

Supporting Information

Chemo- and Diastereoselective *N*-Heterocyclic Carbene-Catalyzed Cross-Benzoin Reactions Using *N*-Boc- α -Amino Aldehydes

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Experimental procedures

General Methods

Anhydrous CH_2Cl_2 , diethyl ether, toluene, and THF were dried using a Braun Solvent Purification System and stored under nitrogen over 4 Å molecular sieves. DMF was dried *via* distillation over CaH_2 . Unless otherwise noted, all reactions were performed under an inert atmosphere of argon.

Preparative thin layer chromatography (TLC) was carried out on glass plates (20×20 cm) pre-coated (0.25 mm) with silica gel 60 F₂₅₄. Materials were detected by visualization under an ultraviolet lamp (254 nm) and/or by treating a 1 cm vertical strip removed from the plate with a solution of phosphomolybdic acid (5%) containing a trace of ceric sulfate in aq. sulfuric acid (5% v/v), or with basic KMnO_4 [KMnO_4 (1.5 g), K_2CO_3 (10 g), 10% aq. NaOH (1.25 mL), in H_2O (200 mL)], followed by charring with a heat gun. Analytical TLC was carried out on glass plates (4×3 cm) pre-coated (0.25 mm) with silica gel 60 F₂₅₄ and was visualized in the same manner as described for preparative TLC.

Flash column chromatography (FCC) was performed according to Still *et al.*¹ with Merck silica gel 60 (0.040–0.063 mm). All mixed solvents eluents are reported as v/v solutions. Unless otherwise noted, all reported compounds were homogenous by thin layer chromatography (TLC) and by ^1H NMR spectroscopy.

Concentration refers to removal of volatiles with a rotary evaporator under vacuum supplied by vacuum pump (ca. 30 Torr). Evacuation at ca. 0.5 Torr with a vacuum pump generally followed rotary evaporation. ^1H NMR and ^{13}C NMR calculations were performed according to reported procedures.^{2,3}

Spectral Data

High resolution mass spectra (HRMS) and low resolution mass spectra (LRMS) were obtained on a VG 70E double focusing high resolution spectrometer; only partial data are reported. Electron impact (EI) ionization was accomplished at 70 eV, chemical ionization (CI) at 50 eV with ammonia as the reagent gas. Alternatively, HRMS was obtained on a LC–MS/MS time-of-flight high resolution spectrometer with electrospray ionization (ESI) from acetonitrile solution.

Infrared spectra were recorded on a Fourier transform interferometer using a diffuse reflectance cell (DRIFT); only diagnostic peaks and/or intense peaks are reported. Unless otherwise noted, all experiments used DRIFT.

Unless otherwise noted, NMR spectra were measured in CDCl₃ solution at 500 MHz or 600 MHz for ¹H and 125 or 150 MHz for ¹³C. Signals due to the solvent (¹³C NMR) or residual protonated solvent (¹H NMR) served as the internal standard: CDCl₃ (7.26 δ_H, 77.16 δ_C); C₆D₆ (7.16 δ_H, 128.39 δ_C); CD₃OD (3.31 δ_H, 49.00 δ_C). The ¹H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), sep (septet), m (multiplet), br (broad), ap (apparent); the list of coupling constants (*J*) corresponds to the order of the multiplicity assignment. Coupling constants are reported to the nearest 0.5 Hz (digital resolution ca. 0.1 Hz/pt) or the nearest 0.1 Hz (digital resolution ca. 0.03 Hz/pt.). The ¹³C NMR assignments were made on the basis of chemical shift.

Specific rotations ([α]_D) are the average of five determinations at ambient temperature using 1 mL, 10 dm cell; the units are 10⁻¹ deg. cm² g⁻¹ and the concentrations (*c*) are reported in g/100 mL. The values reported are rounded to reflect the accuracy of the measured concentrations (the major source of error). HPLC analyses were carried out using an Agilent Technologies 1200 series liquid chromatograph.

Computational Methods

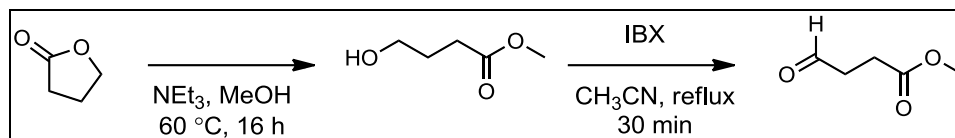
¹H and ¹³C NMR chemical shifts were predicted using the procedure described by Hoyer *et al.*³

Materials

All commercially available aldehydes were purified by bulb-to-bulb distillation prior to use. 2-Iodoxybenzoic acid (IBX) was synthesized according to a literature procedure.⁴ Triazolium precatalyst **1**, **S13** and **S14** were synthesized following reported procedures.^{5,6} ZnCl₂ was dried by heating to 350 °C under vacuum (0.5 Torr) for a period of 16 h.

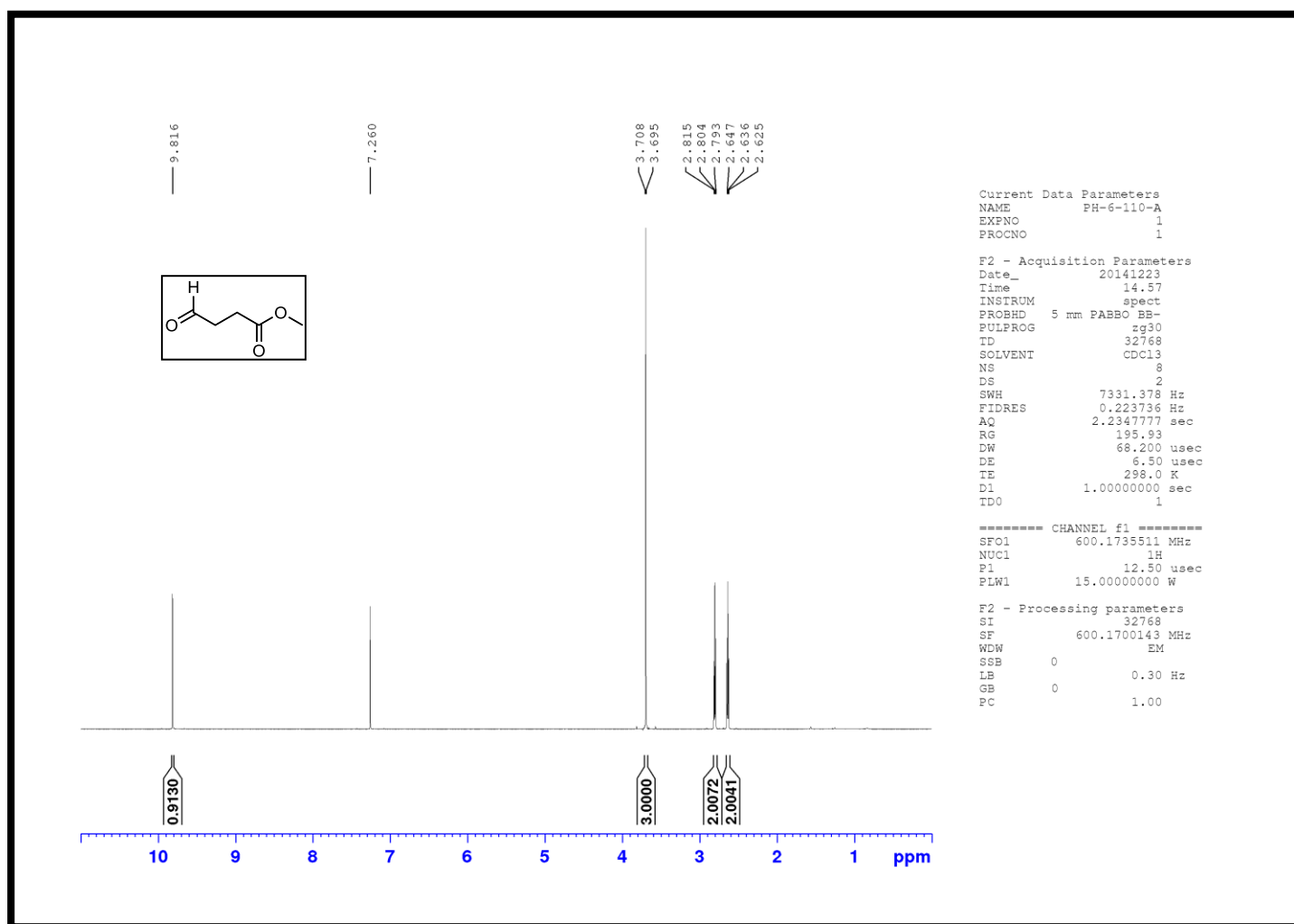
Unless otherwise noted, all other reagents were purchased and used without further purification.

Synthesis of methyl 4-oxobutanoate (S1)



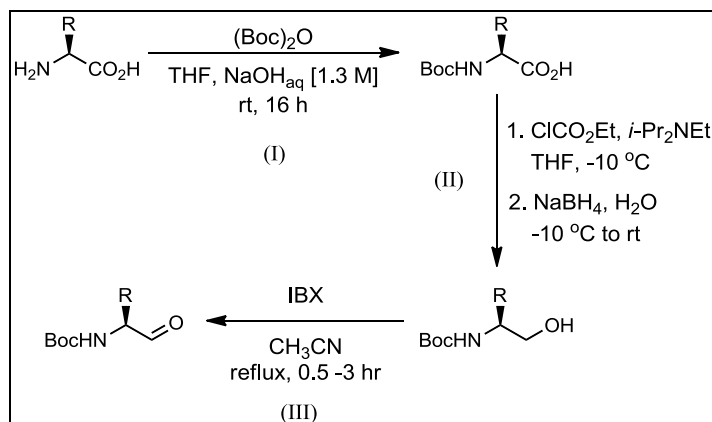
Methyl 4-hydroxybutanoate was prepared according to a previously reported procedure⁷ and carried to the next step without further purification. To a suspension of alcohol (7.46 mmol, 1.0 equiv.) in CH_3CN (37 mL) was added IBX (11.2 mmol, 1.5 equiv.) and heated to reflux. The reaction was monitored by TLC for consumption of starting material (30 min). After completion, the reaction was cooled to room temperature and filtered through a pad of Celite[®] and washed with EtOAc (3×10 mL). The resulting solution was concentrated and purified by chromatography (5:1 hexane:acetone $R_f = 0.22$) to afford a clear colourless oil (552 mg, 64% yield). Spectral data match the previously reported values.⁸

^1H NMR (600 MHz, CDCl_3): δ 9.82 (s, 1H), 3.70 (s, 3H), 2.80 (t, $J = 6.6$ Hz, 2H), 2.64 (t, $J = 6.7$ Hz, 2H).



Synthesis of α -Amino Aldehydes

General procedure A



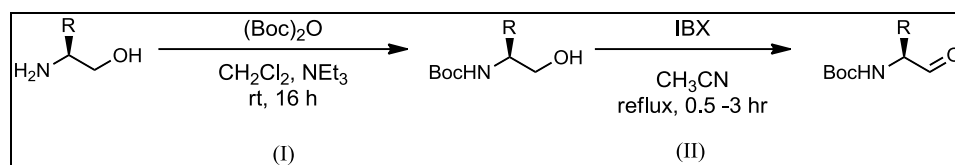
A (I): Using a modified procedure from Nair and co-workers,⁹ the corresponding amino acid (1.0 equiv.) was suspended in THF [0.4 M] and an aqueous solution of NaOH (3.0 equiv. [1.3 M]) was added to this suspension at 0°C . This is followed by the addition of Boc_2O (1.1 equiv.). The ice bath was removed and the mixture was stirred overnight at ambient temperature. After 16 hours, the reaction was cooled to 0°C and acidified to $\text{pH}=3$ using HCl_{aq} [1 M]. The reaction mixture was extracted with ethyl acetate ($\times 3$) and the organic layers were combined and dried over anhydrous MgSO_4 . The resulting suspension was filtered and concentrated *in vacuo*. Depending on the ratio of impurities to the product, the crude product was either taken to the next step without further purification or was purified by chromatography using a mixture of ethyl acetate and hexanes to afford the desired N -Boc-amino acid.

A (II): The reduction of the corresponding amino acids was accomplished by using a modified procedure by Yudin and co-workers¹⁰ The corresponding N -Boc amino acid was dissolved in THF [1 M] and cooled to -10°C . To this solution was added N,N -Diisopropylethylamine (1.0 equiv.) followed by ethyl chloroformate (1 equiv.). The mixture was stirred at this temperature for 15 minutes and the suspension was filtered and washed with THF ($\times 3$). The filtrate was once again cooled to -10°C and NaBH_4 (1.5 equiv.) was added in one portion followed by addition of water [3 M]. The mixture was stirred for an additional 30 minutes and the crude product was extracted with EtOAc ($\times 3$). The combined organic layers were washed with brine and dried over MgSO_4 .

The resulting solution was concentrated *in vacuo* and purified by FCC using a mixture of EtOAc and hexanes to afford the desired *N*-Boc-amino alcohol.

A (III): The oxidation process was carried out according to the previously reported procedure.¹¹ IBX (1.5 equiv.) was added to a solution of *N*-Boc-amino alcohol (1.0 equiv.) in acetonitrile [0.2 M]. The reaction was monitored for complete consumption of starting material (typical reaction time = 45 minutes). After completion, the contents were cooled to room temperature, filtered through a pad of Celite[®] and washed with EtOAc (x3). The resulting solution was concentrated and purified by chromatography.

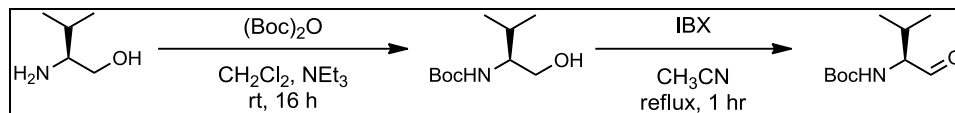
General procedure B



B (I): The Boc protection of amino alcohols was accomplished using a modified procedure.¹²

To a solution of amino alcohol (1.0 equiv.) in CH_2Cl_2 [0.6 M] was added triethylamine (1.1 equiv.) at room temperature. To this solution was added di-*tert*-butyl dicarbonate (Boc_2O) (1.1 equiv.) and stirred at ambient temperature for 16 hours. The reaction was quenched with addition of HCl [1 M] and extracted with CH_2Cl_2 (x3). The combined organic layers were washed with brine and dried over MgSO_4 . The crude product was purified by column chromatography using a mixture of EtOAc and hexanes.

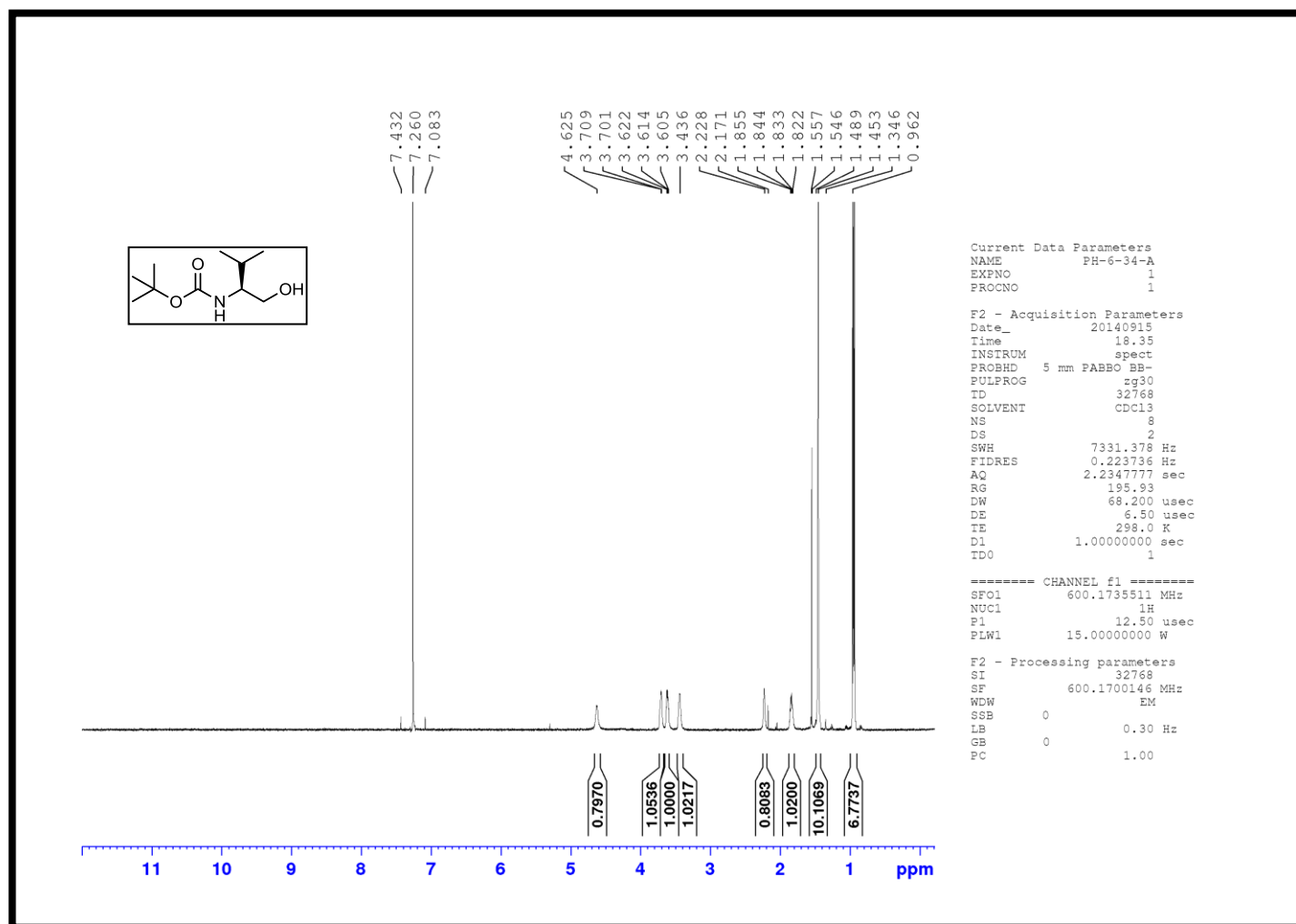
B (II): The oxidation process was carried out according to the previously reported procedure.¹¹ IBX (1.5 equiv.) was added to a solution of *N*-Boc-amino alcohol (1.0 equiv.) in acetonitrile [0.2 M]. The reaction was monitored for complete consumption of starting material (typical reaction time = 45 minutes). After completion, the contents were cooled to room temperature, filtered through a pad of Celite[®] and washed with EtOAc (x3). The resulting solution was concentrated and purified by chromatography.



((S)-tert-butyl 1-hydroxy-3-methylbutan-2-yl)carbamate (N-Boc-L-valinol) (S2)

Prepared according to **general procedure B (I)**. Isolated by column chromatography (3:1 hexane/EtOAc, $R_f = 0.22$) as a colorless oil (2.85 g, 72%). Spectral data match the previously reported values.¹³

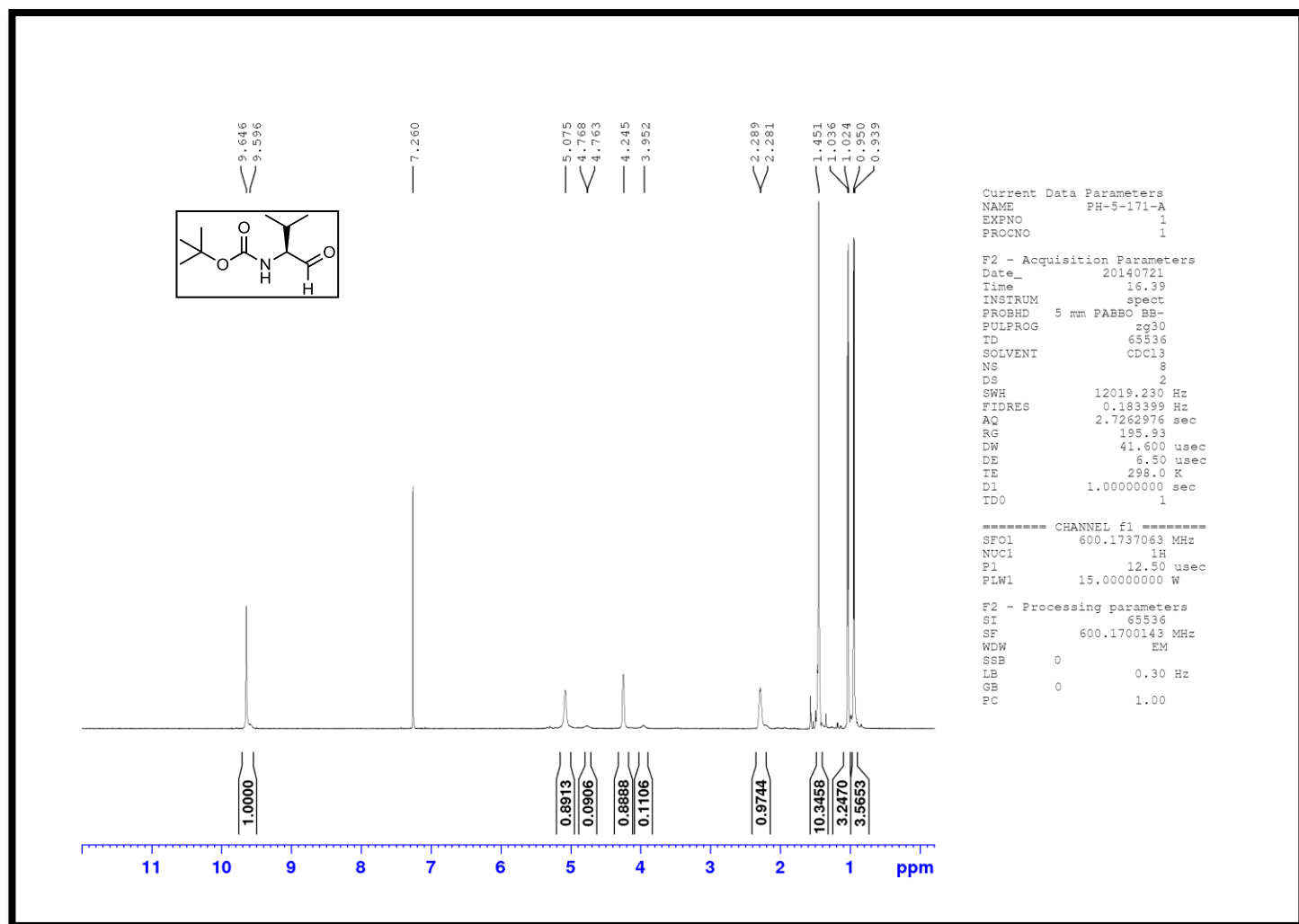
¹H NMR (500 MHz, CDCl₃): δ 4.62 (br s, 1 H), 3.74–3.67 (m, 1 H), 3.64–3.57 (m, 1 H), 3.48–3.39 (m, 1 H), 2.26–2.19 (m, 1 H), 1.88–1.79 (m, 1H), 1.45 (s, 9 H), 0.96 (d, $J = 5.7$ Hz, 3H), 0.93 (d, $J = 5.7$ Hz, 3H).

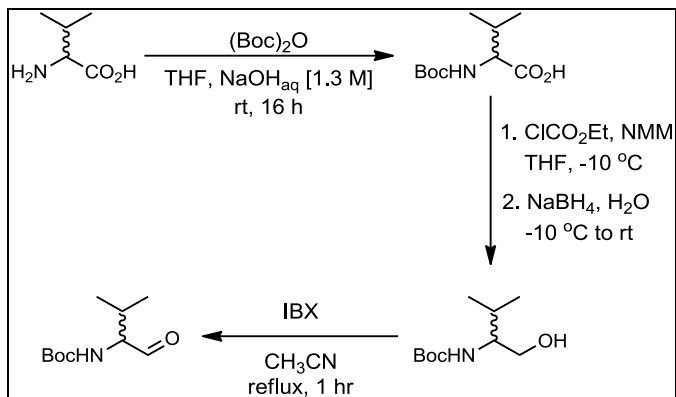


(S)-tert-butyl (3-methyl-1-oxobutan-2-yl)carbamate (N-Boc-L-valinal) (15)

Prepared according to **general procedure B (II)**. Isolated by column chromatography (6:1 hexane/EtOAc, R_f = 0.30) followed by recrystallization from hexane overnight at $-20\text{ }^{\circ}\text{C}$ as a white powder (2.44 g, 83%). Spectral data match the previously reported values.¹⁴

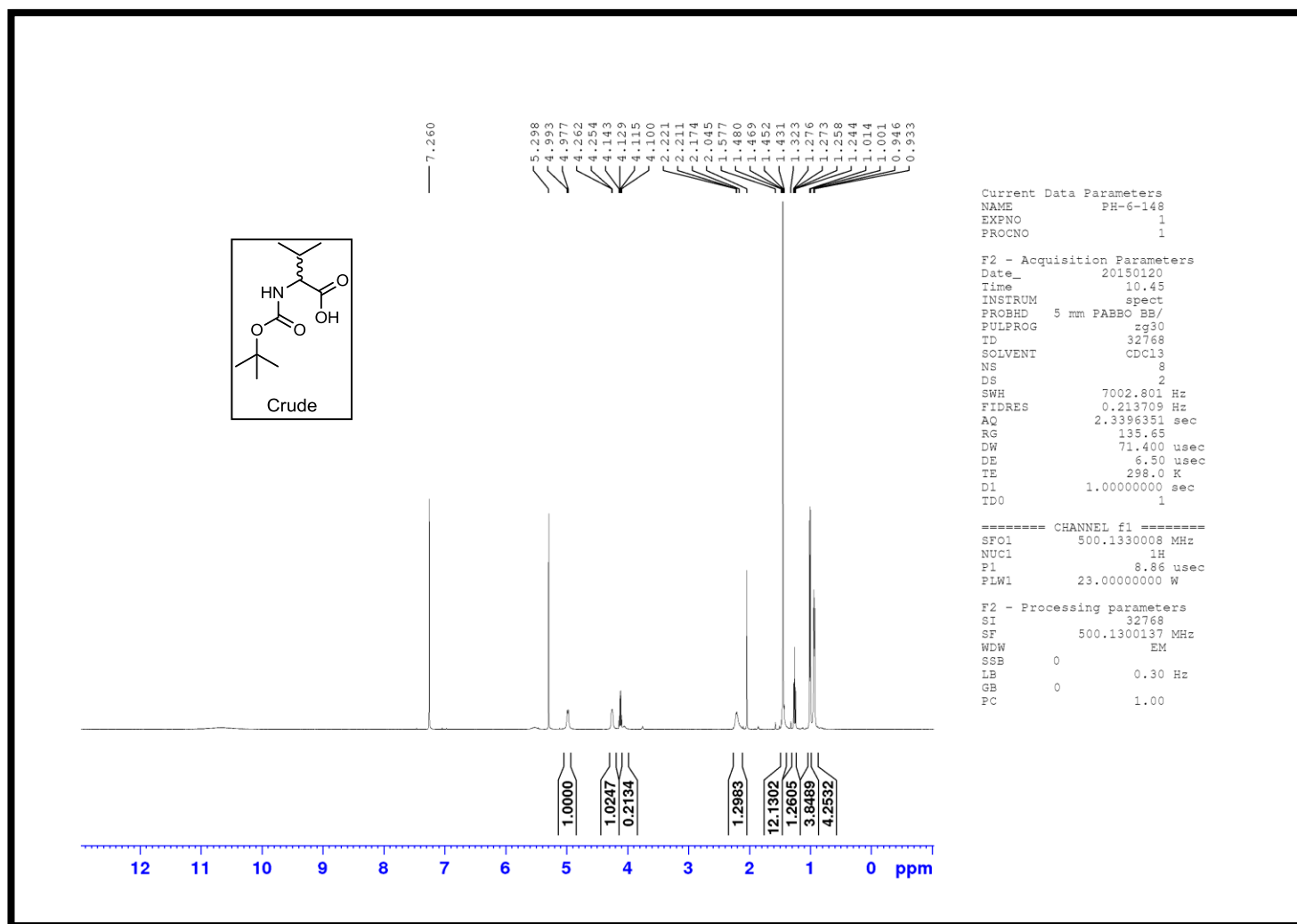
^1H NMR (600 MHz, CDCl_3): mixture of rotamers; δ 9.65 (s, 1 H), 5.07 (br s, 0.9H), 4.76 (br s, 0.1H), 4.25 (br s, 0.9H), 3.95 (br s, 0.1H), 2.35–2.23 (m, 1H), 1.45 (s, 9 H), 1.03 (d, J = 6.9 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H).





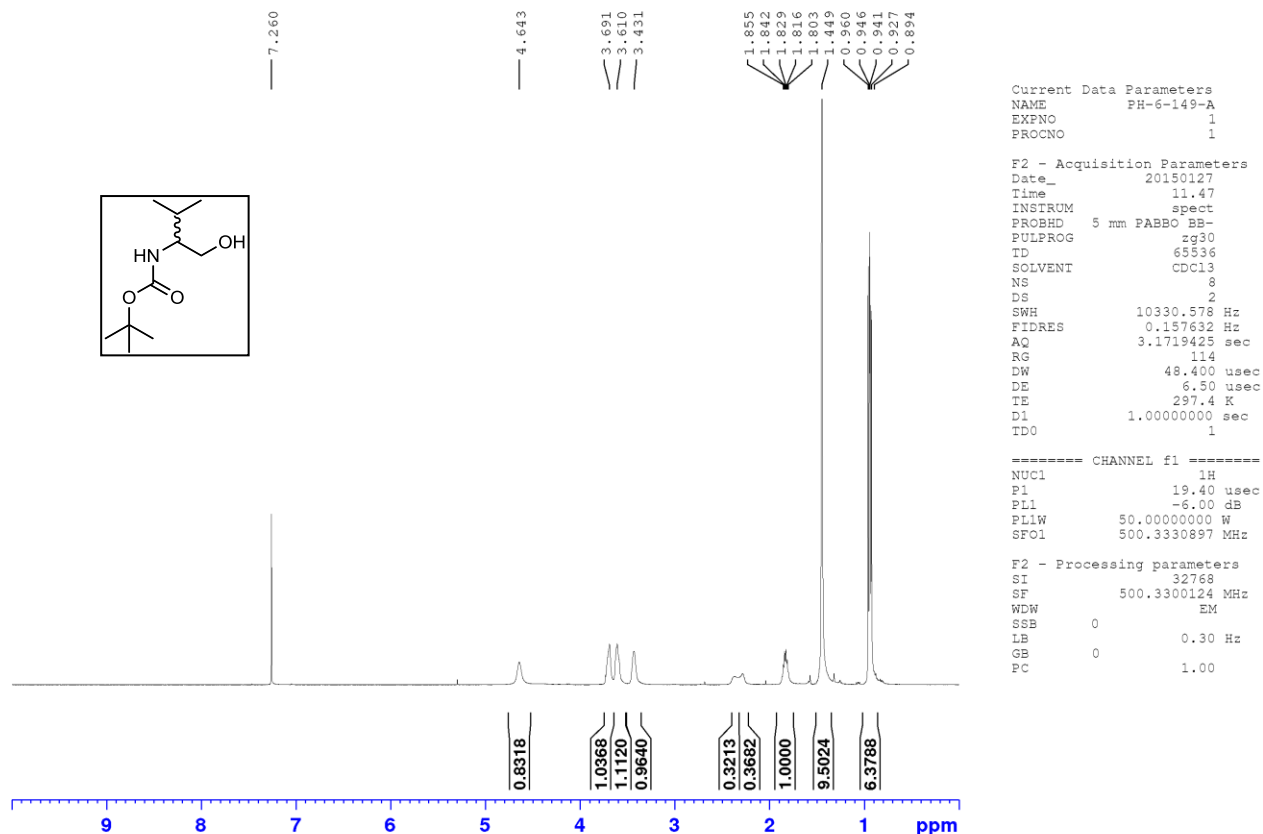
rac-2-((*tert*-butoxycarbonyl)amino)-3-methylbutanoic acid (*rac*-*N*-Boc-*L*-valine) (**S3**)

Prepared according to **general procedure B (I)**. The crude mixture was carried to next step without further purification.



***rac*-tert-butyl (1-hydroxy-3-methylbutan-2-yl)carbamate (*rac*-N-Boc-L-valinol) (S4)**

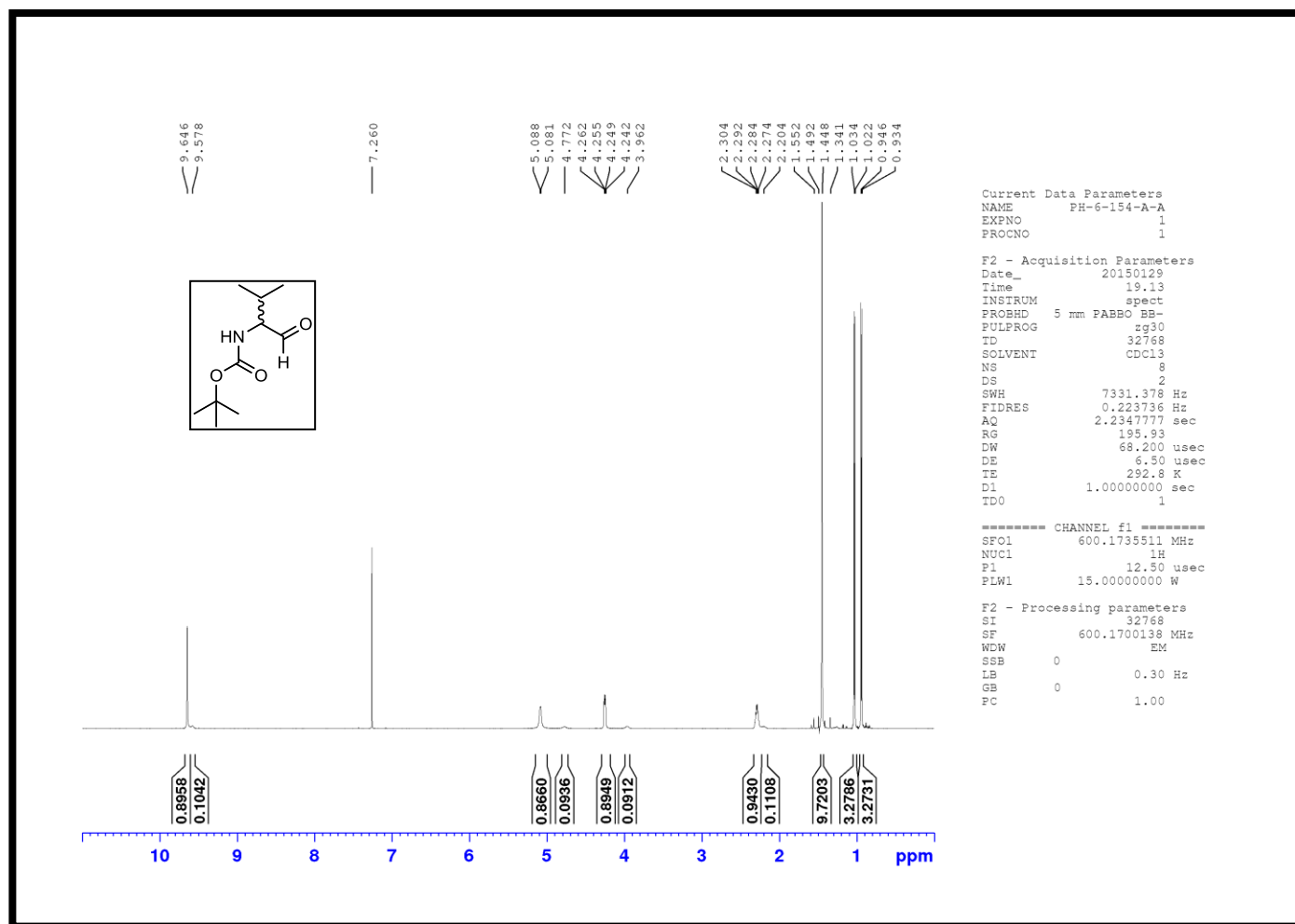
Prepared according to a modified **general procedure B (II)** by replacing *i*-Pr₂NEt with 4-methyl morpholine (NMM). Isolated by recrystallization from a mixture of EtOAc/hexane at -20 °C overnight as a white solid (1.66 g, 89%).

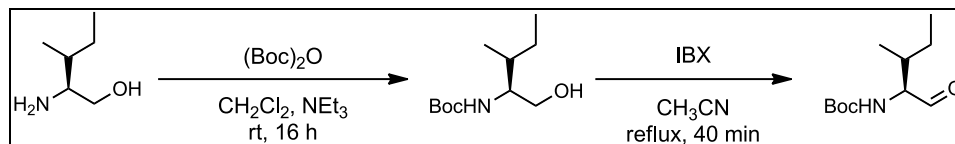


rac-tert-butyl (3-methyl-1-oxobutan-2-yl)carbamate (rac-N-Boc-L-valinal) (S5)

Prepared according to **general procedure B (II)**. Isolated by column chromatography (5:1 hexane/EtOAc, R_f = 0.24) followed by recrystallization from EtOAc/hexanes overnight at $-20\text{ }^{\circ}\text{C}$ as a white solid (700 mg, 71%). Spectral data match the previously reported values.¹⁴

^1H NMR (600 MHz, CDCl_3): mixture of rotamers; δ 9.65 (s, 0.9H), 9.57 (s, 0.1H), 5.09 (d, J = 4.6 Hz, 0.9H), 4.77 (br s, 0.1H), 4.25 (dd, J = 7.7, 4.2 Hz, 0.9H), 3.96 (br s, 0.1H), 2.29 (m, 0.9H), 2.20 (m, 0.1H), 1.45 (s, 9 H), 1.03 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 7.0 Hz, 3H).

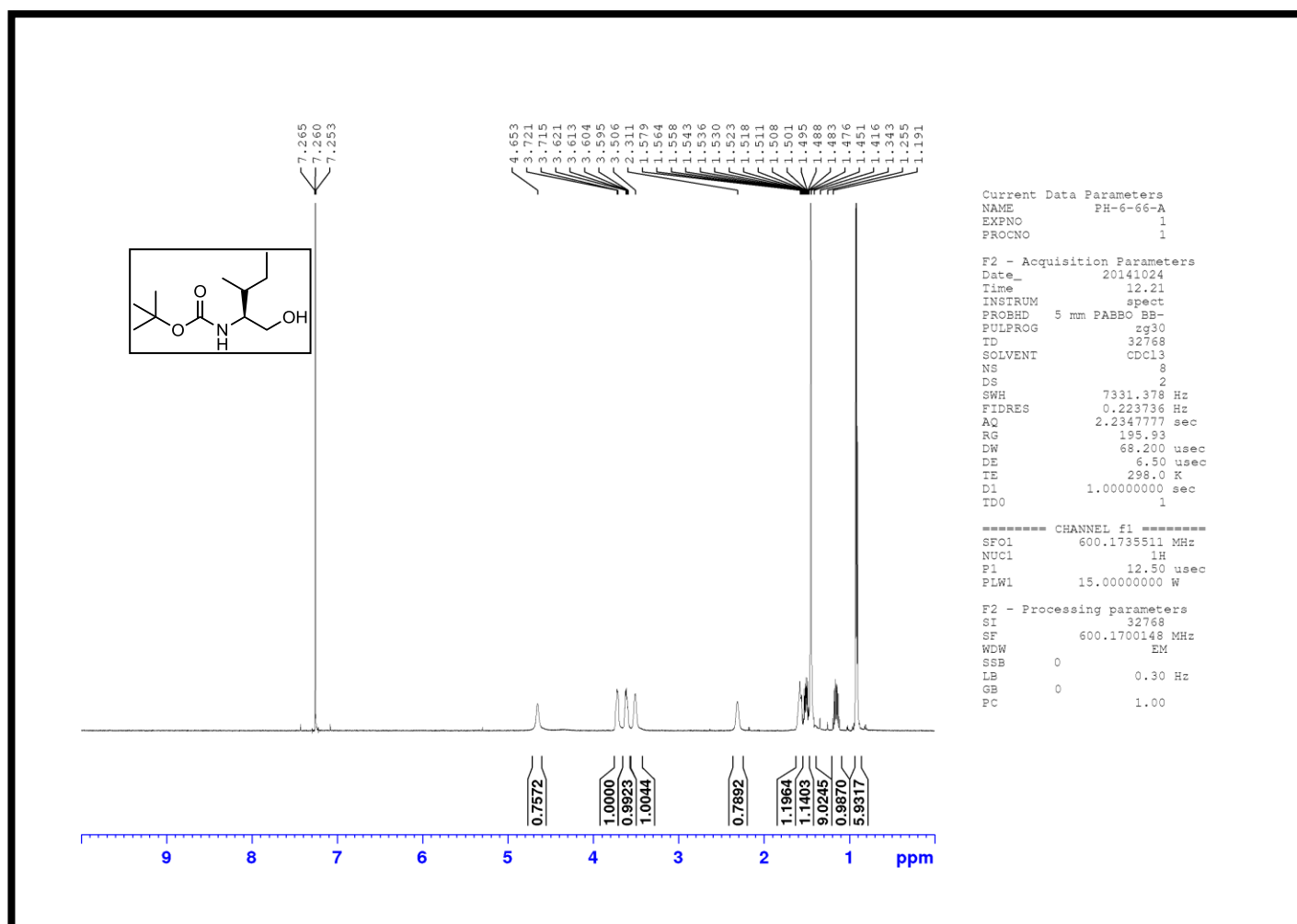




***tert*-butyl ((2*S*,3*S*)-3-methyl-1-oxopentan-2-yl)carbamate (*N*-Boc-L-isoleucinol) (**S6**)**

Prepared according to **general procedure B (I)**. Isolated by column chromatography (3:1 hexane/acetone, $R_f = 0.21$) as a colorless oil (732 mg, 79%). Spectral data match the previously reported values.¹⁵

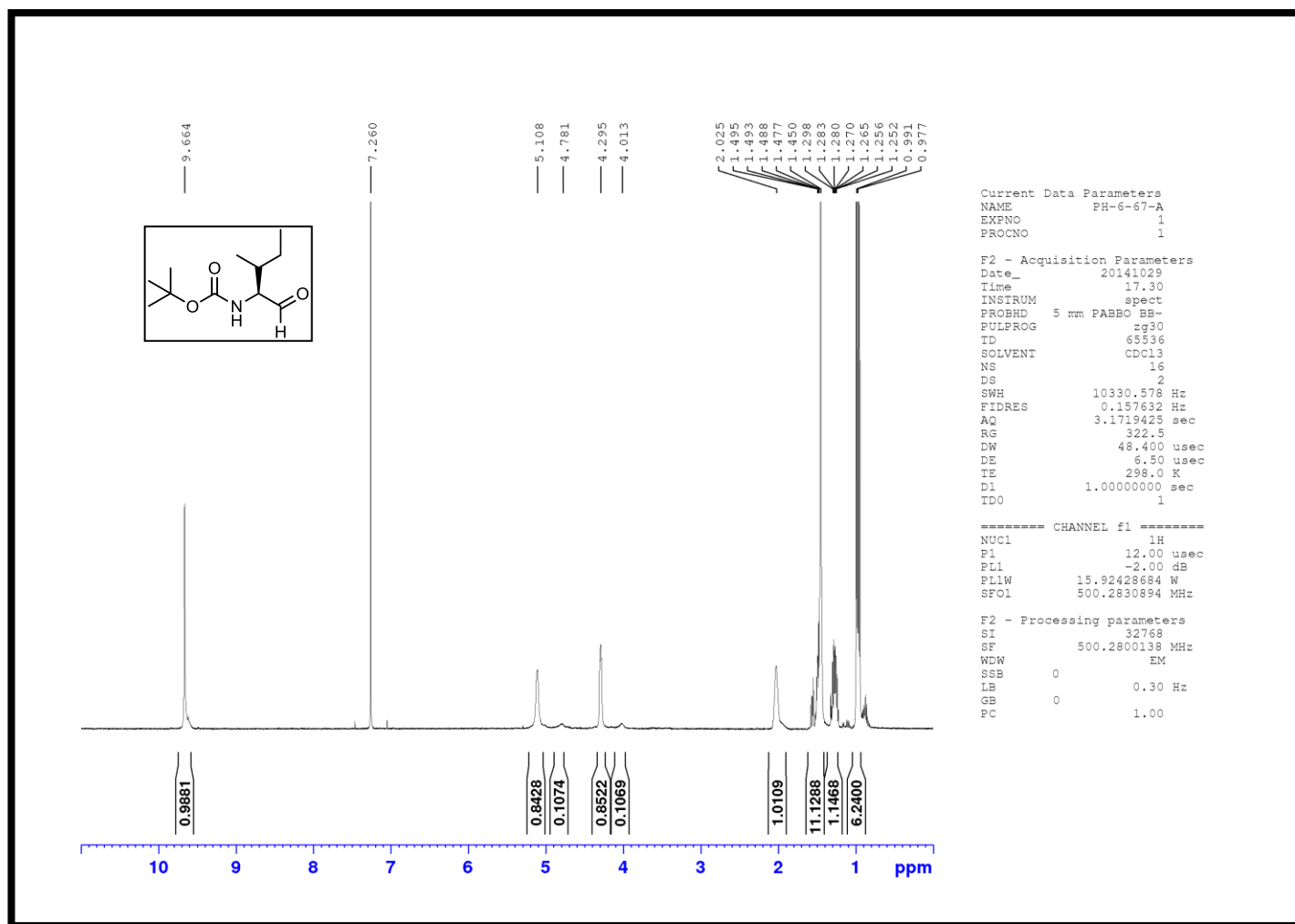
^1H NMR (500 MHz, CDCl_3): δ 3.65 (br s, 1H), 3.74–3.67 (m, 1H), 3.66–3.56 (m, 1H), 3.51 (br, s, 1H), 2.31 (br s, 1H), 1.62–1.55 (m, 1H), 1.54–1.47 (m, 1H), 1.45 (s, 9), 1.20–1.10 (m, 1H), 0.92 (d, $J = 6.4$ Hz, 3H), 0.91 (t, $J = 7$ Hz, 3H).

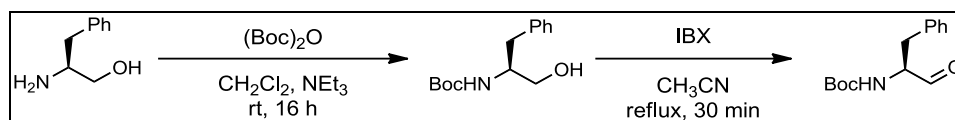


(*S,S*)-tert-butyl (3-methyl-1-oxobutan-2-yl)carbamate (*N*-Boc-L-isoleucinal) (S7)

Prepared according to **general procedure B (II)**. Isolated by column chromatography (9:1 hexane/EtOAc, R_f = 0.30) colourless viscous oil (276 mg, 70%). Spectral data match the previously reported values.¹⁶

¹H NMR (500 MHz, CDCl₃); mixture of rotamers; δ 9.66 (s, 1H), 5.11 (br s, 0.9H), 4.78 (br s, 0.1H), 4.29 (br s, 0.9H), 4.01 (br s, 0.1H), 2.02 (br s, 1H), 1.52–1.45 (m, 1H), 1.45 (s, 9 H), 1.33–1.21 (m, 1H) 0.98 (d, J = 7.1 Hz, 3H), 0.95 (d, J = 7.4 Hz, 3H).

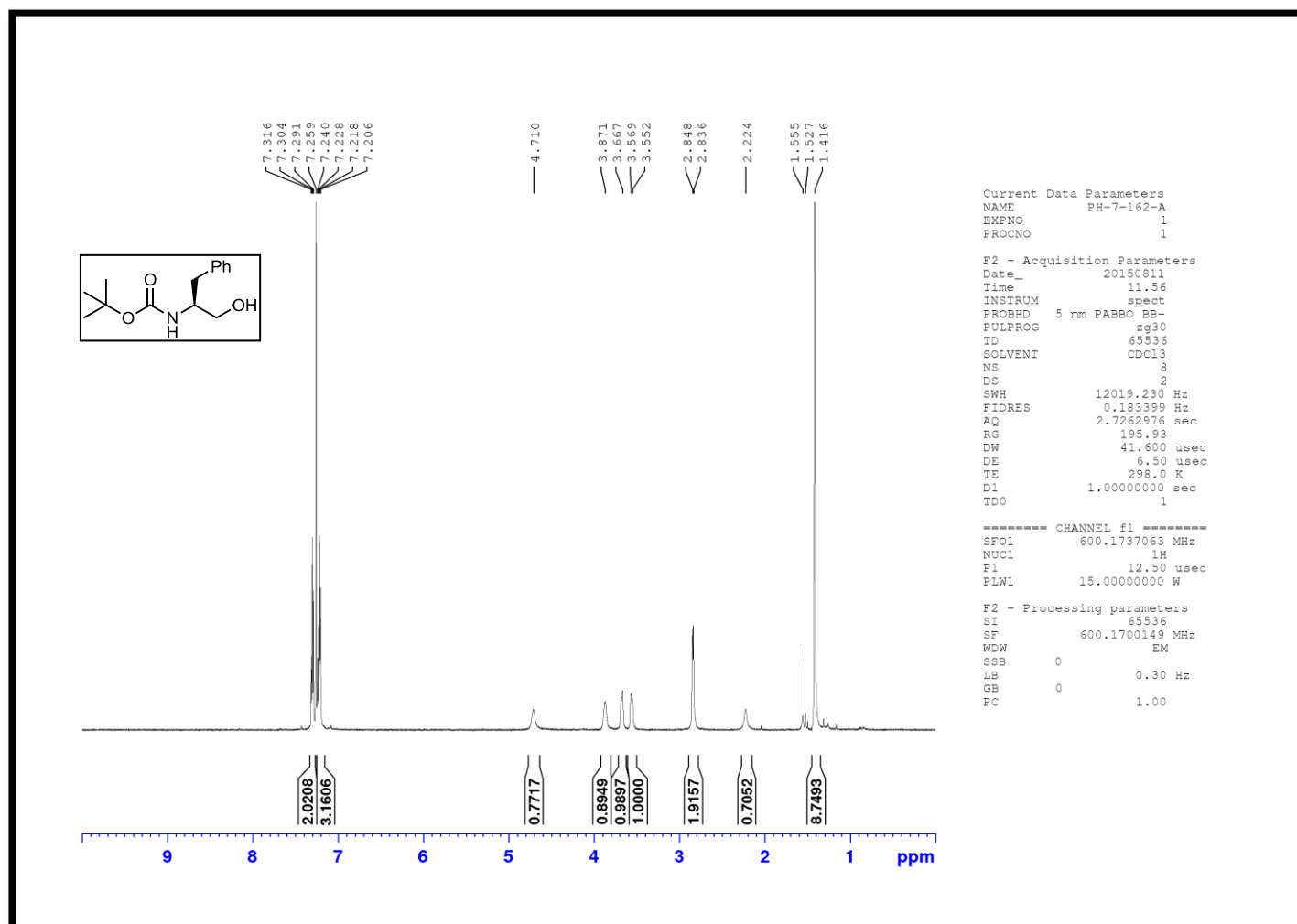




(*S*)-tert-butyl (1-hydroxy-3-phenylpropan-2-yl)carbamate (*N*-Boc-L-phenylalaninol) (S8)

Prepared according to **general procedure A(I)**. Isolated by re-crystallization from a mixture of EtOAc: hexanes at $-20\text{ }^{\circ}\text{C}$ as off-white solids (680 mg, 82%). Spectral data match the previously reported values.¹⁷

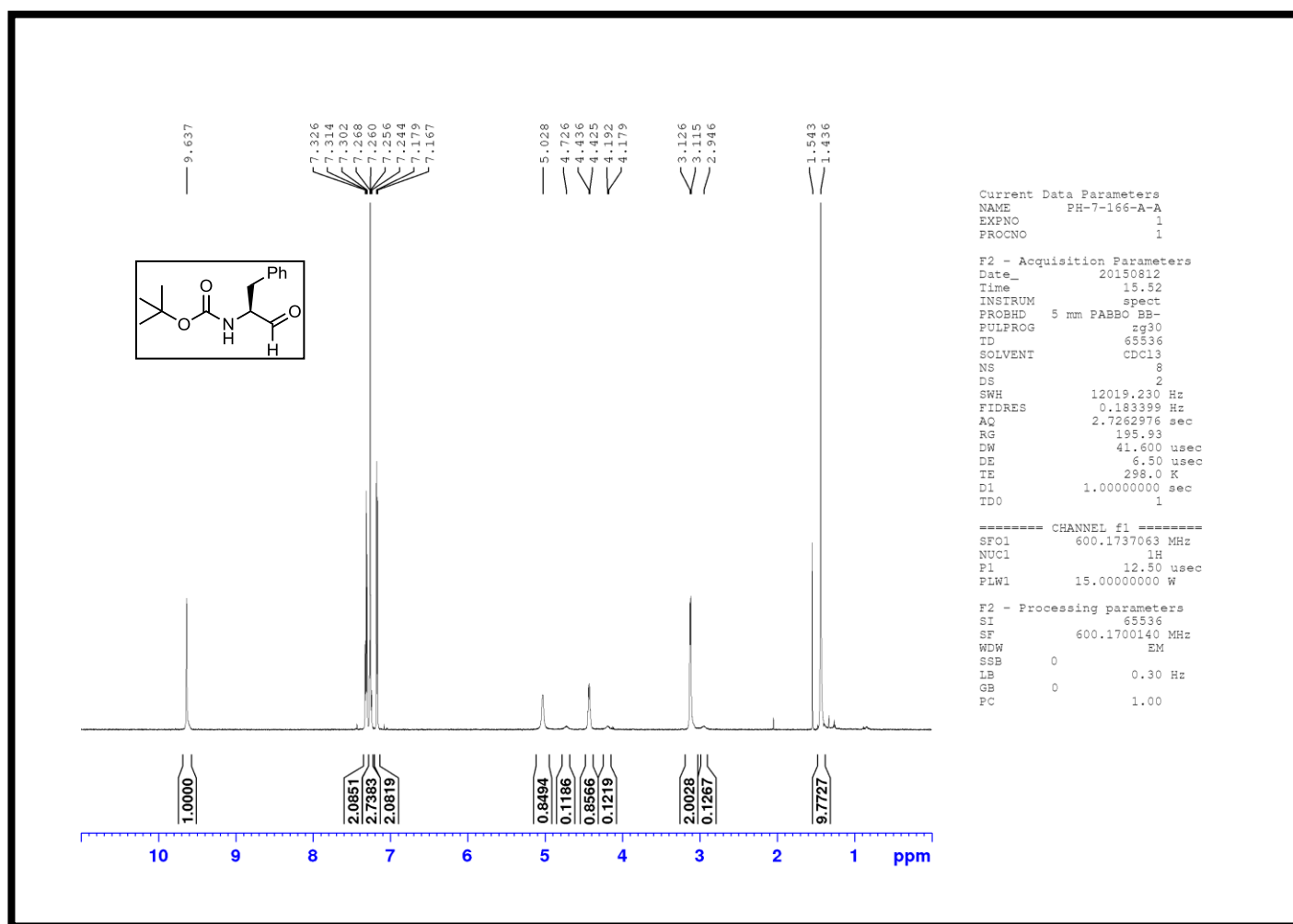
^1H NMR (500 MHz, CDCl_3): δ 7.32–7.28 (m, 2H), 7.25–7.20 (m, 3H), 4.71 (br s, 1H), 3.87 (br s, 1H), 3.71–3.63 (m, 1H), 3.58–3.51 (m, 1H), 2.84 (d, $J = 7.1$, 2H), 2.22 (br s, 1H), 1.42 (s, 9 H).

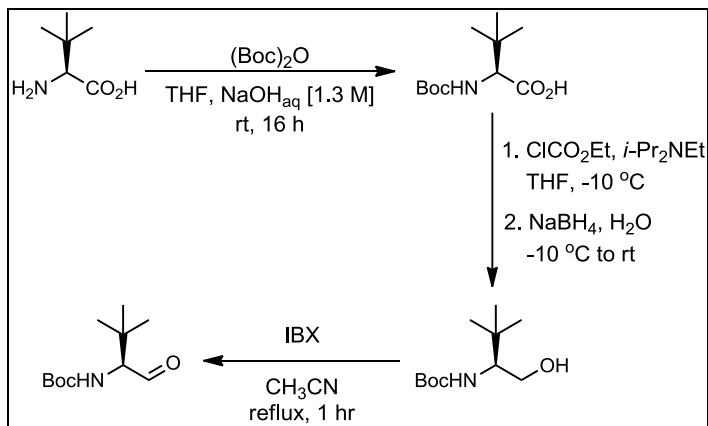


(S)-tert-butyl (1-oxo-3-phenylpropan-2-yl)carbamate (N-Boc-L-phenylalaninal) (S9)

Prepared according to **general procedure A (II)**. Isolated by column chromatography (5:1 hexanes:EtOAc, R_f = 0.2) followed by recrystallization from a mixture of EtOAc/hexane overnight at $-20\text{ }^{\circ}\text{C}$ as a white powder (343 mg, 51%). Spectral data match the previously reported values.¹⁸

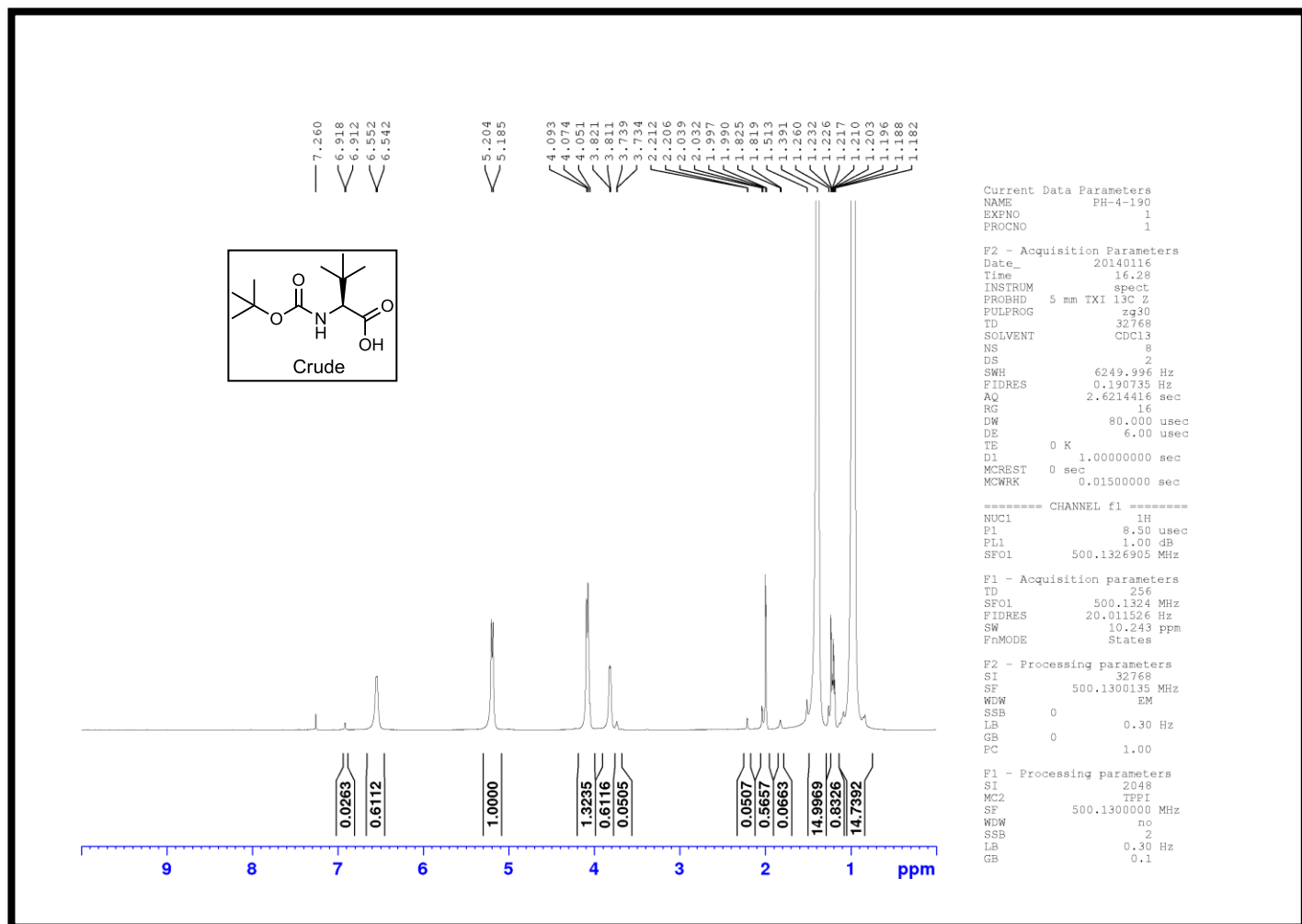
^1H NMR (500 MHz, CDCl_3); mixture of rotamers; δ 9.64 (s, 1H), 7.34–7.28 (m, 2H), 7.27–7.24 (m, 1H), 7.19–7.15 (d, J = 7.1, 2H), 5.03 (br s, 0.9H), 4.73 (br s, 0.1H), 4.47–4.39 (m, 0.9H), 4.22–4.15 (m, 0.1H), 3.12 (d, J = 6.4 Hz, 1.8H), 2.99–2.91 (m, 0.2H), 1.44 (s, 9H).





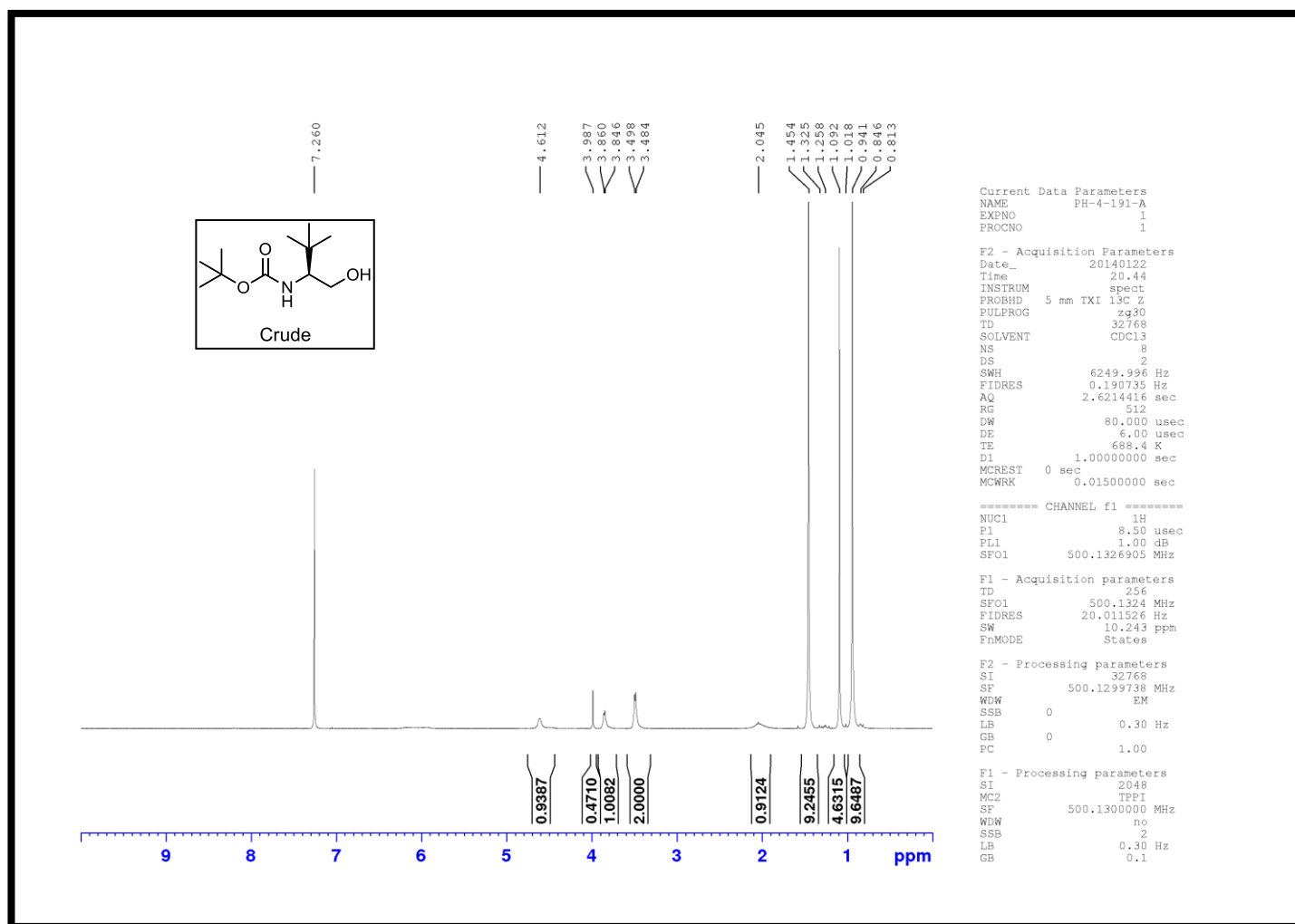
(S)-2-((tert-butoxycarbonyl)amino)-3,3-dimethylbutanoic acid (N-Boc-L-tert-leucine) (S10)

Prepared according to general procedure A (I). The crude reaction mixture was carried to next step without further purification.



(S)-tert-butyl (1-hydroxy-3,3-dimethylbutan-2-yl)carbamate (N-Boc-L-tert-leucinol) (S11)

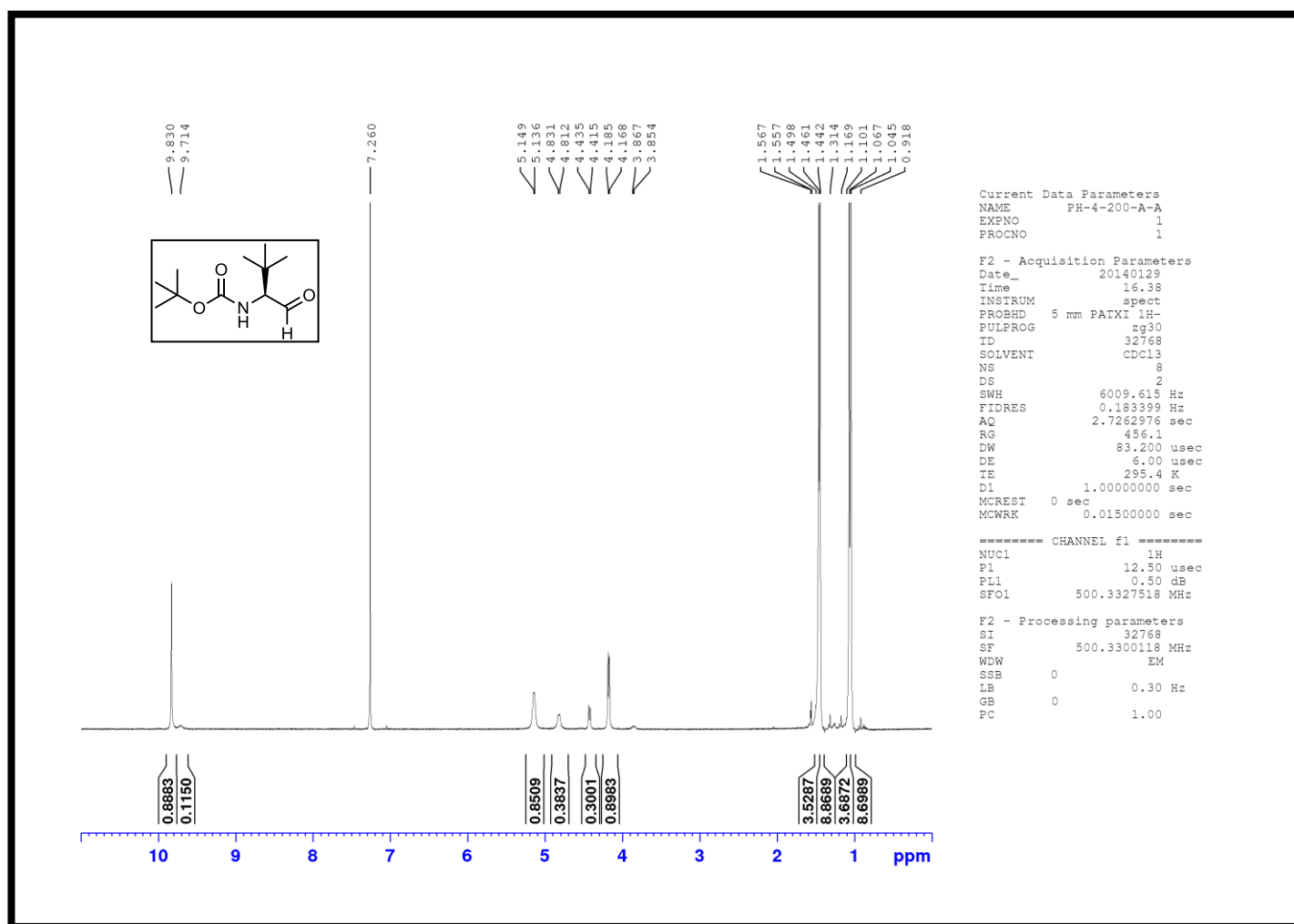
Prepared according to general procedure A (II). Isolated a mixture of product and unknown impurity by chromatography (4:1 hexanes/EtOAc, $R_f=0.2$) as white solids. This mixture was carried to the next step without further purification.



(S)-tert-butyl (3,3-dimethyl-1-oxobutan-2-yl)carbamate (N-Boc-tert-leucinal) (S12)

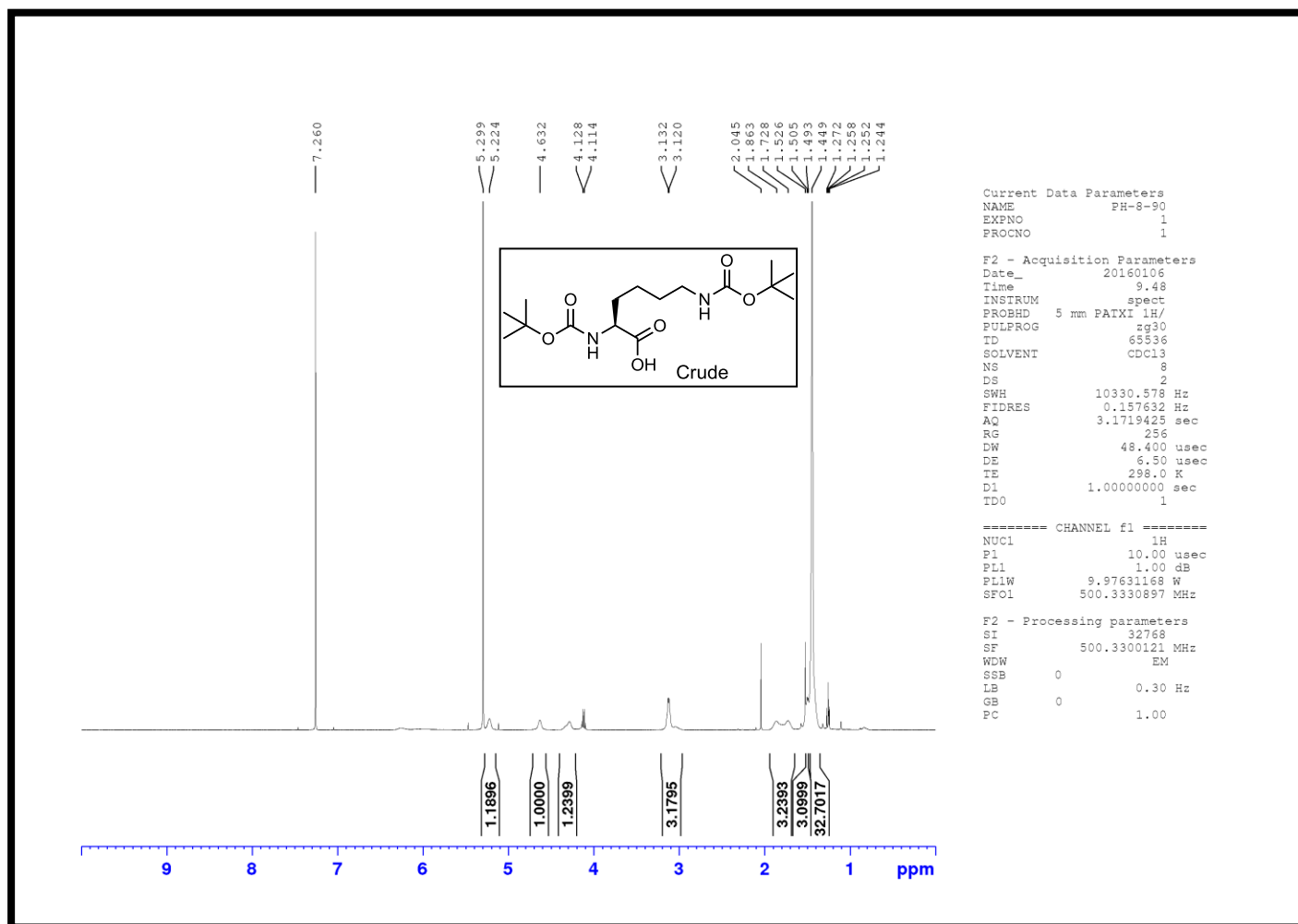
Prepared according to **general procedure A (III)**. Isolated by column chromatography (6:1 Hex/EtOAc, R_f = 0.28) followed by re-crystallization from a mixture of EtOAc:hexanes overnight at $-20\text{ }^{\circ}\text{C}$ as a white needle-like crystals (95 mg, 6% yield over 3 steps). Spectral data match the previously reported values.¹⁹

^1H NMR (600 MHz, CDCl_3); mixture of rotamers; δ 9.83 (s, 0.8H), 9.71 (s, 0.2H), 5.14 (s, 0.8H), 4.82 (s, 0.2H), 4.42 (d, J = 10.2 Hz, 0.2H), 3.95 (d, J = 8.6 Hz, 0.8H), 1.46 (s, 2.7H), 1.44 (s, 7.3H), 1.06 (s, 2.7H), 1.05 (s, 7.3H).



(S)-2,6-bis((tert-butoxycarbonyl)amino)hexanoic acid (Boc-Lys(Boc)-OH) (S13)

Prepared according to a literature procedure.²⁰ The crude reaction mixture was carried to next step without further purification.

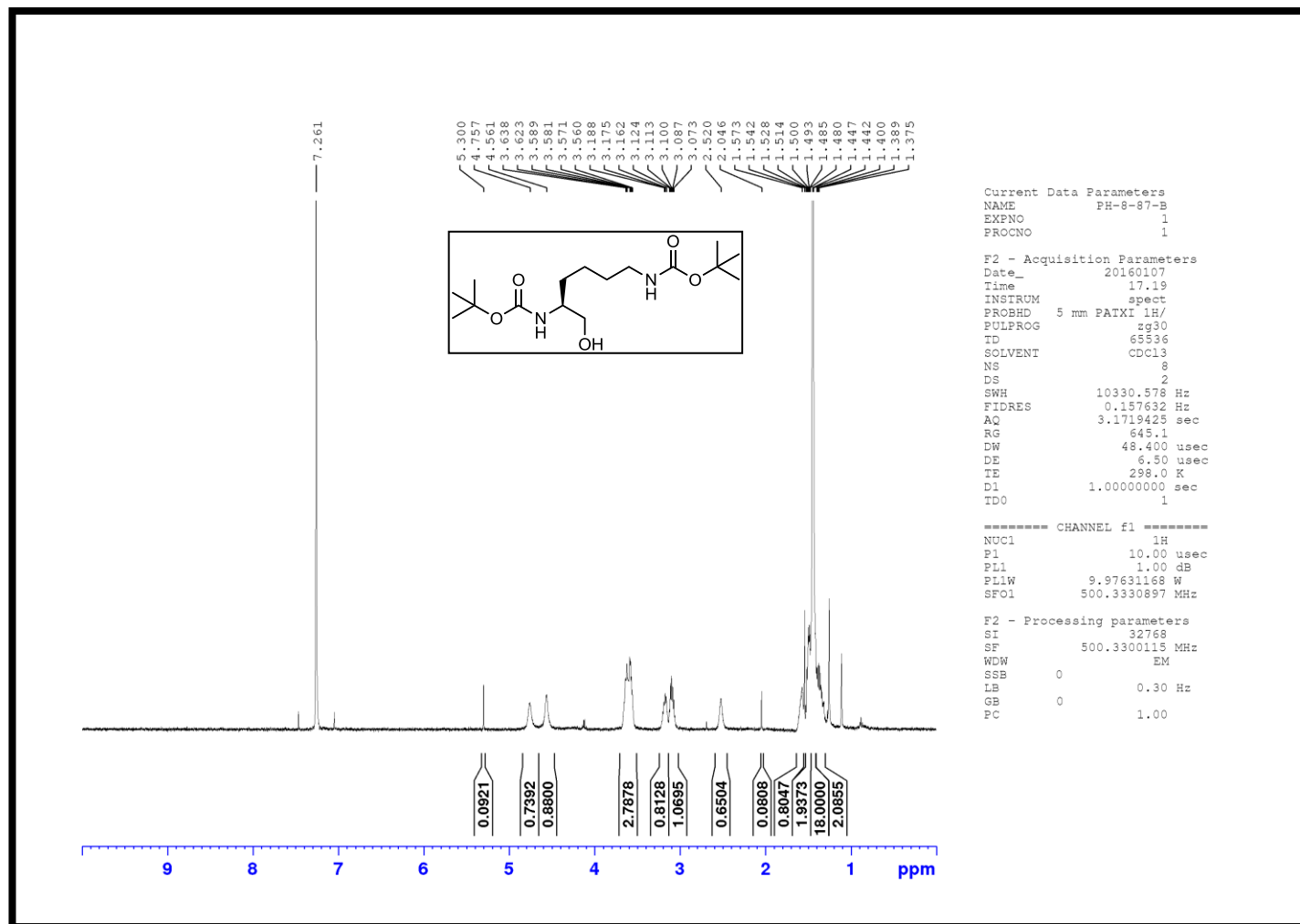


(S)-di-tert-butyl (6-hydroxyhexane-1,5-diyl)dicarbamate (N $_{\alpha}$,N $_{\epsilon}$ -Bis(Boc)lysino)l (S14)

Prepared according to a modified **general procedure B (II)** by replacing *i*-Pr₂NEt with 4-methyl morpholine (NMM). Column chromatography (3:1 hexanes: EtOAc, R_f = 0.20) afforded the title compound as a viscous

colourless oil (99% purity, calcd. 0.547g, 64% over 2 steps). Spectral data match the previously reported values.²¹

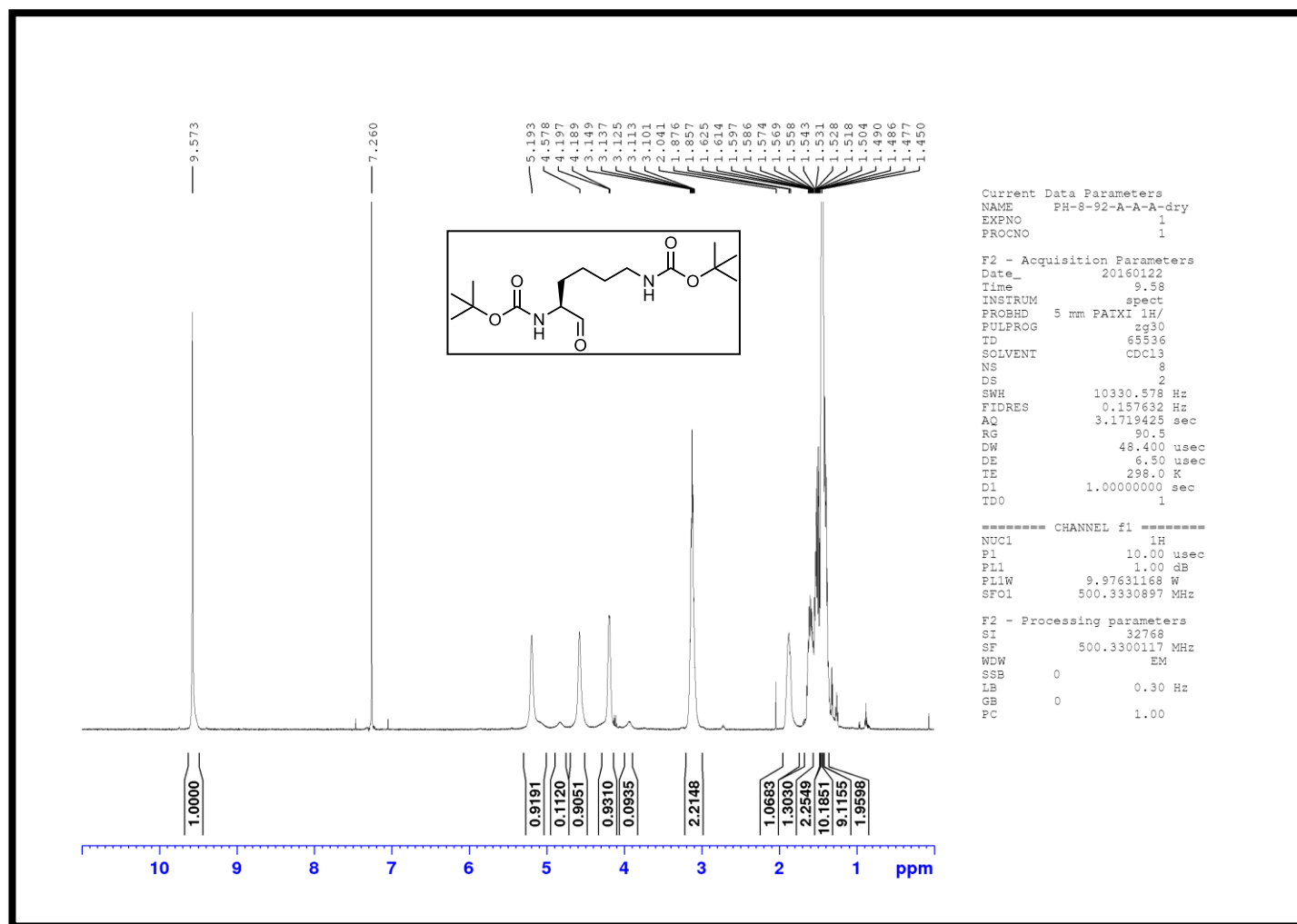
¹H NMR (500 MHz, CDCl₃); δ 4.76 (br s, 1H), 4.56 (br s, 1H), 3.71–3.51 (m, 3H), 3.24–3.14 (m, 1H), 3.13–3.02 (m, 1H), 2.52 (br s, 1H), 1.64–1.56 (m, 1H), 1.53–1.47 (m, 2H), 1.45 (s, 9H), 1.44 (s, 9H), 1.41–1.30 (m, 2H).



(S)-di-tert-butyl (6-oxohexane-1,5-diyl)dicarbamate (N α ,N ϵ -Bis(Boc)lysinal) (S15)

Prepared according to **general procedure B (III)**. Isolated by column chromatography (5:1 hexane:EtOAc, R_f = 0.16) followed by re-crystallization from a mixture of EtOAc:hexanes overnight at –20 °C as a white crystals (202 mg, 68%). Spectral data match the previously reported values.²²

¹H NMR (500 MHz, CDCl₃); Mixture of rotamers; δ 8.57 (s, 1H), 5.19 (s, 0.9H), 4.83 (s, 0.1H), 4.58 (s, 0.9H), 4.19 (ap d, *J* = 4.2 Hz, 0.9H), 3.93 (s, 0.1H), 3.21–2.99 (m, 2H), 1.96–1.75 (m, 1H), 1.68–1.55 (m, 1H), 1.56–1.47 (m, 2H), 1.45 (s, 9H), 1.44 (s, 9H), 1.42–1.34 (m, 2H).



Reaction Optimization

Catalyst screening reactions were performed using valine derivative **15** as the acceptor and furfural (**17**) as the coupling partner (Table 1).

Using catalyst **1** the corresponding α -hydroxy- β -amino ketone was obtained as the major product with good diastereoselectivity with the undesired cross-benzoin and *N*-Boc-alaninal

homo-benzoin reaction pathways suppressed (entry 1). For these reactions, the homo-benzoin product from dimerization of excess furfural (**18**) could easily be removed by column chromatography. Importantly, only trace amounts of the other two possible benzoin products were formed. The use of other catalysts resulted in lower yields or lower diastereomeric ratios of products under the reaction conditions (entries 2-4). Screening of various solvents revealed that the reaction is best performed in toluene or dichloromethane (entries 5-7). The use of various bases showed that catalytic amounts of DBU furnish the cross-benzoin products in higher yield, albeit in lower diastereomeric ratios (entries 8-10). Due to the susceptibility of enantio-enriched *N*-Boc-amino aldehydes towards racemization, Hünig's base was chosen as the optimal base. Optimized conditions were reached by modification of the stoichiometry of reagents; use of 2 equivalents of Hünig's base improved the yield, as did the use of a larger excess of furfural. It is worth mentioning that a large excess of **1** is not a requirement to obtain useful yields of the cross-benzoin products *i.e.* good yields (80%) could be achieved by using 1.5 equivalents of **1** (entries **12-13**).

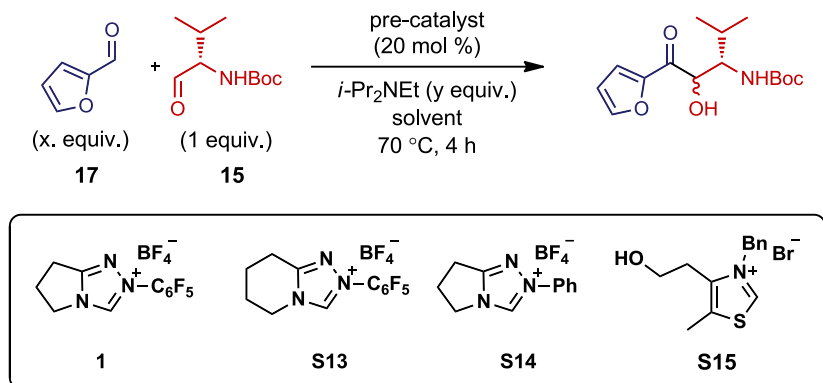
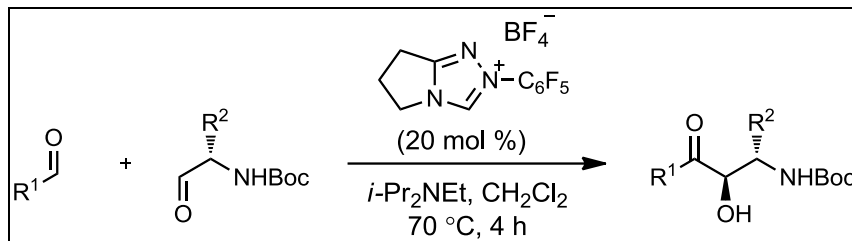


Table 1. Optimization of the reaction conditions

Entry	x equiv.	Pre-catalyst	y equiv.	solvent	base	% NMR yield (d.r.) ^a
1	1.5	1	1	CH ₂ Cl ₂	<i>i</i> -Pr ₂ NEt	74 (7 : 1)
2	1.5	S13	1	CH ₂ Cl ₂	<i>i</i> -Pr ₂ NEt	38 (7 : 1)
3	1.5	S14	1	CH ₂ Cl ₂	<i>i</i> -Pr ₂ NEt	38 (5 : 1)
4	1.5	S15	1	CH ₂ Cl ₂	<i>i</i> -Pr ₂ NEt	64 (6 : 1)
5	1.5	1	1	MeOH	<i>i</i> -Pr ₂ NEt	71 (7 : 1)
6	1.5	1	1	THF	<i>i</i> -Pr ₂ NEt	55 (3 : 1)
7	1.5	1	1	toluene	<i>i</i> -Pr ₂ NEt	72 (6 : 1)
8	1.5	1	1	CH ₂ Cl ₂	CsOAc	71 (5 : 1)
9	1.5	1	1	CH ₂ Cl ₂	DBU	84 (4 : 1)
10	1.5	1	1	CH ₂ Cl ₂	Cs ₂ CO ₃	41 (5 : 1)
11	1.5	1	1	CH ₂ Cl ₂	<i>i</i> -Pr ₂ NEt	75 (9 : 1) ^b
12	1.5	1	2	CH ₂ Cl ₂	<i>i</i> -Pr ₂ NEt	80 (7 : 1)
13	3	1	2	CH ₂ Cl ₂	<i>i</i> -Pr ₂ NEt	83 (7 : 1)

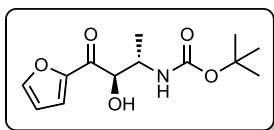
^a Combined yield of both diastereomers determined by ¹H NMR analysis using dimethyl terephthalate as the internal standard. ^b Reaction carried out at 40 °C for 16 hours.

General procedure for NHC-catalyzed cross-benzoin reactions



The corresponding *N*-Boc-amino aldehyde (0.24 mmol, 1.0 equiv.) and triazolium salt **1** (0.048 mmol, 0.2 equiv.) were added to an oven-dried test tube with a Schlenk take-off and fitted with a septum. The vessel was placed under vacuum and re-filled with argon three times to ensure inert atmosphere. The aliphatic or heteroaromatic aldehyde (0.72 mmol, 3 equiv.) and CH₂Cl₂ (0.3 mL, 0.8 M) were added sequentially. Lastly *i*-Pr₂NEt (0.48 mmol, 2 equiv.) was added and the septum was then quickly exchanged for a cold finger. Once inert atmosphere was re-established the flask was sealed and heated to 70 °C for 4 hours. (WARNING: when performed on a larger scale, it is advised to use a water condenser instead of a cold finger to avoid the small pressure buildup that occurs when using a cold finger (see SI p. 62). The crude reaction mixture was cooled to room temperature and quenched by addition of 1M HCl (2 mL). The reaction crude was extracted with CH₂Cl₂ (3×2 mL) and dried over Na₂SO₄. The reaction mixture was purified by column chromatography followed by preparative thin layer chromatography to afford the corresponding cross-benzoin product.

tert-butyl ((2*S*,3*R*)-4-(furan-2-yl)-3-hydroxy-4-oxobutan-2-yl)carbamate (**2**)



Column chromatography (4:1 hexanes: EtOAc) followed by PTLC (7:1 toluene:

EtOAc) afforded the major product as a white solid (26 mg, 41%). Melting range =

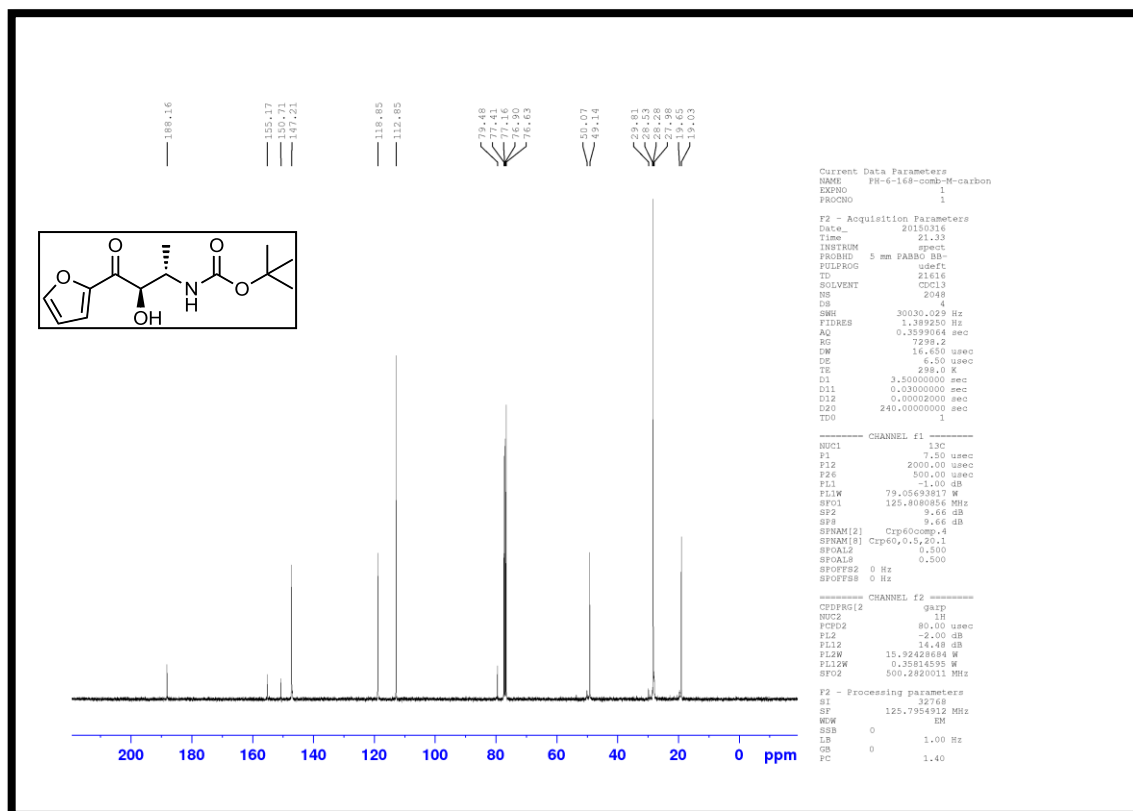
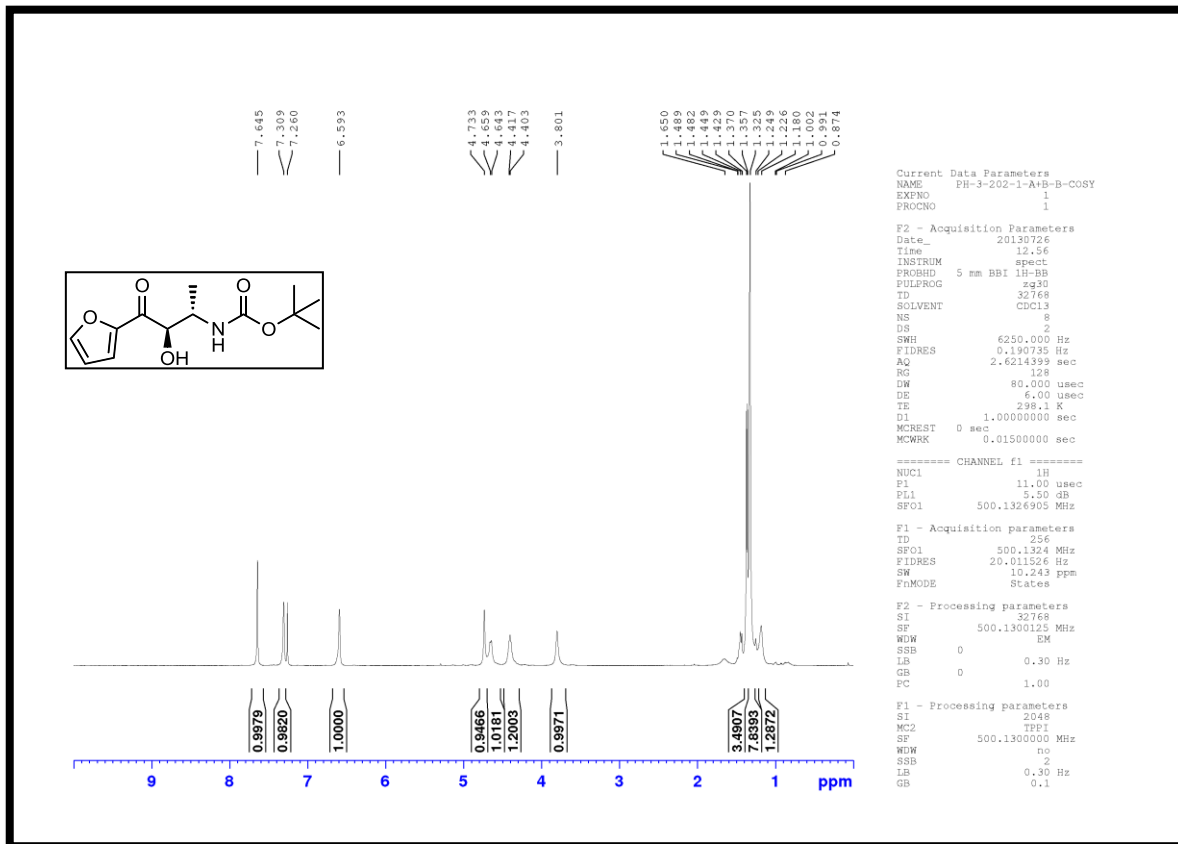
136.2–136.8 °C, *R*_f = 0.20 (20% acetone in hexanes); [α]_D^{25 °C} = +82 (*c* 1.3, CHCl₃); **FTIR** (KBr film) ν_{max}

(cm⁻¹): 3435, 3375, 2977, 2932, 1703, 1680, 1571, 1502, 1466, 1366, 1246, 1166, 1109, 1059, 768; **¹H NMR**

(500 MHz, CDCl₃) Mixture of rotamers: δ 7.65 (s, 1H), 7.31 (br s, 1H), 6.59 (br s, 1H), 4.73 (s, 1H), 4.66 (br d, *J* = 8.3 Hz 1H), 4.46–4.33 (m, 1H), 3.80 (br s, 1H), 1.36 (d, *J* = 6.9 Hz, 3H), 1.33 (s, 7.8H), 1.18 (s, 1.2H);

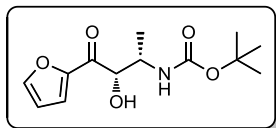
¹³C NMR (125 MHz, CDCl₃) Mixture of rotamers (minor rotamer indicated by asterisk): δ 188.2, 155.2, 150.7,

147.2, 118.9, 112.9, 79.5, 76.6, 50.0*, 49.1, 28.3, 28.0*, 19.7*, 19.0; **HRMS** (CI) m/z : $[M+1]^+$ Calcd for $C_{13}H_{20}NO_5$ 270.1342; Found 270.1337.



The minor diastereomer was also isolated, along with an unidentified impurity:

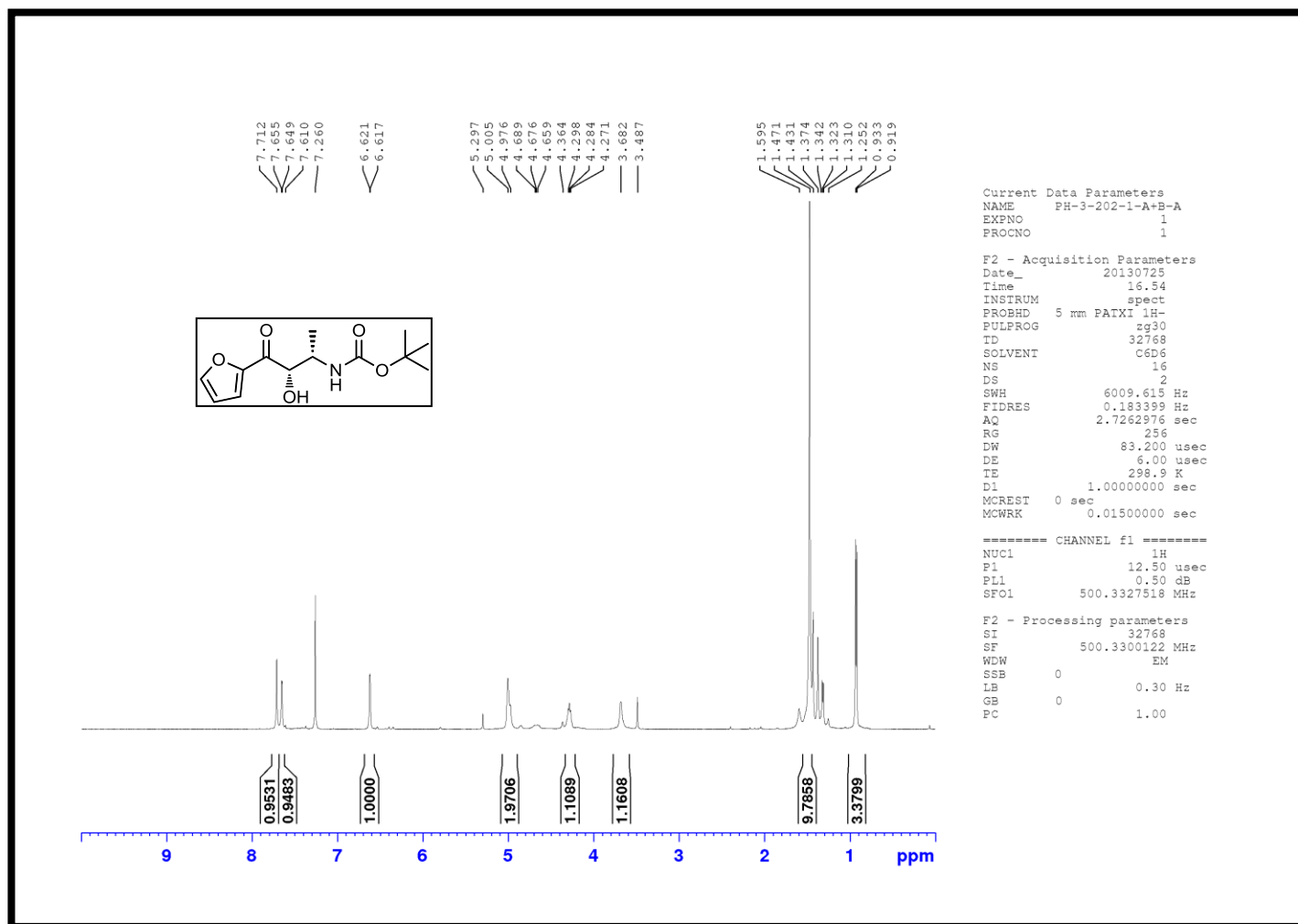
***tert*-butyl ((2*S*,3*S*)-4-(furan-2-yl)-3-hydroxy-4-oxobutan-2-yl)carbamate (S16)**



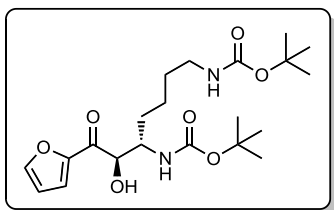
¹H NMR (500 MHz, CDCl₃) δ 7.72 (s, 1H). 7.65 (d, *J* = 3.4 Hz, 1H), 6.62 (d, *J* =

1.9 Hz, 1H), 5.07–4.90 (m, 2H), 4.28 (ap t, *J* = 6.8 Hz, 1H), 3.68 (br s, 1H), 1.47 (s,

9H), 0.93 (t, *J* = 5.3 Hz, 3H).

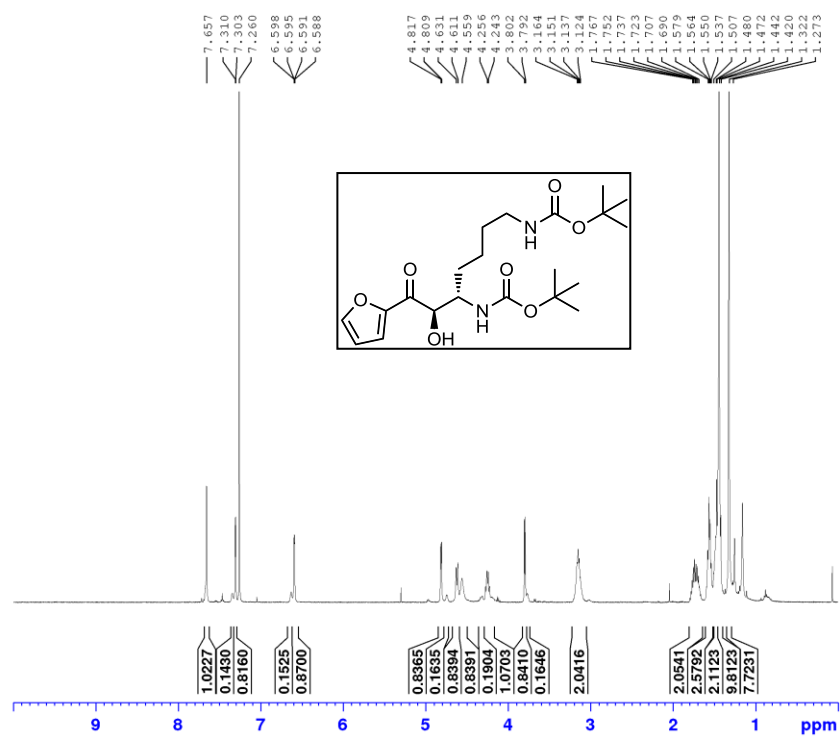


di-*tert*-butyl ((5*S*,6*R*)-7-(furan-2-yl)-6-hydroxy-7-oxoheptane-1,5-diyl)dicarbamate (3)



Column chromatography (3:1 hexanes:Acetone $R_f = 0.15$ (25% acetone in hexanes) followed by PTLC (7:3 toluene: EtOAc) afforded varying mixtures (6:1–9:1) of the two diastereomers (major= 57.4 mg, minor=33.6 mg, 89%). An

analytically pure sample of the major diastereomer was prepared by subjecting a 9:1 mixture of diastereomers to PTLC (6:2:1:1 toluene:hexane:EtOAc:acetone) as a yellow oil; $[\alpha]_D^{26\text{ }^\circ\text{C}} = -105$ (c 0.24, CHCl_3); **FTIR** (KBr film) ν_{max} (cm^{-1}): 3364, 2977, 2932, 1685, 1570, 1391, 1366, 1249, 1170, 768; **^1H NMR** (500 MHz, CDCl_3) Mixture of rotamers: δ 7.66 (s, 1H), 7.31 (s, 0.1H), 7.30 (s, 0.9H), 6.60 (s, 0.1H), 6.59 (s, 0.9H), 4.81 (d, $J = 6.9$ Hz, 0.9H), 4.75 (s, 0.1H), 4.62 (d, $J = 10$ Hz, 0.9H) 4.56 (br s, 1H), 4.33 (d, $J = 11$ Hz, 0.1H), 4.29–4.17 (m, 1H), 3.81 (d, $J = 5.3$ Hz, 0.9H), 3.78–3.74 (m, 0.1H), 3.23–3.05 (m, 2H), 1.81–1.65 (m, 2H), 1.61–1.52 (m, 2H), 1.52–1.46 (m, 2H), 1.44 (s, 9H), 1.32 (s, 9H); **^{13}C NMR** (125 MHz, CDCl_3) Mixture of rotamers (minor rotamer indicated by asterisk): δ 188.2, 156.2, 155.5, 150.6, 147.3, 118.9, 112.9, 79.5, 75.3, 53.0, 40.5, 32.9, 29.8, 28.6, 28.3, 27.9*, 23.4.; **HRMS** (TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{21}\text{H}_{34}\text{N}_2\text{O}_7\text{Na}$ 449.2258; Found 449.2260.

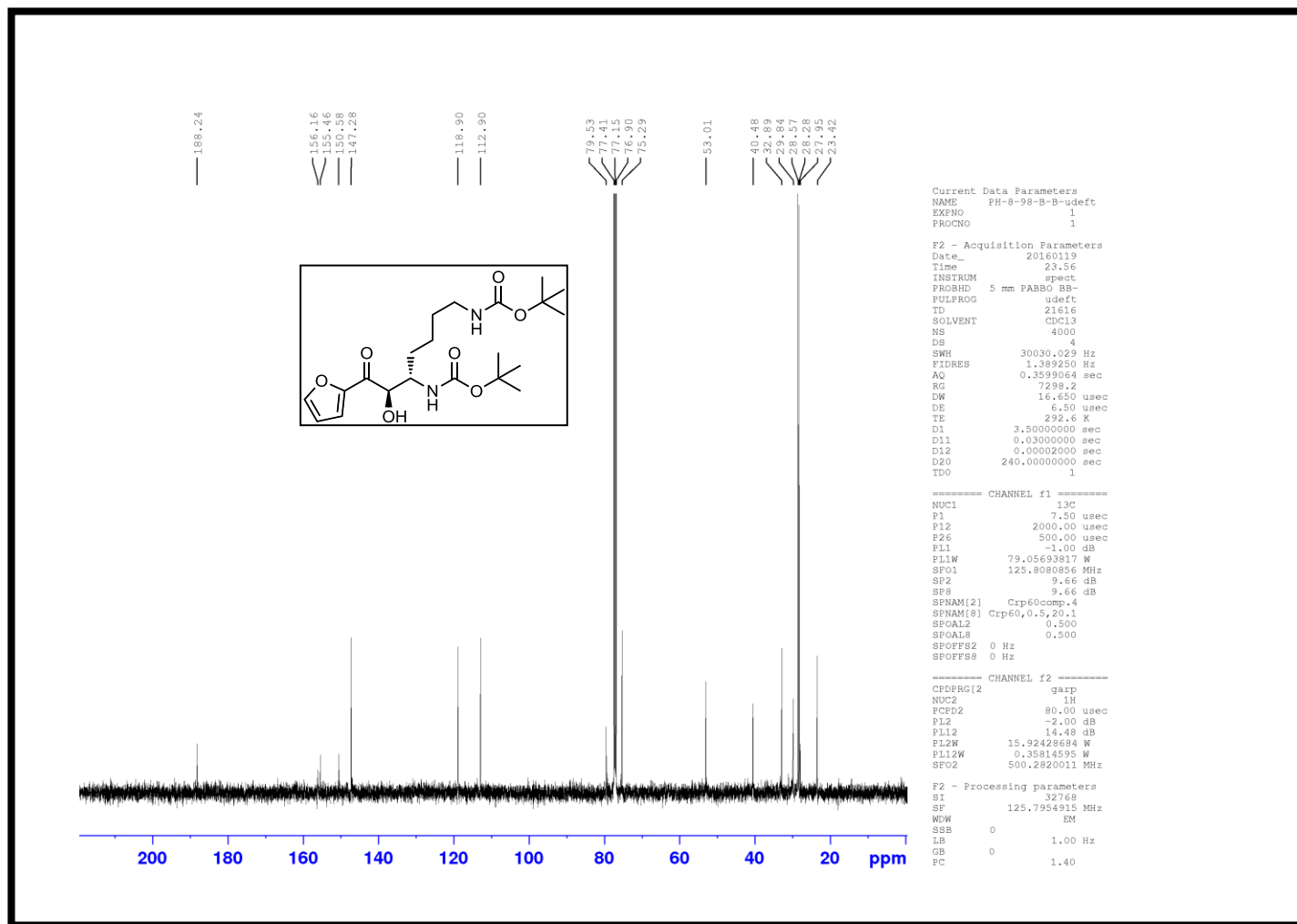


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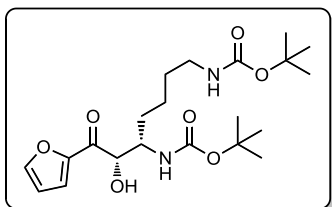
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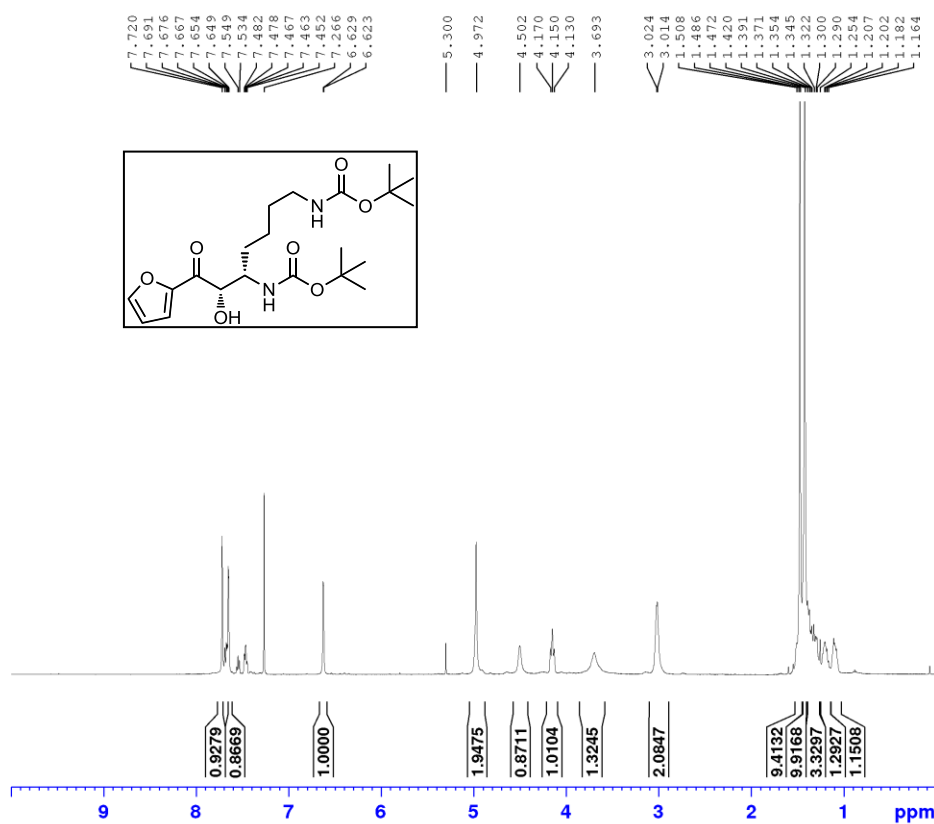


The minor diastereomer was also isolated along with an unknown impurity:

di-tert-butyl ((5S,6S)-7-(furan-2-yl)-6-hydroxy-7-oxoheptane-1,5-diyl)dicarbamate (S17)



¹H NMR (500 MHz, CDCl₃) Mixture of rotamers: δ 7.72 (s, 1H), 7.65 (br s, 1H), 7.63 (br s, 1H), 4.97 (br s, 2H), 4.50 (br s, 1H), 4.15 (ap t, *J* = 10 Hz, 1H), 1.69 (br s, 1H), 3.10–2.90 (m, 2H), 1.47 (s, 9H), 1.44–1.41 (m, 10H), 1.39–1.26 (m, 3H), 1.25–1.14 (m, 1H), 1.14–1.03 (m, 1H).



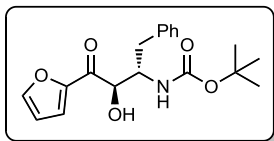
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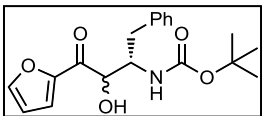
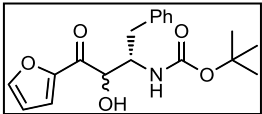
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***tert*-butyl ((2*S*,3*R*)-4-(furan-2-yl)-3-hydroxy-4-oxo-1-phenylbutan-2-yl)carbamate (4)**

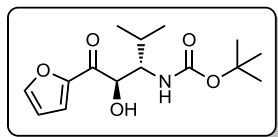


Column chromatography (7:1 toluene: EtOAc) afforded an inseparable 3:1 mixture of two diastereomers (60 mg, 73% yield). R_f = 0.23 (14% EtOAc in toluene); **FTIR** (KBr film) ν_{\max} (cm^{-1}): 3437, 2977, 2930, 1699, 1570, 1497, 1466, 1391, 1367, 1169, 1018,

912, 883, 764; **^1H NMR** (600 MHz, CDCl_3) Mixture of two diastereomers and rotamers. Major diastereomer: δ 7.69 (s, 0.2H), 7.69 (s, 0.8H), 7.49–7.39 (m, 4.3H), 7.38–7.33 (m, 0.7H), 7.29–7.24 (m, 0.8H), 7.14–7.09 (m, 0.8H), 6.80–6.56 (m, 1H), 4.96 (d, J = 9.7 Hz, 0.9H), 4.83–4.74 (m, 1.3H), 4.61–4.52 (m, 1H,), 3.98 (br s, 1H), 3.14 (dd, , J = 13.4, 6.2 Hz, 1H,), 3.08 (dd, , J = 13.0, 9.6 Hz, 1H,), 1.41 (s, 8.4H), 1.19 (s, 1.6H); Minor diastereomer: δ 7.64 (s, 1H,), 7.61 (d, J = 3.3 Hz, 1H,), 7.49–7.39 (m, 1H), 7.38–7.19 (m, 3H), 7.24–7.09 (m, 2H), 6.74–6.63 (m, 1H), 5.19 (d, J = 9.1 Hz, 1H,), 5.11 (s, 0.9H,), 5.06–5.01 (m, 0.1H), , 4.69–4.62 (m, 1H,), 4.06 (s, 1H), 2.82 (dd, , J = 14.3, 9.1 Hz, 1H,), 2.71 (dd, , J = 14.3, 5.5 Hz, 1H,), 1.48 (s, 9H); **^{13}C NMR** (125 MHz, CDCl_3) major diastereomer as a mixture of rotamers (minor rotamer indicated by asterisk): δ 188.2, 155.2, 150.1, 147.3, 146.9*, 137.9, 129.7, 129.6, 128.7, 126.8, 119.0, 118.8*, 112.7, 112.6, 79.6, 76.1, 73.2, 56.1*, 55.0, 39.9, 39.2, 28.3; minor diastereomer: δ 187.2, 155.6, 150.0, 147.9, 137.1, 129.3, 128.3, 126.5, 120.6, 112.8, 177.36, 79.8, 74.1, 55.3, 34.7, 28.4, 27.8; **HRMS** (TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_5$ 368.1468; Found 368.1467.



***tert*-butyl ((2*R*,3*S*)-1-(furan-2-yl)-2-hydroxy-4-methyl-1-oxopentan-3-yl)carbamate (5)**



Column chromatography (4:1 hexanes: EtOAc) followed by PTLC (3:1 hexanes:

EtOAc) afforded the major product as a colourless oil (52 mg, 73%). $R_f = 0.20$ (30%

acetone in hexanes); $[\alpha]_D^{23} = +65$ (c 0.8, CHCl_3); **FTIR** (KBr film) ν_{max} (cm^{-1}): 3446,

3377, 2973, 1710, 1682, 1469, 1390, 1366, 1172, 1020, 769; **^1H NMR** (600 MHz, CDCl_3) Mixture of rotamers:

δ 7.65 (s, 0.2H), 7.64 (s, 0.8H), 7.32 (d, $J = 3.4$ Hz, 0.2H), 7.28 (d, $J = 3.6$ Hz, 0.8H), 6.64–6.61 (m, 0.2H), 6.58

(dd, $J = 3.5, 1.6$ Hz, 0.8H), 5.02 (dd, $J = 5.2, 1.3$ Hz, 0.8H), 4.97 (d, $J = 4.7$ Hz, 0.2H), 4.69 (d, $J = 10.2$ Hz,

0.8H), 4.47 (d, $J = 10.5$ Hz, 0.2H), 3.93 (dd, $J = 9.8, 1.3$ Hz, 0.8H), 3.86–3.81 (m, 0.2H), 3.81 (d, $J = 5.2$ Hz,

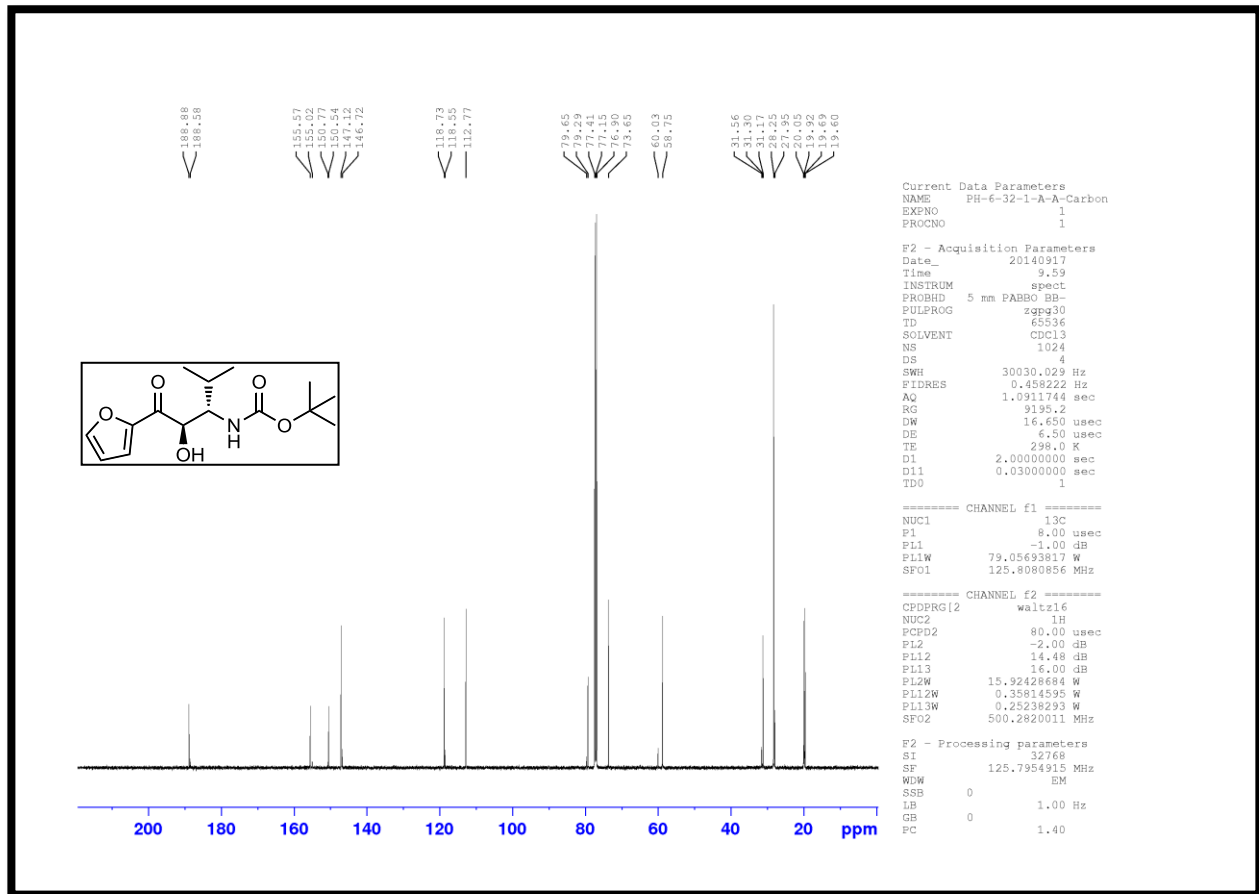
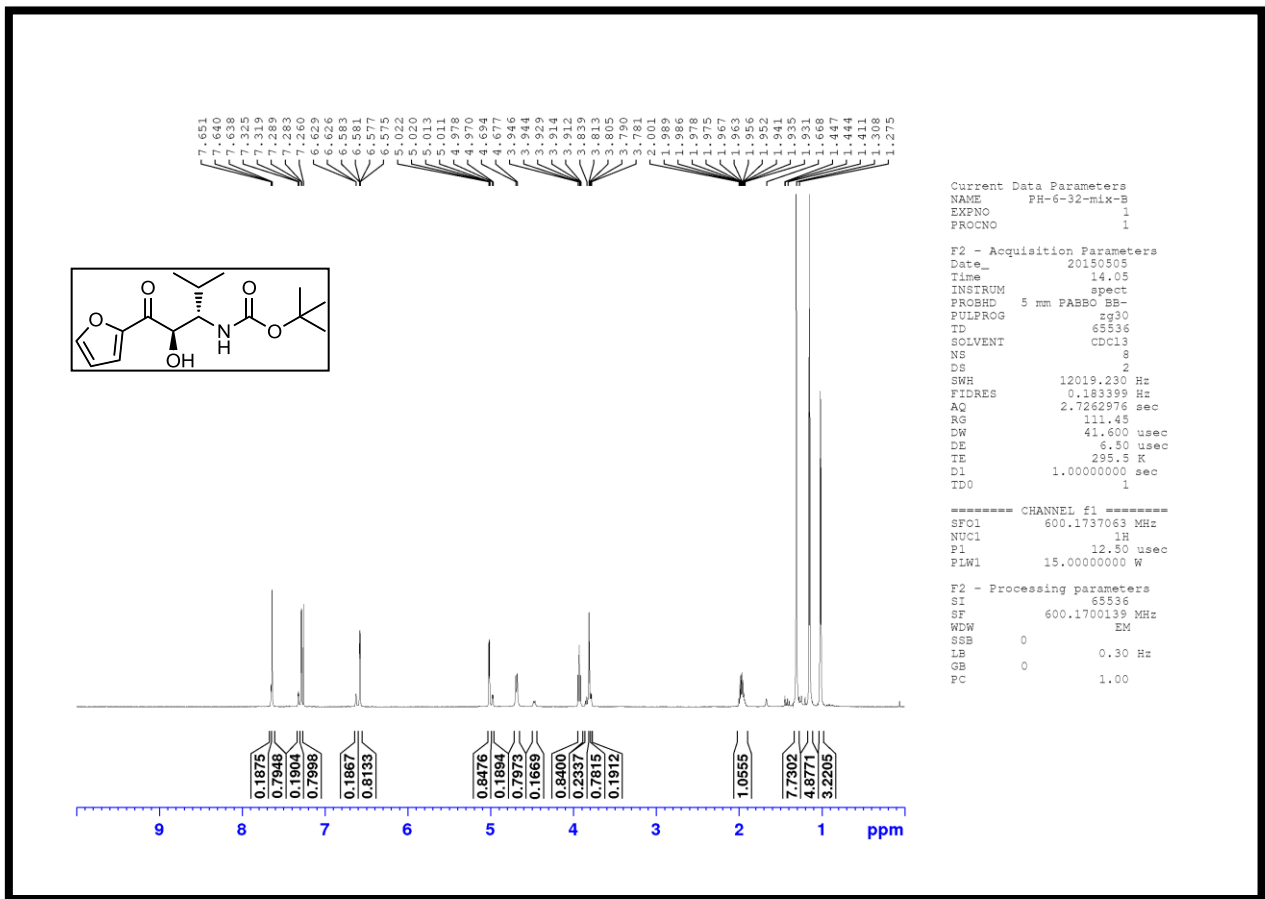
0.8H), 3.79 (d, $J = 5.3$ Hz, 0.2H), 2.02–1.90 (m, 1H), 1.31 (s, 7.7H), 1.15 (d, $J = 6.8$ Hz, 3H), 1.14 (s, 1.3H),

1.01 (d, $J = 6.7$ Hz, 3H); **^{13}C NMR** (125 MHz, CDCl_3) Mixture of rotamers (minor rotamer indicated by

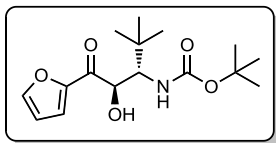
asterisk): δ 188.9, 188.6*, 155.6, 155.02*, 150.8*, 150.5, 147.1, 146.7, 118.7, 118.6*, 112.8, 112.8*, 79.7*,

79.3, 73.7, 60.0*, 58.8, 31.6*, 31.2, 28.3, 28.0*, 20.1*, 19.9, 19.7*, 19.6; **HRMS** (TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd

for $\text{C}_{15}\text{H}_{23}\text{NO}_5\text{Na}$ 320.1468; Found 320.1473.



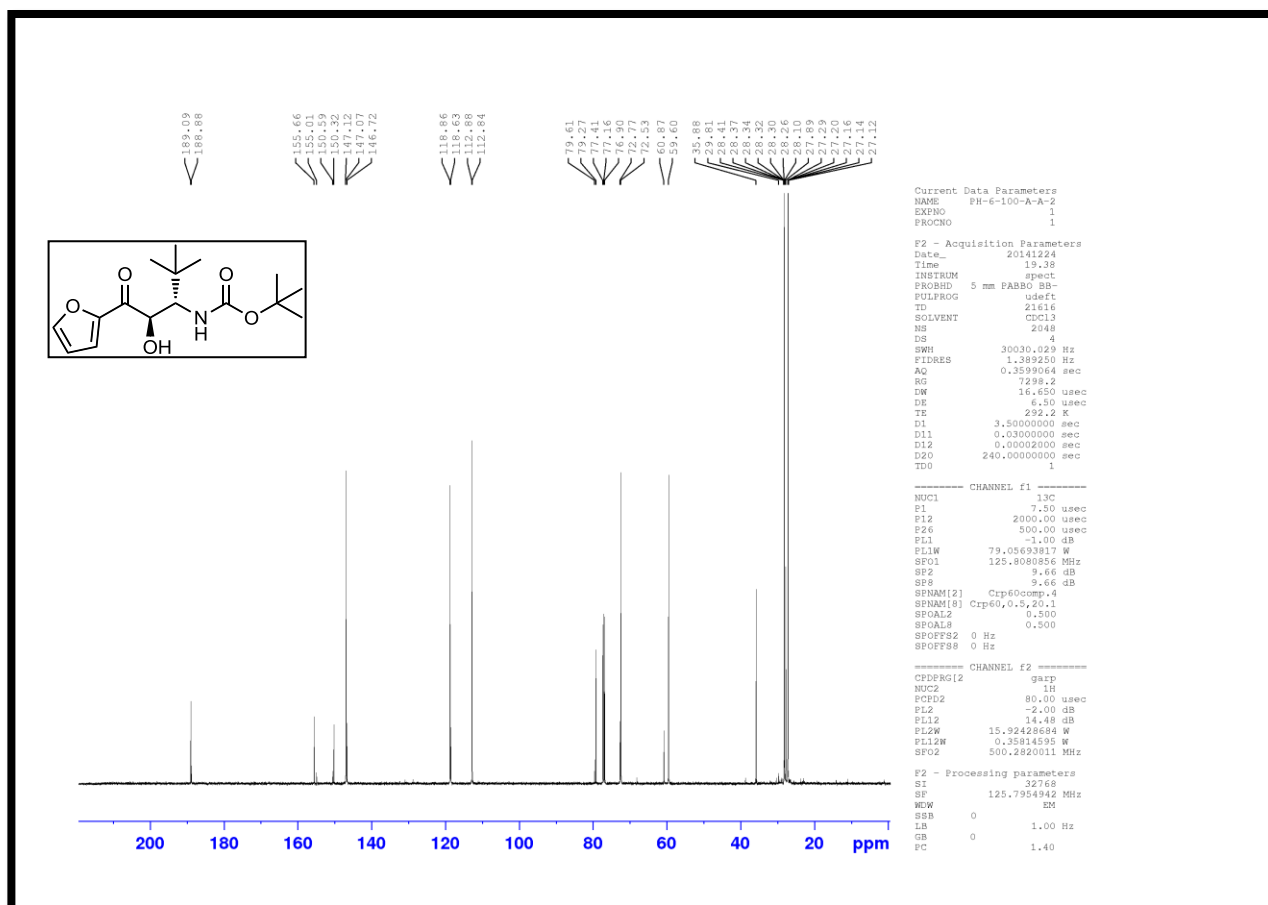
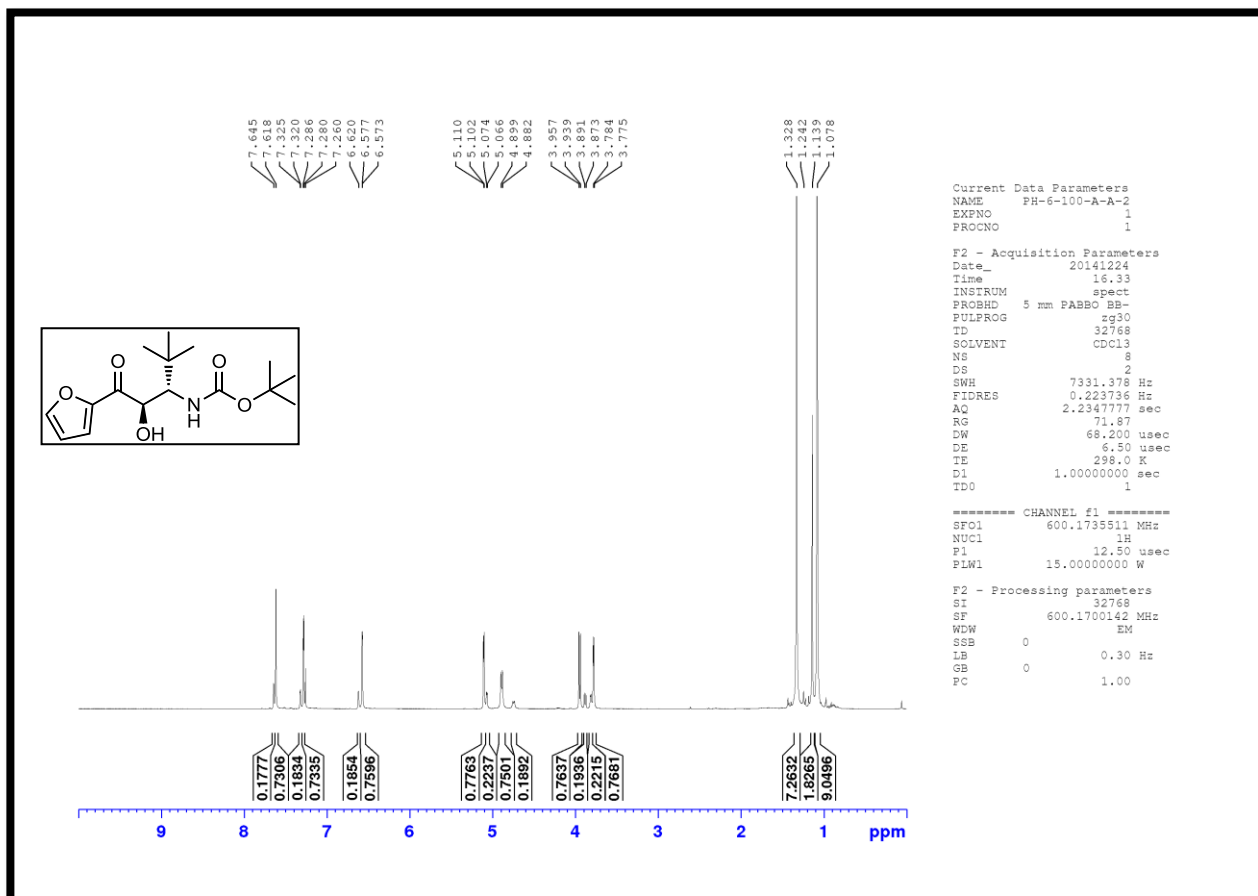
***tert*-butyl ((2*R*,3*S*)-1-(furan-2-yl)-2-hydroxy-4,4-dimethyl-1-oxopentan-3-yl)carbamate (6)**



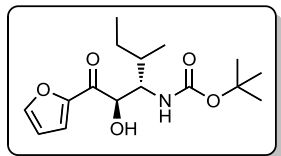
Column chromatography (4:1 hexanes: EtOAc) followed by PTLC (7:1 toluene: EtOAc) afforded the major product as a white solid (52 mg, 73%). Melting range = 84.2–85.6 °C, R_f = 0.24 (20% acetone in hexanes); $[\alpha]_D^{27} = +1.5$ (c 0.5, CHCl_3);

FTIR (KBr film) ν_{max} (cm^{-1}): 3450, 3134, 2965, 1703, 1679, 1571, 1493, 1468, 1367, 1232, 1171, 1059, 768;

^1H NMR (600 MHz, CDCl_3) Mixture of rotamers: δ 7.64 (s, 0.2H), 7.62 (s, 0.8H), 7.32 (d, J = 3.2 Hz, 0.2H), 7.28 (d, J = 3.5 Hz, 0.8H), 6.64–6.60 (m, 0.2H), 6.60–6.54 (m, 0.8H), 5.10 (d, J = 4.9 Hz, 0.8), 5.07 (d, J = 4.8 Hz, 0.2H), 4.89 (d, J = 10.5 Hz, 0.8H), 4.75 (d, J = 10.3 Hz, 0.2H), 3.95 (d, J = 10.7 Hz, 0.8H), 3.88 (d, J = 10.9 Hz, 0.2H), 3.81 (d, J = 5.2 Hz, 0.2H), 3.78 (d, J = 5.2 Hz, 0.8H), 1.33 (s, 7.3H), 1.14 (s, 1.8H), 1.08 (s, 9H); **^{13}C NMR** (125 MHz, CDCl_3) Mixture of rotamers (minor rotamer indicated by asterisk): δ 189.1, 188.9*, 155.7, 155.0*, 150.6*, 150.3, 147.1, 146.7, 118.9, 118.6*, 112.9, 112.8*, 79.6*, 79.3, 72.8*, 72.5, 60.9*, 59.6, 38.8*, 35.9, 28.3, 27.9, 27.3; **HRMS** (TOF) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{16}\text{H}_{26}\text{NO}_5$ 312.1806; Found 312.1801.

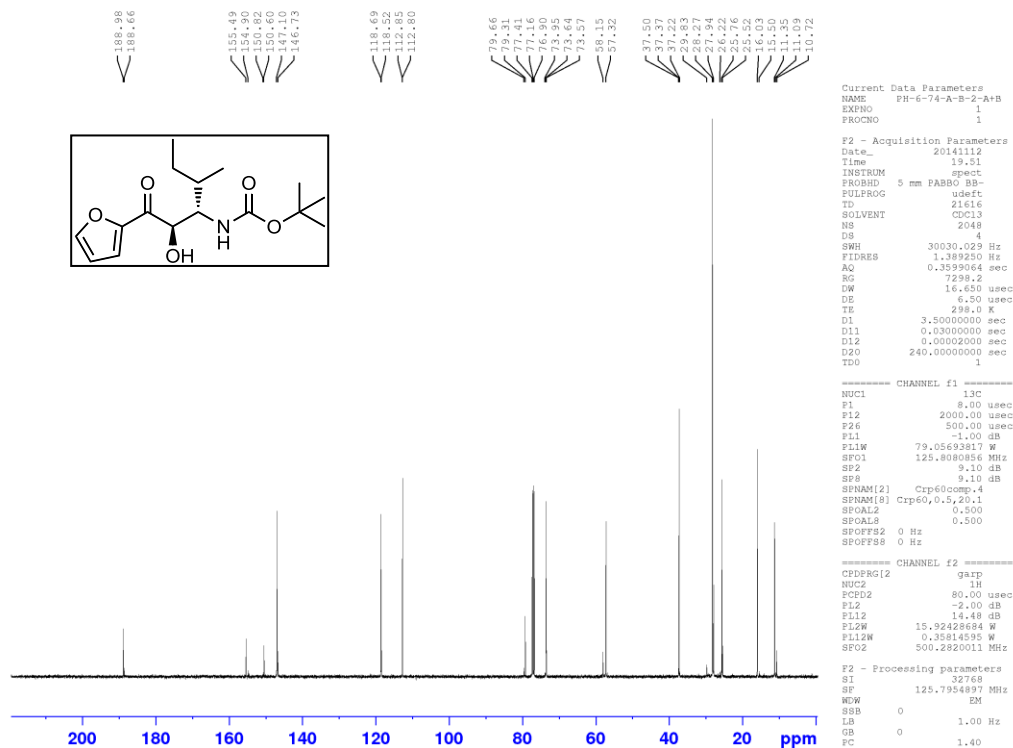
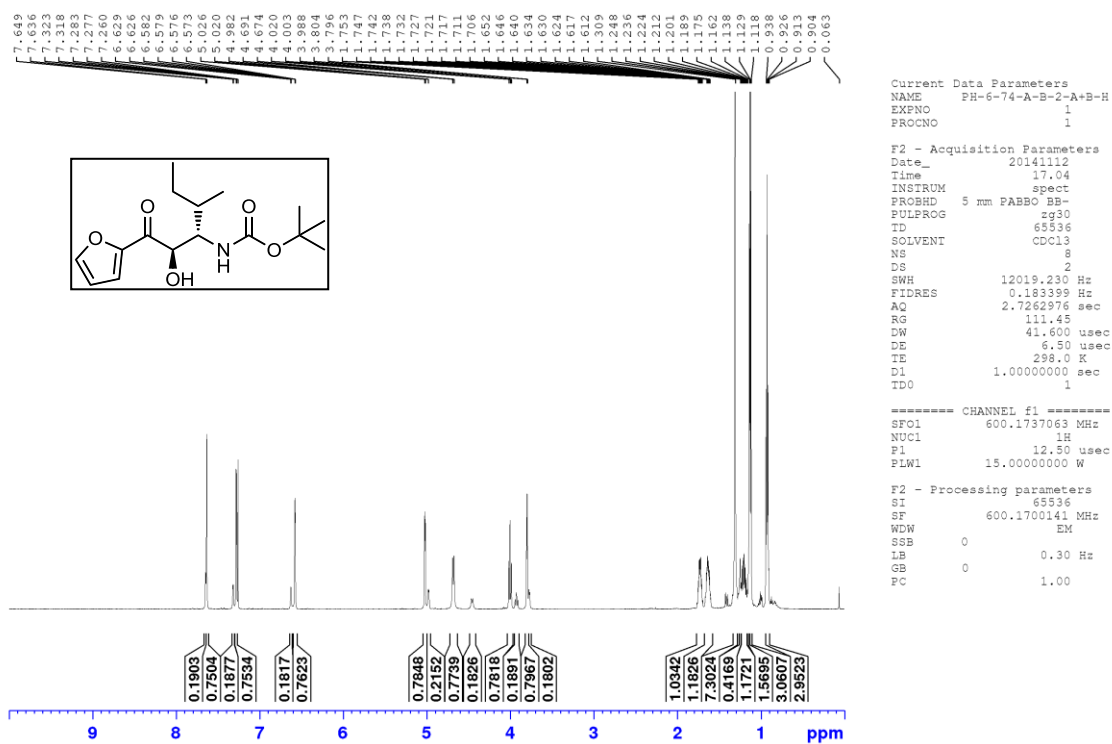


tert-butyl ((2*R*,3*S*,4*R*)-1-(furan-2-yl)-2-hydroxy-4-methyl-1-oxohexan-3-yl)carbamate (7)

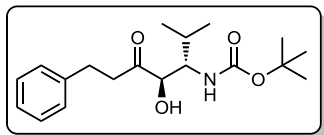


Column chromatography (5:1 hexane:acetone) followed by PTLC (7:1 toluene: EtOAc) afforded the major product as a 13:1 mixture of diastereomers as a colourless oil (58 mg, 71%). An analytically pure sample was prepared by further purification by

PTLC (75:25:0.25 hexanes:EtOAc:MeOH). R_f = 0.20 (20% acetone in hexanes); $[\alpha]_D^{27} = +59$ (c 1.0, CHCl_3); **FTIR** (KBr film) ν_{max} (cm^{-1}): 3447, 3378, 2967, 2932, 1706, 1683, 1468, 1390, 1366, 1172, 1018, 768; **^1H NMR** (600 MHz, CDCl_3) mixture of rotamers: δ 7.65 (s, 0.2H), 7.64 (s, 0.8H), 7.32 (d, J = 2.7 Hz, 0.2H), 7.28 (d, J = 3.5 Hz, 0.8H), 6.64–6.61 (m, 0.2H), 6.58 (dd, J = 3.5, 1.6 Hz, 0.8H), 5.02 (d, J = 4.1 Hz, 0.8H), 4.98 (d, J = 4.3 Hz, 0.2H), 4.68 (d, J = 10.2 Hz, 0.8H), 4.46 (d, J = 10.3 Hz, 0.2H), 4.00 (dd, J = 10.2, 1.3 Hz, 0.8H), 3.92 (t, J = 9.9, 0.2H), 3.80 (d, J = 5.1 Hz, 0.8H), 3.77 (d, J = 5.0 Hz, 0.2H), 1.77–1.68 (m, 1H), 1.68–1.68 (m, 1H), 1.31 (s, 7.5H), 1.24–1.17 (m, 1H), 1.13 (s, 1.5H), 1.12 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 7.4 Hz, 3H); **^{13}C NMR** (125 MHz, CDCl_3) δ mixture of rotamers (minor rotamer indicated by asterisk): 189.0, 188.7*, 155.5, 154.9*, 150.8*, 150.6, 147.1, 146.7, 118.7, 118.5*, 112.8*, 112.8, 79.7*, 79.3, 73.6, 73.6*, 58.1*, 57.3, 37.4, 28.3, 27.9*, 25.8, 25.5*, 16.03, 15.5*, 11.35, 10.72*; **HRMS** (TOF) m/z : $[\text{M} + 1]^+$ Calcd for $\text{C}_{16}\text{H}_{26}\text{NO}_5$ 312.18110; Found 312.18178.



***tert*-butyl ((2*R*,3*S*,4*R*)-1-(furan-2-yl)-2-hydroxy-4-methyl-1-oxohexan-3-yl)carbamate (**8**)**



Column chromatography (3:2 hexanes:Et₂O) followed by PTLC (3:2

hexanes:Et₂O) afforded the major product as a colourless oil (50 mg, 62%). *R*_f =

0.19 (43% Et₂O in hexanes); [α]_D^{24 °C} = -62 (*c* 1.4, CHCl₃); HPLC analysis –

Chiralcel IC column, 5% isopropanol in hexanes, 0.1 mL/min. Major: 21.9 min, minor: 8.80 min. **FTIR** (KBr

film) ν_{max} (cm⁻¹): 3445, 3394, 2967, 2931, 1710, 1497, 1391, 1366, 1242, 1168, 1018, 699; **¹H NMR** (500

MHz, CDCl₃) δ 7.32–7.25 (m, 2H), 7.23–7.17 (m, 3H), 4.66 (d, *J* = 10.3 Hz, 0.9H), 4.45(d, *J* = 10.2 Hz, 0.1H),

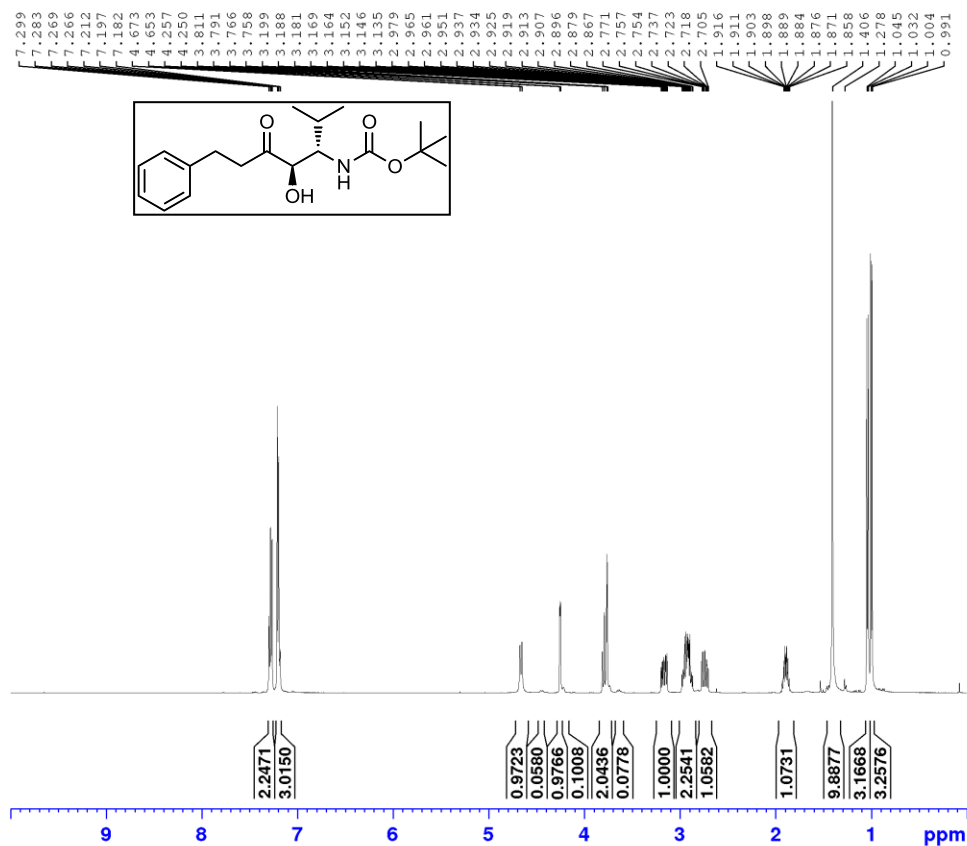
4.25 (d, *J* = 3.1 Hz, 0.9H), 4.22 (s, 0.1H), 3.83–3.71 (m, 2H), 3.64 (t, *J* = 9.9 Hz, 0.1H), 3.17 (ddd, *J* = 14.8,

9.1, 5.7 Hz, 1H), 3.00–2.85 (m, 2H), 2.74 (ddd, *J* = 16.2, 9.0, 6.8 Hz, 1H), 1.95–1.83 (m, 1H), 1.41 (s, 9H),

1.04 (d, *J* = 6.7 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H); **¹³C NMR** (125 MHz, CDCl₃) δ 210.5, 155.9, 140.7, 128.7,

128.4, 126.3, 79.7, 76.6, 58.1, 39.3, 31.0, 29.6, 28.4, 20.0, 19.6; **HRMS** (CI) *m/z*: [M+1] Calcd for C₁₉H₃₀NO₄

336.2175; Found 336.2178.

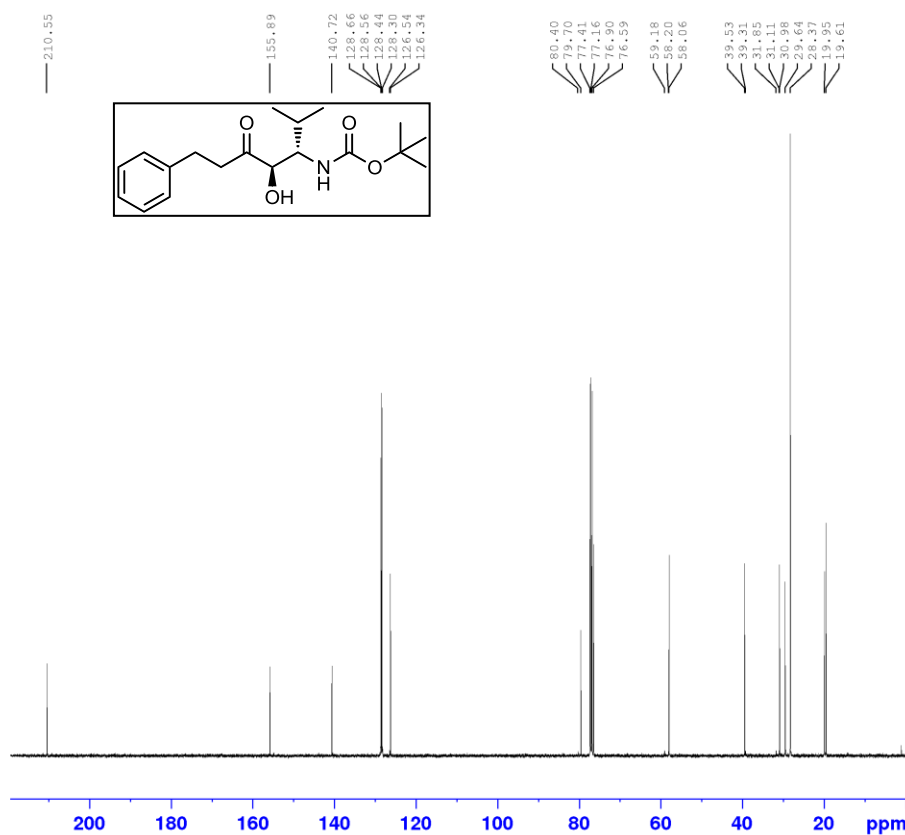


Current Data Parameters
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PROCNO 1

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DS 2
SWH 7002.801 Hz
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AQ 2.3396351 sec
RG 62.43
DW 71.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

===== CHANNEL f1 =====
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NUC1 1H
P1 8.86 usec
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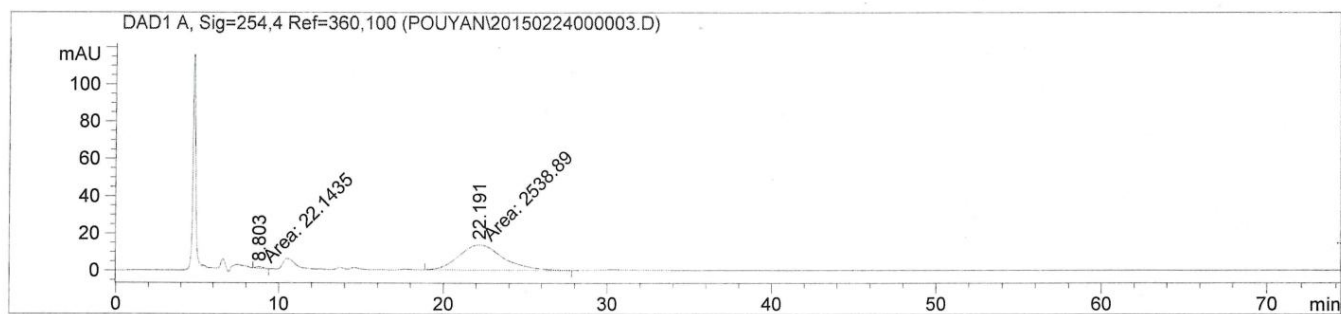


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 D1 2.00000000 sec
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 PL12 14.48 dB
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 PL13W 0.25238293 W
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F2 - Processing parameters
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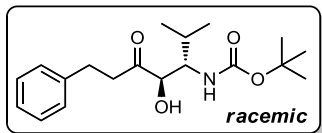


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.803	MM	0.4662	22.14355	7.91628e-1	0.8646
2	22.191	MM	3.1261	2538.88965	13.53607	99.1354

Totals : 2561.03320 14.32770

***rac*-tert-butyl-1-(furan-2-yl)-2-hydroxy-4-methyl-1-oxohexan-3-yl)carbamate (S18)**

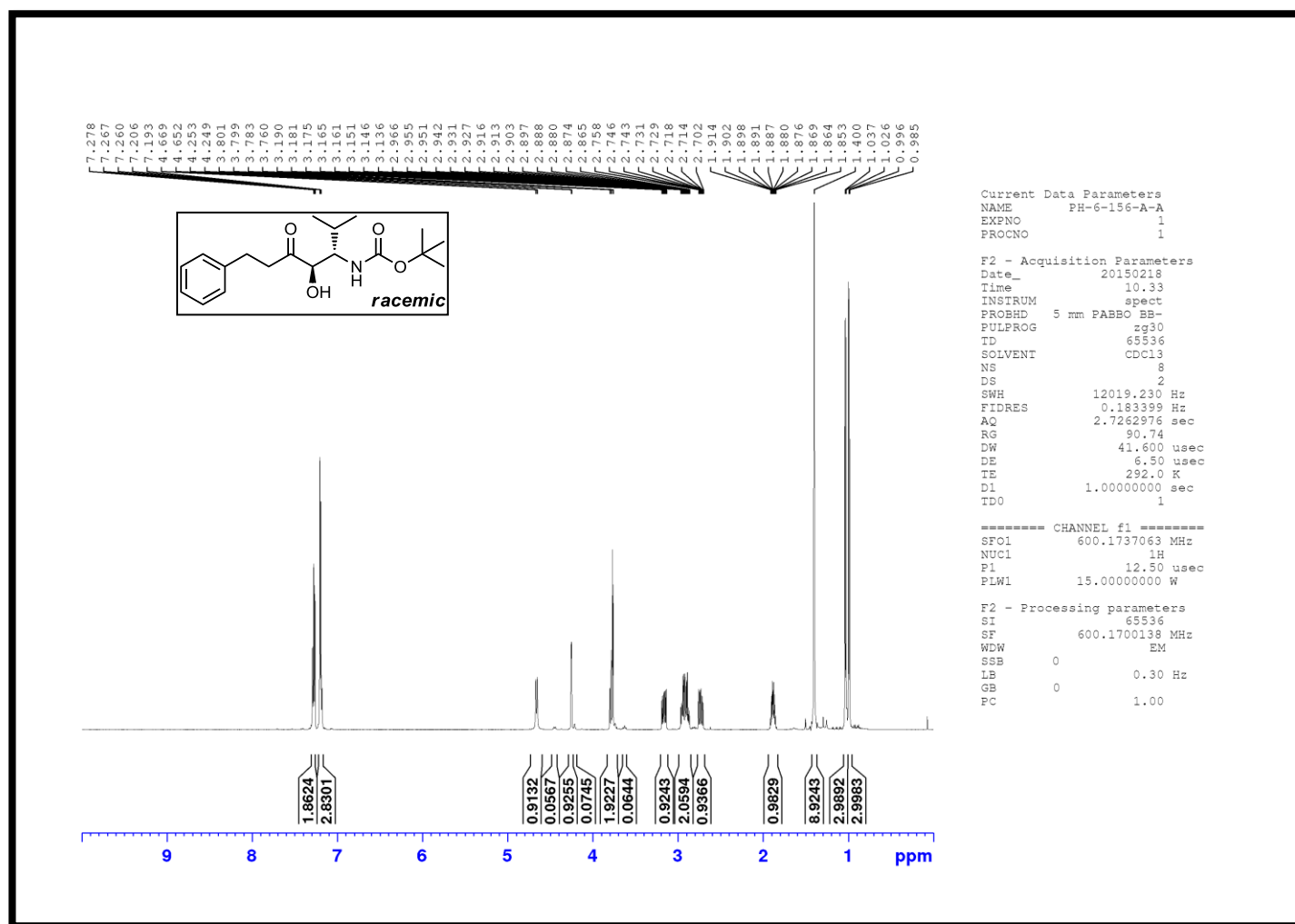


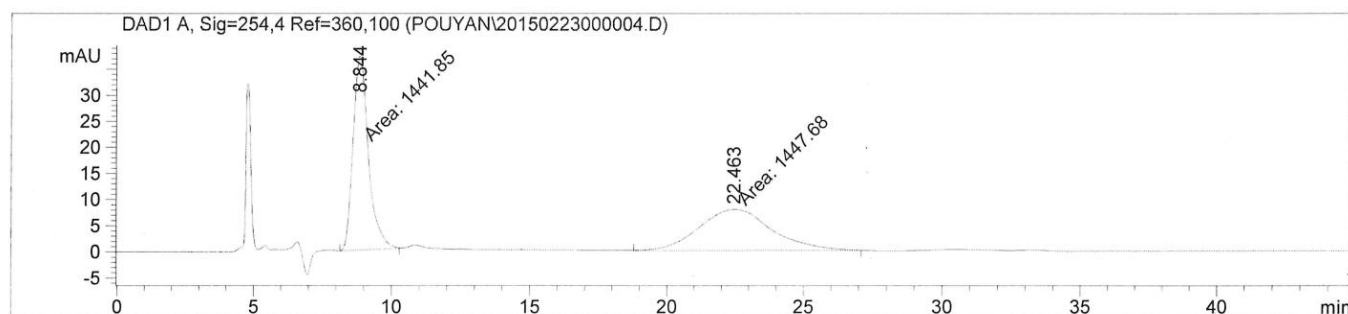
Column chromatography (3:1 hexanes:Et₂O) followed by PTLC (3:2

hexanes:Et₂O) afforded the major product as a colourless oil (36 mg, 44% yield).

R_f = 0.19 (43% Et₂O in hexanes); HPLC analysis – Chiralcel IC column, 5%

isopropanol in hexanes, 0.1 mL/min. 22.5 min and 8.84 min. ¹H NMR (600 MHz, CDCl₃) δ 7.31–7.26 (m, 2H), 7.22–7.17 (m, 3H), 4.66 (d, *J* = 10.3 Hz, 0.9H), 4.45 (d, *J* = 10.5 Hz, 0.1H), 4.25 (d, *J* = 2.5 Hz, 0.9H), 4.21 (s, 0.1H), 3.82–3.71 (m, 2H), 3.63 (t, *J* = 9.7 Hz, 0.1H), 3.16 (ddd, *J* = 14.8, 9.2, 5.6 Hz, 1H), 2.99–2.85 (m, 2H), 2.73 (ddd, *J* = 16.2, 8.9, 6.8 Hz, 1H), 1.94–1.83 (m, 1H), 1.40 (s, 9H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 6.7 Hz, 3H).



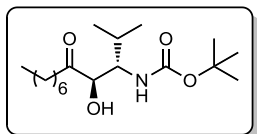


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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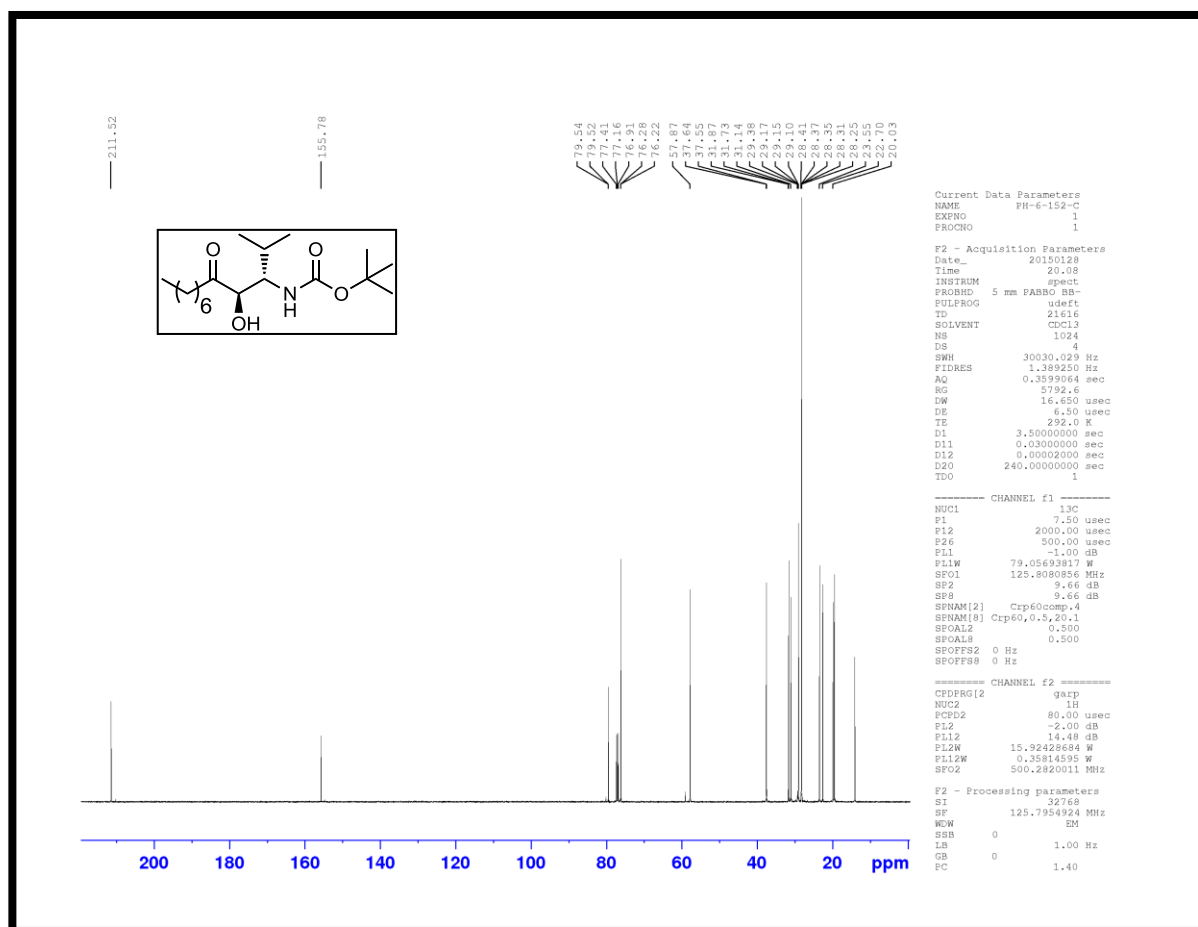
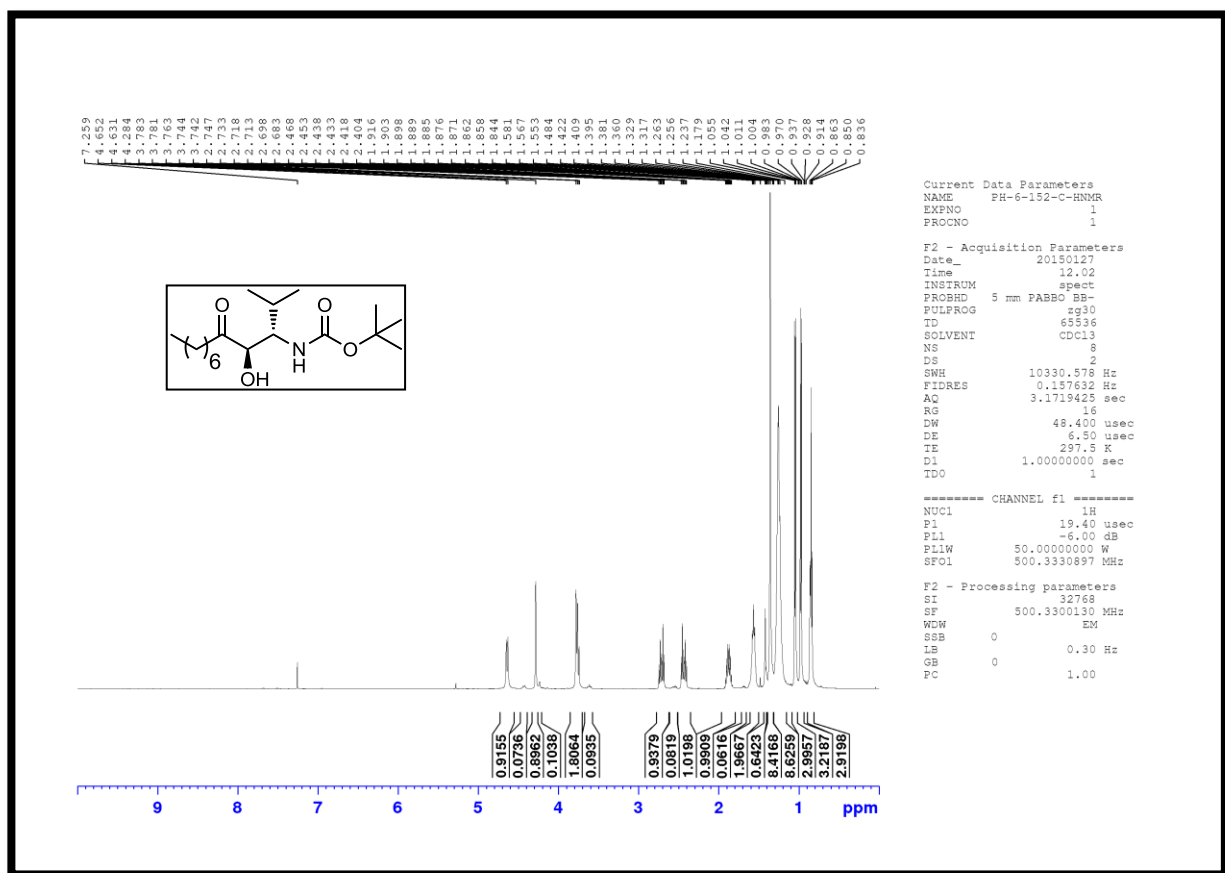
Totals : 2889.53711 44.96281

***tert*-butyl ((3*S*,4*R*)-4-hydroxy-2-methyl-5-oxododecan-3-yl)carbamate (9)**

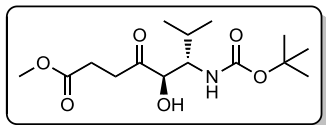


Column chromatography (8:1 hexanes:Et₂O) afforded the major product as a colourless oil (51 mg, 65%). *R_f* = 0.20 (13% Et₂O in hexanes); [α]_D²⁴ °C = -83 (*c* 2.5, CHCl₃); **FTIR** (KBr film) ν_{max} (cm⁻¹): 3448, 3358, 2960, 2930, 2873, 2858, 1713, 1500, 1391, 1366,

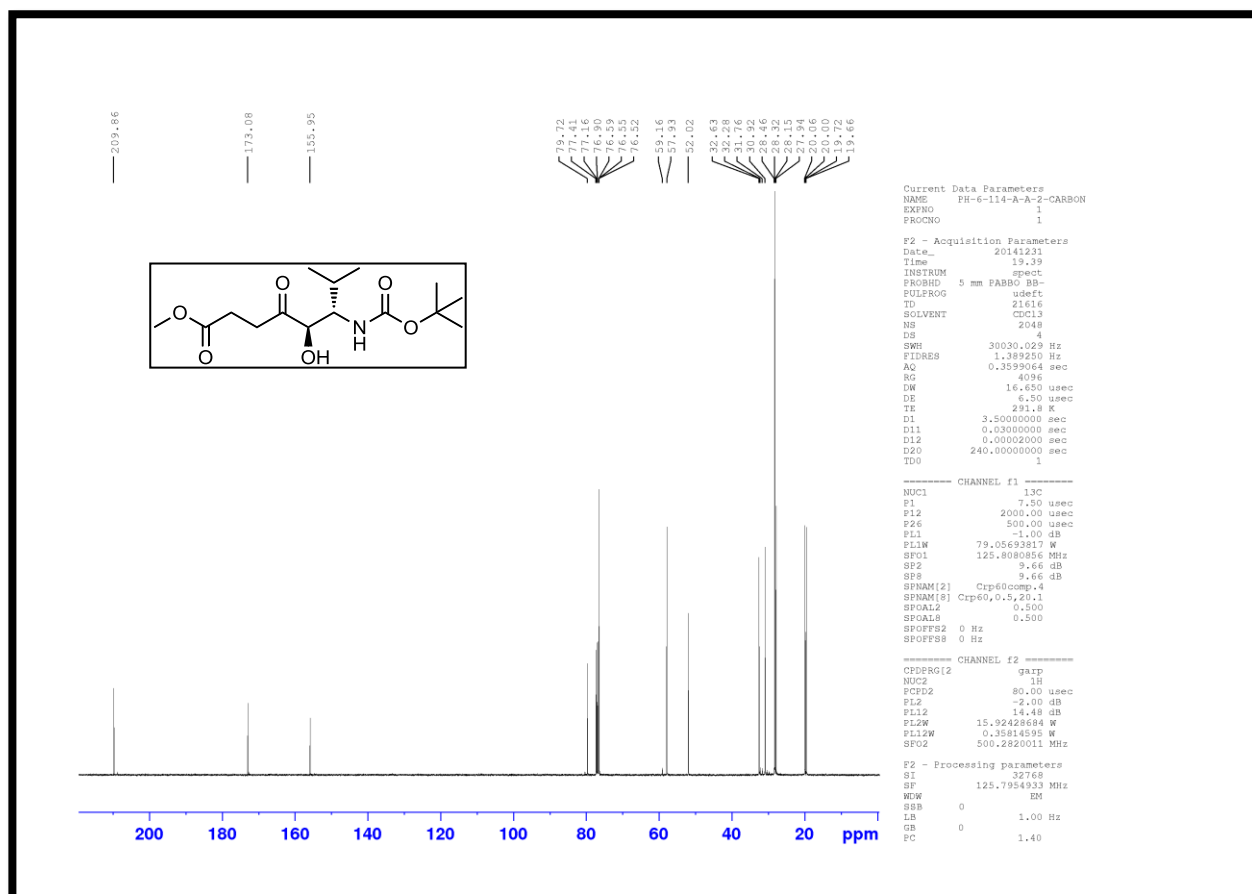
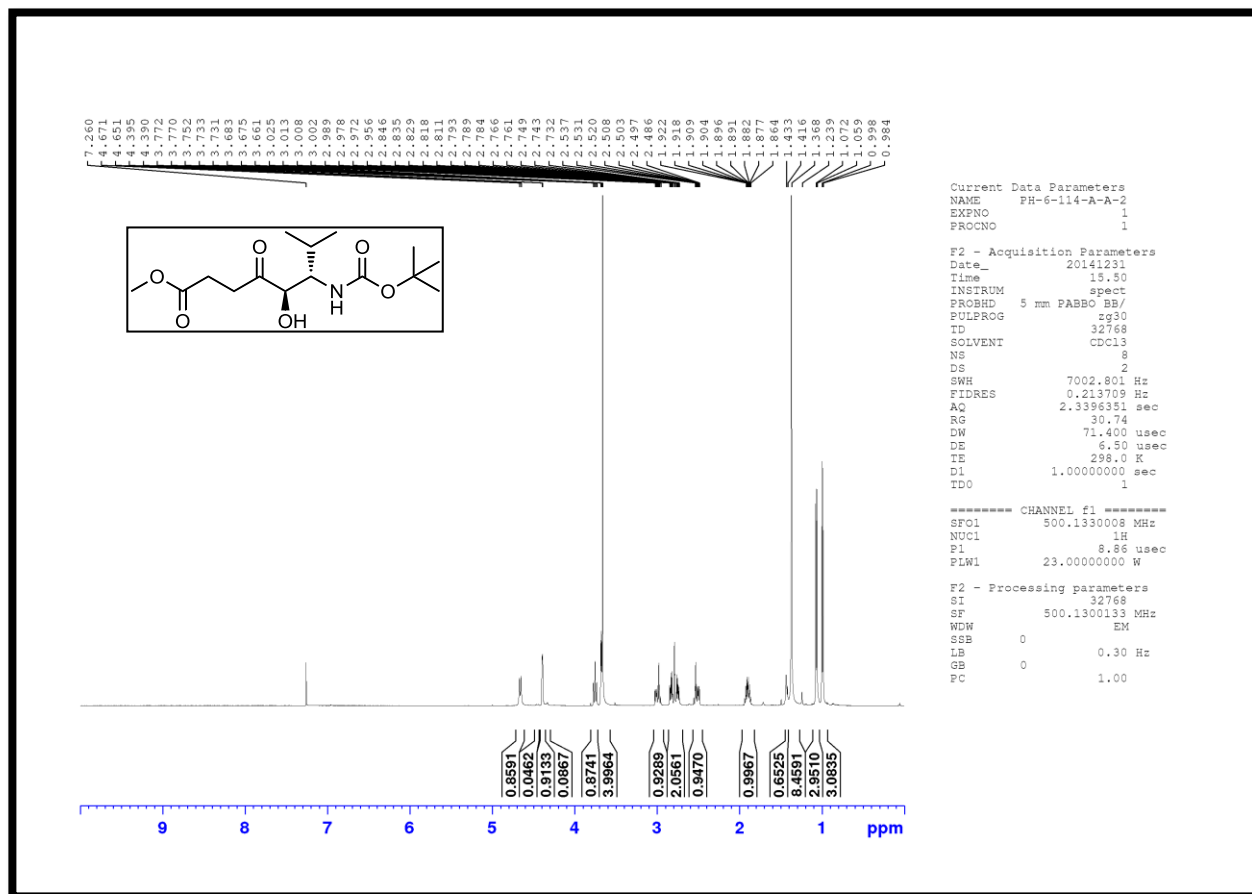
1244, 1172, 1099, 1018, 780; **¹H NMR** (500 MHz, CDCl₃) mixture of rotamers δ 4.64 (d, *J* = 10.3 Hz, 0.9H), 4.43(d, *J* = 10.1 Hz, 0.1H), 4.28 (s, 0.9H), 4.24 (s, 0.1H), 3.86–3.70 (m, 1.8H), 3.63 (t, *J* = 9.7 Hz, 0.1H), 2.72 (dt, *J* = 17.5, 7.4 Hz, 0.9H), 2.61–2.51 (m, 0.1H), 2.44 (dt, *J* = 17.5, 7.4 Hz, 1H), 1.96–1.80 (m, 1H), 1.71–1.66 (m, 0.1H), 1.64–1.50 (m, 1.9H), 1.36 (s, 9H), 1.32–1.15 (m, 8H) 1.05 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.90–0.82 (m, 3H); **¹³C NMR** (125 MHz, CDCl₃) mixture of rotamers (minor rotamer indicated by asterisk) δ 211.5, 155.8, 79.5, 79.5*, 76.3, 76.2*, 59.1*, 57.8, 37.6, 37.5*, 31.9*, 31.7, 31.1, 39.4, 29.4*, 29.1, 28.4*, 28.3, 23.5, 22.7, 20.0*, 20.0, 19.6, 14.2; **HRMS** (FD) *m/z*: [*M*+1] Calcd for C₁₈H₃₆NO₄ 330.26443; Found 330.26529.



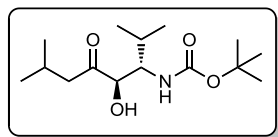
(5*R*,6*S*)-methyl 6-((tert-butoxycarbonyl)amino)-5-hydroxy-7-methyl-4-oxooctanoate (10)



Column chromatography (5:1 hexanes:acetone) followed by PTLC (3:2 hexanes:Et₂O) afforded major as a colourless oil (41 mg, 54%). $R_f = 0.26$ (25% acetone in hexanes); $[\alpha]_D^{28\text{ }^\circ\text{C}} = -99$ (c 1.5, CHCl₃); **FTIR** (KBr film) ν_{max} (cm⁻¹): 3450, 3373, 2971, 2875, 1740, 1712, 1509, 1367, 1241, 1173, 1083, 1045, 748; **¹H NMR** (500 MHz, CDCl₃) Mixture of rotamers δ 4.66 (d, $J = 10.2$ Hz, 0.9H), 4.45 (d, $J = 9.5$ Hz, 0.1H), 4.39 (d, $J = 2.5$ Hz, 0.8H), 4.33 (s, 0.1H), 3.75 (dd, $J = 10.4$, 1.0 Hz, 0.8H), 3.71–3.55 (m, 4H), 3.05–2.92 (m, 1H), 2.87–2.69 (m, 2H), 2.57–2.45 (m, 1H), 1.97–1.82 (m, 1H), 1.43 (s, 0.7H), 1.37 (s, 8.3H), 1.07 (d, $J = 6.7$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H); **¹³C NMR** (125 MHz, CDCl₃) Mixture of rotamers (minor rotamer indicated by asterisk): δ 209.9, 173.1, 155.9, 79.7, 76.6, 59.2, 57.9, 52.0, 32.6, 32.3*, 31.8*, 30.9, 28.3, 27.9, 20.0, 19.7; **HRMS** (TOF) m/z : [M+Na] Calcd for C₁₅H₂₇NO₆Na 340.1731; Found 340.1723.



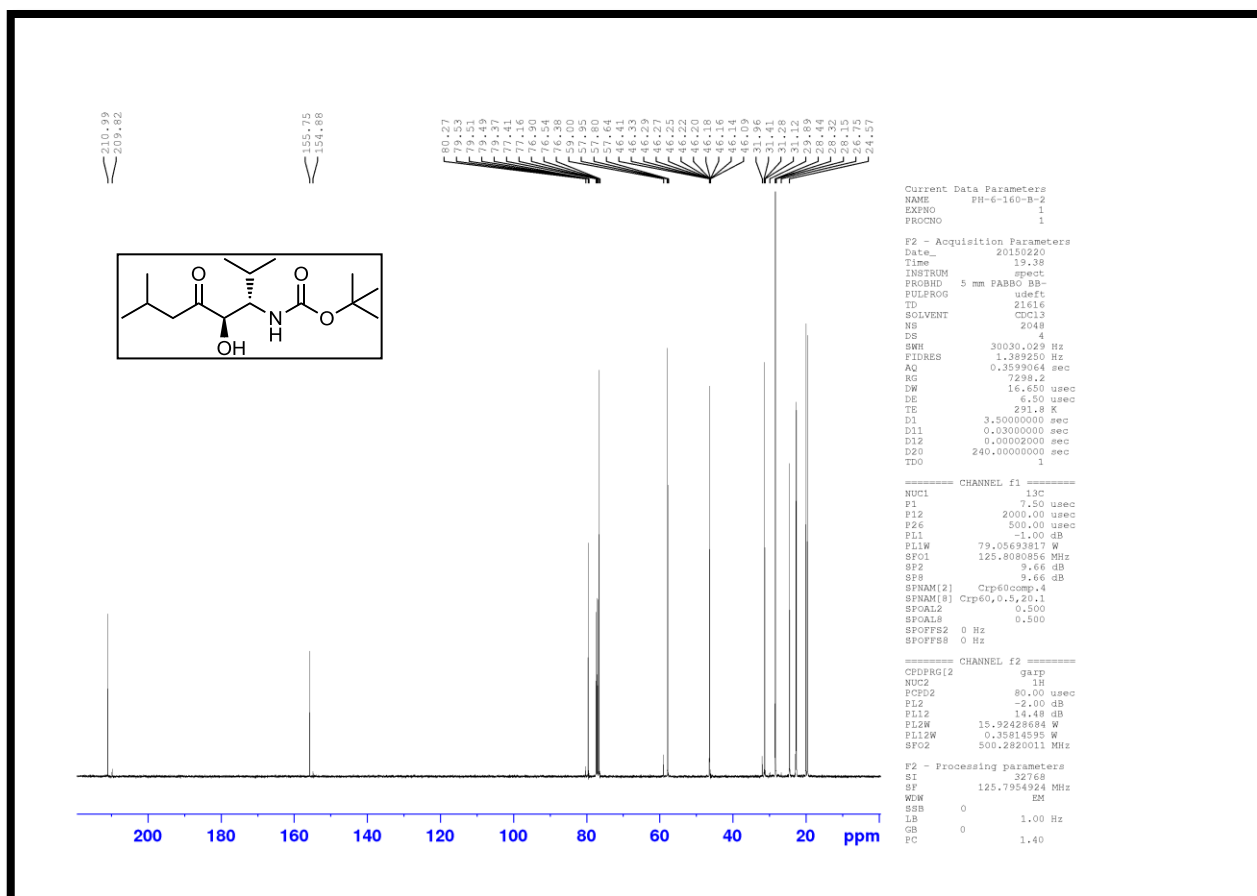
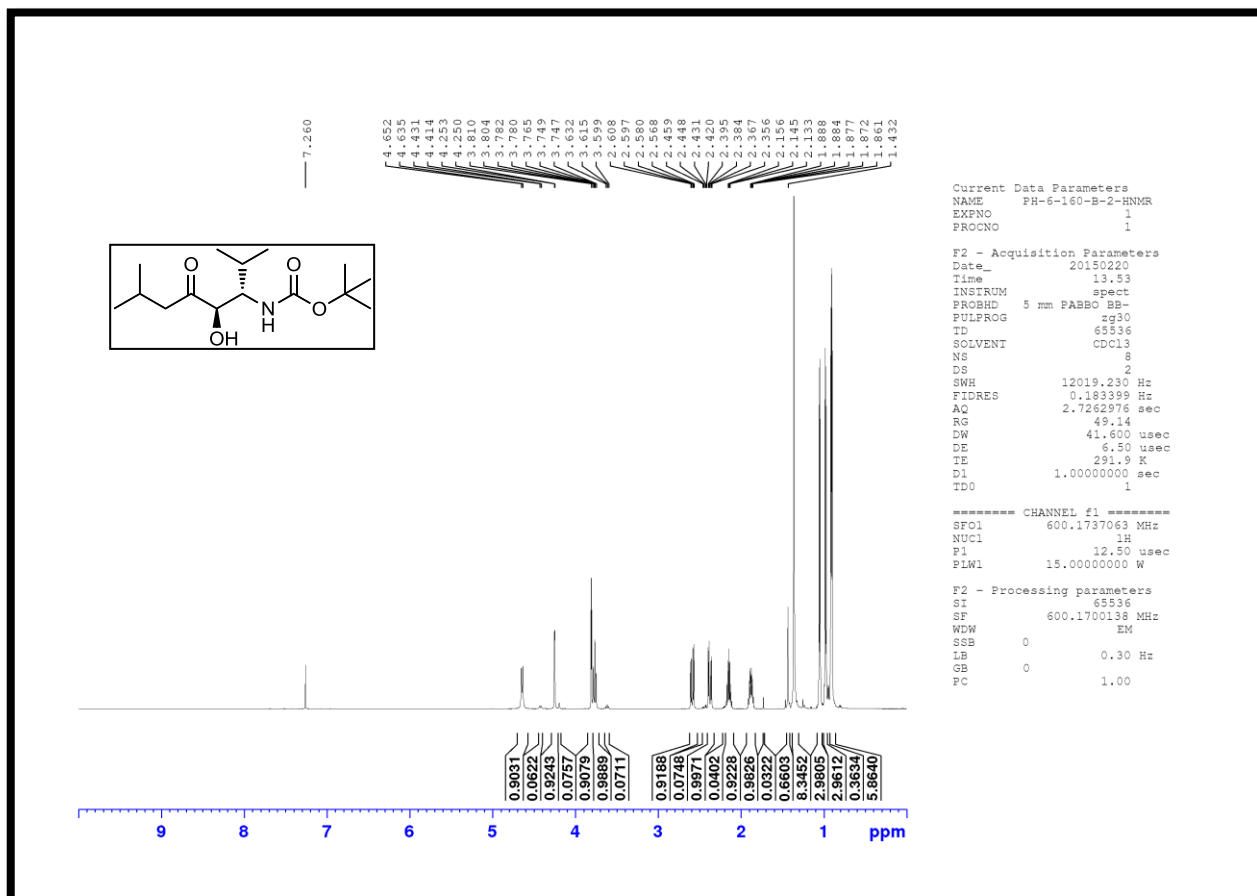
***tert*-butyl ((3*S*,4*R*)-4-hydroxy-2,7-dimethyl-5-oxooctan-3-yl)carbamate (11)**



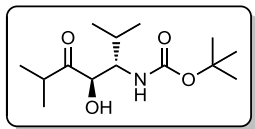
Column chromatography (8:1 hexanes:Et₂O) afforded the major product as white solids (35.5 mg, 56%). *R*_f = 0.21 (13% Et₂O in hexanes); melting range: 96.1–97.2 °C;

[α]_D²⁴ °C = -110 (*c* 1.3, CHCl₃); **FTIR** (KBr film) ν_{max} (cm⁻¹): 3505, 3314, 2962, 2939,

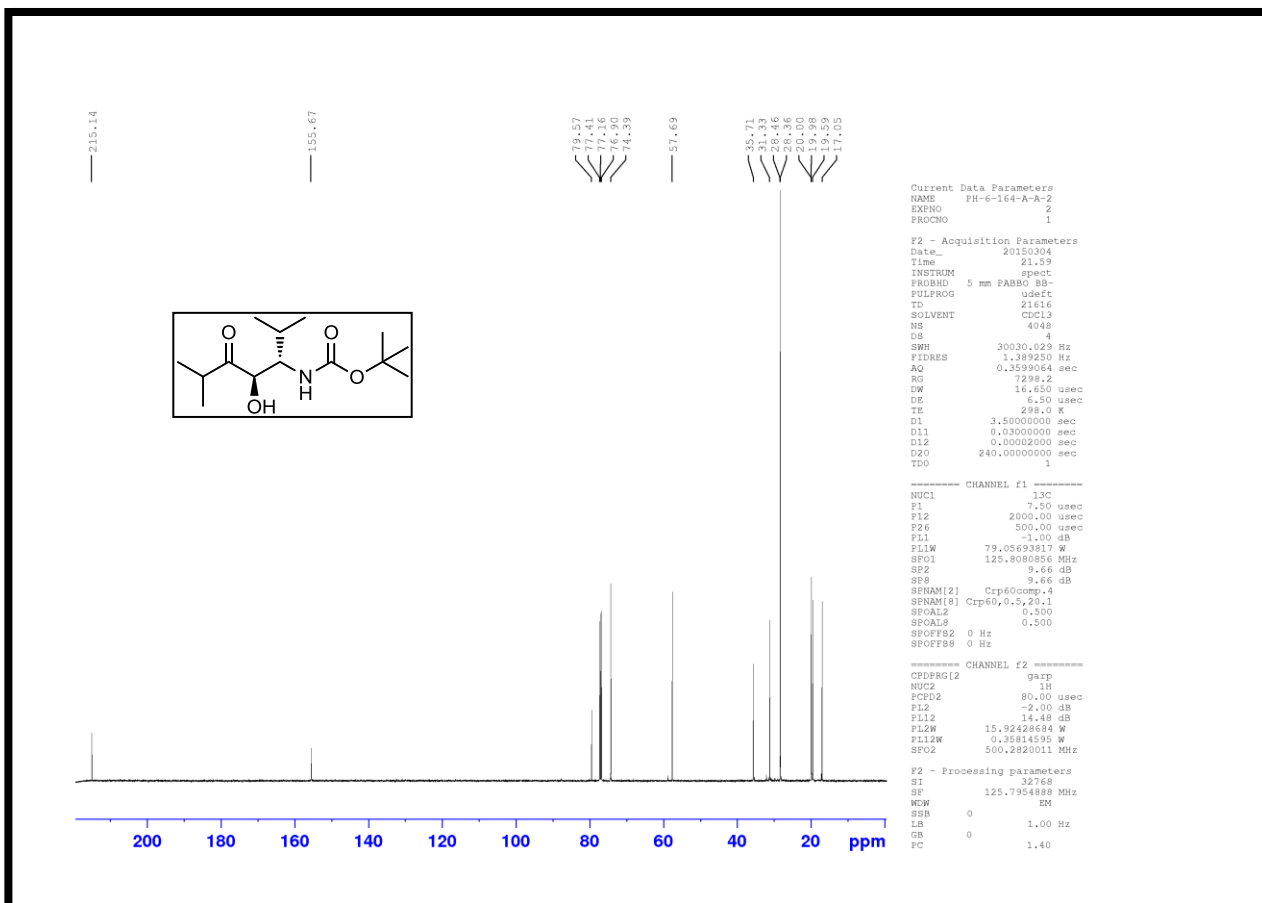
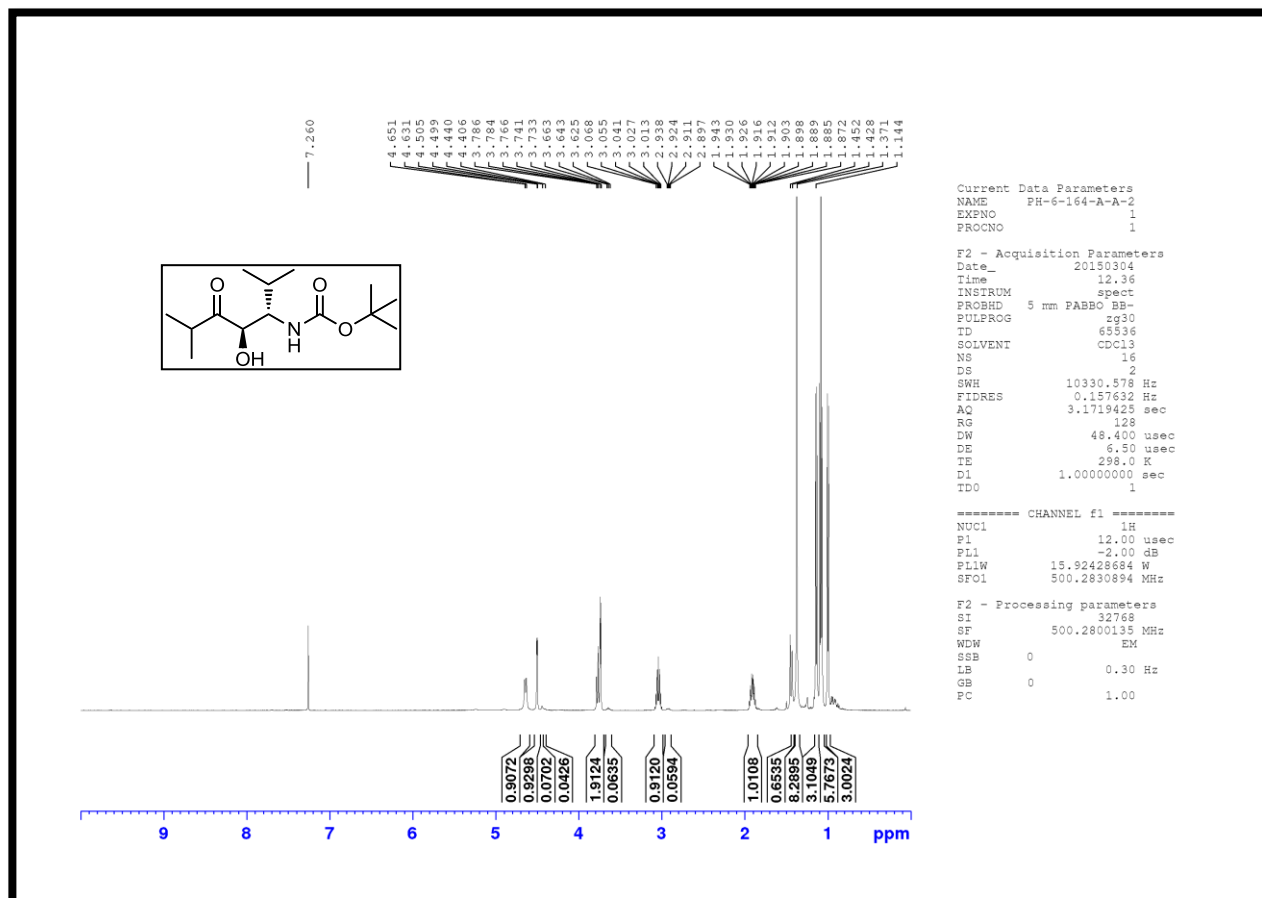
2872, 1706, 1638, 1529, 1389, 1370, 1287, 1171, 1092, 1019, 949; **¹H NMR** (600 MHz, CDCl₃) Mixture of rotamers δ 4.64 (d, *J* = 10.3 Hz, 0.9H), 4.42 (d, *J* = 10.6 Hz, 0.1H), 4.26 (d, *J* = 2.3 Hz, 0.9H), 4.19 (br s, 0.1H), 3.81 (d, *J* = 3.7 Hz, 0.9H), , 3.77 (dt, *J* = 9.2, 1.3 Hz, 0.9H), 3.62 (t, *J* = 10.0 Hz, 0.1H), 2.59 (dd, *J* = 7.0, 17.2 Hz, 0.9 H), 2.44 (dd, *J* = 6.6, 17.0 Hz, 0.1H), 2.38 (dd, *J* = 6.7, 17.1 Hz, 0.9H), 2.22–2.09 (m, 1H), 1.93–1.83 (m, 1H), 1.43 (s, 0.7H), 1.36 (s, 8.3H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 4.0 Hz, 3H), 0.90 (d, *J* = 4.0 Hz, 3H); **¹³C NMR** (125 MHz, CDCl₃) Mixture of rotamers (minor rotamer indicated by asterisk); δ 211.0, 209.8*, 155.7, 154.9*, 80.3*, 79.5, 76.5, 59.0*, 57.8, 46.4*, 46.4, 32.0*, 31.3, 28.4*, 28.3, 24.6, 24.5*, 22.9*, 22.7, 22.6, 20.0*, 20.0, 19.6*, 19.6; **HRMS** (TOF) *m/z*: [M+1] Calcd for C₁₅H₃₀NO₄ 288.2169; Found 288.2170.



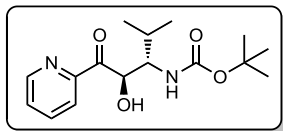
***tert*-butyl((*3S,4R*)-4-hydroxy-2,6-dimethyl-5-oxoheptan-3-yl)carbamate (**12**)**



Column chromatography (6:1 hexanes:Et₂O) afforded the major product as white solids (15 mg, 23%). $R_f = 0.12$ (17% Et₂O in hexanes); melting range: 135.4–138.7 °C; $[\alpha]_D^{24} = -113$ (c 0.8, CHCl₃); **FTIR** (KBr film) ν_{\max} (cm⁻¹): 3505, 3320, 2974, 2941, 2873, 1710, 1676, 1529, 1384, 1246, 1171, 1099, 1032, 1017, 969; **¹H NMR** (500 MHz, CDCl₃) Mixture of rotamers δ 4.64 (d, $J = 10.1$ Hz, 0.9H), 4.50 (d, $J = 2.7$ Hz, 0.9H), 4.44 (s, 0.1H), 4.62 (br s, 0.1H), 3.82–3.70 (m, 1.9H), 3.64 (t, $J = 9.8$ Hz, 0.1H), 3.04 (sep, $J = 6.9$ Hz, 0.9H), 2.96–2.89 (m, 0.1H), 1.96–2.85 (m, 1H), 1.45 (s, 0.7H), 1.43 (s, 8.3H), 1.14 (d, $J = 7.2$ Hz, 3H), 1.08 (dd, $J = 7.1, 6.9$ Hz, 6H), 1.00 (d, $J = 6.8$ Hz, 3H); **¹³C NMR** (125 MHz, CDCl₃) Mixture of rotamers (minor rotamer indicated by asterisk); δ 215.1, 155.7, 79.6, 74.4, 58.9*, 57.7, 35.7, 35.5, 32.3*, 31.3, 28.5*, 28.3, 20.0, 20.0*, 19.6, 17.3*, 17.0; **HRMS** (TOF) m/z : [M+1] Calcd for C₁₄H₂₈NO₄ 274.201285; Found 274.2025.

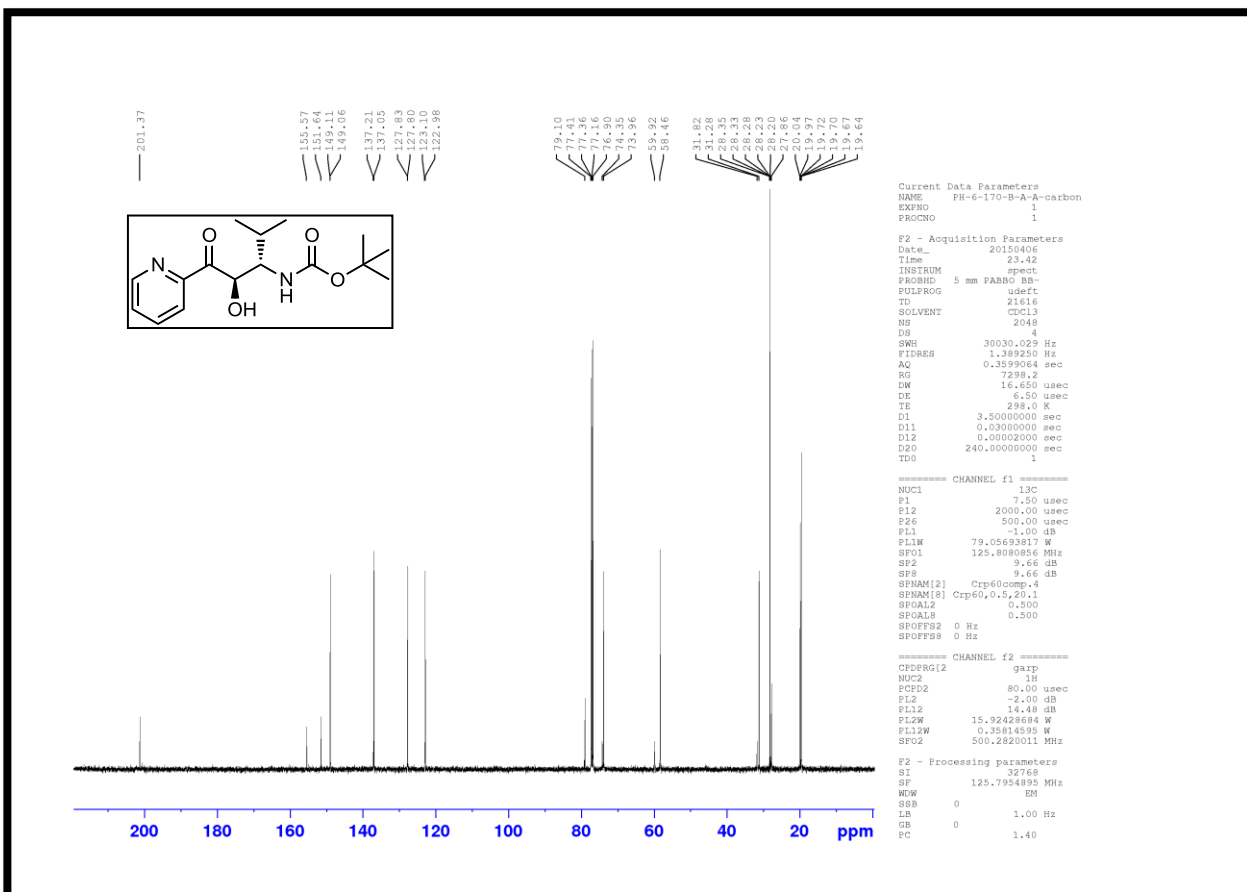
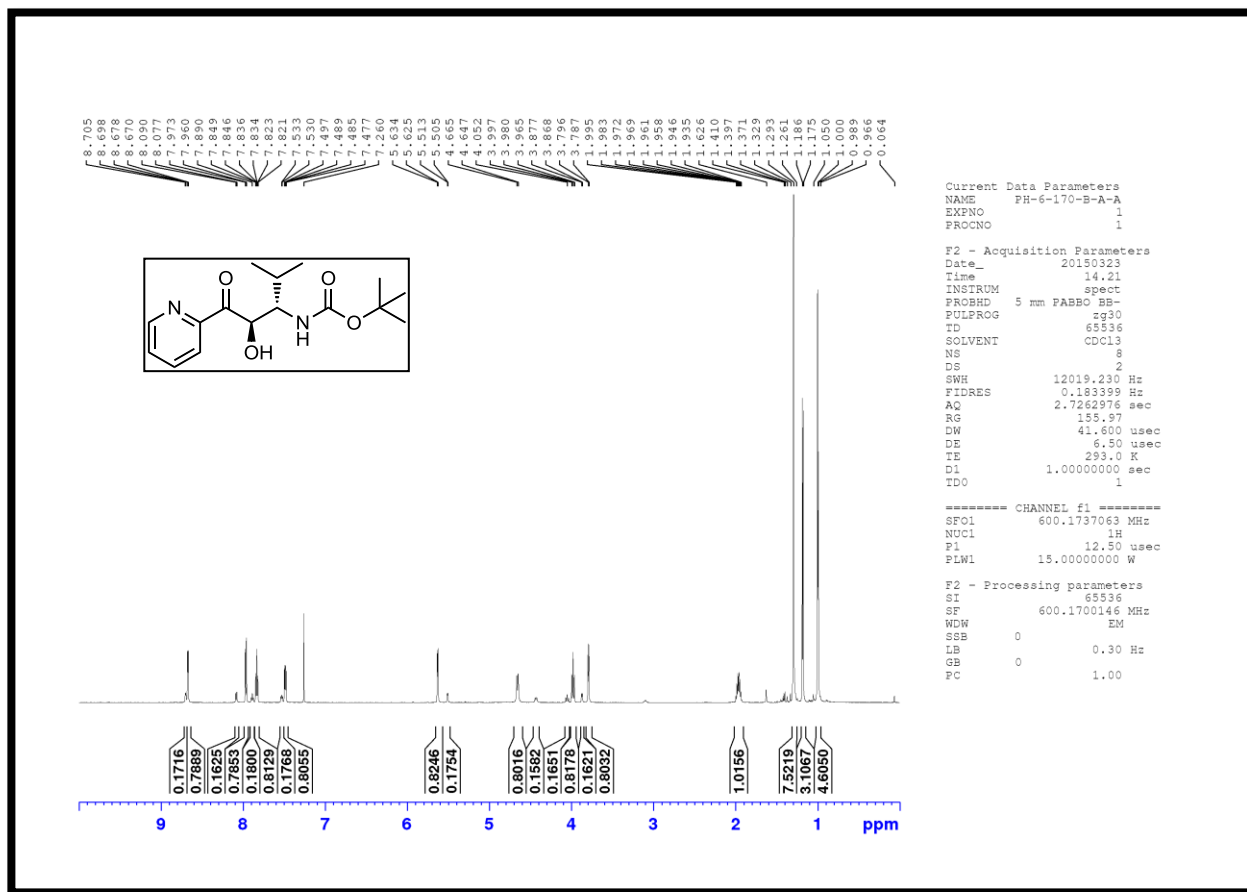


***tert*-butyl ((2*R*,3*S*)-2-hydroxy-4-methyl-1-oxo-1-(pyridin-2-yl)pentan-3-yl)carbamate (**13**)**

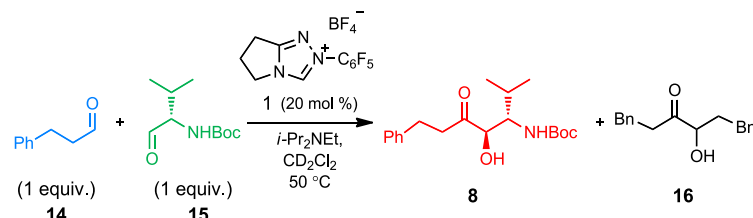


Column chromatography (5:1 hexanes:acetone) afforded the major product with unknown impurity, as a colourless oil (40 mg, 57% yield (54% calculated yield)). An analytically pure sample was prepared by PTLC (85:15:1 hexanes:acetone:NEt₃) R_f =

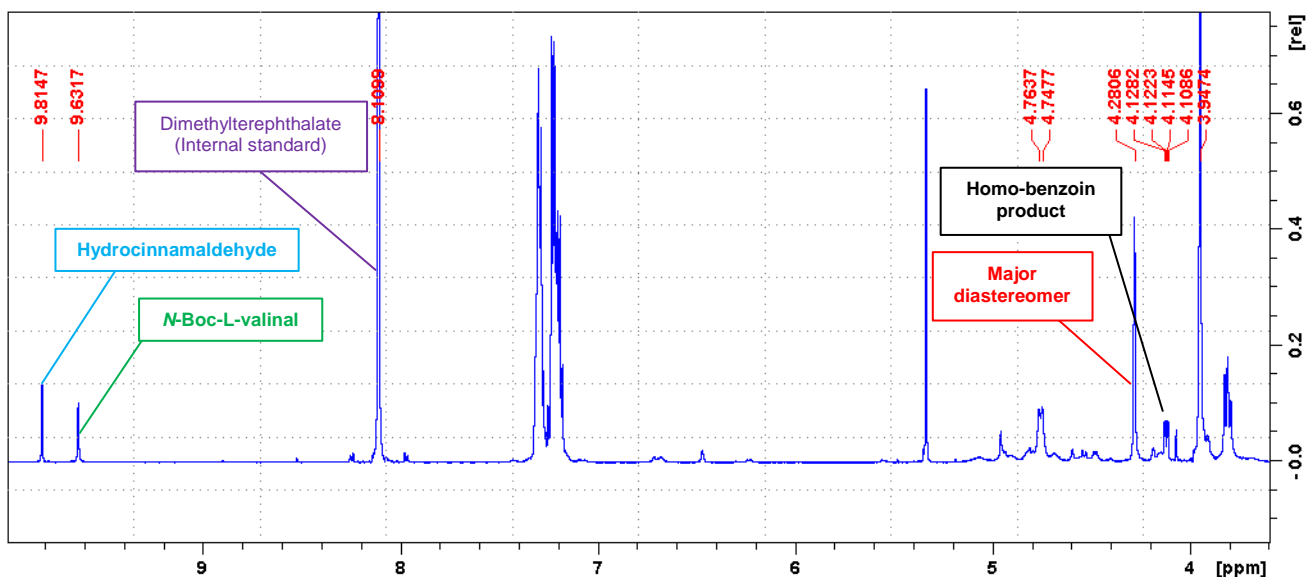
0.28 (20% acetone in hexanes); [α]_D^{24 °C} = +19 (c 0.6, CHCl₃); **FTIR** (KBr film) ν_{max} (cm⁻¹): 3447, 3385, 2973, 2931, 2874, 1704, 1585, 1499, 1391, 1366, 1244, 1172, 1002, 799; **¹H NMR** (600 MHz, CDCl₃) Mixture of rotamers δ 8.70 (d, *J* = 4.4 Hz, 0.2H), 8.67 (d, *J* = 4.6 Hz, 0.8H), 8.08 (d, *J* = 7.8 Hz, 0.2H), 7.97 (d, *J* = 7.8 Hz, 0.8H), 7.89 (dd, *J* = 7.6, 7.6 Hz, 0.2H), 7.83 (ddd *J* = 7.8, 7.8, 1.2 Hz, 0.8H), 7.53 (dd, *J* = 7.2, 4.8 Hz, 0.2H), 7.49 (dd, *J* = 7.2, 4.8 Hz, 0.8H), 5.63 (d, *J* = 5.1 Hz, 0.8H), 5.51 (d, *J* = 4.6 Hz, 0.2H), 4.66 (d, *J* = 10.3 Hz, 0.8H), 4.43 (d, *J* = 10.6 Hz, 0.2H), 4.05 (t, *J* = 9.9 Hz, 0.2H), 3.98 (t, *J* = 9.3 Hz, 0.8H), 3.87 (d, *J* = 5.4 Hz, 0.2H), 3.79 (d, *J* = 5.6 Hz, 0.2H), 2.02–1.91 (m, 1H), 1.29 (s, 7.5H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.00 (s, 1.5H), 0.99 (d, *J* = 6.5 Hz, 3H); **¹³C NMR** (125 MHz, CDCl₃) Mixture of rotamers (minor rotamer indicated by asterisk); δ 201.4, 155.6, 151.6, 149.1*, 149.1, 137.2*, 137.1, 127.8*, 127.8, 123.1*, 123.0, 79.3*, 79.1, 74.3*, 74.0, 59.9*, 58.5, 31.8*, 31.2, 28.3, 27.9*, 20.0*, 20.0, 19.7; **HRMS** (TOF) *m/z*: [M+1] Calcd for C₁₄H₂₈NO₄ 274.201285; Found 274.2025.

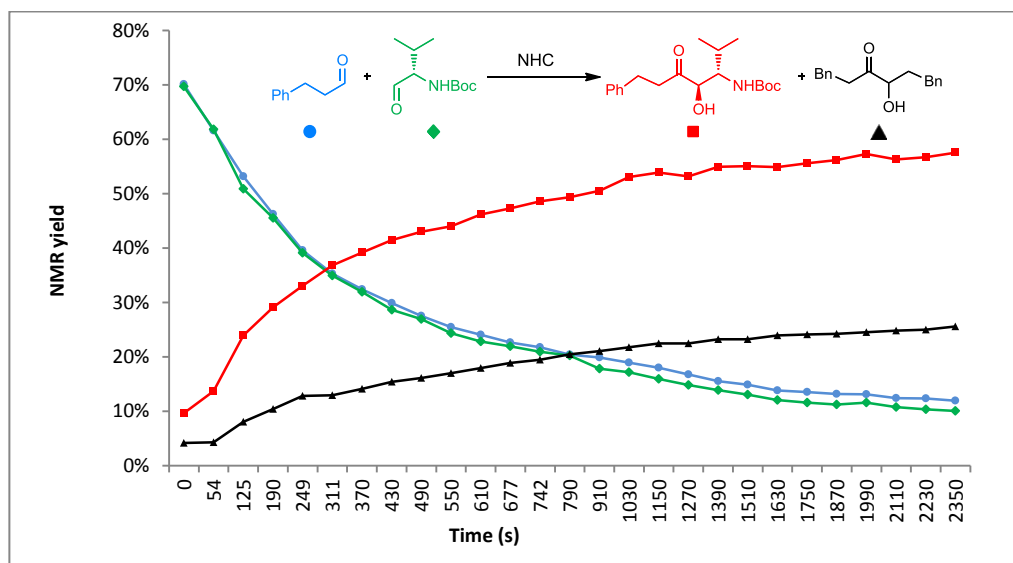


^1H NMR monitoring experiment for the reaction between **14** and **15**

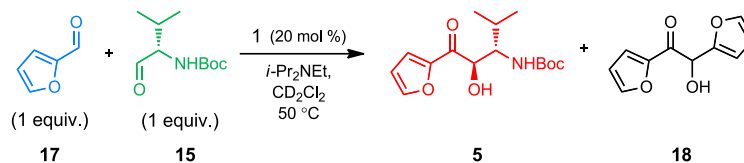


An oven-dried NMR tube was charged with triazolium salt **1** (3 mg, 0.008 mmol, 0.2 equiv.), **15** (0.0053 mL, 0.04 mmol, 1 equiv.), and dimethylterephthalate (7.8 mg, 0.04 mmol, 1 equiv.) and equipped with Schlenk take-off adapter. The NMR tube was placed under vacuum and re-filled with argon three times to ensure inert atmosphere. **14** (0.04 mmol, 1 equiv.) and CH₂Cl₂ (0.5 mL, 0.08 M) were added sequentially under argon atmosphere. Lastly *i*-Pr₂NEt (0.08 mmol, 2 equiv.) was added and the NMR tube was immediately inserted into a pre-heated NMR apparatus (50 °C). Spectra were acquired once per minute for the first 15 minutes and every 2 minutes for the remaining 45 minutes. A typical reaction spectrum (41 min.) is shown below:

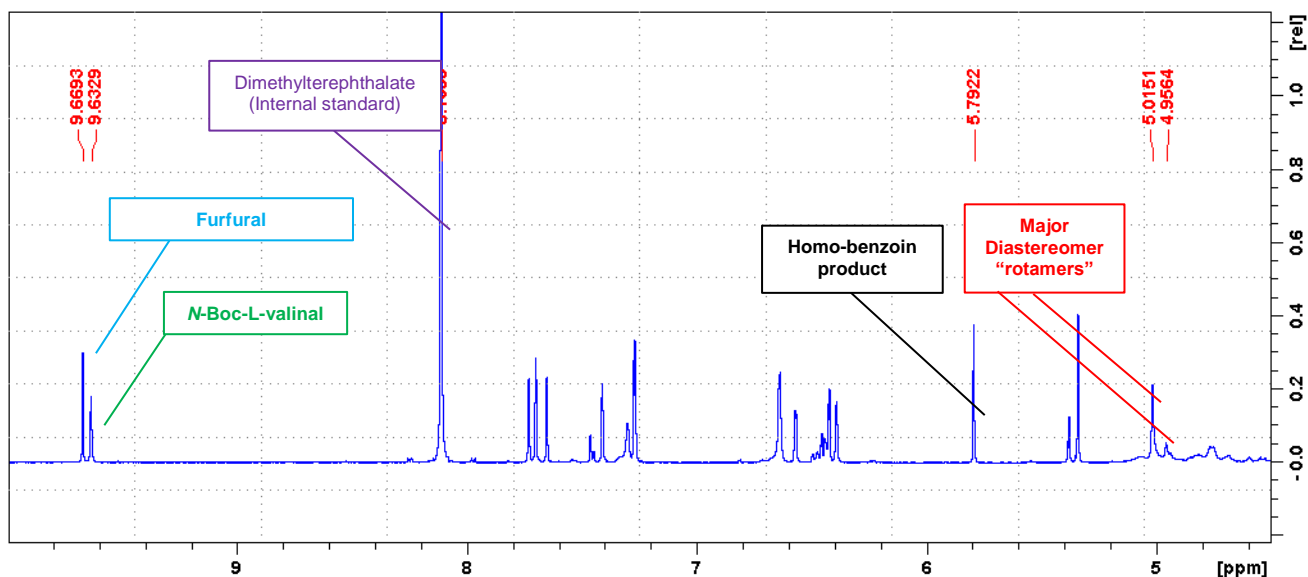


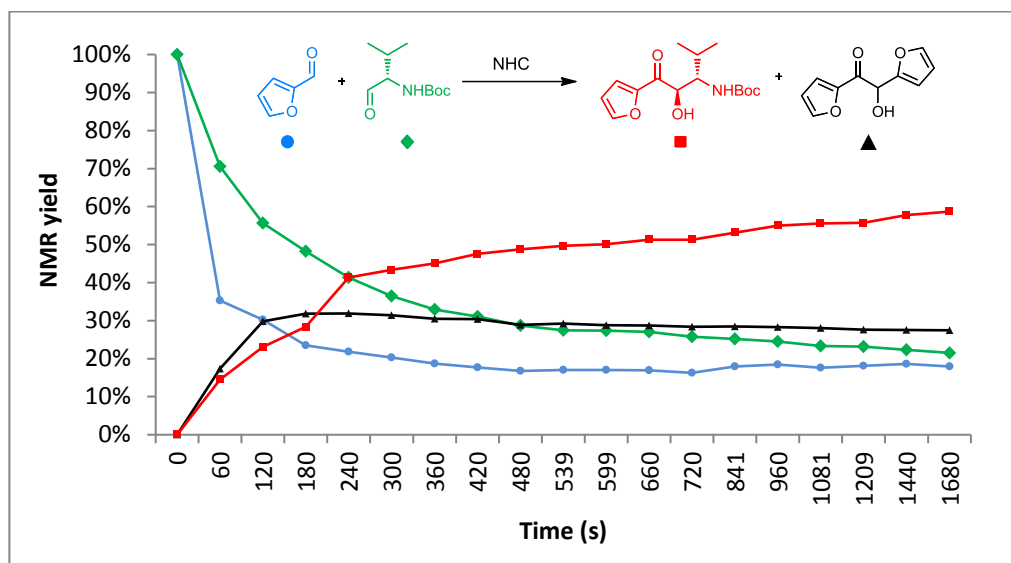


¹H NMR monitoring experiment for the reaction between 17 and 15



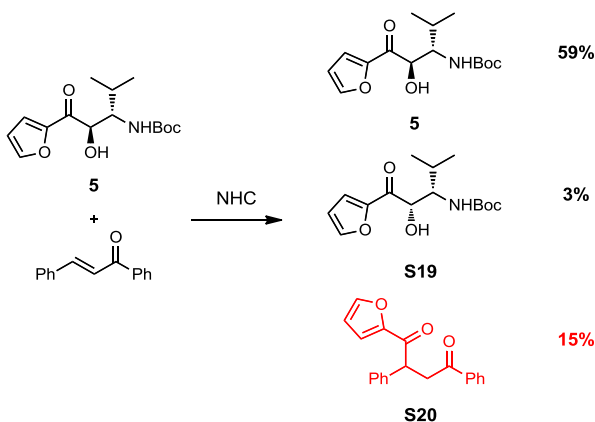
An oven-dried NMR tube was charged with triazolium salt **1** (3 mg, 0.008 mmol, 0.2 equiv.), **15** (0.0053 mL, 0.04 mmol, 1 equiv.), and dimethylterephthalate (7.8 mg, 0.04 mmol, 1 equiv.) and equipped with Schlenk take-off adapter. The NMR tube was placed under vacuum and re-filled with argon three times to ensure inert atmosphere. **17** (0.04 mmol, 1 equiv.) and CH₂Cl₂ (0.5 mL, 0.08 M) were added sequentially under argon atmosphere. Lastly *i*-Pr₂NEt (0.08 mmol, 2 equiv.) was added and the NMR tube was immediately inserted into a pre-heated NMR apparatus (50 °C). Spectra were acquired once per minute for the first 15 minutes and every 2 minutes for the remaining 45 minutes. A typical reaction spectrum (28 min.) is shown below:



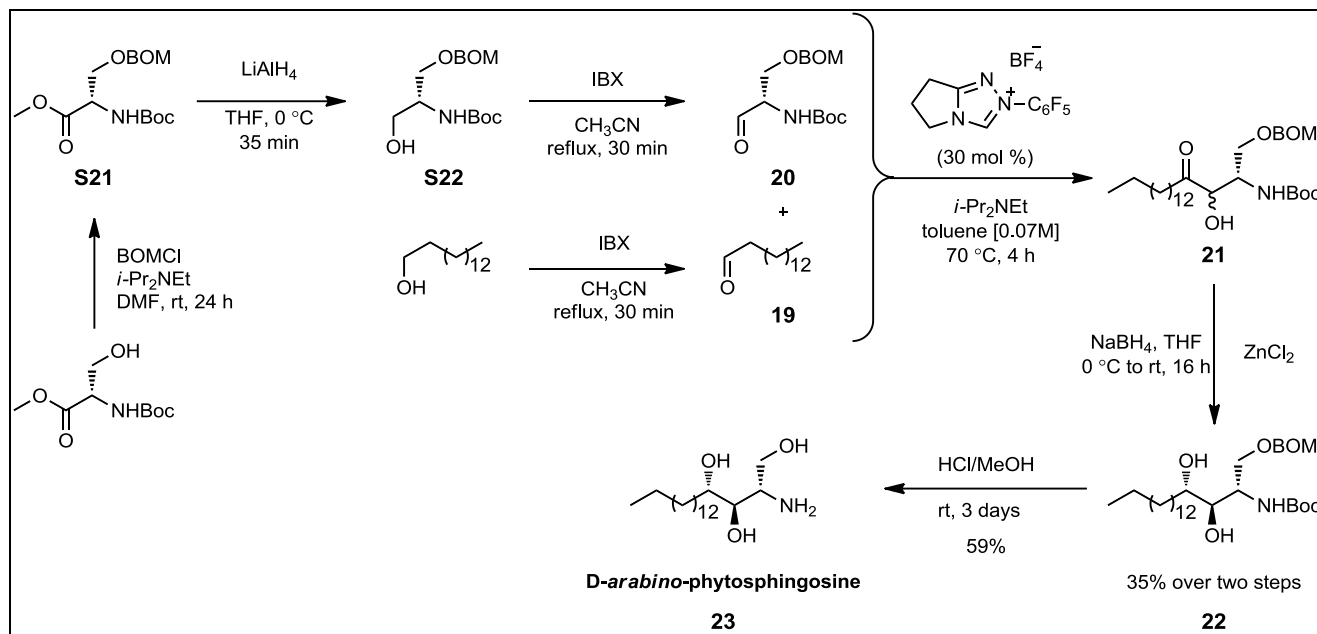


Crossover experiment of major cross-benzoin diastereomer **4** and *trans*-chalcone

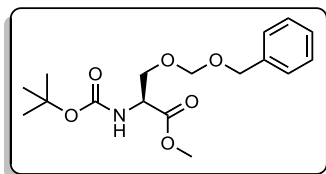
In order to evaluate the reversibility of this pathway, the major diastereomer (**5**) was subjected to reaction conditions with a stoichiometric amount of *trans*-chalcone. If the formation of the product is reversible, the retro-benzoin reaction would lead to re-formation of the Breslow intermediate with furfural. This intermediate could be trapped by the α,β -unsaturated ketone to form the Stetter product (**S20**). It was found that under these conditions **S20** is observed in 15% NMR yield along with 3% of the minor diastereomer (**S19**) and 59% recovered major diastereomer (**4**) (Scheme 4). These results suggest that the pathway leading to the formation of the major product is reversible under the reaction conditions.



Synthesis of D-arabino-phytosphingosine (23)

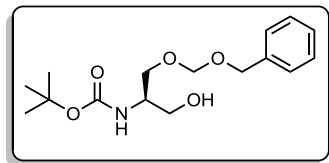


(S)-methyl-3-((benzyloxy)methoxy)-2-((tert-butoxycarbonyl)amino)propanoate ((N-Boc-O-BOM-L-serine ester) (S21))

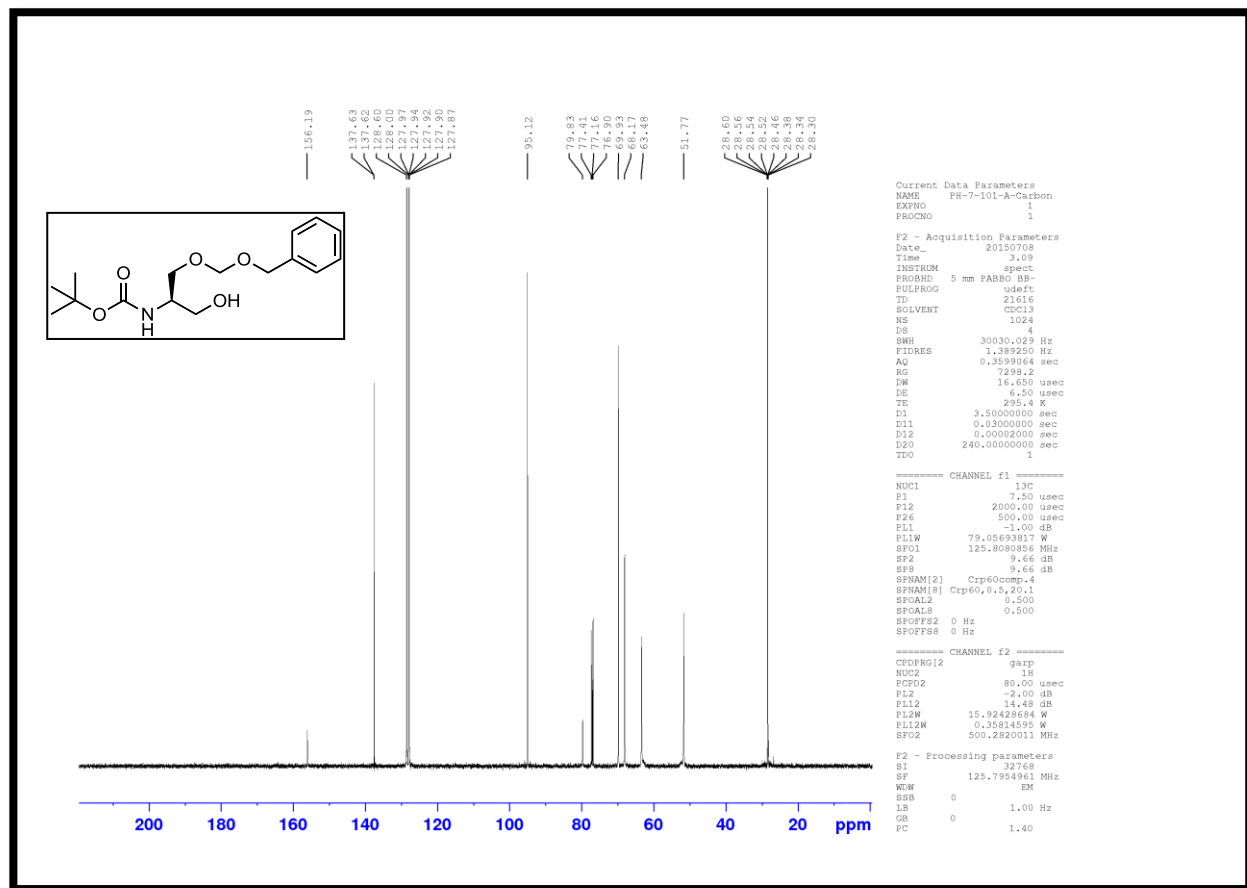
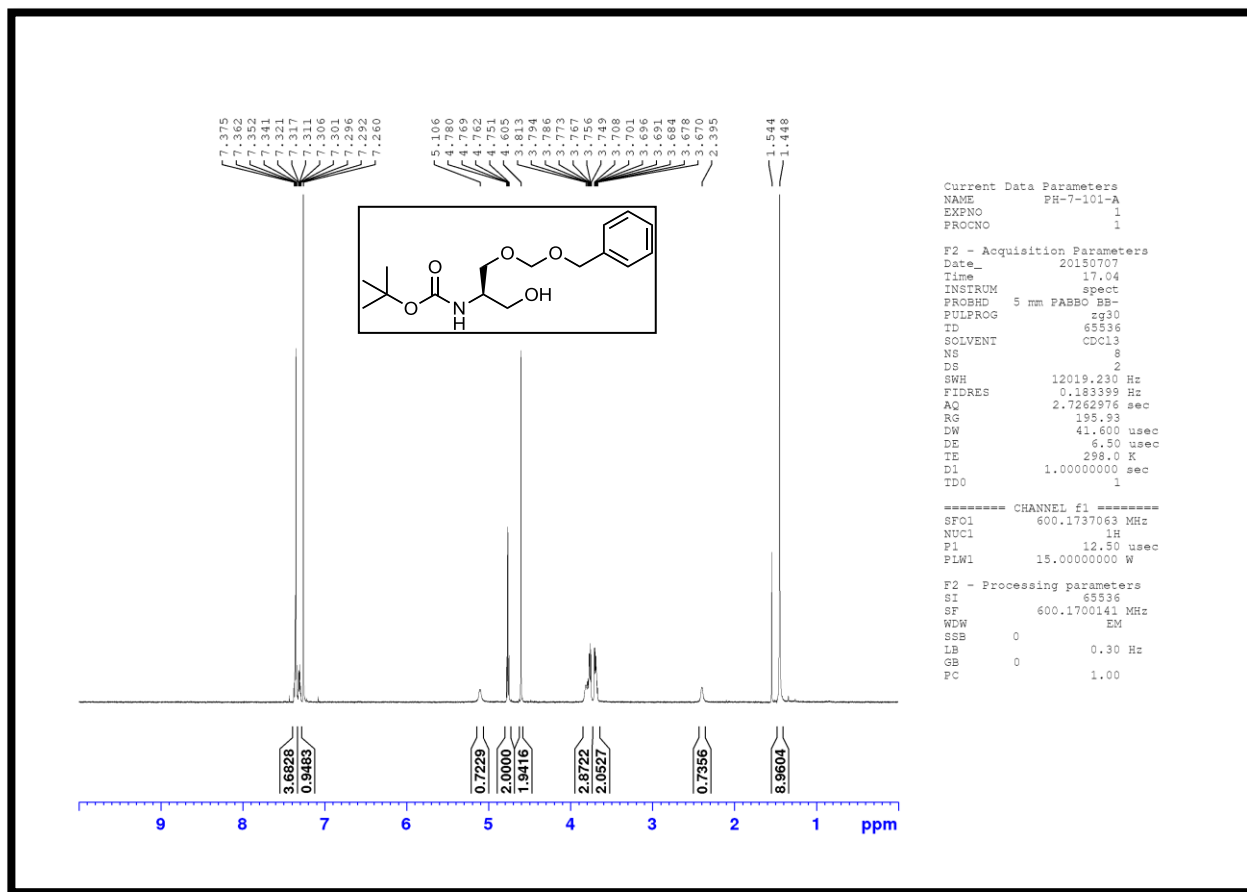


To a solution of *N*-Boc-L-serine ester (2.34 g, 10.7 mmol) in dry DMF (11 mL) was added *i*-Pr₂NEt (6 mL, 34.2 mmol) at room temperature under argon. This was followed by the addition of BOMCl (70% purity) (7.17 g, 32.05 mmol). The mixture was stirred at this temperature for 24 hours. The mixture was diluted in EtOAc (300 mL) and washed sequentially with sat. $\text{NH}_4\text{Cl}_{\text{aq}}$ (200 mL), distilled water (200 mL), and brine (200 mL). The organic layer was dried over MgSO_4 and concentrated. The resulting solution was purified by chromatography (5:1 hexane:EtOAc) to afford a mixture of product and an unknown impurity as clear colourless oil. $R_f = 0.20$ (5:1 hexane:EtOAc). The mixture was carried to next step without further purification.

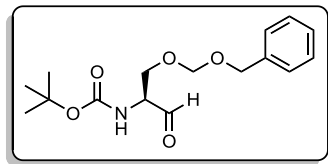
(*R*)-*tert*-butyl (1-((benzyloxy)methoxy)-3-hydroxypropan-2-yl)carbamate (*N*-Boc-O-BOM-L-serinol) (S22)



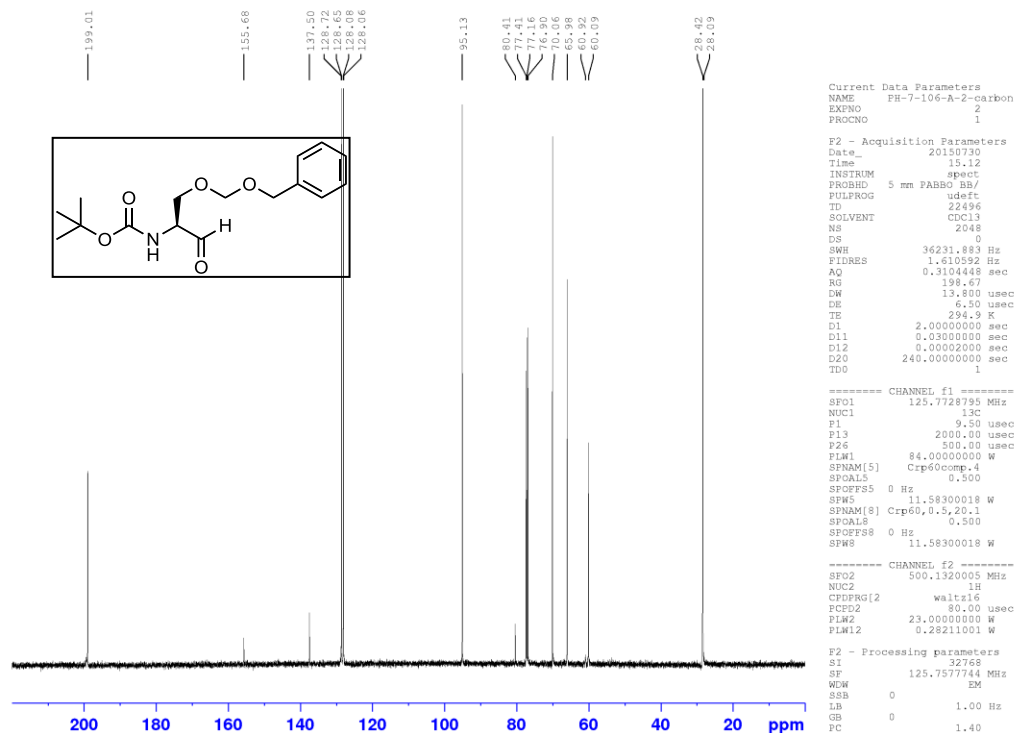
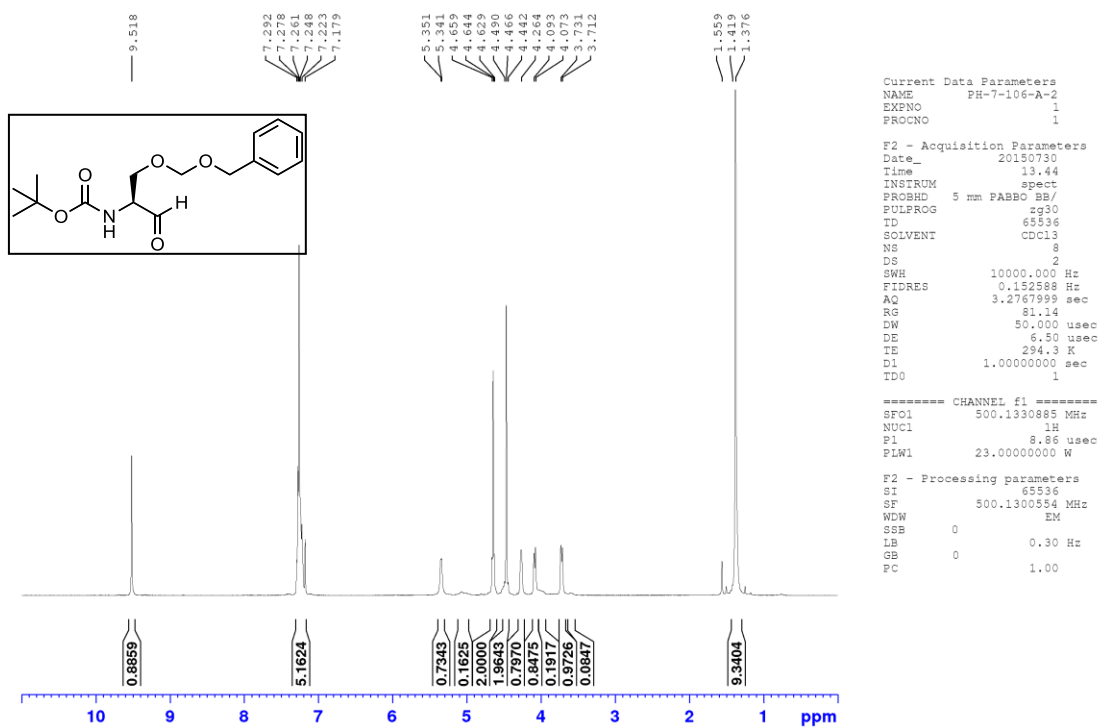
To a suspension of LiAlH_4 in THF (20 mL) was added the crude ester (**S19**) (2.01 g, 5.93 mmol) in dry THF (20 mL) at 0°C . The reaction mixture was stirred at this temperature for 35 minutes and quenched with addition of an aqueous solution of Rochelle's salt [0.5 M] (ca. 20 mL). The reaction was vigorously stirred at room temperature for an additional 2 hours. The reaction mixture was diluted in EtOAc (150 mL) and the layers were separated. The aqueous phase was extracted using EtOAc (2×150 mL) and the combined organic layers were dried over MgSO_4 . The resulting solution was concentrated and purified by chromatography (3:2 hexane:EtOAc) to afford a clear colourless oil (1.46 g, 41% yield over 2 steps). $R_f = 0.20$ (3:2 hexane:EtOAc); $[\alpha]_D^{26} = -1$ (c 0.9, CHCl_3); **FTIR** (KBr film) ν_{max} (cm^{-1}): 3438, 3065, 2976, 2934, 2883, 1694, 1499, 1455, 1367, 1248, 1170, 1046, 738, 699; **^1H NMR** (600 MHz, CDCl_3) δ 7.39–7.33 (m, 4H), 7.33–7.28 (m, 1H), 5.10 (s, 1H), 4.77 (dd, $J = 11.0, 6.7$ Hz, 2H), 4.61 (s, 2H), 3.85–3.73 (m, 3H), 3.73–3.64 (m, 2H), 2.24 (s, 1H), 1.45 (s, 9H); **^{13}C NMR** (125 MHz, CDCl_3) δ 156.2, 137.6, 137.6, 128.6, 128.0, 128.0, 95.1, 79.8, 69.9, 68.2, 63.5, 51.8, 28.5; **HRMS** (TOF) m/z : $[\text{M}+\text{Na}]$ Calcd for $\text{C}_{16}\text{H}_{25}\text{NO}_5\text{Na}$ 334.162495; Found 334, 1641.



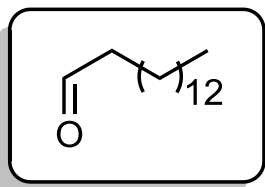
(S)-tert-butyl (1-((benzyloxy)methoxy)-3-oxopropan-2-yl)carbamate (N-Boc-O-BOM-L-serinal)(20)



To a suspension of **S20** (1.28 g, 4.1 mmol) in CH₃CN (41 mL) was added IBX (1.73 g, 6.17 mmol) and heated to reflux. The reaction was monitored for consumption of starting material (30 min). The reaction was cooled to room temperature and filtered through a pad of Celite[®] and washed with EtOAc (3×50 mL). The resulting solution was concentrated and purified by chromatography (3:1 hexane:EtOAc) to afford a clear colourless oil (1.21 g, 95% yield). $R_f = 0.28$ (3:1 hexane:EtOAc); $[\alpha]_D^{26} = -1$ (c 0.9, CHCl₃); **FTIR** (KBr film) ν_{\max} (cm⁻¹): 3349, 2977, 2944, 2887, 1712, 1498, 1368, 1167, 1116, 1048, 748, 699; **¹H NMR** (600 MHz, CDCl₃) Mixture of rotamers: δ 9.52 (s, 1H), 7.31–7.16 (m, 5H), 5.35 (d, $J = 5.1$ Hz, 0.8H), 5.12–4.97 (m, 0.2H), 4.64 (dd, $J = 7.5$, 7.4 Hz, 2H), 4.66 (s, 2H), 4.26 (s, 0.8H), 4.08 (d, $J = 9.9$ Hz, 0.8H), 4.04–3.93 (m, 0.2H), 3.72 (d, $J = 9.5$ Hz, 0.8H), 3.64–3.54 (m, 0.2H), 1.38 (s, 9H); **¹³C NMR** (125 MHz, CDCl₃) Mixture of rotamers (minor rotamer indicated by asterisk); δ 199.0, 155.7, 137.5, 128.6, 128.1, 128.1, 95.1, 80.4, 70.1, 66.0, 60.9*, 60.1, 28.4; **HRMS** (FD) m/z : [M+1] Calcd for C₁₆H₂₄NO₅ 310.16545; Found 310.16431.

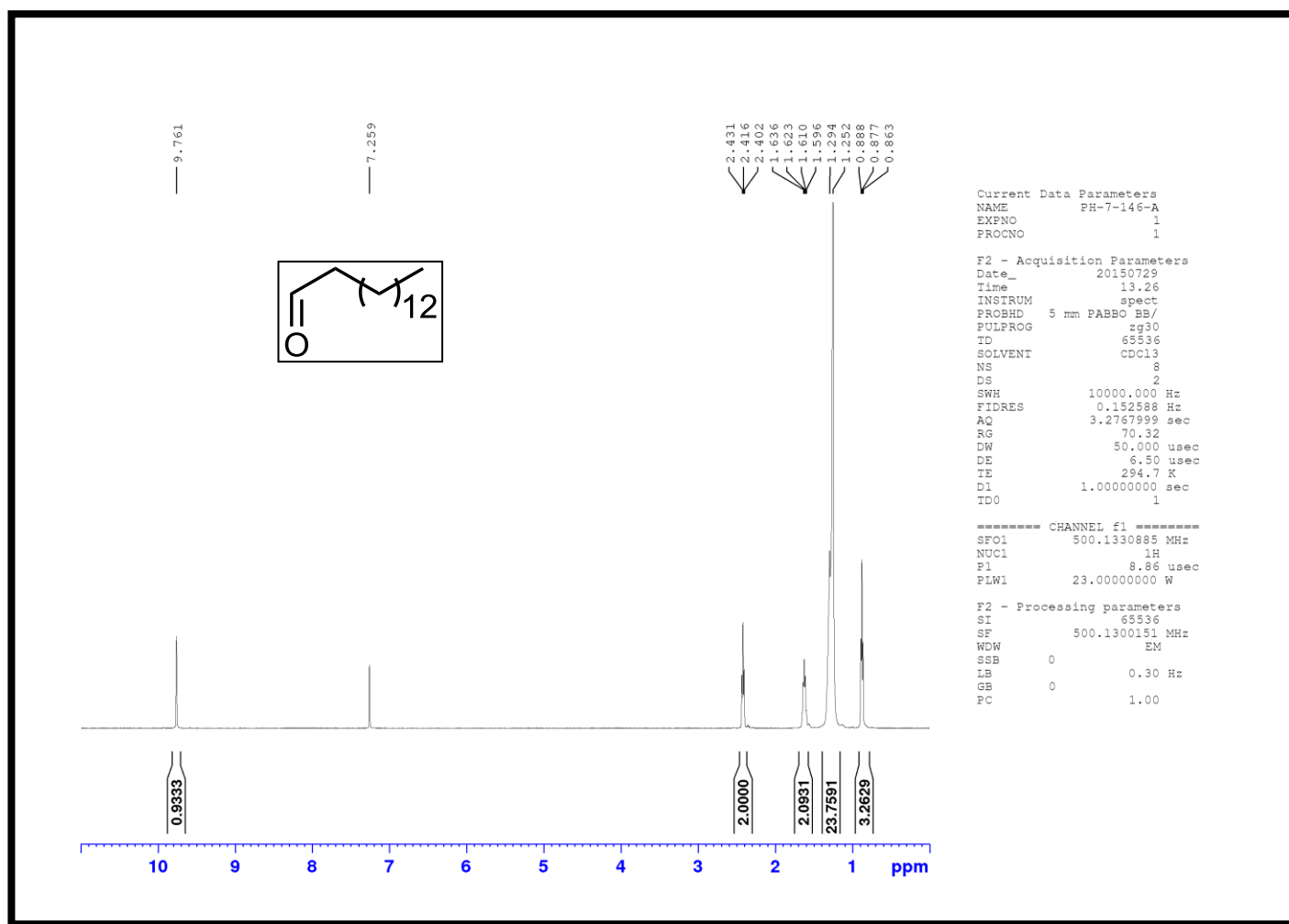


Pentadecanal (19)

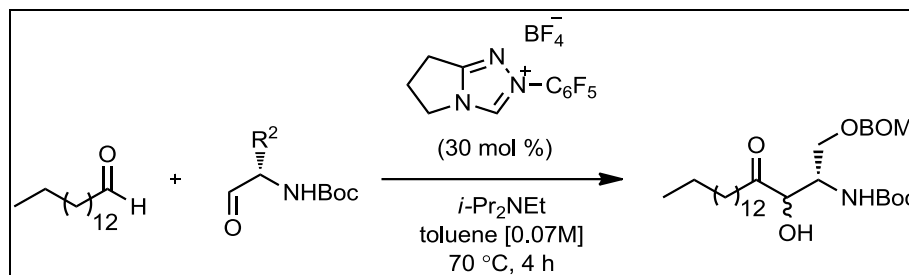


To a suspension of pentadecan-1-ol (2.1 g, 9.21 mmol) in CH_3CN (28 mL) was added IBX (3.87g, 13.82 mmol) and heated to reflux. The reaction was monitored for consumption of starting material (50 min). The reaction was cooled to room temperature and filtered through a pad of Celite[®] and washed with EtOAc (3×50 mL). The resulting solution was concentrated and purified by chromatography (9:1 hexane:EtOAc) to afford a clear colourless oil that solidifies upon refrigeration (1.81 g, 87%) (R_f = 0.31 (9:1 hexane:EtOAc). Spectral data match the previously reported values.²³

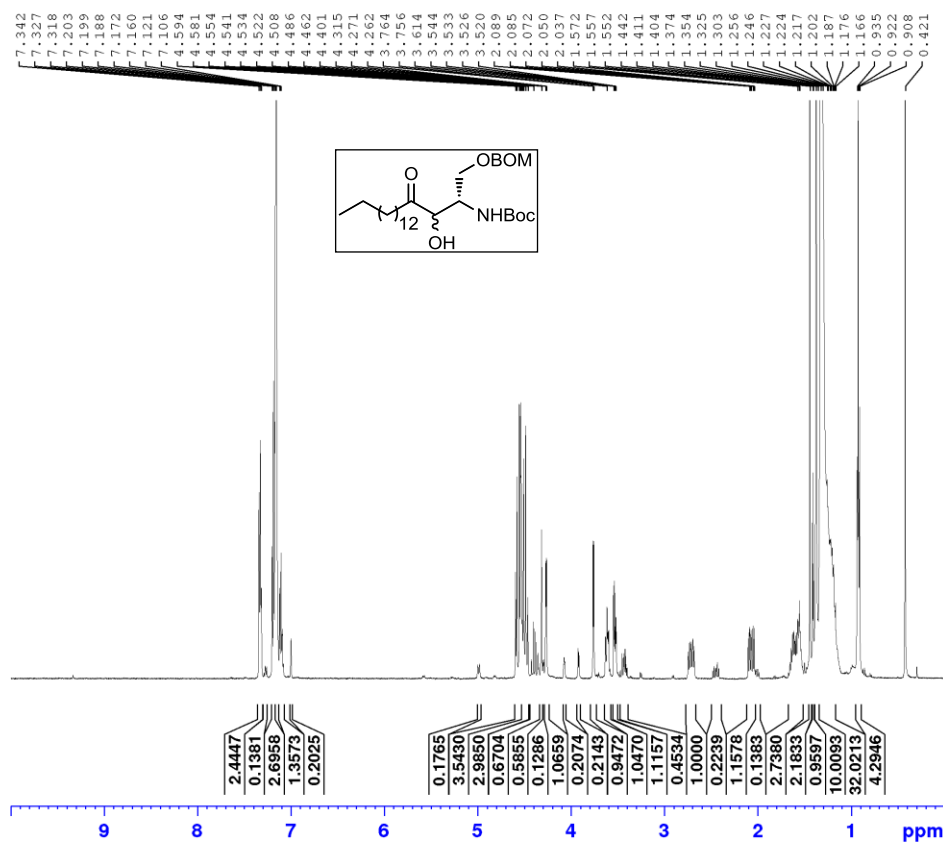
¹H NMR (500 MHz, CDCl_3): δ 9.76 (s, 1H), 2.42 (t, J = 7.3, 2H), 1.70–1.58 (m, 2H), 1.40–1.16 (m, 24 H), 0.88 (t, J = 5.7, 3H).



***tert*-butyl ((2*S*)-1-((benzyloxy)methoxy)-3-hydroxy-4-oxooctadecan-2-yl)carbamate (**21**)**



N-Boc-O-BOM-L-serinal (**20**) (0.3 g, 0.97 mmol.) and triazolium salt **1** (0.106 g, 0.29 mmol) were added to a Schlenk flask and fitted with a septum. The vessel was placed under vacuum and re-filled with argon three times to ensure inert atmosphere. Pentadecanal (1.32 mL, 4.85 mmol) and dry toluene (14 mL) were added sequentially. Lastly *i*-Pr₂NEt (0.34 mL, 1.94 mmol) was added and the septum was then quickly exchanged for a water condenser. The mixture was heated to 70 °C for 4 hours. The reaction was cooled to room temperature and quenched by addition of 1 M HCl (15 mL). The bi-phasic mixture was extracted with CH₂Cl₂ (3x20 mL) and dried over Na₂SO₄. This mixture was purified by column chromatography (7:1 hexane:EtOAc) to afford a 5:1 mixture of diastereomers. *R*_f = 0.20 (7:1 hexane:EtOAc). The resulting mixture was carried to the next step without further purification.



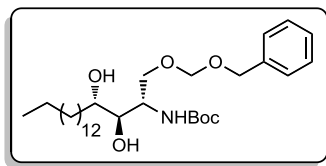
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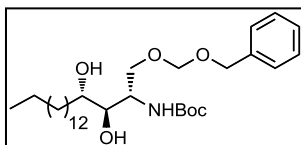
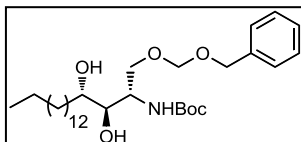
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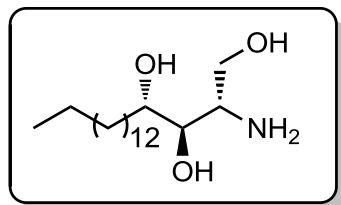
***tert*-butyl ((2*S*,3*R*,4*S*)-1-((benzyloxy)methoxy)-3,4-dihydroxyoctadecan-2-yl)carbamate (**22**)**



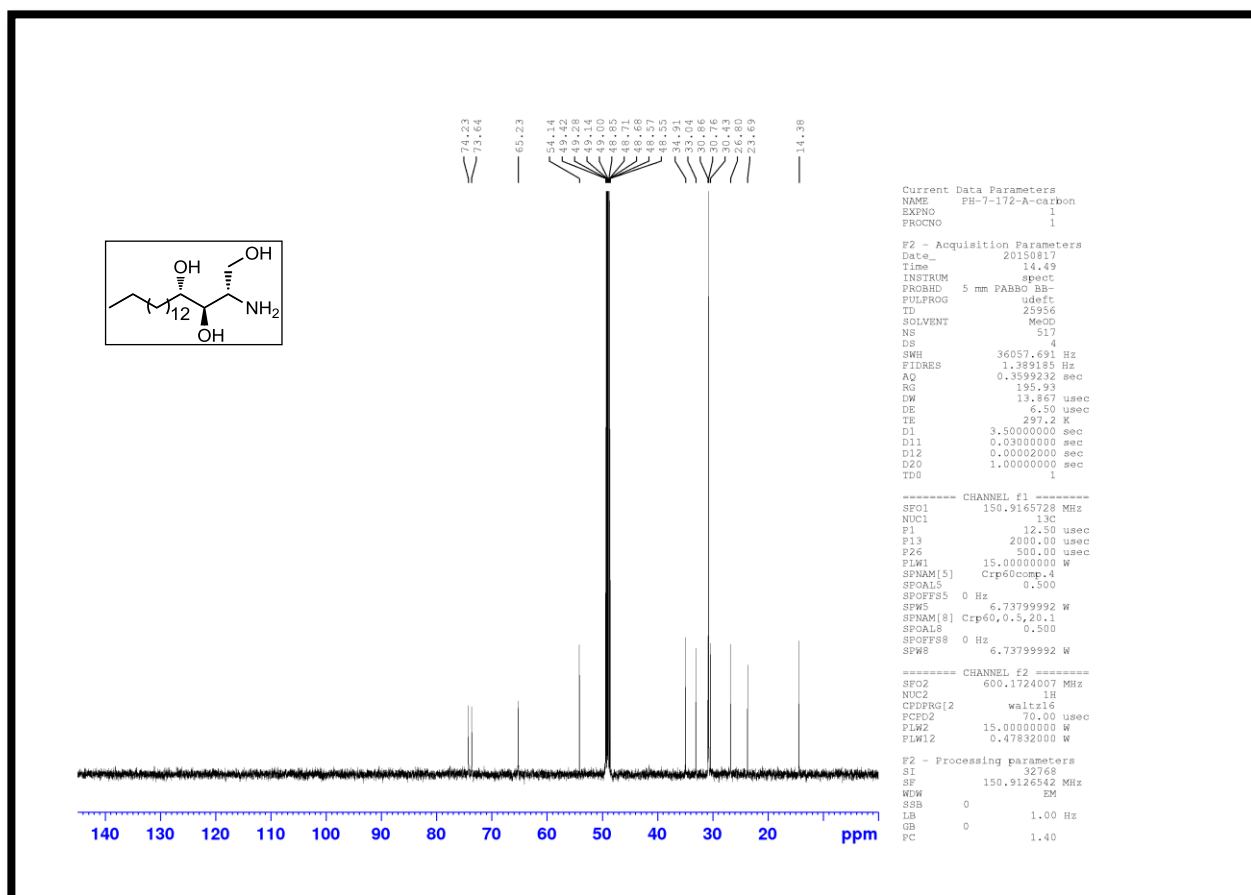
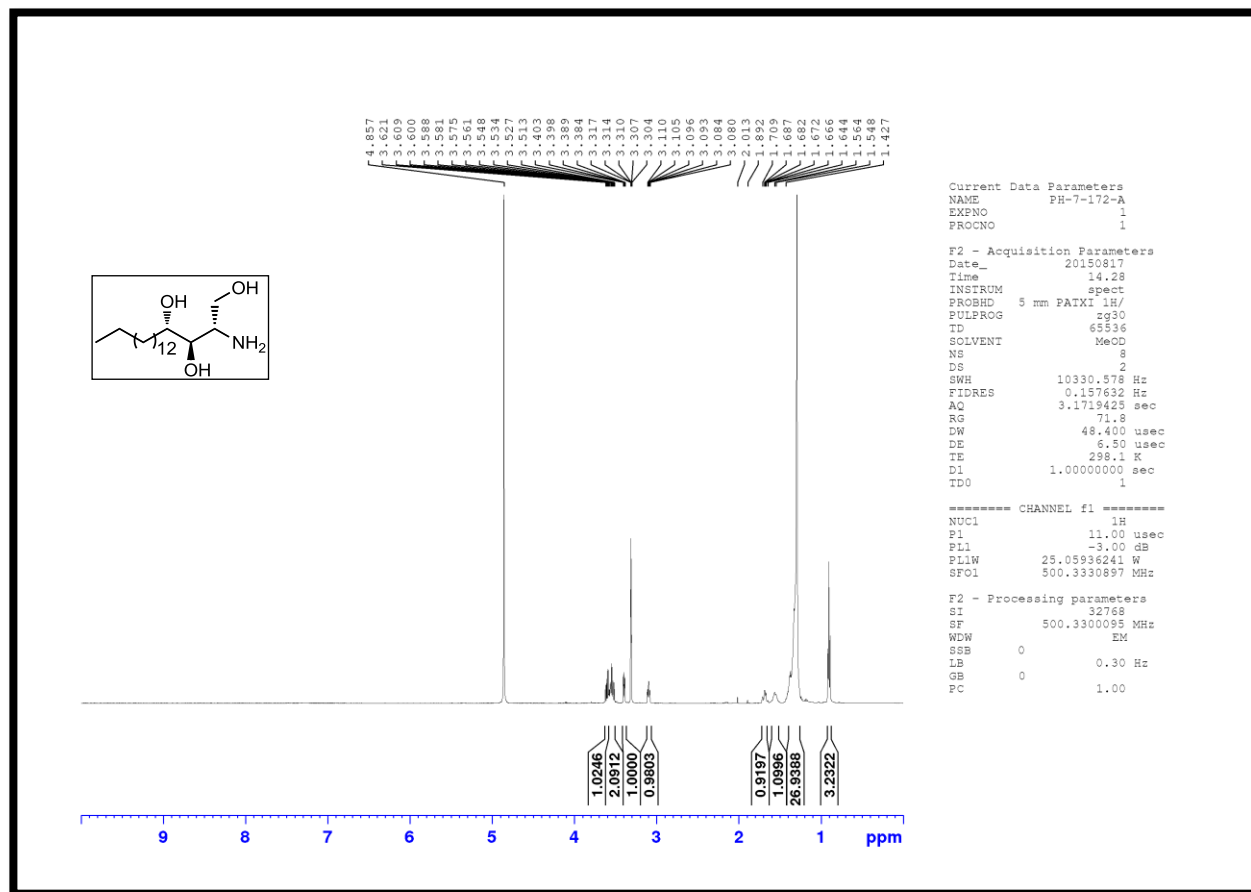
To a pre-cooled (0°C) dry round-bottomed flask containing NaBH₄ (0.44 mmol, 1 equiv.) in THF (1 mL) was added a solution of ZnCl₂ (0.44 mmol, 1 equiv.) in dry Et₂O (0.88 mL) under argon. This mixture was stirred at 0°C for 5 minutes and a solution of **21** (0.44 mmol, 1 equiv.) in THF (3.5 mL) was added. The mixture was gradually warmed to room temperature and stirred at this temperature for 16 h. The reaction was quenched with the slow addition of water at 0°C. The crude mixture was diluted in Et₂O (40 mL) and the layers were separated. The aqueous phase was washed with Et₂O (2×40mL) and the combined organic layers were dried over Na₂SO₄ and then concentrated. Column chromatography (7:1 hexane:acetone) afforded **22** as a white wax (183 mg, 35% over two steps). *R*_f = 0.21 (7:1 hexane:acetone); [*α*]_D^{27 °C} = -47 (*c* 0.9, CHCl₃); **FTIR** (KBr film) *v*_{max} (cm⁻¹): 3430, 2921, 2853, 1683, 1515, 1455, 1361, 1169, 734, 698; **¹H NMR** (600 MHz, C₆D₆) Mixture of rotamers: δ 7.24 (d, *J* = 7.5 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 2H), 7.08 (t, *J* = 7.3 Hz, 1H), 5.44–5.36 (m, 1H), 4.43 (s, 2H), 4.38 (s, 2H), 4.37–4.30 (m, 2H), 3.64–3.53 (m, 4H), 3.01 (d, *J* = 3.2 Hz, 0.8H), 3.07 (d, *J* = 2.8 Hz, 0.2H), 2.04–1.95 (m, 1H), 1.87–1.76 (m, 1H), 1.69–1.52 (m, 2H), 1.88–1.34 (m, 14H), 1.32–1.21 (m, 19 H), 0.90 (t, *J* = 6.8 Hz, 3H); **¹³C NMR** (150 MHz, C₆D₆) Mixture of rotamers (minor rotamer indicated by asterisk); δ 158.1, 138.7, 129.0, 128.4, 128.7, 128.2, 95.4, 80.3, 76.5, 70.4*, 70.4, 70.2, 51.0, 35.3*, 34.0, 32.7*, 32.7, 32.3*, 30.8, 30.7, 30.6, 30.6, 30.6, 30.5, 30.2, 30.2*, 28.7, 26.8, 23.5, 23.4*, 14.7, 14.7*; **HRMS** (TOF) *m/z*: [M+Na] Calcd for C₃₁H₅₅NO₆Na 560.39216; Found 560.3914.



D-arabino-phytosphingosine (23)

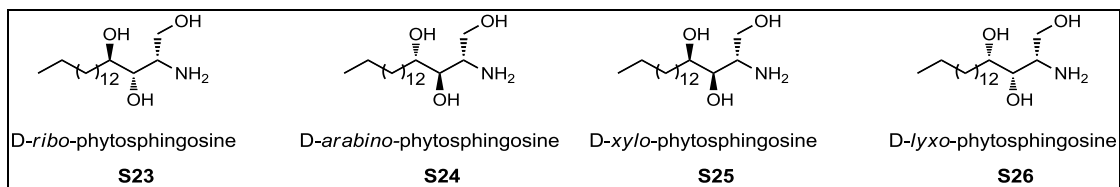


To a mixture of **22** (0.04 mmol, 1 equiv.) in THF (0.6 mL) and MeOH (0.3 mL) was added a freshly prepared solution of acyl chloride (1.12 mmol, 30 equiv.) in MeOH (1 mL) at 0°C. The reaction mixture was sealed and gradually warmed to room temperature. After 3 days, the reaction was quenched by addition of sat. NaHCO₃aq. (1 mL). The solids were filtered and washed with EtOAc (3×5 mL) and concentrated *in vacuo*. The crude was partitioned between in EtOAc (5 mL) and H₂O (2 mL). The layers were separated and the organic layer was washed with water (2×2 mL). The aqueous phase was back extracted with EtOAc (2×3 mL). The combined organic layers were dried over Na₂SO₄ and concentrated. Purification by column chromatography (4:1:0.1 CHCl₃:MeOH:NH₄OH) afforded D-arabino-phytosphingosine as a white solid (7 mg, 59%, 6 LLS, 8% overall yield). $R_f = 0.50$ (4:1:0.1 CHCl₃:MeOH:NH₄OH); Melting range: 78–82 °C (lit: 82–83)²⁴; $[\alpha]_D^{28} = -8$ (*c* 0.4, pyridine), (lit: $[\alpha]_D^{23} = -3.79$ (*c* 0.6, pyridine))²⁴; **FTIR** (KBr film) ν_{\max} (cm⁻¹): 3464, 2985, 2086, 1743, 1374, 1241, 1047, 938, 847; **¹H NMR** (500 MHz, CD₃OD) δ 3.60 (dd, *J* = 10.8, 7.0 Hz, 1H), 3.58–3.51 (m, 1H), 3.53 (dd, *J* = 11.0, 6.4 Hz, 1H), 3.39 (dd, *J* = 7.0, 2.2 Hz, 1H), 3.09 (ddd, *J* = 7.0, 7.9, 2.2 Hz, 1H), 1.73–1.63 (m, 1H), 1.60–1.52 (m, 1H), 1.40–1.26 (m, 26H), 0.90 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (150 MHz, CD₃OD) δ 74.4, 73.8, 65.4, 54.3, 35.1, 33.2, 31.0, 30.9, 30.9, 30.6, 26.9, 23.8, 14.5; **HRMS** (TOF) *m/z*: [M+1] Calcd for C₁₈H₄₀NO₃ 318.300271; Found 318.2994.



¹H NMR and ¹³C NMR spectral data comparison of phytosphingosines S23-S26 and 23

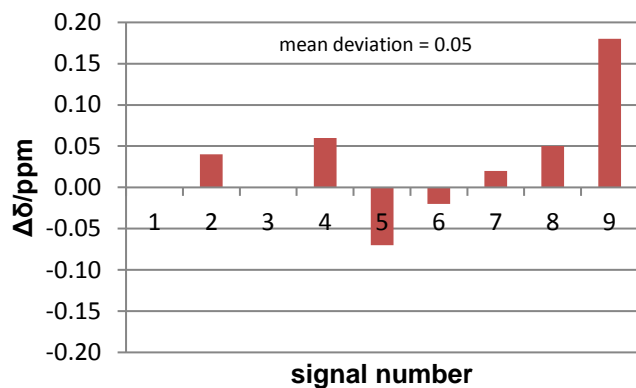
¹H NMR data for phytosphingosines S23-S26 and 23 in CD₃OD



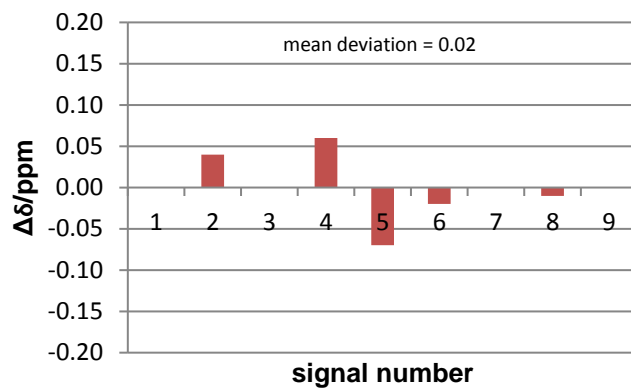
signal number	δ 23 (ppm)	δ S23 ^a (ppm)	Δδ S23 vs. 23 (ppm)	δ S24 ^a (ppm)	Δδ S24 vs. 23 (ppm)	δ S25 ^a (ppm)	Δδ S25 vs. 23 (ppm)	δ S26 ^a (ppm)	Δδ 26 vs. 23 (ppm)
1	0.90	0.90	0.00	0.90	0.00	0.90	0.00	0.87	-0.03
2	1.29	1.33	0.04	1.33	0.04	1.34	0.05	1.32	0.03
3	1.56	1.56	0.00	1.56	0.00	1.47	-0.09	1.47	-0.09
4	1.68	1.74	0.06	1.74	0.06	1.54	-0.14	1.52	-0.16
5	3.09	3.02	-0.07	3.02	-0.07	3.00	-0.09	2.94	-0.15
6	3.39	3.37	-0.02	3.37	-0.02	3.47	0.08	3.34	-0.05
7	3.56	3.58	0.02	3.56	0.00	3.63	0.07	3.64	0.08
8	3.53	3.58	0.05	3.52	-0.01	3.56	0.03	3.54	0.01
9	3.60	3.78	0.18	3.60	0.00	3.65	0.05	3.74	-0.05
mean deviation			0.05		0.02		0.07		0.07

^a Reported literature values.²⁵

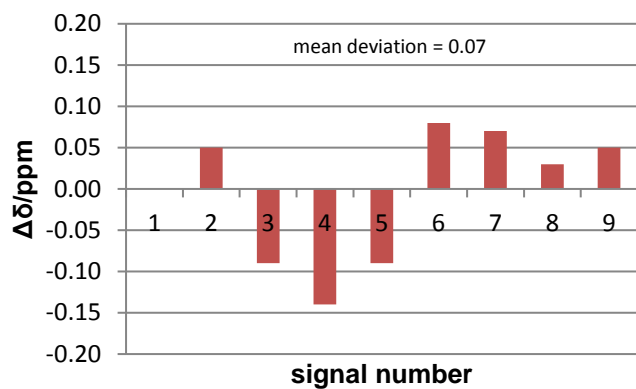
**^1H NMR $\Delta\delta$ vs. signal number
(D-ribo-phytosphingosine (S23) – 23)**



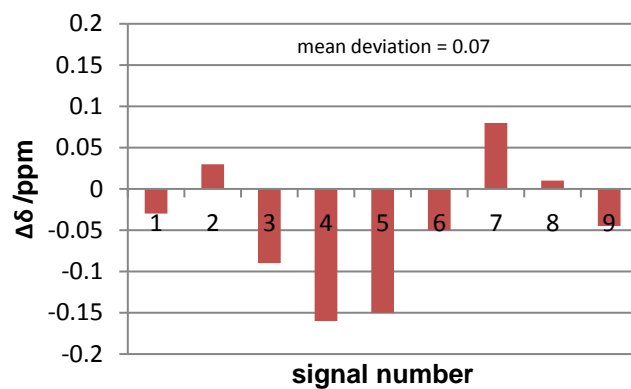
**^1H NMR $\Delta\delta$ vs. signal number
(D-arabino-phytosphingosine (S24) – 23)**



**^1H NMR $\Delta\delta$ vs. signal number
(D-xylo-phytosphingosine (S25) – 23)**



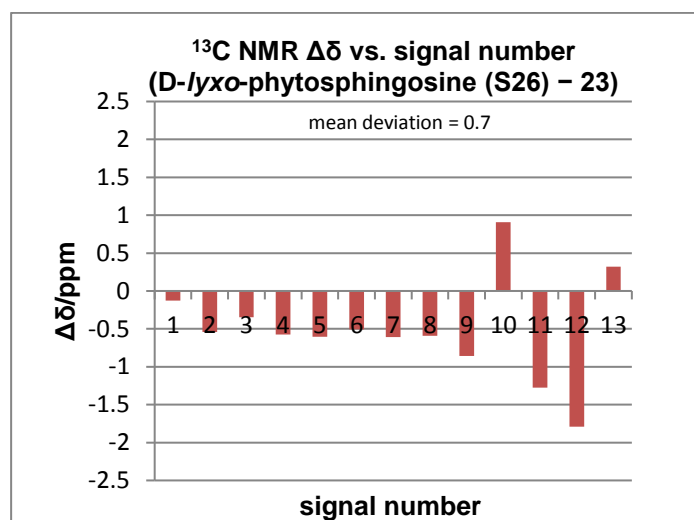
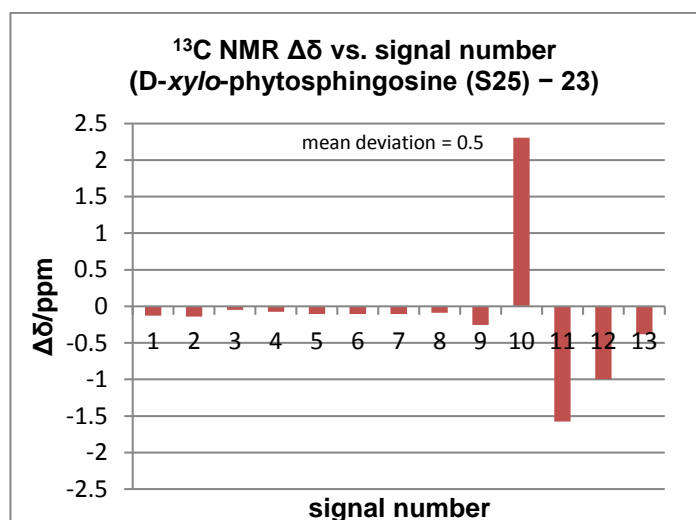
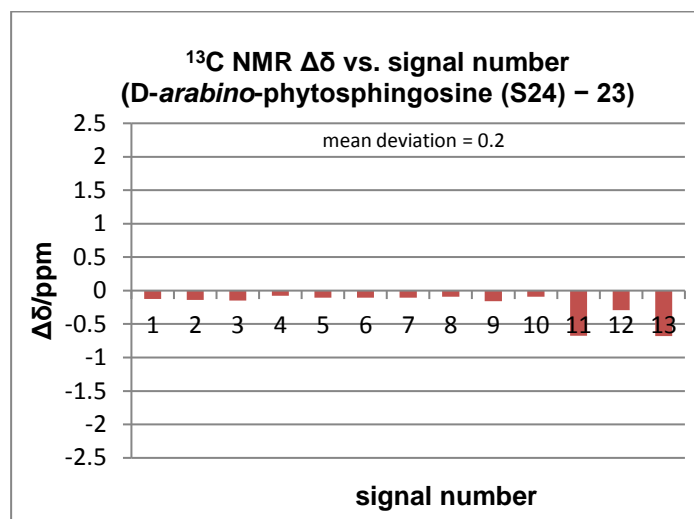
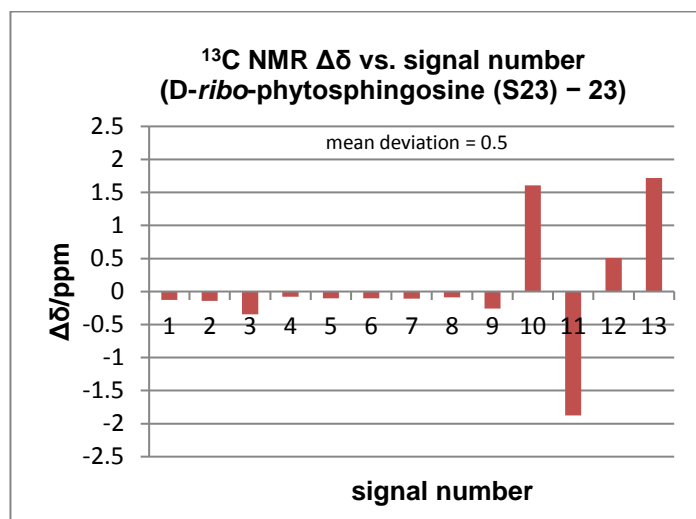
**^1H NMR $\Delta\delta$ vs. signal number
(D-lyxo-phytosphingosine (S26) – 23)**



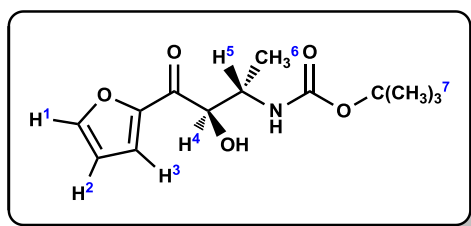
¹³C NMR data for phytosphingosines S23-S26 and 23 in CD₃OD

signal number	δ 23 (ppm)		δ S23 ^a (ppm)	Δδ S23 vs. 23 (ppm)		δ S24 ^a (ppm)	Δδ S24 vs. 23 (ppm)		δ S25 ^a (ppm)	Δδ S25 vs. 23 (ppm)		δ S26 ^a (ppm)	Δδ S26 vs. 23 (ppm)
1	14.5		14.4	-0.1		14.4	0.0		14.4	0.0		14.4	0.0
2	23.8		23.7	-0.1		23.7	-0.1		23.7	-0.1		23.3	-0.5
3	26.9		26.6	-0.3		26.8	-0.1		26.9	0.0		26.6	0.3
4	30.6		30.5	-0.1		30.5	-0.1		30.5	-0.1		30.0	-0.6
5	30.9		30.8	-0.1		30.8	-0.1		30.8	-0.1		30.3	-0.6
6	30.9		30.8	-0.1		30.8	-0.1		30.8	-0.1		30.4	-0.5
7	31.0		30.9	-0.1		30.9	-0.1		30.9	-0.1		30.4	-0.6
8	33.2		33.1	-0.1		33.1	-0.1		33.1	-0.1		32.6	-0.6
9	35.1		34.8	-0.3		34.9	-0.2		34.8	-0.3		34.2	-0.9
10	54.3		55.9	1.6		54.2	-0.1		56.6	2.3		55.2	0.9
11	65.4		63.5	-1.9		64.7	-0.7		63.8	-1.6		64.1	-1.3
12	73.8		74.3	0.5		73.5	-0.3		72.8	-1.0		72.0	-1.8
13	74.4		76.1	1.7		73.7	-0.7		74.0	-0.4		74.7	0.3
mean deviation				0.5			0.2			0.5			0.7

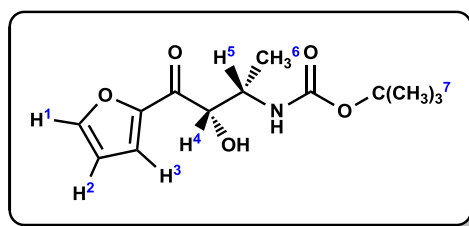
^a Reported literature values.²⁵



Predicted ^1H NMR shifts versus experimental ^1H NMR shifts



anti

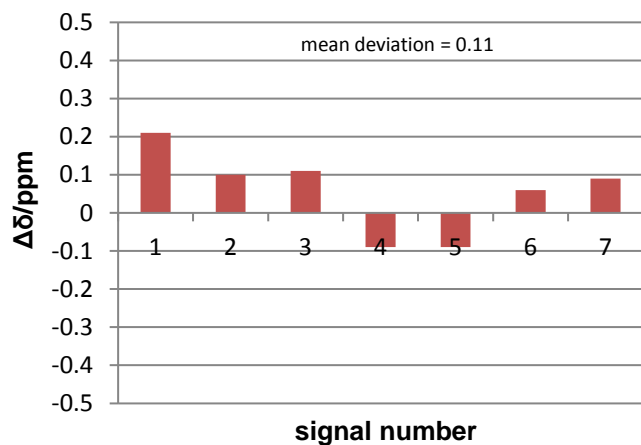


syn

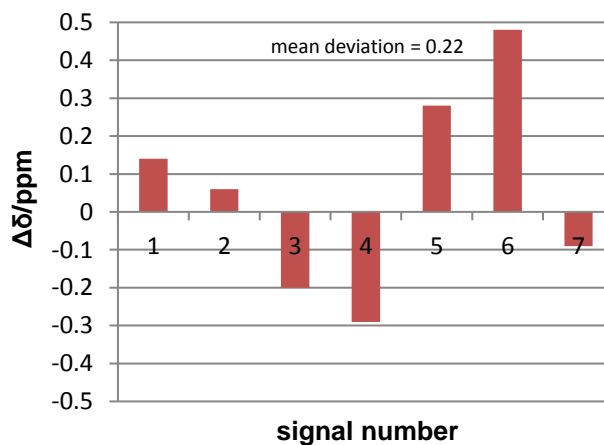
Major isomer (2)

signal number	observed shift (ppm)	calculated shift – anti (ppm)	$\Delta\delta$ obs. vs. calc. anti (ppm)	calculated shift – syn (ppm)	$\Delta\delta$ obs. vs. calc. syn (ppm)
1	7.65	7.44	0.21	7.51	0.14
2	6.59	6.49	0.10	6.53	0.06
3	7.31	7.20	0.11	7.51	-0.20
4	4.66	4.75	-0.09	4.95	-0.29
5	4.40	4.49	-0.09	4.12	0.28
6	1.36	1.30	0.06	0.88	0.48
7	1.33	1.24	0.09	1.42	-0.09
mean deviation			0.11		0.22

^1H NMR $\Delta\delta$ vs. signal number
obs. (2) - calc. *anti*

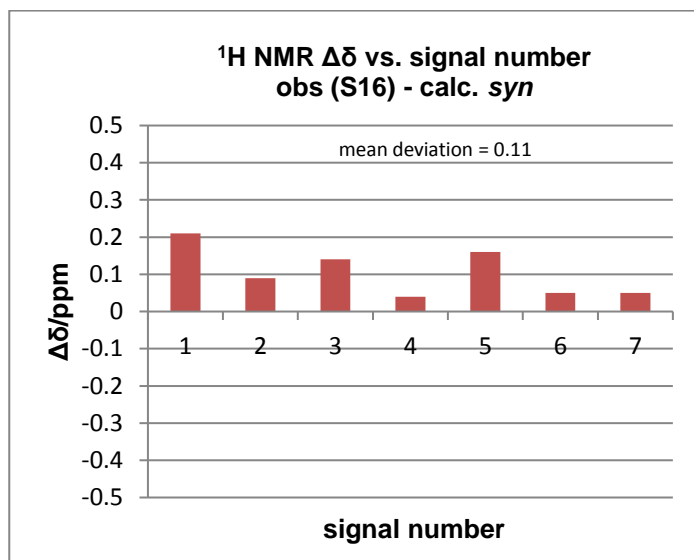
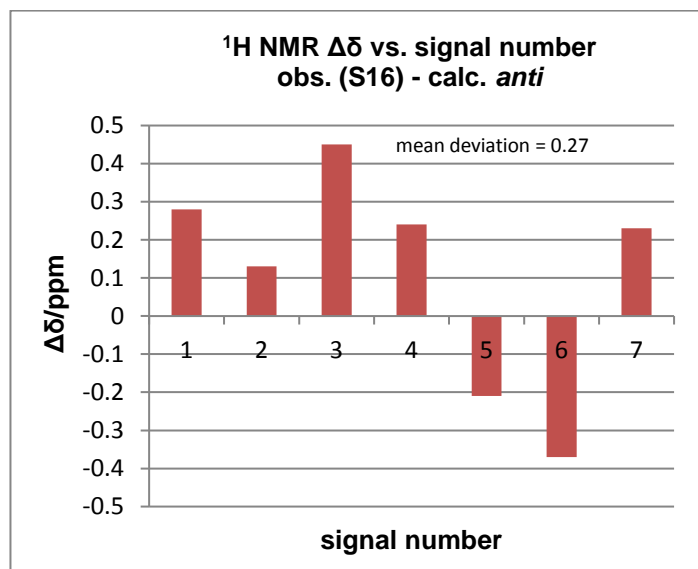


^1H NMR $\Delta\delta$ vs. signal number
obs. (2) - calc. *syn*

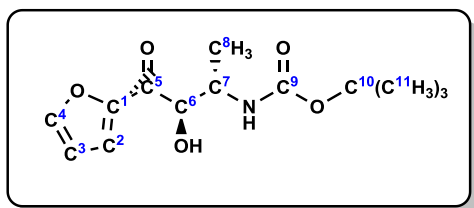


Minor isomer (S16)

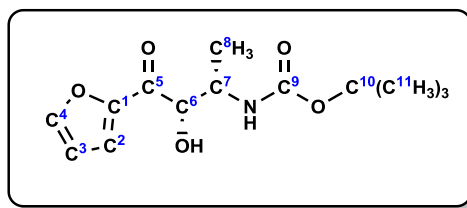
signal number	observed shift (ppm)	calculated shift –anti (ppm)	$\Delta\delta$ obs. vs. calc. anti (ppm)	calculated shift –syn (ppm)	$\Delta\delta$ obs. vs. calc. syn (ppm)
1	7.72	7.44	0.28	7.51	0.21
2	6.62	6.49	0.13	6.53	0.09
3	7.65	7.20	0.45	7.51	0.14
4	4.99	4.75	0.24	4.95	0.04
5	4.28	4.49	-0.21	4.12	0.16
6	0.93	1.30	-0.37	0.88	0.05
7	1.47	1.24	0.23	1.42	0.05
mean deviation			0.27		0.11



Predicted ^{13}C NMR shifts versus experimental ^{13}C NMR shifts



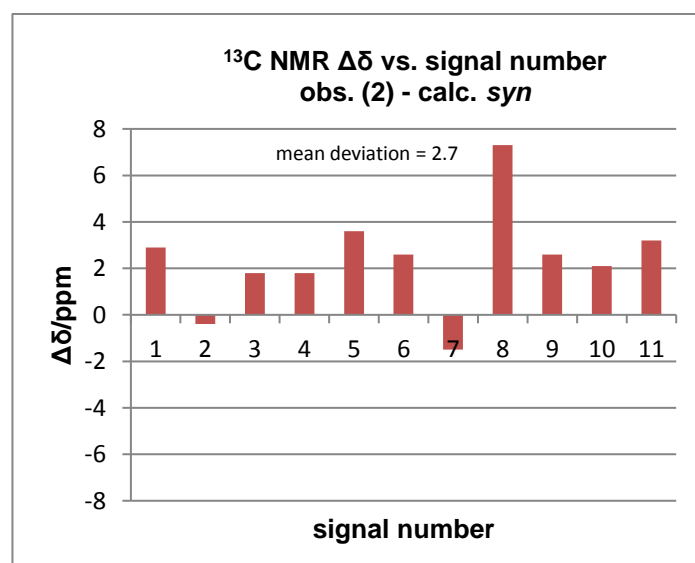
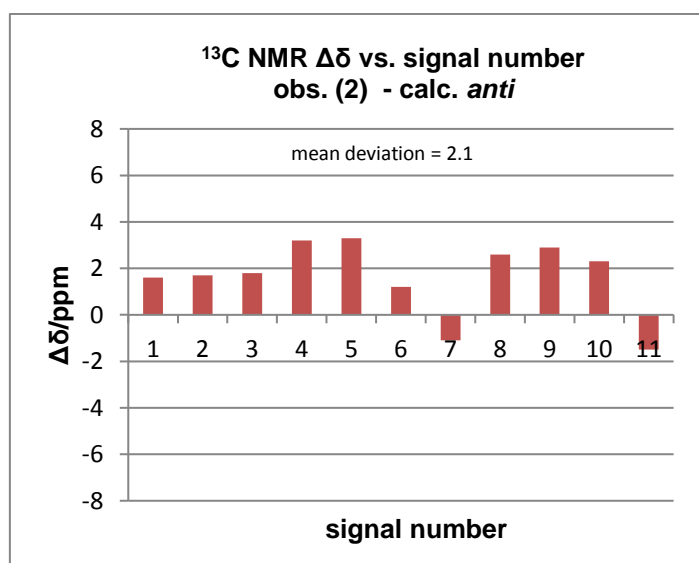
anti



syn

Major isomer (2)

signal number	observed shift (ppm)		calculated shift – anti (ppm)	$\Delta\delta$ obs. vs. calc. anti (ppm)	calculated shift – syn (ppm)	$\Delta\delta$ obs. vs. calc. syn (ppm)
1	150.8		149.2	1.6	147.9	2.9
2	118.9		117.2	1.7	119.3	-0.4
3	112.9		111.1	1.8	111.1	1.8
4	147.3		144.1	3.2	145.5	1.8
5	188.3		185.0	3.3	184.7	3.6
6	76.7		75.5	1.2	74.1	2.6
7	49.2		50.3	-1.1	50.7	-1.5
8	19.1		16.5	2.6	11.8	7.3
9	155.3		152.4	2.9	152.7	2.6
10	79.6		77.3	2.3	77.5	2.1
11	28.4		29.9	-1.5	25.2	3.2
mean deviation				2.1		2.7



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