

Supporting Information for
Brønsted Acid Co-catalysts in Photocatalytic Addition of α -Amino Radicals to Michael Acceptors
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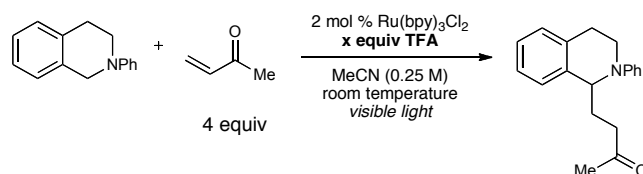
1. General Information

Acetonitrile and CH_2Cl_2 were purified by elution through alumina as described by Grubbs.¹ $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ was purchased from Strem and used without further purification. Trifluoroacetic acid was distilled over magnesium sulfate and stored in a refrigerator between uses. Methyl acrylate was washed with aqueous NaOH and water, dried with CaCl_2 , and distilled immediately prior to use. Substrates from Table 2, entries 1–4,² 6,³ 7,⁴ 8,⁵ and Table 3, entry 3⁶ were prepared as previously described. The syntheses of new substrates are described in the Experimental Section. All other chemicals were purchased from commercial suppliers and used without further purification. All glassware was oven-dried at 130 °C for at least 1 h or flame-dried immediately prior to use. Diastereomer ratios for all compounds were determined by ^1H NMR analysis of the unpurified reaction mixtures. NMR chemical shifts are reported in parts per million (δ) relative to TMS (0.0 ppm) for ^1H NMR data and CDCl_3 (77.23 ppm) for ^{13}C NMR data. Mass spectrometry was performed with an electrospray ionization mass spectrometer. These facilities are funded by the NSF (CHE-9974839, CHE-9304546), NIH (RR08389–01) and the University of Wisconsin.

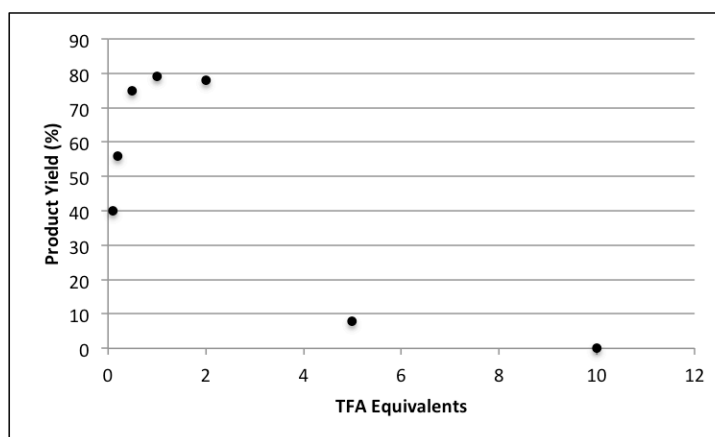
2. Evaluation of TFA Concentration

The effect of the concentration of TFA on the yield of the reaction was evaluated by examining the room-temperature photoaddition reaction between **5** and **6** in the presence of varying amounts of acid. The general procedure for these experiments is as follows. A dry 25 mL Schlenk tube was charged with **5** (1 equiv), **6** (4 equiv), Ru(bpy)₃Cl₂•H₂O (0.02 equiv), the appropriate amount of acid, and acetonitrile (0.25 M) and degassed using three freeze/pump/thaw cycles under nitrogen in the dark. The reaction was stirred while being irradiated with a 23 W (1280 lumen) compact fluorescent lamp at a distance of 30 cm. After 15 h, the mixture was neutralized with K₂CO₃ (2 equiv) and filtered through a silica plug using Et₂O as the eluent. The mixture was concentrated *in vacuo*, and SiMe₃Ph was then added as an internal standard. The yield of product was determined by ¹H NMR analysis of the residue.

Figure S1. Effect of TFA equivalents on the yield of the transformation.



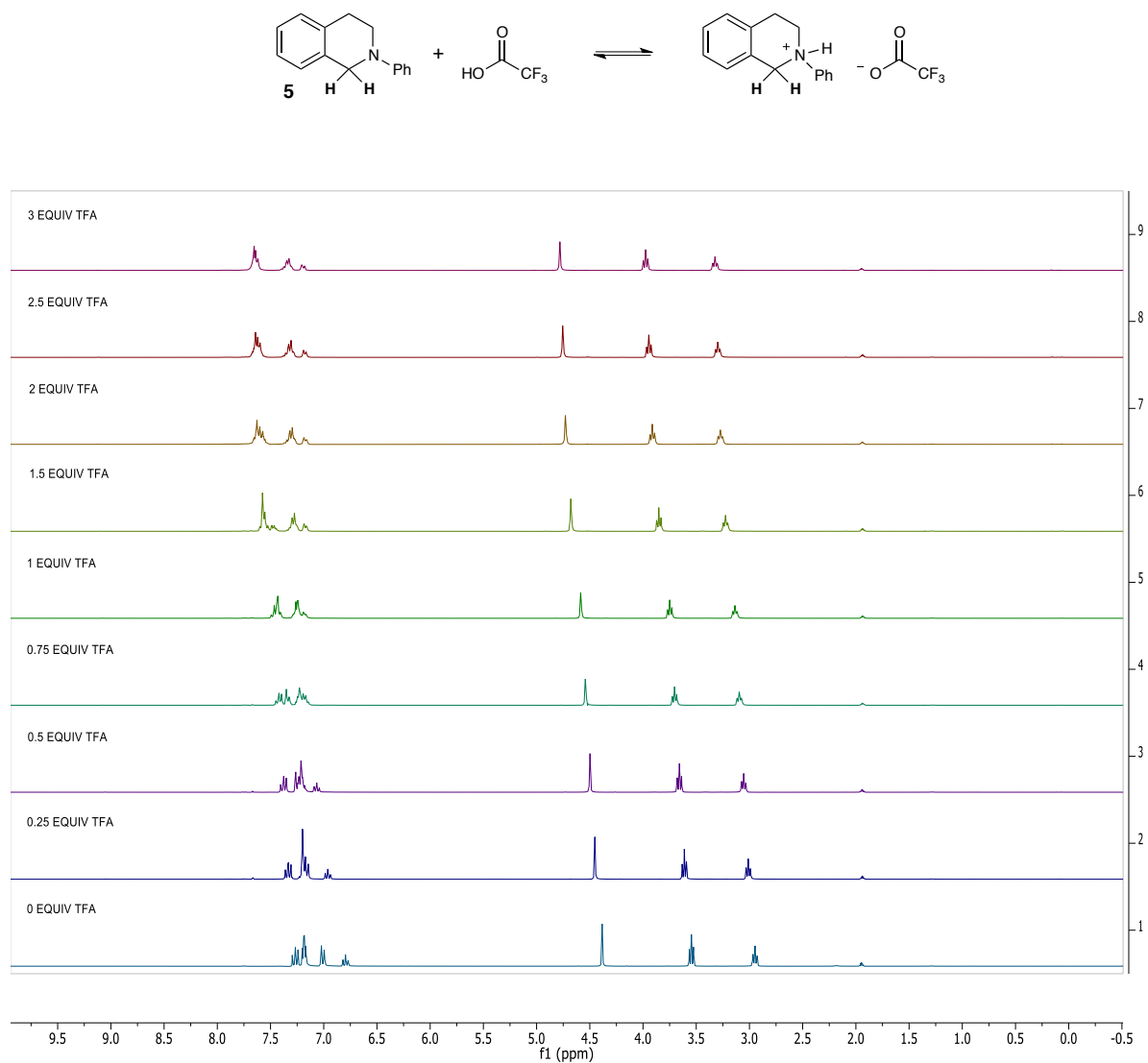
TFA Equivalents	Product Yield (%)
0.1	40
0.2	56
0.5	75
1	79
2	78
5	8
10	0



3. NMR Titration of Isoquinoline **5**.

The starting material **5** (52 mg, 0.25 mmol) was dissolved in MeCN- d_3 (1 mL, 0.25 M) and increasing amounts of TFA were subsequently added. The extent of protonation was evaluated based on the downfield shift of the benzylic protons as observed by $^1\text{H-NMR}$.

Figure S2. $^1\text{H-NMR}$ of 2-phenyl-1,2,3,4-tetrahydroisoquinoline **5** in MeCN- d_3 with different amounts of TFA.



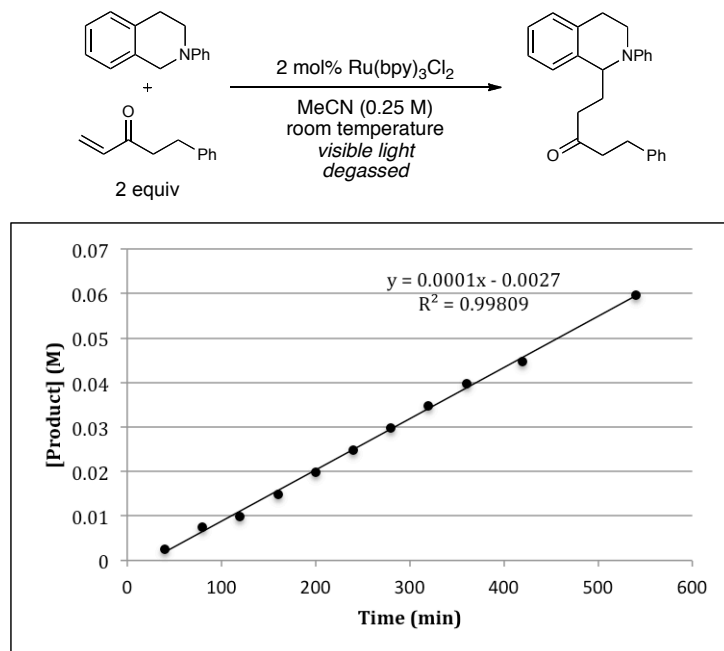
4. Kinetic Isotope Effect Measurements.

The intermolecular kinetic isotope effects were determined by studying the initial rates of reactions with (a) 2-phenyl-1,2,3,4-tetrahydroisoquinoline **5** and 5-phenylpent-1-en-3-one **10**; (b) 1,1-dideutero-1,2,3,4-tetrahydroisoquinoline **5-d₂** and 5-phenylpent-1-en-3-one **10**; and (c) 1,2,3,4-tetrahydroisoquinoline **5** and 1,1,2-trideutero-5-phenylpent-1-en-3-one **10-d₃** under both acidic and neutral conditions.

General procedure for kinetic experiments (initial rates measurements). The experiments were conducted in dry 25 mL Schlenk tubes. Reactions were run to about 25% conversion, and the data ([product] versus time) was analyzed using the initial rates method. The reported value of initial rate is the average of the three kinetic experiments, and the reported error in the initial rate is the standard deviation of those three experiments. A representative example is shown in Figure S3.

Procedure under neutral conditions: For each experiment, the substrate (52 mg, 0.25 mmol), catalyst (3.7 mg, 0.005 mmol), acceptor (80 mg, 0.50 mmol), and naphthalene (internal standard) were added to a dry Schlenk tube under N₂. Then, acetonitrile (1 mL, 0.25 M) was added and the solution was degassed by three freeze/pump/thaw cycles under nitrogen in the dark. The reaction was allowed to stir at room temperature while being irradiated by a 23 W compact fluorescent lamp at a distance of 30 cm. For each time point, the Schlenk's side arm was purged via three vacuum/nitrogen cycles, opened while still being kept under a positive atmosphere of nitrogen, and a small aliquot taken with a needle (previously purged with nitrogen). The aliquot was then diluted in DCM and analyzed by gas chromatography. The yield of product was determined versus naphthalene as the internal standard.

Figure S3. Representative kinetics experiment.



Procedure under acidic conditions: The same general procedure as for neutral conditions was followed except freshly distilled TFA (19 μ L, 0.25 mmol) was also added to the Schlenk tube. For each time point, the Schlenk's side arm was purged via three vacuum/nitrogen cycles, opened while still being kept under a positive atmosphere of nitrogen, and a small aliquot taken with a needle (previously purged with nitrogen). The aliquot was then diluted in DCM, quenched with K₂CO₃, filtered and analyzed by gas chromatography. The yield of product was determined versus naphthalene as the internal standard.

Kinetic isotope effects. Obtained values for rate constants and its use in the calculation of kinetic isotope effects are displayed below.

Figure S4. Computed kinetic isotope effects under neutral conditions.

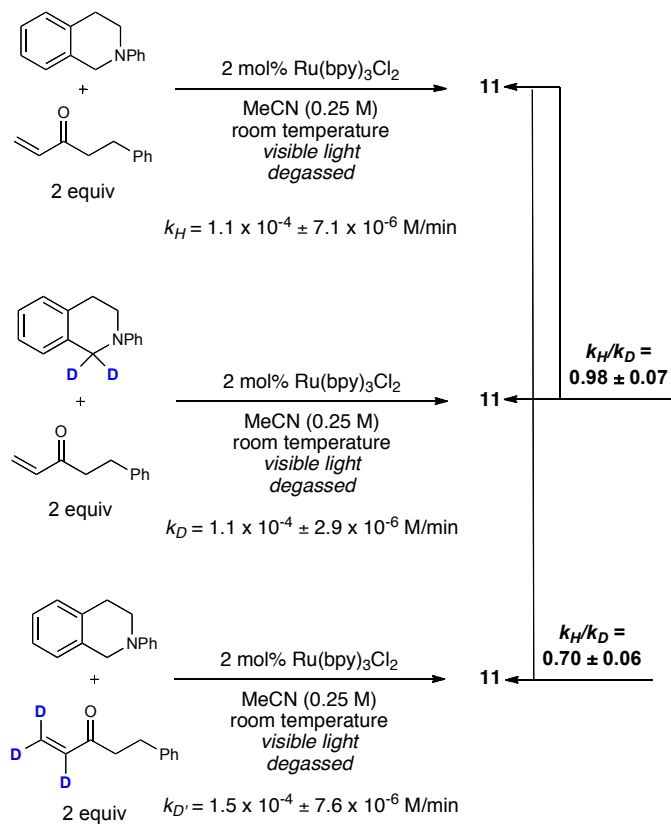
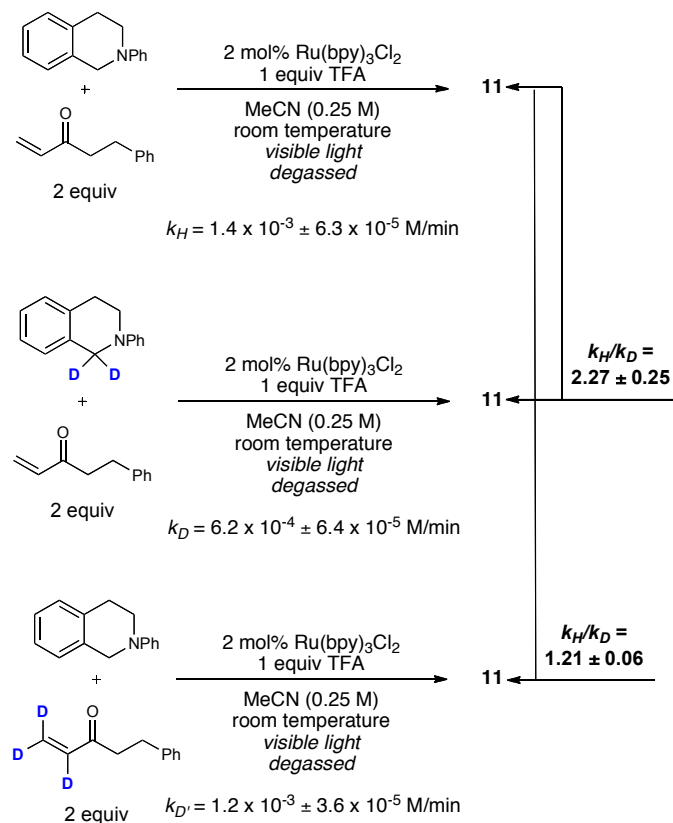


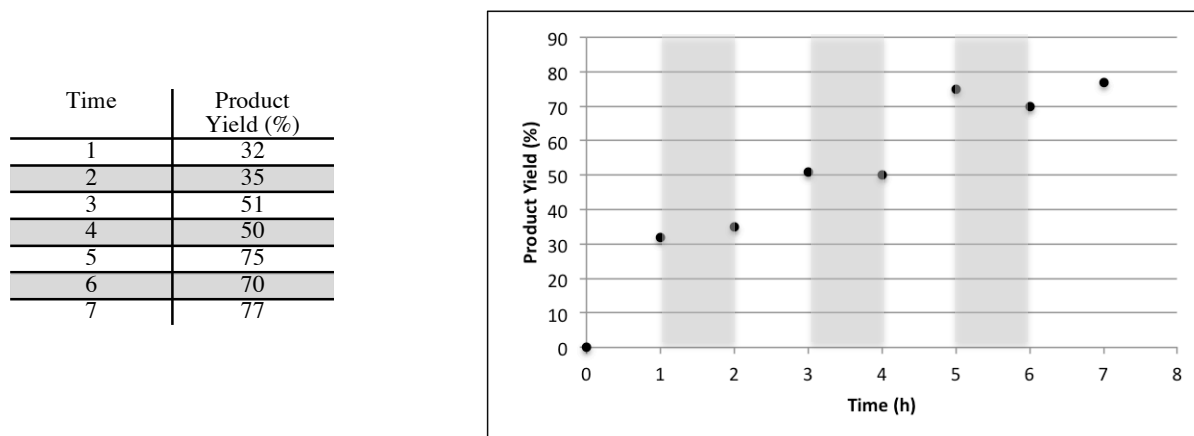
Figure S5. Computed kinetic isotope effects under acidic conditions.



5. Confirmation of Dependence on Light.

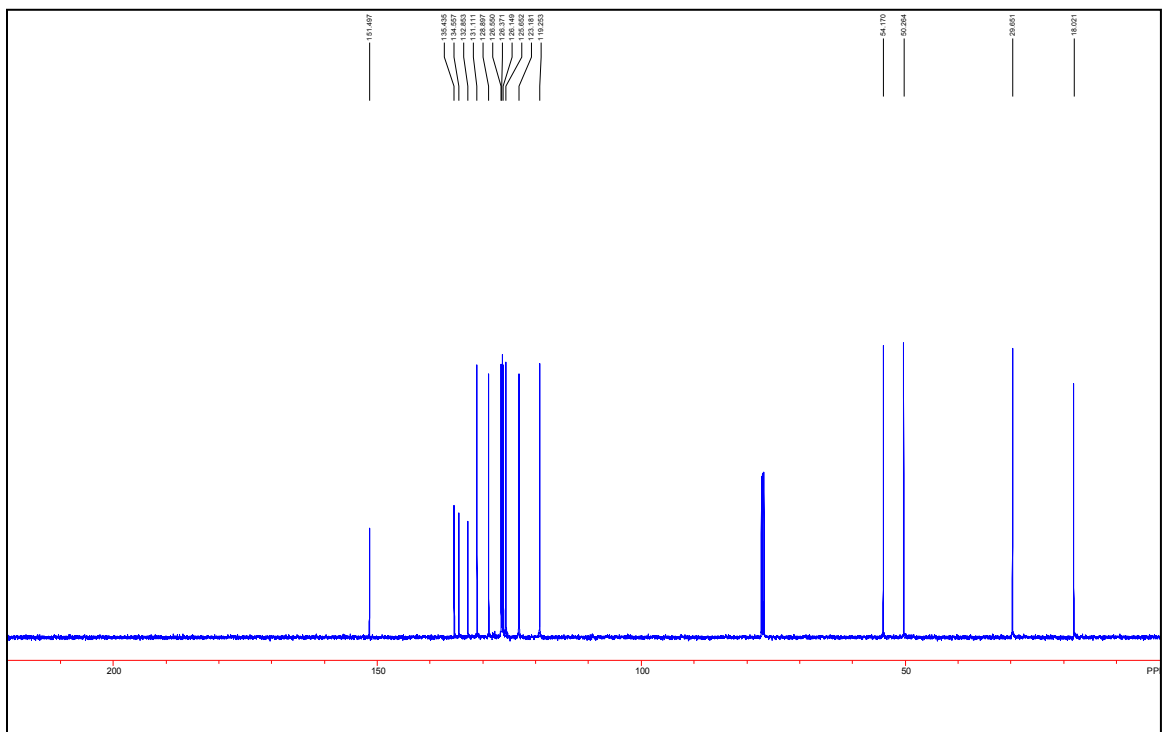
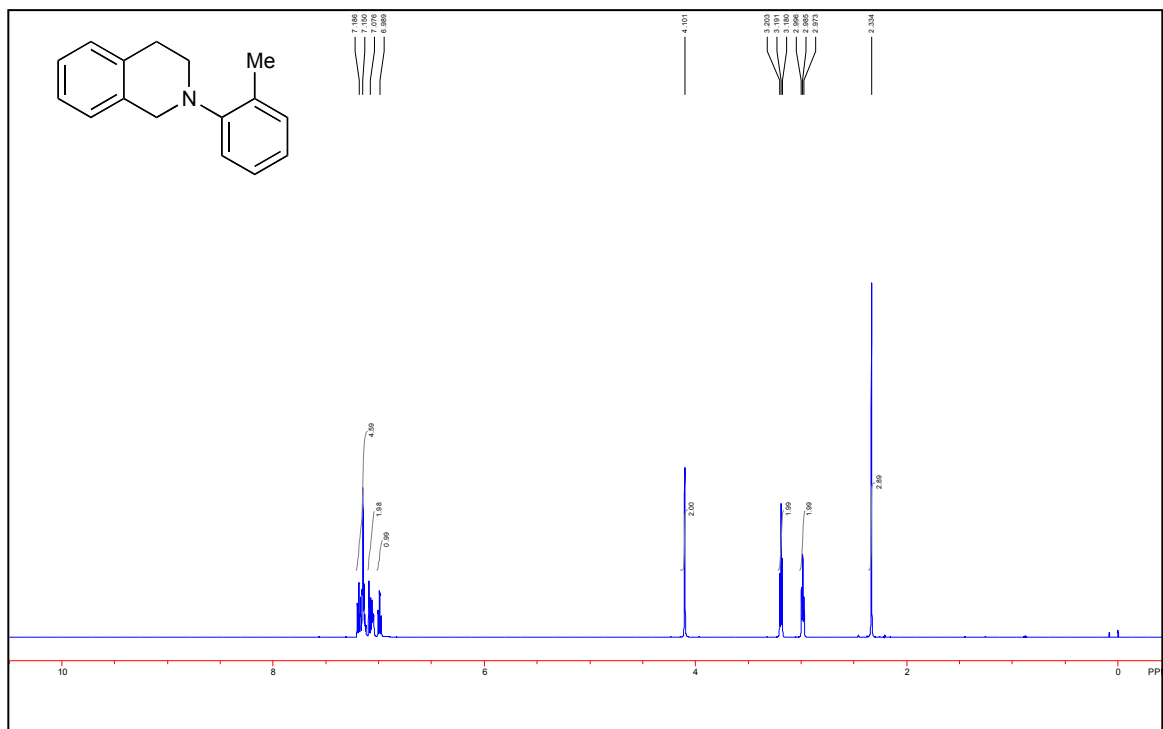
The effect of light on the reaction was evaluated by performing an “on-off” switching light experiment. A dry J. Young valve NMR tube was charged with **5** (1 equiv), **6** (4 equiv), Ru(bpy)₃Cl₂•H₂O (0.02 equiv), TFA (1 equiv), acetonitrile (0.25 M) and phenyltrimethylsilane as an internal standard and degassed using three freeze/pump/thaw cycles under nitrogen in the dark. The homogeneous reaction was irradiated with a 23 W (1280 lumen) compact fluorescent lamp at a distance of 30 cm. The light was turned off and the tube was completely covered with aluminum foil during the following hour increments: 1-2, 3-4, 5-6. The yield of product was determined by ¹H NMR analysis of the reaction mixture.

Figure S6. Light Dependency Experiment

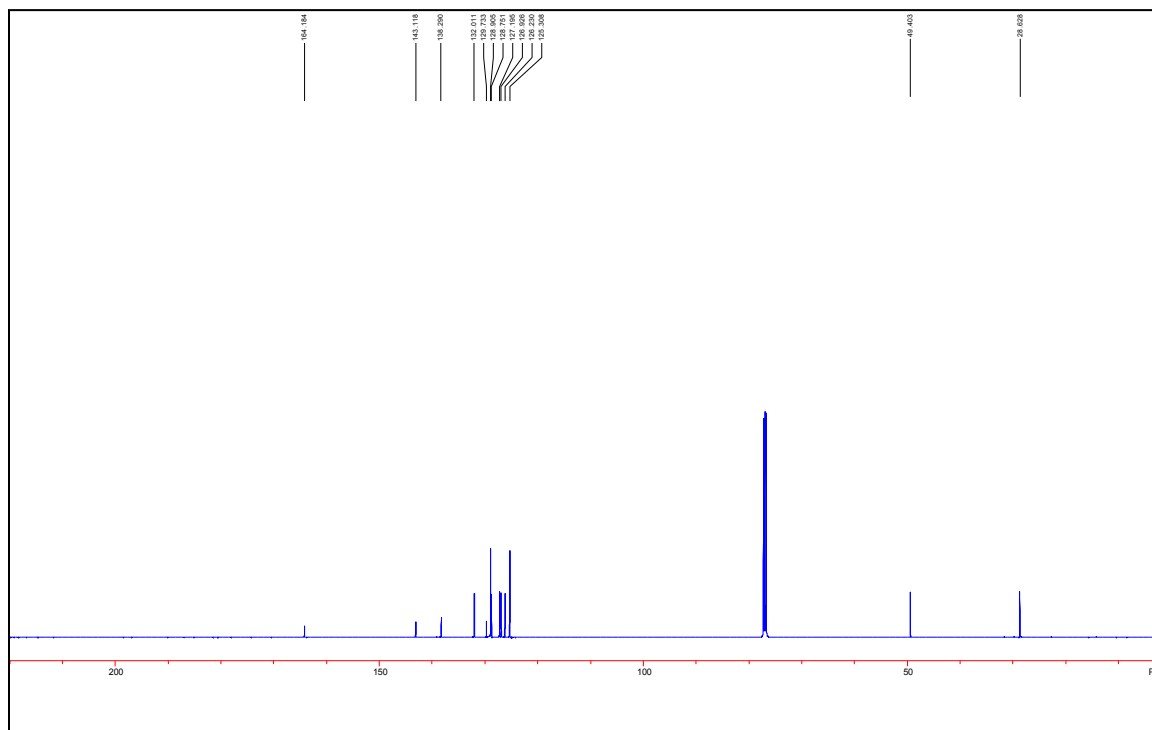
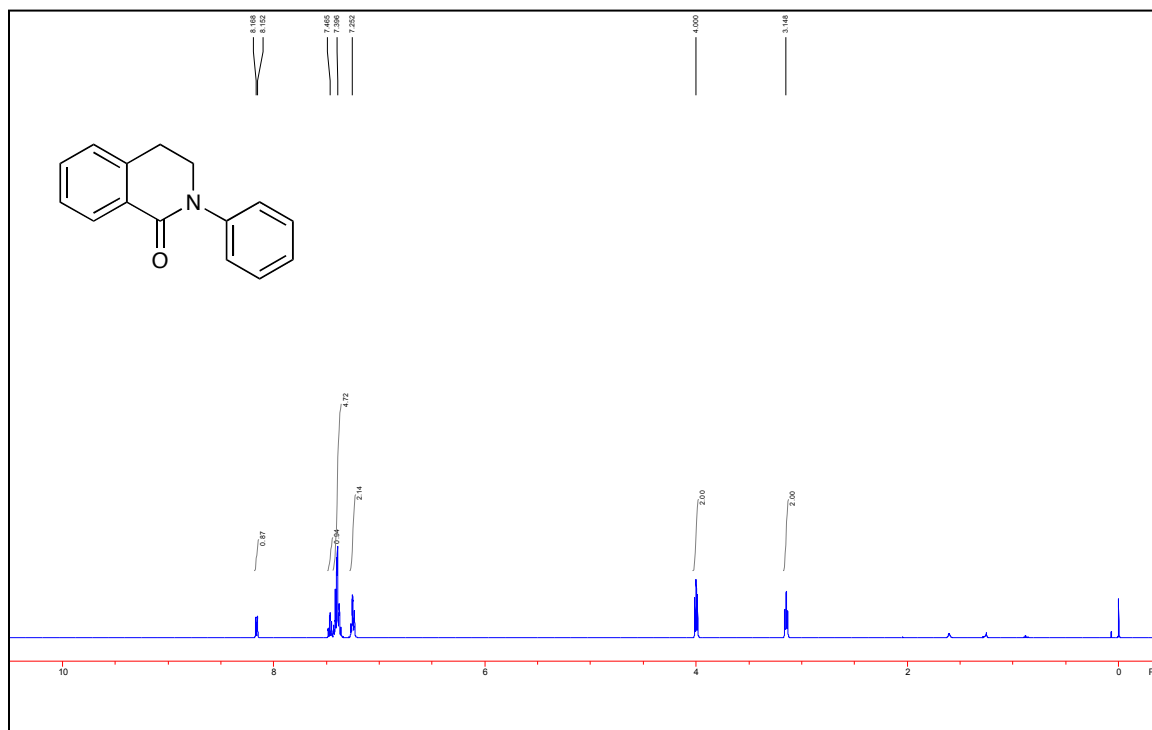


6. NMR Spectra.

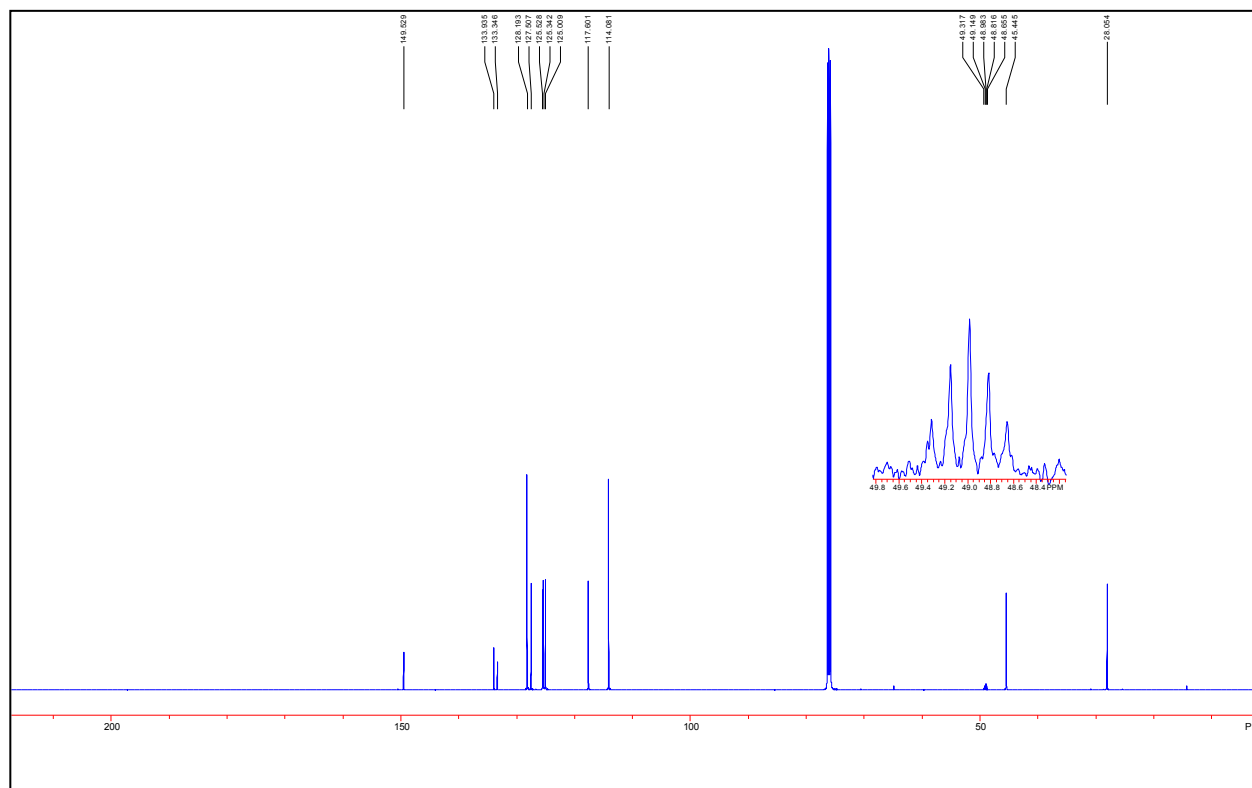
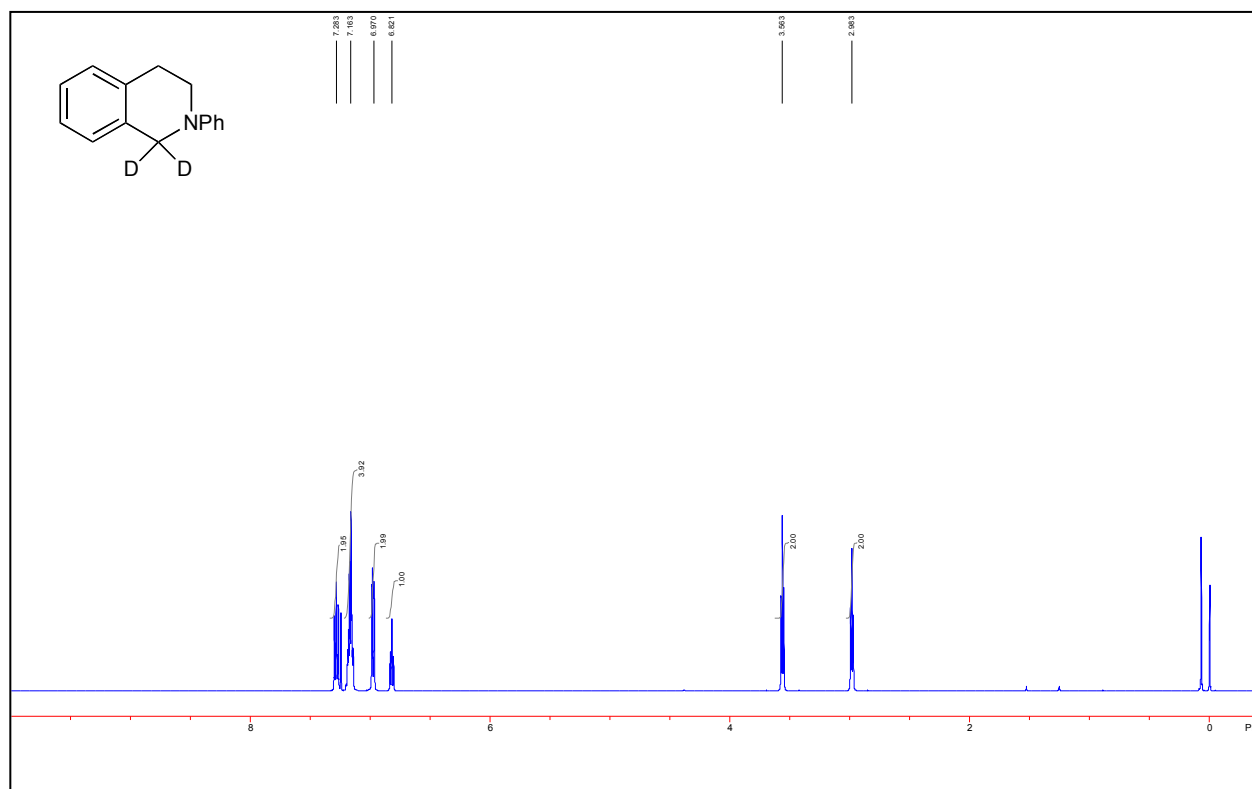
2-(*o*-tolyl)-1,2,3,4-tetrahydroisoquinoline (Table 2, entry 5).



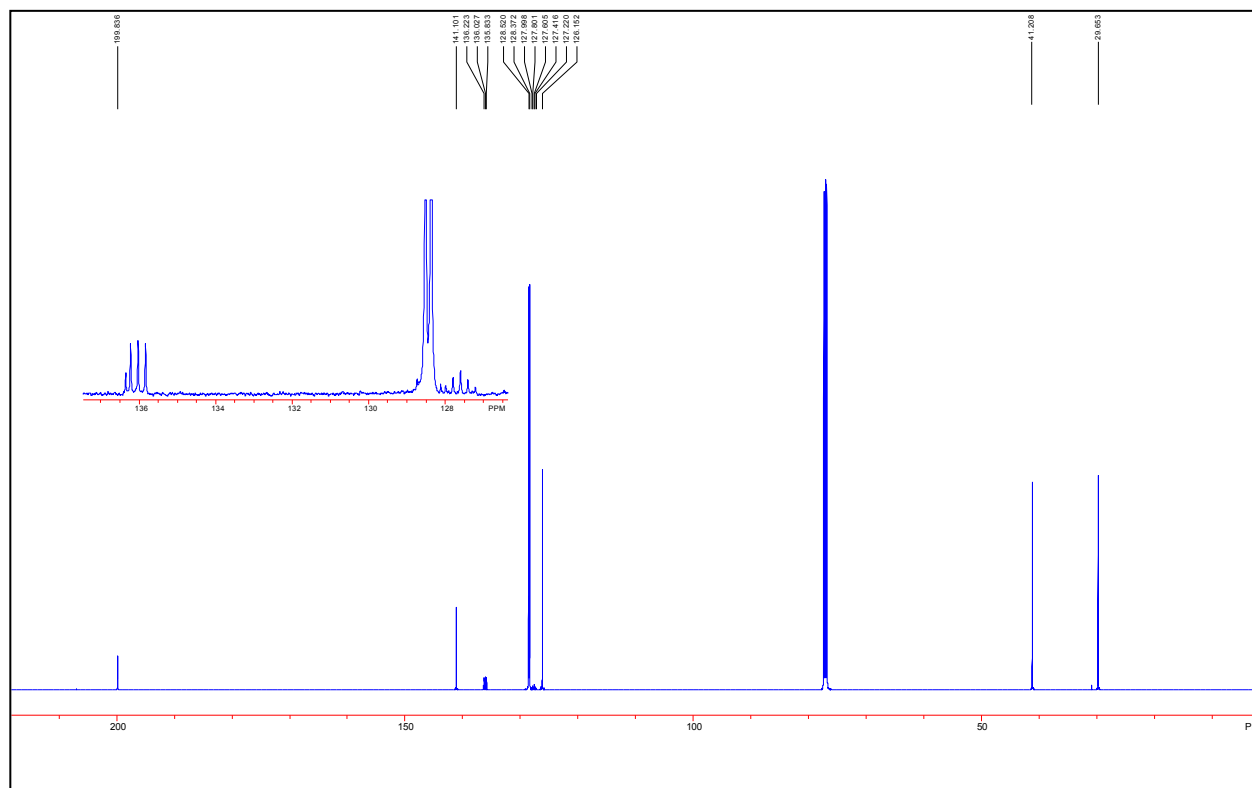
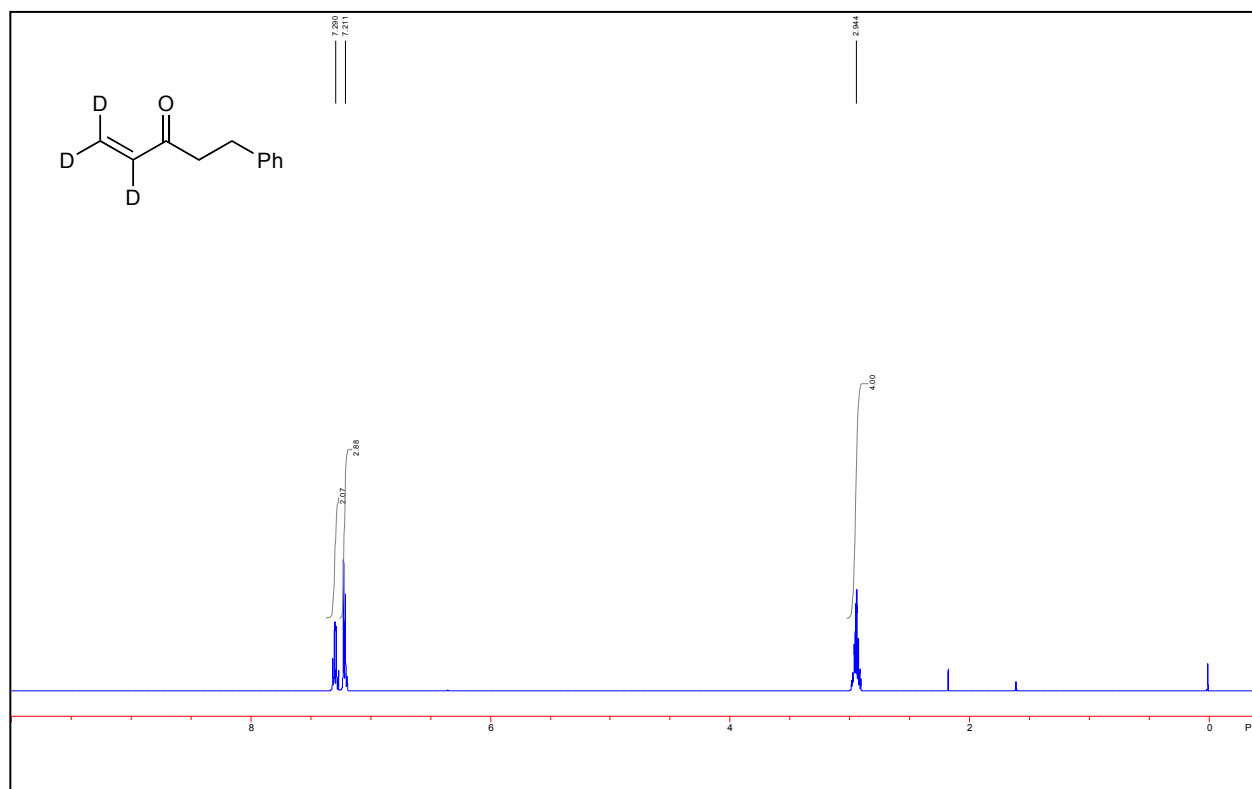
2-phenyl-3,4-dihydroisoquinolin-1(2H)-one.



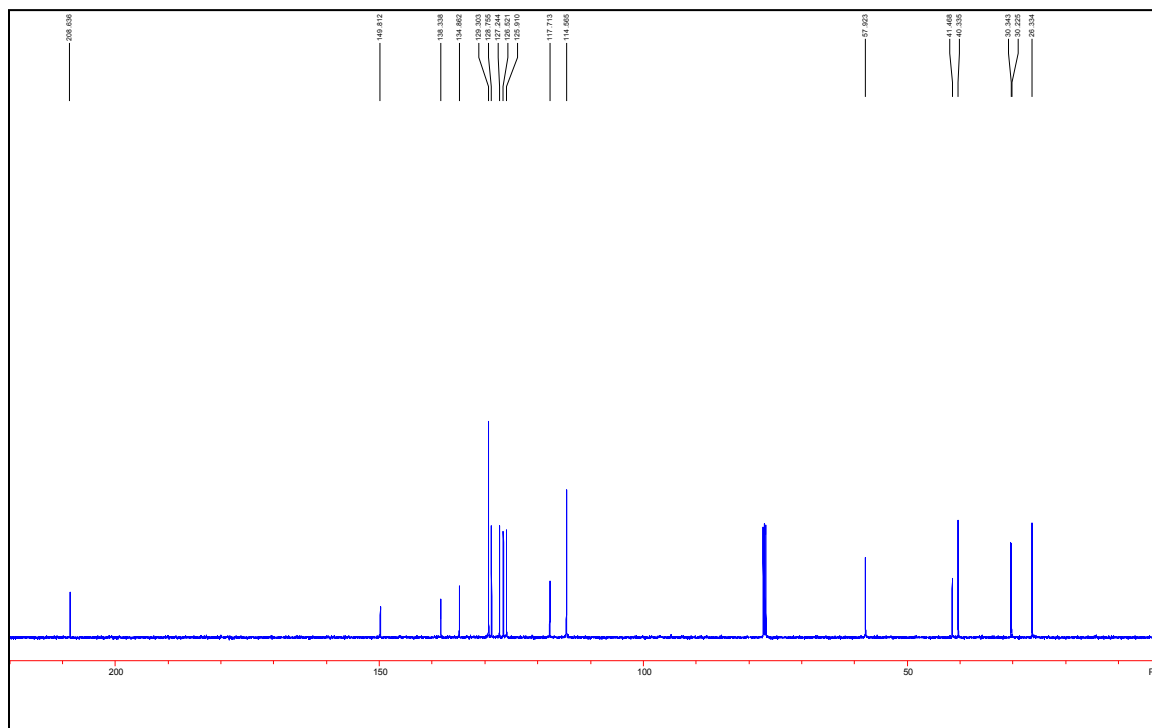
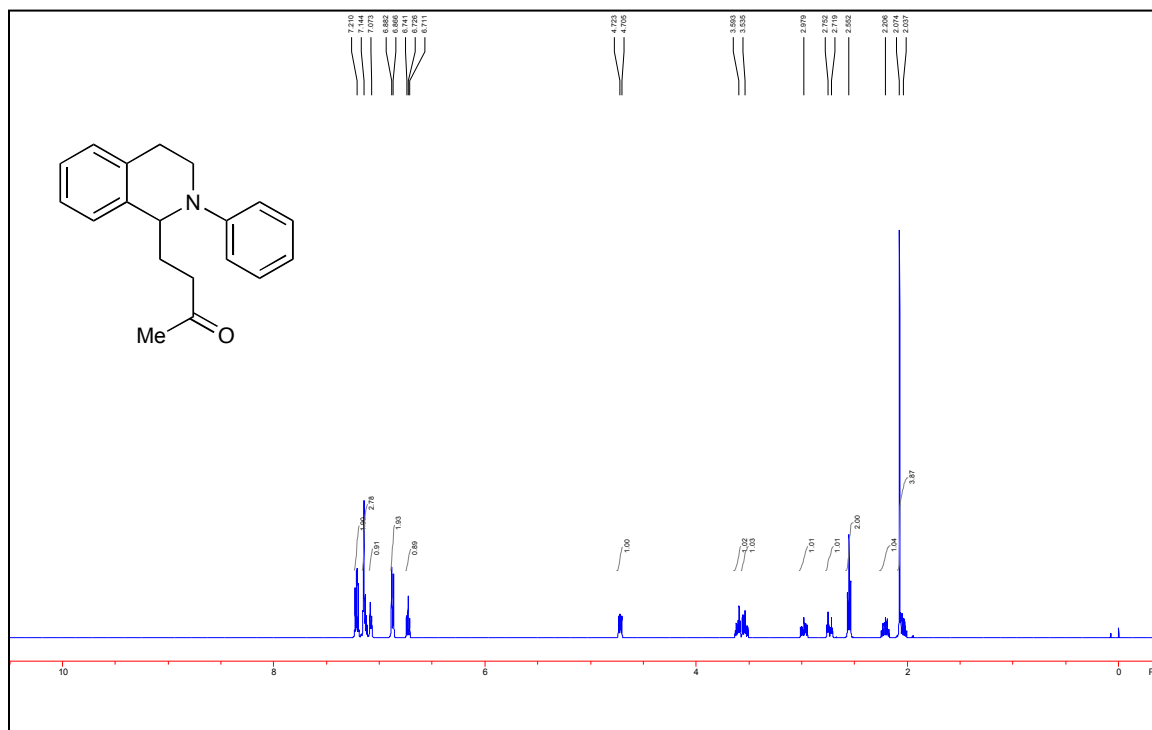
1,1-(²H₂)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (5-d₂).



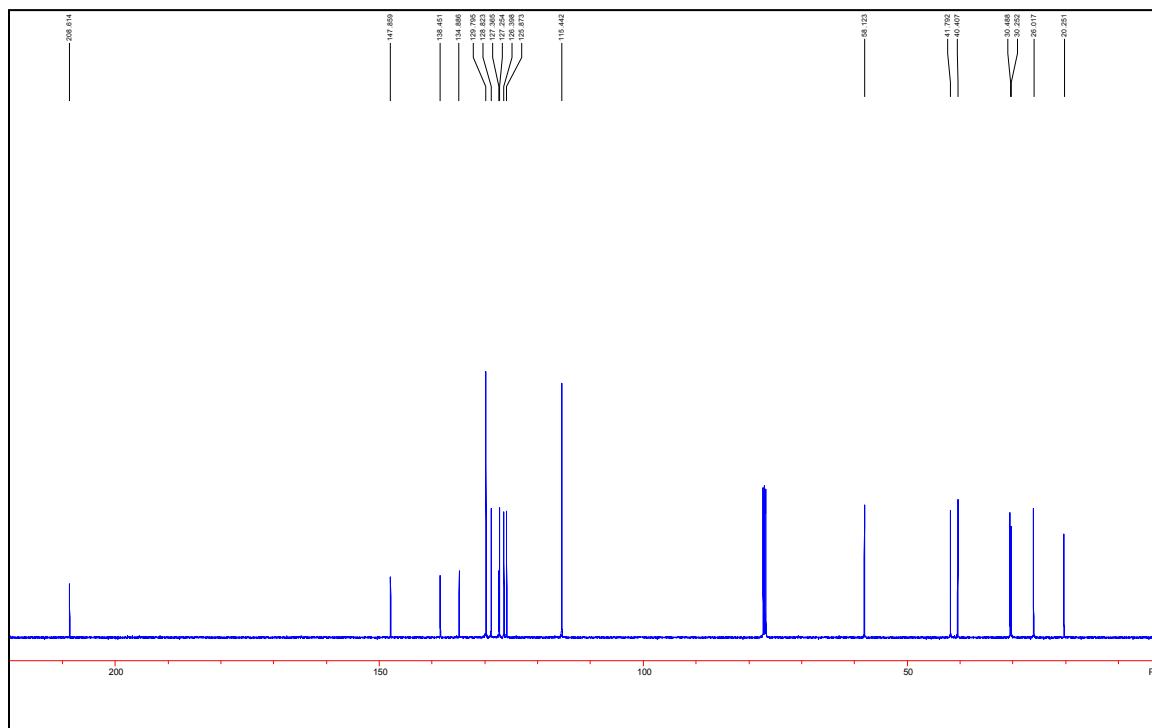
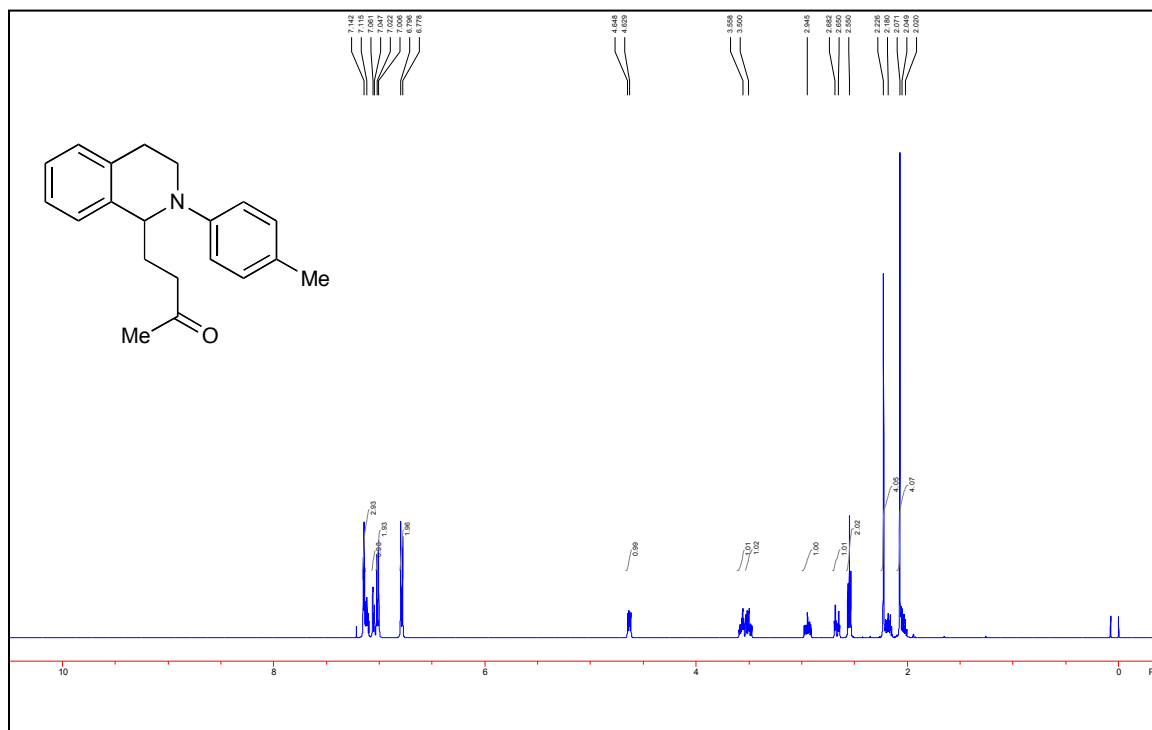
1,1,2-trideutero-5-phenylpent-1-en-3-one. (10-d₃)



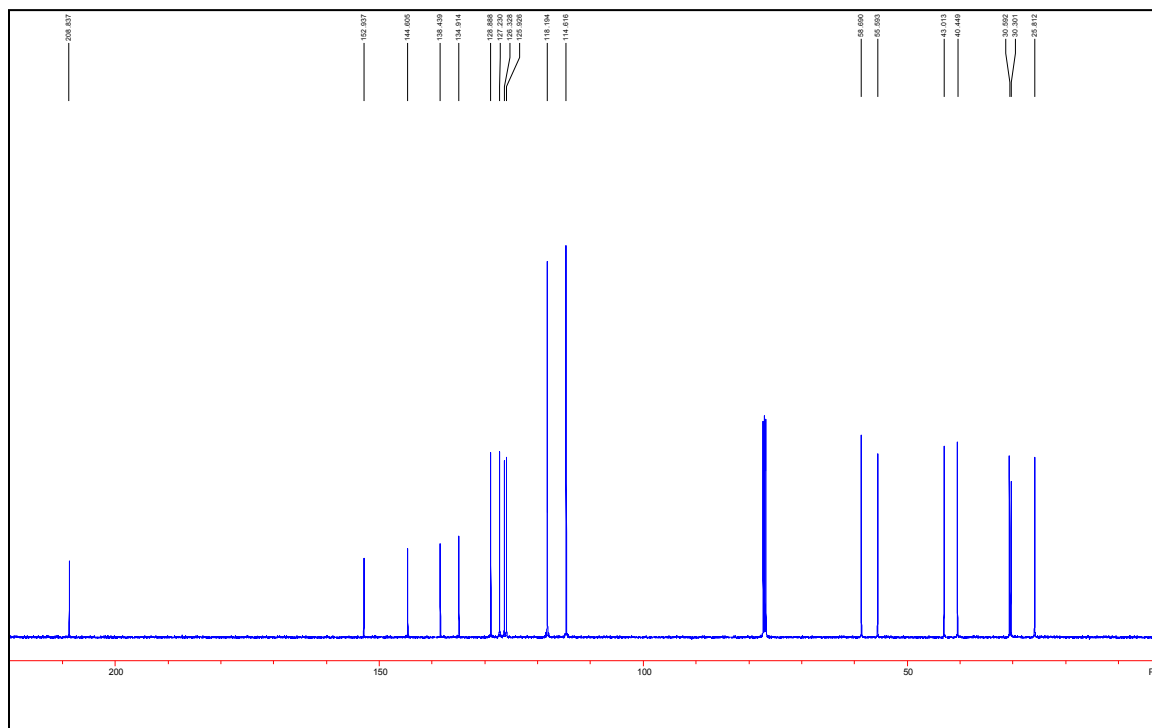
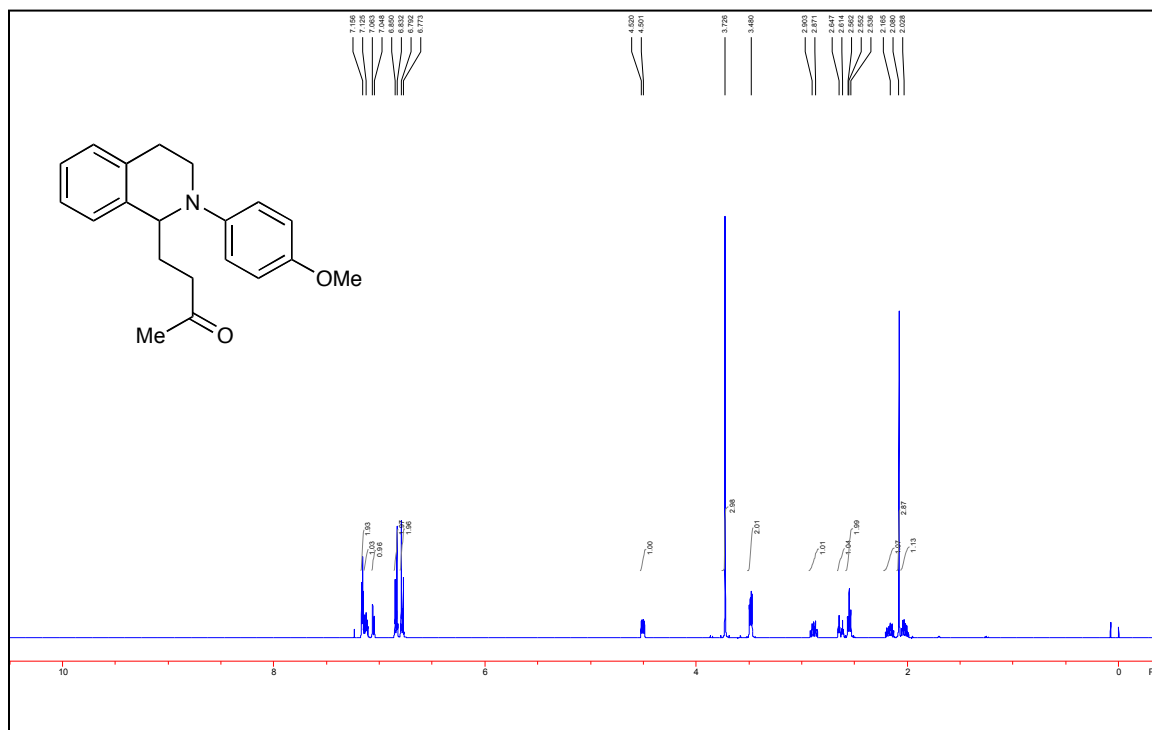
4-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (Table 2, entry 1).



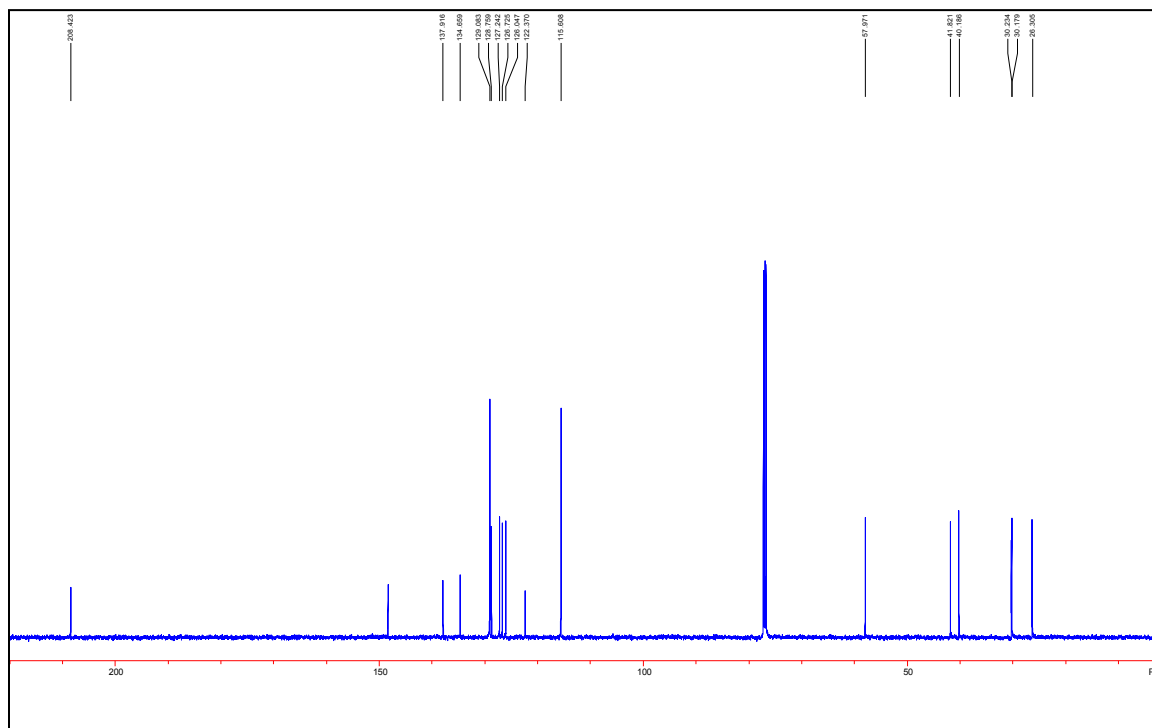
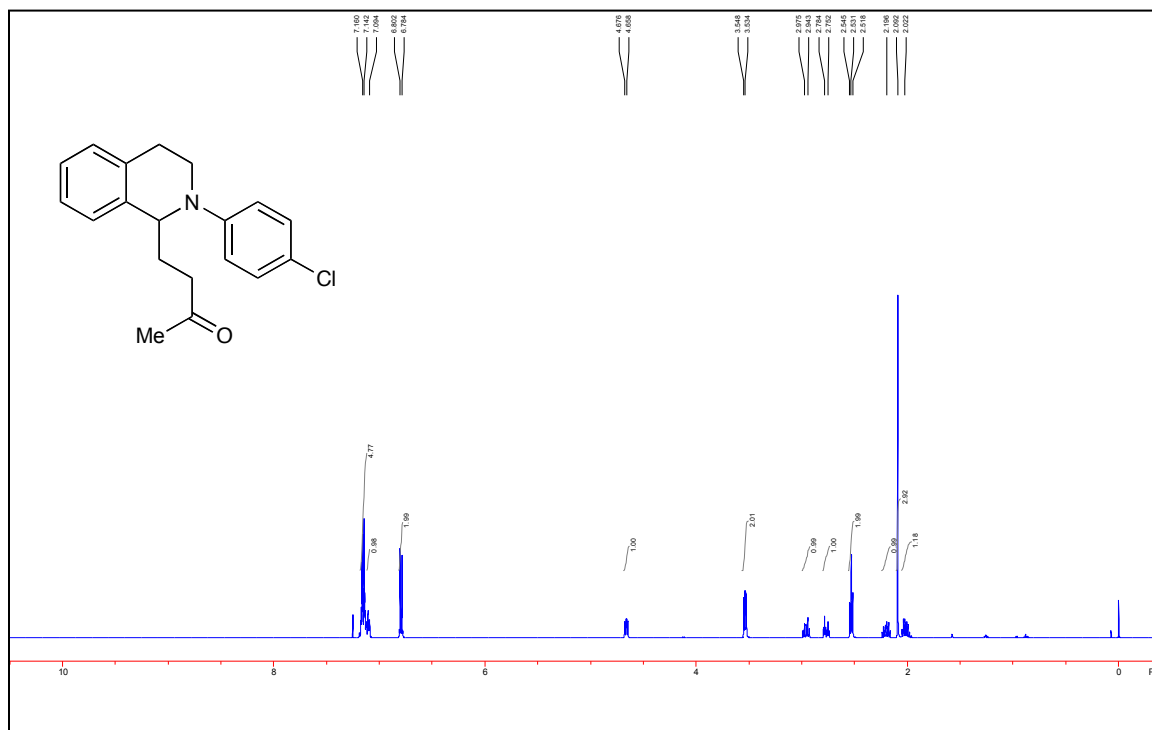
4-(2-(p-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (Table 2, entry 2).



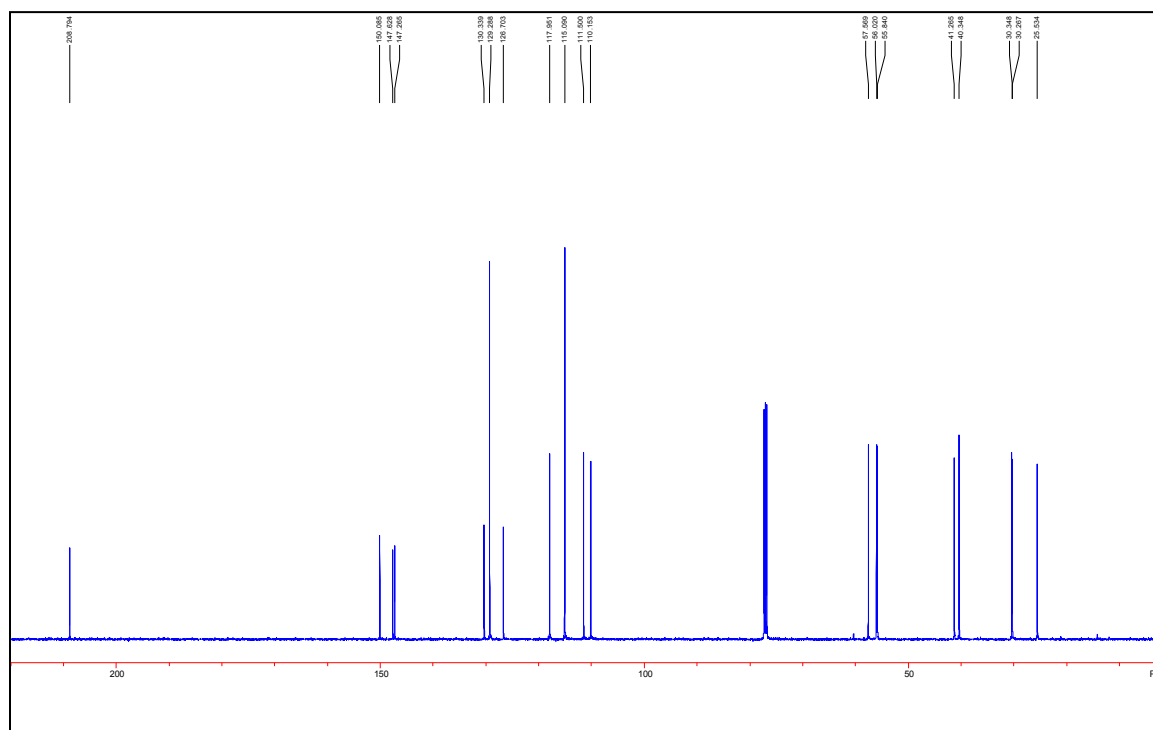
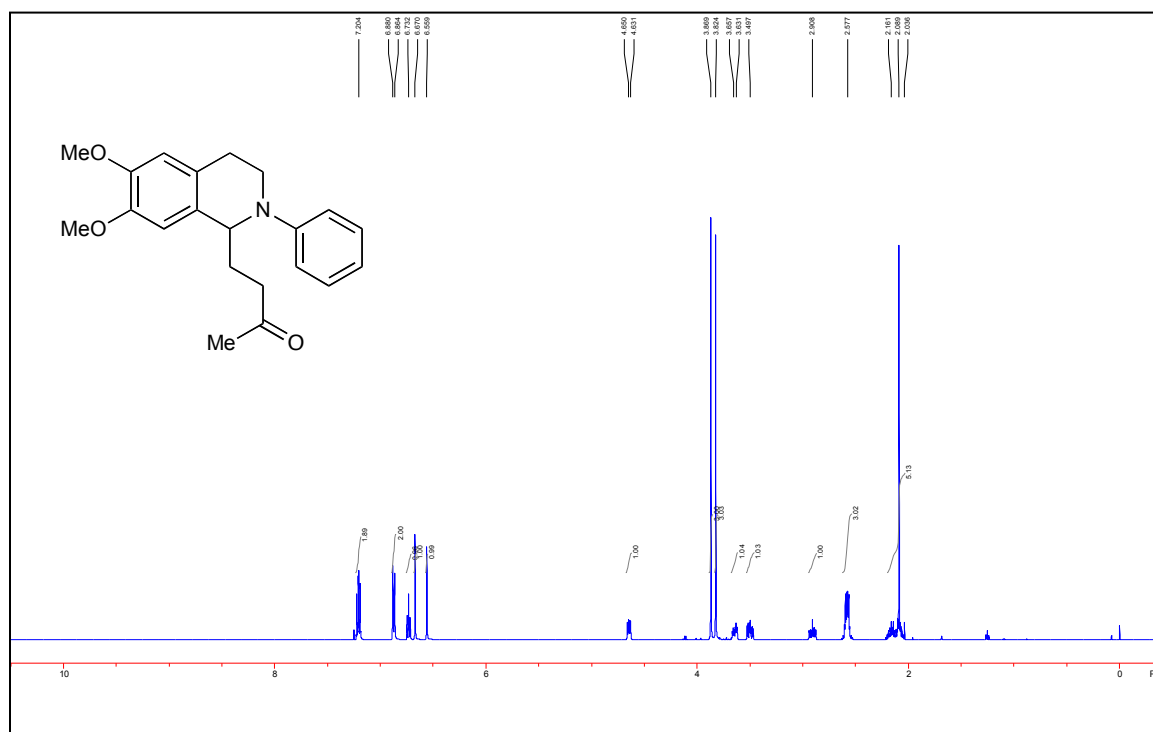
4-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (Table 2, entry 3).



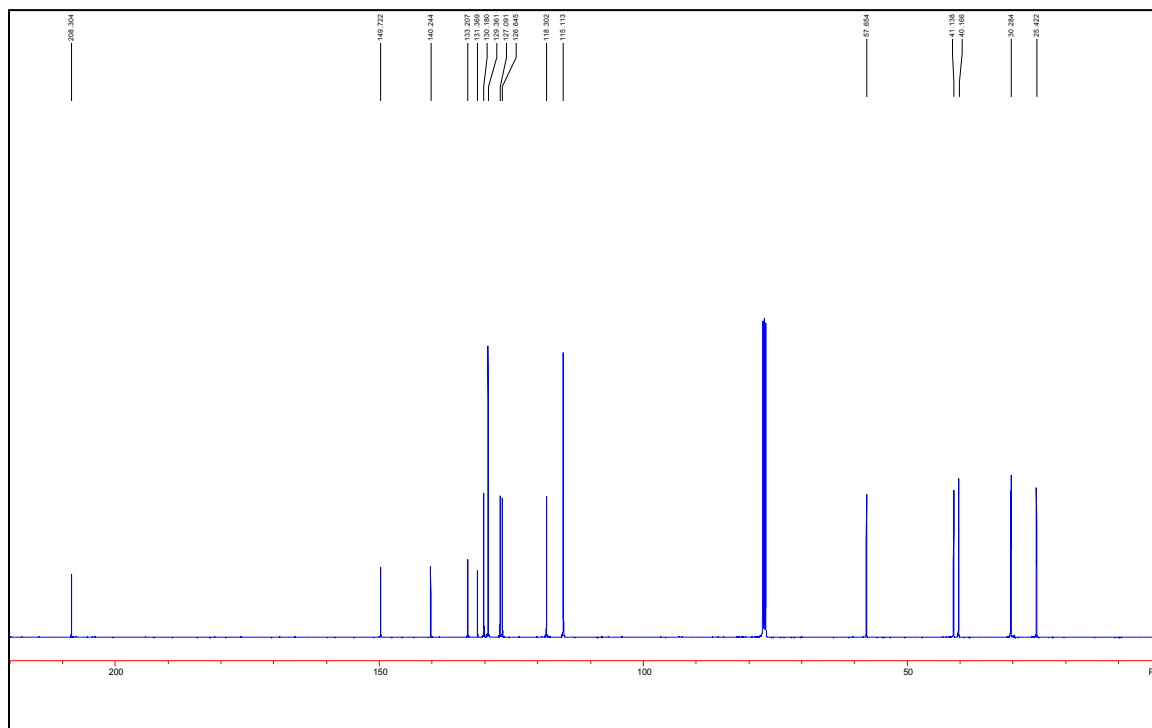
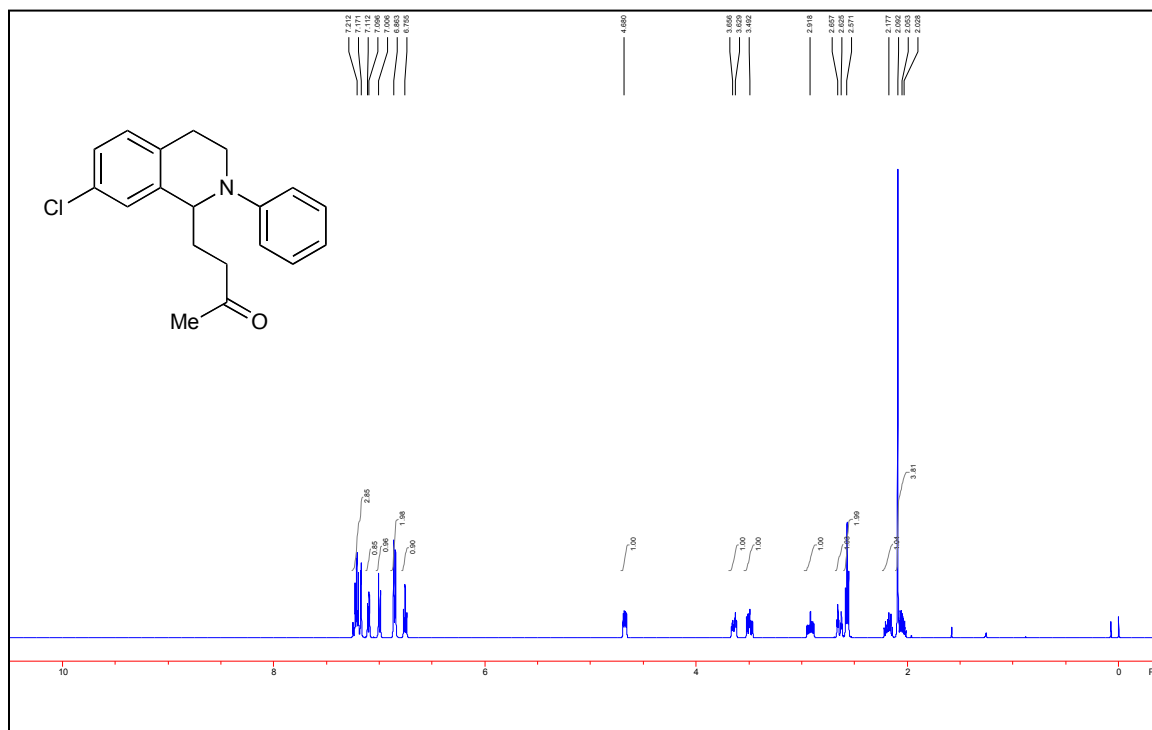
4-(2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (Table 2, entry 4).



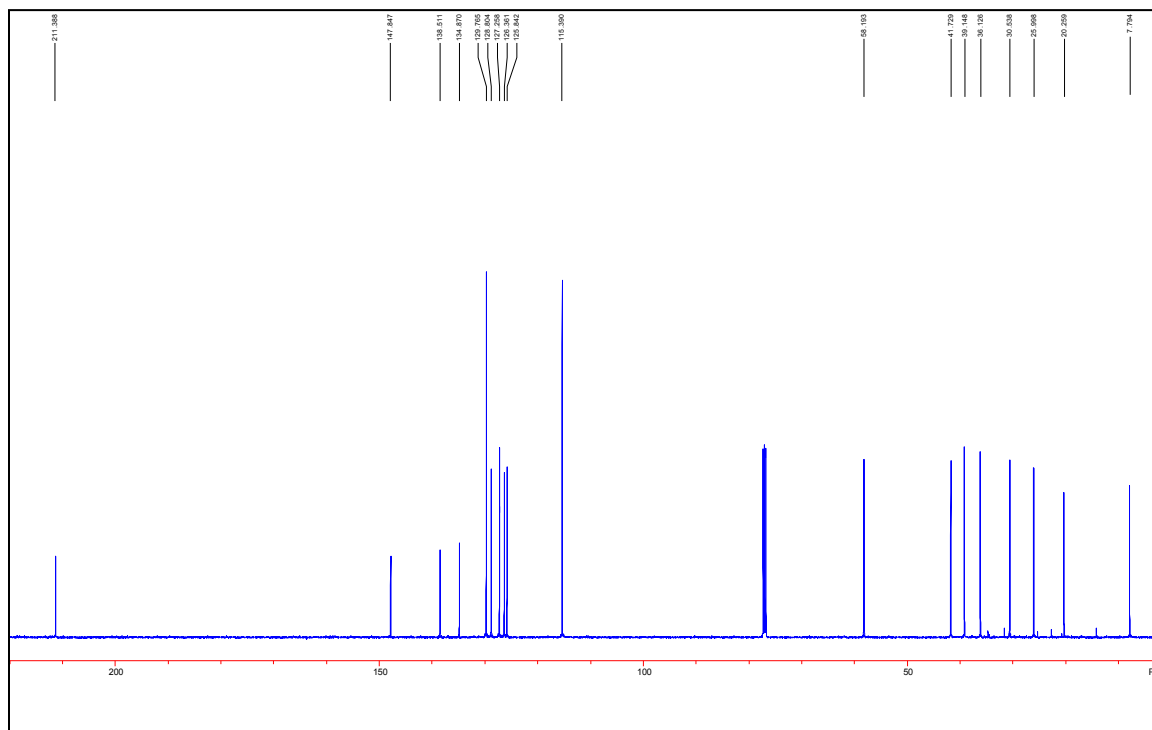
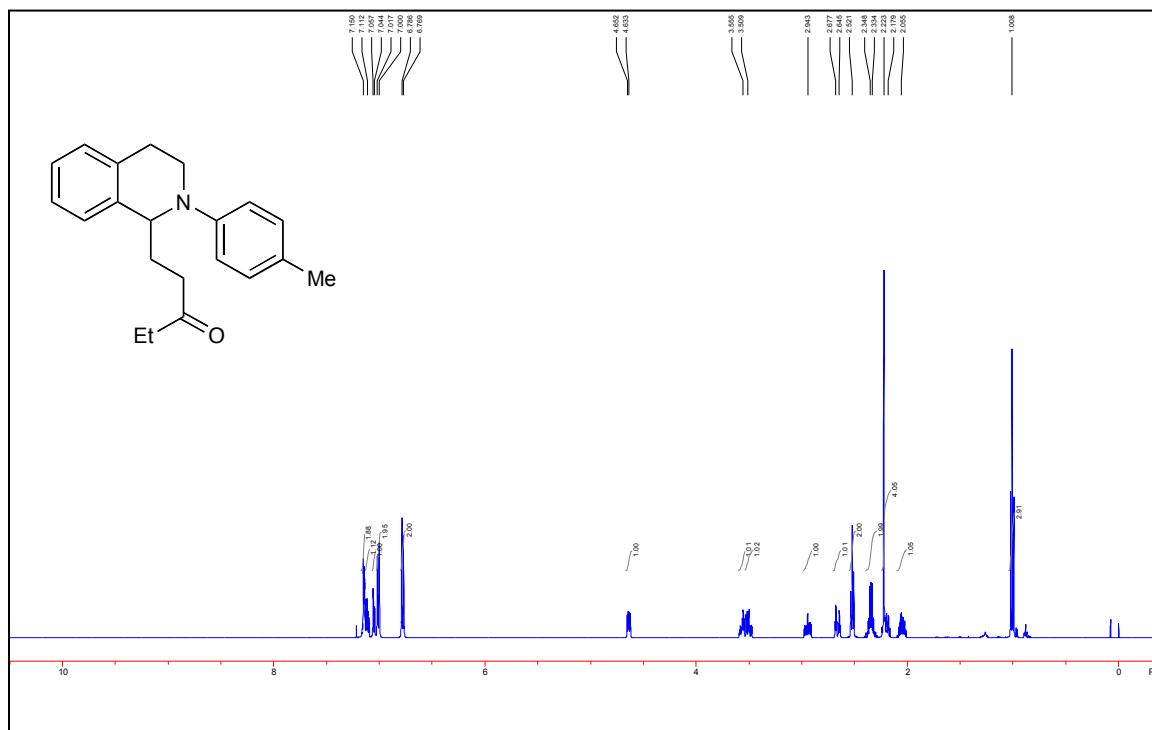
4-(6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (Table 2, entry 6).



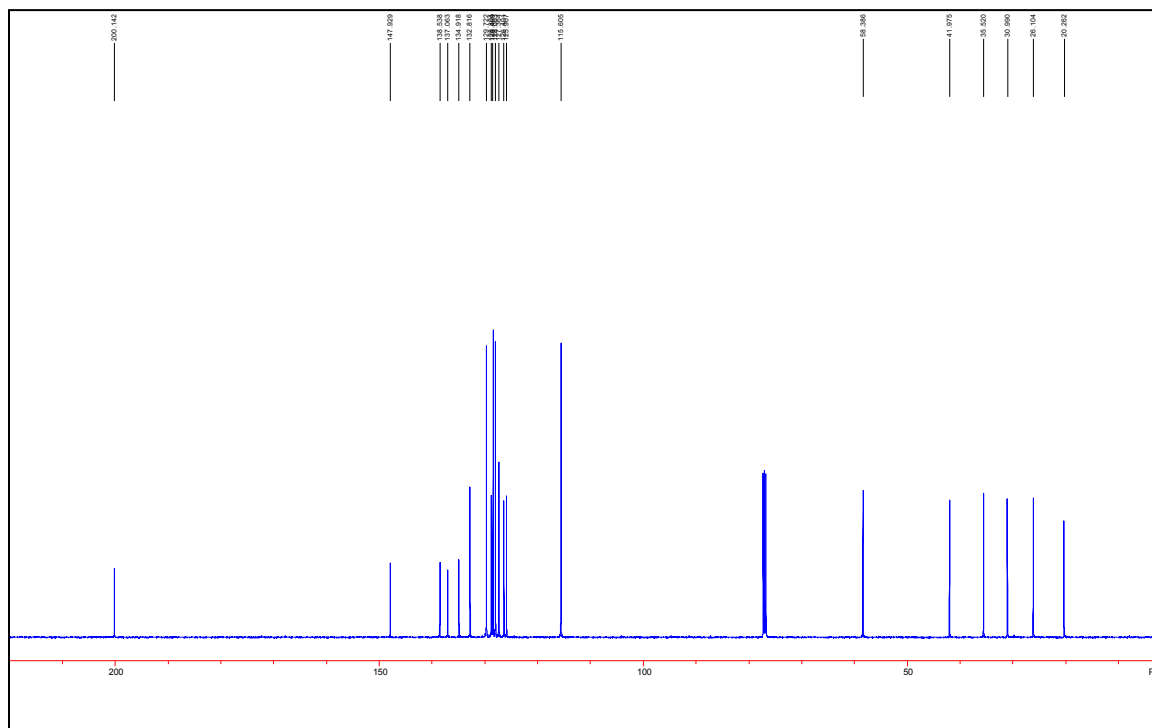
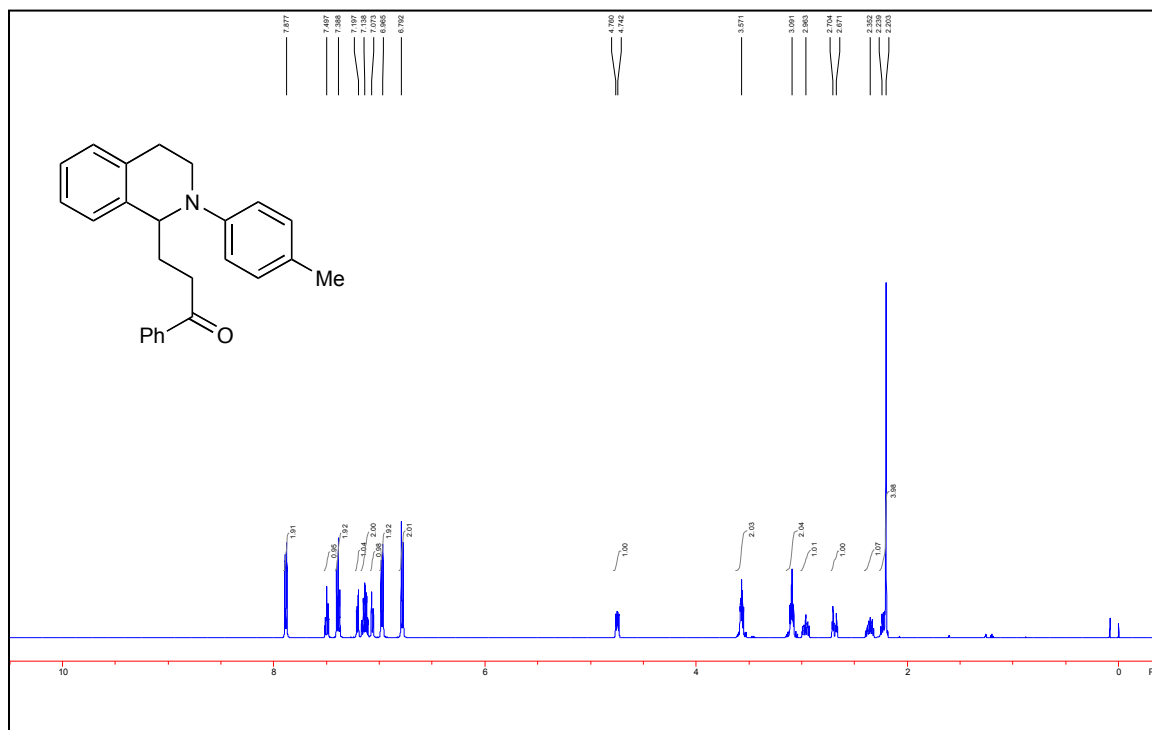
4-(7-chloro-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (Table 2, entry 7).



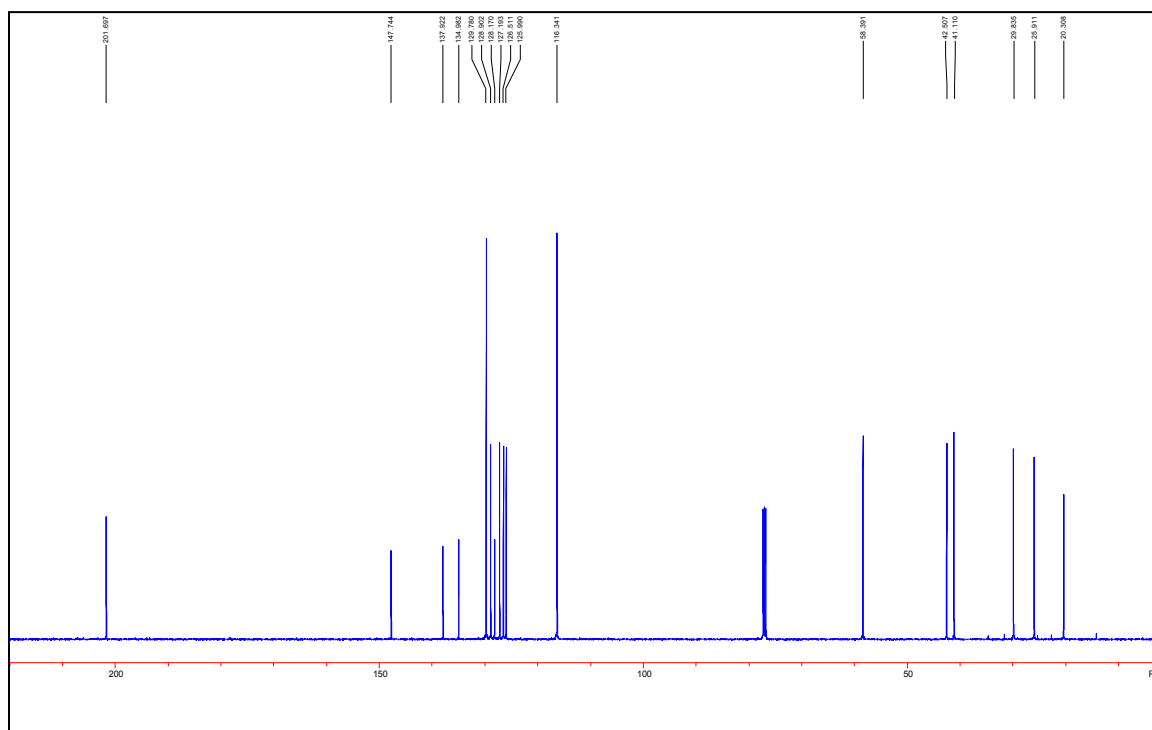
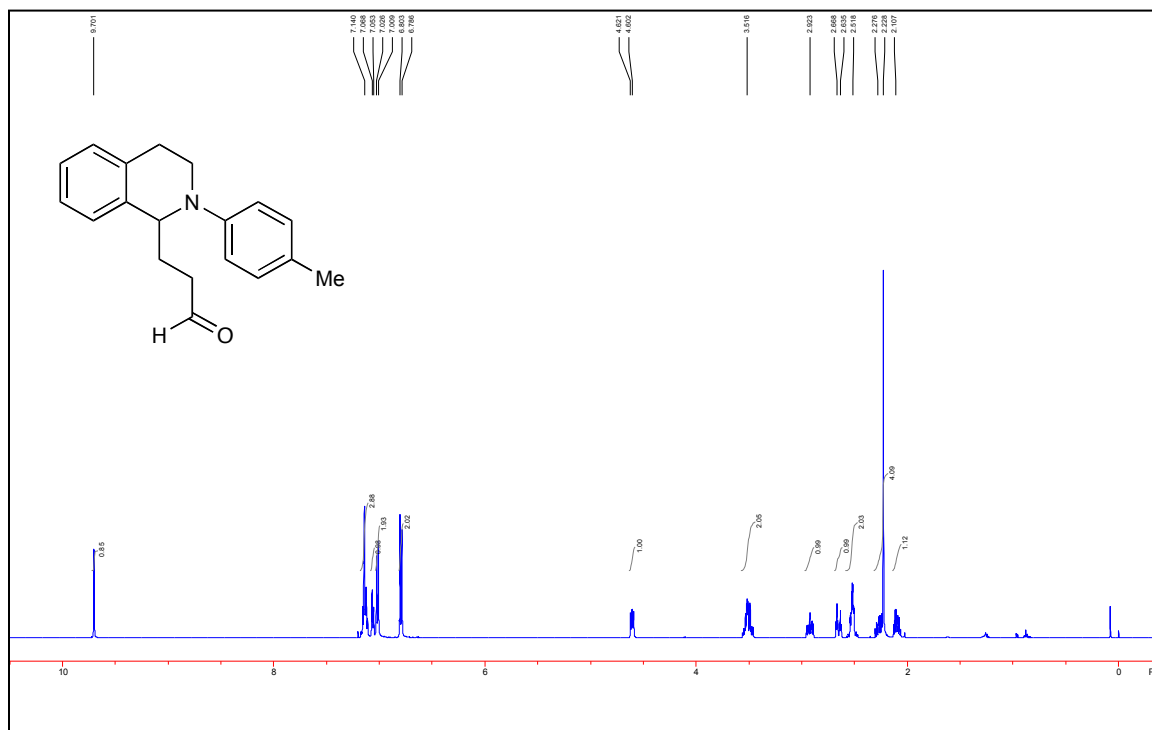
1-(2-(p-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)pentan-3-one (Table 3, entry 1).



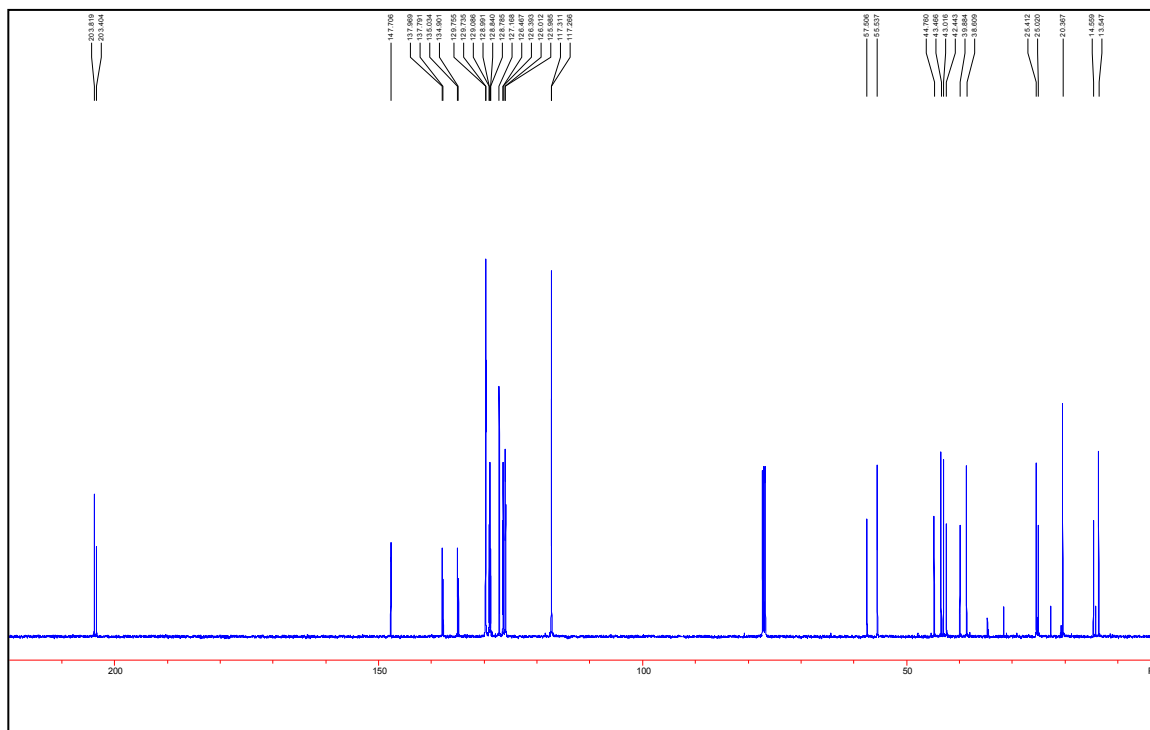
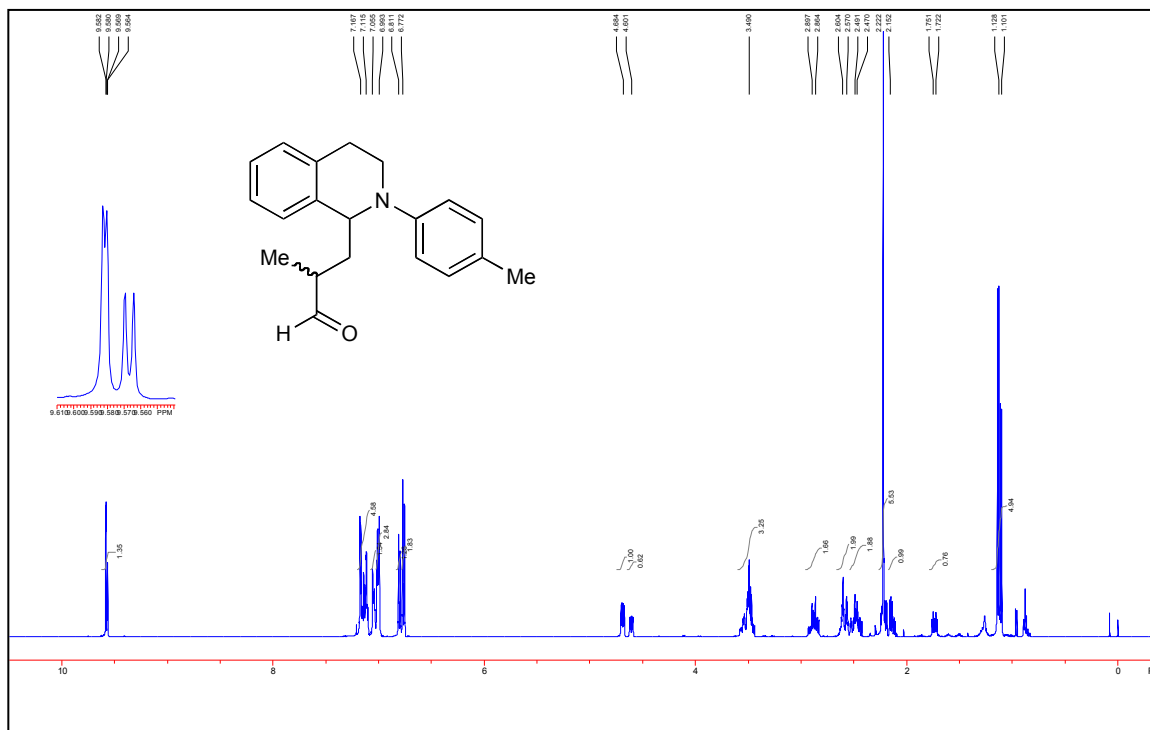
1-phenyl-3-(2-(p-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-1-one (Table 3, entry 2).



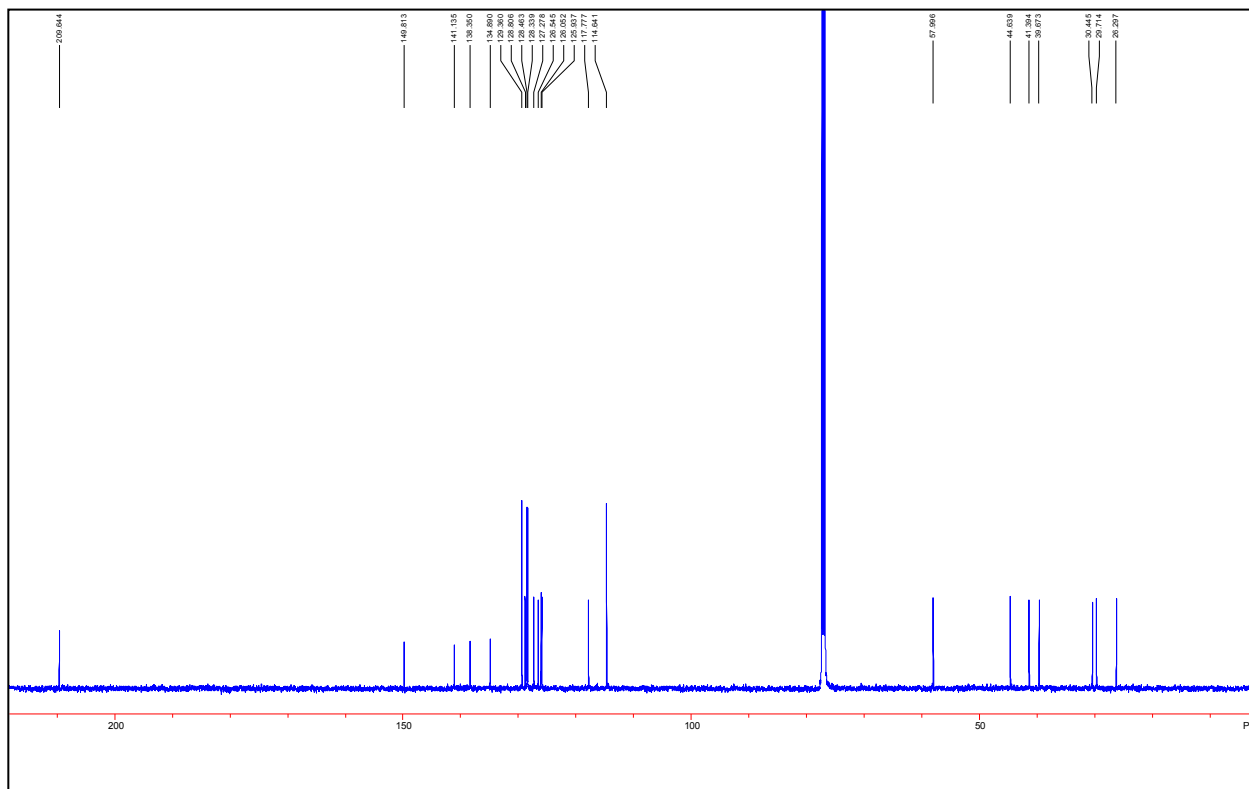
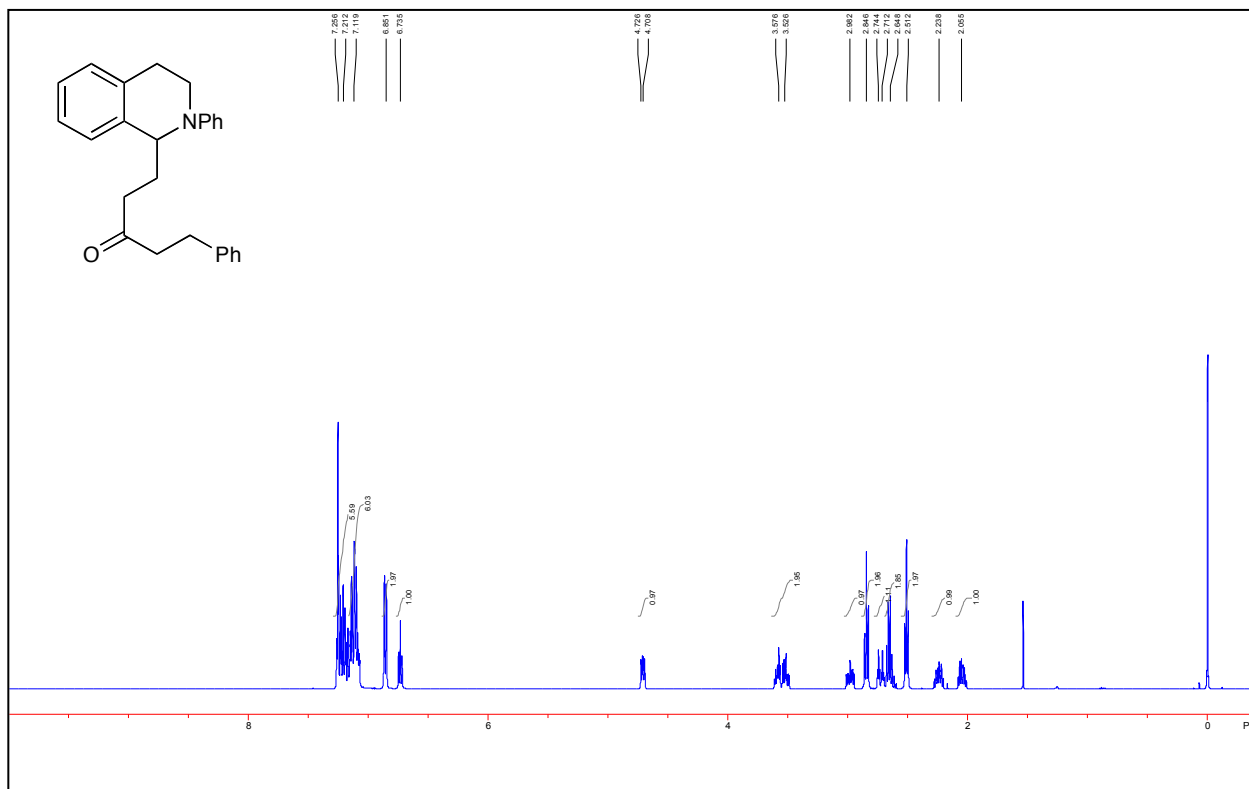
3-(2-(p-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propanal (Table 3, entry 4).



2-methyl-3-(2-(p-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)pentanal (Table 3, entry 5).



1-phenyl-5-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)pentan-3-one (11).



7. References

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- ⁶ Ma, T.; Fu, X.; Kee, C.W.; Zong, L.; Pan, Y.; Huang, K.; Tan, C. H. *J. Am. Chem. Soc.* **2011**, *133*, 2828–2831.