Supporting Information for

Doubly diastereoselective [3,3]-sigmatropic aza-Claisen rearrangements

Stephen G. Davies, A. Christopher Garner, Rebecca L. Nicholson,
James Osborne, Paul M. Roberts, Edward D. Savory,
Andrew D. Smith and James E. Thomson

Department of Chemistry, University of Oxford,
Chemistry Research Laboratory,
Mansfield Road, Oxford, OX1 3TA, UK

steve.davies@chem.ox.ac.uk

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1. Experimental

General Experimental

All 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. 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 solvents were used as supplied (analytical or HPLC grade) 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.

Elemental analyses were recorded by the microanalysis service of the Inorganic Chemistry Laboratory, University of Oxford, UK. 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 as either a thin film on NaCl plates (film) or a KBr disc (KBr), as stated. 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 unless otherwise stated. The field was locked by external referencing to the relevant deuteron resonance. 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 1: Reduction with $LiAlH_4$

A solution of $LiAlH_4$ (1.0 eq) was added dropwise to a stirred solution of ester (1.0 eq) in THF at 0 °C and the resultant mixture was allowed to warm to rt over 16 h. The reaction was quenched with ice and EtOAc at 0 °C, then stirred for 1 h, filtered through Celite (eluent Et_2O) and concentrated *in vacuo*.

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

General Procedure 2: *O*-Benzylation

A solution of alcohol (1.0 eq) in THF was added dropwise *via* cannula to a suspension of sodium hydride (1.2 eq) in THF at 0 °C. After stirring for 15 min, 15-crown-5 (1.3 eq) and BnBr (2.0 eq) were added and the resultant mixture was heated at reflux. After 16 h the reaction mixture was cooled to rt and sat aq NH_4Cl was added. The resultant mixture was extracted with EtOAc, and the combined organic extracts were dried, filtered and concentrated *in vacuo*.

General Procedure 3: *N*-Deallylation

Wilkinson's catalyst (0.05 eq) was added in one portion to a stirred solution of amine (1.0 eq) in $MeCN/H_2O$ (85:15) at rt. The resultant mixture was heated at reflux for 16 h then cooled to rt and concentrated *in vacuo*.

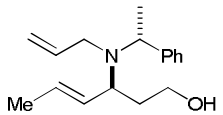
General Procedure 4: *N*-Acylation

Et_3N (2.5 eq) and the requisite acid chloride (2.0 eq) were added sequentially to a stirred solution of amine (1.0 eq) and DMAP (0.1 eq) in CH_2Cl_2 at rt. After stirring for 16 h sat aq NH_4Cl was addedThe layers were separated and the organic layer was washed with sat aq $NaHCO_3$, then dried, filtered and concentrated *in vacuo*.

General Procedure 5: Aza-Claisen rearrangement

TMSCl (2.0 eq) and LiHMDS (1.5 eq) were added sequentially to a stirred solution of amide (1.0 eq) in toluene at rt. The reaction mixture was heated at reflux for 16 h then allowed to cool to rt. Sat aq NH_4Cl was then aadded and the aqueous layer was extracted with EtOAc. The combined organic extracts were then dried, filtered and concentrated *in vacuo*.

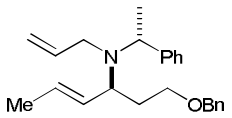
(3*S*,4*E*,α*R*)-3-[*N*-Allyl-*N*-(α-methylbenzyl)amino]hex-4-en-1-ol 12



Following *General Procedure 1*, **11** (10.5 g, 32.0 mmol, 94% de) and $LiAlH_4$ (32.0 mL, 32.0 mmol) in THF (200 mL) afforded **12** (8.10 g, 98%, 94% de) as a yellow oil; $[\alpha]_D^{21}$ –21.9 (*c* 1.2 in $CHCl_3$); ν_{max} (film) 3369 (O–H); δ_H (400 MHz, $CDCl_3$) 1.33-1.43 (1H, m, C(2)H_AH_B), 1.39 (3H, d, *J* 6.9, C(α)CH_3), 1.72 (3H, d, *J* 5.3, C(6)H_3), 1.84-1.90 (1H, m, C(2)H_AH_B), 3.14 (1H, app ddt, *J* 14.4, 8.4, 1.0, C(1')H_AH_B), 3.37 (1H, ddt, *J* 14.4, 5.2, 1.6, C(1')H_AH_B), 3.42 (1H, ddd, *J* 10.8, 9.6, 2.8, C(1)H_AH_B), 3.52 (1H, ddd, *J* 10.8, 6.8, 4.4, C(3)*H*), 3.61 (1H, dt, *J* 10.8, 4.4, C(1)H_AH_B), 4.10 (1H, q, *J* 6.9, C(α)*H*), 4.20-4.40 (1H, br s, O*H*), 5.07-5.15

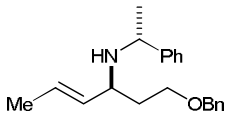
(2H, m, C(3')H_2), 5.49-5.58 (2H, m, C(4)*H*, C(5)*H*), 5.78-5.84 (1H, m, C(2')*H*), 7.23-7.37 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 15.9, 18.1, 34.3, 49.5, 57.3, 58.9, 62.4, 116.9, 126.9, 127.0, 128.0, 128.2, 131.0, 137.4, 144.1; *m/z* (APCI$^+$) 260 ([M+H]+, 57%), 162 ([M–C_6H_9O]$^+$, 100); HRMS (CI$^+$) $C_{17}H_{26}NO^+$ ([M+H]$^+$) requires 260.2014; found 260.2020.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-allyl-*N*-(α-methylbenzyl)amino]hex-4-ene 13



Following *General Procedure 2*, **12** (8.03 g, 31.0 mmol), NaH (1.49 g, 37.2 mmol), 15-crown-5 (8.00 mL, 40.3 mmol), and BnBr (7.38 mL, 62.0 mmol) in THF (150 mL) afforded **13** (8.03 g, 74%, 94% de) as a yellow oil after flash column chromatography (eluent pentane/EtOAc, 99:1); $[\alpha]_D^{24}$ +10.8 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1494 (C=C), 1493 (C=C); δ_H (400 MHz, $CDCl_3$) 1.35 (3H, d, *J* 6.8, C(α)CH_3), 1.60-1.75 (1H, m, C(2)H_AH_B), 1.71 (3H, d, *J* 4.8, C(6)H_3), 1.83-1.95 (1H, m, C(2)H_AH_B), 3.11 (1H, ddt, *J* 14.8, 7.2, 1.2, C(1')H_AH_B), 3.21 (1H, ddt, *J* 14.8, 5.2, 1.6, C(1')H_AH_B), 3.37-3.41 (1H, m, C(α)*H*), 3.41 (2H, t, *J* 6.8, C(1)H_2), 4.38 (1H, d, *J* 11.9, OCH_AH_BPh), 4.44 (1H, d, *J* 11.9, OCH_AH_BPh), 5.03 (1H, ddd, *J* 10.4, 2.2, 1.2, C(3')H_AH_B), 5.09 (1H, ddd, *J* 17.2, 1.8, 1.2, C(3')H_AH_B), 5.43-5.53 (2H, m, C(4)*H*, C(5)*H*), 5.73-5.83 (1H, m, C(2')*H*), 7.18-7.39 (10H, m, 2 × *Ph*); δ_H (100 MHz, $CDCl_3$) 17.5, 18.0, 33.3, 49.4, 56.4, 56.5, 68.2, 72.7, 115.3, 126.2, 126.6, 127.4, 127.6, 127.9, 128.2, 131.7, 138.8, 139.1, 145.8; *m/z* (APCI$^+$) 350 ([M+H]$^+$, 35%), 162 ([M–C_6H_9O]$^+$, 22), 122 ([$C_8H_{12}N$]$^+$, 100); HRMS (CI$^+$) $C_{24}H_{32}NO^+$ ([M+H]$^+$) requires 350.2484; found 350.2483.

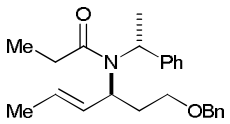
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(α-methylbenzyl)amino]hex-4-ene 14



Following *General Procedure 3*, **13** (3.12 g, 8.94 mmol, 94% de) and $RhCl(PPh_3)_3$ (414 mg, 0.45 mmol) in MeCN/H_2O (85:15, 100 mL) afforded **14** (2.12 g, 79%, >98% de) as an orange oil after flash column chromatography (eluent pentane/EtOAc, 7:1); $[\alpha]_D^{21}$ +58.8 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 3341 (N–H); δ_H (400 MHz, $CDCl_3$) 1.28 (3H, d, *J* 6.5, C(α)CH_3), 1.44-1.49 (1H, br s, N*H*), 1.63 (3H, dd, *J* 6.5, 1.6, C(6)H_3), 1.62-1.70 (1H, m, C(2)H_AH_B), 1.82-1.90 (1H, m, C(2)H_AH_B), 3.17-3.22 (1H, m, C(3)*H*), 3.44-3.56 (1H, m, C(1)H_AH_B), 3.56 (1H, dt, *J* 9.2, 6.0, C(1)H_AH_B), 3.85 (1H, q, *J* 6.5, C(α)*H*), 4.46 (1H, d, *J* 11.9, OCH_AH_BPh), 4.51 (1H, d, *J* 11.9, OCH_AH_BPh), 5.19 (1H, ddq, *J* 15.2, 8.4, 1.6, C(4)*H*), 5.45 (1H, dq, *J* 15.2, 6.5, C(5)*H*), 7.20-7.39 (10H, m, 2 × *Ph*); δ_C (100 MHz, $CDCl_3$) 17.7, 23.2, 35.4, 54.6, 55.5, 67.7, 72.9,

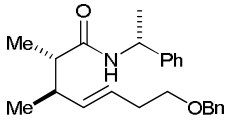
126.4, 126.6, 127.4, 127.6, 128.3, 134.1, 138.6, 146.5; *m/z* (APCI$^+$) 310 ([M+H]$^+$, 60%), 189 ([M–$C_8H_{11}N$]$^+$, 5), 122 ([$C_8H_{12}N$]$^+$, 5); HRMS (CI$^+$) $C_{21}H_{28}NO^+$ ([M+H]$^+$) requires 310.2171; found 310.2177.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-propionyl-*N*-(α-methylbenzyl)amino]hex-4-ene 15



Following *General Procedure 4*, **14** (200 mg, 0.65 mmol), propionyl chloride (0.11 mL, 1.29 mmol), Et_3N (0.23 mL, 1.62 mmol) and DMAP (8 mg, 0.07 mmol) in CH_2Cl_2 (10 mL) afforded **15** as a colourless oil (198 mg, , 84%, >98% de) after flash column chromatography (eluent pentane/EtOAc, 7:1); $[\alpha]_D^{24}$ +32.4 (*c* 1.4 in $CHCl_3$); ν_{max} (film) 1643 (C=O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.04 (3H, t, *J* 7.2, C(3')H_3), 1.57 (3H, d, *J* 7.0, C(α)CH_3), 1.67 (3H, d, *J* 6.5, C(6)H_3), 1.61-1.69 (1H, m, C(2)H_AH$_B$), 1.99-2.06 (1H, m, C(2)H$_A$$H_B$), 2.32 (1H, dq, *J* 15.5, 7.2, C(2')H_AH$_B$), 2.40 (1H, dq, *J* 15.5, 7.2, C(2')H$_A$$H_B$), 3.01-3.11 (2H, m, C(1)H_2), 3.92-4.04 (1H, br s, C(3)*H*), 4.24 (2H, s, OCH_2Ph), 5.07 (1H, q, *J* 7.0, C(α)*H*), 5.56 (1H, dq, *J* 14.5, 6.5, C(5)*H*), 5.75-5.83 (1H, m, C(4)*H*), 7.17-7.41 (10H, m, 2 × *Ph*); δ_C (100 MHz, DMSO-d_6, 363 K) 10.4, 18.2, 19.4, 28.4, 34.3, 55.7, 68.0, 72.6, 127.5, 127.6, 128.0, 128.1, 128.9, 132.4, 139.6, 173.5; *m/z* (APCI$^+$) 366 ([M+H]$^+$, 8%), 189 ([M–C_8H_7]$^+$, 17), 122 ([M–$C_{13}H_{15}O$]$^+$, 100); HRMS (CI$^+$) $C_{24}H_{32}NO_2^+$ ([M+H]$^+$) requires 366.2433; found 366.2432.

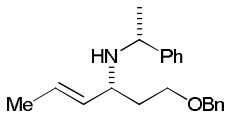
(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2,3-dimethyl-7-benzyloxy-hept-4-enamide 17



Following *General Procedure 5*, **15** (196 mg, 0.54 mmol), LiHMDS (0.80 mL, 0.80 mmol) and TMSCl (0.14 mL, 1.07 mmol) in toluene (10 mL) afforded the crude product in 92% de. Purification by flash column chromatography (eluent petroleum/EtOAc, 5:1) afforded **17** as a white crystalline solid (153 mg, 90%, 92% de). Purification of an aliquot by recrystallisation from petroleum/Et_2O gave an analytical sample of the major diastereoisomer **17** as a white crystalline solid; Found C, 78.7; H, 8.4; N, 3.9%; $C_{24}H_{31}NO_2$ requires C, 78.9; H, 8.55; N, 3.8%; mp 83-85 °C (petroleum/Et_2O); $[\alpha]_D^{21}$ +75.0 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 3285 (N–H), 1641 (C=O), 1547 (C=O); δ_H (400 MHz, $CDCl_3$) 1.00 (3H, d, *J* 6.8, C(3)CH_3), 1.10 (3H, d, *J* 6.9, C(2)CH_3), 1.43 (3H, d, *J* 6.9, C(α)CH_3), 2.02 (1H, dq, *J* 7.0, 6.9, C(2)*H*), 2.32 (2H, m, C(6)H_2), 2.37 (1H, m, (3)*H*), 3.48 (2H, t, *J* 6.9, C(7)H_2), 4.51 (2H, s, OCH_2Ph), 5.12 (1H, m, C(α)*H*), 5.44-5.46 (2H, m, C(4)*H*, C(5)*H*), 5.60 (1H, d, *J* 7.0, N*H*), 7.24-7.38 (10H, m, 2 × *Ph*); δ_C (100 MHz, $CDCl_3$) 14.7, 17.2, 21.6,

33.0, 39.9, 47.2, 48.3, 70.0, 72.8, 126.2, 126.4, 127.3, 127.5, 127.6, 128.3, 128.6, 135.4, 138.5, 143.5, 174.4; *m/z* (APCI$^+$) 366 ([M+H]$^+$, 100%).

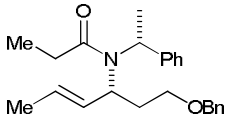
(3*R*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(α-methylbenzyl)amino]hex-4-ene 20



Following *General Procedure 1*, **18** (210 mg, 1.03 mmol, 92% de) and $LiAlH_4$ (1.03 mL, 1.03 mmol) in THF (30 mL) afforded alcohol **19** as a yellow oil (164 mg) which was used immediately in the next step; $[\alpha]_D^{24}$ +103 (*c* 0.8 in $CHCl_3$); ν_{max} (film) 3284 (N–H, O–H), 1108 (C–O); δ_H (400 MHz, $CDCl_3$) 1.31 (3H, d, *J* 6.6, C(α)CH_3), 1.46-53 (1H, m, C(2)H_AH$_B$), 1.57-1.67 (1H, m, C(2)H$_A$$H_B$), 1.71 (3H, dd, *J* 6.3, 1.5, C(6)H_3), 2.91 (1H, ddd, *J* 10.2, 8.5, 3.7, C(3)*H*), 3.60-3.72 (2H, m, C(1)H_2), 3.87 (1H, q, *J* 6.6, C(α)*H*), 5.22 (1H, ddq, *J* 15.2, 8.5, 1.5, C(4)*H*), 5.36 (1H, dq, *J* 15.2, 6.3, C(5)*H*), 7.20-7.36 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 17.7, 25.2, 37.6, 54.7, 58.8, 62.8, 127.0, 127.1, 127.6, 128.6, 132.6, 144.7; *m/z* (APCI$^+$) 220 ([M+H]$^+$, 11%), 105 ([C_8H_9]$^+$, 100); HRMS (CI$^+$) $C_{14}H_{22}NO^+$ ([M+H]$^+$) requires 220.1701; found 220.1398.

Following *General Procedure 2*, **19** (164 mg), NaH (35 mg, 0.87 mmol), 15-crown-5 (0.19 mL, 0.95 mmol), and BnBr (0.17 mL, 1.45 mmol) in THF (15 mL) afforded benzyl ether **20** as a yellow oil (124 mg, 55% over two steps, >98% de) after flash column chromatography (eluent petroleum/EtOAc, 1:2); $[\alpha]_D^{24}$ +34.3 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 3310 (N–H), 1103 (C–O); δ_H (400 MHz, $CDCl_3$) 1.30 (3H, d, *J* 6.8, C(α)CH_3), 1.58 (1H, br s, N*H*), 1.68 (3H, dd, *J* 6.0, 1.2, C(6)H_3), 1.59-1.78 (2H, m, C(2)H_2), 2.84-2.89 (1H, m, C(3)*H*), 3.41-3.52 (2H, m, C(1)H_2), 3.82 (1H, q, *J* 6.8, C(α)*H*), 4.39 (1H, d, *J* 11.9, OCH_AH$_B$Ph), 4.46 (1H, d, *J* 11.9, OCH$_A$$H_B$Ph), 5.19 (1H, ddq, *J* 15.2, 8.4, 1.2, C(4)*H*), 5.29 (1H, dq, *J* 15.2, 6.0, C(5)*H*), 7.20-7.36 (10H, m, 2 × *Ph*); δ_C (100 MHz, $CDCl_3$) 17.2, 25.1, 36.3, 54.6, 54.8, 68.1, 72.9, 127.5, 127.6, 128.3, 128.3, 126.6, 126.7, 128.8, 133.7, 138.5, 145.9; *m/z* (APCI$^+$) 310 ([M+H]$^+$, 100%), 122 ([M–$C_{13}H_{15}O$]$^+$, 46); HRMS (CI$^+$) $C_{21}H_{28}NO^+$ ([M+H]$^+$) requires 310.2171; found 310.2170.

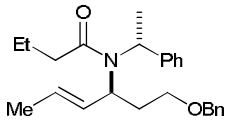
(3*R*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-propionyl-*N*-(α-methylbenzyl)amino]hex-4-ene 21



Following *General Procedure 4*, **20** (59 mg, 0.19 mmol), propionyl chloride (0.03 mL, 0.38 mmol), Et_3N (0.07 mL, 0.48 mmol) and DMAP (2 mg, 0.02 mmol) in CH_2Cl_2 (5 mL) afforded **21** (62 mg, 89%, >98% de) as a colourless oil after flash column chromatography (eluent petroleum/EtOAc, 7:1); $[\alpha]_D^{24}$ –26.0 (*c* 0.7 in $CHCl_3$); ν_{max} (film) 1643 (C=O), 1098 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.02 (3H, t, *J* 7.2, C(3')H_3),

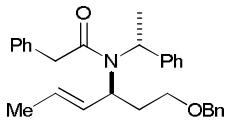
1.42 (3H, d, *J* 6.0, C(6)H_3), 1.60 (3H, d, *J* 7.0, C(α)CH_3), 1.91-1.98 (1H, m, C(2)H_AH_B), 2.10-2.20 (1H, m, C(2)H_AH_B), 2.28-2.42 (2H, m, C(2')H_2), 3.38 (1H, ddd, *J* 10.4, 8.5, 5.2, OCH_AH_BPh), 3.48 (1H, dt, *J* 10.4, 5.2, C(1')H_AH_B), 3.98-4.08 (1H, m, C(3)*H*), 4.42 (1H, d, *J* 11.7, C(1)H_2), 4.50 (1H, d, *J* 11.7, OCH_AH_BPh), 4.88-5.00 (1H, m, C(5)*H*), 5.08 (1H, q, *J* 7.0, C(α)*H*), 5.55 (1H, dd, *J* 15.2, 7.0, C(4)*H*), 7.22-7.38 (10H, m, 2 × *Ph*); δ_C (100 MHz, $CDCl_3$) 9.6, 17.5, 17.7, 27.8, 34.2, 54.9, 55.4, 67.6, 72.8, 127.3, 127.3, 127.4, 127.7, 128.0, 128.1, 128.3, 129.1, 138.4, 140.2, 176.7; *m/z* (APCI$^+$) 365 ([M+H]$^+$, 100%), 178 ([$C_{13}H_{16}$]$^+$, 100); HRMS (CI$^+$) $C_{24}H_{32}NO_2^+$ ([M+H]$^+$) requires 366.2433; found 366.2437.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-butyryl-*N*-(α-methylbenzyl)amino]hex-4-ene 29



Following *General Procedure 4*, **14** (496 mg, 1.61 mmol), butyryl chloride (0.33 mL, 3.21 mmol), Et_3N (0.56 mL, 4.01 mmol) and DMAP (19.6 mg, 0.16 mmol) in CH_2Cl_2 (10 mL) afforded **29** (372 mg, 78%, >98% de) as a yellow oil, after flash column chromatography (eluent petroleum/EtOAc, 7:1); $[\alpha]_D^{25}$ +36.6 (*c* 1.2 in $CHCl_3$); ν_{max} (film) 1644 (C=O), 1099 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 0.91 (3H, t, *J* 7.7, C(4')H_3), 1.57-1.67 (3H, m, C(3')H_2, C(2)H_AH_B), 1.59 (3H, d, *J* 7.0, C(α)CH_3), 1.65 (3H, d, *J* 6.5, C(6)H_3), 1.99-2.09 (1H, m, C(2)H_AH_B), 2.28-2.36 (2H, m, C(2')H_2), 3.09-3.12 (2H, m, C(1)H_2), 3.90-4.08 (1H, br s, C(3)*H*), 4.23 (1H, d, *J* 12.5, OCH_AH_BPh), 4.26 (1H, d, *J* 12.5, OCH_AH_BPh), 5.08 (1H, q, *J* 7.0, C(α)*H*), 5.54-5.59 (1H, br s, C(5)*H*), 5.72-5.84 (1H, br s, C(4)*H*), 7.06-7.37 (10H, m, 2 × *Ph*); δ_C (100 MHz, DMSO-d_6) 13.8, 17.7, 18.3, 18.5, 32.7, 36.0, 52.4, 54.7, 66.9, 71.2, 126.7, 127.2, 127.3, 127.4, 127.9, 128.1, 128.3, 130.9, 138.6, 140.8, 171.3; *m/z* (APCI$^+$) 380 ([M+H]$^+$, 35%), 276 ([M–C_8H_7]$^+$, 30), 192 ([$C_{12}H_{18}N$]$^+$, 100), 189 ([$C_{13}H_{18}O$]$^+$, 13); HRMS (CI$^+$) $C_{25}H_{34}NO_2^+$ ([M+H]$^+$) requires 380.2590; found 380.2588.

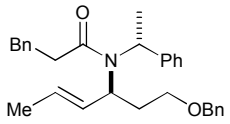
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-phenylacetyl-*N*-(α-methylbenzyl)amino]hex-4-ene 30



Following *General Procedure 4*, **14** (500 mg, 1.62 mmol), phenylacetyl chloride (0.43 mL, 3.24 mmol), Et_3N (0.56 mL, 4.05 mmol) and DMAP (20 mg, 0.16 mmol) in CH_2Cl_2 (10 mL) afforded **30** (270 mg, 39%, >98% de) as a colourless oil after flash column chromatography (eluent pentane/Et_2O, 3:1); $[\alpha]_D^{24}$ +44.3 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 1634 (C=O), 1116 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.53 (3H, d, *J* 6.0, C(α)CH_3), 1.62-1.69 (1H, m, C(2)H_AH_B), 1.62 (3H, d, *J* 5.5, C(6)H_3), 2.02-2.11 (1H, br s, C(2)H_AH_B), 3.03-3.13 (2H, br s, C(1)H_2), 3.75 (1H, d, *J* 15.2, C(2')H_AH_B), 3.78 (1H, d, *J* 15.2, C(2')H_AH_B), 3.80-4.00 (1H, br

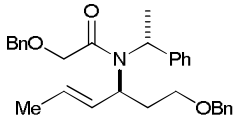
s, C(3)*H*), 4.22 (2H, br s, OCH_2Ph), 5.02-5.14 (1H, br s, C(α)*H*), 5.48 (1H, m, C(5)*H*), 5.71-5.83 (1H, br s, C(4)*H*), 7.14-7.39 (15H, m, 3 × *Ph*); δ_c (125 MHz, DMSO-d_6, 363 K) 18.1, 19.2, 34.2, 42.7, 56.1, 56.2, 67.9, 72.6, 127.2, 128.0, 128.0, 128.3, 128.4, 128.9, 129.1, 129.2, 129.3, 129.7, 131.4, 137.0, 139.4, 141.0, 170.5; *m/z* (APCI$^+$) 428 ([M+H]$^+$, 25%), 240 ([$C_{16}H_{18}NO$]$^+$, 100), 189 ([$C_{13}H_{17}O$]$^+$, 25), 136 ([M–C_8H_8NO]$^+$, 23); HRMS (CI$^+$) $C_{27}H_{34}NO_2^+$ ([M+H]$^+$) requires 428.2590; found 428.2582.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(3'-phenylpropionyl)-*N*-(α-methylbenzyl)amino]hex-4-ene 31



Following *General Procedure 4*, **14** (500 mg, 1.62 mmol), 3-phenylpropionyl chloride (0.48 mL, 3.24 mmol), Et_3N (0.56 mL, 4.05 mmol) and DMAP (20 mg, 0.16 mmol) in CH_2Cl_2 (10 mL) afforded **31** (396 mg, 56%, >98% de) as a colourless oil after flash column chromatography (eluent pentane/EtOAc, 7:1); $[\alpha]_D^{25}$ +14.7 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1640 (C=O), 1099 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.55 (3H, d, *J* 6.8, C(α)CH_3), 1.64 (3H, d, *J* 6.7, C(6)H_3), 1.62-1.69 (1H, m, C(2)H_AH$_B$), 2.00-2.22 (1H, br s, C(2)H$_A$$H_B$), 2.62-2.73 (2H, m, C(3')H_2), 2.80-3.00 (2H, m, C(2')H_2), 3.09-3.13 (2H, m, C(1)H_2), 3.98-4.08 (1H, br s, C(3)*H*), 4.20-4.28 (2H, m, OCH_2Ph), 5.10 (1H, q, *J* 6.8, C(α)*H*), 5.52-5.56 (1H, m, C(5)*H*), 5.74-5.81 (1H, br, m, C(4)*H*), 7.21-7.38 (15H, m, 3 × *Ph*); δ_C (125 MHz, DMSO-d_6, 363 K) 18.0, 19.4, 32.0, 34.5, 36.8, 55.8, 55.9, 68.1, 72.7, 126.6, 127.5, 127.6, 128.0, 128.1, 128.1, 128.8, 128.9, 129.0, 129.1, 129.2, 132.0, 139.6, 142.5, 172.1; *m/z* (APCI$^+$) 442 ([M+H]$^+$, 34%), 254 ([$C_{17}H_{20}NO$]$^+$, 100), 189 ([$C_{13}H_{17}O$]$^+$, 20); HRMS (CI$^+$) $C_{30}H_{36}NO_2^+$ ([M+H]$^+$) requires 442.2746; found 442.2741.

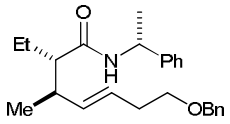
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(2'-benzyloxyacetyl)-*N*-(α-methylbenzyl)amino]hex-4-ene 32



Following *General Procedure 4*, **14** (493 mg, 1.59 mmol), 2-benzyloxyacetyl chloride (0.50 mL, 3.19 mmol), Et_3N (0.55 mL, 3.98 mmol) and DMAP (20 mg, 0.16 mmol) in CH_2Cl_2 (10 mL) afforded **32** (668 mg, 92%, >98% de) as a colourless oil after flash column chromatography (eluent pentane/EtOAc, 7:1); $[\alpha]_D^{25}$ +34.1 (*c* 0.8 in $CHCl_3$); ν_{max} (film) 1644 (C=O), 1100 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.58 (3H, d, *J* 7.0, C(α)CH_3), 1.69 (3H, d, *J* 6.5, C(6)H_3), 1.58-1.69 (1H, m, C(2)H_AH$_B$), 2.02-2.13 (1H, m, C(2)H$_A$$H_B$), 2.99-3.04 (2H, m, C(1)H_2), 3.90-3.95 (1H, m, C(3)*H*), 4.21-4.28 (4H, m, 2 × OCH_2Ph), 4.56-5.60 (2H, m, C(2')H_2), 4.99-5.08 (1H, br s, C(α)*H*), 5.54-5.61 (1H, br s, C(5)*H*), 5.77-5.86 (1H, br s, C(4)*H*), 7.19-7.41 (15H, m, 3 × *Ph*); δ_C (125 MHz, DMSO-d_6) 18.5, 18.6, 33.2, 55.4, 55.6, 67.5, 71.0, 71.9, 73.0, 127.8, 127.9,

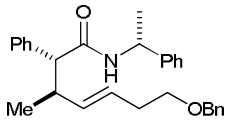
128.3, 128.3, 128.5, 128.5, 128.6, 128.7, 128.9, 129.1, 130.0, 131.1, 138.7, 139.4, 140.1, 168.6; *m/z* ($APCI^+$) 458 ($[M+H]^+$, 48%), 354 ($[M–C_8H_8]^+$, 19), 270 ($[C_{18}H_{22}NO]^+$, 100), 189 ($[C_{13}H_{18}O]^+$, 40), 166 ($[C_{10}H_{14}NO_2]^+$, 40); HRMS $C_{30}H_{36}NO_3^+$ ($[M+H]^+$) requires 458.2695; found 458.2694.

(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-ethyl-3-methyl-7-benzyloxy-hept-4-enamide 33



Following *General Procedure 5*, **29** (348 mg, 0.92 mmol), LiHMDS (1.38 mL, 1.38 mmol) and TMSCl (0.23 mL, 1.84 mmol) in toluene (10 mL) afforded the crude product **33** in 94% de. Purification by flash column chromatography (eluent pentane/EtOAc, 5:1) afforded **33** as a white crystalline solid (307 mg, 88%, 94% de). Purification of an aliquot by recrystallisation from petroleum/Et_2O gave an analytical sample of the major diastereoisomer **33** as a white crystalline solid; Found C, 79.0; H, 8.7; N, 3.7%; $C_{25}H_{33}NO_2$ requires C, 79.1; H, 8.8; N, 3.7%; mp 84-85 °C (petroleum/Et_2O); $[\alpha]_D^{21}$ +57.2 (*c* 1.0 in $CHCl_3$); ν_{max} (KBr) 3312 (N–H), 1641 (C=O), 1104 (C–O); δ_H (400 MHz, $CDCl_3$) 0.85 (3H, t, *J* 7.3, C(2')H_3), 1.05 (3H, d, *J* 6.8, C(3)CH_3), 1.42 (3H, d, *J* 6.9, C(α)CH_3), 1.47-1.66 (2H, m, C(1')H_2), 1.86-1.91 (1H, m, C(2)*H*), 2.32-2.41 (3H, m, C(3)*H*, C(6)H_2), 3.50 (2H, t, *J* 6.9, C(7)H_2), 4.52 (2H, s, OCH_2Ph), 5.13-5.20 (1H, m, C(α)*H*), 5.46 (1H, dt, *J* 15.2, 6.2, C(5)*H*), 5.52 (1H, dd, *J* 15.2, 7.6, C(4)*H*), 6.09 (1H, d, *J* 8.2, N*H*), 7.22-7.37 (10H, m, 2 × *Ph*); δ_C (100 MHz, $CDCl_3$) 12.3, 18.3, 21.8, 23.2, 33.1, 40.1, 48.3, 55.0, 70.2, 72.8, 125.9, 126.3, 127.0, 127.6, 127.6, 128.4, 128.4, 135.7, 138.6, 143.7, 173.8; *m/z* ($APCI^+$) 380 ($[M+H]^+$, 100%).

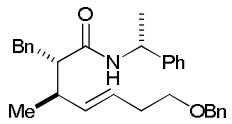
(*R*)-*N*-α-Methylbenzyl (2*R*,3*R*,4*E*)-2-phenyl-3-methyl-7-benzyloxy-hept-4-enamide 34



Following *General Procedure 5*, **30** (271 mg, 0.63 mmol), LiHMDS (0.95 mL, 0.95 mmol) and TMSCl (0.16 mL, 1.27 mmol) in toluene (10 mL) afforded **34** (58 mg, 21%, >95% de) as an orange oil after purification by flash column chromatography (eluent petoroleum/EtOAc, 10:1); $[\alpha]_D^{25}$ +38.3 (*c* 0.7 in $CHCl_3$); ν_{max} (film) 3926 (N–H), 1644 (C=O), 1100 (C–O); δ_H (400 MHz, C_6D_6) 0.93 (3H, d, *J* 6.8, C(3)CH_3), 1.33 (3H, d, *J* 7.0, C(α)CH_3), 2.48 (2H, m, C(6)H_2), 2.69 (1H, d, *J* 10.2, C(2)*H*), 3.23 (1H, m, C(3)*H*), 3.51 (2H, td, *J* 6.9, 1.1, C(7)H_2), 4.48 (2H, s, OCH_2Ph), 5.20 (1H, d, *J* 7.9, N*H*), 5.26 (1H, m, C(α)*H*), 5.67 (1H, dd, *J* 15.5, 7.4, C(4)*H*), 5.78 (1H, dt, *J* 15.5, 6.6, C(5)*H*), 7.16-7.32 (15H, m, 3 × *Ph*); δ_C (100 MHz, $CDCl_3$) 18.2, 21.7, 33.2, 39.6, 48.6, 60.4, 70.0, 72.8, 126.1, 127.1, 127.2, 127.6, 127.7, 128.4, 128.5, 128.5, 128.5, 135.4,

138.6, 138.6, 142.9, 171.7; *m/z* (APCI$^+$) 427 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{29}H_{34}NO_2^+$ ([M+H]$^+$) requires 428.2590; found 428.2588.

(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-benzyl-3-methyl-7-benzyloxy-hept-4-enamide 35



Following *General Procedure 5*, **31** (562 mg, 1.23 mmol), LiHMDS (1.84 mL, 1.84 mmol) and TMSCl (0.31 mL, 2.46 mmol) in toluene (10 mL) afforded **35** as a white crystalline solid (128 mg, 34%, 93% de) after purification by flash column chromatography (eluent pentane/EtOAc, 5:1). Purification of an aliquot by recrystallisation from petroleum/Et_2O gave an analytical sample of the major diastereoisomer **35** as a white crystalline solid; mp 104-106 °C (petroleum/Et_2O); $[\alpha]_D^{25}$ +37.3 (*c* 0.9 in $CHCl_3$); δ_H (400 MHz, C_6D_6) 1.17 (3H, d, *J* 6.8, C(3)CH_3), 1.22 (3H, d, *J* 6.9, C(α)CH_3), 1.89-1.95 (1H, m, C(2)*H*), 2.44 (2H, m, C(6)H_2), 2.53-2.62 (1H, m, C(3)*H*), 2.76 (1H, dd, *J* 13.0, 3.7, C(1')H_AH$_B$), 3.13 (1H, dd, *J* 13.0, 11.4, C(1')H$_A$$H_B$), 3.48 (2H, t, *J* 6.9, C(7)H_2), 4.46 (2H, s, OCH_2Ph), 5.14 (1H, d, *J* 8.3, N*H*), 5.21-5.28 (1H, m, C(α)*H*), 5.63 (1H, dt, *J* 15.2, 6.0, C(5)*H*), 5.69 (1H, dd, *J* 15.2, 7.2, C(4)*H*), 7.06-7.45 (15H, m, 3 × *Ph*); δ_C (100 MHz, $CDCl_3$) 18.3, 21.2, 33.1, 36.3, 39.4, 47.1, 56.1, 70.1, 72.8, 126.0, 126.1, 126.6, 126.9, 127.2, 127.6, 128.3, 128.4, 128.4, 129.0, 134.9, 138.5, 140.1, 142.7, 172.4; ν_{max} (KBr) 3293 (N–H), 1639 (C=O), 1102 (C–O); *m/z* (APCI$^+$) 442 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{30}H_{36}NO_2^+$ ([M+H]$^+$) requires 442.2746; found 442.2750.

X-ray Crystal Structure Determination for 35

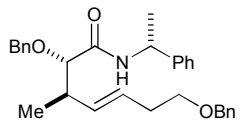
Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[2]

X-ray crystal structure data for **35** [$C_{30}H_{35}NO_2$]: M = 441.61, monoclinic, space group $P\ 2_1$, a = 4.87270(10) Å, b = 10.8284(2) Å, c = 24.6333(6) Å, β = 95.4698(9)°, V = 1293.82(5) Å^3, Z = 2, μ = 0.070 mm^{-1}, colourless block, crystal dimensions = 0.2 × 0.2 × 0.2 mm^3. A total of 2790 unique reflections were measured for 5 < θ < 27 and 2399 reflections were used in the refinement. The final parameters were wR_2 = 0.051 and R_1 = 0.054 [I>0.5σ(I)]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 719633. Copies

[2] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, C. K. Prout and D. J. Watkin, CRYSTALS, 2001, Issue 11, Chemical Crystallography Laboratory, University of Oxford, UK.

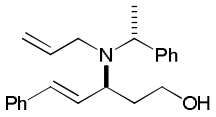
of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-benzyloxy-3-methyl-7-benzyloxy-hept-4-enamide 36



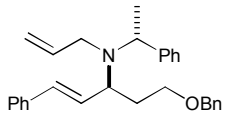
Following *General Procedure 5*, **32** (562 mg, 1.23 mmol), LiHMDS (1.84 mL, 1.84 mmol) and TMSCl (0.31 mL, 2.46 mmol) in toluene (10 mL) afforded **36** as a white crystalline solid (100 mg, 18%, 90% de) after purification by flash column chromatography (eluent Et_2O/petroleum, 1:5). Purification of an aliquot by recrystallisation from petroleum/Et_2O gave an analytical sample of the major diastereoisomer **36** as a white crystalline solid; mp 78-79 °C (pentane/Et_2O); $[\alpha]_D^{25}$ –7.1 (*c* 0.8 in $CHCl_3$); ν_{max} (KBr) 3321 (N–H), 1651 (C=O), 1100 (C–O); δ_H (400 MHz, C_6D_6) 1.19 (3H, d, *J* 6.9, C(3)CH_3), 1.27 (3H, d, *J* 7.0, C(α)CH_3), 2.32-2.37 (2H, m, C(6)H_2), 2.90-2.96 (1H, m, C(3)*H*), 3.38 (2H, t, *J* 6.8, C(7)H_2), 3.94 (1H, d, *J* 3.9, C(2)*H*), 4.34-4.40 (4H, m, 2 × OCH_2Ph), 5.35-5.42 (1H, m, C(α)*H*), 5.55 (1H, dt, *J* 15.4, 6.5, C(5)*H*), 5.64 (1H, dd, *J* 15.4, 7.3, C(4)*H*), 6.72 (1H, d, *J* 8.3, N*H*), 7.12-7.29 (15H, m, 3 × *Ph*); δ_C (100 MHz, $CDCl_3$) 14.5, 21.9, 33.1, 40.0, 48.0, 70.0, 72.8, 73.8, 84.1, 126.1, 127.1, 127.3, 127.5, 128.0, 128.2, 128.4, 128.5, 128.6, 128.7, 133.7, 137.4, 138.5, 143.1, 170.0; *m/z* (APCI$^+$) 442 ([M+H]$^+$, 100%), 353 ([M–C_8H_8]$^+$, 40); HRMS (CI$^+$) $C_{30}H_{36}NO_3^+$ ([M+H]$^+$) requires 458.2695; found 458.2691.

(3*S*,4*E*,α*R*)-3-[*N*-Allyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-en-1-ol 38



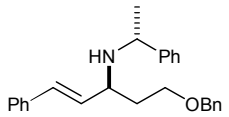
Following *General Procedure 1*, **37** (7.30 g, 18.7 mmol) and $LiAlH_4$ (19.6 mL, 19.6 mmol) in THF (200 mL) afforded **38** (5.72 g, 95%, >98% de) as a colourless oil; $[\alpha]_D^{25}$ –120.8 (*c* 0.7 in $CHCl_3$); ν_{max} (film) 3992 (O–H), 1640 (C=C), 1600 (C=C); δ_H (400 MHz, $CDCl_3$) 1.44 (3H, d, *J* 6.9, C(α)CH_3), 1.46-1.55 (1H, m, C(2)H_AH$_B$), 1.96-2.05 (1H, m, C(2)H$_A$$H_B$), 3.22-3.28 (1H, m, C(1')H_AH$_B$), 3.42-3.53 (2H, m, C(1')H$_A$$H_B$, C(1)$H_AH_B$), 3.65-3.76 (2H, m, C(1)H$_A$$H_B$, C(3)*H*), 3.90-4.10 (1H, br s, O*H*), 4.19 (1H, q, *J* 6.9, C(α)*H*), 5.12-5.20 (2H, m, C(3')H_2), 5.84-5.94 (1H, m, C(2')*H*), 6.34 (1H, dd, *J* 16.1, 7.8, C(4)*H*) 6.44 (1H, d, *J* 16.1, C(5)*H*), 7.23-7.42 (10H, m, 2 × *Ph*); δ_C (100 MHz, $CDCl_3$) 15.9, 34.3, 49.5, 57.3, 59.0, 62.2, 117.4, 126.2, 127.1, 127.5, 128.0, 128.3, 128.6, 129.8, 131.1, 137.0, 137.1, 143.8; *m/z* (APCI$^+$) 322 ([M+H]$^+$, 3), 216 ([M–C_8H_8]$^+$, 11), 162 ([$C_{11}H_{12}O$]$^+$, 27), 161 ([$C_{10}H_{12}N$]$^+$, 100); HRMS (CI$^+$) $C_{22}H_{28}NO^+$ ([M+H]$^+$) requires 322.2171; found 322.2177.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-allyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 39



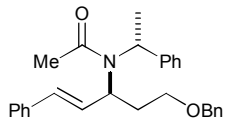
Following *General Procedure 2*, **38** (5.58 g, 17.4 mmol), NaH (834 mg, 20.9 mmol), 15-crown-5 (4.57 mL, 22.6 mmol) and BnBr (4.14 mL, 34.8 mmol) in THF (150 mL) afforded **39** (5.33 g, 75%, >98% de) as a yellow oil after flash column chromatography (eluent pentane/EtOAc, 49:1); $[\alpha]_D^{25}$ –36.1 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1640 (C=C), 1600 (C=C); δ_H (400 MHz, $CDCl_3$) 1.41 (3H, d, *J* 6.8, C(α)C*H*$_3$), 1.76-1.85 (1H, m, C(2)*H*$_A$H$_B$), 1.96-2.07 (1H, m, C(2)H$_A$*H*$_B$), 3.18-3.32 (2H, m, C(1')*H*$_2$), 3.47 (2H, t, *J* 6.5, C(1)*H*$_2$), 3.62-3.68 (1H, m, C(3)*H*), 4.15 (1H, q, *J* 6.8, C(α)*H*), 4.40 (1H, d, *J* 11.9, OC*H*$_A$H$_B$Ph), 4.46 (1H, d, *J* 11.9, OCH$_A$*H*$_B$Ph), 5.05-5.13 (2H, m, C(3')*H*$_2$), 5.80-5.88 (1H, m, C(2')*H*), 6.28 (1H, dd, *J* 16.0, 8.1, C(4)*H*), 6.40 (1H, d, *J* 16.0, C(5)*H*), 7.21-7.43 (15H, m, 3 × *Ph*); δ_C (100 MHz, $CDCl_3$) 17.8, 33.4, 49.5, 56.4, 56.9, 67.9, 72.9, 115.7, 126.2, 126.4, 127.3, 127.4, 127.6, 127.7, 128.0, 128.3, 128.6, 130.9, 131.0, 137.4, 138.7, 138.9, 145.5; *m/z* (CI^+) 412 ($[M+H]^+$, 100%), 251 ($[C_{18}H_{19}O]^+$, 22), 162 ($[C_{10}H_{14}N]^+$, 26); HRMS (CI^+) $C_{29}H_{34}NO^+$ ($[M+H]^+$) requires 412.2640; found 412.2649.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 40



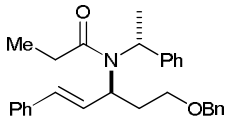
Following *General Procedure 3*, **39** (4.02 g, 9.78 mmol) and $RhCl(PPh_3)_3$ (453 mg, 0.49 mmol) in MeCN/H_2O (85:15, 100 mL) afforded **40** as a colourless oil (3.40 g, 94%, >98% de) after flash column chromatography (eluent pentane/EtOAc, 3:1); $[\alpha]_D^{25}$ +16.4 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 3347 (N–H), 1600 (C=C); δ_H (400 MHz, $CDCl_3$) 1.37 (3H, d, *J* 6.8, C(α)C*H*$_3$), 1.58 (1H, br s, N*H*), 1.77-1.85 (1H, m, C(2)*H*$_A$H$_B$), 1.94-2.02 (1H, m, C(2)H$_A$*H*$_B$), 3.47-3.52 (1H, m, C(3)*H*), 3.53-3.59 (1H, m, C(1)*H*$_A$H$_B$), 3.63-3.67 (1H, m, C(1)H$_A$*H*$_B$), 3.92 (1H, q, *J* 6.8, C(α)*H*), 4.49 (1H, d, *J* 11.9, OC*H*$_A$H$_B$Ph), 4.53 (1H, d, *J* 11.9, OCH$_A$*H*$_B$Ph), 5.99 (1H, dd, *J* 15.9, 8.3, C(4)*H*), 6.41 (1H, d, *J* 15.9, C(5)*H*), 7.21-7.43 (15H, m, 3 × *Ph*); δ_C (100 MHz, $CDCl_3$) 23.2, 35.7, 54.9, 56.1, 67.5, 73.0, 126.3, 126.8, 127.3, 127.5, 127.6, 127.7, 128.3, 128.4, 128.5, 130.6, 133.1, 137.1, 138.5, 146.4; *m/z* ($APCI^+$) 372 ($[M+H]^+$, 5%), 251 ($[M–C_8H_{12}N]^+$, 9); HRMS (CI^+) $C_{26}H_{30}NO^+$ ($[M+H]^+$) requires 372.2327; found 372.2327.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-acetyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 41



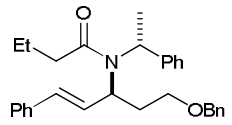
Following *General Procedure 4*, **40** (500 mg, 1.35 mmol), acetyl chloride (0.19 mL, 2.70 mmol), Et_3N (0.47 mL, 3.37 mmol) and DMAP (16 mg, 0.13 mmol) in CH_2Cl_2 (10 mL) afforded **41** as a colourless oil (483 mg, 87%, >98% de) after flash column chromatography (eluent pentane/EtOAc, 3:1); $[\alpha]_D^{25}$ +14.1 (*c* 0.5 in $CHCl_3$); ν_{max} (film) 2860 (C–H), 1643 C=O), 1102 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.64 (3H, d, *J* 6.5, C(α)CH_3), 1.78-1.81 (1H, m, C(2)H_AH$_B$), 2.13 (3H, s, C(2')H_3), 2.17-2.20 (1H, m, C(2)H$_A$$H_B$), 3.21 (2H, t, *J* 6.5 C(1)H_2), 4.21 (1H, br s, C(3)*H*), 4.24-4.33 (2H, m, OCH_2Ph), 5.16 (1H, q, *J* 6.5, C(α)*H*), 6.51-6.58 (2H, br s, C(4)*H*, C(5)*H*), 7.23-7.44 (15H, m, 3 × *Ph*); δ_C (100 MHz, DMSO-d_6) 18.0, 23.6, 32.7, 54.6, 56.0, 66.8, 71.2, 126.2, 126.4, 127.2, 127.5, 127.9, 128.1, 128.2, 128.4, 128.6, 129.5, 130.4, 136.8, 138.6, 140.6, 169.3; *m/z* (APCI$^+$) 414 ([M+H]$^+$, 12%), 251 ([$C_{18}H_{18}O$]$^+$, 10), 164 ([$C_{11}H_{15}NO$]$^+$, 21); HRMS (CI$^+$) $C_{28}H_{32}NO_2^+$ ([M+H]$^+$) requires 414.2433; found 414.2439.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-propionyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 42



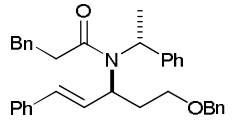
Following *General Procedure 4*, **40** (500 mg, 1.35 mmol), propionyl chloride (0.23 mL, 2.70 mmol), Et_3N (0.47 mL, 3.37 mmol) and DMAP (16 mg, 0.13 mmol) in CH_2Cl_2 (10 mL) afforded **42** as a colourless oil (538 mg, 94%, >98% de) after flash column chromatography (eluent pentane/EtOAc, 7:1); $[\alpha]_D^{25}$ +30.7 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 2977 (C–H), 1644 (C=O), 1101 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.07 (3H, t, *J* 7.3, C(3')H_3), 1.62 (3H, d, *J* 7.0, C(α)CH_3), 1.72-1.77 (1H, m, C(2)H_AH$_B$), 2.17-2.23 (1H, m, C(2)H$_A$$H_B$), 2.37-2.39 (2H, m, C(2')H_2), 4.15-4.25 (1H, m, C(3)*H*), 3.16-3.18 (2H, m, C(1)H_2), 4.24-4.29 (2H, m, OCH_2Ph), 5.18 (1H, q, *J* 7.0, C(α)*H*), 6.51 (1H, d, *J* 16.2, C(5)*H*), 6.57 (1H, dd, *J* 16.2, 6.5, C(4)*H*), 7.16-7.43 (15H, m, 3 × *Ph*); δ_C (100 MHz, DMSO-d_6) 19.0, 21.6, 28.1, 33.6, 55.5, 55.6, 67.7, 72.0, 127.0, 127.2, 127.3, 128.0, 128.4, 129.0, 129.1, 129.2, 129.5, 130.4, 131.8, 137.7, 139.4, 141.5, 173.1; *m/z* (APCI$^+$) 428 ([M+H]$^+$, 5%), 251 ([$C_{18}H_{17}O$]$^+$, 9), 178 ([$C_{11}H_{15}NO$]$^+$, 27); HRMS (CI$^+$) $C_{29}H_{33}NO_2^+$ ([M+H]$^+$) requires 428.2590; found 428.2590.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-butyryl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 43



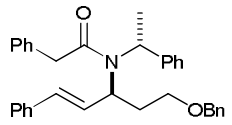
Following *General Procedure 4*, **40** (200 mg, 0.54 mmol), butyryl chloride (0.11 mL, 1.08 mmol), Et_3N (0.19 mL, 1.35 mmol) and DMAP (7 mg, 0.05 mmol) in CH_2Cl_2 (10 mL) afforded **43** as a colourless oil (192 mg, 81%, >98% de) after flash column chromatography (eluent pentane/EtOAc, 7:1); $[\alpha]_D^{25}$ +28.6 (*c* 1.2 in $CHCl_3$); ν_{max} (film) 2964 (C–H), 1640 (C=O), 1101 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 0.93 (3H, t, *J* 7.3, C(4')H_3), 1.58-1.64 (2H, m, C(3')H_2), 1.62 (3H, d, *J* 7.0, C(α)CH_3), 1.68-1.78 (1H, m, C(2)H_AH$_B$), 2.18-2.23 (1H, m, C(2)H$_A$$H_B$), 2.36-2.43 (2H, m, C(2')H_2), 3.16-3.18 (2H, m, C(1)H_2), 4.15-4.25 (1H, m, C(3)*H*), 4.24-4.30 (2H, m, OCH_2Ph), 5.19 (1H, q, *J* 7.0, C(α)*H*), 6.50-6.53 (2H, m, C(4)*H*), 6.55 (1H, m, C(5)*H*), 7.17-7.43 (15H, m, 3 × *Ph*); δ_C (100 MHz, DMSO-d_6) 13.8, 18.3, 18.5, 32.8, 36.0, 52.5, 54.8, 66.8, 71.3, 126.2, 126.4, 127.2, 127.4, 127.9, 128.1, 128.4, 128.6, 129.7, 130.9, 136.9, 138.6, 140.8, 171.6; *m/z* (APCI$^+$) 442 ([M+H]$^+$, 46%), 250 ([$C_{18}H_{18}O$]$^+$, 13), 192 ([$C_{12}H_{17}NO$]$^+$, 74); HRMS (CI$^+$) $C_{29}H_{33}NO_2^+$ ([M+H]$^+$) requires 442.2746; found 442.2743.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(3'-phenylpropionyl)-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 44



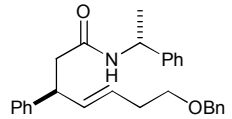
Following *General Procedure 4*, **40** (216 mg, 0.58 mmol), hydrocinnamoyl chloride (0.17 mL, 1.16 mmol), Et_3N (0.20 mL, 1.46 mmol) and DMAP (7 mg, 0.06 mmol) in CH_2Cl_2 (10 mL) afforded **44** as a colourless oil (157 mg, 54%, >98% de) after flash column chromatography (eluent pentane/Et_2O, 5:1); $[\alpha]_D^{25}$ +14.7 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 2860 (C–H), 1639 (C=O), 1099 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.58 (3H, d, *J* 6.5, C(α)CH_3), 1.72-1.75 (1H, m, C(2)H_AH$_B$), 2.10-2.20 (1H, m, C(2)H$_A$$H_B$), 2.71-2.77 (2H, m, C(3')H_2), 2.91-2.94 (2H, m, C(2')H_2), 3.16 (2H, t, *J* 6.2 C(1)H_2), 4.15-4.25 (1H, m, C(3)*H*), 4.20-4.30 (2H, m, OCH_2Ph), 5.19 (1H, q, *J* 6.5, C(α)*H*), 6.47-6.60 (2H, m, C(4)*H*, C(5)*H*), 7.21-7.38 (20H, m, 4 × *Ph*); δ_C (100 MHz, DMSO-d_6) 18.2, 31.1, 32.7, 35.7, 54.8, 54.8, 66.8, 71.2, 125.9, 126.2, 126.4, 127.2, 127.2, 127.4, 127.6, 128.1, 128.2, 128.4, 128.6, 128.6, 129.5, 131.0, 136.8, 138.6, 140.6, 141.5, 171.0; *m/z* (APCI$^+$) 504 ([M+H]$^+$, 19%), 251 ([$C_{18}H_{18}O$]$^+$, 11), 254 ([$C_{11}H_{15}NO$]$^+$, 39); HRMS (CI$^+$) $C_{35}H_{38}NO_2^+$ ([M+H]$^+$) requires 504.2903; found 504.2900.

(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(2'-phenylacetyl)-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 45



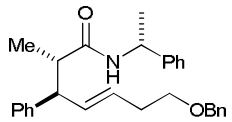
Following *General Procedure 4*, **40** (500 mg, 1.35 mmol), phenylacetyl chloride (0.36 mL, 2.70 mmol), Et_3N (0.47 mL, 3.37 mmol) and DMAP (16 mg, 0.13 mmol) in CH_2Cl_2 (10 mL) afforded **45** as a colourless oil (245 mg, 41%, >98% de) after flash column chromatography (eluent pentane/EtOAc, 7:1); $[\alpha]_D^{21}$ +5.0 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 2860 (C–H), 1634 (C=O), 1117 (C–O); δ_H (500 MHz, DMSO-d_6, 363 K) 1.59 (3H, d, *J* 6.7, C(α)CH_3), 1.75-1.80 (1H, m, C(2)H_AH$_B$), 2.20-2.24 (1H, m, C(2)H$_A$$H_B$), 3.18 (2H, t, *J* 6.5, C(1)H_2), 3.80 (1H, d, *J* 15.0, C(2')H_AH$_B$), 3.85 (1H, d, *J* 15.0, C(2')H$_A$$H_B$), 4.16-4.24 (1H, m, C(3)*H*), 4.20-4.30 (2H, m, OCH_2Ph), 5.19 (1H, q, *J* 6.7, C(α)*H*), 6.42 (1H, d, *J* 16.0, C(5)*H*), 6.52 (1H, dd, *J* 16.0, 7.5, C(4)*H*), 7.02-7.35 (20H, m, 4 × *Ph*); δ_C (100 MHz, DMSO-d_6) 17.8, 32.6, 41.8, 54.9, 55.1, 68.8, 71.1, 126.2, 127.1, 127.1, 127.2, 127.7, 128.1, 128.1, 128.1, 128.3, 128.5, 128.7, 128.7, 129.0, 129.7, 130.0, 136.1, 136.5, 136.8, 138.6, 169.9; *m/z* (APCI$^+$) 490 ([M+H]$^+$, 8%), 372 ([M–C_8H_9O]$^+$, 10), 251 ([$C1_8H_{19}O$]$^+$, 10), 140 ([$C_{16}H_{17}NO$]$^+$, 24); HRMS (CI$^+$) $C_{34}H_{36}NO_2^+$ ([M+H]$^+$) requires 490.2746; found 490.2749.

(*R*)-*N*-α-Methylbenzyl (3*S*,4*E*)-3-phenyl-7-benzyloxy-hept-4-enamide 46



Following *General Procedure 5*, **41** (336 mg, 0.81 mmol), LiHMDS (1.22 mL, 1.22 mmol) and TMSCl (0.21 mL, 1.63 mmol) in toluene afforded recovered starting material **41** (150 mg, 45%) and **46** as an orange oil (19 mg, 6%, 91% de) after purification by flash column chromatography (eluent petroleum/EtOAc, 7:1); $[\alpha]_D^{25}$ +22.8 (*c* 0.7 in $CHCl_3$); ν_{max} (film) 3287 (N–H), 1643 (C=O), 1099 (C–O); δ_H (400 MHz, $CDCl_3$) 1.39 (3H, d, *J* 6.8, C(α)CH_3), 2.35 (1H, m, C(6)H_2), 2.51 (1H, dd, *J* 13.8, 8.0, C(2)H_AH$_B$), 2.60 (1H, dd, *J* 13.8, 7.2, C(2)H$_A$$H_B$), 3.48 (2H, m, C(7)$H_2$), 3.85 (1H, app q, *J* 7.4, C(3)*H*), 4.49 (2H, s, OCH_2Ph), 5.00-5.07 (1H, m, C(α)*H*), 5.46-5.56 (2H, m, C(5)*H*, N*H*), 5.71 (1H, dd, *J* 15.4, 7.2, C(4)*H*), 7.19-7.36 (15H, m, 3 × *Ph*); δ_C (100 MHz, $CDCl_3$) 21.5, 33.0, 43.7, 45.4, 48.4, 69.8, 72.8, 126.6, 127.1, 127.2, 127.5, 126.0, 127.6, 127.6, 128.4, 128.5, 128.7, 132.0, 138.4, 142.3, 143.1, 176.9; *m/z* (APCI$^+$) 414 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{28}H_{32}NO_2^+$ ([M+H]$^+$) requires 414.2433; found 414.2428.

(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-methyl-3-phenyl-7-benzyloxy-hept-4-enamide 47



Following *General Procedure 5*, **42** (357 mg, 0.84 mmol), LiHMDS (1.25 mL, 1.25 mmol) and TMSCl (0.21 mL, 1.67 mmol) in toluene (10 mL) afforded the crude product in 91% de. Purification by flash column chromatography (eluent petroleum/EtOAc, 5:1) afforded **47** as a white crystalline solid (214 mg, 60%, 91% de). Purification of an aliquot by recrystallisation from petroleum/Et_2O gave an analytical sample of the major diastereoisomer **47** as a white crystalline solid; Found C, 81.4; H, 7.8; N, 3.3%; $C_{29}H_{33}NO_2$ requires C, 81.5; H, 7.8; N, 3.3%; ; mp 104-105 °C (petroleum/Et_2O); $[\alpha]_D^{24}$ +92.6 (*c* 1.0 in $CHCl_3$); ν_{max} (KBr) 3341 (N–H), 1648 (C=O), 1103 (C–O); δ_H (400 MHz, $CDCl_3$) 0.94 (3H, d, *J* 6.8, C(2)C*H*$_3$), 1.41 (3H, d, *J* 6.8, C(α)C*H*$_3$), 2.28-2.37 (1H, m, C(6)*H*$_2$), 2.42 (2H, dq, *J* 9.6, 6.8, C(2)*H*), 3.43-3.51 (3H, m, C(3)*H*, C(7)*H*$_2$), 4.48 (2H, s, OC*H*$_2$Ph), 5.08-5.15 (1H, m, C(α)*H*), 5.47-5.54 (1H, m, C(5)*H*), 5.58 (1H, d, *J* 7.7, N*H*), 5.75 (1H, dd, *J* 15.3, 8.5, C(4)*H*), 7.24-7.38 (15H, m, 3 × *Ph*); δ_C (400 MHz, $CDCl_3$) 16.4, 21.6, 33.0, 47.4, 48.4, 52.6, 69.8, 72.8, 126.5, 127.3, 127.5, 128.1, 126.2, 127.6, 128.1, 128.3, 128.6, 128.6, 132.9, 138.4, 142.4, 143.1, 173.9; *m/z* ($APCI^+$) 428 ($[M+H]^+$, 100%).

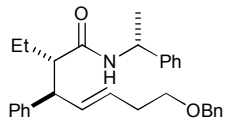
X-ray Crystal Structure Determination for 47

Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation using standard procedures at 150 K. The structure was 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.[3]

X-ray crystal structure data for **47** [$C_{23}H_{33}NNO_2$]: M = 426.91, orthorhombic, space group *P* 2_1 2_1 2_1, *a* = 8.9487(2) Å, *b* = 5.18510(10) Å, *c* = 52.2900(7) Å, *V* = 2426.25(8) Å^3, *Z* = 4, μ = 0.072 mm^{-1}, colourless block, crystal dimensions = 0.1 × 0.1 × 0.1 mm^3. A total of 3067 unique reflections were measured for $5 < \theta < 27$ and 2520 reflections were used in the refinement. The final parameters were wR_2 = 0.159 and R_1 = 0.081 [$I>1.5\sigma(I)$]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 719634. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

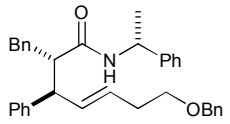
[3] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, C. K. Prout and D. J. Watkin, CRYSTALS, 2001, Issue 11, Chemical Crystallography Laboratory, University of Oxford, UK.

(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-ethyl-3-phenyl-7-benzyloxy-hept-4-enamide 48



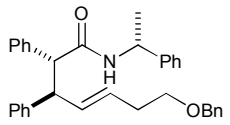
Following *General Procedure 5*, **43** (146 mg, 0.39 mmol), LiHMDS (0.59 mL, 0.59 mmol) and TMSCl (0.10 mL, 0.79 mmol) in toluene (10 mL) afforded **48** as a white crystalline solid (104 mg, 71%, 94% de) after purification by flash column chromatography (eluent petroleum/EtOAc, 5:1). Purification of an aliquot by recrystallisation from petroleum/Et_2O gave an analytical sample of the major diastereoisomer **48** as a white crystalline solid; mp 95-102 °C (petroleum/Et_2O); $[\alpha]_D^{24}$ +85.3 (*c* 0.6 in $CHCl_3$); ν_{max} (KBr) 3278 (N–H), 1634 (C=O), 1094 (C–O); δ_H (400 MHz, $CDCl_3$) 0.76 (3H, t, *J* 6.8, C(2')*H*$_3$), 1.13-1.23 (1H, m, C(1')*H*$_A$H$_B$), 1.40 (3H, d, *J* 6.9, C(α)C*H*$_3$), 1.49-1.58 (1H, m, C(1')H$_A$*H*$_B$), 2.32-2.38 (2H, m, C(6)*H*$_2$), 2.40 (2H, m, C(2)*H*), 3.43-3.52 (3H, m, C(3)*H*, C(7)*H*$_2$), 4.49 (2H, s, OC*H*$_2$Ph), 5.12-5.19 (1H, m, C(α)*H*), 5.51 (1H, dt, *J* 15.2, 6.9, C(5)*H*), 5.70 (1H, d, *J* 8.0 , N*H*), 5.78 (1H, ddt, *J* 15.2, 8.7, 1.3, C(4)*H*), 7.13-7.38 (15H, m, 3 × *Ph*); δ_C (400 MHz, $CDCl_3$) 12.2, 21.5, 24.1, 33.1, 48.4, 52.0, 55.6, 69.8, 72.8, 126.0, 126.3, 126.4, 127.3, 127.5, 127.6, 128.0, 128.3, 128.4, 128.6, 132.9, 138.5, 142.8, 143.2, 173.0; *m/z* (APCI$^+$) 442 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{27}H_{36}NO_2^+$ ([M+H]$^+$) requires 442.2746; found 442.2740.

(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-benzyl-3-phenyl-7-benzyloxy-hept-4-enamide 49



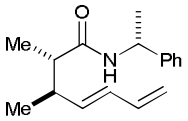
Following *General Procedure 5*, **44** (145 mg, 0.289 mmol), LiHMDS (0.43 mL, 0.434 mmol) and TMSCl (0.07 mL, 0.579 mmol) in toluene (10 mL) afforded **49** (53 mg, 37%, 95% de) as a white crystalline solid after purification by flash column chromatography (eluent petroleum/EtOAc, 10:1); mp 116-118 °C (petroleum/EtOAc); $[\alpha]_D^{23}$ +52.0 (*c* 0.2 in $CHCl_3$); ν_{max} (KBr) 3311 (N–H), 1636 (C=O), 1092 (C–O); δ_H (400 MHz, $CDCl_3$) 1.29 (3H, d, *J* 6.9, C(α)C*H*$_3$), 2.37 (2H, app q, *J* 6.8, C(6)*H*$_2$), 2.46 (1H, dd, *J* 13.2, 3.6, C(1')*H*$_A$H$_B$), 2.55 (1H, ddd, *J* 11.0, 9.2, 3.6, C(2)*H*), 2.83 (1H, dd, *J* 13.2, 11.0, C(1')H$_A$*H*$_B$), 3.49 (2H, dt, *J* 7.0, 1.4, C(7)*H*$_2$), 3.65 (1H, app t, *J* 9.2, C(3)*H*), 5.00 (1H, m, C(α)*H*), 5.28 (1H, d, *J* 8.0, N*H*), 5.56 (1H, dt, *J* 15.2, 7.0, C(5)*H*), 5.80 (1H, tdd, *J* 15.2, 9.2, 1.4, C(4)*H*), 6.79-7.36 (20H, m, 4 × *Ph*); δ_C (100 MHz, $CDCl_3$) 21.1, 33.1, 37.1, 47.8, 51.9, 56.6, 69.8, 72.8, 126.1, 126.7, 126.9, 127.5, 127.6, 127.8, 128.0, 128.3, 128.8, 128.9, 132.5, 134.0, 138.4, 142.5, 171.9; *m/z* (APCI$^+$) 505 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{35}H_{38}NO_2^+$ requires 504.2903; found 504.2899.

(*R*)-*N*-α-Methylbenzyl (2*R*,3*R*,4*E*)-2,3-diphenyl-7-benzyloxy-hept-4-enamide 50



Following *General Procedure 5*, **45** (152 mg, 0.31 mmol), LiHMDS (0.47 mL, 0.47 mmol) and TMSCl (0.08 mL, 0.62 mmol) in toluene (10 mL) afforded **50** (28 mg, 18%, 90% de) as yellow oil after purification by flash column chromatography (eluent petroleum/EtOAc, 10:1); $[\alpha]_D^{25}$ +19.5 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 3313 (N–H), 1651 (C=O), 1602 (C=C), 1100 (C–O); δ_H (400 MHz, $CDCl_3$) 1.42 (3H, d, *J* 6.8, C(α)C*H*$_3$), 2.35-2.40 (2H, m, C(6)*H*$_2$), 3.49 (2H, t, *J* 6.8, C(7)*H*$_2$), 3.57 (1H, d, *J* 10.8, C(2)*H*), 4.10-4.14 (1H, m, C(3)*H*), 4.50 (2H, s, OC*H*$_2$Ph), 5.03-5.07 (1H, m, C(α)*H*), 5.59 (1H, dtd, *J* 15.2, 6.8, 1.4, C(5)*H*), 5.74 (1H, d, *J* 7.8, N*H*), 5.86 (1H, ddt, *J* 15.2, 8.0, 1.4 C(4)*H*), 7.08-7.53 (20H, m, 4 × *Ph*); δ_C (100 MHz, $CDCl_3$) 21.7, 33.2, 48.8, 52.0, 59.2, 69.8, 72.8, 126.1, 126.1, 127.2, 127.7, 128.1, 128.3, 128.3, 128.3, 128.4, 128.5, 128.5, 128.5, 132.9, 137.7, 138.4, 141.5, 142.8, 171.2; *m/z* (APCI$^+$) 489 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{34}H_{36}NO_2^+$ ([M+H]$^+$) requires 490.2746; found 490.2743.

(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2,3-dimethyl-hept-4,6-dienamide 51



Following *General Procedure 5*, **15** (440 mg, 1.21 mmol), LiHMDS (3.62 mL, 3.62 mmol) in toluene (10 mL) afforded the crude product in 88% de. Purification by flash column chromatography (5:1 petroleum:EtOAc) afforded **51** as a white crystalline solid (248 mg, 80%, 88% de), from which the major diastereoisomer **51** was obtained by recrystallisation (petroleum/Et_2O); Found C, 79.2; H, 8.9; N, 5.4%; $C_{17}H_{23}NO$ requires C, 79.3; H, 9.0; N, 5.4%; mp 106-108 °C; $[\alpha]_D^{21}$ +71.3 (*c* 1.2 in $CHCl_3$); ν_{max} (film) 3285 (N–H), 1641 (C=O), 1547 (C=O); δ_H (400 MHz, $CDCl_3$) 1.05 (3H, d, *J* 6.8, C(3)C*H*$_3$), 1.12 (3H, d, *J* 6.9, C(2)C*H*$_3$), 1.45 (3H, d, *J* 6.9, C(α)C*H*$_3$), 2.01-2.08 (1H, m, C(2)*H*), 2.44-2.49 (1H, m, C(3)*H*), 5.01 (1H, dd, *J* 10.3, 1.1, C(7)*H*$_A$), 5.09-5.15 (2H, m, C(α)*H*, C(7)*H*$_B$), 5.59 (1H, br s, N*H*), 5.64 (1H, dd, *J* 15.3, 8.1, C(4)*H*), 6.07 (1H, dd, *J* 15.3, 10.3, C(5)*H*), 6.29, (1H, dd, *J* 17.0, 10.3, C(6)*H*), 7.24-7.38 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.8, 17.0, 21.5, 39.9, 47.2, 48.3, 115.8, 126.2, 127.3, 128.6, 130.8, 137.0, 137.8, 143.1, 174.5; *m/z* (APCI$^+$) 258 ([M+H]$^+$, 100%).

X-ray Crystal Structure Determination for 51

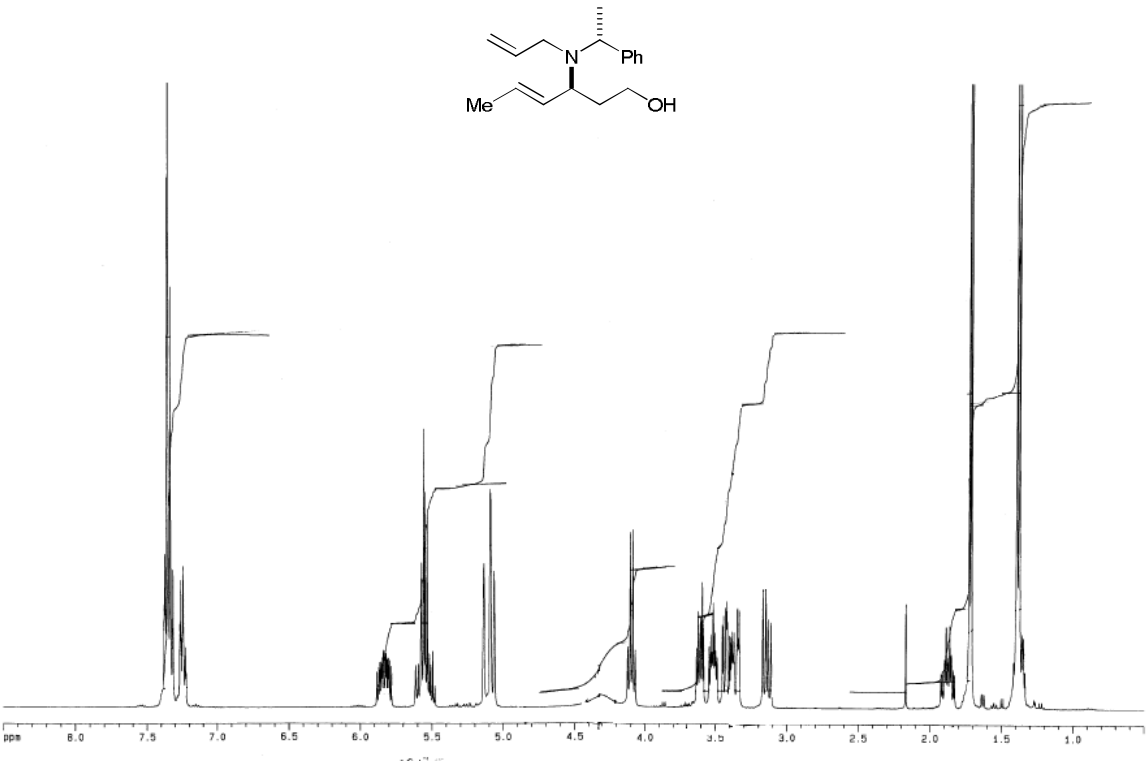
Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[4]

X-ray crystal structure data for **51** [$C_{17}H_{23}NO$]: M = 257.38, monoclinic, space group $P\ 2_1$, a = 12.3683(17) Å, b = 4.9903(8) Å, c = 12.8281(18) Å, β = 93.207(13)°, V = 790.5(2), Å^3, Z = 2, μ = 0.511 mm^{-1}, colourless block, crystal dimensions = 0.4 × 0.4 × 0.8 mm^3. A total of 1796 unique reflections were measured for $5 < \theta < 27$ and 1692 reflections were used in the refinement. The final parameters were wR_2 = 0.061 and R_1 = 0.053 [I>3.0σ(I)]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 719632. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

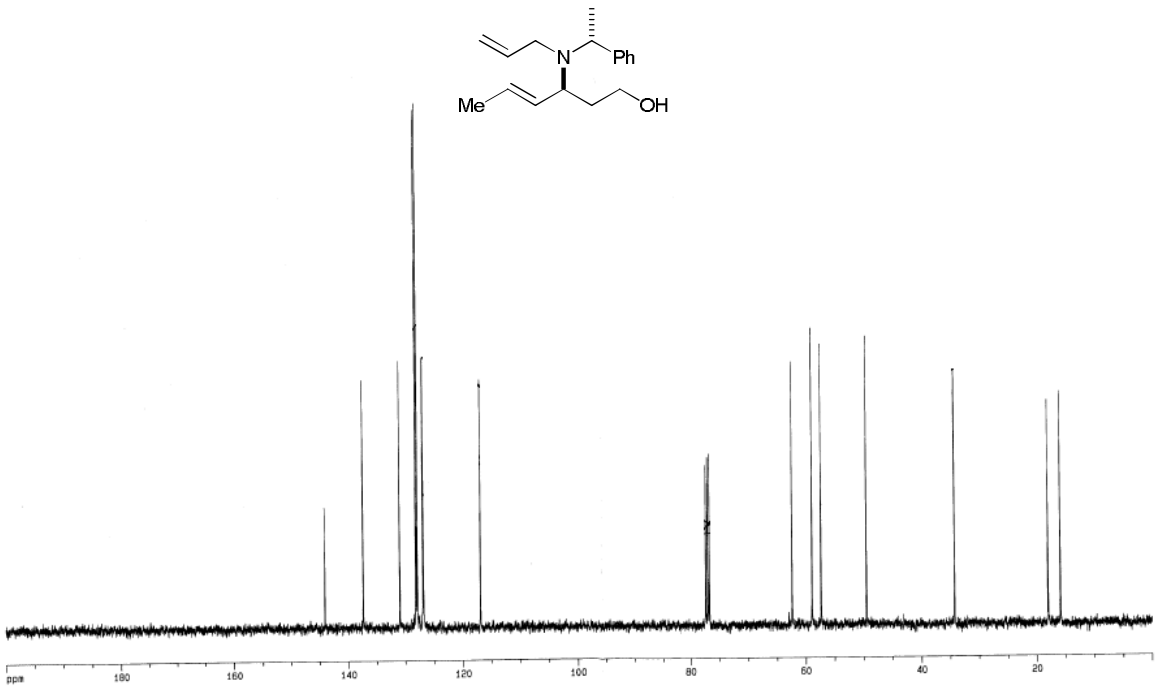
[4] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, C. K. Prout and D. J. Watkin, CRYSTALS, 2001, Issue 11, Chemical Crystallography Laboratory, University of Oxford, UK.

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

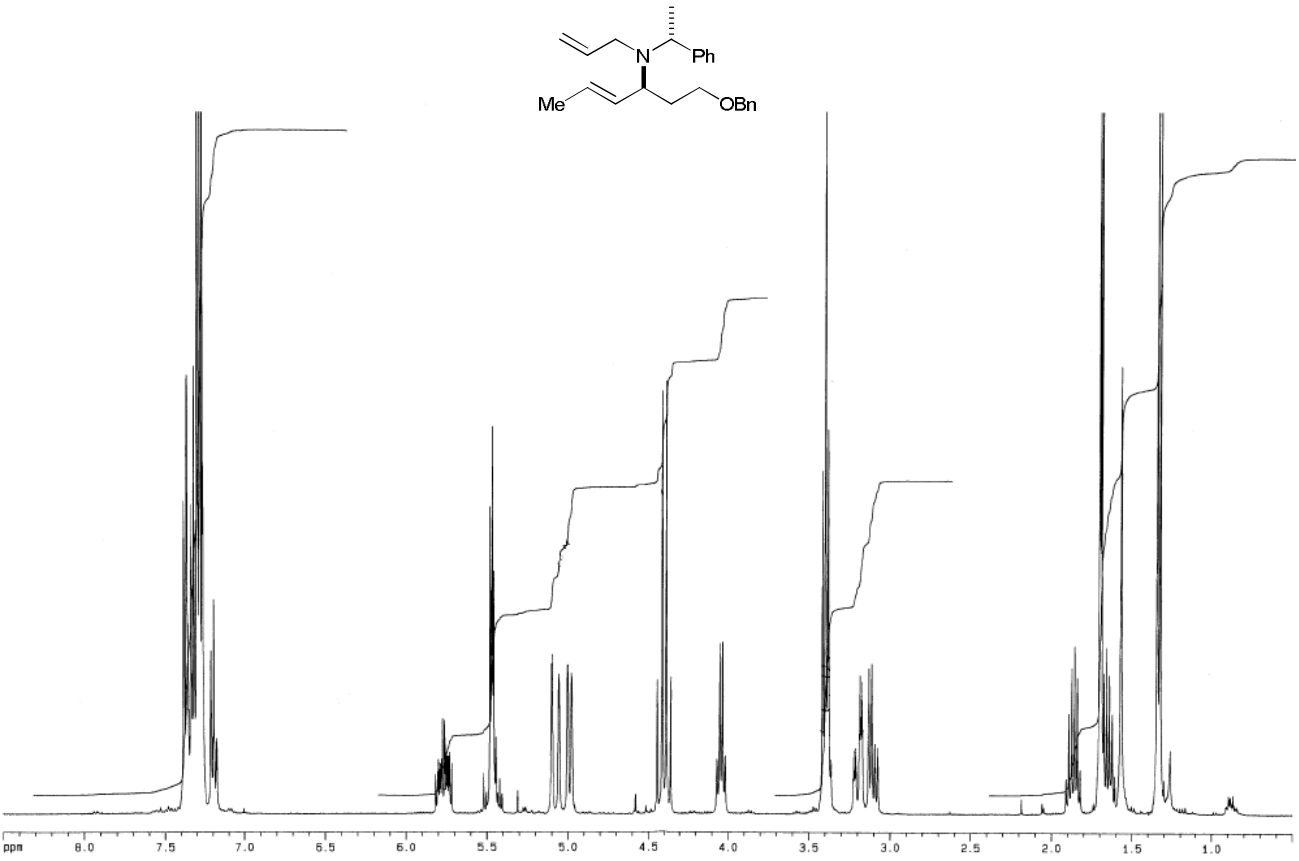
(3*S*,4*E*,α*R*)-3-[*N*-Allyl-*N*-(α-methylbenzyl)amino]hex-4-en-1-ol 12 (400 MHz ^{1}H, $CDCl_3$)



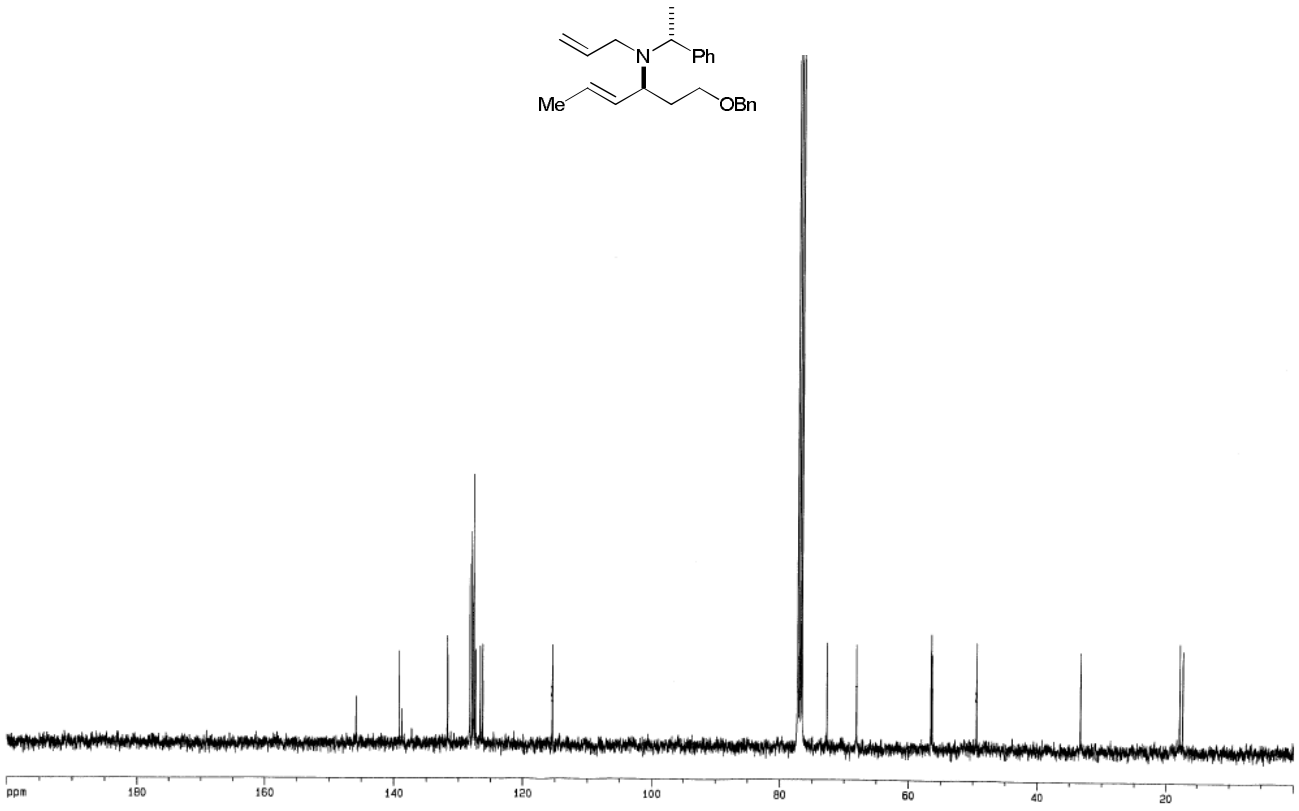
(3*S*,4*E*,α*R*)-3-[*N*-Allyl-*N*-(α-methylbenzyl)amino]hex-4-en-1-ol 12 (100 MHz ^{13}C, $CDCl_3$)



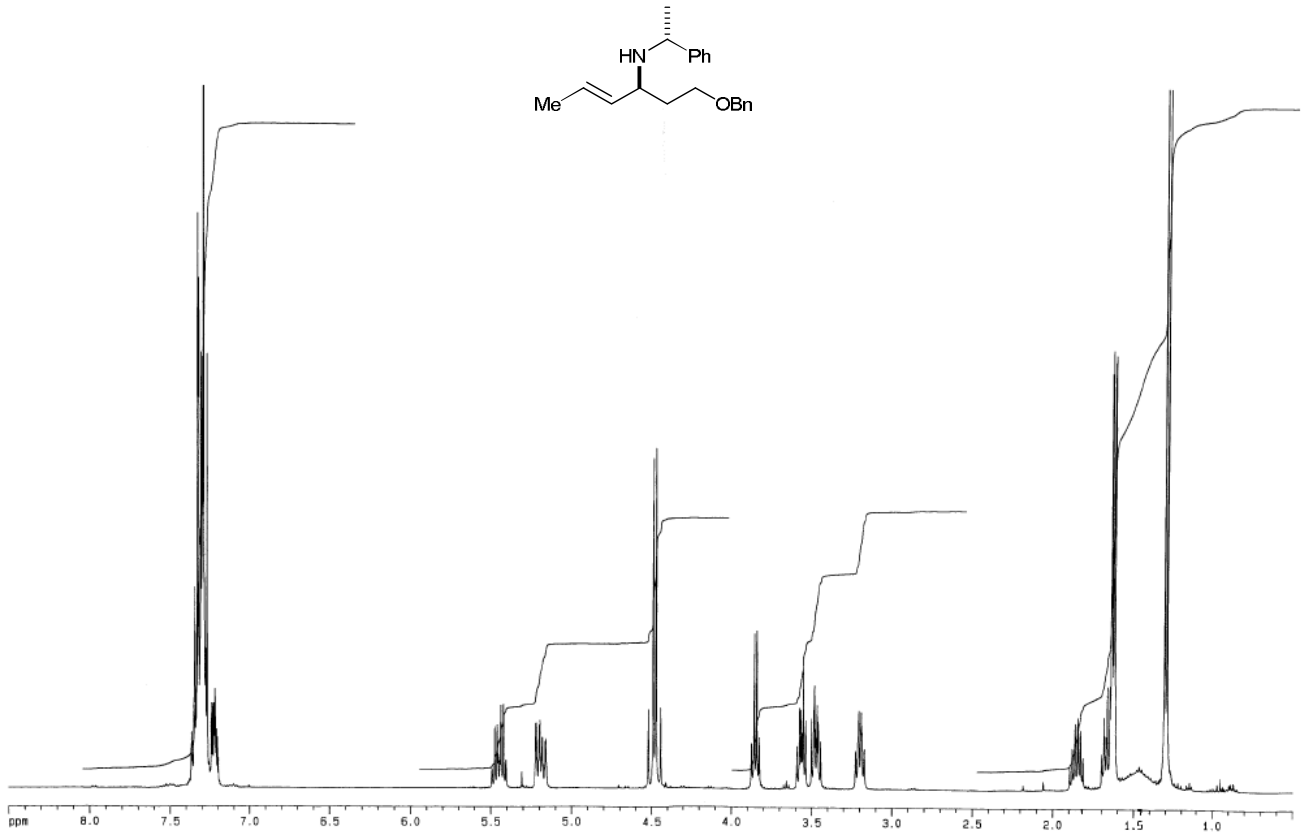
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-allyl-*N*-(α-methylbenzyl)amino]hex-4-ene 13 (400 MHz ^{1}H, $CDCl_3$)



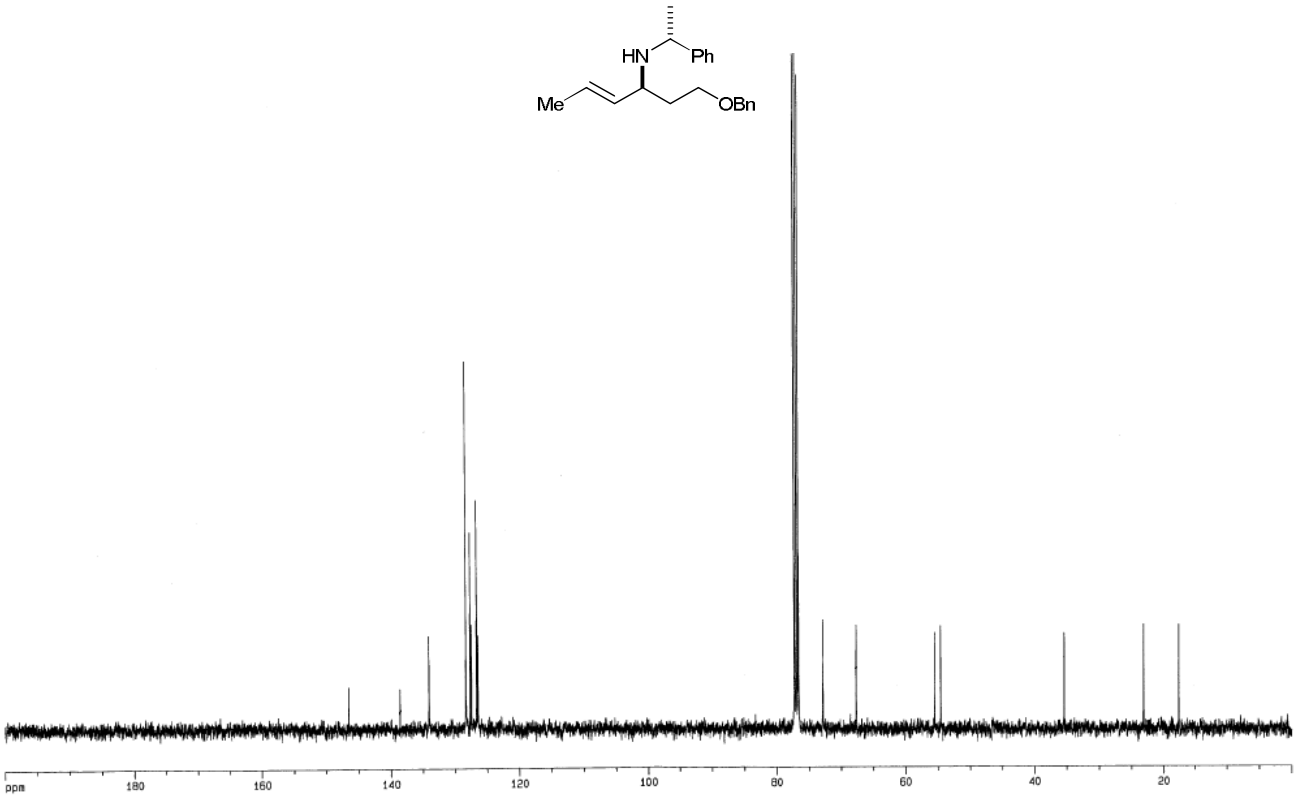
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-allyl-*N*-(α-methylbenzyl)amino]hex-4-ene 13 (100 MHz ^{13}C, $CDCl_3$)



(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(α-methylbenzyl)amino]hex-4-ene 14 (400 MHz ^{1}H, $CDCl_3$)

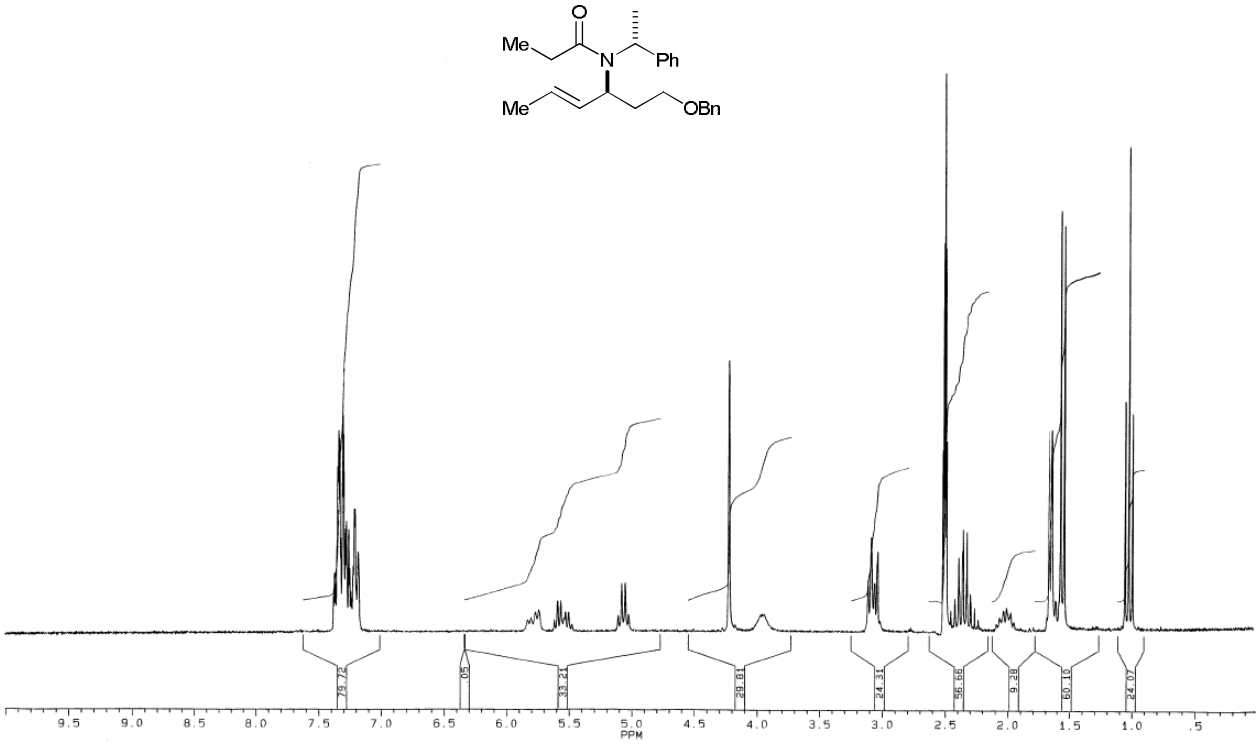


(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(α-methylbenzyl)amino]hex-4-ene 14 (100 MHz ^{13}C, $CDCl_3$)



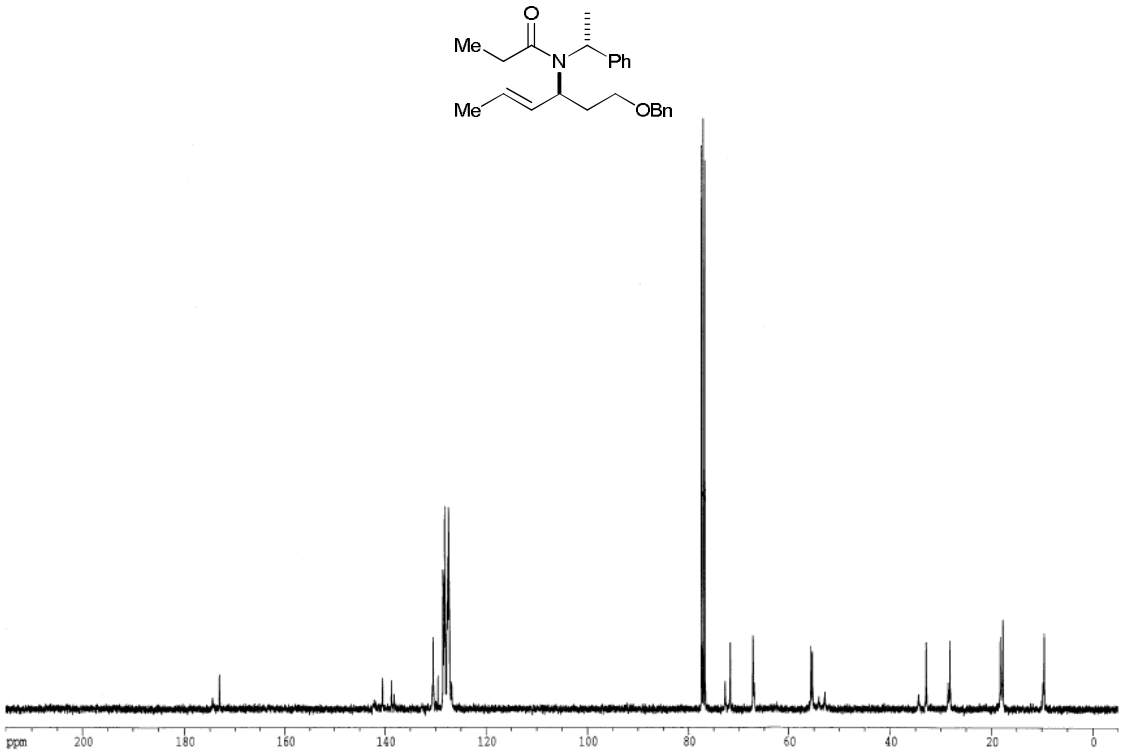
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-propionyl-*N*-(α-methylbenzyl)amino]hex-4-ene 15

(400 MHz ^{1}H, $CDCl_3$, 363 K)

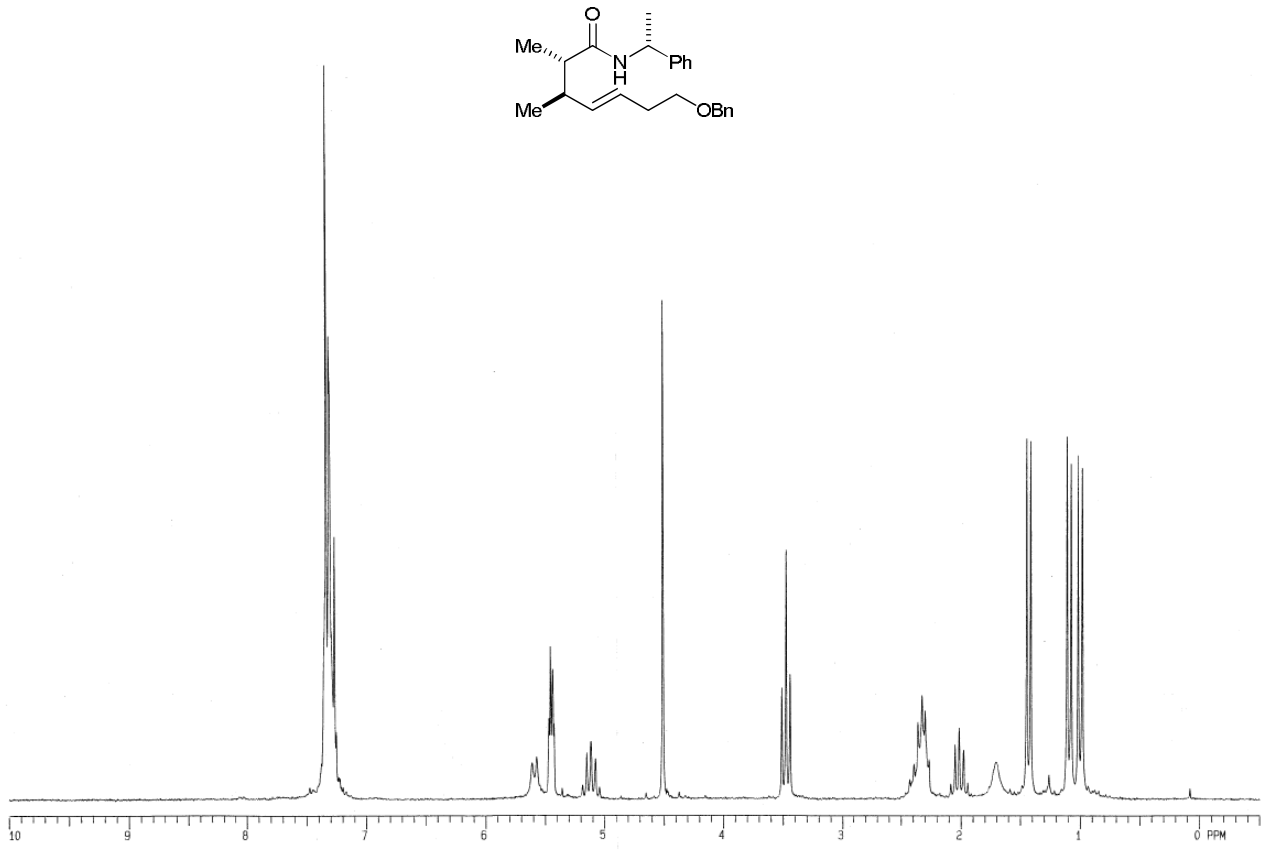


(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-propionyl-*N*-(α-methylbenzyl)amino]hex-4-ene 15

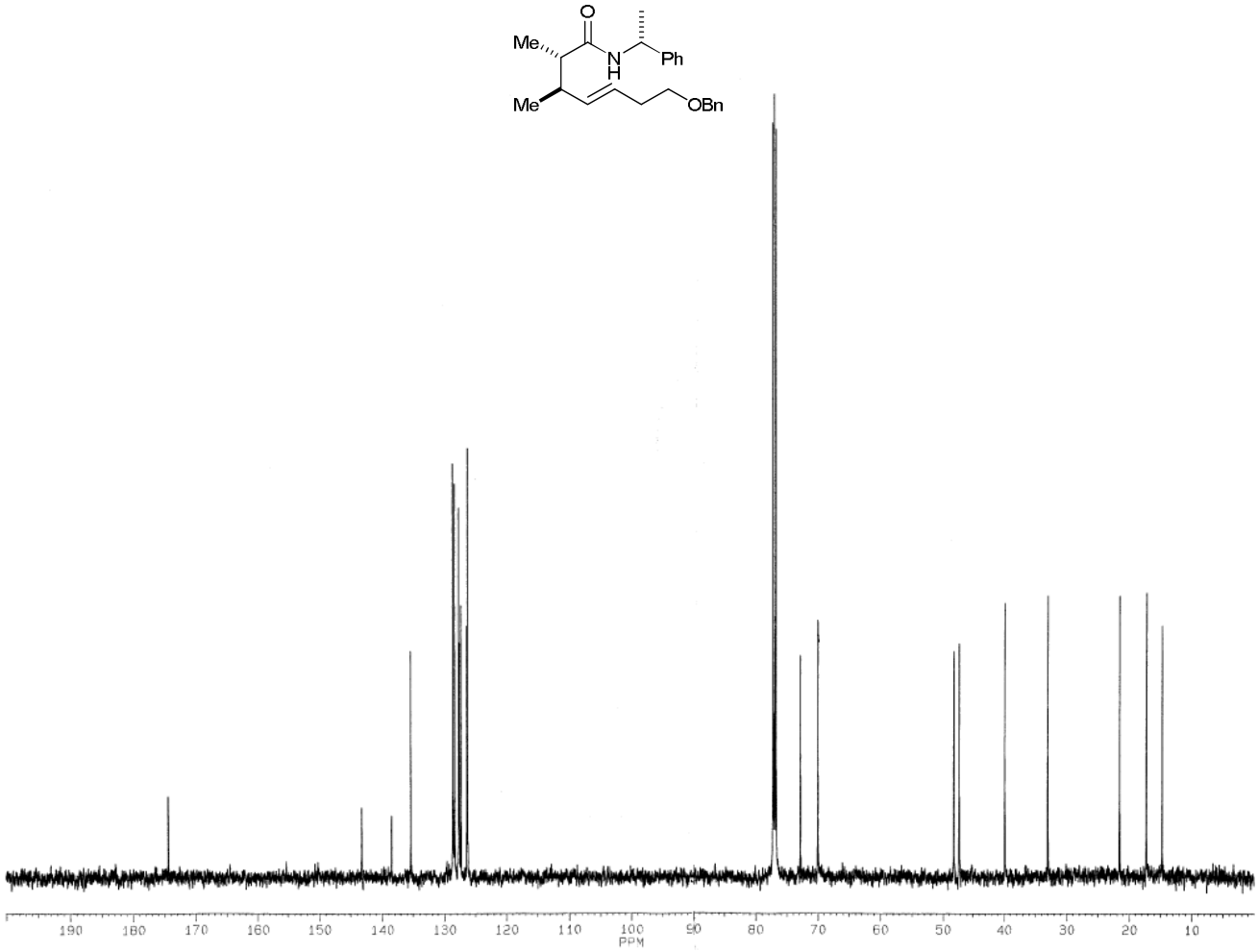
(100 MHz ^{13}C, $CDCl_3$)



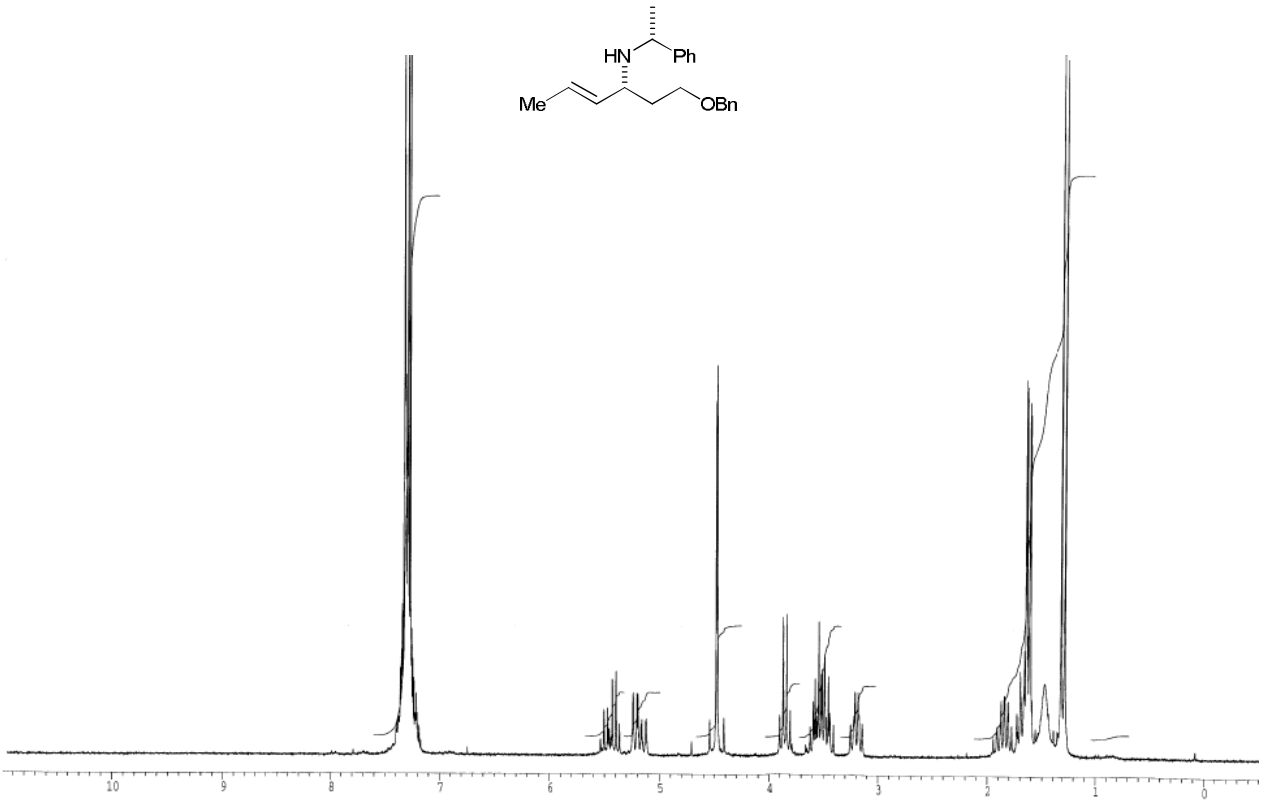
(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2,3-dimethyl-7-benzyloxy-hept-4-enamide 17 (400 MHz ^{1}H, $CDCl_3$)



(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2,3-dimethyl-7-benzyloxy-hept-4-enamide 17 (100 MHz ^{13}C, $CDCl_3$)

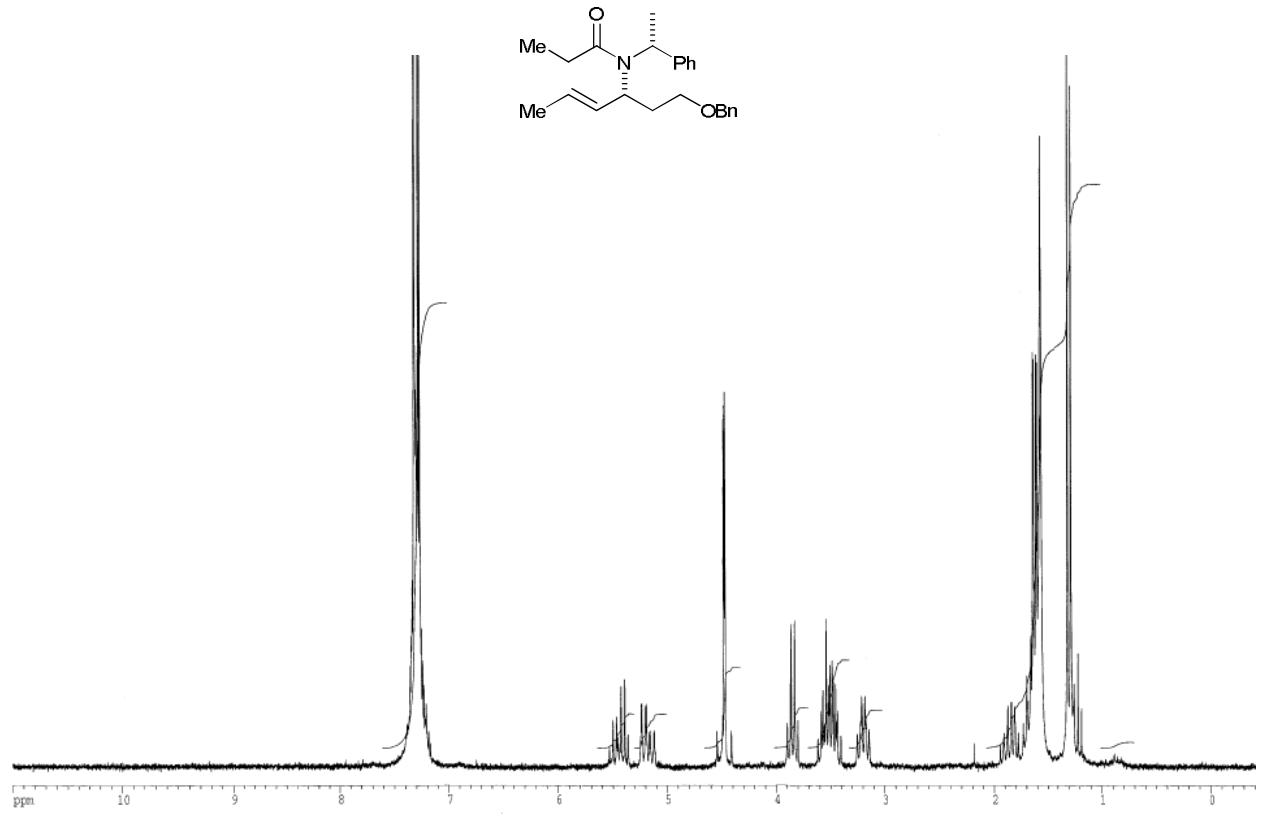


(3*R*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(α-methylbenzyl)amino]hex-4-ene 20 (400 MHz ^{1}H, $CDCl_3$)



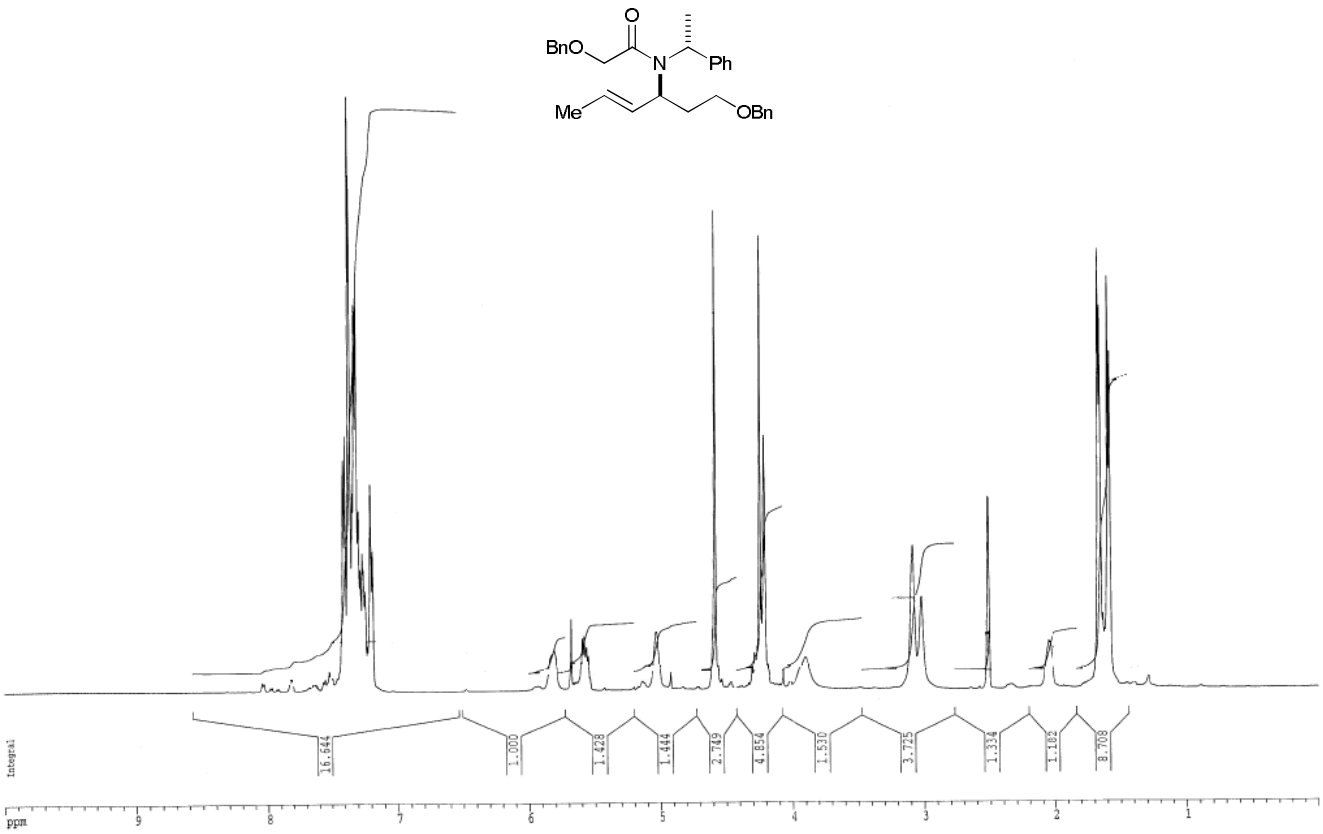
(3*R*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-propionyl-*N*-(α-methylbenzyl)amino]hex-4-ene 21

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



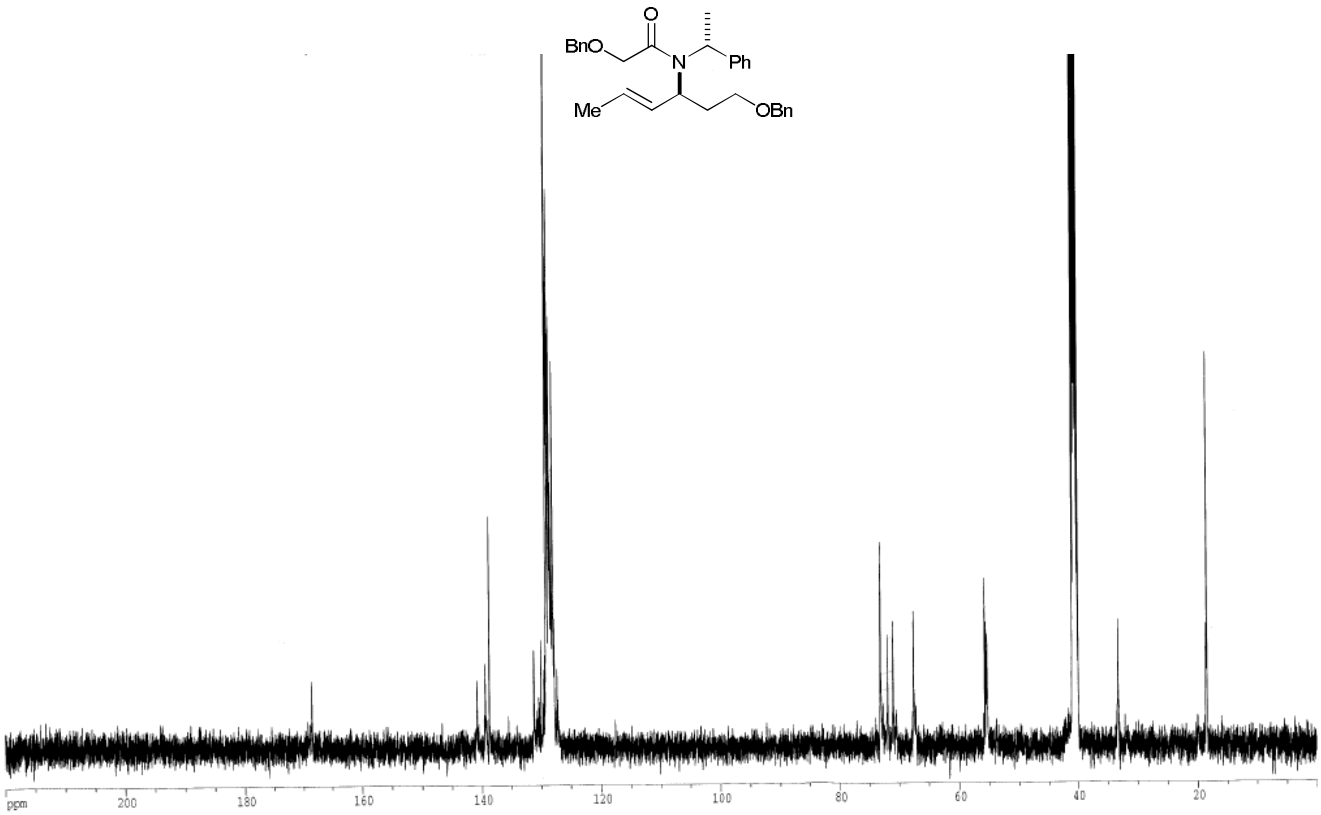
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(2'-benzyloxyacetyl)-*N*-(α-methylbenzyl)amino]hex-4-ene 32

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



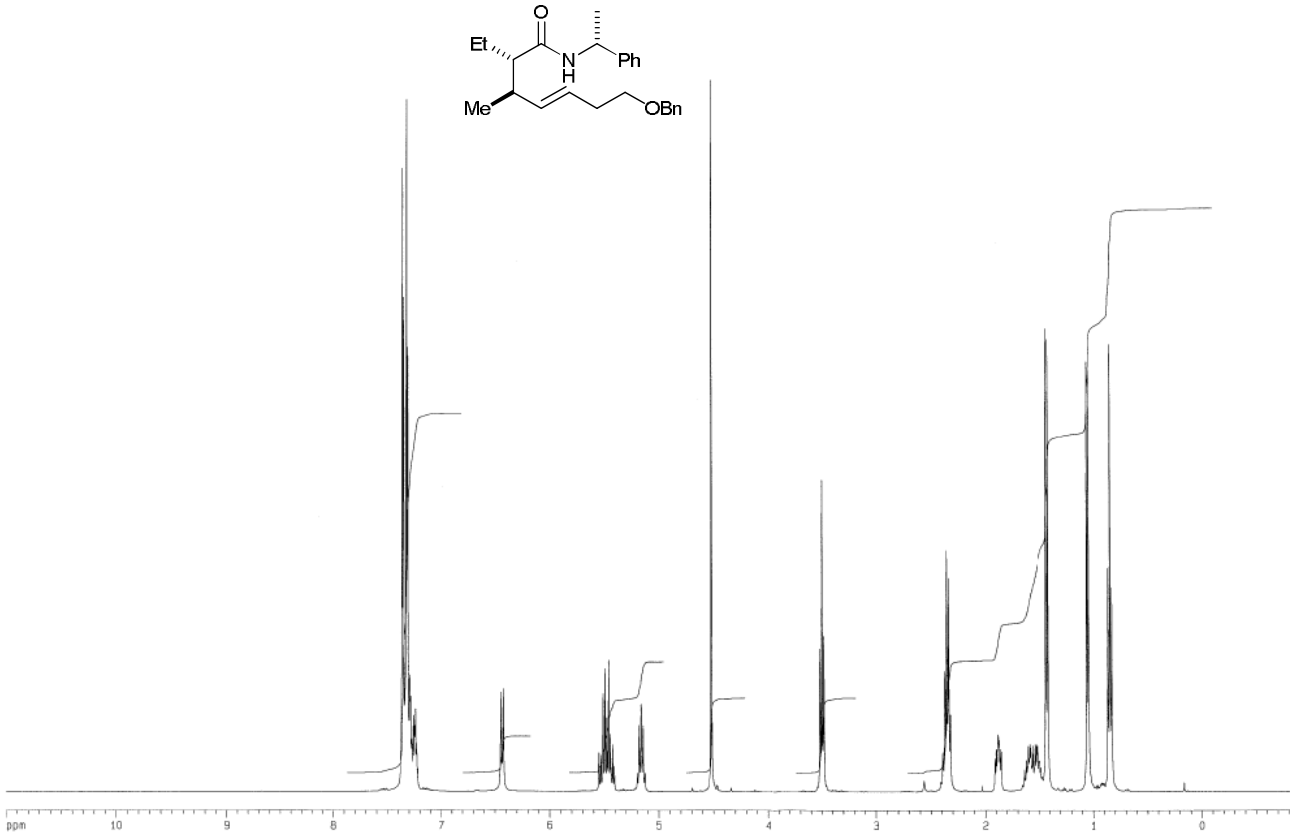
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(2'-benzyloxyacetyl)-*N*-(α-methylbenzyl)amino]hex-4-ene 32

(100 MHz ^{13}C, $CDCl_3$)



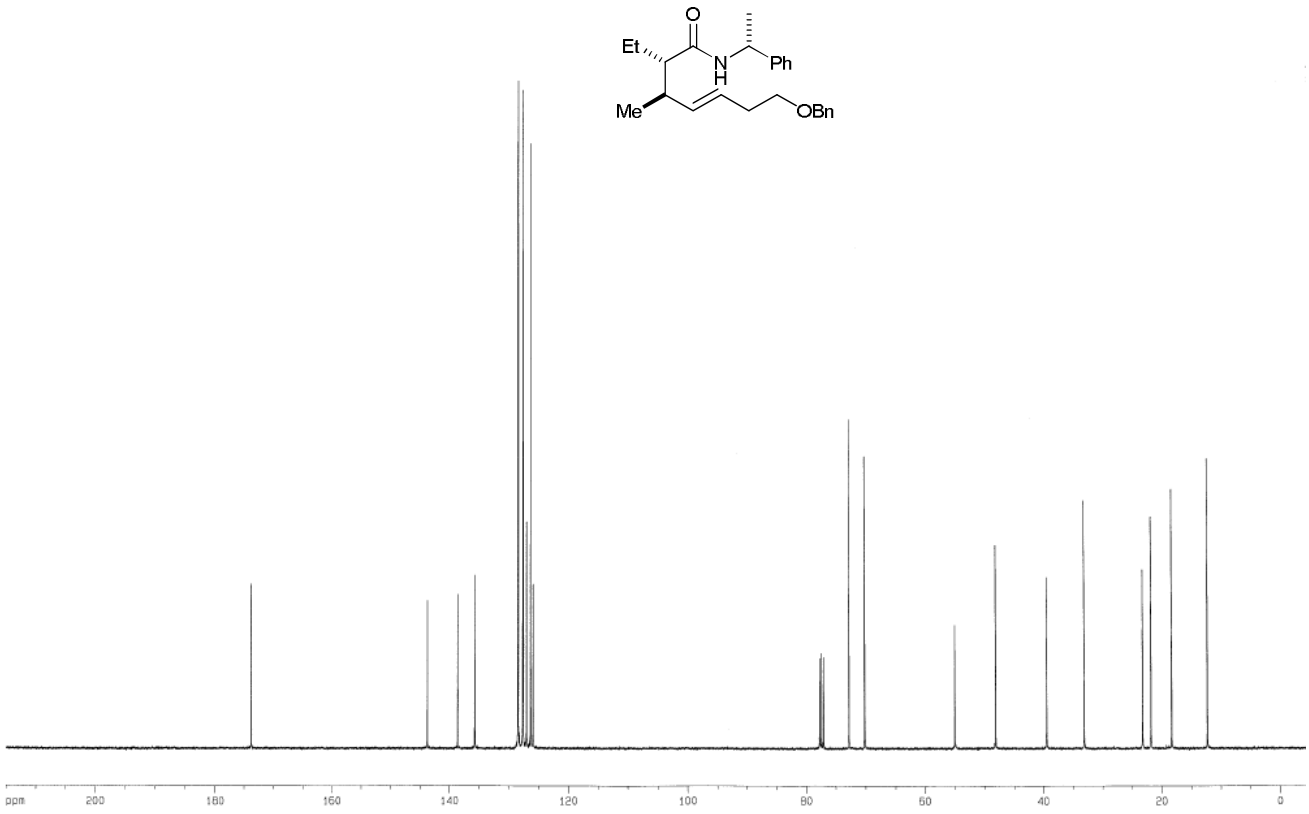
(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-ethyl-3-methyl-7-benzyloxy-hept-4-enamide 33

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



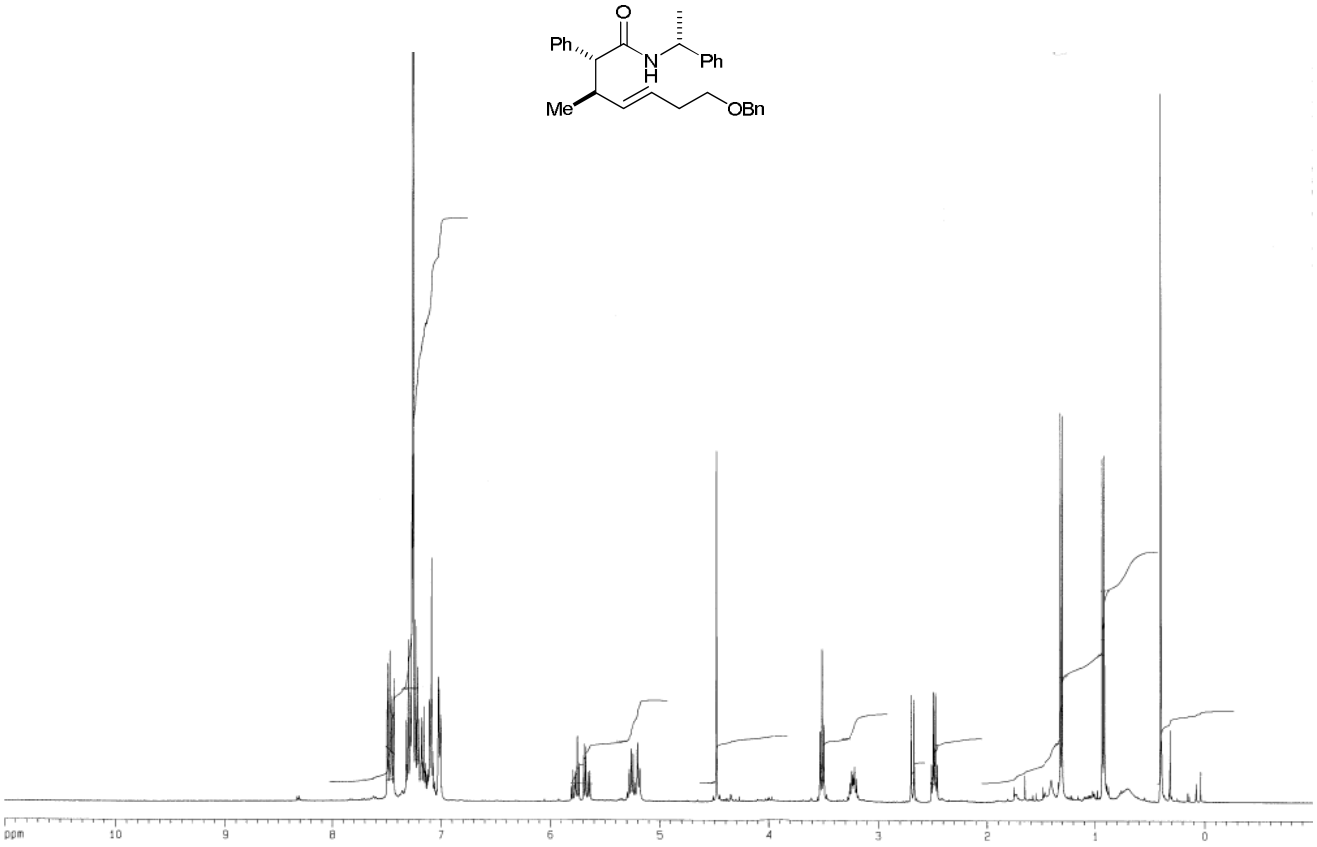
(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-ethyl-3-methyl-7-benzyloxy-hept-4-enamide 33

(100 MHz ^{13}C, $CDCl_3$)



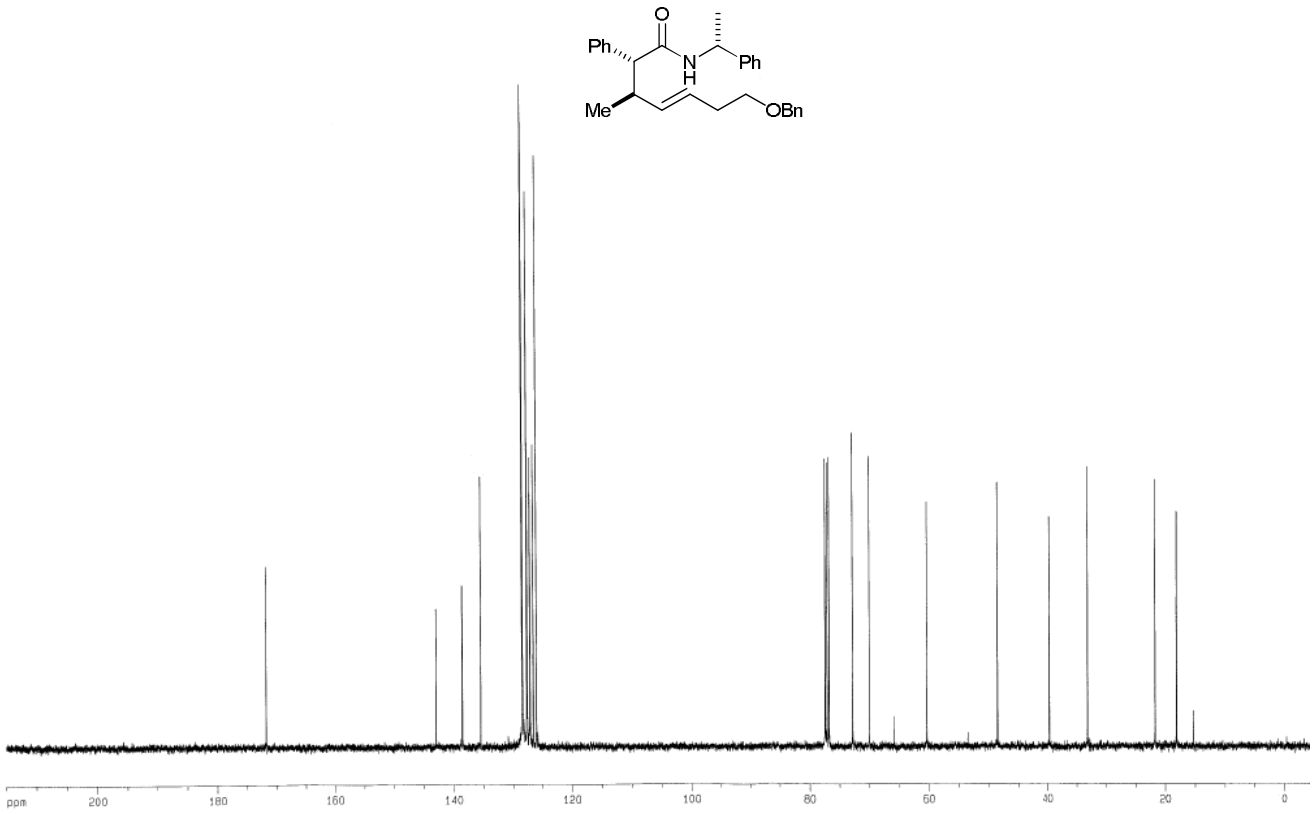
(*R*)-*N*-α-Methylbenzyl (2*R*,3*R*,4*E*)-2-phenyl-3-methyl-7-benzyloxy-hept-4-enamide 34

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



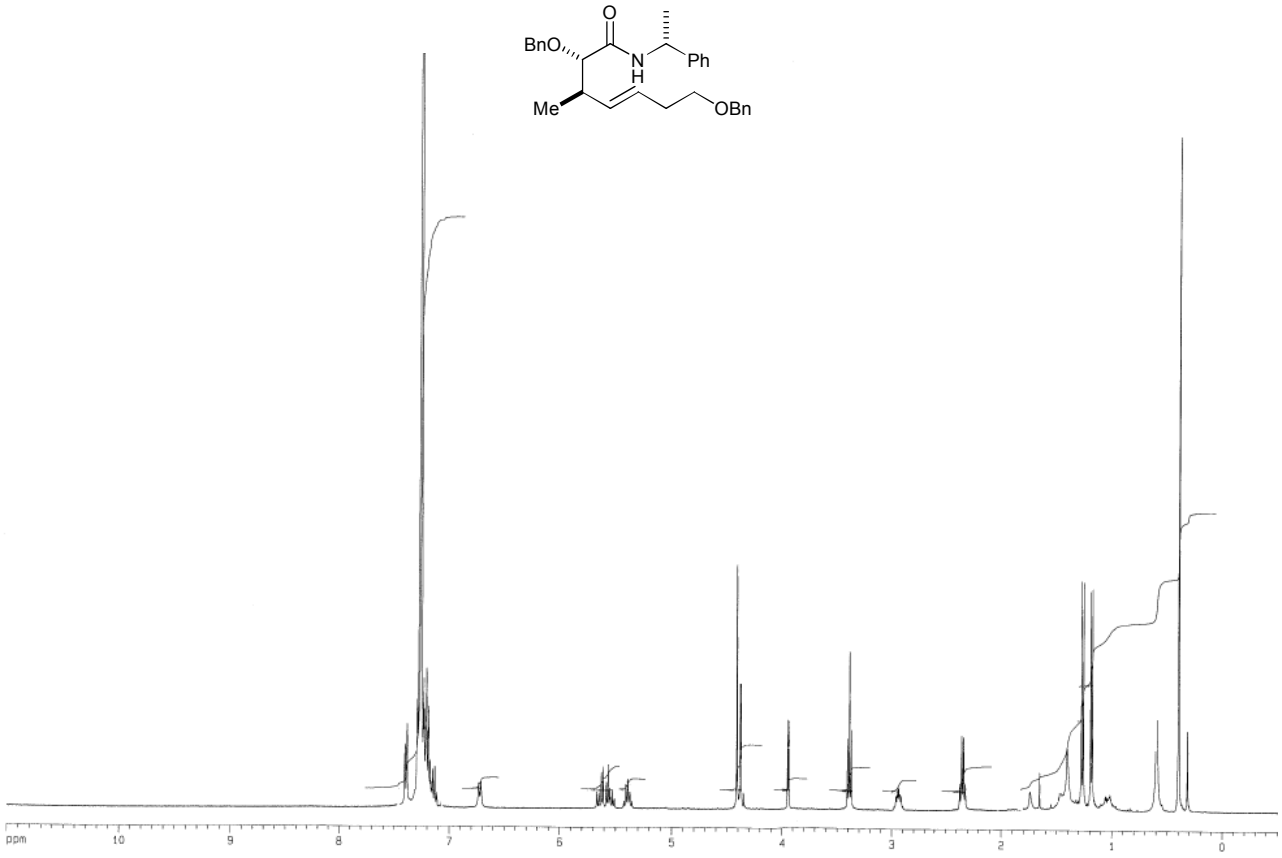
(*R*)-*N*-α-Methylbenzyl (2*R*,3*R*,4*E*)-2-phenyl-3-methyl-7-benzyloxy-hept-4-enamide 34

(100 MHz ^{13}C, $CDCl_3$)

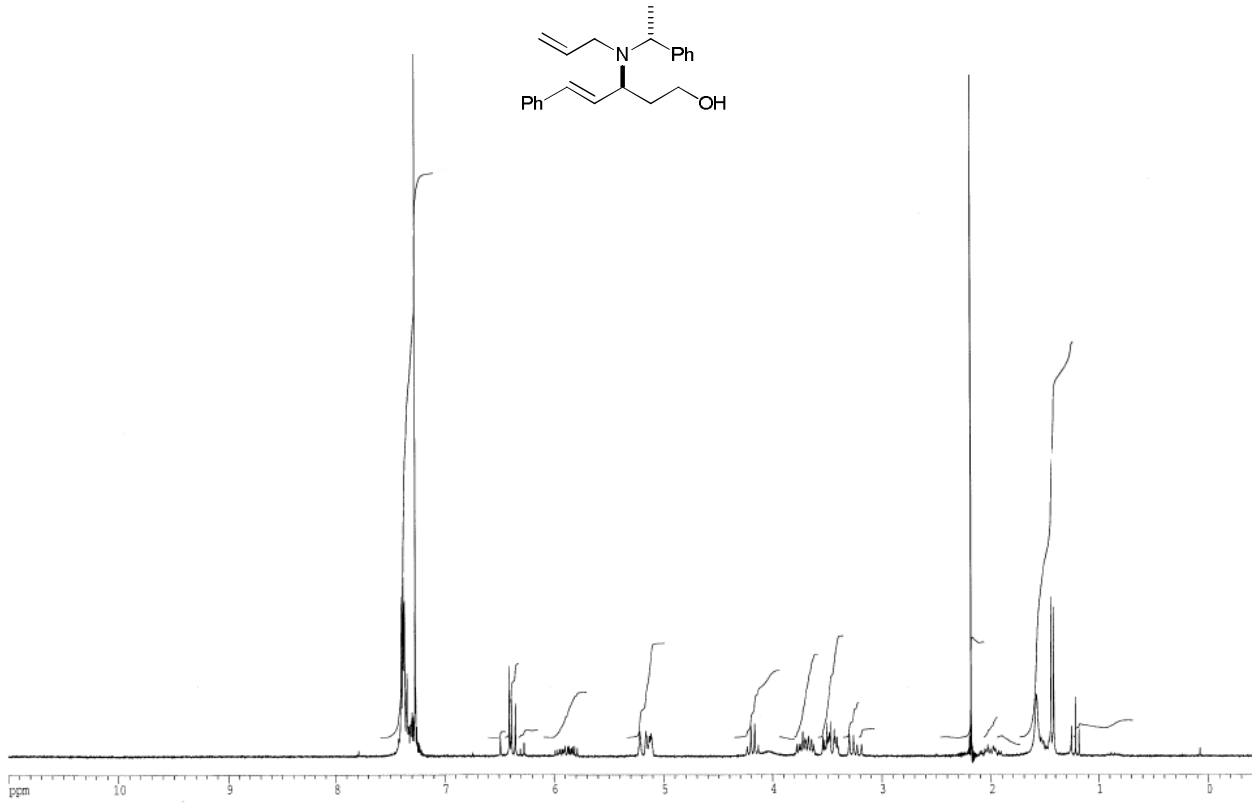


(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-benzyloxy-3-methyl-7-benzyloxy-hept-4-enamide 36

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

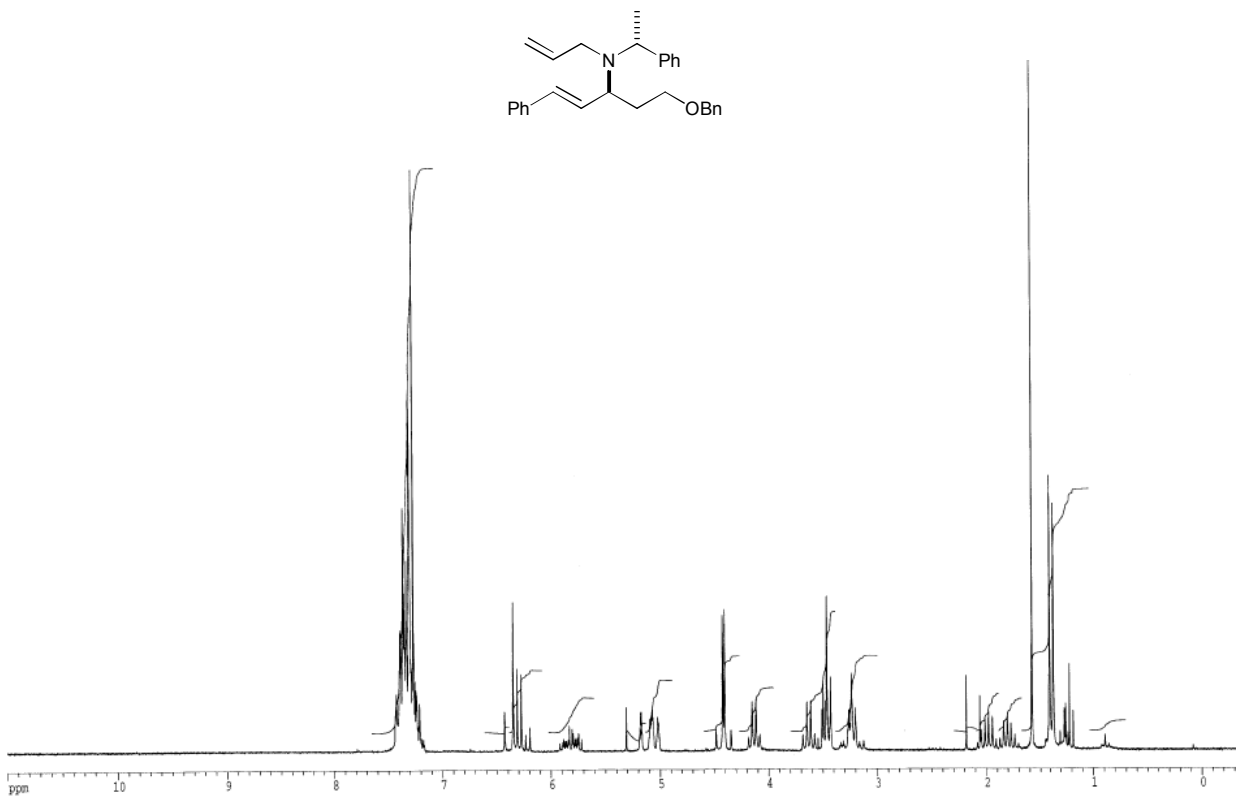


(3*S*,4*E*,α*R*)-3-[*N*-Allyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-en-1-ol 38 (400 MHz ^{1}H, $CDCl_3$)



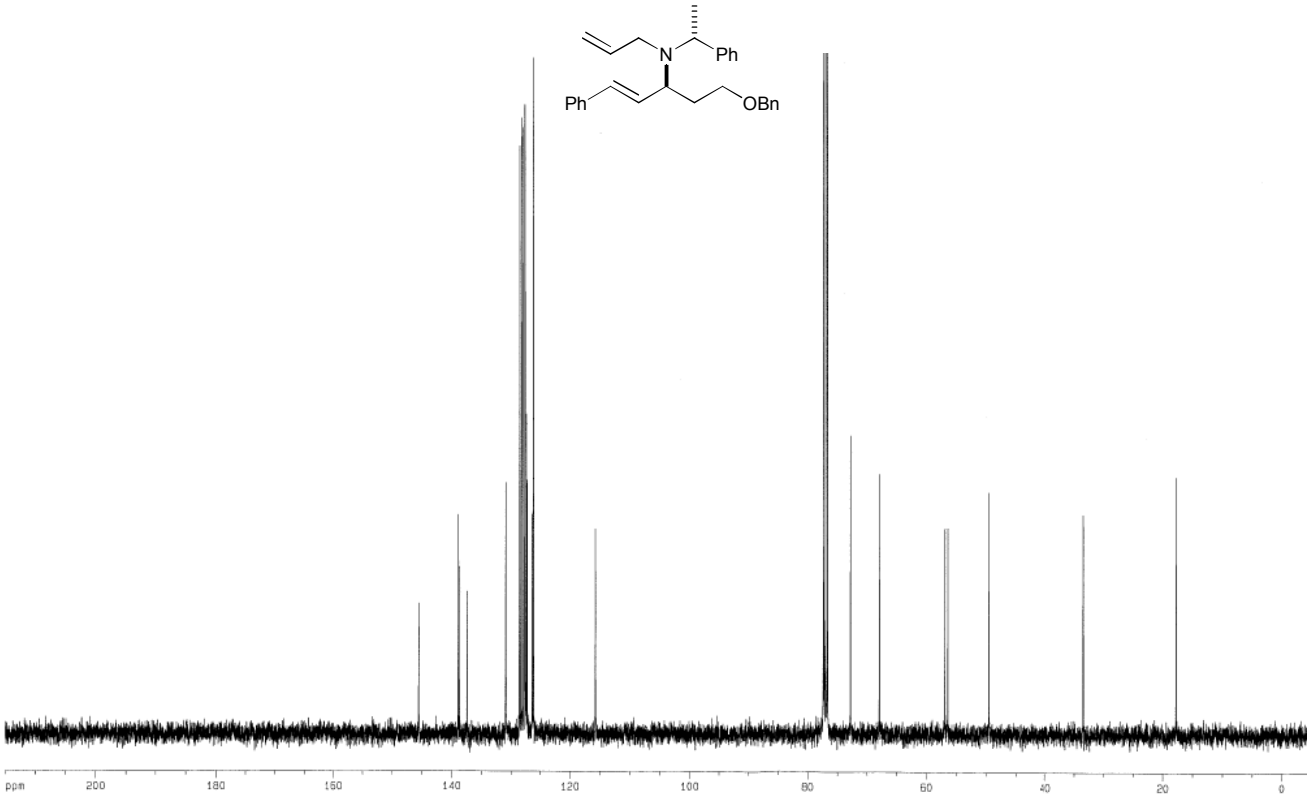
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-allyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 39

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

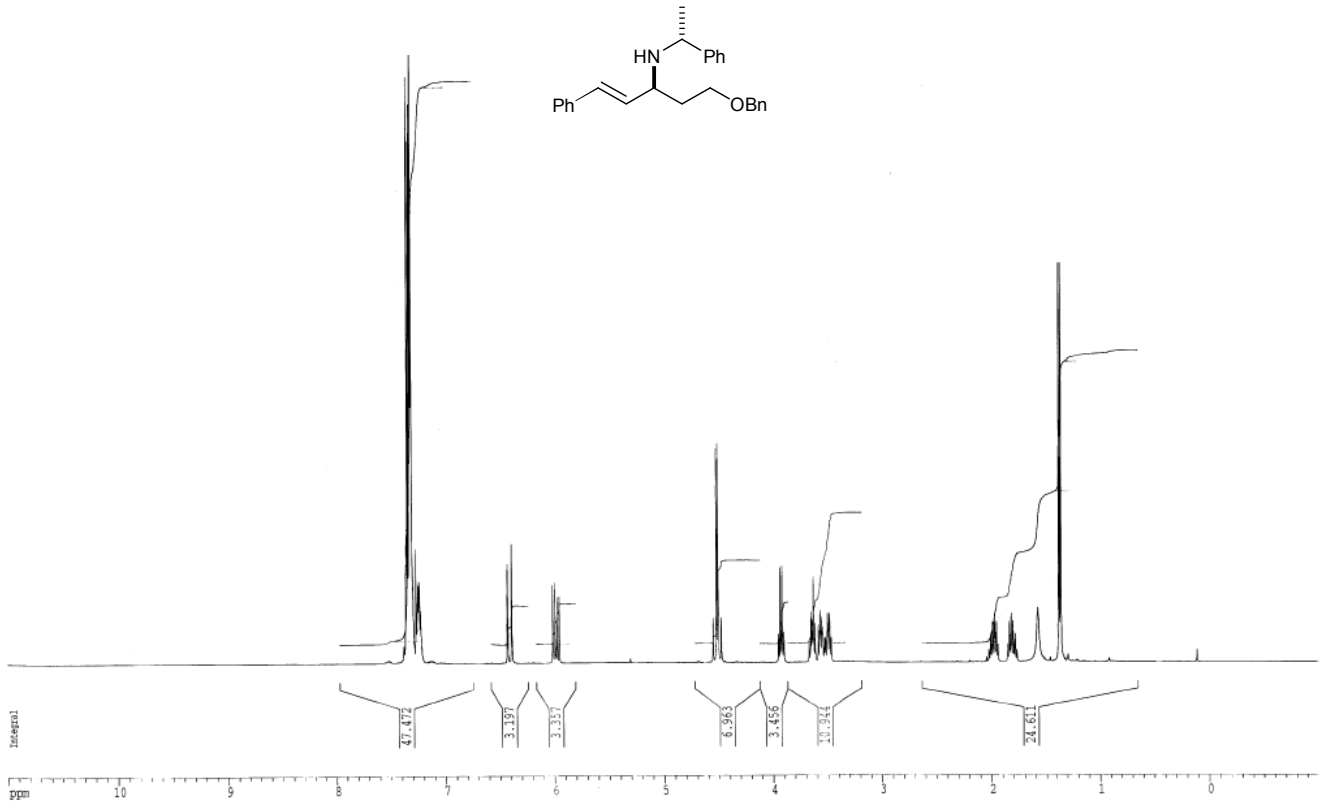


(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-allyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 39

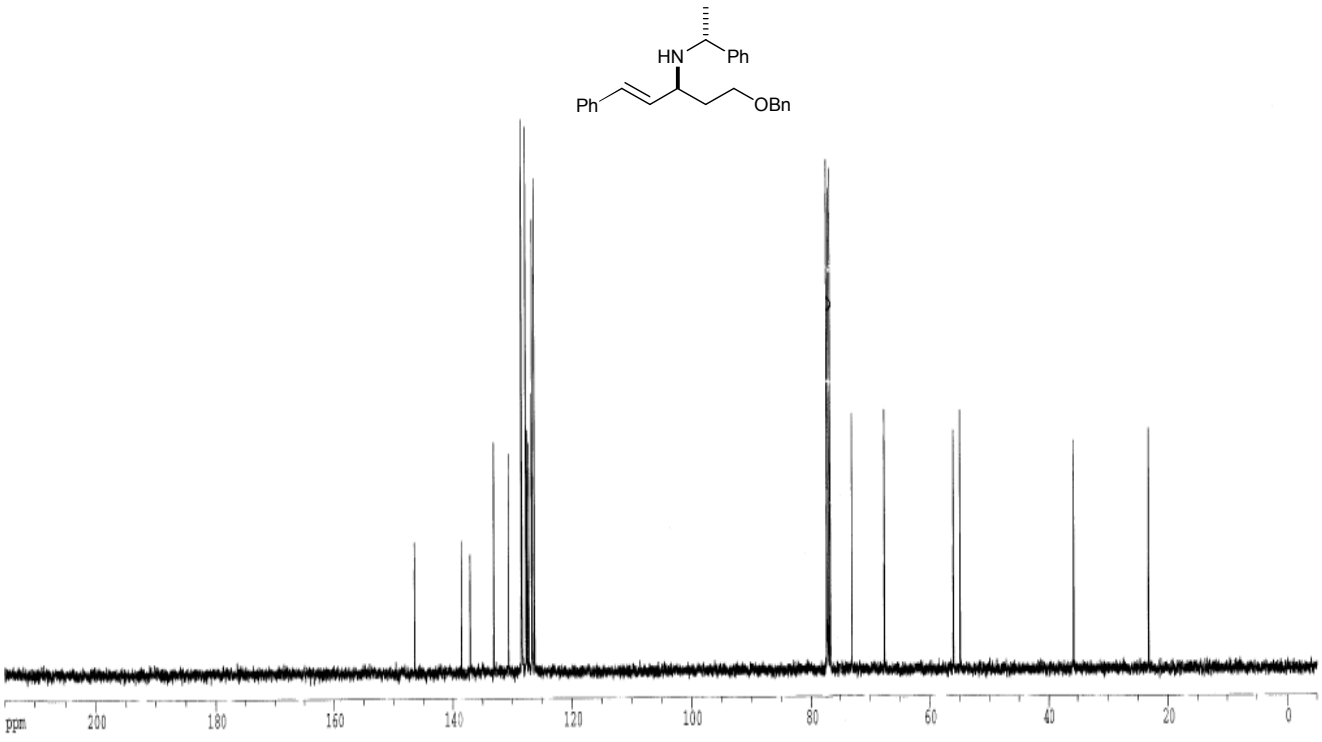
(100 MHz ^{13}C, $CDCl_3$)



(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 40 (400 MHz ^{1}H, $CDCl_3$)

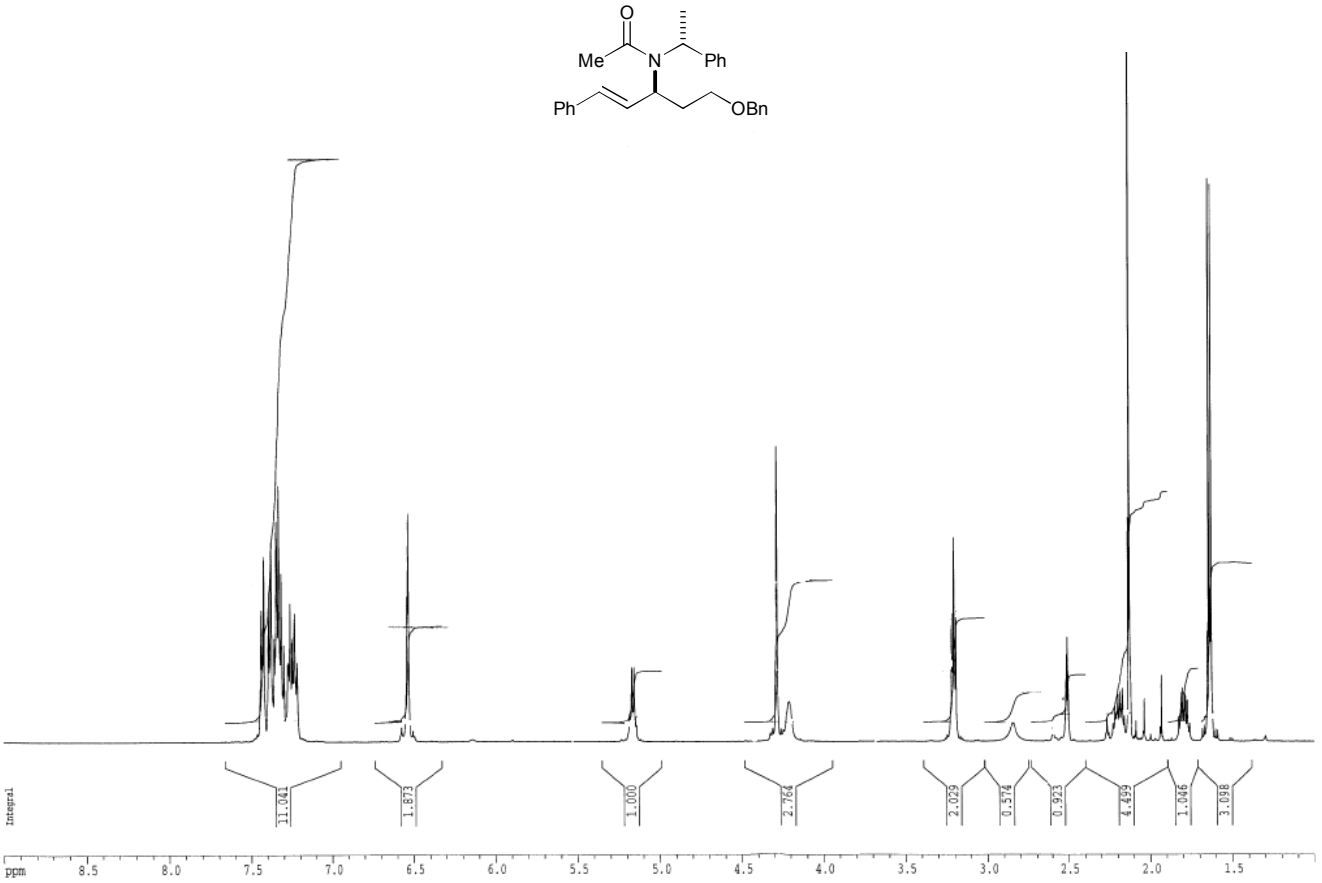


(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 40 (100 MHz ^{13}C, $CDCl_3$)



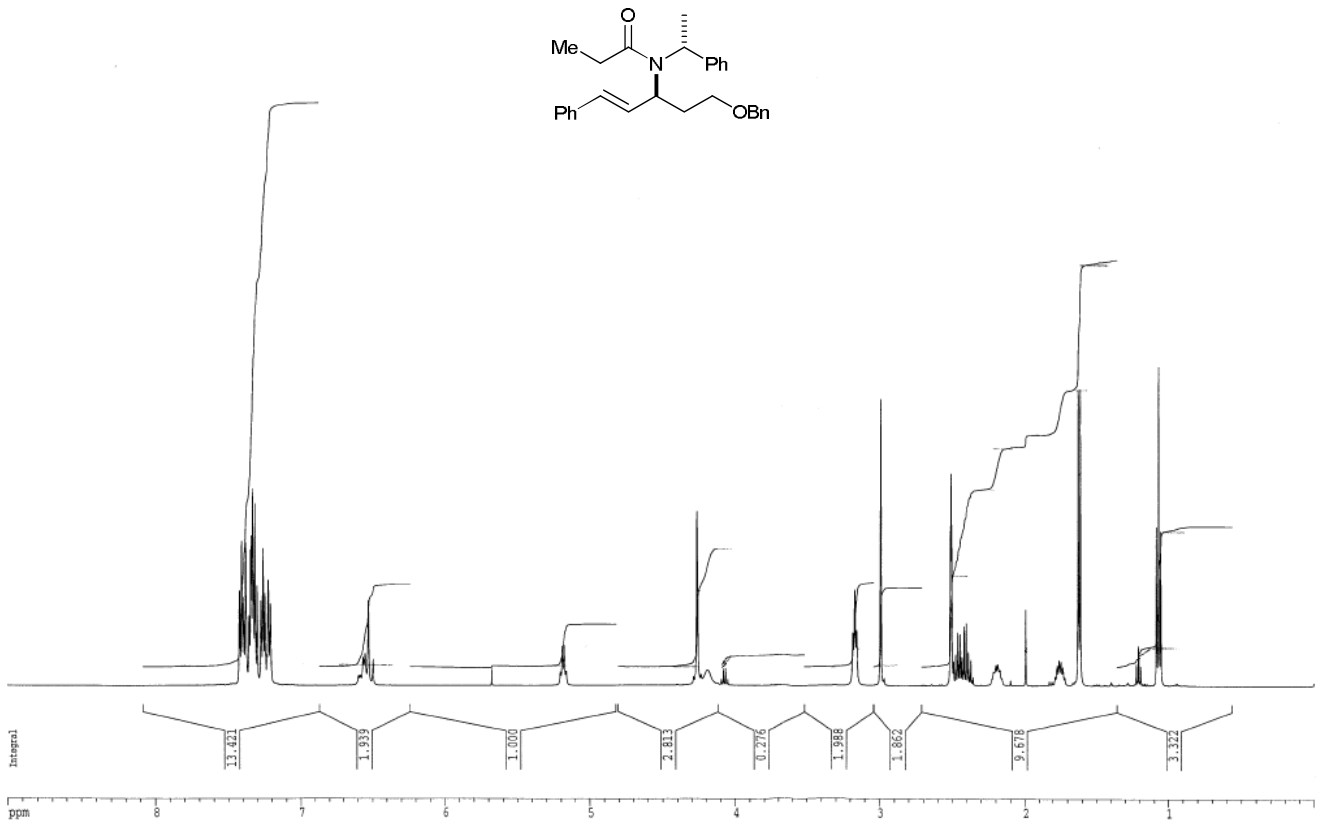
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-acetyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 41

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



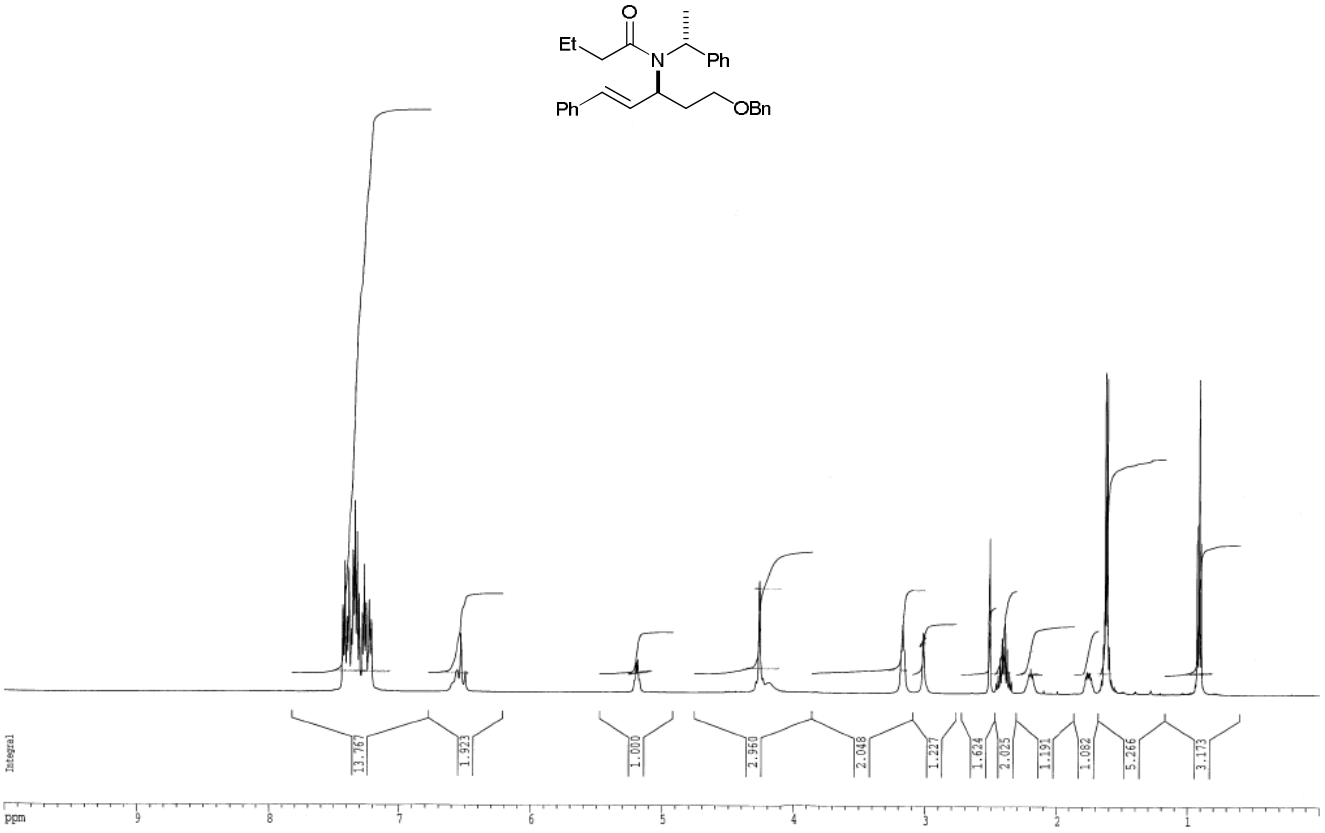
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-propionyl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 42

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



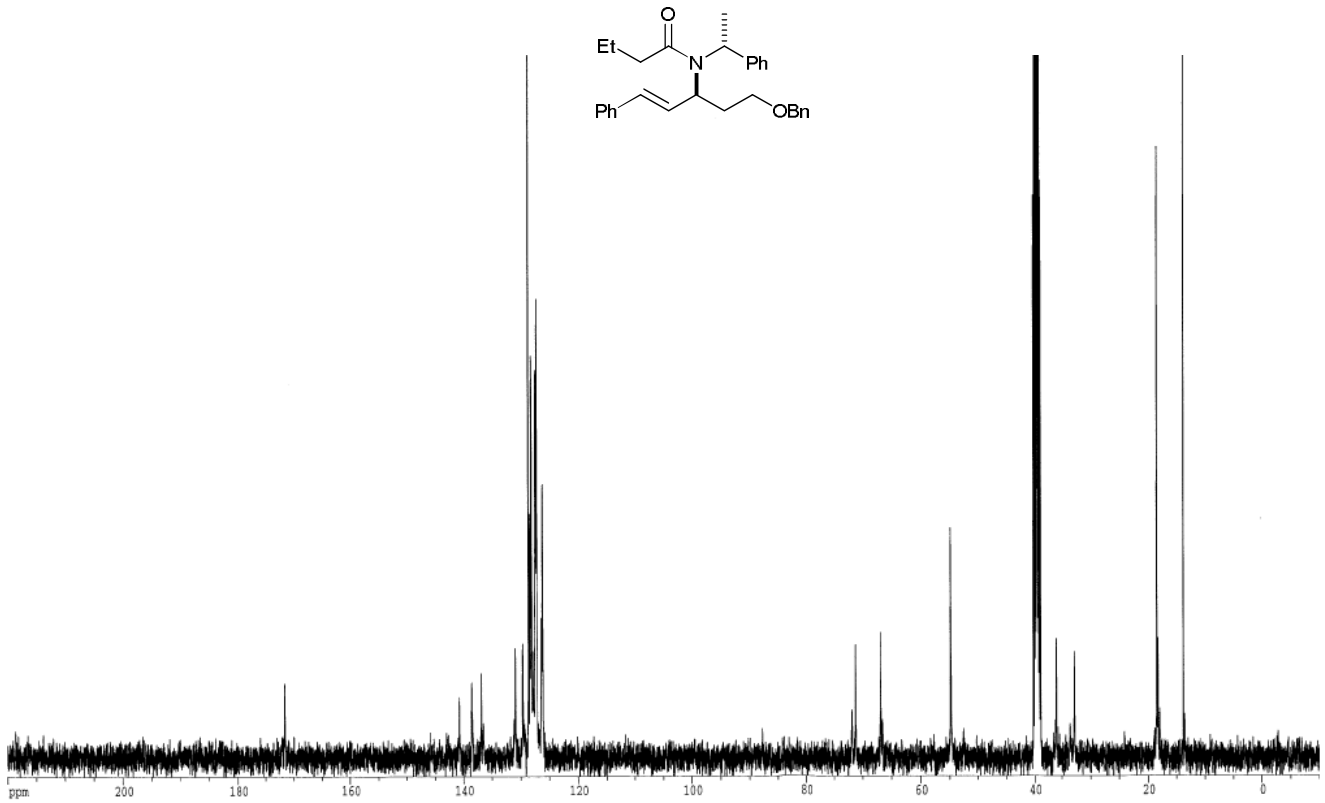
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-butyryl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 43

(400 MHz ^{1}H, $CDCl_3$, 363 K)

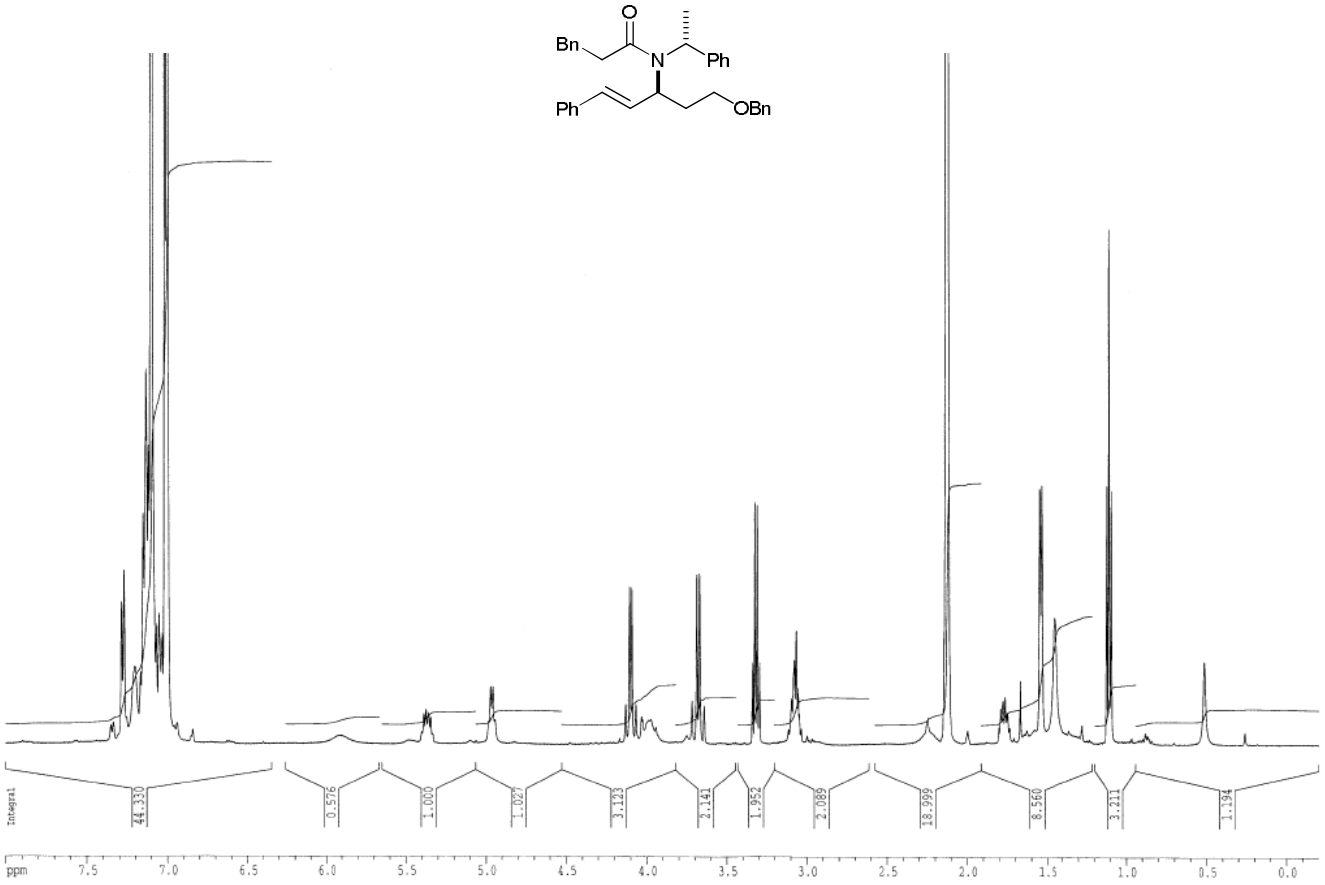


(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-butyryl-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 43

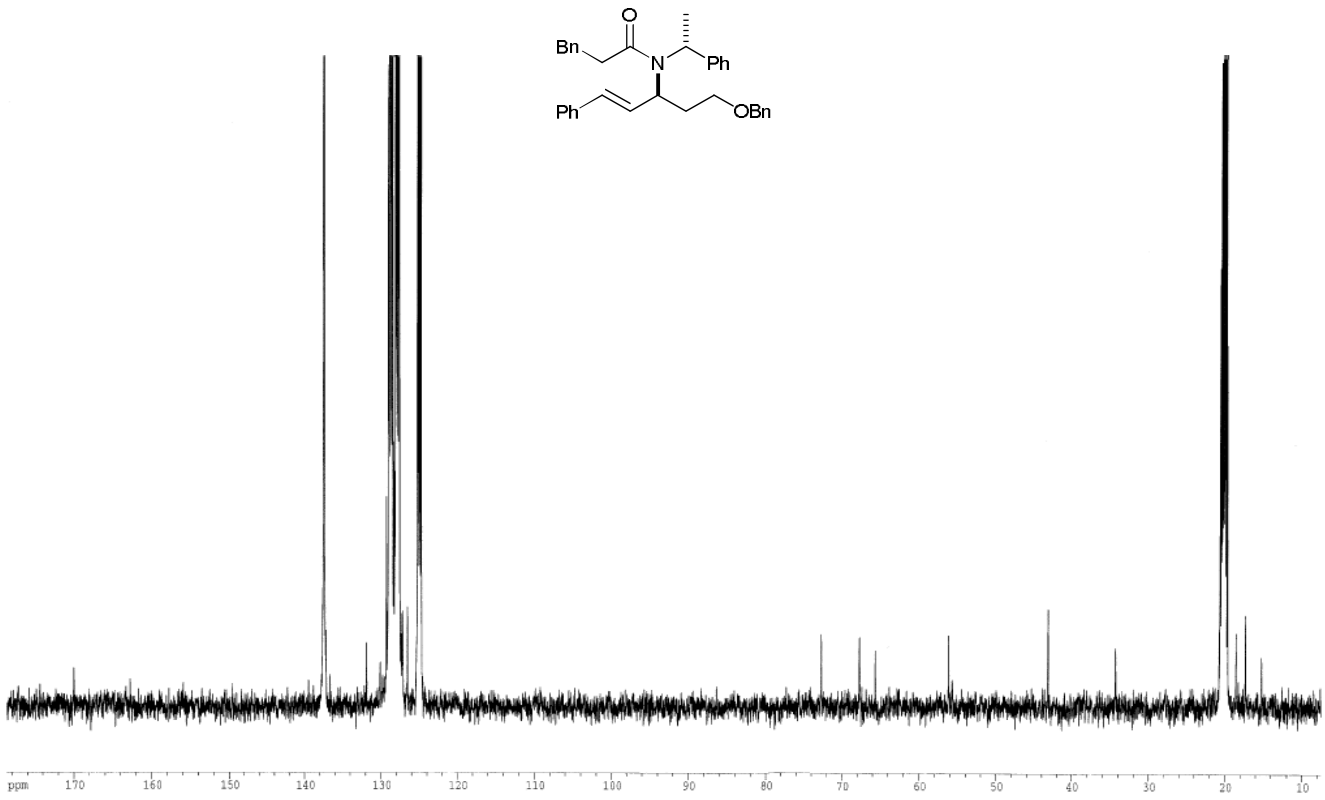
(100 MHz ^{13}C, $CDCl_3$)



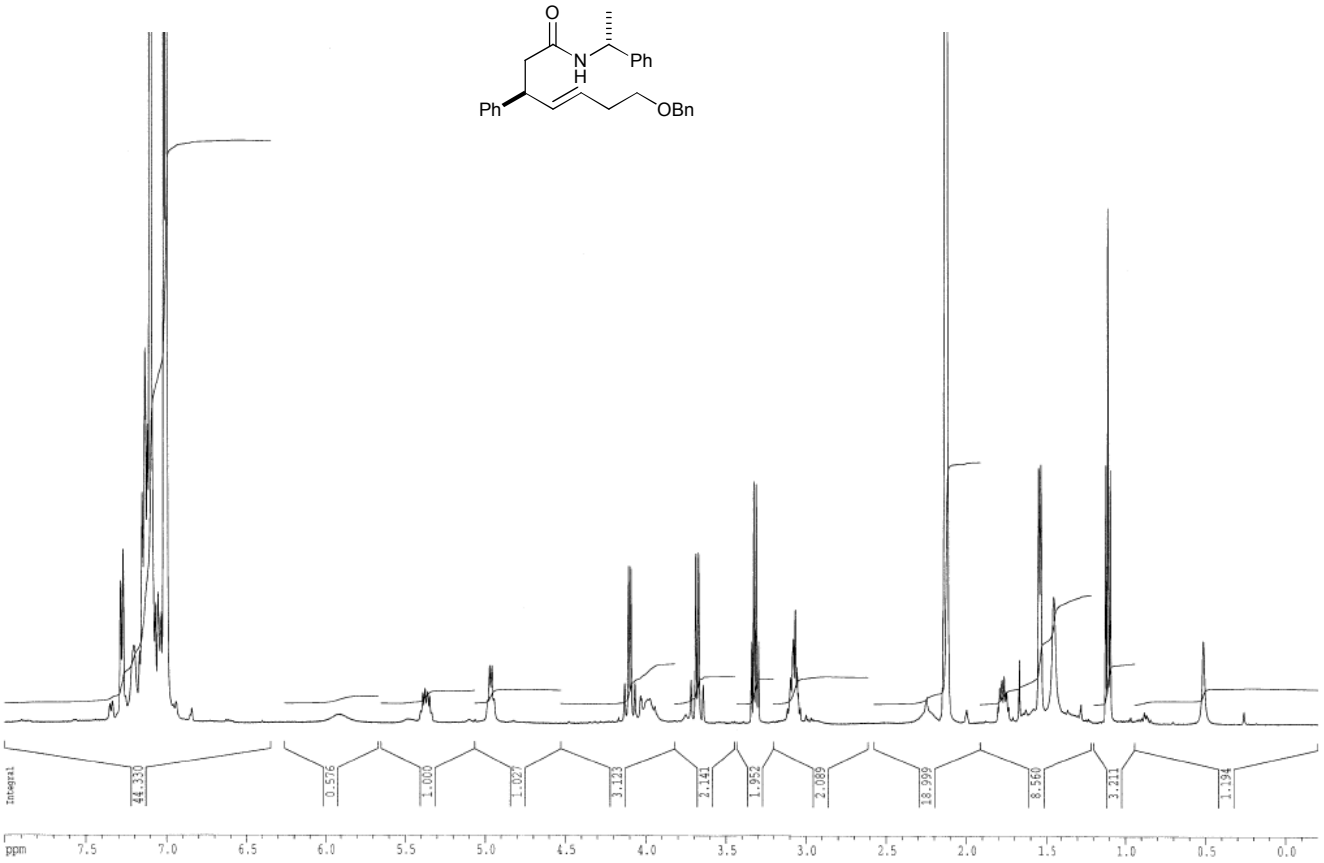
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(3'-phenylpropionyl)-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 44 (400 MHz ^{1}H, $CDCl_3$, 363 K)



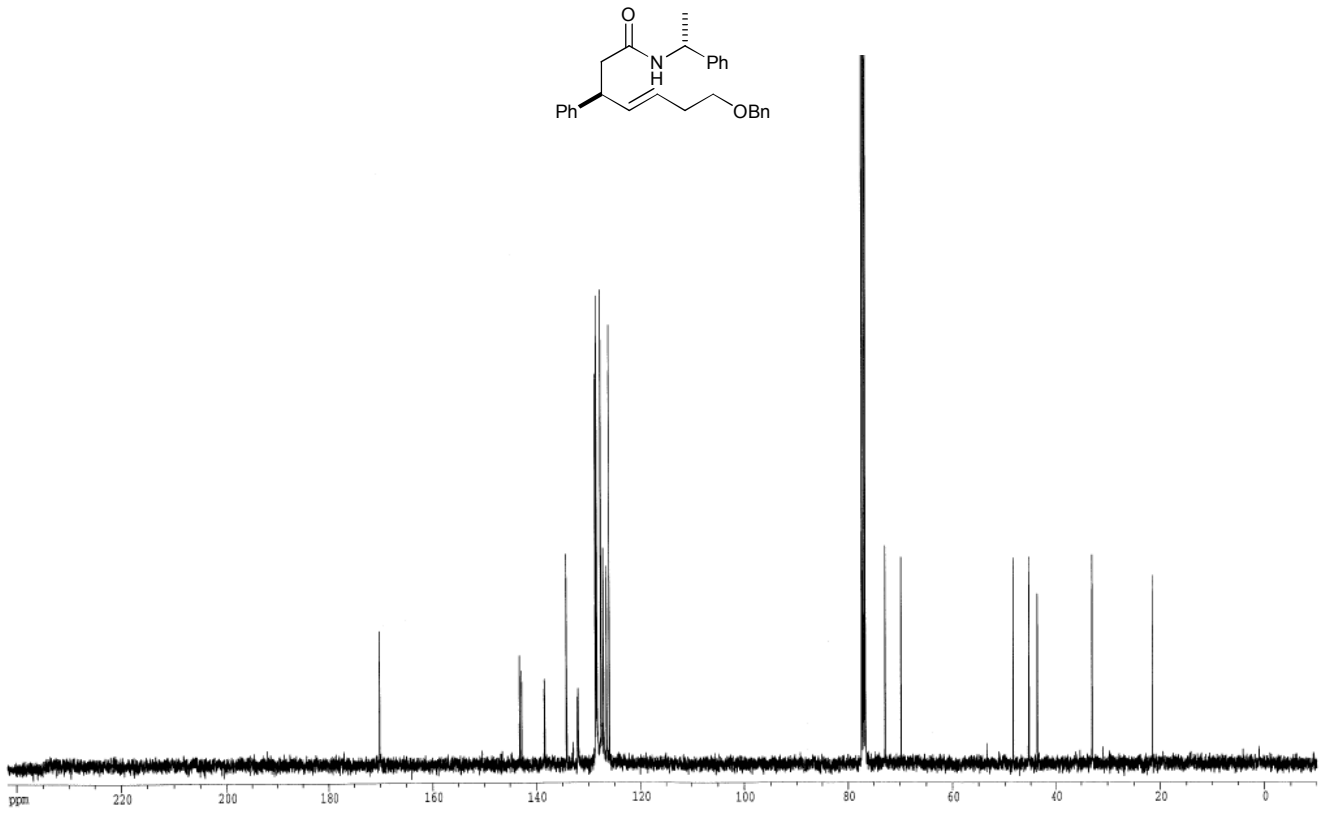
(3*S*,4*E*,α*R*)-1-Benzyloxy-3-[*N*-(3'-phenylpropionyl)-*N*-(α-methylbenzyl)amino]-5-phenyl-pent-4-ene 44 (100 MHz ^{13}C, $CDCl_3$)



(*R*)-*N*-α-Methylbenzyl (3*S*,4*E*)-3-phenyl-7-benzyloxy-hept-4-enamide 46 (400 MHz ^{1}H, $CDCl_3$)

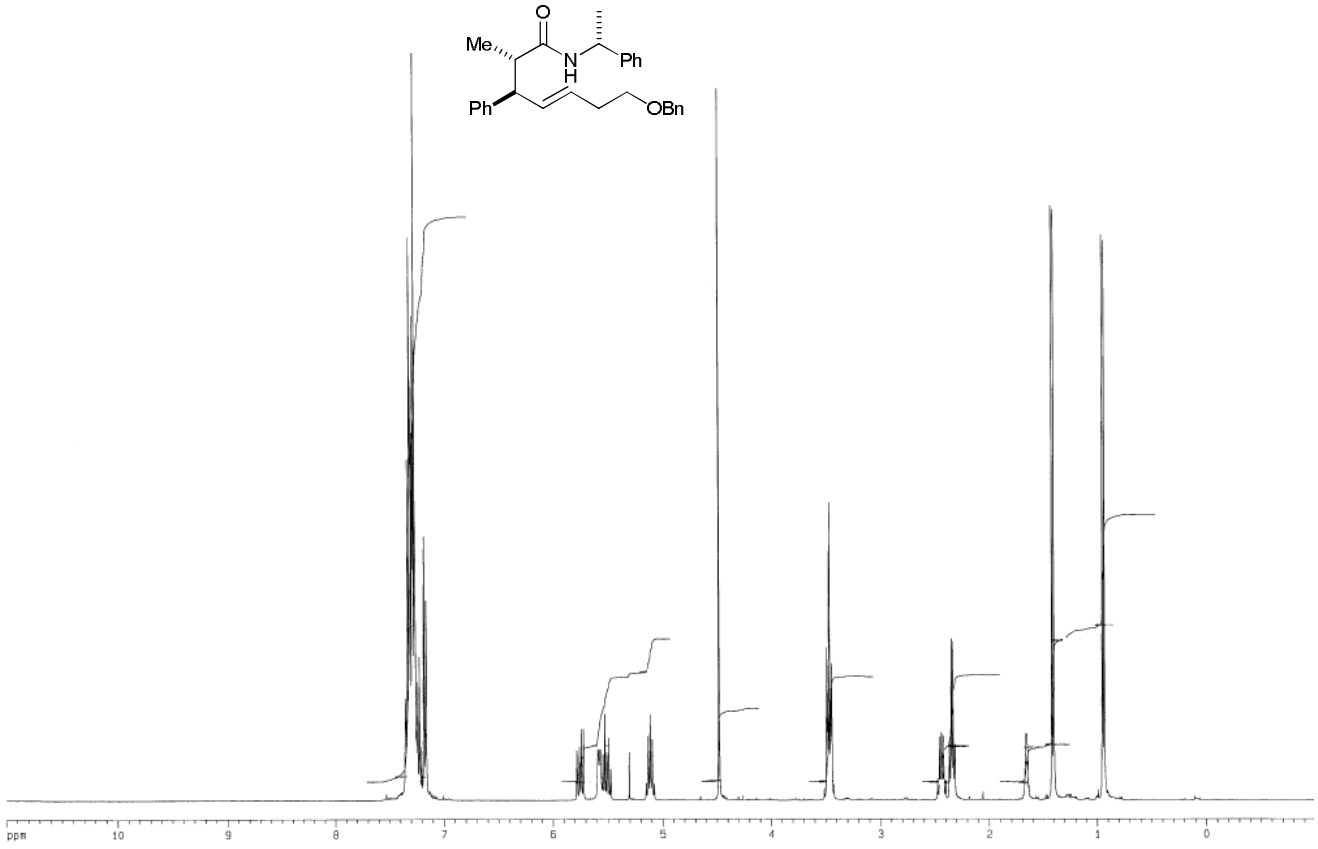


(*R*)-*N*-α-Methylbenzyl (3*S*,4*E*)-3-phenyl-7-benzyloxy-hept-4-enamide 46 (100 MHz ^{13}C, $CDCl_3$)

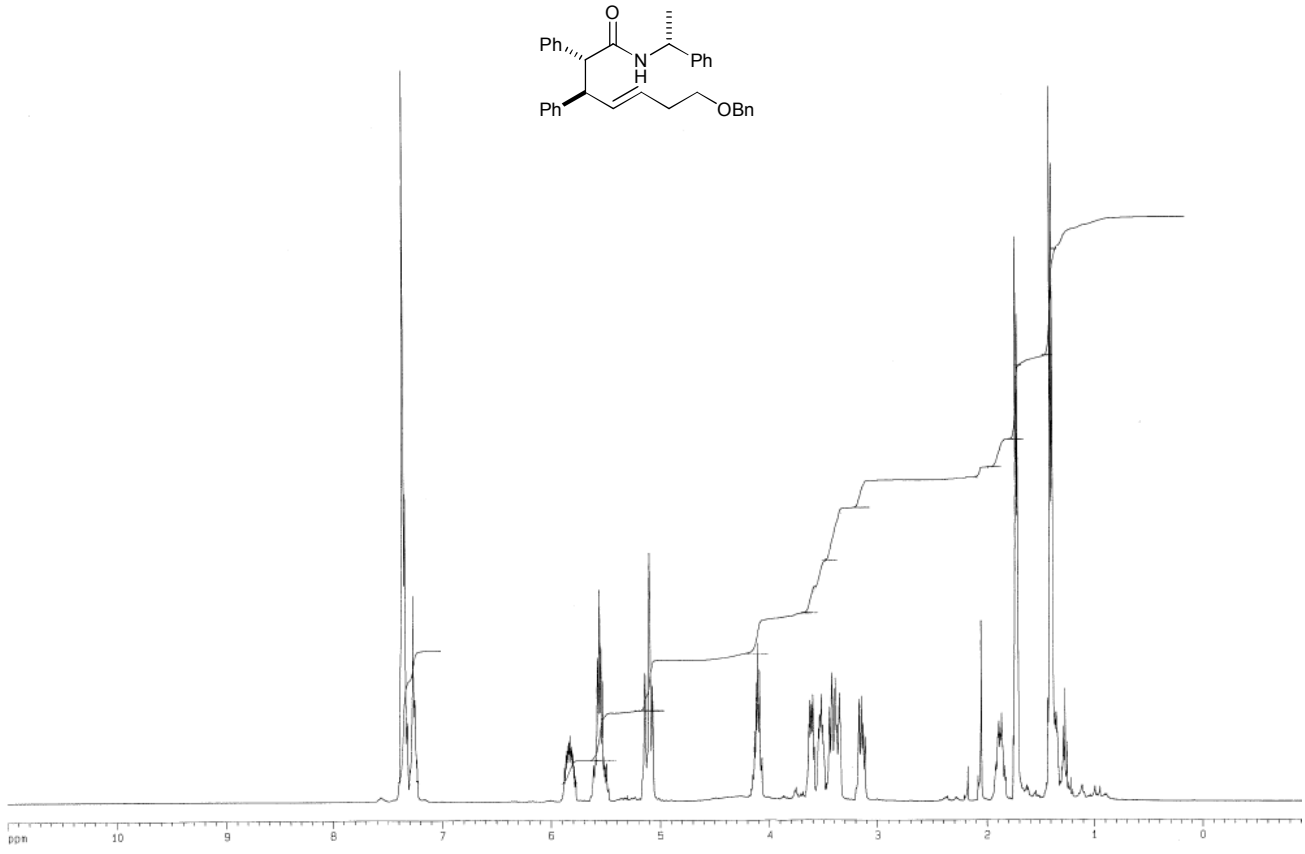


(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-methyl-3-phenyl-7-benzyloxy-hept-4-enamide 47

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

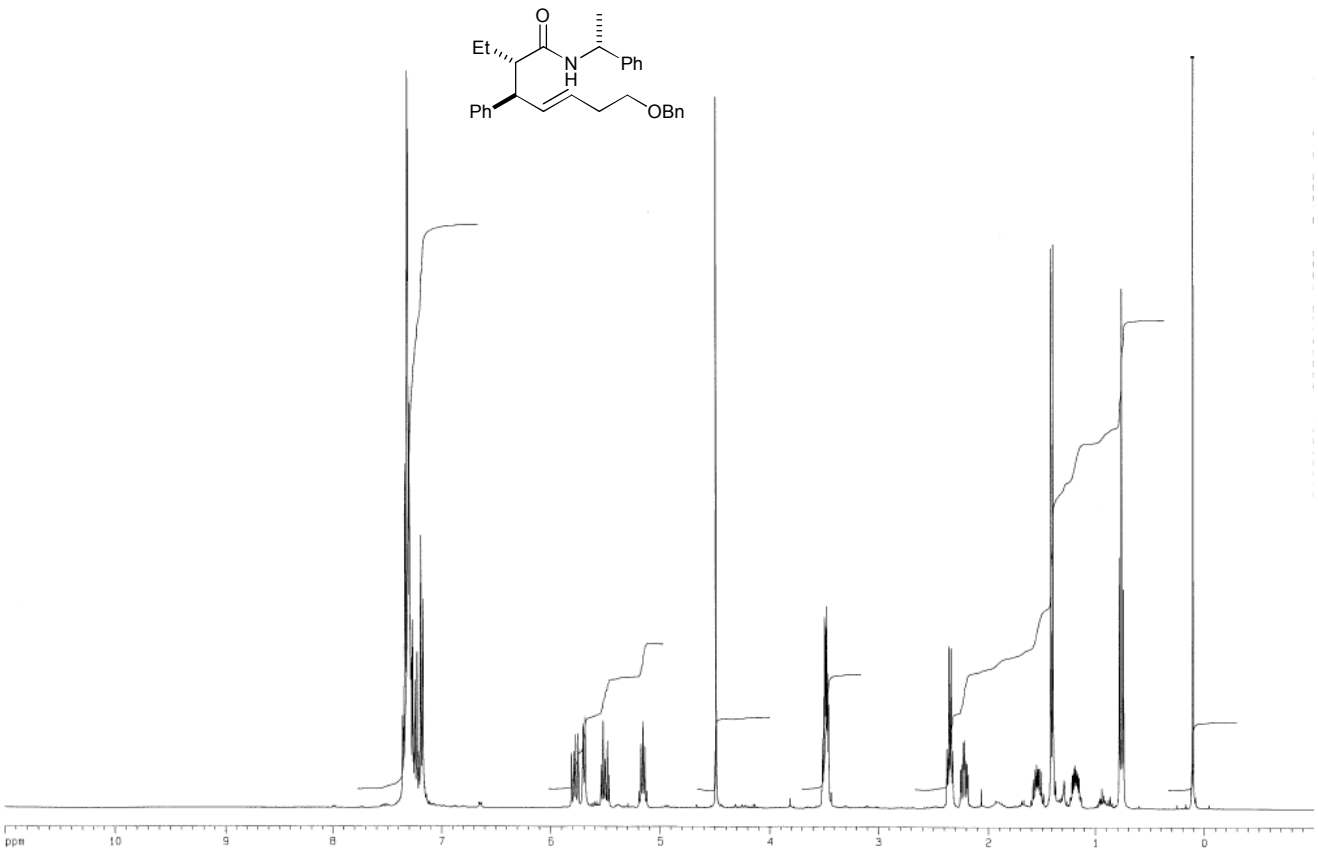


(*R*)-*N*-α-Methylbenzyl (2*R*,3*R*,4*E*)-2,3-diphenyl-7-benzyloxy-hept-4-enamide 50 (400 MHz ^{1}H, $CDCl_3$)



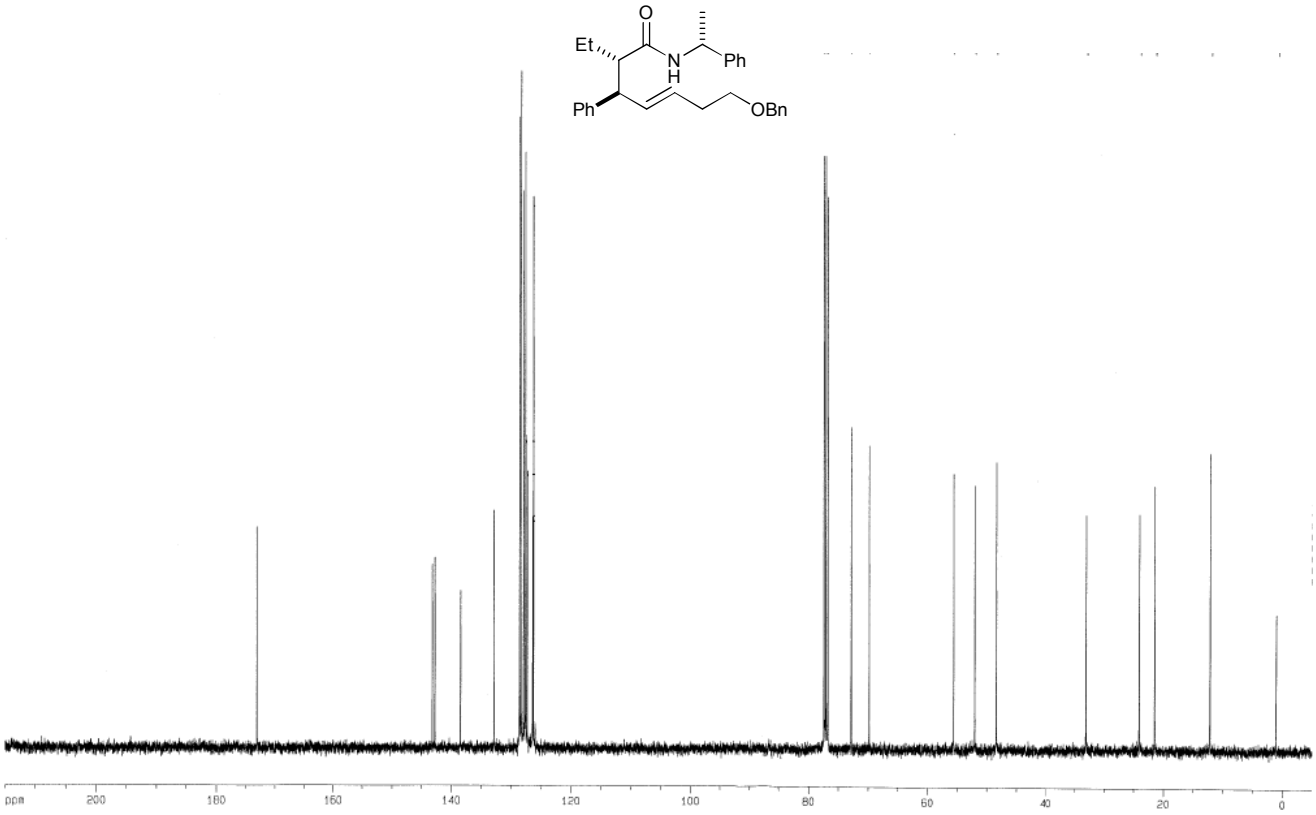
(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-ethyl-3-phenyl-7-benzyloxy-hept-4-enamide 48

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



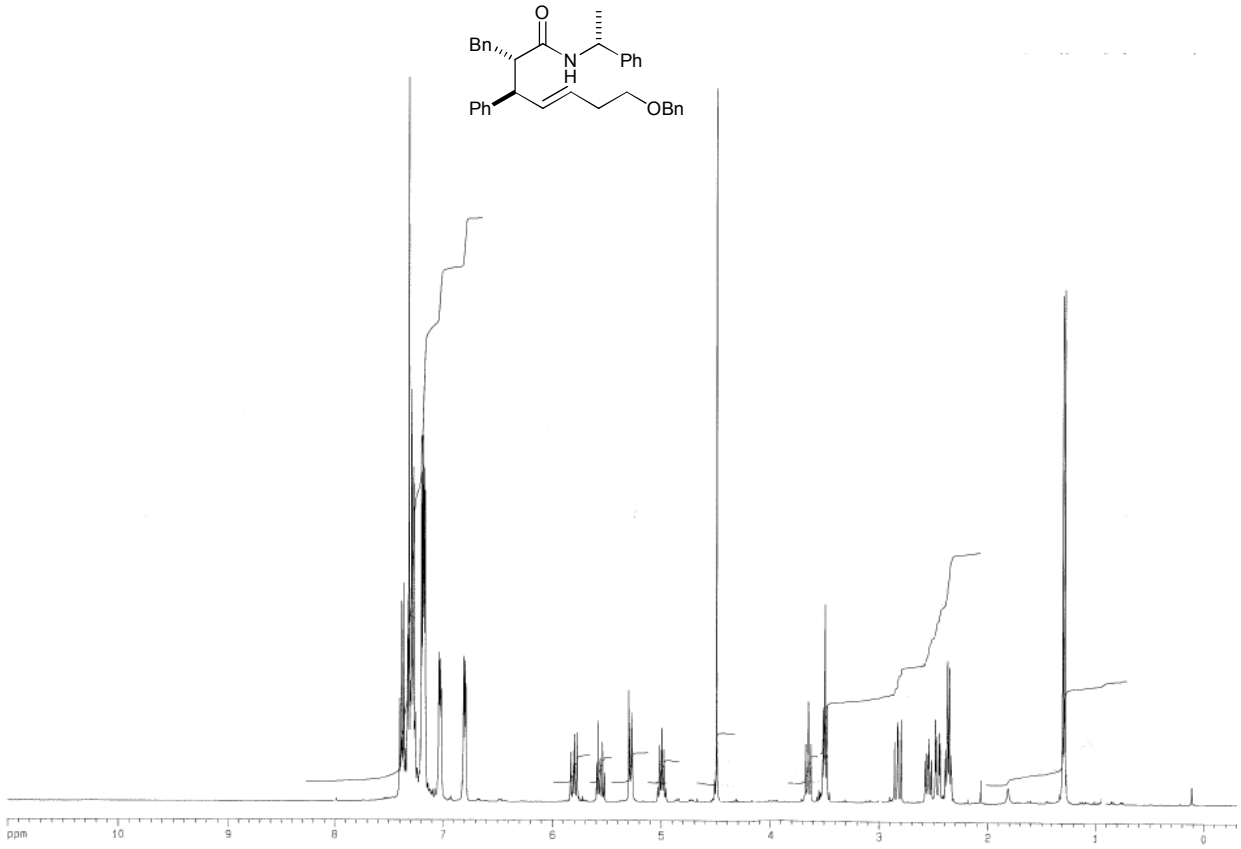
(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-ethyl-3-phenyl-7-benzyloxy-hept-4-enamide 48

(100 MHz ^{13}C, $CDCl_3$)



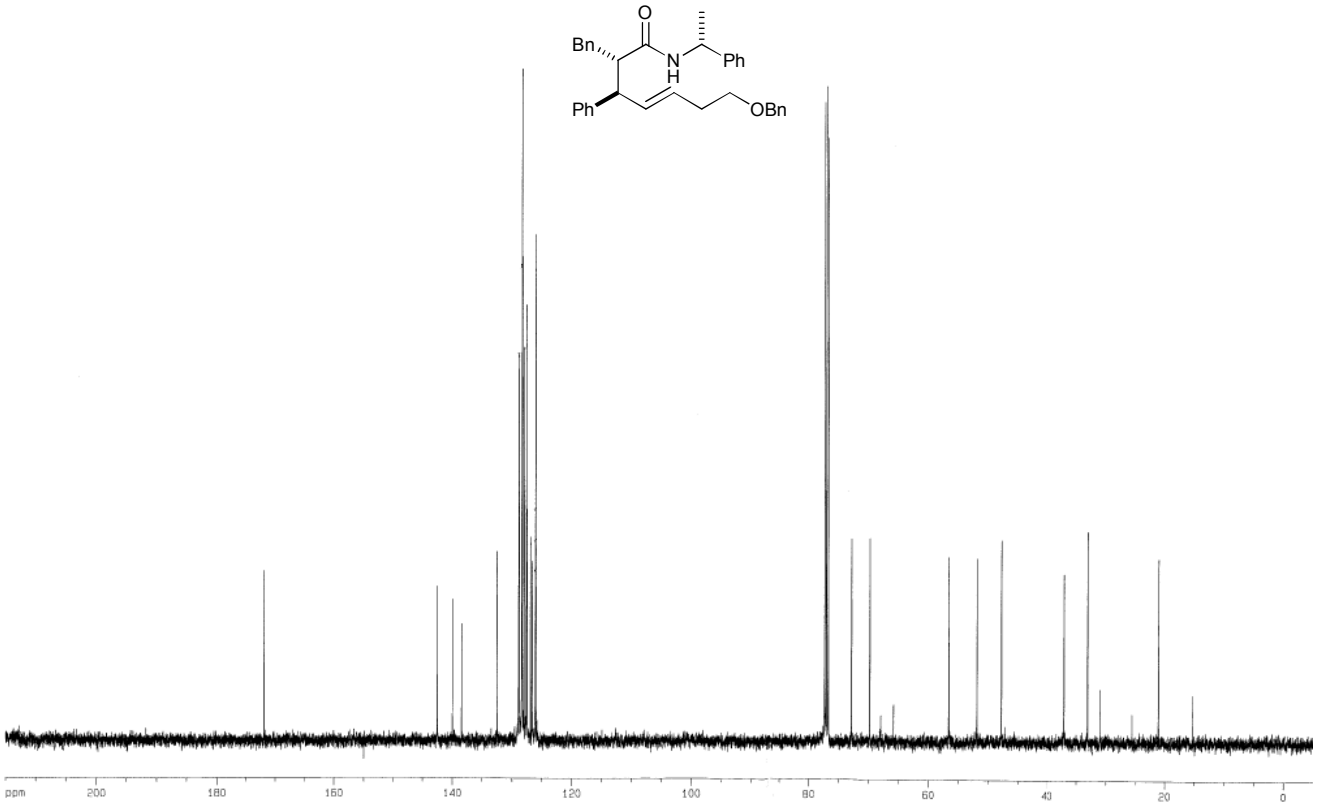
(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-benzyl-3-phenyl-7-benzyloxy-hept-4-enamide 49

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

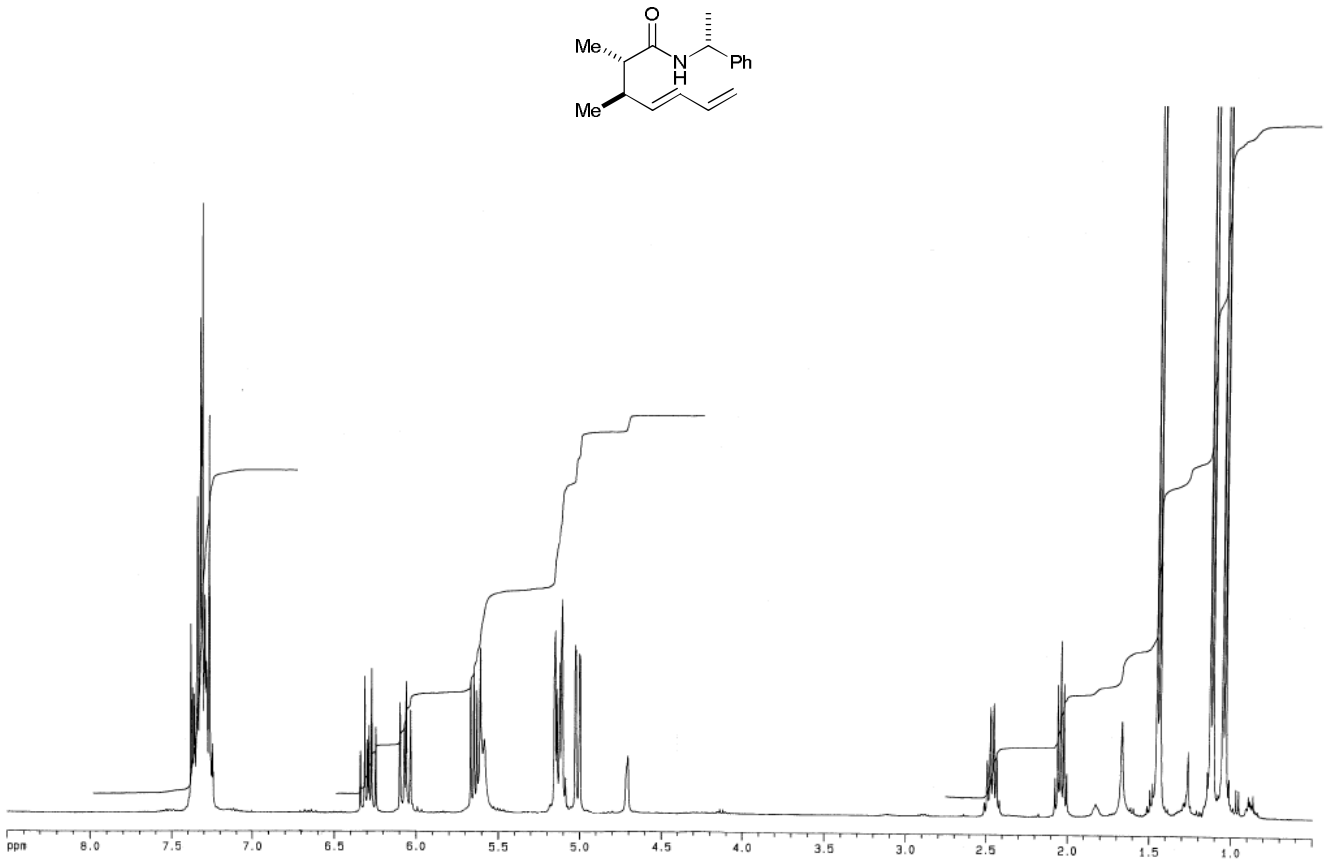


(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2-benzyl-3-phenyl-7-benzyloxy-hept-4-enamide 49

(100 MHz ^{13}C, $CDCl_3$)



(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2,3-dimethyl-hept-4,6-dienamide 51 (400 MHz ^{1}H, $CDCl_3$)



(*R*)-*N*-α-Methylbenzyl (2*S*,3*R*,4*E*)-2,3-dimethyl-hept-4,6-dienamide 51 (100 MHz ^{13}C, $CDCl_3$)