Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Dynamic Kinetic Asymmetric Allylic Amination and Acyl Migration of Vinylaziridines with Imido Carboxylates

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Experimental Procedures

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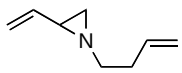
I. General Procedures

General experimental: Flash chromatography was preformed on silica gel (EM Science, Kieselgel 60, 230-400mesh, ASTM) or neutral alumina (Fluka, Aluminum Oxide, type 507, Brockmann grade III, 6% hydrate) using compressed air. TLC was preformed using glass-backed plates coated with 0.2mm silica (Merck, DC-Platten, Kieselgel; 60 F_{254}) or plastic backed plates coated with 0.2mm neutral alumina (EM, 60 F_{254}, Type E). Chiral HPLC analysis was preformed on Daicel Chiralpack columns, eluting with a heptane and isopropanol mixture, using a Thermo Separation Products Spectra SERIES P100 or P200 instruments. NMR spectra were carried out on a Varian Gemini 300 (300 MHz), Mercury 400 (400 MHz), or Unity 500 (500 MHz) instruments and are calibrated to TMS or residual solvent peaks: proton ($CDCl_3$ 7.26ppm, MeOH 4.87ppm) and carbon ($CDCl_3$ 77ppm, MeOH 49.15ppm). Optical rotation was measured on a Jasco DIP-1000 digital polarimeter in 5 cm cells at room temperature. Mass spectra were provided by the Mass Spectrometry Facility of the University of California-San Francisco. IR spectra were performed on a Perkin-Elmer Paragon 500 FT-IR spectrometer. $(\eta^3\text{-}C_3H_5PdCl)_2$,[1] Trost ligand **3**,[2] imide nucleophile (ethyl benzoyl imidocarboxylate,[3] trichloroethyl benzoyl imido carboxylate,[4] *t*-butyl benzoyl imido carboxylate,[5] benzyl benzoyl imido carboxylate,[5] bisbenzyl imido dicarboxylate[6] and *t*-butyl benzyl imido dicarboxylate[6]), aziridine **1**[7] and *N*-2,4-dimethoxybenzyl-2-vinylaziridine[8] were prepared according to literature procedures. All compounds are >95% pure by proton NMR unless otherwise noted. All reagents were used as purchased unless otherwise noted.

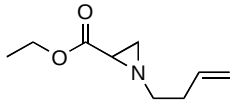
II. Complete Reference 8b

Ohshima, S.; Yanagisawa, M.; Katoh, A.; Fujii, T.; Sano, T.; Matsukuma, S.; Furumai, T.; Fujiu, M.; Watanabe, K.; Yokose, K.; Arisawa, M.; Okuda, T. *J. Antibiot.* **1994**, *47*, 639-647.

III. Synthesis of Novel Vinylaziridines and Novel Imide Nucleophiles

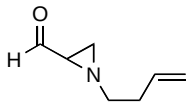


Preparation of *N*-but-3-enyl-2-vinylaziridine



Ethyl 1-(but-3-enyl)aziridine-2-carboxylate

1-Amino-3-butene (prepared by literature procedures)[9] (6.9g, 41mmol) followed by Et_3N (11mL, 7.9g, 82mmol) were added *via* a syringe over ~1min to a solution of ethyl-2,3-dibromopropanoate (5.9mL, 10g, 41mmol) in anhydrous ethanol (200mL) at 0ºC under nitrogen. The solution allowed to warm to room temperature, after which the reaction was stirred at 50ºC in a sealed flask of nitrogen for 20h. The resulting yellow solution was concentrated by distillation (~40º, 25torr). The solid was suspended in ether (500mL) and vigorously stirred for 0.5h. The solids were removed *via* filtration and washed thoroughly with ether. The filtrate was concentrate *in vacuo* to afford the desired aziridine as a yellow oil (6.4g, 93%). This material was used in the next step without further purification. **^{1}H NMR** ($CDCl_3$ 400MHz, δ) 5.88-5.76 (m, 1H), 5.10-5.00 (m, 2H), 4.20 (m, 2H), 2.44-2.34 (m, 4H), 2.18 (dd, J= 3.1, 1.2 Hz, 1H), 2.03 (dd, J= 6.5, 3.1 Hz, 1H), 1.59 (dd, J= 6.5, 1.2 Hz, 1H) 1.28 (t, *J* = 7.0, 3H). **^{13}C NMR** ($CDCl_3$ 100MHz, δ) 170.9, 135.7, 116.3, 61.1, 60.4, 37.5, 34.5, 34.0, 14.2. **IR** (KBr – neat) 3077, 2982, 2938, 2836, 1745, 1642, 1285, 1240, 1187, 1029, 914 cm^{-1}.



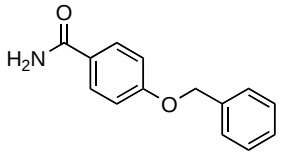
1-(But-3-enyl)aziridine-2-carbaldehyde

DIBAL-H (1M in Hexanes, 151mL, 151mmol) was added dropwise over ~20 min *via* an addition funnel to an anhydrous solution of ester Ethyl 1-(but-3-enyl)aziridine-2-carboxylate (12.2g, 720mmol) in anhydrous methylene chloride (300mL) at -78ºC under nitrogen. The solution was stirred for 4h at -78ºC at which point, the reaction was carefully quenched with a saturated aqueous solution of NaF (90mL) at -78ºC. The resulting mixture was stirred vigorously for 50 min allowing the reaction to warm to room temperature. The mixture was poured into methylene chloride (1L), dried with Na_2SO_4, filtered and concentrated *in vacuo* to the desired aldehyde as a cloudy orange oil. Purification by slica chromatography (0 – 33% ether in pentane) provided the desired aldehyde as an oil (8.8g, 97%) **^{1}H NMR** ($CDCl_3$ 400MHz, δ) 8.88 (d, *J* = 6.8Hz, 1H), 5.88-5.78 (m, 1H), 5.12-5.49 (m, 1H), 5.32-5.04 (m, 1H), 2.47-2.41 (m, 2H), 2.37-2.32 (m, 2H), 2.24 (d, J= 3.1 Hz, 1H), 2.05 (ddd, J= , 1H), 1.78 (d, J= 6.4 Hz, 1H). **^{13}C NMR** ($CDCl_3$ 100MHz, δ) 200.0, 135.5, 116.6, 59.6, 44.6, 34.0, 32.7. **IR** (KBr – neat) 3079, 2981, 2936, 2836, 1723, 1642, 1436, 1362, 1329, 1233, 1211, 1159, 1094, 1052, 997, 916, 865, 774 cm^{-1}.

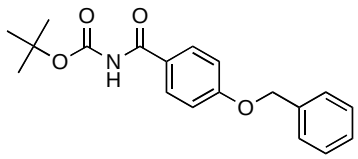
***N*-(But-3-enyl)-2-vinylaziridine:** KHMDS (0.5M in THF, 59mL, 29mmol) was added dropwise over ~20min *via* an addition funnel to an anhydrous suspension of methyltriphenylphosphonium

bromide (12g, 35mmol) in THF (116mL) at -15ºC under nitrogen. The resulting heterogeneous yellow mixture was stirred at -15ºC for 0.25h and at 0ºC for 1h. An anhydrous solution of 1-(But-3-enyl)aziridine-2-carbaldehyde (2.8g, 22mmol) in THF (70mL) was added to the above Wittig reagent dropwise over ~10min at -15ºC. The yellow mixture was stirred at -15º for 15min, warmed to r.t., and stirred at r.t. for 45min under nitrogen. The yellow mixture was poured into a mixture of brine (70mL) and ether (70mL). The layers were separated, and the aqueous portion was extracted with ether (3x100mL). The combined organic extracts were dried with Na_2SO_4, filtered and concentrated by distillation. Purification by silica chromatography (0 – 33% ether in petroleum ether) provided by distillation of the fractions the desired aziridine as a yellow oil in 46% by mass purity contaminated with trimethylsilyl alcohol and diethyl ether (2.2g, at 46% by mass purity, 36% yield). ^{1}H NMR analysis with internal standard shows 17.1μmol aziridine / 10μL of oil. **^{1}H NMR** ($CDCl_3$ 400MHz, δ)5.89-5.79 (m, 1H), 5.73-5.49 (m, 1H), 5.32-5.27 (m, 1H), 5.11-4.99 (m, 3H), 2.40-2.28 (m, 4H), 1.88-1.83 (m, 1H), 1.76 (d, J= 3.3 Hz, 1H), 1.47 (d, J= 6.3 Hz, 1H). **^{13}C NMR** ($CDCl_3$ 100MHz, δ) 138.4, 136.3, 116.0, 115.9, 60.7, 41.1, 35.3, 34.3. **IR** (KBr – neat) 2957, 2924, 2853 cm^{-1}. **EI-HRMS** M=$C_8H_{13}N$, $[M-H]^+$ calcd 122.0970 found 122.0978. **ESI-HRMS** calcd for $C_8H_{13}N$ 123.1 found $[M+H]^+$ 124.1.

***N*-(*t*-Butoxycarbonyl)-benzamide**

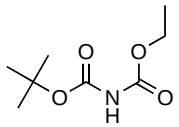


4-(Benzyloxy)benzamide
Benzyl bromide (1.4g, 8.0mmol) was added to a mixture of 4-hydroxybenzamide (1.0g, 7.3mmol) and Cs_2CO_3 (4.8g, 14.7mmol) in anhydrous DMF (20mL). The mixture was stirred at 60^{o}C for 18h. The reaction was cooled to room temperature, diluted with ethyl acetate (300 mL) and washed with water (1x100mL, 4x75 mL). The organic phase was dried with $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by recrystallization (IPA / heptane) to afford 4-(benzyloxy)benzamide as a white solid. **Mp** = 184-195^{o}C (Lit.[10] 186-187^{o}C). **^{1}H NMR** ($CDCl_3$, 400MHz, δ) 7.9-7.8 (m, 2H), 7.5-7.3 (m, 5H), 7.1-7.0 (m, 2H), 5.1 (s, 2H). **IR** (KBr-neat) 3368, 3168, 1623, 1574, 1514, 1423, 1398, 1304, 1251, 1174, 1151, 1012, 842, 794, 762, 733, 698, 616, 535 cm^{-1}. ^{1}H NMR and IR spectra correspond to literature.[10]



***N*-(*t*-Butoxycarbonyl)-benzamide** Oxalyl chloride (0.13 mL, 1.5 mmol) was added dropwise to a solution of 4-(Benzyloxy)benzamide (200mg, 0.9 mmol) in anhydrous dichloroethane (5 mL) at 0^{o}C. The reaction was warmed to room temperature and stirred at reflux for 14h under nitrogen. The reaction was cooled to room temperature and concentrated *in vacuo* to the benzoylisocyanate as a yellow solid. To the crude isocyanate dissolved in anhydrous methylene chloride was added *t*-butyl alcohol (90μL, 0.9mmol). The solution was stirred at room temperature for 18 h; at which point the solvent was removed *in vacuo*. Purification by recrystallization (IPA / heptane) provided the desired imide carboxylate as a white solid. **Mp** = 127 - 129^{o}C. **^{1}H NMR** ($CDCl_3$, 300MHz, δ)

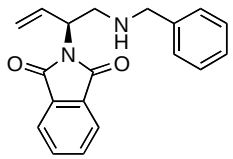
7.91 (sb, 1H), 7.8-7.7 (m, 2H), 7.4-7.3 (m, 5H), 7.0-6.9 (m, 2H), 5.12 (s, 2H), 1.53 (s, 9H). **^{13}C NMR** ($CDCl_3$, 75MHz, δ) 164.5, 162.3, 149.7, 136.0, 129.6, 128.7, 128.3, 127.5, 125.7, 114.8, 82.5, 70.1, 28.0. **IR** (KBr-neat) 3282, 2985, 2935, 1759, 1741, 1673, 1606, 1500, 1454, 1368, 1253, 1216, 1148, 939, 840, 736 cm^{-1} **EI-HRMS** calcd for $C_{19}H_{21}NO_4$ 327.1471 found 327.1464.



***t*-Butyl-ethyl-imido dicarboxylate**

The procedure from Weikert *et. al.*[11] was used for the preparation of the known ethyl isocyanatoformate.[12] Oxalyl chloride (6.3mL, 9.2g, 73mmol) was added dropwise to an anhydrous solution of the urethane (3.8g, 43mmol) in dichloroethane (20 mL). The reaction was stirred at 60ºC for 18h with a drying tube and condenser. One half of the solvent was removed by distillation, and the remaining solution was degassed by bubbling nitrogen through the solution for 0.5h. To the above solution of ethyl isocyanatoformate was added *t*-butyl alcohol (15 mL) dropwise at 40ºC over ~10min. The reaction was stirred at 60ºC for 1h. The reaction was cooled to room temperature, and most of the solvent was removed *in vacuo*. To the oily solid was added chloroform (10mL) and heptane (70mL). After stirring for 0.5h, the solids were removed *via* filtration, and the filtrate was concentrated to the desired imide as a viscous colorless oil (5.0g, 63%) in reasonable purity. **^{1}H NMR** ($CDCl_3$, 500MHz, δ) 7.0 (bs, 1H), 4.23 (q, *J*=7Hz, 2H), 1.50 (s, 9H), 1.29 (t, *J*=7Hz, 3H). **^{13}C NMR** ($CDCl_3$, 125MHz, δ) 151.1, 149.5, 82.4, 62.0, 27.9, 14.2. **IR** (KBr-neat) 3287, 2982, 2937, 1785, 1732, 1522, 1395, 1369, 1306, 1259, 1207, 1099, 784 cm^{-1}. **EI-HRMS** M = $C_8H_{15}NO_4$, $[M\text{-}CH_3]^+$ calcd 174.0766 found 177.0785.

IV. Experimental procedures and spectral data for the dynamic kinetic asymmetric allylic alkylations



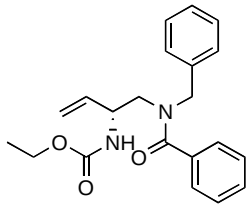
2-((S)-1-(benzylamino)but-3-en-2-yl)-isoindoline-1,3-dione (4)

A flame dried 10ml test tube was charged with $[(\eta^3C_3H_5)PdCl]_2$ (1.1mg, 3μmol), and ligand (R,R) **3** (7.5mg, 9μmol). The tube was flushed with argon and anhydrous and degassed methylene chloride (1 mL) was added to the solids. After stirring for ~10 min at room temperature, aziridine **1** (25mg, 27μL, 0.16mmol) and triethylamine (2.2μL, 1.6mg, 16μmol) were sequentially added to the catalyst solution, and the catalyst and aziridine solution was transferred *via* cannula to a test tube containing phthalimide (23mg, 0.16mmol). The solution was stirred in a nitrogen sealed test tube at room temperature for 18h. The homogeneous yellow to orange solution was concentrated to an oil, and the amine product **4** was isolated *via* alumina chromatography (activity III , 6% hydrate, 45% ether and 0.3% triethylamine in petroleum ether) as a clear thick oil (28mg, 60%). **Chiralpak OD-H HPLC** (20% IPA in heptane, 1 mL / min, 230nm) shows 77% ee in favor of 12.632 over 10.519min. **$[\alpha]_D$** = - 10º (c= 0.80 in $CHCl_3$, 77% ee). **^{1}H NMR** ($CDCl_3$, 400MHz, δ) 7.82 (m, 2H), 7.71 (m, 2H), 7.30-7.16 (m, 5H), 6.22 (ddd,

J=17.0, 10.3, 7.8 Hz, 1H), 5.29 (d, J=17.0 Hz, 1H), 5.23 (d, J= 10.3 Hz, 1H), 4.94 (m, 1H), 3.83 (d, J= 13.0 Hz, 1H), 3.77 (d, J= 13.0 Hz, 1H), 3.29 (dd, J= 11.7, 9.7 Hz, 1H), 3.06 (dd, J= 12.4, 6.5 Hz, 1H), 1.4 (sb, 1H). **^{13}C NMR** ($CDCl_3$ 100MHz, δ) 168.2, 140.0, 133.9, 133.8, 131.9, 128.3, 128.0, 126.9, 123.2, 118.6, 53.5, 53.0, 49.6. **IR** (KBr-neat): 3062, 3028, 2923, 2842, 1771, 1714, 1644, 1614, 1468, 1385, 1007, 718 cm^{-1}. **EI-HRMS** M = $C_{19}H_{18}N_2O_2$ 306.1368, $[M+H]^+$ calcd 307.1447 found 107.1444, $[M-C_7H_7]^+$ calcd 215.0821 fund 215.0807.

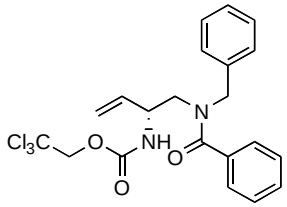
Typical Procedure for the Dynamic Kinetic Asymmetric Addition of Benzoyl-Imidocarboxylates and Imido-dicarboxylates to Vinylaziridines and Vinylepoxides

A flame dried 10ml test tube was charged with $[(\eta^3C_3H_5)PdCl]_2$ (2 mol % to aziridine), and ligand *(S,S)* **3** (6 mol % to aziridine). The tube was flushed with nitrogen and anhydrous and degassed methylene chloride (0.15M to electrophile) was added to the solids. After stirring for ~10 min at room temperature, the aziridine or epoxide was added to the homogeneous orange solution and the catalyst and aziridine solution was cannulated into a test tube containing the imide nucleophile (1.05eq to aziridine). The solution was stirred in an nitrogen sealed test tube at 35°C for 18 h. The homogeneous yellow to orange solution was concentrated to an oil, and the acyl migration product was isolated *via* chromatography.



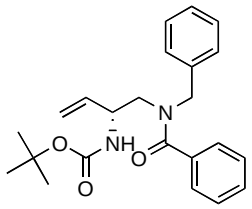
(R) – (+) - Ethyl-1-(N-benzylbenzamido)-but-3-en-2-ylcarbamate (10)

Diamine **10** was prepared from the parent vinylaziridine **1**, ethyl benzoyl imido carboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3** in methylene chloride (1mL). Purification by silica chromatography (50% ether in petroleum ether) provided the desired product as a thick oil (90%). **Chiralpak OD HPLC** (8 % IPA in Heptane, 0.8 ml/min, 230nm) shows 89% ee favor 18.282 over 14.787 min. **$[\alpha]_D$** = + 27° (c= 4.1 in $CHCl_3$, 84% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.45-7.43 (m, 2H), 7.11-7.08 (m, 2H), 7.05-7.03 (m, 6 H), 5.50 (m, 1H), 5.20 (sb, 1H), 5.05 (d, J= 17 Hz, 1H), 4.89 (d, J= 10.3 Hz, 1H), 4.68-4.38 (m, 3H), 4.07 (q, J= 6.6 Hz, 2H), 3.16 (dd, J= 13.7 Hz, 5.0 Hz, 2H), 1.06 (t, J= 6.6 Hz, 3H). **^{13}C NMR** (C_6D_6, 75°C, 125MHz, δ) 173.2, 156.8, 138.0, 137.8, 137.1, 129.8, 129.4, 128.9, 128, 128.1, 127.7, 116.3, 61.2, 53.0, 52.9(b), 49.2(b), 15.1. **IR** (KBr-neat) 3313, 2926, 1714, 1694, 1633, 1531, 1504, 1495, 1417, 1357, 1243, 1078, 923, 726, 698 cm^{-1}. **EI-HRMS** calcd for $C_{21}H_{24}N_2O_3$ 352.1787, $[M-C_2H_5O]^+$ 307.1447 found 307.1452.



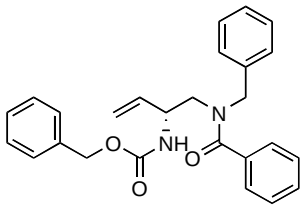
(R) – (+) -2,2,2-trichloroethyl-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (11)

Diamine **11** was prepared from the parent vinylaziridine **1**, trichloroethyl benzoyl imido carboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3** (14mg, 17μmol) in methylene chloride. Purification by silica chromatography (ether in petroleum ether) provided the desired product as a thick oil (84%). **Chiralpak OD HPLC** (20 % IPA in Heptane, 1.0 ml/min, 245nm) shows 93 % ee favor 7.223 over 8.587 min. $[\alpha]_D$ = + 20º (c= 0.42 in $CHCl_3$, 93% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.45-7.43 (m, 2H), 7.11-7.00 (m, 8H), 5.43 (m, 1H), 5.03 (d, J= 17 Hz, 1H), 4.90 (d, J= 11 Hz, 1H), 4.69 (d, J= 12 Hz, 1H), 4.59-4.39 (m, 4H), 3.76 (sb, 1H), 3.14 (dd, J= 14.0, 5.0 Hz, 1H). **^{13}C NMR** (C_6D_6, 75°C, 125MHz, δ) 171.0, 153.5, 136.8, 136.2, 135.7, 128.7, 128.1, 127.8, 126.7, 126.6, 126.0, 115.8, 95.9, 73.4, 52.0, 51(b), 49(b). **IR** (KBr-neat) 3294, 3063, 2948, 1738, 1826, 1520, 1497, 1454, 1422, 1238, 1109, 816, 733, 700 cm^{-1}. **EI-HRMS** M = $C_{21}H_{21}Cl_3N_2O_3$, $[M-C_2H_2Cl_3O]^+$ calcd 307.1447 found 307.1433. **ESI-LRMS** calcd for $C_{21}H_{21}Cl_3N_2O_3$ 454.1 found $[M+H]^+$ 455.1



(R)-(+)-t-butyl-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (7)

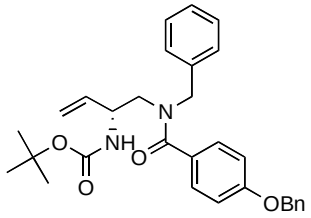
Diamine **7** was prepared from the parent vinylaziridine **1**, *t*-butyl benzoyl imido carboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3** in methylene chloride. Purification by silica chromatography (50% ether in petroleum ether) provided the desired product as a thick oil (95%). **Chiralpak OD HPLC** (8 % IPA in Heptane, 0.8 ml/min, 230nm) shows 89 % ee favor 9.825 over 16.789 min. $[\alpha]_D$ = + 23º (c= 4.3 in $CHCl_3$, 89% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.46 (m, 2H), 7.15-7.05 (m, 8H), 5.48 (m, 1H), 5.03 (d, 16.8 Hz, 1H), 4.88 (d, J= 10.7 Hz, 1H), 4.70-4.39 (m, 3H), 3.76 (sb, 1H), 3.17 (dd, J= 14.3, 5.0 Hz, 1H), 1.46 (s, 9H). **^{13}C NMR** (C_6D_6, 75°C, 125MHz, δ) 173.0, 156.0, 138.1, 137.9, 137.3, 129.8, 129.3, 128.8, 128, 128.0, 127.8, 116.1, 79.5, 52.5, 52.2(b), 50.9(b), 29.0. **IR** (KBr-neat) 3322, 3062, 2977, 2357, 2281, 1714, 1694, 1634, 1504, 1416, 1366, 1163, 696 cm^{-1}. **EI-HRMS** calcd for $C_{23}H_{28}N_2O_3$ 380.2100, $[M-C_4H_9O]^+$ 307.1447 found 307.1441.



(R)-(+)-Benzyl (R)-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (12)

Diamine **12** was prepared from the parent vinylaziridine **1,** benzyl benzoyl imido carboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3** in methylene chloride. Purfication by basic alumina chromatography (activity III, 40% ethyl acetate in petroleum ether) provide the desired product as a thick oil in (75%). **Chiralpak OD HPLC** (20 % IPA in Heptane, 1.0 ml/min, 230nm) shows 90 % ee favor 10.030 over 12.252 min. $[\alpha]_D$ = + 25º (c= 0.90 in $CHCl_3$, 90% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.40-7.38 (m, 2H), 7.28-7.26 (m, 2H), 7.28-7.26 (m, 11H), 5.47 (m, 1H), 5.25 (sb, 1H), 5.15 (d, J= 12.5 Hz, 1H), 5.08-5.01 (m, 2H), 4.88 (d, J= 10.5 Hz, 1H), 4.63 (sb, 1H), 4.57-4.32 (m, 2H), 3.81 (sb, 1H), 3.15 (dd, J= 14.0, 5.0 Hz, 1H). **^{13}C NMR** (C_6D_6, 75°C, 125MHz, δ) 173.2, 156.6, 138.1, 138.0, 137.8, 136.9, 129.8, 129.4, 129.0, 128.9, 128.7, 128.5, 128.3, 127.7, 116.4, 95.9, 73.4, 52.0, 51(b), 49(b). **IR** (KBr-neat) 3310, 3063, 3031, 2936, 1717,

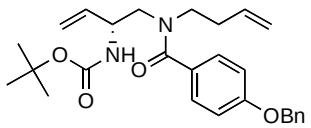
1628, 1602, 1522, 1497, 1455, 1420, 1242, 1076, 1028, 736, 699 cm^{-1}. **ESI–HRMS** calcd for $C_{26}H_{26}N_2O_3$ 414.1943, $[M+H]^+$ calcd 415.2022 found 415.2033.



(R)-(+)-t-butyl-1-(N-benzyl-4-(benzyloxy)benzamido)but-3-en-2-ylcarbamate (13)

Diamine **13** was prepared from the parent vinylaziridine **1** (23mg, 0.15mmol), *t*-butyl p-methyoxybenzoyl imido carboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3** in methylene chloride. Purification by silica chromatography (50% ether in petroleum ether) provided the desired product as a thick oil in (81%). **Chiralpak OD HPLC** (10 % IPA in Heptane, 0.8 ml/min, 230nm) shows 92 % ee favor 18.682 over 26.907 min. $[\alpha]_D$ = + 26º (c= 3.7 in $CHCl_3$, 92% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.48-7.47 (m, 2H), 7.21-7.20 (m, 2H), 7.14-7.02 (m, 8H), 7.77-7.75 (m, 2H), 5.51 (ddd, J= 17.5, 10.3, 5.7 Hz, 1H), 5.06 (d, 17.5 Hz, 1H), 4.99 (sb, 1H), 4.89 (d, J= 10.3 Hz, 1H), 4.72-4.48 (m, 5H), 3.81 (m, 1H), 3.19 (dd, J= 14.0, 5.4 Hz, 1H), 1.46 (s, 9H). **^{13}C NMR** (C_6D_6, 75°C, 125MHz, δ) 173.3, 161.1, 156.4, 138.6, 138.1, 137.8, 130.6, 130.1, 129.7, 129.4, 129.0, 128.7, 128.3, 128.2, 116.3, 115.7, 79.7, 71.0, 53.0(b), 52.9, 49.9(b), 29.3. **IR** (KBr-neat) 3321, 3032, 2978, 2931, 1713, 1697, 1634, 1608, 1513, 1504, 1455, 1424, 1366, 1300, 1174, 1021, 839, 698 cm^{-1}. **EI-HRMS** calcd for $C_{30}H_{34}N_2O_4$, $[M-C_4H_9O]^+$ 413.1865 found 413.1870.

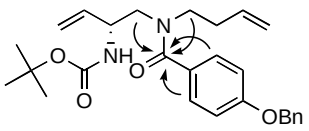
Representative Procedure:

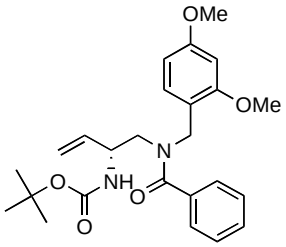


(R)-t-butyl-1-(4-(benzyloxy)-N-(but-3-enyl)benzamido)but-3-en-2-ylcarbamate (14)

A flame dried 10ml test tube was charged with $[(\eta^3C_3H_5)PdCl]_2$ (3mg, 8μmol) and ligand *(S,S)* **3** (20mg, 25μmol). The tube was flushed with nitrogen and anhydrous and degassed methylene chloride (2mL) was added to the solids. After stirring for ~10 min at room temperature, the aziridine (123mg from a 46% pure material (*vida supra*) 0.22mL, 0.41mmol) was added to the homogeneous orange solution and the catalyst and aziridine solution was cannulated into a test containing the *t*-butyl *p*-benzoxybenzoyl imido carboxylate (134mg, 0.41mmol). The solution was stirred in an nitrogen sealed test tube at 35°C for 18 h. The homogeneous yellow to orange solution was concentrated to an oil, and the acyl migration product **14** was isolated *via* chromatography (50% ether in petroleum ether) as an oil (97%). **Chiralpak OD HPLC** (8 % IPA in Heptane, 1.0 ml/min, 230nm) shows 86 % ee favor 15.217 over 17.327 min. $[\alpha]_D$ = + 34º (c= 0.25 in $CHCl_3$, 90% ee). **^{1}H NMR** (DMSO, 500MHz, δ) 7.46-7.45 (m, 2H), 7.41-7.38 (m, 2H), 7.35-7.32 (m, 1H), 7.28-7.27 (m, 2H), 7.05-7.4 (m, 2H), 6.66 (sb, 1H), 5.70 (m, 2H), 5.18-4.96 (m, 4H), 4.29 (sb, 1H), 3.54-3.28 (m, 5H), 2.30-2.2 (m, 2H), 1.41 (s, 9H). **^{13}C NMR** (DMSO, 80°C, 125MHz, δ) 170.6, 158.6, 154.6, 136.7, 136.5, 134.9, 129.3, 127.95, 127.9, 127.4, 127.1, 116.2, 115.1, 114.2, 77.5, 69.2, 49.0, 47.0, 31.6, 30.1, 27.9. **IR** (KBr-neat) 3319, 3073, 3035, 2978, 2932, 1709, 1609, 1576, 1511, 1454, 1412, 1366, 1298, 1244, 1173, 1111, 1080, 1019, 920, 839, 737, 697 cm^{-1}. **EI-HRMS** calcd for $C_{27}H_{34}N_2O_2$ 450.2519 found 450.2529.

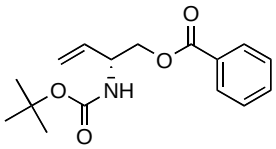
Figure S-1: Key HMBC Correlations for the Acyl Migration Product **14**





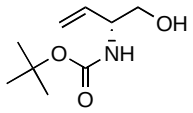
(R) - (+) – *t* - butyl (R) – 1 - (N - (2,4 - dimethoxybenzyl)benzamido) but – 3 – en – 2 – ylcarbamate (15)

Diamine **15** was prepared from *N*-(2,4-dimethoxybenzyl)-2-vinylaziridine, *t*-butyl benzoyl imido carboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3** in methylene chloride. Purification by silica chromatography (20% ethyl acetate in petroleum ether) provided the desired product as a thick oil in (90% yield). **Chiralpak OD HPLC** (20 % IPA in Heptane, 1.0 ml/min, 230nm) shows 87 % ee favor 5.476 over 5.979 min. $[\alpha]_D$ = + 31º (c= 0.67 in $CHCl_3$, 87% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.42-7.34 (m, 5H), 7.04-7.03 (m, 1H), 6.55-6.50 (m, 2H), 6.46 (sb, 1H), 5.75 (m, 1H), 5.13 (d, J= 17.5 Hz, 1H), 5.08 (d, J= 10 Hz, 1H), 4.51 (d, J= 15.5 Hz, 1H), 4.44 (d, J= 15.5, 1H), 4.37 (m, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 3.38 (m, 1H), 3.15 (dd, J= 14.0, 5.0 Hz, 1H), 1.42 (s, 9H). **^{13}C NMR** (DMSO, 100°C, 125MHz, δ) 170.9, 159.8, 157.8, 154.5, 136.7, 128.8, 128.4, 127.5, 126.0, 124.3, 116.8, 114.8, 104.7, 98.5, 77.5, 54.9, 51.2, 48.2(b), 45.5(b), 30.0, 27.8. **IR** (KBr-neat) 3323, 2976, 2935, 1708, 1616, 1508, 1458, 1420, 1293, 1250, 1209, 1159, 1038, 700 cm^{-1}. **EI-HRMS** M = $C_{25}H_{32}N_2O_5$, $[M-C_4H_{10}O]^+$ 366.1580 found 366.1580. **ESI-LRMS** calcd for $C_{25}H_{32}N_2O_5$ 440.2 found $[M+Na]^+$ 463.2.



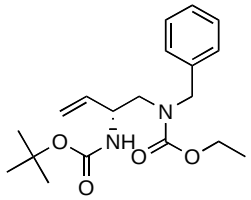
(R)-(+)-*t*-butyl-1-(benzoyloxy)but-3-en-2-ylcarbamate (17)

Ester **17** was prepared from butadiene monoepoxide **16**, *t*-butyl benzoyl imido carboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3** in methylene chloride. Purification by silica chromatography (13% ethyl acetate in petroleum ether) provided the desired product as a white solid in 72% yield. **Mp** = 79-82°C. **Chiralpak AD HPLC** (10 % IPA in Heptane, 1.0 ml/min, 230nm) shows 90 % ee favor 11.415 over 15.672 min. $[\alpha]_D$ = + 41º (c= 0.30 in $CHCl_3$, 90% ee). **^{1}H NMR** ($CDCl_3$, 400MHz, δ) 8.04-8.02 (m, 2H), 7.59-7.55 (m, 1H), 7.46-7.42 (m, 2H), 5.88 (ddd, J= 18.1, 10.6, 4.8 Hz, 1H), 5.33 (d, J= 18.1 Hz, 1H), 5.25 (d, J= 10.6 Hz, 1H), 4.82 (sb, 1H), 4.62 (sb, 1H), 4.37 (d, J= 4.9 Hz, 2H), 1.43 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100MHz, δ) 166.4, 155.2, 134.7, 133.1, 129.7, 129.7, 128.4, 116.7, 79.8, 66.3, 51.7, 28.3. **IR** (KBr-neat) 3352, 2973, 2938, 1719, 1690, 1648, 1529, 1450, 1364, 1289, 1268, 1166, 1130, 1100, 1072, 997, 921, 869, 779 cm^{-1}. **EI-HRMS** M = $C_{16}H_{21}NO_4$, $[M-C_4H_9]^+$ calcd 235.0845 found 235.0846. **ESI-HRMS** calcd for $C_{16}H_{21}NO_4$ 291.1 found $[M+Na]^+$ 314.1.



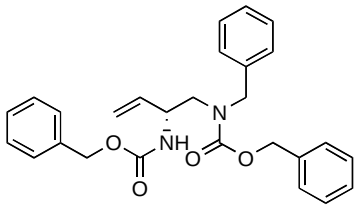
(R)-(+)-*t*-butyl-1-hydroxybut-3-en-2-ylcarbamate (18)

A solution of LiOH (1M aq., 0.4mL, 0.4mmol) and ester **(R)-(+)-17** (95mg, 0.33mmol) in THF (1mL) was stirred at room temperature for 20h, at which point all ester was consumed by TLC. The reaction was diluted with water (2 mL), brine (2 mL) and extracted with methylene chloride (4 x 2 mL). The combined organic extracts were dried with $MgSO_4$, filtered and concentrated *in vacuo* to the desired alcohol in ~95% purity by 1H NMR. $[\alpha]_D$ = + 31º (c= 1.03 in $CHCl_3$). **^{1}H NMR** ($CDCl_3$, 300MHz, δ) 5.82 (ddd, *J* = 17, 10.5, 5.4Hz, 1H), 5.31 – 5.22 (m, 2H), 4.93 (b, 1H), 4.26 (b, 1H), 3.74-3.61 (m, 2H), 2.35 (b, 1H), 1.46 (s, 9H). **IR** (KBr-neat) 3343, 2979, 2933, 2878, 1692, 1526, 1456, 1392, 1367, 1251, 1170, 1073, 1053, 992, 922 cm^{-1}. Optical rotation and 1H NMR corresponds to literature.[13]



(R)-(+)-t-Butyl-1-(N-ethylcarboxyl-benzylamino)-but-3-en-2-ylcarbamate (19)

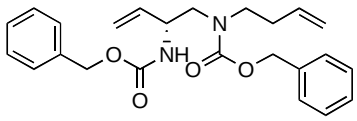
Diamine **19** was prepared from the parent aziridine **1**, ethyl *t*-butyl imido dicarboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3**. Purification by silica chromatography (30% ether in petroleum ether) provided the desired product as a thick oil (71%). **Chiralpak OJ HPLC** (8 % IPA in Heptane, 1.0 ml/min, 225nm) shows 94 % ee favor 5.615 over 6.689 min. $[\alpha]_D$ = + 34º (c= 0.46 in $CHCl_3$, 94% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.2-7.1 (m, 5H), 5.32 (ddd, J= 6.0, 10.5, 17.0 Hz, 1H), 5.05 (d, J= 17.0 Hz, 1H), 4.90 (d, J= 10.5 Hz, 1H), 4.57-4.35 (m, 4H), 4.08 (m, 2H), 3.42 (sb, 1H), 3.07 (dd, J= 14.5, 1.1 Hz, 1H), 1.44 (s, 9H), 1.04 (t, J= 7.0 Hz, 3H). **^{13}C NMR** (C_6D_6, 75°C, 125MHz, δ) 155, 138.9, 137.5, 129.2, 128.7, 128.4, 127.9, 115.9, 79.3, 62.0, 53.0, 51.6, 50.9, 28.9, 15.0. **IR** (KBr-neat) 3343, 2979, 2932, 1698, 1497, 1476, 1423, 1366, 1239, 1170, 1117, 1018, 771, 700 cm^{-1}. **EI-HRMS** calcd for $C_{19}H_{28}N_2O_4$ 348.2049, $[M-C_4H_9O]^+$ calcd 275.1396 found 275.1392.



(R)-Benzyl-1-(N-benzylcarboxyl-benzylamino)-but-3-en-2-ylcarbamate (20)

Diamine **20** was prepared from the parent aziridine **1**, bisbenzyl imido dicarboxylate, $[(\eta^3C_3H_5)PdCl]_2$ and *(S,S)* **3**. Purification by silica chromatography (50% ether in petroleum ether) provided the desired product as a thick oil (67%). **Chiralpak AD HPLC** (20 % IPA in Heptane, 1.0 ml/min, 230nm) shows 92 % ee favor 17.381 over 25.123 min. $[\alpha]_D$ = + 25º (c= 0.35 in $CHCl_3$, 89% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.26-7.22 (m, 2H), 7.22-7.01 (m, 13H), 5.48 (m, 1H), 5.12-4.96 (m, 4H), 4.93 (s, 1H), 4.87 (m, 1H), 4.49 (m, 1H), 4.54-4.26 (m, 3H), 3.40 (sb, 1H), 3.06 (dd, J= 14.8, 5.4 Hz , 1H) . **^{13}C NMR** (C_6D_6, 75°C, 125MHz, δ) 156.4, 150.8, 138.6, 137.7, 137.0, 129.2, 129.0, 128.9, 128.8, 128.7, 128.5, 128.3, 127.9, 116.4, 68.1, 67.2,

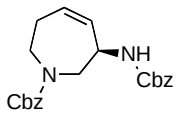
53.6, 51.7, 51.0. **IR** (KBr-neat) 3324, 3031, 2925, 1720, 1702, 1686, 1648, 1236, 1101 cm^{-1}. **EI-HRMS** calcd for $C_{27}H_{28}N_2O_4$ 444.2049, $[M-C_8H_7O_2]^+$ 309.1603 found 309.1600.



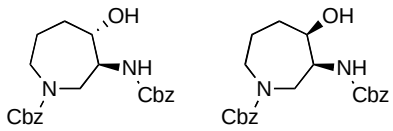
(R)-Benzyl-1-(N-benzylcarboxyl-3-butenylamino)-but-3-en-2-ylcarbamate (21)

A flame dried 10ml test tube was charged with $[(\eta^3C_3H_5)PdCl]_2$ (23mg, 60μmol), and ligand *(S,S)* **3** (150mg, 0.19mmol). The tube was flushed with nitrogen and anhydrous and degassed methylene chloride (11 mL) was added to the solids. After stirring for ~10 min at room temperature, *N*-but-3-enyl-2-vinylaziridine (388mg from a 46% pure material 840mg, 3.15mmol) was added to the homogeneous orange solution of the catalyst. The bisbenzyl imido dicarboxylate (890mg, 3.15mmol) dissolved in anhydrous and degassed methylene chloride (11 mL) was cannulated into the solution of the catalyst and aziridine, and the reaction was stirred at 35°C for 14h. The homogeneous yellow to orange solution was concentrated to an oil, and the acyl migration product **21** (891mg, 69%) was isolated after purification by silica chromatography (50% ether in petroleum ether). **Chiralpak AD HPLC** (10 % IPA in Heptane, 1.0 ml/min, 220nm) shows 88 % ee favor 22.805 over 17.096min. $[\alpha]_D$ = + 20º (c= 0.45 in $CHCl_3$, 87% ee). **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.25-7.21 (m, 4H), 7.14-7.08 (m, 4H), 7.08-7.02 (m, 2H), 5.64-5.46 (m, 2H), 5.09-5.03 (m, 5H), 4.98-4.89 (m, 3H), 4.50-4.42 (m, 1H), 3.35 (sb, 1H), 3.2 (sb, 2H), 3.05 (dd, J= 14.8, 5.4 Hz, 1H), 2.15 (sb, 2H). **^{13}C NMR** (C_6D_6, 75°C, 125MHz, δ) 156.4, 155.0, 138.1, 137.9, 137.1, 135.9, 129.0, 128.9, 128.91, 128.7, 127.8, 127.3, 117.0, 116.4, 67.9, 67.1, 54.0, 51.8, 48.3, 33.5. **IR** (KBr-neat) 3328, 3066, 2949, 1694, 1682, 1644, 1538, 1478, 1455, 1424, 1225, 1165, 1089, 1028, 993, 920, 737, 698 cm^{-1}. **MALDI-HRMS** calcd for $C_{24}H_{28}N_2O_4$ 408.2049 found 408.2283.

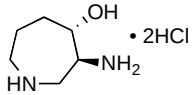
V. Experimental Procedure for the Synthesis of the Azepane Core of Balanol



(R,Z)-Benzyl-1-((benzyloxy)carbonyl)-2,3,6,7-tetrahydro-1H-azepin-3-ylcarbamate (22) A solution of the Grubbs II catalyst (25mg, 29μmol) in anhydrous and degassed methylene chloride (5 mL) was cannulated into a solution of olefin **21** (230mg, 0.56mmol) in anhydrous and degassed methylene chloride (5 mL) under nitrogen. The reaction was stirred at 35°C for 6h; at which point all starting material was consumed. The reaction was cooled to room temperature, concentrated *in vacuo* and purified by silica chromatography (50% ether in petroleum ether) to provide the tetrahydroazepine **22** as a tan amorphous solid (190mg, 90%). Due to the rotamers observed at even elevated temperatures, the material was carried on to the azepane ring for characterization. **^{1}H NMR** (C_6D_6, 75°C, 500MHz, δ) 7.25-7.05 (m, 10H), 6.00-5.60 (2H), 5.2-4.8 (m, 5H), 4.23 (bs, 1H), 3.8-3.4 (4H), 2.4-2.2 (m, 2H).



benzyl (3S) – 1 - ((benzyloxy) - carbonyl) - 4-hydroxyazepan-3-ylcarbamates: Borane (1M in THF, 580μL, 0.58mmol) was added to a solution of tetrahydroazepine **22** (110mg, 0.29mmol) dissolved in anhydrous THF (5 mL) at 0°C. The reaction was stirred at 0°C for 3h at which point all the starting olefin was consumed. The excess borane was quenched by the addition of several drops of water. The mixture was treated with sodium perborate monohydrate (230mg, 2.4mmol) and water (5 mL). The mixture was stirred at room temperature for 6h. The reaction was diluted with water (10 mL) and extracted with ethyl acetate (3x20 mL). The organic extracts were dried with Na_2SO_4, filtered and concentrated *in vacuo* to an oil. Purification by silica chromatography (1% MeOH in methylene chloride) provided the desired regioisomer as a mixture of diastereomers (3S, 4S) and (3S, 4R) (81mg, 70%) and the undersired regioisomers (32mg, 23%). The desired regioisomer was determined to be a 2 : 1 ratio of (3S, 4S) : (3S, 4R) by HPLC analysis. For the mixture of diastereomers: **^{1}H NMR** (benzene, 75 °C, 500 MHz, δ) 7.25-7.06 (m, 10H), 5.11-5.00 (m, 4H), 3.86-2.80 (m, 5H), 1.66-1.15 (m, 5H). The diastereomers were separated by preparatory HPLC [Semi prep: Alltima C18 10μ, length 250mm, ACN in H_2O (20-70%)] and directly subjected to hydrogenolysis.

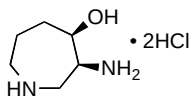


(3S,4S)-(+)-3-aminoazepan-4-ol dihydrochloride (23)

A mixture of (3S, 4S) - benzyl (3S) – 1 - ((benzyloxy) - carbonyl) - 4-hydroxyazepan-3-ylcarbamate (35mg, 90μmol) and 15% $Pd(OH)_2$ / C (10mg) in anhydrous methanol (2 mL) was stirred under an atmosphere of hydrogen for 12h, after which the catalyst was removed by filtration. To the filtrate was added 1M HCl aq (1mL), and the solution was concentrated *in vacuo*. The residue was taken up into water (3 mL) and washed with methylene chloride (3x 1mL), and concentrated to provide the azepane core of (+)-balanol as the bis – hydrochloride salt (15mg, 83%). **$[\alpha]_D$** = + 18° (c= 0.44 in MeOH). **^{1}H NMR** (D_2O, 500 MHz, δ) 3.84-3.81 (m, 1H), 3.59-3.50 (m, 2H), 3.40-3.25 (m, 3H), 2.26-2.05 (m, 1H), 2.04-1.98 (m, 1H), 1.89-1.80 (m, 1H), 1.76-1.69 (m, 1H) **^{13}C NMR** (D_2O, 125 MHz, δ) 71.1, 53.3, 45.9, 42.1, 31.8, 18.4. **IR** (KBr-neat) 3383, 2929, 2850, 1634, 1470, 1956 cm^{-1}.

Literature for **23**:[14]

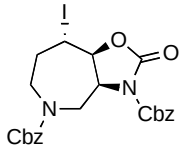
$[\alpha]_D$ = -19.3 (*c* = 0.171 in MeOH) (for the opposite enantiomer) **^{1}H NMR** (D_2O, 400 MHz, δ) 3.75 (m, 1H), 3.6 (m, 2H), 3.21-3.40 (m, 3H), 2.2 (m, 1H), 2.05-2.10 (m, 1H), 1.70-1.80 (m, 2H). **^{13}C NMR** (D_2O, 75.5 MHz) 71.1, 53.3, 45.9, 42.1, 31.8, 18.4.



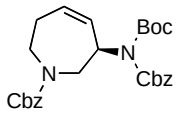
(3S,4R)-(-)-3-aminoazepan-4-ol dihydrochloride (26)

A mixture of (3S, 4R) - benzyl (3S) – 1 - ((benzyloxy) - carbonyl) - 4-hydroxyazepan-3-ylcarbamate (13mg, 33μmol) and 15% $Pd(OH)_2$ / C (5mg) in anhydrous methanol (1 mL) was stirred under an atmosphere of hydrogen for 12h, after which the catalyst was removed by filration. To the filtrate was added 1M HCl aq (1mL), and the solution was concentrated *in vacuo*. The residue was taken up into water (3 mL) and washed with methylene chloride (3x 1mL), and concentrated to provide the azepane **26** as the bis-hydrochloride salt (6.5mg, 97%). **$[\alpha]_D$** = -13° (c= 0.22 in MeOH). **^{1}H NMR** (D_2O, 500 MHz, δ) 4.37-4.28 (m, 1H), 3.85-3.80 (m, 1H), 3.62-

3.58 (m, 1H), 3.43-3.38 (m, 2H), 3.22-3.17 (m, 1H), 2.10-2.00 (m, 2H), 1.87-1.81 (m, 2H). **^{13}C NMR** (D_2O, 125 MHz, δ): 66.9, 51.3, 46.8, 41.4, 31.0, 17.8. **IR** (KBr-neat): 3356, 2927, 1458 cm^{-1}. **ESI-HRMS** calcd for $C_6H_{14}O$ 130.1106, found $[M+H]^+$ calcd 131.1184 found 131.1188.

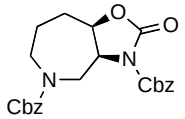


Preparation of (3a*S*,8*S*,8a*S*)-dibenzyl-8-iodo-2-oxo-hexahydro-2*H*-oxazolo[4,5-*c*]azepine-3,5-dicarboxylate (24)



A mixture of (R,Z)-Benzyl-1-((benzyloxy)carbonyl)-2,3,6,7-tetrahydro-1H-azepin-3-ylcarbamate (**22**) (0.997 g, 2.62 mmol), $(BOC)_2O$ (1.144 g, 5.24 mmol) and DMAP (0.160 g, 1.31 mmol) was stirred in 8 mL of CH_3CN. After 14 h, the solution was concentrated and purified by column chromatography on silica gel (diethyl ether: petroleum ether, 1:1) to give the product as a semi-solid (1.20 g, 95%). Due to the rotamers observed at even elevated temperatures, the material was carried on to the deprotected azepane ring for characterization by ^{13}C NMR. $[\alpha]_D$ = -43.7º (*c* = 1.40 in CH_2Cl_2) **^{1}H NMR** ($CDCl_3$, 400MHz δ) 7.44-7.28 (m, 10H), 5.84-5.55 (m, 2H), 5.24-5.05 (m, 5H), 4.20-3.82 (m, 2H), 3.63-3.44 (m, 1H), 3.04-2.86 (m, 1H), 2.48-2.26 (m, 2H), 1.46-1.39 (m, 9H). **IR** (KBr-neat): 2979, 1746, 1704, 1336, 1222, 1155, 1101, 697 cm^{-1}. **EI-HRMS** calcd for $C_{27}H_{32}N_2O_6$ 480.2260, found 480.2282.

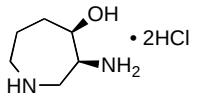
A mixture of the above N-Boc protected intermediate (1.138 g, 2.367 mmol) and NIS (3.047 g, 13.543 mmol) was placed in a 100 mL pressure tube and dissolved in 25 mL of DCE. The mixture was illuminated with a 500W halogen lamp for 3 h, then diluted with 20 mL of CH_2Cl_2 and washed with saturated $Na_2S_2O_3$ (2 x). The aqueous washes were extracted with CH_2Cl_2, and the pooled organics were dried over $MgSO_4$ and evaporated. The crude material was purified by chromatography on silica gel (diethyl ether: petroleum ether, 1.5:1 → 2:1 → 3:1), giving the iodide **24** as a semi-solid (1.08 g, 83%). Due to the rotamers observed at even elevated temperatures, the material was carried on to the deprotected azepane ring for characterization by ^{13}C NMR. $[\alpha]_D$ = 42.9º (*c* = 0.66 in CH_2Cl_2) **^{1}H NMR** ($CDCl_3$, 500MHz δ) 7.47-7.22 (m, 10H), 5.40-5.26 (m, 1H), 5.12 (m, 1H), 4.92-4.70 (m, 4H), 4.60-4.00 (m, 3H), 3.66 (m, 1H), 3.20-3.03 (m, 1H), 2.42-2.26 (m, 1H), 1.94-1.82 (m, 1H). **IR** (KBr-neat): 2956, 1824, 1702, 1423, 1306, 1240, 1111, 1068, 698 cm^{-1}. **EI-HRMS** calcd for $C_{23}H_{23}IN_2O_6$ 550.0601, $[M-C_7H_7]^+$ 459.0053 found 459.0082.



(3a*S*,8a*R*)-dibenzyl 2-oxo-hexahydro-2*H*-oxazolo[4,5-*c*]azepine-3,5-dicarboxylate (25)

A solution of iodide **24** (83 mg, 0.151 mmol) and dilauroylperoxide (21 mg, 0.053 mmol) in 8 mL of degassed cyclohexane was illuminated with a 500W halogen lamp, allowing the heat from the lamp to bring the solution to reflux. After 2h, added another 75 mg of dilauroylperoxide as a solution in 3 mL of cyclohexane. After a total of 5 h the solution was concentrated under vacuum and purified by column chromatography on silica gel (ethyl acetate: petroleum ether, 1.5:1 → 2:1), giving the product **25** as a semi-solid (64 mg, 99%). Due to the rotamers observed at even

elevated temperatures, the material was carried on to the deprotected azepane ring for characterization by ^{13}C NMR. $[\alpha]_D$ = 25.7º (*c* = 2.32 in CH_2Cl_2) **^{1}H NMR** ($CDCl_3$, 500MHz δ) 7.50-7.25 (m, 10H), 5.37-5.12 (m, 2H), 4.90-4.76 (m, 3H), 4.50-4.36 (m, 1H), 4.14-3.95 (m, 1H), 3.85-3.75 (m, 1H), 3.53-3.47 (m, 1H), 3.21 (m, 1H), 2.27 (m, 1H), 2.10-1.84 (m, 2H), 1.65 (m, 1H). **IR** (KBr-neat): 2952, 1815, 1699, 1424, 1384, 1273, 1234, 1096, 754, 698 cm^{-1}. **EI-HRMS** calcd for $C_{23}H_{24}N_2O_6$ 424.1634, $[M-C_7H_7]^+$ 333.1087 found 333.1079.



(3S,4R)-(-)-3-aminoazepan-4-ol dihydrochloride (26)

A solution of **25** (12.8 mg, 30.2 μmol) in 2 mL of concentrated HCl was heated to reflux for 24 h. The solution was concentrated under vacuum and the residue was taken up in 5 mL of H_2O then washed with CH_2Cl_2 (2 x 5 mL). The aqueous layer was concentrated under hard vacuum. To provide the product as a semi-solid (6.0 mg, 98%). Spectral data matched that previously reported (see above).

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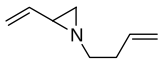
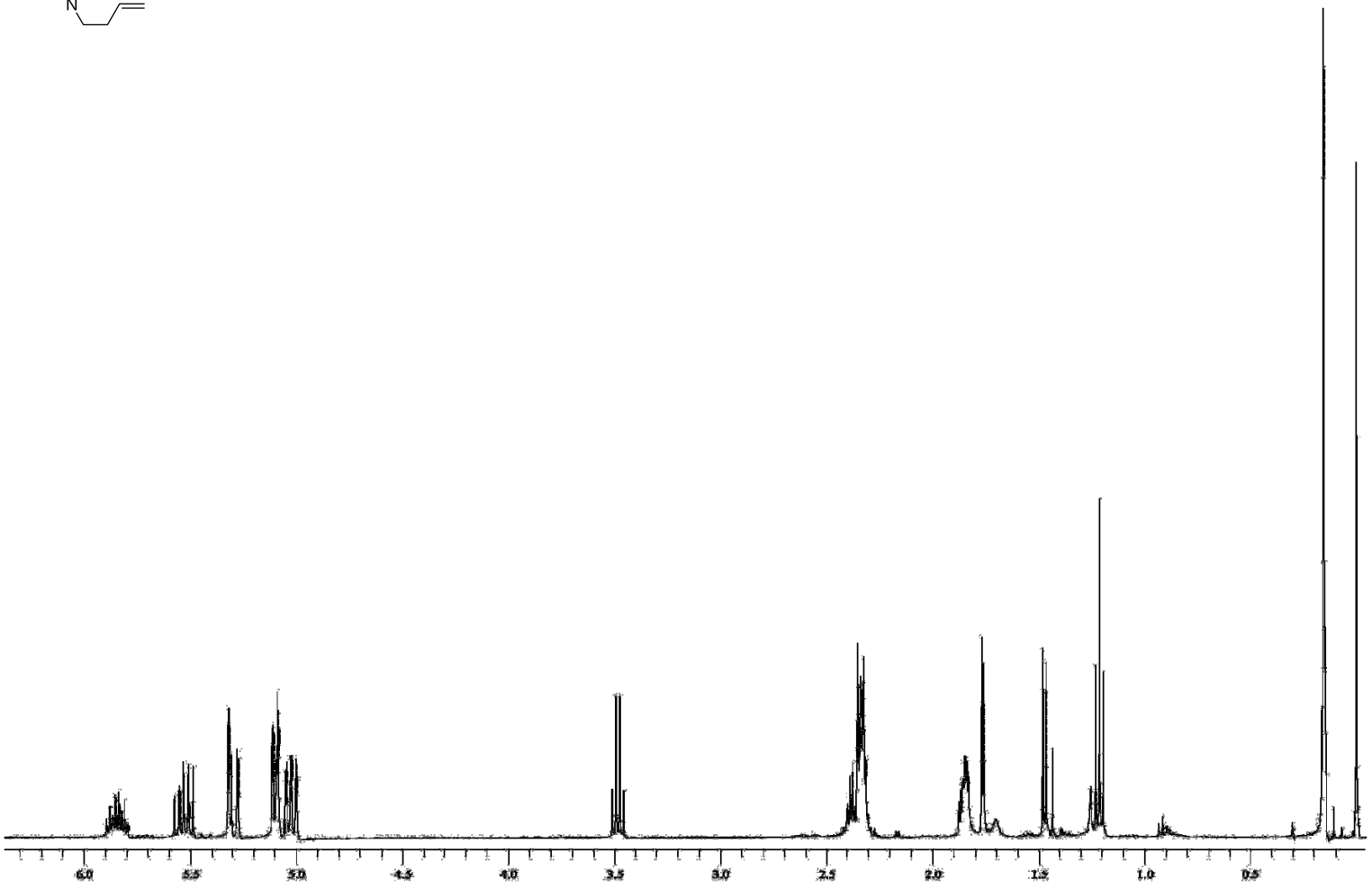
***N*-but-3-enyl-2-vinylaziridine**

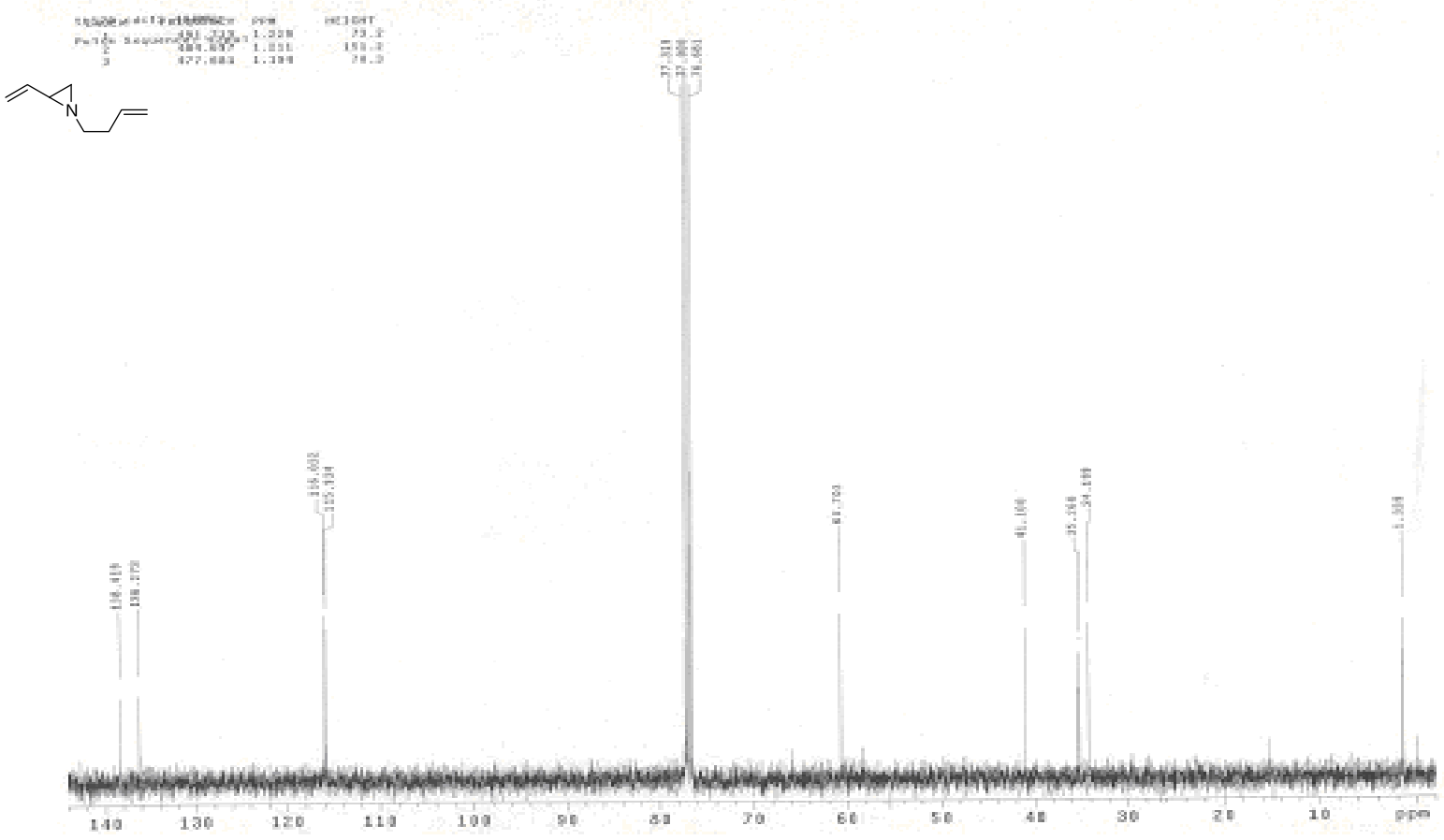
46 wt. %





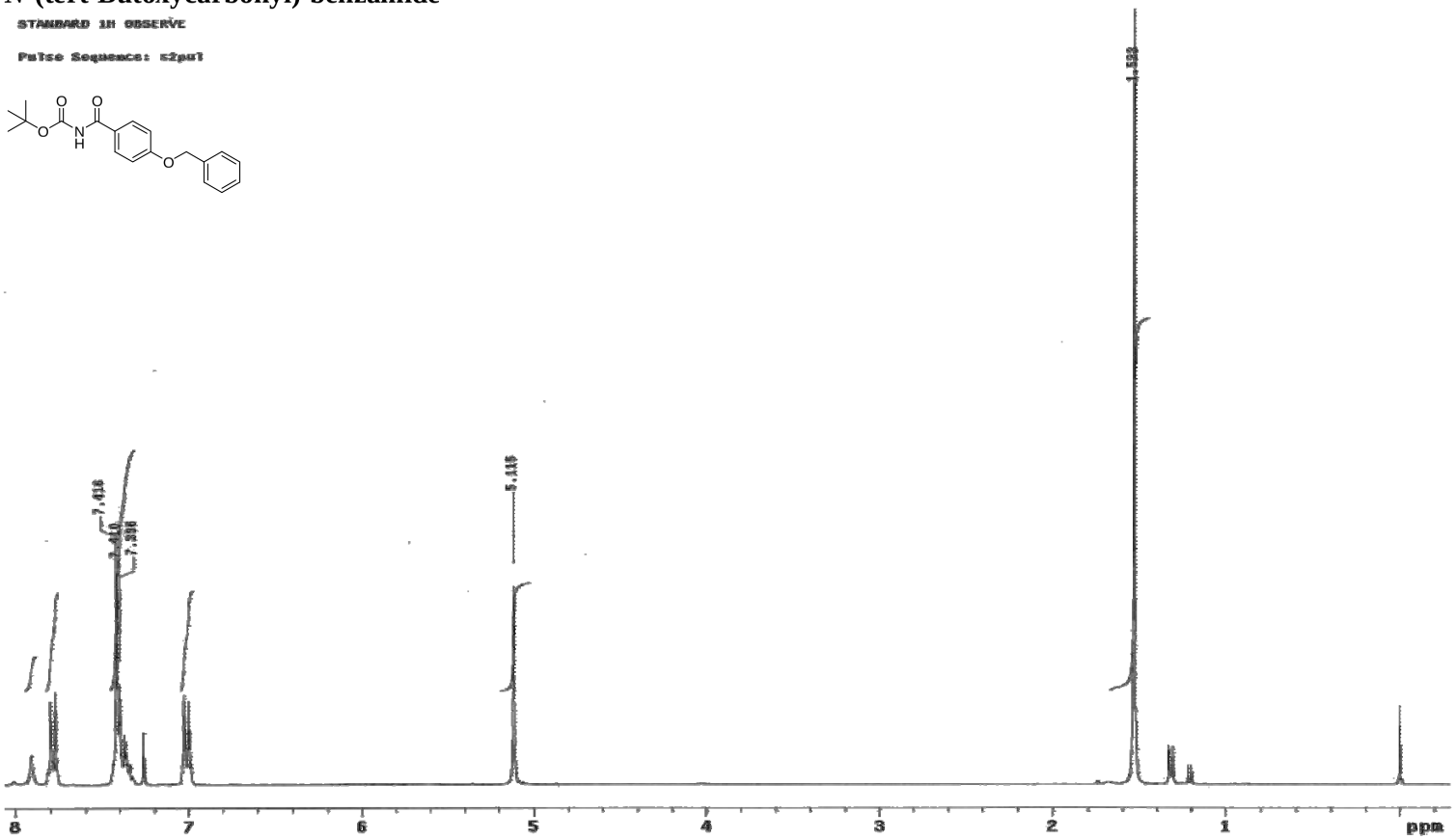
^{1}H NMR ($CDCl_3$ 400MHz)

***N*-but-3-enyl-2-vinylaziridine**



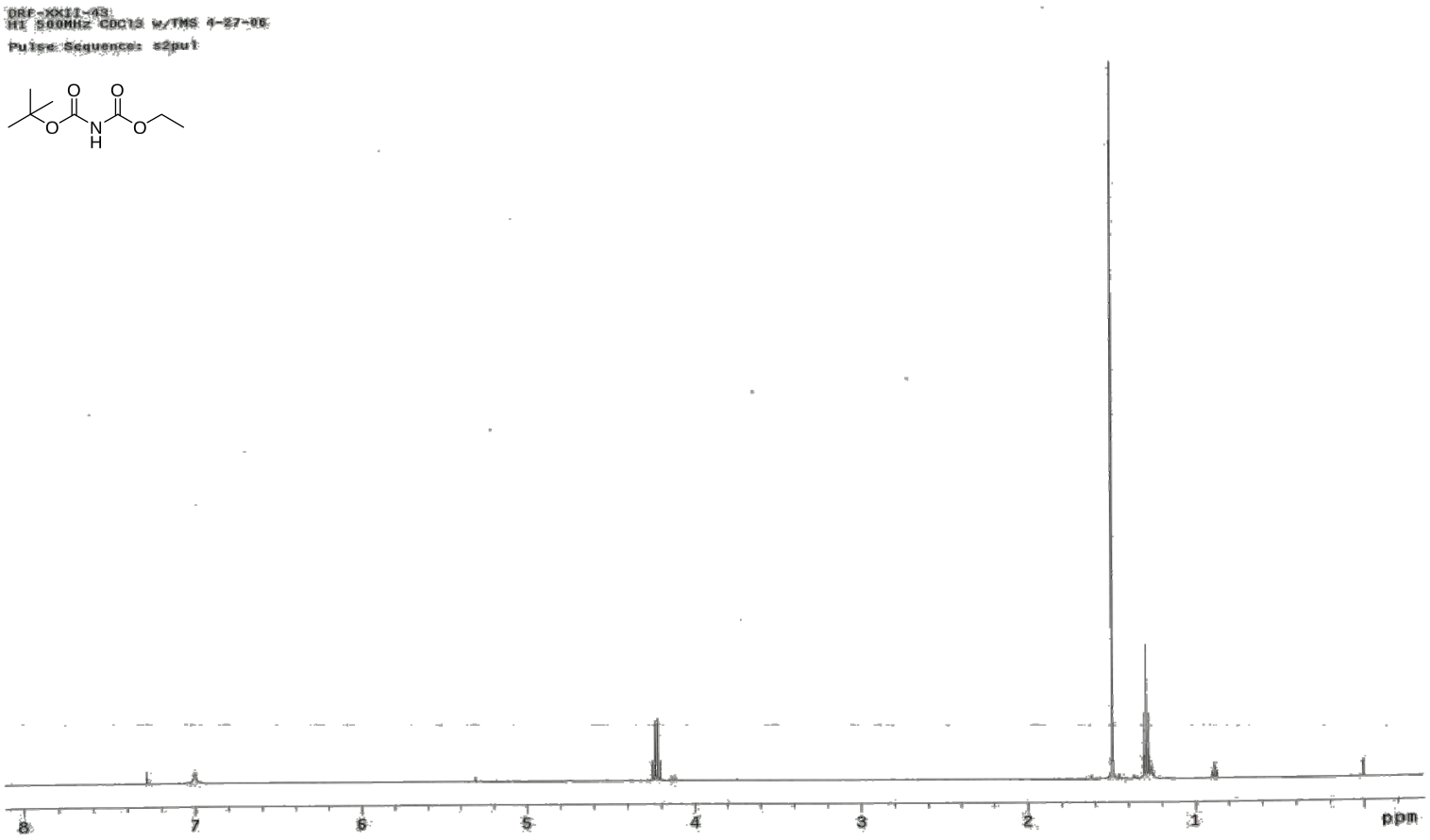
^{13}C NMR ($CDCl_3$ 100MHz)

***N*-(tert-Butoxycarbonyl)-benzamide**



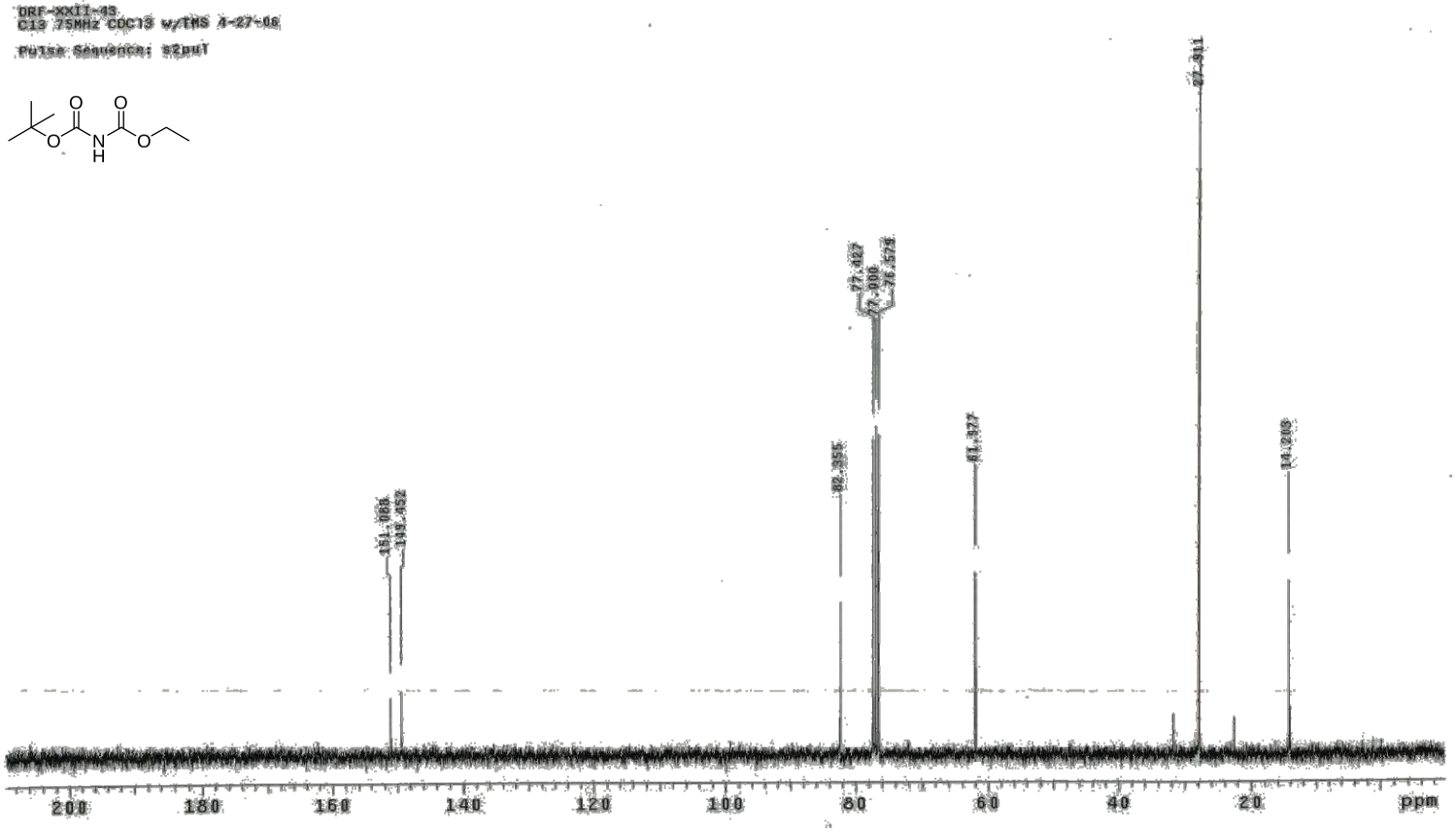
^{1}H NMR ($CDCl_3$, 300MHz)

***t*-Butyl-ethyl-imido dicarboxylate**



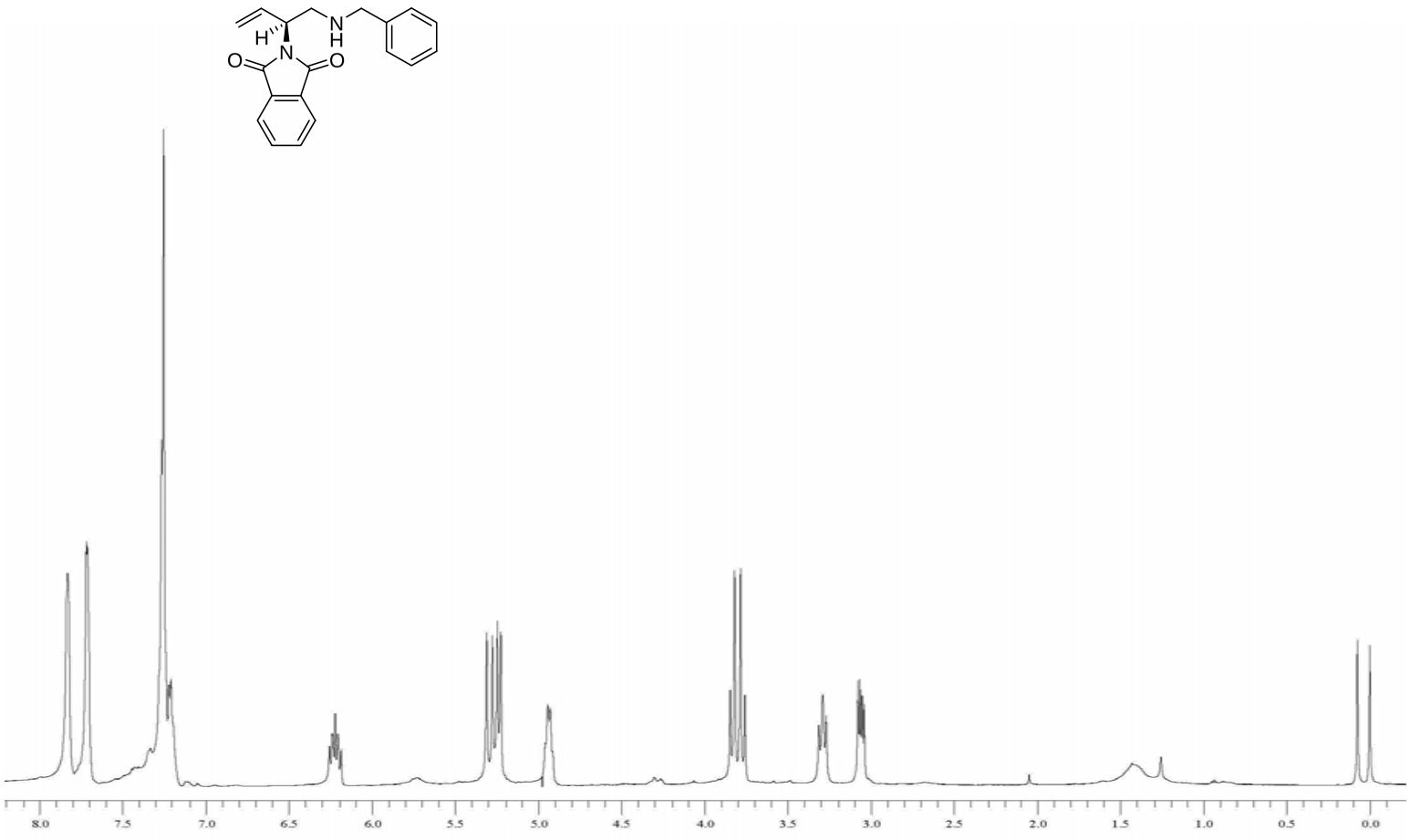
^{1}H NMR ($CHCl_3$, 500MHz)

***t*-Butyl-ethyl-imido dicarboxylate**



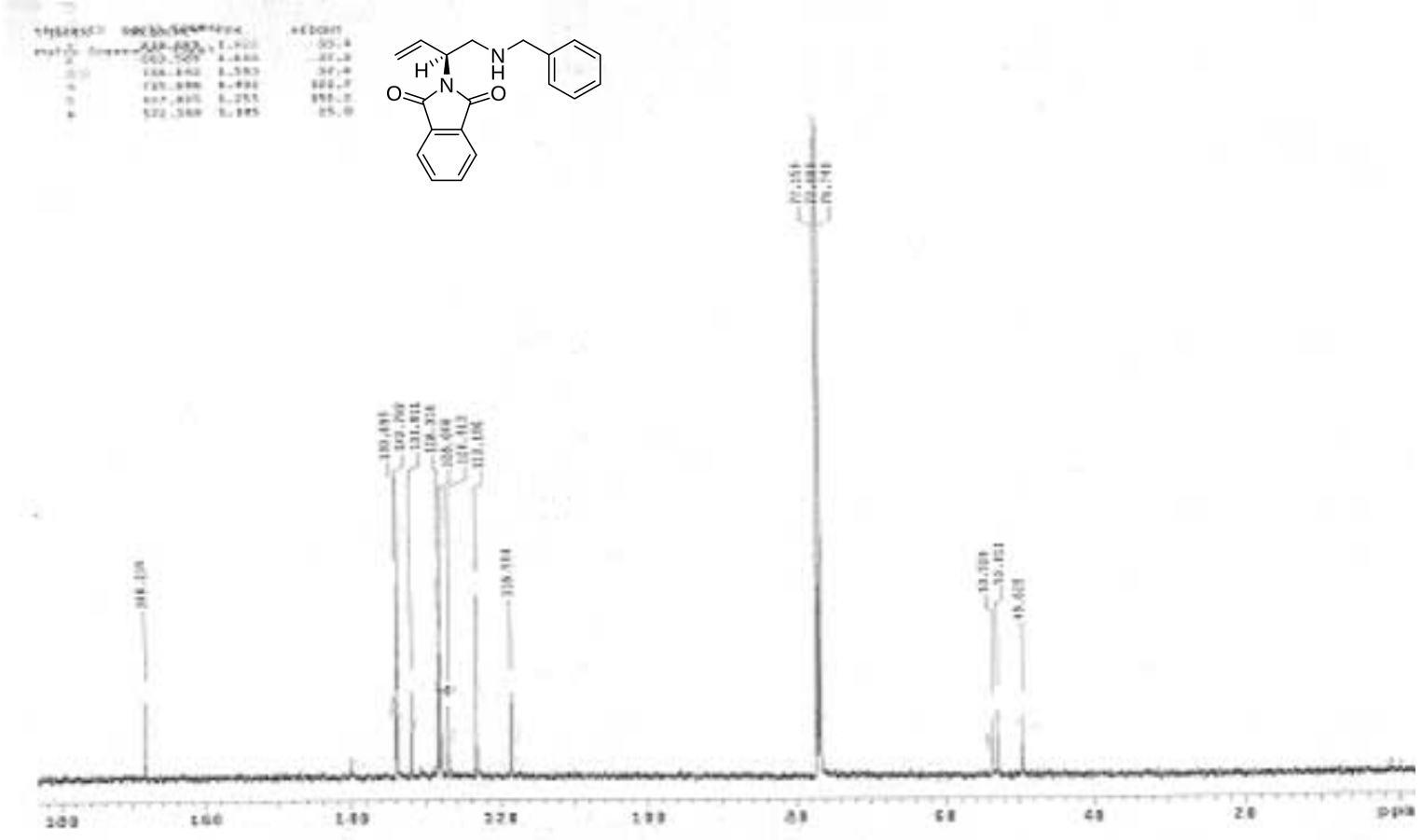
^{13}C NMR ($CHCl_3$, 125MHz)

2-((S)-1-(benzylamino)but-3-en-2-yl)-isoindoline-1,3-dione (4)



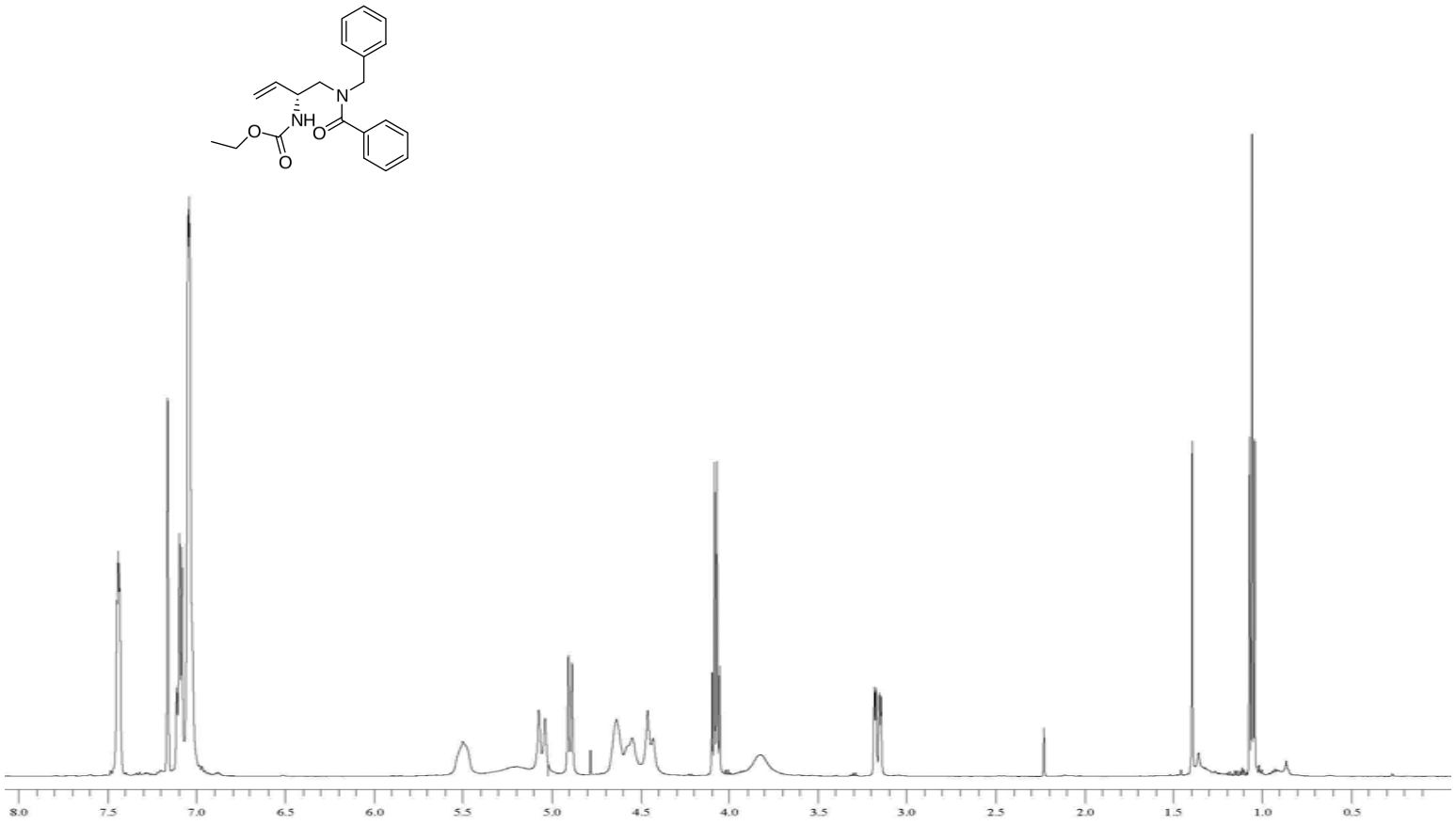
^{1}H NMR ($CDCl_3$, 400MHz)

2-((S)-1-(benzylamino)but-3-en-2-yl)-isoindoline-1,3-dione (4)



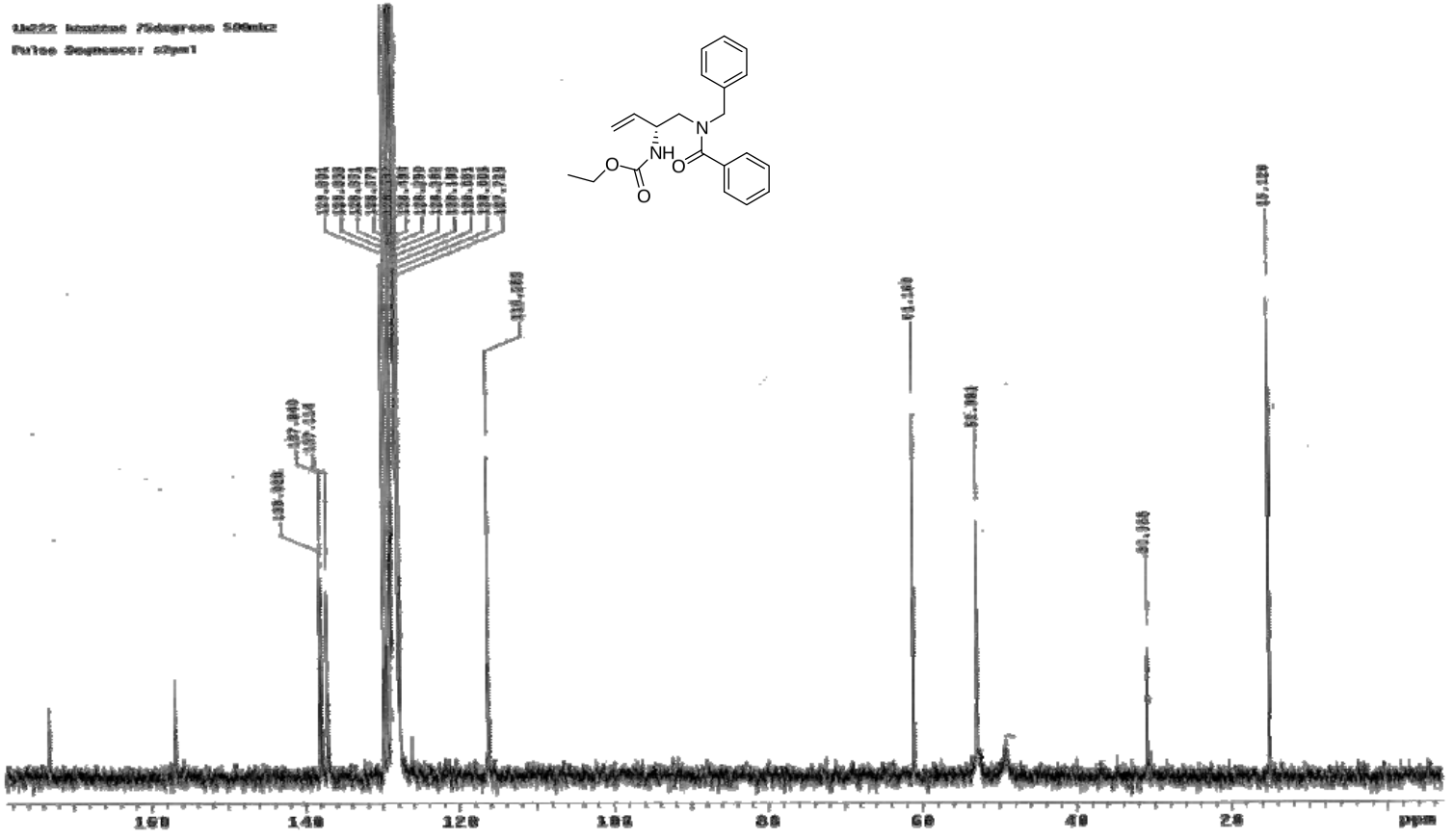
^{13}C NMR ($CDCl_3$ 100MHz)

(R) – (+) - Ethyl-1-(N-benzylbenzamido)-but-3-en-2-ylcarbamate (10)



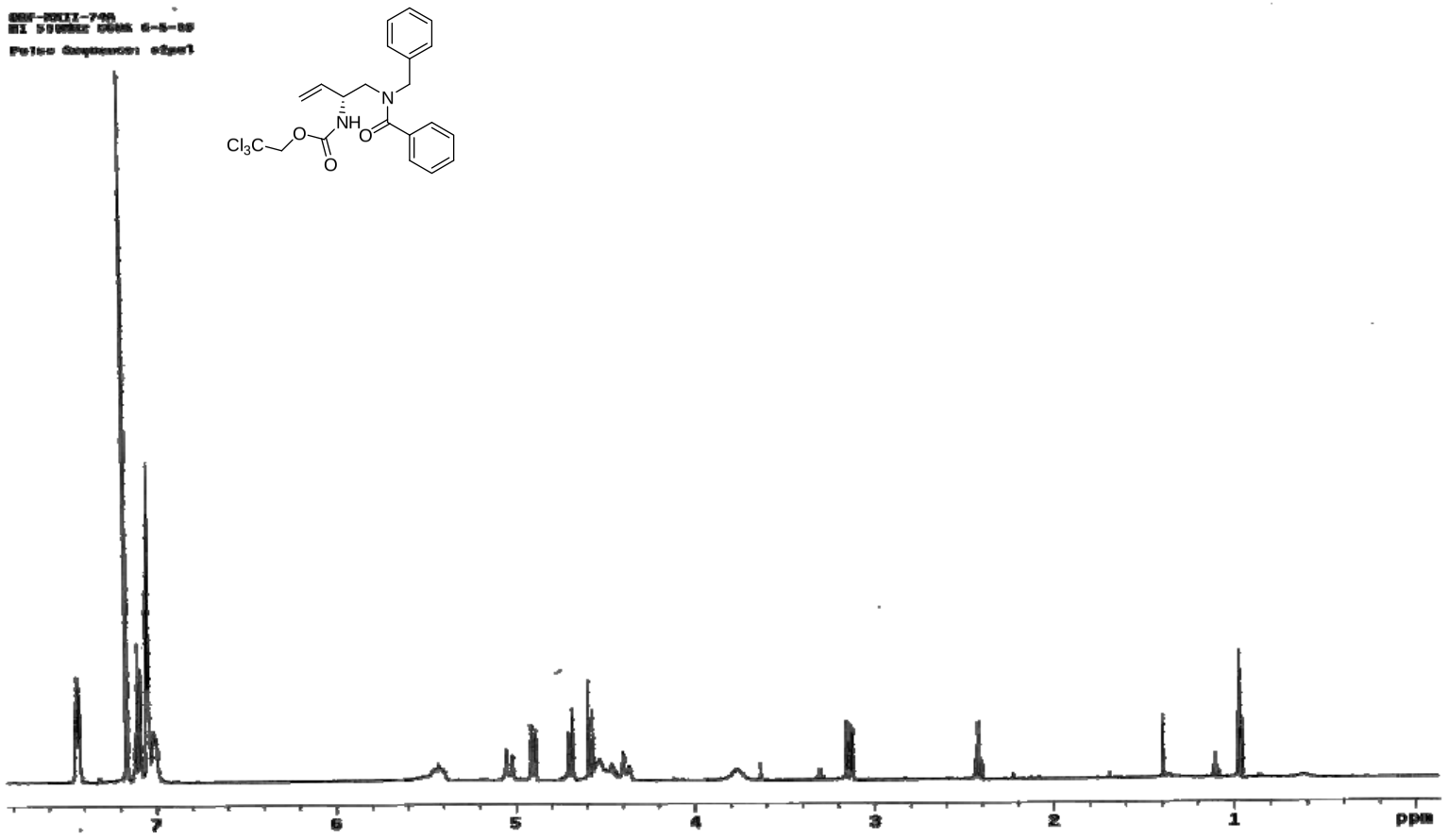
^{1}H NMR (C_6D_6, 75^{o}C, 500MHz)

(R) – (+) - Ethyl-1-(N-benzylbenzamido)-but-3-en-2-ylcarbamate (10)



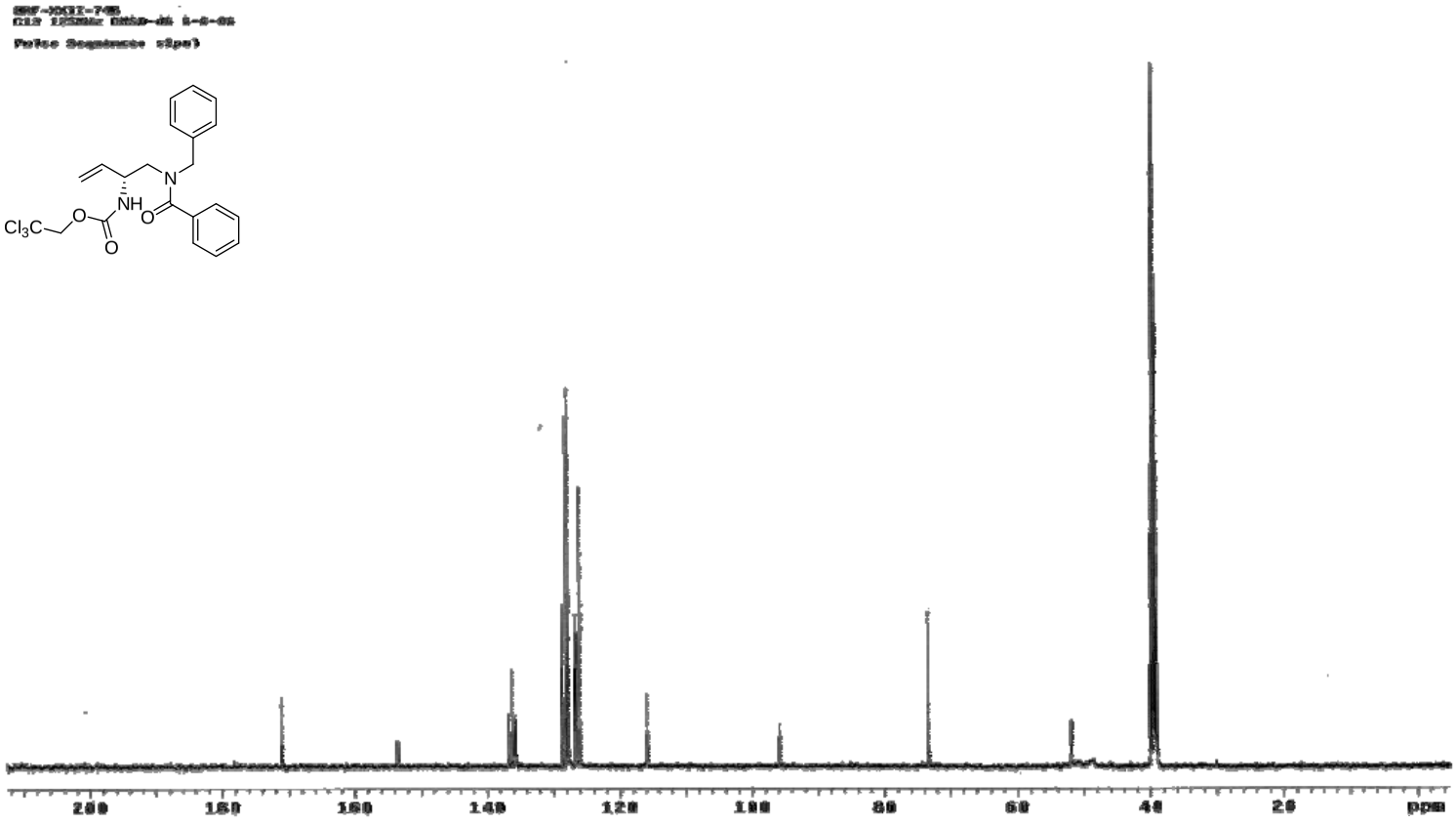
^{13}C NMR (C_6D_6, 75^{o}C, 125MHz)

(R) – (+) -2,2,2-trichloroethyl-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (11)



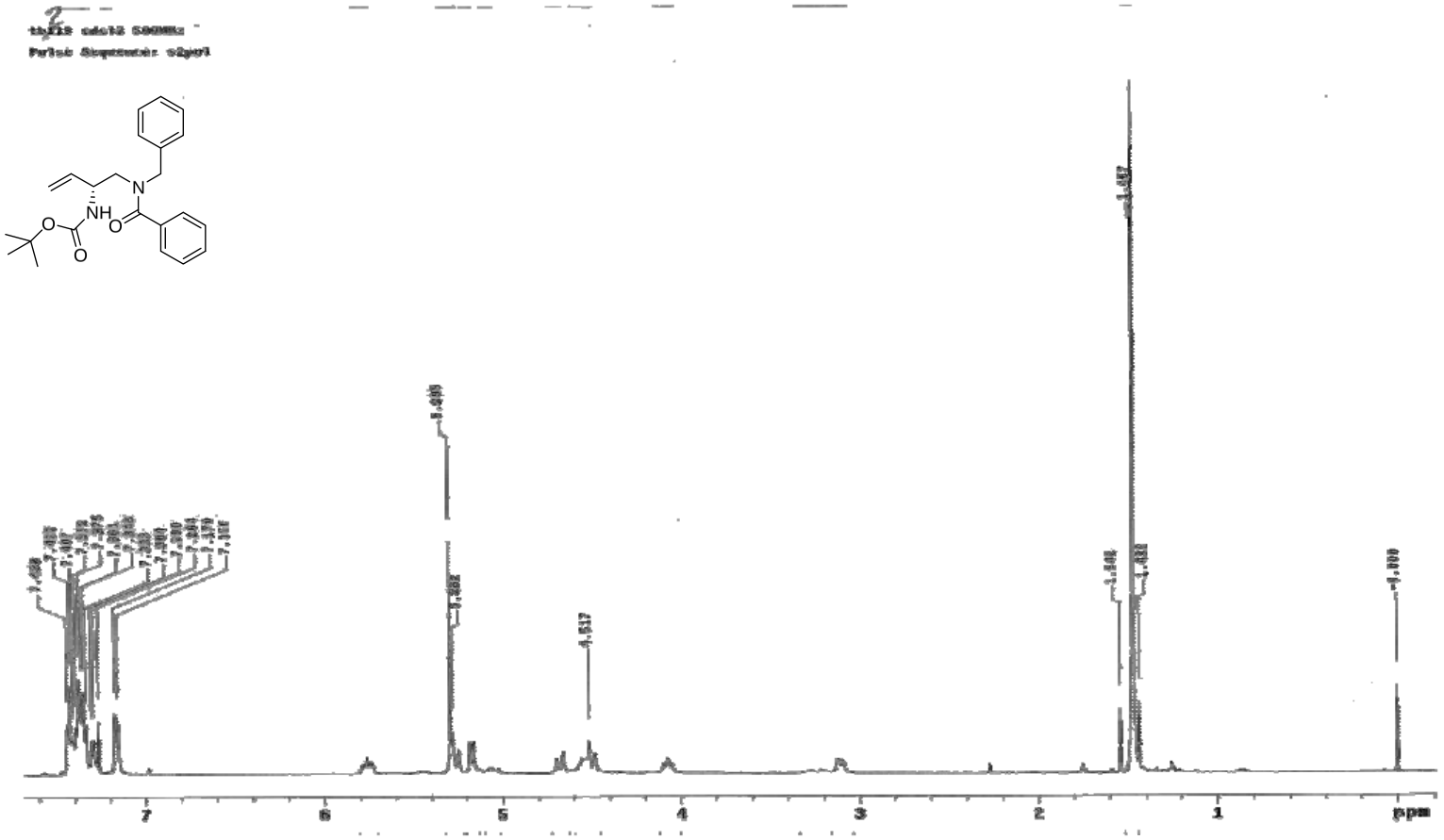
^{1}H NMR (C_6D_6, 75^{o}C, 500MHz)

(R) – (+) -2,2,2-trichloroethyl-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (11)



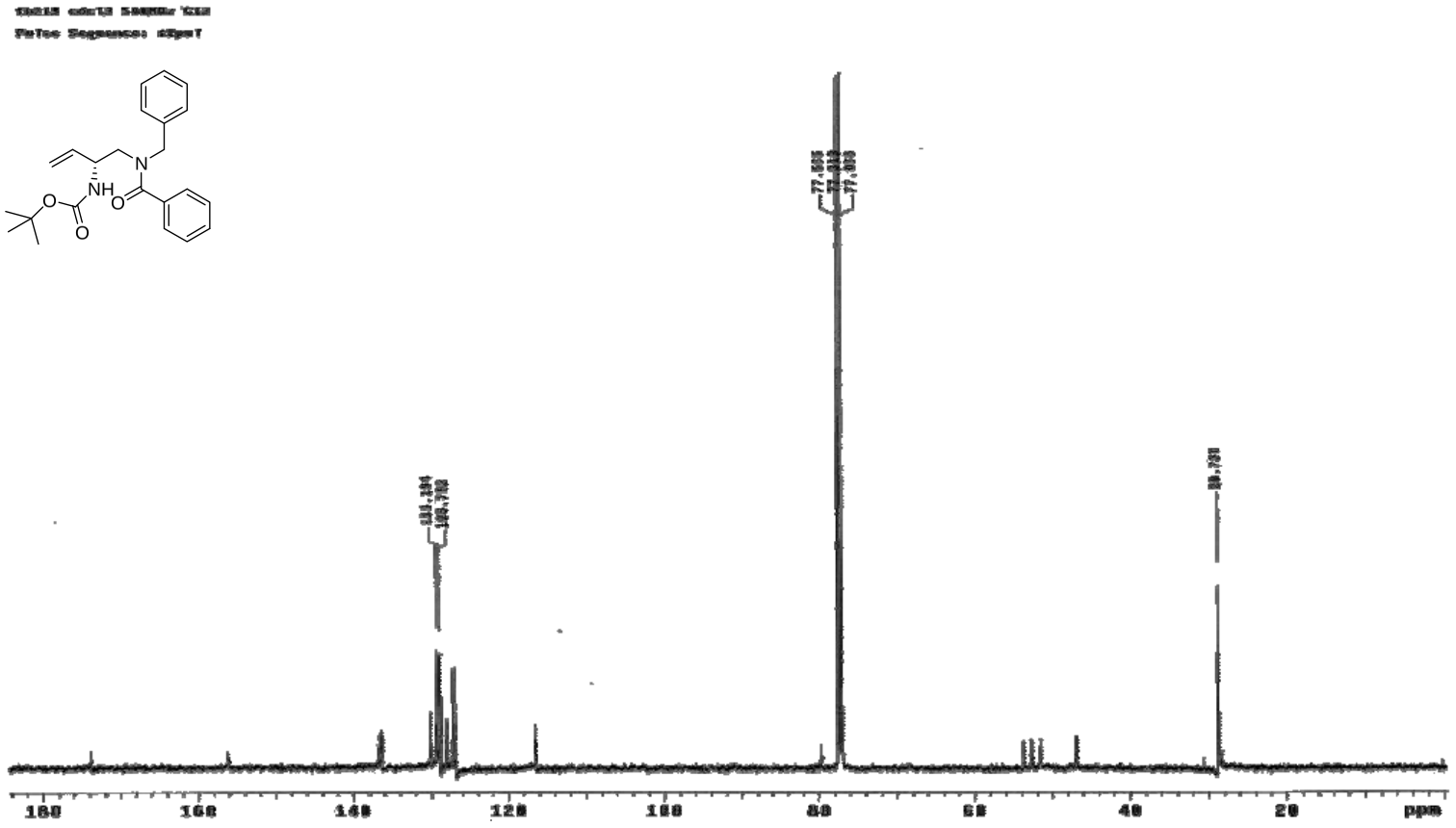
^{13}C NMR (C_6D_6, 75^{o}C, 125MHz)

(R)-(+)-t-butyl-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (7)



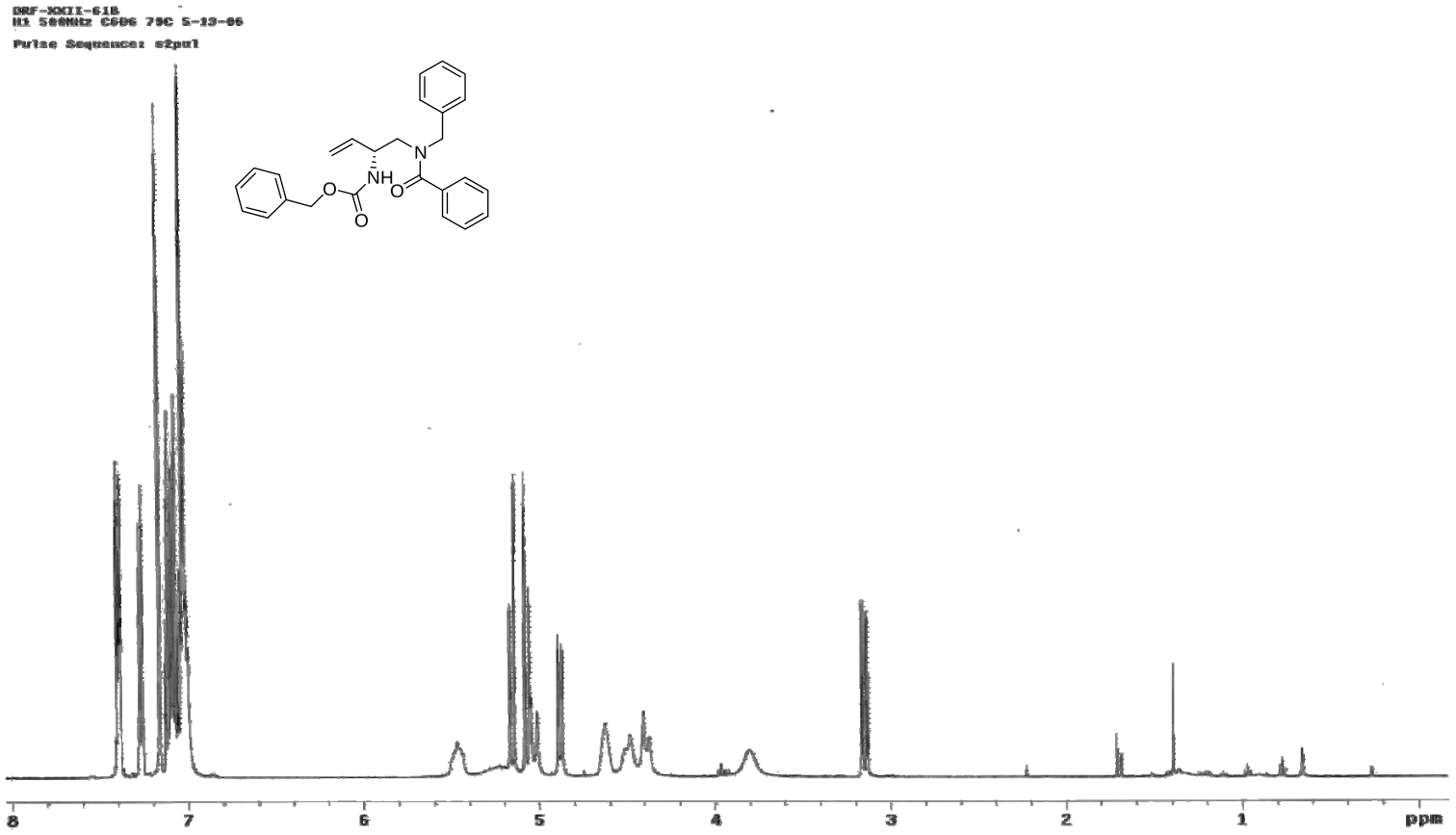
^{1}H NMR (C_6D_6, 75^{o}C, 500MHz)

(R)-(+)-t-butyl-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (7)



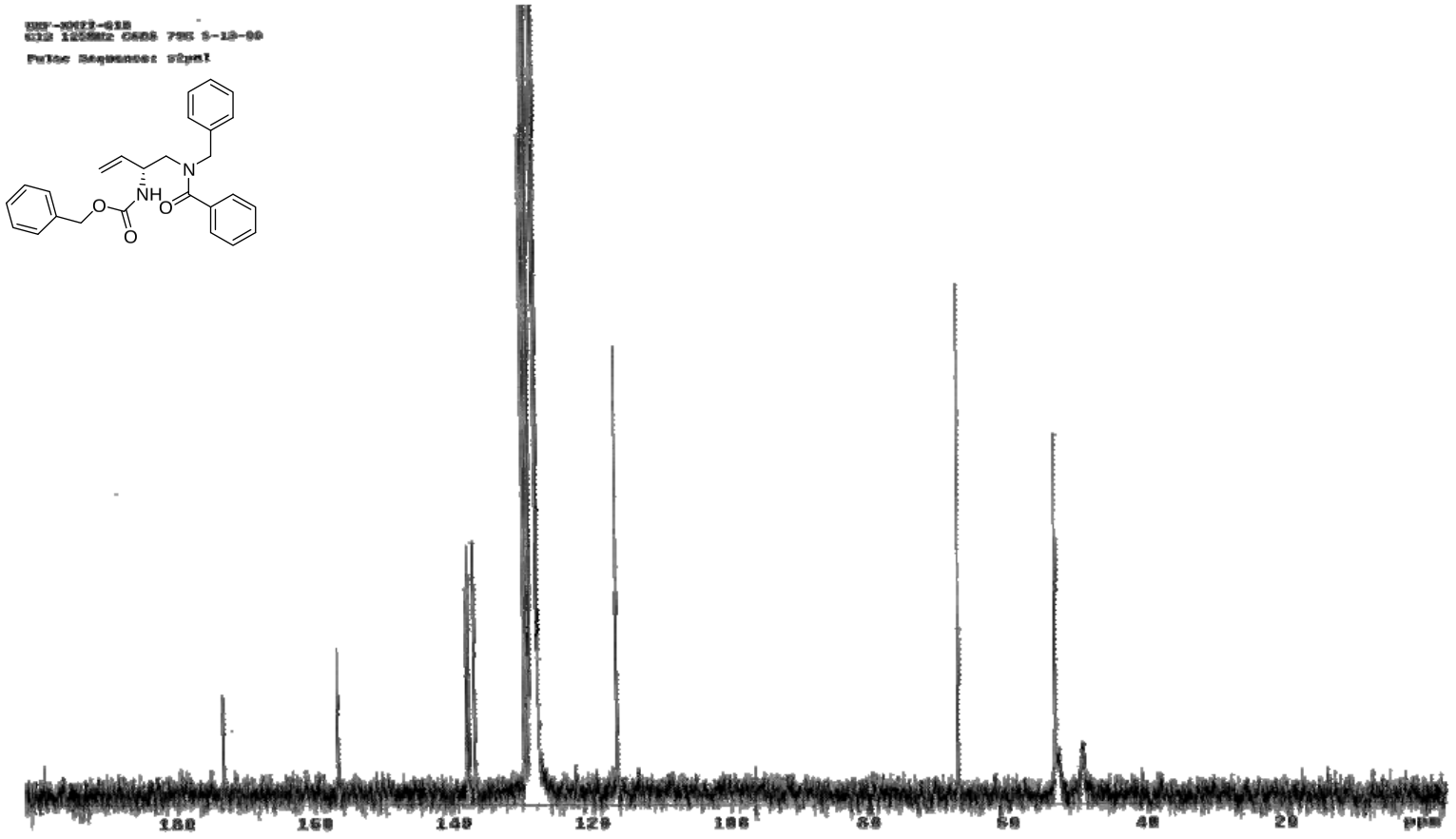
^{13}C NMR (C_6D_6, 75°C, 125MHz)

(R)-(+)-Benzyl (R)-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (12)



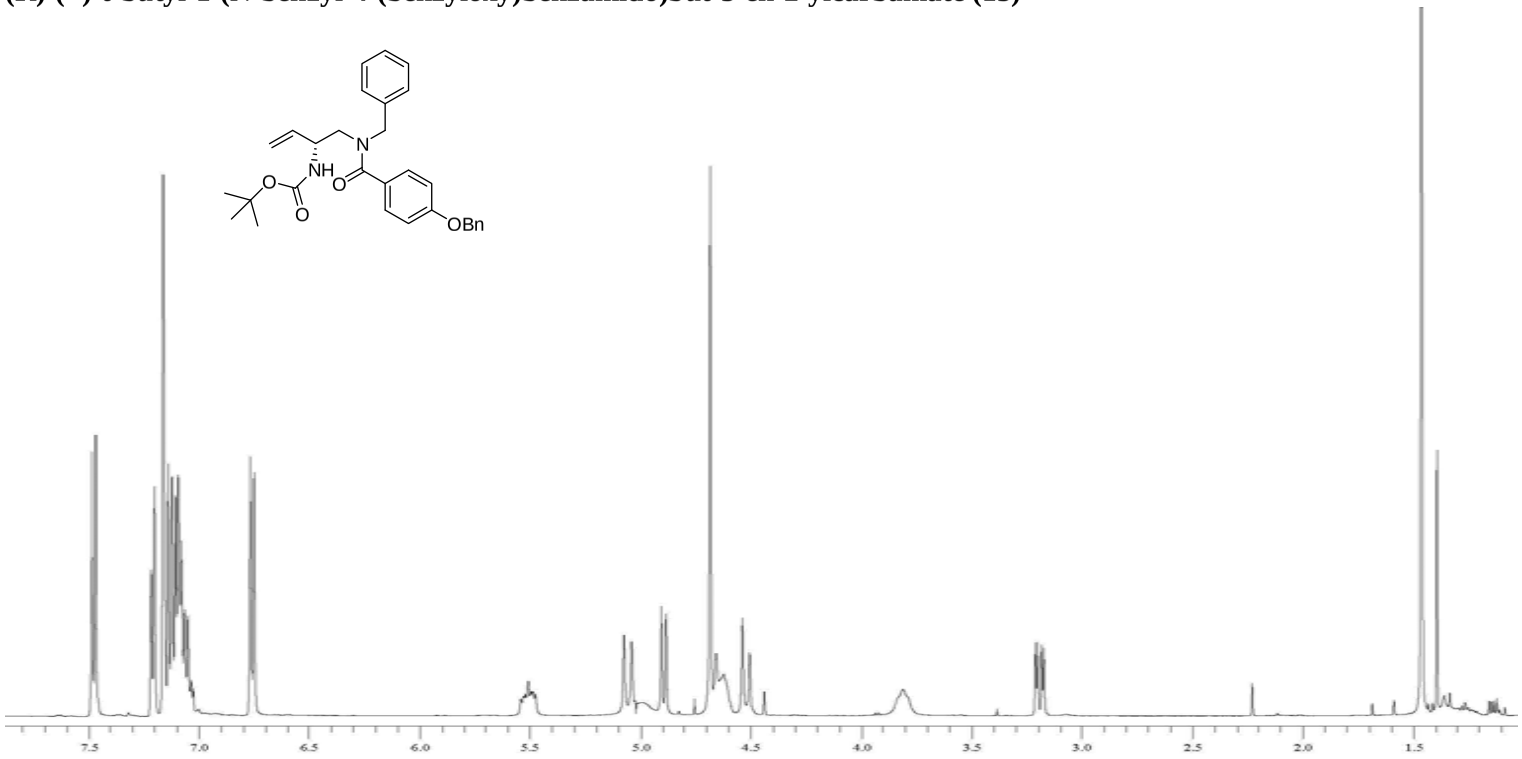
^{1}H NMR (C_6D_6, 75^{o}C, 500MHz)

(R)-(+)-Benzyl (R)-1-(N-benzylbenzamido)but-3-en-2-ylcarbamate (12)



^{13}C NMR (C_6D_6, 75^{o}C, 125MHz)

(R)-(+)-t-butyl-1-(N-benzyl-4-(benzyloxy)benzamido)but-3-en-2-ylcarbamate (13)



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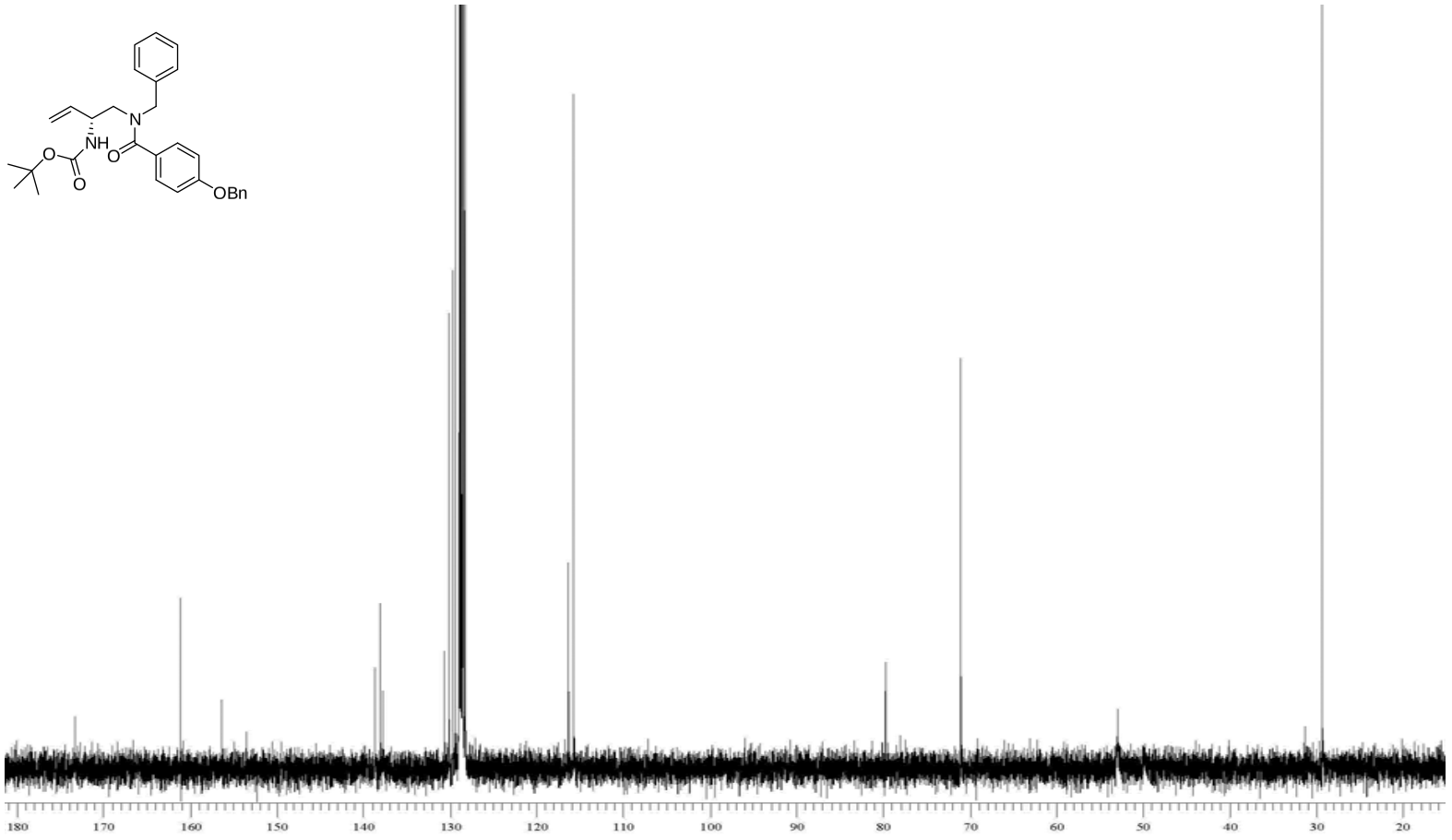
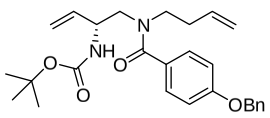
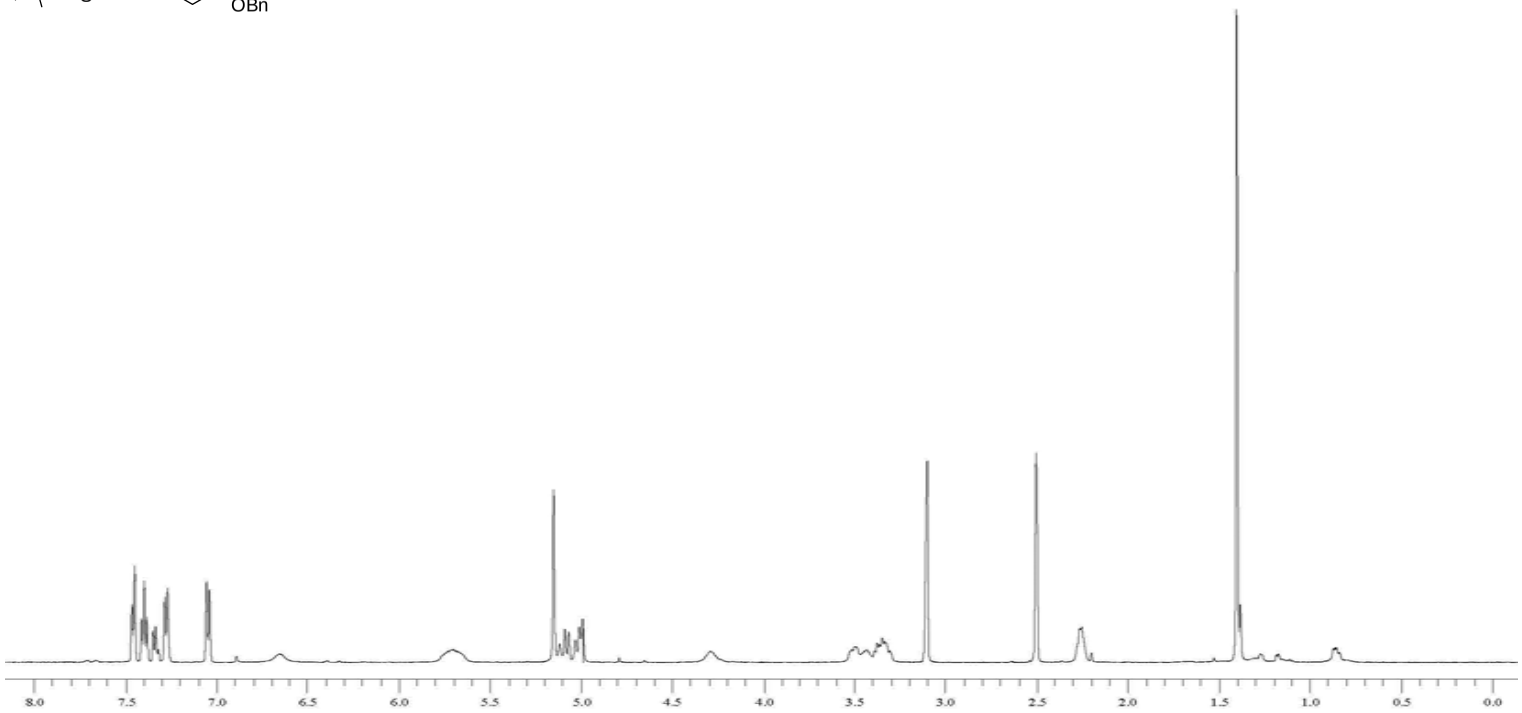
(R)-(+)-t-butyl-1-(N-benzyl-4-(benzyloxy)benzamido)but-3-en-2-ylcarbamate (13)



^{13}C NMR (C_6D_6, 75^{o}C, 125MHz)

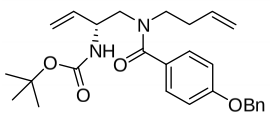
(R)-t-butyl-1-(4-(benzyloxy)-N-(but-3-enyl)benzamido)but-3-en-2-ylcarbamate (14)





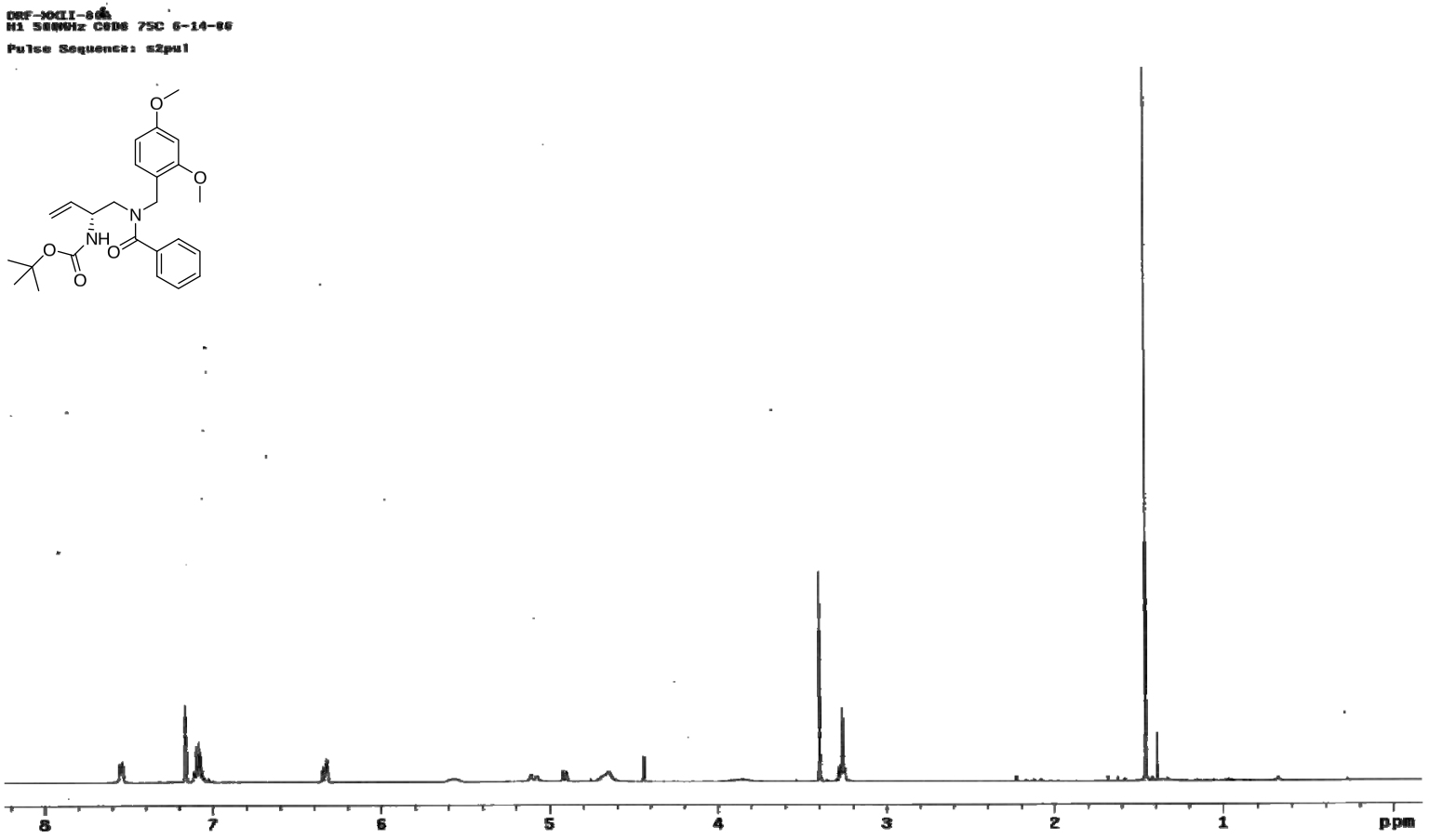
^{1}H NMR (DMSO, 500MHz)

(R)-t-butyl-1-(4-(benzyloxy)-N-(but-3-enyl)benzamido)but-3-en-2-ylcarbamate (14)



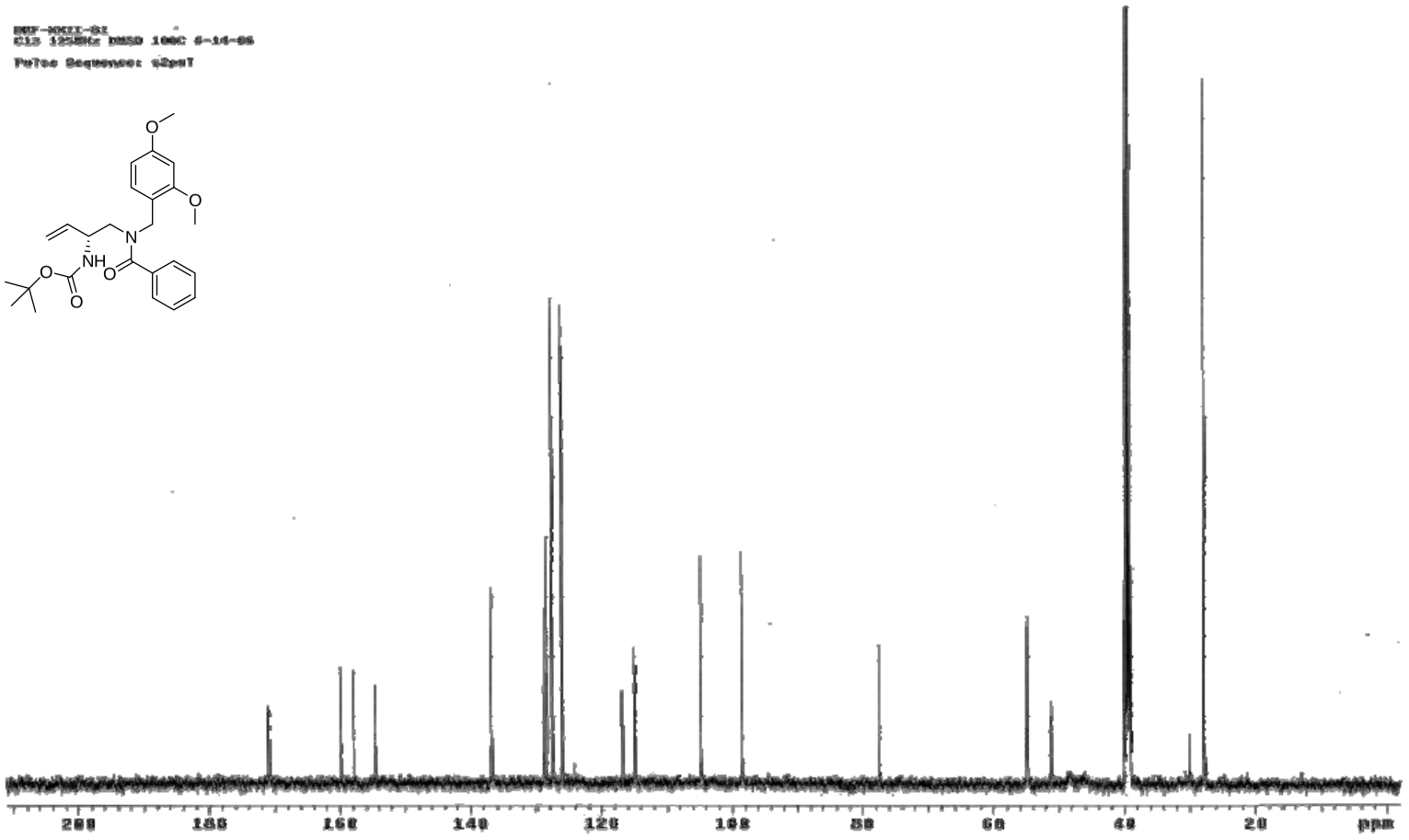
^{13}C NMR (DMSO, 80^{o}C, 125MHz)

(R) - (+) – tert - butyl (R) – 1 - (N - (2,4 - dimethoxybenzyl)benzamido) but – 3 – en – 2 –ylcarbamate (15)



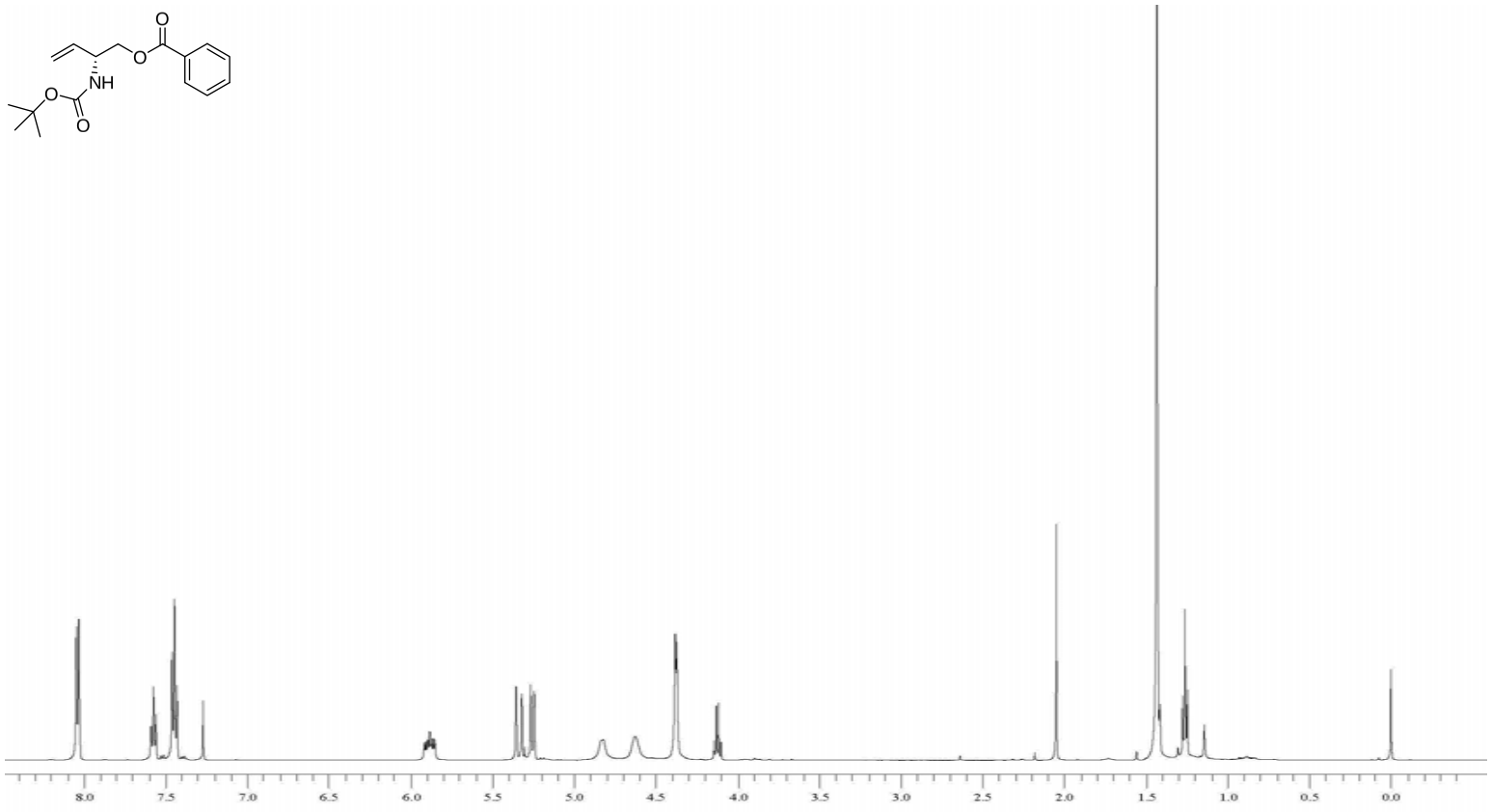
^{1}H NMR (C_6D_6, 75°C, 500MHz)

(R) - (+) – tert - butyl (R) – 1 - (N - (2,4 - dimethoxybenzyl)benzamido) but – 3 – en – 2 –ylcarbamate (15)



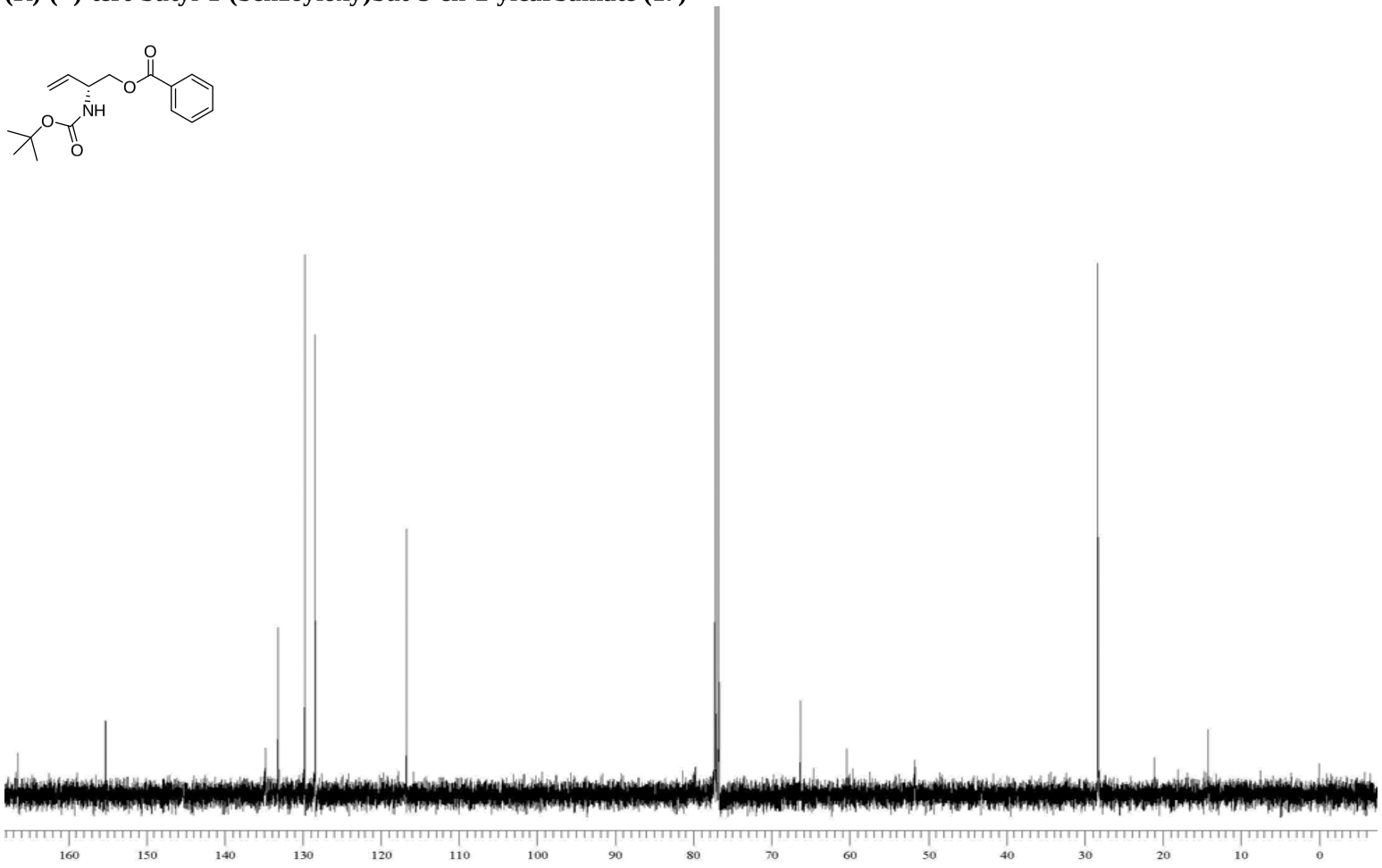
^{13}C NMR (DMSO, 100^{o}C, 125MHz)

(R)-(+)-tert-butyl-1-(benzoyloxy)but-3-en-2-ylcarbamate (17)



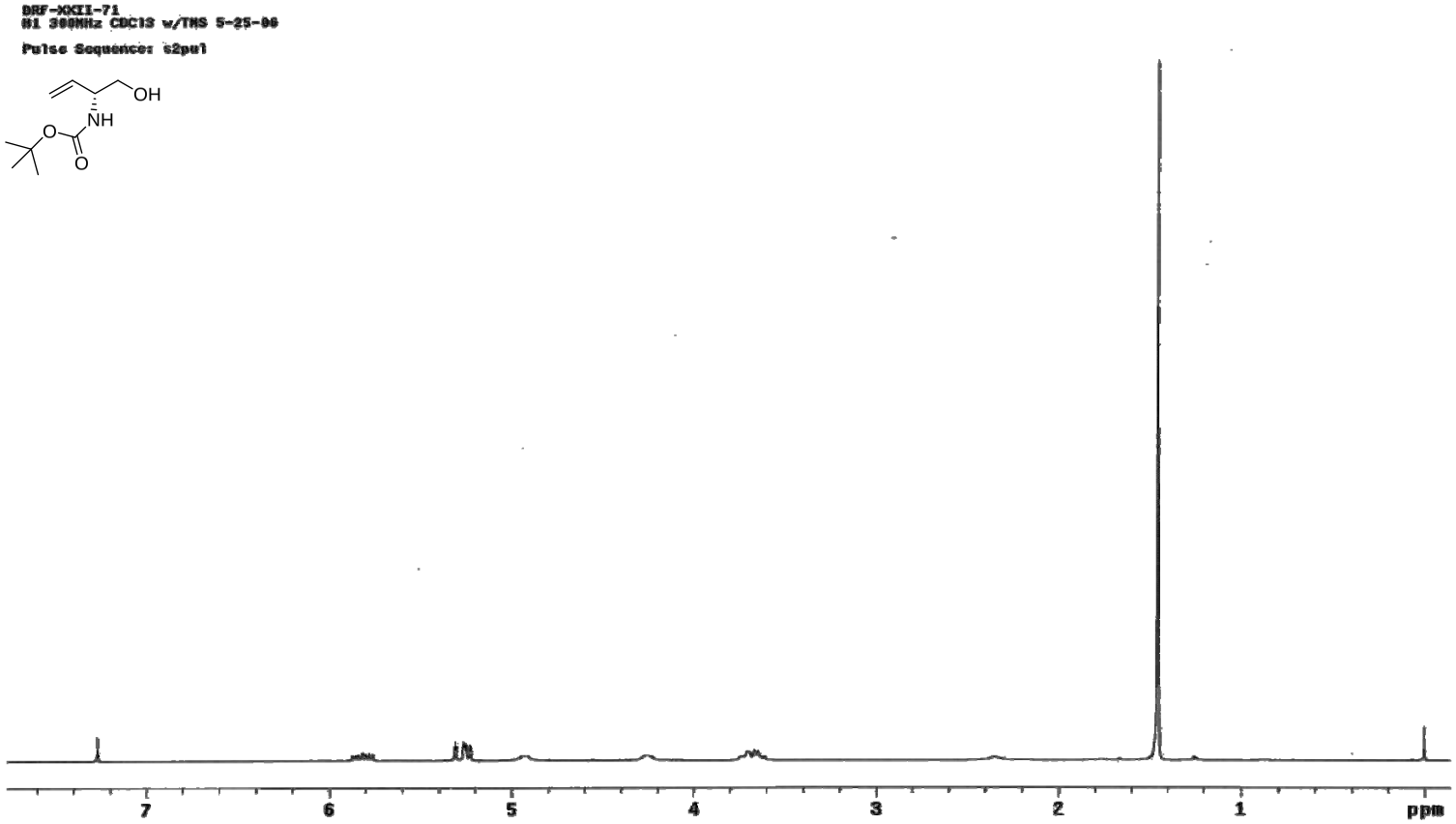
^{1}H NMR ($CHCl_3$, 400MHz)

(R)-(+)-tert-butyl-1-(benzoyloxy)but-3-en-2-ylcarbamate (17)



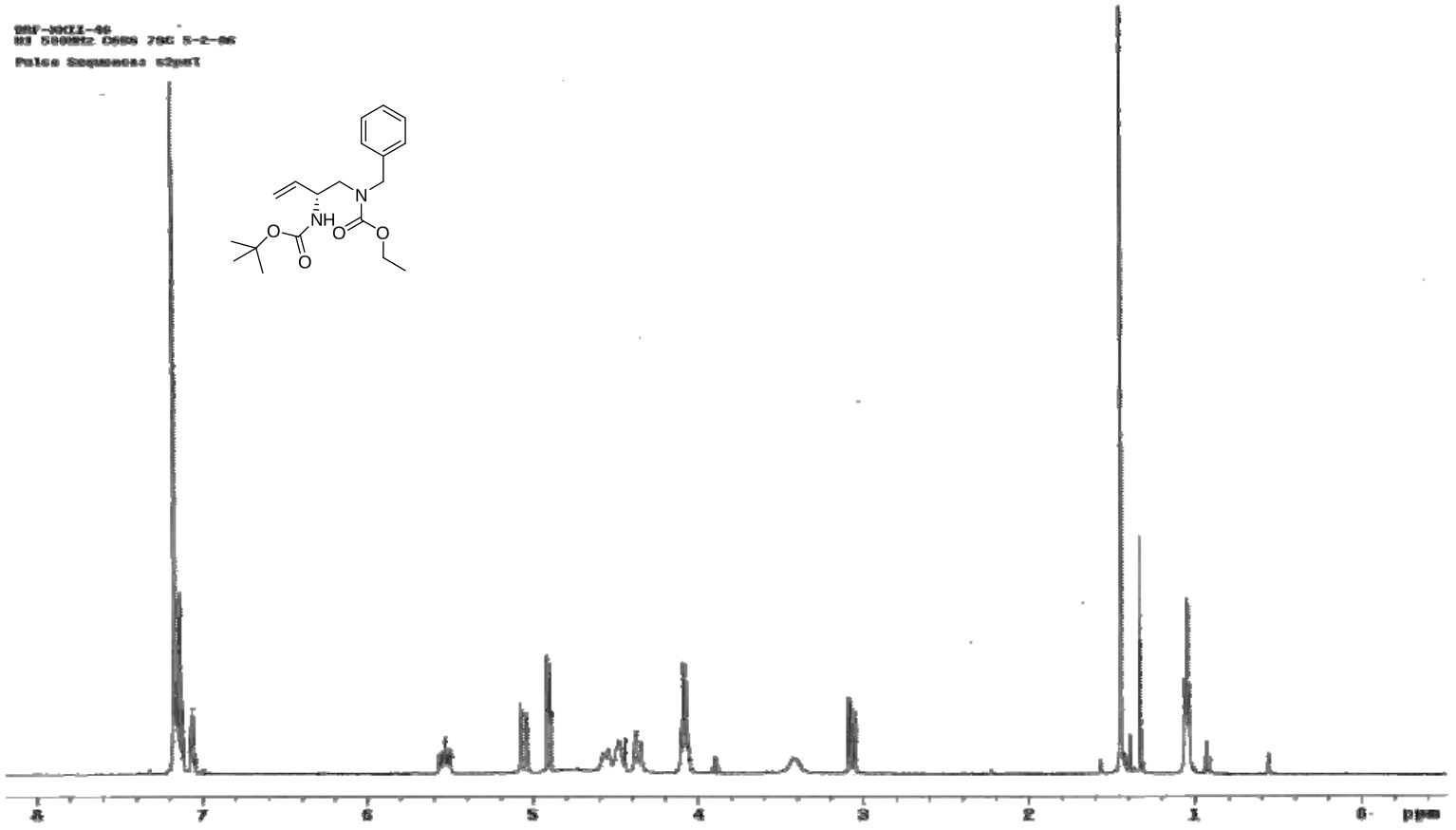
^{13}C NMR ($CHCl_3$, 100MHz)

(R)-(+)-tert-butyl-1-hydroxybut-3-en-2-ylcarbamate (18)



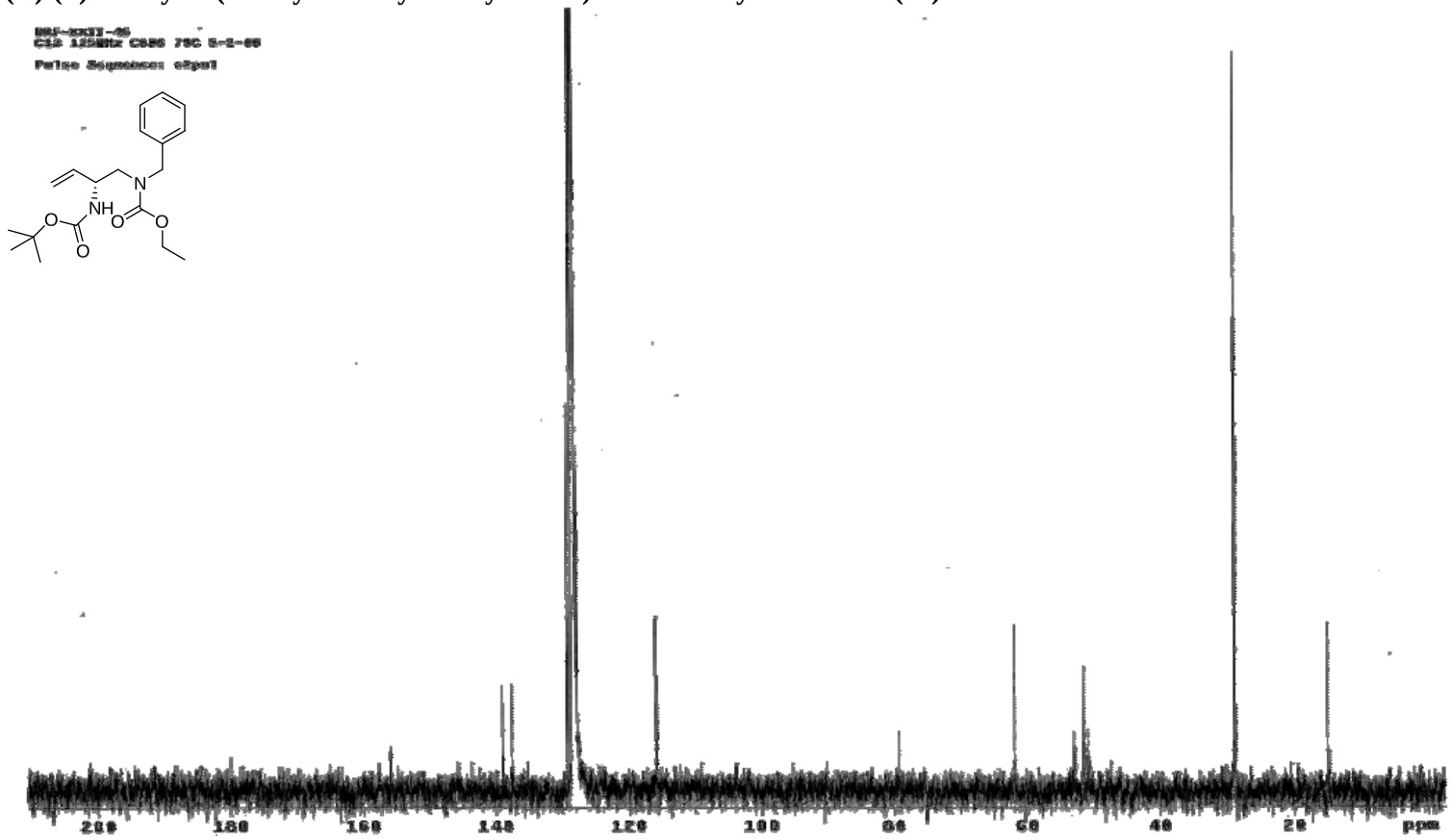
^{1}H NMR ($CHCl_3$, 300MHz)

(R)-(+)-t-Butyl-1-(N-ethylcarboxyl-benzylamino)-but-3-en-2-ylcarbamate (19)



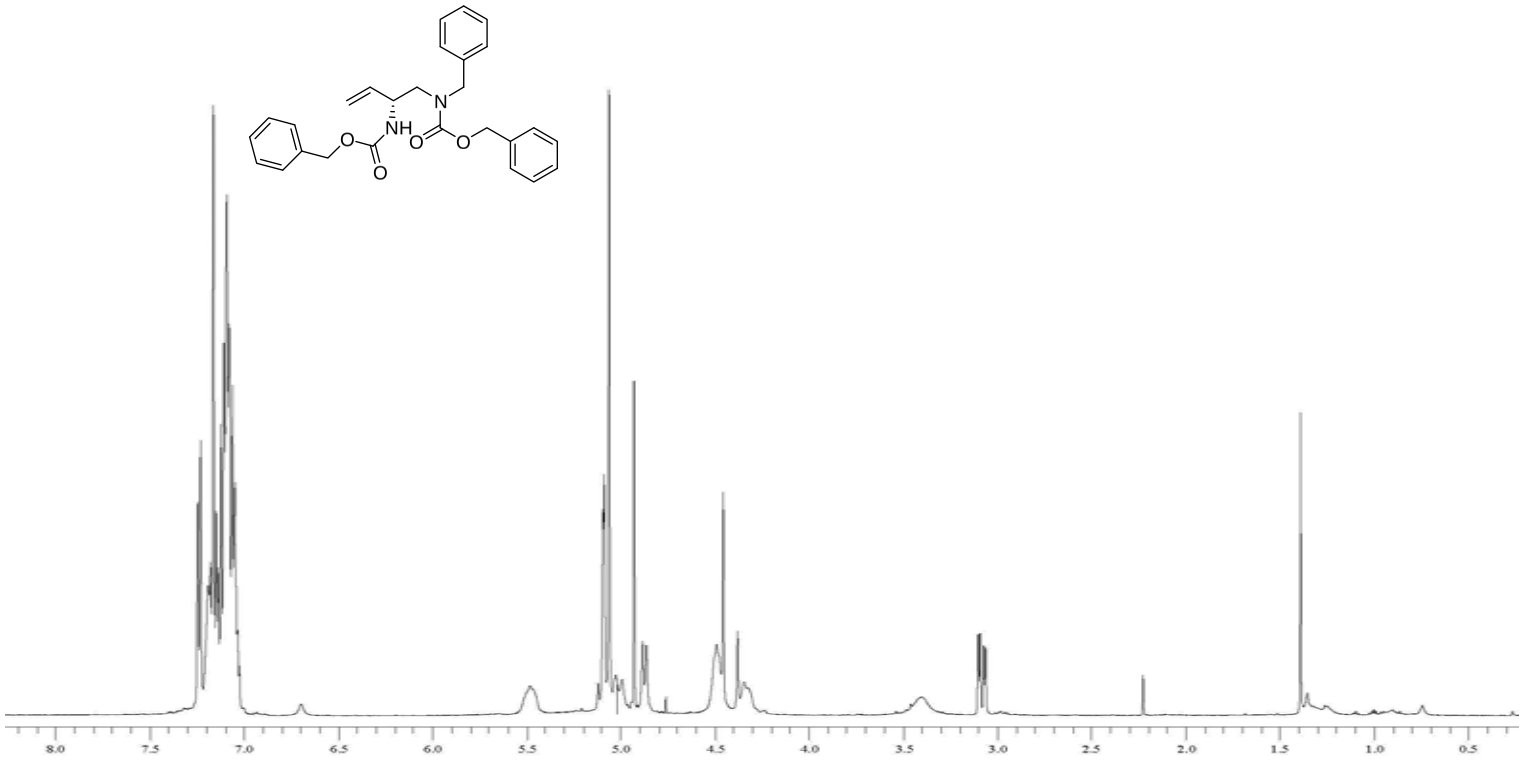
^{1}H NMR (C_6D_6, 75^{o}C, 500MHz)

(R)-(+)-t-Butyl-1-(N-ethylcarboxyl-benzylamino)-but-3-en-2-ylcarbamate (19)



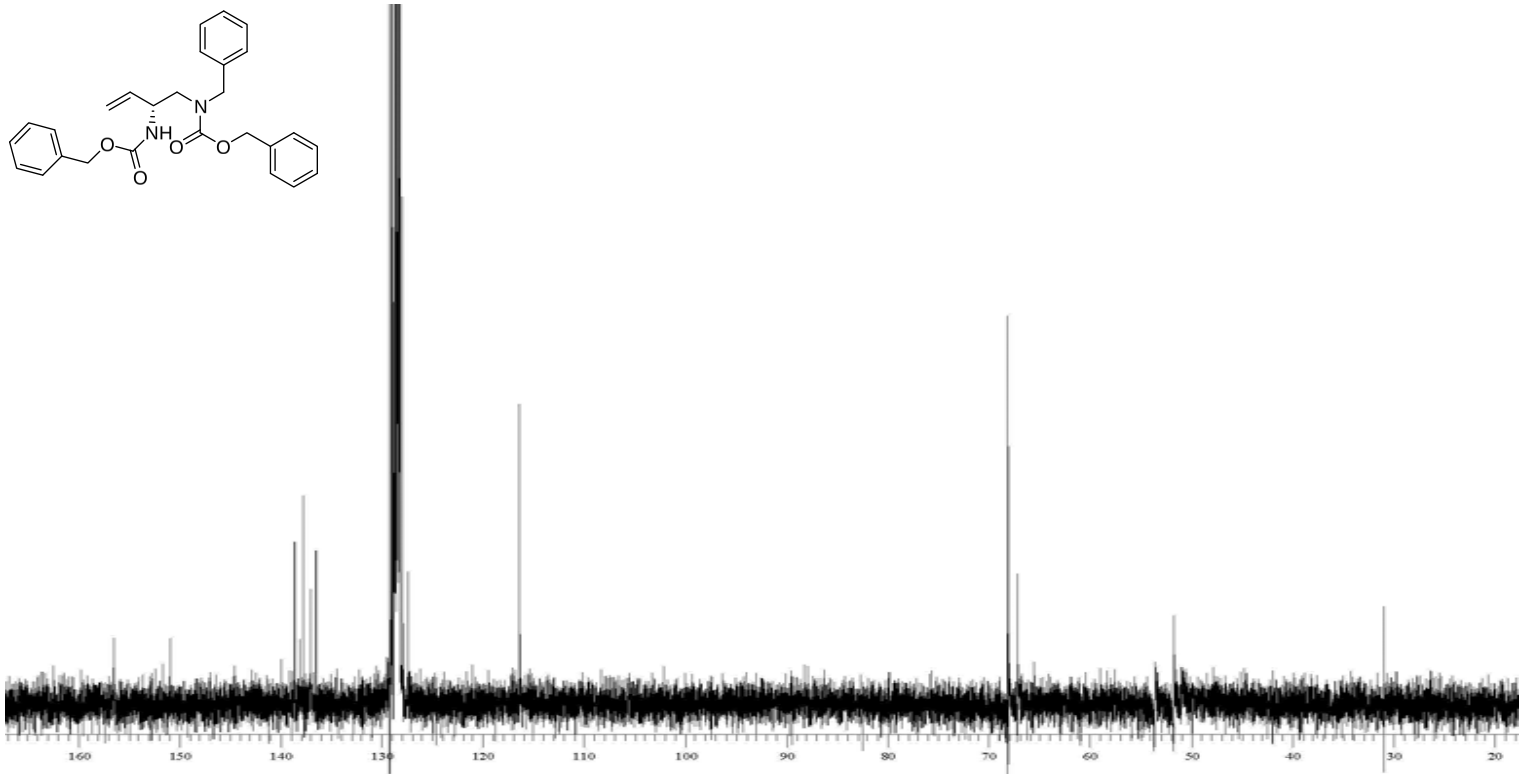
^{13}C NMR (C_6D_6, 75°C, 125MHz)

(R)-Benzyl-1-(N-benzylcarboxyl-benzylamino)-but-3-en-2-ylcarbamate (20)



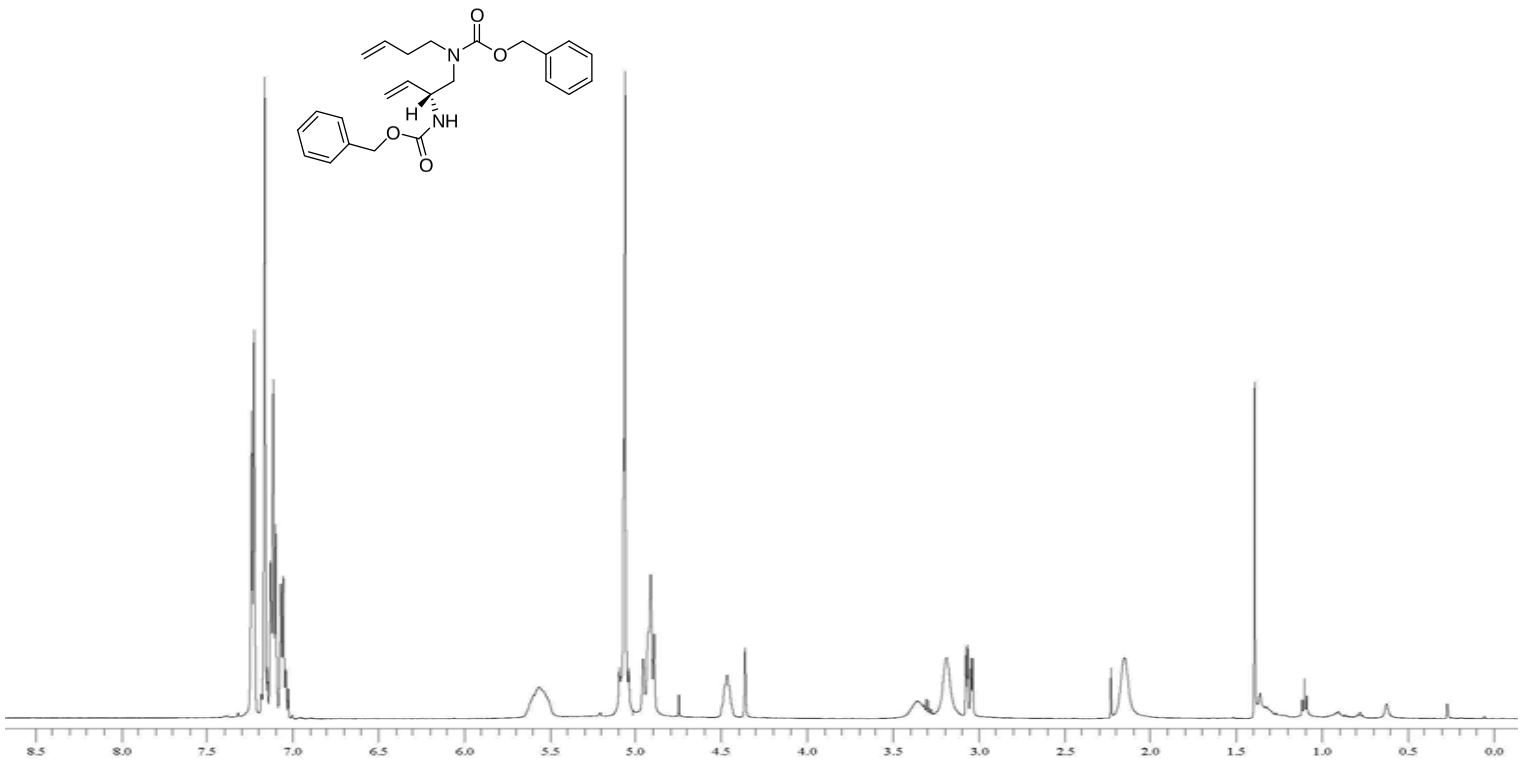
^{1}H NMR (C_6D_6, 75^{o}C, 500MHz)

(R)-Benzyl-1-(N-benzylcarboxyl-benzylamino)-but-3-en-2-ylcarbamate (20)



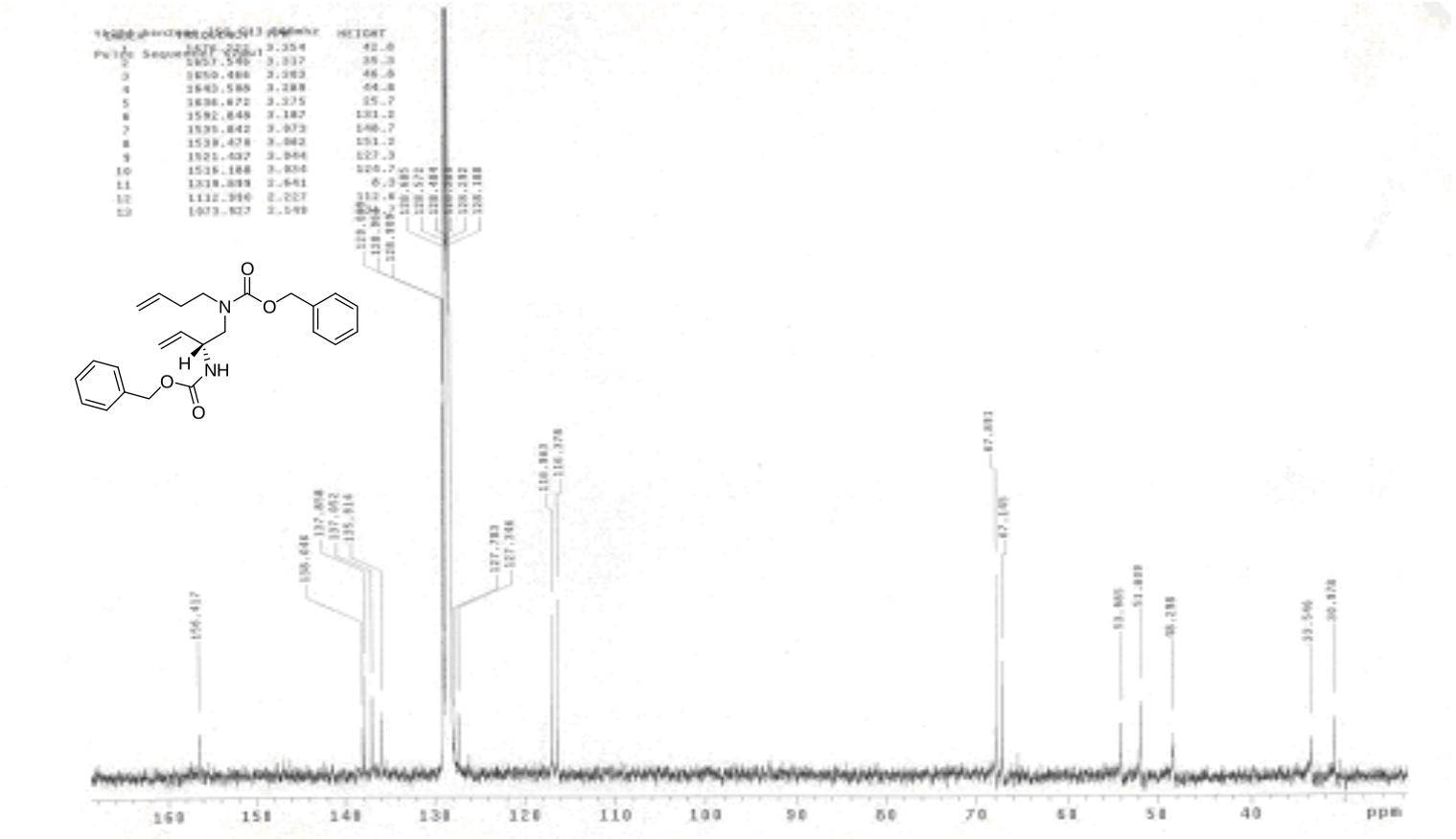
. **^{13}C NMR** (C_6D_6, 75°C, 125MHz)

(R)-Benzyl-1-(N-benzylcarboxyl-3-butenylamino)-but-3-en-2-ylcarbamate (21)



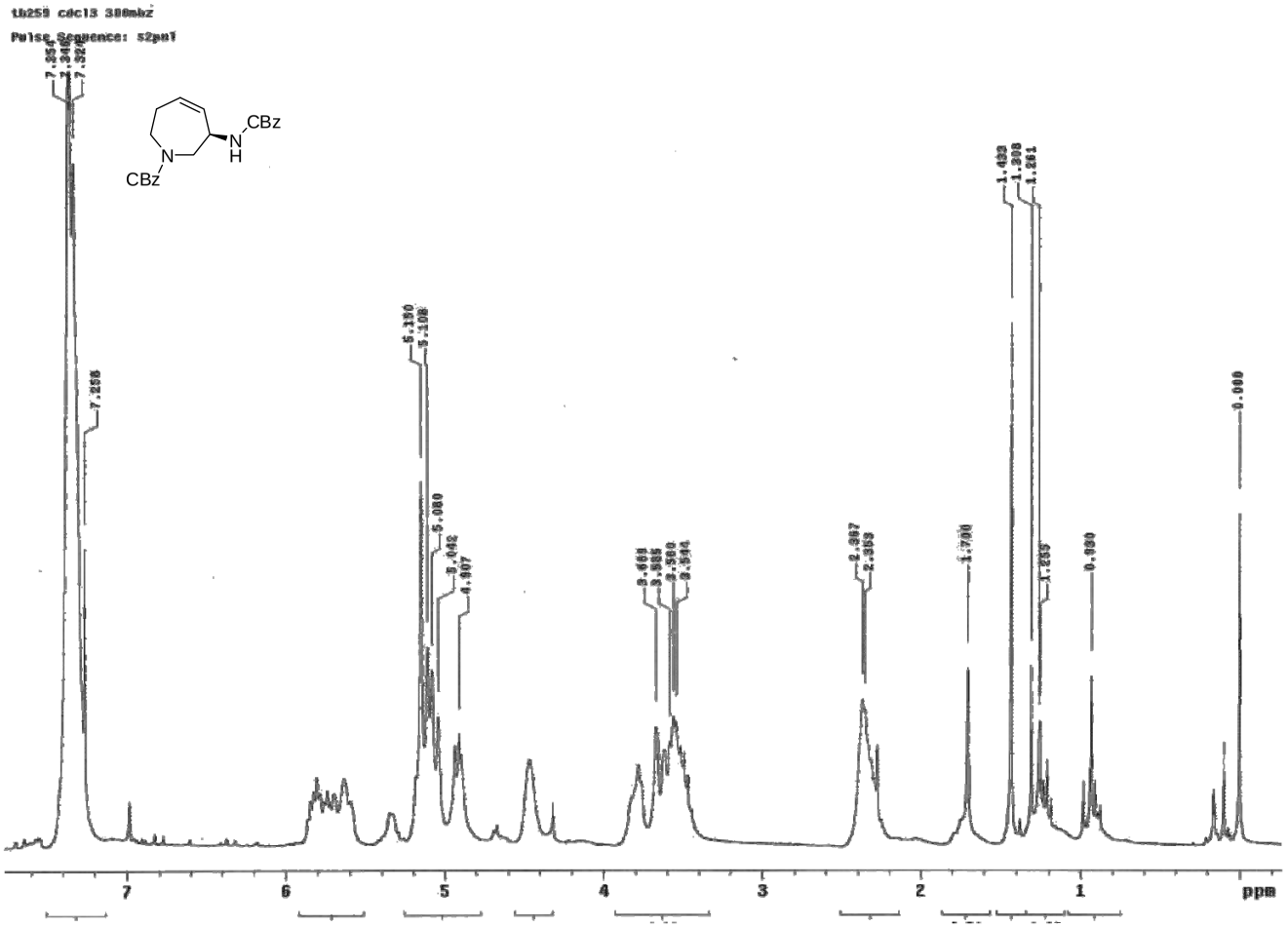
^{1}H NMR (C_6D_6, 75^{o}C, 500MHz)

(R)-Benzyl-1-(N-benzylcarboxyl-3-butenylamino)-but-3-en-2-ylcarbamate (21)



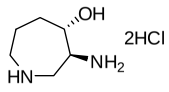
^{13}C NMR (C_6D_6, 75°C, 125MHz)

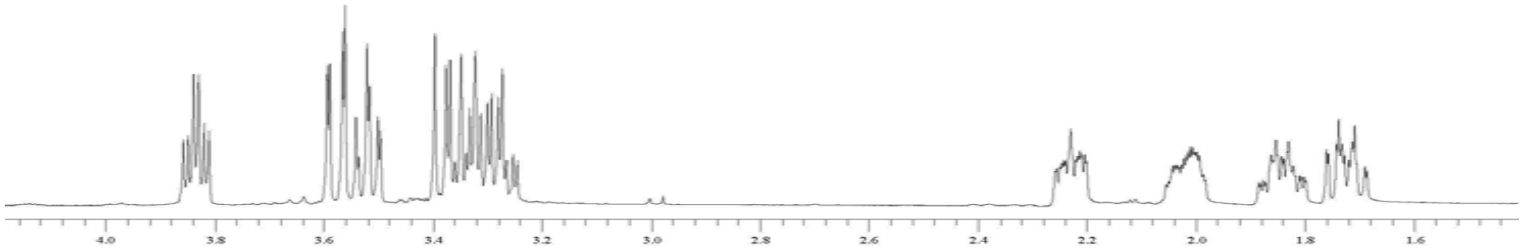
(R,Z)-Benzyl-1-((benzyloxy)carbonyl)-2,3,6,7-tetrahydro-1H-azepin-3-ylcarbamate (22)



^{1}H NMR (C_6D_6, 75°C, 500MHz)

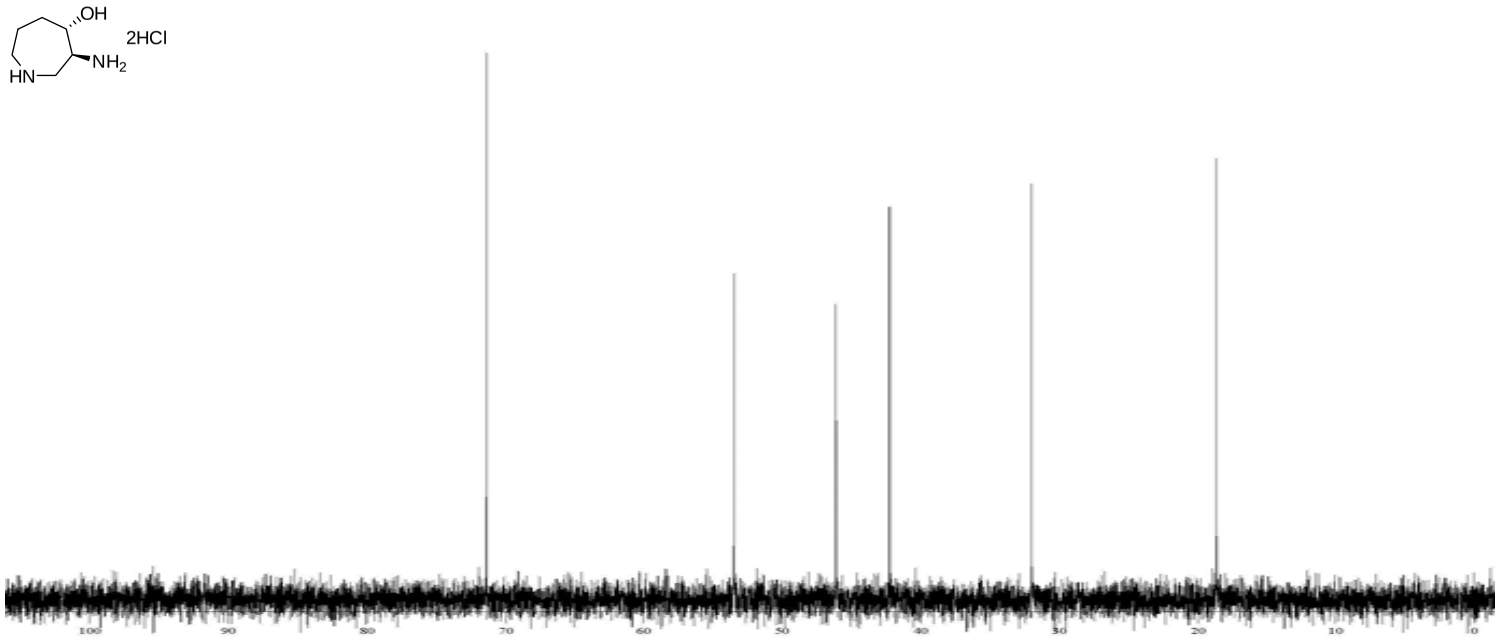
(3S,4S)-(+)-3-aminoazepan-4-ol dihydrochloride (23)





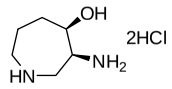
^{1}H NMR (D_2O, 500 MHz)

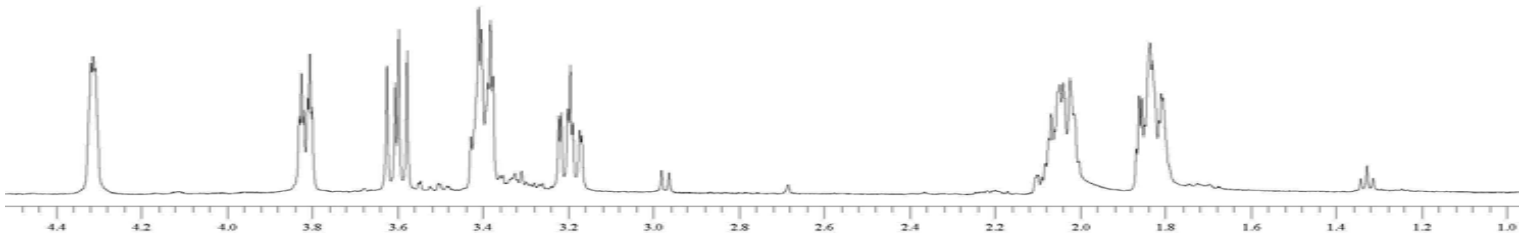
(3S,4S)-(+)-3-aminoazepan-4-ol dihydrochloride (23)



^{13}C NMR (D_2O, 125 MHz)

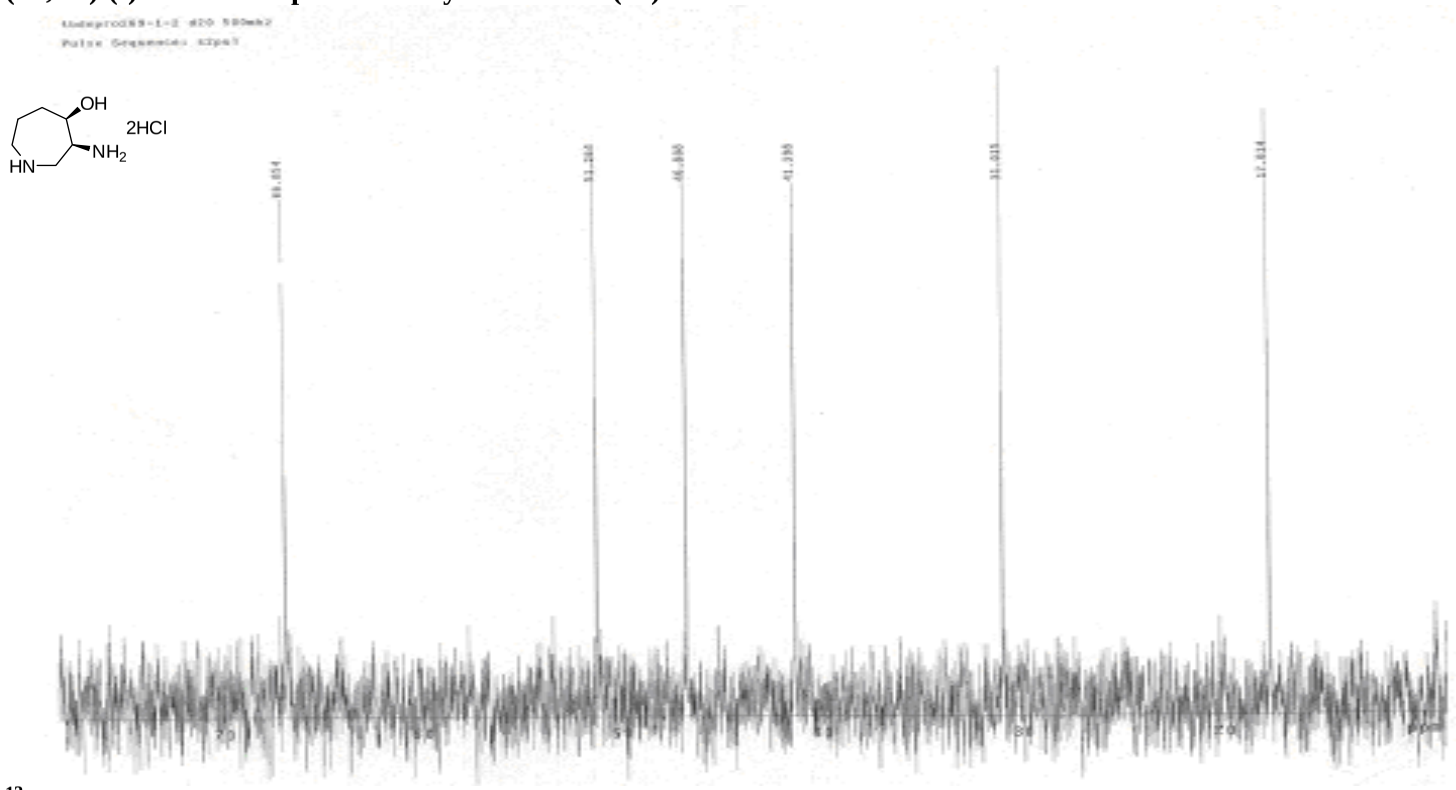
(3S,4R)-(-)-3-aminoazepan-4-ol dihydrochloride (26)





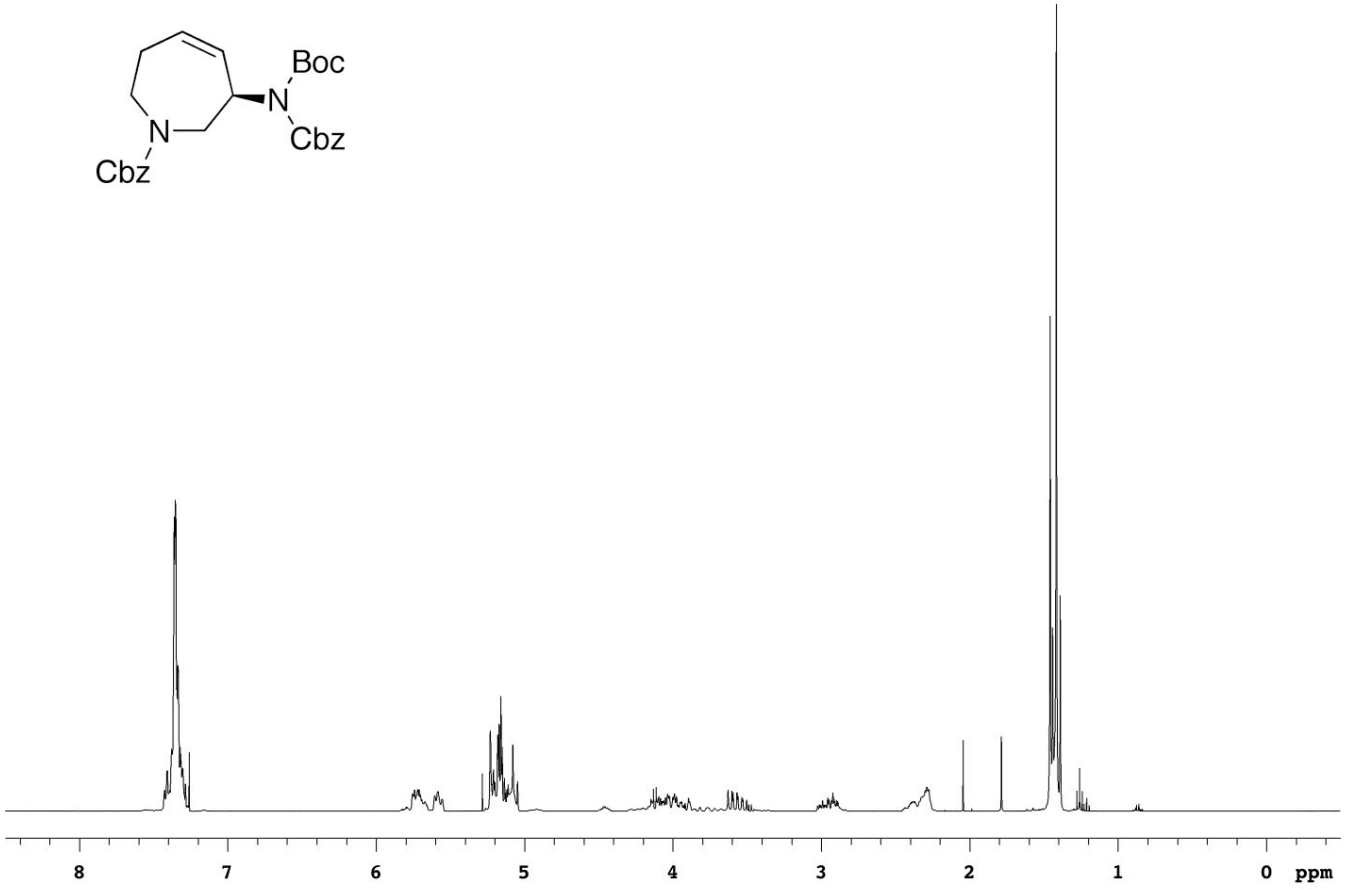
^{1}H NMR (D_2O, 500 MHz)

(3S,4R)-(-)-3-aminoazepan-4-ol dihydrochloride (26)



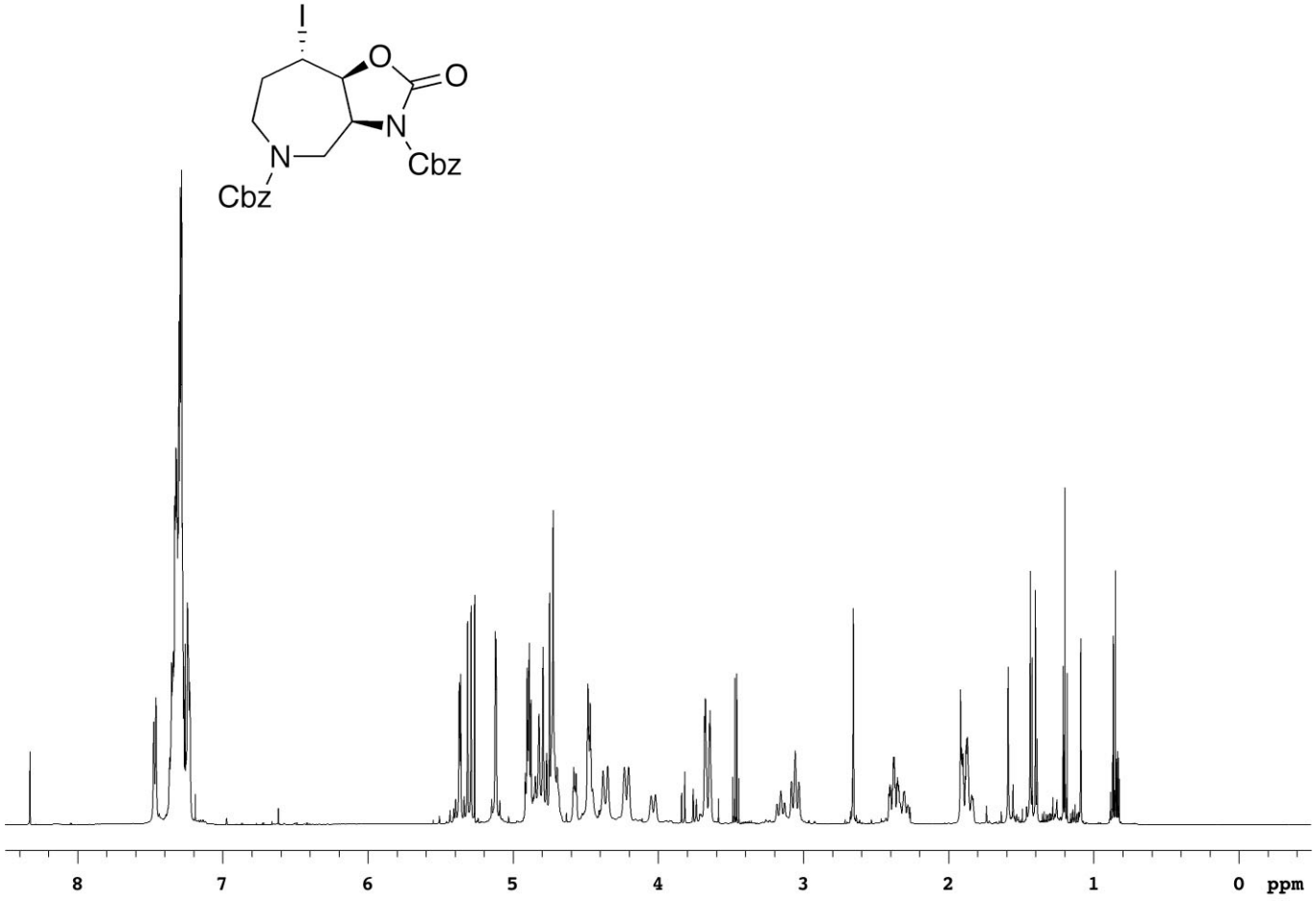
^{13}C NMR (D_2O, 125 MHz)

N-Boc-(R,Z)-Benzyl-1-((benzyloxy)carbonyl)-2,3,6,7-tetrahydro-1H-azepin-3-ylcarbamate



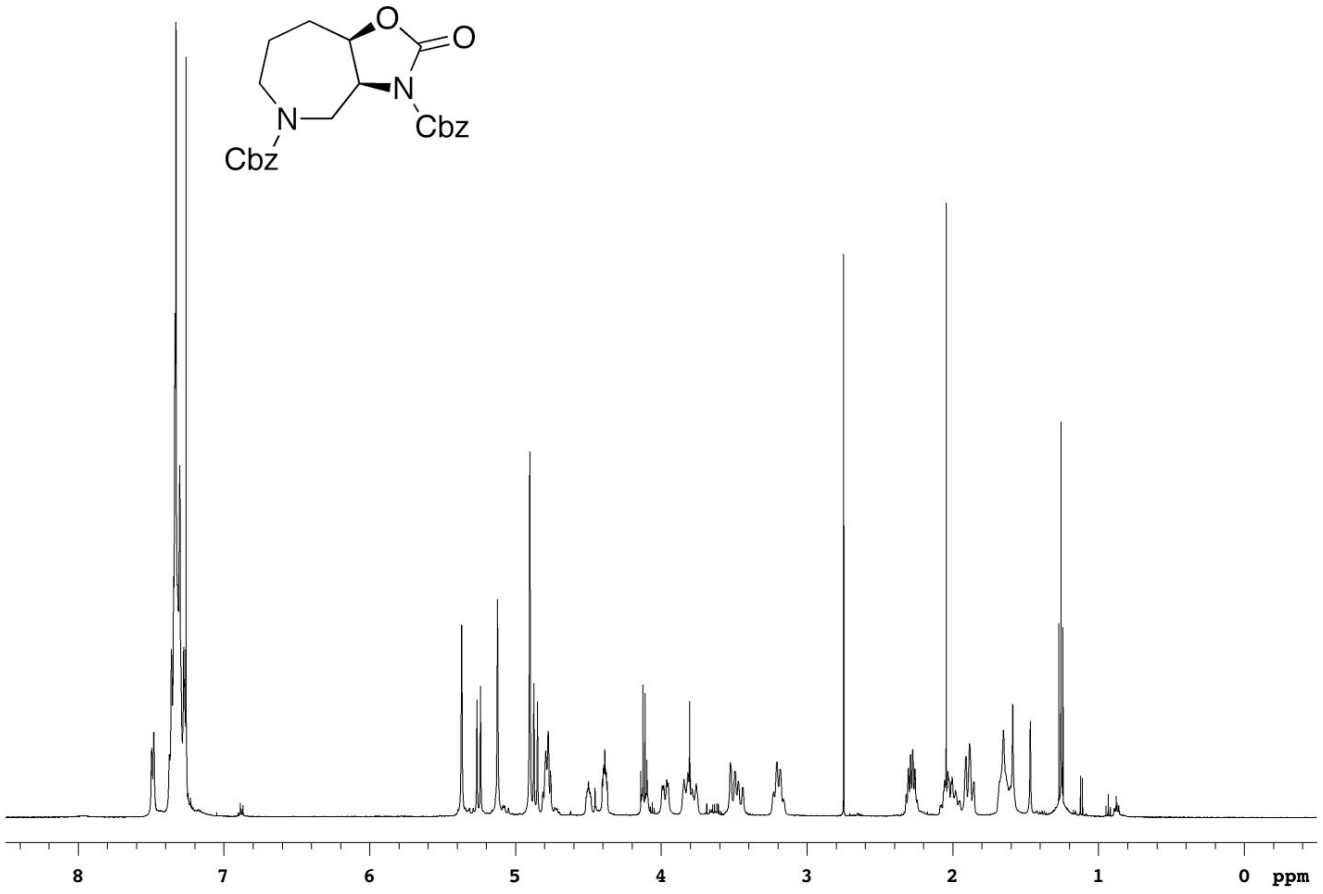
^{1}H NMR ($CDCl_3$, 400 MHz)

8-Iodo-2-oxo-hexahydro-1-oxa-3,5-diaza-azulene-3,5-dicarboxylic acid dibenzyl ester (24)



^{1}H NMR ($CDCl_3$, 500 MHz)

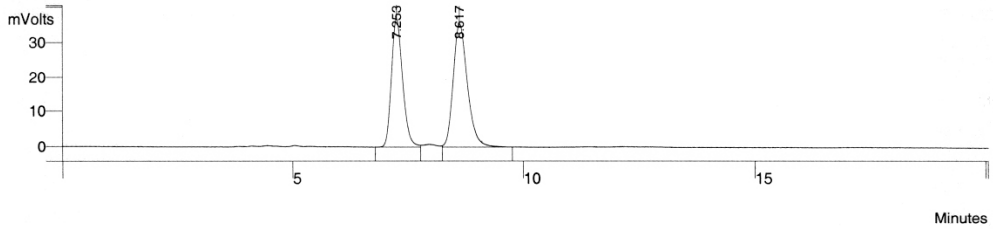
2-Oxo-hexahydro-1-oxa-3,5-diaza-azulene-3,5-dicarboxylic acid dibenzyl ester (25)



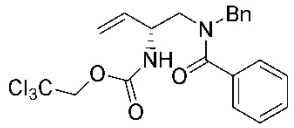
^{1}H NMR ($CDCl_3$, 500 MHz)

(+/-) 11, Chiralpack OD, 20% IPA in heptane

1.0 ml/min, 245nm

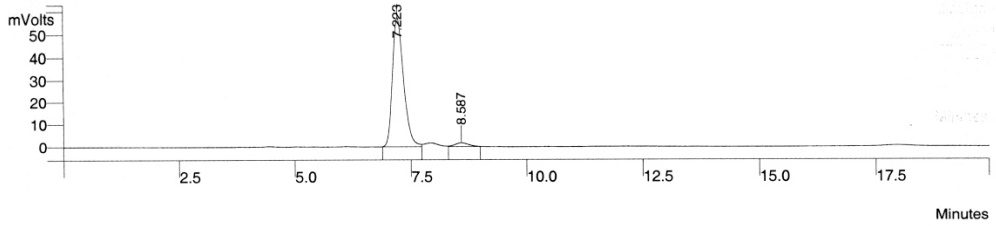


Peak No	Ret. Time (min)	Peak Area	Width 1/2 (sec)	Percent Area
1	7.253	623589	15.4	45.03
2	8.617	761375	19.1	54.97
		1384964		**100.00**

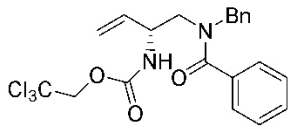


(+) 11, Chiralpack OD, 20% IPA in heptane

1.0ml/min, 245nm

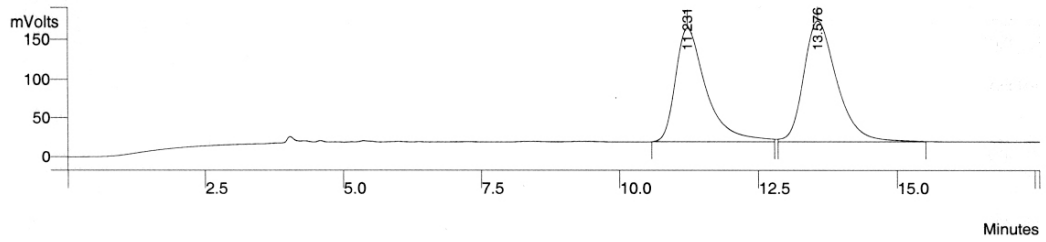


Peak No	Ret. Time (min)	Peak Area	Width 1/2 (sec)	Percent Area
1	7.223	961168	15.4	96.39
2	8.587	35955	17.5	3.61
		997123		**100.00**

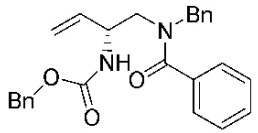


(+/-) 12, Chiralpack OD, 20% IPA in heptane

1.0 ml/min, 230nm

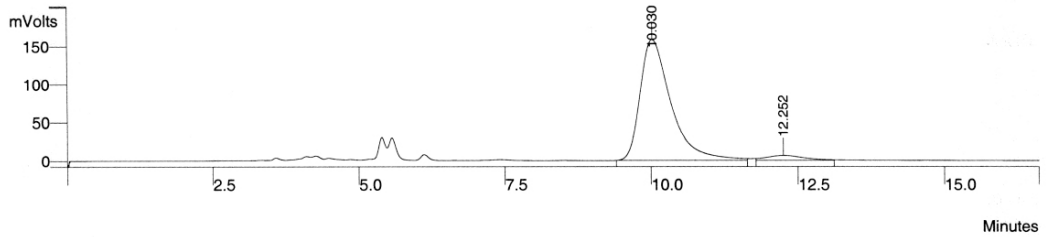


Peak No	Ret. Time (min)	Peak Area	Width 1/2 (sec)	Percent Area
1	11.231	5560850	34.7	46.58
2	13.576	6376336	36.9	53.42
		11937186		**100.00**

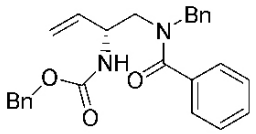


(+) 12, Chiralpack OD, 20% IPA in heptane

1.0 ml/min, 230nm

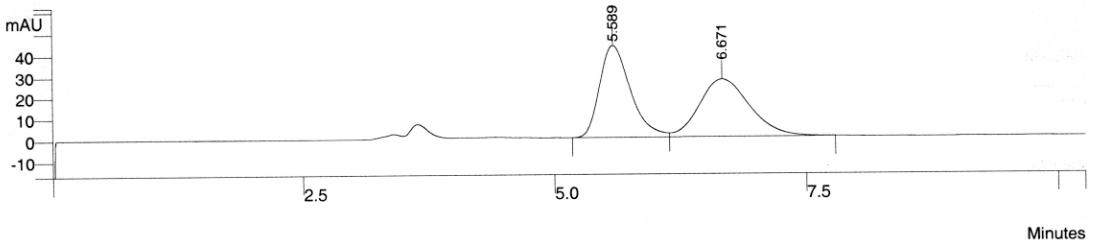


Peak No	Ret. Time (min)	Peak Area	Width 1/2 (sec)	Percent Area
1	10.030	5744488	32.8	95.22
2	12.252	288610	30.4	4.78
		6033098		**100.00**

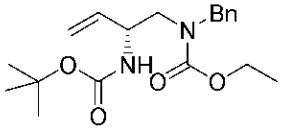


(+/-) 19, Chiralpack OJ, 8% IPA in heptane

1.0 ml/min, 225nm

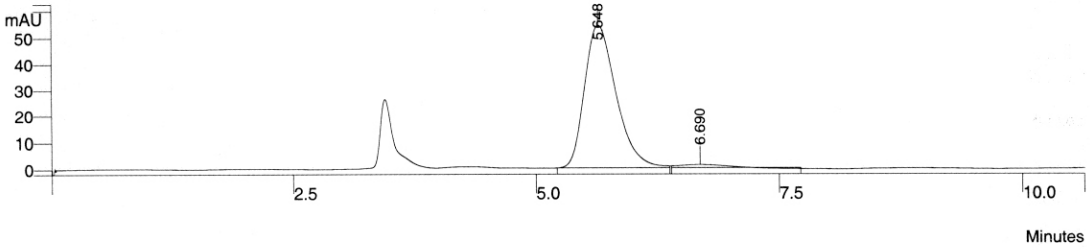


Peak No	Ret. Time (min)	Peak Area	Width 1/2 (sec)	Percent Area
1	5.589	918093	19.4	49.91
2	6.671	921371	32.3	50.09
		1839464		**100.00**



(+) 19, Chiralpack OJ, 8% IPA in heptane

1.0 ml/min, 225nm



Peak No	Ret. Time (min)	Peak Area	Width 1/2 (sec)	Percent Area
1	5.648	1221418	20.6	97.50
2	6.690	31364	18.9	2.50
		1252782		**100.00**