SUPPORTING INFORMATION (PART-1)

Synthesis of Chlorinated Bicyclic C-Fused Tetrahydrofuro[3,2-c]azetidin-2-ones

Ram N. Ram* Neeraj Kumar and Nem Singh

Department of Chemistry, Indian Institute of Technology, Delhi, Hauz Khas, New Delhi-110016, India
Email: rnram@chemistry.iitd.ernet.in

Table of contents:

1. Experimental:

1.1 General remarks:

Dry and freshly distilled solvents were used for carrying out all the reactions. Tetrahedrofuran (THF) and benzene were dried by distillation after a persistent blue color was observed on treating them with enough amount of sodium in the presence of benzophenone. 1,2-Dichloroethane (DCE) was dried by distillation over P_2O_5. IR spectra were recorded on FT IR spectrophotometer of the solid samples as KBr pellet and of the liquid samples as neat liquid film placed between KBr disks. Absorption intensities are indicated by s, m and w for strong, medium and weak absorptions, respectively. NMR spectra were recorded on 300 MHz FT NMR spectrometer in $CDCl_3$ with TMS as internal standard. Multiplicities are indicated by following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of a doublet), dt (doublet of a triplet), td (triplet of a doublet), tt (triplet of a triplet), qd (quartet of a doublet), ddd (doublet of a doublet of a doublet), tdd (triplet of a doublet of a doublet). High resolution mass spectra (HRMS) were recorded on a hybrid quadrupole-TOF LC/MS mass spectrometer using the electron spray (ESI) positive ion mode. Melting points were determined in an electrically heated apparatus by taking the sample in a glass capillary sealed at one end and are uncorrected. The progress of the reaction was monitored by TLC using a glass plate coated with a TLC grade silica gel. Iodine was used for visualizing the spots. Solvents were evaporated on a rotary evaporator under reduced pressure using an aspirator. The products were separated and purified by column chromatography using silica gel (60-120 mesh) or neutral alumina (60-325 mesh) as the solid support. *n*-Hexane and its mixtures with ethyl acetate in variable proportions were used as the solvent for elution.

1.2. General preparative procedures

1.2.1. Imidoyl chlorides:

All the imidoyl chlorides used are known in the literature.[1] These were prepared by the reaction of *sec*.-amides with thionyl chloride according to the reported procedure.[1] A mixture of thionyl chloride (50 mL) and the amide (25 mmol) was refluxed for 2 h in a 100 mL round bottom flask protected with a calcium chloride guard tube. The reaction

mixture was cooled, the condenser was set for downward distillation and the excess thionyl chloride was removed under reduced pressure by distillation. The residual mass was stirred in *n*-hexane (50 mL) at 45-50 ^{o} for 1 h and filtered. Evaporation of the filtrate afforded the imidoyl chloride. The product was further purified by Kugelrohr distillation to give the pure imidoyl chlorides in nearly quantitative yields.

1.2.2 Imidates

The benzimidates were prepared by reaction of imidoyl chlorides with alcohols as per a literature procedure[2] with slight modification. To a suspension of NaH [0.288g, (0.48 g of 60% dispersion in oil), 12 mmol] in THF (10 mL), cooled to 0 °C was added a solution of the respective alcohol (10 mmol) in dry THF (10 mL) drop wise over 15 min. The reaction mixture was stirred for 30 min at 0 °C and another 30 min at room temperature (22-30 ^{o}C). After that the reaction mixture was again cooled to 0 °C and then a solution of the benzimidoyl chloride[1] (10 mmol) in dry THF (10 mL) was added drop wise over 5 min. The ice-bath was then removed and the mixture was stirred at room temperature for 20 h. Then 30 mL ethyl acetate and 10 mL water were successively added to the reaction mixture. The resulting solution was washed with brine (2×10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the imidates of adequate purity in quantitative yields. These imidates were used without any further purification in the next step as they decompose on column chromatography.

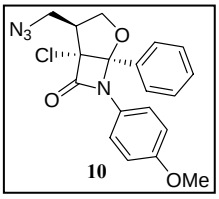
1.2.3. Monocyclic β-lactams 2a-2k, 4, 6, 8:

To a solution of the allylic imidate **1** (10 mmol) in benzene (50 mL) was added triethylamine (2.02 g, 2.8 mL, 20 mmol) through a syringe at room temperature (22-30 ^{o}C). A solution of dichloroacetyl chloride (2.9 g, 1.9 mL, 20 mmol) in benzene (5 mL) was added drop wise over 15 min and the reaction mixture was stirred for 2 h at the same temperature after which time TLC indicated the disappearance of the imidate. The reaction mixture was filtered to separate the hydrochloride salt and the filtrate was washed with brine (3×10 mL), dried over Na_2SO_4 and evaporated under reduced pressure on a rotary evaporator. The residue was purified by column chromatography (neutral alumina, *n*-hexane:EtOAc = 95: 5 v/v) followed by recrystallization from *n*-hexane-diethyl ether to obtain the pure product. Thus, the 3,3-dichloro-β-lactams **2a-2k**, **4**, **6** and **8** were obtained in 48-84% yields.

1.2.4. Tetrahydrofuro[3,2-c]azetidin-2-ones 3a-3k, 5, 7, 9: CuCl/PMDETA-catalyzed ATRC of the substituted 3,3-dichloro-β-lactams 2a-2k, 4, 6, 8:

A two-neck round bottom flask fitted with a rubber septum was connected to a Schlenk tube through a condenser. The flask was evacuated and dried by heating with a flame while the vacuum pump was turned on. The flask was then filled with dry nitrogen. A mixture of the 3,3-dichloro-β-lactams **2a-2k, 4, 6** or **8** (10 mmol), CuCl (0.6 g, 6 mmol, 60 mol%) and a magnetic bar were placed in the flask under continuous flow of nitrogen, which was immediately followed by the addition of degassed dichloroethane (40 mL). To this suspension was injected PMDETA (1.04 g, 1.25 mL, 6 mmol, 60 mol%) and the mixture was heated at reflux with stirring. The progress of the reaction was monitored by TLC, which indicated the completion of the reaction after 4 h. The reaction mixture was cooled, filtered and evaporated to give the crude product which was purified by column chromatography on silica gel column using a mixture of *n*-hexane and ethyl acetate (90:10 v/v) as the eluting solvent followed by recrystallization of the solid products from *n*-hexane-diethyl ether. Thus, the pure fused bicyclic β-lactams **3a-3k, 5, 7** and **9** were obtained in 55-84% yields.

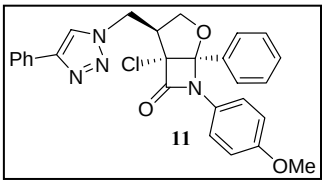
1.3. 4-Azidomethyl-3-chloro-1-(4-methoxyphenyl)-6-phenyltetrahydro furano[3,2-c]azetidin-2-one 10**:**



It was prepared by substitution reaction of the bicyclic lactam **3e** with sodium azide following a typical procedure reported in the literature.[3] To a solution of the β-lactam **3e (**0.378 g, 1 mmol) in 10 mL of DMF was added sodium azide (0.390 g, 6 mmol) and the solution was stirred at 65 °C for 12 h. The solution was diluted with 30 mL of water and extracted twice with 30 mL of ethyl acetate. The organic layer was washed with brine (2×5 mL), dried (Na_2SO_4) and evaporated under reduced pressure. The residual mass was purified by a rapid short path column (silica gel) chromatography using a mixture of *n*-hexane-ethyl acetate (9:1 v/v) to give the pure azide **10** (0.248 g, 65%) which was recrystallized as a white crystals, mp 90-92 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54-7.39 (m, 7H), 6.84-6.81 (m, 2H), 4.64 (dd, *J* = 9.9, 7.5 Hz, 1H), 3.96 (dd, *J* = 12.6, 4.8 Hz, 1H), 3.88 (t, *J* = 10.7 Hz, 1H), 3.77 (s, 3H), 3.62 (t, *J* = 11.4 Hz, 1H), 2.87-2.80 (m, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.2 (C), 157.1 (C), 131.7 (C),

129.9(CH), 128.6 (CH), 127.9 (C), 127.2 (CH), 119.9 (CH), 114.4 (CH), 101.0 (C), 81.0 (C), 69.5 (CH_2), 55.4 (CH_3), 48.89 (CH_2), 48.71 (CH) ppm; IR (KBr): ν_{max} 2998(w), 2923(w), 2835(w), 2102(s), 1765(s), 1512(s), 1380(m), 1249(s), 1059(m), 1031(m), 827(m), 739(w), 691(w) cm^{-1}; HRMS calcd for $[C_{19}H_{17}N_4O_3Cl + K]^+$ 423.0626, found 423.0629.

1.4. 3-chloro-1-(4-methoxyphenyl)-6-pheny-4-(4-phenyl-1,2,3-triazol-1-ylmethyl)tetrahydrofuro[3,2-c]azetidin-2-one 11:



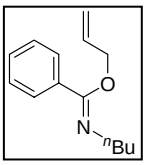
11

It was prepared by a method similar to that reported in the literature for azide-alkyne click reaction.[3] To a solution of the azide **10** (0.193 g, 0.5 mmol) in *t*-BuOH (10 mL) was added phenyl acetylene (0.102 g, 1.0 mmol) through a syringe. This was followed by addition of a solution of $CuSO_4 \cdot 5H_2O$ (0.013 g, 0.05 mmol, 10 mol %) and sodium ascorbate (0.020 g, 0.10 mmol, 20 mol %) in water (2 mL). The solution was stirred at 65 °C for 12 h after which time TLC indicated the disappearance of the azide. The reaction mixture was evaporated under reduced pressure. The residual mass was purified by silica gel column chromatography using a mixture of *n*-hexane and ethyl acetate (80:20) as the solvent for elution to obtain the triazolyl-β-lactam **11** (0.158 g, 65%) which was recrystallized as a yellow crystals, mp: 48-50 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.84 (d, *J* = 7.2 Hz, 2H), 7.50-7.32 (m, 10H), 6.82 (d, *J* = 9.0 Hz, 2H), 4.87-4.70 (m, 2H), 4.64 (dd, *J* = 9.8, 7.7 Hz, 1H), 4.02 (t, *J* = 10.7 Hz, 1H), 3.76 (s, 3H), 3.28-3.22 (m, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.3 (C), 157.2 (C), 147.8 (C), 131.4 (C), 130.2 (C), 130.0 (CH), 128.86 (CH), 128.65 (CH), 128.3 (C), 127.8 (CH), 127.3 (CH), 125.7 (CH), 121.0 (CH), 120.0 (CH), 116.2 (CH), 114.5 (CH), 101.3 (C), 80.8 (C), 69.3 (CH_2), 55.4 (CH_3), 49.2 (CH), 47.8 (CH_2) ppm; IR (KBr): ν_{max} 2923(w), 2851(w), 1763(s), 1511(s), 1454(m), 1382(m), 1247(s), 1033(m), 829(m), 761(m), 696(m) cm^{-1}; HRMS calcd for $[C_{27}H_{23}N_4O_3Cl + K]^+$ 525.1096, found 525.1094.

2. Spectroscopic data

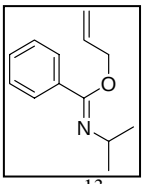
2.1. Imidates

Allyl *N*-butylbenzimidate 1a:



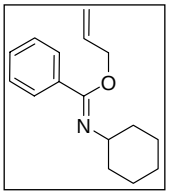
Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.24 (m, 5H), 6.02-5.91 (m, 1H), 5.26 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.11 (dd, *J* = 10.4, 1.4 Hz, 1H), 4.62 (d, *J* = 5.7 Hz, 2H), 3.18 (t, *J* = 6.9 Hz, 2H), 1.48-1.38 (m, 2H), 1.28-1.16 (m, 2H), 0.77 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.5 (C), 133.8 (CH), 132.4 (C), 129.2 (CH), 128.1 (CH), 127.9 (CH), 116.9 (CH_2), 65.9 (CH_2), 49.6 (CH_2), 34.1 (CH_2), 20.3 (CH_2), 13.8 (CH_3) ppm; IR (neat): ν_{max} 3074(w), 2926(s), 2863(m), 1672(s), 1266(s), 1118(m), 699(m) cm^{-1}; HRMS calcd for $[C_{14}H_{19}NO + H]^+$ 218.1545, found 218.1543.

Allyl *N*-isopropylbenzimidate 1b:



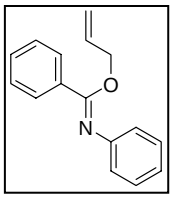
Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47-7.36 (m, 5H), 6.16-6.07 (m, 1H), 5.39 (d, *J* = 17.1 Hz, 1H), 5.24 (d, *J* = 10.2 Hz, 1H), 4.76 (d, *J* = 5.7 Hz, 2H), 3.57 (septet, *J* = 6.3 Hz, 1H), 1.15 (d, *J* = 6.0 Hz, 6H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.2 (C), 133.8 (CH), 132.9 (C), 129.0 (CH), 128.2 (CH), 127.5 (CH), 116.9 (CH_2), 65.9 (CH_2), 49.5 (CH), 24.8 (CH_3) ppm; IR (neat): ν_{max} 3078(w), 3025(w), 2966(s), 2927(s), 1670(s), 1266(s), 1115(s), 700(m) cm^{-1}; HRMS calcd for $[C_{13}H_{17}NO + H]^+$ 204.1388, found 204.1382.

Allyl *N*-cyclohexylbenzimidate 1c:



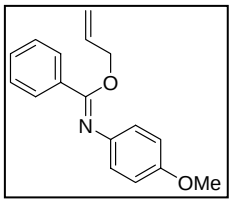
Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.33 (m, 5H), 6.13-6.04 (m, 1H), 5.36 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.21 (d, *J* = 10.5 Hz, 1H), 4.71 (d, *J* = 5.7 Hz, 1H), 3.25-3.17 (m, 1H), 1.76-1.17 (m, 10H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.2 (C), 133.9 (CH), 132.9 (C), 129.1 (CH), 128.2 (CH), 127.6 (CH), 117.0 (CH_2), 65.9 (CH_2), 57.4 (CH), 34.9 (CH_2), 25.7 (CH_2), 24.4 (CH_2) ppm; IR (neat): ν_{max} 3077(w), 2927(s), 2856(m), 1670(s), 1450(m), 1265(s), 699(m) cm^{-1}; HRMS calcd for $[C_{16}H_{21}NO + H]^+$ 244.1701, found 244.1701.

Allyl *N*-phenylbenzimidate 1d[4]:



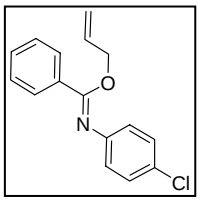
Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33 -7.09 (m, 7H), 6.93 (t, J = 7.4 Hz, 1H), 6.71 (d, *J* = 7.5 Hz, 2H), 6.19-6.06 (m, 1H), 5.43 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.27 (d, *J* = 10.5, 1H), 4.86 (d, *J* = 5.4 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.1 (C), 148.3 (C), 133.2 (CH), 131.3 (C), 129.9 (CH), 129.3 (CH), 128.8 (CH), 127.9 (CH), 122.6 (CH), 121.6 (CH), 117.6 (CH_2), 67.2 (CH_2) ppm; IR (neat): ν_{max} 3068(w), 2925(w), 1659(s), 1267(s), 1113(m), 695(m) cm^{-1}; HRMS calcd for $[C_{16}H_{15}NO + H]^+$ 238.1232, found 238.1226.

Allyl *N*-(4-methoxyphenyl)benzimidate 1e[5]:



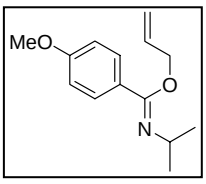
Yellow crystals, mp 50-52 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33-7.17 (m, 5H), 6.71 (d, *J* = 9.0 Hz, 2H), 6.63 (d, *J* = 8.7 Hz, 2H), 6.20-.6.06 (m, 1H), 5.42 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.26 (d, *J* = 10.5 Hz, 1H), 4.85 (d, *J* = 5.1 Hz, 2H), 3.69 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.3 (C), 155.3 (C), 141.4 (C), 133.2 (CH), 131.5 (C), 129.7 (CH), 129.2 (CH), 127.8 (CH), 122.4 (CH), 117.4 (CH_2), 114.1 (CH), 67.0 (CH_2), 55.2 (CH_3) ppm; IR (KBr): ν_{max} 3072(w), 3008(w), 2926(m), 1661(s), 1501(m), 1257(s), 1105(s), 695(m) cm^{-1}; HRMS calcd for $[C_{17}H_{17}NO_2 + H]^+$ 268.1338, found 268.1336.

Allyl *N*-(4-chlorophenyl)benzimidate 1f[5]:



Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.19 (m, 5H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.63 (d, *J* = 8.7 Hz, 2H), 6.18-6.04 (m, 1H), 5.42 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.27 (dd, *J* = 10.4 Hz, 1.1 Hz, 1H), 4.84 (d, *J* = 5.4 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.7 (C), 146.9 (C), 132.9 (CH), 130.9 (C), 130.0 (CH), 129.2 (CH), 128.9 (CH), 128.0 (CH), 127.8 (C), 122.9 (CH), 117.7 (CH_2), 67.3 (CH_2) ppm; IR (neat): ν_{max} 3083(w), 2926(w), 1657(s), 1486(m), 1271(s), 1113(s), 695(m) cm^{-1}; HRMS calcd for $[C_{16}H_{14}NOCl + H]^+$ 272.0842, found 272.0835.

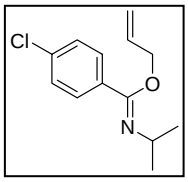
Allyl *N*-isopropyl-4-methoxybenzimidate 1g:



Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 6.12-6.01 (m, 1H), 5.36 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.21 (dd, *J* = 10.4, 1.4 Hz, 1H), 4.69 (d, *J* = 5.7 Hz,

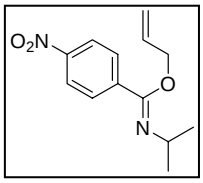
2H), 3.84 (s, 3H), 3.59 (septet, J = 6.2 Hz, 1H), 1.11 (d, J = 6.3 Hz, 6H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 160.1 (C), 157.9 (C), 133.97 (CH), 133.93 (CH), 129.2 (CH), 125.2 (C), 116.8 (CH_2), 114.7 (CH), 113.5 (CH), 65.9 (CH_2), 55.2 (CH_3), 49.5 (CH), 24.9 (CH_3) ppm; IR (neat): ν_{max} 2964(s), 2928(m), 1666(s), 1609(m), 1510(m), 1251(s), 1111(m), 836(m) cm^{-1}; HRMS calcd for $[C_{14}H_{19}NO_2 + H]^+$ 234.1494, found 234.1505.

Allyl *N*-isopropyl-4-chlorobenzimidate 1h:



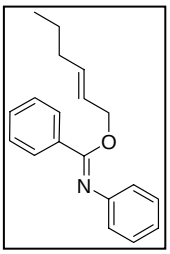
Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (dd, J = 6.7, 1.9 Hz, 2H), 7.28 (dd, J = 6.6, 1.8 Hz, 2H), 6.13-6.03 (m, 1H), 5.35 (dd, J = 17.1, 1.5 Hz, 1H), 5.22 (dd, J = 10.4, 1.4 Hz, 1H), 4.70 (td, J = 5.6, 1.4 Hz, 2H), 3.49 (septet, J = 6.2 Hz, 1H), 1.10 (d, J = 6.0 Hz, 6H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 157.1 (C), 135.1 (C), 133.6 (CH), 131.2 (C), 129.1 (CH), 128.5 (CH), 117.2 (CH_2), 66.1 (CH_2), 49.6 (CH), 24.8 (CH_3) ppm; IR (neat): ν_{max} 3083(w), 2967(s), 2927(m), 1670(s), 1266(s), 1113(s) cm^{-1}; HRMS calcd for $[C_{13}H_{16}ClNO + H]^+$ 238.0999, found 238.0992.

Allyl *N*-isopropyl-4-nitrobenzimidate 1i:



Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.29 (d, J = 8.7 Hz, 2H), 7.50 (d, J = 9.0 Hz, 2H), 6.11-6.00 (m, 1H), 5.36 (dd, J = 17.4, 1.5 Hz, 1H), 5.24 (dd, J = 10.5, 1.2 Hz, 1H), 4.72 (d, J = 5.7 Hz, 2H), 3.42 (septet, J = 6.2 Hz, 1H), 1.11 (d, J = 6.0 Hz, 6H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 155.9 (C), 148.1 (C), 139.0 (C), 133.3(CH), 128.8 (CH), 123.6 (CH), 117.6 (CH_2), 66.4 (CH_2), 49.8 (CH), 24.8 (CH_3) ppm; IR (neat): ν_{max} 3082(w), 2967(m), 2928(m), 1673(s), 1526(s), 1350(s), 1268(s), 1111(m) cm^{-1}; HRMS calcd for $[C_{13}H_{16}N_2O_3 + H]^+$ 249.1239, found 249.1233.

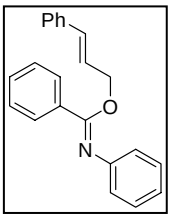
***E*-Hex-2enyl *N*-phenylbenzimidate 1j[2]:**



Yellowish viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32-7.12 (m, 7H), 6.93 (t, J = 7.4 Hz, 1H), 6.71 (d, J = 7.5 Hz, 2H), 5.92-5.73 (m, 2H), 4.80 (d, J = 5.4 Hz, 2H), 2.08 (q, J = 6.8 Hz, 2H), 1.44 (sextet, J = 7.4 Hz, 2H), 0.93 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.3 (C), 148.4 (C), 135.5 (CH), 131.5 (C), 129.7 (CH), 129.3 (CH), 128.8 (CH), 127.8 (CH), 124.8 (CH), 122.4 (CH), 121.6 (CH), 67.3 (CH_2), 34.4 (CH_2), 22.1 (CH_2), 13.7 (CH_3) ppm; IR (neat): ν_{max} 3063(w), 3026(w), 2958(m), 2927(m), 1658(s),

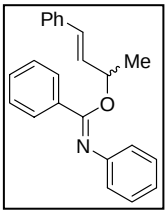
1262(s), 1110(s), 695(m) cm^{-1}; HRMS calcd for $[C_{19}H_{21}NO + H]^+$ 280.1701, found 280.1703.

Cinnamyl *N*-phenylbenzimidate 1k[4]:



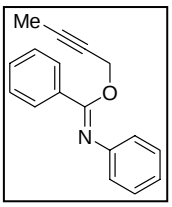
Yellowish viscous liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 7.43-7.22 (m, 12H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.86-6.80 (m, 3H), 6.58 (td, *J* = 15.9, 6.1 Hz, 1H), 5.10 (dd, *J* = 6.0, 0.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.1 (C), 148.3 (C), 136.6 (C), 133.4 (CH), 131.3 (C), 129.9 (CH), 129.3 (CH), 128.9 (CH), 128.5 (CH), 127.9 (CH), 127.8 (CH), 126.6 (CH), 124.3 (CH), 122.6 (CH) , 121.6 (CH), 67.0(CH_2) ppm; IR (neat): ν_{max} 3026(w), 2923(m), 1657(s), 1265(s),1110(s), 696(m) cm^{-1}.

***E*-4-Phenylbut-3-en-2-yl-*N*-phenylbenzimidate[6]:**



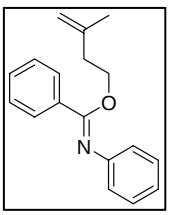
Yellow crystals, mp 76-78 °C (*n*-hexane-ether); ^1H NMR (300 MHz, $CDCl_3$): δ 7.43-7.13 (m, 13H), 6.93 (t, *J* = 7.1 Hz, 1H), 6.75-6.69 (m, 2H), 6.38 (dd, *J* = 15.9, 6.3 Hz, 1H), 5.91 (m, 1H), 1.58 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 157.5 (C), 148.5 (C), 136.8 (C), 131.7 (C), 131.0 (CH), 129.9 (CH), 129.7 (CH), 129.3 (CH), 128.8 (CH), 128.5 (CH), 127.9 (CH), 127.6 , (CH) 126.5 (CH), 122.4 (CH), 121.5 (CH), 71.8 (CH), 20.3 (CH_3) ppm; IR (KBr): ν_{max} 3026(w), 2978(w), 2925(w), 1652(s), 1258(s),, 1109(s), 694(m) cm^{-1}; HRMS calcd for $[C_{23}H_{21}NO + Na]^+$ 350.1521, found 350.1530.

But-2-ynyl-*N*-phenylbenzimidate:



Yellowish viscous liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 7.34-7.14 (m, 7H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.71 (d, *J* = 8.1 Hz, 2H), 4.93 (q, *J* = 2.4 Hz, 2H), 1.89 (t, *J* = 2.4 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 157.5 (C), 147.9 (C), 130.8 (C), 130.0 (CH), 129.4 (CH), 128.8 (CH), 127.9 (CH), 122.7 (CH), 121.5 (CH), 82.7 (C), 74.2 (C), 54.8 (CH_2), 3.7 (CH_3) ppm; IR (neat): ν_{max} 3063(w), 2925(w), 1662(s), 1263(s), 1107(s), 695(m) cm^{-1}; HRMS calcd for $[C_{17}H_{15}NO + H]^+$ 250.1232, found 250.1236.

3-Methylbut-3-enyl *N*-phenylbenzimidate:

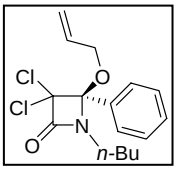


Yellowish viscous liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 7.31-7.12 (m, 7H), 6.92 (t, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 2H), 4.85 (s, 2H), 4.47 (t, *J* = 6.8 Hz, 2H), 2.54 (t, *J* = 6.8 Hz, 2H), 1.83 (s, 3H) ppm; ^{13}C NMR (75.5

MHz, $CDCl_3$): δ 158.5 (C), 148.5 (C), 142.3 (C), 131.4 (C), 129.7 (CH), 129.3 (CH), 128.8 (CH), 127.8 (CH), 122.4 (CH), 121.5 (CH), 112.0 (CH_2), 64.6 (CH_2), 36.9 (CH_2), 22.6 (CH_3) ppm; IR (neat): ν_{max} 3069(w), 3028(w), 2927(m), 1659(s), 1265(s), 1114(s), 695(m) cm^{-1}; HRMS calcd for $[C_{18}H_{19}NO + Na]^+$ 288.1364, found 288.1368.

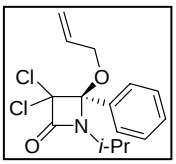
2.2. Monocyclic β-lactams

4-(Allyloxy)-1-butyl-3,3-dichloro-4-phenylazetidin-2-one 2a:



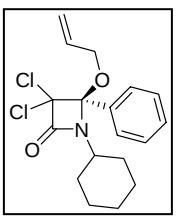
Yield: 78%; yellowish crystals, mp 45-47 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46-7.40 (m, 5H), 6.00-5.87 (m, 1H), 5.44 (d, *J* = 17.1 Hz, 1H), 5.25 (d, *J* = 10.5 Hz, 1H), 4.26 (dd, *J* = 12.9, 4.5 Hz, 1H), 4.16 (dd, *J* = 12.9, 4.5 Hz, 1H), 3.53-3.43 (m, 1H), 3.24-3.14 (m, 1H), 1.98-1.83 (m, 2H), 1.40 (sextet, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 162.6 (C), 133.3 (C), 132.9 (CH), 129.9 (CH), 128.6 (CH), 127.9 (CH), 116.8 (CH_2), 98.9 (C), 89.8 (C), 67.3 (CH_2), 43.6 (CH_2), 30.1 (CH_2), 20.5 (CH_2), 13.6 (CH_3) ppm; IR (KBr): ν_{max} 3063(w), 2963(m), 2931(m), 2871(w), 1789(s), 1393(m), 1106(s), 929(m), 692(m) cm^{-1}; HRMS calcd for $[C_{16}H_{19}NO_2Cl_2 + Na]^+$ 350.0691, found 350.0679.

4-(Allyloxy)-3,3-dichloro-1-isopropyl -4-phenylazetidin-2-one 2b:



Yield: 84%; white crystals, mp 63-65 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (s, 5H), 6.00-5.87 (m, 1H), 5.45 (d, *J* = 17.1 Hz, 1H), 5.25 (d, *J* = 10.2 Hz, 1H), 4.26 (dd, *J* = 12.6, 3.9 Hz, 1H), 4.14 (dd, *J* = 12.9, 4.2 Hz, 1H), 3.62 (septet, *J* = 6.6 Hz, 1H), 1.63 (d, *J* = 6.6 Hz, 3H), 1.49 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 161.9 (C), 133.6 (C), 132.9 (CH), 129.9 (CH), 128.5 (CH), 127.8 (CH), 116.8 (CH_2), 99.2 (C), 89.7 (C), 67.4 (CH_2), 48.0 (CH), 21.3 (CH_3), 20.9 (CH_3) ppm; IR (KBr): ν_{max} 2984(w), 2035(w), 1780(s), 1325(m), 1146(m), 1114(m), 695(w) cm^{-1}; HRMS calcd for $[C_{15}H_{17}NO_2Cl_2 + H]^+$ 314.0715, found 314.0710.

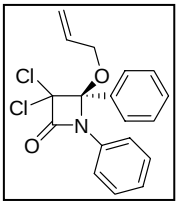
4-(Allyloxy)- 3,3-dichloro-1-cyclohexyl-4-phenylazetidin-2-one 2c:



Yield: 82%; white crystals, mp 92-94 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48-7.46 (m, 5H), 6.00-5.90 (m, 1H), 5.46 (dd, *J* = 16.8, 1.5 Hz, 1H), 5.26 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.23 (dd, *J* = 12.9, 4.5 Hz,

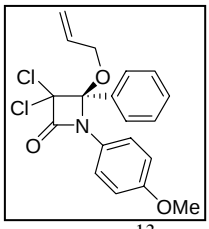
1H), 4.16 (dd, *J* = 12.9, 4.8 Hz, 1H), 3.19-3.14 (m, 1H), 2.25-2.19 (m, 2H), 2.10-1.83 (m, 5H), 1.31-1.17 (m, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 161.9 (C), 133.5 (C), 132.9 (CH), 129.9 (CH), 128.6 (CH), 127.8 (CH), 116.7 (CH_2), 99.1 (C), 89.6 (C), 67.4 (CH_2), 55.9 (CH), 31.4 (CH_2), 30.8 (CH_2), 25.8 (CH_2), 25.5 (CH_2), 24.9 (CH_2) ppm; IR (KBr): ν_{max} 2935(m), 2860(w), 1780(s), 1102(m), 980(w), 694(w) cm^{-1}; HRMS calcd for $[C_{18}H_{21}NO_2Cl_2 + H]^+$ 354.1028, found 354.1018.

4-(Allyloxy)- 3,3-dichloro-1,4-diphenylazetidin-2-one 2d:



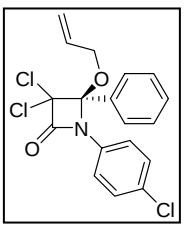
Yield: 78%; white crystals, mp 62-64 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47-7.19 (m, 10H), 6.03-5.90 (m, 1H), 5.39 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.25 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.74 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.18 (dd, *J* = 12.3, 5.4 Hz, 1H), ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.1 (C), 135.6 (C), 133.7 (C), 132.5 (CH), 129.7 (CH), 129.3 (CH), 128.2 (CH), 127.4 (CH), 125.9 (CH), 118.5 (CH), 117.4 (CH_2), 98.6 (C), 89.9 (C), 67.0 (CH_2) ppm; IR (KBr): ν_{max} 3063(w), 2927(w), 1784(s), 1493(m), 1371(s), 1123(m), 759(m), 731(m), 692(m) cm^{-1}; HRMS calcd for $[C_{18}H_{15}NO_2Cl_2 + Na]^+$ 370.0378, found 370.0365.

4-(Allyloxy)-3,3-dichloro-1-(4-methoxyphenyl)-4-phenylazetidin-2-one 2e:



Yield: 84%; colourless viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44-7.35 (m, 7H), 6.83 (dd, *J* = 7.2, 2.1 Hz, 2H), 5.96-5.85 (m, 1H), 5.34 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.21 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.68 (ddd, *J* = 12.3, 3.3, 1.5 Hz, 1H), 4.12 (dd, 12.3, 5.4 Hz, 1H), 3.78 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.7 (C), 157.4 (C), 133.9 (C), 132.6 (CH), 129.7 (CH), 128.8 (C), 128.2 (CH), 127.5 (CH), 120.1 (CH), 117.4 (CH_2), 114.5 (CH), 98.6 (C), 90.0 (C), 67.0 (CH_2), 55.4 (CH_3) ppm; IR (neat): ν_{max} 3072(w), 2933(w), 1783(s), 1510(s), 1253(s), 1131(m), 839(m), 702(w) cm^{-1}; HRMS calcd for $[C_{19}H_{17}NO_3Cl_2 + Na]^+$ 400.0483, found 400.0485.

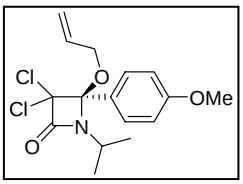
4-(Allyloxy)-3,3-dichloro-1-(4-chlorophenyl)-4-phenylazetidin-2-one 2f:



Yield: 76%; white crystals, mp 70-72 °C (*n*-pentane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47-7.37 (m, 7H), 7.28 (d, *J* = 9.0 Hz, 2H), 5.96-5.87 (m, 1H), 5.34 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.21 (dd, *J* = 10.4, 1.4 Hz, 1H), 4.70 (ddd, *J* = 12.3, 3.5, 1.7 Hz, 1H), 4.10 (dd, 12.3, 5.4 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.1 (C), 134.2 (C), 133.5 (C), 132.4 (CH), 131.5 (C),

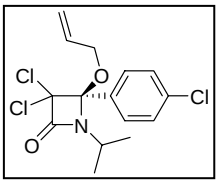
130.0 (CH), 129.6 (CH), 128.4 (CH), 127.4 (CH), 120.0 (CH), 117.7 (CH_2), 98.8 (C), 90.0 (C), 67.1 (CH_2) ppm; IR (KBr): ν_{max} 3102(w), 2917(w), 1783(s), 1491(s), 1363(s), 1122(m), 830(m), 772(m) cm^{-1}; HRMS calcd for $[C_{18}H_{14}NO_2Cl_3 + Na]^+$ 403.9988, found 404.0005.

4-(Allyloxy)-3,3-dichloro-1-isopropyl -4-(4-methoxyphenyl)azetidin-2-one 2g:



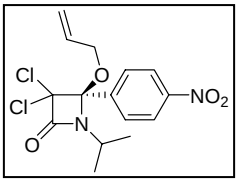
Yield: 76%; white crystals, mp 70-72 °C (*n*-hexane-ether);^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (d, *J* = 9.0 Hz, 2H), 6.98 (d, *J* = 8.7 Hz, 2H), 5.99-5.87 (m, 1H), 5.45 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.25 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.24 (dd, *J* = 12.9, 4.5 Hz, 1H), 4.14 (dd, *J* = 12.8, 4.7 Hz, 1H), 3.86 (s, 3H), 3.58 (septet, *J* = 6.6 Hz, 1H), 1.61 (d, *J* = 6.6 Hz, 3H), 1.48 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 162.1 (C), 160.7 (C), 133.0 (CH), 129.3 (CH), 125.4 (C), 116.7 (CH_2), 113.9 (CH), 99.2 (C), 90.1 (C), 67.3 (CH_2), 55.3 (CH_3), 47.8 (CH), 21.4 (CH_3), 21.0 (CH_3) ppm; IR (KBr): ν_{max} 3074(w), 2982(m), 2938(w), 1782(s), 1611(m), 1512(m), 1318(s), 1251(s), 1182(m), 1091(m), 864(m), 690(w) cm^{-1}; HRMS calcd for $[C_{16}H_{19}NO_3Cl_2 + H]^+$ 344.0820 found, 344.0811.

4-(Allyloxy)-3,3-dichloro-4-(4-chlorophenyl)-1-isopropylazetidin-2-one 2h:



Yield: 80%; white crystals, mp: 82-84 °C (*n*-hexane-ether);^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 5.99-5.87 (m, 1H), 5.44 (d, *J* = 17.1 Hz, 1H), 5.26 (d, *J* = 10.5 Hz, 1H), 4.32 (d, *J* = 12.9 Hz, 1H), 4.13 (dd, *J* = 12.9, 4.5 Hz, 1H), 3.59 (septet, *J* = 6.5 Hz, 1H), 1.58 (d, *J* = 6.6 Hz, 3H), 1.48 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 161.8 (C), 136.0 (C), 132.7 (CH), 132.5 (C), 129.3 (CH), 128.8 (CH), 117.0 (CH_2), 98.8 (C), 89.6 (C), 67.4 (CH_2), 48.0 (CH), 21.2 (CH_3), 20.9 (CH_3) ppm; IR (KBr): ν_{max} 3088 (w), 2984(w), 2940(w), 1784(s), 1324(m), 1092(s), 980(m), 861(m), 691(w) cm^{-1}; HRMS calcd for $[C_{15}H_{16}NO_2Cl_3 + H]^+$ 348.0325, found 348.0324.

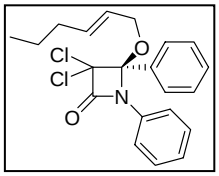
4-(Allyloxy)-3,3-dichloro-1-isopropyl-4-(4-nitrophenyl)azetidin-2-one 2i:



Yield: 78%; yellow crystals, mp: 95-97 °C (*n*-hexane-DCM);^{1}H NMR (300 MHz, $CDCl_3$): δ 8.33 (td, *J* = 9.0, 2.1 Hz, 2H), 7.70 (td, *J* = 8.7, 2.1 Hz, 2H), 6.00-5.9 (m, 1H), 5.45 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.30 (dd, *J* = 10.8, 1.5 Hz, 1H), 4.44 (tdd, *J* = 12.9, 4.5, 1.8 Hz, 1H), 4.14 (tdd, *J* = 12.9, 4.8, 1.7 Hz, 1H), 3.66 (septet, *J* = 6.5 Hz, 1H), 1.56 (d, *J* = 6.6 Hz,

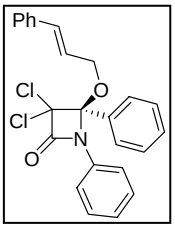
3H), 1.49 (d, J = 6.6 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 161.3 (C), 148.6 (C), 141.1 (C), 132.3 (CH), 129.0 (CH), 123.5 (CH), 117.3 (CH_2), 98.4 (C), 89.3 (C), 67.4 (CH_2), 48.1 (CH), 21.1 (CH_3), 20.8 (CH_3) ppm; IR (KBr): ν_{max} 3090(w), 2981(w), 1785(s), 1525(s), 1350(m), 1319(m), 1096(m), 842(m), 687(m) cm^{-1}; HRMS calcd for $[C_{15}H_{16}N_2O_4Cl_2 + H]^+$ 359.0565, found 359.0560.

***E*-3,3-Dichloro-4-(hex-2-enyloxy)-1,4-diphenylazetidin-2-one 2j:**



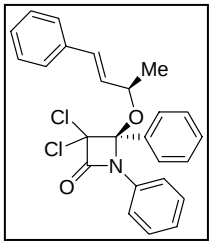
Yield: 76%; colourless viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.15 (m, 10H), 5.71-5.51 (m, 2H), 4.64 (dd, J = 11.1, 5.1 Hz, 1H), 4.07 (dd, J = 11.3, 5.9 Hz, 1H), 1.99 (q, J = 6.7 Hz, 2H), 1.37 (sextet, J = 7.0 Hz, 2H), 0.88 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.3 (C), 135.8 (C), 135.4 (CH), 134.0 (C), 129.6 (CH), 129.3 (CH), 128.2 (CH), 127.5 (CH), 125.9 (CH), 124.4 (CH), 118.7 (CH), 98.7 (C), 90.0 (C), 67.2 (CH_2), 34.3 (CH_2), 22.0 (CH_2), 13.6 (CH_3) ppm; IR (neat): ν_{max} 3035(w), 2959(w), 2928(w), 1788(s), 1496(m), 1369(m), 1129(m), 756(w), 688(w) cm^{-1}; HRMS calcd for $[C_{21}H_{21}NO_2Cl_2 + H]^+$ 390.1028, found 390.1032.

3,3-Dichloro-4-(cinnamyloxy)-1,4-diphenylazetidin-2-one 2k



Yield: 72%; white crystals, mp: 85-87 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56-7.21 (m, 15H), 6.63 (d, J = 15.9 Hz, 1H), 6.32 (td, J = 15.9, 6.0 Hz, 1H), 4.91 (dd, J = 12.0, 5.4 Hz, 1H), 4.35 (dd, J = 12.2, 6.2 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.2 (C), 136.2 (C), 135.7 (C), 133.8 (C), 133.1 (CH), 129.7 (CH), 129.3 (CH), 128.5 (CH), 128.2 (CH), 127.9 (CH), 127.4 (CH), 126.5 (CH), 126.0 (CH), 123.7 (CH), 118.6 (CH), 98.7 (C), 90.0 (C), 67.0 (CH_2) ppm; IR (KBr): ν_{max} 3073(w), 3030(w), 1787(s), 1596(w), 1495(m), 1371(s), 1129(s), 755(m), 690(m) cm^{-1}; HRMS calcd for $[C_{24}H_{19}NO_2Cl_2 + Na]^+$ 446.0691, found 446.0695.

***E*-3,3-Dichloro-1,4-diphenyl-4-(4-phenylbut-3-en-2-yloxy)azetidin-2-one 4:**

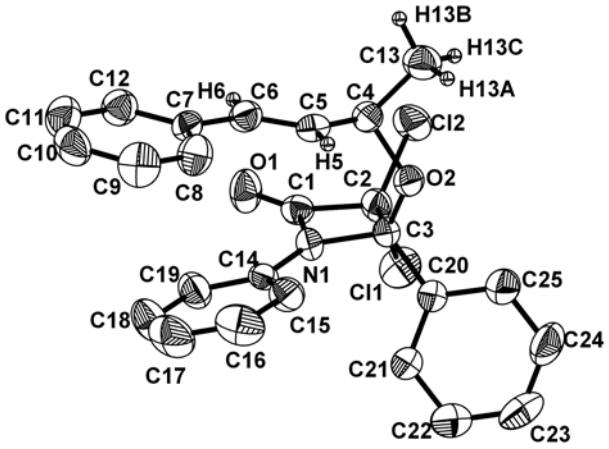


Yield: 48%; *RR*, *SS* racemic mixture of a single diastereoisomer, white crystals, mp 124-126 °C (*n*-hexane-ether);^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.31 (m, 7H), 7.13-7.11 (m, 3H), 6.99 (t, J = 8.0 Hz, 2H), 6.90-6.88 (m, 2H), 6.75 (t, J = 7.5 Hz, 1H), 6.01 (d, J = 16.2 Hz, 1H), 5.83 (dd, J = 15.9, 7.8 Hz, 1H), 4.97 (quintet, J = 6.5 Hz, 1H), 1.53 (d, J =

6.3 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.7 (C), 136.0 (C), 135.7 (C), 134.0 (C), 131.0 (CH), 130.6 (CH), 129.6 (CH), 128.5 (CH), 127.98 (CH), 127.95 (CH), 127.5 (CH), 126.3 (CH), 125.2 (CH), 119.4 (CH), 99.4 (C), 90.2 (C), 74.6(CH), 22.8 (CH_3) ppm; IR (KBr): ν_{max} 3038(w), 2977(w), 2926(w), 1783(s), 1494(m), 1366(s), 1066(m), 1029(m), 752(m), 688(m) cm^{-1}; HRMS calcd for $[C_{25}H_{21}NO_2Cl_2 + Na]^+$ 460.0847, found 460.0851.

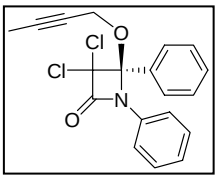
X-ray crystal structure data of 4

Formula sum: $C_{25}H_{21}Cl_2NO_2$, Formula weight: 438.33; Crystal system: monoclinic; Space group: C2/c; Unit cell dimensions: *a* = 17.803(6) Å, *b* = 9.984(3) Å, *c* = 25.300(9) Å, α = 90.00(0) °, β = 103.671(3) °, γ = 90.00(0) °; Cell volume = 4369(2) $Å^3$, Z = 8; Density calculated = 1.332 g/cm^3; R_{All} = 0.1444. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (CCDC 772888)



ORTEP diagram of monocyclic β-lactam 4

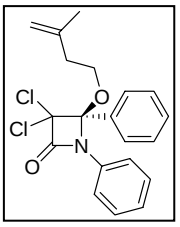
4-(But-2-ynyloxy)-3,3-dichloro-1,4-diphenylazetidin-2-one 6:



Yield: 72%; white crystals, mp 124-126 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.18 (m, 10H), 4.78 (qd, *J* = 14.4, 2.3 Hz, 1H), 4.35 (qd, *J* = 14.4, 2.3 Hz, 1H), 1.80 (t, *J* = 2.4 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.0 (C), 135.4 (C), 133.4 (C), 129.7 (CH), 129.2 (CH), 128.2 (CH), 127.5 (CH), 126.0 (CH), 118.8 (CH), 98.7 (C), 89.8 (C), 83.5 (C), 73.5 (C), 55.4 (CH_2), 3.6 (CH_3) ppm; IR (KBr): ν_{max} 3071(w), 2927(w),

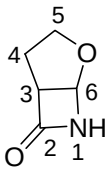
2245(w), 1788(s), 1495(m), 1377(s), 1260(m), 1128(s), 1076(m), 756(m), 686(m) cm^{-1}; HRMS calcd for $[C_{19}H_{15}NO_2Cl_2 + H]^+$ 360.0558, found 360.0554.

3,3-Dichloro-4-(3-methylbut-3-enyloxy)-1,4-diphenylazetidin-2-one 8:

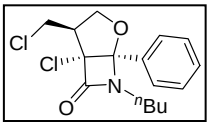


Yield: 84%; colourless viscous liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 7.49-7.15 (m, 10H), 4.78 (s, 1H), 4.72 (s, 1H), 4.27 (dd, *J* = 15.8, 6.8 Hz, 1H), 3.68 (dd, *J* = 15.8, 7.0 Hz, 1H), 2.40 (t, *J* = 6.8 Hz, 2H), 1.69 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.3 (C), 141.6 (C), 135.9 (C), 134.0 (C), 129.6 (CH), 129.3 (CH), 128.2 (CH), 127.5 (CH), 125.9 (CH), 118.5 (CH), 112.5 (CH_2), 98.6 (C), 90.0 (C), 64.7 (CH_2), 37.6 (CH_2), 22.6 (CH_3) ppm; IR (neat): ν_{max} 3071(w), 2924(w), 1788(s), 1496(m), 1369(s), 1134(m), 757(w), 689(w) cm^{-1}; HRMS calcd for $[C_{20}H_{19}NO_2Cl_2 + Na]^+$ 398.0691, found 398.0703.

2.3. Bicyclic β-lactams

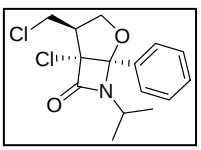


1-Butyl-3-chloro-4-chloromethyl-6-phenyltetrahydrofuro[3,2-c]azetidin-2-one 3a:



Yield: 77%; yellowish solid, mp 35-37 °C (*n*-hexane-ether); ^1H NMR (300 MHz, $CDCl_3$): δ 7.47 (s, 5H), 4.67 (t, *J* = 8.6 Hz, 1H), 3.98 (dd, *J* = 11.3, 4.1 Hz, 1H), 3.86 (t, *J* = 10.8 Hz, 1H), 3.69 (t, *J* = 11.3 Hz, 1H), 3.38 (quintet, *J* = 7.4 Hz, 1H), 2.99-2.80 (m, 2H), 1.62-1.53 (m, 2H), 1.30 (sextet, *J* = 7.3 Hz, 2H), 0.88 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 162.5 (C), 131.8 (C), 129.8 (CH), 128.5 (CH), 127.2 (CH), 101.4 (C), 81.2 (C), 69.9 (CH_2), 50.8 (CH), 41.0 (CH_2), 40.2 (CH_2), 30.3 (CH_2), 20.5 (CH_2), 13.5(CH_3) ppm; IR (KBr): ν_{max} 3064(w), 2959(s), 2870(m), 1775(s), 1451(m), 1389(s), 1320(m), 1055(s), 993(m), 743(m), 706(m) cm^{-1}; HRMS calcd for $[C_{16}H_{19}NO_2Cl_2 + Na]^+$ 350.0691, found 350.0699

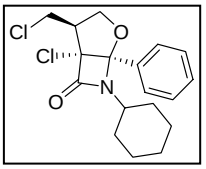
3-Chloro-4-chloromethyl-1-isopropyl-6-phenyltetrahydrofuro[3,2-c]azetidin-2-one 3b:



Yield: 75%; yellow crystals, mp 88-90 °C ;^1H NMR (300 MHz, $CDCl_3$): δ 7.56-7.53 (m, 2H), 7.46-7.44 (m, 3H), 4.67 (dd, *J* = 9.8, 7.7

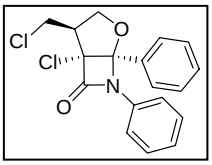
Hz, 1H), 3.98 (dd, *J* = 11.4, 3.9 Hz, 1H), 3.89 (t, *J* = 10.7 Hz, 1H), 3.70 (t, *J* = 11.4 Hz, 1H), 3.57 (septet, *J* = 6.8 Hz, 1H), 2.89-2.78 (m, 1H), 1.39 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 162.2 (C), 132.7 (C), 129.7 (CH), 128.3 (CH), 127.2 (CH), 101.5 (C), 80.7 (C), 69.8 (CH_2), 50.9 (CH), 46.1 (CH), 41.0 (CH_2), 21.3 (CH_3), 20.8 (CH_3) ppm; IR (KBr): ν_{max} 3063(w), 2980(w), 2873(w), 1764(s), 1333(m), 1303(m), 1039(m), 742(w) cm^{-1}; HRMS calcd for $[C_{15}H_{17}NO_2Cl_2 + Na]^+$ 336.0534, found 336.0534.

3-Chloro-4-chloromethyl-1-cyclohexyl-6-phenyltetrahydrofuro[3,2-c]azetidin-2-one 3c:



Yield: 74%; yellow crystals, mp 75-77 °C (*n*-hexane-ether);^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58-7.54 (m, 2H), 7.47-7.45 (m, 3H), 4.67 (dd, *J* = 9.9, 7.5 Hz, 1H), 3.98 (dd, *J* = 11.4, 4.1 Hz, 1H), 3.92 (t, *J* = 11.3 Hz, 1H), 3.71 (t, *J* = 11.4 Hz, 1H), 3.22 (tt, *J* = 11.7, 3.9 Hz, 1H), 2.90-2.81 (m, 1H), 2.11-1.10 (m, 10H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 162.1 (C), 132.7 (C), 129.6 (CH), 128.3 (CH), 127.2 (CH), 101.4 (C), 80.7 (C), 69.8 (CH_2), 53.7 (CH), 50.9 (CH), 41.0 (CH_2), 31.4 (CH_2), 30.8 (CH_2), 25.3 (CH_2), 25.0 (CH_2), 24.9 (CH_2) ppm; IR (KBr): ν_{max} 3065(w), 2937(m), 2859(w), 1768(s), 1360(m), 1297(m), 1043(m), 993(w), 743(w) cm^{-1}; HRMS calcd for $[C_{18}H_{21}NO_2Cl_2 + Na]^+$ 376.0847, found 376.0838.

3-Chloro-4-chloromethyl-1,6-diphenyltetrahydrofuro[3,2-c]azetidin-2-one 3d:

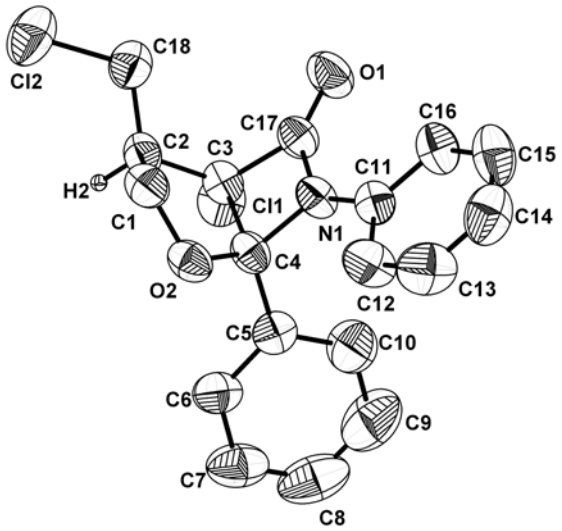


Yield: 79%; white crystals, mp 130-132 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.43 (m, 7H), 7.30-7.25 (m, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 4.74 (dd, *J* = 10.1, 7.4 Hz, 1H), 4.04 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.91 (t, *J* = 10.8 Hz, 1H), 3.72 (t, *J* = 11.4 Hz, 1H), 3.06-2.96 (m, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.5 (C), 134.7 (C), 131.6 (C), 130.0 (CH), 129.2 (CH), 128.7 (CH), 127.2 (CH), 125.5 (CH), 118.5 (CH), 101.7 (C), 81.3 (C), 70.3 (CH_2), 51.3 (CH), 40.7 (CH_2) ppm; IR (KBr): ν_{max} 3008(w), 2923(w), 1770(s), 1501(m), 1384(m), 1055(m), 748(m), 690(w) cm^{-1}; HRMS calcd for $[C_{18}H_{15}NO_2Cl_2 + Na]^+$ 370.0378, found 370.0372.

X-ray crystal structure data of 3d

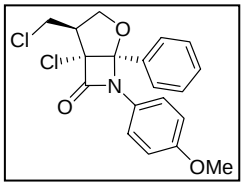
Formula sum: $C_{18}H_{15}Cl_2NO_2$, Formula weight: 348.21; Crystal system: monoclinic; Space group: P2(1)/c; Unit cell dimensions: *a* = 12.976(3) Å, *b* = 17.547(4) Å, *c* = 7.4994(15)

Å, α = 90.00(0) °, β = 101.304(3) °, γ = 90.00(0) °; Cell volume = 1674.4(6) $Å^3$, Z = 4; Density calculated = 1.368 g/cm^3; R_{All} = 0.0845. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (CCDC 747465)



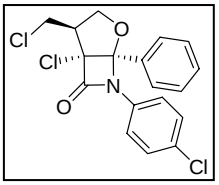
ORTEP diagram of bicyclic β-lactam 3d

3-Chloro-4-chloromethyl-1-(4-methoxyphenyl)-6-phenyltetrahydrofuro[3,2-c]azetidin-2-one 3e:



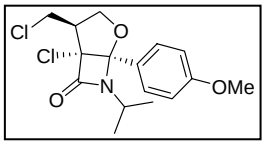
Yield: 72%; white crystals, mp 113-115 °C (*n*-hexane-ether);[1]H NMR (300 MHz, $CDCl_3$): δ 7.51-7.41 (m, 5H), 7.38 (d, *J* = 9.0 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.72 (dd, *J* = 9.9, 7.5 Hz, 1H), 4.03 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.90 (t, *J* = 10.8 Hz, 1H), 3.75 (s, 3H), 3.72 (t, *J* = 11.4 Hz, 1H, overlapped with the singlet at δ 3.75), 3.03-2.96 (m, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.0 (C), 157.1 (C), 131.6 (C), 129.9 (CH), 128.6 (CH), 127.9 (C), 127.2 (CH), 119.9 (CH), 114.4 (CH), 101.6 (C), 81.3 (C), 70.2 (CH_2), 55.4 (CH_3), 51.2 (CH), 40.7 (CH_2) ppm; IR (KBr): ν_{max} 3067(w), 3023(w), 2954(w), 2913(w), 1765(s), 1511(s), 1448(m), 1391(m), 1296(m), 1248(s), 1128(m), 1039(m), 822(m), 726(m) cm^{-1}; HRMS calcd for $[C_{19}H_{17}NO_3Cl_2 + Na]^+$ 400.0483, found 400.0480.

3-Chloro-4-chloromethyl-1-(4-chlorophenyl)-6-phenyltetrahydrofuro[3,2-c]azetidin-2-one 3f:



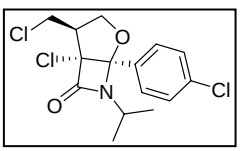
Yield: 66%; white crystals, mp 146-148 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46-7.44 (m, 5H), 7.38 (d, *J* = 8.7 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 4.73 (t, *J* = 8.7 Hz, 1H), 4.02 (dd, *J* = 11.4, 3.9 Hz, 1H), 3.89 (t, *J* = 10.8 Hz, 1H), 3.70 (t, *J* = 11.4 Hz, 1H), 3.05-2.94 (m, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.4 (C), 133.1 (C), 131.2 (C), 130.8 (C), 130.1 (CH), 129.4 (CH), 128.7 (CH), 127.1 (CH), 119.7 (CH), 101.7 (C), 81.4 (C), 70.3 (CH_2), 51.2(CH), 40.5 (CH_2) ppm; IR (KBr): ν_{max} 3063(w), 3008(w), 2958(w), 1770(s), 1498(m), 1382(m), 1128(m), 1056(m) 822(m), 749(w) cm^{-1}. Anal. Calcd for $C_{18}H_{14}Cl_3NO_2$ C: 56.50; H: 3.69; N: 3.66. Found C: 56.37; H: 3.57; N: 3.94; HRMS calcd for $[C_{18}H_{14}NO_2Cl_3 + Na]^+$ 403.9988, found 403.9991.

3-Chloro-4-chloromethyl-1-isopropyl-6-(4-methoxyphenyl)tetrahydrofuro[3,2-c]azetidin-2-one 3g:



Yield: 73%; white crystals, mp 95-97 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (d, *J* = 9.0 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 4.64 (dd, *J* = 9.9, 7.5 Hz, 1H), 3.97 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.86 (t, *J* = 10.6 Hz, 1H), 3.84 (s, 3H, overlapped with the triplet at δ 3.86), 3.69 (t, *J* = 11.4 Hz, 1H), 3.55 (septet, *J* = 6.8 Hz, 1H), 2.86-2.80 (m, 1H), 1.38 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 162.2 (C), 160.6 (C), 128.6 (CH), 124.5 (C), 113.7 (CH), 101.5 (C), 80.8 (C), 69.6 (CH_2), 55.3 (CH_3), 50.9 (CH), 45.9 (CH), 41.0 (CH_2), 21.2 (CH_3), 20.8 (CH_3) ppm; IR (KBr): ν_{max} 2977(m), 2913(w), 1766(s), 1612(m), 1515(m), 1300(s), 1250(s) 1181(s), 1043(m), 844(m), 786(m) cm^{-1}; HRMS calcd for $[C_{16}H_{19}NO_3Cl_2 + H]^+$ 344.0820, found 344.0824.

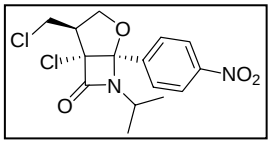
3-Chloro-4-chloromethyl-1-isopropyl-6-(4-chlorophenyl)tetrahydrofuro[3,2-c]azetidin-2-one 3h:



Yield: 74%; white crystals, mp 85-87 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 4.66 (dd, *J* = 9.9, 7.5 Hz, 1H), 3.97 (dd, *J* = 11.6, 4.1 Hz, 1H), 3.88 (t, *J* = 10.8 Hz, 1H), 3.69 (t, *J* = 11.4 Hz, 1H), 3.57 (septet, *J* = 6.8 Hz, 1H), 2.88-2.77 (m, 1H), 1.37 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (75.5

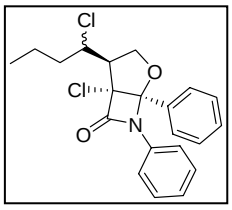
MHz, $CDCl_3$): δ 162.0 (C), 135.8 (C), 131.3 (C), 128.7 (CH), 128.6 (CH), 101.0 (C), 80.7 (C), 69.8 (CH_2), 50.8 (CH), 46.1 (CH), 40.8 (CH_2), 21.2 (CH_3), 20.8 (CH_3) ppm; IR (KBr): ν_{max} 2980(w), 2927(w), 1769(s), 1379(m), 1337(m), 1298(m), 1053(m), 1011(w), 843(w), 781(w), 722(w) cm^{-1}; HRMS calcd for $[C_{15}H_{16}NO_2Cl_3 + Na]^+$ 370.0144, found 370.0144.

3-Chloro-4-chloromethyl-1-isopropyl-6-(4-nitrophenyl)tetrahydrofuro[3,2-c]azetidin-2-one 3i:



Yield: 79%; yellow crystals, mp 138-140°C (*n*-hexane-DCM); ^1H NMR (300 MHz, $CDCl_3$): δ 8.29 (d, *J* = 8.7 Hz, 2H), 7.74 (d, *J* = 8.7 Hz, 2H), 4.70 (dd, *J* = 9.9, 7.5 Hz, 1H), 3.97-3.87 (m, 2H), 3.67 (t, *J* = 11.4 Hz, 1H), 3.58 (septet, *J* = 6.8 Hz, 1H, overlapped with the triplet at δ 3.67), 2.88-2.80 (m, 1H), 1.35 (d, *J* = 6.9 Hz, 3H), 1.20 (d, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 161.6 (C), 148.7 (C), 139.8 (C), 128.5 (CH), 123.5 (CH), 100.5 (C), 80.9 (C), 70.1 (CH_2), 50.8 (CH), 46.3 (CH), 40.6 (CH_2), 21.2 (CH_3), 20.9 (CH_3) ppm; IR (KBr): ν_{max} 3082(w), 2981(w), 2924(w), 1768(s), 1526(s), 1347(s), 1052(m), 854(w), 715(w) cm^{-1}; HRMS calcd for $[C_{15}H_{16}N_2O_4Cl_2 + Na]^+$ 381.0385, found 381.0383.

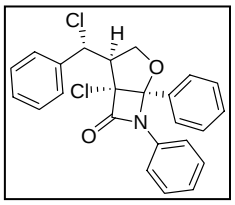
3-Chloro-4-(1-chlorobutyl)-1,6-diphenyltetrahydrofuro[3,2-c]azetidin-2-one 3j:



Yield: 84%; colourless viscous liquid; mixture of two diastereomers (91:09); ^1H NMR (300 MHz, $CDCl_3$): δ 7.61-7.39 (m, 7H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), [4.80 (dd, *J* = 10.2, 7.8 Hz) (major diastereoisomer) + 4.59 (dd, *J* = 9.6, 7.8 Hz) (minor diastereoisomer), 1H], [partially overlapping signals 4.32-4.30 (m) (minor diastereoisomer) + 4.23 (dt, *J* = 10.1, 2.6 Hz) (major diastereoisomer), 1H], 4.01 (t, *J* = 10.7 Hz, 1H), [3.29 (dd, *J* = 9.3, 3.6 Hz) (minor diastereoisomer) + 3.04 (dt, *J* = 10.8, 7.5 Hz) (major diastereoisomer), 1H], 2.42-2.31 (m, 1H), 1.95-1.82 (m, 1H), 1.80-1.65 (m, 1H), 1.63-1.45 (m, 1H), [1.03 (t, *J* = 7.4 Hz) (major diastereoisomer) + 0.89 (t, *J* = 7.2 Hz) (minor diastereoisomer), 3H] ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ [159.5 (C) (minor diastereoisomer), 159.1 (C) (major diastereoisomer)], 134.8 (C), 132.0 (C), 129.8 (CH), 129.2 (CH), 128.5 (CH), [127.4 (CH) (minor diastereoisomer), 127.3 (CH) (major diastereoisomer)], [125.3 (CH) (major diastereoisomer), 125.2 (CH) (minor

diastereoisomer)], 118.4 (CH), [102.7 (C) (major diastereoisomer), 101.4 (C) (minor diastereoisomer)], [81.5 (C) (minor diastereoisomer), 80.7 (C) (major diastereoisomer)], [71.6 (CH_2) (major diastereoisomer), 68.2 (CH_2) (minor diastereoisomer)], [61.9 (CH) (major diastereoisomer), 58.3 (CH) (major diastereoisomer)], [55.1 (CH) (minor diastereoisomer), 54.8 (CH) (major diastereoisomer)], [38.1 (CH_2) (major diastereoisomer), 37.9 (CH_2) (minor diastereoisomer)], [19.4 (CH_2) (minor diastereoisomer), 18.9 (CH_2) (major diastereoisomer)], [13.3 (CH_3) (minor diastereoisomer), 13.1 (CH_3) (major diastereoisomer)] ppm; IR (neat): ν_{max} 3066(m), 2960(s), 2928(s), 2874(s), 1764(s), 1597(s), 1498(s), 1374(s), 1295(s), 1071(s), 1036(s), 995(m), 747(s), 688(s), 618(m) cm^{-1}; HRMS calcd for $[C_{21}H_{21}NO_2Cl_2 + H]^+$ 390.1028, found 390.1028.

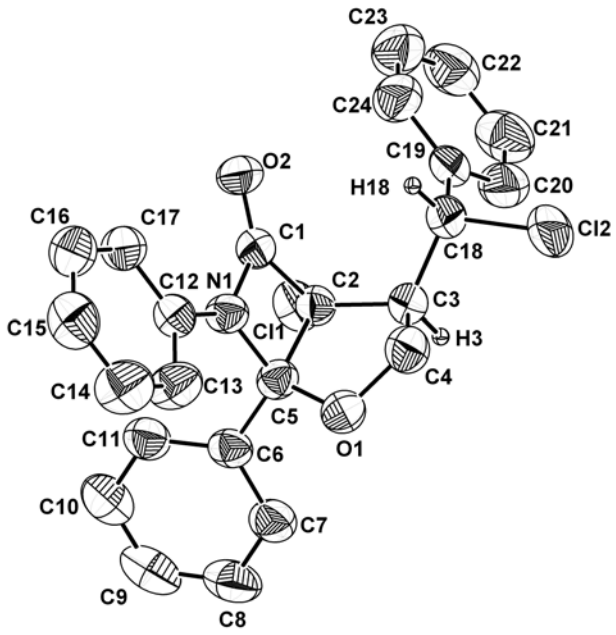
3-Chloro-4-{(chloro)(phenyl)methyl}-1,6-diphenyltetrahydrofuro[3,2-c]azetidin-2-one 3k:



Yield: 55%; white crystals, mp 132-134 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (d, *J* = 7.8 Hz, 2H), 7.52-7.28 (m, 12H), 7.17 (t, *J* = 7.4 Hz, 1H), 5.25 (d, *J* = 10.8 Hz, 1H), 4.90 (dd, *J* = 10.2, 7.5 Hz, 1H), 4.17 (t, *J* = 10.8 Hz, 1H), 3.36 (td, *J* = 11.1, 7.5 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 159.5 (C), 138.7 (C), 134.8 (C), 131.9 (C), 129.8 (CH), 129.2 (CH), 129.0 (CH), 128.5 (CH), 128.4 (CH), 128.1 (CH), 127.3 (CH), 125.5 (CH), 118.6 (CH), 102.7 (C), 80.8 (C), 70.8 (CH_2), 61.4 (CH), 56.1 (CH) ppm; IR (KBr): ν_{max} 3063(w), 2927(w), 2873(w), 1768(s), 1494(m), 1379(m), 1294(w), 1040(m), 754(w), 694(m) cm^{-1}; HRMS calcd for $[C_{24}H_{19}NO_2Cl_2 + Na]^+$ 446.0691, found 446.0689.

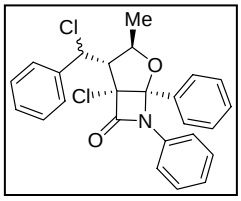
X-ray crystal structure data of 3k:

Formula sum: $C_{24}H_{19}Cl_2NO_2$, Formula weight: 424.30; Crystal system: monoclinic; Space group: P2(1)/c; Unit cell dimensions: *a* = 11.4549(11) Å, *b* = 16.0115(16) Å, *c* = 11.6598(12) Å, α = 90.00(0) °, β = 104.850(2) °, γ = 90.00(0) °; Cell volume = 2067.1(4) $Å^3$, Z = 4; Density calculated = 1.363 g/cm^3; R_{All} = 0.0402. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (CCDC 739846).



ORTEP diagram of bicyclic β-lactam 3k

3-Chloro-4-{(chloro)(phenyl)methyl}-5-methyl-1,6-diphenyltetrahydrofuro[3,2-c]azetidin-2-one 5:

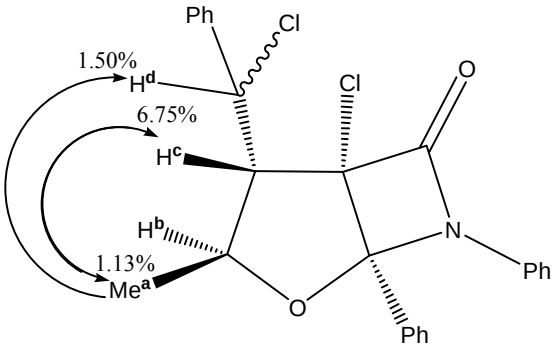


Yield: 68%; white solid, mp 48-50°C; mixture of two diastereoisomers (78:22); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66-6.84 (m, 15 H), [5.43 (br s) (major diastereoisomer) + 5.28 (d, *J* = 5.4 Hz) (minor diastereoisomer), 1H], [partially overlapping signals 5.23-5.22 (m, 1H) (minor diastereoisomer) + 5.17 (dq, *J* = 7.1, 1.8 Hz) (major diastereoisomer), 1 H], [3.38 (dd, *J* = 5.3, 3.5 Hz) (minor diastereoisomer) + 3.11 (t, *J* = 1.8 Hz) (major diastereoisomer), 1H], [1.22 (d, *J* = 6.9 Hz) (minor diastereoisomer) + 1.08 (d, *J* = 7.2 Hz) (major diastereoisomer), 3H] ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ [162.7 (C) (major diastereoisomer) + 162.2 minor diastereoisomer)], [138.6 (C) (major diastereoisomer) + 137.2 (C) (minor diastereoisomer)], 134.9 (C), [132.2 (C) (major diastereoisomer) + 131.9 (C) (minor diastereoisomer)], [129.7 (CH) (major diastereoisomer) + 129.4 (CH) (minor diastereoisomer)], [129.1 (CH) (major diastereoisomer) + 128.92 (CH) (minor diastereoisomer)], [128.87 (CH) (major diastereoisomer) + 128.7 (CH) (minor diastereoisomer)], [128.4 (CH) (minor diastereoisomer) + 128.3 (CH) (major diastereoisomer)], [128.2 (CH) (minor

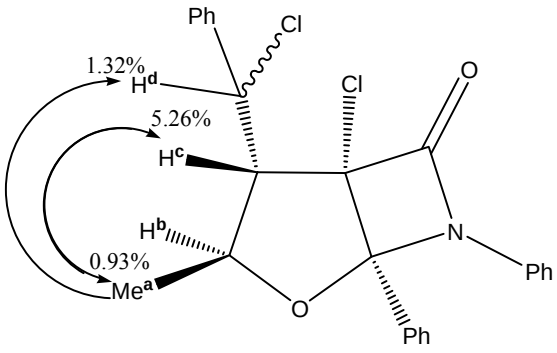
diastereoisomer) + 127.9 (CH) (major diastereoisomer)], [127.1 (CH) (minor diastereoisomer) + 126.9 (CH) (major diastereoisomer)], [125.2 (CH) (major diastereoisomer) + 125.1 (CH) (minor diastereoisomer)], [118.7 (CH) (major diastereoisomer) + 118.6 (CH) (minor diastereoisomer)], [103.5 (C) (major diastereoisomer) + 102.0 (C) (minor diastereoisomer)], [82.8 (C) (major diastereoisomer) +82.7 (C) (minor diastereoisomer)], [80.4 (CH) (minor diastereoisomer) + 79.3 (CH) (major diastereoisomer)], [60.9 (CH) (major diastereoisomer) + 60.5 (CH) (minor diastereoisomer)], [56.8 (CH) (minor diastereoisomer) + 54.9 (CH) (major diastereoisomer)], [23.1 (CH_3) (major diastereoisomer) + 22.3 (CH_3) (minor diastereoisomer)] ppm; IR (KBr): ν_{max} 3063(w), 2978(w), 1771(s), 1597(m), 1496(m), 1378(s), 1061(m), 755(m), 698(m) cm^{-1}; HRMS calcd for $[C_{25}H_{21}NO_2Cl_2 + Na]^+$ 460.0847, found 460.0849.

Stereochemistry of 5 by NOE

2D NOSEY spectrum showed similar correlations for the major and minor diastereomers. It showed that the methyl protons H^a (following Fig.) were correlated to both H^c and H^d protons and the proton H^c was also correlated to the proton H^b in both the diastereomers, thus providing little information on the stereochemistry in the absence of accurate volume integrals (NOSEY spectra are generally quite noisy), except probably that both the isomers had similar stereochemistry at the stereogenic centres of the tetrahydrofuran ring. This type of NOE correlation between both *cis* and *trans* protons in tetrahydrofurans has



Bicyclic β-lactam 5 (Major isomer)



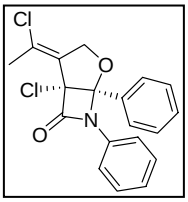
Bicyclic β-lactam 5 (Minor isomer)

Percentage enhancements of relevant proton-signals in difference NOE spectra

been observed earlier and has been rationalized in terms of similar spatial distances between them.[7] However, the *cis* proton still shows higher NOE enhancement than the *trans* proton. Therefore 1D NOE spectra were recorded to determine the relative NOE enhancements more accurately. The percentage NOE enhancements were calculated from the absolute area integrals of the signals before and after irradiation of a particular signal. The aliphatic protons of the two isomers were not sufficiently separated from each other to allow irradiation of the protons of one diastereomer specifically with complete exclusion of that of the other isomer. However, the signals of each isomer could be irradiated, as far as possible, selectively with partial irradiation of that of the other isomer. The spectra are shown in Part II of the Supporting Information along with the spectra of the other compounds. The results are shown pictorially in the above figure.

It was observed that irradiation of the methyl protons H^a caused considerably large enhancement of the H^c proton signal both in the major (6.75%) and minor (5.26%) isomers. The benzylic methine proton H^d was enhanced to a lower extent (1.50 and 1.32% in these isomers, respectively). Similarly, irradiation of the signal due to H^c enhanced the H^a signal reasonably well by 1.13 and 0.93% in the major and minor isomers, respectively. The H^b proton was also enhanced in both the isomers but the percentage enhancements could not be determined accurately because the signals of the major and minor isomers were overlapping. It was not possible to determine the effect of irradiating H^b on H^d accurately because these signals were very close to each other. Though the structures of the two diastereomers did not allow a better comparison to be made, these results might be considered to suggest that the methyl group and the benzylic side-chain were probably *trans* to each other in both the isomers and the two isomers probably differed in the stereochemistry of the benzylic centre of the side-chain.

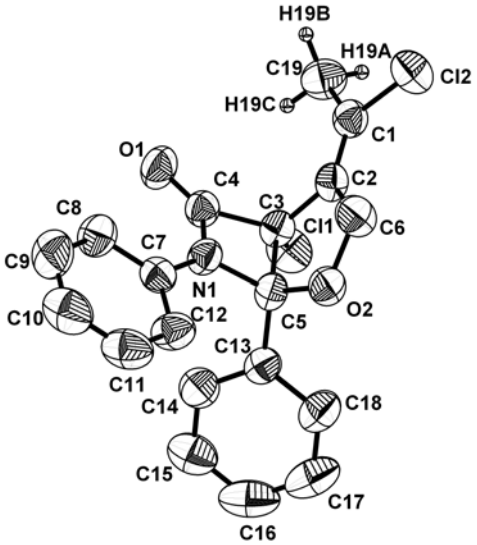
***E*-3-Chloro-4-(1-chloroethylidene)-1,6-diphenyltetrahydrofuro[3,2-c]azetidin-2-one7:**



Yield: 65%; white crystals, mp 92-94 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55-7.42 (m, 7H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 5.28 (qd, *J* = 14.4, 2.0 Hz, 1H), 4.88 (qd, *J* = 14.4, 2.4 Hz, 1H), 2.52 (t, *J* = 2.1 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 158.5 (C), 135.5 (C), 133.2 (C), 132.6 (C), 130.0 (CH), 129.2 (CH), 128.6 (CH), 127.5 (CH), 125.2 (CH), 118.3 (CH), 104.4 (C), 77.9 (C), 73.6 (CH_2), 23.5 (CH_3) ppm; IR (KBr): ν_{max} 3069(w), 2920(w), 2865(w), 1781(s), 1498(m), 1375(s), 1114(m), 1056(m), 745(m), 690(m) cm^{-1}; HRMS calcd for $[C_{19}H_{15}NO_2Cl_2 + Na]^+$ 382.0378, found 382.0374.

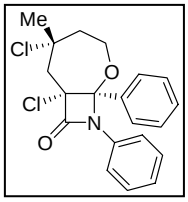
X-ray crystal structure data of 7:

Formula sum: $C_{19}H_{15}Cl_2NO_2$, Formula weight: 360.22; Crystal system: monoclinic; Space group: C2/c; Unit cell dimensions: *a* = 27.270(4) Å, *b* = 7.7951(121) Å, *c* = 18.080(3) Å, α = 90.00(0) °, β = 115.837(2) °, γ = 90.00(0) °; Cell volume = 3459.1(9) $Å^3$, Z = 8; Density calculated = 1.383 g/cm^3; R_{All} = 0.0592. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (CCDC 750464).



ORTEP diagram of bicyclic β-lactam 7

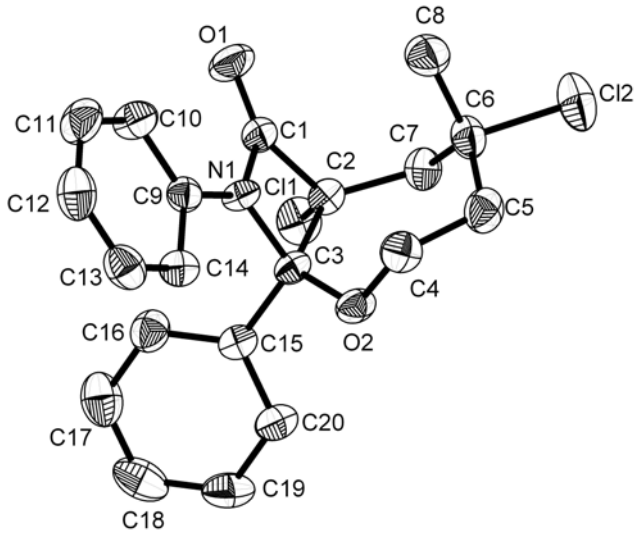
5,7-Dichloro-5-methyl-1,9-diphenyl-2-oxa-9-azabicyclo[5.2.0]nonan-8-one 9:



Yield: 62%; white crystals, mp 135-136 °C (*n*-hexane-ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.8 Hz, 2H), 7.38-7.24 (m, 7H), 7.15 (t, *J* = 7.5 Hz, 1H), 3.96 (td, *J* = 13.8, 3.6 Hz, 1H), 3.82 (t, *J* = 12.9 Hz, 1H), 3.11 (dd, *J* = 14.9, 2.3 Hz, 1H), 2.99 (d, *J* = 15.0 Hz, 1H), 2.67 (dt, *J* = 13.2, 3.3 Hz, 1H), 2.21 (d, *J* = 14.7 Hz, 1H), 1.83 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 163.0 (C), 135.97 (C), 135.94 (C), 129.5 (CH), 129.1 (CH), 128.0 (CH), 127.0 (CH), 125.5 (CH), 118.1 (CH), 99.3 (C), 79.7 (C), 68.7 (C), 60.9 (CH_2), 51.4 (CH_2), 48.0 (CH_2), 28.7 (CH_3) ppm; IR (KBr): ν_{max} 3062(w), 2977(w), 2955(w), 1780(s), 1595(m), 1497(m), 1373(s), 1132(s), 1096(m), 755(m), 695(m) cm^{-1}; HRMS calcd for $[C_{20}H_{19}NO_2Cl_2 + H]^+$ 376.0871, found 376.0873.

X-ray crystal structure data of 9:

Formula sum: $C_{20}H_{19}Cl_2NO_2$, Formula weight: 376.26; Crystal system: monoclinic; Space group: P2(1)/c; Unit cell dimensions: *a* = 11.291(5) Å, *b* = 15.222(7) Å, *c* = 21.328(10) Å, α = 90.00(0) °, β = 96.717(9) °, γ = 90.00(0) °; Cell volume = 3641(3) $Å^3$, Z = 8; Density calculated = 1.373 g/cm^3; R_{All} = 0.1319. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (CCDC 739845).

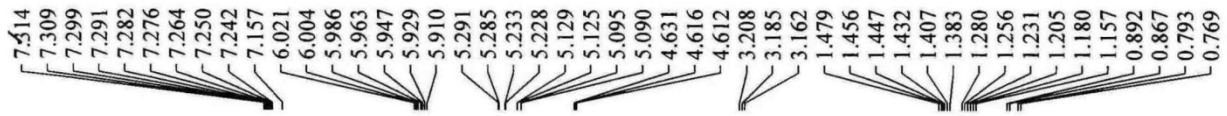


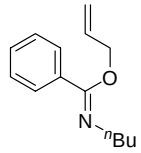
ORTEP diagram of bicyclic β-lactam 9

3. References:

1. (a) Van den Hoven, B. G.; Alper, H. *J. Am. Chem. Soc.* **2001,** *123,* 10214-10220. (b) Riggs, R. L.; Morton, C. J. H.; Slawin, A. M. Z.; Smith, D. M.; Westwood, N. J.; Austen, W. S. D.; Stuart, K. E. *Tetrahedron* **2005**, *61*, 11230-11243.
2. Calter, M.; Hollis, T. K.; Overman, L. E.; Ziller, J.; Zipp, G. G. *J. Org. Chem.* **1997**, *62,* 1449-1456.
3. Aucagne, V.; Leigh, D. A. *Org. Lett.* **2006**, *8*, 4505-4507.
4. Engman, L. *J. Org. Chem.* **1993**, *58*, 2394-2401.
5. Ma, J.; Cui, X.; Yang, D.; Wu, J.; Song, M.; Wu, Y. *Appl. Organomet. Chem.* **2008**, *22*, 624-628.
6. Schenck, T. G.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2058-2066.
7. (a) Quideau, S.; Ralph, J. *J Chem. Soc., Perkin Trans 1* **1993**, 653-659. (b) Sutterer, A.; Moeller, K. D. *J. Am. Chem. Soc.* **2000,** *122,* 5636-5637.

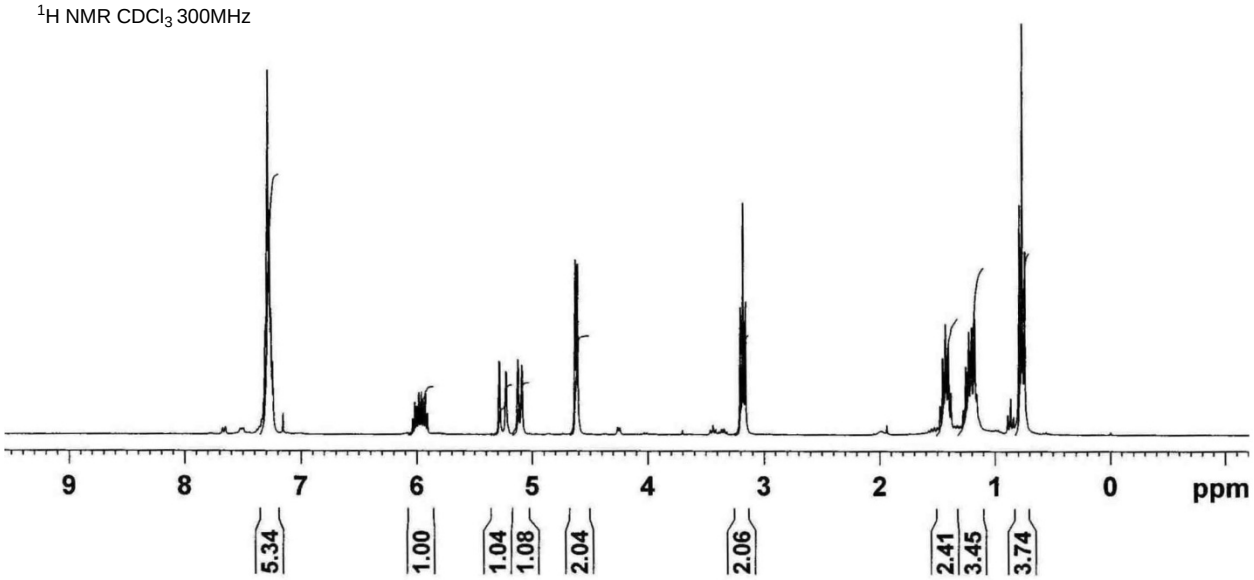
4. ^{1}H and ^{13}C NMR spectra of the imidates, monocyclic β-lactams and bicyclic β-lactams

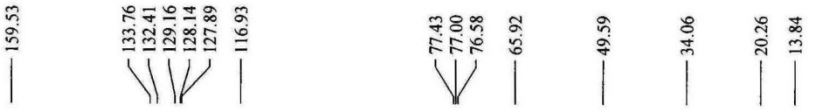


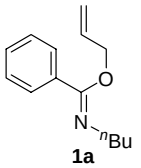


1a

^{1}H NMR $CDCl_3$ 300MHz

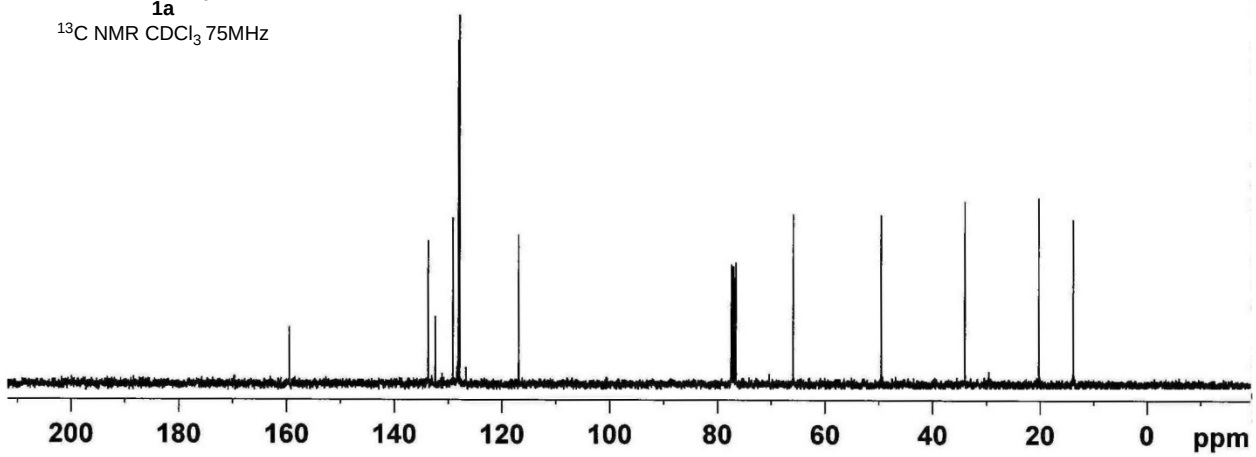


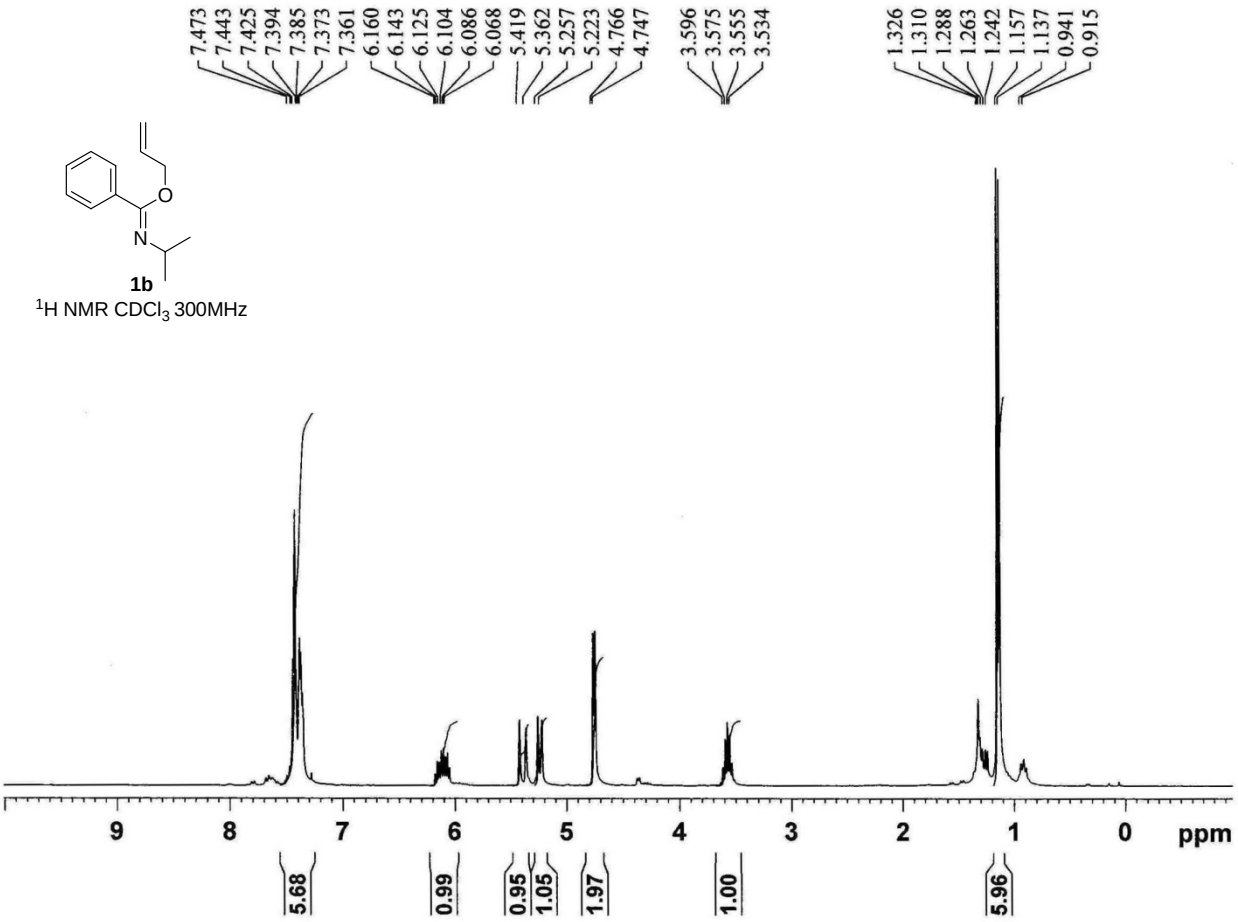




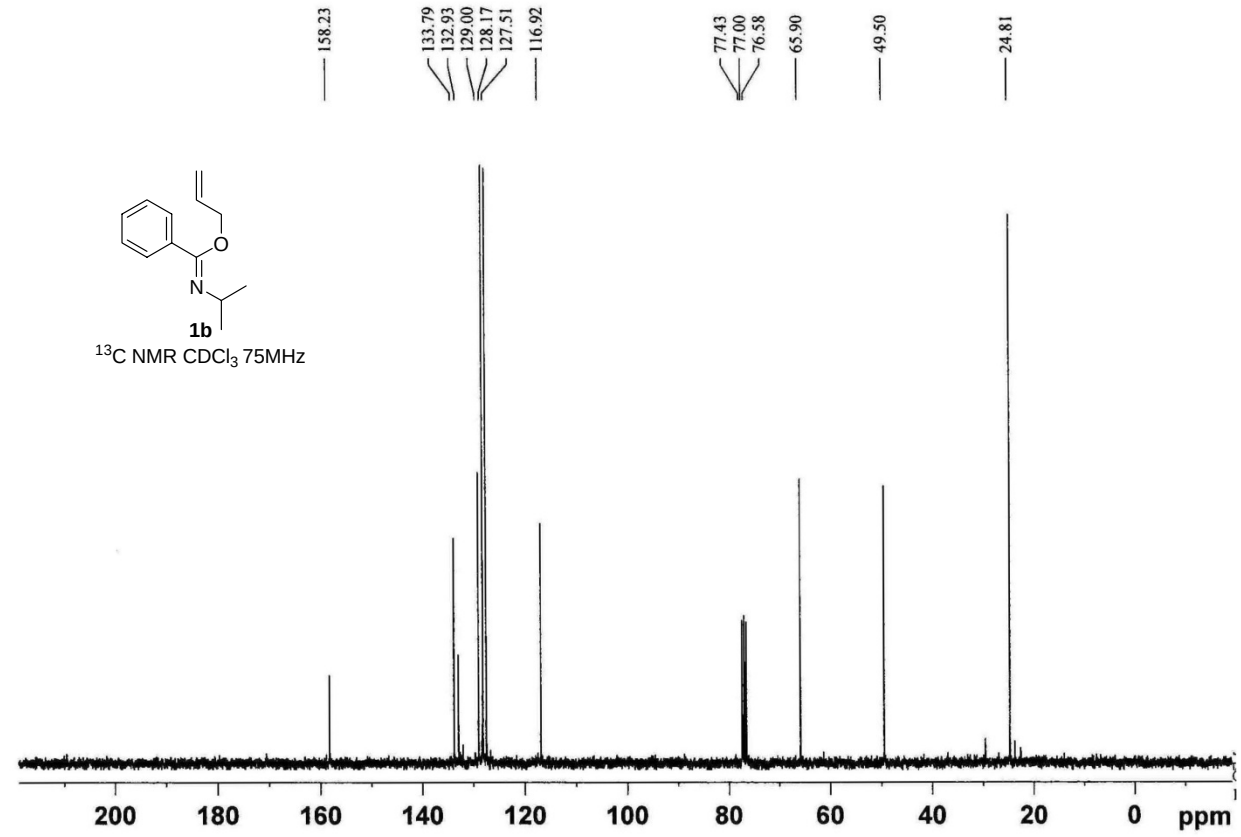
1a

^{13}C NMR $CDCl_3$ 75MHz

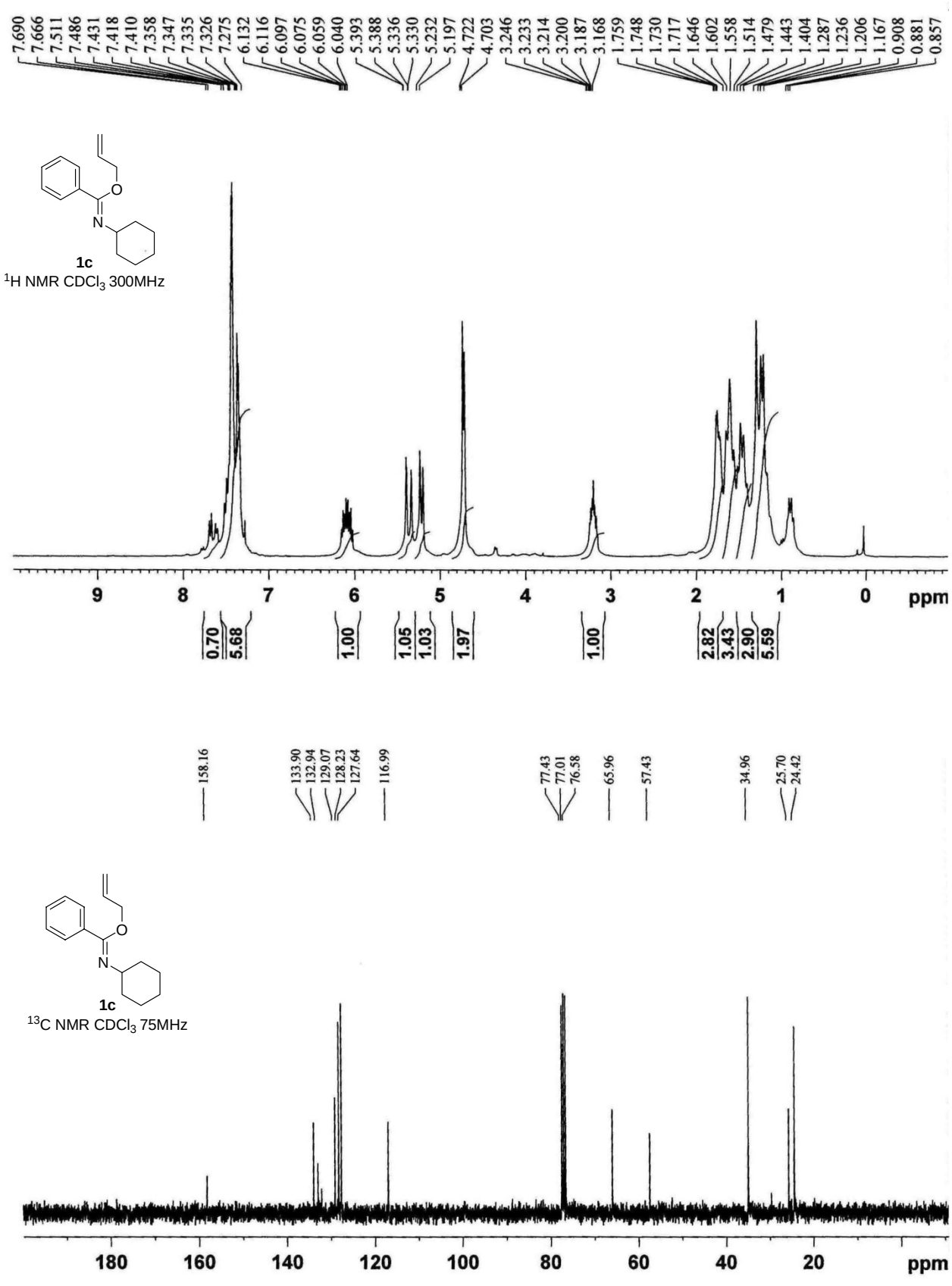


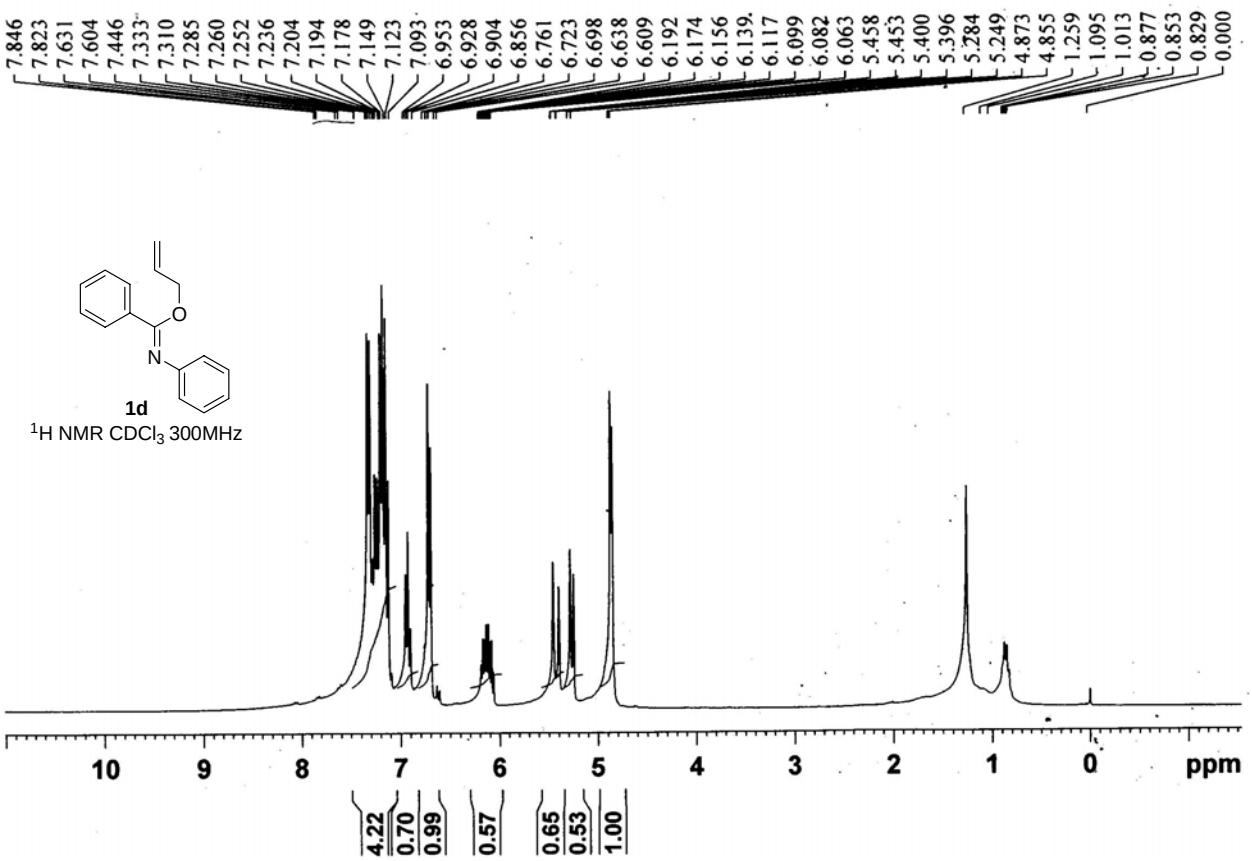


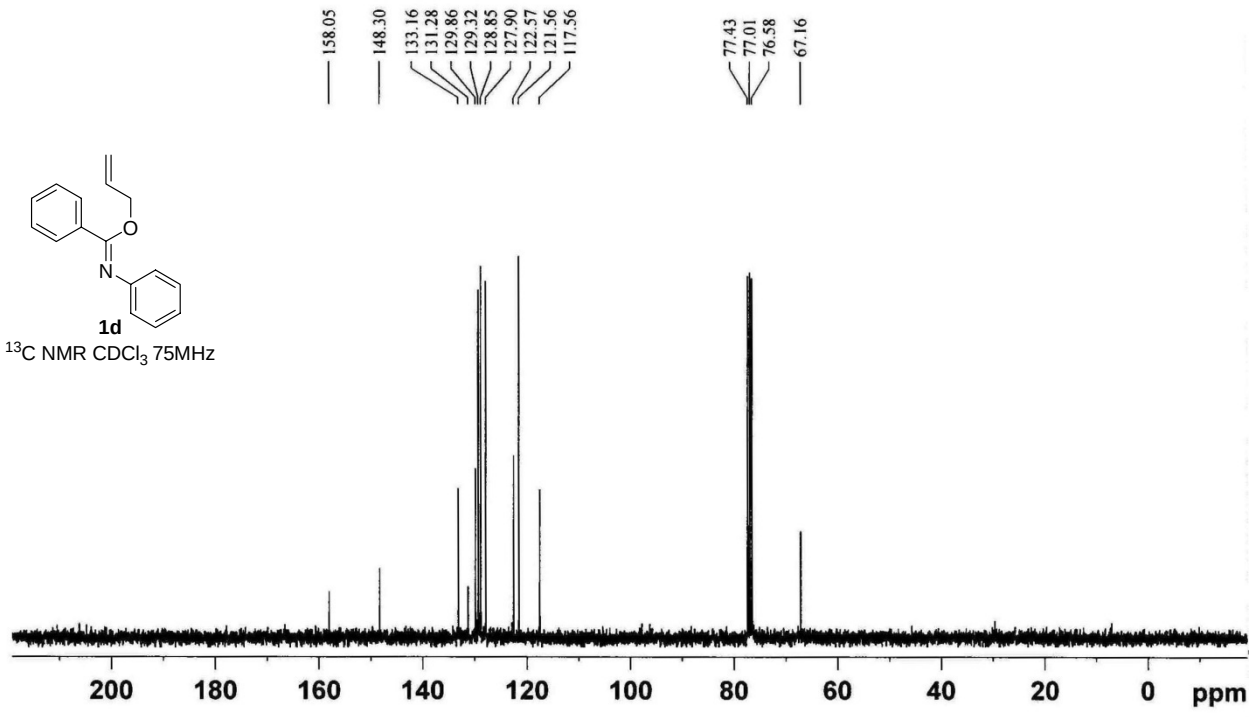
^{1}H NMR $CDCl_3$ 300MHz

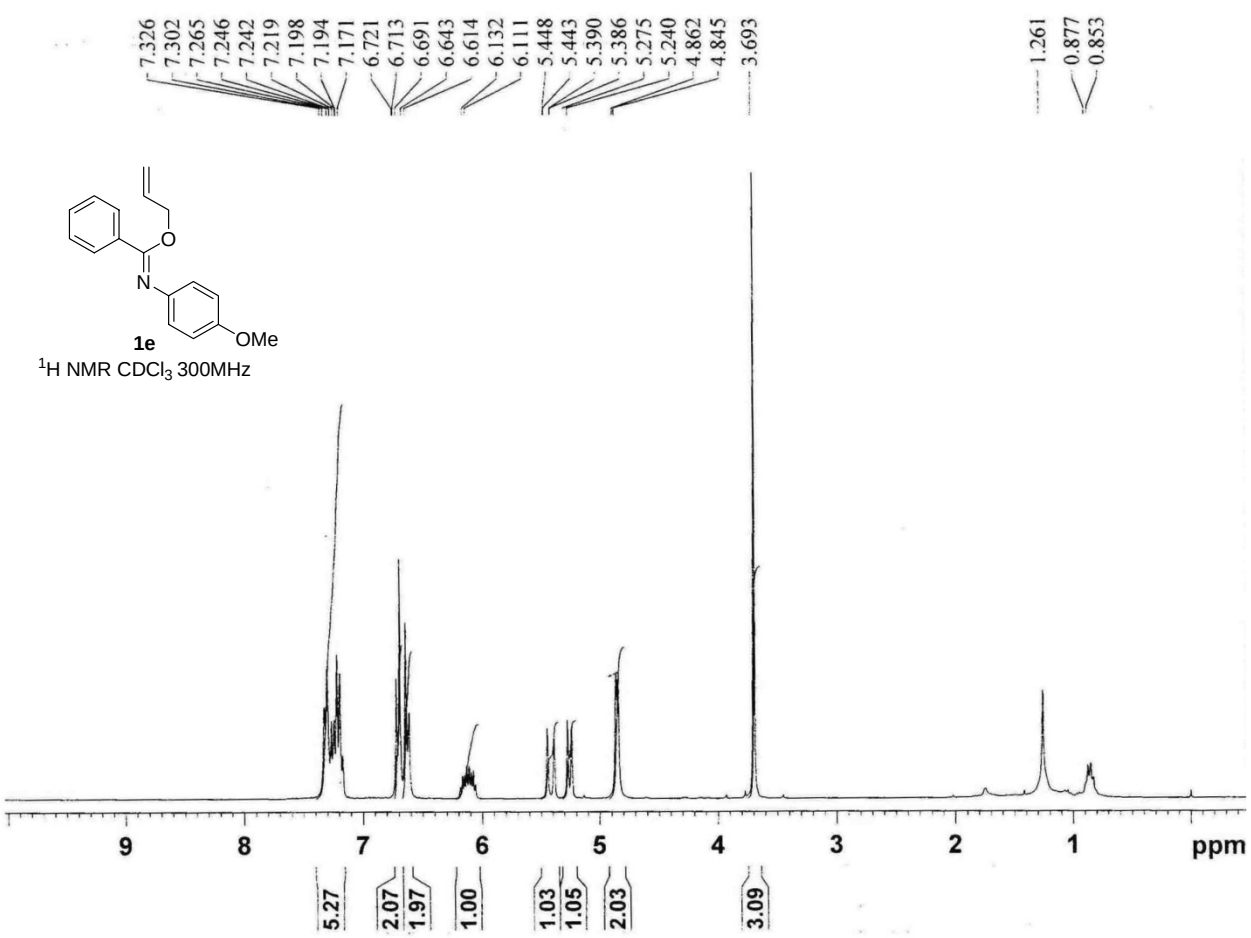


^{13}C NMR $CDCl_3$ 75MHz


7.690
7.666
7.511
7.486
7.431
7.418
7.410
7.358
7.347
7.335
7.326
7.275
6.132
6.116
6.097
6.075
6.059
6.040
5.393
5.388
5.336
5.330
5.232
5.197
4.722
4.703
3.246
3.233
3.214
3.200
3.187
3.168
1.759
1.748
1.730
1.717
1.646
1.602
1.558
1.514
1.479
1.443
1.404
1.287
1.236
1.206
1.167
0.908
0.881
0.857
O
N
1c
1H NMR CDCl3 300MHz
9
8
7
6
5
4
3
2
1
0
ppm
0.70
5.68
1.00
1.05
1.03
1.97
1.00
2.82
3.43
2.90
5.59
158.16
133.90
132.94
129.07
128.23
127.64
116.99
77.43
77.01
76.58
65.96
57.43
34.96
25.70
24.42
O
N
1c
13C NMR CDCl3 75MHz
180
160
140
120
100
80
60
40
20
ppm

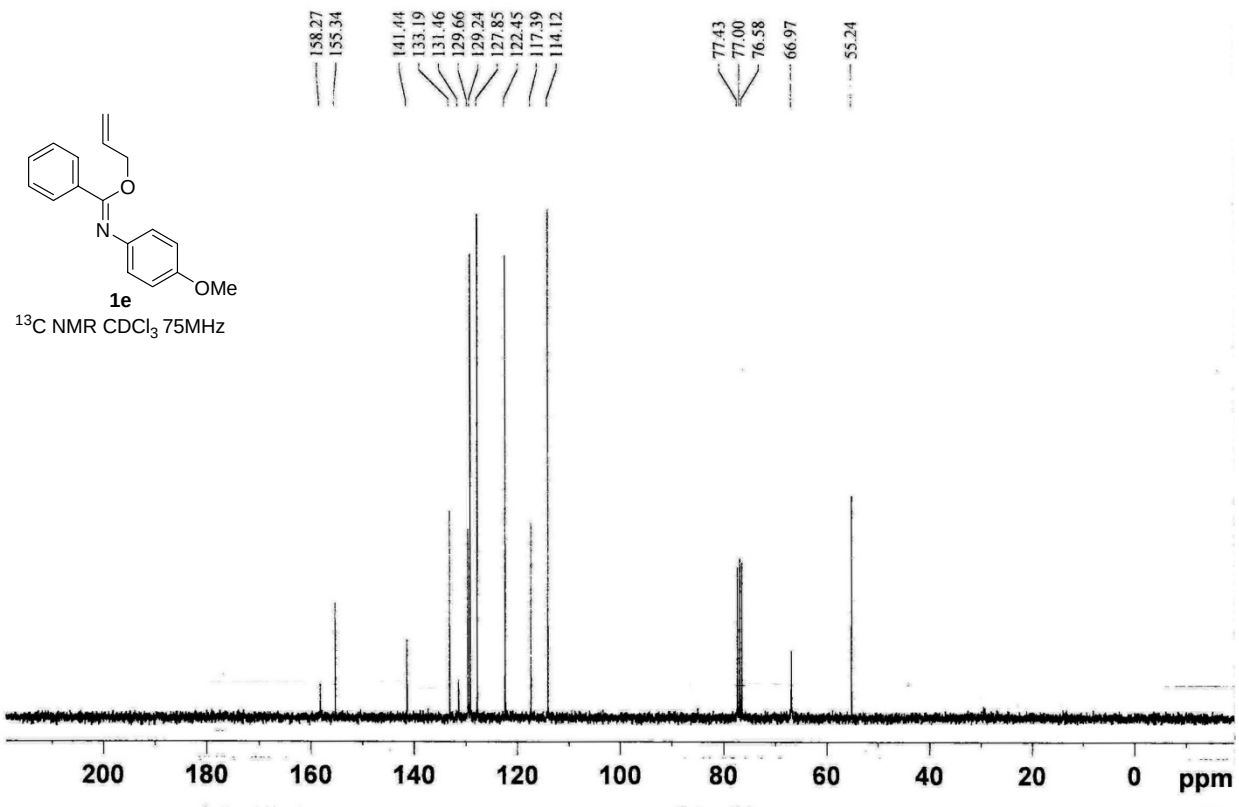

7.846
7.823
7.631
7.604
7.446
7.333
7.310
7.285
7.260
7.252
7.236
7.204
7.194
7.178
7.149
7.123
7.093
6.953
6.928
6.904
6.856
6.761
6.723
6.698
6.638
6.609
6.192
6.174
6.156
6.139
6.117
6.099
6.082
6.063
5.458
5.453
5.400
5.396
5.284
5.249
4.873
4.855
1.259
1.095
1.013
0.877
0.853
0.829
0.000
O
N
1d
1H NMR CDCl3 300MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
4.22
0.70
0.99
0.57
0.65
0.53
1.00


158.05
148.30
133.16
131.28
129.86
129.32
128.85
127.90
122.57
121.56
117.56
77.43
77.01
76.58
67.16
O
N
1d
13C NMR CDCl3 75MHz
200
180
160
140
120
100
80
60
40
20
0
ppm



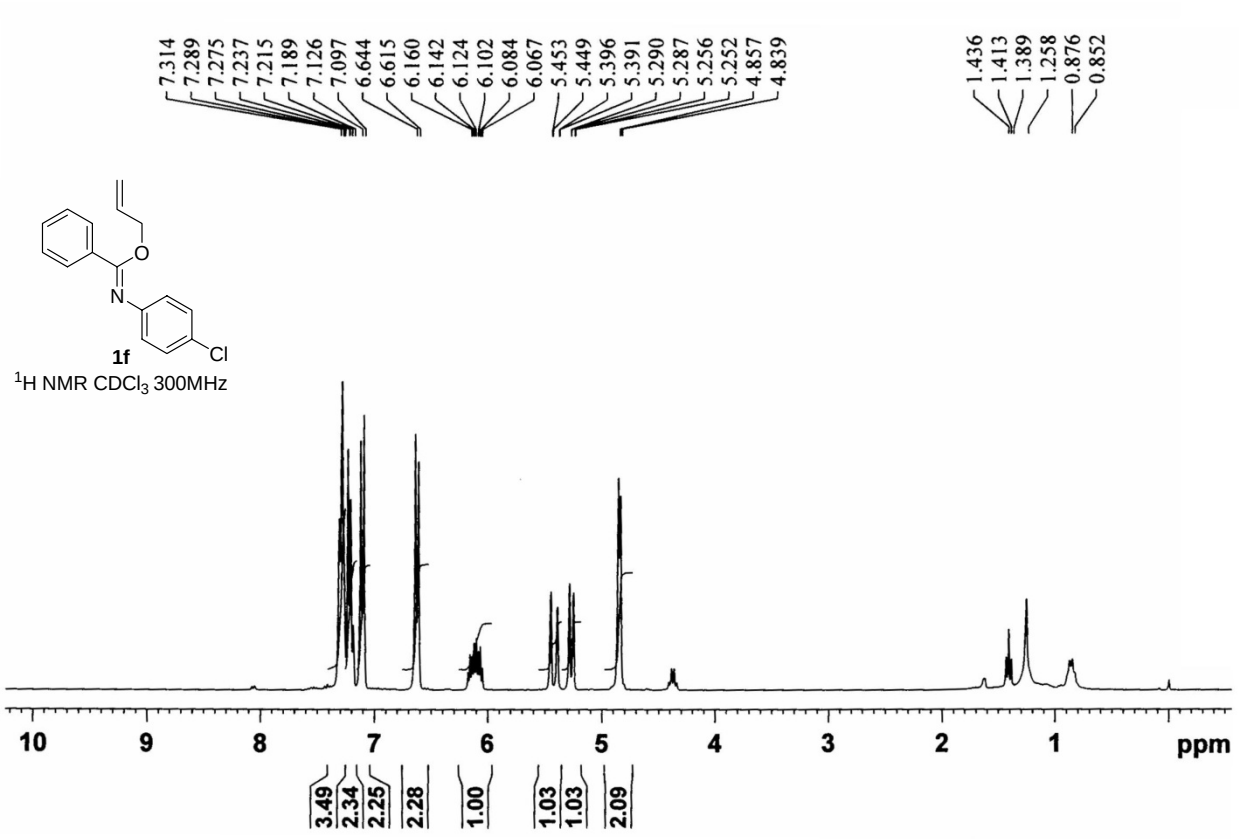
1e

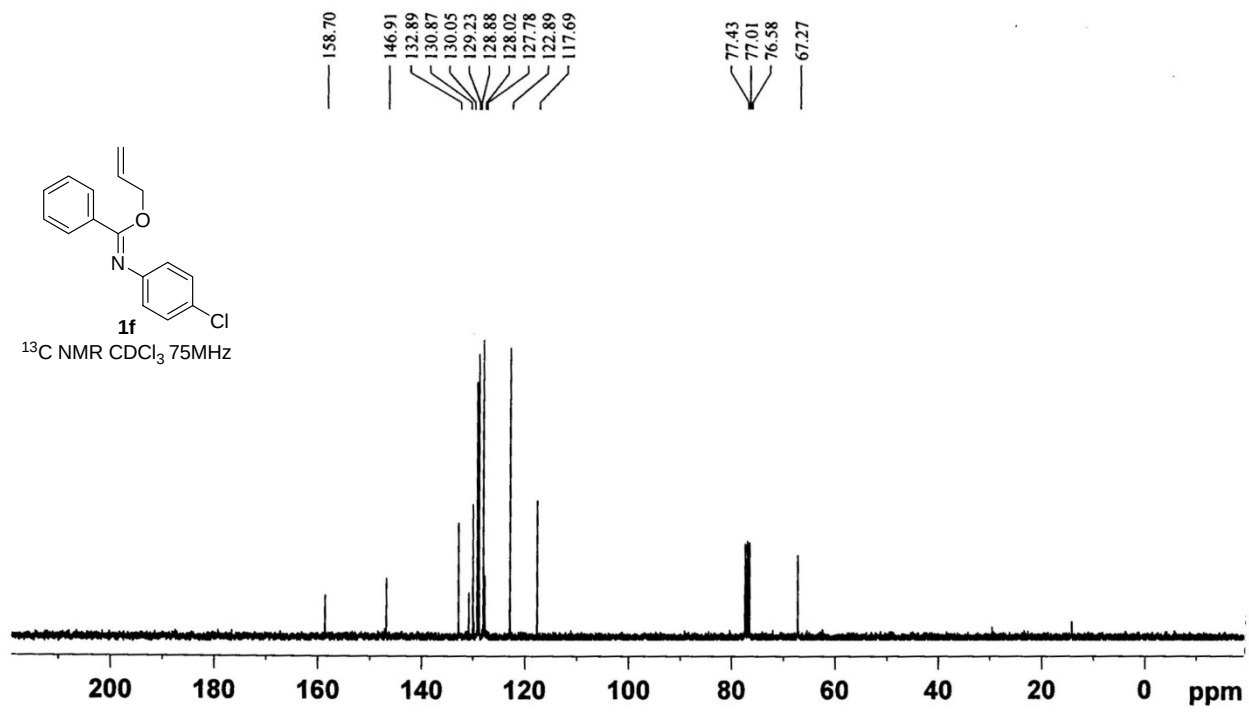
^{1}H NMR $CDCl_3$ 300MHz

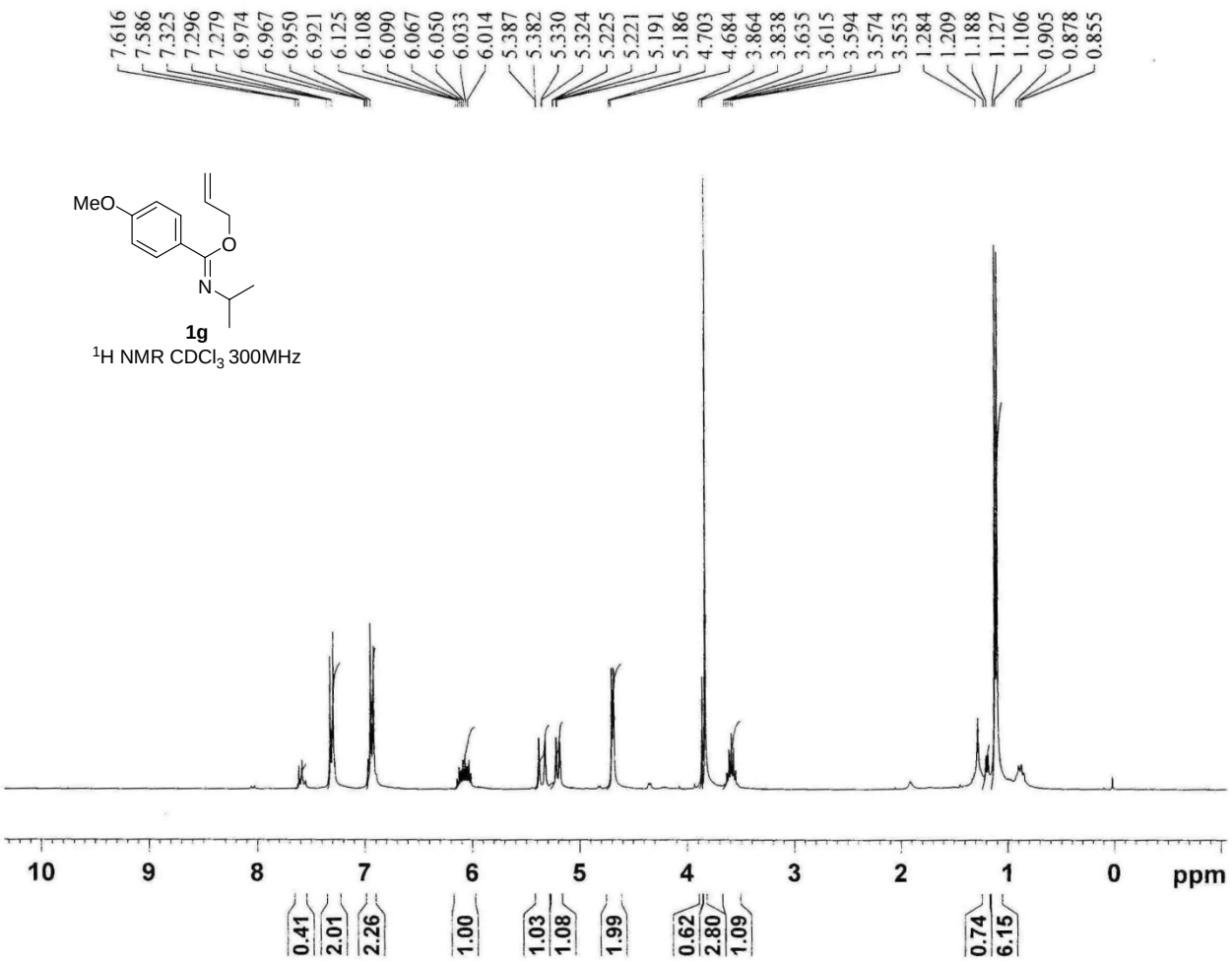


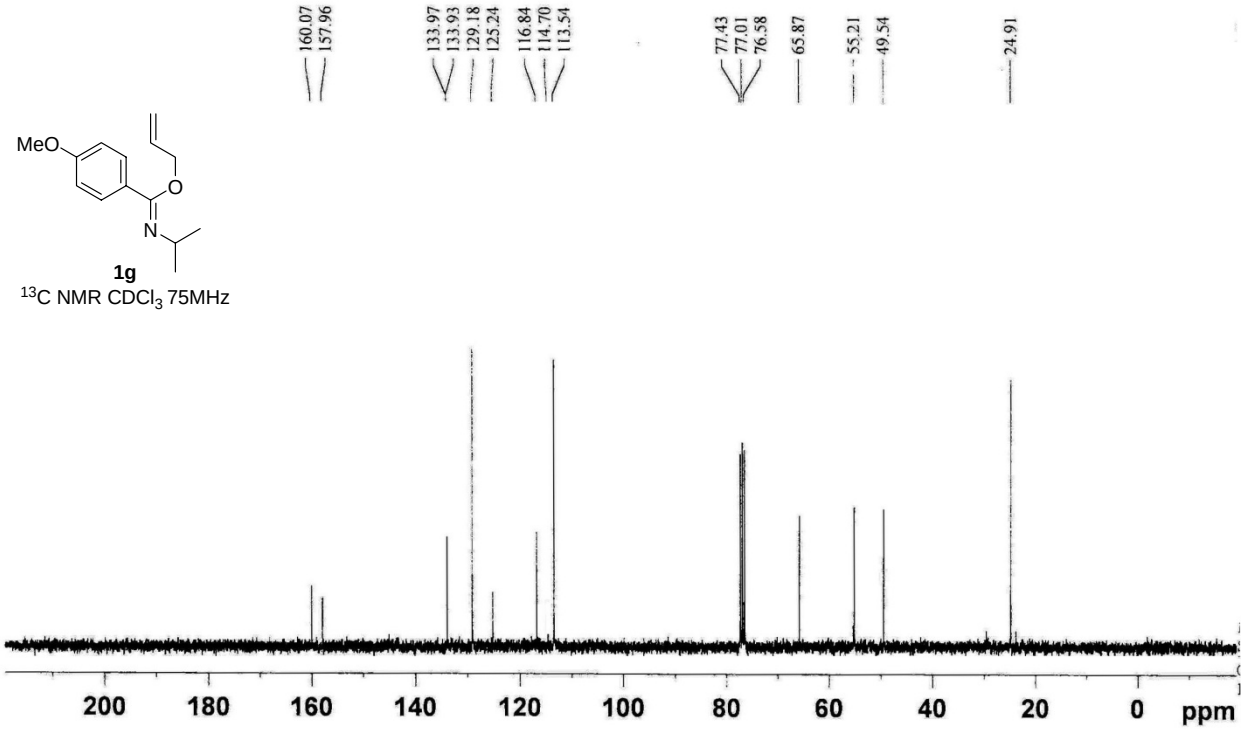
1e

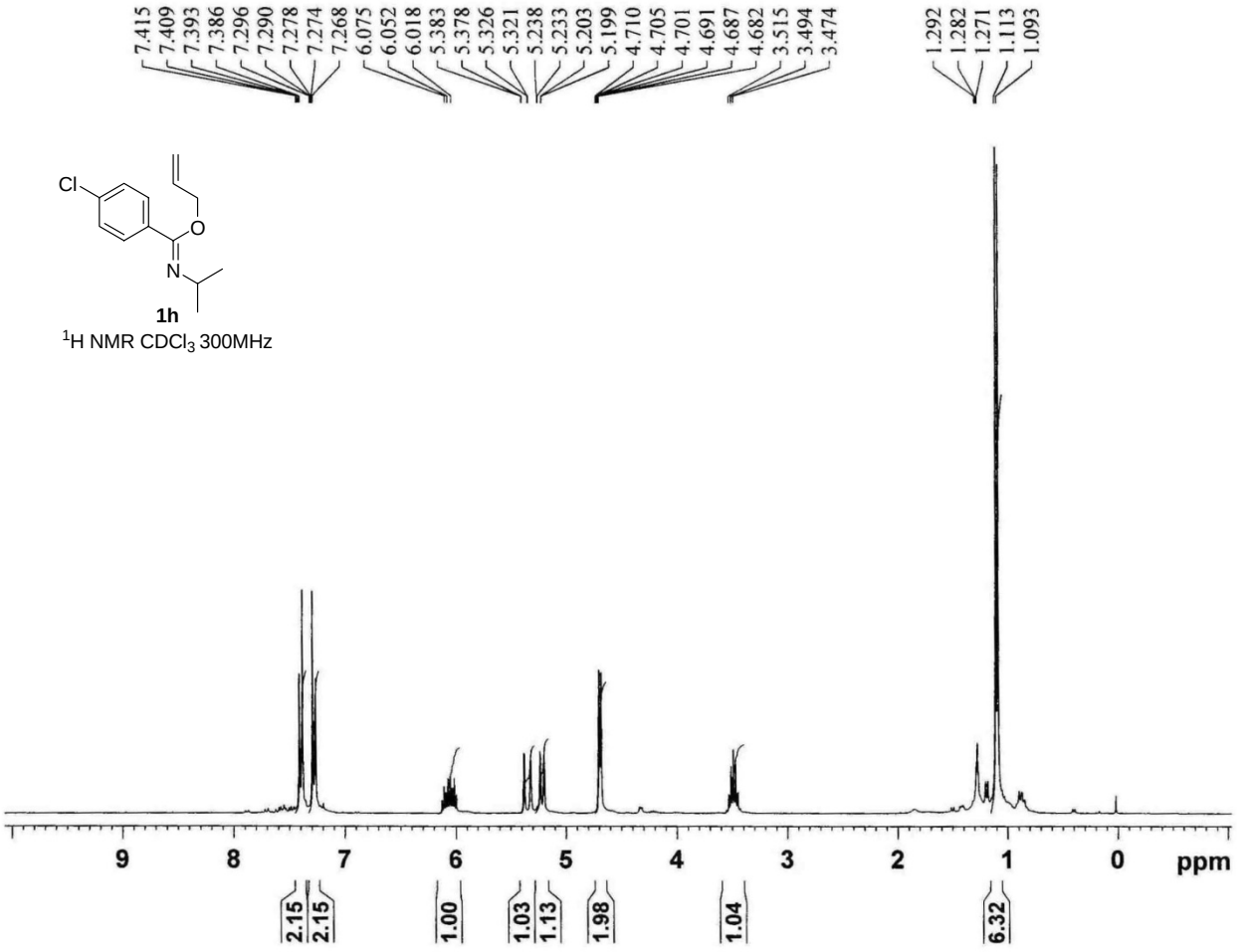
^{13}C NMR $CDCl_3$ 75MHz

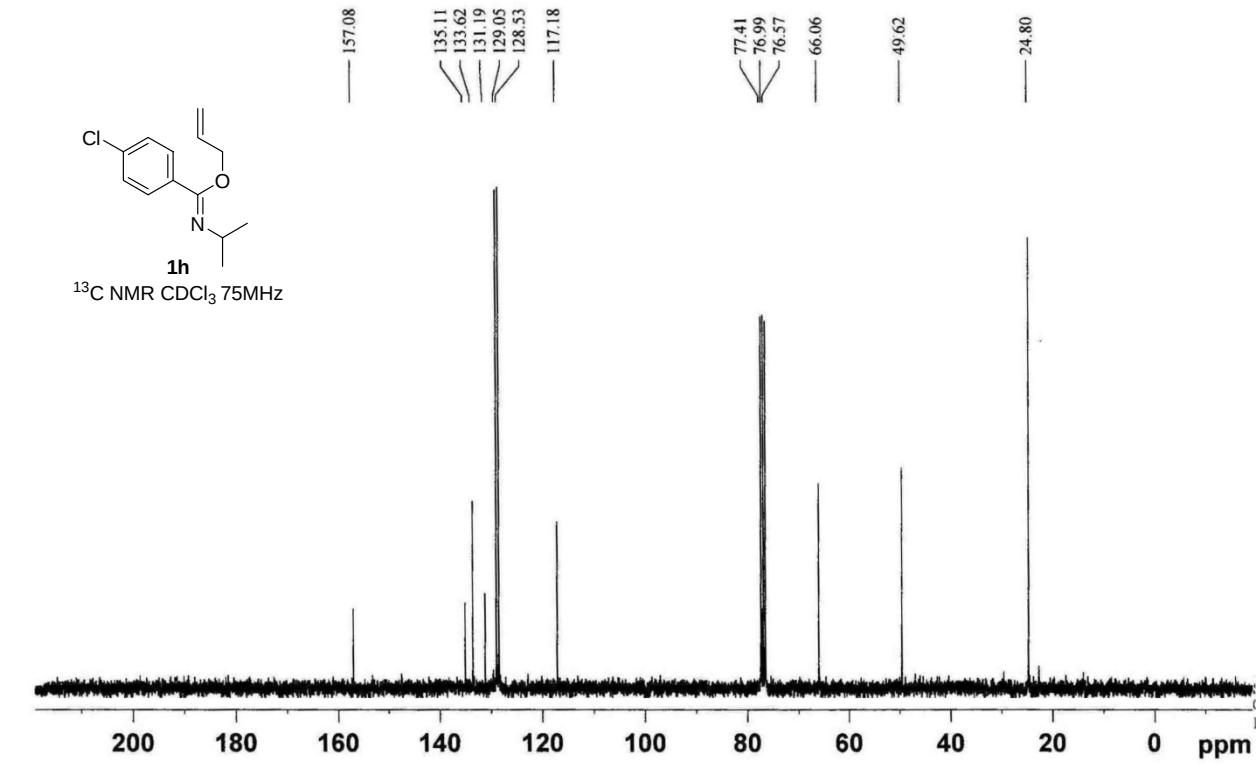

7.314
7.289
7.275
7.237
7.215
7.189
7.126
7.097
6.644
6.615
6.160
6.142
6.124
6.102
6.084
6.067
5.453
5.449
5.396
5.391
5.290
5.287
5.256
5.252
4.857
4.839
1.436
1.413
1.389
1.258
0.876
0.852
O
N
Cl
1f
1H NMR CDCl3 300MHz
10
9
8
7
6
5
4
3
2
1
ppm
3.49
2.34
2.25
2.28
1.00
1.03
1.03
2.09

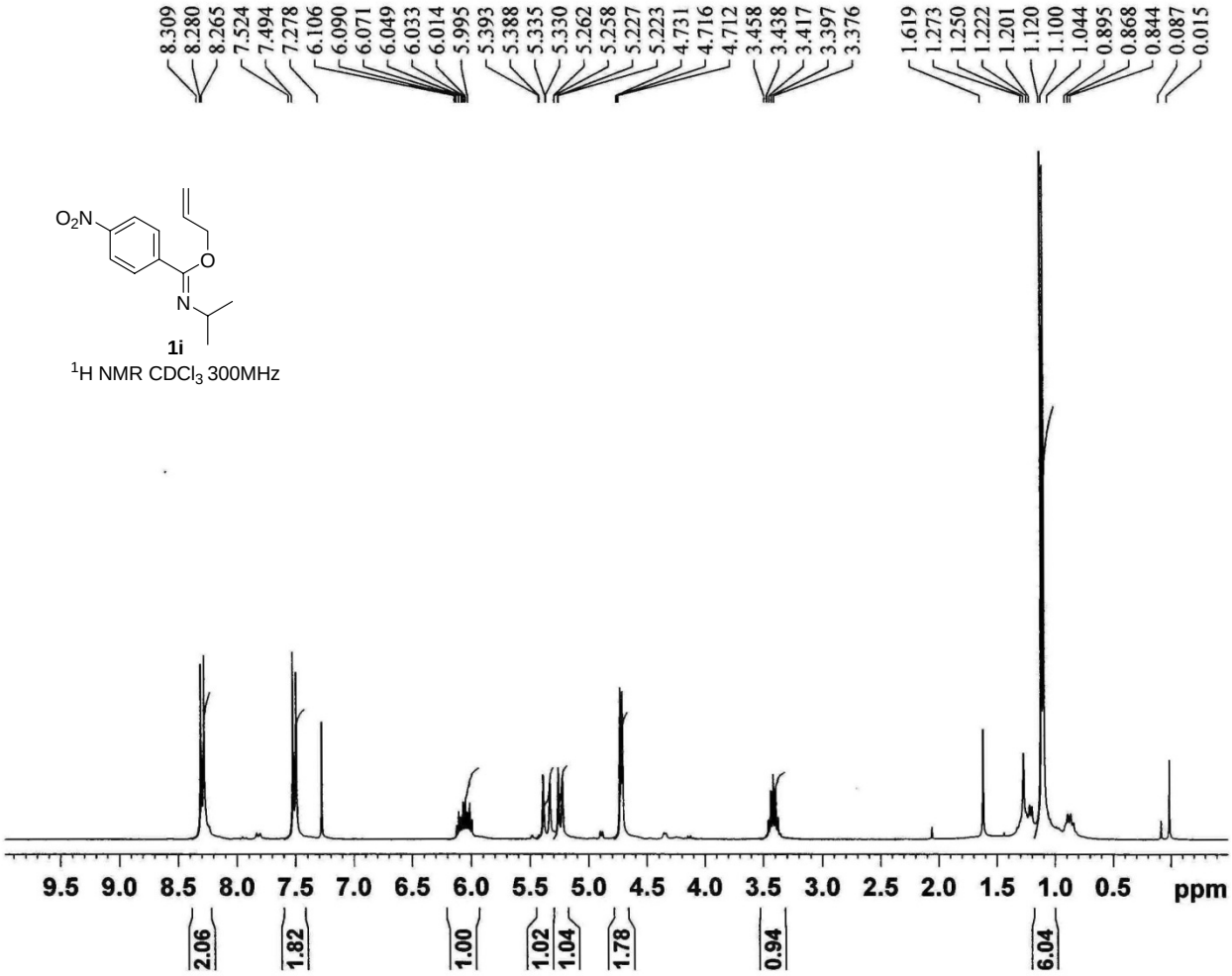

158.70
146.91
132.89
130.87
130.05
129.23
128.88
128.02
127.78
122.89
117.69
77.43
77.01
76.58
67.27
O
N
Cl
1f
13C NMR CDCl3 75MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

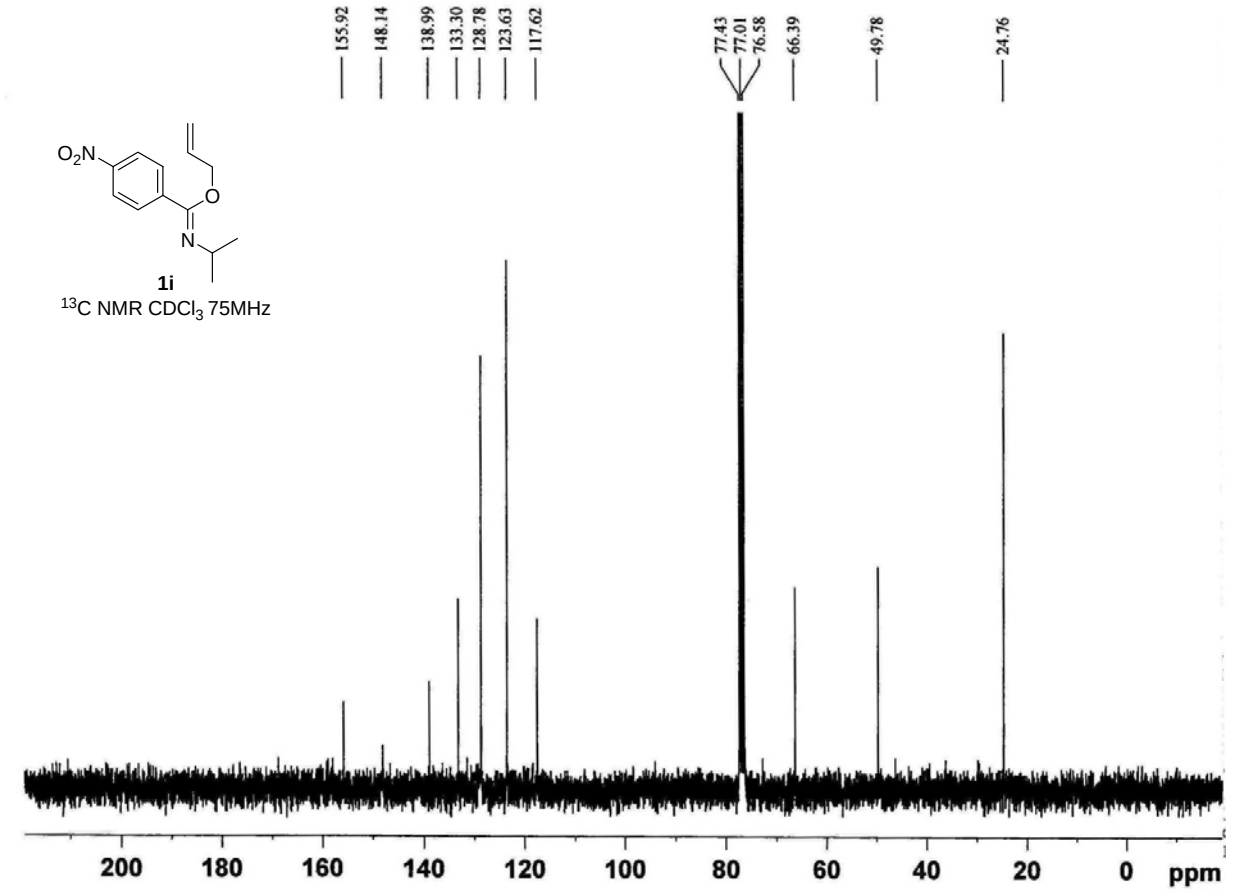

7.616
7.586
7.325
7.296
7.279
6.974
6.967
6.950
6.921
6.125
6.108
6.090
6.067
6.050
6.033
6.014
5.387
5.382
5.330
5.324
5.225
5.221
5.191
5.186
4.703
4.684
3.864
3.838
3.635
3.615
3.594
3.574
3.553
1.284
1.209
1.188
1.127
1.106
0.905
0.878
0.855
MeO
O
N
1g
1H NMR CDCl3 300MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
0.41
2.01
2.26
1.00
1.03
1.08
1.99
0.62
2.80
1.09
0.74
6.15

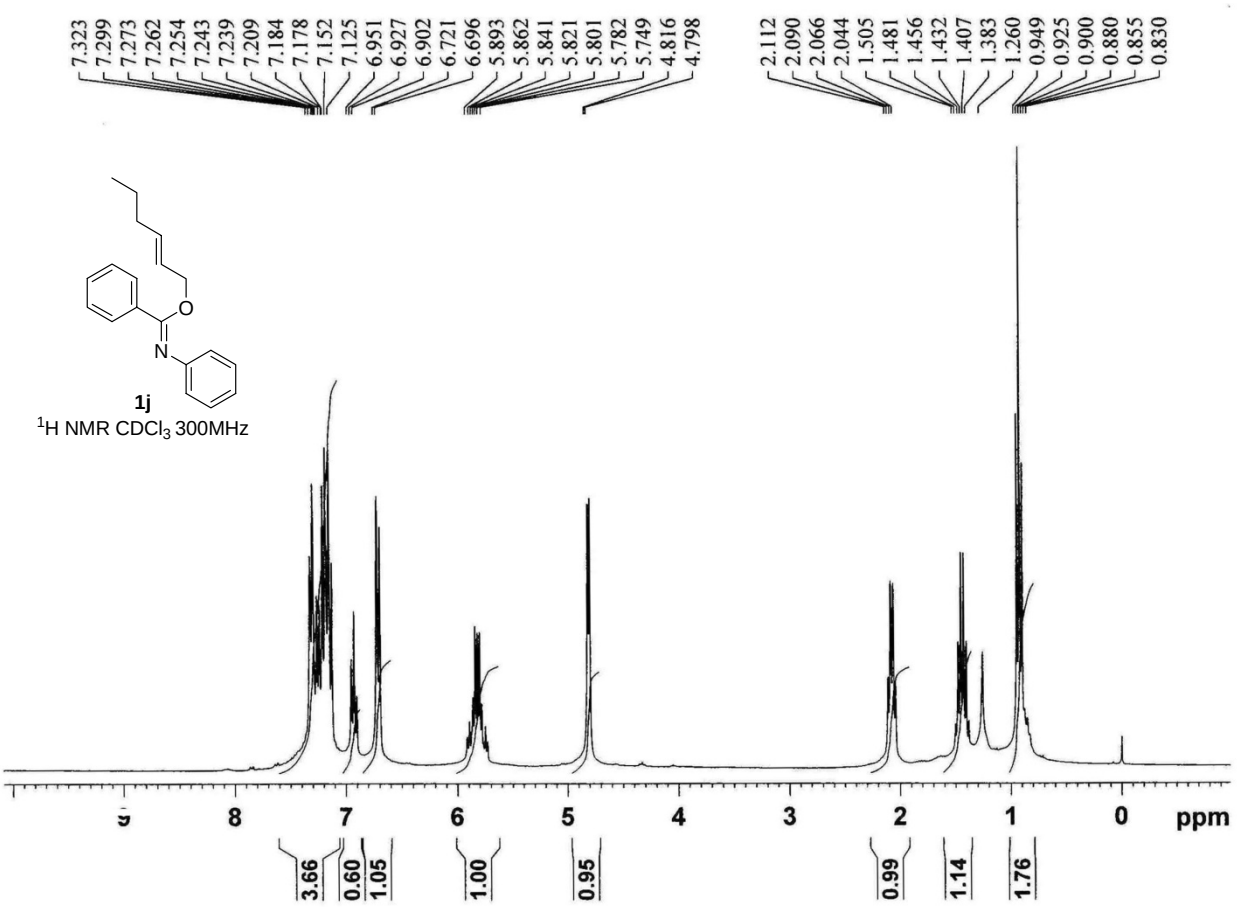

160.07
157.96
133.97
133.93
129.18
125.24
116.84
114.70
113.54
77.43
77.01
76.58
65.87
55.21
49.54
24.91
MeO
O
N
1g
13C NMR CDCl3 75MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

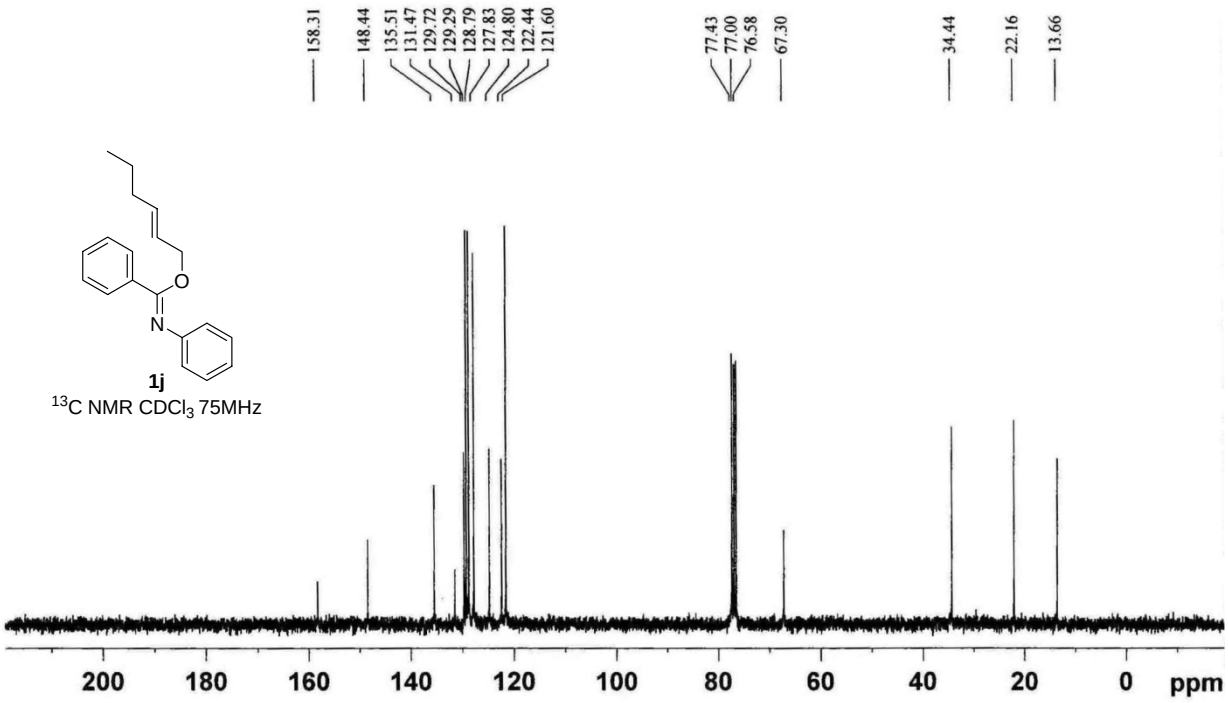

7.415
7.409
7.393
7.386
7.296
7.290
7.278
7.274
7.268
6.075
6.052
6.018
5.383
5.378
5.326
5.321
5.238
5.233
5.203
5.199
4.710
4.705
4.701
4.691
4.687
4.682
3.515
3.494
3.474
1.292
1.282
1.271
1.113
1.093
Cl
O
N
1h
1H NMR CDCl3 300MHz
9
8
7
6
5
4
3
2
1
0
ppm
2.15
2.15
1.00
1.03
1.13
1.98
1.04
6.32

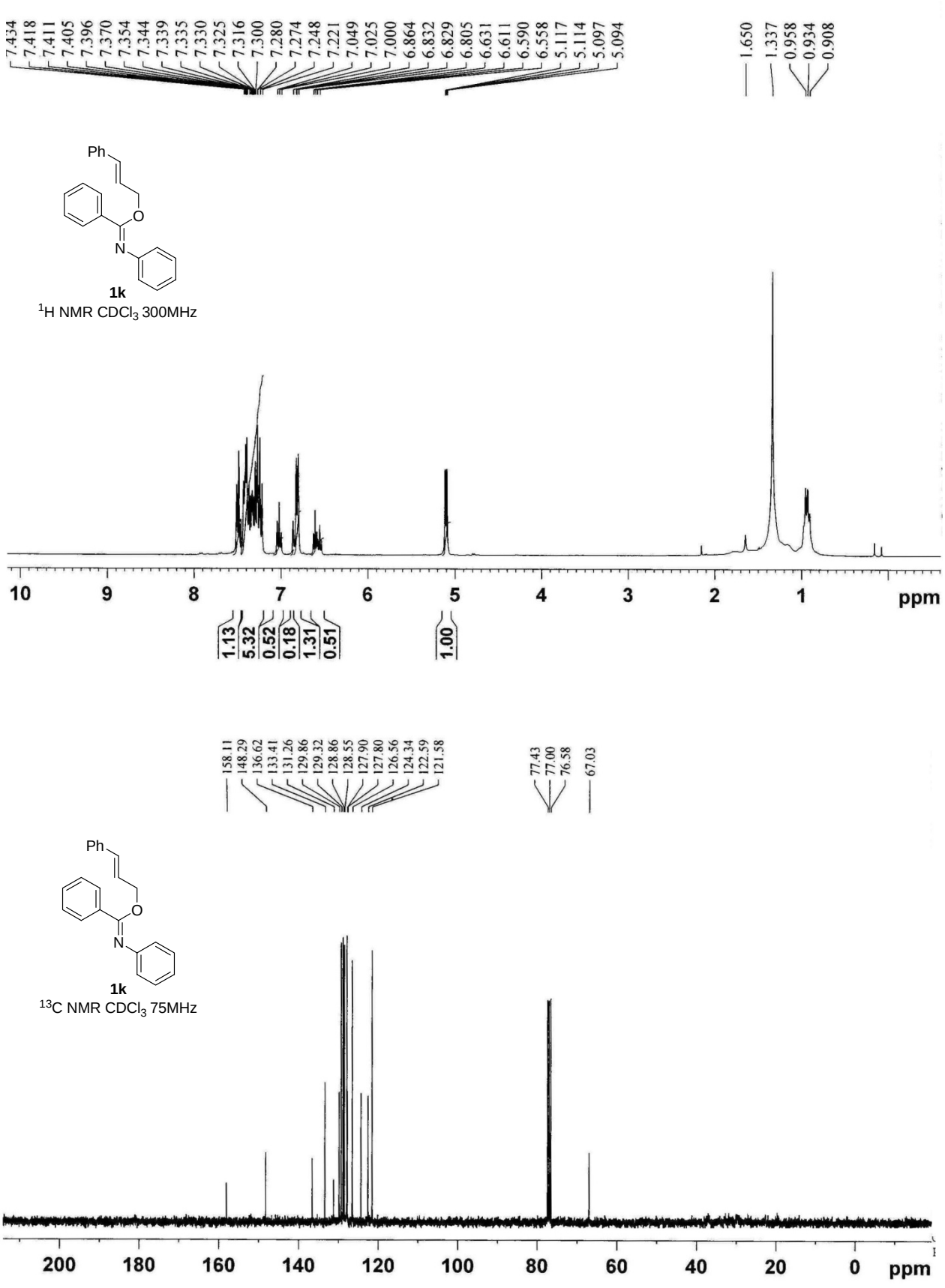

157.08
135.11
133.62
131.19
129.05
128.53
117.18
77.41
76.99
76.57
66.06
49.62
24.80
Cl
O
N
1h
13C NMR CDCl3 75MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

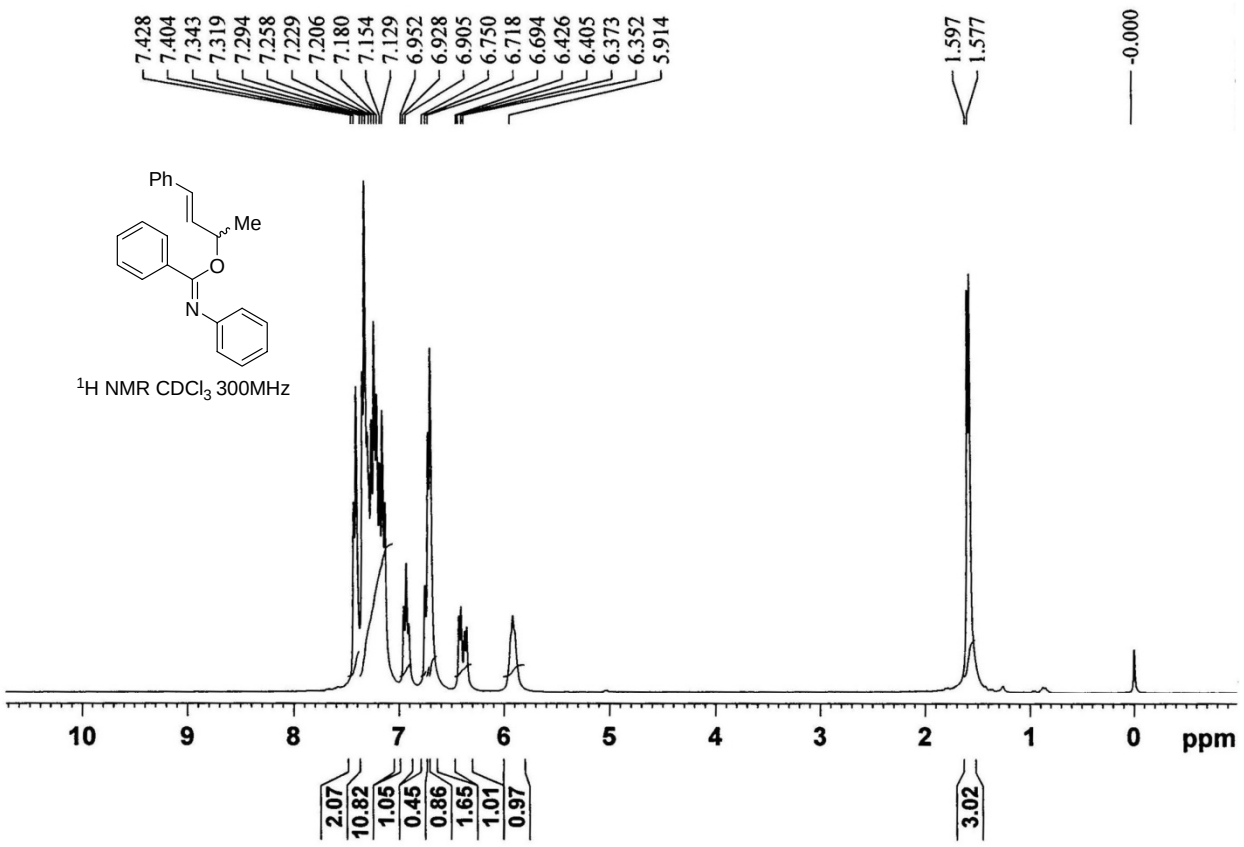

8.309
8.280
8.265
7.524
7.494
7.278
6.106
6.090
6.071
6.049
6.033
6.014
5.995
5.393
5.388
5.335
5.330
5.262
5.258
5.227
5.223
4.731
4.716
4.712
3.458
3.438
3.417
3.397
3.376
1.619
1.273
1.250
1.222
1.201
1.120
1.100
1.044
0.895
0.868
0.844
0.087
0.015
O2N
O
N
1i
1H NMR CDCl3 300MHz
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.06
1.82
1.00
1.02
1.04
1.78
0.94
6.04


155.92
148.14
138.99
133.30
128.78
123.63
117.62
77.43
77.01
76.58
66.39
49.78
24.76
O2N
O
N
1i
13C NMR CDCl3 75MHz
200 180 160 140 120 100 80 60 40 20 0 ppm

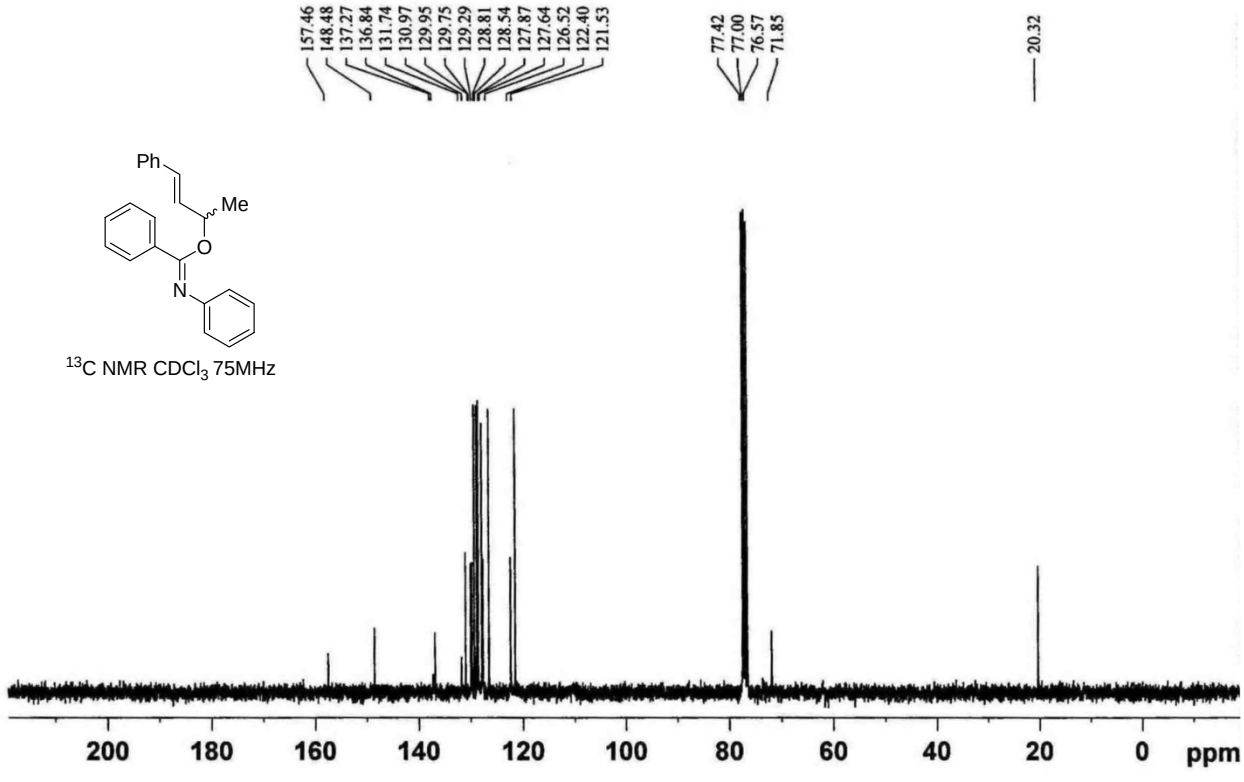

7.323
7.299
7.273
7.262
7.254
7.243
7.239
7.209
7.184
7.178
7.152
7.125
6.951
6.927
6.902
6.721
6.696
5.893
5.862
5.841
5.821
5.801
5.782
5.749
4.816
4.798
2.112
2.090
2.066
2.044
1.505
1.481
1.456
1.432
1.407
1.383
1.260
0.949
0.925
0.900
0.880
0.855
0.830
O
N
1j
1H NMR CDCl3 300MHz
8
7
6
5
4
3
2
1
0
ppm
3.66
0.60
1.05
1.00
0.95
0.99
1.14
1.76


158.31
148.44
135.51
131.47
129.72
129.29
128.79
127.83
124.80
122.44
121.60
77.43
77.00
76.58
67.30
34.44
22.16
13.66
O
N
1j
13C NMR CDCl3 75MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

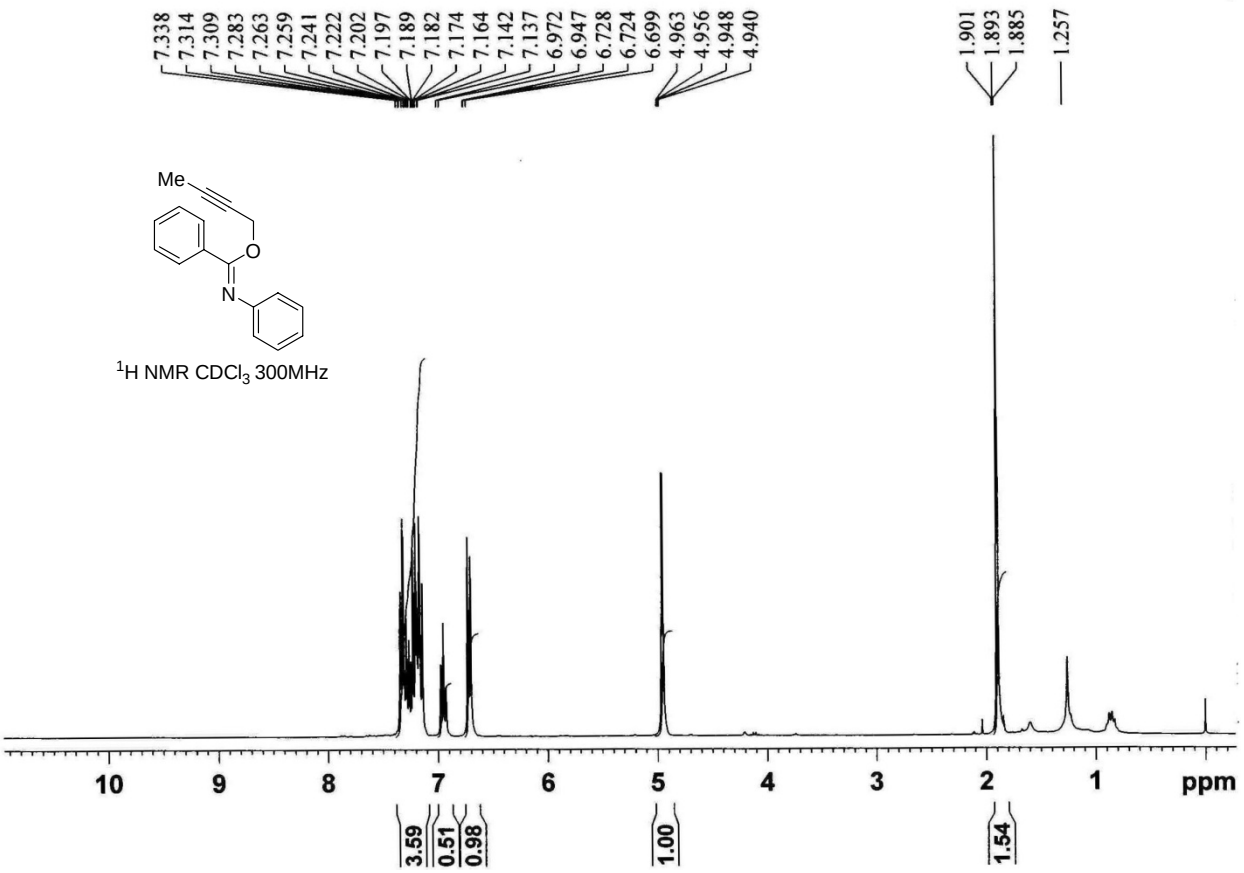

7.434
7.418
7.411
7.405
7.396
7.370
7.354
7.344
7.339
7.335
7.330
7.325
7.316
7.300
7.280
7.274
7.248
7.221
7.049
7.025
7.000
6.864
6.832
6.829
6.805
6.631
6.611
6.590
6.558
5.117
5.114
5.097
5.094
1.650
1.337
0.958
0.934
0.908
Ph
O
N
1k
1H NMR CDCl3 300MHz
10
9
8
7
6
5
4
3
2
1
ppm
1.13
5.32
0.52
0.18
1.31
0.51
1.00
158.11
148.29
136.62
133.41
131.26
129.86
129.32
128.86
128.55
127.90
127.80
126.56
124.34
122.59
121.58
77.43
77.00
76.58
67.03
Ph
O
N
1k
13C NMR CDCl3 75MHz
200
180
160
140
120
100
80
60
40
20
0
ppm



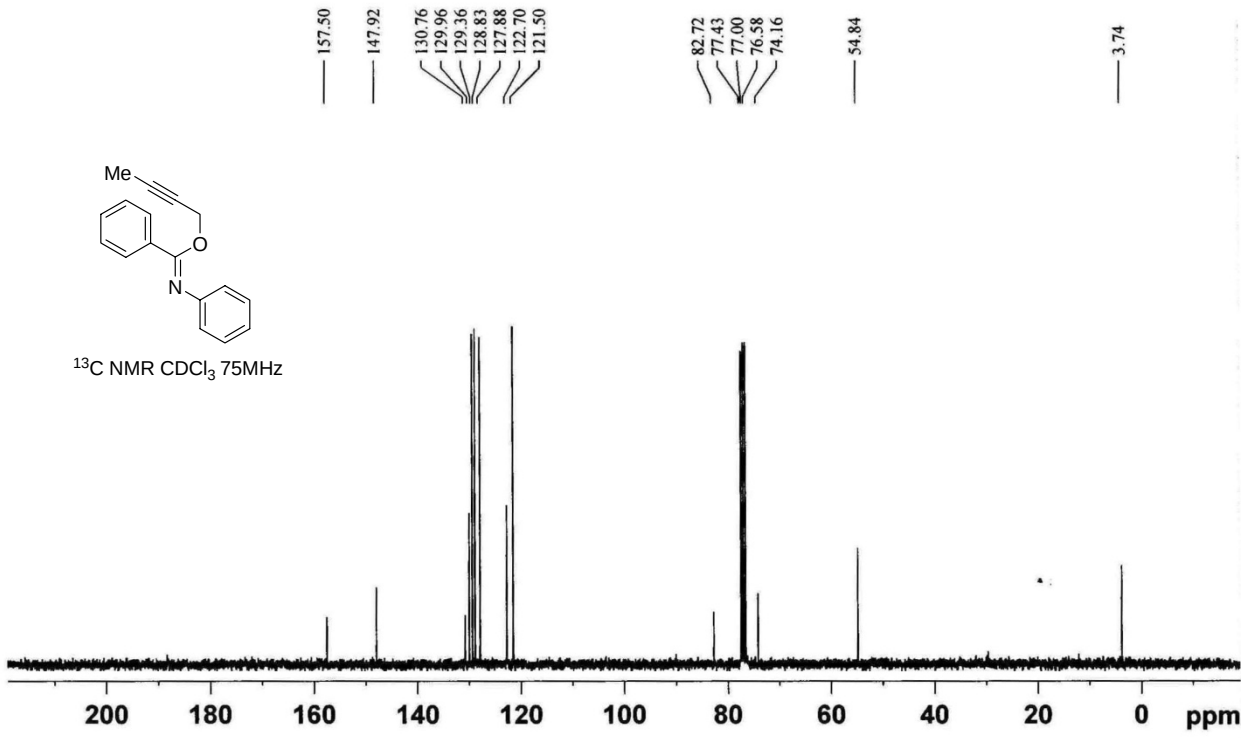
^{1}H NMR $CDCl_3$ 300MHz



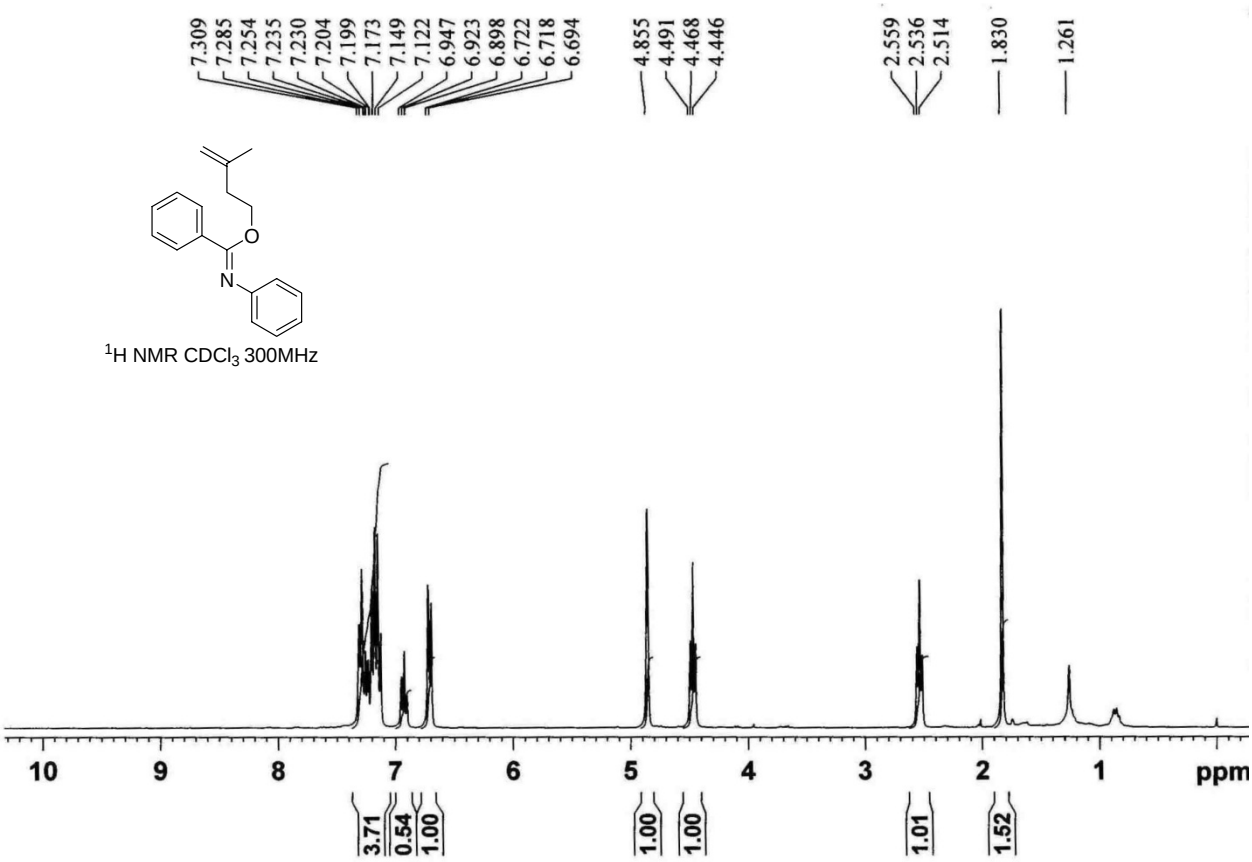
^{13}C NMR $CDCl_3$ 75MHz



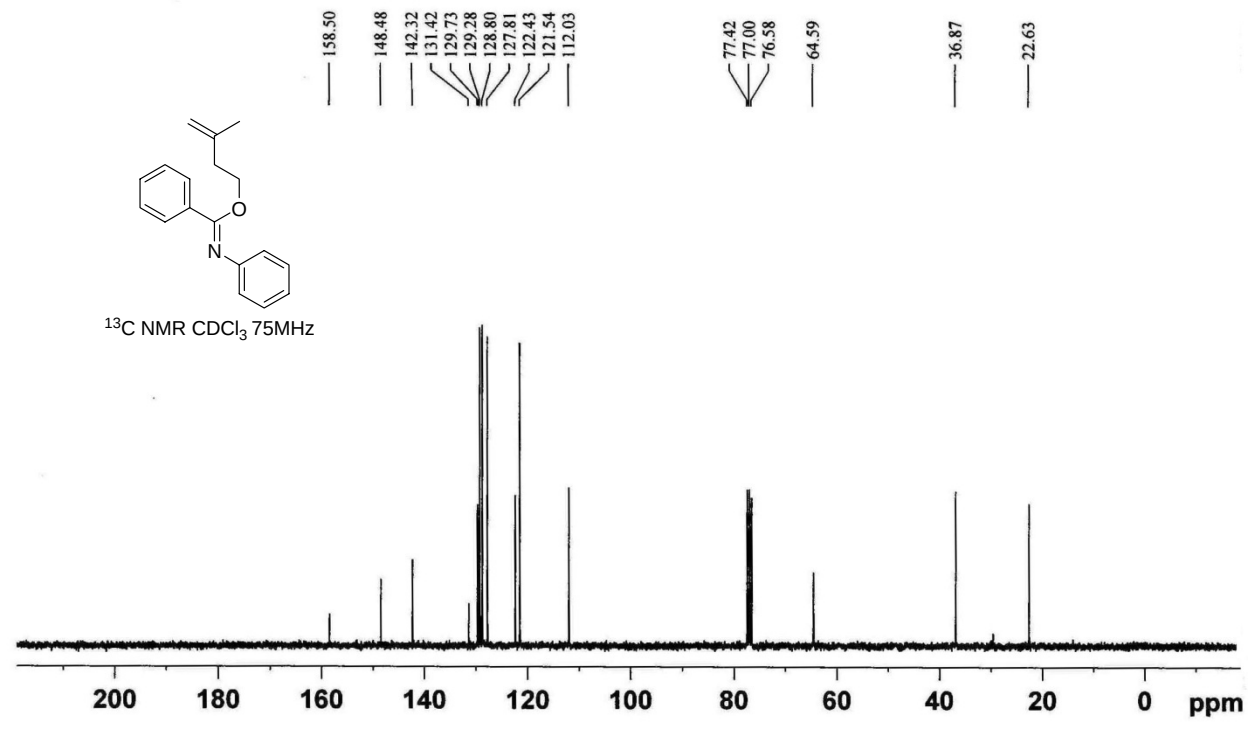
^{1}H NMR $CDCl_3$ 300MHz



^{13}C NMR $CDCl_3$ 75MHz



^{1}H NMR $CDCl_3$ 300MHz



^{13}C NMR $CDCl_3$ 75MHz