Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information for

On the origins of diastereoselectivity in the conjugate additions of the antipodes of lithium *N*-benzyl-(*N*-α-methylbenzyl)amide to enantiopure *cis*- and *trans*-dioxolane containing α,β-unsaturated esters

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Experimental

General Experimental Details

Reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. BuLi was purchased from Sigma-Aldrich (as a solution in hexanes) and titrated against diphenylacetic acid before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.[1] Water was purified by an Elix® UV-10 system. All other reagents were used as supplied without prior purification. Organic layers were dried over $MgSO_4$. Thin layer chromatography was performed on aluminium plates coated with 60 F_{254} silica. Plates were visualised using UV light (254 nm), iodine, 1% aq $KMnO_4$, or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed on Kieselgel 60 silica.

Melting points were recorded on a Gallenkamp Hot Stage apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter with a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer on an ATR module. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded on Bruker Avance spectrometers in the deuterated solvent stated. Spectra were recorded at rt. The field was locked by external referencing to the relevant deuteron resonance. When the diastereotopic methyl groups of acetonide and isopropyl functionalities could not be unambiguously assigned, the descriptors *Me*CMe and *Me*CHMe were employed. Low-resolution mass spectra were recorded on either a VG MassLab 20–250 or a Micromass Platform 1 spectrometer. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m × 0.25 mm) using amyl acetate as a lock mass.

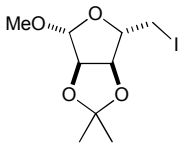
General Procedure: Lithium amide conjugate addition to an α,β-unsaturated ester

BuLi (1.94 equiv) was added dropwise to a stirred solution of the requisite amine (2.0 equiv) in either THF or Et_2O (as stated) at −78 °C or −20 °C, respectively, and stirring was continued for 30 min. A solution of the requisite α,β-unsaturated ester (1.0 equiv) in either THF or Et_2O (as stated) was then added via cannula and the reaction mixture was stirred for 2 h (for THF) or 5 h (for Et_2O). Satd aq NH_4Cl was then added and the reaction mixture was partitioned between Et_2O and H_2O. The aqueous layer was extracted with three portions

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

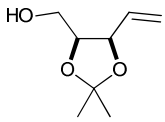
of Et_2O and the combined organic extracts were washed sequentially with 10% aq citric acid, satd aq $NaHCO_3$ and brine, then dried and concentrated *in vacuo*.

(2*R*,3*R*,4*S*,5*S*)-2-Methoxy-3,4-*O*-isopropylidene-3,4-dihydroxy-5-iodomethyltetrahydrofuran 36



Conc aq HCl (2.0 mL) was added to a solution of D-ribose **35** (50.0 g, 0.333 mol) in acetone/MeOH (v/v 1:1, 700 mL). The resultant solution was heated at 60 °C for 1 h then allowed to cool to rt and neutralised by the addition of Na_2CO_3 (~10 g). The resultant suspension was filtered through Celite® (eluent EtOAc) and the filtrate was concentrated *in vacuo*. The residue was dissolved in EtOAc (250 mL) and the resultant solution was washed with H_2O (250 mL). The aqueous layer was extracted with EtOAc (2 × 250 mL) and the combined organic extracts were dried and concentrated *in vacuo*. PPh_3 (105 g, 0.40 mol) and imidazole (34.0 g, 0.500 mol) were added to the residue and the resultant mixture was dissolved in PhMe/MeCN (v/v 5:1, 1 L). I_2 (101 g, 0.399 mol) was then added and the reaction mixture was heated at 60 °C for 1 h, then allowed to cool to rt and diluted with Et_2O (250 mL). The resultant mixture was washed sequentially with 10% aq $Na_2S_2O_3$ (1 L), H_2O (1 L) and brine (1 L), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **36** as an orange oil (66.4 g, 64%, >99:1 dr);[2,3] $[\alpha]_D^{24}$ −72.3 (*c* 1.0 in $CHCl_3$); {lit.[4] $[\alpha]_D^{24}$ −79.8 (*c* 1.0 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.34 (3H, s, *Me*CMe), 1.49 (3H, s, *Me*CMe), 3.17 (1H, app t, *J* 10.1, CH_AH$_B$I), 3.30 (1H, dd, *J* 10.1, 5.8, CH$_A$*H*$_B$I), 3.38 (3H, s, O*Me*), 4.45 (1H, app dd, *J* 10.1, 5.8, C(5)*H*), 4.64 (1H, app d, *J* 5.8, C(4)*H*), 4.78 (1H, app d, *J* 5.8, C(3)*H*), 5.06 (1H, app s, C(2)*H*).

(4*S*,5*R*)-2,2-Dimethyl-4-hydroxymethyl-5-vinyl-1,3-dioxolane 37

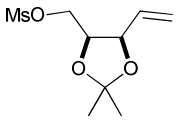


BuLi (2.1 M in hexanes, 31.7 mL, 66.7 mmol) was added to a solution of **36** (20.9 g, 66.7 mmol, >99:1 dr) in THF (340 mL) at −78 °C and the resultant solution was stirred at −78 °C for 2 h. DIBAL-H (1.0 M in THF, 100 mL, 100 mmol) was then added via cannula and the resultant mixture was allowed to warm to rt over 16 h. Acetone (500 mL) and satd aq sodium potassium tartrate (500 mL) were added sequentially and stirring was

[2] Paquette, L. A.; Bailey, S. *J. Org. Chem.* **1995**, *60*, 7849.
[3] Anderson, R. J.; Dixon, R. M.; Golding, B. T. *J. Organometallic. Chem.* **1992**, *437*, 227.
[4] Ivanova, N. A.; Valiullina, Z. R.; Shitikova, O. V.; Muftakhov, M. S. *Russ. J. Org. Chem.* **2007**, *43*, 742.

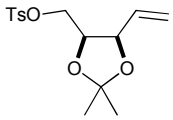
continued for 1 h at rt. The reaction mixture was then partitioned between brine (300 mL) and EtOAc (300 mL), and the aqueous layer was extracted with EtOAc (300 mL). The combined organic extracts were then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 2:1) gave **37** as a pale yellow oil (9.60 g, 91%, >99:1 dr);[5] $[\alpha]_D^{24}$ −45.7 (*c* 1.0 in $CHCl_3$); {lit.[6] $[\alpha]_D^{24}$ −44.0 (*c* 4.9 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.40 (3H, s, *Me*CMe), 1.52 (3H, s, *Me*CMe), 1.94 (1H, s, O*H*), 3.58 (2H, app t, *J* 5.5, CH_2OH), 4.24-4.30 (1H, m, C(4)*H*), 4.65 (1H, app t, *J* 7.0, C(5)*H*), 5.29 (1H, dd, *J* 10.4, 1.0, CH=CH_AH$_B$), 5.40 (1H, dd, *J* 17.4, 1.0, C=CH$_A$$H_B$), 5.87 (1H, ddd, *J* 17.4, 10.4, 7.0, C*H*=CH$_2$).

(4*S*,5*R*)-2,2-Dimethyl-4-(methanesulfonyloxy)methyl-5-vinyl-1,3-dioxlane 38



MsCl (12.2 mL, 158 mmol), Et_3N (50.9 mL, 364 mmol) and DMAP (10 mg) were added to a stirred solution of **37** (5.00 g, 31.6 mmol, >99:1 dr) in CH_2Cl_2 (760 mL) at 0 °C. The resultant mixture was allowed to warm to rt and stirring was continued at rt for 3 h. H_2O (450 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (250 mL). The combined organic extracts were washed sequentially with 1.0 M aq HCl (500 mL), satd aq $NaHCO_3$ (500 mL) and brine (500 mL), then dried and concentrated *in vacuo* to give **38** as an orange oil (7.46 g, quant, >99:1 dr), which was used without purification;[7] δ_H (400 MHz, $CDCl_3$) 1.40 (3H, s, *Me*CMe), 1.53 (3H, s, *Me*CMe), 3.07 (3H, s, SO_2*Me*), 4.13 (1H, dd, *J* 10.8, 7.5, CH_AH$_B$OMs), 4.20 (1H, dd, *J* 10.8, 4.1, CH$_A$$H_B$OMs), 4.43 (1H, ddd, *J* 7.5, 6.9, 4.1, C(4)*H*), 4.72 (1H, app t, *J* 6.9, C(5)*H*), 5.34 (1H, app dt, *J* 10.4, 1.2, CH=CH_AH$_B$), 5.46 (1H, app dt, *J* 17.3, 1.2, CH=CH$_A$$H_B$), 5.81 (1H, ddd, *J* 17.3, 10.4, 6.9, C*H*=CH$_2$).

(4*S*,5*R*)-2,2-Dimethyl-4-(*p*-toluenesulfonyloxy)methyl-5-vinyl-1,3-dioxolane 39

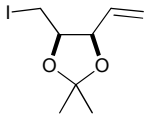


TsCl (3.01 g, 15.8 mmol), Et_3N (3.96 mL, 36.3 mmol) and DMAP (10 mg) were added to a stirred solution of **37** (500 mg, 3.16 mmol, >99:1 dr) in CH_2Cl_2 (76 mL) at 0 °C. The resultant mixture was allowed to warm to rt and stirring was continued at rt for 48 h. H_2O (60 mL) was then added and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were washed sequentially with 1.0 M aq HCl (70 mL), satd aq $NaHCO_3$ (70 mL) and brine (70 mL), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 3:1) gave **39** as a yellow solid (939 mg, 95%, >99:1

[5] Yadav, J. S.; Reddy, B. V. S.; Srinivasa Reddy, K. *Tetrahedron* **2003**, *59*, 5333.
[6] Haefele, B.; Schrocter, D.; Jaeger, V. *Angew. Chem.* **1986**, *98*, 89.
[7] Jaeger, V.; Huemmer, W.; Stahl, U.; Gracza, T. *Synthesis*, **1991**, *9*, 769.

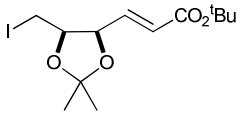
dr);[8] mp 49–53 °C; {lit.[9] mp 51–52 °C)}; $[\alpha]_D^{24}$ −36.5 (*c* 1.0 in $CHCl_3$); {lit.[8] $[\alpha]_D^{24}$ −37.5 (*c* 1.9 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.34 (3H, s, *Me*CMe), 1.39 (3H, s, *Me*CMe), 2.46 (3H, s, Ar*Me*), 3.90 (1H, dd, *J* 10.2, 6.8, CH_AH$_B$OTs), 4.01 (1H, dd, *J* 10.2, 5.2, CH$_A$$H_B$OTs), 4.34 (1H, app dt, *J* 6.8, 5.2, C(4)*H*), 4.65 (1H, app t, *J* 6.8, C(5)*H*), 5.24 (1H, app dt, *J* 10.3, 1.3, CH=CH_AH$_B$), 5.39 (1H, app dt, *J* 17.3, 1.3, CH=CH$_A$$H_B$), 5.71 (1H, ddd, *J* 17.3, 10.3, 6.8, C*H*=CH$_2$), 7.35 (2H, d, *J* 8.4, *Ar*), 7.79 (2H, d, *J* 8.4, *Ar*).

(*R*,*R*)-2,2-Dimethyl-4-iodomethyl-5-vinyl-1,3-dioxolane 40



PPh_3 (396 mg, 1.51 mmol) and imidazole (129 mg, 1.89 mmol) were added to a solution of **37** (200 mg, 1.26 mmol, >99:1 dr) in PhMe/MeCN (v/v 5:1, 4 mL). I_2 (384 mg, 1.51 mmol) was then added and the resultant mixture was heated at 60 °C for 1 h. The reaction mixture was allowed to cool to rt, diluted with Et_2O (5 mL) and washed sequentially with 10% aq $Na_2S_2O_3$ (5 mL), H_2O (5 mL) and brine (5 mL), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 2:1) gave **40** as a pale yellow oil (244 mg, 72%, >99:1 dr); $[\alpha]_D^{24}$ −13.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2986, 2935 (C–H); δ_H (400 MHz, $CDCl_3$) 1.34 (3H, s, *Me*CMe), 1.47 (3H, s, *Me*CMe), 3.02 (1H, dd, *J* 10.2, 6.3, CH_AH$_B$I), 3.10 (1H, dd, *J* 10.2, 7.5, CH$_A$$H_B$I), 4.40 (1H, app dt, *J* 7.5, 6.3, C(4)*H*), 4.59 (1H, app t, *J* 6.3, C(5)*H*), 5.29 (1H, d, *J* 10.6, CH=CH_AH$_B$), 5.39 (1H, d, *J* 17.4, CH=CH$_A$$H_B$), 5.81 (1H, ddd, *J* 17.4, 10.6, 6.3, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 4.0 (*C*H$_2$I), 25.6, 28.2 (C*Me*$_2$), 78.4 (*C*(4)), 79.1 (*C*(5)), 109.0 (*C*Me$_2$), 119.3 (CH=*C*H$_2$), 132.4 (*C*H=CH$_2$); *m*/*z* (FI^+) 268 ($[M]^+$, 100%); HRMS (FI^+) $C_8H_{13}IO_2^+$ ($[M]^+$) requires 267.9955; found 267.9966.

***tert*-Butyl (*R*,*R*,*E*)-4,5-*O*-isopropylidene-4,5-dihydroxy-6-iodohex-2-enoate 42**

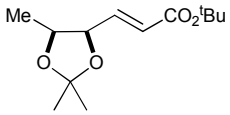


Hoveyda-Grubbs II (1.55 g, 1.82 mmol) was added to a degassed solution of **40** (4.89 g, 18.2 mmol, >99:1 dr) and *tert*-butyl acrylate (7.01 mL, 54.7 mmol) in CH_2Cl_2 (94 mL) and the resultant mixture was heated at reflux for 24 h. The reaction mixture was then allowed to cool to rt and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 20:1) gave **42** as a pale yellow solid (4.45 g, 66%, >99:1 dr); mp 39–43 °C; $[\alpha]_D^{24}$ −0.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3031, 2978, 2934, 2903, 2852, 2361, 2342 (C–H), 1696 (C=O), 1645 (C=C); δ_H (400 MHz, $CDCl_3$) 1.39 (3H, s, *Me*CMe), 1.50 (9H, s, C*Me*$_3$), 1.53 (3H, s,

[8] Gypser, A.; Flasche, M.; Scharf, H. D. *Liebigs Ann. Chem.* **1994**, *8*, 775.
[9] Wershofen, S.; Scarf, H. D. *Synthesis* **1988**, 11, 854.

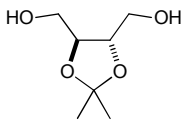
*Me*CMe), 3.02 (1H, dd, *J* 10.4, 6.5, C(6)H_A), 3.13 (1H, dd, *J* 10.4, 7.5, C(6)H_B), 4.52 (1H, app q, *J* 6.5, C(5)*H*), 4.79 (1H, app dt, *J* 6.5, 1.3, C(4)*H*), 6.09 (1H, dd, *J* 15.5, 1.3, C(2)*H*), 6.81 (1H, dd, *J* 15.5, 6.5, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 3.1 (*C*(6)), 25.5, 28.0 (C*Me*$_2$), 28.1 (C*Me*$_3$), 76.9 (*C*(4)), 78.5 (*C*(5)), 80.8 (*C*Me$_3$), 109.6 (*C*Me$_2$), 125.8 (*C*(2)), 139.8 (*C*(3)), 165.0 (*C*(1)); *m*/*z* (ESI$^+$) 759 ([2M+Na]$^+$, 100%), 391 ([M+Na]$^+$, 53%); HRMS (ESI$^+$) $C_{13}H_{21}INaO_4^+$ ([M+Na]$^+$) requires 391.0377; found 391.0365.

tert-Butyl (4*R*,5*S*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-2-enoate 31



Pd/C (2.27% w/w of substrate, 23 mg) and Et_3N (5.20 mL, 27.2 mmol) were added to a solution of **42** (1.00 g, 2.72 mmol, >99:1 dr) in MeOH (179 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 24 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give a 90:10 mixture of **31** and **42**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 5:1) gave **42** as a yellow solid (110 mg, 10%, >99:1 dr) and **31** as a pale yellow oil (480 mg, 73%, >99:1 dr); $[\alpha]_D^{24}$ +3.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2982, 2937, 2905 (C–H), 1714 (C=O), 1659 (C=C); δ_H (400 MHz, $CDCl_3$) 1.17 (3H, d, *J* 6.3, C(6)H_3), 1.38 (3H, s, *Me*CMe), 1.49 (9H, s, C*Me*$_3$), 1.53 (3H, s, *Me*CMe), 4.42 (1H, app quintet, *J* 6.3, C(5)*H*), 4.64 (1H, app t, *J* 6.3, C(4)*H*), 6.00 (1H, app d, *J* 15.7, C(2)*H*), 6.73 (1H, dd, *J* 15.7, 6.3, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 16.2 (*C*(6)), 25.4, 28.0 (C*Me*$_2$), 28.1 (C*Me*$_3$), 74.0 (*C*(5)), 77.7 (*C*(4)), 80.6 (*C*Me$_3$), 108.6 (*C*Me$_2$), 124.9 (*C*(2)), 142.3 (*C*(3)), 165.3 (*C*(1)); *m*/*z* (ESI$^+$) 265 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{13}H_{22}NaO_4^+$ ([M+Na]$^+$) requires 265.1410; found 265.1403.

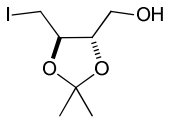
(*S*,*S*)-2,2-Dimethyl-4,5-bis(hydroxymethyl)-1,3-dioxolane 45



DMP (12.0 mL, 96.9 mmol) and TsOH (128 mg, 0.65 mmol) were added to a solution of dimethyl L-tartrate **44** (11.5 g, 64.6 mmol) in PhMe (75 mL). The resultant mixture was fitted with a Dean-Stark apparatus and heated at reflux for 16 h. The reaction mixture was then cooled to rt and satd aq $NaHCO_3$ (50 mL) was added. The resultant mixture was stirred at rt for 15 min then the aqueous layer was extracted with EtOAc (2 × 30 mL). The combined organic extracts were sequentially washed with H_2O (40 mL) and brine (40 mL), then dried and concentrated *in vacuo* to give dimethyl (*R*,*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate as a

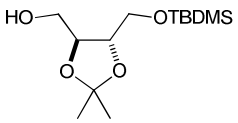
yellow oil (13.5 g, 96%, >99:1 dr);[10] $[\alpha]_D^{24}$ −56.1 (*c* 1.0 in MeOH); {lit.[11] $[\alpha]_D^{24}$ −49.1 (*c* 1.0 in MeOH)}; δ_H (400 MHz, $CDCl_3$) 1.50 (6H, s, C*Me*$_2$), 3.83 (6H, s, CO_2*Me*), 4.82 (2H, s, C(4)*H*, C(5)*H*). $LiAlH_4$ (1.0 M in THF, 100 mL, 100 mmol) was added dropwise to a stirred solution of dimethyl (*R*,*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (9.32 g, 42.7 mmol, >99:1 dr) in THF (160 mL) at 0 °C. The resultant mixture was heated at reflux for 16 h then allowed to cool to rt. 10% aq NaOH (150 mL), H_2O (70 mL) and EtOAc (150 mL) were added and the resultant mixture was stirred at rt for 1 h. The reaction mixture was then filtered through Celite® (eluent EtOAc) and the filtrate was dried and concentrated *in vacuo* to give **45** as a pale yellow oil (6.55 g, 91%, >99:1 dr);[12] δ_H (400 MHz, $CDCl_3$) 1.44 (6H, s, C*Me*$_2$), 2.52 (2H, br s, O*H*), 3.67–3.74 (2H, m, CH_AH$_B$OH), 3.81–3.87 (2H, m, CH$_A$$H_B$OH), 4.02–4.05 (2H, m, C(4)*H*, C(5)*H*).

(4*R*,5*S*)-2,2-Dimethyl-4-iodomethyl-5-hydroxymethyl-1,3-dioxolane 46



PPh_3 (323 mg, 1.23 mmol) and imidazole (84 mg, 1.2 mmol) were added to a solution of **45** (200 mg, 1.23 mmol, >99:1 dr) in PhMe/MeCN (v/v 5:1, 4 mL). I_2 (313 mg, 1.23 mmol) was then added and the resultant solution was heated at 60 °C for 1 h then allowed to cool to rt. Et_2O (3 mL) was added and the reaction mixture was washed sequentially with satd aq $Na_2S_2O_3$ (5 mL), H_2O (5 mL) and brine (5 mL), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 4:1, 1% Et_3N) gave **46** as an orange oil (52 mg, 16%, >99:1 dr); $[\alpha]_D^{24}$ −3.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3432 (O–H), 2986, 2933, 2878 (C–H); δ_H (400 MHz, $CDCl_3$) 1.43 (3H, s, *Me*CMe), 1.46 (3H, s, *Me*CMe), 2.09 (1H, br s, O*H*), 3.30 (2H, app d, *J* 5.5, CH_2I), 3.65–3.75 (1H, m, CH_AH$_B$OH), 3.85–3.99 (3H, m, C(4)*H*, C(5)*H*, CH$_A$$H_B$OH); δ_C (100 MHz, $CDCl_3$) 5.8 (*C*H$_2$I), 27.4, 27.4 (C*Me*$_2$), 62.4 (*C*H$_2$OH), 75.9 (*C*(4)), 81.8 (*C*(5)), 109.7 (*C*Me$_2$); *m*/*z* (FI$^+$) 272 ([M]$^+$, 100%); HRMS (FI$^+$) $C_7H_{13}IO_3^+$ ([M]$^+$) requires 271.9904; found 271.9984.

(*S*,*S*)-2,2-Dimethyl-4-(*tert*-butyldimethylsilyloxy)methyl-5-hydroxymethyl-1,3-dioxolane 49

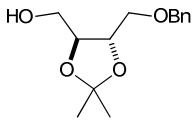


NaH (60% dispersion in mineral oil, 123 mg, 3.08 mmol) was stirred in 30–40 °C petrol (5 mL) for 10 min. The petrol was removed via cannula, then THF (5 mL) was added and the resultant mixture was cooled to 0 °C.

[10] Moon Kim, B.; Bae, S. J.; So, S. M.; Yoo, H. T.; Chang, S. K.; Lee, J. H.; Kang, J. S. *Org. Lett.* **2001**, *3*, 2349.
[11] Li, B.; Xuemer, Y.; Yang, K.; Fu, E. *Synthetic Commun.* **2005**, *35*, 2603.
[12] Flezmann, W.; Castagnolo, D.; Rosenbeiger, D.; Mulzer, J. *J. Org. Chem.* **2007**, *72*, 2182.

A solution of **45** (500 mg, 3.08 mmol, >99:1 dr) in THF (5 mL) was added via cannula and the resultant mixture was allowed to warm to rt and stirred at rt for 45 min. TBDMSCl (464 mg, 3.08 mmol) was then added and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then diluted with Et_2O (8 mL) and washed with satd aq $NaHCO_3$ (2 × 12 mL). The aqueous layer was separated and extracted with Et_2O (2 × 8 mL) and the combined organic extracts were dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 5:1) gave **49** as a pale yellow oil (425 mg, 50%, >99:1 dr);[13] $[\alpha]_D^{24}$ +14.5 (*c* 1.0 in $CHCl_3$); {lit.[14] $[\alpha]_D^{24}$ +15.3 (*c* 7.5 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 0.09 (6H, s, Si*Me*$_2$), 0.91 (9H, s, SiC*Me*$_3$), 1.41 (3H, s, *Me*CMe), 1.42 (3H, s, *Me*CMe), 2.38 (1H, dd, *J* 8.3, 4.4, O*H*), 3.64–3.81 (3H, m, C*H*$_2$OH, C*H*$_A$H$_B$OSi), 3.86–3.92 (2H, m, C(4)*H*, CH$_A$*H*$_B$OSi), 4.00 (1H, dt, *J* 7.5, 4.6, C(5)*H*).

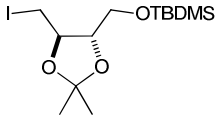
(*S*,*S*)-2,2-Dimethyl-4-benzyloxymethyl-5-hydroxymethyl-1,3-dioxolane 50



NaH (60% dispersion in mineral oil, 50 mg, 1.23 mmol) was stirred in 30–40 °C petrol (2 mL) for 10 min. The petrol was removed via cannula, then THF (2 mL) was added and the resultant suspension was cooled to 0 °C. A solution of **45** (200 mg, 1.23 mmol, >99:1 dr) in THF (2 mL) was added via cannula and the resultant mixture was allowed to warm to rt then stirred for 45 min. BnBr (0.15 mL, 1.23 mmol) was then added and the resultant solution was stirred at rt for 16 h. The reaction mixture was diluted with Et_2O (5 mL) and washed with satd aq $NaHCO_3$ (2 × 10 mL). The aqueous layer was separated and extracted with Et_2O (2 × 6 mL) and the combined organic extracts were dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 7:3) gave **50** as a pale yellow oil (170 mg, 55%, >99:1 dr);[15] $[\alpha]_D^{24}$ +8.6 (*c* 1.0 in $CHCl_3$); {lit.[16] $[\alpha]_D^{20}$ +8.7 (*c* 1.2 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.47 (3H, s, *Me*CMe), 1.48 (3H, s, *Me*CMe), 2.23 (1H, app q, *J* 4.3, O*H*), 3.61 (1H, dd, *J* 9.9, 5.8, C*H*$_A$H$_B$OBn), 3.70–3.77 (2H, m, C*H*$_A$H$_B$OH, CH$_A$*H*$_B$OBn), 3.83 (1H, dt, *J* 11.6, 4.4, CH$_A$*H*$_B$OH), 3.97–4.02 (1H, m, C(4)*H*), 4.09–4.14 (1H, m, C(5)*H*), 4.64 (2H, app s, C*H*$_2$Ph), 7.33–7.44 (5H, m, *Ph*).

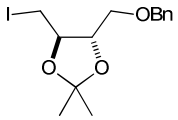
[13] Suzuki, M.; Kambe, M.; Tokuyama, H.; Fukuyama, T. *J. Org. Chem.*, **2004**, *69*, 2831.
[14] Clough, S.; Raggatt, M. E.; Simpson, T. J.; Willis, C. L.; Whiting, A.; Wrigley, S. K. *J. Chem. Soc. Perkin Trans. 1* **2000**, *15*, 2475.
[15] Fox, D. T.; Poulter, C. D. *J. Org. Chem.* **2005**, *70*, 1978.
[16] Kakinuma, H.; Tsuchiya, Y.; Tanaka, M; Horito, S.; Hashimoto, H. *Carbohyd. Res.* **1994**, *264*, 237.

(4*R*,5*S*)-2,2-Dimethyl-4-iodomethyl-5-(*tert*-butyldimethylsilyloxy)methyl-1,3-dioxolane 51



PPh_3 (427 mg, 1.80 mmol) and imidazole (153 mg, 2.25 mmol) were added to a solution of **49** (390 mg, 1.50 mmol, >99:1 dr) in PhMe/MeCN (v/v 5:1, 5 mL). I_2 (457 mg, 1.80 mmol) was then added and the resultant mixture was heated at 60 °C for 1 h. The reaction mixture was then allowed to cool to rt, diluted with Et_2O (5 mL) and the resultant mixture was washed sequentially with 10% aq $Na_2S_2O_3$ (7 mL), H_2O (7 mL) and brine (7 mL), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **51** as a yellow oil (551 mg, 95%, >99:1 dr);[17] $[\alpha]_D^{24}$ −3.3 (*c* 1.0 in $CHCl_3$); {lit.[17] for enantiomer $[\alpha]_D^{24}$ +2.8 (*c* 5.0 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 0.09 (6H, s, Si*Me*$_2$), 0.91 (9H, s, SiC*Me*$_3$), 1.41 (3H, s, *Me*CMe), 1.47 (3H, s, *Me*CMe), 3.31 (1H, dd, *J* 10.6, 5.1, C*H*$_A$H$_B$I), 3.42 (1H dd, *J* 10.6, 4.8, CH$_A$*H*$_B$I), 3.70–3.92 (4H, m, C*H*$_2$OSi, C(4)*H*, C(5)*H*).

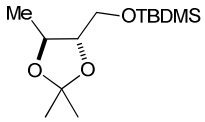
(4*R*,5*S*)-2,2-Dimethyl-4-iodomethyl-5-benzyloxymethyl-1,3-dioxolane 52



PPh_3 (1.00 g, 3.81 mmol) and imidazole (324 mg, 4.76 mmol) were added to a solution of **50** (800 mg, 3.17 mmol, >99:1 dr) in PhMe/MeCN (v/v 5:1, 10 mL). I_2 (966 mg, 3.81 mmol) was then added and the resultant solution was heated at 60 °C for 1 h. Et_2O (6 mL) was added and the resultant mixture was washed sequentially with satd aq $Na_2S_2O_3$ (10 mL), H_2O (10 mL) and brine (10 mL), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 2:1) gave **52** as a pale yellow oil (939 mg, 82%, >99:1 dr);[18] $[\alpha]_D^{24}$ −9.6 (*c* 1.0 in $CHCl_3$); {lit.[19] $[\alpha]_D^{23}$ −10.1 (*c* 2.1 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.43 (3H, s, *Me*CMe), 1.48 (3H, s, *Me*CMe), 3.29 (1H, dd, *J* 10.6, 5.5, C*H*$_A$H$_B$I), 3.36 (1H, dd, *J* 10.6, 5.1, CH$_A$*H*$_B$I), 3.64 (1H, dd, *J* 10.2, 5.1, C*H*$_A$H$_B$OBn), 3.68 (1H, dd, *J* 10.2, 5.1, CH$_A$*H*$_B$OBn), 3.87 (1H, app dt, *J* 7.5, 5.1, C(4)*H*), 3.98 (1H, app dt, *J* 7.5, 5.1, C(5)*H*), 4.60 (2H, app s, C*H*$_2$Ph), 7.28–7.40 (5H, m, *Ph*).

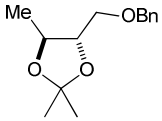
[17] White, J. D.; Kuntiyong, P.; Lee, T. H. *Org. Lett.* **2006**, *8*, 6039.
[18] Mori, K.; Takeuchi, T.; *Tetrahedron* **1988**, *44*, 333.
[19] Kakinuma, H.; Tsuchiya, Y.; Tanaka, M; Horito, S.; Hashimoto, H. *Carbohyd. Res.* **1994**, *264*, 237.

(*S*,*S*)-2,2-Dimethyl-4-(*tert*-butyldimethylsilyloxy)methyl-5-methyl-1,3-dioxolane 53



$Pd(OH)_2/C$ (50% w/w of substrate, 161 mg) and Et_3N (0.51 mL, 2.70 mmol) were added to a solution of **51** (321 mg, 0.89 mmol, >99:1 dr) in MeOH (5 mL) at rt. The resultant solution was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 24 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **53** as a pale yellow oil (191 mg, 83%, >99:1 dr); $[\alpha]_D^{24}$ +13.4 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2986, 2956, 2931, 2859 (C–H); δ_H (400 MHz, $CDCl_3$) 0.07 (6H, s, Si*Me*$_2$), 0.88 (9H, s, SiC*Me*$_3$), 1.29 (3H, d, *J* 6.1, C(5)*Me*), 1.34 (3H, s, *Me*CMe), 1.39 (3H, s, *Me*CMe), 3.56 (1H, ddd, *J* 8.2, 5.5, 4.1, C(4)*H*), 3.65 (1H, dd, *J* 10.6, 5.5, C*H*$_A$H$_B$OSi), 3.76 (1H, dd, *J* 10.6, 4.1, CH$_A$*H*$_B$OSi), 3.97 (1H, dq, *J* 8.2, 6.1, C(5)*H*); δ_C (100 MHz, $CDCl_3$) −5.5 (Si*Me*$_2$), 18.2 (*C*(5)*Me*), 18.3 (Si*C*Me$_3$), 25.8 (SiC*Me*$_3$), 26.8, 27.8 (C*Me*$_2$), 63.3 (*C*H$_2$OSi), 74.9 (*C*(5)), 82.4 (*C*(4)), 108.1 (*C*Me$_2$); *m*/*z* (ESI$^+$) 283 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{13}H_{28}NaO_3Si^+$ ([M+Na]$^+$) requires 283.1700; found 283.1699.

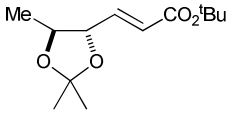
(*S*,*S*)-2,2-Dimethyl-4-benzyloxymethyl-5-methyl-1,3-dioxolane 54



$Pd(OH)_2/C$ (50% w/w of substrate, 100 mg) and Et_3N (0.20 mL, 1.66 mmol) were added to a solution of **52** (200 mg, 0.55 mmol, >99:1 dr) in MeOH (5 mL) at rt. The resultant solution was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 24 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 10:1) gave **54** as a yellow oil (117 mg, 92%, >99:1 dr);[20] $[\alpha]_D^{24}$ +10.4 (*c* 1.0 in $CHCl_3$); {lit.[20] $[\alpha]_D^{21}$ +10.1 (*c* 1.4 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.30 (3H, d, *J* 6.1, C(5)*Me*), 1.41 (3H, s, *Me*CMe), 1.44 (3H, s, *Me*CMe), 3.56 (1H, dd, *J* 10.2, 4.4, C*H*$_A$H$_B$OBn), 3.61 (1H, dd, *J* 10.2, 5.5, CH$_A$*H*$_B$OBn), 3.74–3.79 (1H, m, C(4)*H*), 3.94 (1H, dq, *J* 8.2, 6.1, C(5)*H*), 4.58 (1H, d, *J* 12.2, C*H*$_A$H$_B$Ph), 4.62 (1H, d, *J* 12.2, CH$_A$*H*$_B$Ph), 7.28–7.38 (5H, m, *Ph*).

[20] Kita, Y.; Itoh, F.; Tamura, O.; Ke, Y. Y.; Miki, T.; Tamura, Y. *Chem. Pharm. Bull.* **1989**, *37*, 1446.

tert-Butyl (_S_,_S_,_E_)-4,5-_O_-isopropylidene-4,5-dihydroxyhex-2-enoate 32



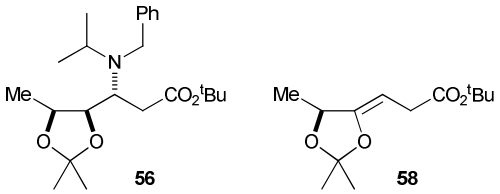
*Method A (from **46**)*: $Pd(OH)_2/C$ (50% w/w of substrate, 260 mg) and Et_3N (1.11 mL, 5.73 mmol) were added to a solution of **46** (520 mg, 1.91 mmol, >99:1 dr) in MeOH (30 mL) at rt. The solution was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **47** as a brown oil (638 mg); δ_H (400 MHz, $CDCl_3$) 1.29 (3H, d, *J* 5.8, C(5)*Me*), 1.40 (3H, s, *Me*CMe), 1.43 (3H, s, *Me*CMe), 3.58–3.67 (2H, m, C*H*$_2$OH), 3.78–3.83 (1H, m, C(4)*H*), 3.98–4.05 (1H, m, C(5)*H*). DMSO (0.20 mL, 2.85 mmol) was then added dropwise to a solution of $(COCl)_2$ (0.14 mL, 2.63 mmol) in CH_2Cl_2 (16 mL) at −78 °C and the resultant mixture was left to stir for 10 min. A solution of **47** (320 mg) in CH_2Cl_2 (1.6 mL) was added dropwise and the resultant mixture was left to stir at −78 °C for 1 h. Et_3N (0.85 mL, 4.38 mmol) was added and the reaction mixture was allowed to warm to rt. *tert*-Butyl (triphenylphosphoranylidene)acetate (824 mg, 2.19 mmol) was added and the resultant mixture was left to stir at rt for 16 h. Satd aq Na_2CO_3 (12 mL) was then added and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were dried and concentrated *in vacuo* to give a 65:35 [(*E*):(*Z*)] mixture of diastereoisomers. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 15:1) gave **32** as a colourless oil (66 mg, 29% from **46**, >99:1 dr); $[\alpha]_D^{24}$ +11.1 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2982, 2934, 2875 (C−H), 1715 (C=O), 1661 (C=C); δ_H (400 MHz, $CDCl_3$) 1.31 (3H, d, *J* 6.1, C(6)*H*$_3$), 1.42 (3H, s, *Me*CMe), 1.44 (3H, s, *Me*CMe), 1.49 (9H, s, C*Me*$_3$), 3.84 (1H, dq, *J* 8.5, 6.1, C(5)*H*), 4.05 (1H, ddd, *J* 8.5, 6.1, 1.3, C(4)*H*), 6.04 (1H, dd, *J*, 15.7, 1.3, C(2)*H*), 6.75 (1H, dd, *J* 15.7, 6.1, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 16.6 (*C*(6)), 26.7, 27.3 (C*Me*$_2$), 28.0 (C*Me*$_3$), 76.4 (*C*(5)), 80.7 (*C*Me$_3$), 81.7 (*C*(4)), 109.1 (*C*Me$_2$), 124.8 (*C*(2)), 142.1 (*C*(3)), 165.2 (*C*(1)); *m/z* (ESI^+) 265 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{13}H_{22}NaO_4^+$ ($[M+Na]^+$) requires 265.1410; found 265.1419.

*Method B (from **53**)*: TBAF (1.0 M in THF, 9.60 mL, 9.60 mmol) was added to a solution of **53** (500 mg, 1.92 mmol) in THF (5 mL) at rt and the resultant solution was stirred at rt for 18 h. Et_2O (3 mL) was then added and the resultant mixture was washed with H_2O (5 mL) then dried and concentrated *in vacuo* to give **47** as a brown oil (280 mg). DMSO (0.18 mL, 2.50 mmol) was added dropwise to a solution of $(COCl)_2$ (0.19 mL, 35.5 mmol) in CH_2Cl_2 (20 mL) at −78 °C and the resultant mixture was left to stir for 10 min. A solution of **47** (280 mg) in CH_2Cl_2 (1.5 mL) was added dropwise and the resultant mixture was left to stir at −78 °C for 1 h. Et_3N (0.53 mL, 3.84 mmol) was added and the reaction mixture was allowed to warm to rt. *tert*-Butyl (triphenylphosphoranylidene)acetate (723 mg, 1.92 mmol) was added and the resultant mixture was left to stir for at rt for 16 h. Satd aq Na_2CO_3 (15 mL) was then added and the aqueous layer was extracted with CH_2Cl_2 (3

× 10 mL). The combined organic extracts were then dried and concentrated *in vacuo* to give a 69:31 [(*E*):(*Z*)] mixture of diastereoisomers. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **32** as pale yellow oil (168 mg, 36% from **53**, >99:1 dr). Further elution gave (*S*,*S*,*Z*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-2-enoate as a pale yellow oil (76 mg, 16% from **53**, >99:1 dr); $[\alpha]_D^{24}$ +47.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2983, 2935, 2871 (C–H), 1718 (C=O), 1653 (C=C); δ_H (400 MHz, $CDCl_3$) 1.33 (3H, d, *J* 6.1, C(6)*H*$_3$), 1.43 (3H, s, *Me*CMe), 1.45 (3H, s, *Me*CMe), 1.49 (9H, s, C*Me*$_3$), 3.80 (1H, dq, *J* 8.5, 6.1, C(5)*H*), 5.22 (1H, app t, *J* 8.5, C(4)*H*), 5.86 (1H, d, *J* 11.8, C(2)*H*), 6.03 (1H, dd, *J* 11.8, 8.5, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 16.9 (*C*(6)), 26.9, 27.1 (C*Me*$_2$), 27.9 (C*Me*$_3$), 76.7 (*C*(5)), 77.2 (*C*(4)), 80.4 (*C*Me$_3$), 108.7 (*C*Me$_2$), 124.6 (*C*(2)), 143.7 (*C*(3)), 164.5 (*C*(1)); *m*/*z* (ESI^+) 265 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{13}H_{22}NaO_4^+$ ($[M+Na]^+$) requires 265.1410; found 265.1409.

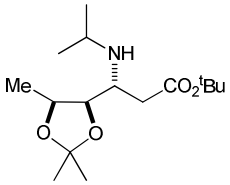
*Method C (from **54**)*: 10% Pd/C (60% w/w of substrate, 4.20 g) was added to a solution of **54** (7.00 g, 29.6 mmol) in EtOAc/AcOH (v/v 8:1, 144 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 24 h. The reaction mixture was then filtered through Celite® (eluent EtOAc) and the filtrate was concentrated *in vacuo*. The residue was dissolved in $CHCl_3$ (100 mL) and washed with H_2O (100 mL). The aqueous layer was extracted with $CHCl_3$ (3 × 50 mL) and the combined organic extracts were dried and concentrated *in vacuo* to give **47** as a brown oil (4.33 g). DMSO (2.74 mL, 38.5 mmol) was added dropwise to a solution of $(COCl)_2$ (3.00 mL, 35.5 mmol) in CH_2Cl_2 (260 mL) at −78 °C and the resultant mixture was left to stir for 10 min. A solution of **47** (4.33 g) in CH_2Cl_2 (20 mL) was added dropwise and the resultant mixture was left to stir at −78 °C for 1 h. Et_3N (11.5 mL, 59.2 mmol) was added and the reaction mixture was allowed to warm to rt. *tert*-Butyl (triphenylphosphoranylidene)acetate (11.1 g, 29.6 mmol) was added and the resultant mixture was left to stir for at rt 16 h. Satd aq Na_2CO_3 (150 mL) was then added and the aqueous layer was extracted with CH_2Cl_2 (3 × 60 mL). The combined organic extracts were dried and concentrated *in vacuo* to give a 68:32 [(*E*):(*Z*)] mixture of diastereoisomers. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **32** as pale yellow oil (2.69 g, 38% from **54**, >99:1 dr). Further elution gave (*S*,*S*,*Z*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-2-enoate as a pale yellow oil (1.25 g, 17% from **54**, >99:1 dr).

***tert*-Butyl (3*R*,4*R*,5*S*)-3-(*N*-benzyl-*N*-isopropylamino)-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 56 and *tert*-butyl (*S*,*Z*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-3-enoate 58**



Following the general procedure, BuLi (2.5 M in hexanes, 1.60 mL, 4.00 mmol) and *N*-benzyl-*N*-isopropylamine (0.68 mL, 4.1 mmol) in THF (10 mL) were reacted with **31** (500 mg, 2.06 mmol, >99:1 dr) in THF (30 mL) at −78 °C to give an 82:18 mixture of **56** and **58**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **58** as a yellow oil (90 mg, 18%, >99:1 dr); $[\alpha]_D^{24}$ −3.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2980, 2931, 2858 (C–H), 1733 (C=O); δ_H (500 MHz, $CDCl_3$) 1.37 (3H, d, *J* 6.3, C(6)H_3), 1.40 (3H, s, *Me*CMe), 1.45 (9H, s, CMe_3), 1.51 (3H, s, *Me*CMe), 3.01 (1H, dd, *J* 17.7, 6.9, C(2)H_A), 3.07 (1H, dd, *J* 17.7, 6.9, C(2)H_B), 4.29 (1H, app td, *J* 6.9, 1.6, C(3)*H*), 4.68 (1H, app qd, *J* 6.3, 1.6, C(5)*H*); δ_C (125 MHz, $CDCl_3$) 19.7 (*C*(6)), 25.0, 26.9 (CMe_2), 28.1 (CMe_3), 31.9 (*C*(2)), 72.8 (*C*(3)), 80.2 (*C*Me_3), 86.0 (*C*(5)), 110.1 (*C*Me_2), 155.5 (*C*(4)), 171.9 (*C*(1)); *m*/*z* (ESI^+) 265 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{13}H_{22}NaO_4^+$ ($[M+Na]^+$) requires 265.1410; found 265.1402. Further elution gave **56** as an orange oil (330 mg, 41%, >99:1 dr); $[\alpha]_D^{24}$ +23.5 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3086, 3063, 3027, 2977, 2934, 2875 (C–H), 1727 (C=O); δ_H (400 MHz, $CDCl_3$) 1.04 (3H, d, *J* 6.6, *Me*CHMe), 1.05 (3H, d, *J* 6.6, *Me*CHMe), 1.16 (3H, d, *J* 6.3, C(6)H_3), 1.28 (3H, s, *Me*CMe), 1.38 (3H, s, *Me*CMe), 1.49 (9H, s, CMe_3), 2.34 (1H, dd, *J* 15.2, 5.6, C(2)H_A), 2.61 (1H, dd, *J* 15.2, 6.7, C(2)H_B), 2.99 (1H, septet, *J* 6.6, C*H*Me_2), 3.55 (1H, app dt, *J* 6.7, 5.6, C(3)*H*), 3.69 (1H, d, *J* 14.9, NC$H_A$$H_B$Ph), 3.82 (1H, d, *J* 14.9, NC$H_A$$H_B$Ph), 4.15 (1H, dd, *J* 6.3, 5.6, C(4)*H*), 4.29 (1H, app quintet, *J* 6.3, C(5)*H*), 7.19–7.37 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 15.8 (*C*(6)), 20.4, 21.0 (CH*Me*$_2$), 25.3, 27.6, (C*Me*$_2$), 28.2 (C*Me*$_3$), 37.0 (*C*(2)), 49.8 (*C*H_2Ph), 50.0 (*C*HMe_2), 54.1 (*C*(3)), 73.9 (*C*(5)), 79.1 (*C*(4)), 80.0 (*C*Me_3), 107.2 (*C*Me_2), 126.5 (*p*-*Ph*), 128.0, 128.4 (*o*,*m*-*Ph*), 141.7 (*i*-*Ph*), 172.2 (*C*(1)); *m*/*z* (ESI^+) 392 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{23}H_{38}NO_4^+$ ($[M+H]^+$) requires 392.2795; found 392.2786.

***tert*-Butyl (3*R*,4*R*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 59**



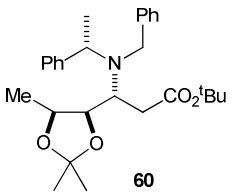
*Method A (from **56**)*: $Pd(OH)_2$/C (50% w/w of substrate, 77 mg) was added to a solution of **56** (154 mg, 0.30 mmol, >99:1 dr) in MeOH (6 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent

MeOH) and the filtrate was concentrated *in vacuo* to give **59** as a white solid (112 mg, 97%, >99:1 dr); mp 50–55 °C; $[\alpha]_D^{24}$ −12.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3313 (N–H), 2974, 2935, 2873 (C–H), 1712 (C=O); δ_H (400 MHz, $CDCl_3$) 0.98 (3H, d, *J* 6.2, *Me*CHMe), 1.01 (3H, d, *J* 6.2, *Me*CHMe), 1.24 (3H, d, *J* 6.2, C(6)H_3), 1.30 (3H, s, *Me*CMe), 1.42 (3H, s, *Me*CMe), 1.45 (9H, s, CMe_3), 2.40 (1H, dd, *J* 15.5, 5.2, C(2)H_A), 2.58 (1H, dd, *J* 15.5, 4.4, C(2)H_B), 2.92 (1H, septet, *J* 6.2, C*H*Me_2), 3.08 (1H, ddd, *J* 8.0, 5.2, 4.4, C(3)*H*), 3.97 (1H, dd, *J* 8.0, 6.2, C(4)*H*), 4.33 (1H, app quintet, *J* 6.2, C(5)*H*); δ_C (100 MHz, $CDCl_3$) 15.7 (*C*(6)), 22.3, 24.2 (CH*Me*$_2$), 25.5, 28.0 (C*Me*$_2$), 28.1 (C*Me*$_3$), 37.0 (*C*(2)), 44.8 (*C*HMe_2), 51.4 (*C*(3)), 73.9 (*C*(5)), 79.2 (*C*(4)), 80.2 (*C*Me_3), 107.3 (*C*Me_2), 171.8 (*C*(1)); *m*/*z* (FI^+) 301 ($[M]^+$, 100%); HRMS (FI^+) $C_{16}H_{31}NO_4^+$ ($[M]^+$) requires 301.2248; found 301.2252.

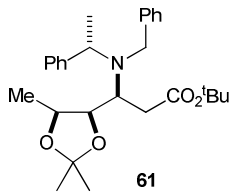
*Method B (from **60**)*: $Pd(OH)_2$/C (50% w/w of substrate, 69 mg) was added to a solution of **60** (137 mg, 0.30 mmol, >99:1 dr) in MeOH/acetone (v/v 9:1, 6 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **59** as a white solid (72 mg, 79%, >99:1 dr).

*Method C (from **63**)*: $Pd(OH)_2$/C (50% w/w of substrate, 66 mg) was added to a solution of **63** (132 mg, 0.29 mmol, >99:1 dr) in MeOH/acetone (v/v 9:1, 6 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **59** as a white solid (76 mg, 87%, >99:1 dr).

tert-Butyl (3*R*,4*R*,5*S*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 60 and _tert_-butyl-(3*S*,4*R*,5*S*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 61



60

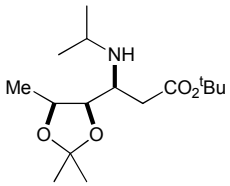


61

Following the general procedure, BuLi (2.5 M in hexanes, 3.98 mL, 9.99 mmol) and (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (2.17 g, 10.3 mmol) in Et_2O (10 mL) were reacted with **31** (500 mg, 2.06 mmol, >99:1 dr) in Et_2O (30 mL) −20 °C to give an 85:15 mixture of **60** and **61**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 100:1 increased to 20:1) gave **60** as a yellow oil (296 mg, 39%, >99:1 dr); $[\alpha]_D^{24}$ +8.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3085, 3062, 3028, 2979, 2935, 2879 (C–H), 1727 (C=O); δ_H (400 MHz, $CDCl_3$) 1.12 (3H, d, *J* 6.6, C(6)H_3), 1.24 (3H, s, *Me*CMe), 1.36 (3H, s, *Me*CMe), 1.39 (3H, d, *J* 7.0, C(α)*Me*),

1.45 (9H, s, C*Me*$_3$), 2.21 (1H, dd, *J* 15.6, 6.8, C(2)*H*$_A$), 2.26 (1H, dd, *J* 15.6, 5.4, C(2)*H*$_B$), 3.68–3.74 (1H, m, C(3)*H*), 3.70 (1H, d, *J* 14.9, NC*H*$_A$H$_B$Ph), 3.80 (1H, d, *J* 14.9, NCH$_A$*H*$_B$Ph), 3.95 (1H, q, *J* 7.0, C(α)*H*), 4.09 (1H, app t, *J* 6.1, C(4)*H*), 4.30–4.37 (1H, m, C(5)*H*), 7.20–7.37 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.2 (*C*(6)), 19.4 (C(α)*Me*), 25.4, 27.8 (C*Me*$_2$), 28.1 (C*Me*$_3$), 36.0 (*C*(2)), 50.4 (*C*H$_2$Ph), 54.2 (*C*(3)), 59.2 (*C*(α)), 73.9 (*C*(5)), 78.8 (*C*(4)), 79.8 (*C*Me$_3$), 107.1 (*C*Me$_2$), 126.7, 127.1 (*p-Ph*), 128.0, 128.1, 128.1, 128.2 (*o*,*m-Ph*), 141.5, 143.1 (*i-Ph*), 171.6 (*C*(1)); *m*/*z* (ESI$^+$) 454 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{40}NO_4^+$ ([M+H]$^+$) requires 454.2952; found 454.2956. Further elution gave **61** as a yellow oil (231 mg, 12%, >99:1 dr); $[\alpha]_D^{24}$ −38.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3084, 3063, 3029, 2977, 2933, 2870 (C–H), 1727 (C=O); δ_H (400 MHz, $CDCl_3$) 0.92 (3H, d, *J* 6.3, C(6)*H*$_3$), 1.23 (3H, d, *J* 6.8, C(α)*Me*), 1.33 (3H, s, *Me*CMe), 1.50 (3H, s, *Me*CMe), 1.50 (9H, s, C*Me*$_3$), 1.78 (1H, dd, *J* 14.8, 2.6, C(2)*H*$_A$), 2.29 (1H, dd, *J* 14.8, 10.0, C(2)*H*$_B$), 3.47 (1H, app td, *J* 10.0, 2.6, C(3)*H*), 3.83 (1H, d, *J* 15.7, NC*H*$_A$H$_B$Ph), 3.98–4.05 (1H, m, C(5)*H*), 4.06 (1H, d, *J* 15.7, NCH$_A$*H*$_B$Ph), 4.12 (1H, dd, *J* 10.0, 5.1, C(4)*H*), 4.35 (1H, q, *J* 6.8, C(α)*H*), 7.18–7.52 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.4 (*C*(6)), 21.1 (C(α)*Me*), 26.1, 28.2 (C*Me*$_2$), 28.7 (C*Me*$_3$), 38.4 (*C*(2)), 50.1 (*C*H$_2$Ph), 55.2 (*C*(3)), 62.3 (*C*(α)), 74.2 (*C*(5)), 78.7 (*C*(4)), 80.5 (*C*Me$_3$), 107.9 (*C*Me$_2$), 126.3, 126.7 (*p-Ph*), 127.8, 127.9, 128.0, 128.5 (*o*,*m-Ph*), 143.2, 145.3 (*i-Ph*), 170.8 (*C*(1)); *m*/*z* (ESI$^+$) 454 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{40}NO_4^+$ ([M+H]$^+$) requires 454.2952; found 454.2966.

tert-Butyl (3*S*,4*R*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 62

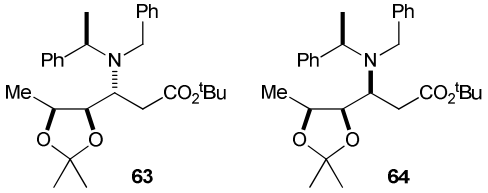


*Method A (from **61**)*: $Pd(OH)_2$/C (50% w/w of substrate, 40 mg) was added to a solution of **61** (80 mg, 0.30 mmol, >99:1 dr) in MeOH/acetone (v/v 9:1, 6 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent EtOAc) and the filtrate was concentrated *in vacuo* to give **62** as a white solid (52 mg, 99%, >99:1 dr); $[\alpha]_D^{24}$ +14.4 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3333 (N–H), 2977, 2934, 2873 (C–H), 1726 (C=O); δ_H (400 MHz, $CDCl_3$) 1.04 (3H, d, *J* 6.2, *Me*CHMe), 1.06 (3H, d, *J* 6.2, *Me*CHMe), 1.29 (3H, d, *J* 6.3, C(6)*H*$_3$), 1.33 (3H, s, *Me*CMe), 1.45 (3H, s, *Me*CMe), 1.46 (9H, s, C*Me*$_3$), 2.30 (1H, dd, *J* 15.4, 5.8, C(2)*H*$_A$), 2.34 (1H, dd, *J* 15.4, 5.6, C(2)*H*$_B$), 2.93 (1H, septet, *J* 6.2, C*H*Me$_2$), 3.19 (1H, ddd, *J* 6.3, 5.8, 5.6, C(3)*H*), 4.02 (1H, app t, *J* 6.3, C(4)*H*), 4.33 (1H, app quintet, *J* 6.3, C(5)*H*); δ_C (100 MHz, $CDCl_3$) 15.9 (*C*(6)), 22.3, 24.3 (CH*Me*$_2$), 25.4, 27.8 (C*Me*$_2$), 28.1 (C*Me*$_3$), 38.8 (*C*(2)), 45.4 (*C*HMe$_2$), 51.3 (*C*(3)), 73.5 (*C*(5)), 79.9 (*C*(4)), 80.6 (*C*Me$_3$),

107.6 (*C*Me$_2$), 171.5 (*C*(1)); *m*/*z* (ESI$^+$) 302 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{32}NO_4^+$ ([M+H]$^+$) requires 302.2326; found 302.2313.

*Method B (from **64**)*: Pd(OH)$_2$/C (50% w/w of substrate, 38 mg) was added to a solution of **64** (75 mg, 0.17 mmol, >99:1 dr) in MeOH/acetone (v/v 9:1, 3 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **62** as a pale yellow oil (41 mg, 84%, >99:1 dr).

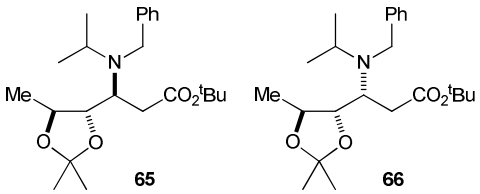
tert-Butyl (3*R*,4*R*,5*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 63 and _tert_-butyl (3*S*,4*R*,5*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 64



Following the general procedure, BuLi (2.5 M in hexanes, 1.60 mL, 4.00 mmol) and (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (873 mg, 41.3 mmol) in Et$_2$O (10 mL) were reacted with **31** (500 mg, 2.06 mmol, >99:1 dr) in Et$_2$O (30 mL) at −20 °C to give a 60:40 mixture of **63** and **64**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et$_2$O, 100:1 increased to 10:1) gave **63** as a white solid (356 mg, 38%, >99:1 dr); mp 74–79 °C; $[\alpha]_D^{24}$ +65.2 (*c* 1.0 in CHCl$_3$); ν_{max} (ATR) 3086, 3063, 3029, 2978, 2932, 2873, 2807 (C−H), 1724 (C=O); δ_H (400 MHz, CDCl$_3$) 1.01 (3H, d, *J* 6.5, C(6)*H*$_3$), 1.14 (3H, s, *Me*CMe), 1.32 (3H, s, *Me*CMe), 1.36 (3H, d, *J* 6.8, C(α)*Me*), 1.54 (9H, s, C*Me*$_3$), 2.27 (1H, dd, *J* 15.2, 4.8, C(2)*H*$_A$), 2.53 (1H, dd, *J* 15.2, 7.6, C(2)*H*$_B$), 3.48 (1H, dd, *J* 6.5, 3.9, C(4)*H*), 3.64 (1H, d, *J* 15.3, NC*H*$_A$H$_B$Ph), 3.69 (1H, ddd, *J* 7.6, 4.8, 3.9, C(3)*H*), 3.83 (1H, q, *J* 6.8, C(α)*H*), 3.94 (1H, quintet, *J* 6.5, C(5)*H*), 3.98 (1H, d, *J* 15.3, NCH$_A$*H*$_B$Ph), 7.22–7.46 (10H, m, *Ph*); δ_C (100 MHz, CDCl$_3$) 15.3 (*C*(6)), 18.4 (C(α)*Me*), 24.9, 27.2 (C*Me*$_2$), 28.2 (C*Me*$_3$), 37.1 (*C*(2)), 50.7 (*C*H$_2$Ph), 53.4 (*C*(3)), 57.9 (*C*(α)), 73.6 (*C*(5)), 77.8 (*C*(4)), 80.1 (*C*Me$_3$), 106.9 (*C*Me$_2$), 126.7, 127.1 (*p-Ph*), 128.0, 128.1, 128.2, 128.6 (*o*,*m-Ph*), 141.4, 142.5 (*i-Ph*), 172.2 (*C*(1)); *m*/*z* (ESI$^+$) 454 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{40}NO_4^+$ ([M+H]$^+$) requires 454.2952; found 454.2953. Further elution gave **64** as a white solid (205 mg, 22%, >99:1 dr); mp 57–62 °C; $[\alpha]_D^{24}$ −28.0 (*c* 1.0 in CHCl$_3$); ν_{max} (ATR) 3085, 3064, 3025, 2979, 2934, 2874, 2854 (C−H), 1703 (C=O); δ_H (400 MHz, CDCl$_3$) 1.10 (3H, d, *J* 6.6, C(6)*H*$_3$), 1.40 (3H, s, *Me*CMe), 1.46 (9H, s, C*Me*$_3$), 1.53 (3H, d, *J* 6.8, C(α)*Me*), 1.55 (3H, s, *Me*CMe), 1.79 (1H, dd, *J* 15.0, 2.7, C(2)*H*$_A$), 2.28 (1H, dd, *J* 15.0, 10.4, C(2)*H*$_B$), 3.67 (1H, app td, *J* 10.4, 2.7, C(3)*H*), 3.73 (1H, d, *J* 14.0, NC*H*$_A$H$_B$Ph), 3.93 (1H, d, *J* 14.0, NCH$_A$*H*$_B$Ph), 4.07–4.14 (1H, m, C(5)*H*), 4.21 (1H, q, *J* 6.8,

C(α)*H*), 4.25 (1H, dd, *J* 10.4, 5.1, C(4)*H*), 7.12–7.50 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.5 (*C*(6)), 19.4 (C(α)*Me*), 26.0, 28.8 (C*Me*$_2$), 28.1 (C*Me*$_3$), 37.4 (*C*(2)), 51.2 (*C*H$_2$Ph), 53.7 (*C*(3)), 58.6 (*C*(α)), 74.4 (*C*(5)), 79.1 (*C*(4)), 80.4 (*C*Me$_3$), 108.1 (*C*Me$_2$), 126.4, 126.4 (*p-Ph*), 127.7, 127.7, 128.0, 129.2 (*o,m-Ph*), 141.4, 146.3 (*i-Ph*), 170.7 (*C*(1)); *m/z* (ESI$^+$) 454 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{40}NO_4^+$ ([M+H]$^+$) requires 454.2952; found 454.2945.

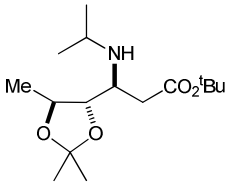
tert-Butyl (*S*,*S*,*S*)-3-(*N*-benzyl-*N*-isopropylamino)-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 65 and _tert_-butyl (3*R*,4*S*,5*S*)-3-(*N*-benzyl-*N*-isopropylamino)-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 66



Following the general procedure, BuLi (2.5 M in hexanes, 1.60 mL, 4.00 mmol) and *N*-benzyl-*N*-isopropylamine (0.68 mL, 4.13 mmol) in THF (15 mL) were reacted with **32** (500 mg, 2.06 mmol, >99:1 dr) in THF (25 mL) at −78 °C to give an 82:18 mixture of **65** and **66**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **66** as a yellow oil (114 mg, 14%, >99:1 dr); $[\alpha]_D^{24}$ −15.5 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2977, 2935, 2872, 2720 (C−H), 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 0.98 (3H, d, *J* 6.4, *Me*CHMe), 1.01 (3H, d, *J* 6.4, *Me*CHMe), 1.09 (3H, d, *J* 6.5, C(6)*H*$_3$), 1.30 (3H, s, *Me*CMe), 1.32 (3H, s, *Me*CMe), 1.48 (9H, s, C*Me*$_3$), 2.67 (1H, dd, *J* 14.8, 8.0, C(2)*H*$_A$), 2.70 (1H, dd, *J* 14.8, 5.9, C(2)*H*$_B$), 3.18 (1H, septet, *J* 6.4, *CH*Me$_2$), 3.18–3.23 (1H, m, C(3)*H*), 3.48 (1H, dd, *J* 8.3, 2.8, C(4)*H*), 3.54 (1H, d, *J* 14.0, NC*H*$_A$H$_B$Ph), 4.06 (1H, d, *J* 14.0, NCH$_A$*H*$_B$Ph), 4.22 (1H, dq, *J* 8.3, 6.5, C(5)*H*), 7.17–7.38 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 17.1, 17.3 (CH*Me*$_2$), 22.7 (*C*(6)), 26.9, 27.2 (C*Me*$_2$), 28.1 (C*Me*$_3$), 35.8 (*C*(2)), 48.7 (*C*HMe$_2$), 51.1 (*C*(3)), 51.3 (*C*H$_2$Ph), 73.1 (*C*(5)), 80.5 (*C*Me$_3$), 85.3 (*C*(4)), 107.3 (*C*Me$_2$), 126.5 (*p-Ph*), 128.1, 128.6 (*o,m-Ph*), 141.3 (*i-Ph*), 172.1 (*C*(1)); *m/z* (ESI$^+$) 392 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{23}H_{38}NO_4^+$ ([M+Na]$^+$) requires 392.2795; found 392.2805. Further elution gave **65** as a colourless oil (440 mg, 55%, >99:1 dr); $[\alpha]_D^{24}$ −24.2 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2977, 2933, 2875, 2718, (C−H), 1727 (C=O); δ_H (400 MHz, $CDCl_3$) 1.05 (3H, d, *J* 6.7, *Me*CHMe), 1.08 (3H, d, *J* 6.7, *Me*CHMe), 1.31 (3H, s, *Me*CMe), 1.32 (3H, d, *J* 5.6, C(6)*H*$_3$), 1.38 (3H, s, *Me*CMe), 1.49 (9H, s, C*Me*$_3$), 2.43 (1H, dd, *J* 15.5, 5.7, C(2)*H*$_A$), 2.61 (1H, dd, *J* 15.5, 6.6, C(2)*H*$_B$), 3.01 (1H, septet, *J* 6.7, C*H*Me$_2$), 3.41 (1H, app dt, *J* 6.1, 4.1, C(3)*H*), 3.69 (1H, d, *J* 14.7, NC*H*$_A$H$_B$Ph), 3.78 (1H, d, *J* 14.7, NCH$_A$*H*$_B$Ph), 3.68–3.77 (2H, m, C(4)*H*, C(5)*H*), 7.19–7.37 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.7 (*C*(6)), 19.7, 20.5 (CH*Me*$_2$), 26.9, 27.4 (C*Me*$_2$), 28.1 (C*Me*$_3$), 35.4 (*C*(2)), 48.4 (*C*HMe$_2$), 50.1 (*C*H$_2$Ph), 54.4 (*C*(3)), 75.7, 83.9 (*C*(4), *C*(5)), 80.0 (*C*Me$_3$), 108.0 (*C*Me$_2$), 126.6 (*p-Ph*), 128.0,

128.6 (*o*,*m*-*Ph*), 141.0 (*i*-*Ph*), 172.3 (*C*(1)); *m*/*z* (ESI$^+$) 392 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{23}H_{38}NO_4^+$ ([M+H]$^+$) requires 392.2795; found 392.2790.

tert-Butyl (*S*,*S*,*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 67

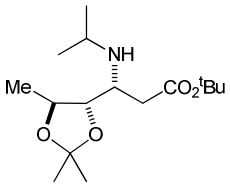


*Method A (from **65**)*: Pd(OH)$_2$/C (50% w/w of substrate, 125 mg) was added to a solution of **65** (250 mg, 0.64 mmol, >99:1 dr) in MeOH (12.9 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **67** as a pale yellow solid (176 mg, 92%, >99:1 dr); mp 38–42 °C; $[\alpha]_D^{24}$ +2.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3345, 3325 (N–H), 2975, 2932, 2873 (C–H), 1707 (C=O); δ_H (400 MHz, $CDCl_3$) 1.01 (3H, d, *J* 6.1, *Me*CHMe), 1.03 (3H, d, *J* 6.1, *Me*CHMe), 1.34 (3H, d, *J* 5.9, C(6)H_3), 1.37 (3H, s, *Me*CMe), 1.39 (3H, s, *Me*CMe), 1.46 (9H, s, CMe_3), 2.37 (1H, dd, *J* 15.3, 6.1, C(2)H_A), 2.50 (1H, dd, *J* 15.3, 5.1, C(2)H_B), 2.91 (1H, septet, *J* 6.1, C*H*Me$_2$), 3.06 (1H, app q, *J* 5.6, C(3)*H*), 3.57 (1H, dd, *J* 8.1, 5.6, C(4)*H*), 3.89 (1H, dq, *J* 8.1, 5.9, C(5)*H*); δ_C (100 MHz, $CDCl_3$) 19.2 (*C*(6)), 22.9, 23.8 (CH*Me*$_2$), 27.0, 27.3 (C*Me*$_2$), 28.1 (C*Me*$_3$), 37.2 (*C*(2)), 45.5 (*C*HMe$_2$), 53.4 (*C*(3)), 75.2 (*C*(5)), 80.5 (*C*Me$_3$), 84.1 (*C*(4)), 107.9 (*C*Me$_2$), 171.8 (*C*(1)); *m*/*z* (ESI$^+$) 302 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{32}NO_4^+$ ([M+H]$^+$) requires 302.2326; found 302.2331.

*Method B (from **69**)*: Pd(OH)$_2$/C (50% w/w of substrate, 117 mg) was added to a solution of **69** (335 mg, 0.52 mmol, 98:2 dr) in MeOH/acetone (v/v 9:1, 8 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **67** as a pale yellow solid (129 mg, 99%, 98:2 dr).

*Method C (from **71**)*: Pd(OH)$_2$/C (50% w/w of substrate, 22 mg) was added to a solution of **71** (44 mg, 0.10 mmol, 82:18 dr) in MeOH/acetone (v/v 9:1, 2 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **67** as a pale yellow solid (28 mg, 97%, 82:18 dr).

tert-Butyl (3*R*,4*S*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 68

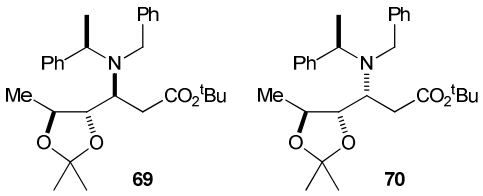


*Method A (from **66**)*: $Pd(OH)_2/C$ (50% w/w of substrate, 48 mg) was added to a solution of **66** (95 mg, 0.24 mmol, >99:1 dr) in MeOH (4.9 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left stir to under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **68** as a pale yellow oil (48 mg, 66%, >99:1 dr); $[\alpha]_D^{24}$ −15.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3343 (N–H), 2970, 2932, 2872 (C–H), 1726 (C=O); δ_H (400 MHz, $CDCl_3$) 0.98 (3H, d, *J* 6.2, *Me*CHMe), 1.03 (3H, d, *J* 6.2, *Me*CHMe), 1.28 (3H, d, *J* 6.1, C(6)H_3), 1.38 (6H, app s, CMe_2), 1.45 (9H, s, CMe_3), 2.38 (1H, dd, *J* 14.9, 6.3, C(2)H_A), 2.43 (1H, dd, *J* 14.9, 6.6, C(2)H_B), 2.88 (1H, septet, *J* 6.2, C*H*Me_2), 3.09 (1H, ddd, *J* 6.6, 6.3, 3.0, C(3)*H*), 3.58 (1H, dd, *J* 8.3, 3.0, C(4)*H*), 4.12 (1H, dq, *J* 8.3, 6.1 C(5)*H*); δ_C (100 MHz, $CDCl_3$) 18.1 (*C*(6)), 22.6, 23.9 (CH*Me*$_2$), 26.9, 27.4 (C*Me*$_2$), 28.0 (C*Me*$_3$), 38.7 (*C*(2)), 45.5 (*C*HMe_2), 51.3 (*C*(3)), 73.0 (*C*(5)), 80.6 (*C*Me_3), 84.3 (*C*(4)), 107.9 (*C*Me_2), 171.7 (*C*(1)); *m/z* (ESI^+) 302 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{16}H_{32}NO_4^+$ ($[M+H]^+$) requires 302.2326; found 302.2320.

*Method B (from **70**)*: $Pd(OH)_2/C$ (50% w/w of substrate, 44 mg) was added to a solution of **70** (88 mg, 0.19 mmol, >99:1 dr) in MeOH/acetone (v/v 9:1, 3.6 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left stir to under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **68** as a pale yellow oil (57 mg, 98%, >99:1 dr).

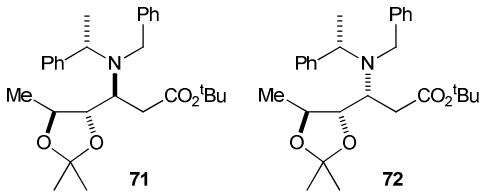
*Method C (from **72**)*: $Pd(OH)_2/C$ (50% w/w of substrate, 100 mg) was added to a solution of **72** (200 mg, 0.44 mmol, >99:1 dr) in MeOH/acetone (v/v 9:1, 8 mL) at rt. The resultant mixture was degassed and saturated with H_2, then left to stir under an atmosphere of H_2 (1 atm) for 16 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **68** as a pale yellow oil (120 mg, 90%, >99:1 dr).

tert-Butyl (3*S*,4*S*,5*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 69 and _tert_-butyl (3*R*,4*S*,5*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 70



Following the general procedure, BuLi (2.5 M in hexanes, 1.60 mL, 4.00 mmol) and (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (872 mg, 4.13 mmol) in THF (10 mL) were reacted with **32** (500 mg, 2.06 mmol, >99:1 dr) in THF (30 mL) at −78 °C to give a 76:24 mixture of **69** and **70**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **70** as a pale yellow oil (119 mg, 13%, >99:1 dr); $[\alpha]_D^{24}$ +33.6 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3087, 3065, 3028, 2979, 2933, 2890 (C–H), 1722 (C=O); δ_H (400 MHz, $CDCl_3$) 0.38 (3H, d, *J* 6.1, C(6)H_3), 1.28 (3H, s, *Me*CMe), 1.35 (3H, s, *Me*CMe), 1.40 (3H, d, *J* 6.8, C(α)*Me*), 1.51 (9H, s, CMe_3), 2.78 (1H, dd, *J* 14.8, 3.5, C(2)H_A), 2.84 (1H, dd, *J* 14.8, 9.6, C(2)H_B), 3.25 (1H, ddd, *J* 9.6, 3.5, 2.3, C(3)*H*), 3.34 (1H, dd, *J* 8.3, 2.3, C(4)*H*), 3.70 (1H, d, *J* 13.4, NC$H_A$$H_B$Ph), 3.92 (1H, dq, *J* 8.3, 6.1, C(5)*H*), 3.96 (1H, q, *J* 6.8, C(α)*H*), 4.39 (1H, d, *J* 13.4, NC$H_A$$H_B$Ph), 7.17–7.57 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 10.9 (C(α)*Me*), 16.5 (*C*(6)), 26.7, 27.3 (CMe_2), 28.1 (CMe_3), 36.6 (*C*(2)), 49.6 (*C*(3)), 52.9 (*C*H_2Ph), 56.0 (*C*(α)), 72.8 (*C*(5)), 80.6 (*C*Me_3), 85.2 (*C*(4)), 107.1 (*C*Me_2), 126.9, 127.0 (*p-Ph*), 128.0, 128.3, 128.5, 129.0 (*o,m-Ph*), 141.0, 143.4 (*i-Ph*), 172.0 (*C*(1)); *m/z* (ESI$^+$) 476 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{39}NNaO_4^+$ ([M+Na]$^+$) requires 476.2771; found 476.2755. Further elution gave **69** as a pale yellow oil (440 mg, 47%, 98:2 dr); $[\alpha]_D^{24}$ −22.4 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3085, 3062, 3028, 2978, 2932, 2875, 2814 (C–H), 1726 (C=O); δ_H (400 MHz, $CDCl_3$) 1.33 (3H, d, *J* 4.3, C(6)H_3), 1.33 (3H, s, *Me*CMe), 1.37 (3H, s, *Me*CMe), 1.41 (3H, d, *J* 6.9, C(α)*Me*), 1.42 (9H, s, CMe_3), 2.06 (1H, dd, *J* 16.0, 4.2, C(2)H_A), 2.32 (1H, dd, *J* 16.0, 7.5, C(2)H_B), 3.59–3.65 (1H, m, C(3)*H*), 3.62 (1H, d, *J* 14.4, NC$H_A$$H_B$Ph), 3.74–3.81 (2H, m, C(4)*H*, C(5)*H*), 3.85 (1H, d, *J* 14.4, NC$H_A$$H_B$Ph), 3.94 (1H, q, *J* 6.9, C(α)*H*), 7.20–7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.5 (*C*(6)), 19.3 (C(α)*Me*), 26.8, 27.4 (CMe_2), 28.0 (CMe_3), 34.0 (*C*(2)), 51.2 (*C*H_2Ph), 54.2 (*C*(3)), 57.6 (*C*(α)), 75.6, 84.3 (*C*(4), *C*(5)), 80.0 (*C*Me_3), 108.0 (*C*Me_2), 126.7, 127.0 (*p-Ph*), 128.0, 128.0, 128.2, 128.4 (*o,m-Ph*), 140.9, 142.8 (*i-Ph*), 171.9 (*C*(1)); *m/z* (ESI$^+$) 476 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{39}NNaO_4^+$ ([M+Na]$^+$) requires 476.2771; found 476.2762.

tert-Butyl (_S_,_S_,_S_,_S_)-3-[_N_-benzyl-_N_-(α-methylbenzyl)amino]-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 71 and _tert_-butyl (3_R_,4_S_,5_S_,α_S_)-3-[_N_-benzyl-_N_-(α-methylbenzyl)amino]-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 72



Following the general procedure, BuLi (2.5 M in hexanes, 1.60 mL, 4.00 mmol) and (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (872 mg, 4.13 mmol) in THF (1 mL) were reacted with **32** (500 mg, 2.06 mmol, >99:1 dr) in THF (3 mL) at −78 °C to give a 16:84 mixture of **71** and **72**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 20:1) gave **72** as a pale yellow oil (530 mg, 57%, >99:1 dr); $[\alpha]_D^{24}$ −8.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3084, 3062, 3027, 2978, 2932, 2871, 2811 (C−H), 1724 (C=O); δ_H (400 MHz, $CDCl_3$) 1.24 (3H, d, *J* 6.1, C(6)H_3), 1.26 (3H, s, *Me*CMe), 1.32 (3H, s, *Me*CMe), 1.34 (3H, d, *J* 7.1, C(α)*Me*), 1.43 (9H, s, CMe_3), 1.74 (1H, dd, *J* 15.8, 2.5, C(2)H_A), 2.43 (1H, dd, *J* 15.8, 10.7, C(2)H_B), 3.48 (1H, app td, *J* 10.7, 2.5, C(3)*H*), 3.55 (1H, d, *J* 14.9, NC$H_A$$H_B$Ph), 3.57 (1H, dd, *J* 8.3, 2.5, C(4)*H*), 3.82 (1H, q, *J* 7.1, C(α)*H*), 4.36 (1H, d, *J* 14.9, NC$H_A$$H_B$Ph), 4.51 (1H, dq, *J* 8.3, 6.1, C(5)*H*), 7.22–7.55 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 17.5 (*C*(6)), 20.1 (C(α)*Me*), 26.9, 27.1 (CMe_2), 28.1 (CMe_3), 34.0 (*C*(2)), 50.0 (*C*(3)), 53.0 (*C*H_2Ph), 58.0 (*C*(α)), 72.9 (*C*(5)), 80.3 (*C*Me_3), 85.1 (*C*(4)), 107.5 (*C*Me_2), 126.5, 127.2 (*p-Ph*), 127.9, 128.1, 128.2, 128.3 (*o*,*m-Ph*), 141.3, 141.4 (*i-Ph*), 171.7 (*C*(1)); *m*/*z* (ESI$^+$) 476 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{39}NNaO_4^+$ ([M+Na]$^+$) requires 476.2771; found 476.2755. Further elution gave **71** as a pale yellow oil (91 mg, 10%, 82:18 dr); ν_{max} (ATR) 3085, 3063, 3028, 2979, 2932, 2877 (C−H), 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.01 (3H, d, *J* 6.1, C(6)H_3), 1.25 (3H, s, *Me*CMe), 1.31 (3H, s, *Me*CMe), 1.36 (3H, d, *J* 7.1, C(α)*Me*), 1.52 (9H, s, CMe_3), 2.48 (1H, dd, *J* 15.8, 5.8, C(2)H_A), 2.63 (1H, dd, *J* 15.8, 5.4, C(2)H_B), 3.32 (1H, dq, *J* 7.8, 6.1, C(5)*H*), 3.42–3.49 (2H, m, C(3)*H*, C(4)*H*), 3.80 (1H, d, *J* 14.7, NC$H_A$$H_B$Ph), 3.93 (1H, d, *J* 14.7, NC$H_A$$H_B$Ph), 3.95 (1H, q, *J* 7.1, C(α)*H*), 7.21–7.48 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.0 (C(α)*Me*), 18.3 (*C*(6)), 26.7, 27.4 (CMe_2), 28.2 (CMe_3), 35.3 (*C*(2)), 51.5 (*C*H_2Ph), 53.7 (*C*(3)), 57.2 (*C*(α)), 74.9 (*C*(5)), 80.3 (*C*Me_3), 84.1 (*C*(4)), 107.9 (*C*Me_2), 126.7, 127.0 (*p-Ph*), 128.1, 128.2, 128.2, 128.7 (*o*,*m-Ph*), 141.2, 143.4 (*i-Ph*), 172.4 (*C*(1)); *m*/*z* (ESI$^+$) 476 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{39}NNaO_4^+$ ([M+Na]$^+$) requires 476.2771; found 476.2760.

X-ray crystal structure determination for 59, 63, 64 and 67

Data were collected using a Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation using standard procedures at 150 K. The structures were solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[21,22]

X-ray crystal structure data for **59** [$C_{16}H_{31}NO_4$]: M = 301.43, monoclinic, space group $P\,2_1$, a = 5.7565(2) Å, b = 19.4300(8) Å, c = 8.1386(3) Å, β = 96.168(2)º, V = 905.02(6) Å^3, Z = 2, μ = 0.078 mm^{-1}, colourless prism, crystal dimensions = 0.07 × 0.08 × 0.26 mm. A total of 2122 unique reflections were measured for $5 < \theta < 27$ and 1907 reflections were used in the refinement. The final parameters were wR_2 = 0.094 and R_1 = 0.043 [$I > -3.0\sigma(I)$].

X-ray crystal structure data for **63** [$C_{28}H_{39}NO_4$]: M = 453.62, monoclinic, space group $P\,2_1$, a = 7.9717(2) Å, b = 12.5518(3) Å, c = 13.0678(3) Å, β = 95.5854(9)º, V = 1301.35(5) Å^3, Z = 2, μ = 0.076 mm^{-1}, colourless block, crystal dimensions = 0.18 × 0.23 × 0.27 mm. A total of 3107 unique reflections were measured for $5 < \theta < 27$ and 2549 reflections were used in the refinement. The final parameters were wR_2 = 0.117 and R_1 = 0.046 [$I > -3.0\sigma(I)$].

X-ray crystal structure data for **64** [$C_{28}H_{39}NO_4$]: M = 453.62, orthorhombic, space group $P\,2_1\,2_1\,2_1$, a = 9.3260(2) Å, b = 13.7383(3) Å, c = 20.3169(6) Å, V = 2603.07(11) Å^3, Z = 4, μ = 0.076 mm^{-1}, colourless block, crystal dimensions = 0.12 × 0.15 × 0.16 mm. A total of 3316 unique reflections were measured for $5 < \theta < 27$ and 2639 reflections were used in the refinement. The final parameters were wR_2 = 0.098 and R_1 = 0.045 [$I > -3.0(I)$].

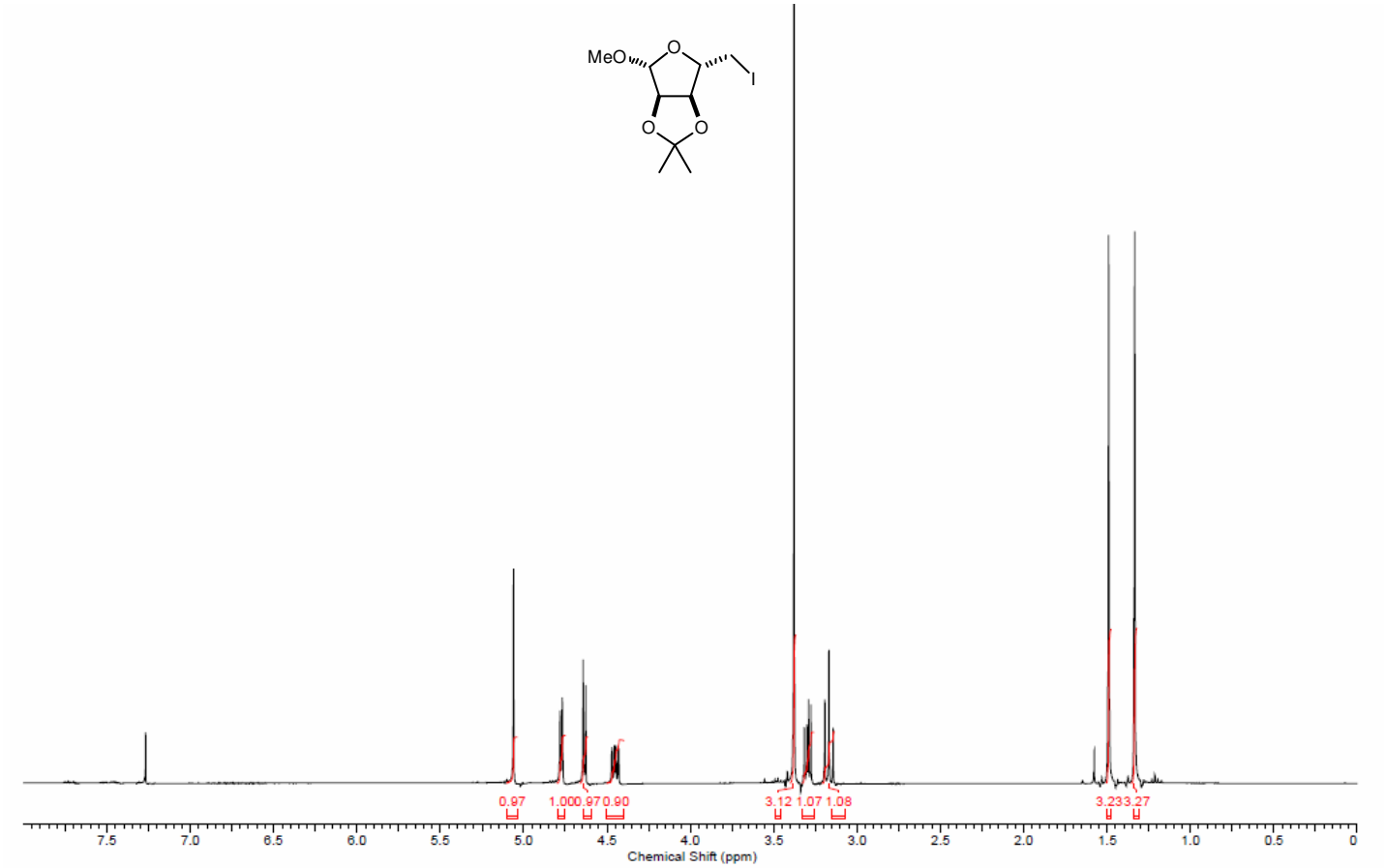
X-ray crystal structure data for **67** [$C_{16}H_{31}NO_4$]: M = 301.43, monoclinic, space group $C\,2$, a = 22.1832(6) Å, b = 5.8375(2) Å, c = 14.5119(4) Å, β = 105.8953(12)º, V = 1807.36(9) Å^3, Z = 4, μ = 0.078 mm^{-1}, colourless prism, crystal dimensions = 0.14 × 0.17 × 0.90 mm. A total of 2239 unique reflections were measured for $5 < \theta < 27$ and 2239 reflections were used in the refinement. The final parameters were wR_2 = 0.121 and R_1 = 0.049 [$I > -3.0(I)$].

[21] Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, C. K.; Watkin, D. J. *J. Appl. Crystallogr.* **2003**, *36*, 1487.

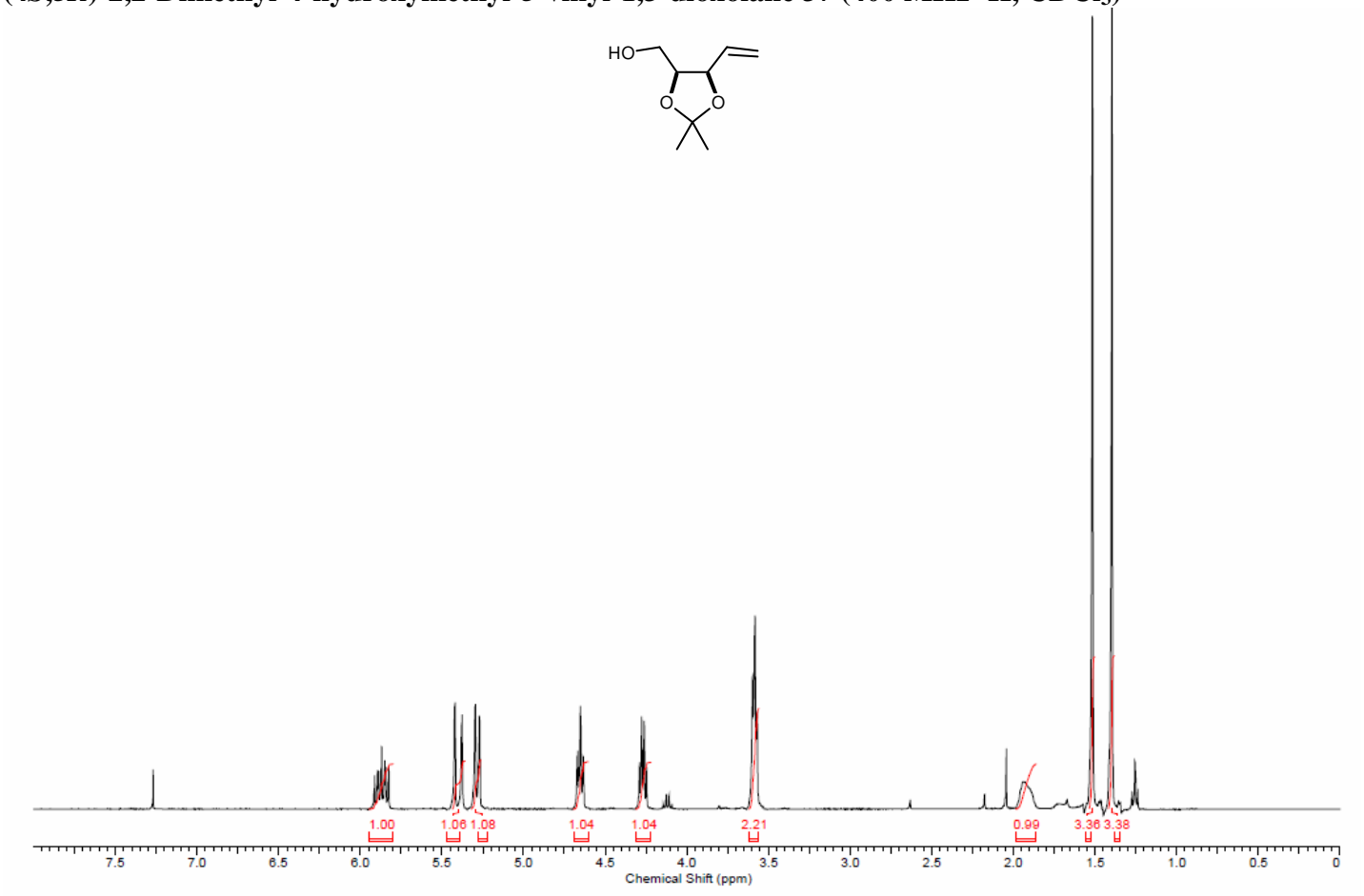
[22] Crystallographic data (excluding structure factors) for compounds **59**, **63**, **64** and **67** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 846621–846624, respectively. Copies of these data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

(2*R*,3*R*,4*S*,5*S*)-2-Methoxy-3,4-*O*-isopropylidene-3,4-dihydroxy-5-iodomethyltetrahydrofuran 36

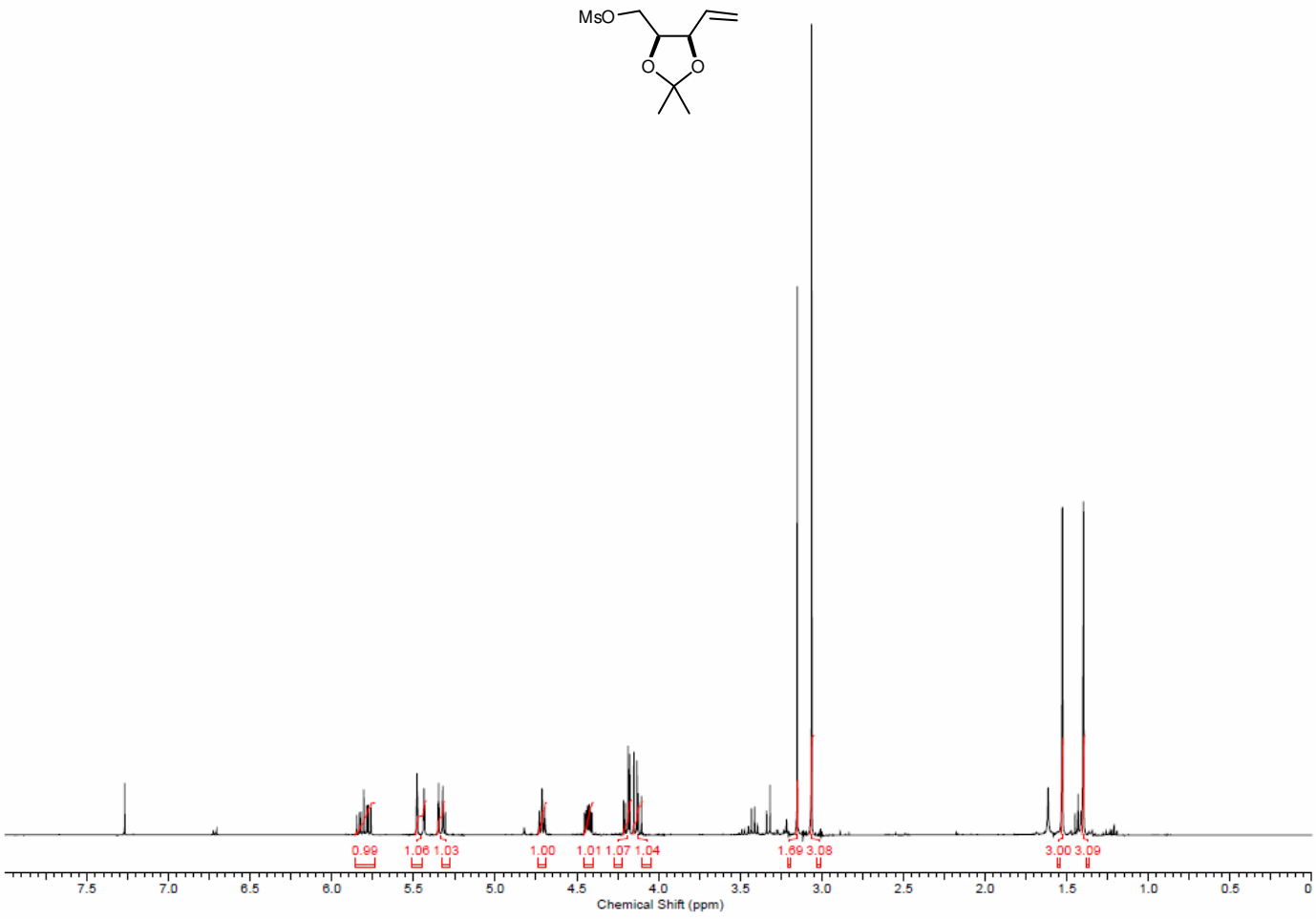
(400 MHz ^{1}H, $CDCl_3$)



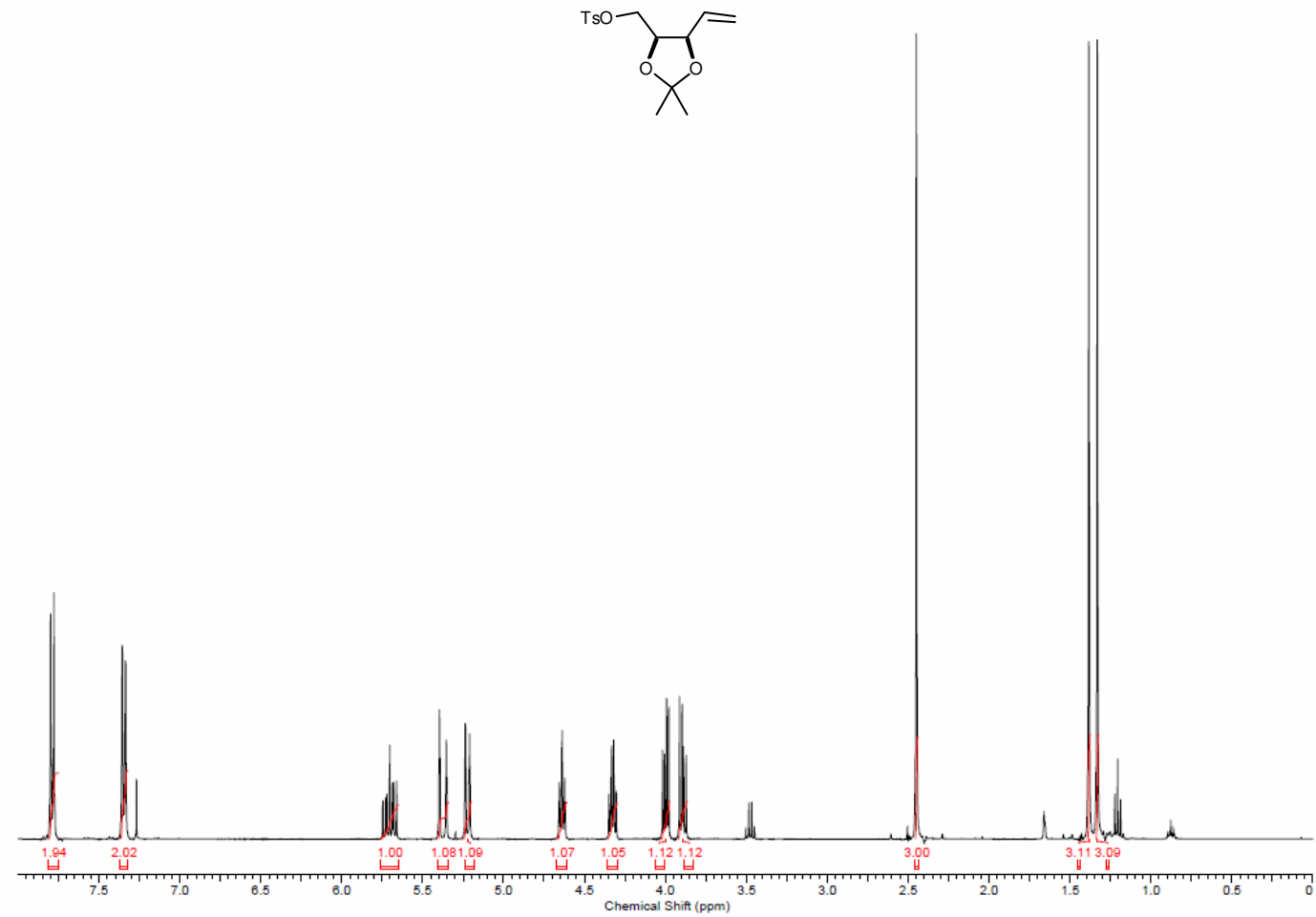
(4*S*,5*R*)-2,2-Dimethyl-4-hydroxymethyl-5-vinyl-1,3-dioxolane 37 (400 MHz ^{1}H, $CDCl_3$)



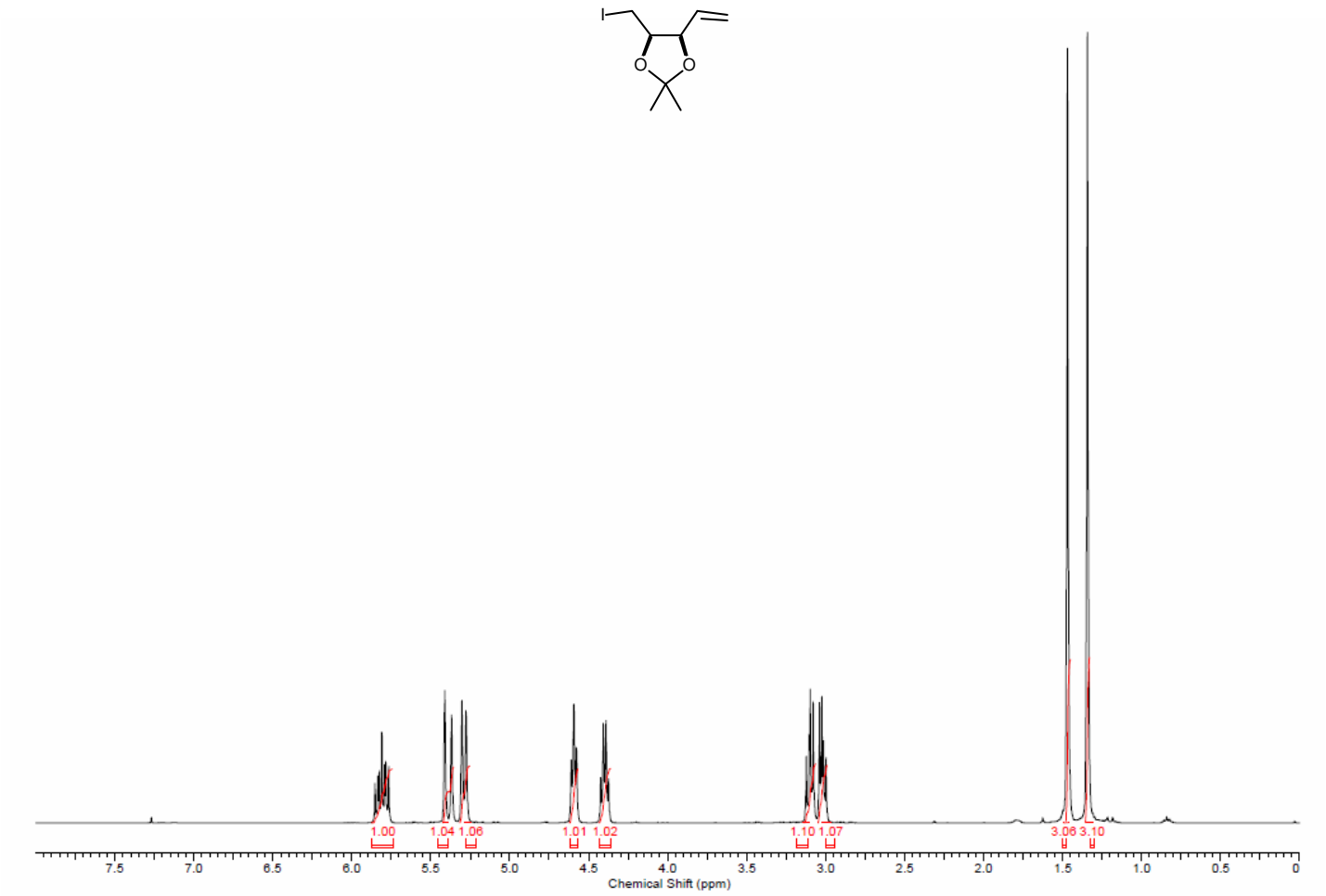
(4*S*,5*R*)-2,2-Dimethyl-4-(methanesulfonyloxy)methyl-5-vinyl-1,3-dioxolane 38 (400 MHz ^{1}H, $CDCl_3$)



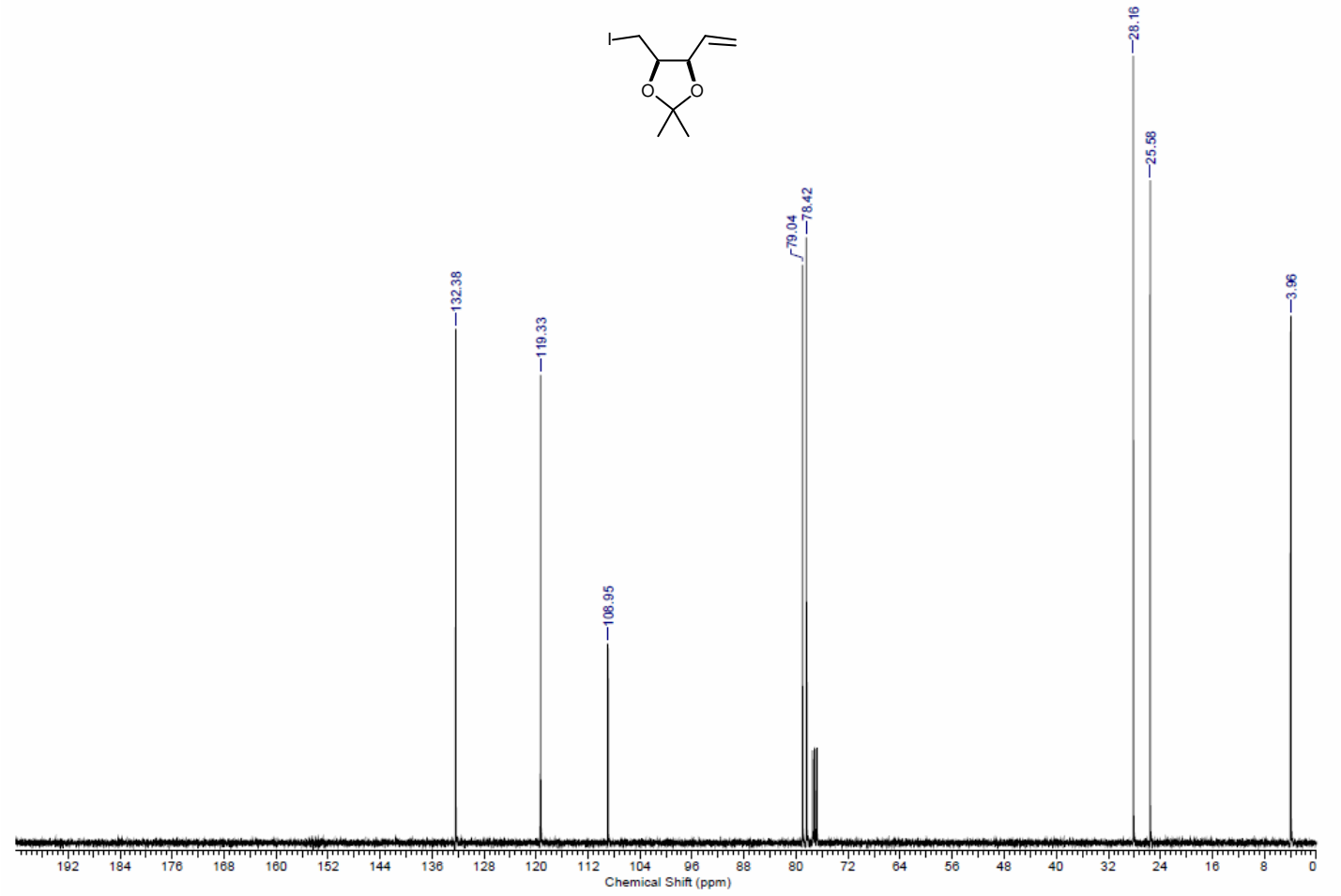
(4*S*,5*R*)-2,2-Dimethyl-4-(*p*-toluenesulfonyloxy)methyl-5-vinyl-1,3-dioxolane 39 (400 MHz ^{1}H, $CDCl_3$)



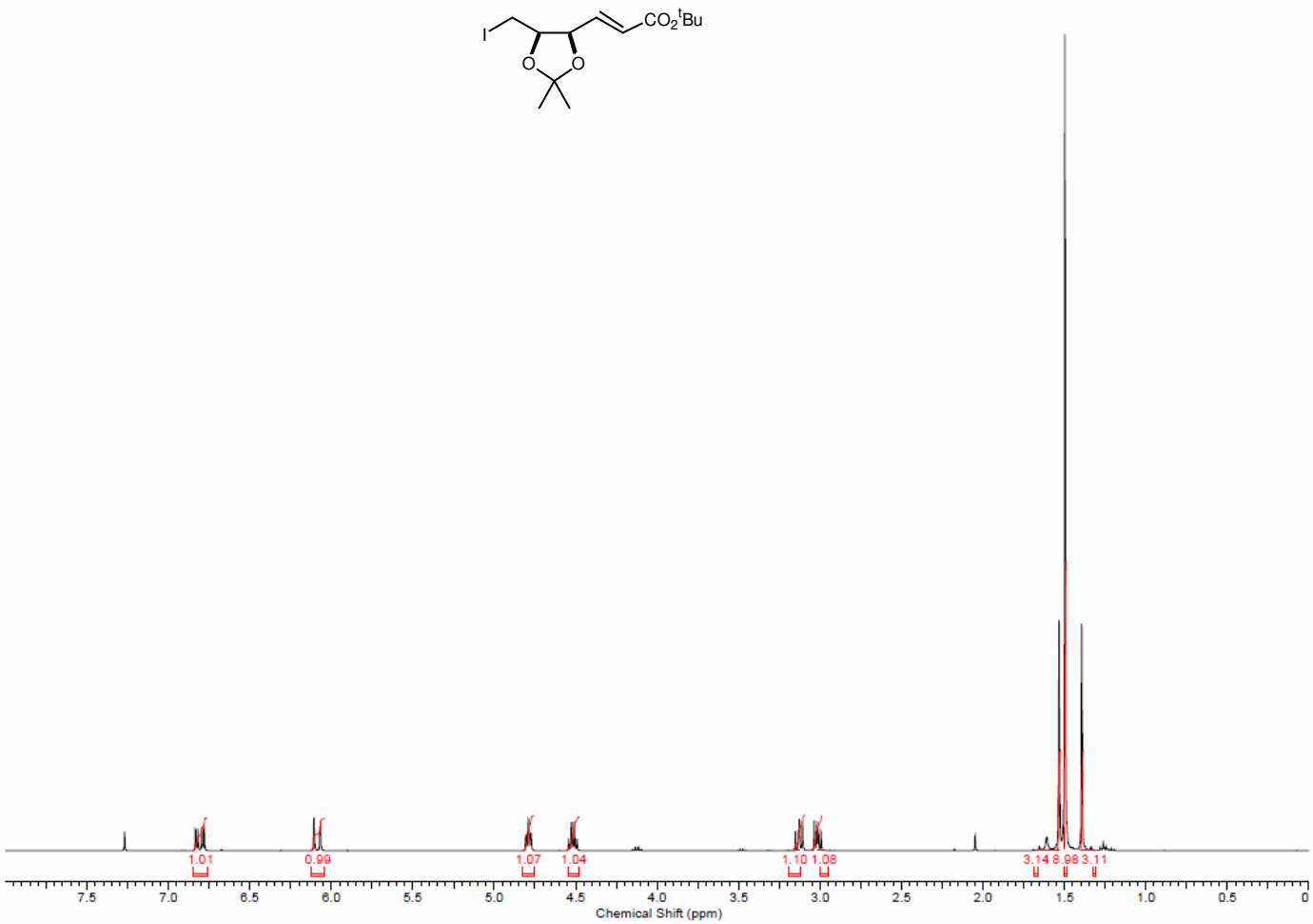
(*R*,*R*)-2,2-Dimethyl-4-iodomethyl-5-vinyl-1,3-dioxolane 40 (400 MHz ^{1}H, $CDCl_3$)



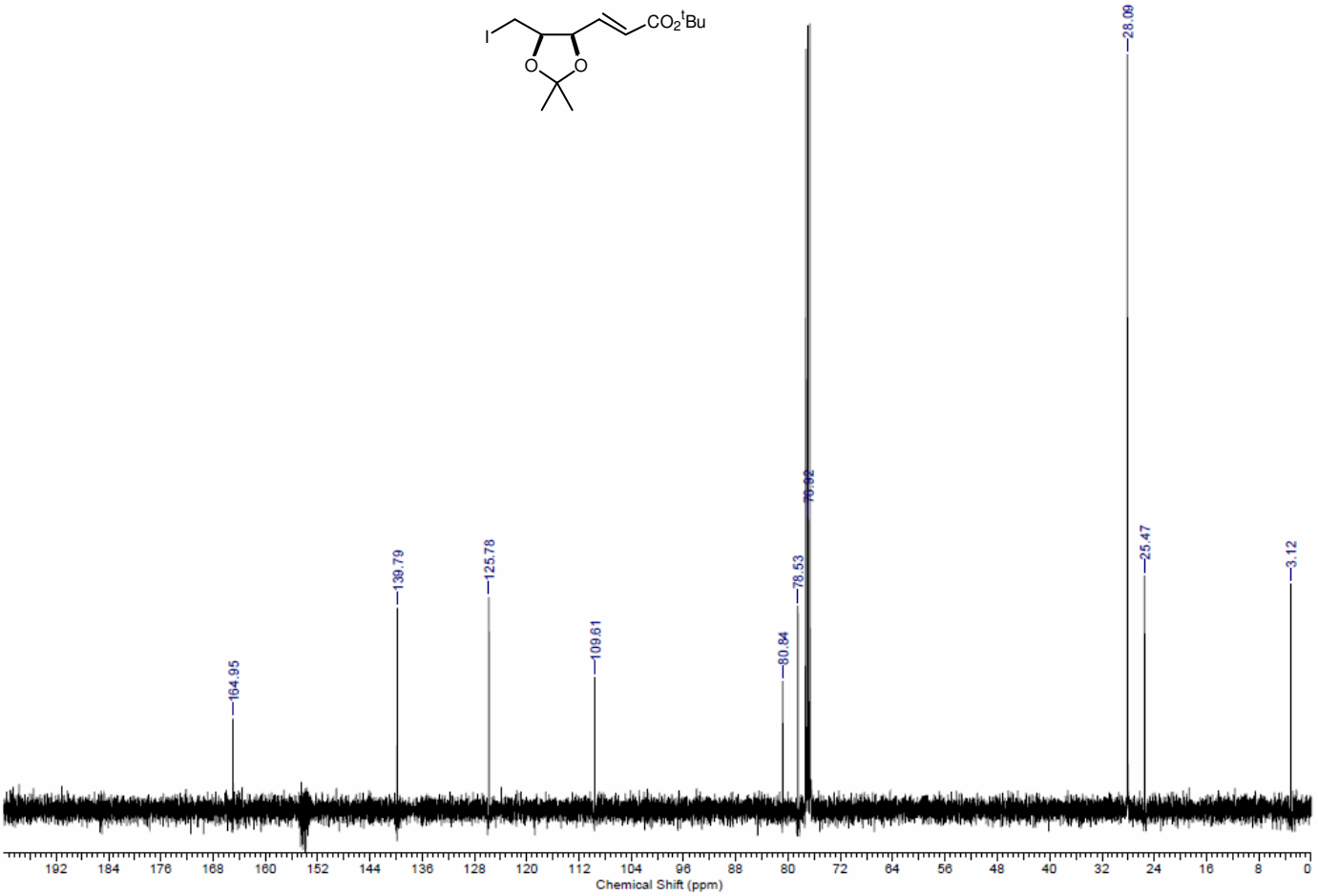
(*R*,*R*)-2,2-Dimethyl-4-iodomethyl-5-vinyl-1,3-dioxolane 40 (100 MHz ^{13}C, $CDCl_3$)



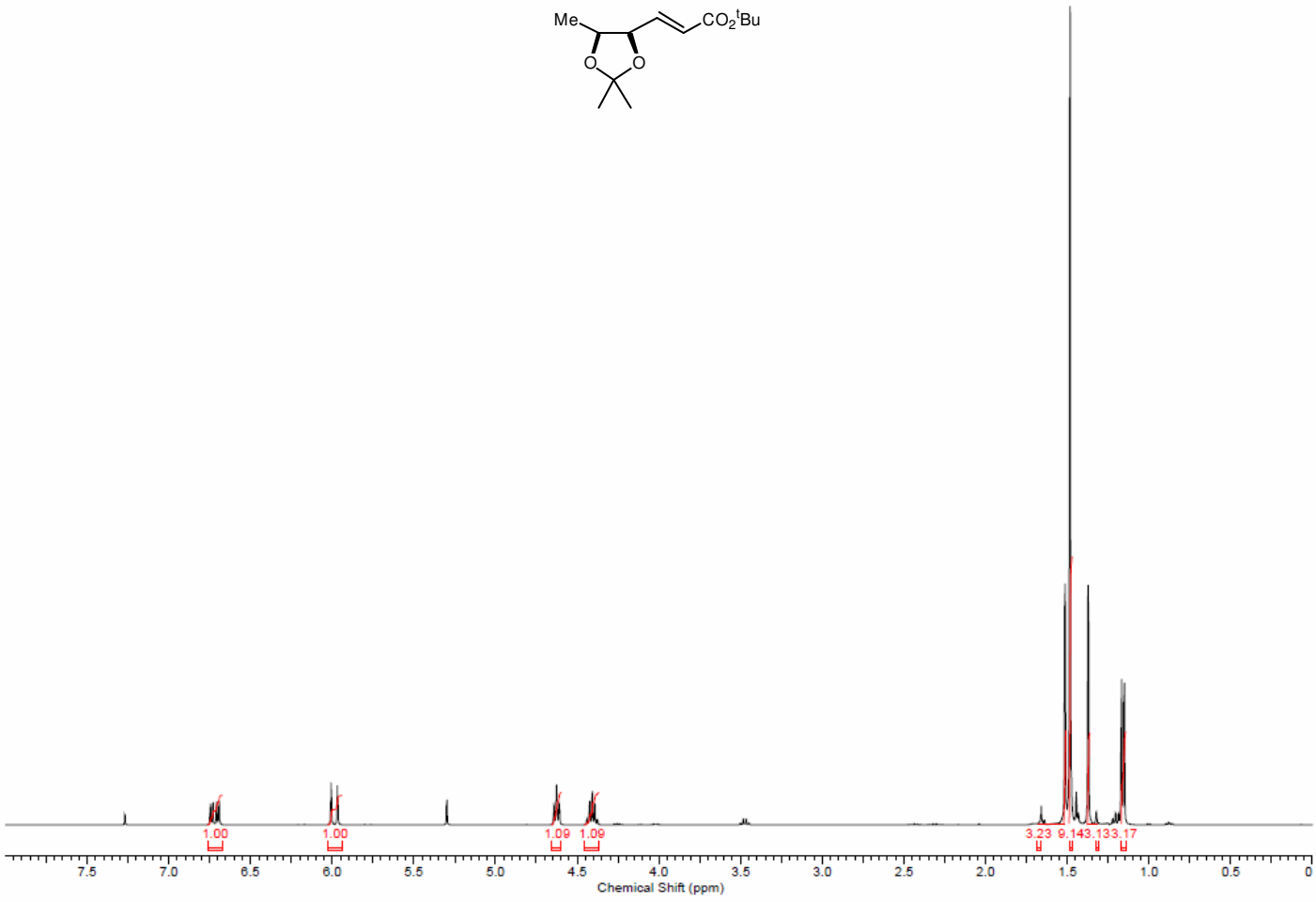
***tert*-Butyl (*R*,*R*,*E*)-4,5-*O*-isopropylidene-4,5-dihydroxy-6-iodohex-2-enoate 42 (400 MHz ^{1}H, $CDCl_3$)**



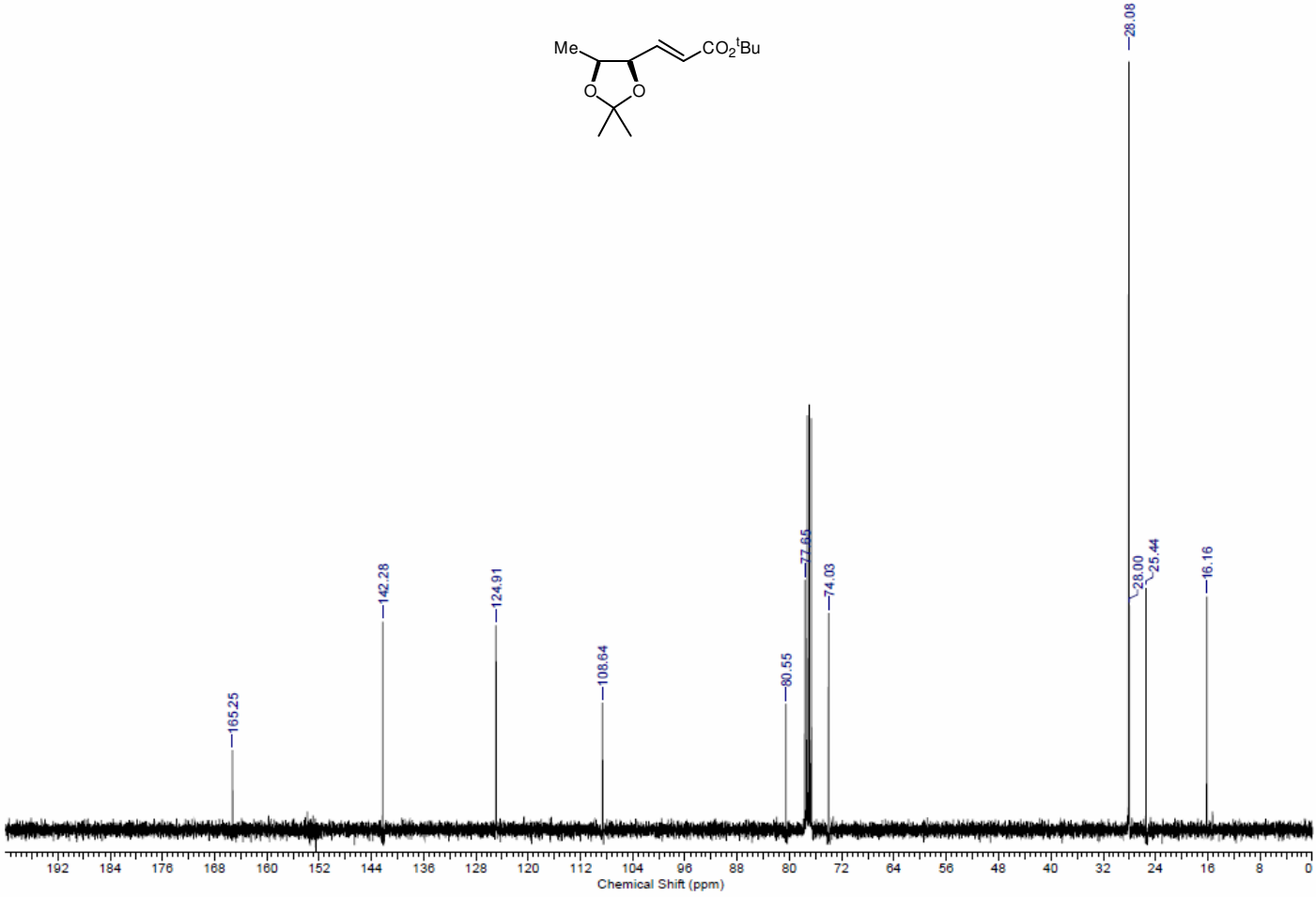
***tert*-Butyl (*R*,*R*,*E*)-4,5-*O*-isopropylidene-4,5-dihydroxy-6-iodohex-2-enoate 42 (100 MHz ^{13}C, $CDCl_3$)**



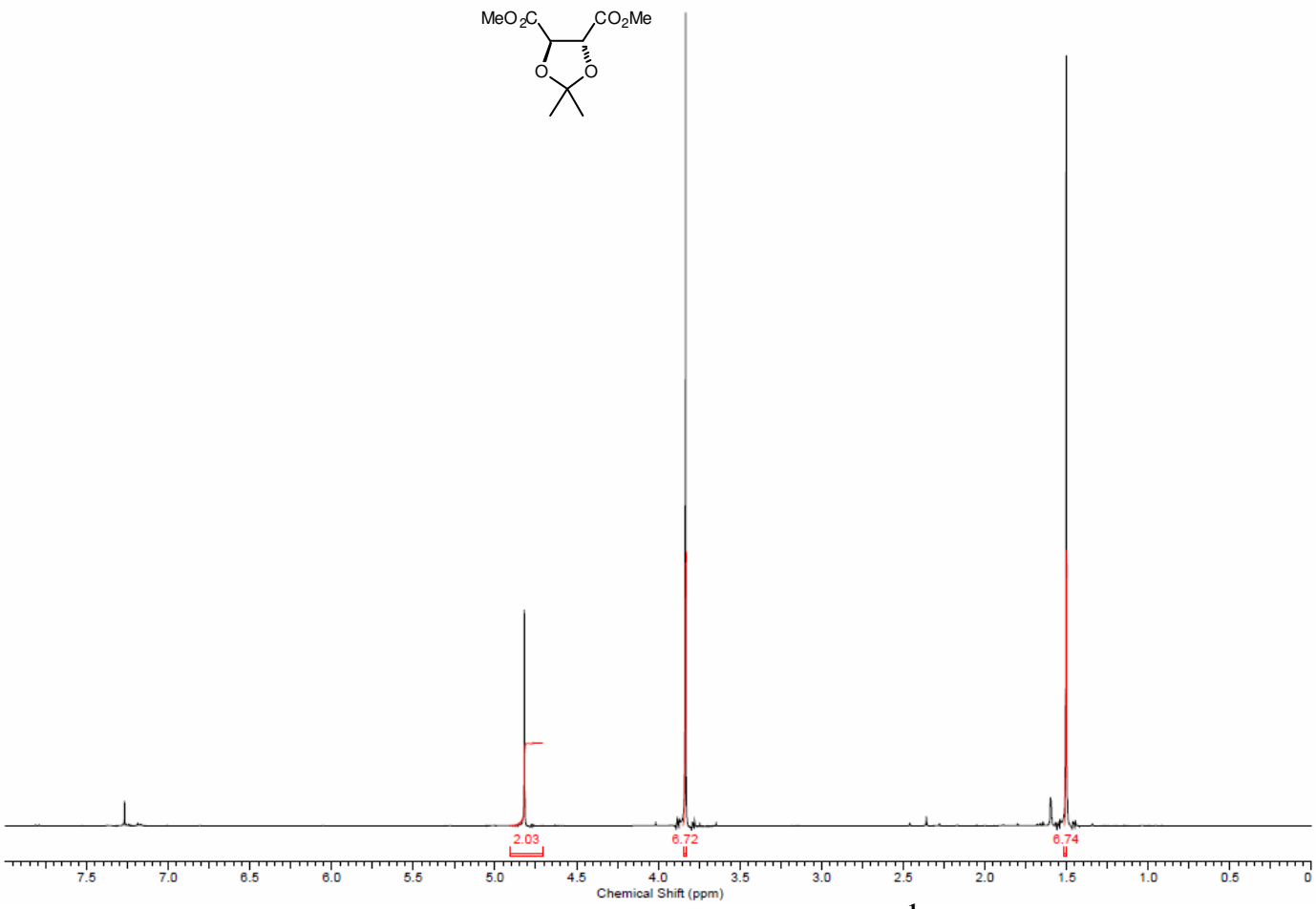
tert-Butyl (4_R_,5_S_)-4,5-_O_-isopropylidene-4,5-dihydroxyhex-2-enoate 31 (400 MHz ^{1}H, $CDCl_3$)



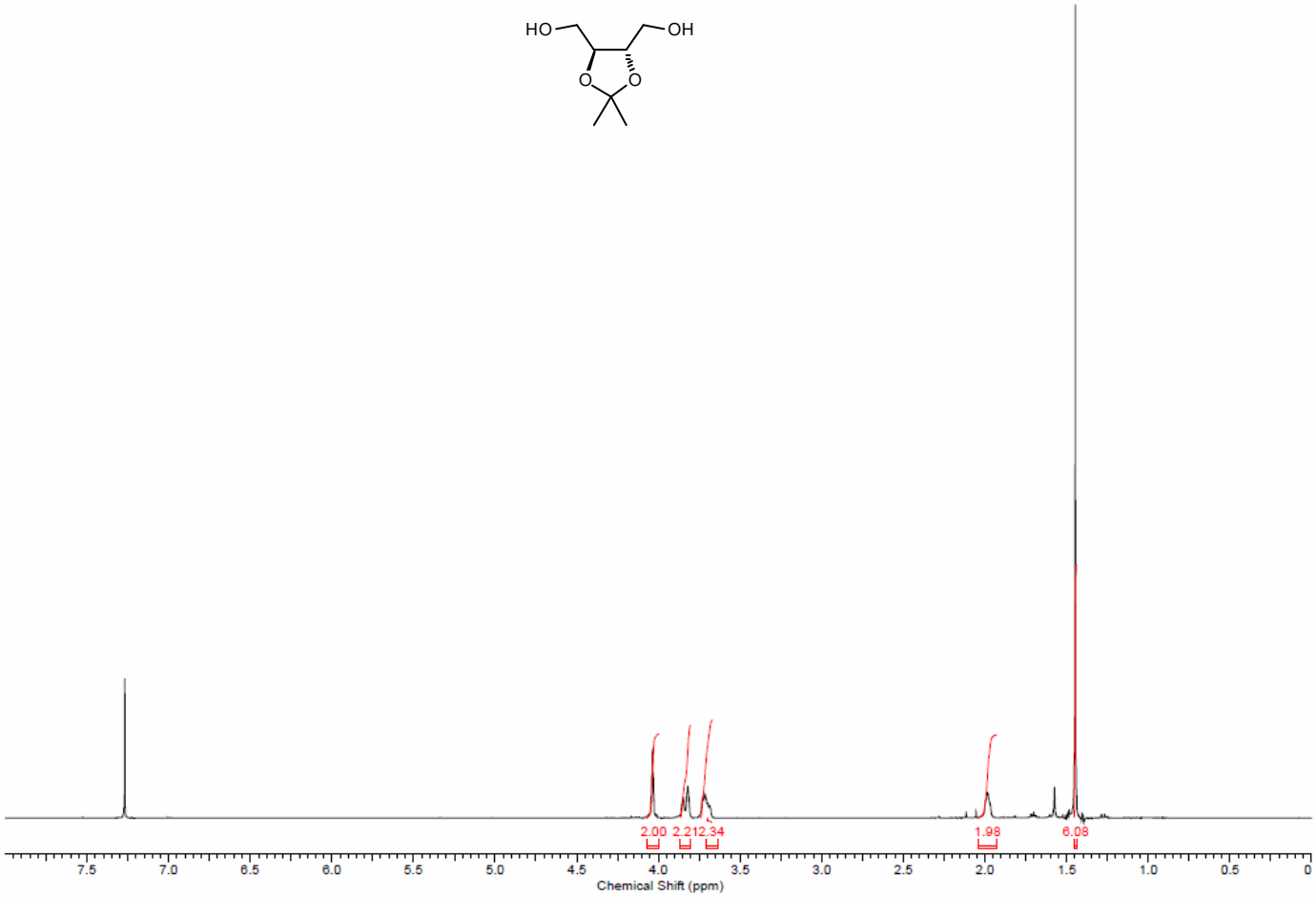
tert-Butyl (4_R_,5_S_)-4,5-_O_-isopropylidene-4,5-dihydroxyhex-2-enoate 31 (100 MHz ^{13}C, $CDCl_3$)



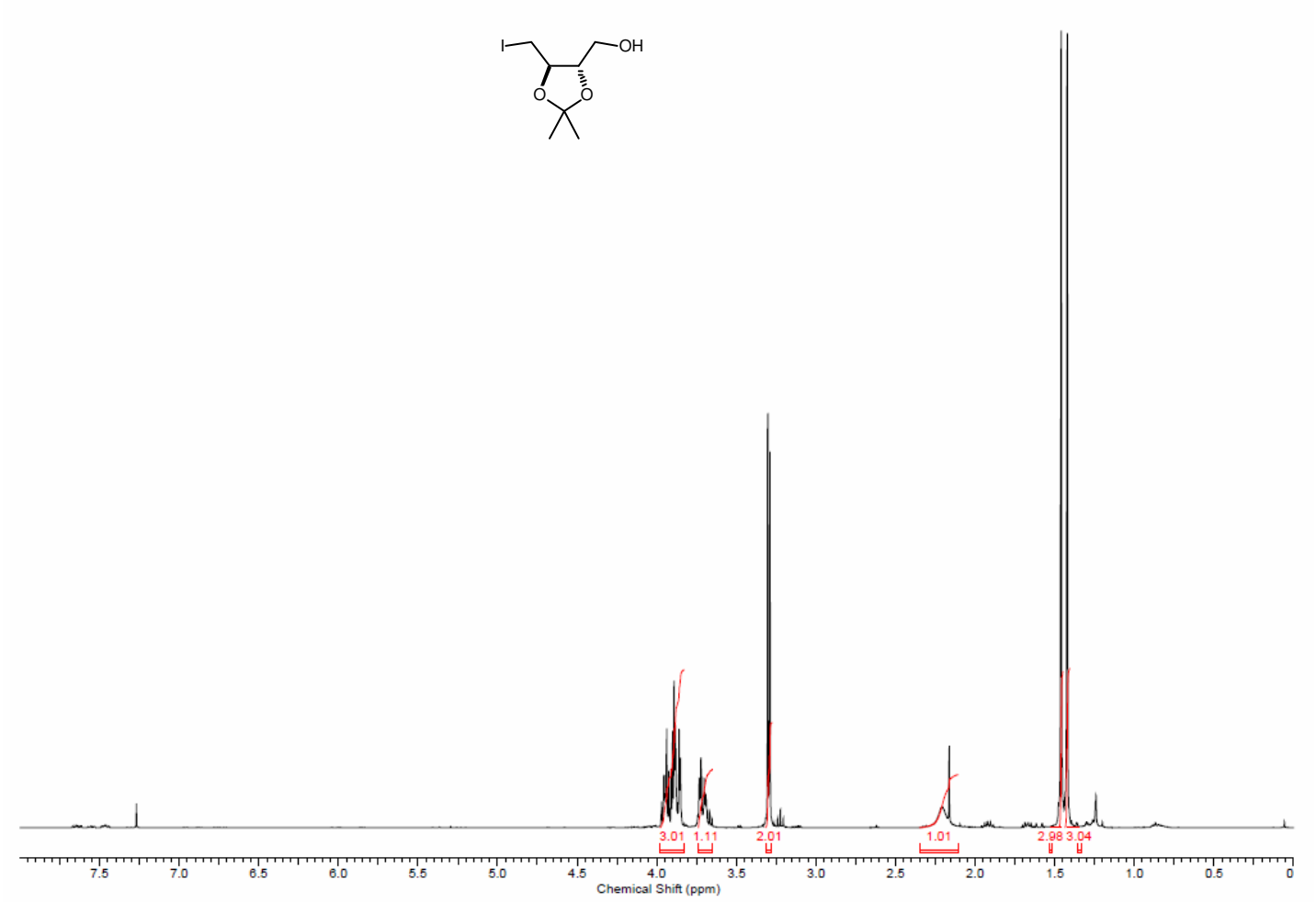
Dimethyl (*R*,*R*)-2,2-Dimethyl-1,3-dioxolane-4,5-dicarboxylate (400 MHz ^{1}H, $CDCl_3$)



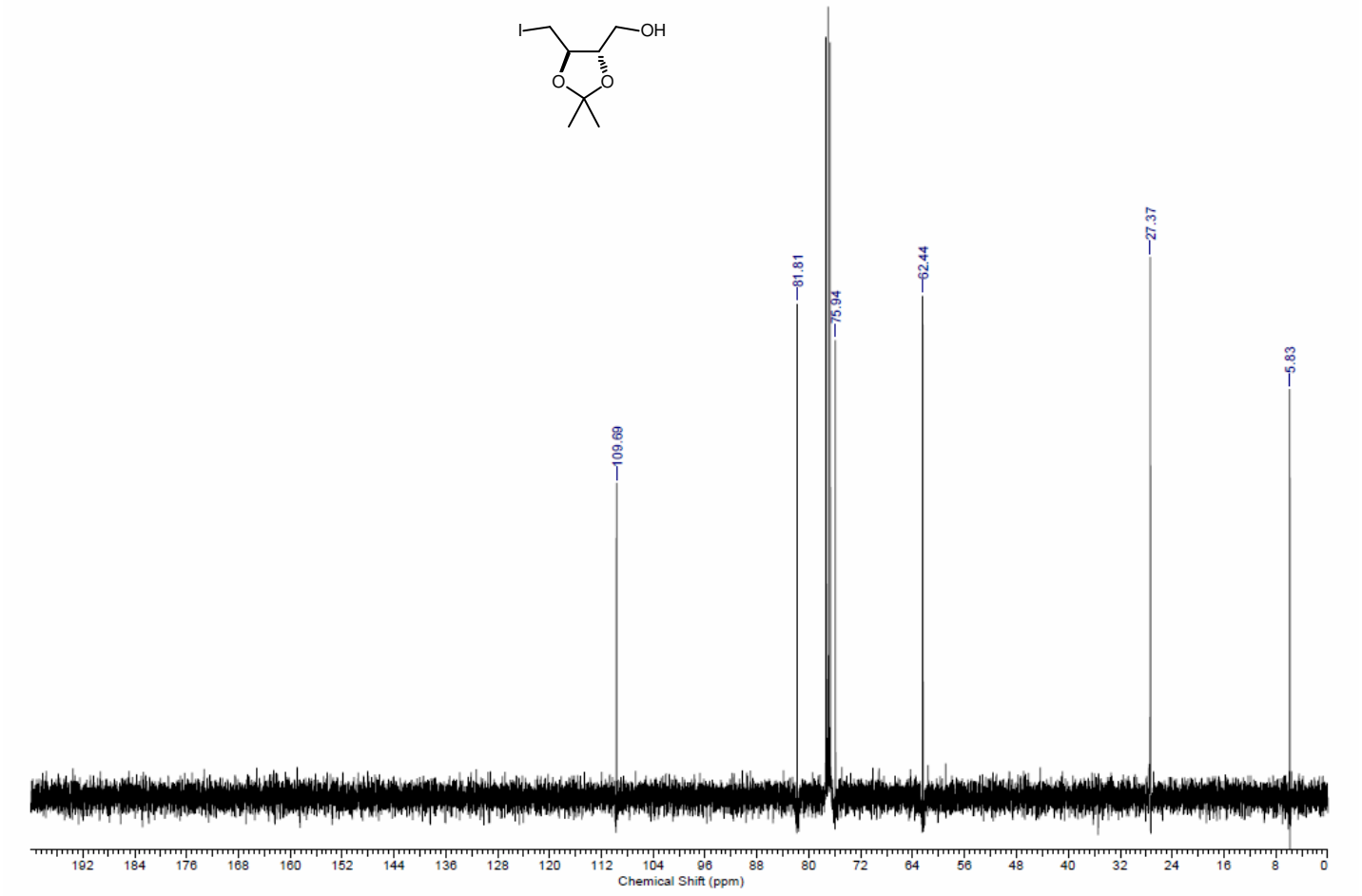
(*S*,*S*)-2,2-Dimethyl-4,5-bis(hydroxymethyl)-1,3-dioxolane 45 (400 MHz ^{1}H, $CDCl_3$)



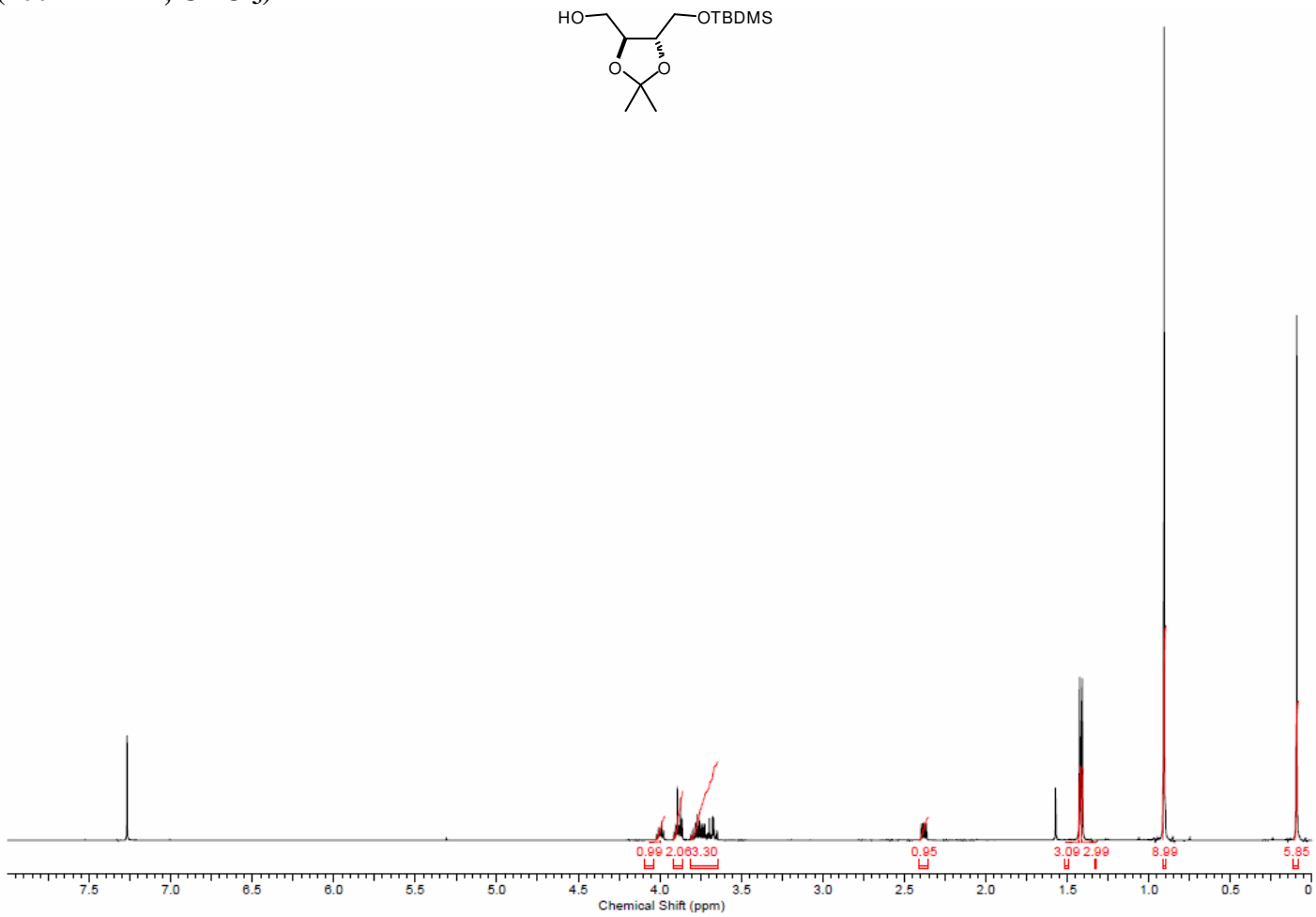
(4*R*,5*S*)-2,2-Dimethyl-4-iodomethyl-5-hydroxymethyl-1,3-dioxolane 46 (400 MHz ^{1}H, $CDCl_3$)



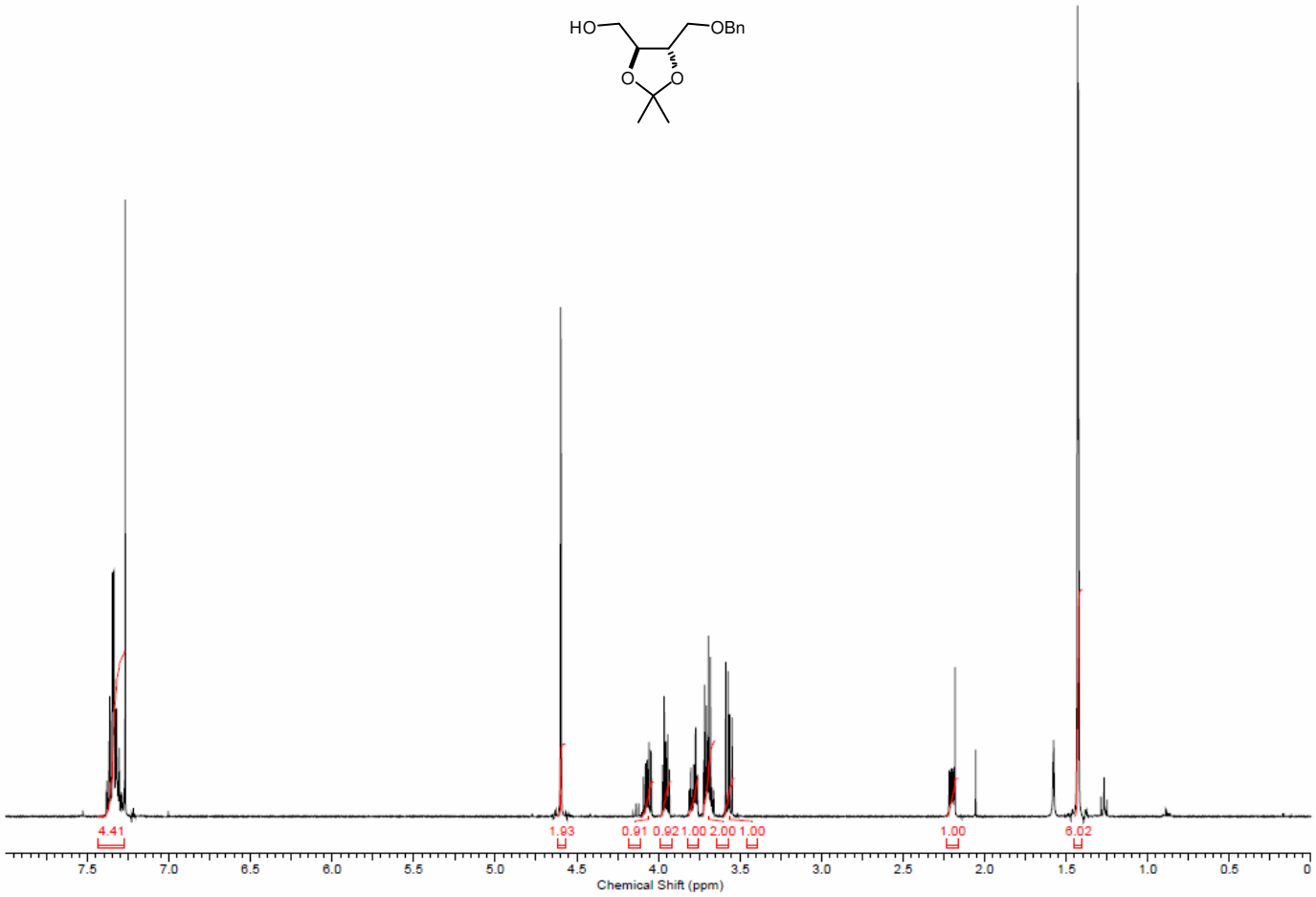
(4*R*,5*S*)-2,2-Dimethyl-4-iodomethyl-5-hydroxymethyl-1,3-dioxolane 46 (100 MHz ^{13}C, $CDCl_3$)



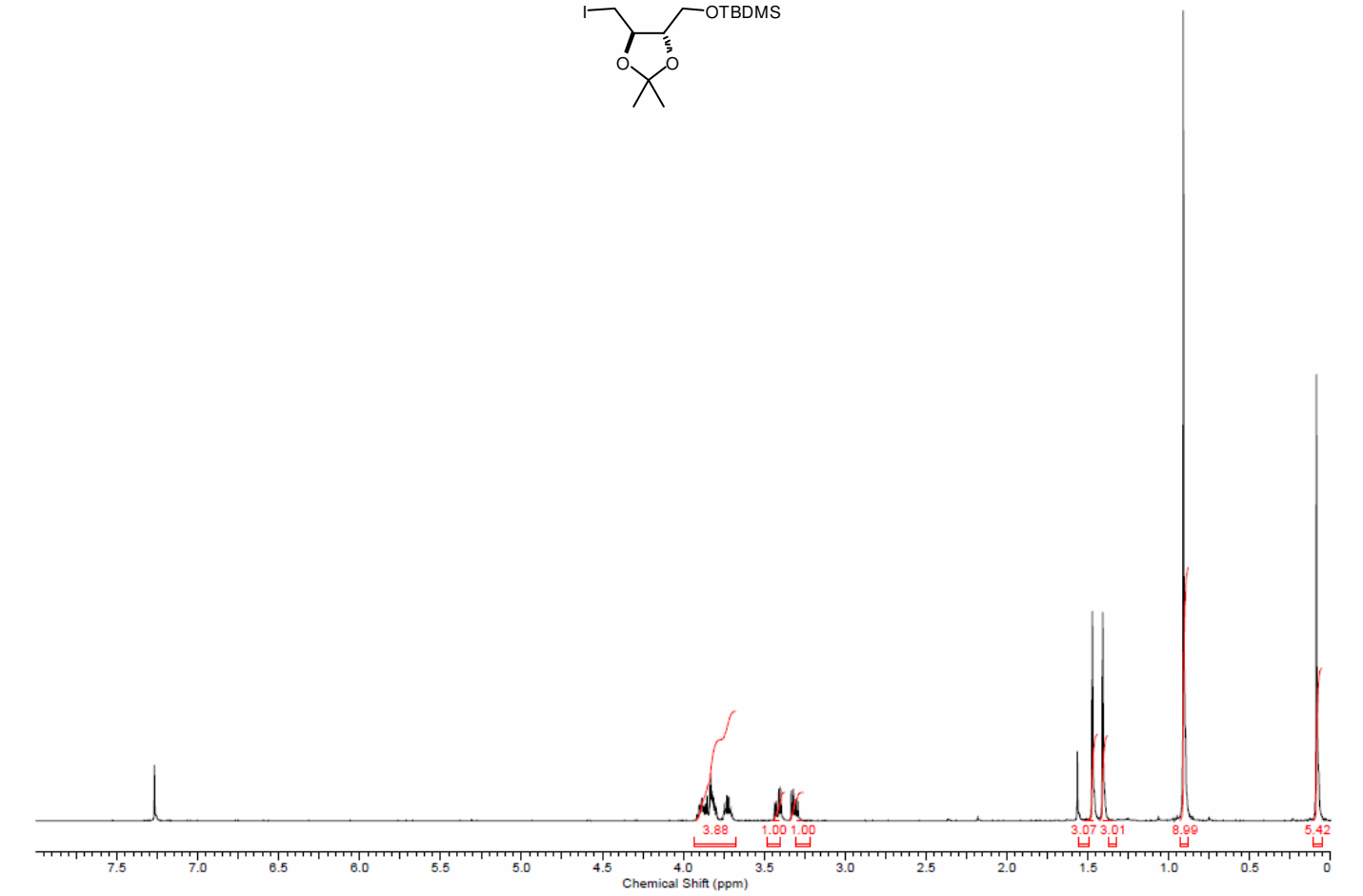
(*S*,*S*)-2,2-Dimethyl-4-(*tert*-butyldimethylsilyloxy)methyl-5-hydroxymethyl-1,3-dioxolane 49 (400 MHz ^{1}H, $CDCl_3$)



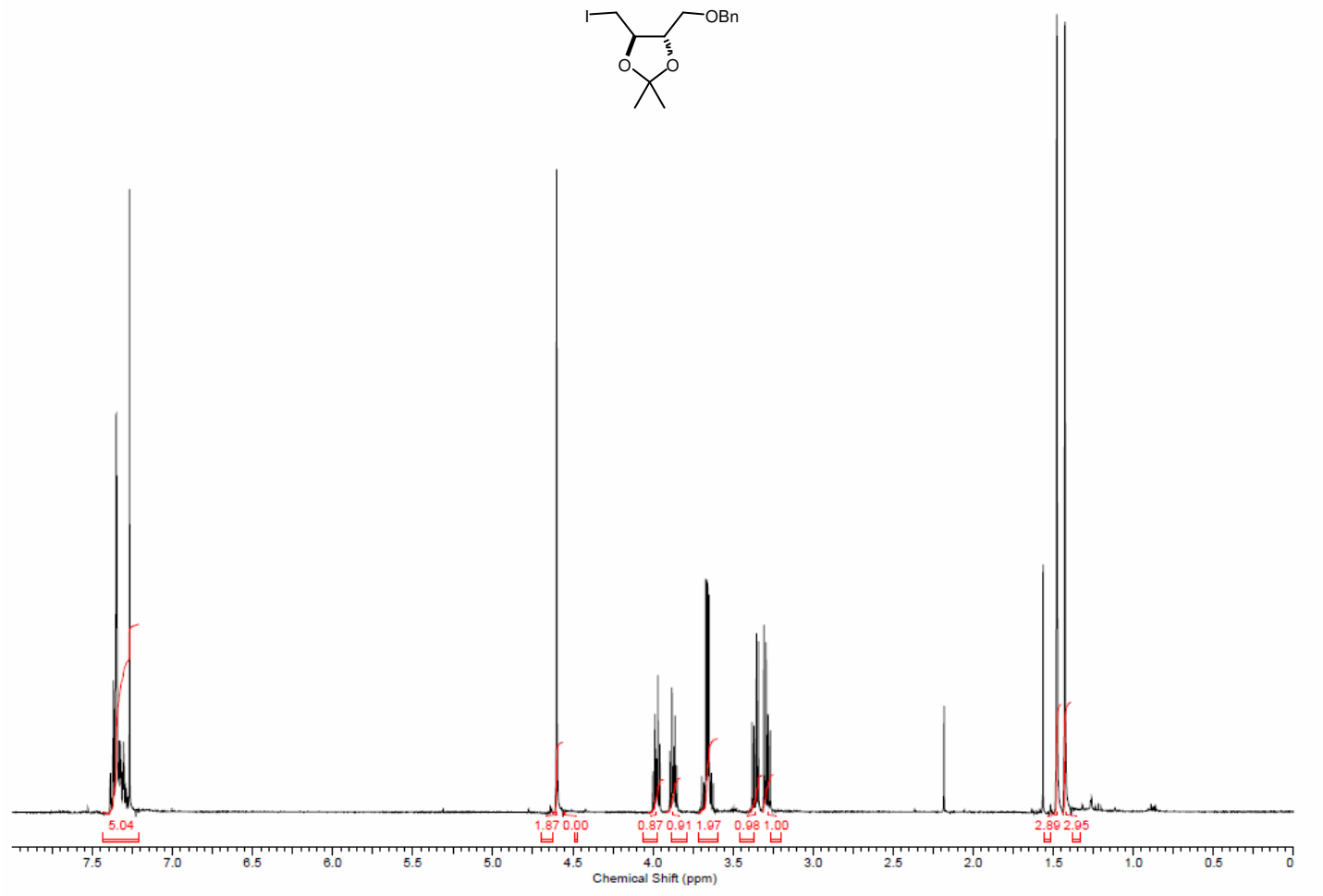
(*S*,*S*)-2,2-Dimethyl-4-benzyloxymethyl-5-hydroxymethyl-1,3-dioxolane 50 (400 MHz ^{1}H, $CDCl_3$)



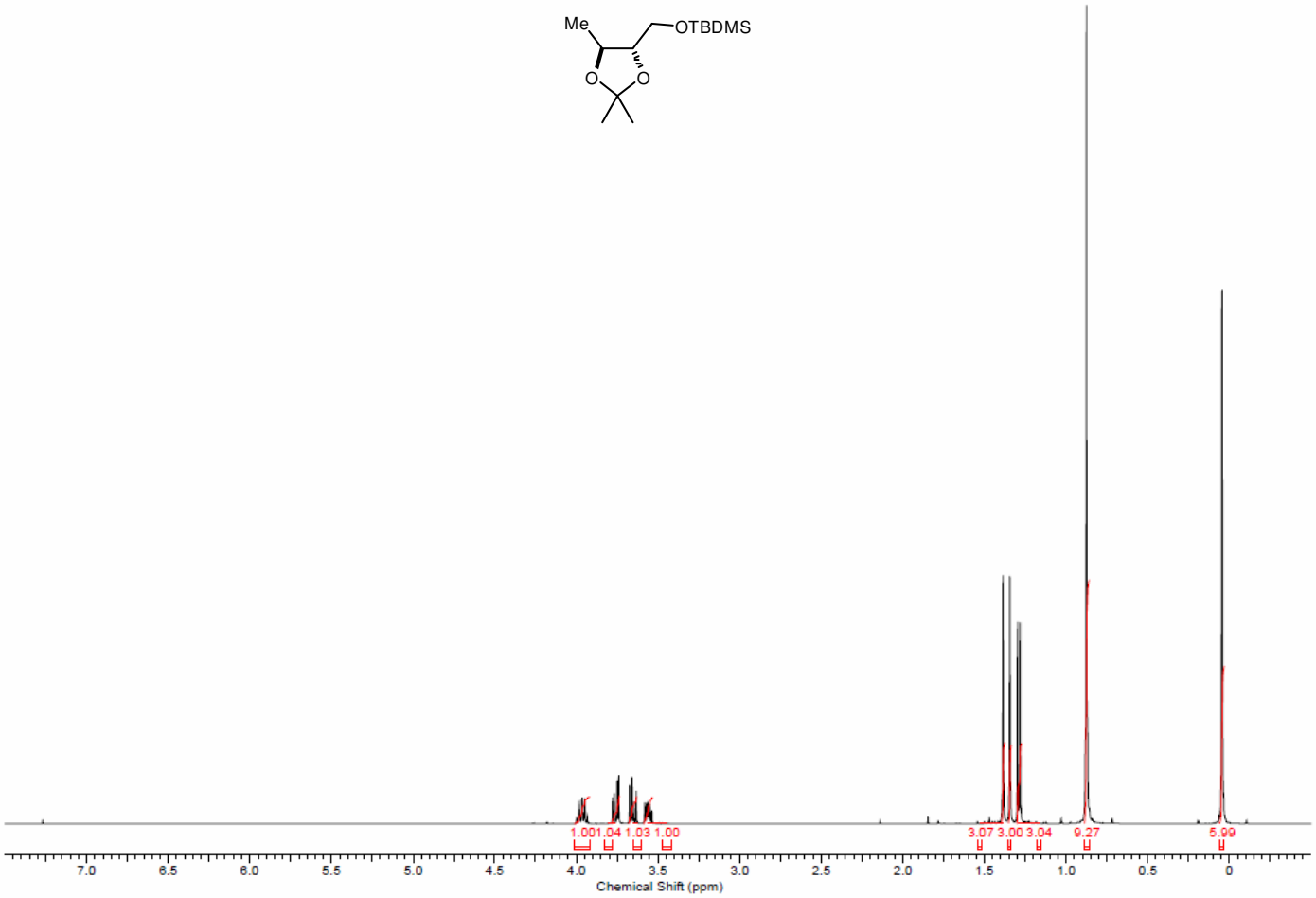
(4*R*,5*S*)-2,2-Dimethyl-4-iodomethyl-5-(*tert*-butyldimethylsilyloxy)methyl-1,3-dioxolane 51 (400 MHz ^{1}H, $CDCl_3$)



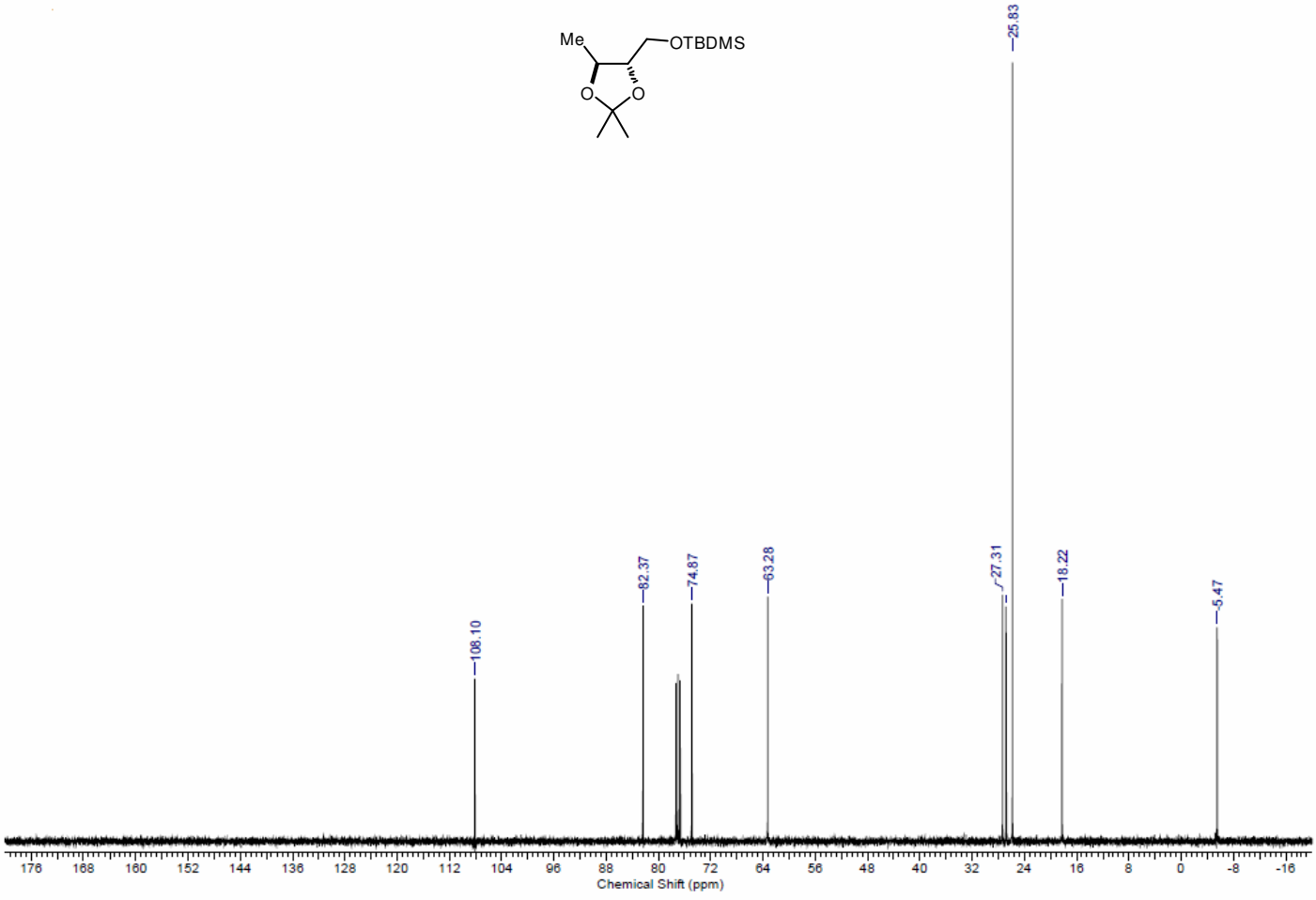
(4*R*,5*S*)-2,2-Dimethyl-4-iodomethyl-5-benzyloxymethyl-1,3-dioxolane 52 (400 MHz ^{1}H, $CDCl_3$)



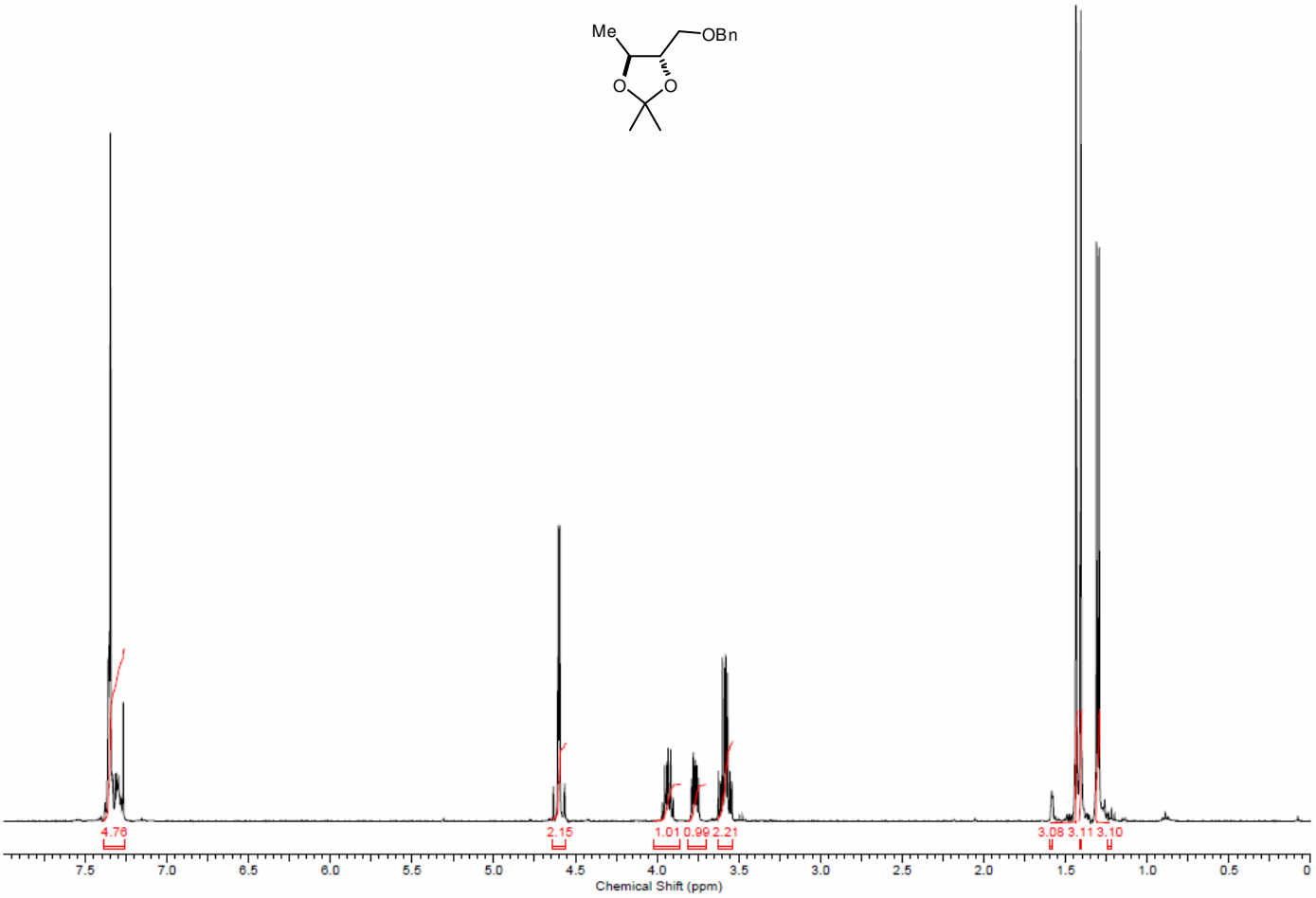
(*S*,*S*)-2,2-Dimethyl-4-(*tert*-butyldimethylsilyloxy)methyl-5-methyl-1,3-dioxolane 53 (400 MHz ^{1}H, $CDCl_3$)



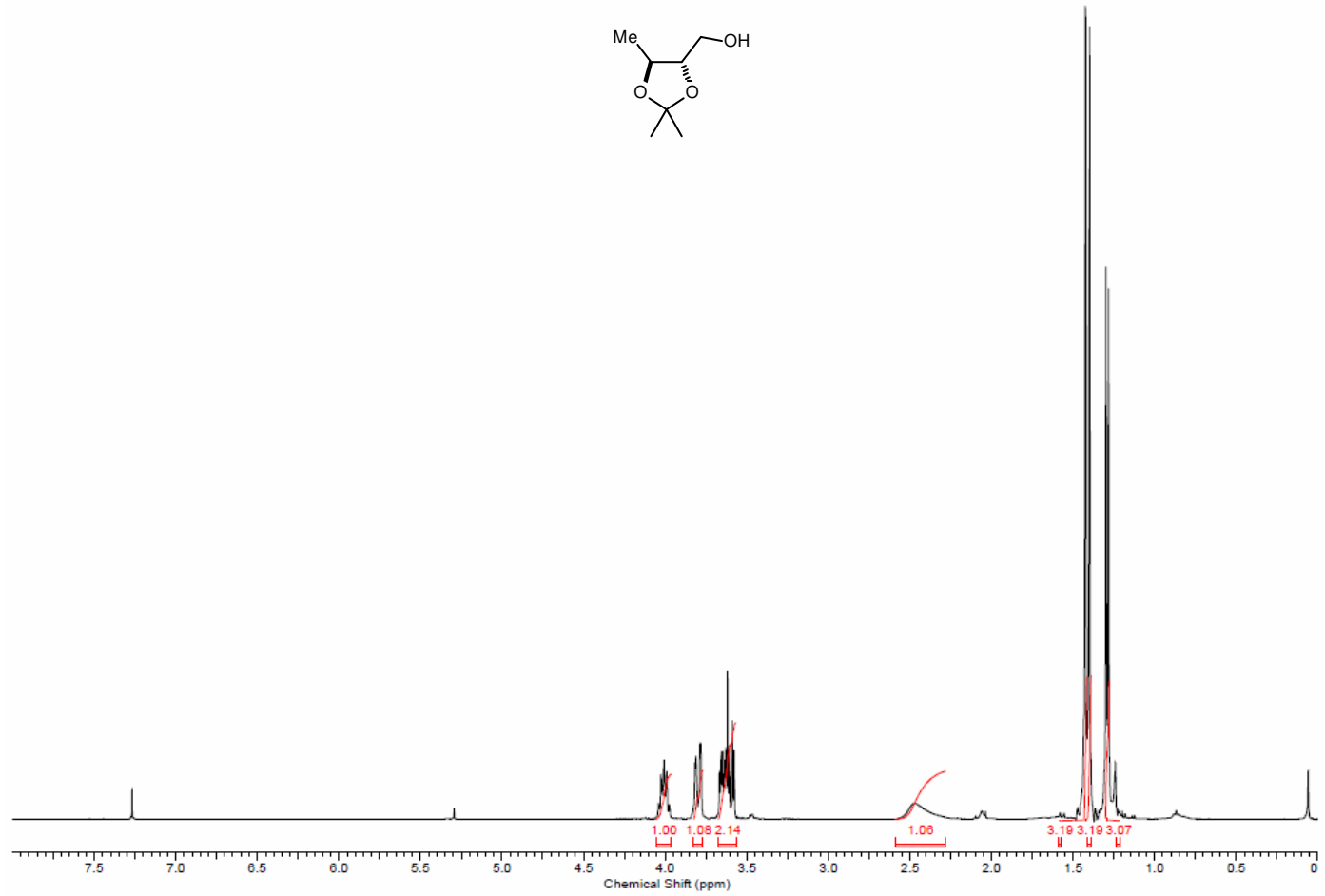
(*S*,*S*)-2,2-Dimethyl-4-(*tert*-butyldimethylsilyloxy)methyl-5-methyl-1,3-dioxolane 53 (100 MHz ^{13}C, $CDCl_3$)



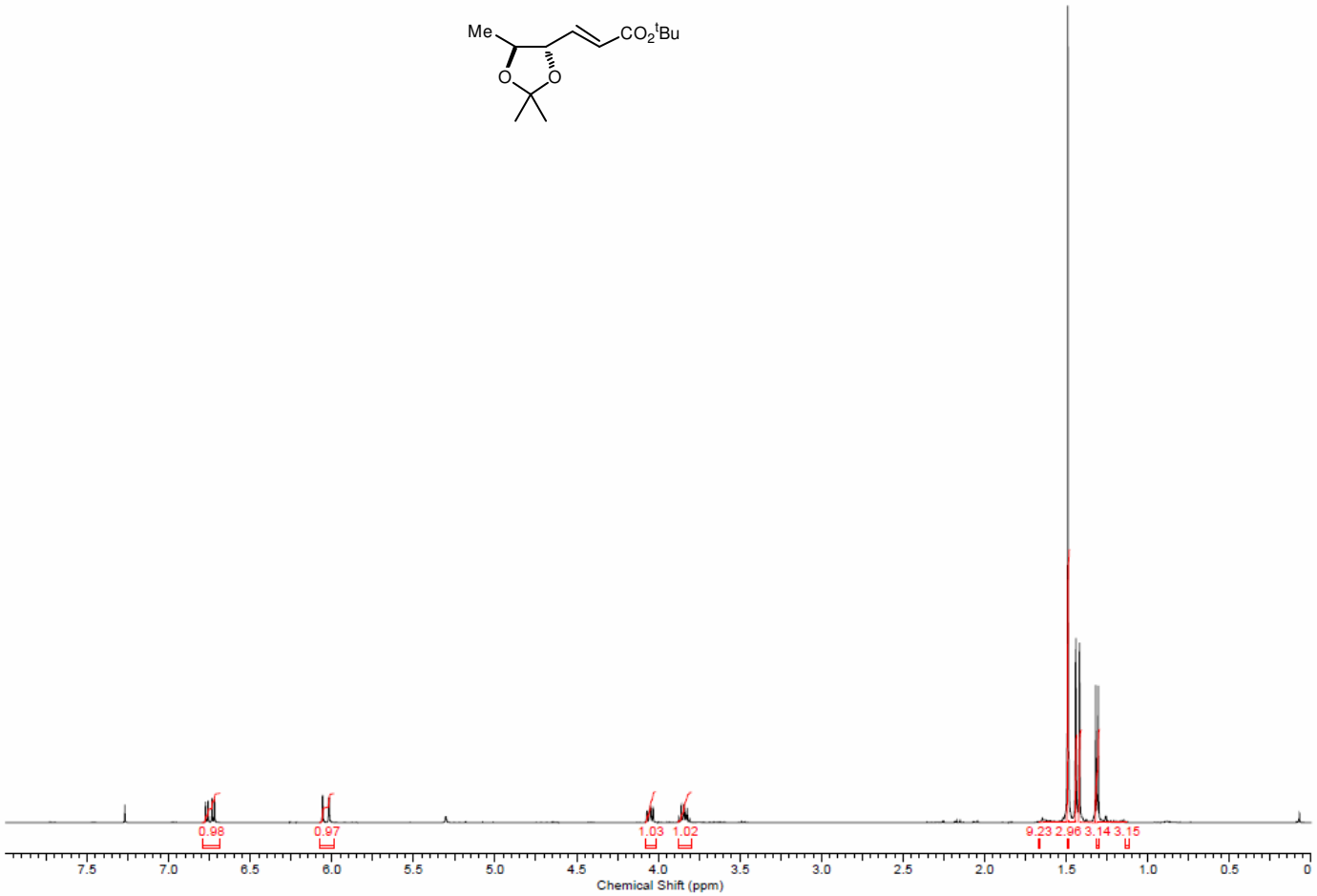
(*S*,*S*)-2,2-Dimethyl-4-benzyloxymethyl-5-methyl-1,3-dioxolane 54 (400 MHz ^{1}H, $CDCl_3$)



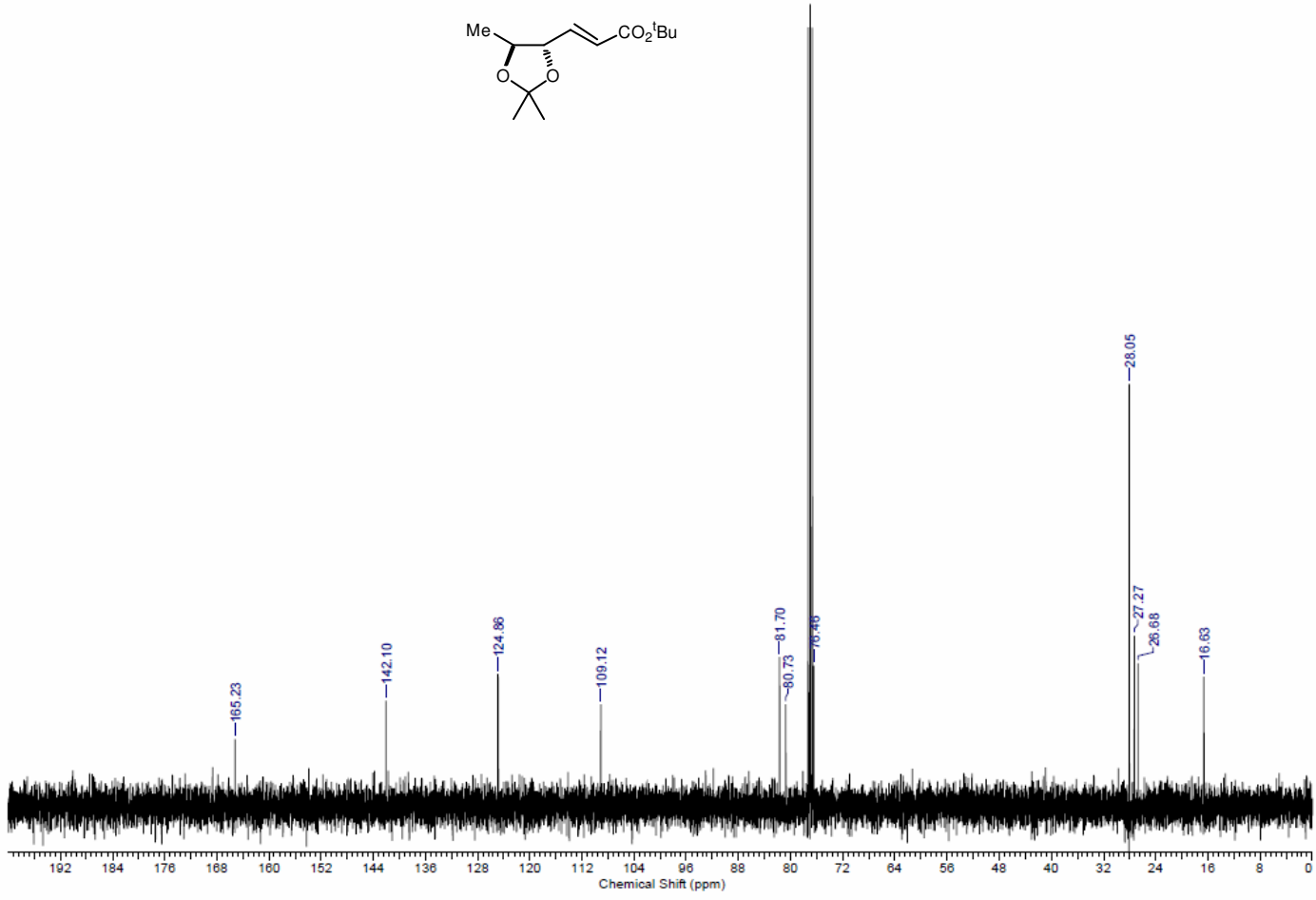
(*S*,*S*)-2,2-Dimethyl-4-hydroxymethyl-5-methyl-1,3-dioxolane 47 (400 MHz ^{1}H, $CDCl_3$)



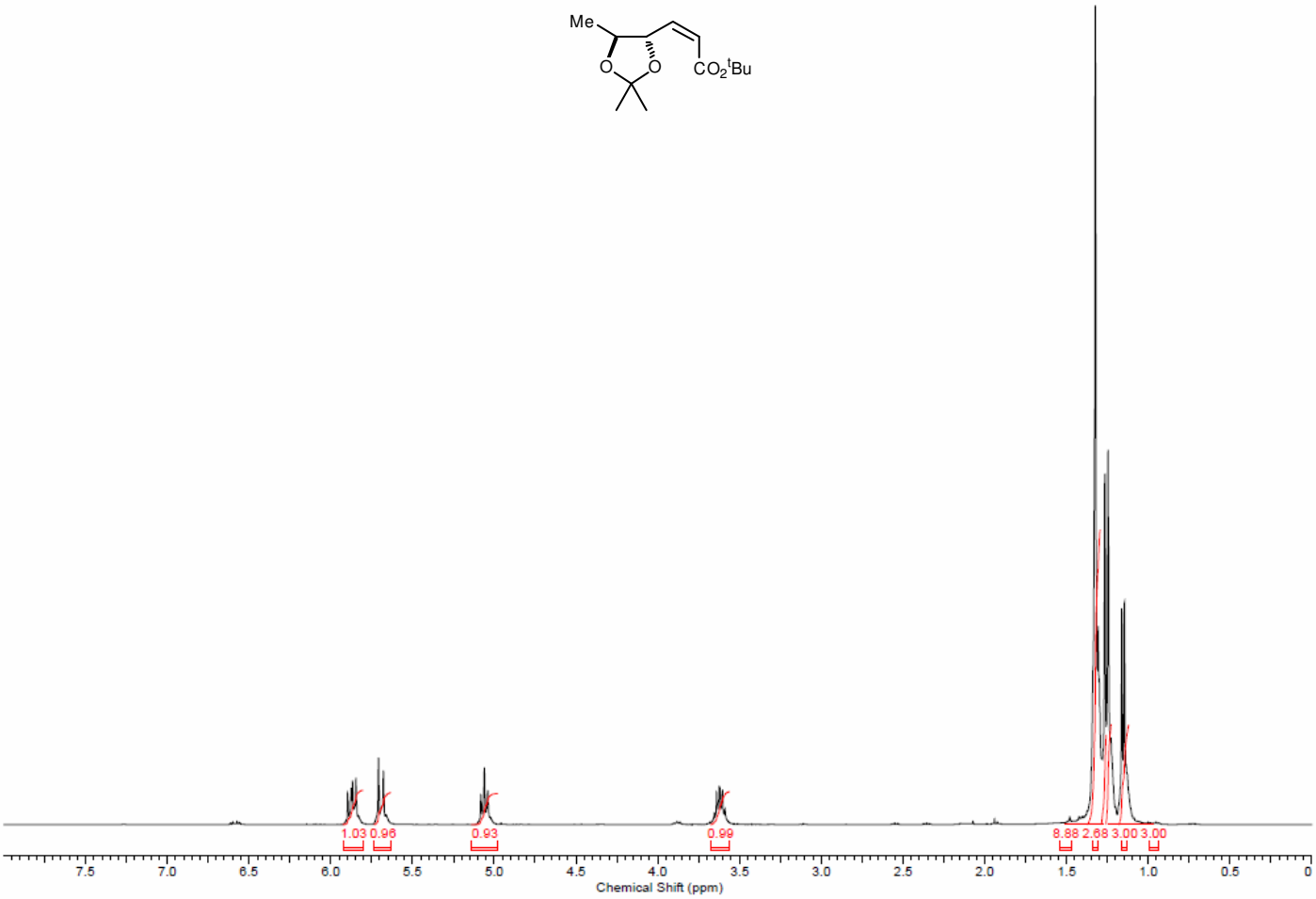
***tert*-Butyl (*S*,*S*,*E*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-2-enoate 32 (400 MHz ^{1}H, $CDCl_3$)**



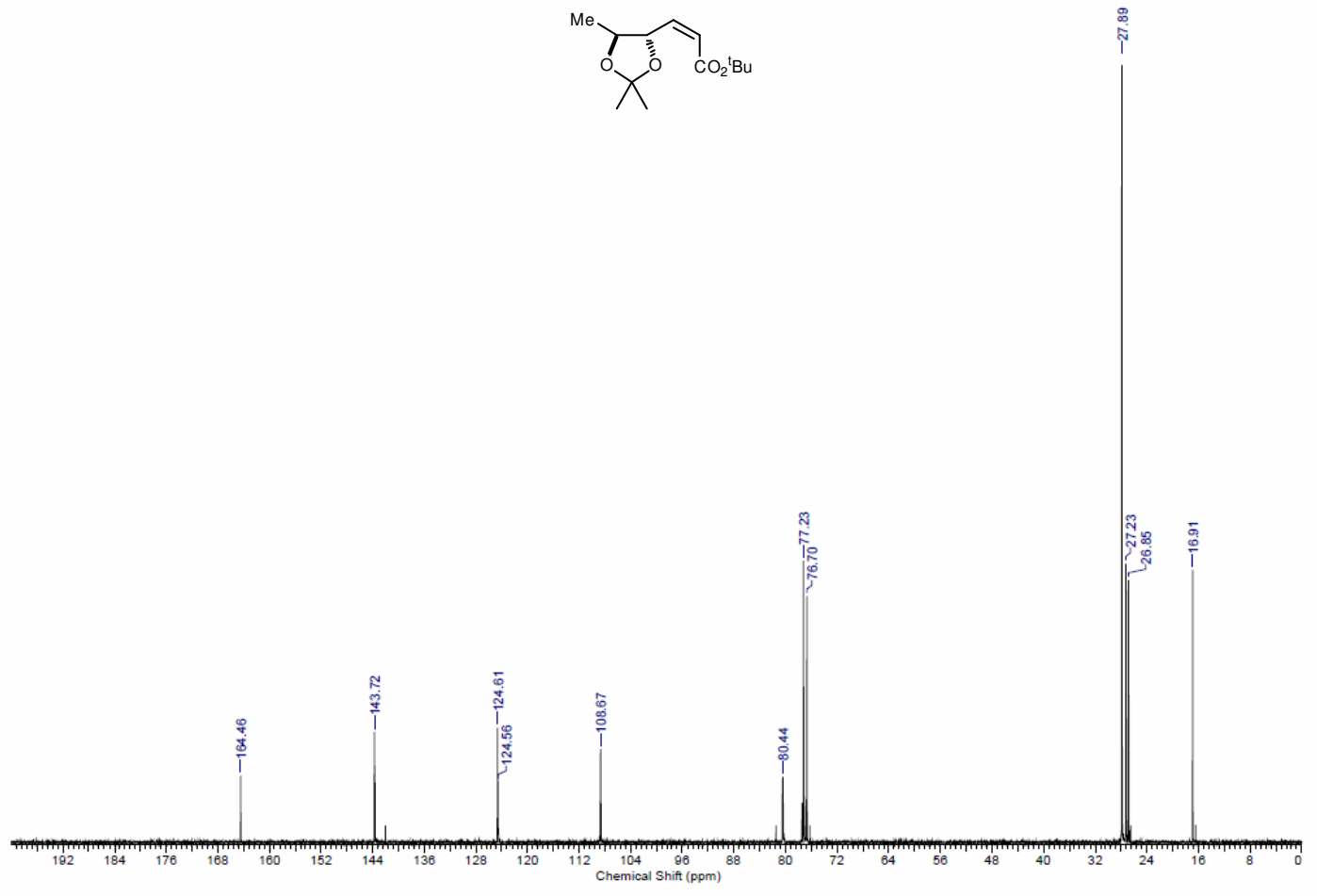
***tert*-Butyl (*S*,*S*,*E*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-2-enoate 32 (100 MHz ^{13}C, $CDCl_3$)**



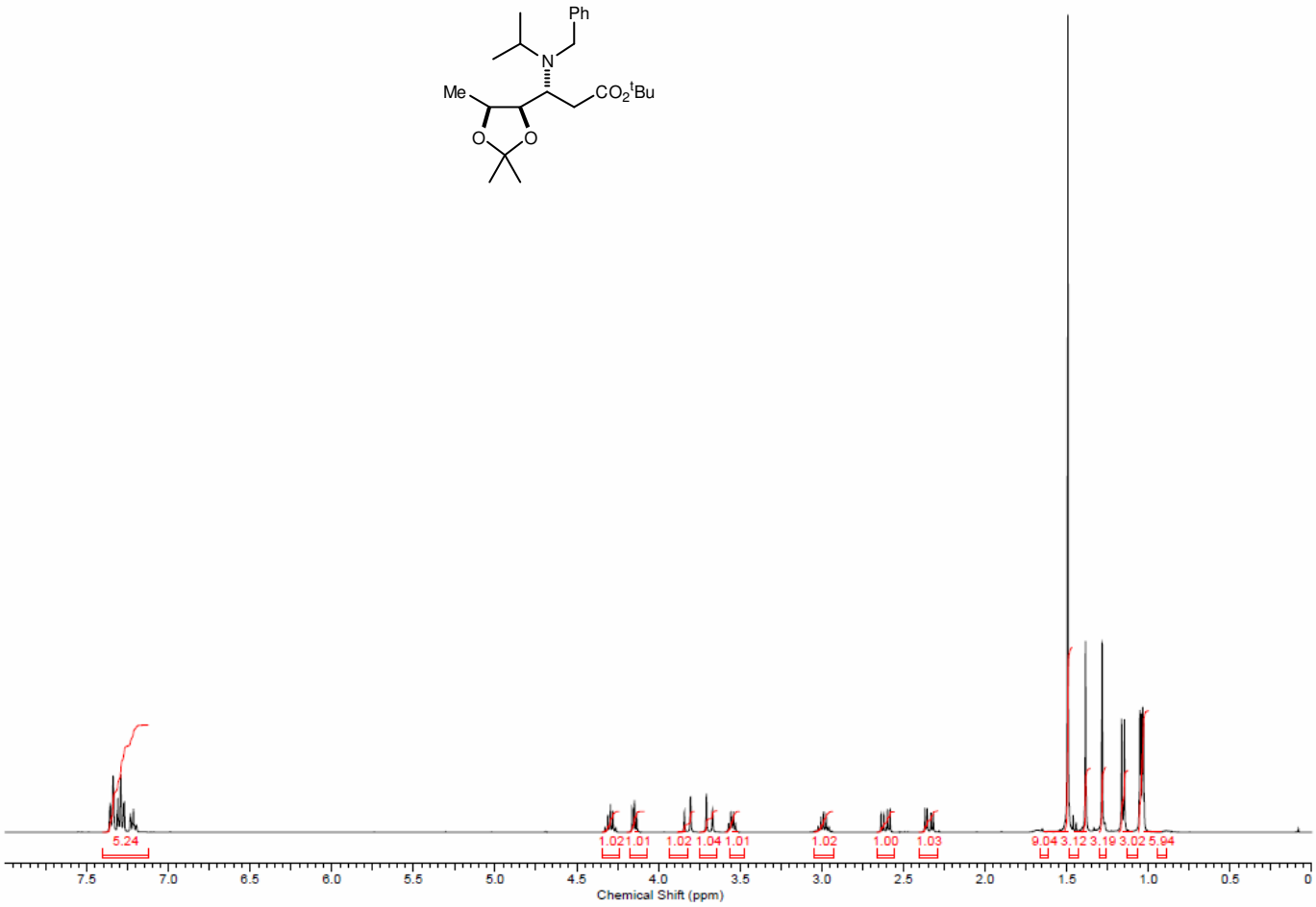
***tert*-Butyl (*S*,*S*,*Z*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-2-enoate (400 MHz ^{1}H, $CDCl_3$)**



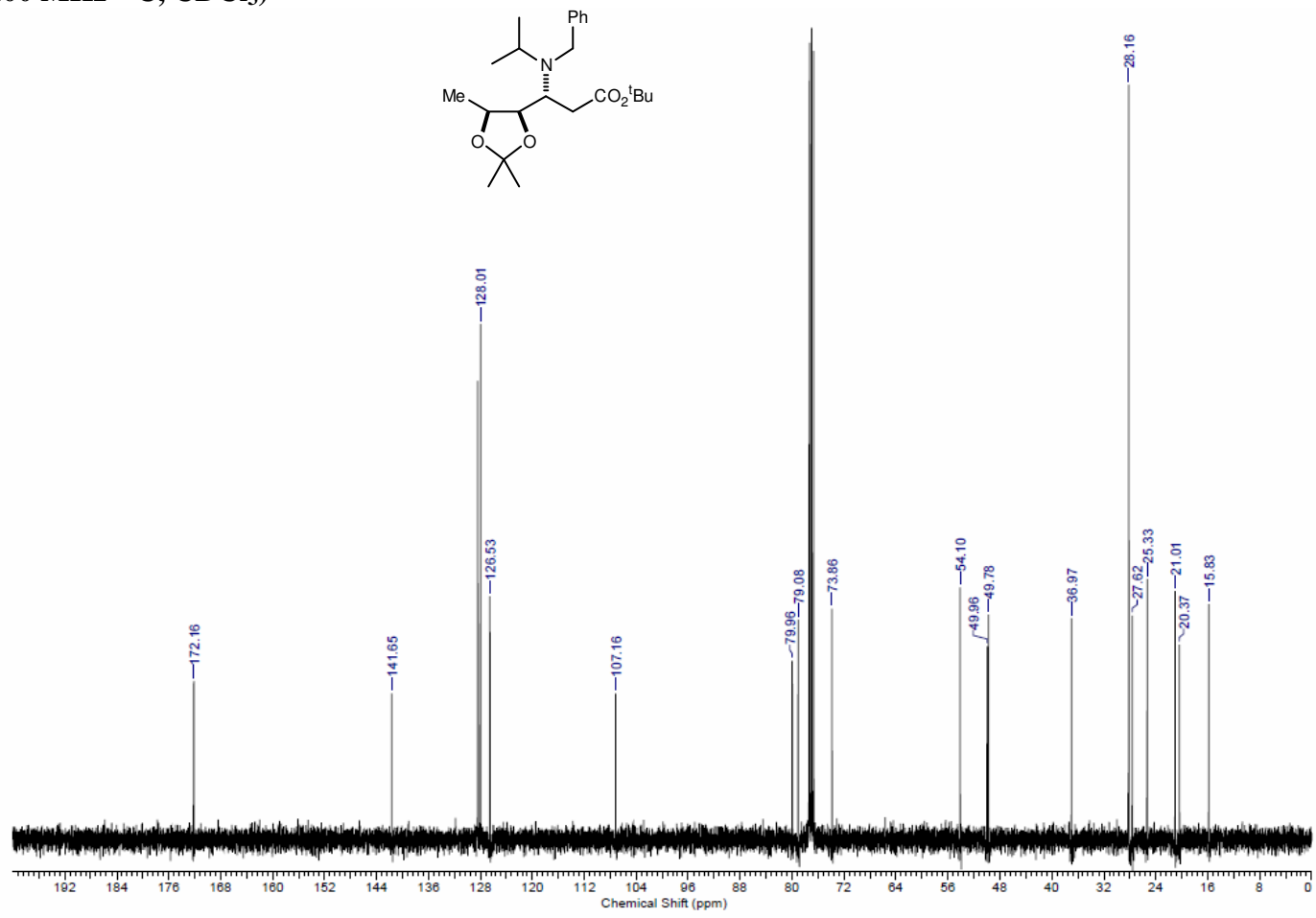
***tert*-Butyl (*S*,*S*,*Z*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-2-enoate (100 MHz ^{13}C, $CDCl_3$)**



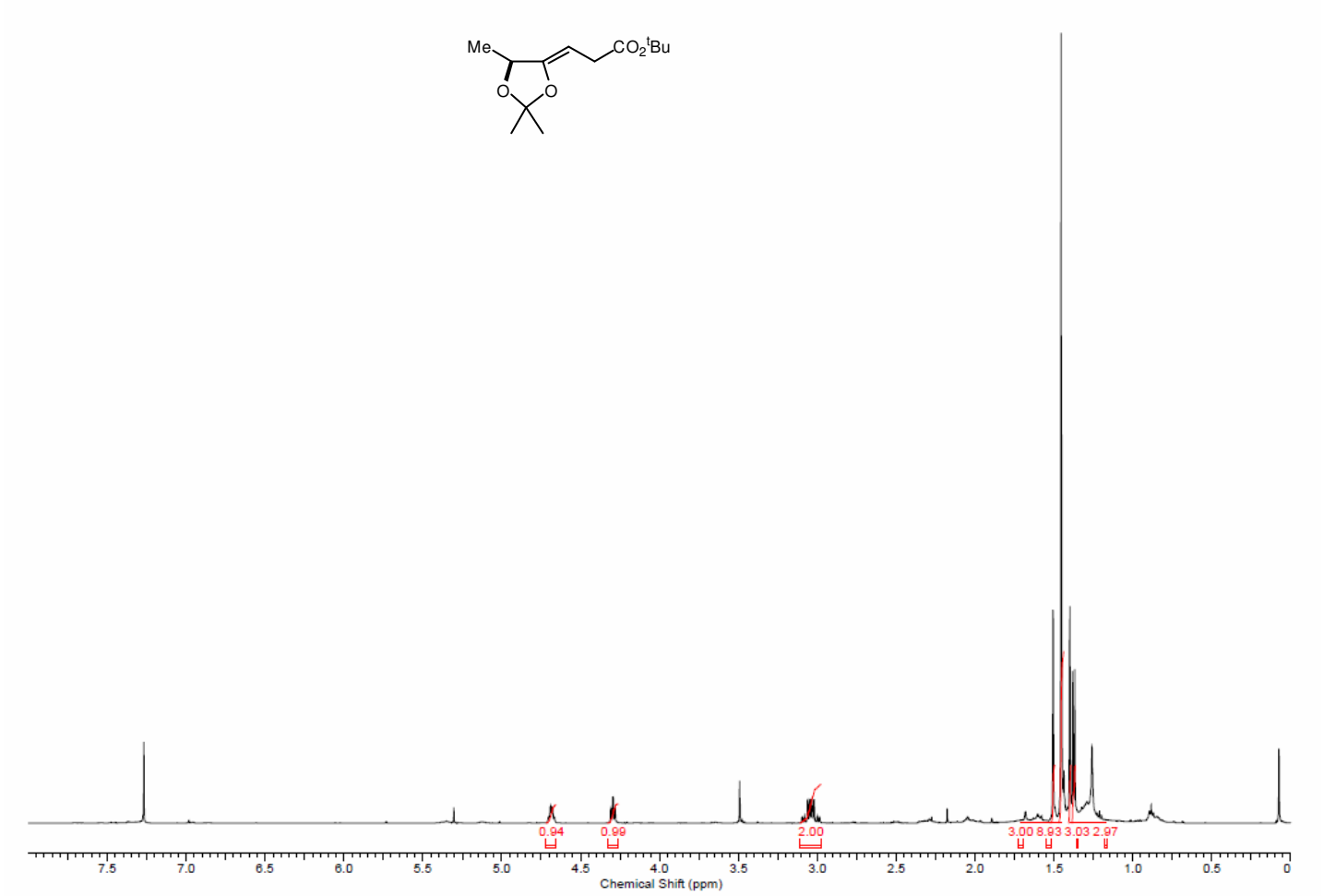
tert-Butyl (3_R_,4_R_,5_S_)-3-(_N_-benzyl-_N_-isopropylamino)-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 56 (400 MHz ^{1}H, $CDCl_3$)



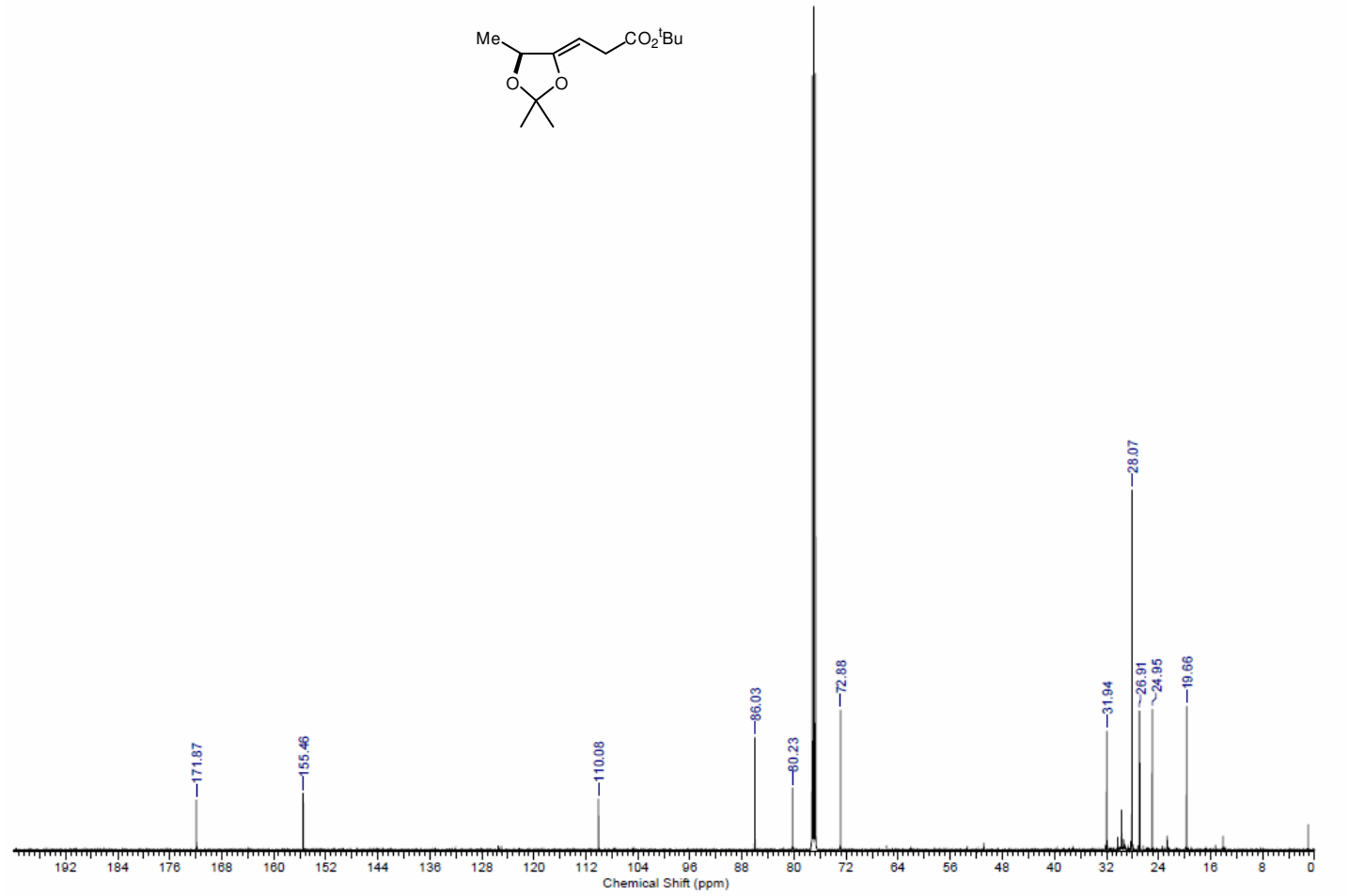
tert-Butyl (3_R_,4_R_,5_S_)-3-(_N_-benzyl-_N_-isopropylamino)-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 56 (100 MHz ^{13}C, $CDCl_3$)



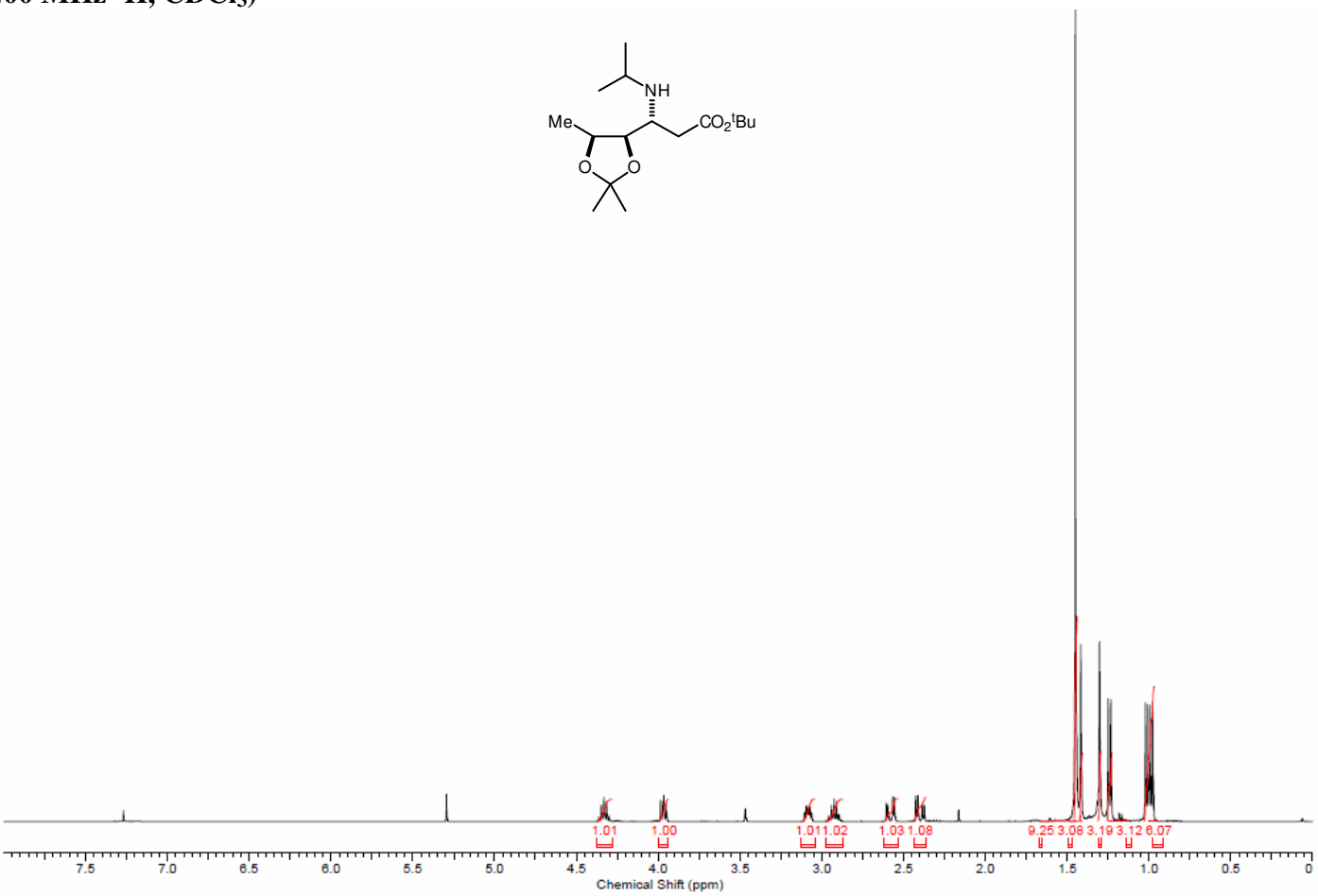
***tert*-Butyl (*S*,*Z*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-3-enoate 58 (500 MHz ^{1}H, $CDCl_3$)**



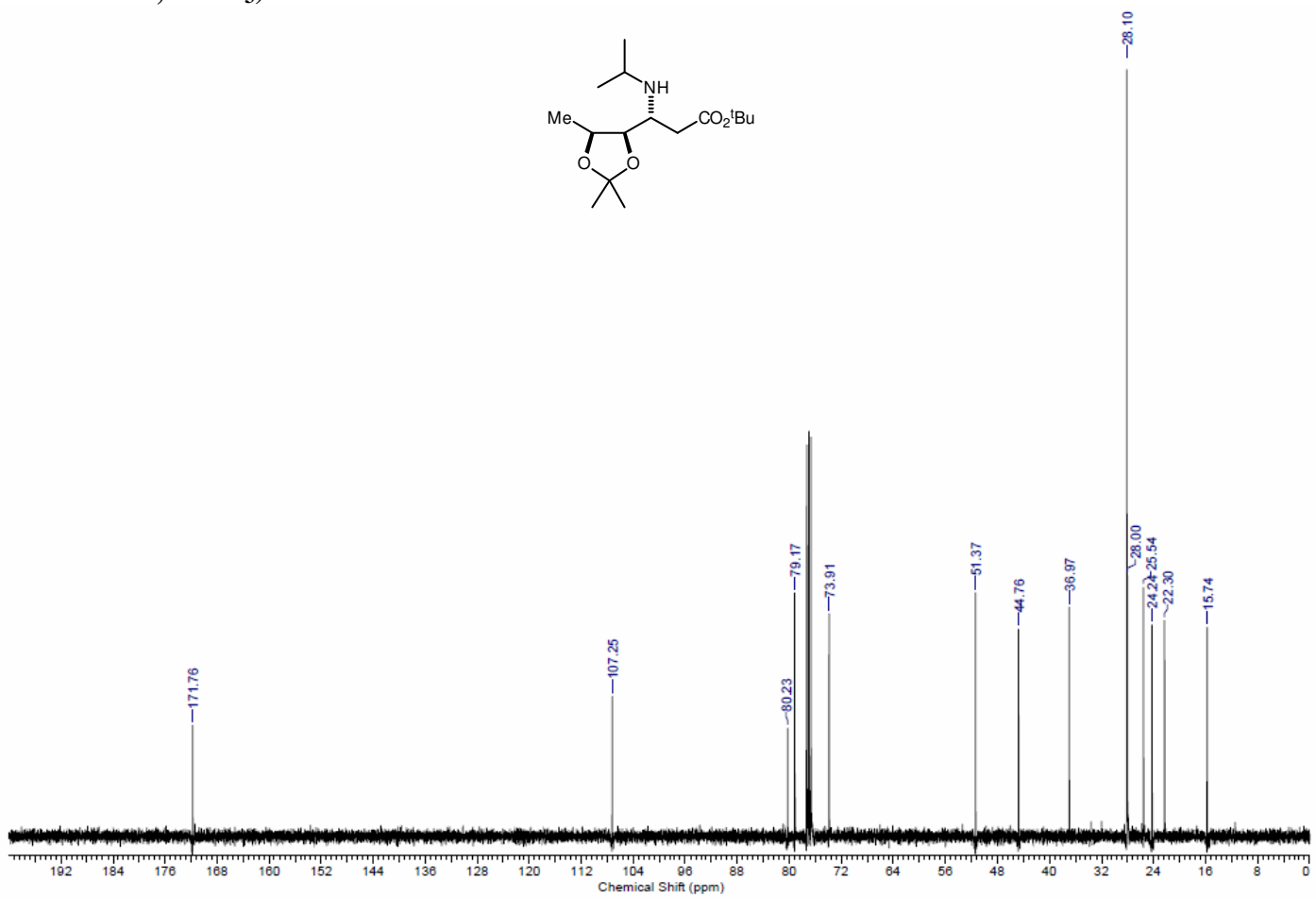
***tert*-Butyl (*S*,*Z*)-4,5-*O*-isopropylidene-4,5-dihydroxyhex-3-enoate 58 (125 MHz ^{13}C, $CDCl_3$)**



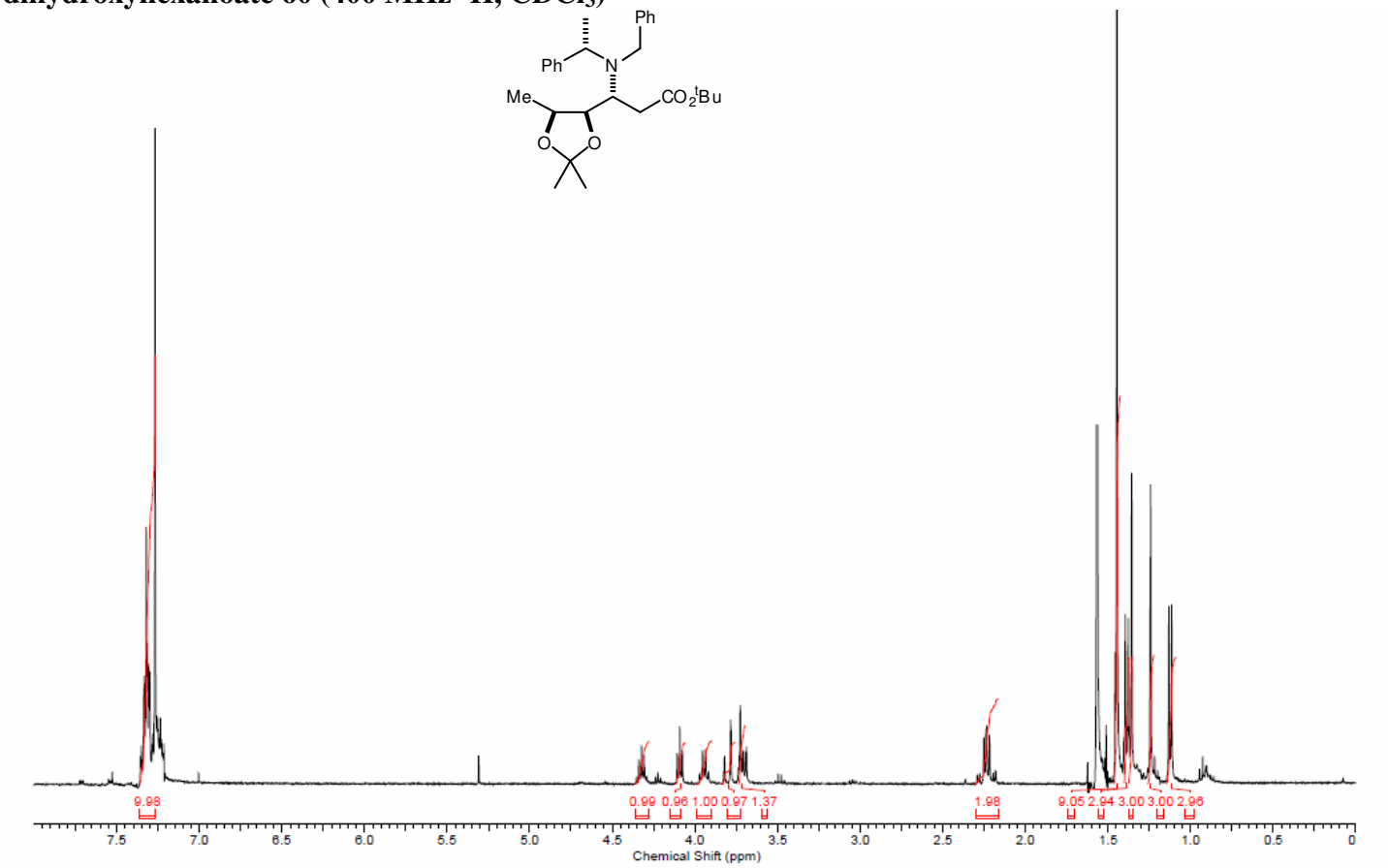
***tert*-Butyl (3*R*,4*R*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 59 (400 MHz ^{1}H, $CDCl_3$)**



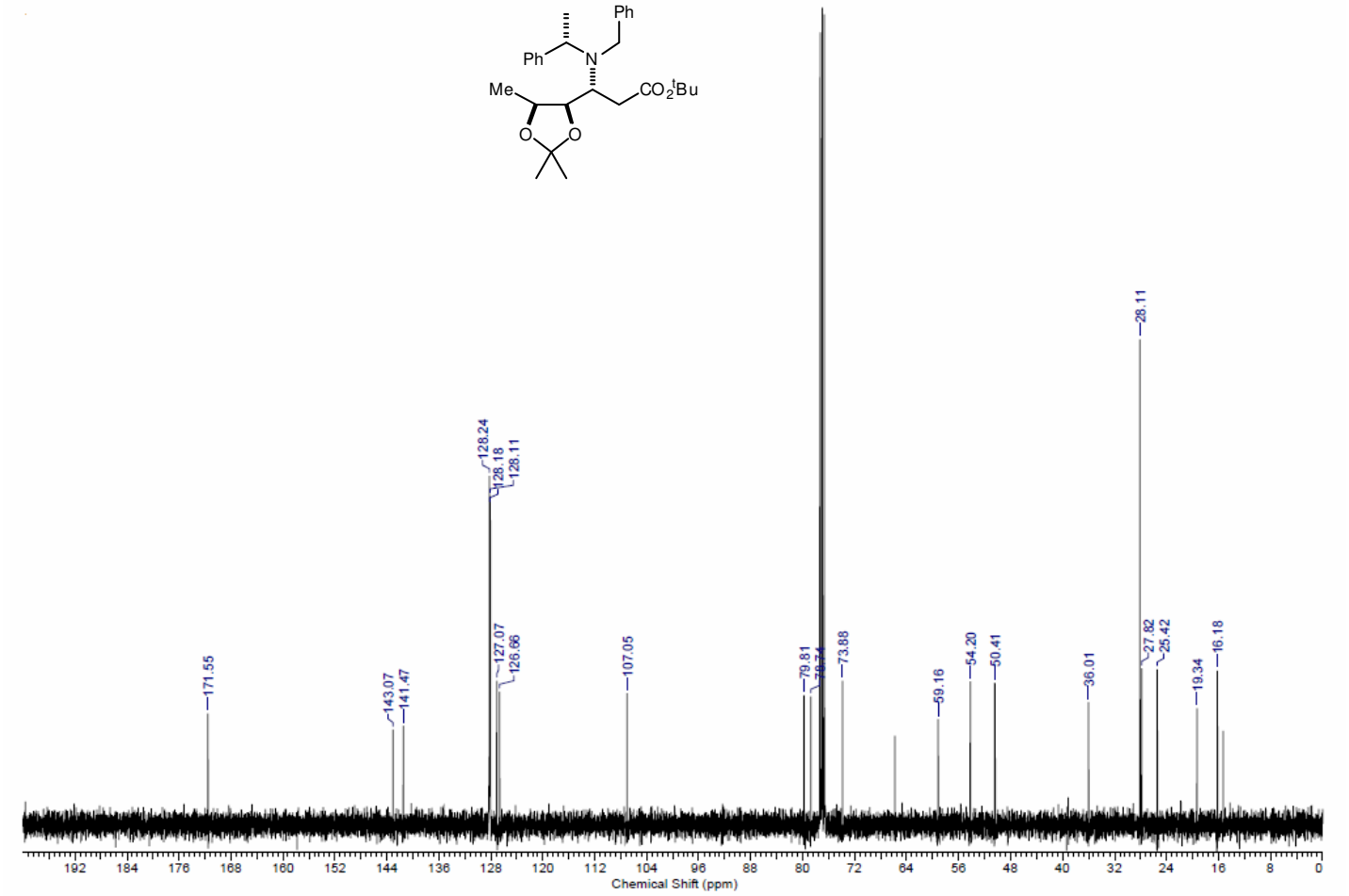
***tert*-Butyl (3*R*,4*R*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 59 (100 MHz ^{13}C, $CDCl_3$)**



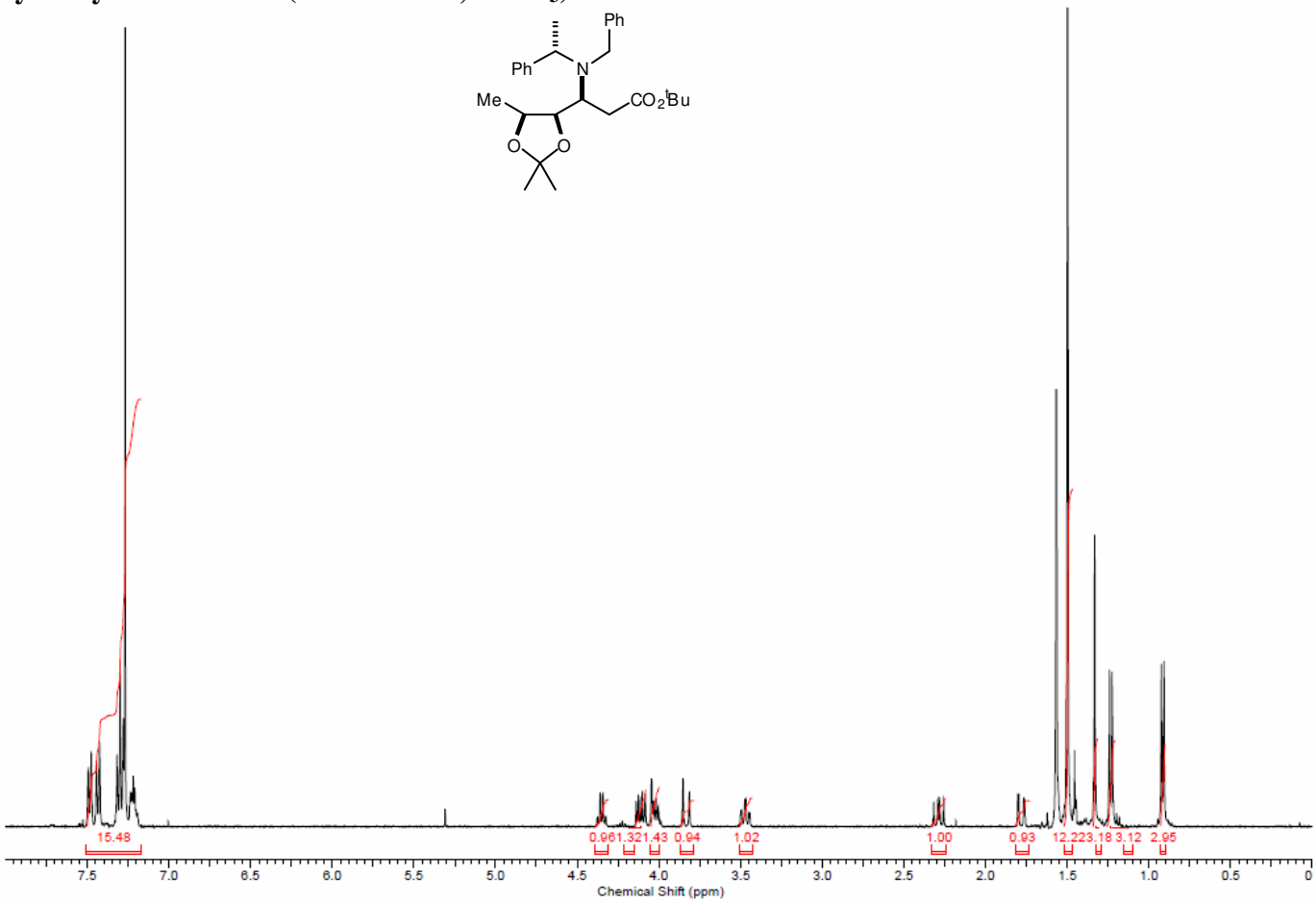
***tert*-Butyl (3*R*,4*R*,5*S*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 60 (400 MHz ^{1}H, $CDCl_3$)**



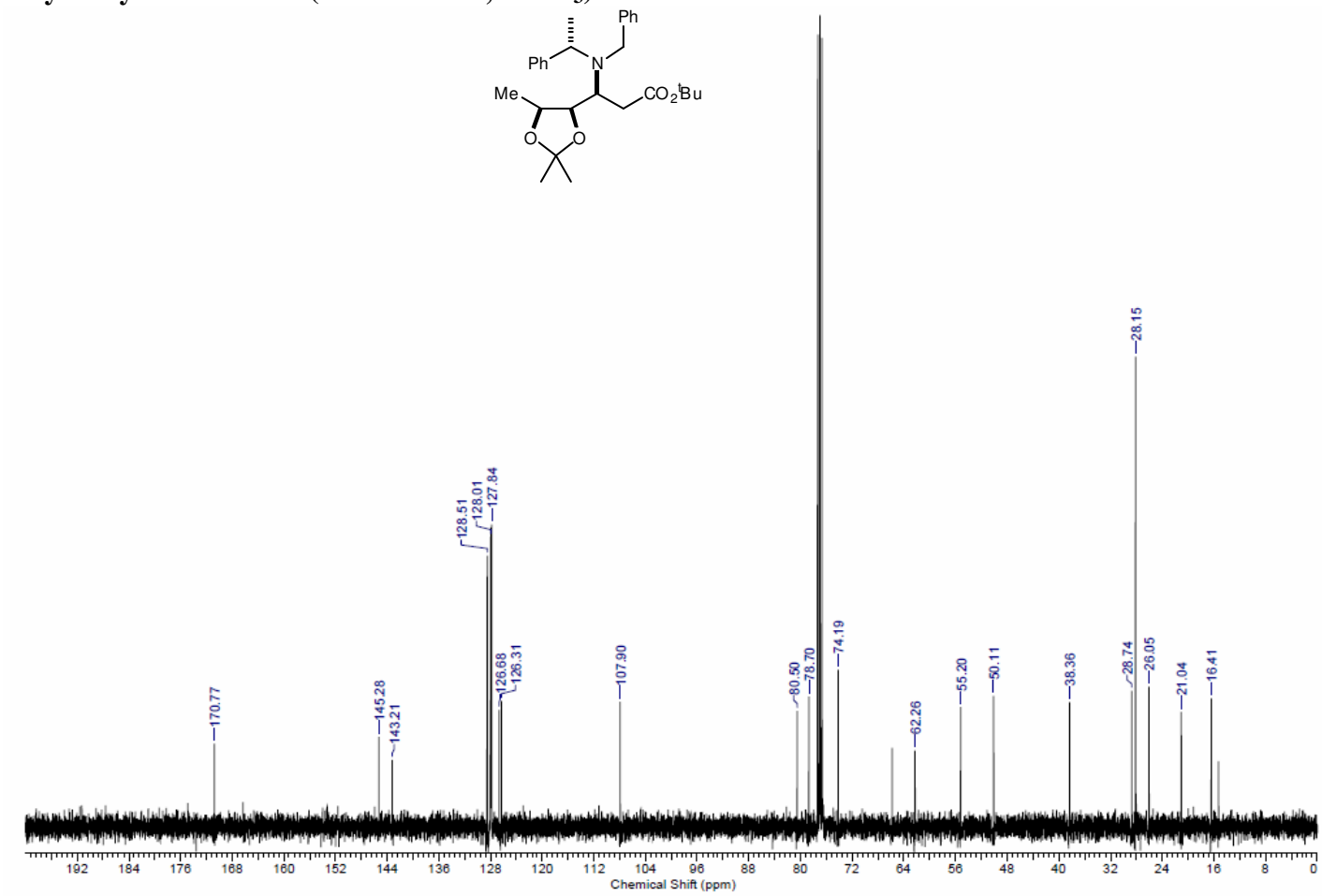
***tert*-Butyl (3*R*,4*R*,5*S*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 60 (100 MHz ^{13}C, $CDCl_3$)**



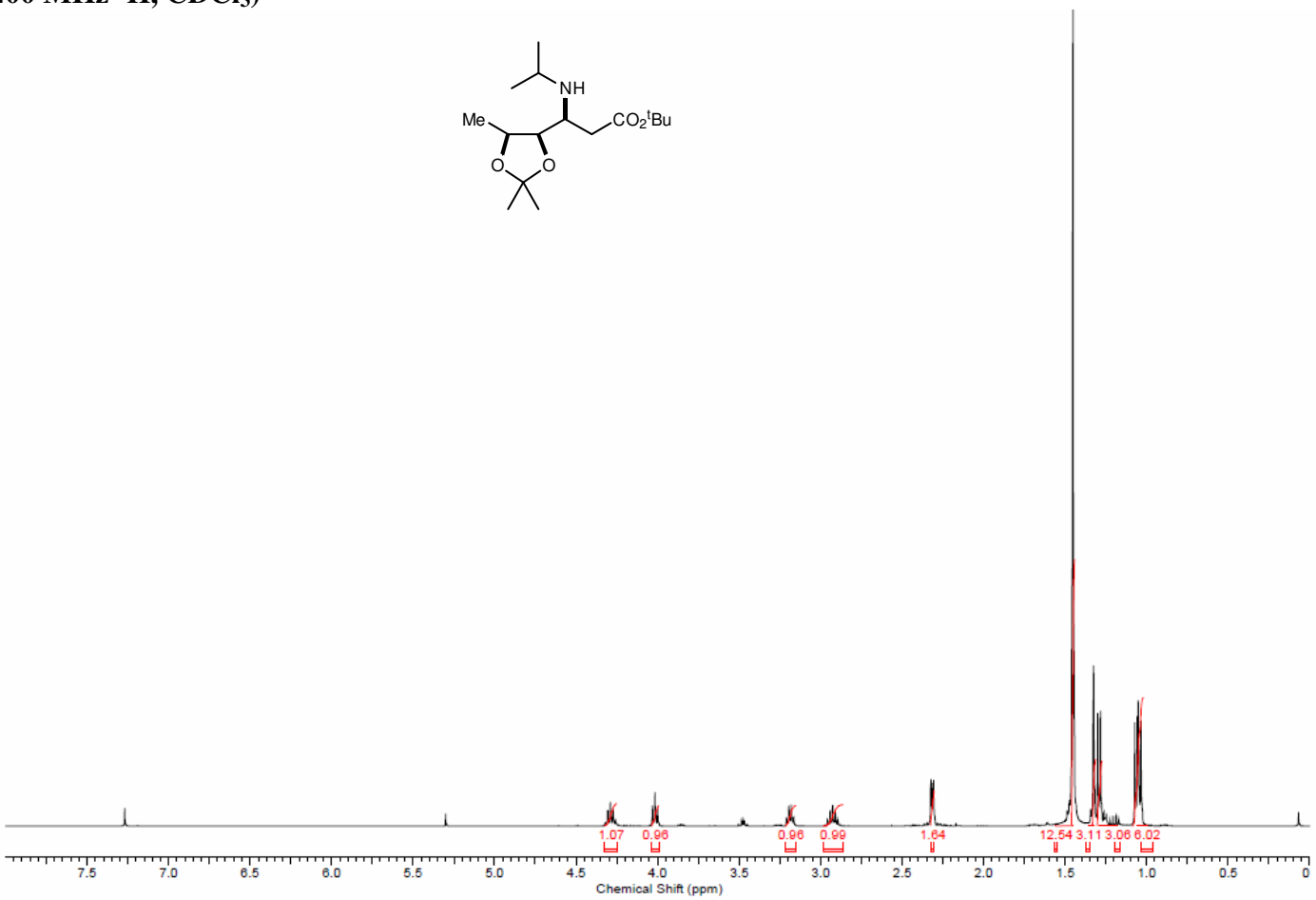
***tert*-Butyl (3*S*,4*R*,5*S*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 61 (400 MHz ^{1}H, $CDCl_3$)**



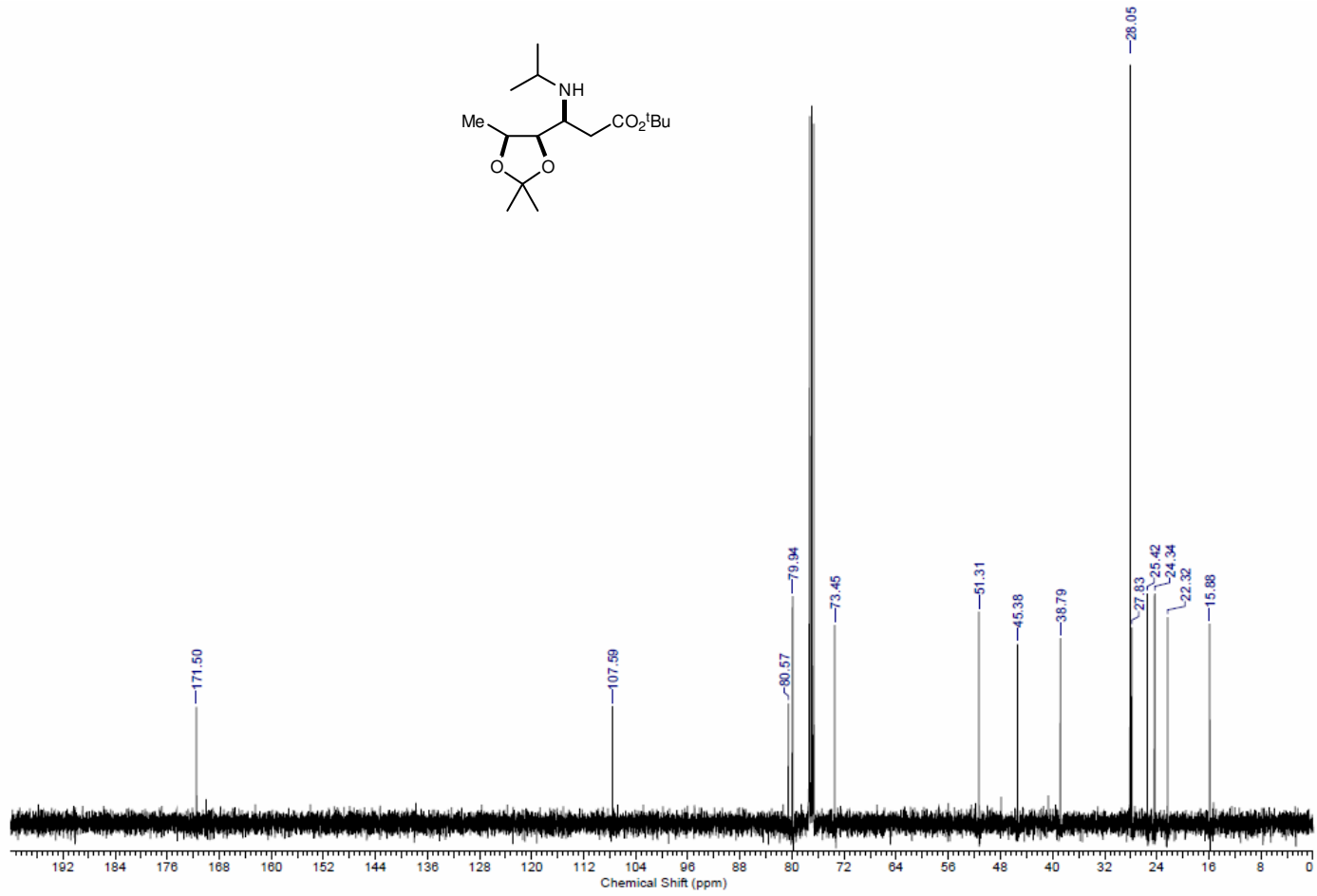
***tert*-Butyl (3*S*,4*R*,5*S*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 61 (100 MHz ^{13}C, $CDCl_3$)**



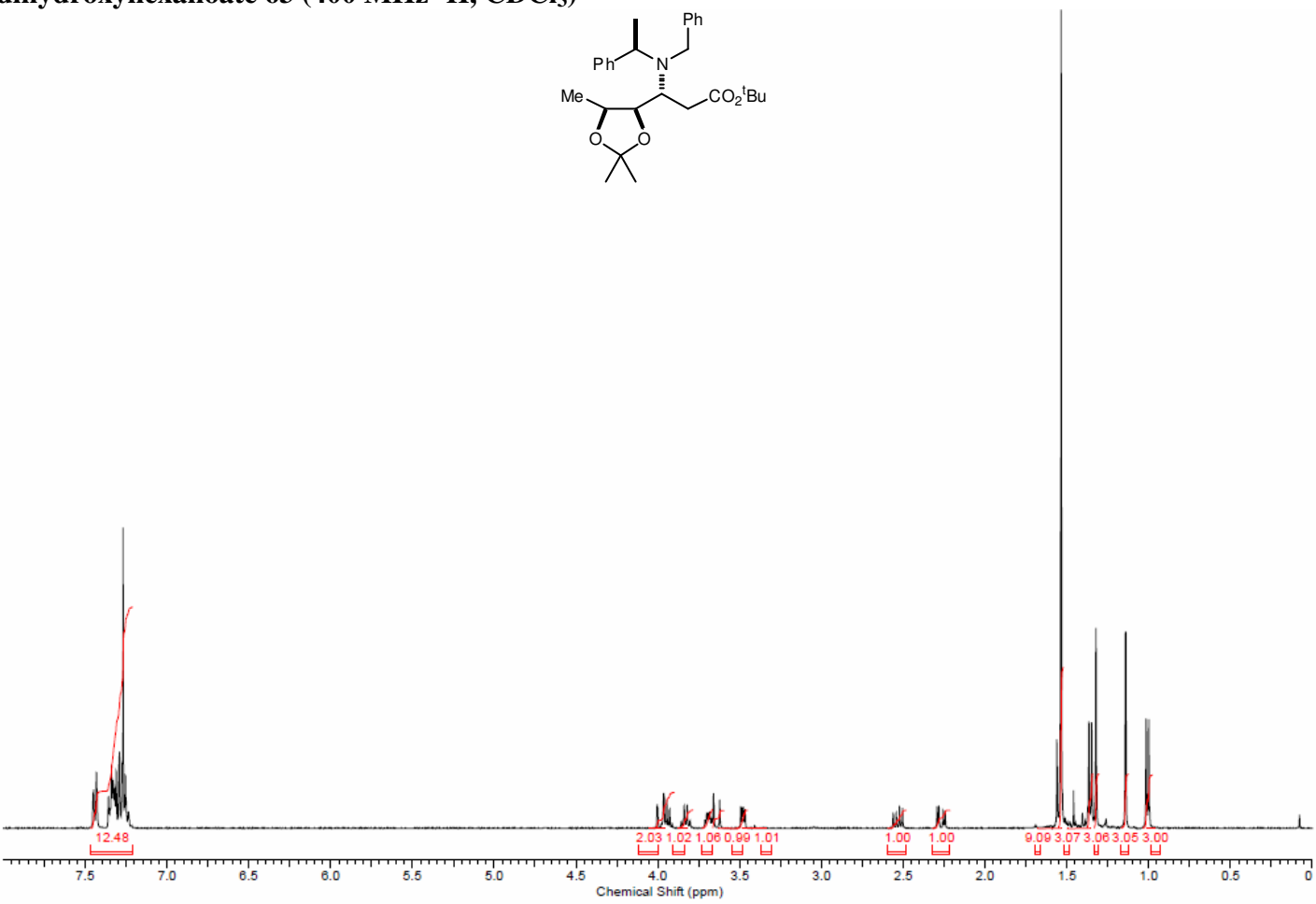
***tert*-Butyl (3*S*,4*R*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 62 (400 MHz ^{1}H, $CDCl_3$)**



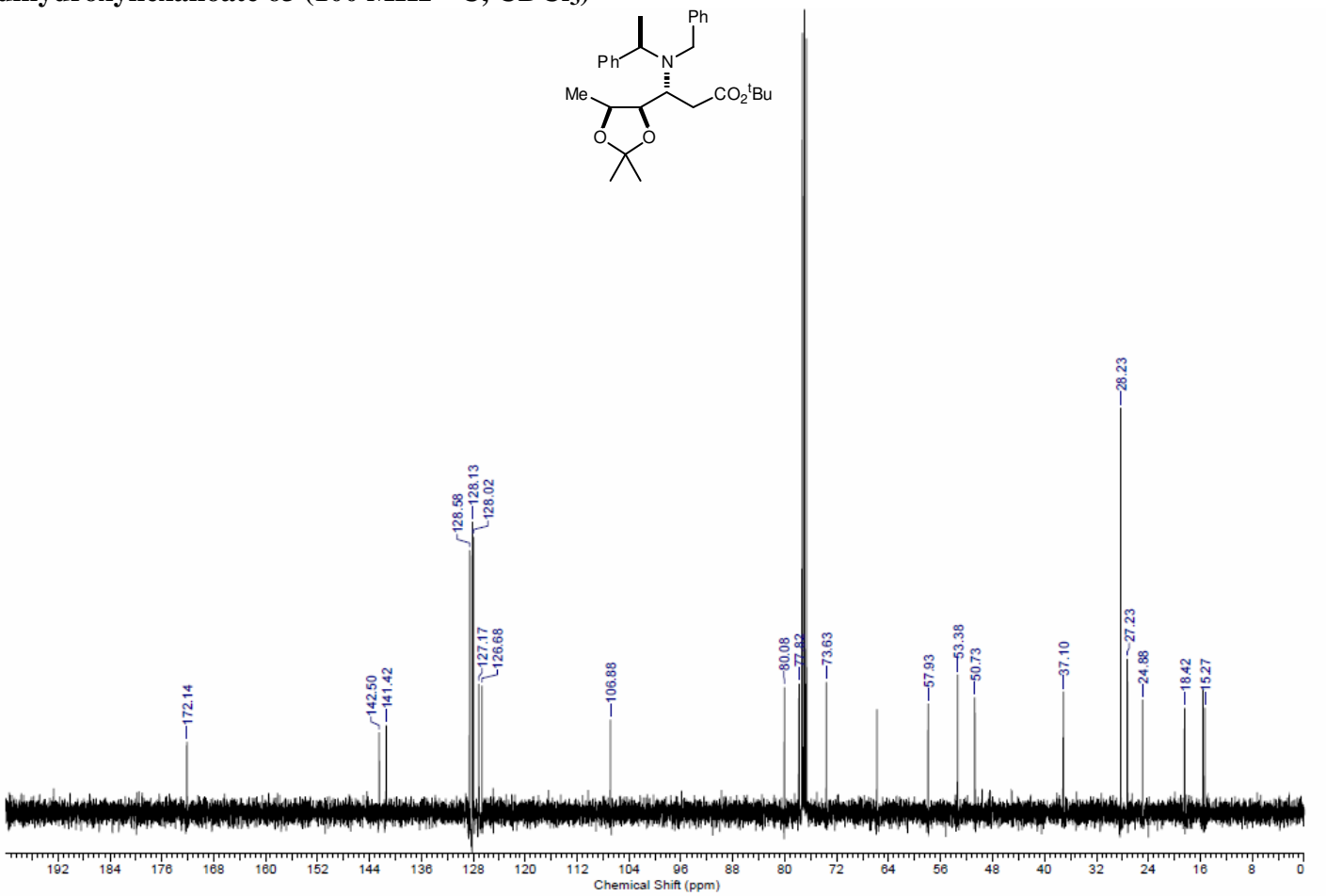
***tert*-Butyl (3*S*,4*R*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 62 (100 MHz ^{13}C, $CDCl_3$)**



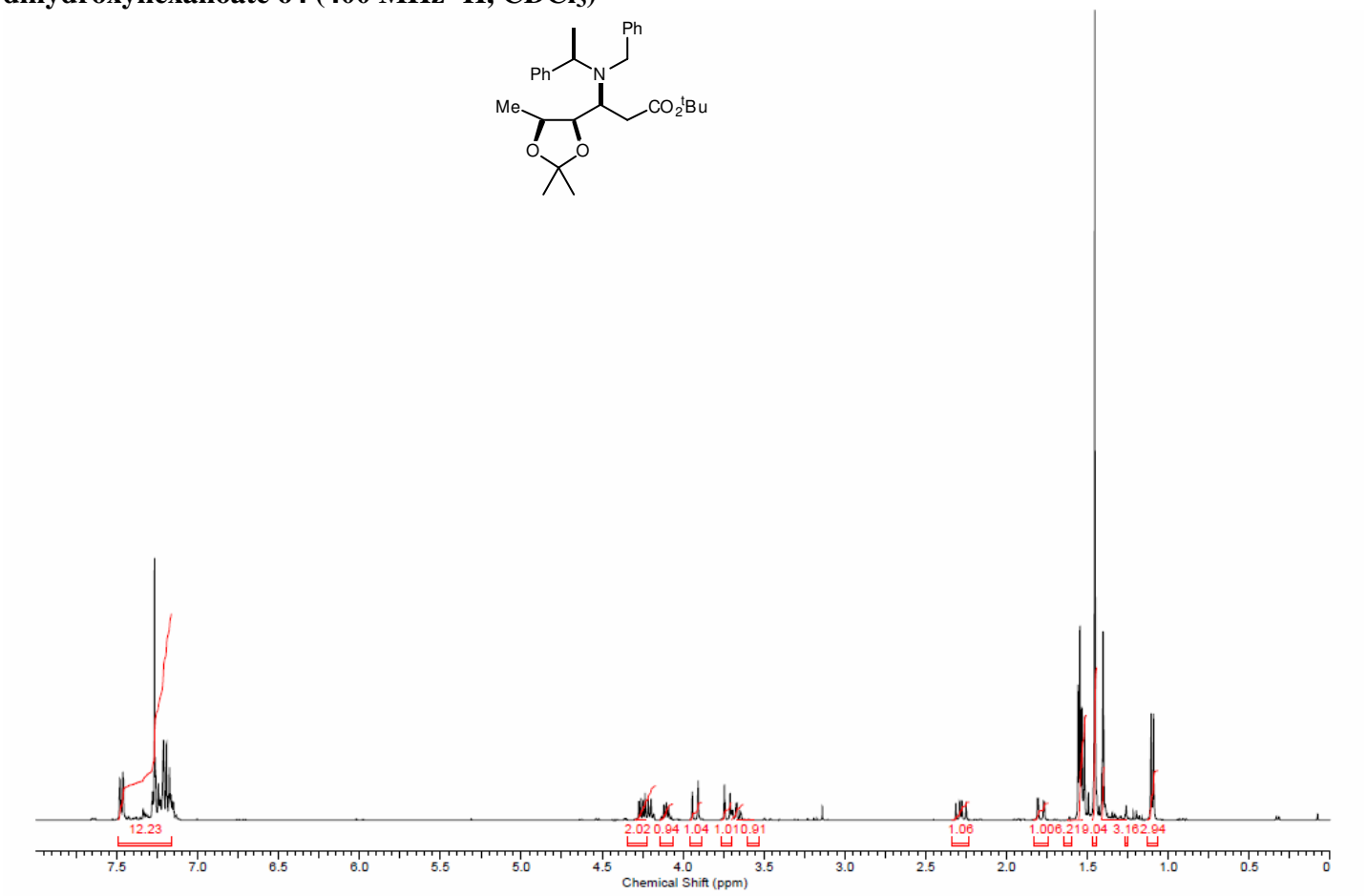
tert-Butyl (3_R_,4_R_,5_S_,α_R_)-3-[_N_-benzyl-_N_-(α-methylbenzyl)amino]-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 63 (400 MHz ^{1}H, $CDCl_3$)



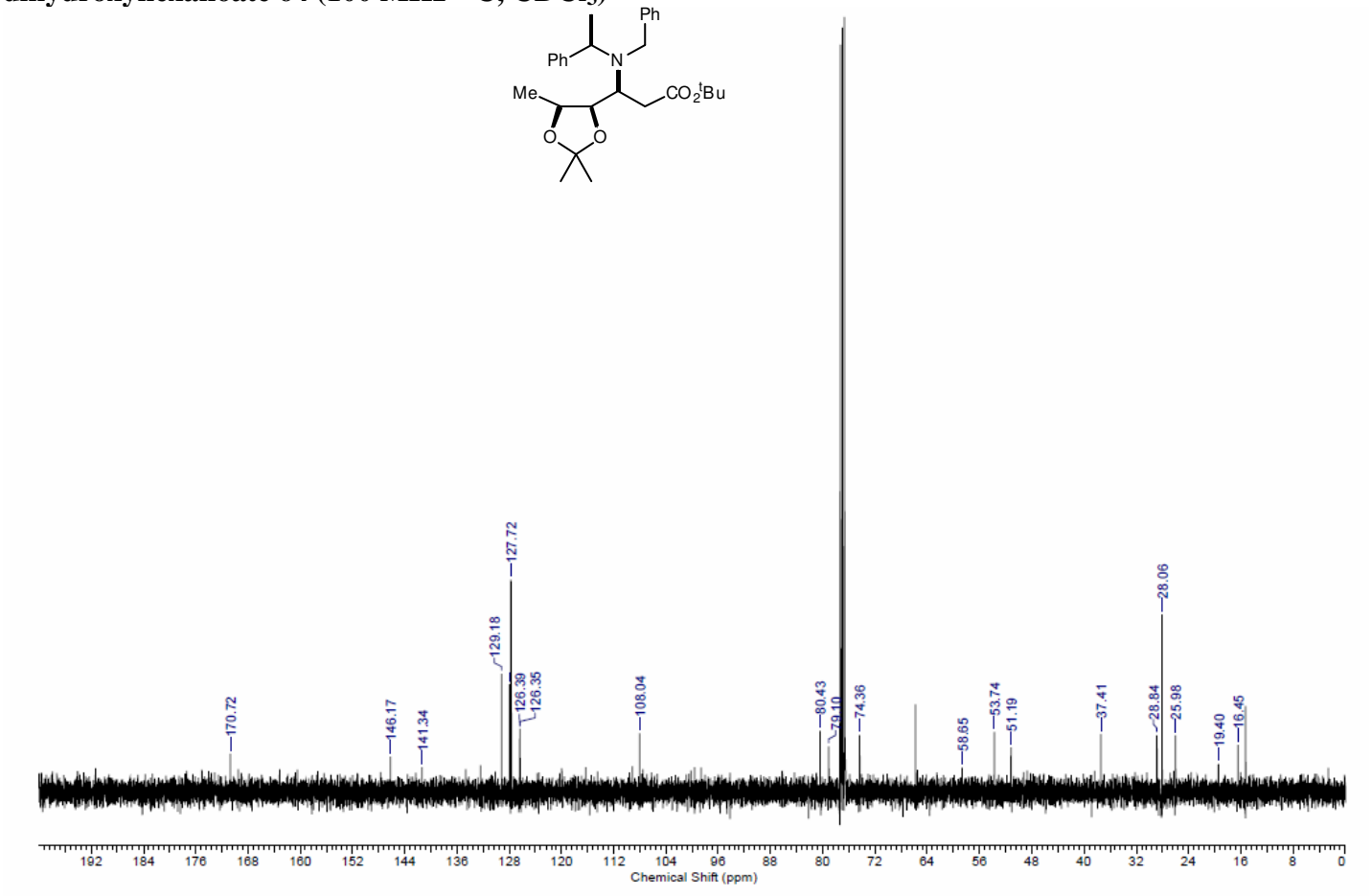
tert-Butyl (3_R_,4_R_,5_S_,α_R_)-3-[_N_-benzyl-_N_-(α-methylbenzyl)amino]-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 63 (100 MHz ^{13}C, $CDCl_3$)



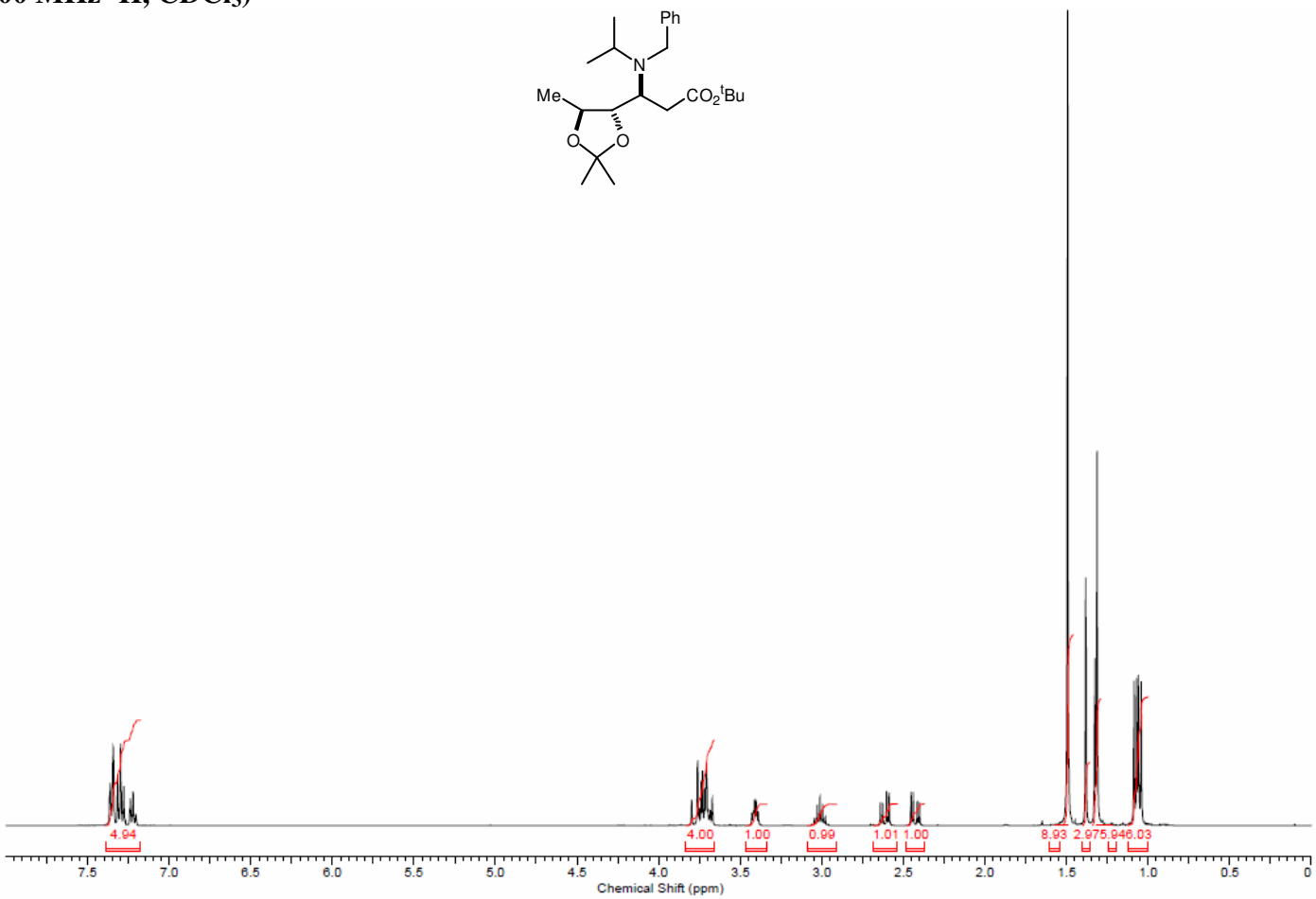
***tert*-Butyl (3*S*,4*R*,5*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 64 (400 MHz ^{1}H, $CDCl_3$)**



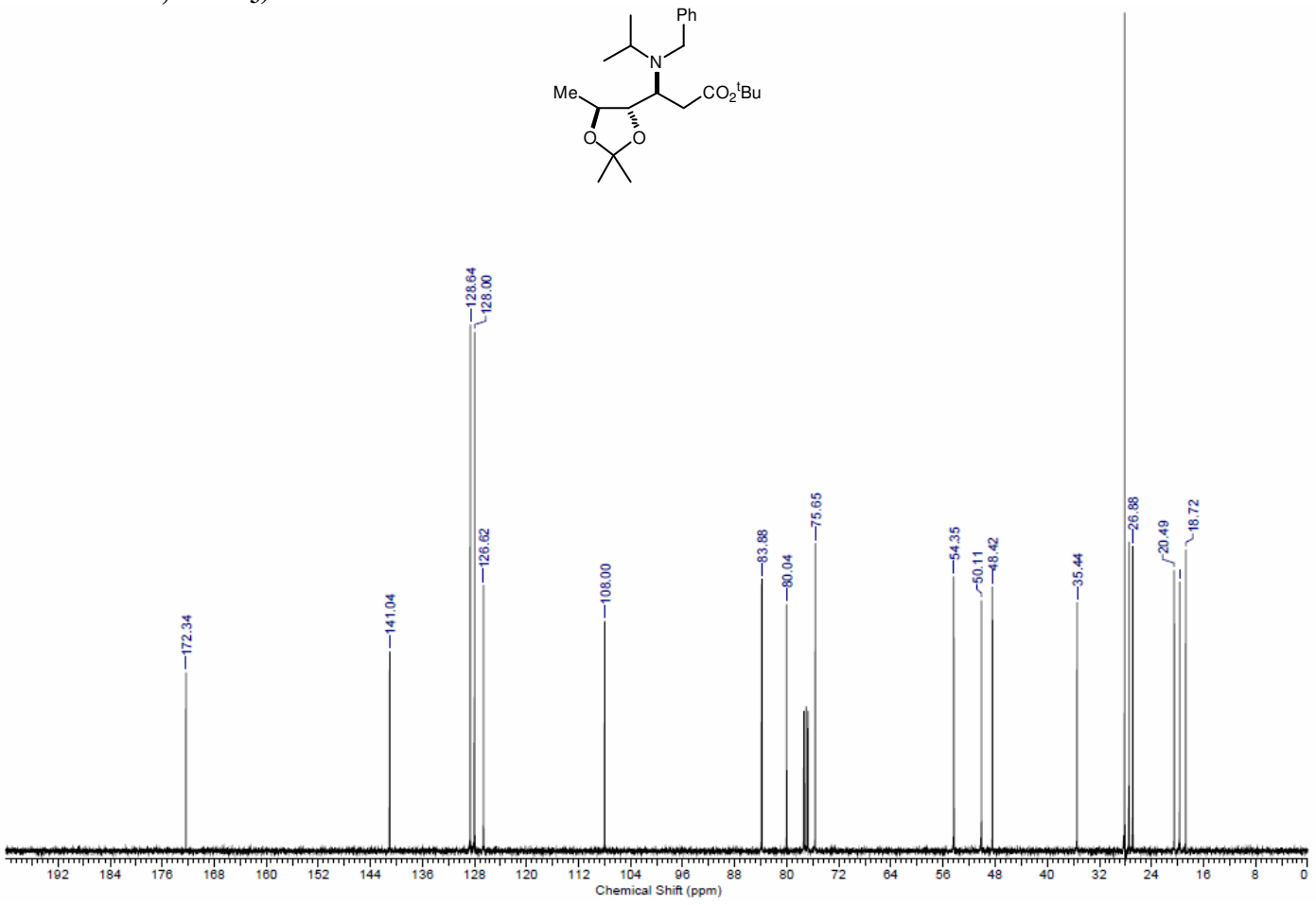
***tert*-Butyl (3*S*,4*R*,5*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 64 (100 MHz ^{13}C, $CDCl_3$)**



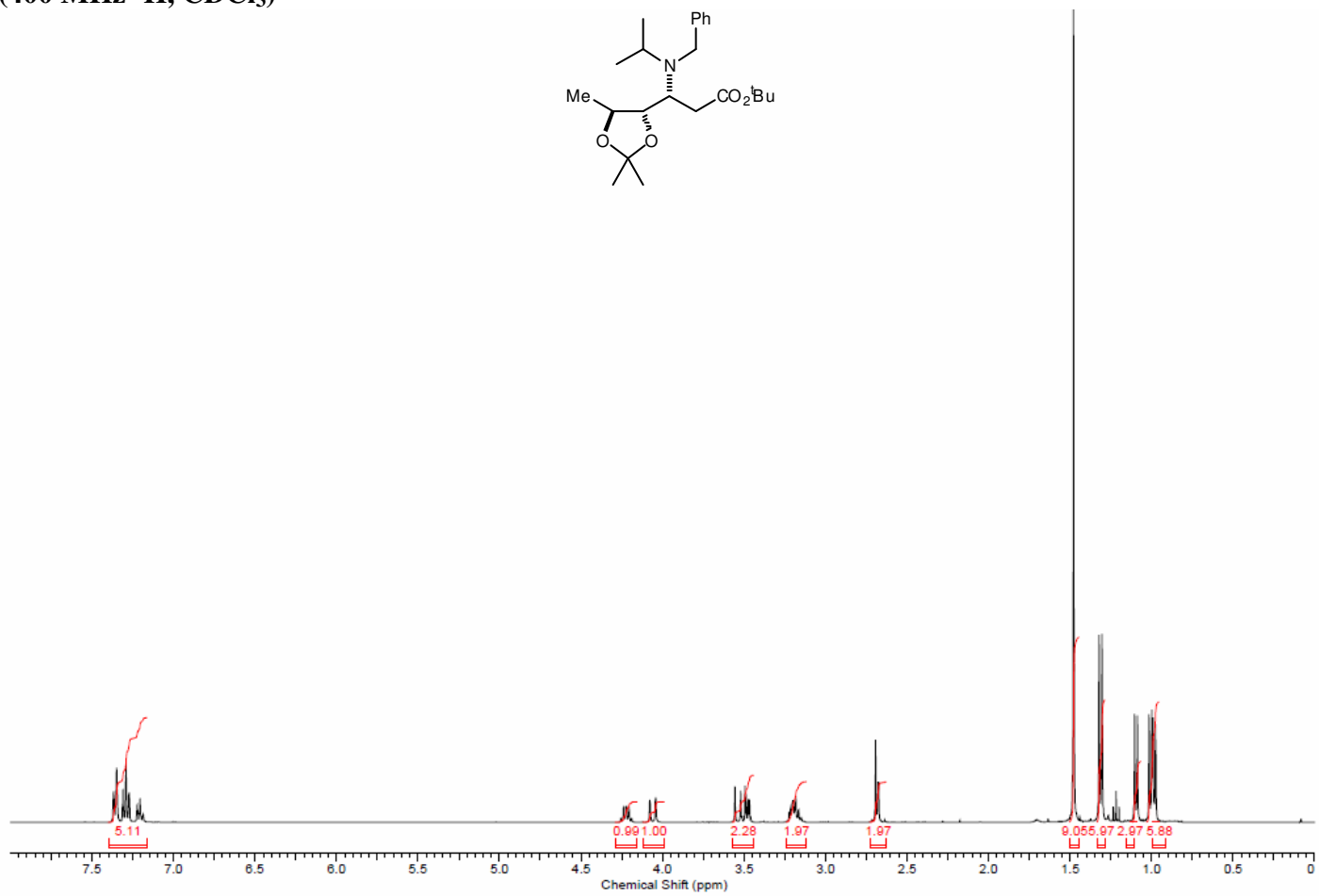
***tert*-Butyl (*S*,*S*,*S*)-3-(*N*-benzyl-*N*-isopropylamino)-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 65 (400 MHz ^{1}H, $CDCl_3$)**



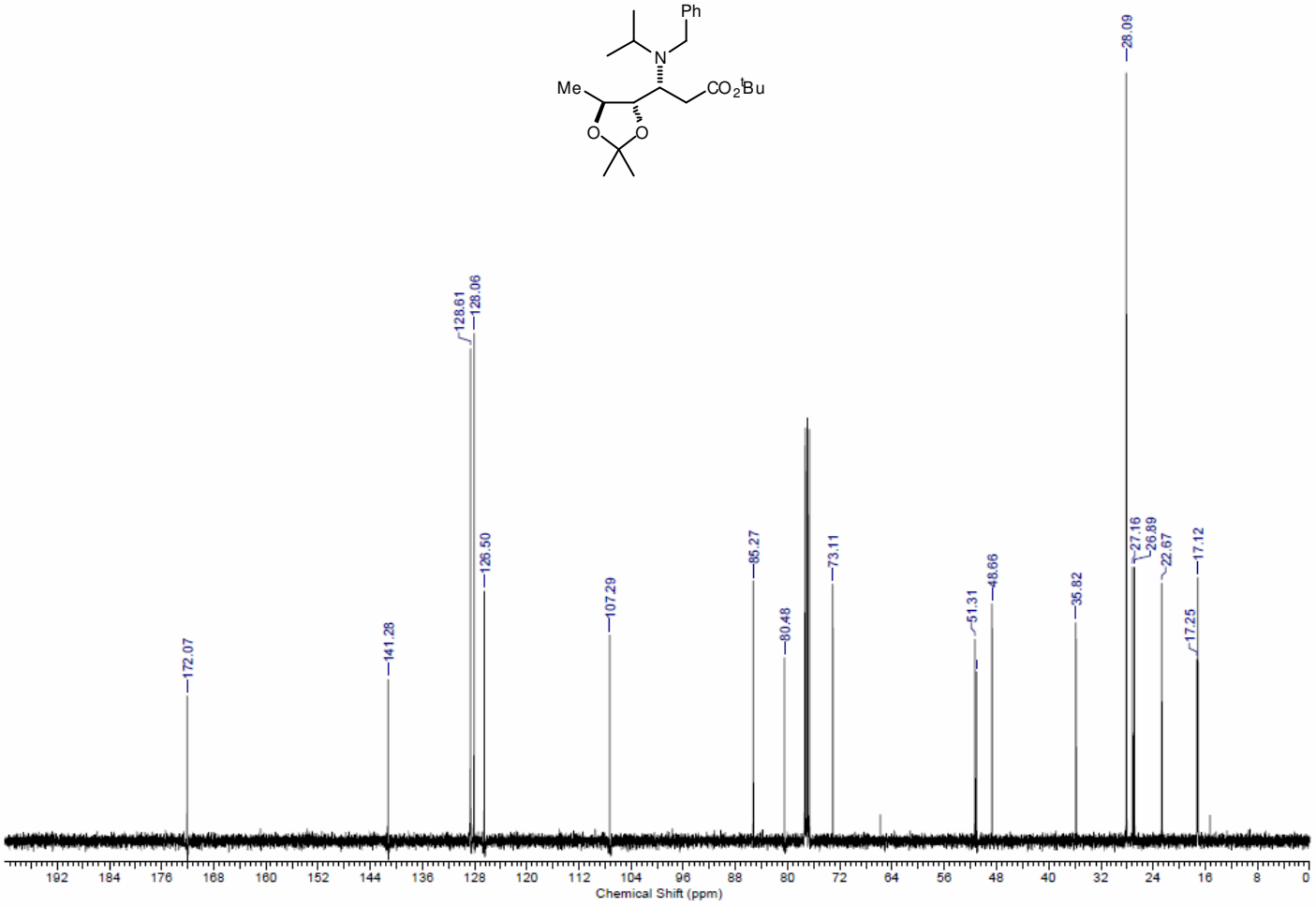
***tert*-Butyl (*S*,*S*,*S*)-3-(*N*-benzyl-*N*-isopropylamino)-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 65 (100 MHz ^{13}C, $CDCl_3$)**



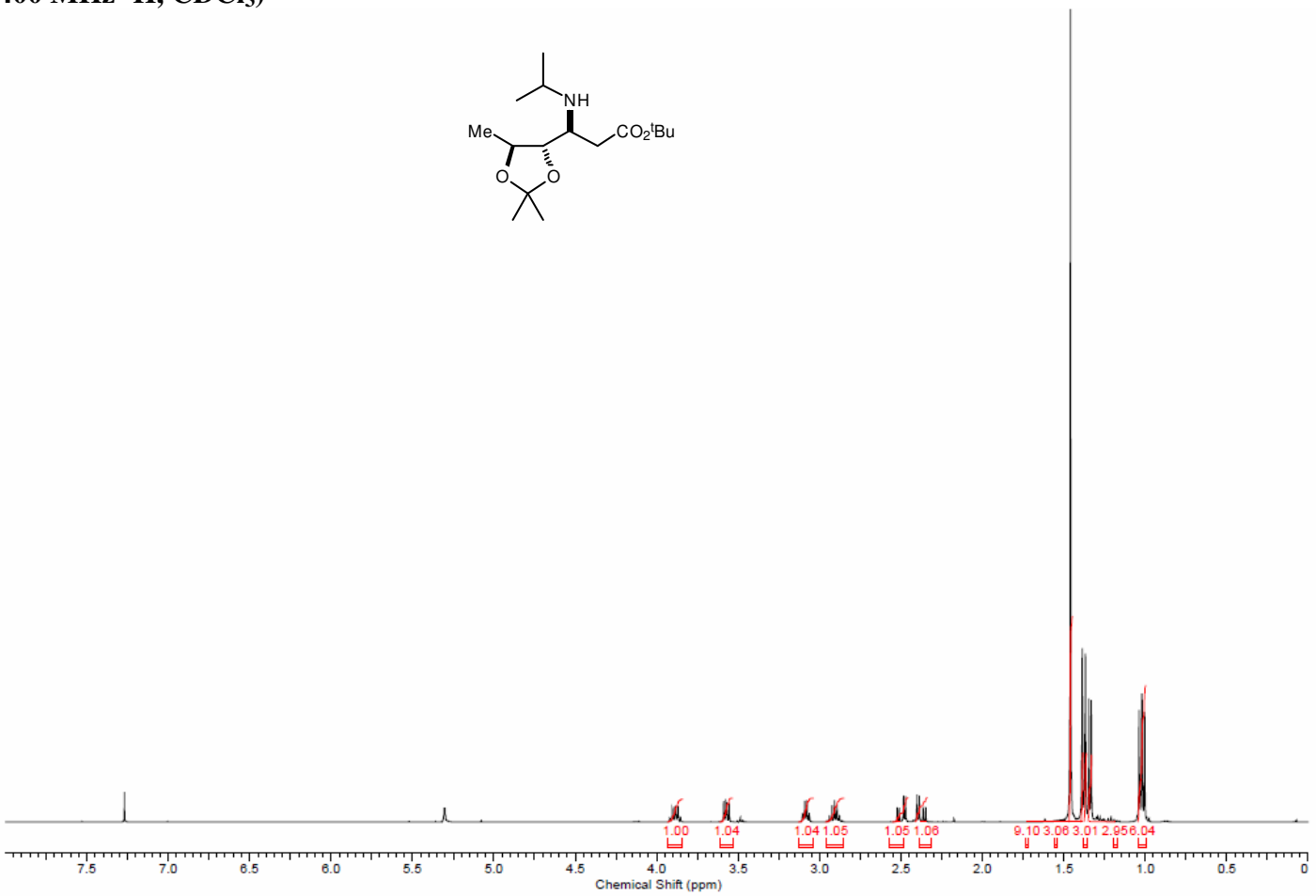
tert-Butyl (3_R_,4_S_,5_S_)-3-(_N_-benzyl-_N_-isopropylamino)-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 66 (400 MHz ^{1}H, $CDCl_3$)



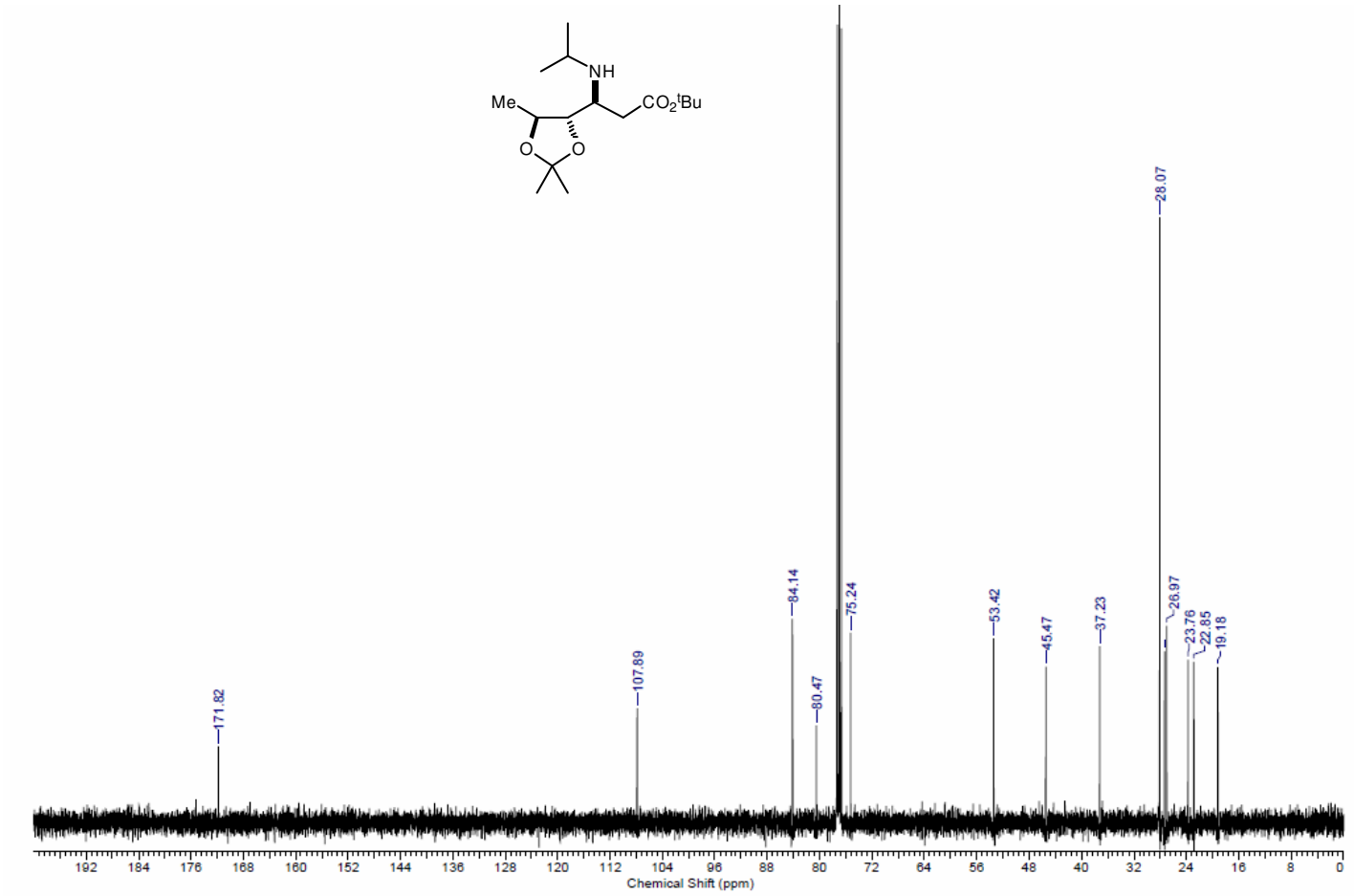
tert-Butyl (3_R_,4_S_,5_S_)-3-(_N_-benzyl-_N_-isopropylamino)-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 66 (100 MHz ^{13}C, $CDCl_3$)



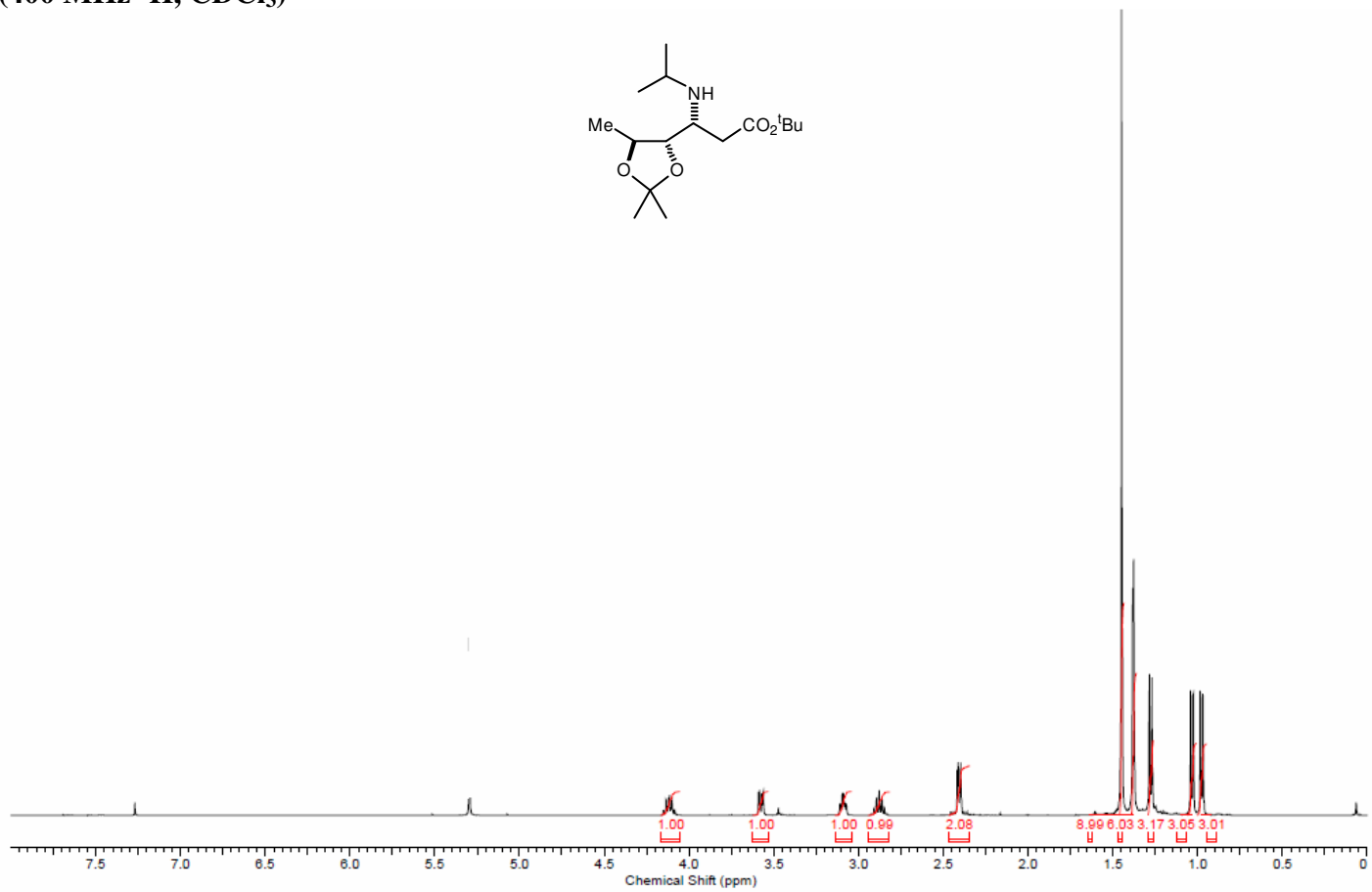
***tert*-Butyl (*S*,*S*,*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 67 (400 MHz ^{1}H, $CDCl_3$)**



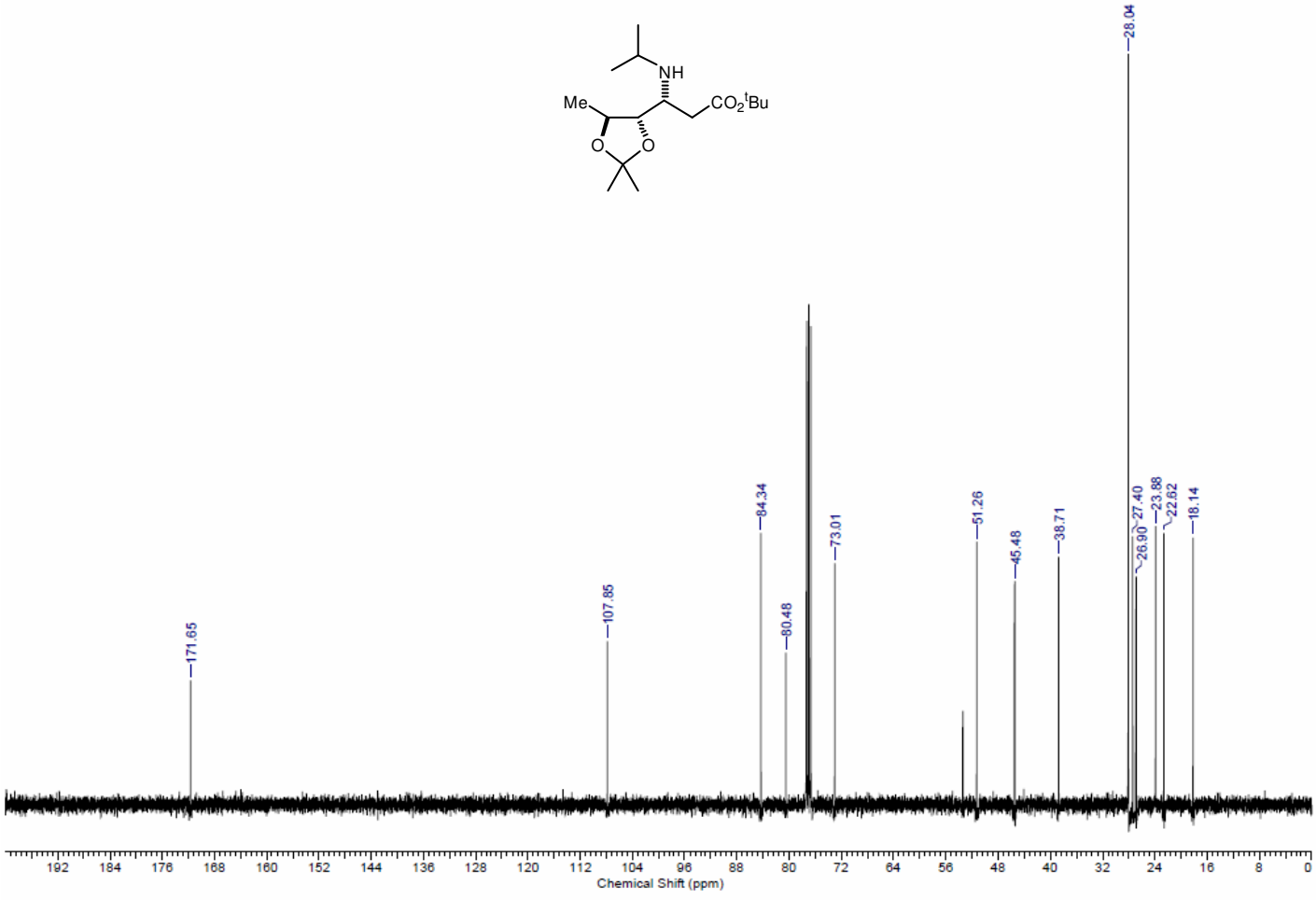
***tert*-Butyl (*S*,*S*,*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 67 (100 MHz ^{13}C, $CDCl_3$)**



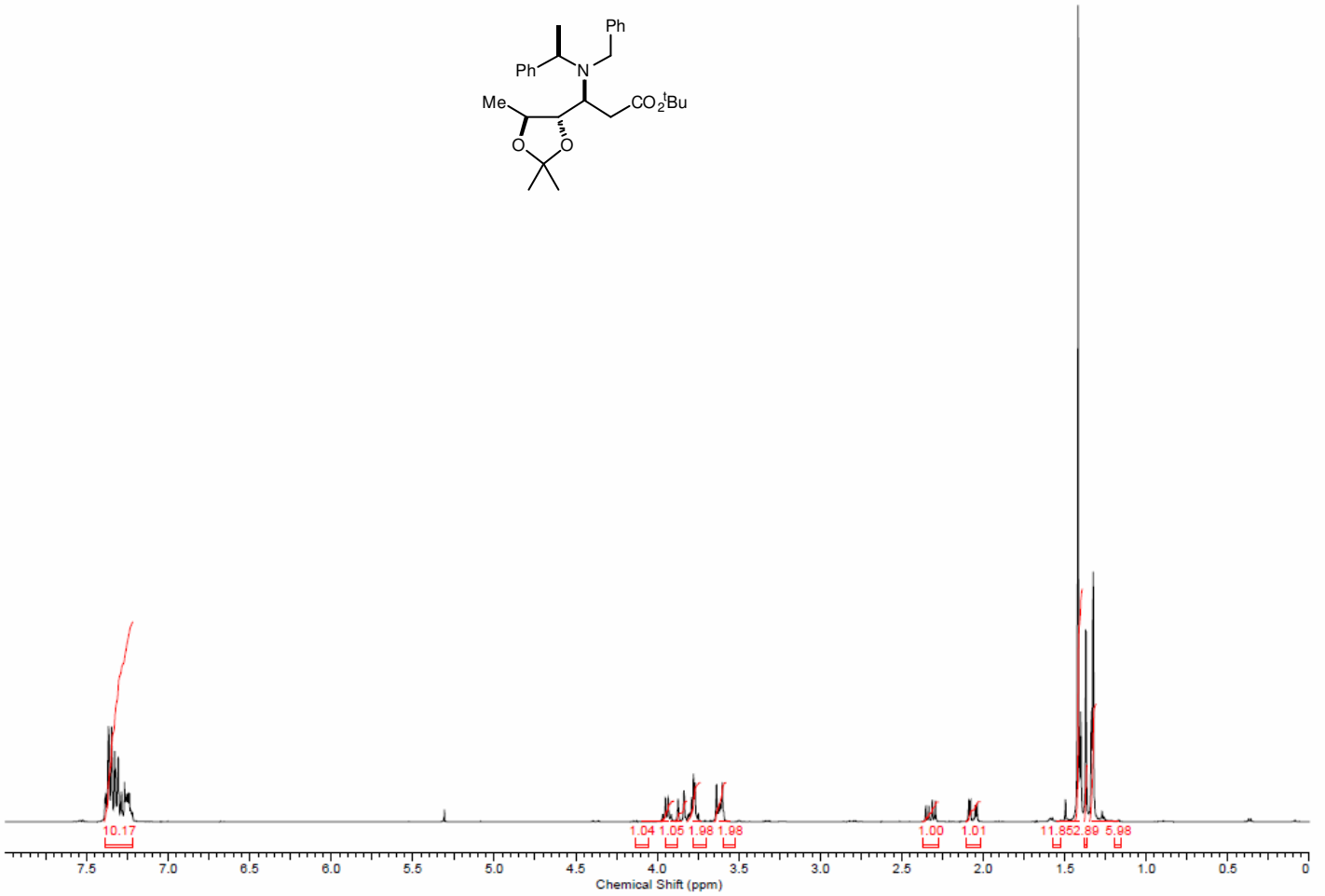
***tert*-Butyl (3*R*,4*S*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 68 (400 MHz ^{1}H, $CDCl_3$)**



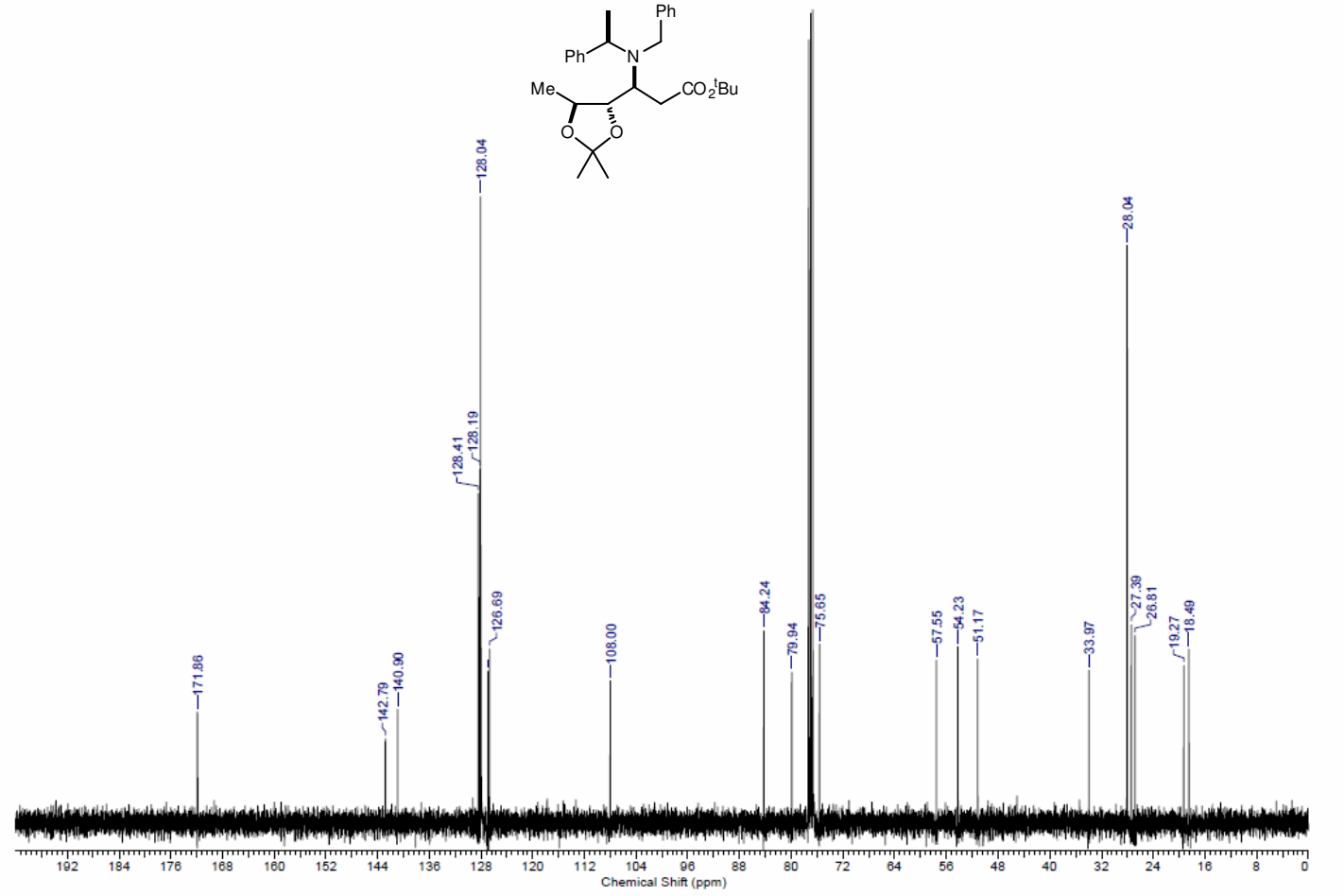
***tert*-Butyl (3*R*,4*S*,5*S*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 68 (100 MHz ^{13}C, $CDCl_3$)**



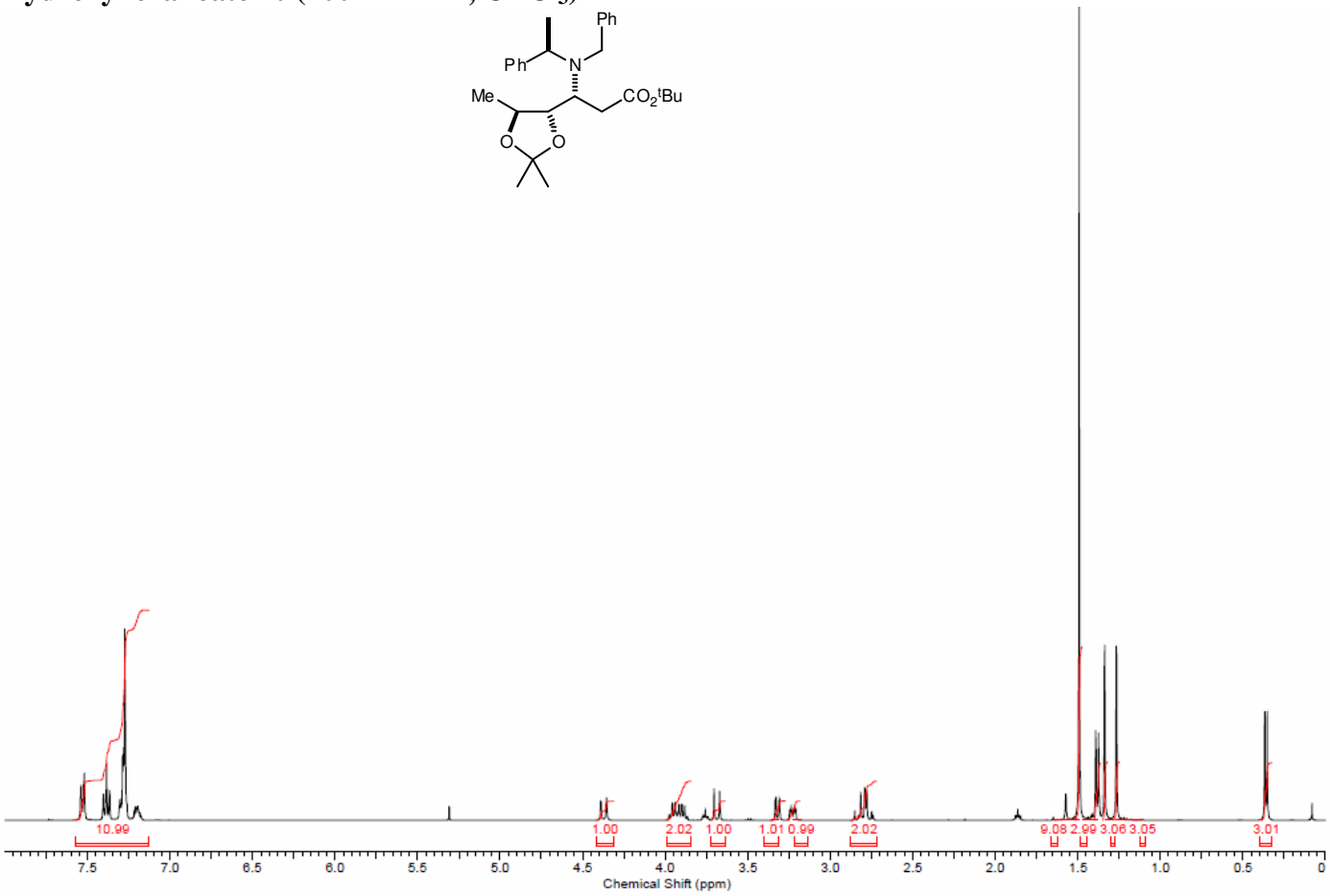
***tert*-Butyl (3*S*,4*S*,5*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 69 (400 MHz ^{1}H, $CDCl_3$)**



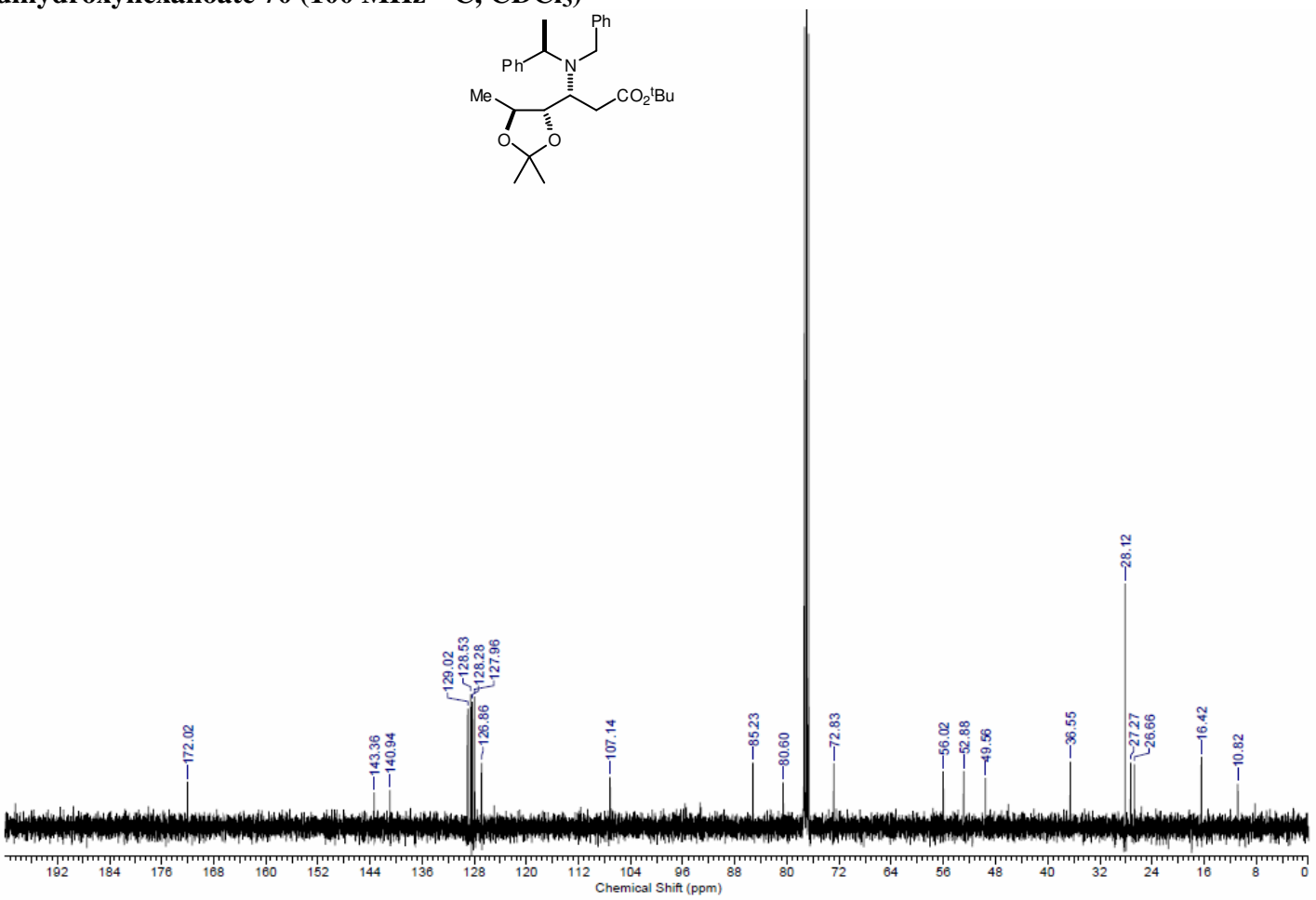
***tert*-Butyl (3*S*,4*S*,5*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 69 (100 MHz ^{13}C, $CDCl_3$)**



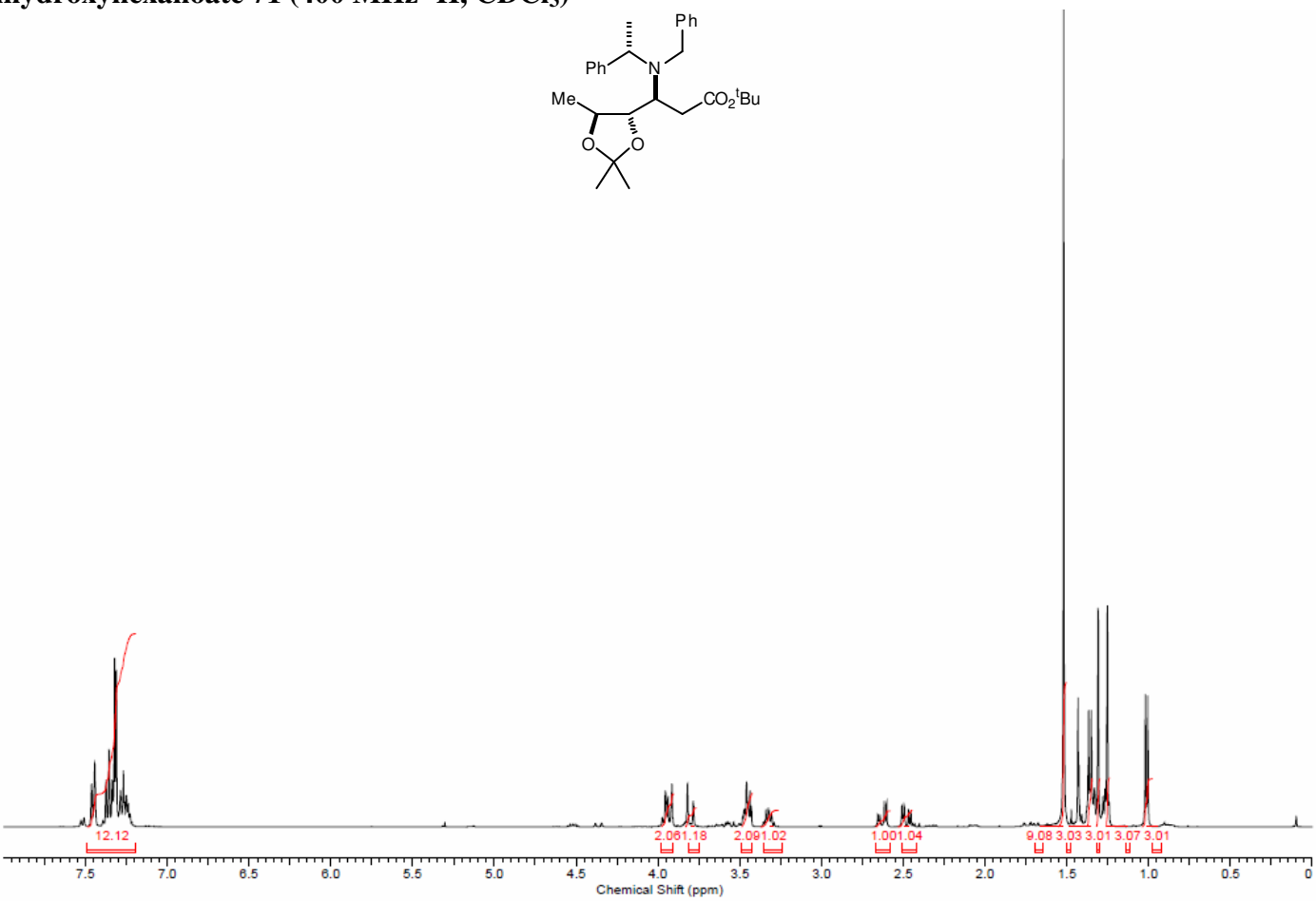
tert-Butyl (3_R_,4_S_,5_S_,α_R_)-3-[_N_-benzyl-_N_-(α-methylbenzyl)amino]-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 70 (400 MHz ^{1}H, $CDCl_3$)



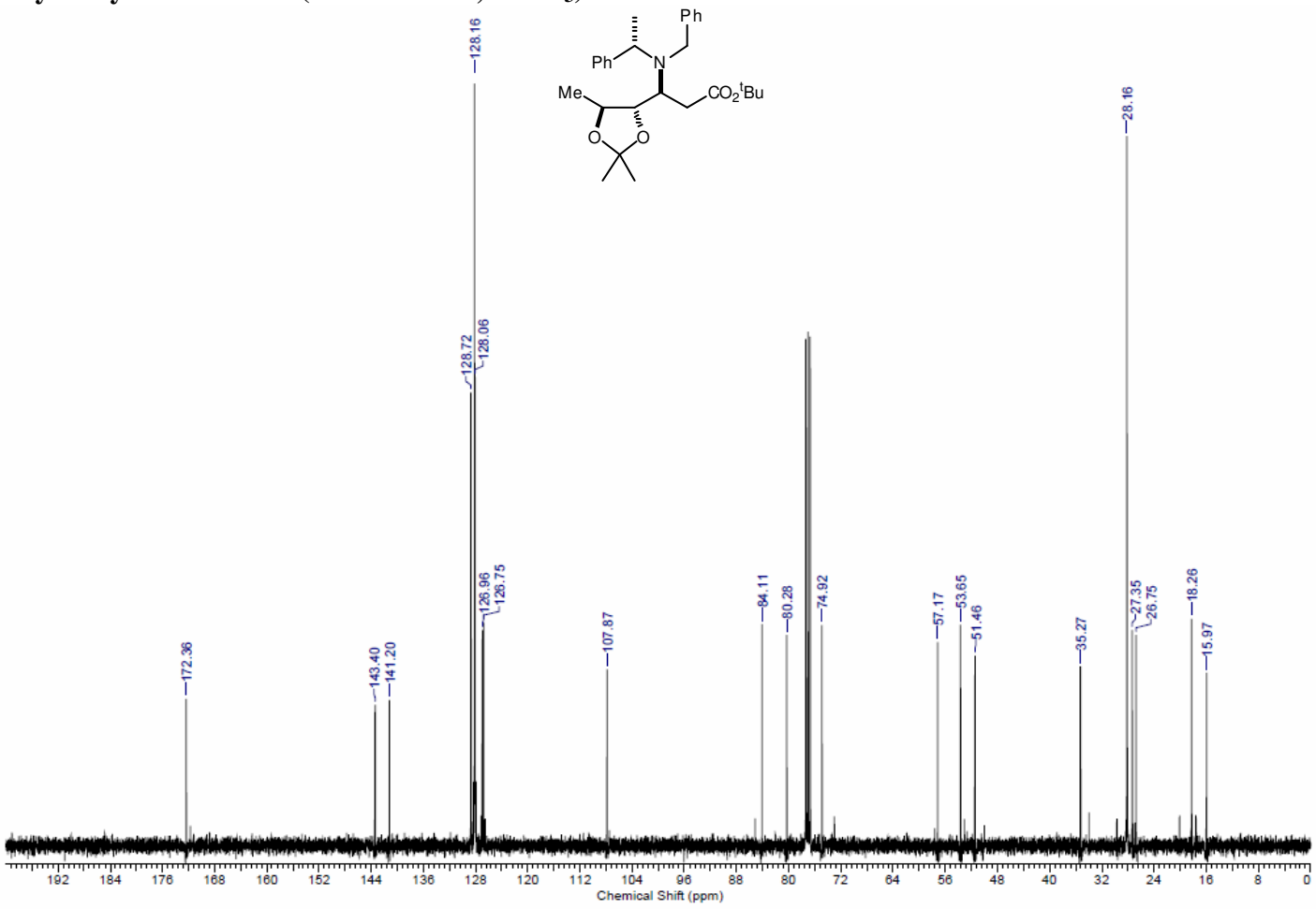
tert-Butyl (3_R_,4_S_,5_S_,α_R_)-3-[_N_-benzyl-_N_-(α-methylbenzyl)amino]-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 70 (100 MHz ^{13}C, $CDCl_3$)



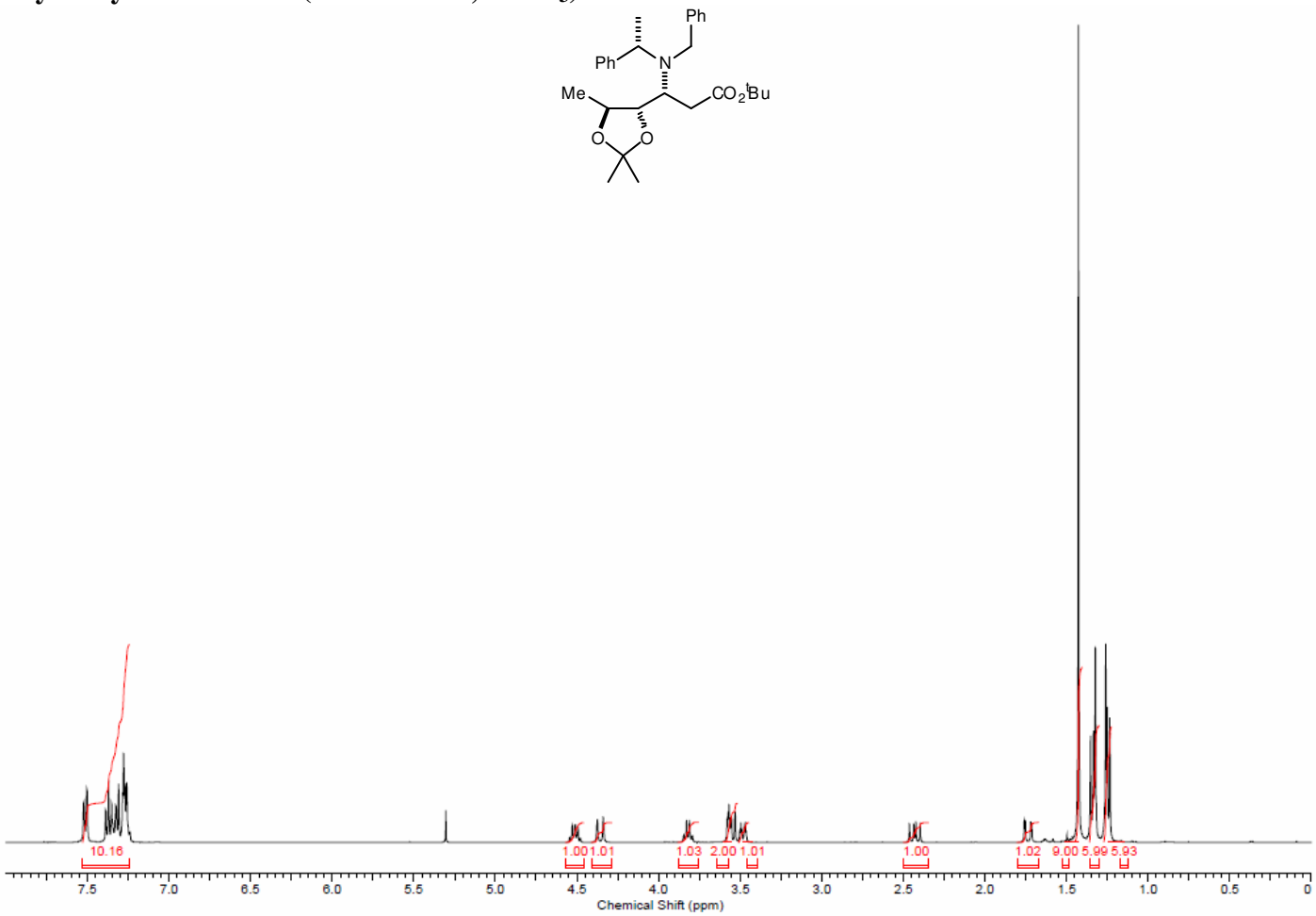
***tert*-Butyl (*S*,*S*,*S*,*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 71 (400 MHz ^{1}H, $CDCl_3$)**



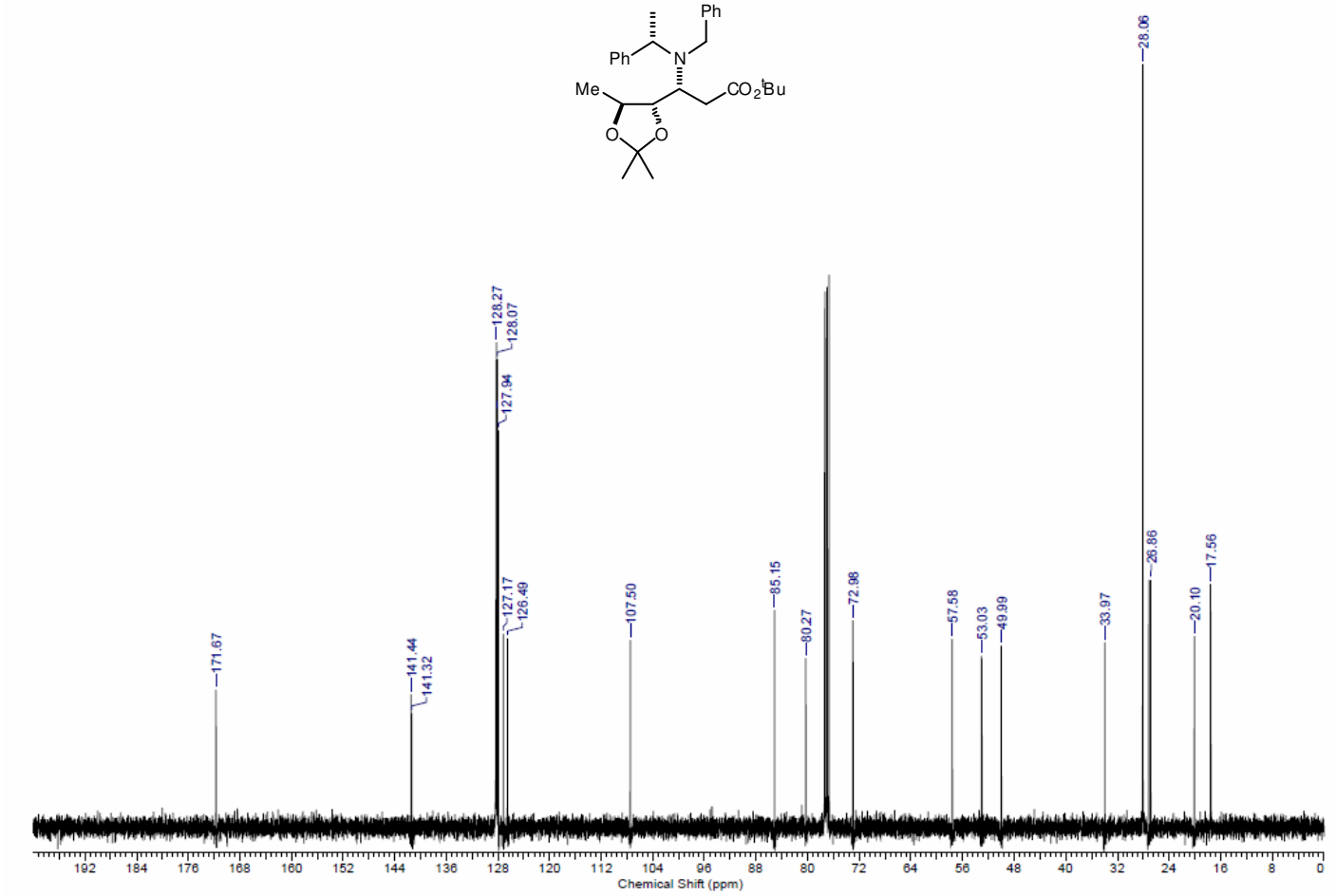
***tert*-Butyl (*S*,*S*,*S*,*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-4,5-dihydroxyhexanoate 71 (100 MHz ^{13}C, $CDCl_3$)**



tert-Butyl (3_R_,4_S_,5_S_,α_S_)-3-[_N_-benzyl-_N_-(α-methylbenzyl)amino]-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 72 (400 MHz ^{1}H, $CDCl_3$)



tert-Butyl (3_R_,4_S_,5_S_,α_S_)-3-[_N_-benzyl-_N_-(α-methylbenzyl)amino]-4,5-_O_-isopropylidene-4,5-dihydroxyhexanoate 72 (100 MHz ^{13}C, $CDCl_3$)



2. Molecular Modelling Calculations

The following Chem3D representations depict minimum energy conformations **31A** and **32A** (obtained from MM2 force field molecular modelling calculations) of α,β-unsaturated esters **31** and **32**. In each case, conformations **31A** and **32A** are viewed along the C(3)–C(4) bonds, and selected H atoms are omitted for clarity. These findings are entirely consistent with our proposed models which rationalise the diastereoselectivity observed upon the conjugate additions of the antipodes of lithium *N*-benzyl-(*N*-α-methylbenzyl)amide **1** to α,β-unsaturated esters **31** and **32**.