

Supplementary Material

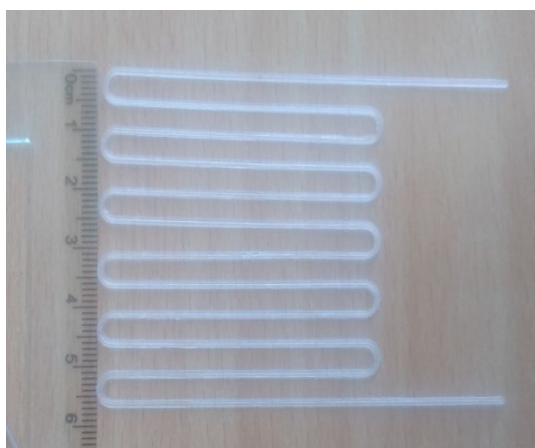
Visible Light Promoted Photoredox C(sp³)-H Bond Functionalization of Tetrahydroisoquinolines in Flow

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General Remarks:

All reactions were monitored by thin-layer chromatography using Merck 60 F254 precoated silica gel plates (0.25 mm thickness). Preparative thin layer chromatography was performed using Merck 60 F254 silica gel purchased from Merck KGA. Column chromatography was carried out on silica gel (12-26, ICN Biomedicals) using petrol ether/ethyl acetate as eluents. ¹H-NMR and ¹³C-NMR spectra were measured on a Bruker Ultrashield Advance III spectrometer (¹H at 500 MHz, ¹³C at 125 MHz) and Varian 400 spectrometer (¹H at 400 MHz, ¹³C at 100 MHz) using CDCl₃ as solvent with TMS as internal standard. Chemical shifts (δ) are given in parts per million (ppm) and coupling constants are given in Hertz (Hz). The proton spectra are reported as follows δ/ppm (multiplicity, coupling constant J/Hz, number of protons). High-resolution mass spectral analyses (HRMS) were carried out using Bruker ESI-TOF MS. IR spectra were measured on a PerkinElmer FT-IR 1725X spectrophotometer using ATR technique. The peak intensities are defined as very strong (vs), strong (s), middle (m) or weak (w).

For PDMS microreactor fabrication we used SYLGARD silicone elastomer kit 184 obtained by Dow Corning Corporation. This is a two-part liquid component kit consisting of base and curing agents. Microchannels are designed with 3-D printer Wanhao Duplicator i3 Mini using transparent ABS (1,75mm) as a filament (Fig.S1.a). SYLGARD Components are well mixed 10 minutes in weight mix ratio 10:1 (base: curing agent). During mixing, air bubbles are formed, which were degassed under a vacuum. One part of PDMS was transferred into a Petri dish and heated in the oven at 60 °C for 20-30 min (Fig.S1.b). ABS printed filament was placed over baked PDMS. Then, the remaining amount of PDMS was poured out over ABS filament (1 mm layer thickness) and left for 48h at room temperature (Fig.S1.c). The PDMS with embedded ABS filament was then removed from a Petri dish and baked for about 10 minutes at 60 °C (Fig.S1.d). To enable free entrance and exit from microreactor, one side of PDMS was cut (Fig.S1.e). The removal of ABS filament from PDMS was achieved by placing the whole system in acetone overnight. The formed microchannels were cleaned from ABS with a syringe and acetone. Finally, the obtained microreactor was left in the oven at 60 °C for 24h to remove acetone completely. Reactors with internal volume of 500 μ L are obtained. Microreactor in operation (Figure S2).



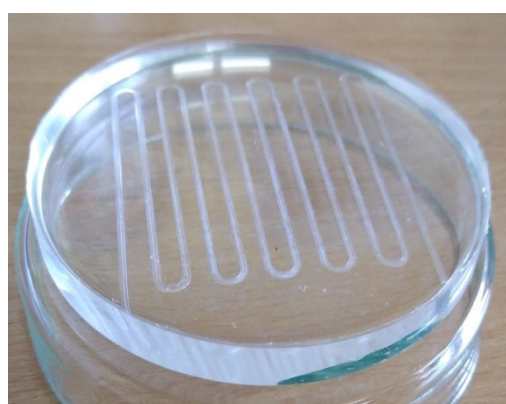
a)



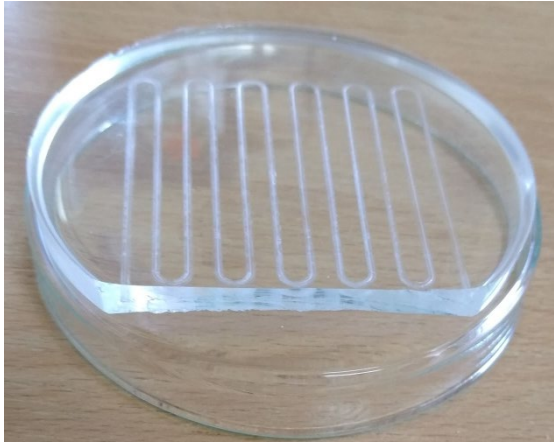
b)



c)



d)



e)

Figure S1. PDMS microreactor fabrication

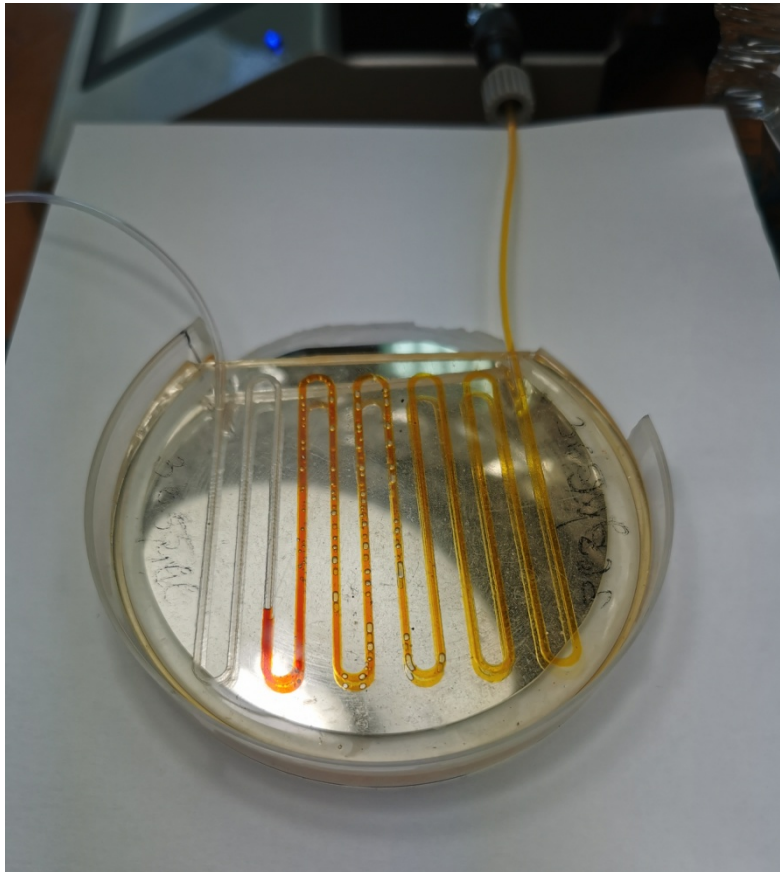


Figure S2. PDMS microreactor in operation. Air bubbles appearing in the microchannel due to the porosity of PDMS, change of colour is evident from light yellow to dark orange as reaction progresses

For fabrication of FEP reactor the FEP tubing is wrapped in figure eights around glass tube so that a total of 100 cm (corresponding to 450 μ L total volume) is used. The tubing is secured in place by 2 plastic joint clips. The coiled tubing is then placed approximately 2 cm from the LED stripes placed inside metal housing. An aluminum mirror is then placed above the coiled tubing to close the metal housing. At the bottom of the housing cooling fan is placed in order to maintain desired room temperature. The photoreactor tubing is connected to the syringe pump by means of a conical adapter (IDEX Health and Science, Part # P-797) which contains the appropriate female nut, ferrule and washer. Figure S3 depicts the assembled reactor.

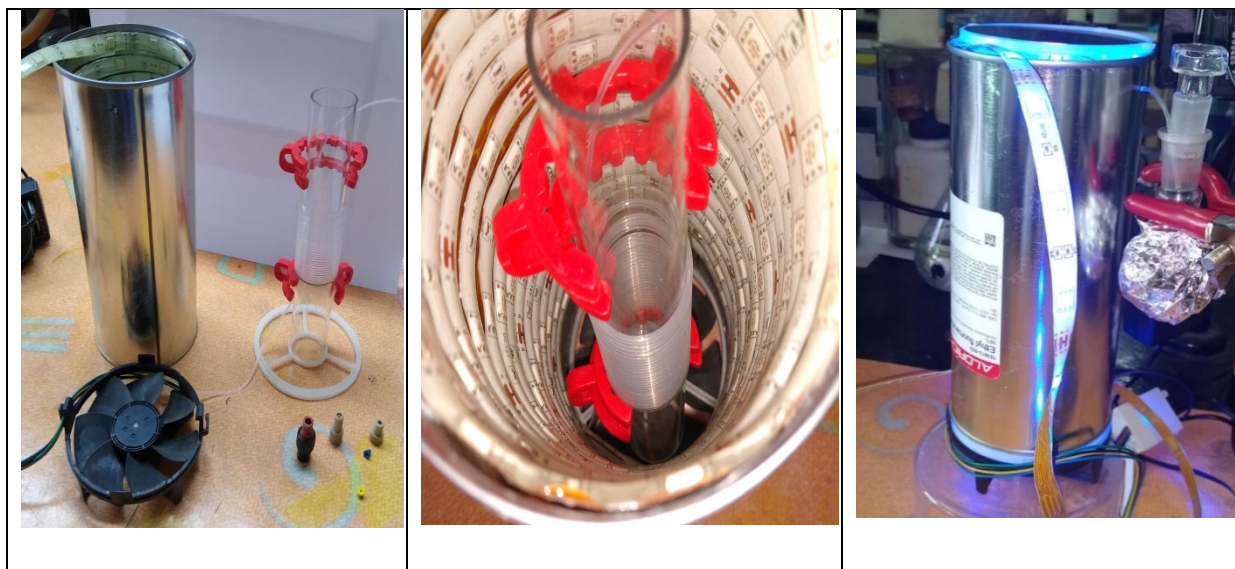


Figure S3. Setup of FEP tube microreactor including cooling fan, led stripes, mirror top and metal housing

For fabrication of silicone/glass microreactor photolithography was used along with wet-etching of pyrex glass and anodic bonding technique. A close up photograph of the assembled photoreactor is shown in Figure S4.

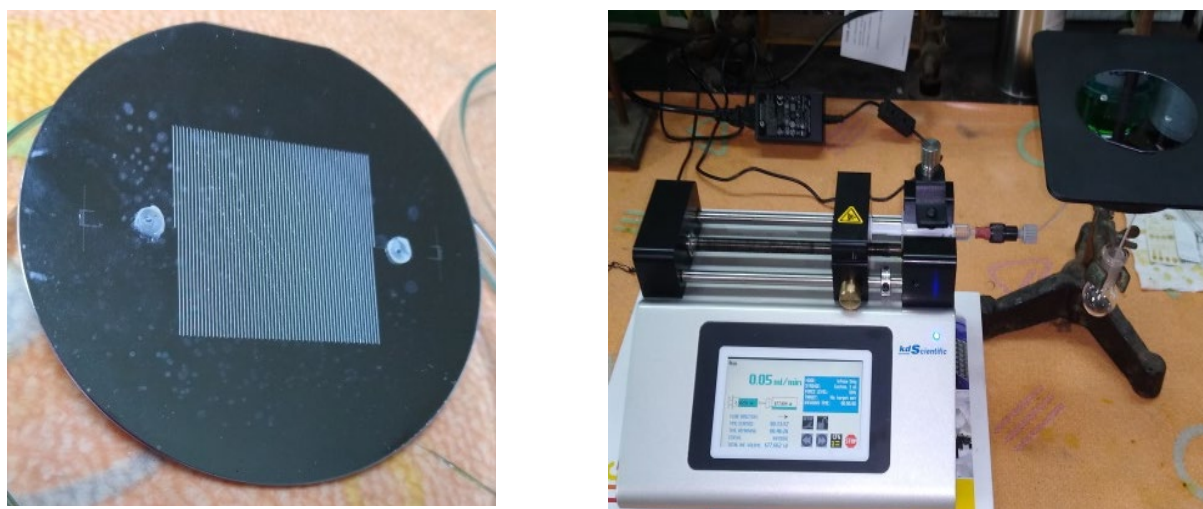


Figure S4. Glass/silicon microreactor V_{total} = 25 μ L

Table S1. Optimization of the photoredox THIQ oxidation/Mannich addition in batch

Entry ^a	Solvent	OrganoCatalyst (x mol%)	Photocatalyst (x mol%)	CFL Lamp	Time (h)	Yield (%) ^b	Prec. ^c
1	CH ₃ CN	L-Proline (30mol%)	[Ru(bpy) ₃]Cl ₂ (1 mol%)	15 W	24	67	Y
2	CH ₃ CN	L-Proline (30mol%)	[Ru(bpy) ₃]Cl ₂ (1 mol%)	8W	24	71	Y
3	CH ₃ CN	L-Proline (10mol%)	[Ru(bpy) ₃]Cl ₂ (1 mol%)	8W	24	73	Y
4	CH ₃ CN	/	[Ru(bpy) ₃]Cl ₂ (1 mol%)	8W	24	/	N
5	MeOH	L-Proline (10mol%)	[Ru(bpy) ₃]Cl ₂ (1 mol%)	8W	24	85	N
6	MeOH	McMillan I gen. (10mol%)	[Ru(bpy) ₃]Cl ₂ (1 mol%)	8W	24	6	N
7	MeOH	McMillan II gen. (10mol%)	[Ru(bpy) ₃]Cl ₂ (1 mol%)	8W	24	15	N
8	MeOH	L-Proline (10mol%)	[Ru(bpz) ₃][PF ₆] ₂ (1 mol%)	8W	24	57	Y
9	MeOH	L-Proline (10mol%)	Eosin Y (2 mol%)	8W	24	64	N
10 ^d	MeOH	L-Proline (10mol%)	[Ru(bpy) ₃]Cl ₂ (1 mol%)	8W		86	N

^a Reaction conditions : Tetrahydroisoquinoline (0.25 mmol, 1 equiv.), Ru cat. (0.0025 mmol, 1 mol%) L-Proline (0.075 mmol, 0.3 equiv.) and acetone (10 equiv.) were added to solvent (2 mL) and irradiated with designated CFL lamp and stirred for designated period of time; ^b Isolated yield after column chromatography; ^c "Y": Precipitation observed, "N": no precipitation observed, all reactants are soluble in designated solvent; ^d 1 equivalent of methyl viologen as terminal oxidant was added.

Table S2. Optimization of the photoredox THIQ oxidation/alkynylation reaction in flow and comparison to batch conditions

at the outset or in the FLASK

Entry	Reactor type	Copper source	Photosensitizer	Retention time (h)	Light source	Yield (%)
1	batch	CuOTf·½C ₆ H ₆	[Ru(bpy) ₃]Cl ₂	24h	8W	58
2	PDMS	CuOTf·½C ₆ H ₆	[Ru(bpy) ₃]Cl ₂	2h	8W	44
3	PDMS	(MeCN) ₄ CuPF ₆	[Ru(bpy) ₃]Cl ₂	2h	8W	40
4	PDMS	(MeCN) ₄ CuPF ₆	[Ru(bpz) ₃](PF ₆) ₂	2h	8W	31
5	PDMS	CuOTf·½C ₆ H ₆	[Ru(bpy) ₃]Cl ₂	2h	White LED	22
6	PDMS	CuOTf·½C ₆ H ₆	[Ru(bpy) ₃]Cl ₂	2h	26W	20
7	PDMS+flask	CuOTf·½C ₆ H ₆	[Ru(bpy) ₃]Cl ₂	2h+18 h	8W	99

With 2h residence time for oxidation reaction at concentration of 0.25M and taking into account total internal volume of PDMS reactor of 0.5ml (flow rate 0.25 ml/h), total output is calculated to be 1.5 mmol of starting compound per day per reactor.

General procedure I, THIQ oxidation/Mannich reaction in flow

Tetrahydroisoquinoline (0.25 mmol, 1 equiv.), Ru(bpy)₃Cl₂·6H₂O (0.0025 mmol, 1 mol%), L-Proline (0.0025 mmol, 0.1 equiv.) and ketone (5-10 equiv.) were added to MeOH (1 mL) and pumped through microfluidic device by means of syringe pump. System is irradiated with CFL lamp, residence time depends on the substrate applied (2h or 6h depending on substrate). Upon completion of reaction, excess of solvent was evaporated under reduced pressure on the vacuum evaporator. Residue was submitted for ¹H NMR analysis. Purification was performed using SiO₂ column chromatography with petrol ether/ethyl acetate as an eluents.

General procedure II, THIQ oxidation/Strecker reaction in flow

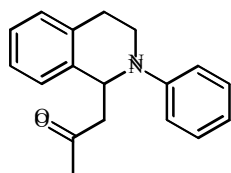
Tetrahydroisoquinoline (0.25 mmol, 1 equiv.), Ru(bpy)₃Cl₂·6H₂O (0.0025 mmol, 1 mol%), TMSCN (0.3 mmol, 1.2 equiv) were added to acetonitrile (1 mL) and pumped through microfluidic device by means of syringe pump. System is irradiated with 8w CFL lamp, residence time of 2h was applied. Upon completion of reaction, excess of solvent and reagents was evaporated under reduced pressure on the vacuum evaporator. Residue was submitted for

¹H NMR analysis. Purification was performed using SiO₂ column chromatography with petrol ether/ethyl acetate as an eluents.

General procedure III, THIQ oxidation/alkynylation reaction in flow

Tetrahydroisoquinoline (0.25 mmol, 1 equiv.), Ru(bpy)₃Cl₂*6H₂O (0.0025 mmol, 1 mol%), were added to acetonitrile (1 mL) and pumped through microfluidic device by means of syringe pump. System is irradiated with CFL lamp, residence time of 2h was applied. Subsequently in recipient flask were added phenylacetylene (1.25 mmol, 5 equiv.), Cu catalyst (0.025 mmol, 0.1 equiv) in CH₂Cl₂ and mixture was stirred at room temperature overnight. Upon completion of reaction, excess of solvent was evaporated under reduced pressure on the vacuum evaporator. Residue was submitted for ¹H NMR analysis. Purification was performed using SiO₂ column chromatography with petrol ether/ethyl acetate as an eluents.

1-(2-Phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (2a)



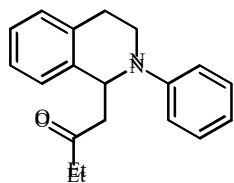
General procedure I was followed with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (52.3 mg, 0.25 mmol), acetone (145.2 mg, 0.185 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction

mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (58 mg, 88 %) as yellowish oil.

R_f = 0.53 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.24 (t, 2H, ArH, *J* = 7.8 Hz), 7.12-7.15 (m, 4H, ArH), 6.93 (d, 2H, ArH, *J* = 8.5 Hz), 6.77 (t, 1H, *J* = 7.0 Hz), 5.39 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.64 (dt, 1H, *J* = 5.5 Hz, 13.0 Hz), 3.52 (ddd, 1H, *J* = 4.4 Hz, 8.9 Hz, 12.5 Hz), 3.02-3.07 (m, 2H), 2.81 (dd, 2H, *J* = 7.2, 16.2 Hz), 2.06 (s, 3H, CH₃); ¹³C NMR (CDCl₃, 125.8 MHz): δ 207.2, 148.8, 138.3, 134.4, 129.3, 128.6, 126.83, 126.78, 126.3, 118.2, 114.8, 54.8, 50.2, 42.0, 31.1, 27.2.

Spectroscopic data are in agreement with the published data.^{S1}

1-(2-Phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (2b)

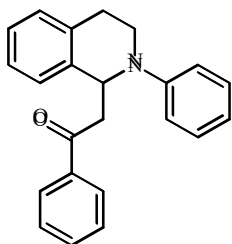


General procedure I was followed with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (52.3 mg, 0.25 mmol), ethyl methyl ketone (180.3 mg, 0.224 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude

reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (62 mg, 89 %) as yellowish oil.

Rf = 0.62 (Petrol Ether/EtOAc : 7/1); **¹H NMR** (CDCl₃, 500 MHz): δ 7.26 (t, 2H, ArH, *J* = 8.0 Hz), 7.13-7.18 (m, 4H, ArH), 6.95 (d, 2H, ArH, *J* = 8.5 Hz), 6.78 (t, 1H, ArH, *J* = 7.2 Hz), 5.43 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.65 (dt, 1H, *J* = 5.2 Hz, 12.5 Hz), 3.54 (ddd, 1H, *J* = 4.5 Hz, 8.6 Hz, 12.9 Hz), 3.02-3.10 (m, 2H), 2.77-2.87 (m, 2H), 2.36 (dq, 1H, *J* = 7.3, 17.9 Hz), 2.26 (dq, 1H, *J* = 7.3, 17.9 Hz), 0.99 (t, 3H, *J* = 7.2 Hz); **¹³C NMR** (CDCl₃, 125.8 MHz): δ 209.9, 148.8, 138.3, 134.4, 129.3, 128.6, 126.8, 126.7, 126.2, 118.1, 114.6, 55.1, 48.9, 41.9, 37.2, 27.2, 7.5; Spectroscopic data are in agreement with the published data.^{S1}

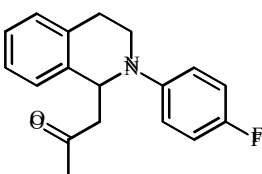
1-Phenyl-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)ethanone (2c)



General procedure I was followed with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (52.3 mg, 0.25 mmol), acetophenone (300.4 mg, 0.292 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (68 mg, 83 %)

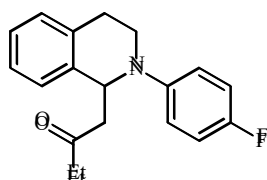
as yellowish oil. **Rf** = 0.61 (Petrol Ether/EtOAc : 7/1); **¹H NMR** (CDCl₃, 500 MHz): δ 7.87 (d, 2H, ArH, *J* = 7.5 Hz), 7.54 (t, 1H, ArH, *J* = 7.2 Hz), 7.42 (t, 2H, ArH, *J* = 7.8 Hz), 7.11-7.27 (m, 7H, ArH), 6.99 (d, 1H, ArH, *J* = 8.0 Hz), 6.77 (t, 1H, ArH, *J* = 7.2 Hz), 5.69 (dd, 1H, C(1)H, *J* = 5.5 Hz, 7.0 Hz), 3.63-3.71 (m, 2H), 3.60 (dd, 1H, *J* = 4.8 Hz, 16.8 Hz), 3.42 (dd, 1H, *J* = 7.2, 16.8 Hz), 3.10-3.16 (m, 1H), 2.95 (dt, 1H, *J* = 5.0 Hz, 16.0 Hz); **¹³C NMR** (CDCl₃, 125.8 MHz): δ 198.6, 148.7, 138.5, 137.2, 134.5, 133.1, 129.3, 128.5, 128.1, 127.1, 126.8, 126.2, 117.9, 114.3, 55.0, 45.3, 42.1, 27.5; Spectroscopic data are in agreement with the published data.^{S2}

1-(2-(4-Fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (2d)



General procedure I was followed with 2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (69.3 mg, 0.25 mmol), acetone (145.2 mg, 0.185 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (67 mg, 95 %) as yellowish oil. **Rf** = 0.45 (Petrol Ether/EtOAc : 7/1); **¹H NMR** (CDCl₃, 500 MHz): δ 7.13-7.20 (m, 4H, ArH), 6.89-6.97 (m, 4H, ArH), 5.31 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.59 (dt, 1H, *J* = 4.9, 12.5 Hz), 3.48-3.53 (m, 1H), 3.00-3.06 (m, 2H), 2.76-2.83 (m, 2H), 2.09 (s, 3H, CH₃); **¹³C NMR** (CDCl₃, 125.8 MHz): δ 207.1, 156.4 (d, *J* = 237.6 Hz), 145.7, 138.0, 134.1, 128.8, 126.74, 126.72, 126.3, 117.1 (d, *J* = 7.6 Hz), 115.6 (d, *J* = 22.1 Hz), 55.5, 50.0, 42.6, 30.9, 26.7; Spectroscopic data are in agreement with the published data.^{S1}

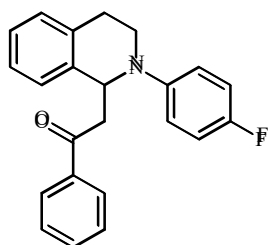
1-(2-(4-Fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (2e)



General procedure I was followed with 2-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (71.8 mg, 0.25 mmol), ethyl

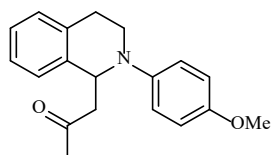
methyl ketone (180.3 mg, 0.224 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (63 mg, 85%) as yellowish oil. **Rf** = 0.52 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.12-7.18 (m, 4H, ArH), 6.88-6.96 (m, 4H, ArH), 5.32 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.58 (dt, 1H, *J* = 5.0 Hz, 13.0 Hz), 3.48-3.53 (m, 1H), 2.99-3.07 (m, 2H), 2.74-2.81 (m, 2H), 2.36 (dq, 1H, *J* = 7.2, 17.7 Hz), 2.28 (dq, 1H, *J* = 7.2, 17.7 Hz), 0.99 (t, 3H, *J* = 7.2 Hz); ¹³C NMR (CDCl₃, 125.8 MHz): δ 209.8, 156.4 (d, *J* = 237.8 Hz), 145.7, 138.1, 134.2, 128.8, 126.8, 126.2, 116.9 (d, *J* = 7.2 Hz), 115.6 (d, *J* = 22.0 Hz), 55.8, 48.8, 42.5, 37.2, 26.8, 7.5; Spectroscopic data are in agreement with the published data.^{S3}

2-(2-(4-Fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethanone (2f)



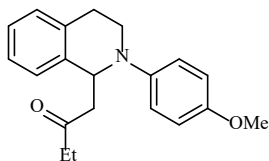
General procedure I was followed with 2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (69.3 mg, 0.25 mmol), acetophenone (300.4 mg, 0.292 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (72 mg, 84 %) as yellowish oil. **Rf** = 0.57 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.85 (d, 2H, ArH, *J* = 7.5 Hz), 7.53 (t, 1H, ArH, *J* = 7.5 Hz), 7.41 (t, 2H, ArH, *J* = 7.8 Hz), 7.21 (d, 1H, ArH, *J* = 7.5 Hz), 7.12-7.17 (m, 3H, ArH), 6.92 (d, 4H, ArH, *J* = 6.5 Hz), 5.57 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.56-3.61 (m, 3H), 3.34 (dd, 1H, *J* = 6.5 Hz, 16.5 Hz), 3.06-3.12 (m, 1H), 2.87 (dt, 1H, *J* = 4.1 Hz, 16.0 Hz); ¹³C NMR (CDCl₃, 125.8 MHz): δ 198.6, 156.3 (d, *J* = 237.0 Hz), 145.6, 138.3, 137.2, 134.2, 133.1, 128.7, 128.5, 128.1, 127.0, 126.8, 126.3, 116.6 (d, *J* = 7.2 Hz), 115.6 (d, *J* = 22.1 Hz), 55.8, 45.1, 42.6, 27.1; Spectroscopic data are in agreement with the published data.^{S2}

1-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (2g)



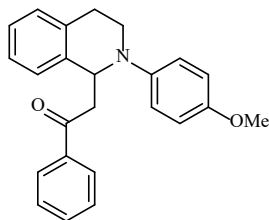
General procedure I was followed with 2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (60 mg, 0.25 mmol), acetone (145.2 mg, 0.185 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH/CH₃CN=1/1 (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (65 mg, 88 %) as yellowish oil. **Rf** = 0.65 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 400 MHz): δ 7.17 – 7.03 (m, 4H), 6.89 (d, *J* = 9.1 Hz, 2H), 6.83-6.73 (m, 2H), 5.22 (t, *J* = 6.4 Hz, 1H), 3.73 (s, 3H), 3.58 – 3.49 (m, 1H), 3.49 – 3.36 (m, 1H), 3.07 – 2.88 (m, 2H), 2.81 – 2.64 (m, 2H), 2.04 (s, 3H); ¹³C NMR (CDCl₃, 101 MHz): δ 207.3, 153.3, 143.6, 138.2, 134.3, 128.9, 126.8, 126.6, 126.1, 118.4, 114.6, 55.9, 55.6, 49.9, 42.9, 30.8, 26.7; Spectroscopic data are in agreement with the published data.^{S1}

1-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (2h)



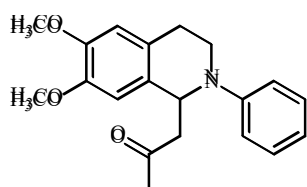
General procedure I was followed with 2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (60 mg, 0.25 mmol), ethyl methyl ketone (180.3 mg, 0.224 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH/CH₃CN=1/1 (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (61 mg, 79%) as yellowish oil. **Rf** = 0.62 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 400 MHz): δ 7.18-7.08 (m, 4H), 6.91 (d, *J* = 9.1 Hz, 2H), 6.81 (d, *J* = 9.1 Hz, 2H), 5.27 (t, *J* = 6.4 Hz, 1H), 3.74 (s, 3H), 3.60 – 3.51 (m, 1H), 3.51 – 3.39 (m, 1H), 3.07 – 2.92 (m, 2H), 2.74 (ddd, *J* = 15.8, 10.7, 5.2 Hz, 2H), 2.39 – 2.19 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz): δ 210.0, 153.1, 143.6, 138.3, 134.3, 128.8, 126.8, 126.5, 126.1, 118.1, 114.6, 56.1, 55.6, 48.7, 42.6, 37.0, 26.8, 7.5. Spectroscopic data are in agreement with the published data.^{S4}

2-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethanone (2i)



General procedure I was followed with 2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (60 mg, 0.25 mmol), acetophenone (300.4 mg, 0.292 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH/CH₃CN=1/1 (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (62.5 mg, 70 %) as yellowish solid. **Rf** = 0.66 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 400 MHz): δ 7.82 (d, *J* = 7.3 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.21 – 7.05 (m, 4H), 6.92 (d, *J* = 9.1 Hz, 2H), 6.78 (d, *J* = 9.1 Hz, 2H), 5.51 (t, *J* = 6.0 Hz, 1H), 3.71 (s, 3H), 3.60-3.50 (m, 3H), 3.28 (dd, *J* = 16.3, 6.6 Hz, 1H), 3.13 – 3.01 (m, 1H), 2.82 (dt, *J* = 16.3, 4.1 Hz, 1H) ¹³C NMR (CDCl₃, 101 MHz): δ 198.7, 152.9, 143.6, 138.5, 137.3, 134.3, 132.9, 128.8, 128.4, 128.1, 127.0, 126.6, 126.1, 117.8, 114.6, 56.2, 55.6, 44.9, 42.7, 27.2. Spectroscopic data are in agreement with the published data.^{S5}

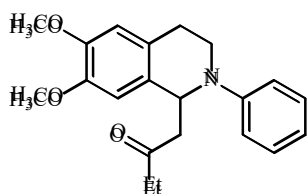
1-(6,7-Dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (2j)



General procedure I was followed with 6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinoline (67.3 mg, 0.25 mmol), acetone (145.2 mg, 0.185 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (77 mg, 95 %) as yellowish oil. **Rf** = 0.30 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.24 (t, 2H, ArH, *J* = 8.0 Hz), 6.93 (d, 2H, ArH, *J* = 8.0 Hz), 6.78 (t, 1H, ArH, *J* = 7.2 Hz), 6.69 (s, 1H, C(5)H or C(8)H), 6.61 (s, 1H, C(5)H or C(8)H), 5.30 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.84 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 3.66 (dt, 1H, *J* = 5.0 Hz, 13.0 Hz), 3.49 (ddd, 1H, *J* = 4.5 Hz, 9.7 Hz, 12.8 Hz), 3.04 (dd, 1H, *J* = 5.5 Hz, 16.5 Hz), 2.97 (ddd, 1H, *J* = 5.8 Hz, 9.8 Hz, 15.8 Hz),

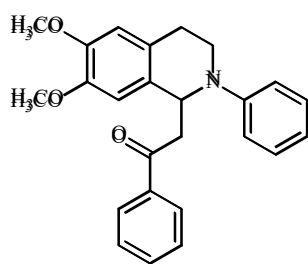
2.82 (dd, 1H, $J = 6.8$ Hz, 12.2 Hz), 2.70 (dt, 1H, $J = 4.2$ Hz, 16.0 Hz), 2.08 (s, 3H, COCH₃); ¹³C NMR (CDCl₃, 125.8 MHz): δ 207.6, 148.9, 147.7, 147.3, 130.1, 129.2, 126.2, 118.4, 115.1, 111.3, 109.7, 55.9, 55.8, 54.5, 50.1, 41.9, 31.1, 26.5; Spectroscopic data are in agreement with the published data.^{S1}

1-(6,7-Dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (2k)



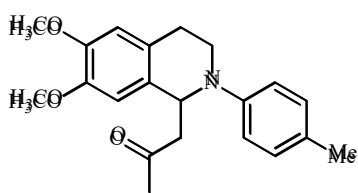
General procedure I was followed with 6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinoline (67.3 mg, 0.25 mmol), ethyl methyl ketone (180.3 mg, 0.224 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (75.5 mg, 89 %) as yellowish oil. **Rf** = 0.29 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.24 (t, 2H, ArH, $J = 8.2$ Hz), 6.95 (d, 2H, ArH, $J = 8.5$ Hz), 6.78 (t, 1H, ArH, $J = 7.0$ Hz), 6.66 (s, 1H, C(5)H or C(8)H), 6.61 (s, 1H, C(5)H or C(8)H), 5.32 (t, 1H, C(1)H, $J = 6.5$ Hz), 3.85 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 3.66 (dt, 1H, $J = 5.0$ Hz, 13.0 Hz), 3.50 (ddd, 1H, $J = 4.2$ Hz, 9.2 Hz, 12.5 Hz), 3.02 (dd, 1H, $J = 5.2$ Hz, 15.8 Hz), 2.96-3.02 (m, 1H), 2.78 (dd, 1H, $J = 7.0$ Hz, 16.0 Hz), 2.72 (dt, 1H, $J = 4.4$ Hz, 16.0 Hz), 2.37 (dq, 1H, $J = 7.4$ Hz, 17.8 Hz), 2.28 (dq, 1H, $J = 7.2$ Hz, 17.8 Hz), 0.99 (t, 3H, COCH₂CH₃, $J = 7.2$ Hz); ¹³C NMR (CDCl₃, 125.8 MHz): δ 210.3, 148.9, 147.7, 147.3, 130.2, 129.3, 126.2, 118.2, 114.9, 111.3, 109.7, 55.9, 55.8, 54.9, 48.8, 41.8, 37.4, 26.6, 7.5; Spectroscopic data are in agreement with the published data.^{S4}

2-(6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethanone (2l)



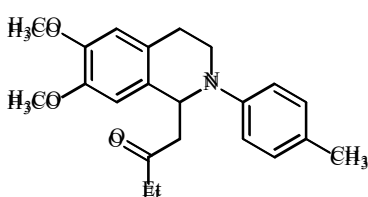
General procedure I was followed with 6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinoline (67.3 mg, 0.25 mmol), acetophenone (300.4 mg, 0.292 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (71 mg, 73 %) as yellowish oil. **Rf** = 0.29 (Petrol Ether/EtOAc : 3/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.85 (d, 2H, ArH, $J = 7.5$ Hz), 7.52 (t, 1H, ArH, $J = 7.5$ Hz), 7.41 (t, 2H, ArH, $J = 7.8$ Hz), 7.24 (t, 2H, ArH, $J = 7.5$ Hz), 6.98 (d, 2H, ArH, $J = 8.5$ Hz), 6.76 (t, 1H, ArH, $J = 7.2$ Hz), 6.70 (s, 1H, C(5)H or C(8)H), 6.63 (s, 1H, C(5)H or C(8)H), 5.36 (dd, 1H, C(1)H, $J = 5.0$ Hz, 7.0 Hz), 3.84 (s, 3H, OCH₃), 3.74 (s, 3H, OCH₃), 3.68 (dt, 1H, $J = 5.2$ Hz, 12.5 Hz), 3.32-3.61 (m, 2H), 3.39 (dd, 1H, $J = 7.5$ Hz, 16.0 Hz), 3.03 (ddd, 1H, $J = 5.8$ Hz, 8.4 Hz, 15.6 Hz), 2.81 (dt, 1H, $J = 4.4$ Hz, 16.0 Hz); ¹³C NMR (CDCl₃, 125.8 MHz): δ 199.1, 148.9, 147.8, 147.3, 137.3, 133.1, 130.4, 129.3, 128.5, 128.1, 126.3, 118.1, 114.7, 111.3, 110.1, 55.9 (2C overlapped), 55.0, 45.1, 42.0, 27.0; Spectroscopic data are in agreement with the published data.^{S6}

1-(6,7-Dimethoxy-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (2m)



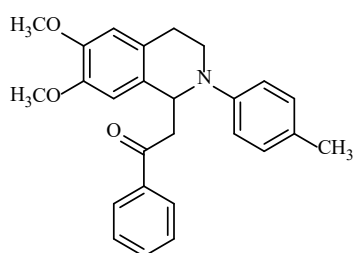
General procedure I was followed with 6,7-dimethoxy-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline (70.8 mg, 0.25 mmol), acetone (145.2 mg, 0.185 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (70 mg, 83 %) as yellowish oil. **Rf** = 0.38 (Petrol Ether/EtOAc : 3/1); **¹H NMR** (CDCl₃, 500 MHz): δ 7.05 (d, 2H, ArH, *J* = 8.0 Hz), 6.86 (d, 2H, ArH, *J* = 8.0 Hz), 6.68 (s, 1H, C(5)H or C(8)H), 6.59 (s, 1H, C(5)H or C(8)H), 5.24 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.842 (s, 3H, OCH₃), 3.838 (s, 3H, OCH₃), 3.64 (ddd, 1H, *J* = 4.0 Hz, 5.0 Hz, 12.9 Hz), 3.46 (ddd, 1H, *J* = 4.1 Hz, 10.1 Hz, 13.1 Hz), 3.02 (dd, 1H, *J* = 6.0 Hz, 16.0 Hz), 2.95 (ddd, 1H, *J* = 5.8 Hz, 10.2 Hz, 16.0 Hz), 2.79 (dd, 1H, *J* = 7.0 Hz, 16.0 Hz), 2.66 (brdt, 1H, *J* = 3.5 Hz, 16.0 Hz), 2.25 (s, 3H, ArCH₃), 2.08 (s, 3H, COCH₃); **¹³C NMR** (CDCl₃, 125.8 MHz): δ 207.7, 147.7, 147.3, 147.0, 130.1, 129.8, 128.1, 126.2, 116.0, 111.4, 109.7, 55.9, 55.8, 54.9, 49.9, 42.1, 31.0, 26.3, 20.3; Spectroscopic data are in agreement with the published data.^{S7}

1-(6,7-Dimethoxy-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (2n)



General procedure I was followed with 6,7-dimethoxy-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline (70.8 mg, 0.25 mmol), ethyl methyl ketone (180.3 mg, 0.224 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (66 mg, 75 %) as yellowish oil. **Rf** = 0.52 (Petrol Ether/EtOAc : 3/1); **¹H NMR** (CDCl₃, 500 MHz): δ 7.05 (d, 2H, ArH, *J* = 8.2 Hz), 6.86 (d, 2H, ArH, *J* = 8.2 Hz), 6.65 (s, 1H, C(5)H or C(8)H), 6.29 (s, 1H, C(5)H or C(8)H), 5.26 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.84 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 3.63 (dt, 1H, *J* = 4.8 Hz, 12.0 Hz), 3.46 (ddd, 1H, *J* = 4.2 Hz, 10.2 Hz, 12.5 Hz), 2.94-3.01 (m, 2H), 2.75 (dd, 1H, *J* = 7.0 Hz, 15.5 Hz), 2.67 (brdt, 1H, *J* = 3.5 Hz, 16.0 Hz), 2.36 (dq, 1H, *J* = 7.3 Hz, 17.9 Hz), 2.28 (dq, partially hidden by COCH₂CH₃ signal, 1H, *J* = 7.3 Hz, 17.9 Hz), 0.98 (t, 3H, COCH₂CH₃, *J* = 7.5 Hz); **¹³C NMR** (CDCl₃, 125.8 MHz): δ 210.4, 147.7, 147.3, 147.0, 130.2, 129.8, 127.9, 126.2, 115.8, 111.3, 109.6, 55.9, 55.8, 55.3, 48.6, 41.9, 37.3, 26.5, 20.3, 7.5; Spectroscopic data are in agreement with the published data.^{S8}

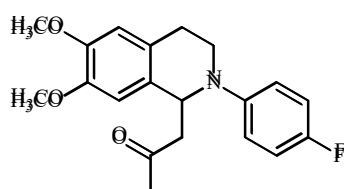
1-(6,7-Dimethoxy-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (2o)



General procedure I was followed with 6,7-dimethoxy-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline (70.8 mg, 0.25 mmol), ethyl methyl ketone (180.3 mg, 0.224 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped

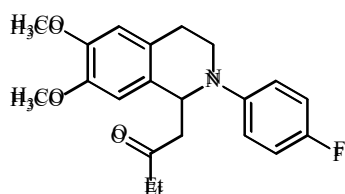
through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (71 mg, 71 %) as yellowish oil. **Rf** = 0.53 (Petrol Ether/EtOAc : 3/1); **¹H NMR** (CDCl₃, 400 MHz): δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 6.69 (s, 1H), 6.61 (s, 1H), 5.50 (t, *J* = 4 Hz, 1H), 3.83 (s, 3H), 3.73 (s, 3H), 3.69 – 3.60 (m, 1H), 3.58 – 3.46 (m, 2H), 3.35 (dd, *J* = 16.1, 7.2 Hz, 1H), 3.02 (ddd, *J* = 15.6, 9.6, 5.7 Hz, 1H), 2.76 (dt, *J* = 16.0, 4.3 Hz, 1H), 2.23 (s, 3H); **¹³C NMR** (CDCl₃, 101 MHz): δ 199.2, 147.7, 147.2, 146.9, 137.4, 133.0, 130.4, 129.8, 128.5, 128.1, 127.8, 126.2, 115.5, 111.3, 109.9, 55.8, 55.4, 44.8, 42.1, 26.9, 20.3; **IR** (ATR): ν = 2987 (m), 2834 (m), 1679 (s), 1612 (m), 1514 (vs), 1449 (m), 1273 (s), 1249 (s), 1116 (m), 1021 (m); **HRMS**: *m/z* (ESI/TOF) calc for C₂₆H₂₇NO₃ (M⁺) 401.1991, found 401.1990;

1-(2-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (2p)



General procedure I was followed with 2-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (71.8 mg, 0.25 mmol), acetone (145.2 mg, 0.185 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (72 mg, 84 %) as yellowish oil. **Rf** = 0.36 (Petrol Ether/EtOAc : 3/1); **¹H NMR** (CDCl₃, 500 MHz): δ 6.86-6.94 (m, 4H, ArH), 6.66 (s, 1H, C(5)H or C(8)H), 6.59 (s, 1H, C(5)H or C(8)H), 5.18 (t, 1H, C(1)H, *J* = 6.2 Hz), 3.838 (s, 3H, OCH₃), 3.831 (s, 3H, OCH₃), 3.58 (ddd, 1H, *J* = 3.8 Hz, 5.2 Hz, 12.8 Hz), 3.46 (ddd, 1H, *J* = 4.2 Hz, 10.5 Hz, 16.0 Hz), 3.01 (dd, 1H, *J* = 6.2 Hz, 16.2 Hz), 2.92 (ddd, 1H, *J* = 5.8 Hz, 10.2 Hz, 16.0 Hz), 2.78 (dd, 1H, *J* = 6.5 Hz, 16.0 Hz), 2.64 (dt, 1H, *J* = 7.2 Hz, 16.0 Hz), 2.09 (s, 3H, COCH₃); **¹³C NMR** (CDCl₃, 125.8 MHz): δ 207.5, 156.6 (d, *J* = 238.0 Hz), 147.8, 147.5, 145.9, 129.8, 126.0, 117.5 (d, *J* = 7.4 Hz), 115.6 (d, *J* = 22.4 Hz), 111.4, 109.6, 55.9, 55.8, 55.3, 50.0, 42.6, 31.0, 26.0; Spectroscopic data are in agreement with the published data.^{S8}

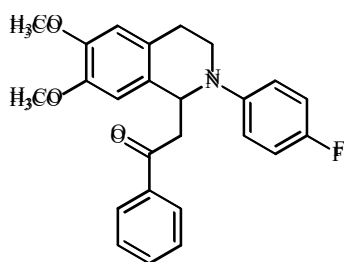
1-(2-(4-Fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (2r)



General procedure I was followed with 2-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (71.8 mg, 0.25 mmol), ethyl methyl ketone (180.3 mg, 0.224 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (77 mg, 86 %) as yellowish oil. **Rf** = 0.34 (Petrol Ether/EtOAc : 3/1); **¹H NMR** (CDCl₃, 500 MHz): δ 6.87-6.94 (m, 4H, ArH), 6.62 (s, 1H, C(5)H or C(8)H), 6.59 (s, 1H, C(5)H or C(8)H), 5.20 (t, 1H, C(1)H, *J* = 6.5 Hz), 3.84 (s, 3H, OCH₃), 3.82 (s, 3H,

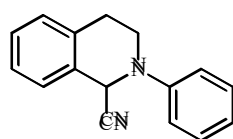
OCH₃), 3.57 (ddd, 1H, *J* = 3.9 Hz, 5.4 Hz, 12.9 Hz), 3.43-3.49 (m, 1H), 2.99 (dd, 1H, *J* = 6.5 Hz, 16.0 Hz), 2.88-2.98 (m, 1H), 2.74 (dd, 1H, *J* = 6.5 Hz, 15.5 Hz), 2.66 (dt, 1H, *J* = 3.8 Hz, 16.0 Hz), 2.26-2.40 (m, 2H, COCH₂CH₃), 0.99 (t, 3H, COCH₂CH₃, *J* = 7.2 Hz); ¹³C NMR (CDCl₃, 125.8 MHz): δ 210.2, 156.5 (d, *J* = 238.1 Hz), 147.8, 147.4, 145.8, 129.9, 126.0, 117.25 (d, *J* = 7.4 Hz), 115.6 (d, *J* = 22.0 Hz), 111.4, 109.5, 55.9, 55.8, 55.6, 48.7, 42.4, 37.3, 26.2, 7.5; Spectroscopic data are in agreement with the published data.^{S8}

2-(2-(4-Fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethanone (2s)



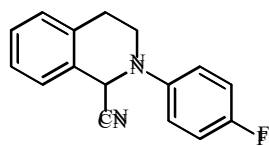
General procedure I was followed with 2-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (71.8 mg, 0.25 mmol), acetophenone (300.4 mg, 0.292 ml, 2.5 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), and L-proline (2.9 mg, 0.025 mmol) in MeOH (2 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (74 mg, 73 %) as yellowish oil. **Rf** = 0.34 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.85 (d, 2H, ArH, *J* = 7.5 Hz), 7.53 (d, 1H, ArH, *J* = 7.5 Hz), 7.41 (t, 2H, ArH, *J* = 7.5 Hz), 6.92 (d, 4H, ArH, *J* = 6.5 Hz), 6.67 (s, 1H, C(5)H or C(8)H), 6.62 (s, 1H, C(5)H or C(8)H), 5.44 (t, 1H, C(1)H, *J* = 6.0 Hz), 3.84 (s, 3H, OCH₃), 3.74 (s, 3H, OCH₃), 3.52-3.63 (m, 3H), 3.33 (dd, 1H, *J* = 6.8 Hz, 16.2 Hz), 3.00 (ddd, 1H, *J* = 6.1 Hz, 9.6 Hz, 15.9 Hz), 2.74 (brd, 1H, *J* = 16.0 Hz); ¹³C NMR (CDCl₃, 125.8 MHz): δ 199.0, 156.4 (d, *J* = 237.5 Hz), 147.8, 147.4, 145.8, 137.3, 133.2, 130.1, 128.6, 128.1, 126.1, 117.1 (d, *J* = 7.3 Hz), 115.6 (d, *J* = 22.1 Hz), 111.4, 109.9, 55.9 (3C overlapped), 44.9, 42.6.3, 26.6; Spectroscopic data are in agreement with the published data.^{S8}

2-Phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (3a)



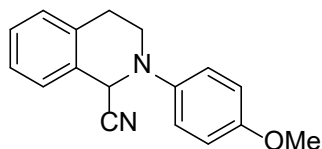
General procedure II was followed with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (52.3 mg, 0.25 mmol), trimethylsilyl cyanide (29.8 mg, 0.038 ml, 0.3 mmol) and Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), in CH₃CN (1 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (56 mg, 95 %) as colourless solid. **Rf** = 0.44 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.36 (t, 2H, ArH, *J* = 8.0 Hz), 7.22-7.32 (m, 4H, ArH), 7.08 (d, 2H, ArH, *J* = 8.0 Hz), 7.02 (t, 1H, ArH, *J* = 7.2 Hz), 5.51 (s, 1H, C(1)H), 3.76 (dddd, 1H, *J* = 1.0 Hz, 3.0 Hz, 6.0 Hz, 12.5 Hz), 3.47 (ddd, 1H, *J* = 3.9 Hz, 10.9 Hz, 12.1 Hz), 3.14 (ddd, 1H, *J* = 5.9 Hz, 10.6 Hz, 16.4 Hz), 2.95 (dt, 1H, *J* = 3.4 Hz, 16.5 Hz); ¹³C NMR (CDCl₃, 125.8 MHz): δ 148.3, 134.5, 129.5 (2C overlapped), 129.3, 128.7, 127.0, 126.8, 121.8, 117.7, 117.5, 53.1, 44.1, 28.4; Spectroscopic data are in agreement with the published data.^{S9}

2-(4-Fluorophenyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (3b)



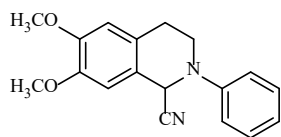
General procedure II was followed with 2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (69.3 mg, 0.25 mmol), trimethylsilyl cyanide (29.8 mg, 0.038 ml, 0.3 mmol), and Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), in CH₃CN (1 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (56 mg, 89 %) as colourless solid. **Rf** = 0.38 (Petrol Ether/EtOAc : 3/1); **¹H NMR** (CDCl₃, 500 MHz): δ 7.21-7.31 (m, 4H, ArH), 7.02-7.08 (m, 4H, ArH), 5.38 (s, 1H, C(1)H), 3.61 (dddd, 1H, *J* = 1.0 Hz, 2.2 Hz, 6.2 Hz, 12.3 Hz), 3.44 (dt, 1H, *J* = 4.0 Hz, 11.8 Hz), 3.14 (ddd, 1H, *J* = 6.0 Hz, 10.8 Hz, 16.5 Hz), 2.93 (dt, 1H, *J* = 3.0 Hz, 16.0 Hz); **¹³C NMR** (CDCl₃, 125.8 MHz): δ 158.6 (d, *J* = 242.2 Hz), 145.1, 134.2, 129.42, 129.36, 128.8, 127.0, 126.8, 120.4 (d, *J* = 7.9 Hz), 117.4, 116.2 (d, *J* = 22.4 Hz), 54.7, 44.7, 28.5; Spectroscopic data are in agreement with the published data.^{S10}

2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (3c)



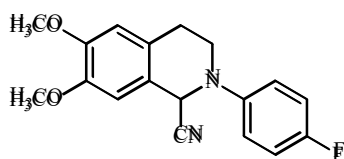
General procedure II was followed with 2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (60 mg, 0.25 mmol), trimethylsilyl cyanide (29.8 mg, 0.038 ml, 0.3 mmol), and Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), in CH₃CN (1 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (55 mg, 84 %) as colourless solid. **Rf** = 0.45 (Petrol Ether/EtOAc : 7/1); **¹H NMR** (CDCl₃, 400 MHz): δ 7.32 – 7.17 (m, 4H), 7.08 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 5.35 (s, 1H), 3.79 (s, 3H), 3.57 (dd, *J* = 12.2, 6.1 Hz, 1H), 3.43 (td, *J* = 11.7, 4.0 Hz, 1H), 3.15 (ddd, *J* = 17.1, 11.1, 6.3 Hz, 1H), 2.96 – 2.87 (m, 1H); **¹³C NMR** (CDCl₃, 125.8 MHz): δ 155.7, 142.6, 134.3, 129.7, 129.4, 128.6, 127.0, 126.7, 120.9, 117.6, 114.8, 55.5, 55.5, 44.9, 28.7; Spectroscopic data are in agreement with the published data.^{S11}

2-(4-Fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (3d)



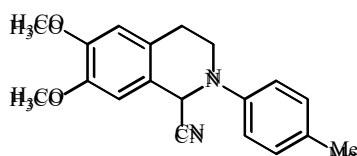
General procedure II was followed with 6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinoline (67.3 mg, 0.25 mmol), trimethylsilyl cyanide (29.8 mg, 0.038 ml, 0.3 mmol), and Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), in CH₃CN (1 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (73.5 mg, 100 %) as colourless solid. **Rf** = 0.45 (Petrol Ether/EtOAc : 3/1); **¹H NMR** (CDCl₃, 400 MHz): δ = 7.39-7.34 (m, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 7.07-7.02 (m, 1H), 6.70 (s, 1H), 6.67 (s, 1H), 5.46 (s, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.82-3.77 (m, 1H), 3.48 (ddd, *J* = 3.5, 11, 12 Hz, 1H), 3.11 (ddd, *J* = 6.0, 11, 16 Hz, 1H), 2.88 (ddd, *J* = 3, 3.8, 16.4 Hz, 1H); **¹³C NMR** (CDCl₃, 101 MHz): δ = 149.4, 148.3, 148.0, 129.4, 126.7, 122.1, 121.0, 117.9, 117.7, 111.5, 56.2, 55.9, 53.3, 44.3, 28.2; Spectroscopic data are in agreement with the published data.^{S12}

2-(4-Fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (3e)



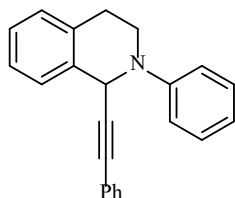
General procedure II was followed with 2-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (71.8 mg, 0.25 mmol), trimethylsilyl cyanide (29.8 mg, 0.038 ml, 0.3 mmol), and Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), in CH₃CN (1 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (71 mg, 91 %) as colourless solid. **Rf** = 0.44 (Petrol Ether/EtOAc : 3/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.05-7.06 (m, 4H, ArH), 6.72 (s, 1H, C(5)H or C(8)H), 6.68 (s, 1H, C(5)H or C(8)H), 5.33 (s, 1H, C(1)H), 3.882 (s, 3H, OCH₃), 3.876 (s, 3H, OCH₃), 3.61 (brdd, 1H, *J* = 5.5 Hz, 12.5 Hz), 3.41 (dt, 1H, *J* = 4.0 Hz, 11.8 Hz), 3.08 (ddd, 1H, *J* = 5.8 Hz, 10.8 Hz, 16.2 Hz), 2.83 (dt, 1H, *J* = 2.5 Hz, 15.0 Hz); ¹³C NMR (CDCl₃, 125.8 MHz): δ 158.6 (d, *J* = 242.2 Hz), 149.4, 148.1, 145.1 (d, *J* = 2.1 Hz), 126.5, 120.9, 120.5 (d, *J* = 8.1 Hz), 117.6, 116.1 (d, *J* = 22.4 Hz), 111.5, 109.3, 56.0, 55.9, 54.5, 44.8, 28.1. Spectroscopic data are in agreement with the published data.^{S8}

6,7-Dimethoxy-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (3f)



General procedure II was followed with 6,7-dimethoxy-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline (70.8 mg, 0.25 mmol), trimethylsilyl cyanide (29.8 mg, 0.038 ml, 0.3 mmol), and Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), in CH₃CN (1 mL). The reaction was pumped through microflow reactor irradiated with 8W CFL lamp, for 2 h. Crude reaction mixture was purified by column chromatography on silica gel (petrolether/ethylacetate = 3/1) to give the title compound (65.5 mg, 85 %) as colourless solid. **Rf** = 0.53 (Petrol Ether/EtOAc : 3/1); ¹H NMR (CDCl₃, 500 MHz): δ 7.16 (d, 2H, ArH, *J* = 8.5 Hz), 6.99 (d, 2H, ArH, *J* = 8.5 Hz), 6.73 (s, 1H, C(5)H or C(8)H), 6.67 (s, 1H, C(5)H or C(8)H), 5.38 (s, 1H, C(1)H), 3.88 (s, 6H, 2OCH₃), 3.69 (brdd, 1H, *J* = 5.5 Hz, 12.5 Hz), 3.40 (td, 1H, *J* = 3.8 Hz, 10.9 Hz), 3.07 (ddd, 1H, *J* = 5.8 Hz, 11.0 Hz, 16.2 Hz), 2.82 (brdt, 1H, *J* = 2.2 Hz, 15.5 Hz), 2.31 (s, 3H, ArCH₃); ¹³C NMR (CDCl₃, 125.8 MHz): δ 149.3, 148.0, 146.3, 131.8, 130.0, 126.8, 121.2, 118.4, 117.8, 111.5, 109.3, 56.0, 55.9, 53.9, 44.4, 28.1, 20.5; Spectroscopic data are in agreement with the published data.^{S8}

2-phenyl-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (4a)

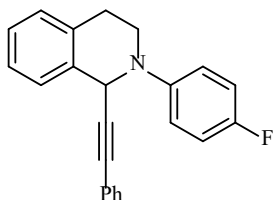


General procedure III was followed with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (52.3 mg, 0.25 mmol), Ru(bpy)₃Cl₂ (1.9 mg, 0.0025 mmol), in CH₃CN (1 mL). The reaction was pumped through microflow reactor irradiated with 11W CFL lamp, for 2 h. Recipient flask contained CuOTf·½C₆H₆ (12.6 mg, 0.025 mmol) and phenylacetylene (137 μl, 1.25 mmol) in 1 ml CH₂Cl₂. The mixture was stirred overnight, evaporated and purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (76.5 mg, 99 %) as yellowish oil.

Rf = 0.85 (Petrol Ether/EtOAc : 7/1); ¹H NMR (CDCl₃, 400 MHz): δ 7.31–7.21 (m, 5 H), 7.17–7.09 (m, 6 H), 7.04 (dd, *J* = 8.4, 1 Hz, 2H), 6.85 (t, *J* = 7.6 Hz, 1 H), 5.59 (s, 1 H), 3.66-

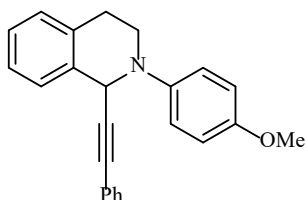
3.58 (m, 2H), 3.08 (ddd, $J = 16.0, 10.0, 6.0$ Hz, 1 H), 2.90 (dt, $J = 16.0, 4.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 149.4, 135.2, 134.2, 131.6, 128.9, 128.7, 127.9, 127.8, 127.3, 127.1, 126.1, 122.8, 119.5, 116.6, 88.6, 84.7, 52.3, 43.5, 29.0; Spectroscopic data are in agreement with the published data.^{S13}

2-(4-fluorophenyl)-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (4b)



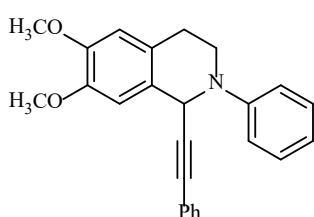
General procedure III was followed with 2-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (71.8 mg, 0.25 mmol), $\text{Ru}(\text{bpy})_3\text{Cl}_2$ (1.9 mg, 0.0025 mmol), in CH_3CN (1 mL). The reaction was pumped through microflow reactor irradiated with 11W CFL lamp, for 2 h. Recipient flask contained $\text{CuOTf} \cdot \frac{1}{2}\text{C}_6\text{H}_6$ (12.6 mg, 0.025 mmol) and phenylacetylene (137 μl , 1.25 mmol) in 1 ml CH_2Cl_2 . The mixture was stirred overnight, evaporated and purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (72mg, 88 %) as yellowish oil. $R_f = 0.80$ (Petrol Ether/EtOAc : 7/1); ^1H NMR (CDCl_3 , 400 MHz): δ 7.42-7.35 (m, 1H), 7.33-7.22 (m, 8H), 7.12-7.05 (m, 2H), 7.05-6.98 (m, 2H), 5.55 (s, 1H), 3.65-3.60 (m, 2H), 3.22-3.14 (m, 1H), 2.96 (dt, $J = 3.6, 16.3$ Hz, 1H). ^{13}C NMR (CDCl_3 , 101 MHz): δ 157.6 (d, $J = 240$ Hz), 146.5, 135.1, 134.2, 131.8 (2C), 129.0, 128.1 (3C), 127.6, 127.4, 126.3, 123.0, 119.5 (d, $J = 8$ Hz, 2C), 115.6 (d, $J = 22$ Hz, 2C), 88.2, 85.5, 53.7, 44.1, 29.0; Spectroscopic data are in agreement with the published data.^{S14}

2-(4-methoxyphenyl)-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (4c)



General procedure III was followed with 2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (60 mg, 0.25 mmol), $\text{Ru}(\text{bpy})_3\text{Cl}_2$ (1.9 mg, 0.0025 mmol), in CH_3CN (1 mL). The reaction was pumped through microflow reactor irradiated with 11W CFL lamp, for 2 h. Recipient flask contained $\text{CuOTf} \cdot \frac{1}{2}\text{C}_6\text{H}_6$ (12.6 mg, 0.025 mmol) and phenylacetylene (137 μl , 1.25 mmol) in 1 ml CH_2Cl_2 . The mixture was stirred overnight, evaporated and purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (69mg, 82 %) as yellowish oil. $R_f = 0.70$ (Petrol Ether/EtOAc : 7/1); ^1H NMR (CDCl_3 , 400 MHz): δ 7.38-7.35 (m, 1H), 7.31-7.27 (m, 2H), 7.26 – 7.17 (m, 6H), 7.15 – 7.08 (m, 2H), 6.94 – 6.87 (m, 2H), 5.52 (s, 1H), 3.79 (s, 3H), 3.70 – 3.60 (m, 1H), 3.56 (ddd, $J = 8.9, 6.1, 1.9$ Hz, 1H), 3.15 (ddd, $J = 16.7, 10.7, 6.2$ Hz, 1H), 2.98 – 2.89 (m, 1H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 154.2, 144.1, 135.4, 134.0, 131.7, 129.0, 128.0, 127.9, 127.5, 127.1, 126.1, 123.1, 120.2, 114.4, 88.5, 85.5, 55.6, 54.4, 44.2, 29.0; Spectroscopic data are in agreement with the published data.^{S13}

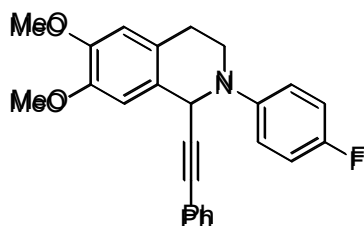
6,7-dimethoxy-2-phenyl-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (4d)



General procedure III was followed with 6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinoline (67.3 mg, 0.25 mmol), $\text{Ru}(\text{bpy})_3\text{Cl}_2$ (1.9 mg, 0.0025 mmol), in CH_3CN (1 mL). The reaction was pumped through microflow reactor irradiated with 11W CFL lamp,

for 2 h. Recipient flask contained $\text{CuOTf} \cdot \frac{1}{2}\text{C}_6\text{H}_6$ (12.6 mg, 0.025 mmol) and phenylacetylene (137 μl , 1.25 mmol) in 1 ml CH_2Cl_2 . The mixture was stirred overnight, evaporated and purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (78.5 mg, 85 %) as yellowish oil. **Rf** = 0.15 (Petrol Ether/EtOAc : 7/1); **^1H NMR** (CDCl_3 , 400 MHz): δ 7.39–7.33 (m, 4 H), 7.28–7.26 (m, 2 H), 7.17 (d, J = 8 Hz, 2 H), 6.96 (t, J = 7.0 Hz, 1 H), 6.93 (s, 1 H), 6.72 (s, 1 H), 5.63 (s, 1 H), 3.98 (s, 3 H), 3.92 (s, 3 H), 3.88–3.79 (m, 1 H), 3.68 (m, 1 H), 3.10 (ddd, J = 6.0, 10.9, 16.0 Hz, 1 H), 2.92 (dt, J = 3, 16 Hz, 1 H); **^{13}C NMR** (CDCl_3 , 101 MHz): δ 149.8, 148.4, 147.6, 131.9, 129.4, 128.4, 128.1, 127.3, 126.6, 123.2, 119.8, 116.9, 111.4, 110.3, 88.9, 84.9, 56.2, 55.9, 52.3, 43.5, 28.6; Spectroscopic data are in agreement with the published data.^{S15}

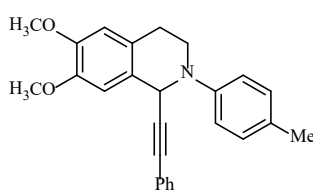
2-(4-fluorophenyl)-6,7-dimethoxy-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (4e)



General procedure III was followed with 2-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (71.8 mg, 0.25 mmol), $\text{Ru}(\text{bpy})_3\text{Cl}_2$ (1.9 mg, 0.0025 mmol), in CH_3CN (1 mL). The reaction was pumped through microflow reactor irradiated with 11W CFL lamp, for 2 h. Recipient flask contained $\text{CuOTf} \cdot \frac{1}{2}\text{C}_6\text{H}_6$ (12.6 mg, 0.025 mmol) and phenylacetylene (137 μl , 1.25 mmol) in 1 ml CH_2Cl_2 . The

mixture was stirred overnight, evaporated and purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (78.5 mg, 80 %) as yellowish oil. **Rf** = 0.24 (Petrol Ether/EtOAc : 7/1); **^1H NMR** (CDCl_3 , 400 MHz): δ 7.31 – 7.17 (m, 5H), 7.11 – 7.05 (m, 2H), 7.05 – 6.98 (m, 2H), 6.84 (s, 1H), 6.66 (s, 1H), 5.46 (s, 1H), 3.90 (s, 1H), 3.88 (s, 1H), 3.62 – 3.56 (m, 2H), 3.11 – 3.02 (m, 1H), 2.84 (dt, J = 15.9, 3.2 Hz, 1H). **^{13}C NMR** (CDCl_3 , 101 MHz): δ 158.7, 156.8, 148.6, 147.9, 146.7, 131.9, 128.4, 127.2, 126.3, 123.1, 119.8, 119.7, 115.8, 115.6, 111.6, 110.4, 88.5, 85.5, 56.3, 56.1, 53.7, 44.3, 28.7; **IR** (ATR): ν = 2933 (w), 2833 (w), 1611 (w), 1509 (vs), 1463 (m), 1247 (s), 1118 (s), 1027 (w), 816 (w); **HRMS** (ESI) m/z calculated for $\text{C}_{25}\text{H}_{22}\text{FNO}_2^+$ ($[\text{M}^+]$) 387.1635, found 387.1631.

6,7-dimethoxy-1-(phenylethynyl)-2-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline (4f)



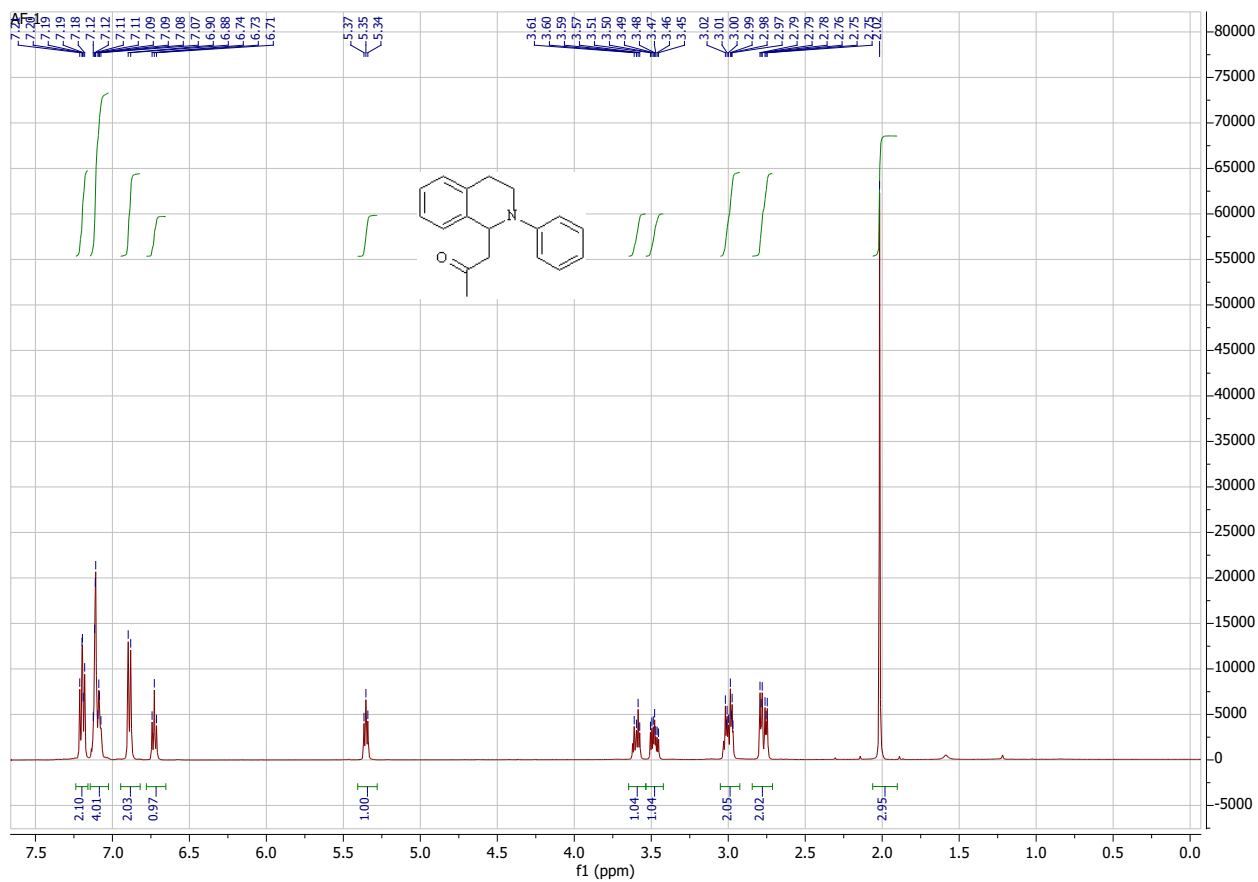
General procedure III was followed with 6,7-dimethoxy-2-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline (70.8 mg, 0.25 mmol), $\text{Ru}(\text{bpy})_3\text{Cl}_2$ (1.9 mg, 0.0025 mmol), in CH_3CN (1 mL). The reaction was pumped through microflow reactor irradiated with 11W CFL lamp, for 2 h. Recipient flask contained $\text{CuOTf} \cdot \frac{1}{2}\text{C}_6\text{H}_6$ (12.6 mg, 0.025 mmol) and phenylacetylene (137 μl , 1.25 mmol) in 1 ml CH_2Cl_2 . The mixture was stirred overnight, evaporated and purified by column chromatography on silica gel (petrolether/ethylacetate = 7/1) to give the title compound (86 mg, 90%) as yellowish oil. **Rf** = 0.29 (Petrol Ether/EtOAc : 7/1); **^1H NMR** (CDCl_3 , 400 MHz): δ 7.33–7.26 (m, 2H), 7.25–7.18 (m, 3H), 7.15–7.08 (m, 2H), 7.06–7.01 (m, 2H), 6.84 (s, 1H), 6.65 (s, 1H), 5.51 (s, 1H), 3.88 (d, J = 11 Hz, 6H), 3.73 – 3.56 (m, 2H), 3.06 (ddd, J = 16.6, 10.5, 6.4 Hz, 1H), 2.85–2.78 (m, 1H), 2.29 (s, 3H); **^{13}C NMR** (CDCl_3 , 101 MHz): δ 148.2, 147.6, 147.5, 131.7, 129.6, 129.4, 128.0, 127.9, 127.3, 126.3, 123.1, 117.6, 111.4, 110.2, 88.7, 84.9, 56.1, 55.9, 52.7, 43.7, 28.4, 20.45; **IR** (ATR): ν = 3000 (m), 2917 (m), 2832 (m), 1612 (m), 1516 (vs),

1463 (s), 1407 (s), 1260 (s), 1248 (s), 1213 (s), 1117 (s); **HRMS** (ESI) m/z calculated for $C_{26}H_{25}NO_2^+$ ([M⁺]) 383.1885, found 383.1878.

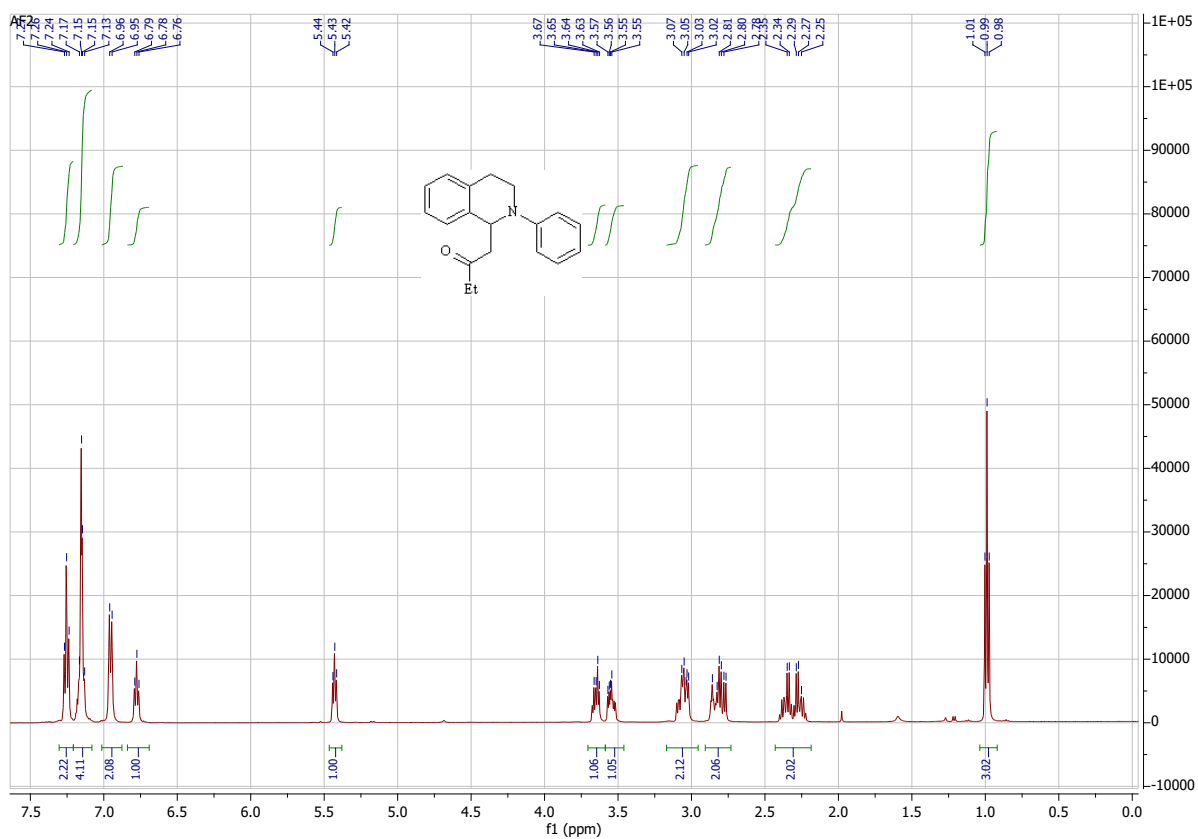
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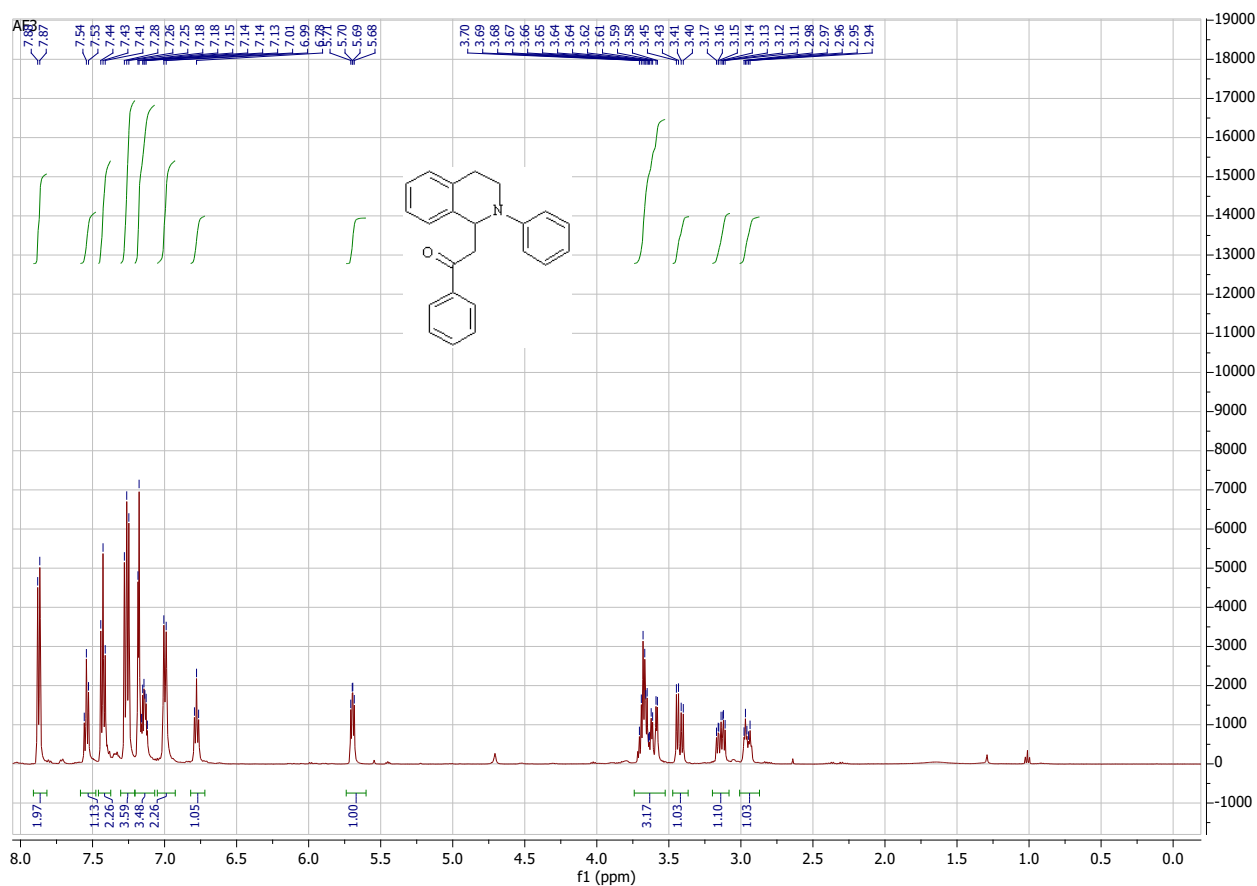
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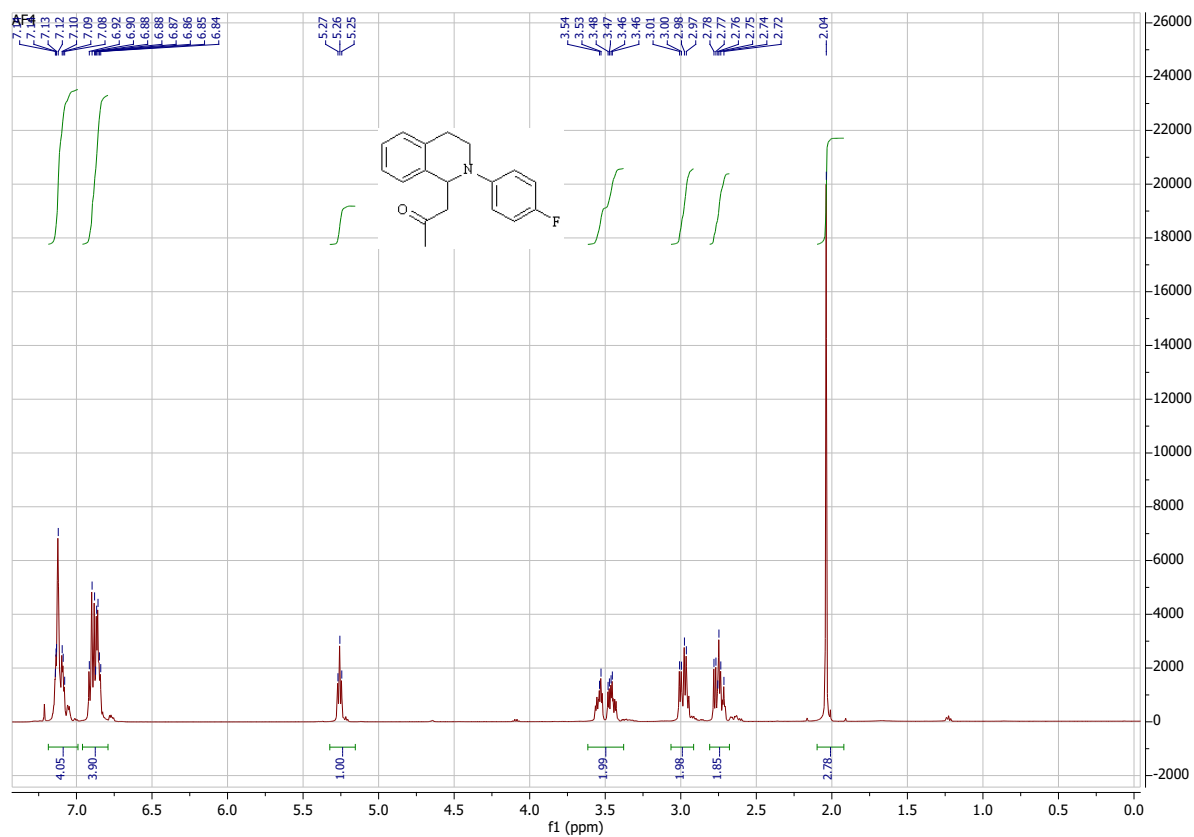
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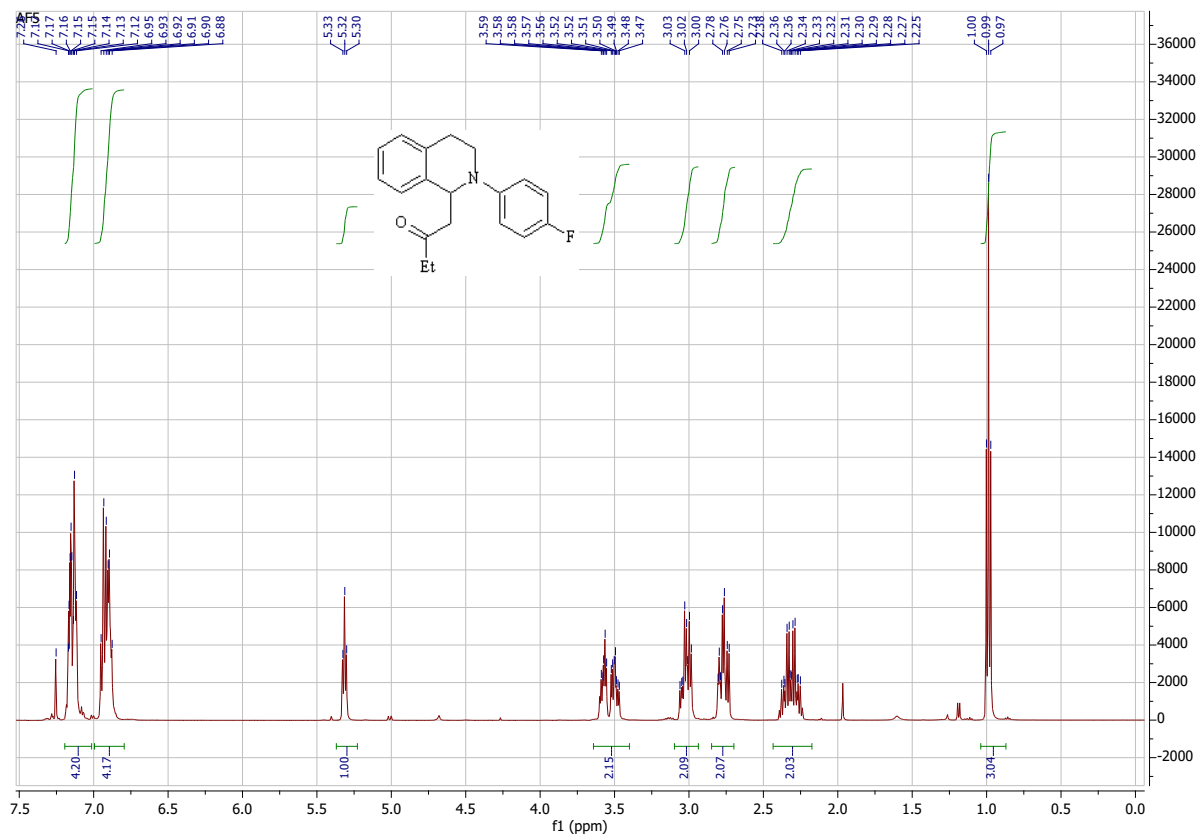
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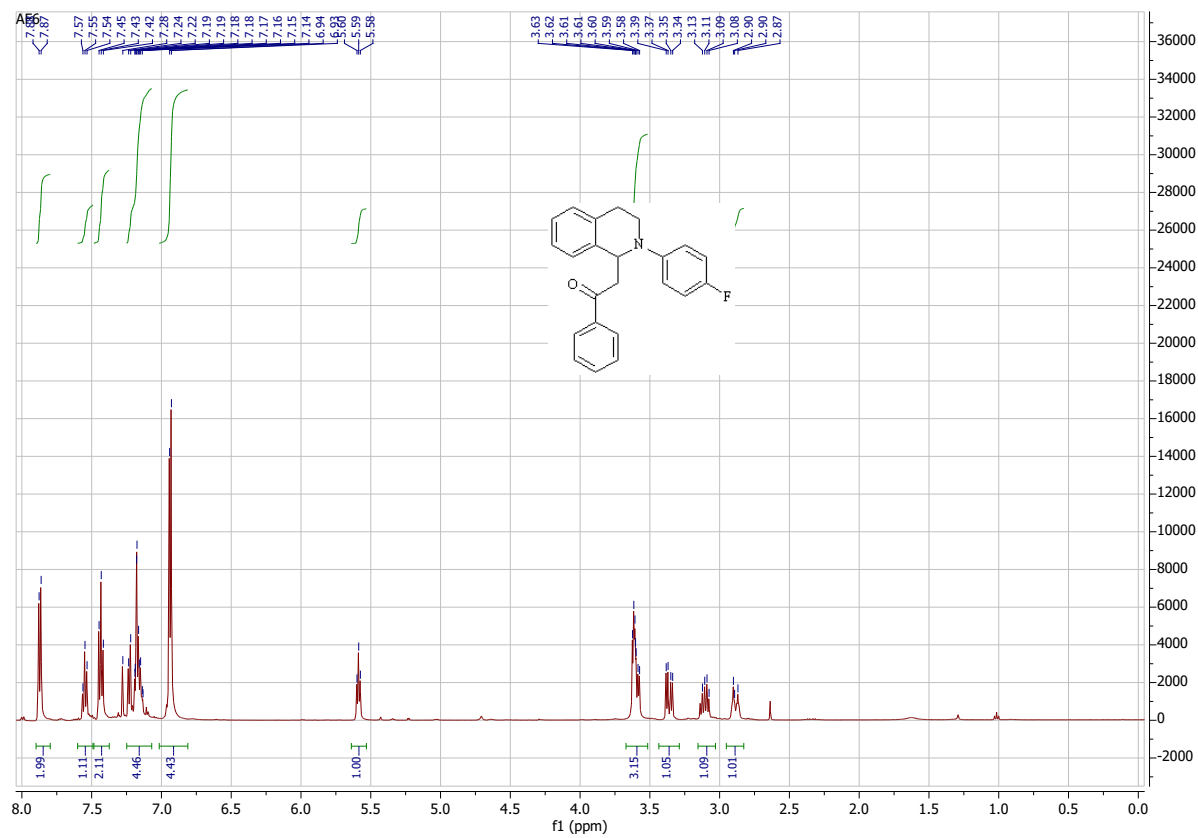
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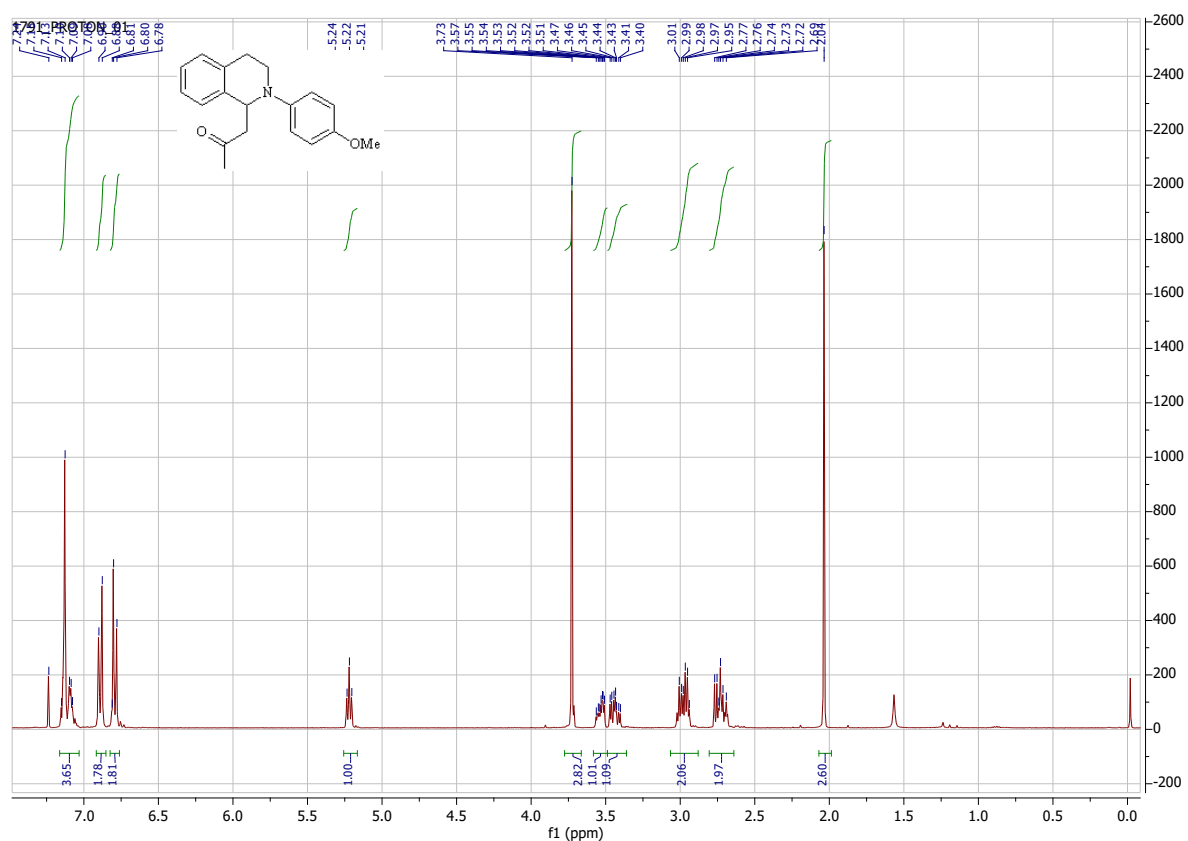
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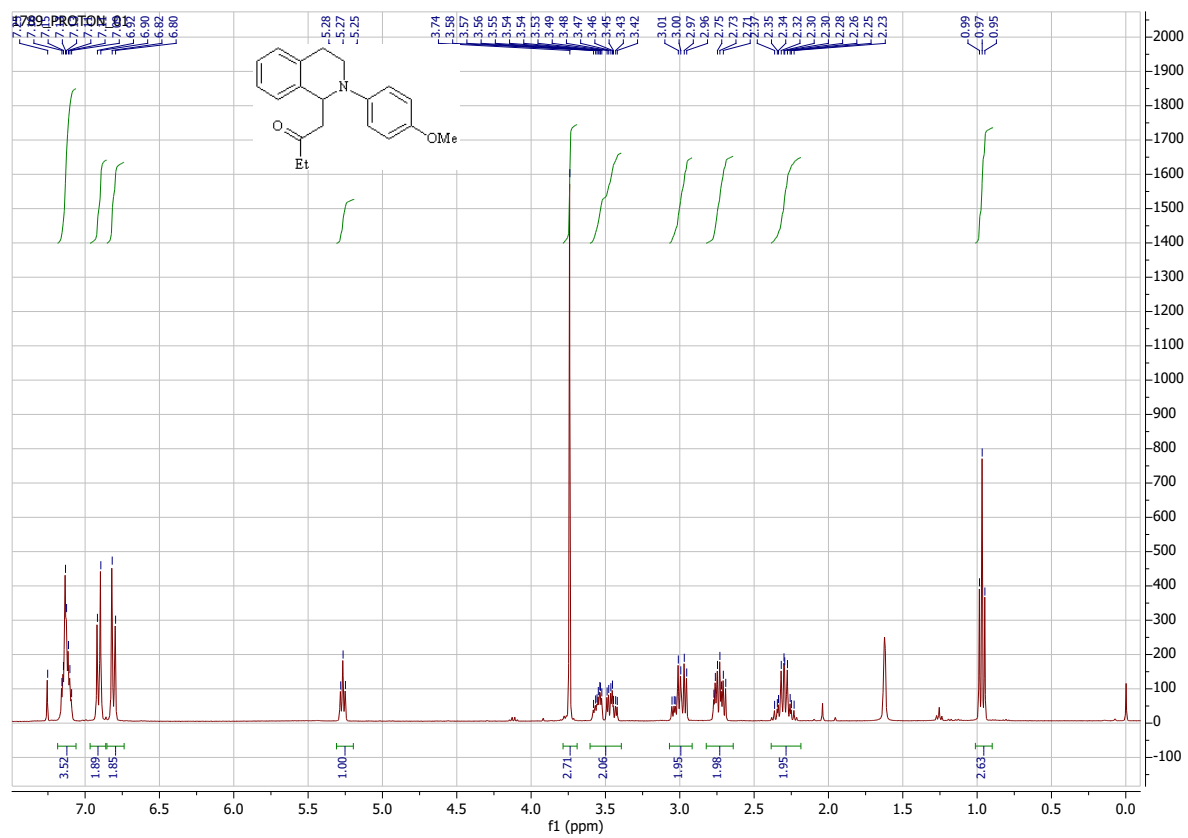
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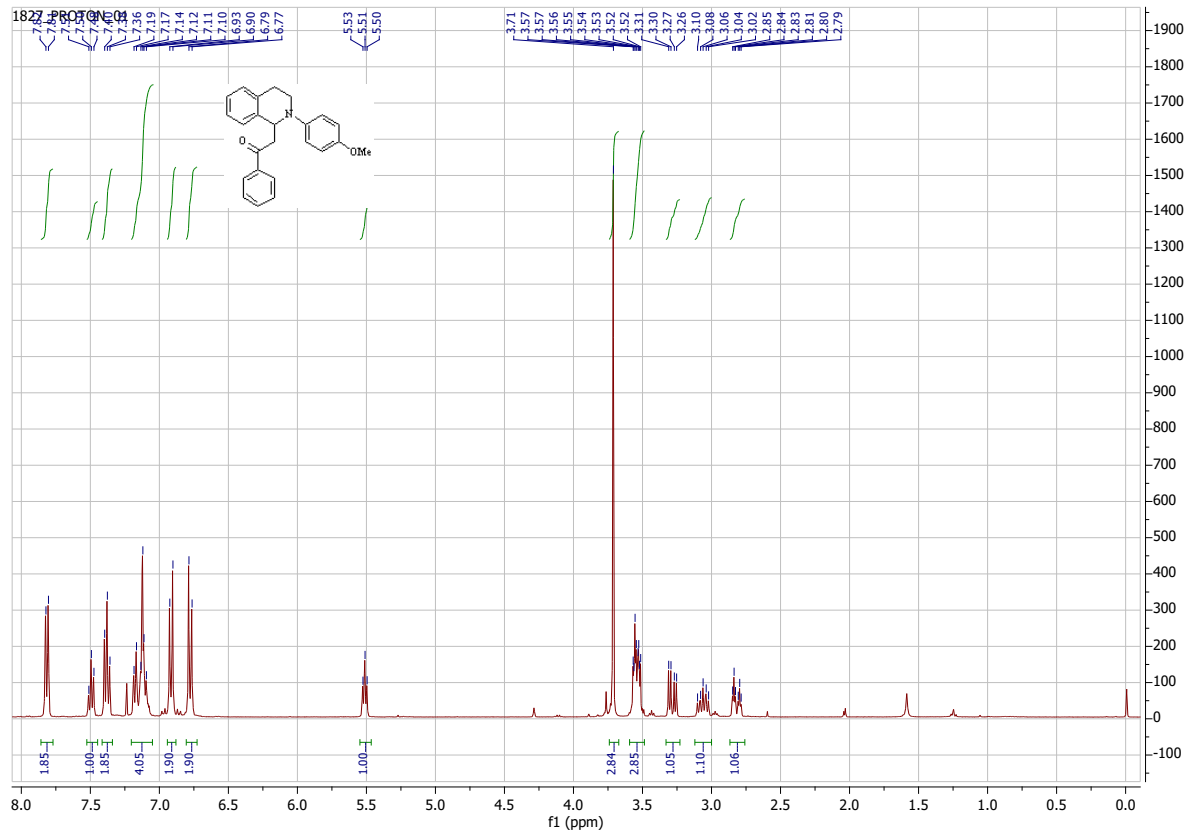
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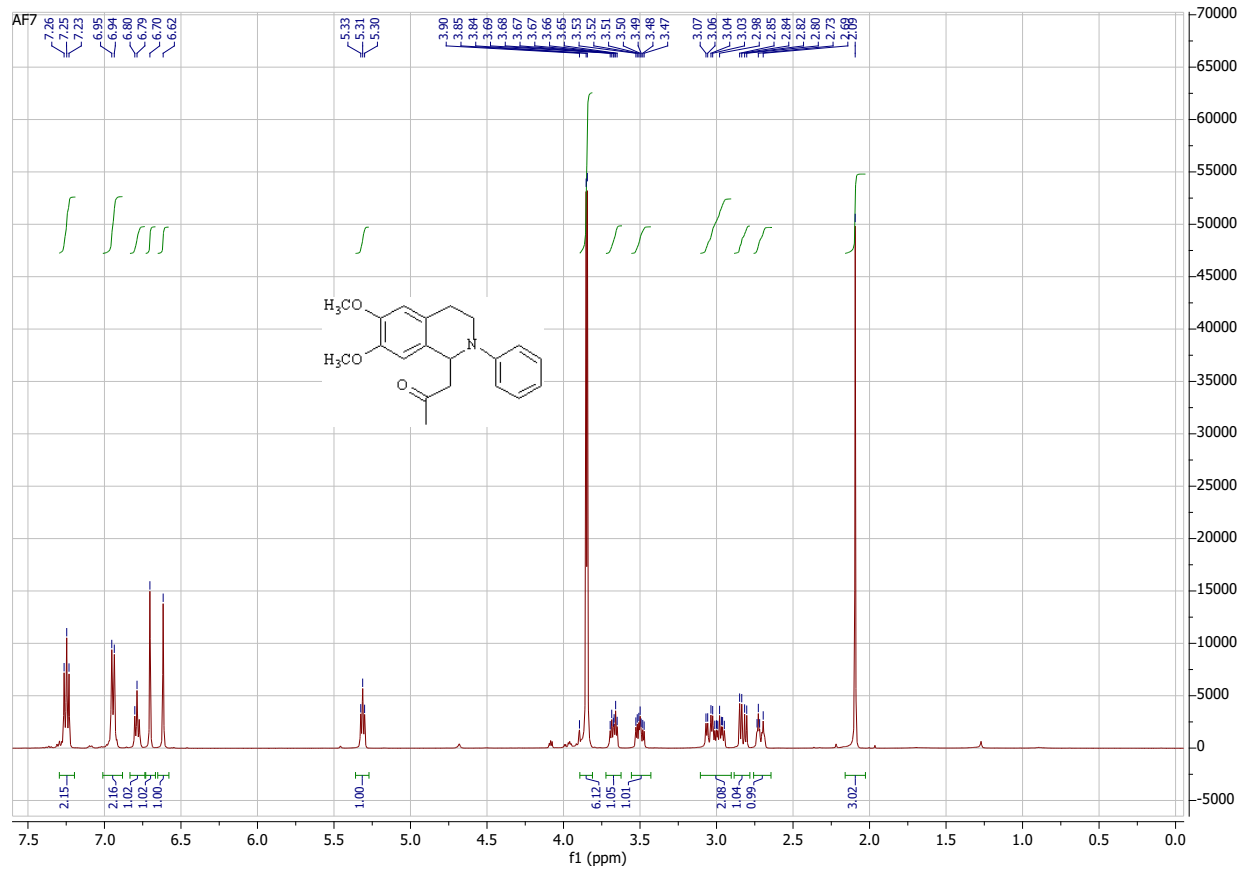
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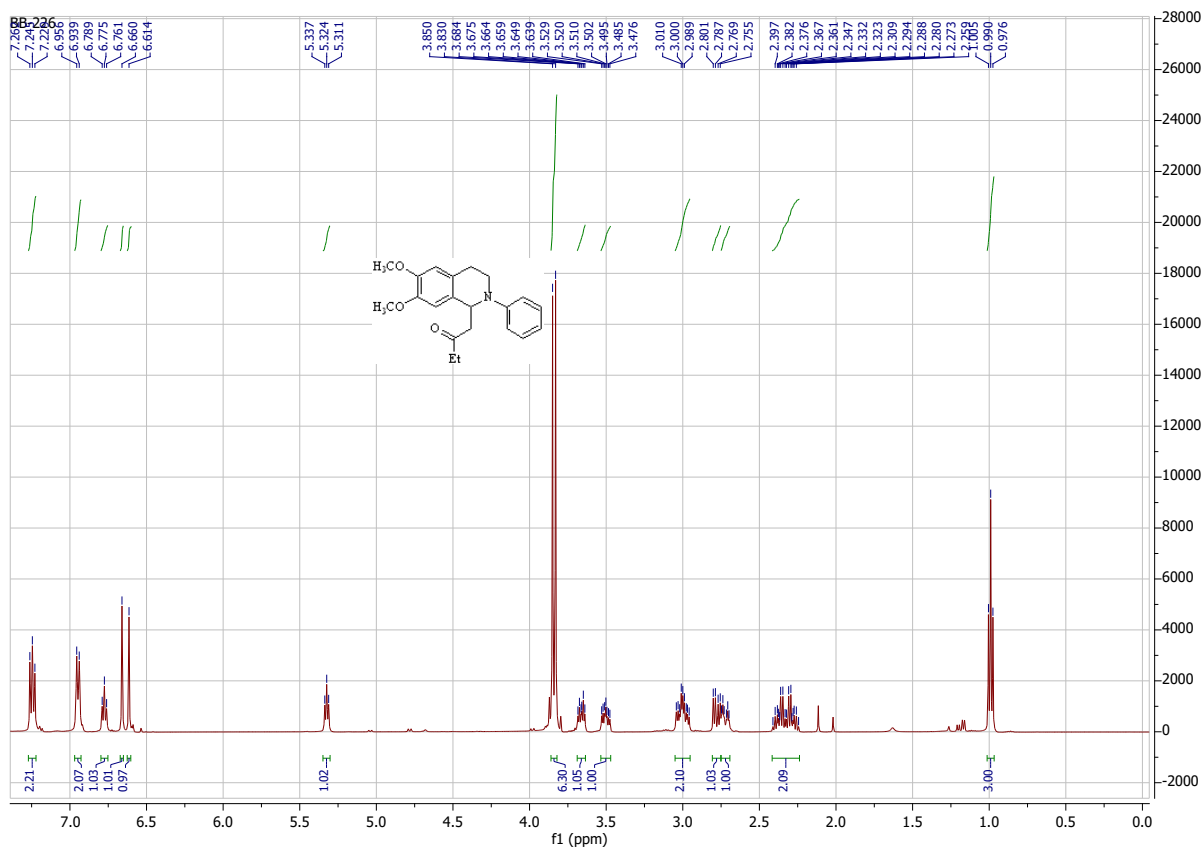
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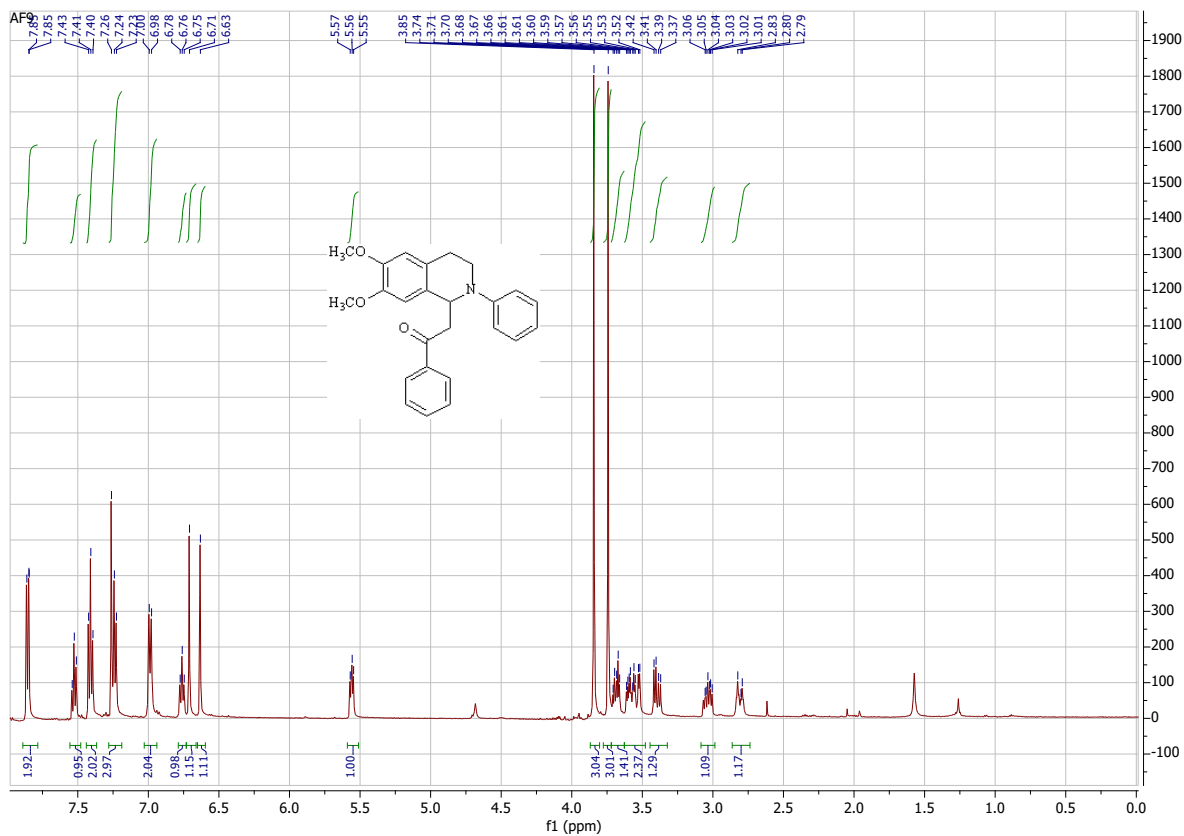
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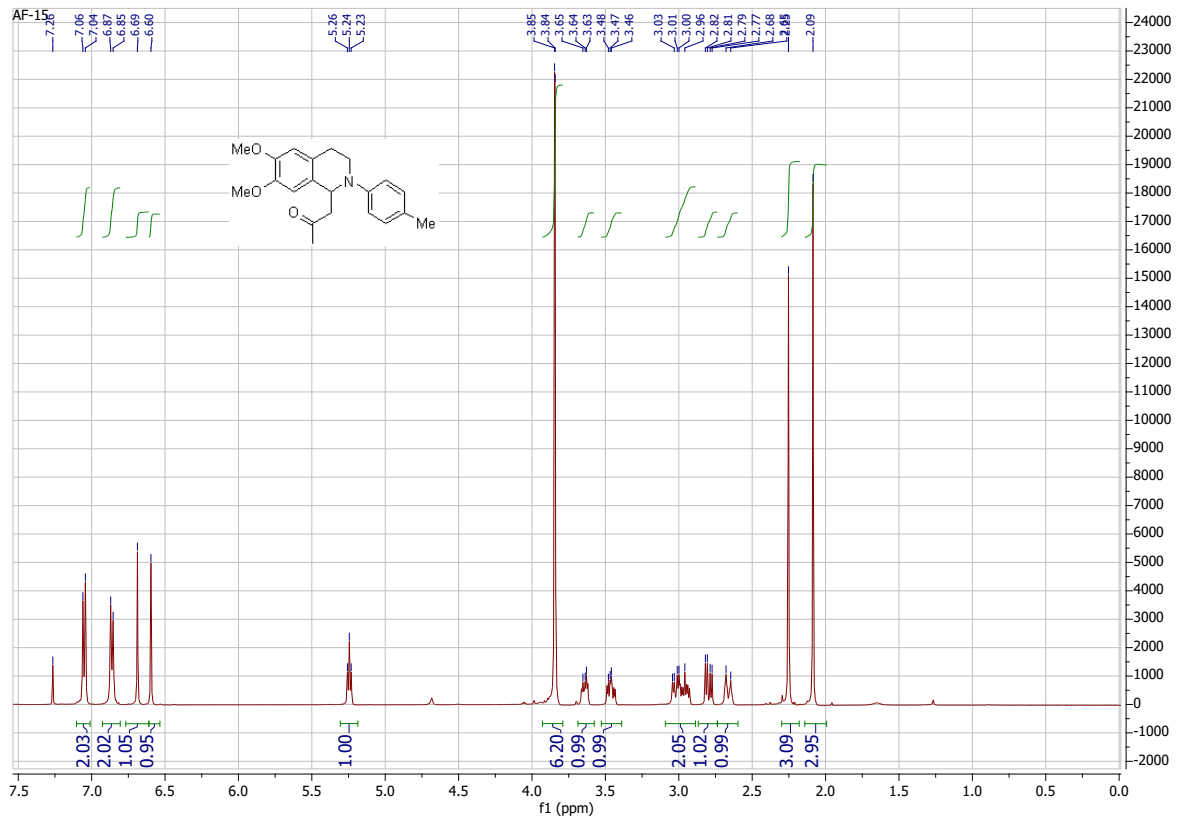
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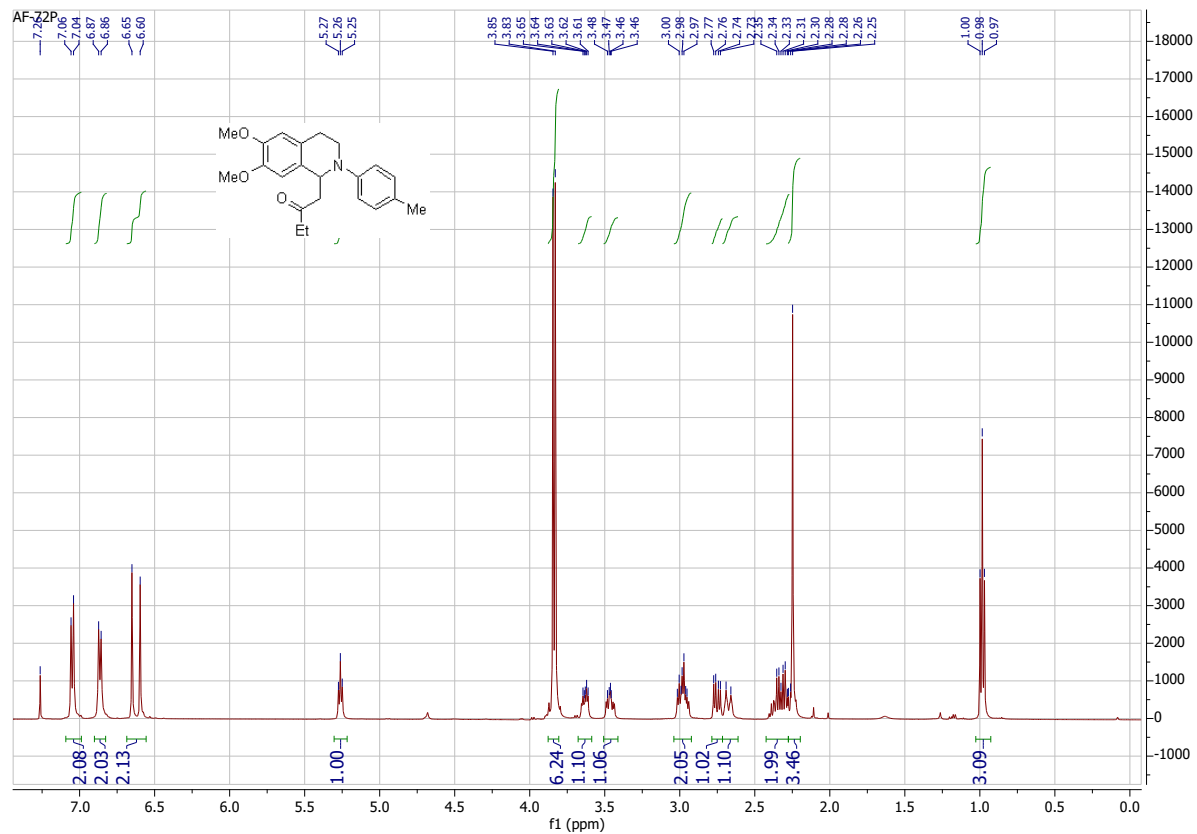
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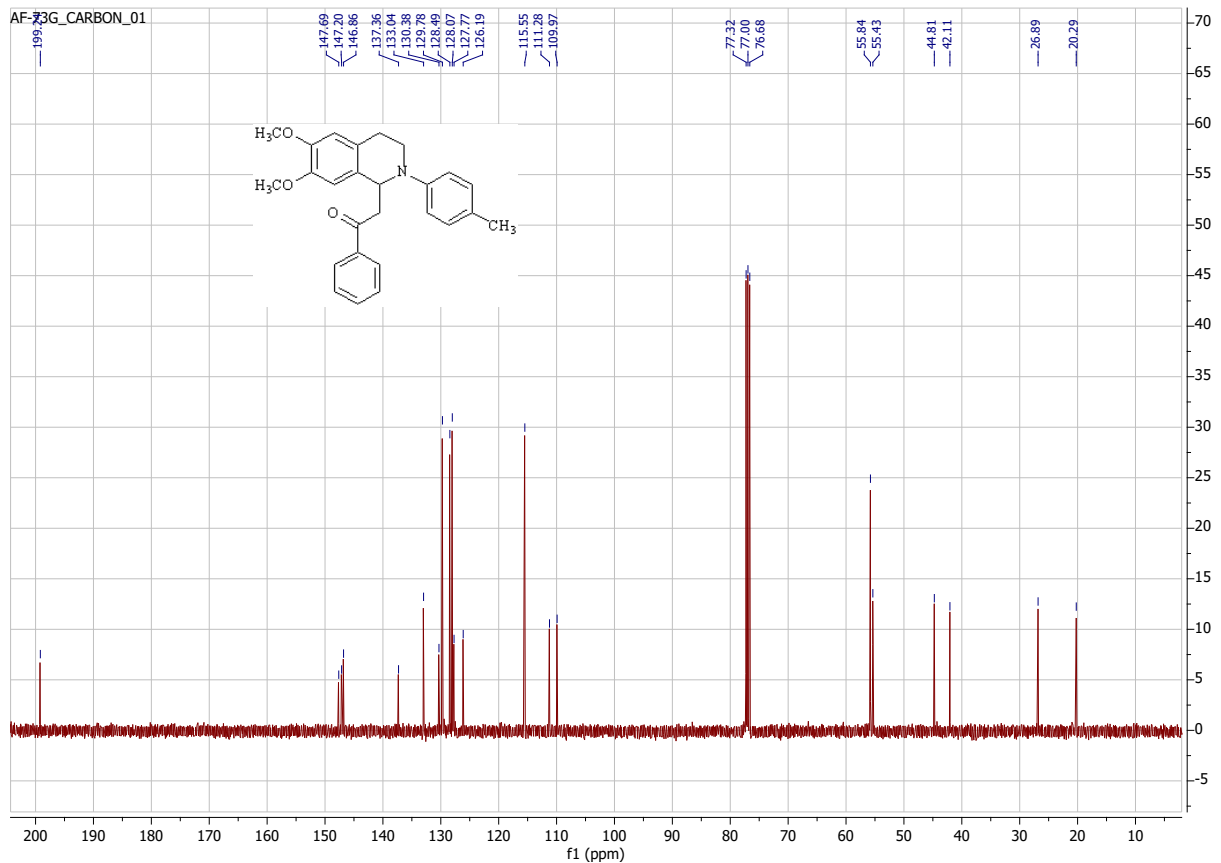
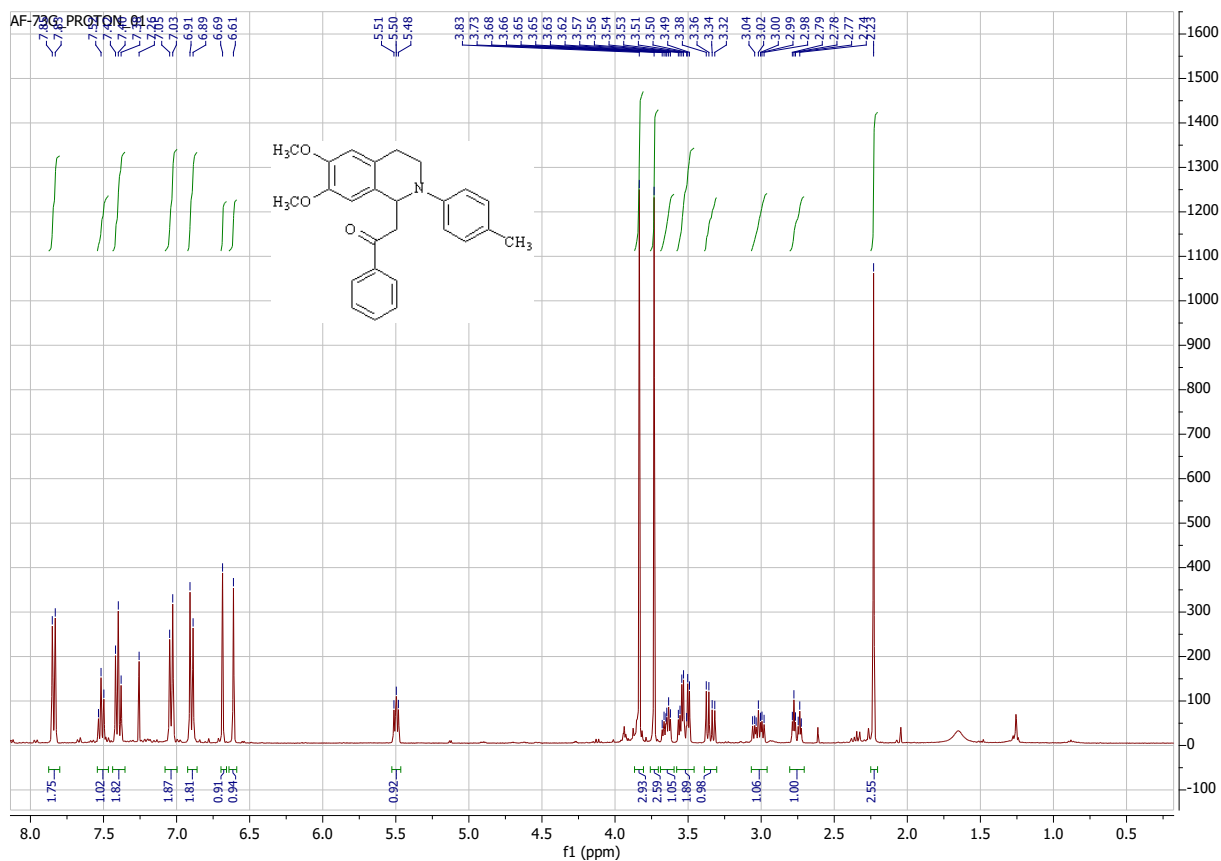
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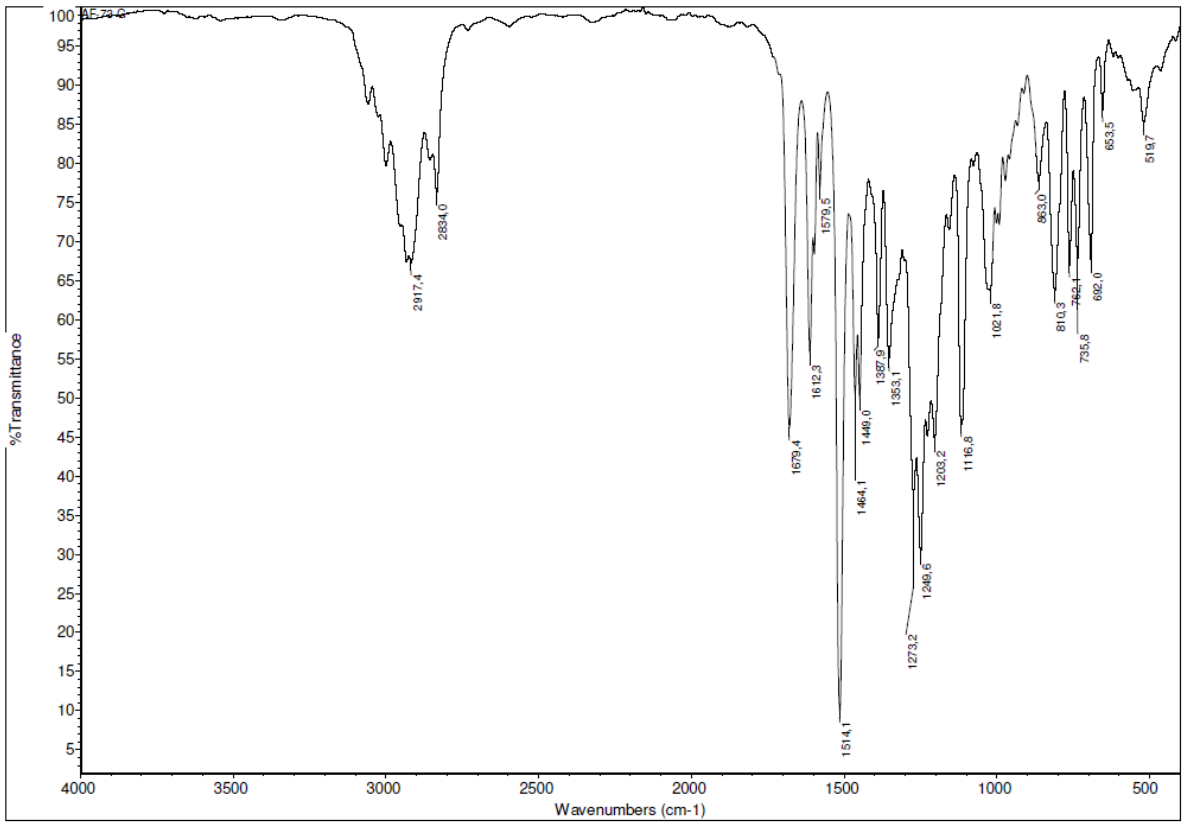


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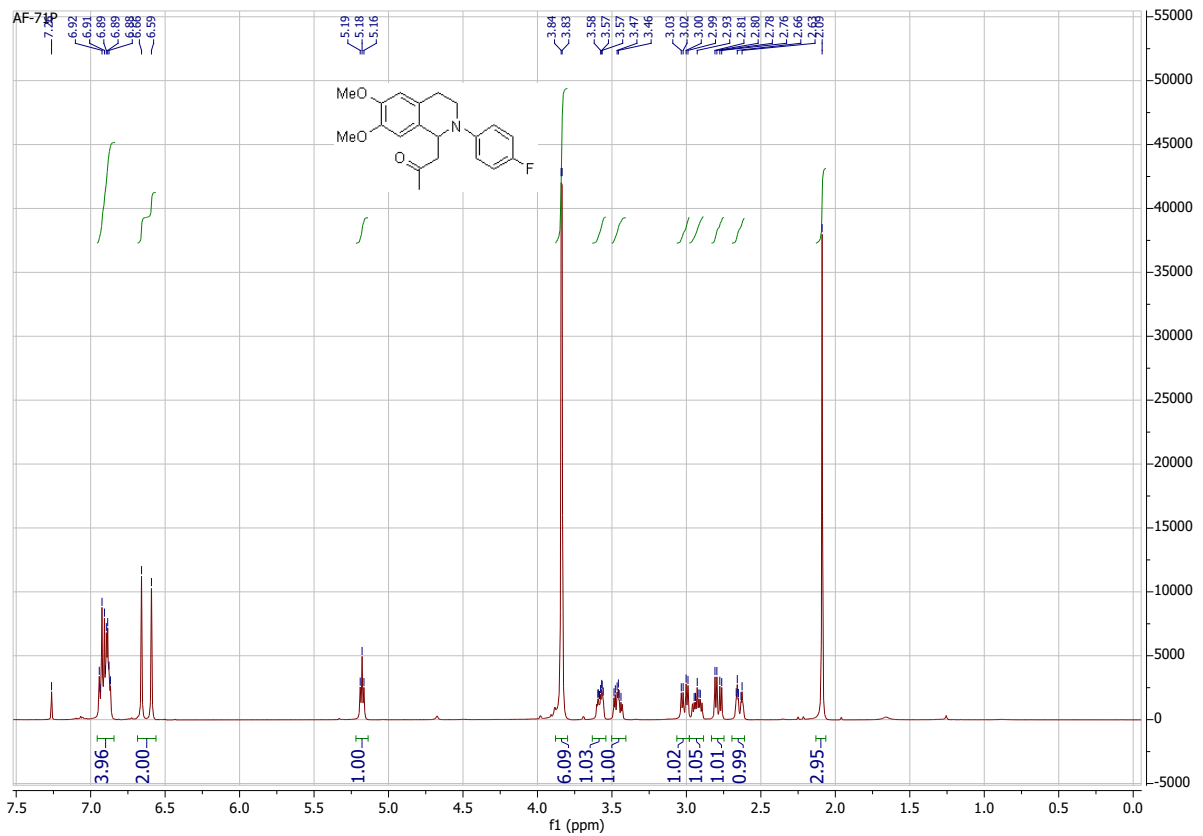


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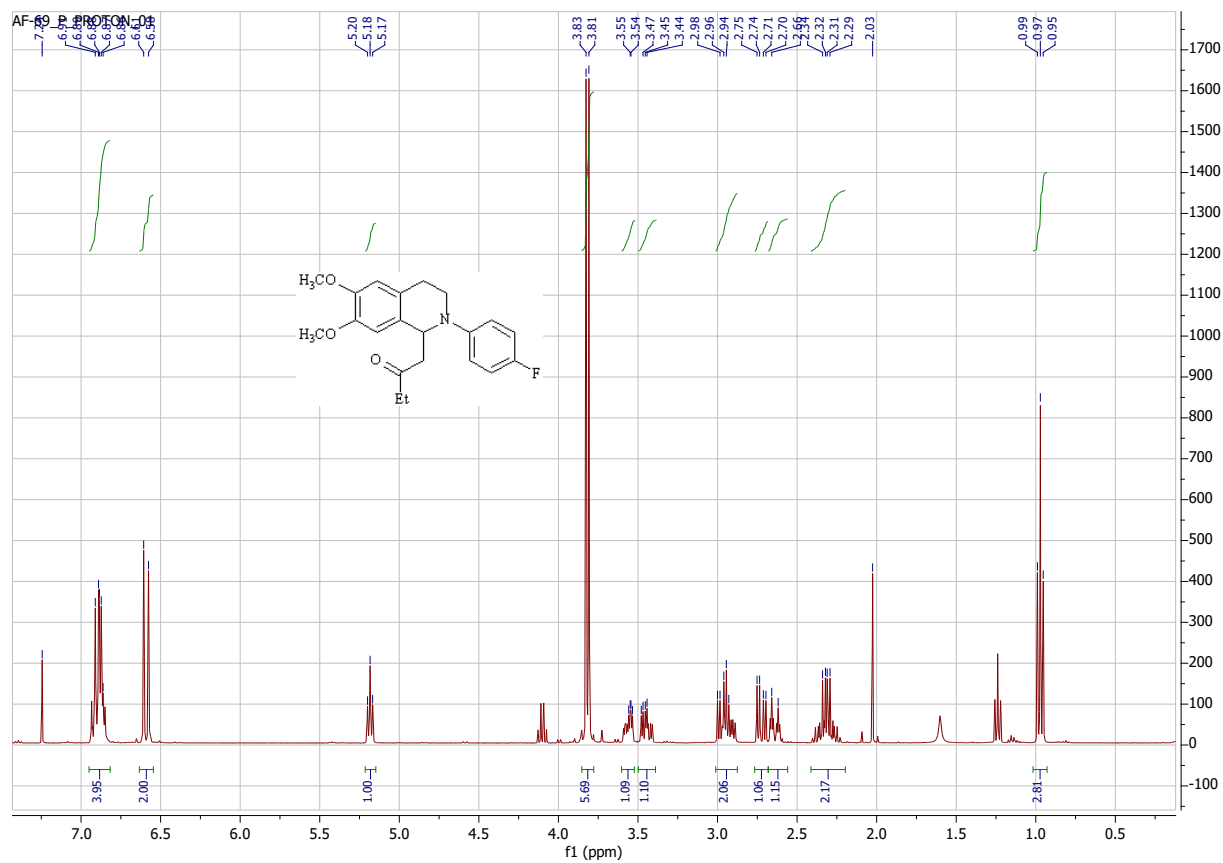




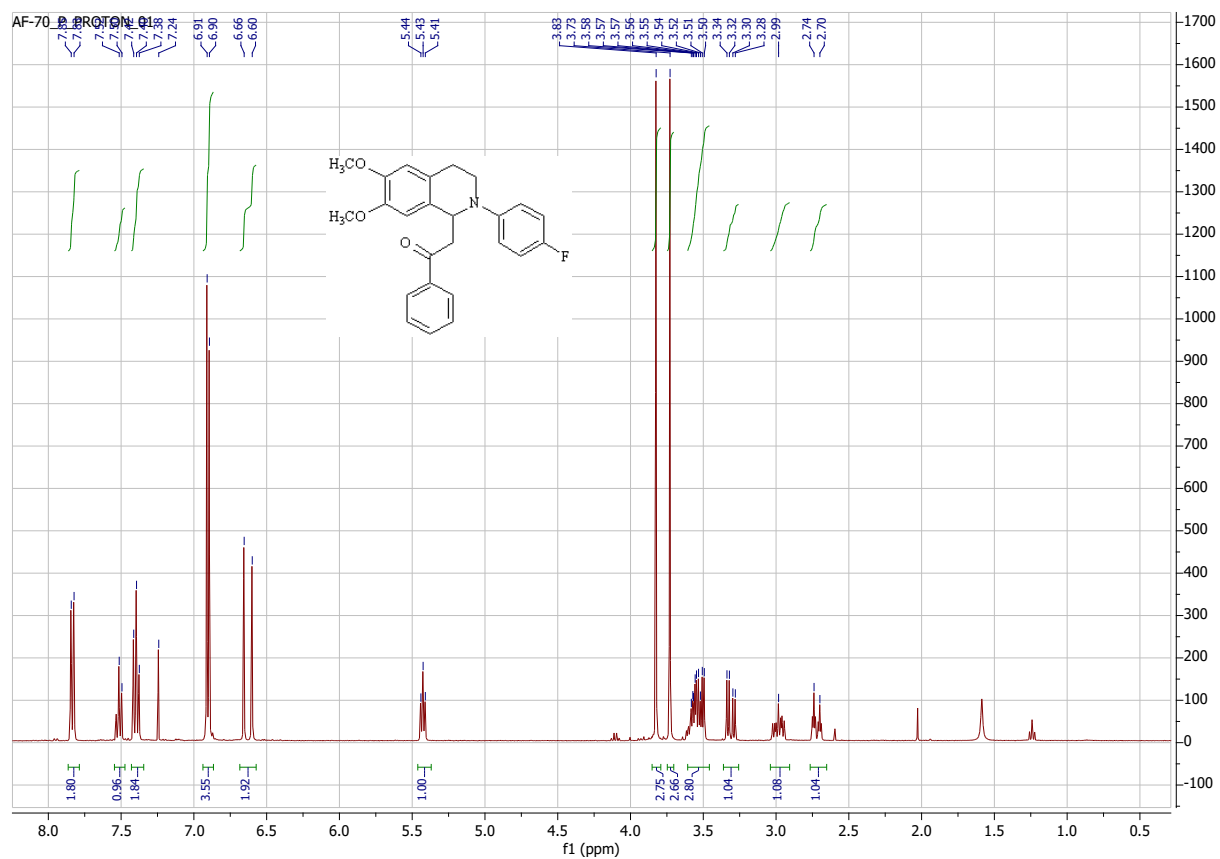
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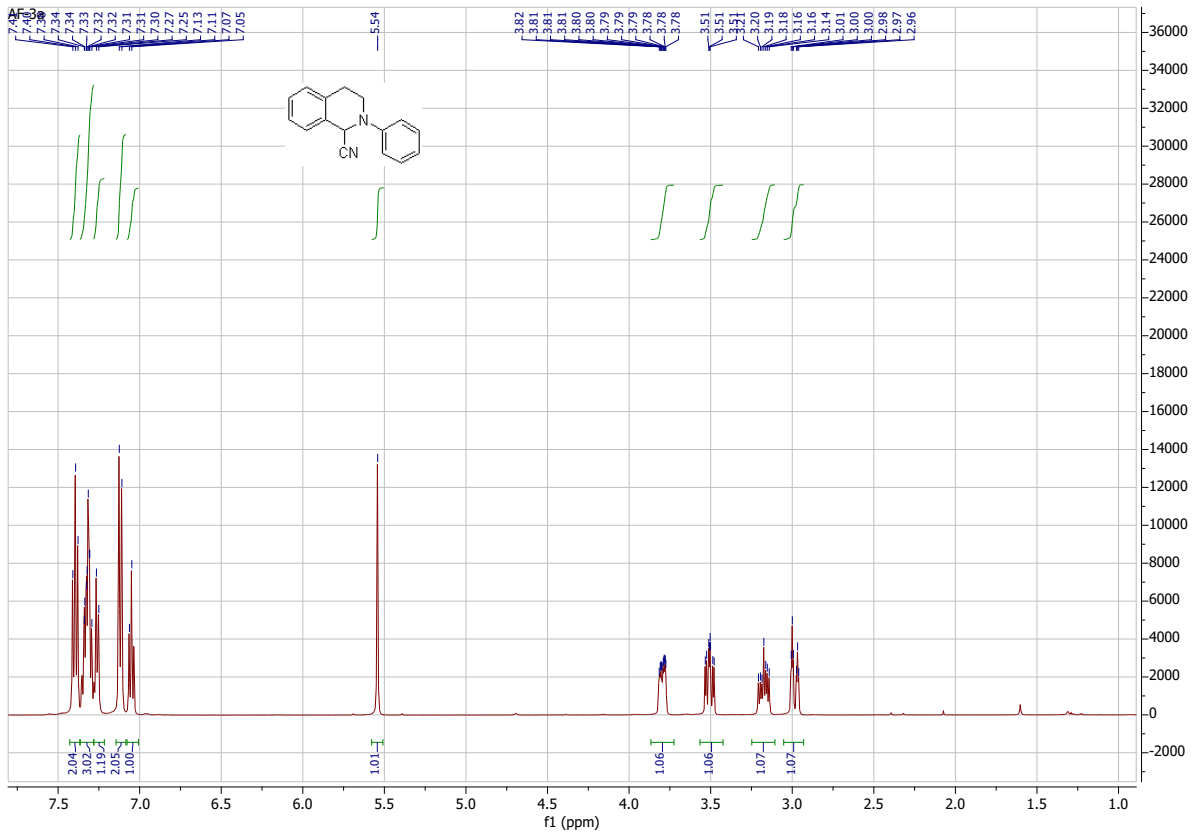
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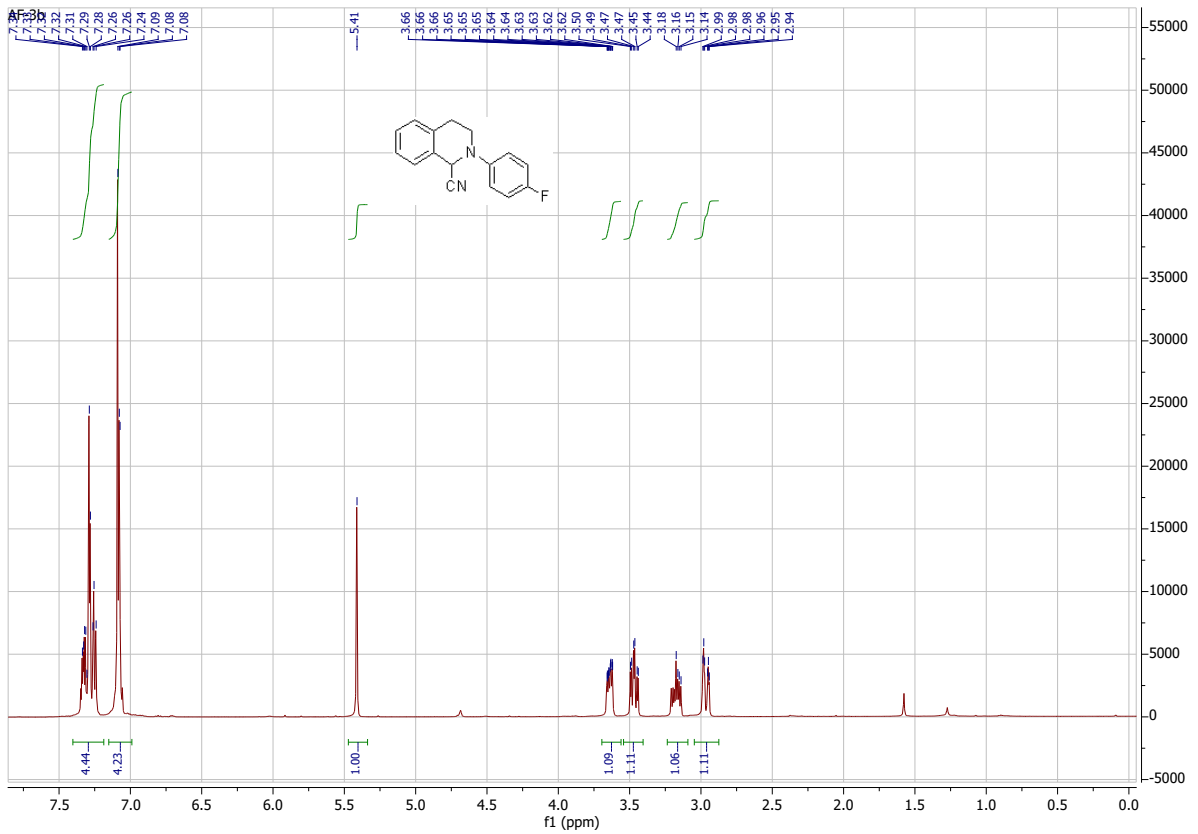
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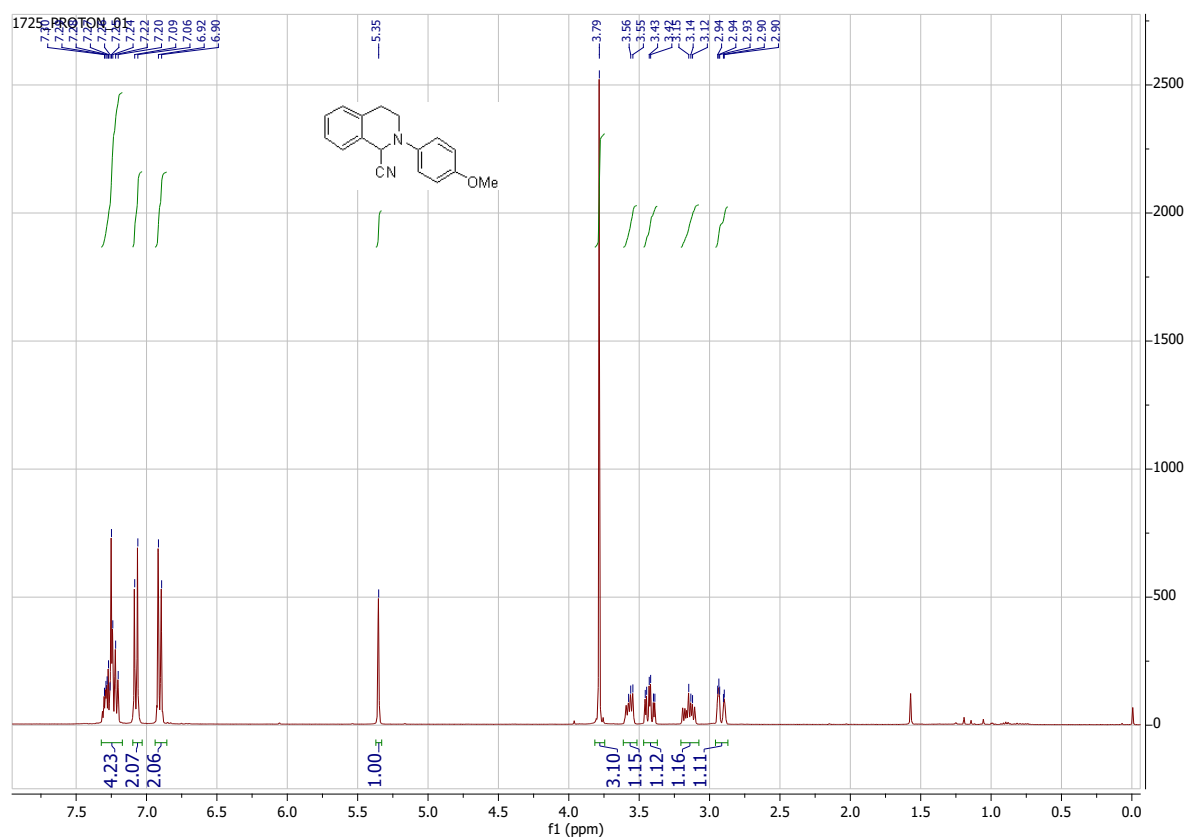
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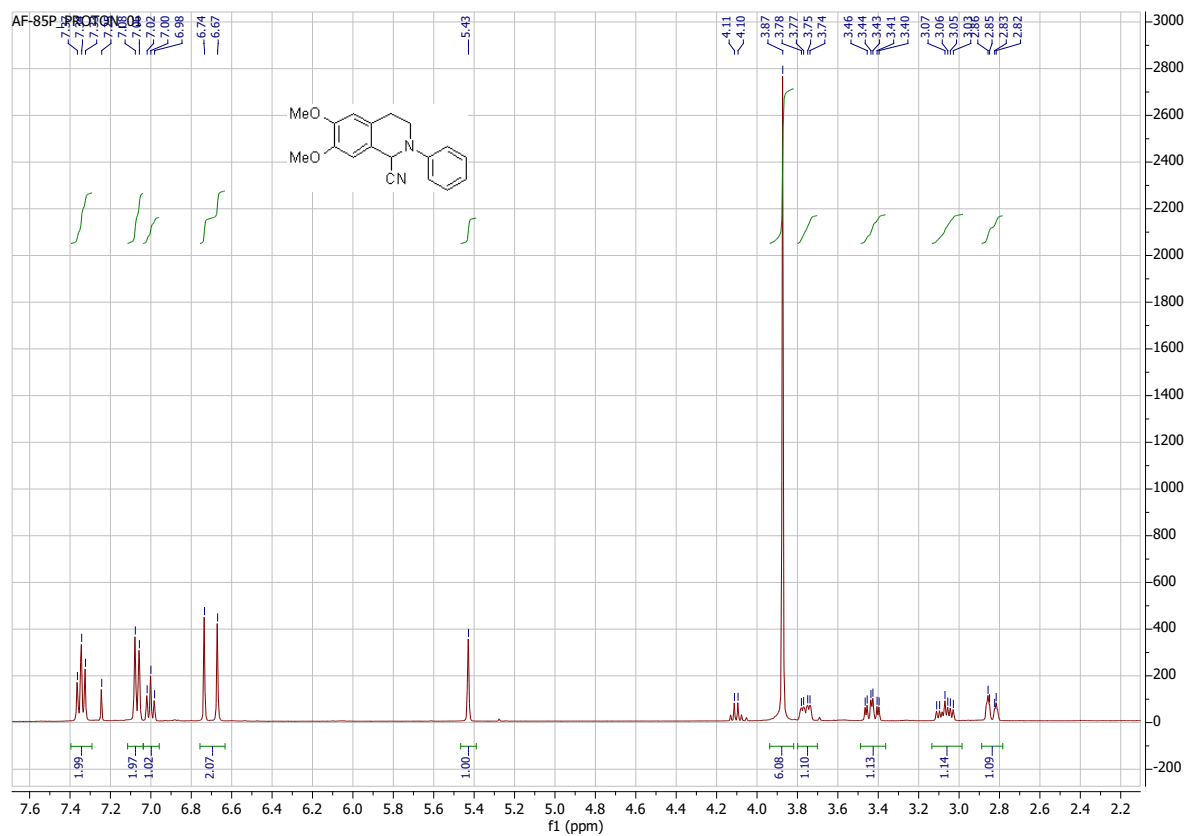
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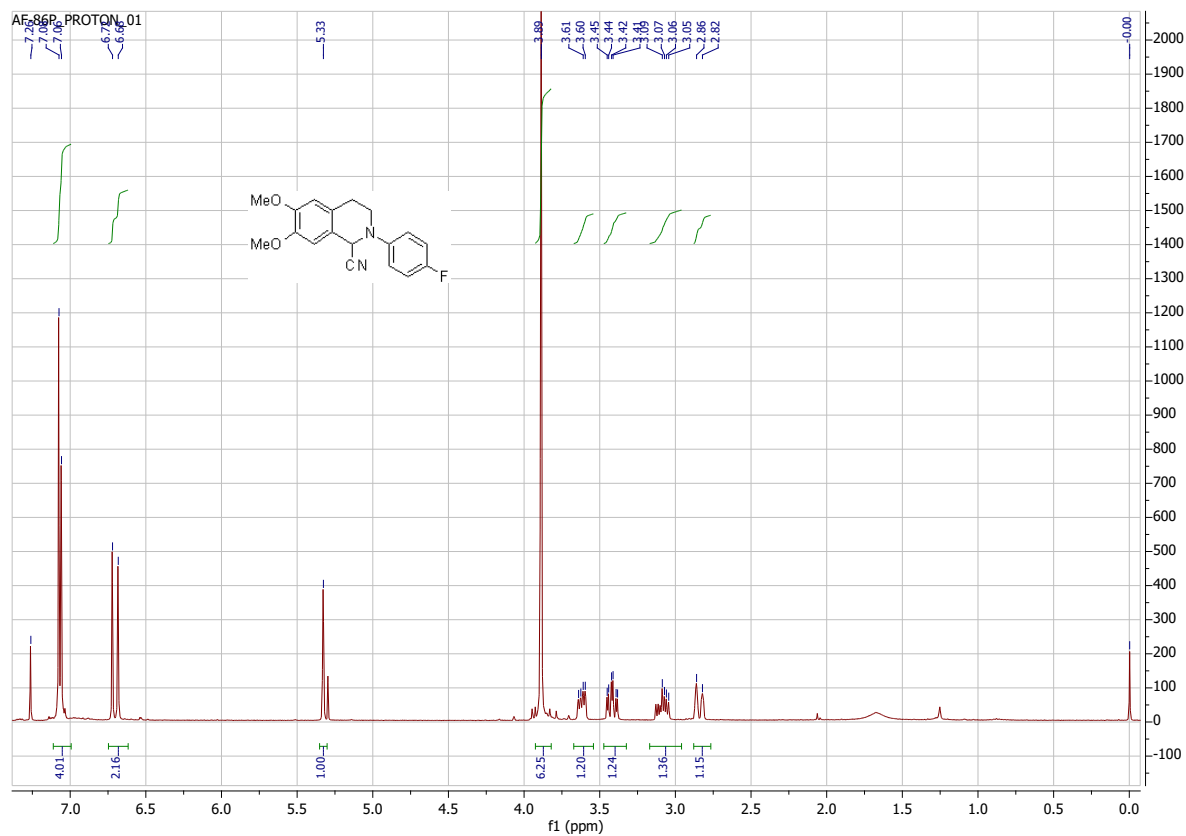
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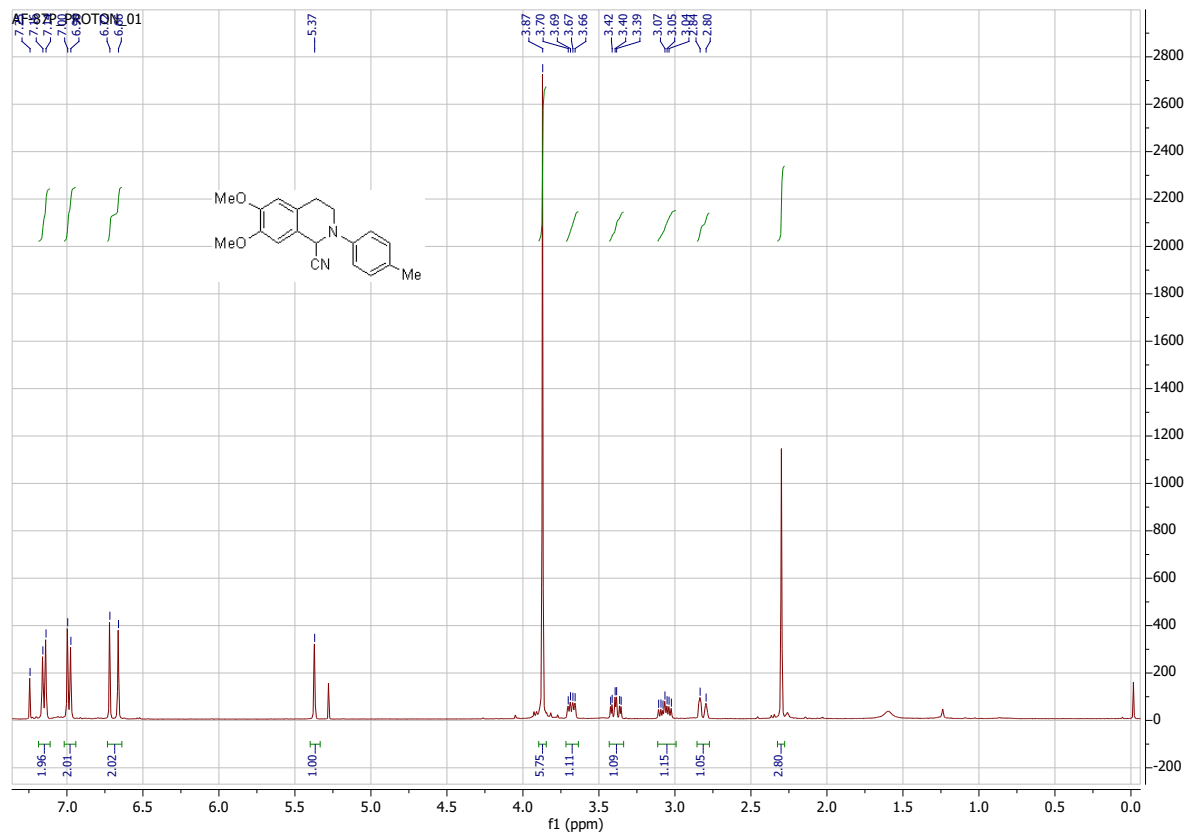
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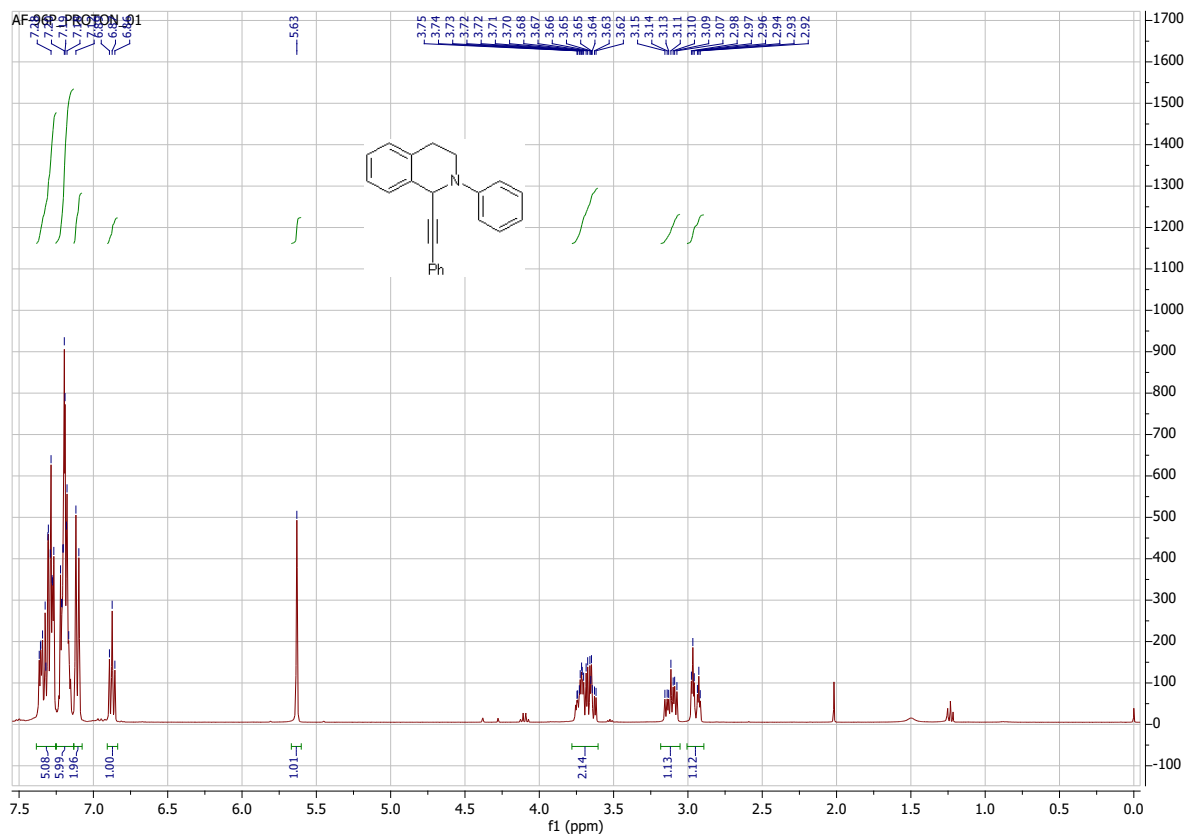
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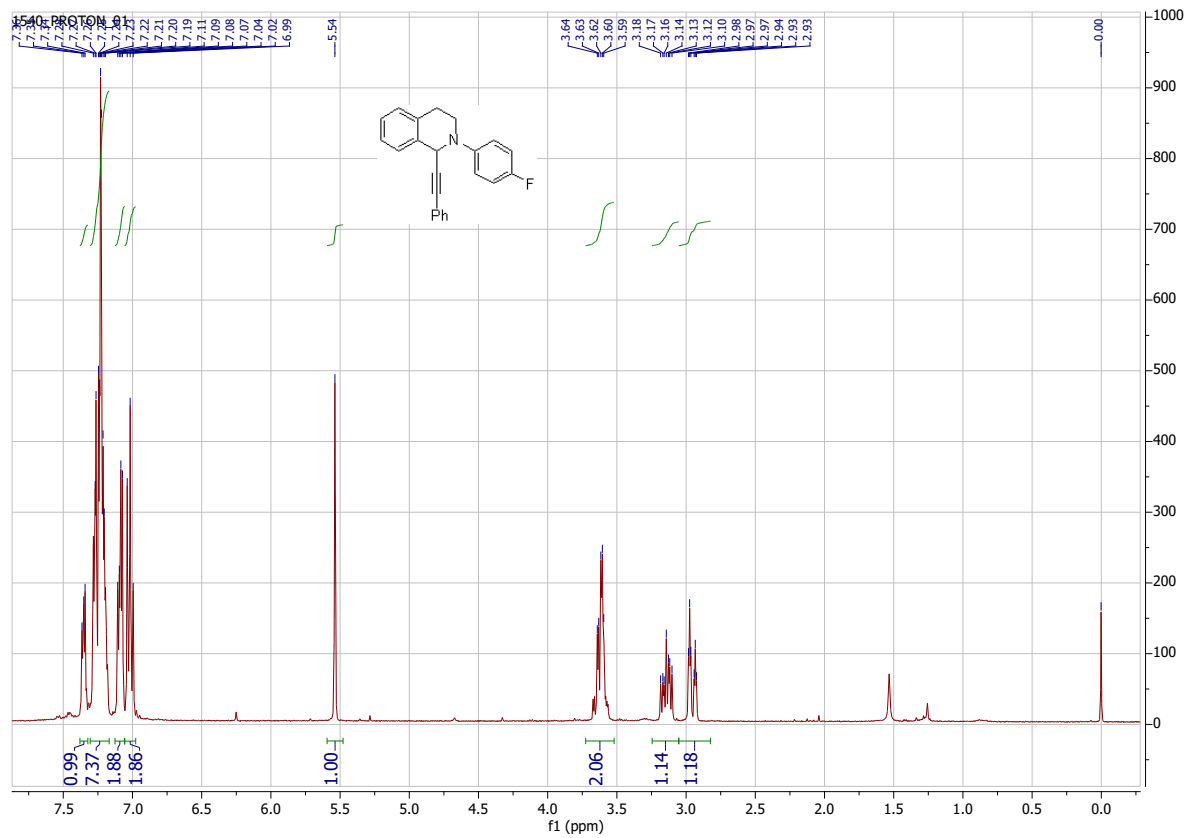
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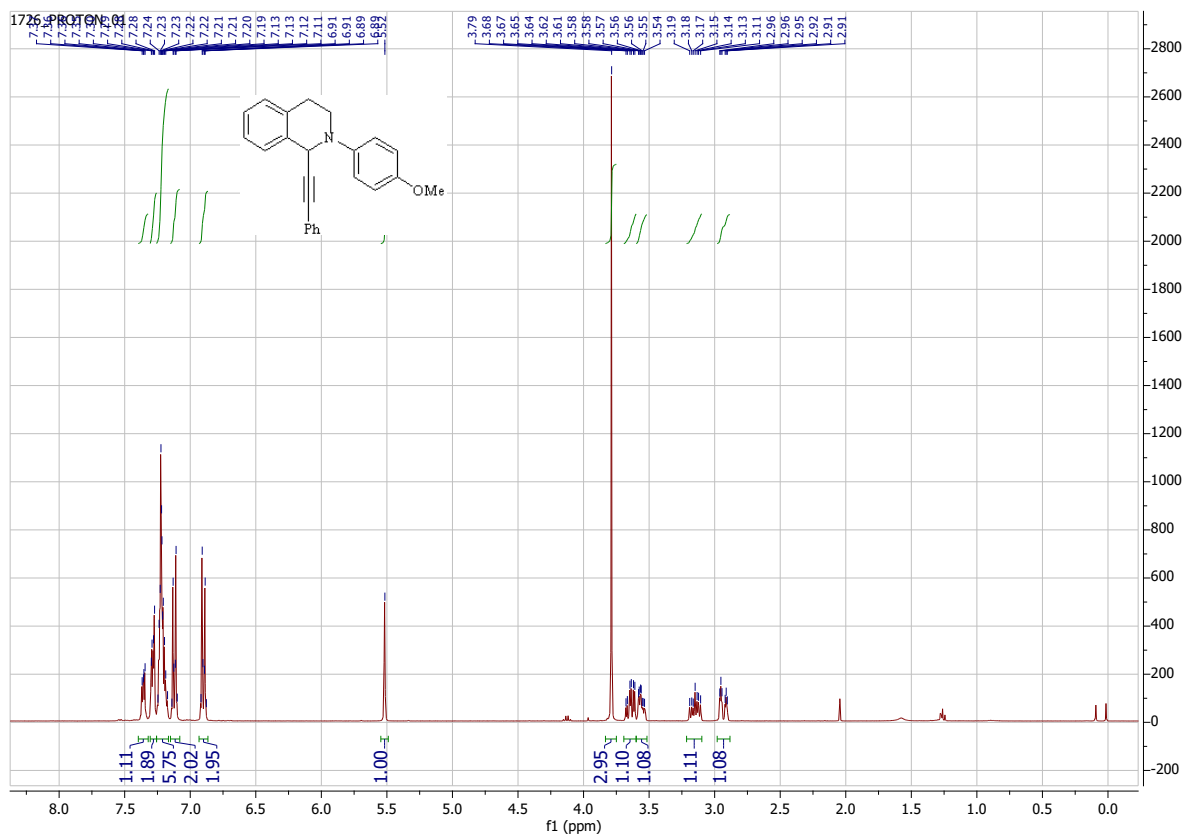
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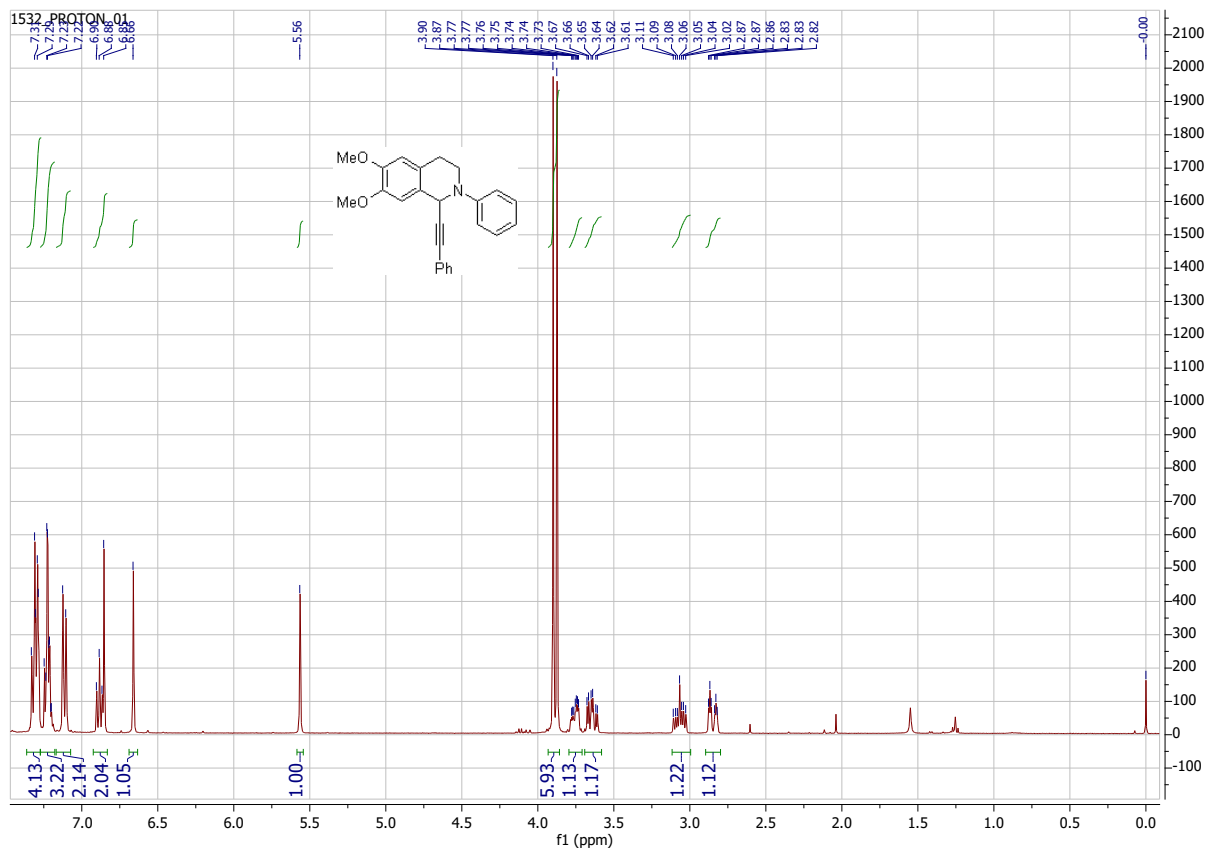
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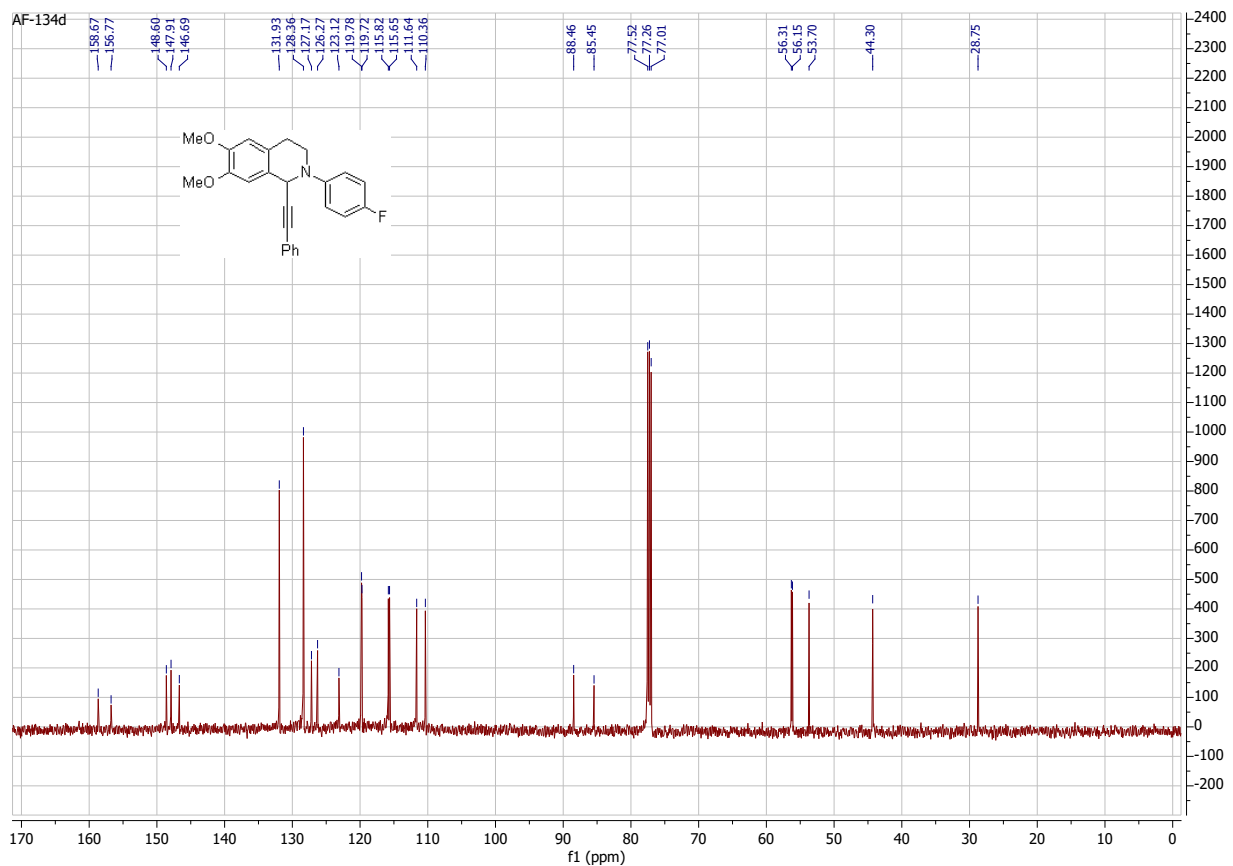
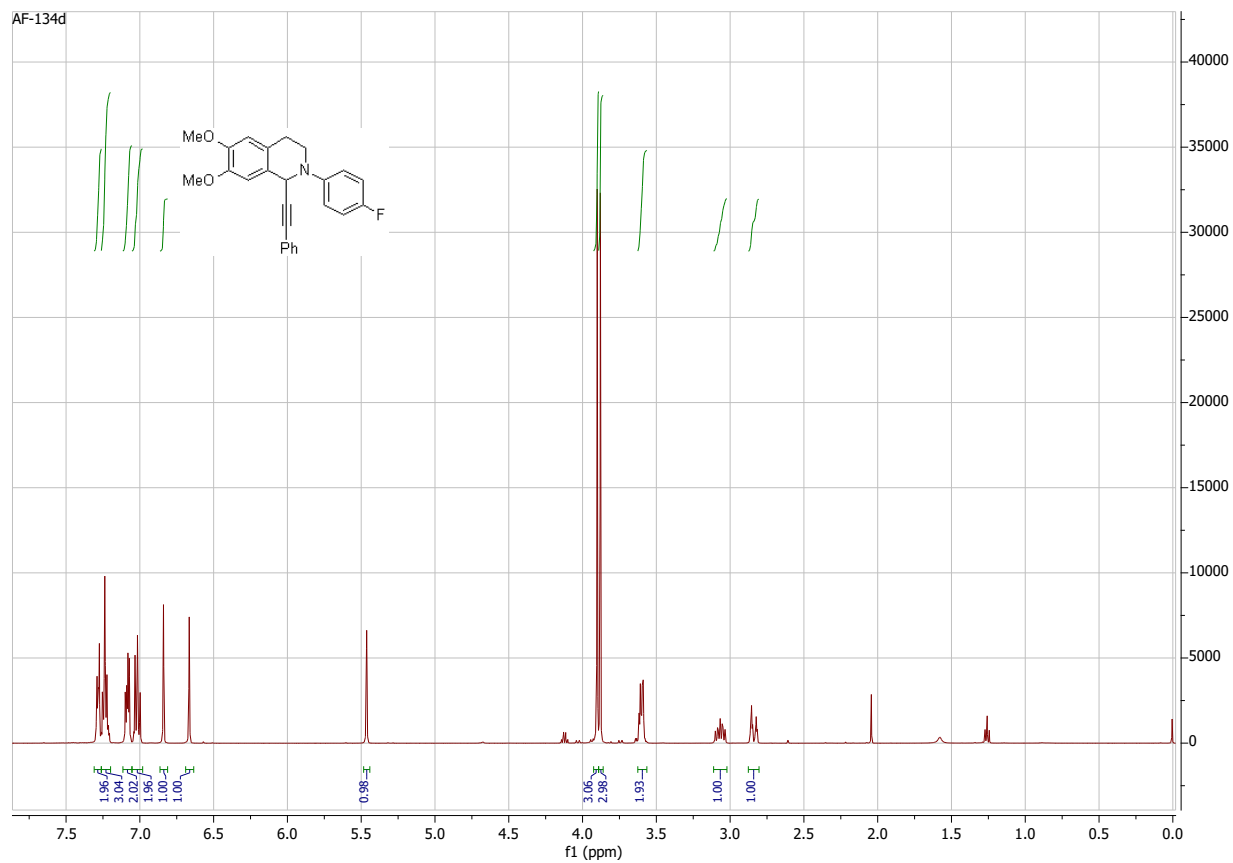
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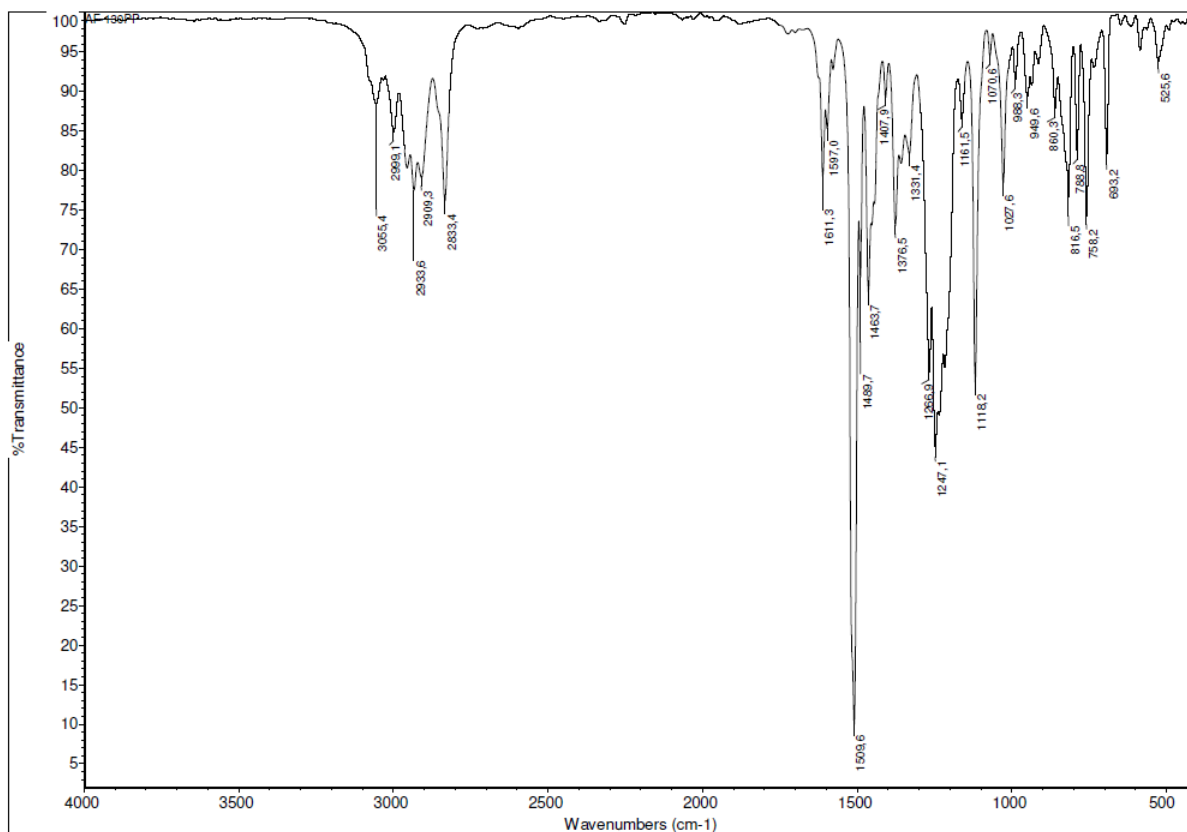


4d



4e





4f

