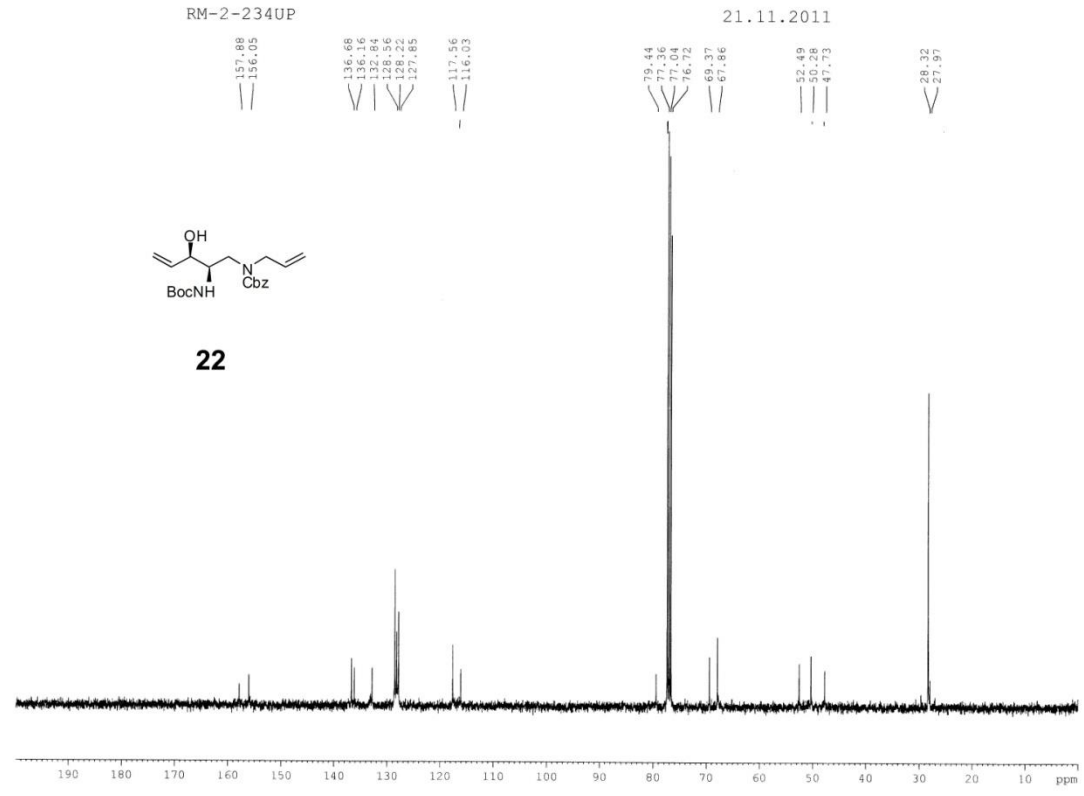
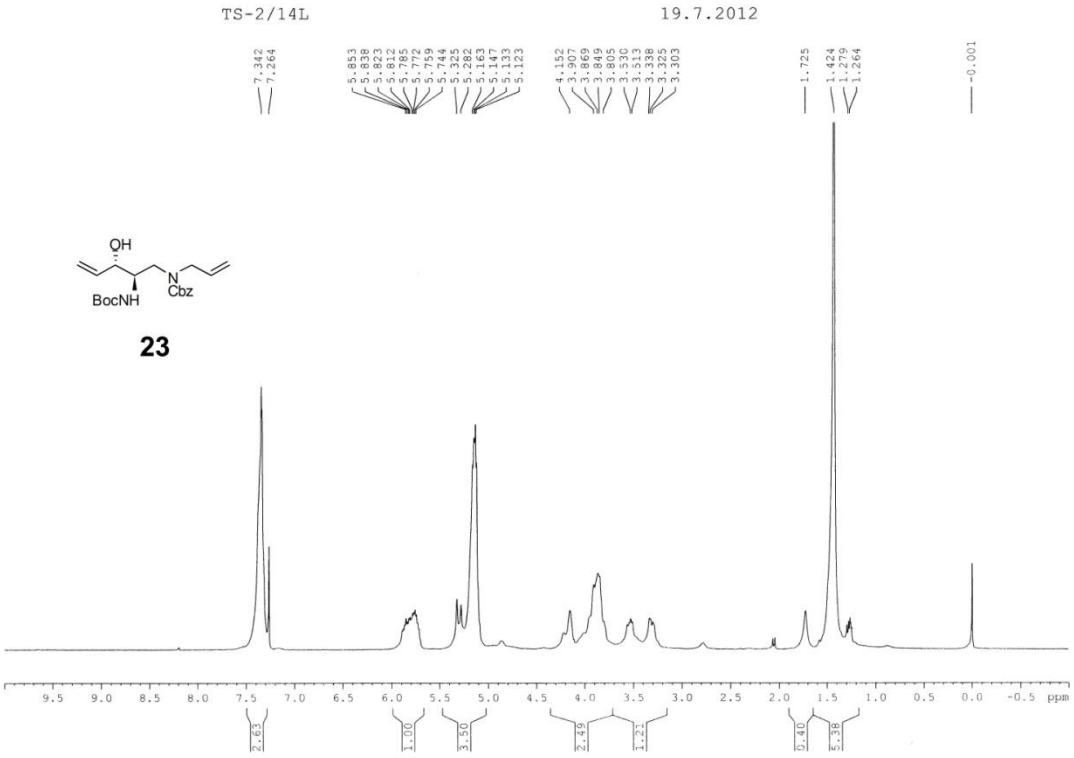
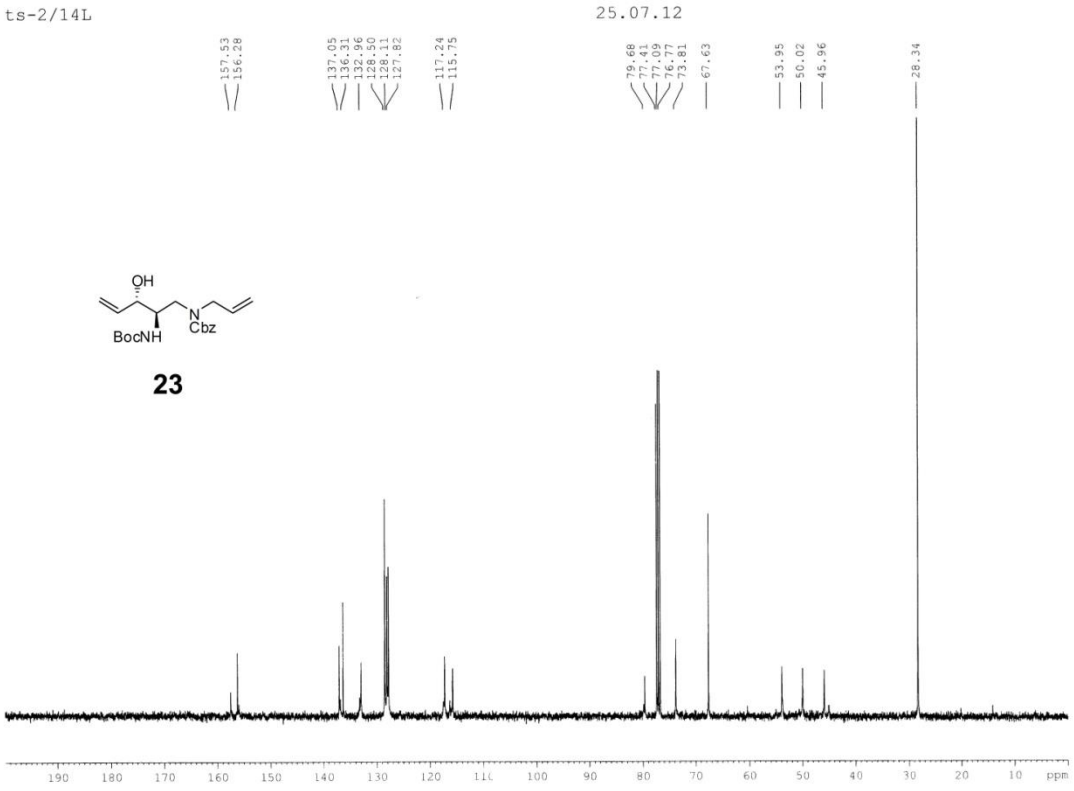


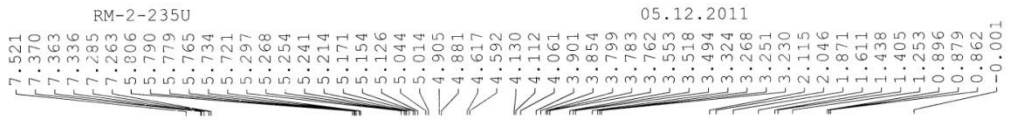


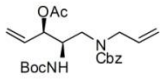

RM-2-234UP
18.11.2011
7.358
7.348
7.342
7.262
5.849
5.838
5.823
5.811
5.796
5.780
5.769
5.755
5.741
5.391
5.349
5.213
5.184
5.153
4.955
4.934
4.164
4.088
4.032
4.019
3.991
3.980
3.898
3.854
3.840
3.814
3.801
3.735
3.682
3.648
3.621
3.166
3.154
3.132
1.634
1.565
1.483
1.474
1.410
1.254
0.070
0.007
-0.001
-0.008
OH
N
Cbz
BocNH
22
9
8
7
6
5
4
3
2
1
0
ppm
6.71
0.77
2.11
1.00
6.32
0.64
3.83
3.19
0.64
2.70
12.71


RM-2-234UP
21.11.2011
157.88
156.05
136.68
136.16
132.84
128.56
128.22
127.85
117.56
116.03
79.44
77.36
77.04
76.72
69.37
67.86
52.49
50.28
47.73
28.32
27.97
OH
N
Cbz
BocNH
22
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

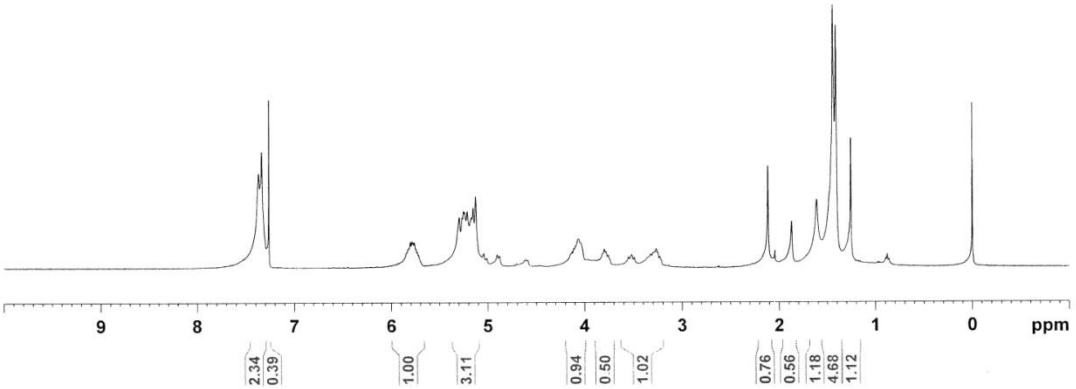

TS-2/14L
19.7.2012
7.342
7.264
5.853
5.838
5.823
5.812
5.785
5.772
5.759
5.744
5.325
5.282
5.163
5.147
5.133
5.123
4.152
3.907
3.869
3.849
3.805
3.530
3.513
3.398
3.385
3.303
1.725
1.424
1.279
1.264
-0.001
OH
N
Cbz
BocNH
23
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
2.63
1.00
3.50
2.49
1.23
5.40
5.38


ts-2/14L
25.07.12
157.53
156.28
137.05
136.31
132.96
128.50
128.11
127.82
117.24
115.75
79.68
77.41
77.09
76.77
73.81
67.63
53.95
50.02
45.96
28.34
OH
N
Cbz
BocNH
23
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


RM-2-235U
05.12.2011
7.521
7.370
7.363
7.336
7.285
7.263
5.806
5.790
5.779
5.765
5.734
5.721
5.297
5.268
5.254
5.241
5.214
5.171
5.154
5.126
5.044
5.014
4.905
4.881
4.617
4.592
4.130
4.112
4.061
3.901
3.854
3.799
3.783
3.762
3.553
3.518
3.494
3.324
3.268
3.251
3.230
2.115
2.046
1.871
1.611
1.438
1.405
1.253
0.896
0.879
0.862
-0.001


OAc
N
Cbz
BocNH

24


9
8
7
6
5
4
3
2
1
0
ppm
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3.11
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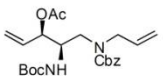
0.50
1.02
0.76
0.56
1.18
4.68
1.12


RM-2-250Lo (253)
20-3-2012
170.46
170.33
157.27
155.85
155.47
136.50
136.24
133.25
133.09
132.75
128.69
128.49
128.34
128.01
127.68
118.29
118.15
117.67
117.14
79.91
79.44
77.37
77.05
76.73
73.68
67.81
67.42
51.02
50.51
49.72
49.29
45.37
44.71
35.42
28.32
21.05
20.78


OAc
N
Cbz
BocNH

24

190
180
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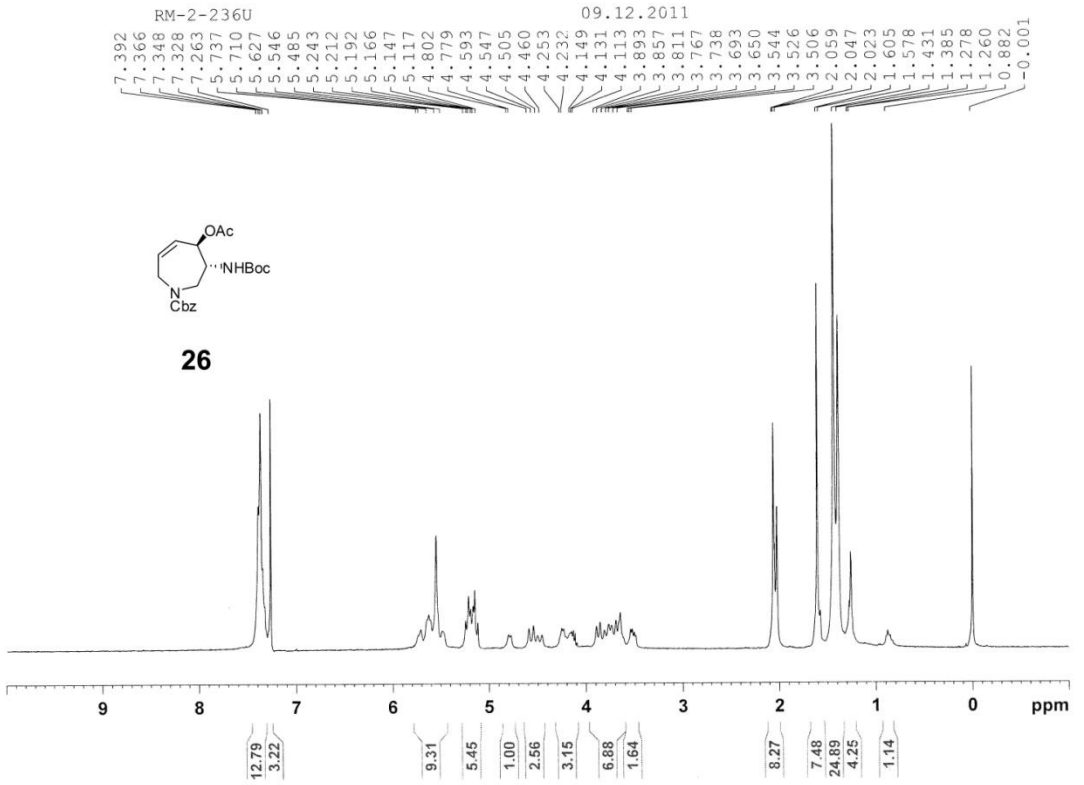
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


RM-2-236U
09.12.2011
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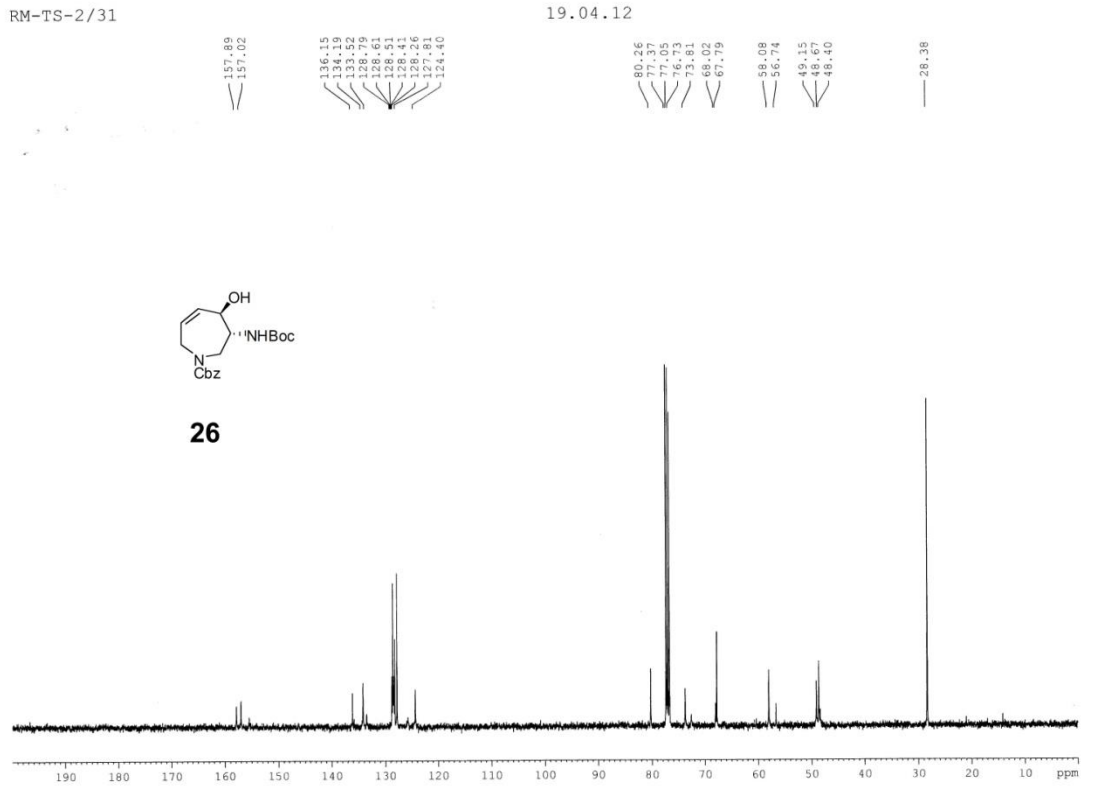
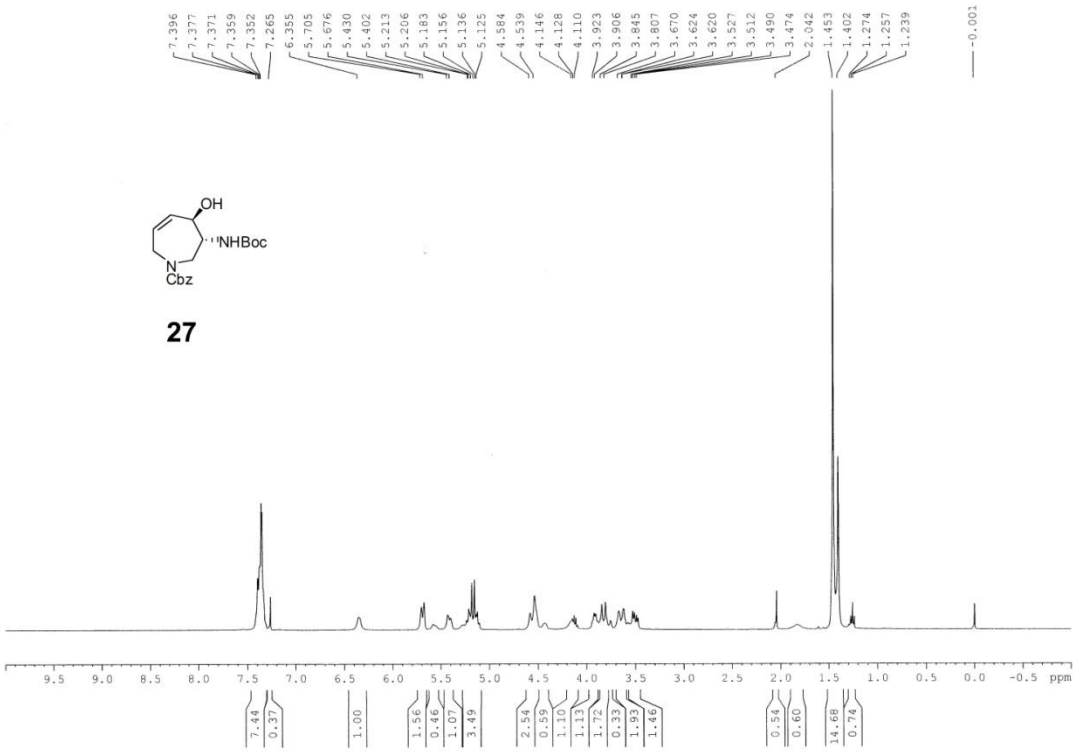
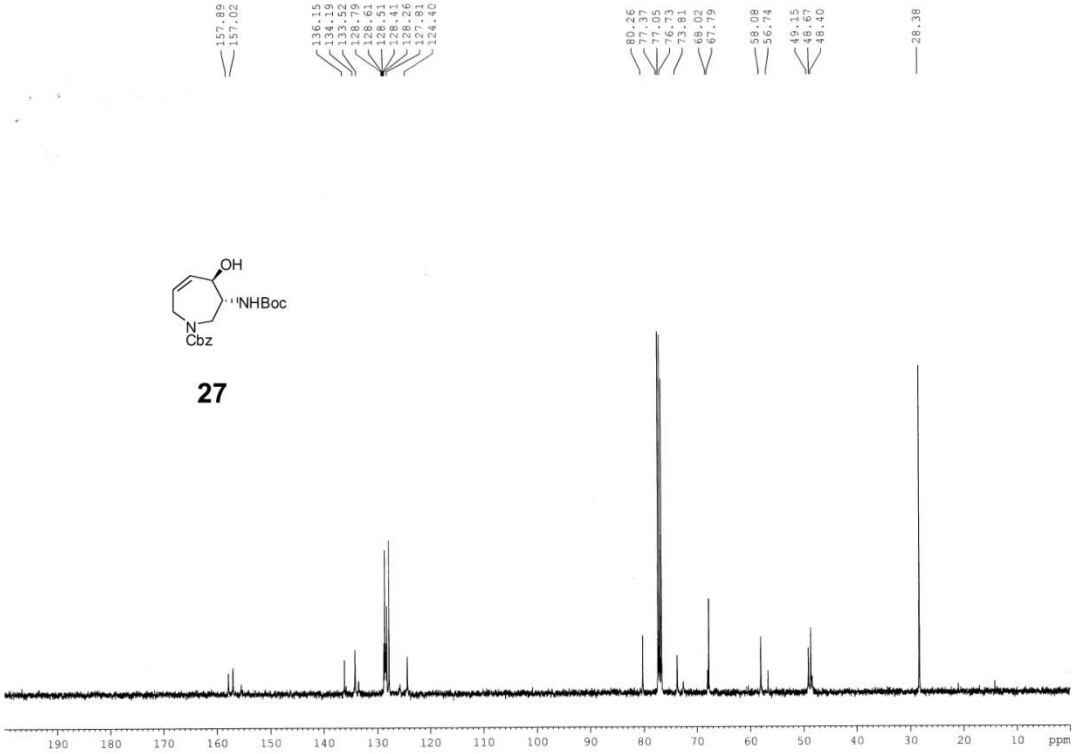
NHBoc
N
Cbz
26
ppm


RM-TS-2/31
19.04.12
OH
NHBoc
N
Cbz
26
ppm

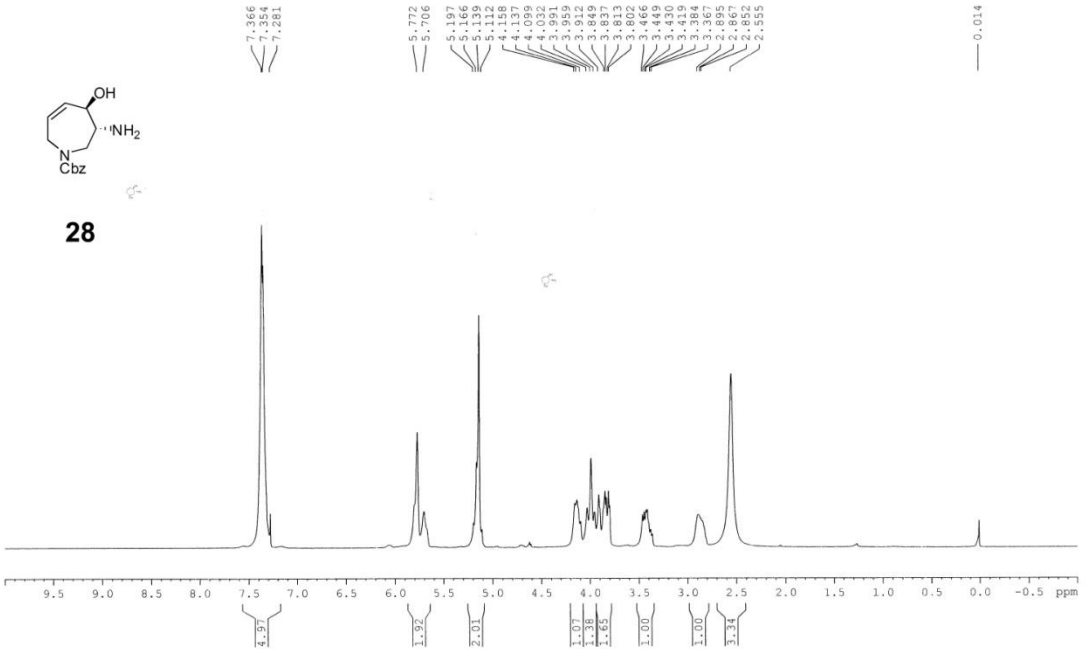
RM-TS-2/31 19.04.12



RM-TS-2/31 19.04.12

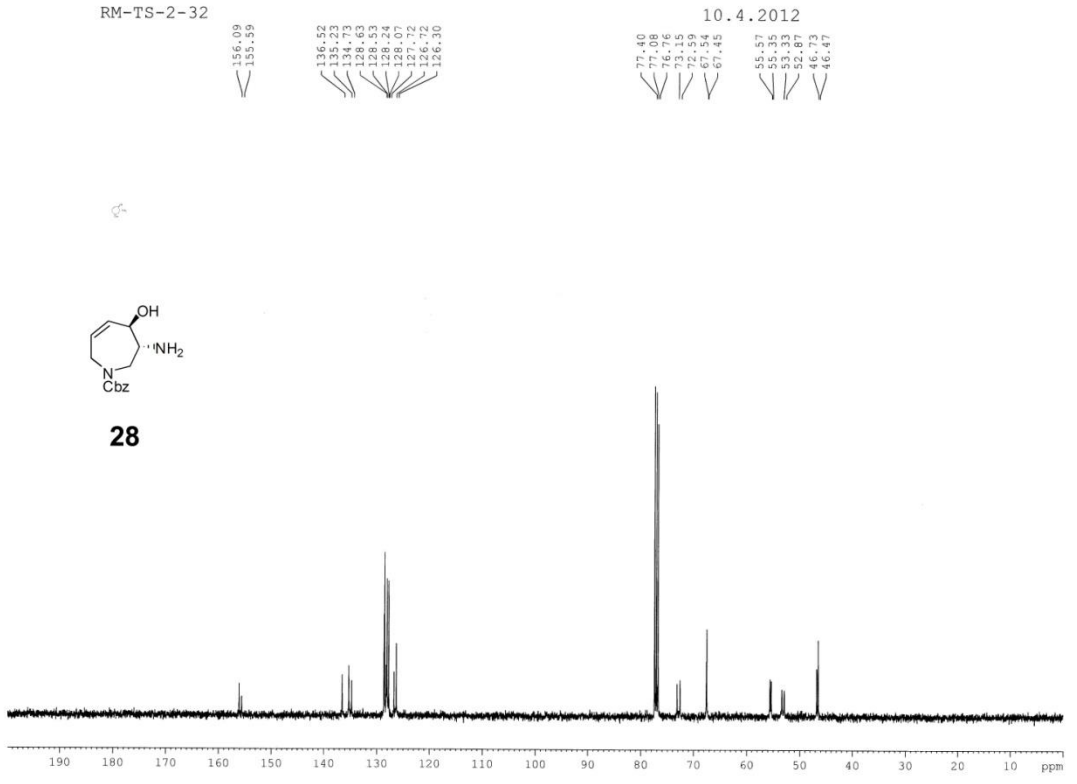


RM-TS-2-32 10.04.12



28

RM-TS-2-32 10.4.2012



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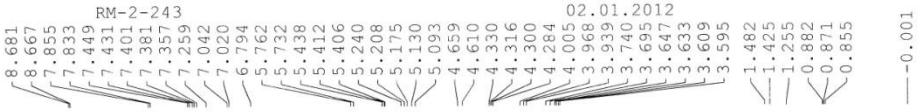
RM-2-243
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7.449
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7.401
7.381
7.357
7.259
7.042
7.020
6.794
5.762
5.732
5.438
5.412
5.406
5.240
5.208
5.175
5.130
5.093
4.659
4.610
4.330
4.316
4.300
4.284
4.005
3.968
3.939
3.740
3.695
3.647
3.633
3.609
3.595
1.482
1.425
1.255
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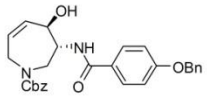
0.871
0.855
-0.001


OH
NH
N
Cbz
O
OBn

29

9
8
7
6
5
4
3
2
1
0
ppm
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2.07
10.88
0.93
1.93
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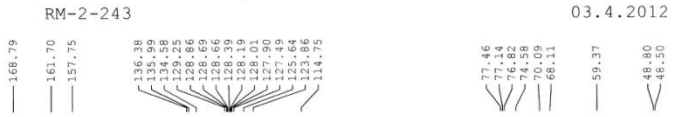
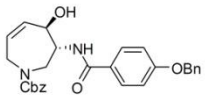
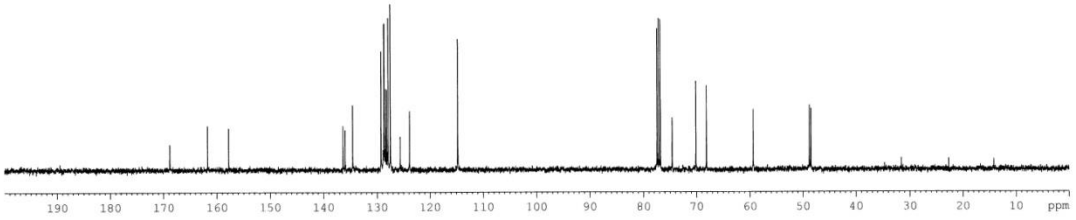
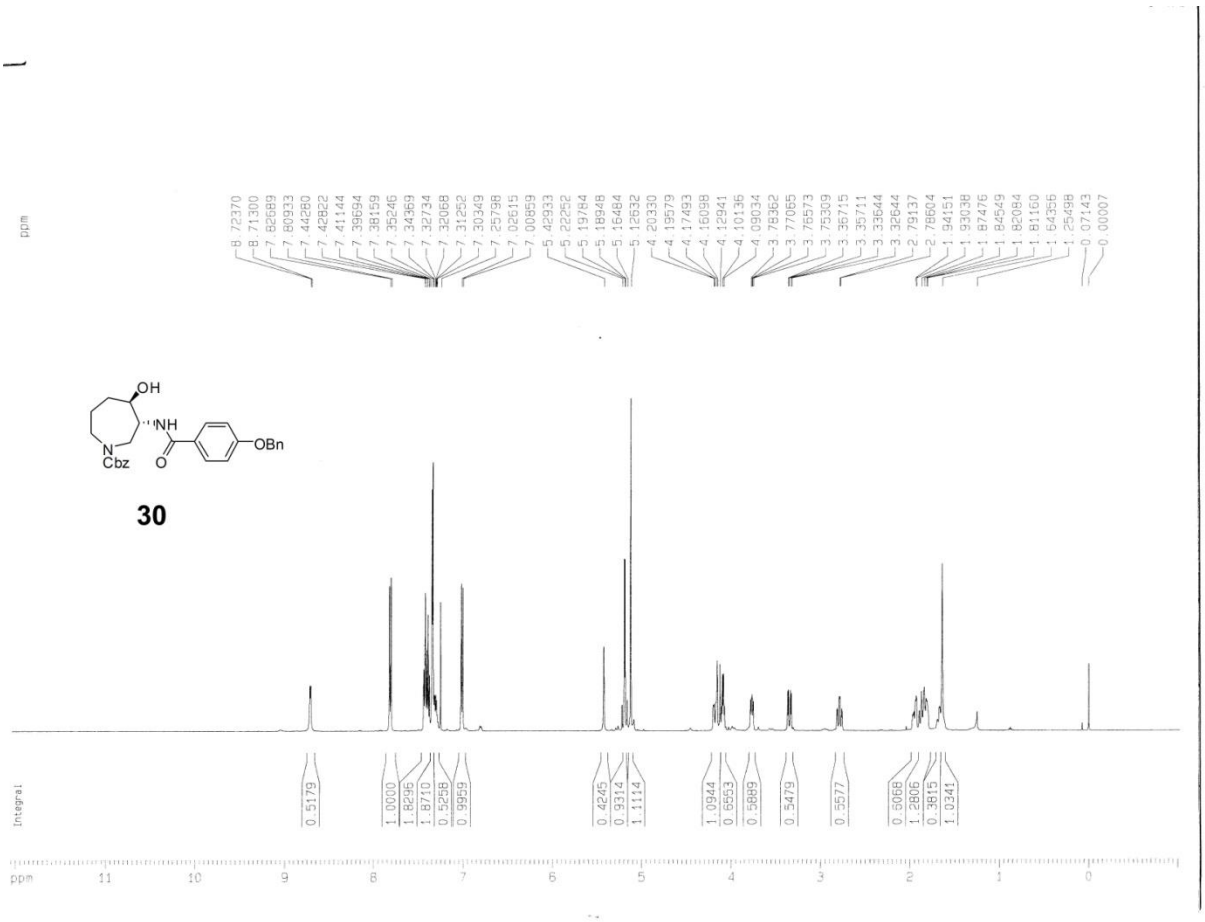
2.52
2.23
1.10
1.24
1.26
1.08
1.12
0.95
0.67


RM-2-243
03.4.2012
168.79
161.70
157.75
136.38
135.99
134.58
129.25
128.86
128.69
128.66
128.39
128.19
128.01
127.90
127.49
125.64
123.86
114.75
77.46
77.14
76.82
74.58
70.09
68.11
59.37
48.80
48.50


OH
NH
N
Cbz
O
OBn

29


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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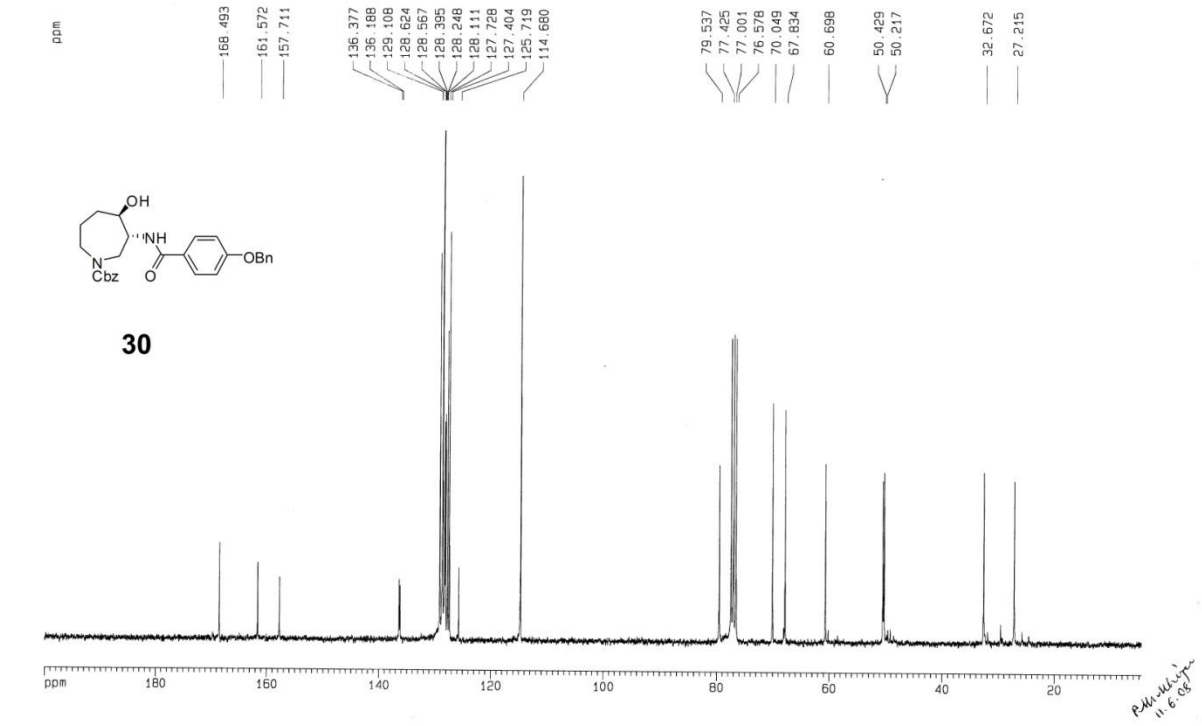
8.72370
8.71300
7.82689
7.80933
7.44280
7.42822
7.41144
7.39694
7.38159
7.35246
7.34369
7.32734
7.32068
7.31252
7.30349
7.25798
7.02615
7.00859
5.42933
5.22252
5.19784
5.18948
5.16484
5.12632
4.20330
4.19579
4.17493
4.16098
4.12941
4.10136
4.09034
3.78362
3.77065
3.76573
3.75309
3.36715
3.35711
3.33644
3.32644
2.79137
2.78604
1.94151
1.93038
1.87476
1.84549
1.82084
1.81160
1.64356
1.25498
0.07143
0.00007
OH
NH
N
Cbz
O
OBn
30
Integral
0.5179
1.0000
1.8295
1.8710
0.5258
0.9959
0.4245
0.9314
1.1114
1.0944
0.6553
0.5889
0.5479
0.5577
0.6068
1.2806
0.3815
1.0341
ppm
11
10
9
8
7
6
5
4
3
2
1
0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136.377
136.188
129.108
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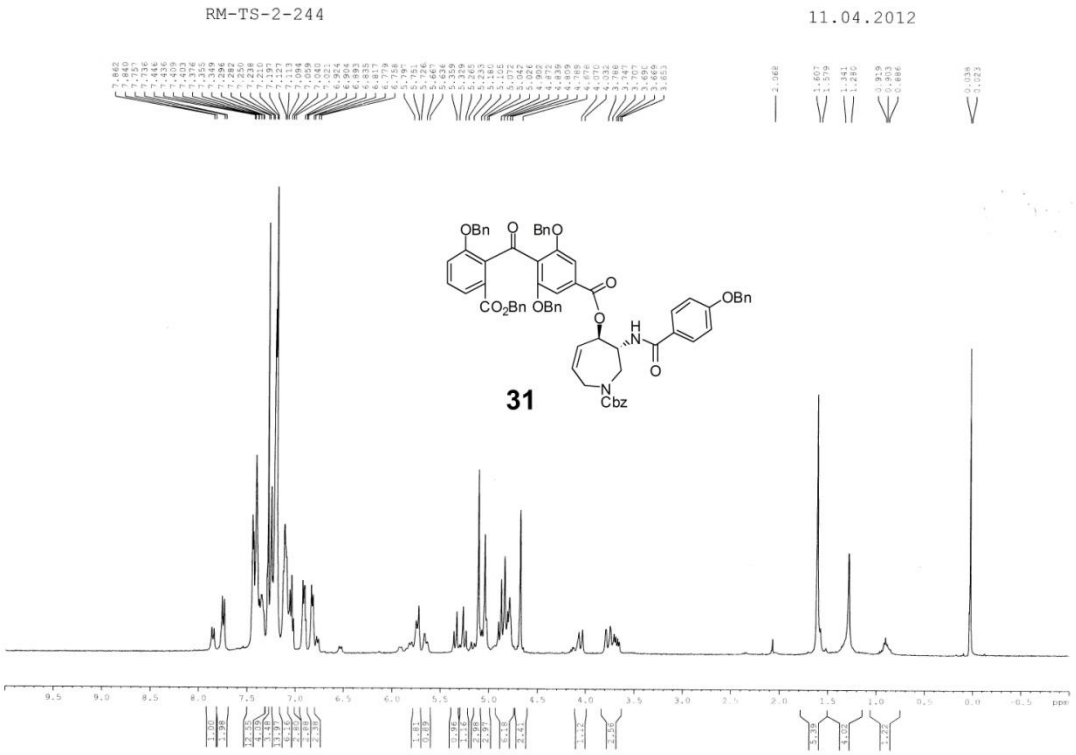
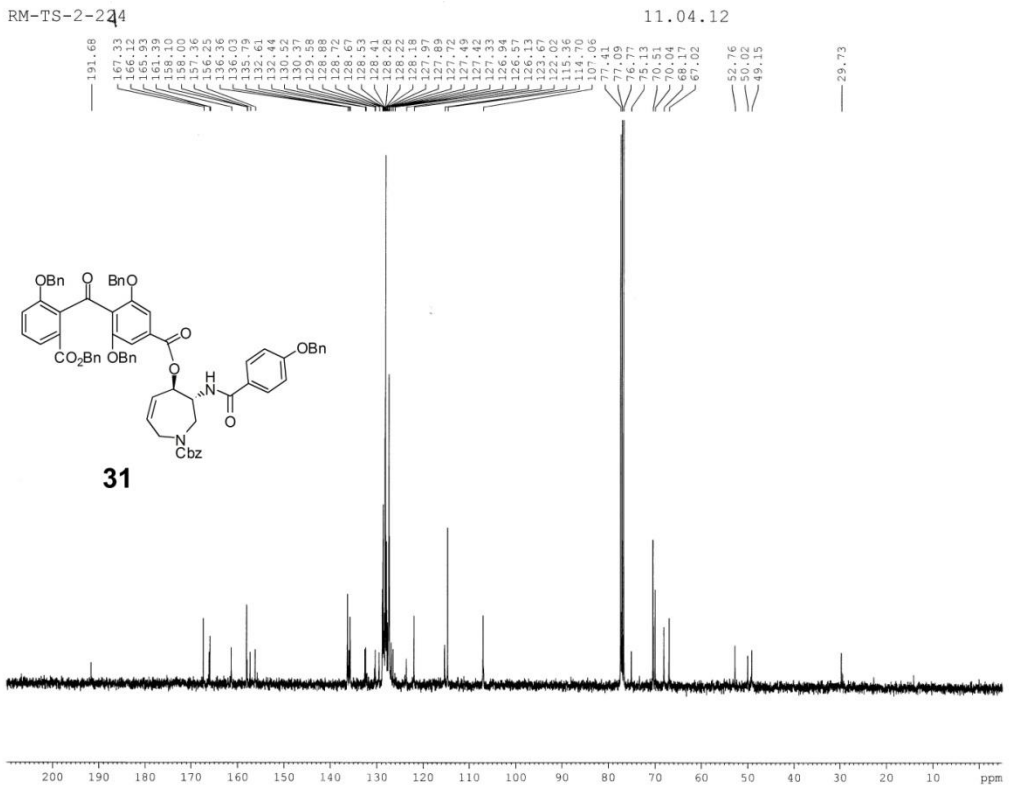
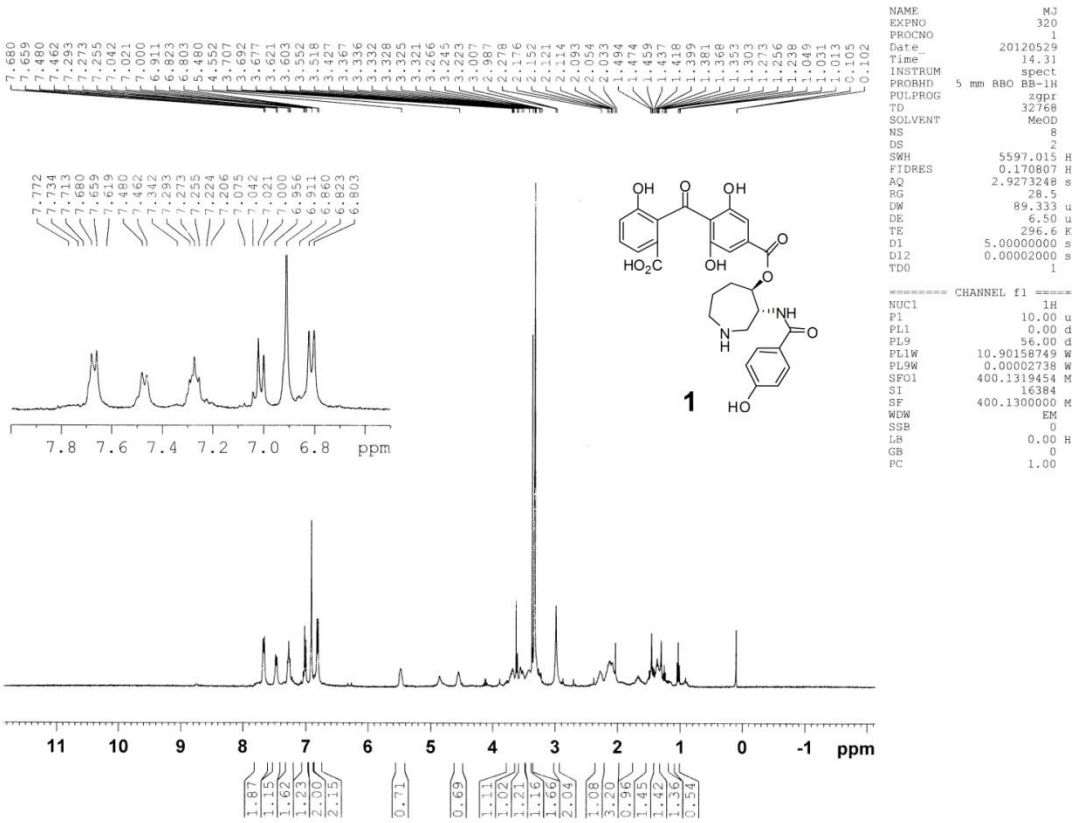
128.567
128.395
128.248
128.111
127.728
127.404
125.719
114.680
79.537
77.425
77.001
76.578
70.049
67.834
60.698
50.429
50.217
32.672
27.215
OH
NH
N
Cbz
O
OBn
30
ppm
180
160
140
120
100
80
60
40
20


RM-TS-2-244
11.04.2012
OBn
BnO
CO2Bn OBn
OBn
Cbz
31


RM-TS-2-244
11.04.12
OBn
BnO
CO2Bn OBn
OBn
Cbz
31

water suppressed RM 2/254



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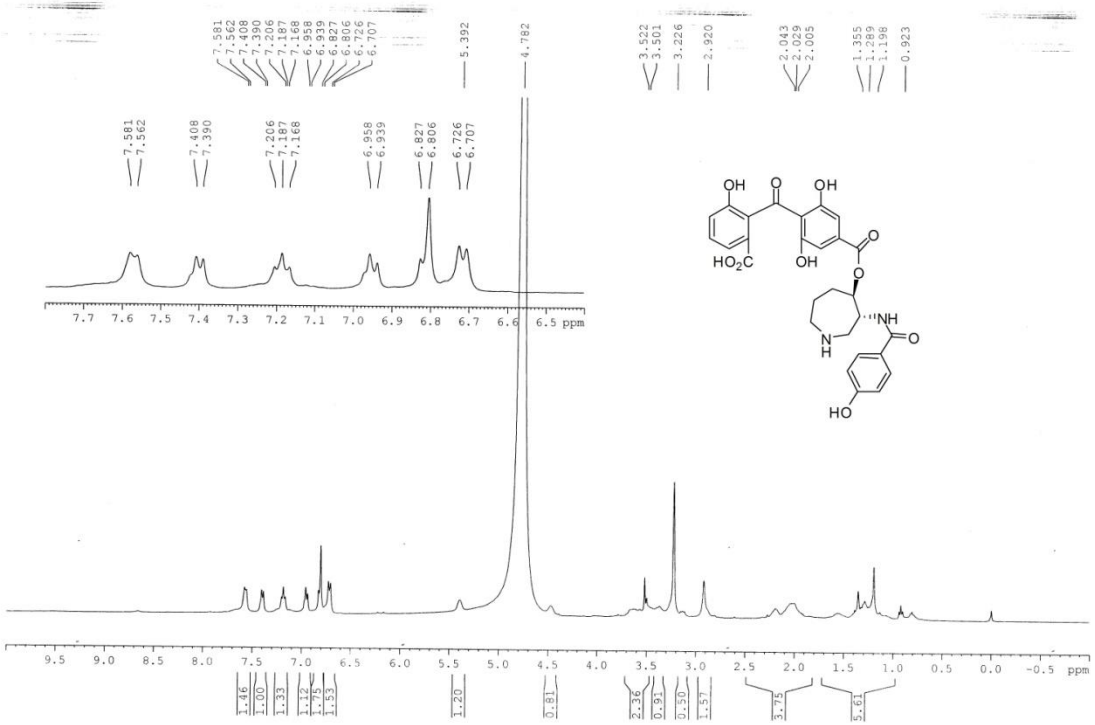
EXPNO	320
PROCNO	1
Date_	20120529
Time	14.31
INSTRUM	spect
PROBHD	5 mm BBO BB-1H
PULPROG	zgpr
TD	32768
SOLVENT	MeOD
NS	8
DS	2
SWH	5597.015 H
FIDRES	0.170807 H
AQ	2.9273248 s
RG	28.5
DW	89.333 u
DE	6.50 u
TE	296.6 K
D1	5.00000000 s
D12	0.00002000 s
TD0	1
========	CHANNEL f1 ======
NUC1	1H
P1	10.00 u
PL1	0.00 d
PL9	56.00 d
PL1W	10.90158749 W
PL9W	0.00002738 W
SFO1	400.1319454 M
SI	16384
SF	400.1300000 M
WDW	EM
SSB	0
LB	0.00 H
GB	0
PC	1.00

TS-2/44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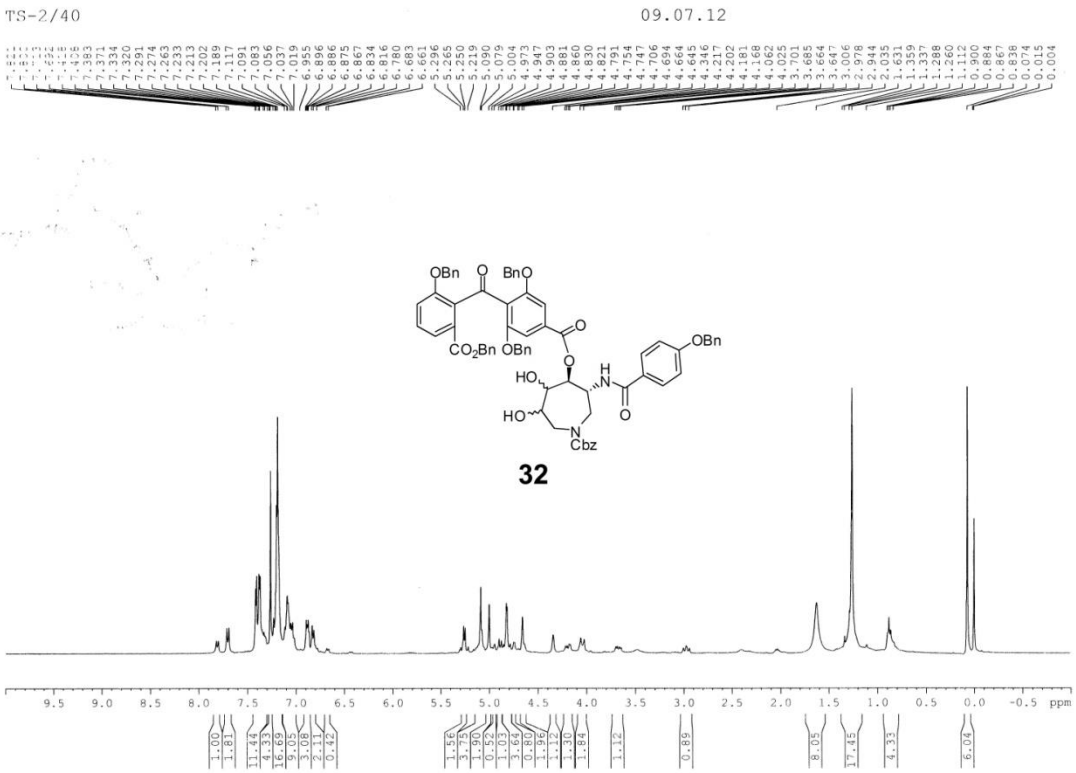
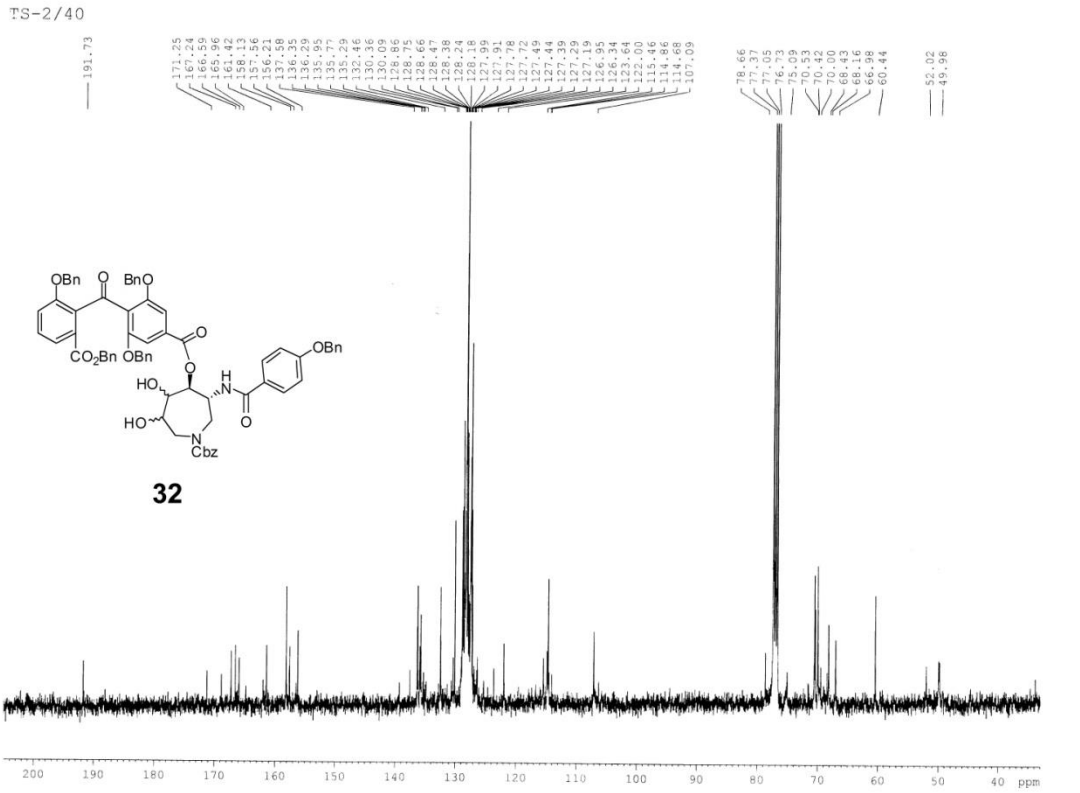
7.187
7.168
6.958
6.939
6.827
6.806
6.726
6.707
5.392
4.782
3.522
3.501
3.226
2.920
2.043
2.029
2.005
1.355
1.289
1.198
0.923
OH
O
OH
HO2C
OH
O
O
NH
N
H
O
HO
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
1.46
1.00
1.33
1.12
1.75
1.53
1.20
0.81
2.36
0.91
0.50
1.57
3.75
5.61


TS-2/40
09.07.12
32


TS-2/40
32

^{1}H NMR data of compound **30**(500 MHz, $CDCl_3$)	^{1}H NMR data of compound **30** (500 MHz, $CDCl_3$) reported by Nicolaou *et. al.*	^{13}C NMR data of compound **30**	^{13}C NMR data of compound **30** reported
8.72 (d, *J* = 5.4 Hz, 1H),	8.75 (d, *J* = 5.5 Hz,1H),	168.5	168.5
7.81 (d, *J* = 8.8 Hz, 2H),	7.82 (ddd, *J* = 8.8, 2.8, 1.9 Hz, 2H)	161.6	161.5
7.44-7.29 (m, 10H),	7.45-7.29 (m, 10H),	157.7	157.7
7.02 (d, *J* = 8.8 Hz, 2H),	7.02 (ddd, *J* =8.8, 2.8, 1.9 Hz, 2H)	136.4	136.3
5.43 (br s, 1H), 5.20 (AB q, *J* = 12.3 Hz, 2H),	5.21, 5.18 (AB , *J* = 12.3 Hz, 2H)	136.2	136.1
5.13 (s, 2H),	5.13 (s, 2H),	129.1	129.1
4.20 (dd, J=14.2, 3.75Hz, 1H) 4.16 (d, *J* = 15.8 Hz, 1H)	4.19 (dd, *J* = 14.3, 3.8 Hz,1H), 4.15 (d, *J* = 15.4 Hz, 1H),	128.6	128.62
		128.4	128.56
4.10- 4.06 (m, 1H),	4.10 (m, 1H),	128.2	128.2
3.76 (dd, *J* =8.9, 6.5Hz, 1H),	3.77 (ddd, *J* =10.2, 6.1, 1.6 Hz, 1H)	128.1	128.1
3.34 (dd, *J* =15.3, 5.1 Hz,1H)	3.35 (dd, *J* = 15.4, 5.1 Hz, 1H),	127.7	127.7
2.79 (dt, *J* = 3.4, 13.6Hz, 1H)	2.79 (ddd,*J* =14.3, 13.2, 3.5 Hz,1H)	127.4	127.4
1.97-1.93 (m, 1H), 1.90-1.81 (m, 2H),	1.95-1.81 (m, 3H),	125.7	125.6
		114.7	114.6
1.70-1.67 (m, 1H).	1.66 (m, 1H).	79.5	79.7
		70.0	70.0
		67.8	67.8
		60.7	60.7
		50.4	50.4
		50.2	50.2
		32.7	32.7
		27.2.	27.3.

^{1}H NMR(500 MHz, $CDCl_3$) data of (−)-balanol reported by Nicolaou *et. al* [2]	^{1}H NMR(500 MHz, $CDCl_3$) data of compound **1**
7.60 (d, *J* = 8.7, 2 H)	δ 7.58 (d, *J* = 8.4 Hz, 2H)
7.26 (d, *J* = 7.3 Hz, 1 H)	7.39 (d, *J* = 7.2 Hz, 1H)
7.17 (dd, *J* = 7.9, 7.9 Hz, 1H)	7.18 (t, *J* = 9.0 Hz, 1H)
6.91 (s, 2H)	6.94 (d, *J* = 8.4 Hz, 1H)
6.79 (d, *J* = 7.7Hz, 1H)	6.82 (s, 2H)
6.76 (d, *J* = 8.7 Hz, 2H)	6.71 (d, *J* = 7.6 Hz, 2H)
5.29 (m, 1H)	5.39 (m, 1H)
4.33 (br m, 1H)	4.47 (m, 1H)
3.44-2.98 (br m, 4H)	3.52-2.92 (m, 4H)
2.11-1.85 (br m, 4H)	2.19-2.02 (m, 4H)

References

1. Hollinshead, S. P.; Nichols, J. B.; Wilson, J. W. *J. Org. Chem.* **1994,** *59,* 6703–6709. doi:10.1021/jo00101a032
2. Nicolaou, K. C.; Koide, K.; Bunnage, M. E. *Chem.–Eur. J.* **1995,** *1,* 454–466. doi:10.1002/chem.19950010711
3. Nicolaou, K. C.; Bunnage, M. E.; Koide, K. *J. Am. Chem. Soc.* **1994,** *116,* 8402–8403. doi:10.1021/ja00097a072
4. Lampe, J. W.; Hughes, P. F.; Biggers, C. K.; Smith, S. H.; Hu, H. *J. Org. Chem.* **1994,** *59,* 5147–5148. doi:10.1021/jo00097a014