Electricity-Driven Sustainable Synthesis of 2-Aminobenzonitriles through C-C bond cleavage of isatins: Post-Functionalization via One-Pot Integration with Enzyme Catalysis

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1. Experimental section

1.1 Experimental set-up

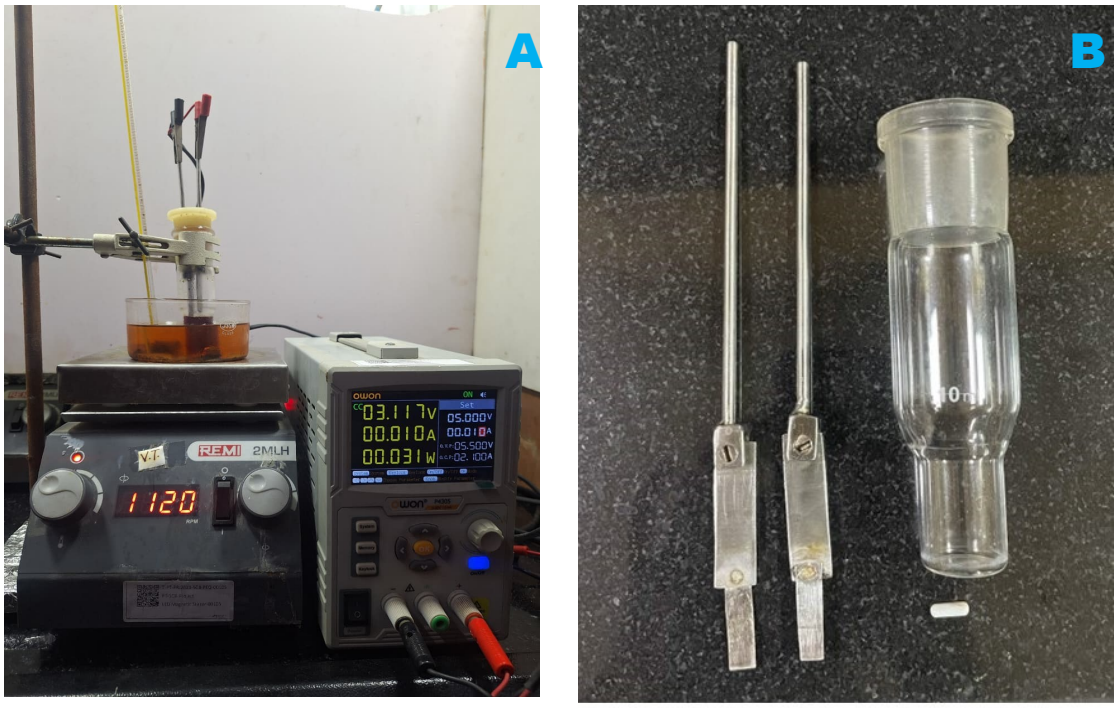
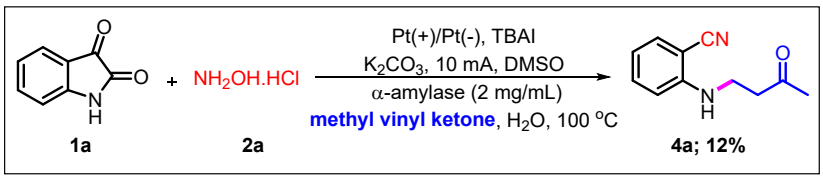


Figure S1: (A) Experimental set-up assembly (B) Electrochemical vial, Platinum sheet electrodes, magnetic stirrer bar

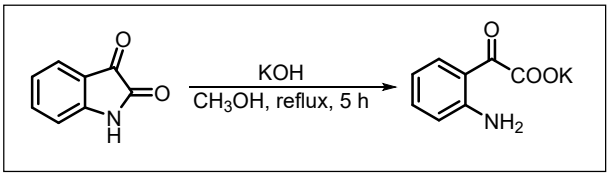
1.2 General procedure for the synthesis of β-amino carbonyl compounds in a one-step one-pot.

In a reaction vial equipped with a magnetic stir bar, Isatin (1a) (20 mg, 1 equiv.), hydroxylamine (2a) (14 mg, 1.5 equiv.), TBAI (75 mg, 1.5 equiv.), and K_2CO_3 (19 mg, 1 equiv.) were added to 1 mL of DMSO, followed by α-amylase (2 mg/mL), methyl vinyl ketone (18 µL, 1.5 equiv.), and 2 mL of water (v/v). The resulting reaction mixture was subjected to a constant current of 10 mA in an undivided cell equipped with platinum electrodes serving as both anode and cathode, and heated to 100 °C. The reaction was stirred for 12 h, and its progress was monitored by thin-layer chromatography (TLC). Upon completion, the mixture was extracted with ethyl acetate and the combined organic layers were dried over anhydrous sodium sulphate. After evaporation of the solvent under reduced pressure, the crude residue was purified by column chromatography on silica gel (60–120 mesh) using hexane/ethyl acetate as the eluent to afford the desired product.



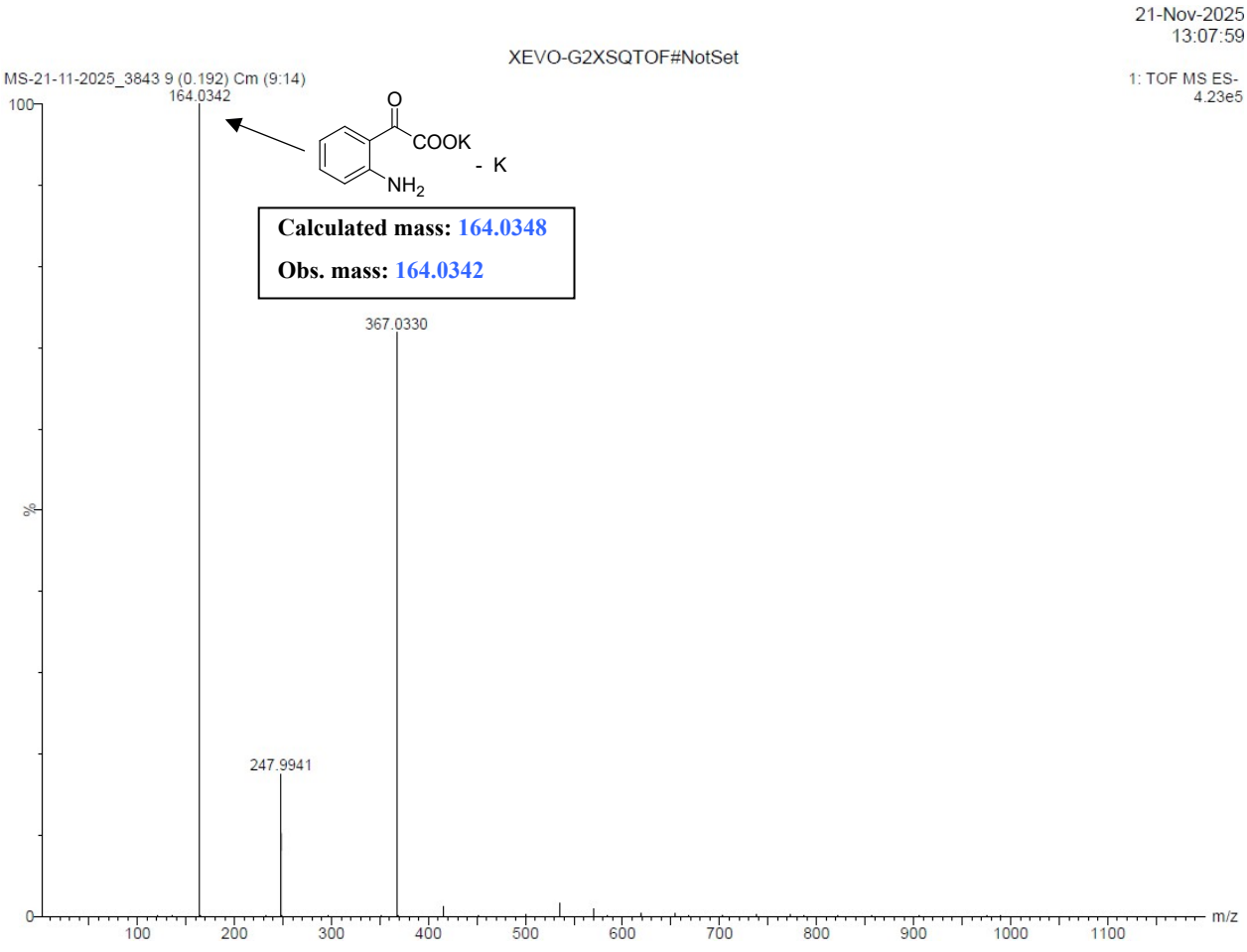
Scheme S1: One-step one-pot synthesis of β-aminocarbonyls

1.3 General procedure for the synthesis of potassium 2-(2-aminophenyl)-2-oxoacetate salt. In a round-bottom flask equipped with a magnetic stir bar, isatin (500 mg, 1.0 equiv.) and potassium hydroxide (209 mg, 1.1 equiv.) were added, and the resulting mixture was refluxed at 60 °C for 5 h in 15 mL methanol. The resulting salt precipitate was collected by filtration.



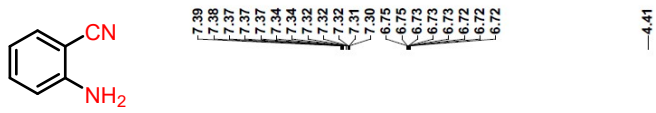
Scheme S2: Synthesis of sodium 2-(2-aminophenyl)-2-oxoacetate salt

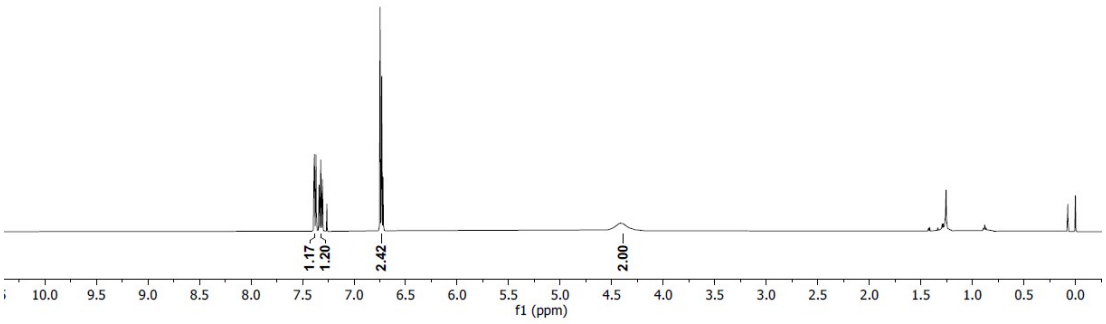
HRMS spectra of potassium 2-(2-aminophenyl)-2-oxoacetate salt

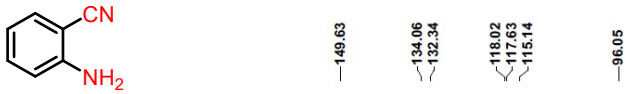


2. Copies of ^{1}H NMR and $^{13}C\{1H\}$ NMR data of compounds

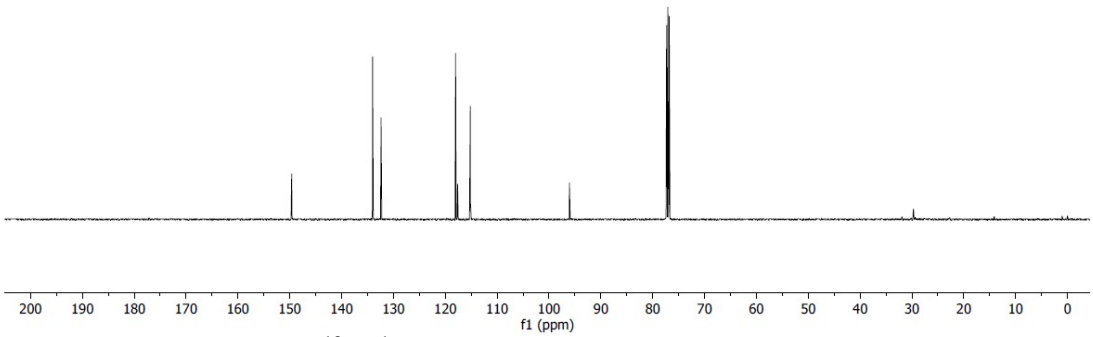
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) spectra of 3a



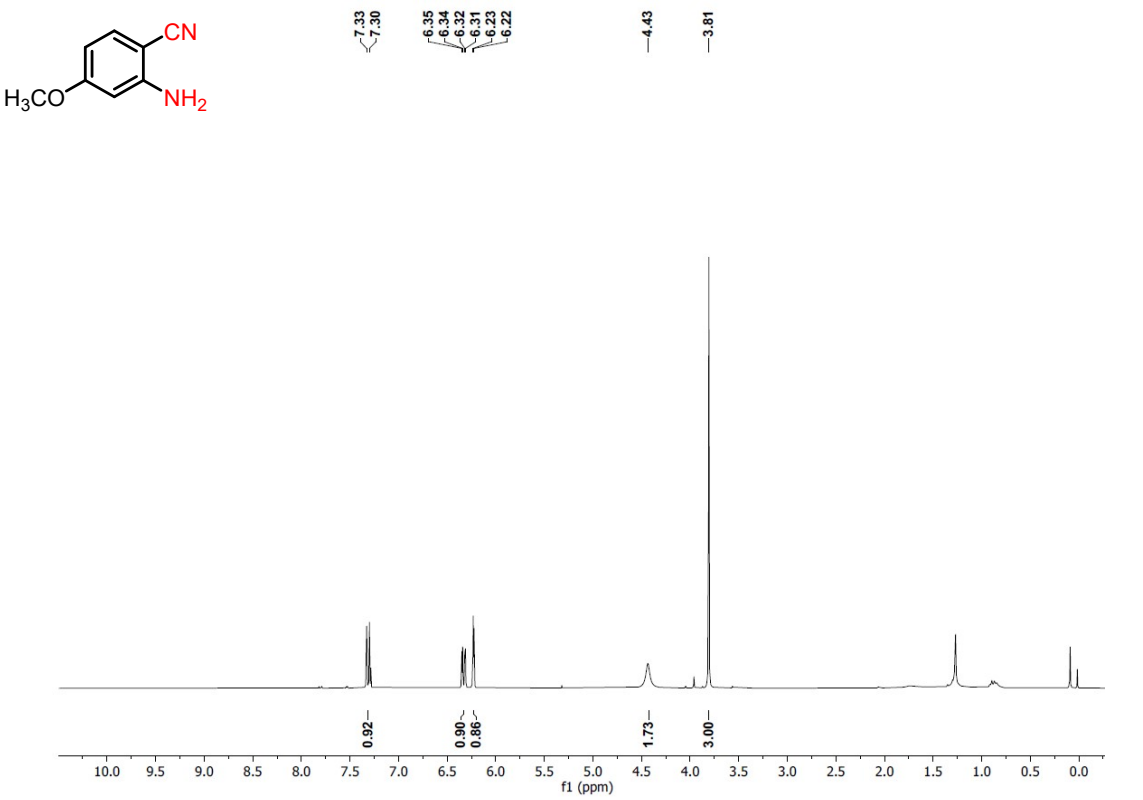




^{1}H

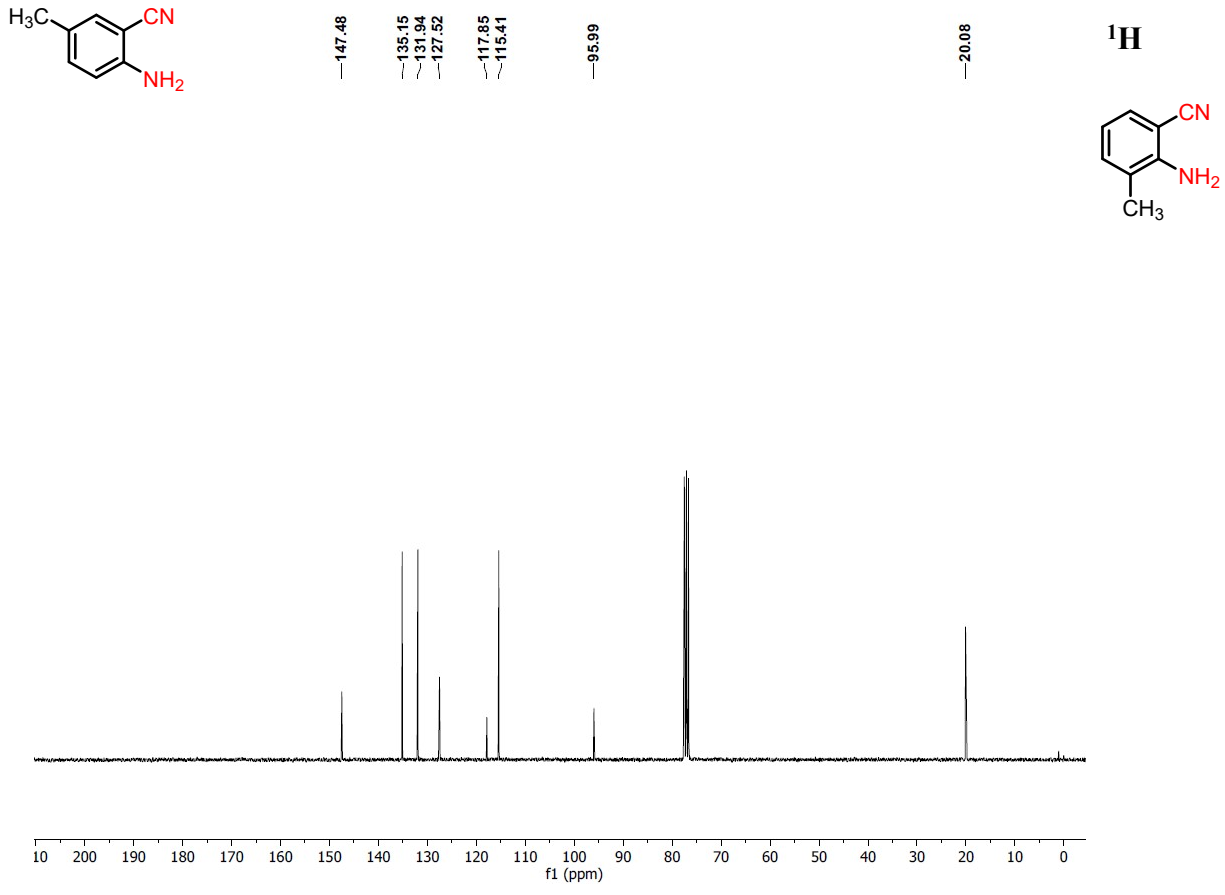


NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 3b

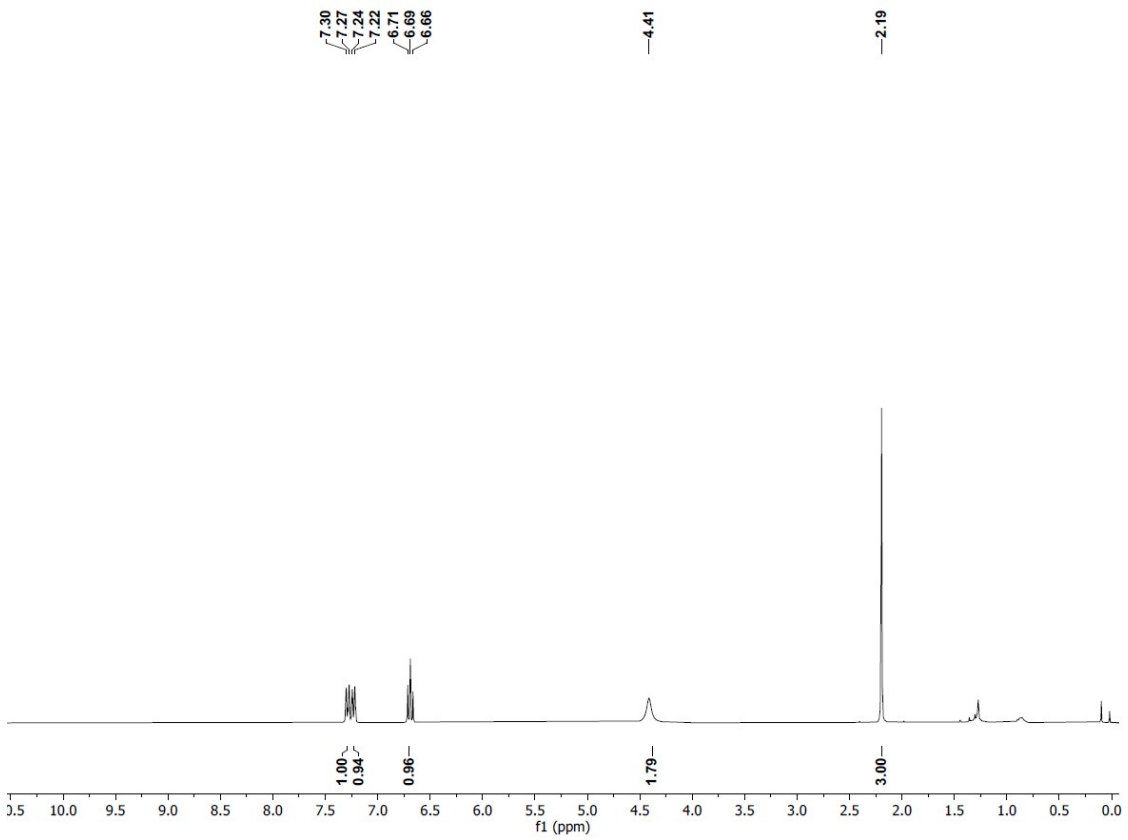


^{1}H

NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 3c



NMR (300 MHz, $CDCl_3$) and $^{13}C\{^1H\}$ NMR (76 MHz, $CDCl_3$) spectra of 3d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7.22
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6.69
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2.19
1.00
0.94
0.96
1.79
3.00
f1 (ppm)


CN
NH2
CH3


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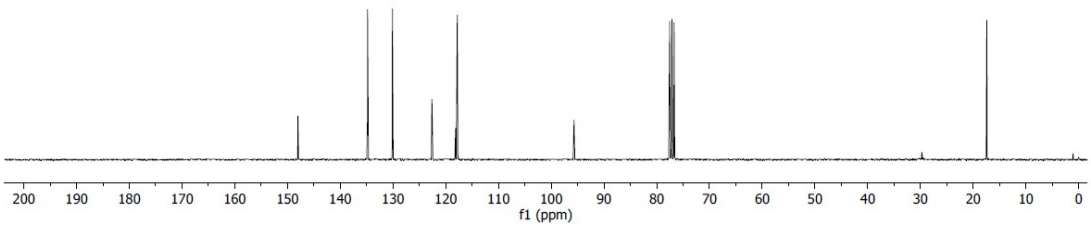
130.11
122.62
118.13
117.57
95.67
17.42


f1 (ppm)

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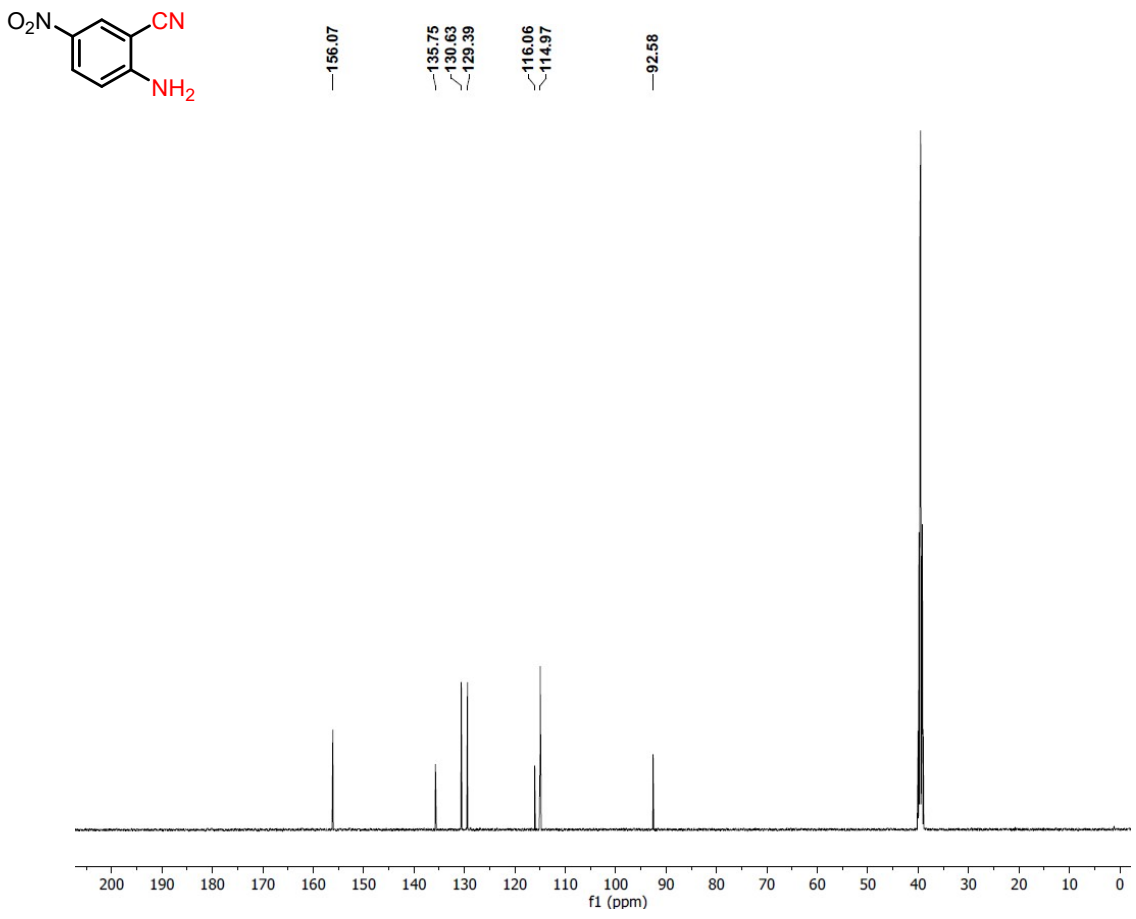
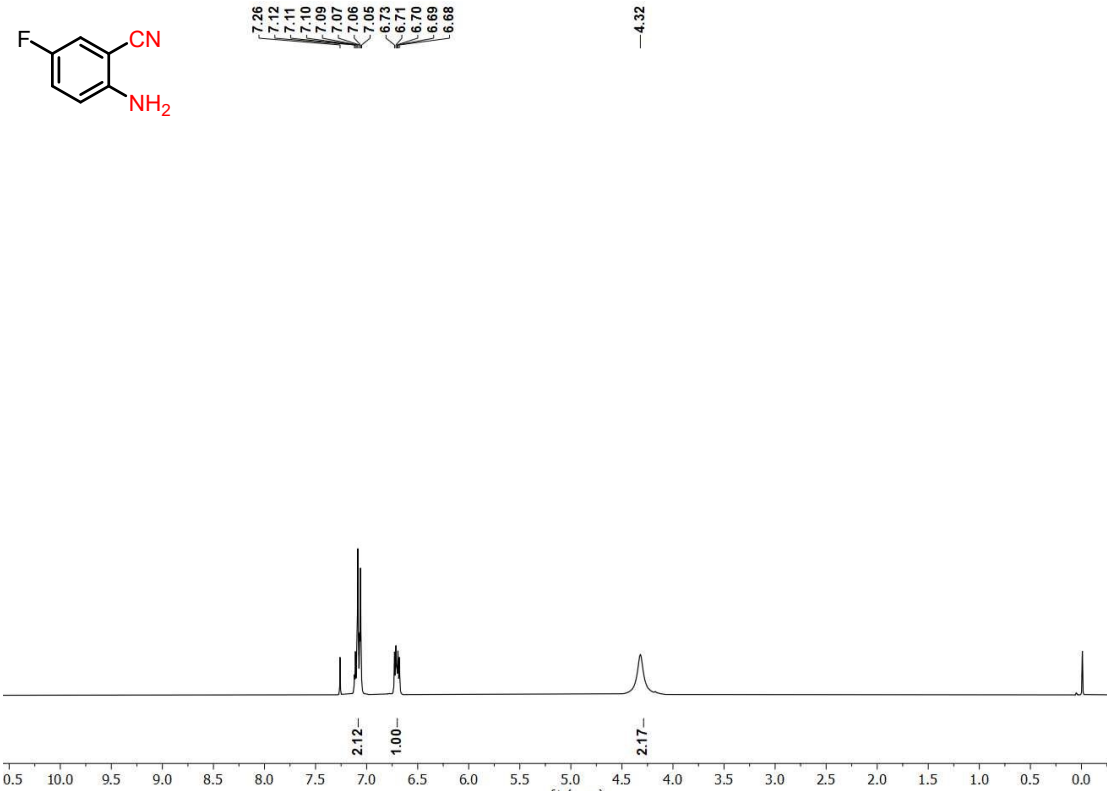
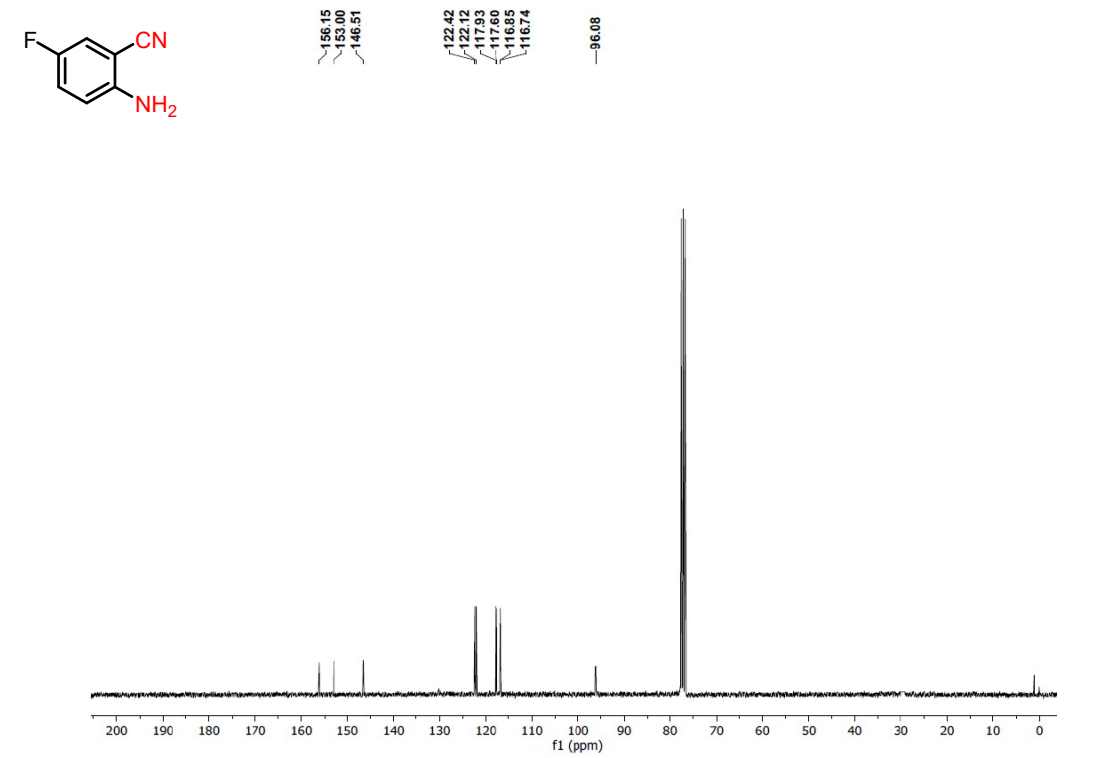


^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 3f





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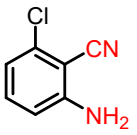
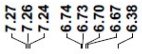
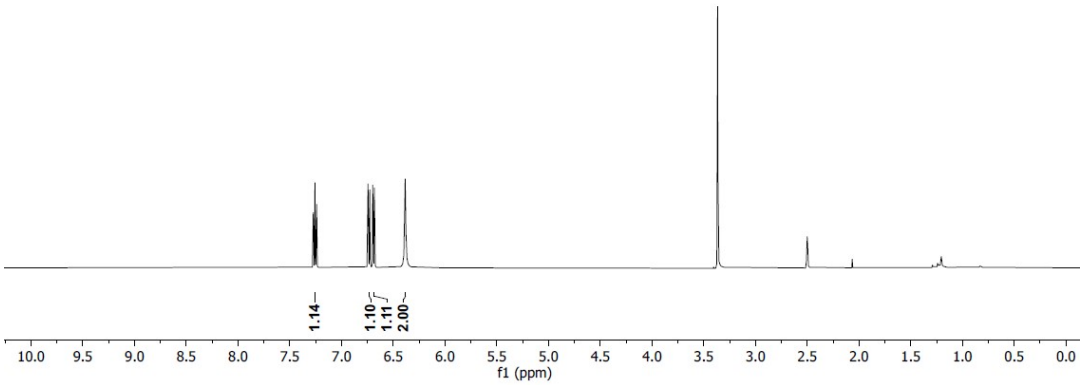
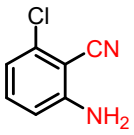
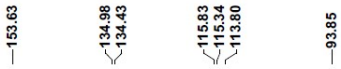
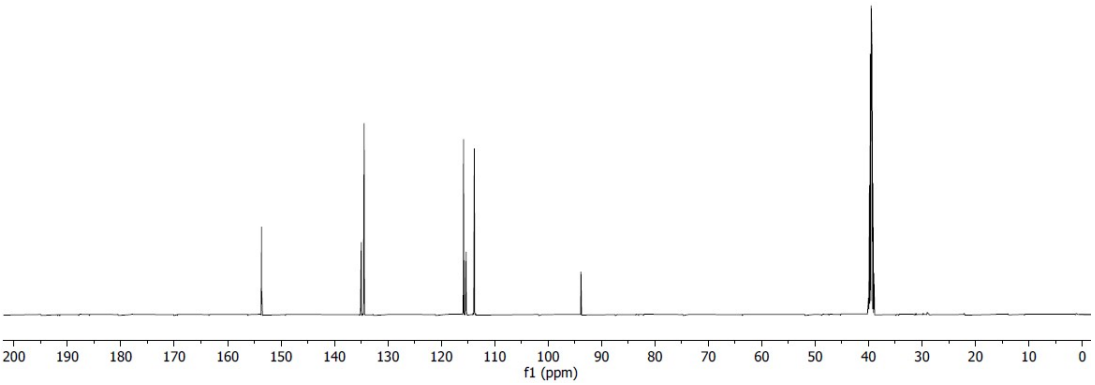




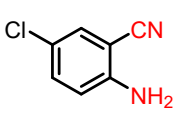


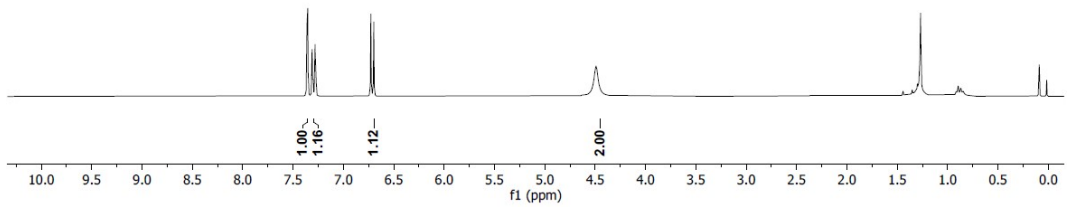


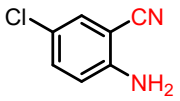


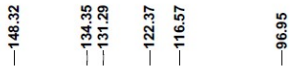


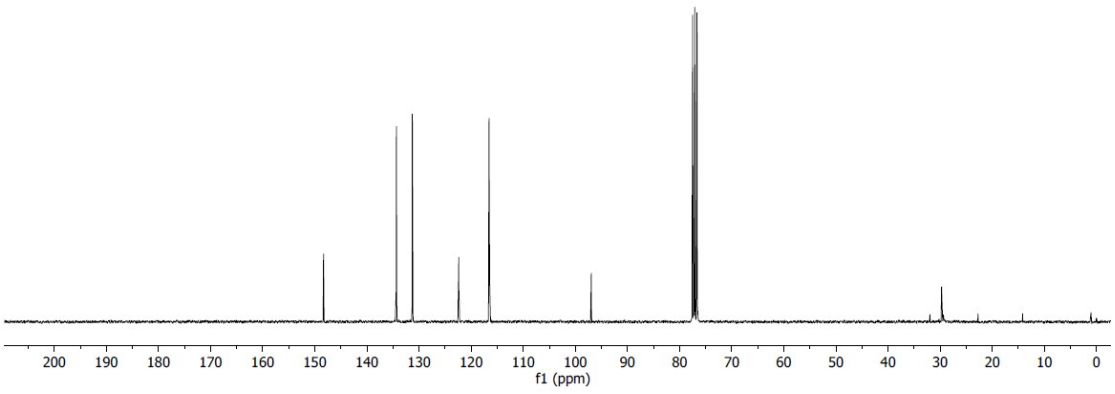
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 3h



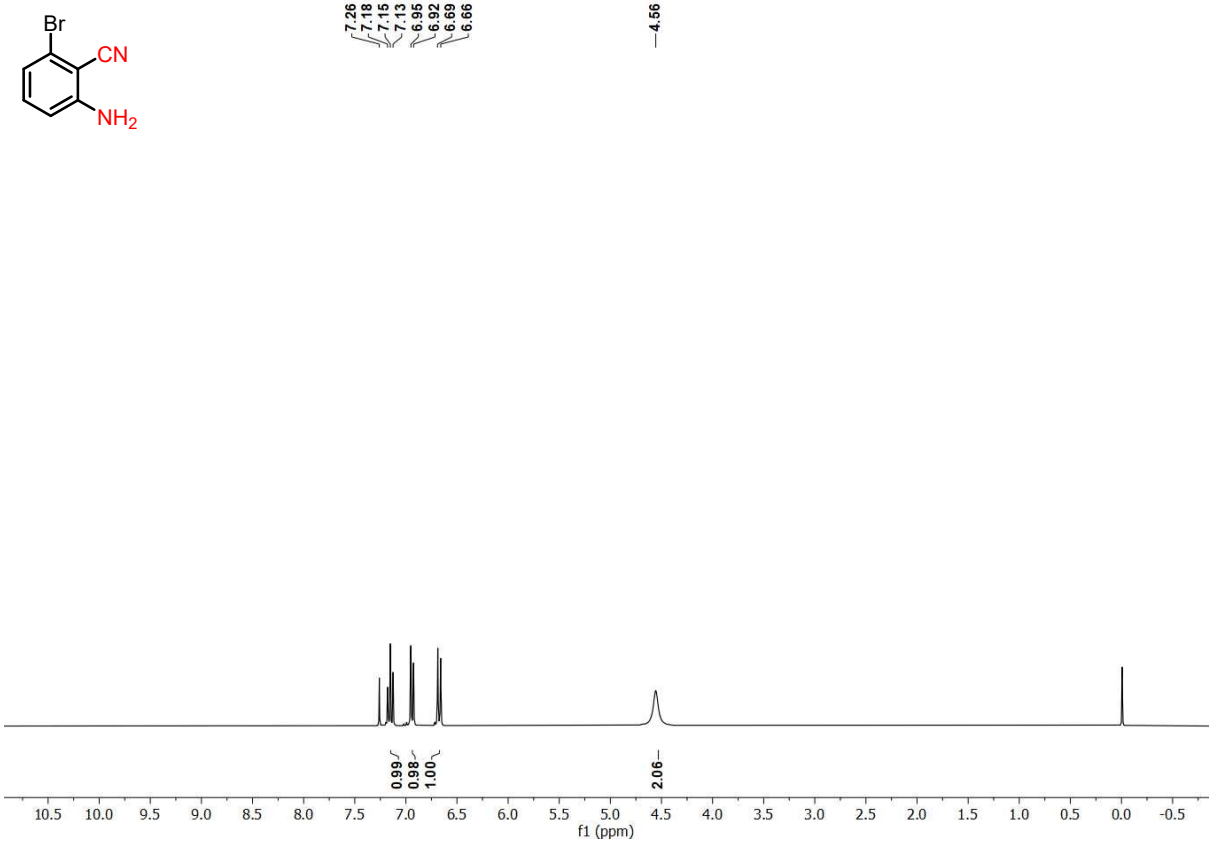


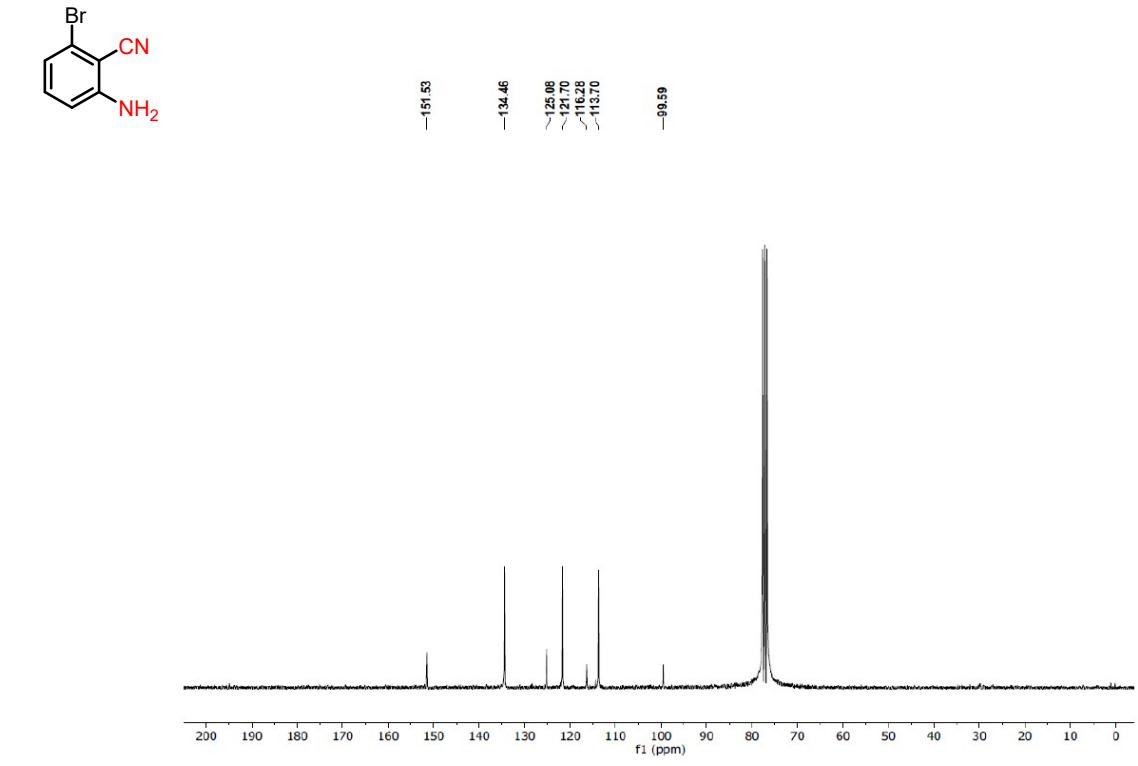




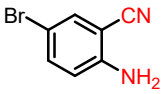


^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) spectra of 3i





^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) spectra of 3j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CN
NH2


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6.65
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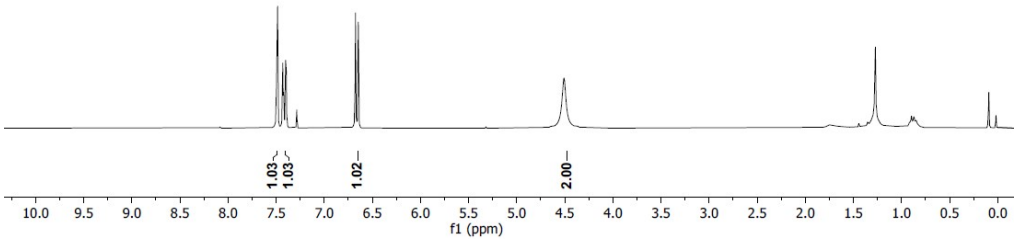
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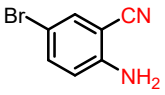
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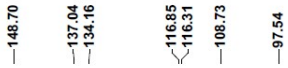
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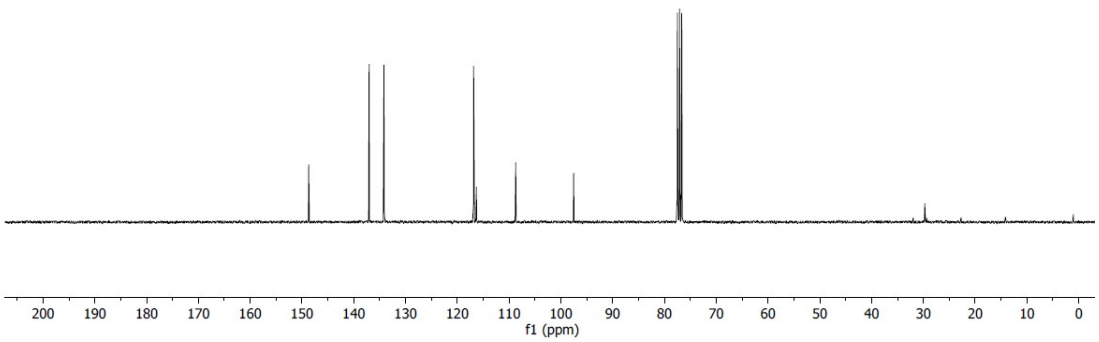
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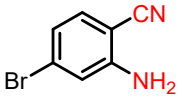
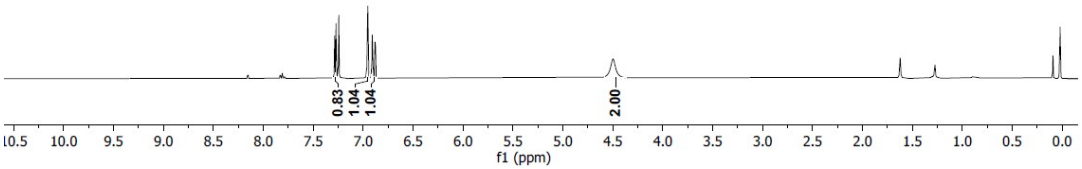
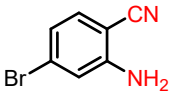
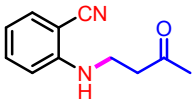
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^1H\}$ NMR (76 MHz, $CDCl_3$) spectra of 3k



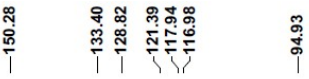


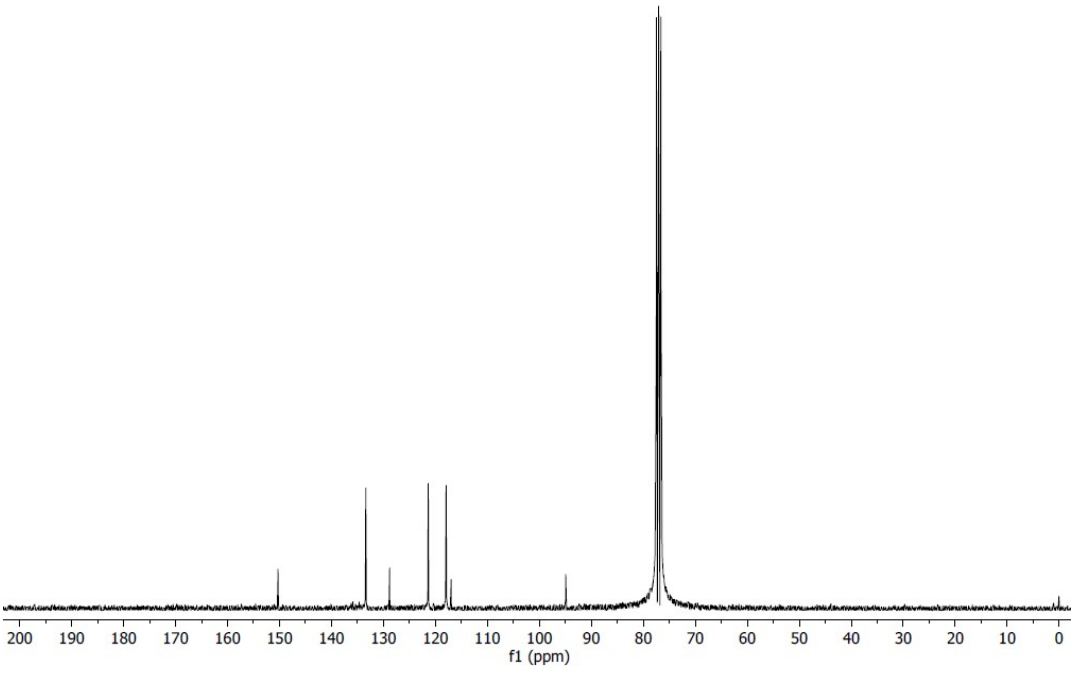


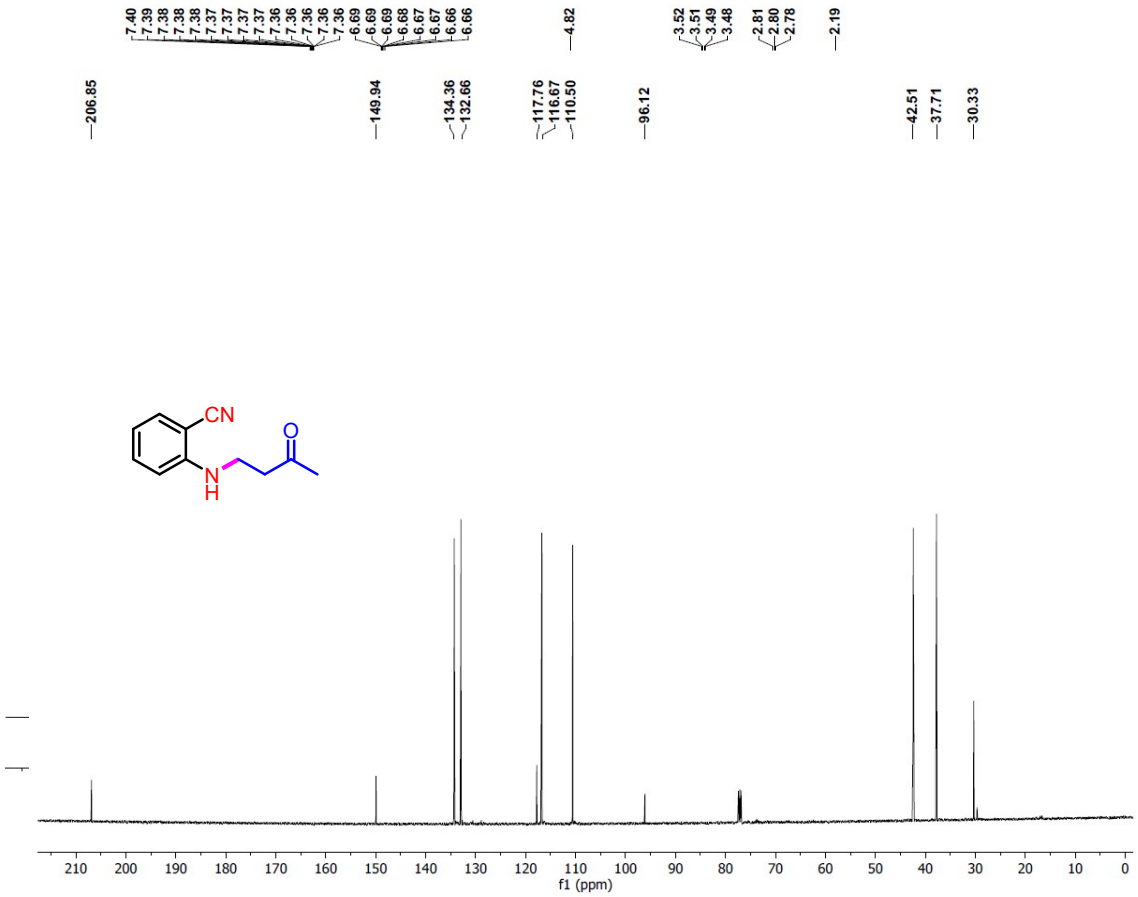
^{1}H NMR (500 MHz, $CDCl_3$) and



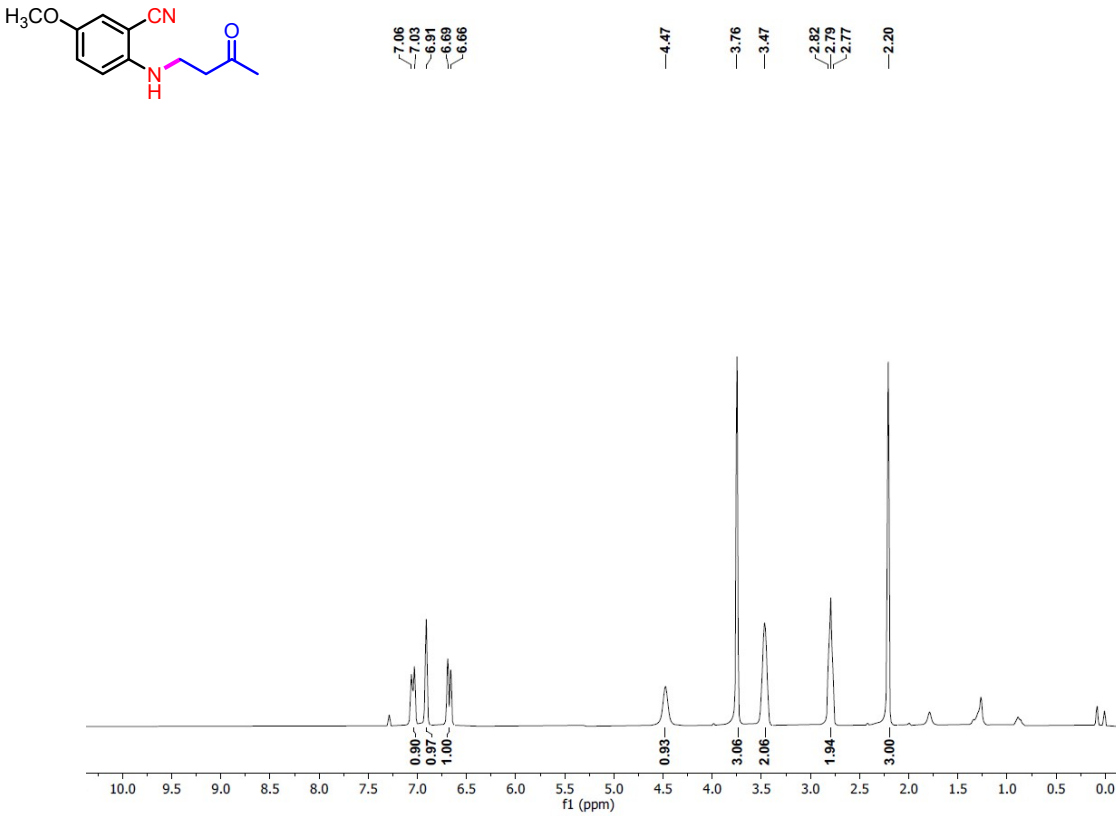
$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) spectra of 4a







^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 4b



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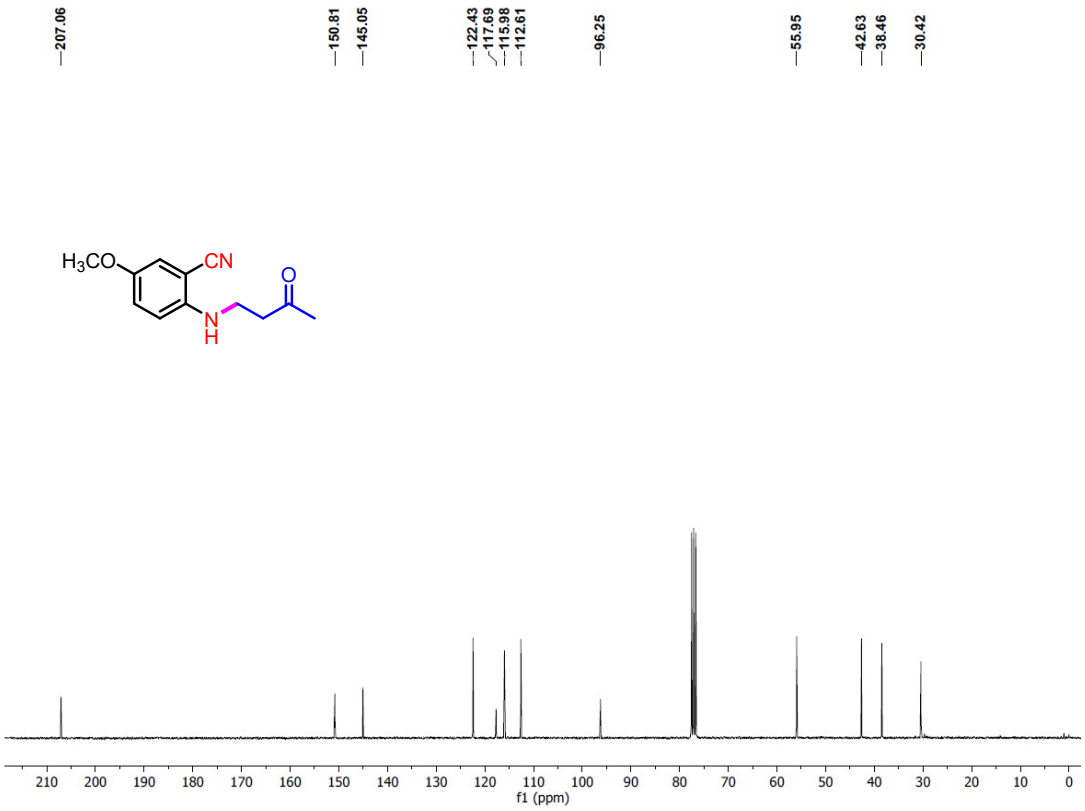
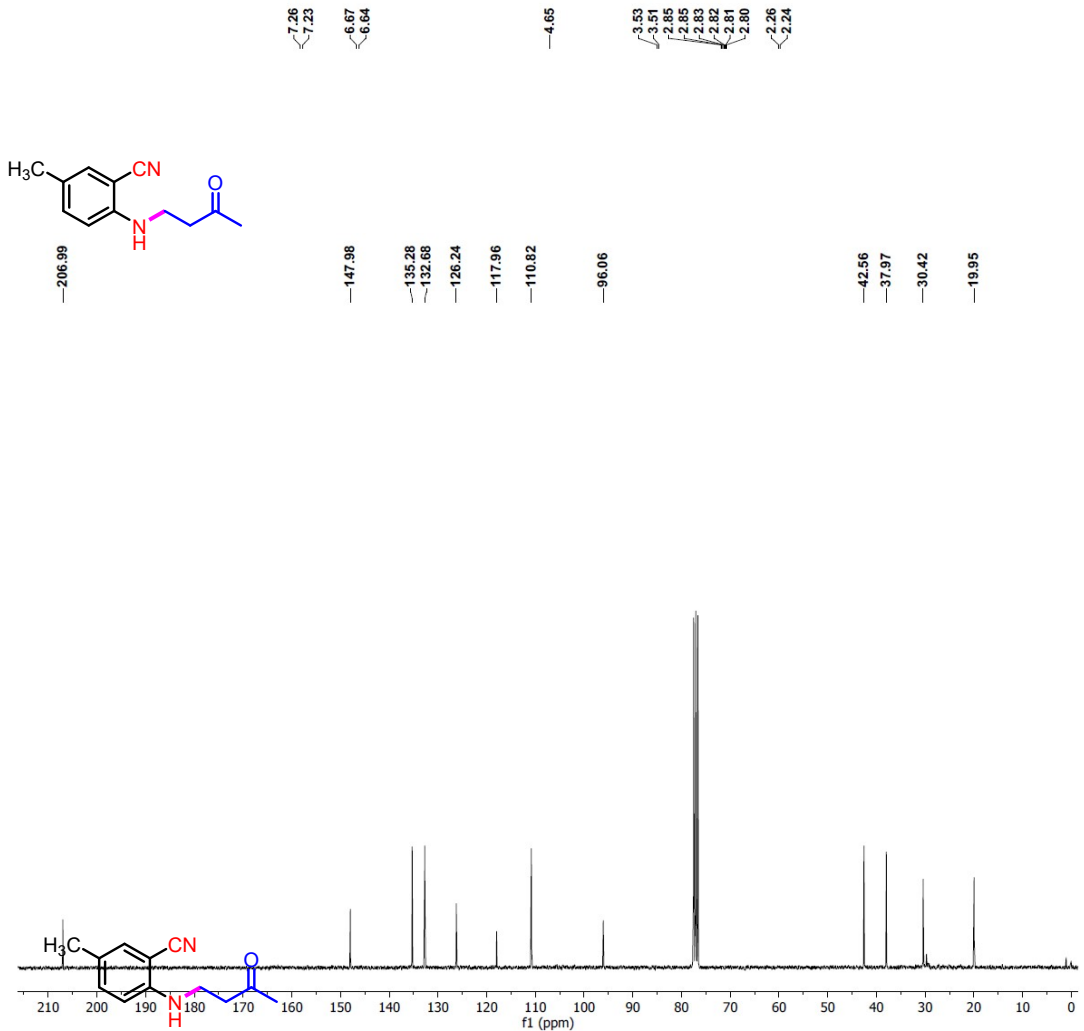


NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 4c



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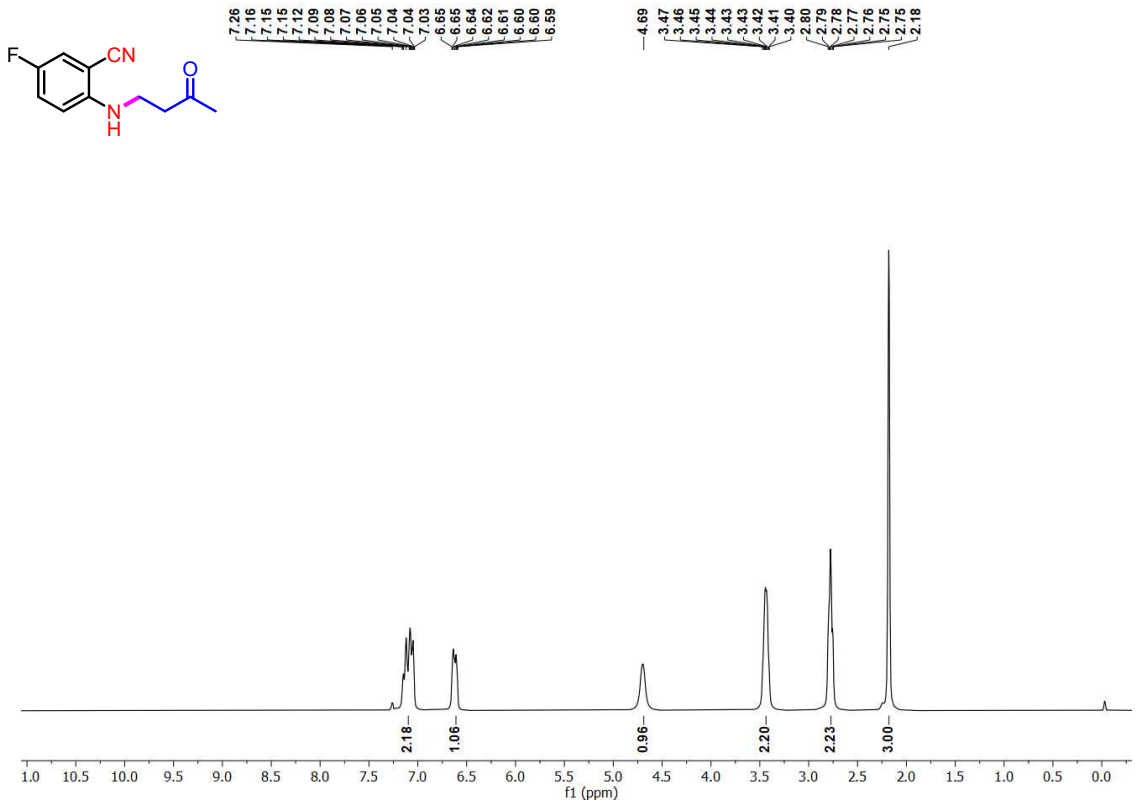

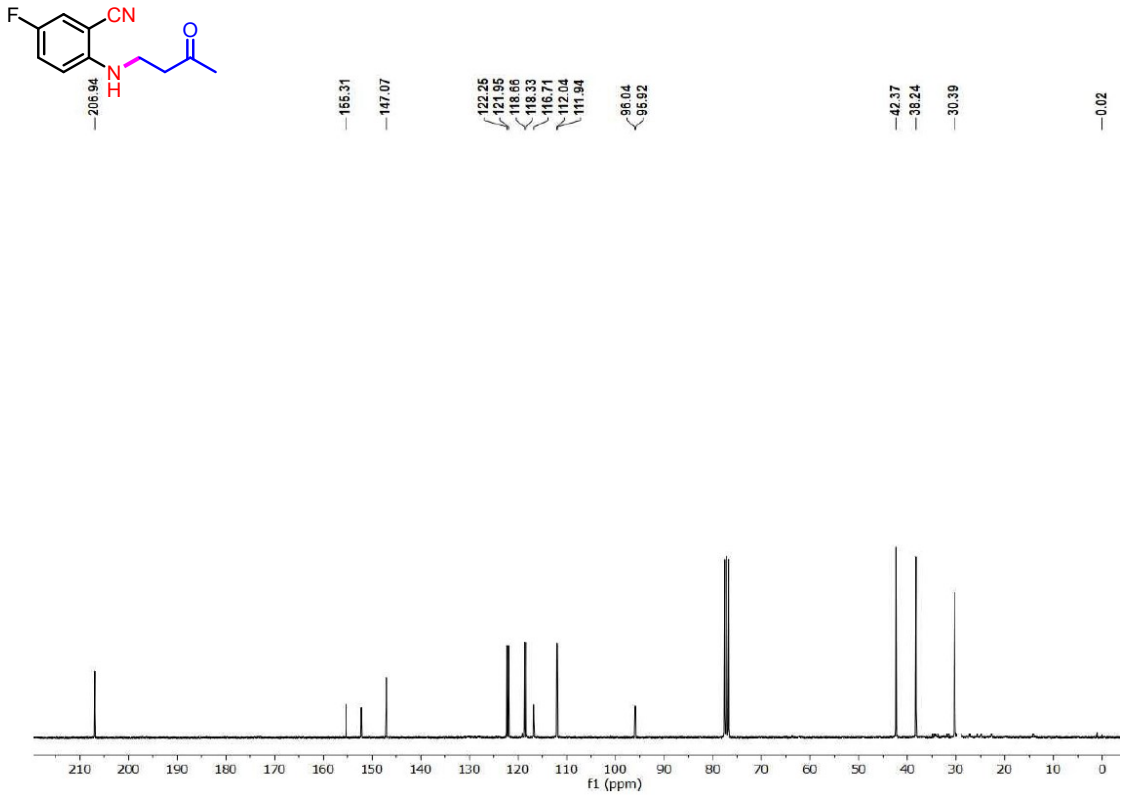

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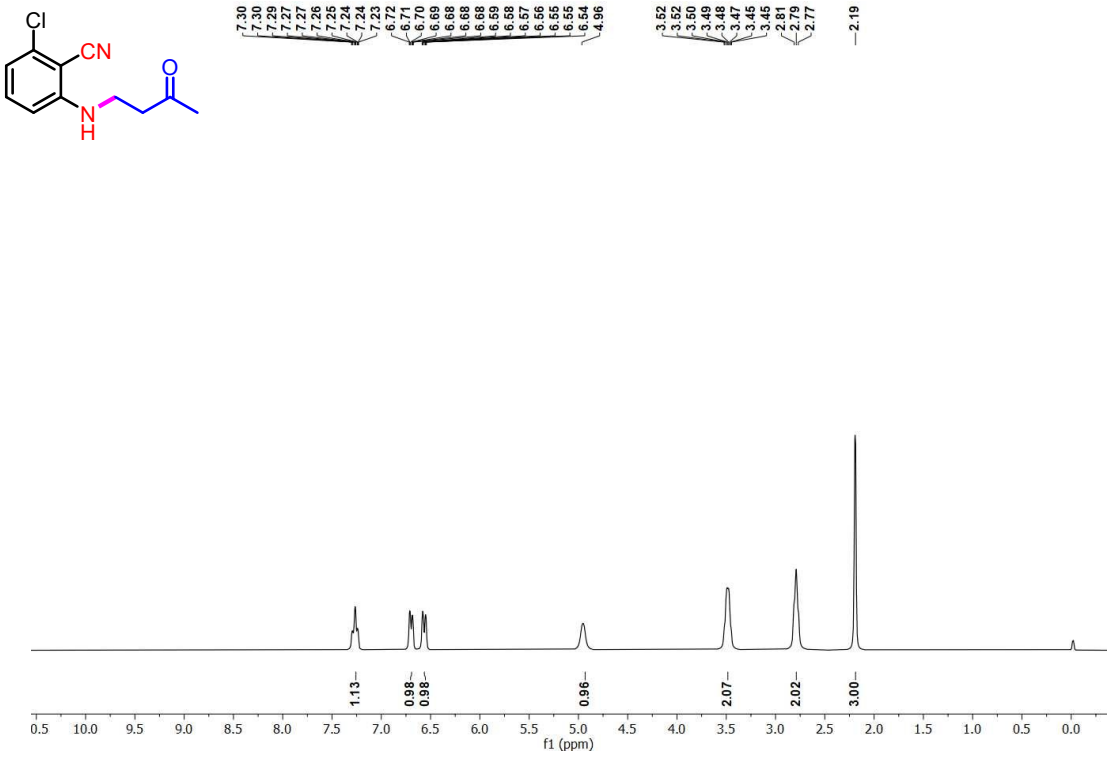
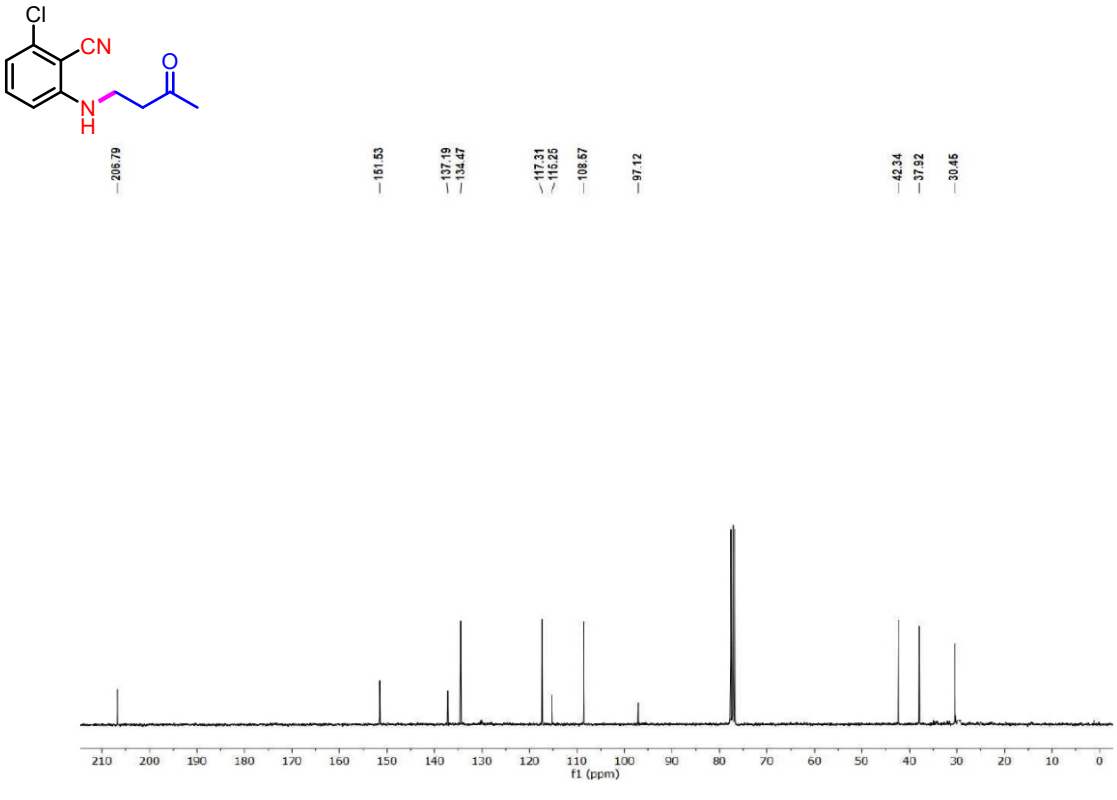
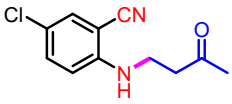
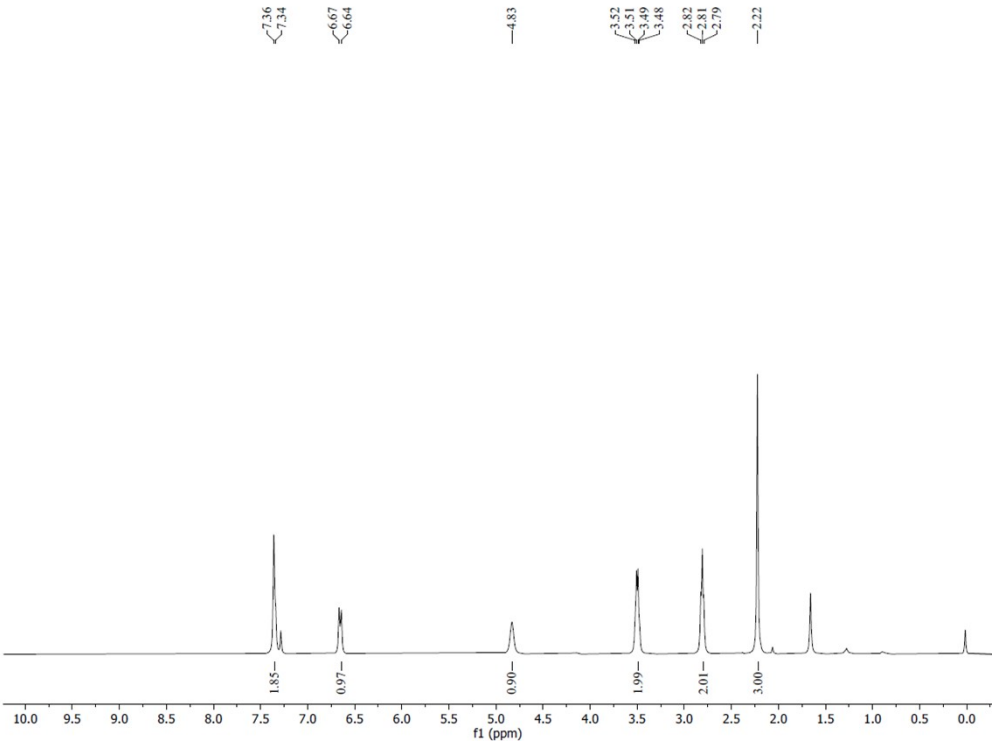
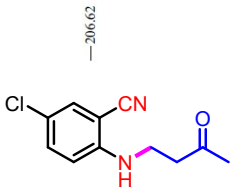




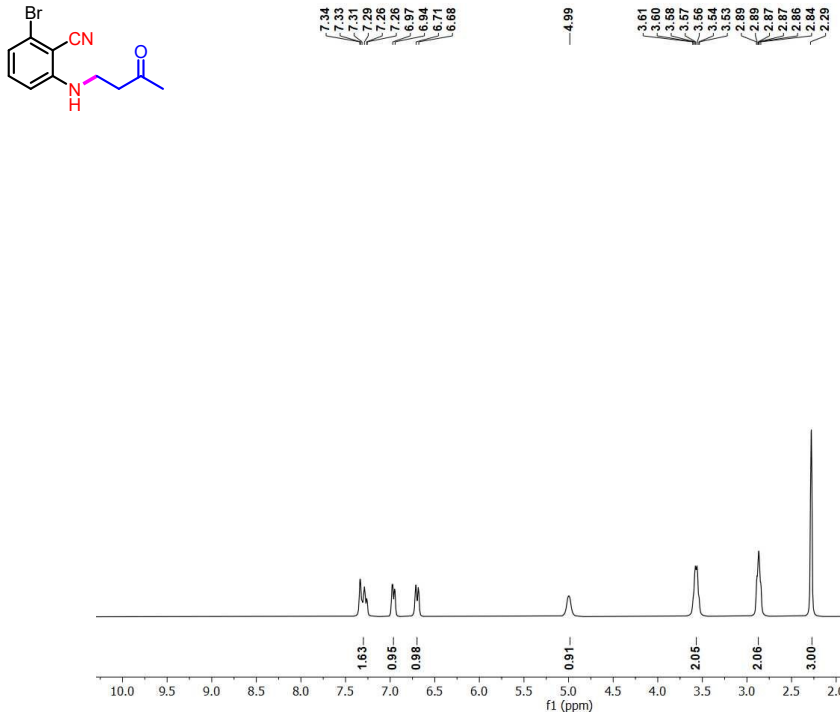
^{1}H NMR (400 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectra of 4f

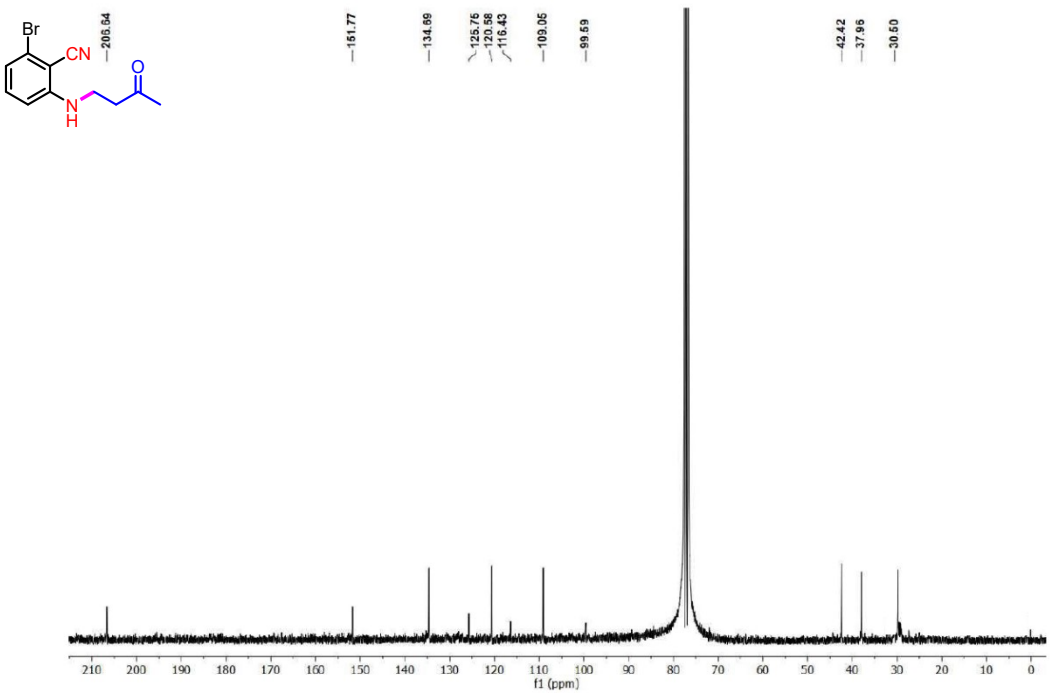




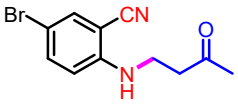


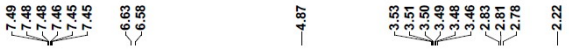
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 4g

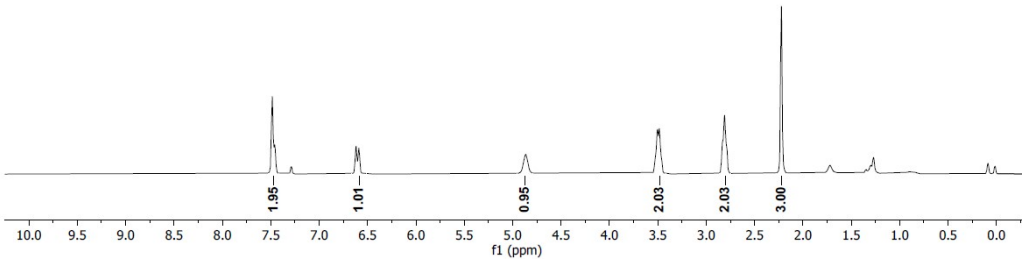


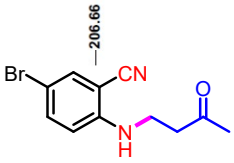


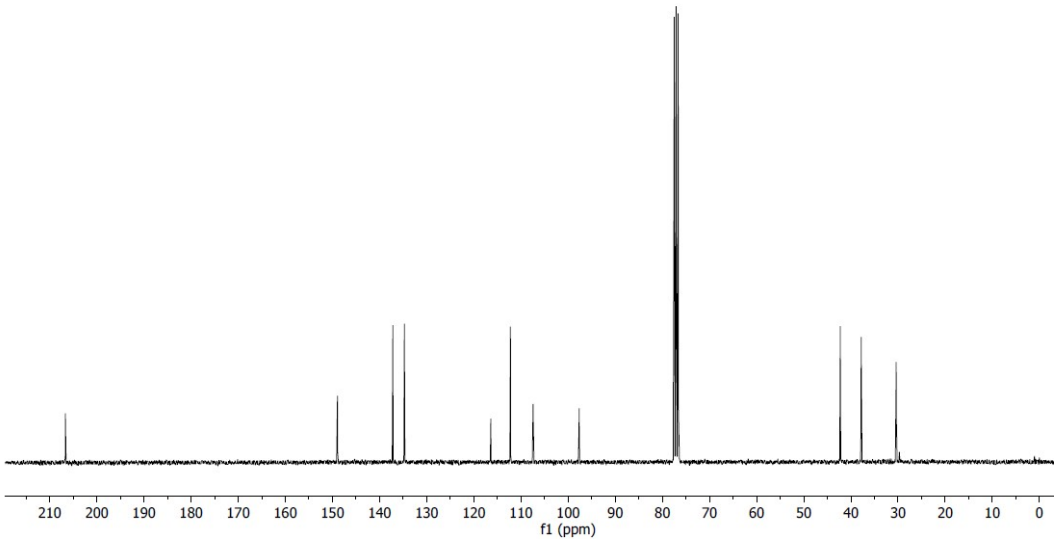
^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) spectra of 4h



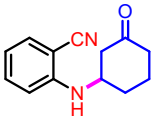


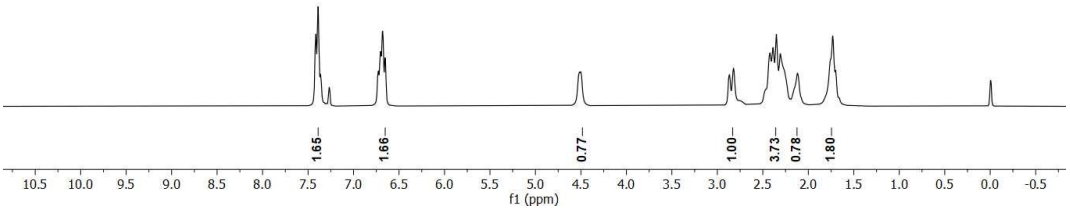


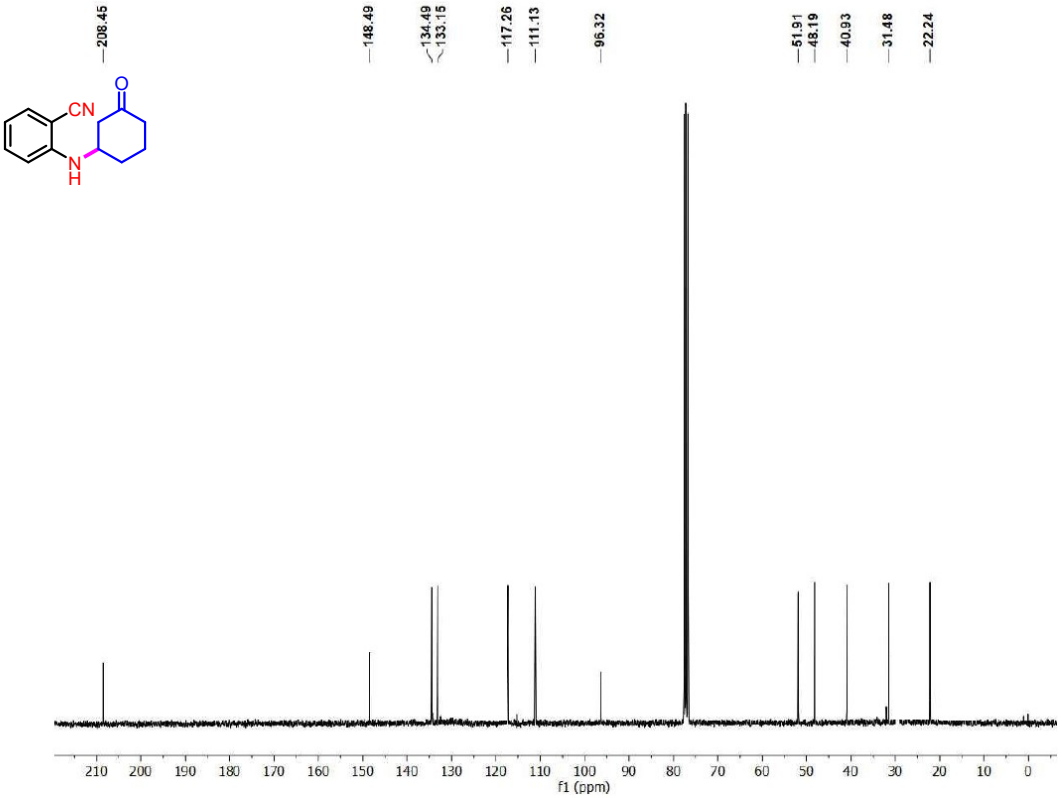




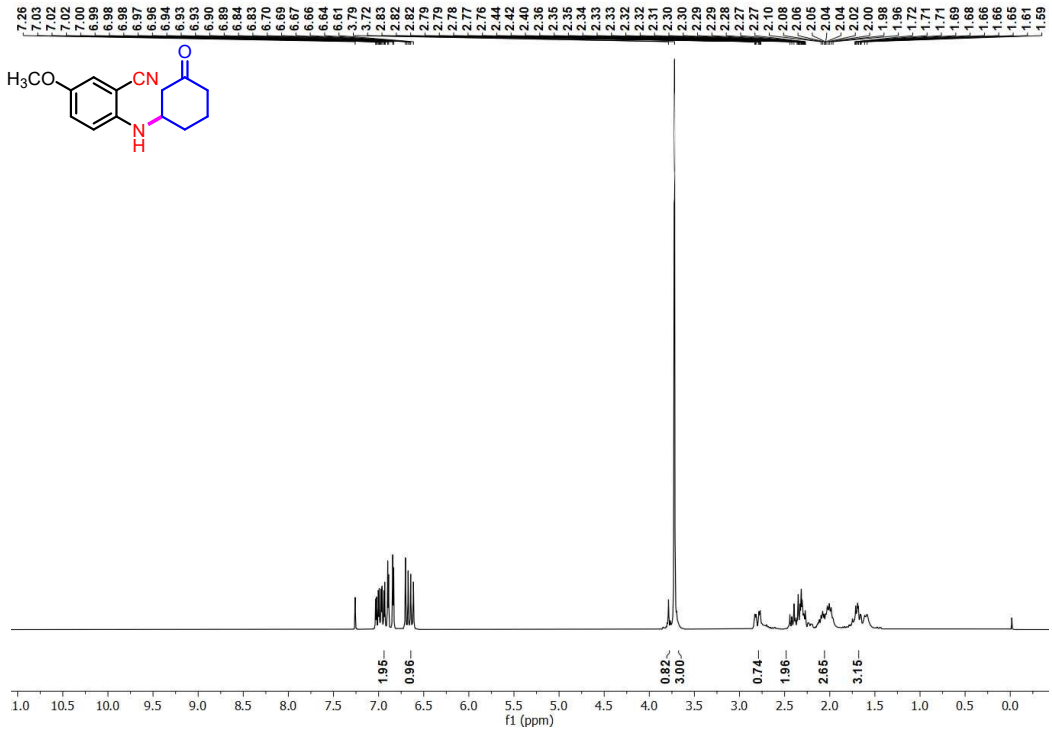
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 4i

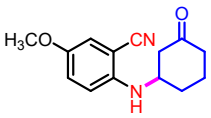




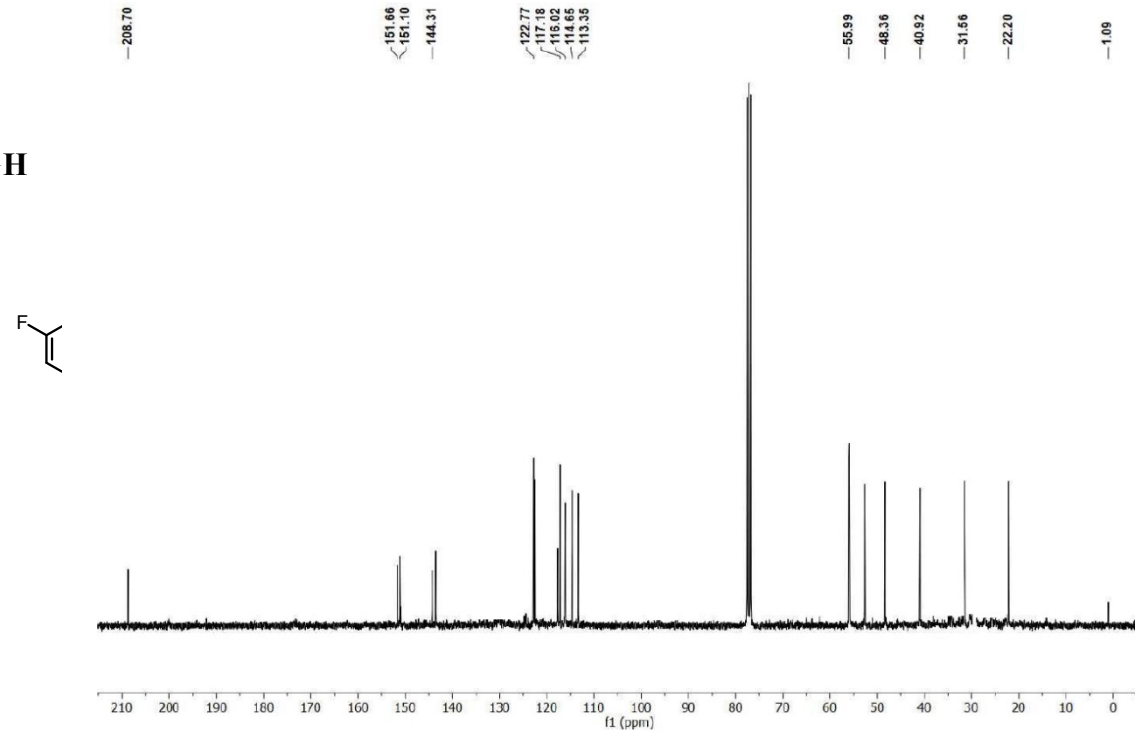


^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 4j

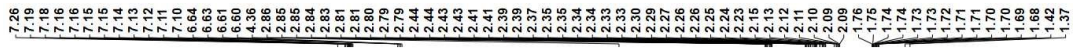


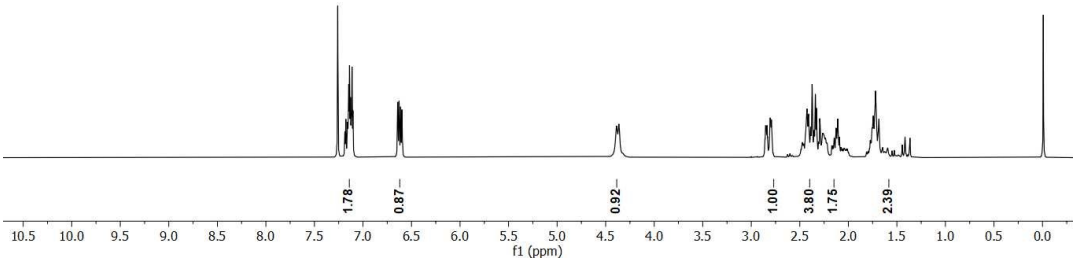


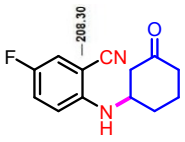
^{1}H



NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (76 MHz, $CDCl_3$) spectra of 4k




1.78
0.87
0.92
1.00
3.80
1.75
2.39
f1 (ppm)


F
CN
O
N
H

208.30
152.42
145.49
122.49
122.19
118.94
118.61
116.73
112.64
112.54
96.43
96.31
52.41
48.18
40.92
31.56
22.23
0.13
f1 (ppm)