Palladium-Catalyzed Hydroacyloxylation of Ynamides

Donna L. Smith,[a] William R. F. Goundry,[b] and Hon Wai Lam*,[a]

[a] *EaStCHEM, School of Chemistry, University of Edinburgh, Joseph Black Building, The King's Buildings, West Mains Road, Edinburgh, EH9 3JJ, United Kingdom*

[b] *AstraZeneca Process Research and Development, Charter Way, Silk Road Business Park, Macclesfield, Cheshire, SK10 2NA, United Kingdom*

Supplementary Information

Contents **Page**

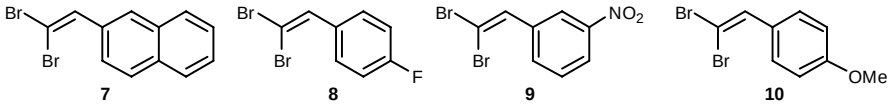
General Information

All non-aqueous reactions were carried out under a nitrogen atmosphere in oven-dried apparatus. Toluene was dried and purified by passage through activated alumina columns using a solvent purification system from http://www.glasscontoursolventsystems.com. All commercially available reagents were used as received. Thin layer chromatography (TLC) was performed on Merck DF-Alufoilien $60F_{254}$ 0.2 mm precoated plates. Product spots were visualized by UV light at 254 nm, and subsequently developed using potassium permanganate or vanillin solution as appropriate. Flash column chromatography was carried out using silica gel (Fisher Scientific 60Å particle size 35-70 micron) employing the method of Still and co-workers.[1] Melting points are uncorrected. Infra-red spectra were recorded as a thin film on sodium chloride plates or as a solid on an ATR IR spectrometer.

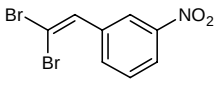
1. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

^{1}H NMR spectra were recorded on a Bruker AVA500 (500 MHz) or a Bruker AVA400 (400 MHz) spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm) downfield of tetramethylsilane, using residual protonated solvent as internal standard ($CDCl_3$ at 7.27 ppm, $(CD_3)_2SO$ at 2.50 ppm). Abbreviations used in the description of resonances are: s (singlet), d (doublet), t (triplet), q, (quartet), app (apparent), m (multiplet), br (broad). Coupling constants (*J*) are quoted to the nearest 0.1 Hz. Proton-decoupled ^{13}C NMR spectra were recorded on a Bruker AVA500 (125.8 MHz) spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm) downfield of tetramethylsilane, using deuterated solvent as internal standard ($CDCl_3$ at 77.0 ppm, $(CD_3)_2SO$ at 39.5 ppm). Assignments were made using the DEPT sequence with secondary pulses at 90° and 135°. ^{19}F NMR spectra were recorded on a Bruker AVA400 (376 MHz) spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm) downfield of $CFCl_3$ (δ = 0 ppm), using fluorobenzene as internal standard (C_6H_5F at –113.2 ppm). High resolution mass spectra were recorded using electrospray ionization (ES) or atmospheric solids analysis probe (ASAP) techniques on a Finnigan MAT 900 XLT spectrometer, a Finnigan MAT 95XP spectrometer, or a Thermofisher LTQ Orbitrap XL spectrometer at the EPSRC National Mass Spectrometry Service Centre, University of Wales, Swansea. Optical rotations were performed on an Optical Activity POLAAR 20 polarimeter.

Preparation of Dibromoalkenes



Dibromoalkenes **7**,[2] **8**,[3] **9**,[4] and **10**[2] were prepared according to a previously described method.[2] Spectroscopic data for **7**,[2] **8**,[3] and **10**[2] were consistent with those reported. Characterization data for **9** have not been reported previously, and are therefore listed below:

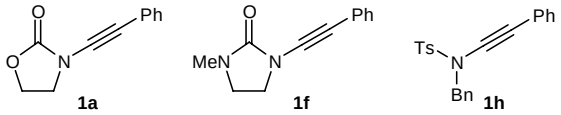


1-(2,2-Dibromovinyl)-3-nitrobenzene (9). Yellow solid R_f = 0.79 (10% EtOAc/hexane); m.p. 54-56 °C; IR (solid) 3086, 1520 (N-O), 1473, 1352 (N-O), 903, 837, 802, 731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (1H, t, *J* = 1.7 Hz, Ar**H**), 8.21 (1H, dd, *J* = 8.3, 1.4 Hz, Ar**H**), 7.84 (1H, d, *J* = 7.8 Hz, Ar**H**), 7.57 (1H, t, *J* = 8.1 Hz, Ar**H**), 7.55 (1H, s, =C**H**); ^{13}C

2. Rao, M. L. N.; Jadhav, D. N.; Dasgupta, P. *Org. Lett.* **2010**, *12*, 2048–2051.
3. Shastin, A. V.; Korotchenko, V. N.; Nenajdenko, V. G.; Balenkova, E. S. *Synthesis* **2001**, 2081–2085.
4. Wang, L.; Yang, F.; Yang, X.; Guan, X; Hu, C.; Liu, T.; He, Q.; Yang, B.; Hu, Y. *Eur. J. Med. Chem.* **2011**, *46*, 285–296.

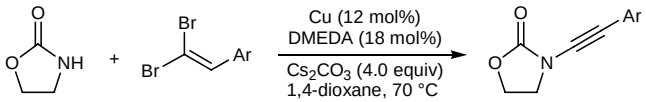
NMR (125.8 MHz, $CDCl_3$) δ 148.2 (C), 136.8 (C), 134.5 (CH), 134.2 (CH), 129.4 (CH), 123.2 (CH), 123.2 (CH), 93.3 (C).

Preparation of Ynamides

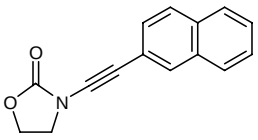


Ynamides **1a**,[5] **1f**,[5] and **1h**[6] were prepared as described previously.

Preparation of Ynamides From Dibromoalkenes: General Procedure A



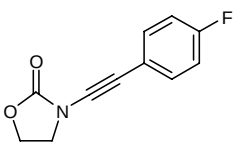
Following the procedure of Evano and co-workers,[7] to a suspension of 2-oxazolidinone (1.0 equiv), CuI (0.12 equiv), and Cs_2CO_3 (4.0 equiv) in 1,4-dioxane (2 mL/mmol of 2-oxazolidinone) was added the appropriate dibromoalkene (1.5 equiv) using 1,4-dioxane (10 mL). DMEDA (0.18 equiv) was added and the reaction mixture was heated at 70 °C for 40 h. The mixture was filtered through a pad of silica gel using EtOAc (100 mL) as eluent. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography to give the desired ynamide.



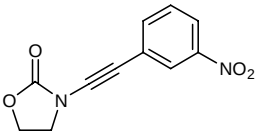
3-Naphthalen-2-ylethynyloxazolidin-2-one (1b). The title compound was prepared according to General Procedure A using 2-oxazolidinone (1.80 g, 12.4 mmol) and dibromoalkene **7** (5.80 g, 18.6 mmol) and purified by column chromatography (30% EtOAc/hexane→60% EtOAc/hexane) to give a pale yellow solid (1.11 g), which was recrystallized from $CHCl_3$ to give a white solid (352 mg, 12%). (Further recrystallization of the mother liquor was not carried out.) R_f = 0.46 (60% EtOAc/hexane); m.p. 173-175 °C; IR (film) 3052, 2986, 2252, 1755 (C=O), 1478, 1416, 1213, 1156, 738, 703 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2SO$) δ 8.04 (1H, d, *J* = 1.3 Hz, Ar**H**), 7.93-7.90 (3H, m, Ar**H**), 7.56-7.51 (2H, m, Ar**H**), 7.48 (1H, dd, *J* = 8.5, 1.7 Hz, Ar**H**), 4.51-4.48 (2H, m, C**H**$_2$O), 4.07-4.03 (2H, m, C**H**$_2$N); ^{13}C NMR (125.8 MHz, $(CD_3)_2SO$) δ 155.8 (C), 132.6 (C), 132.1 (C), 130.4 (CH), 128.3 (CH), 127.8 (CH), 127.65 (CH), 127.56 (CH),

5. Gourdet, B.; Lam, H. W. *J. Am. Chem. Soc.* **2009**, *131*, 3802–3803.
6. Gourdet, B.; Rudkin, M. E.; Watts, C. A.; Lam, H. W. *J. Org. Chem.* **2009**, *74*, 7849–7858.
7. Coste, A.; Karthikeyan, G.; Couty, F.; Evano, G. *Angew. Chem., Int. Ed.* **2009**, *48*, 4381–4385.

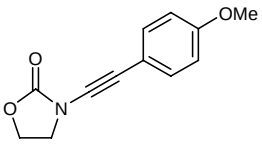
126.8 (2 x CH), 119.2 (C), 81.0 (C), 70.4 (C), 63.7 (CH_2), 46.6 (CH_2); HRMS (ES) Exact mass calcd for $C_{15}H_{15}N_2O_2$ $[M+NH_4]^+$: 255.1128, found: 255.1132.



3-(4-Fluorophenylethynyl)oxazolidin-2-one (1c). The title compound was prepared according to General Procedure A using 2-oxazolidinone (2.26 g, 26.0 mmol) and dibromoalkene **8** (10.9 g, 39.0 mmol) and purified by column chromatography (5% EtOAc/hexane→60% EtOAc/hexane) to give a white solid (1.60 g, 30%). R_f = 0.39 (50% EtOAc/hexane); m.p. 112-114 °C; IR (film) 3054, 2986, 1775 (C=O), 1601, 1513, 1415, 1265, 1206, 740, 705 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.41 (2H, m, Ar**H**), 7.04-6.99 (2H, m, Ar**H**), 4.52-4.49 (2H, m, C**H**$_2$O), 4.03-4.00 (2H, m, C**H**$_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 162.5 (C, d, J = 250.0 Hz), 155.9 (C), 133.7 (2 x CH, d, J = 8.4 Hz), 118.2 (C, d, J = 3.5 Hz) 115.6 (2 x CH, d, J = 22.0 Hz), 78.5 (C), 70.2 (C), 63.0 (CH_2), 47.0 (CH_2); ^{19}F NMR (376 MHz, $CDCl_3$) δ –111.0 (1F, tt, J = 8.6, 5.3 Hz); HRMS (ES) Exact mass calcd for $C_{11}H_{12}FN_2O_2$ $[M+NH_4]^+$: 223.0877, found: 223.0876.



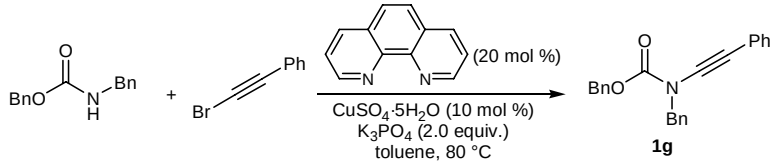
3-(3-Nitrophenylethynyl)oxazolidin-2-one (1d). The title compound was prepared according to General Procedure A using 2-oxazolidinone (1.10 g, 12.7 mmol) and dibromoalkene **9** (5.83 g, 19.0 mmol). The residue was purified by column chromatography (30% EtOAc/hexane→50% EtOAc/hexane) to give a yellow solid (830 mg, 28%). R_f = 0.41 (60% EtOAc/Hexane); m.p. 114-116 °C; IR (film) 3055, 2986, 2926, 2263, 1780 (C=O), 1534 (N-O), 1409, 1353 (N-O), 1265, 739 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (1H, t, J = 1.9 Hz, Ar**H**), 8.14 (1H, ddd, J = 8.3, 2.3, 1.0 Hz, Ar**H**), 7.73 (1H, dt, J = 7.7, 2.2 Hz, Ar**H**), 7.50 (1H, t, J = 8.0 Hz, Ar**H**), 4.56-4.53 (2H, m, C**H**$_2$O), 4.08-4.05 (2H, m, C**H**$_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.5 (C), 148.1 (C), 136.9 (CH), 129.3 (CH), 125.9 (CH), 124.2 (C), 122.7 (CH), 81.4 (C), 69.5 (C), 63.2 (CH_2), 46.8 (CH_2); HRMS (ES) Exact mass calcd for $C_{11}H_{12}N_3O_4$ $[M+NH_4]^+$: 250.0822, found: 250.0825.



3-(4-Methoxyphenylethynyl) oxazolidin-2-one (1e).[8] The title compound was prepared according to General Procedure A using 2-oxazolidinone (1.22 g, 14.0 mmol) and dibromoalkene **10** (6.12 g, 21.0 mmol). The residue was purified by

column chromatography (5% EtOAc/hexane→50% EtOAc/hexane) to give a yellow solid (1.61 mg, 53%) that displayed spectral data consistent with those reported previously.[8]

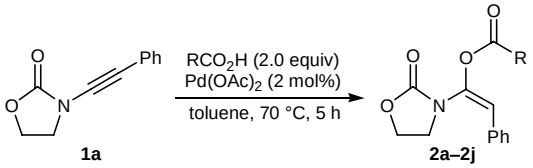
N-Benzyl-*N*-phenylethynylcarbamic acid benzyl ester (1g)



Following a slight modification of the procedure of Hsung and co-workers,[9] a mixture of 1-bromo-2-phenylacetylene (3.13 g, 17.3 mmol), benzylcarbamic acid benzyl ester[10] (3.80 g, 15.7 mmol), K_3PO_4 (6.67 g, 31.4 mmol), $CuSO_4{\cdot}5H_2O$ (392 mg, 1.60 mmol) and 1,10-phenanthroline (566 mg, 3.60 mmol) in toluene (40 mL) was heated at 80 °C for 24 h. After cooling to room temperature, the mixture was filtered through a short pad of silica gel using EtOAc (200 mL) as the eluent, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (5% EtOAc/hexane→10% EtOAc/hexane) to give the *ynamide* **1g** (2.53 g, 47%) as a pale orange solid. R_f = 0.65 (30% EtOAc/hexane); m.p. 50-60 °C; IR (film) 3033, 2948, 2248, 1726 (C=O), 1598, 1442, 1400, 1289, 1231, 901 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47-7.25 (15H, m, Ar**H**), 5.29 (2H, s, C**H**$_2$), 4.75 (2H, s, C**H**$_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.0 (C), 135.8 (C), 135.6 (C), 130.8 (CH), 128.6 (4 x CH), 128.5 (2 x CH), 128.23 (2 x CH), 128.18 (2 x CH), 128.1 (CH), 127.7 (2 x CH), 127.4 (CH), 123.2 (C), 82.9 (C), 71.5 (C), 68.6 (CH_2), 53.9 (CH_2); Exact mass calcd for $C_{23}H_{23}N_2O_2$ $[M+NH_4]^+$: 359.1754, found: 359.1758.

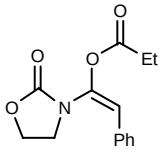
Palladium-Catalyzed Hydroacyloxylation of Ynamides

Hydroacyloxylation of Ynamide 1a: General Procedure B



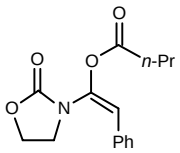
8. (a) Jia, W.; Jiao, N. *Org. Lett.* **2010**, *12*, 2000–2003. (b) Hamada, T.; Ye, X.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130*, 833–835.
9. Zhang, Y.; Hsung, R. P.; Tracey, M. R.; Kurtz, K. C. M.; Vera, E. L. *Org. Lett.* **2004**, *6*, 1151–1154.
10. Prepared according to a literature procedure: Dubé, D.; Scholte, A. A. *Tetrahedron Lett.* **1999**, *40*, 2295–2298.

A solution of ynamide **1a** (75 mg, 0.40 mmol), the appropriate carboxylic acid (0.80 mmol), and $Pd(OAc)_2$ (1.8 mg, 0.008 mmol) in toluene (4 mL) was heated at 70 °C in a sealed tube for 5 h. After cooling to room temperature, saturated aqueous $NaHCO_3$ solution (15 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography gave the desired α-acyloxyenamide.



Propionic acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2a). *On a 0.40 mmol scale:* The title compound was prepared according to General Procedure B using propionic acid (60 µL, 0.80 mmol) and purified by column chromatography (50% EtOAc/hexane) to give a light brown oil (80 mg, 76%). R_f = 0.54 (50% EtOAc/hexane); IR (film) 3059, 2986, 2920, 1768 (C=O), 1675, 1481, 1448, 1399, 1226, 1108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39-7.35 (2H, m, Ar**H**), 7.34-7.28 (3H, m, Ar**H**), 6.24 (1H, s, =C**H**), 4.37-4.33 (2H, m, C$\mathbf{H}_2$O), 3.72-3.68 (2H, m, C$\mathbf{H}_2$N), 2.56 (2H, q, *J* = 7.5 Hz, C$\mathbf{H}_2$CH$_3$), 1.23 (3H, t, *J* = 7.5 Hz, C$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 173.0 (C), 155.6 (C), 137.6 (C), 132.0 (C), 128.7 (2 x CH), 128.1 (3 x CH), 115.4 (CH), 63.1 (CH_2), 44.5 (CH_2), 27.1 (CH_2), 8.8 (CH_3); HRMS (ES) Exact mass calcd for $C_{14}H_{16}NO_4$ $[M+H]^+$: 262.1074, found: 262.1075.

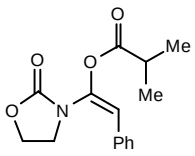
On a 3.0 mmol scale: A solution of ynamide **1a** (562 mg, 3.00 mmol), propionic acid (246 µL, 3.30 mmol), and $Pd(OAc)_2$ (6.7 mg, 0.03 mmol) in toluene (30 mL) was heated at 70 °C for 18 h. Saturated aqueous $NaHCO_3$ solution (50 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (15% EtOAc/hexane→30% EtOAc/hexane) gave the α-acyloxyenamide **2a** as a colorless oil (620 mg, 79%).



Butyric acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2b).

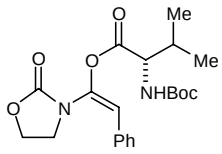
The title compound was prepared according to General Procedure B using butyric acid (73 µL, 0.80 mmol) and purified by column chromatography (50% EtOAc/hexane) to give a brown oil (96 mg, 87%). R_f = 0.54 (50% EtOAc/hexane); IR (film) 2966, 2934, 2877, 1770 (C=O), 1675, 1448, 1399, 1226, 1108, 1037 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39-7.28 (5H, m, Ar**H**), 6.24 (1H, s, =C**H**), 4.37-4.32 (2H, m, C$\mathbf{H}_2$O), 3.72-3.67 (2H, m, C$\mathbf{H}_2$N), 2.50 (2H, t, *J* = 7.4 Hz, C$\mathbf{H}_2$CH$_2$CH$_3$), 1.75 (2H, sextet, *J* = 7.4 Hz, C$\mathbf{H}_2$CH$_3$) 1.02 (3H, t, *J* = 7.4 Hz, C$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 172.1 (C), 155.5 (C), 137.5 (C), 132.0 (C), 128.7 (2 x CH), 128.0 (3 x CH),

115.4 (CH), 63.1 (CH_2), 44.4 (CH_2), 35.5 (CH_2), 18.1 (CH_2), 13.5 (CH_3); HRMS (ES) Exact mass calcd for $C_{15}H_{18}NO_4$ $[M+H]^+$: 276.1230, found: 276.1232.

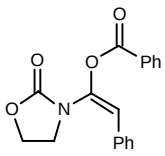


Isobutyric acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2c). *Using 2.0 equiv of carboxylic acid:* The title compound was prepared according to General Procedure B using isobutyric acid (74 μL, 0.80 mmol) and purified by column chromatography (20% EtOAc/hexane→25% EtOAc/hexane) to give a cream solid (95 mg, 86%). R_f = 0.61 (50% EtOAc/hexane); m.p. 62-64 °C; IR (film) 3057, 2981, 1768 (C=O), 1676, 1401, 1265, 1224, 1111, 1089, 735; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.28 (5H, m, Ar**H**), 6.25 (1H, s, =C**H**), 4.37-4.34 (2H, m, C$\mathbf{H}_2$O), 3.72-3.69 (2H, m, C$\mathbf{H}_2$N), 2.78 (1H, septet, *J* = 7.0 Hz, C**H**$(CH_3)_2$), 1.30 (6H, d, *J* = 7.0 Hz, CH(C$\mathbf{H}_3$)$_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 175.7 (C), 155.5 (C), 137.7 (C), 132.0 (C), 128.7 (2 x CH), 128.0 (3 x CH), 115.3 (CH), 63.1 (CH_2), 44.5 (CH_2), 33.8 (CH), 18.7 (2 x CH_3); HRMS (ES) Exact mass calcd for $C_{15}H_{21}N_2O_4$ $[M+NH_4]^+$: 293.1496, found: 293.1496.

Using 1.1 equiv of carboxylic acid: A repeat of the above reaction using isobutyric acid (41 μL, 0.44 mmol) under otherwise identical conditions gave the title compound (93 mg, 84%) as a cream solid.

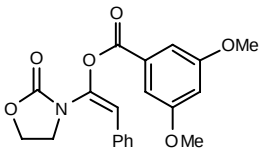


(*E*)-1-(2-Oxo-1,3-oxazolidin-3-yl)-2-phenylethenyl 2-{[(*tert*-butoxy)carbonyl]amino}-3-methylbutanoate (2d). The title compound was prepared according to General Procedure B using L-Boc-valine-OH (174 mg, 0.80 mmol) and purified by column chromatography (20% EtOAc/hexane→25% EtOAc/hexane) to give an orange gum (173 mg, >95%). R_f = 0.54 (50% EtOAc/hexane); $[\alpha]_D^{20}$ +15.5 (*c* 1.04 $CHCl_3$); IR (film) 3056, 2987, 2921, 1774 (C=O), 1676, 1532, 1353, 1266, 1111, 737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.28 (5H, m, Ar**H**), 6.30 (1H, s, =C**H**), 5.00 (1H, br d, *J* = 8.6 Hz, N**H**), 4.37-4.33 (3H, m, C**H**N and C$\mathbf{H}_2$O), 3.78-3.68 (2H, m, C$\mathbf{H}_2$N), 2.35-2.29 (1H, m, C**H**$(CH_3)_2$), 1.48 (9H, s, C(C$\mathbf{H}_3$)$_3$), 1.06 (3H, d, *J* = 6.9 Hz, CH(C$\mathbf{H}_3$)$_2$), 0.98 (3H, d, *J* = 6.9 Hz, CH(C$\mathbf{H}_3$)$_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 171.2 (C), 155.7 (C), 155.4 (C), 137.0 (C), 131.7 (C), 128.8 (2 x CH), 128.3 (CH), 128.1 (2 x CH), 117.0 (CH), 80.1 (C), 63.2 (CH_2), 58.7 (CH), 44.3 (CH_2), 30.7 (CH), 28.3 (3 x CH_3), 19.3 (CH_3), 17.4 (CH_3); HRMS (ES) Exact mass calcd for $C_{21}H_{32}N_3O_6$ $[M+NH_4]^+$: 422.2286, found: 422.2283.



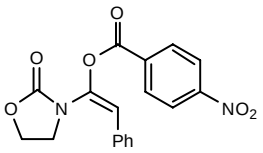
Benzoic acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2e). The title compound was prepared according to General Procedure B using benzoic acid (98 mg, 0.80 mmol) and purified by column chromatography (20% EtOAc/hexane) to give a

pale orange gum (124 mg, >95%). R_f = 0.59 (50% EtOAc/hexane); IR (film) 3062, 3019, 2916, 1767 (C=O), 1739 (C=O), 1675, 1449, 1399, 1264, 1225 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.16 (2H, app dd, *J* = 8.4, 1.3 Hz, Ar**H**), 7.65 (1H, app tt, *J* = 7.5, 1.3 Hz, Ar**H**), 7.53-7.49 (2H, m, Ar**H**), 7.42-7.37 (4H, m, Ar**H**), 7.35-7.30 (1H, m, Ar**H**), 6.42 (1H, s, =C**H**), 4.40-4.36 (2H, m, C$\mathbf{H}_2$O), 3.83-3.79 (2H, m, C$\mathbf{H}_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 165.3 (C), 155.6 (C), 137.6 (C), 134.0 (CH), 132.0 (C), 130.4 (2 x CH), 128.8 (2 x CH), 128.7 (2 x CH), 128.4 (C), 128.2 (CH), 128.1 (2 x CH), 116.5 (CH), 63.2 (CH_2), 44.5 (CH_2); HRMS (ES) Exact mass calcd for $C_{18}H_{16}NO_4$ $[M+H]^+$: 310.1074, found: 310.1074.



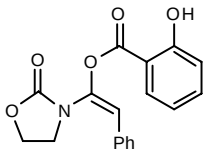
3,5-Dimethoxybenzoic acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2f). *Using 2.0 equiv. of carboxylic acid:* The title compound was prepared according to General Procedure B using 3,5-dimethoxybenzoic acid (146 mg, 0.80 mmol) and purified by column chromatography (50% EtOAc/hexane) to give a light brown oil (123 mg, 83%). R_f = 0.44 (50% EtOAc/hexane); IR (film) 3058, 2963, 2938, 2841, 1767 (C=O), 1735 (C=O), 1677, 1595, 1205, 1040 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.38 (4H, m, Ar**H**), 7.34-7.31 (1H, m, Ar**H**), 7.30 (2H, d, *J* = 2.4 Hz, Ar**H**), 6.73 (1H, t, *J* = 2.4 Hz, Ar**H**), 6.41 (1H, s, =C**H**), 4.39-4.36 (2H, m, C$\mathbf{H}_2$O), 3.86 (6H, s, 2 x OC$\mathbf{H}_3$), 3.82-3.78 (2H, m, C$\mathbf{H}_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 165.0 (C), 160.8 (2 x C), 155.5 (C), 137.5 (C), 131.9 (CH), 130.1 (C), 128.8 (2 x CH), 128.2 (CH), 128.1 (2 x CH), 116.6 (CH), 107.7 (2 x CH), 106.0 (CH), 63.1 (CH_2), 55.6 (2 x CH_3), 44.5 (CH_2); HRMS (ASAP) Exact mass calcd for $C_{20}H_{20}NO_6$ $[M+H]^+$: 370.1285, found: 370.1289.

Using 1.1 equiv of carboxylic acid: A repeat of the above reaction using 3,5-dimethoxybenzoic acid (80 mg, 0.44 mmol) under otherwise identical conditions gave the title compound (132 mg, 89%) as a colorless oil.

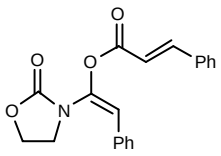


4-Nitrobenzoic acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2g). The title compound was prepared according to General Procedure B using 4-nitrobenzoic acid (134 mg, 0.80 mmol) and purified by column chromatography (25% EtOAc/hexane→35% EtOAc/hexane) to give a pale yellow solid (99 mg, 70%). R_f = 0.50 (50% EtOAc/hexane); m.p. 142-144 °C; IR (film) 2923, 2876, 1766 (C=O), 1677, 1527 (N-O), 1399, 1263, 1224, 1069 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.34 (4H, br s, Ar**H**), 7.43-7.36 (4H, m, Ar**H**), 7.36-7.31 (1H, m, Ar**H**), 6.43 (1H, s, =C**H**), 4.42-4.38 (2H, m, C$\mathbf{H}_2$O), 3.81-3.77 (2H, m, C$\mathbf{H}_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 163.3 (C), 155.5 (C), 151.0 (C), 137.4 (C), 133.8 (C), 131.54 (C), 131.47 (2 x

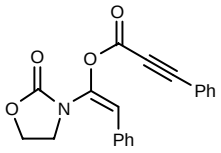
CH), 128.9 (2 x CH), 128.4 (CH), 128.1 (2 x CH), 123.7 (2 x CH), 116.4 (CH), 63.2 (CH_2), 44.5 (CH_2); HRMS (ES) Exact mass calcd for $C_{18}H_{18}N_3O_6$ $[M+NH_4]^+$: 372.1190, found: 372.1193.



2-Hydroxybenzoic acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2h). The title compound was prepared according to General Procedure B using salicylic acid (111 mg, 0.80 mmol) and purified by column chromatography (15% EtOAc/hexane→20% EtOAc/hexane) to give a colorless oil (98 mg, 75%). R_f = 0.69 (60% EtOAc/hexane); IR (film) 3253 (OH, br), 3058, 3026, 2917, 1770 (C=O), 1691 (C=O), 1614, 1483, 1401, 1205 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 10.24 (1H, s, O**H**), 8.03 (1H, dd, *J* = 8.0, 1.5 Hz, Ar**H**), 7.56-7.52 (1H, m, Ar**H**), 7.42-7.36 (4H, m, Ar**H**), 7.35-7.31 (1H, m, Ar**H**), 7.03 (1H, d, *J* = 8.4 Hz, Ar**H**), 6.96 (1H, t, *J* = 7.6 Hz, Ar**H**), 6.44 (1H, s, =C**H**), 4.41-4.37 (2H, m, C$\mathbf{H}_2$O), 3.81-3.78 (2H, m, C$\mathbf{H}_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 168.7 (C), 162.1 (C), 155.3 (C), 136.9 (CH), 136.7 (C), 131.6 (C), 130.7 (CH), 128.8 (2 x CH), 128.4 (CH), 128.1 (2 x CH), 119.7 (CH), 117.7 (CH), 117.2 (CH), 110.9 (C), 63.1 (CH_2), 44.3 (CH_2); HRMS (ES) Exact mass calcd for $C_{18}H_{16}NO_5$ $[M+H]^+$: 326.1023, found: 326.1028.



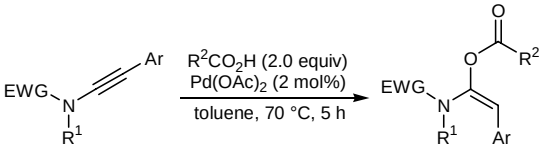
(*E*)-3-Phenylacrylic acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2i). The title compound was prepared according to General Procedure B using *trans*-cinnamic acid (119 mg, 0.80 mmol) and purified by column chromatography (10% EtOAc/hexane→20% EtOAc/hexane) to give a colorless oil (107 mg, 80%). R_f = 0.59 (50% EtOAc/hexane); IR (film) 3059, 2987, 2917, 1766 (C=O), 1729 (C=O), 1676, 1633, 1448, 1223, 1127 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (1H, d, *J* = 16.0 Hz, CH=C**H**Ph), 7.58-7.56 (2H, m, Ar**H**), 7.43-7.36 (7H, m, Ar**H**), 7.32-7.29 (1H, m, Ar**H**), 6.56 (1H, d, *J* = 16.0 Hz, C**H**=CHPh), 6.36 (1H, s, =C**H**), 4.39-4.36 (2H, m, C$\mathbf{H}_2$O), 3.78-3.75 (2H, m, C$\mathbf{H}_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 165.3 (C), 155.7 (C), 147.8 (CH), 137.5 (C), 133.9 (C), 132.1 (C), 131.0 (CH), 129.0 (2 x CH), 128.8 (2 x CH), 128.4 (2 x CH), 128.1, (3 x CH), 116.3 (CH), 116.0 (CH), 63.2 (CH_2), 44.5 (CH_2); HRMS (ES) Exact mass calcd for $C_{20}H_{18}NO_4$ $[M+H]^+$: 336.1230, found: 336.1227.



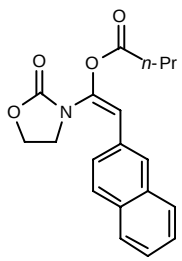
Phenylpropynoic acid (*E*)-1-(2-oxo-oxazolidin-3-yl)-2-phenylvinyl ester (2j). The title compound was prepared according to a modification of General Procedure B in that 4.0 equivalents of phenylpropiolic acid (234 µL, 1.60 mmol) was used and the reaction time was 24 h. The residue was purified by column chromatography (10%

EtOAc/hexane→20% EtOAc/hexane) to give a brown oil (98 mg, 73%). R_f = 0.54 (50% EtOAc/hexane); IR (film) 3058, 2988, 2916, 2225, 1771 (C=O), 1727 (C=O), 1678, 1400, 1280, 1139 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (2H, d, *J* = 7.4 Hz, Ar**H**), 7.50 (1H, t, *J* = 7.4 Hz, Ar**H**), 7.45-7.30 (7H, m, Ar**H**), 6.42 (1H, s, =C**H**), 4.40 (2H, t, *J* = 8.0 Hz, C$\mathbf{H}_2$O), 3.76 (2H, t, *J* = 8.0 Hz, C$\mathbf{H}_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.3 (C), 152.0 (C), 136.6 (C), 133.3 (2 x CH), 131.6 (C), 131.2 (CH), 128.8 (2 x CH), 128.7 (2 x CH), 128.4 (CH), 128.1 (2 x CH), 118.9 (C), 117.4 (CH), 89.8 (C), 79.5 (C), 63.1 (CH_2), 44.3 (CH_2); HRMS (ES) Exact mass calcd for $C_{20}H_{16}NO_4$ $[M+H]^+$: 334.1074, found: 334.1078.

Hydroacyloxylation of Various Ynamides: General Procedure C

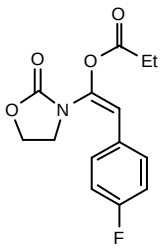


A solution of the appropriate ynamide (0.40 mmol), the appropriate carboxylic acid (0.80 mmol), and $Pd(OAc)_2$ (1.8 mg, 0.008 mmol) in toluene (4 mL) was heated at 70 °C in a sealed tube for 5 h. After cooling to room temperature, saturated aqueous $NaHCO_3$ solution (15 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography gave the desired α-acyloxyenamide.

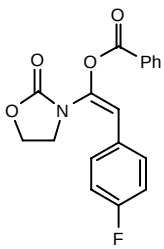


Butyric acid (*E*)-2-naphthalen-2-yl-1-(2-oxo-oxazolidin-3-yl)vinyl ester (3a). The title compound was prepared according to General Procedure C using ynamide **1b** (95 mg, 0.40 mmol) and butyric acid (73 μL, 0.80 mmol) and purified by column chromatography (15% EtOAc/hexane→20% EtOAc/hexane) to give a pale orange solid (99 mg, 76%). R_f = 0.68 (60% EtOAc/hexane); m.p. 93-95 °C; IR (neat) 2972, 2930, 2874, 1763 (C=O), 1748 (C=O), 1676, 1402, 1230, 1107, 1005 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.83-7.80 (3H, m, Ar**H**), 7.76 (1H, s, Ar**H**), 7.51-7.46 (3H, m, Ar**H**), 6.39 (1H, s, =C**H**), 4.33 (2H, t, *J* = 8.0 Hz, C$\mathbf{H}_2$O), 3.70 (2H, t, *J* = 8.0 Hz, C$\mathbf{H}_2$N), 2.53 (2H, t, *J* = 7.4 Hz, C$\mathbf{H}_2$$CH_2CH_3$), 1.77 (2H, sextet, *J* = 7.4 Hz, C$\mathbf{H}_2$$CH_3$), 1.04 (3H, t, *J* = 7.4 Hz, C$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 172.2 (C), 155.6 (C), 137.8 (C), 133.2 (C), 132.7 (C), 129.5 (C), 128.4 (CH), 128.0 (CH), 127.7 (CH), 127.6 (CH), 126.5 (CH), 126.5 (CH), 125.3 (CH), 115.3 (CH), 63.1 (CH_2), 44.7 (CH_2), 35.5 (CH_2),

18.2 (CH_2), 13.5 (CH_3); HRMS (ES) Exact mass calcd for $C_{19}H_{20}NO_4$ $[M+H]^+$: 326.1387, found: 326.1390.

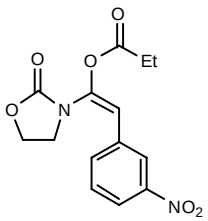


Propionic acid (*E*)-2-(4-fluorophenyl)-1-(2-oxo-oxazolidin-3-yl)vinyl ester (3b). The title compound was prepared according to General Procedure C using ynamide **1c** (82 mg, 0.40 mmol) and propionic acid (60 µL, 0.80 mmol) and purified by column chromatography (20% EtOAc/hexane→30% EtOAc/hexane) to give a light green oil (86 mg, 77%). R_f = 0.51 (50% EtOAc/hexane); IR (film) 3071, 2986, 2919, 1764 (C=O), 1677, 1508, 1398, 1228, 1108, 731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.27 (2H, m, Ar**H**), 7.06-7.02 (2H, m, Ar**H**), 6.19 (1H, s, =C**H**), 4.36-4.33 (2H, m, C$\mathbf{H}_2$O), 3.69-3.66 (2H, m, C$\mathbf{H}_2$N), 2.53 (2H, q, *J* = 7.5 Hz, C$\mathbf{H}_2$CH$_3$), 1.21 (3H, t, *J* = 7.5 Hz, CH$_2$C$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 172.9 (C), 162.1 (C, d, *J* = 248.6 Hz), 155.4 (C), 137.4 (C, d, *J* = 1.6 Hz), 129.8 (2 x CH, d, *J* = 8.1 Hz), 128.1 (C, d, *J* = 3.5 Hz), 115.8 (2 x CH, d, *J* = 21.7 Hz), 114.6 (CH), 63.1 (CH_2), 44.4 (CH_2), 27.0 (CH_2), 8.7 (CH_3); ^{19}F NMR (376.3 MHz, $CDCl_3$) δ –112.8 (1F, tt, *J* = 8.5, 5.4 Hz); HRMS (ASAP) Exact mass calcd for $C_{14}H_{15}FNO_4$ $[M+H]^+$: 280.0980, found: 280.0979.

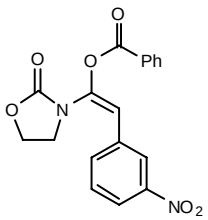


Benzoic acid (*E*)-2-(4-fluorophenyl)-1-(2-oxo-oxazolidin-3-yl)vinyl ester (3c). *Using 2.0 equiv. of carboxylic acid:* The title compound was prepared according to General Procedure C using ynamide **1c** (82 mg, 0.40 mmol) and benzoic acid (98 mg, 0.80 mmol) and purified by column chromatography (50% EtOAc/hexane) to give a yellow oil (106 mg, 81%). R_f = 0.60 (50% EtOAc/hexane); IR (film) 3069, 3012, 2918, 1766 (C=O), 1738 (C=O), 1678, 1508, 1398, 1227, 1085 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (2H, dd, *J* = 8.3, 1.2 Hz, Ar**H**), 7.66-7.63 (1H, m, Ar**H**), 7.50 (2H, t, *J* = 7.8 Hz, Ar**H**), 7.37-7.34 (2H, m, Ar**H**), 7.09-7.06 (2H, m, Ar**H**), 6.37 (1H, s, =C**H**), 4.40-4.37 (2H, m, C$\mathbf{H}_2$O), 3.81-3.78 (2H, m, C$\mathbf{H}_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 165.1 (C), 162.2 (C, d, *J* = 248.8 Hz), 155.4 (C), 137.4 (C, d, *J* = 1.7 Hz), 134.1 (CH), 130.3 (2 x CH), 129.8 (2 x CH, d, *J* = 8.1 Hz), 128.6 (2 x CH), 128.2 (C), 128.1 (C, d, *J* = 3.5 Hz), 115.8 (2 x CH, d, *J* = 21.7 Hz), 115.7 (CH), 63.1 (CH_2), 44.4 (CH_2); ^{19}F NMR (376.3 MHz, $CDCl_3$) δ –112.7 (1F, tt, *J* = 8.6, 5.4 Hz); HRMS (ASAP) Exact mass calcd for $C_{18}H_{15}FNO_4$ $[M+H]^+$: 328.0980, found: 328.0982.

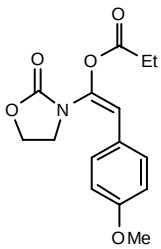
Using 1.1 equiv of carboxylic acid: A repeat of the above reaction using benzoic acid (54 mg, 0.44 mmol) for a reaction time of 6 h under otherwise identical conditions gave the title compound (109 mg, 83%) as a yellow oil.



Propionic acid (*E*)-2-(3-nitrophenyl)-1-(2-oxo-oxazolidin-3-yl)vinyl ester (3d). The title compound was prepared according to General Procedure C using ynamide **1d** (93 mg, 0.40 mmol) and propionic acid (60 μL, 0.80 mmol) and purified by column chromatography (20% EtOAc/hexane→40% EtOAc/hexane) to give a cream solid (82 mg, 67%). R_f = 0.60 (70% EtOAc/hexane); m.p. 59-62 °C; IR (film) 3063, 2987, 2918, 1769 (C=O), 1674, 1530 (N-O), 1398, 1352 (N-O), 1224, 1109 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.20 (1H, s, Ar**H**), 8.14-8.12 (1H, m, Ar**H**), 7.64 (1H, d, *J* = 7.8 Hz, Ar**H**), 7.54 (1H, t, *J* = 8.0 Hz, Ar**H**), 6.28 (1H, s, =C**H**), 4.45-4.42 (2H, m, C**H**$_2$O), 3.78-3.74 (2H, m, C**H**$_2$N), 2.57 (2H, q, *J* = 7.5 Hz, C**H**$_2$CH$_3$), 1.24 (3H, t, *J* = 7.5 Hz, C**H**$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 172.6 (C), 154.8 (C), 148.5 (C), 139.3 (C), 134.1 (C), 134.0 (CH), 129.7 (CH), 122.6 (2 x CH), 113.2 (CH), 63.0 (CH_2), 44.5 (CH_2), 27.1 (CH_2), 8.7 (CH_3); HRMS (ASAP) Exact mass calcd for $C_{14}H_{15}N_2O_6$ $[M+H]^+$: 307.0925, found: 307.0922.

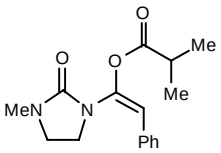


Benzoic acid (*E*)-2-(3-nitrophenyl)-1-(2-oxo-oxazolidin-3-yl)vinyl ester (3e). The title compound was prepared according to General Procedure C using ynamide **1d** (93 mg, 0.40 mmol) and benzoic acid (98 mg, 0.80 mmol) and purified by column chromatography (20% EtOAc/hexane→30% EtOAc/hexane) to give a cream solid (111 mg, 78%). R_f = 0.45 (50% EtOAc/hexane); m.p. 128-130 °C; IR (film) 3092, 2912, 1774 (C=O), 1745 (C=O), 1680, 1524 (N-O), 1342 (N-O), 1219, 1128, 1051 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.25 (1H, s, Ar**H**), 8.14 (3H, d, *J* = 7.9 Hz, Ar**H**), 7.71-7.65 (2H, m, Ar**H**), 7.56 (1H, t, *J* = 8.0 Hz, Ar**H**), 7.52 (2H, t, *J* = 7.7 Hz, Ar**H**), 6.44 (1H, s, =C**H**), 4.49-4.45 (2H, m, C**H**$_2$O), 3.89-3.86 (2H, m, C**H**$_2$N); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 164.8 (C), 154.8 (C), 148.4 (C), 139.3 (C), 134.3 (CH), 134.1 (C), 134.0 (CH), 130.4 (2 x CH), 129.7 (CH), 128.7 (2 x CH), 127.9 (C), 122.63 (CH), 122.60 (CH), 114.1 (CH), 63.0 (CH_2), 44.5 (CH_2); HRMS (ASAP) Exact mass calcd for $C_{18}H_{15}N_2O_6$ $[M+H]^+$: 355.0925, found: 355.0926.



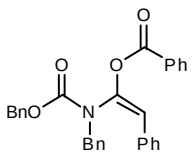
Propionic acid (*E*)-2-(4-methoxyphenyl)-1-(2-oxo-oxazolidin-3-yl)vinyl ester (3f). The title compound was prepared according to a slight modification of General Procedure C using ynamide **1e** (87 mg, 0.40 mmol) and propionic acid (60 μL, 0.80 mmol) in that an increased loading of $Pd(OAc)_2$ (3.6 mg, 0.016 mmol) was employed. Purification by column chromatography (20% EtOAc/hexane→35% EtOAc/hexane) gave a white solid (50 mg, 43%). R_f = 0.53 (60% EtOAc/hexane); m.p. 106-108 °C; IR (film) 3054,

2986, 1769 (C=O), 1608, 1513, 1421, 1265, 738, 705 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.7 Hz, Ar**H**), 6.90 (2H, d, *J* = 8.7 Hz, Ar**H**), 6.19 (1H, s, =C**H**), 4.38-4.33 (2H, m, C$\mathbf{H}_2$O), 3.82 (3H, s, OC$\mathbf{H}_3$), 3.74-3.69 (2H, m, C$\mathbf{H}_2$N), 2.54 (2H, q, *J* = 7.5 Hz, C$\mathbf{H}_2$CH$_3$), 1.22 (3H, t, *J* = 7.5 Hz, CH$_2$C$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 173.2 (C), 159.3 (C), 155.7 (C), 136.2 (C), 129.4 (2 x CH), 124.3 (C), 115.4 (CH), 114.2 (2 x CH), 63.1 (CH_2), 55.2 (CH_3), 44.3 (CH_2), 27.1 (CH_2), 8.8 (CH_3); HRMS (ES) Exact mass calcd for $C_{15}H_{18}NO_5$ $[M+H]^+$: 292.1179, found: 292.1182.



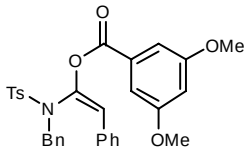
Isobutyric acid (*E*)-1-(3-methyl-2-oxoimidazolidin-1-yl)-2-phenylvinyl ester (3g). *Using 2.0 equiv. of carboxylic acid:* The title compound was prepared according to General Procedure C using ynamide **1f** (80 mg, 0.40 mmol) and isobutyric acid (74 μL, 0.80 mmol) and purified by column chromatography (30% EtOAc/hexane→35% EtOAc/hexane) to give a yellow oil (86 mg, 74%). R_f = 0.51 (70% EtOAc/hexane); IR (film) 3059, 2975, 2877, 1751 (C=O), 1715 (C=O), 1670, 1495, 1388, 1275, 1092 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.27 (4H, m, Ar**H**), 7.22-7.18 (1H, m, Ar**H**), 6.06 (1H, s, =C**H**), 3.51-3.36 (2H, m, C$\mathbf{H}_2$N), 3.33 (2H, dd, *J* = 9.4, 6.7 Hz, C$\mathbf{H}_2$N), 2.81 (3H, s, NC$\mathbf{H}_3$), 2.72 (1H, septet, *J* = 7.0 Hz, C**H**(CH$_3$)$_2$), 1.24 (6H, d, *J* = 7.0 Hz, CH(C$\mathbf{H}_3$)$_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 175.9 (C), 157.6 (C), 139.8 (C), 132.9 (C), 128.4 (2 x CH), 128.1 (2 x CH), 127.3 (CH), 113.3 (CH), 45.1 (CH_2), 41.7 (CH_2), 33.7 (CH), 31.0 (CH_3), 18.8 (2 x CH_3); HRMS (ASAP) Exact mass calcd for $C_{16}H_{21}N_2O_3$ $[M+H]^+$: 289.1547, found: 289.1541.

Using 1.1 equiv of carboxylic acid: A repeat of the above reaction using isobutyric acid (41 μL, 0.44 mmol) under otherwise identical conditions gave the title compound (82 mg, 71%) as a yellow oil.



Benzoic acid (*E*)-1-(benzylbenzyloxycarbonylamino)-2-phenylvinyl ester (3h). The title compound was prepared according to a slight modification of General Procedure C using ynamide **1g** (137 mg, 0.40 mmol) and benzoic acid (98 mg, 0.80 mmol) in that the reaction time was 24 h. Purification by column chromatography (10% EtOAc/hexane→20% EtOAc/hexane) gave a yellow oil (104 mg, 56%). R_f = 0.61 (30% EtOAc/hexane); IR (film) 3066, 3019, 2954, 1743 (C=O), 1712 (C=O), 1601, 1450, 1397, 1216, 1062 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (2H, br s, Ar**H**), 7.57 (1H, t, *J* = 7.5 Hz, Ar**H**), 7.40 (2H, t, *J* = 7.7 Hz, Ar**H**), 7.33 (2H, br s, Ar**H**), 7.29-7.17 (13H, m, Ar**H**), 6.38 (1H, s, =C**H**), 5.14 (2H, s, C$\mathbf{H}_2$), 4.65 (2H, br s, C$\mathbf{H}_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 163.8 (C), 155.1 (C), 139.7 (C), 136.8 (C), 135.8 (C), 133.4 (CH), 132.7 (C), 130.0 (2 x CH), 129.1 (C), 128.7 (2 x CH), 128.6 (2 x CH), 128.3 (2

x CH), 128.3 (2 x CH), 128.3 (2 x CH), 128.0 (2 x CH), 127.9 (2 x CH), 127.8 (CH), 127.5 (CH), 117.3 (CH), 68.0 (CH_2), 51.5 (CH_2), due to overlapping signals in the aromatic region, two CH signals were not observed; HRMS (ES) Exact mass calcd for $C_{30}H_{26}NO_4$ $[M+H]^+$: 464.1856, found: 464.1849.

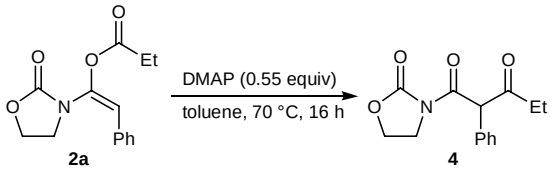


3,5-Dimethoxybenzoic acid (*E*)-1-[benzyl-(toluene-4-sulfonyl)amino]-2-phenylvinyl ester (3i). *Using 2.0 equiv. of carboxylic acid:* The title compound was prepared according to a slight modification of General Procedure C using ynamide **1h** (145 mg, 0.40 mmol) and 3,5-dimethoxybenzoic acid (146 mg, 0.80 mmol) in that the reaction was heated for 24 h. Purification by column chromatography (15% EtOAc/hexane) gave an orange oil (196 mg, 90%). R_f = 0.39 (30% EtOAc/hexane); IR (CH_2Cl_2) 3062, 3030, 2940, 2840, 1741 (C=O), 1665, 1596, 1456, 1353, 1205 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (2H, d, *J* = 8.2 Hz, Ar**H**), 7.37-7.34 (2H, m, Ar**H**), 7.25-7.17 (7H, m, Ar**H**), 7.17-7.11 (3H, m, Ar**H**), 6.91 (2H, d, *J* = 2.3 Hz, Ar**H**), 6.68 (1H, t, *J* = 2.3 Hz, Ar**H**), 6.51 (1H, s, =C**H**), 4.50 (2H, s, C$\mathbf{H}_2$N), 3.83 (6H, s, 2 x OC$\mathbf{H}_3$) 2.36 (3H, s, ArC$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 163.8 (C), 160.6 (2 x C), 144.0 (C), 136.9 (C), 136.5 (C), 134.4 (C), 132.0 (C), 130.8 (C), 129.6 (4 x CH), 128.7 (2 x CH), 128.2 (2 x CH), 128.11 (2 x CH), 128.06 (CH), 128.04 (CH), 127.9 (2 x CH), 123.3 (CH), 107.7 (2 x CH), 105.9 (CH), 55.6 (2 x CH_3), 52.6 (CH_2), 21.4 (CH_3); HRMS (ES) Exact mass calcd for $C_{31}H_{33}N_2O_6S$ $[M+NH_4]^+$: 561.2054, found: 561.2051.

Using 1.1 equiv of carboxylic acid: A repeat of the above reaction using 3,5-dimethoxybenzoic acid (80 mg, 0.44 mmol) under otherwise identical conditions gave the title compound (160 mg, 74%) as an orange oil.

Further Reactions of α-Acyloxyenamide 2a

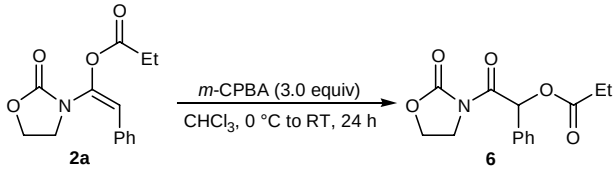
1-(2-Oxo-oxazolidin-3-yl)-2-phenylpentane-1,3-dione (4)



A solution of α-acyloxyenamide **2a** (105 mg, 0.40 mmol) and DMAP (27 mg, 0.22 mmol) in toluene (8 mL) was heated at 70 ºC for 16 h. The mixture was concentrated *in vacuo* and the residue was purified by column chromatography (15% EtOAc/hexane→23% EtOAc/hexane) to give the β-ketoimide **4** (95 mg, 91%) as a white solid. R_f = 0.55 (60% EtOAc/hexane); m.p. 116-118 °C; IR (solid) 2964, 2924,

1757 (C=O), 1703 (C=O), 1487, 1394, 1238, 1109, 1039, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.32 (3H, m, Ar**H**), 7.29-7.26 (2H, m, Ar**H**), 5.83 (1H, s, C**H**Ph), 4.50-4.39 (2H, m, C$\mathbf{H}_2$O), 4.14 (1H, ddd, *J* = 10.9, 9.5, 7.0 Hz, C$\mathbf{H}_2$N), 4.02 (1H, ddd, *J* = 10.9, 9.3, 6.8 Hz, C$\mathbf{H}_2$N), 2.67 (1H, dq, *J* = 18.2, 7.3 Hz, C$\mathbf{H}_2$$CH_3$), 2.40 (1H, dq, *J* = 18.2, 7.3 Hz, C$\mathbf{H}_2$$CH_3$), 0.99 (3H, t, *J* = 7.3 Hz, CH_2C$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 205.1 (C), 168.0 (C), 153.9 (C), 131.8 (C), 130.2 (2 x CH), 128.8 (2 x CH), 128.4 (CH), 64.3 (CH), 62.4 (CH_2), 42.6 (CH_2), 34.6 (CH_2), 7.6 (CH_3); HRMS (ES) Exact mass calcd for $C_{14}H_{16}NO_4$ $[M+H]^+$: 262.1074, found: 262.1070.

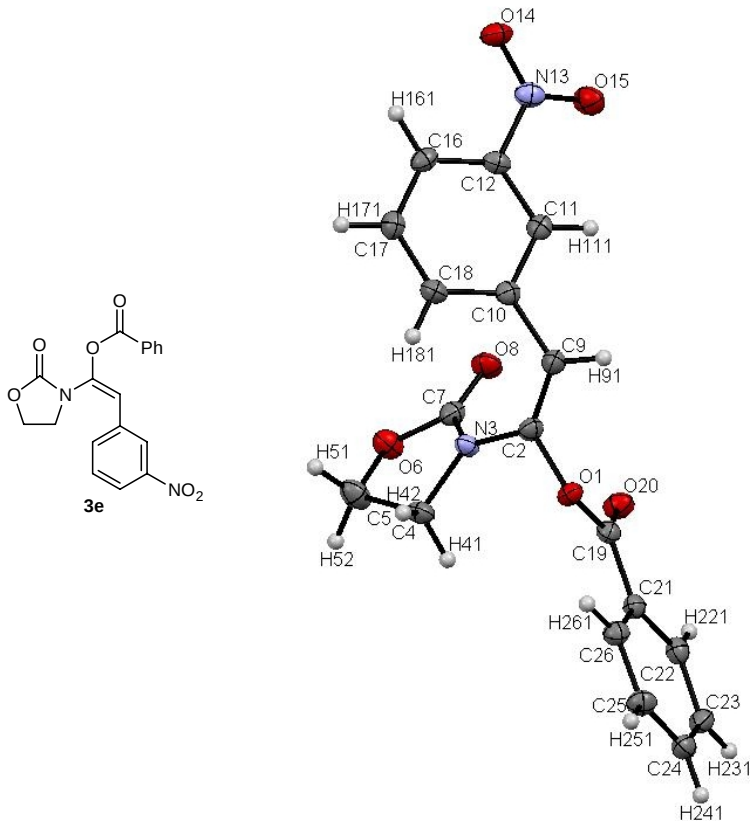
Propionic acid 2-oxo-2-(2-oxo-oxazolidin-3-yl)-1-phenylethyl ester (6)



To a solution of *m*-CPBA (223 mg, 70%, 0.90 mmol) in $CHCl_3$ (3 mL) at 0 ºC was rapidly added a solution of α-acyloxyenamide **2a** (78 mg, 0.30 mmol) in $CHCl_3$ (2 mL + 1 mL rinse) *via* cannula. The reaction was allowed to warm to room temperature over 2 h, and then stirred for a further 22 h. Saturated aqueous Na_2SO_3 solution (10 mL) was added and the mixture was stirred for 30 min. The mixture was diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (2 x 20 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (40% Et_2O/hexane→45% Et_2O/hexane) gave the *α-acyloxyimide* **6** (66 mg, 79%) as a colorless oil. R_f = 0.34 (80% Et_2O/hexane); IR (film) 3023, 2986, 2926, 1784 (C=O), 1739 (C=O), 1712 (C=O), 1389, 1217, 1176, 757 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.61-7.56 (2H, m, Ar**H**), 7.41-7.37 (3H, m, Ar**H**), 7.06 (1H, s, C**H**Ph), 4.47-4.42 (1H, m, C$\mathbf{H}_2$O), 4.37-4.32 (1H, m, C$\mathbf{H}_2$O), 4.11 (1H, ddd, *J* = 10.8, 9.6, 7.2 Hz, C$\mathbf{H}_2$N), 3.90 (1H, ddd, *J* = 10.9, 9.4, 6.3 Hz, C$\mathbf{H}_2$N), 2.50 (1H, dq, *J* = 16.7, 7.6 Hz, C$\mathbf{H}_2$$CH_3$), 2.43 (1H, dq, *J* = 16.7, 7.5 Hz, C$\mathbf{H}_2$$CH_3$), 1.18 (3H, t, *J* = 7.5 Hz, CH_2C$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 174.2 (C), 169.0 (C), 152.8 (C), 132.8 (C), 129.5 (CH), 129.0 (2 x CH), 128.7 (2 x CH), 73.3 (CH), 62.5 (CH_2), 42.4 (CH_2), 27.1 (CH_2), 8.8 (CH_3); HRMS (ES) Exact mass calcd for $C_{14}H_{19}N_2O_5$ $[M+NH_4]^+$: 295.1288, found: 295.1294.

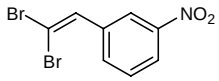
Regio-/Stereochemical Determinations

- The structure of **3e** was determined by X-ray crystallography:

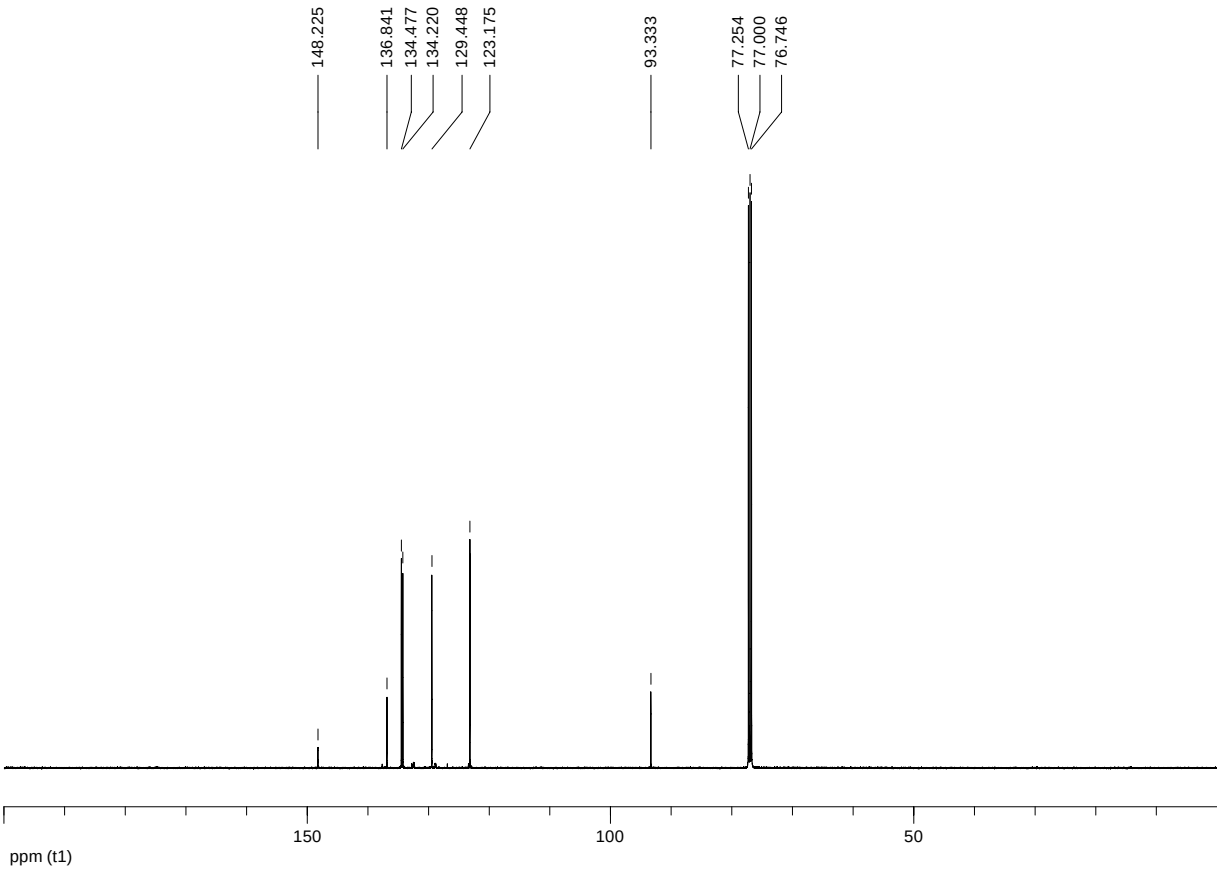


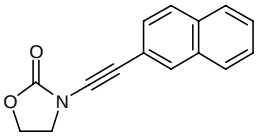
- The formation of products **4** and **6** from **2a** lends further support for the regioselectivity of the reaction producing **2a**.
- The regio- and stereoselectivities of the remaining ynamide hydroacyloxylation reactions were assigned by analogy.

NMR Spectra of New Compounds

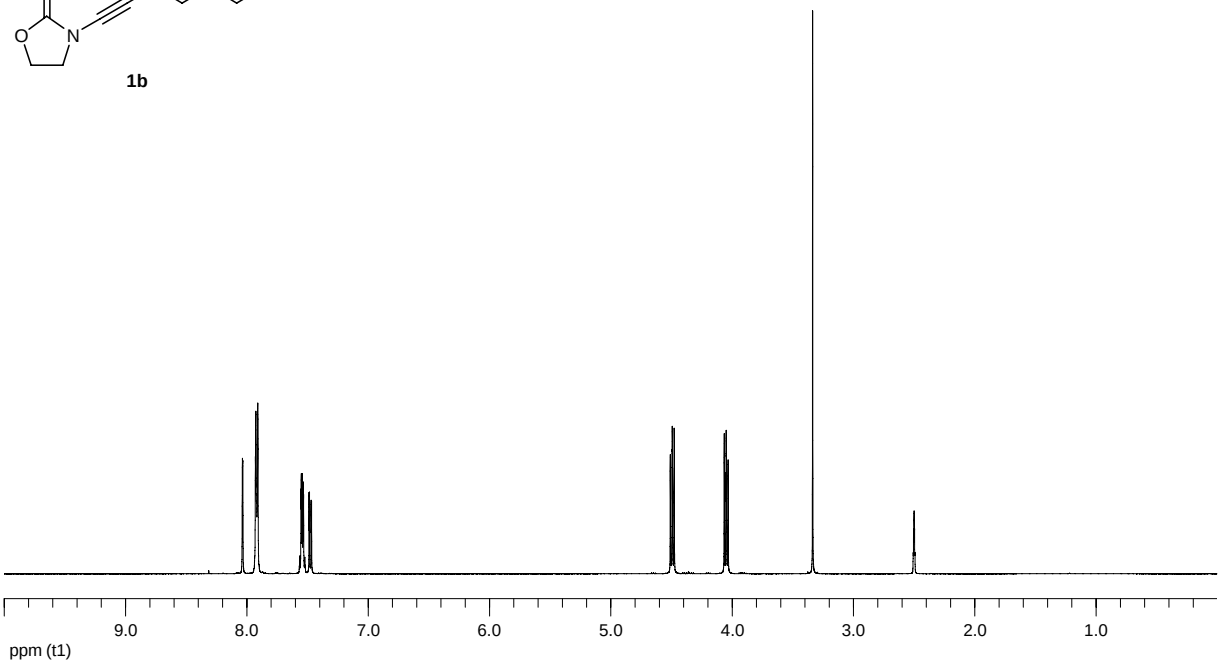


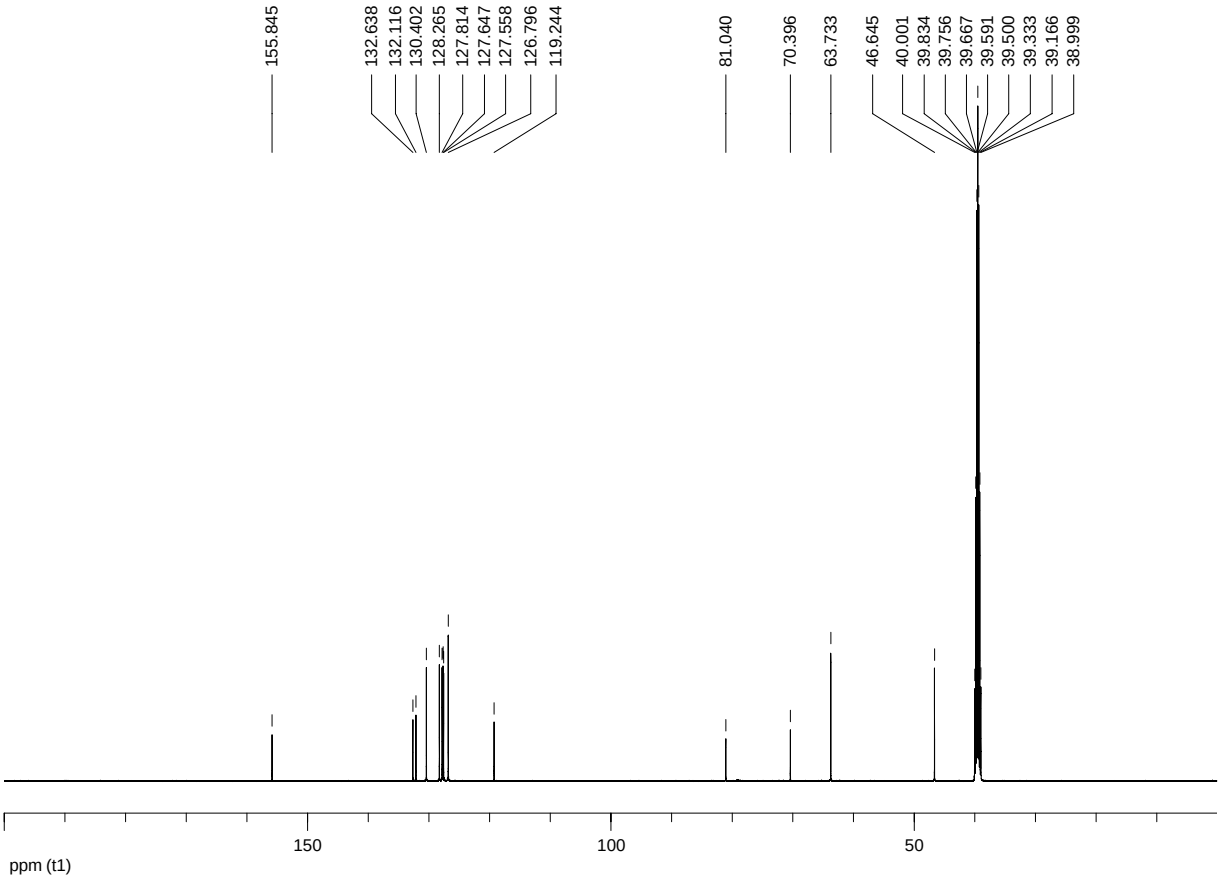
9

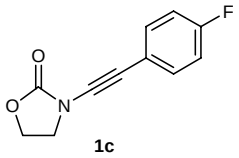




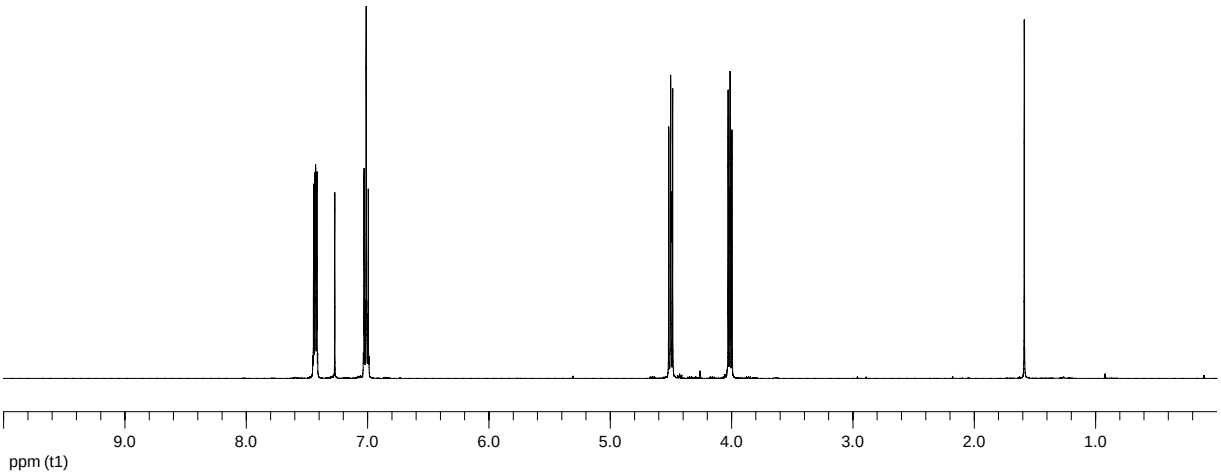
1b

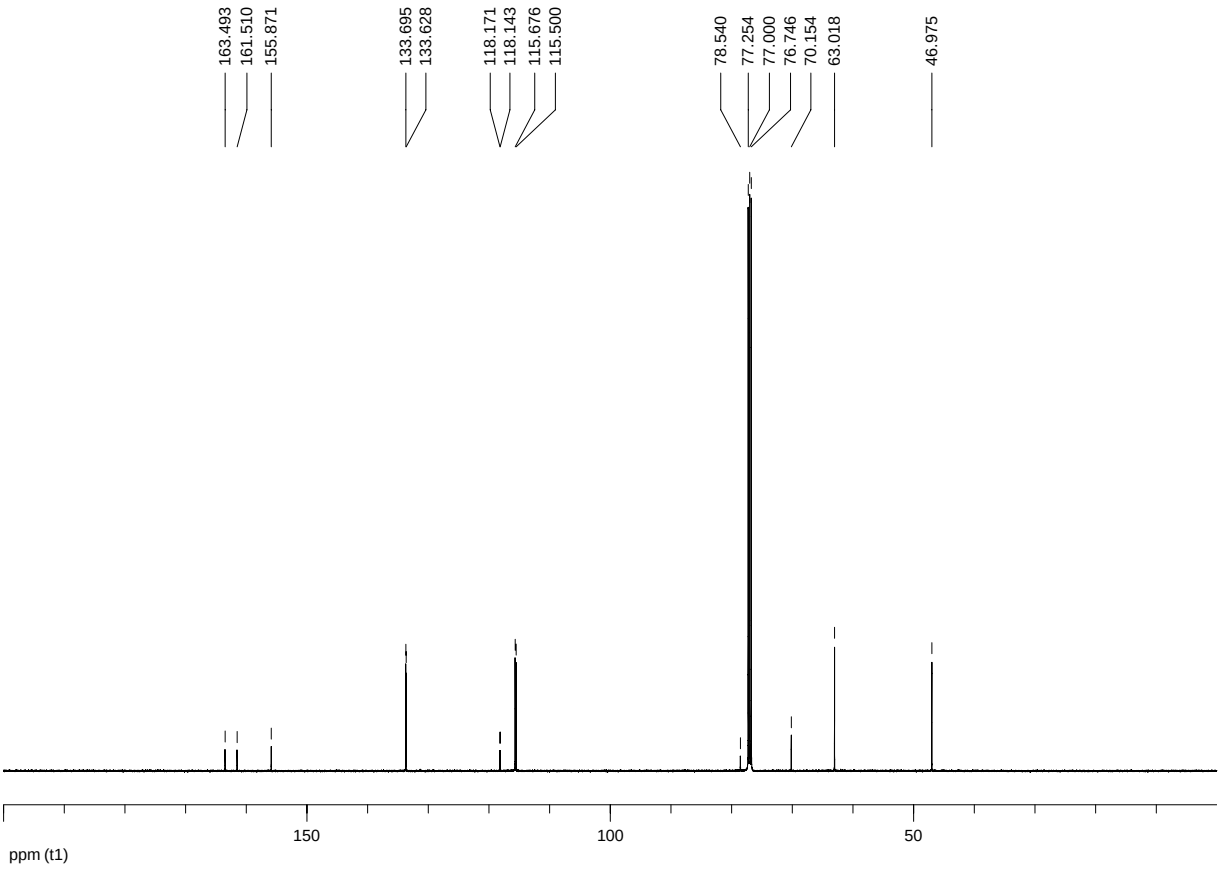


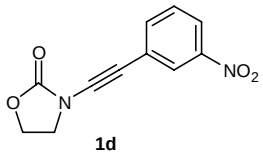




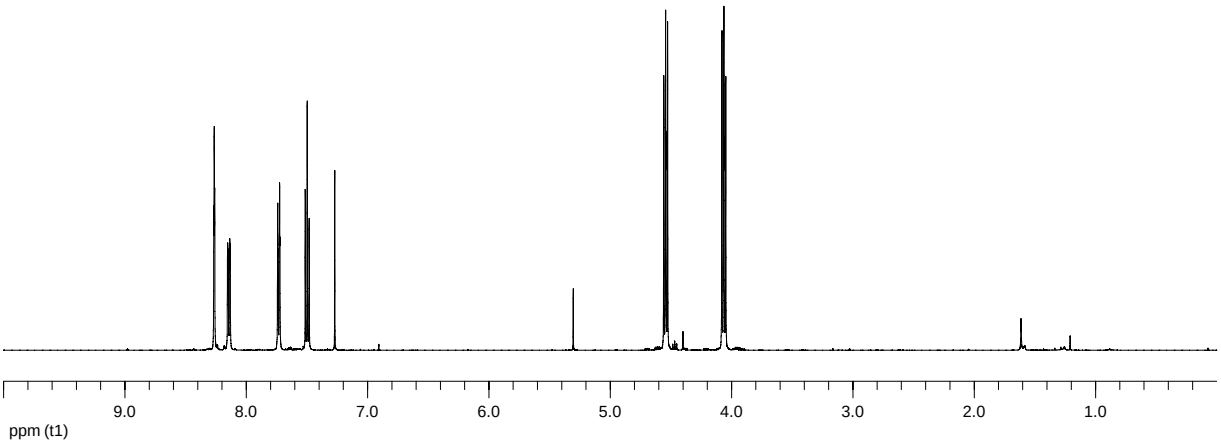
1c

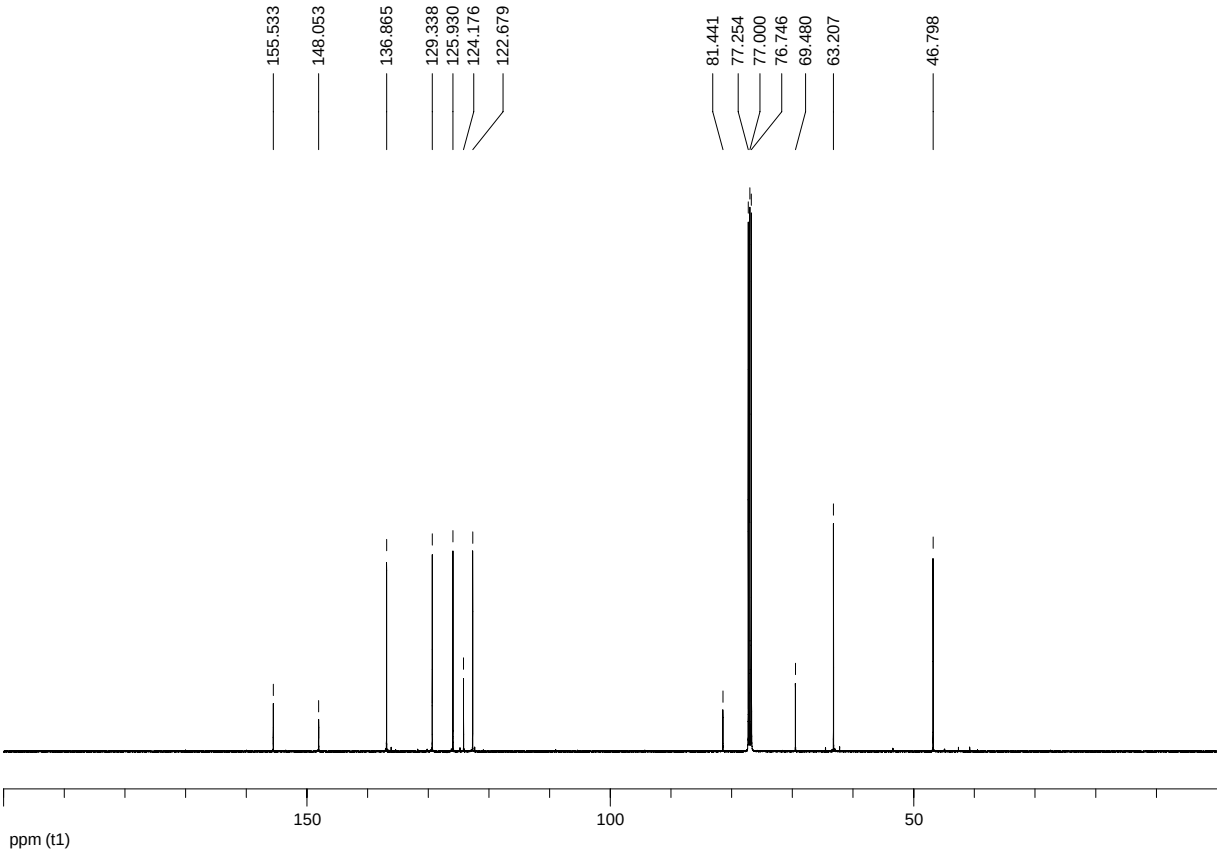


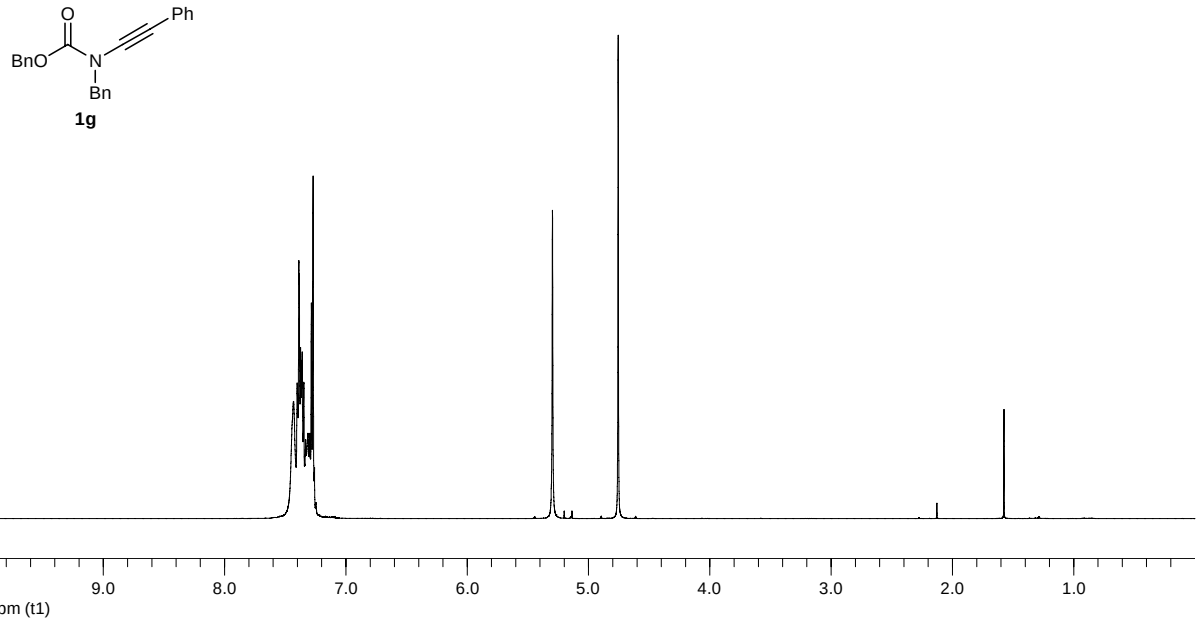


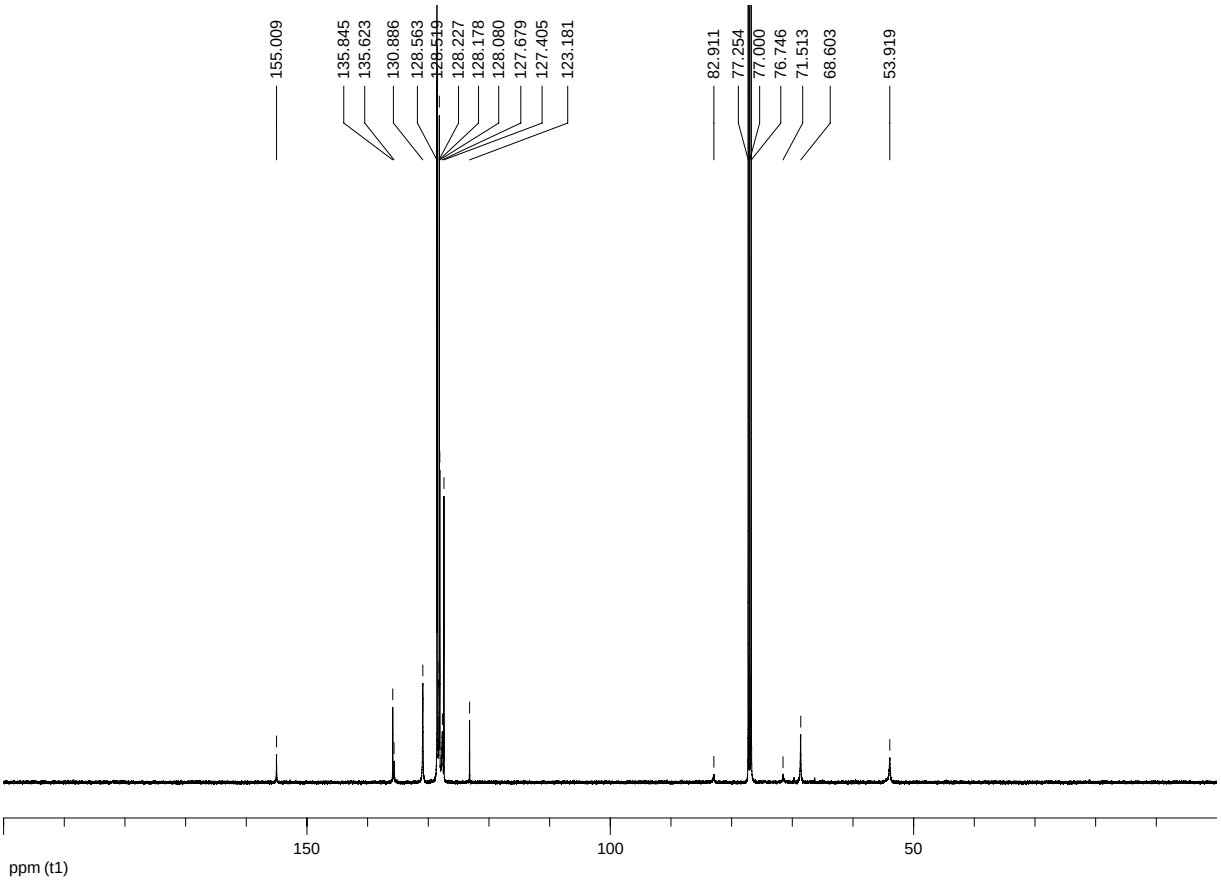


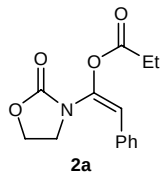
1d



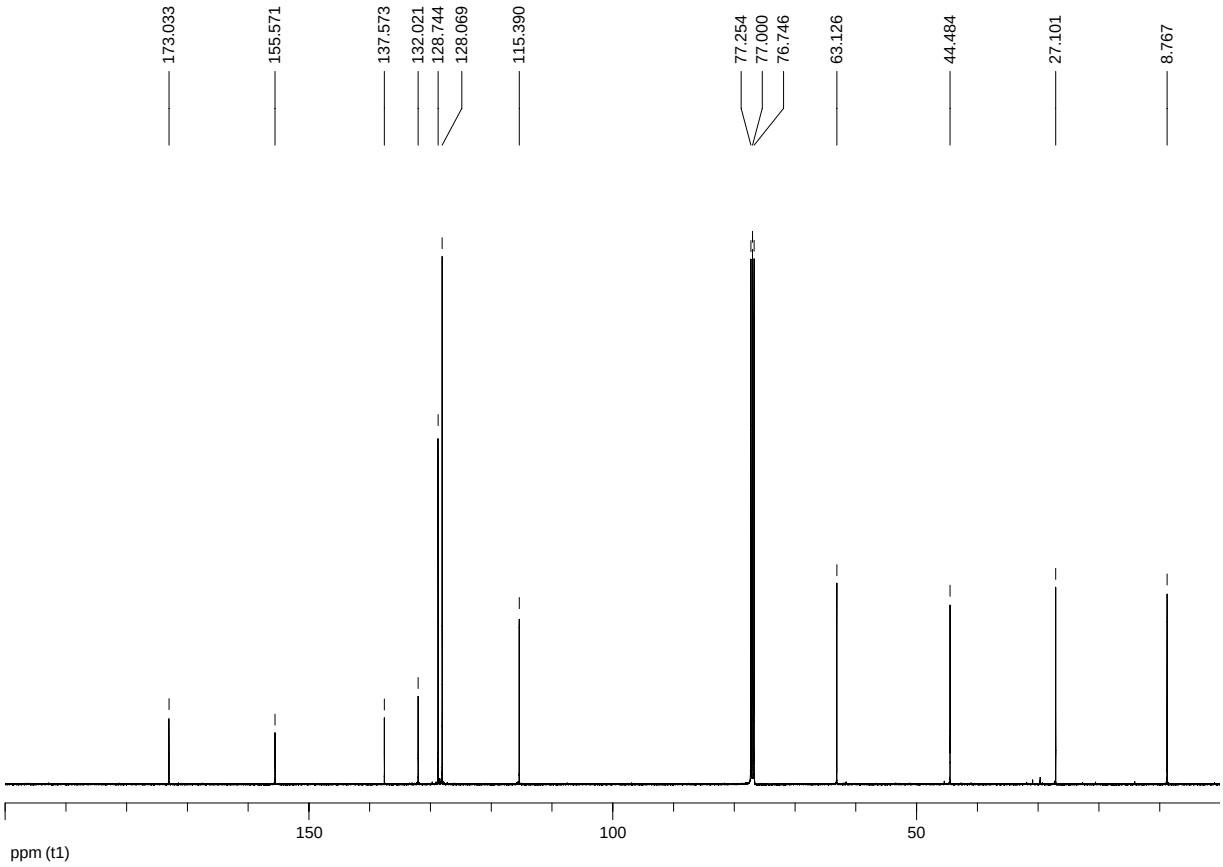


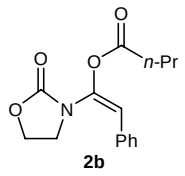




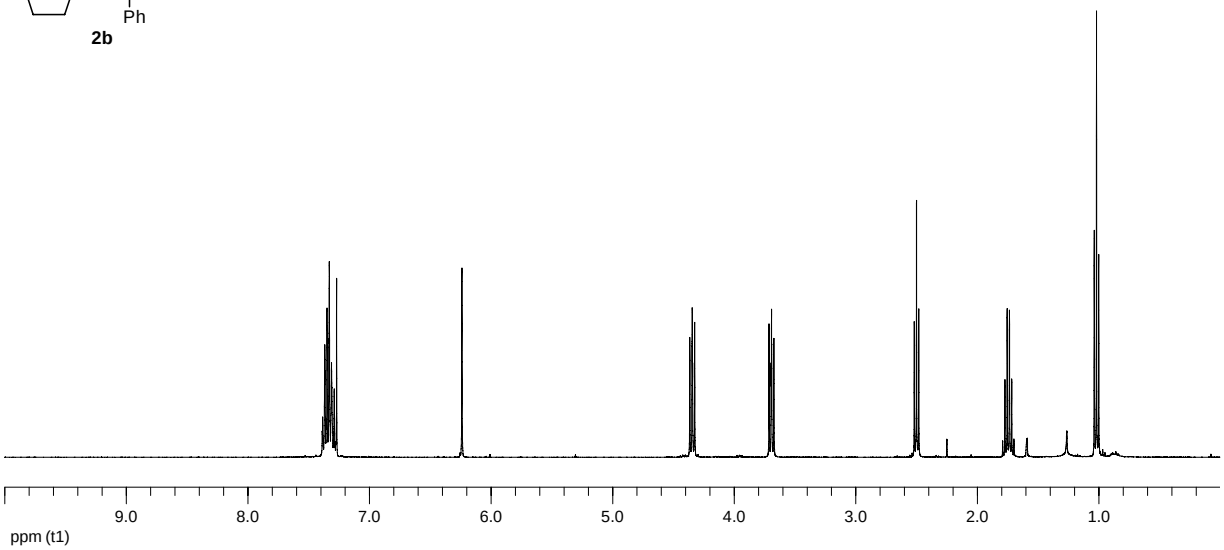


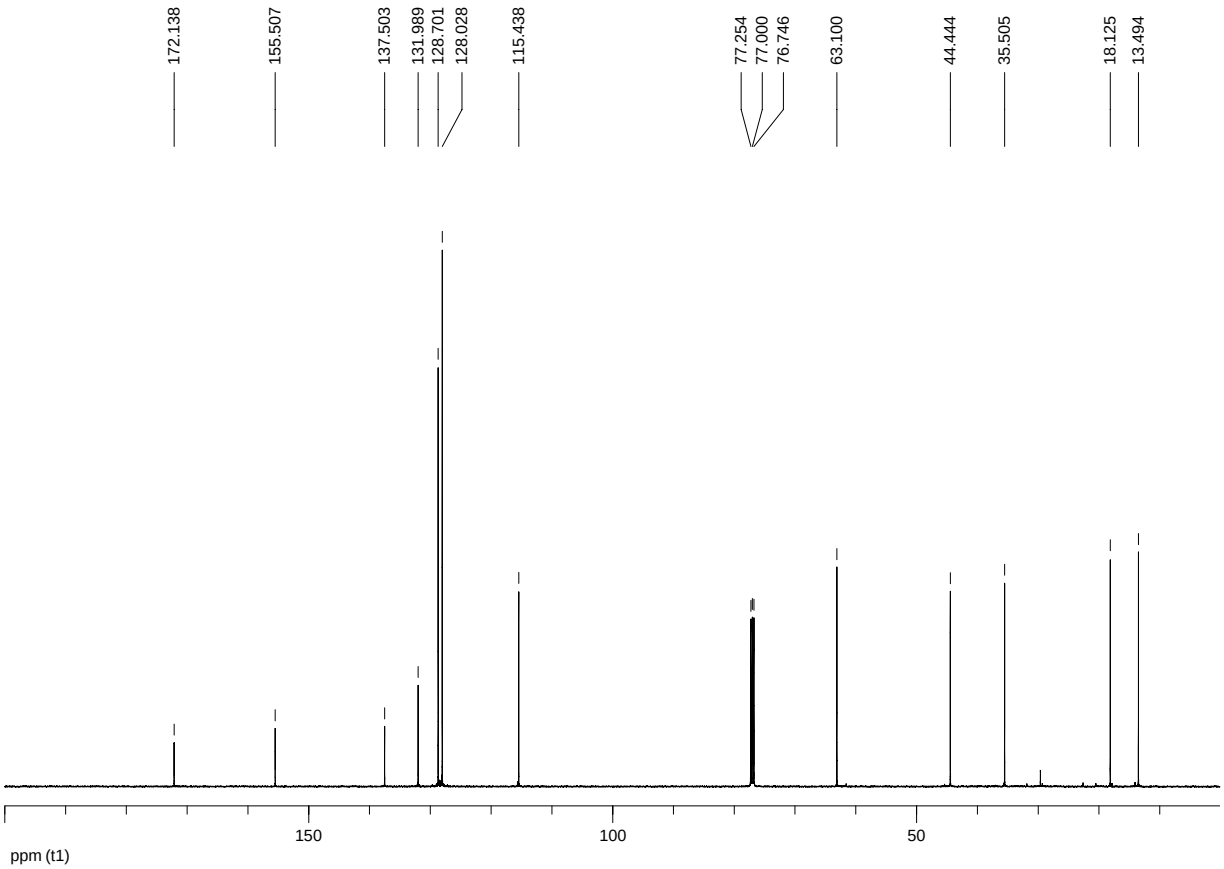
2a

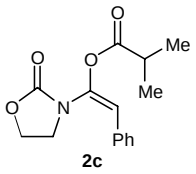




2b

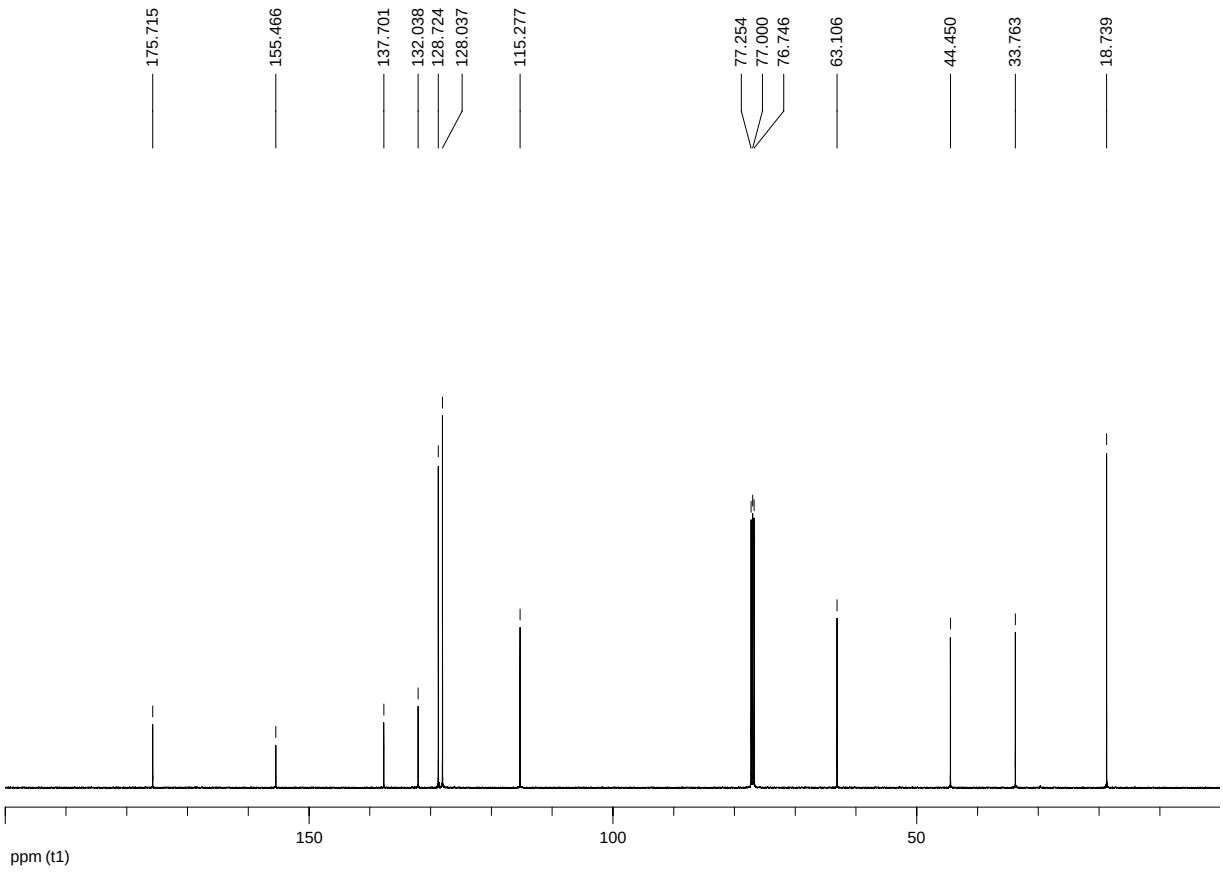


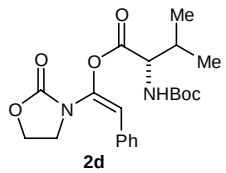



O
O
O
Me
Me
O
N
Ph

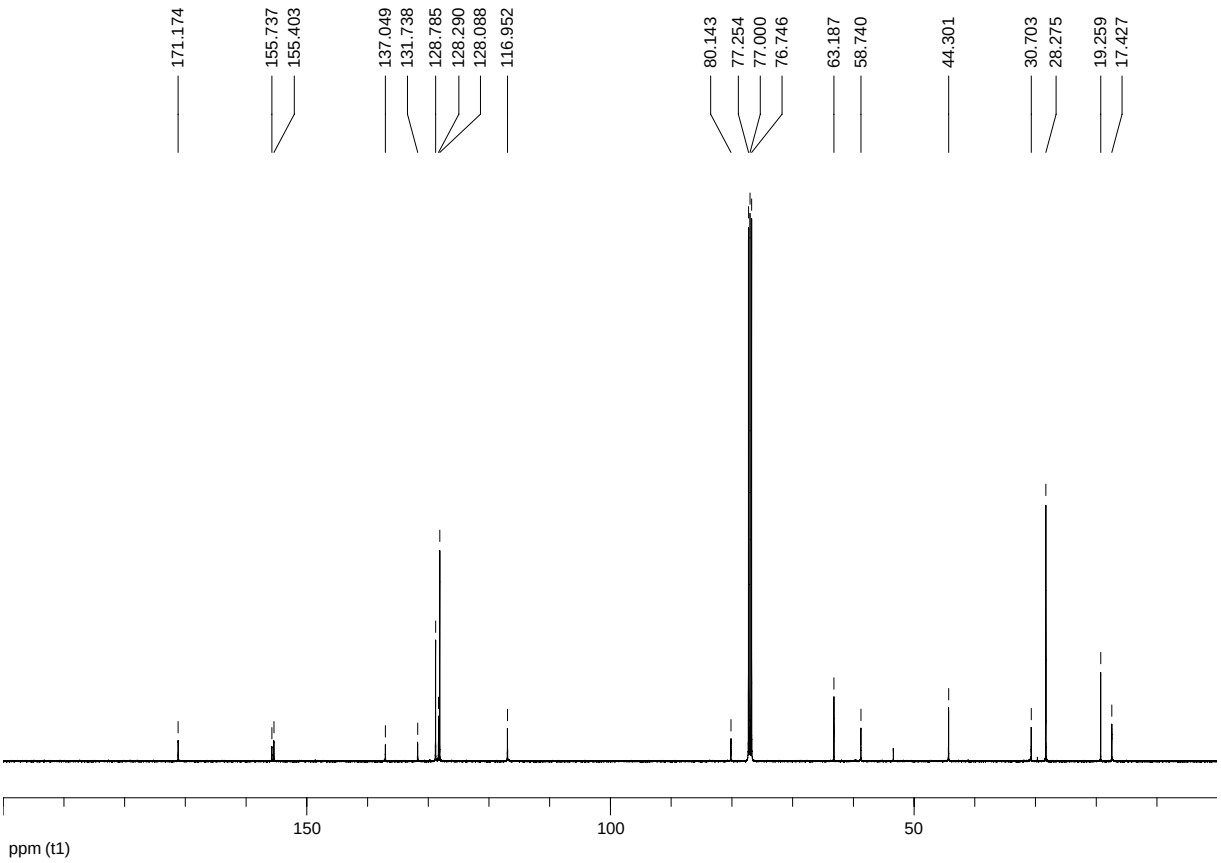
2c

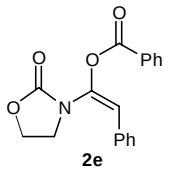
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


175.715
155.466
137.701
132.038
128.724
128.037
115.277
77.254
77.000
76.746
63.106
44.450
33.763
18.739
150
100
50
ppm (t1)

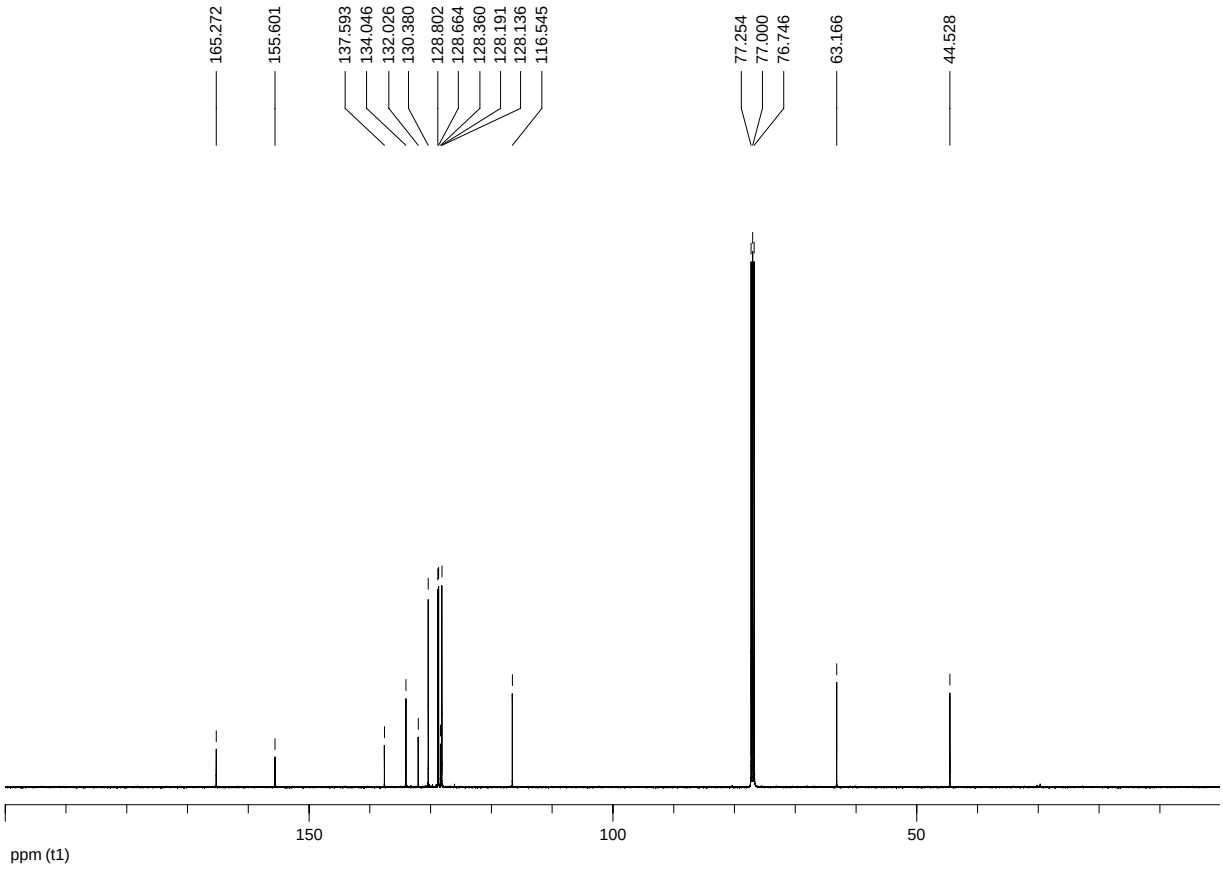


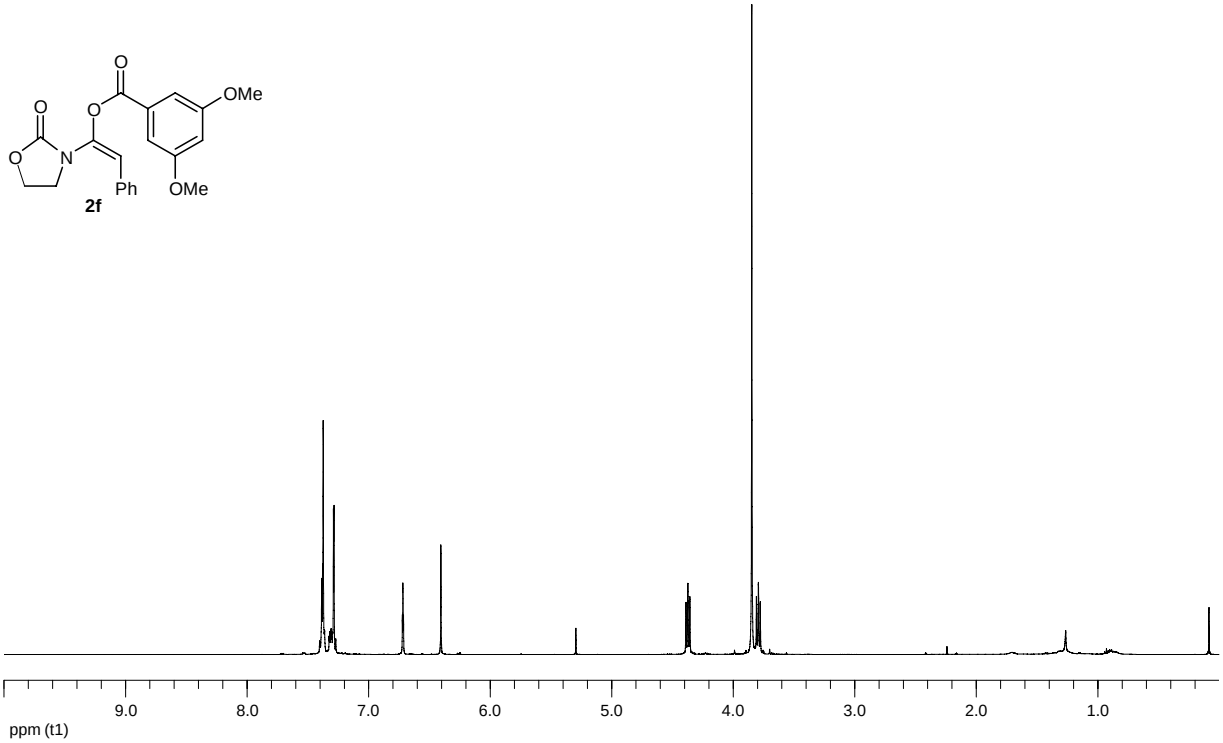
2d



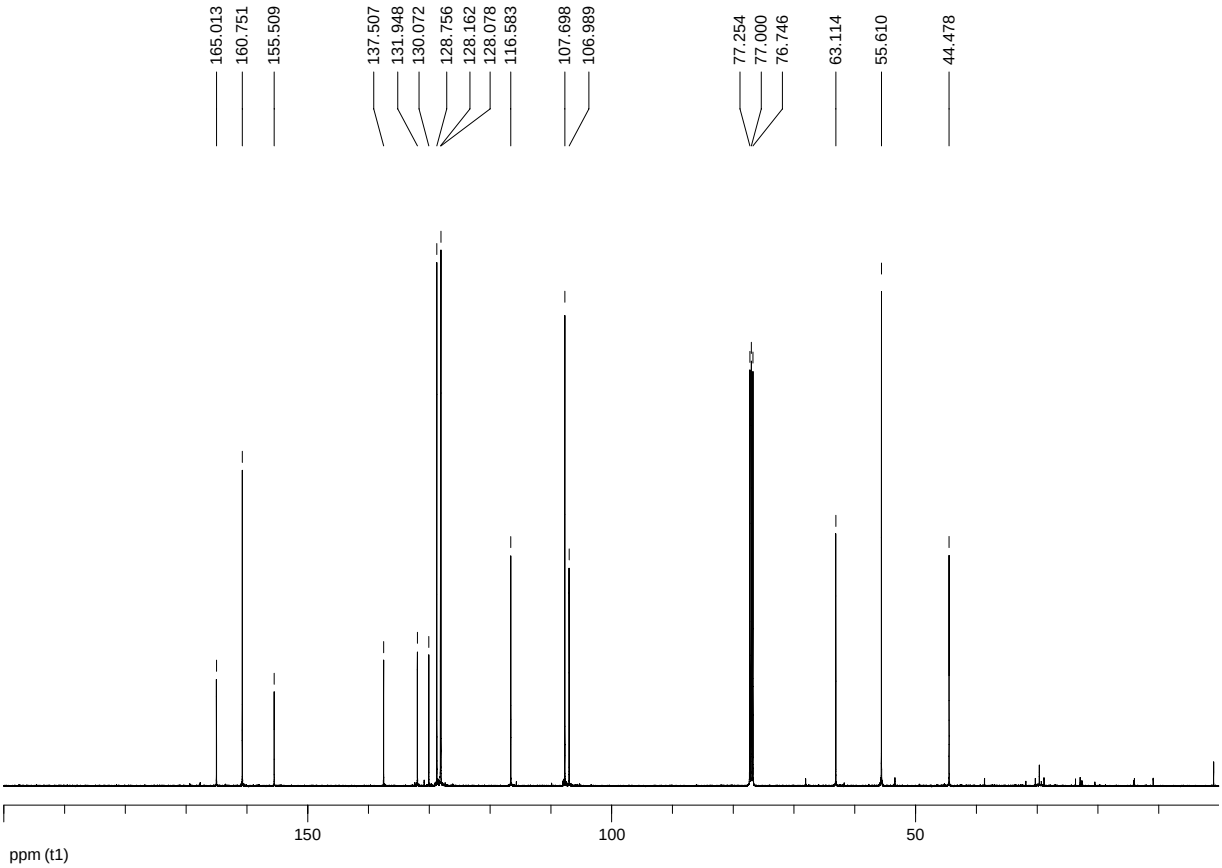


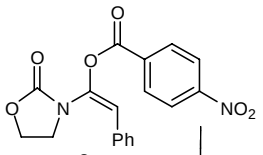
2e



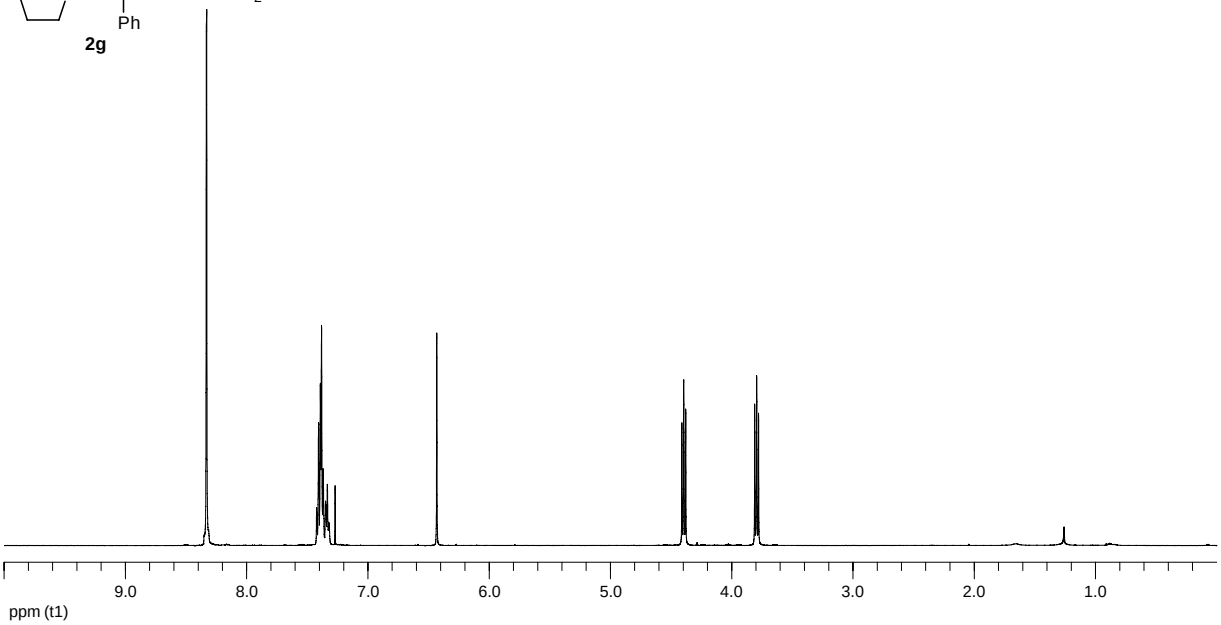


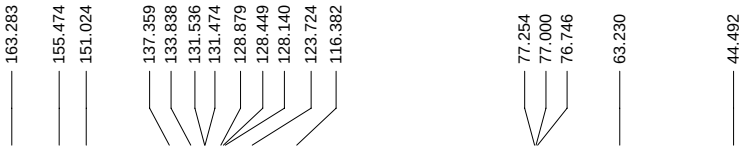
2f

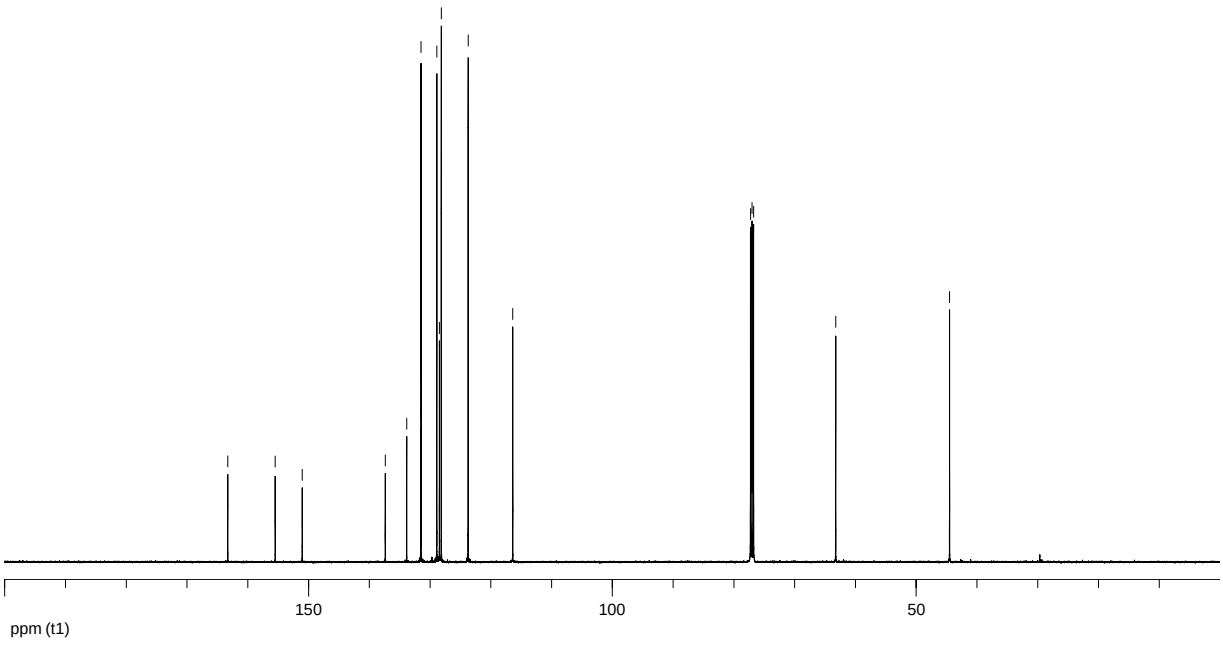


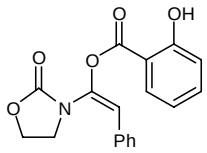


2g

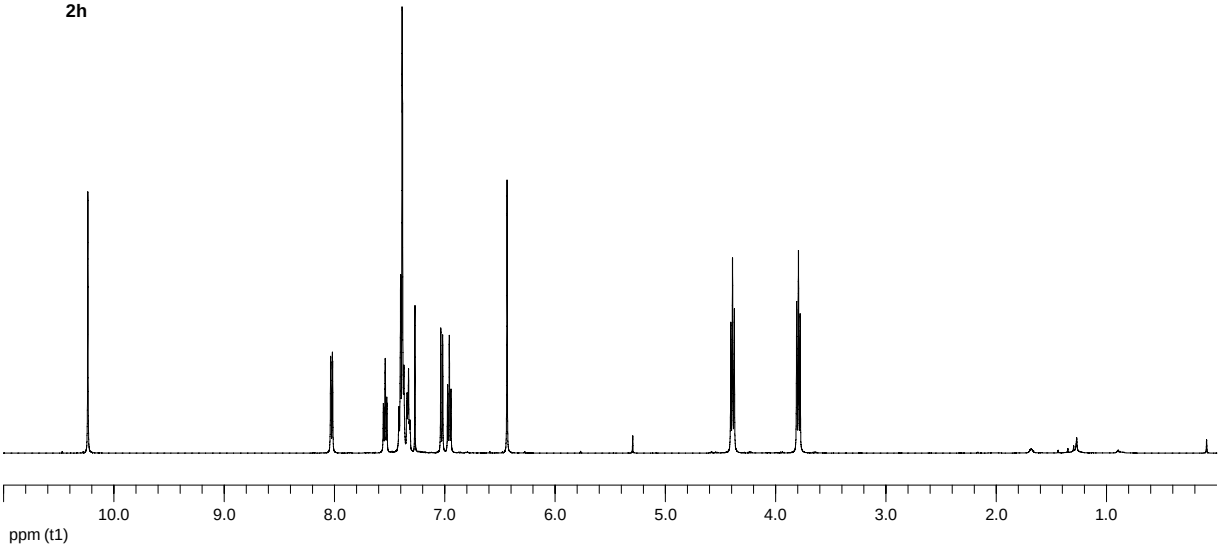


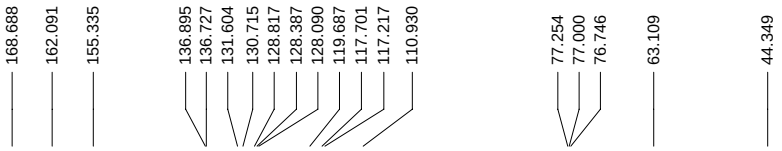


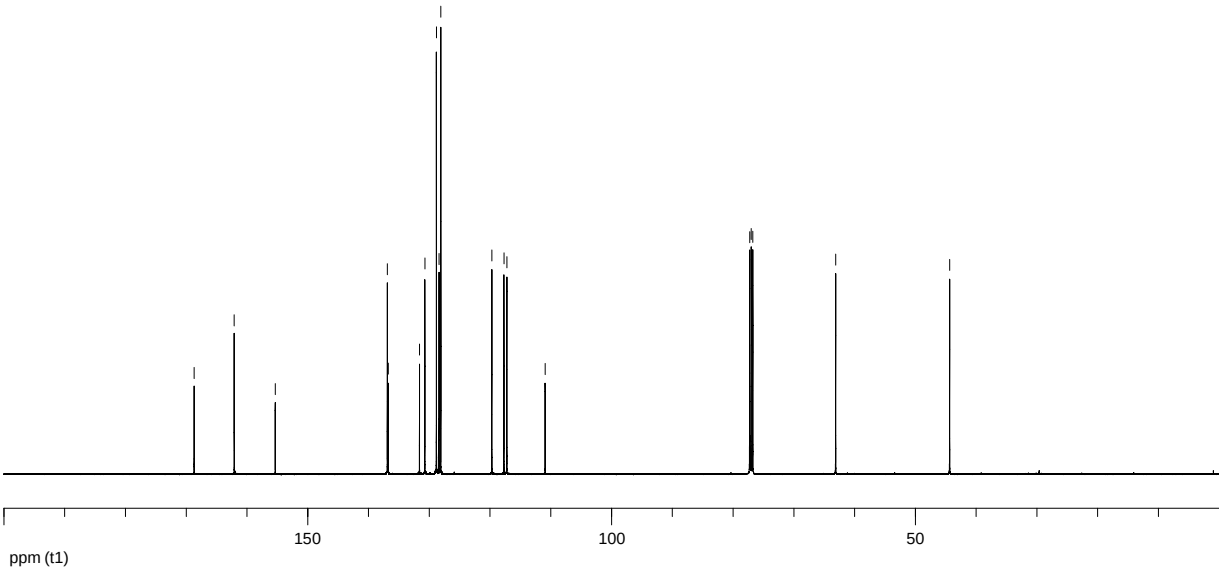


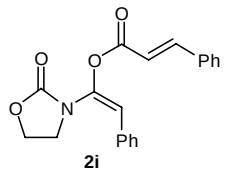


2h

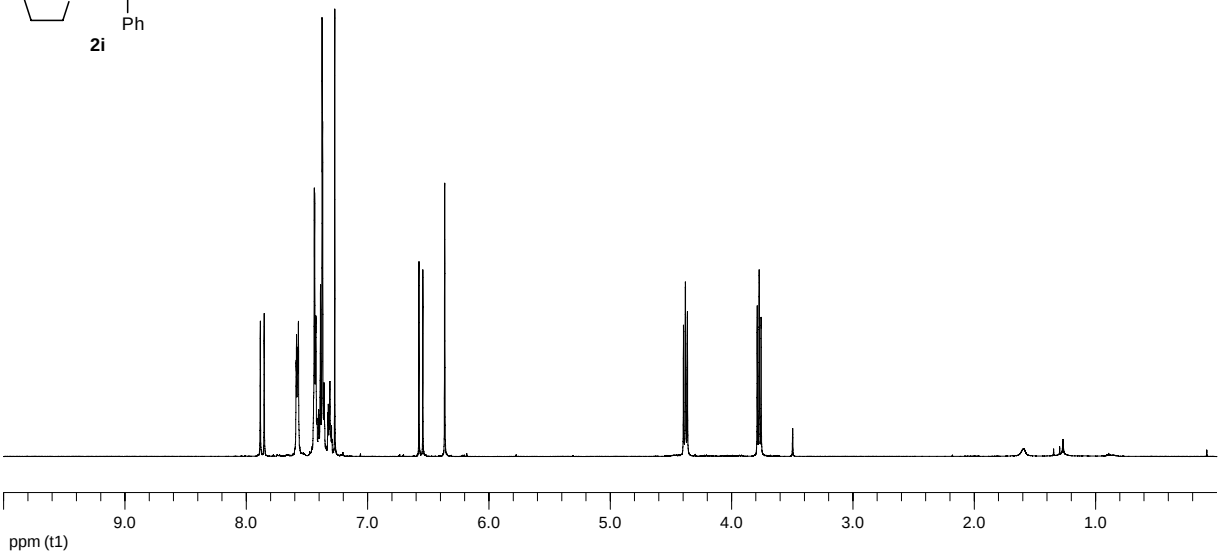


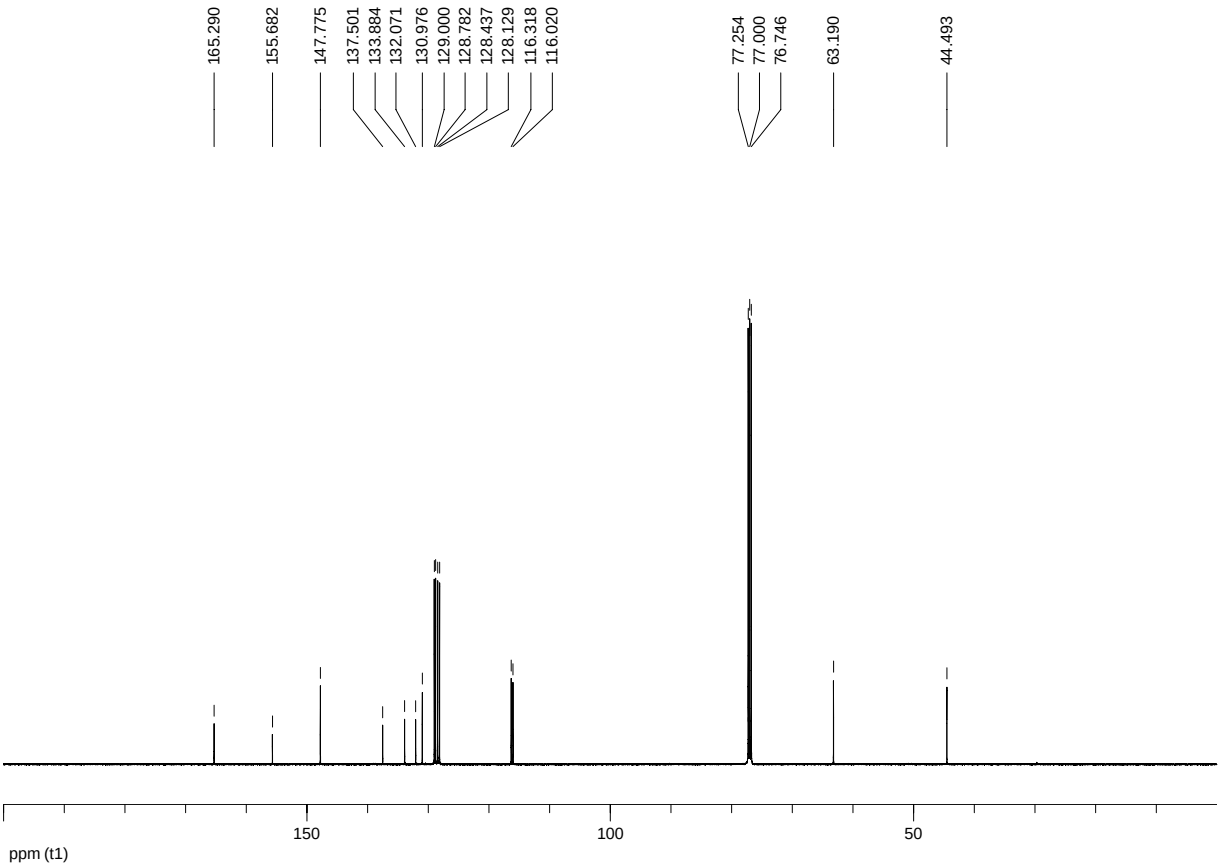


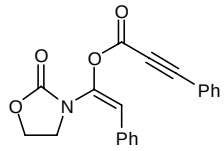




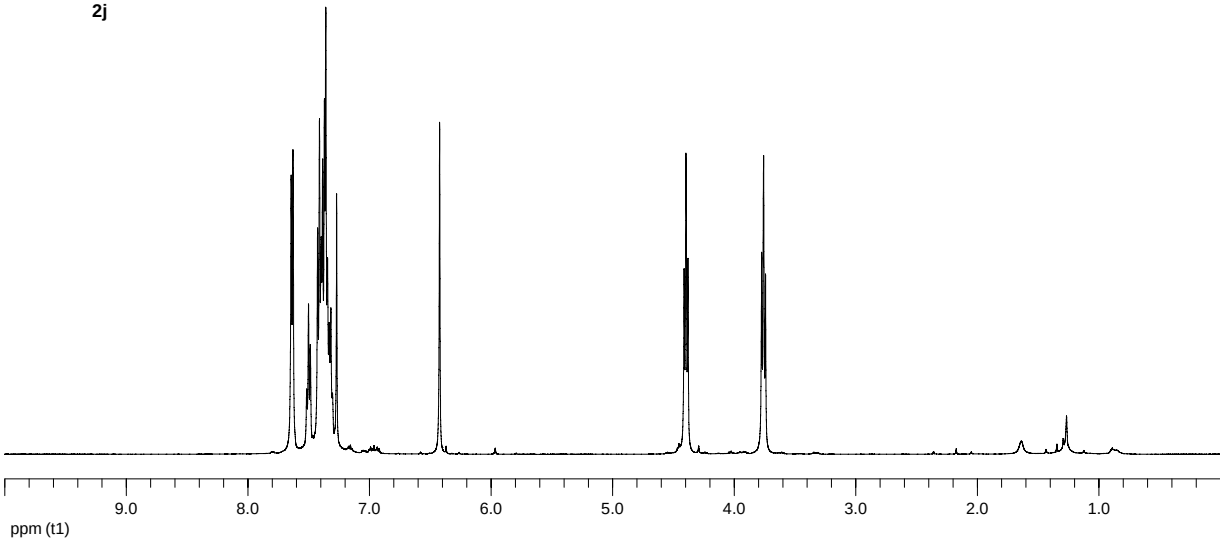
2i

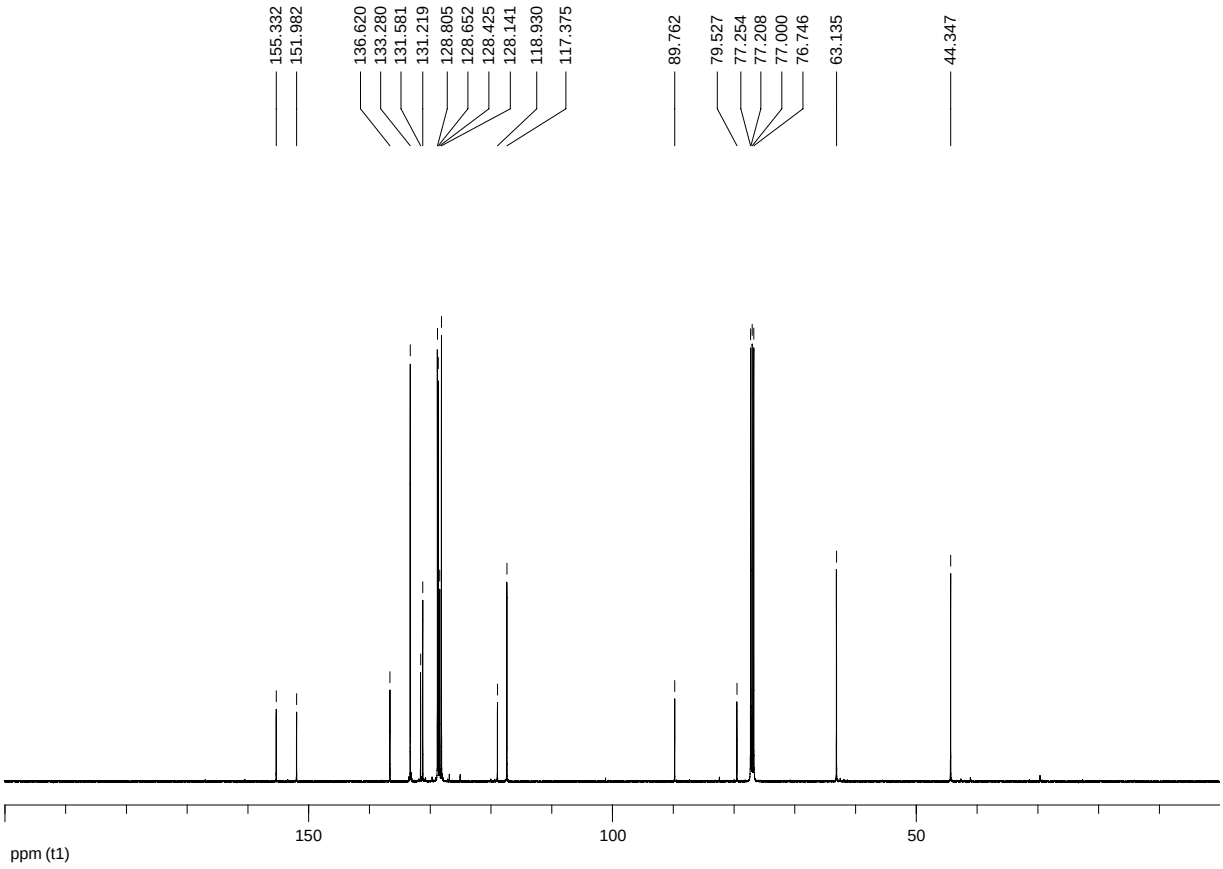


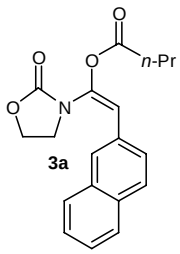




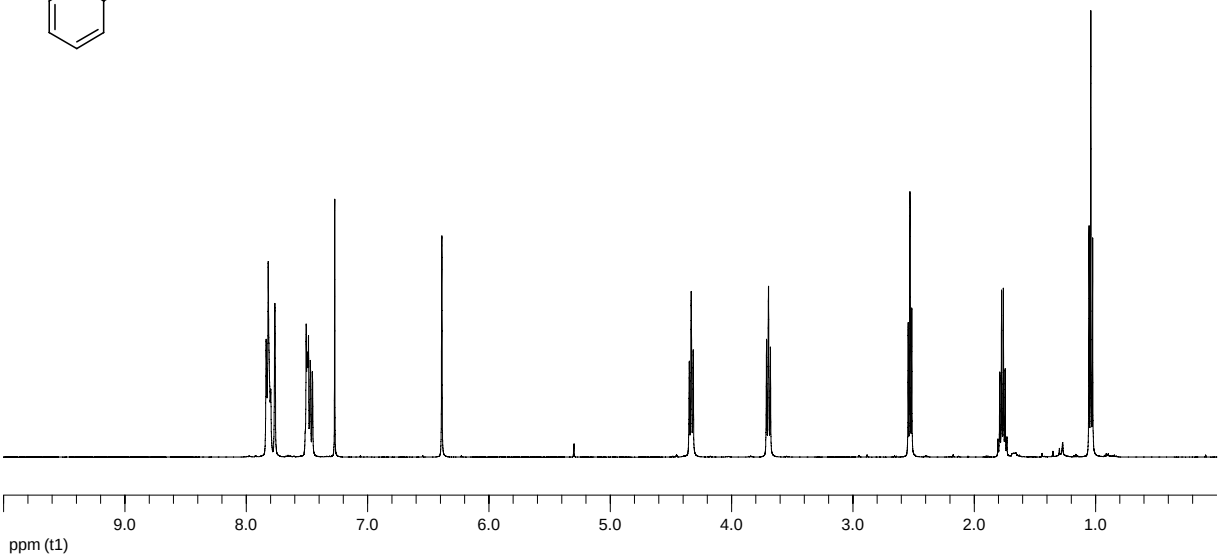
2j

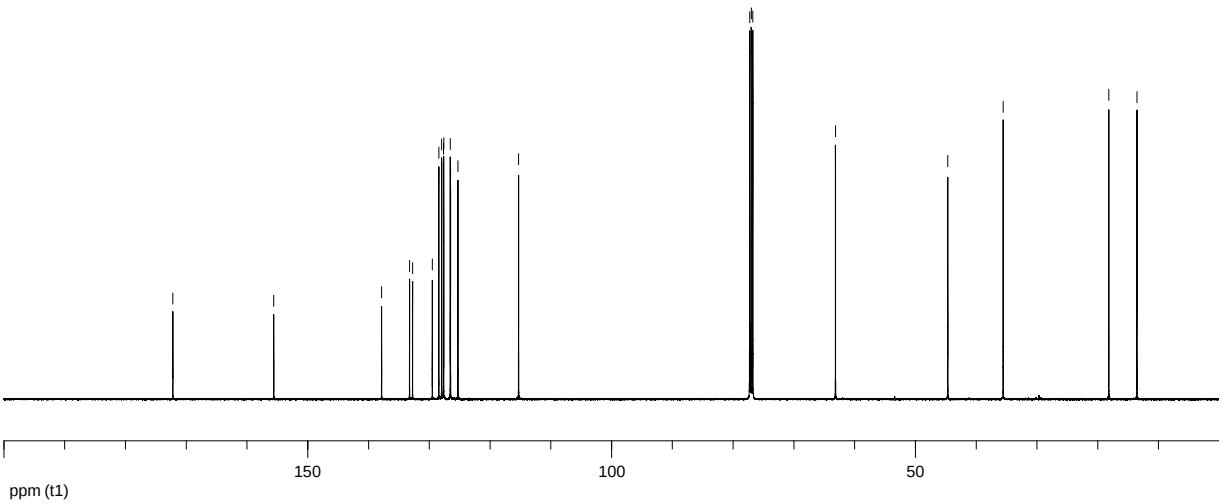


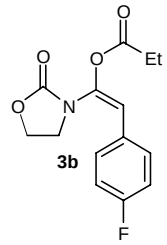




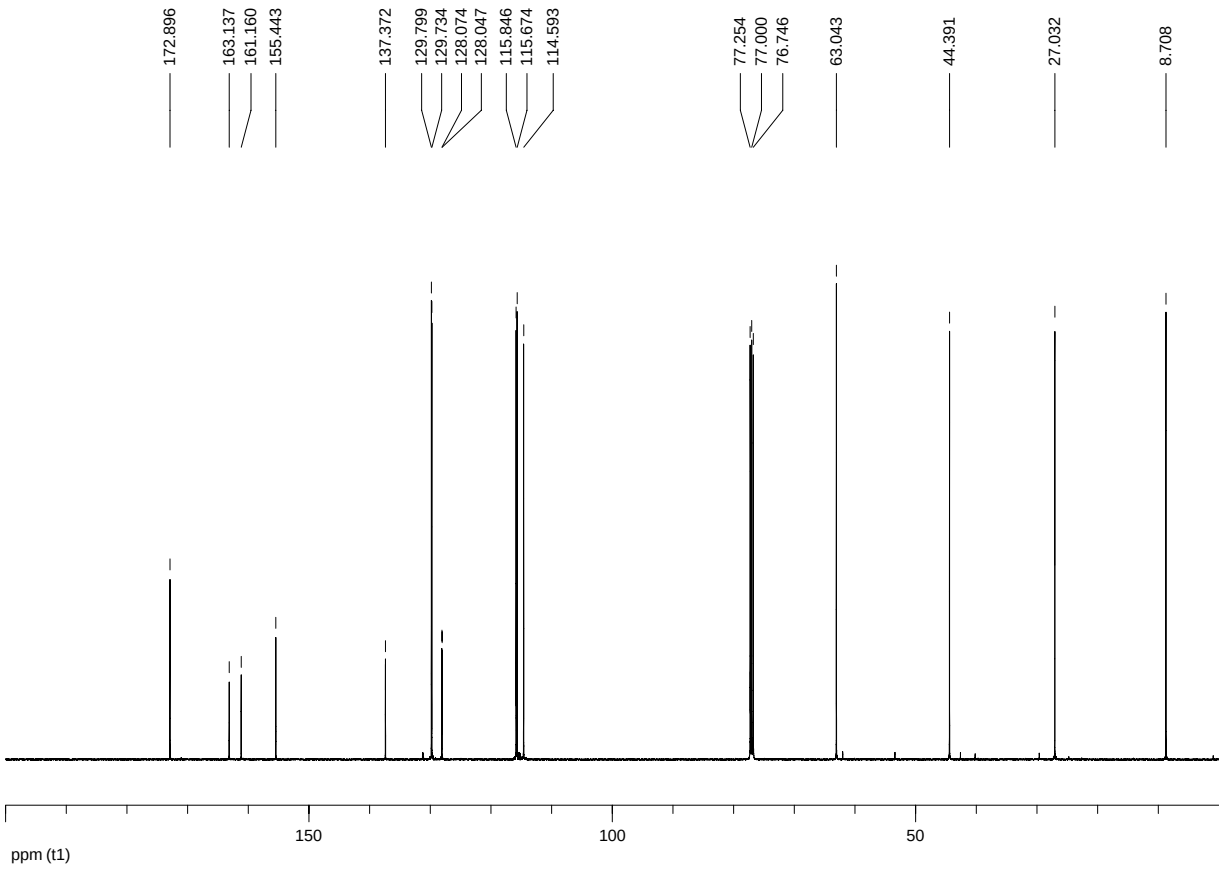
3a

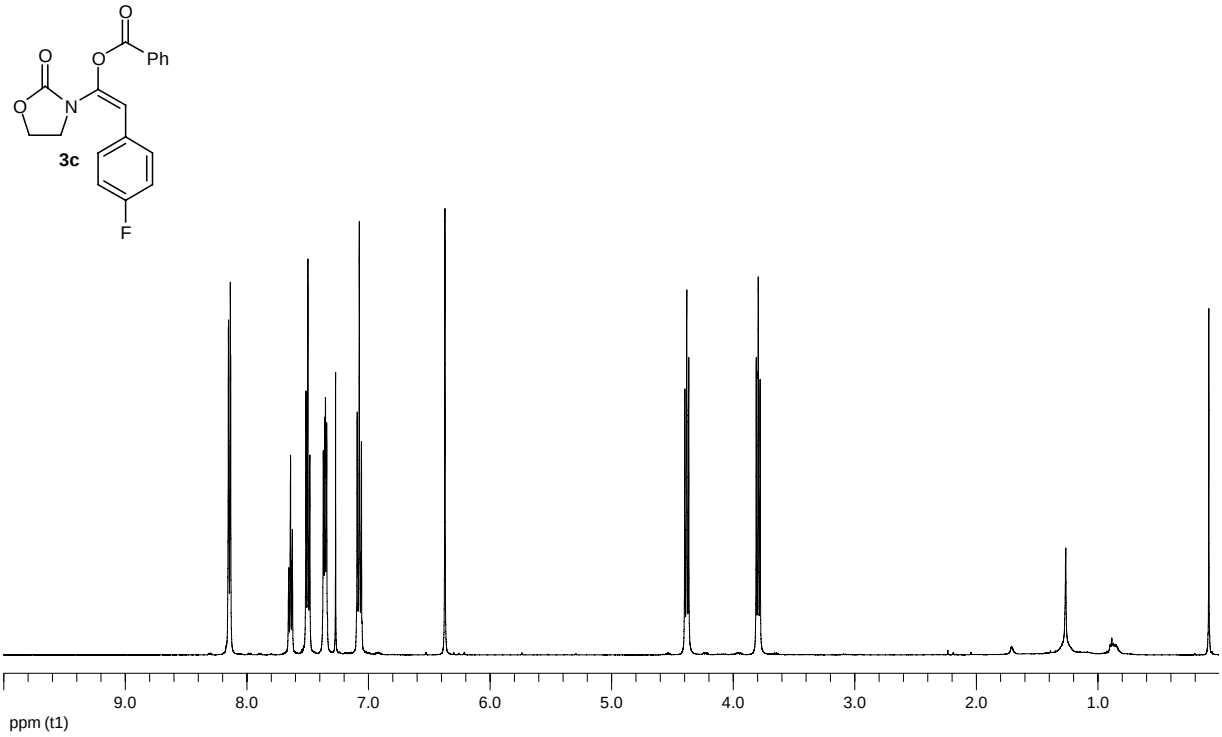


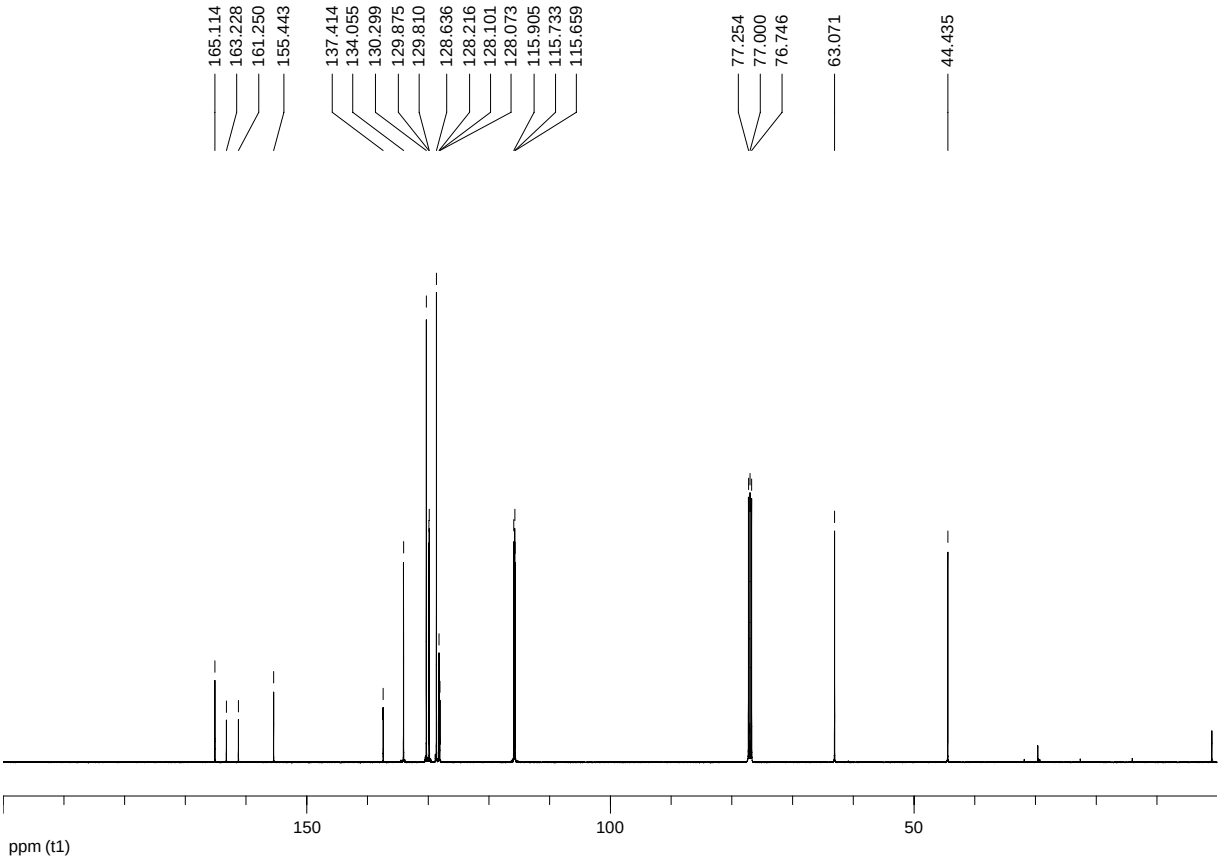


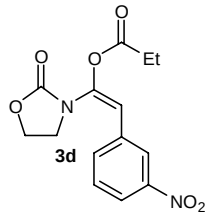


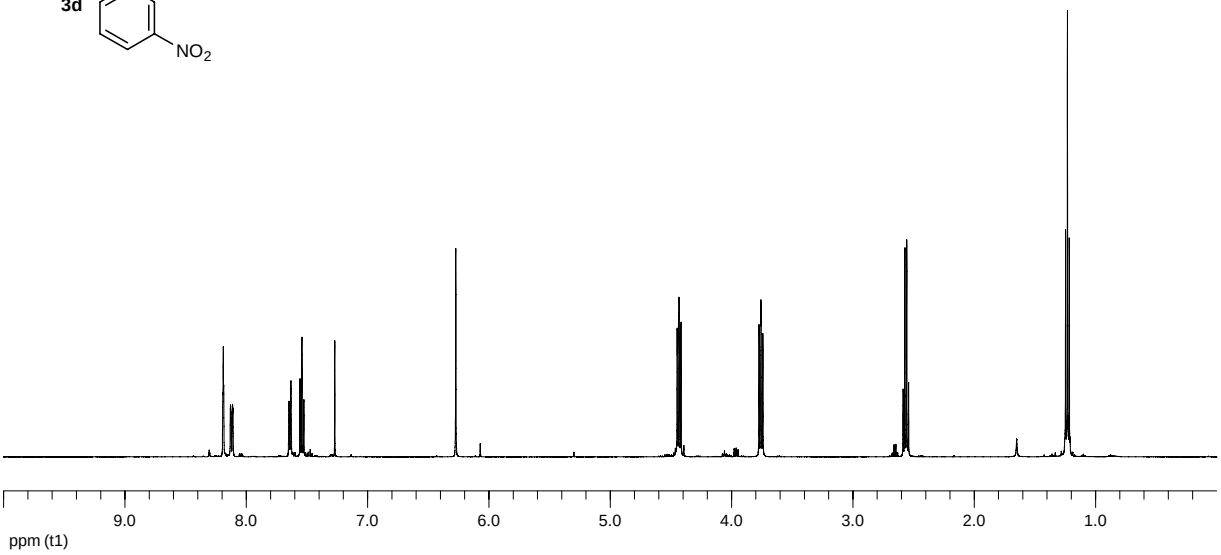
3b

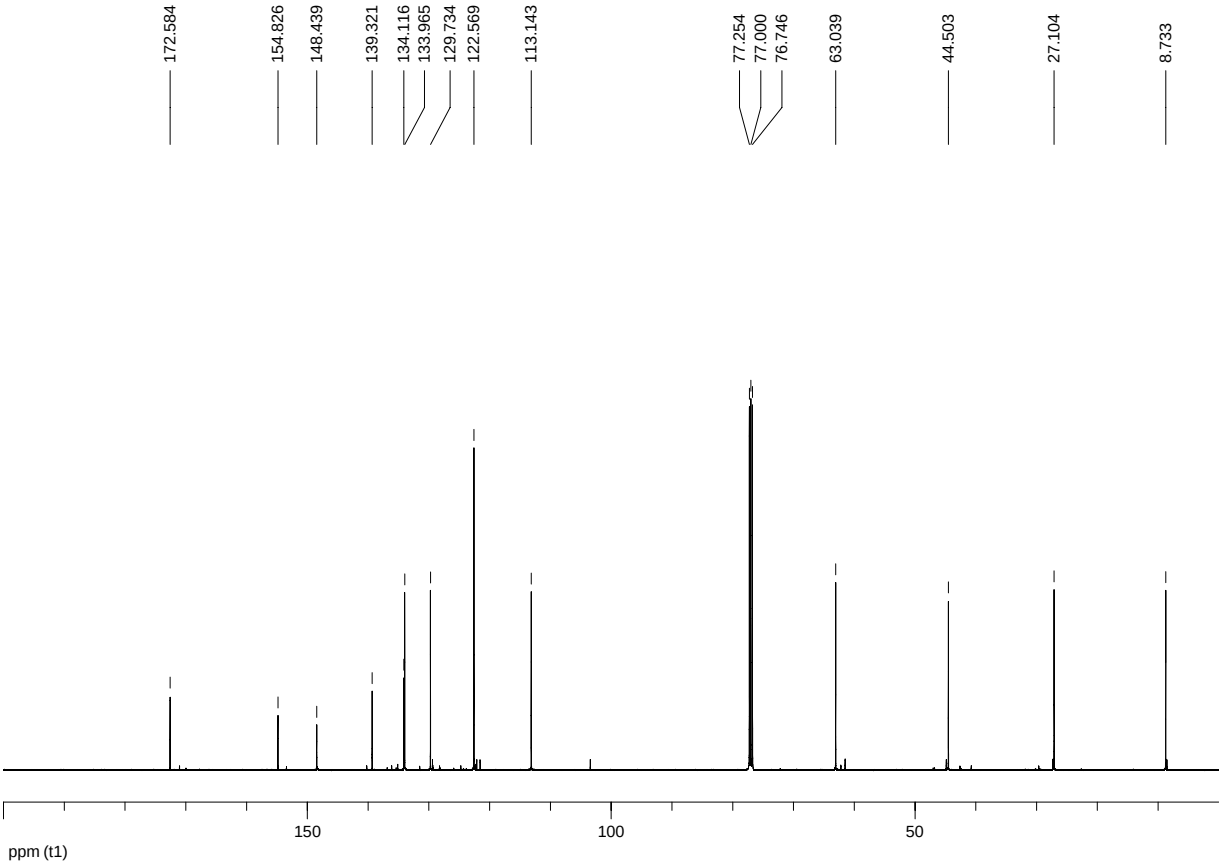


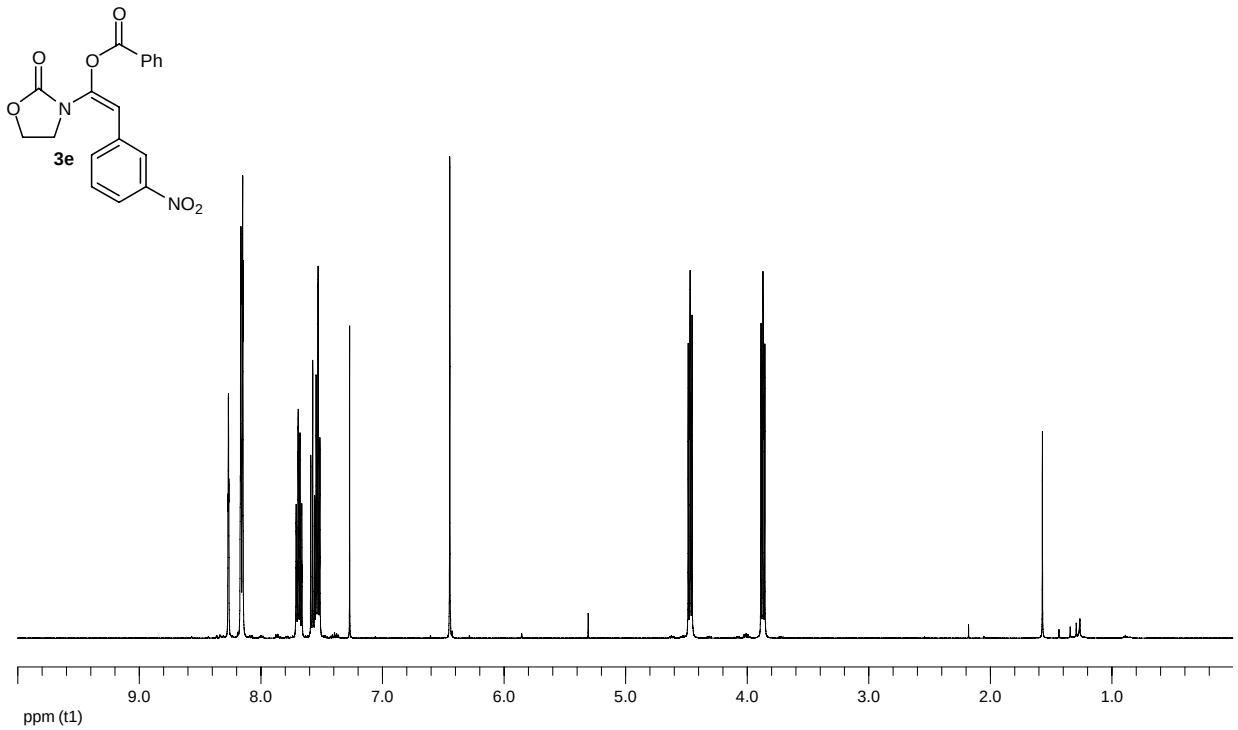


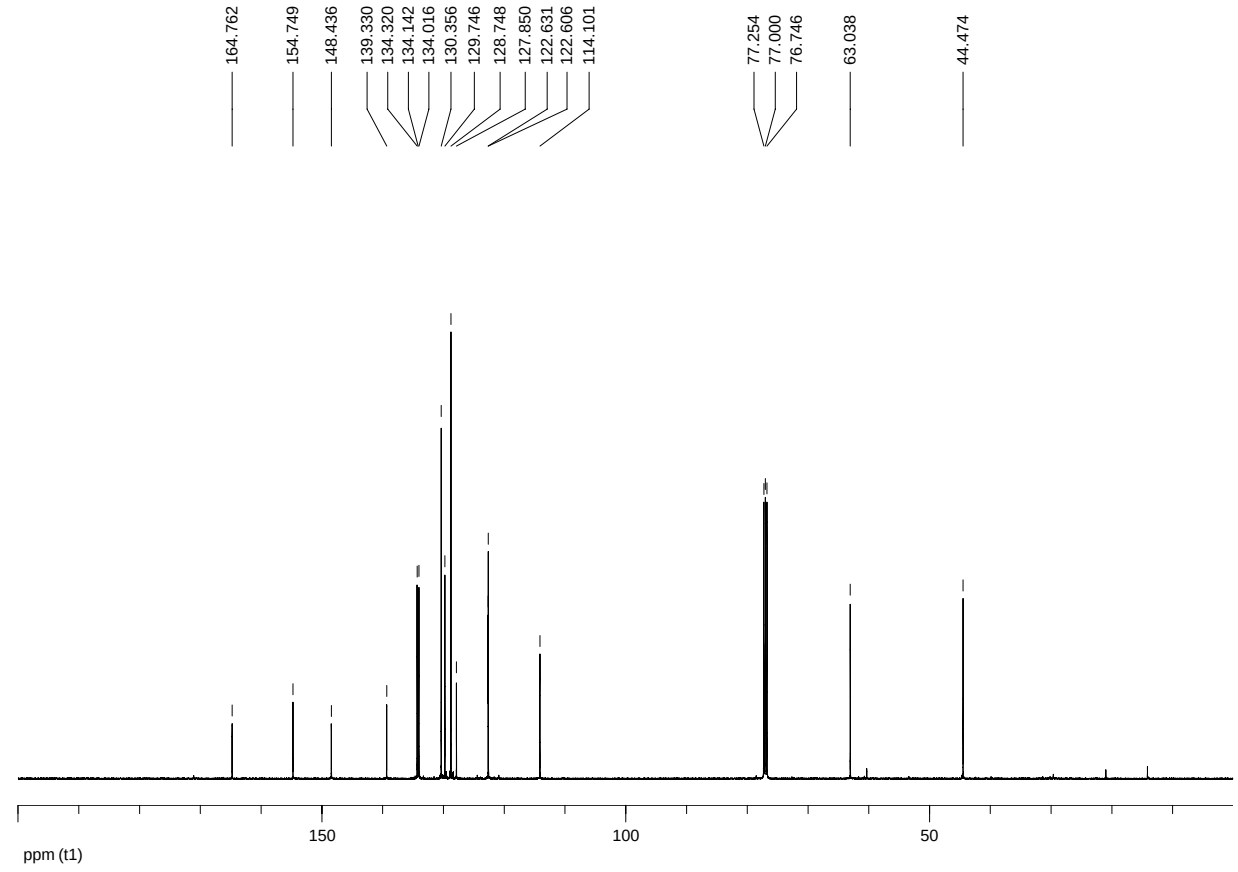


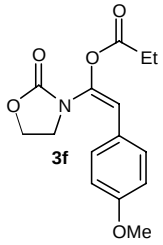




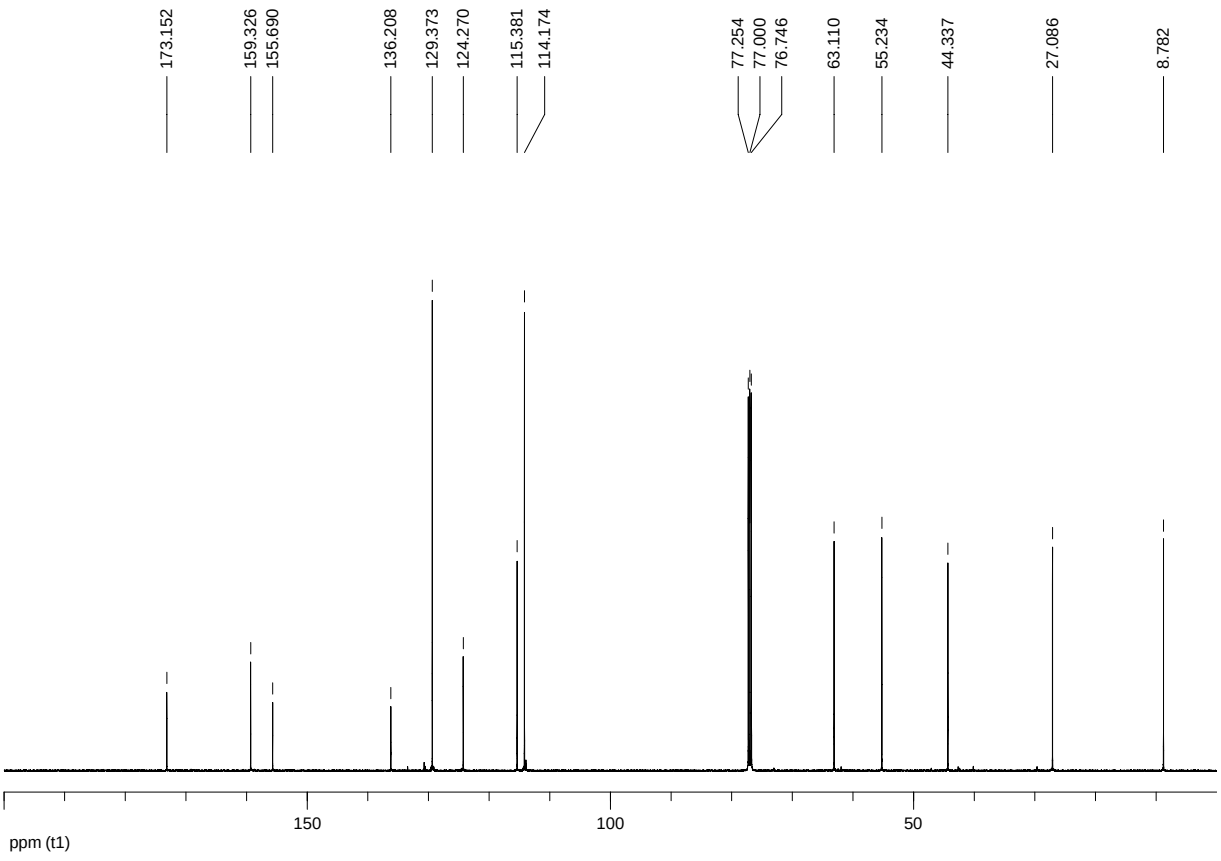


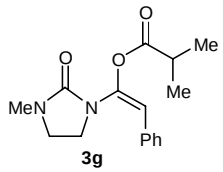

O
O
Ph
O
N
3e
NO2
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


164.762
154.749
148.436
139.330
134.320
134.142
134.016
130.356
129.746
128.748
127.850
122.631
122.606
114.101
77.254
77.000
76.746
63.038
44.474
150
100
50
ppm (t1)

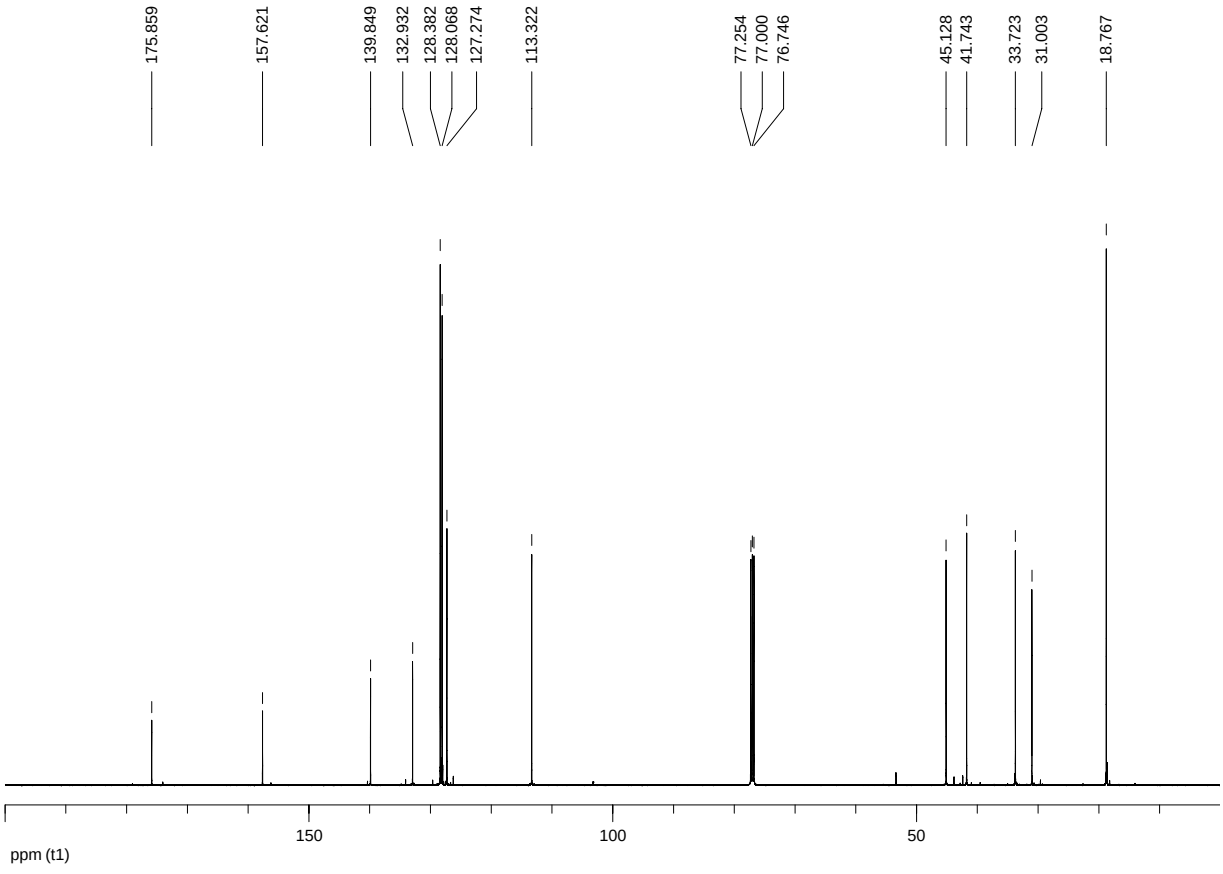


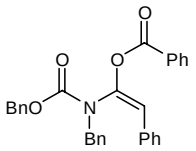
3f



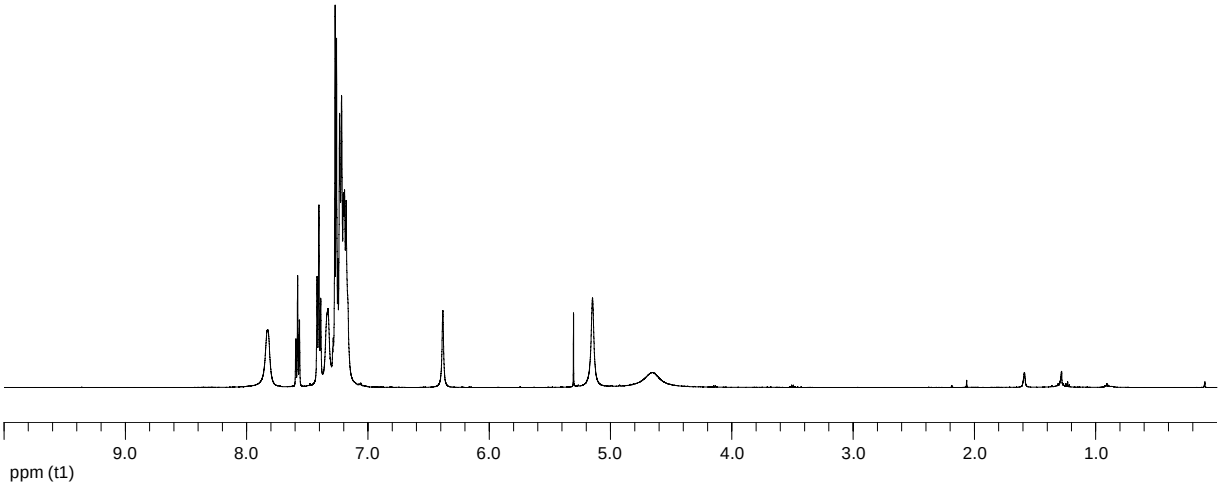


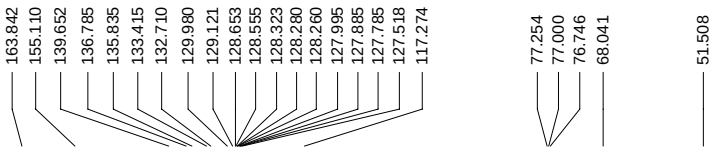
3g

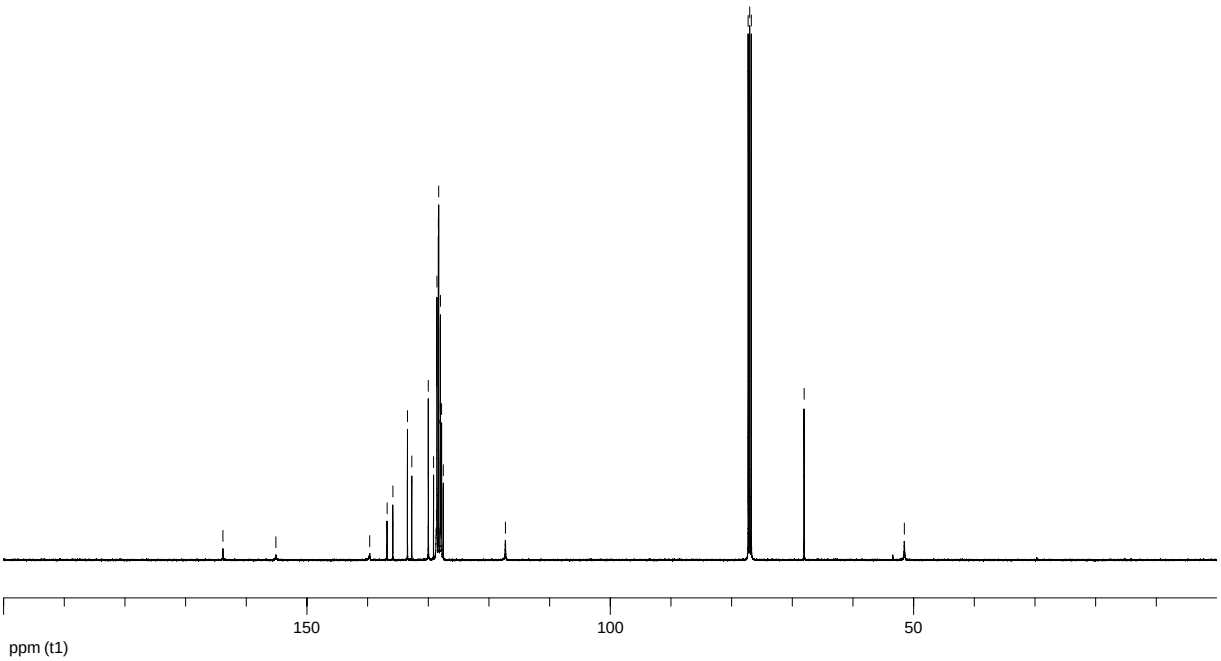


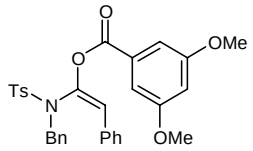


3h

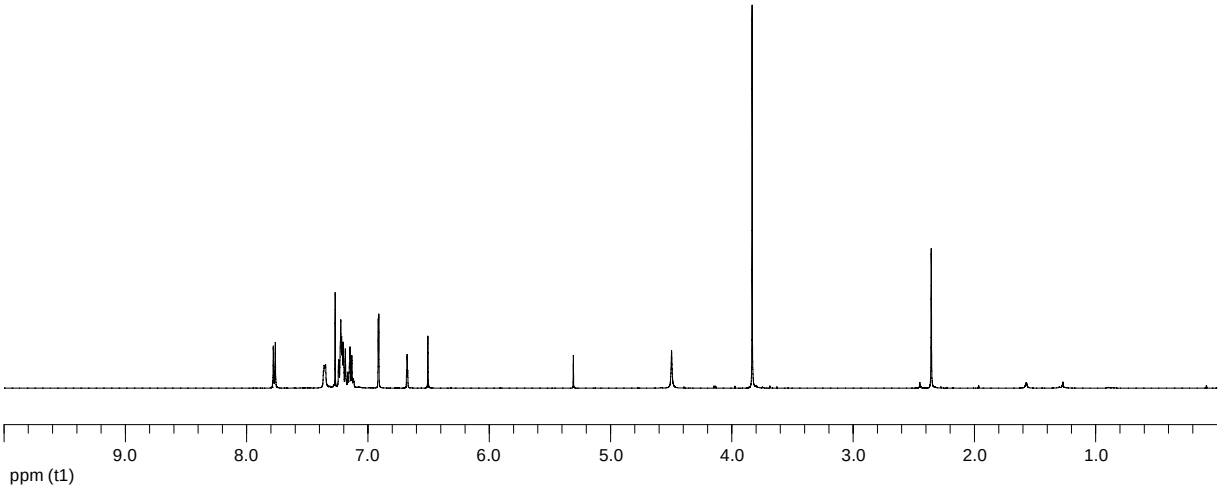


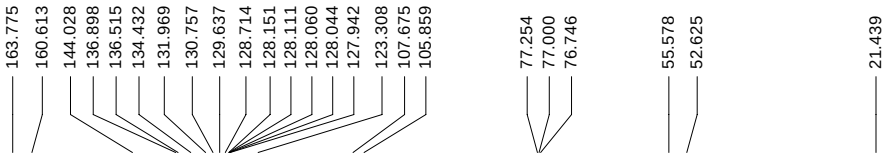


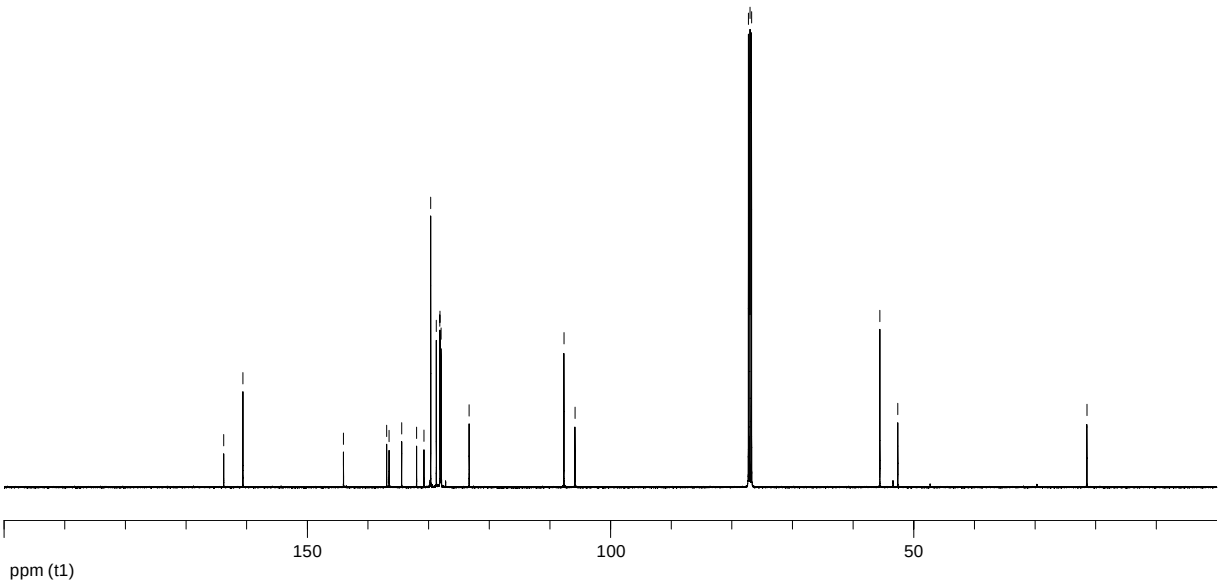


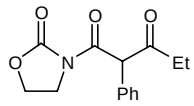


3i

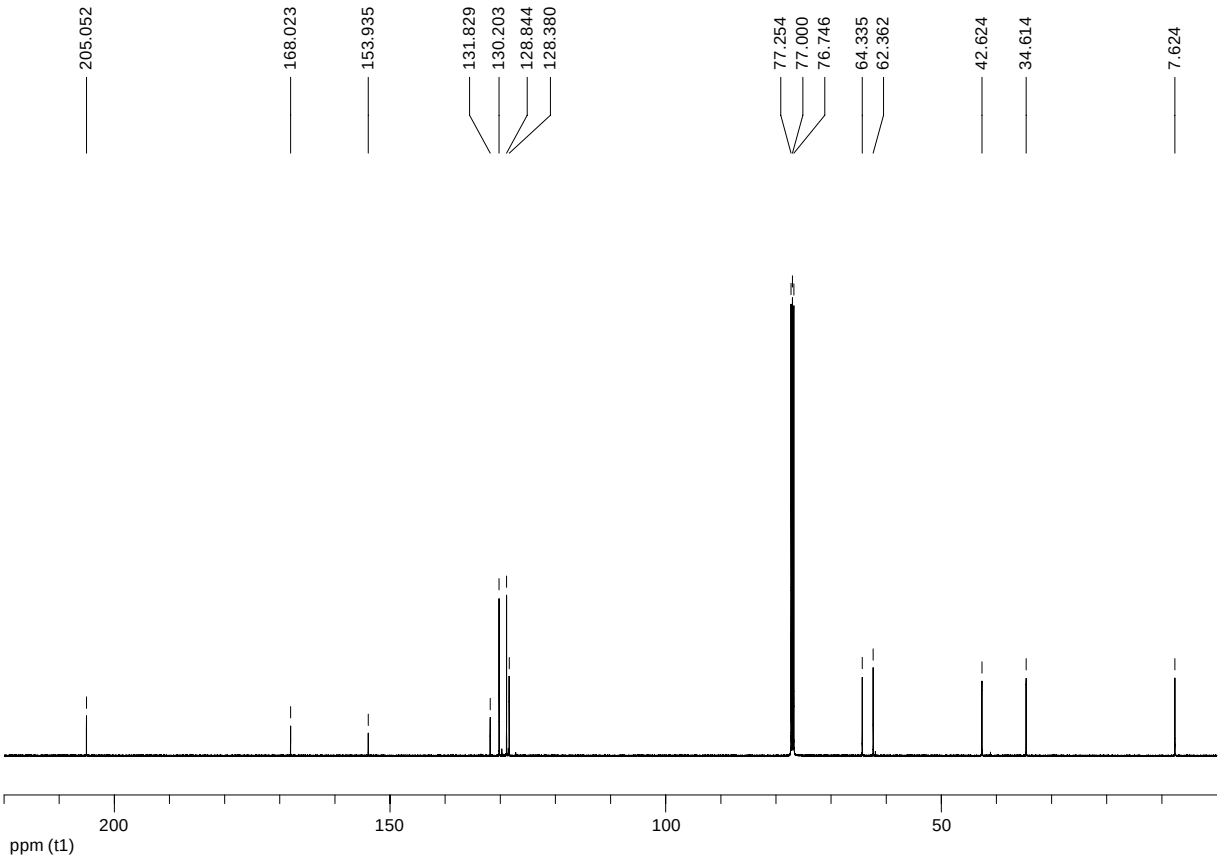


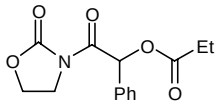






4





6