

Electronic Supplementary Information

Catalytic cascade synthesis of cyanohydrin esters via water/O₂-induced cyanide transfer from K₃Fe(CN)₆

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Table of Contents

Optimization of the reaction conditions.....	S2
Mechanistic studies.....	S3
X-ray structure report of 3a.....	S16
Preparative methods.....	S17
Reference.....	S38
¹ H and ¹³ C NMR spectra of compounds	S39

Table S1 Optimization of the Reaction Conditions for the Synthesis of Cyanohydrin Esters^a

Sl. No.	Catalyst	Additive	Solvent (mL)	3a (%)	4(%)
1	PdCl ₂	-	DMSO	0	0
2	NiBr ₂	-	DMSO	0	0
3	FeCl ₂	-	DMSO	0	0
4	FeCl ₃	-	DMSO	0	0
5	CoCl ₂	-	DMSO	0	0
6	BrMn(CO) ₅	-	DMSO	0	0
7	CuBr ₂	-	DMSO	55	20
8	CuI	-	DMSO	30	50
9	Cu(OAc) ₂	-	DMSO	15	60
10	CuF ₂	-	DMSO	38	50
11	CuCl ₂	-	DMSO	48	39
12	Cu ₂ O	-	DMSO	10	60
13	Cu(acac) ₂	-	DMSO	23	55
14	CuBr	-	DMSO	30	60
15	CuBr ₂	Terpyridine	DMSO	50	30
16	CuBr ₂	Picolinic acid	DMSO	50	25
17	CuBr ₂	(S)- BINAP	DMSO	55	30
18	CuBr ₂	8-aminoquinoline	DMSO	55	20
19	CuBr ₂	1, 10-Phenanthroline	DMSO	0	0
20	CuBr ₂	Pyridine N-oxide	DMSO	0	0
21	CuBr ₂	Xphos	DMSO	55	20
22	CuBr ₂	DPPE	DMSO	53	25
23 ^b	CuBr ₂	-	DMSO	45	30
24	CuBr₂	-	Oxygenated DMSO	86	<5
25 ^c	CuBr ₂	-	Oxygenated DMSO	65	15
26 ^d	CuBr ₂	-	Oxygenated DMSO	60	20
27 ^e	CuBr ₂	-	degassed DMSO	0	0
28 ^f	CuBr ₂	-	Oxygenated DMSO	40	50
29 ^g	CuBr ₂	-	Oxygenated DMSO	52	21
30	CuBr ₂	-	DMF	0	0
31	CuBr ₂	-	DCE	0	0
32	CuBr ₂	-	Toluene	0	0
33	CuBr ₂	-	DMAc	0	0
34	CuBr ₂	-	Chlorobenzene	0	0
35	CuBr ₂	-	Xylene	0	0
36	CuBr ₂	-	1,2-dichlorobenzene	0	0
37	CuBr ₂	-	<i>n</i> -butanol	0	0
38	-	-	Oxygenated DMSO	0	10

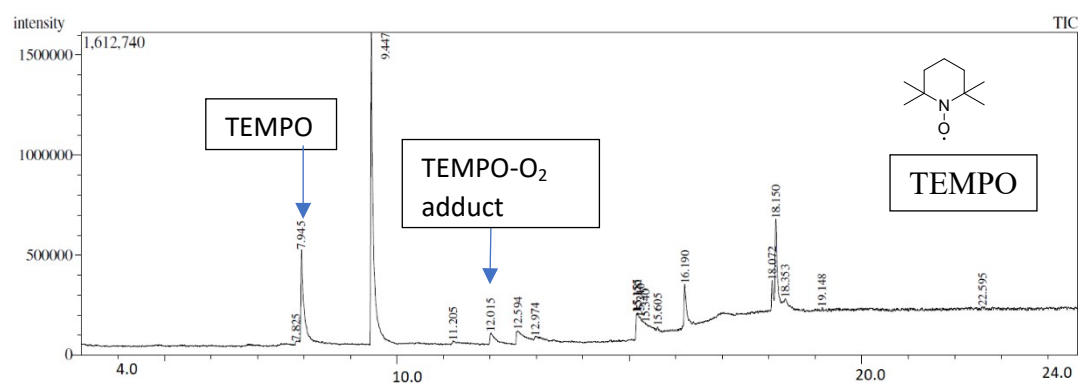
^a Reaction Conditions: **1a** (0.5 mmol), K₃Fe(CN)₆ (1.0 mmol, 2.0 eq.), CuBr₂ (0.1 mmol, 0.2 eq., 20 mol %), Additive (0.02 mmol, 0.2 eq., 4 mol%), anhydrous DMSO (0.5 mL), 120 °C, 48 h, isolated yield of pure product, ^b CuBr₂ (15 mol%), ^c Air, ^d 110 °C, ^e Degassed and anhydrous DMSO and N₂ atmosphere, ^f 130 °C, ^g K₃Fe(CN)₆ (0.75 mmol, 1.5 eq.).

Mechanistic study

Radical scavenging experiment with 2-phenylacetophenone (1a) in the presence of TEMPO

A 20 mL crimp cap vial was charged with **1a** (98 mg, 0.5 mmol, 1.0 eq), copper (II) bromide (22 mg, 0.1 mmol, 20 mol%), potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) and TEMPO (156 mg, 1.0 mmol, 2.0 eq). The vial was then closed with a cap by a crimper tool and the reaction mixture was then evacuated and backfilled with nitrogen. To it, oxygenated DMSO (0.5 mL) was added. The reaction mixture was stirred at 120 °C for 48 h on an aluminium block. After cooling, an aliquot (0.2 mL) from the reaction mixture was withdrawn and diluted with EtOAc (2.0 mL), and washed with water (1.0 mL). The organic layer was dried over Na₂SO₄, and subsequently submitted to GC-MS, which shows the formation of the TEMPO(O₂) adduct (*m/z* = 188). The rest of the solvent from the crude reaction mixture was evaporated and the residue was then directly subjected to flash column chromatography on silica-gel to recover the starting material **1a** (75 mg, 76%).

GCMS spectrum of the reaction between 2-phenylacetophenone (1a) with K₃Fe(CN)₆ and copper (II) bromide in the presence of TEMPO



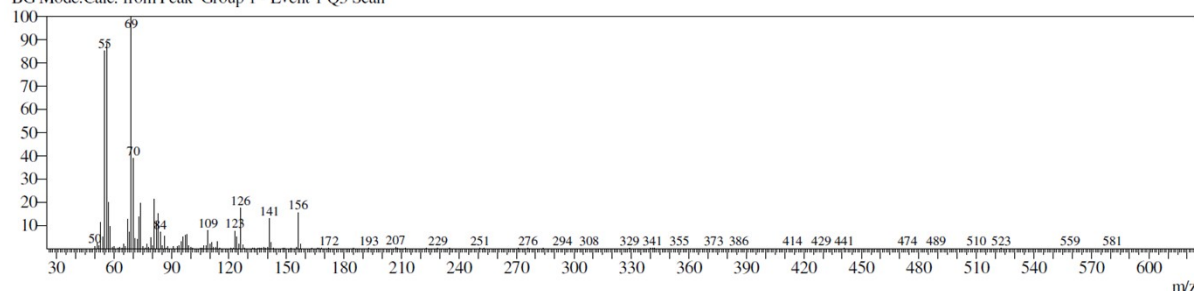
GCMS Spectrum of TEMPO (*m/z* = 156, *R_t* = 7.945)

Line#:2 R.Time:7.945(Scan#:950)

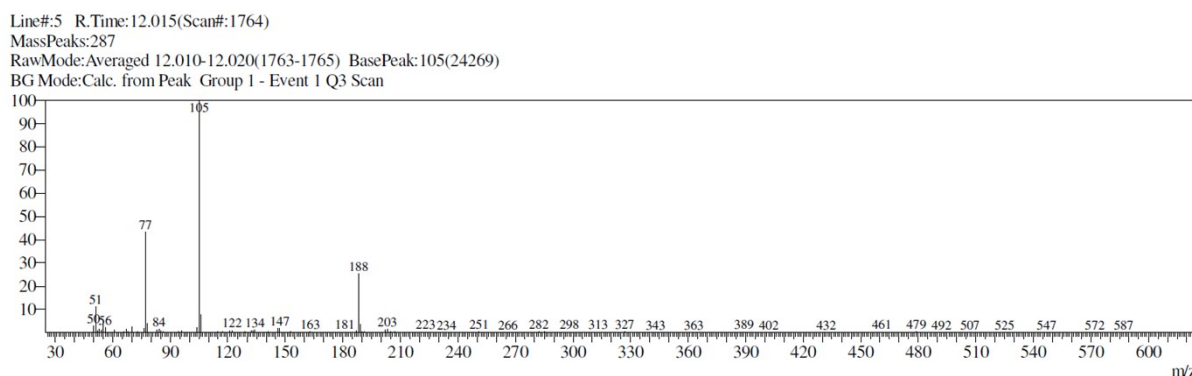
MassPeaks:370

RawMode:Averaged 7.940-7.950(949-951) BasePeak:69(71159)

BG Mode:Calc. from Peak Group 1 - Event 1 Q3 Scan



GCMS Spectrum of TEMPO(O₂) adduct (m/z = 188, R_t = 12.015)



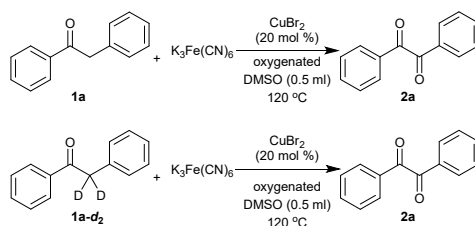
Radical scavenging experiment with 2-phenylacetophenone (**1a**) in the presence of BHT

A 20 mL crimp cap vial was charged with **1a** (98 mg, 0.5 mmol, 1.0 eq), copper (II) bromide (22 mg, 0.1 mmol, 20 mol%), potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) and BHT (220 mg, 1.0 mmol, 2.0 eq). The vial was then closed with a cap by a crimper tool and the reaction mixture was then evacuated and backfilled with nitrogen. To it, oxygenated DMSO (0.5 mL) was added. The reaction mixture was stirred at 120 °C for 48 h on an aluminium block. The reaction mixture was extracted with ethyl acetate (3 x 20 mL) and water (10 mL). The organic layer was dried over Na₂SO₄, filtered & evaporated and the residue was then directly subjected to flash column chromatography on silica-gel to recover the starting material **1a** (90 mg, 92%). **3a** was not formed at all as observed by GC-MS.

Determination of KIE for the copper catalyzed oxygenation of **1a** with O₂ by independent parallel experiments

Two independent reactions with **1a** and **1a-d₂** under the optimal reaction conditions were conducted: Two 20 mL crimp cap vials were independently charged with either **1a** (98 mg, 0.5 mmol, 1.0 eq.) or **1a-d₂** (99 mg, 0.5 mmol, 1.0 eq.). To each of them, copper (II) bromide (22 mg, 0.1 mmol, 20 mol%) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) were added and the vessels were closed with the help of a crimper tool. The reaction vessels were evacuated and backfilled with nitrogen (x 3). Subsequently, oxygenated and anhydrous DMSO (0.5 mL), was added to both vials and stirred at 120 °C on an aluminium block for the required time as indicated in the following table. An aliquot of 0.1 mL was withdrawn periodically and passed through a small bed of silica gel and monitored by GC analysis (Figure S1). A comparison of the two individual reactions showed a kinetic isotope effect of 4.32 for the oxygenation of **1a**

i.e., the formation of **2a** starting from **1a**. This indicates that the C–H bond cleavage of **1a** in the oxygenation process took place in the rate determining step.



Time (min)	0	4	8	12	16	20
2a (%) from 1a	0	5.32	16.89	32.61	42.93	48.22
2a (%) from 1a-d₂	0	2.63	4.51	7.75	10.24	11.92

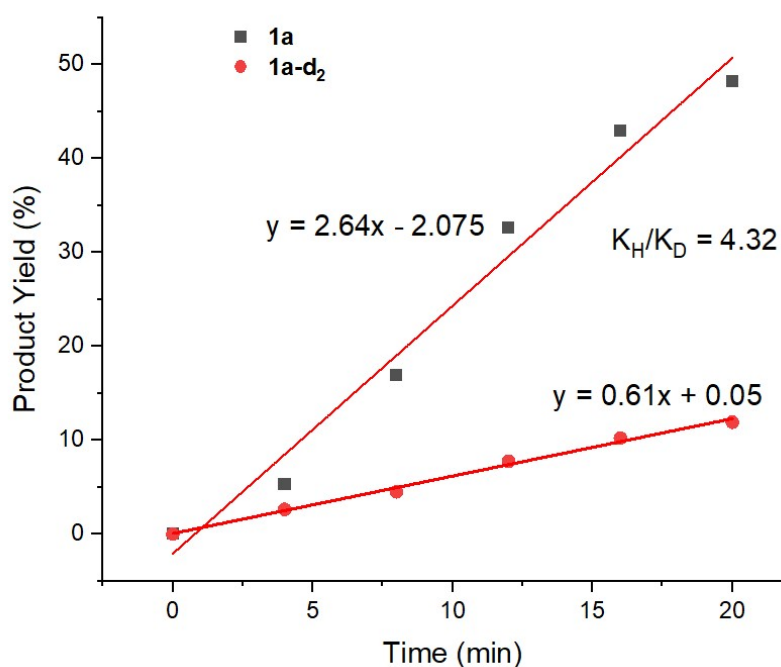
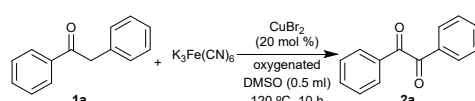


Figure S1. Determination of KIE by independent parallel experiments with **1a** and **1a-d₂**

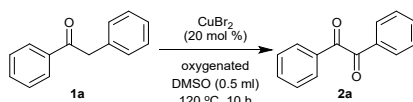
Isolation of benzil (**2a**) as an intermediate in the reaction between 2-phenylacetophenone **1a** and $K_3Fe(CN)_6$ in the presence of $CuBr_2$



A 20 mL crimp cap vial was charged with a magnetic stirring bar, **1a** (98 mg, 0.5 mmol, 1.0 eq), copper (II) bromide (22 mg, 0.1 mmol, 20 mol%) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). The vial was then closed with a cap by a crimper tool and the reaction mixture

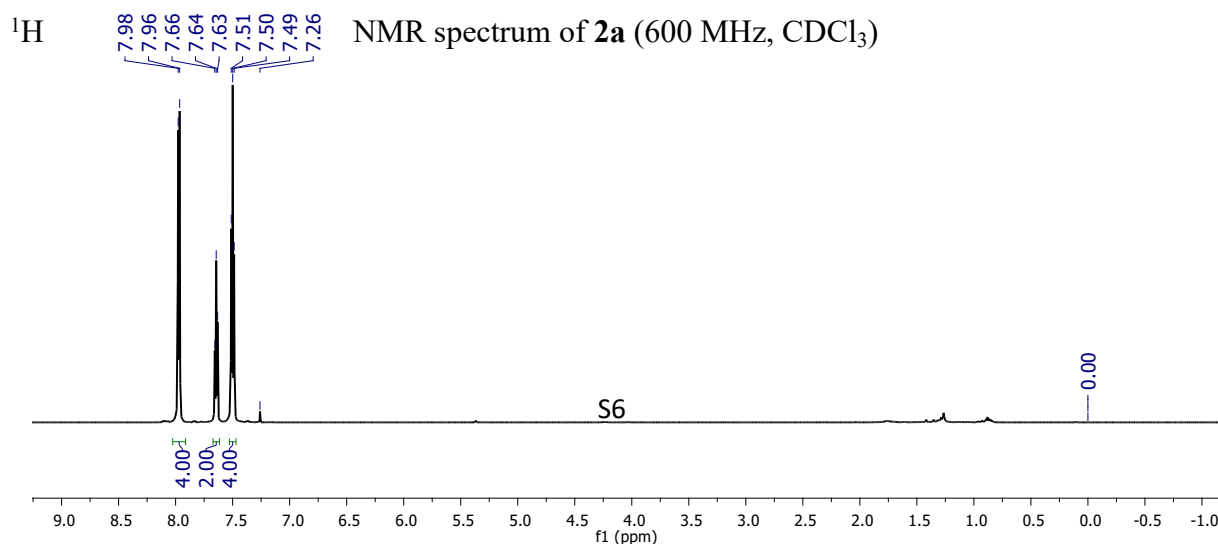
was then evacuated and backfilled with nitrogen. To it, oxygenated DMSO (0.5 mL) was added. The reaction mixture was stirred at 120 °C on an aluminium block. The progress of the reaction was monitored by GC analysis. After 10 h, the reaction mixture was allowed to cool down and water (10 mL) was added to it. The reaction mixture was then extracted with ethyl acetate (3 x 20 mL) and the organic layer was dried over Na₂SO₄, filtered, evaporated under vacuum and the residue was then directly subjected to flash column chromatography on silica-gel to obtain **2a** (101 mg, 96%) which was confirmed by NMR. ¹H NMR (600 MHz, CDCl₃) δ 7.97 (d, *J* = 8.4 Hz, 4H), 7.64 (t, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 4H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 194.7 (2C), 135.0 (2C), 133.1 (2C), 130.0 (4C), 129.1 (4C) ppm. All spectral data were in accord with the literature.¹

Isolation of Benzil (**2a**) as an intermediate by reaction between 2-phenylacetophenone **1a** with CuBr₂

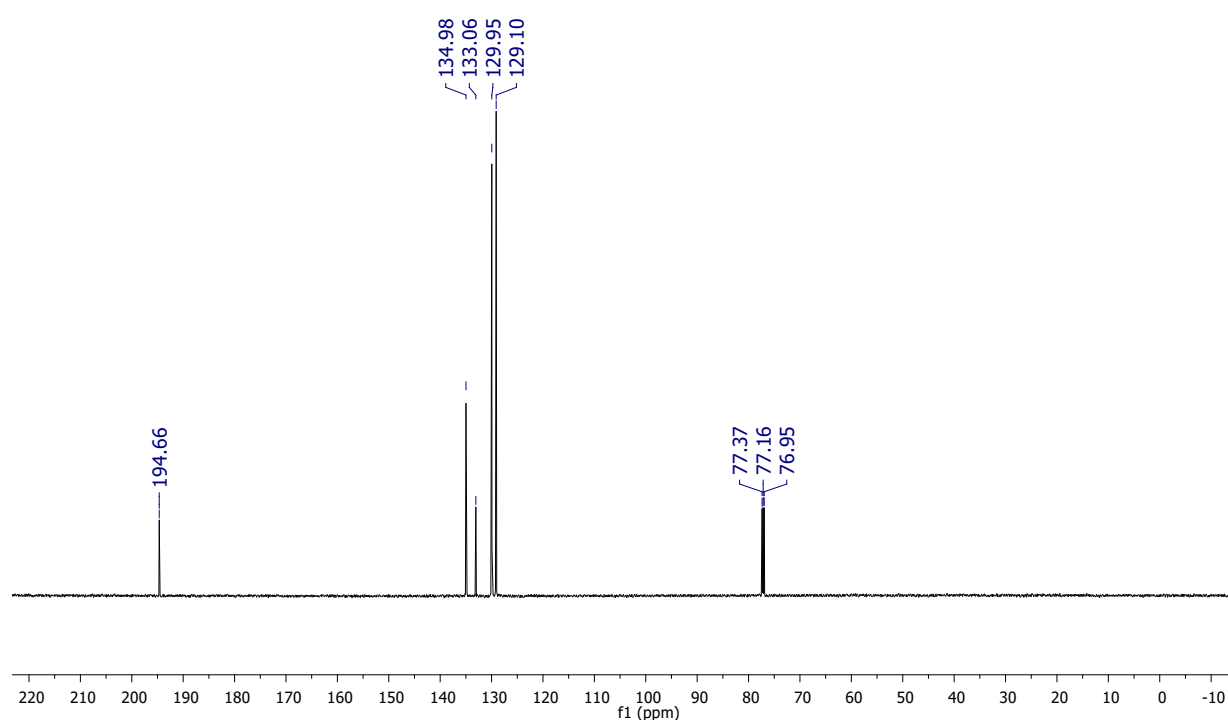


A 20 mL crimp cap vial was charged with a magnetic stirring bar, **1a** (98 mg, 0.5 mmol, 1.0 eq) and copper (II) bromide (22 mg, 0.1 mmol, 20 mol%). The vial was then closed with a cap by a crimper tool and the reaction mixture was then evacuated and backfilled with nitrogen. To it, oxygenated DMSO (0.5 mL) was added. The reaction mixture was stirred at 120 °C on an aluminium block. The progress of the reaction was monitored by GC. After 10 h, the reaction mixture was allowed to cool down and water (10 mL) was added to it. The reaction mixture was then extracted with ethyl acetate (3 x 20 mL) and the organic layer was dried over Na₂SO₄, filtered, evaporated under vacuum and the residue was then directly subjected to flash column chromatography on silica-gel to obtain **2a** (99 mg, 94%) which was confirmed by ¹H and ¹³C NMR. All spectral data are in accord with the literature.¹

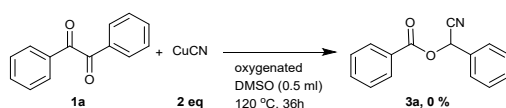
¹H NMR spectrum of **2a** (600 MHz, CDCl₃)



^{13}C NMR spectrum of **2a** (151 MHz, CDCl_3)



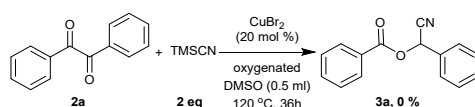
Reaction of **2a** with CuCN



A 20 mL crimp cap vial, equipped with a magnetic stirring bar, was charged with **2a** (105 mg, 0.5 mmol, 1.0 eq) and CuCN (90 mg, 1.0 mmol, 2.0 eq). The vial was then closed with a cap by a crimper tool and the reaction mixture was then evacuated and backfilled with nitrogen (x 3). To it, oxygenated DMSO (0.5 mL) was added. The reaction mixture was stirred at 120 °C

for 36 h on an aluminium block. After cooling, an aliquot (0.2 mL) from the reaction mixture was passed through a small bed of silica gel, diluted with EtOAc (2.0 mL), and washed with water (1.0 mL). The organic layer was analysed via GC analysis, which did not show the formation of **3a**. This indicates that the cyanohydrin ester formation does not involve a copper-mediated cyanide attack.

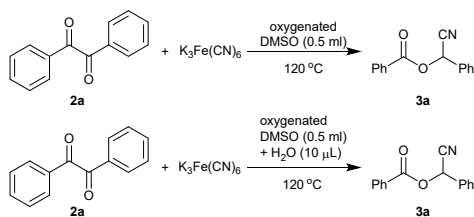
Reaction of **2a** with TMSCN in presence of CuBr_2



A 20 mL crimp cap vial, equipped with a magnetic stirring bar, was charged with **2a** (105 mg, 0.5 mmol, 1.0 eq), copper(II) bromide (22 mg, 0.1 mmol, 20 mol%), and the vessel was closed with the help of a crimper tool. The vessel was then evacuated and backfilled with nitrogen (x 3). Subsequently, oxygenated DMSO (0.5 mL) was added to the reaction vial followed by the addition of TMSCN (99 mg, 1.0 mmol, 2.0 eq). The reaction mixture was stirred on an aluminium block at 120 °C for 36 h. After which, an aliquot of 0.2 mL was withdrawn and passed through a small bed of silica gel, diluted with EtOAc (2.0 mL) and washed with water (1.0 mL). The organic layer was analysed via GC analysis, which did not show the formation of **3a**. This indicates that the cyanohydrin ester formation does not involve a copper-mediated cyanide attack.

Effect of water addition

Two 20 mL crimp cap vials were charged with **2a** (105 mg, 0.5 mmol, 1.0 eq), potassium ferricyanide (329 mg, 1 mmol, 2 eq) and the vessels were closed with the help of a crimper tool. The vessels were then evacuated and backfilled with nitrogen (x 3). Subsequently, oxygenated DMSO (0.5 mL) was added to both reaction mixtures. In one of the vials, water (10 μL) was added. Both the reaction vessels were stirred on an aluminium block at 120 °C. An aliquot of 50 μL was withdrawn periodically and passed through a small bed of silica gel and monitored by GC at the required time interval, particularly at a lower concentration of **3a** (i.e., lower conversion of **2a**) as indicated in the following table. A comparison on the rate of the two independent reactions were plotted as shown in Figure S3.



Time (min)	3a (%) (without water)	3a (%) (with 10 μ L water)
0	0	0
30	0.17	0.73
60	0.48	3.8
90	1.86	10.73
120	3.44	11.32
150	4.93	16.1
180	5.22	20.97

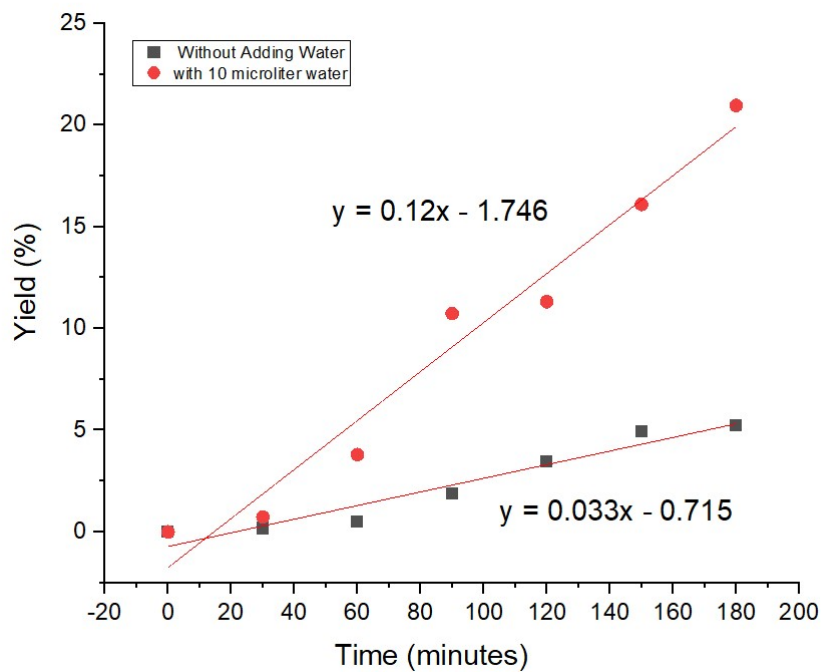
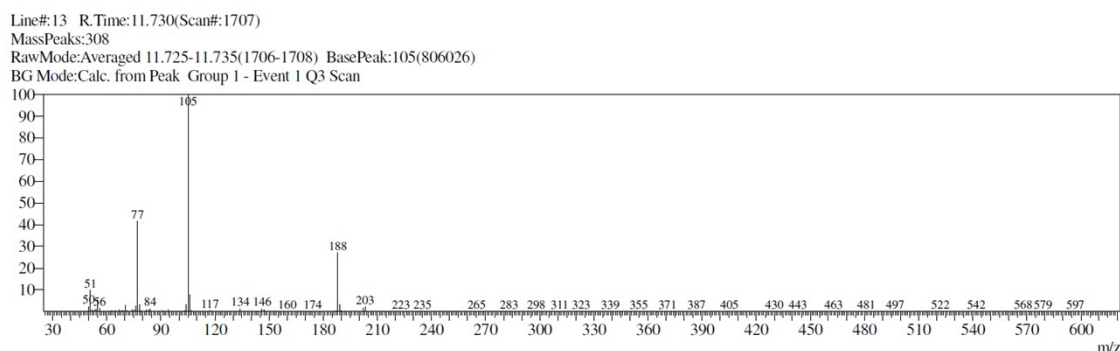


Figure S2. Effect of addition of traces of water in the conversion of **2a** to **3a**

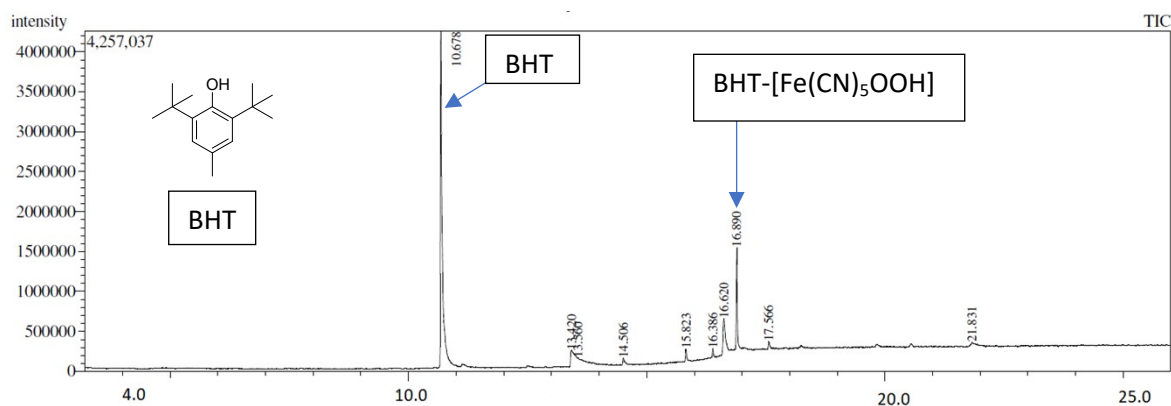
GCMS Spectrum of TEMPO(O₂) adduct ($m/z = 188$, $R_t = 11.73$)



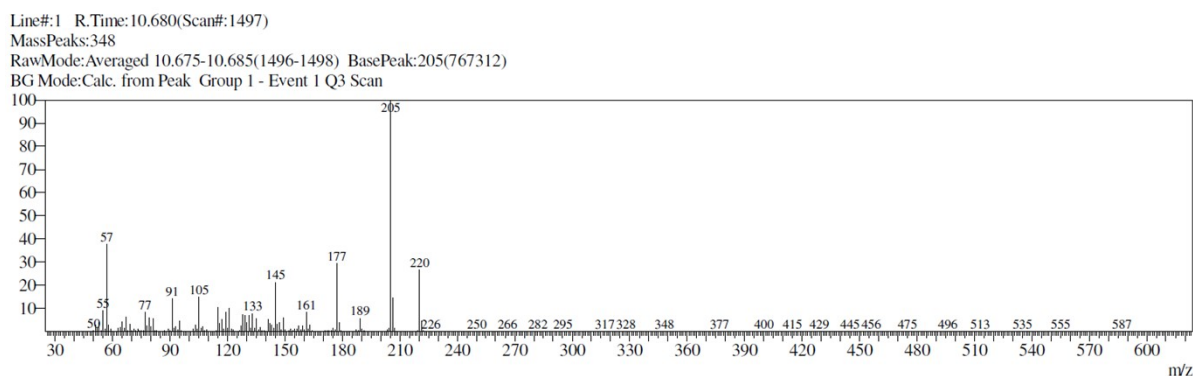
Radical scavenging experiment with benzil (**2a**) in the presence of BHT

A 20 mL crimp cap vial was charged with **2a** (105 mg, 0.5 mmol, 1.0 eq), potassium ferricyanide (329 mg, 1.0 mmol, 2 eq), and BHT (220 mg, 1.0 mmol, 2.0 eq). The vial was then closed with a cap by a crimper tool and the reaction mixture was then evacuated and backfilled with nitrogen. To it, oxygenated DMSO (0.5 mL) was added. The reaction mixture was stirred at 120 °C for 36 h on an aluminium block. After cooling, an aliquot (0.2 mL) from the reaction mixture was withdrawn and diluted with EtOAc (2.0 mL), and washed with water (1.0 mL). The organic layer was dried over Na₂SO₄, and subsequently submitted to GC-MS, which shows the formation of the BHT-[Fe(CN)₅OOH] adduct ($m/z = 438$). The rest of the solvent from the crude reaction mixture was evaporated and the residue was then directly subjected to flash column chromatography on silica-gel to recover the starting material benzil **2a** (80 mg, 76%).

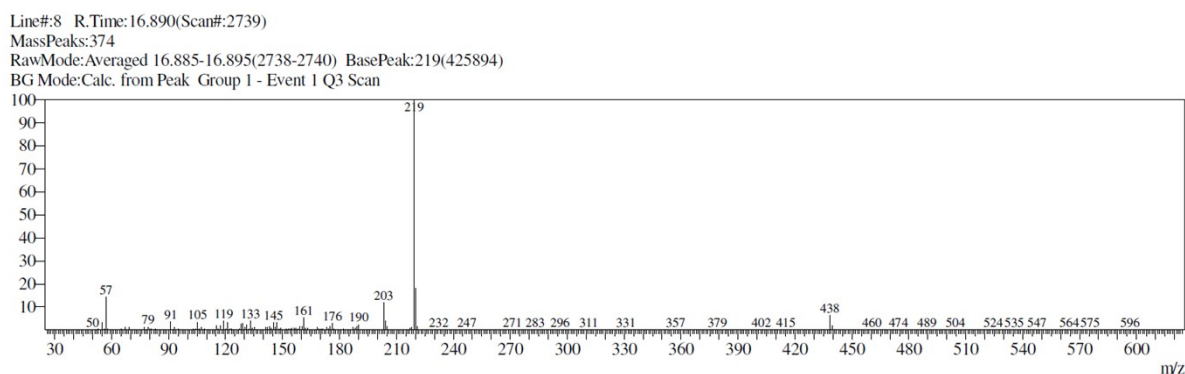
GCMS spectrum of the reaction between benzil (**2a**) and K₃Fe(CN)₆ with BHT



GCMS Spectrum of BHT ($m/z = 220$, $R_t = 10.680$)



GCMS Spectrum of BHT-[Fe(CN)₅OOH] adduct ($m/z = 438$, $R_t = 16.890$)



EPR Study

A 20 mL crimp cap vial was charged with **2a** (105 mg, 0.5 mmol, 1.0 eq), and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) The vial was then closed with a cap by a crimper tool and the reaction vessel was then evacuated and backfilled with nitrogen. To it, oxygenated and anhydrous DMSO (0.5 mL) was added. The reaction mixture was stirred at 120 °C for 36 h on an aluminium block. An aliquot (0.1 mL) from the reaction mixture was withdrawn typically at 0 min, 30 min, 60 min, 120 min and 10 h and 30 h. A signal appeared at $g = 2.15$ remains unchanged, indicating the formation of superoxide anion.²

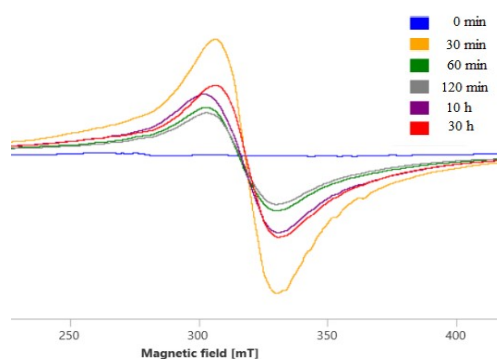
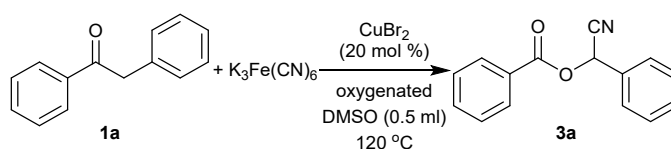


Figure S3. A. EPR spectra at -160 °C of the reaction between **2a** (0.5 mmol) and K₃Fe(CN)₆ (1.0 mmol) in DMSO (0.5 mL) at 120 °C

Effect of variation of amount of $K_3Fe(CN)_6$

20 mL crimp cap vials, equipped with a magnetic stirring bar, were charged with **1a** (98 mg, 0.5 mmol, 1.0 eq), copper(II) bromide (22 mg, 0.1 mmol, 20 mol%), potassium ferricyanide (0 eq, 0.6 eq, 1.2 eq, 1.8 eq & 2.0 eq) and the vessels were closed with the help of a crimper tool. The vessels were then evacuated and backfilled with nitrogen (x 3). Subsequently, oxygenated DMSO (0.5 mL) was added to both reaction mixtures. The reaction mixture was stirred at 120 °C for 48 h on an aluminium block. After cooling, an aliquot (0.2 mL) from the reaction mixture was passed through a small bed of silica gel, diluted with EtOAc (2.0 mL), and washed with water (1.0 mL). The organic layer was analysed via GC analysis, to calculate the yield of the product **3a**.



Sl. No.	1	2	3	4	5
$K_3Fe(CN)_6$ (eq.)	0	0.6	1.2	1.8	2.0
3a from 1a (%)	0	11.0	60.0	72.0	86.0

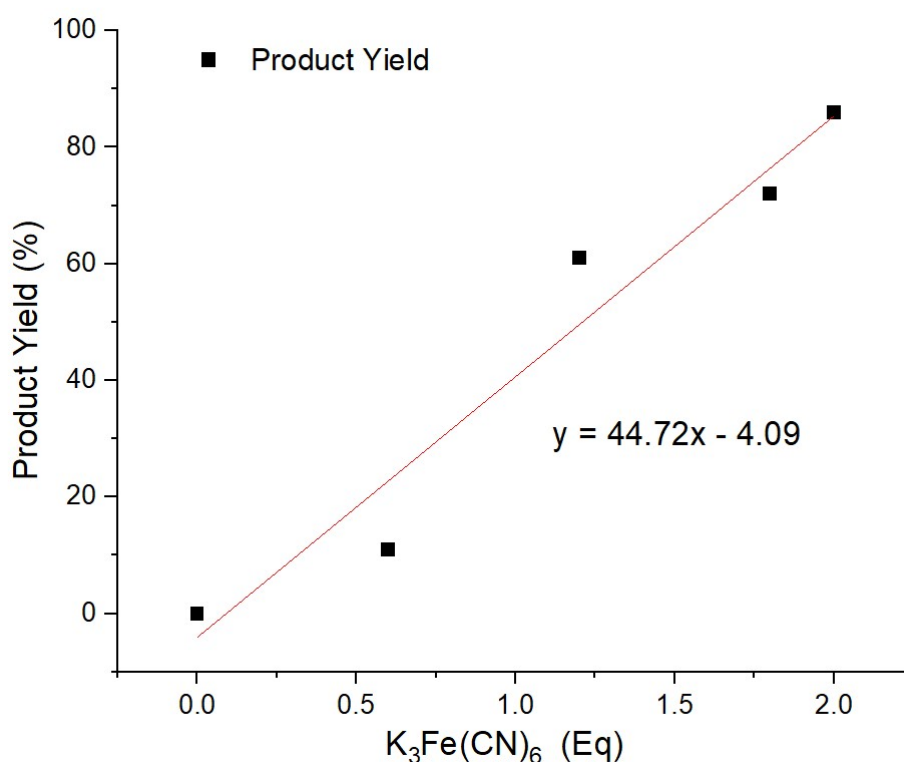


Figure S4. Effect of $K_3Fe(CN)_6$ variation on yield of **3a** from **1a**

Deuterium labelling study in the reaction of **2a** with $K_3Fe(CN)_6$ in the presence of D_2O

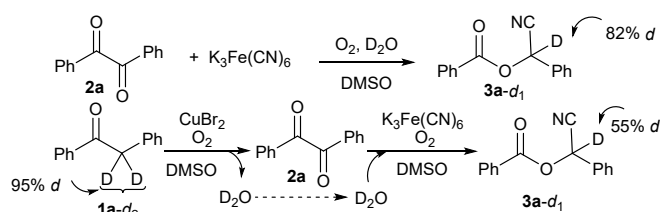
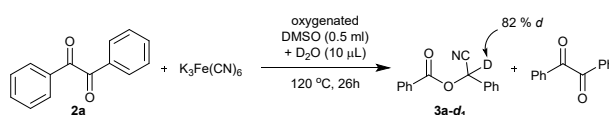


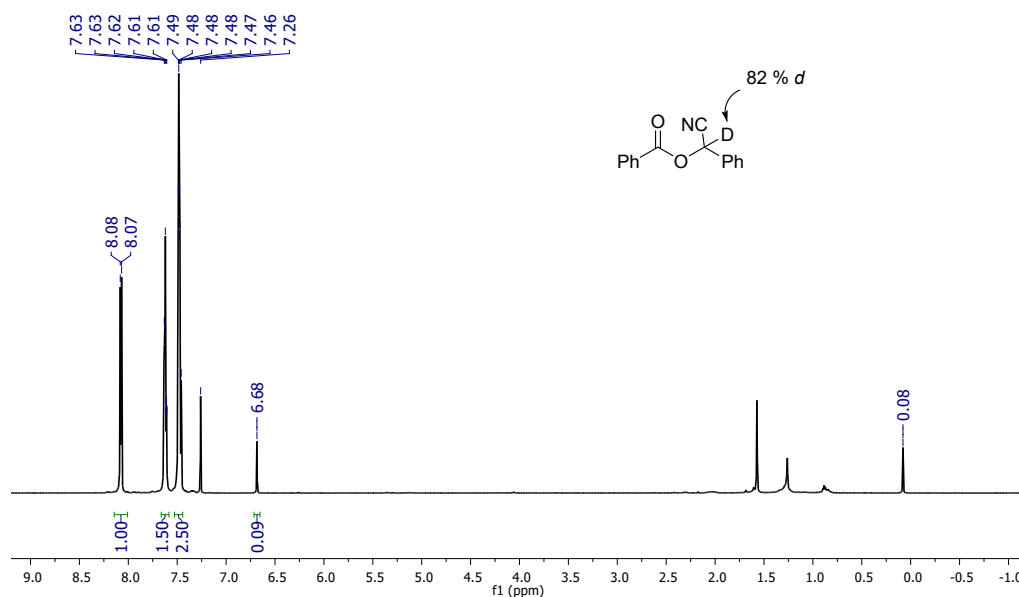
Figure S5. Evidences in support of the proposed mechanism

Deuterium labelling study in the reaction of **2a** with $K_3Fe(CN)_6$ in the presence of D_2O

A 20 mL crimp cap vial was charged with **2a** (105 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). The vial was closed with a cap by a crimper tool and the reaction vessel was then evacuated and backfilled with nitrogen (x 3). To it, oxygenated and anhydrous DMSO (0.5 mL) was added followed by D_2O (10 μ L). The reaction was stirred on an aluminium block at 120 °C. After 24 h, the reaction mixture was allowed to cool to room temperature and ethyl acetate (20 mL) was added to it. The reaction mixture was then filtered through anhydrous Na_2SO_4 and low volatiles were evaporated through rotary evaporator. The residual DMSO from the crude mixture was then separated via Kugelrohr distillation at 120 °C and 10 mbar vacuum. The residue was purified by flash column chromatography on silica gel to obtain **3a-d₁** (75.0 mg, 0.31 mmol, 63%) with 82% *d* enrichment (confirmed by 1H NMR).

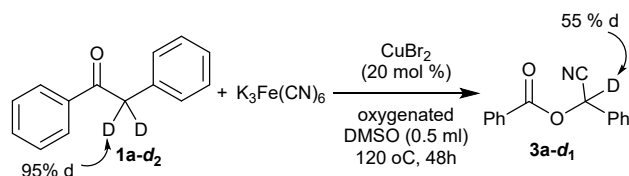


1H NMR spectrum of **3a-d₁** (600 MHz, $CDCl_3$)

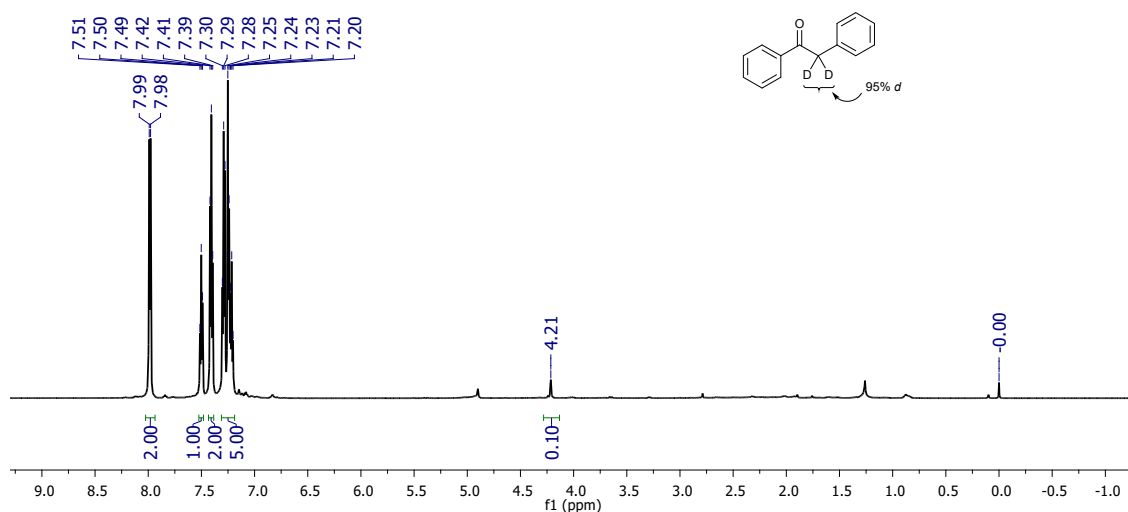


Deuterium labelling study in the reaction of **1a-d₂** with **K₃Fe(CN)₆**

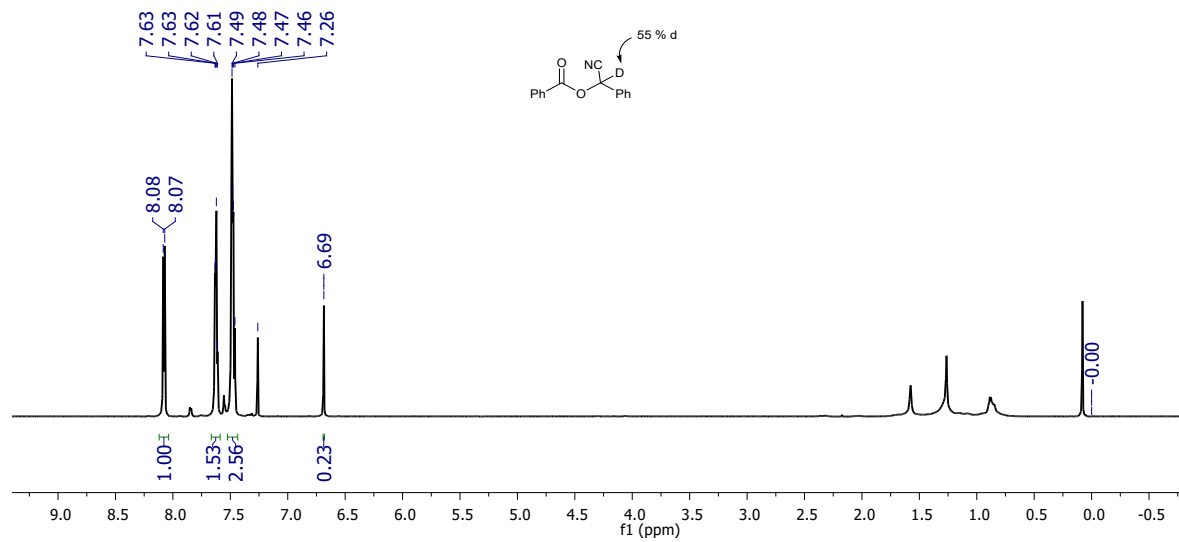
A 20 mL crimp cap vial was charged with **1a-d₂** (98 mg, 0.5 mmol, 1.0 eq.), CuBr₂ (22 mg, 0.1 mmol, 20 mol%) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq.) The vial was closed with a cap by a crimper tool and the reaction vessel was then evacuated and backfilled with nitrogen (x 3). To it, oxygenated and anhydrous DMSO (0.5 mL) was added and the mixture was stirred on an aluminium block at 120 °C. After 48 h, the reaction mixture was allowed to cool to room temperature and ethyl acetate (20 mL) was added to it. The reaction mixture was filtered through anhydrous Na₂SO₄ and low volatiles were evaporated through rotary evaporator. The residual DMSO from the crude mixture was then separated via Kugelrohr distillation at 120 °C and 10 mbar vacuum. The residue was purified by flash column chromatography on silica gel to obtain **3a-d₁** (85 mg, 0.36 mmol, 72%) with 55% *d* enrichment (confirmed by ¹H NMR).



¹H NMR spectrum of **1a-d₂** (600 MHz, CDCl₃):



^1H NMR spectrum of **3a-d₁** (600 MHz, CDCl_3)



X-ray Structure Report for 3a

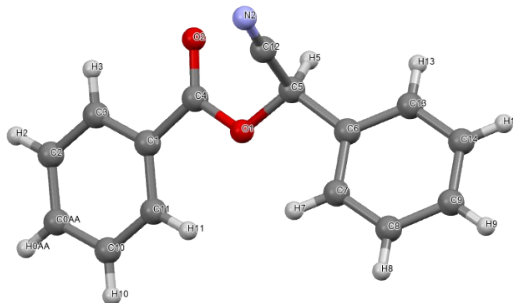


Figure 1. ORTEP diagram of **3a** (50% probability factor for the thermal ellipsoids)

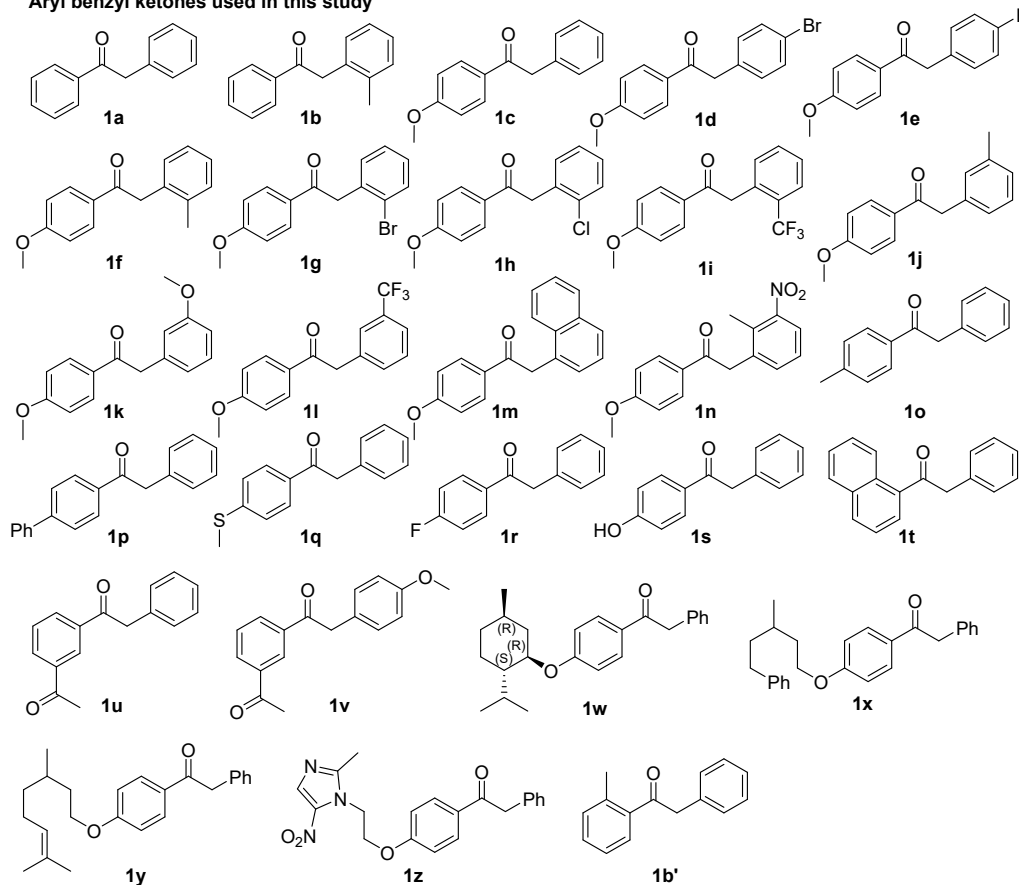
Empirical formula	C ₁₅ H ₁₁ NO ₂
Formula weight	237.26
Temperature/K	298
Crystal system	Monoclinic
Space group	P 21/c
a/Å	14.6245 (10)
b/Å	11.4172 (8)
c/Å	7.6696 (3)
a/o	90
b/o	102.208 (3)
g/o	90
Volume/Å ³	1251.64 (15)
Z	4
rcalc g/cm ³	1.259
m/mm-1	0.084
F(000)	496.0
Crystal size/mm ³	0.46 × 0.11 × 0.08
Radiation	MoK α (λ = 0.71073)
2 θ range for data collection/o	2.9–26.3°
Index ranges	-17 ≤ h ≤ 17, -13 ≤ k ≤ 13, -9 ≤ l ≤ 9
Reflections collected	2205
Independent reflections	1728
Data/restraints/parameters	2205/0/163
Goodness-of-fit on F ²	1.105
Final R indexes [I ≥ 2σ (I)]	R1 = 0.0631, wR2 = 0.1467
Final R indexes [all data]	R1 = 0.0499, wR2 = 0.1332
Largest diff. peak/hole/e Å ⁻³	0.163/ -0.197
CCDC	2173504

Preparative methods and characterization of new compounds

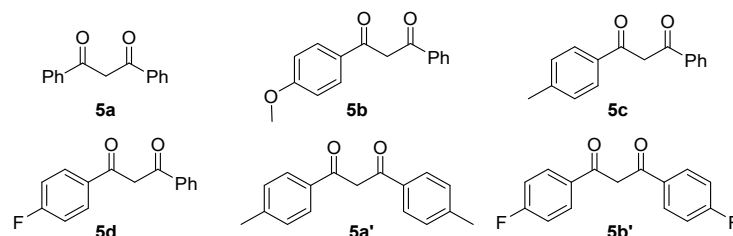
General Methods. IR spectra were recorded on a Perkin-Elmer Spectrum GX FT-IR spectrophotometer. NMR spectra were recorded on Jeol Resonance ECZ 600R spectrometer (600 MHz for ^1H NMR, 151 MHz for ^{13}C NMR, 565 MHz for ^{19}F) and/or Bruker AvanceII 500 spectrometer (500 MHz for ^1H NMR, 126 MHz for ^{13}C NMR). Chemical shifts were reported in ppm on the δ scale relative to Me_4Si ($\delta = 0.00$ for ^1H -NMR), CDCl_3 ($\delta = 77.160$ for ^{13}C -NMR) and $\text{DMSO-}d_6$ ($\delta = 39.52$ for ^{13}C -NMR). Additional peaks at $\delta = 1.56\text{--}1.61$ ppm in ^1H -NMR spectra of compounds recorded in CDCl_3 and $\delta = 3.39$ ppm in ^1H -NMR spectra of compounds recorded in $\text{DMSO-}d_6$ correspond to water, present if any. Multiplicities are indicated as: br (broad), s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Coupling constants (J) are reported in Hertz (Hz). Melting Points of solid compounds were measured by Thermo Scientific MEL TEMP instrument. GC spectral data were recorded on a Shimadzu GC-2014. HRMS (ESI) spectra were recorded on a Micromass Q-ToF microTM instrument. GCMS spectral data were acquired on a Shimadzu GC-2010 Plus coupled with GCMS-TQ8040 instrument. Single crystal structures were determined using a Bruker D8 QUEST (CCD) diffractometer. Fractional distillations were conducted by a Kugelrohr apparatus BUCHI Glass Oven B-55. All low-temperature reactions were performed in a Siskin Profichill RFC-90 immersion cooler instrument. All reactions that required heating were conducted in an oil bath or aluminium-block under continuous stirring by a magnetic stirrer equipped with a hot plate and temperature controller. For thin-layer chromatography (TLC) analysis throughout this work, Macherey-Nagel pre-coated TLC plates (silica gel 60 F254 0.25 mm) were used.¹ Unless otherwise mentioned, all solvents including DMSO, DMF, Toluene and THF were dehydrated (dried) by standard techniques before use. Anhydrous DMSO, employed in this study, was degassed by freeze-thaw technique and subsequently, oxygenated by purging with molecular oxygen before use. All other solvents and commercially available compounds were used without further purification. The recrystallization of compound **3a** was performed by dissolving the compound in DCM and layered with hexane at -20 °C.

Preparation of aryl benzyl ketones and 1,3-diketones

Aryl benzyl ketones used in this study

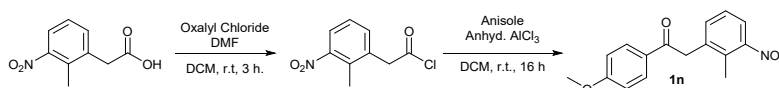


1,3- β -diketones used in this study



Substrate **1a** was commercially available. Substrates **1b–1m**, **1o–1u** were prepared by reported methods and characterized by matching their ^1H and ^{13}C NMR. Substrate **5a** was commercially available and **5b–5a'** were prepared by a reported method and characterized by matching their ^1H and ^{13}C NMR.⁶ Substrates **1n**, **1v–1z** and **5b'** were prepared as follows:

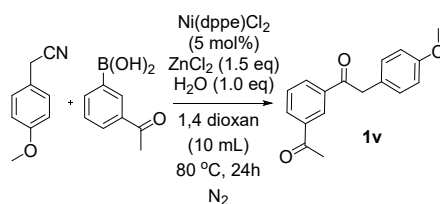
1-(4-methoxyphenyl)-2-(2-methyl-3-nitrophenyl)ethan-1-one (1n) was prepared according to a modified literature report.³



Step 1: A 100 mL round bottom flask, equipped with a magnetic bead and septum, was charged with 2-(2-methyl-3-nitrophenyl)acetic acid (1.95 g, 10 mmol, 1.0 eq). The flask was evacuated and backfilled with nitrogen (x 3). It was then placed in an ice bath followed by addition of dry DCM (38 mL) and 6-8 drops of DMF. To it, was added oxalyl chloride (1.65 g, 13 mmol, 1.3 eq). The reaction mixture was then stirred at room temperature for 3 h. The volatiles were evaporated under reduced pressure and the resulting crude acid chloride was subjected to the next step without further purification.

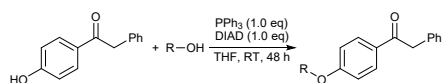
Step 2: A 100 mL RB flask equipped with a magnetic bar, was charged with anhydrous AlCl₃ (1.73 g, 13.0 mmol, 1.3 eq). The flask was evacuated and backfilled with nitrogen (x 3) and then placed in an ice bath (0 °C), followed by the addition of dry DCM (10 mL). Anisole 1.40 g, 13.0 mmol, 1.3 eq) was then dissolved in DCM (5 mL) and added to the above flask. To the resulting mixture, 2-(2-methyl-3-nitrophenyl)acetyl chloride (2.13 g, 10.0 mmol, 1.0 eq.), as obtained in step 1, in DCM (5 mL) was added dropwise. After 30 minutes, the ice bath was removed and the reaction was stirred further overnight at room temperature (monitored by TLC). After completion, the reaction mixture was poured into ice-cold water and stirred for 30 minutes. The aqueous part was then extracted with DCM (3 x 30 mL), the combined organic layers was washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuum. The residue was purified by flash column chromatography on silica gel to provide the desired aryl benzyl ketone **1n**. White solid (600 mg, 2.3 mmol, 23.5%). R_f = 0.5 (Hexane: Ether = 8:2). M.P = 86 °C. IR (KBr): ν = 3325, 2922, 2844, 1673, 1517, 828, 730 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 8.01 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.5 Hz, 2H), 4.38 (s, 2H), 3.89 (s, 3H), 2.33 (s, 3H) ppm. ¹³C NMR (151 MHz, CDCl₃): δ 194.6, 164.0, 151.4, 137.1, 134.8, 131.6, 130.7 (2C), 129.5, 126.4, 123.1, 114.1(2C), 55.7, 43.3, 15.6. HRMS (ESI): *m/z* calcd. for C₁₆H₁₆NO₄ [M + H]⁺, 286.1074, found 286.1079.

1-(3-acetylphenyl)-2-(4-methoxyphenyl)ethan-1-one (1v) was prepared according to a modified literature procedure.⁴

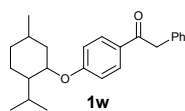


A 50 mL round-bottomed flask equipped with a stir bar was charged with 4-methoxy phenyl acetonitrile (5.0 mmol), 3-acetyl phenylboronic acid (2.0 equiv.), Ni(dppe)Cl₂ (5 mol%), ZnCl₂ (1.5 equiv.). The flask was evacuated and backfilled with nitrogen (x 3). Then H₂O (1.0 equiv.) and dioxane (10 mL) were added in turn to the round-bottomed flask through the rubber septum using syringes under nitrogen flow. The reaction mixture was allowed to stir for 24 h at 80 °C. After the mixture was cooled to room temperature, the reaction mixture was diluted with ethyl acetate, followed by filtration through a pad of silica gel with several washings. The filtrate was concentrated under reduced pressure and then purified by flash column chromatography on silica gel to afford the ketone **1v**. White Solid (0.5 g, 1.86 mmol, 37%). R_f = 0.5 (Hexane: Ether = 8:2). MP = 76 °C. IR ν = 3054, 2929, 2856, 2342, 1688, 1266, 733 cm⁻¹. ¹H NMR (600 MHz, CDCl₃) δ 8.57 (s, 1H), 8.19-8.18 (m, 1H), 8.14- 8.12 (m, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.20-7.18 (m, 2H), 6.88, 6.88- 6.86 (m, 2H), 4.27 (s, 2H), 3.78 (s, 3H), 2.64 (s, 3H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 197.4, 197.4, 158.8, 137.6, 137.0, 133.1, 132.6, 130.6, 129.2, 128.6, 126.1, 114.4, 55.4, 45.1, 26.8 ppm. HRMS (ESI): *m/z* calcd. for C₁₇H₁₇O₃ [M + H]⁺, 269.1158, found 269.1157.

Substrates (**1w-1z**) were prepared according to a modified literature procedure.⁵



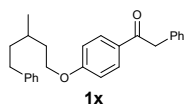
General Procedure A: A 100 mL round bottom flask equipped with a stir bar was charged with 1-(4-hydroxyphenyl)-2-phenylethan-1-one (0.637g, 3.0 mmol, 1.0 eq) and the corresponding alcohol (1.0 eq). The flask was evacuated and back-filled with nitrogen (x 3) and then placed in an ice bath (0 °C), followed by the addition of dry THF (0.1 M). Then PPh₃ (1.0 eq) and DIAD (1.0 eq) were added sequentially to it. The suspension was then stirred vigorously at room temperature for 48 h. The volatiles were then evaporated under reduced pressure and purified by column chromatography on silica gel.



1-(4-((2-isopropyl-5-methylcyclohexyl)oxy)phenyl)-2-phenylethan-1-one

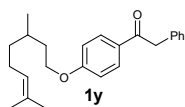
(1w) was prepared according to the general procedure **A** starting from 1-(4-hydroxyphenyl)-2-phenylethan-1-one (0.637g, 3.0 mmol, 1.0 eq) and 2-isopropyl-5-methylcyclohexan-1-ol (menthol) (469 mg, 3.0 mmol, 1.0 eq). Yield = 250 mg, 0.71 mmol, 24%. Yellow solid R_f = 0.5 (Hexane: Ether = 9:1). M.P = 68 °C. IR (KBr): ν = 2944, 2354, 1685, 1601, 1244 cm⁻¹. ¹H NMR (600 MHz, CDCl₃) δ 7.98 (d, *J* = 9.0 Hz, 2H) 7.33-7.22 (m, 5H), 6.91 (d, *J* = 8.4 Hz, 2H), 4.71(s, 1H), 4.22 (s, 2H), 2.09-2.06 (m, 1H), 1.79-1.74 (m, 2H), 1.66-1.60 (m, 2H), 1.59-1.53 (m, 1H), 1.09-1.01 (m, 2H), 0.98-0.94 (m, 1H),

0.92 (d, $J = 6.6$ Hz, 3H), 0.83-0.81 (q, $J = 6.6$ Hz, 6H) ppm. ^{13}C NMR (151 MHz,) δ 196.2, 162.6, 135.2, 131.2 (2C), 129.5 (2C), 129.2, 128.8 (2C), 126.9, 115.1 (2C), 73.83, 47.75, 45.32, 37.71, 34.97, 29.41, 26.33, 24.92, 22.34, 21.13, 20.87 ppm. HRMS (ESI): m/z calcd. For $\text{C}_{24}\text{H}_{31}\text{O}_2$ $[\text{M} + \text{H}]^+$, 351.2319, found, 351.2329.



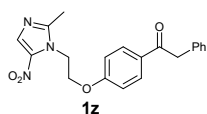
1-(4-((3-methyl-5-phenylpentyl)oxy)phenyl)-2-phenylethan-1-one (1x)

was prepared according to the general procedure A starting from 1-(4-hydroxyphenyl)-2-phenylethan-1-one (0.637g, 3.0 mmol, 1.0 eq) and 3-methyl-5-phenylpentan-1-ol (mefrosol) (535 mg, 3.0 mmol, 1.0 eq). Yield = 350 mg, 0.94 mmol, 31%. Yellow solid $R_f = 0.5$ (Hexane: Ether = 9:1). M.P = 50 °C. IR (KBr): $\nu = 2925$, 2356, 1682, 1600, 1258, 730 cm^{-1} . ^1H NMR (600 MHz, CDCl_3) δ 7.98-7.96 (m, 2H), 7.31-7.22, 7.17-7.15 (m, 3H), 6.89-6.87 (m, 2H), 4.20 (s, 2H), 4.06-3.99 (m, 2H), 2.70-2.65 (m, 1H), 2.62-2.57 (m, 1H), 1.91-1.85 (m, 1H), 1.73-1.63 (m, 3H), 1.53-1.51 (m, 1H), 1.01 (d, $J = 6.6$ Hz, 6H) ppm. ^{13}C NMR (151 MHz, CDCl_3) δ 196.3, 163.2, 142.7, 135.1, 131.0 (2C), 129.6, 129.5 (2C), 128.7 (2C), 128.4 (4C), 126.8, 125.8, 114.3 (2C), 66.50, 45.32, 38.92, 35.94, 33.39, 29.61, 19.63 ppm. HRMS (ESI): m/z calcd. For $\text{C}_{26}\text{H}_{29}\text{O}_2$ $[\text{M} + \text{H}]^+$, 373.2162, found, 373.2210.



1-(4-((3,7-dimethyloct-6-en-1-yl)oxy)phenyl)-2-phenylethan-1-one (1y)

was prepared according to the general procedure A starting from 1-(4-hydroxyphenyl)-2-phenylethan-1-one (0.637g, 3.0 mmol, 1.0 eq) and 3,7-Dimethyl-6-octen-1-ol (β -citronellol) (469 mg, 3.0 mmol, 1.0 eq). Yield = 210 mg, 0.6 mmol, 20 %. Yellow liquid. $R_f = 0.5$ (Hexane: Ether = 9:1). IR (neat): $\nu = 2931$, 2342, 1670, 1600, 1265 cm^{-1} . ^1H NMR (600 MHz, CDCl_3) δ 7.98-7.97 (m, 2H), 7.32-7.22 (m, 5H), 6.91 (d, $J = 9$ Hz, 2H), 5.10 (t, $J = 7.2$ Hz, 1H), 4.22 (s, 2H), 4.07-4.01(m, 2H), 2.07-1.95 (m, 2H), 1.87- 1.82 (m, 1H), 1.70-1.66 (m, 4H), 1.60 (s, 4H), 1.42-1.36 (m, 3H), 1.25-1.20 (m, 1H), 0.96 (d, $J = 6.6$ Hz, 3H) ppm. ^{13}C NMR (151 MHz, CDCl_3) δ 196.4, 163.3, 135.2, 131.5, 131.1(2C), 129.6, 129.5 (2C), 128.8 (2C), 126.9, 124.7, 114.4 (2C), 66.7, 45.4, 37.2, 36.1, 29.6, 25.9, 25.6, 19.7, 17.8. HRMS (ESI): m/z calcd. For $\text{C}_{24}\text{H}_{31}\text{O}_2$ $[\text{M} + \text{H}]^+$, 351.2319, found, 351.2361.

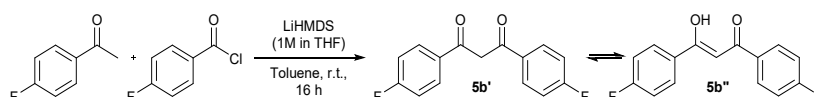


1-(4-(2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethoxy)phenyl)-2-phenylethan-1-

one (1z) was prepared according to the general procedure A starting from 1-(4-hydroxyphenyl)-2-phenylethan-1-one (0.637g, 3.0 mmol, 1.0 eq) and 2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethan-1-ol (Metronidazole) (513 mg, 3.0 mmol, 1.0 eq) for 96 h. Yield = 260 mg, 0.71 mmol, 24 %. White Solid. MP =125-130 °C. $R_f = 0.5$ (Hexane: EtOAc

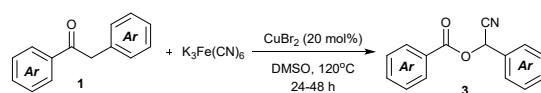
= 1:1). IR (neat): $\nu = 3129, 2936, 2363, 1677, 1186 \text{ cm}^{-1}$. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.96(t, $J = 4.8$ Hz, 3H), 7.30 (t, $J = 7.8$ Hz, 2H), 7.24 (d, $J = 7.2$ Hz, 3H), 6.84 (d, $J = 9$ Hz, 2H) 4.72 (t, $J = 4.8$ Hz, 2H), 4.37 (t, $J = 4.8$ Hz, 2H), 4.21 (s, 2H), 2.61 (s, 3H) ppm. $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 196.2, 161.6, 151.8, 138.5, 134.8, 133.5, 131.1(2C), 130.6, 129.5 (2C), 128.8 (2C), 127.0, 114.2 (2C), 66.9, 45.9, 45.4, 14.8 ppm. HRMS (ESI): m/z calcd. For $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}_4$ $[\text{M} + \text{H}]^+$, 366.1448, found, 366.1433.

(Z)-1,3-bis(4-fluorophenyl)-3-hydroxyprop-2-en-1-one (5b') was prepared according to a modified literature report.⁶



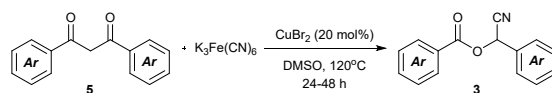
A 100 mL RB flask, equipped with a magnetic stirring bar and a septum, was charged with a solution of 1-(4-fluorophenyl)ethan-1-one (691 mg, 5 mmol, 1.0 eq) in dry THF (10 mL). The resulting solution was stirred at 0 °C for 30 min under N_2 atmosphere, followed by the dropwise addition of LiHMDS (7.5 mL, 7.5 mmol 1 M in THF, 1.5 eq) over 10 min via a syringe. After stirring at 0 °C for an additional 1 h, 4-fluorobenzoyl chloride (1.59 g, 10.0 mmol, 2.0 eq) was added in one portion. The reaction mixture was continued to stir for 5 min at 0 °C and then placed for stirring at room temperature for 16 h (the progress of the reaction was monitored by TLC) before being quenched with saturated NH_4Cl solution. The resulting suspension was dispersed into ethyl acetate (50 mL), extracted with ethyl acetate (30 mL x 3), washed with brine (25 mL x 2), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography to afford 1,3-bis(4-fluorophenyl)propane-1,3-dione **5b'** mainly in its enol form **5b''**. Yield = 0.8 g, 3.07 mmol, 62%. Colourless solid. $R_f = 0.5$ (Hexane: Ether = 9:1). M.P. = 110 °C. IR (KBr): $\nu = 3075, 2925, 1602, 1227, 782 \text{ cm}^{-1}$. $^1\text{H NMR}$ (600 MHz, CDCl_3): δ 16.77 (s, 1H), 7.90 – 7.86 (m, 4H), 7.07 – 7.03 (m, 4H), 6.63 (s, 1H) ppm. $^{13}\text{C NMR}$ (151 MHz, CDCl_3): δ 184.6, 166.4, 164.7, 131.8 (2C), 131.7, 129.7 (2C), 129.7 (2C) 116.0 (2C), 115.9 (2C), 92.6 ppm. $^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -105.94, -105.96, -105.97, -105.99 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{15}\text{H}_9\text{F}_2\text{O}_2$ $[\text{M} - \text{H}]^-$, 259.0565, found, 259.0559.

General procedure B: Copper catalysed transformation of aryl benzyl ketones to cyanohydrin esters with $\text{K}_3\text{Fe}(\text{CN})_6$



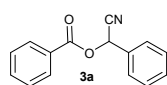
A 20 mL crimp cap vial was charged with aryl benzyl ketone **1** (0.5 mmol, 1.0 eq), copper (II) bromide (22 mg, 0.1 mmol, 0.2 eq), and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). The vial was then closed with the help of a crimper tool. The vessel was evacuated and backfilled with nitrogen (x 3). To it, oxygenated DMSO (0.5 mL) was added and the reaction mixture was stirred at 120 °C for the required time (the progress of the reaction was monitored by TLC). After cooling, the reaction mixture was diluted with ethyl acetate (10 mL) and washed with water (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 25 mL), and the organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuum. The residue was purified by flash column chromatography on silica gel to provide the corresponding cyanohydrin ester **3**.

General procedure C: Copper catalysed transformation of 1, 3-di-ketones to cyanohydrin esters with K₃Fe(CN)₆



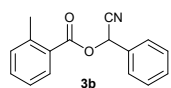
A 20 mL crimp cap vial was charged with a magnetic stirring bar, 1, 3-di-ketones **5** (0.5 mmol, 1.0 eq), copper (II) bromide (22 mg, 0.1 mmol, 0.2 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). The vial was then closed with the help of a crimper tool. The vessel was evacuated and backfilled with nitrogen (x 3). To it, oxygenated DMSO (0.5 mL) was added and the reaction mixture was stirred at 120 °C for the required time (the progress of the reaction was monitored by TLC). After cooling, the reaction mixture was diluted with ethyl acetate (10 mL) and washed with water (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 25 mL), and the organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuum. The residue was purified by flash column chromatography on silica gel to provide the corresponding cyanohydrin ester **3**.

Characterization of cyanohydrin esters:

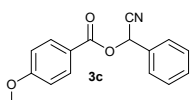


Cyano(phenyl)methyl benzoate (**3a**) was prepared according to the general procedure **B** or **C** starting from 2-phenylacetophenone **1a** (98 mg, 0.5 mmol, 1.0 eq) or 1,3-diphenylpropane-1,3-dione **5a** (137 mg, 0.5 mmol, 1.0 eq) respectively. Yield = 102 mg, 0.43 mmol, 86% (**B**); (97 mg, 0.41 mmol, 82% (**C**)). White solid. R_f = 0.5

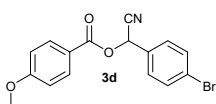
(Hexane:Ether = 9:1). All characterization data are in agreement with that as reported in the literature.⁷ ¹H NMR (600 MHz, CDCl₃): δ 8.09 (d, *J* = 7.8 Hz, 2H), 7.64-7.61 (m, 3H), 7.49-7.46 (m, 5H), 6.70 (s, 1H) ppm. ¹³C NMR (151 MHz, CDCl₃): δ 164.7, 134.2, 132.0, 130.5, 130.2 (2C), 129.4 (2C), 128.7 (2C), 128.2, 127.9 (2C), 116.3, 63.4 ppm.



cyano(phenyl)methyl 2-methylbenzoate (3b) was prepared according to the general procedure **B** by the reaction between 2-phenyl-1-(*o*-tolyl)ethan-1-one **1b** (105 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) or by the reaction between 2-phenyl-1-(*o*-tolyl)ethan-1-one **1b'** (105 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). Yield = 58 mg, 0.23 mmol, 46% from **1b**; 54 mg, 0.22 mmol, 43% from **1b'**. Yellow liquid. *R*_f = 0.5 (Hexane:Ether = 9:1). ¹H NMR (600 MHz, CDCl₃): δ 7.97-7.95 (m, 1H), 7.62-7.61 (m, 2H), 7.48-7.47 (m, 3H), 7.46-7.44 (m, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 5.4 Hz, 1H), 6.65 (s, 1H), 2.62 (s, 3H) ppm. ¹³C NMR (151 MHz, CDCl₃): δ 165.2, 141.6, 133.4, 132.2, 131.2, 130.5, 129.4 (2C), 128.0 (3C), 127.3, 126.1, 116.5, 63.2, 22.0 ppm. HRMS (ESI): *m/z* calcd. For C₁₆H₁₃NaNO₂ [M + Na]⁺, 247.0838, found, 274.0843.

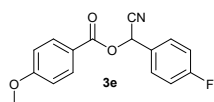


Cyano(phenyl)methyl 4-methoxybenzoate (3c) was prepared according to the general procedure **B** or **C** starting from 1-(4-methoxyphenyl)-2-phenylethan-1-one **1c** (113 mg, 0.5 mmol, 1.0 eq) using CuBr₂ (22 mg, 0.1 mmol, 0.2 eq) or 1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione **5b** (127 mg, 0.5 mmol, 1.0 eq) using CuBr₂ (17 mg, 0.075 mmol, 0.15 eq) respectively. Yield = 124 mg, 0.46 mmol, 93% (**B**); 122 mg, 0.46 mmol, 91% (**C**). Yellow liquid. *R*_f = 0.5 (Hexane: Ether = 9:1). All characterization data are in agreement with that as reported in the literature.⁸ ¹H NMR (600 MHz, CDCl₃): δ 8.03 (d, *J* = 8.4 Hz, 2H), 7.61(t, *J* = 3.0 Hz, 2H), 7.47 (t, *J* = 3.0 Hz, 3H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.67 (s, 1H), 3.87 (s, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃): δ 164.4, 132.4 (2C), 132.3, 130.4, 129.4 (2C), 127.9 (2C), 120.5, 116.5, 114.1 (3C), 63.2, 55.7 ppm.



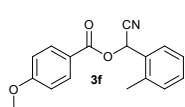
(4-Bromophenyl)(cyano)methyl 4-methoxybenzoate (3d) was prepared according to general procedure **B** by the reaction between 2-(4-bromophenyl)-1-(4-methoxyphenyl)ethan-1-one **1d** (152 mg, 0.5 mmol, 1.0

eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) for 72 h. Yield = 133 mg, 0.38 mmol, 77%. Yellow liquid. $R_f = 0.5$ (Hexane: Ether = 9:1). All characterization data are in agreement with that as reported in the literature.⁹ $^1\text{H NMR}$ (600 MHz, CDCl_3): δ 8.00 (d, $J = 9.0$ Hz, 2H), 7.61 (d, $J = 8.4$ Hz, 2H), 7.49 (d, $J = 8.4$ Hz, 2H), 6.95-6.93 (m, 2H), 6.62 (s, 1H), 3.87 (s, 3H) ppm. $^{13}\text{C NMR}$ (151 MHz, CDCl_3): δ 164.5, 164.3, 132.7, 132.4 (2C), 131.3, 129.6 (3C), 124.9, 120.2, 116.1, 114.1 (2C), 62.6, 55.7 ppm.



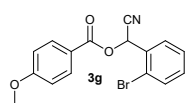
Cyano(4-fluorophenyl)methyl 4-methoxybenzoate (**3e**) was prepared

according to general procedure **B** by the reaction between 2-(4-fluorophenyl)-1-(4-methoxyphenyl)ethan-1-one **1e** (122 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). Yield = 117 mg, 0.41 mmol, 82%. White solid. $R_f = 0.5$ (Hexane: Ether = 9:1). MP = 160 °C. IR (KBr): $\nu = 2928, 2854, 2359, 1730, 195, 1267, 761$ cm^{-1} . $^1\text{H NMR}$ (600 MHz, CDCl_3): δ 8.01 (d, $J = 9$ Hz, 2H), 7.62-7.60 (m, 2H), 7.16 (t, $J = 8.5$ Hz, 2H), 6.94 (d, $J = 9.0$ Hz, 2H), 6.64 (s, 1H), 3.87 (s, 3H) ppm. $^{13}\text{C NMR}$ (151 MHz, CDCl_3): δ 164.9, 164.4 (d, $J = 22.7$ Hz), 162.9, 163.05, 132.4, 130.2 (d, $J = 9.1$ Hz), 128.3, 120.3, 116.6, 116.5, 116.4, 114.1, 62.5, 55.7 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{16}\text{H}_{13}\text{FNO}_3$ $[\text{M} + \text{H}]^+$, 286.0874, found 286.0877.



Cyano(o-tolyl)methyl 4-methoxybenzoate (**3f**) was prepared according to

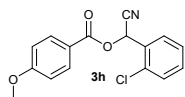
general procedure **B** by the reaction between 1-(4-methoxyphenyl)-2-(*o*-tolyl)ethan-1-one **1f** (120 mg, 0.5 mmol, 1.0 eq.) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). Yield = 73 mg, 0.305 mmol, 61%. Yellow solid. $R_f = 0.5$ (Hexane: Ether = 9:1). All characterization data are in agreement with that as reported in the literature.¹⁰ $^1\text{H NMR}$ (600 MHz, CDCl_3): δ 8.03-8.00 (m, 2H), 7.66 (d, $J = 7.5$, 1H), 7.38-7.35 (m, 1H), 7.31 (t, $J = 7.0$ Hz, 1H), 7.27 (d, $J = 9.5$ Hz, 1H), 6.95-6.92 (m, 2H), 6.67 (s, 1H), 3.87 (s, 3H), 2.49 (s, 3H) ppm. $^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 164.4, 164.4, 136.9, 132.4 (2C), 131.5, 130.6, 130.3, 128.7, 126.9, 120.5, 116.4, 114.1 (2C), 61.5, 55.7, 19.2. HRMS (ESI): m/z calcd. for $\text{C}_{17}\text{H}_{15}\text{NaNO}_3$ $[\text{M} + \text{Na}]^+$, 304.0944, found 304.0945.



(2-Bromophenyl)(cyano)methyl 4-methoxybenzoate (**3g**) was prepared

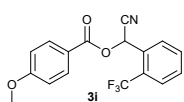
according to general procedure **B** by the reaction between 2-(2-bromophenyl)-1-(4-methoxyphenyl)ethan-1-one **1g** (153 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). Yield = 100 mg, 0.29 mmol, 58%. White solid. $R_f = 0.5$ (Hexane:

Ether = 9:1). MP = 112 °C. IR (KBr): ν = 3146, 2359, 1726, 1597, 753 cm^{-1} . ^1H NMR (600 MHz, CDCl_3): δ 8.04-8.02 (d, J = 9.0 Hz, 2H), 7.82-7.80 (m, 1H), 7.68-7.66 (m, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.37-7.35 (m, 1H), 6.95 (d, J = 9.0 Hz, 2H), 6.88 (s, 1H), 3.87 (s, 3H) ppm. ^{13}C NMR (151 MHz, CDCl_3): δ 164.5, 164.1, 133.7, 132.4 (2C), 131.9, 131.6, 129.7, 128.4, 123.3, 120.3, 115.7, 114.1 (2C), 63.0, 55.7 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{16}\text{H}_{13}\text{BrNO}_3$ [$\text{M} + \text{H}$] $^+$, 346.0073, found 346.0082.



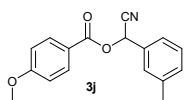
(2-Chlorophenyl)(cyano)methyl 4-methoxybenzoate (**3h**) was prepared according to general procedure **B** by the reaction between 2-(2-chlorophenyl)-

1-(4-methoxyphenyl)ethan-1-one **1h** (130 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) for 72 h. Yield = 98 mg, 0.33 mmol, 65%. Yellow solid. R_f = 0.5 (Hexane: Ether = 9:1). MP = 110 °C. IR (KBr): ν = 2922, 2846, 2291, 1733, 1250, 600 cm^{-1} . ^1H NMR (600 MHz, CDCl_3) δ 8.03 (d, J = 8.4 Hz, 2H), 7.80-7.79 (m, 1H), 7.49-7.47 (m, 1H), 7.43-7.41 (m, 2H), 6.95 (s, 1H), 6.93 (s, 1H), 6.92 (s, 1H), 3.87 (s, 3H) ppm. ^{13}C NMR (151 MHz, CDCl_3) δ 164.4, 164.1, 133.7, 132.4 (2C), 131.8, 130.5, 129.9, 129.6, 127.8, 120.2, 115.7, 114.1 (2C), 60.7, 55.7 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{16}\text{H}_{12}\text{ClNaNO}_3$ [$\text{M} + \text{Na}$] $^+$, 324.0398, found 324.0406.



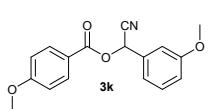
Cyano(2-(trifluoromethyl)phenyl)methyl 4-methoxybenzoate (**3i**) was prepared according to general procedure **B** by the reaction between 1-(4-methoxyphenyl)-2-(2-(trifluoromethyl)phenyl)ethan-1-one **1i** (147 mg, 0.5

mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). Yield = 107 mg, 0.32 mmol, 64%. Yellow liquid. R_f = 0.5 (Hexane: Ether = 9:1). IR (neat): ν = 3129, 2358, 1727, 1405, 775 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 8.03 (d, J = 6.5 Hz, 2H), 8.00 (s, 1H), 7.79-7.72 (m, 2H), 7.62 (t, J = 7.5 Hz, 1H), 6.94 (s, 1H), 6.93 (s, 1H), 6.91 (s, 1H), 3.86 (s, 3H), ppm. ^{13}C NMR (126 MHz, CDCl_3): δ 164.5, 164.0, 133.1, 132.4 (2C), 130.7, 130.3, 130.1, 128.5 (q, $J_{\text{C-F}}$ = 126.0 Hz), 126.9 (d, $J_{\text{C-F}}$ = 19.0 Hz), 123.7 (d, $J_{\text{C-F}}$ = 272.4 Hz), 120.14, 115.9, 114.1 (2C), 59.8, 55.7 ppm. ^{19}F NMR (565 MHz, CDCl_3): δ -58.75 ppm. HRMS (ESI): m/z calcd. For $\text{C}_{17}\text{H}_{13}\text{F}_3\text{NO}_3$ [$\text{M} + \text{H}$] $^+$, 336.0843, found 336.0842.



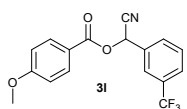
Cyano(*m*-tolyl)methyl 4-methoxybenzoate (**3j**) was prepared according to general procedure **B** by the reaction between 1-(4-methoxyphenyl)-2-(*m*-

tolyl)ethan-1-one **1j** (120 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). Yield = 90 mg, 0.32 mmol, 64%. Yellow liquid. $R_f = 0.5$ (Hexane: Ether = 9:1). IR (neat): $\nu = 3057, 2935, 2841, 2309, 1726, 1252, 741 \text{ cm}^{-1}$. $^1\text{H NMR}$ (600 MHz, CDCl_3): $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.94 (d, $J = 8.4 \text{ Hz}$, 2H), 7.32 (d, $J = 10.2 \text{ Hz}$, 2H), 7.27 (t, $J = 7.2 \text{ Hz}$, 1H), 7.19 (t, $J = 7.2 \text{ Hz}$, 1H), 6.86 (d, $J = 8.4 \text{ Hz}$, 2H), 6.55 (s, 1H), 3.79 (s, 3H), 2.33 (s, 3H) ppm. $^{13}\text{C NMR}$ (151 Hz, CDCl_3): δ 164.5, 164.4, 139.4, 132.4 (2C), 132.1, 131.2, 129.3, 128.6, 125.1, 120.6, 116.6, 114.1 (2C), 63.2, 55.7, 21.5 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{17}\text{H}_{16}\text{NO}_3$ $[\text{M} + \text{H}]^+$, 282.1125, found 282.1119.



Cyano(3-methoxyphenyl)methyl 4-methoxybenzoate (**3k**) was prepared according to general procedure **B** by the reaction between 2-(3-methoxyphenyl)-1-(4-methoxyphenyl)ethan-1-one-methane **1k** (128 mg,

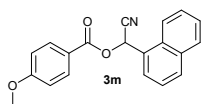
0.5 mmol, 1.0 eq.) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). Yield = 107 mg, 0.36 mmol, 72%. Yellow liquid. $R_f = 0.5$ (Hexane: Ether = 8:2). IR (neat): $\nu = 3057, 2932, 2355, 1732, 1260, 736 \text{ cm}^{-1}$. $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 8.04-8.02 (m, 2H), 7.38 (t, $J = 8.0 \text{ Hz}$, 1H), 7.18 (d, $J = 7.5 \text{ Hz}$, 1H), 7.12 (t, $J = 2.0 \text{ Hz}$, 1H), 7.01-6.98 (m, 1H), 6.94 (d, $J = 9.0 \text{ Hz}$, 2H), 6.63 (s, 1H), 3.87 (s, 3H), 3.85 (s, 3H) ppm. $^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 164.4, 160.3, 133.5, 132.5 (2C), 132.4, 130.5, 120.5, 120.1, 116.5, 116.0, 114.1(2C), 113.4, 63.1, 55.7, 55.6 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{17}\text{H}_{15}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$, 320.0894, found 320.0895.



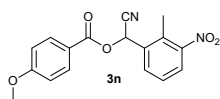
Cyano(3-(trifluoromethyl)phenyl)methyl 4-methoxy benzoate (**3l**) was prepared according to general procedure **B** by the reaction between 1-(4-methoxyphenyl)-2-(3-(trifluoromethyl)phenyl)ethan-1-one **1l** (147 mg, 0.5 mmol, 1.0 eq) and

potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) for 72 h. Yield = 122 mg, 0.37 mmol, 73%. Yellow liquid. $R_f = 0.5$ (Hexane: Ether = 9:1). IR (neat): $\nu = 3052, 2356, 1730, 1264, 739 \text{ cm}^{-1}$. $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 8.03 (d, $J = 9.0 \text{ Hz}$, 2H), 7.87 (s, 1H), 7.83 (d, $J = 7.5 \text{ Hz}$, 1H), 7.75 (d, $J = 7.5 \text{ Hz}$, 1H), 7.63 (t, $J = 7.5 \text{ Hz}$, 1H), 6.95 (d, $J = 9 \text{ Hz}$, 2H), 6.72 (s, 1H), 3.88 (s, 3H) ppm. $^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 164.6, 164.2, 133.3, 132.5 (2C), 132.0 (d, $J_{\text{C-F}} = 33.14 \text{ Hz}$), 131.3, 130.1, 127.3, 124.8, 122.5, 120.0, 115.9, 114.2 (2C), 62.5, 55.7 ppm. ^{19}F

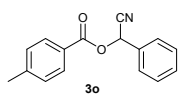
NMR (565 MHz, CDCl₃): δ -62.7 ppm. HRMS (ESI): m/z calcd. for C₁₇H₁₃F₃NO₃ [M + H]⁺, 336.0842, found 336.0840.



Naphthalen-1-yl)methyl 4-methoxybenzoate (3m) was prepared according to general procedure **B** by the reaction between (4-methoxyphenyl)(naphthalen-1-yl)ethanone **1m** (138 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 98 mg, 0.31 mmol, 62%. Light Yellow liquid. R_f = 0.5 (Hexane: Ether = 9:1). IR (neat): ν = 2929, 2351, 1664, 1263, 605 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 8.15 (d, J = 8.4 Hz, 1H), 8.00 (t, J = 9 Hz, 3H), 7.95 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 6.6 Hz, 1H), 7.64 (t, J = 8.4 Hz, 1H), 7.58 (t, J = 7.8 Hz, 1H), 7.55 (t, J = 7.8 Hz, 1H), 7.24 (s, 1H), 6.91 (d, J = 8.4 Hz, 2H), 3.85 (3H) ppm. ¹³C NMR (151 MHz, CDCl₃): δ 164.5, 164.4, 134.2, 132.5 (2C), 131.7, 130.4, 129.3, 127.9, 127.8, 127.5, 126.8, 125.3, 122.9, 120.4, 116.5, 114.1 (2C), 61.9, 55.7 ppm. HRMS (ESI): m/z calcd. for C₂₀H₁₅NaNO₃ [M + H]⁺, 340.0944, found 340.0950.

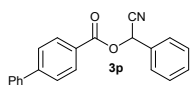


Cyano(2-methyl-3-nitrophenyl)methyl 4-methoxybenzoate (3n) was prepared according to general procedure **B** by the reaction between 1-(4-methoxyphenyl)-2-(2-methyl-3-nitrophenyl)ethan-1-one **1n** (136 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq.). Yield = 99 mg, 0.29 mmol, 57%. Yellow solid. R_f = 0.5 (Hexane: Ether = 8:2). MP = 74 °C. IR (KBr): ν = 3102, 2924, 2362, 1726, 1252, 765 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.03-8.00 (m, 2H), 7.93-7.88 (m, 2H), 7.49 (t, J = 8 Hz, 1H), 6.97-6.94 (m, 2H), 6.82 (s, 1H), 3.89 (s, 3H), 2.61 (s, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ 164.7, 164.0, 151.8, 133.3, 132.7, 132.5 (2C), 131.5, 127.6, 126.1, 119.8, 115.6, 114.3 (2C), 61.0, 55.7, 15.0. HRMS (ESI): m/z calcd. for C₁₇H₁₄N₂NaO₅ [M + Na]⁺, 327.0975, found 327.0981.

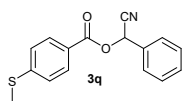


Cyano(phenyl)methyl 4-methylbenzoate (3o) was prepared according to general procedure **B** or **C** starting from 2-phenyl-1-(*p*-tolyl)ethan-1-one **1o** (105 mg, 0.5 mmol, 1.0 eq) or 1-phenyl-3-(*p*-tolyl)propane-1,3-dione **5c** (119 mg, 0.5 mmol, 1.0 eq) respectively. Yield = 106 mg, 0.42 mmol, 84% (**B**); 106 mg, 0.42 mmol, 84% (**C**). Yellow liquid. IR (neat): ν = 3147, 2925, 2340, 1727, 1259, 765 cm⁻¹. R_f = 0.5 (Hexane: Ether

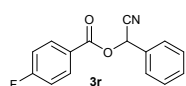
= 8:2). ¹H NMR (600 MHz, CDCl₃) δ 7.96-7.95 (m, 2H), 7.62-7.60 (m, 2H), 7.48-7.46 (m, 3H), 7.25 (d, *J* = 7.8 Hz, 2H), 6.66 (s, 1H), 2.41 (s, 3H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 164.8, 145.2, 132.1, 130.5, 130.2 (2C), 129.5 (2C), 129.4 (2C), 127.9 (2C), 125.4, 116.4, 63.3, 21.9 ppm. HRMS (ESI): *m/z* calcd. for C₁₆H₁₄NO₂ [M + H]⁺, 252.1019, found 252.1022.



Cyano(phenyl)methyl [1,1'-biphenyl]-4-carboxylate (3p) was prepared according to general procedure **B** by the reaction between [1,1'-biphenyl]-4-yl(phenyl)ethanone **1p** (136 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 118 mg, 0.38 mmol, 75%. Orange solid. *R_f* = 0.5 (Hexane: Ether = 9:1). MP = 120 °C. IR (KBr): *ν* = 3138, 2952, 2357, 1730, 1257, 709 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 8.14-8.13 (m, 2H), 7.69-7.68 (m, 2H), 7.65-7.61 (m, 4H), 7.49-7.48 (m, 3H), 7.46 (s, 2H), 7.41(t, *J* = 7.8 Hz, 1H), 6.70 ppm (s, 1H). ¹³C NMR (151 MHz, CDCl₃): δ 164.7, 147.1, 139.8, 132.1, 130.8 (2C), 130.6, 129.5 (2C), 129.2 (2C), 128.6, 128.0 (2C), 127.5 (4C), 126.9, 116.4, 63.5 ppm. HRMS (ESI): *m/z* calcd. for C₂₁H₁₆NO₂ [M + H]⁺, 314.1176, found 314.1182.

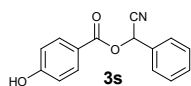


Cyano(phenyl)methyl 4-(methylthio)benzoate (3q) was prepared according to general procedure **B** by the reaction between (4-(methylthio)phenyl)(phenyl)ethanone **1q** (121 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 91 mg, 0.32 mmol, 64%. Yellow liquid. *R_f* = 0.5 (Hexane: Ether = 9:1). IR (neat): *ν* = 2918, 2351, 1726, 1262, 753 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 7.96-7.94 (m, 2H), 7.62-7.60 (m, 2H), 7.48 (t, *J* = 3.6 Hz, 3H), 7.27 (s, 1H), 7.25 (s, 1H), 6.66 (s, 1H), 2.51 (s, 3H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 164.5, 147.6, 132.1, 130.5, 130.5 (2C), 129.5 (2C), 128.0 (2C), 125.1 (2C), 124.1, 116.4, 63.4, 14.9 ppm. HRMS (ESI): *m/z* calcd. for C₁₆H₁₄NO₂S [M + H]⁺, 284.0740, found 284.0744.

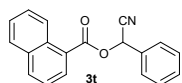


Cyano(phenyl)methyl 4-fluorobenzoate (3r) was prepared according to general procedure **B** or **C** starting from 1-(4-fluorophenyl)(phenyl)ethanone **1r** (107 mg, 0.5 mmol, 1.0 eq) using CuBr₂ (22 mg, 0.1 mmol, 0.2 eq) for 72 h or 1-(4-fluorophenyl)-3-phenylpropane-1,3-dione **5e** (121 mg, 0.5 mmol, 1.0 eq) using CuBr₂ (17 mg, 0.075 mmol, 0.15 eq) respectively. Yield = 50 mg, 0.19 mmol, 39% (**B**); 92 mg, 0.36 mmol, 72% (**C**). Yellow liquid. *R_f* = 0.5 (Hexane: Ether = 9:1). All characterization data are in

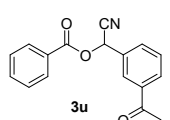
agreement with that as reported in the literature.¹¹ ¹H NMR (600 MHz, CDCl₃): δ 8.10-8.08 (m, 2H), 7.62-7.60 (m, 2H), 7.49-7.47 (m, 3H), 7.15-7.12 (m, 2H), 6.66 (s, 1H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 167.4, 165.7, 163.8, 132.9 (d, *J*_{C-F} = 9.4 Hz), 131.9, 130.6, 130.2, 129.5 (2C), 128.8, 128.0 (2C), 124.5, 116.1 (d, *J*_{C-F} = 22.2 Hz), 63.6 ppm. ¹⁹F NMR (565 MHz, CDCl₃): δ -103.01, -103.03, -103.05 ppm.



cyano(phenyl)methyl 4-hydroxybenzoate (3s) was prepared according to general procedure **B** starting from 1-(4-hydroxyphenyl)-2-phenylethan-1-one **1s** (106 mg, 0.5 mmol, 1.0 eq). Yield = 84 mg, 0.33 mmol, 66%. Yellow liquid. *R*_f = 0.5 (Hexane: EtOAc = 8:2). IR (neat): ν = 3396, 2923, 2854, 2365, 1721, 1261 cm⁻¹. ¹H NMR (600 MHz, CDCl₃) δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.61-7.59 (m, 2H), 7.47 (t, *J* = 3 Hz, 3H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.65 (s, 1H), 6.16 (s, 1H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 164.5, 161.2, 132.7 (2C), 132.1, 130.5, 129.4 (2C), 127.9 (2C), 120.5, 116.5, 115.7 (2C), 63.3 ppm. HRMS (ESI): *m/z* calcd. for C₁₅H₁₂NO₃ [M + H]⁺, 254.0812, found 254.0810.

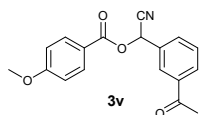


Cyano(phenyl)methyl 1-naphthoate (3t) was prepared according to general procedure **B** by the reaction between 1-(naphthalen-2-yl)-2-phenylethan-1-one **1t** (123 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq). Yield = 59 mg, 0.20 mmol, 41%. Yellow solid. *R*_f = 0.5 (Hexane: Ether = 9:1). All characterization data are in agreement with that as reported in the literature.¹² ¹H NMR (600 MHz, CDCl₃): δ 8.96 (d, *J* = 9.0 Hz, 1H), 8.28-8.27 (m, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.68-7.64 (m, 3H), 7.58-7.56 (t, *J* = 7.8 Hz, 1H), 7.52-7.49 (m, 4H), 6.77 (s, 1H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 165.2, 135.0, 134.0, 132.1, 131.7, 131.5, 130.6, 129.5 (2C), 128.9, 128.6, 128.1 (2C), 126.7, 125.6, 124.6, 124.5, 116.5, 63.4 ppm.

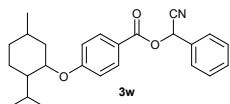


(3-acetylphenyl)(cyano)methyl benzoate (3u) was prepared according to general procedure **B** by the reaction between 1-(3-acetylphenyl)-2-phenylethan-1-one **1u** (114 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 110 mg, 0.39 mmol, 79%. White solid. *R*_f = 0.5 (Hexane: Ether = 6:4). MP = 92 °C. IR (KBr): ν = 3073, 2948, 2843, 2364, 1730, 1224, 1739, 1266 cm⁻¹. ¹H NMR (600 MHz, CDCl₃): δ 8.20 (s, 1H), 8.08 - 8.06 (m, 3H), 7.85, 7.84 (d, *J* = 7.2 Hz,

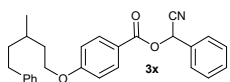
1H), 7.63-7.60 (m, 2H), 7.49-7.47 (m, 2H) 6.72 (d, $J = 8.4$ Hz, 1H) 2.65 (s, 3H) ppm. ^{13}C NMR (151 MHz, CDCl_3) δ 197.0, 164.7, 138.2, 134.4, 132.8, 132.3, 130.4, 130.3 (2C), 129.9, 128.9 (2C), 127.8, 116.3, 116.0, 63.1, 26.8 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{17}\text{H}_{14}\text{NO}_3$ [$\text{M} + \text{H}$] $^+$ 279.0923, found 279.0922.



(3-acetylphenyl)(cyano)methyl 4-methoxybenzoate (**3v**) was prepared according to general procedure **A** by the reaction between 1-(3-acetylphenyl)-2-(4-methoxyphenyl)ethan-1-one **1v** (134 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 121 mg, 0.38 mmol, 78%. Yellow liquid. $R_f = 0.5$ (Hexane: Ethyl Acetate = 8:2). IR (neat): $\nu = 3440, 2959, 2927, 2363, 1725, 1607, 1427, 1087, 1266$ cm^{-1} . ^1H NMR (600 MHz, CDCl_3) δ 8.18 (s, 1H), 8.06-8.01 (m, 4H), 7.83 (d, $J = 7.83$ Hz, 1H), 7.60 (t, $J = 7.8$ Hz, 1H), 6.96-6.93 (m, 2H), 6.71 (s, 1H), 3.88 (s, 3H), 2.65 (s, 3H) ppm. NMR (151 MHz, CDCl_3) δ 197.0, 164.6, 164.3, 138.2, 133.1, 132.5 (2C), 132.30, 130.3, 129.9, 127.7, 120.2, 116.2, 114.2 (2C), 62.8, 55.7, 26.8 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{18}\text{H}_{16}\text{NO}_4$ [$\text{M} + \text{H}$] $^+$ 310.1074, found 310.1074.

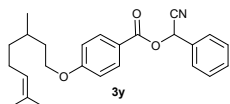


cyano(phenyl)methyl 4-((2-isopropyl-5-methylcyclohexyl)oxy)benzoate (**3w**) was prepared according to general procedure **B** by the reaction between 1-(4-((2-isopropyl-5-methylcyclohexyl)oxy)phenyl)-2-phenylethan-1-one (**1w**) (175 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 125 mg, 0.32 mmol, 64%. Yellow liquid. $R_f = 0.5$ (Hexane: Ether = 9:1). IR (neat): $\nu = 3055, 2988, 2360, 1734, 1717, 1508$ cm^{-1} . ^1H NMR (600 MHz, CDCl_3) δ 8.01-7.99 (m, 2H), 7.61-7.59 (m, 2H), 7.47 (t, $J = 3.6$ Hz, 3H), 6.92 (d, $J = 9$ Hz, 2H), 6.67 (s, 1H), 4.72 (s, 1H), 2.08-2.05 (m, 1H), 1.80-1.75 (m, 2H), 1.66-1.61 (m, 2H), 1.08-1.02 (m, 2H), 0.96-0.94 (m, 1H), 0.92 (d, $J = 6.6$ Hz, 3H), 0.84-0.81 (q, $J = 4.2$ Hz, 6H) ppm. ^{13}C NMR (151 MHz, CDCl_3) δ 164.5, 163.4, 132.5 (2C), 132.4, 130.4, 129.4 (2C), 127.9 (2C), 119.7, 116.6, 115.3 (2C), 74.1, 63.1, 47.7, 37.67, 35.0, 29.4, 26.3, 24.9, 22.3, 21.1, 20.8 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{25}\text{H}_{30}\text{NO}_3$ [$\text{M} + \text{H}$] $^+$ 392.2220, found 392.2203.



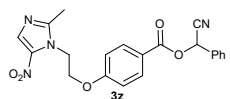
cyano(phenyl)methyl 4-((3-methyl-5-phenylpentyl)oxy)benzoate (**3x**) was prepared according to general procedure **B** by the reaction between 1-(4-

((3-methyl-5-phenylpentyl)oxy)phenyl)-2-phenylethan-1-one (**1x**) (186 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 141 mg, 0.34 mmol, 68%. Colourless liquid. $R_f = 0.5$ (Hexane: Ether = 8:1). IR (neat): $\nu = 3055, 2933, 2358, 1730, 1606, 1265, 704 \text{ cm}^{-1}$. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.00 (d, $J = 9\text{ Hz}$, 2H), 7.61- 7.60 (m, 2H), 7.47 (t, $J = 3.2 \text{ Hz}$, 3H), 7.27 (t, $J = 7.8 \text{ Hz}$, 2H), 7.18 (d, $J = 6.6 \text{ Hz}$, 3H) 6.90 (d, $J = 8.4 \text{ Hz}$, 2H), 6.66 (s, 1H), 4.09-4.02 (m, 2H), 2.72-2.67 (m, 1H), 2.63-2.58 (m, 1H), 1.93-1.87 (m, 1H), 1.77-1.63 (m, 4H), 1.55-1.51 (m, 1H), 1.02 (d, $J = 6.6 \text{ Hz}$, 3H) ppm. $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 164.5, 164.0, 142.7, 132.4 (2C), 132.3, 130.4, 129.4 (2C), 128.5 (4C), 128.0 (2C), 125.9, 120.3, 116.5, 114.6 (2C), 66.7, 63.2, 39.0, 36.0, 33.4, 29.6, 19.7 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{27}\text{H}_{28}\text{NO}_3$ $[\text{M} + \text{H}]^+$ 414.2064, found 414.2049.



cyano(phenyl)methyl 4-((3,7-dimethyloct-6-en-1-yl)oxy)benzoate (**3y**)

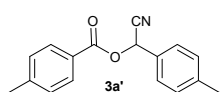
was prepared according to general procedure **B** by the reaction between 1-(4-((3,7-dimethyloct-6-en-1-yl)oxy)phenyl)-2-phenylethan-1-one (**1y**) (175 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 111 mg, 0.285 mmol, 57%. Colourless liquid. $R_f = 0.5$ (Hexane: Ether = 8:1). IR (neat): $\nu = 2931, 2342, 1670, 1600, 1265 \text{ cm}^{-1}$. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.00 (d, $J = 9 \text{ Hz}$, 2H), 7.62-7.60 (m, 2H), 7.47 (t, $J = 3.6 \text{ Hz}$, 3H), 6.92 (d, $J = 9 \text{ Hz}$, 2H), 6.66 (s, 1H), 5.10 (t, $J = 7.2 \text{ Hz}$, 1H), 4.07-4.03 (m, 2H), 2.04-1.97 (m, 3H), 1.87-1.84 (m, 1H), 1.68 (s, 3H), 1.60 (s, 3H), 1.41-1.37 (m, 1H), 1.26-1.20 (m, 2H), 0.96 (d, $J = 6.6 \text{ Hz}$, 3H) ppm. $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 164.5, 164.0, 132.4 (2C), 132.3, 131.6, 130.4, 129.4 (2C), 128.0 (2C), 124.7, 120.2, 116.547, 114.6 (2C), 66.8, 63.2, 37.2, 36.0, 29.6, 25.9, 25.6, 19.7, 17.8 ppm. HRMS (ESI): m/z calcd. for $\text{C}_{25}\text{H}_{30}\text{NO}_3$ $[\text{M} + \text{H}]^+$ 392.2220, found 392.2206.



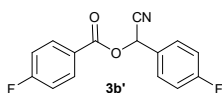
cyano(phenyl)methyl 4-(2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethoxy)benzoate (**3z**)

was prepared according to general procedure **B** by the reaction between 1-(4-(2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethoxy)phenyl)-2-phenylethan-1-one (**1z**) (183 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329, 1.0 mmol, 2.0 eq). Yield = 130 mg, 0.32 mmol, 64%. Yellow liquid. $R_f = 0.5$ (Hexane: EtOAc = 1:1). IR (neat): $\nu = 2955, 2926, 2853, 2254, 1732, 1508, 910 \text{ cm}^{-1}$. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.99 (d, $J = 9 \text{ Hz}$, 2H), 7.98 (s, 1H), 7.61- 7.60 (m, 2H), 7.48 (t, $J = 3 \text{ Hz}$, 3H), 6.86 (d, $J = 8.4 \text{ Hz}$, 2H), 6.65 (s, 1H) (t, $J = 4.8 \text{ Hz}$, 2H), 4.40 (t, $J = 4.8 \text{ Hz}$, 2H), 2.63 (s, 3H), ppm. $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 164.2, 162.4, 151.8, 133.5, 132.6 (2C), 132.1, 130.5, 129.4 (2C), 128.8, 128.0

(2C), 121.6, 116.3, 114.4 (2C), , 67.0, 63.4, 45.9, 14.8 ppm. HRMS (ESI): m/z calcd. for $C_{21}H_{19}N_4O_5$ $[M + H]^+$ 407.1350, found 407.1340.

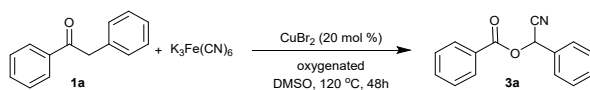


Cyano(p-tolyl)methyl 4-methylbenzoate (3a') was prepared according to general procedure C by the reaction between (*Z*)-3-hydroxy-1,3-di-*p*-tolylprop-2-en-1-one **5a'** (126 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) for 72 h. Yield = 93 mg, 0.25 mmol, 70%. Yellow solid. R_f = 0.5 (Hexane: Ether = 9:1). All characterization data are in agreement with that as reported in the literature.¹³ 1H NMR (600 MHz, $CDCl_3$): δ 7.86(d, J = 7.2 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.20-7.16 (m, 4H), 6.55 (s, 1H), 2.33 (s, 3H), 2.31 (s, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.8, 145.1, 140.7, 130.3 (2C), 130.0 (2C), 129.5 (2C), 129.2, 128.0 (2C), 125.6, 116.6, 63.2, 21.9, 21.4 ppm.



Cyano(4-fluorophenyl)methyl 4-fluorobenzoate (3b') was prepared according to general procedure C by the reaction between (*Z*)-1,3-bis(4-fluorophenyl)-3-hydroxyprop-2-en-1-one **5b'** (130 mg, 0.5 mmol, 1.0 eq) and potassium ferricyanide (329 mg, 1.0 mmol, 2.0 eq) for 72 h. Yield = 100 mg, 0.37 mmol, 73%. Yellow solid. R_f = 0.5 (Hexane: Ether = 9:1). IR (neat): ν = 3076, 2920, 2220, 1738, 1247, 765 cm^{-1} . 1H NMR (600 MHz, $CDCl_3$): δ 8.10-8.07 (m, 2H), 7.63-7.61 (m, 2H), 7.19-7.13 (m, 4H), 6.64 (s, 1H), ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.5, 165.3 (d, J = 141.6 Hz), 163.7, 163.2, 133.0 (d, J_{C-F} = 9.2 Hz, 2C), 130.3 (d, J_{C-F} = 8.6 Hz, 2C), 127.9, 124.4, 116.7 (d, J_{C-F} = 22.7 Hz, 2C), 116.2 (d, J_{C-F} = 22.3 Hz, 2C), 63.0 ppm. ^{19}F NMR (565 MHz, $CDCl_3$): δ -102.2, -102.2, -108.6, -108.6 ppm. HRMS (ESI): m/z calcd. for $C_{15}H_9F_2NNaO_2$ $[M + Na]^+$, 296.0494, found 296.0511.

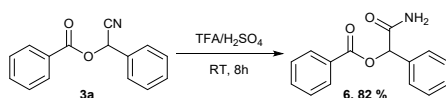
Representative procedure for the gram-scale synthesis of 3a



A 50 mL round bottom flask equipped with a stirring bar and septum, was charged with **1a** (1.5 g, 7.64 mmol, 1.0 eq), copper (II) bromide (341 mg, 1.53 mmol, 0.2 eq), and potassium

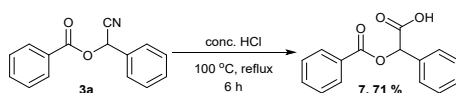
ferricyanide (5.3 g, 15.28 mmol, 2.0 eq). The RB flask was evacuated and back-filled with nitrogen (x 3). To it, oxygenated DMSO (8 mL) was added and the reaction mixture was stirred at 120 °C for the required time (the progress of the reaction was monitored by TLC). After cooling, the reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (20 mL). The aqueous layer was extracted with ethyl acetate (3 x 25 mL), and the organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuum. The residue was purified by flash column chromatography on silica gel to provide the corresponding cyanohydrin ester **3a** (1.45g, 6.1 mmol, 80%).

Conversion of **3a** to 2-amino-2-oxo-1-phenylethyl benzoate (**6**)



A 20 mL reaction tube equipped with a stirring bar and septum, was charged with **3a** (95 mg, 0.4 mmol), trifluoroacetic acid TFA (420 μL) and conc. H₂SO₄ (140 μL). The reaction was allowed to stir for 8 h at room temperature (TLC). After completion, the reaction mixture was poured into ice-cold water (5.0 mL). The resulting mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuum. The residue was purified by flash column chromatography on silica-gel to provide the corresponding amide **6**. Yield = 82 mg, 0.32 mmol, 82%. White solid. R_f = 0.5 (Hexane:EtOAc = 8:2). All characterization data are in agreement with that as reported in the literature.¹³ ¹H NMR (600 MHz, DMSO): δ 8.09-8.07 (m, 2H), 7.83 (s, 1H), 7.70-7.67 (m, 1H), 7.62-7.60 (m, 2H), 7.57-7.54 (m, 2H), 7.45-7.42 (m, 2H), 7.40-7.37 (m, 1H), 7.34 (s, 1H), 6.04 (s, 1H) ppm. ¹³C NMR (151 MHz, DMSO): δ 169.7, 165.0, 136.0, 133.7, 129.5 (2C), 129.2, 128.8 (2C), 128.6, 128.5 (2C), 127.2 (2C), 75.7 ppm.

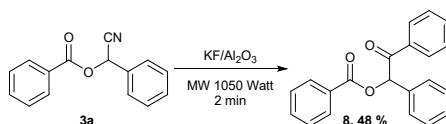
Conversion of **3a** to 2-(benzoyloxy)-2-phenylacetic acid (**7**)



A 20 mL reaction tube equipped with a magnetic stirring bar and condenser, was charged with **3a** (143 mg, 0.6 mmol) and conc. hydrochloric acid (1.0 mL). The reaction mixture was

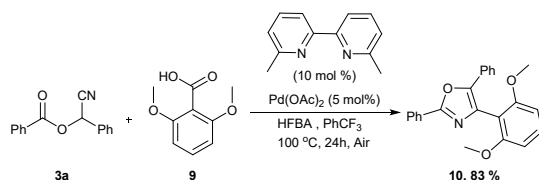
refluxed at 100 °C, for 6 h (TLC). After completion, the reaction mixture was poured into water (10 mL). The resulting mixture was extracted with EtOAc (3 x 15 mL) and the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuum. The residue was purified by flash column chromatography on silica-gel to provide the corresponding carboxylic acid **7**. Yield = 109 mg, 0.42 mmol, 71%. White solid. R_f = 0.5 (Hexane:EtOAc = 8:2). All characterization data are in agreement with that as reported in the literature.¹⁴ ¹H NMR (600 MHz, CDCl₃) δ 9.29 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.61-7.58 (m, 3H), 7.47-7.41 (m, 5H), 6.18 (s, 1H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 174.5, 166.0, 133.1, 133.5, 130.1 (2C), 129.6, 129.1 (2C), 129.1, 128.6 (2C), 127.8 (2C), 74.6 ppm.

Conversion of **3a** to 2-oxo-1,2-diphenylethyl benzoate (**8**)



A 100 mL round bottom flask equipped with a stirrer bar, was charged with **3a** (118 mg, 0.5 mmol) and potassium fluoride on alumina (250 mg). The reaction mixture was heated in a microwave oven at 1050 watt for 2 min. After completion, the reaction mixture was diluted with ethyl acetate (10 mL). The resulting mixture was filtered and solid residue was washed with EtOAc (3 x 10 mL). The combined organic layers were extracted with EtOAc (3 x 15 mL) and water (10 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuum. The residue was purified by flash column chromatography on silica-gel to provide the corresponding ketone **8**. Yield = 76 mg, 0.24 mmol, 48%. White solid. R_f = 0.5 (Hexane:Ether = 9.1). All characterization data are in agreement with that as reported in the literature.¹⁵ ¹H NMR (600 MHz, CDCl₃): δ 8.14-8.12 (m, 2H), 8.02-8.00 (m, 2H), 7.59-7.56 (m, 3H), 7.55-7.52 (m, 1H), 7.46-7.36 (m, 7H), 7.10 (s, 1H) ppm. ¹³C NMR (151 MHz, CDCl₃): δ 193.9, 166.2, 134.9, 133.9, 133.6, 133.5, 130.1 (2C), 129.6, 129.5, 129.3 (2C), 129.0 (2C), 128.8 (4C), 128.6 (2C), 78.1 ppm.

Synthesis of functionalized oxazoles (**10**)



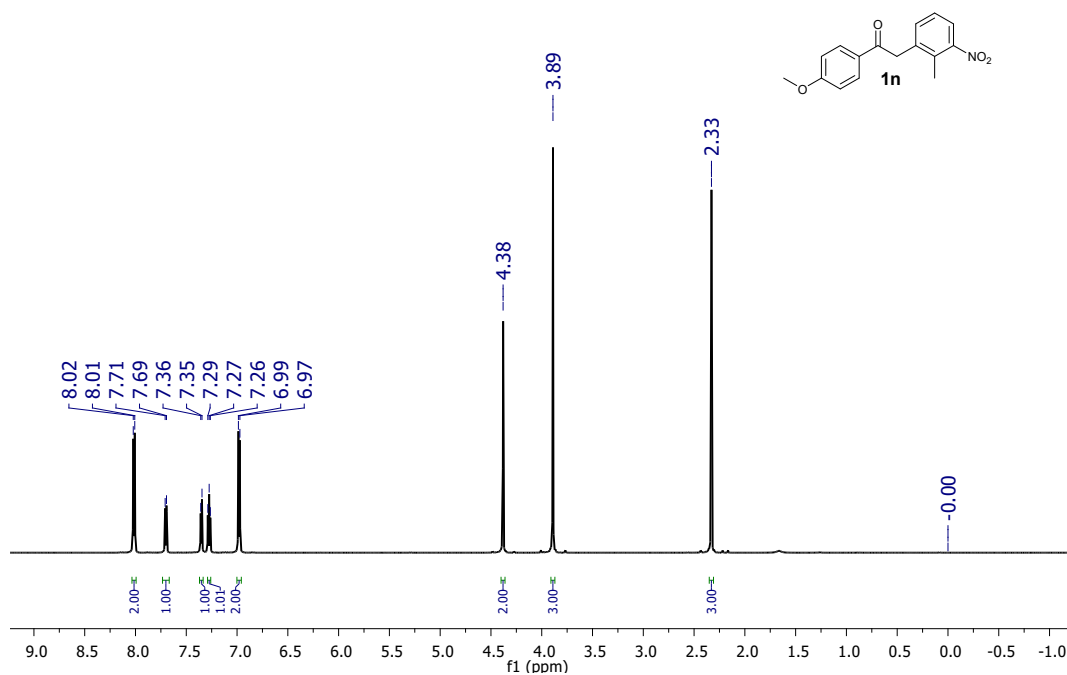
A 20 mL reaction tube, equipped with a magnetic stirring bar and septum, was charged with **3a** (118 mg, 0.5 mmol), 2,6-dimethoxybenzoic acid (273 mg, 1.5 mmol, 3.0 equiv), Pd(OAc)₂ (0.025 mmol, 5 mol%, 3.0 mg), 6,6'-dimethyl-2,2'-dipyridyl (0.05 mmol, 10 mol%, 39 mg) and HFBA (0.5 mmol, 1 equiv, 107 mg) were dissolved in benzotrifluoride (1.7 mL). The reaction mixture was then heated at 100 °C (oil bath) with vigorous stirring for 24 hours in air. After the reaction equilibrium, the mixture was poured into ethyl acetate, which was washed with saturated NaHCO₃ (2 × 10 mL) and then brine (1 × 10 mL). After the aqueous layer was extracted with ethyl acetate, the combined organic layers were dried over anhydrous Na₂SO₄ and evaporated under vacuum. The filtrate was concentrated in vacuo and purified by a silica gel packed flash chromatography column with hexane:ether (9:1) as the eluent to afford the desired products **8**. Yield = 129 mg, 0.42 mmol, 83%. White solid. R_f = 0.5 (Hexane:EtOAc = 8:2). All characterization data are in agreement with that as reported in the literature.¹⁶ ¹H NMR (600 MHz, CDCl₃): δ 8.18-8.17 (m, 2H), 7.52-7.50 (m, 2H), 7.47-7.42 (m, 3H), 7.37 (t, *J* = 8.4 Hz, 1H), 7.29-7.27 (m, 2H), 7.23-7.21 (m, 1H), 6.65 (s, 1H), 6.64 (s, 1H), 3.68 (6H) ppm. ¹³C NMR (151 MHz, CDCl₃): δ 159.9, 159.2, 147.1, 130.8, 130.1 (2C), 130.0, 129.4, 128.7 (2C), 128.5 (2C), 127.9, 127.6, 126.6 (2C), 124.8 (2C), 110.6, 104.4 (2C), 56.1 (2C) ppm.

References

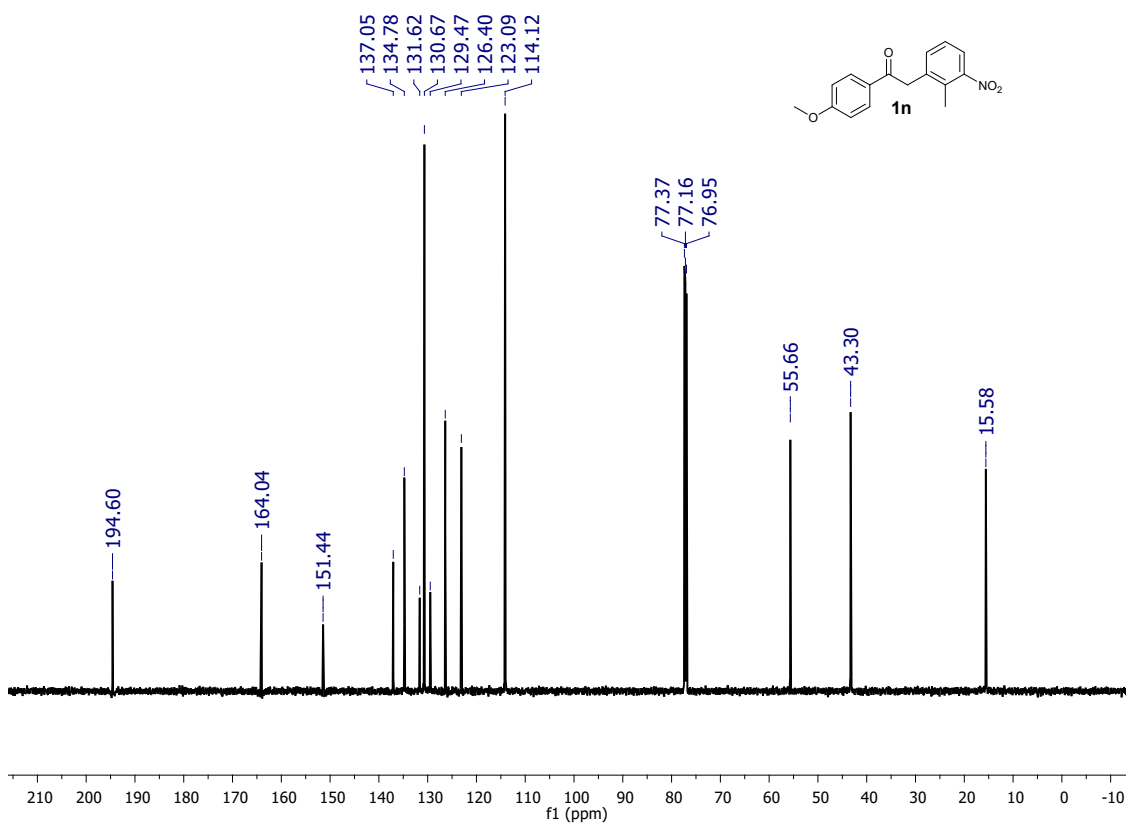
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^1H and ^{13}C NMR spectra of new substrates

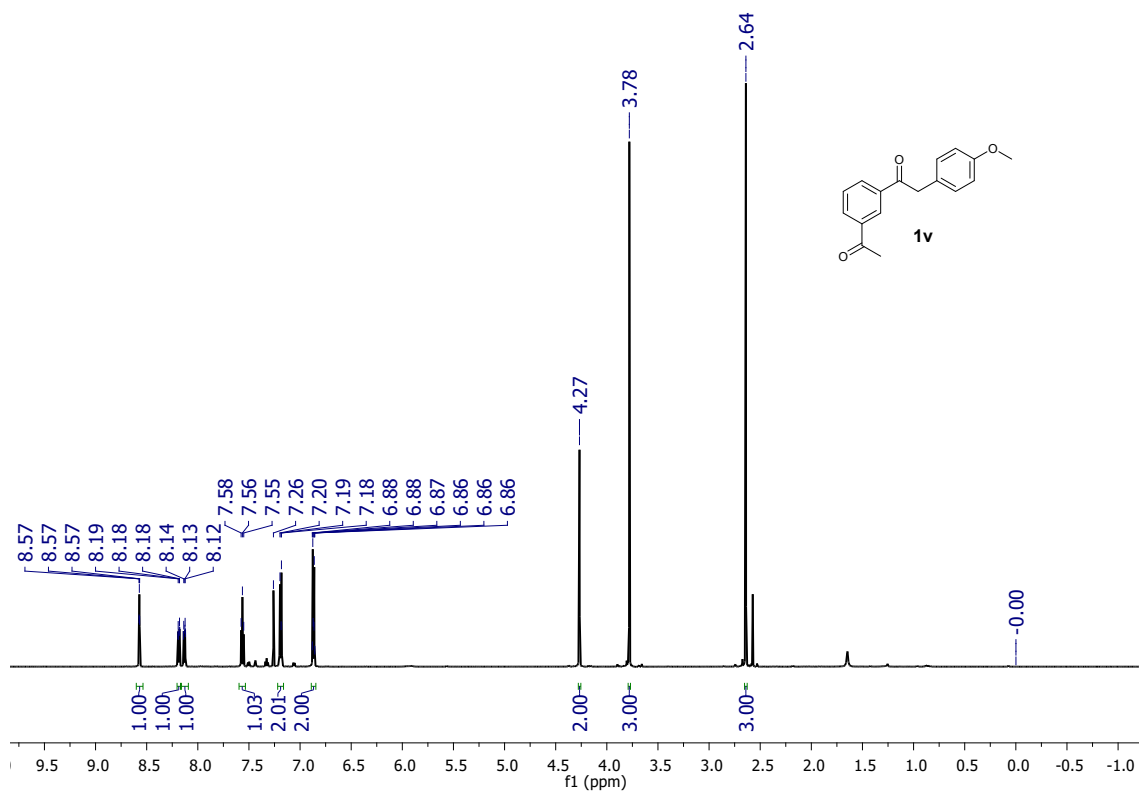
^1H NMR (600 MHz, CDCl_3):



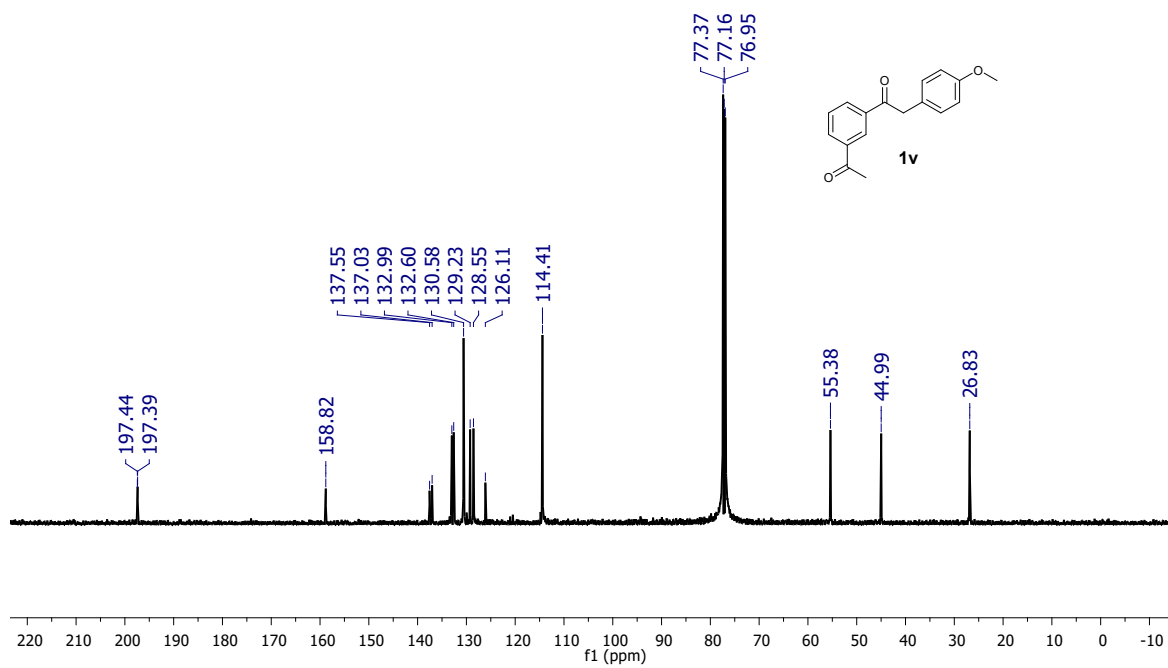
^{13}C NMR (126 MHz, CDCl_3):



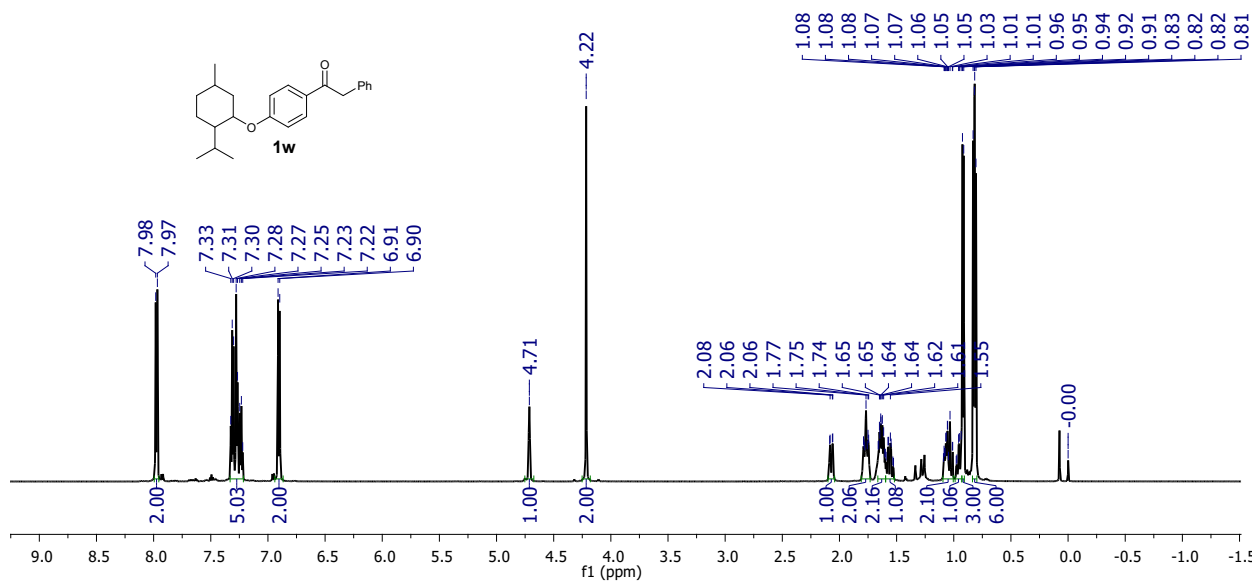
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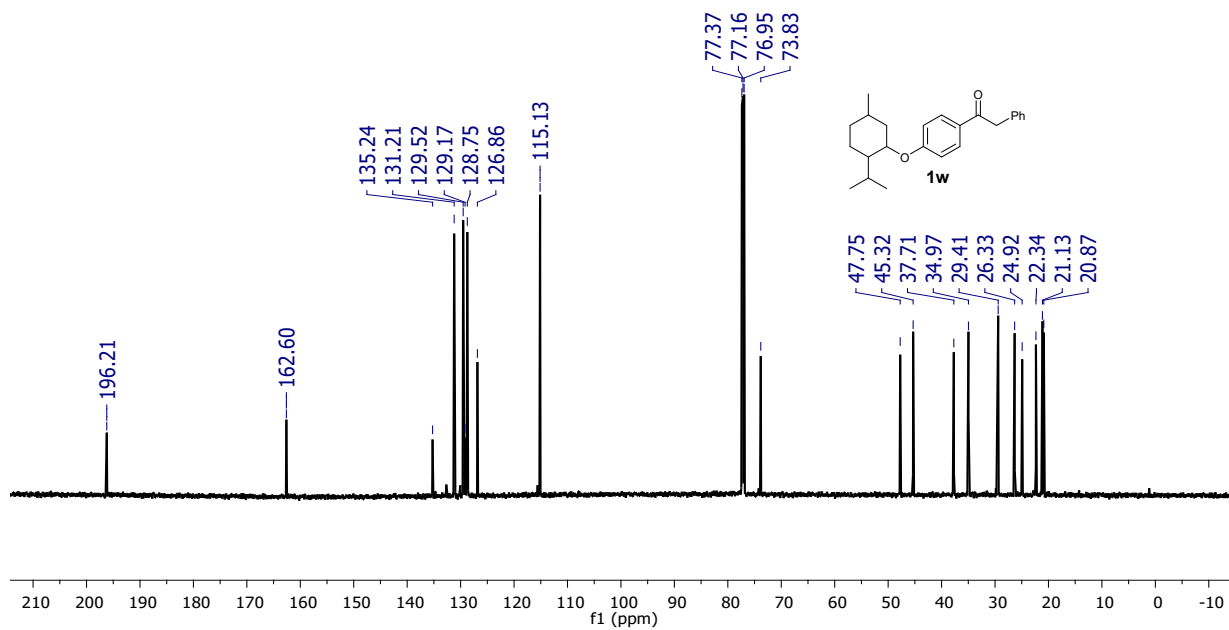
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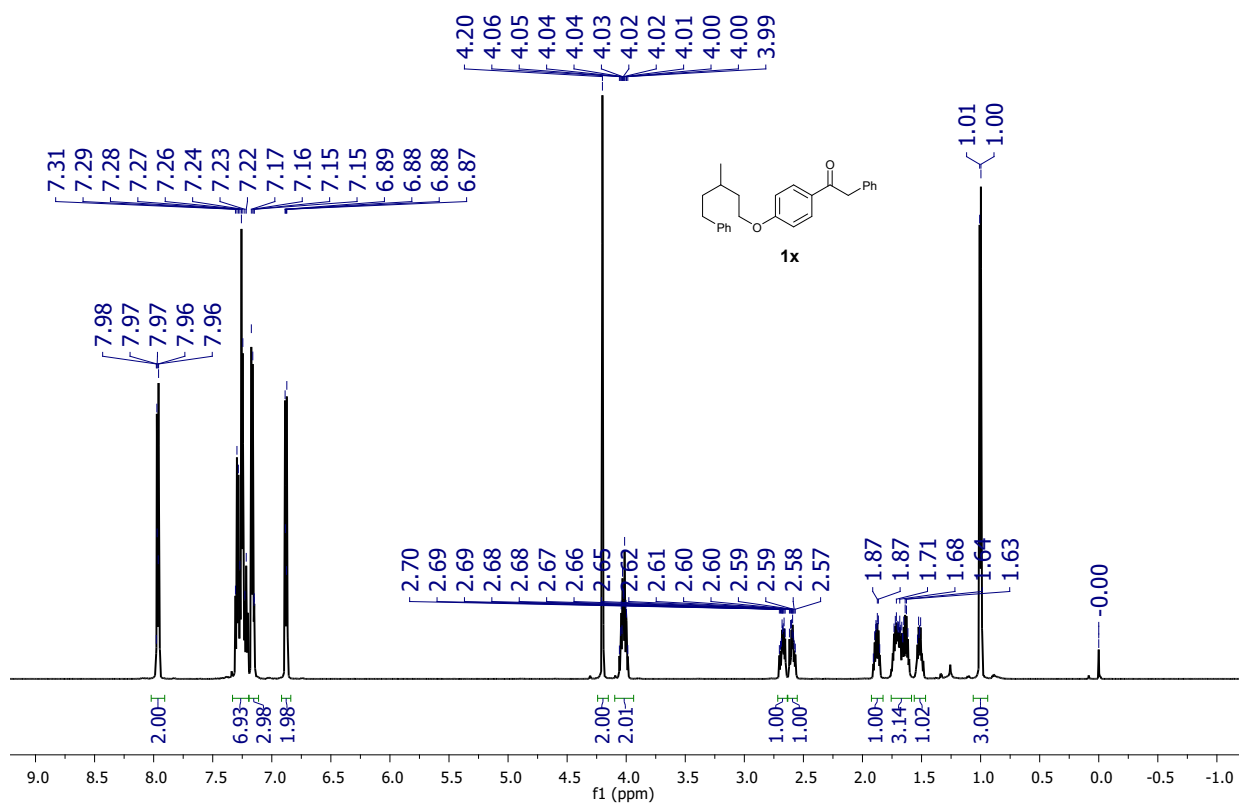
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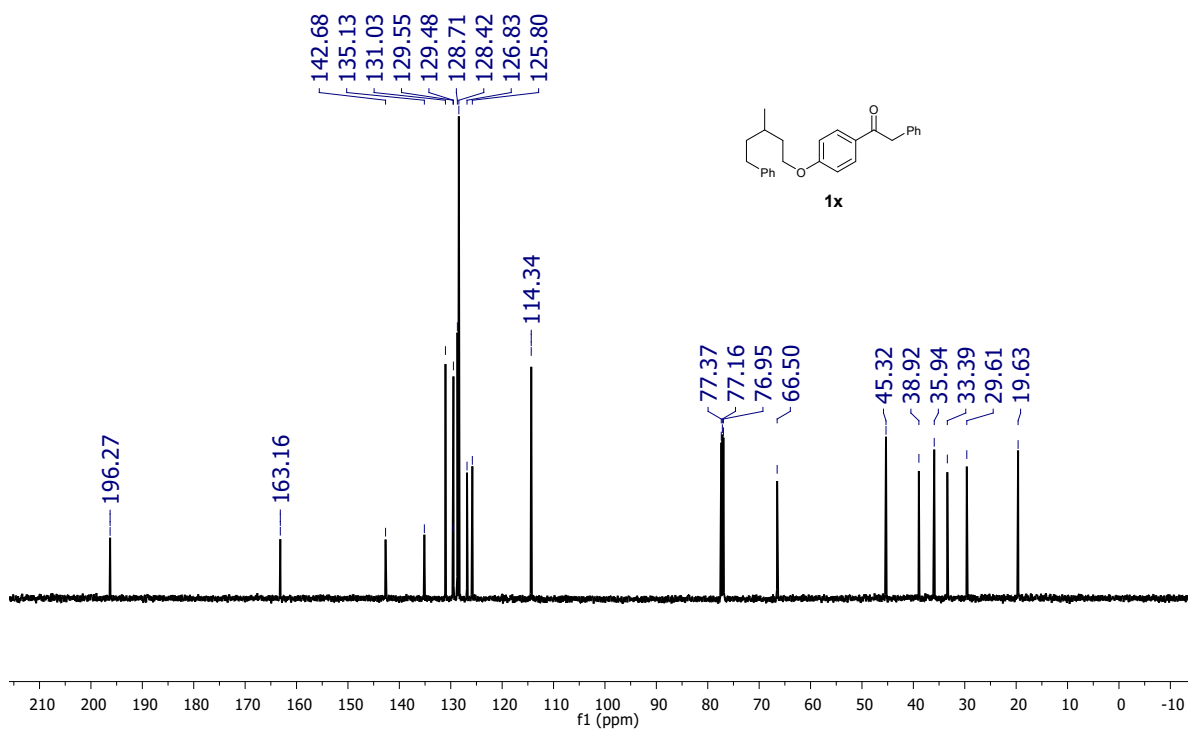
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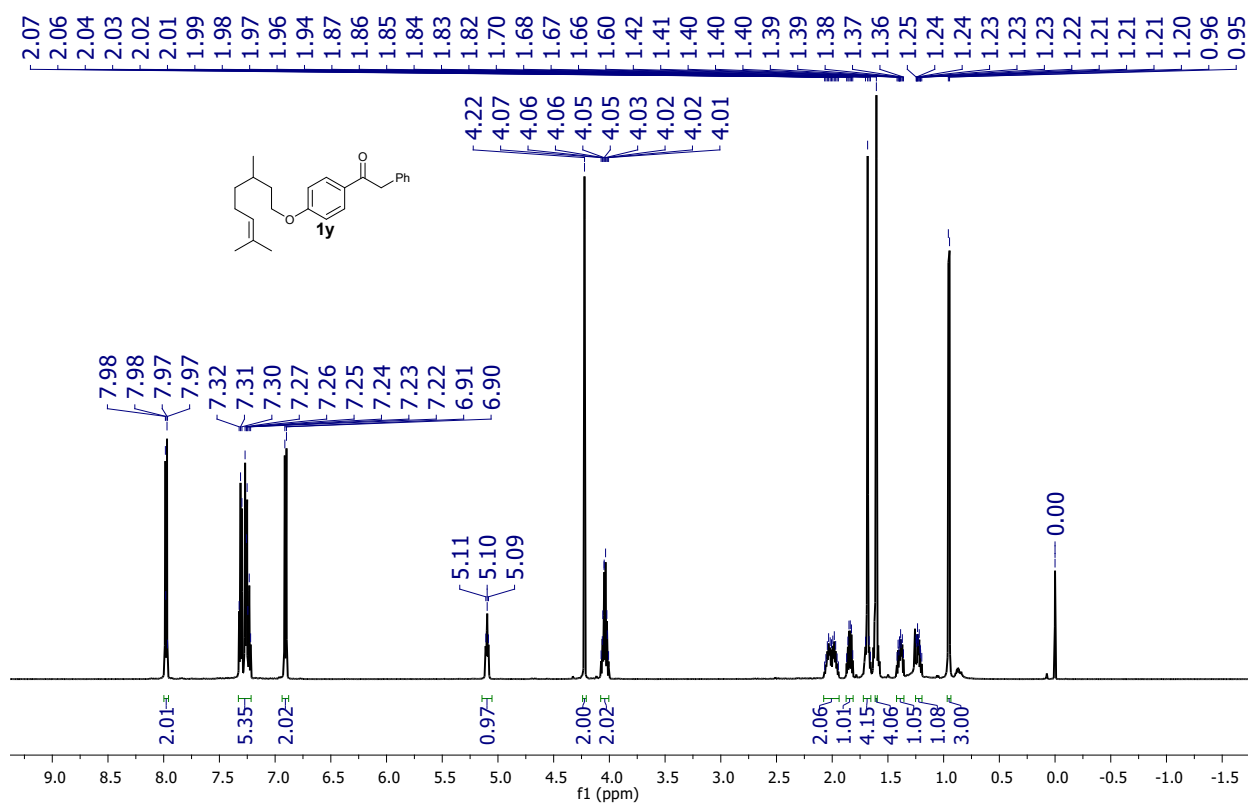
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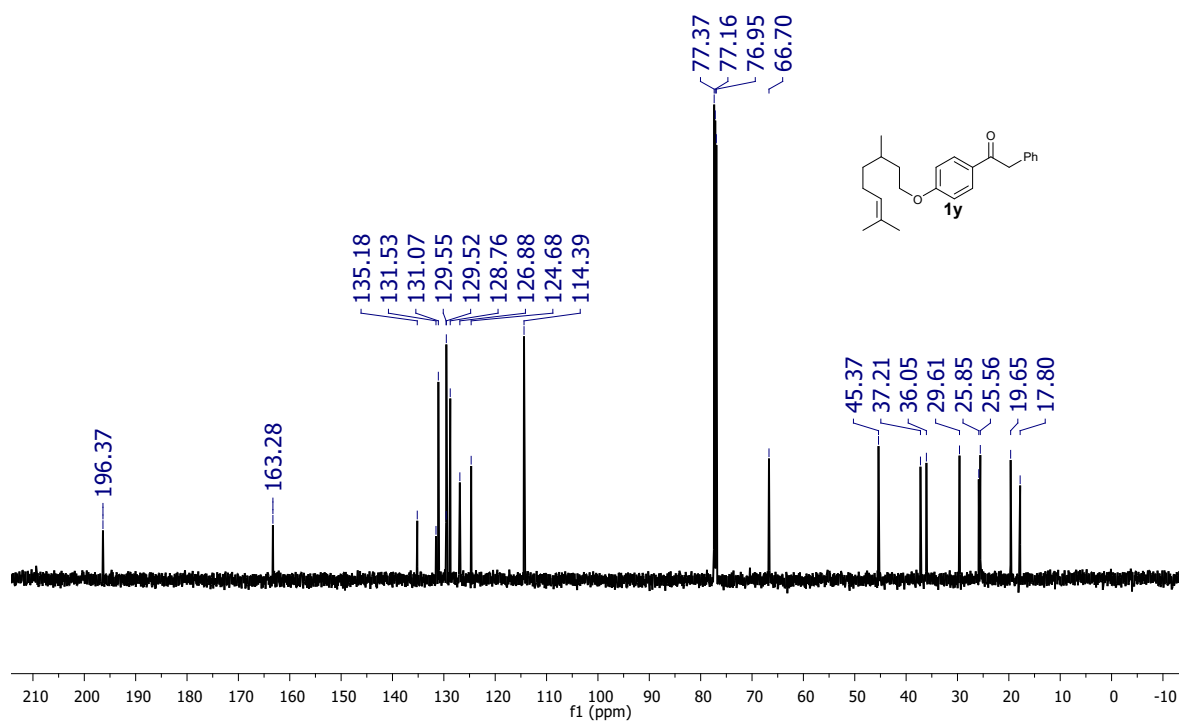
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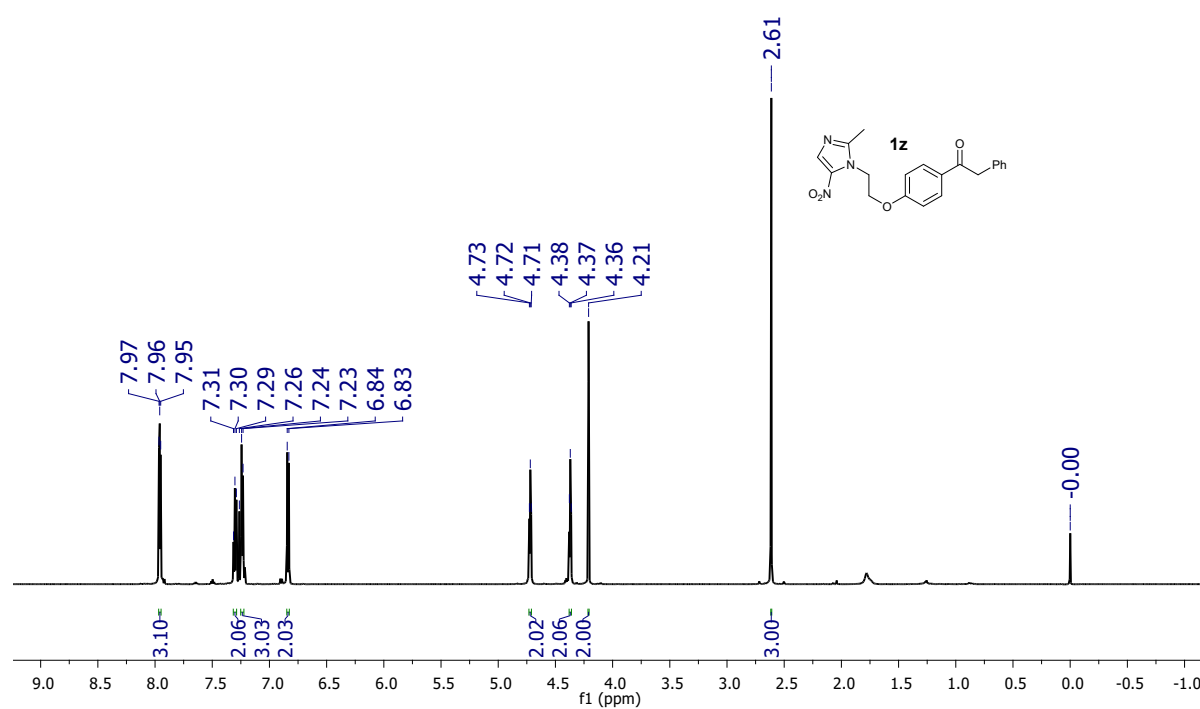
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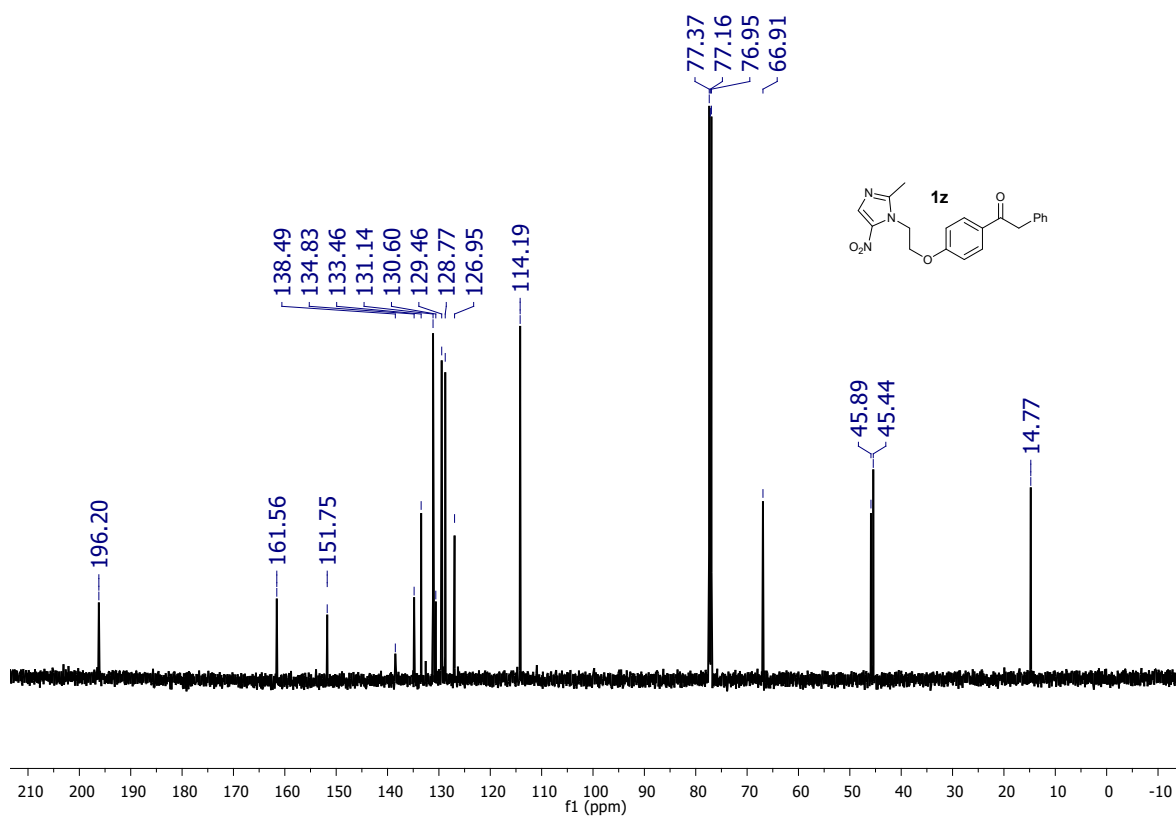
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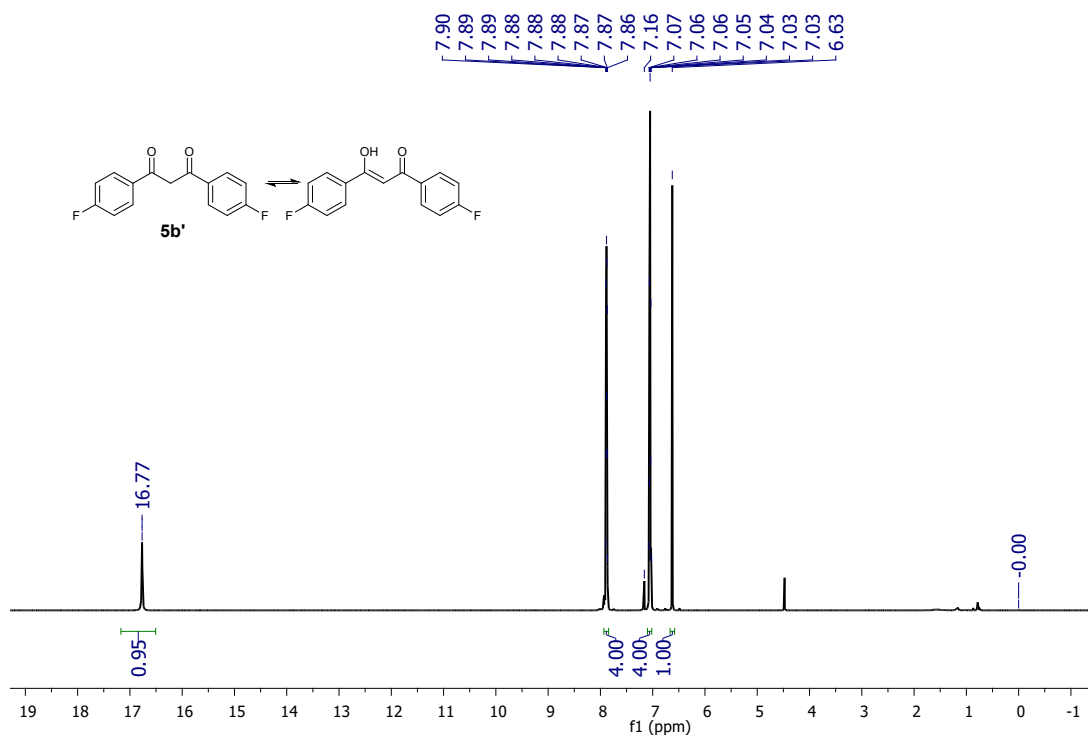
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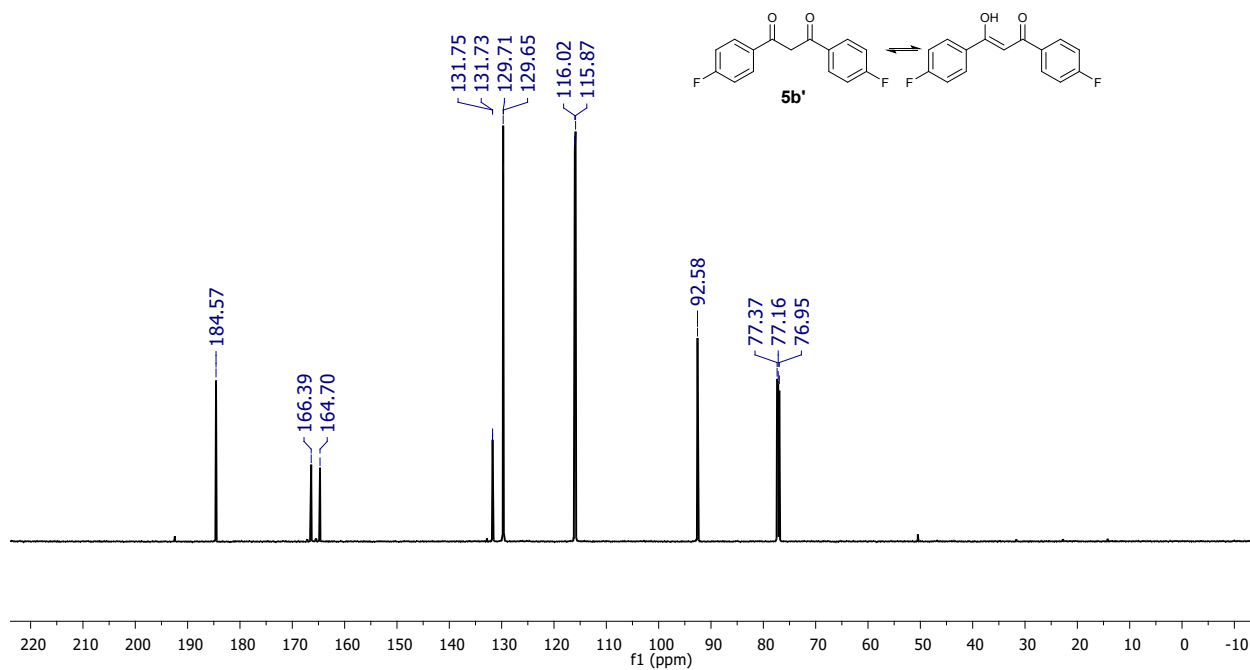
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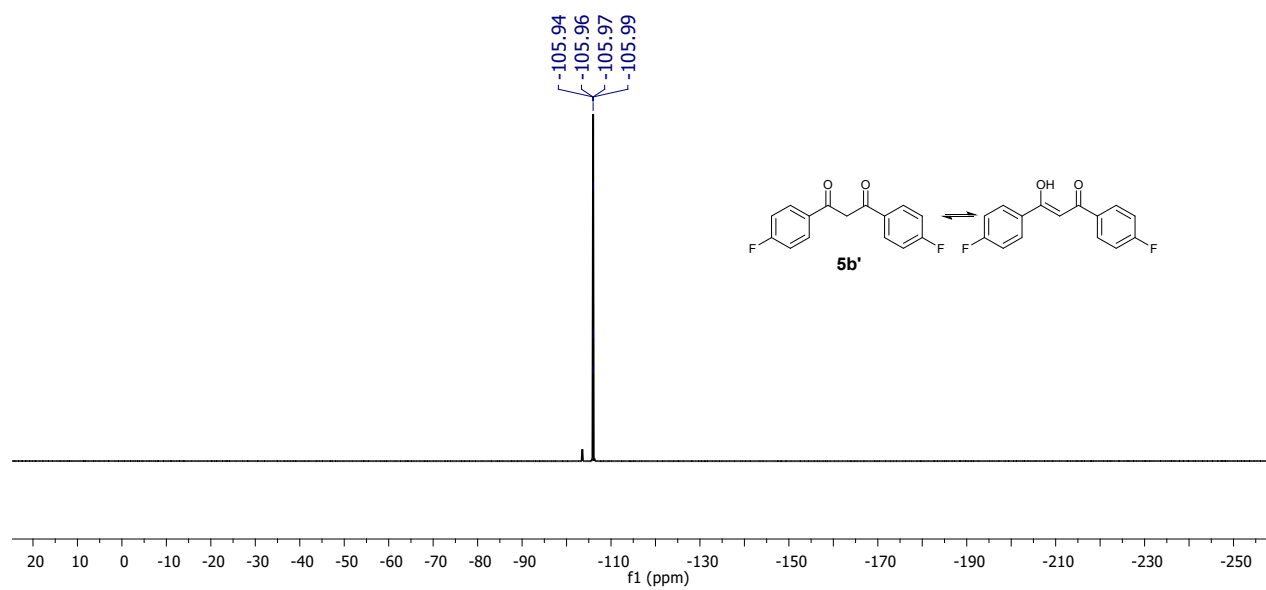
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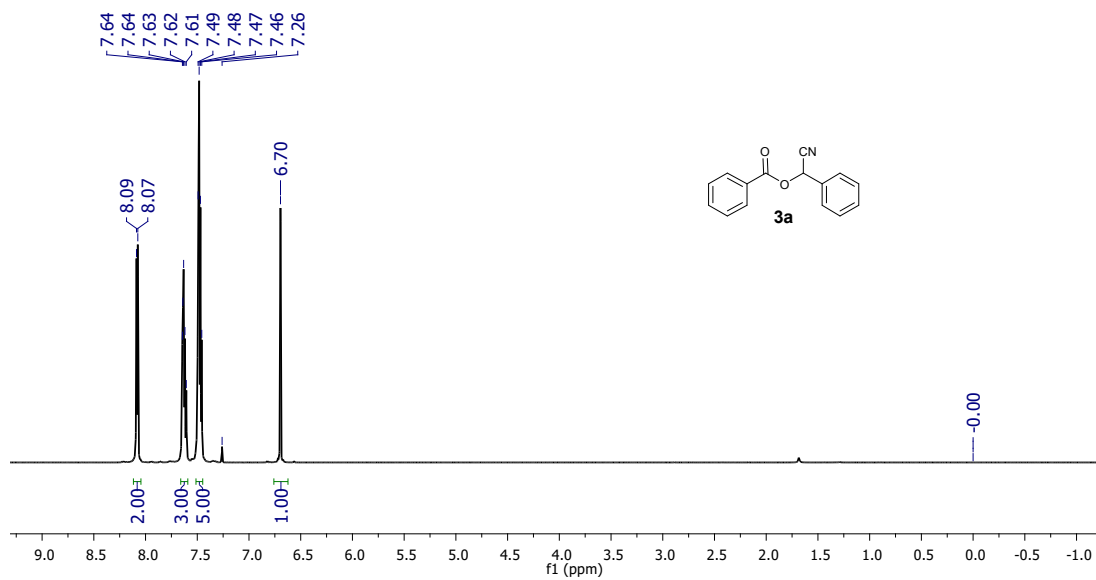
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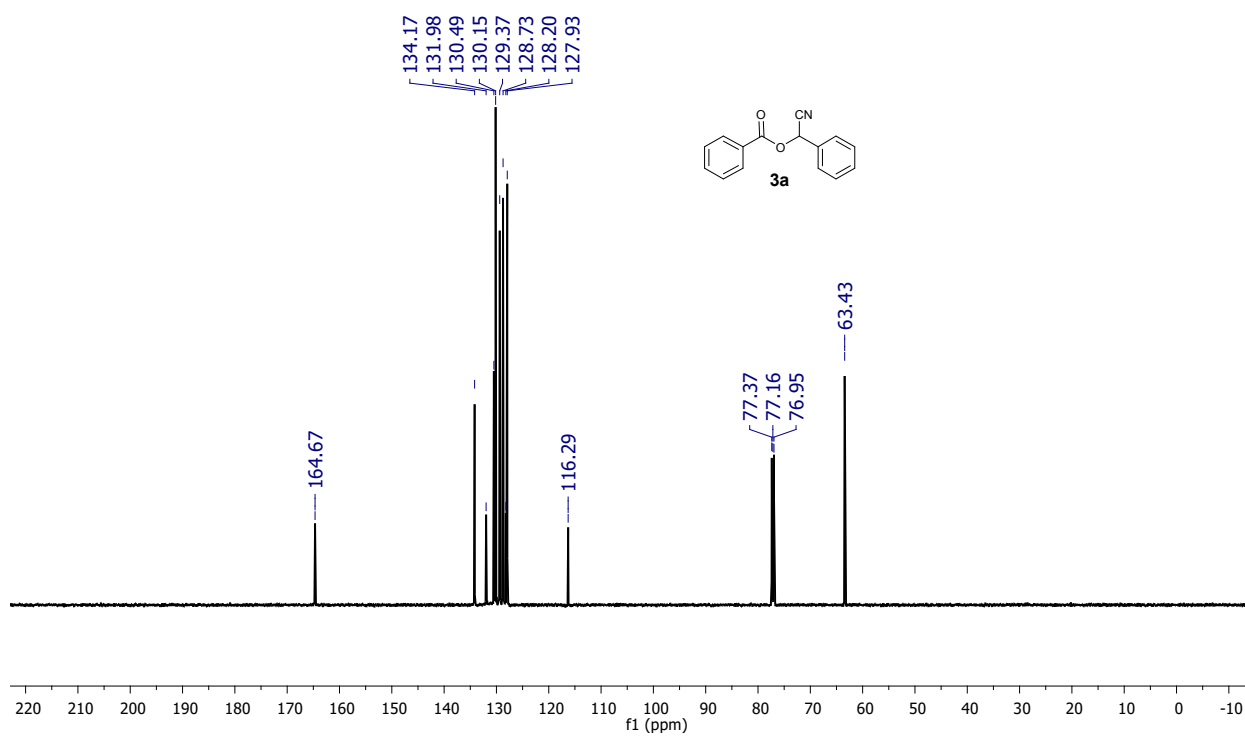
^{19}F NMR (565 MHz, CDCl_3):



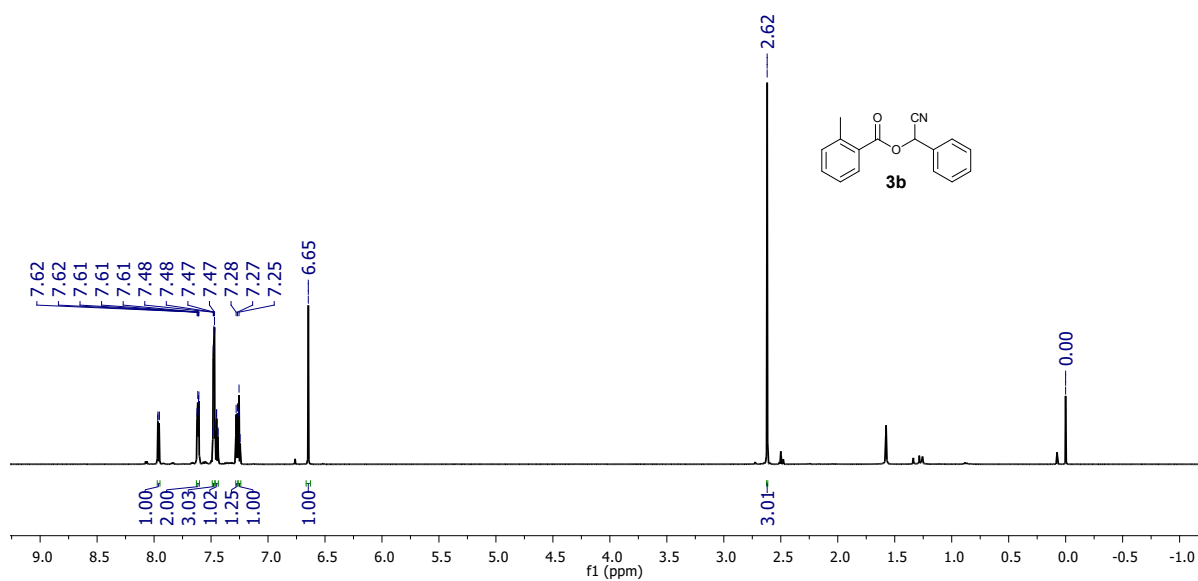
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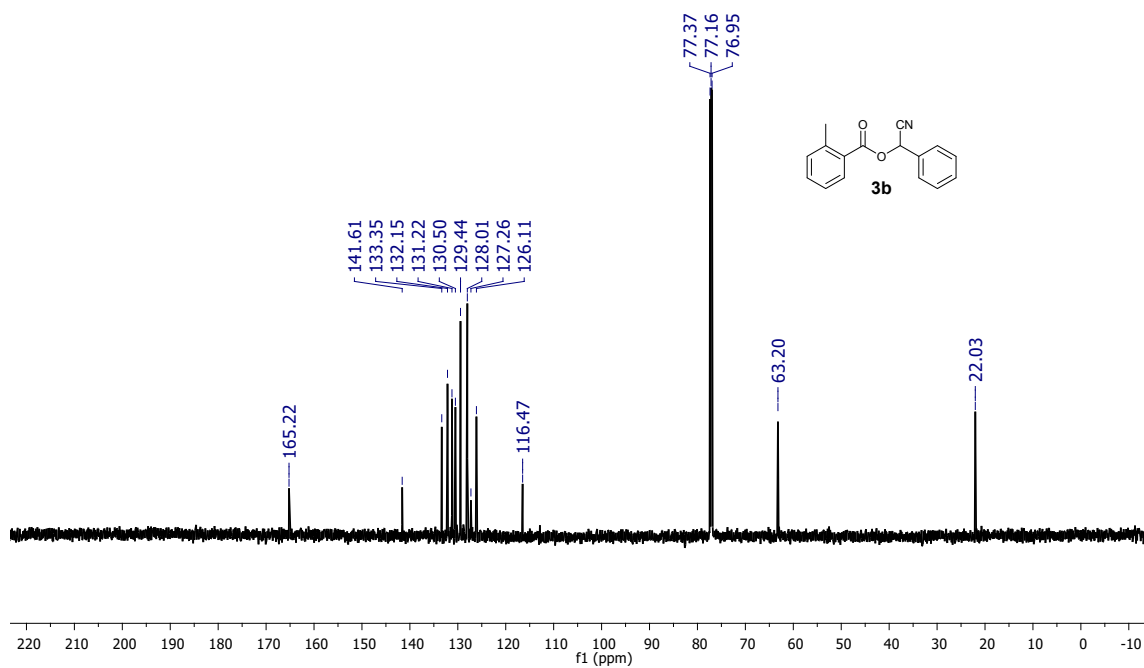
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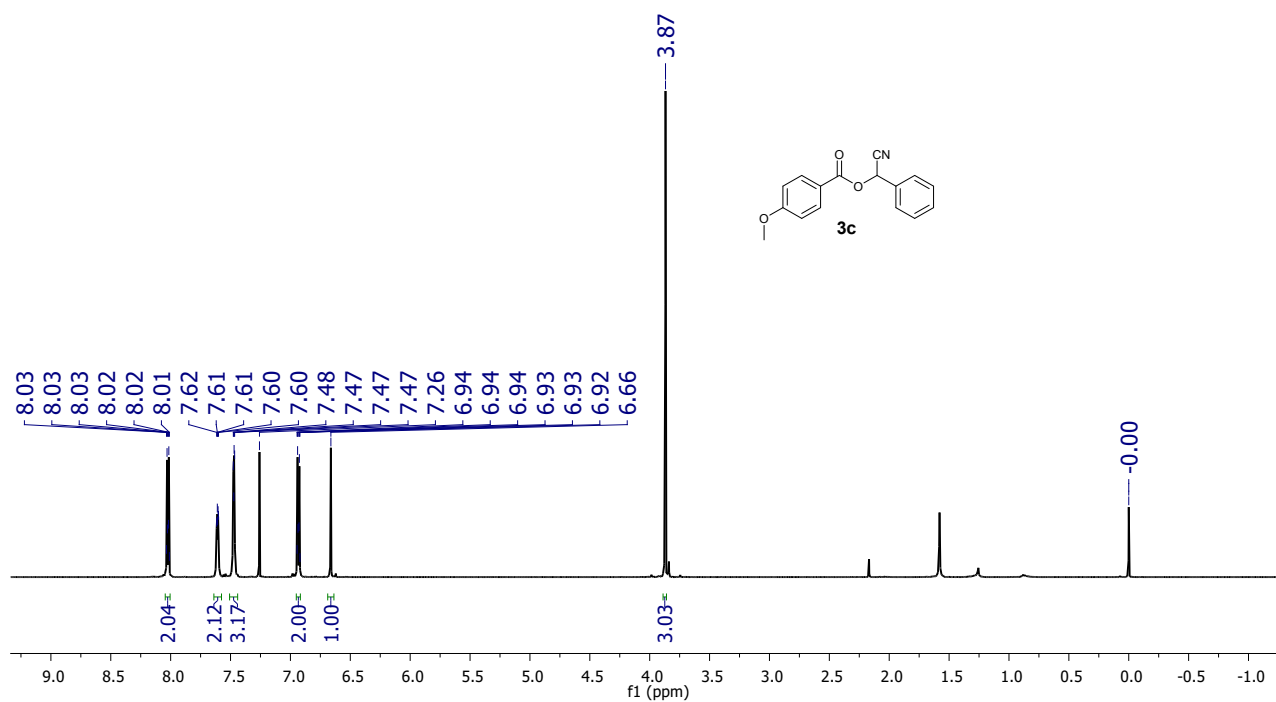
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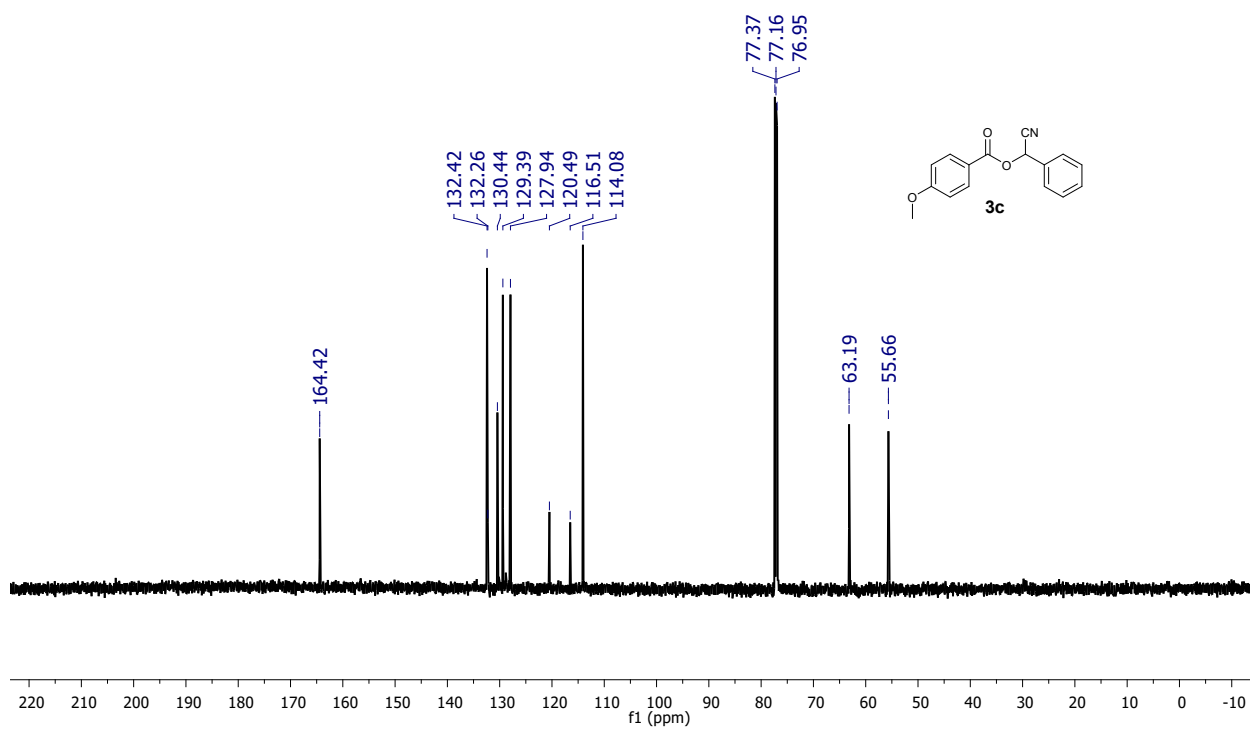
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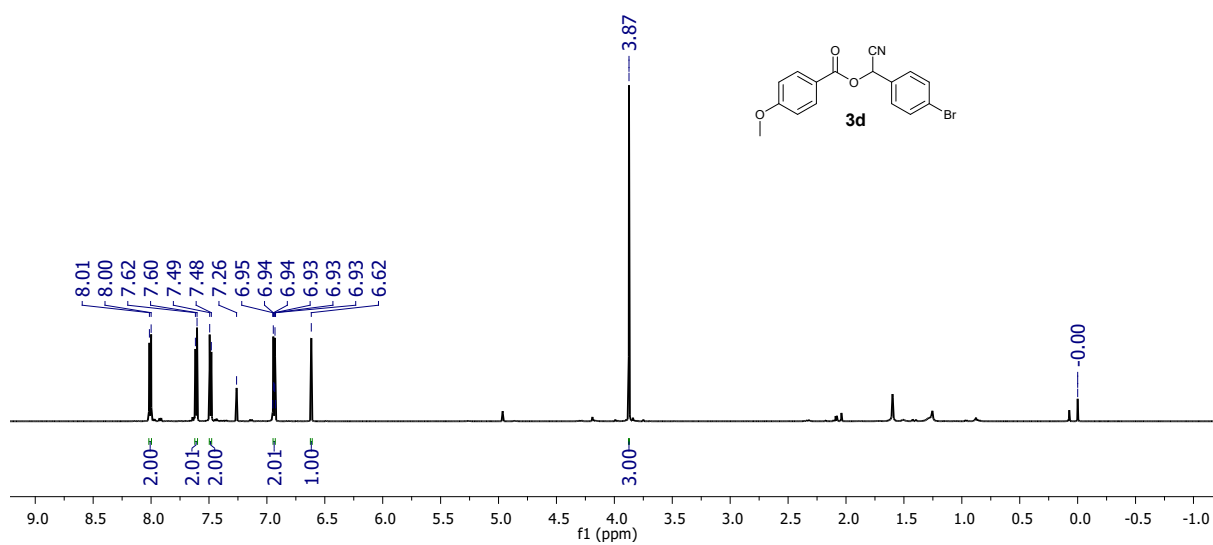
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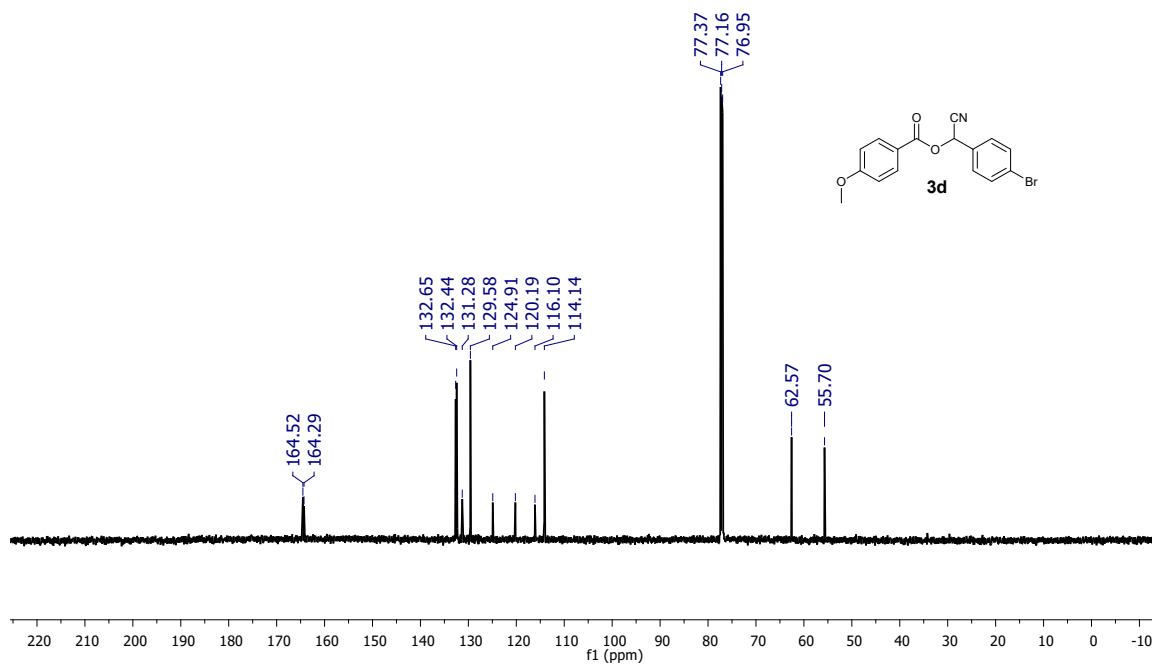
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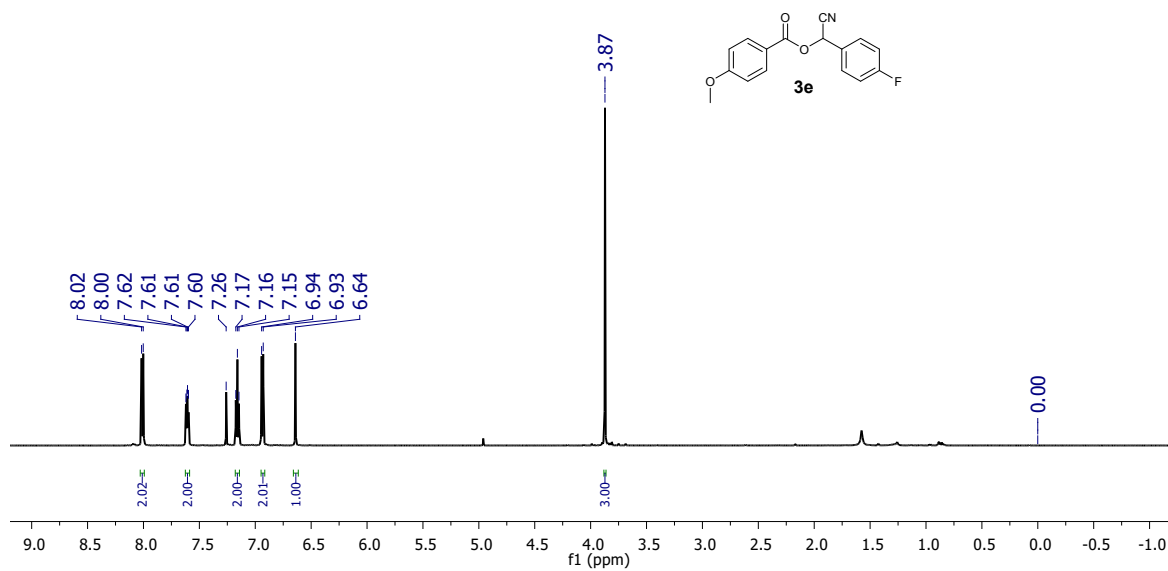
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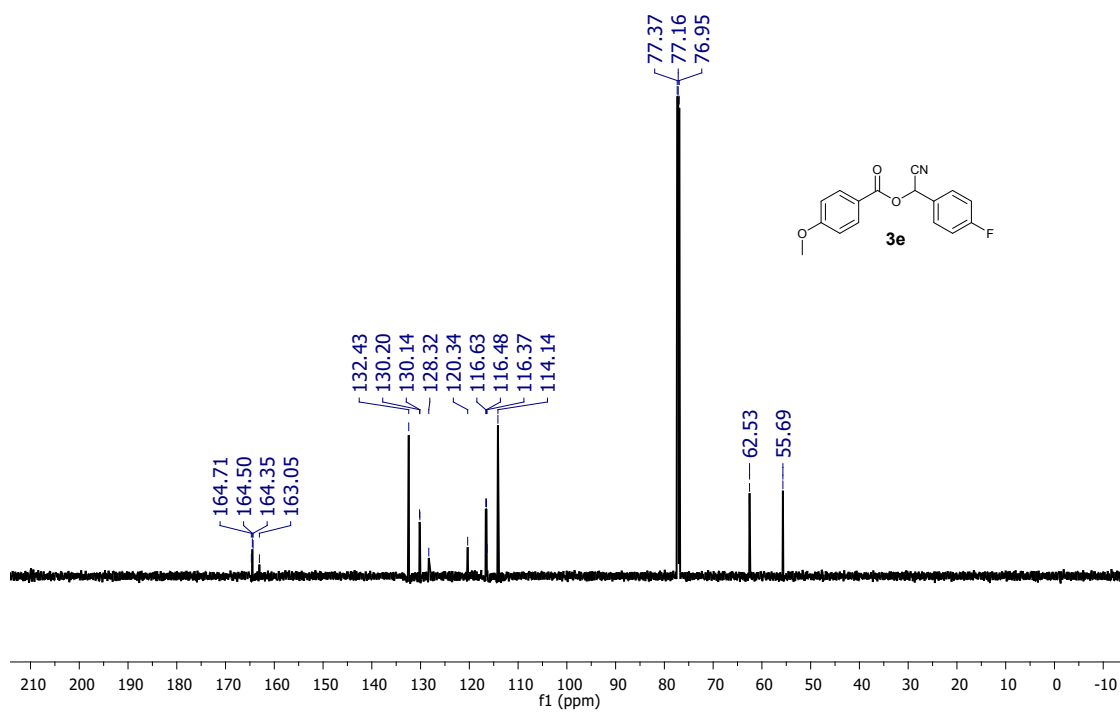
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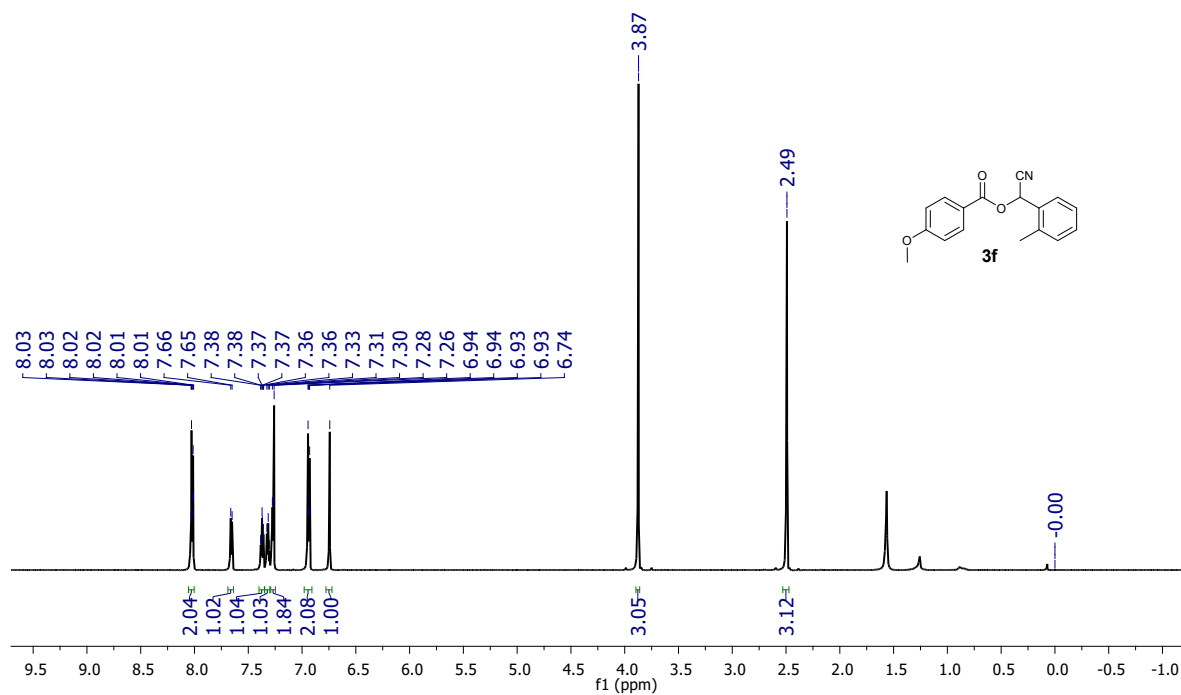
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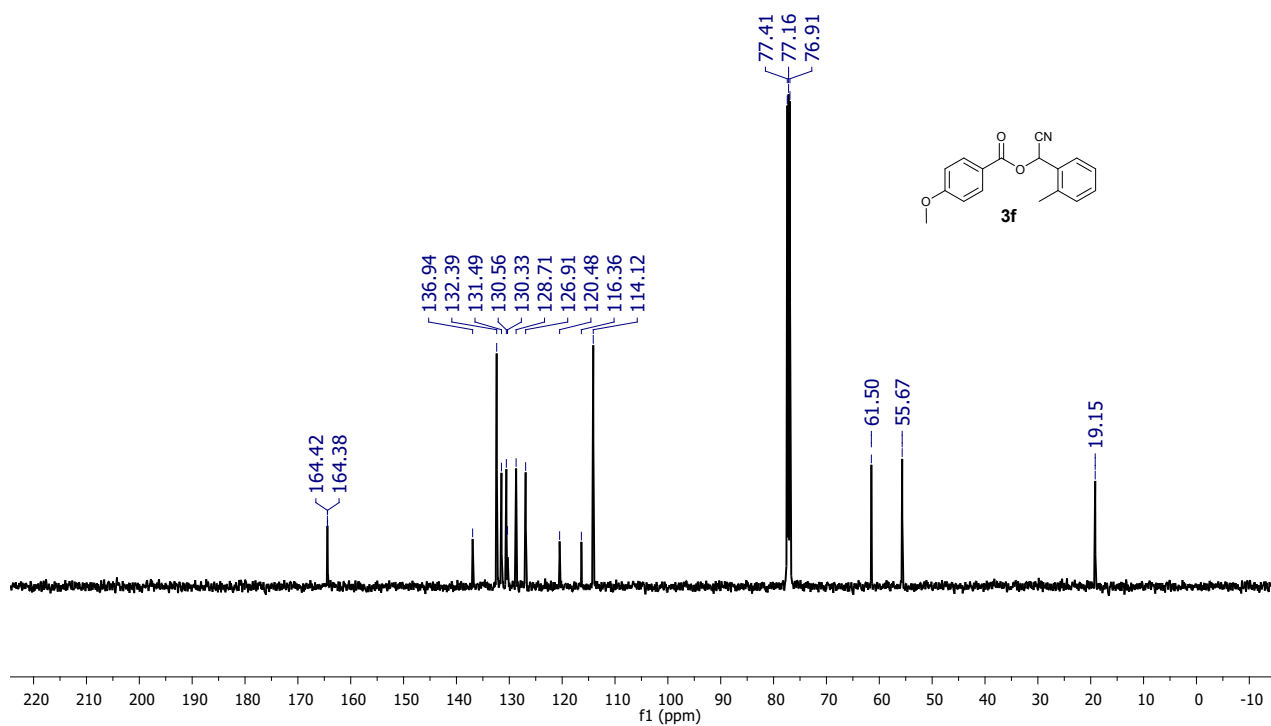
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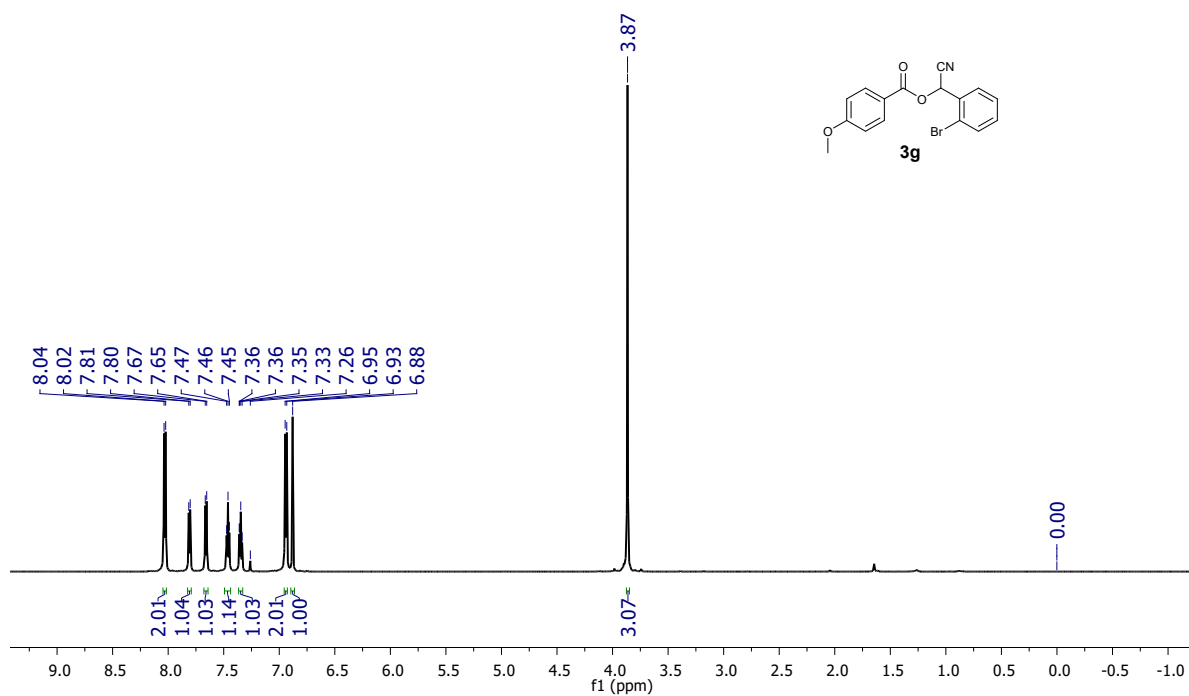
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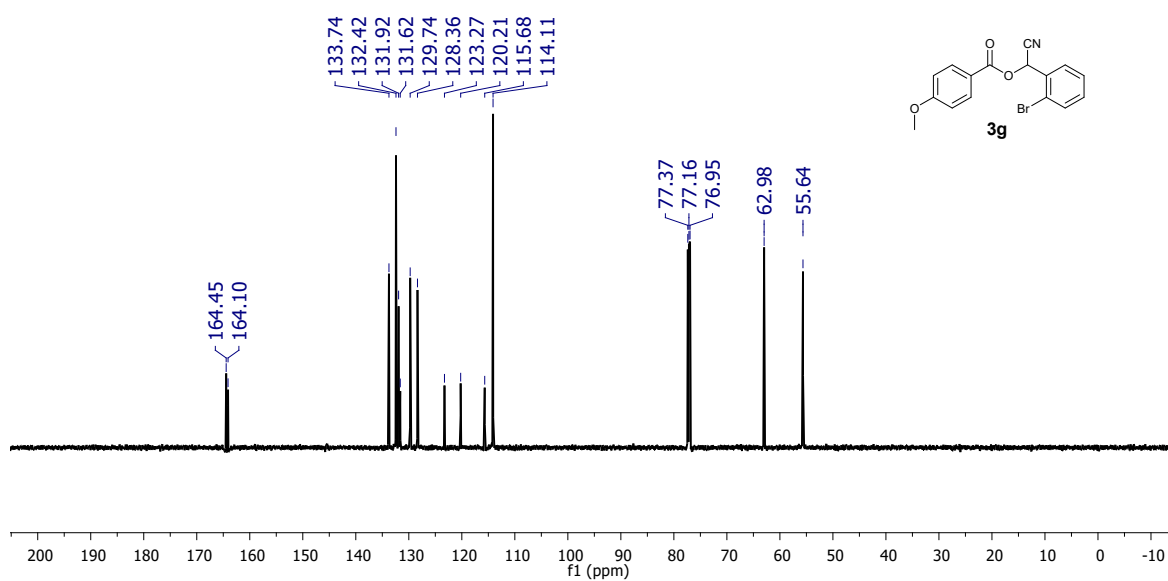
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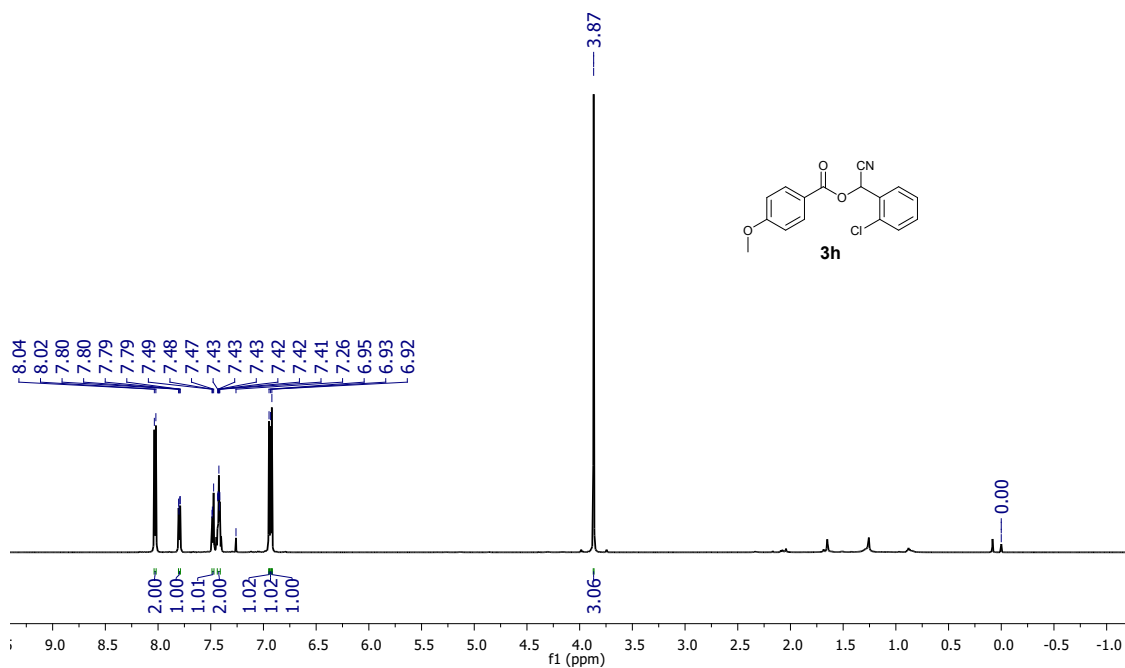
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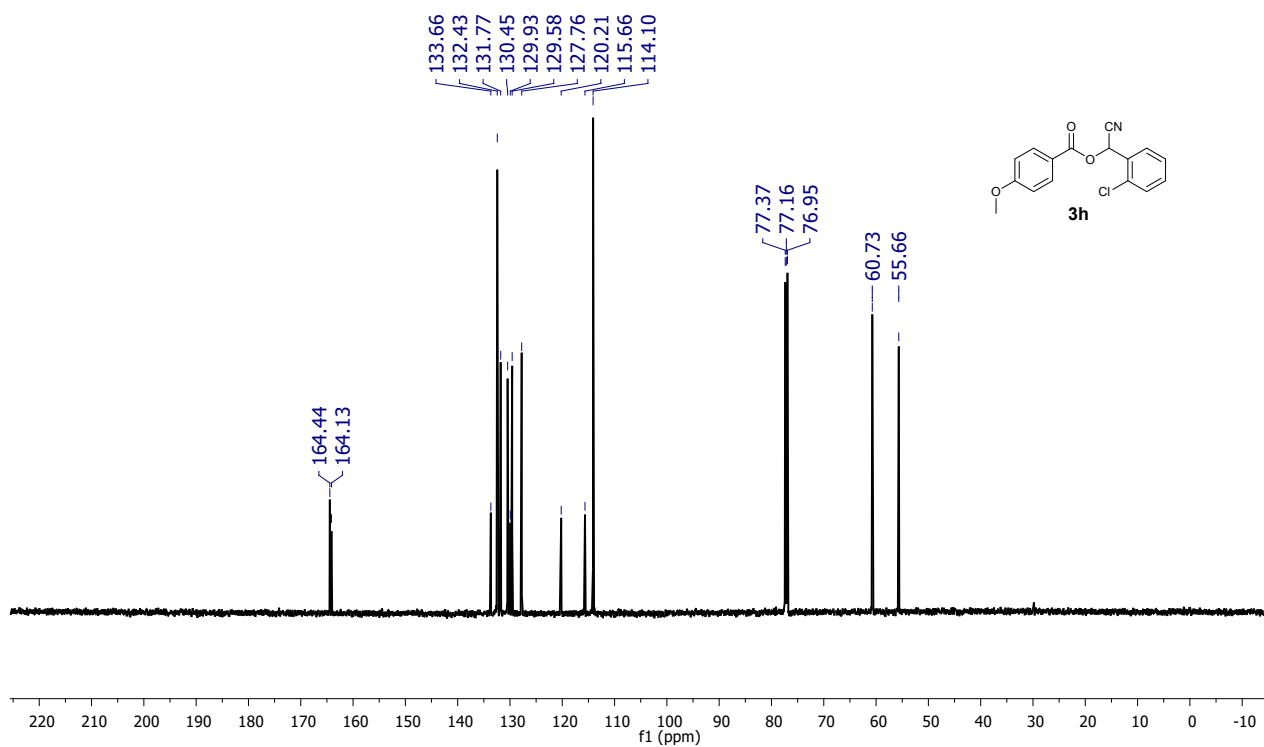
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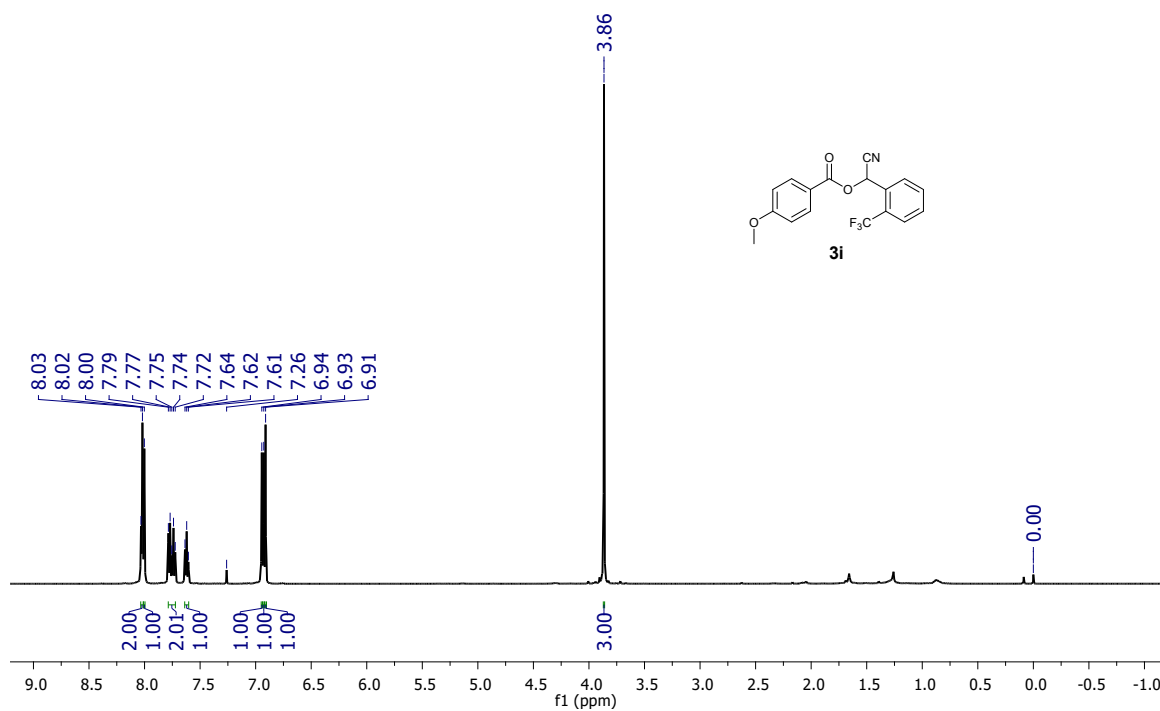
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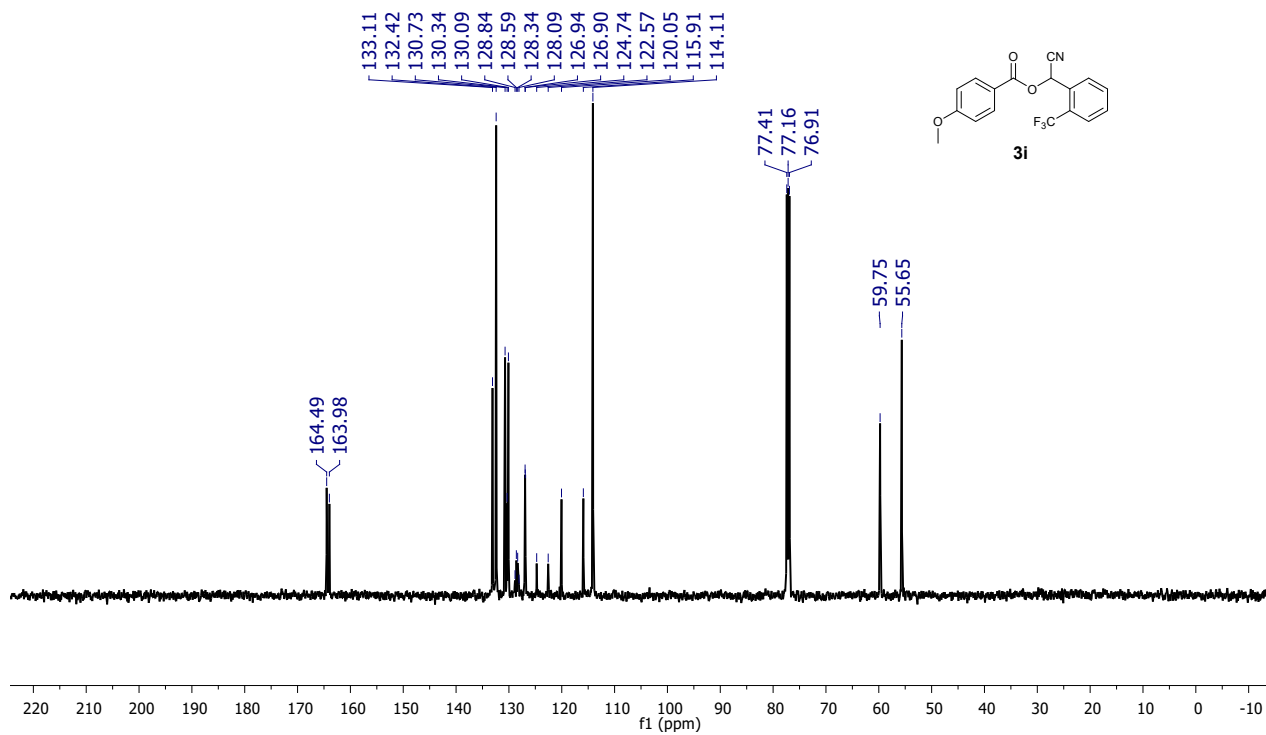
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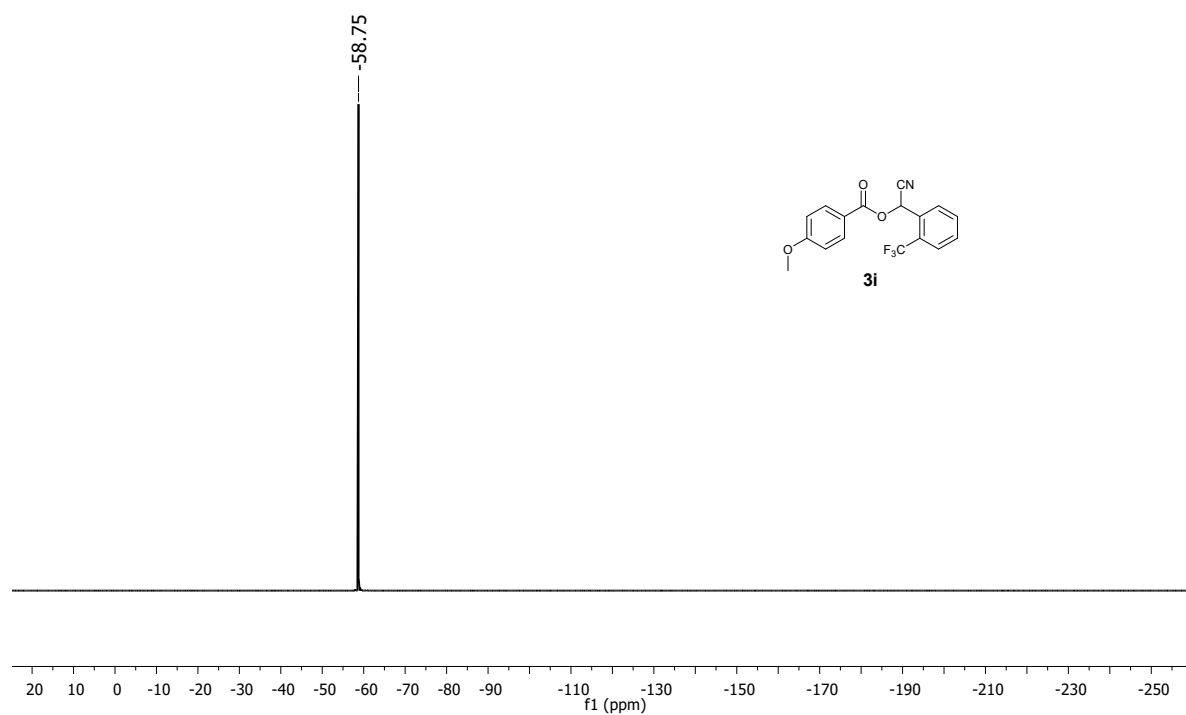
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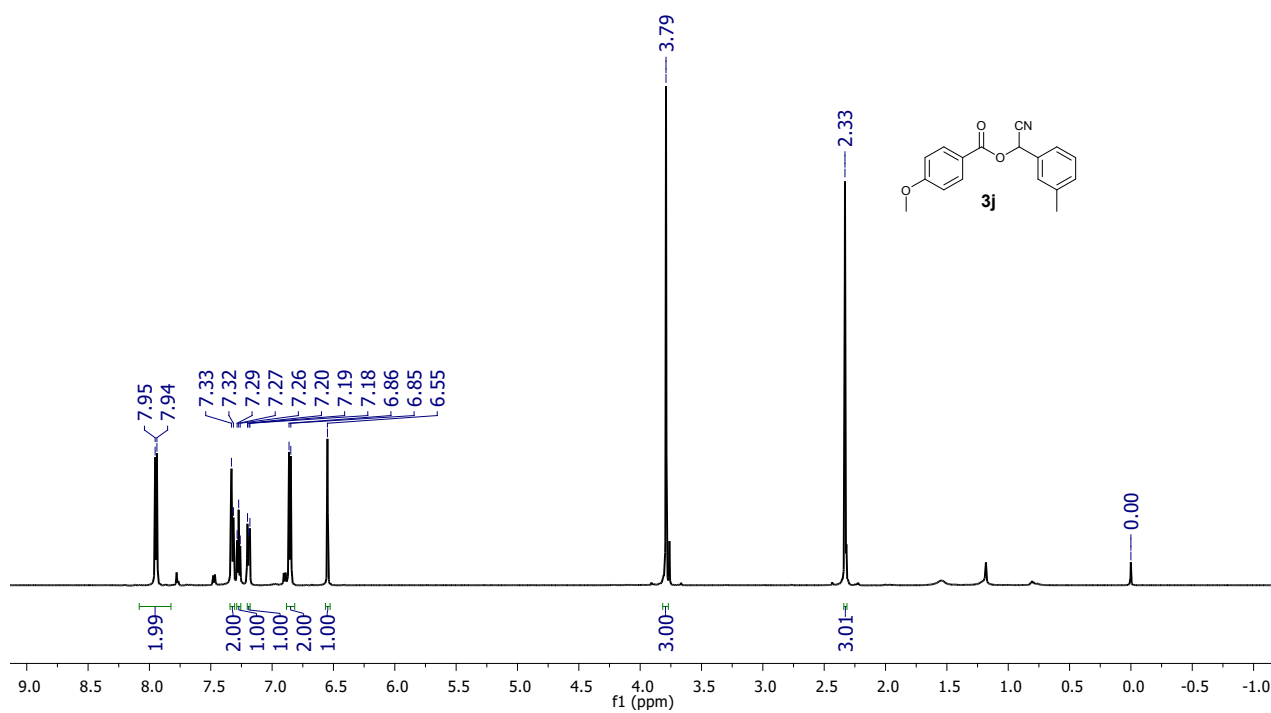
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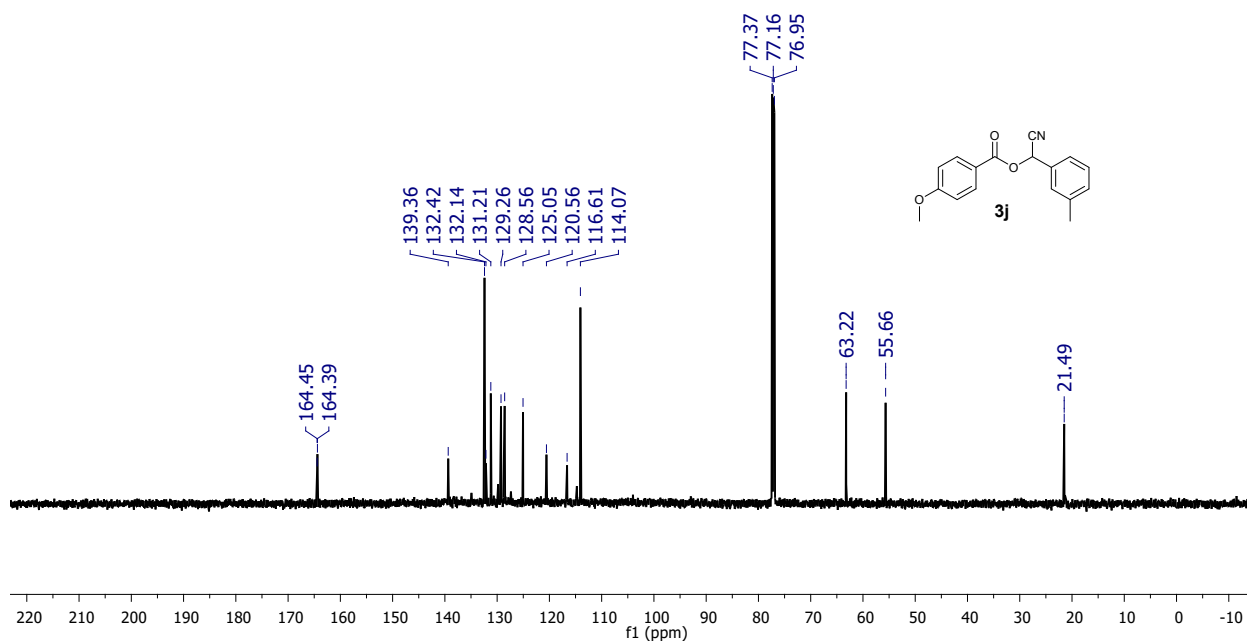
^{19}F NMR (565 MHz, CDCl_3):



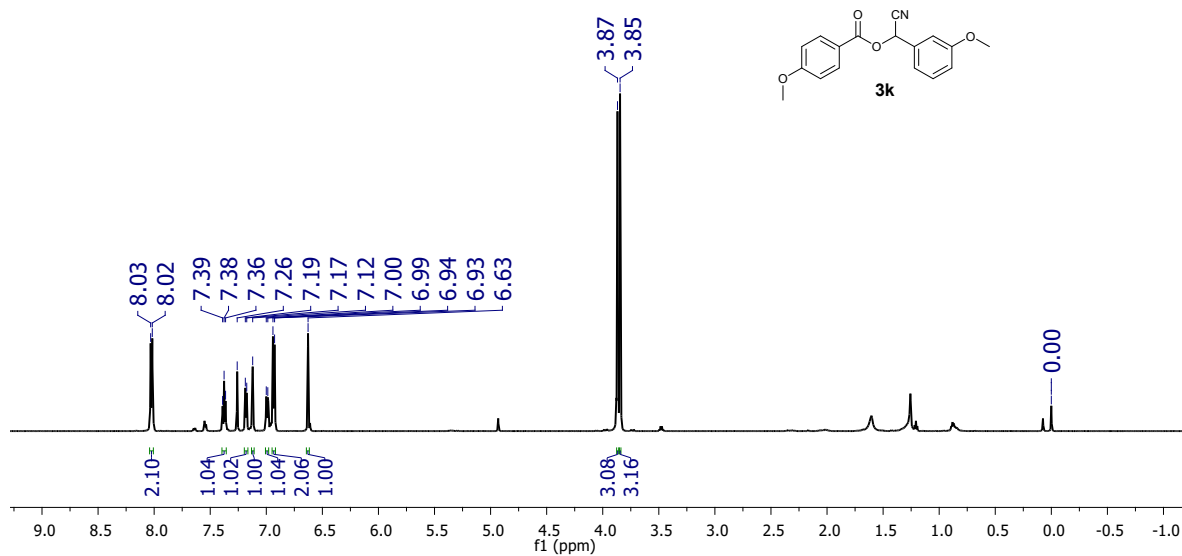
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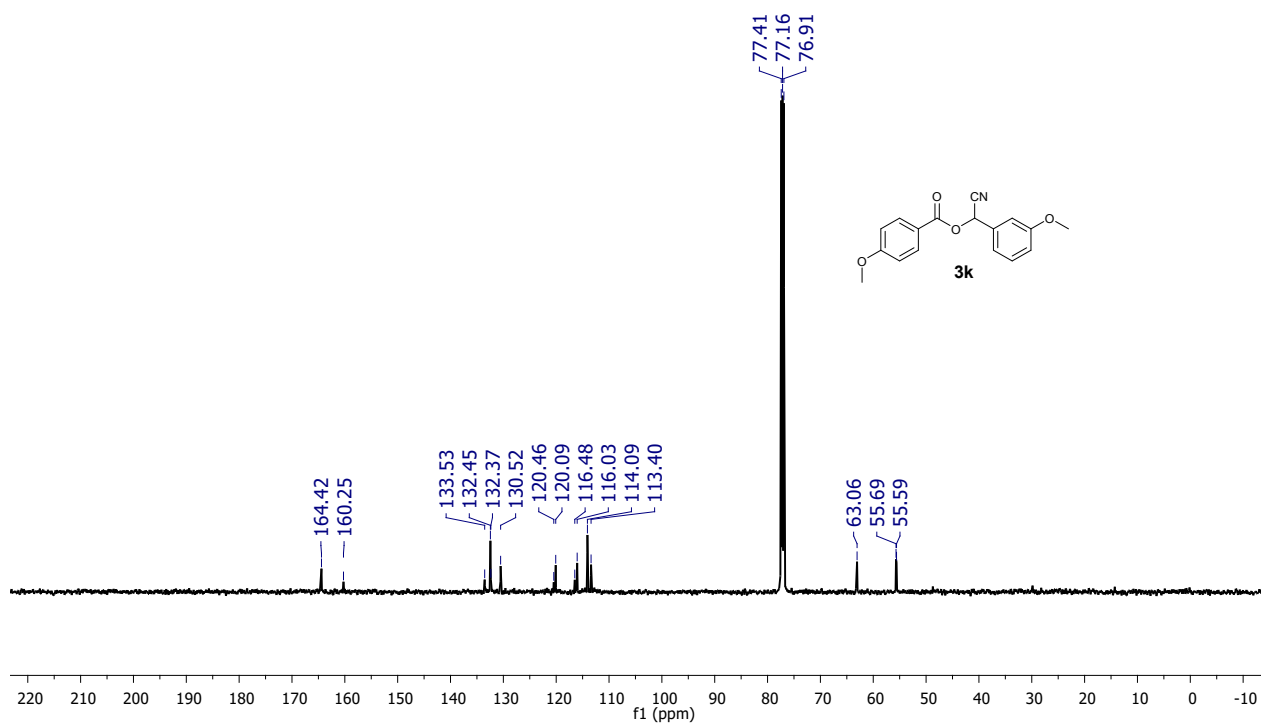
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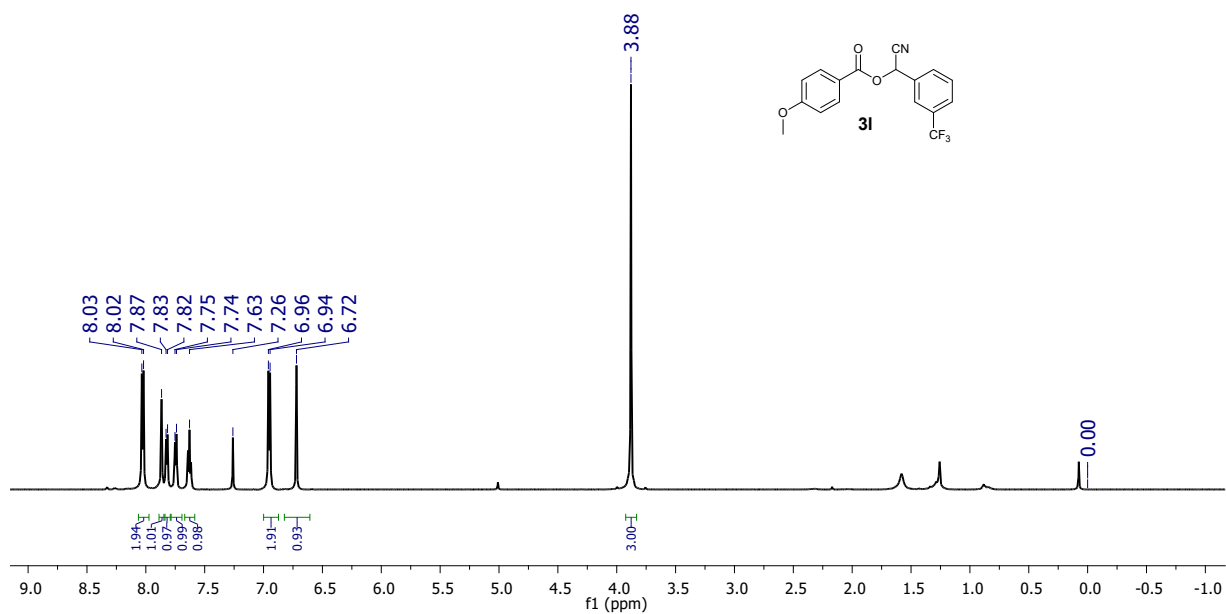
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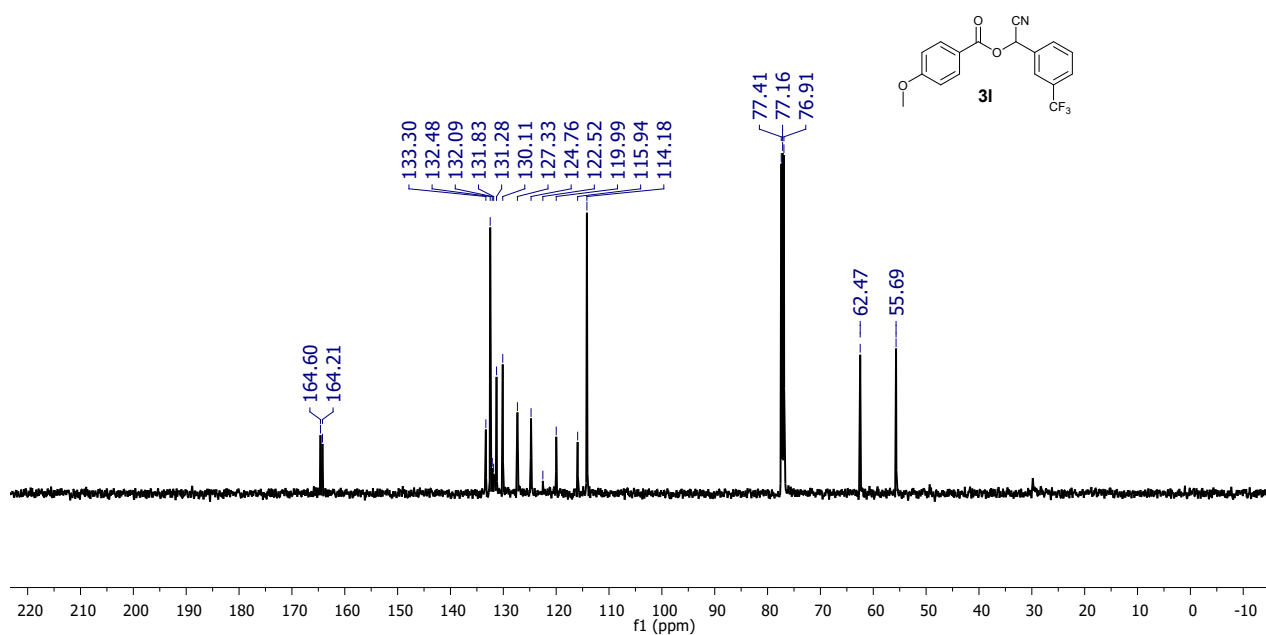
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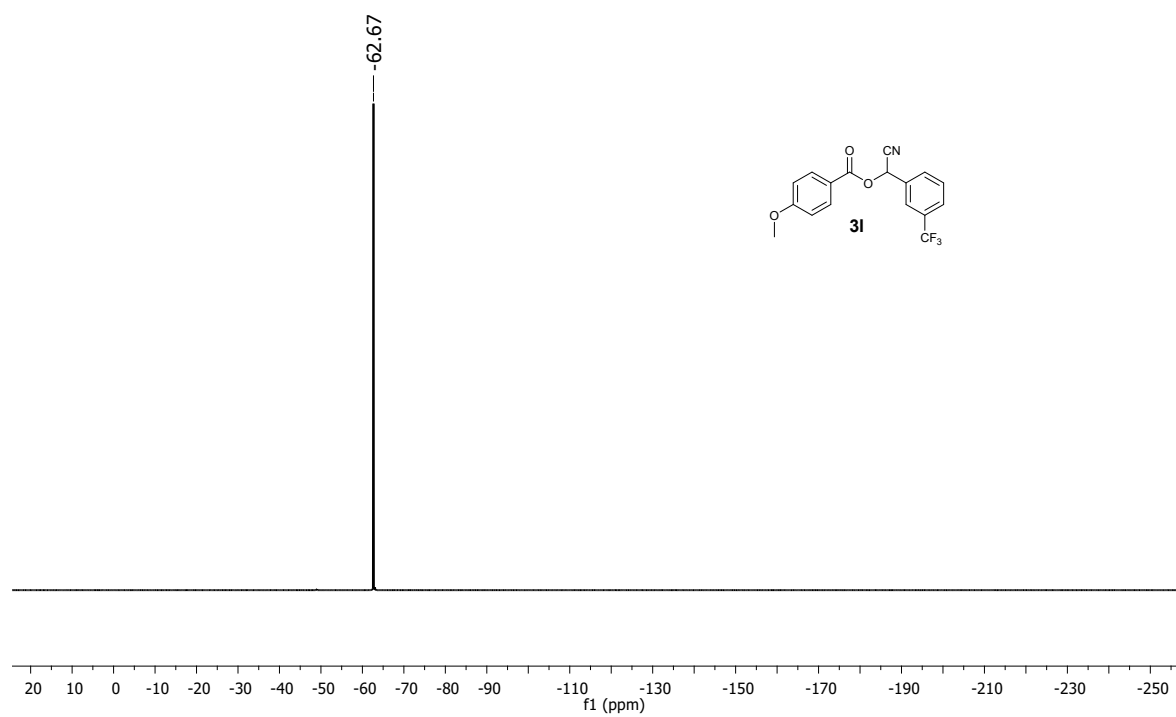
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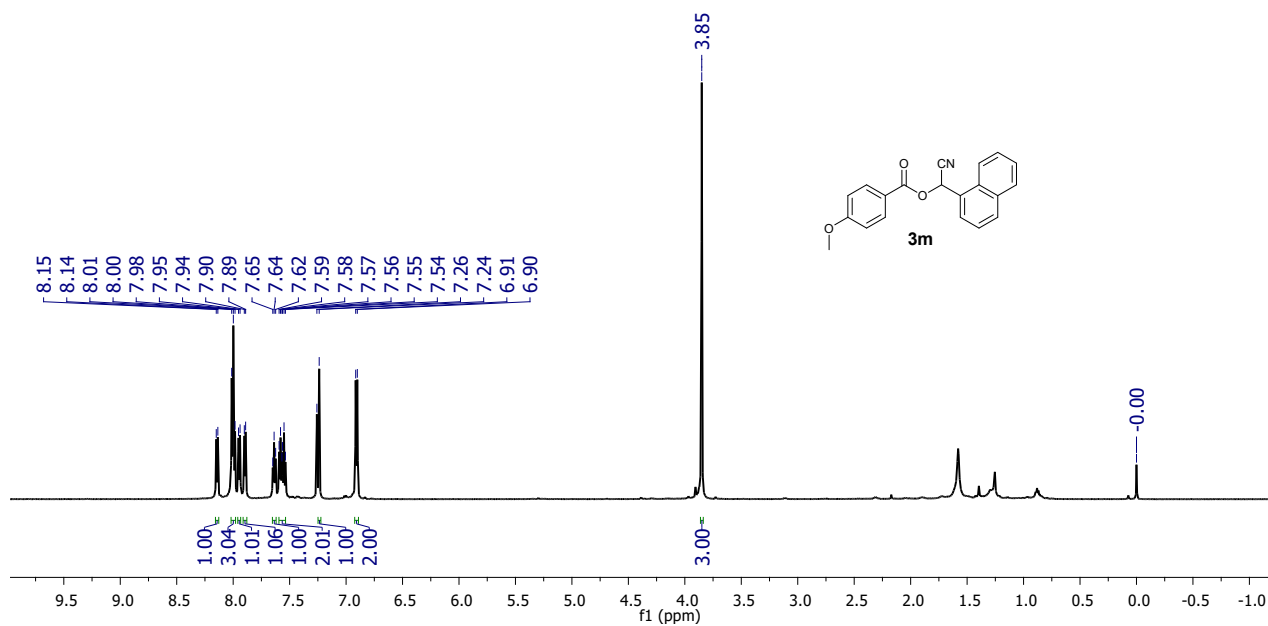
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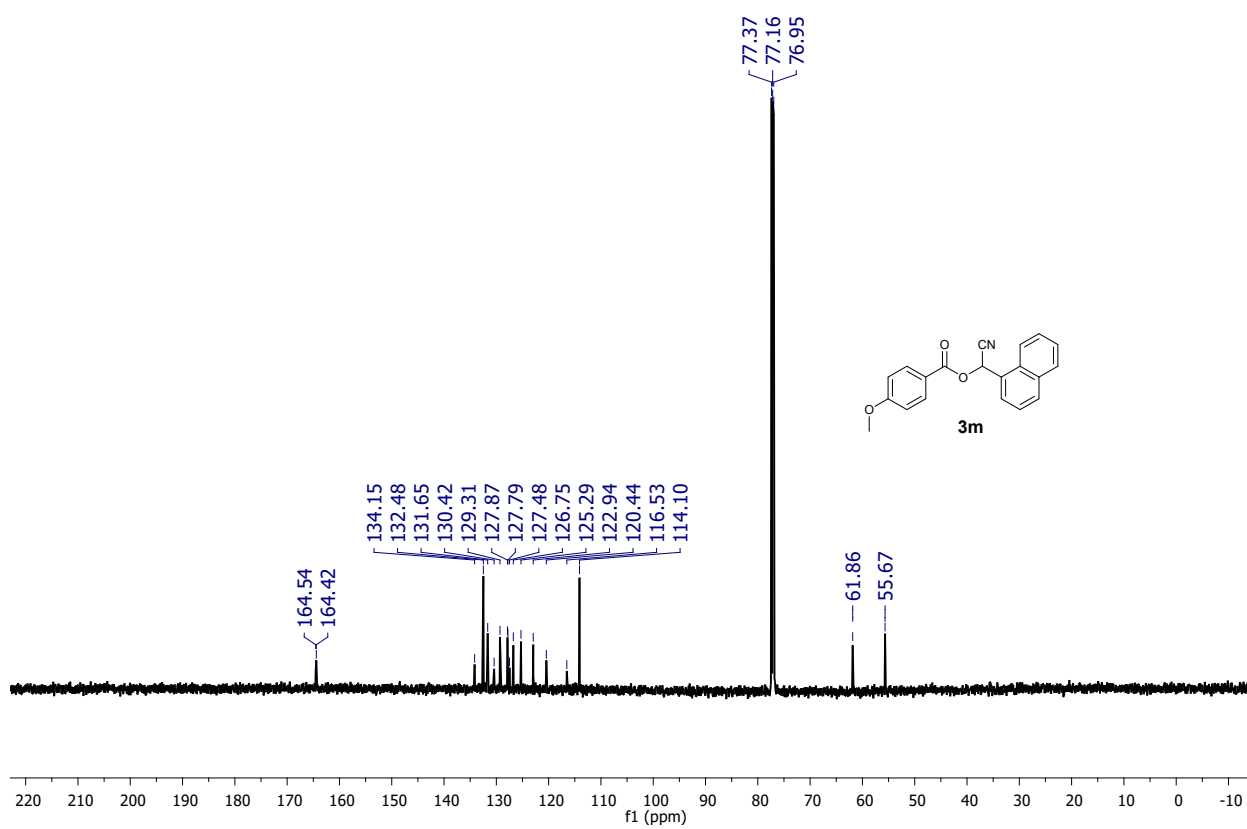
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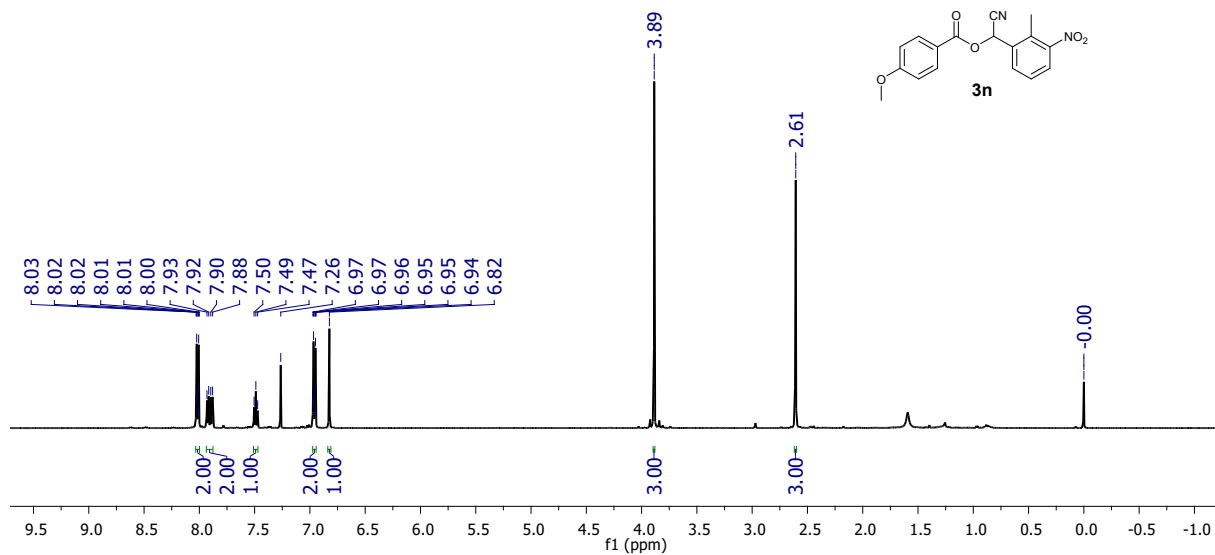
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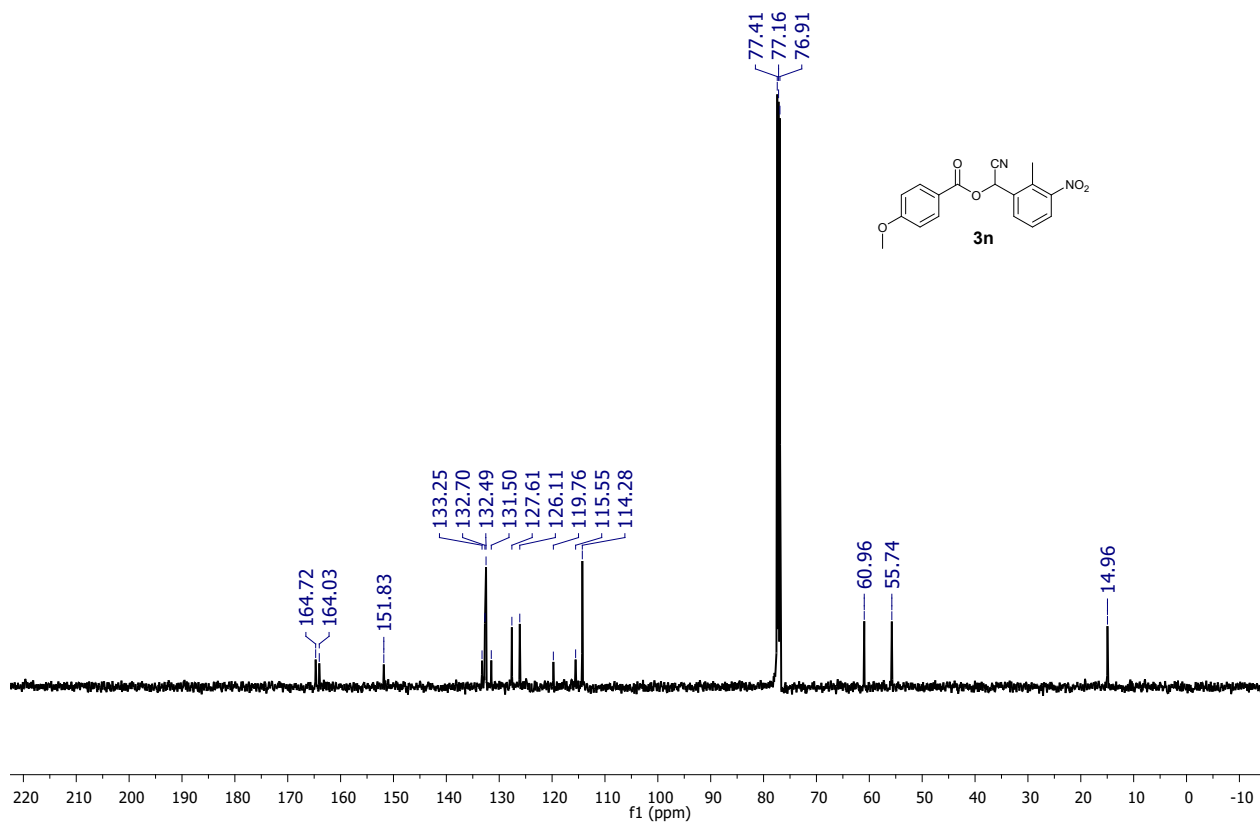
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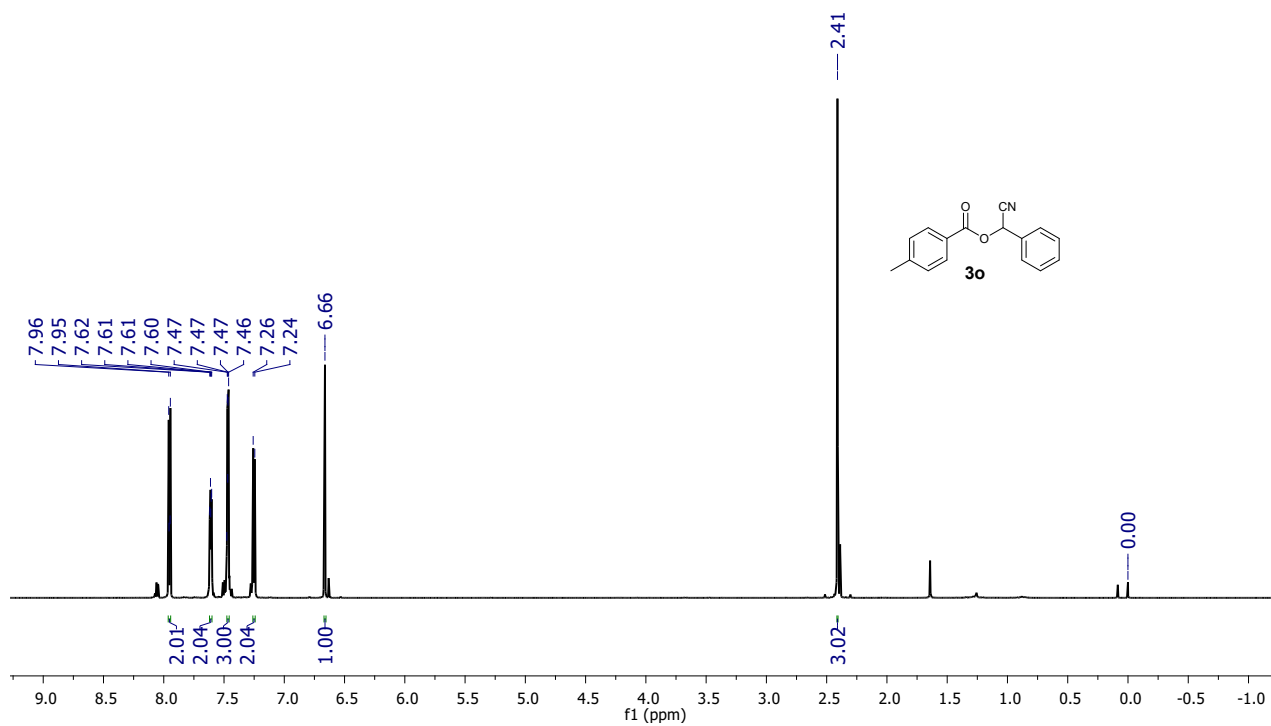
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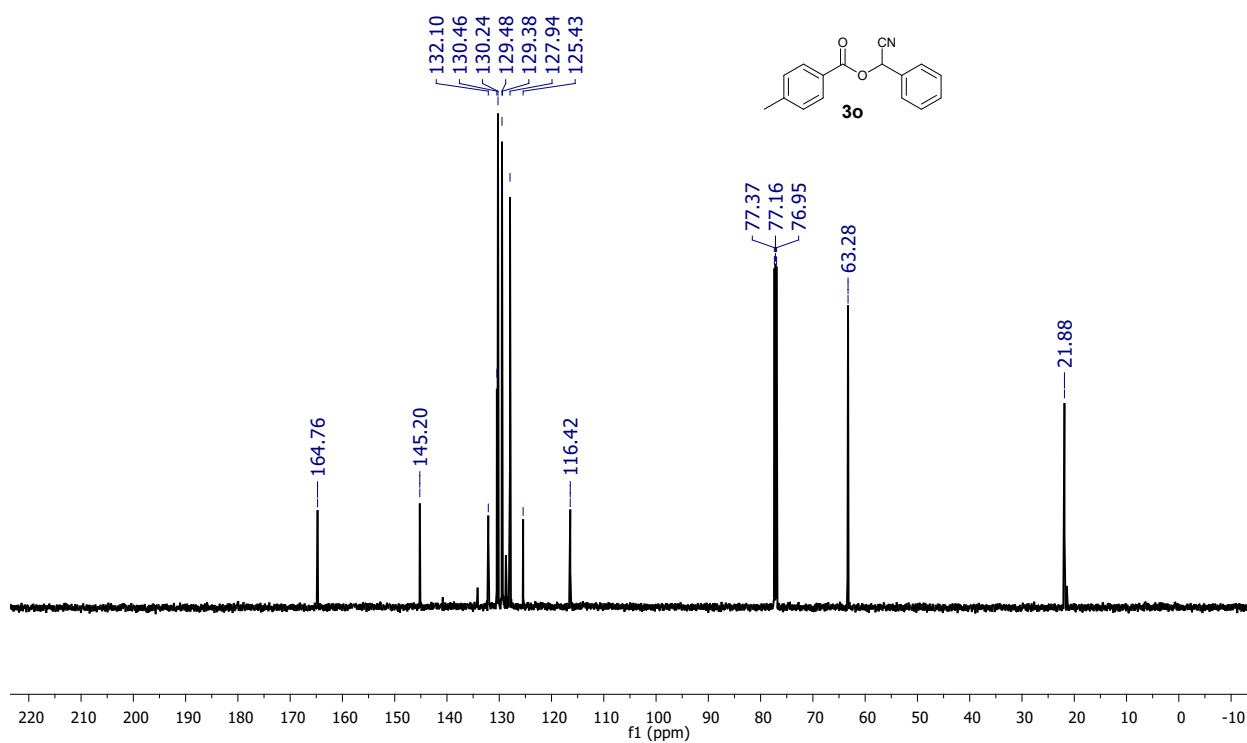
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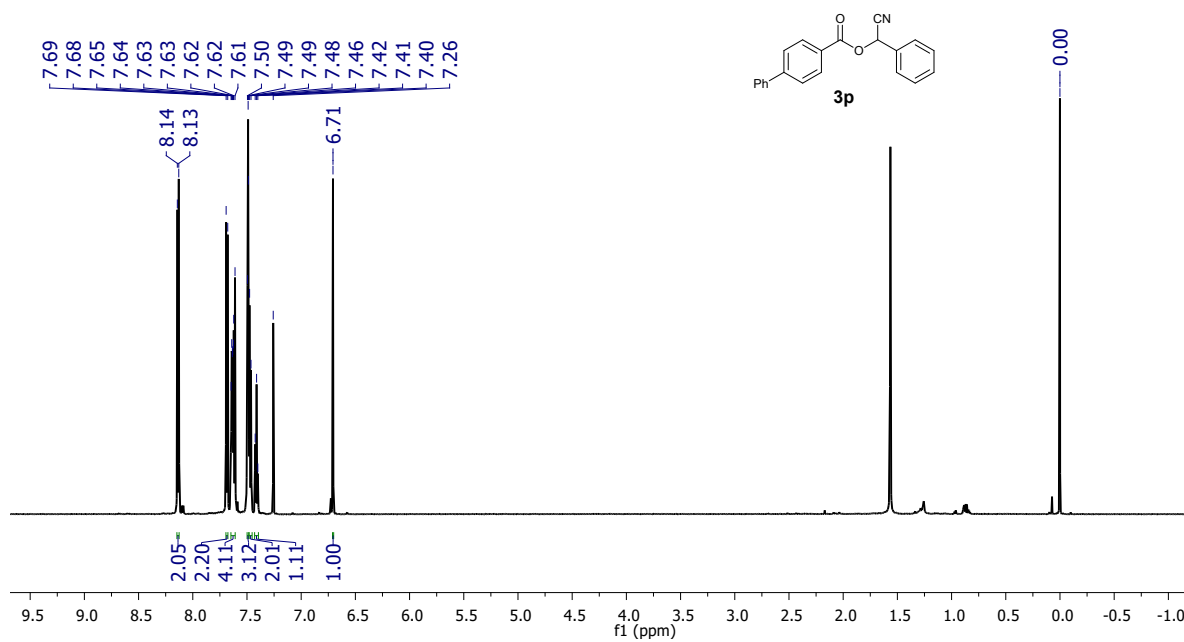
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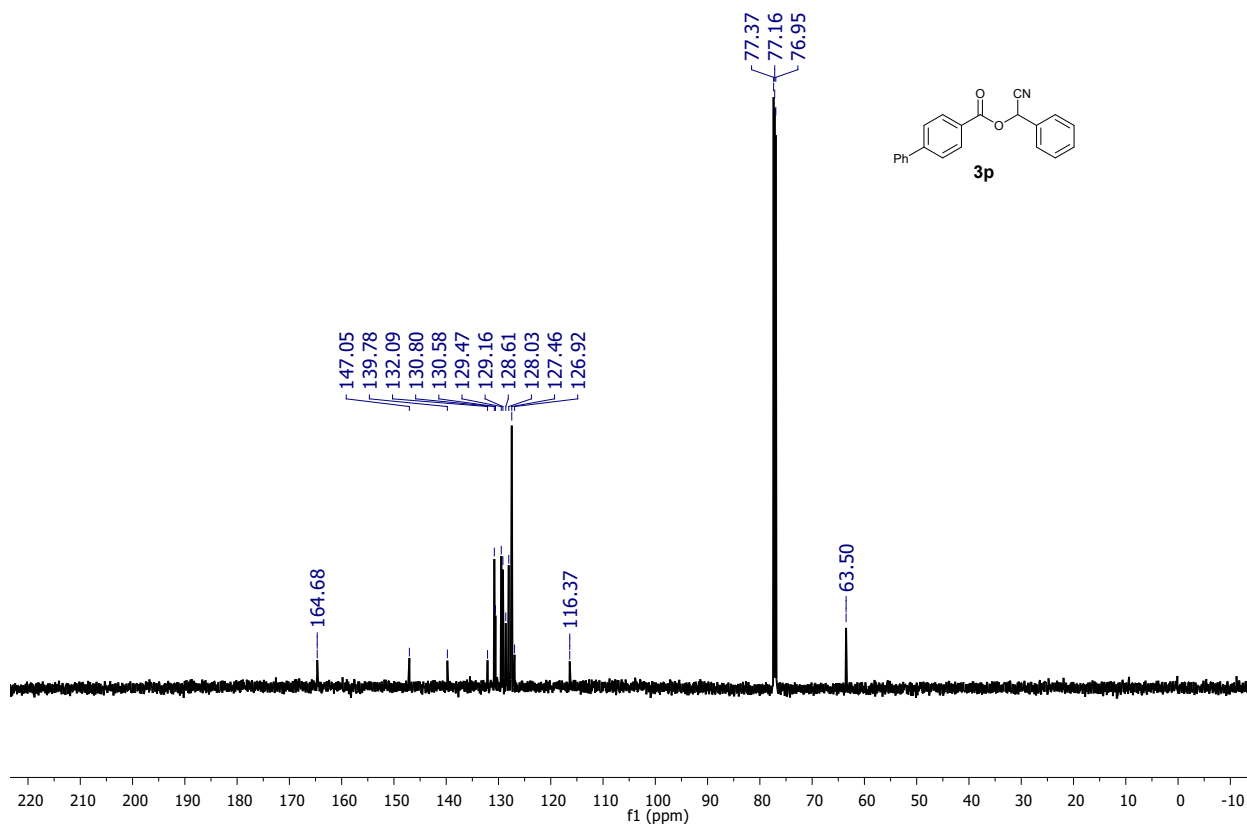
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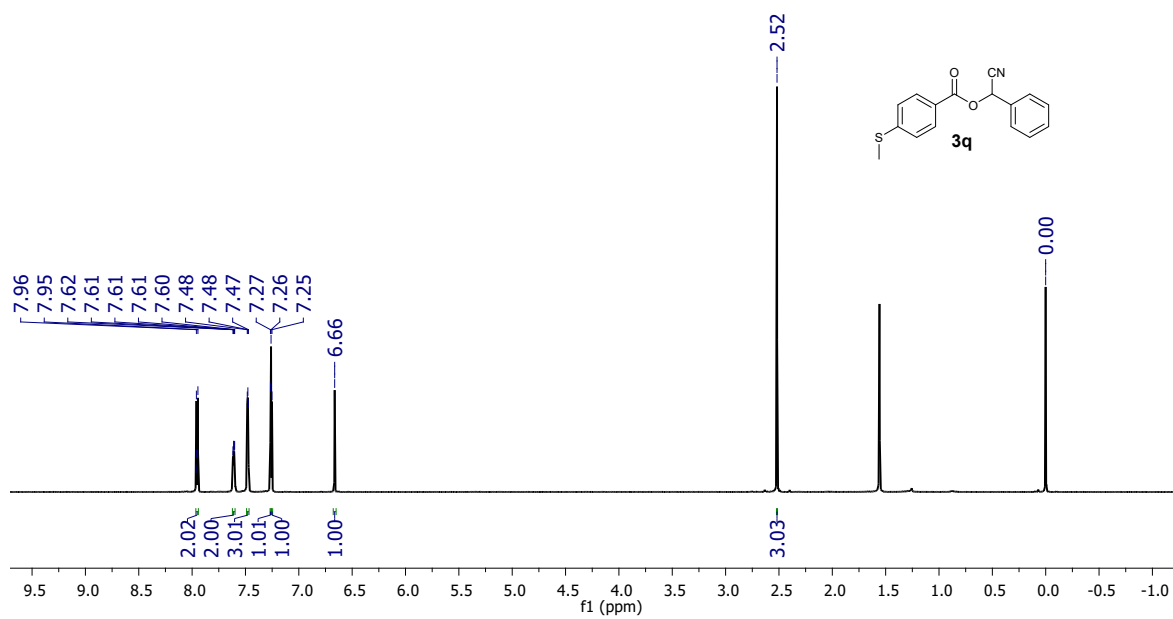
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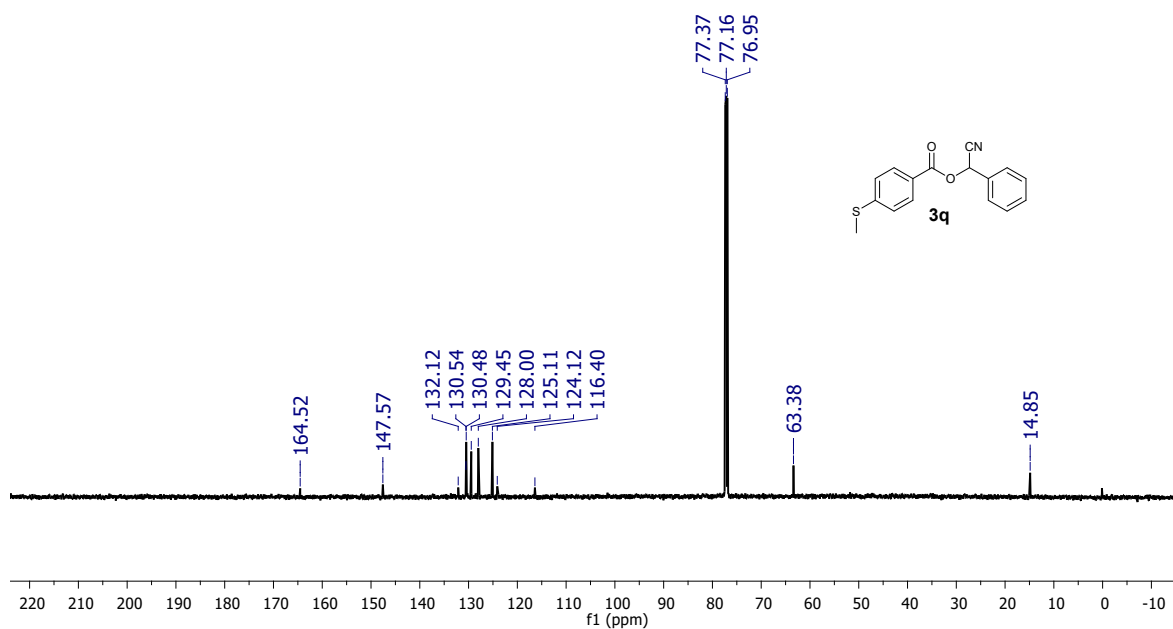
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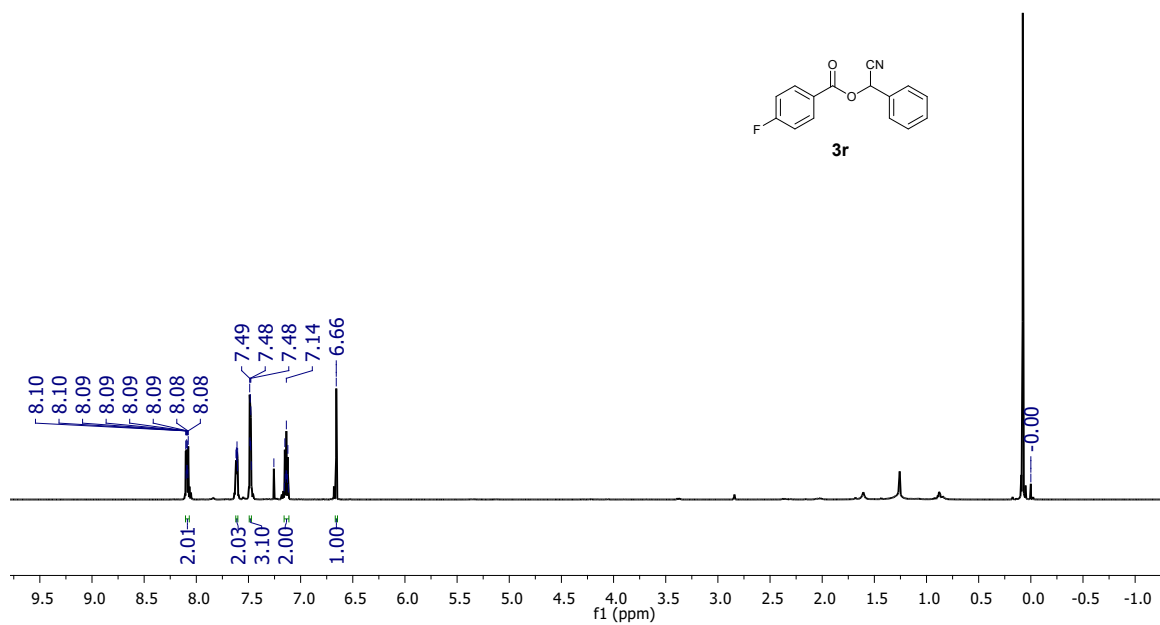
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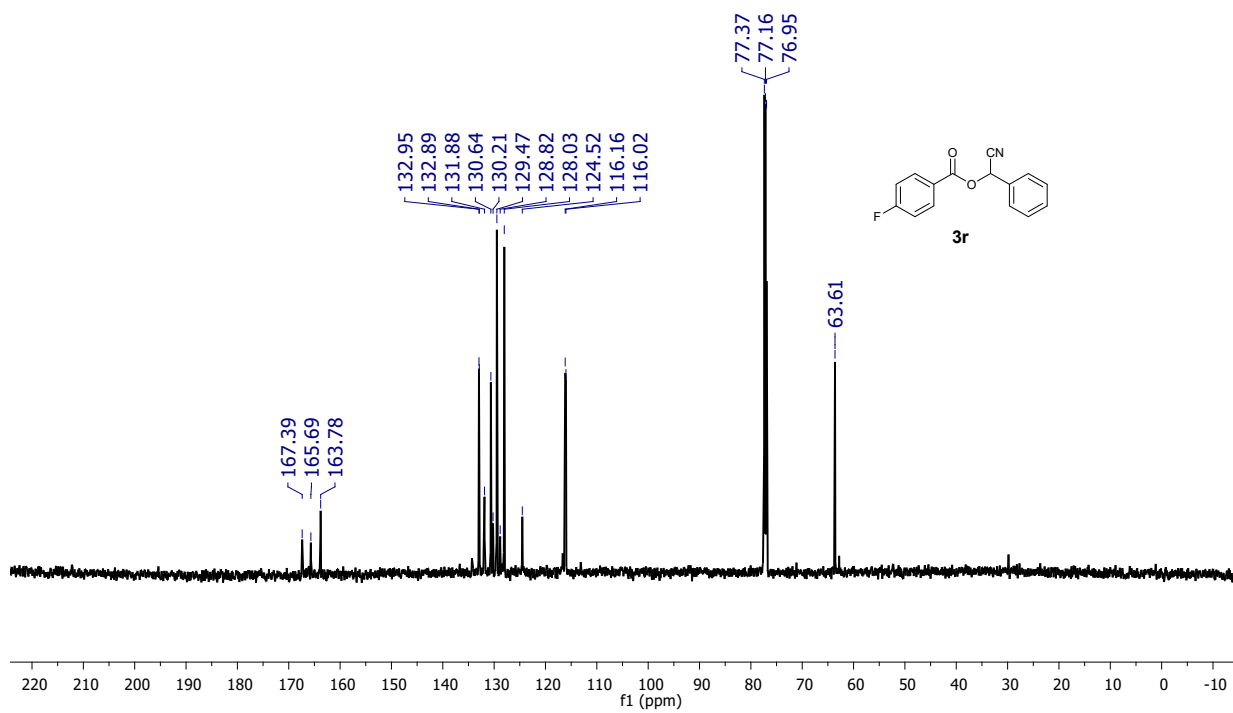
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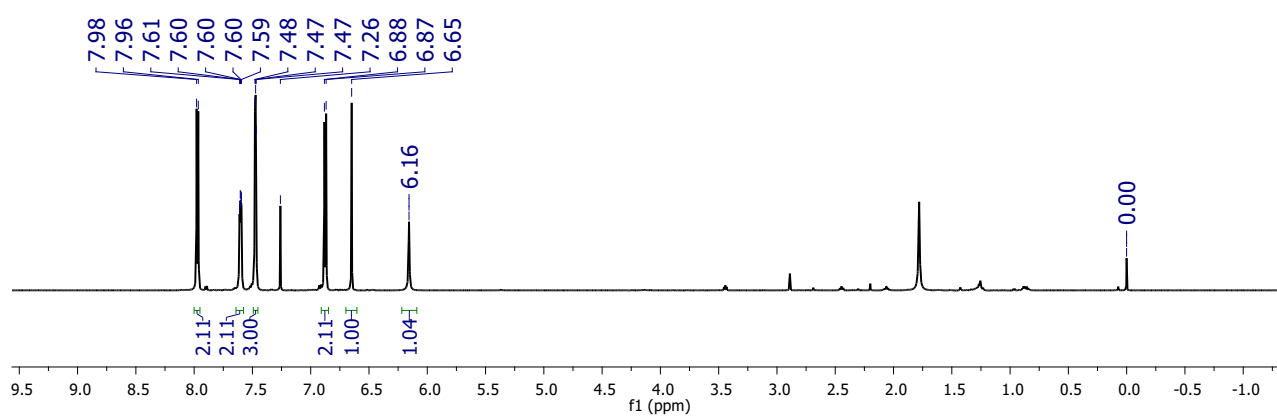
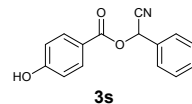
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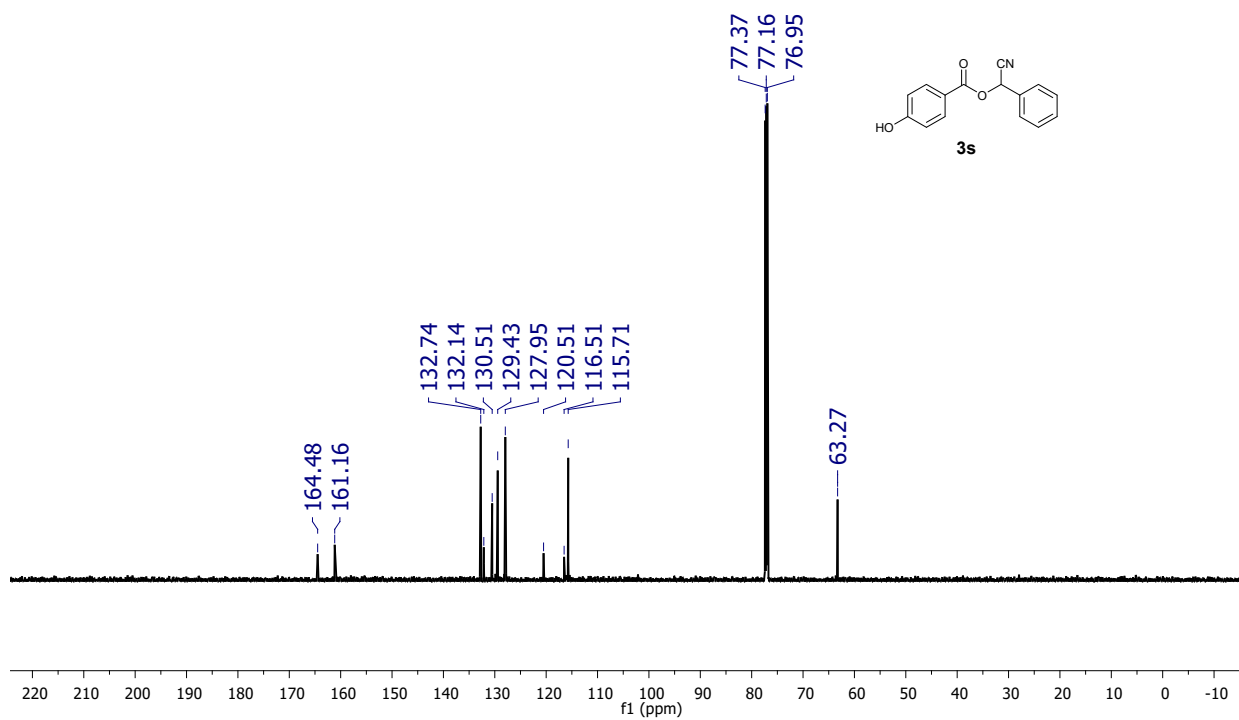
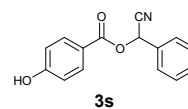
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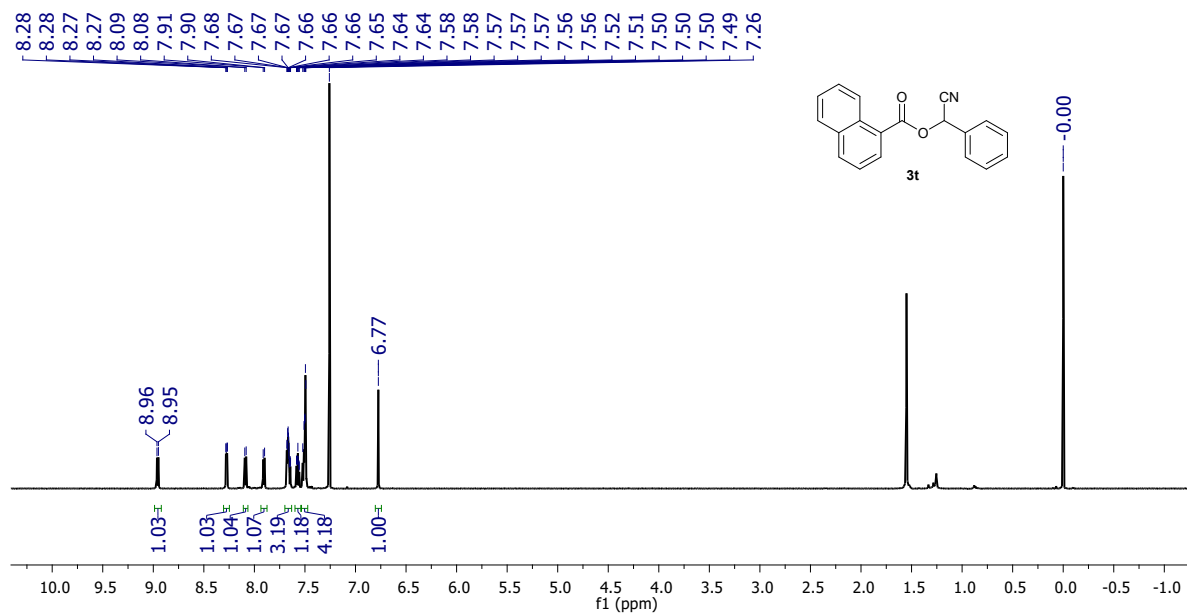
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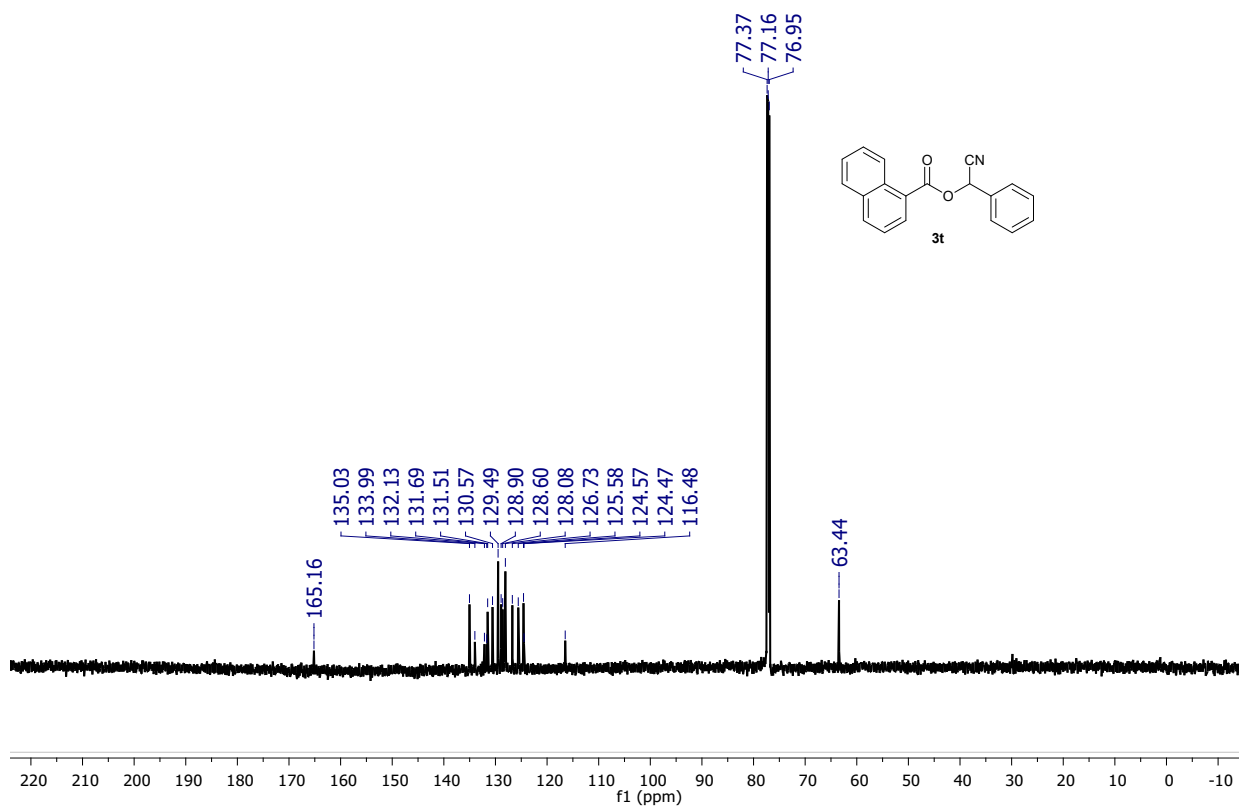
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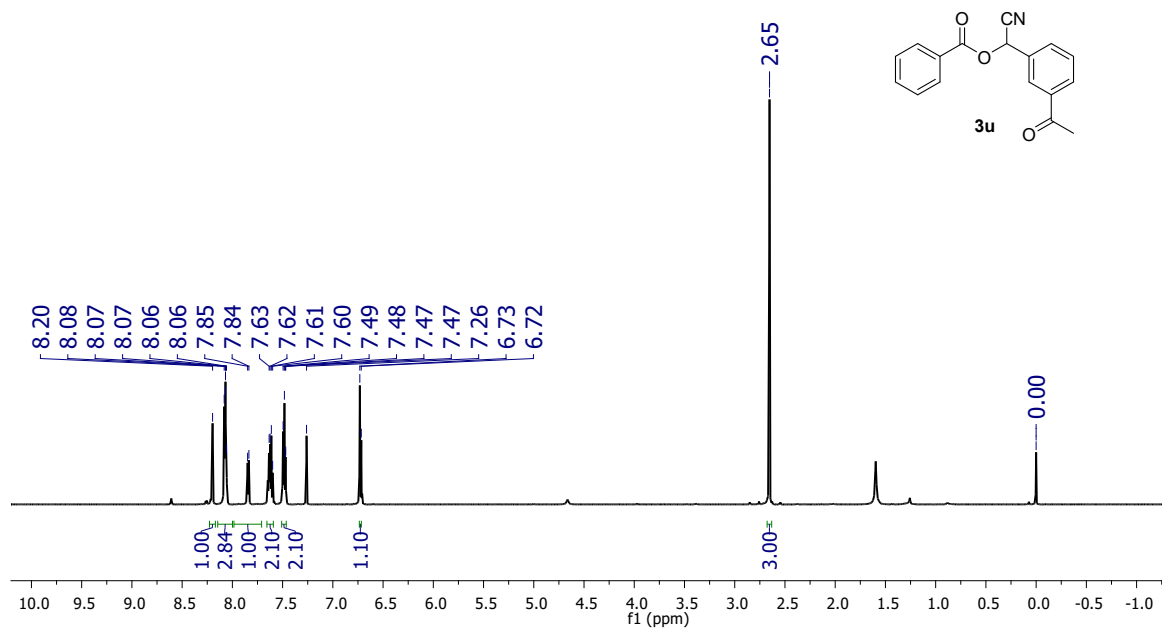
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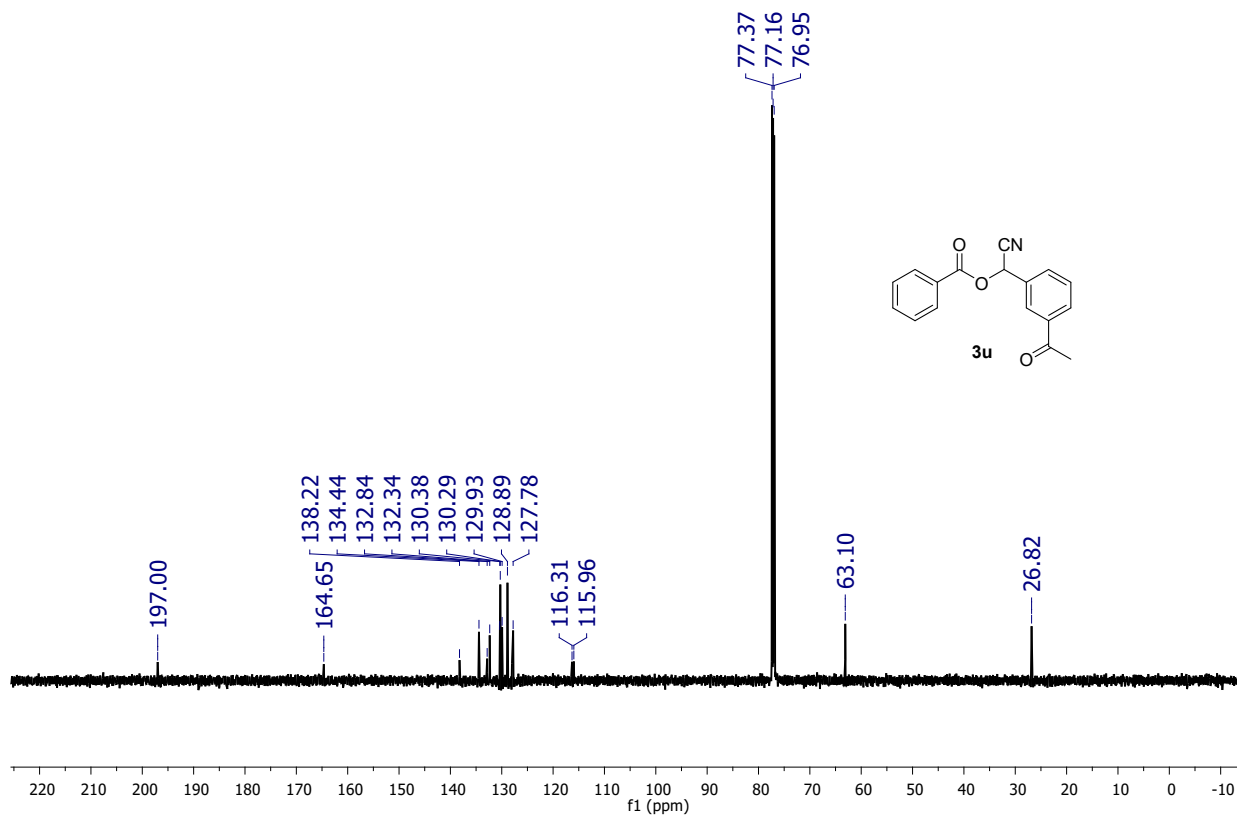
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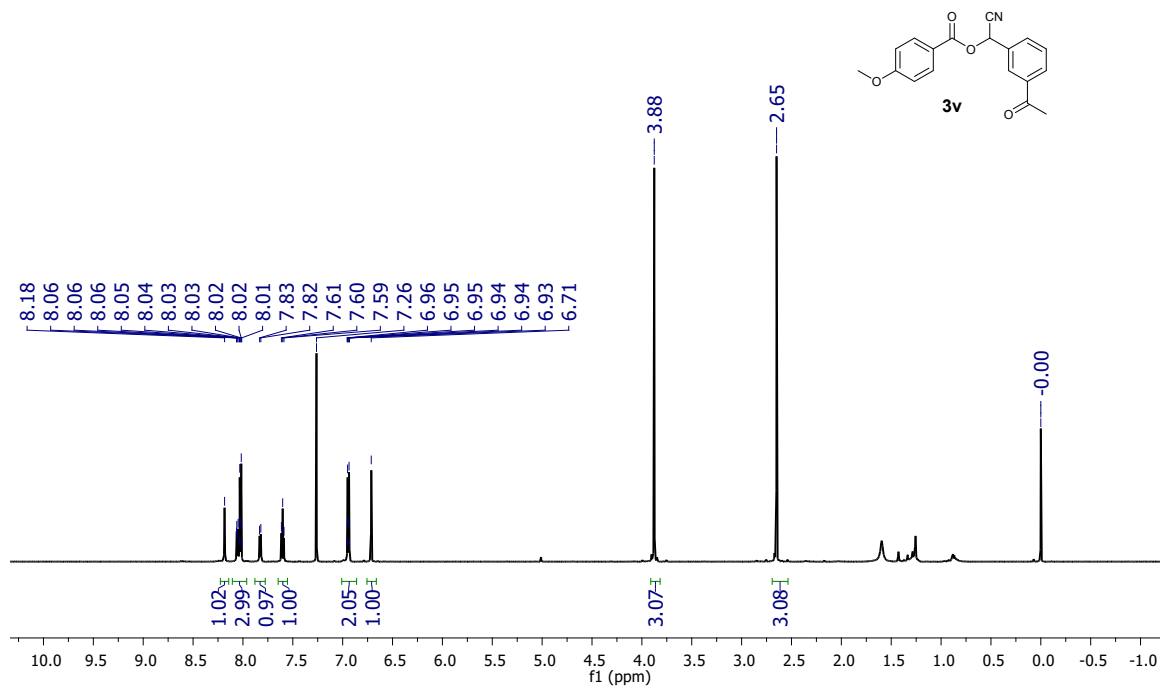
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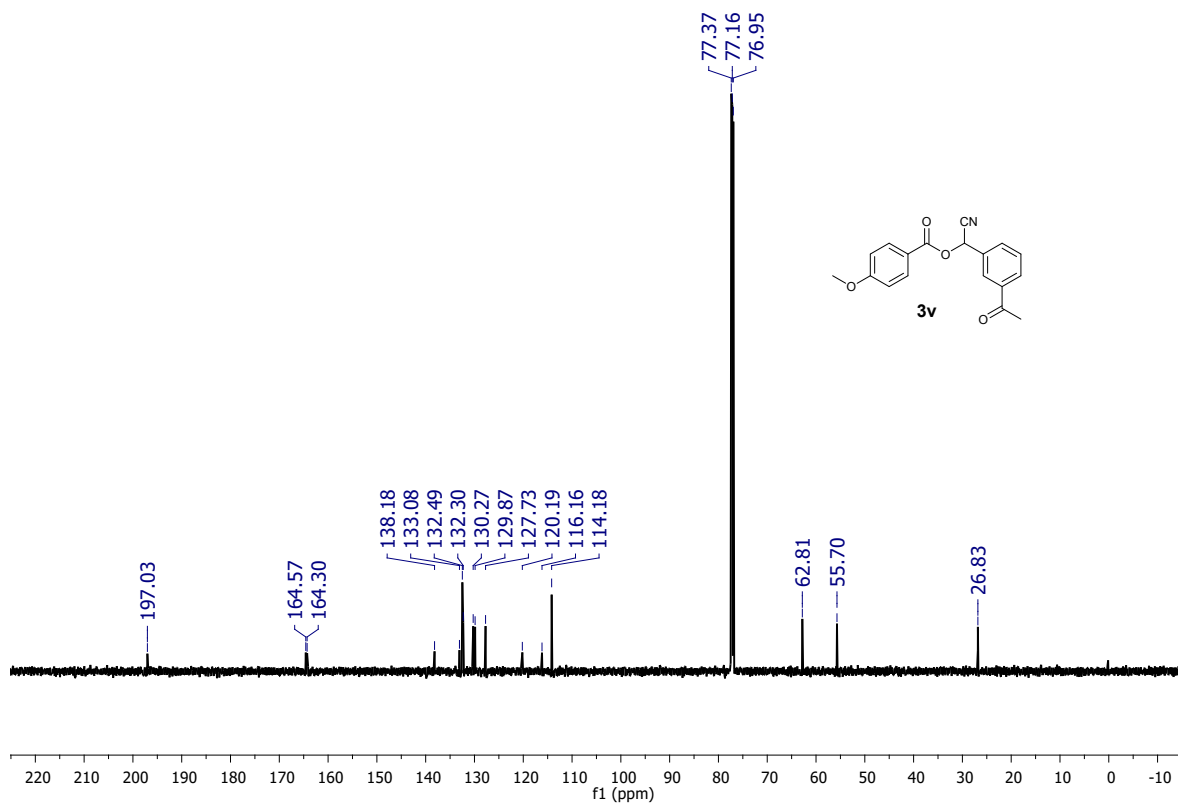
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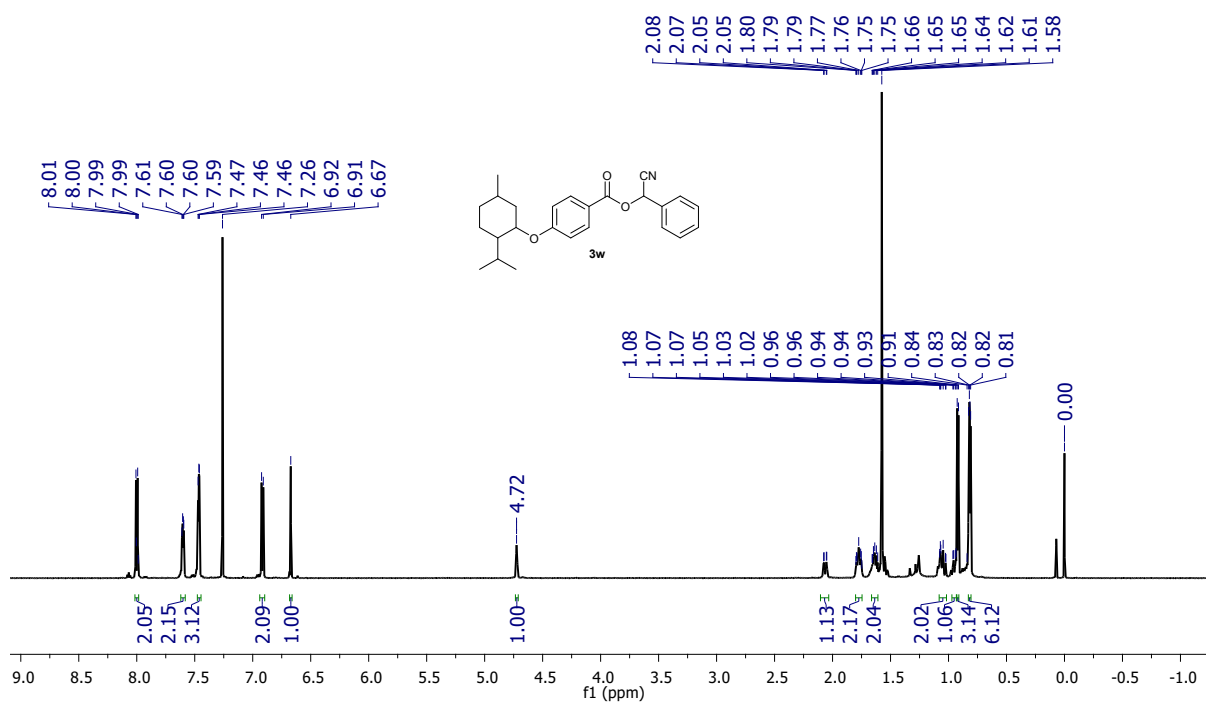
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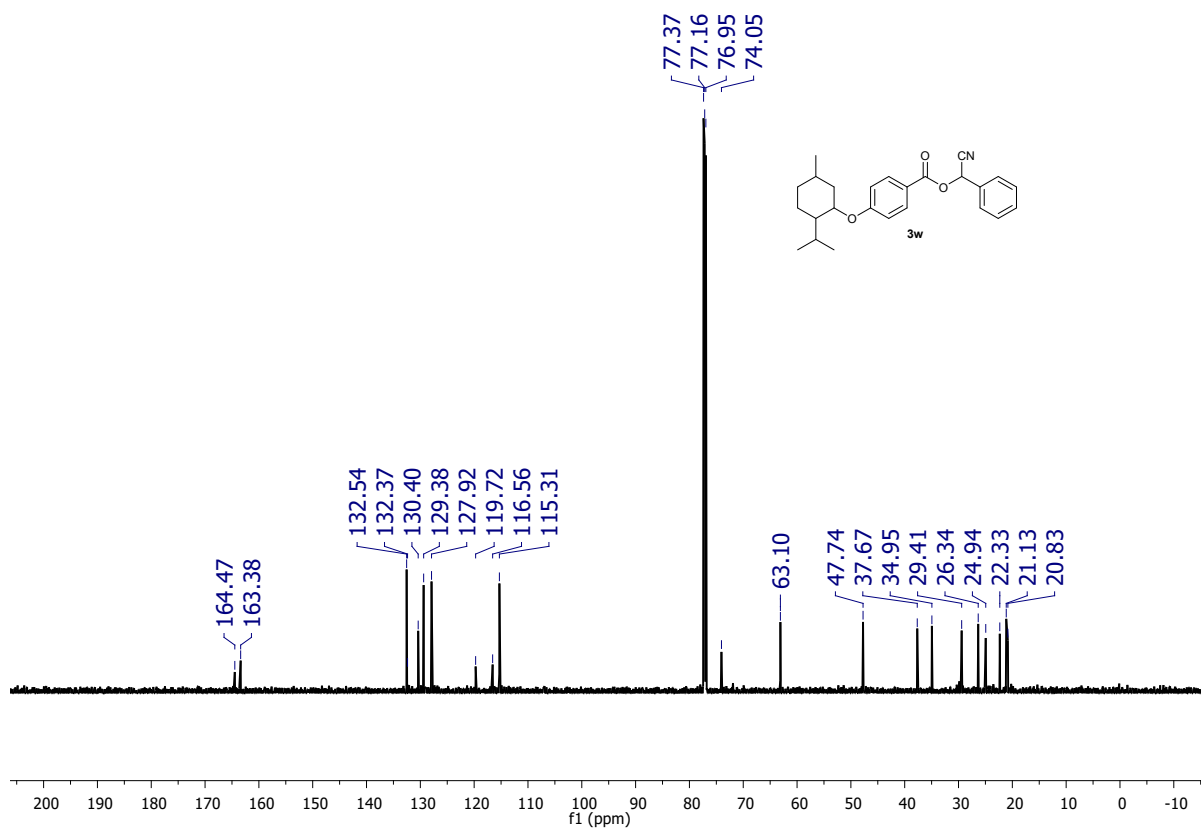
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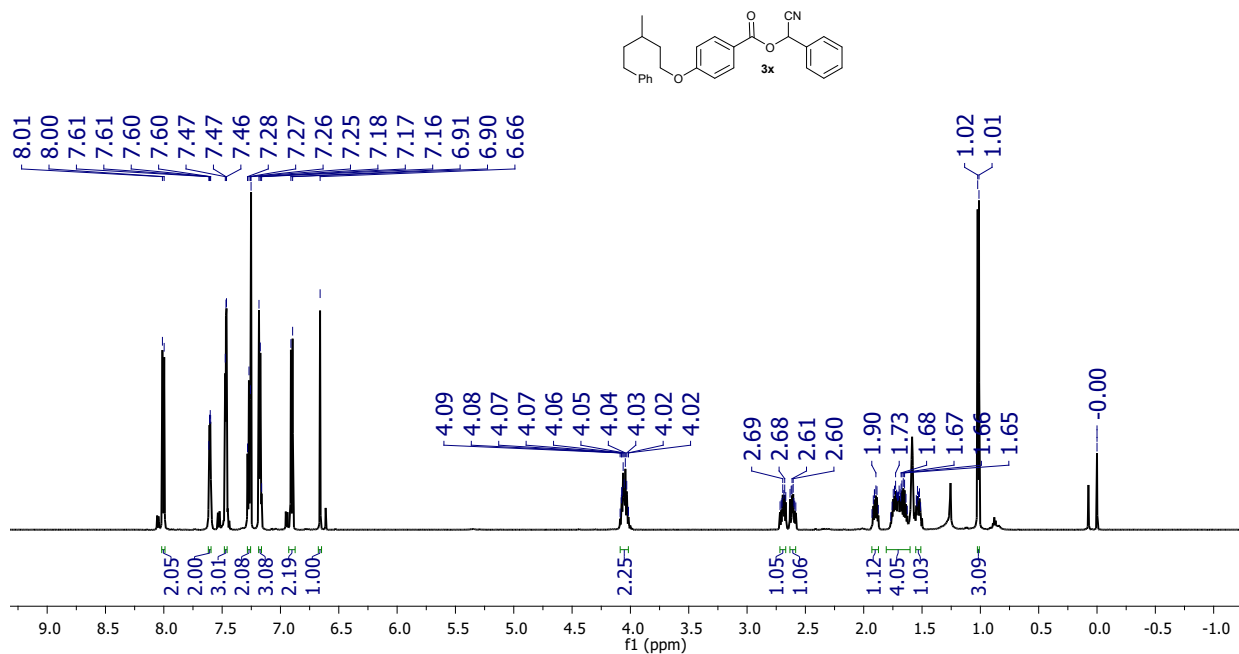
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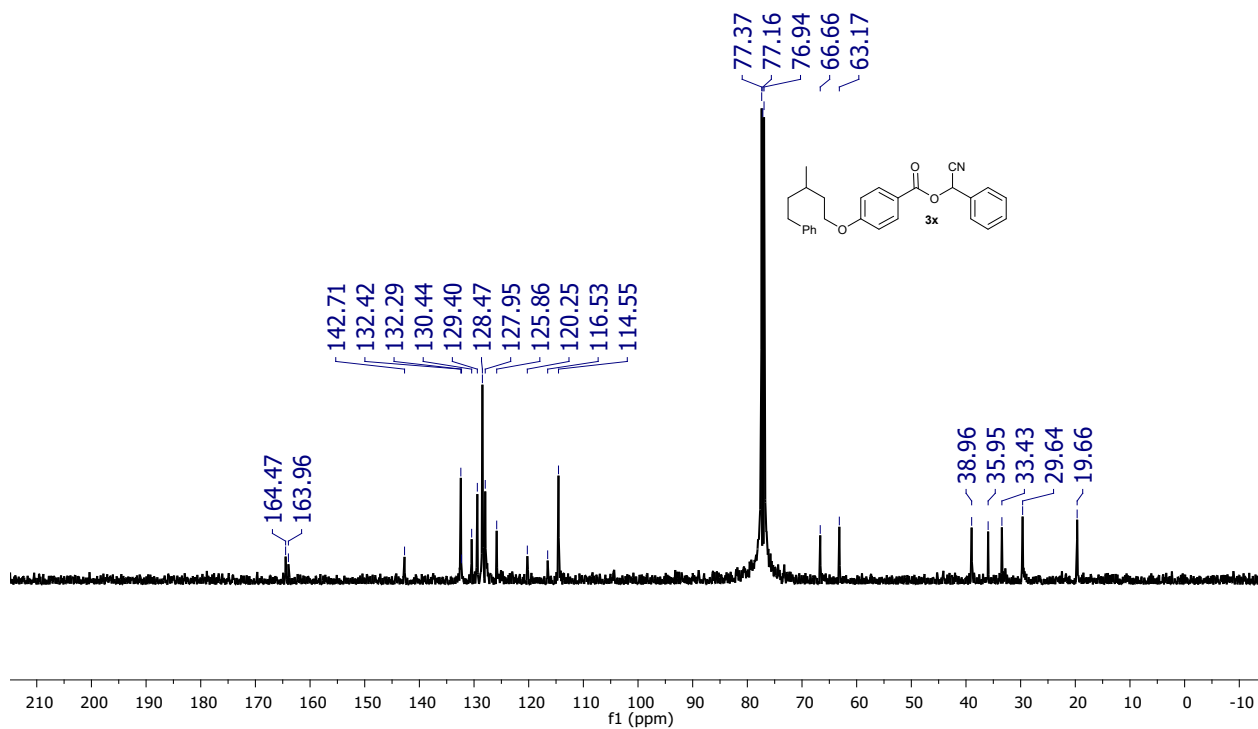
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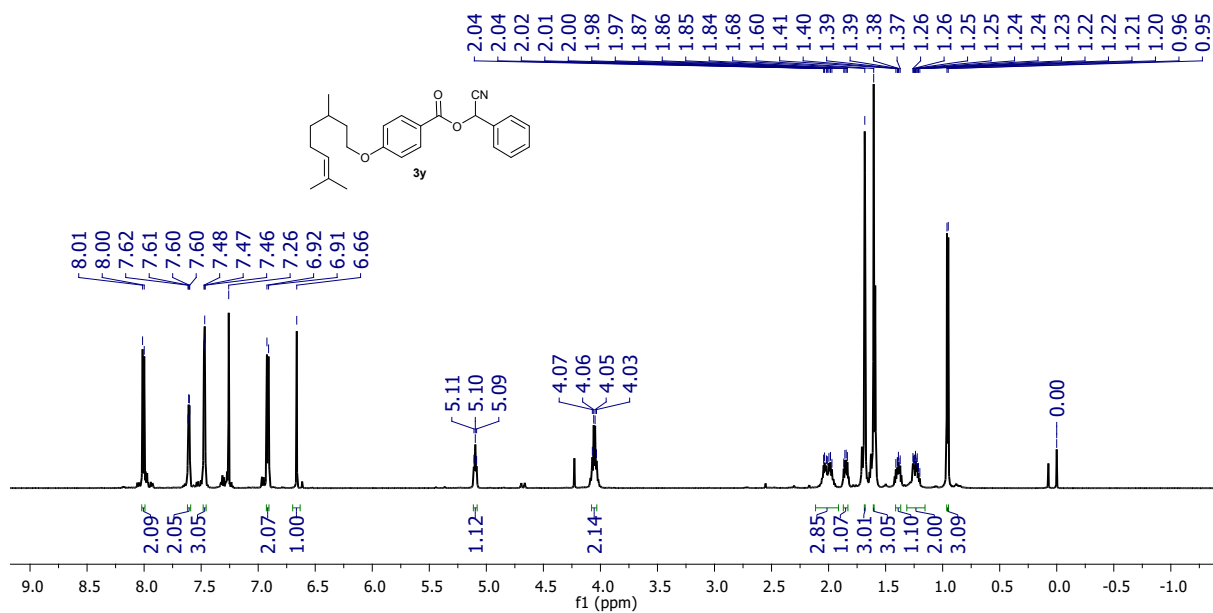
^1H NMR (600 MHz, CDCl_3):



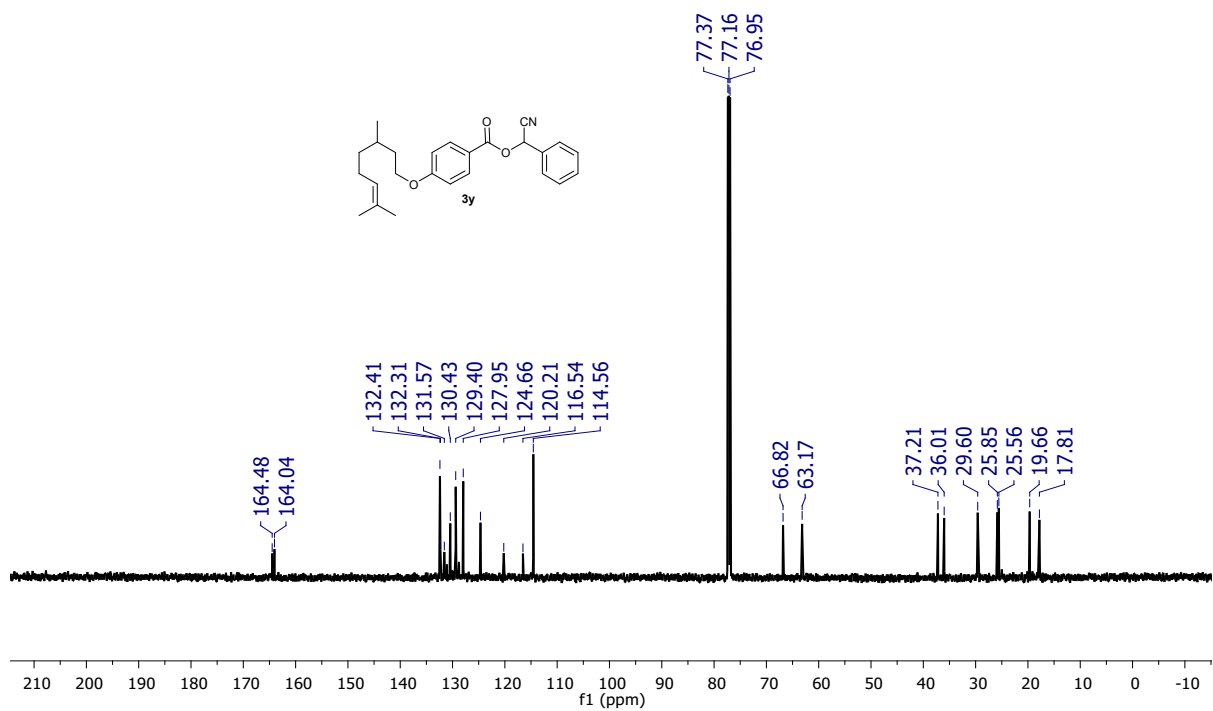
^{13}C NMR (151 MHz, CDCl_3):



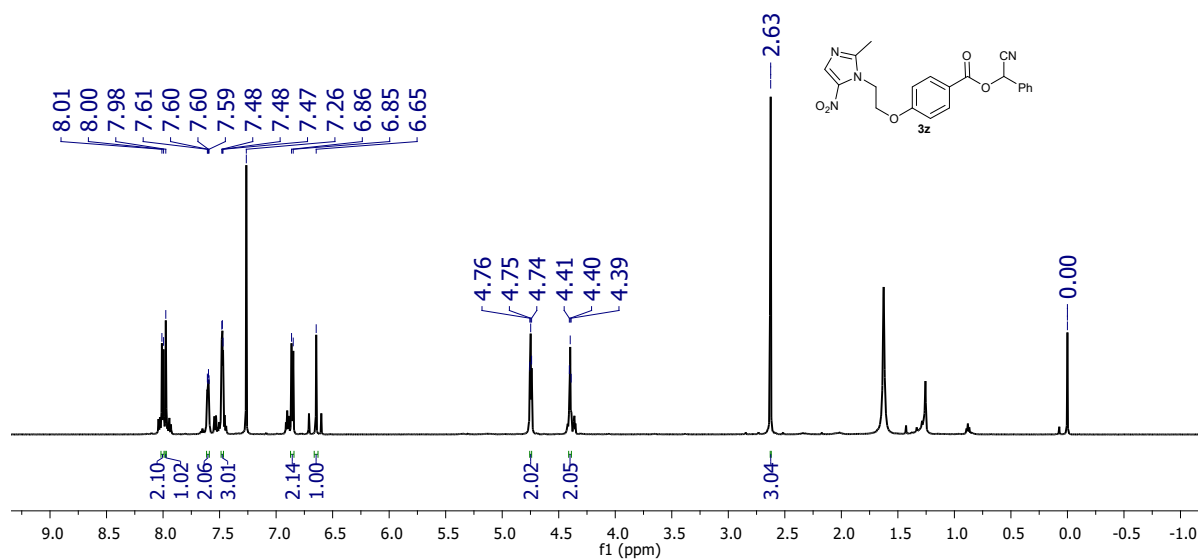
^1H NMR (600 MHz, CDCl_3):



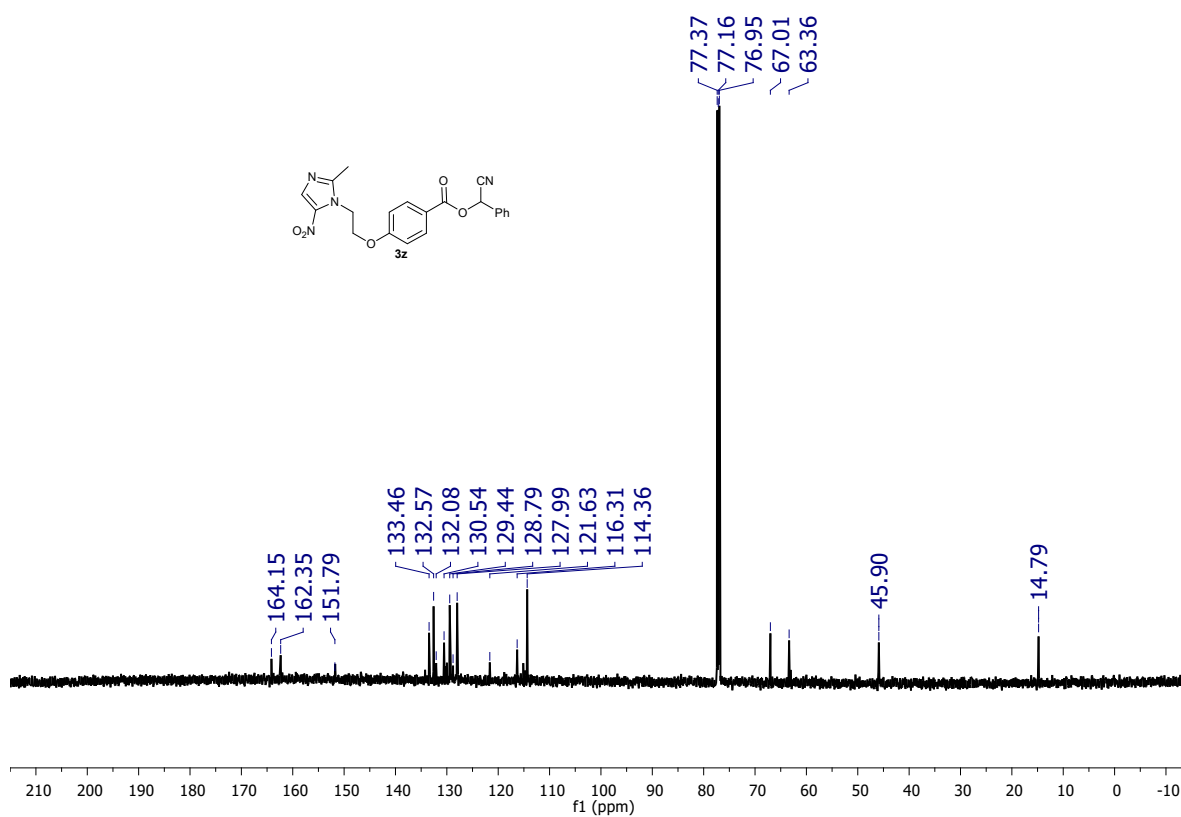
^{13}C NMR (151 MHz, CDCl_3):



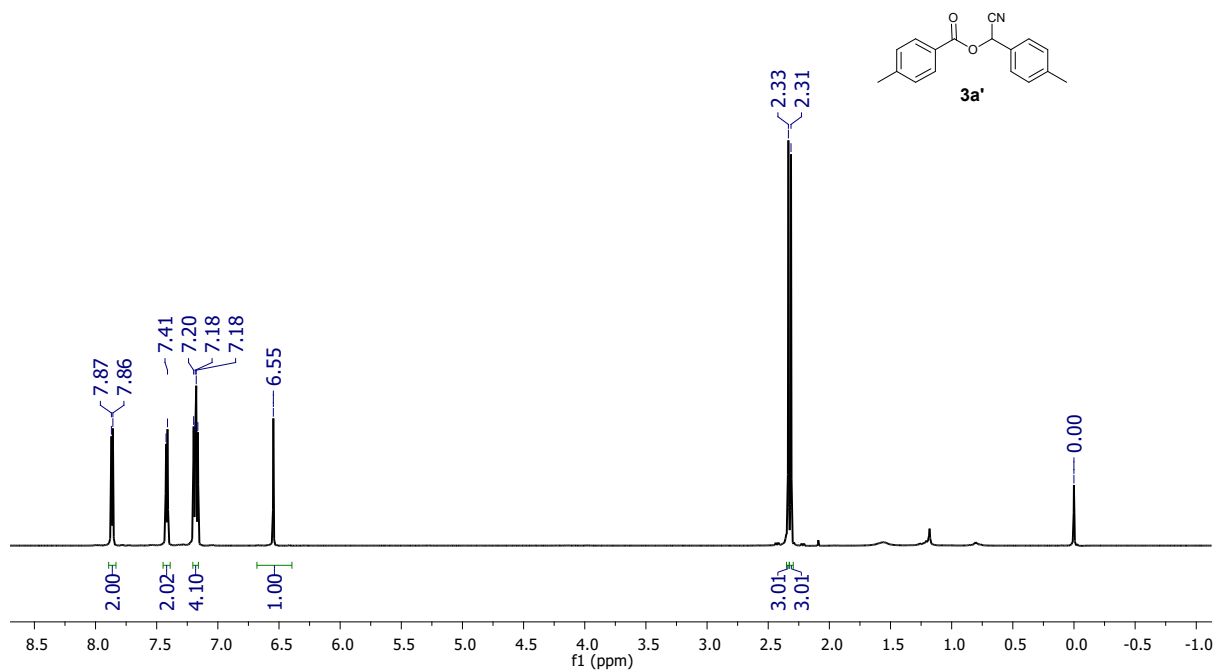
^1H NMR (600 MHz, CDCl_3):



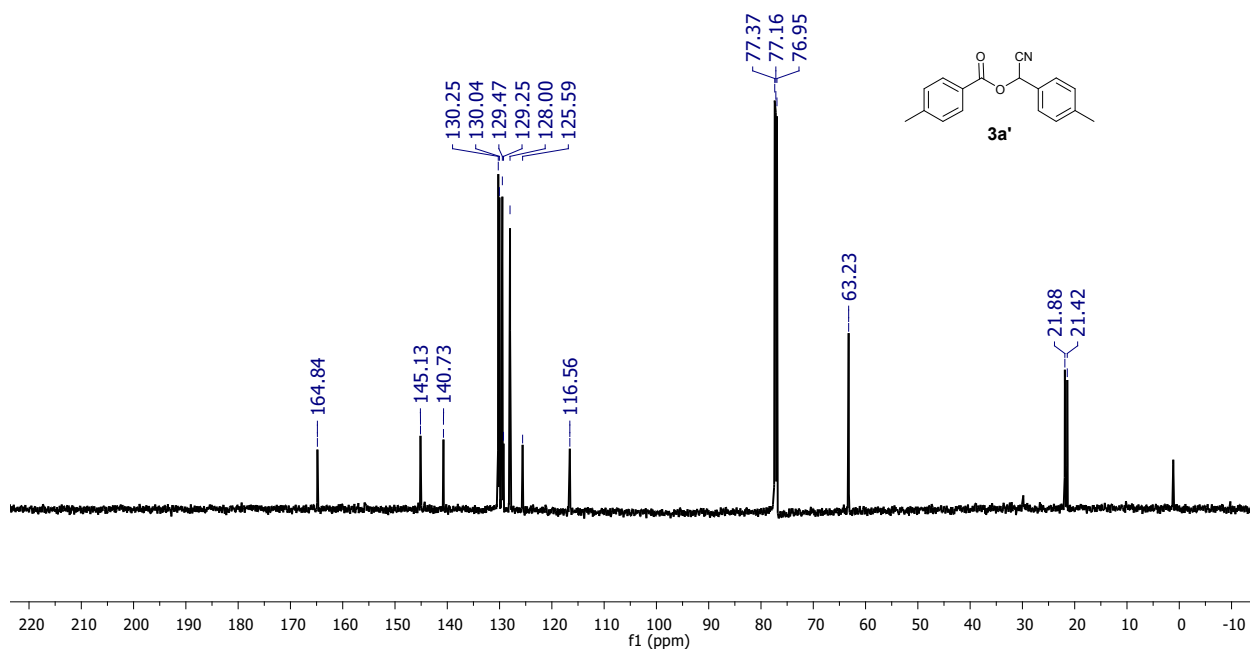
^{13}C NMR (151 MHz, CDCl_3):



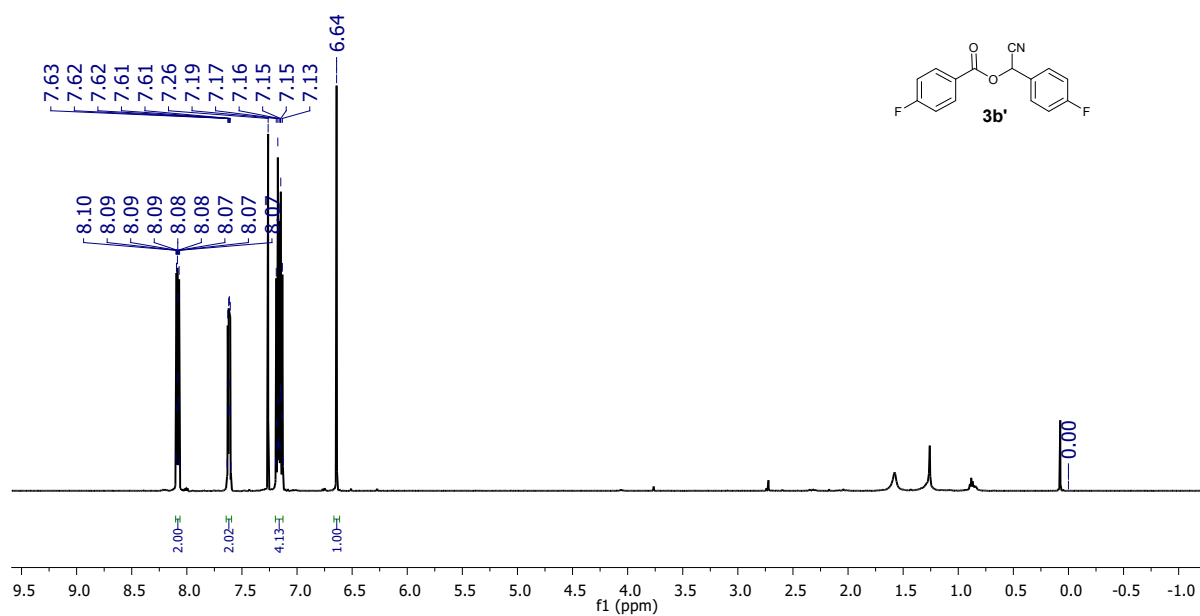
^1H NMR (600 MHz, CDCl_3):



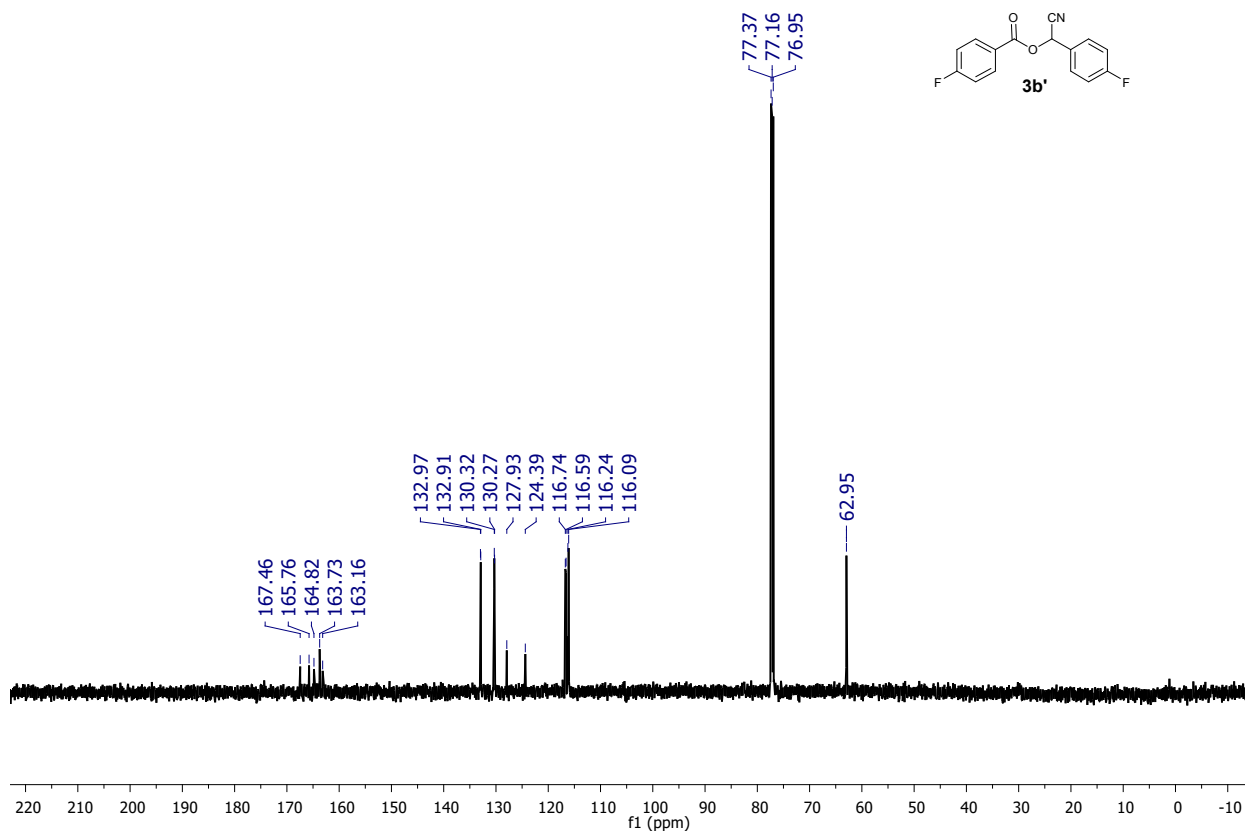
^{13}C NMR (151 MHz, CDCl_3):



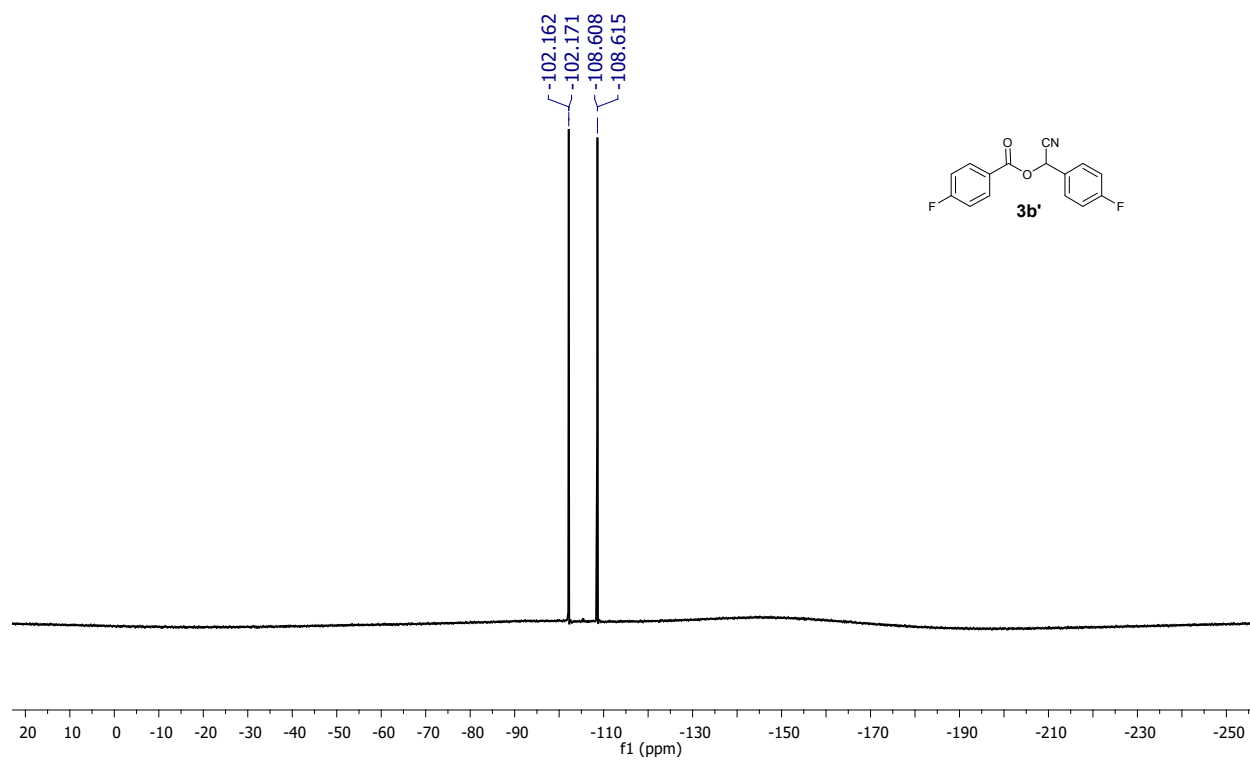
^1H NMR (600 MHz, CDCl_3):



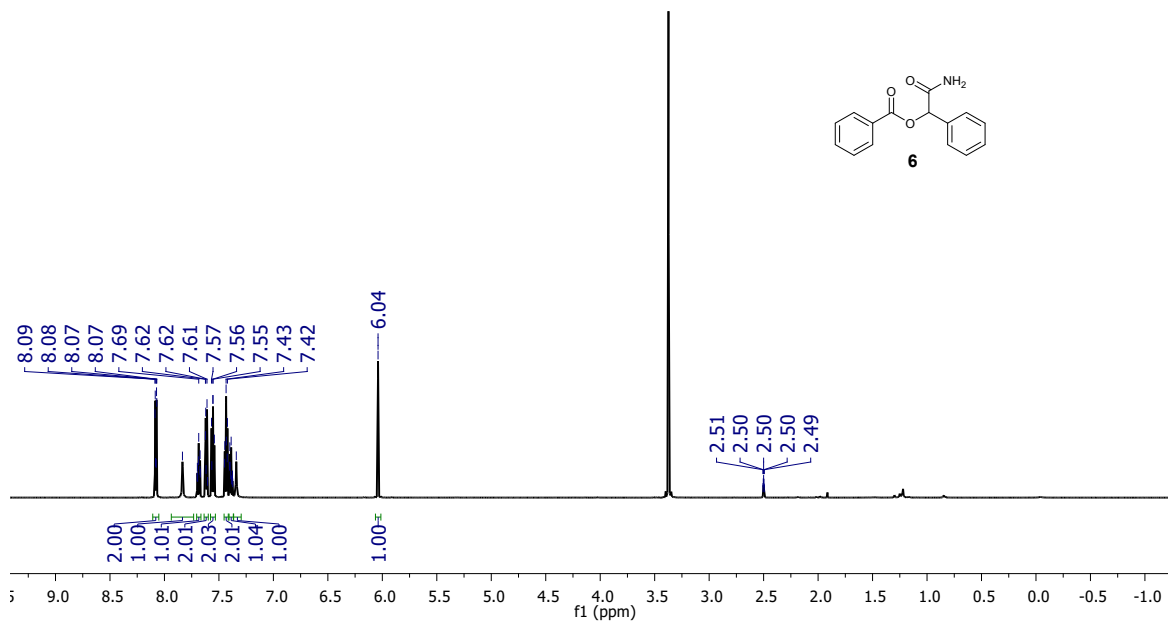
^{13}C NMR (151 MHz, CDCl_3):



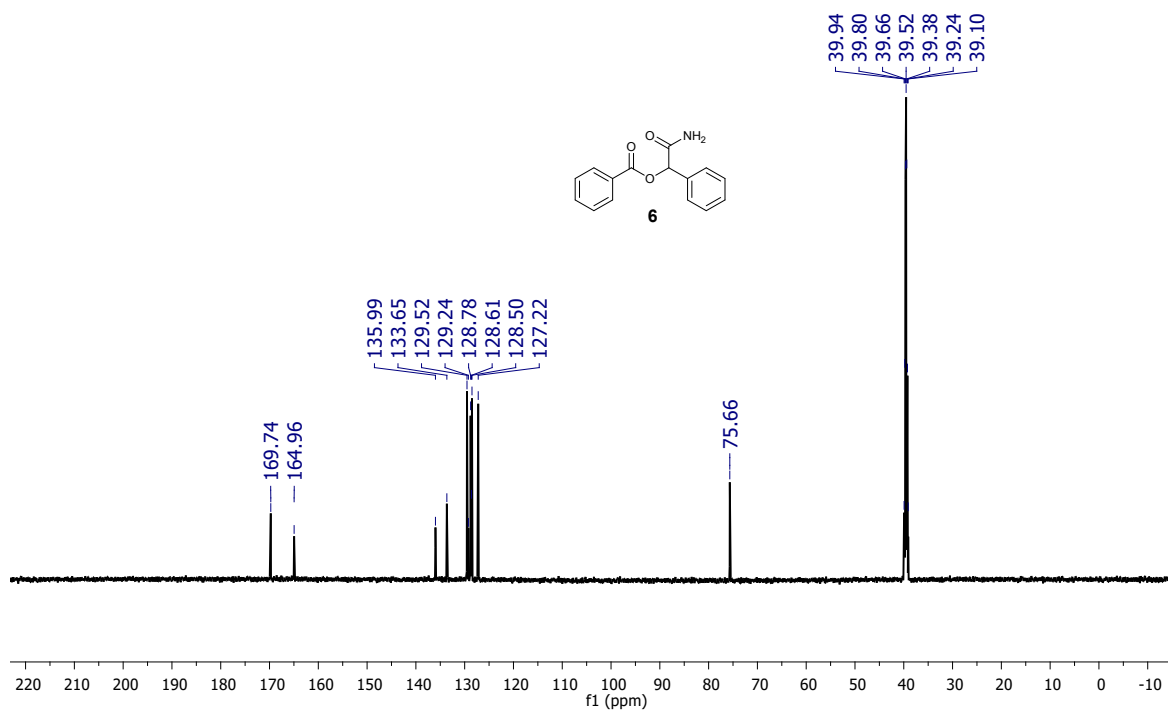
^{19}F NMR (565 MHz, CDCl_3):



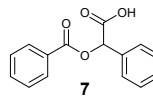
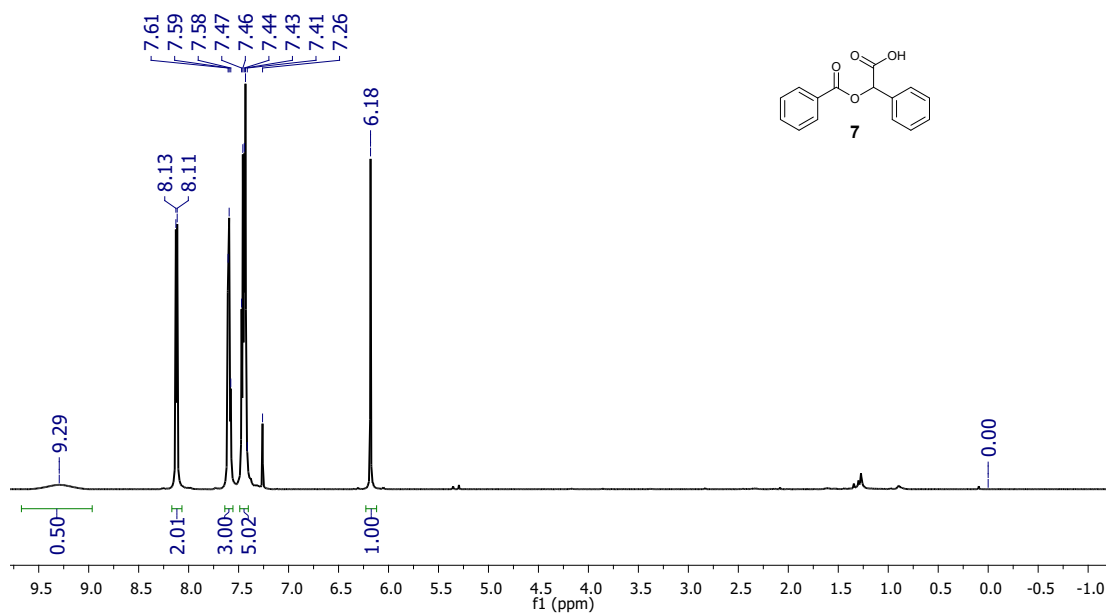
^1H NMR (600 MHz, DMSO):



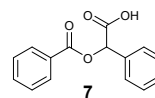
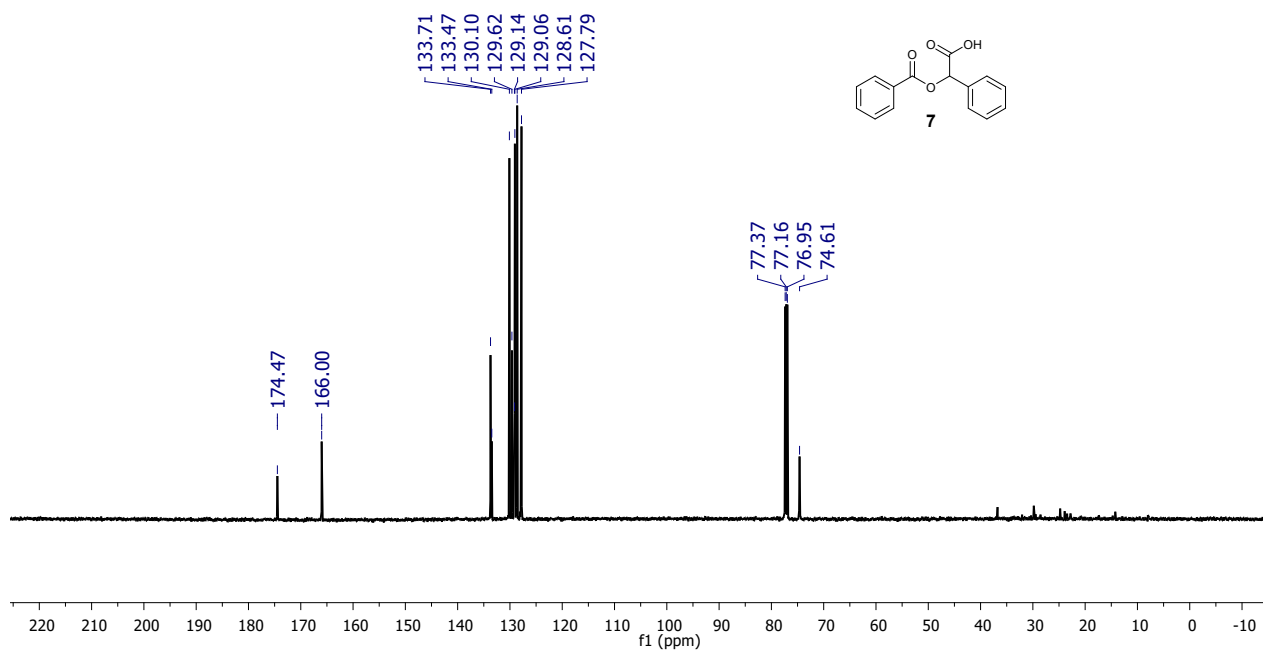
^{13}C NMR (151 MHz, DMSO):



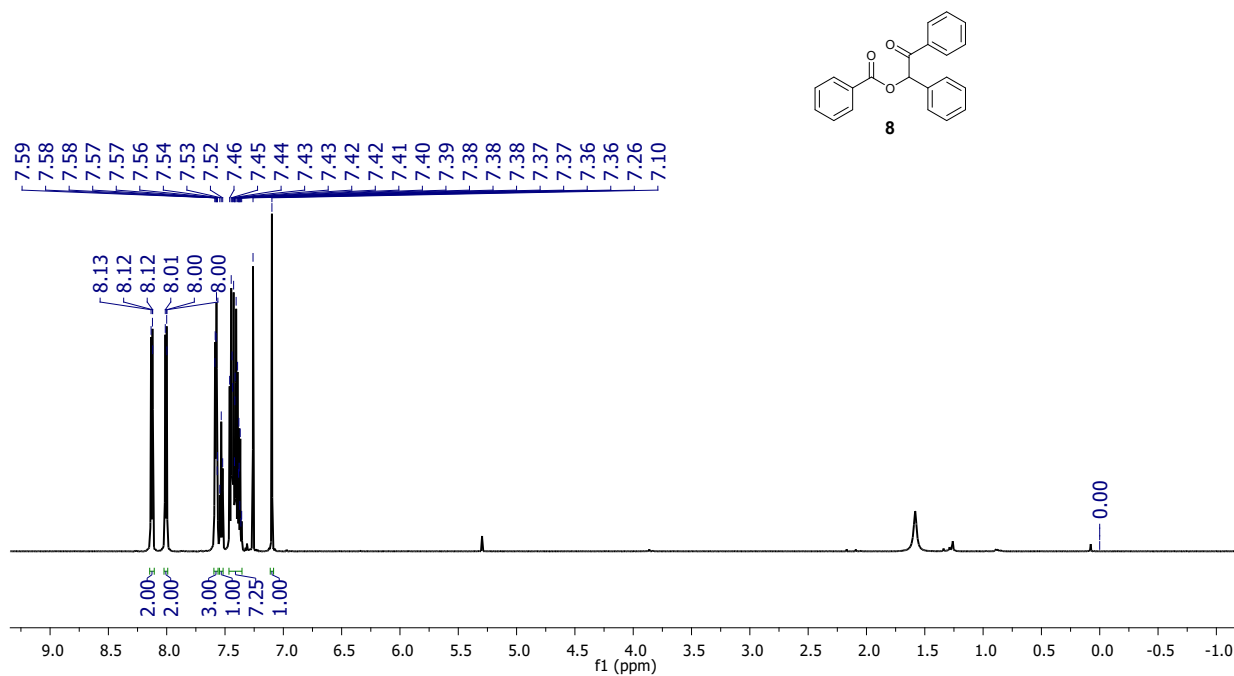
^1H NMR (600 MHz, CDCl_3):



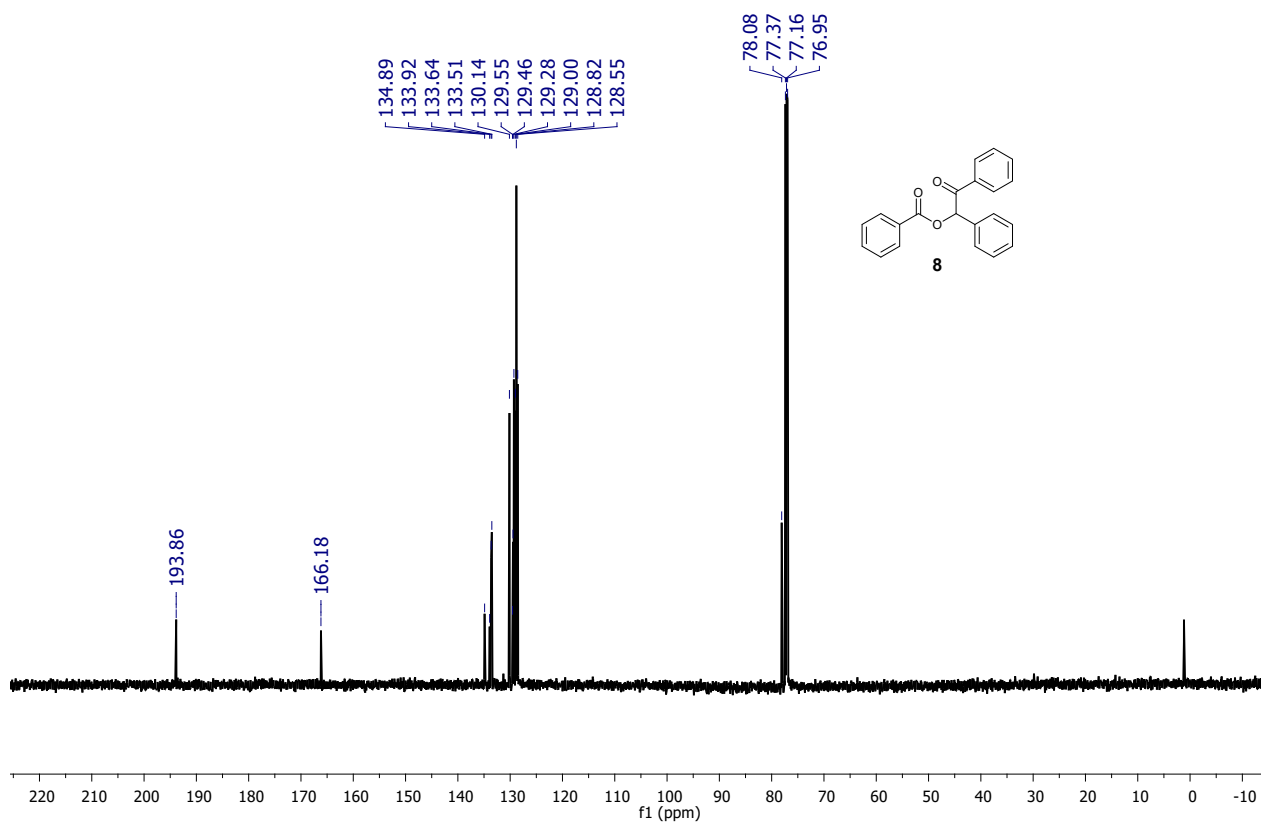
^{13}C NMR (151 MHz, CDCl_3):



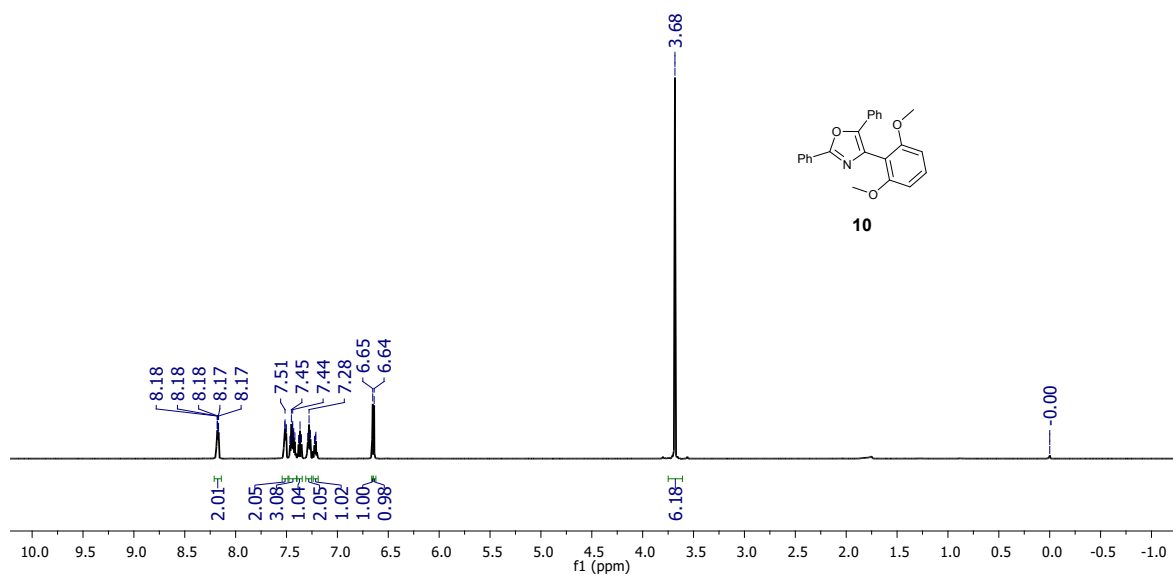
^1H NMR (600 MHz, CDCl_3):



^{13}C NMR spectrum of **8** (151 MHz, CDCl_3):



^1H NMR (600 MHz, CDCl_3):



^{13}C NMR (151 MHz, CDCl_3):

