Electronic Supplementary Material (ESI) for ChemComm.

SUPPORTING INFORMATION

Electrochemical Alkene Azidocyanation *via* 1,4-Nitrile Migration

Alex C. Seastram,[a] Mishra Deepak Hareram,[a] Thomas M. B. Knight,[a] and Louis C. Morrill*[a]

*E-mail: MorrillLC@cardiff.ac.uk

[a] *Cardiff Catalysis Institute, School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff, CF10 3AT, UK.*

Table of Contents

1. General Information 2
2. Experimental and Characterisation Data 4
    2.1 General Procedures – Substrate Synthesis 4
    2.2 Characterisation of Substrate Precursors 8
    2.3 Characterisation of Substrates 59
    2.4 General Procedure 6 – Electrochemical Alkene Azidocyanation 101
    2.5 Characterisation of Products 101
    2.6 Alternative Transformations 148
    2.7 Product Derivatisation 154
3. Optimisation Studies 159
    3.1 Optimisation 159
4. Mechanistic Studies 164
    4.1 Cyclic Voltammetry Studies 164
    4.2 Mechanistic Experiments 165
5. References 170

1. General Information

Unless otherwise stated, all non-electrochemical reactions were conducted in flame-dried glassware under an atmosphere of dry nitrogen, sealed with septum seals and were stirred with Teflon-coated magnetic stirrer bars. Unless stated otherwise, all electrochemical reactions were performed using oven-dried ElectraSyn vials under an atmosphere of dry nitrogen, sealed with an ElectraSyn Teflon cap fitted with a graphite anode and platinum foil cathode and were stirred with Teflon-coated magnetic stirrer bars. Dry acetonitrile (MeCN), dichloromethane (CH_2Cl_2), and tetrahydrofuran (THF) were obtained after passing these previously degassed solvents through activated alumina columns (Mbraun, SPS-800). Tetra-*n*-butylammonium hexafluorophosphate ($TBAPF_6$) and tetra-*n*-butylammonium tetrafluoroborate ($TBABF_4$) were recrystallised from ethanol or water, respectively, and dried in the oven before use. All other solvents and commercial reagents were used as supplied without further purification unless stated otherwise.

All electrochemical reactions were conducted using an ElectraSyn 2.0 apparatus, purchased from IKA. Graphite, reticulated vitreous carbon (RVC), and platinum foil electrodes were purchased from IKA and are of uniform dimensions. Graphite electrodes were cut from a sheet of carbon foil (2 mm thickness) purchased from Goodfellow. The electrodes were cut to the dimension of 8 mm × 52 mm using a Startrite Bandsaw (model 18-T-5), with a Starrett Durate SFB High Carbon Steel Blade, 2870 mm × 10 mm × 0.65 mm, 3 mm pitch, regular tooth. Graphite electrodes could be used several times by renewing the top surface of the graphite, this was achieved by scraping away the top layer with a razor blade, sonicating in MeCN for 5 minutes, followed by oven-drying for 30 mins. Platinum electrodes were cut from a sheet of platinum foil (0.05 mm thickness) purchased from Goodfellow using scissors. Platinum electrodes were washed with water and acetone, then burned over a Bunsen burner before every reaction.

Cyclic voltammetry (CV) experiments were conducted using an Autolab PGSTAT204, controlled using Nova 2.1 software. The working electrode was a glassy carbon disc (3 mm dia., BASi part number MF-2012), the counter electrode was a Pt-wire (BASi part number MW-4130) and a Ag/$AgNO_3$ reference electrode was used (BASi part number MF-2052).

Room temperature (rt) refers to 20-25 °C. Ice/water and CO_2(s)/acetone baths were used to obtain temperatures of 0 °C and -78 °C respectively. All reactions involving heating were conducted using DrySyn blocks and a contact thermometer.

Analytical thin layer chromatography was carried out using aluminium plates coated with silica (Kieselgel 60 F_{254} silica) and visualisation was achieved using ultraviolet light (254 nm), followed by staining with a 1% aqueous $KMnO_4$ solution. Flash column chromatography was performed using Kieselgel 60 silica in the solvent system stated.

Melting points were recorded on a Gallenkamp melting point apparatus and are reported corrected by linear calibration to benzophenone (47 - 49 °C) and benzoic acid (121 - 123 °C).

Infrared spectra were recorded on a Shimadzu IRAffinity-1 Fourier Transform ATR spectrometer as thin films using a Pike MIRacle ATR accessory. Characteristic peaks are quoted (ν_{max} / cm^{-1}).

^{1}H, ^{13}C and ^{19}F NMR spectra were obtained on a Bruker Avance 300 (300 MHz ^{1}H, 75 MHz ^{13}C), Bruker Avance 400 (400 MHz ^{1}H, 101 MHz ^{13}C, 376 MHz ^{19}F) or a Bruker Avance 500 (500 MHz ^{1}H, 126 MHz ^{13}C) spectrometer at rt unless otherwise stated and in the solvent stated. Chemical shifts are reported in parts per million (ppm) relative to the residual solvent signal. All coupling constants, J, are quoted in Hz. Multiplicities are reported with the following symbols: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, app = apparent and combinations of these were used to denote higher order multiplicities.

High resolution mass spectrometry (HRMS, *m/z*) data was acquired at Cardiff University on a Micromass LCT Spectrometer.

“Petrol” refers to the fraction boiling in the range of 40-60 °C unless otherwise stated.

Current density values for the anode, j_{anode}, were calculated by dividing the current, i, passed during electrolysis by the exposed active surface area of the electrode. The exposed active surface of the electrode was calculated to be the submerged surface of the electrode that was directly facing the other electrode, since electrons travel through the shortest available circuit (See Figure S1). See electrochemical General Procedure for specific current density values.

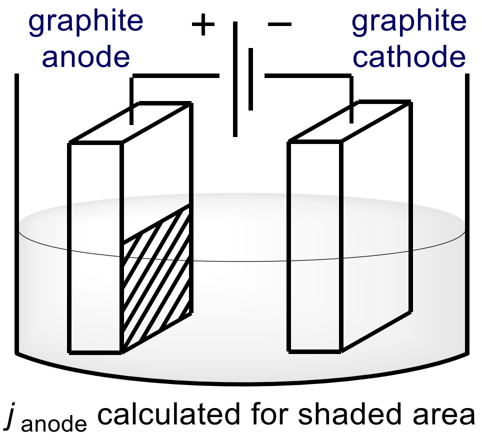
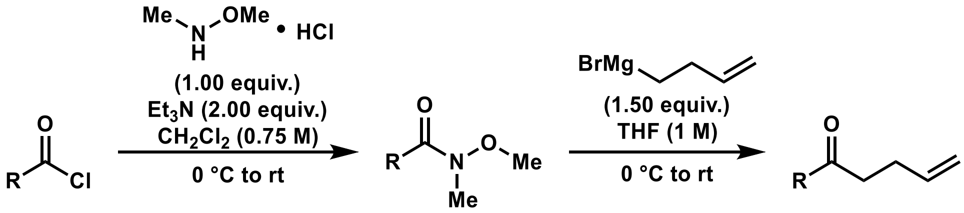


Figure S1 – Current density calculation visual aid

2. Experimental and Characterisation Data

2.1 General Procedures – Substrate Synthesis

2.1.1 General Procedure 1: Synthesis of Ketones from Acid Chlorides



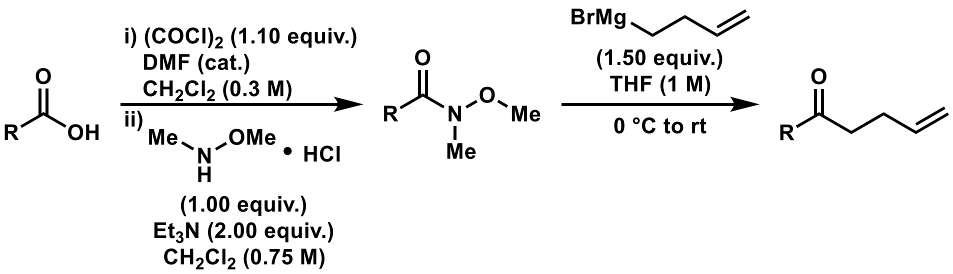
Synthesis of Aryl Weinreb Amide

To a flame-dried RBF fitted with a septum seal was added *N*,*O*-dimethylhydroxylamine hydrochloride (1.00 equiv.) in anhydrous CH_2Cl_2 (0.75 M). The solution was cooled to 0 °C and the appropriate acid chloride (1.00 equiv.) was added dropwise followed by dropwise addition of triethylamine (2.00 equiv.). The reaction suspension was stirred at rt for 30 min before being quenched with a saturated solution of $NaHCO_3$ (aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (× 3). The combined organics were washed with water, then brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude Weinreb amide that was used without further purification.

Formation of Aryl Ketone

To a three-neck RBF fitted with a condenser, stopper, and septum seal was added magnesium (1.65 equiv.) and the system was flame-dried. After cooling, a crystal of iodine was added before the system was subjected to vacuum-nitrogen exchange cycles (× 3). Anhydrous THF (1 M with respect to 4-bromobut-1-ene) was added, followed by the dropwise addition of 4-bromobut-1-ene (1.50 equiv.). After complete addition, the mixture was stirred for 5 min at rt or until the exotherm has ceased, before being heated to reflux for 2-3 h. The reaction was allowed to cool to rt, then further cooled to 0 °C. A solution of Weinreb amide (1.00 equiv.) in anhydrous THF (2 M) was added slowly and the reaction was stirred overnight at rt before being quenched with a saturated solution of NH_4Cl (aq.), and a few drops of 1 M HCl (aq.). EtOAc was added, the layers were separated, and the aqueous layer was further extracted with EtOAc (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography to afford the desired compound.

2.1.2 General Procedure 2 – Synthesis of Ketones from Carboxylic Acids



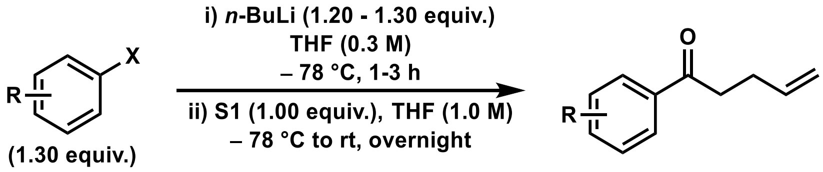
Synthesis of Weinreb Amide

To a flame-dried RBF fitted with a septum seal was added the appropriate carboxylic acid (1.00 equiv.) in CH_2Cl_2 (0.3 M). The solution was cooled to 0 °C before oxalyl chloride (1.10 equiv.) was added dropwise followed by the addition of DMF (cat.). The reaction was then allowed to warm to rt and stirred until gas evolution ceased. *N*,*O*-Dimethylhydroxylamine hydrochloride (1.00 equiv.) was added followed by dropwise addition of triethylamine (3.00 equiv.). The reaction suspension was stirred at rt for 30 min before being quenched with a saturated solution of $NaHCO_3$ (aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (× 3). The combined organics were washed with water, then brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude Weinreb amide that was used without further purification.

Formation of Aryl Ketone

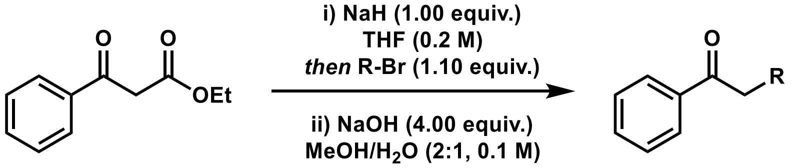
To a three-neck RBF fitted with a condenser, stopper, and septum seal was added magnesium (1.65 equiv.) and the system was flame-dried. After cooling, a crystal of iodine was added before the system was subjected to vacuum-nitrogen exchange cycles (× 3). Anhydrous THF (1 M with respect to 4-bromobut-1-ene) was added, followed by the dropwise addition of 4-bromobut-1-ene (1.50 equiv.). After complete addition, the mixture was stirred for 5 min at rt or until the exotherm has ceased, before being heated to reflux for 2-3 h. The reaction was allowed to cool to rt, then further cooled to 0 °C. A solution of Weinreb amide (1.00 equiv.) in anhydrous THF (2 M) was added slowly and the reaction was stirred overnight at rt before being quenched with a saturated solution of NH_4Cl (aq.) and a few drops of 1 M HCl (aq.). EtOAc was added, the layers were separated, and the aqueous layer was further extracted with EtOAc (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography to afford the desired compound.

2.1.3 General Procedure 3 – Synthesis of Ketones from Aryl Halides



To a flame-dried RBF fitted with a septum seal was added a solution of alkyl or aryl halide (1.20 – 1.30 equiv.) in anhydrous THF (0.3 M). The mixture was cooled to -78 °C, and a solution of *n*-BuLi in hexanes (1.20 – 1.30 equiv.) was added dropwise. The reaction mixture was left to stir for 1-3 h before a solution of **S1** (1.00 equiv.) in anhydrous THF (1.0 M) was added dropwise. The solution was left to stir for 1-3 h whilst warming to rt. A saturated solution of NH_4Cl (aq.) was added dropwise, followed by EtOAc, and the layers were separated. The aqueous layer was further extracted with EtOAc (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography to afford the desired compound.

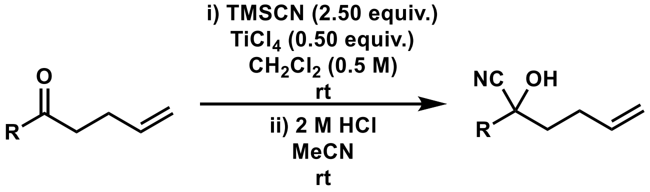
2.1.4 General Procedure 4 – Synthesis of α-Substituted Ketones from β-Ketoesters



Following a literature procedure,[1] to a flame dried RBF was added ethylbenzoyl acetate (1.00 equiv.) in THF (0.2 M). Sodium hydride (60% dispersion in mineral oil, 1.00 equiv.) was added portion-wise, and the reaction was stirred at rt for 1 h. The appropriate allylic bromide (1.10 equiv.) was added, and the reaction was heated at 40 °C overnight. After cooling to rt, the suspension was diluted with Et_2O, followed by water. The layers were separated, and the aqueous layer was further extracted with Et_2O (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product that was used in the next step without further purification.

To a RBF was added the crude product (1.00 equiv.) in 2:1 MeOH/water (0.1 M), and NaOH (4.00 equiv.) was added. The reaction was heated to reflux for 20 h, before being cooled to rt and concentrated under reduced pressure. EtOAc was added, the layers were separated, and the aqueous layer was further extracted with EtOAc (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography to afford the desired compound.

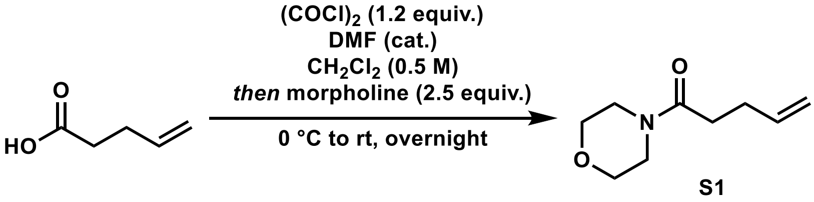
2.1.5 General Procedure 5 – Synthesis of Cyanohydrins from Ketones



To a flame-dried RBF fitted with a septum seal was added the appropriate ketone (1.00 equiv.) in anhydrous CH_2Cl_2 (0.5 M). Trimethylsilyl cyanide (2.50 equiv.) was added slowly, followed by titanium (IV) tetrachloride (0.50 equiv.) and the reaction mixture was stirred at rt overnight. The reaction mixture was concentrated under reduced pressure and the resulting residue was dissolved in MeCN (0.2 M), before an identical volume of 2 M HCl (aq.) was added. The resulting biphasic mixture was stirred at rt for 1 h, before being diluted with water. The layers were separated, and the aqueous layer was extracted with EtOAc (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the cyanohydrins that were used without further purification.

2.2 Characterisation of Substrate Precursors

1-Morpholinopent-4-en-1-one (S1)

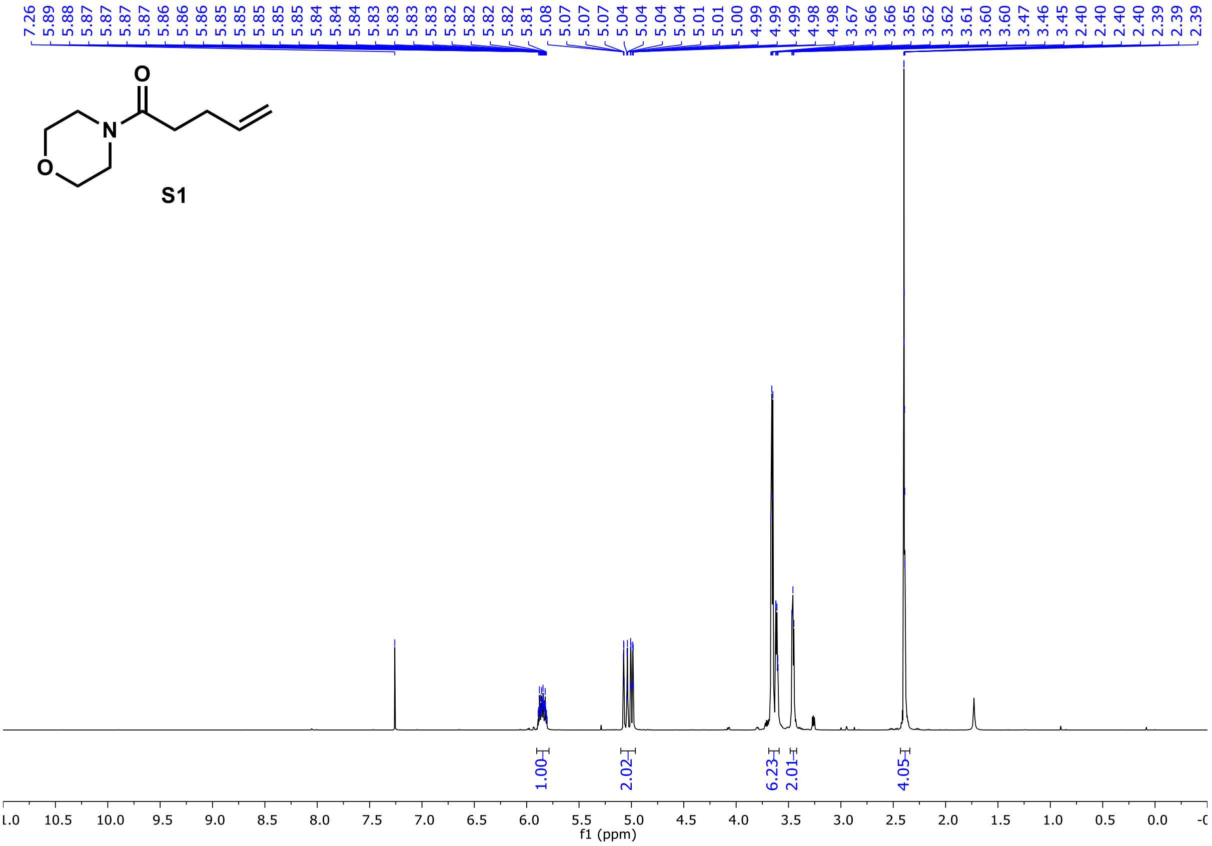


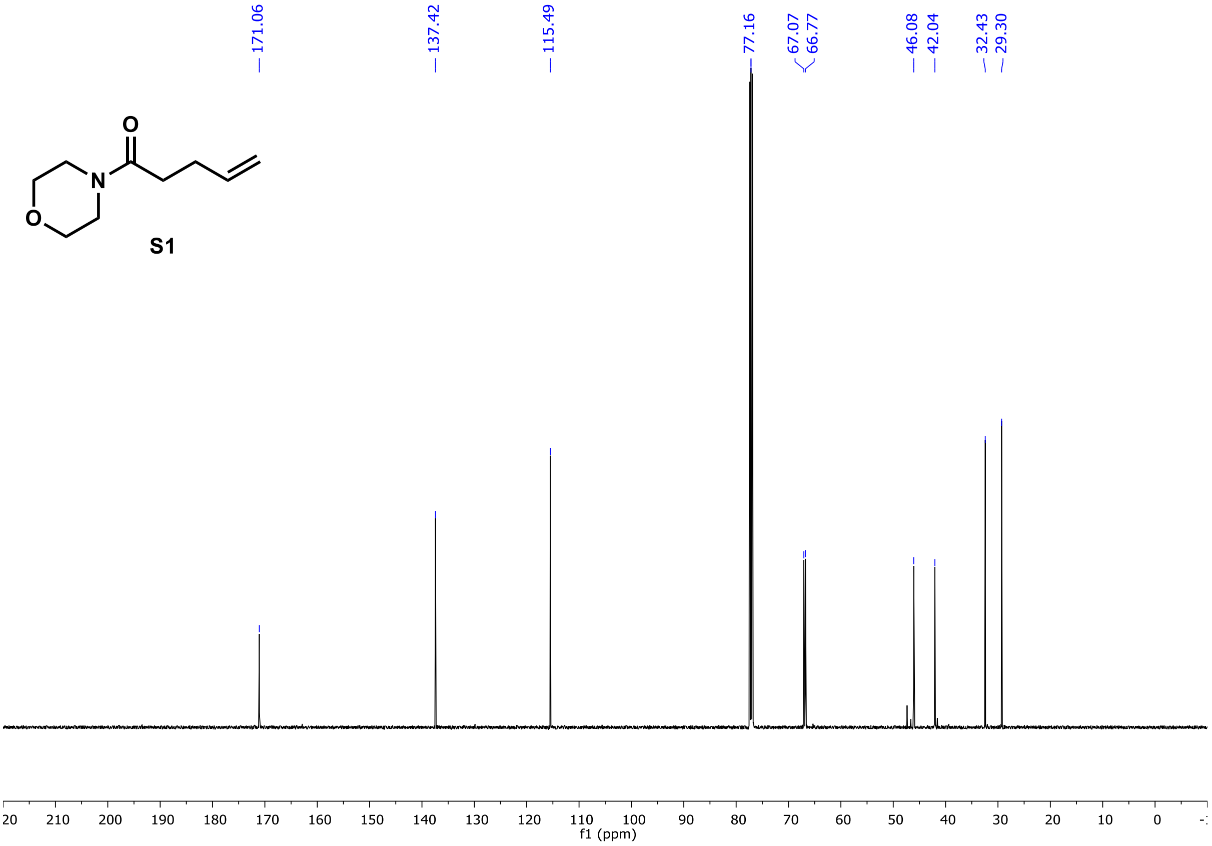
To a flame-dried RBF was added 4-pentenoic acid (10.2 mL, 100 mmol) in anhydrous CH_2Cl_2 (200 mL, 0.5 M). The solution was cooled to 0 °C, and oxalyl chloride (8.90 mL, 105 mmol) was added dropwise, followed by the addition of DMF (3 drops). The reaction was warmed to rt and stirred until gas evolution ceased, at which point morpholine (21.9 mL, 250 mmol) was added. The reaction was stirred at rt overnight before being quenched with 2 M HCl (aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (× 3). The combined organics were then washed with 2 M HCl (aq.) then brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford **S1** (14.3 g, 85%) as a yellow oil that was used without any further purification.

R_f = 0.18 (25% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.37 – 2.42 (4H, m), 3.44 – 3.47 (2H, m), 3.60 – 3.68 (6H, m), 4.98 – 5.08 (2H, m), 5.80 – 5.90 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 29.3, 32.4, 42.0, 46.1, 66.8, 67.1, 115.5, 137.4, 171.1.

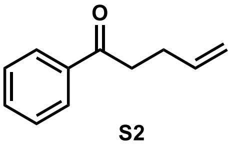
These data are in accordance with the literature.[2]

^{1}H and ^{13}C NMR spectra of **S1**





1-Phenylpent-4-en-1-one (S2)

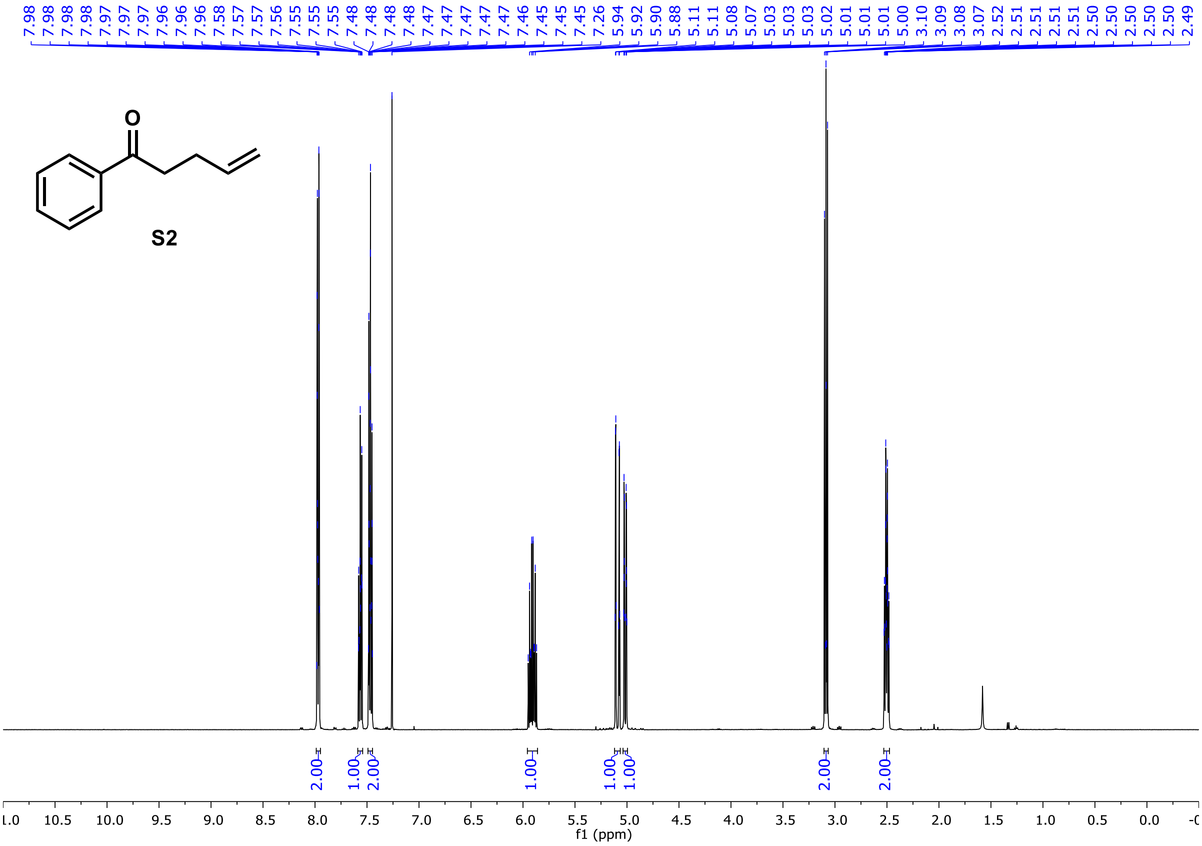


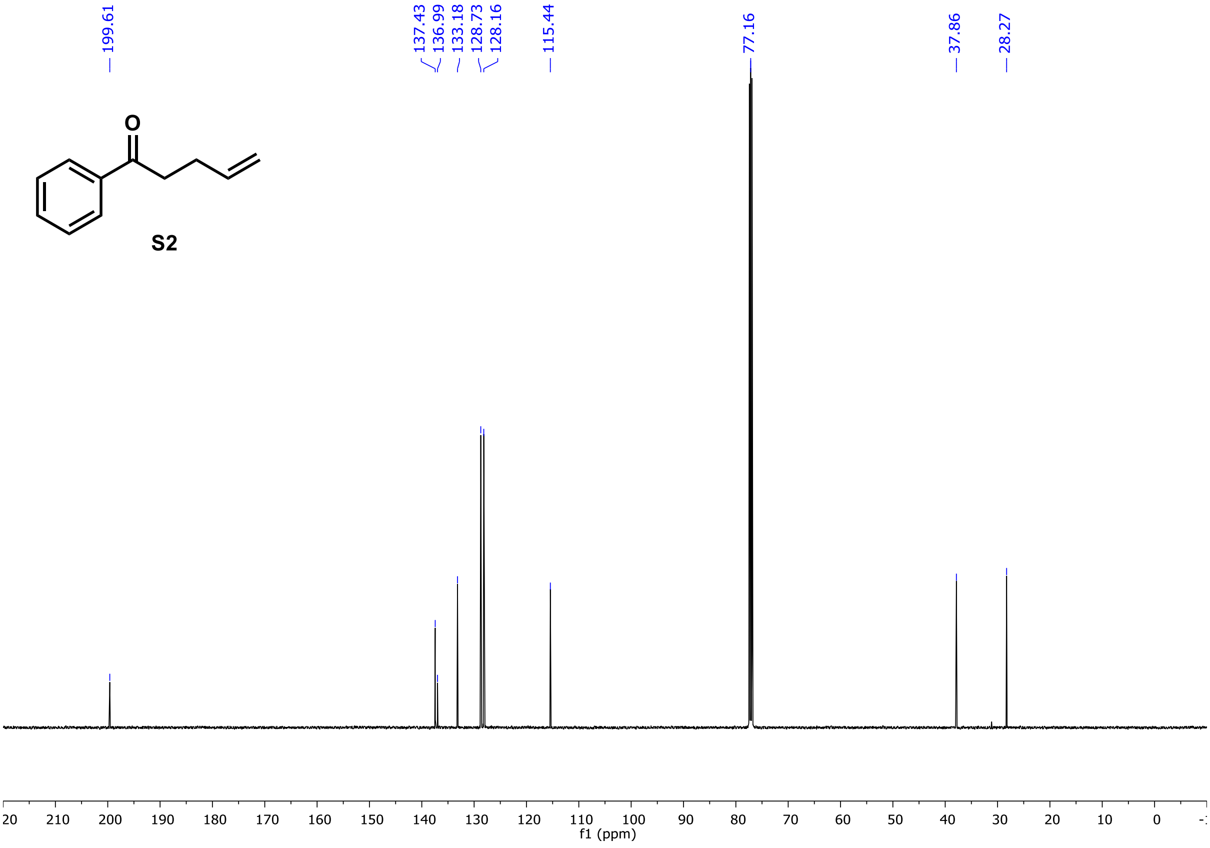
S2

Prepared according to General Procedure 1 using *N*,*O*-dimethylhydroxylamine hydrochloride (4.88 g, 50.0 mmol) in CH_2Cl_2 (67 mL), benzoyl chloride (5.80 mL, 50.0 mmol), and triethylamine (14.0 mL, 100 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (2.00 g, 82.5 mmol) in THF (75 mL), and 4-bromobut-1-ene (7.60 mL, 75.0 mmol). The aryl ketone was prepared through the addition of the Weinreb amide in THF (25 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S2** (6.36 g, 79%) as a colourless oil.

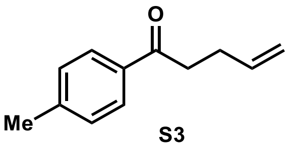
R_f = 0.38 (5% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3080, 2918, 1684, 1597, 1448, 1205, 912, 743, 689; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.48 – 2.52 (2H, m), 3.07 – 3.10 (2H, m), 5.00 – 5.03 (1H, m), 5.07 – 5.12 (1H, m), 5.91 (1H, ddt, *J* 16.9, 10.2, 6.5), 7.45 – 7.49 (2H, m), 7.55 – 7.58 (1H, m), 7.96 – 7.98 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.3, 37.9, 115.4, 128.2, 128.7, 133.2, 137.0, 137.4, 199.6; **HRMS** (ES+) $C_{11}H_{12}O$ $[M+H]^+$ requires 160.0966, found 161.0970 (+ 2.5 ppm).

^{1}H and ^{13}C NMR spectra of **S2**





1-(*p*-Tolyl)pent-4-en-1-one (S3)



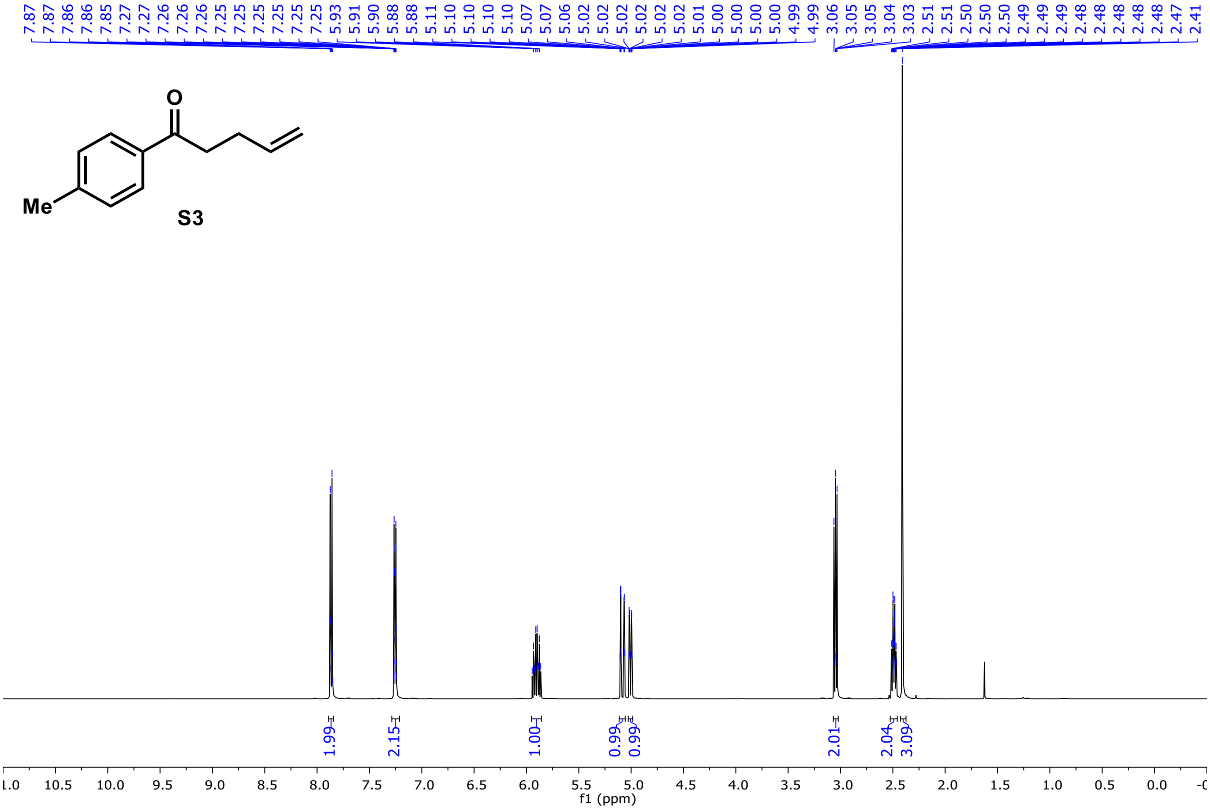
S3

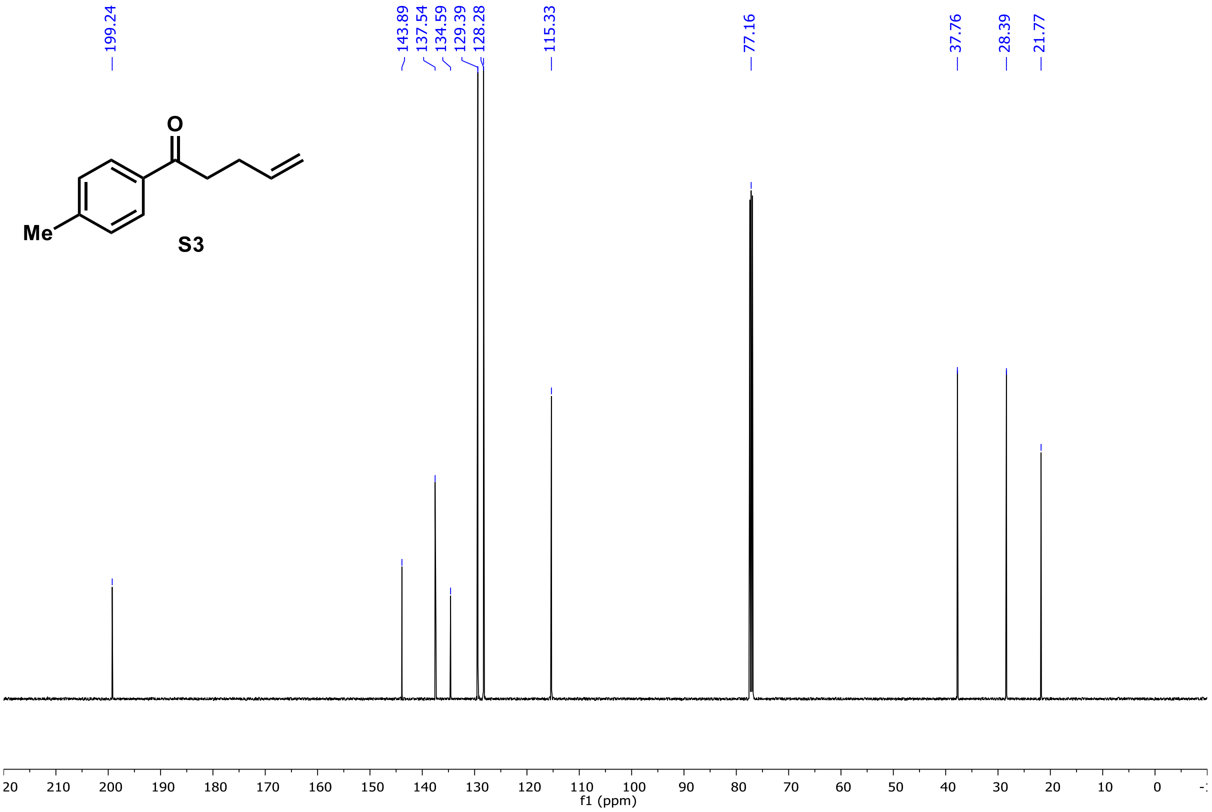
Prepared according to General Procedure 3 using **S1** (846 mg, 5.00 mmol), 4-bromotoluene (1.11 g, 6.50 mmol), and ^{n}BuLi (2.4 M in hexanes, 2.71 mL, 6.50 mmol) in THF (27 mL). The resultant crude material was purified by flash column chromatography (2.5% EtOAc/petrol, silica gel) to afford **S3** (394 mg, 45%) as a colourless oil.

R$_f$ = 0.57 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.41 (3H, s), 2.46 – 2.52 (2H, m), 3.03 – 3.07 (2H, m), 4.98 – 5.03 (1H, m), 5.06 – 5.11 (1H, m), 5.85 – 5.95 (1H, m). 7.24 – 7.27 (2H, m), 7.85 – 7.88 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 21.8, 28.4, 37.8, 115.3, 128.3, 129.4, 134.6, 137.5, 143.9, 199.2.

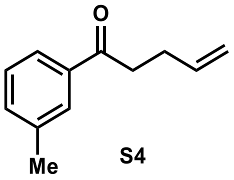
These data are in accordance with the literature.[3]

^{1}H and ^{13}C NMR spectra of **S3**





1-(*m*-Tolyl)pent-4-en-1-one (S4)



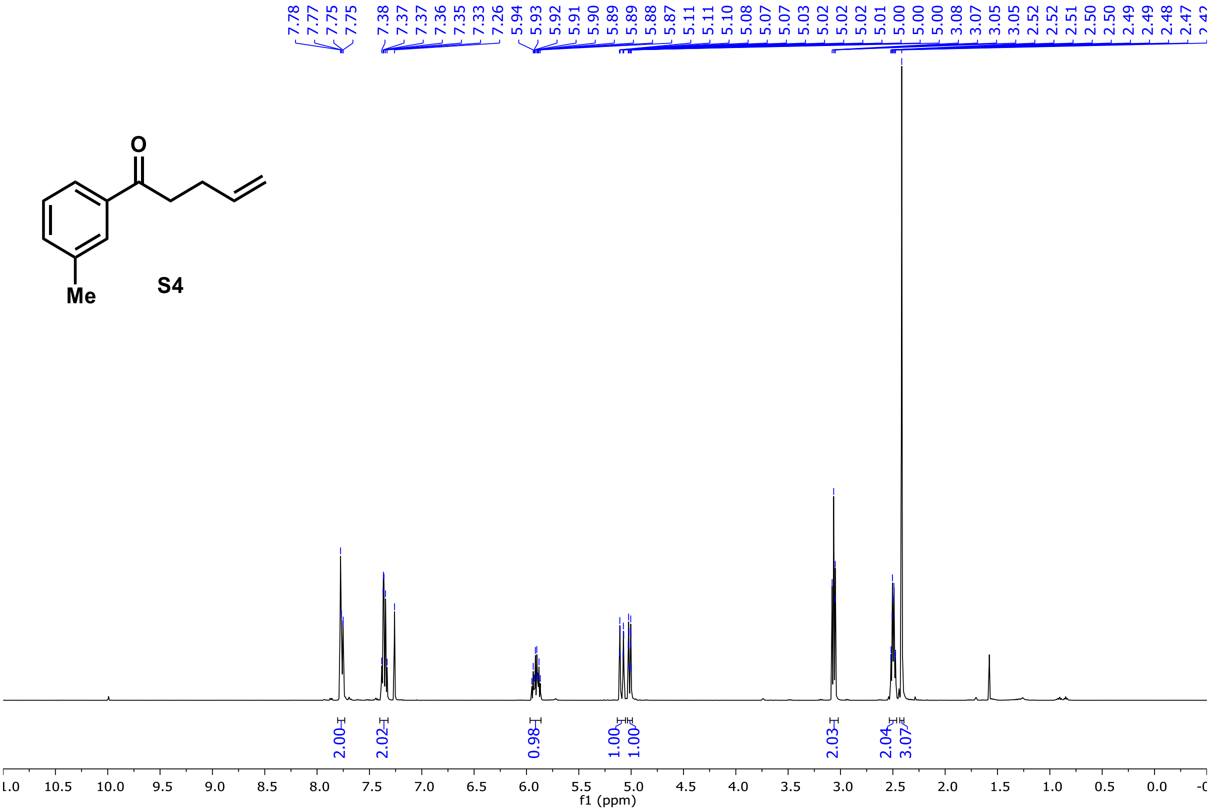
S4

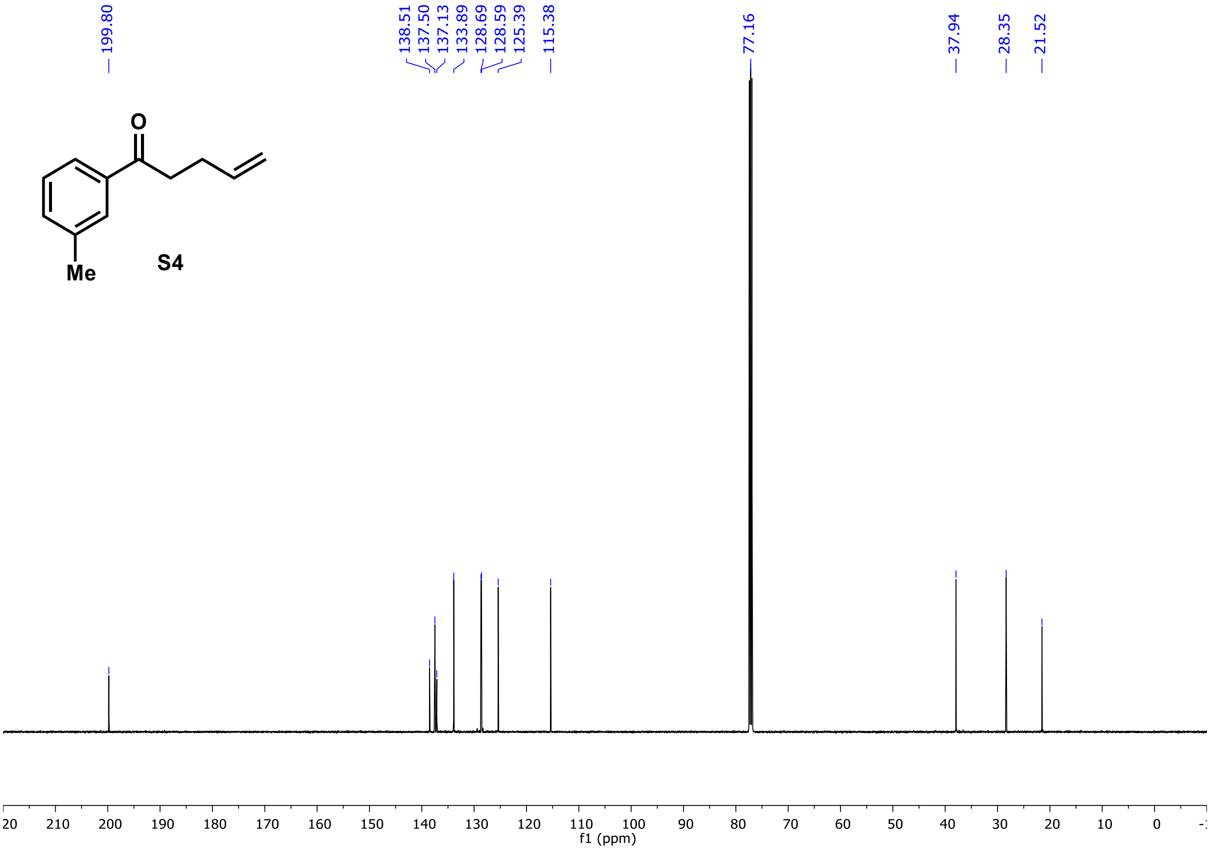
Prepared according to General Procedure 3 using **S1** (1.52 g, 9.00 mmol), 3-bromotoluene (1.42 mL, 11.7 mmol), and ^{n}BuLi (2.5 M in hexanes, 4.68 mL, 11.7 mmol) in THF (50 mL). The resultant crude material was purified by flash column chromatography (0-1% EtOAc/petrol, silica gel) to afford **S4** (1.26 g, 80%) as a colourless oil.

R_f = 0.38 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.42 (3H, s), 2.47 – 2.52 (2H, m), 3.05 – 3.08 (2H, m), 5.00 – 5.03 (1H, m), 5.07 – 5.11 (1H, m), 5.87 – 5.95 (1H, m), 7.33 – 7.38 (2H, m), 7.75 – 7.78 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 21.5, 28.4, 37.9, 115.4, 125.4, 128.6, 128.7, 133.9, 137.1, 137.5, 138.5, 199.8.

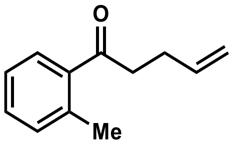
These data are in accordance with the literature.[4]

^{1}H and ^{13}C NMR spectra of **S4**





1-(*o*-Tolyl)pent-4-en-1-one (S5)



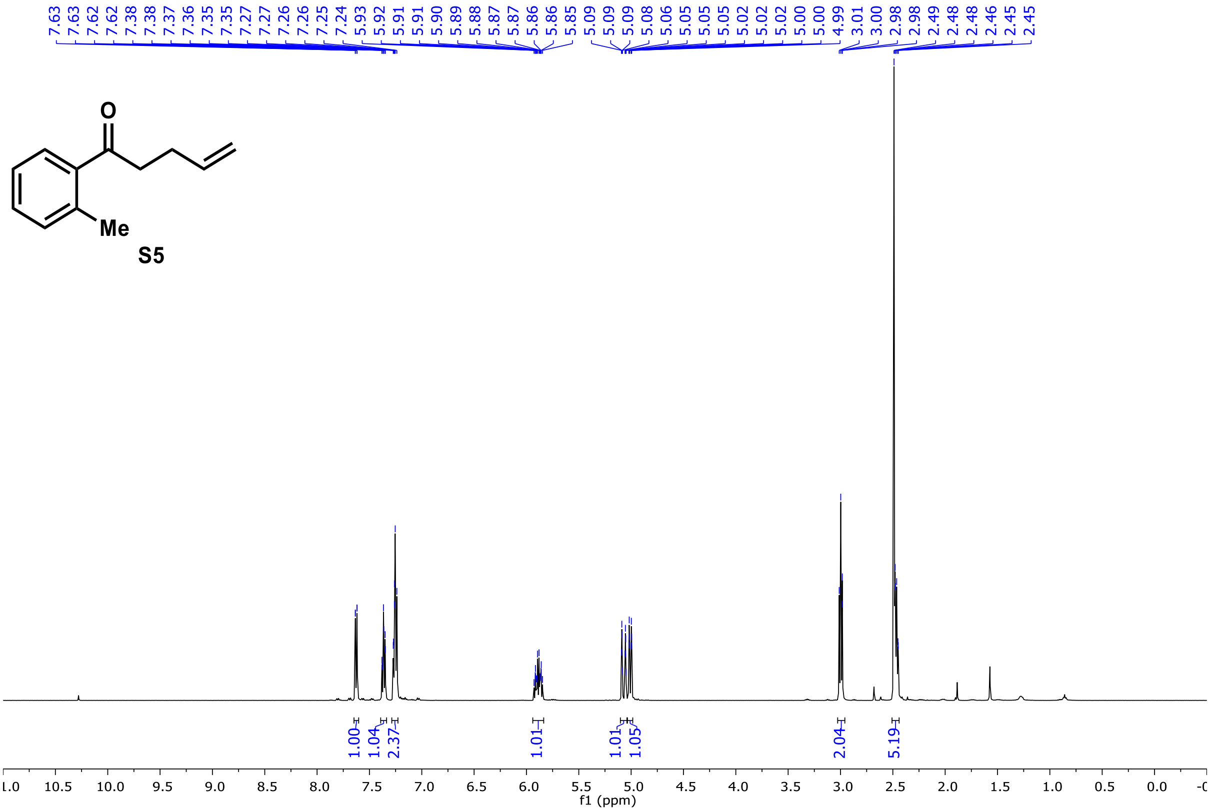
S5

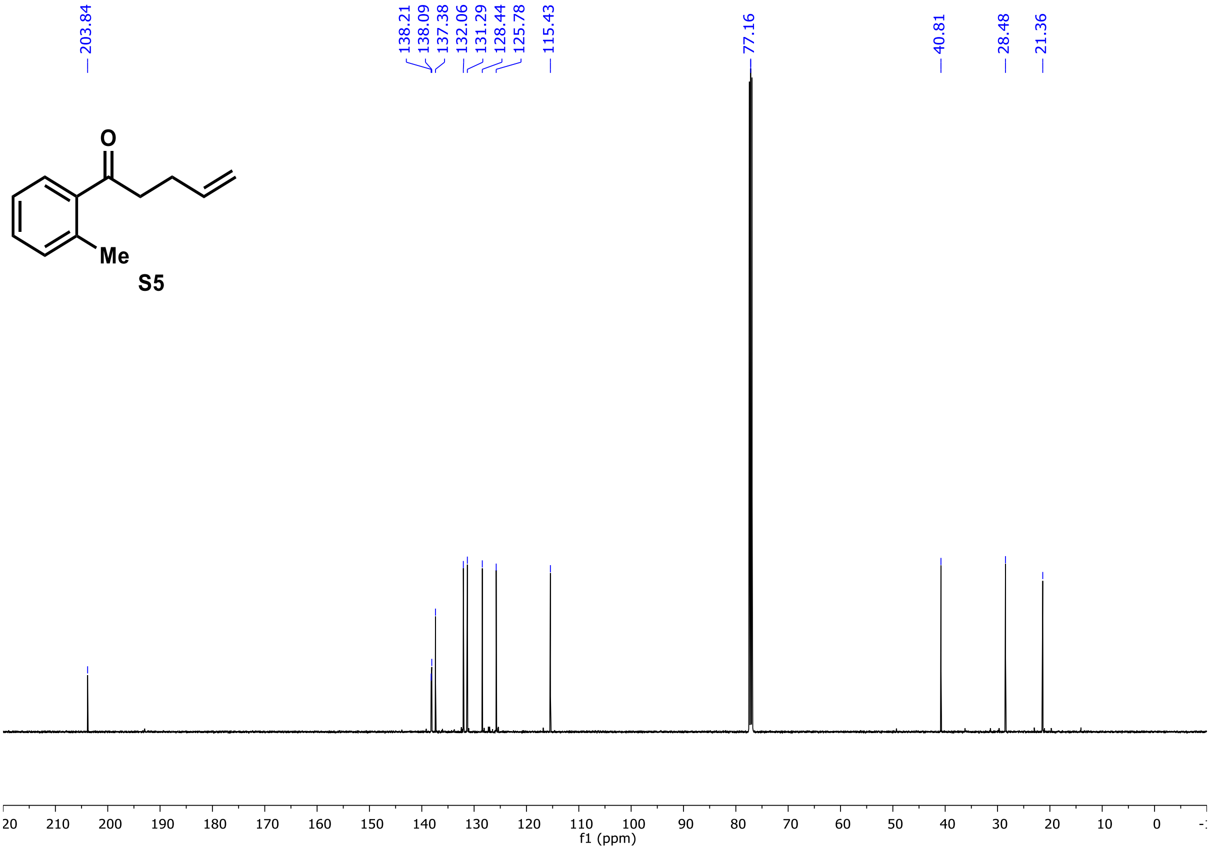
Prepared according to General Procedure 3 using **S1** (1.52 g, 9.00 mmol), 2-bromotoluene (1.41 mL, 11.7 mmol), and ^{n}BuLi (2.5 M in hexanes, 4.68 mL, 11.7 mmol) in THF (50 mL). The resultant crude material was purified by flash column chromatography (1% EtOAc/petrol, silica gel) to afford **S5** (622 mg, 40%) as a pale-yellow oil.

R$_f$ = 0.38 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.45 – 2.49 (5H, m), 2.98 – 3.01 (2H, m), 4.99 – 5.02 (1H, m), 5.05 – 5.09 (1H, m), 5.85 – 5.93 (1H, m), 7.24 – 7.27 (2H, m), 7.35 – 7.38 (1H, m), 7.62 – 7.63 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 21.4, 28.5, 40.8, 115.4, 125.8, 128.4, 131.3, 132.1, 137.4, 138.1, 138.2, 203.8.

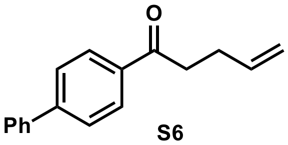
These data are in accordance with the literature.[5]

^{1}H and ^{13}C NMR spectra of **S5**





1-([1,1’-Biphenyl]-4-yl)pent-3-en-1-one (S6)

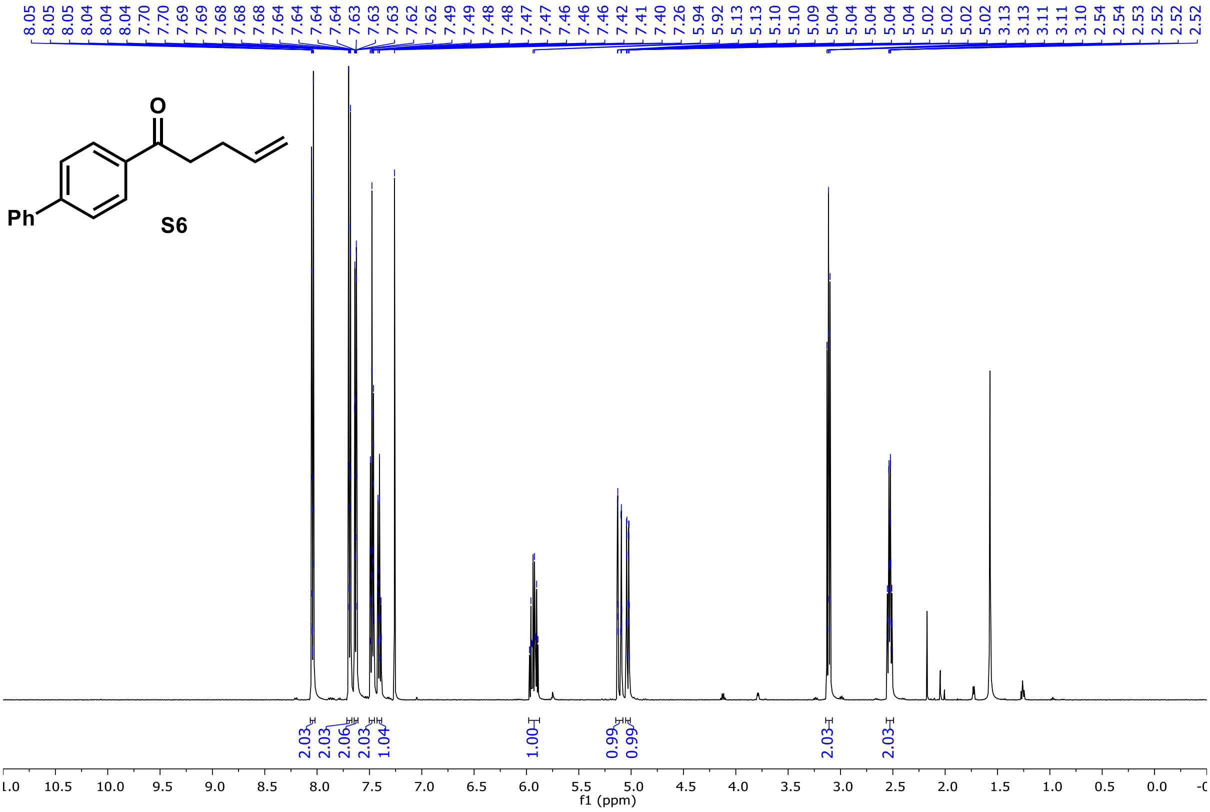


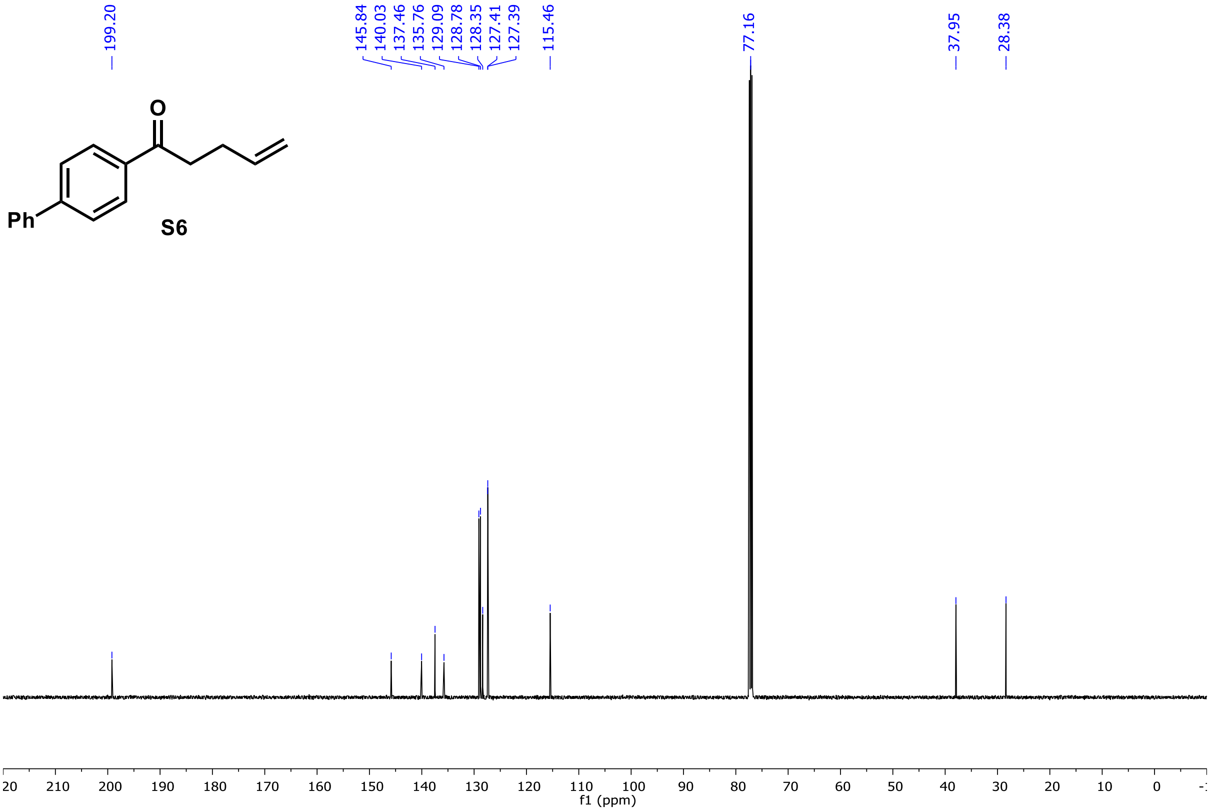
S6

Prepared according to General Procedure 3 using **S1** (1.692 g, 10.0 mmol), 4-bromo-1,1’-biphenyl (2.80 g, 12.0 mmol), and ^{n}BuLi (2.4 M in hexanes, 5.00 mL, 12.0 mmol) in THF (53 mL). The resultant crude material was purified by flash column chromatography (2.5% EtOAc/petrol, silica gel) to afford **S6** (1.58 g, 67%) as a white solid.

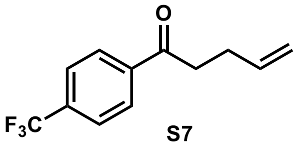
R$_f$ = 0.51 (5% EtOAc/petrol); **M.p.:** 81-83 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3038, 1676, 1601, 1199, 982, 903, 754, 687; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.50 – 2.56 (2H, m), 3.08 – 3.15 (2H, m), 5.00 – 5.05 (1H, m), 5.08 – 5.15 (1H, m), 5.89 – 5.99 (1H, m), 7.38 – 7.43 (1H, m), 7.45 – 7.50 (2H, m), 7.61 – 7.65 (2H, m), 7.67 – 7.71 (2H, m), 8.02 – 8.06 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 28.4, 38.0, 115.5, 127.39, 127.41, 128.4, 128.8, 129.1, 135.8, 137.5, 140.0, 145.8, 199.2; **HRMS** (CI+) $C_{17}H_{16}O$ [M+H]$^+$ requires 237.1274, found 237.1276 (+ 1.0 ppm).

^{1}H and ^{13}C NMR spectra of **S6**





1-(4-(Trifluoromethyl)phenyl)pent-4-en-1-one (S7)



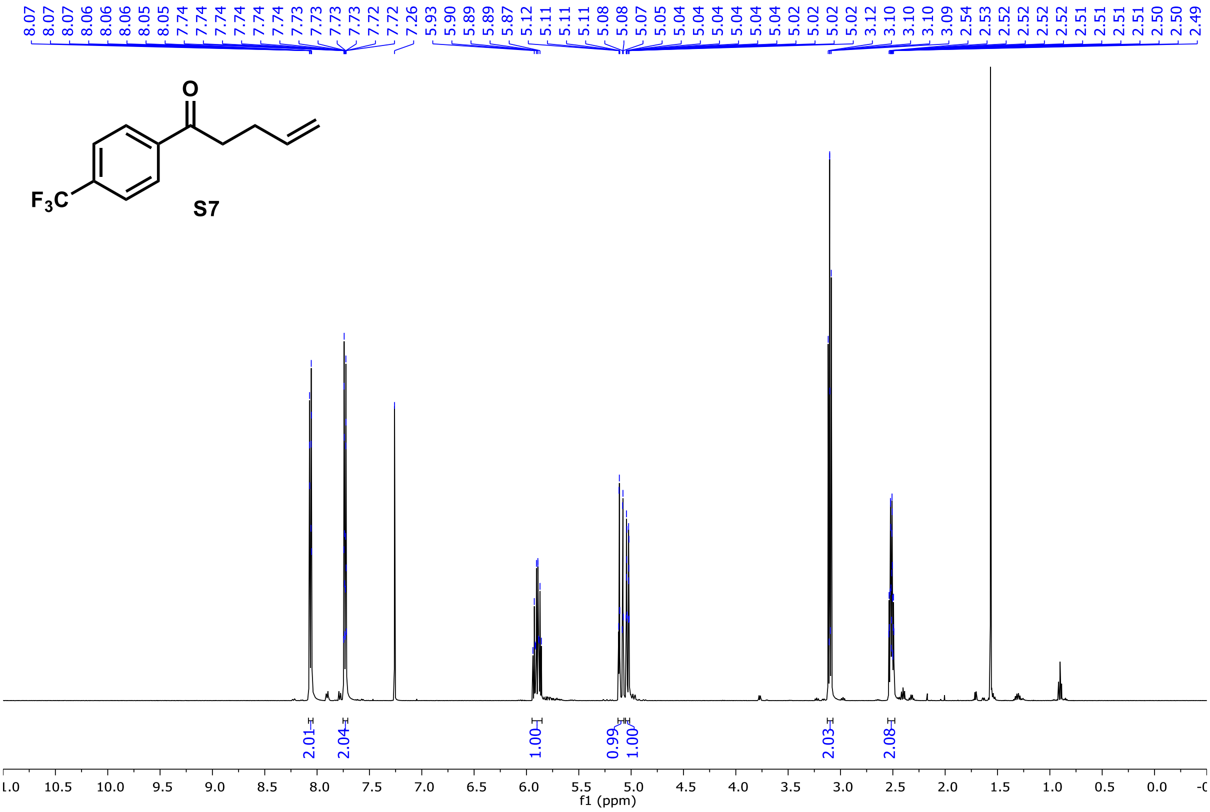
S7

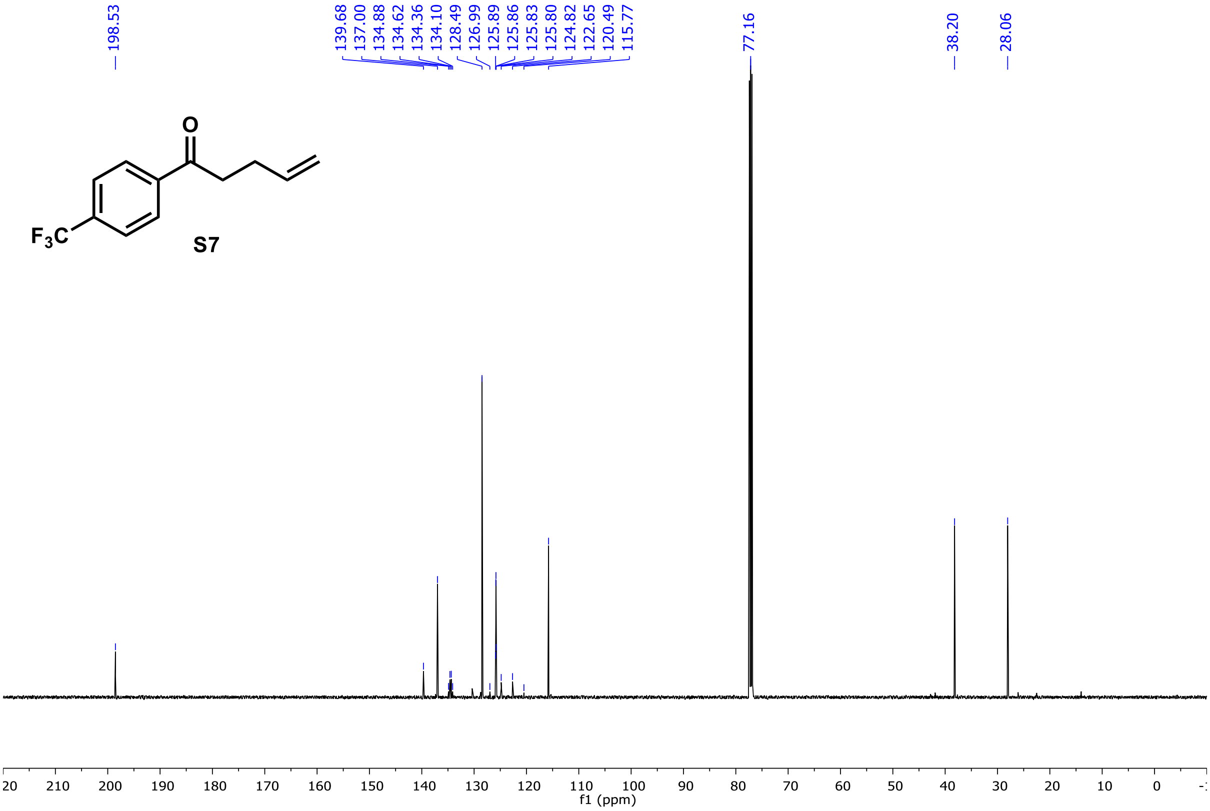
Prepared according to General Procedure 3 using **S1** (1.69 g, 10.0 mmol), 1-bromo-4-(trifluoromethyl)benzene (1.82 mL, 13.0 mmol), and ^{n}BuLi (2.4 M in hexanes, 5.40 mL, 13.0 mmol) in THF (54 mL). The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S7** (1.65 g, 72%) as a colourless oil.

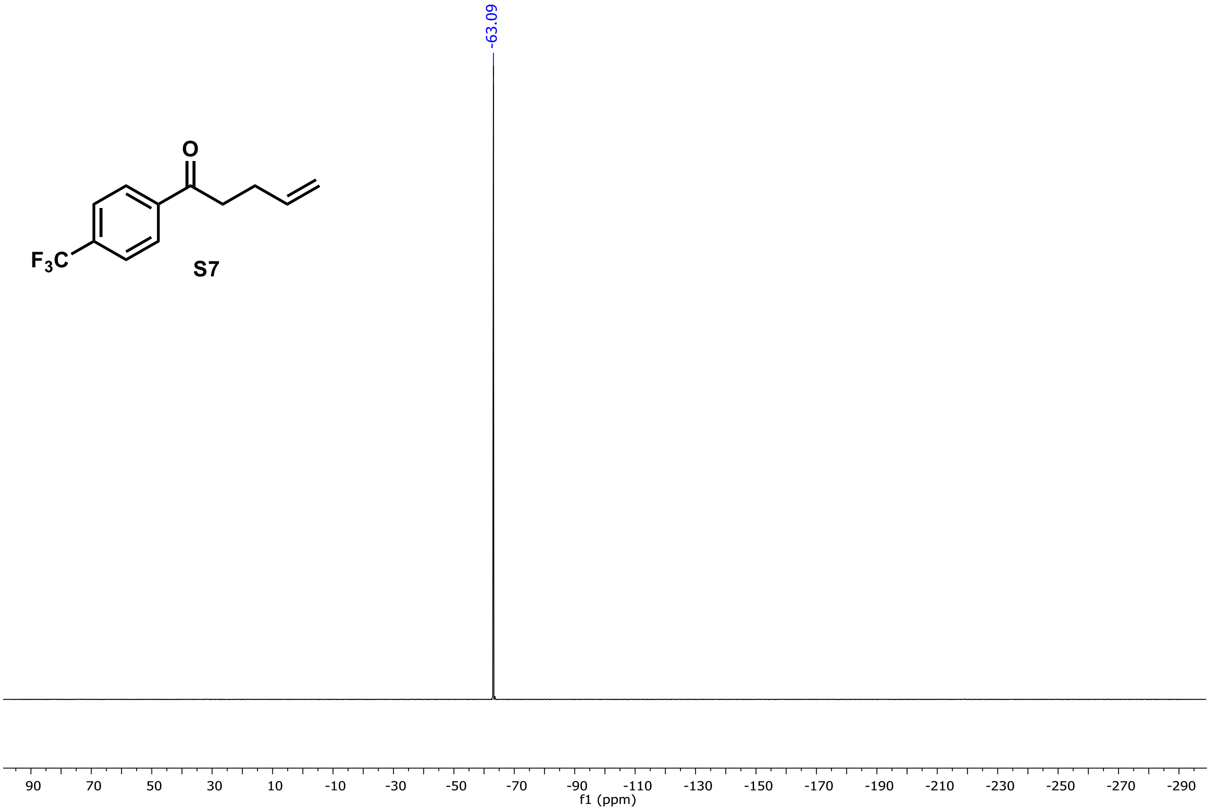
R$_f$ = 0.63 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.49 – 2.55 (2H, m), 3.07 – 3.14 (2H, m), 5.00 – 5.05 (1H, m), 5.07 – 5.14 (1H, m), 5.84 – 5.96 (1H, m), 7.70 – 7.77 (2H, m), 8.03 – 8.10 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 28.1, 38.2, 115.8, 123.7 (q, *J* 272.7), 125.8 (q, *J* 3.8), 128.5, 134.5 (q, *J* 32.7), 137.0, 139.7, 198.5; **^{19}F{^{1}H} NMR (376 MHz, CDCl$_3$)** δ_F = – 63.09.

These data are in accordance with the literature.[6]

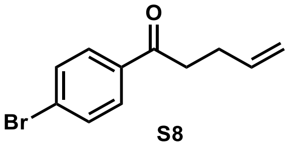
^{1}H, ^{13}C, and ^{19}F NMR spectra of **S7**




198.53
139.68
137.00
134.88
134.62
134.36
134.10
128.49
126.99
125.89
125.86
125.83
125.80
124.82
122.65
120.49
115.77
77.16
38.20
28.06
O
F3C
S7
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-:
f1 (ppm)


-63.09
O
F3C
S7
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
-270
-290
f1 (ppm)

1-(4-Bromophenyl)pent-4-en-1-one (S8)



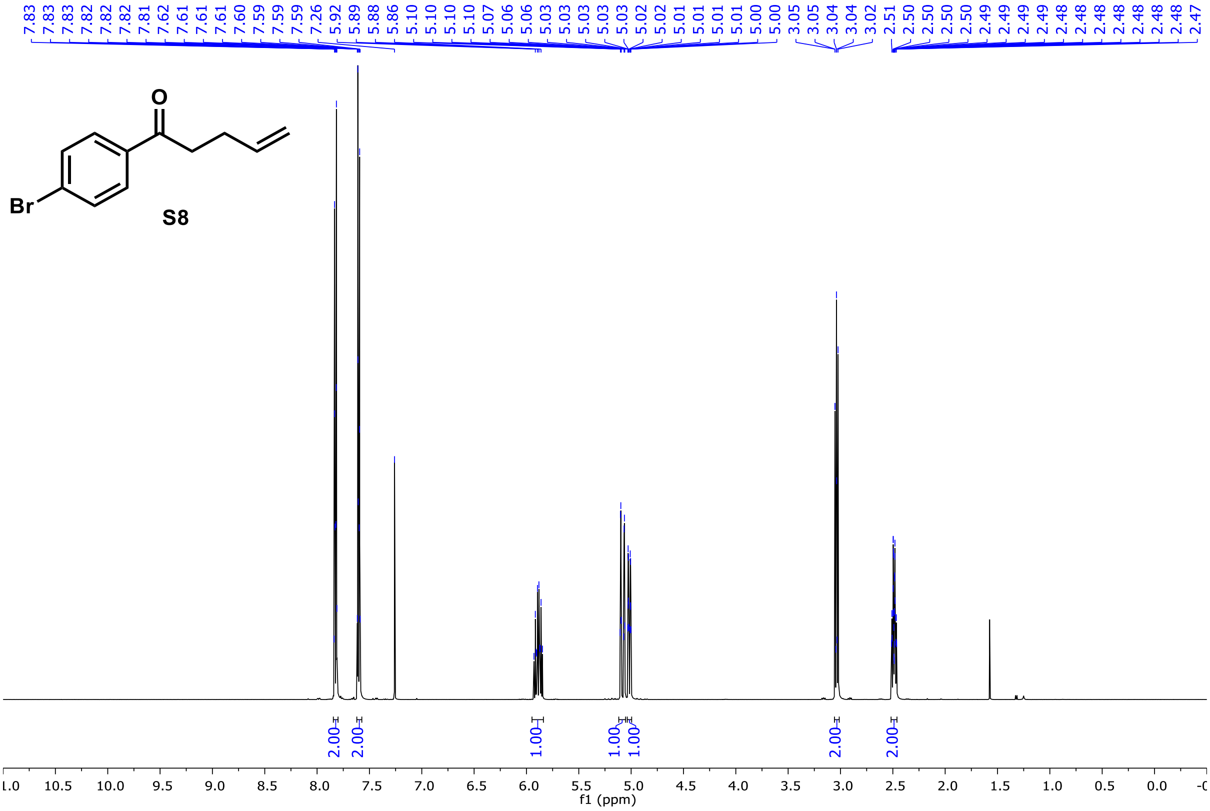
S8

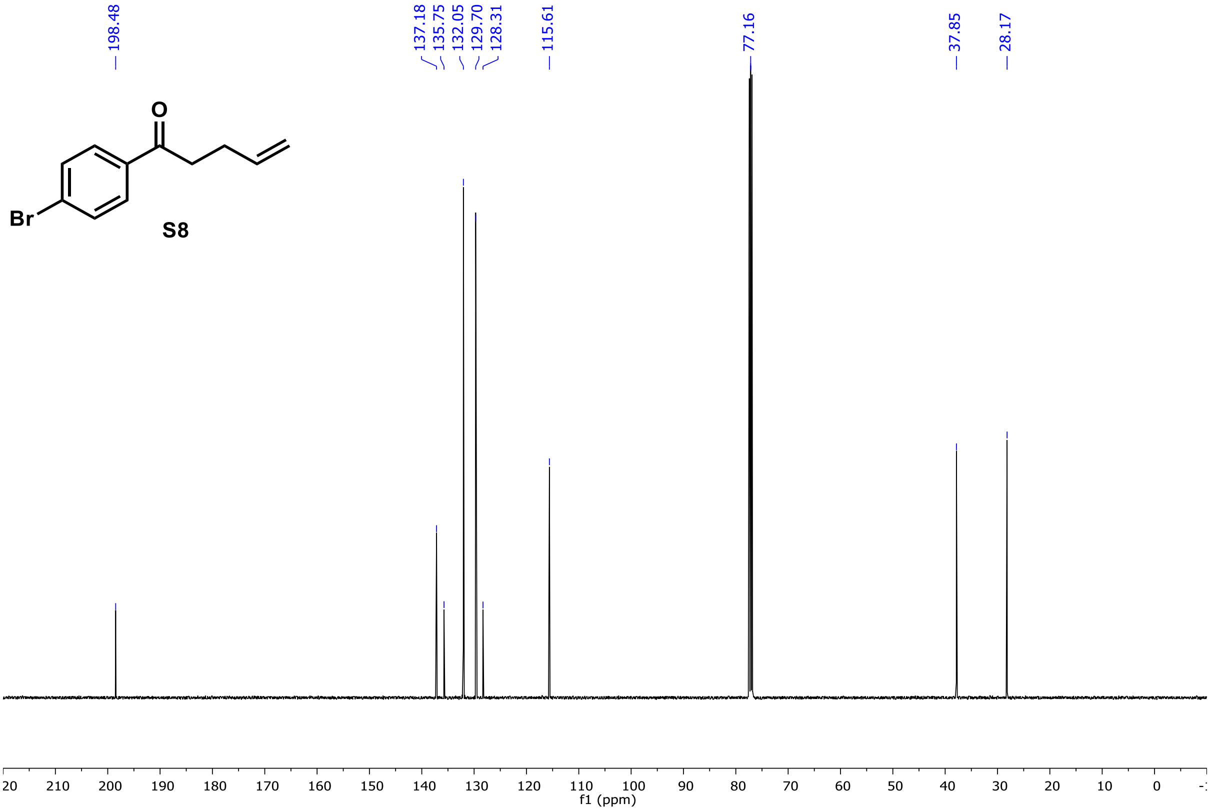
Prepared according to General Procedure 1 using *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30.0 mmol) in CH_2Cl_2 (40 mL), 4-bromobenzoyl chloride (6.58 g, 30.0 mmol), and triethylamine (8.36 mL, 60.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (1.20 g, 49.5 mmol) in THF (45 mL), and 4-bromobut-1-ene (4.57 mL, 45.0 mmol). The aryl ketone was prepared through the addition of the Weinreb amide in THF (15 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S8** (5.62 g, 78%) as a white solid.

R_f = 0.52 (10% EtOAc/petrol); **M.p.:** 49-51 °C; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.46 – 2.51 (2H, m), 3.02 – 3.05 (2H, m), 5.00 – 5.03 (1H, m), 5.06 – 5.11 (1H, m), 5.89 (1H, ddt, *J* 16.8, 10.2, 6.5), 7.59 – 7.62 (2H, m), 7.81 – 7.84 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.2, 37.9, 115.6, 128.3, 129.7, 132.1, 135.8, 137.2, 198.5.

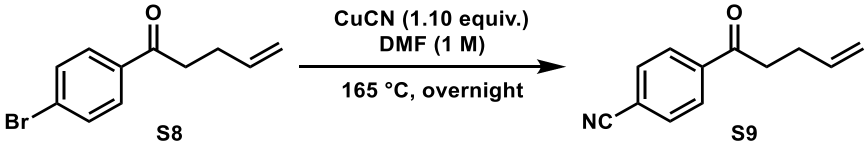
These data are in accordance with the literature.[7]

^{1}H and ^{13}C NMR spectra of **S8**





4-(Pent-4-enoyl)benzonitrile (S9)

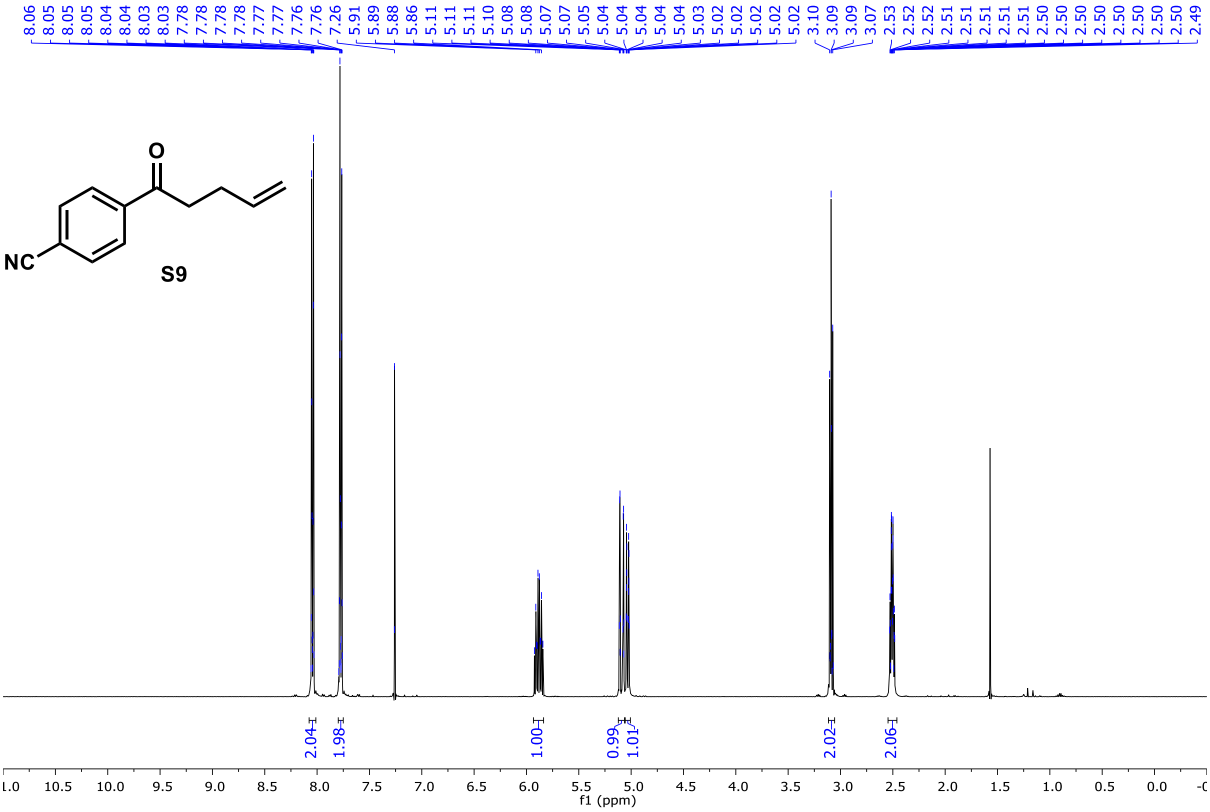


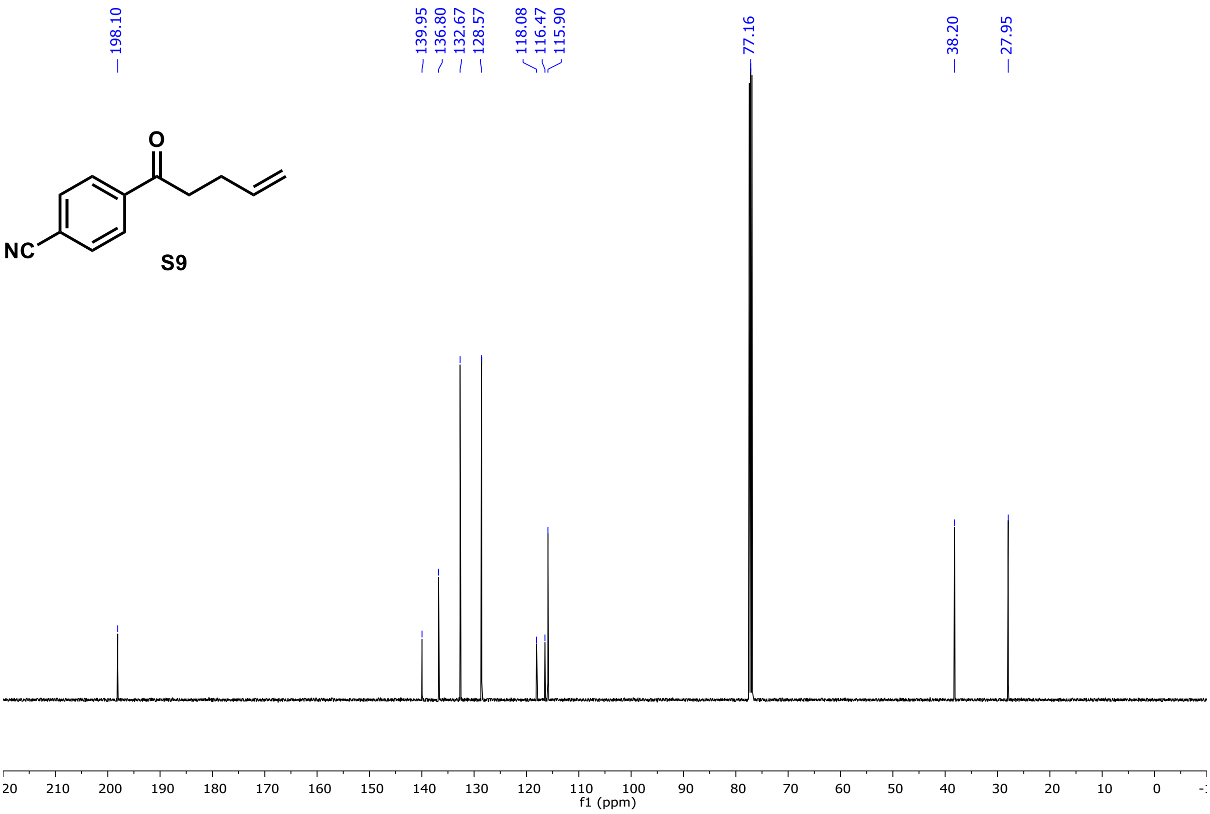
Following a literature procedure,[8] to a flame-dried Schlenk tube was added **S8** (2.39 g, 10.0 mmol) in anhydrous DMF (10 mL, 1 M). Copper (I) cyanide (985 mg, 11.0 mmol) was added portion-wise, and the resulting solution was heated to 165 °C overnight. The reaction was cooled, and water was added, followed by CH_2Cl_2. The layers were separated, and the aqueous layer was further extracted with CH_2Cl_2 (× 3). The combined organics were washed with 10% NaCN (aq.) solution, water (× 4), then brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography (10% EtOAc/petrol, silica gel) to afford **S9** (1.62 g, 87%) as a yellow solid.

R_f = 0.14 (10% EtOAc/petrol); **M.p.:** 48-50 °C; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.48 – 2.53 (2H, m), 3.07 – 3.10 (2H, m), 5.02 – 5.05 (1H, m), 5.07 – 5.11 (1H, m), 5.84 – 5.92 (1H, m), 7.76 – 7.79 (2H, m), 8.03 – 8.06 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.0, 38.2, 115.9, 116.5, 118.1, 128.6, 132.7, 136.8, 140.0, 198.1.

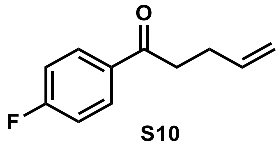
These data are in accordance with the literature.[7]

^{1}H and ^{13}C NMR spectra of **S9**





1-(4-Fluorophenyl)pent-4-en-1-one (S10)

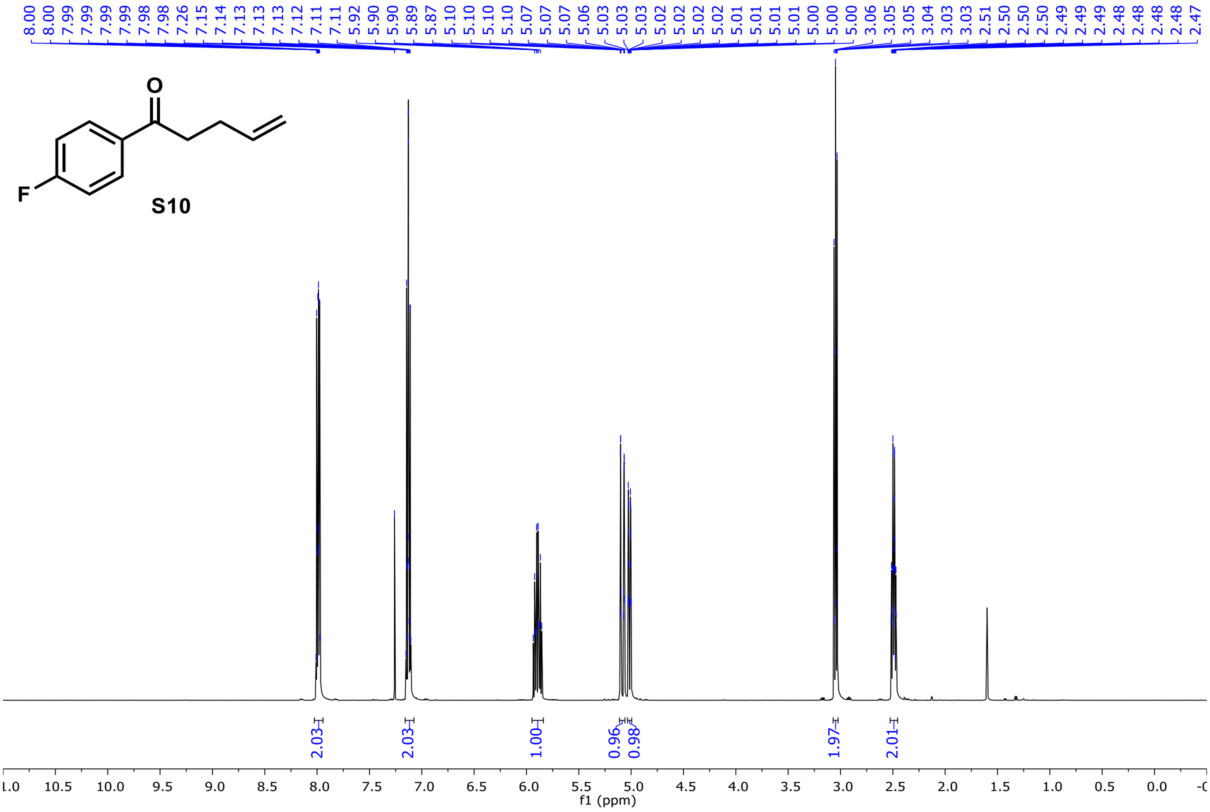


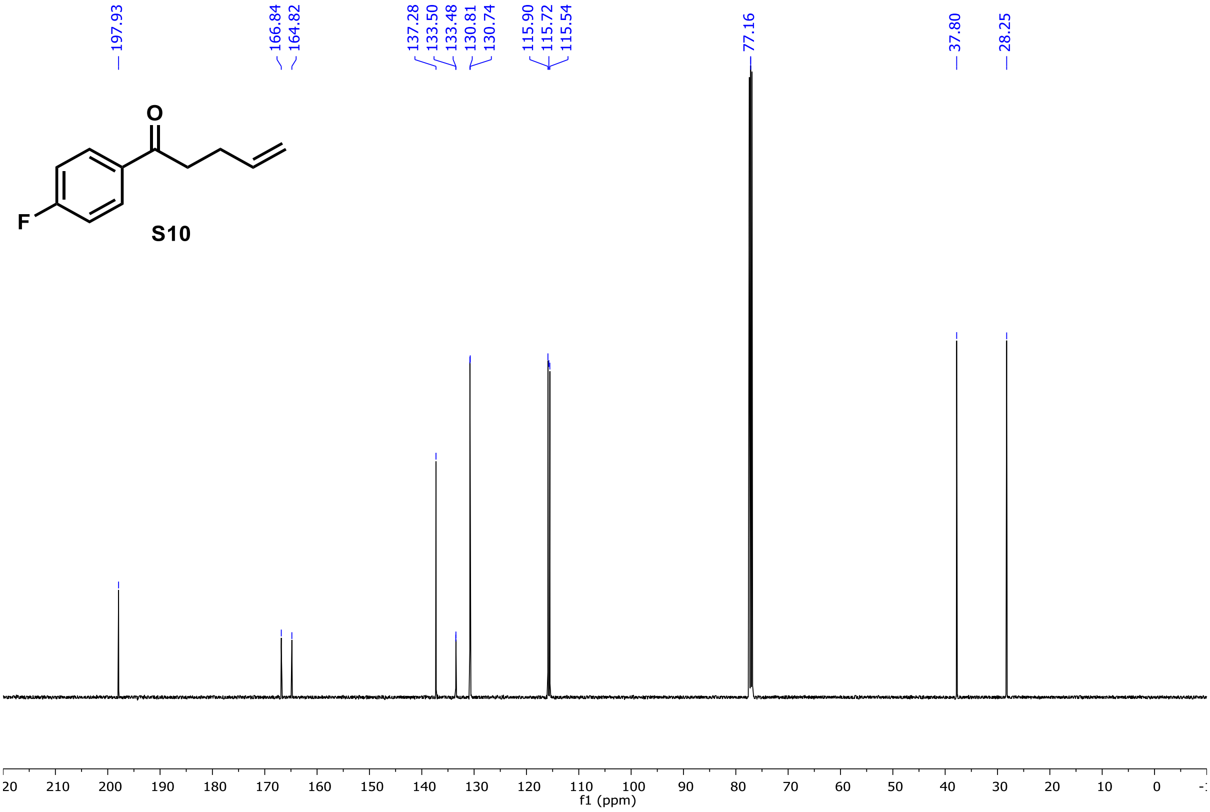
S10

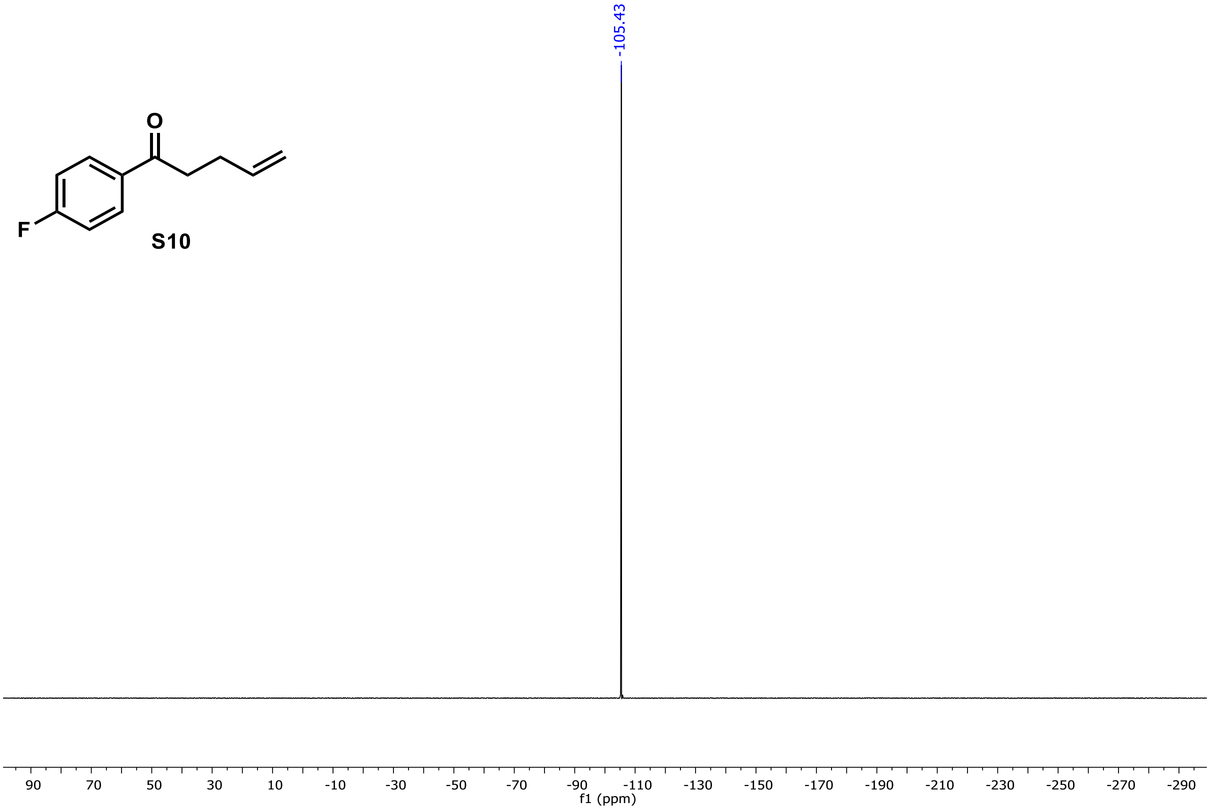
Prepared according to General Procedure 1 using *N*,*O*-dimethylhydroxylamine hydrochloride (483 mg, 5.00 mmol) in CH_2Cl_2 (7 mL), 4-fluorobenzoyl chloride (591 μL, 5.00 mmol), and triethylamine (1.39 mL, 10.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (201 mg, 8.25 mmol) in THF (7.5 mL), and 4-bromobut-1-ene (761 μL, 7.50 mmol). The aryl ketone was prepared through the addition of the Weinreb amide in THF (5 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S10** (609 mg, 68%) as a colourless oil.

R_f = 0.54 (5% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3078, 1684, 1597, 1227, 1206, 1155, 853; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.47 – 2.52 (2H, m), 3.01 – 3.08 (2H, m), 4.98 – 5.05 (1H, m), 5.04 – 5.13 (1H, m), 5.83 – 5.95 (1H, m), 7.08 – 7.17 (2H, m), 7.95 – 8.03 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.3, 37.8, 115.5, 115.8 (d, *J* 21.8), 130.8 (d, *J* 9.3), 133.5 (d, *J* 3.1), 137.3, 165.8 (d, *J* 254.5), 193.9; **^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$)** δ_F = – 105.43; **HRMS** (ES+) $C_{11}H_{11}OF$ $[M+H]^+$ requires 179.0872, found 179.0873 (+ 0.6 ppm).

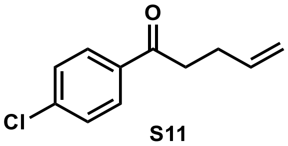
^{1}H, ^{13}C, and ^{19}F NMR spectra of **S10**







1-(4-Chlorophenyl)pent-4-en-1-one (S11)

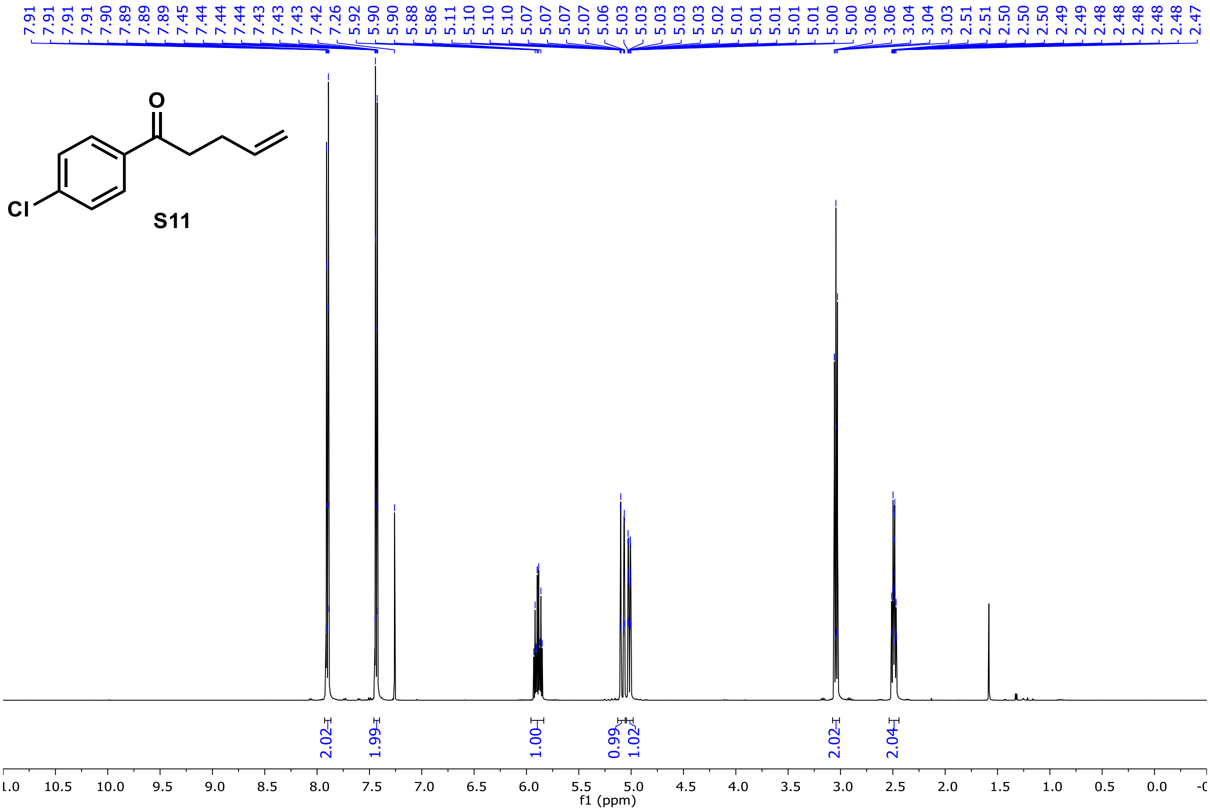


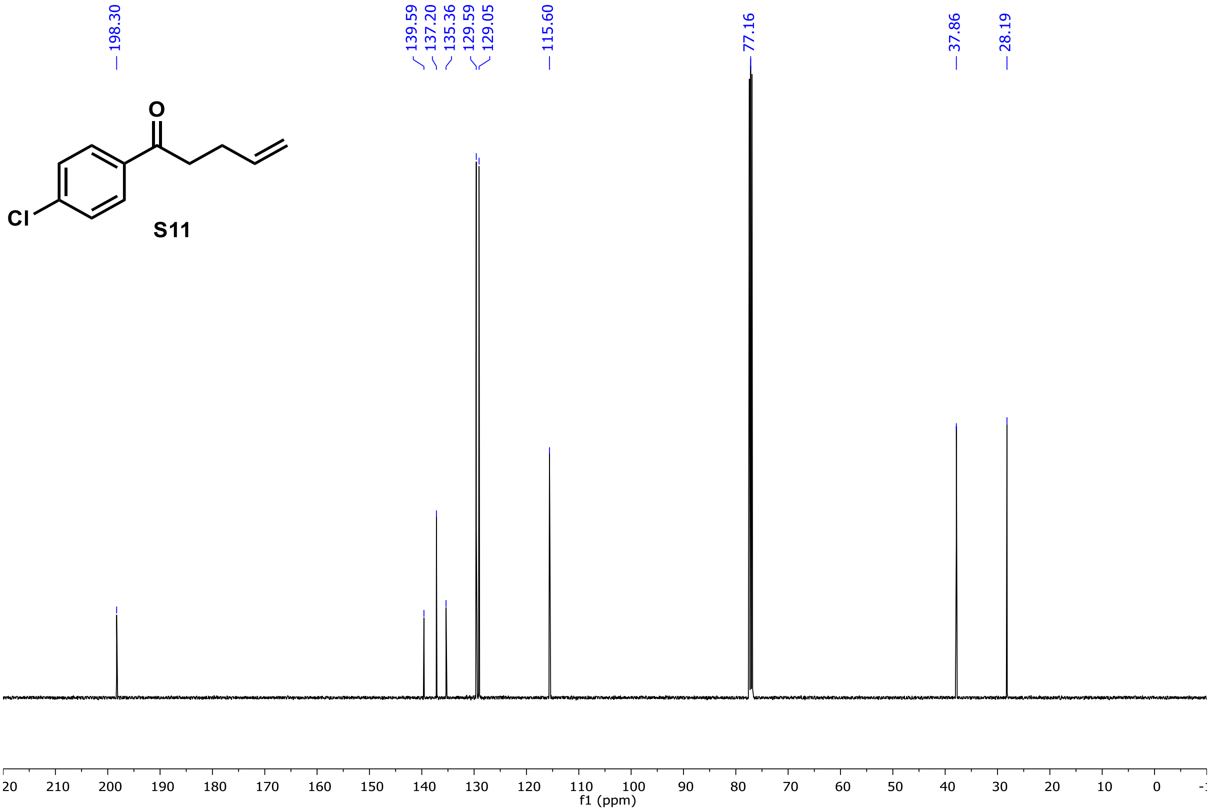
S11

Prepared according to General Procedure A using *N*,*O*-dimethylhydroxylamine hydrochloride (483 mg, 5.00 mmol) in CH_2Cl_2 (7 mL), 4-chlorobenzoyl chloride (641 μL, 5.00 mmol), and triethylamine (1.39 mL, 10.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (201 mg, 8.25 mmol) in THF (7.5 mL), and 4-bromobut-1-ene (761 μL, 7.50 mmol). The aryl ketone was prepared through the addition of the Weinreb amide in THF (5 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S11** (569 mg, 61%) as a yellow oil.

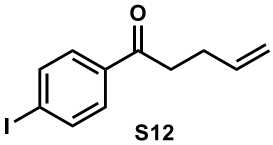
R_f = 0.57 (5% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3076, 1683, 1587, 1400, 1204, 1090; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.46 – 2.52 (2H, m), 3.01 – 3.08 (2H, m), 4.98 – 5.04 (1H, m), 5.06 – 5.13 (1H, m), 5.83 – 5.95 (1H, m), 7.42 – 7.45 (2H, m), 7.88 – 7.92 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.2, 37.9, 115.6, 129.1, 129.6, 135.4, 137.2, 139.6, 198.3; **HRMS** (ES+) $C_{11}H_{11}OCl$ $[M+H]^+$ requires 195.0577, found 195.0578 (+ 0.5 ppm).

^{1}H and ^{13}C NMR spectra of **S11**





1-(4-Iodophenyl)pent-4-en-1-one (S12)



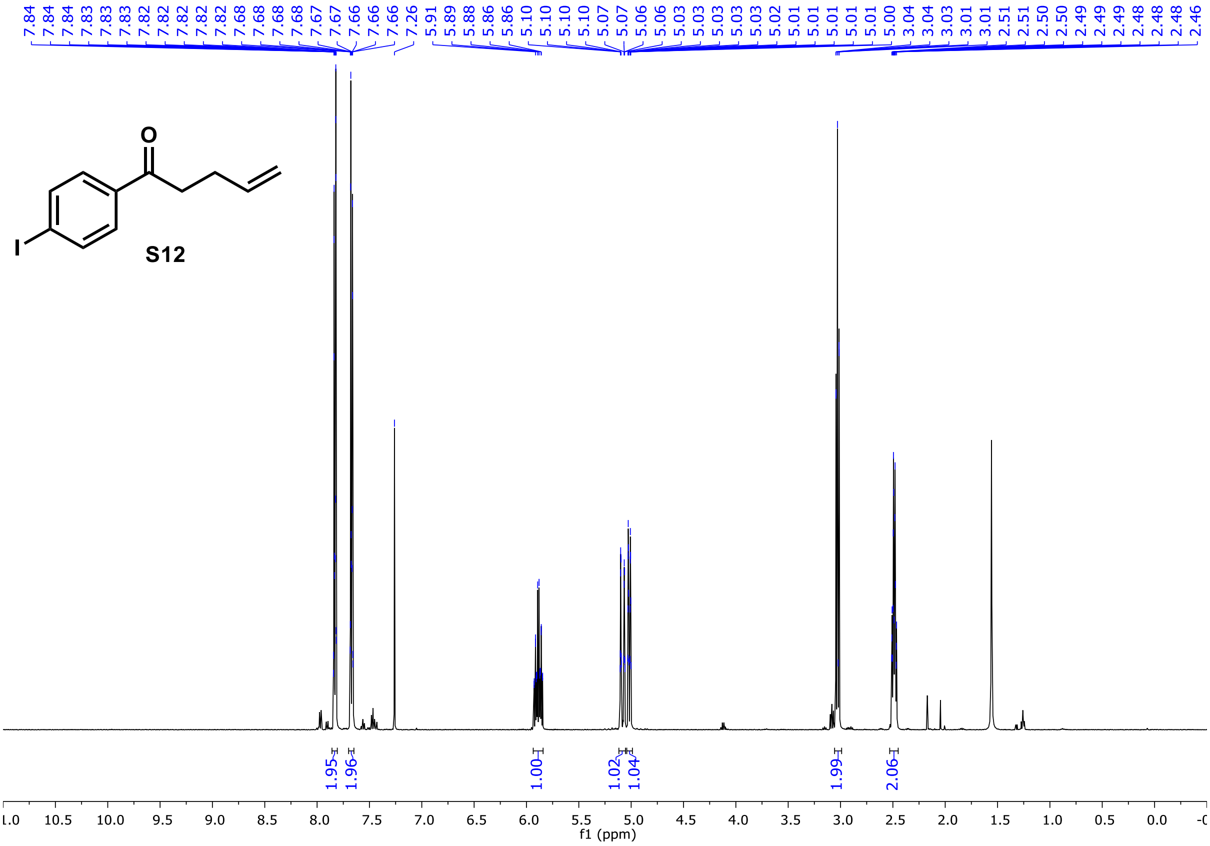
S12

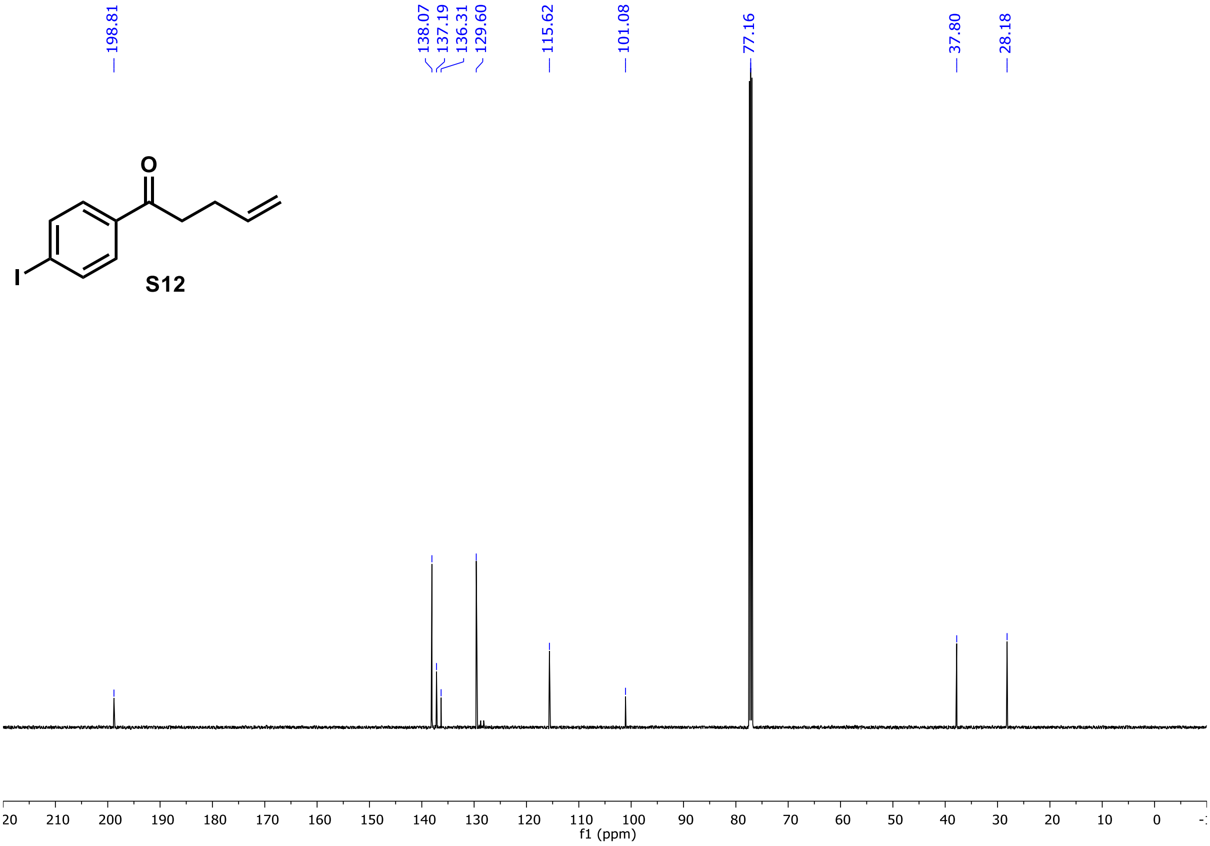
Prepared according to General Procedure 1 using *N*,*O*-dimethylhydroxylamine hydrochloride (975 mg, 10.0 mmol) in CH_2Cl_2 (15 mL), 4-iodobenzoyl chloride (2.66 g, 10.0 mmol), and triethylamine (2.79 mL, 20.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (401 mg, 16.5 mmol) in THF (15 mL), and 4-bromobut-1-ene (1.52 mL, 15.0 mmol). The aryl ketone was prepared through the addition of the Weinreb amide in THF (5 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (2.5-5% EtOAc/petrol, silica gel) to afford **S12** (388 mg, 14%) as a white solid.

R_f = 0.43 (5% EtOAc/petrol); **M.p.:** 64-66 °C; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.46 – 2.51 (2H, m), 3.01 – 3.04 (2H, m), 5.00 – 5.03 (1H, m), 5.06 – 5.11 (1H, m), 5.85 – 5.93 (1H, m), 7.66 – 7.68 (2H, m), 7.82 – 7.84 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.2, 37.8, 101.1, 115.6, 129.6, 136.3, 137.2, 138.1, 198.8.

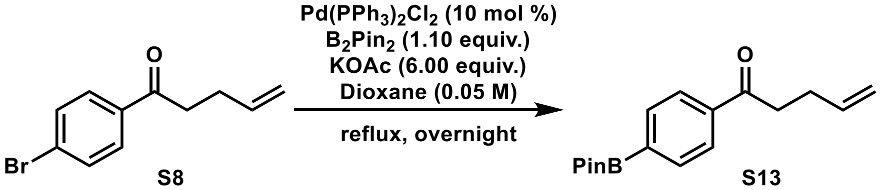
These data are in accordance with the literature.[9]

^{1}H and ^{13}C NMR spectra of **S12**





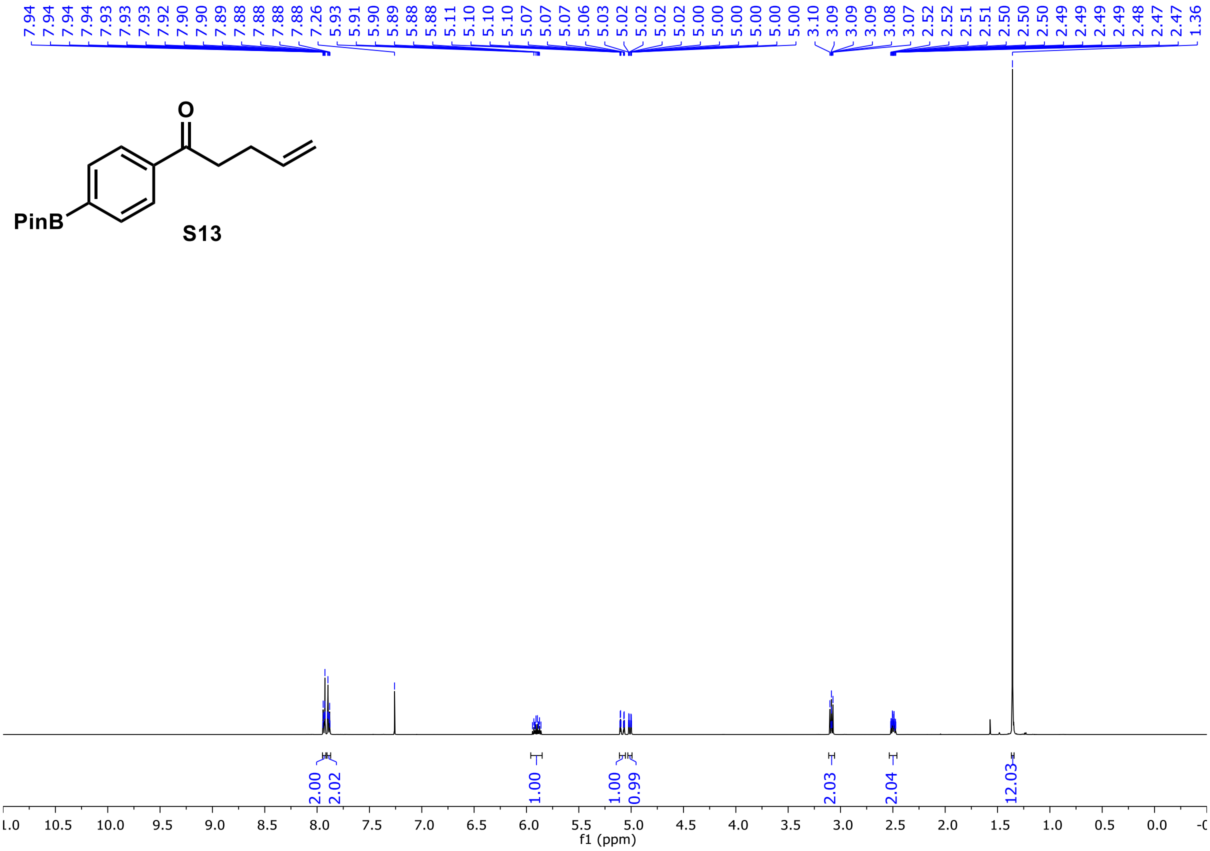
1-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pent-4-en-1-one (S13)

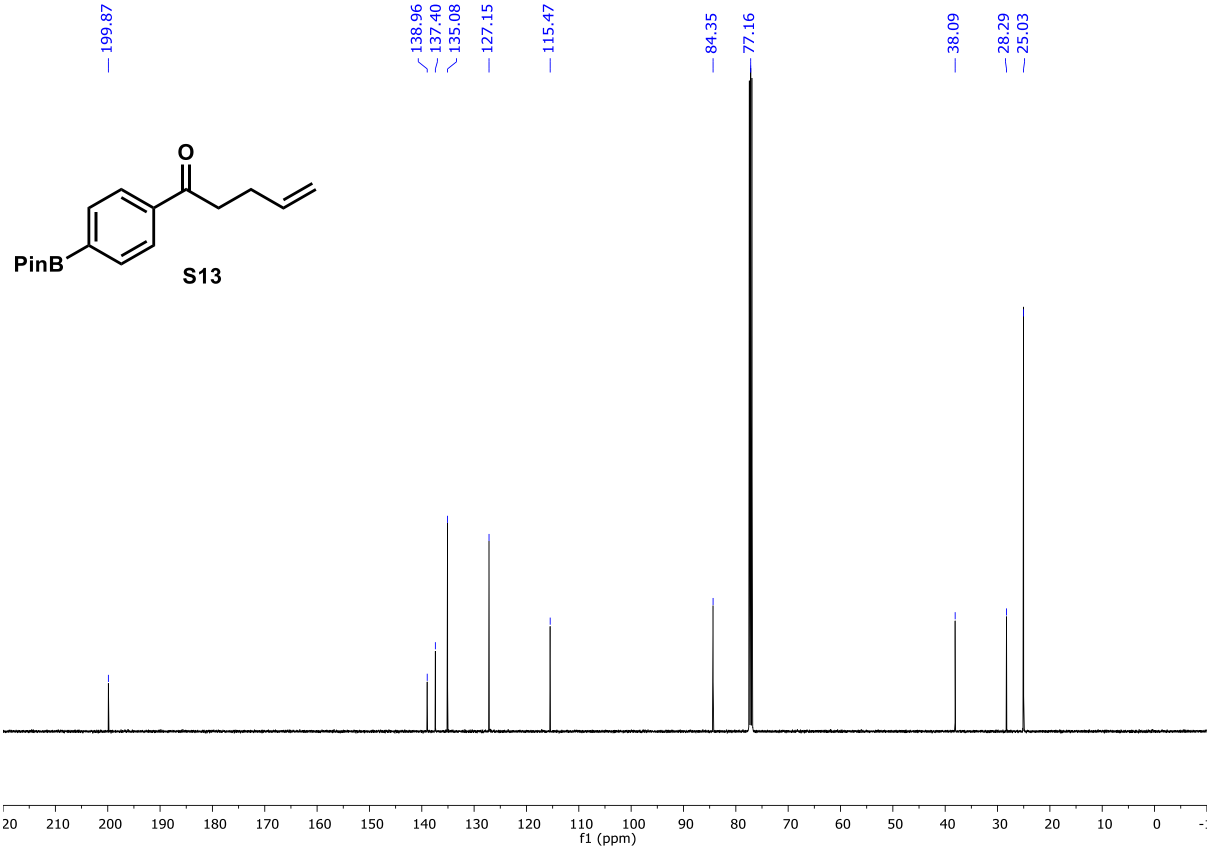


Following a literature procedure,[10] to a flame-dried three-neck RBF fitted with a condenser was added **S8** (1.20 g, 5.00 mmol), $Pd(PPh_3)_2Cl_2$ (351 mg, 0.50 mmol), B_2Pin_2 (1.40 g, 5.50 mmol), and KOAc (2.94 g, 30.0 mmol) and the system was subjected to vacuum-nitrogen exchange cycles (× 3). 1,4-Dioxane (100 mL) which has been previously purged with nitrogen gas for 20 min was then added, and the resulting suspension was refluxed overnight. Upon cooling, the mixture was filtered through celite, washing with EtOAc, and the filtrate was concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography (2.5-10% EtOAc/petrol, silica gel) to afford **S13** (972 mg, 68%) as a colourless oil.

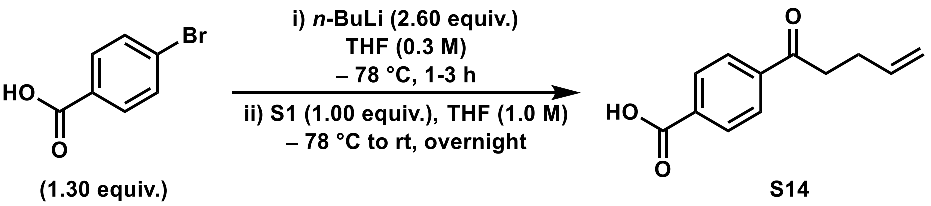
R_f = 0.21 (10% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 2978, 1686, 1506, 1356, 1142, 1088, 856, 652; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.36 (12H, s), 2.47 – 2.52 (2H, m), 3.07 – 3.10 (2H, m), 5.00 – 5.03 (1H, m), 5.06 – 5.11 (1H, m), 5.86 – 5.94 (1H, m), 7.88 – 7.90 (2H, m), 7.92 – 7.94 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 25.0, 28.3, 38.1, 84.4, 115.5, 127.2, 135.1, 137.4, 139.0, 199.9; **HRMS** (ES+) $C_{17}H_{23}{}^{11}BO$ $[M+H]^+$ requires 287.1819, found 287.1826 (+ 2.4 ppm).

^{1}H and ^{13}C NMR spectra of **S13**





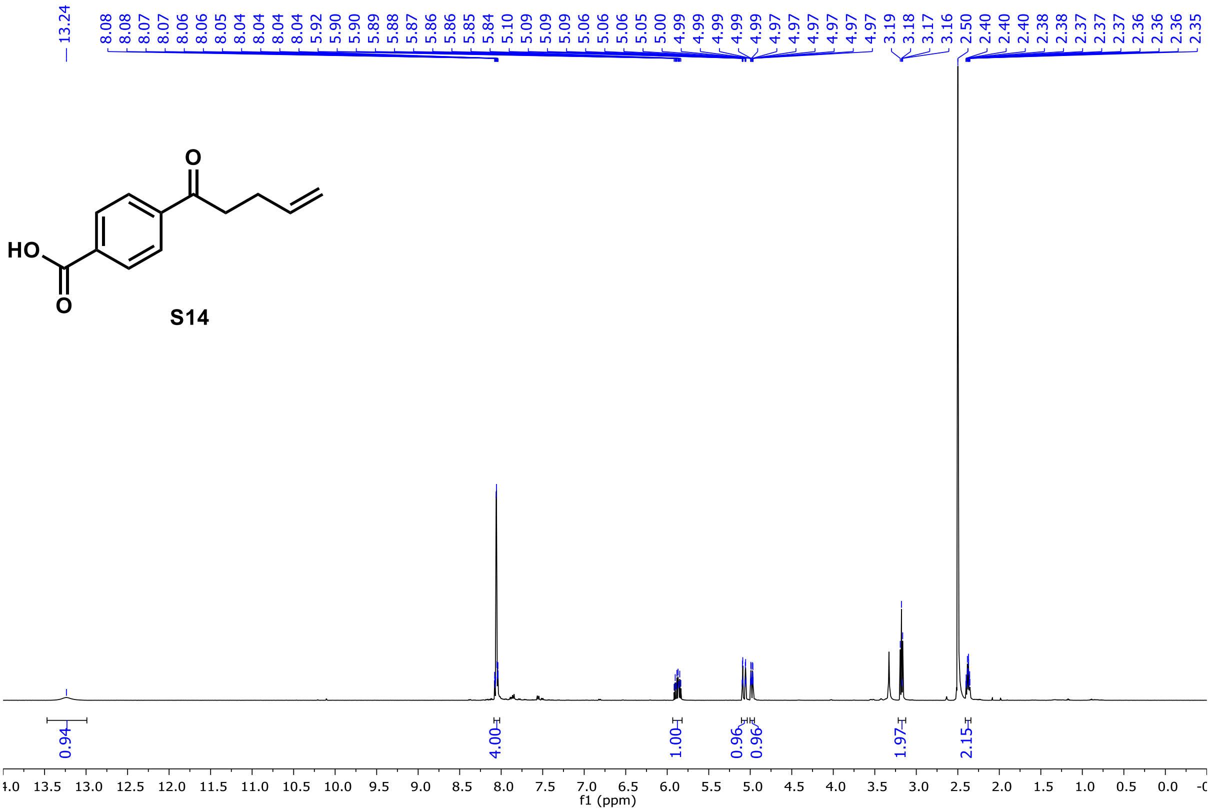
4-(Pent-4-enoyl)benzoic acid (S14)

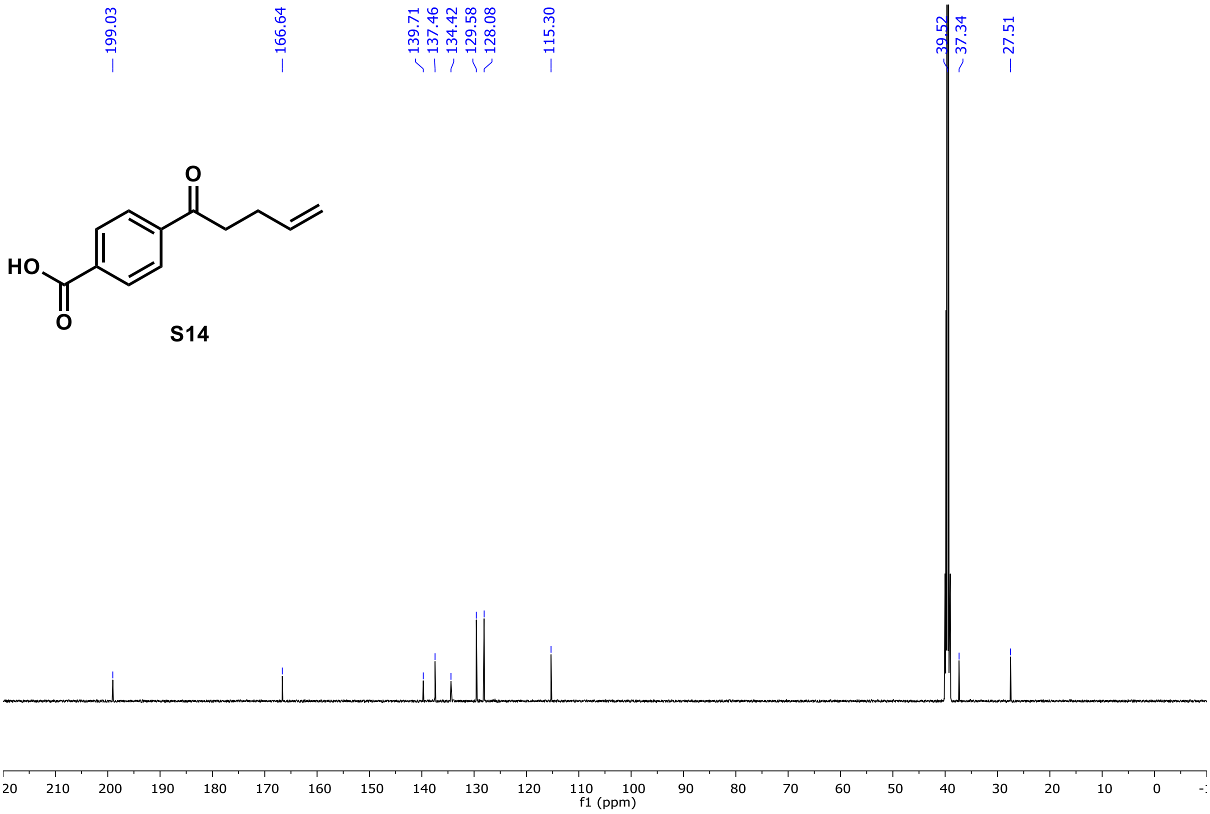


To a flame-dried RBF fitted with a septum seal was added a solution 4-bromobenzoic acid (7.84 g, 39.0 mmol) in anhydrous THF (130 mL, 0.3 M). The mixture was cooled to -78 °C, and a solution of *n*-BuLi (2.4 M in hexanes, 32.5 mL, 78.0 mmol) was added dropwise. The reaction mixture was left to stir for 1 h before a solution of **S1** (5.08 g, 30.0 mmol) in anhydrous THF (30 mL, 1.0 M) was added dropwise. The solution was left to stir for 15 min, before a saturated solution of NH_4Cl (aq.) (50 mL) was added. The mixture was warmed to rt and 1 M HCl (aq.) was added. The layers were separated, and the aqueous layer was further extracted with EtOAc (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was suspended in hexane and stirred vigorously, resulting in the formation of a solid. The precipitate was filtered and resuspended in CH_2Cl_2. Slow addition of hexane resulted in the formation of a precipitate that was filtered, and dried under a high vacuum to afford **S14** (2.45 g, 40%) as an off-white solid.

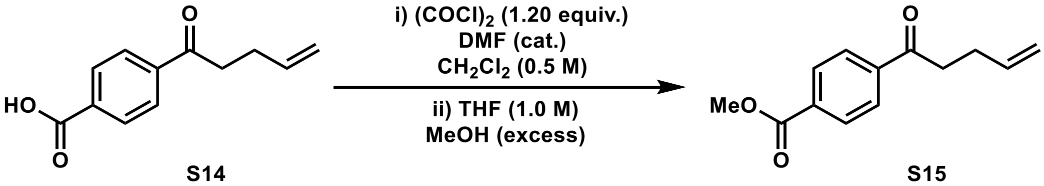
R_f = 0.06 (50% EtOAc/petrol); **M.p.:** 154-156 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 2941, 2847, 2544, 1678, 1645, 1504, 1406, 1273, 1204, 930, 901, 752; **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ_H = 2.35 – 2.40 (2H, m), 3.16 – 3.19 (2H, m), 4.97 – 5.00 (1H, m), 5.05 – 5.10 (1H, m), 5.84 – 5.92 (1H, m), 8.04 – 8.08 (4H, m), 13.24 (1H, br s); **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ_C = 27.5, 37.3, 115.3, 128.1, 129.6, 134.4, 137.5, 139.7, 166.6, 199.0; **HRMS** (CI+) $C_{12}H_{12}O_3$ $[M+H]^+$ requires 205.0859, found 205.0859 (– 0.1 ppm).

^{1}H and ^{13}C NMR spectra of **S14**





Methyl 4-(pent-4-enoyl)benzoate (S15)

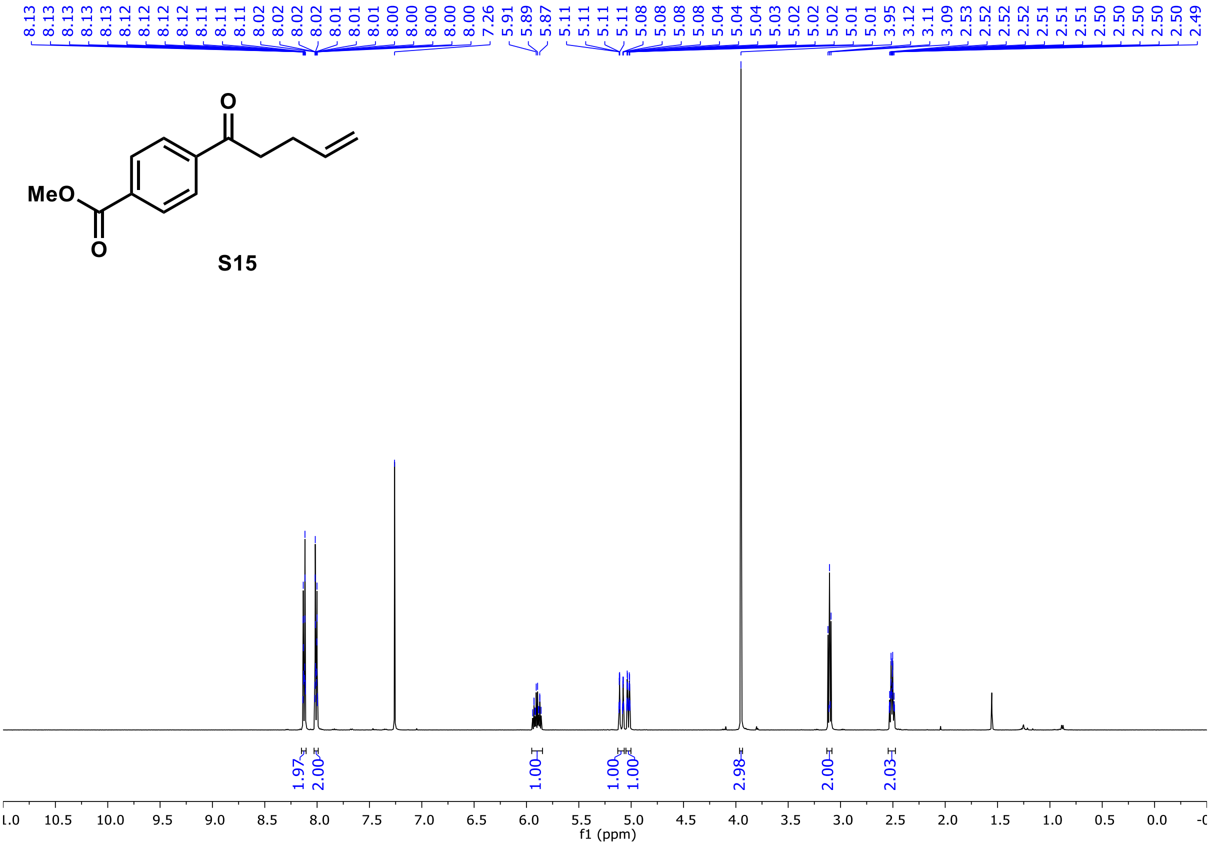


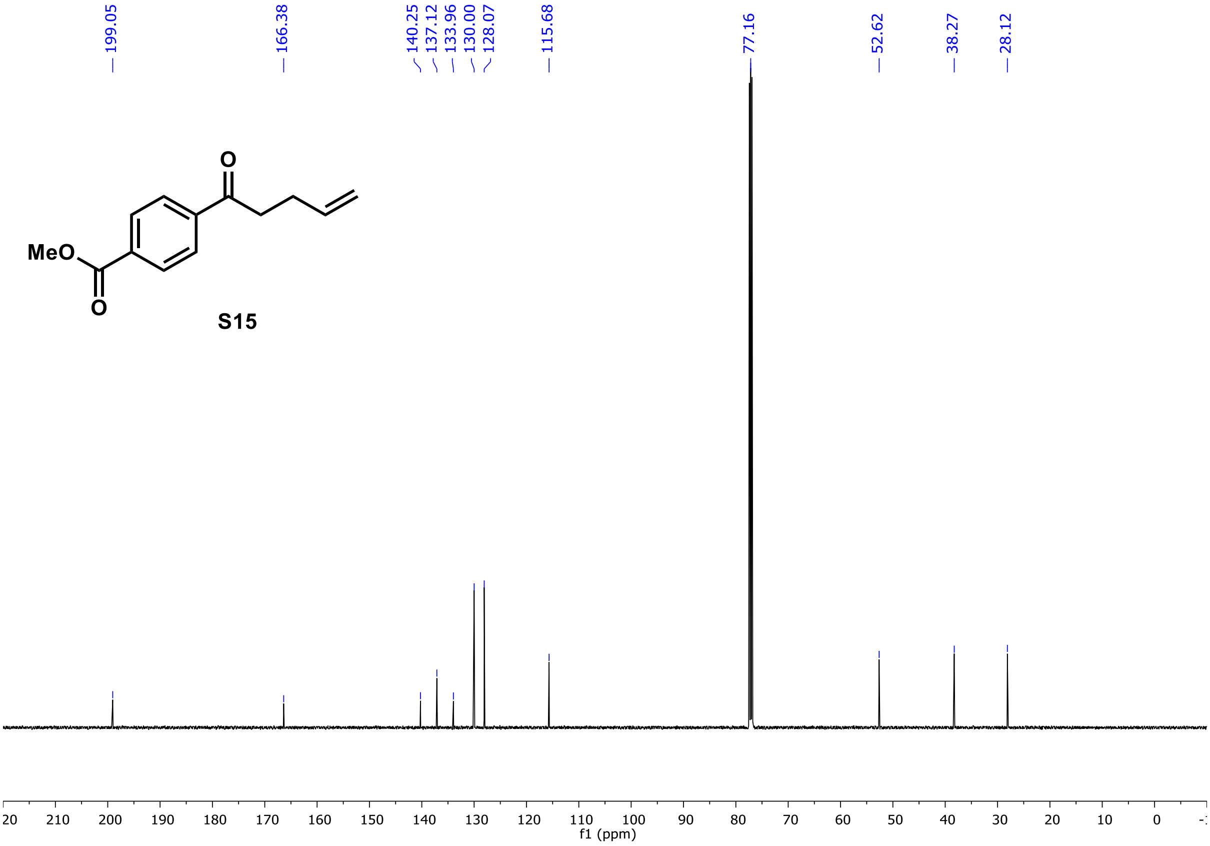
To a flame-dried RBF was added **S14** (90 mg, 0.44 mmol) in anhydrous CH_2Cl_2 (2 mL, 0.25 M). The solution was cooled to 0 °C, and oxalyl chloride (45 μL, 0.53 mmol) was added dropwise, followed by the addition of DMF (1 drop). The reaction was warmed to rt and stirred until gas evolution ceased. The mixture was concentrated under reduced pressure, and the resulting crude material was dissolved in anhydrous THF (1 mL, 1.0 M). MeOH (10 mL) was added, and the reaction was stirred at rt overnight before being quenched with a saturated solution of $NaHCO_3$ (aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (× 2). The combined organics were then washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatograph (10-20% EtOAc/petrol, silica gel) to afford **S15** (78 mg, 81%) as a white solid.

R_f = 0.36 (15% EtOAc/petrol); **M.p.:** 79-81 °C; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.49 – 2.53 (2H, m), 3.09 – 3.12 (2H, m), 3.95 (3H, s), 5.01 – 5.04 (1H, m), 5.07 – 5.12 (1H, m), 5.90 (1H, ddt, *J* 16.9, 10.2, 6.5), 8.00 – 8.02 (2H, m), 8.11 – 8.14 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.1, 38.3, 52.6, 115.7, 128.1, 130.0, 134.0, 137.1, 140.3, 166.4, 199.1.

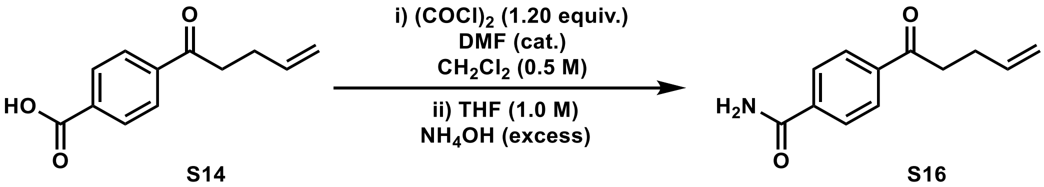
These data are in accordance with the literature.[11]

^{1}H and ^{13}C NMR spectra of **S15**





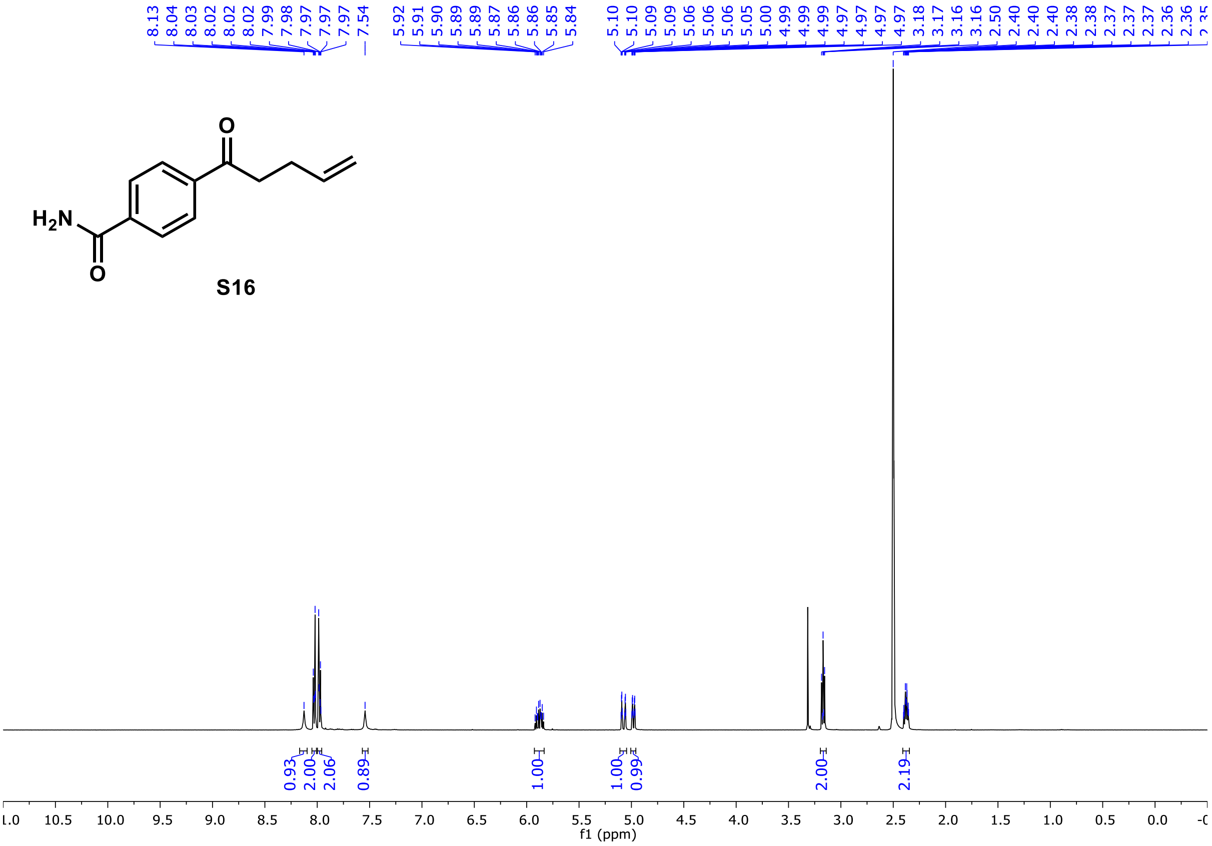
4-(Pent-4-enoyl)benzamide (S16)

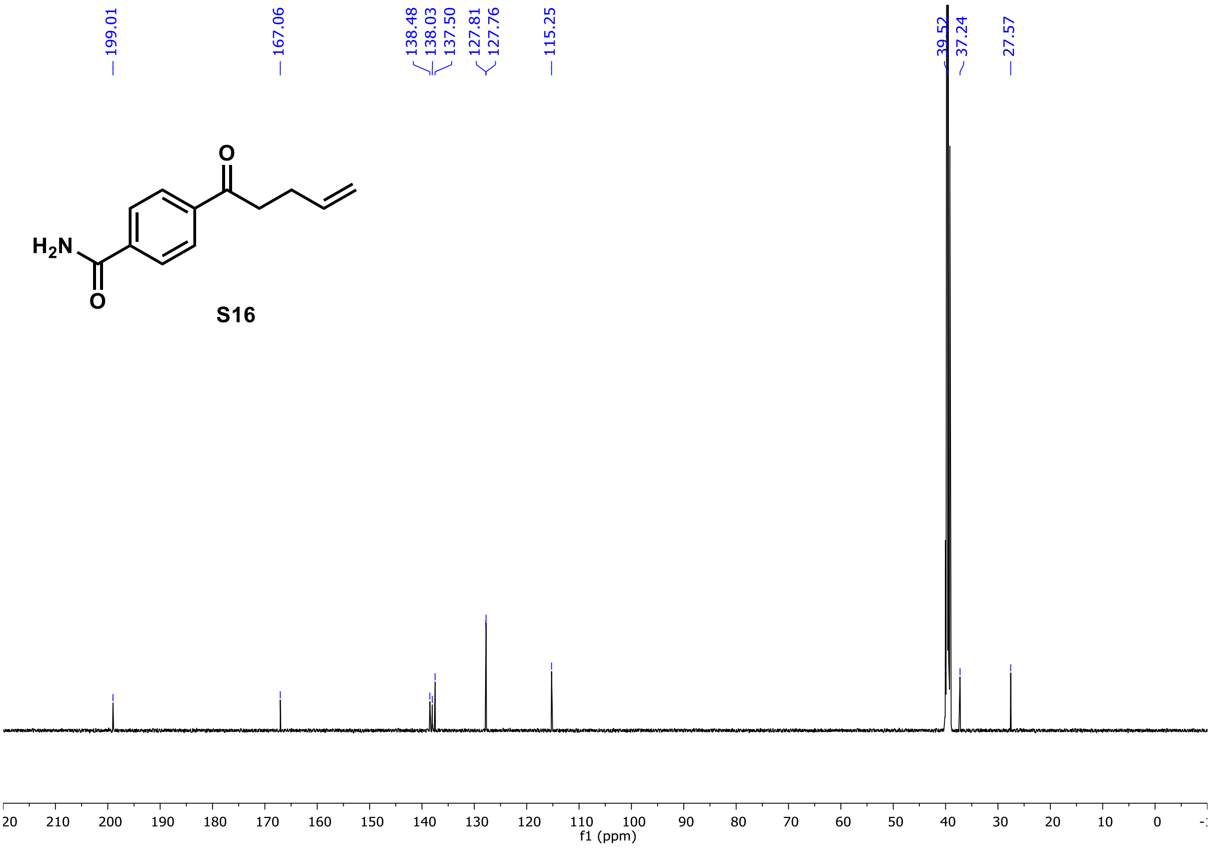


To a flame-dried RBF was added **S14** (613 mg, 3.00 mmol) in anhydrous CH_2Cl_2 (6 mL, 0.5 M). The solution was cooled to 0 °C, and oxalyl chloride (305 µL, 3.60 mmol) was added dropwise, followed by the addition of DMF (3 drops). The reaction was warmed to rt and stirred until gas evolution ceased. The mixture was concentrated under reduced pressure, and the resultant crude material was dissolved in THF (3.0 mL, 1.0 M) before being added slowly to 35% NH_3 solution (aq.) (excess) and stirred at rt overnight before being diluted with EtOAc. The layers were separated, and the aqueous layer was further extracted with EtOAc (× 3). The combined organics were then washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resultant crude material was purified by recrystallisation (CH_2Cl_2) to afford **S16** (221 mg, 36%) as a white solid.

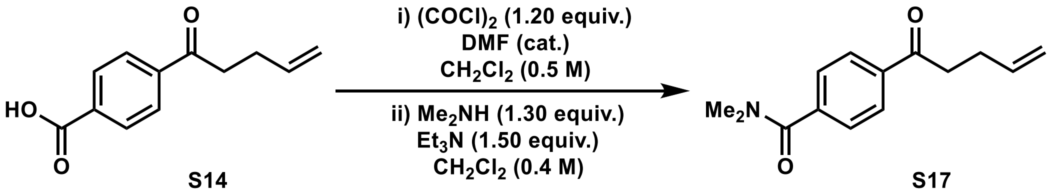
R_f = 0.27 (80% EtOAc/petrol); **M.p.:** 168-170 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3385, 3186, 1678, 1649, 1618, 1568, 1409, 1303, 1273, 1207, 910, 860, 783; **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ_H = 2.35 – 2.40 (2H, m), 3.16 – 3.18 (2H, m), 4.97 – 5.00 (1H, m), 5.05 – 5.10 (1H, m), 5.88 (1H, ddt, *J* 16.8, 10.2, 6.4), 7.54 (1H, br s), 7.97 – 7.99 (2H, m), 8.02 – 8.04 (2H, m), 8.13 (1H, br s); **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ_C = 27.6, 37.2, 115.3, 127.7, 127.8, 137.5, 138.0, 138.5, 167.1, 199.0; **HRMS** (CI+) $C_{12}H_{13}NO_2$ [M+H]$^+$ requires 204.1019, found 204.1019 (+ 0.1 ppm).

^{1}H and ^{13}C NMR spectra of **S16**





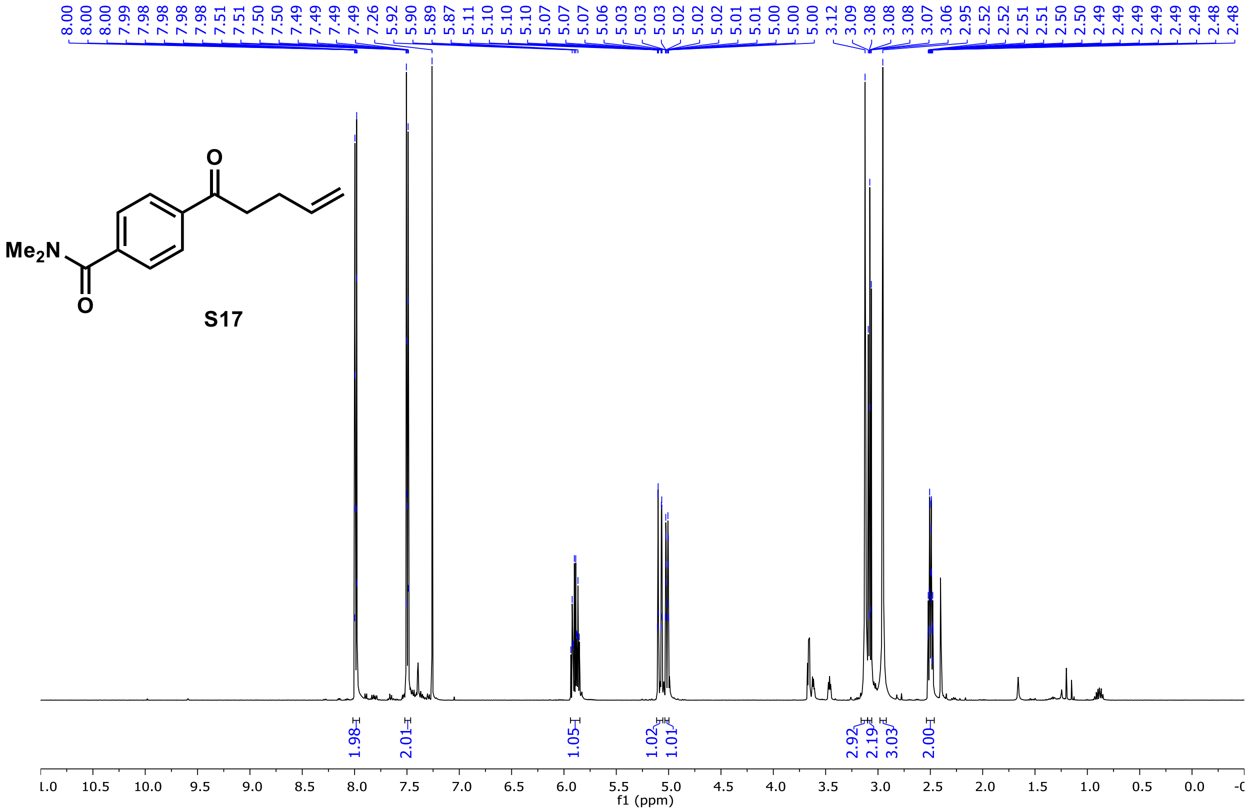
N,*N*-Dimethyl-4-(pent-4-enoyl)benzamide (S17)



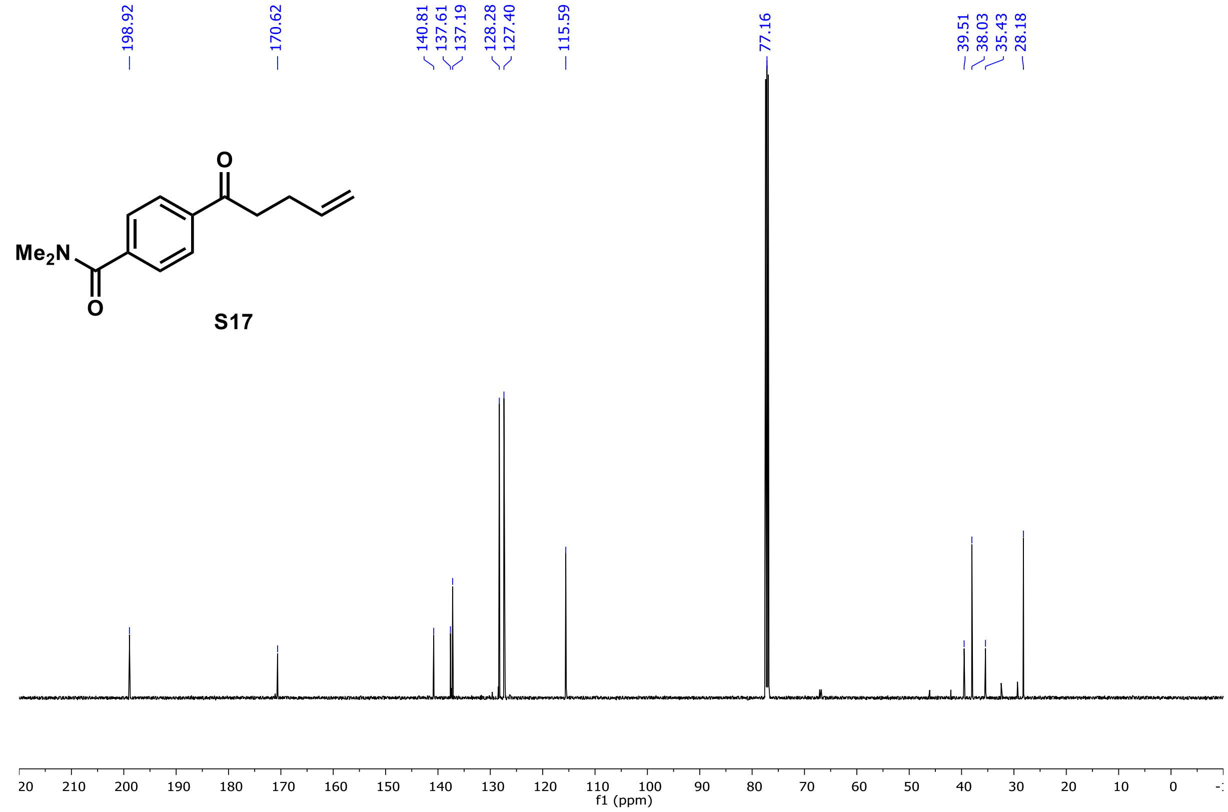
To a flame-dried RBF was added **S14** (613 mg, 3.00 mmol) in anhydrous CH_2Cl_2 (6 mL, 0.5 M). The solution was cooled to 0 °C, and oxalyl chloride (305 µL, 3.60 mmol) was added dropwise, followed by the addition of DMF (3 drops). The reaction was warmed to rt and stirred until gas evolution ceased. The mixture was concentrated under reduced pressure, and the resulting crude material was dissolved in anhydrous CH_2Cl_2 (7.5 mL, 0.4 M). Dimethylamine (2.0 M in toluene, 1.95 mL, 3.90 mmol) and triethylamine (627 µL, 4.50 mmol) were added dropwise and the reaction was stirred at rt overnight before being quenched with water. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (× 3). The combined organics were then washed with a saturated solution of $NaHCO_3$ (aq.), followed by water, then brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatograph (50% EtOAc/petrol, silica gel) to afford **S17** (458 mg, 66%) as a yellow solid.

R_f = 0.16 (50% EtOAc/petrol); **M.p.:** 46-48 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 2938, 1676, 1618, 1508, 1423, 1264, 1206, 1080, 985, 908, 845, 756; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.47 – 2.52 (2H, m), 2.95 (3H, s), 3.06 – 3.09 (2H, m), 3.12 (3H, s), 5.00 – 5.03 (1H, m), 5.06 – 5.11 (1H, m), 5.85 – 5.93 (1H, m), 7.49 – 7.51 (2H, m), 7.98 – 8.00 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.2, 35.4, 38.0, 39.5, 115.6, 127.4, 128.3, 137.2, 137.6, 140.8, 170.6, 198.9; **HRMS** (ES+) $C_{14}H_{17}NO_2$ $[M+H]^+$ requires 232.1338, found 232.1342 (+ 1.7 ppm).

^{1}H and ^{13}C NMR spectra of **S17**

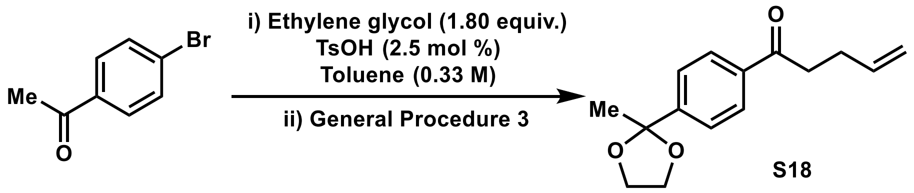


S17



S17

1-(4-(2-Methyl-1,3-dioxolan-2-yl)phenyl)pent-4-en-1-one (S18)

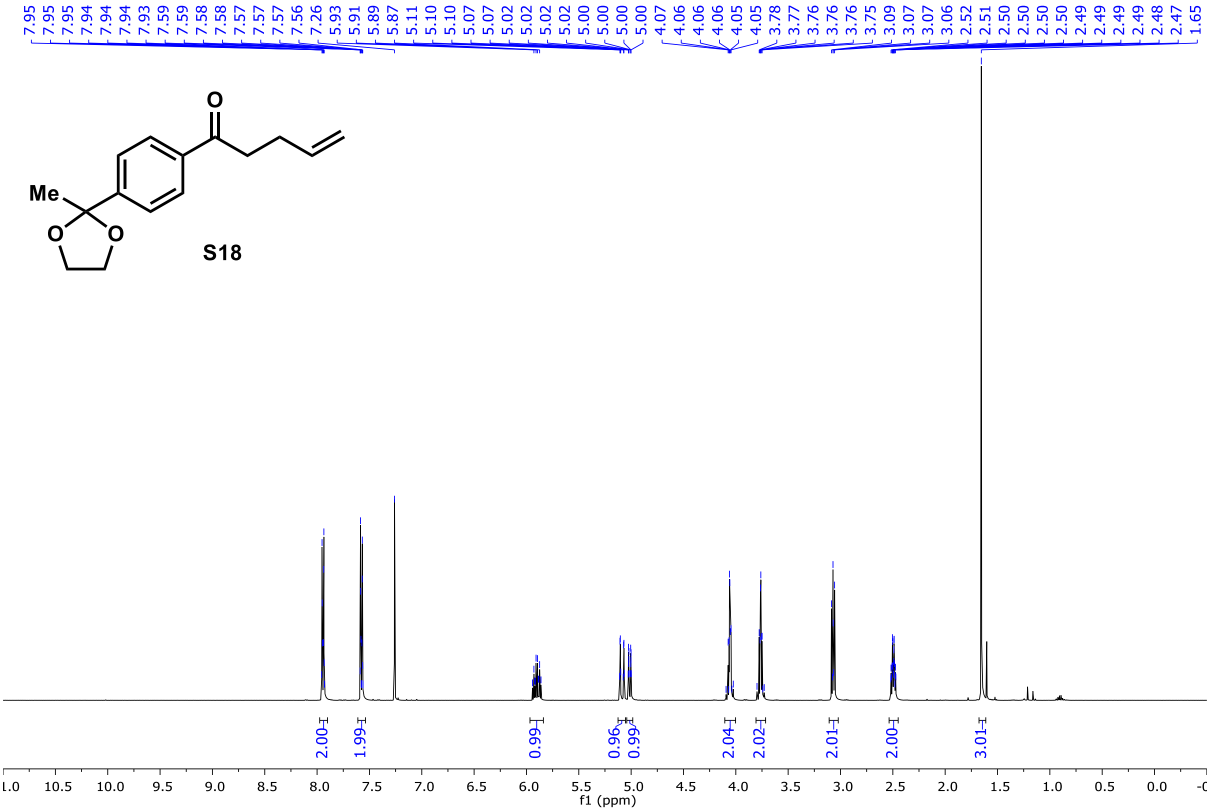


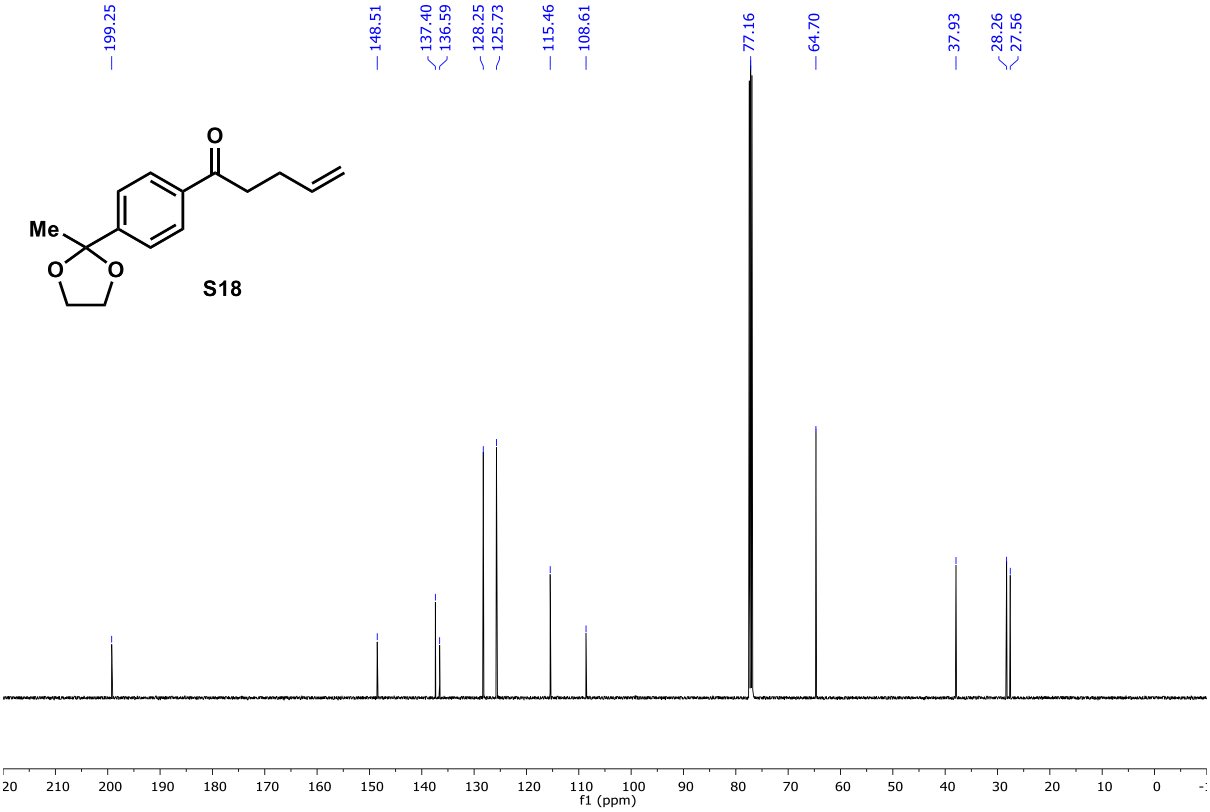
To an RBF fitted with a Dean-Stark condenser was added 4’-bromoacetophenone (3.98 g, 20.0 mmol), *para*-toluenesulfonic acid (95.0 mg, 0.50 mmol), and ethylene glycol (2.00 mL, 36.0 mmol) in toluene (60 mL, 0.33 M). The mixture was heated to reflux overnight, before being cooled, washed with a saturated solution of $NaHCO_3$ (aq.) (2 × 20 mL), and the aqueous layer was further extracted with EtOAc (3 × 30 mL). The combined organics were washed with brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude ketal that was used without further purification.

The crude ketal (2.53 g, 10.4 mmol) was then subjected to the conditions of General Procedure 3 using **S1** (1.35 g, 8.00 mmol), and ^{n}BuLi (2.40 M in hexanes, 4.33 mL, 10.4 mmol) in THF (43 mL). The resultant crude material was purified by flash column chromatography (5-10% EtOAc/petrol, silica gel) to afford **S18** (1.21 g, 61%) as a colourless oil.

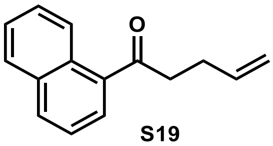
R_f = 0.23 (10% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 2988, 2889, 2349, 1682, 1607, 1404, 1373, 1244, 1198, 1034, 874; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.65 (3H, s), 2.47 – 2.52 (2H, m), 3.06 – 3.09 (2H, m), 3.73 – 3.80 (2H, m), 4.02 – 4.09 (2H, m), 5.00 – 5.03 (1H, m), 5.07 – 5.11 (1H, m), 5.86 – 5.94 (1H, m), 7.56 – 7.59 (2H, m), 7.93 – 7.96 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 27.6, 28.3, 37.9, 64.7, 108.6, 115.5, 125.7, 128.3, 136.6, 137.4, 148.5, 199.3; **HRMS** (CI+) $C_{15}H_{18}O_3$ $[M+H]^+$ requires 247.1329, found 247.1328 (–0.5 ppm).

^{1}H and ^{13}C NMR spectra of **S18**





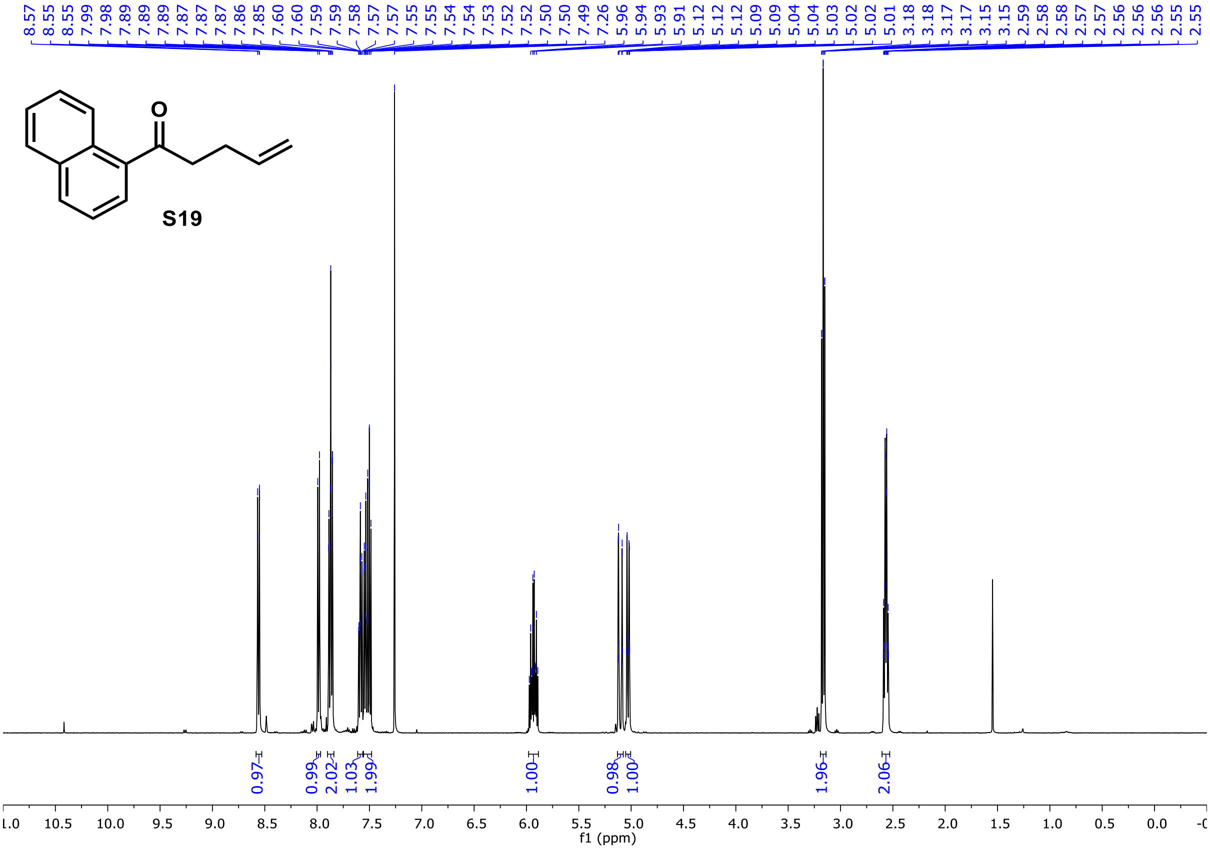
1-(Naphthalen-1-yl)pent-4-en-1-one (S19)

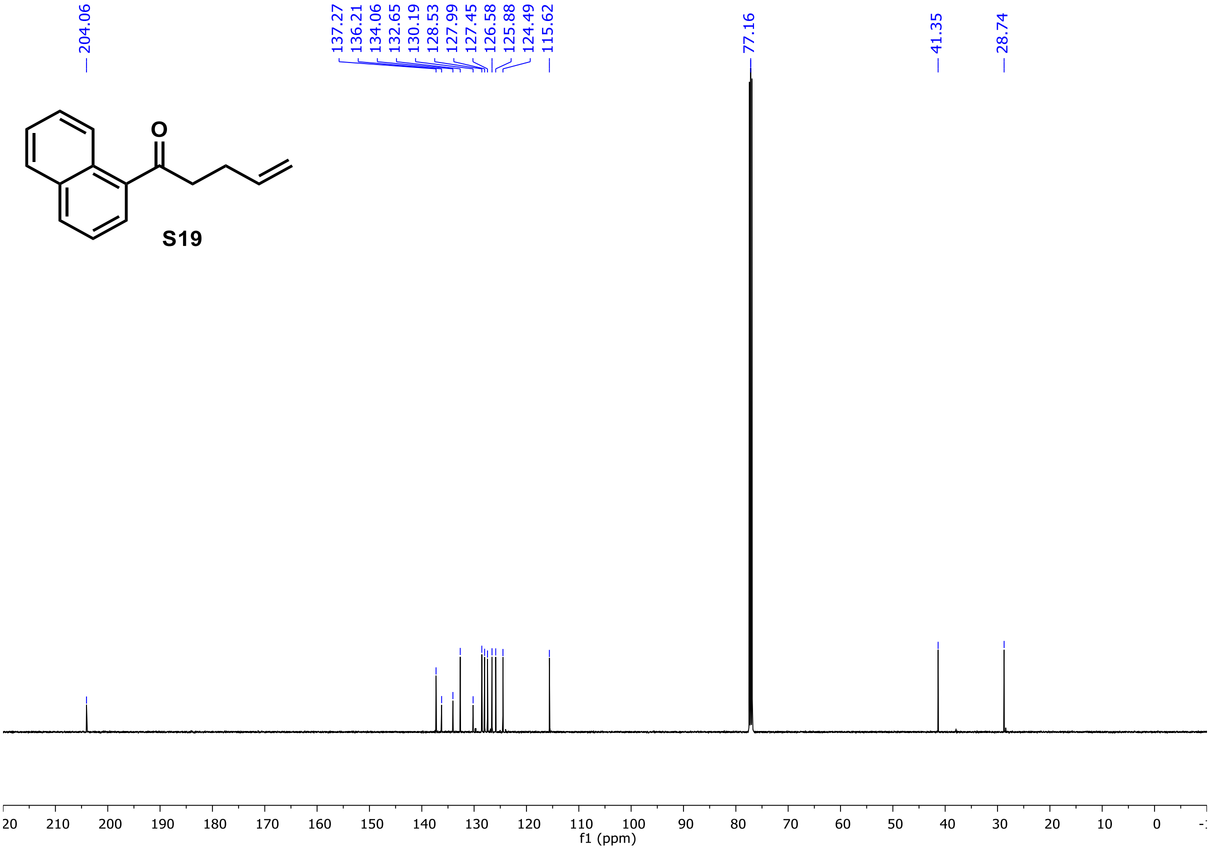

S19

Prepared according to General Procedure 3 using **S1** (1.52 g, 9.00 mmol), 1-bromonaphthalene (1.63 mL, 11.7 mmol), and ^{n}BuLi (2.5 M in hexanes, 4.68 mL, 11.7 mmol) in THF (50 mL). The resultant crude material was purified by flash column chromatography (0-1% EtOAc/petrol, silica gel) to afford **S19** (756 mg, 40%) as a pale-yellow oil.

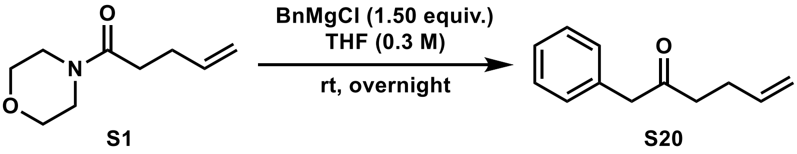
R$_f$ = 0.26 (5% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3049, 2976, 2914, 2360, 1678, 1639, 1506, 1435, 1276, 1172, 1089, 997; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.54 – 2.59 (2H, m), 3.15 – 3.18 (2H, m), 5.01 – 5.04 (1H, m), 5.08 – 5.13 (1H, m), 5.93 (1H, ddt, *J* 16.8, 10.2, 6.5), 7.49 – 7.55 (2H, m), 7.57 – 7.60 (1H, m), 7.85 – 7.89 (2H, m), 7.98 – 7.99 (1H, m), 8.55 – 8.57 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 28.7, 41.4, 115.6, 124.5, 125.9, 126.9, 127.5, 128.0, 128.5, 130.2, 132.7, 134.1, 136.2, 137.3, 204.1; **HRMS** (CI+) $C_{15}H_{14}O$ [M]$^+$ requires 210.1039, found 210.1039 (– 0.2 ppm).

<u>^{1}H and ^{13}C NMR spectra of **S19**</u>





1-Phenylhex-5-en-2-one (S20)

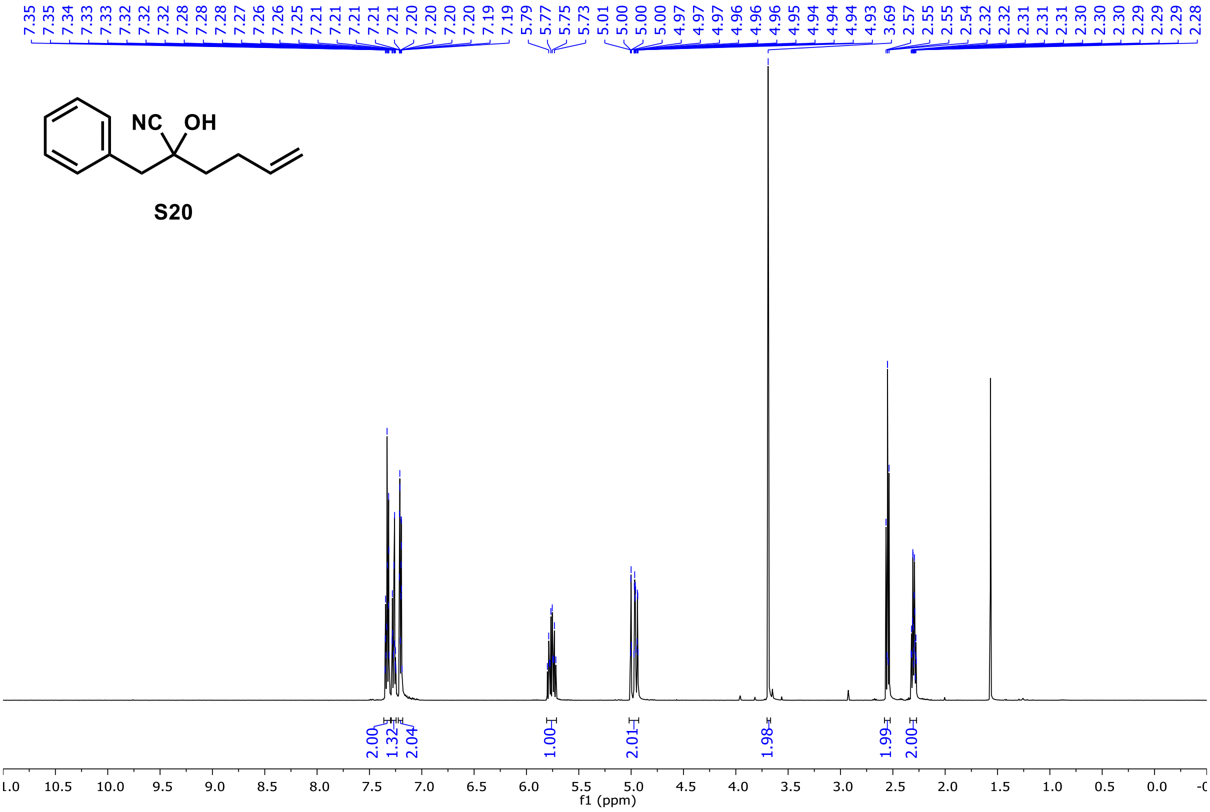


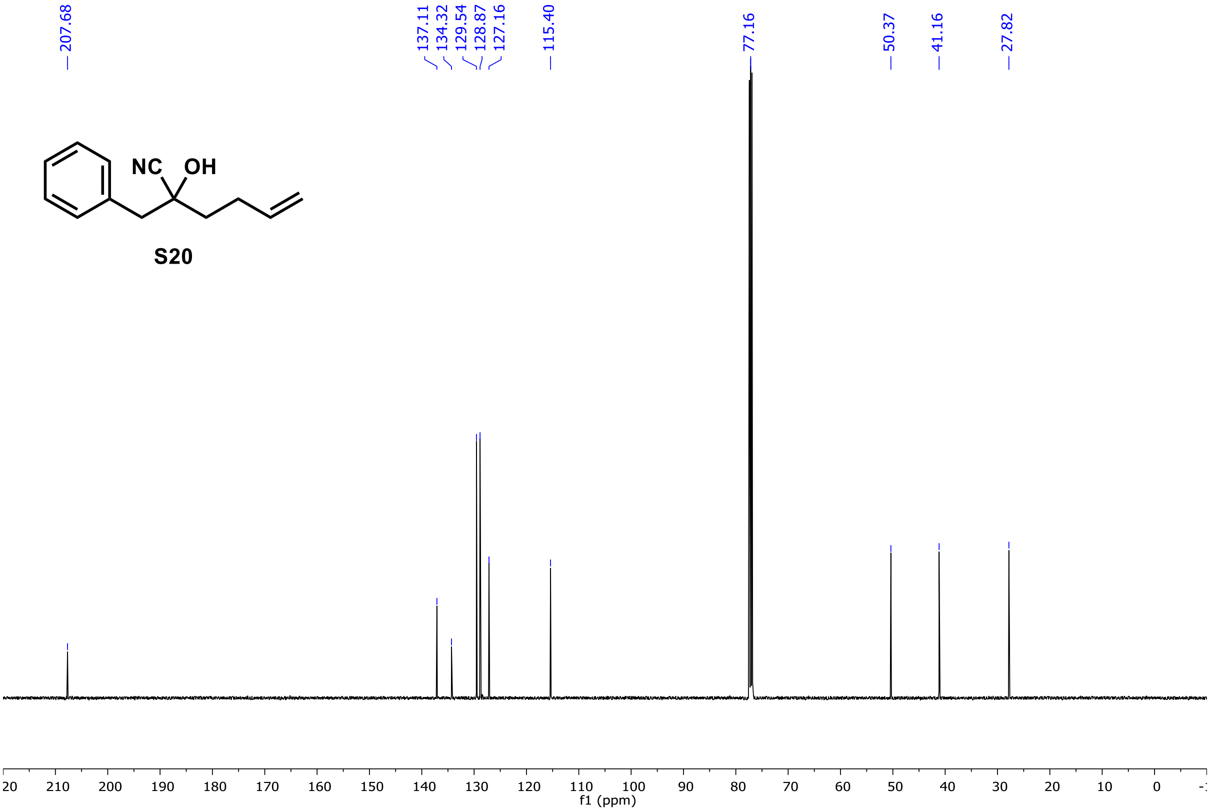
To a flame-dried RBF fitted with a septum seal was added benzyl magnesium chloride (1.4 M in THF, 10.7 mL, 15.0 mmol). After cooling to 0 °C under an N_2 atmosphere, **S1** (1.692 g, 10.0 mmol) in THF (30 mL, 0.3 M) was added dropwise. After complete addition, the resulting mixture was left to warm to rt and stirred overnight. A saturated solution of NH_4Cl (aq.) was added, followed by a few drops of 1 M HCl (aq.), and the mixture was diluted with Et_2O. The layers were separated, and the aqueous layer was further extracted with Et_2O (× 2). The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S20** (503 mg, 28%) as a pale-yellow oil.

R_f = 0.46 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.27 – 2.33 (2H, m), 2.52 – 2.59 (2H, m), 3.69 (2H, s), 4.93 – 5.01 (2H, m), 5.70 – 5.82 (1H, m), 7.19 – 7.22 (2H, m), 7.25 – 7.29 (1H, m), 7.31 – 7.36 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 27.8, 41.2, 50.4, 115.4, 127.2, 128.9, 129.5, 134.3, 137.1, 207.7.

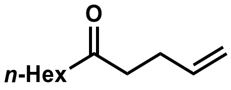
These data are in accordance with the literature.[12]

^{1}H and ^{13}C NMR spectra of **S20**





Undec-1-en-5-one (S21)

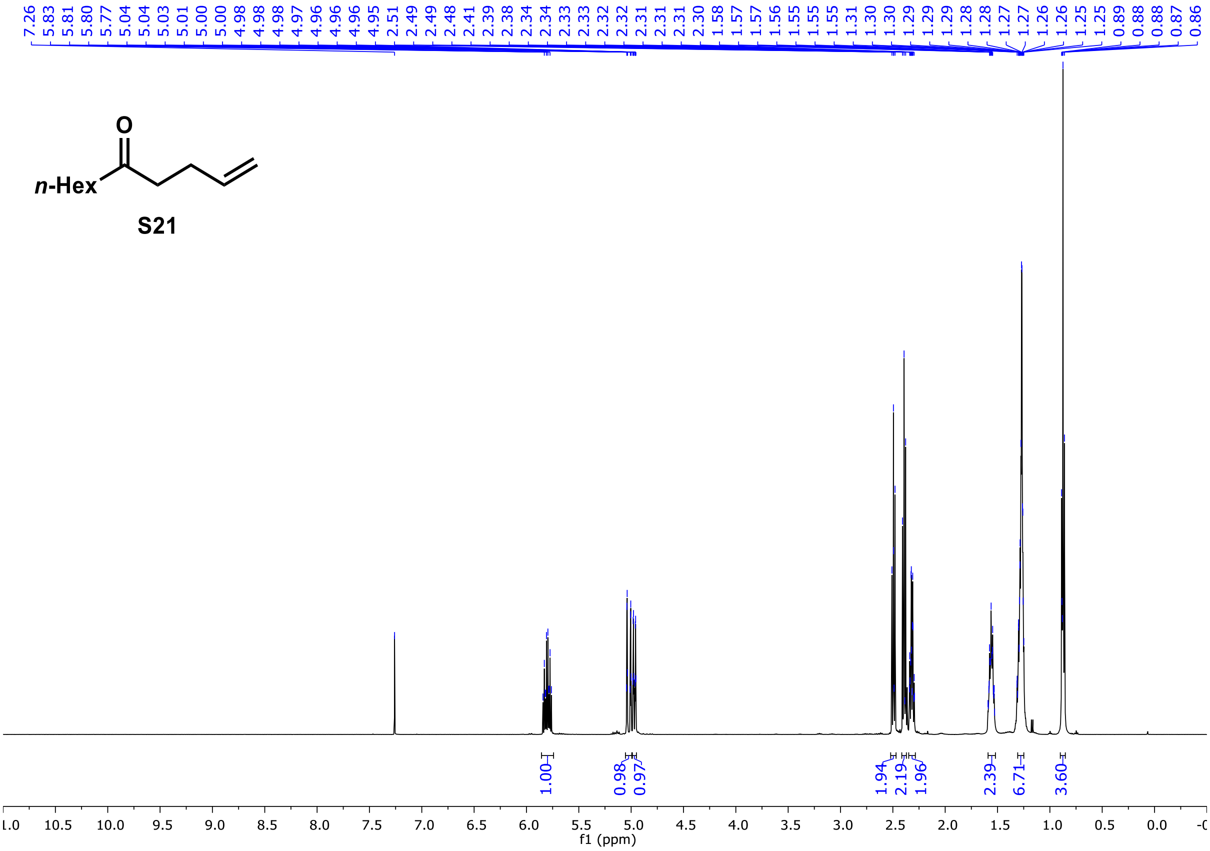


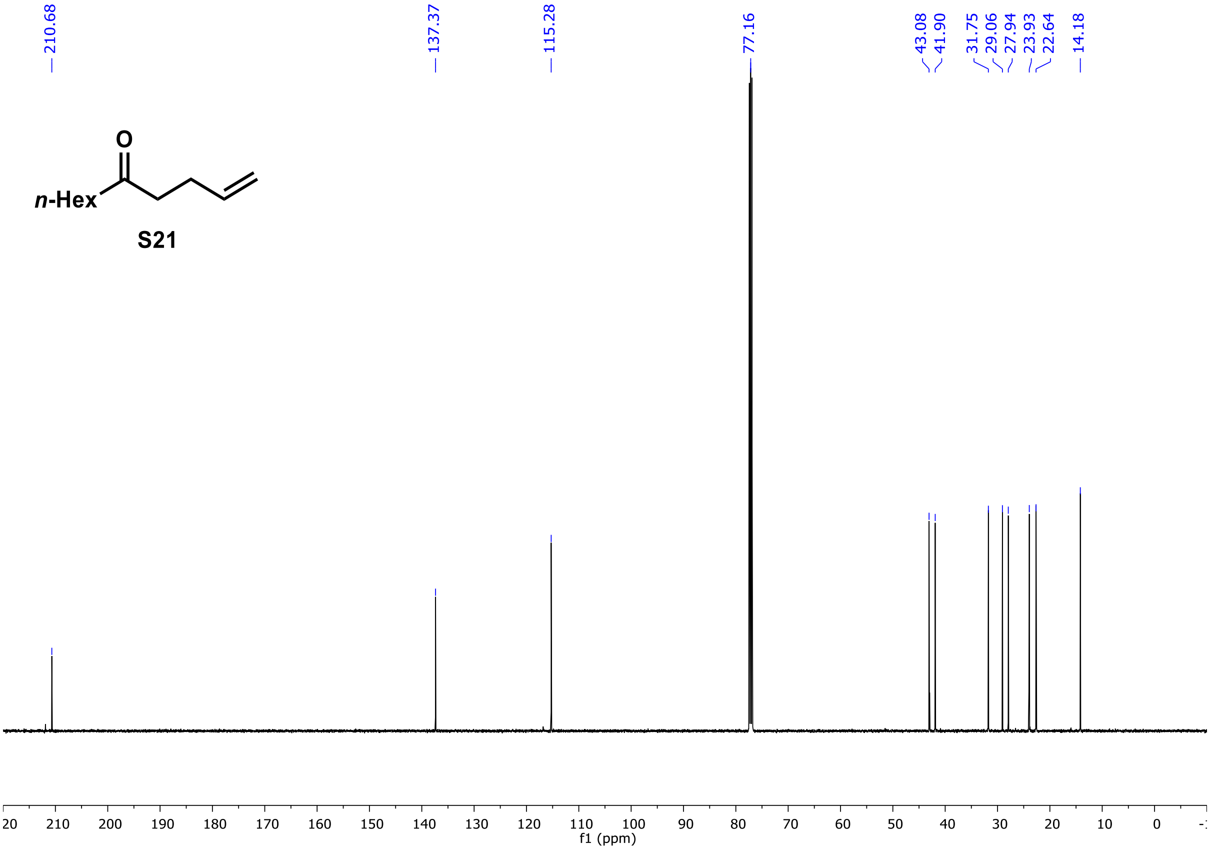
S21

Prepared according to General Procedure 2 using heptanoic acid (4.25 mL, 30.0 mmol), oxalyl chloride (2.83 mL, 33.0 mmol), DMF (3 drops), *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30.0 mmol) in CH_2Cl_2 (70 mL), and triethylamine (12.5 mL, 90.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (401 mg, 16.5 mmol) in THF (15 mL), and 4-bromobut-1-ene (1.52 mL, 15.0 mmol). The alkyl ketone was prepared through the addition of the Weinreb amide (1.73 g, 10.0 mmol) in THF (10 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S21** (1.08 g, 64%) as a colourless oil.

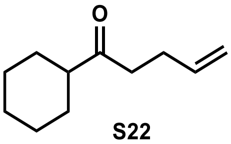
R_f = 0.28 (5% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3078, 2955, 2927, 2856, 1715, 1641, 1458, 1412, 1371, 1130, 1067, 995, 912; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 0.86 – 0.89 (3H, m), 1.25 – 1.31 (6H, m), 1.53 – 1.59 (2H, m), 2.29 – 2.34 (2H, m), 2.38 – 2.41 (2H, m), 2.48 – 2.51 (2H, m), 4.95 – 4.98 (1H, m), 5.00 – 5.04 (1H, m), 5.76 – 5.84 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 14.2, 22.6, 23.9, 27.9, 29.1, 31.8, 41.9, 43.1, 115.3, 137.4, 210.7; **HRMS** (CI+) $C_{11}H_{20}O$ $[M+H]^+$ requires 169.1587, found 169.1587 (– 0.1 ppm).

^{1}H and ^{13}C NMR spectra of **S21**





1-Cyclohexylpent-4-en-1-one (S22)

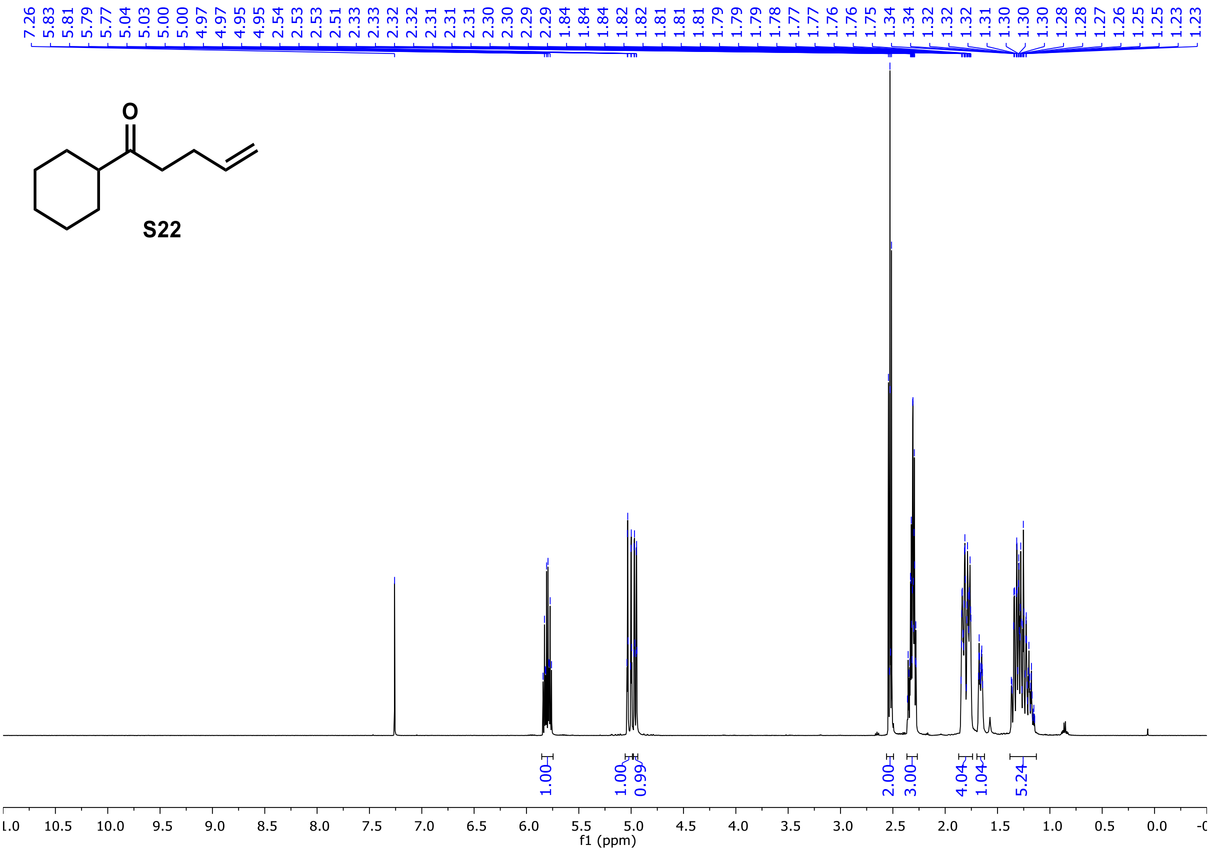

S22

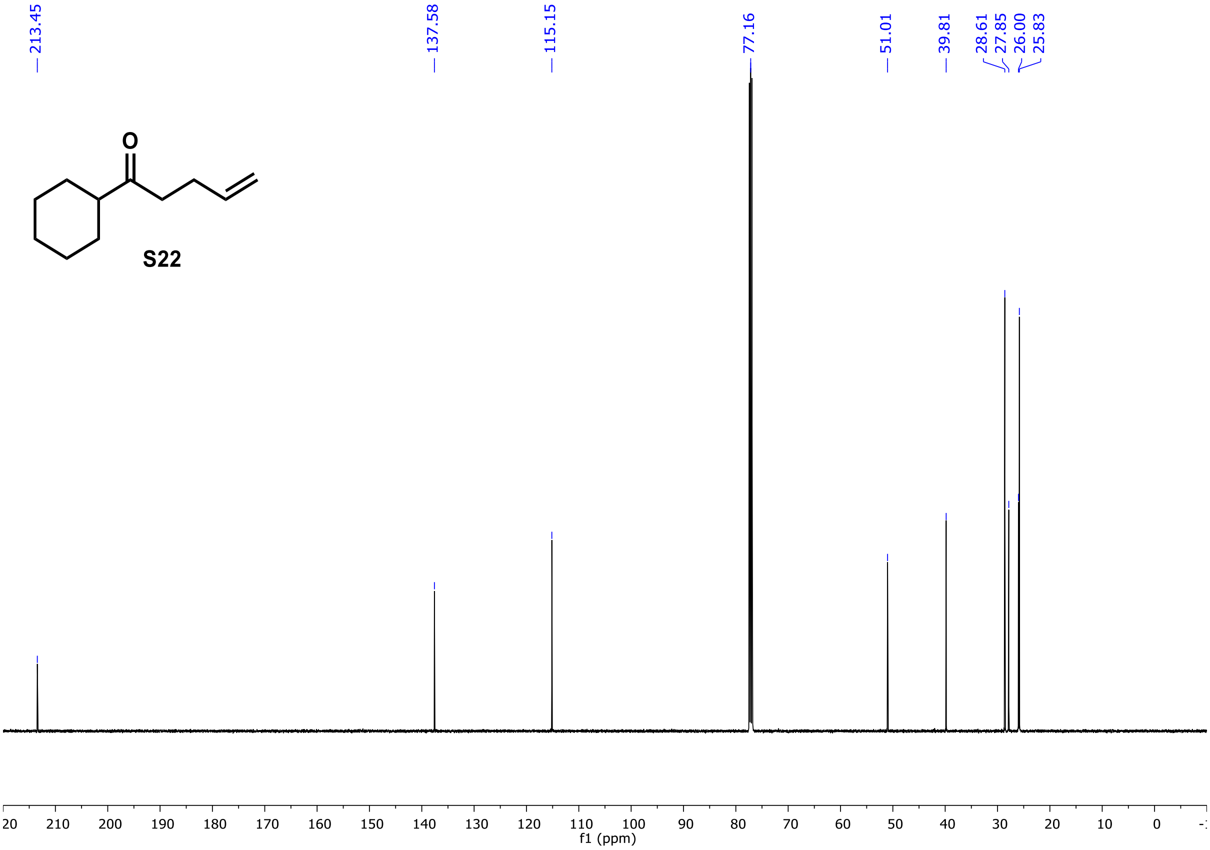
Prepared according to General Procedure 2 using cyclohexanecarboxylic acid (3.80 g, 30.0 mmol), oxalyl chloride (2.83 mL, 33.0 mmol), DMF (3 drops), *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30.0 mmol) in CH_2Cl_2 (70 mL), and triethylamine (12.5 mL, 90.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (401 mg, 16.5 mmol) in THF (15 mL), and 4-bromobut-1-ene (1.52 mL, 15.0 mmol). The alkyl ketone was prepared through the addition of the Weinreb amide (1.60 g, 10.0 mmol) in THF (10 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S22** (450 mg, 27%) as a colourless oil.

R_f = 0.26 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.15 – 1.37 (5H, m), 1.64 – 1.68 (1H, m), 1.75 – 1.85 (4H, m), 2.28 – 2.36 (3H, m), 2.51 – 2.54 (2H, m), 4.94 – 4.97 (1H, m), 5.00 – 5.04 (1H, m), 5.76 – 5.84 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 25.8, 26.0, 27.9, 28.6, 39.8, 51.0, 115.2, 137.6, 213.5.

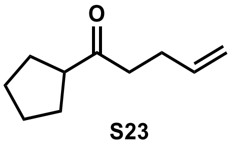
These data are in accordance with the literature.[13]

^{1}H and ^{13}C NMR spectra of **S22**





1-Cyclopentylpent-4-en-1-one (S23)



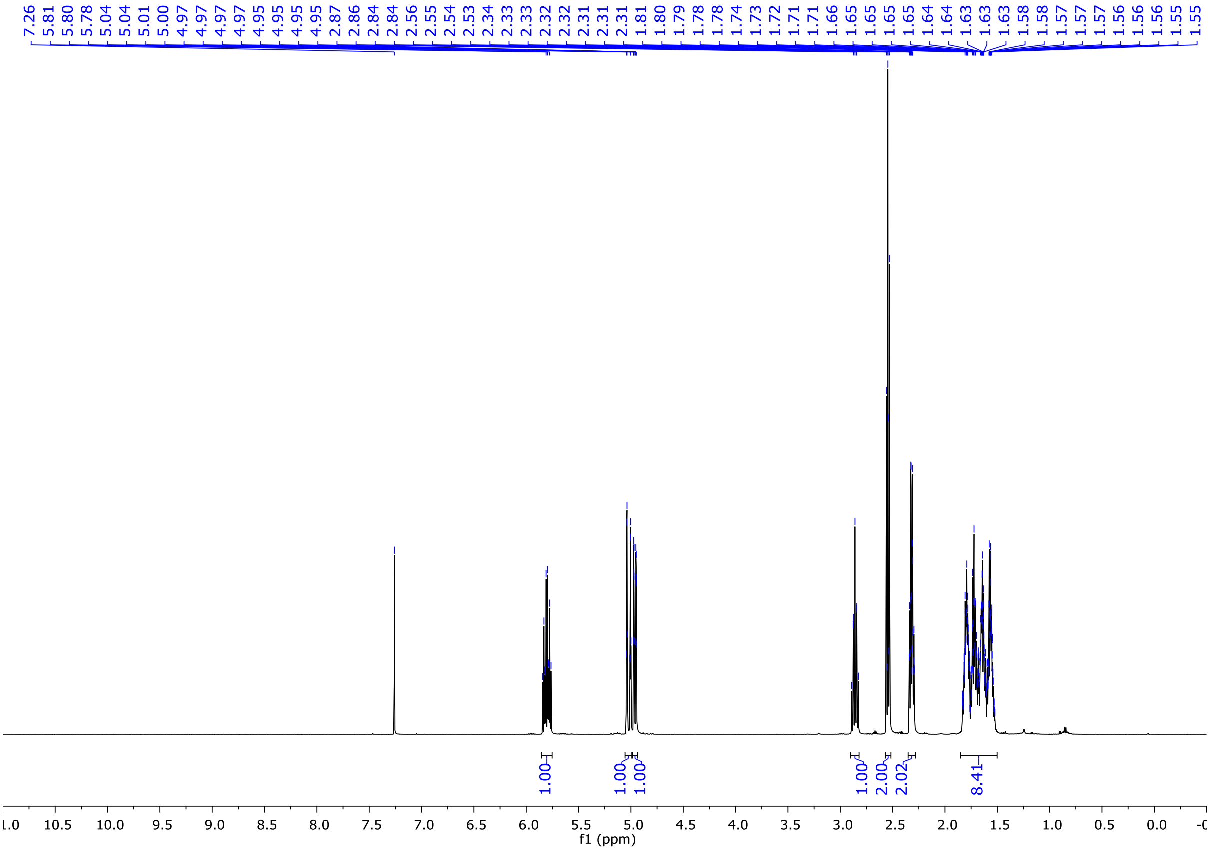
S23

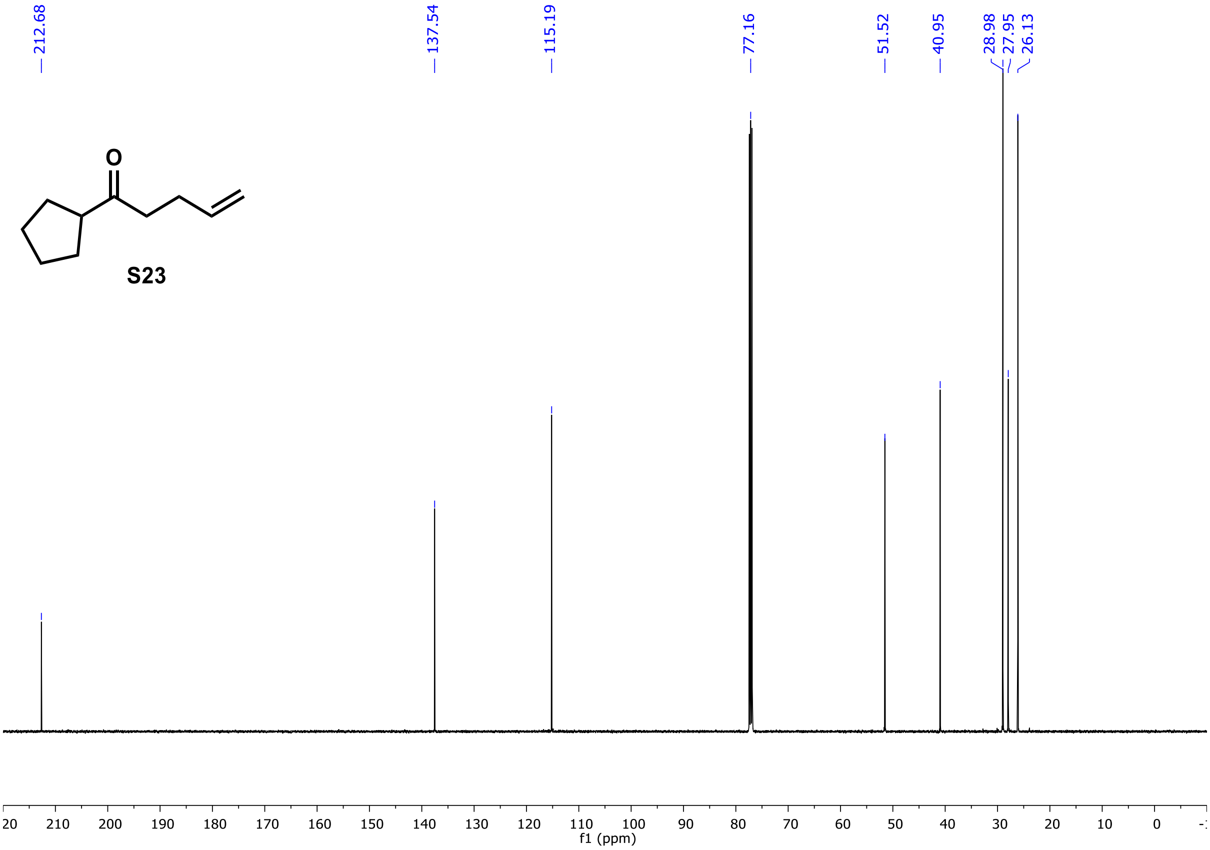
Prepared according to General Procedure 2 using cyclopentanecarboxylic acid (3.60 mL, 30.0 mmol), oxalyl chloride (2.83 mL, 33.0 mmol), DMF (3 drops), *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30.0 mmol) in CH_2Cl_2 (70 mL), and triethylamine (12.5 mL, 90.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (401 mg, 16.5 mmol) in THF (15 mL), and 4-bromobut-1-ene (1.52 mL, 15.0 mmol). The alkyl ketone was prepared through the addition of the Weinreb amide (1.60 g, 10.0 mmol) in THF (10 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S23** (920 mg, 60%) as a colourless oil.

R_f = 0.42 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.55 – 1.83 (8H, m), 2.29 – 2.34 (2H, m), 2.53 – 2.56 (2H, m), 2.83 – 2.89 (1H, m), 4.95 – 4.98 (1H, m), 5.00 – 5.04 (1H, m), 5.76 – 5.84 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 26.1, 27.9, 29.0, 40.9, 51.5, 115.2, 137.5, 212.7.

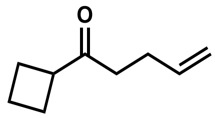
These data are in accordance with the literature.[14]

^{1}H and ^{13}C NMR spectra of **S23**





1-Cyclobutylpent-4-en-1-one (S24)

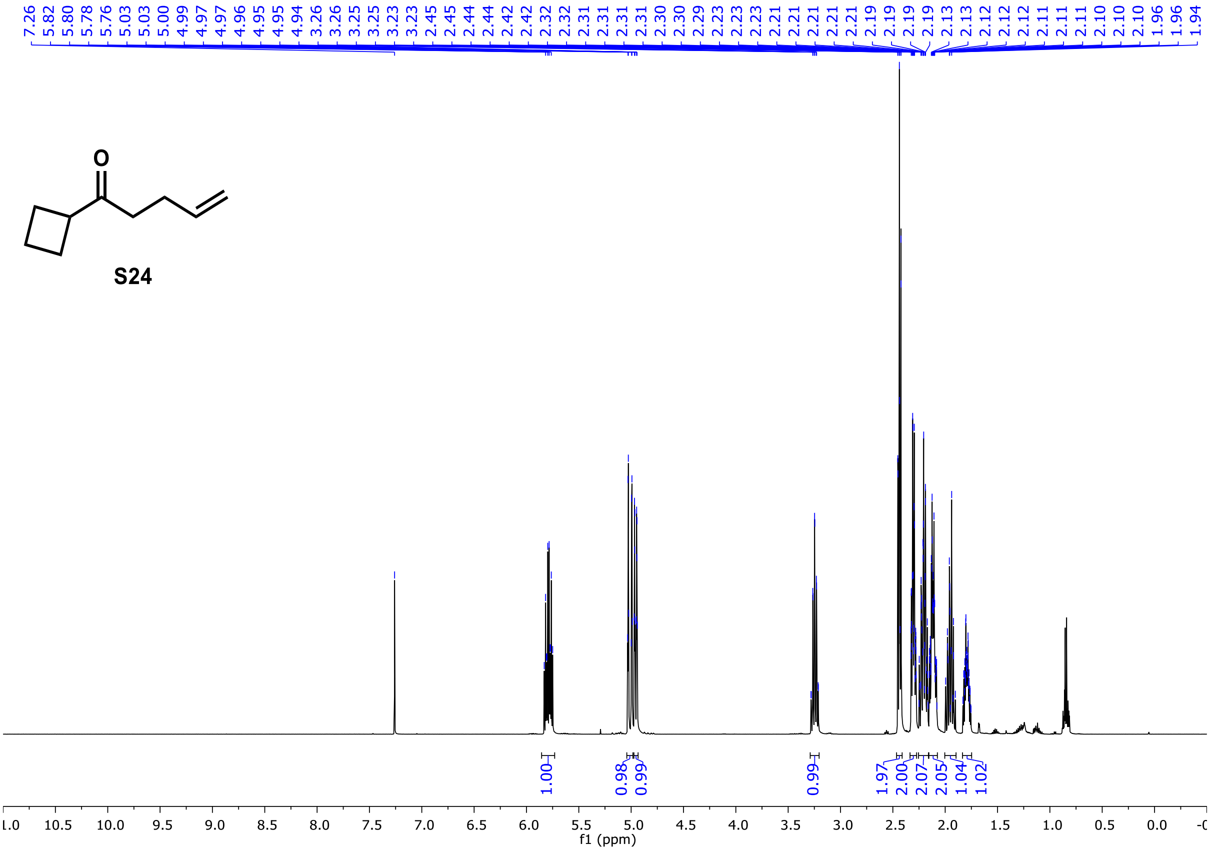


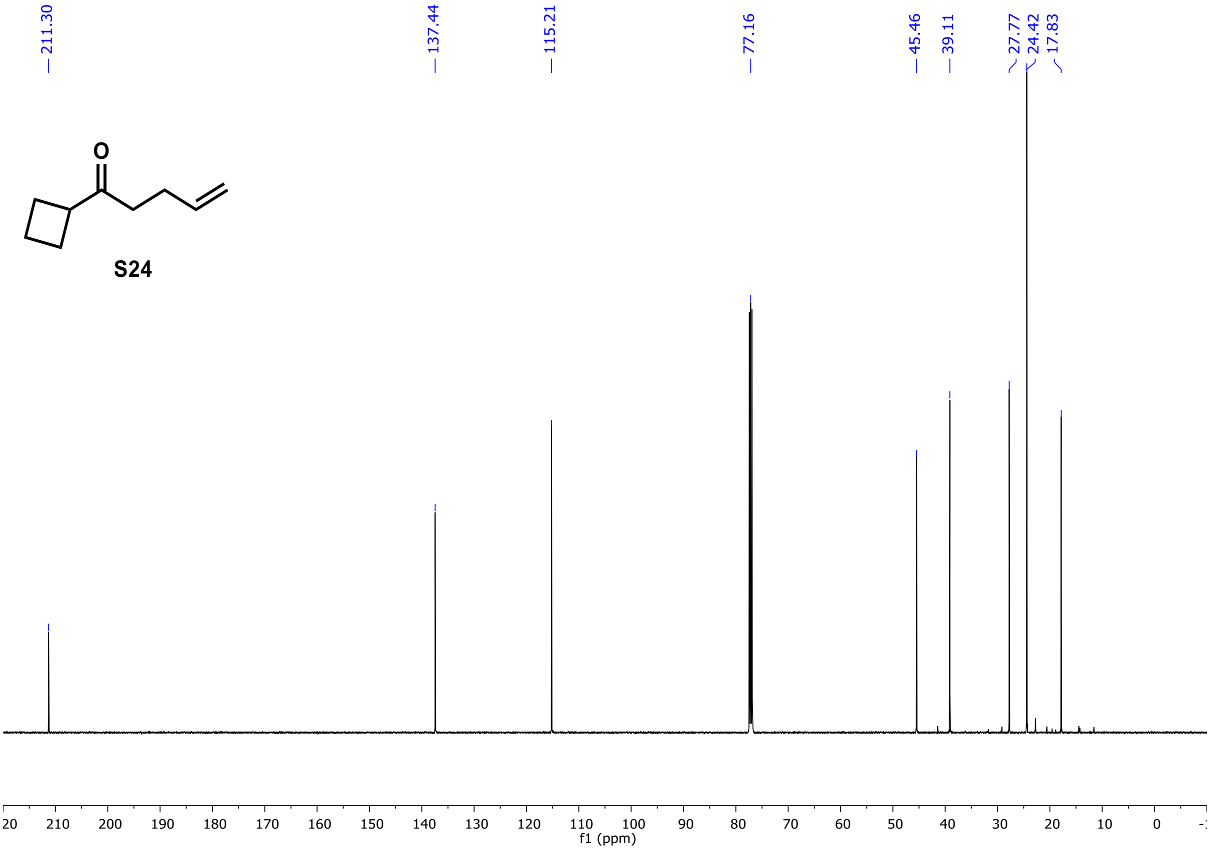
S24

Prepared according to General Procedure 2 using cyclobutanecarboxylic acid (2.40 mL, 25.0 mmol), oxalyl chloride (2.39 mL, 27.5 mmol), DMF (3 drops), *N*,*O*-dimethylhydroxylamine hydrochloride (2.44 g, 25.0 mmol) in CH_2Cl_2 (60 mL), and triethylamine (10.5 mL, 75.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (1.00 g, 41.3 mmol) in THF (40 mL), and 4-bromobut-1-ene (3.80 mL, 37.5 mmol). The alkyl ketone was prepared through the addition of the Weinreb amide in THF (25 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S24** (890 mg, 63%) as a colourless oil.

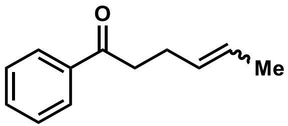
R_f = 0.39 (5% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 2980, 2943, 1705, 1641, 1437, 1410, 1367, 1244, 1123, 995, 912; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.75 – 1.83 (1H, m), 1.90 – 2.00 (1H, m), 2.08 – 2.15 (2H, m), 2.16 – 2.25 (2H, m), 2.28 – 2.33 (2H, m), 2.42 – 2.45 (2H, m), 3.21 – 3.28 (1H, m), 4.94 – 4.97 (1H, m), 4.99 – 5.03 (1H, m), 5.75 – 5.83 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 17.8, 24.4, 27.8, 39.1, 45.5, 115.2, 137.4, 211.3; **HRMS** (CI+) $C_9H_{14}O$ $[M+H]^+$ requires 139.1117, found 139.1117 (± 0.0 ppm).

^{1}H and ^{13}C NMR spectra of **S24**





1-Phenylhex-4-en-1-one (S25)



S25

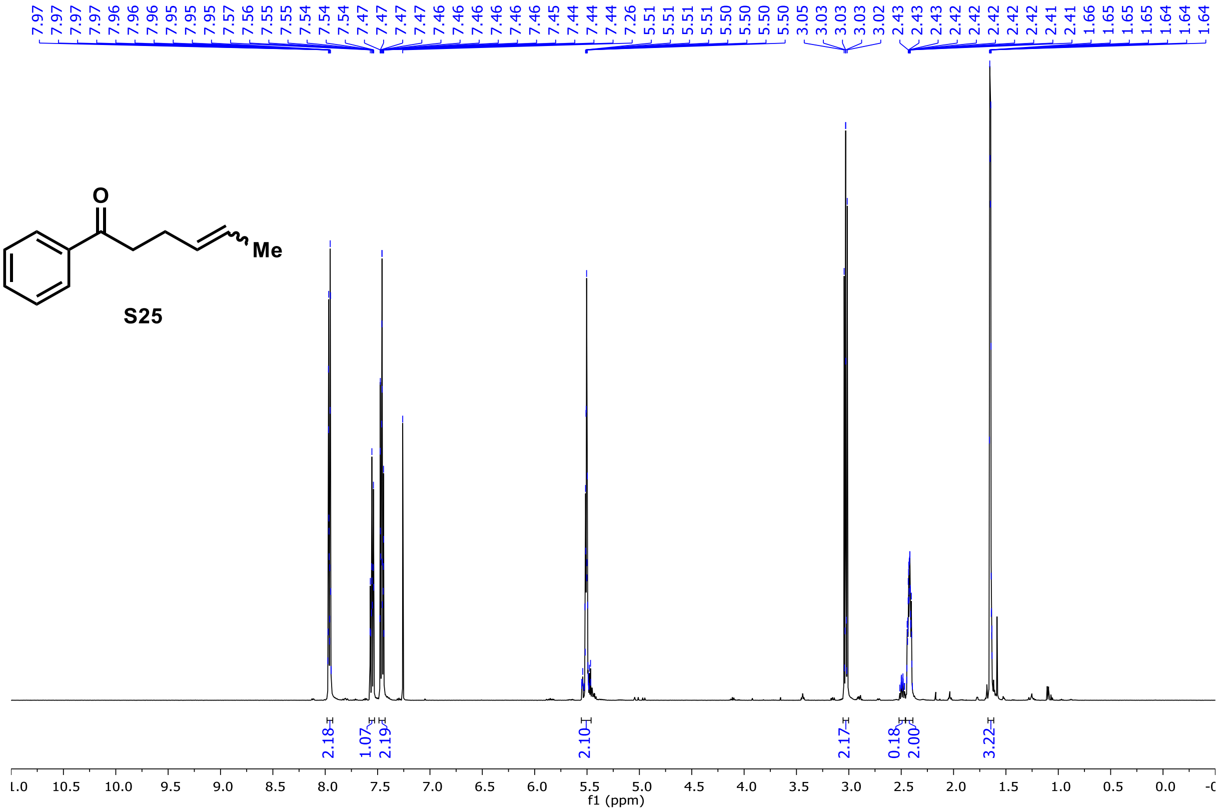
Prepared according to General Procedure 4 using ethylbenzoyl acetate (866 μL, 5.00 mmol) in THF (25 mL), sodium hydride (60% dispersion in mineral oil, 200 mg, 5.00 mmol), and 1-bromobut-2-ene (*E*:*Z* ratio = 93:7, 743 mg, 5.50 mmol). The crude product was dissolved in 2:1 MeOH/water (50 mL), and treated with NaOH (800 mg, 20.0 mmol). The resultant crude material was purified by flash column chromatography (2.5% EtOAc/petrol, silica gel) to afford **S25** (473 mg, 55%) as a low-melting white solid with an approximate *E*:*Z* ratio of 92:8.

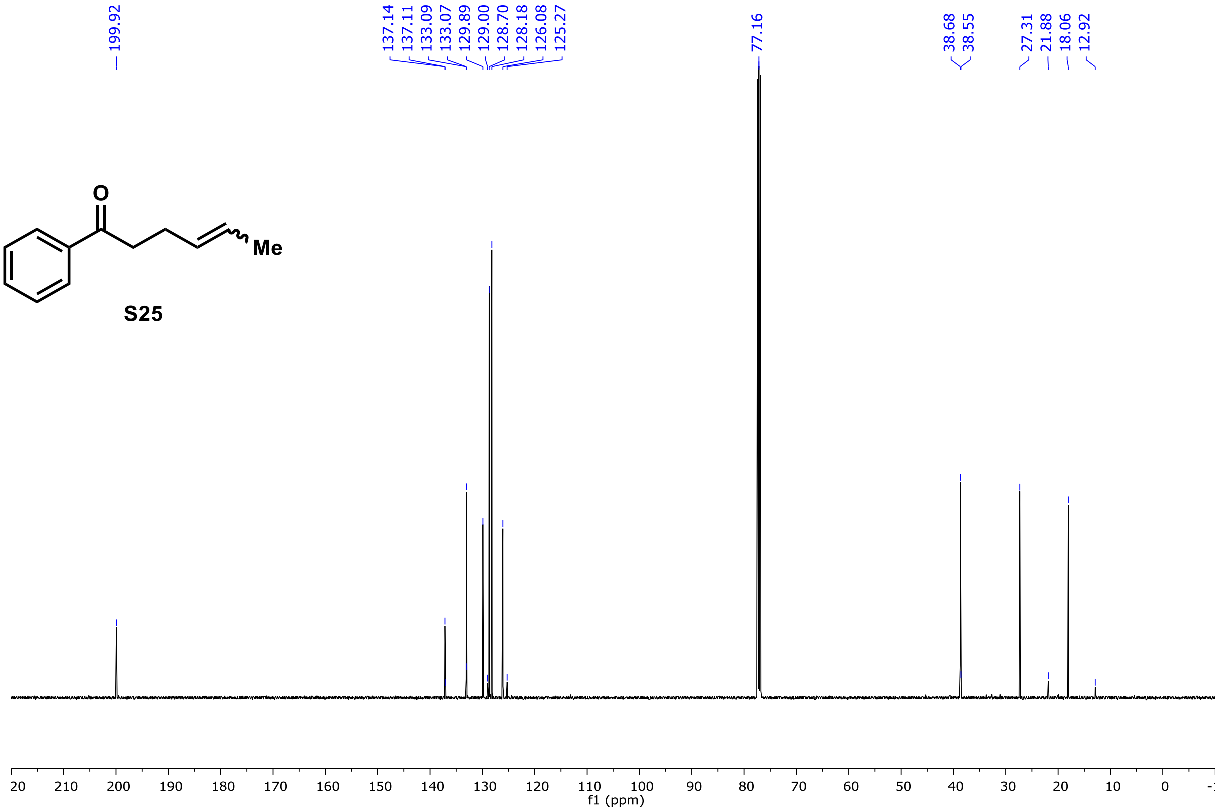
R_f = 0.60 (5% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 2920, 1680, 1449, 1368, 1202, 970, 737, 685; **HRMS** (ES+) $C_{12}H_{14}O$ $[M+H]^+$ requires 175.1123, found 175.1116 (– 4.0 ppm).

Data for (*E*)*-isomer:* **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.63 – 1.66 (3H, m), 2.39 – 2.45 (2H, m), 3.00 – 3.06 (2H, m), 5.46 – 5.56 (2H, m), 7.42 – 7.50 (2H, m), 7.52 – 7.59 (1H, m), 7.94 – 7.98 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 18.1, 27.3, 38.7, 126.1, 128.2, 128.7, 129.9, 133.1, 137.1, 199.9;

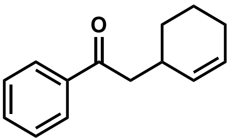
Data for (*Z*)*-isomer (selected):* **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.47 – 2.51 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 12.9, 21.9, 38.6, 125.3, 129.0, 133.1, 137.1.

¹H and ¹³C NMR spectra of **S25**





2-(Cyclohex-2-en-1-yl)-1-phenylethan-1-one (S26)



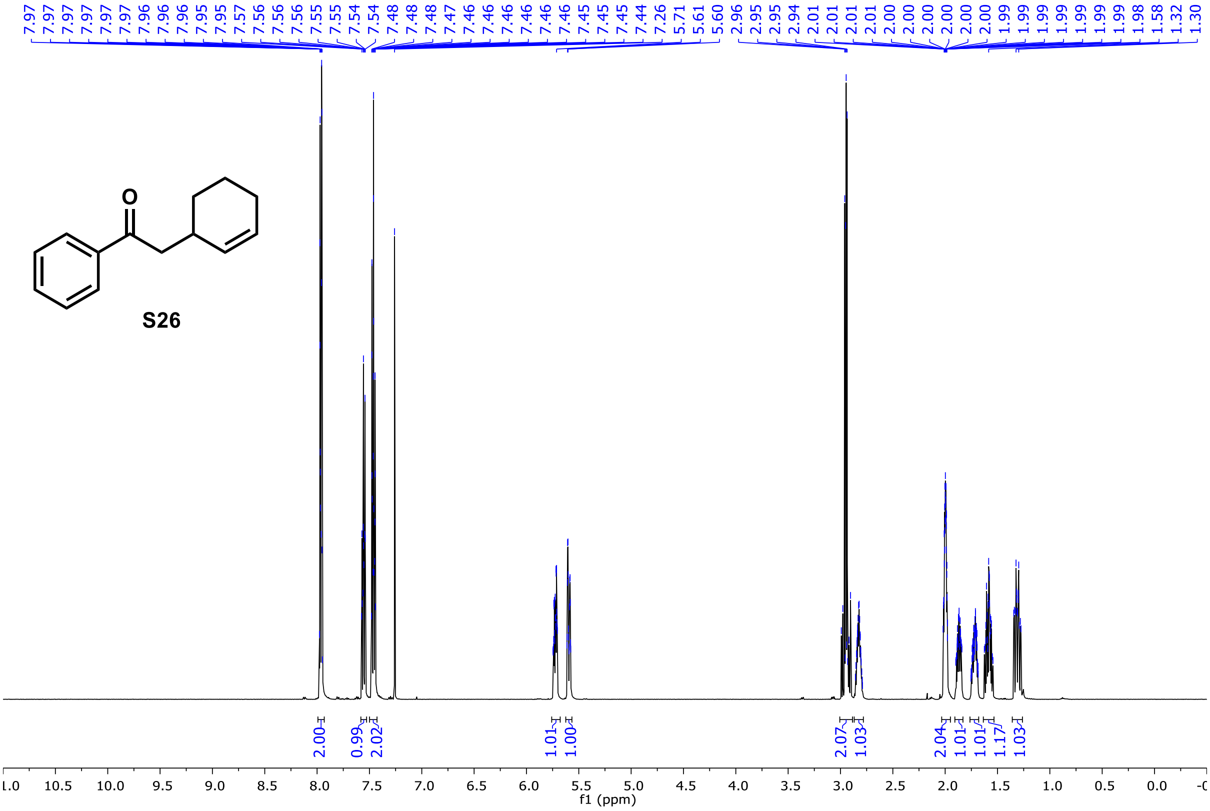
S26

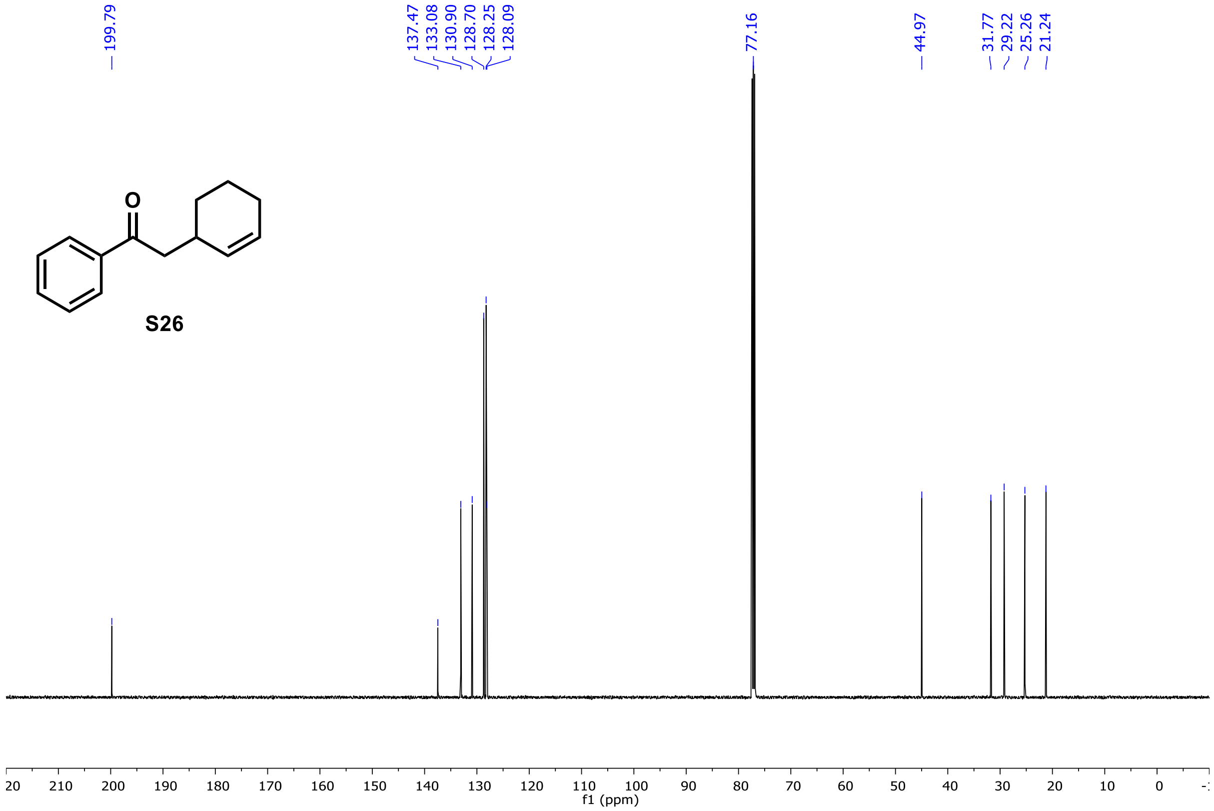
Prepared according to General Procedure 4 using ethylbenzoyl acetate (866 µL, 5.00 mmol) in THF (25 mL), sodium hydride (60% dispersion in mineral oil, 200 mg, 5.00 mmol), and 3-bromocyclohexene (633 µL, 5.50 mmol). The crude product was dissolved in 2:1 MeOH/water (50 mL), and treated with NaOH (800 mg, 20.0 mmol). The resultant crude material was purified by flash column chromatography (2.5% EtOAc/petrol, silica gel) to afford **S26** (626 mg, 63%) as a white solid.

R$_f$ = 0.66 (5% EtOAc/petrol); **M.p.:** 39-41 °C; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.26 – 1.36 (1H, m), 1.52 – 1.65 (1H, m), 1.66 – 1.77 (1H, m), 1.82 – 1.92 (1H, m), 1.96 – 2.04 (2H, m), 2.77 – 2.86 (1H, m), 2.89 – 3.01 (2H, m), 5.56 – 5.63 (1H, m), 5.68 – 5.77 (1H, m), 7.42 – 7.50 (2H, m), 7.52 – 7.59 (1H, m), 7.93 – 8.00 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 21.2, 25.3, 29.2, 31.8, 45.0, 128.1, 128.3, 128.7, 130.9, 133.1, 137.5, 199.8.

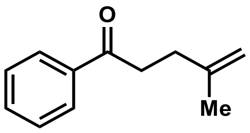
These data are in accordance with the literature.[15]

<u>^{1}H and ^{13}C NMR spectra of **S26**</u>





4-Methyl-1-phenylpent-4-en-1-one (S27)



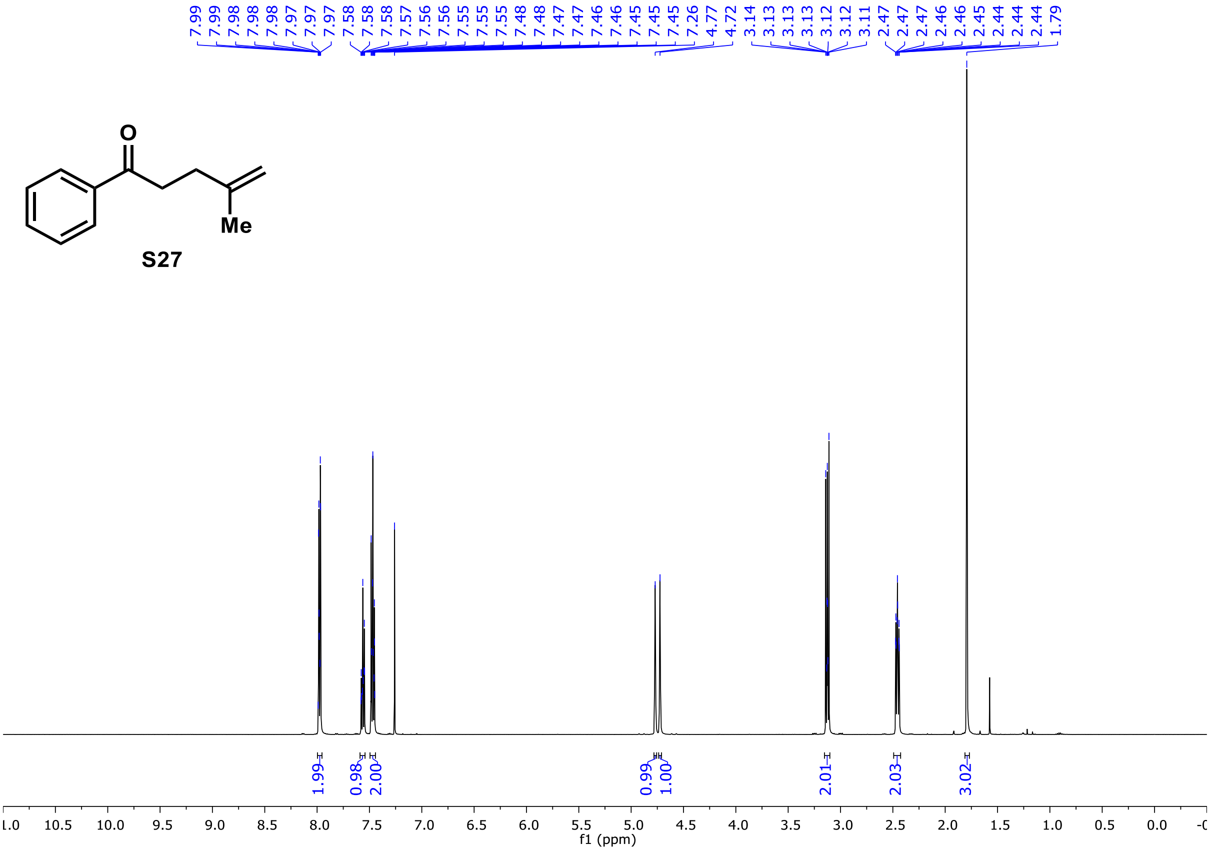
S27

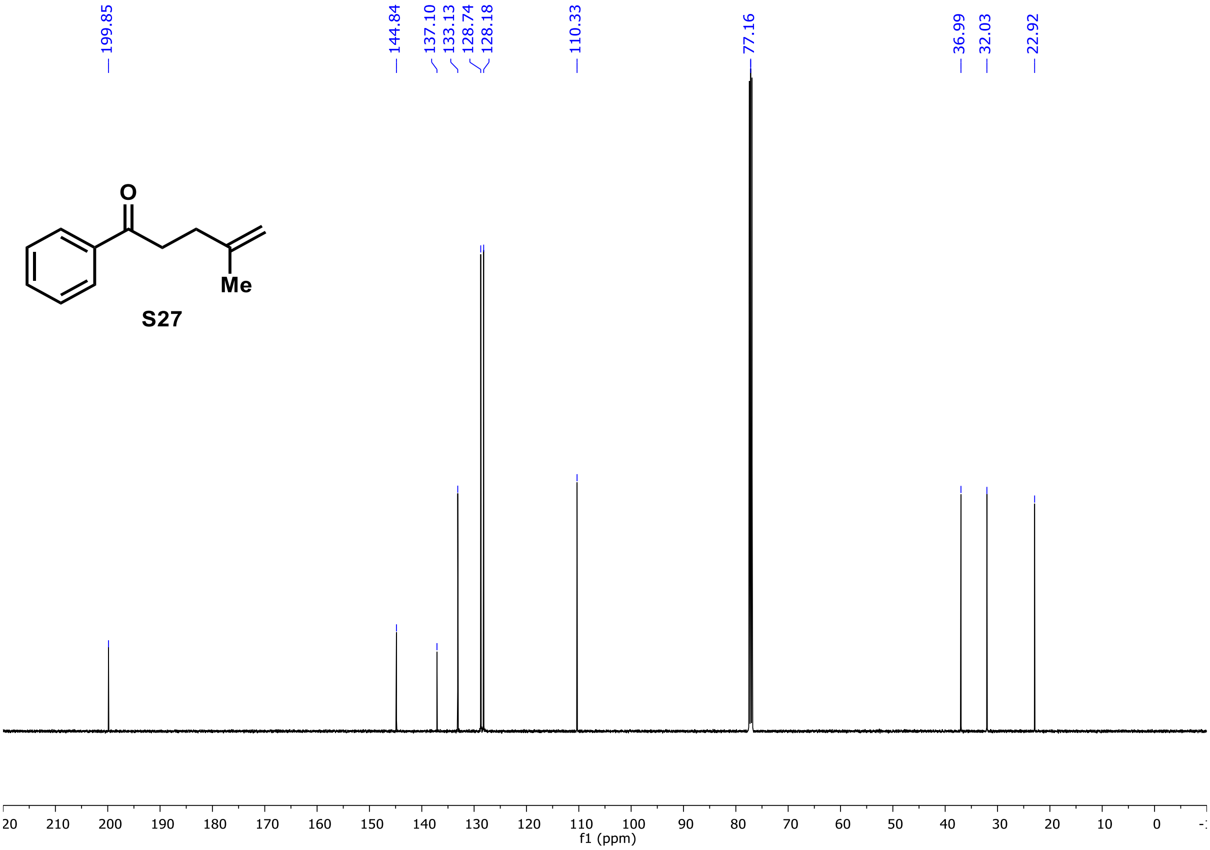
Prepared according to General Procedure 4 using ethylbenzoyl acetate (1.73 mL, 10.0 mmol) in THF (50 mL), sodium hydride (60% dispersion in mineral oil, 400 mg, 10.0 mmol), and 3-bromo-2-methylprop-1-ene (1.11 mL, 11.0 mmol). The crude product was dissolved in 2:1 MeOH/water (100 mL), and treated with NaOH (1.60 g, 40.0 mmol). The resultant crude material was purified by flash column chromatography (2% EtOAc/petrol, silica gel) to afford **S27** (1.09 g, 63%) as a yellow oil.

R_f = 0.56 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.79 (3H, s), 2.44 – 2.47 (2H, m), 3.11 – 3.14 (2H, m), 4.72 (1H, app s), 4.77 (1H, app s), 7.45 – 7.48 (2H, m), 7.55 – 7.58 (1H, m), 7.97 – 7.99 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 22.9, 32.0, 37.0, 110.3, 128.2, 128.7, 133.1, 137.1, 144.8, 199.9.

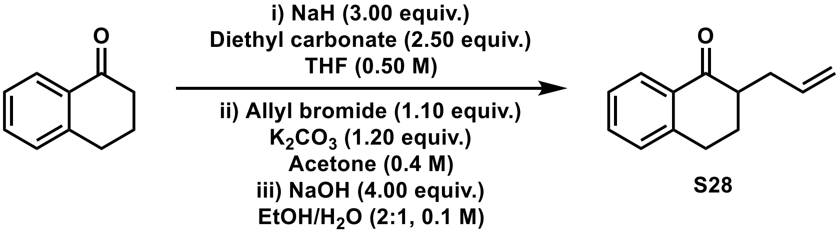
These data are in accordance with the literature.[16]

^{1}H and ^{13}C NMR spectra of **S27**





2-Allyl-3,4-dihydronaphthalen-1(2*H*)-one (S28)



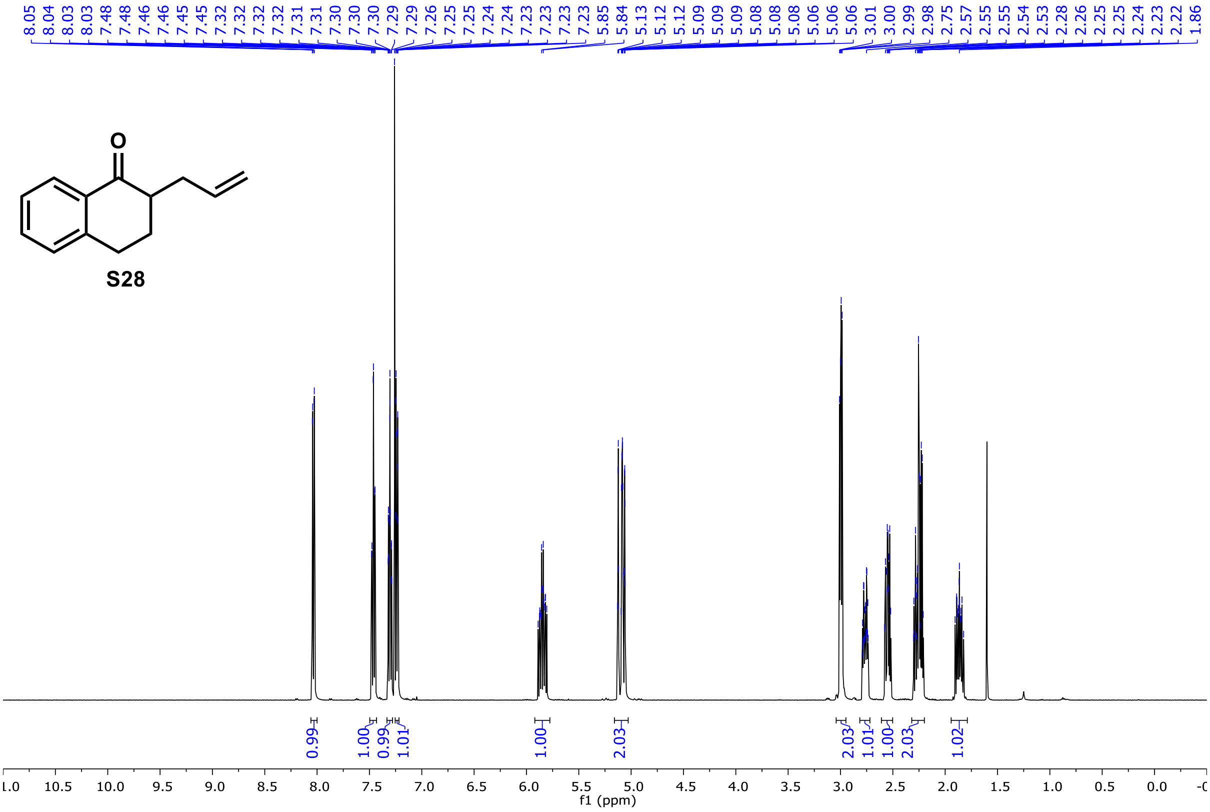
To a flame-dried RBF was added NaH (60% suspension in mineral oil, 1.20 g, 30.0 mmol) in THF (20 mL). The suspension was cooled to 0 °C, diethyl carbonate (5.46 mL, 25.0 mmol) was added and the mixture was stirred at 0 °C for 30 min. α-Tetralone (1.33 mL, 10.0 mmol) was added dropwise, and the mixture was refluxed for 4 h. Upon cooling, a saturated solution of $NaHCO_3$ (aq.) was added. The layers were separated, and the aqueous layer was further extracted with Et_2O (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude *β*-ketoester that was used without further purification.

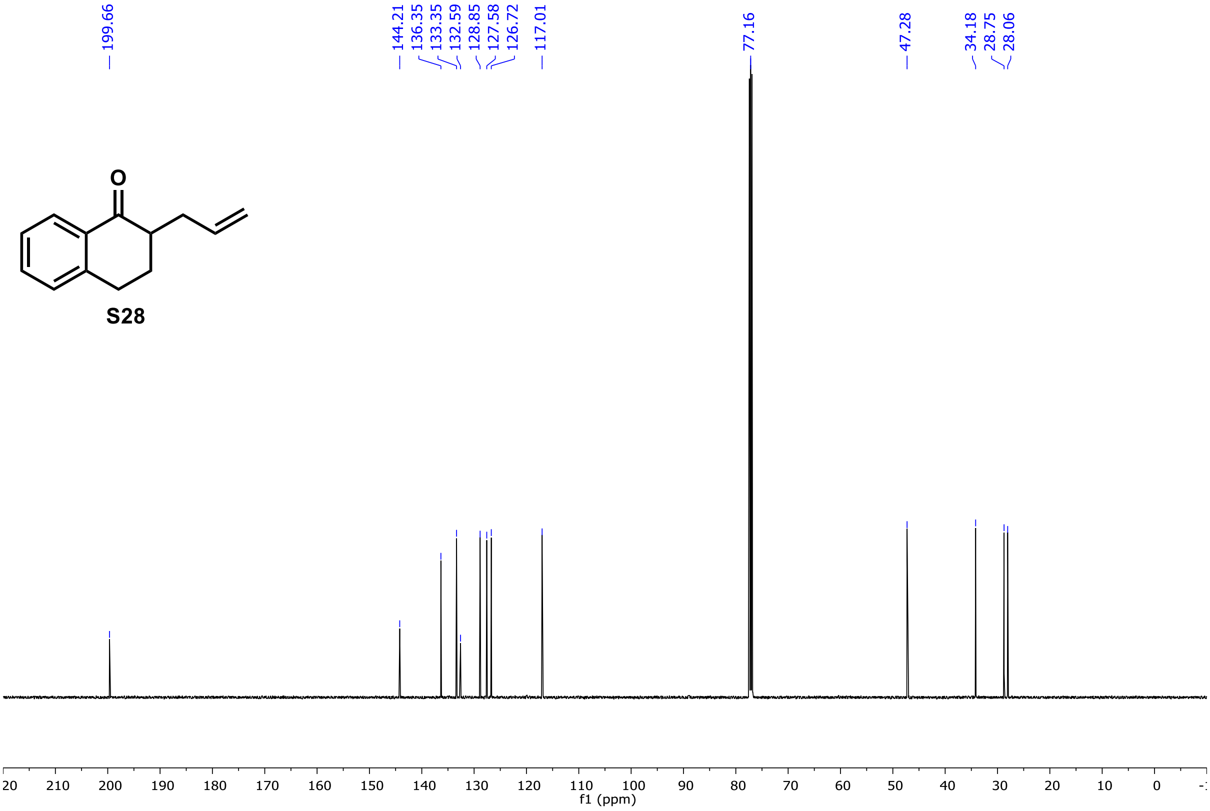
The *β*-ketoester was dissolved in acetone (25 mL), then allyl bromide (952 μL, 11.0 mmol) and K_2CO_3 (1.66 g, 12.0 mmol) were added, and the resulting suspension was refluxed overnight. Upon cooling, the mixture was filtered, and the filtrate was concentrated under reduced pressure. The crude oil was then dissolved in a 2:1 mixture of $EtOH/H_2O$ (100 mL), NaOH (1.60 g, 40.0 mmol) was added, and the reaction was heated to reflux overnight. Upon cooling to rt the solution was concentrated under reduced pressure. EtOAc was added, the layers were separated, and the aqueous layer was further extracted with EtOAc (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography (5% EtOAc/petrol, silica gel) to afford **S28** (560 mg, 30%) as a colourless oil.

R_f = 0.42 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.82 – 1.91 (1H, m), 2.21 – 2.30 (2H, m), 2.52 – 2.58 (1H, m), 2.74 – 2.79 (1H, m), 2.98 – 3.01 (2H, m), 5.06 – 5.13 (2H, m), 5.81 – 5.89 (1H, m), 7.23 – 7.26 (1H, m), 7.29 – 7.32 (1H, m), 7.45 – 7.48 (1H, app td, *J* 7.5, 1.5), 8.03 – 8.05 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.1, 28.8, 34.2, 47.3, 117.0, 126.7, 127.6, 128.9, 132.6, 133.4, 136.4, 144.2, 199.7.

These data are in accordance with the literature.[17]

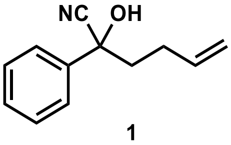
^{1}H and ^{13}C NMR spectra of **S28**





2.3 Characterisation of Substrates

2-Hydroxy-2-phenylhex-5-enenitrile (1)



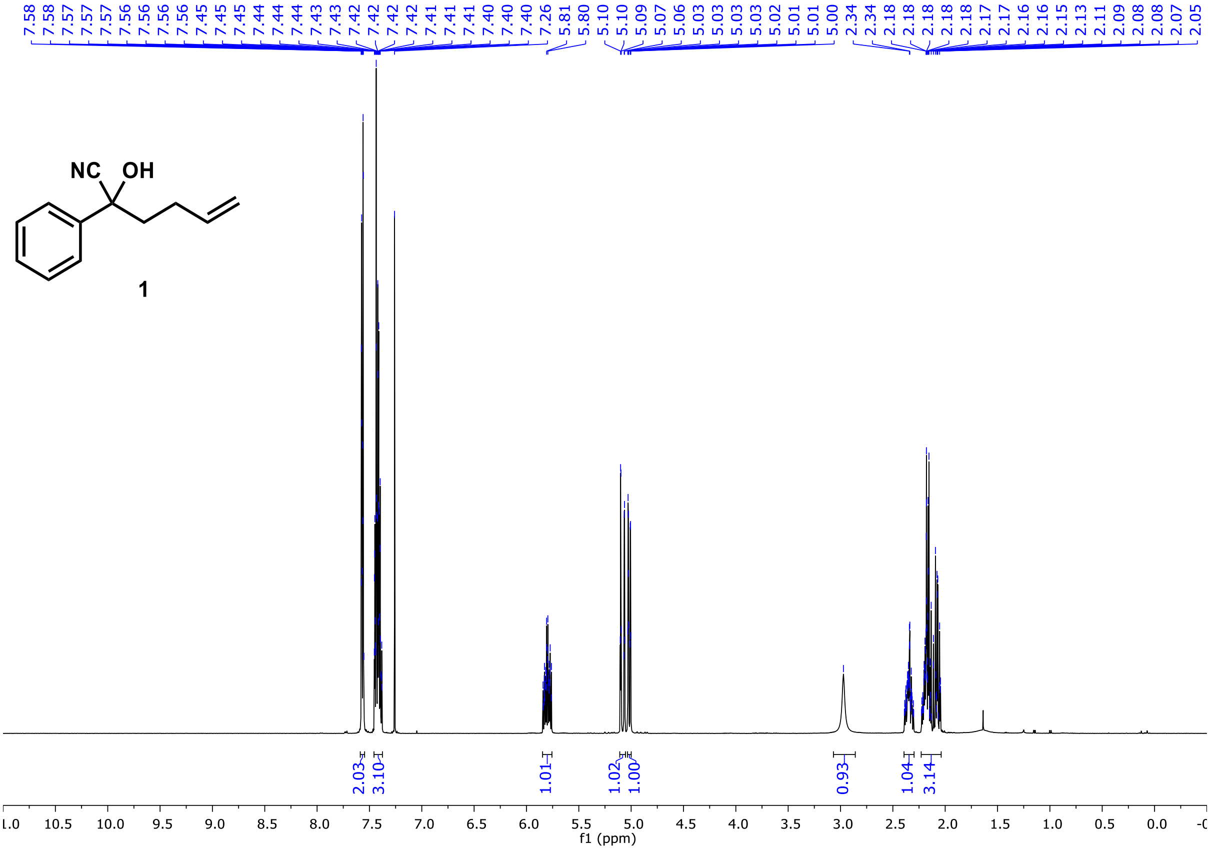
1

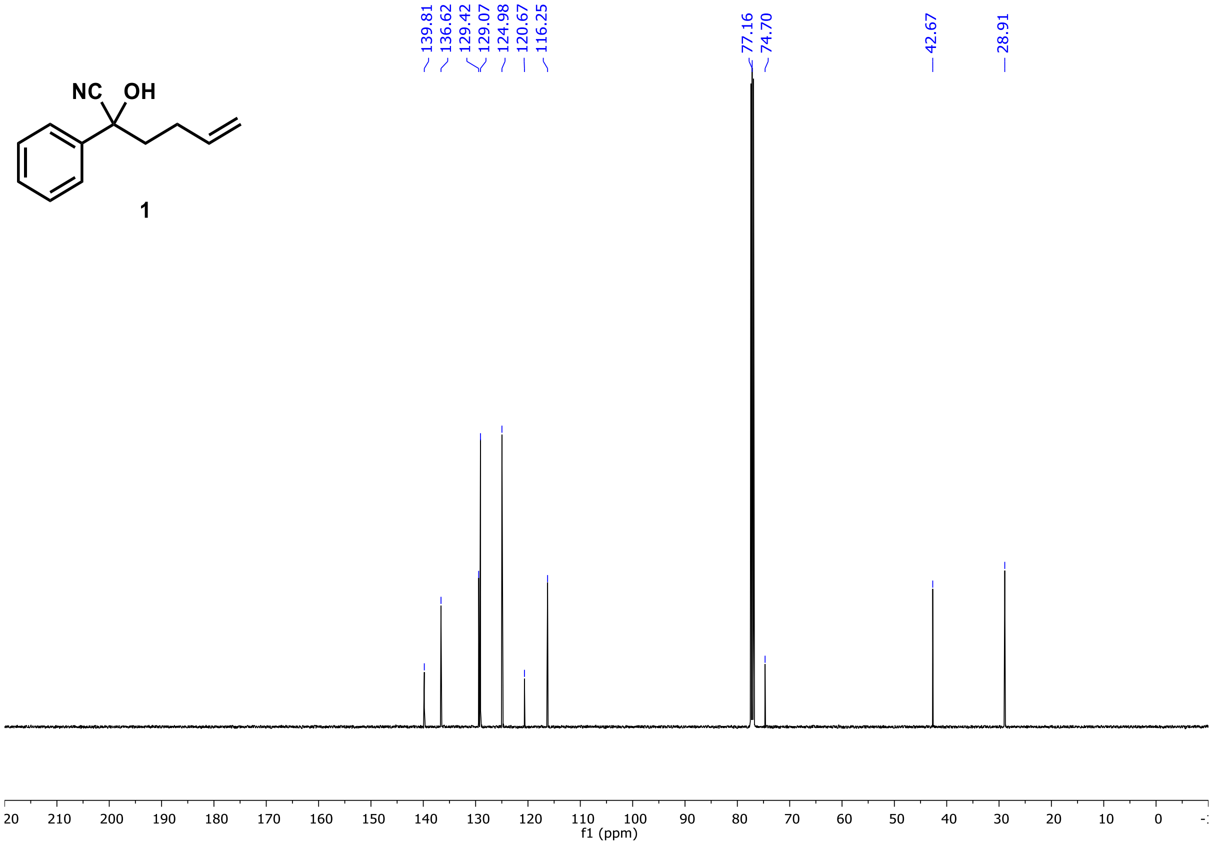
Prepared according to General Procedure 5 using **S2** (5.77 g, 36.0 mmol) in CH_2Cl_2 (72 mL), trimethylsilyl cyanide (11.3 mL, 90.0 mmol), and $TiCl_4$ (2.00 mL, 18.0 mmol), followed by MeCN (180 mL) and 2 M HCl (180 mL) to afford **1** (6.68 g, 99%) as a yellow oil that was used without further purification.

R_f = 0.22 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.04 – 2.23 (3H, m), 2.30 – 2.39 (1H, m), 2.97 (1H, br s), 5.00 – 5.03 (1H, m), 5.04 – 5.12 (1H, m), 5.76 – 5.85 (1H, m), 7.38 – 7.46 (3H, m), 7.55 – 7.58 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.9, 42.7, 74.7, 116.3, 120.7, 125.0, 129.1, 129.4, 136.6, 139.8.

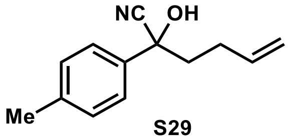
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **1**





2-Hydroxy-2-(*p*-tolyl)hex-5-enenitrile (S29)



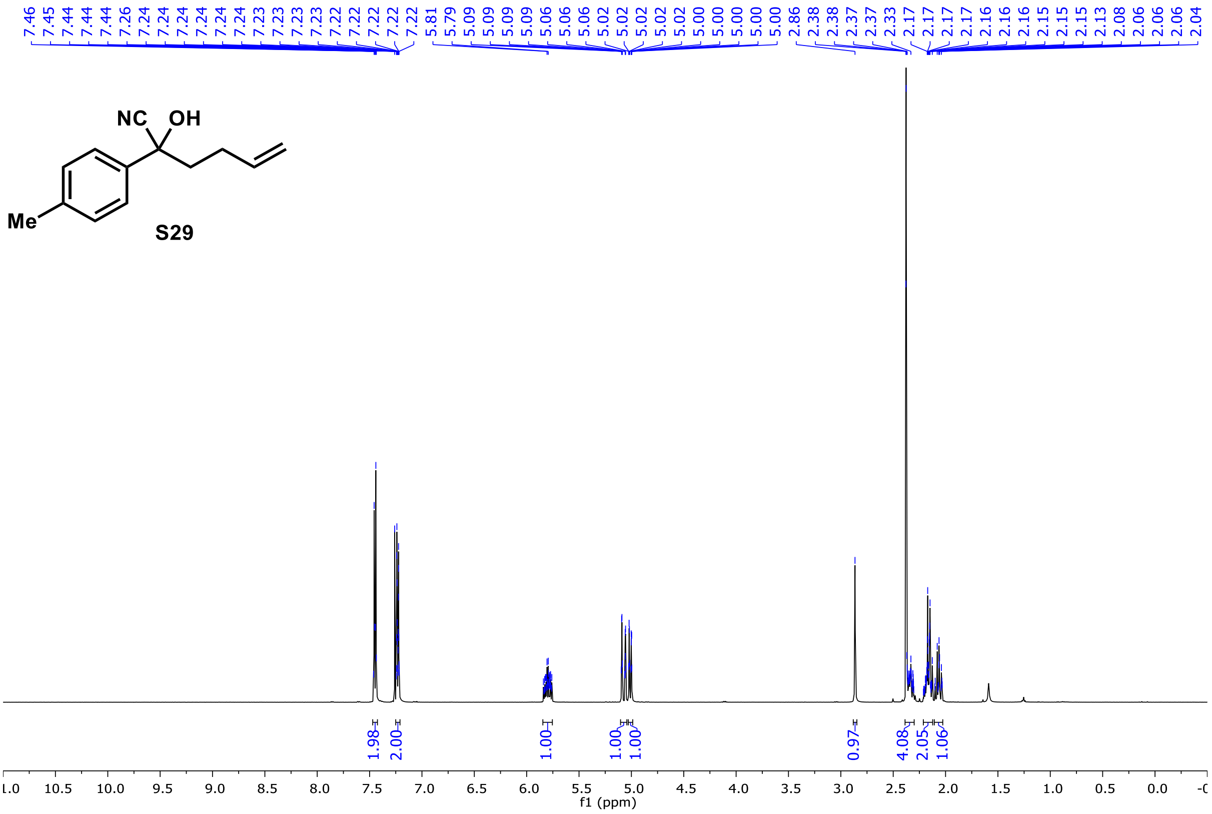
S29

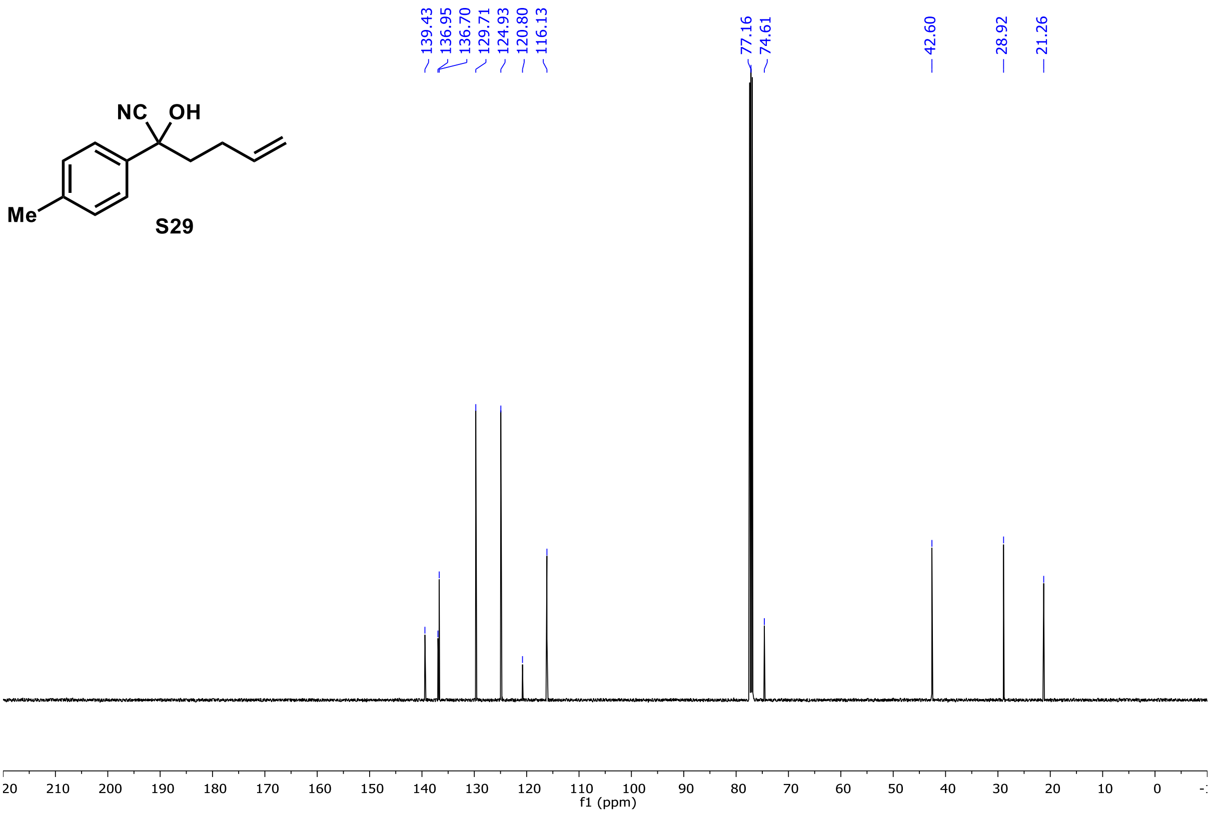
Prepared according to General Procedure 5 using **S3** (348 g, 2.00 mmol) in CH_2Cl_2 (4 mL), trimethylsilyl cyanide (626 μL, 2.50 mmol), and $TiCl_4$ (110 μL, 0.50 mmol), followed by MeCN (10 mL) and 2 M HCl (10 mL) to afford **S29** (345 mg, 86%) as a yellow oil that was used without further purification.

R_f = 0.19 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.03 – 2.11 (1H, m), 2.12 – 2.21 (2H, m), 2.30 – 2.39 (4H, m), 2.86 (1H, br s), 4.98 – 5.04 (1H, m), 5.03 – 5.12 (1H, m), 5.74 – 5.86 (1H, m), 7.20 – 7.25 (2H, m), 7.42 – 7.48 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 21.3, 28.9, 42.6, 74.6, 116.1, 120.8, 124.9, 129.7, 136.7, 136.9, 139.4.

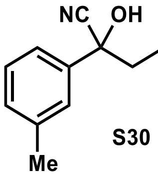
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **S29**





2-Hydroxy-2-(*m*-tolyl)hex-5-enenitrile (S30)



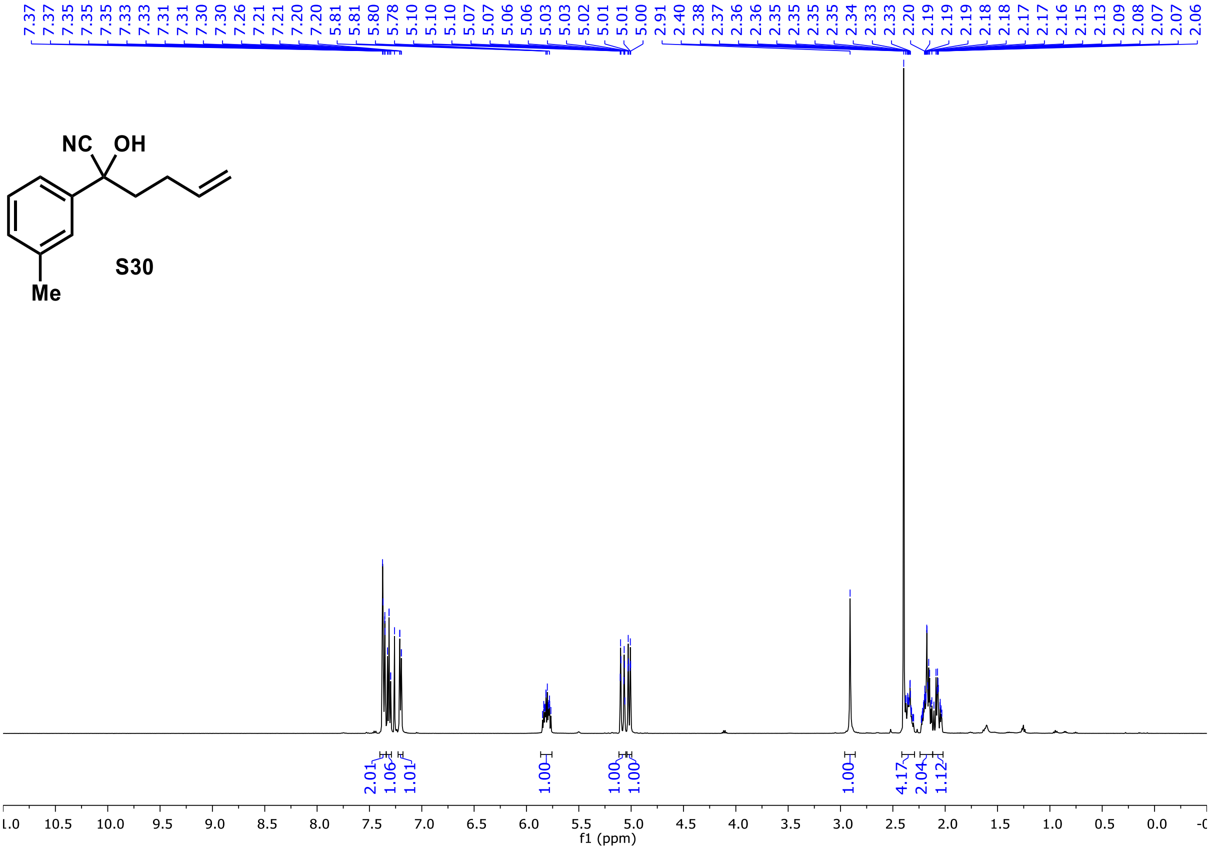
S30

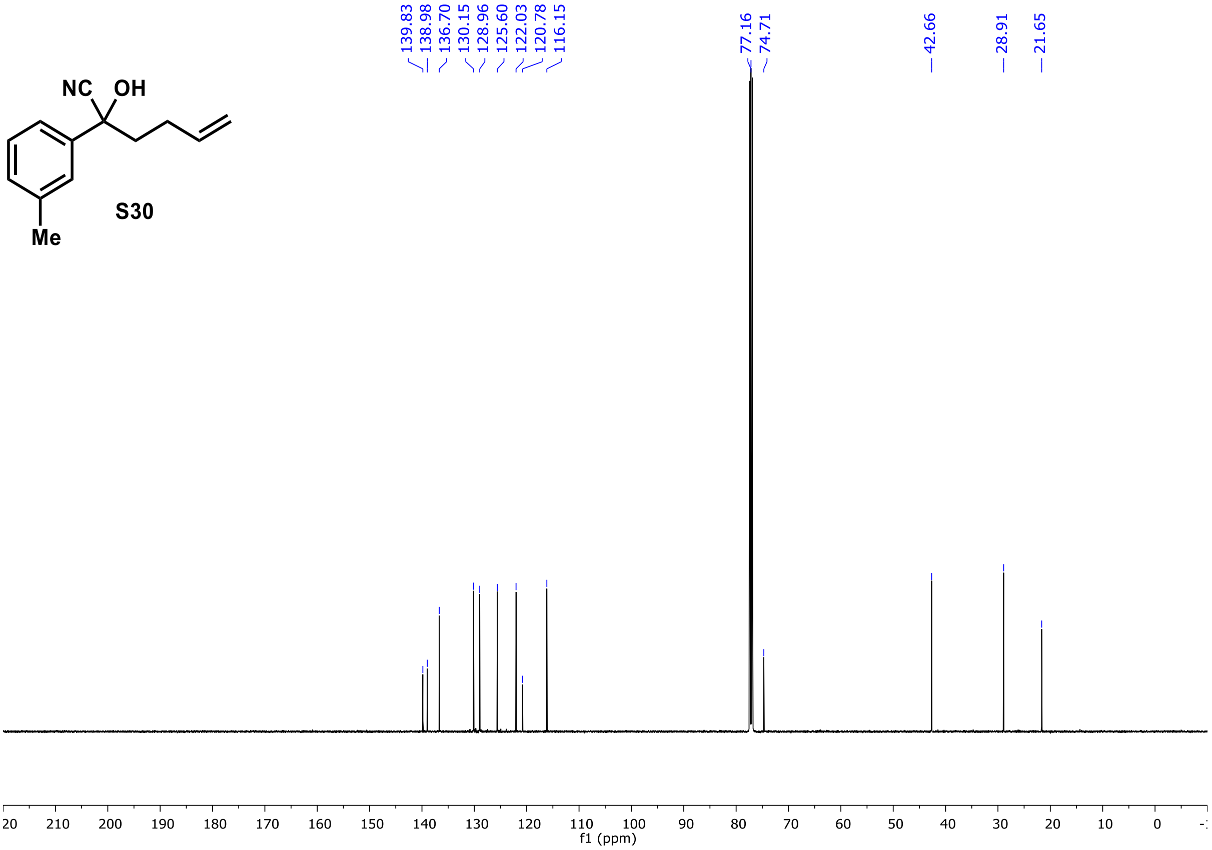
Prepared according to General Procedure 5 using **S4** (871 mg, 5.00 mmol) in CH_2Cl_2 (10 mL), trimethylsilyl cyanide (1.56 mL, 12.5 mmol), and $TiCl_4$ (274 µL, 2.50 mmol), followed by MeCN (25 mL) and 2 M HCl (25 mL) to afford **S30** (951 mg, 94%) as a yellow oil that was used without further purification.

R$_f$ = 0.23 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.03 – 2.11 (1H, m), 2.13 – 2.23 (2H, m), 2.30 – 2.38 (1H, m), 2.40 (3H, s), 2.91 (1H, br s), 5.00 – 5.03 (1H, m), 5.06 – 5.10 (1H, m), 5.77 – 5.85 (1H, m), 7.20 – 7.21 (1H, m), 7.30 – 7.33 (1H, m), 7.35 – 7.37 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 21.7, 28.9, 42.7, 74.7, 116.2, 120.8, 122.0, 125.6, 128.9, 130.2, 136.7, 139.0, 139.8.

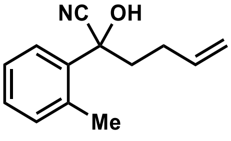
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **S30**





2-Hydroxy-2-(*o*-tolyl)hex-5-enenitrile (S31)



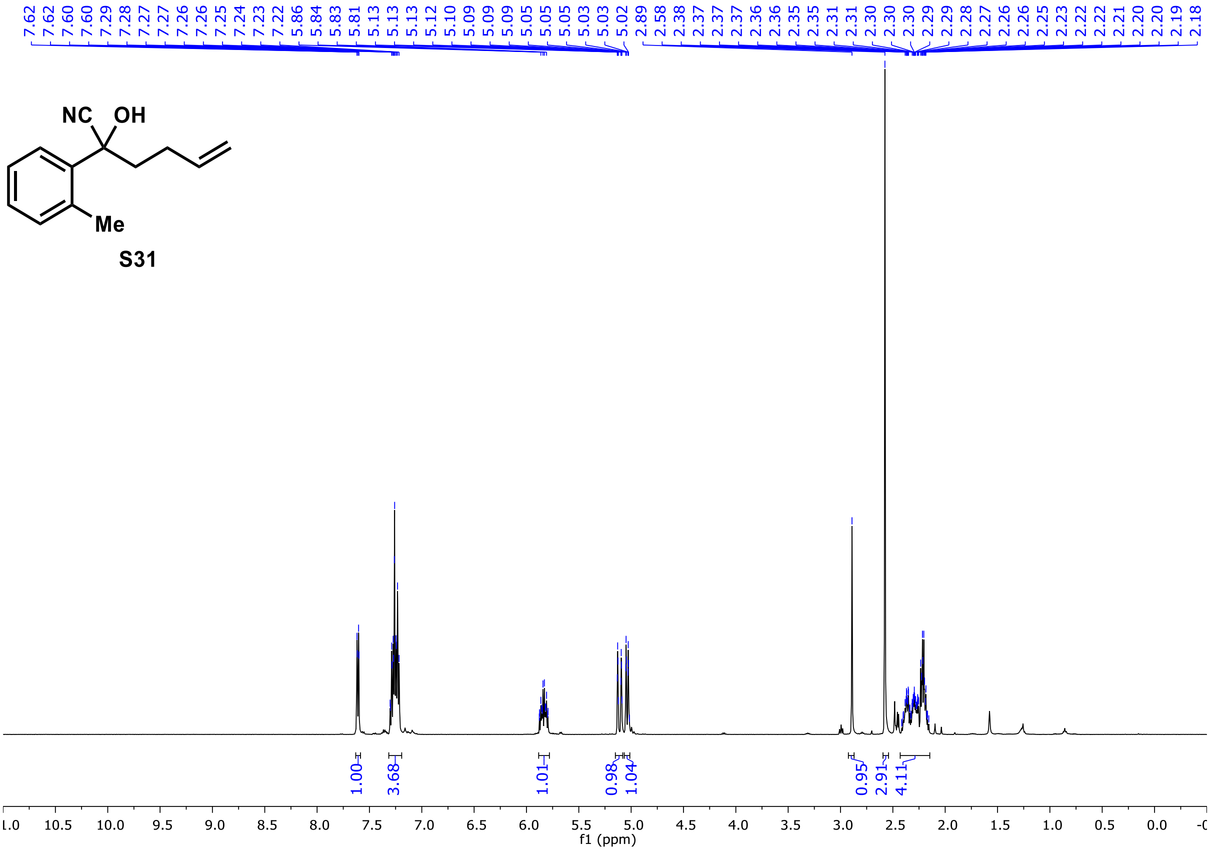
S31

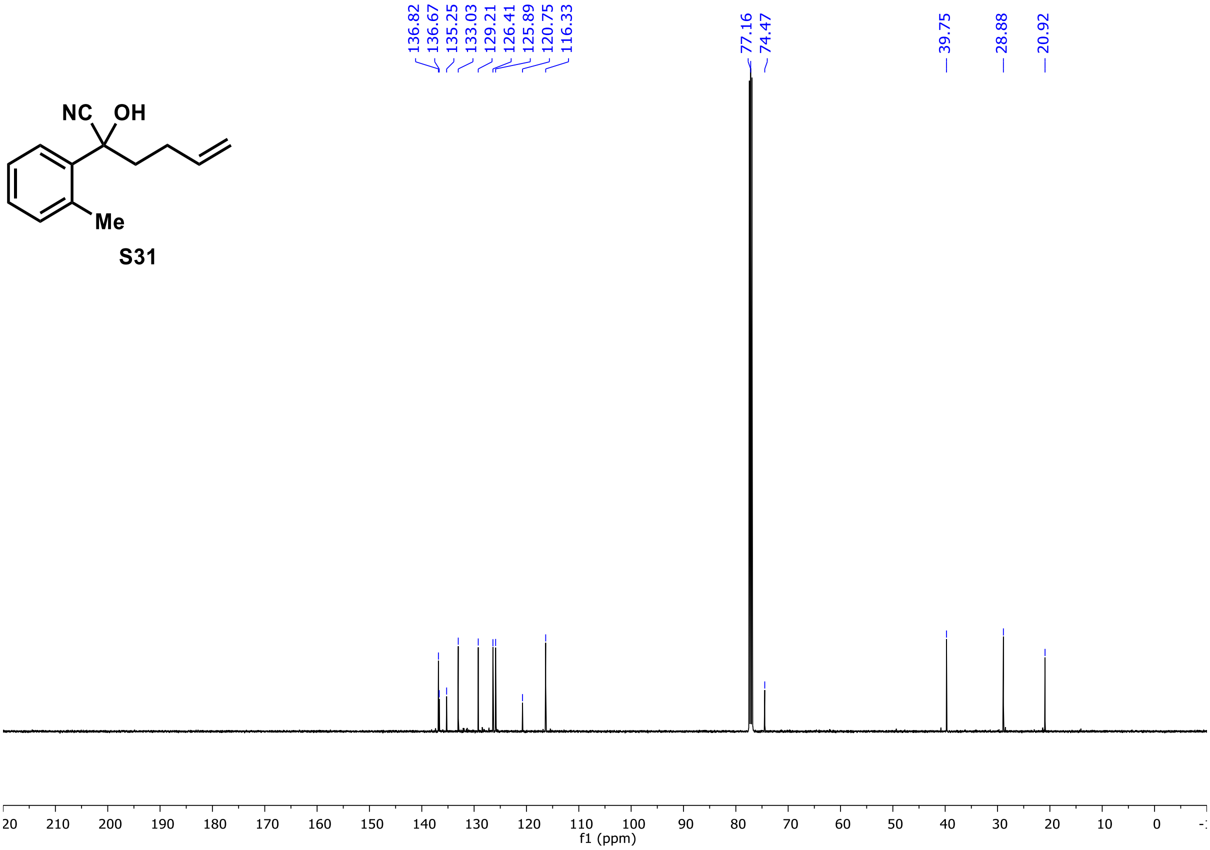
Prepared according to General Procedure 5 using **S5** (523 mg, 3.00 mmol) in CH_2Cl_2 (6 mL), trimethylsilyl cyanide (938 µL, 7.50 mmol), and $TiCl_4$ (164 µL, 1.50 mmol), followed by MeCN (15 mL) and 2 M HCl (15 mL) to afford **S31** (578 mg, 96%) as a yellow oil that was used without further purification.

R_f = 0.20 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.16 – 2.42 (4H, m), 2.58 (3H, s), 2.89 (1H, br s), 5.02 – 5.05 (1H, m), 5.09 – 5.13 (1H, m), 5.79 – 5.88 (1H, m), 7.22 – 7.30 (3H, m), 7.60 – 7.62 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 20.9, 28.9, 39.8, 74.5, 116.3, 120.8, 125.9, 126.4, 129.2, 133.0, 135.3, 136.7, 136.8.

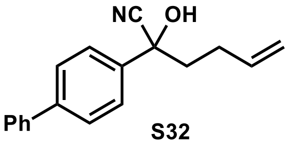
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **S31**





2-([1,1’-biphenyl]-4-yl)-2-hydroxyhex-5-enenitrile (S32)



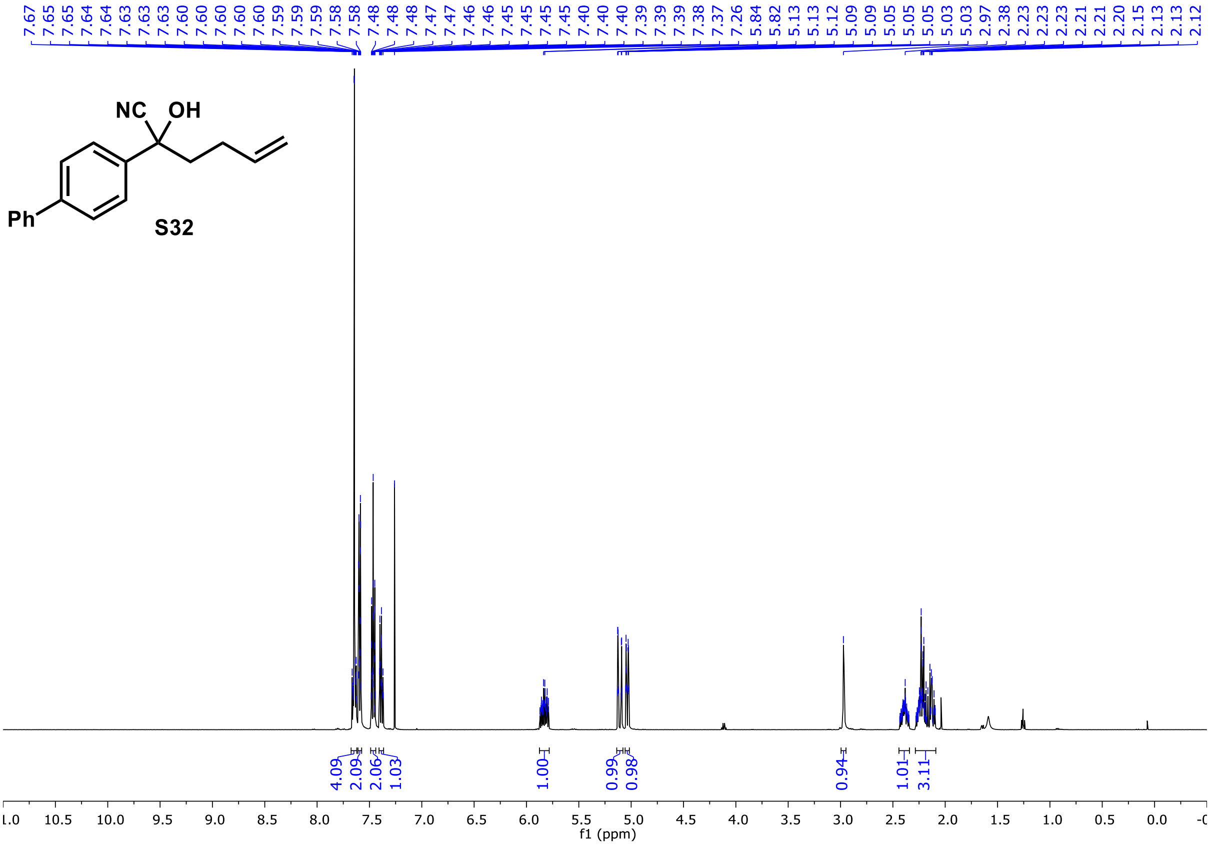
S32

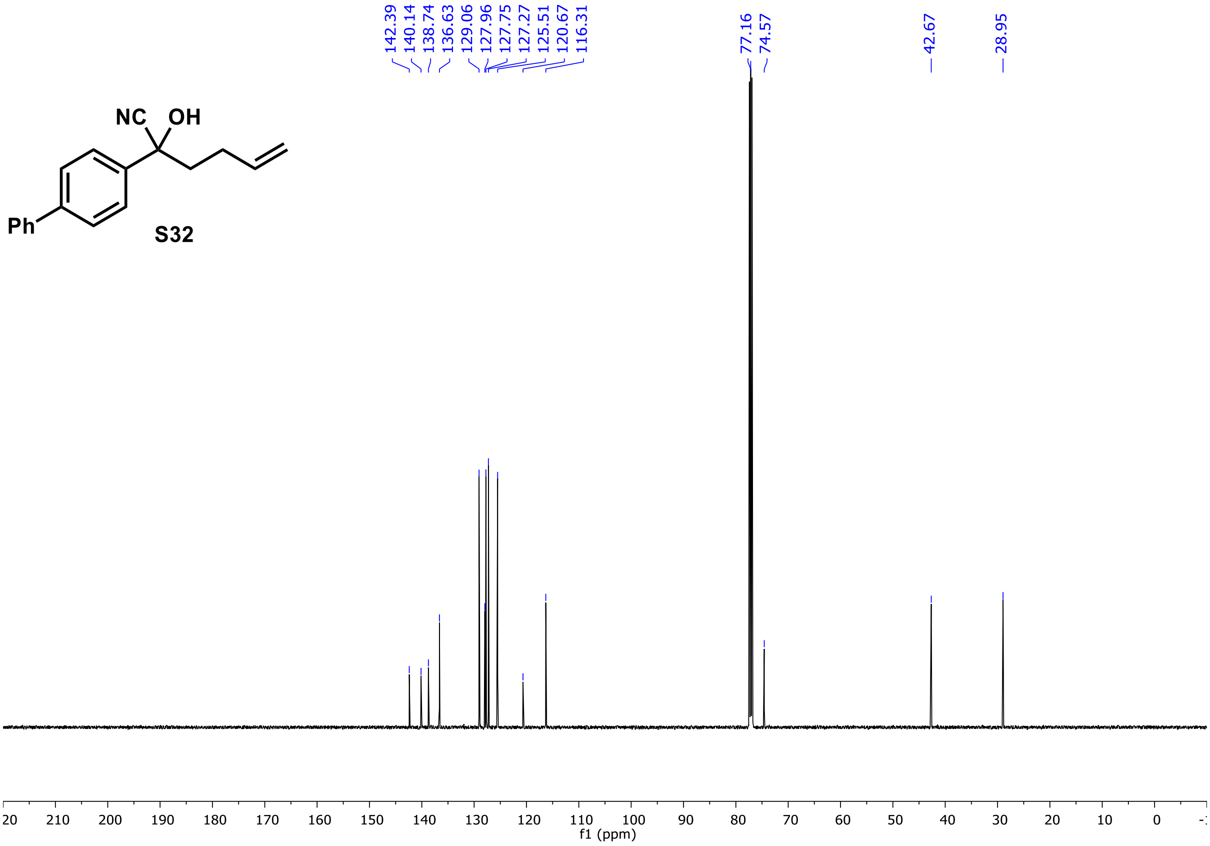
Prepared according to General Procedure 5 using **S6** (1.18 g, 5.00 mmol) in CH_2Cl_2 (10 mL), trimethylsilyl cyanide (1.55 mL, 12.5 mmol), and $TiCl_4$ (274 µL, 2.50 mmol), followed by MeCN (25 mL) and 2 M HCl (25 mL) to afford **S32** (1.25 g, 95%) as an off-white solid that was used without further purification.

R_f = 0.13 (10% EtOAc/petrol); **M.p.:** 81-83 °C; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.09 – 2.28 (3H, m), 2.34 – 2.44 (1H, m), 2.97 (1H, br s), 5.02 – 5.05 (1H, m), 5.07 – 5.15 (1H, m), 5.79 – 5.87 (1H, m), 7.35 – 7.42 (1H, m), 7.44 – 7.50 (2H, m), 7.56 – 7.62 (2H, m), 7.60 – 7.69 (4H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 29.0, 42.7, 74.6, 116.3, 120.7, 125.5, 127.2, 127.8, 128.0, 129.1, 136.6, 138.7, 140.1, 142.4.

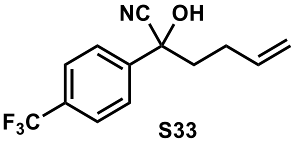
These data are in accordance with the literature.[18]

<u>^{1}H and ^{13}C NMR spectra of **S32**</u>





2-Hydroxy-2-(4-(trifluoromethyl)phenyl)hex-5-enenitrile (S33)



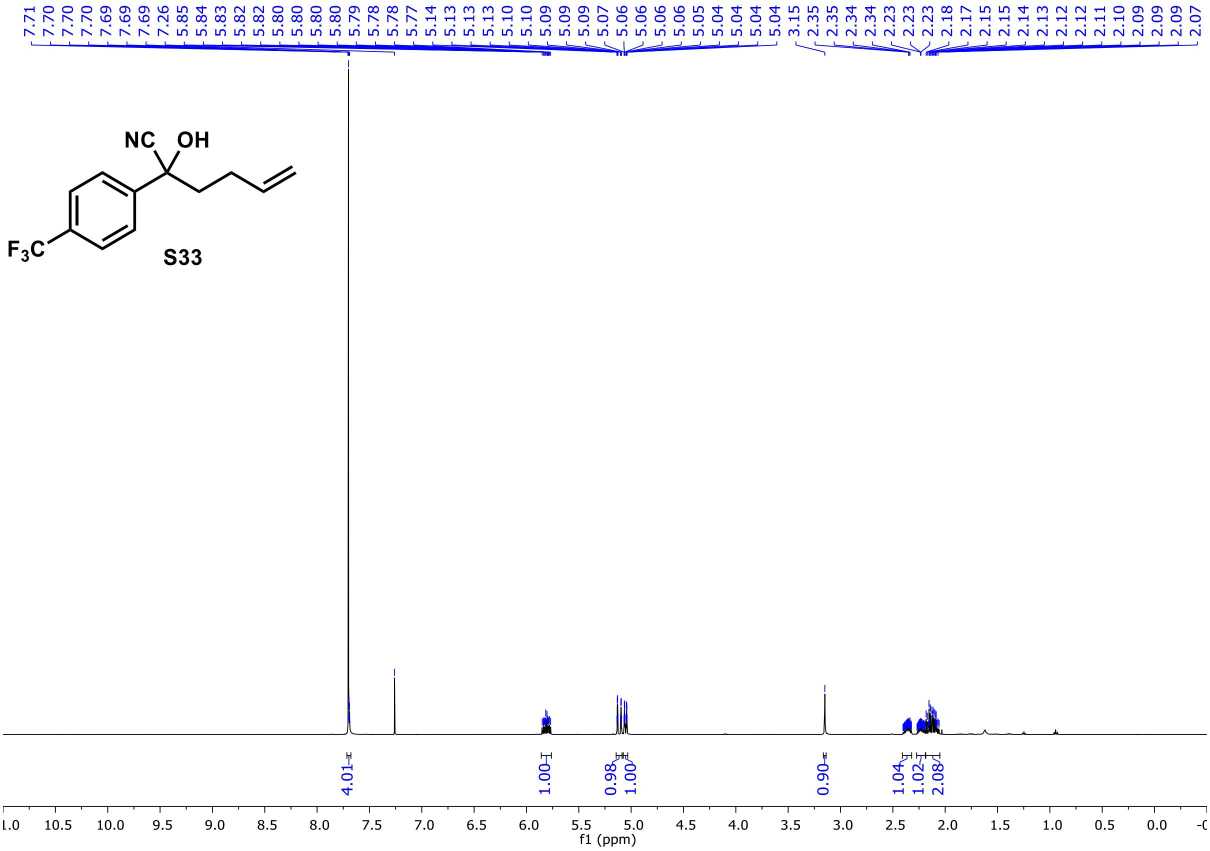
S33

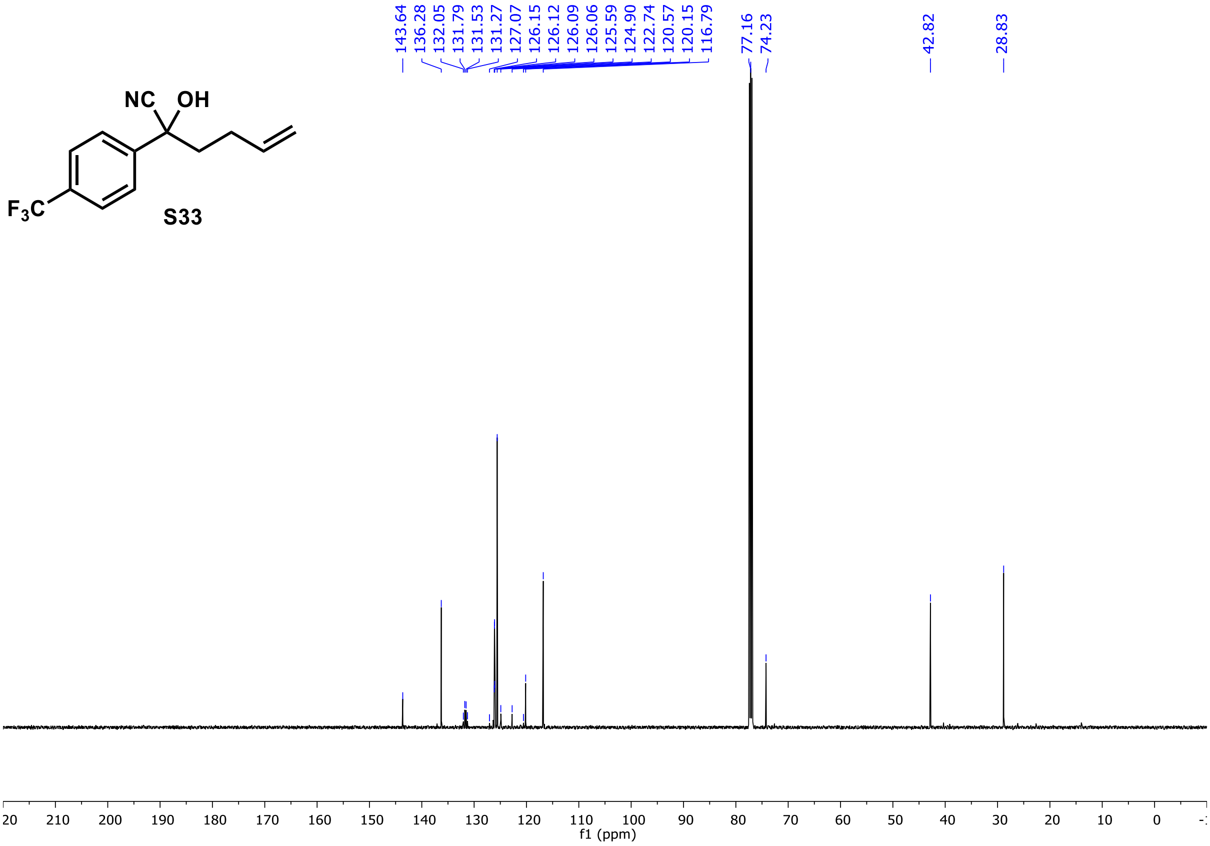
Prepared according to General Procedure 5 using **S7** (1.14 g, 5.00 mmol) in CH_2Cl_2 (10 mL), trimethylsilyl cyanide (1.55 mL, 12.5 mmol), and $TiCl_4$ (274 μL, 2.50 mmol), followed by MeCN (25 mL) and 2 M HCl (25 mL) to afford **S33** (1.26 g, 99%) as a yellow oil that was used without further purification.

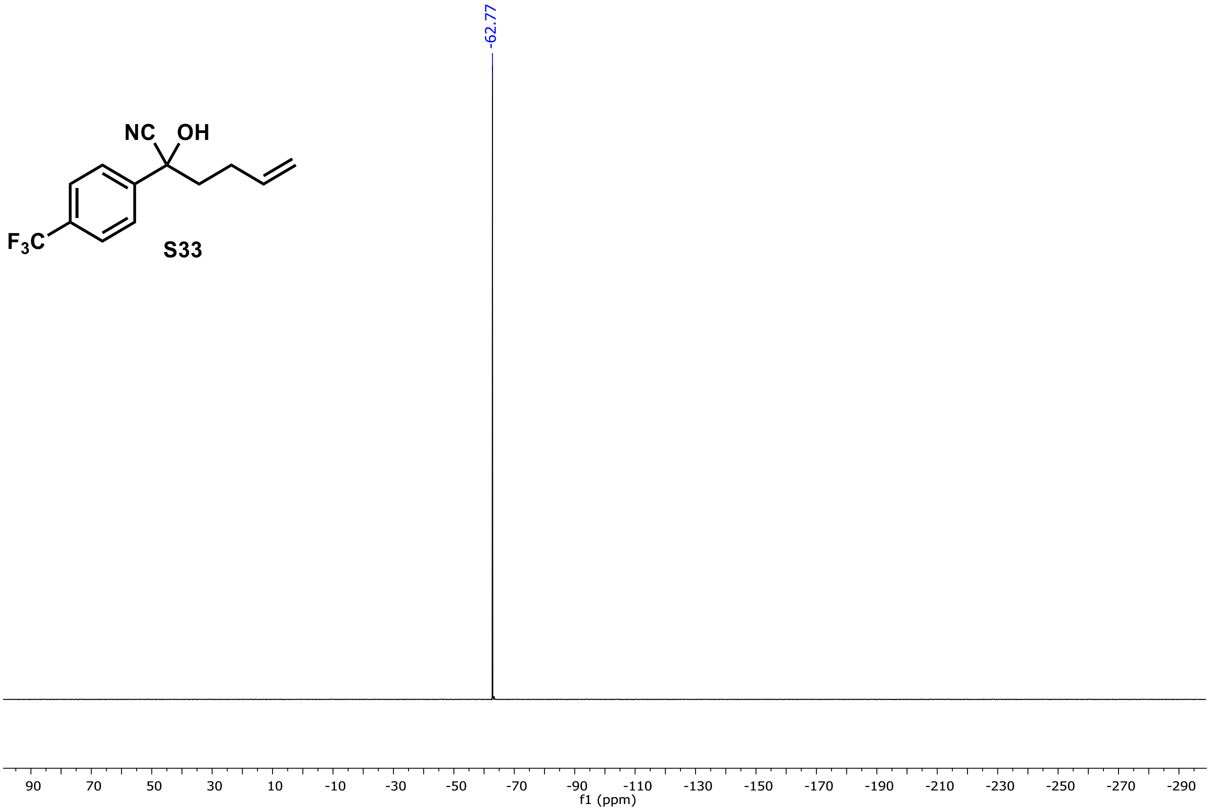
R_f = 0.22 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.06 – 2.18 (2H, m), 2.19 – 2.27 (1H, m), 2.32 – 2.41 (1H, m), 3.15 (1H, br s), 5.04 – 5.07 (1H, m), 5.09 – 5.16 (1H, m), 5.75 – 5.87 (1H, m), 7.70 (4H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.8, 42.8, 74.2, 116.8, 120.2, 123.8 (q, *J* 272.4), 125.6, 126.1 (q, *J* 3.7), 131.7 (q, *J* 32.8), 136.3, 143.6; **^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$)** δ_F = – 62.77.

These data are in accordance with the literature.[18]

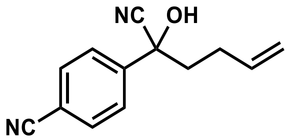
^{1}H, ^{13}C, and ^{19}F NMR spectra of **S33**







4-(1-Cyano-1-hydroxypent-4-en-1-yl)benzonitrile (S34)

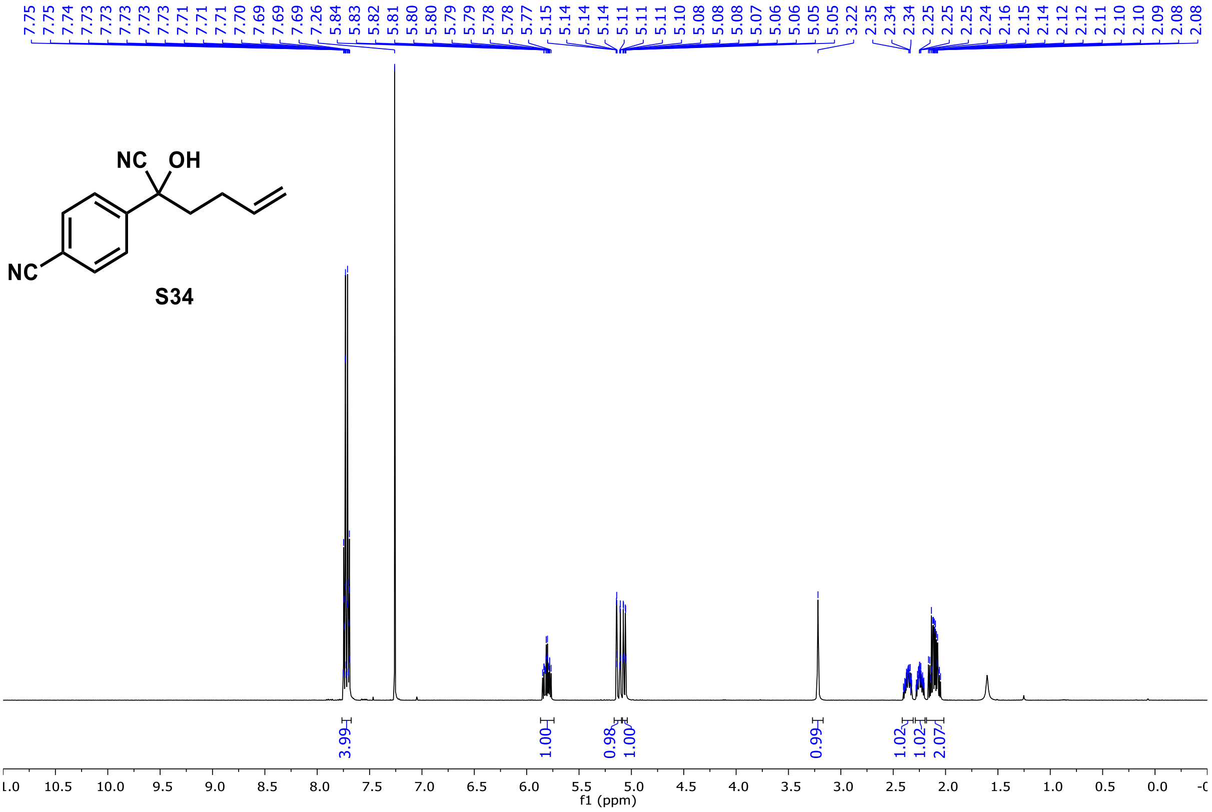


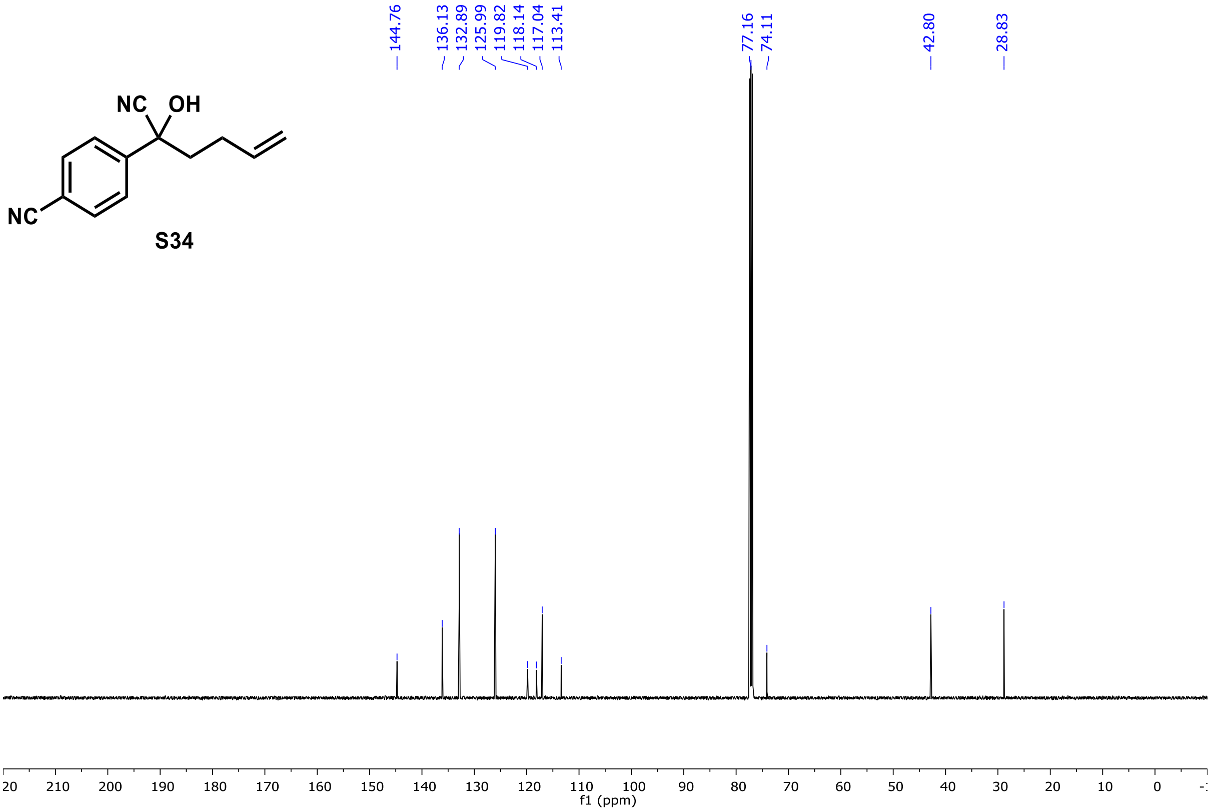
S34

Prepared according to General Procedure 5 using **S9** (463 mg, 2.50 mmol) in CH_2Cl_2 (5 mL), trimethylsilyl cyanide (782 μL, 6.25 mmol), and $TiCl_4$ (137 μL, 1.25 mmol), followed by MeCN (12.5 mL) and 2 M HCl (12.5 mL) to afford **S34** (530 mg, 99%) as a yellow oil that was used without further purification.

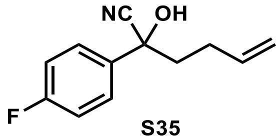
R_f = 0.16 (10% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3393, 3078, 2926, 2232, 1641, 1609, 1406, 1072, 916, 839; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.05 – 2.16 (2H, m), 2.20 – 2.28 (1H, m), 2.32 – 2.40 (1H, m), 3.22 (1H, br s), 5.05 – 5.08 (1H, m), 5.10 – 5.15 (1H, m), 5.77 – 5.85 (1H, m), 7.69 – 7.75 (4H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.8, 42.8, 74.1, 113.4, 117.0, 118.1, 119.8, 126.0, 132.9, 136.1, 144.8; **HRMS** (EI+) $C_{13}H_{12}N_2O$ [M-H]$^+$ requires 211.0866, found 211.0866 (– 0.1 ppm).

^{1}H and ^{13}C NMR spectra of **S34**





2-(4-Fluorophenyl)-2-hydroxyhex-5-enenitrile (S35)



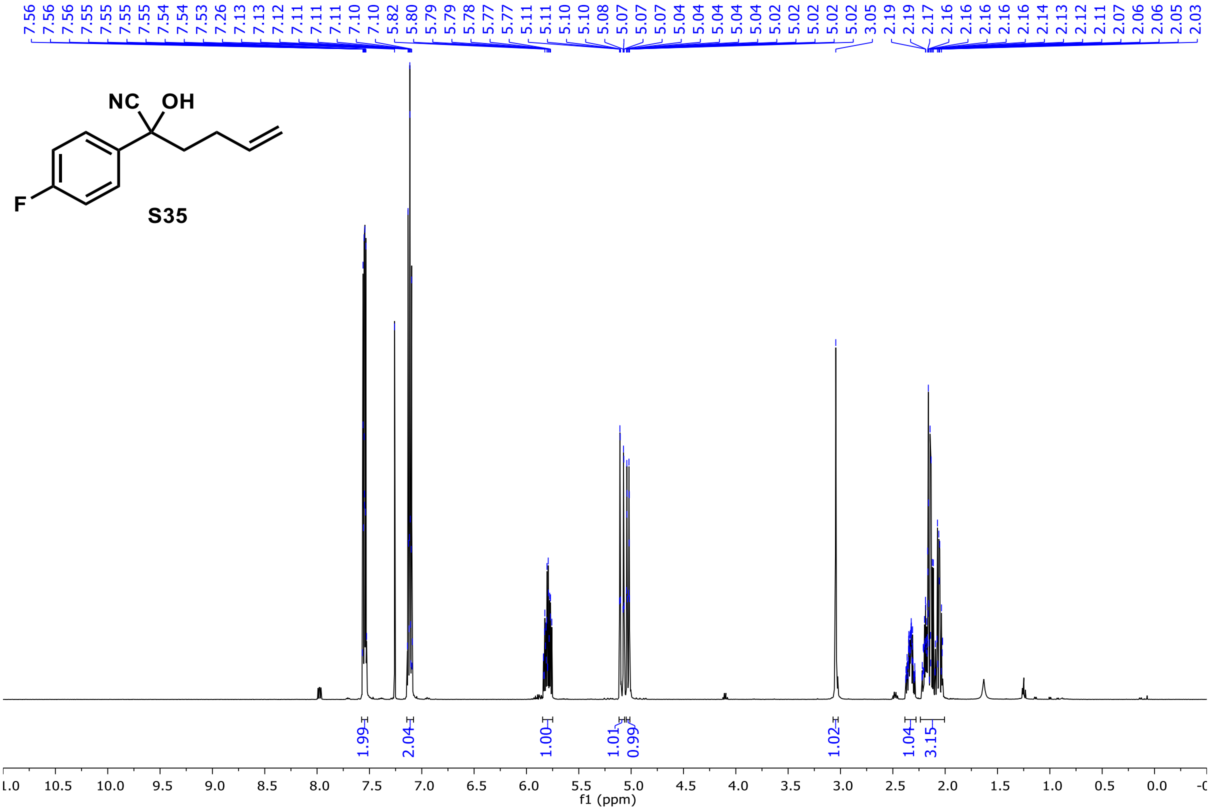
S35

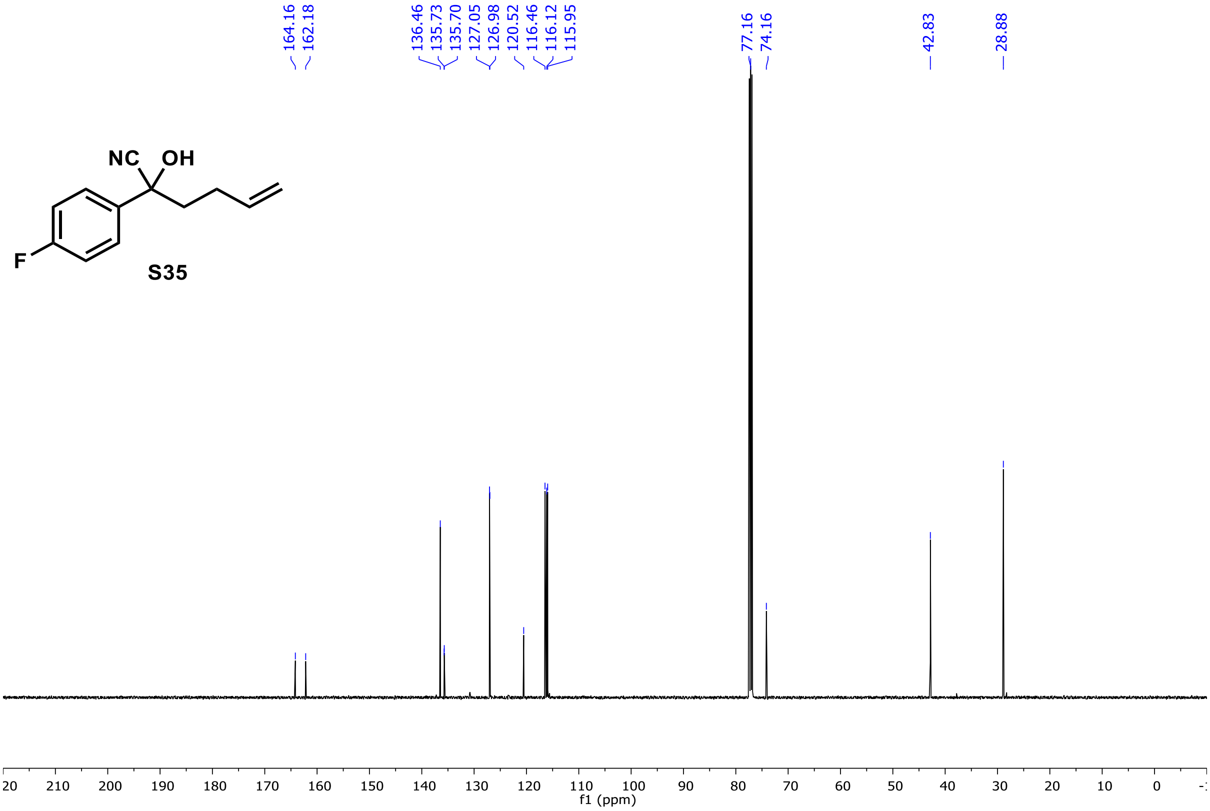
Prepared according to General Procedure 5 using **S10** (446 mg, 2.50 mmol) in CH_2Cl_2 (5 mL), trimethylsilyl cyanide (782 μL, 6.25 mmol), and $TiCl_4$ (137 μL, 1.25 mmol), followed by MeCN (12.5 mL) and 2 M HCl (12.5 mL) to afford **S35** (489 mg, 95%) as a yellow oil that was used without further purification.

R_f = 0.19 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.02 – 2.22 (3H, m), 2.29 – 2.38 (1H, m), 3.05 (1H, br s), 5.02 – 5.04 (1H, m), 5.07 – 5.11 (1H, m), 5.76 – 5.84 (1H, m), 7.09 – 7.14 (2H, m), 7.53 – 7.57 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.9, 42.8, 74.2, 116.0 (d, *J* 21.9), 116.5, 120.5, 127.0 (d, *J* 8.5), 135.7, (d, *J* 3.3), 136.5, 163.2 (d, *J* 248.9); **^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$)** δ_F = – 112.21.

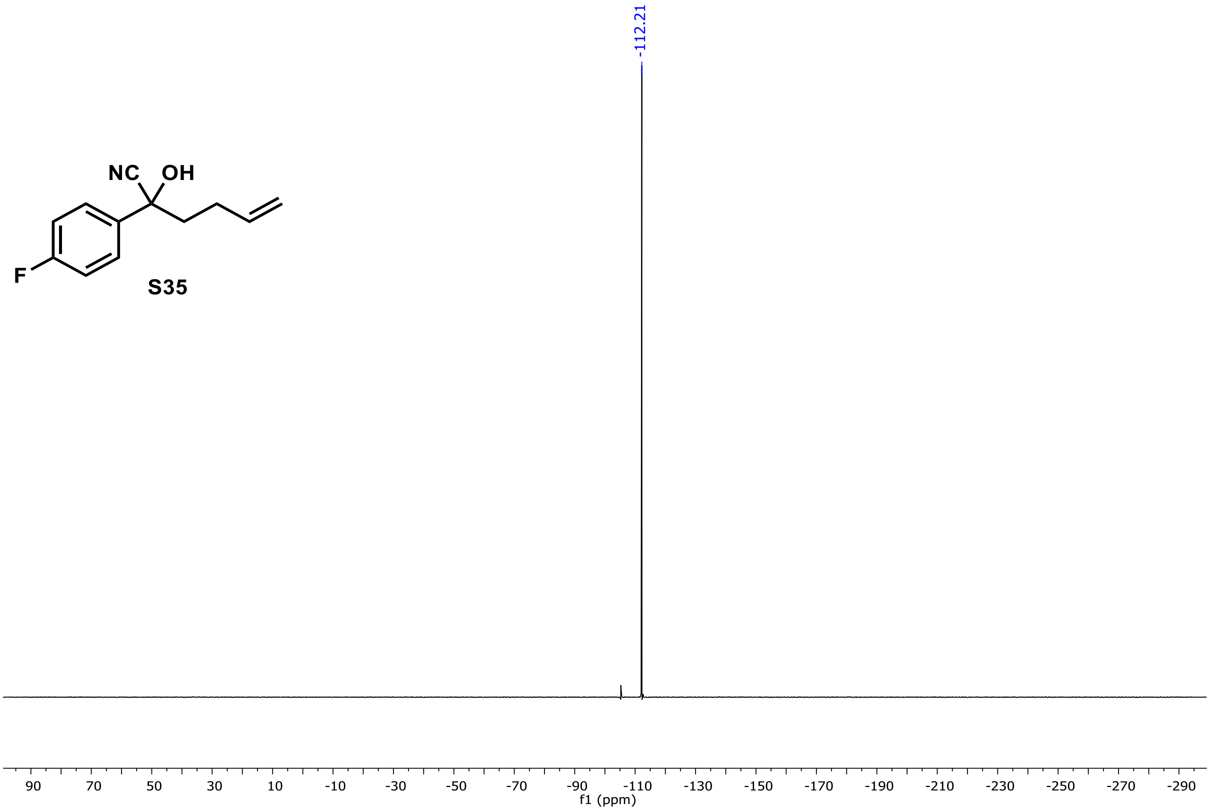
These data are in accordance with the literature.[18]

^{1}H, ^{13}C, and ^{19}F NMR spectra of **S35**



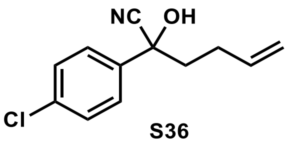

S35

164.16
162.18
136.46
135.73
135.70
127.05
126.98
120.52
116.46
116.12
115.95
77.16
74.16
42.83
28.88
NC
OH
F
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


S35

-112.21
NC
OH
F
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
-270
-290
f1 (ppm)

2-(4-Chlorophenyl)-2-hydroxyhex-5-ene-nitrile (S36)



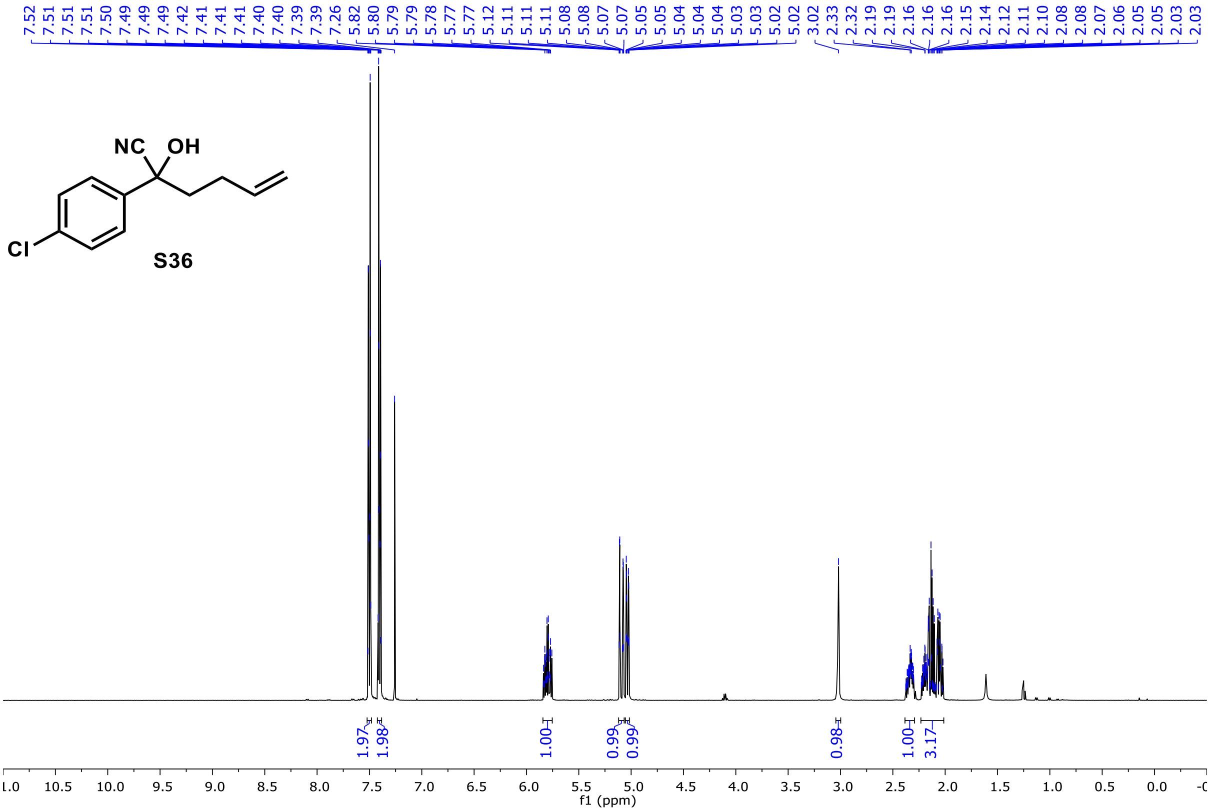
S36

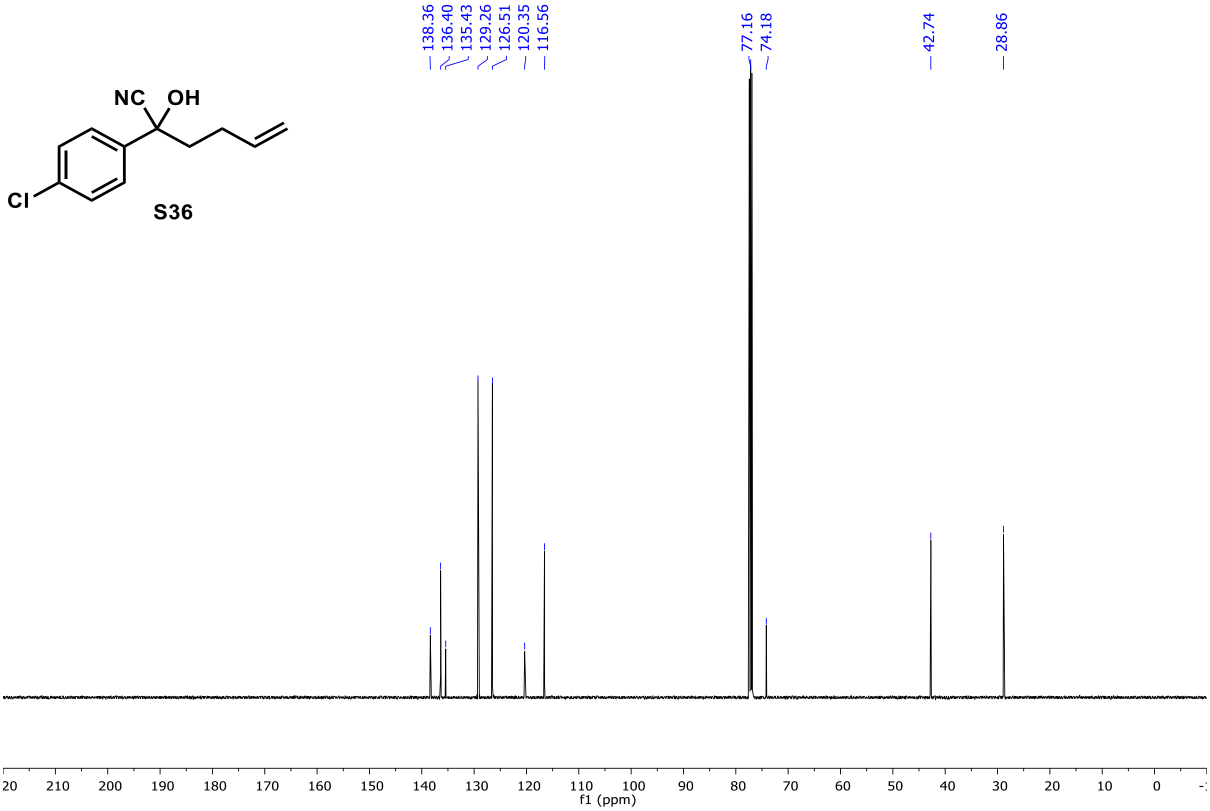
Prepared according to General Procedure 5 using **S11** (487 mg, 2.50 mmol) in CH_2Cl_2 (5 mL), trimethylsilyl cyanide (782 μL, 6.25 mmol), and $TiCl_4$ (137 μL, 1.25 mmol), followed by MeCN (12.5 mL) and 2 M HCl (12.5 mL) to afford **S36** (563 g, 99%) as a yellow oil that was used without further purification.

R_f = 0.22 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.02 – 2.22 (3H, m), 2.30 – 2.36 (1H, m), 3.02 (1H, br s), 5.02 – 5.05 (1H, m), 5.07 – 5.12 (1H, m), 5.76 – 5.84 (1H, m), 7.39 – 7.42 (2H, m), 7.49 – 7.52 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.9, 42.7, 74.2, 116.6, 120.4, 126.5, 129.3, 135.4, 136.4, 138.4.

These data are in accordance with the literature.[18]

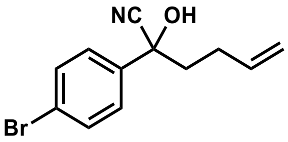
<u>^{1}H and ^{13}C NMR spectra of **S36**</u>





S36

2-(4-Bromophenyl)-2-hydroxyhex-5-enenitrile (S37)



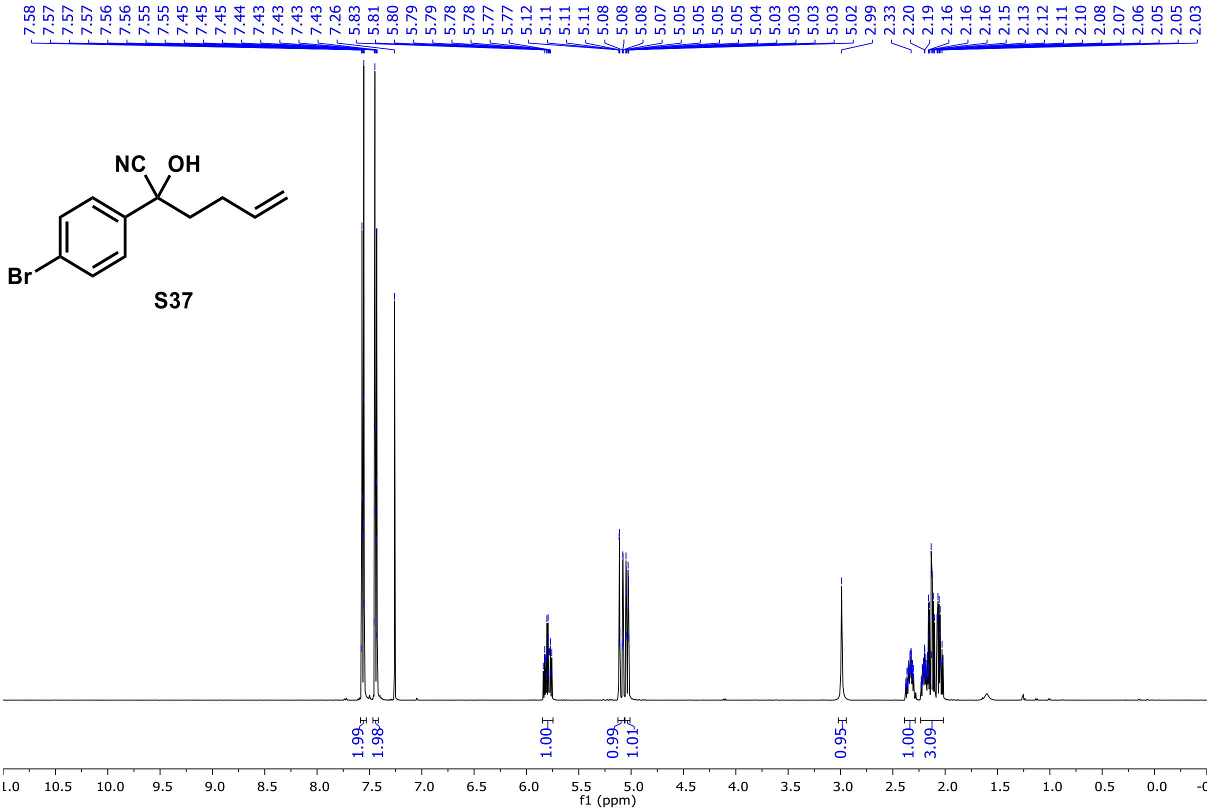
S37

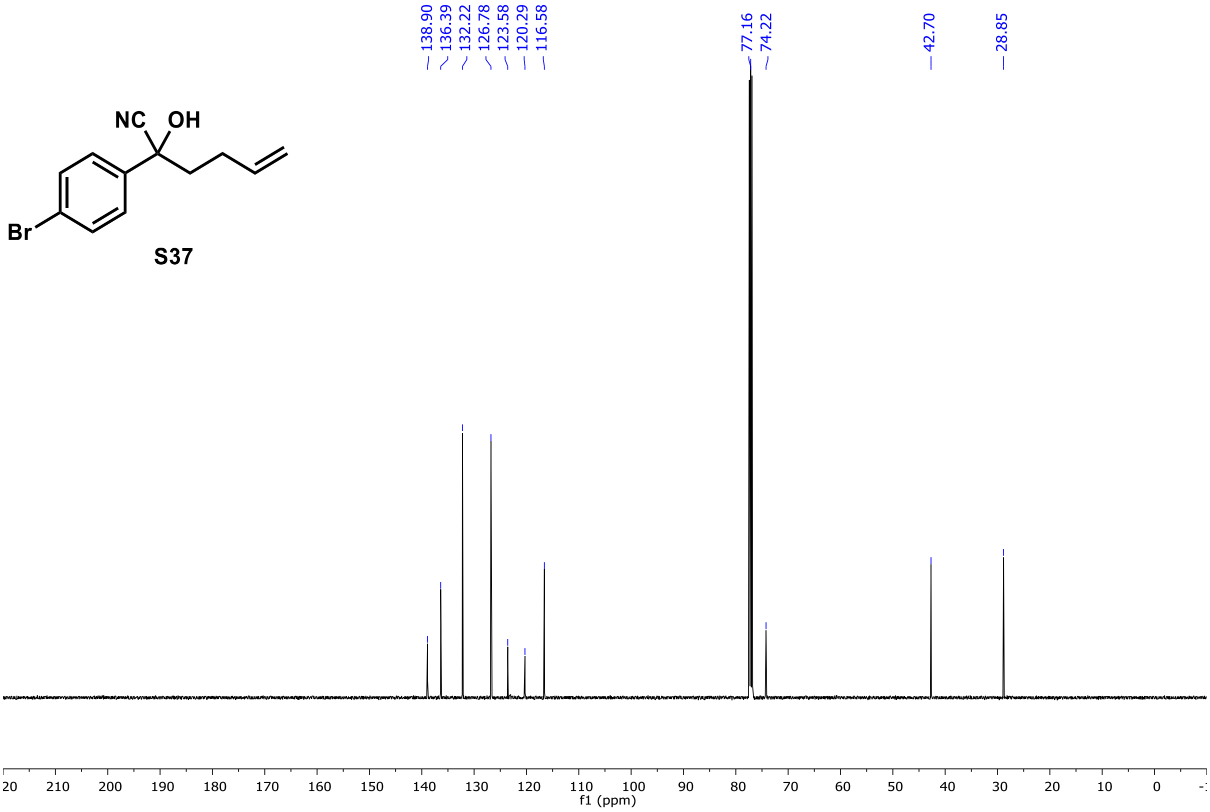
Prepared according to General Procedure 5 using **S8** (598 mg, 2.50 mmol) in CH_2Cl_2 (5 mL), trimethylsilyl cyanide (782 µL, 6.25 mmol), and $TiCl_4$ (137 µL, 1.25 mmol), followed by MeCN (12.5 mL) and 2 M HCl (12.5 mL) to afford **S37** (636 mg, 96%) as a yellow oil that was used without further purification.

R_f = 0.14 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.02 – 2.33 (3H, m), 2.30 – 2.36 (1H, m), 2.99 (1H, br s), 5.02 – 5.05 (1H, m), 5.07 – 5.12 (1H, m), 5.76 – 5.84 (1H, m), 7.43 – 7.45 (2H, m), 7.55 – 7.58 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.9, 42.7, 74.2, 116.6, 120.3, 123.6, 126.8, 132.2, 136.4, 138.9.

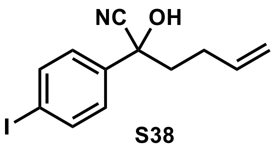
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **S37**





2-Hydroxy-2-(4-iodophenyl)hex-5-enenitrile (S38)



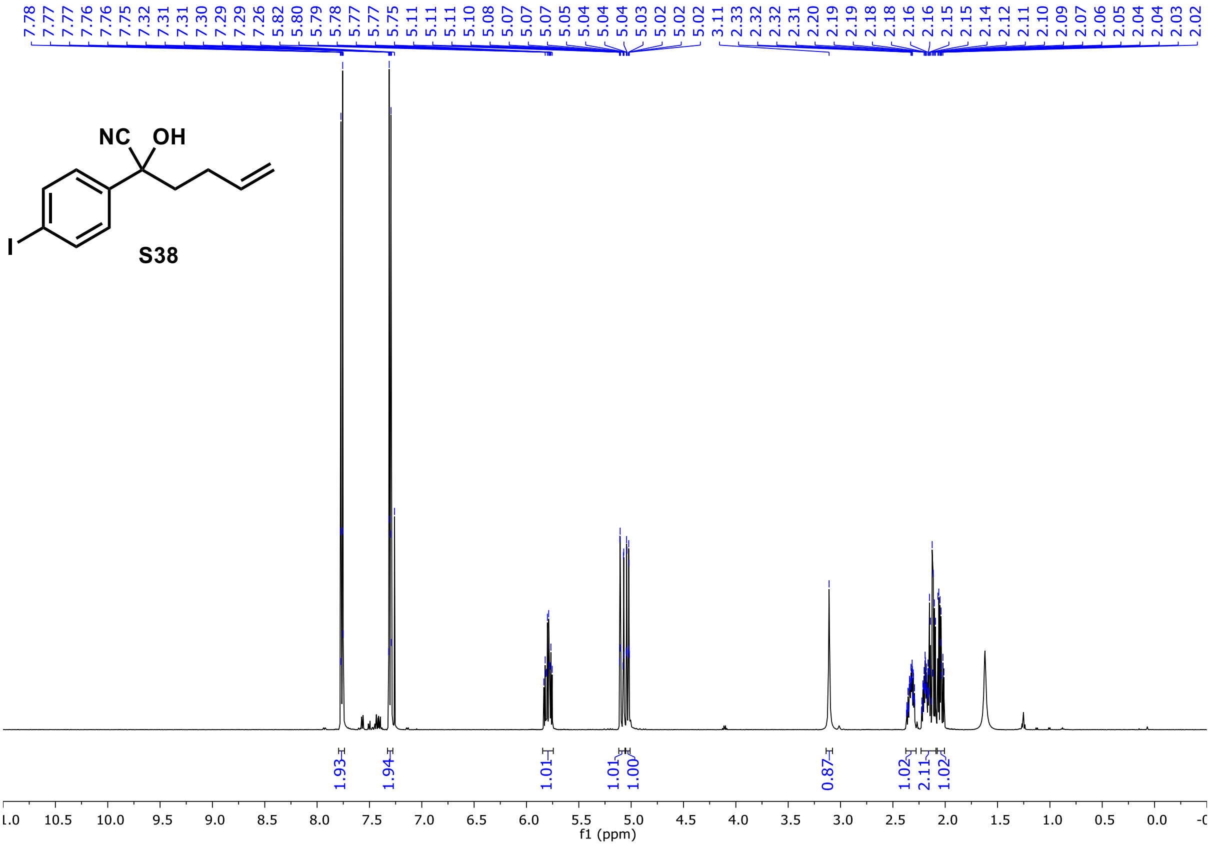
S38

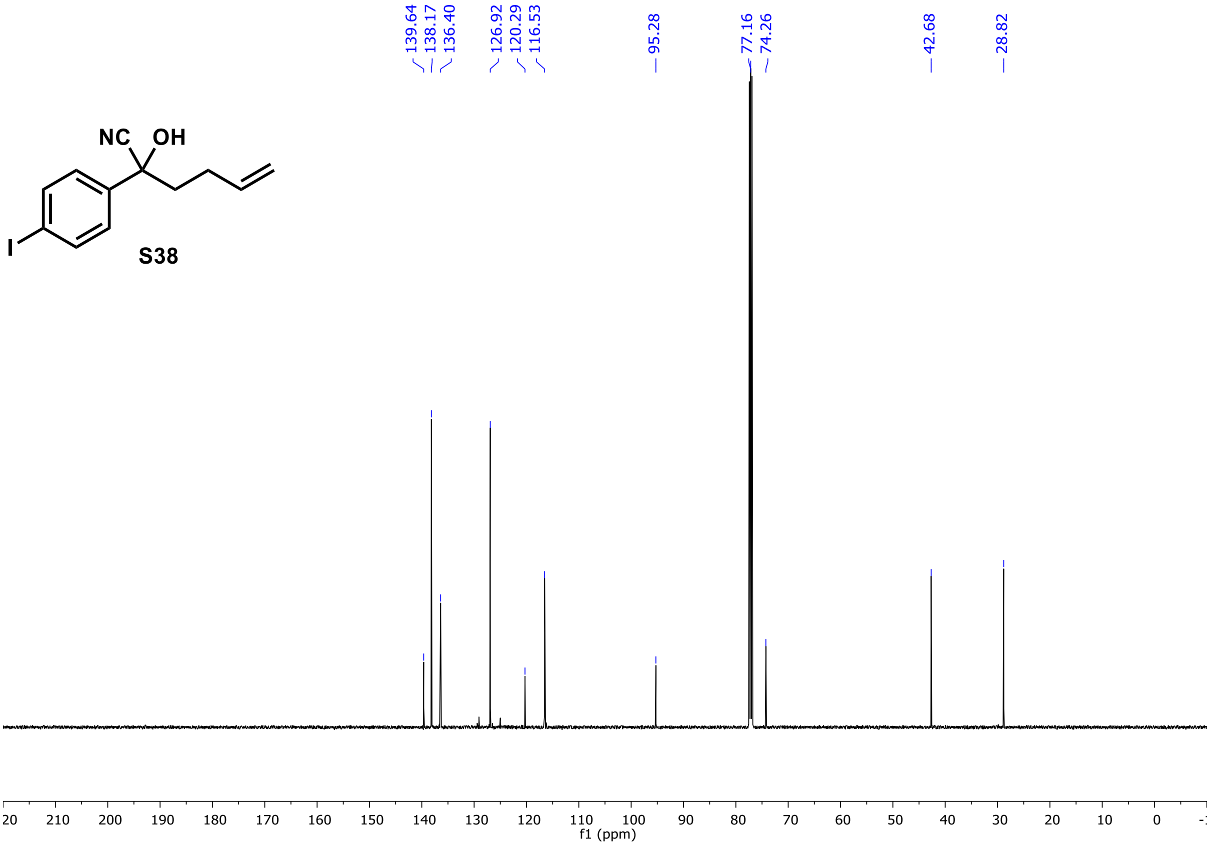
Prepared according to General Procedure 5 using **S12** (286 mg, 1.00 mmol) in CH_2Cl_2 (2 mL), trimethylsilyl cyanide (313 µL, 2.50 mmol), and $TiCl_4$ (55 µL, 0.50 mmol), followed by MeCN (5 mL) and 2 M HCl (5 mL) to afford **S38** (300 mg, 96%) as a yellow oil that was used without further purification.

R_f = 0.14 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.01 – 2.07 (1H, m), 2.09 – 2.22 (2H, m), 2.29 – 2.37 (1H, m), 3.11 (1H, br s), 5.02 – 5.04 (1H, m), 5.07 – 5.11 (1H, m), 5.75 – 5.83 (1H, m), 7.29 – 7.32 (2H, m), 7.75 – 7.78 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 28.8, 42.7, 74.3, 95.3, 116.5, 120.3, 126.9, 136.4, 138.2, 139.6.

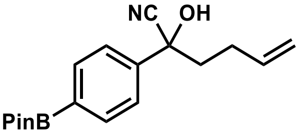
These data are in accordance with the literature.[19]

^{1}H and ^{13}C NMR spectra of **S38**





2-Hydroxy-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)hex-5-enenitrile (S39)

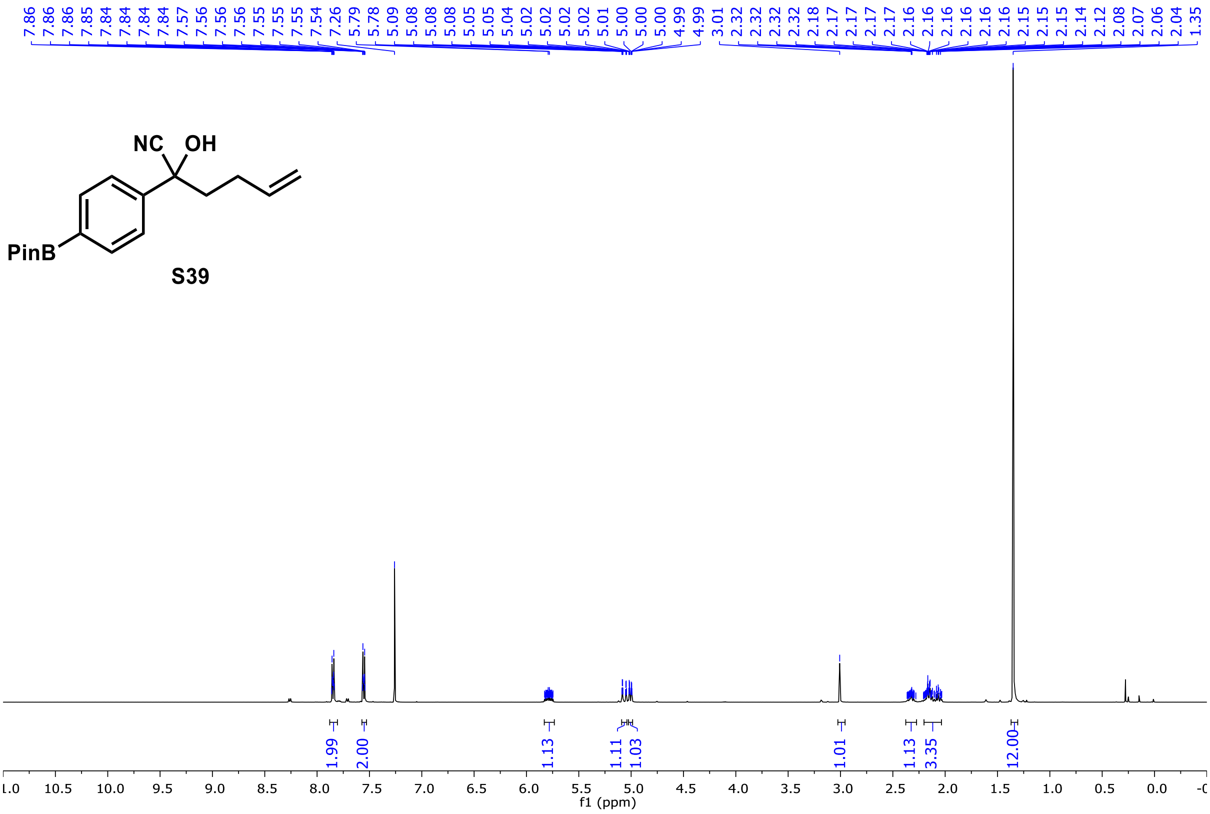


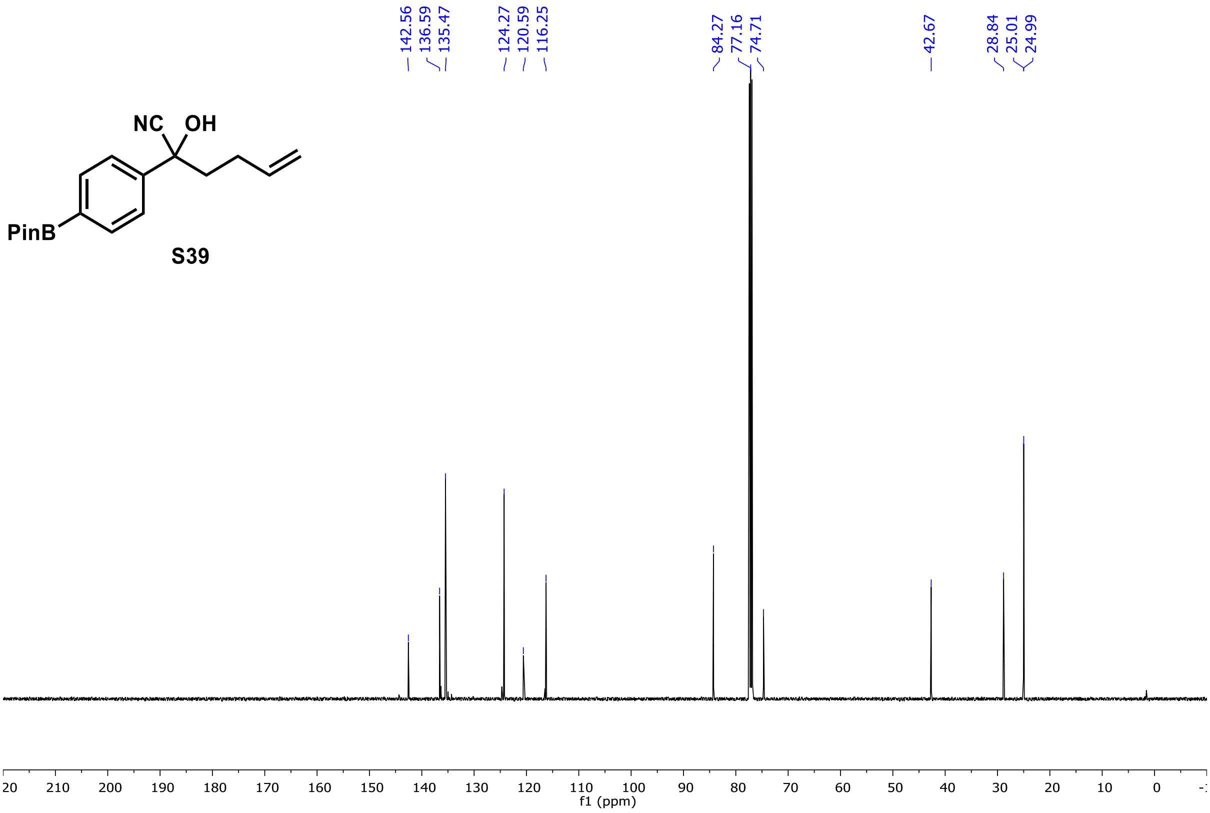
S39

Prepared according to General Procedure 5 using **S13** (572 mg, 2.00 mmol) in CH_2Cl_2 (4 mL), trimethylsilyl cyanide (626 µL, 5.00 mmol), and $TiCl_4$ (110 µL, 1.00 mmol), followed by MeCN (10 mL) and 2 M HCl (10 mL) to afford **S39** (610 mg, 98%) as a yellow solid that was used without further purification.

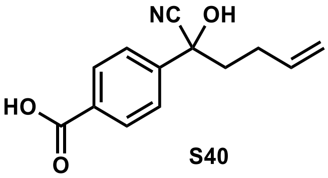
R_f = 0.27 (20% EtOAc/petrol); **M.p.:** 77-79 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3402, 2978, 2930, 2238, 1610, 1400, 1360, 1132, 1088, 753; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.35 (12H, s), 2.03 – 2.20 (3H, m), 2.30 – 2.36 (1H, m), 3.01 (1H, br s), 4.99 – 5.02 (1H, m), 5.04 – 5.09 (1H, m), 5.75 – 5.83 (1H, m), 7.54 – 7.57 (2H, m), 7.84 – 7.86 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 24.9, 25.0, 28.8, 42.7, 74.7, 84.3, 116.3, 120.6, 124.3, 135.5, 136.6, 142.6; **HRMS** (EI+) $C_{18}H_{24}{}^{11}BNO_3$ [M-H]$^+$ requires 312.1766, found 312.1763 (– 0.9 ppm).

^{1}H and ^{13}C NMR spectra of **S39**





4-(1-Cyano-1-hydroxypent-4-en-1-yl)benzoic acid (S40)

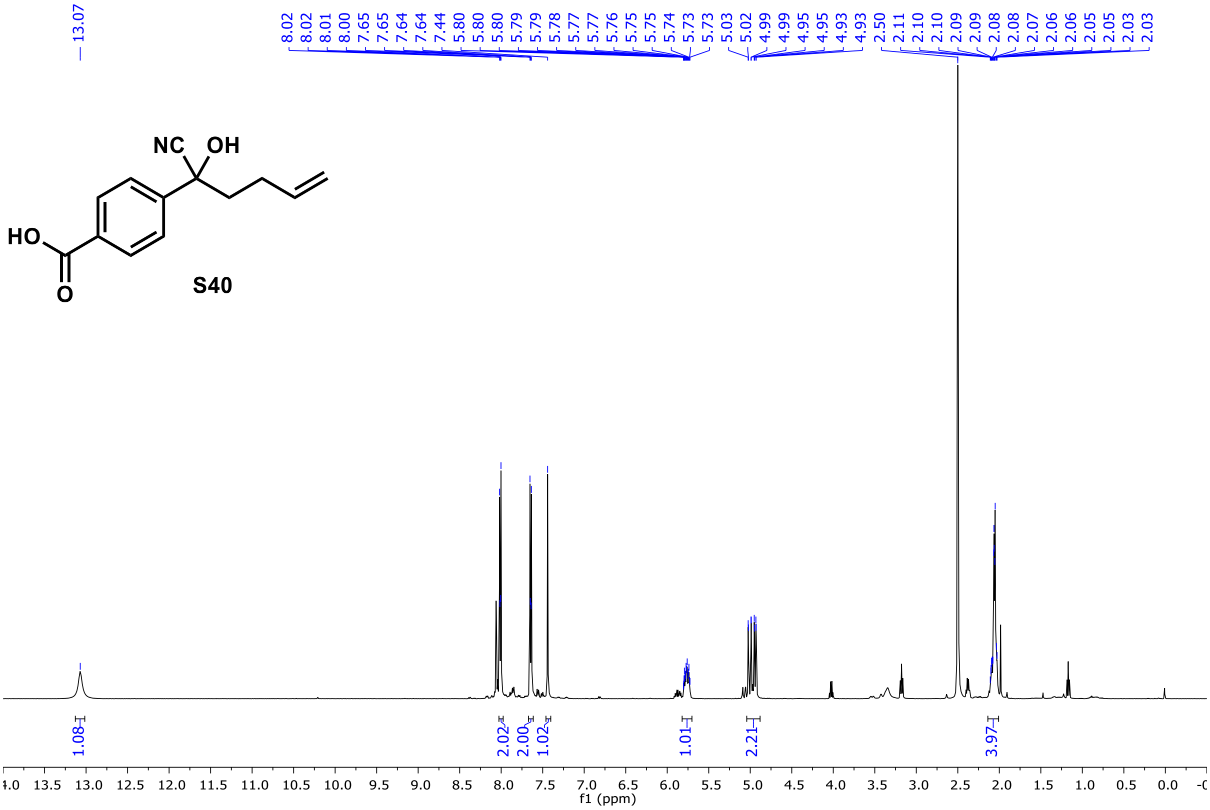


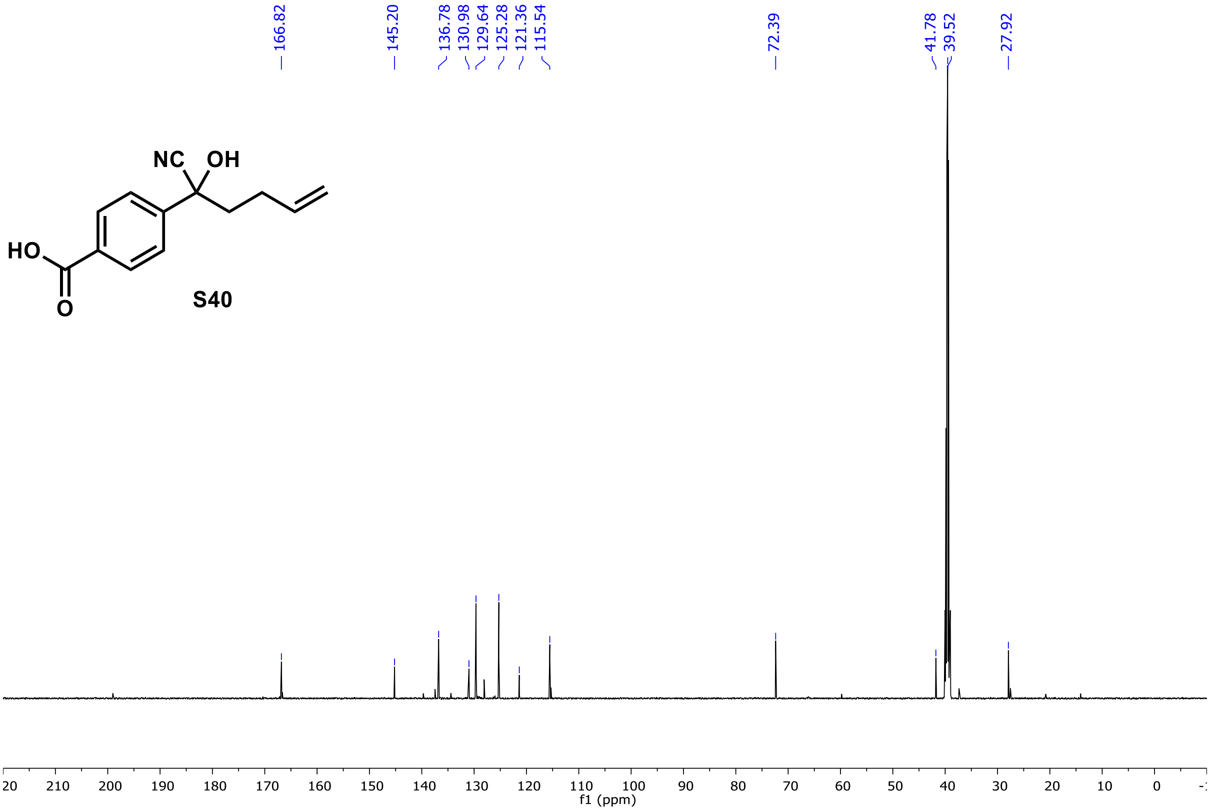
S40

Prepared according to General Procedure 5 using **S14** (306 mg, 1.50 mmol) in CH_2Cl_2 (7 mL), trimethylsilyl cyanide (469 µL, 3.75 mmol), and $TiCl_4$ (82 µL, 0.75 mmol), followed by MeCN (7.5 mL) and 2 M HCl (7.5 mL) to afford **S40** (298 mg, 86%) as an orange solid that was used without further purification.

R_f = 0.09 (50% EtOAc/petrol); **M.p.:** 105-107 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3397, 2849, 2669, 2550, 2253, 1686, 1610, 1417, 1287, 1078, 914, 864; **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ_H = 2.03 – 2.11 (4H, m), 4.93 – 5.03 (2H, m), 5.73 – 5.80 (1H, m), 7.44 (1H, s), 7.64 – 7.65 (2H, m), 8.00 – 8.02 (2H, m), 13.07 (1H, br s); **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ_C = 27.9, 41.8, 72.4, 115.5, 121.4, 125.3, 129.6, 131.0, 136.8, 145.2, 166.8; **HRMS** (ES+) $C_{13}H_{13}NO_3$ $[M+H]^+$ requires 232.0974, found 232.0968 (– 2.6 ppm).

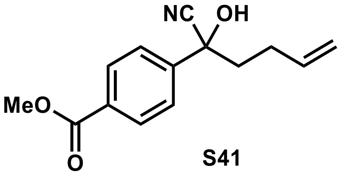
<u>^{1}H and ^{13}C NMR spectra of **S40**</u>





S40

Methyl 4-(1-cyano-1-hydroxypent-4-en-1-yl)benzoate (S41)

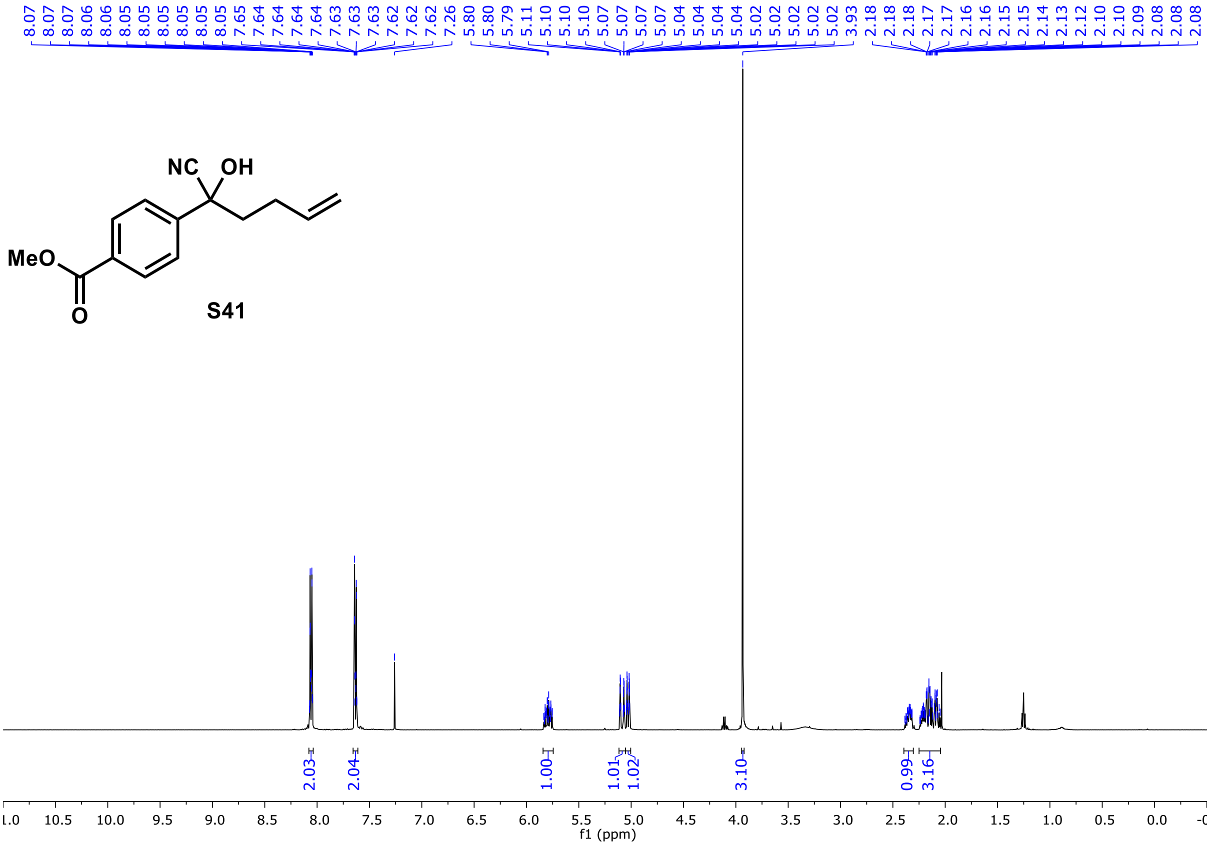


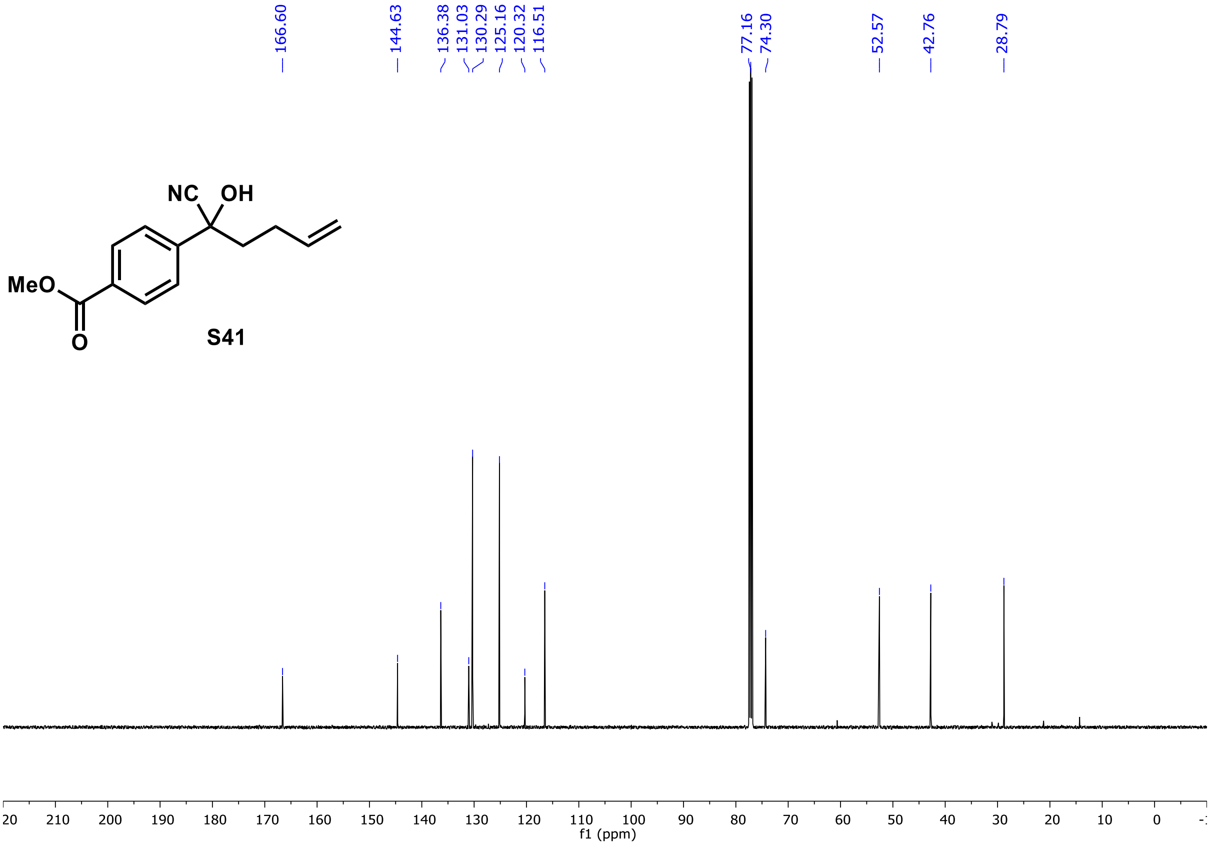
S41

Prepared according to General Procedure 5 using **S15** (218 mg, 1.00 mmol) in CH_2Cl_2 (2 mL), trimethylsilyl cyanide (313 µL, 2.50 mmol), and $TiCl_4$ (55 µL, 0.50 mmol), followed by MeCN (5 mL) and 2 M HCl (5 mL) to afford **S41** (234 mg, 95%) as an orange oil that was used without further purification.

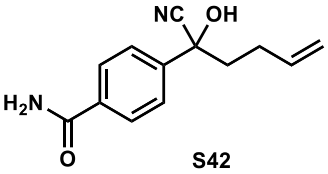
R_f = 0.23 (20% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3410 (br), 2955, 1724, 1641, 1610, 1436, 1409, 1278, 1188, 1109, 1018, 916; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.05 – 2.24 (3H, m), 2.32 – 2.38 (1H, m), 3.93 (3H, m), 5.01 – 5.04 (1H, m), 5.06 – 5.11 (1H, m), 5.75 – 5.83 (1H, m), 7.62 – 7.65 (2H, m), 8.05 – 8.07 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.8, 42.8, 52.6, 74.3, 116.5, 120.3, 125.2, 130.3, 131.0, 136.4, 144.6, 166.6; **HRMS** (AP+) $C_{14}H_{14}NO_3$ $[M+H]^+$ requires 244.0974, found 244.0982 (+ 3.3 ppm).

^{1}H and ^{13}C NMR spectra of **S41**





4-(1-Cyano-1-hydroxypent-3-en-1-yl)benzamide (S42)

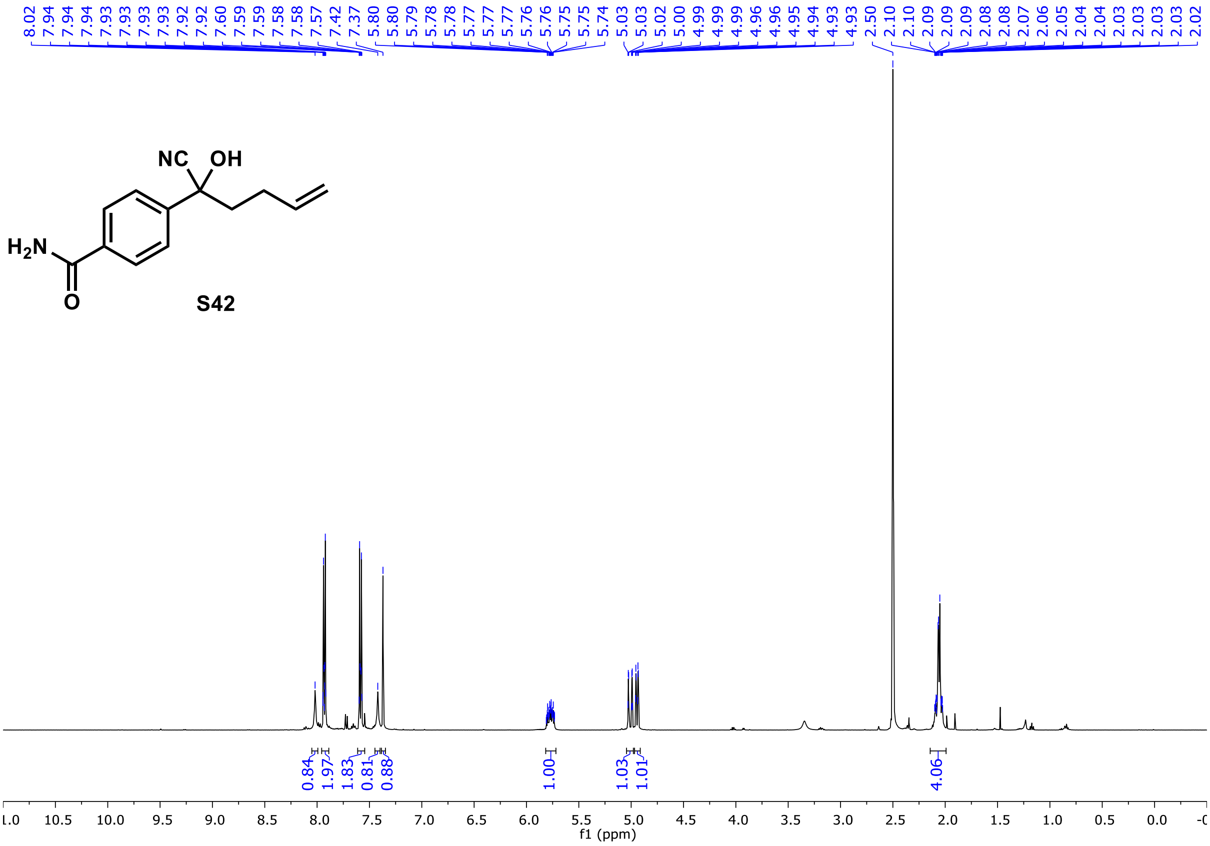


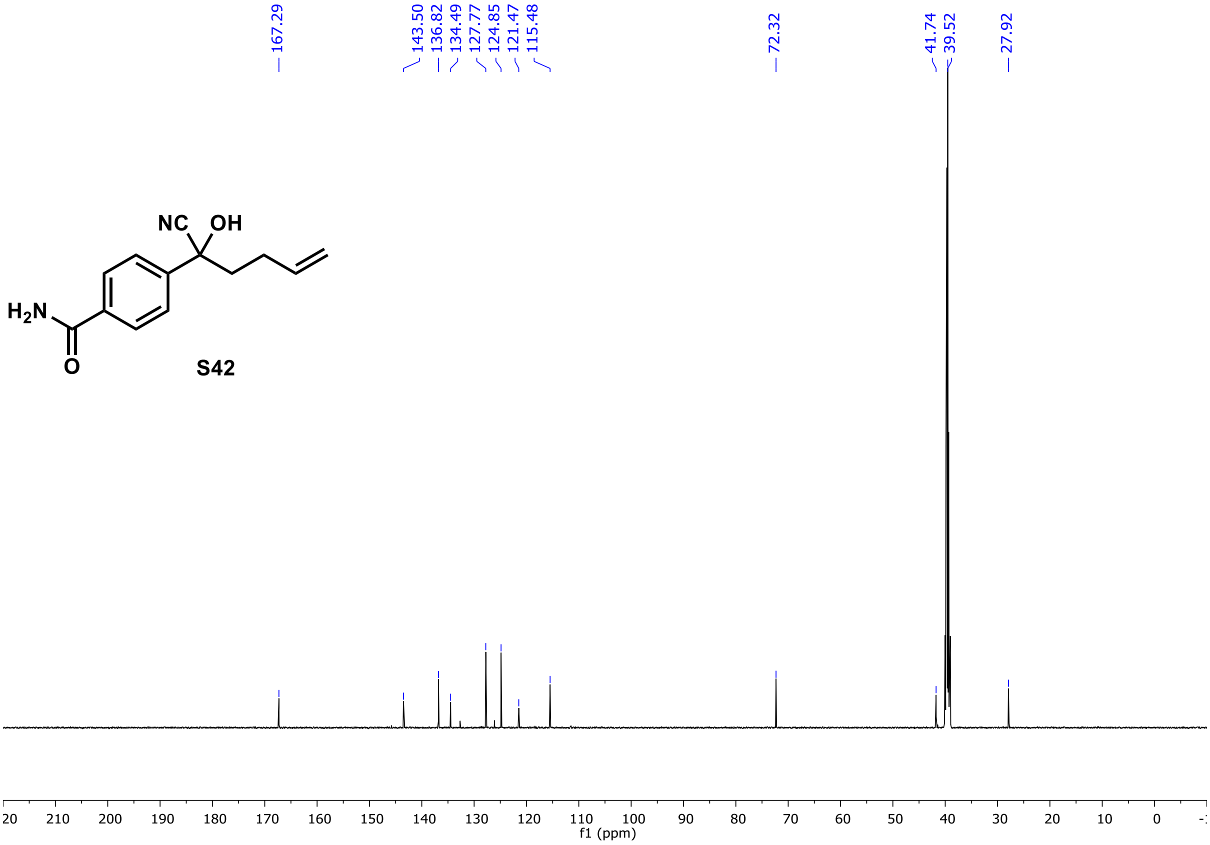
S42

Prepared according to General Procedure 5 using **S16** (184 mg, 0.90 mmol) in CH_2Cl_2 (4 mL), trimethylsilyl cyanide (563 μL, 4.50 mmol), and $TiCl_4$ (100 μL, 0.90 mmol), followed by MeCN (4.5 mL) and 2 M HCl (4.5 mL) to afford **S42** (159 mg, 77%) as an orange solid that was used without further purification.

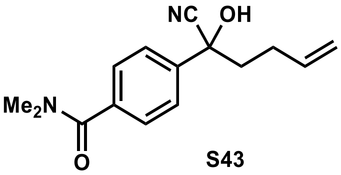
R$_f$ = 0.24 (80% EtOAc/petrol); **M.p.:** 118-120 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3414, 3192, 2922, 1653, 1610, 1566, 1413, 1300, 1269, 1207, 1143, 1124, 1072, 991, 910; **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ_H = 2.02 – 2.10 (4H, m), 4.93 – 4.96 (1H, m), 4.99 – 5.03 (1H, m), 5.73 – 5.81 (1H, m), 7.37 (1H, s), 7.42 (1H, br s), 7.57 – 7.60 (2H, m), 7.92 – 7.94 (2H, m), 8.02 (1H, br s); **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ_C = 27.9, 41.7, 73.3, 115.5, 121.5, 124.9, 127.8, 134.5, 136.8, 143.5, 167.3; **HRMS** (ES+) $C_{13}H_{14}N_2O_2$ $[M+H]^+$ requires 232.1134, found 231.1139 (+ 2.2 ppm).

^{1}H and ^{13}C NMR spectra of **S42**





4-(1-Cyano-1-hydroxypent-4-en-1-yl)-*N*,*N*-dimethylbenzamide (S43)

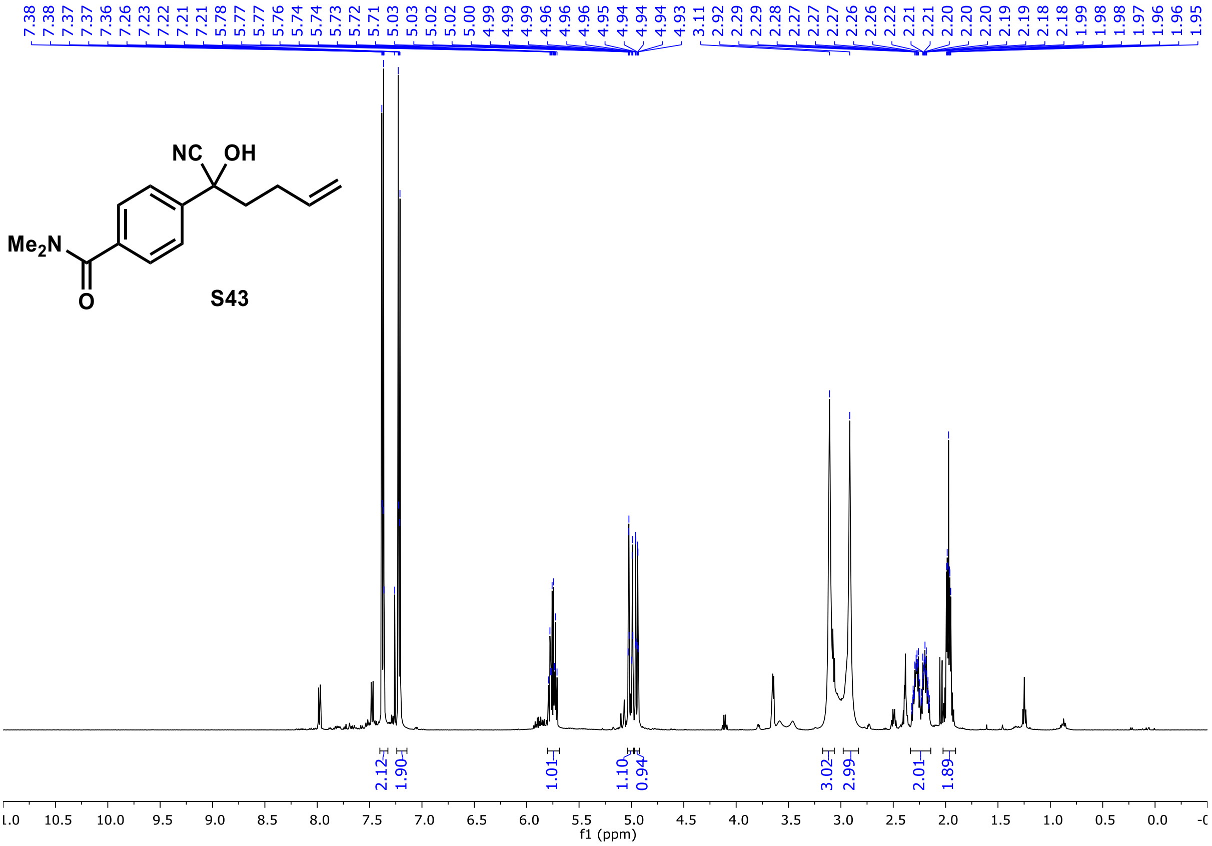


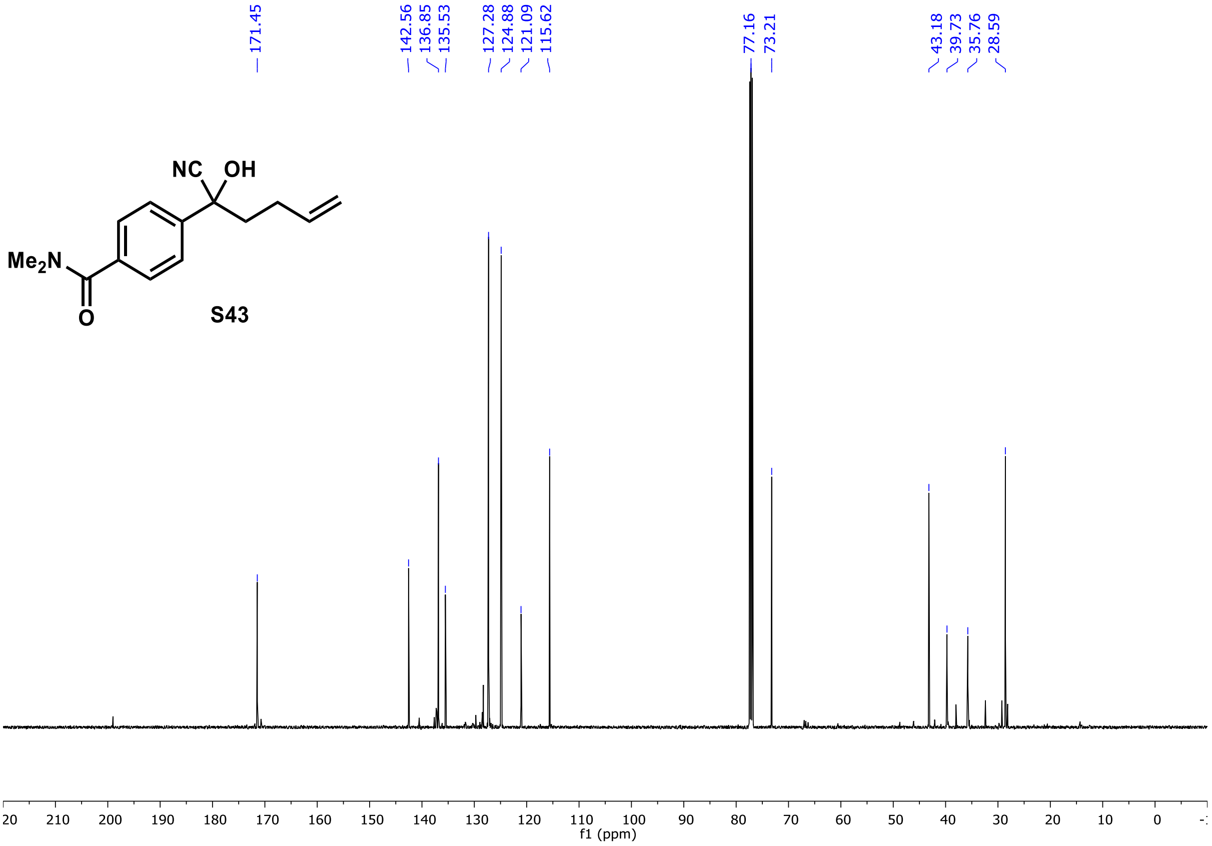
S43

Prepared according to General Procedure 5 using **S17** (347 mg, 1.50 mmol) in CH_2Cl_2 (3 mL), trimethylsilyl cyanide (469 µL, 3.75 mmol), and $TiCl_4$ (82 µL, 0.75 mmol), followed by MeCN (7.5 mL) and 2 M HCl (7.5 mL) to afford **S43** (346 mg, 89%) as an orange oil that was used without further purification.

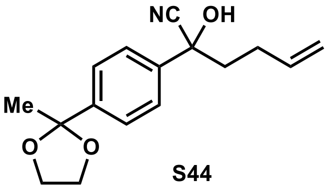
R$_f$ = 0.19 (60% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3242, 2927, 1608, 1517, 1448, 1398, 1265, 1083, 1018, 914, 846; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.95 – 1.99 (2H, m), 2.15 – 2.32 (2H, m), 2.92 (3H, s), 3.11 (3H, s), 4.93 – 4.96 (1H, m), 4.99 – 5.03 (1H, m), 5.75 (1H, ddt, *J* 16.8, 10.2, 6.5), 7.21 – 7.23 (2H, m), 7.36 – 7.38 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 28.6, 35.8, 39.7, 43.2, 73.2, 115.6, 121.1 124.9, 127.3, 135.5, 136.9, 142.6, 171.5; **HRMS** (ES+) $C_{15}H_{18}N_2O_2$ [M+H]$^+$ requires 259.1447, found 259.1448 (+ 0.4 ppm).

^{1}H and ^{13}C NMR spectra of **S43**





2-Hydroxy-2-(4-(2-methyl-1,3-dioxolan-2-yl)phenyl)hex-5-enenitrile (S44)

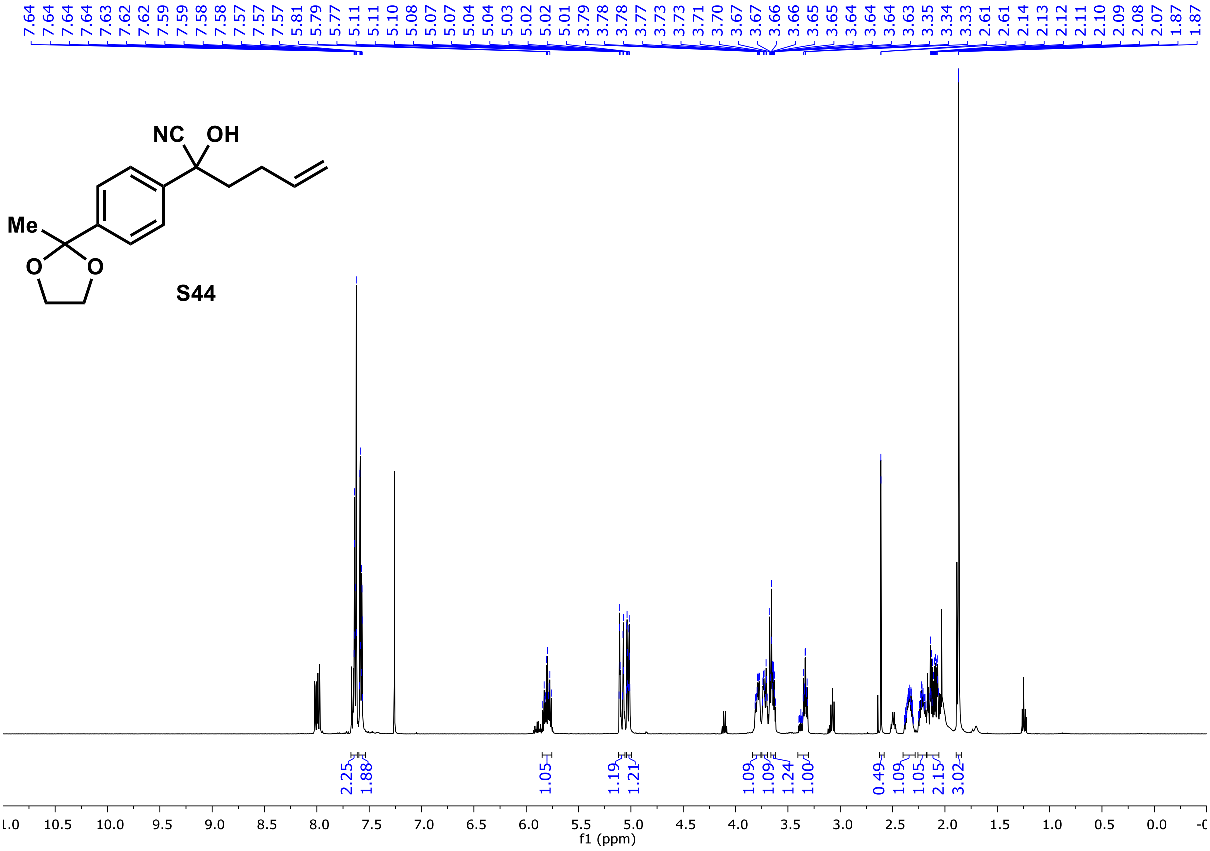


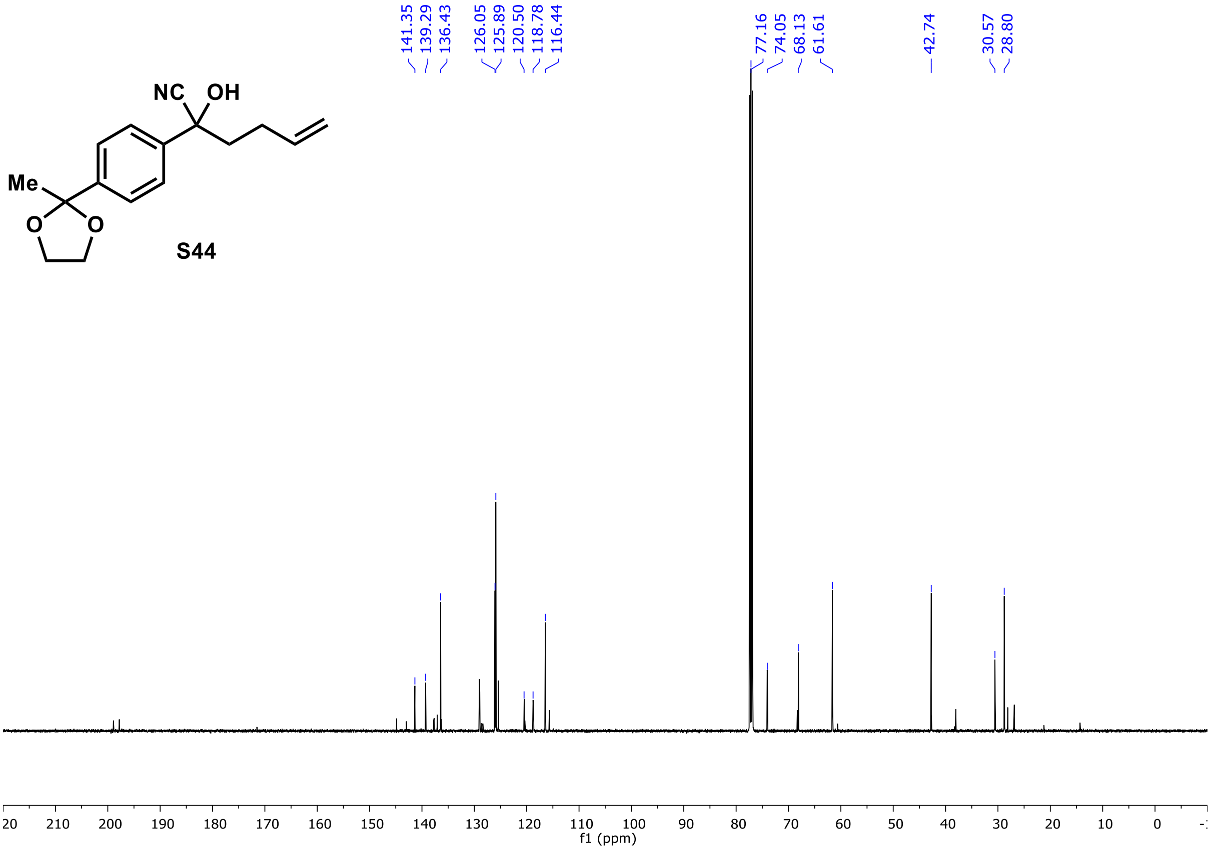
S44

Prepared according to General Procedure 5 using **S18** (616 mg, 2.50 mmol) in CH_2Cl_2 (5 mL), trimethylsilyl cyanide (782 μL, 6.25 mmol), and $TiCl_4$ (137 μL, 1.25 mmol), followed by MeCN (12.5 mL) and 2 M HCl (12.5 mL) to afford **S44** (683 mg, 99%) as a yellow oil that was used without further purification.

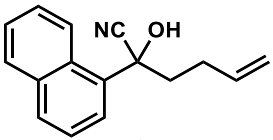
R_f = 0.13 (30% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3366, 2932, 2326, 1406, 1373, 1229, 1113, 1078, 1044, 1016, 837; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.87 (3H, s), 2.06 – 2.14 (2H, m), 2.18 – 2.25 (1H, m), 2.30 – 2.39 (1H, m), 2.61 (s, 1H), 3.31 – 3.39 (1H, m), 3.62 – 3.67 (1H, m), 3.70 – 3.74 (1H, m), 3.77 – 3.81 (1H, m), 5.01 – 5.04 (1H, m), 5.07 – 5.11 (1H, m), 5.76 – 5.84 (1H, m), 7.56 – 7.59 (2H, m), 7.62 – 7.64 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 28.8, 30.6, 42.7, 61.6, 68.1, 74.1, 116.4, 118.8, 120.5, 125.9, 126.1, 136.4, 139.3, 141.4; **HRMS** (ES+) $C_{16}H_{19}NO_3$ $[M+H]^+$ requires 274.1443, found 274.1441 (– 0.7 ppm).

^{1}H and ^{13}C NMR spectra of **S44**





2-Hydroxy-2-(naphthalen-1-yl)hex-5-enenitrile (S45)



S45

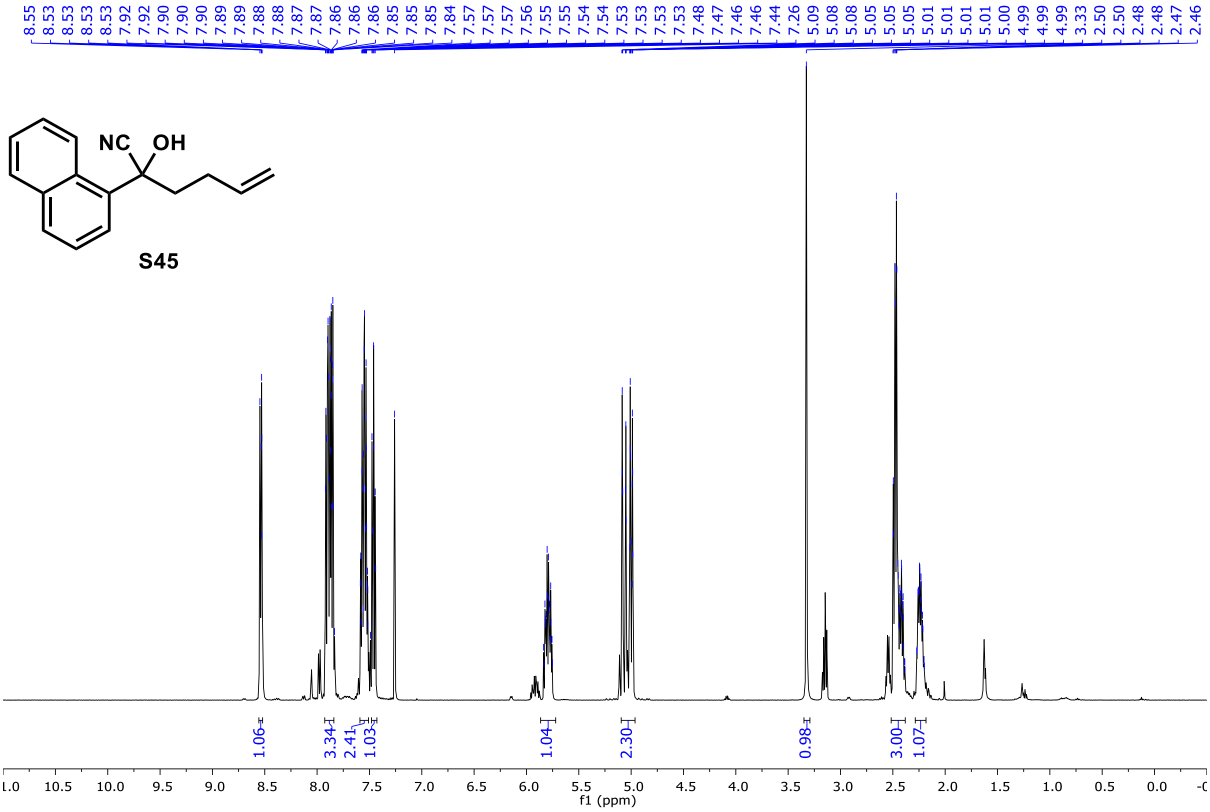
Prepared according to General Procedure 5 using **S19** (631 mg, 3.00 mmol) in CH_2Cl_2 (6 mL), trimethylsilyl cyanide (938 µL, 7.50 mmol), and $TiCl_4$ (164 µL, 1.50 mmol), followed by MeCN (15 mL) and 2 M HCl (15 mL) to afford **S45** (641 mg, 90%) as an orange oil that was used without further purification.

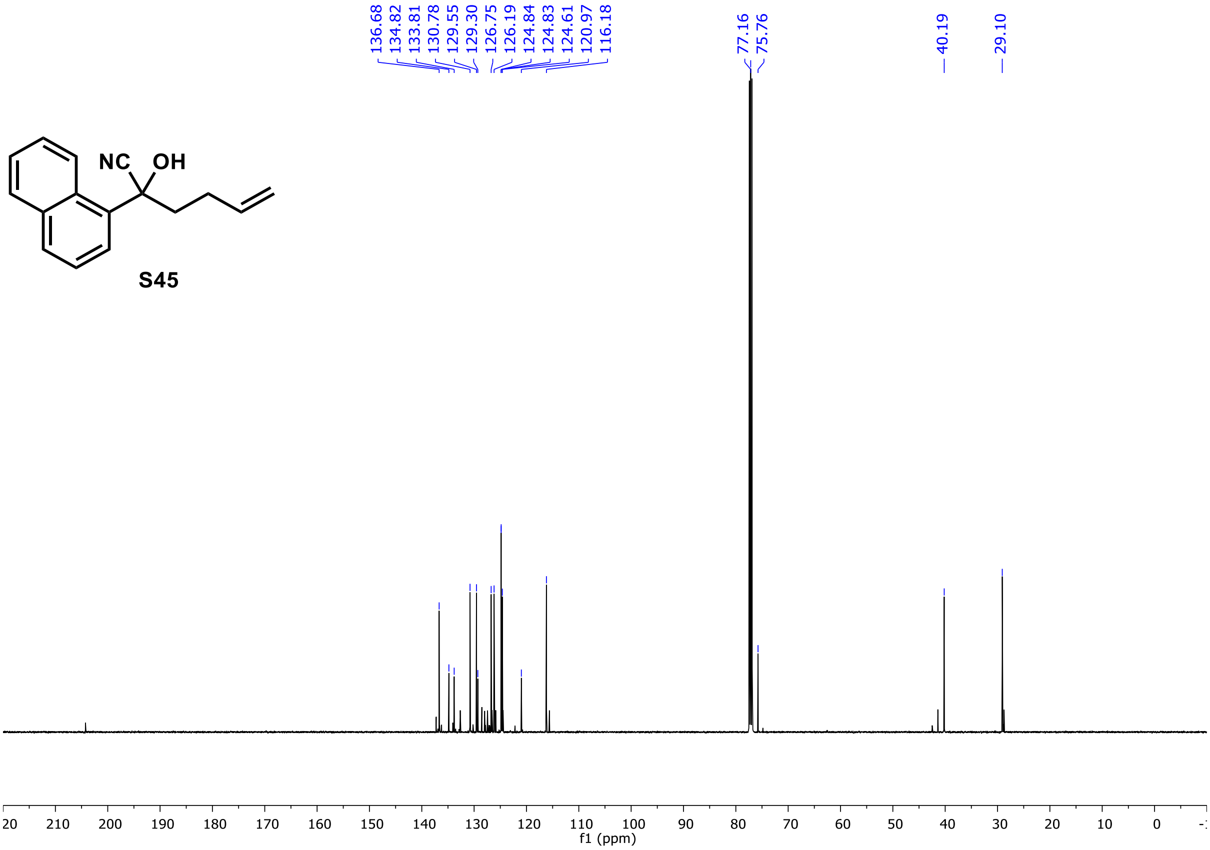
R_f = 0.57 (30% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.20 – 2.27 (1H, m), 2.38 – 2.50 (3H, m), 3.33 (1H, s), 4.98 – 5.09 (2H, m), 5.75 – 5.84 (1H, m), 7.44 – 7.49 (1H, m), 7.51 – 7.59 (2H, m), 7.83 – 7.92 (3H, m), 8.53 – 8.55 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 29.1, 40.2, 75.8, 116.2, 121.0, 124.6, 124.8 (2C), 126.2, 126.8, 129.3, 129.6, 130.8, 133.8, 134.8, 136.7.

28.5, 39.6, 75.2, 115.6, 120.4, 124.0, 124.3 (2C), 125.6, 126.2, 128.7, 129.0, 130.2, 133.2, 134.2, 136.1.

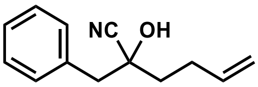
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **S45**





2-Benzyl-2-hydroxyhex-5-enenitrile (S46)



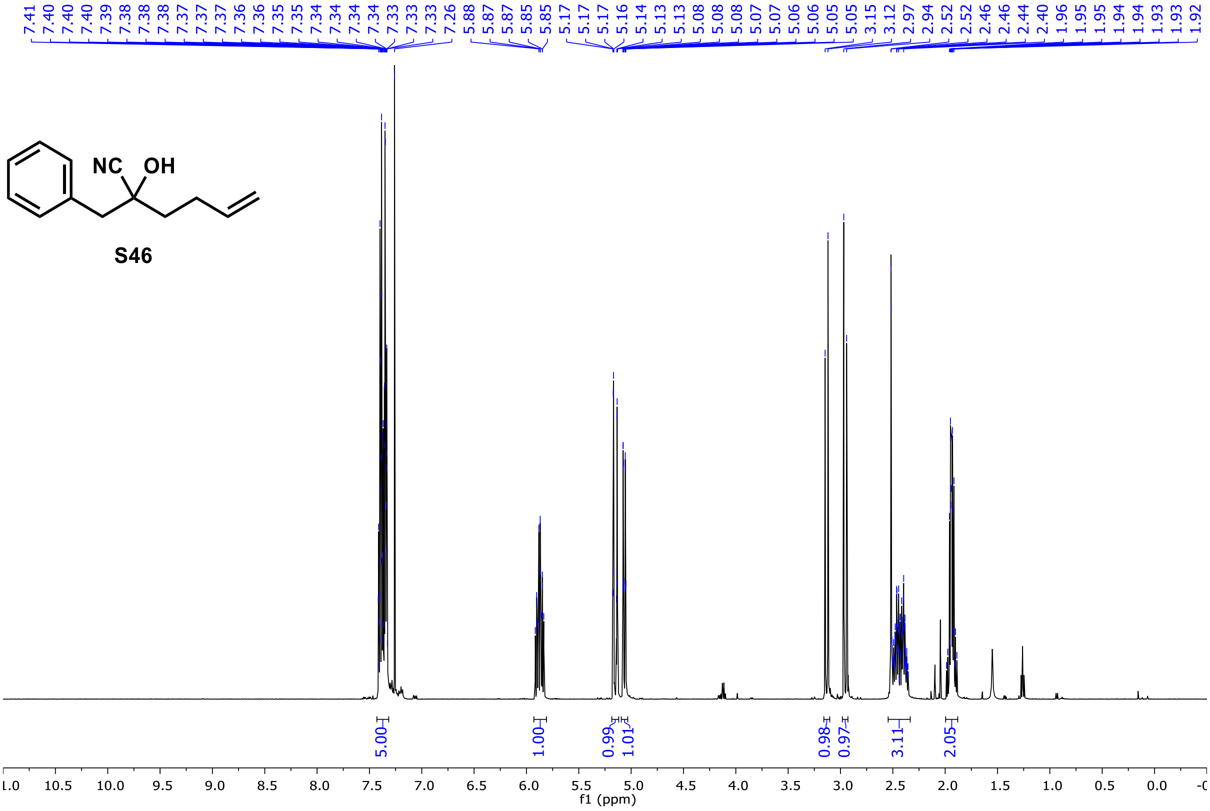
S46

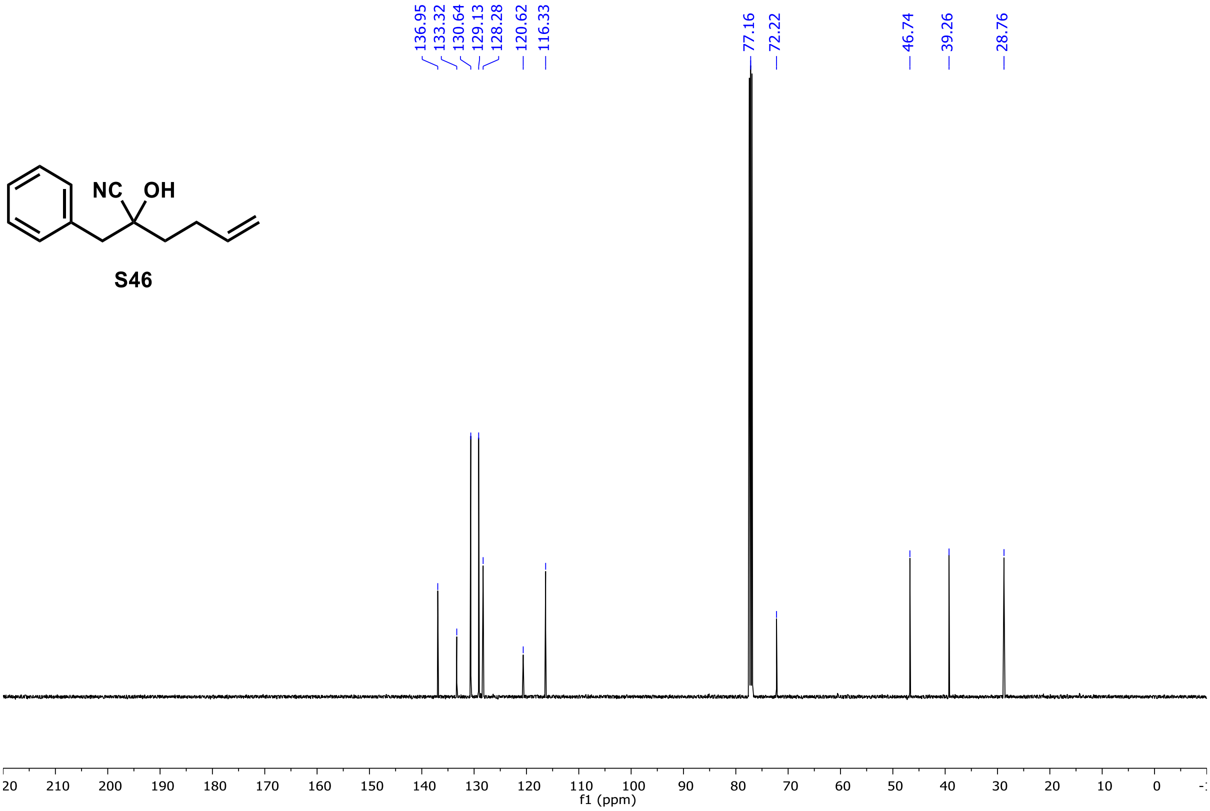
Prepared according to General Procedure 5 using **S20** (436 mg, 2.50 mmol) in CH_2Cl_2 (5 mL), trimethylsilyl cyanide (782 µL, 6.25 mmol), and $TiCl_4$ (137 µL, 1.25 mmol), followed by MeCN (12.5 mL) and 2 M HCl (12.5 mL) to afford **S46** (454 mg, 90%) as a colourless oil that was used without further purification.

R$_f$ = 0.16 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.87 – 2.01 (2H, m), 2.33 – 2.54 (3H, m), 2.95 (1H, d, *J* 13.7), 3.13 (1H, d, *J* 13.7), 5.03 – 5.09 (1H, m), 5.12 – 5.19 (1H, m), 5.81 – 5.94 (1H, m), 7.31 – 7.44 (5H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 28.8, 39.3, 46.7, 72.2, 116.3, 120.6, 128.3, 129.1, 130.6, 133.3, 137.0.

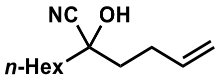
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **S46**





(But-3-en-1-yl)-2-hydroxyoctanenitrile (S47)

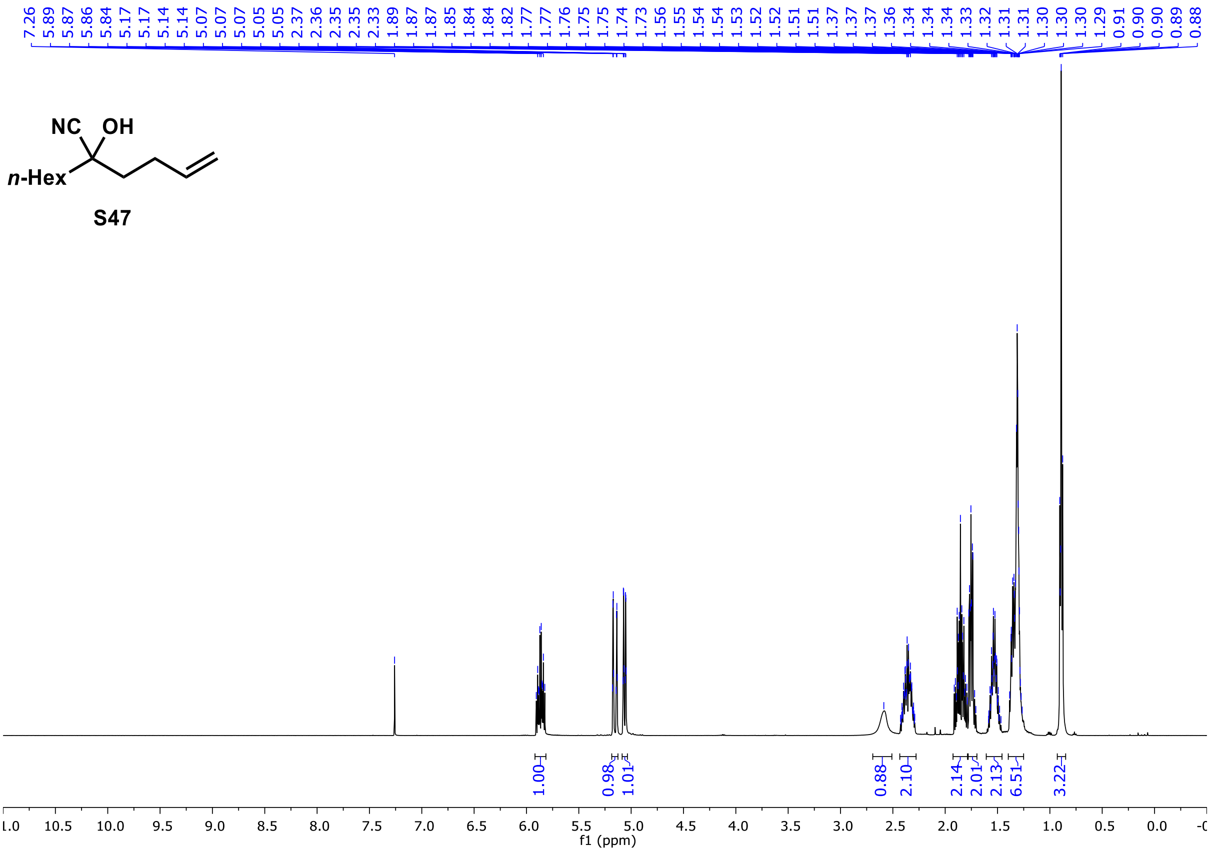


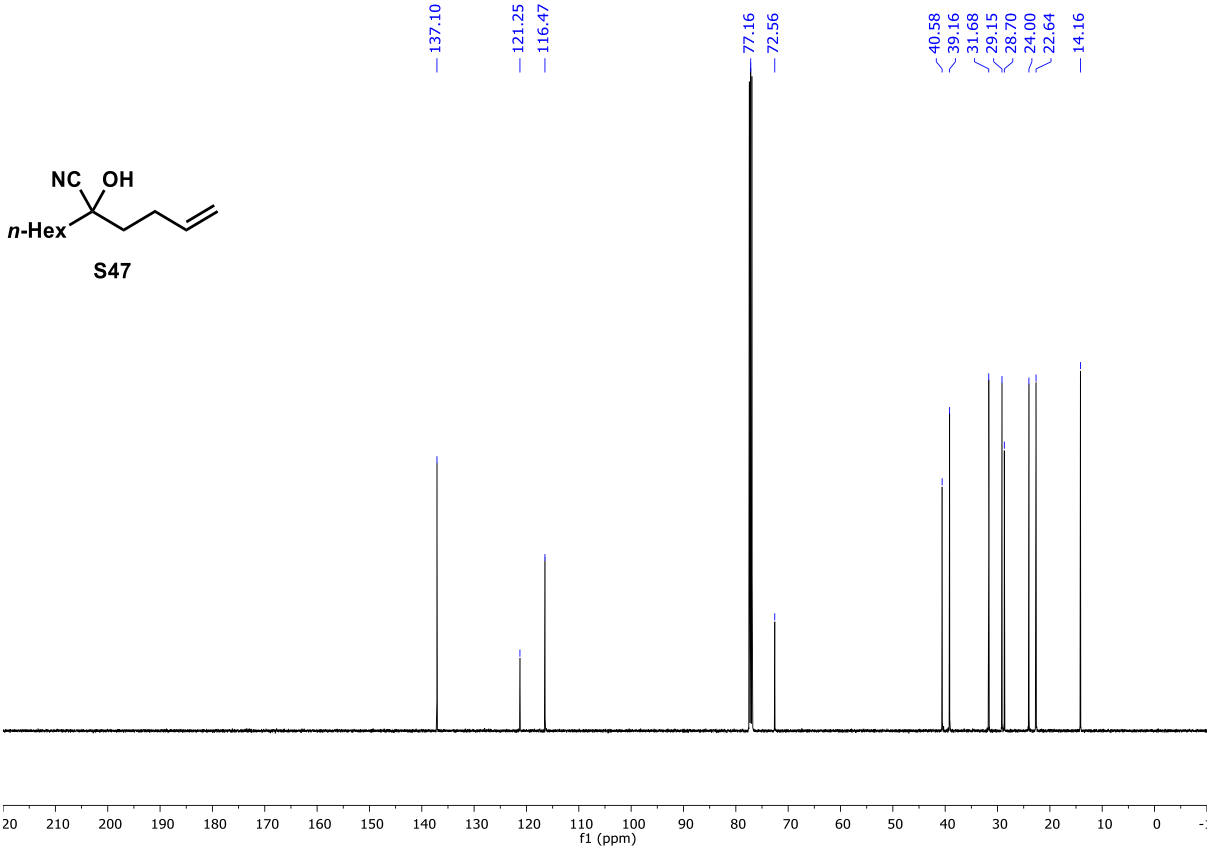
S47

Prepared according to General Procedure 5 using **S21** (503 mg, 3.00 mmol) in CH_2Cl_2 (6 mL), trimethylsilyl cyanide (938 μL, 7.50 mmol), and $TiCl_4$ (164 μL, 1.50 mmol), followed by MeCN (15 mL) and 2 M HCl (15 mL) to afford **S47** (450 mg, 80%) as a colourless oil that was used without further purification.

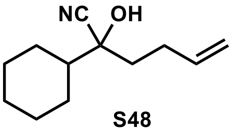
R_f = 0.34 (20% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3431, 2954, 2928, 2859, 2241, 1643, 1454, 1379, 1142, 1067, 993, 912; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 0.88 – 0.91 (3H, m), 1.26 – 1.38 (6H, m), 1.47 – 1.59 (2H, m), 1.71 – 1.77 (2H, m), 1.79 – 1.91 (2H, m), 2.29 – 2.43 (2H, m), 2.59 (1H, br s), 5.05 – 5.08 (1H, m), 5.13 – 5.18 (1H, m), 5.82 – 5.91 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 14.2, 22.6, 24.0, 28.7, 29.2, 31.7, 39.2, 40.6, 72.6, 116.5, 121.3, 137.1; **HRMS** (CI+) $C_{12}H_{21}NO$ [M-CN]$^+$ requires 169.1587, found 169.1588 (+ 0.9 ppm).

^{1}H and ^{13}C NMR spectra of **S47**





2-Cyclohexyl-2-hydroxyhex-5-enenitrile (S48)

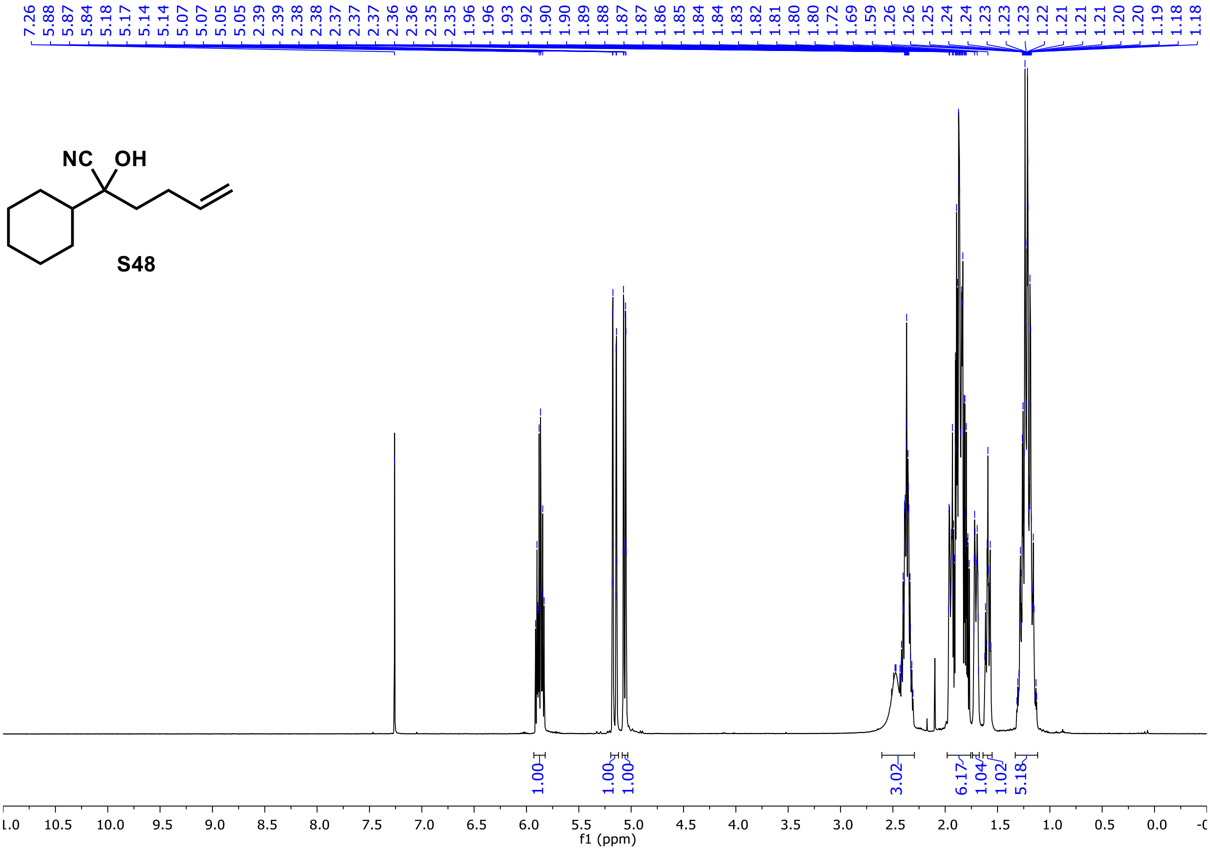


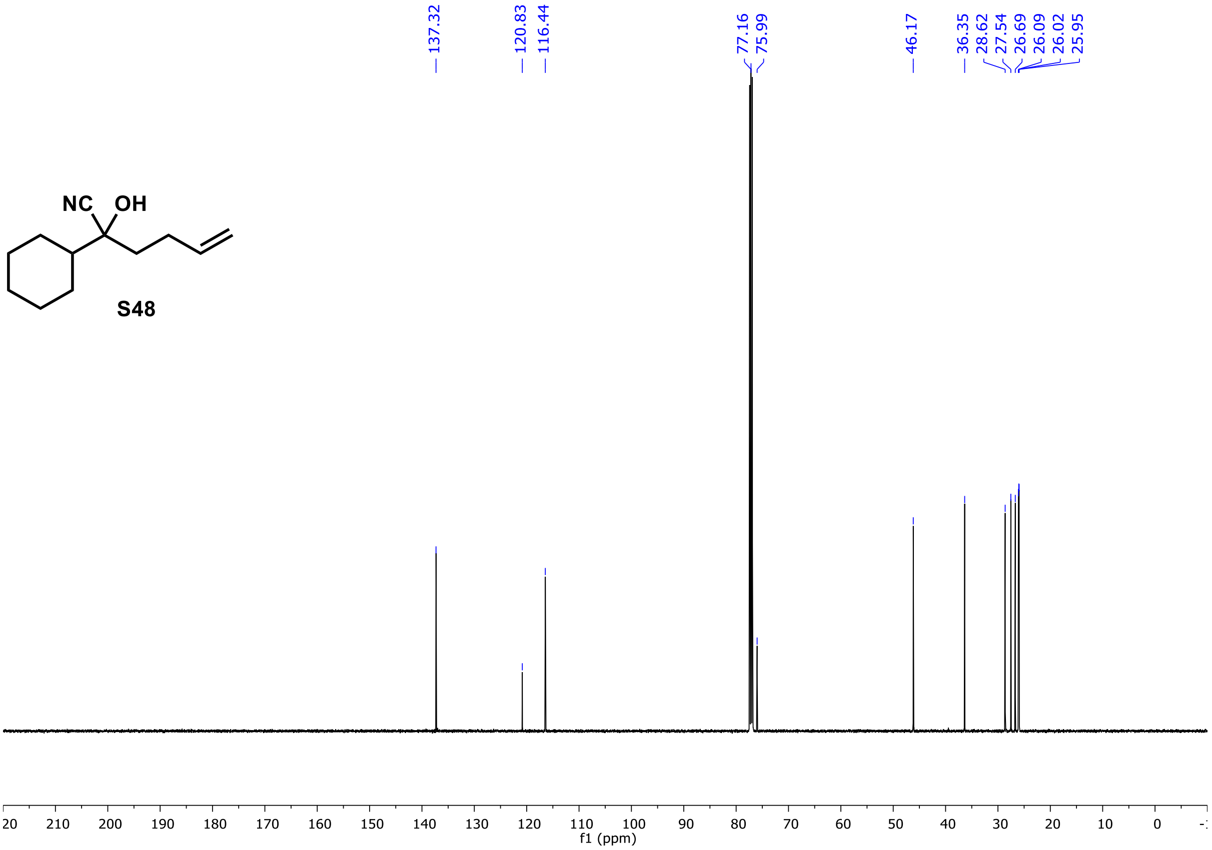
S48

Prepared according to General Procedure 5 using **S22** (498 mg, 3.00 mmol) in CH_2Cl_2 (6 mL), trimethylsilyl cyanide (938 µL, 7.50 mmol), and $TiCl_4$ (164 µL, 1.50 mmol), followed by MeCN (15 mL) and 2 M HCl (15 mL) to afford **S48** (425 mg, 73%) as a pale-yellow oil that was used without further purification.

R$_f$ = 0.36 (20% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3437, 3080, 2930, 2855, 2241, 1643, 1450, 1304, 1244, 1152, 1109, 1070, 914; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.13 – 1.31 (5H, m), 1.56 – 1.62 (1H, m), 1.68 – 1.73 (1H, m), 1.77 – 1.97 (6H, m), 2.31 – 2.51 (3H, m), 5.05 – 5.08 (1H, m), 5.14 – 5.18 (1H, m), 5.83 – 5.91 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 25.9, 26.0, 26.1, 26.7, 27.5, 28.6, 36.4, 46.2, 76.0, 116.4, 120.8, 137.3; **HRMS** (CI+) $C_{12}H_{19}NO$ [M-CN]$^+$ requires 167.1430, found 167.1430 (± 0.0 ppm).

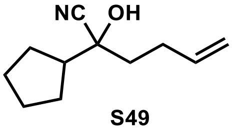
^{1}H and ^{13}C NMR spectra of **S48**





S48

2-Cyclopentyl-2-hydroxyhex-5-enenitrile (S49)

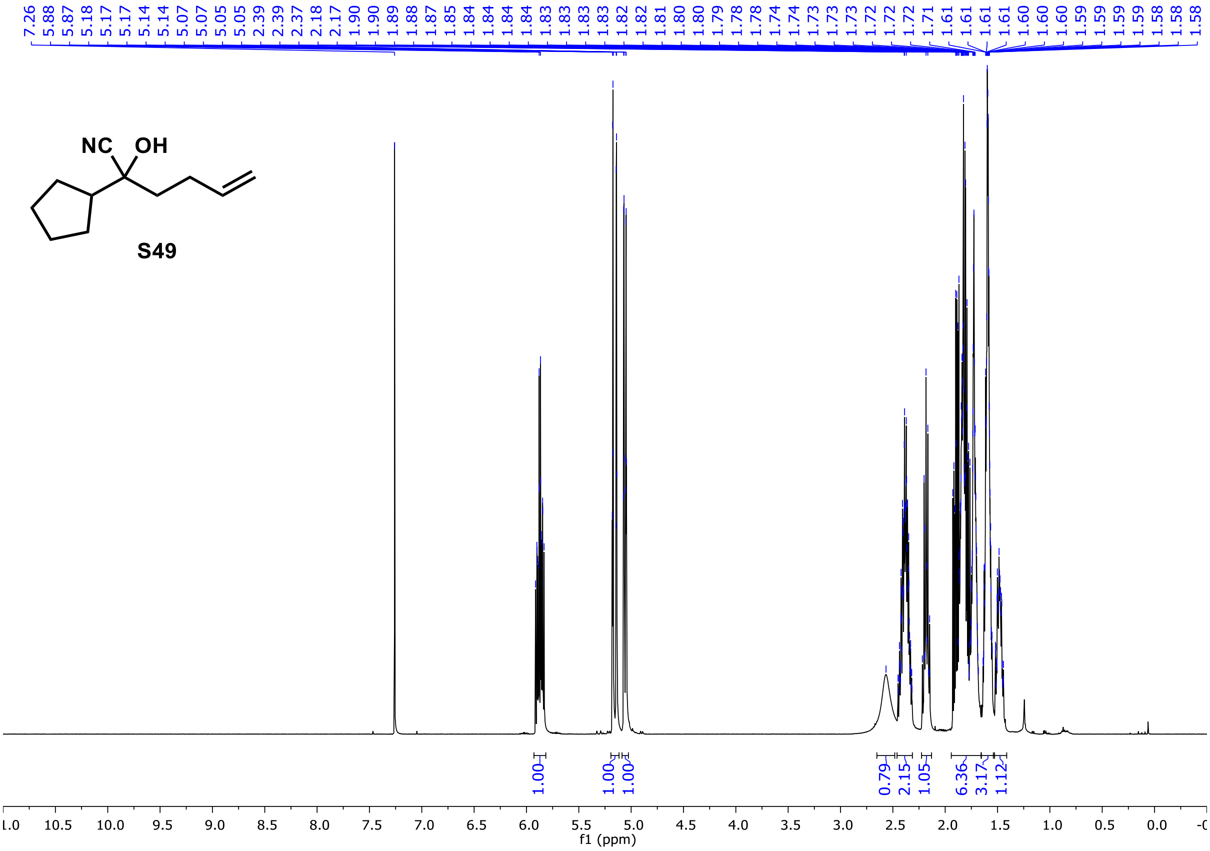


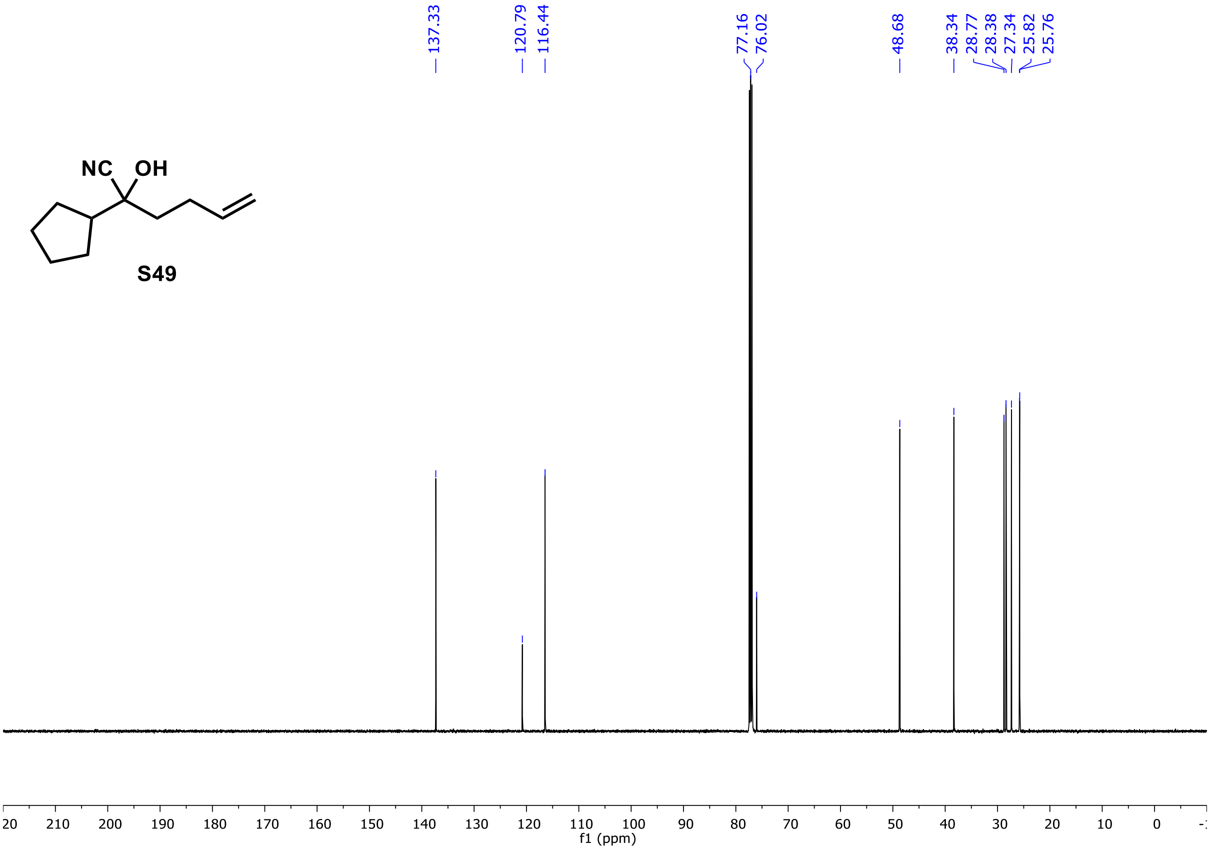
S49

Prepared according to General Procedure 5 using **S23** (454 mg, 3.00 mmol) in CH_2Cl_2 (6 mL), trimethylsilyl cyanide (938 μL, 7.50 mmol), and $TiCl_4$ (164 μL, 1.50 mmol), followed by MeCN (15 mL) and 2 M HCl (15 mL) to afford **S49** (430 mg, 81%) as a pale-yellow oil that was used without further purification.

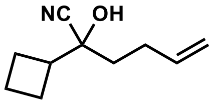
R_f = 0.33 (20% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3433, 3080, 2955, 2870, 2237, 1643, 1450, 1382, 1302, 1065, 993, 916; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.44 – 1.52 (1H, m), 1.55 – 1.64 (3H, m), 1.69 – 1.93 (6H, m), 2.15 – 2.22 (1H, m), 2.32 – 2.45 (2H, m), 2.57 (1H, br s), 5.04 – 5.07 (1H, m), 5.14 – 5.18 (1H, m), 5.83 – 5.91 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 25.7, 25.8, 27.3, 28.4, 28.8, 38.3, 48.7, 76.0, 116.4, 120.8, 137.3; **HRMS** (CI+) $C_{11}H_{17}NO$ [M-CN]$^+$ requires 153.1274, found 153.1273 (– 0.8 ppm).

^{1}H and ^{13}C NMR spectra of **S49**





2-Cyclobutyl-2-hydroxyhex-5-enenitrile (S50)

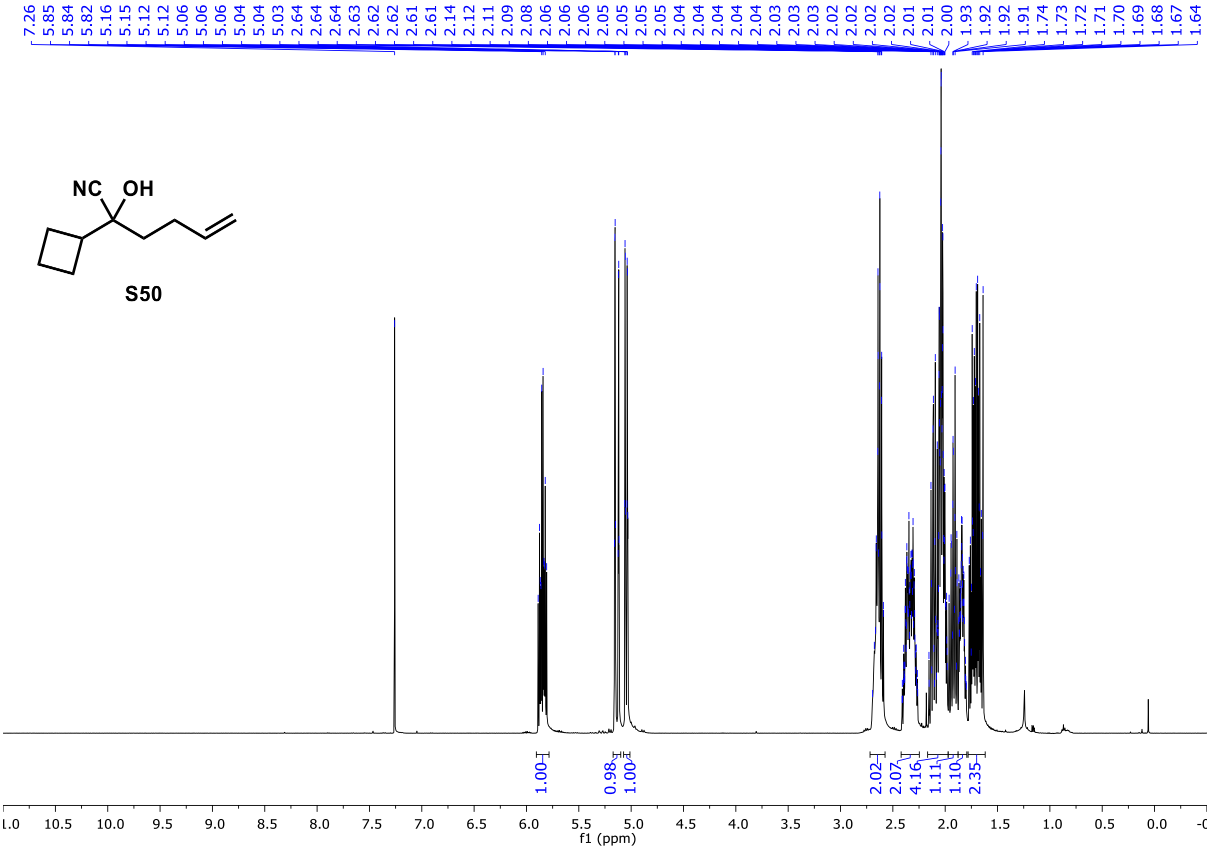


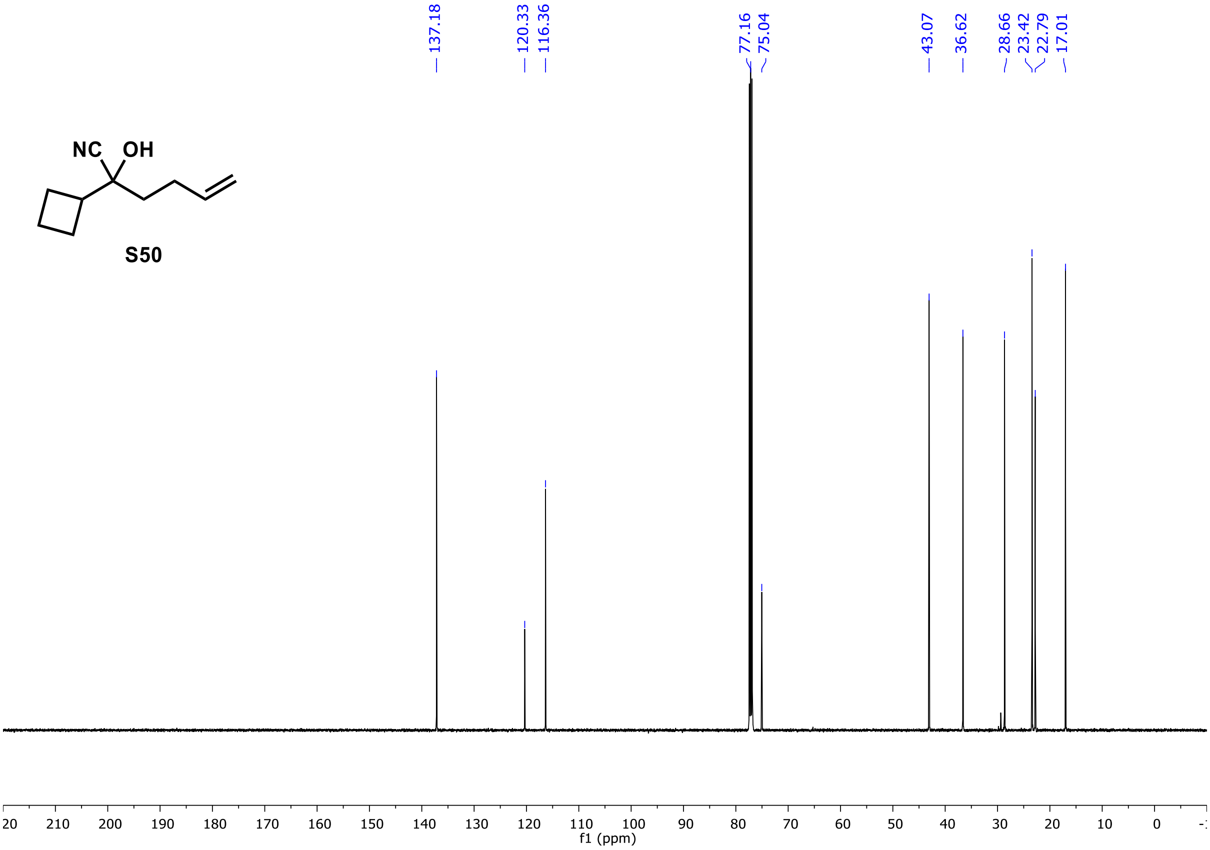
S50

Prepared according to General Procedure 5 using **S24** (415 mg, 3.00 mmol) in CH$_2$Cl$_2$ (6 mL), trimethylsilyl cyanide (938 µL, 7.50 mmol), and TiCl$_4$ (164 µL, 1.50 mmol), followed by MeCN (15 mL) and 2 M HCl (15 mL) to afford **S50** (390 mg, 79%) as a yellow oil that was used without further purification.

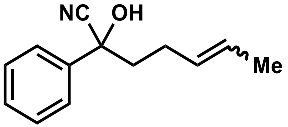
R$_f$ = 0.37 (20% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3433, 2980, 2945, 2864, 2239, 1643, 1438, 1382, 1250, 1148, 1092, 1022, 995, 916; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.64 – 1.77 (2H, m), 1.80 – 1.87 (1H, m), 1.89 – 1.96 (1H, m), 1.98 – 2.16 (4H, m), 2.26 – 2.41 (2H, m), 2.59 – 2.69 (2H, m), 5.03 – 5.06 (1H, m), 5.12 – 5.16 (1H, m), 5.81 – 5.89 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 17.0, 22.8, 23.4, 28.7, 36.6, 43.1, 75.0, 116.4, 120.3, 137.2; **HRMS** (CI+) C$_{10}$H$_{15}$NO [M-CN]$^+$ requires 139.1117, found 139.1116 (– 1.2 ppm).

^{1}H and ^{13}C NMR spectra of **S50**




S50

2-Hydroxy-2-phenylhept-5-enenitrile (S51)


S51

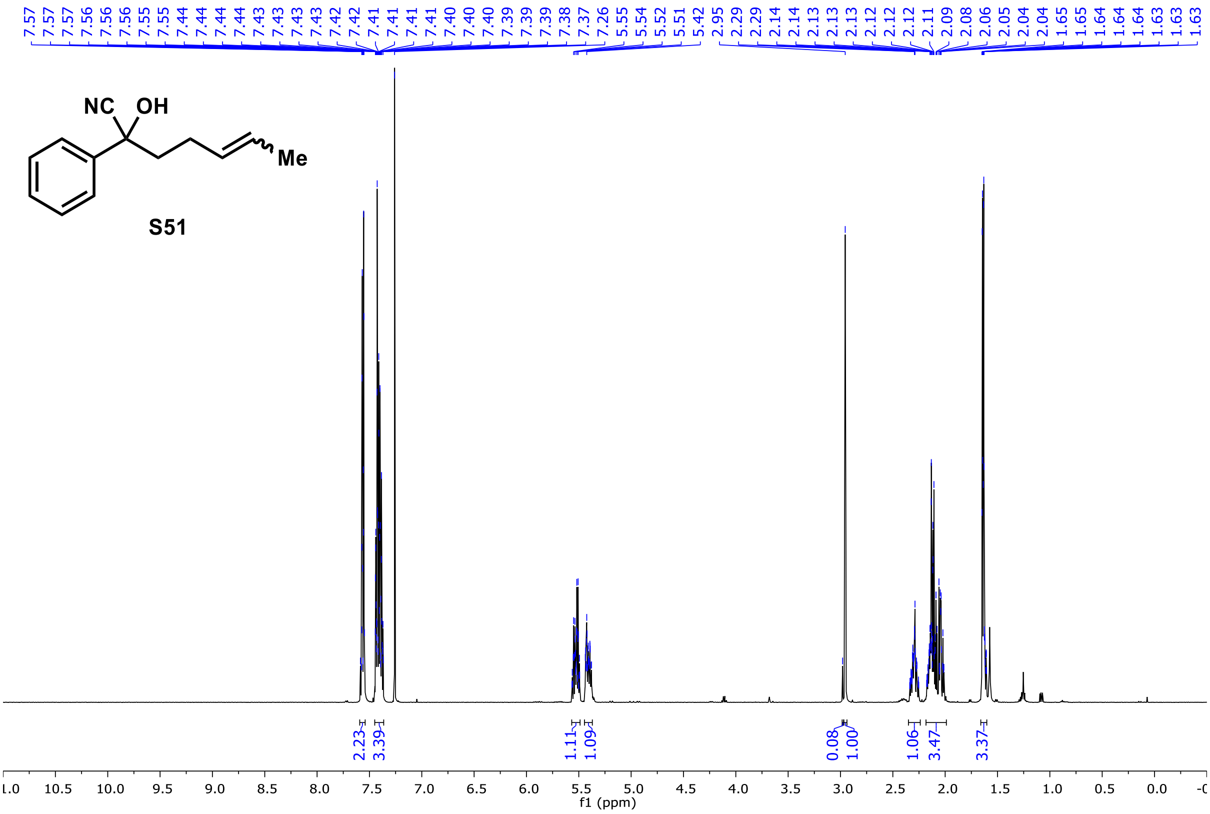
Prepared according to General Procedure 5 using **S25** (348 mg, 2.00 mmol) in CH_2Cl_2 (4 mL), trimethylsilyl cyanide (626 µL, 5.00 mmol), and $TiCl_4$ (110 µL, 1.00 mmol), followed by MeCN (10 mL) and 2 M HCl (10 mL) to afford **S51** (342 mg, 85%) as a yellow solid in an approximate *E*:*Z* ratio of 93:7, that was used without further purification.

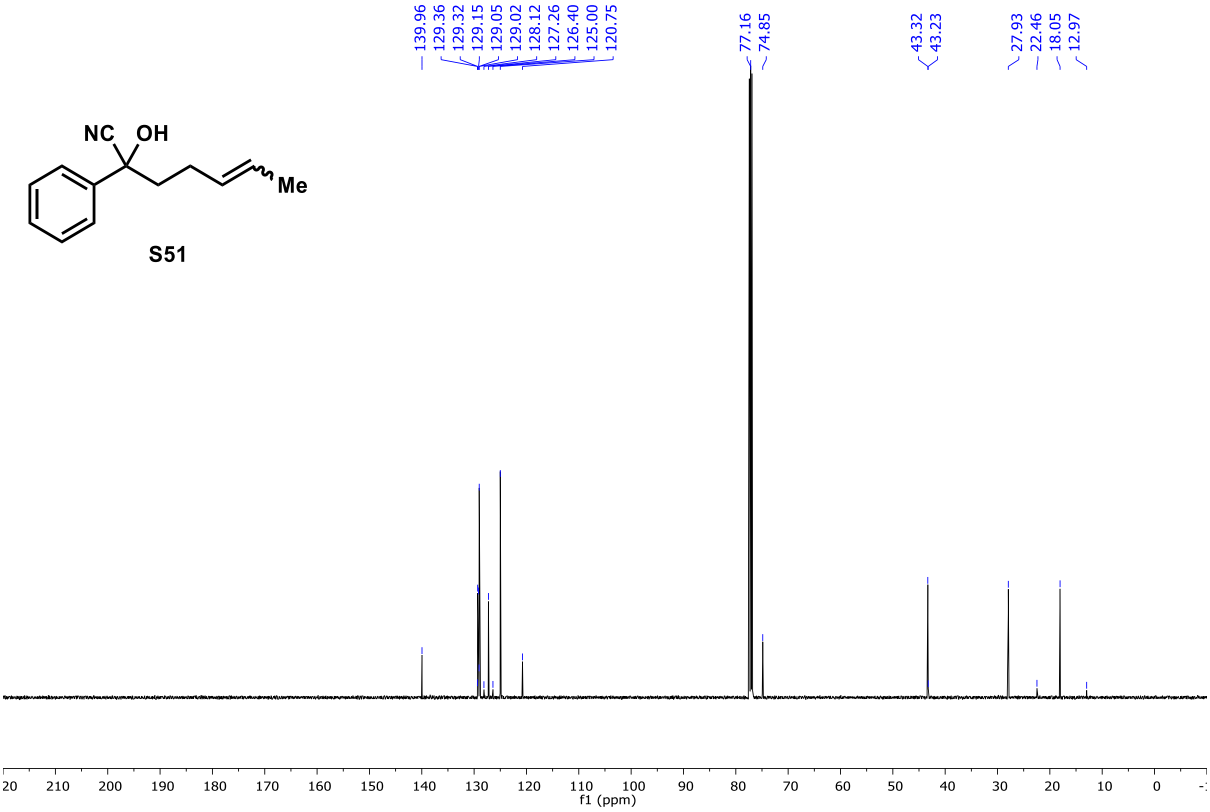
R$_f$ = 0.14 (10% EtOAc/petrol); **M.p.:** 56-58 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3372, 2963, 2933, 2245, 1446, 1377, 1066, 959, 700; **HRMS** (EI+) $C_{13}H_{15}NO$ $[M]^+$ requires 201.1148, found 201.1149 (+ 0.3 ppm).

Data for (*E*)-**S51***:* **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.60 – 1.65 (3H, m), 2.01 – 2.18 (3H, m), 2.27 – 2.33 (1H, m), 2.95 (1H, br s), 5.38 – 5.44 (1H, m), 5.49 – 5.56 (1H, m), 7.37 – 7.44 (3H, m), 7.55 – 7.59 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 18.1, 27.9, 43.3, 74.9, 120.8, 125.0, 127.3, 129.0, 129.2, 129.3, 140.0;

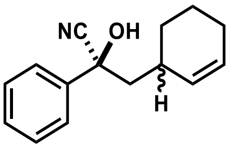
Data for (*Z*)-**S51** *(selected):* **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.98 (1H, br s); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 13.0, 22.5, 43.2, 126.4, 128.1, 129.1, 129.4.

^{1}H and ^{13}C NMR spectra of **S51**





3-(Cyclohex-2-en-1-yl)-2-hydroxy-2-phenylpropanenitrile (S52)



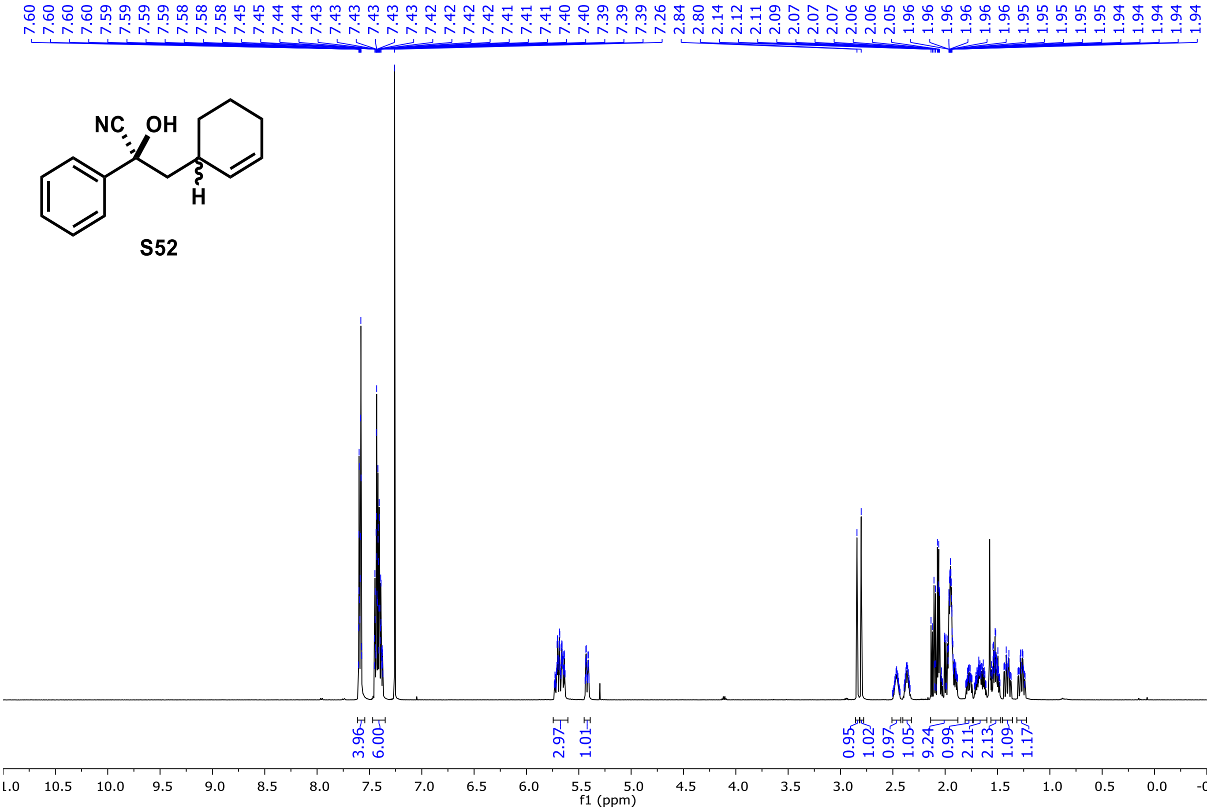
S52

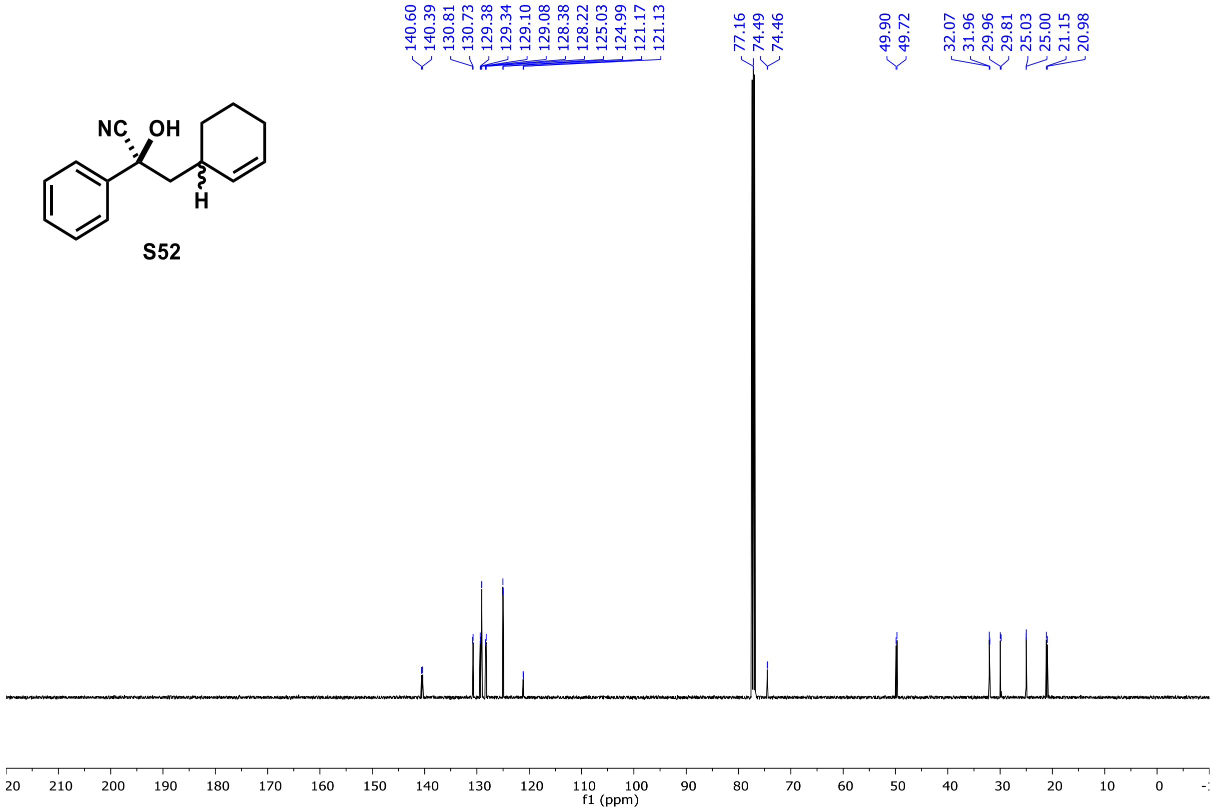
Prepared according to General Procedure 5 using **S26** (501 mg, 2.50 mmol) in CH_2Cl_2 (5 mL), trimethylsilyl cyanide (782 µL, 6.25 mmol), and $TiCl_4$ (137 µL, 1.25 mmol), followed by MeCN (12.5 mL) and 2 M HCl (12.5 mL) to afford **S52** (501 mg, 88%) as an orange oil that was used without further purification. The compound was obtained as a 1:1 inseparable mixture of diastereoisomers.

R_f = 0.14 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.24 – 1.30 (1H, m), 1.37 – 1.44 (1H, m), 1.48 – 1.56 (2H, m), 1.61 – 1.72 (2H, m), 1.74 – 1.80 (1H, m), 1.88 – 2.14 (9H, m), 2.33 – 2.39 (1H, m), 2.43 – 2.50 (1H, m), 2.80 (1H, br s), 2.84 (1H, br s), 5.40 – 5.44 (1H, m), 5.63 – 5.73 (3H, m), 7.37 – 7.45 (6H, m), 7.57 – 7.60 (4H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 21.0, 21.2, 25.0, 25.1, 29.8, 30.0, 32.0, 32.1, 49.7, 49.9, 74.4, 74.5, 121.1, 121.2, 124.9, 125.0, 128.2, 128.4, 129.0, 129.1, 129.3, 129.4, 130.7, 130.8, 140.4, 140.6.

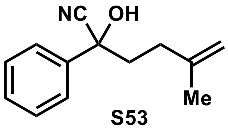
These data are in accordance with the literature.[18]

<u>^{1}H and ^{13}C NMR spectra of **S52**</u>





2-Hydroxy-5-methyl-2-phenylhex-5-enenitrile (S53)



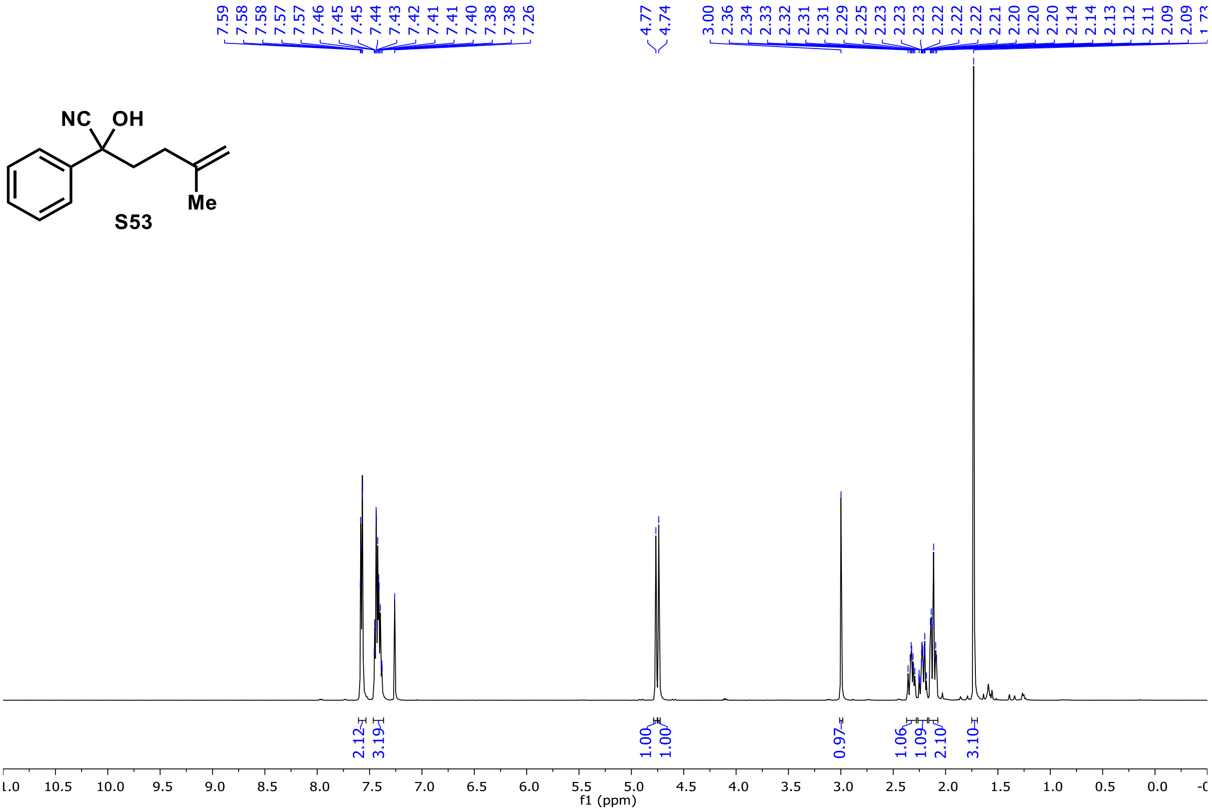
S53

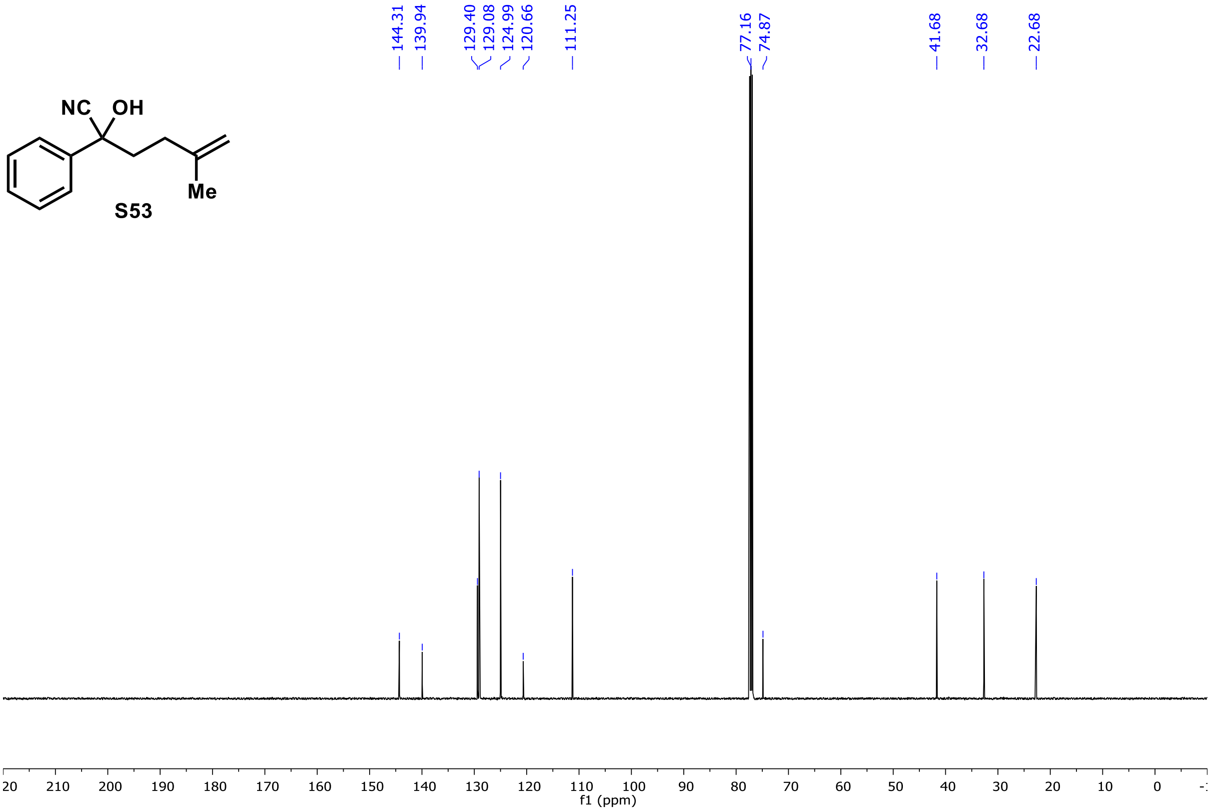
Prepared according to General Procedure 5 using **S27** (871 mg, 5.00 mmol) in CH_2Cl_2 (10 mL), trimethylsilyl cyanide (1.56 mL, 12.5 mmol), and $TiCl_4$ (274 µL, 2.50 mmol), followed by MeCN (25 mL) and 2 M HCl (25 mL) to afford **S53** (993 mg, 99%) as an orange oil that was used without further purification.

R_f = 0.17 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.73 (3H, s), 2.09 – 2.14 (2H, m), 2.18 – 2.26 (1H, m), 2.29 – 2.36 (1H, m), 3.00 (1H, br s), 4.74 (1H, app s), 4.77 (1H, app s), 7.38 – 7.46 (3H, m), 7.57 – 7.59 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 22.7, 32.7, 41.7, 74.9, 111.3, 120.7, 125.0, 129.1, 129.4, 139.9, 144.3.

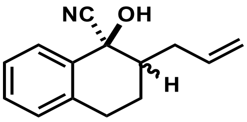
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **S53**





2-Allyl-1-hydroxy-1,2,3,4-tetrahydronaphthalene-1-carbonitrile (S54)

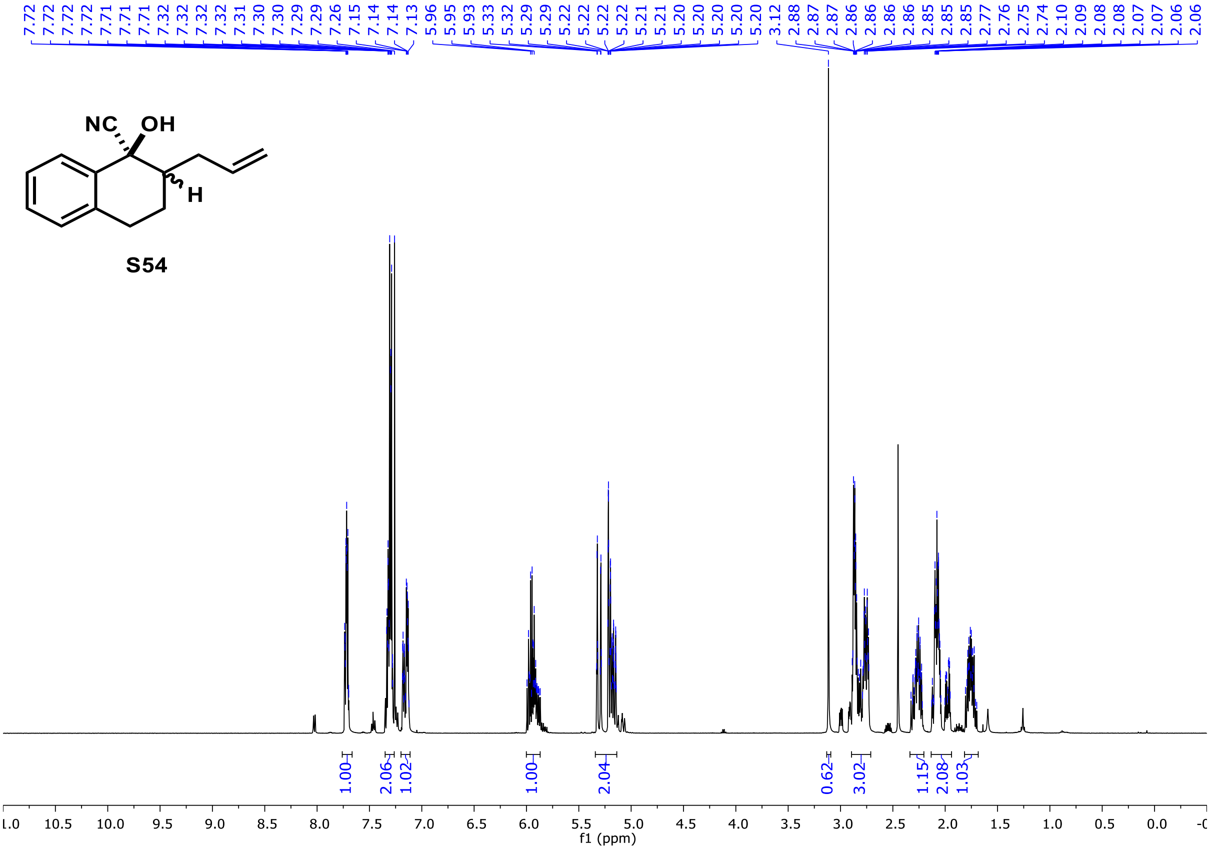


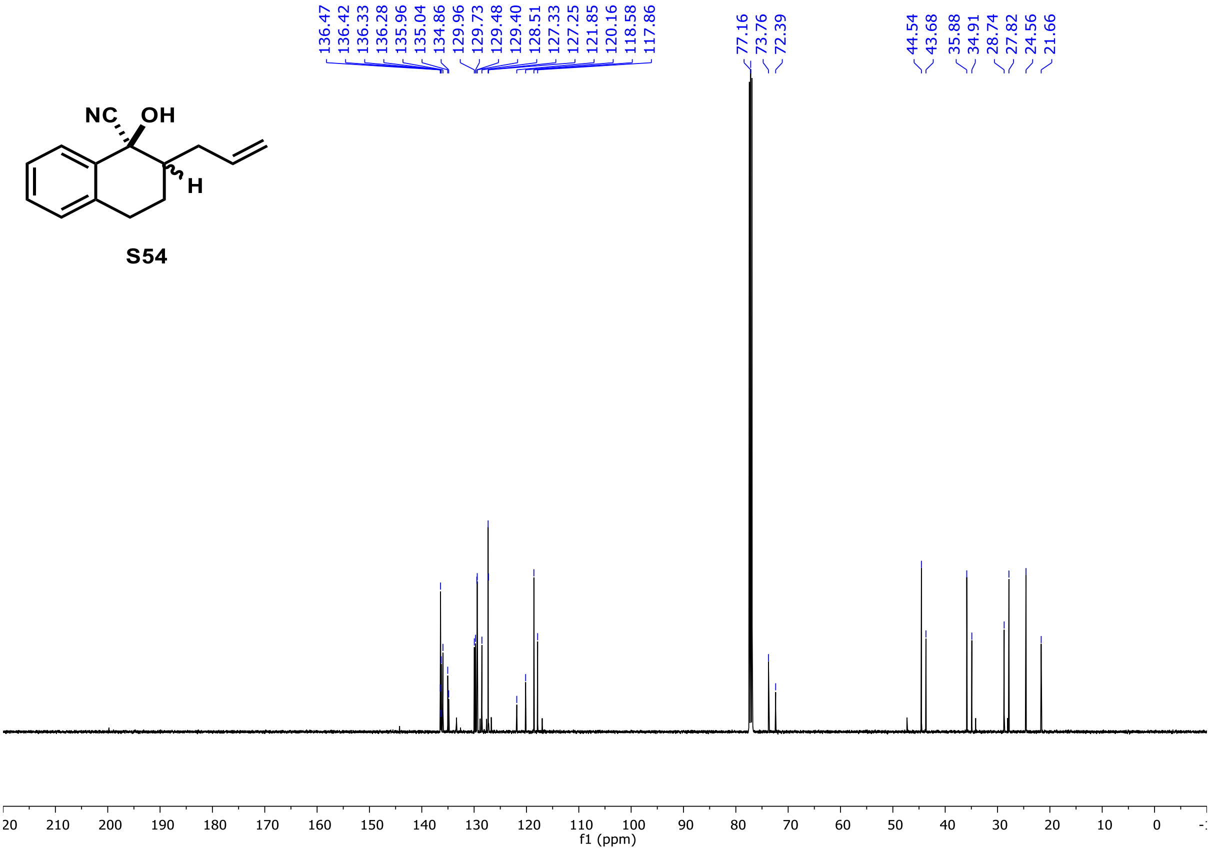
S54

Prepared according to General Procedure 5 using **S28** (373 mg, 2.00 mmol) in CH_2Cl_2 (4 mL), trimethylsilyl cyanide (626 μL, 5.00 mmol), and $TiCl_4$ (110 μL, 1.00 mmol), followed by MeCN (10 mL) and 2 M HCl (10 mL) to afford **S54** (411 mg, 97%) as an orange oil that was used without further purification. Analysis of the reaction mixture indicated a diastereomeric ratio of 3:2.

R_f = 0.33 (20% EtOAc/petrol); **FTIR** (v_{max} cm^{-1}, thin film) 3408, 2928, 2349, 2326, 1641, 1452, 1363, 1201, 991, 913, 761; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.70 – 1.81 (1H, m), 1.95 – 2.10 (2H, m), 2.22 – 2.33 (1H, m), 2.73 – 2.89 (3H, m), 3.12 (1H, s), 5.14 – 5.33 (2H, m), 5.87 – 5.99 (1H, m), 7.12 – 7.18 (1H, m), 7.28 – 7.34 (2H, m), 7.70 – 7.74 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 21.7, 24.6, 27.8, 28.7, 34.9, 35.9, 43.7, 44.5, 72.4, 73.8, 117.9, 118.6, 120.2, 121.9, 127.2, 127.3, 128.5, 129.4, 129.5, 129.7, 130.0 134.9, 135.0, 136.0, 136.2, 136.3, 136.4, 136.5; **HRMS** (ES+) $C_{14}H_{15}NO$ $[M-H]^+$ requires 212.1075, found 212.1079 (+ 1.9 ppm).

^{1}H and ^{13}C NMR spectra of **S54**


7.72
7.72
7.72
7.72
7.71
7.71
7.32
7.32
7.32
7.32
7.31
7.30
7.30
7.29
7.29
7.26
7.15
7.14
7.14
7.13
5.96
5.95
5.93
5.33
5.32
5.29
5.29
5.22
5.22
5.22
5.22
5.22
5.21
5.21
5.20
5.20
5.20
5.20
3.12
2.88
2.87
2.87
2.86
2.86
2.86
2.86
2.85
2.85
2.77
2.76
2.75
2.74
2.10
2.09
2.08
2.07
2.07
2.06
2.06
NC
OH
H
S54
1.00
2.06
1.02
1.00
2.04
0.62
3.02
1.15
2.08
1.03
10.5
10.0
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
0.0
f1 (ppm)

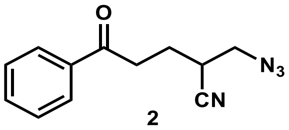

136.47
136.42
136.33
136.28
135.96
135.04
134.86
129.96
129.73
129.48
129.40
128.51
127.33
127.25
121.85
120.16
118.58
117.86
77.16
73.76
72.39
44.54
43.68
35.88
34.91
28.74
27.82
24.56
21.66
NC
OH
H
S54
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

2.4 General Procedure 6 – Electrochemical Alkene Azidocyanation

To an oven-dried 10 mL ElectraSyn vial equipped with a magnetic stirrer bar, was added the appropriate cyanohydrin (0.30 mmol), $Mn(OTf)_2$ (11 mg, 0.03 mmol), and NaN_3 (98 mg, 1.50 mmol). The threaded glass was wrapped with PTFE tape and connected to the ElectraSyn cap, which was fitted with a graphite anode and platinum foil cathode. The vial was subjected to vacuum-nitrogen exchange cycles (× 3), anhydrous MeCN (5.4 mL) was added, followed by TFA (600 μL), and the mixture was stirred until complete solvation of the NaN_3. The mixture was purged *via* bubbling with N_2 gas for 10 minutes. Electrolysis at 10 mA (j_{anode} = 7.8 mA/cm^2) was conducted for 4 h under N_2 at rt with continuous stirring. After electrolysis was complete, the reaction mixture was diluted with EtOAc (10 mL) and washed with a saturated solution of $NaHCO_3$ (aq.) (2 × 15 mL). The layers were separated, and the aqueous layer was further extracted with EtOAc (3 × 10 mL). The combined organics were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography to afford the desired product.

2.5 Characterisation of Products

2-(Azidomethyl)-5-oxo-5-phenylpentanenitrile (2)



2

Prepared according to General Procedure 6 using **1** (56 mg). The resultant crude material was purified by flash column chromatography (20% EtOAc/petrol, silica gel) to afford **2** (35 mg, 51%) as an orange solid.

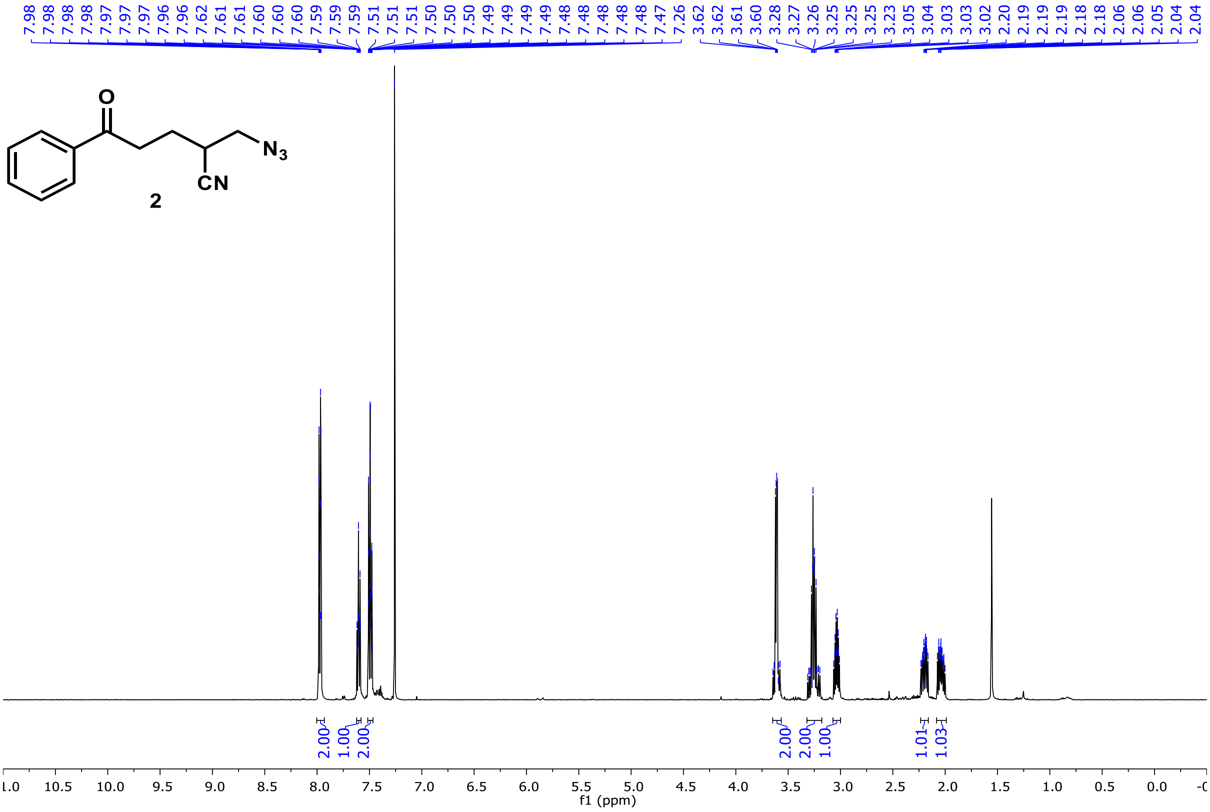
1.0 mmol scale

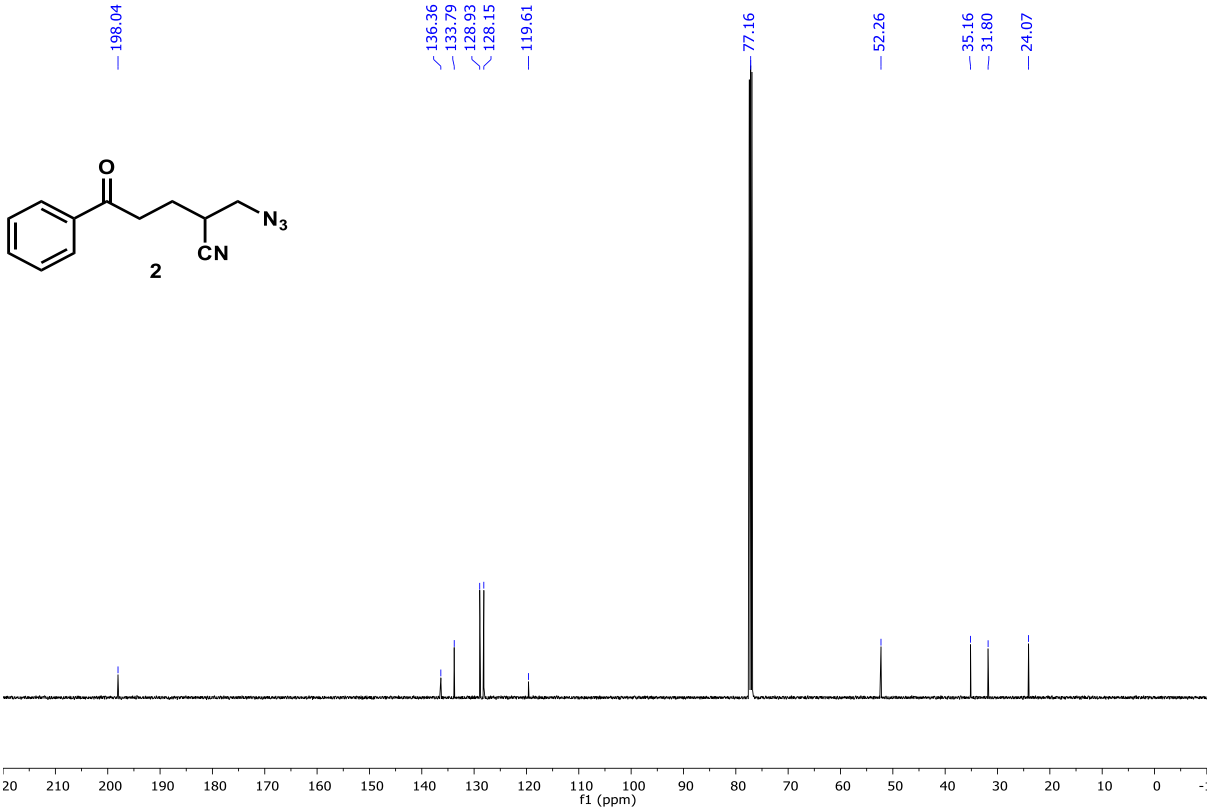
To an oven-dried 20 mL ElectraSyn vial equipped with a magnetic stirrer bar, was added **1** (187 mg, 1.00 mmol), $Mn(OTf)_2$ (35 mg, 0.10 mmol), and NaN_3 (325 mg, 5.00 mmol). The threaded glass was wrapped with PTFE tape and connected to the ElectraSyn cap, which was fitted with a graphite anode and platinum foil cathode. The vial was subjected to vacuum-nitrogen exchange cycles (× 3), anhydrous MeCN (5.4 mL) was added, followed by TFA (600 μL), and the mixture was stirred until complete solvation of the NaN_3. The mixture was purged *via* bubbling with N_2 gas for 10 minutes. Electrolysis at 10 mA (j_{anode} = 4.0 mA/cm^2) was conducted for 13 h 20 min under N_2 at rt with continuous stirring. After electrolysis was complete, the reaction mixture was diluted with EtOAc (50 mL) and washed with a saturated solution of $NaHCO_3$ (aq.) (2 × 50 mL). The layers were separated, and the aqueous layer was further extracted with EtOAc (3 × 50 mL). The combined organics were washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography to afford the **2** (146 mg, 64%) as an orange solid.

R_f = 0.16 (20% EtOAc/petrol); **M.p.:** 45-47 °C; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.98 – 2.09 (1H, m), 2.14 – 2.25 (1H, m), 2.99 – 3.08 (1H, m), 3.18 – 3.33 (2H, m), 3.56 – 3.67 (2H, m), 7.45 – 7.53 (2H, m), 7.57 – 7.64 (1H, m), 7.94 – 8.01 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 24.1, 31.8, 35.2, 52.3, 119.6, 128.2, 128.9, 133.8, 136.4, 198.0.

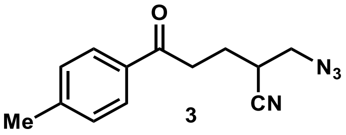
These data are in accordance with the literature.[18]

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





2-(Azidomethyl)-5-oxo-5-(*p*-tolyl)pentanenitrile (3)



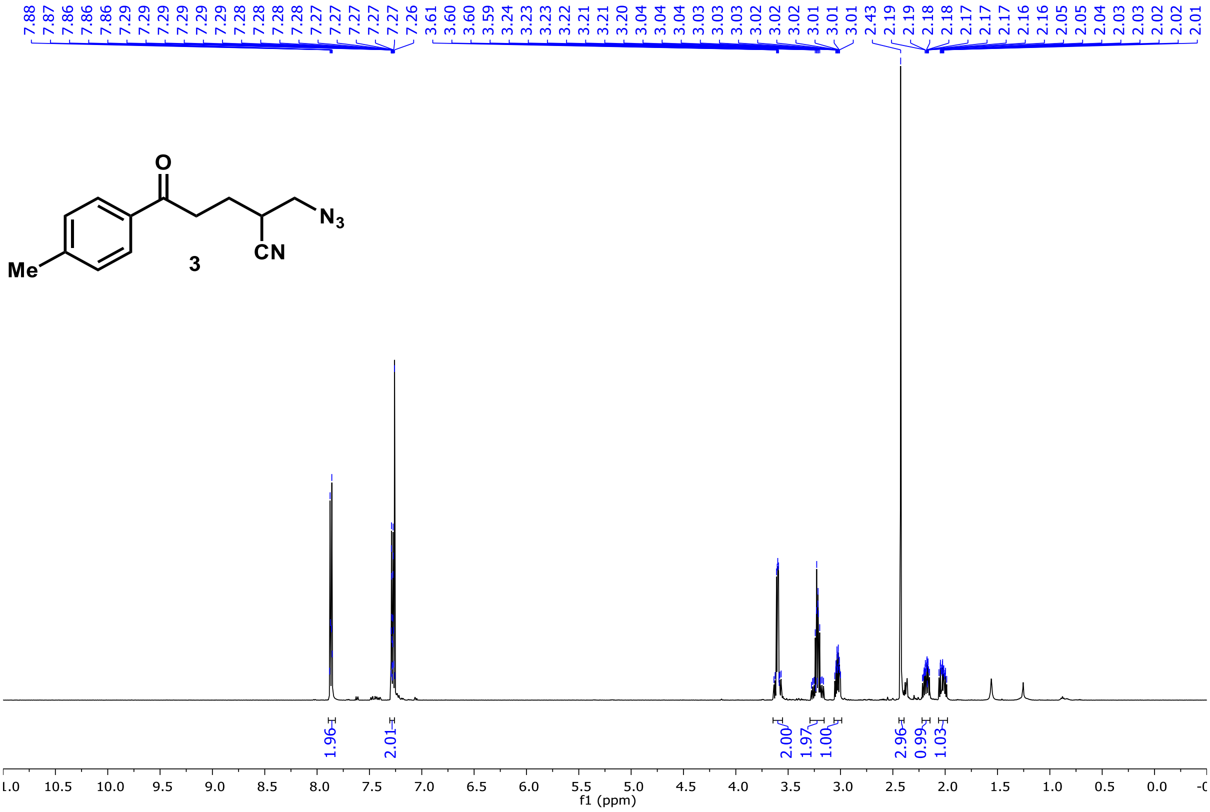
3

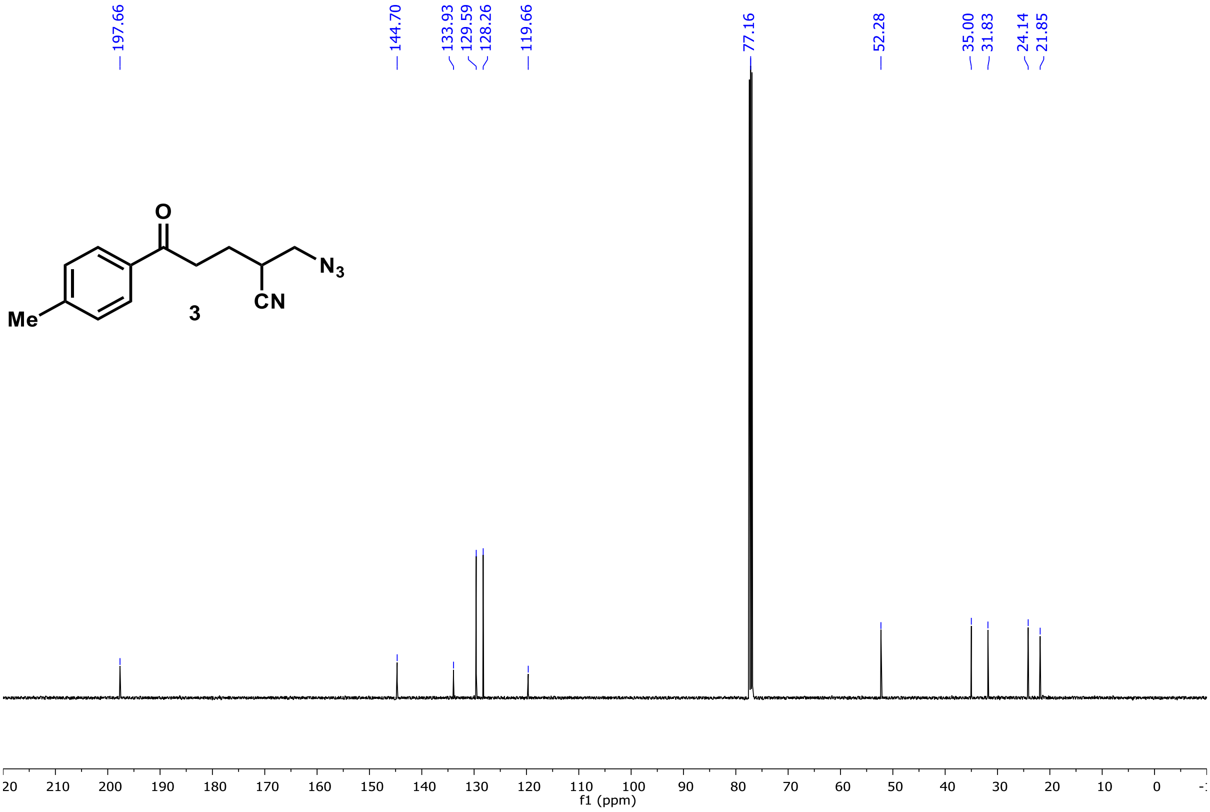
Prepared according to General Procedure 6 using **S29** (60 mg). The resultant crude material was purified by flash column chromatography (5-15% EtOAc/*n*-hexane, silica gel) to afford **3** (35 mg, 48%) as a yellow oil.

R$_f$ = 0.19 (20% EtOAc/*n*-hexane); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.99 – 2.06 (1H, m), 2.15 – 2.22 (1H, m), 2.43 (3H, s), 3.00 – 3.05 (1H, m), 3.16 – 3.28 (2H, m), 3.57 – 3.64 (2H, m), 7.27 – 7.29 (2H, m), 7.86 – 7.88 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 21.9, 24.1, 31.8, 35.0, 52.3, 119.7, 128.3, 129.6, 133.9, 144.7, 197.7.

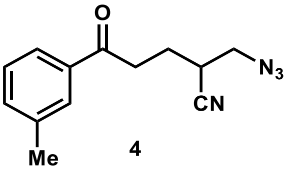
These data are in accordance with the literature.[18]

^1H and ^{13}C NMR spectra of **3**





2-(Azidomethyl)-5-oxo-5-(*m*-tolyl)pentanenitrile (4)



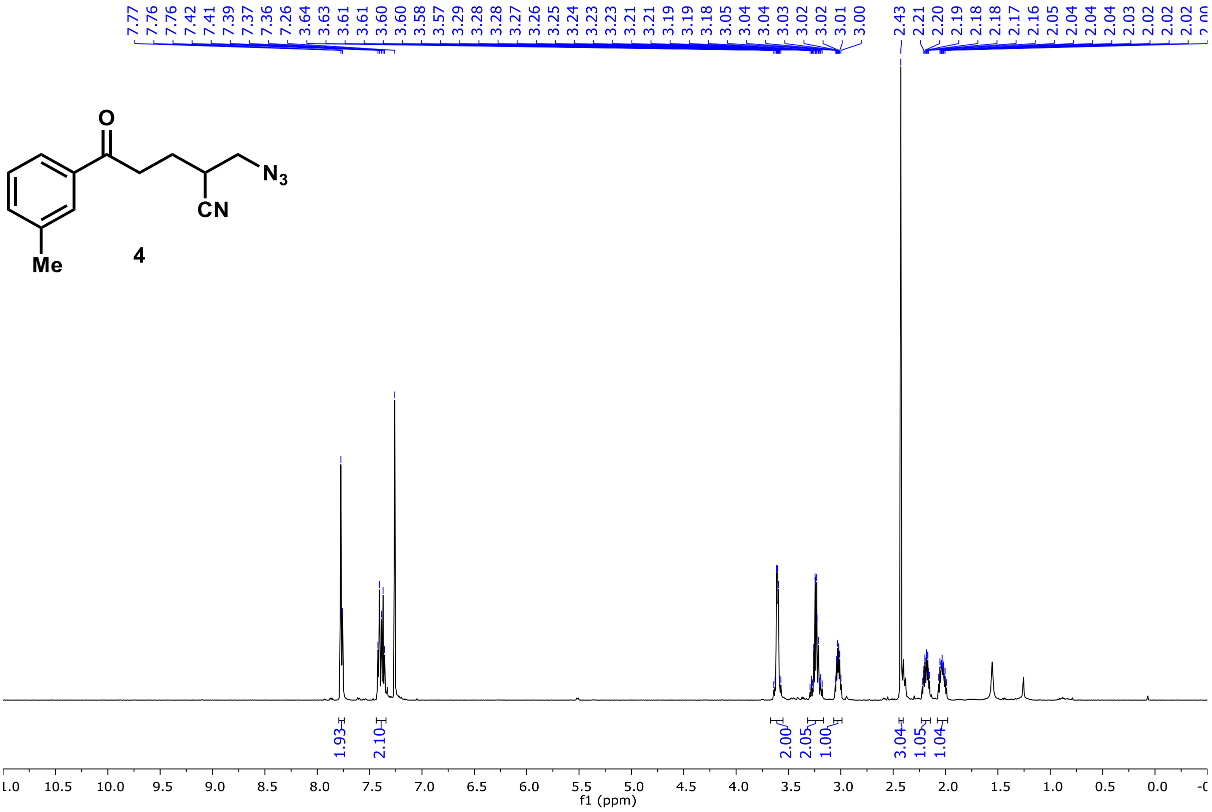
4

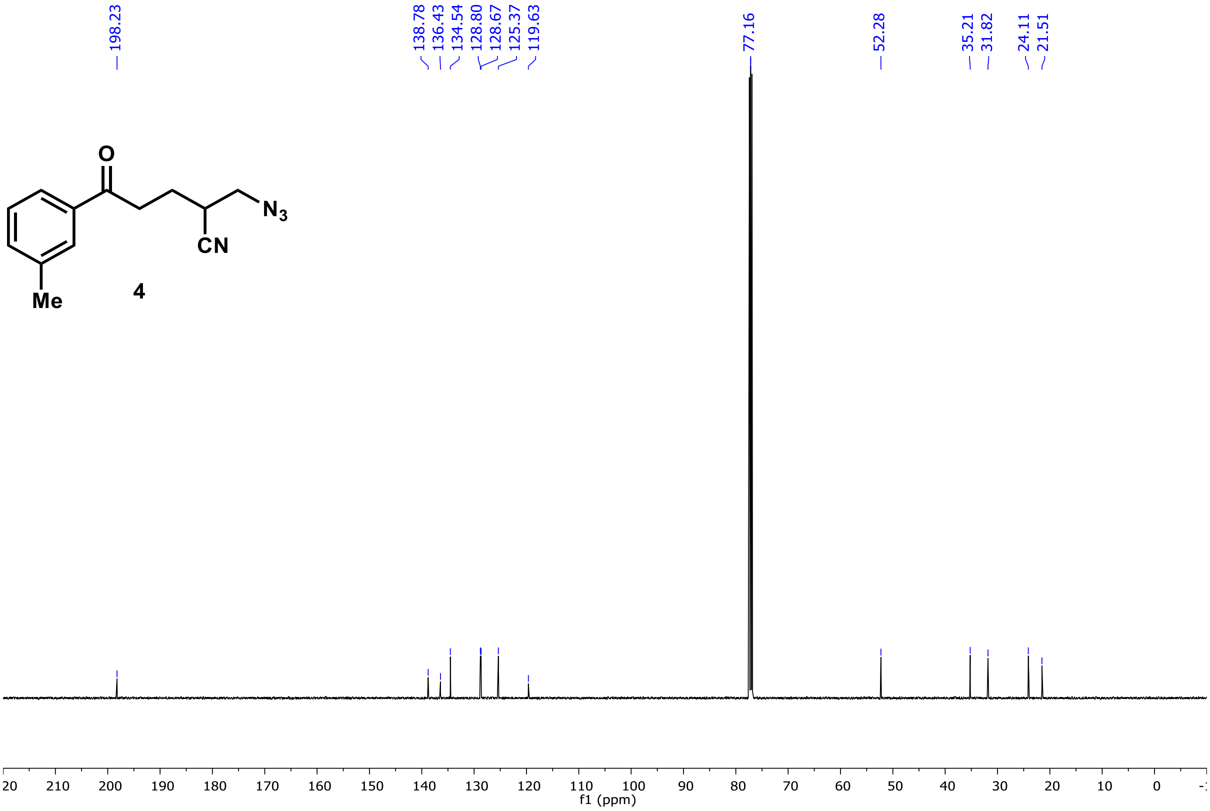
Prepared according to General Procedure 6 using **S30** (60 mg). The resultant crude material was purified by flash column chromatography (5-15% EtOAc/*n*-hexane, silica gel) to afford **4** (35 mg, 48%) as a yellow oil.

R$_f$ = 0.40 (30% EtOAc/*n*-hexane); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.99 – 2.07 (1H, m), 2.15 – 2.22 (1H, m), 2.43 (3H, s), 3.00 – 3.05 (1H, m), 3.18 – 3.29 (2H, m), 3.57 – 3.64 (2H, m), 7.36 – 7.42 (2H, m), 7.75 – 7.78 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 21.5, 24.1, 31.8, 35.2, 52.3, 119.6, 125.4, 128.7, 128.8, 134.5, 136.4, 138.8, 198.2.

These data are in accordance with the literature.[18]

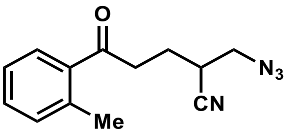
<u>^{1}H and ^{13}C NMR spectra of **4**</u>





4

2-(Azidomethyl)-5-oxo-5-(*o*-tolyl)pentanenitrile (5)



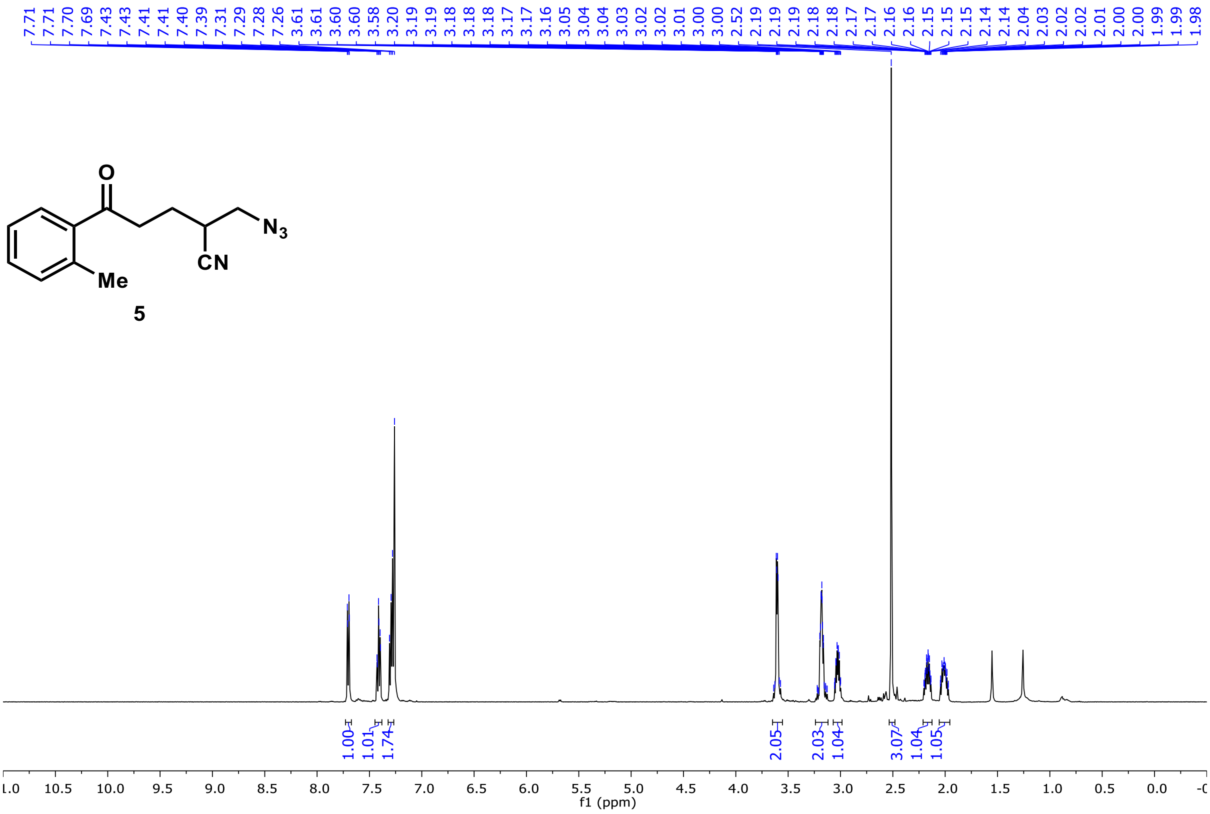
5

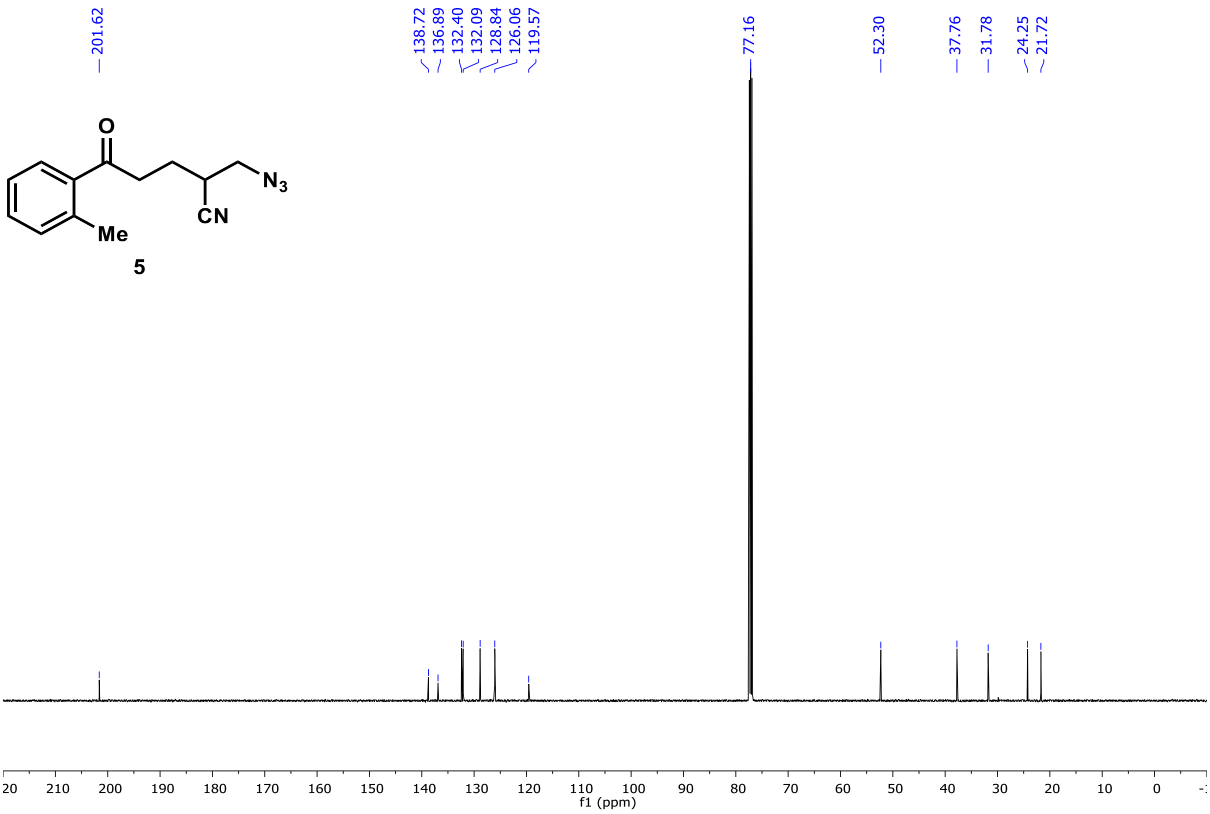
Prepared according to General Procedure 6 using **S31** (60 mg). The resultant crude material was purified by flash column chromatography (5-15% EtOAc/*n*-hexane, silica gel) to afford **5** (34 mg, 47%) as a yellow oil.

R_f = 0.38 (30% EtOAc/*n*-hexane); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.97 – 2.05 (1H, m), 2.14 – 2.20 (1H, m), 2.52 (3H, s), 3.00 – 3.06 (1H, m), 3.13 – 3.22 (2H, m), 2.57 – 3.64 (2H, m), 7.27 – 7.31 (2H, m), 7.39 – 7.43 (1H, m), 7.69 – 7.71 (1H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 21.7, 24.3, 31.8, 37.8, 52.3, 119.6, 126.1, 128.8, 132.1, 132.4, 136.9, 138.8, 201.6.

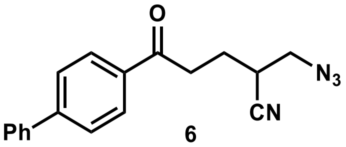
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **5**





5-([1,1'-Biphenyl]-5-yl)-2-(azidomethyl)-5-oxopentanenitrile (6)



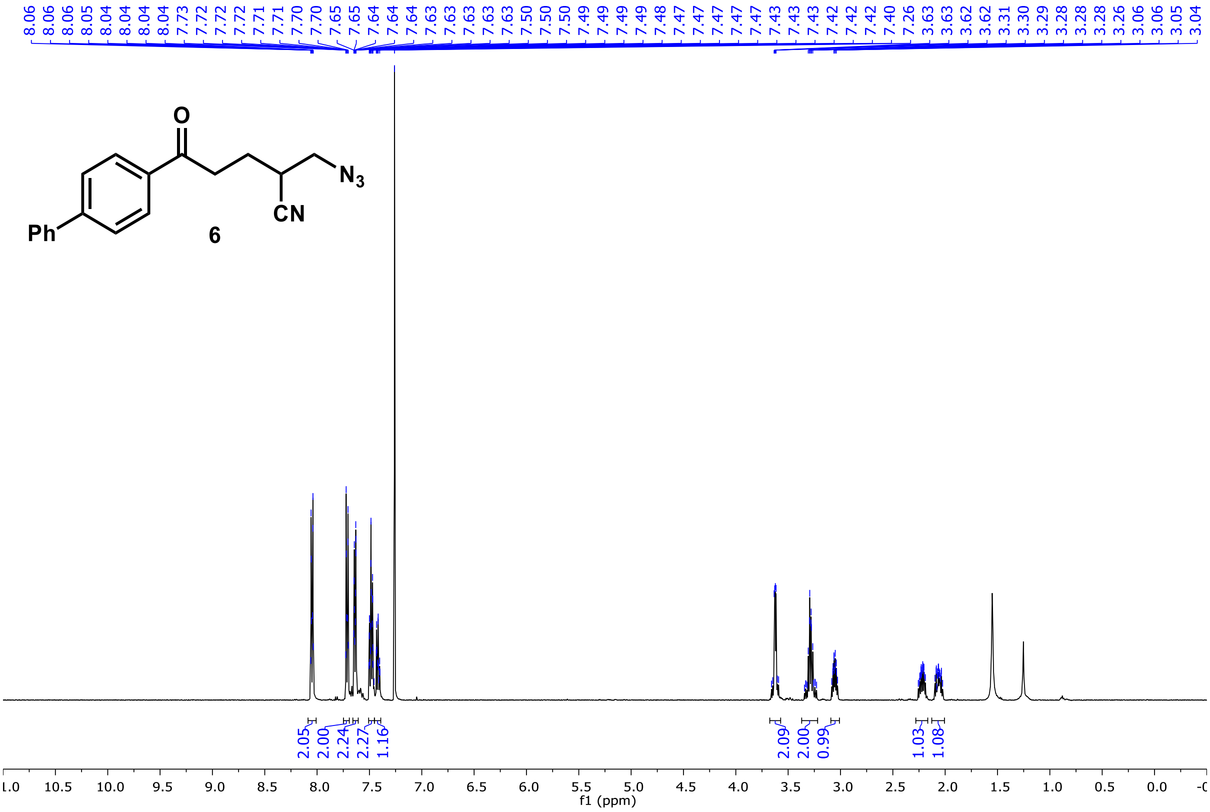
6

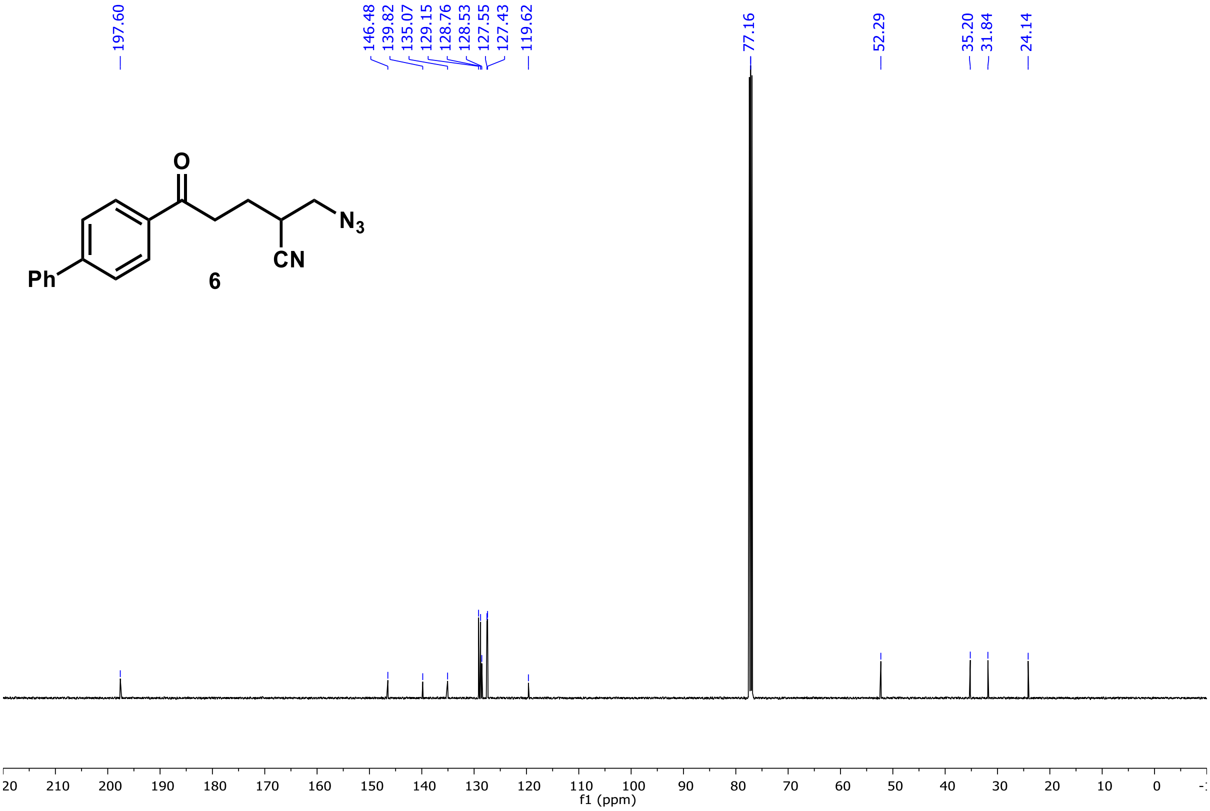
Prepared according to General Procedure 6 using **S32** (79 mg). The resultant crude material was purified by flash column chromatography (5-20% EtOAc/*n*-hexane, silica gel) to afford **6** (38 mg, 42%) as a white solid.

R$_f$ = 0.13 (20% EtOAc/*n*-hexane); **M.p.:** 123-125 °C; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.00 – 2.12 (1H, m), 2.17 – 2.28 (1H, m), 3.02 – 3.09 (1H, m), 3.22 – 3.38 (2H, m), 3.58 – 3.67 (2H, m), 7.39 – 7.44 (1H, m), 7.45 – 7.52 (2H, m), 7.63 – 7.65 (2H, m), 7.70 – 7.74 (2H, m), 8.03 – 8.06 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 24.1, 31.8, 35.2, 52.3, 119.6, 127.4, 127.6, 128.5, 128.8, 129.2, 135.1, 139.8, 146.5, 197.6.

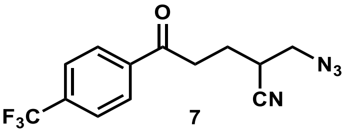
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **6**





2-(Azidomethyl)-5-oxo-5-(4-(trifluoromethyl)phenyl)pentanenitrile (7)



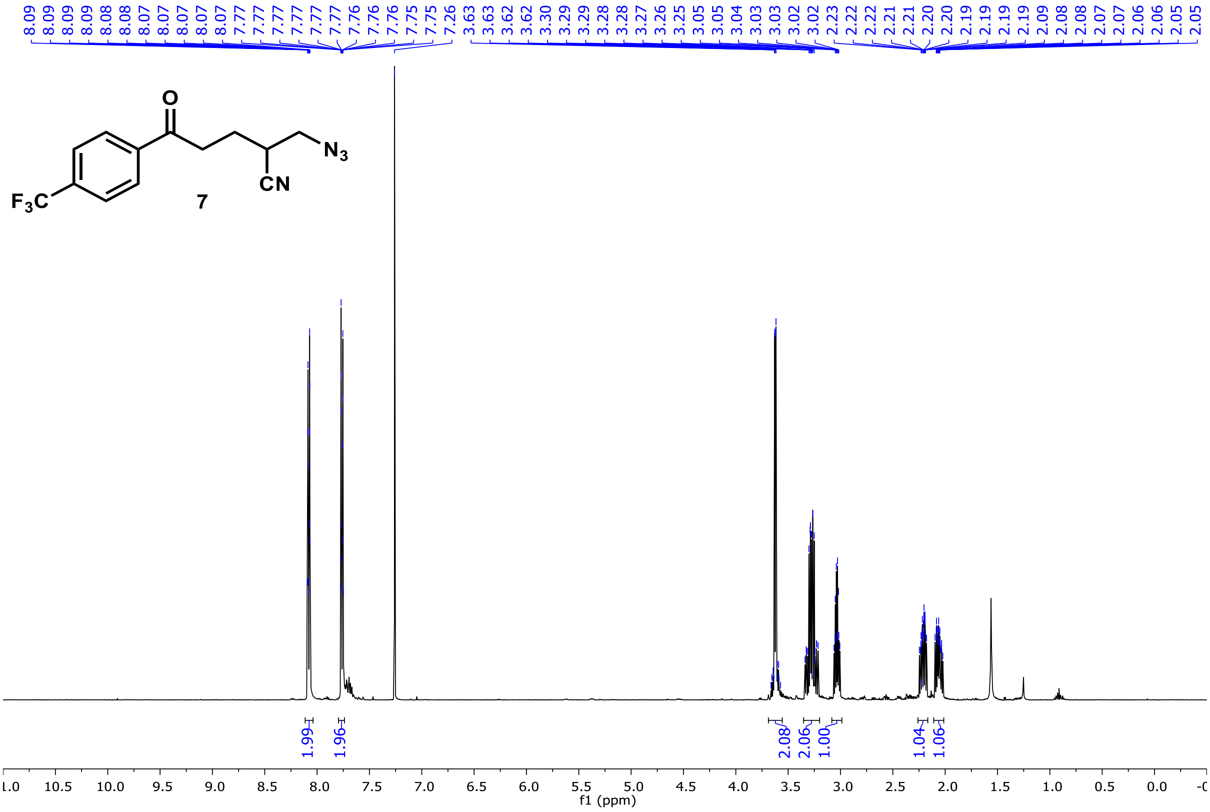
7

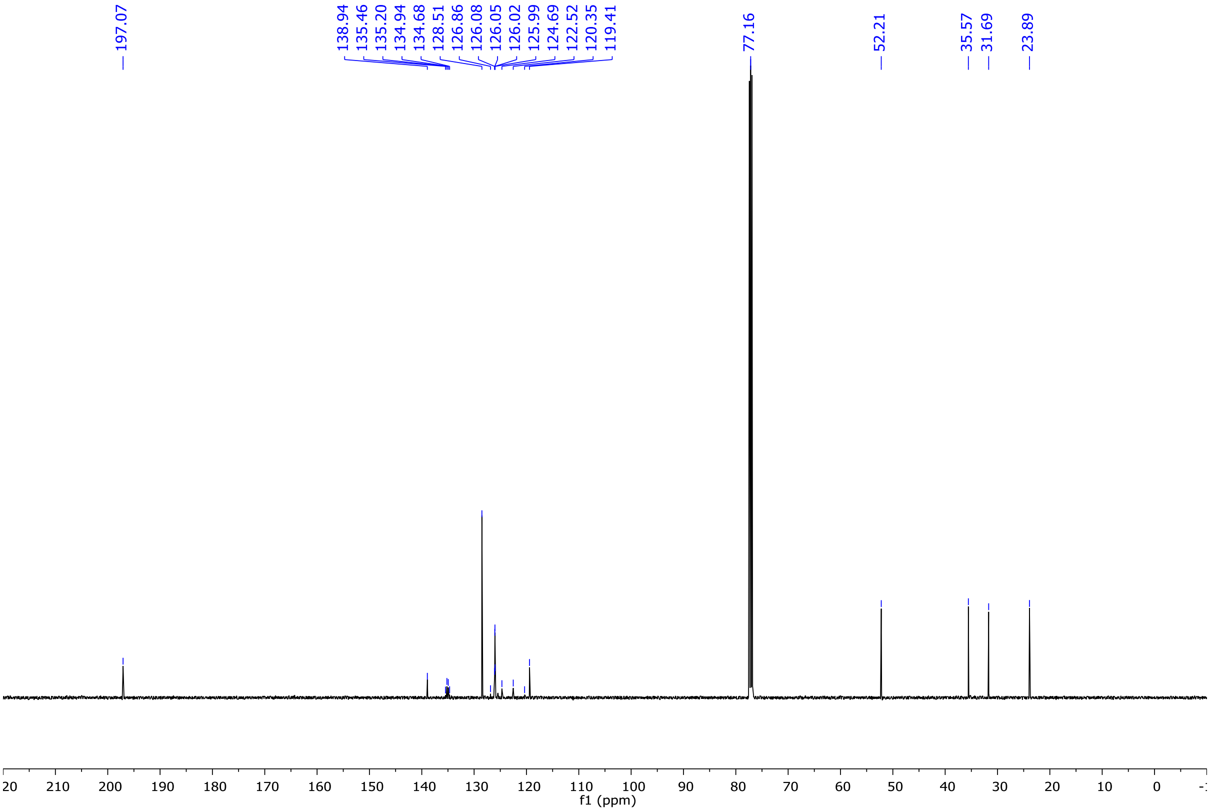
Prepared according to General Procedure 6 using **S33** (77 mg). The resultant crude material was purified by flash column chromatography (20% EtOAc/*n*-hexane, silica gel) to afford **7** (39 mg, 44%) as a yellow oil.

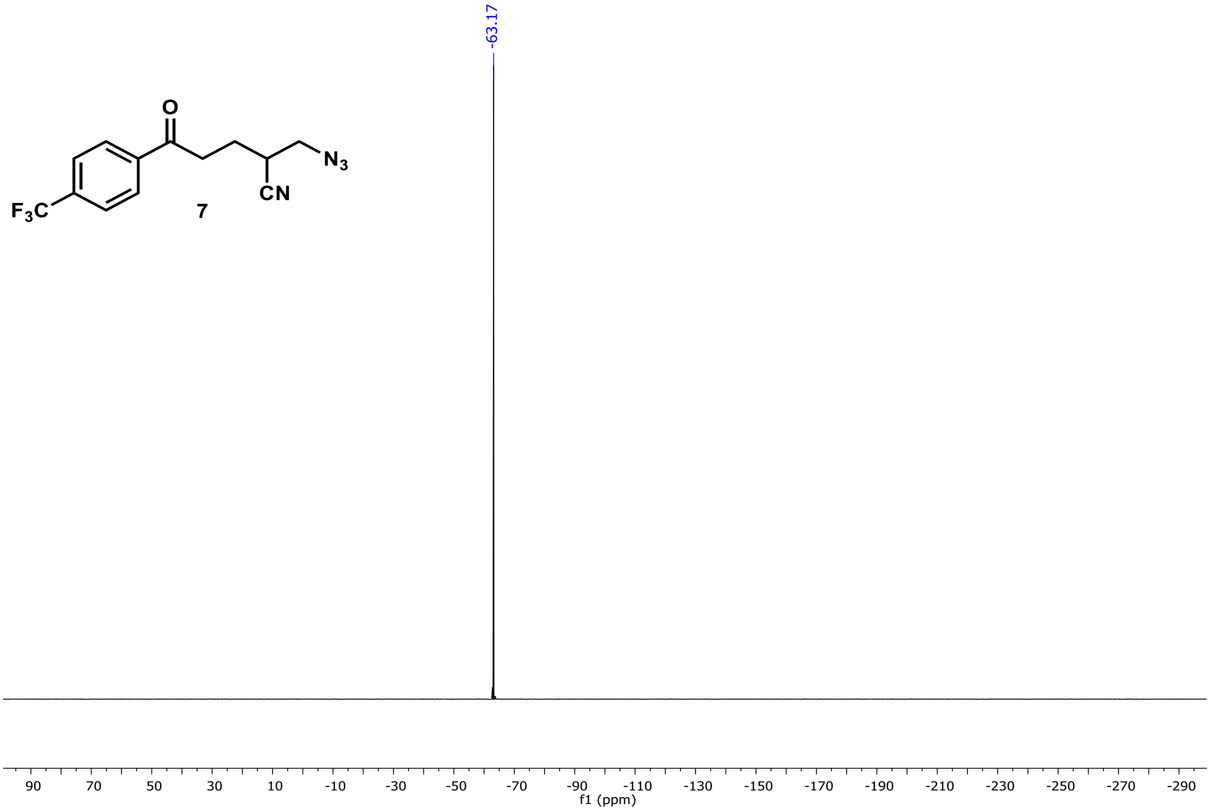
R_f = 0.19 (20% EtOAc/*n*-hexane); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.00 – 2.16 (1H, m), 2.16 – 2.27 (1H, m), 2.99 – 3.08 (1H, m), 3.20 – 3.36 (2H, m), 3.35 – 3.69 (2H, m), 7.73 – 7.80 (2H, m), 8.06 – 8.11 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 23.9, 31.7, 35.6, 52.2, 119.4, 123.6 (q, *J* 272.9), 126.0 (q, *J* 3.7), 128.5, 135.1 (q, *J* 32.8), 138.9, 197.1; **^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$)** δ_F = – 63.17.

These data are in accordance with the literature.[18]

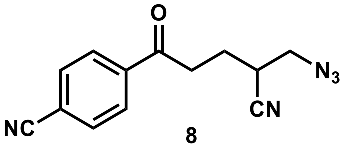
^{1}H, ^{13}C, and ^{19}F NMR spectra of **7**







4-(5-Azido-4-cyanopentanoyl)benzonitrile (8)

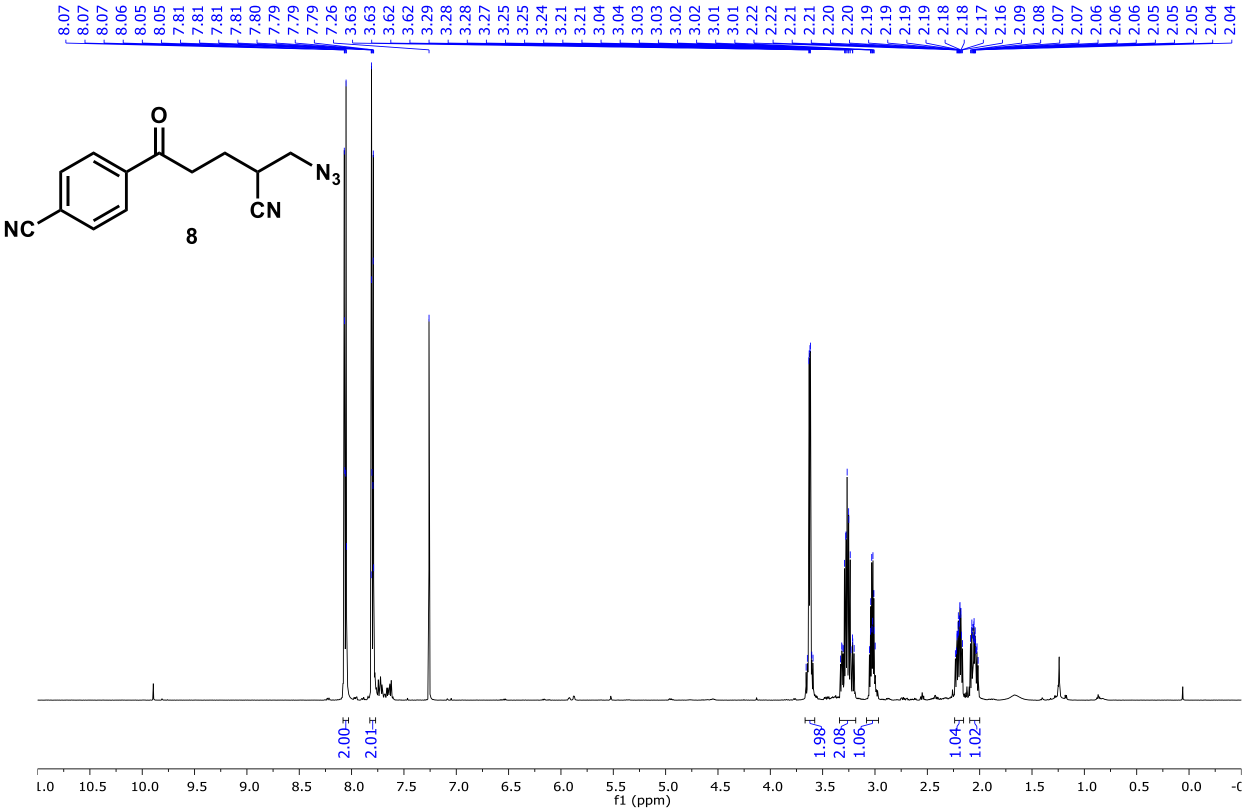


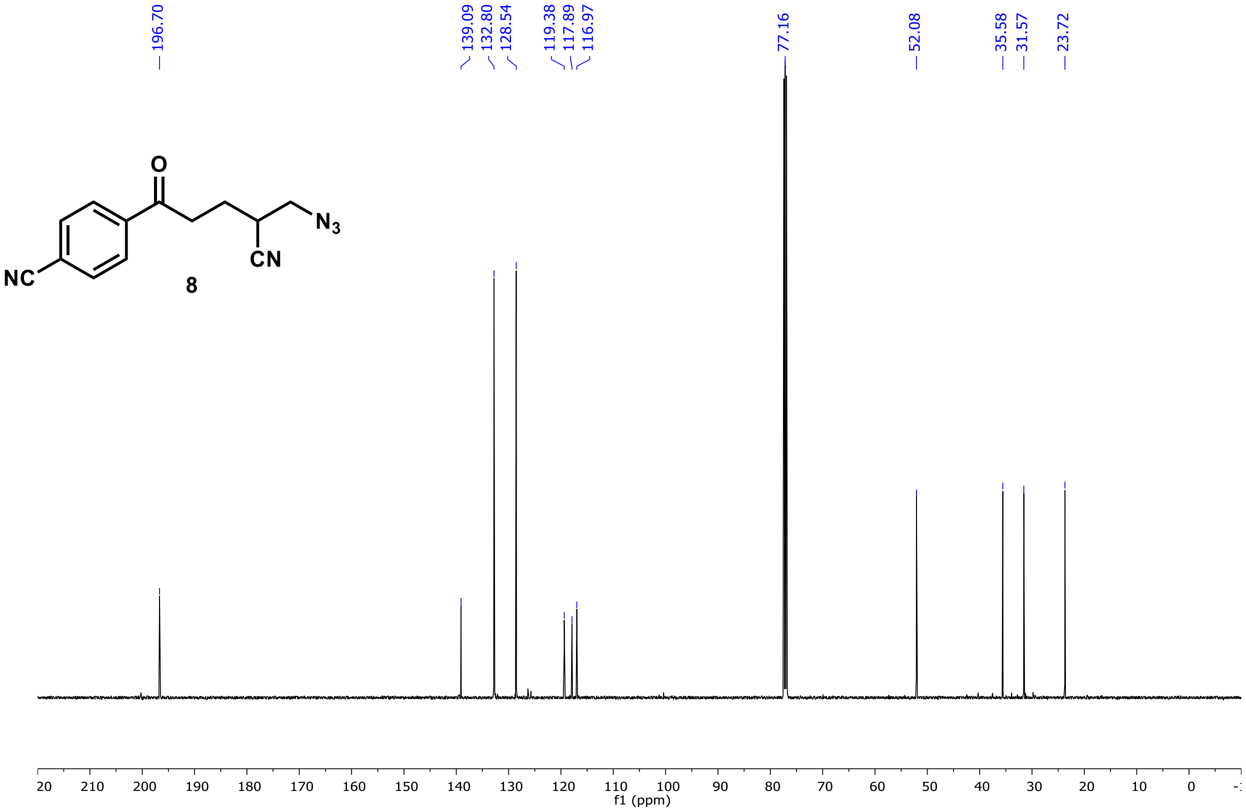
8

Prepared according to General Procedure 6 using **S34** (64 mg). The resultant crude material was purified by flash column chromatography (5-30% EtOAc/*n*-hexane, silica gel) to afford **8** (34 mg, 45%) as an orange oil.

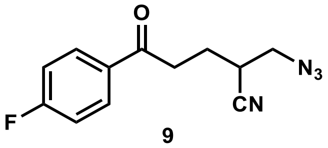
R_f = 0.16 (30% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 2938, 2230, 2102, 1688, 1404, 1206, 984, 831; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.01 – 2.09 (1H, m), 2.16 – 2.23 (1H, m), 3.00 – 3.05 (1H, m), 3.20 – 3.33 (2H, m), 3.59 – 3.66 (2H, m), 7.79 – 7.81 (2H, m), 8.05 – 8.07 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 23.7, 31.6, 35.6, 52.1, 117.0, 117.9, 119.4, 128.5, 132.8, 139.1, 196.7; **HRMS** (CI+) $C_{13}H_{11}N_5O$ [M-N$_2$+H]$^+$ requires 226.0975, found 226.0974 (– 0.6 ppm).

^{1}H and ^{13}C NMR spectra of **8**





2-(Azidomethyl)-5-(4-fluorophenyl)-5-oxopentanenitrile (9)



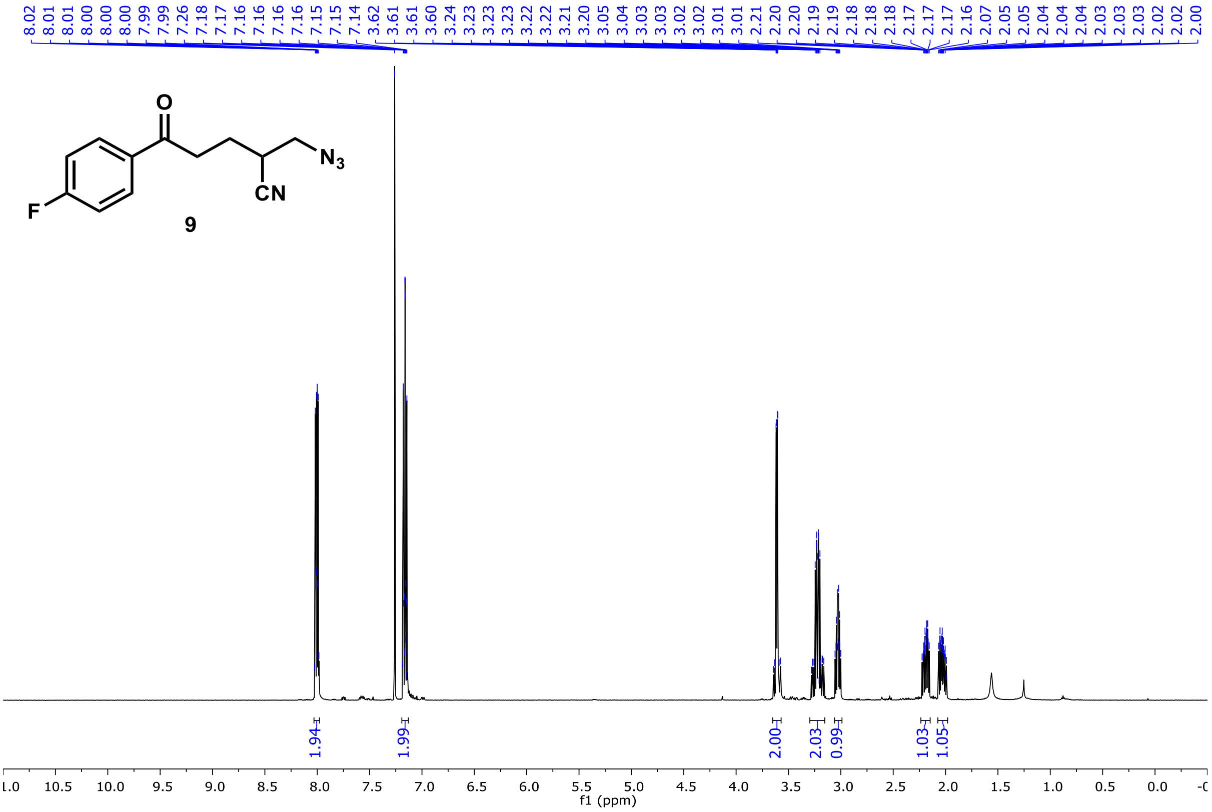
9

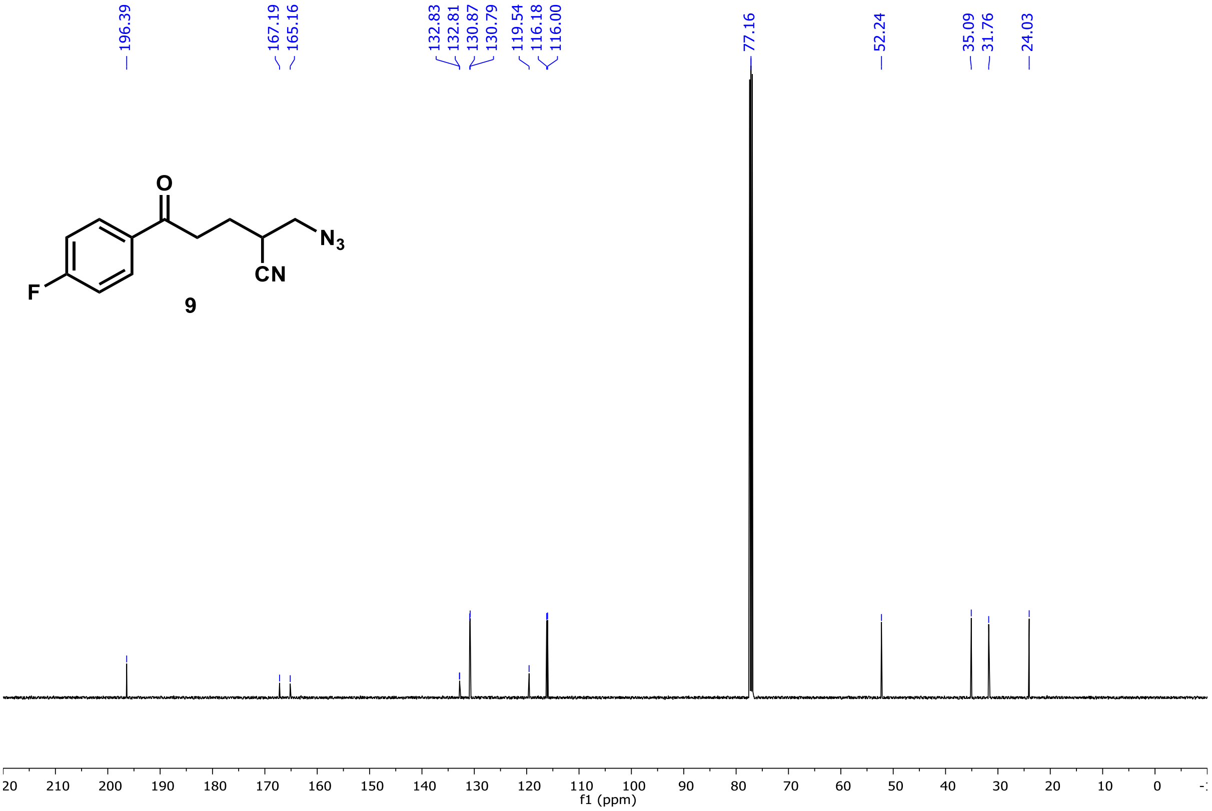
Prepared according to General Procedure 6 using **S35** (62 mg). The resultant crude material was purified by flash column chromatography (5-15% EtOAc/*n*-hexane, silica gel) to afford **9** (32 mg, 43%) as a yellow oil.

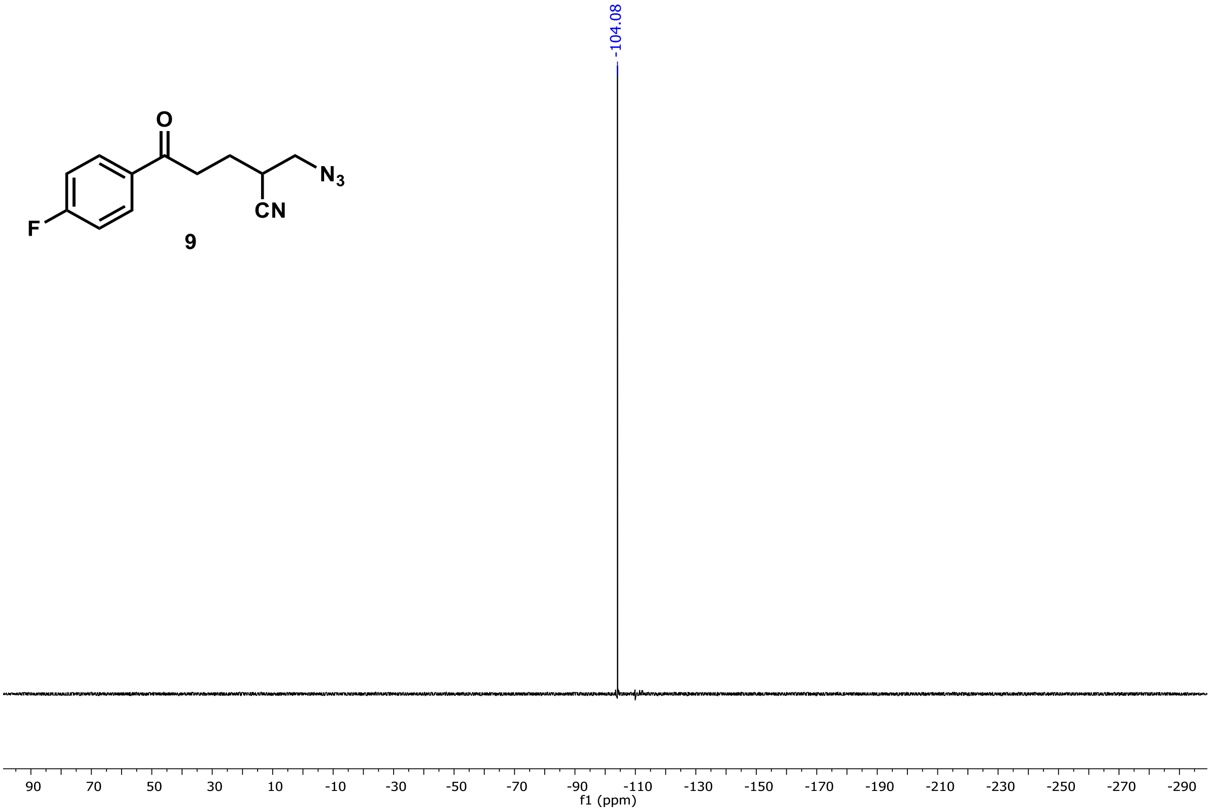
R$_f$ = 0.16 (20% EtOAc/*n*-hexane); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.99 – 2.07 (1H, m), 2.16 – 2.22 (1H, m), 3.00 – 3.06 (1H, m), 3.16 – 3.28 (2H, m), 3.58 – 3.64 (2H, m), 7.14 – 7.18 (2H, m), 7.98 – 8.02 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 24.0, 31.8, 35.1, 52.2, 116.1 (d, *J* 21.9), 119.5, 130.8 (d, *J* 9.4), 132.8 (d, *J* 3.0), 166.2 (d, *J* 255.8), 196.4; **^{19}F{^{1}H} NMR (376 MHz, CDCl$_3$)** δ_F = – 104.08.

These data are in accordance with the literature.[18]

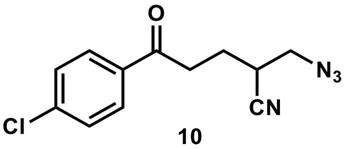
^{1}H, ^{13}C, and ^{19}F NMR spectra of **9**




196.39
167.19
165.16
132.83
132.81
130.87
130.79
119.54
116.18
116.00
77.16
52.24
35.09
31.76
24.03
O
N3
CN
F
9
f1 (ppm)


-104.08
O
N3
CN
F
9
f1 (ppm)

2-(Azidomethyl)-5-(4-chlorophenyl)-5-oxopentanenitrile (10)



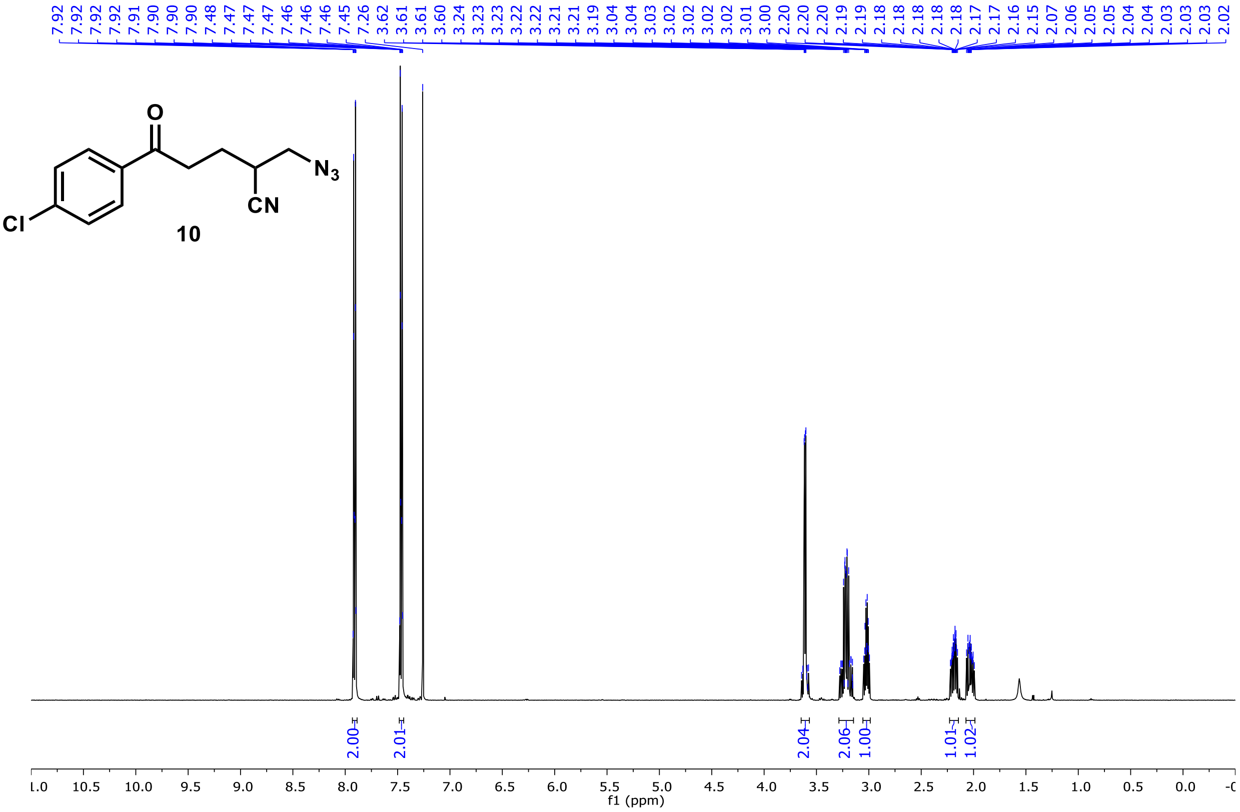
10

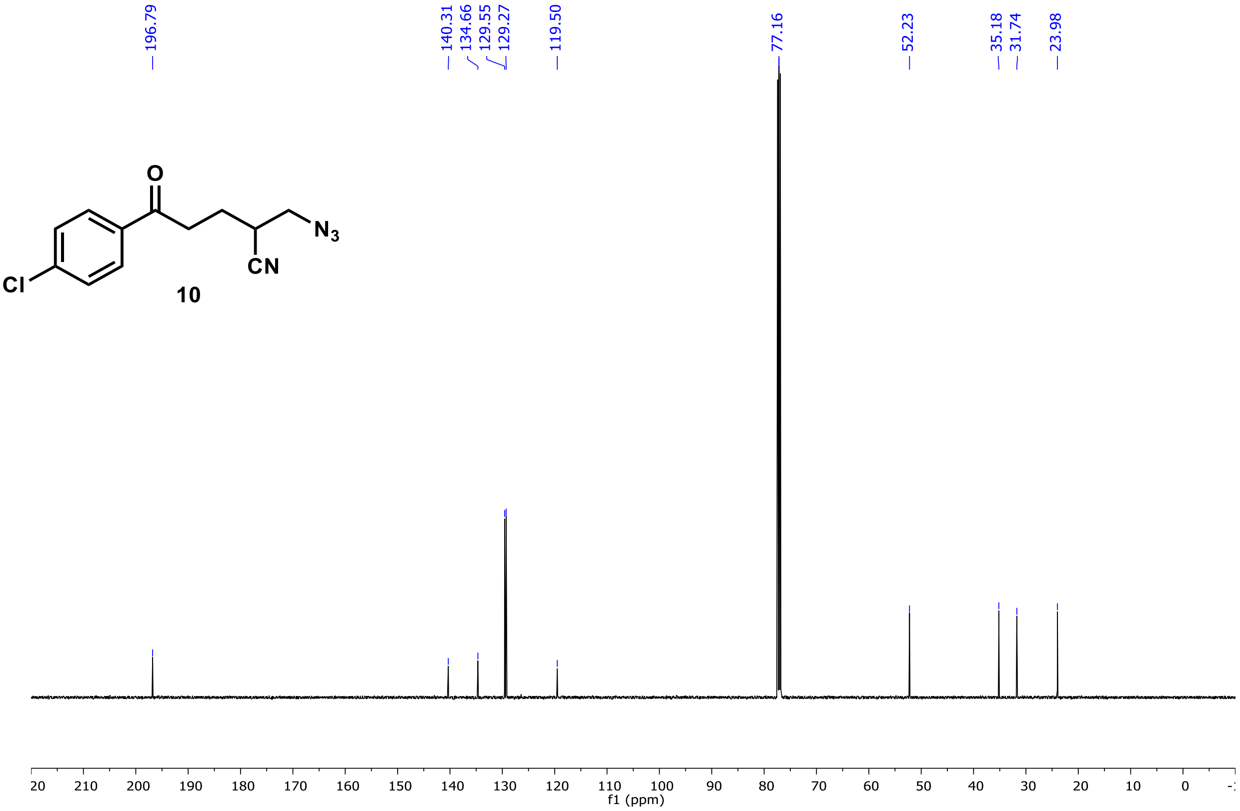
Prepared according to General Procedure 6 using **S36** (67 mg). The resultant crude material was purified by flash column chromatography (5-15% EtOAc/*n*-hexane, silica gel) to afford **10** (38 mg, 48%) as a white solid.

R$_f$ = 0.16 (20% EtOAc/*n*-hexane); **M.p.:** 51-53 °C; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.97 – 2.09 (1H, m), 2.13 – 2.24 (1H, m), 2.97 – 3.07 (1H, m), 3.15 – 3.28 (2H, m), 3.57 – 3.64 (2H, m), 7.45 – 7.48 (2H, m), 7.90 – 7.93 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 24.0, 31.7, 35.2, 52.2, 119.5, 129.3, 129.6, 134.7, 140.3, 196.8.

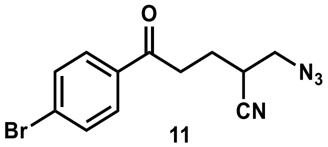
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **10**





2-(Azidomethyl)-5-(4-bromophenyl)-5-oxopentanenitrile (11)



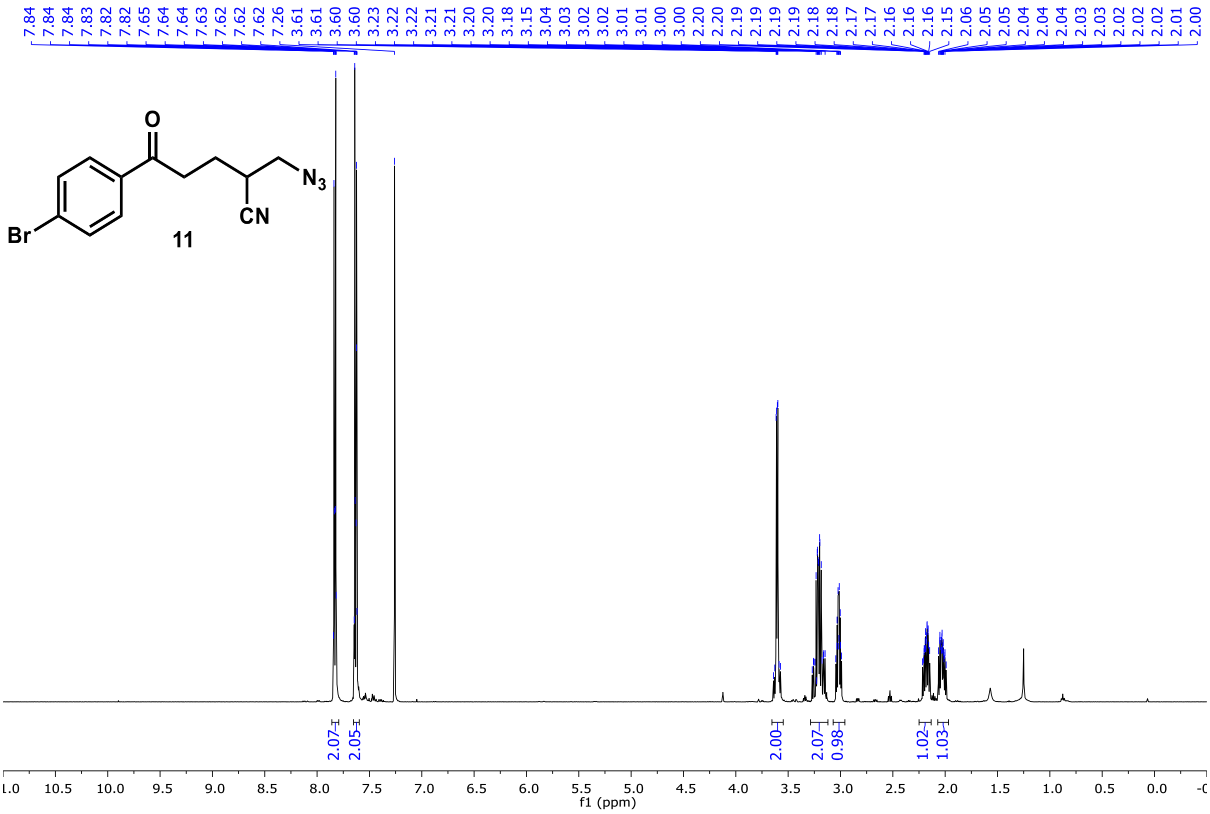
11

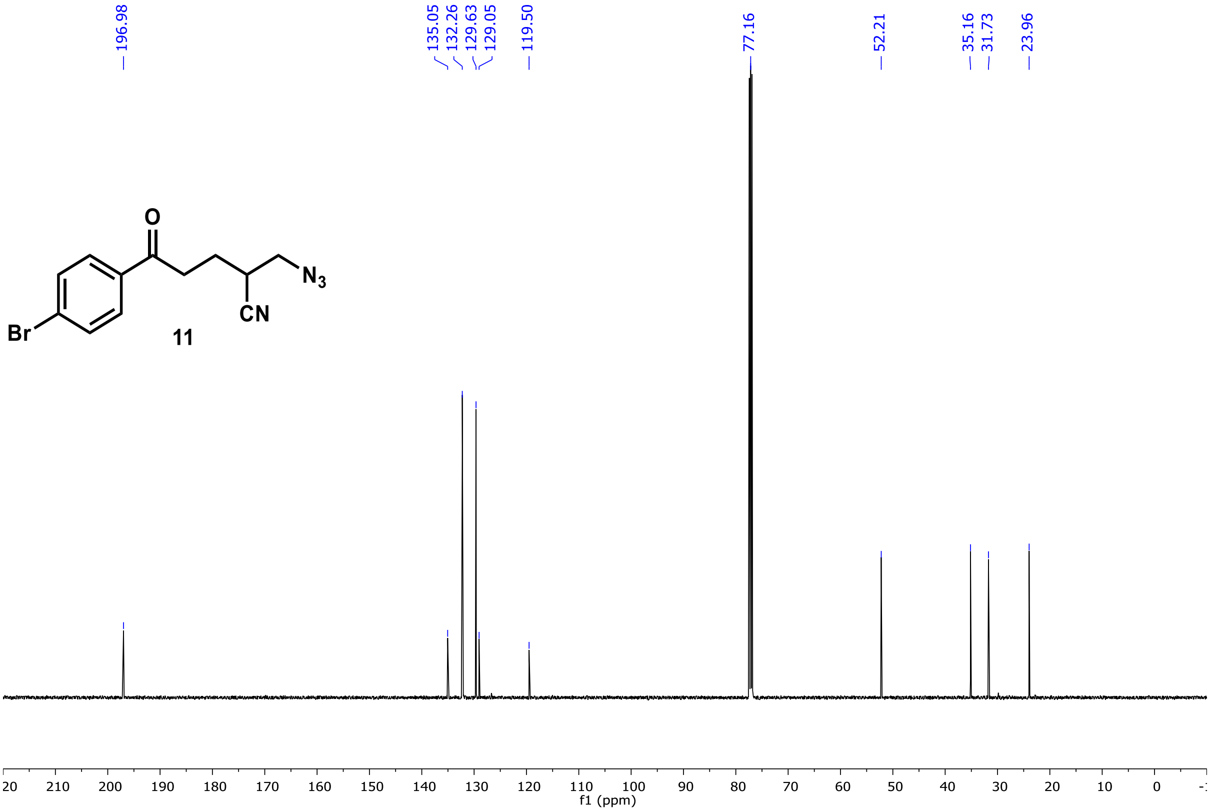
Prepared according to General Procedure 6 using **S37** (80 mg). The resultant crude material was purified by flash column chromatography (5-20% EtOAc/*n*-hexane, silica gel) to afford **11** (41 mg, 44%) as a yellow solid.

R_f = 0.24 (20% EtOAc/*n*-hexane); **M.p.:** 92-94 °C; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 1.99 – 2.06 (1H, m), 2.15 – 2.22 (1H, m), 2.99 – 3.04 (1H, m), 3.15 – 3.27 (2H, m), 3.57 – 3.64 (2H, m), 7.62 – 7.65 (2H, m), 7.82 – 7.84 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 24.0, 31.7, 35.2, 52.2, 119.5, 129.1, 129.6, 132.3, 135.1, 197.0.

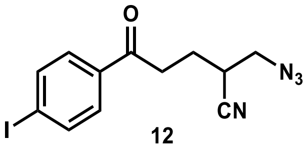
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **11**





2-(Azidomethyl)-5-(4-iodophenyl)-5-oxopentanenitrile (12)

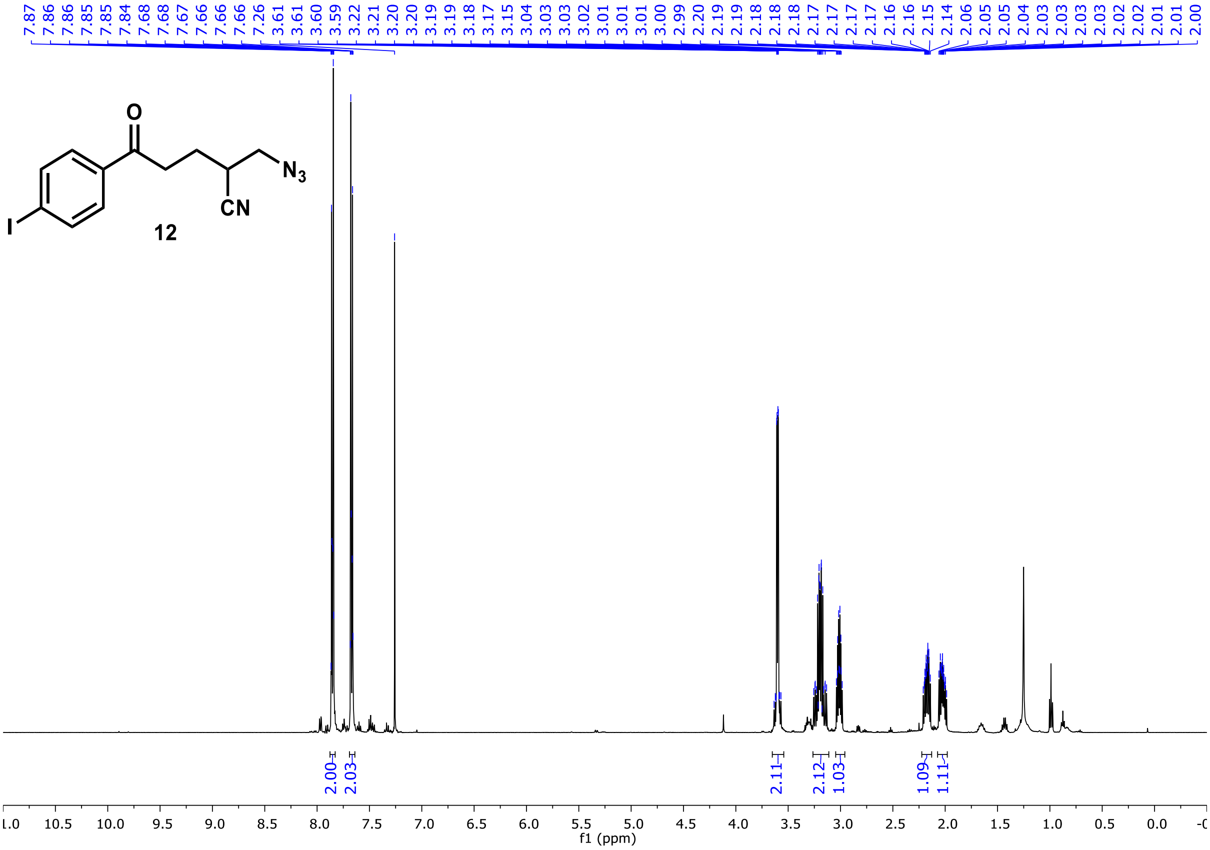


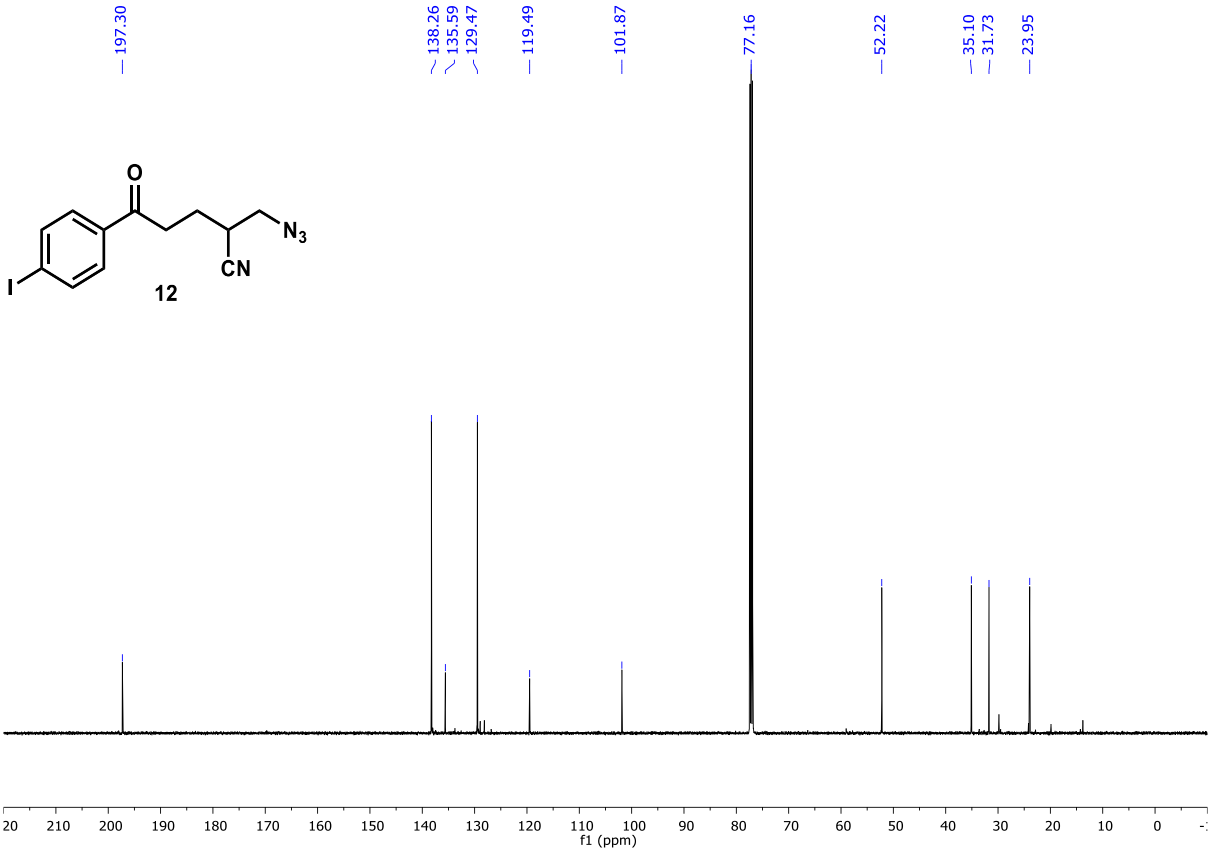
12

Prepared according to General Procedure 6 using **S38** (94 mg). The resultant crude material was purified by flash column chromatography (5-12% EtOAc/*n*-hexane, silica gel) to afford **12** (37 mg, 35%) as an orange oil.

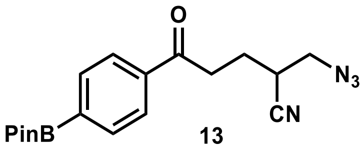
R$_f$ = 0.17 (20% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 2926, 2243, 2100, 1681, 1579, 1560, 1450, 1392, 1273, 1219, 1205, 1180, 1056, 1004, 977; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.99 – 2.06 (1H, m), 2.14 – 2.21 (1H, m), 2.98 – 3.04 (1H, m), 3.13 – 3.26 (2H, m), 3.57 – 3.63 (2H, m), 7.66 – 7.68 (2H, m), 7.84 – 7.87 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 23.4, 31.7, 35.1, 52.2, 101.9, 119.5, 129.5, 135.6, 138.3, 197.3; **HRMS** (AP+) $C_{12}H_{11}N_2OI$ [M-N$_2$+H]$^+$ requires 326.9994, found 326.9997 (+ 0.9 ppm).

^{1}H and ^{13}C NMR spectra of **12**





2-(Azidomethyl)-5-oxo-5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pentanenitrile (13)

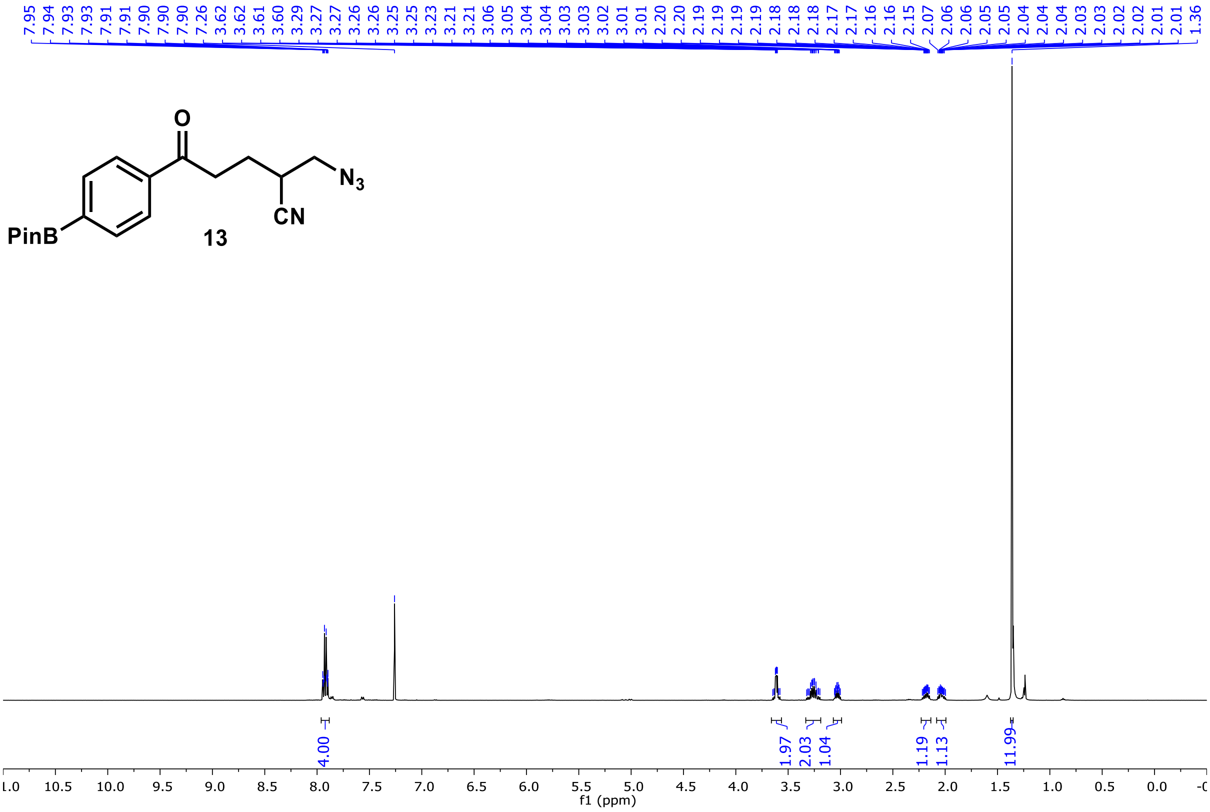


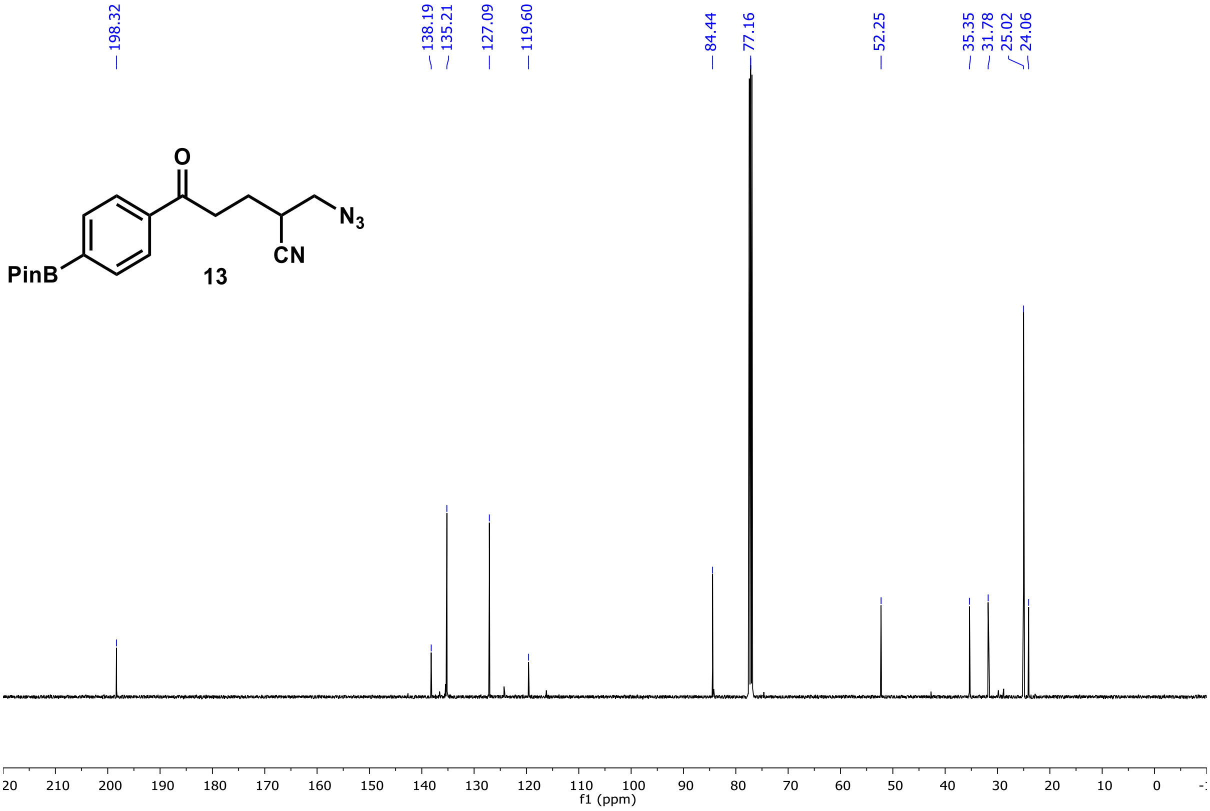
13

Prepared according to General Procedure 6 using **S39** (94 mg), but electrolysis was run for 5 h instead of 4 h. ^{1}H NMR analysis of the crude reaction mixture indicated a 46% yield. **13** was purified by flash column chromatography (5-25% EtOAc/*n*-hexane, silica gel) as a yellow oil.

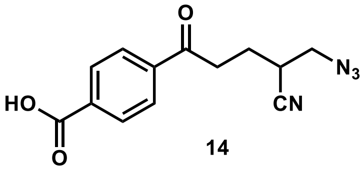
R$_f$ = 0.38 (30% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 2980, 2929, 2360, 2106, 1685, 1508, 1398, 1359, 1327, 1273, 1143, 1089, 1018, 962; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.36 (12H, s), 2.00 – 2.07 (1H, m), 2.15 – 2.22 (1H, m), 3.00 – 3.06 (1H, m), 3.20 – 3.32 (2H, m), 3.58 – 3.65 (2H, m), 7.90 – 7.95 (4H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 24.1, 25.0, 31.8, 35.4, 52.3, 84.4, 119.6, 127.1, 135.2, 138.2, 198.3; **HRMS** (ES+) $C_{18}H_{23}{}^{11}BN_4O_3$ [M-N$_2$+H]$^+$ requires 327.1880, found 327.1882 (+ 0.6 ppm).

^{1}H and ^{13}C NMR spectra of **13**





4-(5-Azido-4-cyanopentanoyl)benzoic acid (14)

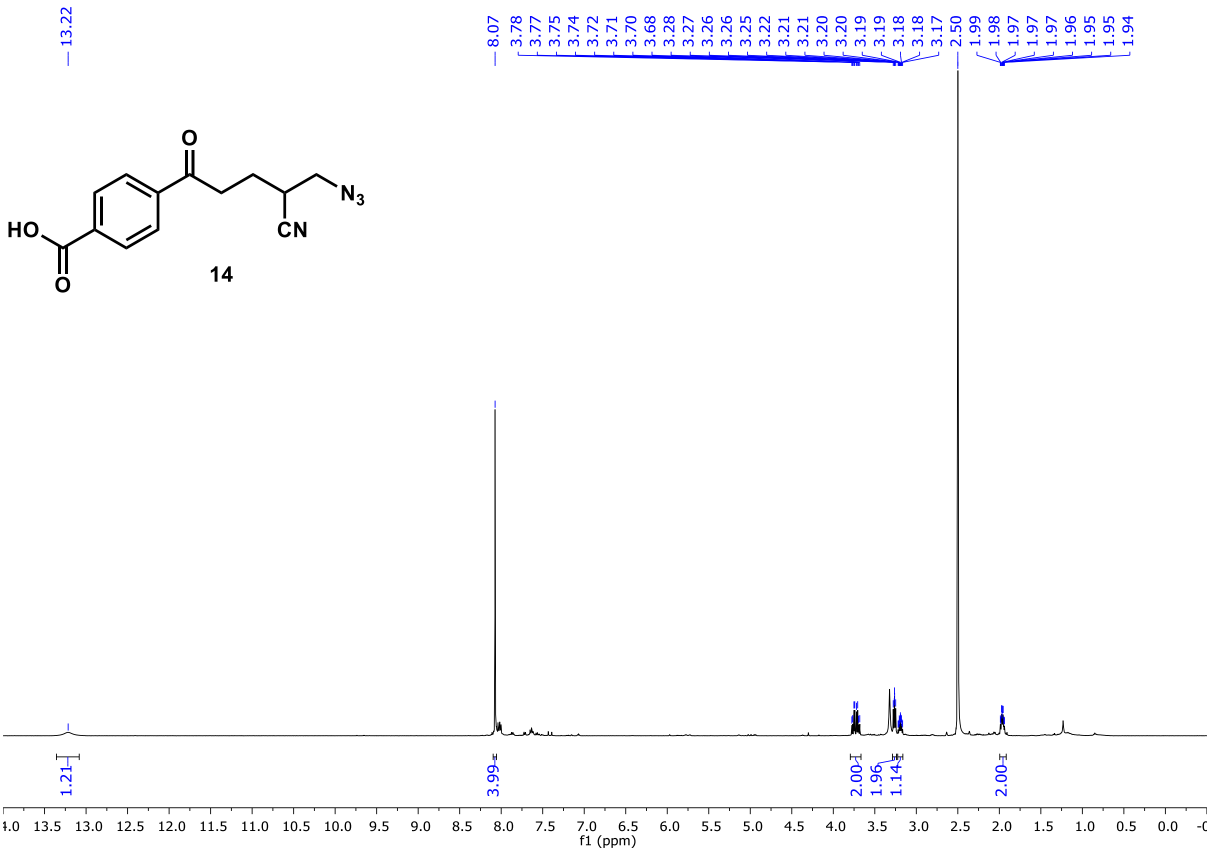


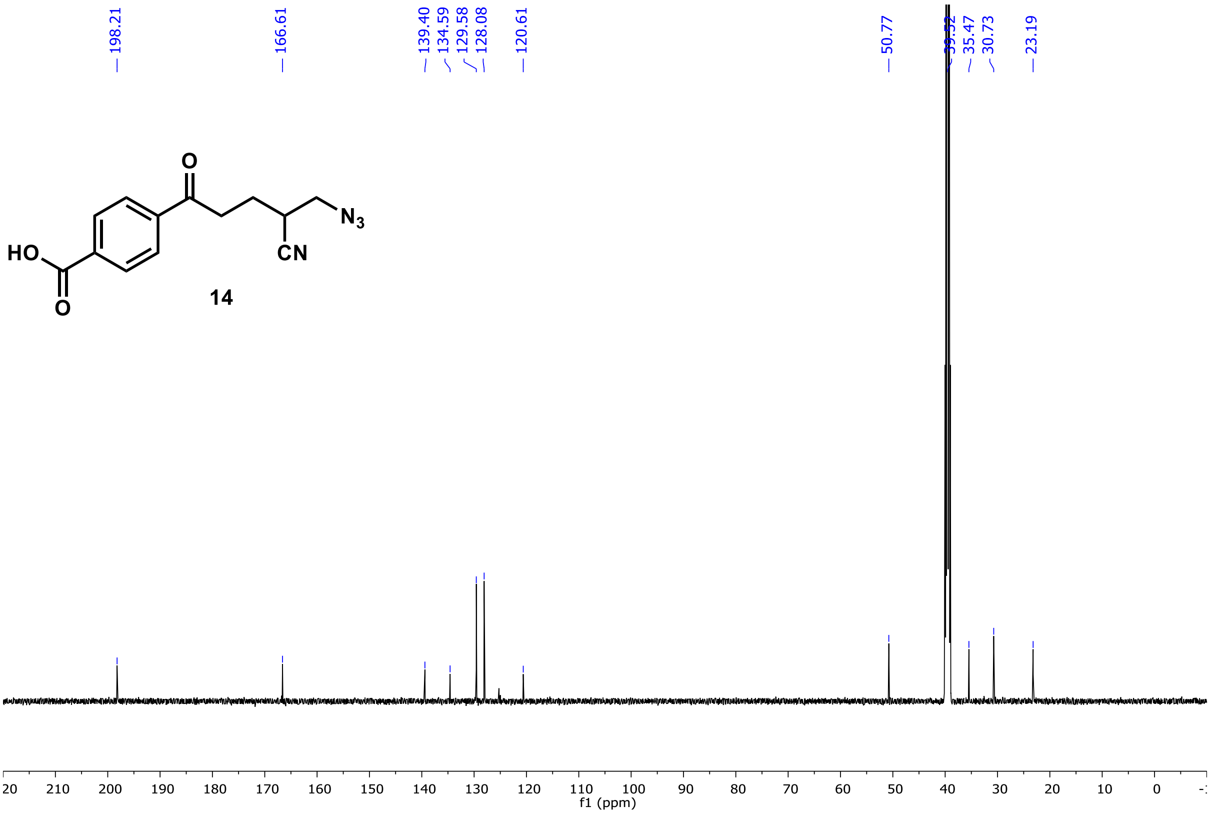
14

Prepared according to General Procedure 6 using **S40** (69 mg), but electrolysis was run for 5 h instead of 4 h. In this example the organic layers were washed with water instead of a saturated solution of $NaHCO_3$ (aq.). ^{1}H NMR analysis of the crude reaction mixture indicated a 45% yield. **14** was purified by flash column chromatography (40-100% EtOAc/*n*-hexane, silica gel) as a yellow solid.

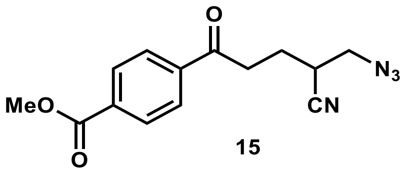
R$_f$ = 0.24 (80% EtOAc/*n*-hexane); **M.p.:** 127-129 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 2922, 2850, 2669, 2546, 2268, 2106, 1678 (br), 1610, 1506, 1425, 1409, 1282, 1205, 1128, 1116, 1014, 981; **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ_H = 1.94 – 1.99 (2H, m), 3.17 – 3.22 (1H, m), 3.25 – 3.28 (2H, m), 3.68 – 3.78 (2H, m), 8.07 (4H, s), 13.22 (1H, br s); **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ_C = 23.2, 30.7, 35.5, 50.8, 120.6, 128.1, 129.6, 134.6, 139.4, 166.6, 198.2; **HRMS** (ASAP+) $C_{13}H_{12}N_4O_3$ [M-N_2+H]$^+$ requires 245.0926, found 245.0930 (+ 1.6 ppm).

<u>^{1}H and ^{13}C NMR spectra of **14**</u>





Methyl 4-(5-azido-4-cyanopentanoyl)benzoate (15)

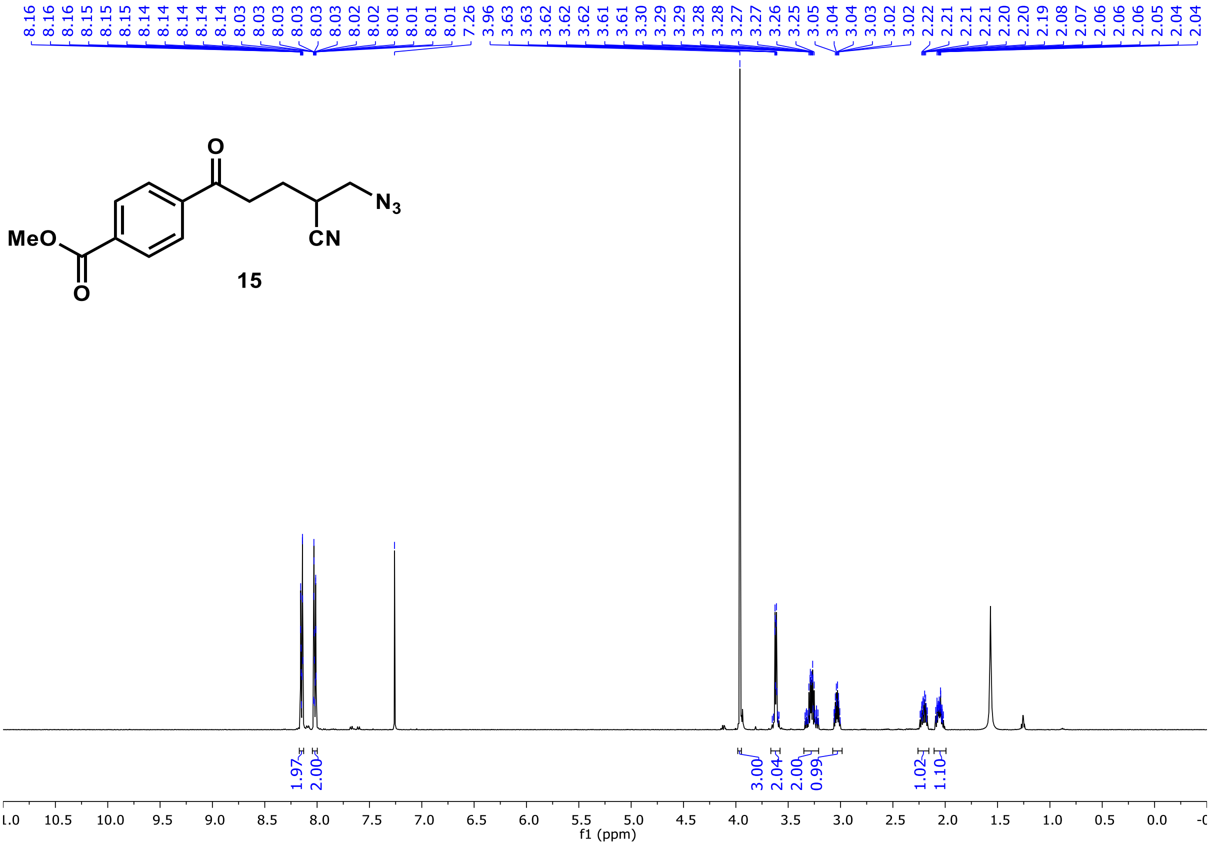


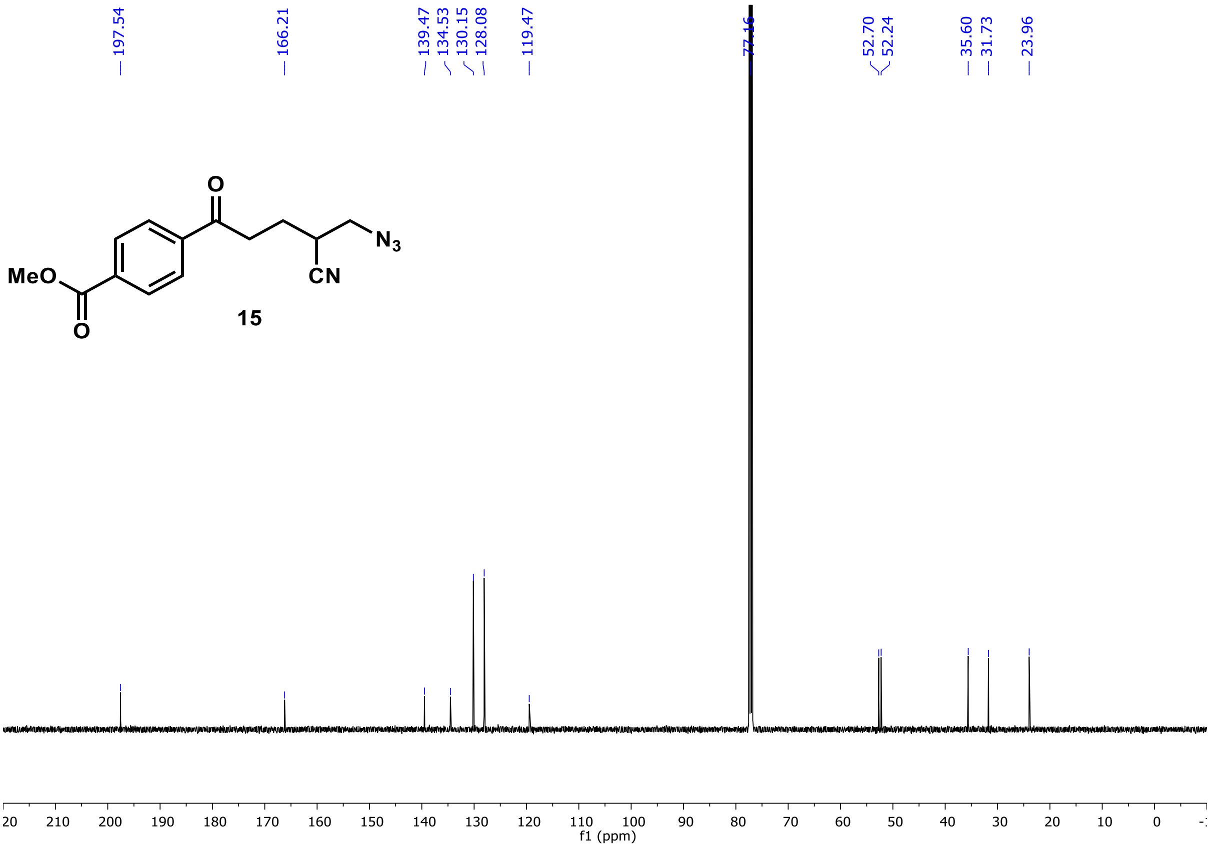
15

Prepared according to General Procedure 6 using **S41** (74 mg). The resultant crude material was purified by flash column chromatography (20-30% EtOAc/*n*-hexane, silica gel) to afford **15** (64 mg, 75%) as a white solid.

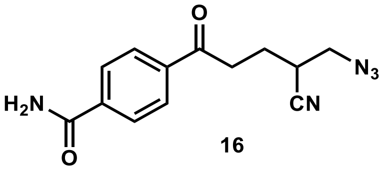
R_f = 0.21 (30% EtOAc/*n*-hexane); **M.p.:** 66-68 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 2958, 2899, 2202, 2118, 1712, 1681, 1571, 1454, 1433, 1408, 1355, 1282, 1261, 1192, 1111, 1020, 983, 950; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.02 – 2.09 (1H, m), 2.17 – 2.24 (1H, m), 3.00 – 3.06 (1H, m), 3.21 – 3.34 (2H, m), 3.59 – 3.65 (2H, m), 3.96 (3H, s), 8.01 – 8.03 (2H, m), 8.14 – 8.16 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 24.0, 31.7, 35.6, 52.2, 52.7, 119.5, 128.1, 130.2, 134.5, 139.5, 166.2, 197.5; **HRMS** (AP+) $C_{14}H_{14}N_4O_3$ $[M-N_2+H]^+$ requires 259.1083, found 259.1088 (+ 1.9 ppm).

^{1}H and ^{13}C NMR spectra of **15**





4-(5-Azido-4-cyanopentanoyl)benzamide (16)

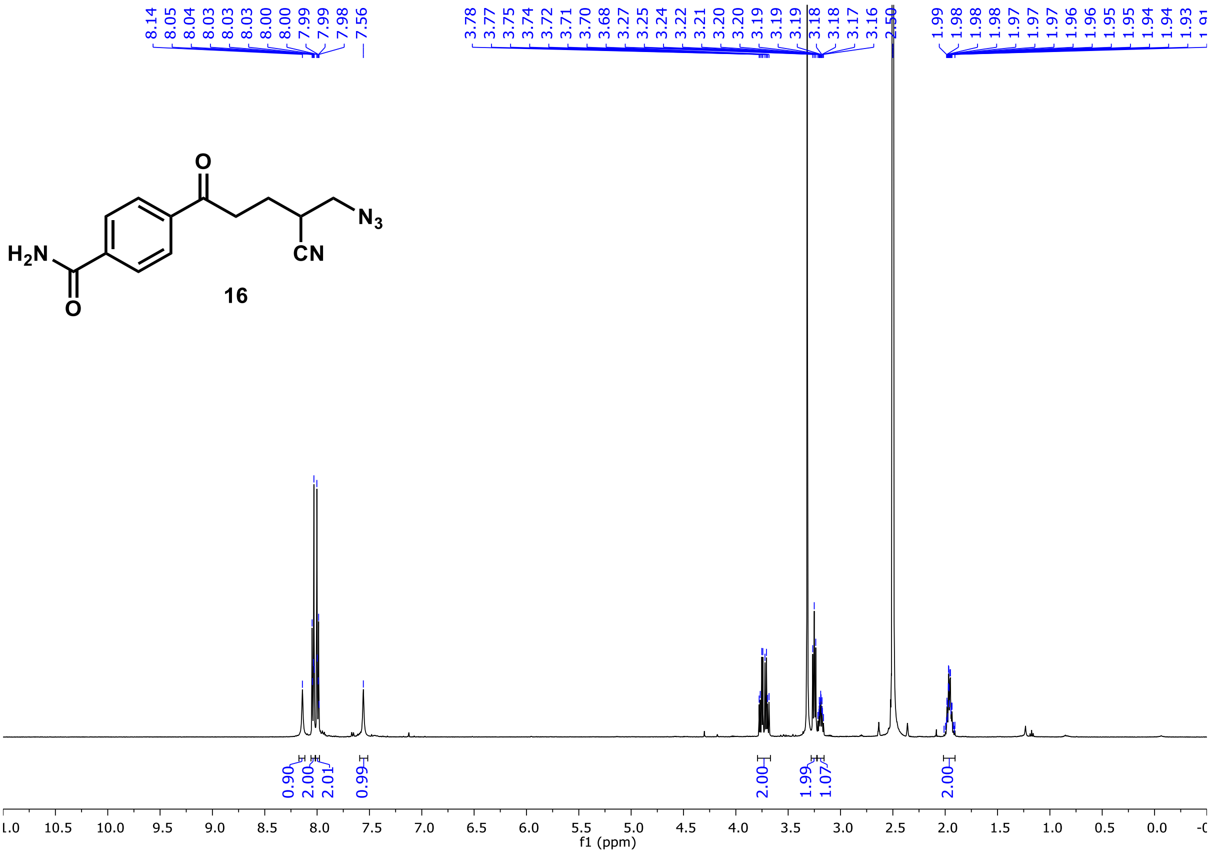


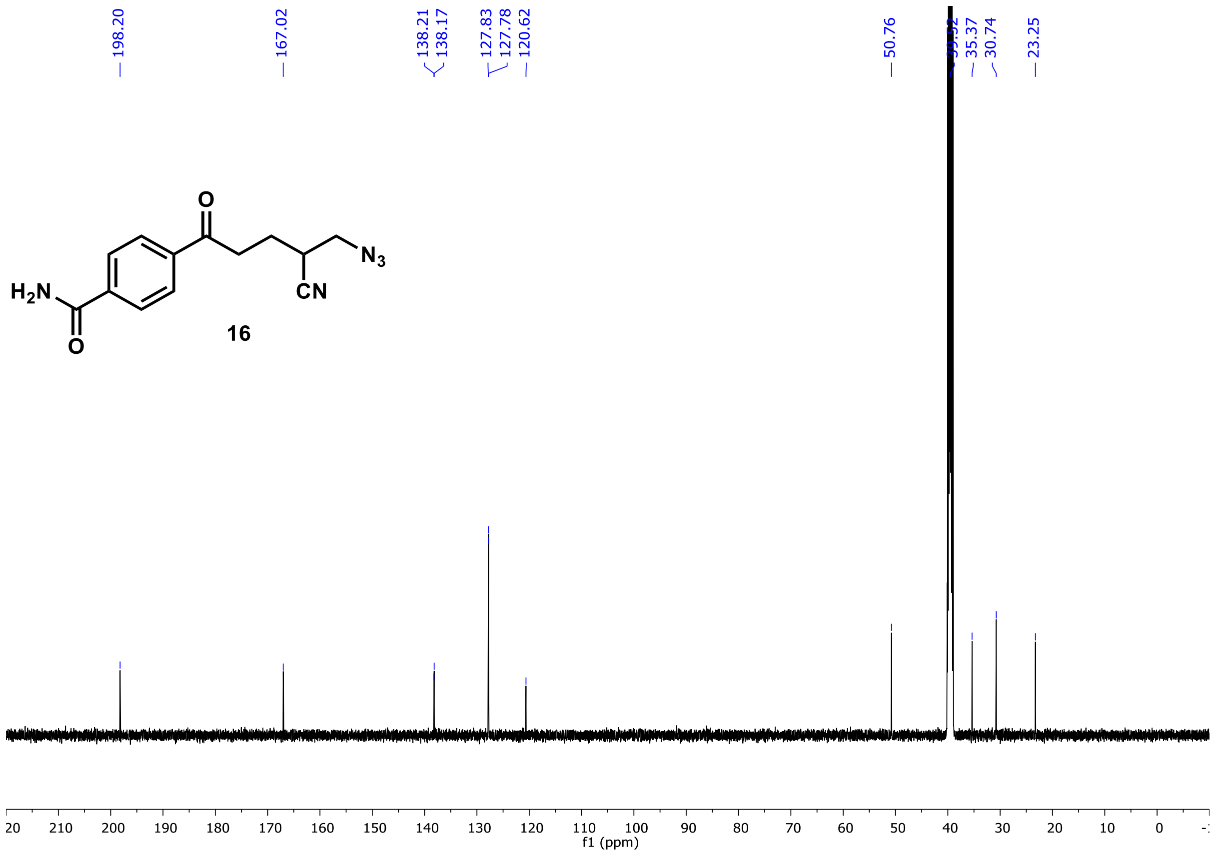
16

Prepared according to General Procedure 6 using **S42** (69 mg). The resultant crude material was purified by flash column chromatography (50-90% EtOAc/*n*-hexane, silica gel) to afford **16** (25 mg, 31%) as a white solid.

R_f = 0.16 (80% EtOAc/*n*-hexane); **M.p.:** 136-138 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3414, 3377, 3165, 2923, 2243, 2092, 1683, 1651, 1620, 1564, 1506, 1409, 1392, 1257, 1203, 1147, 1120, 1016, 981; **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ_H = 1.91 – 2.01 (2H, m), 3.16 – 3.22 (1H, m), 3.24 – 3.27 (2H, m), 3.68 – 3.78 (2H, m), 7.56 (1H, br s), 7.98 – 8.00 (2H, m), 8.03 – 8.05 (2H, m), 8.14 (1H, br s); **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ_C = 23.3, 30.7, 35.4, 50.8, 120.6, 127.7, 127.8, 138.1, 132.2, 167.0, 198.2; **HRMS** (ES–) $C_{13}H_{13}N_5O_2$ [M-H]$^-$ requires 270.0991, found 270.0884 (+ 1.1 ppm).

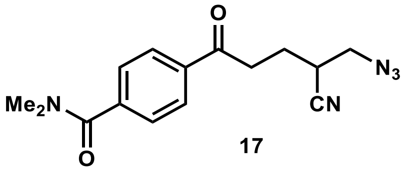
^{1}H and ^{13}C NMR spectra of **16**





16

4-(5-Azido-4-cyanopentanoyl)-*N*,*N*-dimethylbenzamide (17)

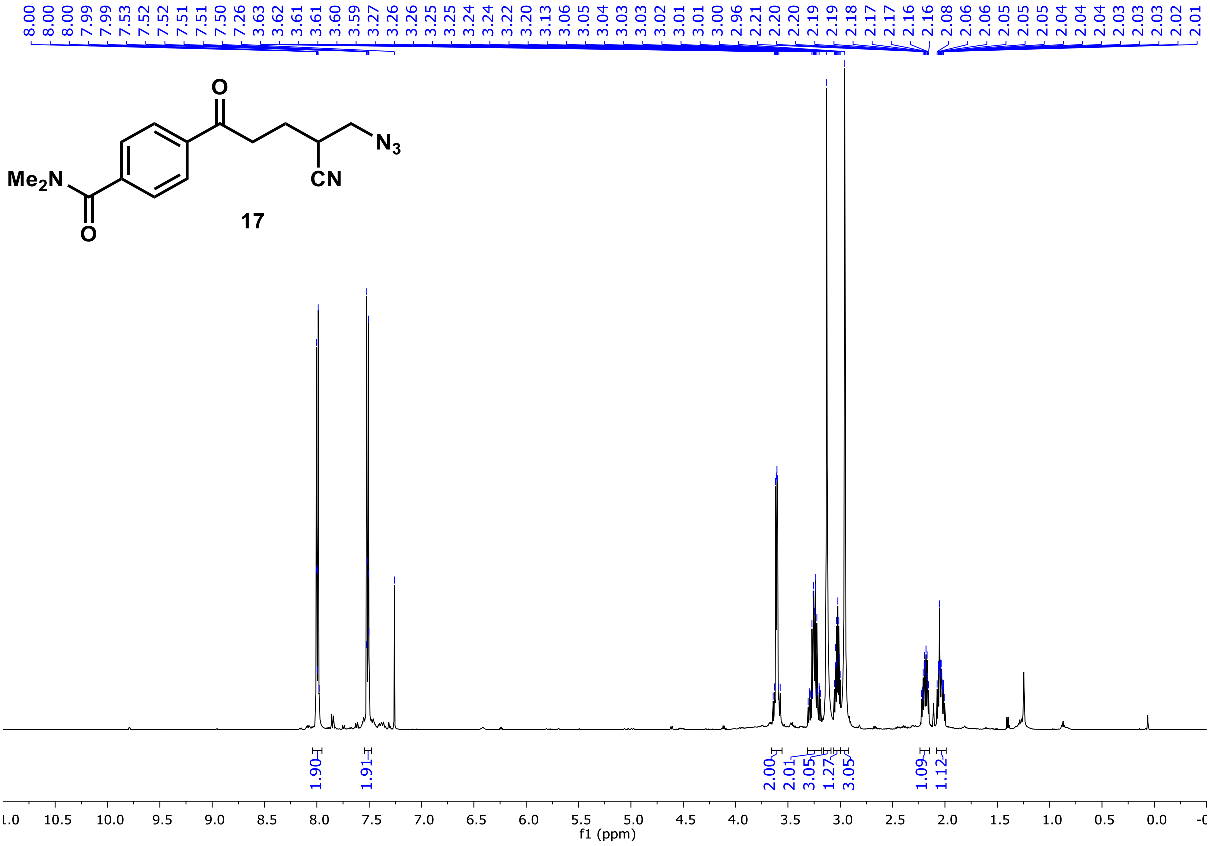


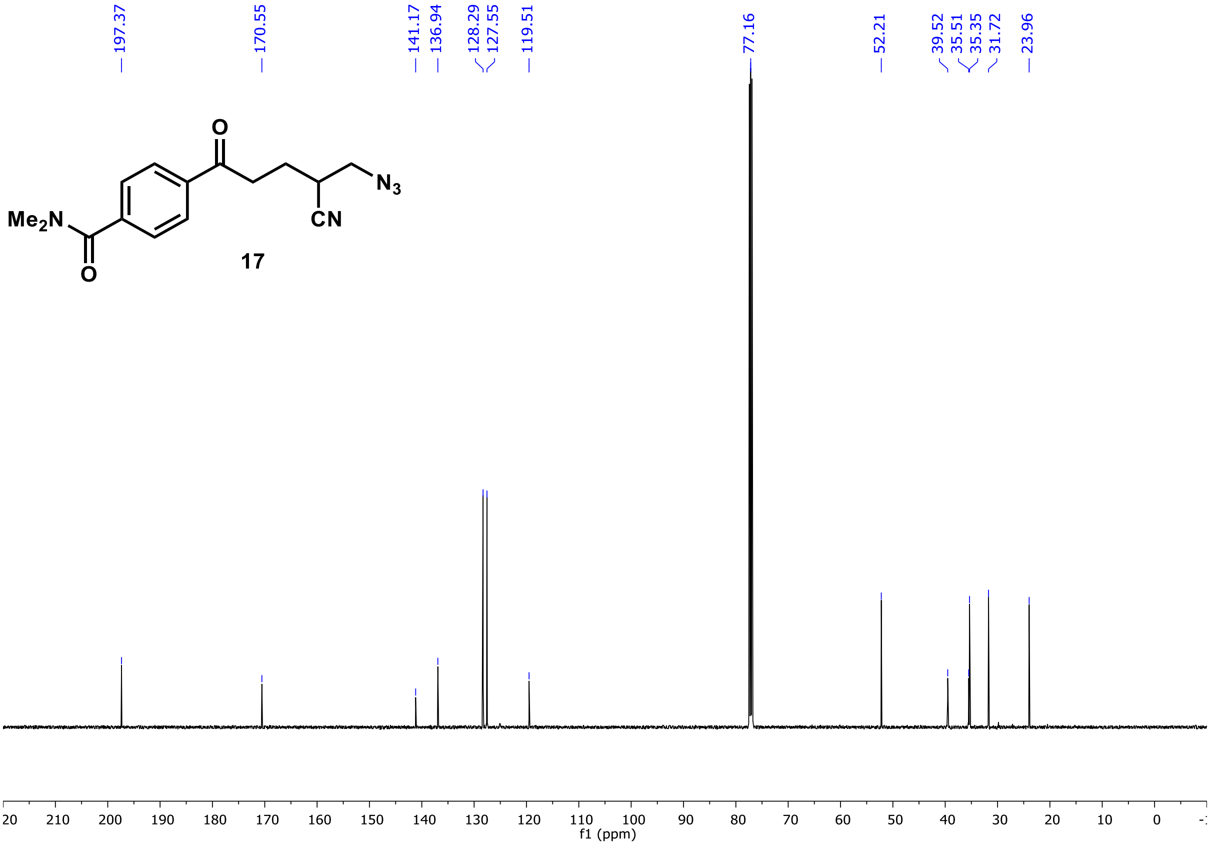
17

Prepared according to General Procedure 6 using **S43** (77 mg). The resultant crude material was purified by flash column chromatography (60-90% EtOAc/*n*-hexane, silica gel) to afford **17** (37 mg, 41%) as a yellow oil.

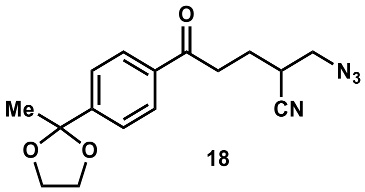
R$_f$ = 0.22 (80% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 2933, 2243, 2102, 1683, 1624 (br), 1566, 1512, 1452, 1400, 1265, 1211, 1081, 1016, 981, 918; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.00 – 2.08 (1H, m), 2.16 – 2.22 (1H, m), 2.96 (3H, s), 3.00 – 3.06 (1H, m), 3.13 (3H, m), 3.19 – 3.31 (2H, m), 3.57 – 3.64 (2H, m), 7.50 – 7.53 (2H, m), 7.98 – 8.00 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 24.0, 31.7, 35.3, 35.5, 39.5, 52.2, 119.5, 127.6, 128.3, 136.9, 141.2, 170.6, 197.4; **HRMS** (ES+) $C_{15}H_{17}N_5O_2$ [M+H]$^+$ requires 300.1460, found 300.1457 (– 1.0 ppm).

^{1}H and ^{13}C NMR spectra of **17**





2-(Azidomethyl)-5-(4-(2-methyl-1,3-dioxolan-2-yl)phenyl)-5-oxopentanenitrile (18)

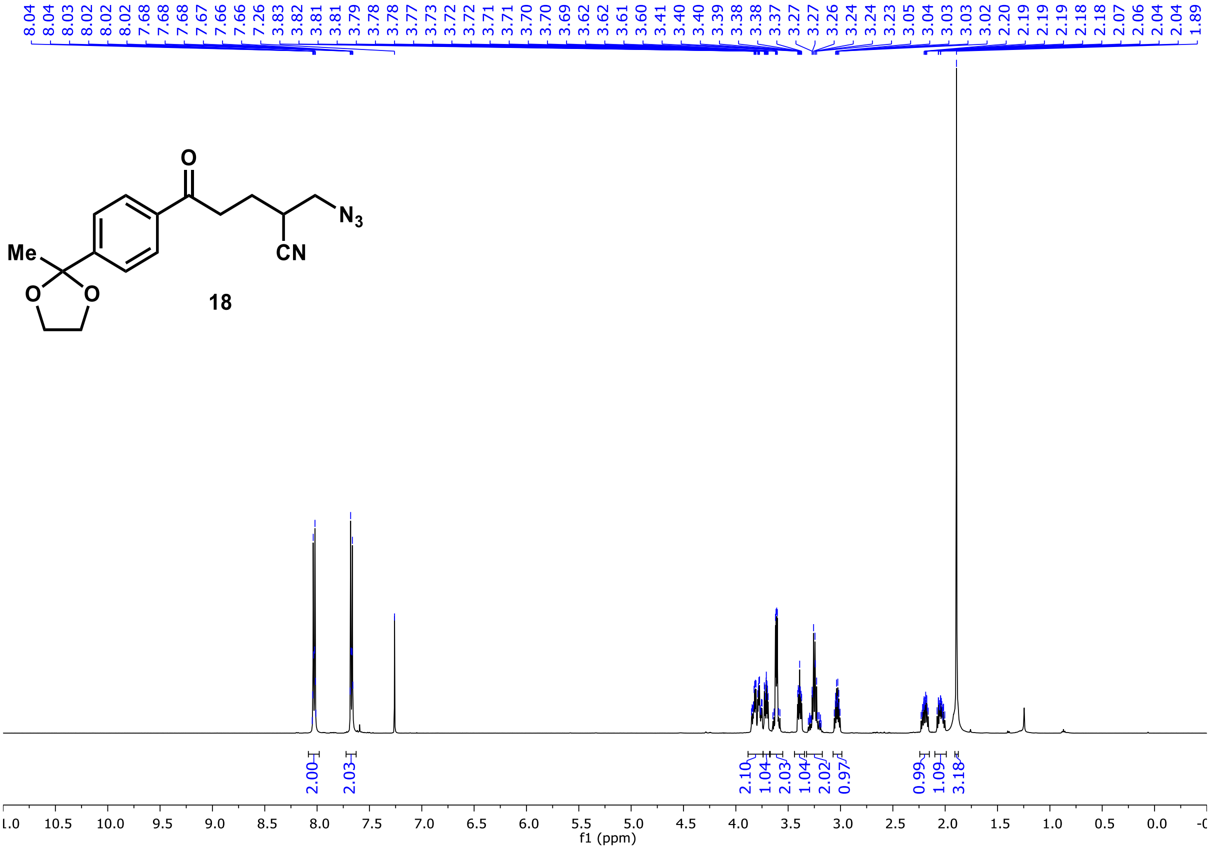


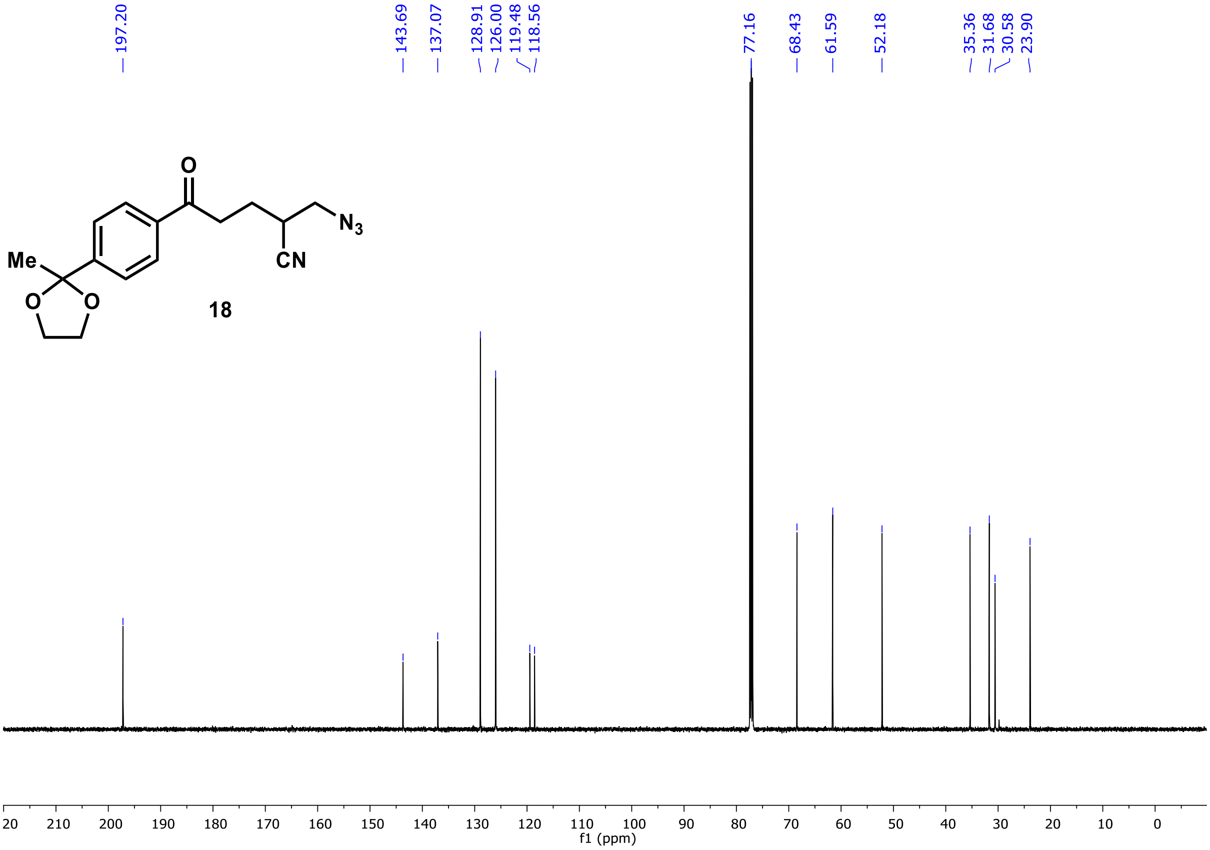
18

Prepared according to General Procedure 6 using **S44** (82 mg). The resultant crude material was purified by flash column chromatography (10-50% EtOAc/*n*-hexane, silica gel) to afford **18** (28 mg, 30%) as an orange oil.

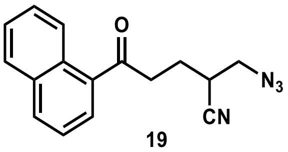
R$_f$ = 0.22 (50% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 3447, 2934, 2347, 2104, 1684, 1609, 1406, 1225, 1111, 1080, 1044, 831; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.89 (3H, s), 2.00 – 2.08 (1H, m), 2.16 – 2.23 (1H, m), 3.00 – 3.06 (1H, m), 3.19 – 3.31 (2H, m), 3.37 – 3.41 (1H, m), 3.58 – 3.65 (2H, m), 3.69 – 3.73 (1H, m), 3.75 – 3.85 (2H, m), 7.66 – 7.68 (2H, m), 8.01 – 8.05 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 23.9, 30.6, 31.7, 35.3, 52.2, 61.6, 68.4, 118.6, 119.5, 126.0, 128.9, 137.1, 143.7, 197.2; **HRMS** (ES+) $C_{16}H_{18}N_4O_3$ [M+H]$^+$ requires 315.1457, found 315.1461 (+ 1.3 ppm).

^{1}H and ^{13}C NMR spectra of **18**





2-(Azidomethyl)-5-(naphthalen-1-yl)-5-oxopentanenitrile (19)



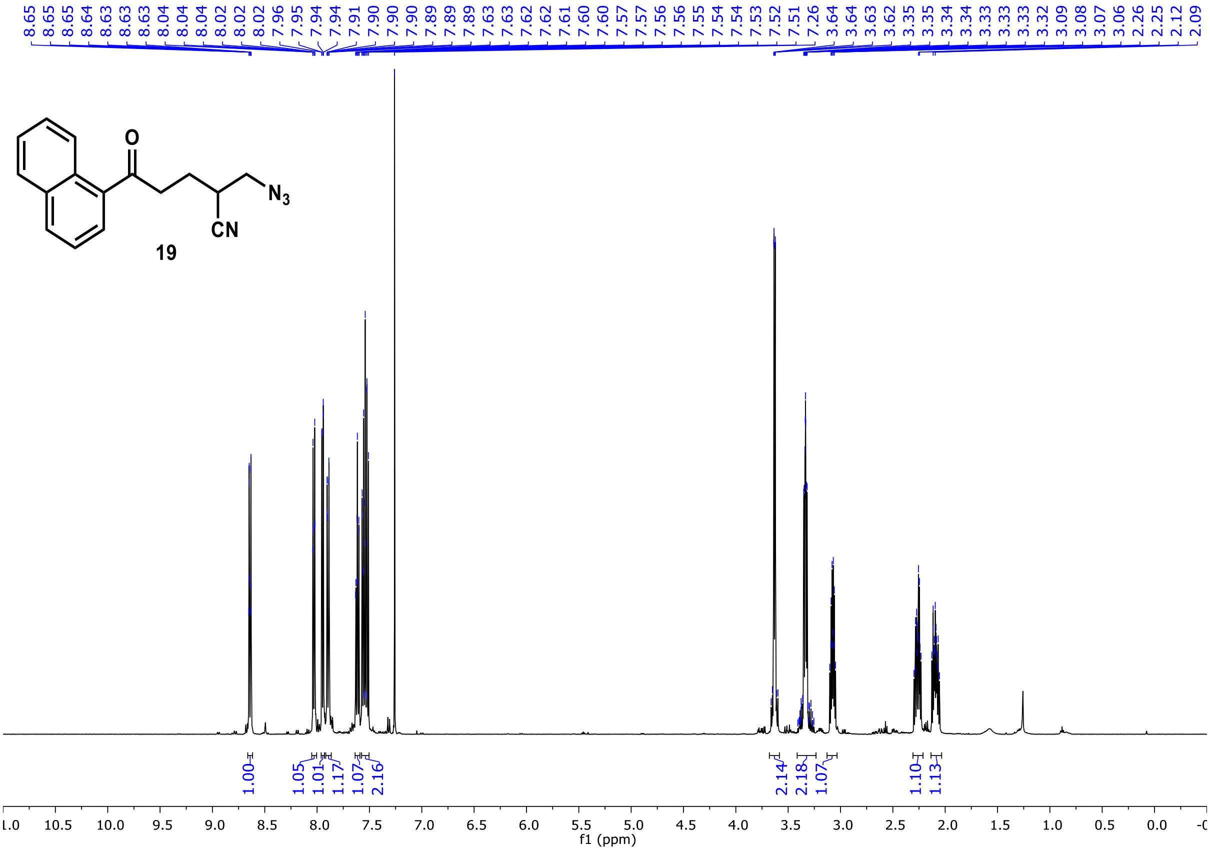
19

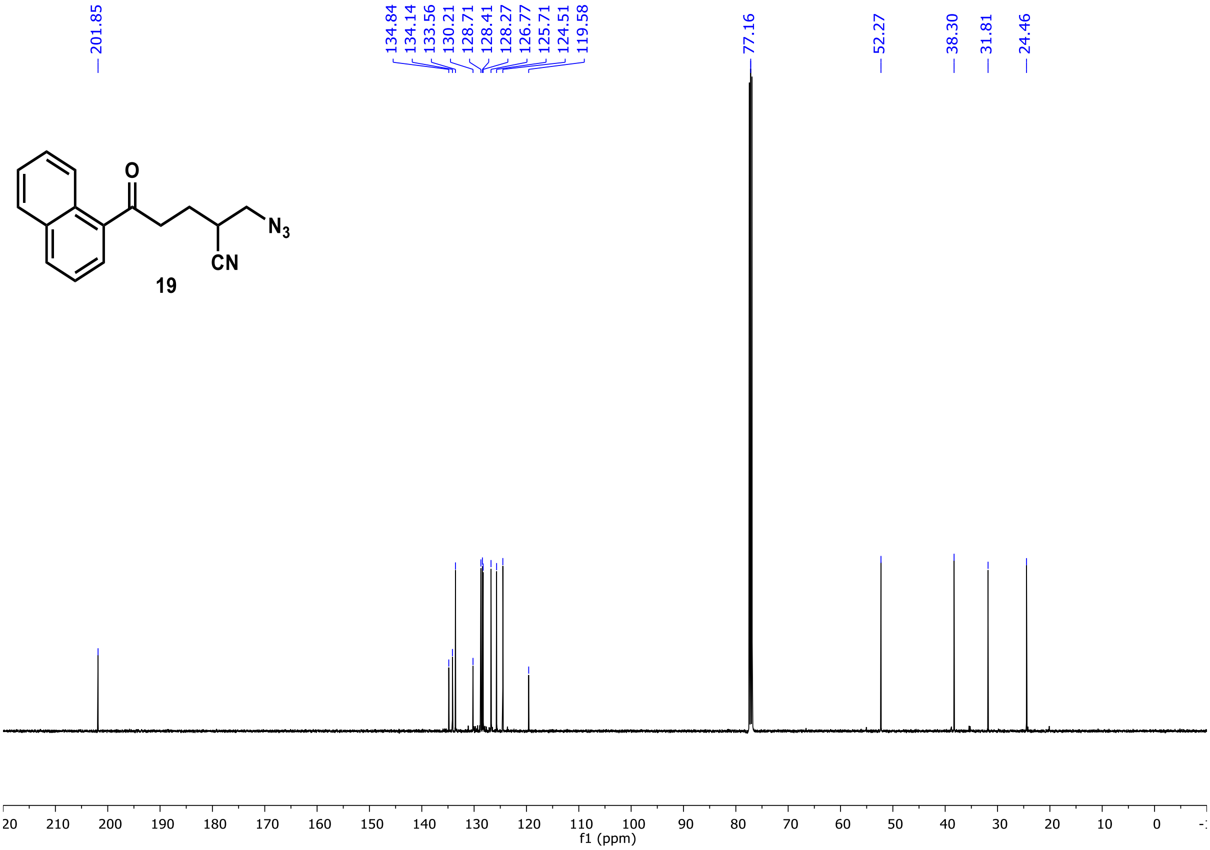
Prepared according to General Procedure 6 using **S45** (71 mg). The resultant crude material was purified by flash column chromatography (5-25% EtOAc/*n*-hexane, silica gel) to afford **19** (28 mg, 34%) as a yellow oil.

R$_f$ = 0.28 (30% EtOAc/*n*-hexane); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 2.05 – 2.13 (1H, m), 2.23 – 2.30 (1H, m), 3.05 – 3.10 (1H, m), 3.25 – 3.41 (2H, m), 3.60 – 3.66 (2H, m), 7.51 – 7.57 (2H, m), 7.60 – 7.63 (1H, m), 7.89 – 7.91 (1H, m), 7.94 – 7.96 (1H, m), 8.02 – 8.04 (1H, m), 8.63 – 8.65 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 24.5, 31.8, 38.3, 52.3, 119.6, 124.5, 125.7, 126.8, 128.3, 128.4, 128.7, 130.2, 133.6, 134.1, 134.8, 201.9.

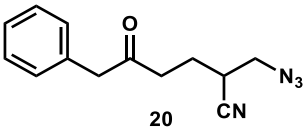
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **19**





2-(Azidomethyl)-5-oxo-6-phenylhexanenitrile (20)



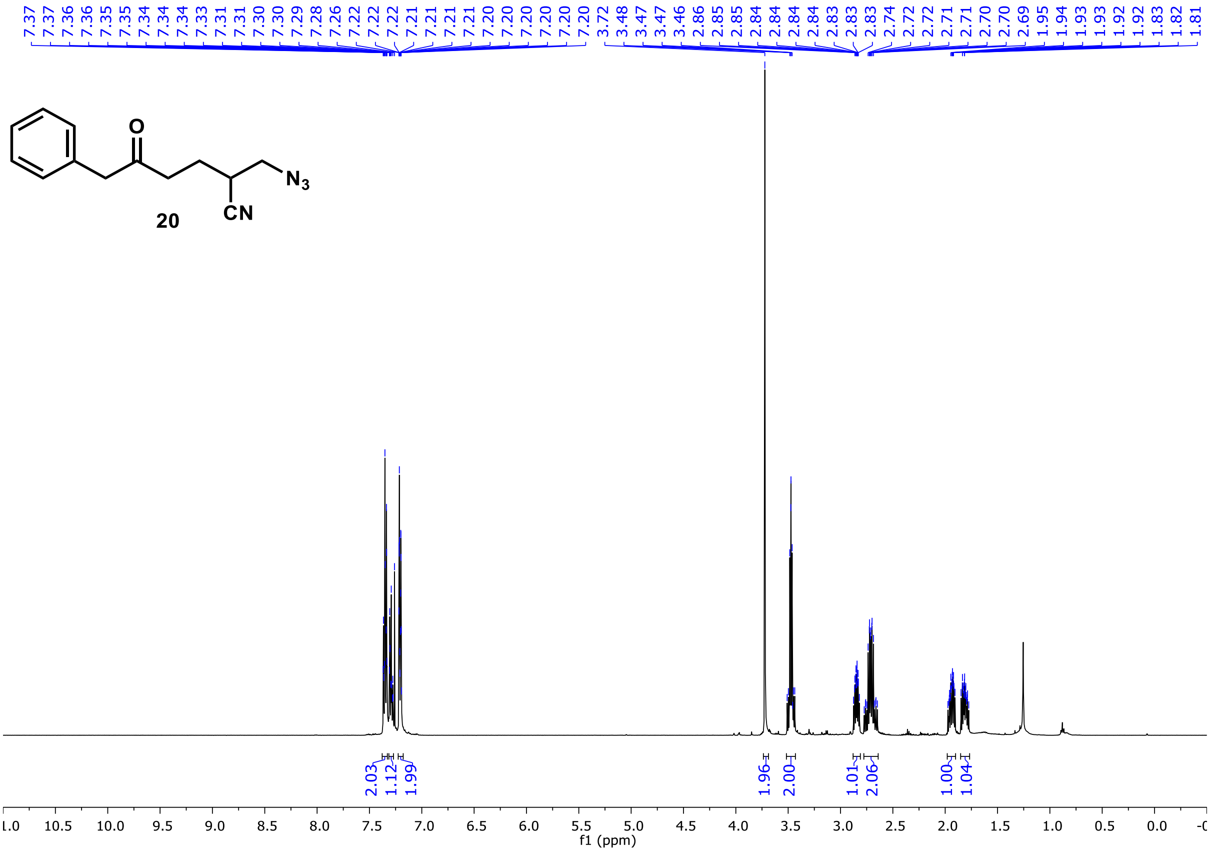
20

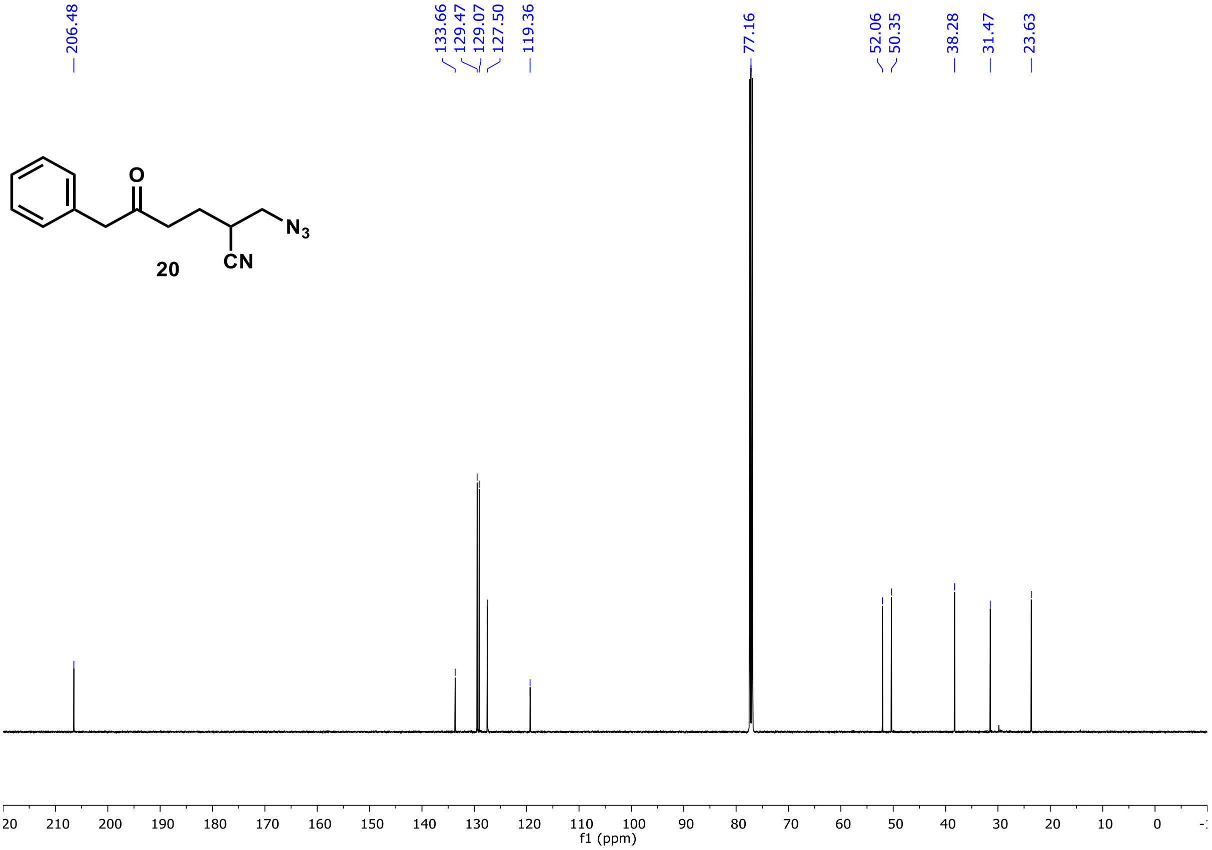
Prepared according to General Procedure 6 using **S46** (60 mg), but electrolysis was run for 5 h instead of 4 h. The resultant crude material was purified by flash column chromatography (5-20% EtOAc/*n*-hexane, silica gel) to afford **20** (33 mg, 45%) as a yellow oil.

R$_f$ = 0.21 (30% EtOAc/*n*-hexane); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.77 – 1.85 (1H, m), 1.91 – 1.97 (1H, m), 2.65 – 2.77 (2H, m), 2.82 – 2.88 (1H, m), 3.44 – 3.51 (2H, m), 3.72 (2H, s), 7.19 – 7.22 (2H, m), 7.27 – 7.31 (1H, m), 7.33 – 7.37 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 23.6, 31.5, 38.3, 50.4, 52.1, 119.4, 127.5, 129.1, 129.5, 133.7, 206.5.

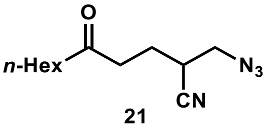
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **20**





2-(Azidomethyl)-5-oxoundecanenitrile (21)

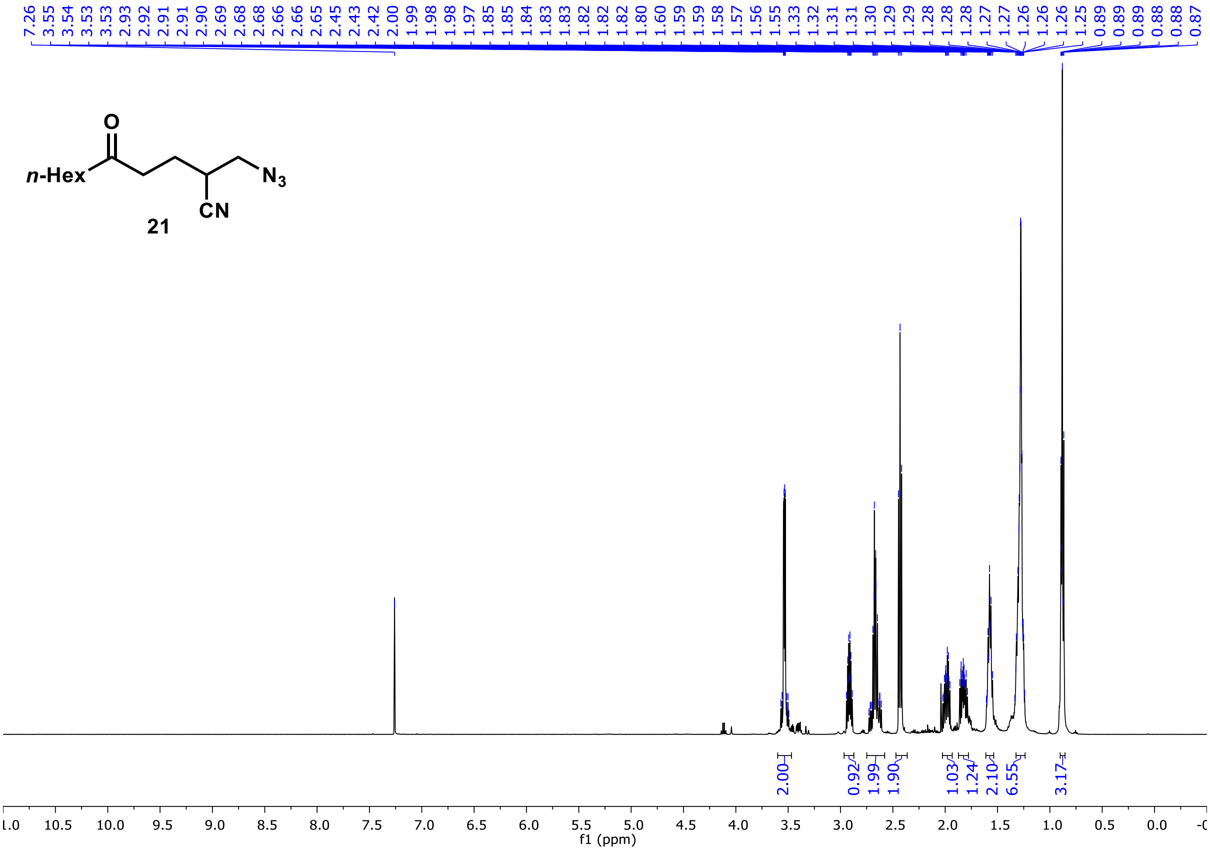


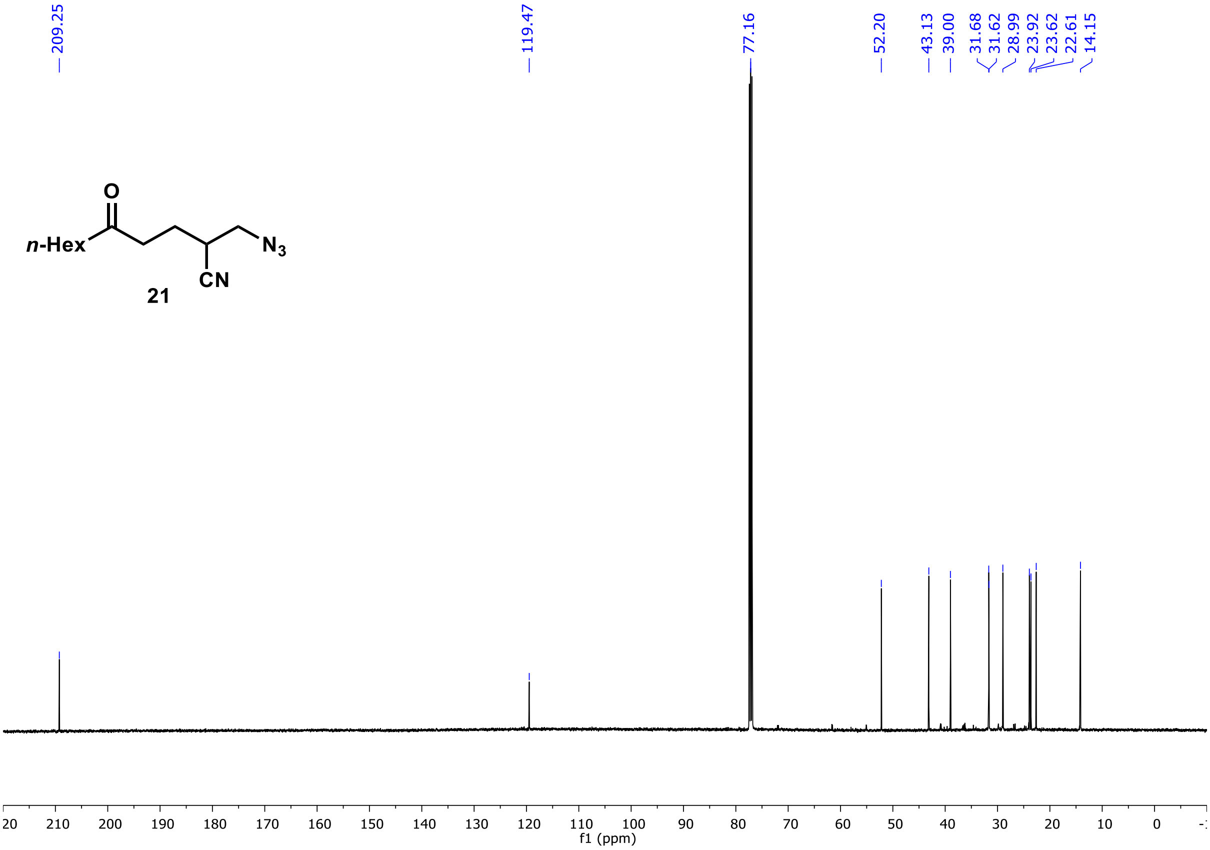
21

Prepared according to General Procedure 6 using **S47** (63 mg). The resultant crude material was purified by flash column chromatography (5-25% EtOAc/*n*-hexane, silica gel) to afford **21** (21 mg, 27%) as a yellow oil.

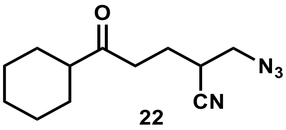
R_f = 0.37 (15% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 2964, 2930, 2858, 2243, 2104, 1713, 1456, 1412, 1377, 1279, 1159, 1128, 951, 815; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 0.87 – 0.89 (3H, m), 1.24 – 1.33 (6H, m), 1.55 – 1.61 (2H, m), 1.79 – 1.86 (1H, m), 1.95 – 2.02 (1H, m), 2.43 (2H, t, *J* 7.5), 2.61 – 2.73 (2H, m), 2.89 – 2.94 (1H, m), 3.49 – 3.57 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 14.2, 22.6, 23.6, 23.9, 29.0, 31.6, 31.7, 39.0, 43.1, 52.2, 119.5, 209.3; **HRMS** (AP+) $C_{12}H_{20}N_4O$ [M-N$_2$+H]$^+$ requires 209.1654, found 209.1658 (+ 1.9 ppm).

^{1}H and ^{13}C NMR spectra of **21**





2-(Azidomethyl)-5-cyclohexyl-5-oxopentanenitrile (22)

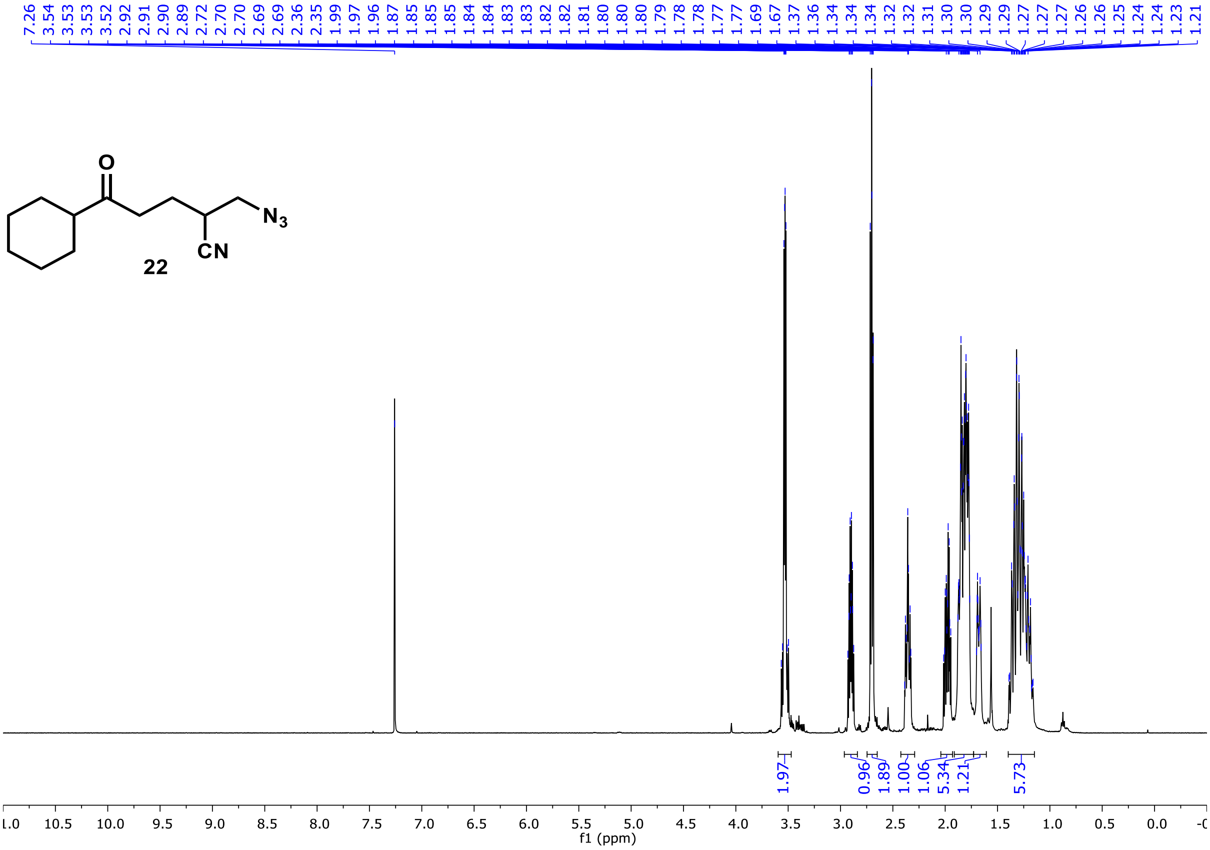


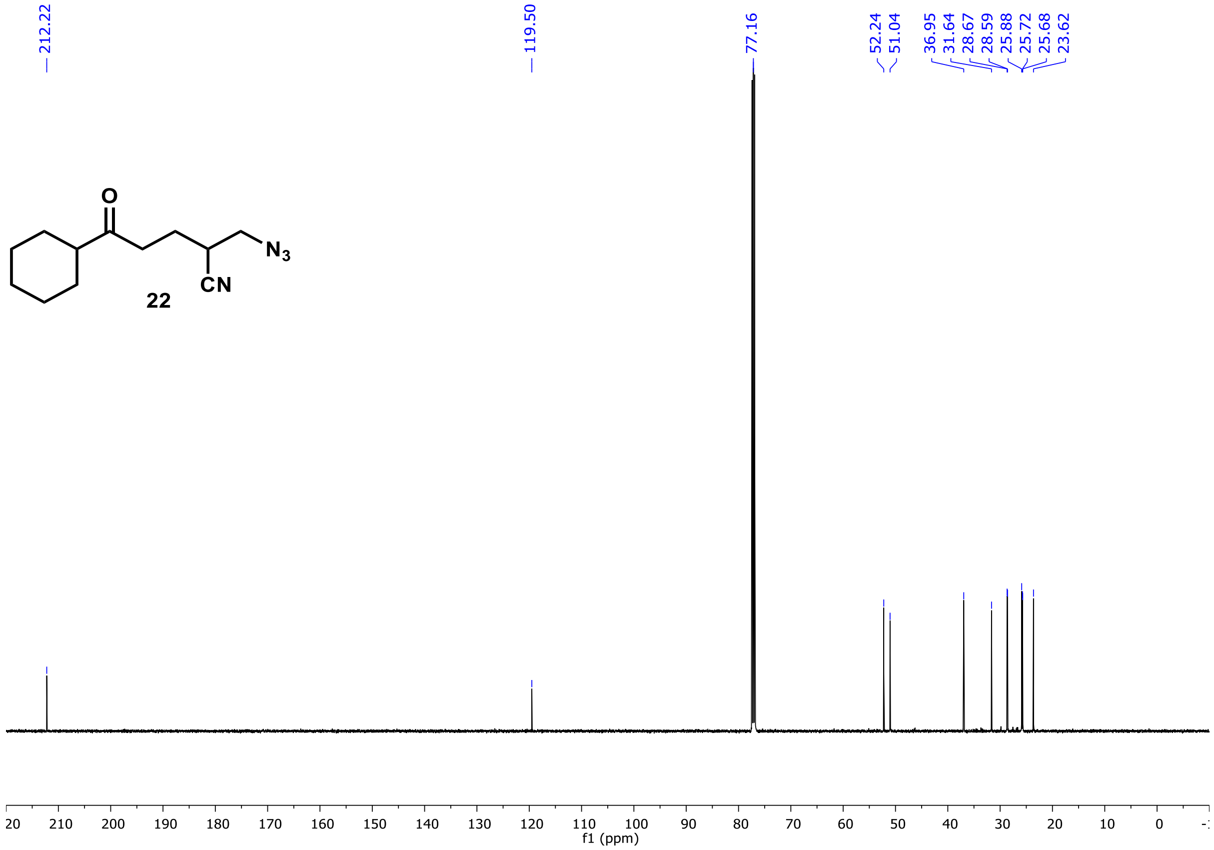
Prepared according to General Procedure 6 using **S48** (58 mg). The resultant crude material was purified by flash column chromatography (5-25% EtOAc/*n*-hexane, silica gel) to afford **22** (28 mg, 40%) as a colourless oil.

R$_f$ = 0.34 (15% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ$_H$ = 1.16 – 1.39 (5H, m), 1.66 – 1.70 (1H, m), 1.77 – 1.88 (5H, m), 1.95 – 2.01 (1H, m), 2.33 – 2.39 (1H, m), 2.69 – 2.72 (2H, m), 2.87 – 2.93 (1H, m), 3.50 – 3.57 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ$_C$ = 23.6, 25.6, 25.7, 25.9, 28.6, 28.7, 31.6, 36.9, 51.0, 52.2, 119.5, 212.2.

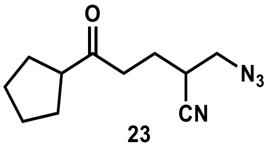
These data are in accordance with the literature.[18]

<u>^{1}H and ^{13}C NMR spectra of **22**</u>





2-(Azidomethyl)-5-cyclopentyl-5-oxopentanenitrile (23)

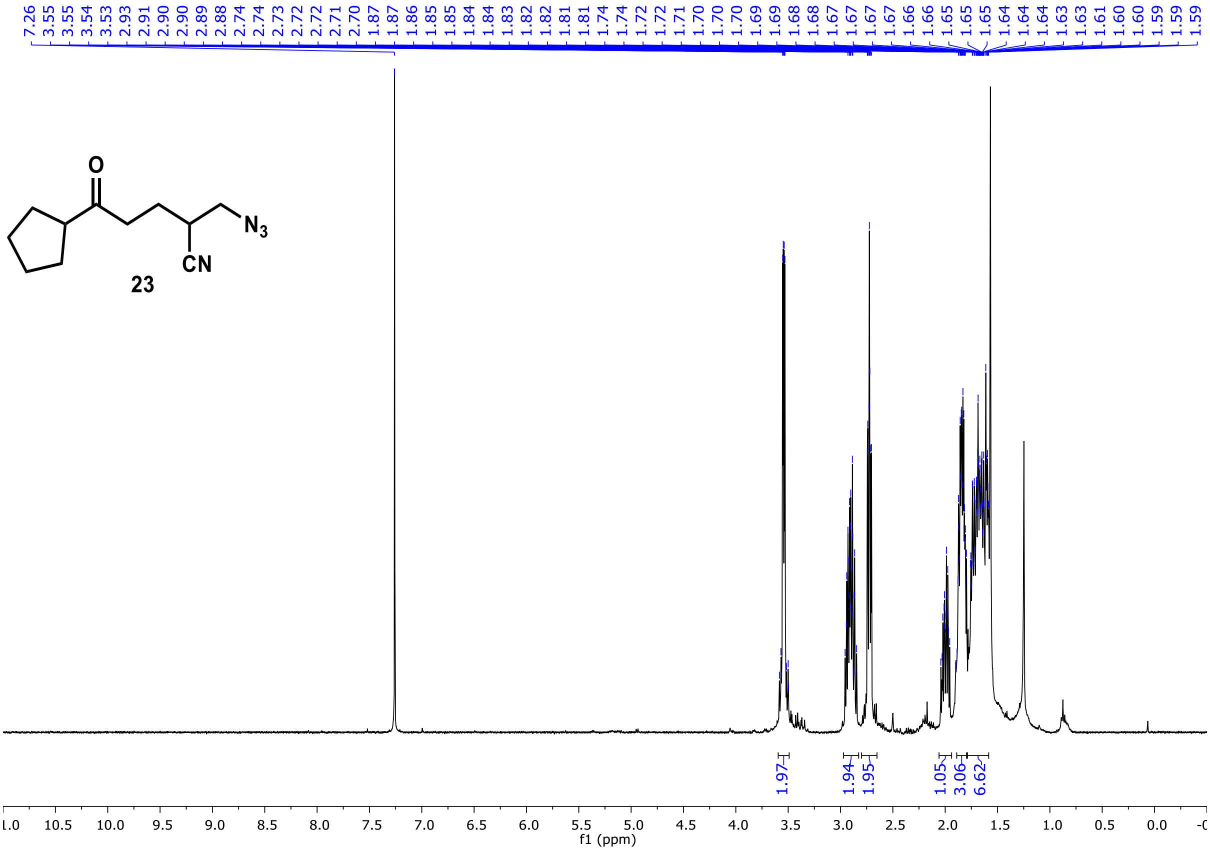


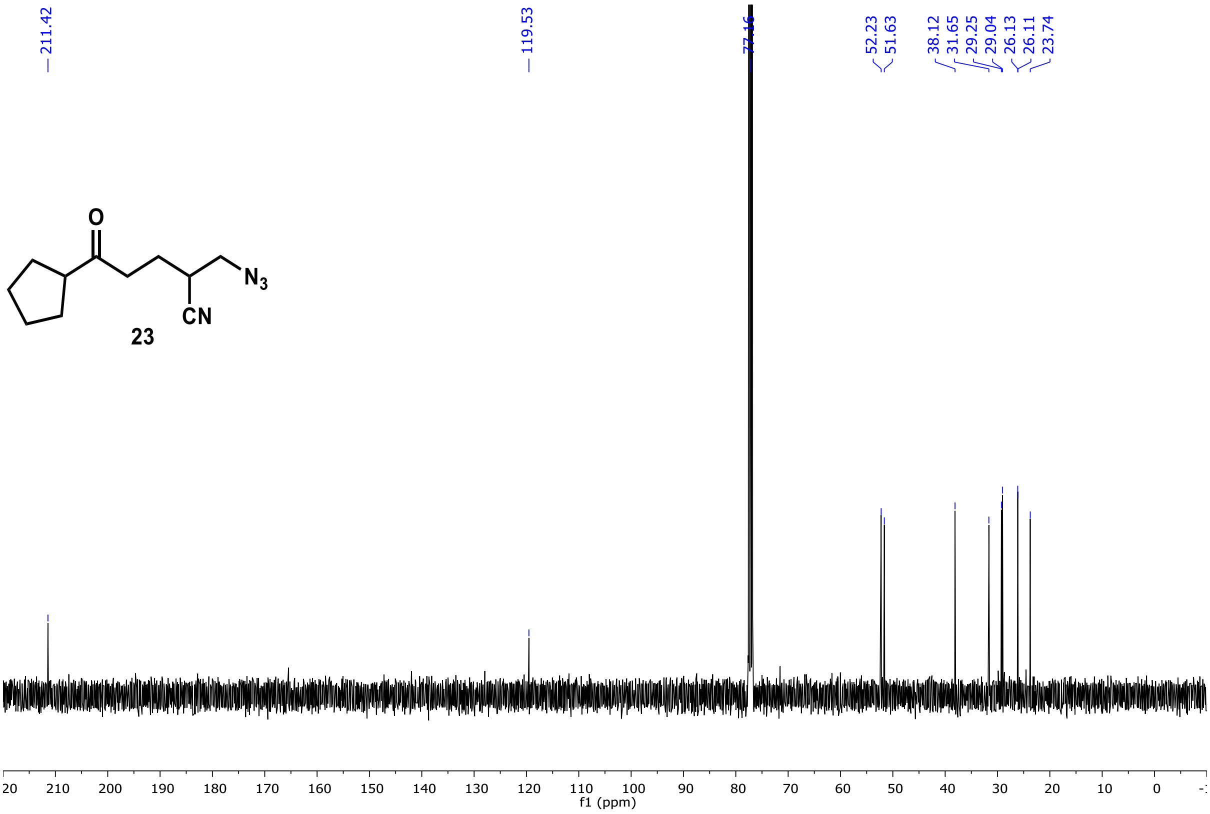
23

Prepared according to General Procedure 6 using **S49** (54 mg). The resultant crude material was purified by flash column chromatography (5-25% EtOAc/*n*-hexane, silica gel) to afford **23** (21 mg, 31%) as a pale-yellow oil.

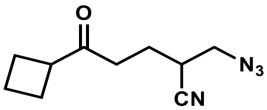
R_f = 0.35 (15% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 2957, 2870, 2243, 2106, 1707, 1452, 1358, 1279, 1113, 1018; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H = 1.59 – 1.76 (6H, m), 1.80 – 1.90 (3H, m), 1.96 – 2.04 (1H, m), 2.70 – 2.74 (2H, m), 2.85 – 2.96 (2H, m), 3.50 – 3.58 (2H, m); **^{13}C NMR (101 MHz, CDCl$_3$)** δ_C = 23.7, 26.1 (2C), 29.0, 29.2, 31.7, 38.1, 51.6, 52.2, 119.5, 211.4; **HRMS** (CI+) $C_{11}H_{16}N_4O$ [M-N$_2$+H]$^+$ requires 193.1341, found 193.1334 (– 3.6 ppm).

^{1}H and ^{13}C NMR spectra of **23**





2-(Azidomethyl)-5-cyclobutyl-5-oxopentanenitrile (24)

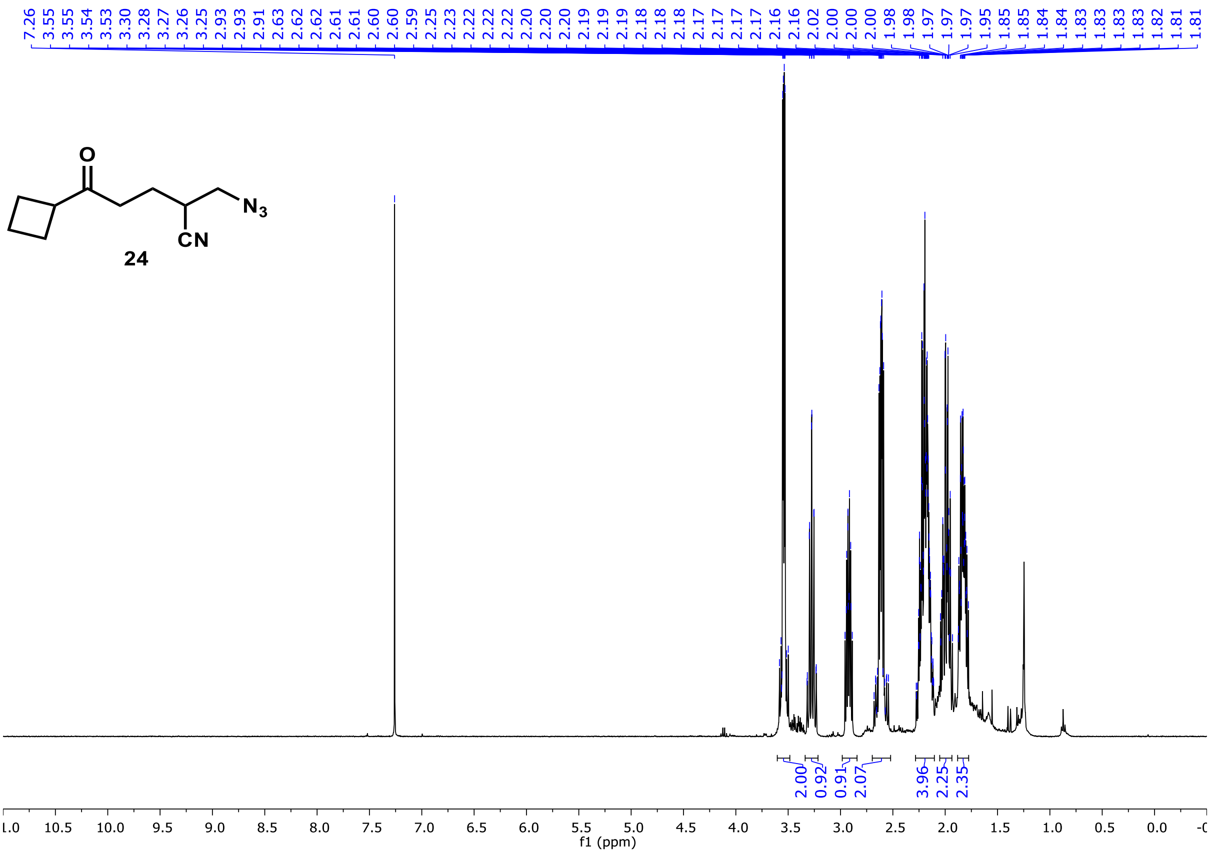


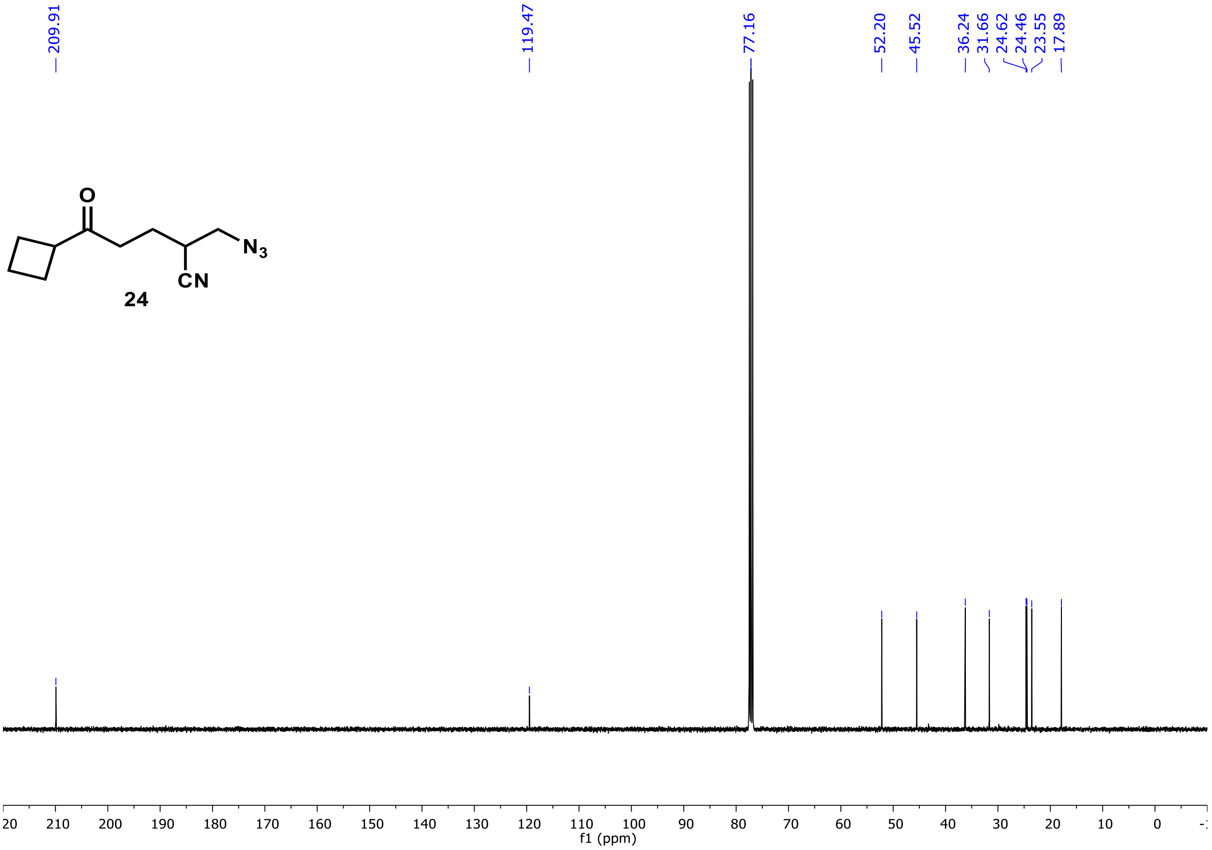
24

Prepared according to General Procedure 6 using **S50** (50 mg). The resultant crude material was purified by flash column chromatography (5-25% EtOAc/*n*-hexane, silica gel) to afford **24** (24 mg, 39%) as a colourless oil.

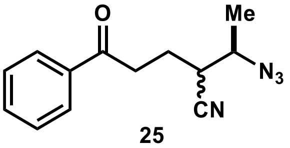
R$_f$ = 0.31 (15% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 2943, 2868, 2243, 2102, 1705, 1452, 1356, 1277, 1126, 982; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H = 1.78 – 1.88 (2H, m), 1.93 – 2.04 (2H, m), 2.11 – 2.27 (4H, m), 2.54 – 2.68 (2H, m), 2.89 – 2.96 (1H, m), 3.23 – 3.32 (1H, m), 3.50 – 3.58 (2H, m); **^{13}C NMR (101 MHz, CDCl$_3$)** δ_C = 17.9, 23.4, 24.5, 24.6, 31.7, 36.2, 45.5, 52.2, 119.5, 209.9; **HRMS** (AP+) $C_{10}H_{14}N_4O$ [M-N$_2$+H]$^+$ requires 179.1184, found 179.1188 (+ 2.2 ppm).

^{1}H and ^{13}C NMR spectra of **24**





2-(1-Azidoethyl)-5-oxo-5-phenylpentanenitrile (25)



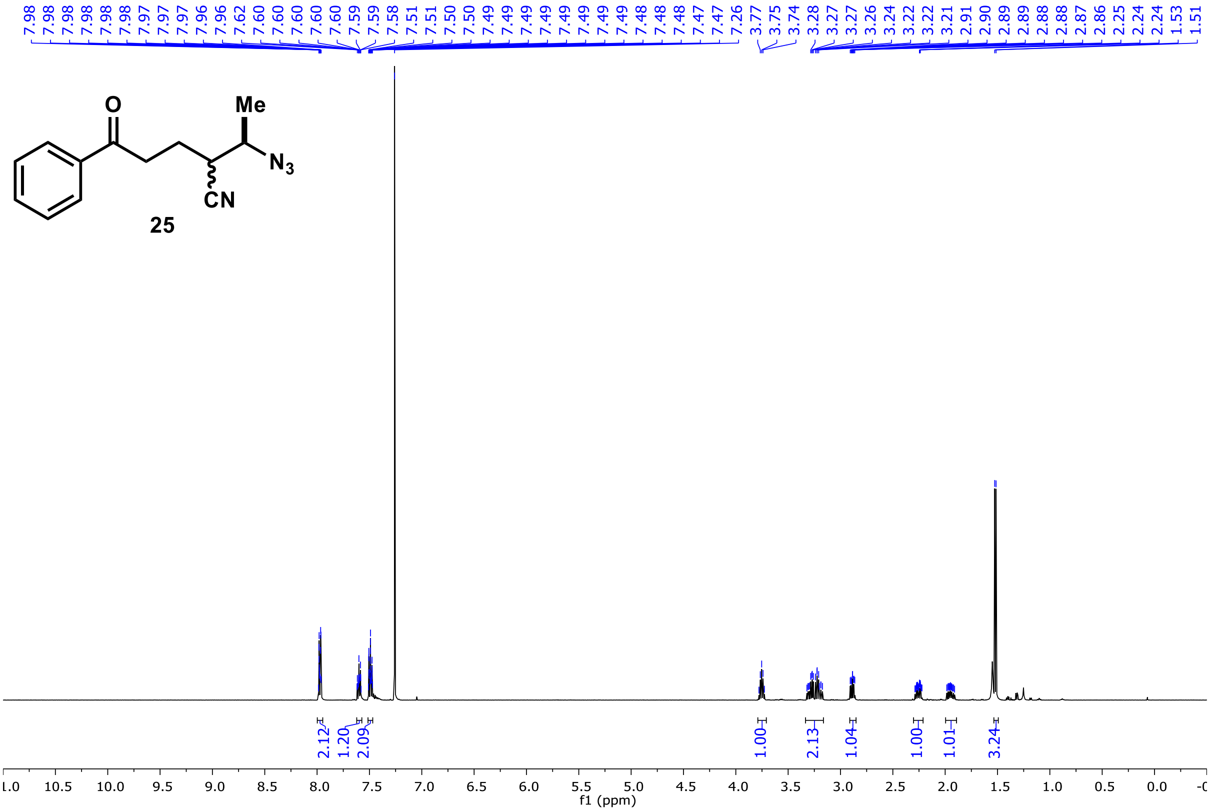
25

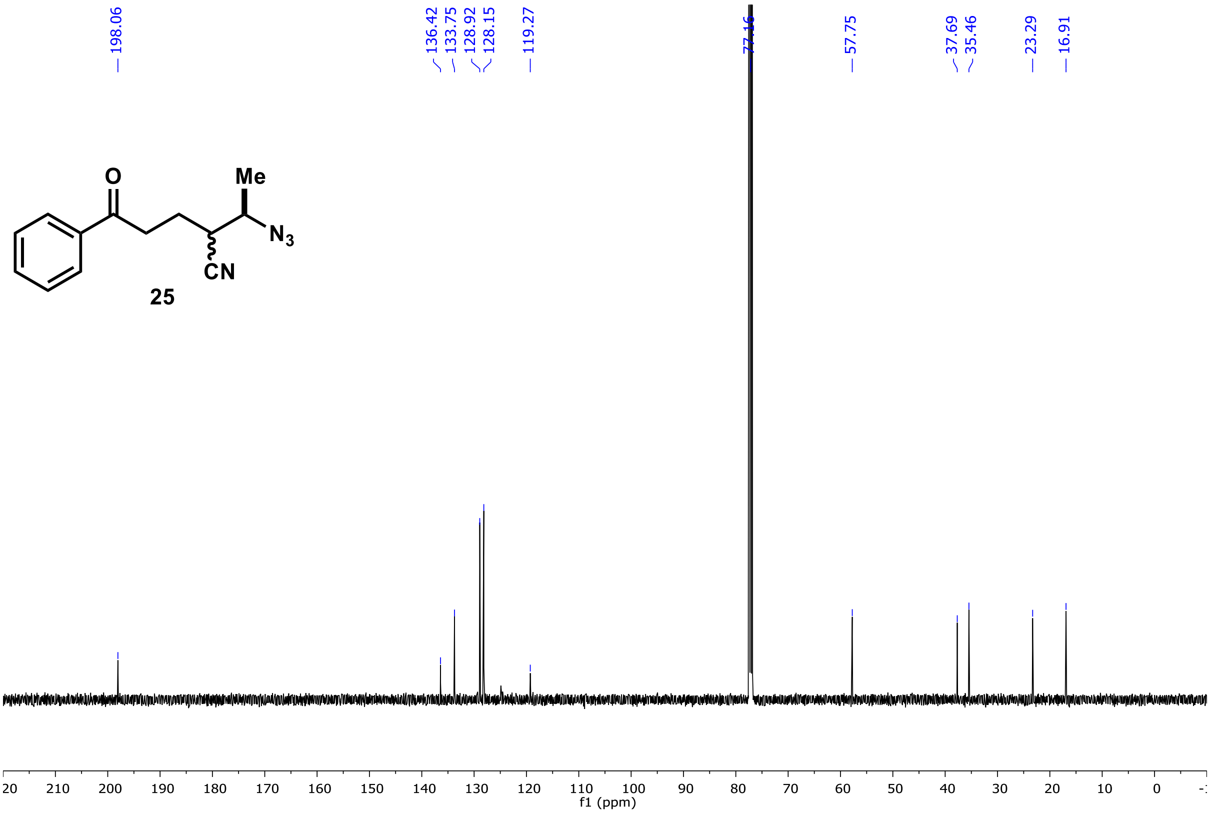
Prepared according to General Procedure 6 using **S51** (60 mg). The resultant crude material was purified by flash column chromatography (5-15% EtOAc/*n*-hexane, silica gel) to afford the separable diastereoisomers **25-1** (17 mg, 23%) and **25-2** (14 mg, 19%) as yellow oils. Analysis of the crude reaction mixture indicated a diastereomeric ratio of 1:1.

Data for **25-1**

R_f = 0.42 (30% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 2980, 2245, 2115, 2097, 1672, 1446, 1261, 1209, 974, 738, 685; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.52 (3H, d. *J* 6.6), 1.91 – 1.98 (1H, m), 2.22 – 2.29 (1H, m), 2.86 – 2.91 (1H, m), 3.17 – 3.32 (2H, m), 3.73 – 3.78 (1H, m), 7.47 – 7.51 (2H, m), 7.58 – 7.62 (1H, m), 7.96 – 7.99 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 16.9, 23.3, 35.5, 37.7, 57.8, 119.3, 128.2, 128.9, 133.8, 136.4, 198.1; **HRMS** (ES+) $C_{13}H_{14}N_4O$ [M-N$_2$]$^+$ requires 215.1184, found 215.1180 (– 1.9 ppm).

^{1}H and ^{13}C NMR spectra of **25-1**

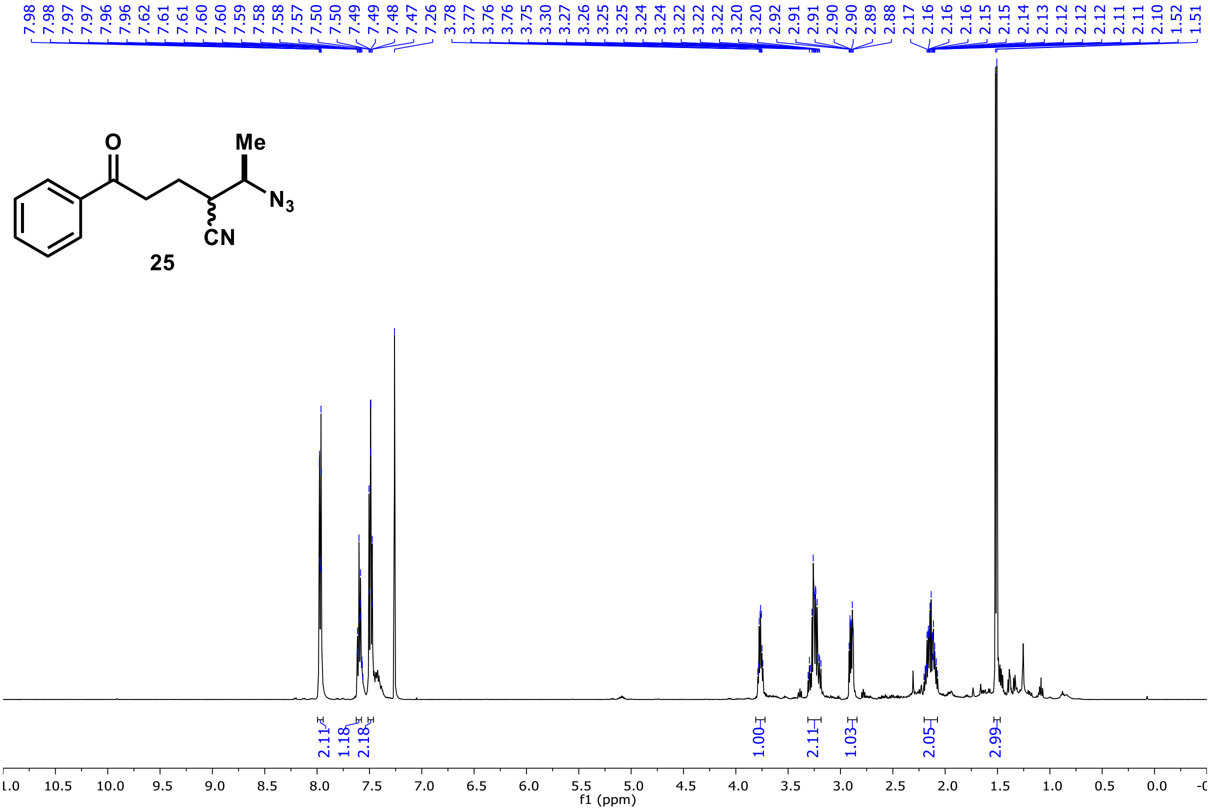


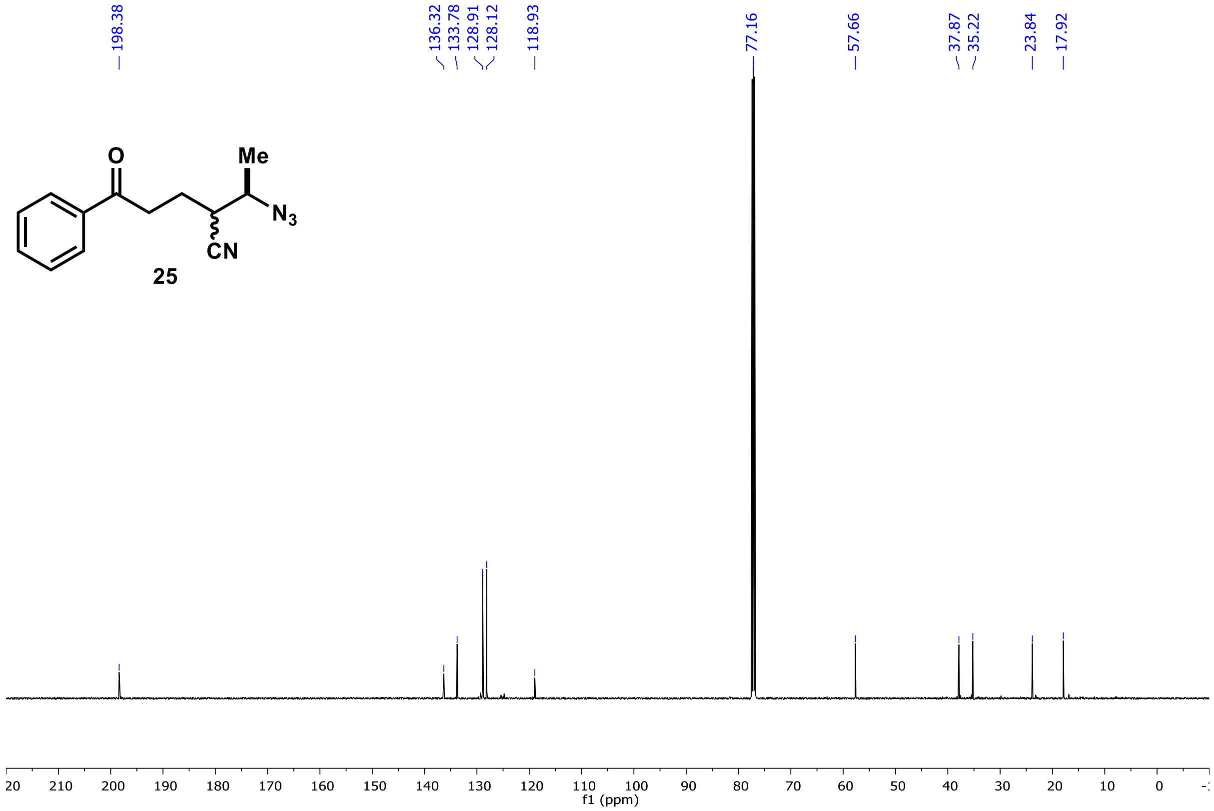


Data for **25-2**

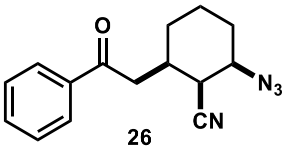
R$_f$ = 0.33 (30% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 2976, 2926, 2360, 2243, 2102, 1681, 1635, 1597, 1581, 1448, 1255, 1209, 1180, 1001; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.51 (3H, d, *J* 6.6), 2.07 – 2.20 (2H, m), 2.88 – 2.92 (1H, m), 3.19 – 3.31 (2H, m), 3.74 – 3.79 (1H, m), 7.47 – 7.50 (2H, m), 7.56 – 7.62 (1H, m), 7.96 – 7.98 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 17.9, 23.8, 35.2, 37.9, 57.7, 118.9, 128.1, 128.9, 133.8, 136.3, 198.4; **HRMS** (ES+) $C_{13}H_{14}N_4O$ [M-N$_2$+H]$^+$ requires 215.1184, found 215.1177 (– 3.3 ppm).

^{1}H and ^{13}C NMR spectra of **25-2**





2-Azido-6-(2-oxo-2-phenylethyl)cyclohexane-1-carbonitrile (26)



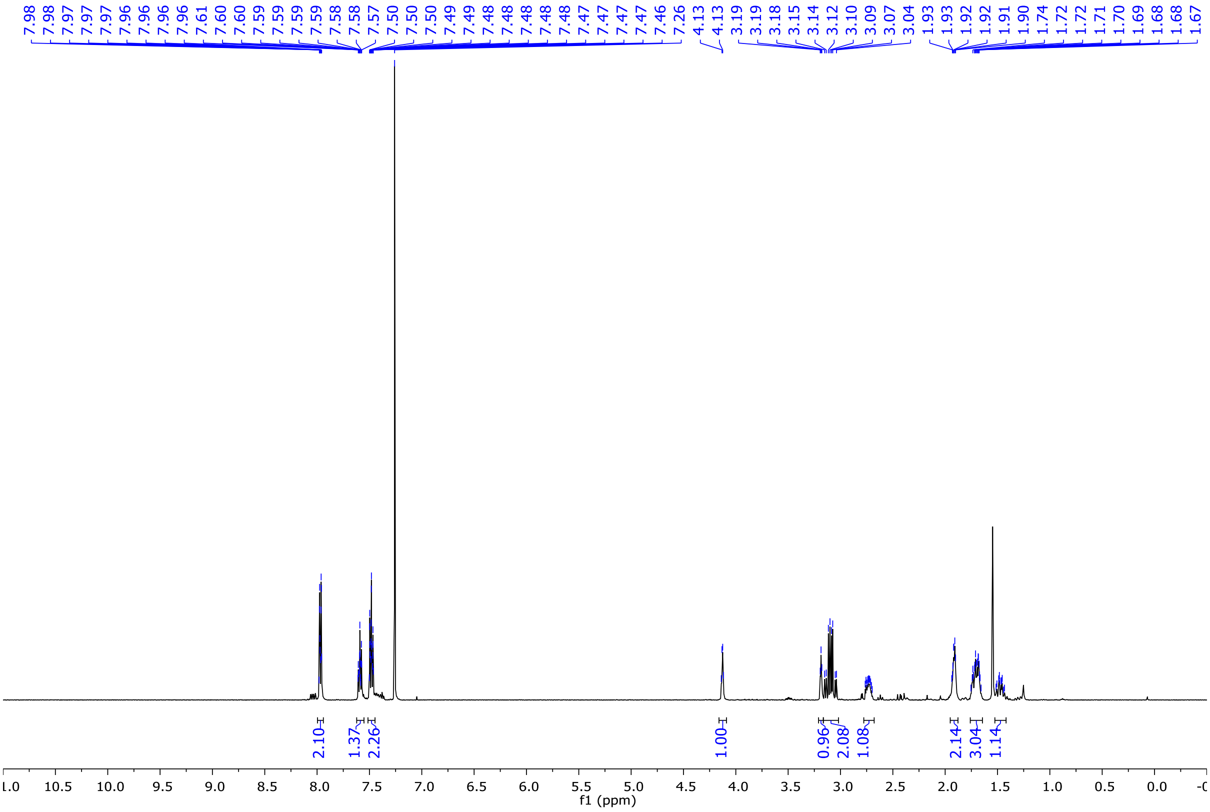
26

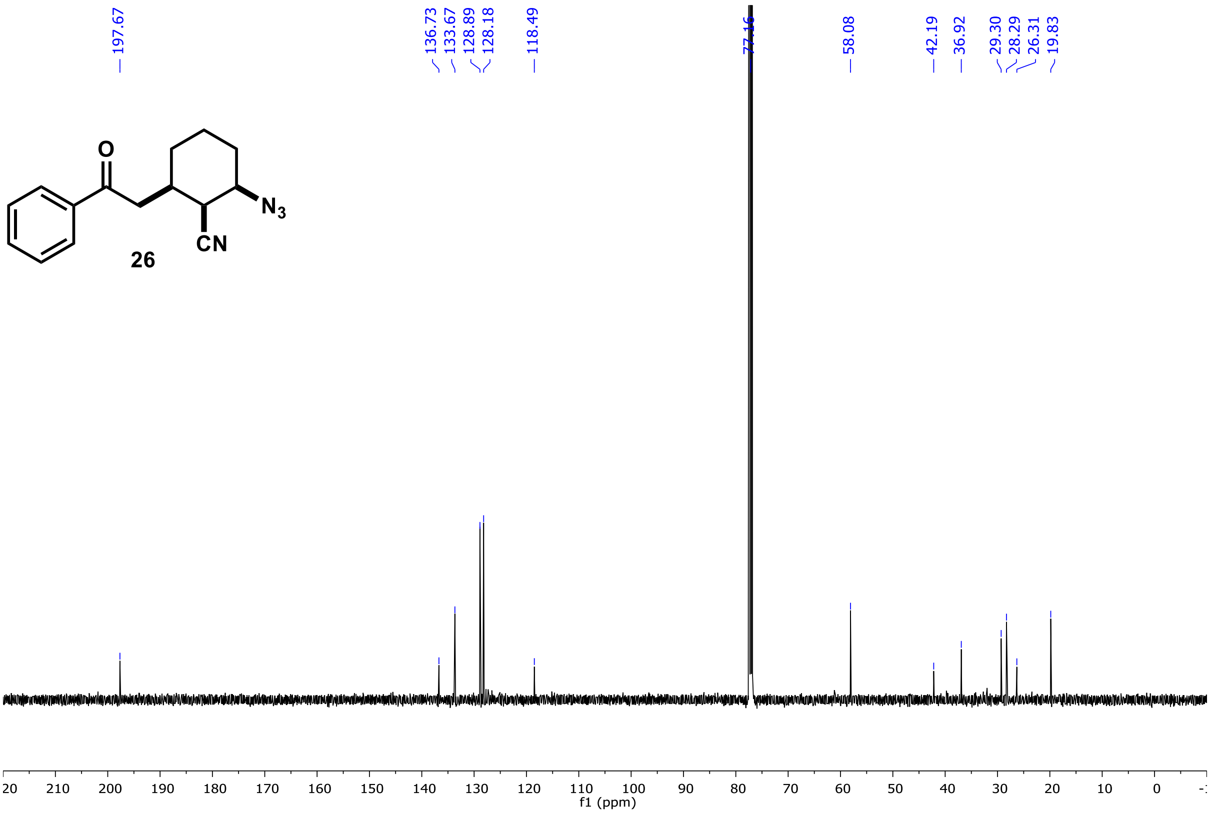
Prepared according to General Procedure 6 using **S52** (68 mg). The resultant crude material was purified by flash column chromatography (5-10% EtOAc/*n*-hexane, silica gel) to afford **26** (30 mg, 37%) as a white solid. Analysis of the crude reaction mixture indicated a diastereomeric ratio of > 20:1.

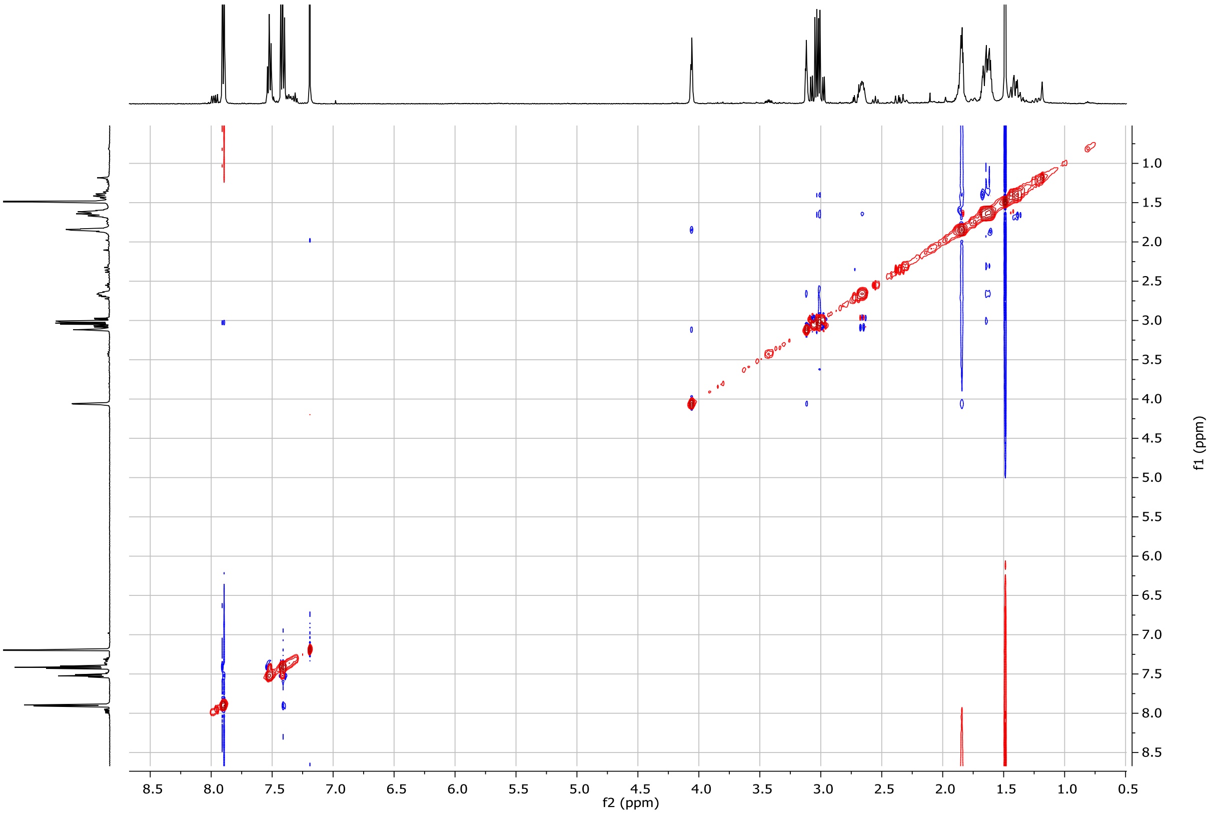
R$_f$ = 0.40 (20% EtOAc/*n*-hexane); **M.p.:** 62-64 °C; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.43 – 1.51 (1H, m), 1.66 – 1.75 (3H, m), 1.90 – 1.94 (2H, m), 2.70 – 2.76 (1H, m), 3.04 – 3.15 (2H, m), 3.18 – 3.19 (1H, m), 4.12 – 4.14 (1H, m), 7.46 – 7.50 (2H, m), 7.57 – 7.61 (1H, m), 7.96 – 7.98 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 19.8, 26.3, 28.3, 29.3, 36.9, 42.2, 58.1, 118.5, 128.2, 128.9, 133.7, 136.7, 197.7.

These data are in accordance with the literature.[18]

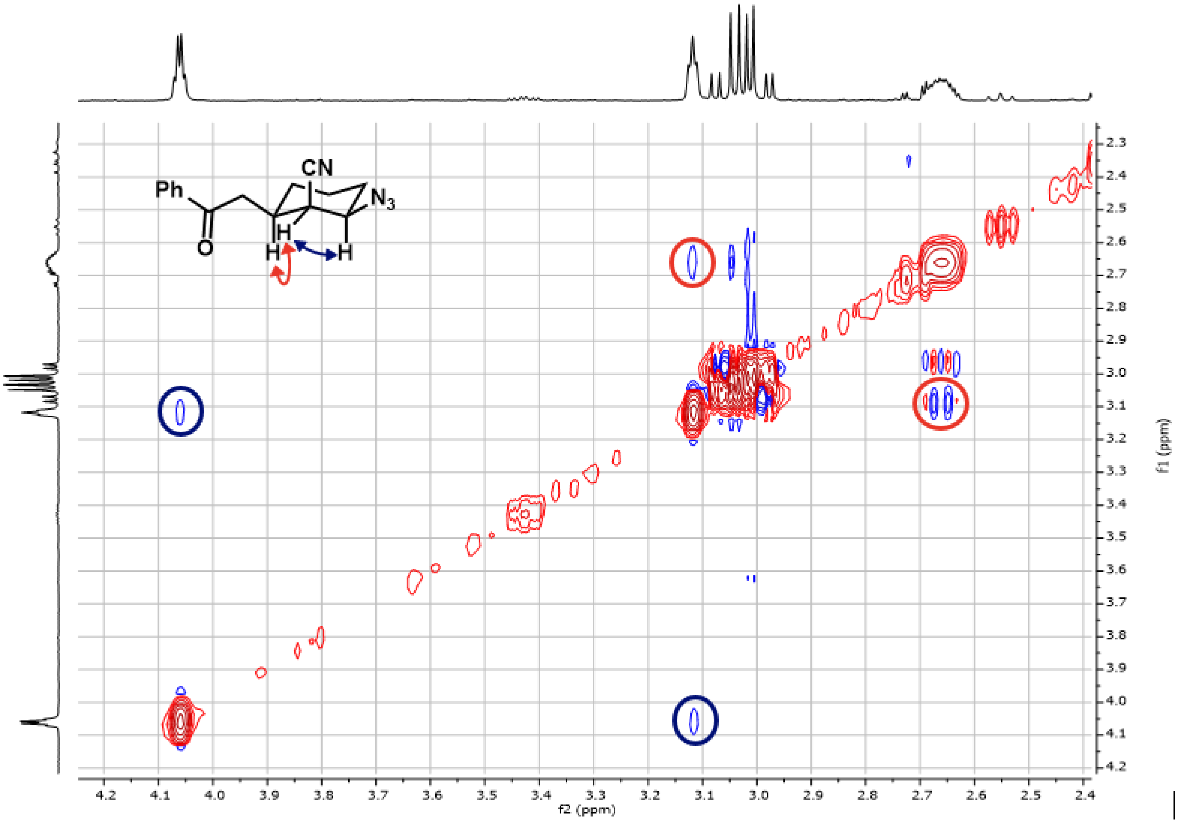
^{1}H and ^{13}C and NOESY NMR spectra of **26**



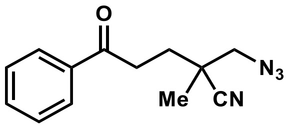




NOESY Spectrum Expansion



2-(Azidomethyl)-2-methyl-5-oxo-5-phenylpentanenitrile (27)



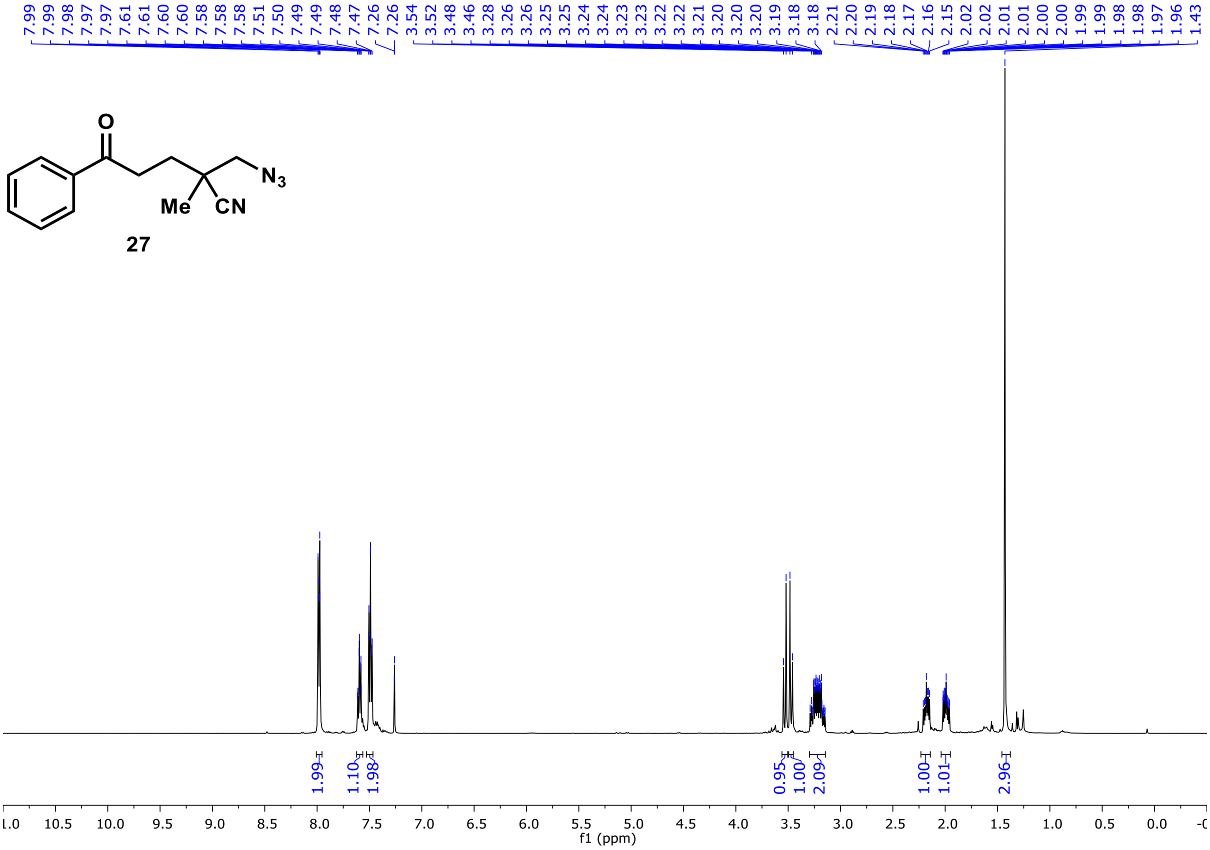
27

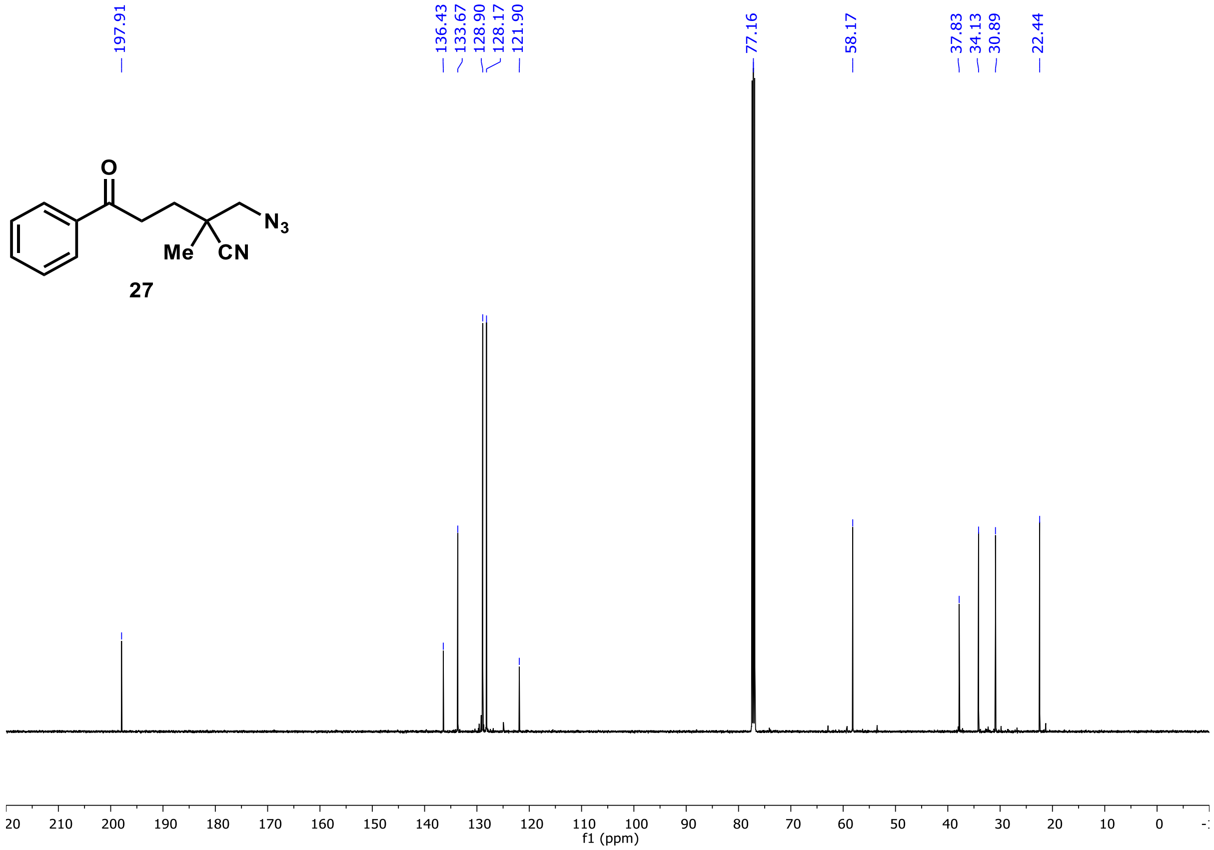
Prepared according to General Procedure 6 using **S53** (60 mg). The resultant crude material was purified by flash column chromatography (5-15% EtOAc/*n*-hexane, silica gel) to afford **27** (32 mg, 44%) as an orange oil.

R$_f$ = 0.30 (30% EtOAc/*n*-hexane); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.43 (3H, s), 1.96 – 2.02 (1H, m), 2.15 – 2.21 (1H, m), 3.15 – 3.29 (2H, m), 3.47 (1H, d, *J* 12.2), 3.53 (1H, d, *J* 12.2), 7.47 – 7.51 (2H, m), 7.58 – 7.61 (1H, m), 7.97 – 7.99 (2H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 22.4, 30.9, 34.1, 37.8, 58.2, 121.9, 128.2, 128.9, 133.7, 136.4, 197.9.

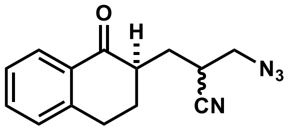
These data are in accordance with the literature.[18]

^{1}H and ^{13}C NMR spectra of **27**





3-Azido-2-((1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)propanenitrile (28)



28

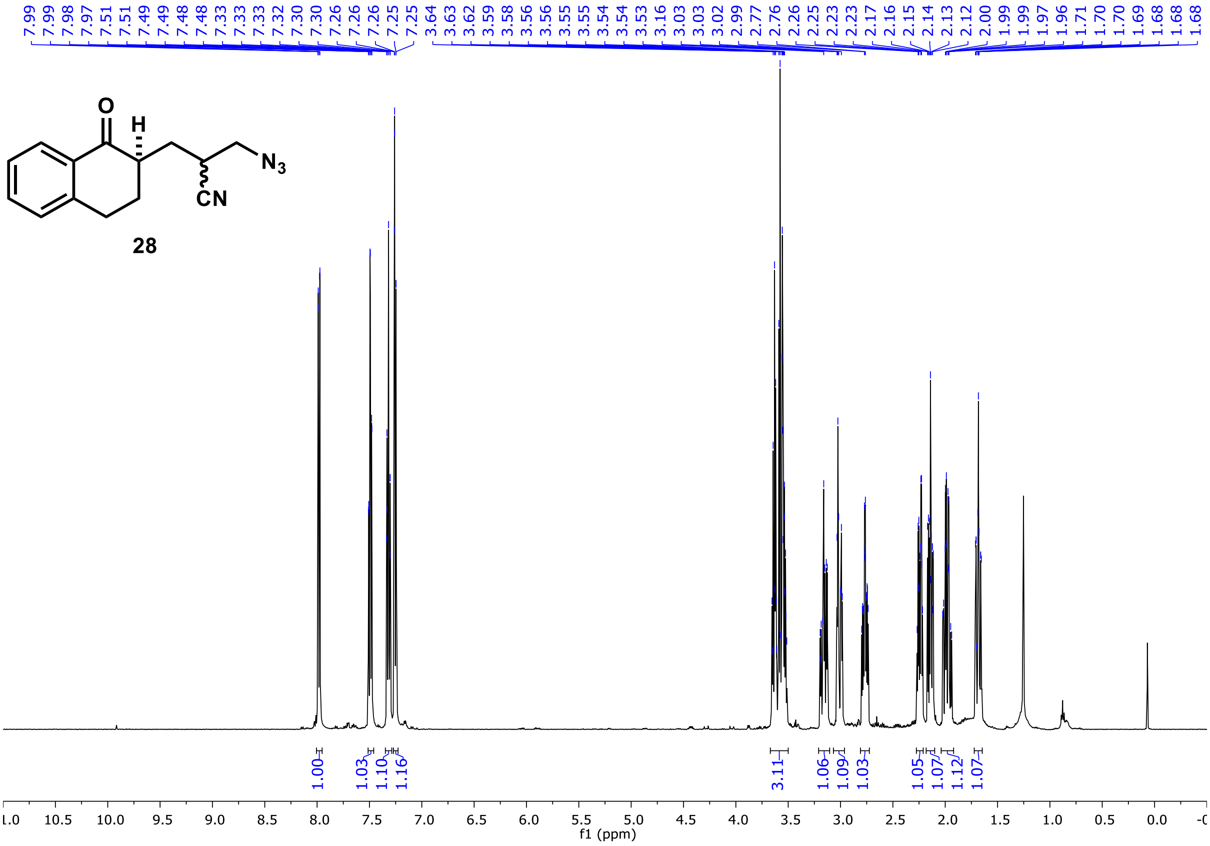
Prepared according to General Procedure 6 using **S54** (64 mg). The resultant crude material was purified by flash column chromatography (5-15% EtOAc/*n*-hexane, silica gel) to afford the separable diastereoisomers **28-1** (17 mg, 22%) and **28-2** (18 mg, 24%) as yellow oils. Analysis of the crude reaction mixture indicated a diastereomeric ratio of 1:1.

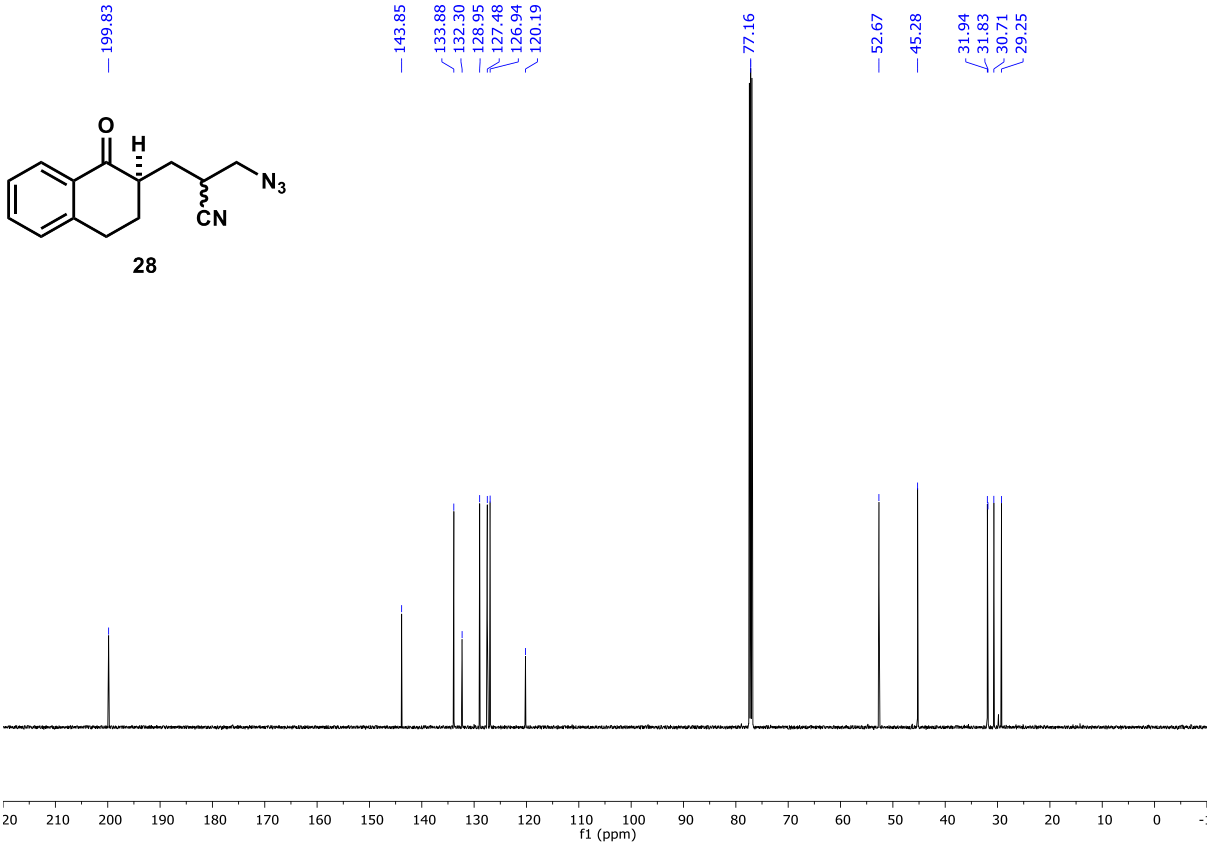
Data for **28-1**

R$_f$ = 0.41 (30% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 2918, 2870, 2848, 2243, 2160, 2108, 1672, 1598, 1450, 1436, 1361, 1350, 1273, 1228, 1143, 972, 931; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.66 – 1.71 (1H, m), 1.94 – 2.02 (1H, m), 2.11 – 2.17 (1H, m), 2.22 – 2.27 (1H, m), 2.74 – 2.80 (1H, m), 2.98 – 3.03 (1H, m), 3.13 – 3.19 (1H, m), 3.51 – 3.65 (3H, m), 7.25 – 7.26 (1H, m), 7.30 – 7.33 (1H, m), 7.48 – 7.51 (1H, m), 7.97 – 7.99 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 29.3, 30.7, 31.8, 31.9, 45.3, 52.7, 120.2, 126.9, 127.5, 128.9, 132.3,

133.9, 143.9, 199.8; **HRMS** (ASAP+) $C_{14}H_{14}N_4O$ $[M-N_2+H]^+$ requires 227.1184, found 227.1187 (+ 1.3 ppm).

^{1}H and ^{13}C NMR spectra of **28-1**

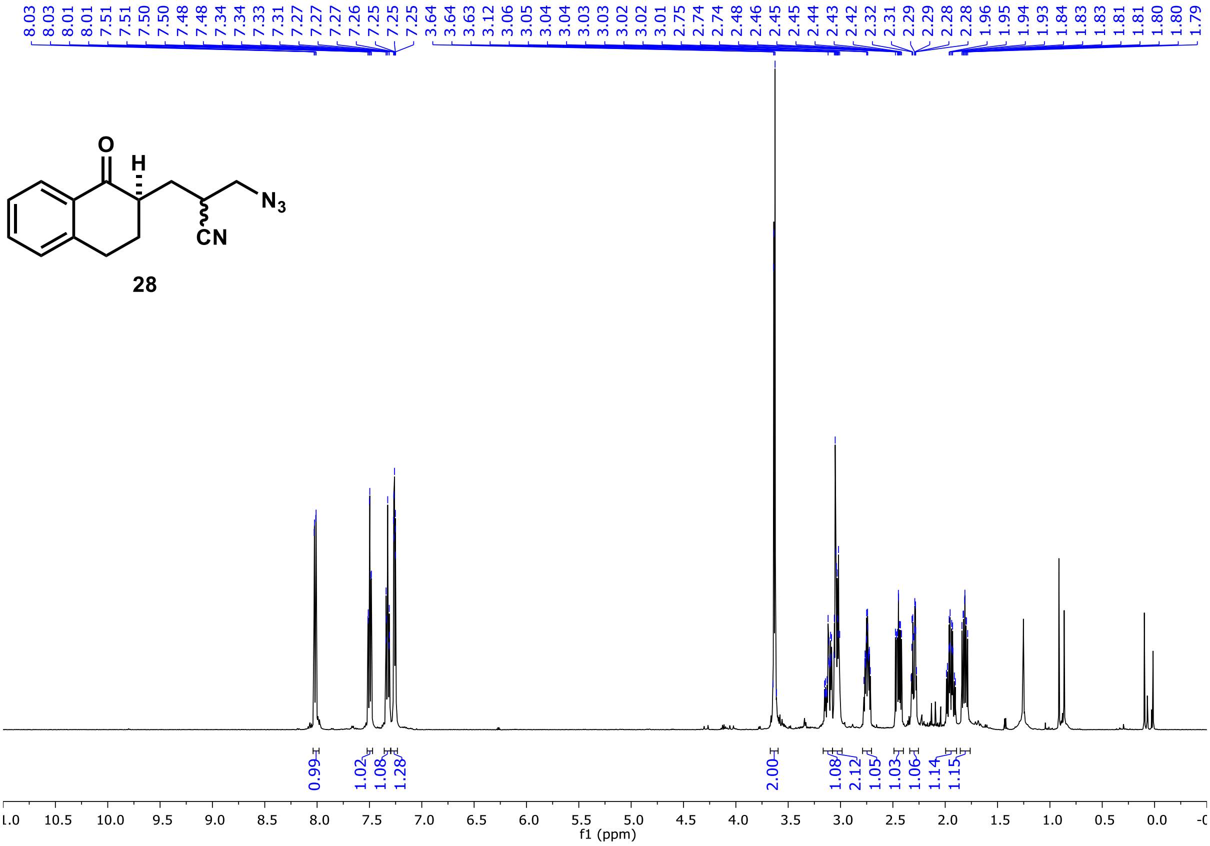


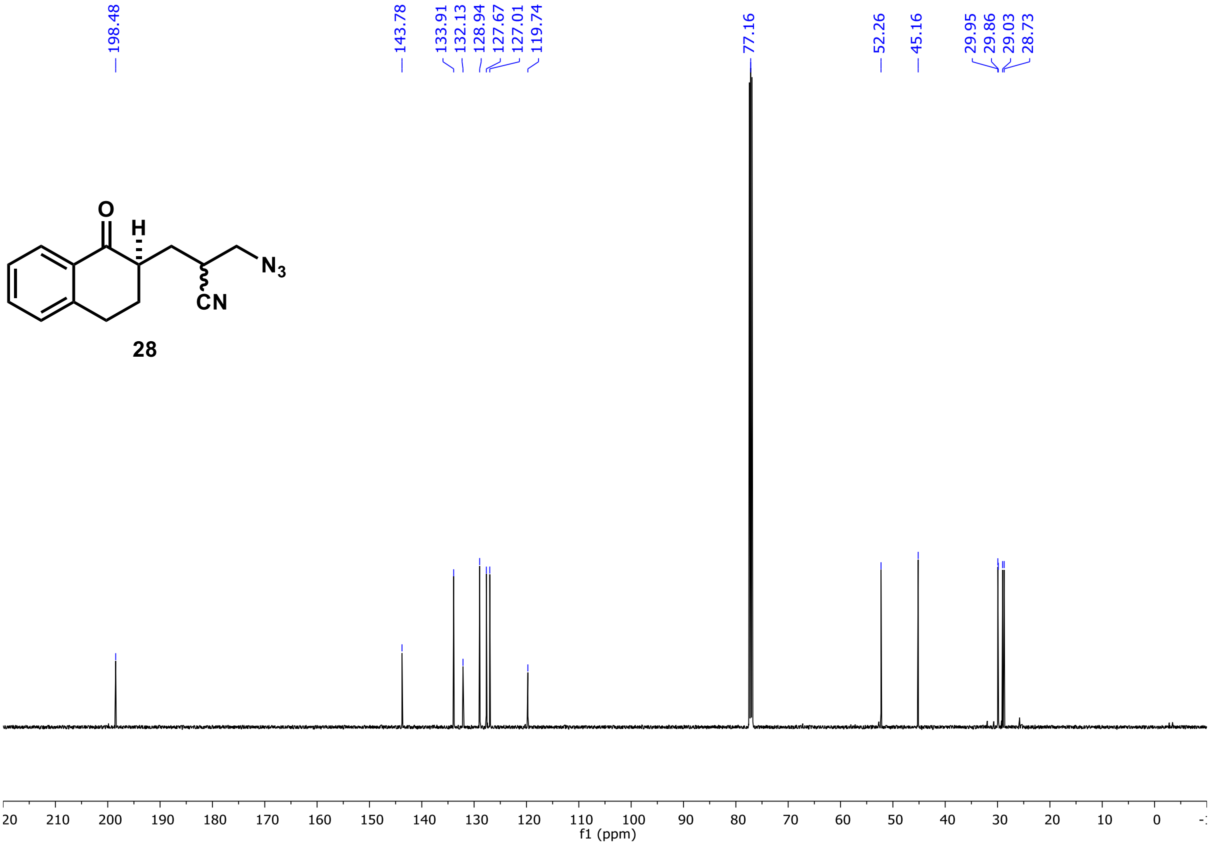


Data for **28-2**

R$_f$ = 0.38 (30% EtOAc/*n*-hexane); **FTIR** (ν_{max} cm^{-1}, thin film) 2931, 2243, 2100, 1674, 1598, 1454, 1274, 1224, 1155, 1099, 1001, 929; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.79 – 1.84 (1H, m), 1.90 – 1.99 (1H, m), 2.27 – 2.33 (1H, m), 2.42 – 2.48 (1H, m), 2.72 – 2.78 (1H, m), 3.01 – 3.06 (2H, m), 3.09 – 3.15 (1H, m), 3.61 – 3.64 (2H, m), 7.25 – 7.27 (1H, m), 7.31 – 7.34 (1H, m), 7.48 – 7.51 (1H, m) 8.01 – 8.03 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 28.7, 29.0, 29.9, 30.0, 45.2, 52.3, 119.7, 127.0, 127.7, 128.9, 132.1, 133.9, 143.8, 198.5; **HRMS** (ASAP+) $C_{14}H_{14}N_4O$ [M-N$_2$+H]$^+$ requires 227.1184, found 227.1189 (+ 2.2 ppm).

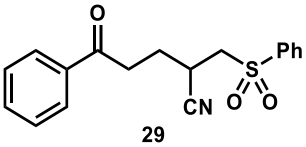
^{1}H and ^{13}C NMR spectra of **28-2**





2.6 Alternative Transformations

5-Oxo-5-phenyl-1-((phenylsulfonyl)methyl)pentanenitrile (29)

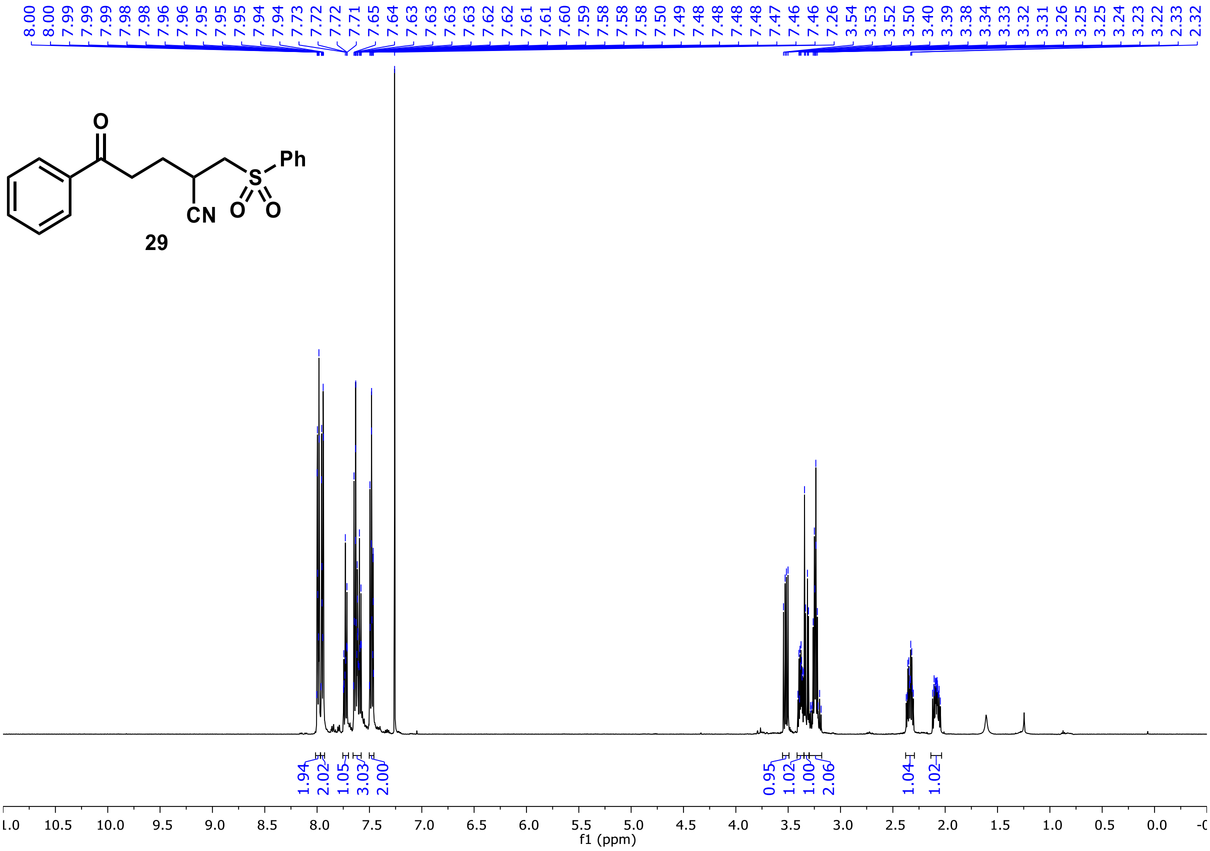


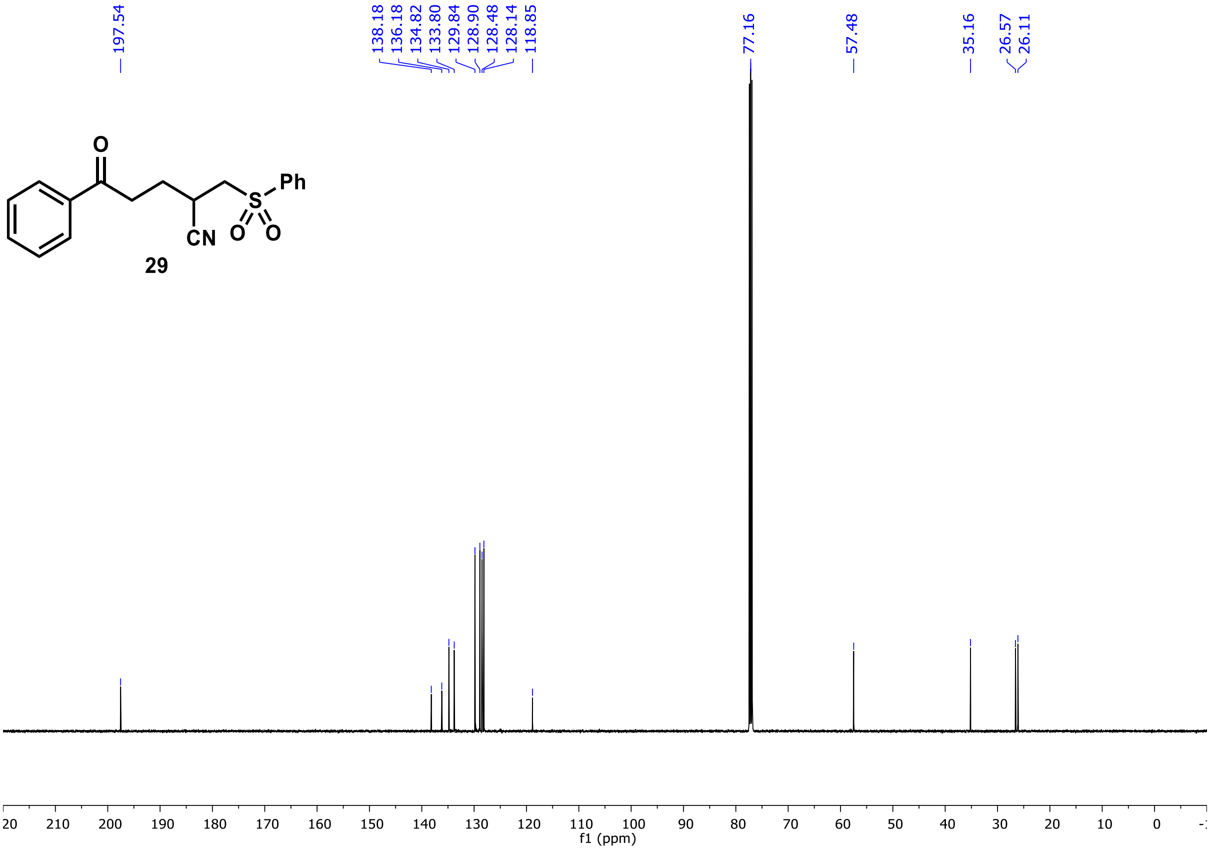
29

Prepared according to General Procedure 6 using **1** (56 mg), but with $NaSO_2Ph$ (246 mg, 1.50 mmol) in place of NaN_3. The resultant crude material was purified by flash column chromatography (5-30% EtOAc/*n*-hexane, silica gel) to afford **29** (40 mg, 41%) as a white solid.

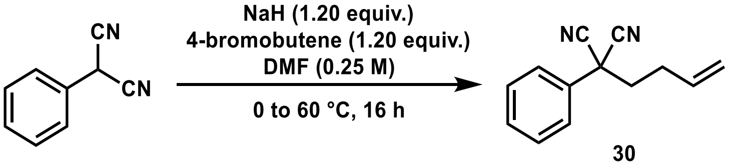
R_f = 0.16 (30% EtOAc/*n*-hexane); **M.p.:** 102-104 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3059, 2991, 2937, 2239, 1685, 1597, 1583, 1446, 1294, 1278, 1199, 1138, 1083, 997; **^1H NMR (500 MHz, $CDCl_3$)** δ_H = 2.05 – 2.12 (1H, m), 2.30 – 2.37 (1H, m), 3.18 – 3.29 (2H, m), 3.32 (1H, dd, *J* 13.9, 5.0), 3.35 – 3.41 (1H, m), 3.52 (1H, dd, *J* 13.9, 7.8), 7.46 – 7.50 (2H, m), 7.58 – 7.65 (3H, m), 7.71 – 7.75 (1H, m), 7.94 – 7.96 (2H, m), 7.98 – 8.00 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 26.1, 26.6, 35.2, 57.5, 118.9, 128.1, 128.5, 128.9, 129.8, 133.8, 134.8, 136.2, 138.2, 197.5; **HRMS** (ES+) $C_{18}H_{17}NO_3S$ $[M+Na]^+$ requires 350.0827, found 350.0827 (± 0.0 ppm).

^{1}H and ^{13}C NMR spectra of **29**





2-(But-3-en-1-yl)-2-phenylmalononitrile (30)



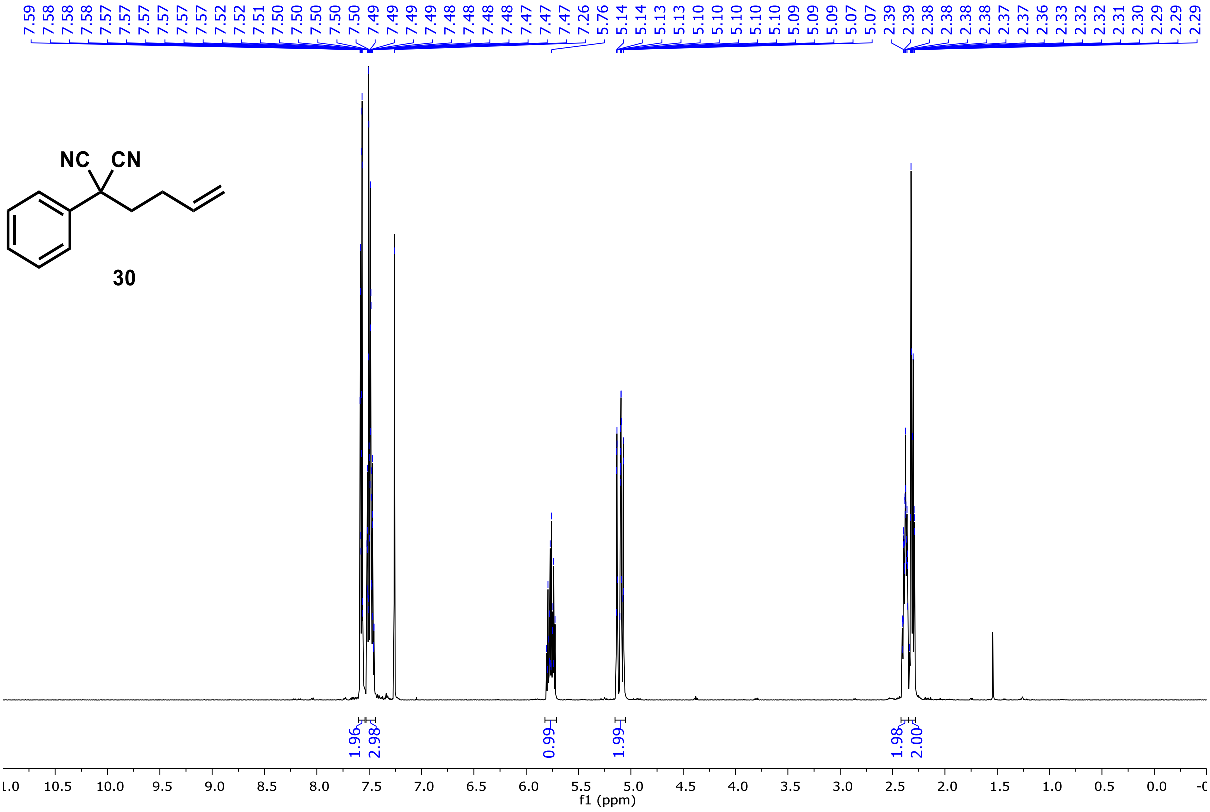
30

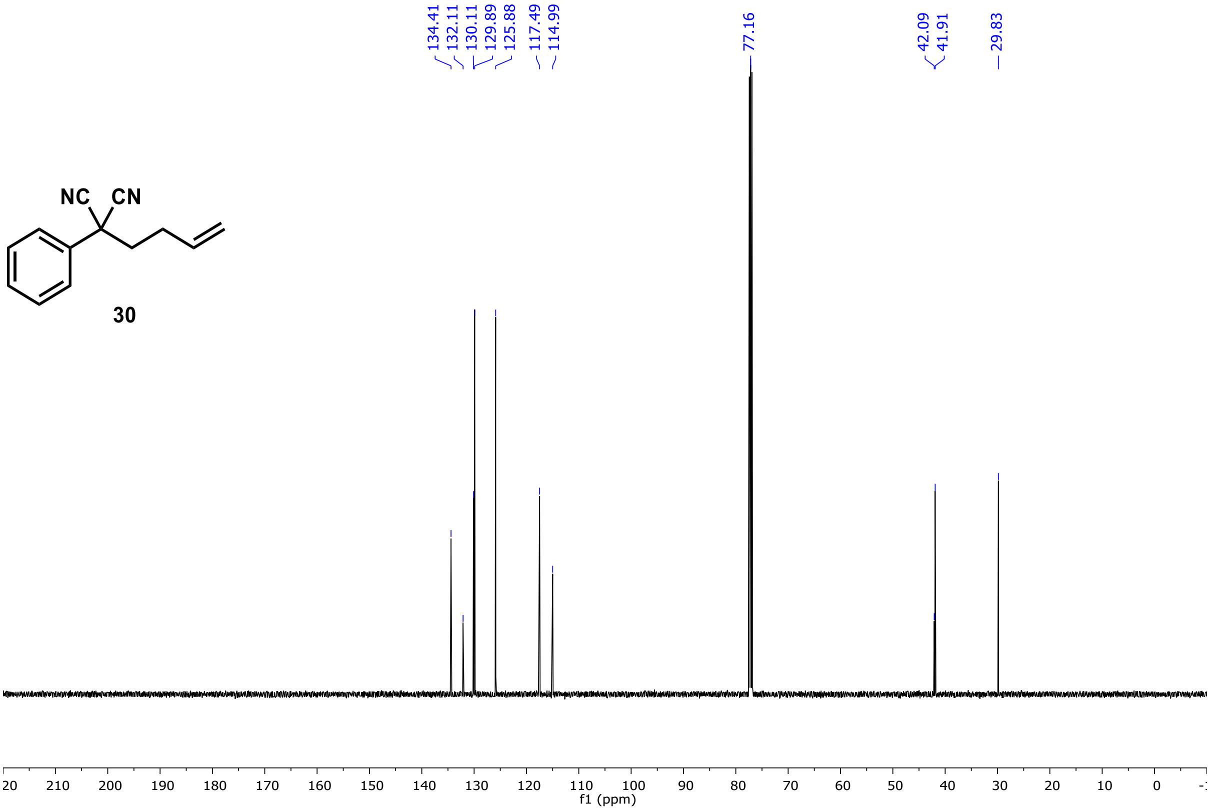
To a flame-dried three-neck RBF fitted with a condenser was added sodium hydride (60% dispersion in mineral oil, 480 mg, 12.0 mmol) in DMF (40 mL, 0.25 M). 2-Phenylmalononitrile (1.42 g, 10.0 mmol) was added at 0 °C and the reaction was stirred at rt for 1 h. 4-bromobut-1-ene (1.22 mL, 12.0 mmol) was added dropwise, and the mixture was heated to 60 °C overnight. Upon completion, the reaction was cooled to rt before a saturated solution of NH_4Cl (aq.) and EtOAc were added. The layers were separated, and the aqueous layer was extracted with EtOAc (× 3). The combined organics were washed with water (× 5) then brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography (10% EtOAc/petrol, silica gel) to afford **30** (1.68 g, 86%) as a pale-yellow oil.

R_f = 0.46 (10% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 2.29 – 2.34 (2H, m), 2.35 – 2.41 (2H, m), 5.07 – 5.14 (2H, m), 5.72 – 5.80 (1H, m), 7.45 – 7.52 (3H, m), 7.55 – 7.59 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 29.8, 41.9, 42.1, 115.0, 117.5, 125.9, 129.9, 130.1, 132.1, 134.4.

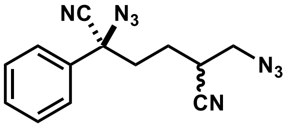
These data are in accordance with the literature.[20]

^{1}H and ^{13}C NMR spectra of **30**





2-Azido-5-(azidomethyl)-2-phenylhexanedinitrile (31)



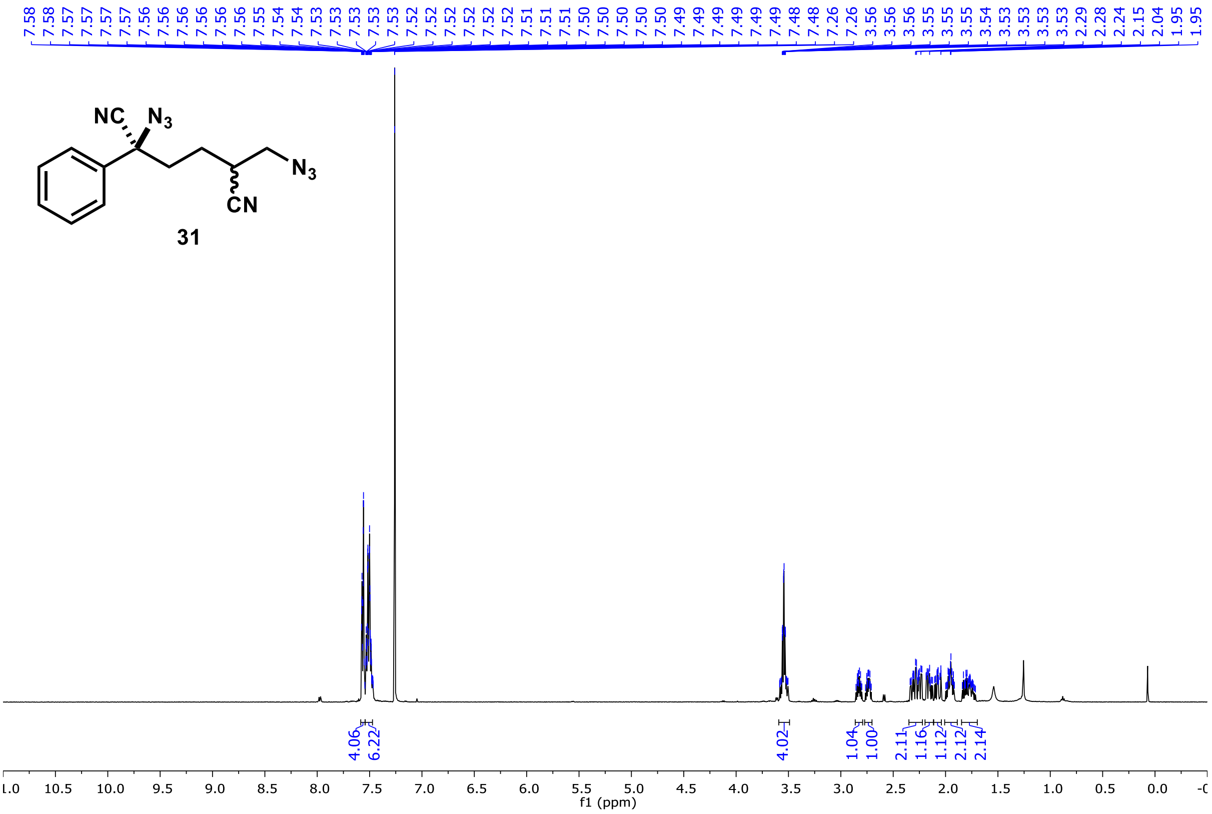
31

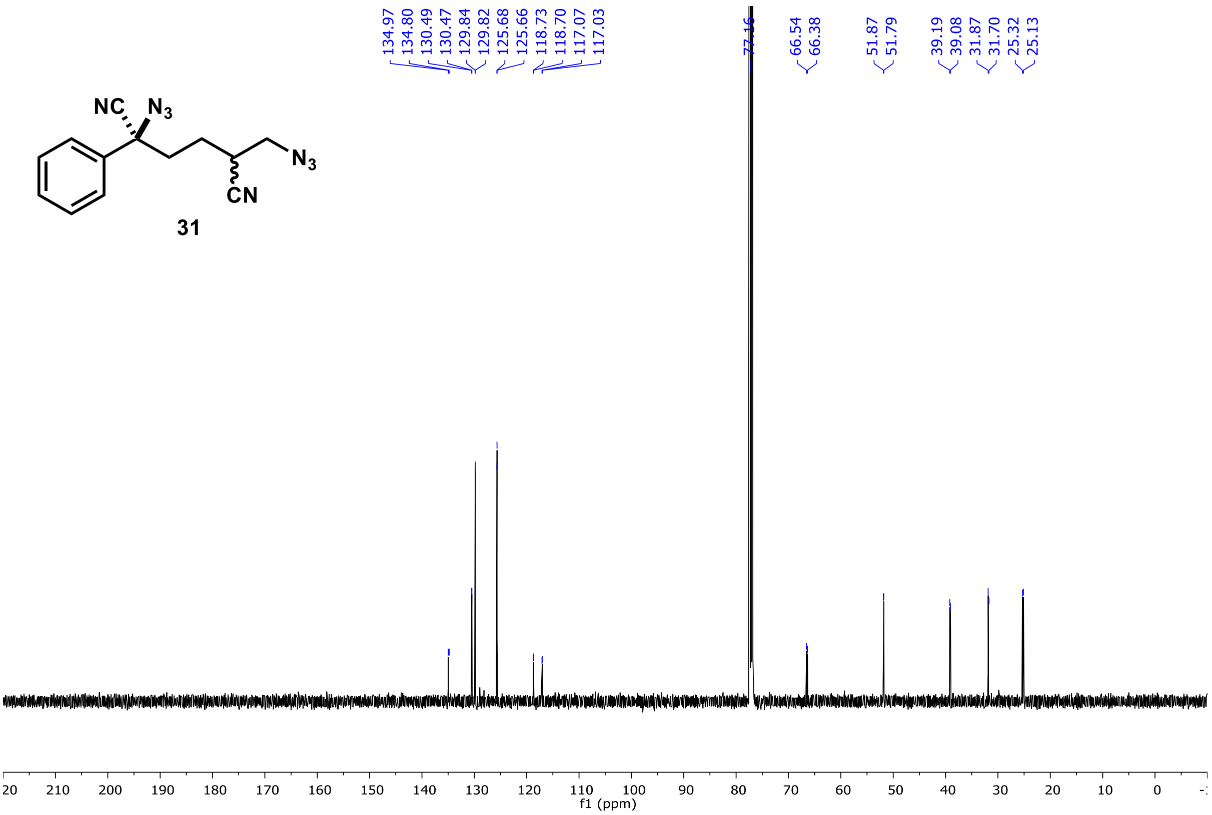
Prepared according to General Procedure 6 using **30** (59 mg). The resultant crude material was purified by flash column chromatography (10-20% EtOAc/*n*-hexane, silica gel) to afford **31** (29 mg, 34%) as a yellow oil. Analysis of the crude reaction mixture indicated a diastereomeric ratio of 1:1.

R$_f$ = 0.19 (20% EtOAc/petrol); **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 1.71 – 1.84 (2H, m), 1.92 – 1.99 (2H, m), 2.04 – 2.10 (1H, m), 2.12 – 2.19 (1H, m), 2.23 – 2.34 (2H, m), 2.71 – 2.76 (1H, m), 2.80 – 2.85 (1H, m), 3.50 – 3.58 (4H, m), 7.47 – 7.54 (6H, m), 7.55 – 7.58 (4H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 25.1, 25.3, 31.7, 31.9, 39.1, 39.2, 51.8, 51.9, 66.4, 66.5, 117.0, 117.1, 118.7 (2C), 125.7 (2C), 129.8 (2C), 130.5 (2C), 134.8, 135.0.

These data are in accordance with the literature.[20]

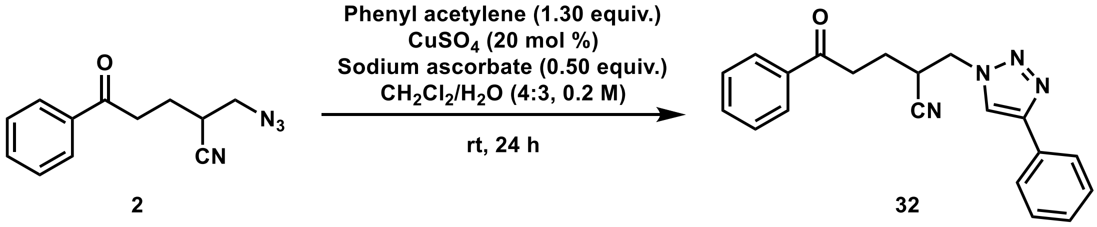
^{1}H and ^{13}C NMR spectra of **31**




NC
N3
N3
CN
31
134.97
134.80
130.49
130.47
129.84
129.82
125.68
125.66
118.73
118.70
117.07
117.03
77.16
66.54
66.38
51.87
51.79
39.19
39.08
31.87
31.70
25.32
25.13
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

2.7 Product Derivatisation

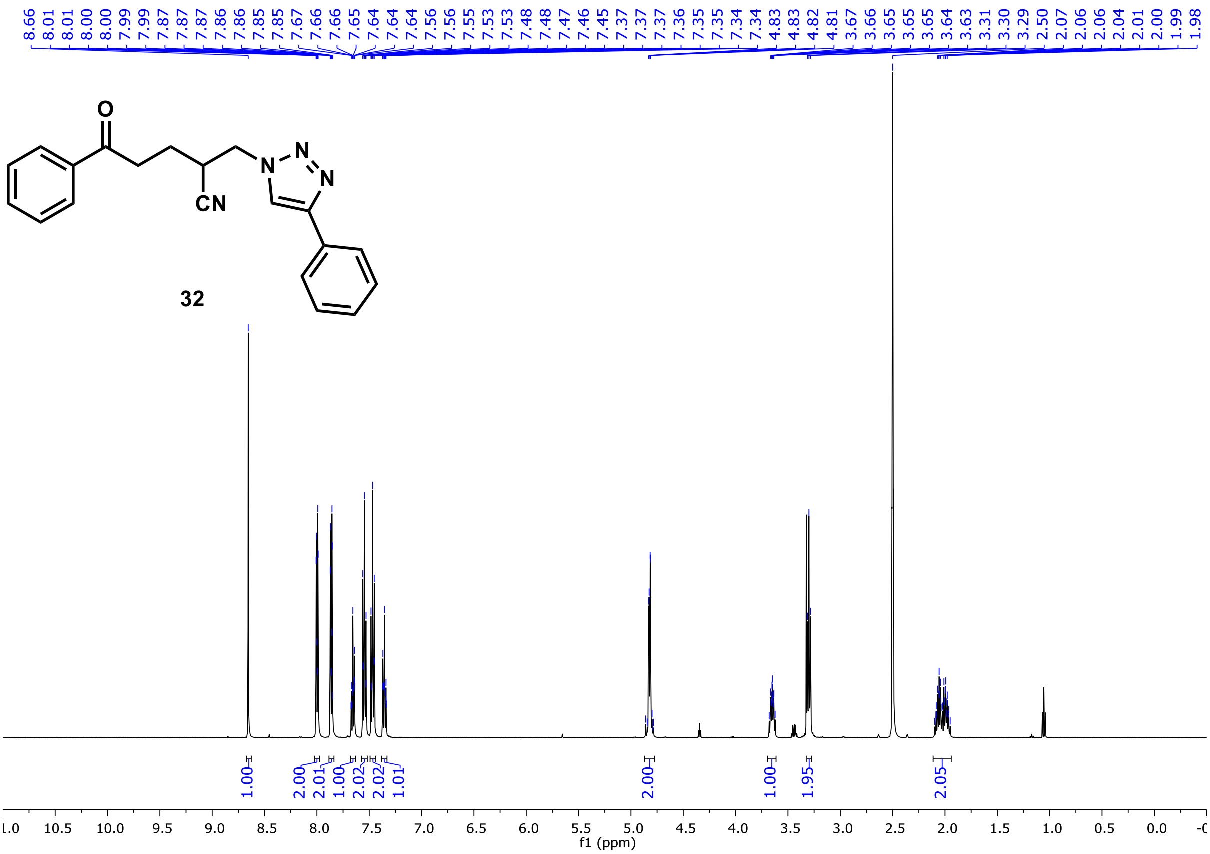
5-Oxo-5-phenyl-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)pentanenitrile (32)

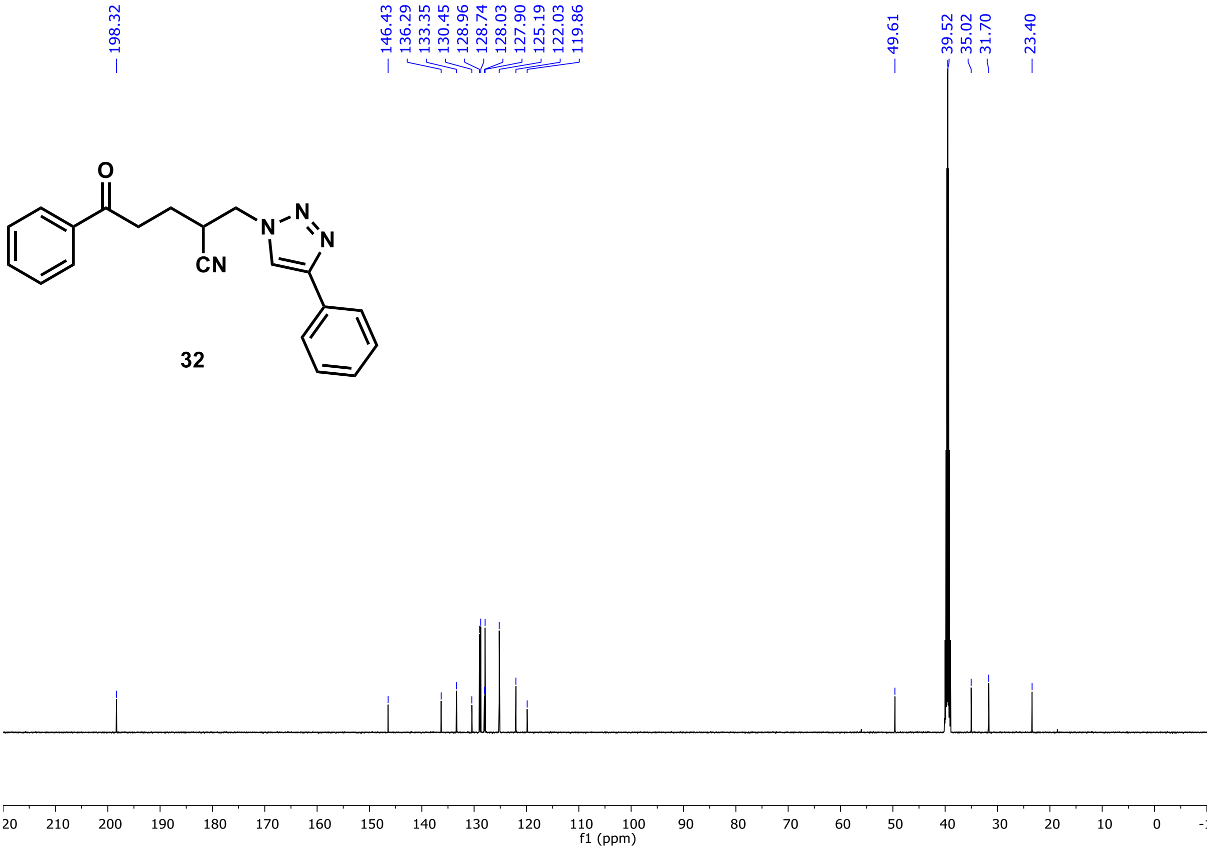


Following a literature procedure,[21] to a flame-dried microwave vial was added **2** (228 mg, 1.00 mmol) and phenylacetylene (143 µL, 1.30 mmol) in CH_2Cl_2 (2.9 mL). H_2O (2.1 mL) was added, followed by $CuSO_4$ (32 mg, 0.20 mmol). Sodium ascorbate (99 mg, 0.50 mmol) was added portion-wise, and the reaction mixture was stirred at rt for 24 h. CH_2Cl_2 was added, followed by H_2O and 1 M HCl (aq.). The layers were separated, and the aqueous layer was further extracted with EtOAc (× 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant crude material was purified by recrystallisation (EtOH) to afford **32** (155 mg, 47%) as a white solid.

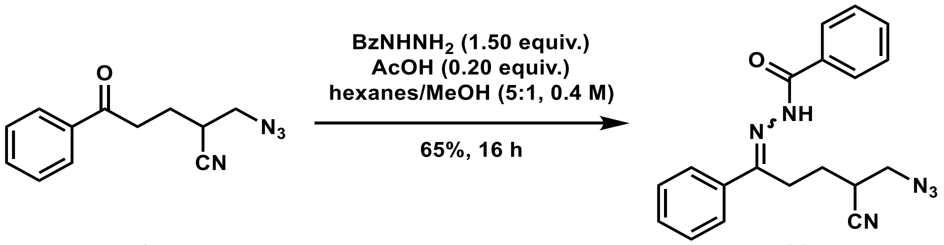
R_f = 0.12 (30% EtOAc/petrol); **M.p.:** 178-180 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3086, 2960, 2241, 1739, 1678, 1597, 1462, 1444, 1365, 1226, 1205, 1083, 1041, 974; **^{1}H NMR (500 MHz, DMSO-*d*$_6$)** δ_H = 1.95 – 2.10 (2H, m), 3.30 (2H, t, *J* 7.3), 3.62 – 3.68 (1H, m), 4.79 – 4.86 (2H, m), 7.34 – 7.37 (1H, m), 7.45 – 7.48 (2H, m), 7.53 – 7.56 (2H, m), 7.64 – 7.67 (1H, m), 7.85 – 7.87 (2H, m), 7.99 – 8.01 (2H, m), 8.66 (1H, s); **^{13}C NMR (126 MHz, DMSO-*d*$_6$)** δ_C = 23.4, 31.7, 35.0, 49.6, 119.9, 122.0, 125.2, 127.9, 128.0, 128.7, 129.0, 130.5, 133.4, 136.3, 146.4, 198.3; **HRMS** (CI+) $C_{20}H_{18}N_4O$ $[M+H]^+$ requires 331.1553, found 331.1554 (+ 0.1 ppm).

^{1}H and ^{13}C NMR spectra of **32**





N'-(5-Azido-4-cyano-1-phenylpentylidene)benzohydrazide (33)

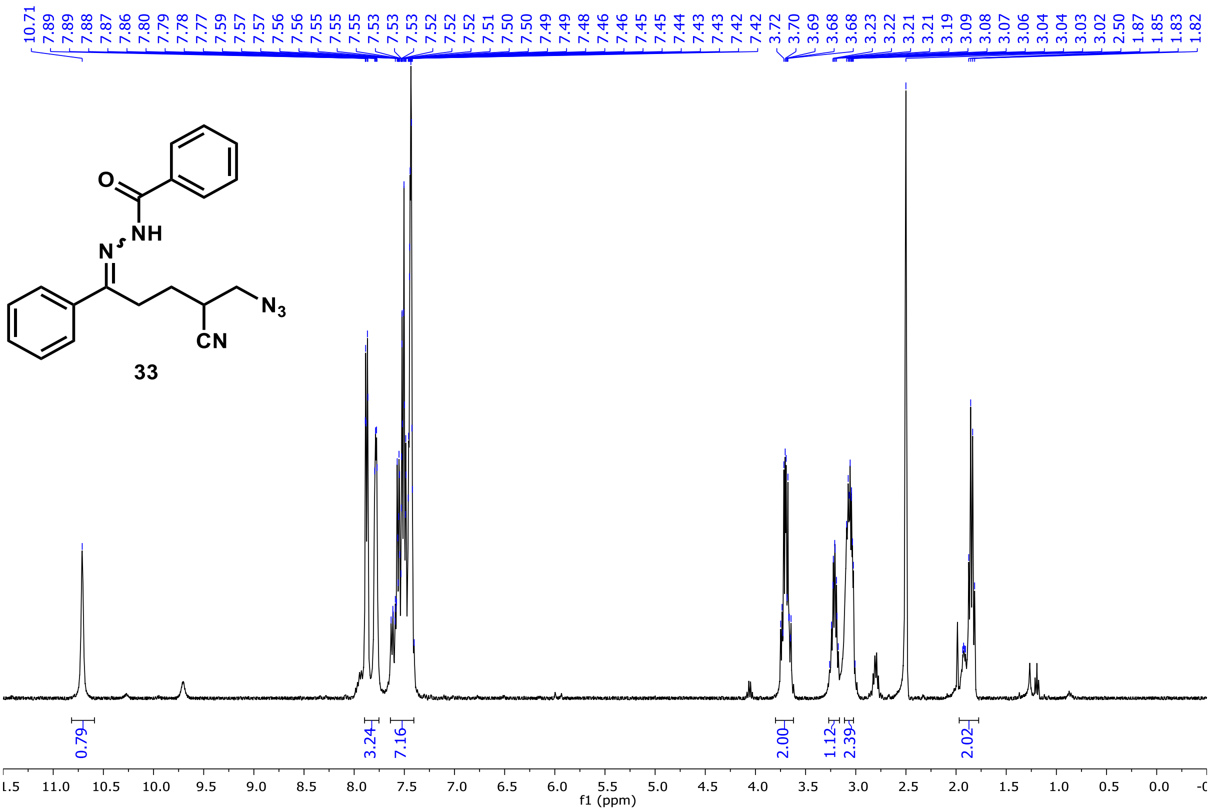


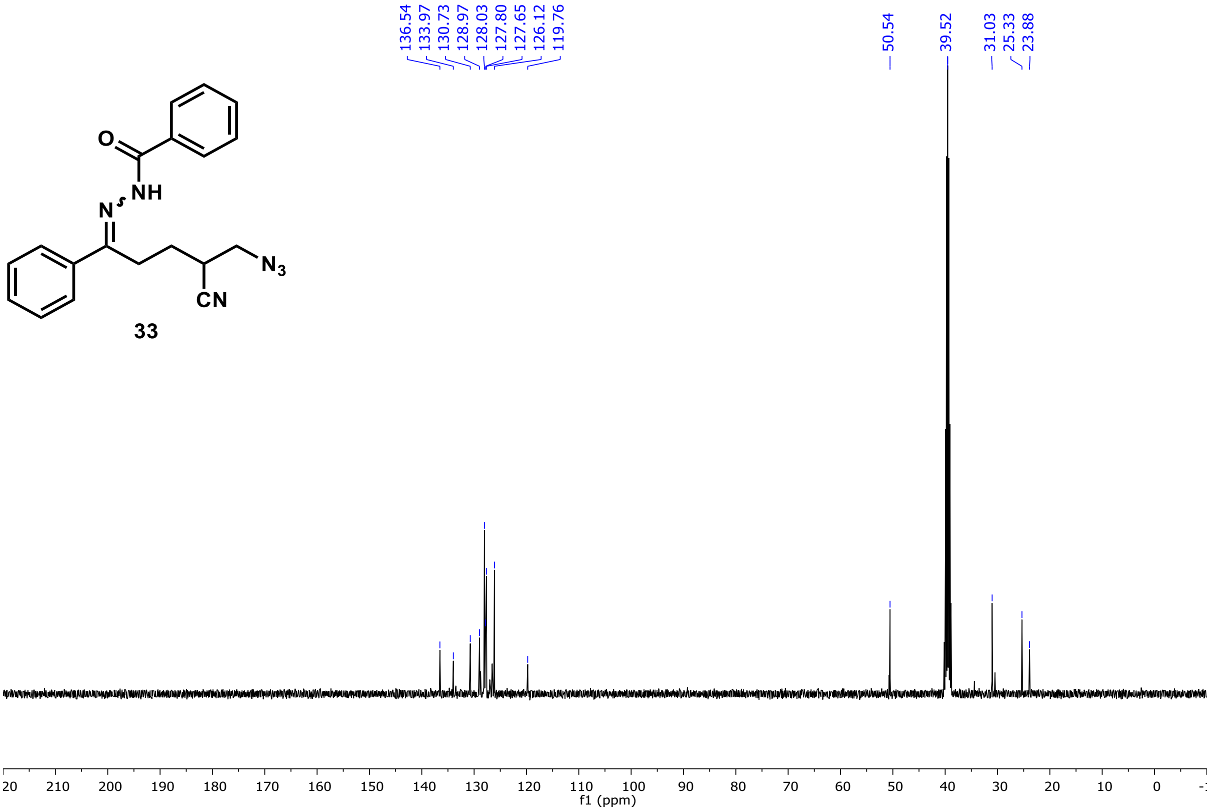
2 33

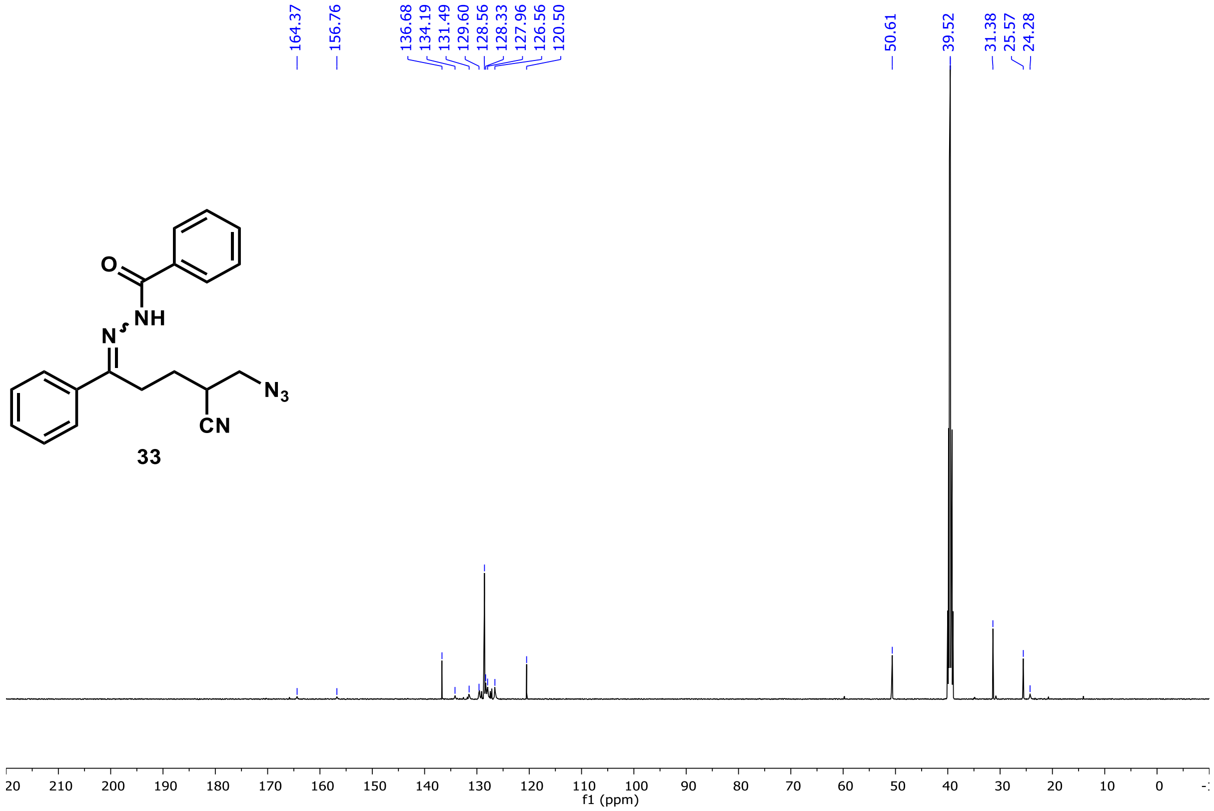
Following a literature procedure,[22] to a RBF was added **2** (114 mg, 0.50 mmol) and AcOH (6 mg, 0.10 mmol) in hexanes (1 mL) and MeOH (0.25 mL). The reaction mixture was heated to reflux overnight. Upon cooling, the mixture was concentrated under reduced pressure. The resultant crude material was purified by flash column chromatography (20-60% EtOAc/petrol, silica gel) to afford **33** (153 mg, 88%) as a pale-yellow solid.

R_f = 0.11 (30% EtOAc/petrol); **M.p.:** 141-143 °C; **FTIR** (ν_{max} cm^{-1}, thin film) 3199, 2931, 2235, 2104, 1639, 1535, 1489, 1463, 1450, 1330, 1278, 1130, 1072; **^{1}H NMR (400 MHz, DMSO-*d*$_6$, 80 °C)** δ_H = 1.82 – 1.93 (2H, m), 3.01 – 3.09 (2H, m), 3.17 – 3.26 (1H, m), 3.65 – 3.75 (2H, m), 7.40 – 7.63 (7H, m), 7.77 – 7.89 (3H, m), 10.71 (1H, br s); **^{13}C NMR (101 MHz, DMSO-*d*$_6$, 80 °C)** δ_C = 23.9, 25.3, 31.0, 50.5, 119.8, 126.1, 127.7, 127.8, 128.0, 129.0, 130.7, 134.0, 136.6; **(126 MHz, DMSO-*d*$_6$, 25 °C)** δ_C = 156.8, 164.4; **HRMS** (ES+) $C_{19}H_{18}N_6O$ [M+H]$^+$ requires 347.1620, found 347.1627 (+ 2.0 ppm).

^{1}H (80 °C), ^{13}C (80 °C), and ^{13}C (25 °C) NMR spectra of **33**



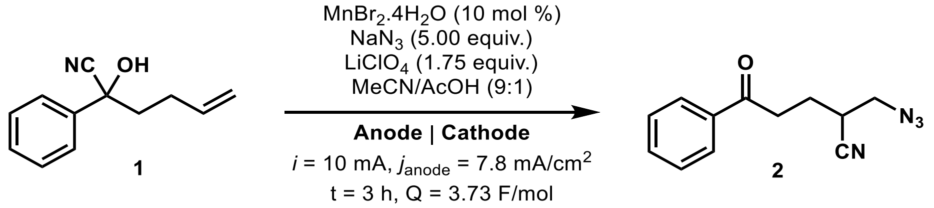



164.37
156.76
136.68
134.19
131.49
129.60
128.56
128.33
127.96
126.56
120.50
50.61
39.52
31.38
25.57
24.28
O
NH
N
N3
CN
33
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3. Optimisation Studies

3.1 Optimisation

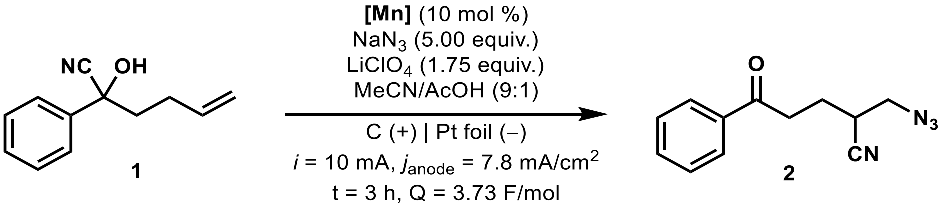
3.1.1 Electrode Material Screen



Entry^a	**Anode**	**Cathode**	**1**^{b} **(%)**	**2**^{b} **(%)**
1	Graphite	Graphite	35	23
2	**Graphite**	**Pt foil**	**32**	**31**
3	RVC	Pt foil	53	17
4	RVC	Graphite	22	25

^{a} Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. ^{b} Yield after 3 h as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard.

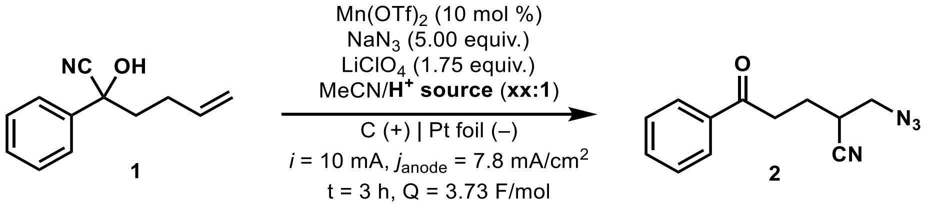
3.1.2 Manganese Salt Screen



Entry^a	**[Mn]**	**1**^{b} **(%)**	**2**^{b} **(%)**
1	$MnBr_2.4H_2O$	32	31
2	$Mn(acac)_2$	31	29
3	$MnCl_2.4H_2O$	21	31
4	$Mn(OAc)_2$	41	19
5	$Mn(OAc)_2.4H_2O$	37	33
6	**$Mn(OTf)_2$**	**37**	**31**

^{a} Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. ^{b} Yield after 3 h as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard.

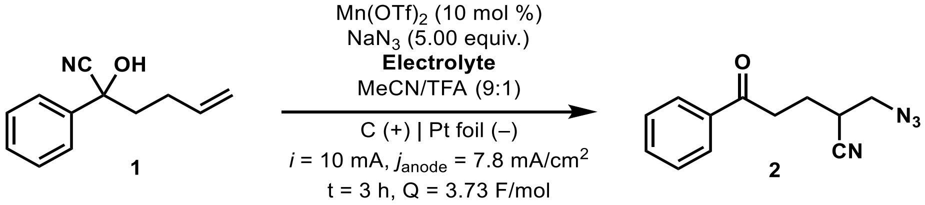
3.1.3 Proton Source Screen



Entry[a]	H$^+$ source	Solvent Ratio	**1**[b] (%)	**2**[b] (%)
1	AcOH	9:1	37	31
2	HFIP	9:1	17	0
3	TFE	9:1	13	0
4	Formic Acid	9:1	40	20
5	**TFA**	**9:1**	**29**	**48**
6	TFA	4:1	31	27
7	TFA	19:1	17	51

[a] Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. [b] Yield after 3 h as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard.

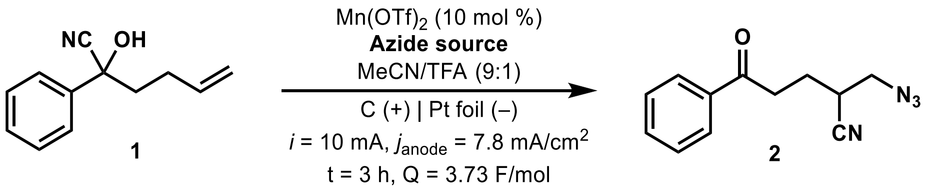
3.1.4 Electrolyte Screen



Entry[a]	Electrolyte	Loading (equiv.)	**1**[b] (%)	**2**[b] (%)
1	$LiClO_4$	1.75	29	48
2	$TBAPF_6$	1.75	34	34
3	$TBABF_4$	1.75	36	23
4	TBAOAc	1.75	7	16
5	$TBAClO_4$	1.75	23	47
6	$TEABF_4$	1.75	42	29
7	$TBAN_3$	1.75	7	26
8	$LiClO_4$	3.00	28	43
9	$LiClO_4$	2.00	29	36
10	$LiClO_4$	1.00	20	47
11	**None**	**0.00**	**21**	**52**

[a] Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. [b] Yield after 3 h as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard.

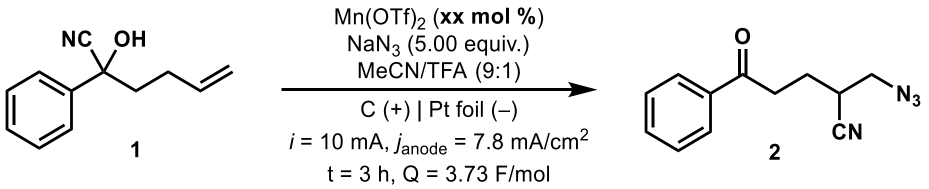
3.1.5 Azide Source Screen



Entry[a]	Azide Source	Loading (equiv.)	**1**[b] (%)	**2**[b] (%)
1	**NaN_3**	**5.00**	**21**	**52**
2	TBAN$_3$	5.00	11	14
3	NaN_3	2.50	42	5
4	NaN_3	7.50	20	51
5	NaN_3	10.0	0	56

[a] Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. [b] Yield after 3 h as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard.

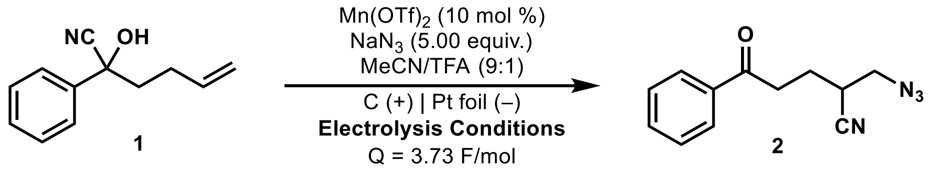
3.1.6 Manganese Salt Loading Screen



Entry[a]	Loading (mol %)	**1**[b] (%)	**2**[b] (%)
1	2.5	36	33
2	5	40	27
3	**10**	**21**	**52**
4	20	27	34

[a] Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. [b] Yield after 3 h as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard.

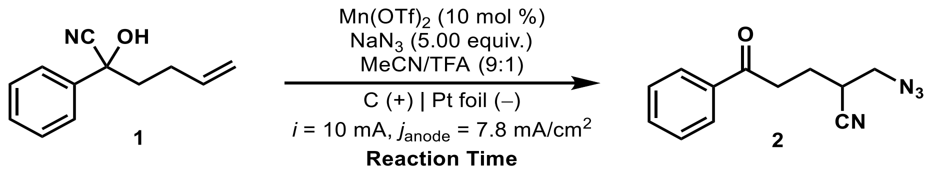
3.1.7 Electrolysis Conditions Screen



Entry[a]	**Conditions**	**1**[b] **(%)**	**2**[b] **(%)**
1[c]	i = 4 mA; j_{anode} = 3.1 mA/cm^2	0	23
2[d]	i = 8 mA; j_{anode} = 6.2 mA/cm^2	35	30
3[e]	**i = 10 mA; j_{anode} = 7.8 mA/cm^2**	**21**	**52**
4[f]	i = 12 mA; j_{anode} = 9.4 mA/cm^2	36	32
5[g]	i = 20 mA; j_{anode} = 15.6 mA/cm^2	34	38
6	E_{cell} = 2 V	0	46

[a] Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. [b] Yield as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard. [c] 7 h 30 min reaction time. [d] 3 h 45 min reaction time. [e] 3 h reaction time. [f] 2 h 30 min reaction time. [g] 1 h 30 min reaction time.

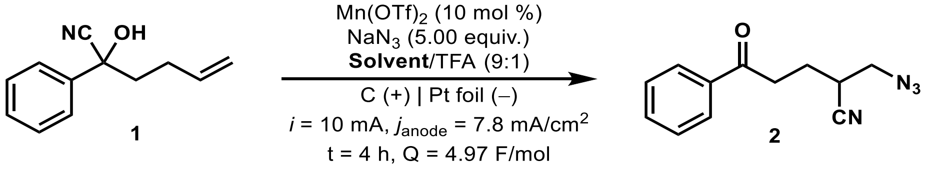
3.1.8 Reaction Time Screen



Entry[a]	**Reaction Time**	**1**[b] **(%)**	**2**[b] **(%)**
1	t = 1 h 36 min, Q = 2.00 F/mol	46	29
2	t = 3 h, Q = 3.73 F/mol	21	52
3	**t = 4 h, Q = 4.97 F/mol**	**0**	**55 (51)**
4	t = 5 h, Q = 6.22 F/mol	0	42
5	t = 6 h, Q = 7.46 F/mol	0	41

[a] Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. [b] Yield as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard. Isolated yield given in parentheses.

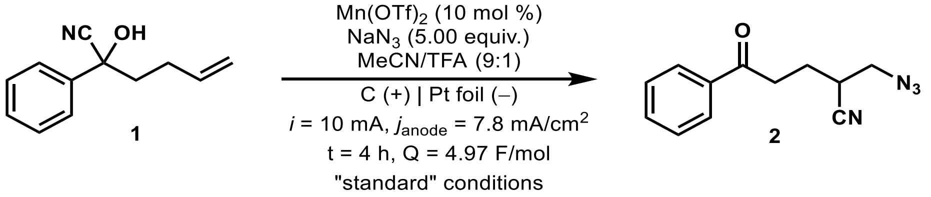
3.1.9 Solvent Conditions Screen



Entry[a]	Solvent	**1**[b] (%)	**2**[b] (%)
1	**MeCN**	**0**	**55 (51)**
2	THF	99	0
3	DMF	51	14
4	DMA	69	10
5	DMSO	12	32

[a] Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. [b] Yield as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard. Isolated yield given in parentheses.

3.1.10 Deviation from "Standard" Conditions



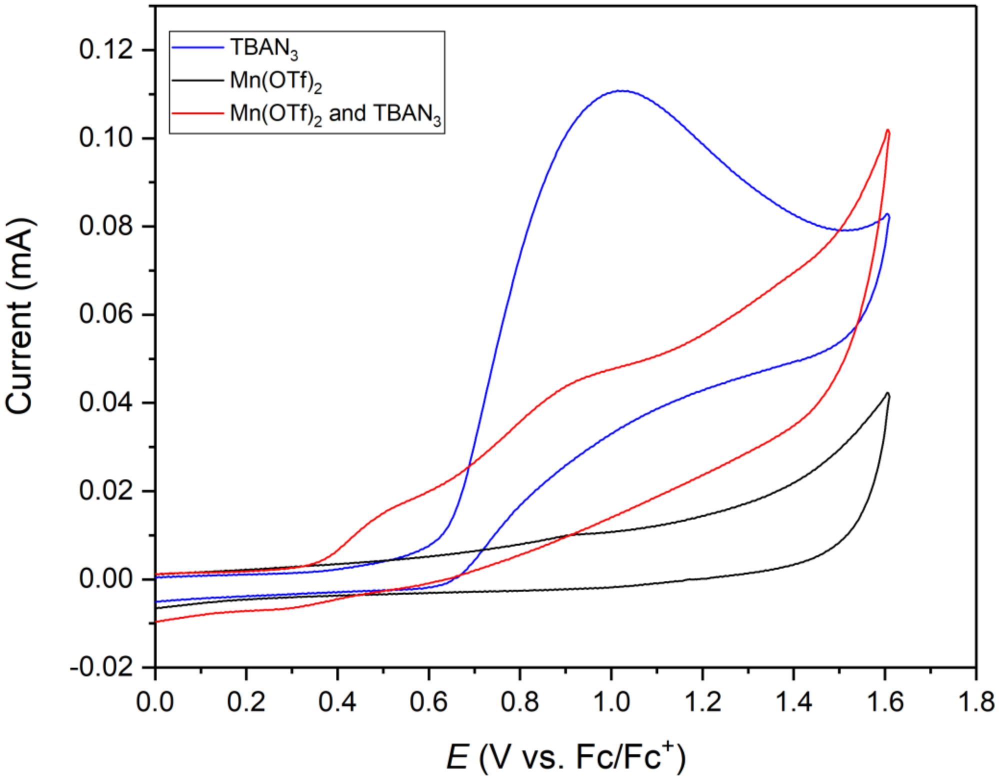
Entry[a]	Variation from "standard" conditons	**1**[b] (%)	**2**[b] (%)
1	**None**	**< 2**	**55 (51)**
2	No electricity	94	< 2
3	No $Mn(OTf)_2$	34	23
4	$E_{cell} = 2.4$ V	< 2	55
5[c]	$i = 12.5$ mA, $j_{anode} = 9.8$ mA/cm^2	4	32
6[d]	$i = 7.5$ mA, $j_{anode} = 5.9$ mA/cm^2	< 2	42
7	$LiClO_4$ (1.75 equiv.) as supporting electrolyte	20	38
8	Graphite cathode instead of Pt foil	6	23
9	Ni plate cathode instead of Pt foil	10	43
10	$MnBr_2.4H_2O$ instead of $Mn(OTf)_2$	< 2	34
11	$Mn(OAc)_2.4H_2O$ instead of $Mn(OTf)_2$	< 2	48
12	AcOH instead of TFA	20	30
13	NaN_3 (2.5 equiv.)	29	19
14	$Mn(OTf)_2$ (5 mol %)	8	50
15[e]	Q = 6.22 F/mol	< 2	42
16[f]	Q = 2 F/mol	46	29

[a] Reactions performed using 0.3 mmol of cyanohydrin **1** using the ElectraSyn 2.0 batch electrochemical reactor. [**1**] = 0.05 M. [b] Yield as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard. Isolated yield given in parentheses. [c] 192 min reaction time. [d] 320 min reaction time. [e] 180 min reaction time. [f] 96 min reaction time.

4. Mechanistic Studies

4.1 Cyclic Voltammetry Studies

General Information: Cyclic voltammetry (CV) experiments were conducted with a Metrohm Autolab PGSTAT204 potentiostat and Nova 2.1 software. For all experiments, a glassy carbon working electrode (3 mm dia., BASi), a platinum wire counter electrode, and a Ag/$AgNO_3$ reference electrode were employed. All data were collected at room temperature. The solution of interest was purged with N_2 for 5 minutes before data collection. After data collection, ferrocene (5 mᴍ) was added, and an additional scan was run. The parent data was referenced relative to the Fc/Fc^+ couple that was recorded. In these studies, $TBAN_3$ was used in place of NaN_3 due to its higher solubility in MeCN, and AcOH was used in place of TFA due to its lower acidity. Both $TBAN_3$ and AcOH proved competent in alkene azidocyanation (see section 3).

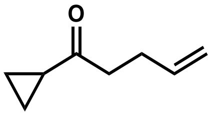


Cyclic Voltammogram of $Mn(OTf)_2$, $TBAN_3$, and their mixture in MeCN (6 mL) with AcOH (240 μL) and $LiClO_4$ (0.1 ᴍ). a (black line) – $Mn(OTf)_2$ (2.0 mᴍ); b (blue line) – $TBAN_3$ (10 mᴍ); c (red line) – $Mn(OTf)_2$ (2.0 mm) and $TBAN_3$ (10 mᴍ). ***Scan rate: 100 mV/s***

4.2 Mechanistic Experiments

4.2.1 Substrate Synthesis

1-Cyclopropylpent-4-en-1-one (S55)



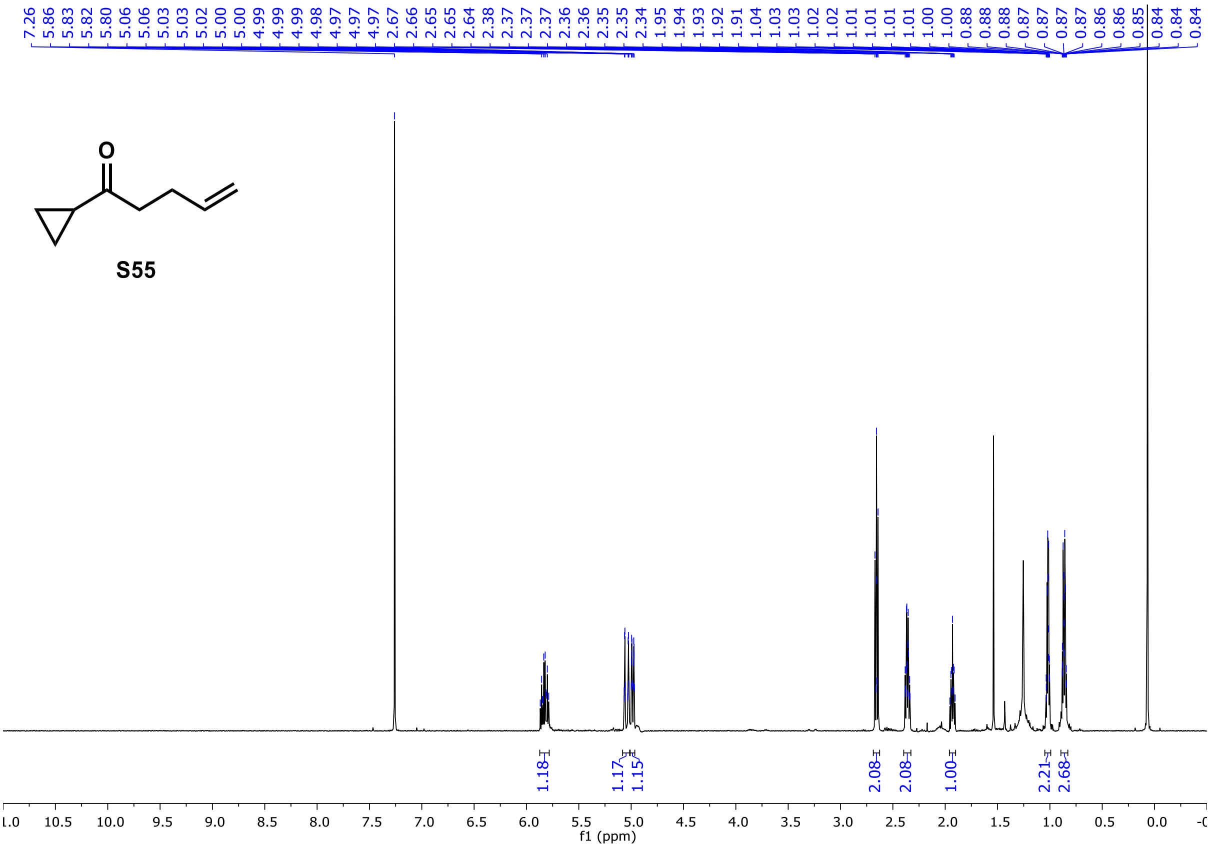
S55

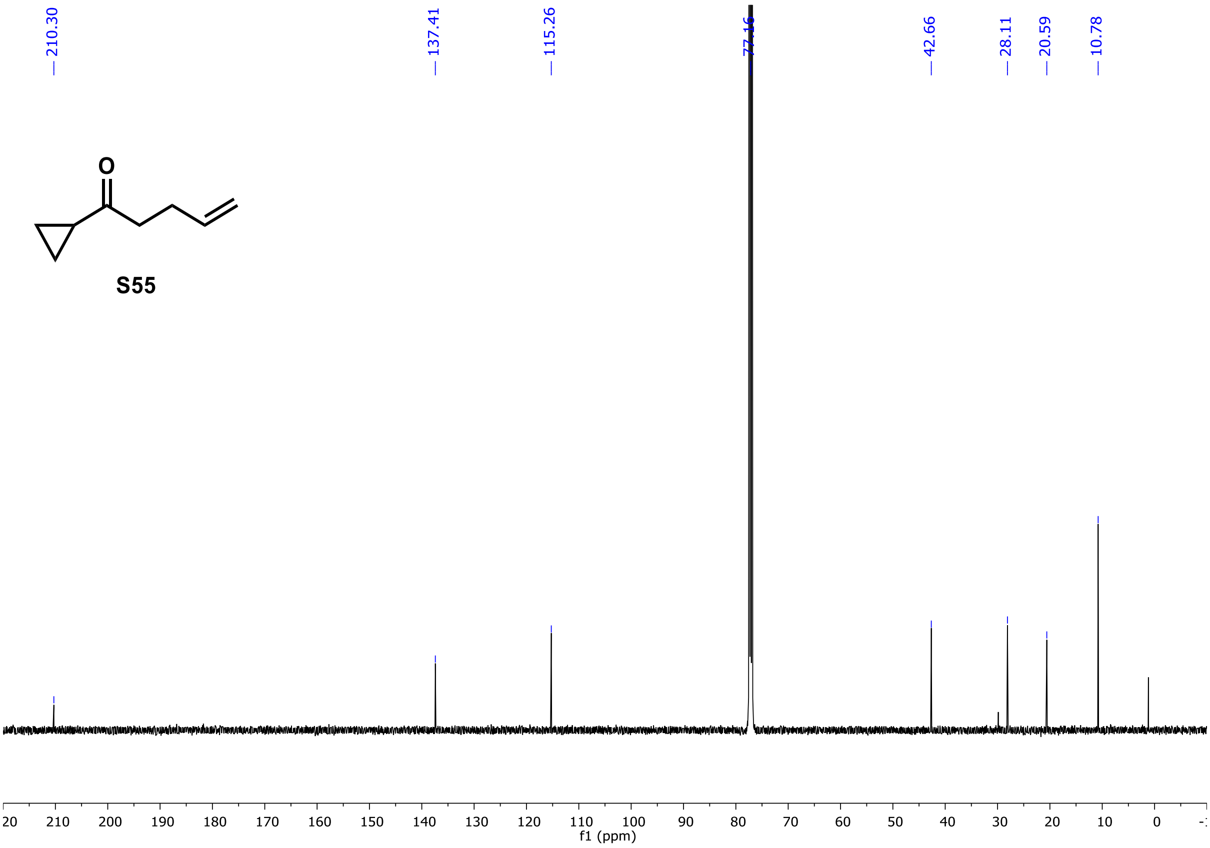
Prepared according to General Procedure 2 using cyclopropanecarboxylic acid (960 μL, 12.0 mmol), oxalyl chloride (1.14 mL, 13.2 mmol), DMF (3 drops), *N*,*O*-dimethylhydroxylamine hydrochloride (1.17 g, 12.0 mmol) in CH_2Cl_2 (35 mL), and triethylamine (5.02 mL, 36.0 mmol) to form the crude Weinreb amide. The Grignard reagent was prepared using magnesium (277 mg, 11.4 mmol) in THF (10 mL), and 4-bromobut-1-ene (1.06 mL, 10.4 mmol). The alkyl ketone was prepared through the addition of the Weinreb amide in THF (25 mL) to the solution of Grignard reagent. The resultant crude material was purified by flash column chromatography (5% Et_2O/*n*-pentane, silica gel) to afford **S55** (250 mg, 29%) as a colourless oil.

R_f = 0.45 (5% EtOAc/petrol); **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 0.84 – 0.88 (2H, m), 1.00 – 1.04 (2H, m), 1.91 – 1.96 (1H, m), 2.34 – 2.39 (2H, m), 2.64 – 2.67 (2H, m), 4.97 – 5.00 (1H, m), 5.02 – 5.07 (1H, m), 5.83 (1H, ddt, *J* 16.9, 10.2, 6.5); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 10.8, 20.6, 28.1, 42.7, 115.3, 137.4, 210.3.

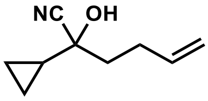
These data are in accordance with the literature.[23]

^{1}H and ^{13}C NMR spectra of **S55**





2-Cyclopropyl-2-hydroxyhex-5-enenitrile (34)

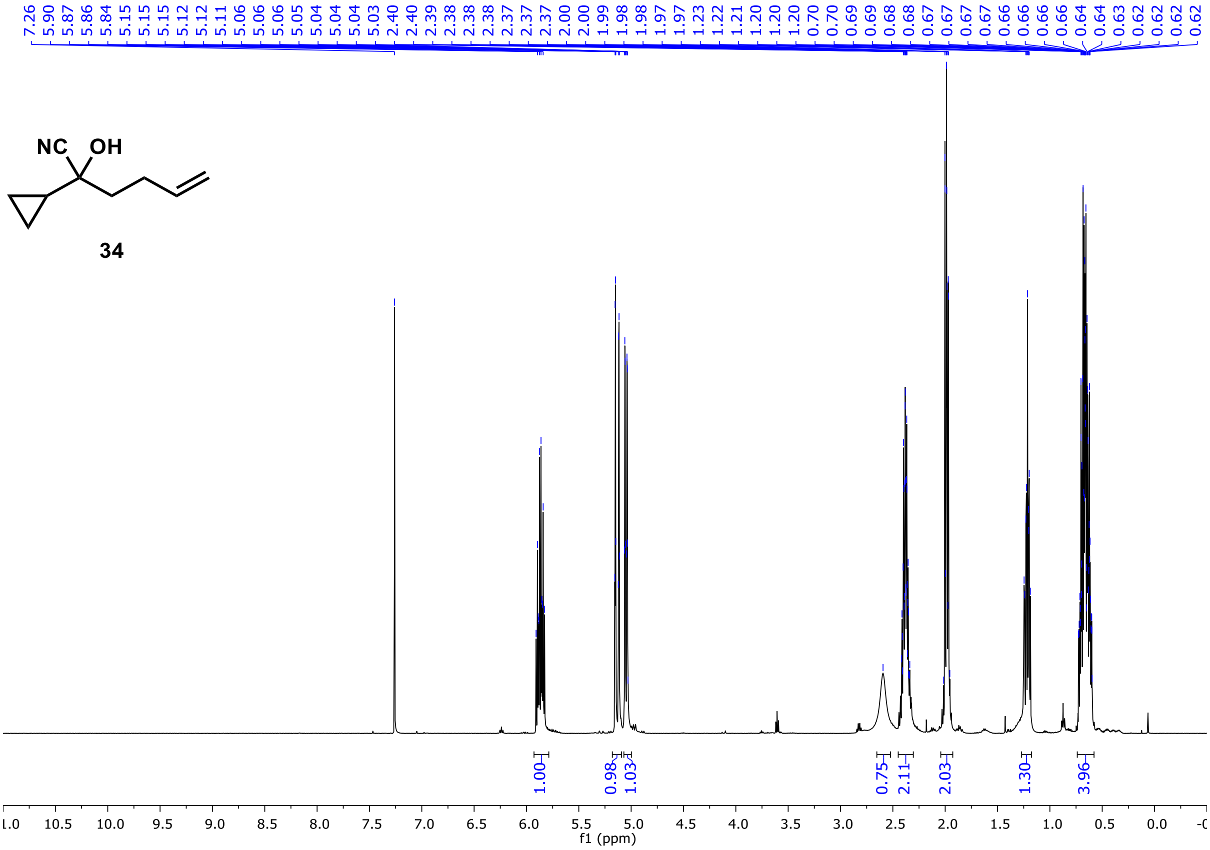


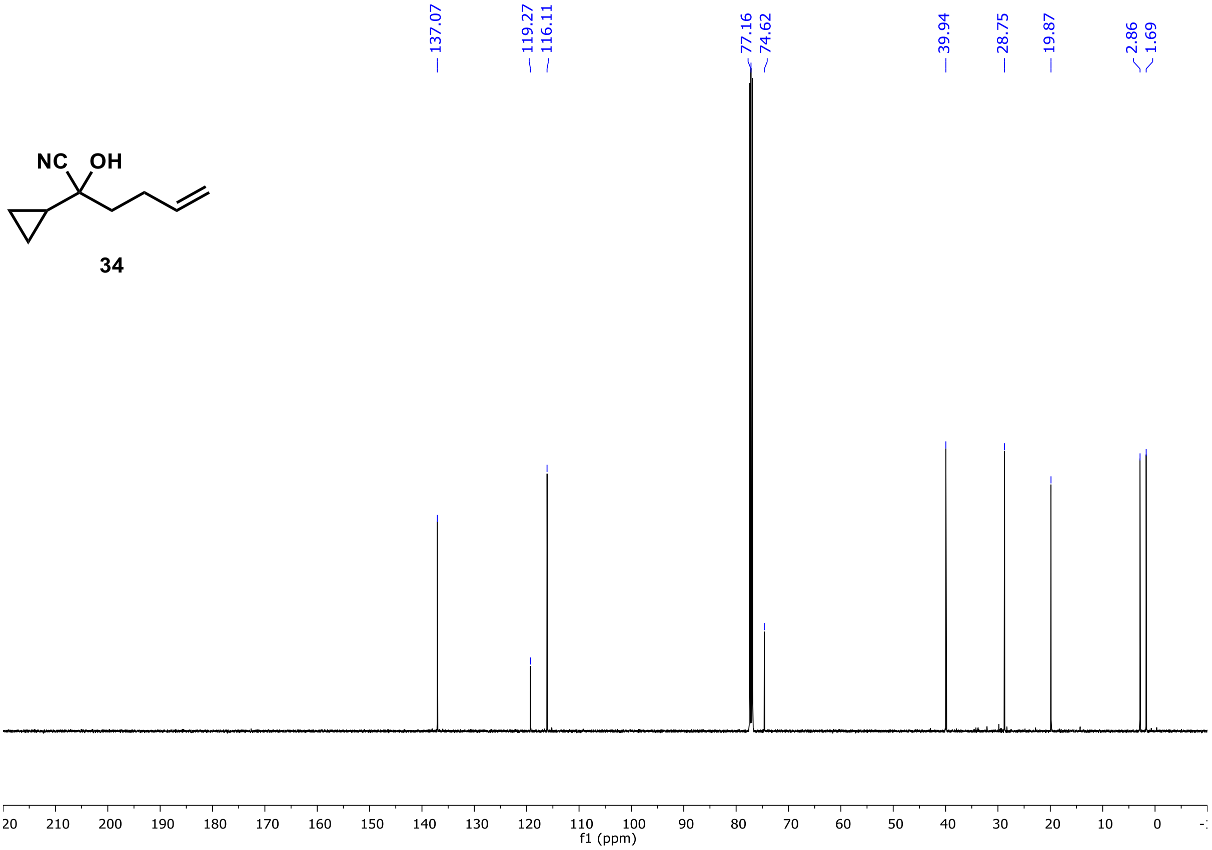
34

Prepared according to General Procedure 5 using **S55** (250 mg, 2.00 mmol) in CH_2Cl_2 (4 mL), trimethylsilyl cyanide (626 µL, 5.00 mmol), and $TiCl_4$ (110 µL, 1.00 mmol), followed by MeCN (10 mL) and 2 M HCl (10 mL) to afford **34** (270 mg, 88%) as a brown oil that was used without further purification.

R$_f$ = 0.38 (20% EtOAc/petrol); **FTIR** (ν_{max} cm^{-1}, thin film) 3424, 3082, 3013, 2926, 2855, 2349, 2326, 2241, 1643, 1418, 1057, 1028, 918; **^{1}H NMR (500 MHz, CDCl$_3$)** δ_H = 0.60 – 0.73 (4H, m), 1.19 – 1.25 (1H, m), 1.96 – 2.01 (2H, m), 2.34 – 2.42 (2H, m), 2.59 (1H, br s), 5.03 – 5.06 (1H, m), 5.11, 5.16 (1H, m), 5.83 – 5.91 (1H, m); **^{13}C NMR (126 MHz, CDCl$_3$)** δ_C = 1.7, 2.9, 19.9, 28.8, 39.9, 74.6, 116.1, 119.3, 137.1; **HRMS** (CI+) $C_9H_{13}NO$ [M-CN]$^+$ requires 125.0961, found 125.0961 (– 0.1 ppm).

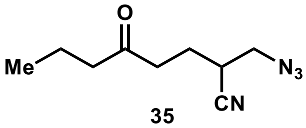
<u>^{1}H and ^{13}C NMR spectra of **34**</u>





4.2.2 Radical Clock Experiment

2-(Azidomethyl)-5-oxooctanenitrile (35)

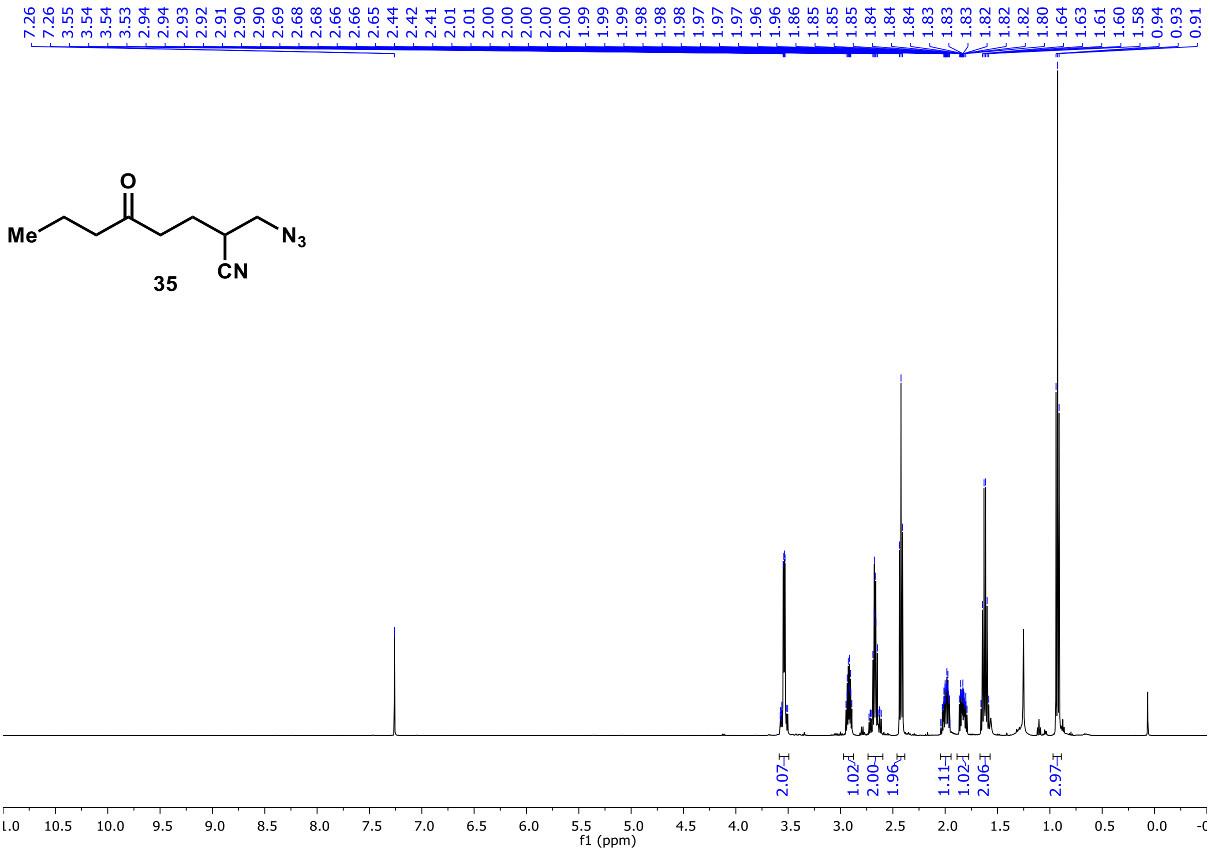


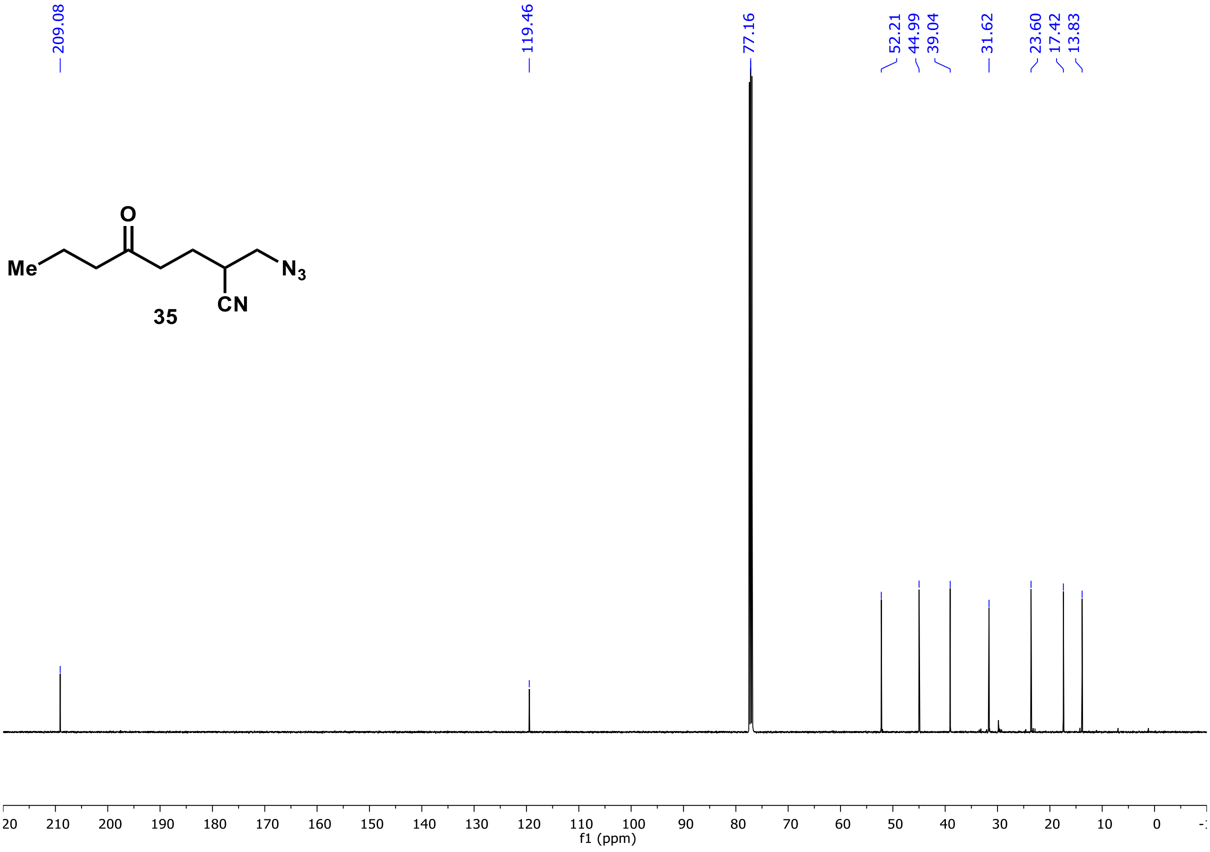
35

Prepared according to General Procedure 6 using **34** (45 mg). The resultant crude material was purified by flash column chromatography (5-25% EtOAc/*n*-hexane, silica gel) to afford **35** (21 mg, 36%) as a colourless oil.

R_f = 0.28 (15% EtOAc/petrol); **FTIR** (v_{max} cm^{-1}, thin film) 2963, 2934, 2104, 1713, 1458, 1318, 1362, 1281, 1126; **^{1}H NMR (500 MHz, $CDCl_3$)** δ_H = 0.93 (3H, t, *J* 7.4), 1.58 – 1.66 (2H, app h, *J* 7.3), 1.79 – 1.86 (1H, m), 1.95 – 2.04 (1H, m), 2.42 (2H, t, *J* 7.3), 2.61 – 2.73 (2H, m), 2.89 – 2.95 (1H, m), 3.50 – 3.58 (2H, m); **^{13}C NMR (126 MHz, $CDCl_3$)** δ_C = 13.8, 17.4, 23.6, 31.6, 39.0, 45.0, 52.2, 119.5, 209.1; **HRMS** (CI+) $C_9H_{14}N_2O$ $[M-N_2+H]^+$ requires 167.1179, found 167.1178 (– 0.5 ppm).

^{1}H and ^{13}C NMR spectra of **35**





5. References

1 J. Davies, N. S. Sheikh and D. Leonori, *Angew. Chem., Int. Ed.*, 2017, **56**, 13361–13365.

2 S. Samadi and A. Orellana, *ChemCatChem*, 2016, **8**, 2472–2475.

3 S. Giboulot, F. Liron, G. Prestat, B. Wahl, M. Sauthier, Y. Castanet, A. Mortreux and G. Poli, *Chem. Commun.*, 2012, **48**, 5889–5891.

4 F. Huang and S. Zhang, *Org. Lett.*, 2019, **21**, 7430–7434.

5 C. S. Penkett, J. A. Woolford, T. W. Read and R. J. Kahan, *J. Org. Chem.*, 2011, **76**, 1295–1304.

6 J. Wu, X. Yang, Z. He, X. Mao, T. A. Hatton and T. F. Jamison, *Angew. Chem., Int. Ed.*, 2014, **53**, 8416–8420.

7 D. M. Hodgson, P. G. Humphreys, S. M. Miles, C. A. J. Brierley and J. G. Ward, *J. Org. Chem.*, 2007, **72**, 10009–10021.

8 K. Usami, E. Yamaguchi, N. Tada and A. Itoh, *Org. Lett.*, 2018, **20**, 5714–5717.

9 S. Arava, J. N. Kumar, S. Maksymenko, M. A. Iron, K. N. Parida, P. Fristrup and A. M. Szpilman, *Angew. Chem., Int. Ed.*, 2017, **56**, 2599–2603.

10 S. Wang, L. Ma, Q. Wang, P. Shao, D. Ma, S. Yuan, P. Lei, P. Li, X. Feng and B. Wang, *J. Mater. Chem. C*, 2018, **6**, 5369–5374.

11 W. S. Bechara, G. Pelletier and A. B. Charette, *Nat. Chem.*, 2012, **4**, 228–234.

12 J. F. Hayes, M. Shipman and H. Twin, *J. Org. Chem.*, 2002, **67**, 935–942.

13 E. W. Thomas and J. R. Szmuszkovicz, *J. Org. Chem.*, 1990, **55**, 6054–6058.

14 D. L. J. Clive and M. P. Pham, *J. Org. Chem.*, 2009, **74**, 1685–1690.

15 E. C. Burger and J. A. Tunge, *Org. Lett.*, 2004, **6**, 4113–4115.

16 R. Suresh, A. K. Simlandy and S. Mukherjee, *Org. Lett.*, 2018, **20**, 1300–1303.

17 J. A. Murphy, M. Mahesh, G. McPheators, R. Vijaya Anand, T. M. McGuire, R. Carlinga and A. R. Kennedy, *Org. Lett.*, 2007, **9**, 3233–3236.

18 Z. Wu, R. Ren and C. Zhu, *Angew. Chem., Int. Ed.*, 2016, **55**, 10821–10824.

19 Y. Kwon and Q. Wang, *Org. Lett.*, 2020, **22**, 4141–4145.

20 C. Chang, H. Zhang, X. Wu and C. Zhu, *Chem. Commun.*, 2022, **58**, 1005–1008.

21 X. Creary, A. Anderson, C. Brophy, F. Crowell and Z. Funk, *J. Org. Chem.*, 2012, **77**, 8756–8761.

22 X. L. Yang, X. X. Peng, F. Chen and B. Han, *Org. Lett.*, 2016, **18**, 2070–2073.

23 T. Kato, H. Kondo, M. Nishino, M. Tanaka, G. Hata and A. Miyake, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 2958–2961.