Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting information

1,4-Refunctionalization of β-Diketones to γ-Keto Nitriles via C-C Single Bond Cleavage

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Experimental details and spectroscopic data

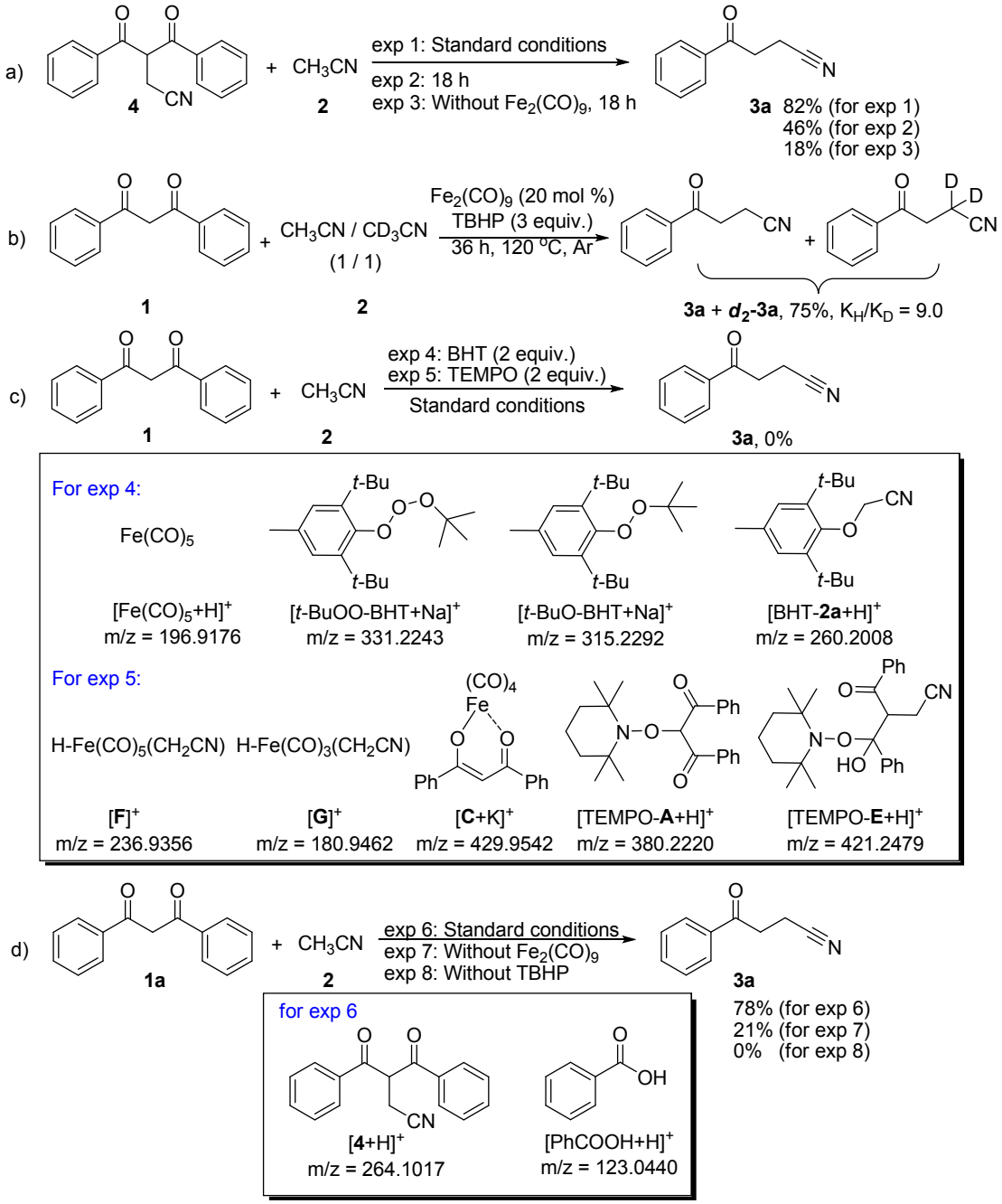
Contents:

1. General information

All reactions were performed under Ar atmosphere using quartz tube. Solvents were dried and degassed by standard methods before they were used. 1,3-diketones were purchased from commercial suppliers and used without further purification or synthesized according to the method in the literature. Silica gel was purchased from Qing Dao Hai Yang Chemical Industry Co. ^{1}H NMR spectra was recorded on a Bruker DPX-400 (400 MHz) spectrometer with deuteraterated chloroform as solutions, the chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane. ^{13}C NMR spectra was recorded at 100 MHz on Bruker DPX-400. The chemical shifts δ are reported relative to residual $CHCl_3$ (δ = 77.00 ppm). ^{19}F NMR spectra was recorded at 376.5 MHz on Bruker DPX-400, the chemical shifts δ are reported relative to $CFCl_3$ (δ = 0 ppm) as internal standard. The multiplicity of signals is designated by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). High resolution mass spectra were obtained on an Agilent Technologies 1290-6540 UHPLC/Accurate-Mass Quadrupole Time-of-Flight LC/MS spectrometer using electrospray ionization (ESI, Fragmentor: 180 V). Aryl-1,3-butanedione, 1-phenyl-1,3-alkanedione[2] and 1,3-diaryl diketones[3] were synthesized according literature data.

2. Control experiment for mechanistic studies

Scheme S1. Mechanistic studies.



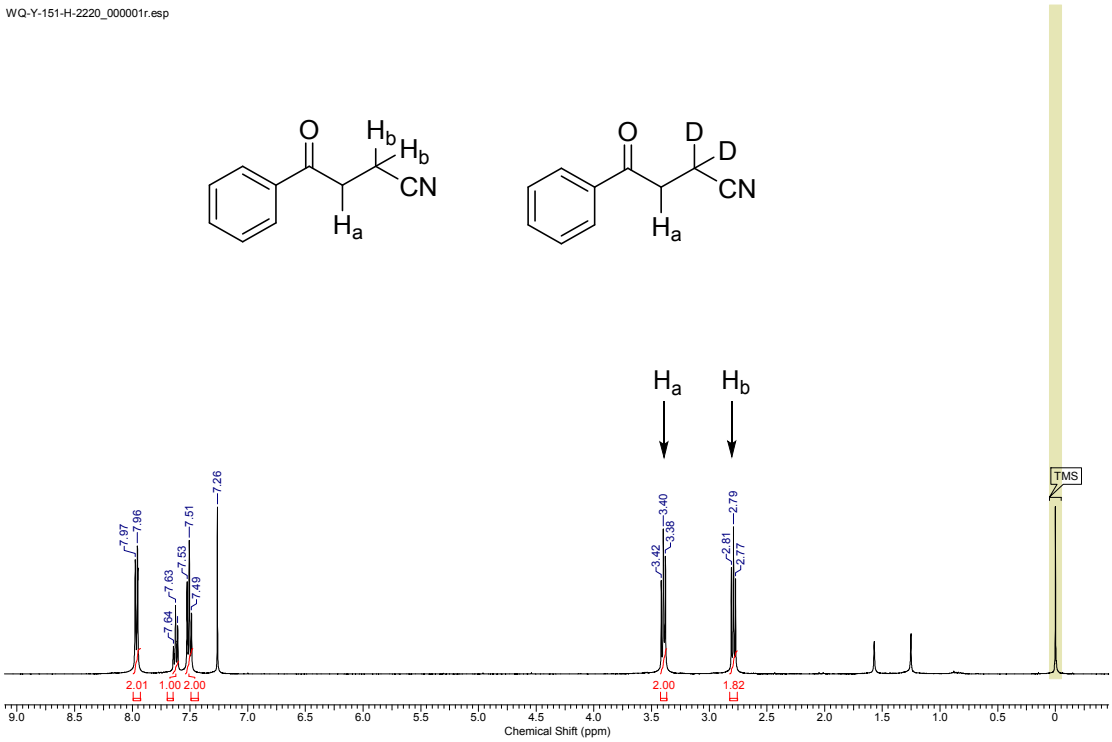


Figure S1. ^{1}H NMR spectrum of reaction b

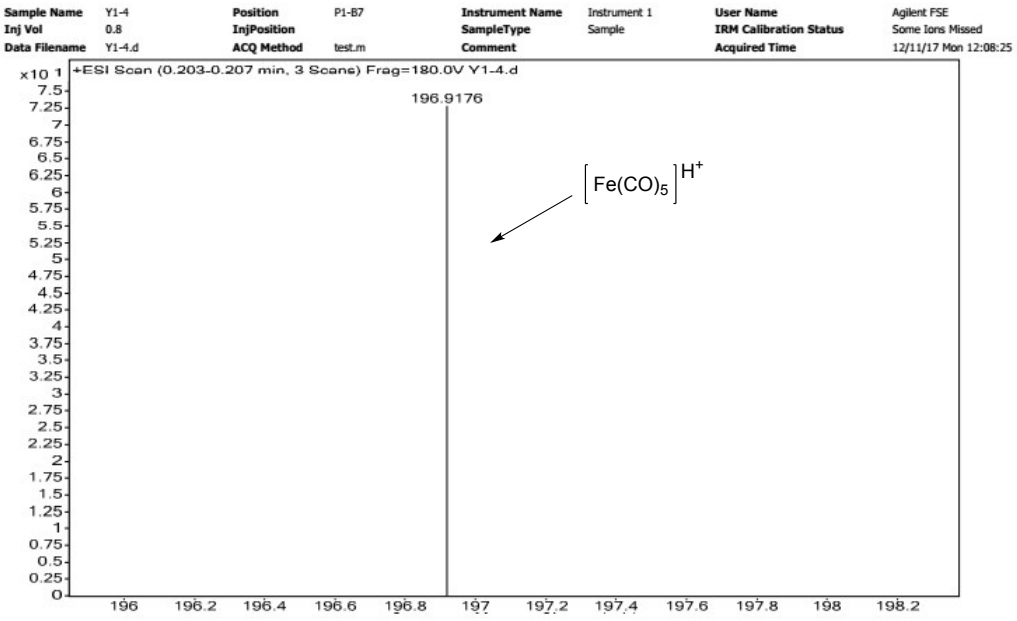


Figure S2. HRMS spectrum of compound $[Fe(CO)_5+H]^+$ for exp 1

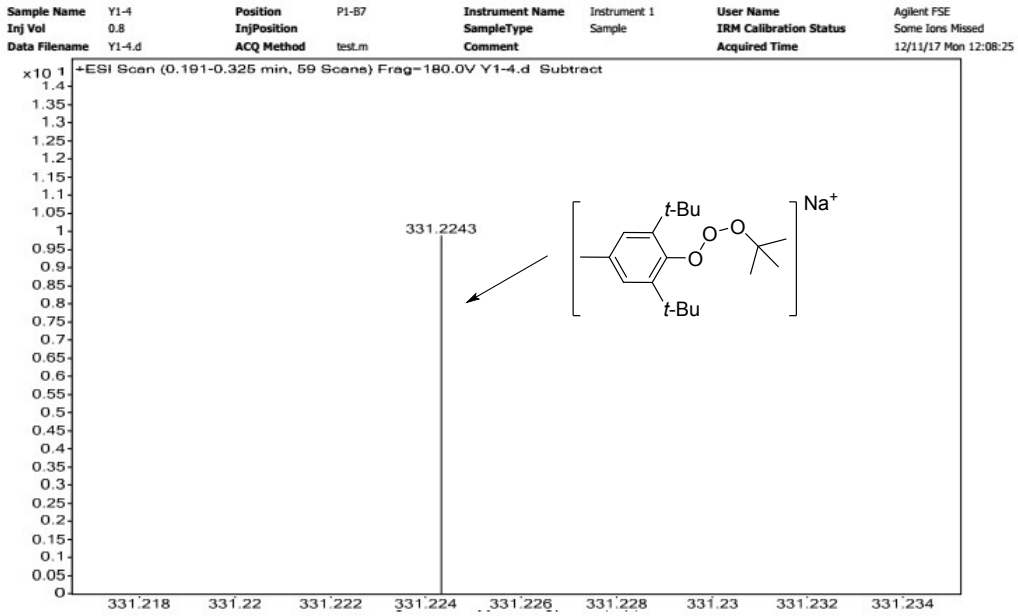


Figure S3. HRMS spectrum of compound [*t*-BuOO-BHT+Na]$^+$ for exp 1

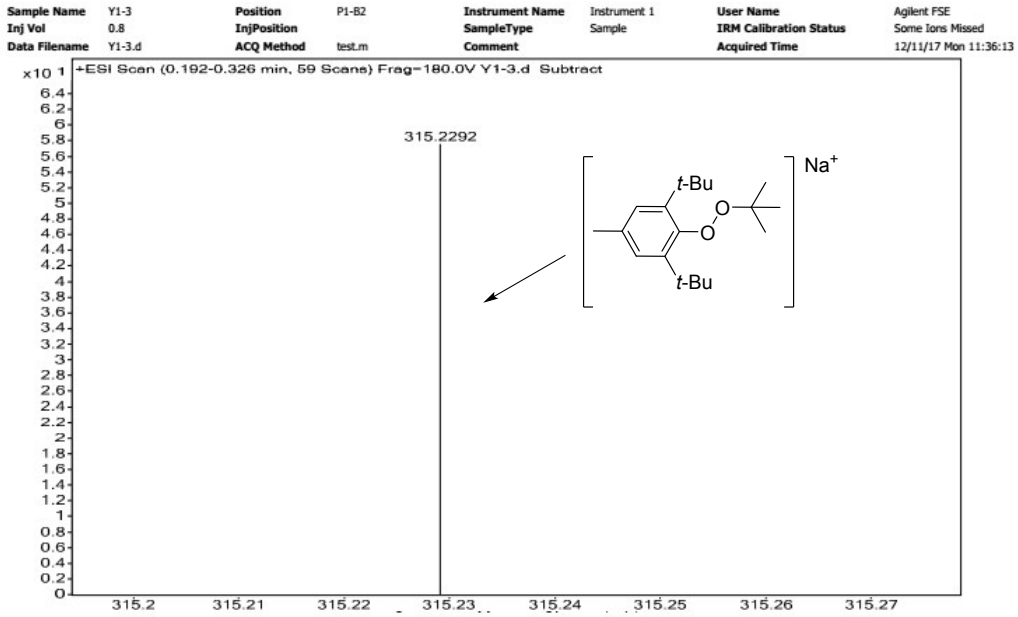


Figure S4. HRMS spectrum of compound [*t*-BuO-BHT+Na]$^+$ for exp 1

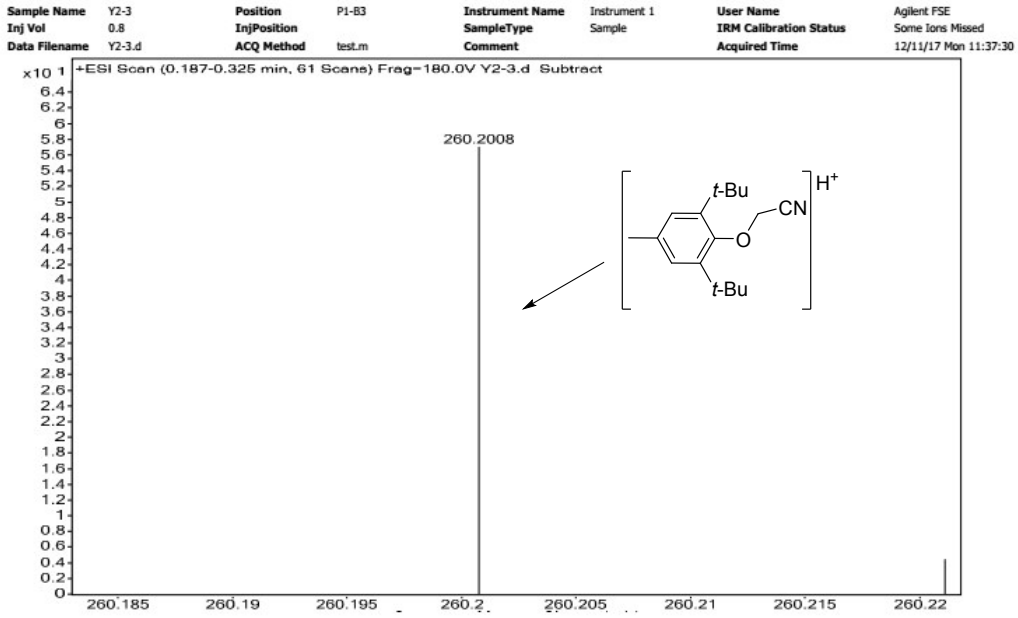


Figure S5. HRMS spectrum of compound [BHT-**2a**+H]$^+$ for exp 1

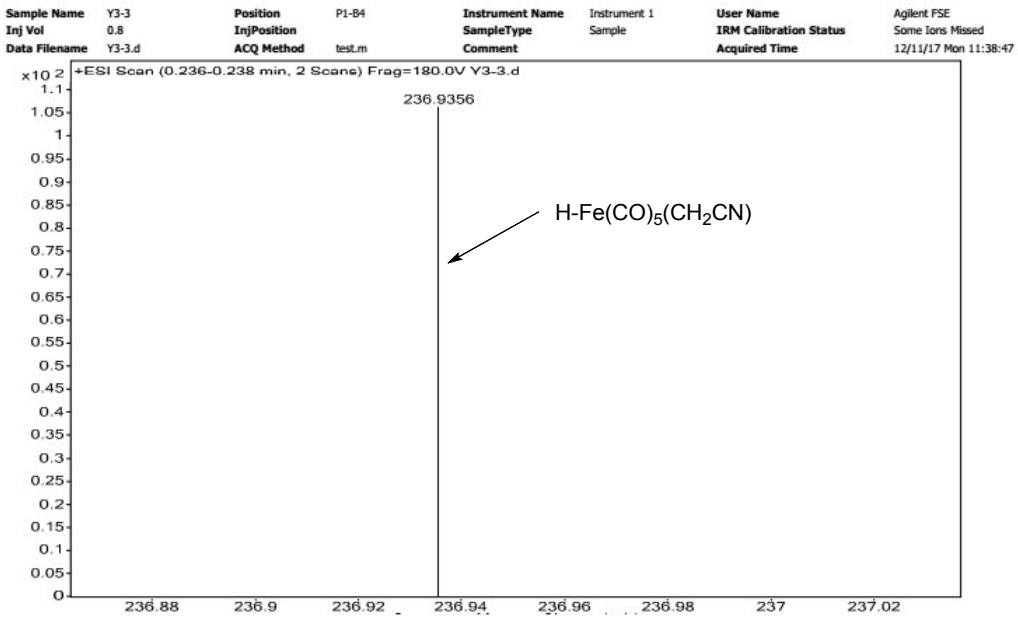


Figure S6. HRMS spectrum of compound [**F**]$^+$ for exp 2

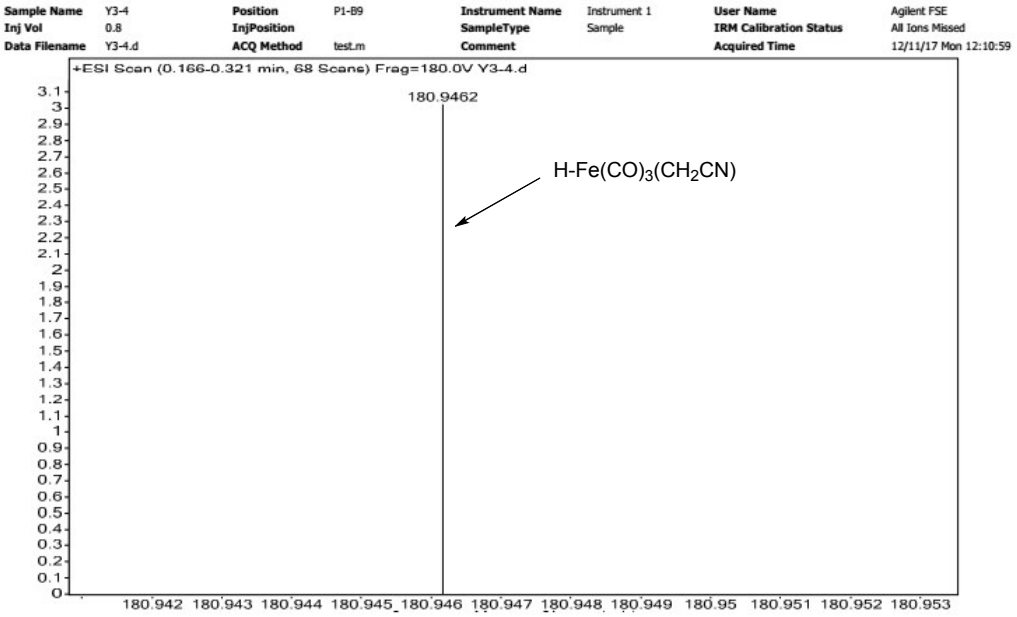


Figure S7. HRMS spectrum of compound [**G**]$^+$ for exp 2

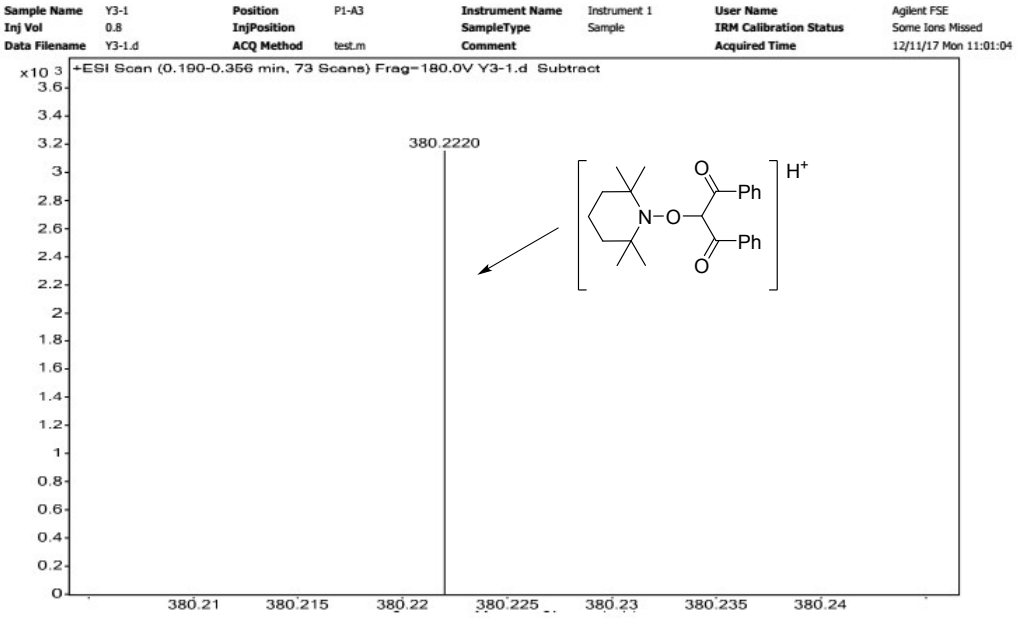


Figure S8. HRMS spectrum of compound [TEMPO-**1a**+H]$^+$ for exp 2

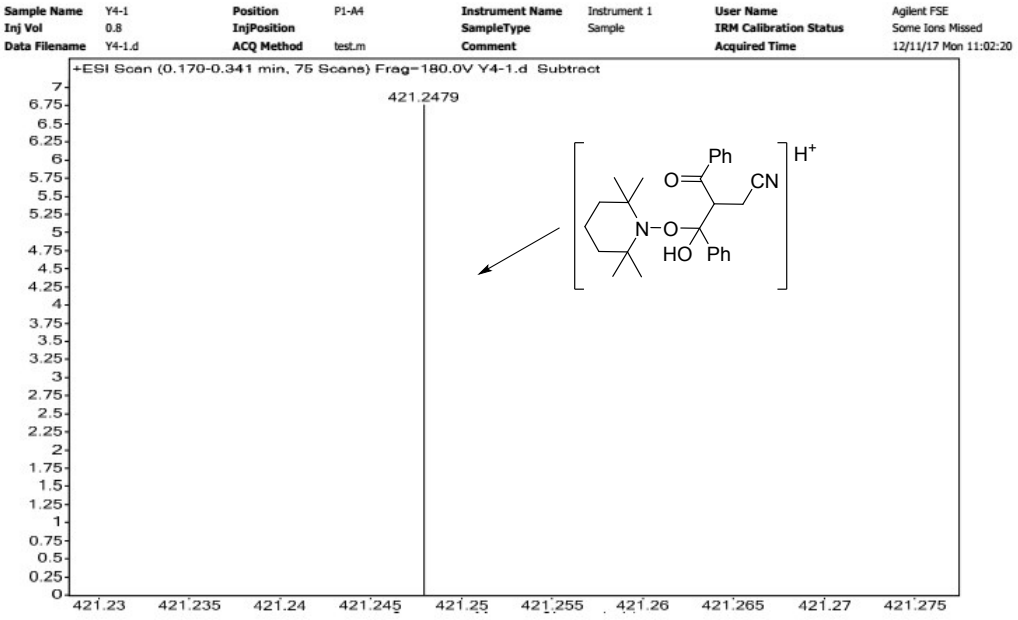


Figure S9. HRMS spectrum of compound [TEMPO-**E**+H]$^+$ for exp 2

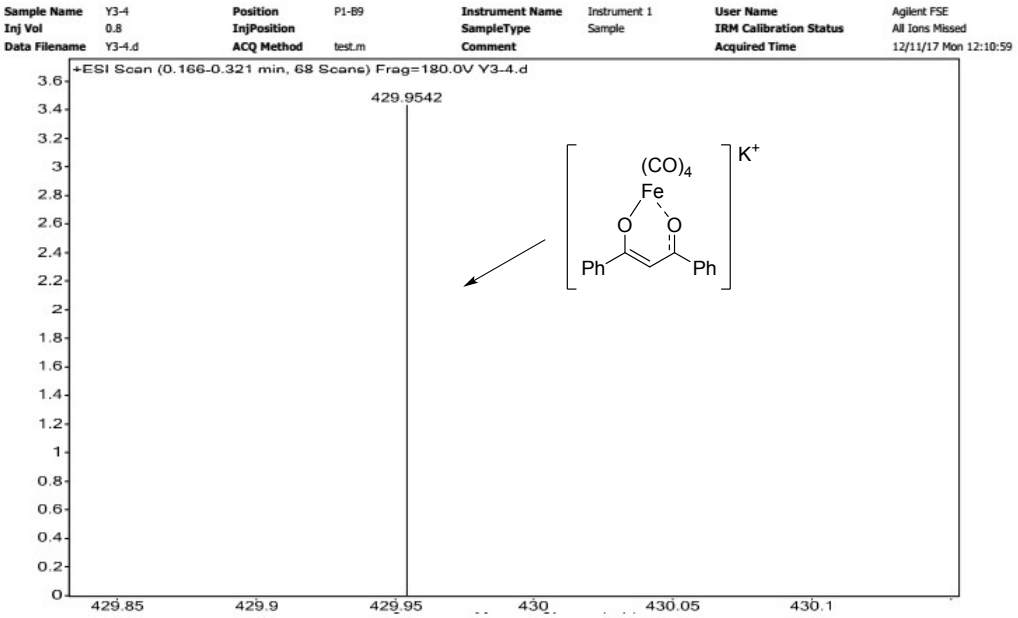


Figure S10. HRMS spectrum of compound [**C**+K]$^+$ for exp 2

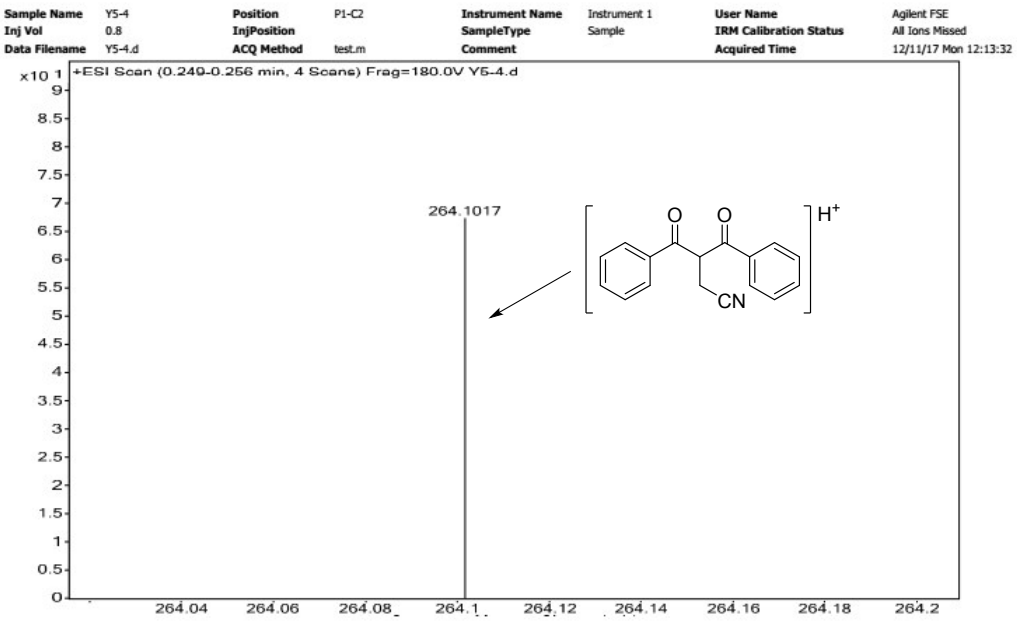


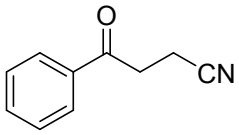
Figure S11. HRMS spectrum of compound [**F**+H]$^+$ for exp 3

3. General procedure for the synthesis of product 3

To a reaction tube equipped with a magnetic stirring bar were added $Fe_2(CO)_9$ (20% mmol) and 1,3-diketones (0.25 mmol). Under a Ar atmosphere, TBHP (3.0 equiv), CH_3CN (2 mL) were added. The resulting mixture was heated at 120°C for 36 h. The solvent was removed under vacuum, and the residue was purified by flash chromatography (SiO_2, petroleum ether/ethyl acetate = 1:5).

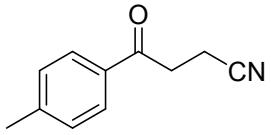
4. Characterization data

γ-oxo-Benzenebutanenitrile (3a)[4]:



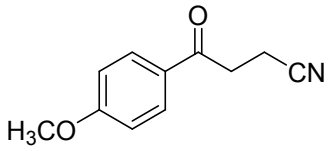
Light yellow solid (33 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97-7.95 (m, 2H), 7.64-7.61 (m, 1H), 7.53-7.49 (m, 2H), 3.40 (t, J = 7.2 Hz, 2H), 2.79 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.36, 135.56, 133.97, 128.92, 128.05, 119.29, 34.29, 11.84. HRMS (ESI) calcd. for $C_{10}H_9NO$ (M+H)+: 160.0757, found: 160.0757.

4-methyl-γ-oxo-Benzenebutanenitrile (3b)[4]:



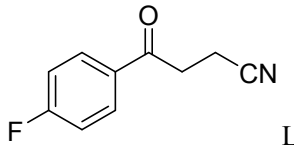
White solid (32.8 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.85 (m, 2H), 7.30-7.28 (m, 2H), 3.36 (t, J = 7.2 Hz, 2H), 2.77 (t, J = 7.2 Hz, 2H). 2.43 (s, 3H), ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.95, 140.5293, 133.14, 129.57, 128.16, 119.37, 34.15, 21.77, 11.84. HRMS (ESI) calcd. for $C_{11}H_{11}NO$ $(M+H)^+$: 174.0913, found: 174.0914.

4-methoxy-γ-oxo-Benzenebutanenitrile (3c)[5]:



White solid (40.6 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96-7.92 (m, 2H), 6.98-6.94 (m, 2H), 3.89 (s, 3H), 3.34 (t, J = 7.2 Hz, 2H), 2.77 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.79, 164.08, 130.36, 129.69, 119.45, 114.03, 55.59, 33.89, 11.89. HRMS (ESI) calcd. for $C_{11}H_{11}NO_2$ $(M+H)^+$: 190.0863, found: 190.0862.

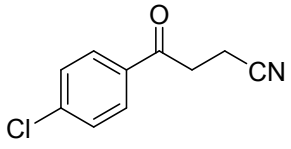
4-fluoro-γ-oxo-Benzenebutanenitrile (3d)[4]:



Light yellow solid (32.3 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02-7.97 (m, 2H), 7.20-7.15 (m, 2H), 3.37 (t, J = 7.1 Hz, 2H), 2.78 (t, J = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.77, 166.18 (d, $J_{C\text{-}F}$ = 256.0 Hz), 132.05 (d, $J_{C\text{-}F}$ = 3.0 Hz), 130.76 (d, $J_{C\text{-}F}$ =

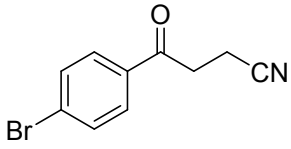
9.5 Hz), 119.16, 116.11 (d, $J_{C\text{-}F}$ = 22.0 Hz), 34.21, 11.83. ^{19}F NMR (376 MHz, $CDCl_3$): δ -103.47. HRMS (ESI) calcd. for $C_{10}H_8FNO$ $(M+H)^+$: 178.0663, found: 178.0664.

4-chloro-γ-oxo-Benzenebutanenitrile (3e)[4]:



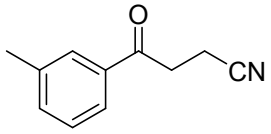
White solid (33.8 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91-7.89 (m, 2H), 7.49-7.47 (m, 2H), 3.36 (t, J = 7.2 Hz, 2H), 2.78 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.16, 140.52, 133.88, 129.44, 129.28, 119.06, 34.28, 11.80. HRMS (ESI) calcd. for $C_{10}H_8ClNO$ $(M+H)^+$: 194.0367, found: 194.0365.

4-bromo-γ-oxo-Benzenebutanenitrile (3f):



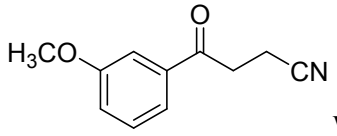
White solid (38.6 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.81 (m, 2H), 7.66-7.63 (m, 2H), 3.36 (t, J = 7.2 Hz, 2H), 2.78 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.37, 134.27, 132.27, 129.52, 129.29, 119.06, 34.27, 11.79. HRMS (ESI) calcd. for $C_{10}H_8BrNO$ $(M+H)^+$: 237.9862, found: 237.9864.

3-methyl-γ-oxo-Benzenebutanenitrile (3h)[4]:



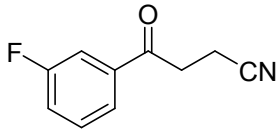
Light yellow solid (29.5 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77-7.74 (m, 2H), 7.44-7.36 (m, 2H), 3.38 (t, J = 7.3 Hz, 2H), 2.78 (t, J = 7.3 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.53, 138.79, 135.61, 134.72, 128.77, 128.56, 125.26, 119.30, 34.32, 21.39, 11.85. HRMS (ESI) calcd. for $C_{11}H_{11}NO$ $(M+H)^+$: 174.0913, found: 174.0912.

3-methoxy-γ-oxo-Benzenebutanenitrile (3i):



White solid (34.0 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.48 (m, 2H), 7.42-7.38 (m, 1H), 7.17-7.14 (m, 1H), 3.89 (s, 3H), 3.38 (t, J = 7.1 Hz, 2H), 2.78 (t, J = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.19, 160.00, 136.93, 129.89, 120.59, 120.38, 119.20, 112.28, 55.52, 34.40, 11.87. HRMS (ESI) calcd. for $C_{11}H_{11}NO_2$ $(M+H)^+$: 190.0863, found: 190.0863.

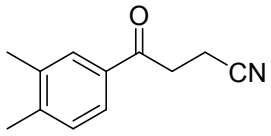
3-fluoro-γ-oxo-Benzenebutanenitrile (3j):



Light yellow solid (27.8 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75-7.73 (m, 1H), 7.66-7.64 (m, 1H), 7.52-7.47 (m, 1H), 7.35-7.31 (m, 1H), 3.37 (t, J = 7.2 Hz, 2H),

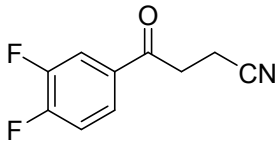
2.79 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.15, 162.93 (d, $J_{C\text{-}F}$ = 249.4 Hz), 137.57 (d, $J_{C\text{-}F}$ = 5.9 Hz), 130.67 (d, $J_{C\text{-}F}$ = 8.1 Hz), 123.81 (d, $J_{C\text{-}F}$ = 2.9 Hz), 121.06 (d, $J_{C\text{-}F}$ = 21.3 Hz), 118.99, 114.83 (d, $J_{C\text{-}F}$ = 22.7 Hz), 34.48, 11.79. ^{19}F NMR (376 MHz, $CDCl_3$): δ -111.00. HRMS (ESI) calcd. for $C_{10}H_8FNO$ $(M+H)^+$: 178.0663, found: 178.0662.

3,4-dimethyl-γ-oxo-Benzenebutanenitrile (3m):



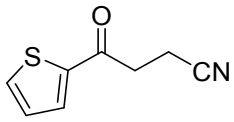
White solid (32.7 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (s, 1H), 7.69-7.67 (m, 1H), 7.25-7.23 (m, 1H), 3.36 (t, J = 7.2 Hz, 2H), 2.76 (t, J = 7.2 Hz, 2H), 2.33 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.20, 143.67, 137.33, 133.53, 130.07, 129.13, 125.76, 119.42, 34.15, 20.16, 19.85, 11.86. HRMS (ESI) calcd. for $C_{12}H_{13}NO$ $(M+H)^+$: 188.1070, found: 188.1070.

3,4-difluoro-γ-oxo-Benzenebutanenitrile (3n):



White solid (31.2 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.78 (m, 1H), 7.77-7.73 (m, 1H), 7.33-7.29 (m, 1H), 3.35 (t, J = 7.1 Hz, 2H), 2.79 (t, J = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.92, 154.12 (m), 150.58 (m), 132.65 (m), 125.15 (m), 118.92, 117.92 (d, $J_{C\text{-}F}$ = 17.6 Hz), 117.44 (m), 34.25, 11.79. ^{19}F NMR (376 MHz, $CDCl_3$): δ -127.93, 135.06. HRMS (ESI) calcd. for $C_{10}H_7F_2NO$ $(M+H)^+$: 196.0568, found: 196.0569.

γ-oxo-2-Thiophenebutanenitrile (3o)[6]:



White solid (33.8 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76-7.74 (m, 1H), 7.72-7.71 (m, 1H), 7.18-7.16 (m, 1H), 3.34 (t, J = 7.3 Hz, 2H), 2.78 (t, J = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.17, 142.52, 134.68, 132.48, 128.42, 119.00, 34.65, 11.80. HRMS (ESI) calcd. for C_8H_7NOS $(M+H)^+$: 166.0321, found: 166.0320.

5. References

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2 J. K. Kim, E. Shokova, V. Tafeenko and V. Kovalev, *Beilstein J. Org. Chem.*, 2014, **10**, 2270.

3 (a) A. G. Hu, W. B. Lin, *Org. Lett.,* 2005, **7**, 455; (b) H. Zhang, D. D. Feng, H. B. Sheng, X. B. Ma, J. W. Wan and Q. Tang, *RSC Adv.,* 2014, **4**, 6417.

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6. NMR spectra of γ-Keto Nitriles

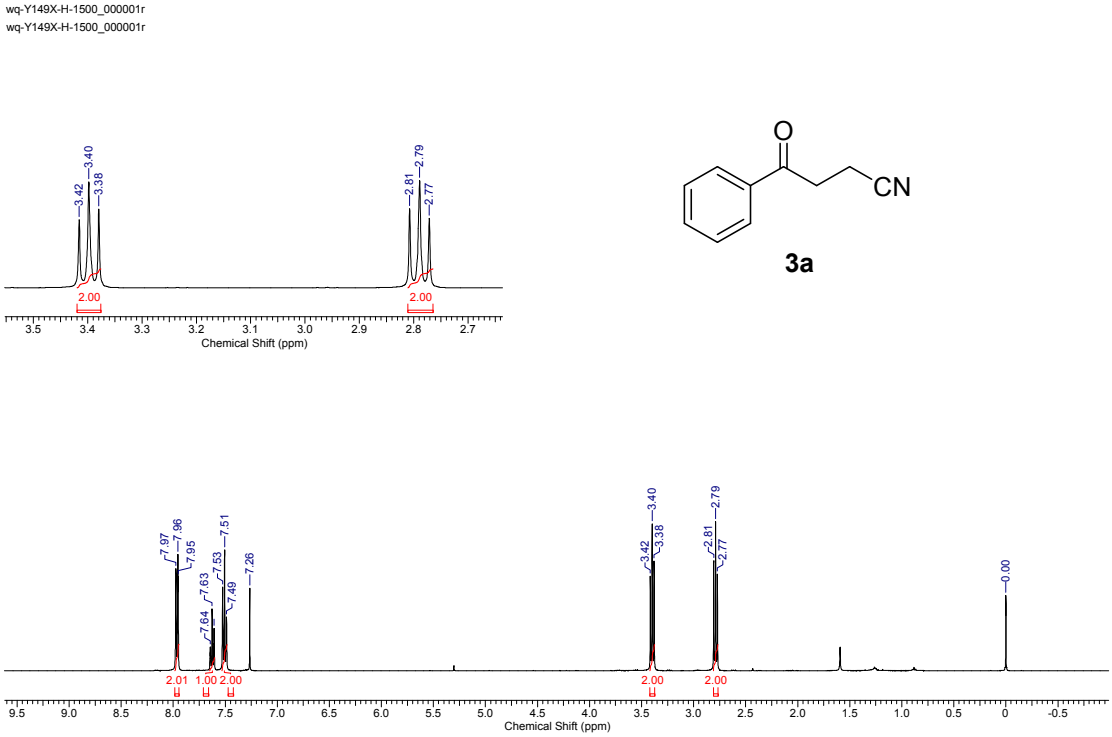


Figure S12. ^{1}H NMR spectrum of compound **3a**

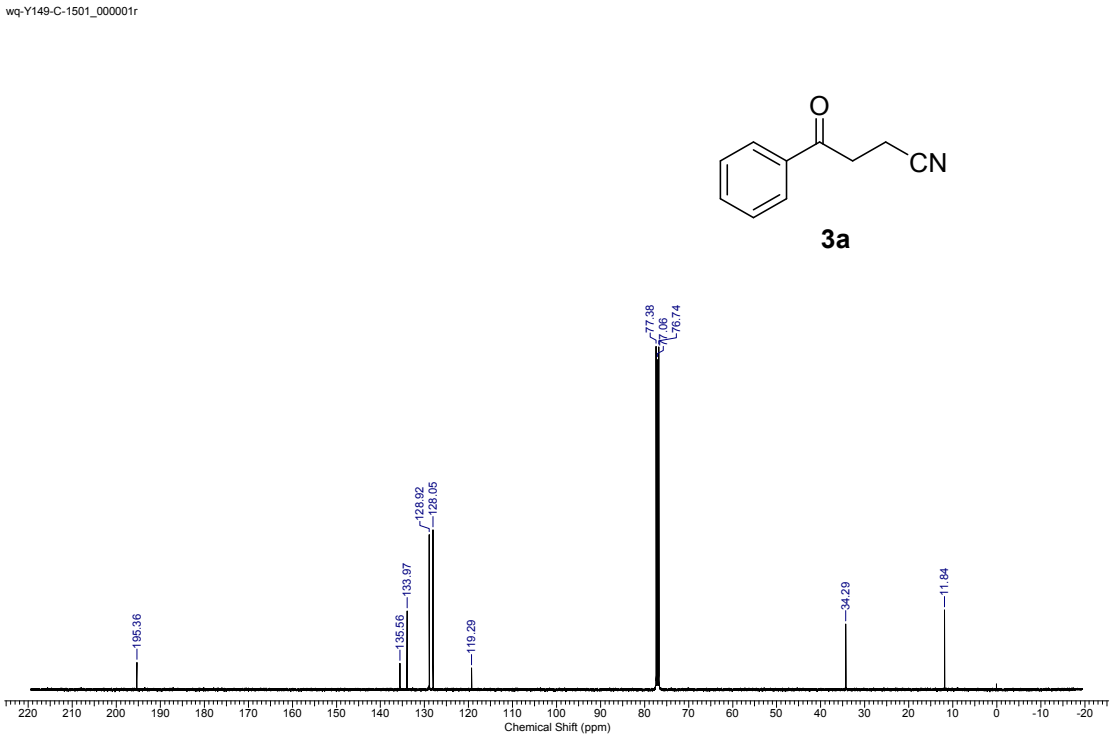


Figure S13. ^{13}C NMR spectrum of compound **3a**

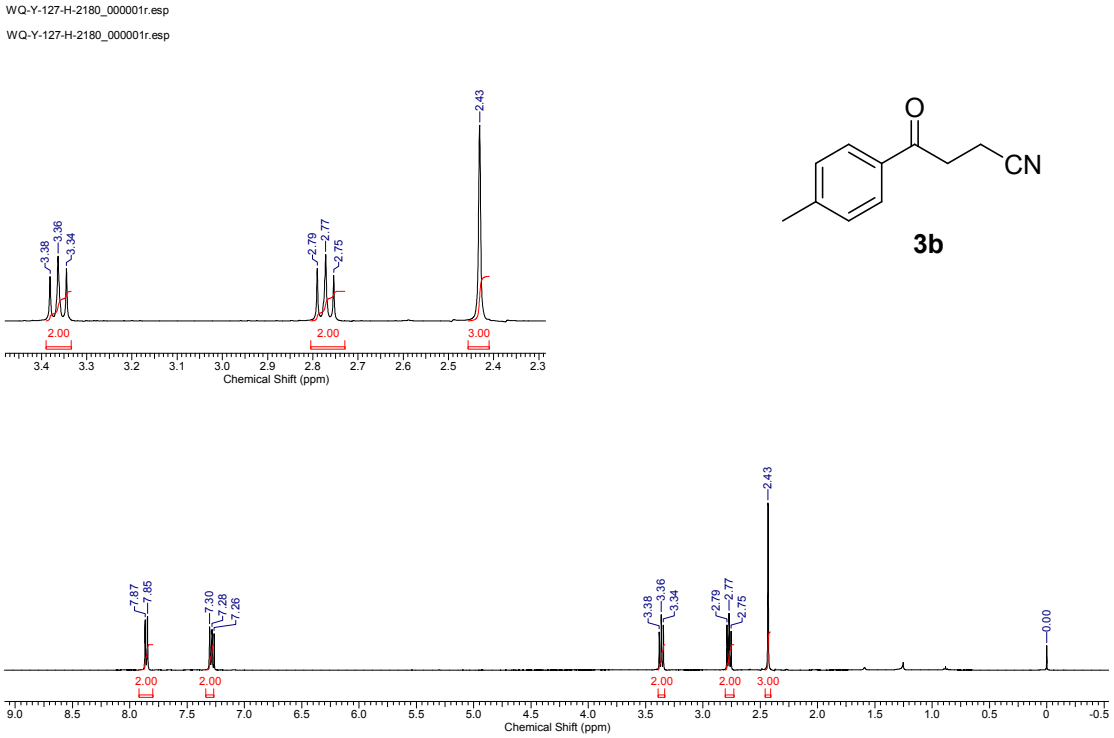


Figure S14. ^{1}H NMR spectrum of compound **3b**

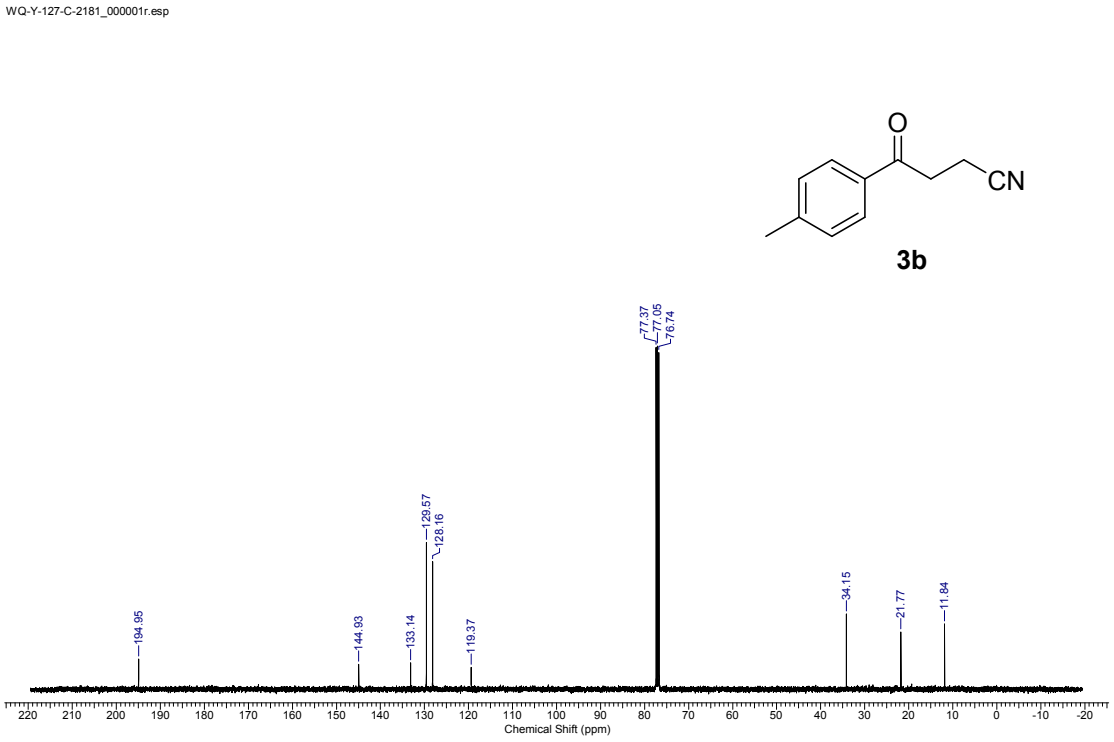


Figure S15. ^{13}C NMR spectrum of compound **3b**

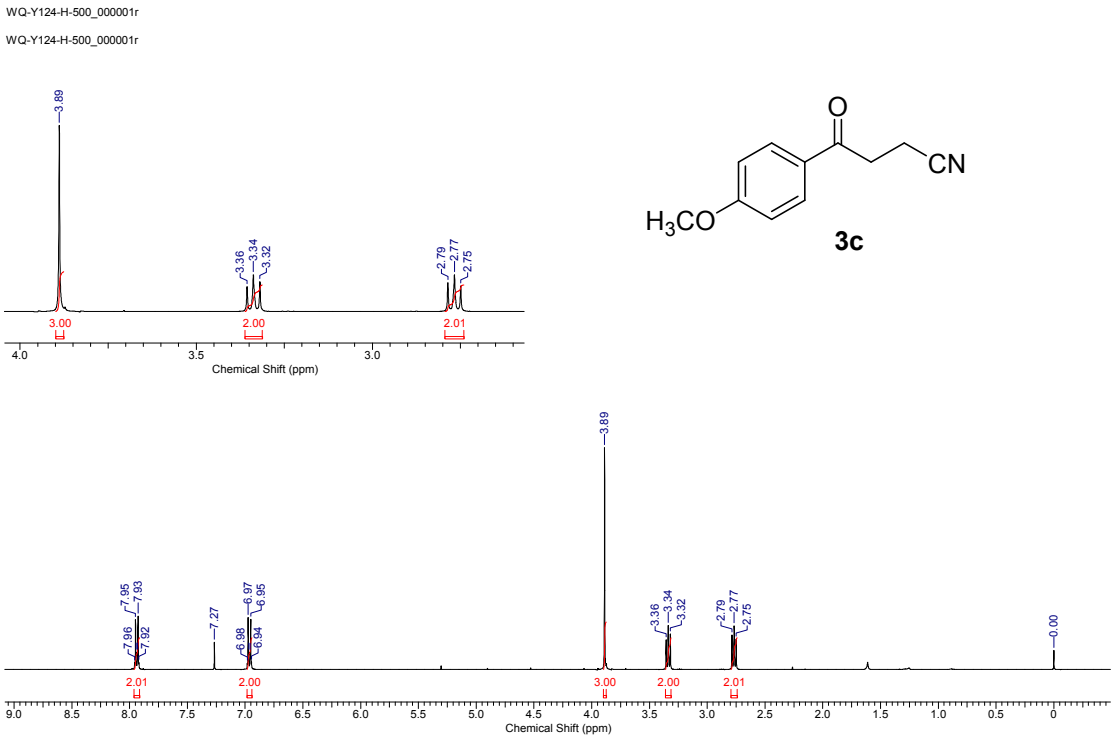


Figure S16. ^{1}H NMR spectrum of compound **3c**

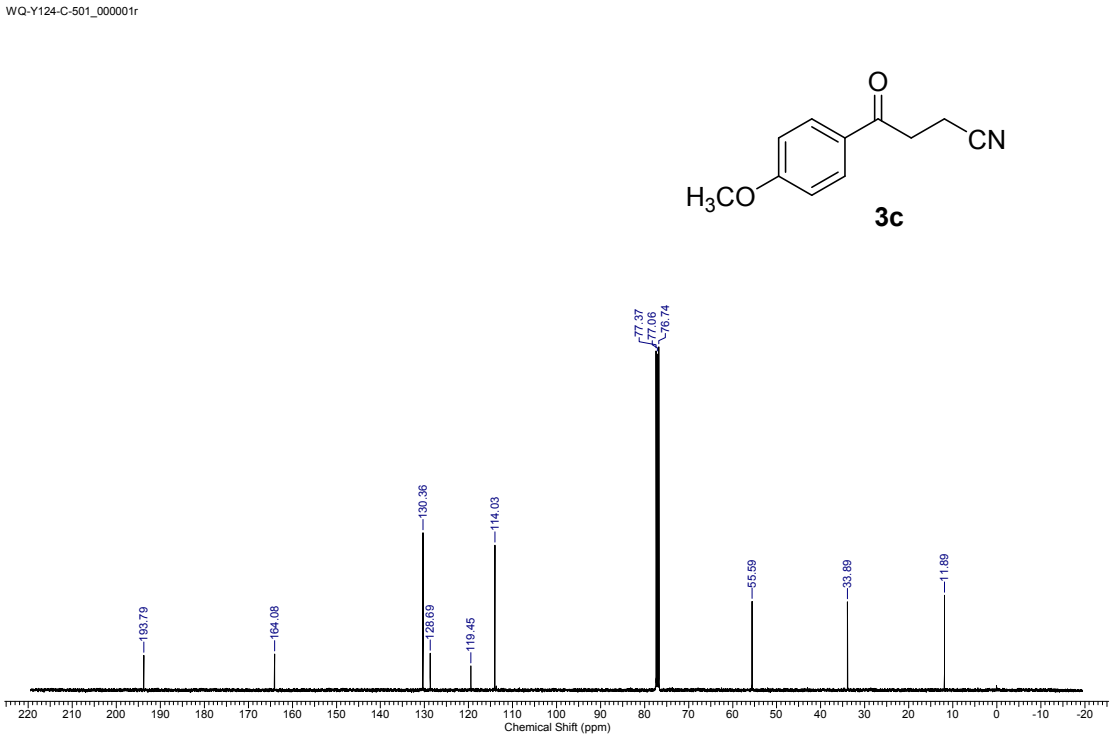
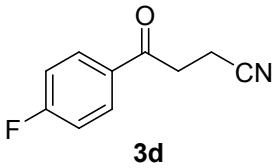


Figure S17. ^{13}C NMR spectrum of compound **3c**



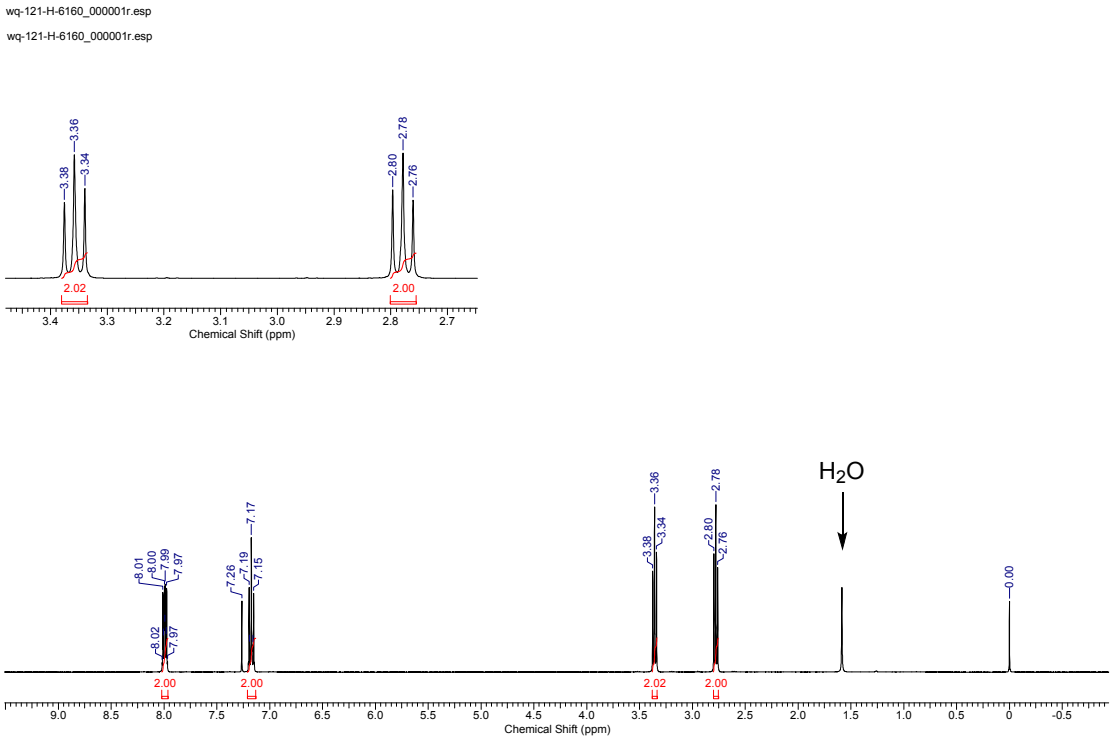


Figure S18. ^{1}H NMR spectrum of compound **3d**

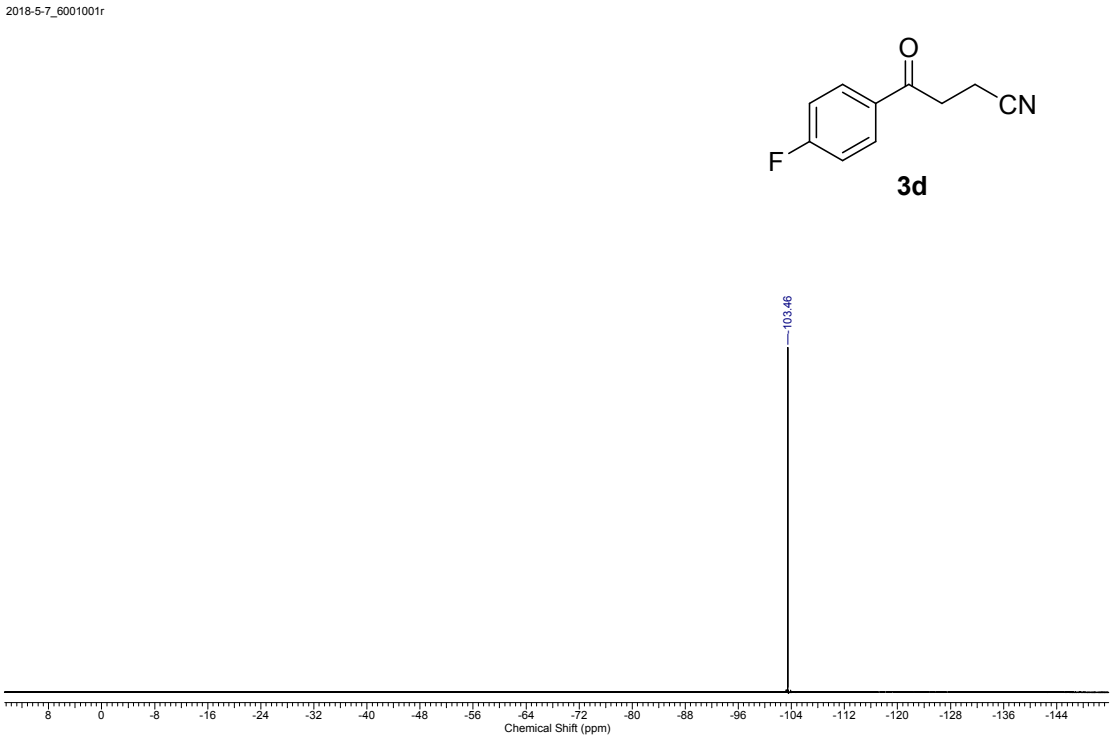


Figure S19. ^{19}F NMR spectrum of compound **3d**

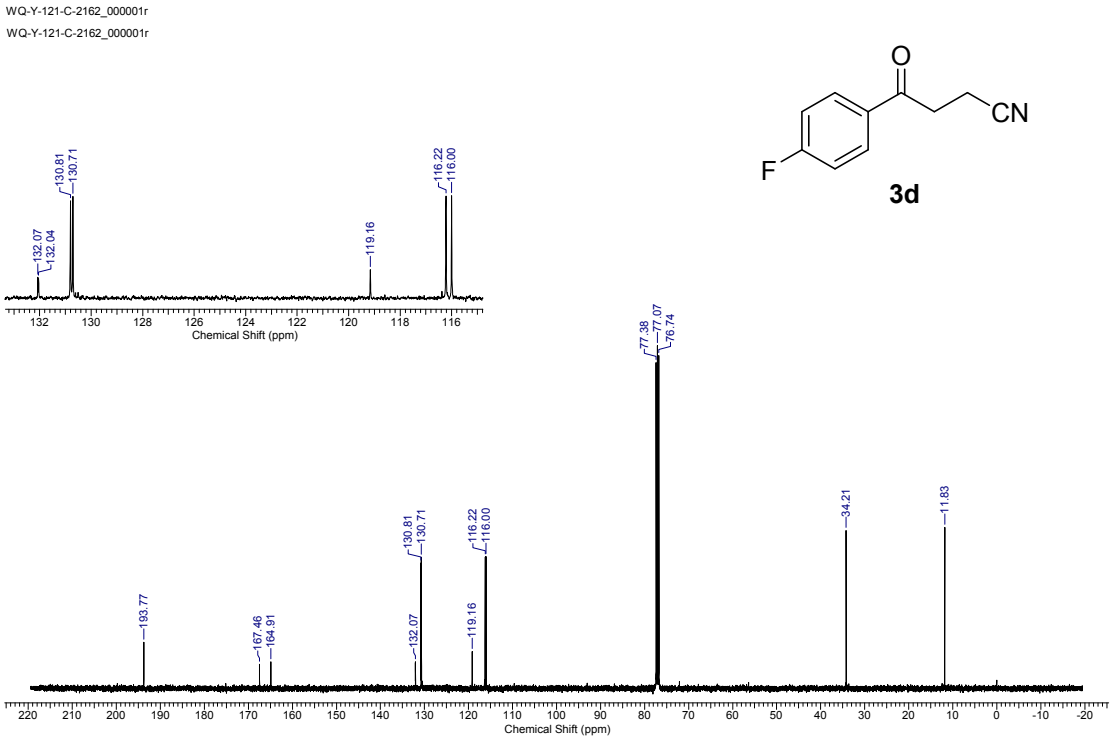


Figure S20. ^{13}C NMR spectrum of compound **3d**

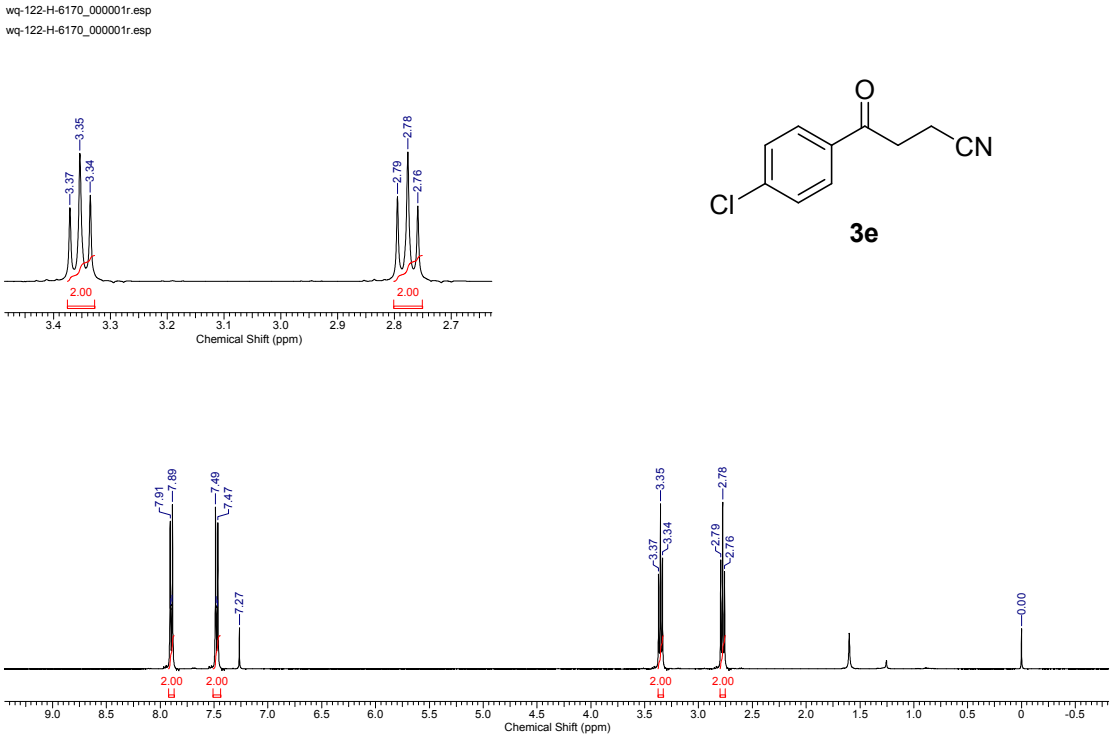


Figure S21. ^{1}H NMR spectrum of compound **3e**

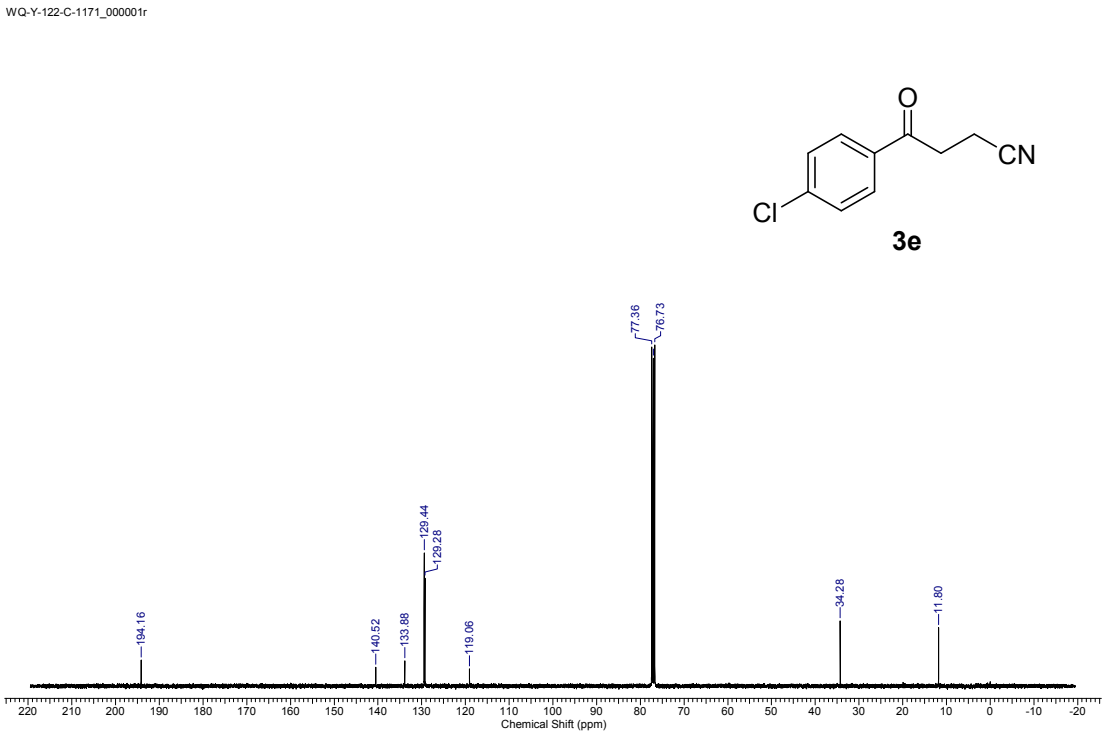


Figure S22. ^{13}C NMR spectrum of compound **3e**

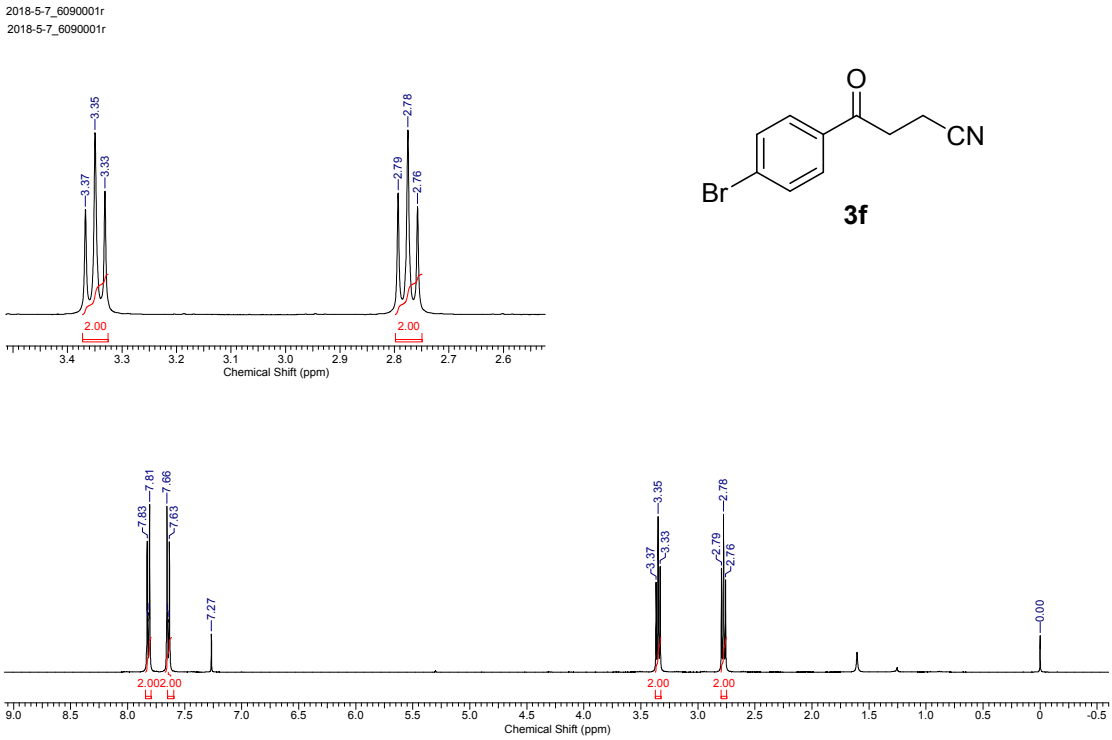


Figure S23. ^{1}H NMR spectrum of compound **3f**

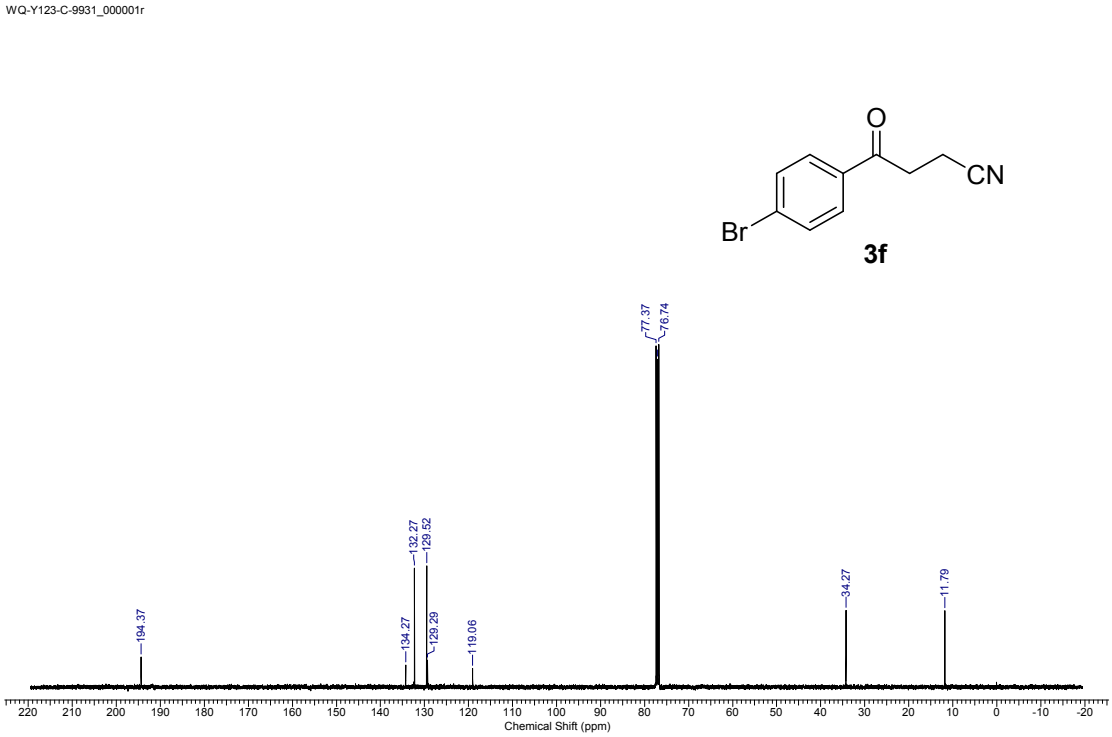


Figure S24. ^{13}C NMR spectrum of compound **3f**

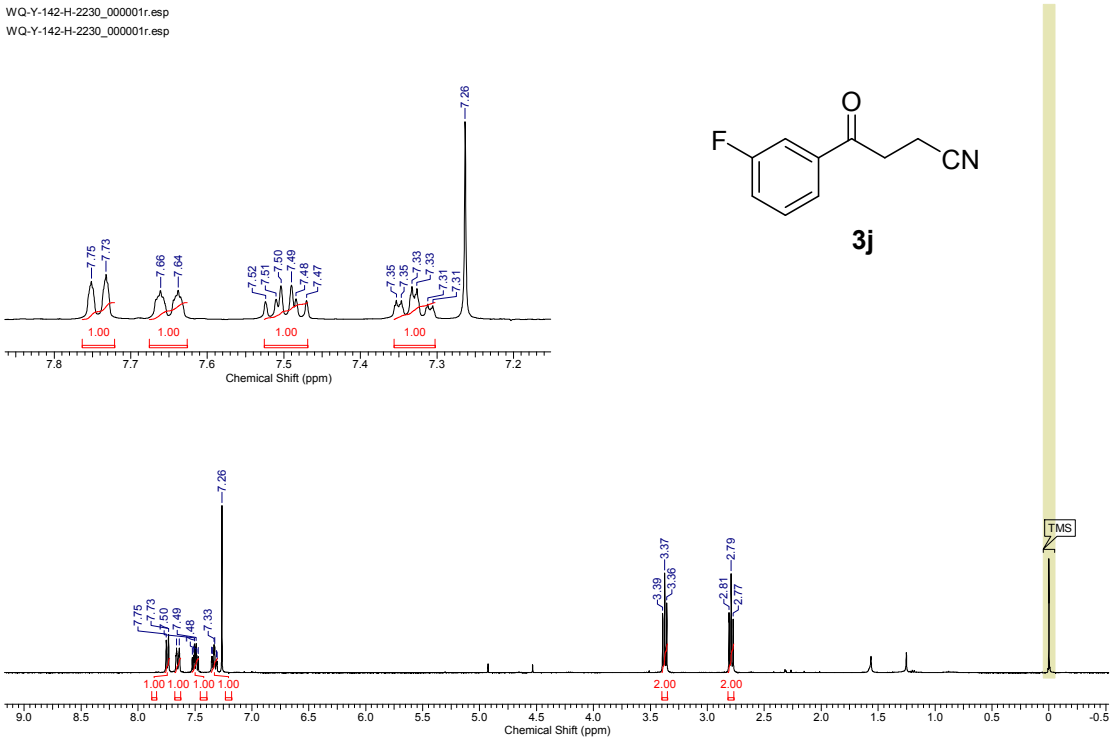


Figure S25. ^{1}H NMR spectrum of compound **3j**

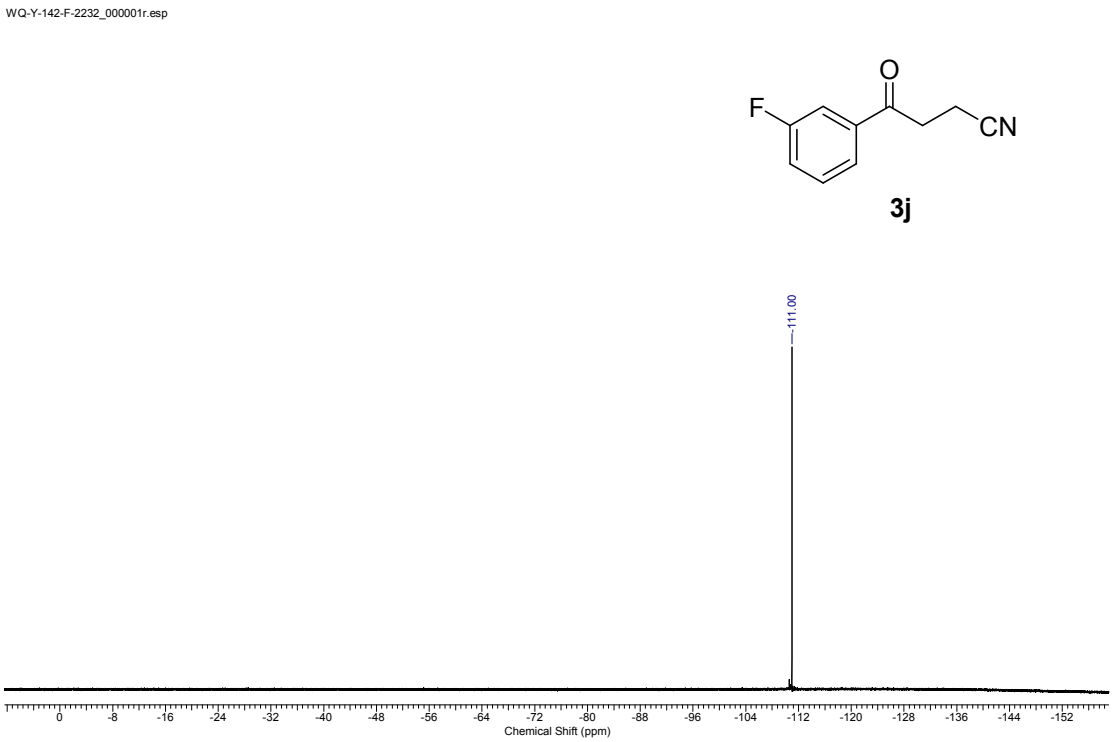


Figure S26. ^{19}F NMR spectrum of compound **3j**

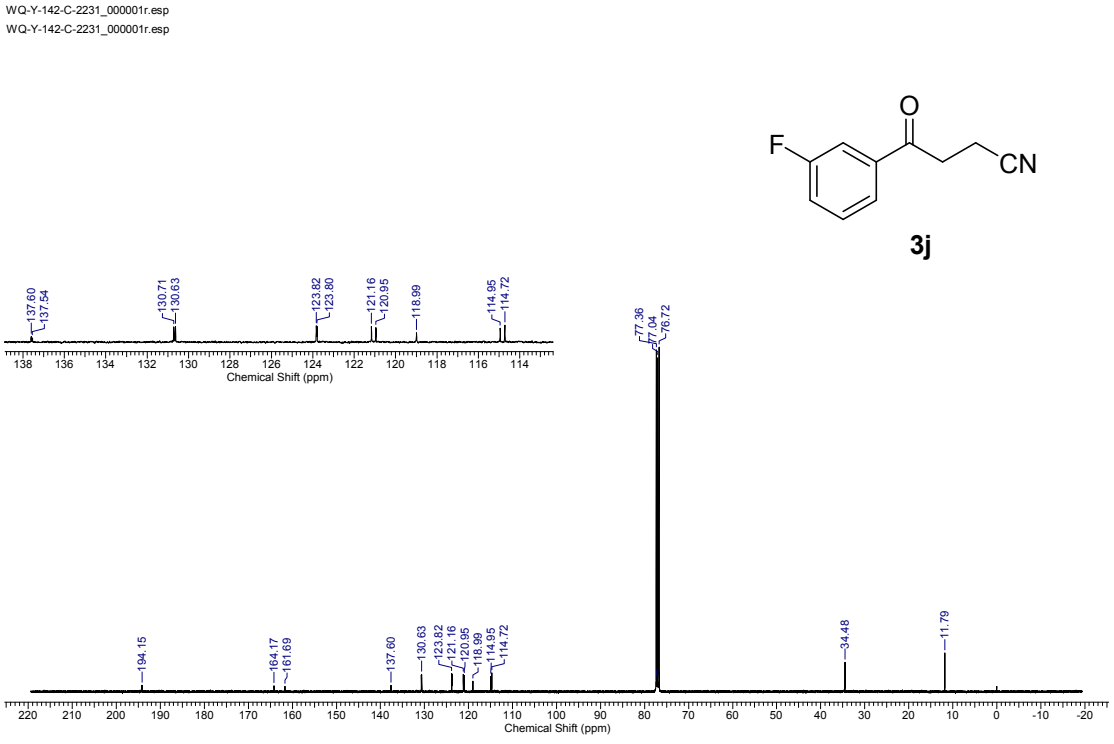


Figure S27. ^{13}C NMR spectrum of compound **3j**

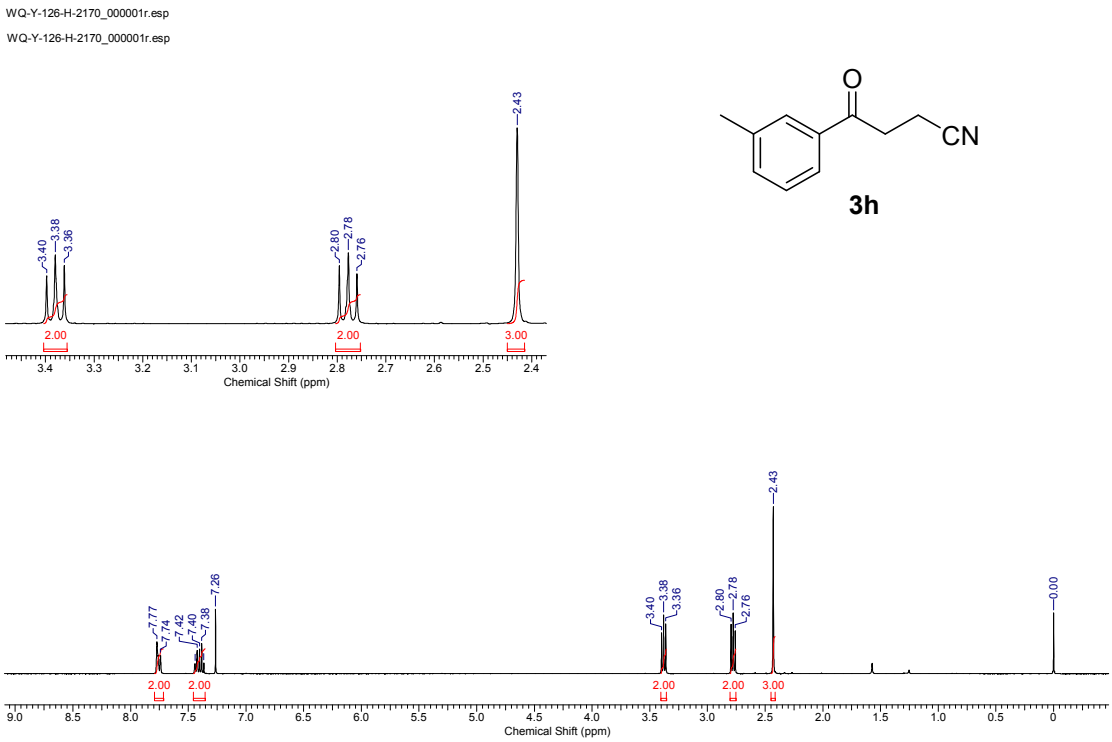


Figure S28. ^{1}H NMR spectrum of compound **3h**

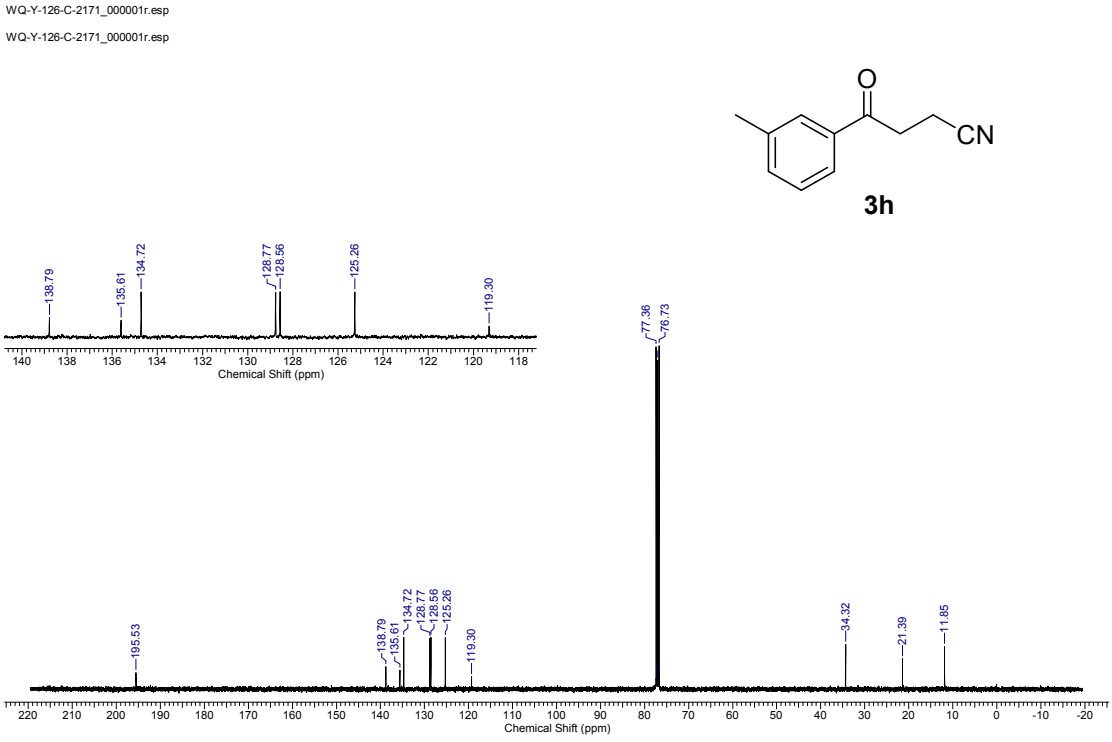


Figure S29. ^{13}C NMR spectrum of compound **3h**

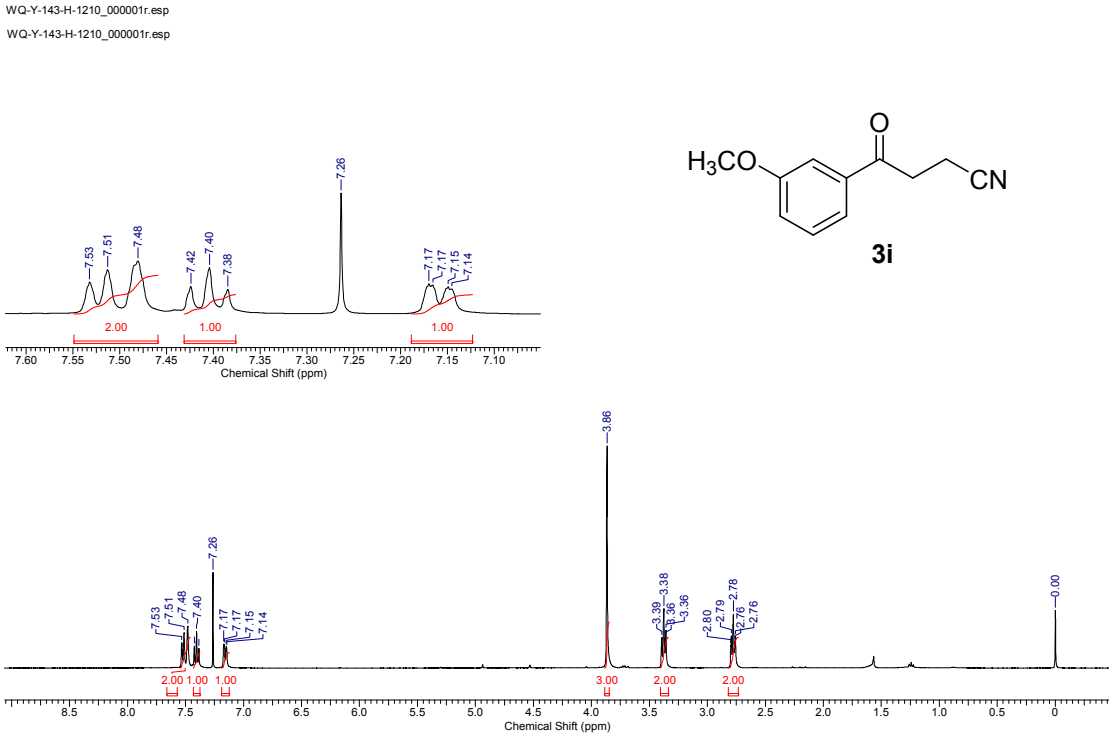


Figure S30. ^{1}H NMR spectrum of compound **3i**

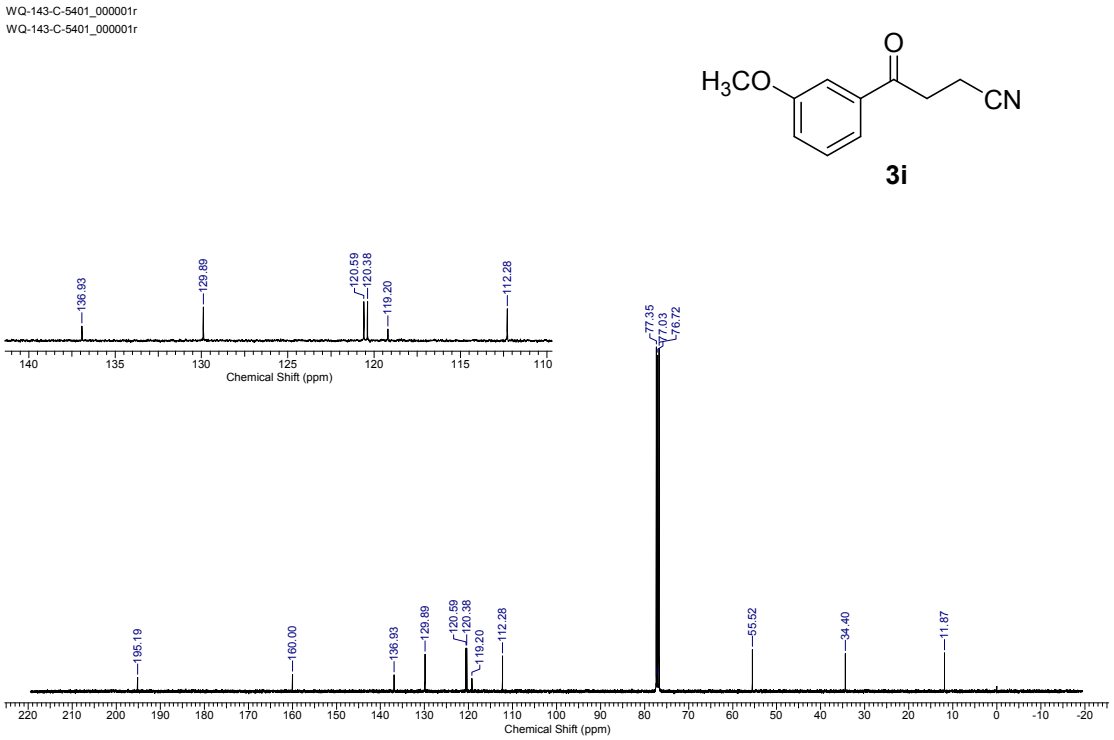


Figure S31. ^{13}C NMR spectrum of compound **3i**

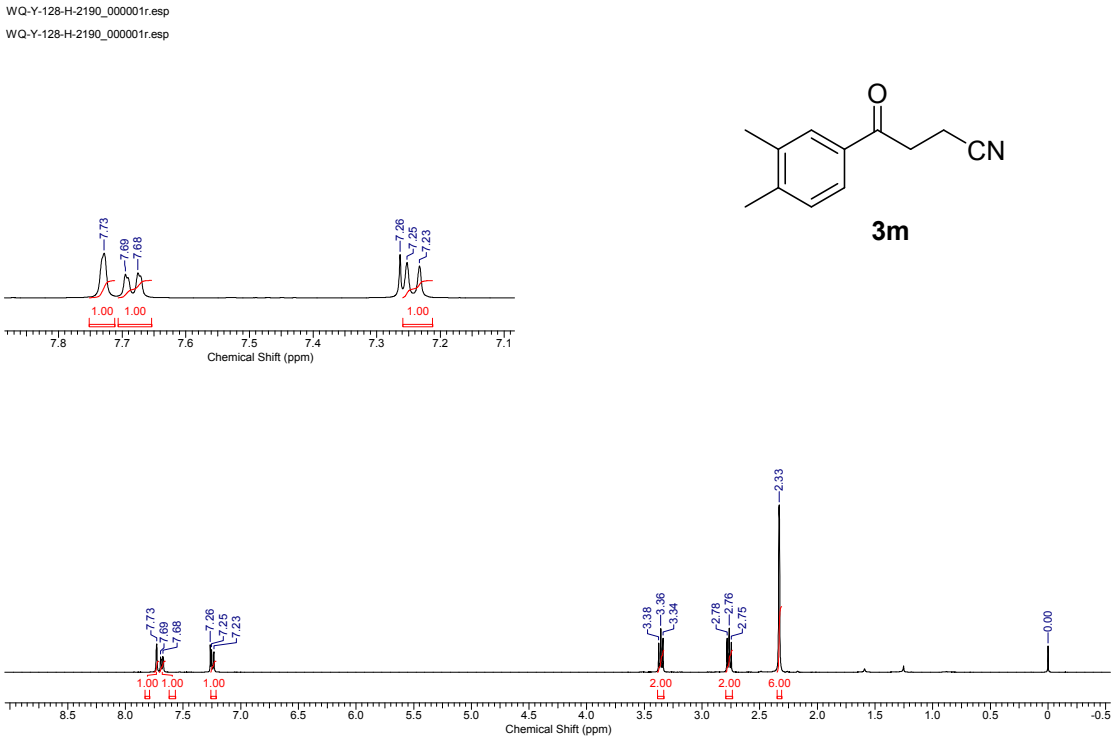


Figure S32. ^{1}H NMR spectrum of compound **3m**

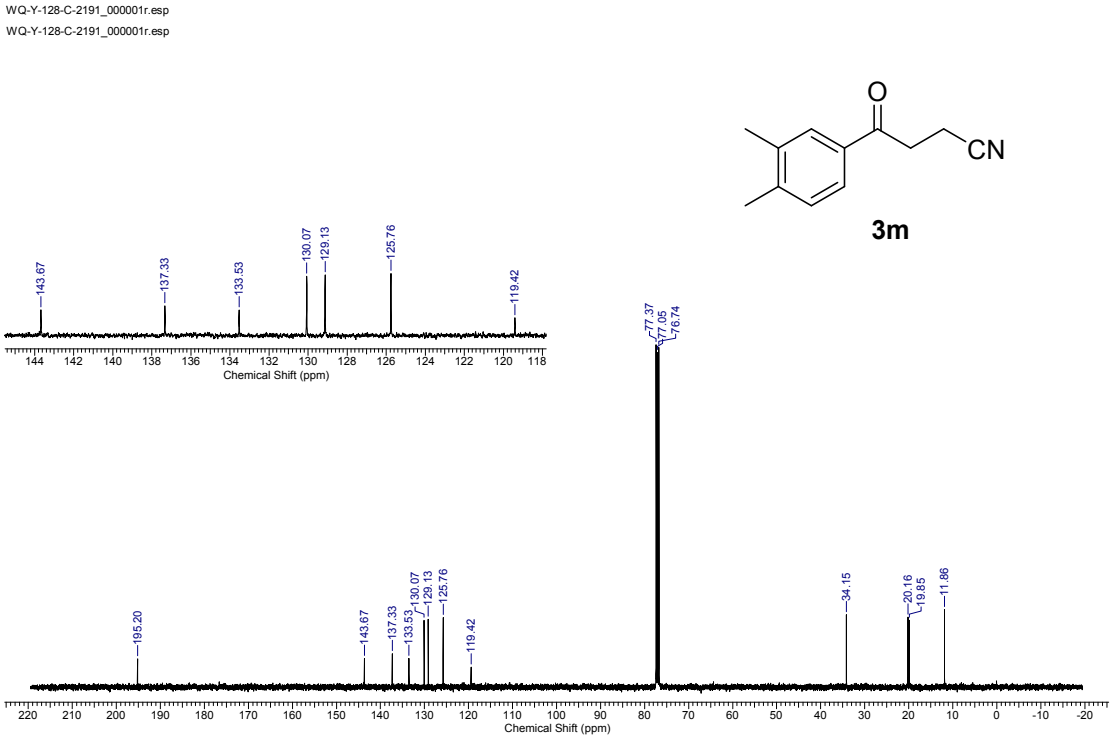


Figure S33. ^{13}C NMR spectrum of compound **3m**

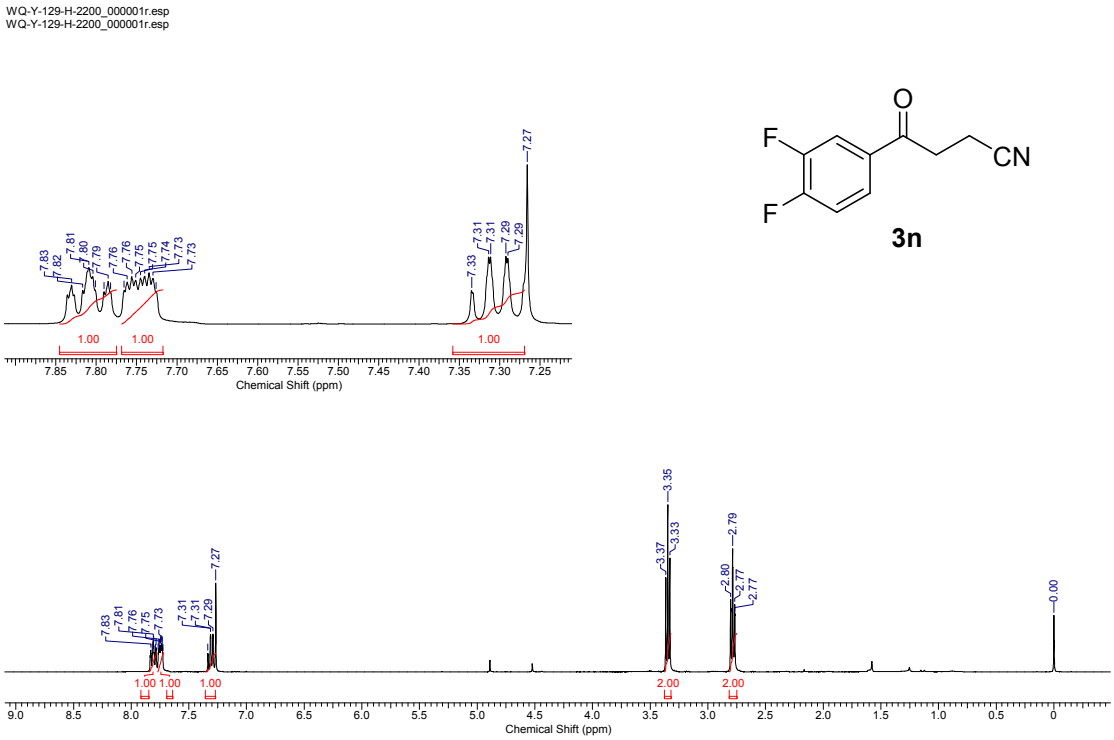


Figure S34. ^{1}H NMR spectrum of compound **3n**

Figure S35. ^{19}F NMR spectrum of compound **3n**

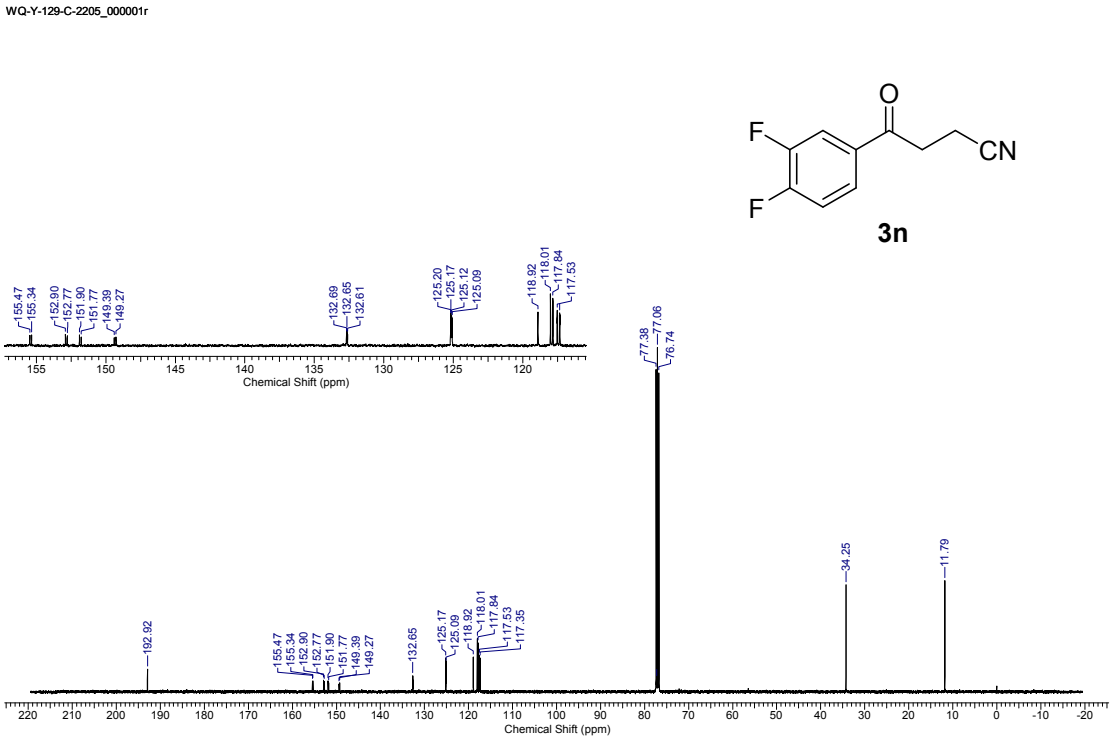


Figure S36. ^{13}C NMR spectrum of compound **3n**

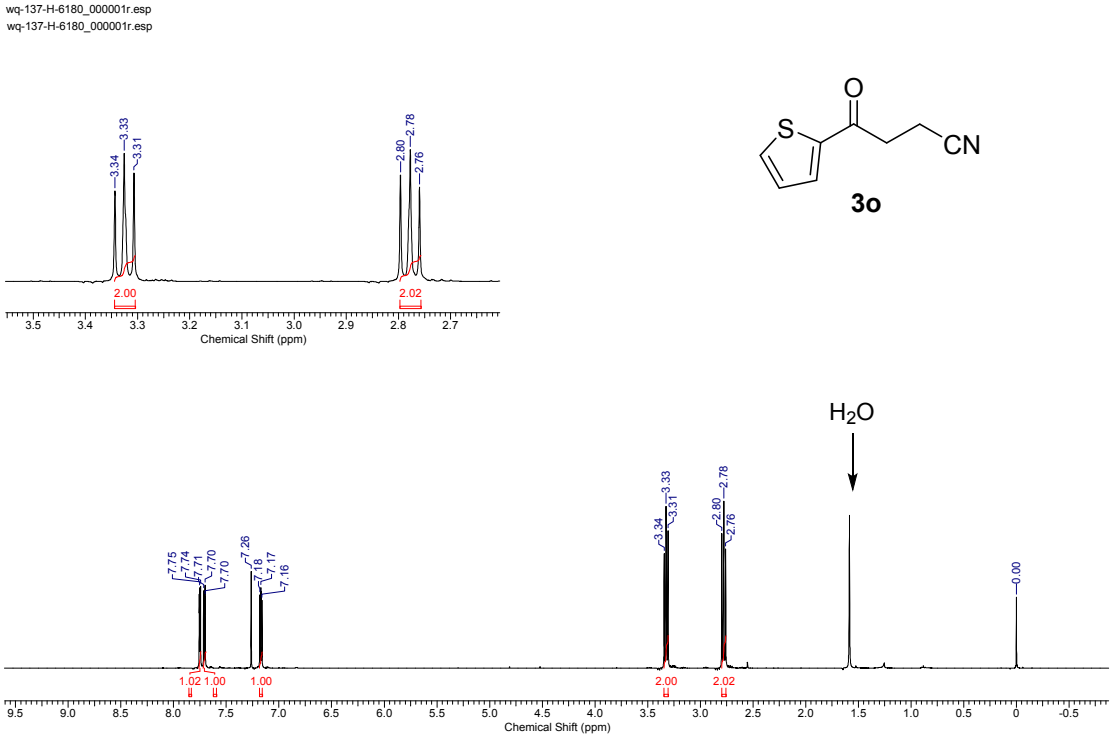


Figure S37. ^{1}H NMR spectrum of compound **3o**

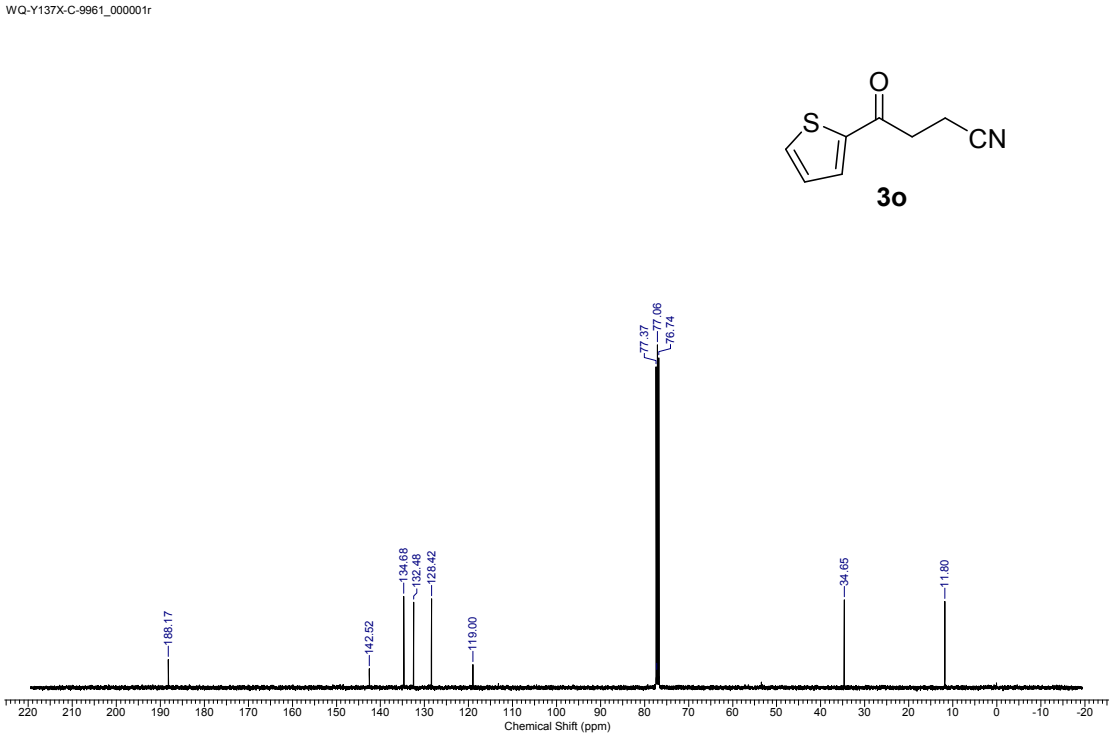


Figure S38. ^{13}C NMR spectrum of compound **30**

7. Determination of Structure of 3a

The structure of **3a** was determined by the X-ray diffraction. Recrystallized from EtOH/dichloromethane. Further information can be found in the CIF file. This crystal was deposited in the Cambridge Crystallographic Data Centre and assigned as CCDC **1818651**.

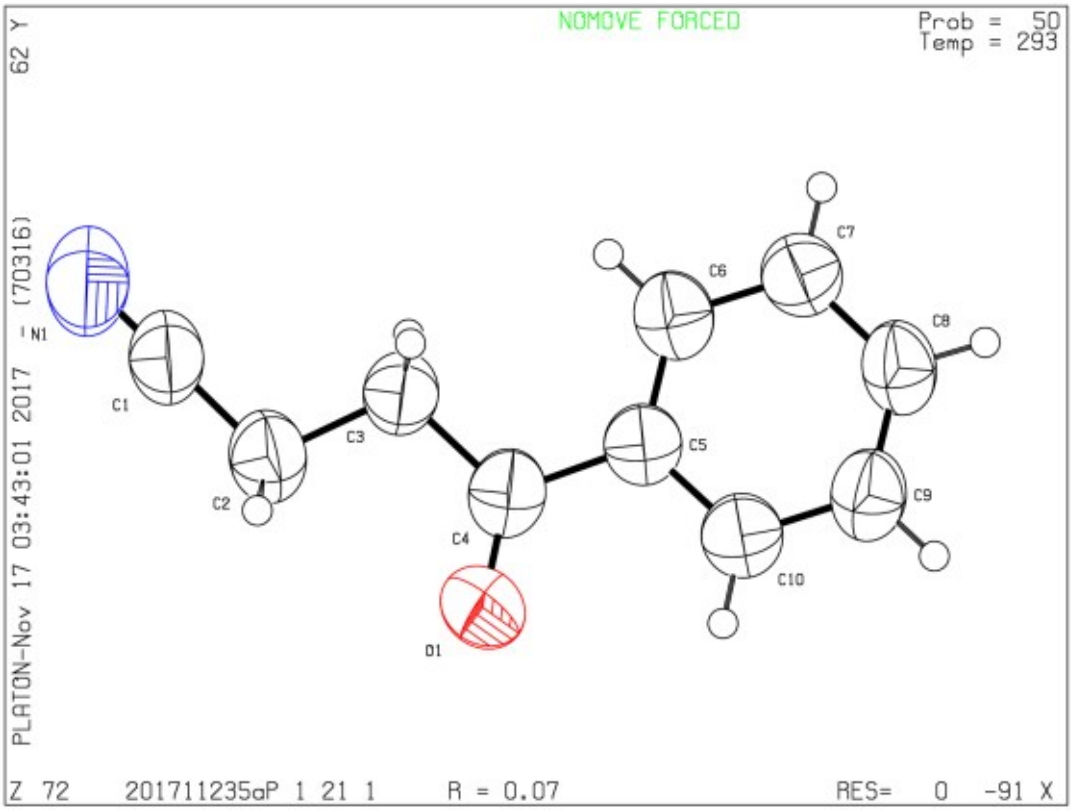


Table 1 Crystal data and structure refinement for 201711235a.

Identification code	201711235a
Empirical formula	$C_{10}H_9NO$
Formula weight	159.18
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	7.5235(7)
b/Å	5.5446(8)
c/Å	10.2976(10)
α /°	90
β /°	99.850(10)
γ /°	90
Volume/Å^3	423.23(9)
Z	2
ρ_{calc}g/cm^3	1.249

μ/mm^{-1}	0.653
F(000)	168.0
Crystal size/mm^3	0.21 × 0.15 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.716 to 134.05
Index ranges	-8 ≤ h ≤ 7, -6 ≤ k ≤ 4, -12 ≤ l ≤ 12
Reflections collected	1646
Independent reflections	1126 [R_{int} = 0.0187, R_{sigma} = 0.0445]
Data/restraints/parameters	1126/1/110
Goodness-of-fit on F^2	1.054
Final R indexes [I>=2σ (I)]	R_1 = 0.0682, wR_2 = 0.1904
Final R indexes [all data]	R_1 = 0.0863, wR_2 = 0.2218
Largest diff. peak/hole / e $Å^{-3}$	0.23/-0.24
Flack parameter	0.1(3)