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Supporting Information

Heteropolyacid ionic liquids heterogeneously catalyzed syntheseis of isochromans via Oxa-Pictete-Spengler cyclization in dimethyl carbonate

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1 General Information

The starting materials were commercially available and were used without further purification. The products were isolated by column chromatography on silica gel (200-300 mesh) using petroleum ether (60-90°C) and ethyl acetate. All compounds were characterized by ^{1}H NMR, ^{13}C NMR and mass spectroscopy, which were consistent with those reported in related literatures. NMR spectra were determined on Bruker Ascend 500 in $CDCl_3$. ^{1}H NMR chemical shifts were referenced to residual solvent as determined relative to $CDCl_3$ (7.26 ppm). The ^{13}C NMR chemical shifts were reported in ppm relative to the carbon resonance of $CDCl_3$ (central peak is 77.0 ppm). ^{1}H NMR peaks were labelled as singlet (s), doublet (d), triplet (t), and multiplet (m). The coupling constants, *J*, are reported in Hertz (Hz). EI-MS data were performed on Agilent 7000C. GC analyses were performed on an Agilent 7890B equipped with a capillary column (HP-5, 30 m × 0.25 μm) using a flame ionization detector.

2 POMs-based Ionic Liquids

2.1 Synthesis of POM-based Ionic Liquids[1, 2]

3-Ethyl-5-(2-Hydroxyethyl)-4-methylthiazol-3-ium (HEMT) (1 mmol) was charged into a 250 mL flask, followed by the dropwise addition of aqueous solution of 12-Phosphomolybdic acid (1 mmol), then it was further stirred at ambient temperature for 12 h. Afterwards, the solvent was removed by rotary evaporator and the residue solid was dried under vacuum at 80 ℃for 12 h to obtain the final product $[HEMTH]H_2[PMo_{12}O_{40}]$. $[HEMTH]_3[PMo_{12}O_{40}]$ and $[HEMTH]_2H[PMo_{12}O_{40}]$, were prepared by similar procedures with their respective stoichiometric compositions. i.e., 3 mmol, and 2 mmol of HEMT, respectively. Accordingly, $[HBMTH]H_2[PMo_{12}O_{40}]$ and $[HMTH]H_2[PMo_{12}O_{40}]$ were prepared using 3-Benzyl-5-(2-Hydroxyethyl)-4-methylthiazol-3-ium (HBMT), 5-(2-Hydroxyethyl)-4-methylthiazole (HMT) and 12-Phosphomolybdic acid as the raw materials with the similar procedure. All of the ionic liquids were characterized and consistent with those reported in the literature.

2.2 FT-IR data of the catalysts

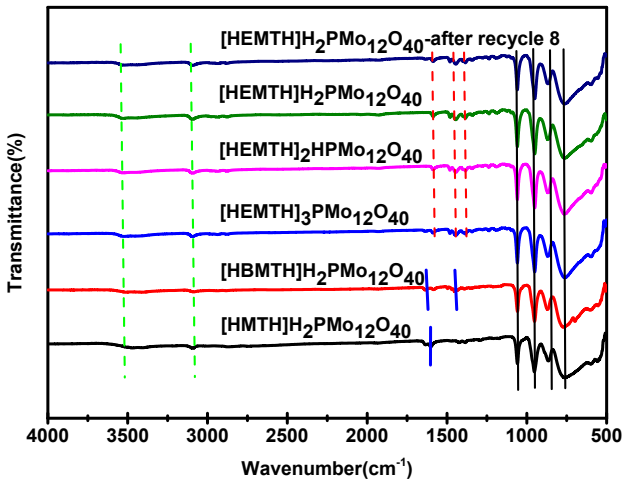


Figure S1

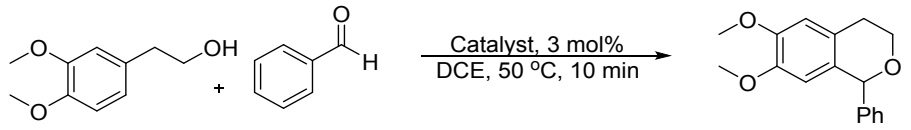
2.3 Typical procedure for direct Oxa-Pictet-Spengler reaction of arylethanols with aldehys.

To a 4 mL reaction vial, 2-(3,4-dimethoxyphenyl)ethan-1-ol (0.6 mmol), benzaldehyde (0.66 mmol), $[HEMTH]H_2[PMo_{12}O_{40}]$ (4 mol%) and DMC (3 mL) were added. Then the reaction was carried out in screw cap vials with a Teflon seal at 70 ^{o}C for desired time. After cooling to room temperature, the mixture was further purified by column chromatography (petroleum ether/EtOAc) to afford the desired products.

catalyst activation method: after each cycle, the product was extracted by ethyl ether for several times. Subsequently, the catalyst layer was dried under vacuum for 3 h at 50 ^{o}C for next run.

3 Optimization of the reaction conditions

Table S1. Examination of the catalysts.

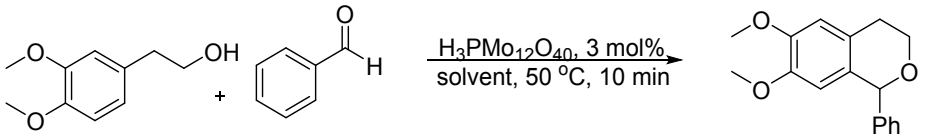


1a 0.2 mmol + **2a** 0.22 mmol → **3a**

Entry	Catalyst	Conv.(%)	Yield (%)[a]
1	----	45	0
2	$H_3PW_{12}O_{40}$	99	54
3	$H_4SiW_{12}O_{40}$	99	43
4	**$H_3PMo_{12}O_{40}$**	**99**	**80**

[a] The conversions and yields were determined by GC with biphenyl as the internal standard

Table S2. Examination of solvents.

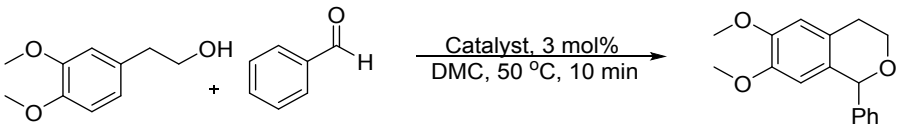


1a 0.2 mmol + **2a** 0.22 mmol → **3a**

Entry	Solvent (1 mL)	Conv. (%)	Yield (%)[a]
1	H_2O	99	0
2	PC	99	54
3	EC	99	35
4	CPME	99	82
5	**DMC**	**99**	**89**
6	Ph-Cl	99	80
7	DCE	99	80
8	Toluene	99	82
9	CH_3CN	99	87
10	CH_3NO_2	99	86

[a] The conversions and yields were determined by GC with biphenyl as the internal standard

Table S3. Examination of the ILs-$H_3PMo_{12}O_{40}$.

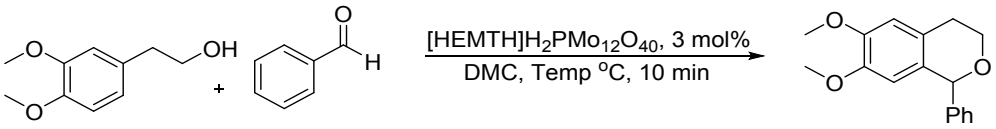


1a 0.2 mmol + **2a** 0.22 mmol → **3a**

Entry	ILs-Catalyst	Conv. (%)	Yield (%)[a]
1	**$H_3PMo_{12}O_{40}$**	**99**	**89**
2	$[HMTH]H_2PMo_{12}O_{40}$	99	61
3	**$[HEMTH]H_2PMo_{12}O_{40}$**	**99**	**65**
4	$[HBMTH]H_2PMo_{12}O_{40}$	88	13
5	$[HEMTH]_2HPMo_{12}O_{40}$	84	0
6	$[HEMTH]_3PMo_{12}O_{40}$	75	0

[a] The conversions and yields were determined by GC with biphenyl as the internal standard

Table S4. The investigation of the reaction temperature.

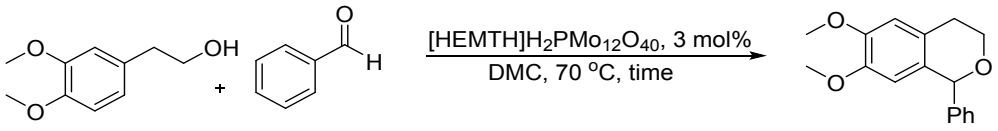


1a 0.2 mmol + **2a** 0.22 mmol → **3a**

Entry	T (°C)	Conv. (%)	Yield (%)[a]
1	30	99	48
2	40	99	59
3	50	99	65
4	55	99	72
5	60	99	78
6	65	99	81
7	**70**	**99**	**85**
8	80	99	85

[a] The conversions and yields were determined by GC with biphenyl as the internal standard

Table S5. The investigation of the reaction time.

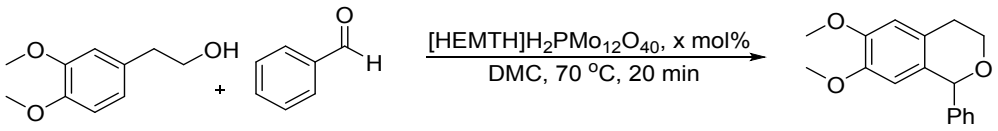


1a 0.2 mmol + **2a** 0.22 mmol → **3a**

Entry	Time (min)	Conv. (%)	Yield (%)[a]
1	1	99	62
2	3	99	71
3	5	99	78
4	7	99	80
5	10	99	85
6	15	99	88
7	**20**	**99**	**91**
8	25	99	91

[a] The conversions and yields were determined by GC with biphenyl as the internal standard

Table S6. Optimization of catalyst loading.

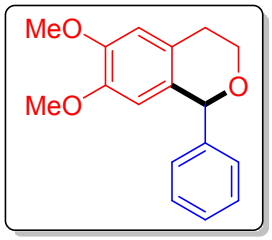


1a 0.2 mmol + **2a** 0.22 mmol → **3a**

Entry	loading (mol%)	Conv. (%)	Yield (%)[a]
1	1	99	59
2	1.5	99	71
3	2	99	77
4	2.5	99	86
5	3	99	91
6	3.5	99	93
7	**4**	**99**	**95**
8	4.5	99	95

[a] The conversions and yields were determined by GC with biphenyl as the internal standard

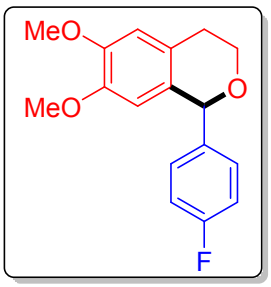
4 Characterization of Substrates and Products



6,7-dimethoxy-1-phenylisochromane (3a)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.29-7.37 (m, 5H), 6.66 (s, 1H), 6.24 (s, 1H), 5.69 (s, 1H), 4.12-4.16 (m, 1H), 3.87-3.92 (m, 4H), 3.65 (s, 3H), 3.01-3.07 (m, 1H), 2.72-2.77 (m, 1H);

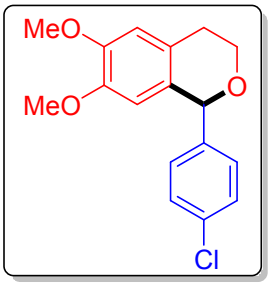
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.84, 147.24, 142.20, 128.94, 128.46, 128.17, 126.09, 111.15, 109.68, 79.18, 63.60, 55.89, 28.38.



1-(4-fluorophenyl)-6,7-dimethoxyisochromane (3b)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.17-7.18 (m, 2H), 6.90-6.93 (m, 2H), 6.55 (s, 1H), 6.09 (s, 1H), 5.55 (s, 1H), 4.00-4.01 (m, 1H), 3.75-3.79 (m, 4H), 3.54-3.55 (s, 3H), 2.91-2.94 (m, 1H), 2.60-2.63 (m, 1H);

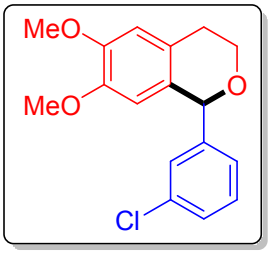
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 162.54 (d, J = 246.96 Hz), 147.95, 147.30, 138.19 (d, J = 2.52 Hz), 130.65 (d, J = 8.82 Hz), 128.73, 126.10, 115.29 (d, J = 21.42 Hz), 111.20, 109.54, 78.44, 63.64, 55.86, 28.30.



1-(4-chlorophenyl)-6,7-dimethoxyisochromane (3c)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.30-7.32 (m, 2H), 7.23-7.25 (m, 2H), 6.65 (s, 1H), 6.18 (s, 1H), 5.65 (s, 1H), 4.09-4.13 (m, 1H), 3.87-3.89 (m, 4H), 3.66 (s, 3H), 2.99-3.05 (m, 1H), 2.70-2.75 (m, 1H);

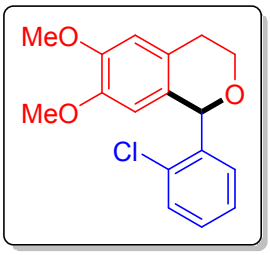
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 148.02, 147.36, 140.80, 133.93, 130.30, 128.61, 128.38, 126.10, 111.25, 109.51, 78.40, 63.60, 55.90, 28.28.



1-(3-chlorophenyl)-6,7-dimethoxyisochromane (3d)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.27-7.30 (m, 3H), 7.20-7.22 (m, 1H), 6.66 (s, 1H), 6.22 (s, 1H), 5.65 (s, 1H), 4.10-4.14 (m, 1H), 3.85-3.90 (m, 4H), 3.68 (s, 3H), 3.00-3.06 (m, 1H), 2.71-2.76 (m, 1H);

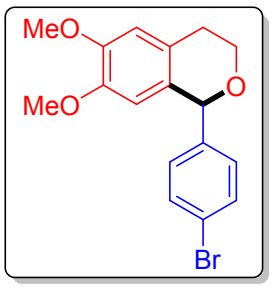
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 148.04, 147.37, 144.31, 134.34, 129.70, 129.01, 128.35, 128.06, 127.11, 126.09, 111.27, 109.49, 78.47, 63.60, 55.95, 55.90, 28.25.



1-(2-chlorophenyl)-6,7-dimethoxyisochromane (3e)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.32-7.34 (m, 1H), 7.06-7.17 (m, 3H), 6.57 (s, 1H), 6.16 (s, 1H), 6.11(s, 1H), 4.02-4.06 (m, 1H), 3.78-3.85 (m, 4H), 3.57 (s, 3H), 2.92-2.98 (m, 1H), 2.63-2.68 (m, 1H);

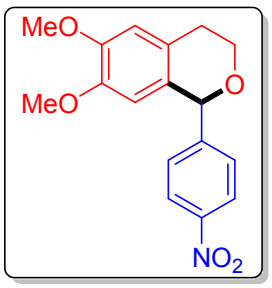
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.94, 147.43, 139.80, 134.21, 130.69, 129.60, 129.30, 128.21, 126.95, 126.21, 111.21, 109.22, 74.98, 63.66, 55.89, 28.28.



1-(4-bromophenyl)-6,7-dimethoxyisochromane (3f)[6]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.45-7.47 (m, 2H), 7.17-7.19 (m, 2H), 6.65 (s, 1H), 6.18 (s, 1H), 5.63 (s, 1H), 4.08-4.12 (m, 1H), 3.85-3.88 (m, 4H), 3.66 (s, 3H), 2.98-3.04 (m, 1H), 2.70-2.75 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 148.00, 147.34, 141.30, 131.57, 130.66, 128.26, 126.08, 122.17, 111.23, 109.45, 78.43, 63.59, 55.93, 55.90, 28.28.

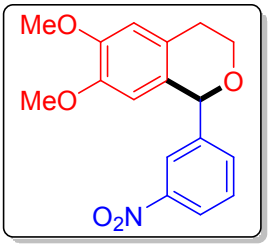


6,7-dimethoxy-1-(4-nitrophenyl)isochromane (3g)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.16-8.20 (m, 2H), 7.46-7.50 (m, 2H), 6.63-6.67 (m, 1H), 6.11-6.14 (m, 1H), 5.71-5.75 (m, 1H), 4.08-4.13 (m, 1H), 3.85-3.90 (m, 4H), 3.61-3.64 (m, 3H), 3.00-3.07

(m, 1H), 2.71-2.76 (m, 1H);

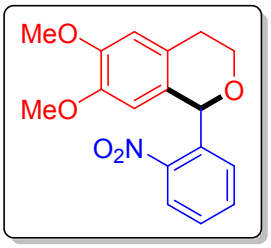
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 149.46, 148.28, 147.70, 147.53, 129.68, 127.35, 126.07, 123.68, 111.47, 109.23, 78.06, 63.83, 55.93, 28.18.



6,7-dimethoxy-1-(3-nitrophenyl)isochromane (3h)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.15-8.18 (m, 2H), 7.64-7.66 (m, 1H), 7.50-7.53 (m, 1H), 6.67 (s, 1H), 6.15 (s, 1H), 5.76 (s, 1H), 4.09-4.13 (m, 1H), 3.87-3.91 (m, 4H), 3.64 (s, 3H), 3.02-3.08 (m, 1H), 2.72-2.77 (m, 1H);

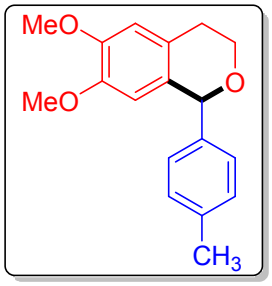
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 148.34, 148.32, 147.56, 144.52, 134.94, 129.42, 127.34, 126.23, 123.78, 123.19, 111.52, 109.34, 78.11, 63.85, 55.99, 55.92, 28.19.



6,7-dimethoxy-1-(2-nitrophenyl)isochromane (3i)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.83-7.84 (m, 1H), 7.49-7.52 (m, 1H), 7.72-7.45 (m, 1H), 7.32-7.33 (m, 1H), 6.66 (s, 1H), 6.34 (s, 1H), 6.29 (s, 1H), 4.03-4.07 (m, 1H), 3.85-3.90 (m, 4H), 3.67 (s, 3H), 3.00-3.06 (m, 1H), 2.71-2.76 (m, 1H);

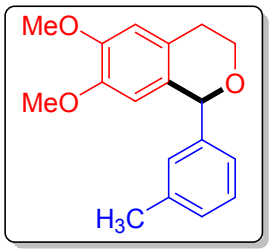
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 149.90, 148.23, 147.50, 136.65, 132.62, 131.22, 128.85, 127.49, 126.20, 123.90, 111.36, 109.71, 73.27, 63.90, 55.97, 55.90, 28.08.



6,7-dimethoxy-1-(p-tolyl)isochromane (3j)[4]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.14-7.20 (m, 4H), 6.65 (s, 1H), 6.25 (s, 1H), 5.66 (s, 1H), 4.10-4.14 (m, 1H), 3.85-3.90 (m, 4H), 4.08-4.13 (m, 1H), 3.85-3.90 (m, 4H), 3.66 (s, 3H), 2.99-3.05 (m, 1H), 2.71-2.76 (m, 1H), 2.35 (s, 3H);

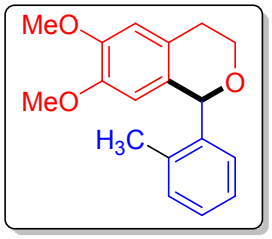
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.83, 147.25, 139.25, 137.81, 129.10, 128.87, 126.14, 111.16, 109.78, 78.88, 63.36, 55.92, 55.89, 28.40, 21.23.



6,7-dimethoxy-1-(m-tolyl)isochromane (3k)[7]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.21-7.25 (m, 1H),7.08-7.12 (m, 3H), 6.65 (s, 1H), 6.24 (s, 1H), 5.64 (s, 1H), 4.12-4.16 (m, 1H), 3.85-3.90 (m, 4H), 3.66 (s, 3H), 3.01-3.07 (m, 1H), 2.70-2.75 (m, 1H), 2.33 (s, 3H);

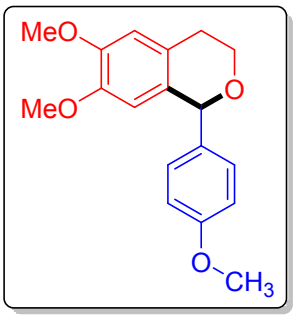
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.86, 147.26, 142.09, 138.13, 129.53, 129.06, 128.94, 128.24, 126.11, 126.07, 111.18, 109.83, 79.25, 63.64, 55.95, 55.89, 28.41, 21.46.



6,7-dimethoxy-1-(o-tolyl)isochromane (3l)[7]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.09-7.12 (m, 2H),7.09-7.12 (m, 1H), 6.96-6.97 (m,1H), 6.56 (s, 1H), 6.10 (s, 1H), 5.79 (s, 1H), 4.00-4.04 (m, 1H), 3.75-3.78 (m, 4H), 3.54 (s, 3H), 2.88-2.94 (m, 1H),2.63-2.67 (m, 1H), 2.29 (s, 3H);

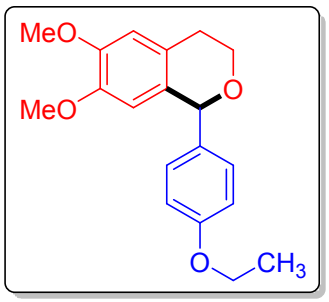
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.83, 147.41, 139.76, 137.51, 130.95, 129.86, 129.06, 128.09, 126.25, 125.66, 111.23, 109.31, 77.05, 63.52, 55.90, 28.36, 19.35.



6,7-dimethoxy-1-(4-methoxyphenyl)isochromane (3m)[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.21-7.22 (m, 2H), 6.85-6.87 (m, 2H), 6.64 (s, 1H), 6.23 (s, 1H), 5.64 (s, 1H), 4.09-4.13 (m, 1H), 3.83-3.88 (m, 4H), 3.78 (s, 3H), 3.65 (s, 3H), 2.98-3.04 (m, 1H), 2.70-2.74 (m, 1H);

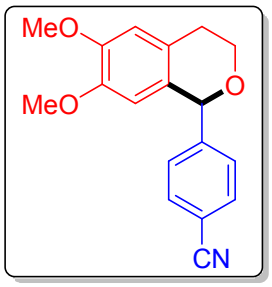
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 159.41, 147.79, 147.20, 134.48, 130.19, 129.22, 126.14, 113.74, 111.11, 109.70, 78.66, 63.42, 55.88, 55.26, 28.38.



1-(4-ethoxyphenyl)-6,7-dimethoxyisochromane (3n)[7]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.20 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 6.64 (s, 1H), 6.23 (s, 1H), 5.63 (s, 1H), 4.14 – 4.09 (m, 1H), 4.01 (q, J = 7.0 Hz, 2H), 3.87 (s, 4H), 3.65 (s, 3H), 3.05 – 2.91 (m, 1H), 2.72 (d, J = 16.1 Hz, 1H), 1.40 (t, J = 7.0 Hz, 3H);

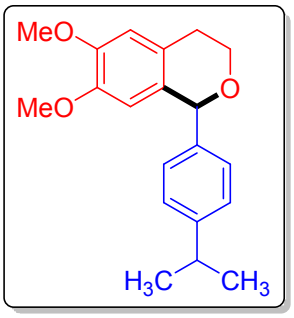
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 158.78, 147.76, 147.17, 134.30, 130.18, 129.24, 126.13, 114.29, 111.06, 109.69, 78.69, 63.44, 55.88, 28.38, 14.87.



4-(6,7-dimethoxyisochroman-1-yl)benzonitrile (3o)[4]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.64 (d, *J* = 8 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 6.66 (s, 1H), 6.13 (s, 1H), 5.70 (s, 1H), 4.09-4.13 (m, 1H), 3.86-3.91 (m, 4H), 3.66 (s, 3H), 3.00-3.06 (m, 1H), 2.72-2.77 (m, 1H);

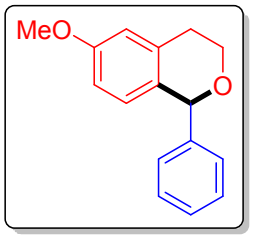
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 148.21, 147.46, 132.34, 129.56, 127.38, 126.08, 118.77, 111.98, 111.36, 109.21, 78.36, 63.78, 55.94, 55.92, 28.18.



1-(4-isopropylphenyl)-6,7-dimethoxyisochromane (3p)[6]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.19-7.23 (m, 4H), 6.65 (s, 1H), 6.28 (s, 1H), 5.67 (s, 1H), 4.09-4.13 (m, 1H), 3.87-3.90 (m, 4H), 3.67 (s, 3H), 2.98-3.04 (m, 1H), 2.88-2.93 (m, 1H), 2.72-2.76 (m, 1H), 1.24 (d, J = 7 Hz, 6H);

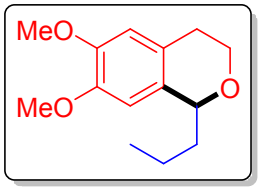
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 148.78, 147.79, 147.19, 139.52, 128.96, 128.90, 126.50, 126.19, 111.10, 109.79, 78.81, 63.33, 55.97, 55.88, 33.89, 28.41, 24.04, 23.98.



6-methoxy-1-phenylisochromane (3q)[8]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.21-7.23 (m, 5H), 6.52-6.59 (m, 3H), 5.57 (s, 1H), 4.04-4.08 (m, 1H), 3.65-3.81 (m, 4H), 3.00-3.04 (m, 1H), 2.64-2.98 (m, 1H);

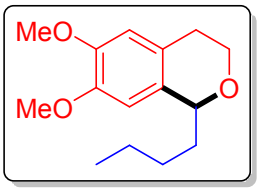
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 158.21, 142.49, 135.21, 129.74, 128.90, 128.49, 128.15, 113.23, 112.37, 79.52, 63.89, 55.26, 29.24.



6,7-dimethoxy-1-propylisochromane (3r)[4]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.56 (d, J = 20 Hz, 2H), 4.67 (d, J = 10 Hz, 1H), 4.07-4.11 (m, 1H), 3.84 (s, 6H), 3.70-3.74 (m, 1H), 2.85-2.91 (m, 1H), 2.56-2.60 (m, 1H), 1.72-1.84 (m, 2H), 1.44-1.53 (m, 2H), 0.95 (t, J = 7.5 Hz,15 Hz, 3H);

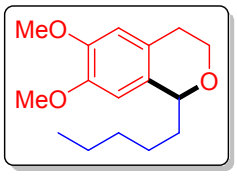
^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.37, 130.43, 125.97, 111.40, 107.83, 75.35, 63.15, 56.01, 55.84, 38.26, 28.69, 18.57, 14.20.



1-butyl-6,7-dimethoxyisochromane (3s)[4]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.55 (d, J = 20 Hz, 2H), 4.66 (d, J = 11 Hz, 1H), 4.07-4.11 (m, 1H), 3.83 (s, 6H), 3.69-3.73 (m, 1H), 2.85-2.91 (m, 1H), 2.55-2.59 (m, 1H), 1.72-1.87 (m, 2H), 1.29-1.44 (m, 4H), 0.90 (t, J = 7.0 Hz,14 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.37, 130.41, 125.99, 111.39, 107.84, 75.56, 63.20, 55.99, 55.82, 35.80, 28.69, 27.46, 22.86, 14.16.

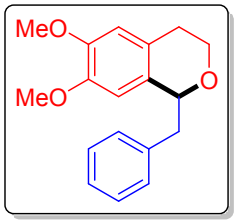


6,7-dimethoxy-1-pentylisochromane (3t)[4]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.56 (d, J = 20 Hz, 2H), 4.67 (d, J = 8 Hz, 1H), 4.08-4.12 (m, 1H), 3.84 (s, 6H), 3.70-3.75 (m, 1H), 2.86-2.91 (m, 1H), 2.57-2.61 (m, 1H), 1.72-1.86 (m, 2H), 1.27-1.47 (m, 4H), 0.88 (t, J = 7.5 Hz,15 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.37, 130.43, 125.98, 111.39, 107.83, 75.60, 63.20, 56.00,

55.83, 36.08, 32.02, 28.69, 25.00, 22.71, 14.14.



1-benzyl-6,7-dimethoxyisochromane (3u)[5]

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.17-7.21 (m, 4H), 7.10-7.13 (m, 1H), 6.48 (s, 1H), 6.37 (s, 1H), 4.85-4.88 (m, 1H), 3.99-4.03 (m, 1H), 3.74 (s, 3H), 3.61-3.65 (m, 4H), 2.96-3.07 (m, 2H), 2.69-2.75 (m, 1H), 2.49-2.54 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 147.58, 147.17, 138.83, 129.64, 129.57, 128.32, 126.33, 126.19, 111.46, 108.30, 76.34, 62.83, 55.90, 42.83, 28.66.

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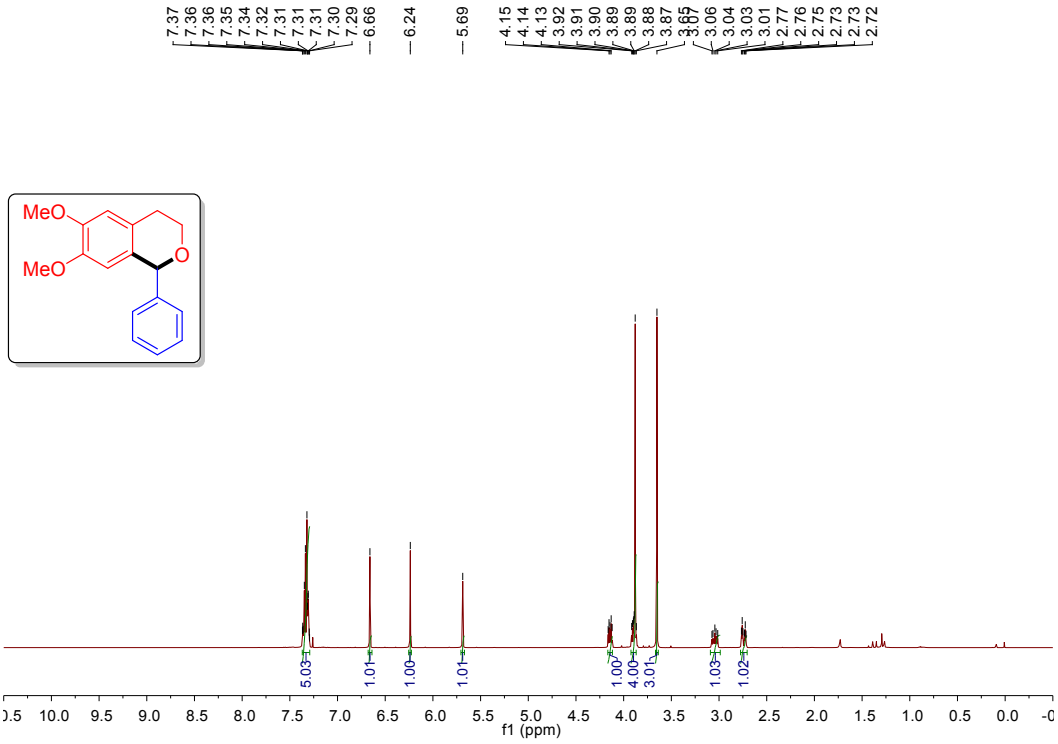
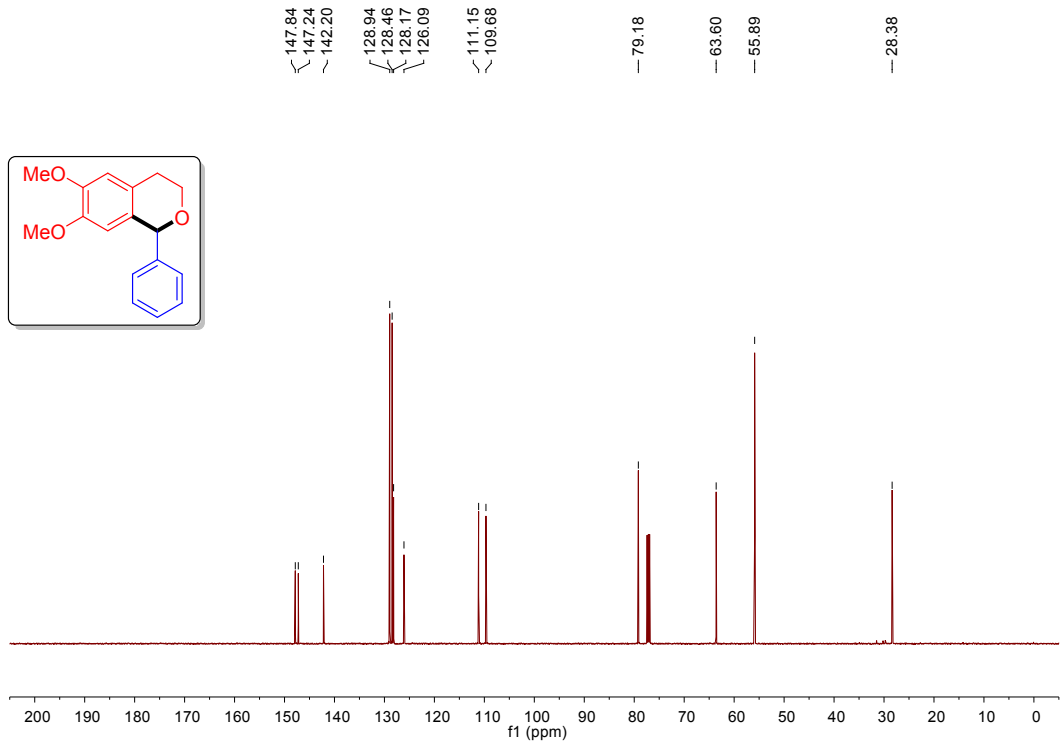
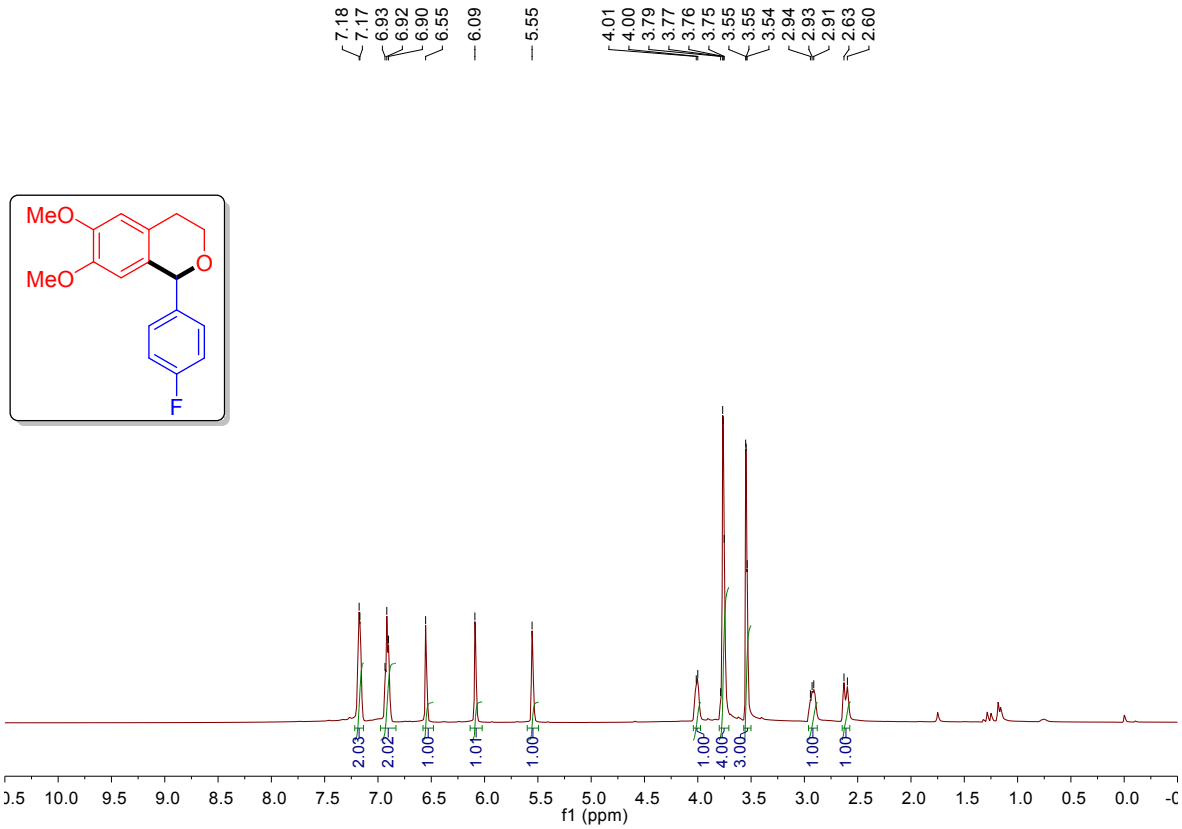
5 NMR Spectra



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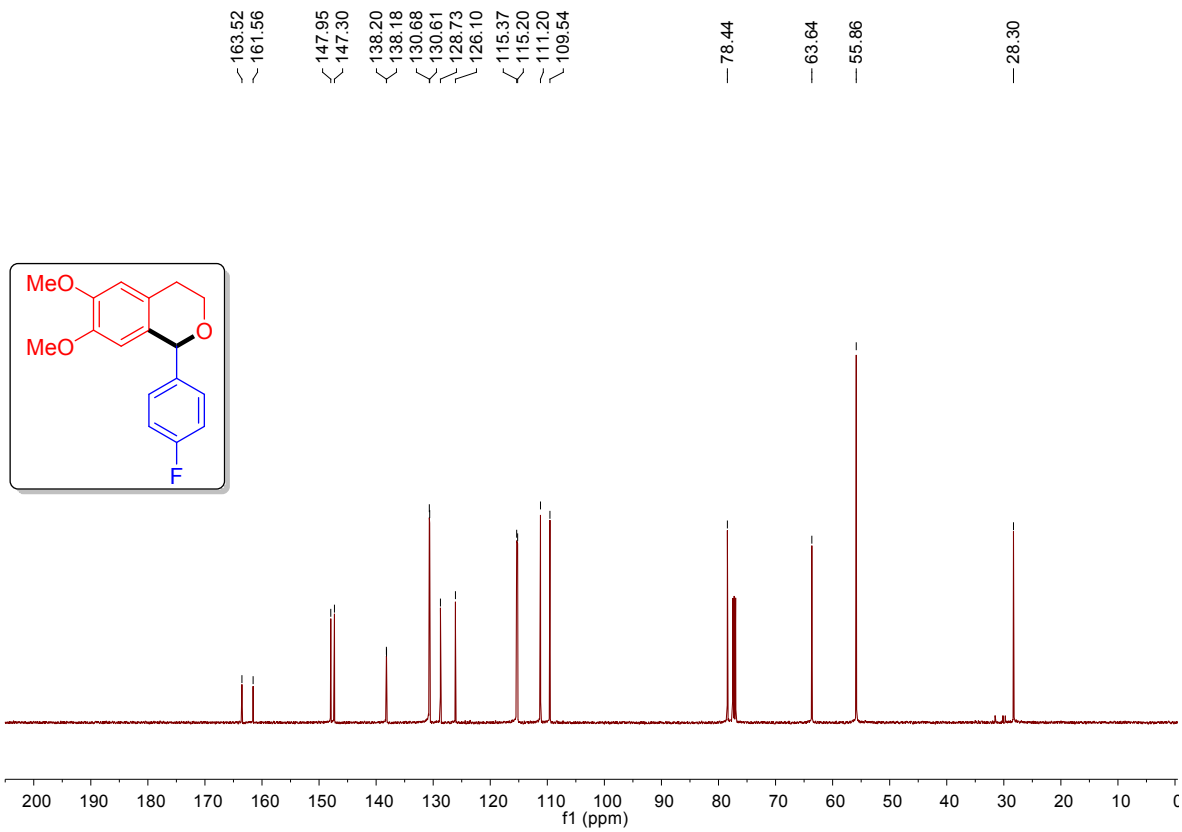
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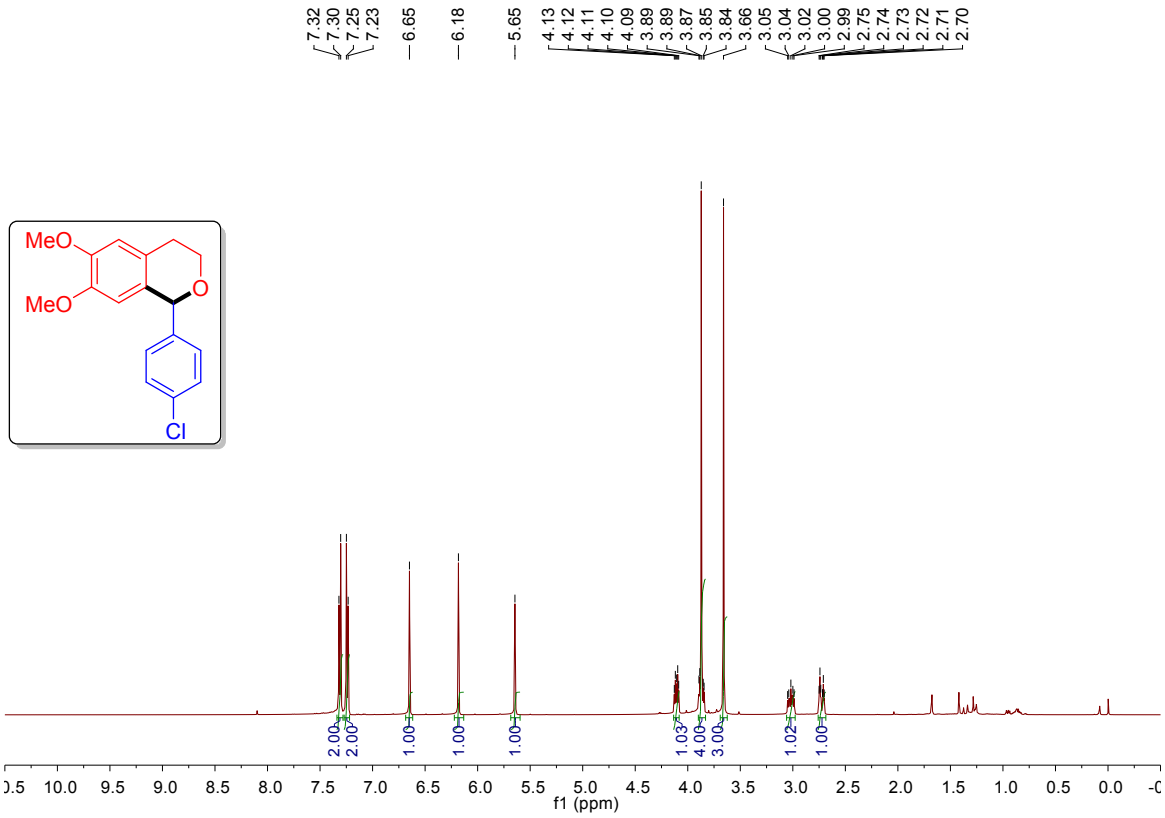
F
f1 (ppm)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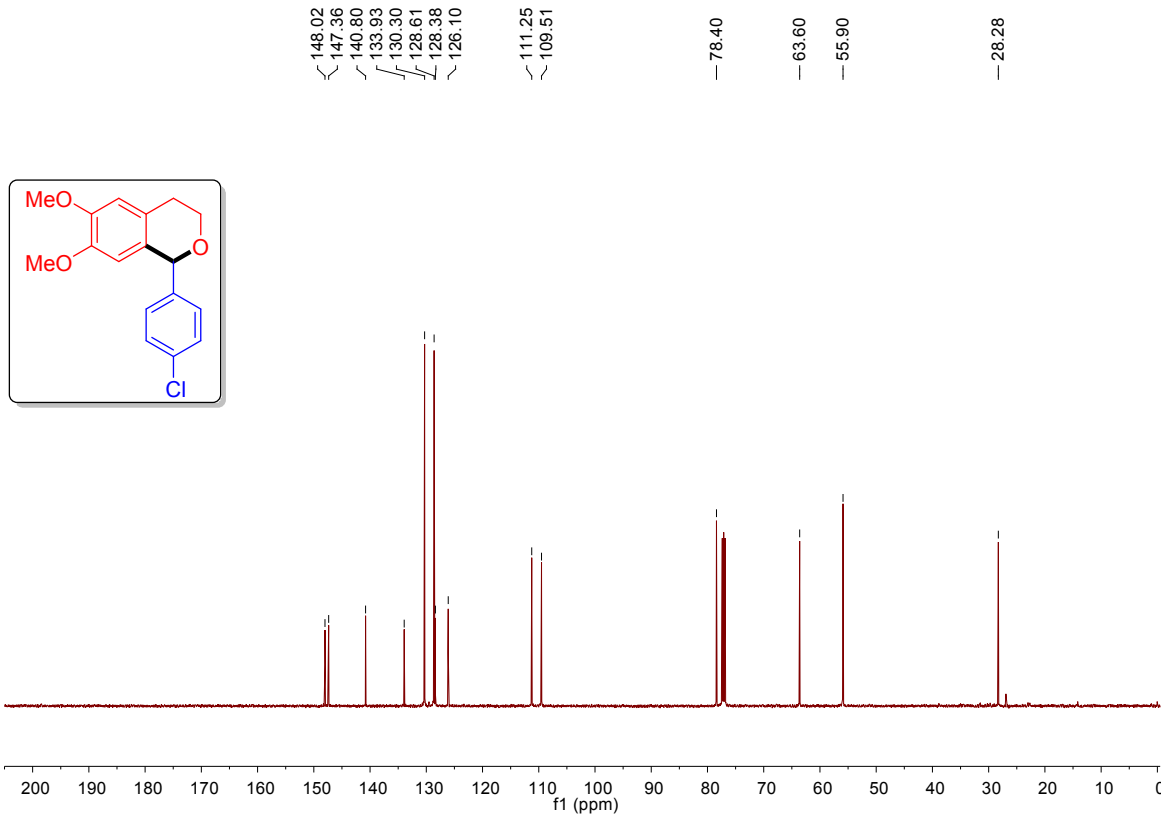
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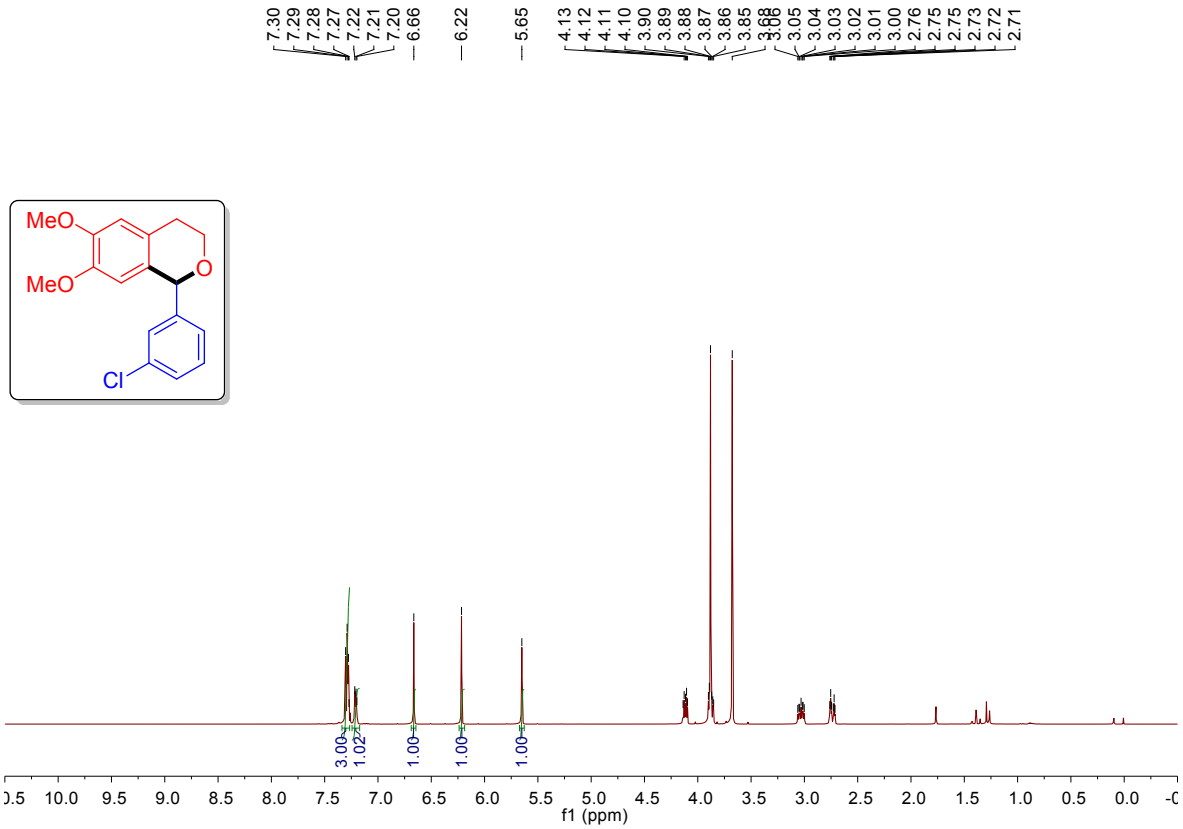
Cl
f1 (ppm)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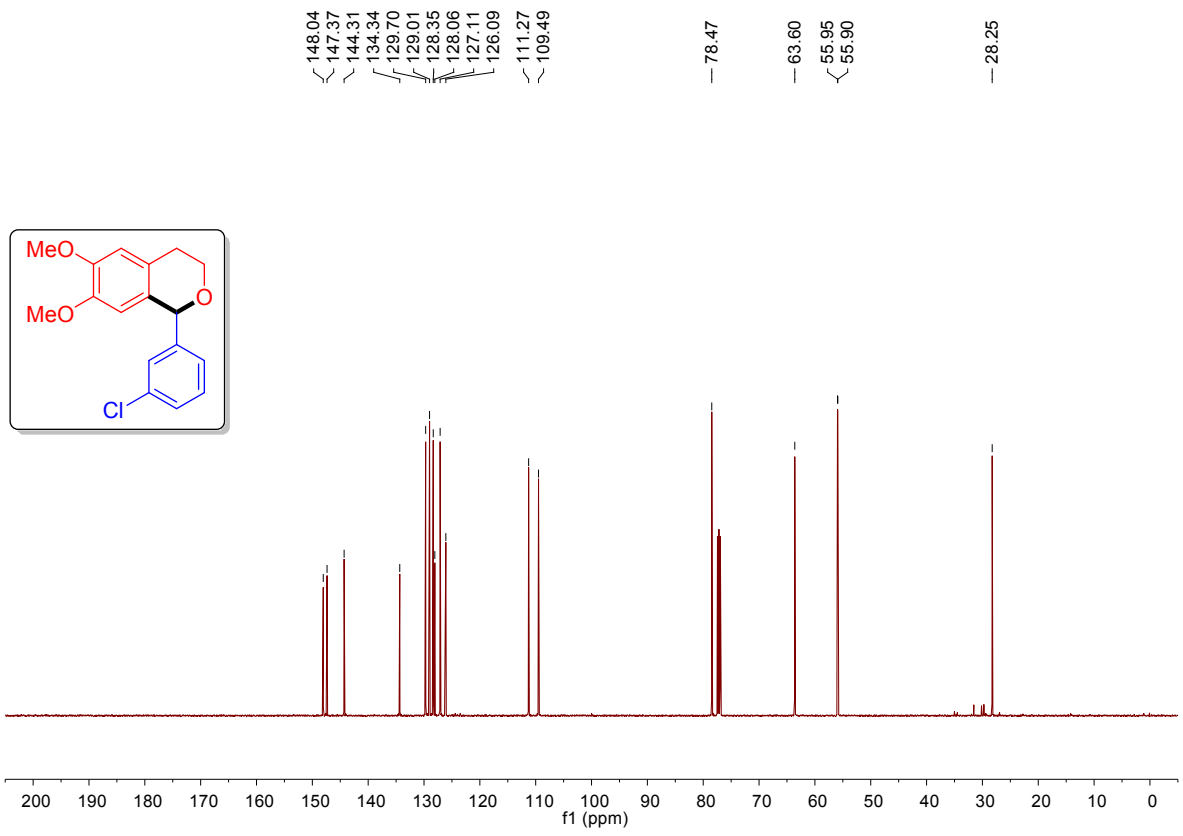
f1 (ppm)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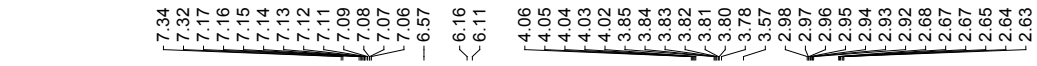
Cl
f1 (ppm)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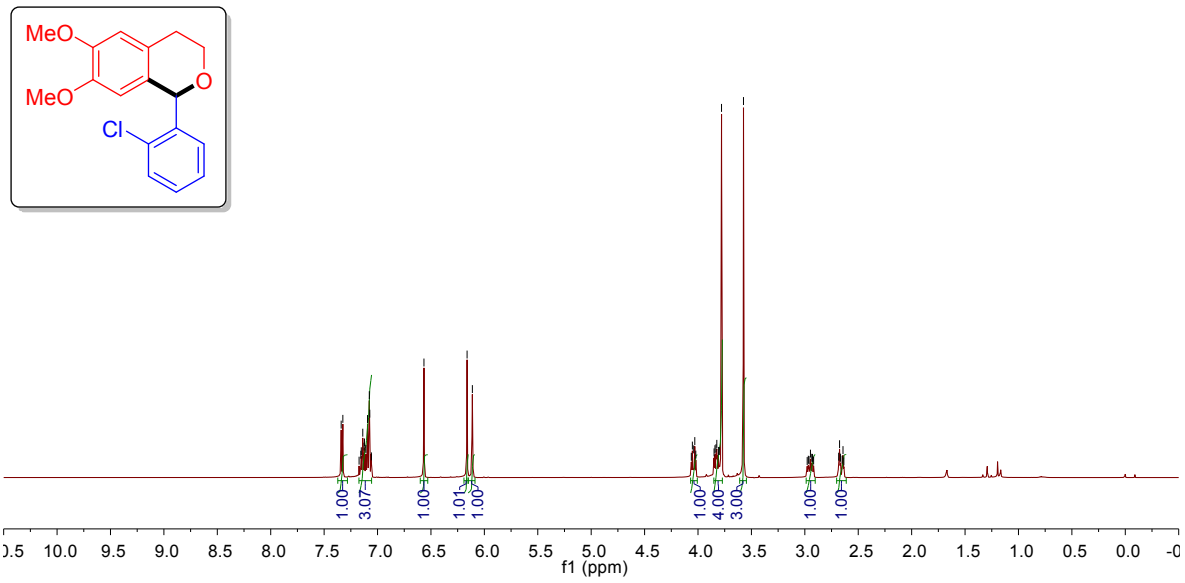
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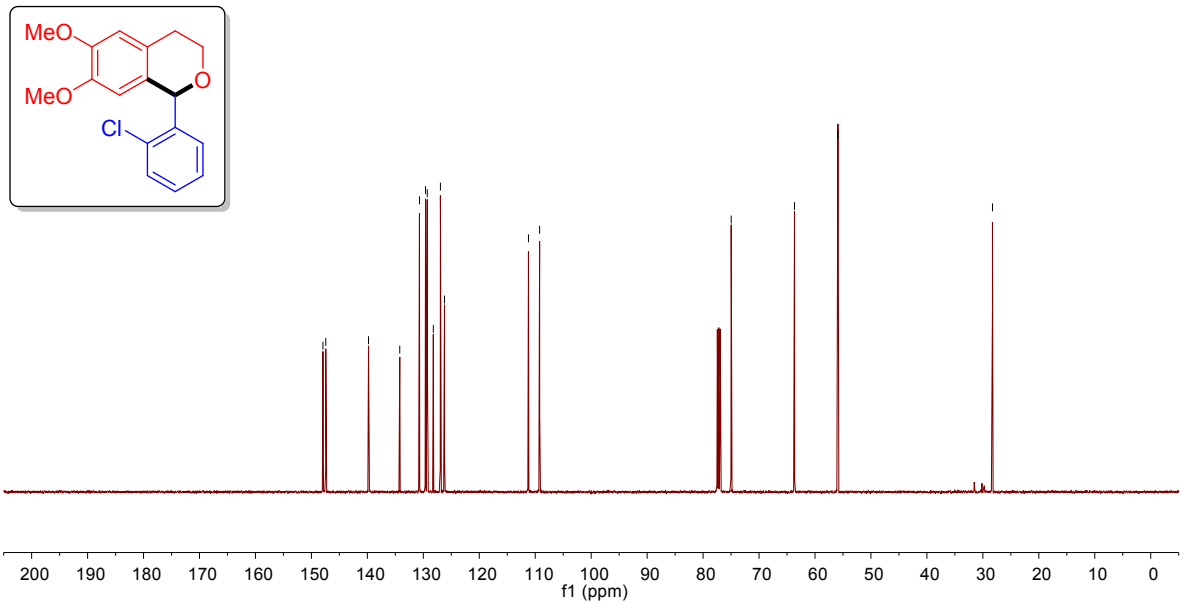
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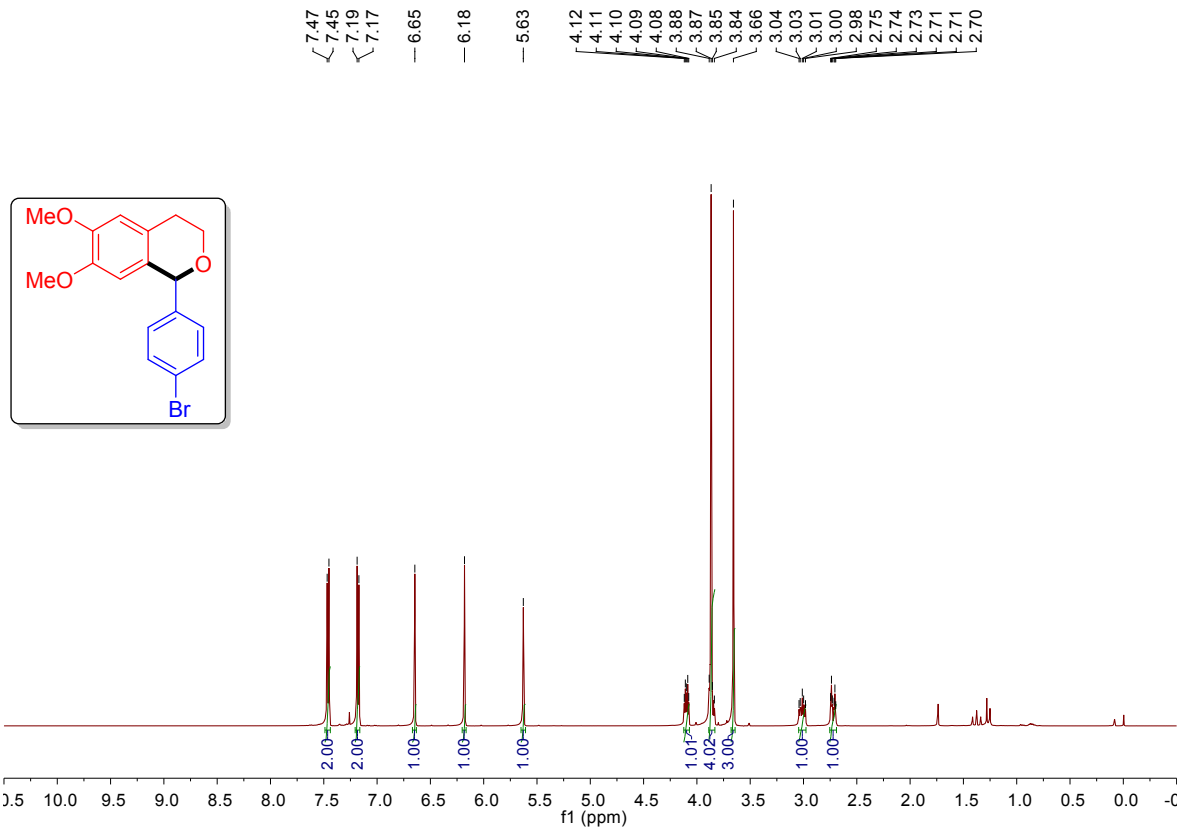
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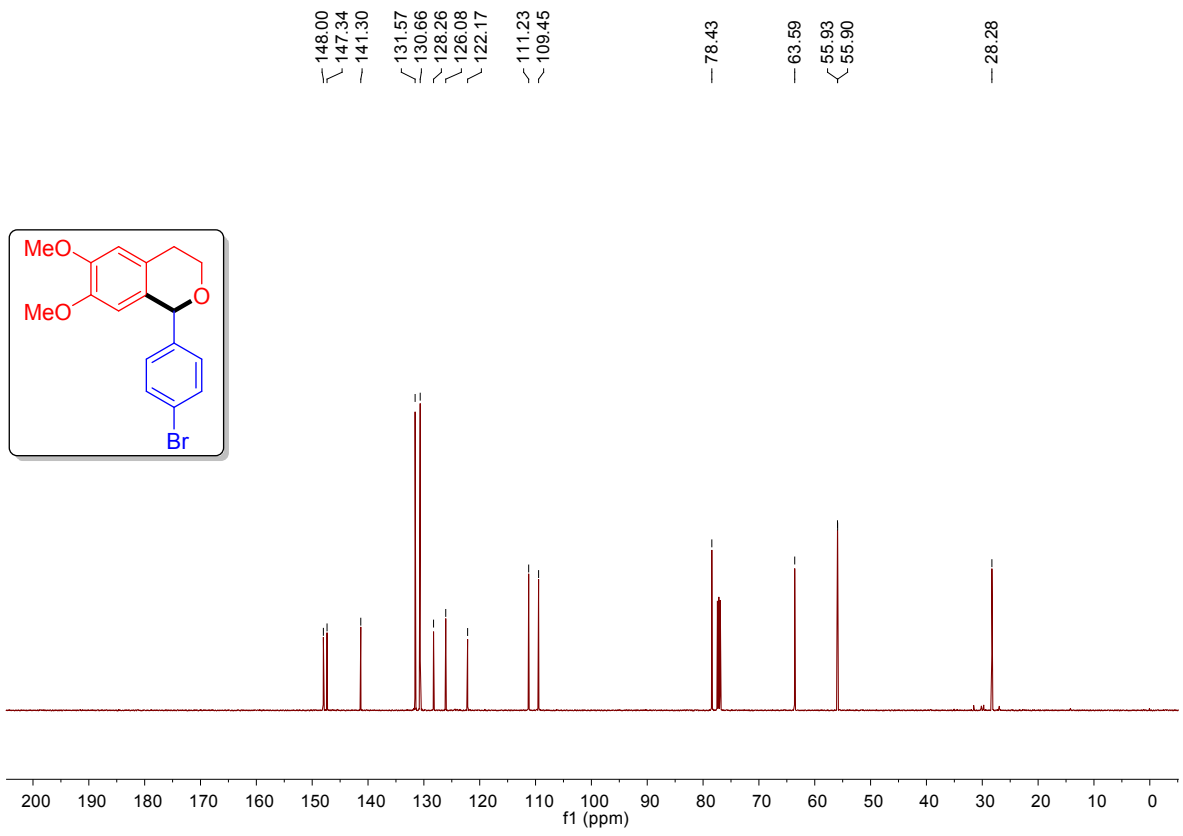
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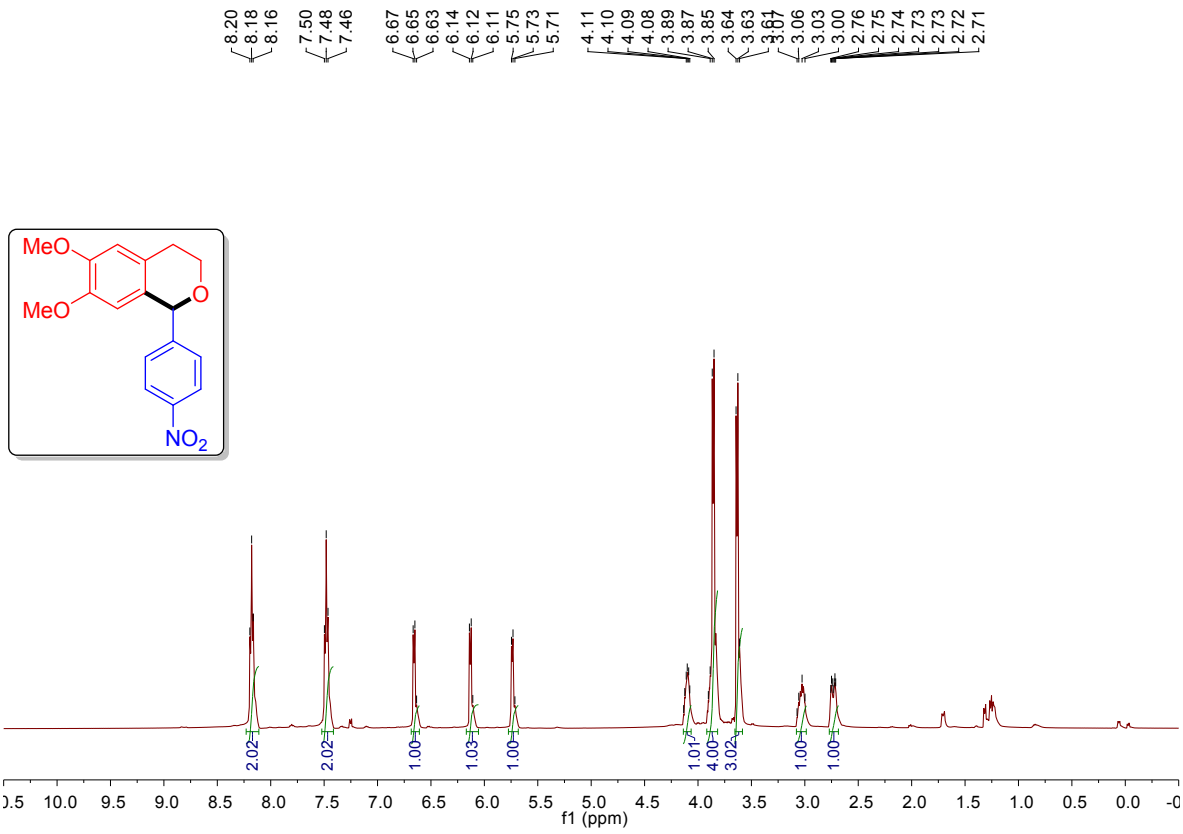
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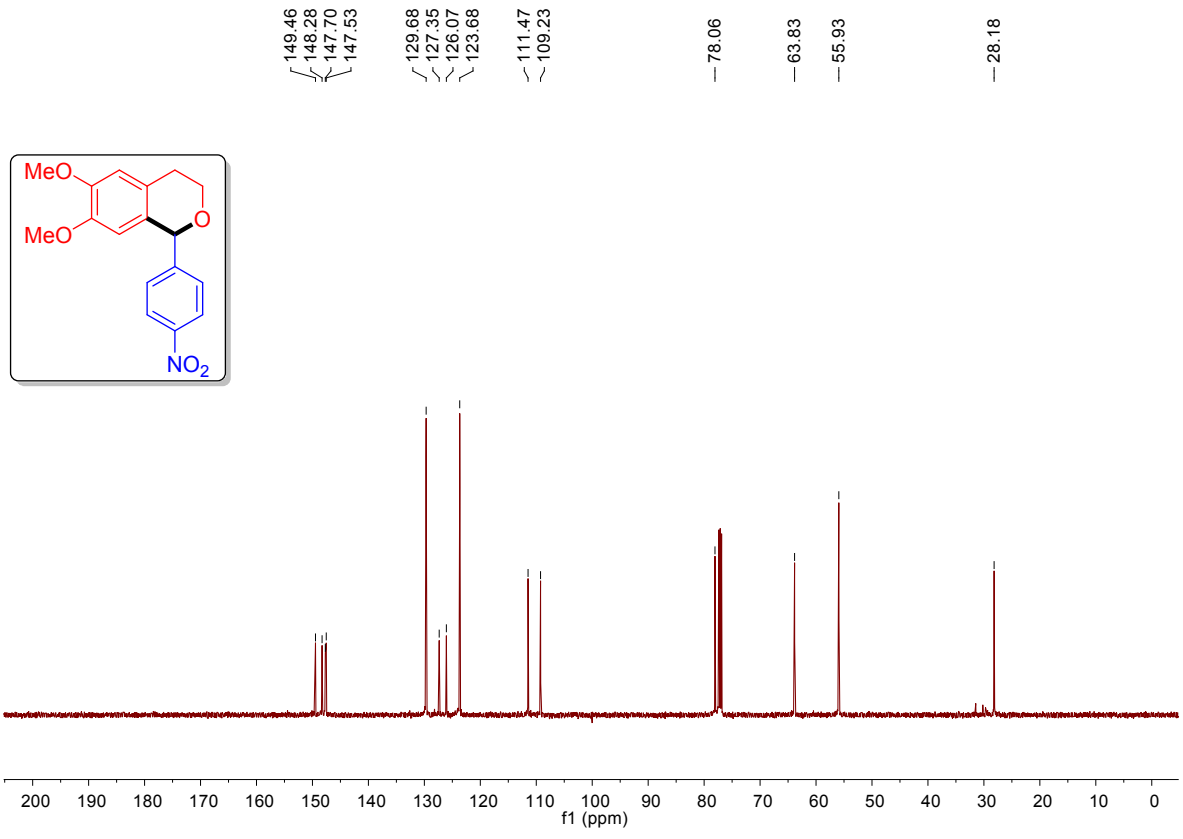
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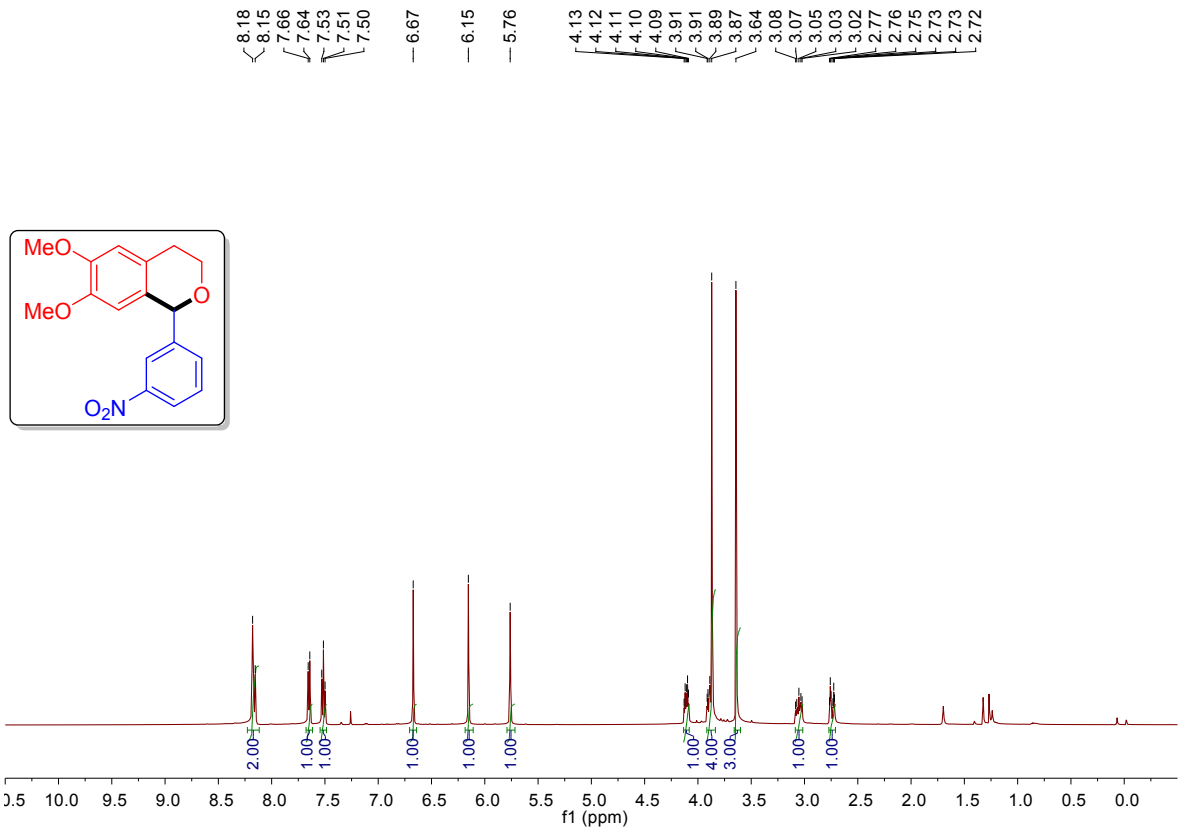
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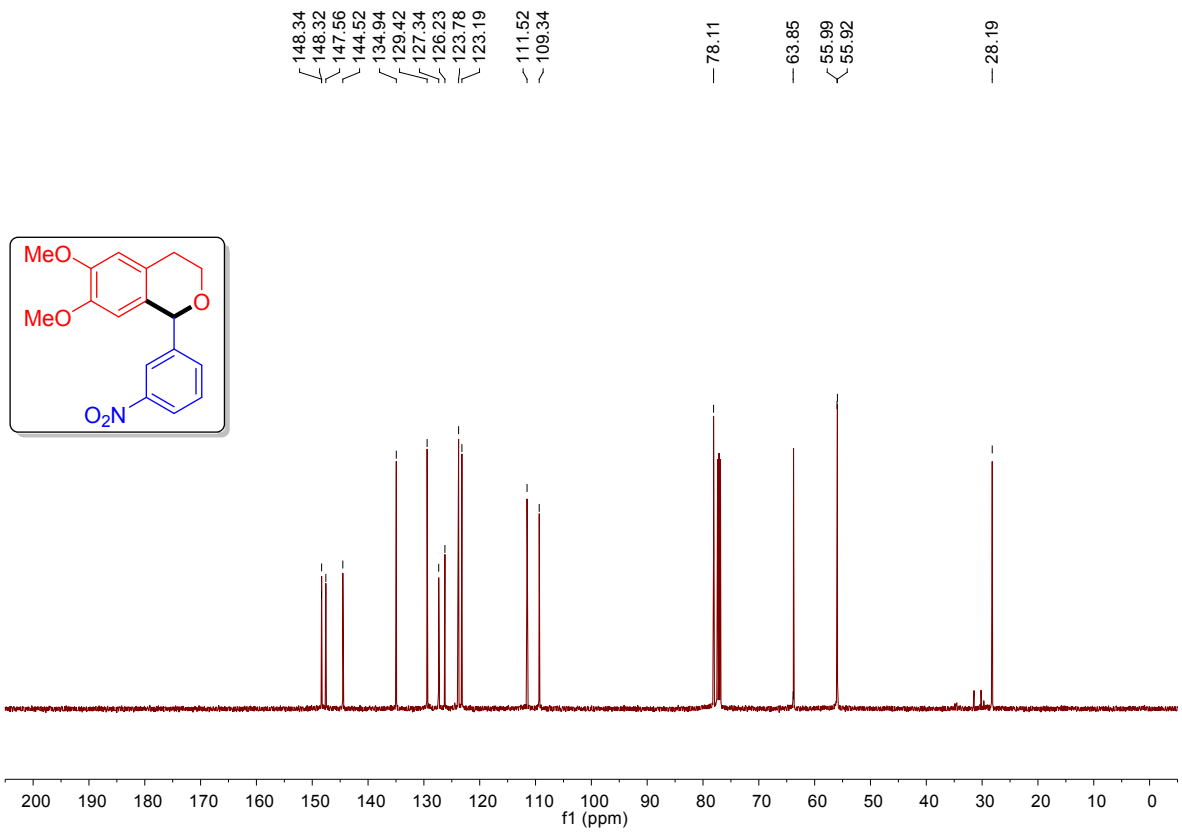
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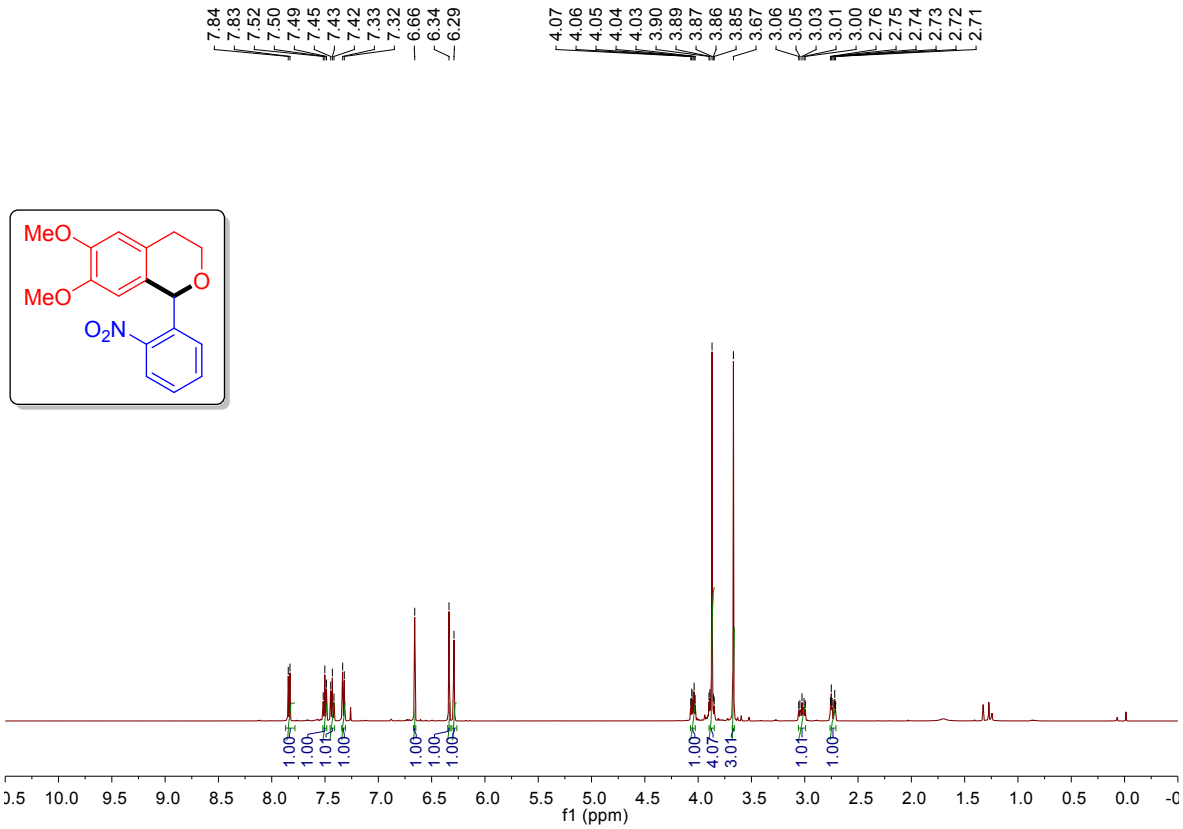
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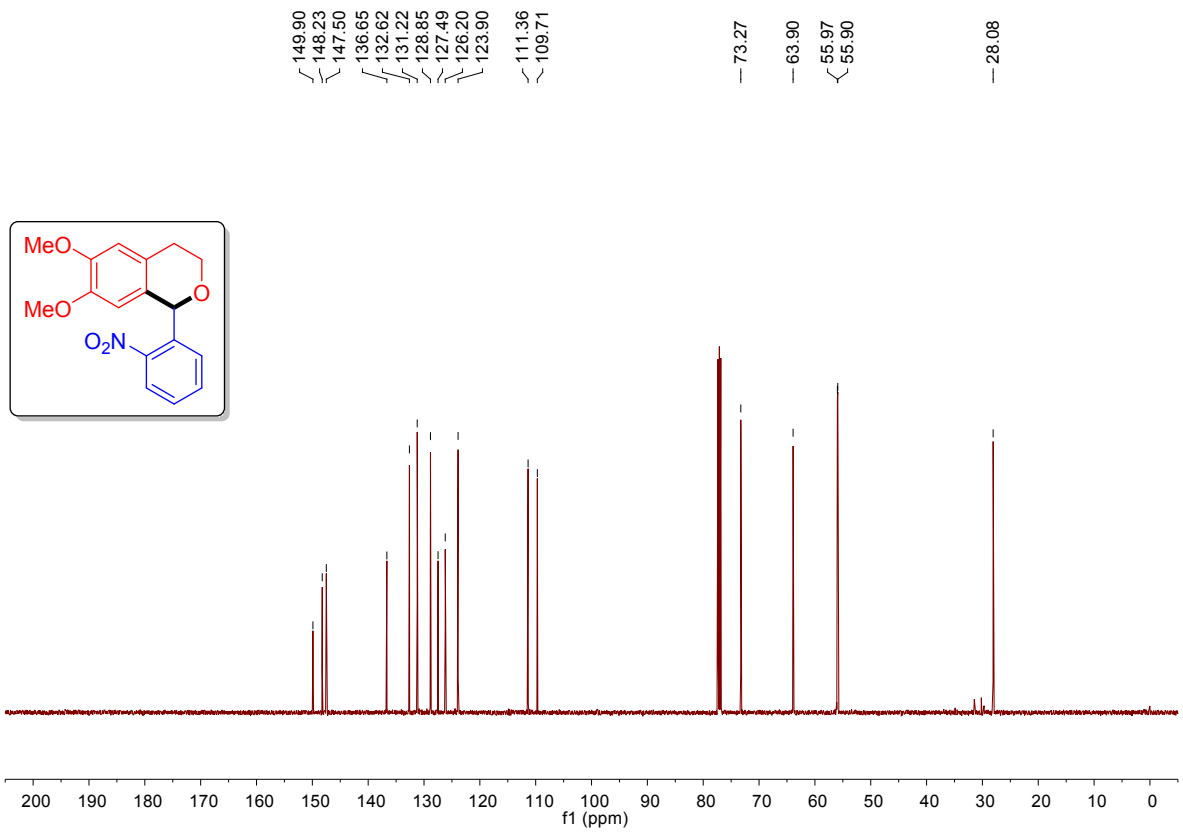
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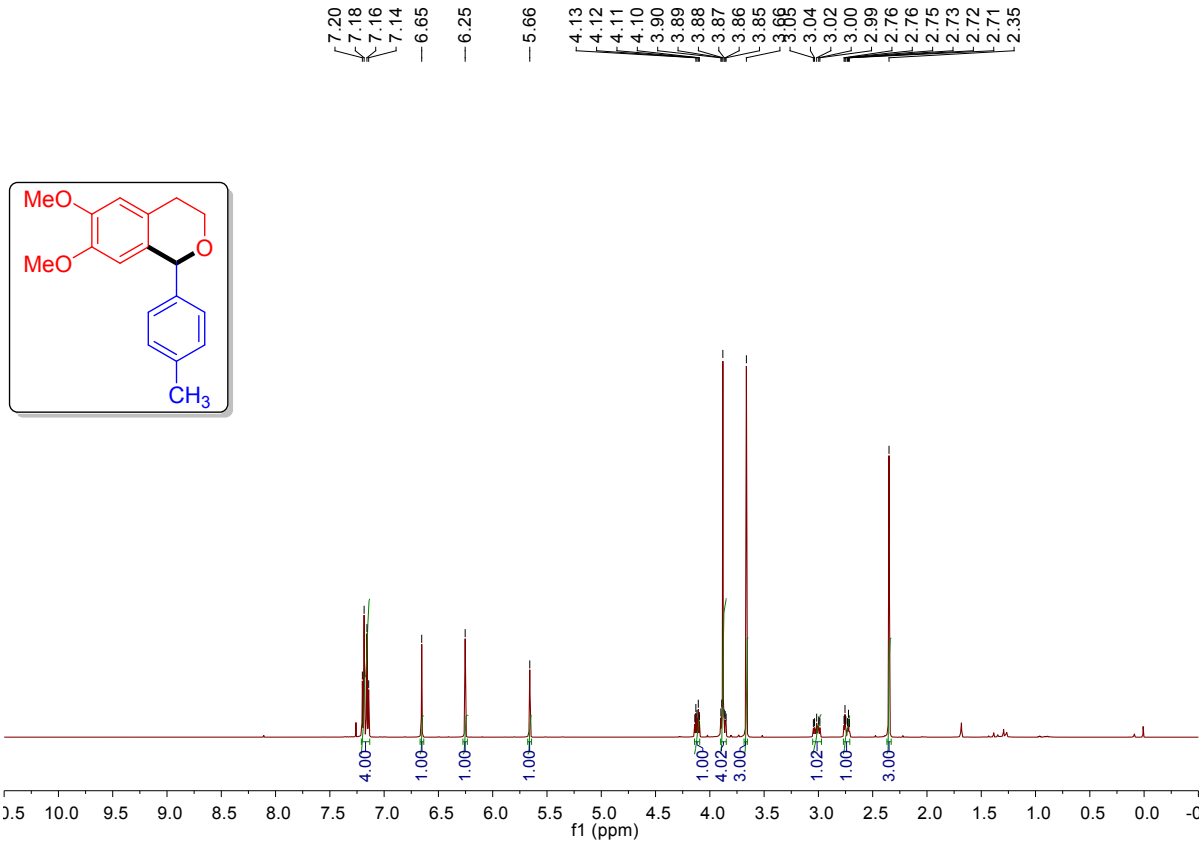
MeO
MeO
O
O2N
f1 (ppm)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4.13
4.12
4.11
4.10
3.90
3.89
3.88
3.87
3.86
3.85
3.04
3.02
3.00
2.99
2.76
2.76
2.75
2.73
2.72
2.71
2.35
MeO
MeO
O
CH3
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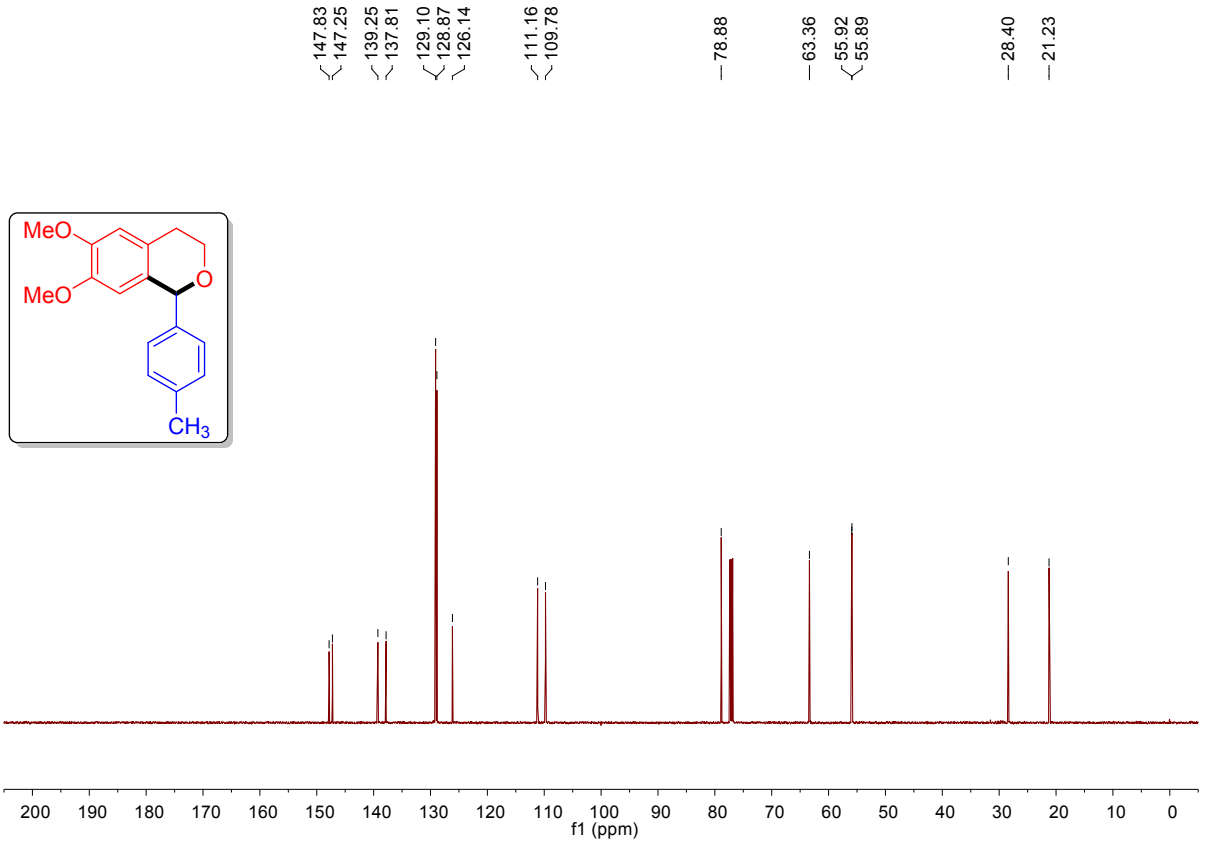
1.00
1.00
1.00
4.02
3.00
1.02
1.00
3.00
f1 (ppm)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128.87
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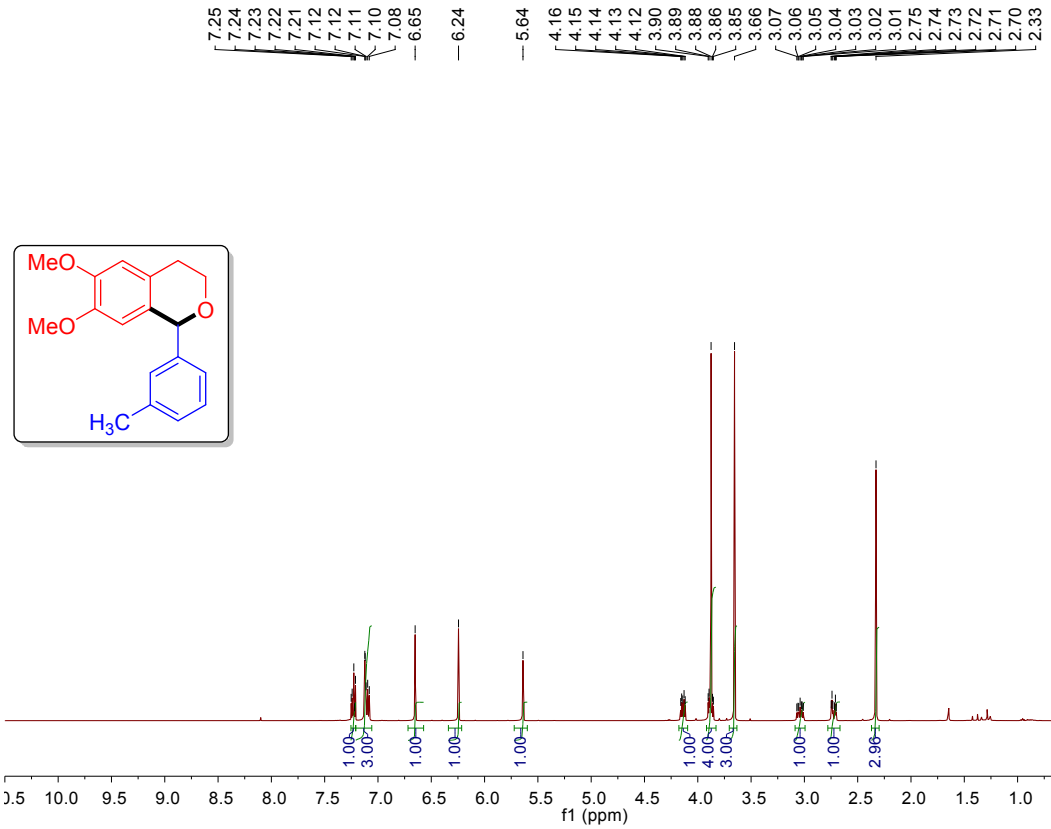
MeO
O
CH3
f1 (ppm)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6.24
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4.15
4.14
4.13
4.12
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3.88
3.86
3.85
3.66
3.07
3.06
3.05
3.04
3.03
3.02
3.01
2.75
2.74
2.73
2.72
2.71
2.70
2.33
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MeO
O
H3C
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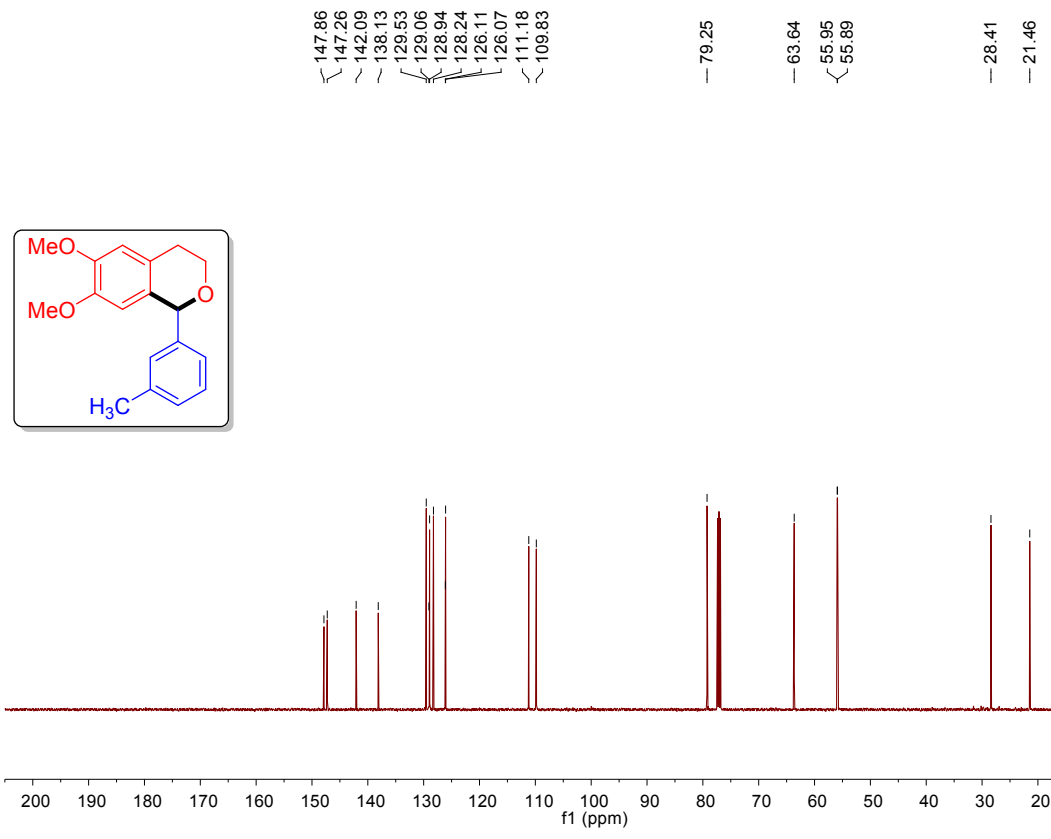
1.00
1.00
1.00
4.00
3.00
1.00
1.00
2.96
f1 (ppm)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126.07
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63.64
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55.89
28.41
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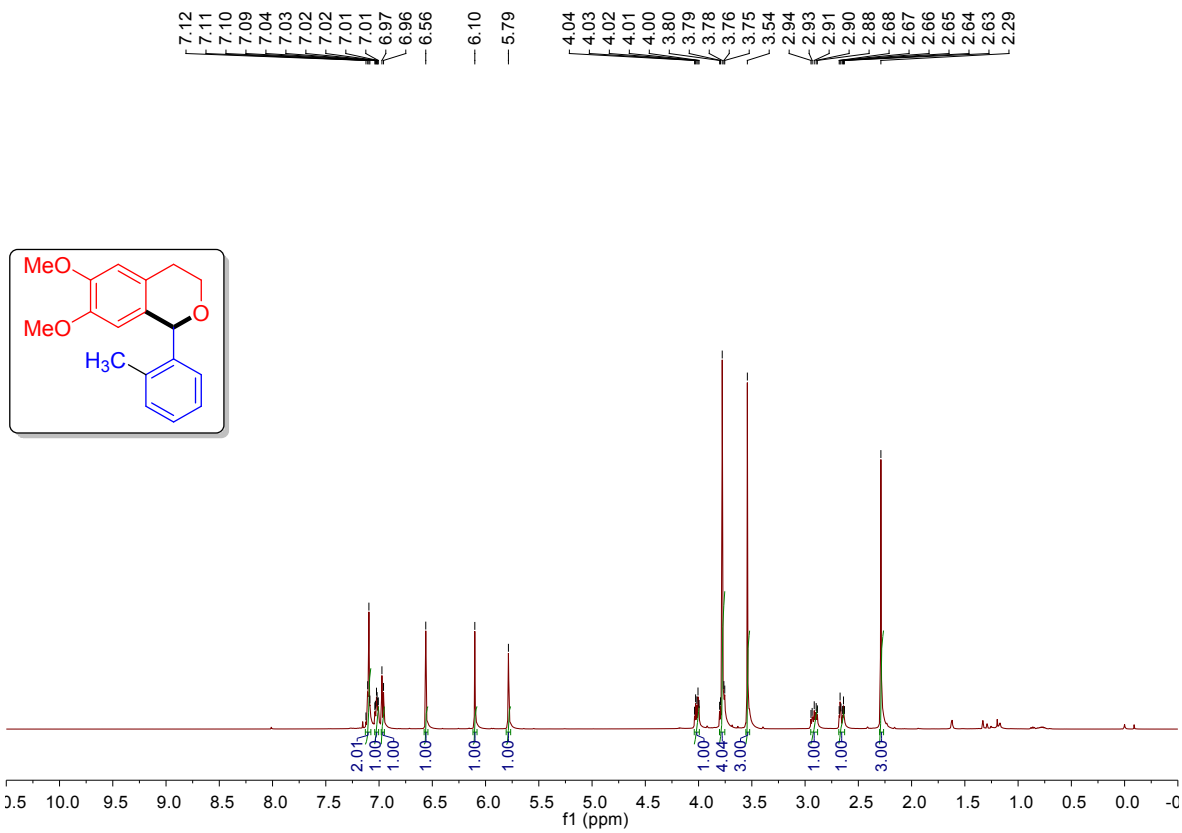
MeO
O
H3C
f1 (ppm)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7.11
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7.02
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6.96
6.56
6.10
5.79
4.04
4.03
4.02
4.01
4.00
3.80
3.79
3.78
3.76
3.75
3.54
2.94
2.93
2.91
2.90
2.88
2.68
2.67
2.66
2.65
2.64
2.63
2.29
MeO
MeO
O
H3C
2.01
1.00
1.00
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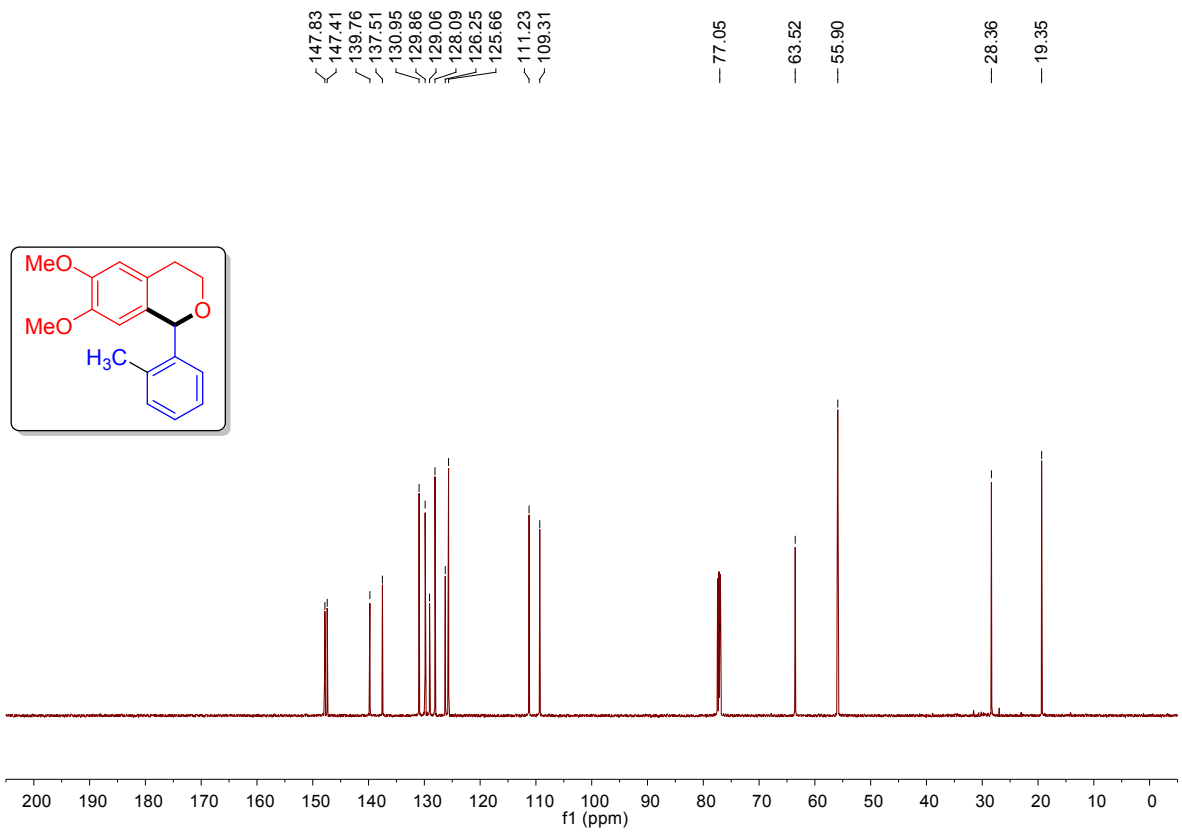
1.00
1.00
1.00
4.04
3.00
1.00
1.00
3.00
f1 (ppm)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129.86
129.06
128.09
126.25
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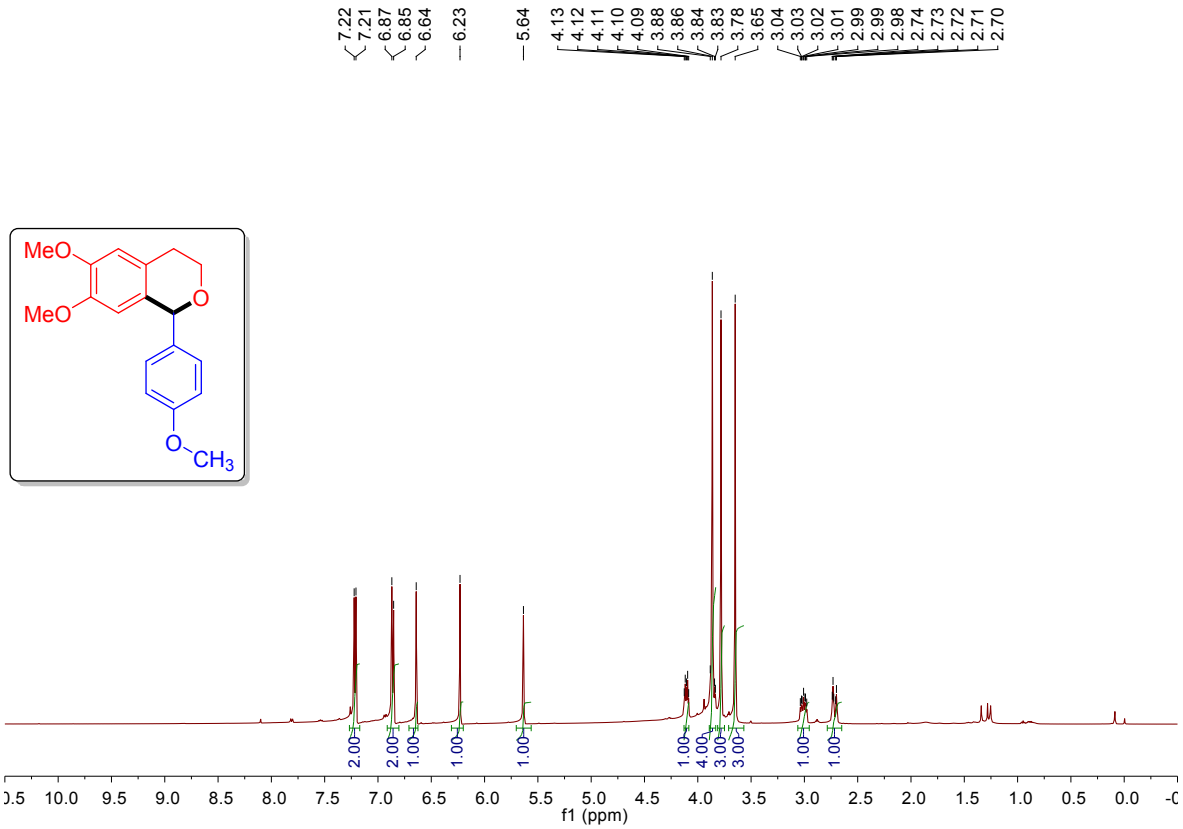
63.52
55.90
28.36
19.35
MeO
MeO
O
H3C
f1 (ppm)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5.64
4.13
4.12
4.11
4.10
4.09
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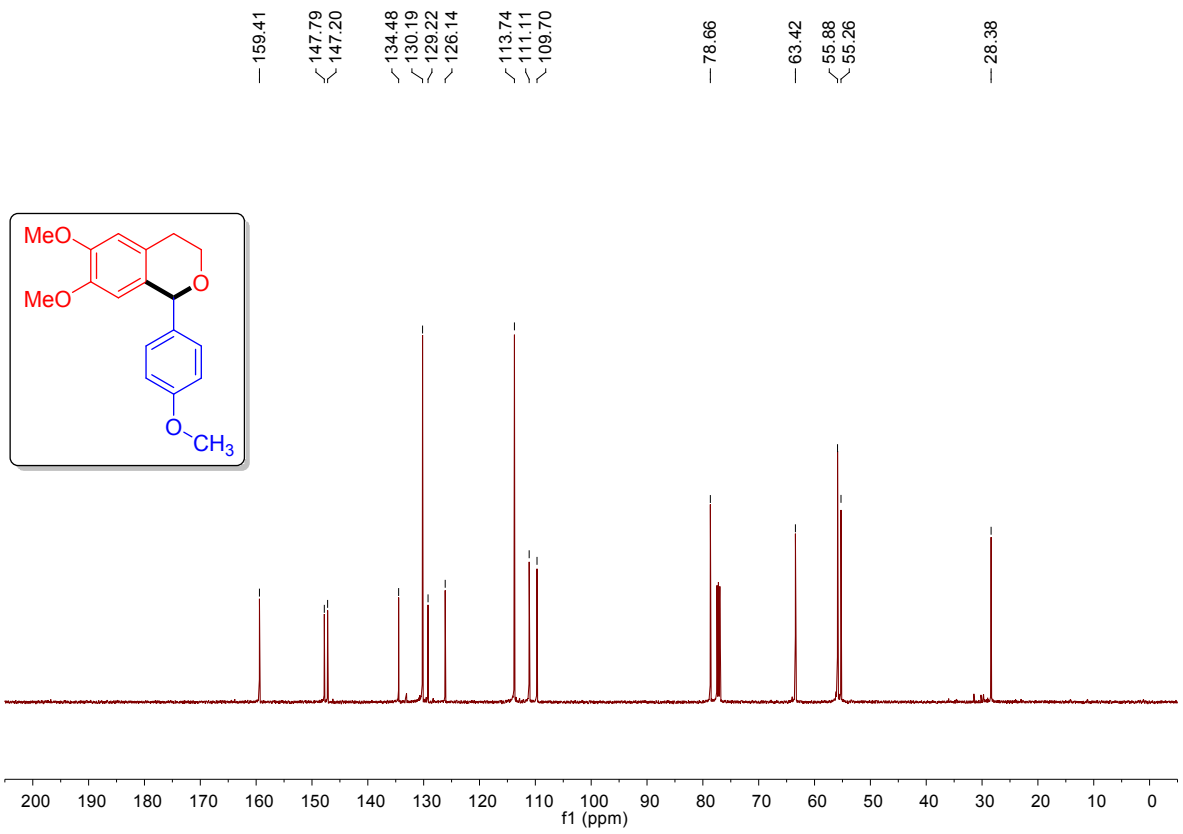
3.86
3.84
3.83
3.78
3.65
3.04
3.03
3.02
3.01
2.99
2.99
2.98
2.74
2.73
2.72
2.71
2.70
MeO
MeO
O
O
CH3
2.00
2.00
1.00
1.00
1.00
1.00
4.00
3.00
3.00
1.00
1.00
f1 (ppm)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130.19
129.22
126.14
113.74
111.11
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78.66
63.42
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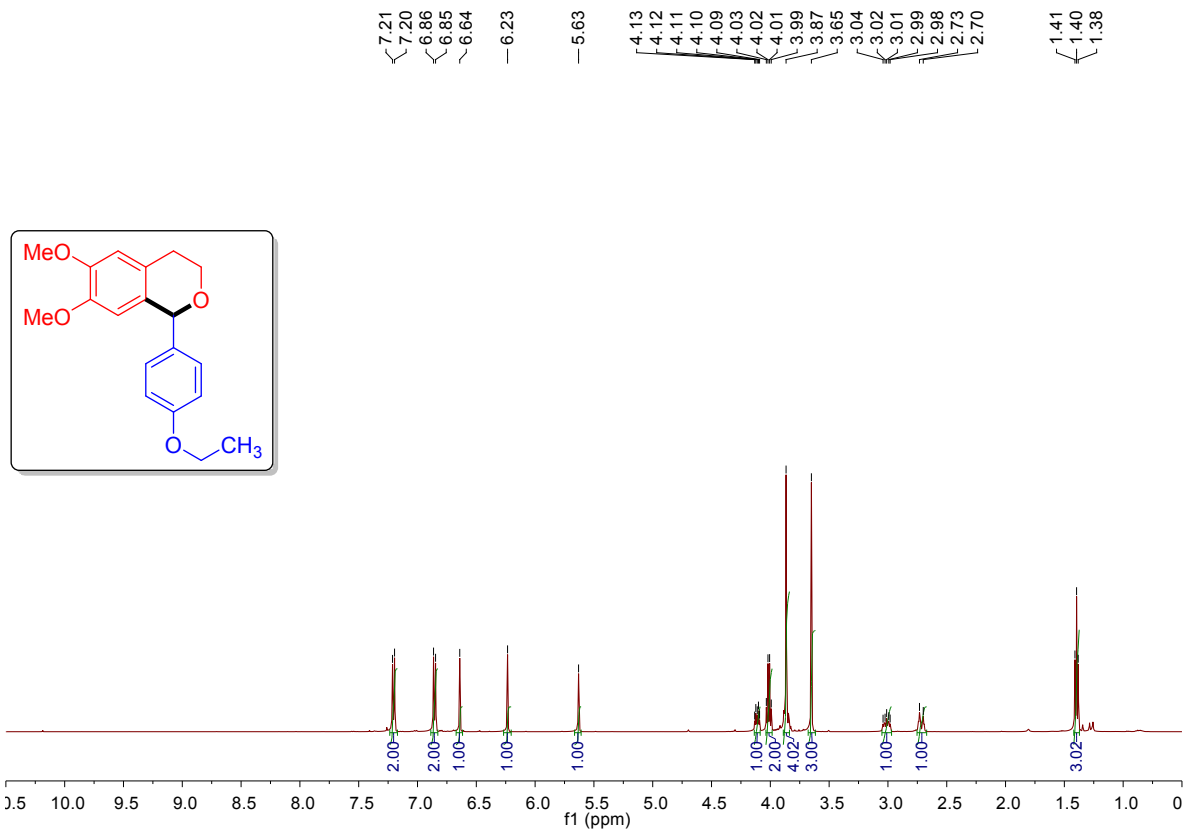
28.38
MeO
MeO
O
O
CH3
f1 (ppm)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6.64
6.23
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4.13
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4.11
4.10
4.09
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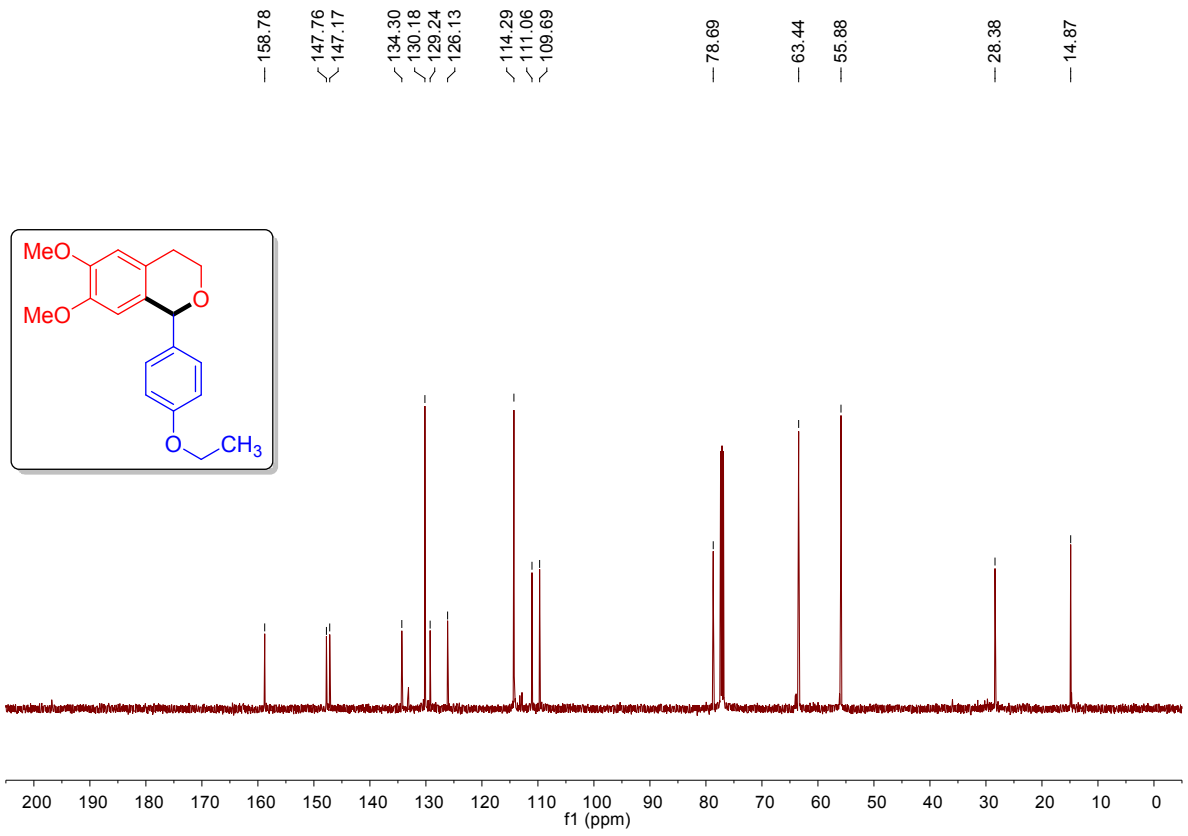
4.02
4.01
3.99
3.87
3.65
3.04
3.02
3.01
2.99
2.98
2.73
2.70
1.41
1.40
1.38
MeO
MeO
O
O
CH3
2.00
2.00
1.00
1.00
1.00
1.00
2.00
4.02
3.00
1.00
1.00
3.02
f1 (ppm)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129.24
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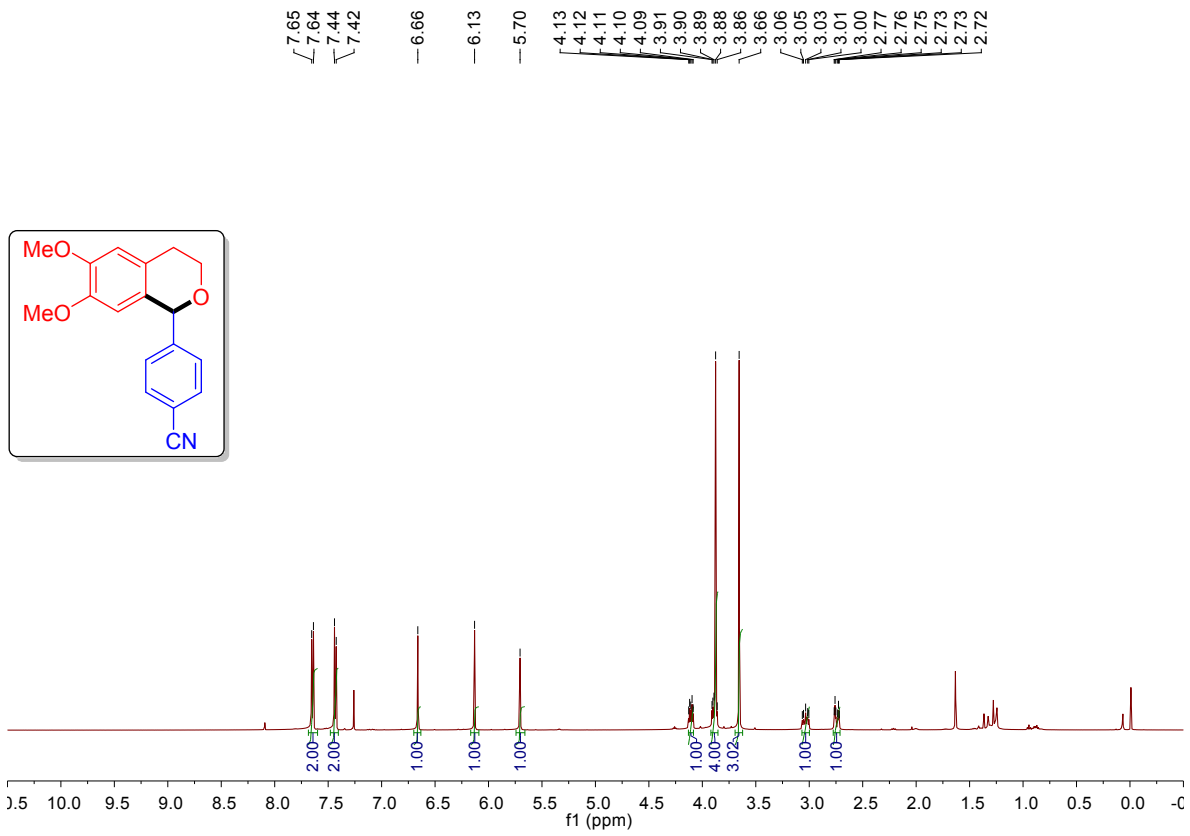
78.69
63.44
55.88
28.38
14.87
MeO
MeO
O
O
CH3
f1 (ppm)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7.64
7.44
7.42
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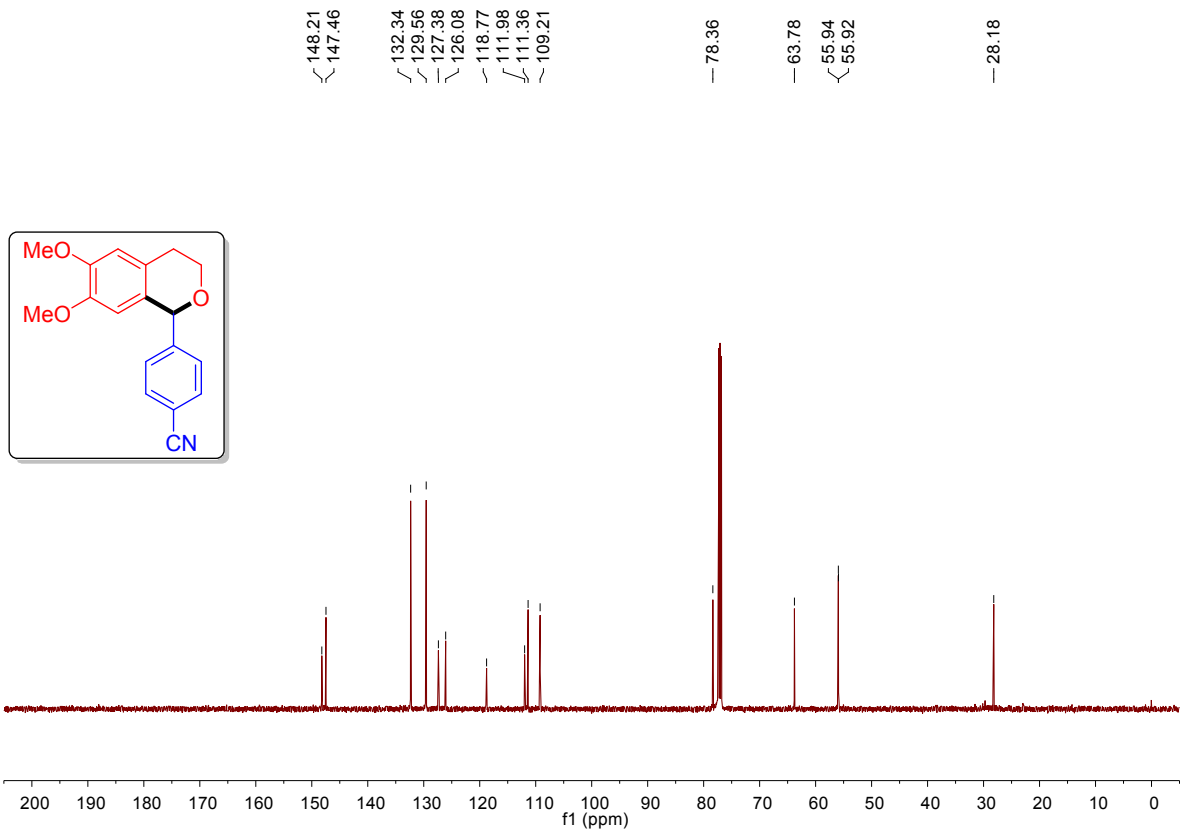
6.13
5.70
4.13
4.12
4.11
4.10
4.09
3.91
3.90
3.89
3.88
3.86
3.66
3.06
3.05
3.03
3.01
3.00
2.77
2.76
2.75
2.73
2.73
2.72
MeO
MeO
O
CN
2.00
2.00
1.00
1.00
1.00
1.00
4.00
3.02
1.00
1.00
f1 (ppm)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126.08
118.77
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78.36
63.78
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55.92
28.18
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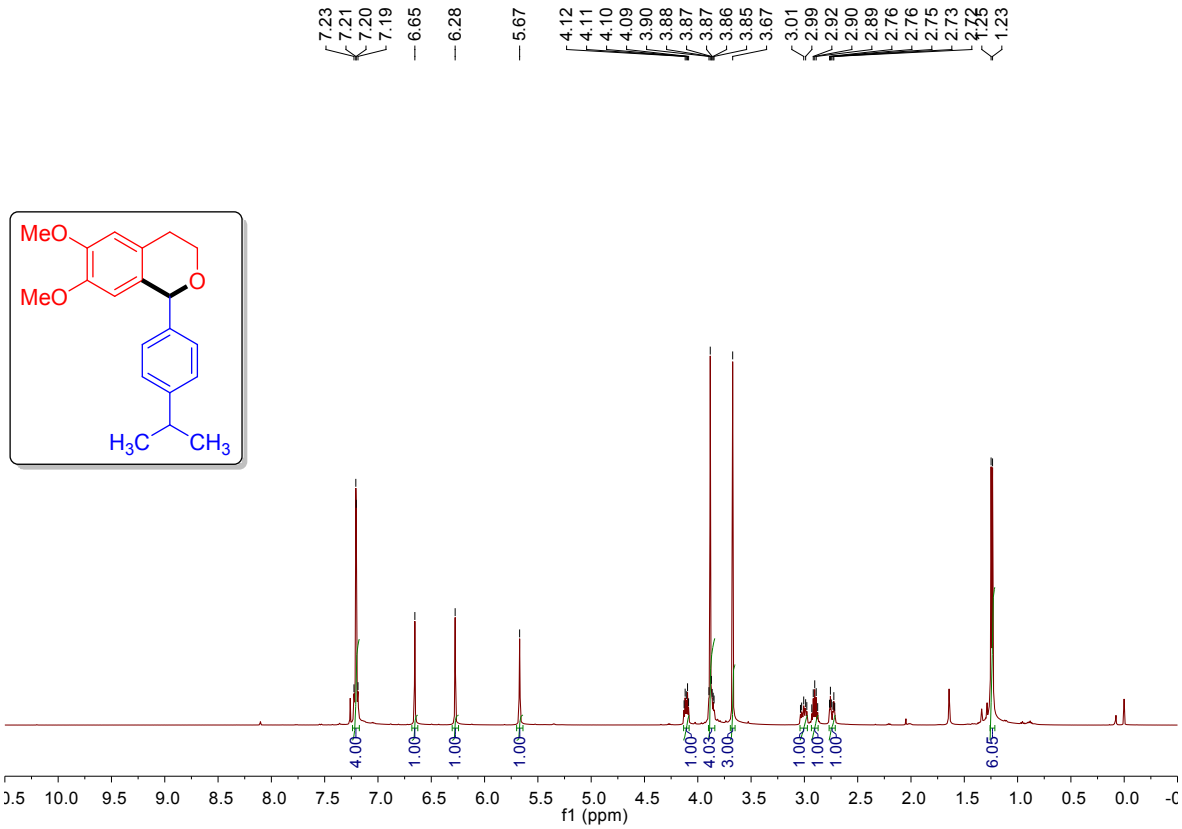
MeO
O
CN
f1 (ppm)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7.21
7.20
7.19
6.65
6.28
5.67
4.12
4.11
4.10
4.09
3.90
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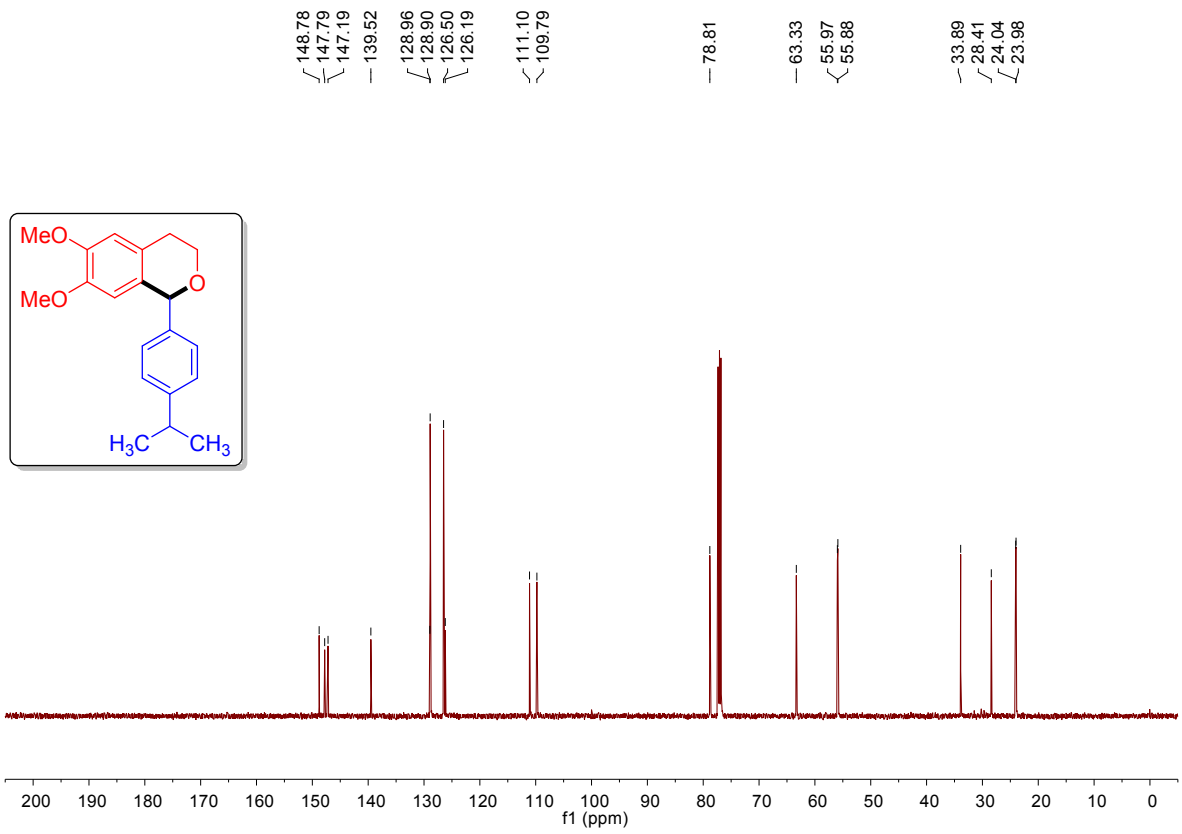
3.87
3.87
3.86
3.85
3.67
3.01
2.99
2.92
2.90
2.89
2.76
2.76
2.75
2.73
1.25
1.23
MeO
MeO
O
H3C
CH3
4.00
1.00
1.00
1.00
1.00
4.03
3.00
1.00
1.00
1.00
6.05
f1 (ppm)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126.50
126.19
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109.79
78.81
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33.89
28.41
24.04
23.98
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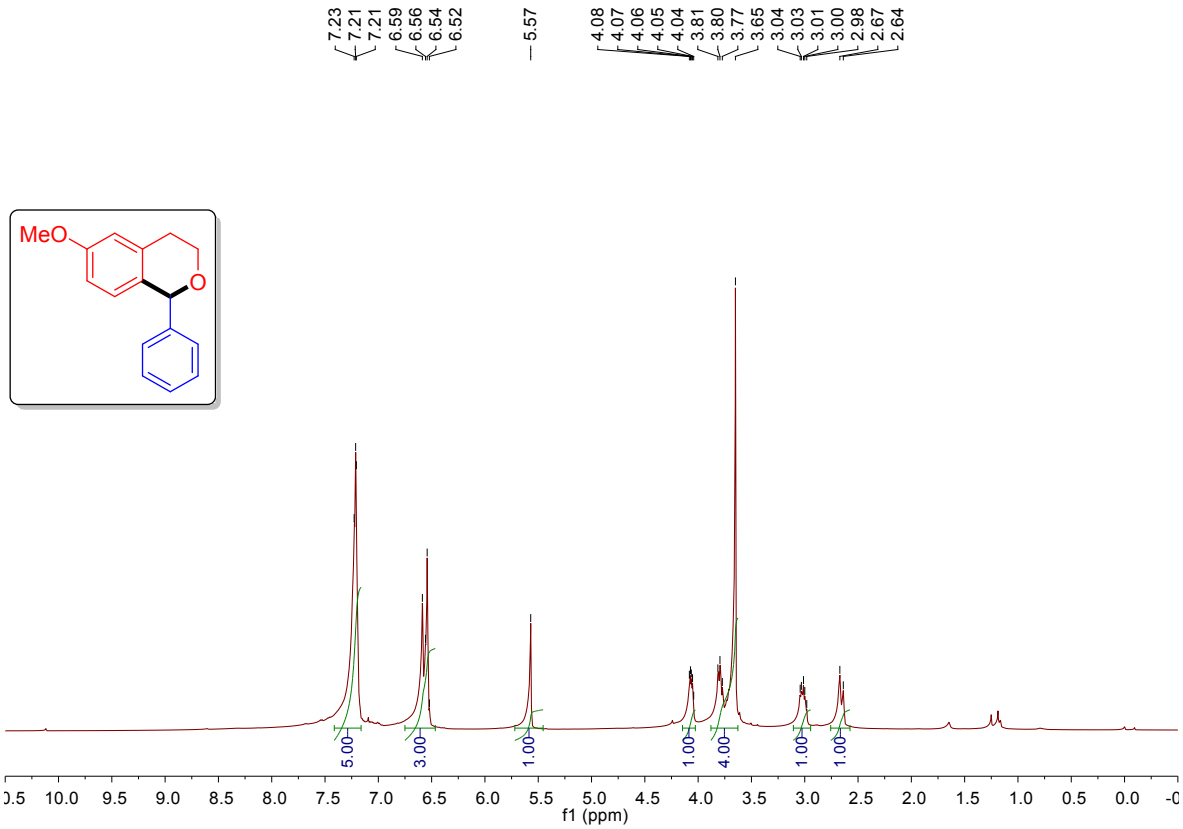
MeO
O
H3C
CH3
f1 (ppm)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6.54
6.52
5.57
4.08
4.07
4.06
4.05
4.04
3.81
3.80
3.77
3.65
3.04
3.03
3.01
3.00
2.98
2.67
2.64
MeO
O
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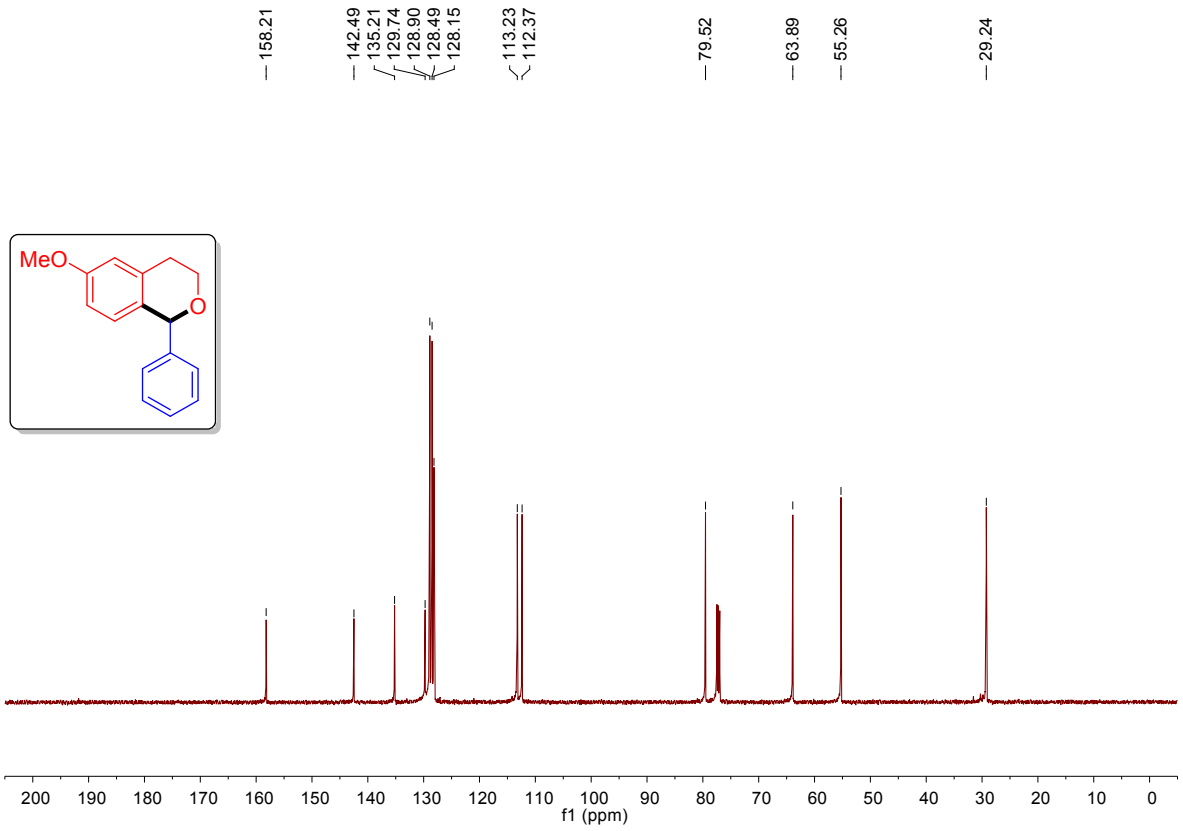
3.00
1.00
1.00
4.00
1.00
1.00
f1 (ppm)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135.21
129.74
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128.15
113.23
112.37
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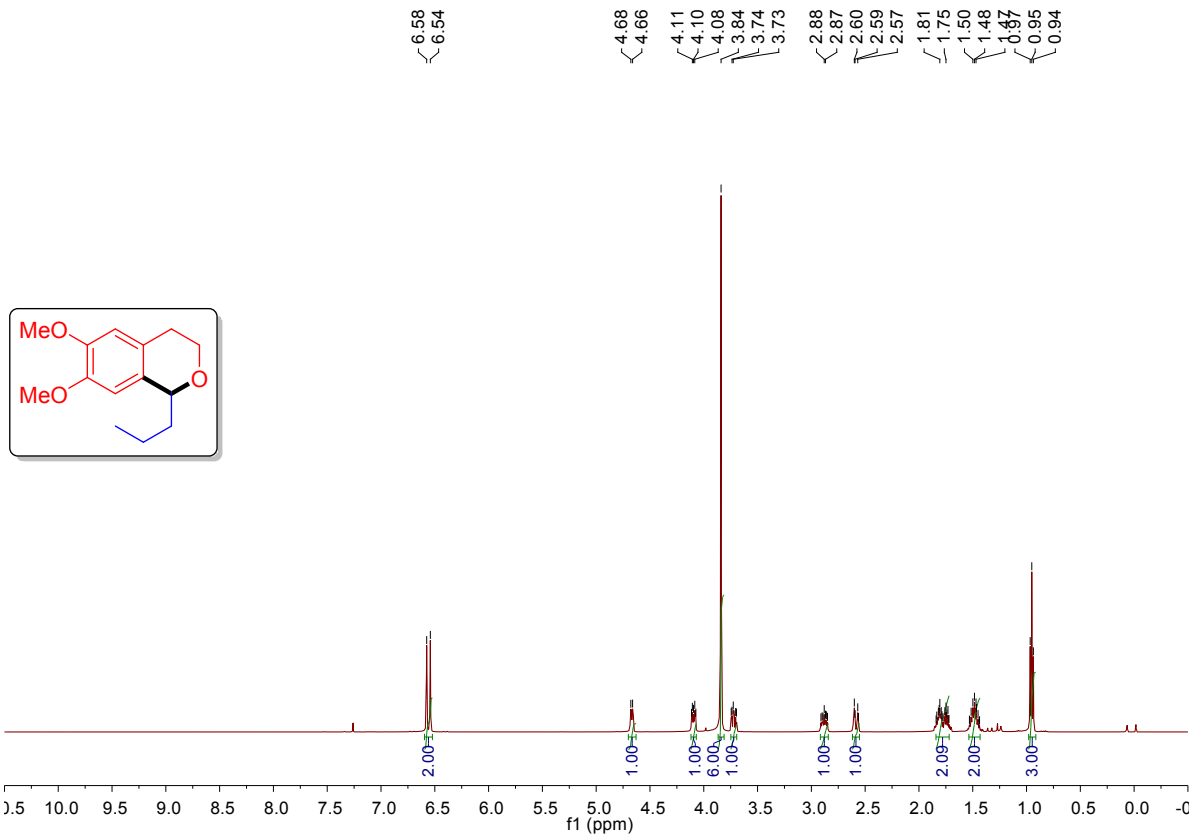
63.89
55.26
29.24
MeO
O
f1 (ppm)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4.10
4.08
3.84
3.74
3.73
2.88
2.87
2.60
2.59
2.57
1.81
1.75
1.50
1.48
0.95
0.94
MeO
MeO
O
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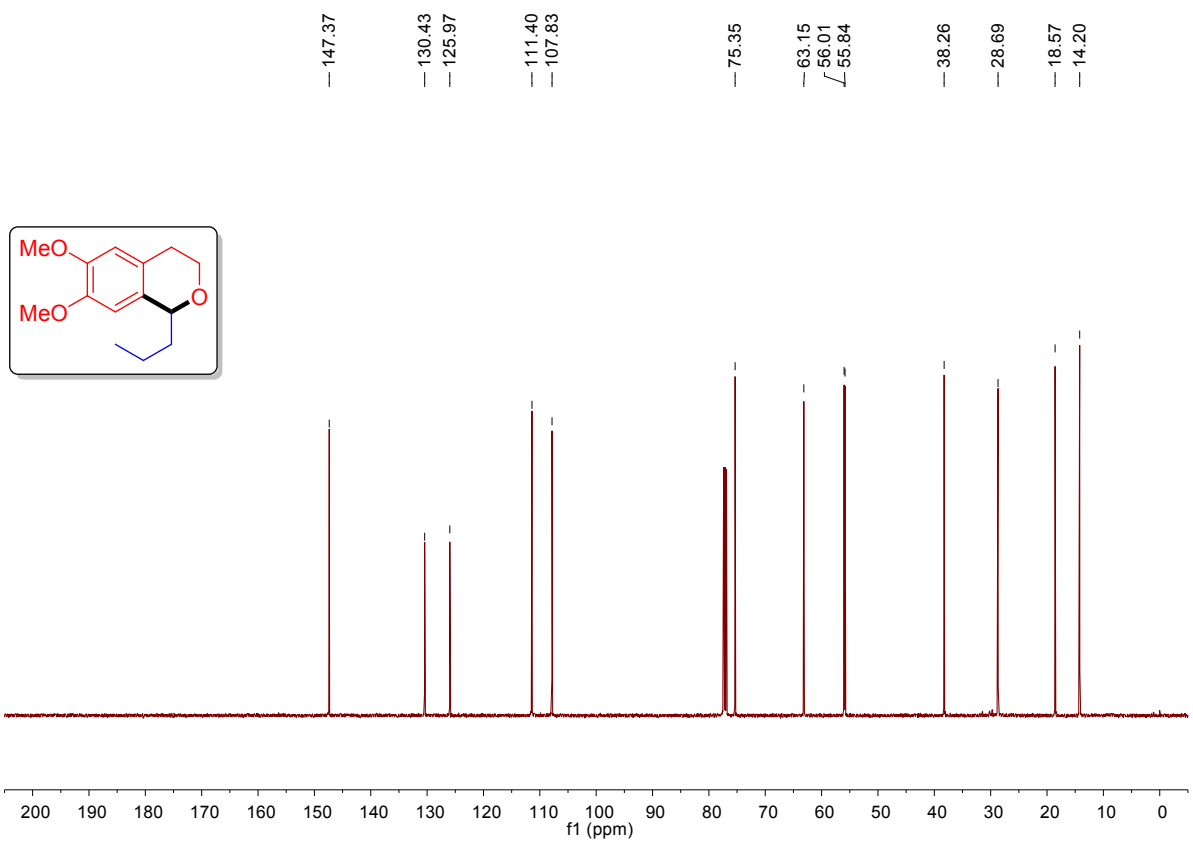
1.00
1.00
6.00
1.00
1.00
1.00
2.09
2.00
3.00
f1 (ppm)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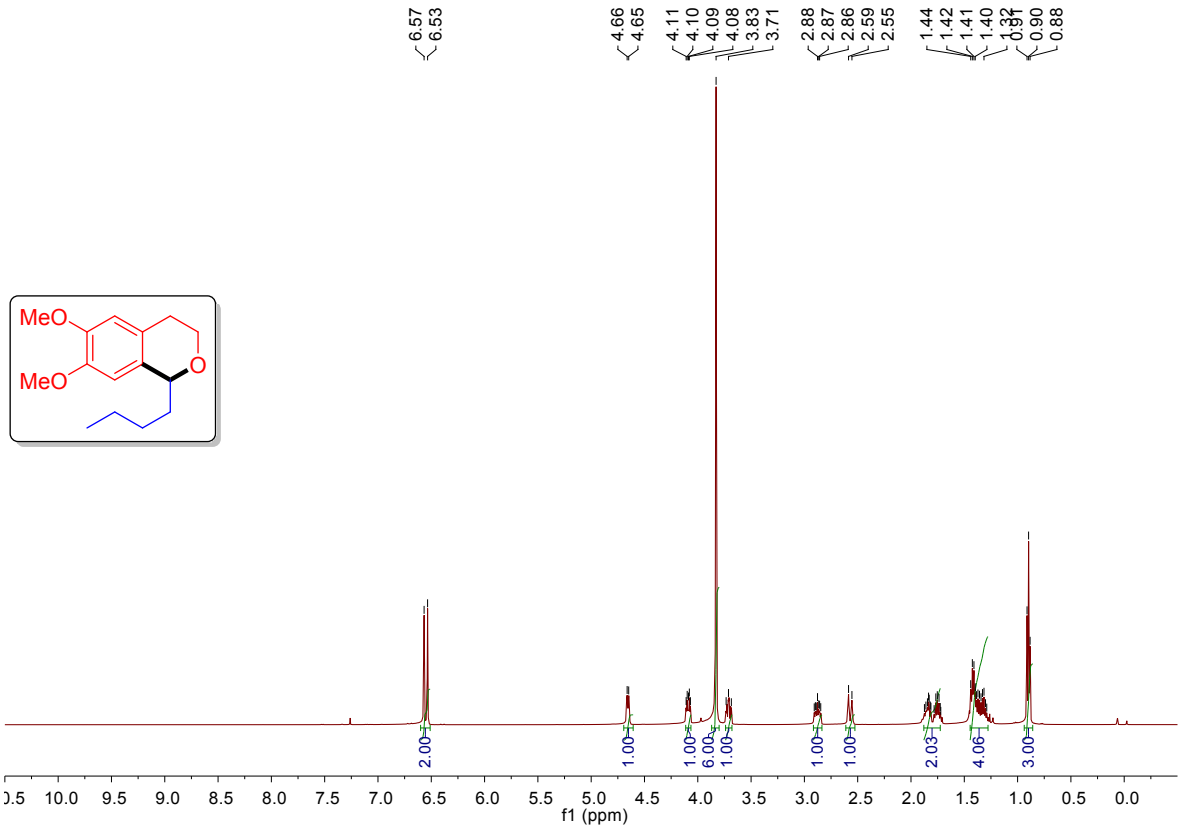
55.84
38.26
28.69
18.57
14.20
MeO
MeO
O
f1 (ppm)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2.86
2.59
2.55
1.44
1.42
1.41
1.40
0.91
0.90
0.88
MeO
MeO
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2.00
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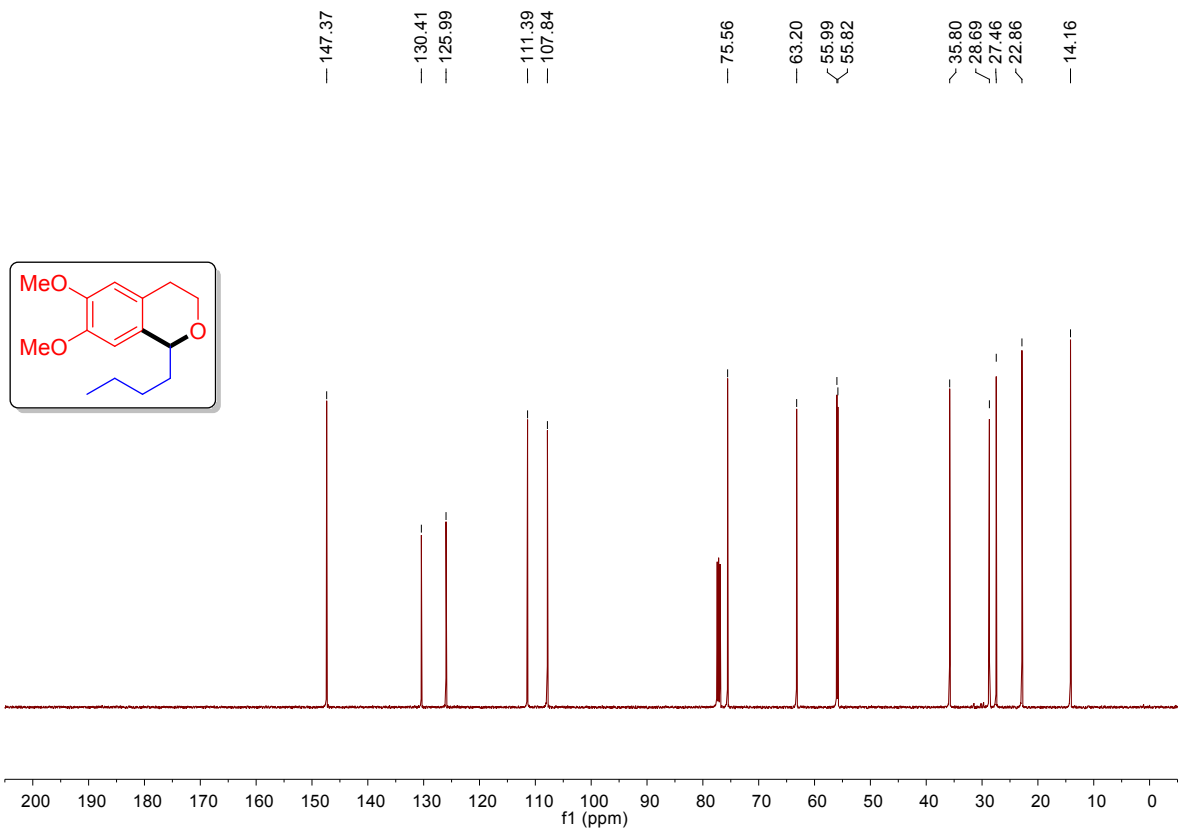
1.00
6.00
1.00
1.00
1.00
2.03
4.06
3.00
f1 (ppm)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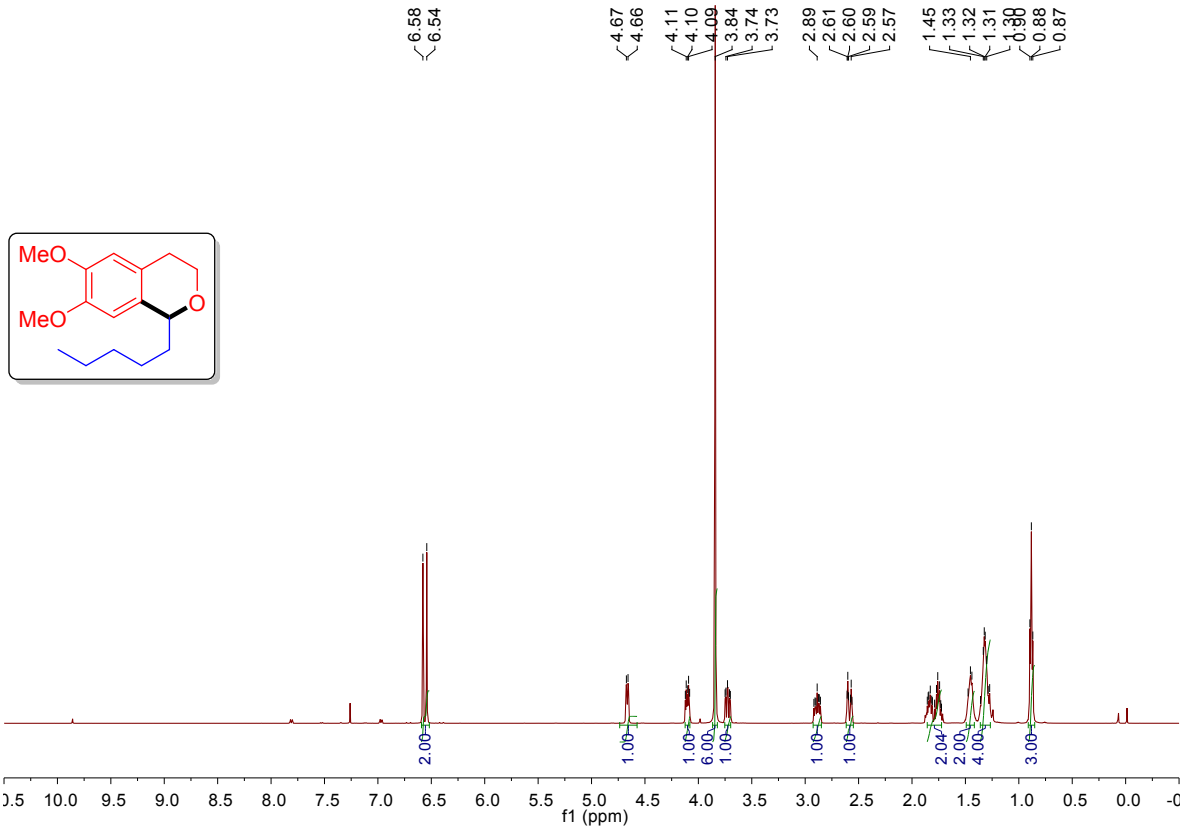
35.80
28.69
27.46
22.86
14.16
MeO
MeO
O
f1 (ppm)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4.10
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3.84
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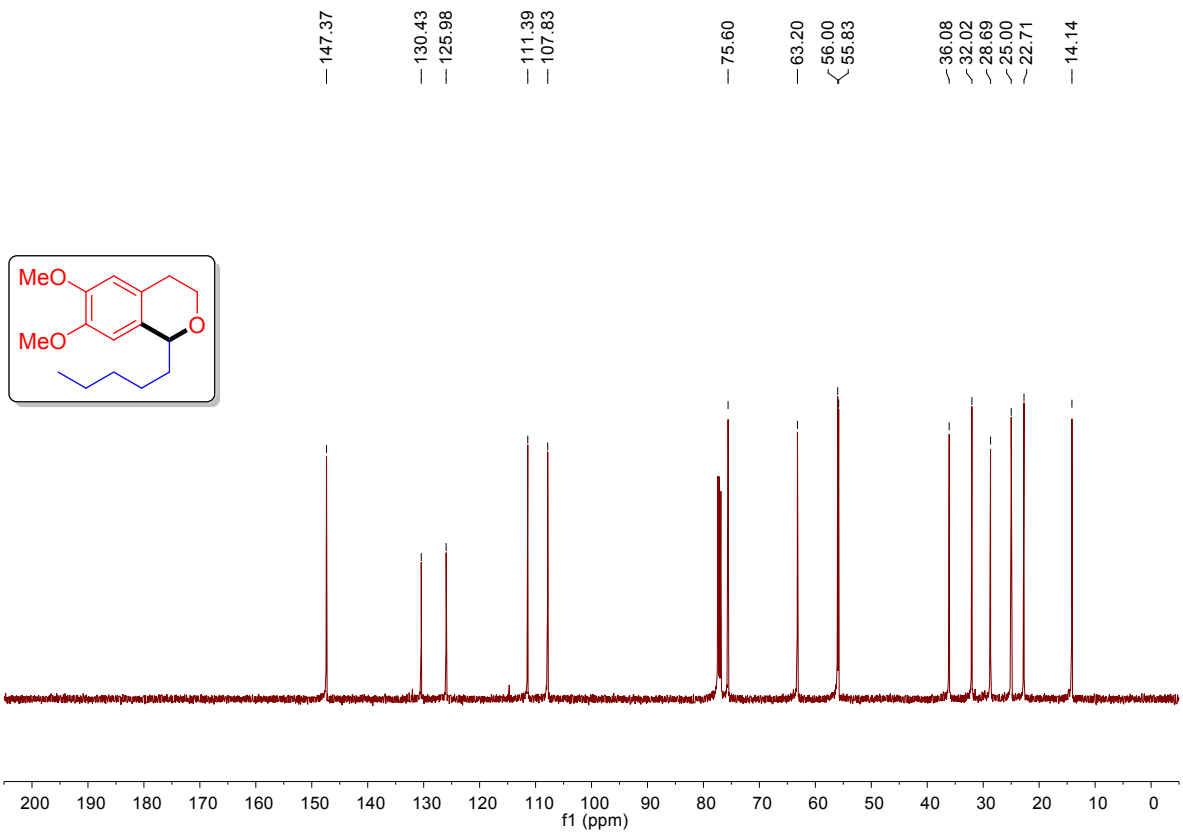
3.73
2.89
2.61
2.60
2.59
2.57
1.45
1.33
1.32
1.31
1.30
0.90
0.88
0.87
MeO
MeO
O
2.00
1.00
1.00
6.00
1.00
1.00
1.00
2.04
2.00
4.00
3.00
f1 (ppm)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111.39
107.83
75.60
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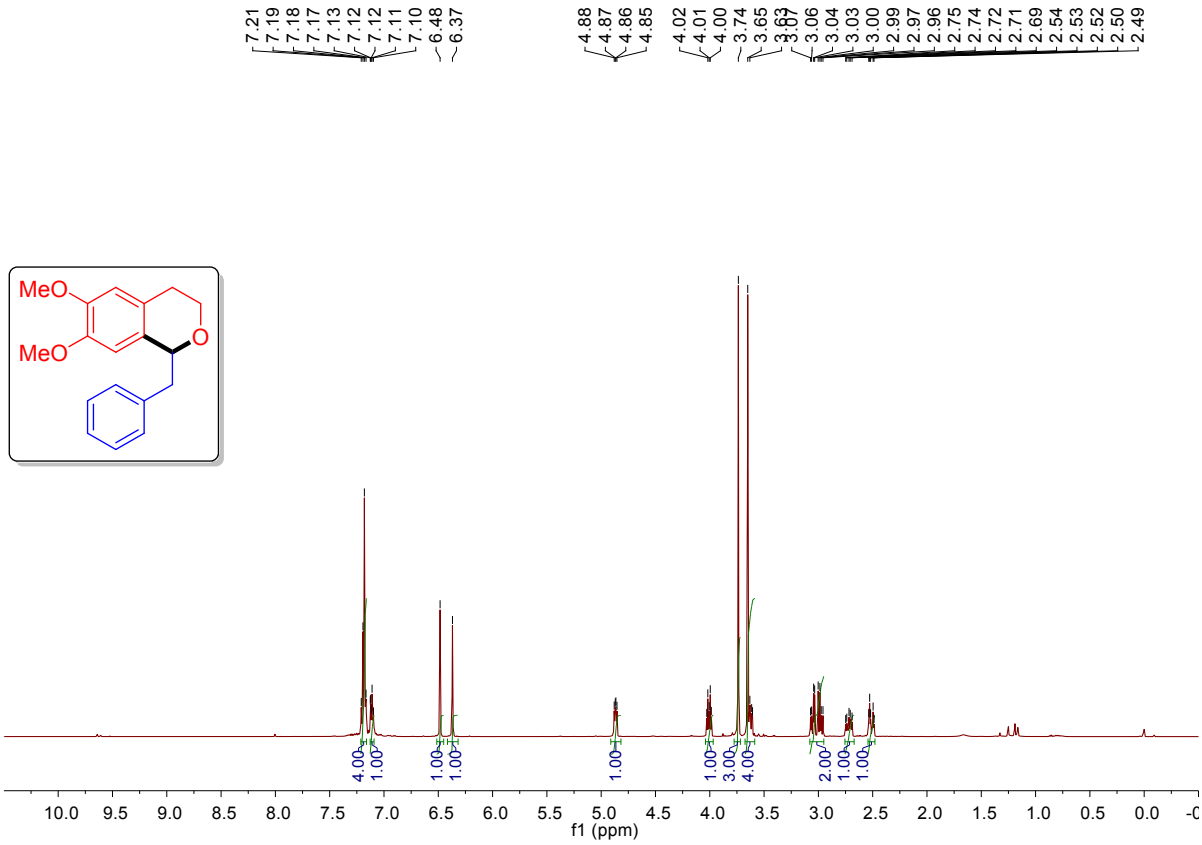
36.08
32.02
28.69
25.00
22.71
14.14
MeO
MeO
O
f1 (ppm)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7.19
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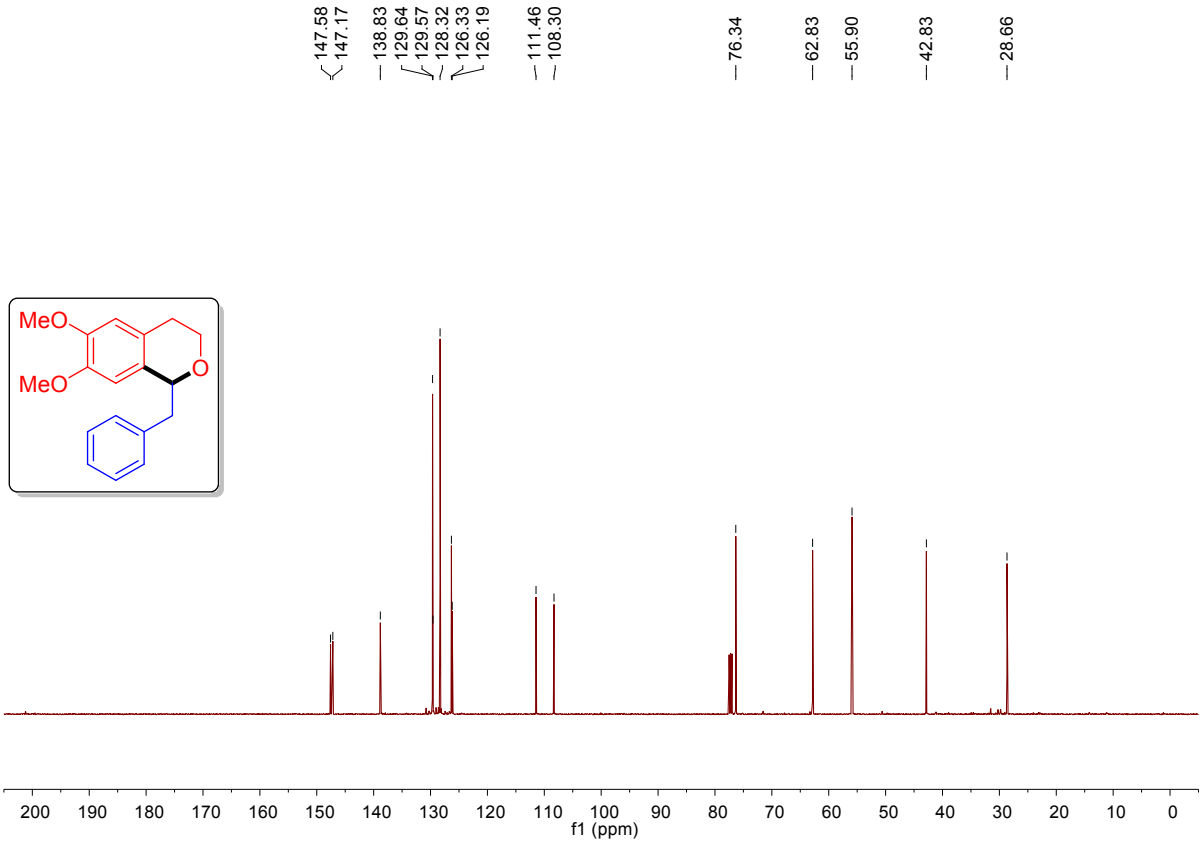
4.88
4.87
4.86
4.85
4.02
4.01
4.00
3.74
3.65
3.63
3.07
3.06
3.04
3.03
3.00
2.99
2.97
2.96
2.75
2.74
2.72
2.71
2.69
2.54
2.53
2.52
2.50
2.49
MeO
MeO
O
4.00
1.00
1.00
1.00
1.00
1.00
3.00
4.00
2.00
1.00
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.32
126.33
126.19
111.46
108.30
76.34
62.83
55.90
42.83
28.66
MeO
MeO
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

6 Notes and references

[1] Zhang W, Leng Y, Zhao P, et al. Heteropolyacid salts of n-methyl-2-pyrrolidonium as highly efficient and reusable catalysts for prins reactions of styrenes with formalin. *Green chemistry*, 2011, 13(4): 832-834.

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[3] Saeed A. Oxa-pictet–spengler reaction in water. Synthesis of some (±)-1-aryl-6, 7-dimethoxyisochromans. *Chinese Chemical Letters*, 2010, 21(3): 261-264.

[4] Zhou J, Wang C, Xue D, et al. Synthesis of isochromans via fe (otf) 2-catalyzed oxa-pictet–spengler cyclization. *Tetrahedron*, 2018, 74(49): 7040-7046.

[5] Saito A, Takayama M, Yamazaki A, et al. Synthesis of tetrahydroisoquinolines and isochromans via pictet–spengler reactions catalyzed by brønsted acid–surfactant-combined catalyst in aqueous media. *Tetrahedron*, 2007, 63(19): 4039-4047.

[6] Product class 5: seven-membered hetarenes with two or more heteroatoms. Science of Synthesis (2004), 17, 929-977. Publisher: (Georg Thieme Verlag,) CODEN:SSCYJ9

[7] Peng Z, Wang Y, Yu Z, et al. Direct Arylation of Benzyl Ethers with Organozinc Reagents. *J. Org. Chem,* 2018, 83(15): 7900–7906.

[8] Wang Z, Mao Y, Guan H, et al Direct oxidative C(sp^3)-H cyanation of secondary benzylic ethers. *Chinese Chemical Letters*, 2019, 30(6): 261–264.