

Supporting Information

Synthesis of isoindolinones by Pd-catalyzed coupling between *N*-methoxybenzamide and styrene derivatives

Changkun Xia,[†] Andrew J. P. White and King Kuok (Mimi) Hii*

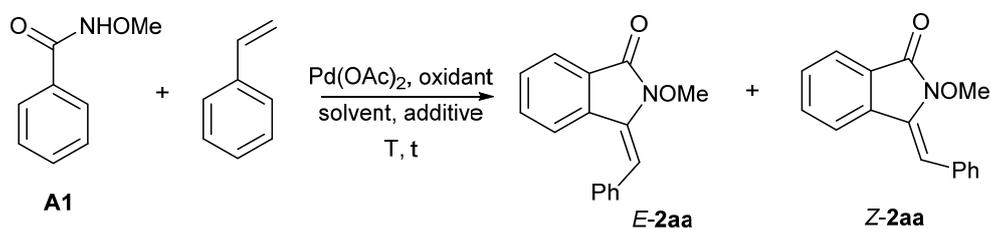
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Table S1. Screening reaction conditions for the coupling between *N*-methoxybenzamide (A1) and styrene.^[a]

Entry	Styrene/eq.	Oxidant	Solvent	Additive	T/°C	t/h	Yield/%
1	2	K ₂ S ₂ O ₈	CH ₂ Cl ₂	TFA	50	24	NR
2	2	(NH ₄) ₂ S ₂ O ₈	CH ₂ Cl ₂	TFA	50	24	NR
3	2	PhCO ₃ t-Bu	EtOAc	TFA	rt or 70	24	NR
4	2	BQ	AcOH	TFA	80	48	NR
5	2	BQ	AcOH		80	48	30
6	2	BQ	AcOH	TFA	80	48	33
7	2	BQ	AcOH	TFA	70	48	34
8	2	BQ	AcOH	TFA	100	48	NR
9	2	BQ	AcOH		100	48	27
10	2	BQ	AcOH	TFA	100	48	30
11	2	BQ	EtOAc	TFA	80	24	NR
12	3	BQ ^[b]	AcOH	TFA	70	48	69
13	3	BQ	AcOH (1.5 mL)	TFA	70	24	66
14	2	BQ ^[c] /O ₂	AcOH	TFA	70	48	34
15	3	Cu(OAc) ₂ / O ₂	AcOH	TFA	80	24	48
16	3	Cu(OAc) ₂ / O ₂	AcOH	TFA	90	24	60
17	3	Cu(OAc) ₂ / O ₂	AcOH	none	90	24	44
18	3	Cu(OAc) ₂ / O ₂	AcOH	TFA	100	24h	50

[a] General conditions: **A1** (0.3 mmol), styrene (0.6 or 0.9 mmol, as indicated), Pd(OAc)₂ (0.015 mmol), oxidant (0.6 mmol) or Cu(OAc)₂ (0.06 mmol, 20 mol%) with O₂ balloon, solvent (3 mL), TFA (0.3 mmol, if added). [b] 2.5 equiv [c] 1 equiv

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Table S2. Crystal Data and Structure Refinement Parameters for **2aa**, **4aa** and **4'aa**.

	E-2aa	4aa	4'aa
Formula	C ₁₆ H ₁₃ NO ₂	C ₁₆ H ₁₅ NO ₂	C ₁₅ H ₁₃ NO
Crystal Size (mm ³)	0.56 x 0.50 x 0.20	0.59 x 0.37 x 0.25	0.20 x 0.15 x 0.10
Molecular mass	251.27	253.29	223.26
Crystal system	Monoclinic,	Orthorhombic	Monoclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 2 ₁ 2 ₁ 2 ₁	<i>P</i> 2 ₁ / <i>c</i>
<i>a</i> (Å)	9.1382(5)	8.5662(4)	12.6365(8)
<i>b</i> (Å)	11.9472(6)	10.7642(6)	8.5132(4)
<i>c</i> (Å)	11.4848(7)	14.3417(7)	12.1579(8)
α (°)	90	90	90
β (°)	97.094(6)	90	116.664(8)
γ (°)	90	90	90
<i>V</i> (Å ³)	1244.26(12)	1322.42(11)	1168.82(15)
<i>Z</i>	4	8	4
<i>T</i> , K	173	173	173
<i>D</i> _{calc} (g·cm ⁻³)	1.341	1.272	1.269
<i>F</i> (000)	528	536	472
Range of <i>h</i> , <i>k</i> , <i>l</i>	-10 ≤ <i>h</i> ≤ 6, -9 ≤ <i>k</i> ≤ 15, -15 ≤ <i>l</i> ≤ 14	-11 ≤ <i>h</i> ≤ 7, -13 ≤ <i>k</i> ≤ 9, -18 ≤ <i>l</i> ≤ 16	-16 ≤ <i>h</i> ≤ 15, -11 ≤ <i>k</i> ≤ 10, -15 ≤ <i>l</i> ≤ 14
Reflections collected	4403	3345	4118
Data / restrain/parameters	2504 / 0 / 174	2134 / 0 / 203	2324 / 1 / 158
Goodness-of-fit on <i>F</i> ²	1.039	1.084	1.063
<i>R</i> ₁ , <i>wR</i> ₂ [<i>I</i> > 2σ(<i>I</i>)]	0.0389, 0.0866	0.0368, 0.0735	0.0462, 0.0987
<i>R</i> ₁ , <i>wR</i> ₂ (all data)	0.0548, 0.0954	0.0445, 0.0785	0.0644, 0.1110

$$^a R_1 = \sum (|F_0| - |F_c|) / \sum |F_0| \quad wR_2 = \left[\frac{\sum w(F_0^2 - F_c^2)^2}{\sum w(F_0^2)^2} \right]^{0.5}$$

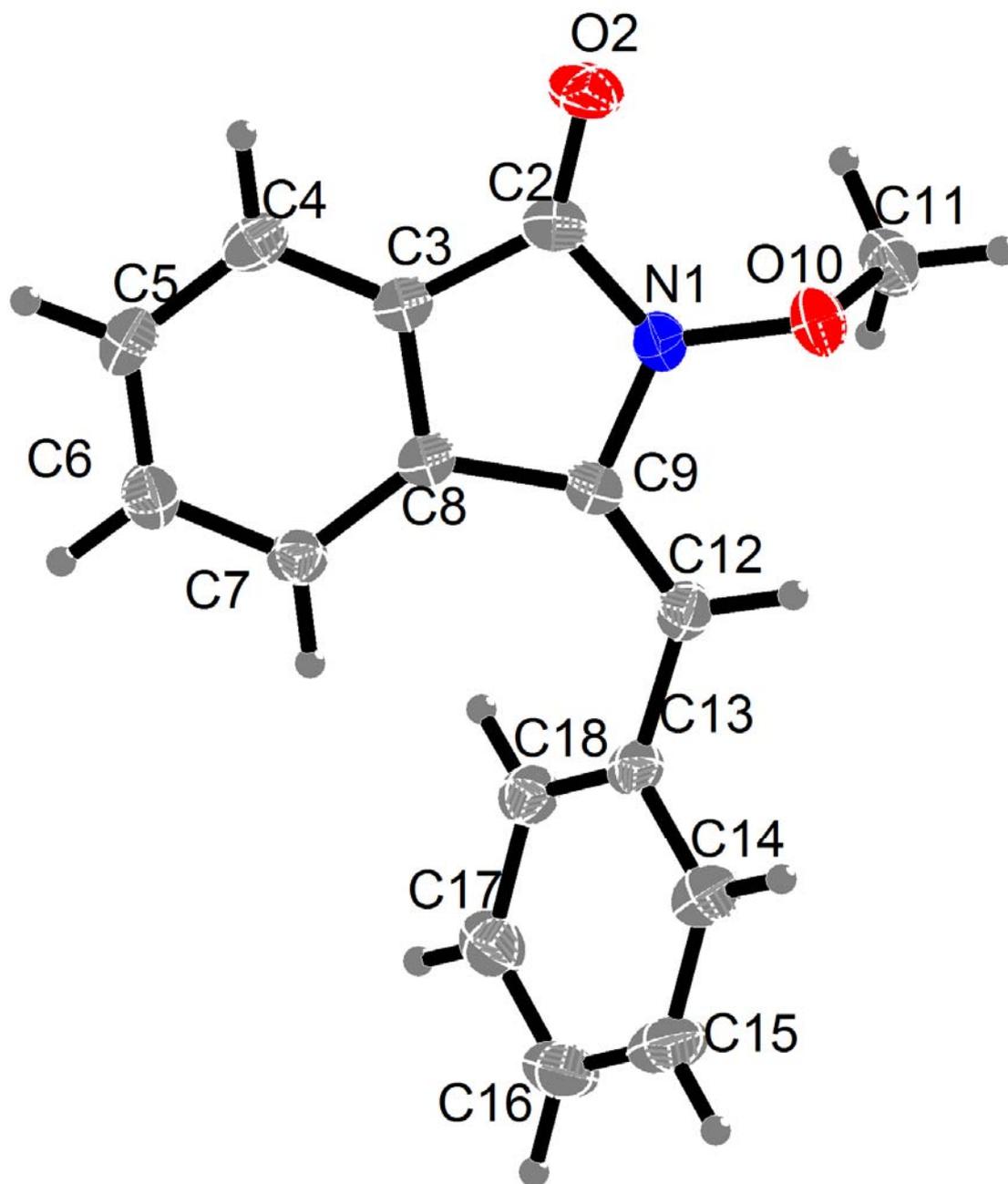


Fig. S1 X-ray diffraction of *E*-2aa with thermal ellipsoids plotted at 50% level

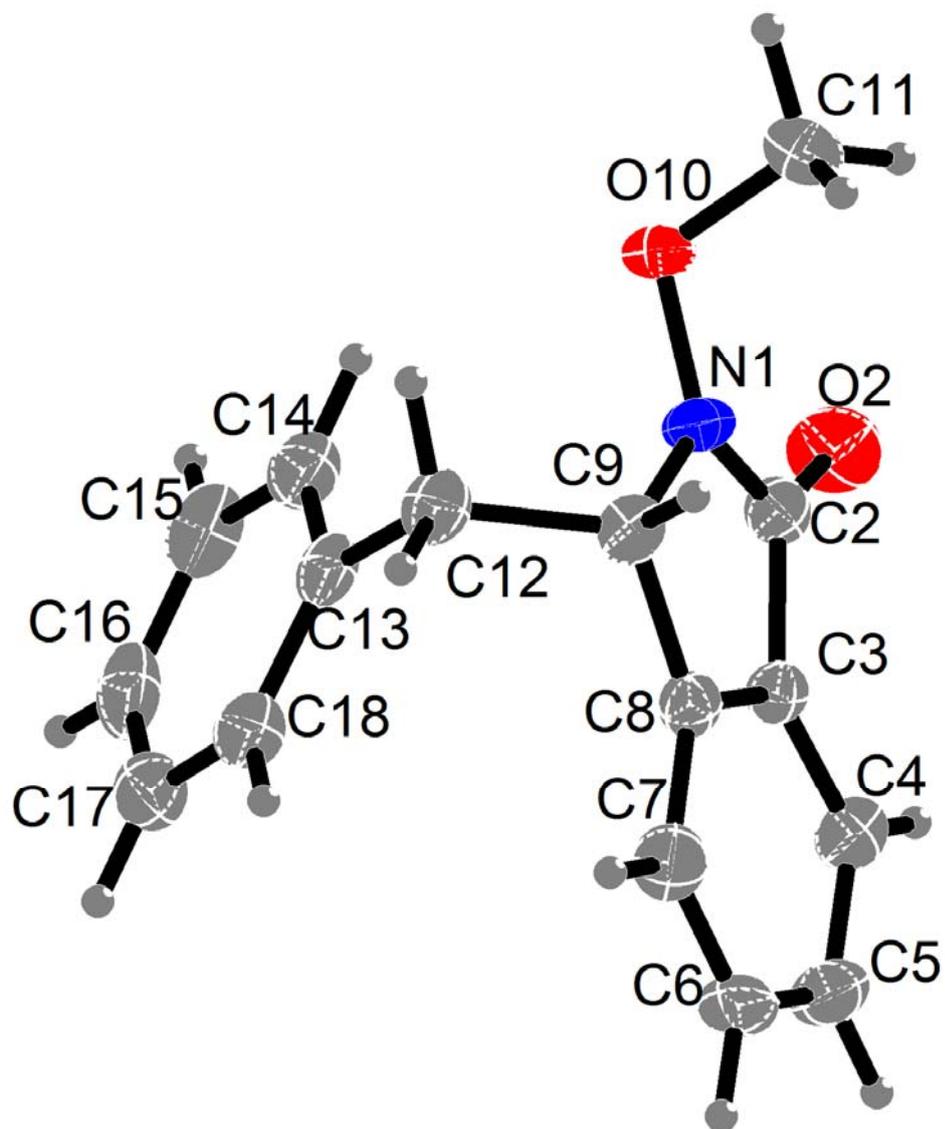


Fig. S2 X-ray diffraction of **4aa** with thermal ellipsoids plotted at 50% level

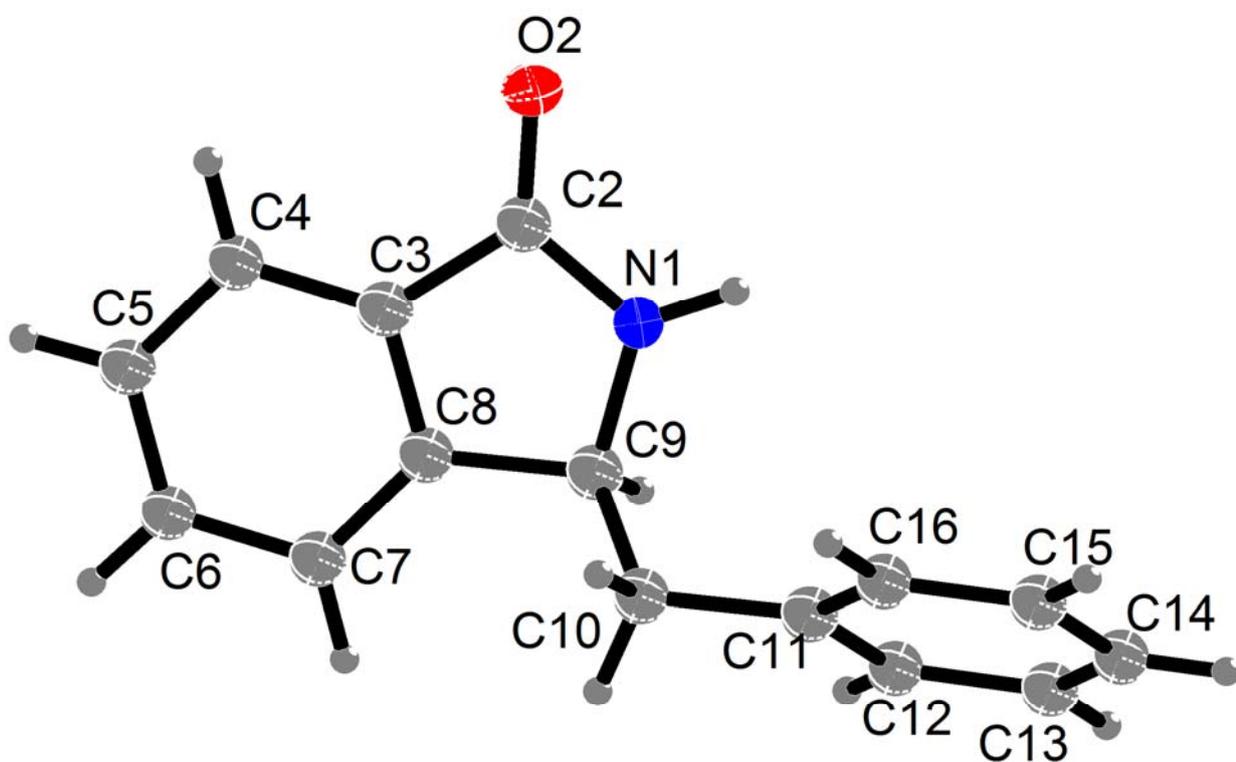
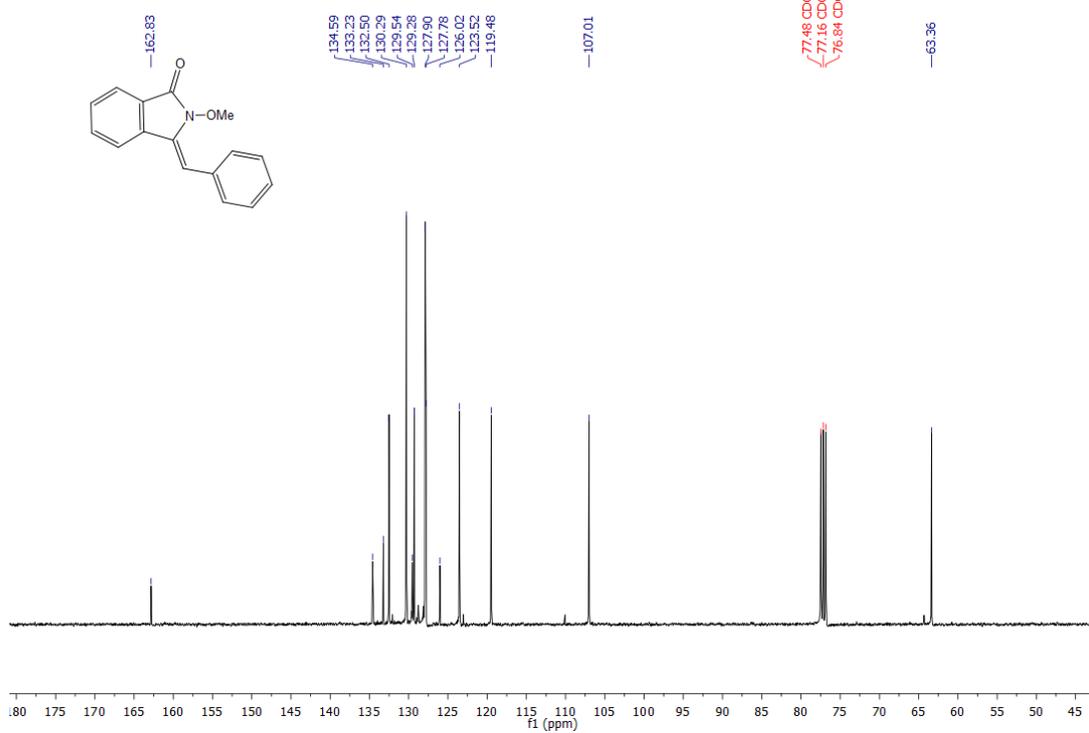
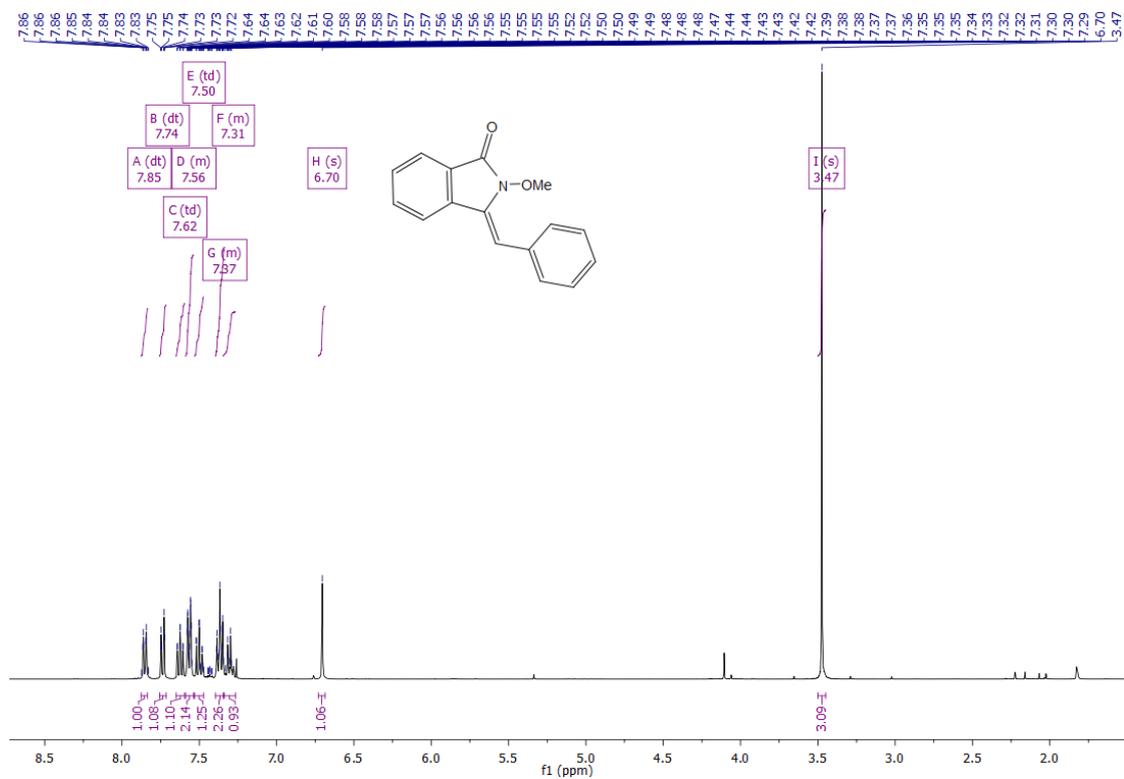


Fig. S3 X-ray diffraction of **4'aa** with thermal ellipsoids plotted at 50% level

Supporting Information

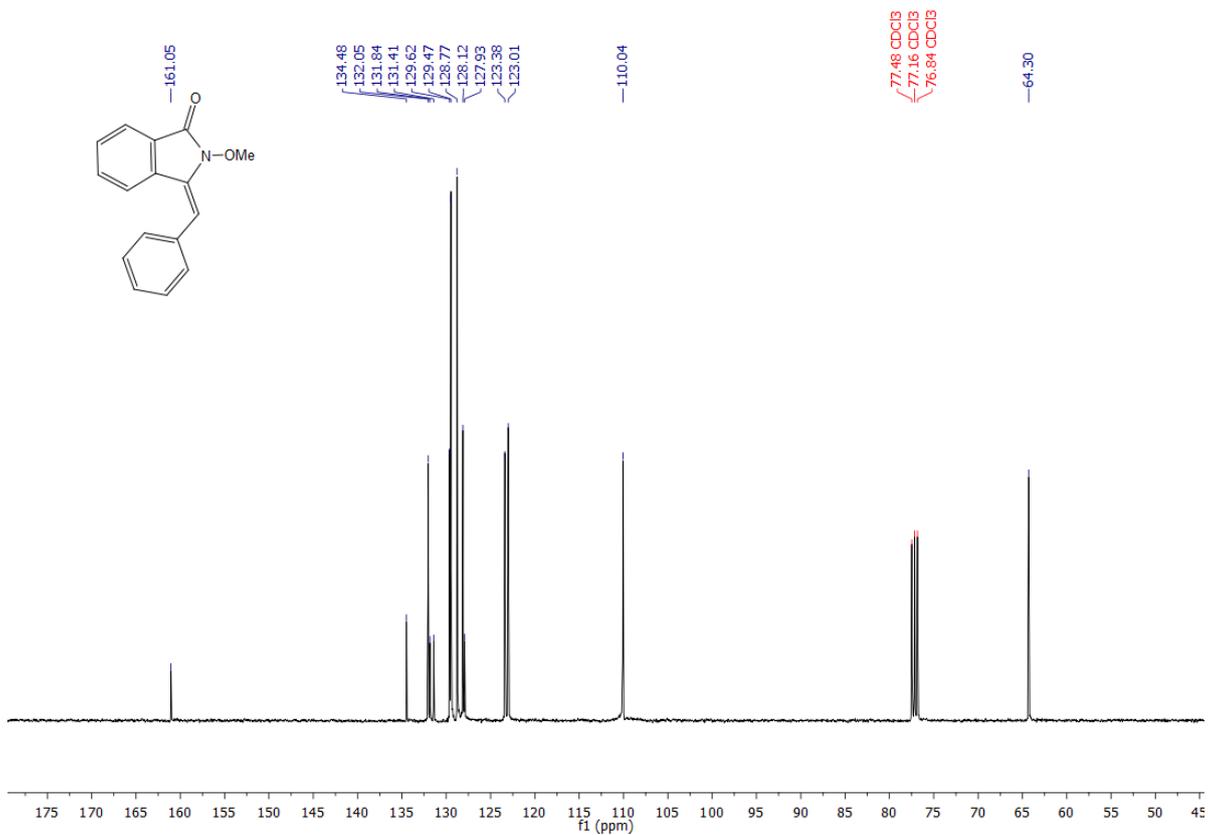
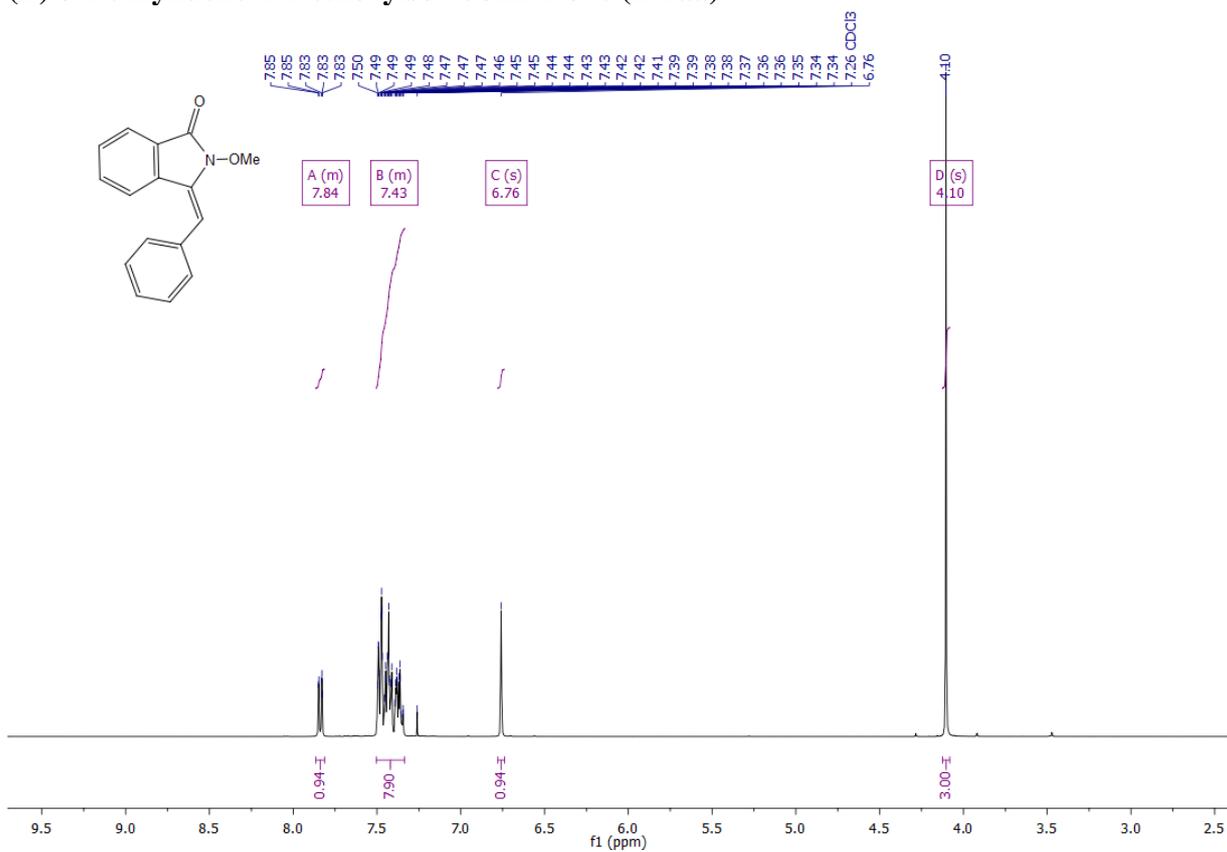
^1H and ^{13}C NMR spectra of isolated compounds.

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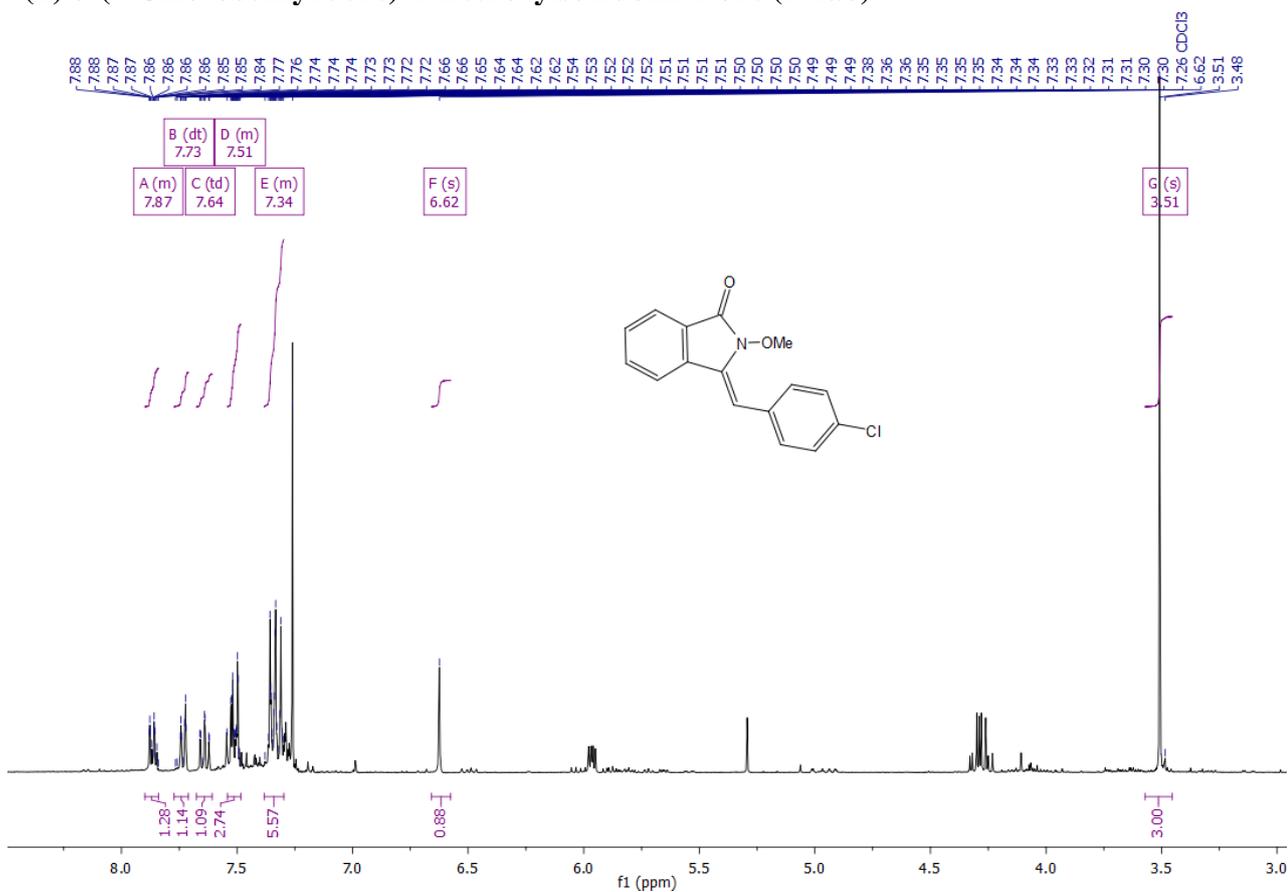
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(E)-3-Benzylidene-2-methoxyisoindolin-1-one (E-2aa)



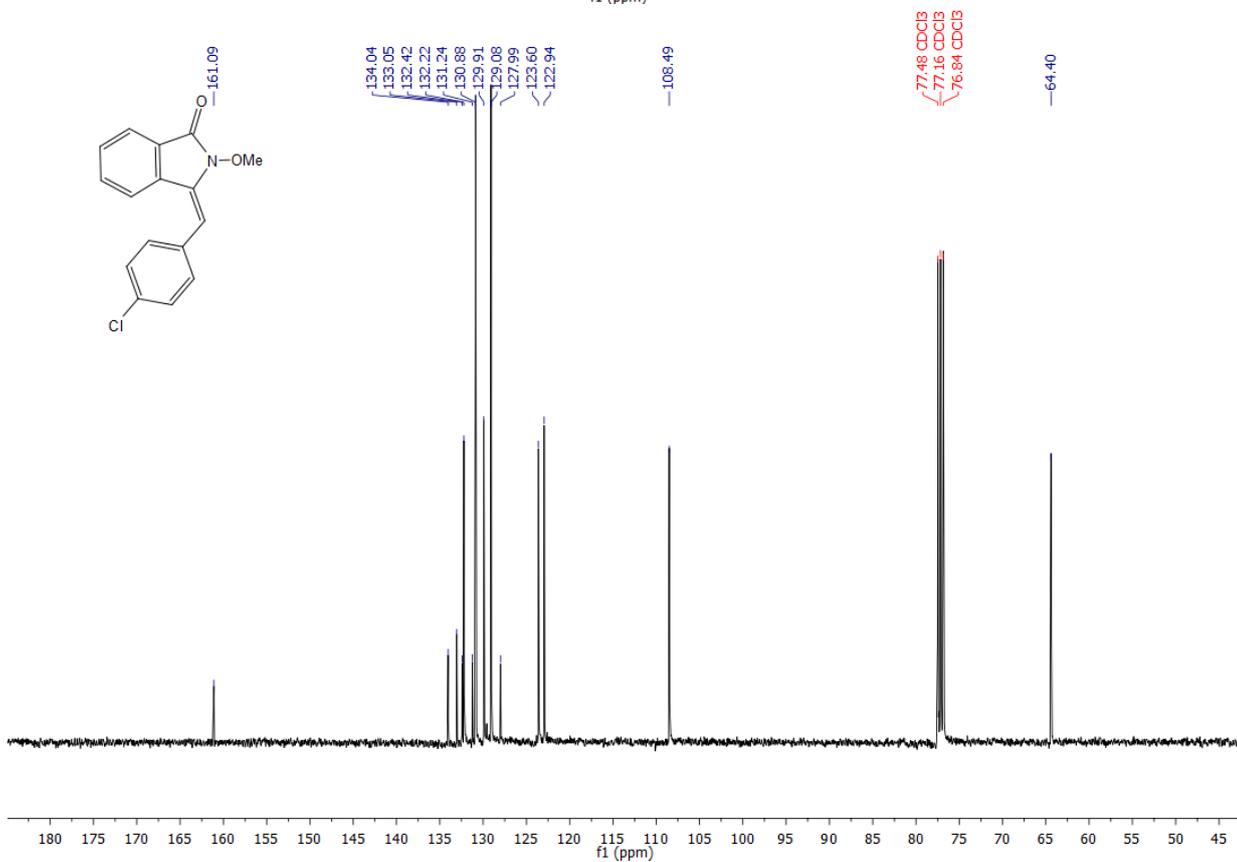
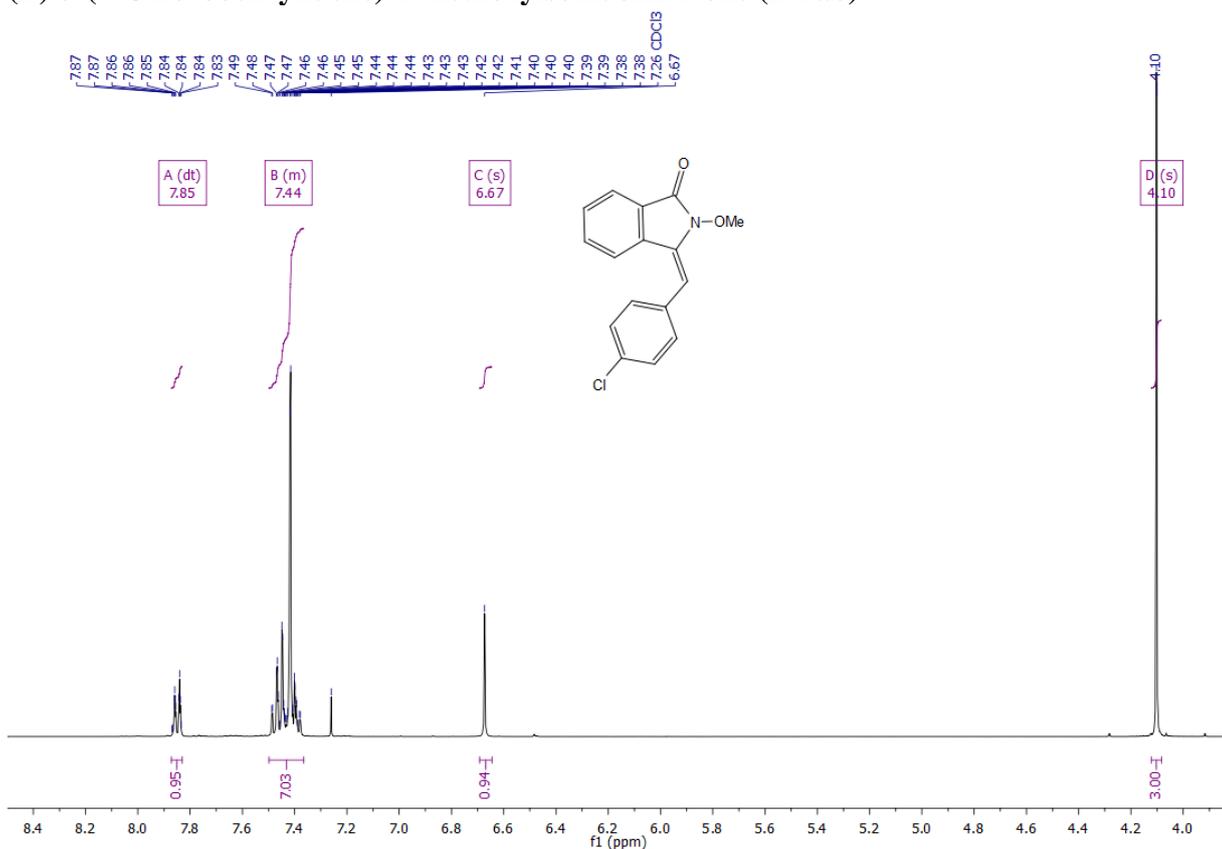
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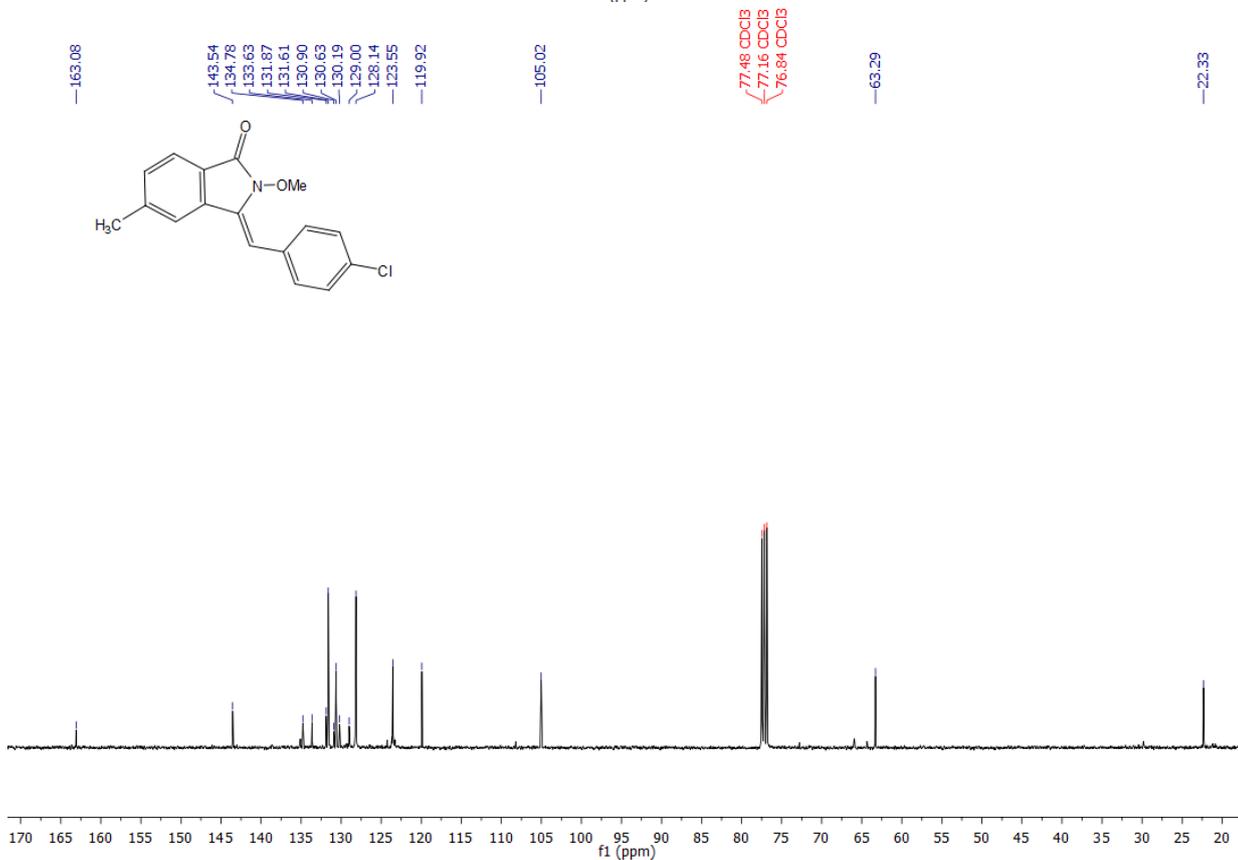
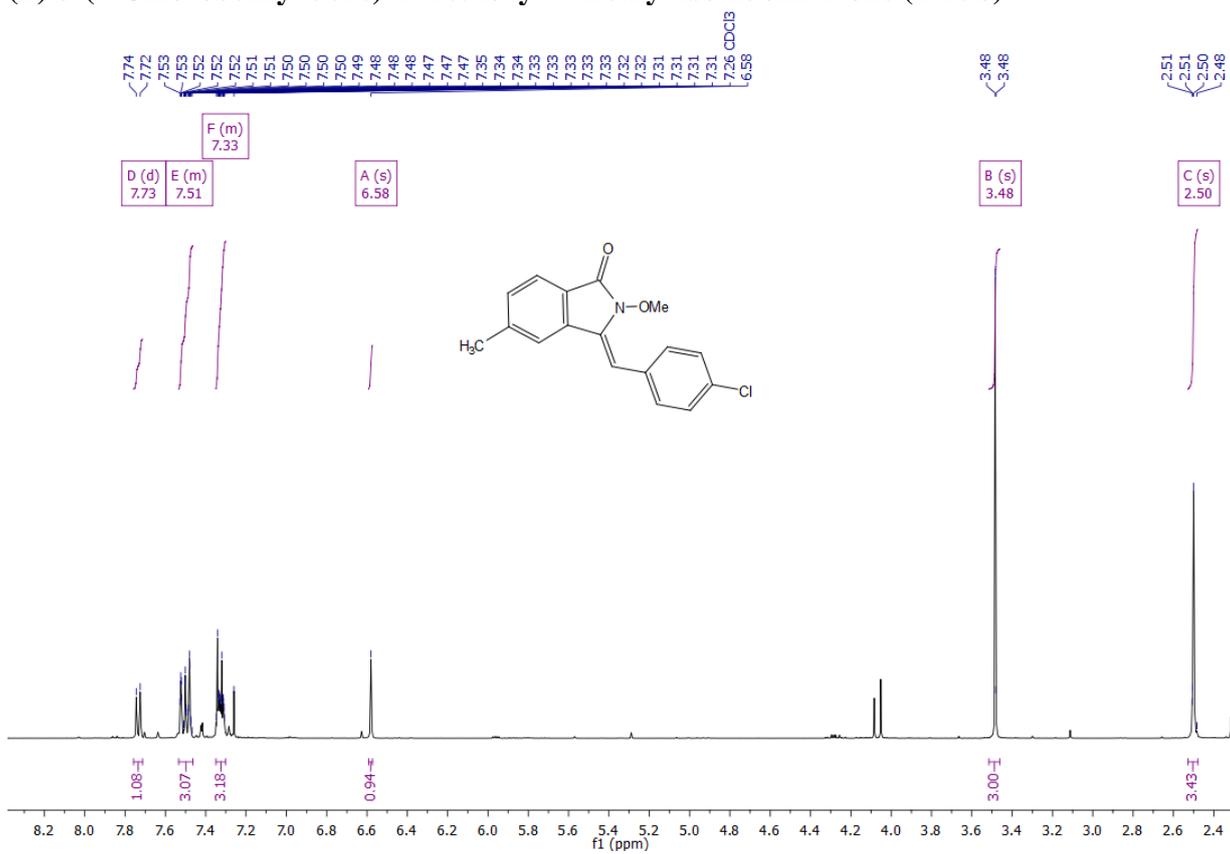
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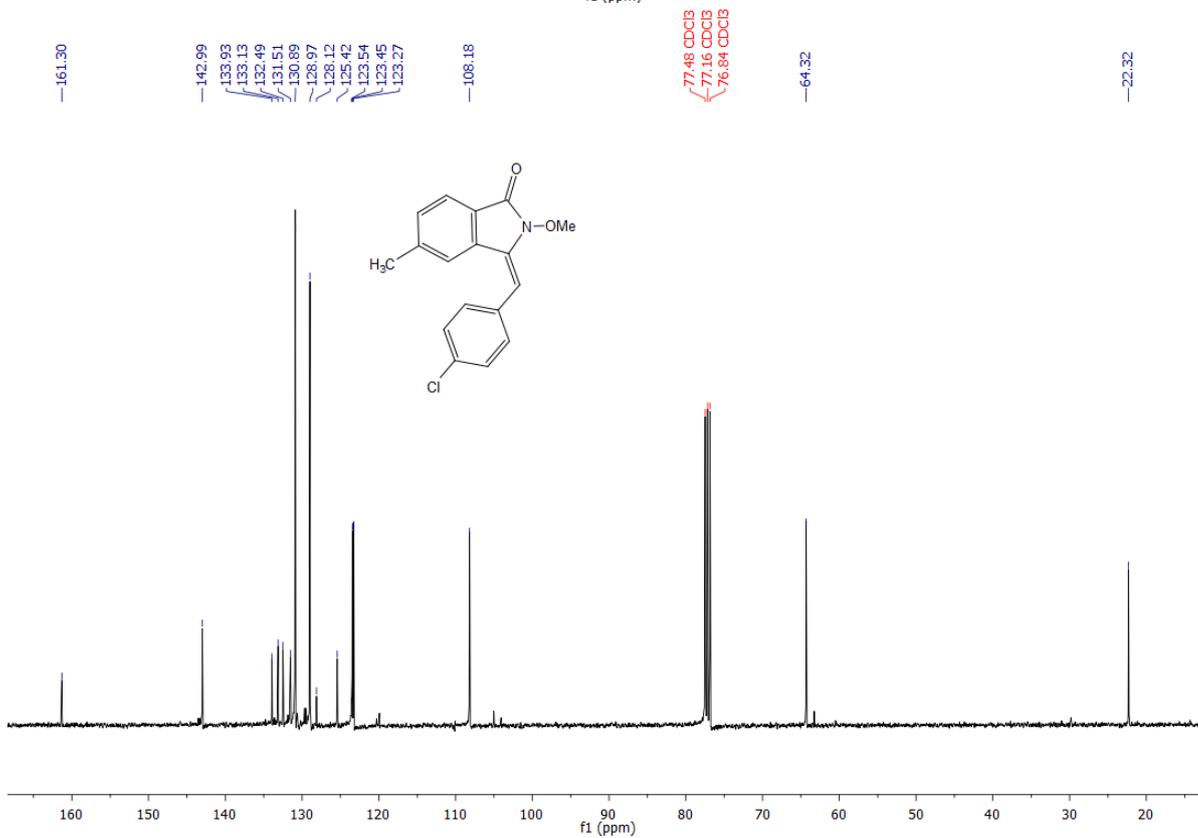
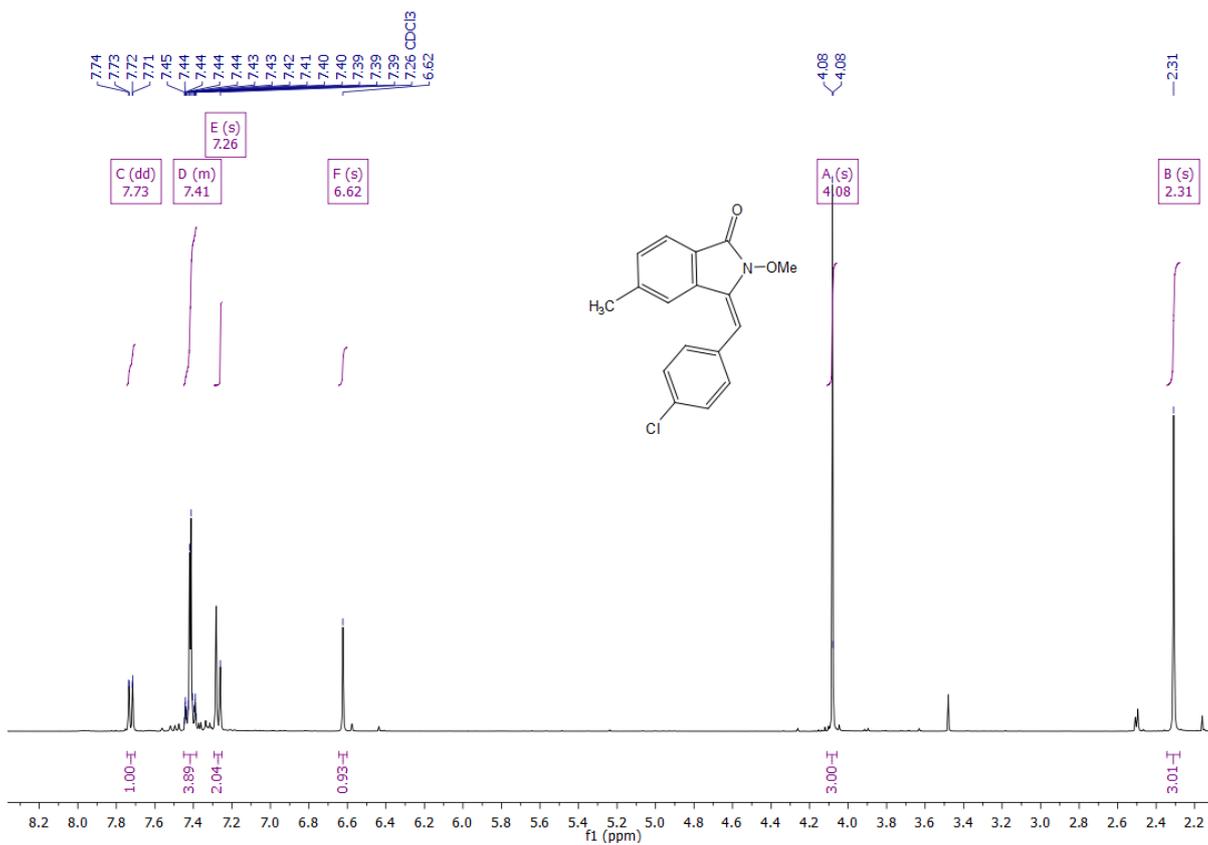


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(Z)-3-(4-Chlorobenzylidene)-2-methoxy-5-methyl-isoindolin-1-one (Z-2db)

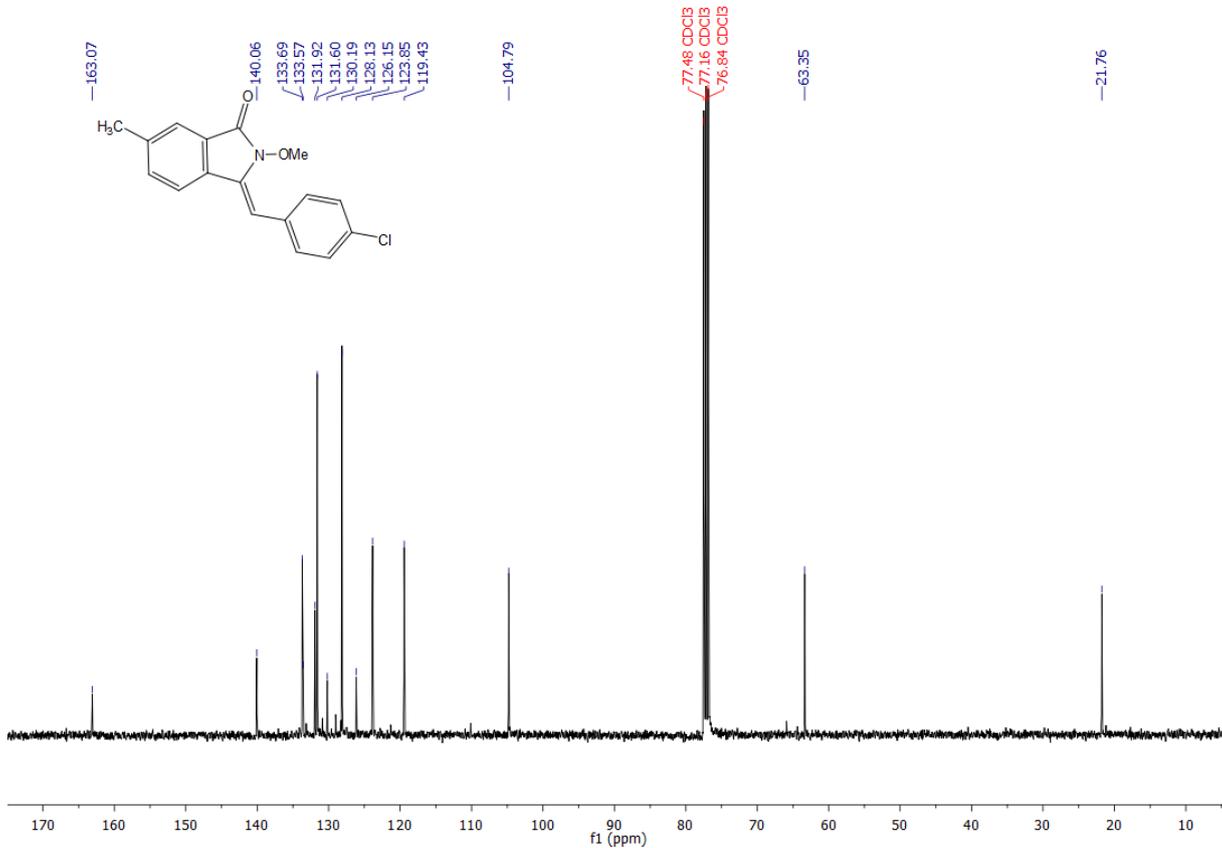
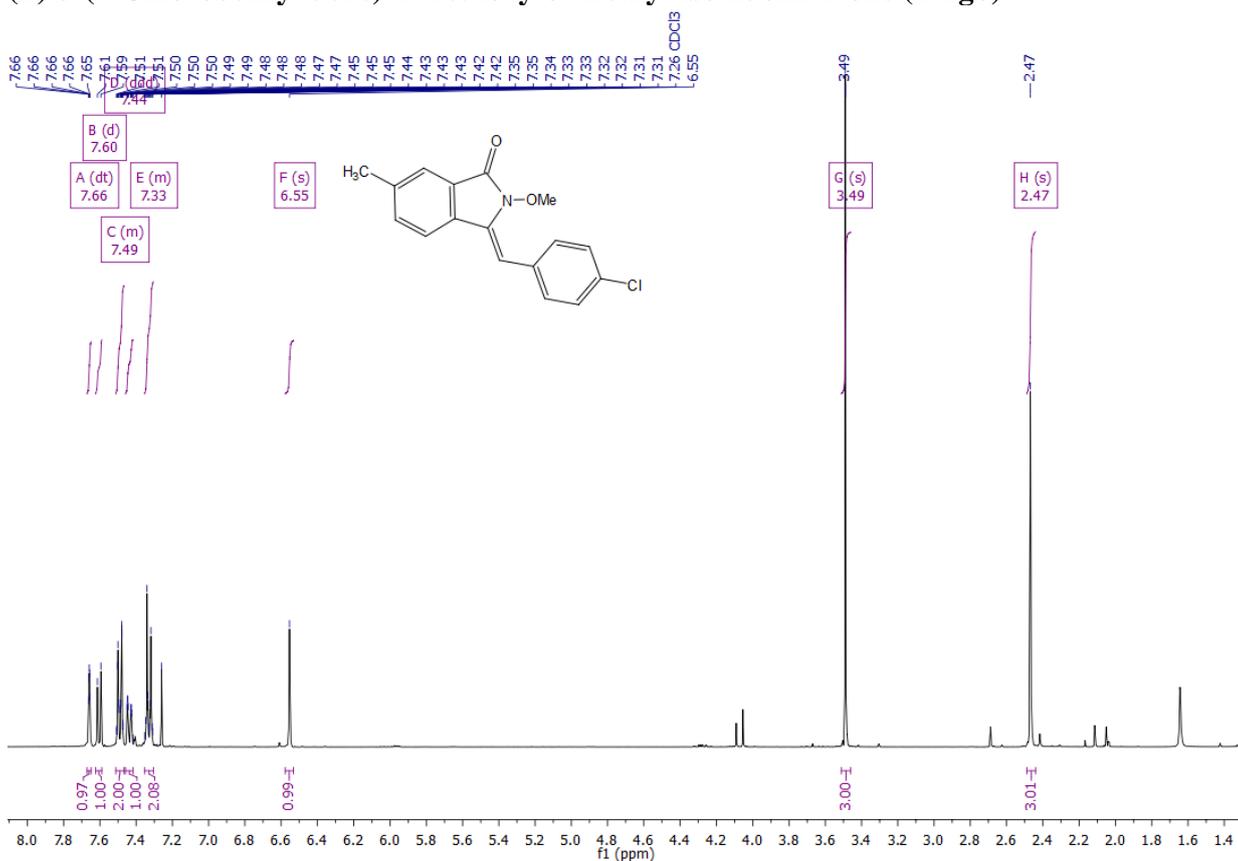


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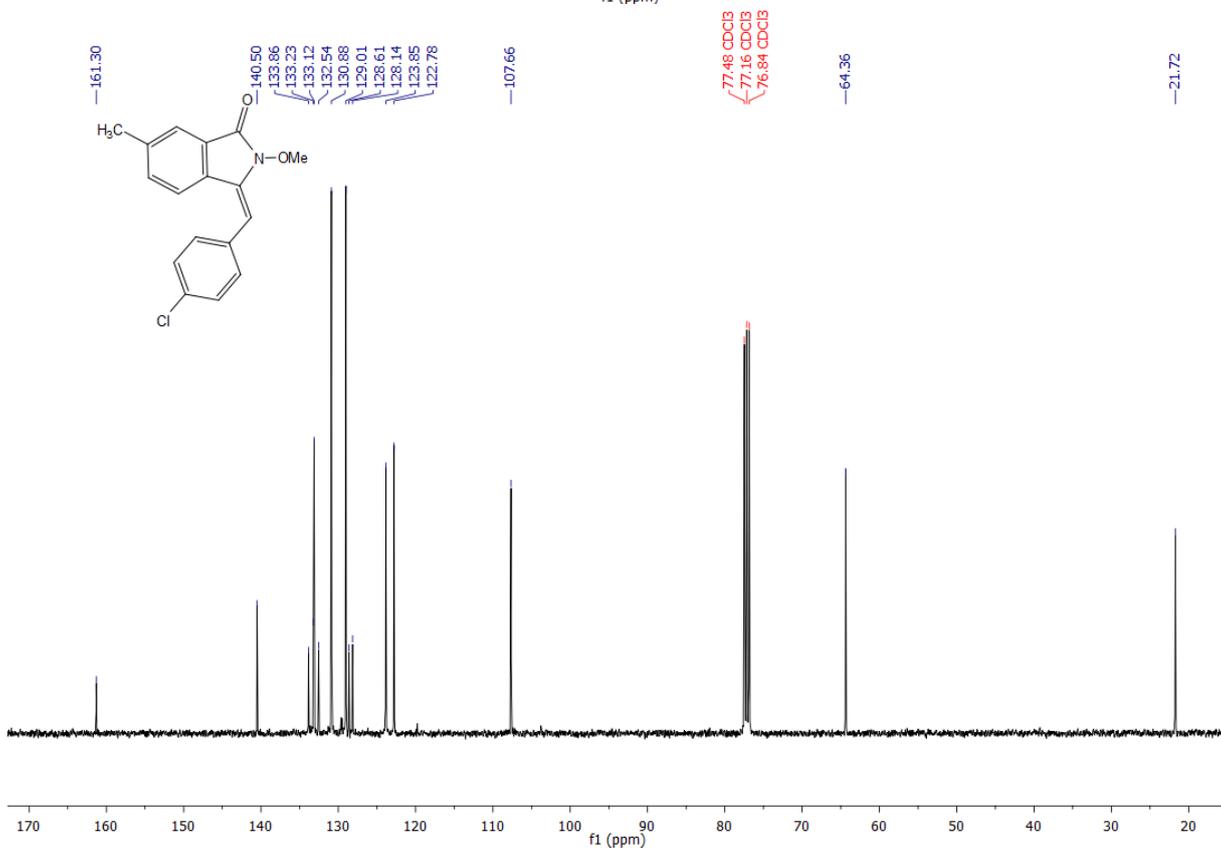
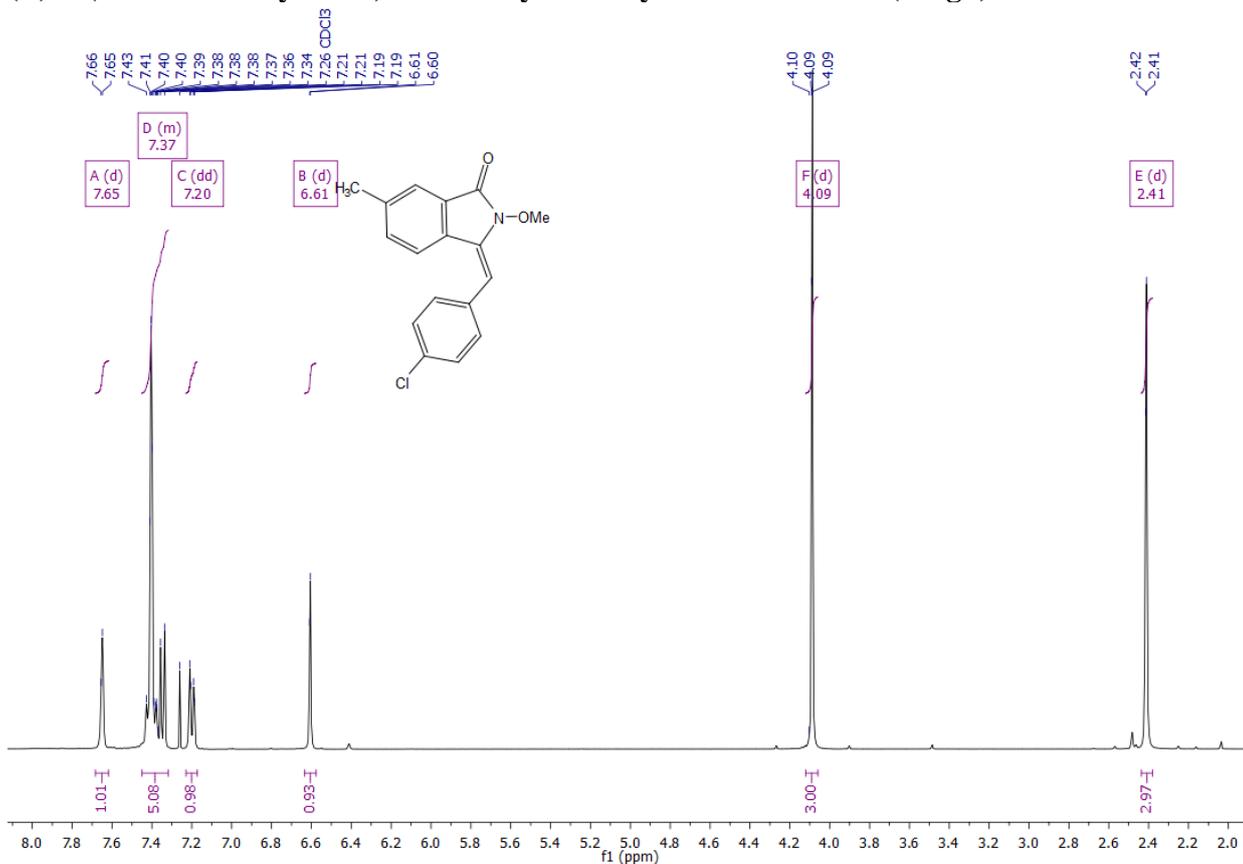
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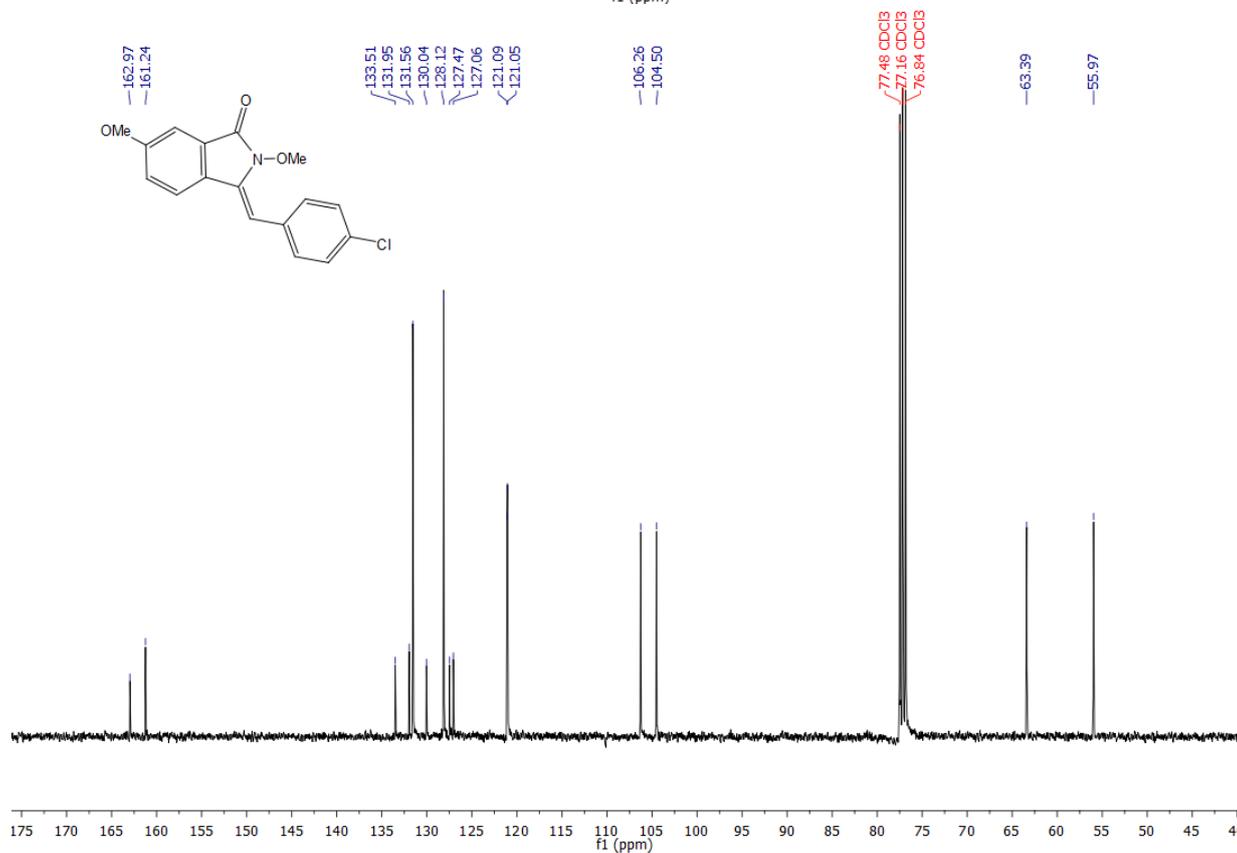
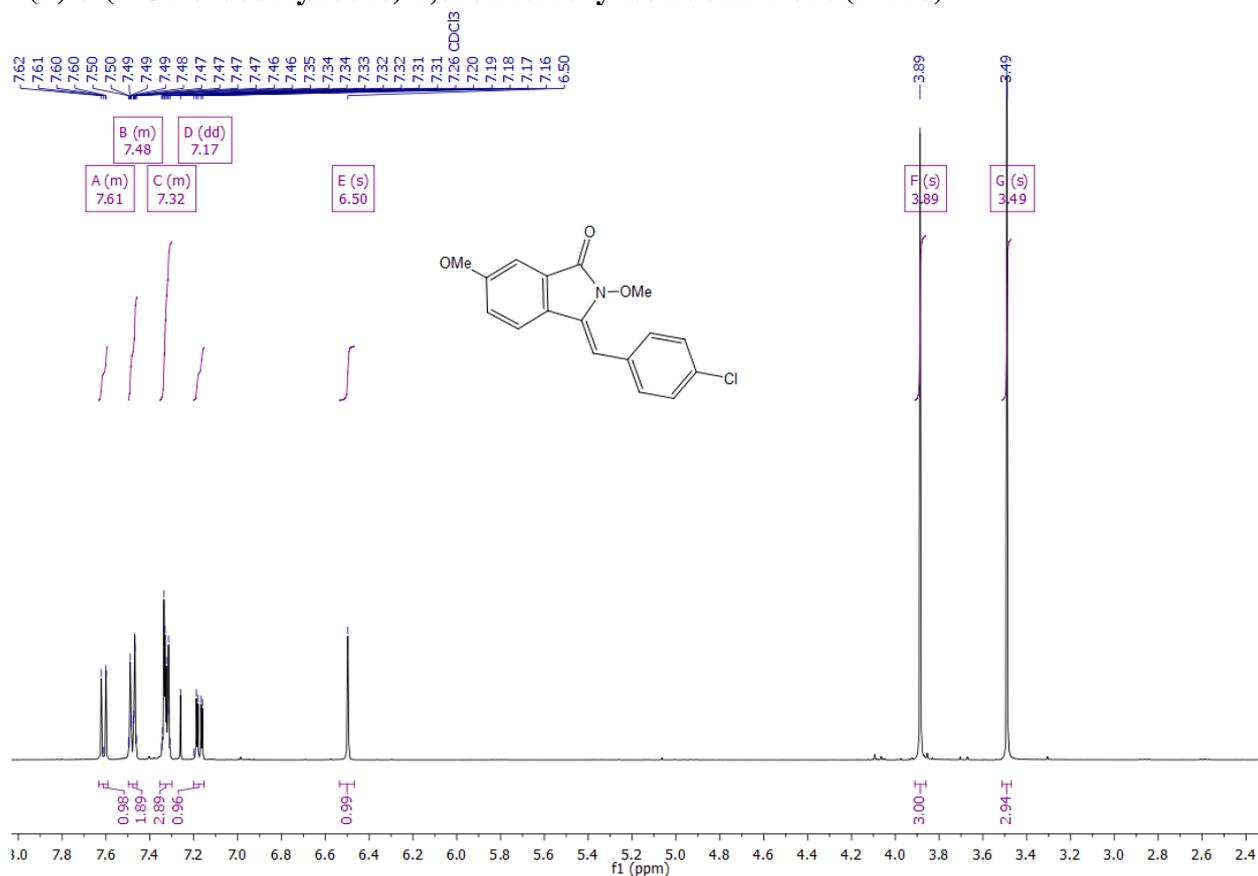
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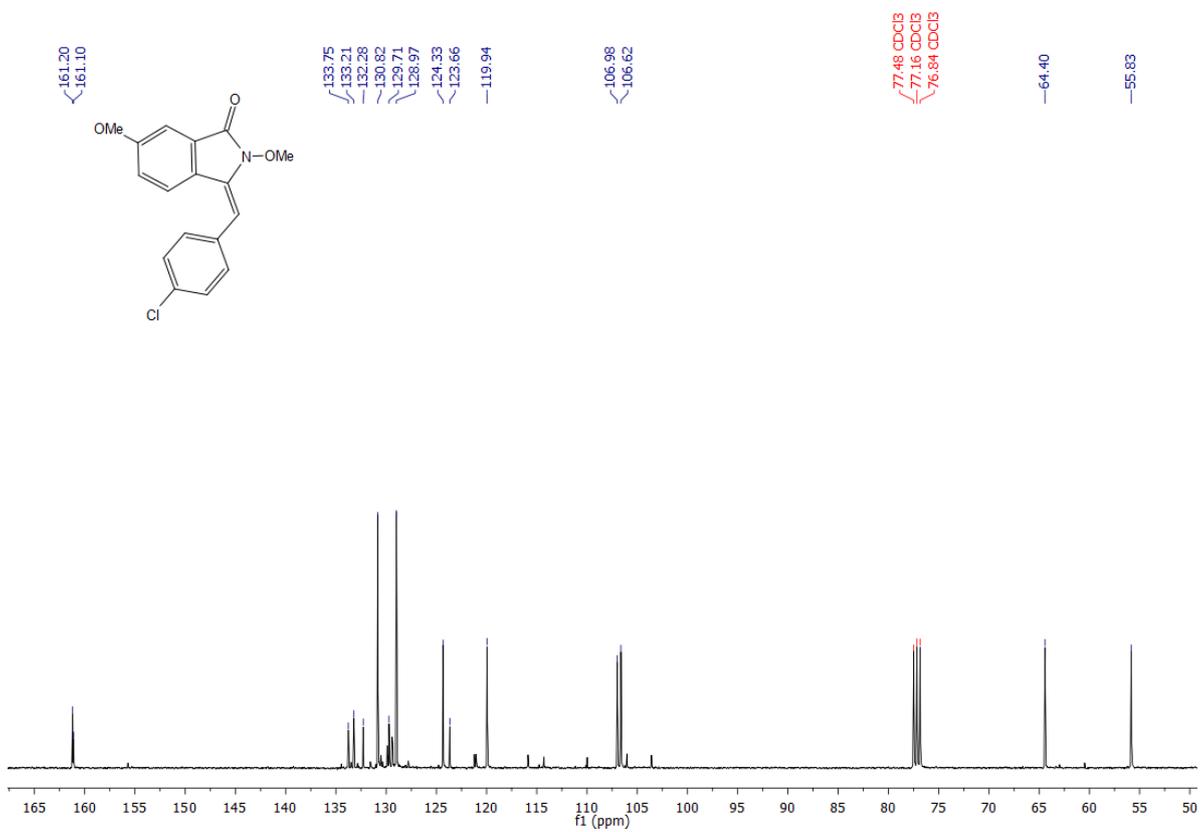
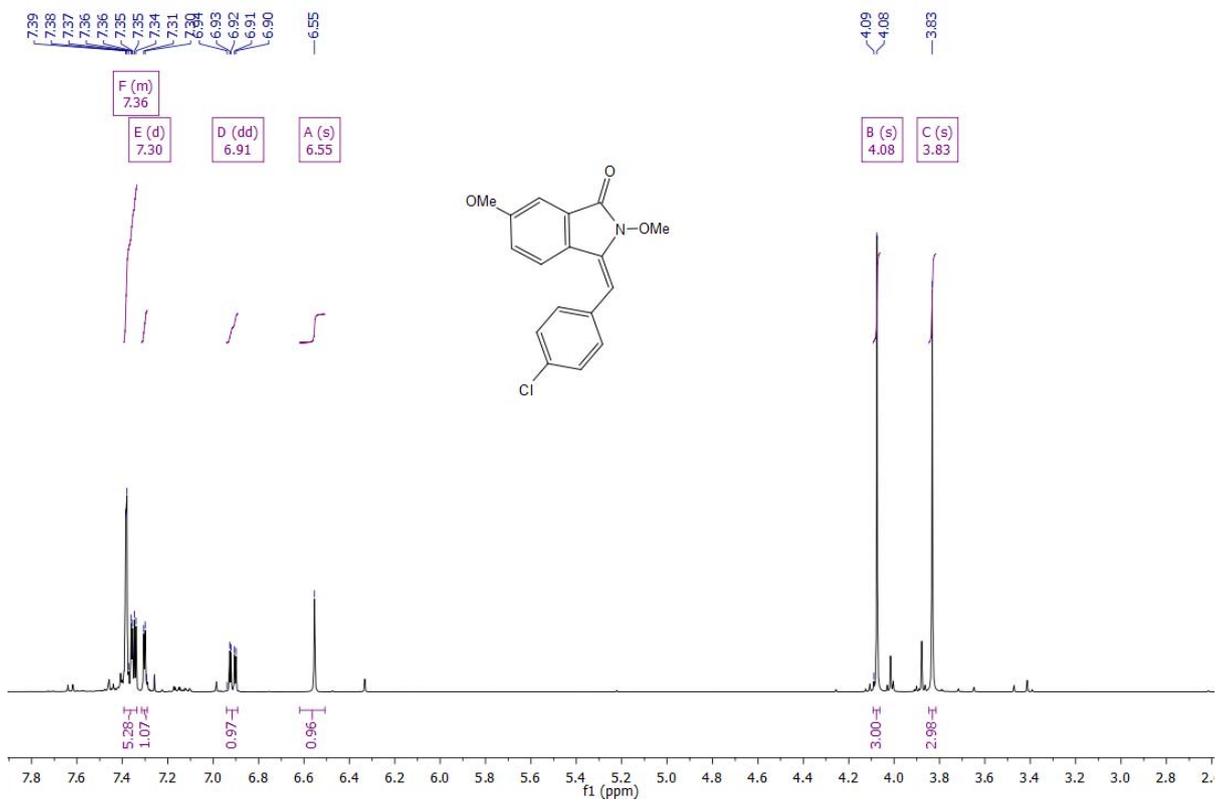


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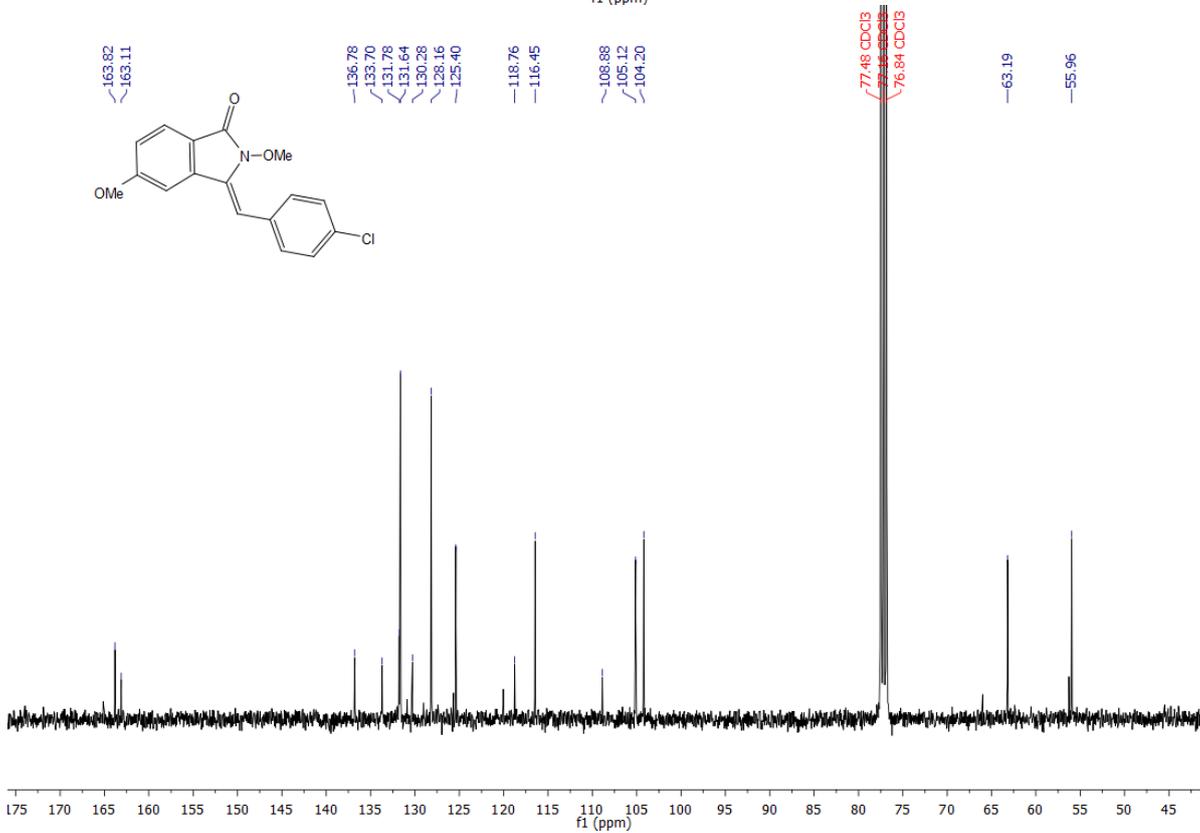
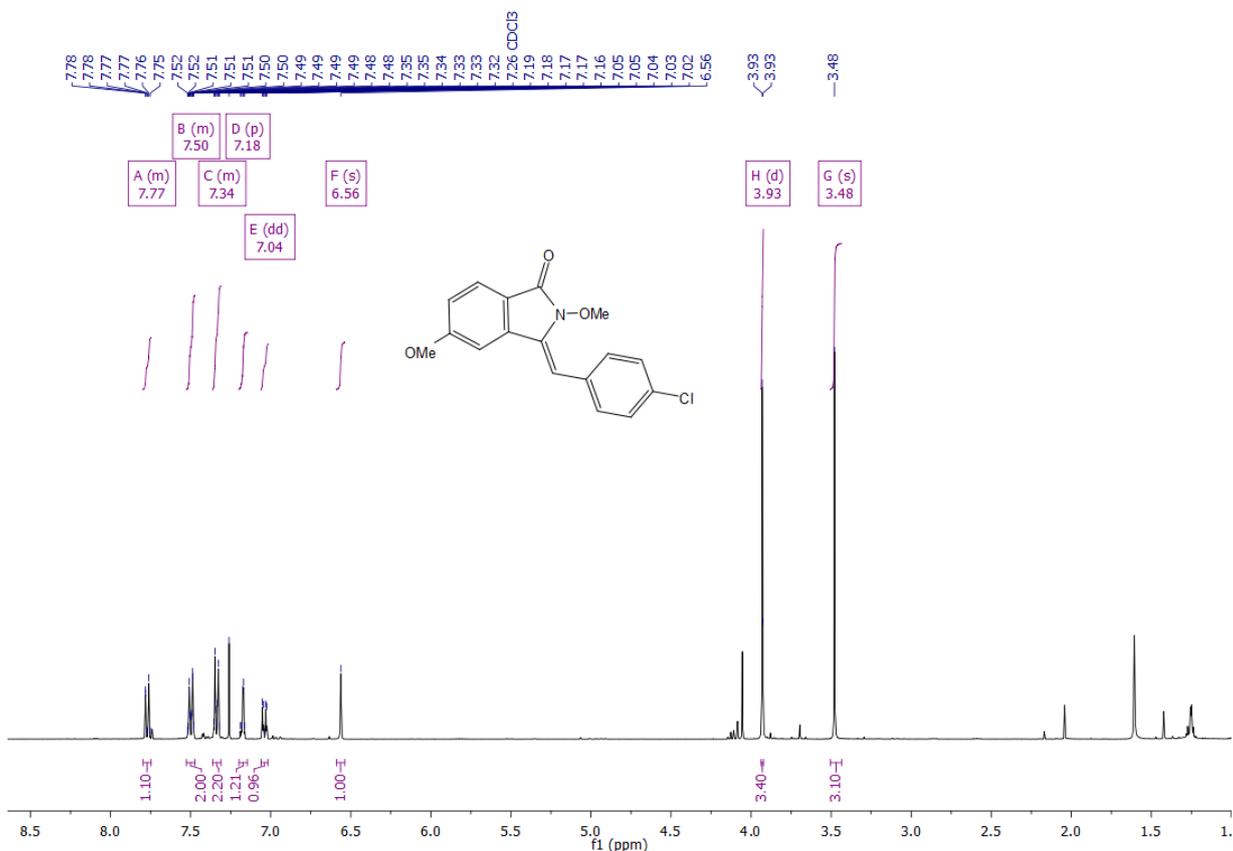
(Z)-3-(4-Chlorobenzylidene)-2,6-dimethoxy-isoindolin-1-one (Z-2hb)



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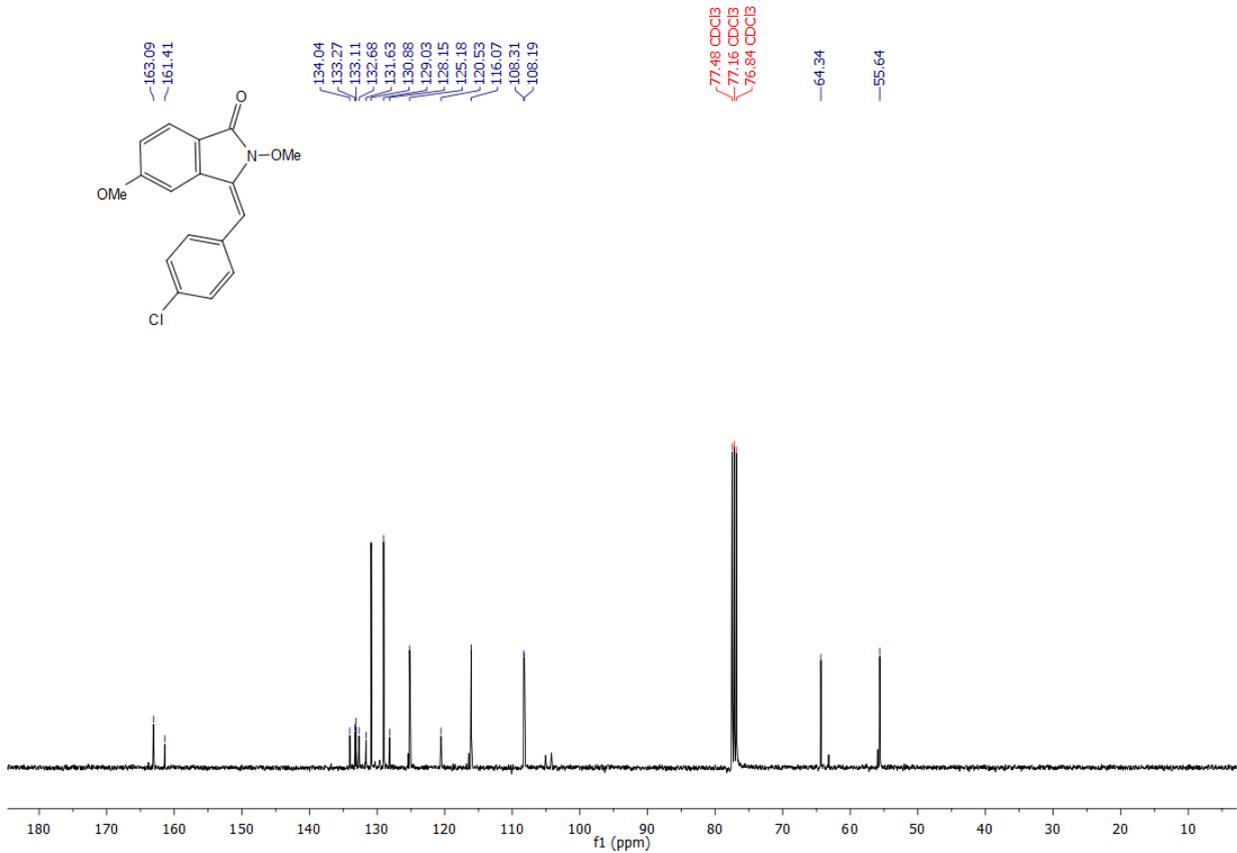
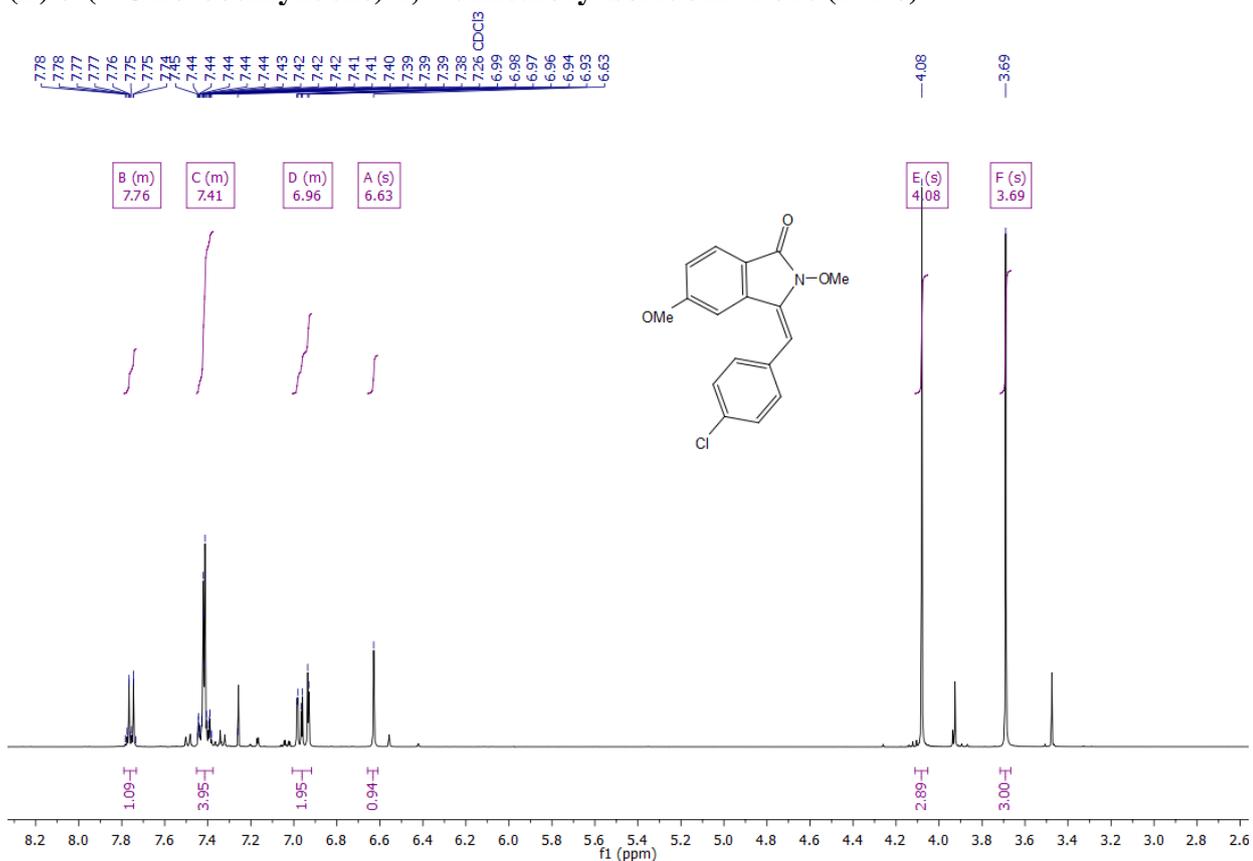
(E)-3-(4-Chlorobenzylidene)-2,6-dimethoxyisoindolin-1-one (E-2hb)

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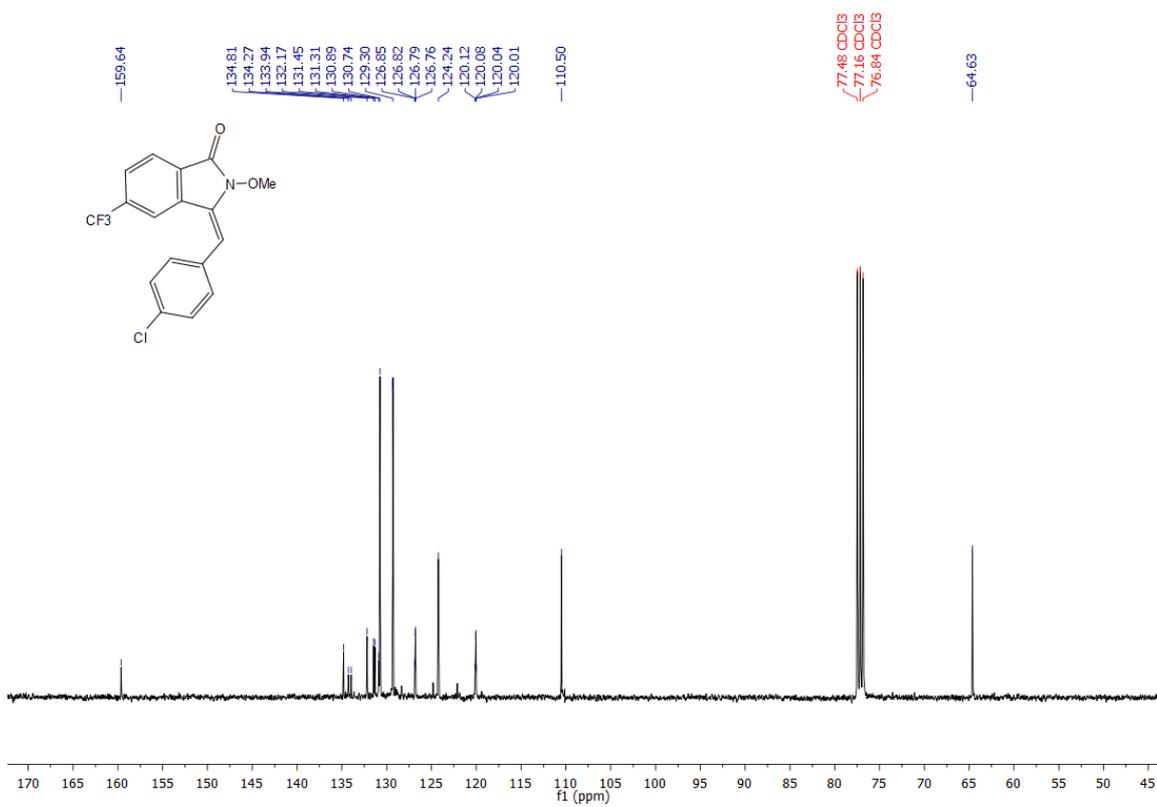
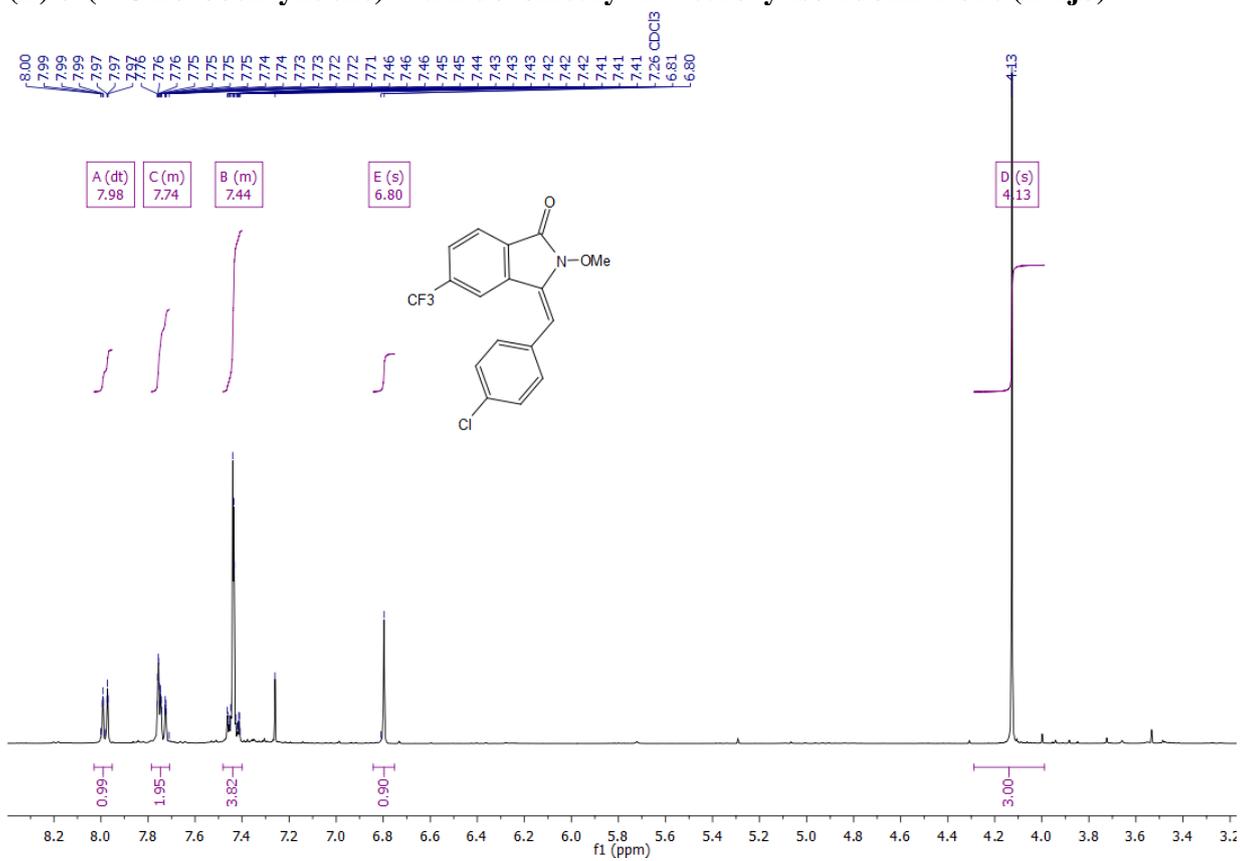
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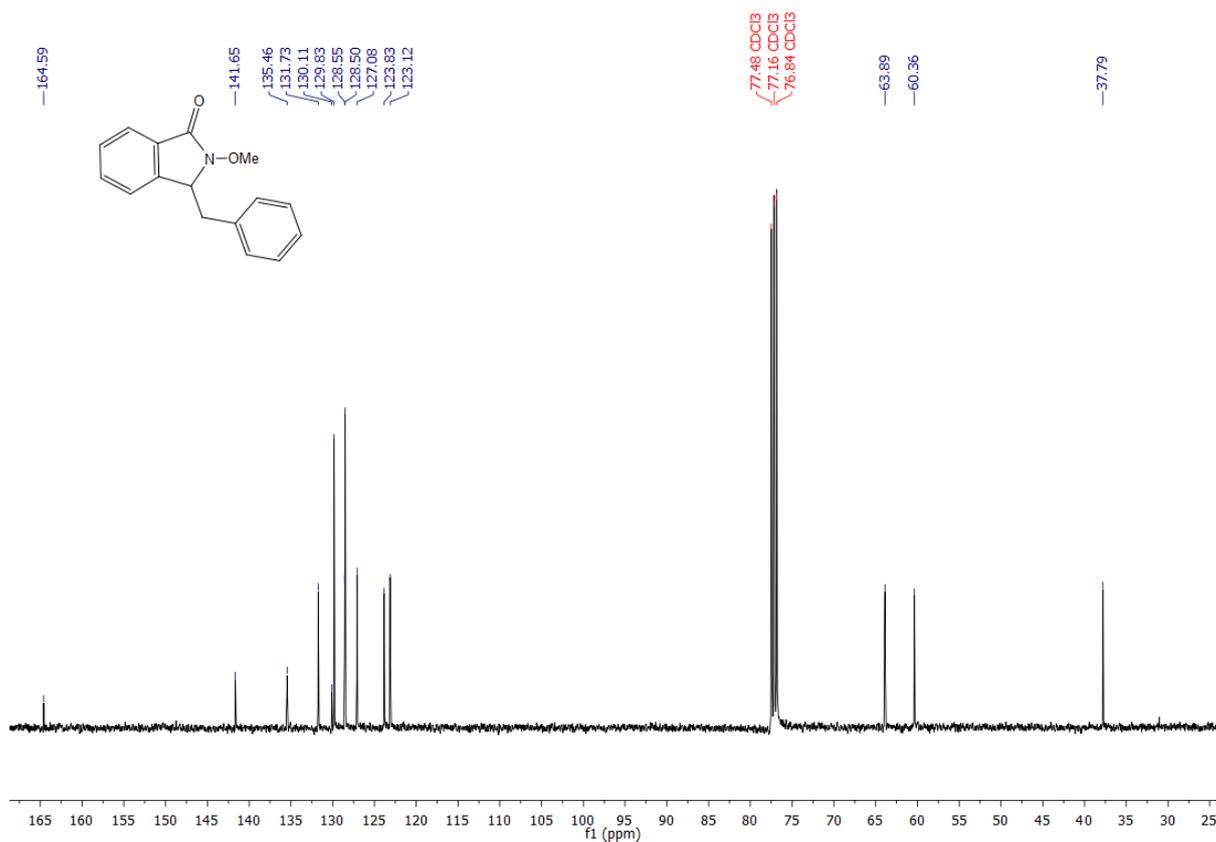
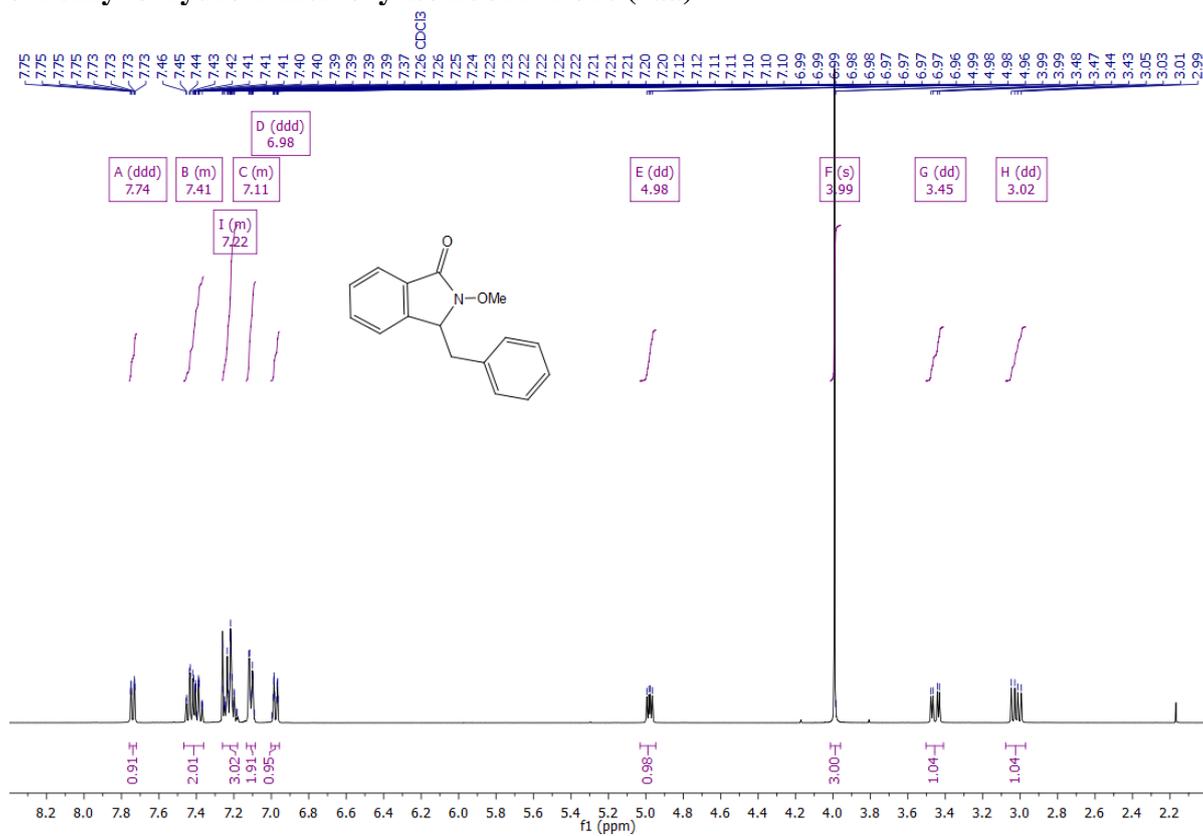
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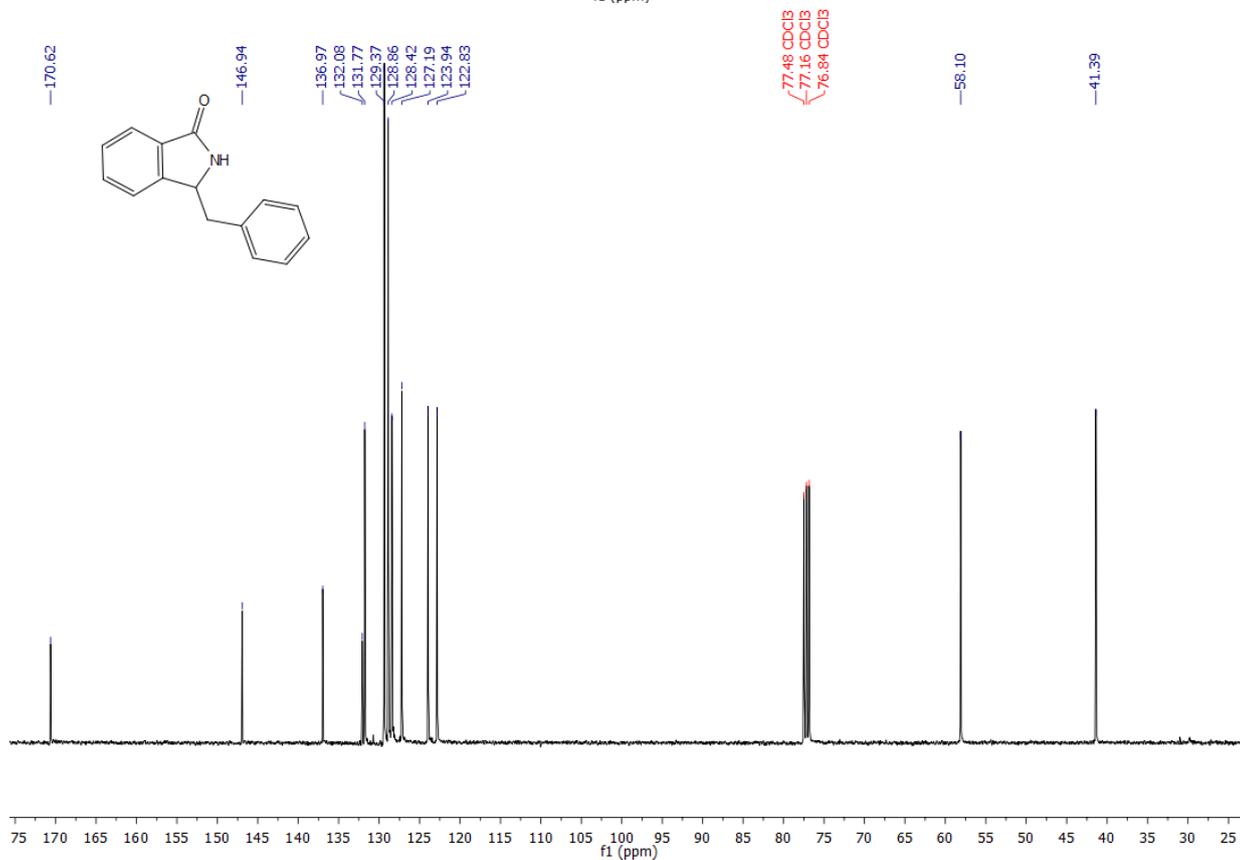
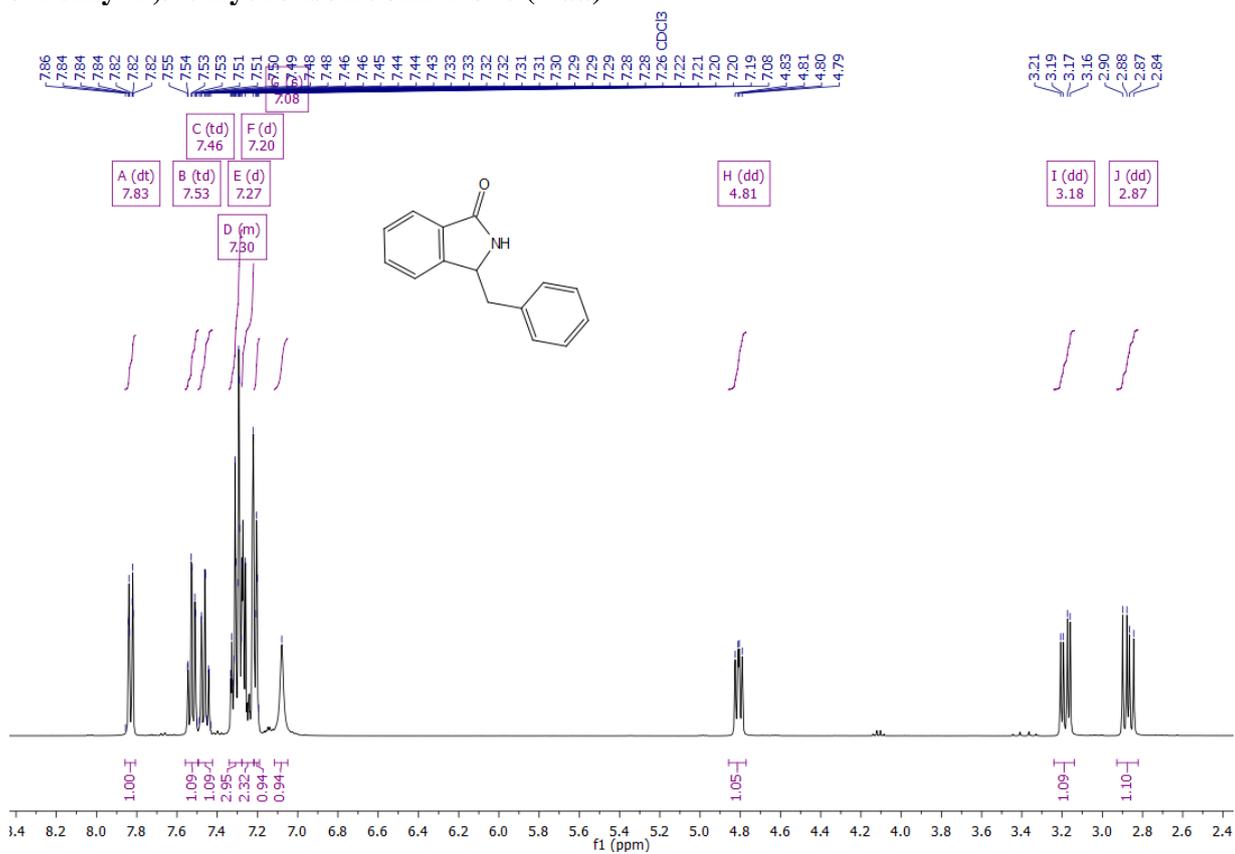
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3-Benzyl-3-hydro-2-methoxy-isoindolin-1-one (4aa)



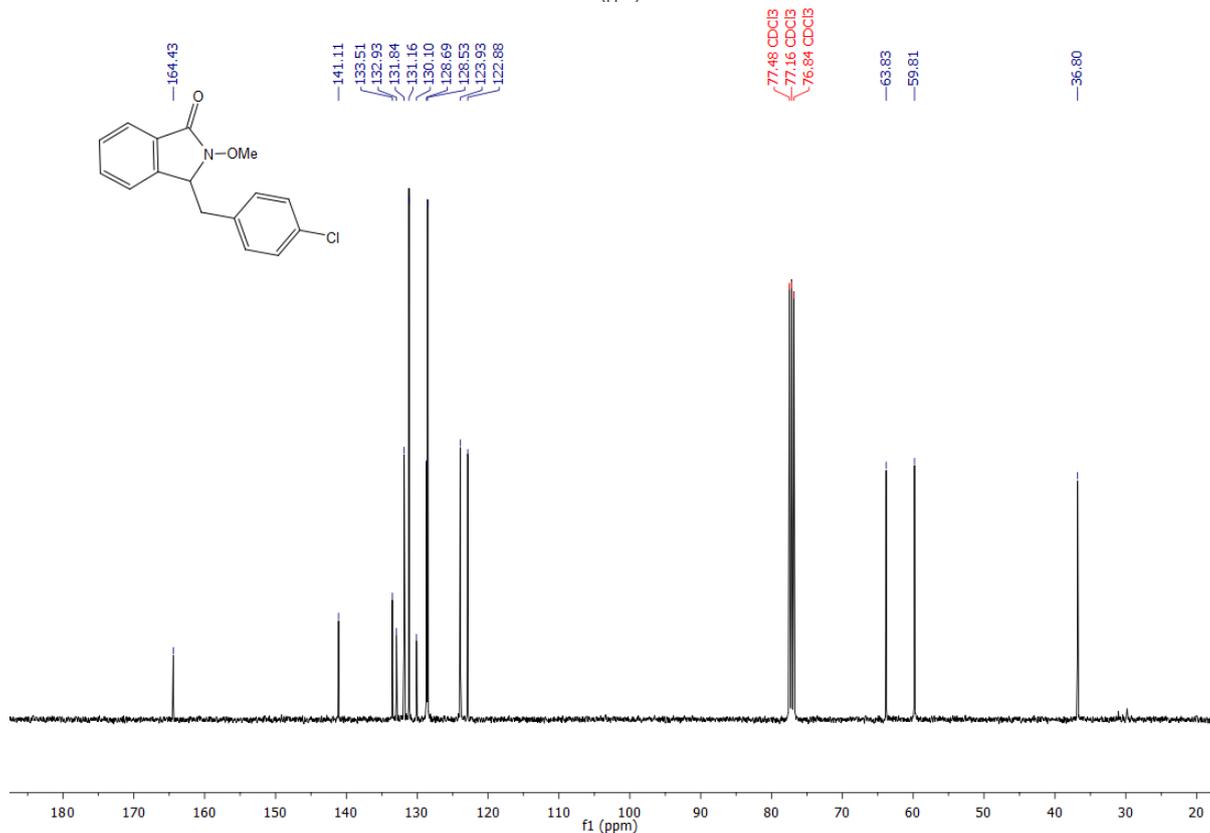
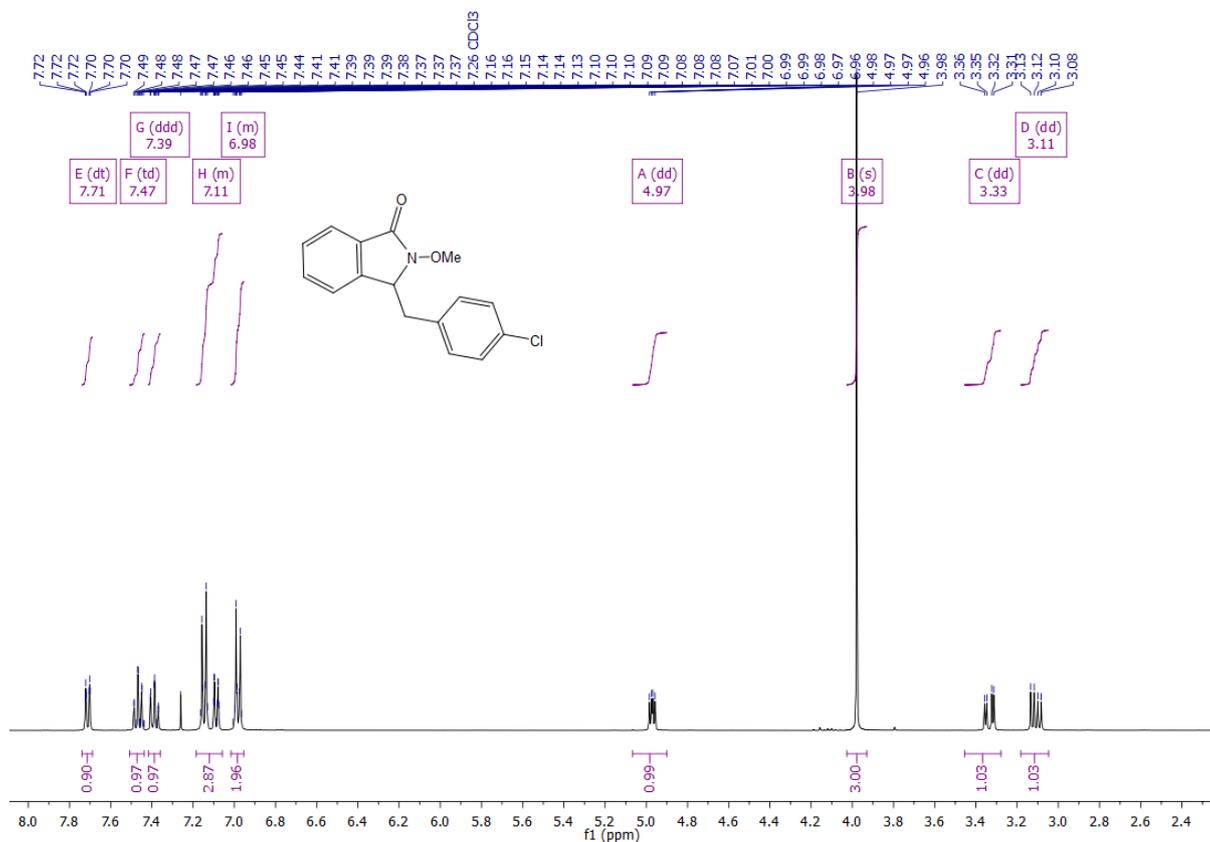
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3-Benzyl-2,3-dihydro-isoindolin-1-one (4'aa)



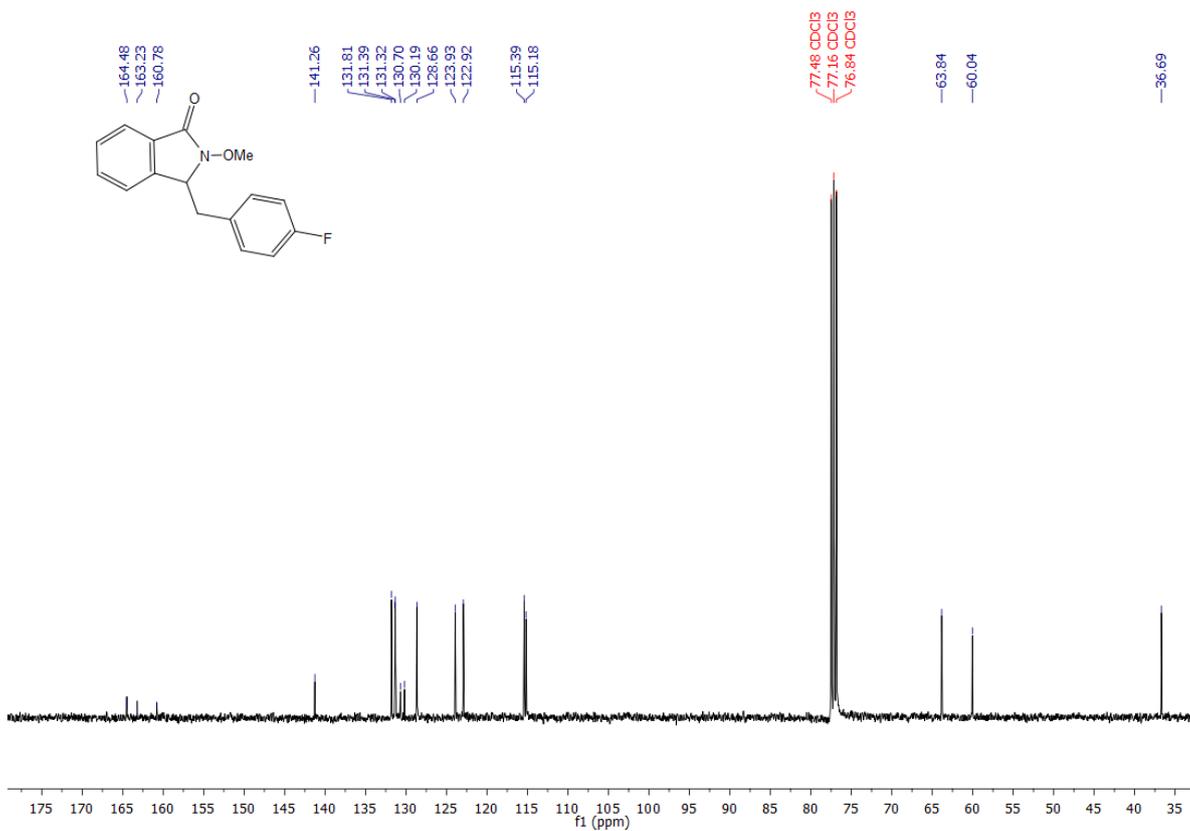
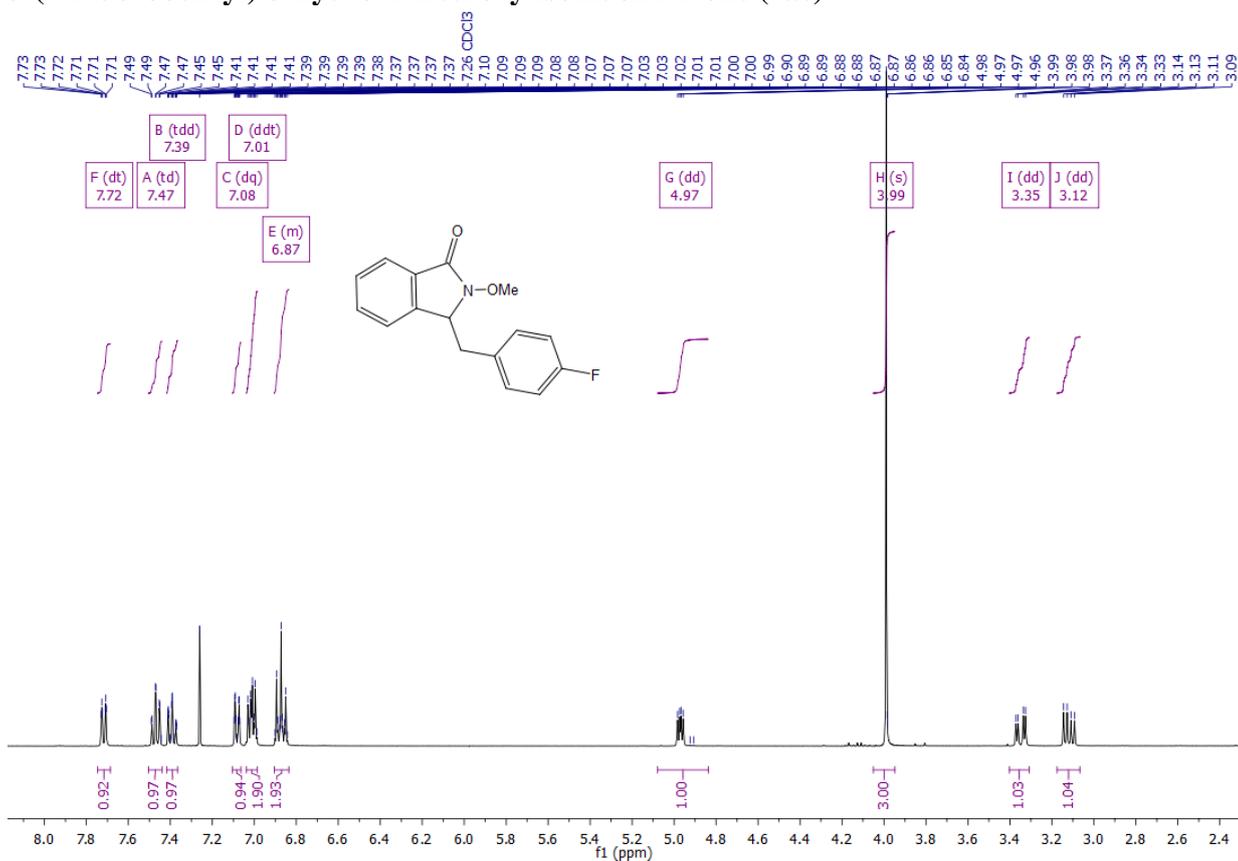
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3-(4-Chlorobenzyl)-3-hydro-2-methoxy-isoindolin-1-one (4ab)



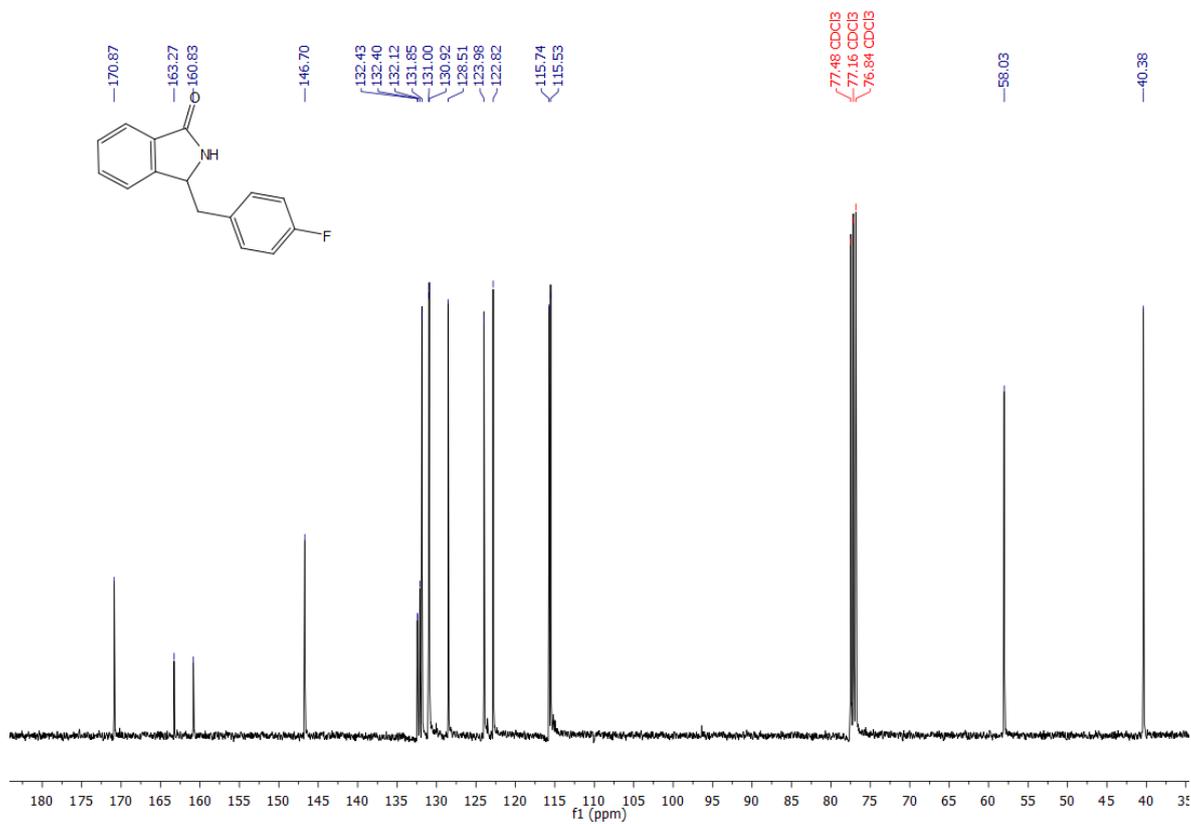
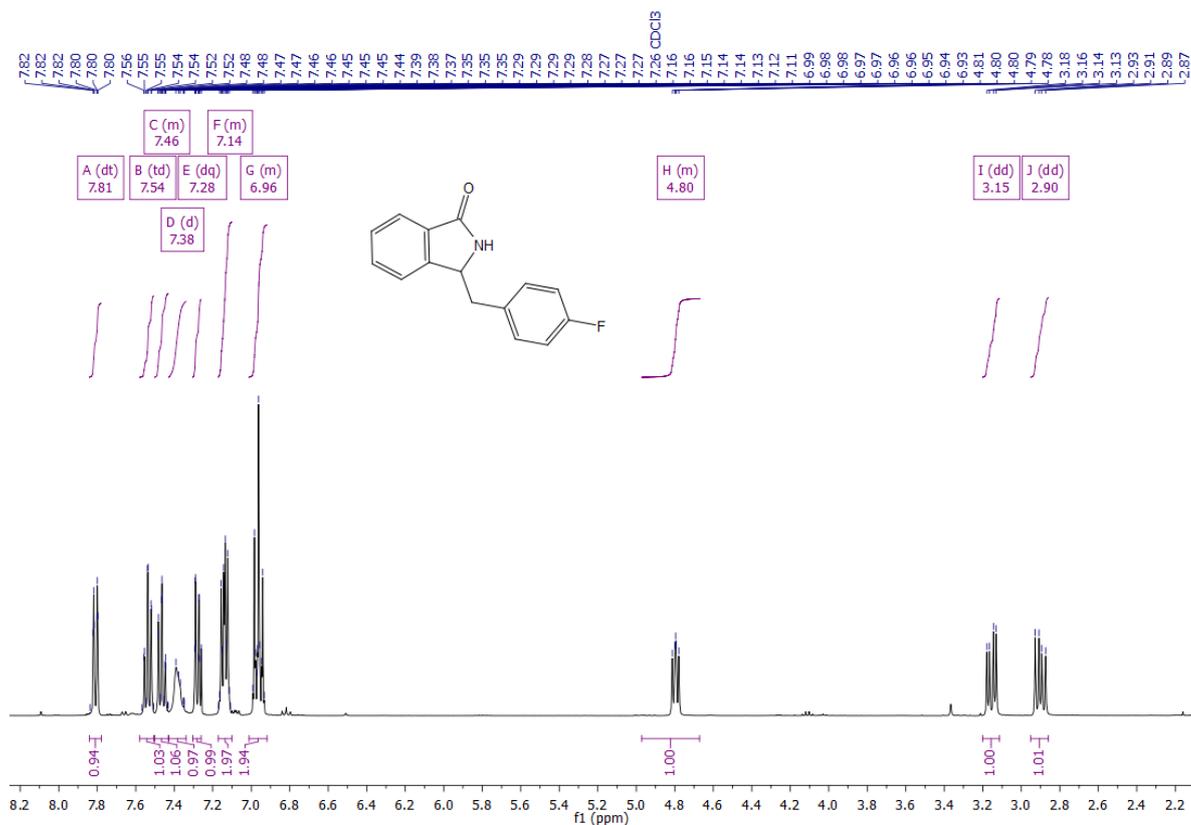
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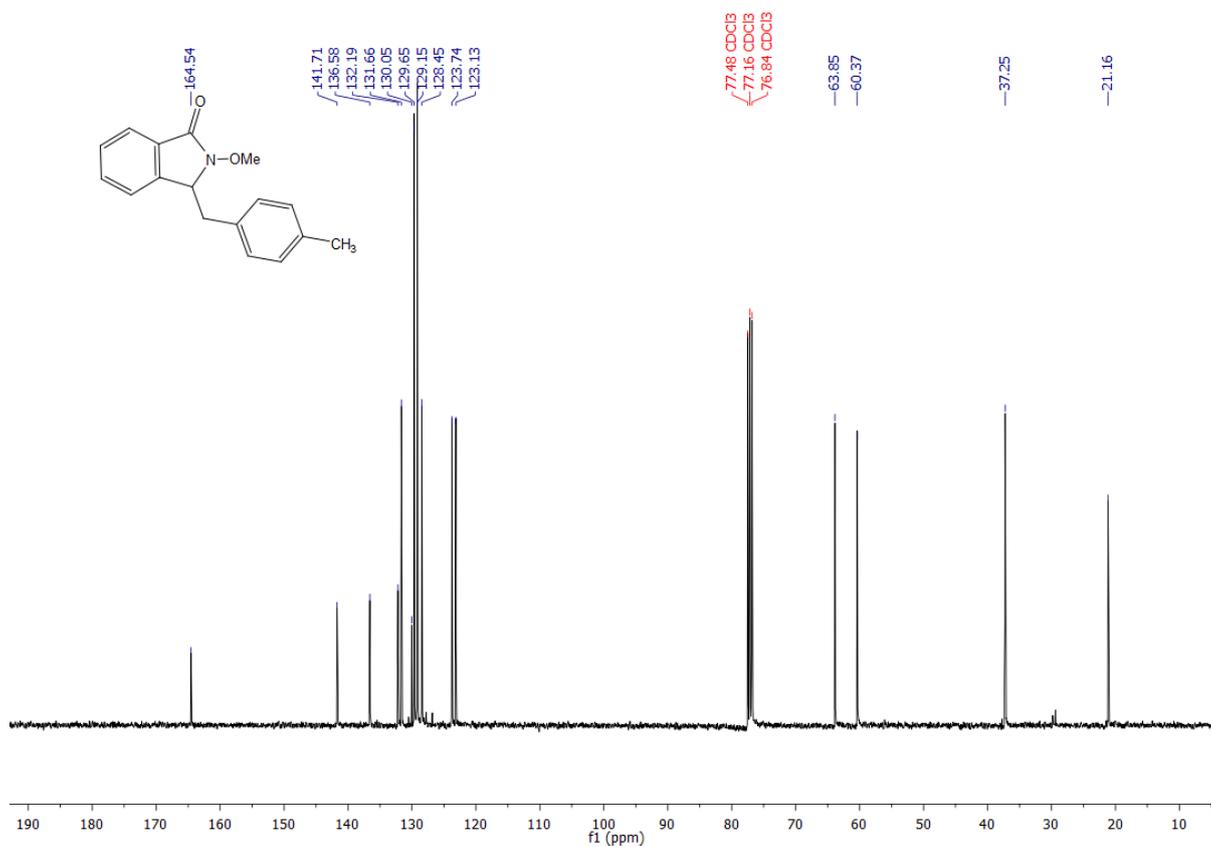
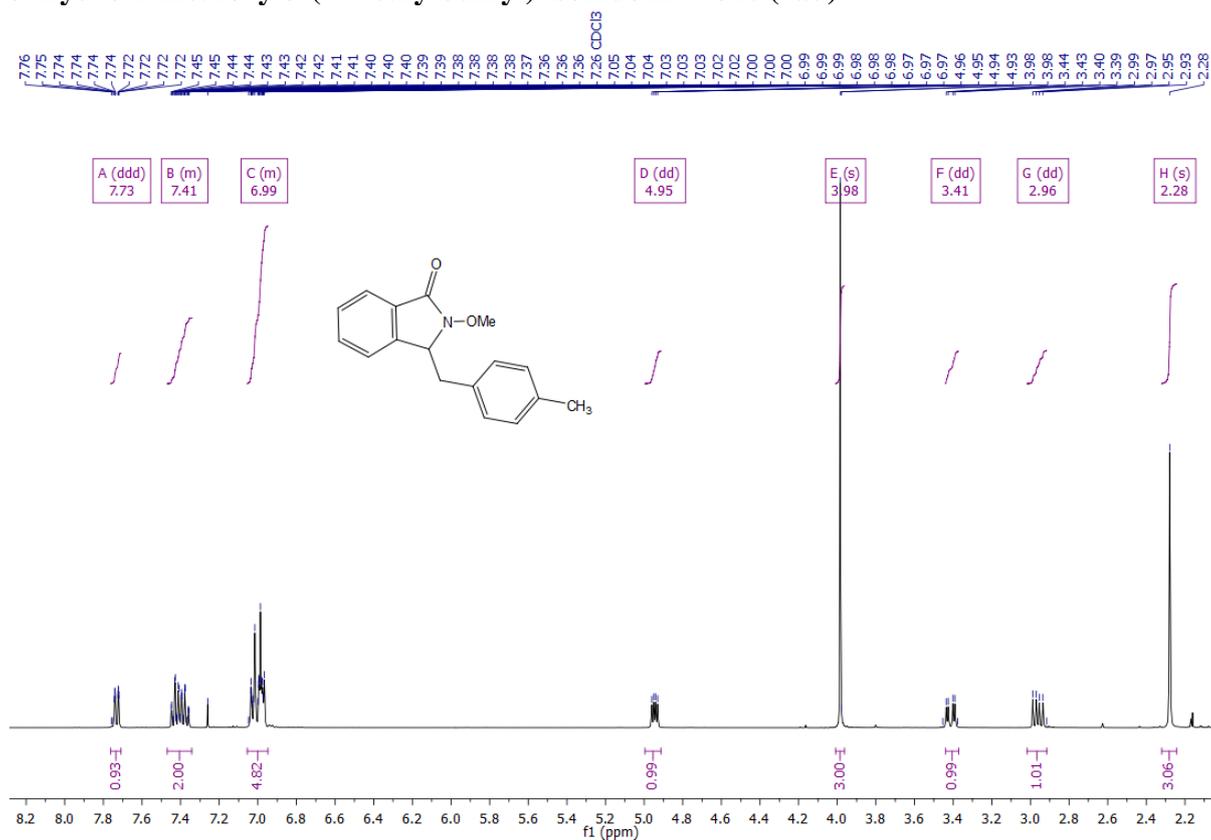
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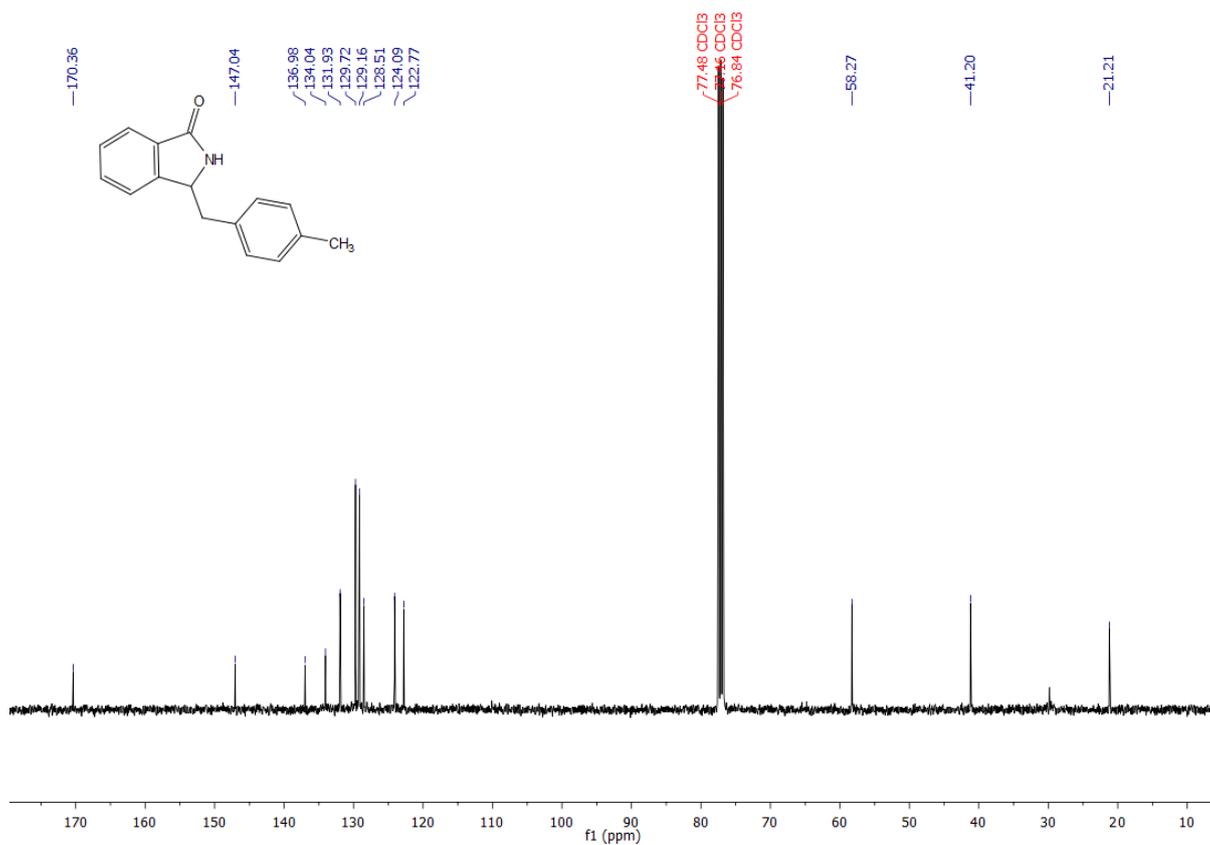
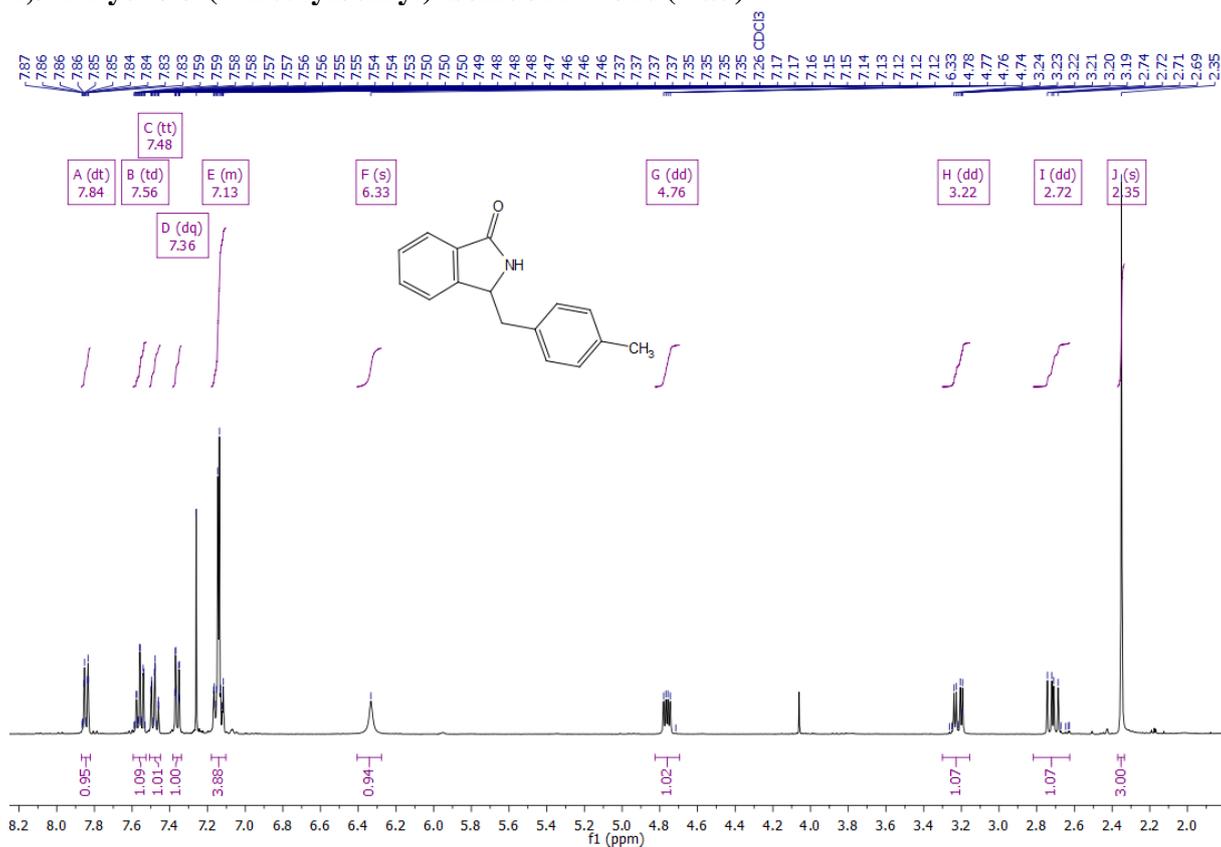
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3-Hydro-2-methoxy-3-(4-methylbenzyl)-isoindolin-1-one (4ad)



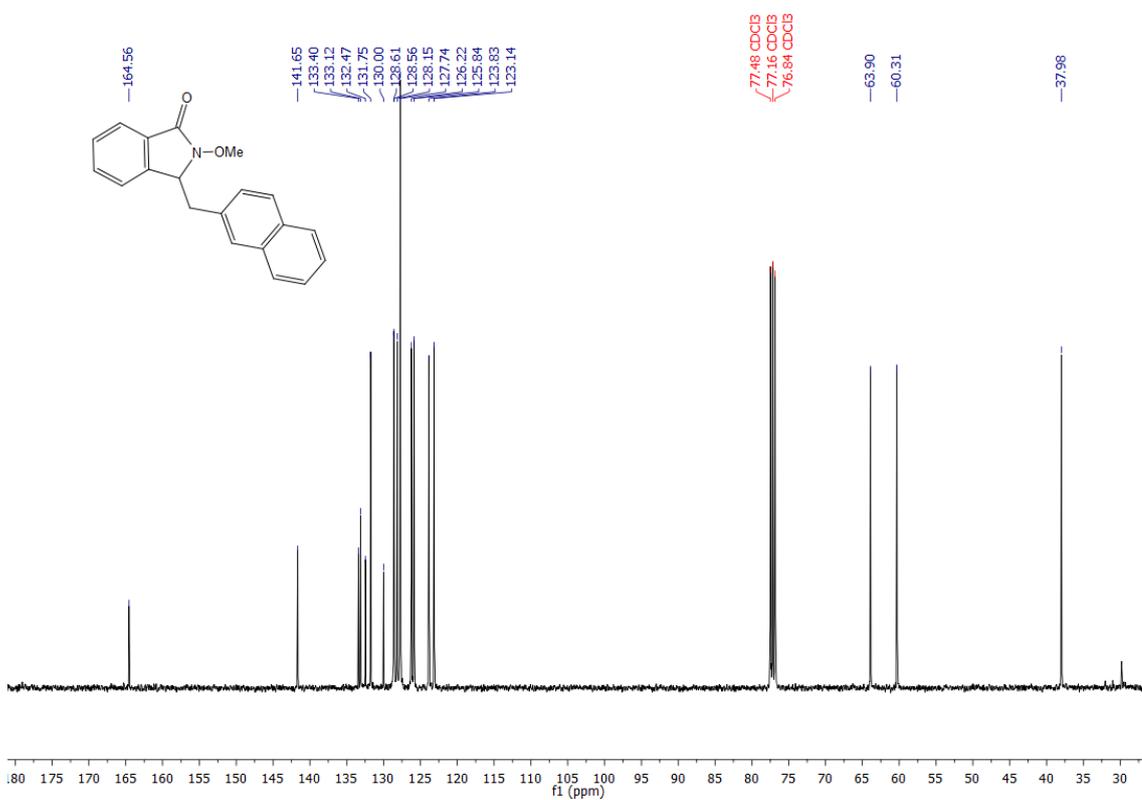
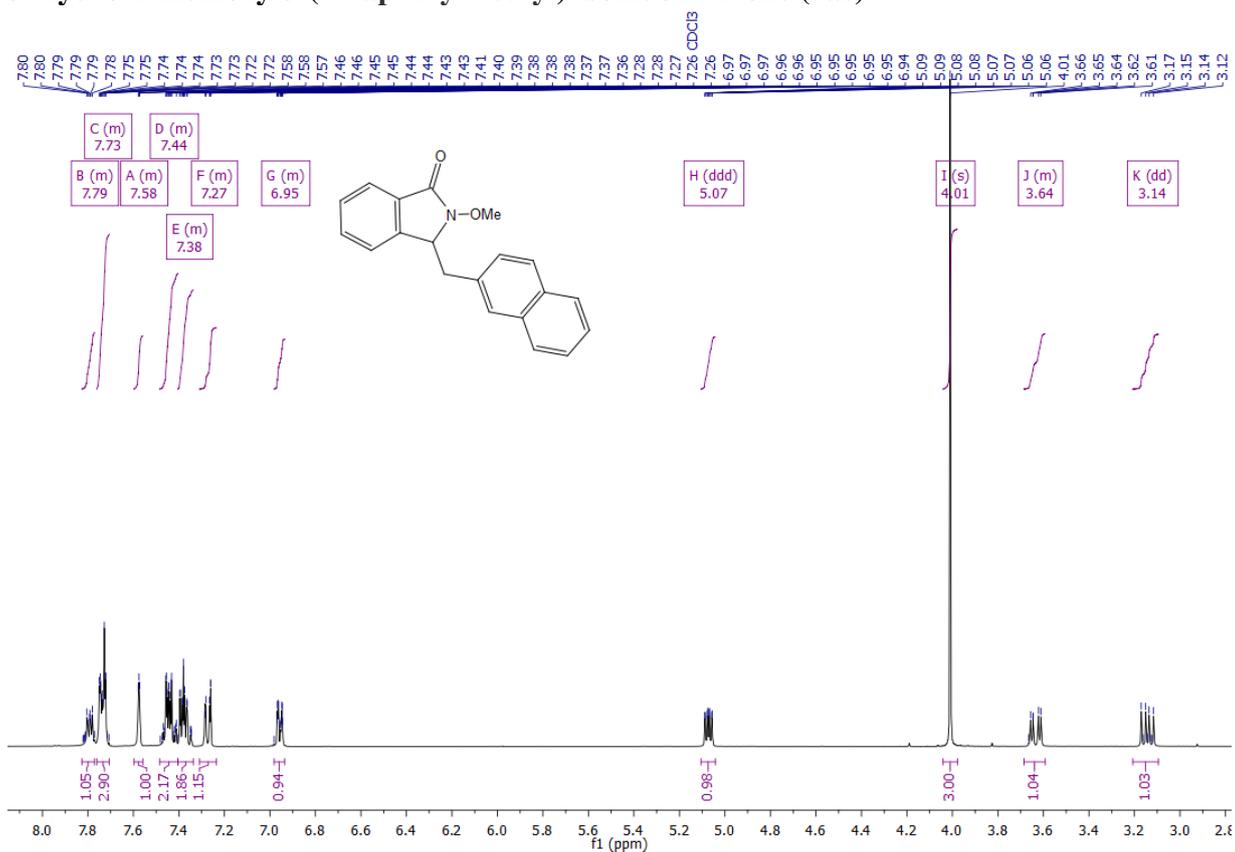
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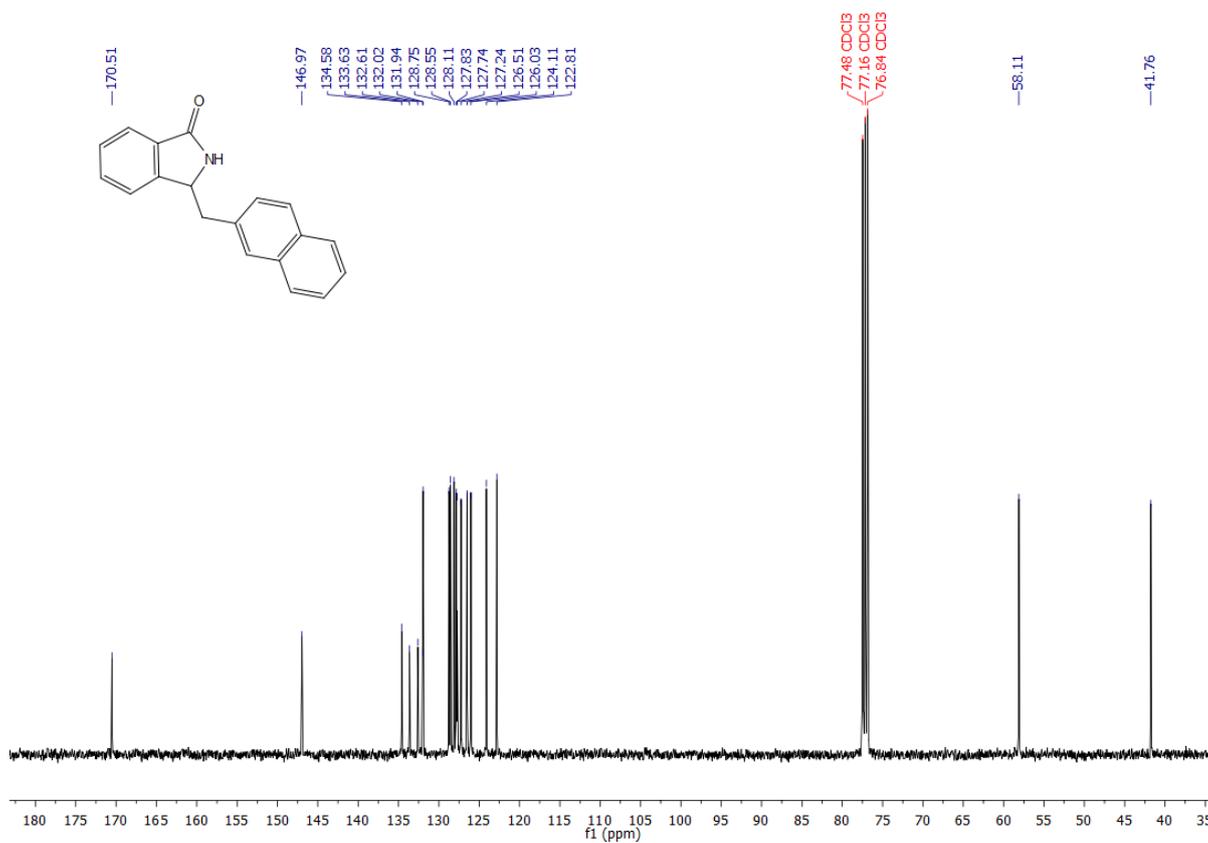
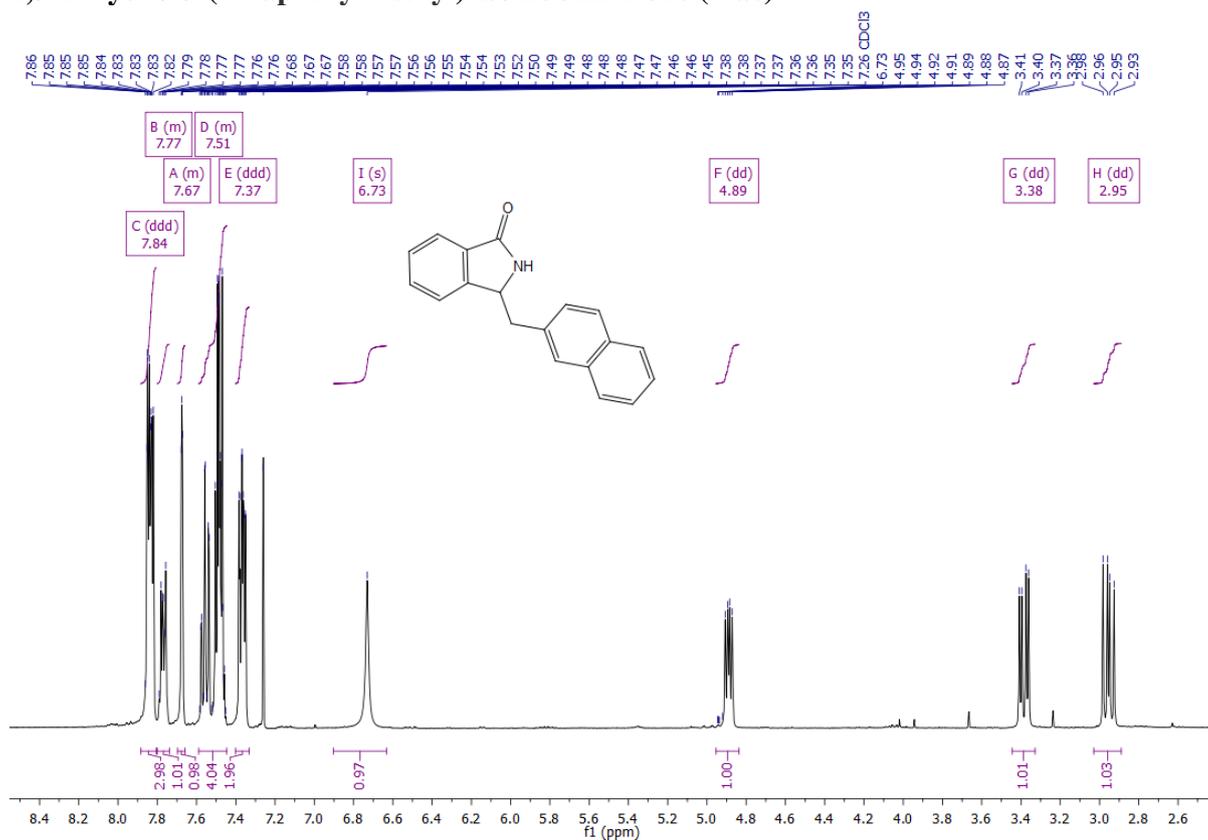
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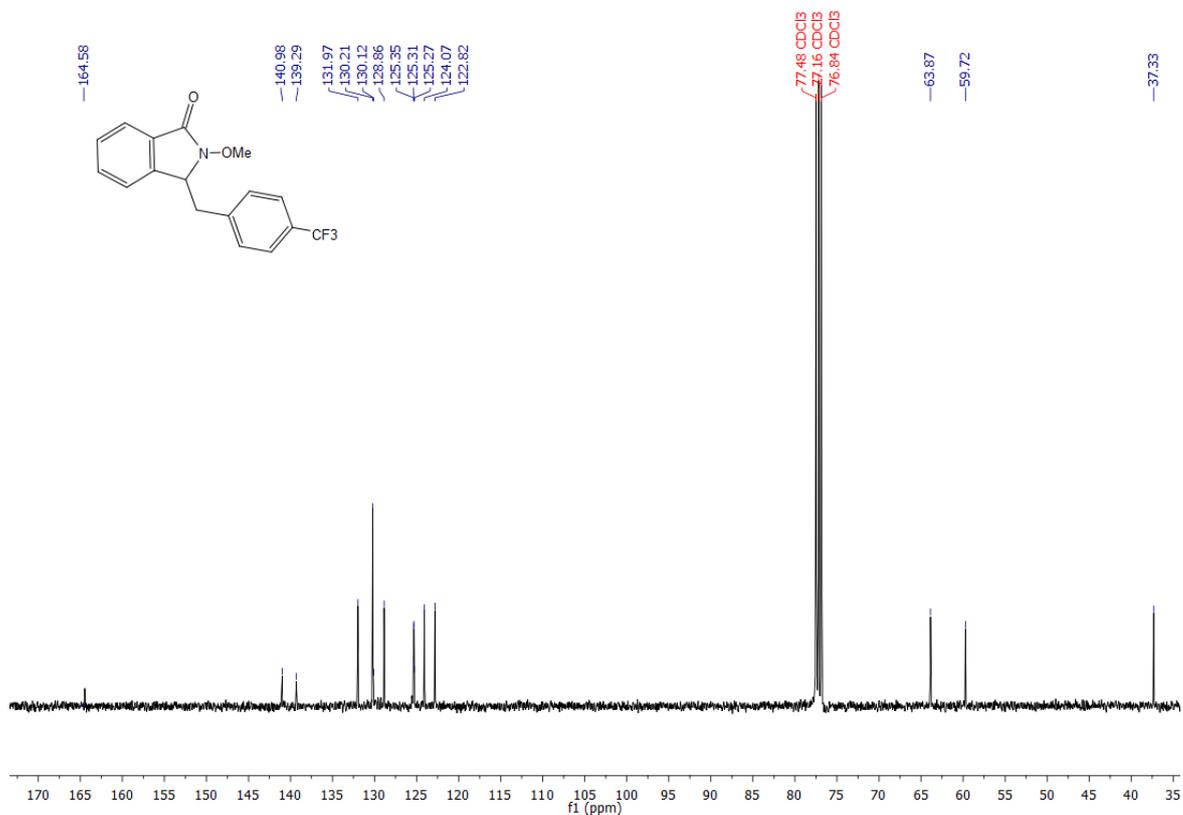
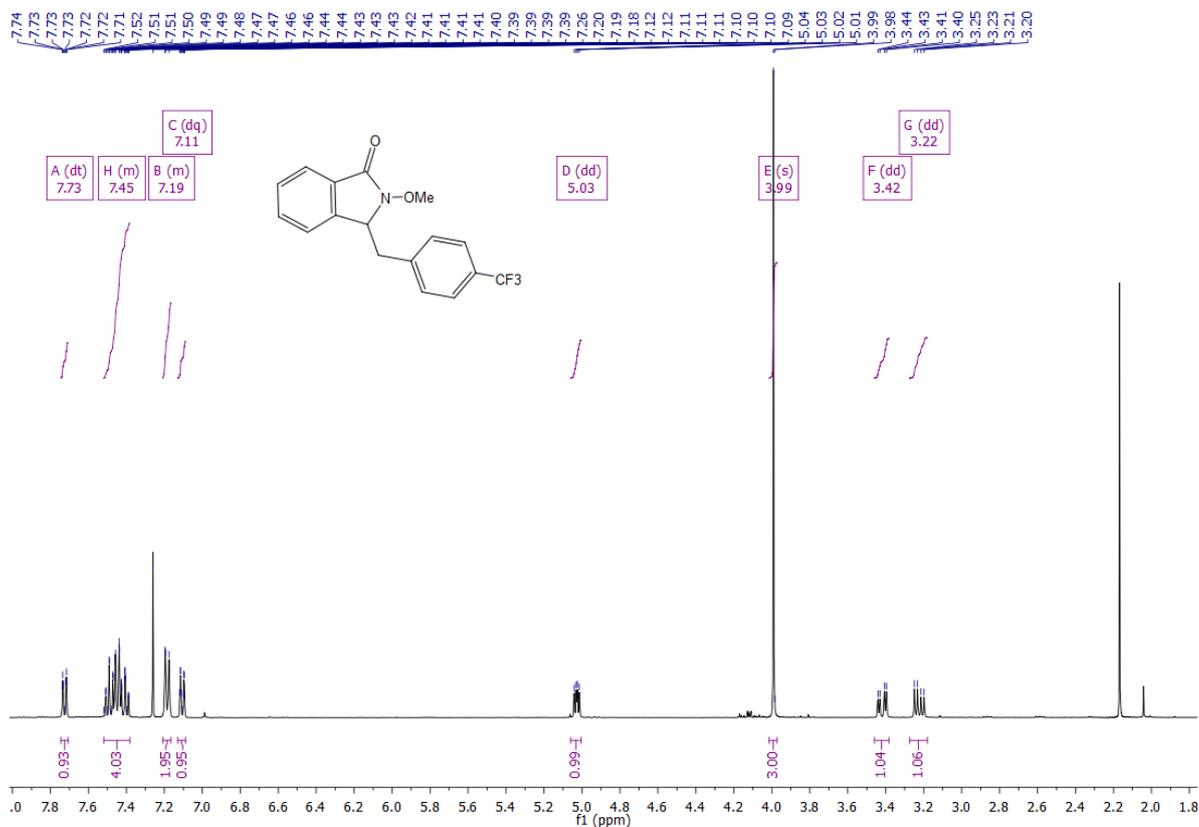
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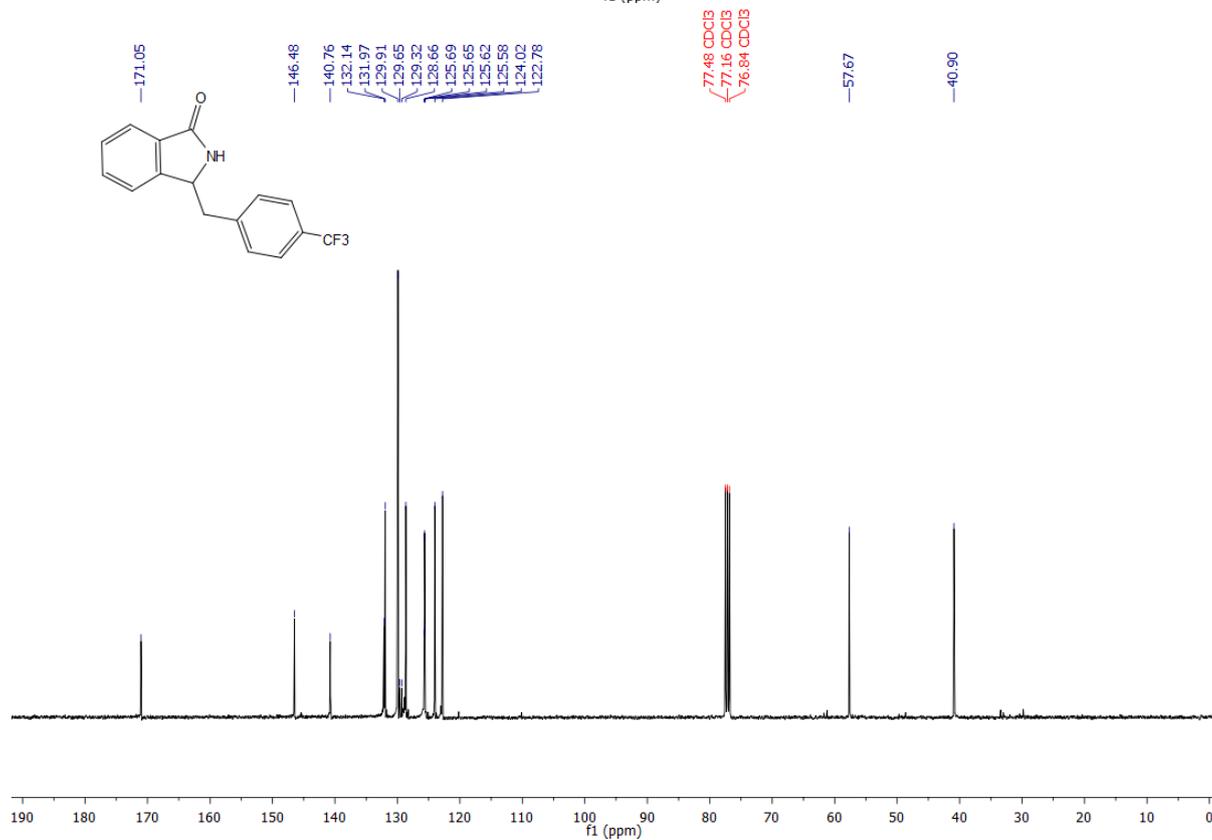
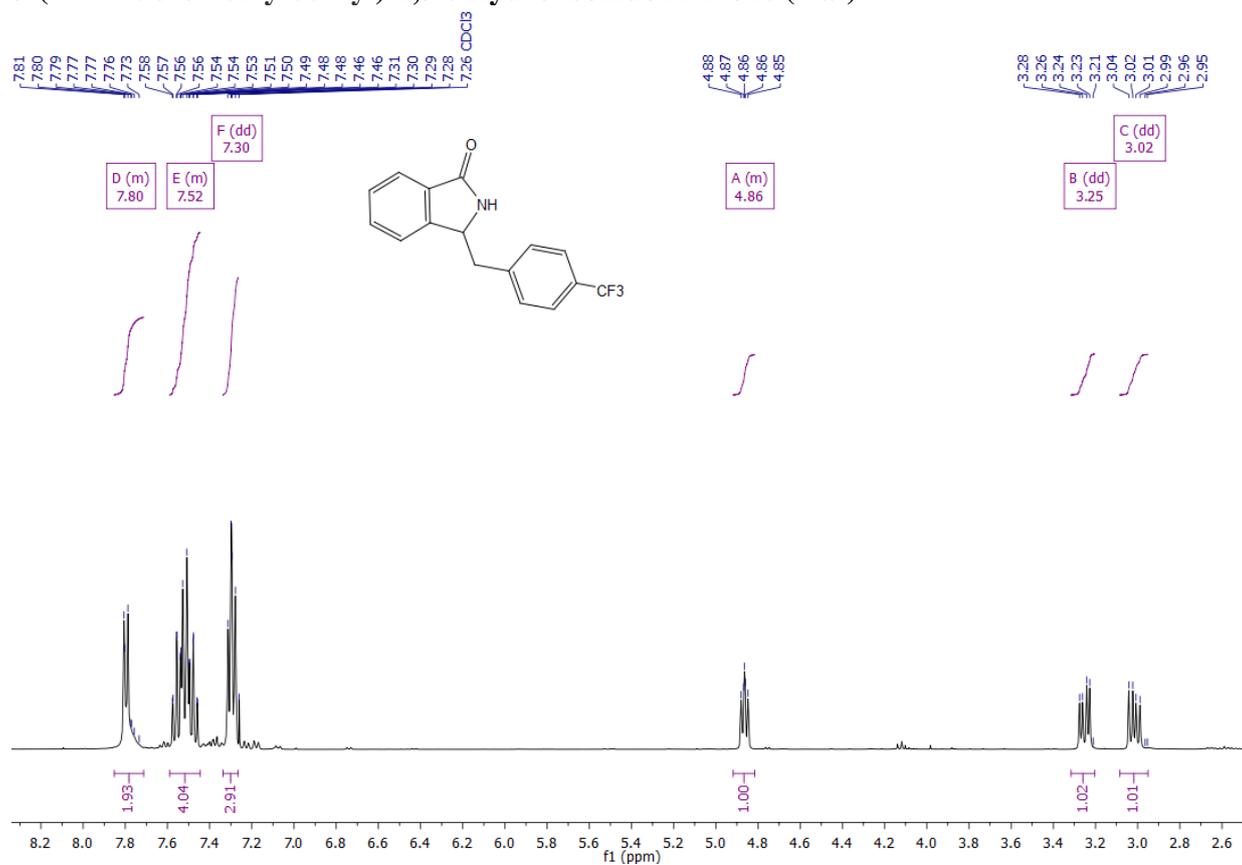
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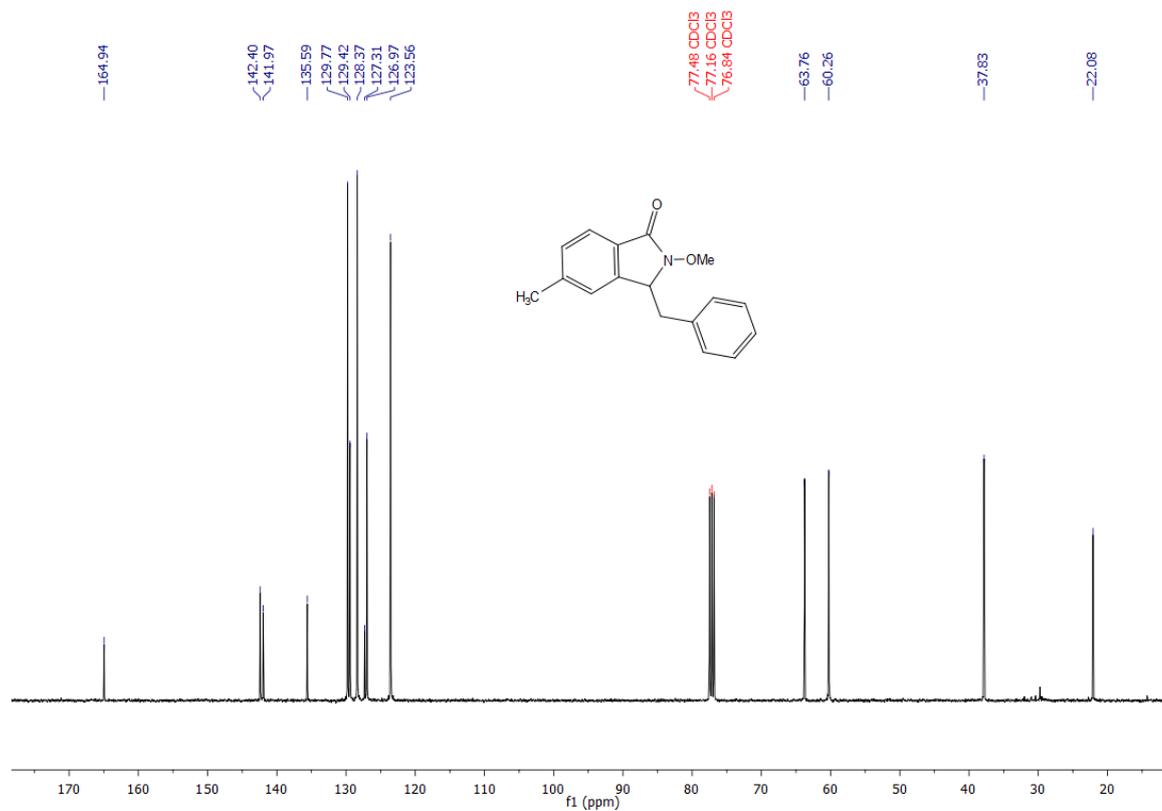
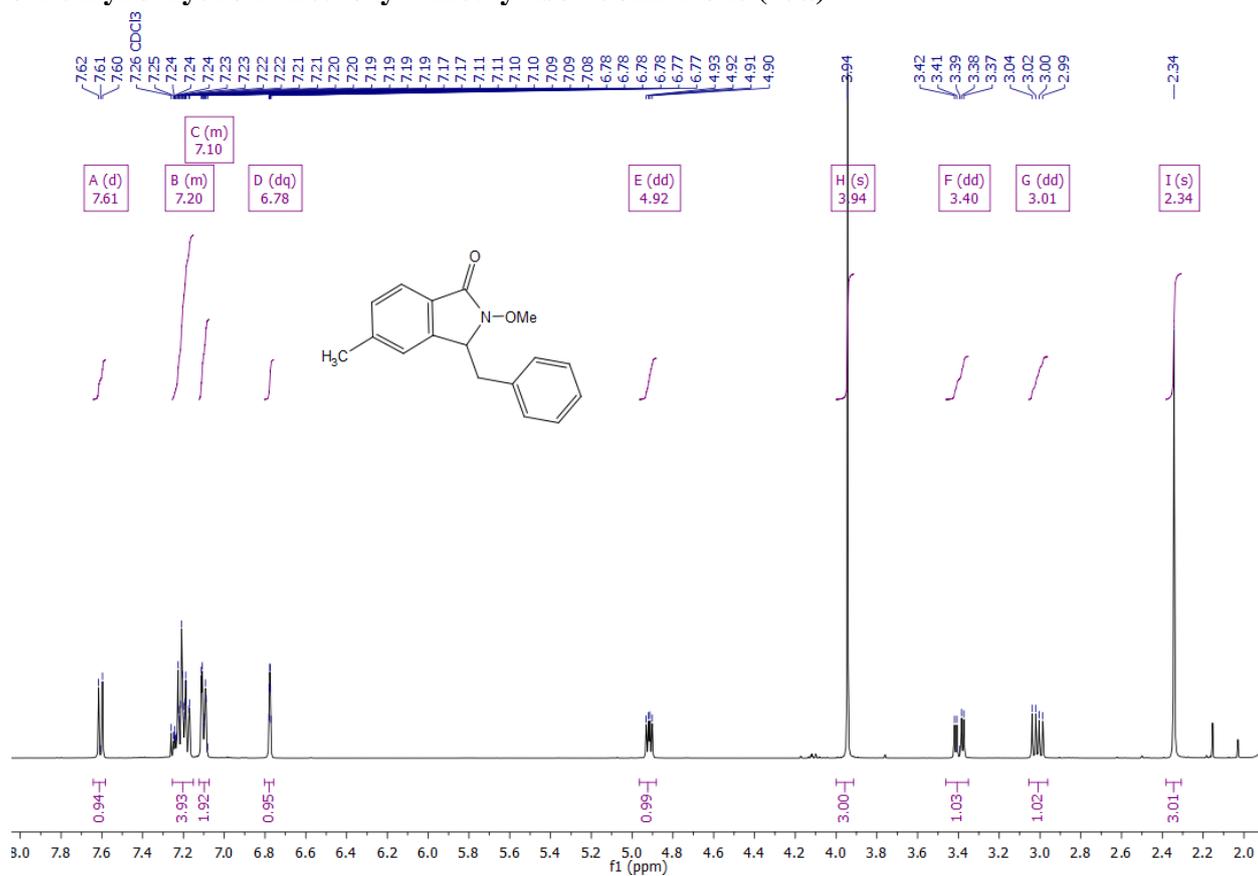
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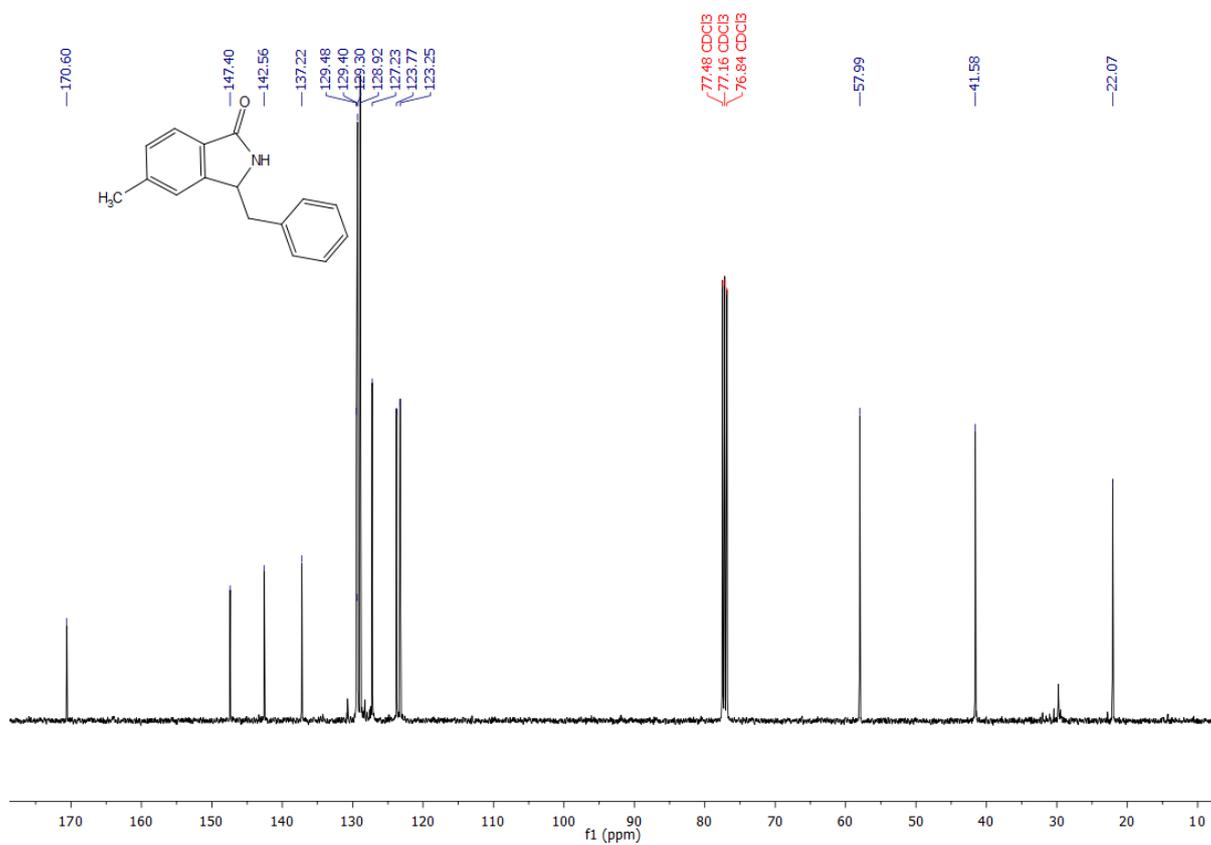
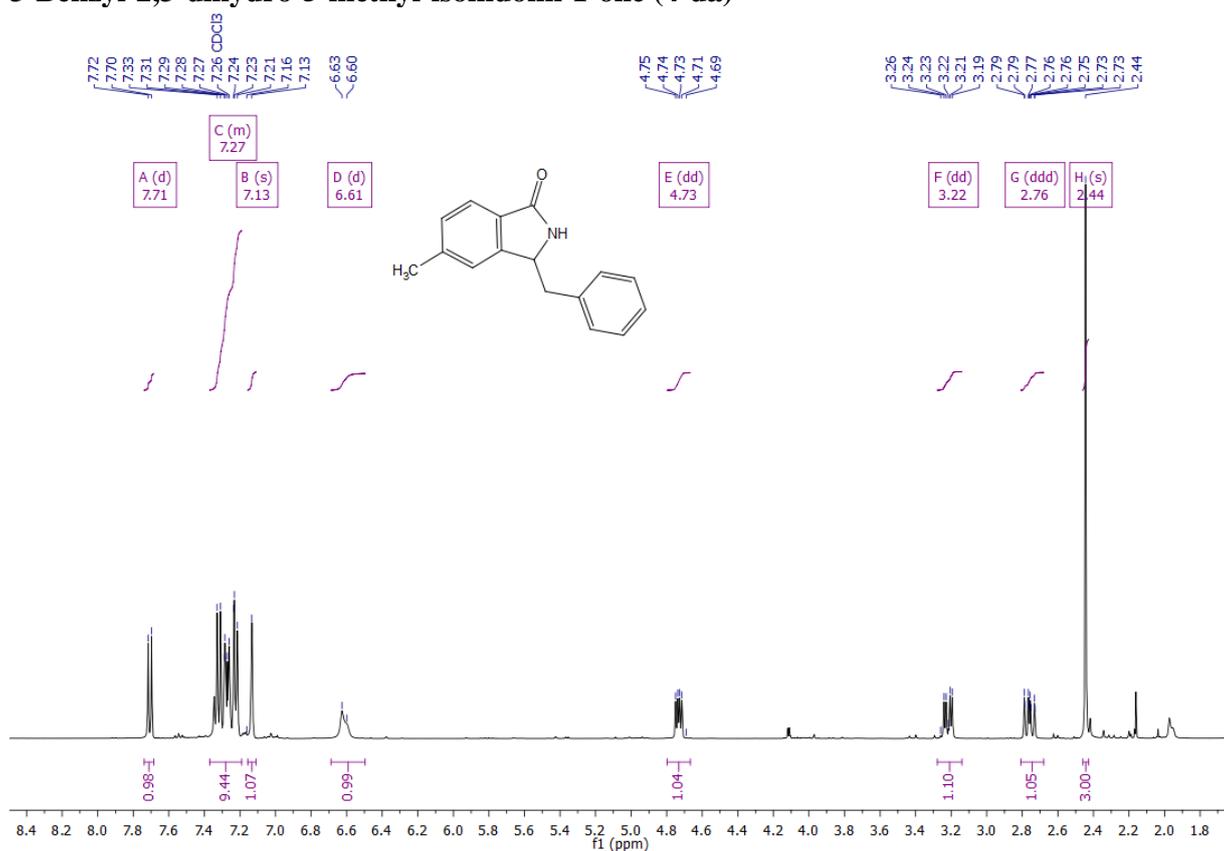
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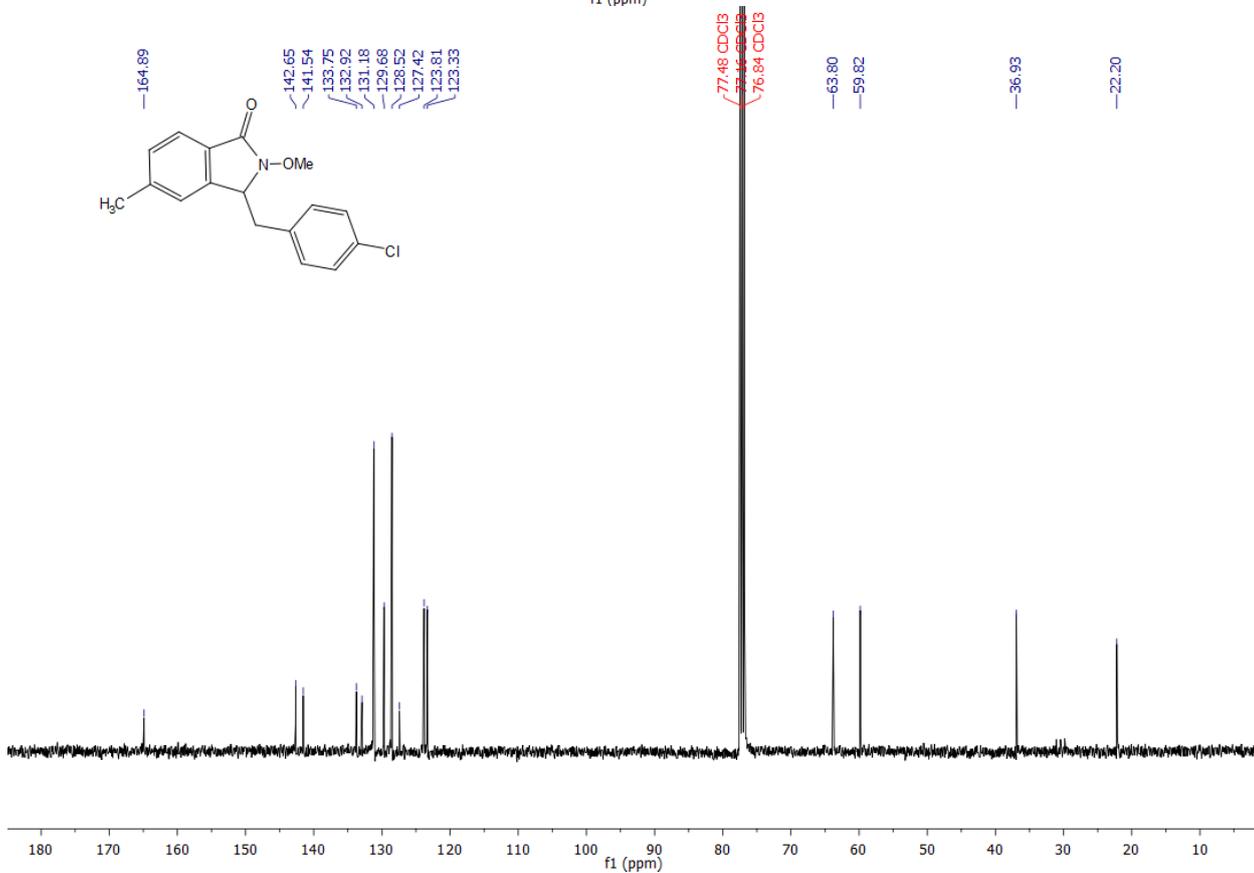
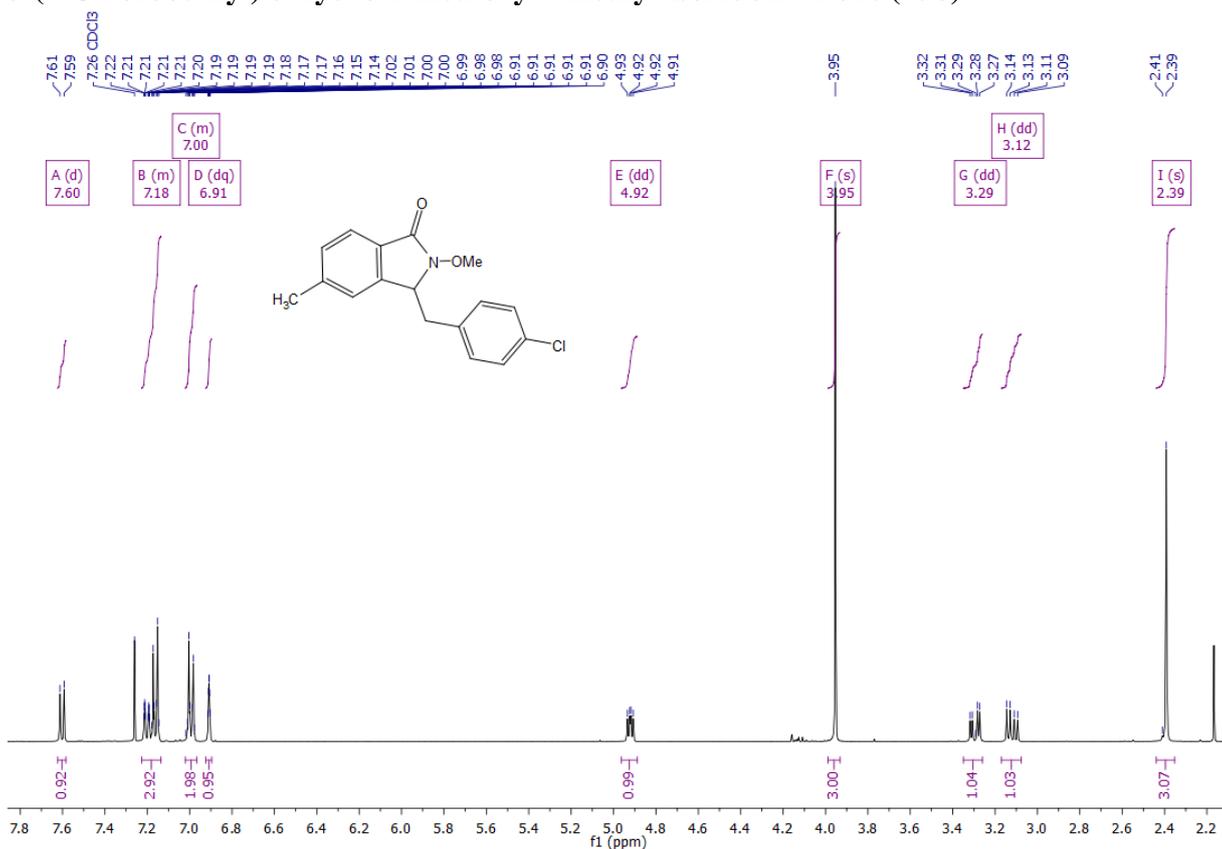
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3-Benzyl-2,3-dihydro-5-methyl-isindolin-1-one (4'da)



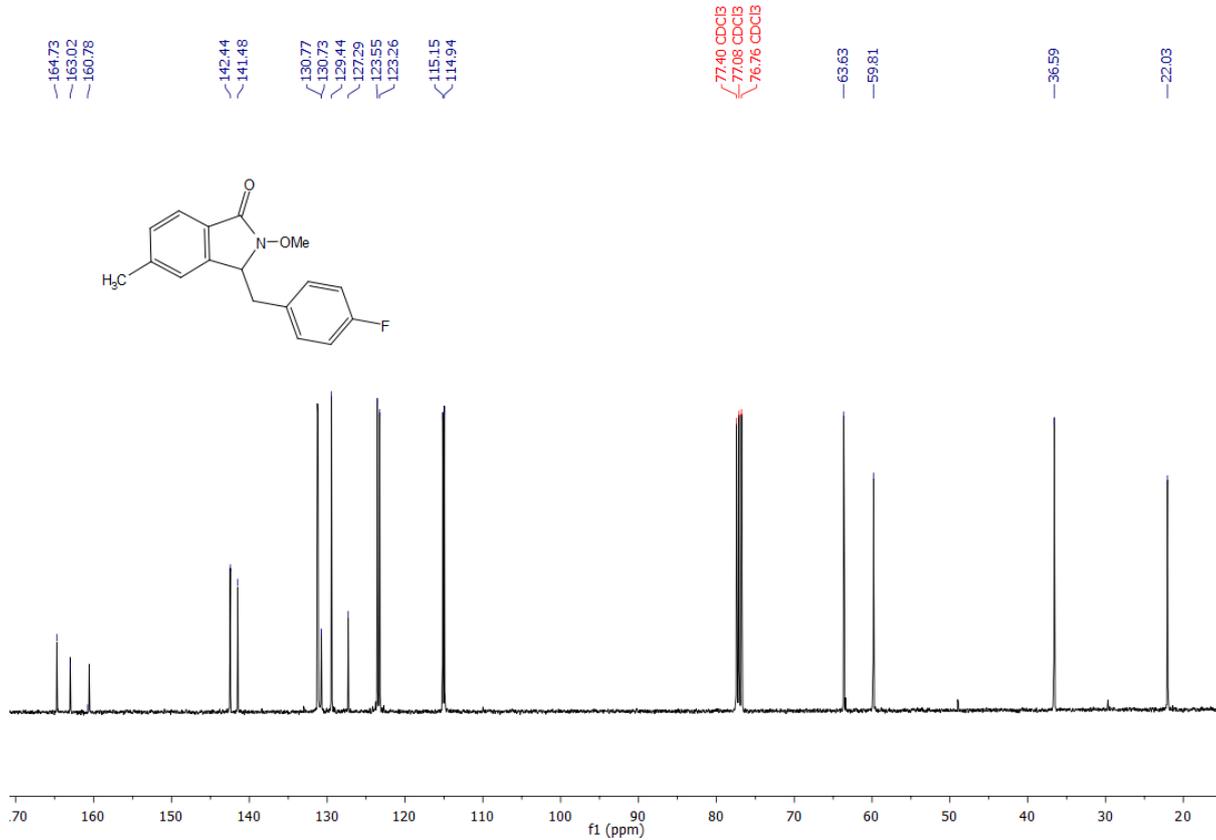
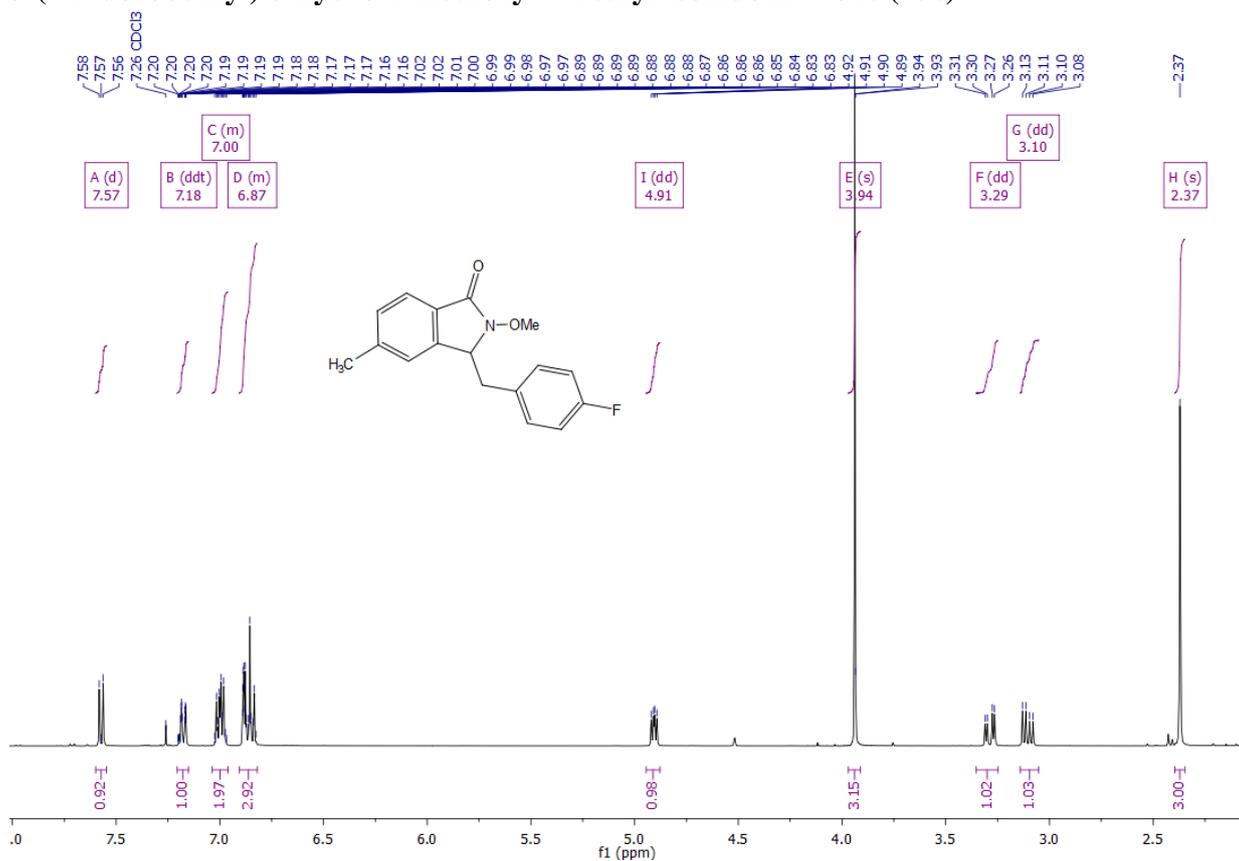
Supporting Information

3-(4-Chlorobenzyl)-3-hydro-2-methoxy-5-methyl-indolin-1-one (4db)



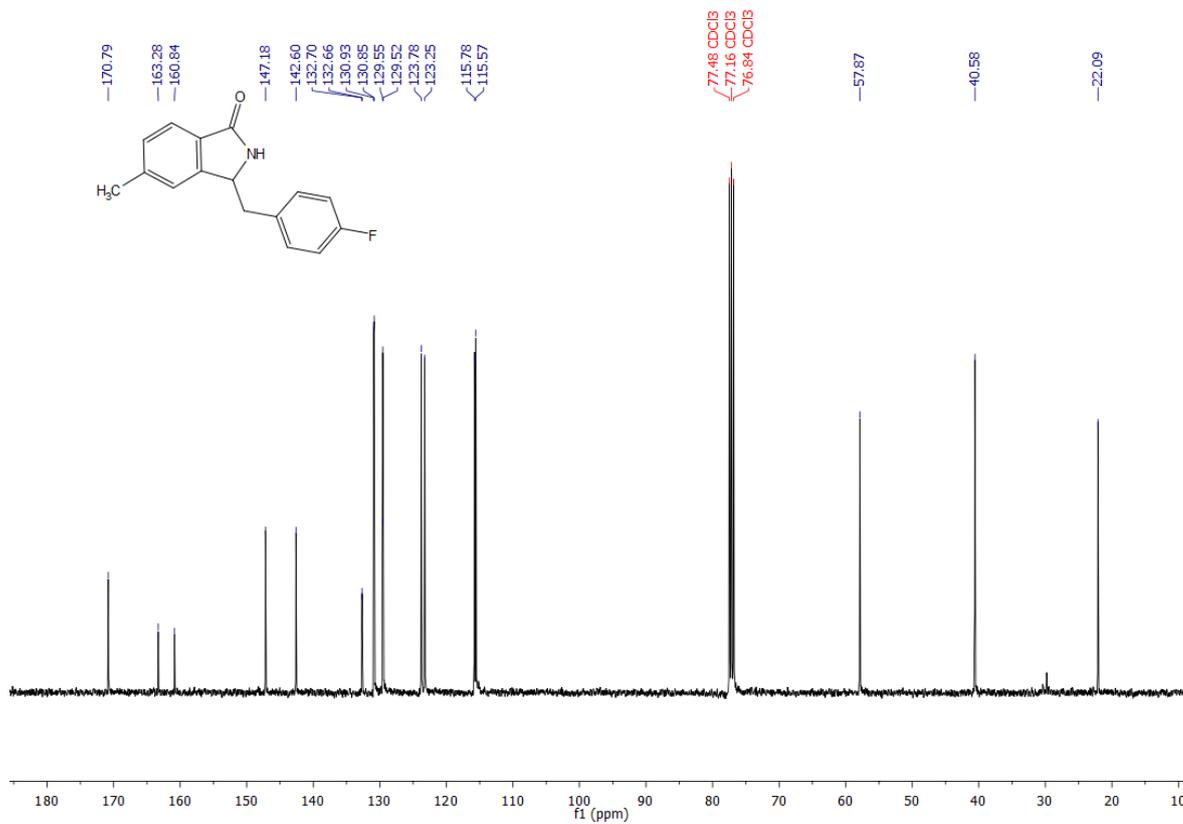
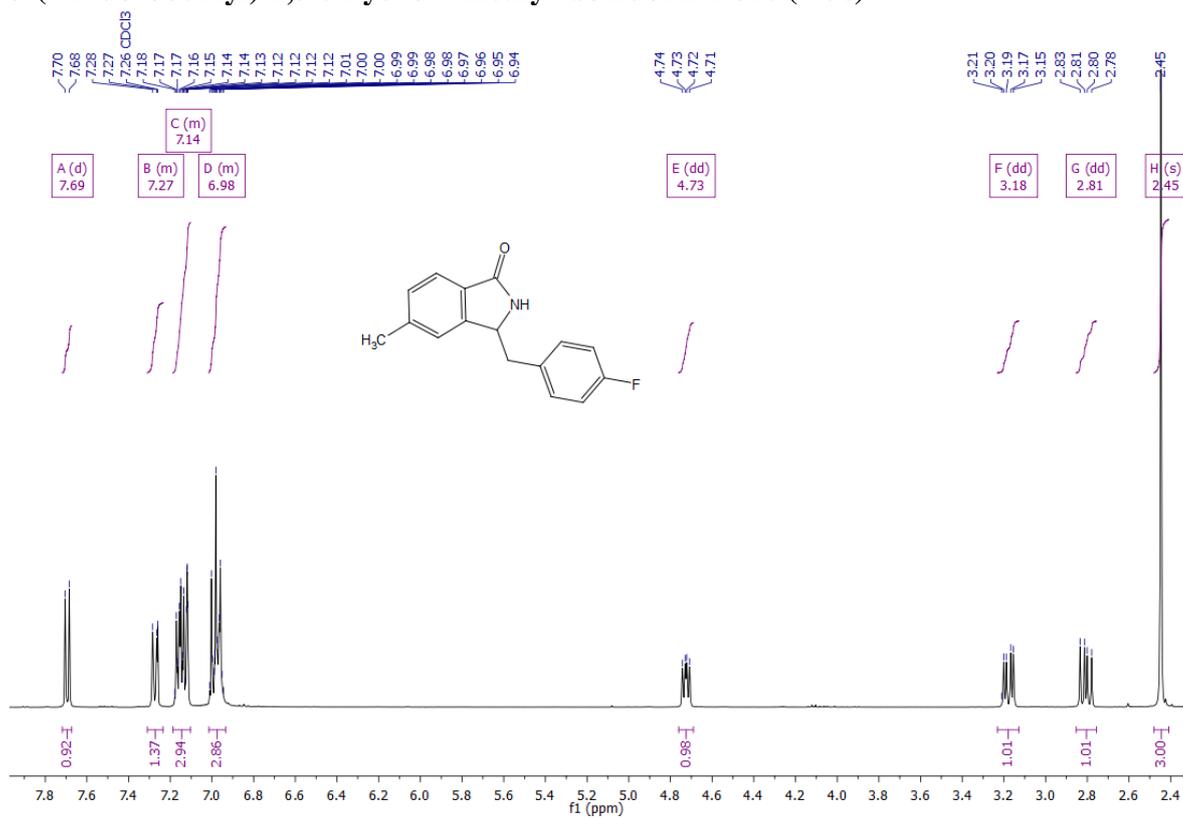
Supporting Information

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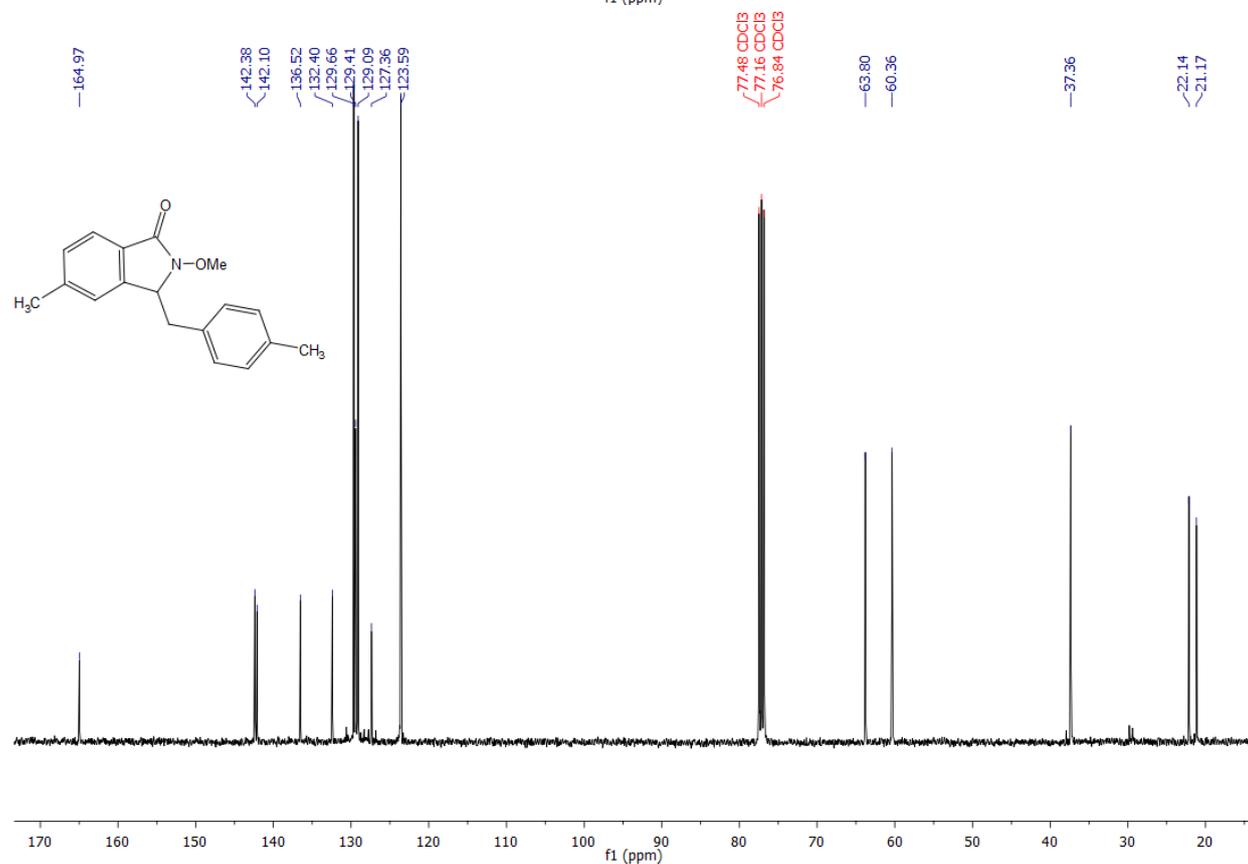
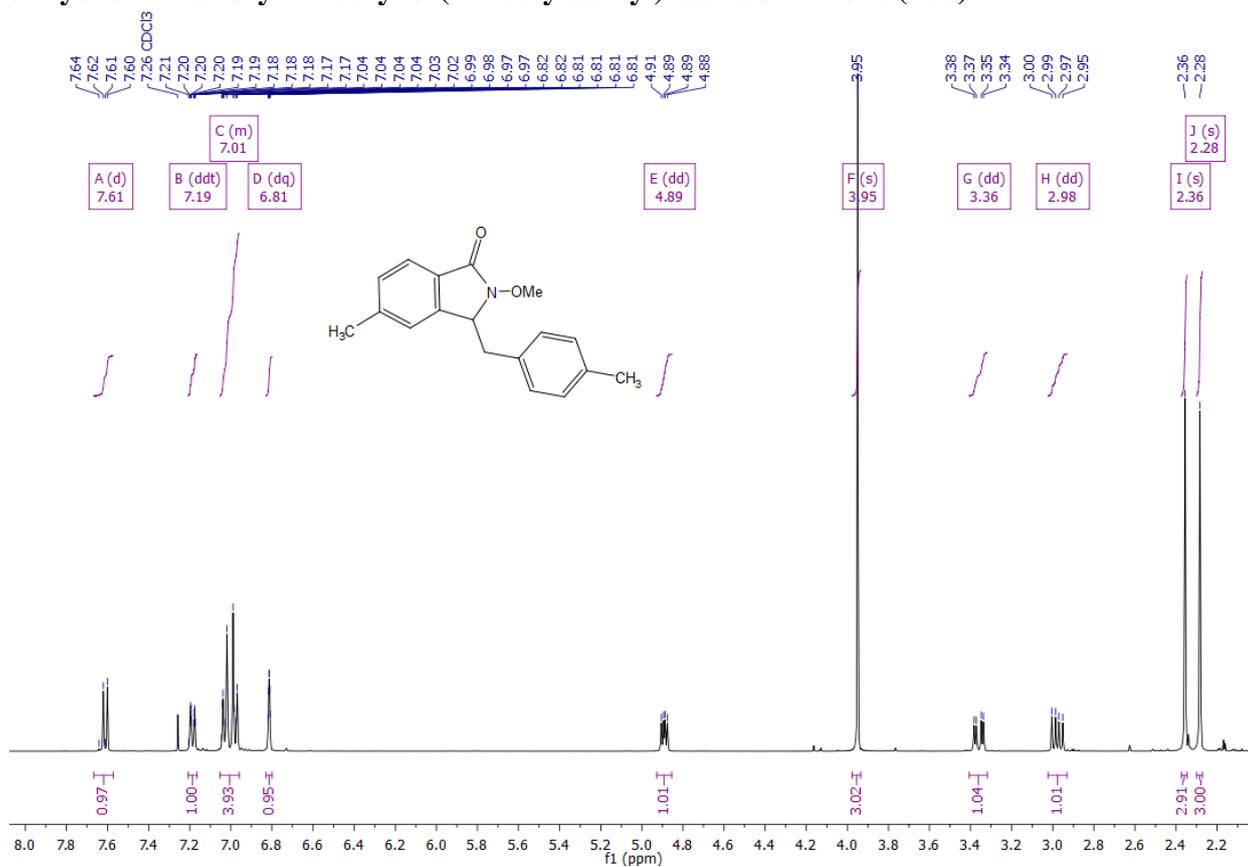
Supporting Information

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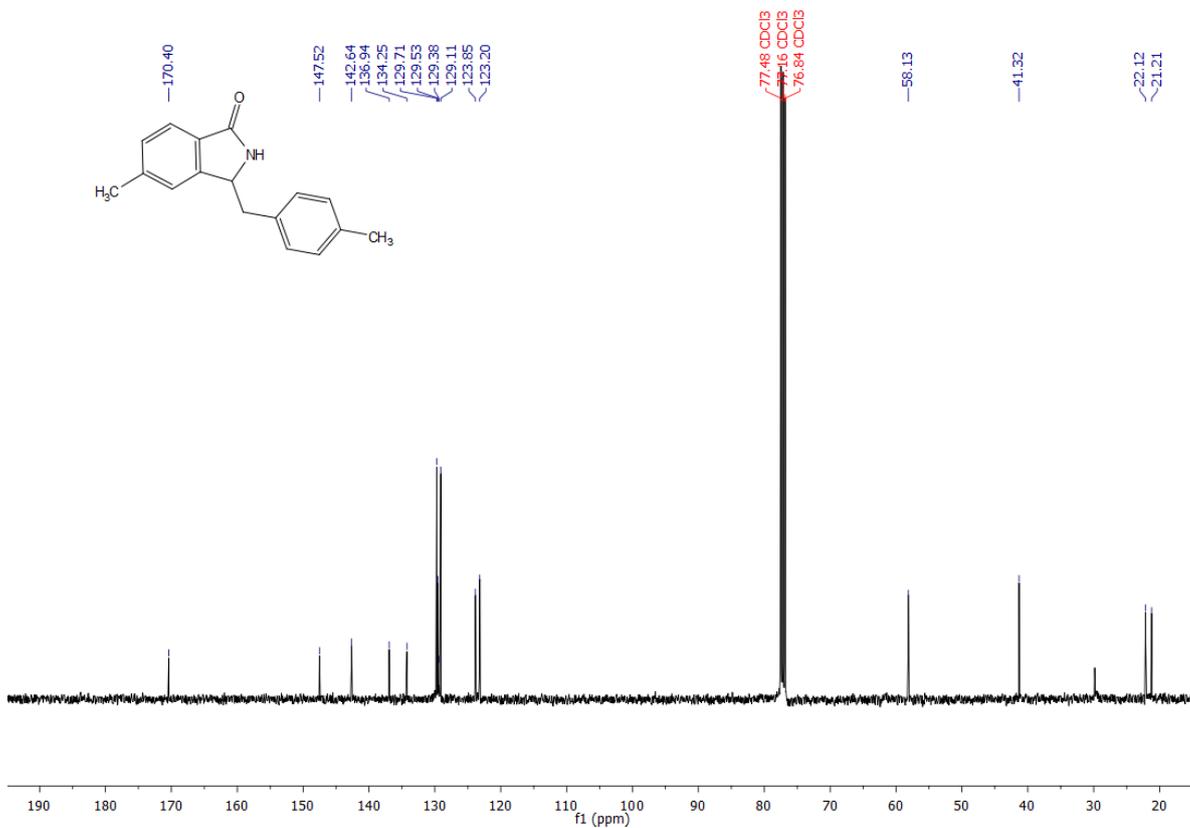
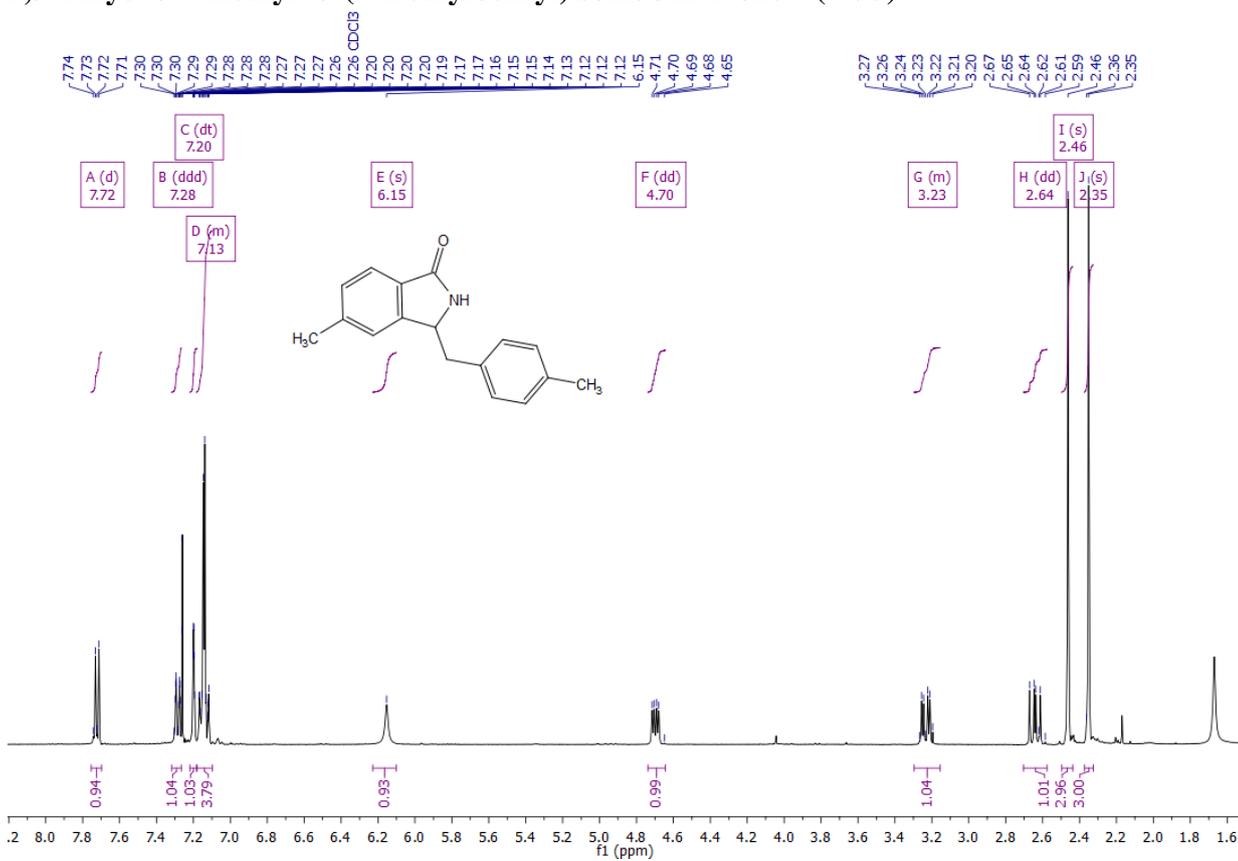
Supporting Information

3-Hydro-2-methoxy-5-methyl-3-(4-methylbenzyl)-isoindolin-1-one (4dd)



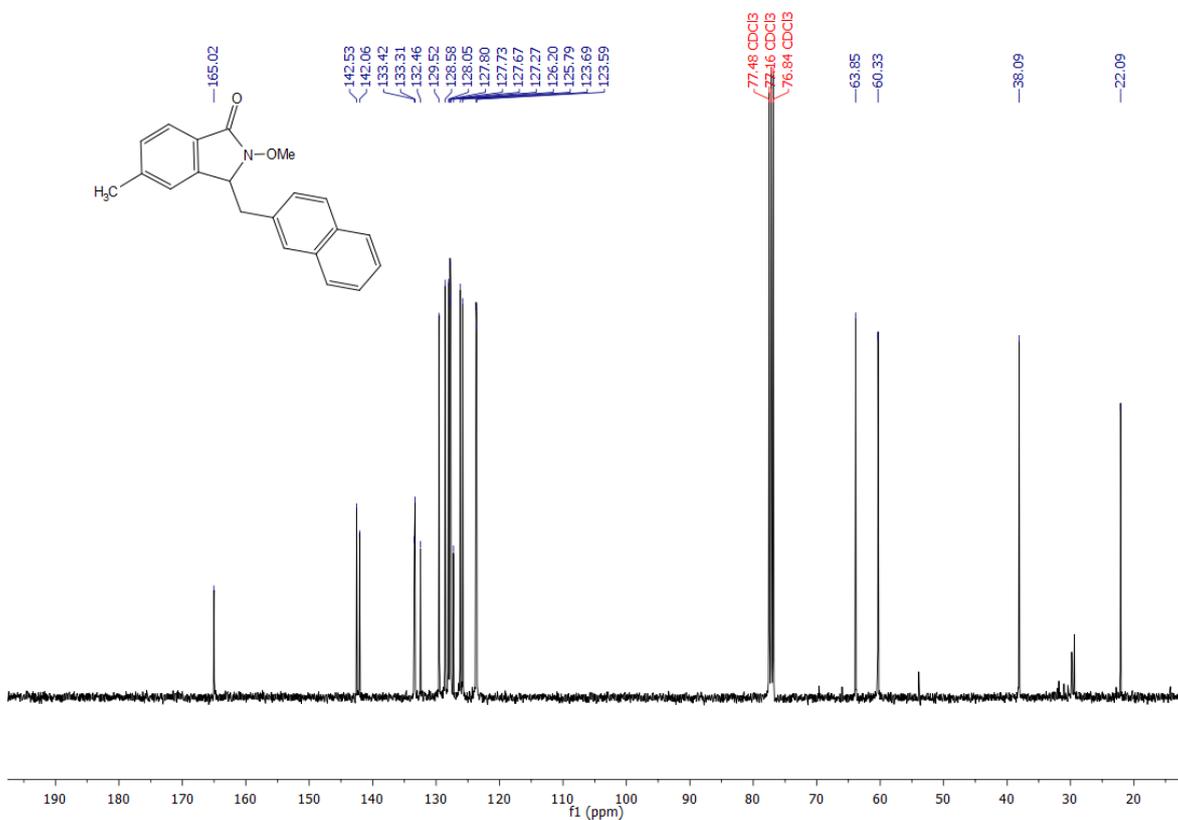
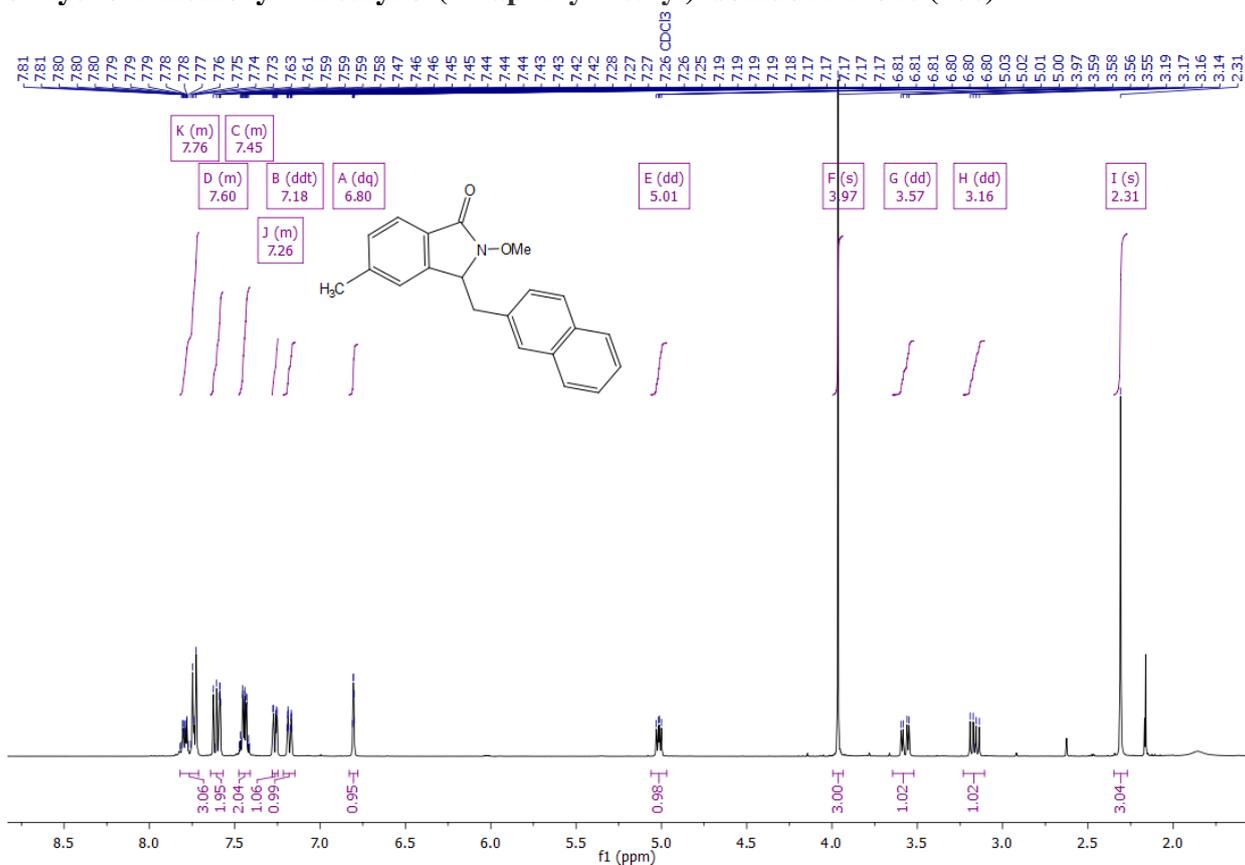
Supporting Information

2,3-Dihydro-5-methyl--3-(4-methylbenzyl)isoindolin-1-one (4'dd)



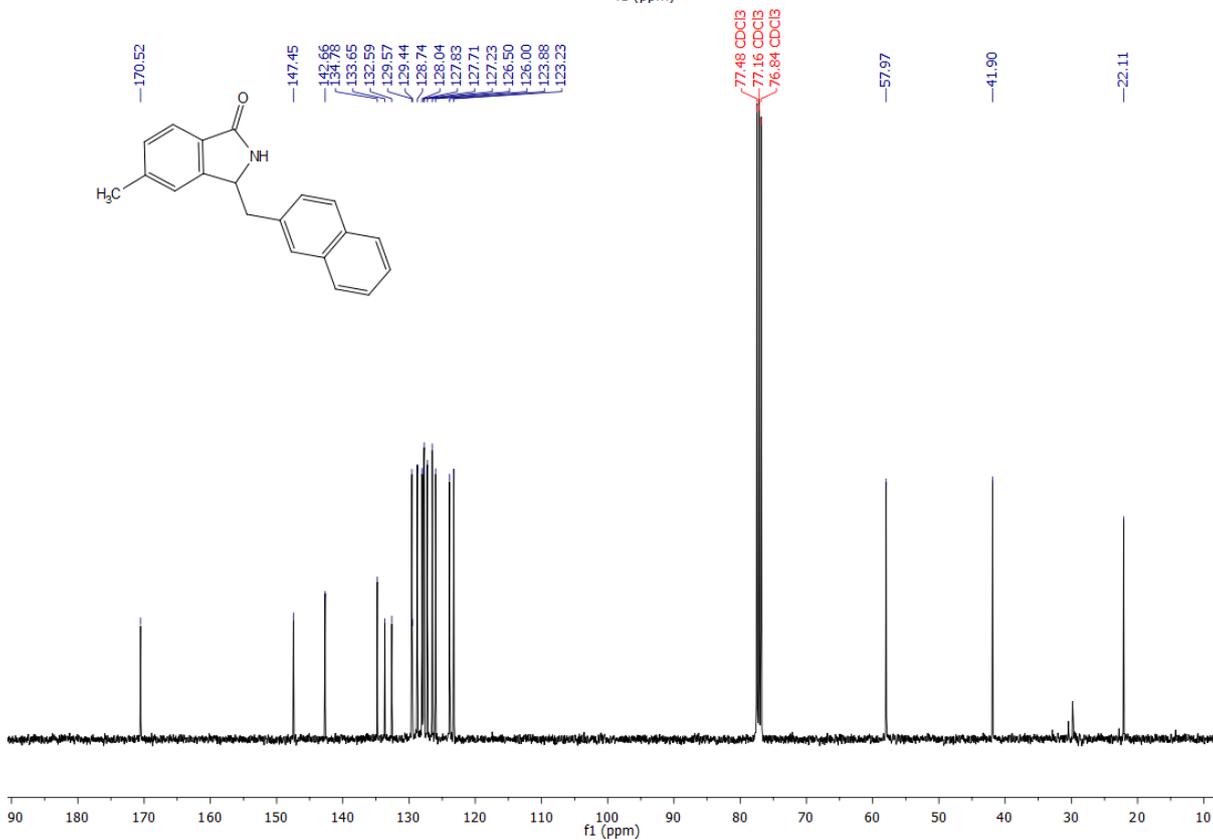
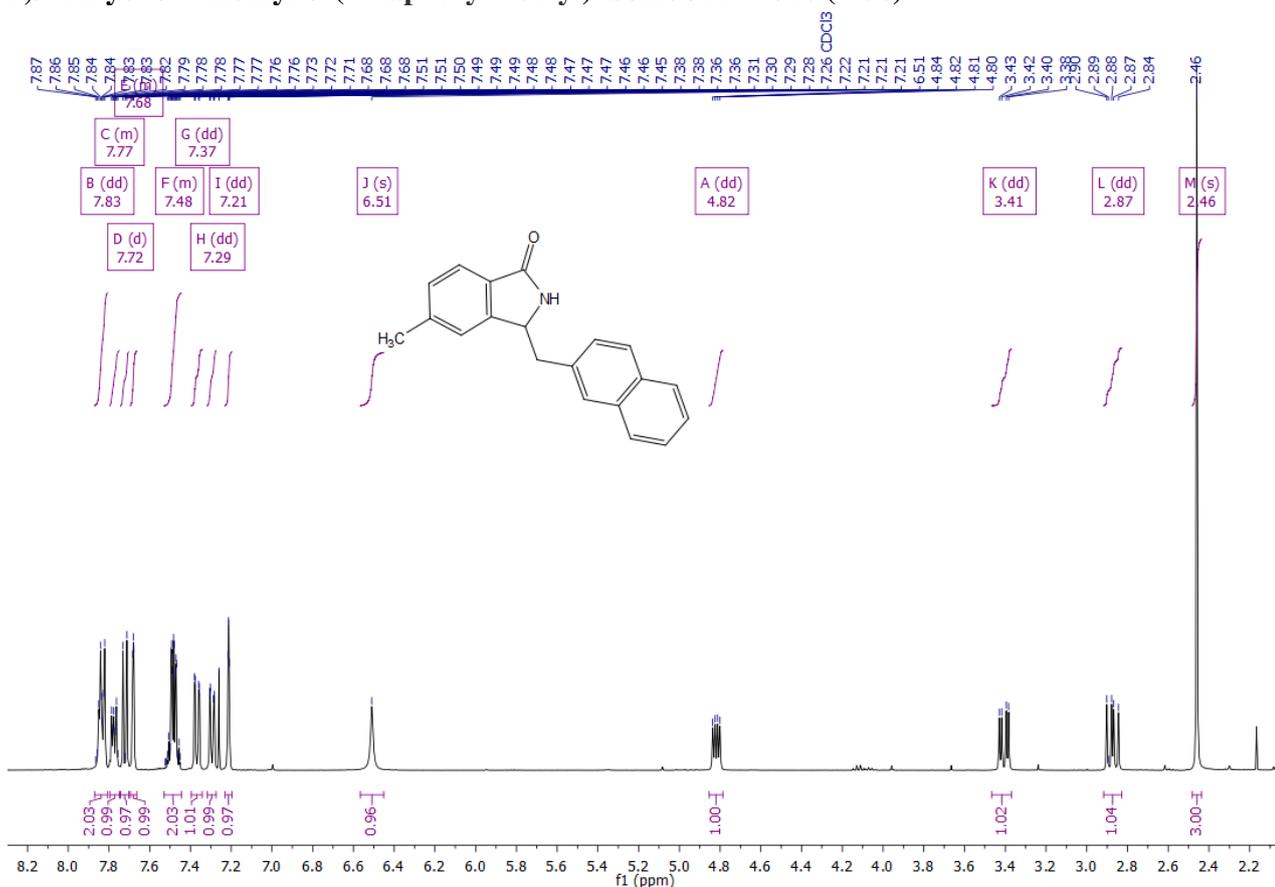
Supporting Information

3-Hydro-2-methoxy-5-methyl-3-(2-naphthylmethyl)-isoindolin-1-one (4de)



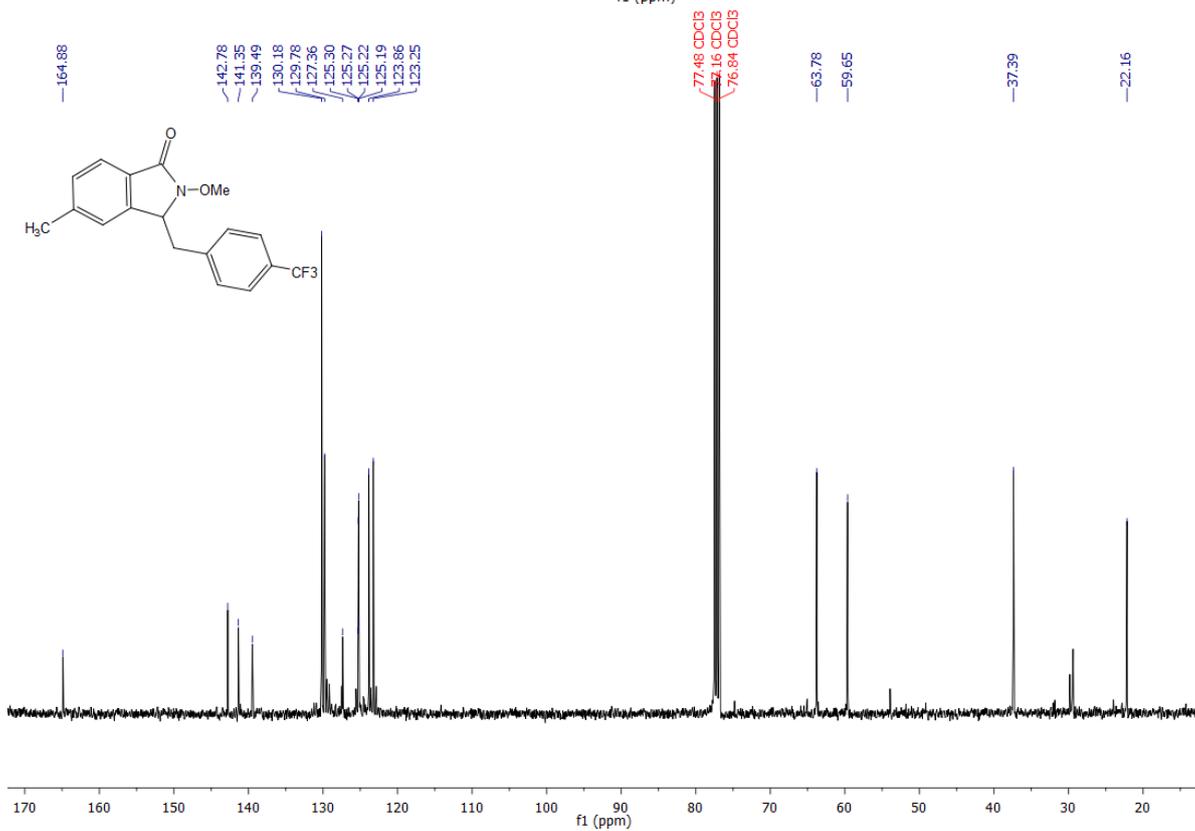
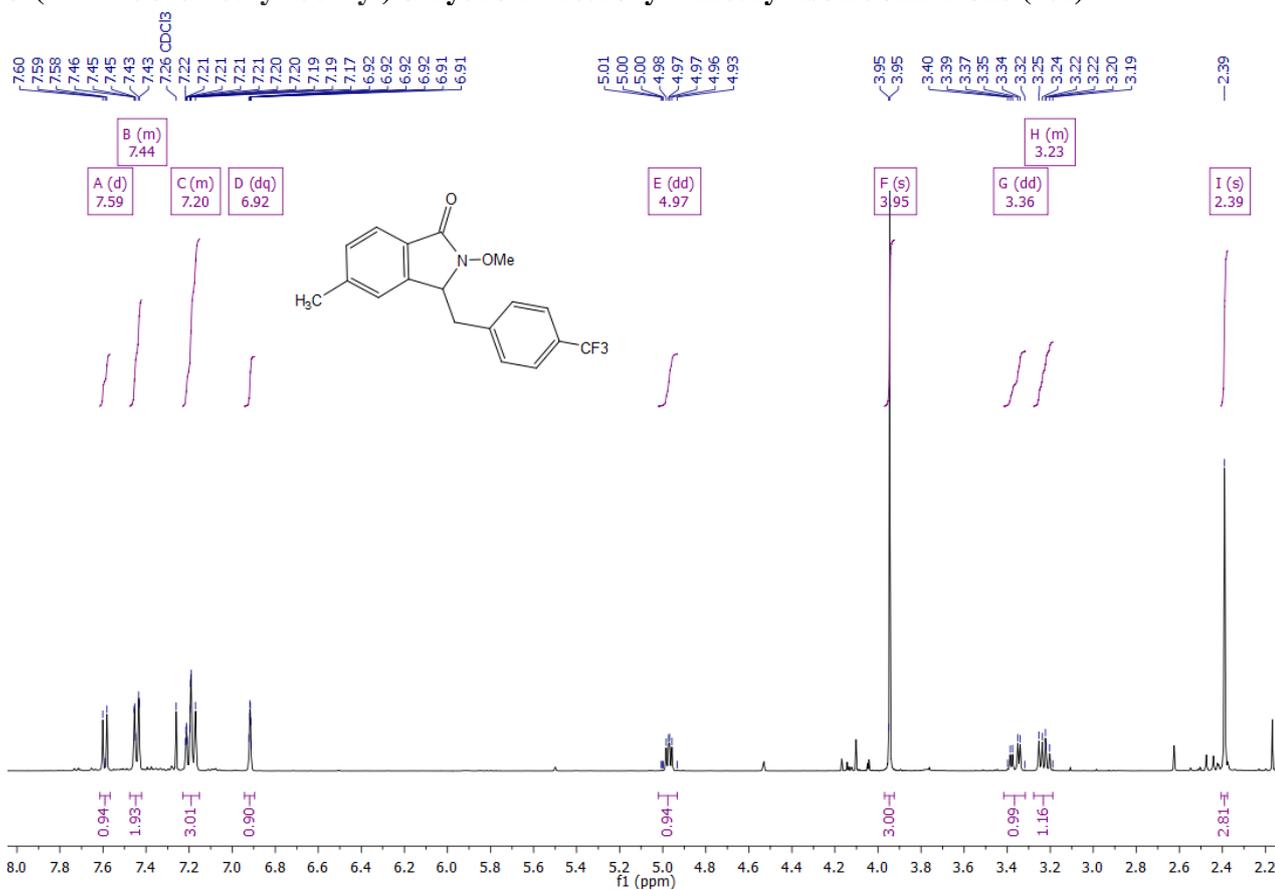
Supporting Information

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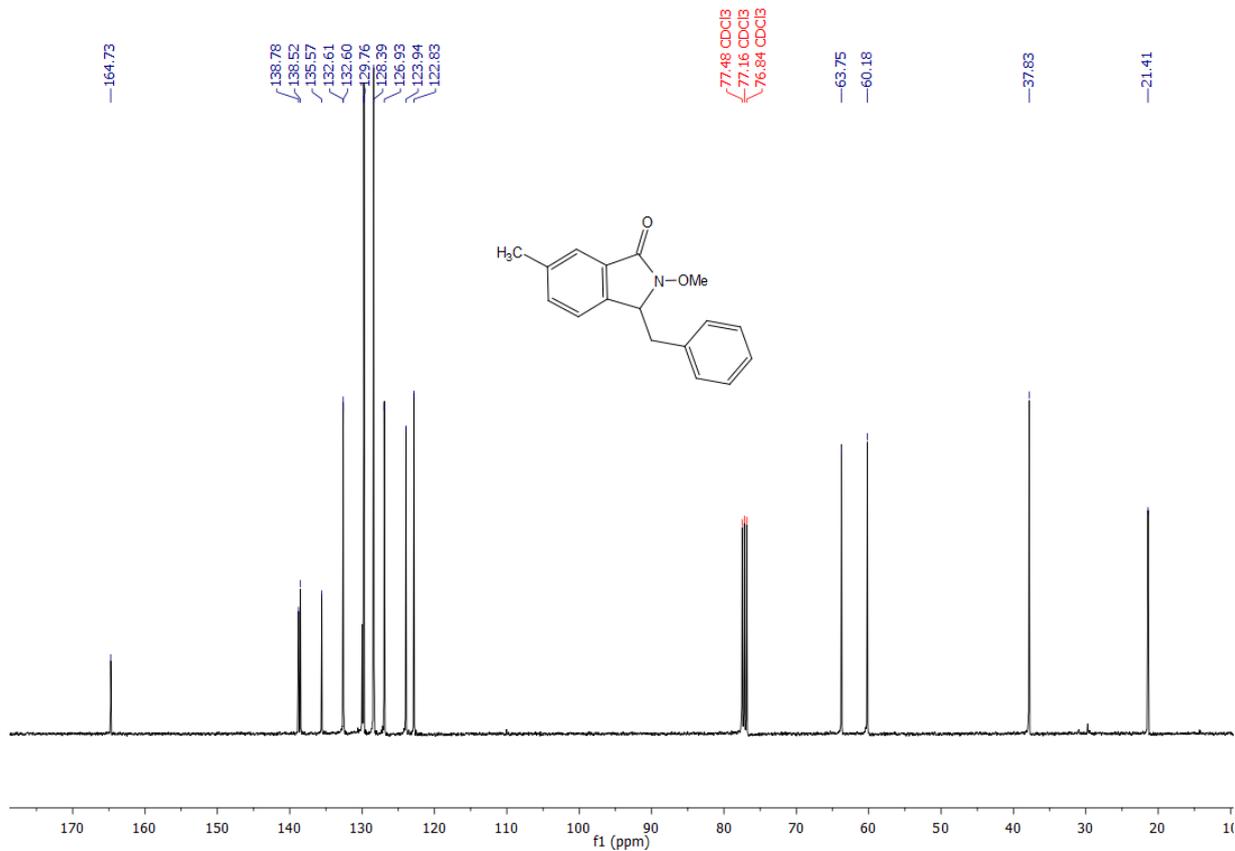
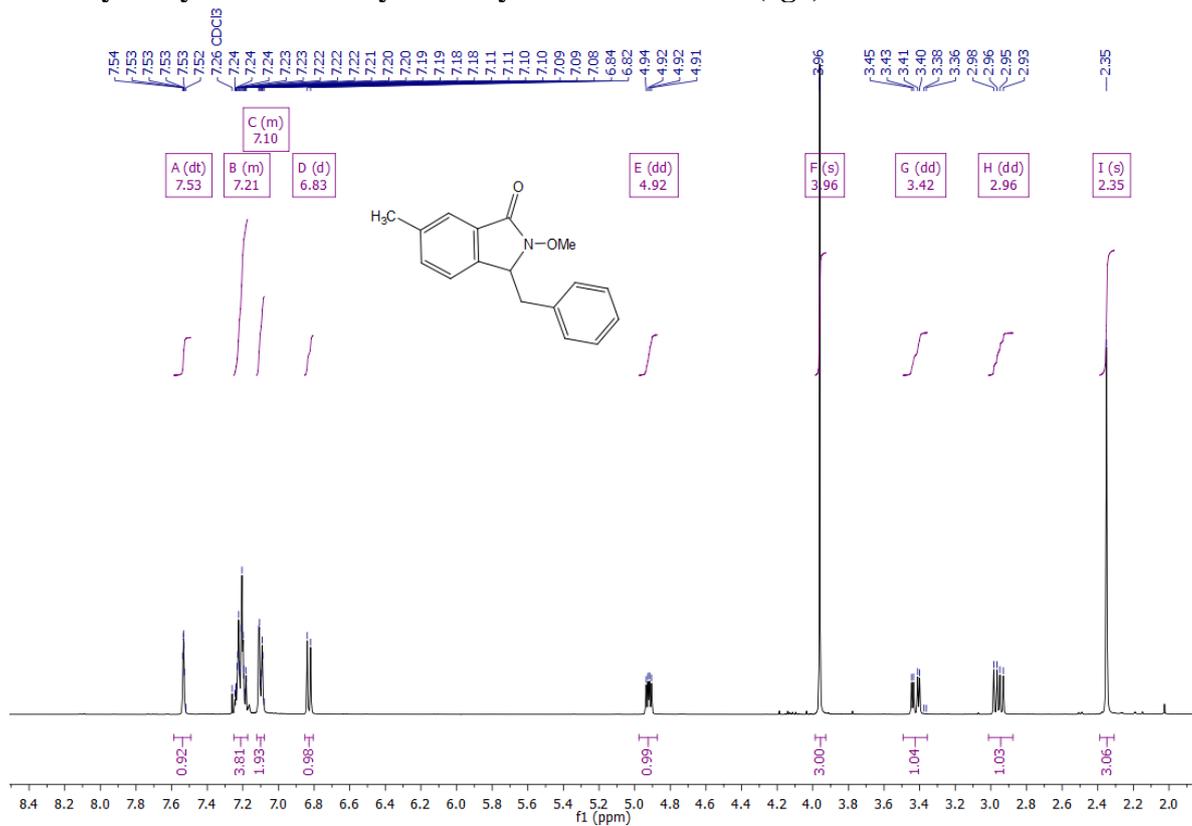
Supporting Information

3-(4-Trifluoromethyl-benzyl)-3-hydro-2-methoxy-5-methyl-isoindolin-1-one (4df)



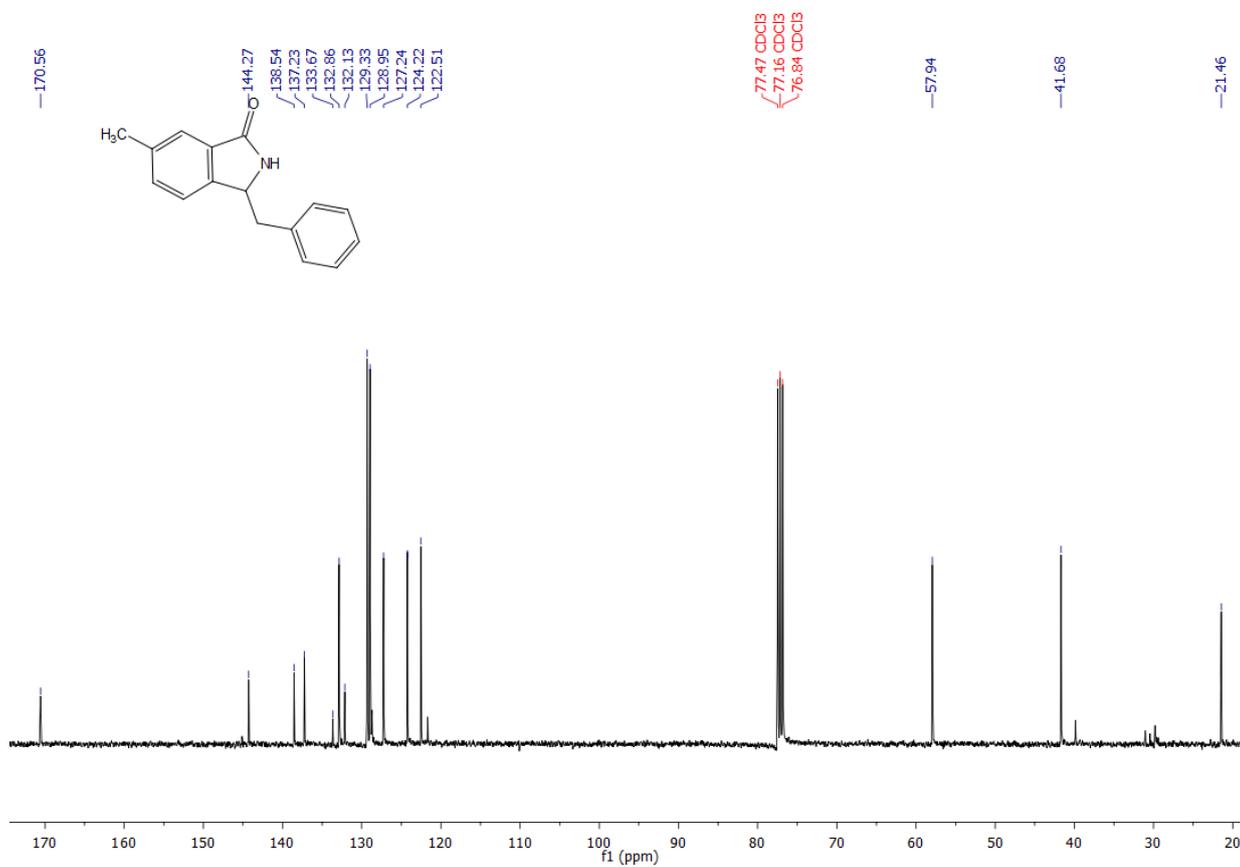
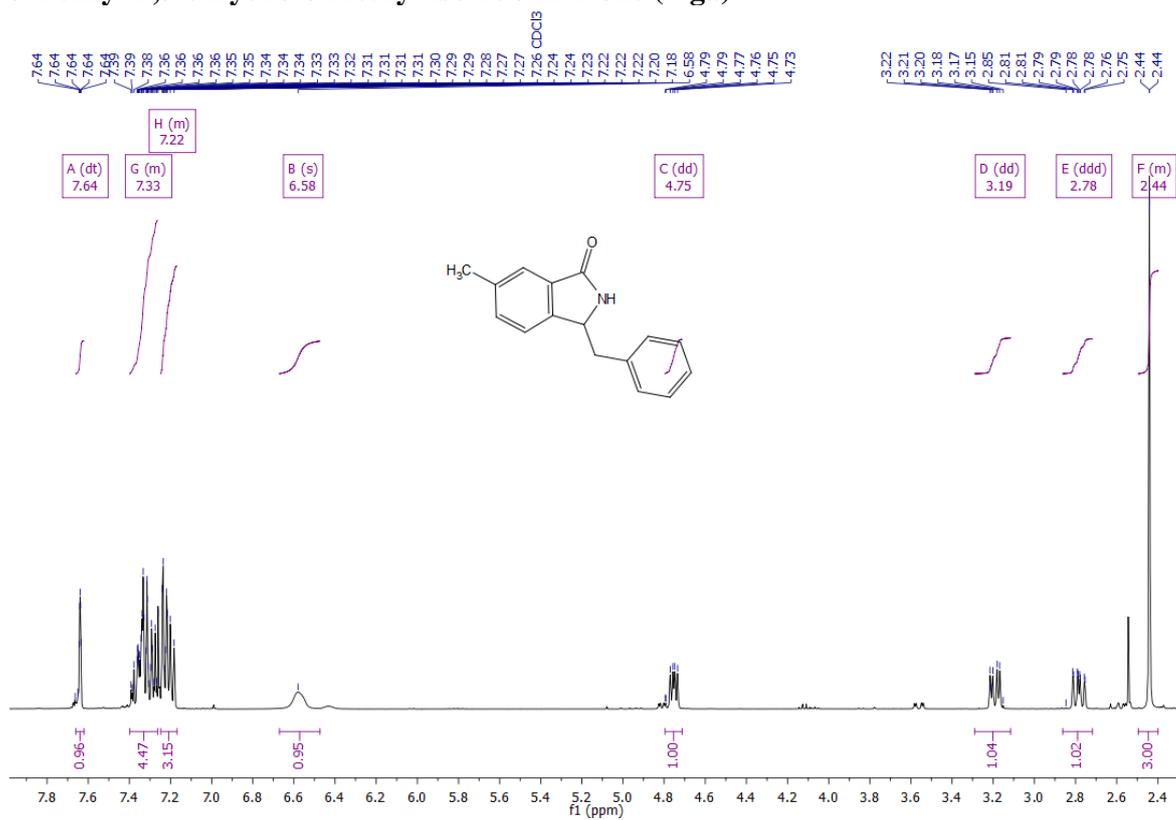
Supporting Information

3-Benzyl-3-hydro-2-methoxy-6-methyl-isoindolin-1-one (4ga)



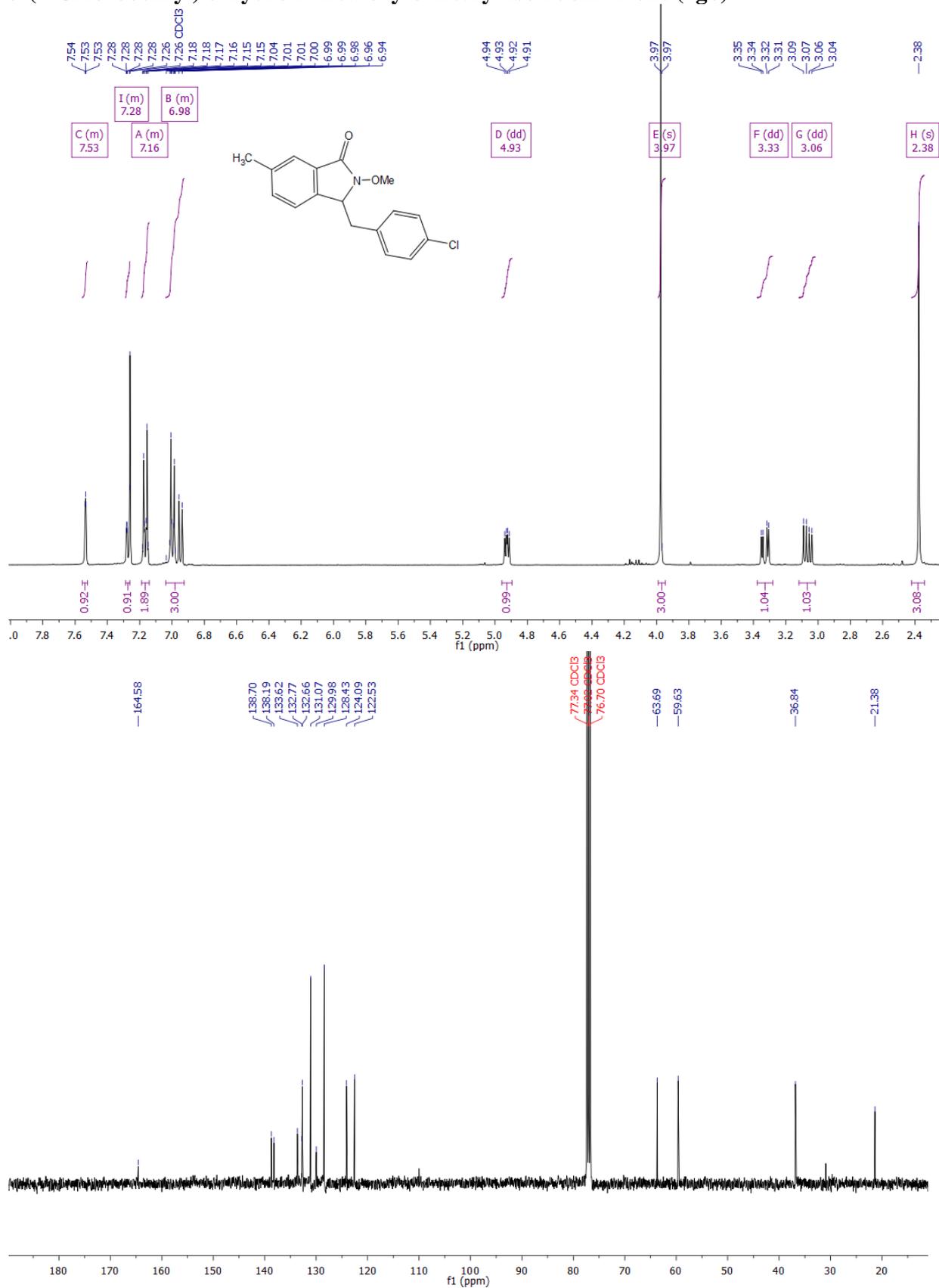
Supporting Information

3-Benzyl-2,3-dihydro-6-methyl-isoindolin-1-one (4'ga)



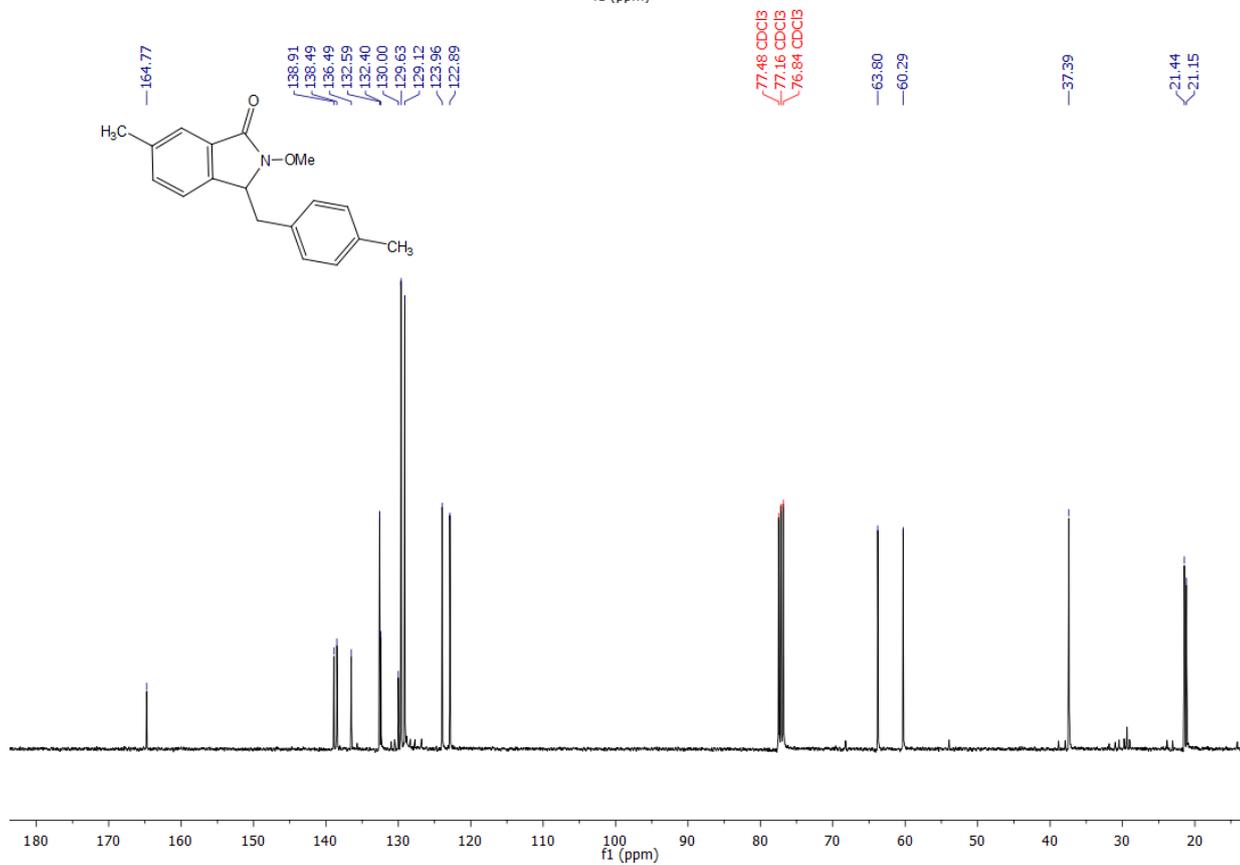
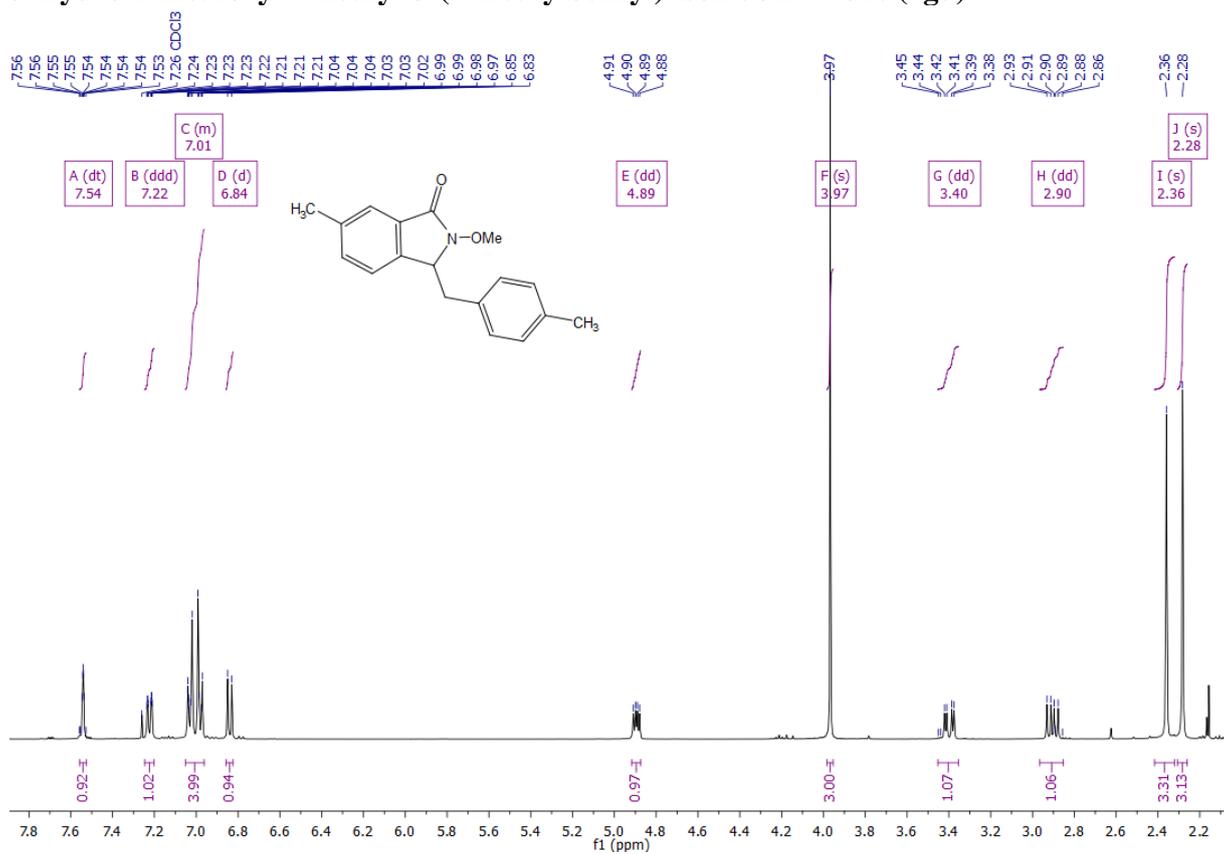
Supporting Information

3-(4-Chlorobenzyl)-3-hydro-2-methoxy-6-methyl-isindolin-1-one (4gb)



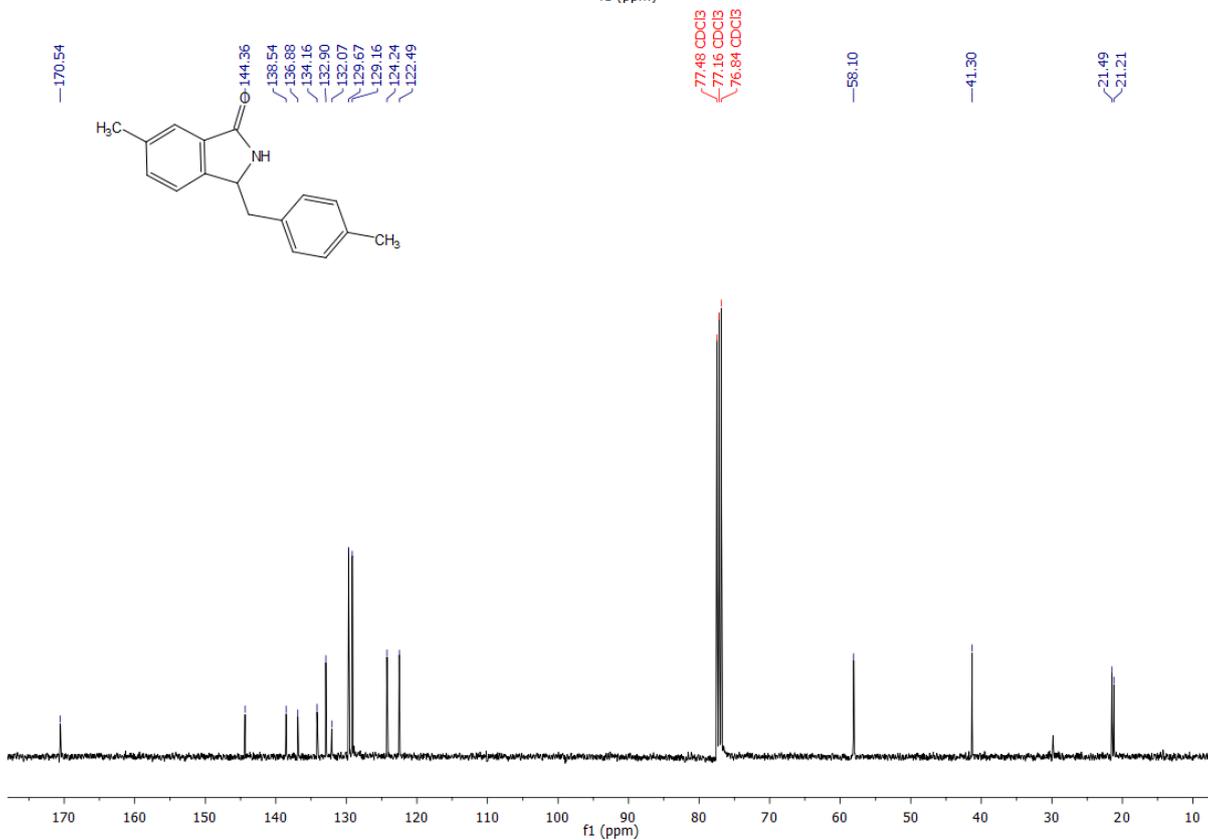
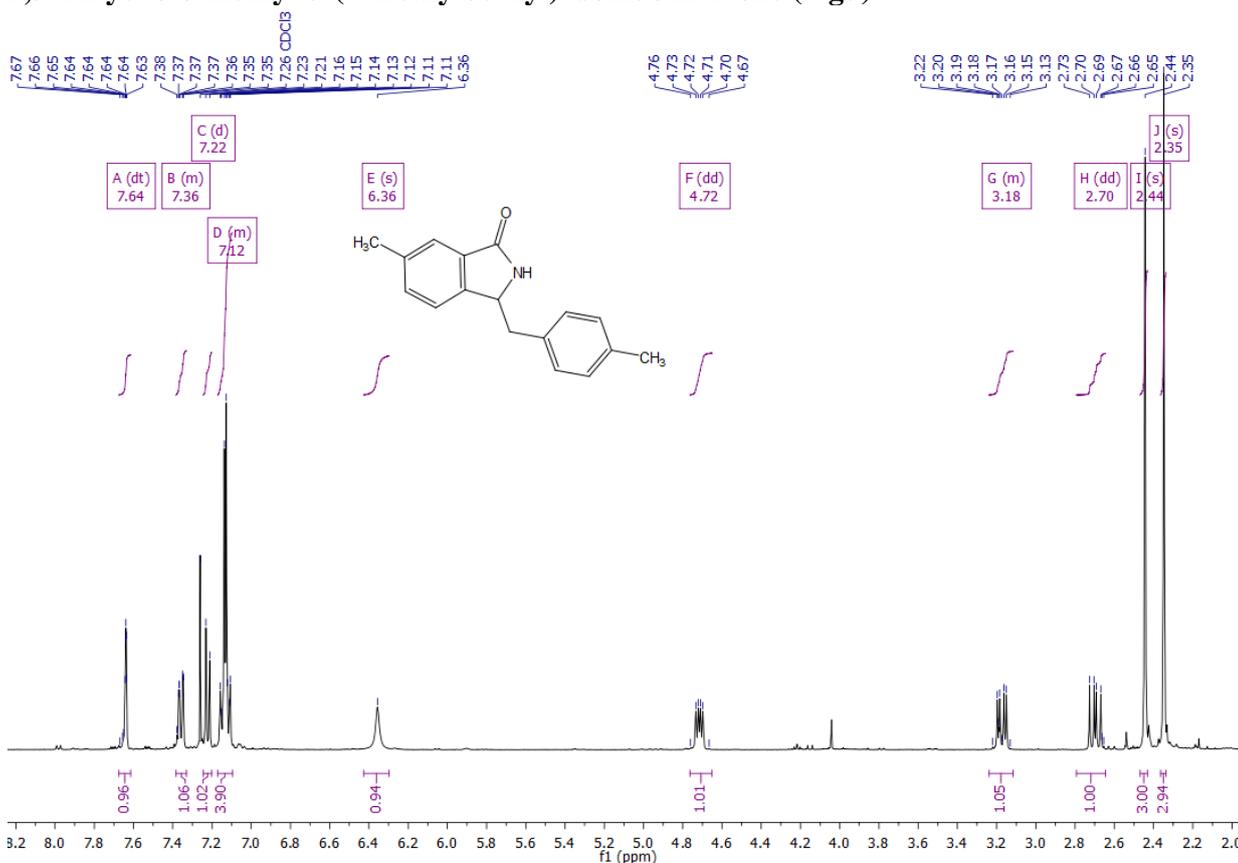
Supporting Information

3-Hydro-2-methoxy-5-methyl-3-(4-methylbenzyl)-isoindolin-1-one (4gd)

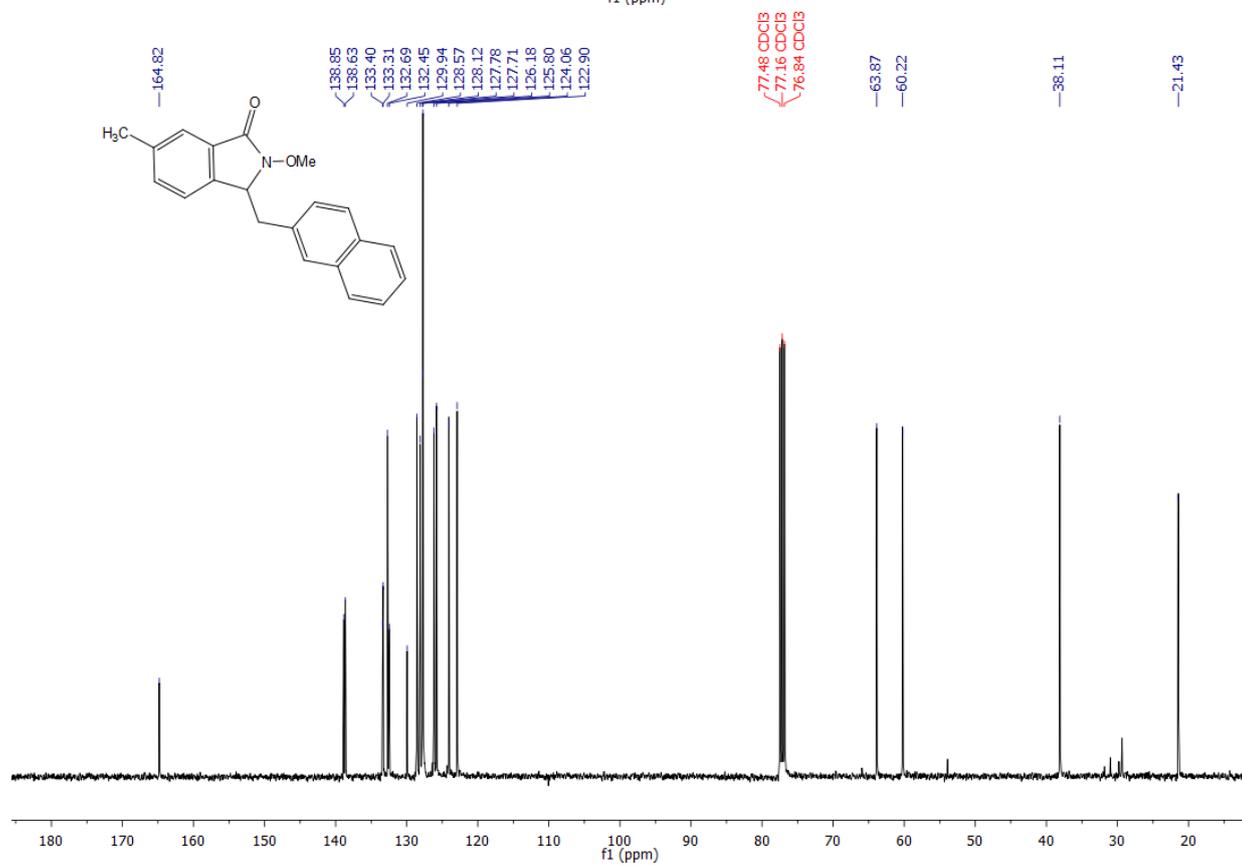


Supporting Information

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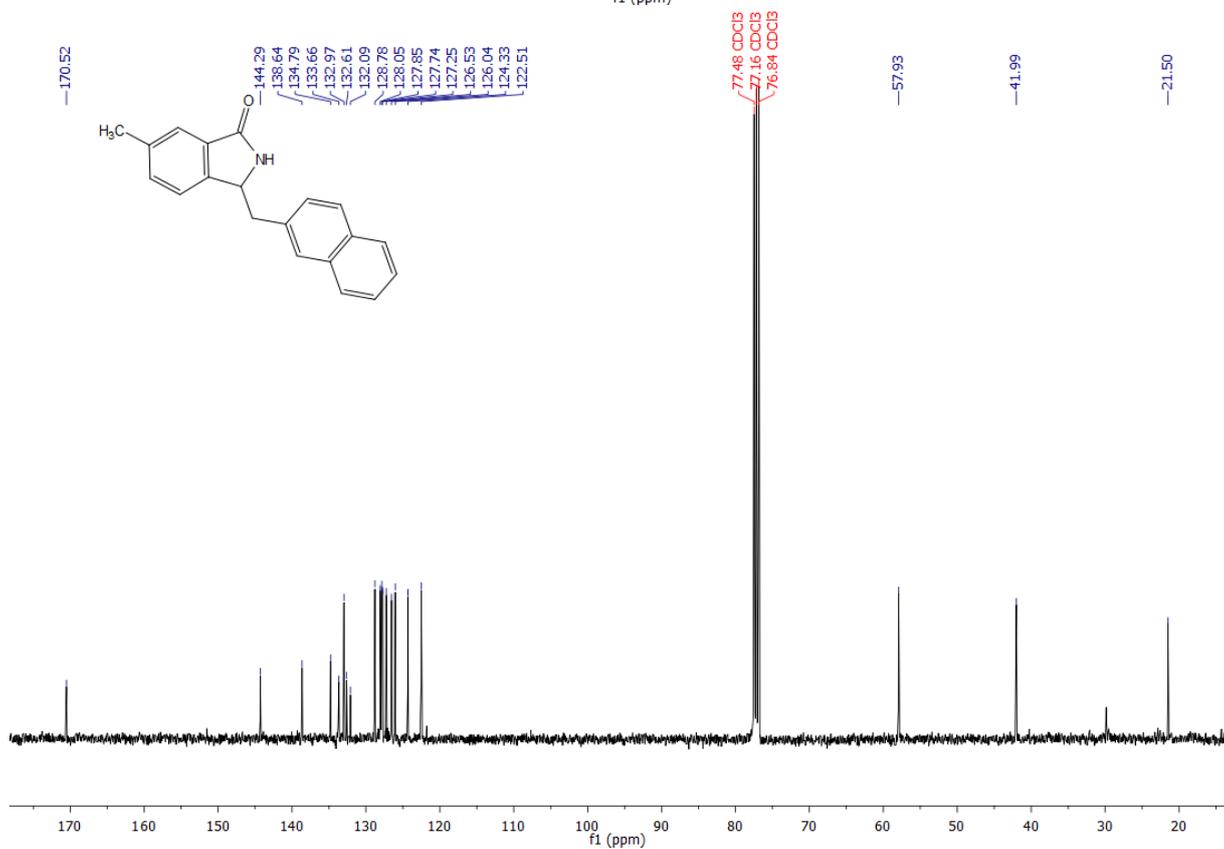
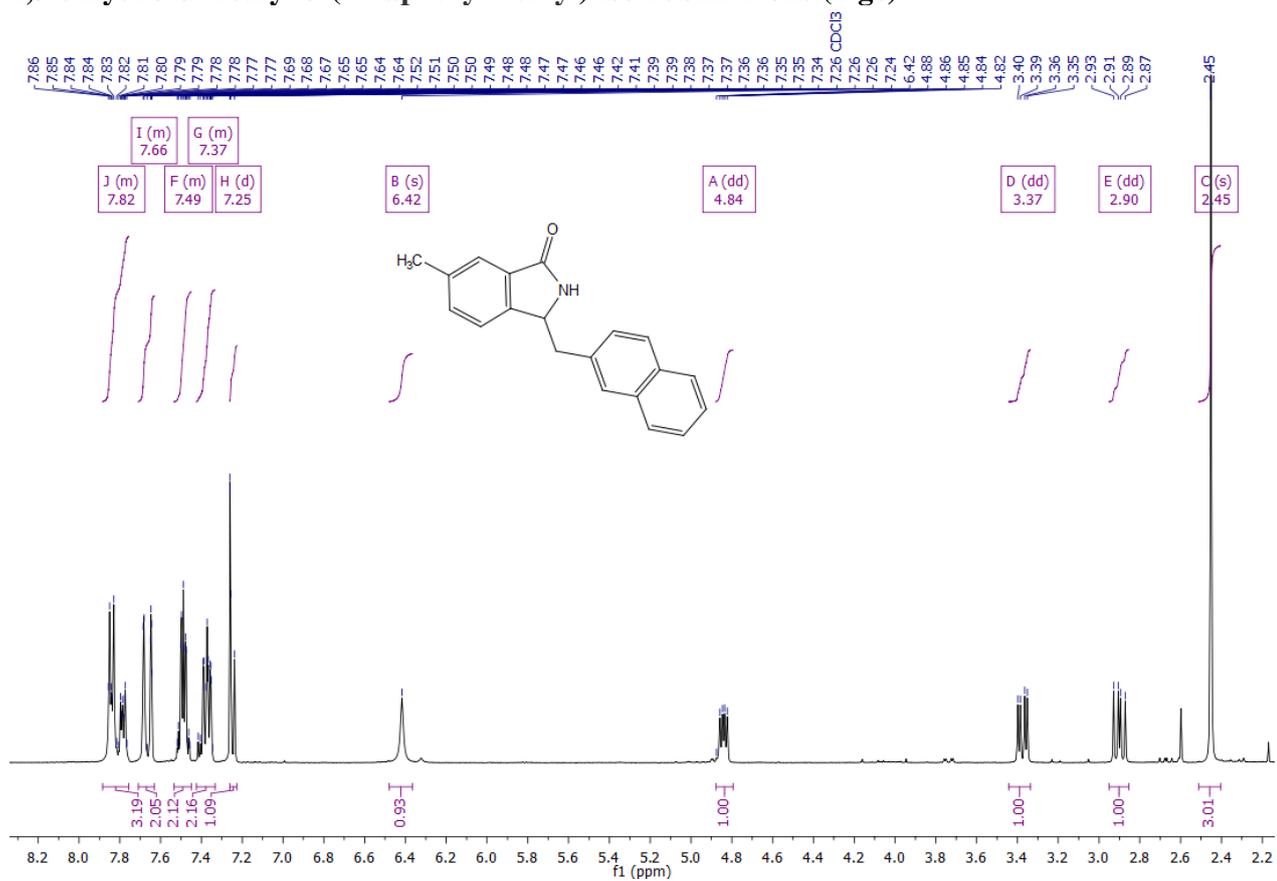


Supporting Information

3-Hydro-2-methoxy-6-methyl-3-(2-naphthylmethyl)-isoindolin-1-one (4ge)

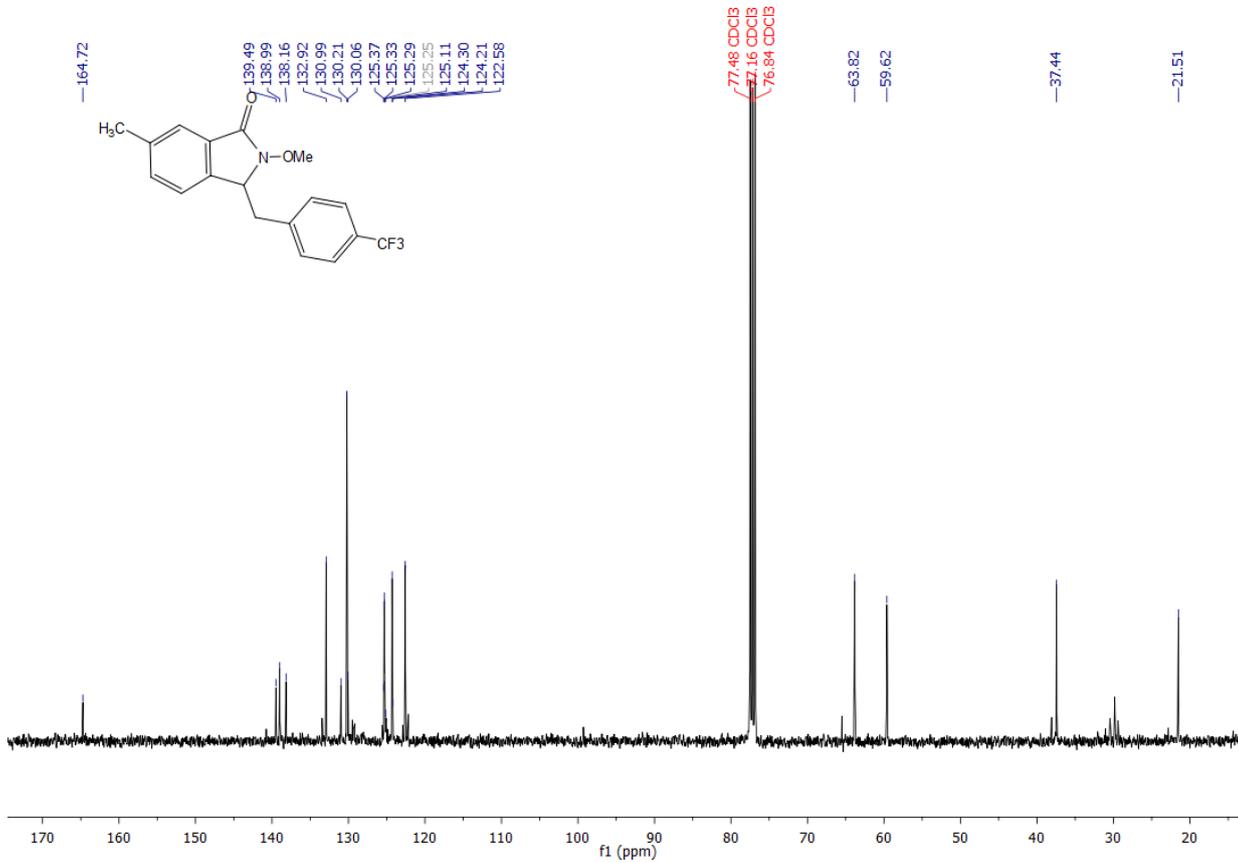
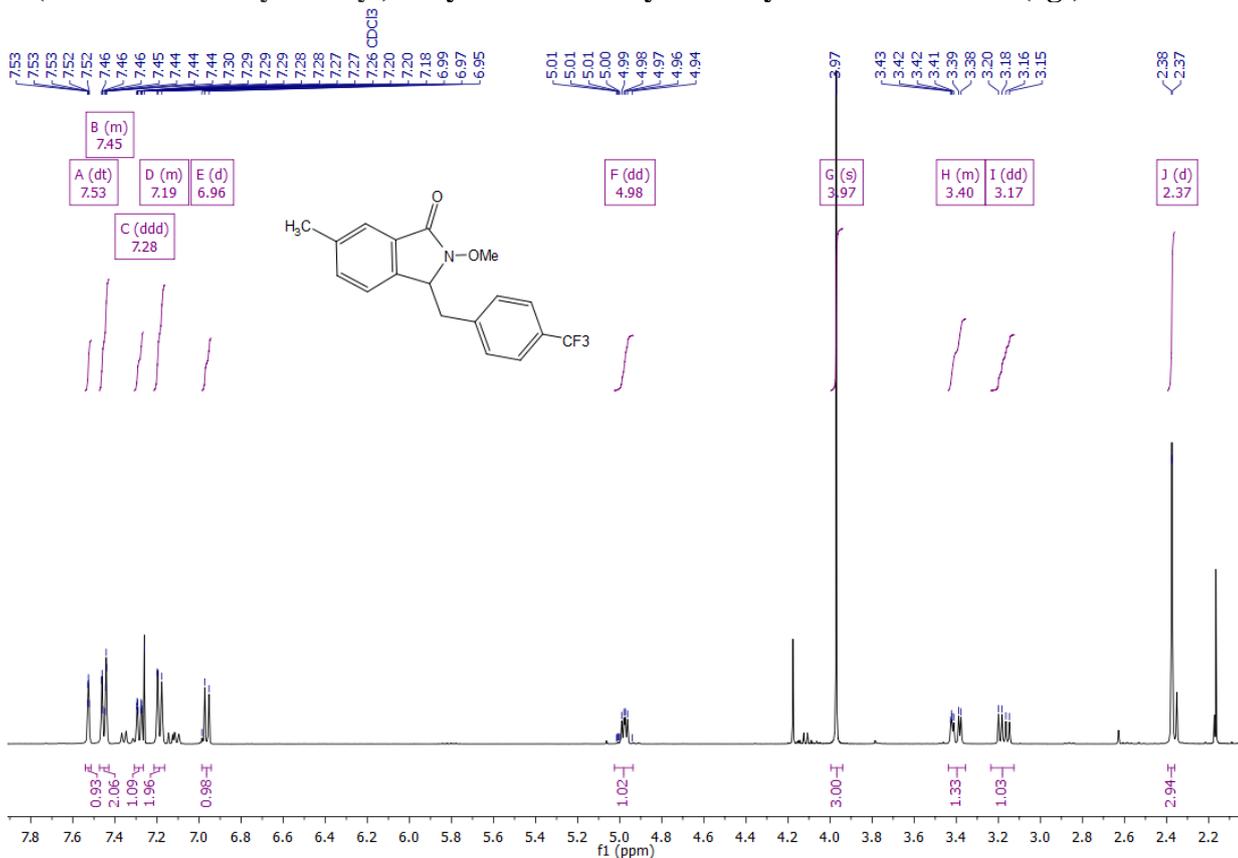
Supporting Information

2,3-dihydro-6-methyl-3-(2-naphthylmethyl)-isoindolin-1-one (4'ge)



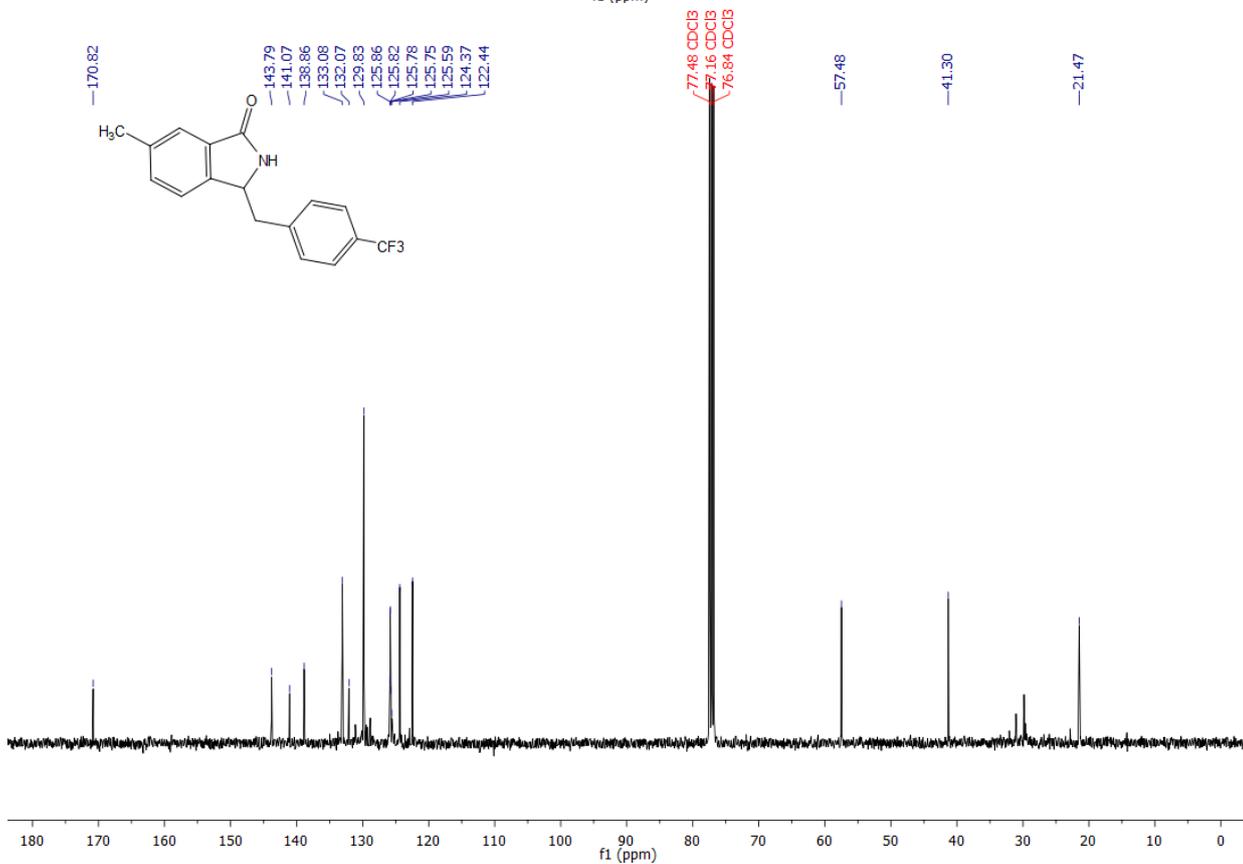
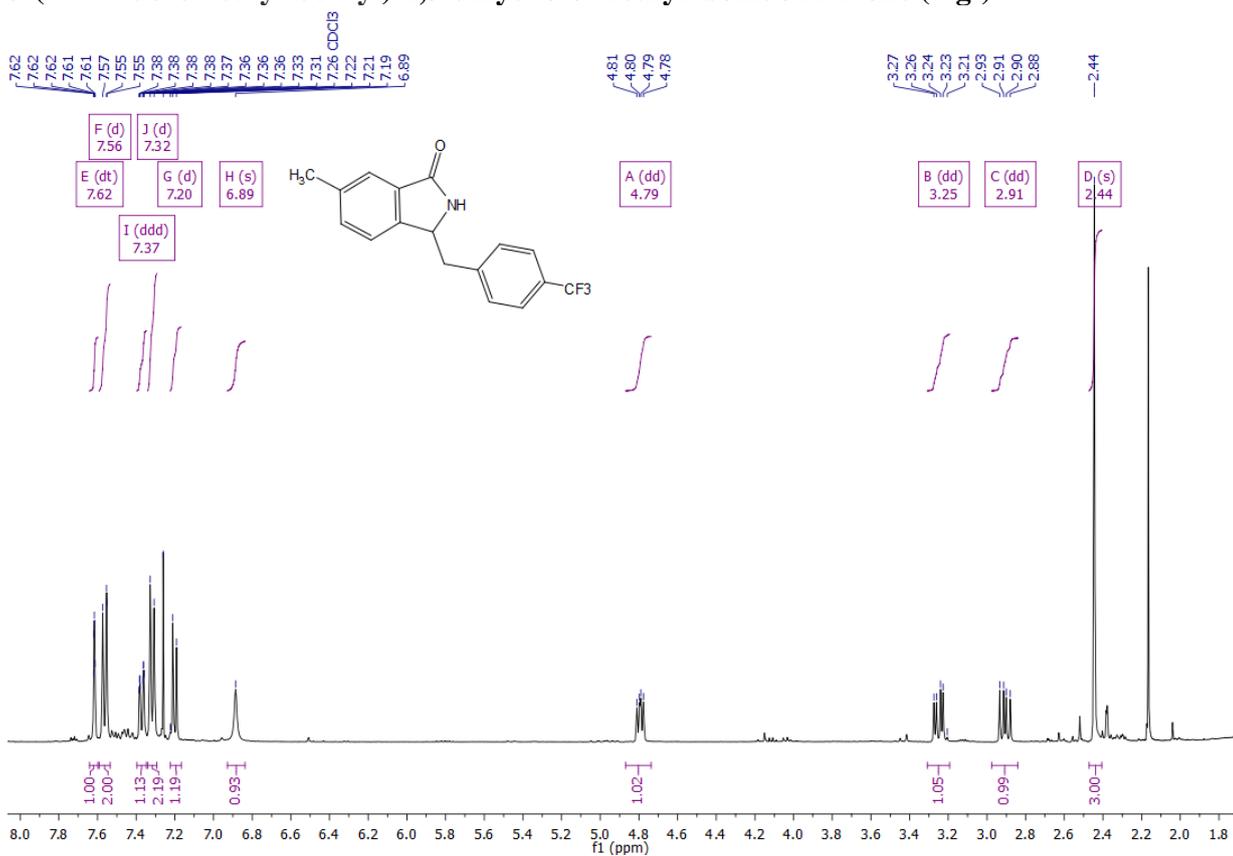
Supporting Information

3-(4-Trifluoromethyl-benzyl)-3-hydro-2-methoxy-6-methyl-isoindolin-1-one (4gf)



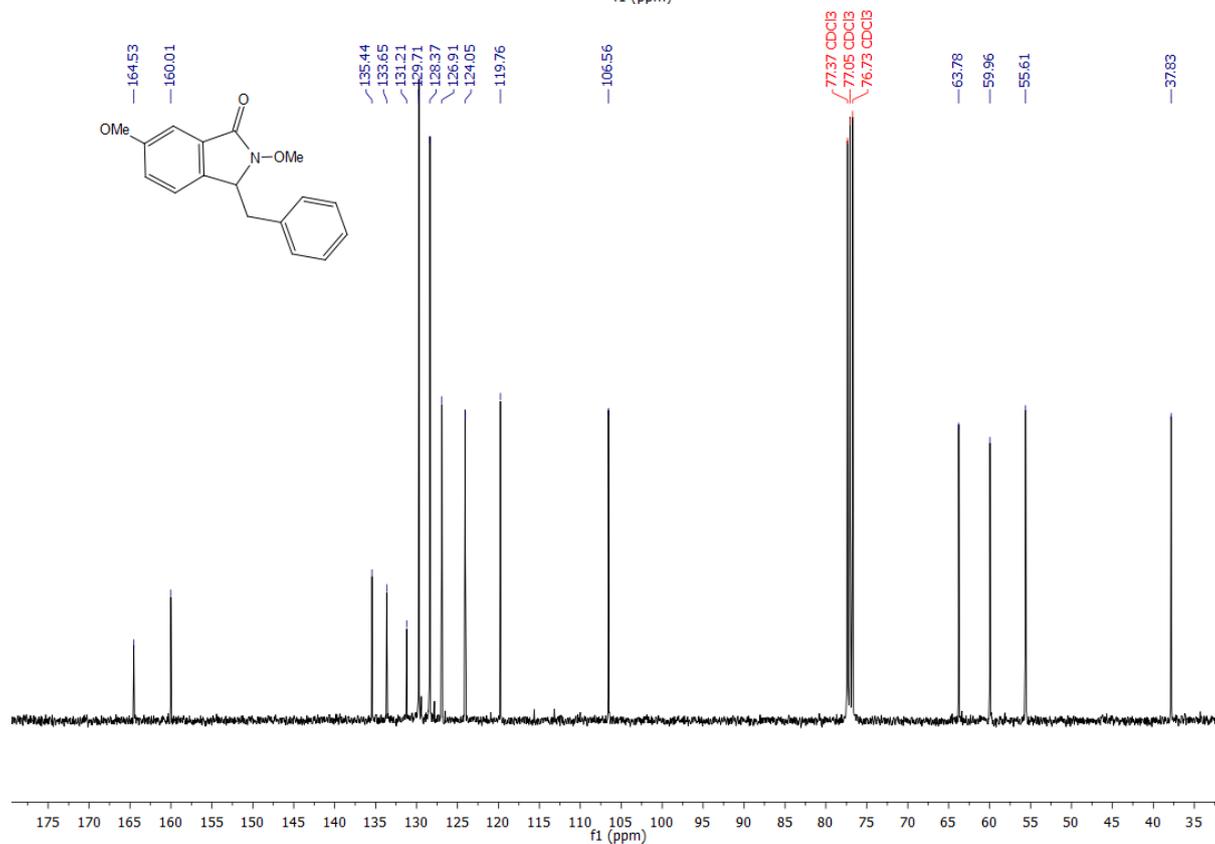
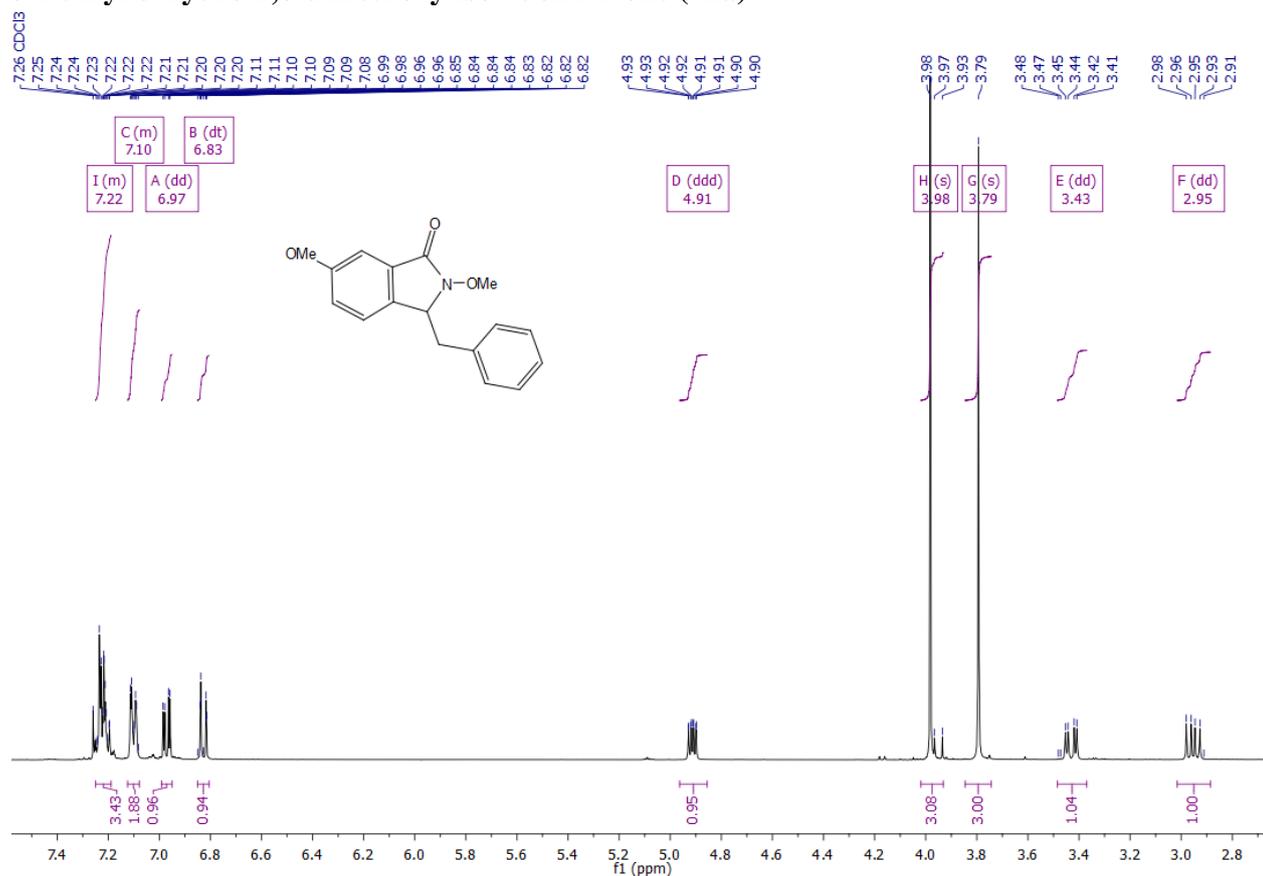
Supporting Information

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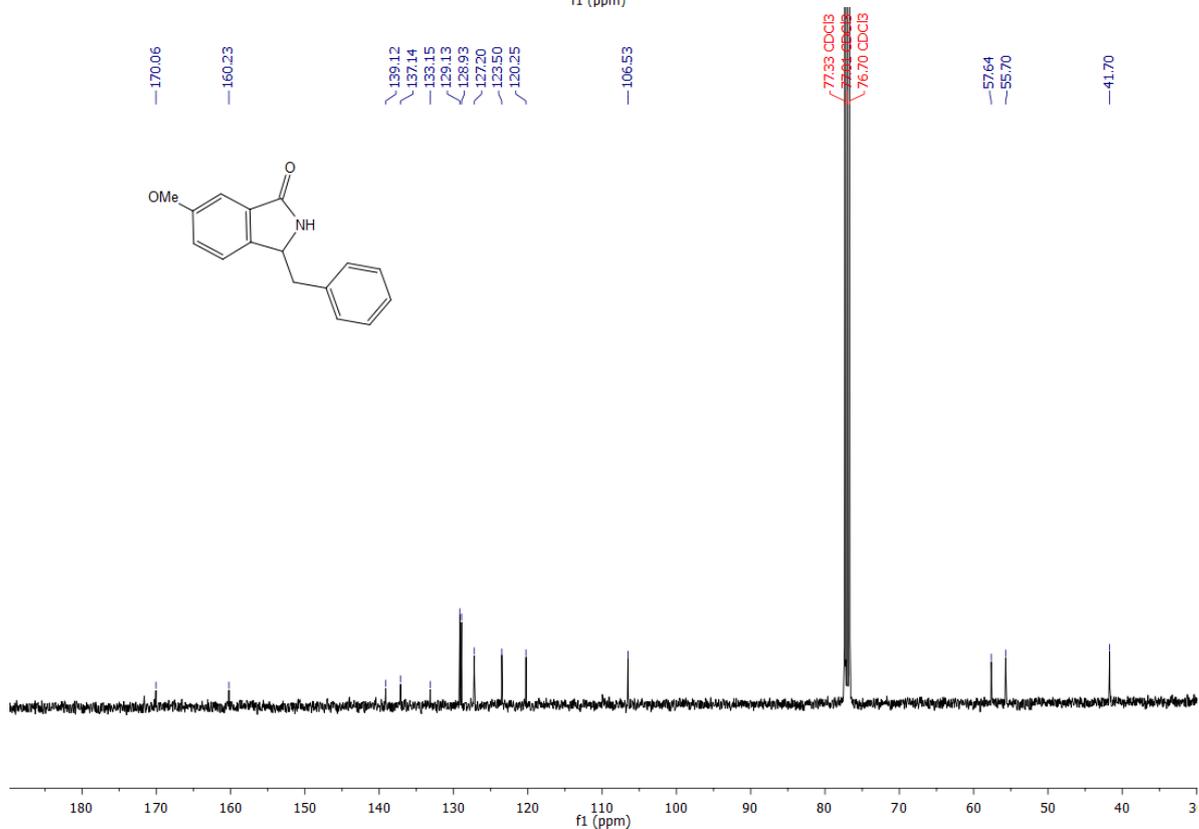
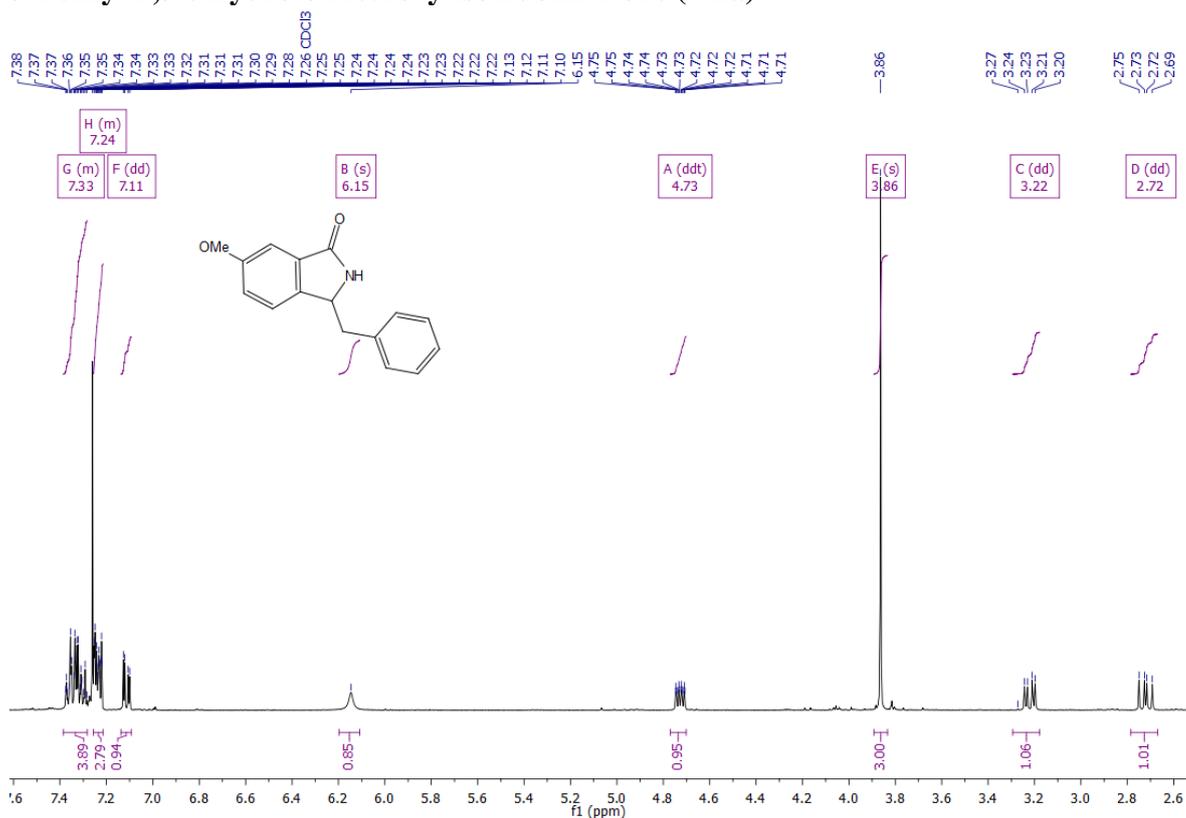
Supporting Information

3-Benzyl-3-hydro-2,6-dimethoxy-isoindolin-1-one (4ha)



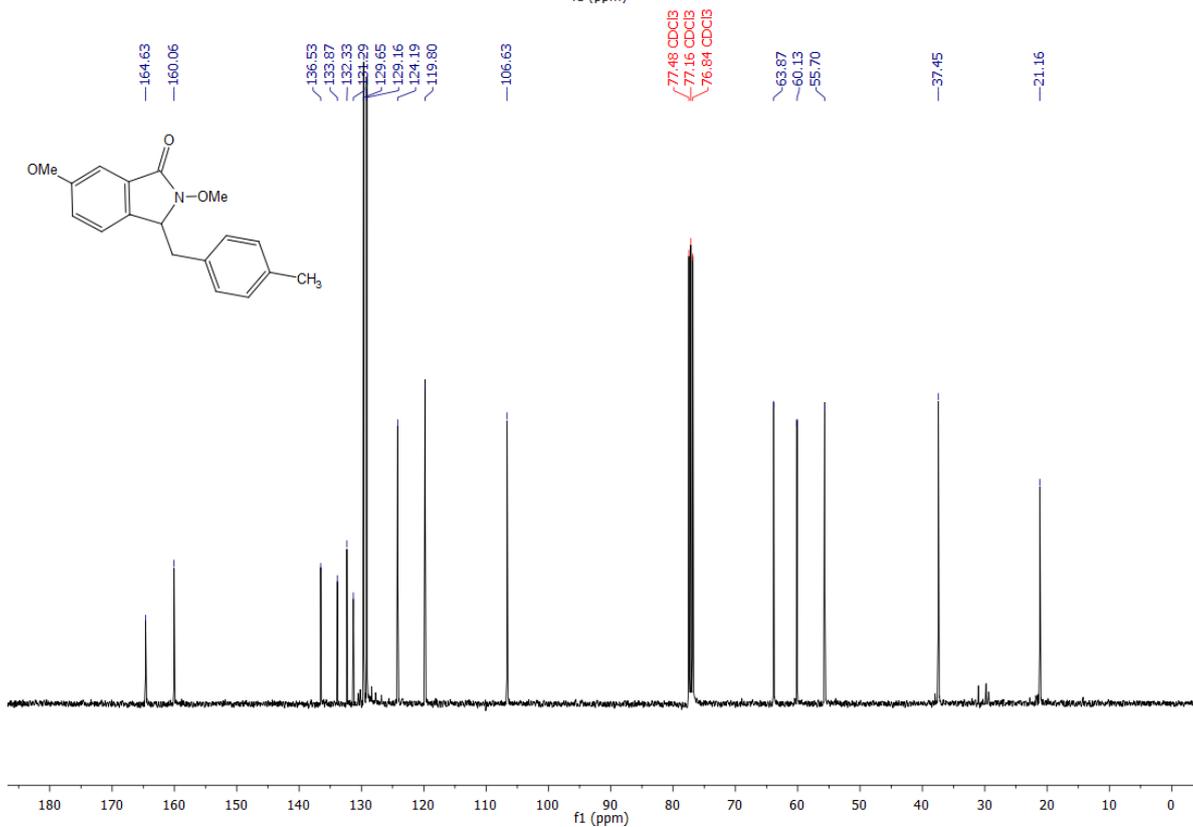
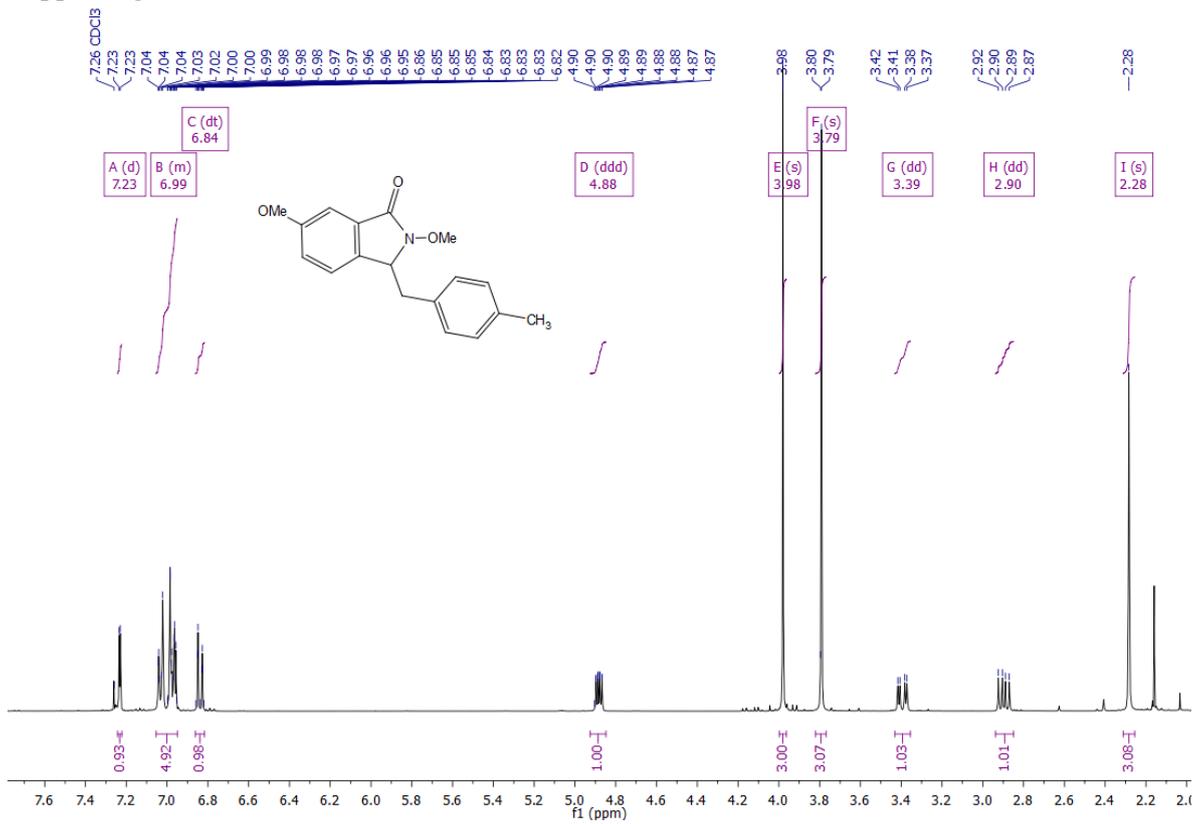
Supporting Information

3-Benzyl-2,3-dihydro-6-methoxy-isoindolin-1-one (4'ha)



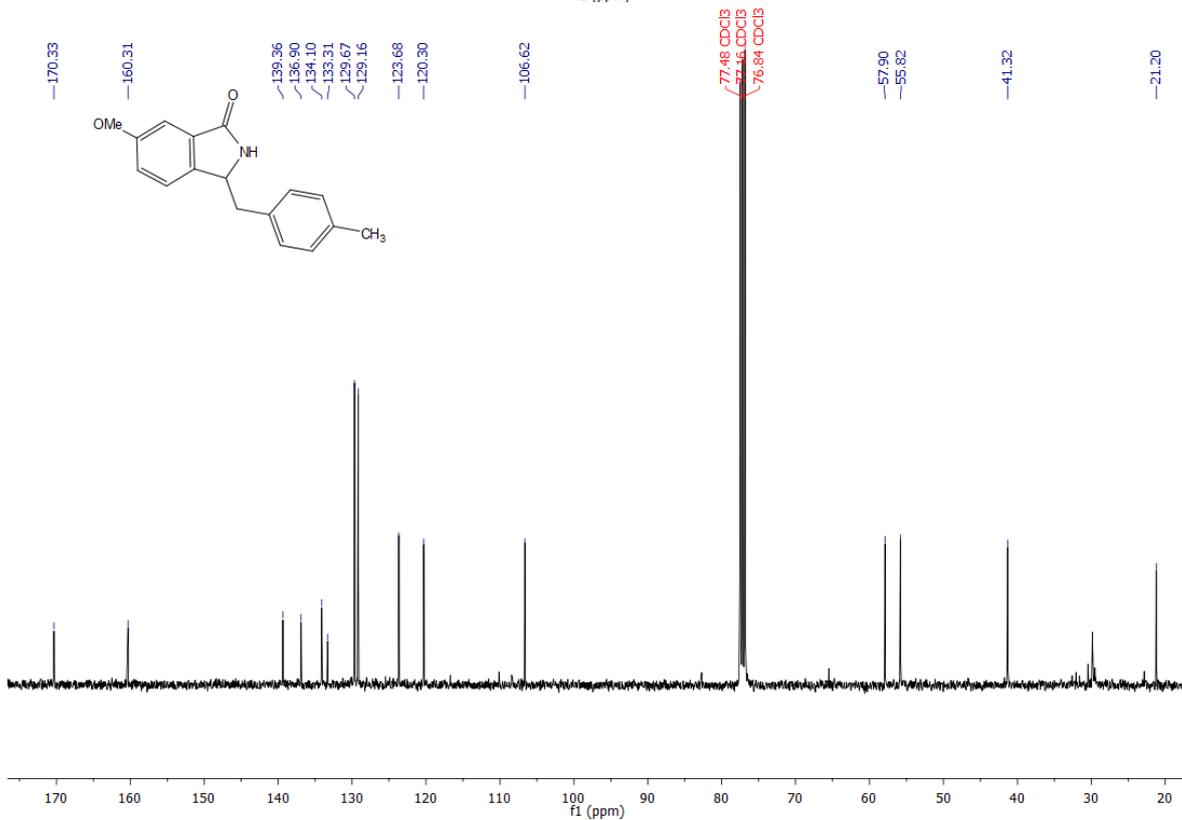
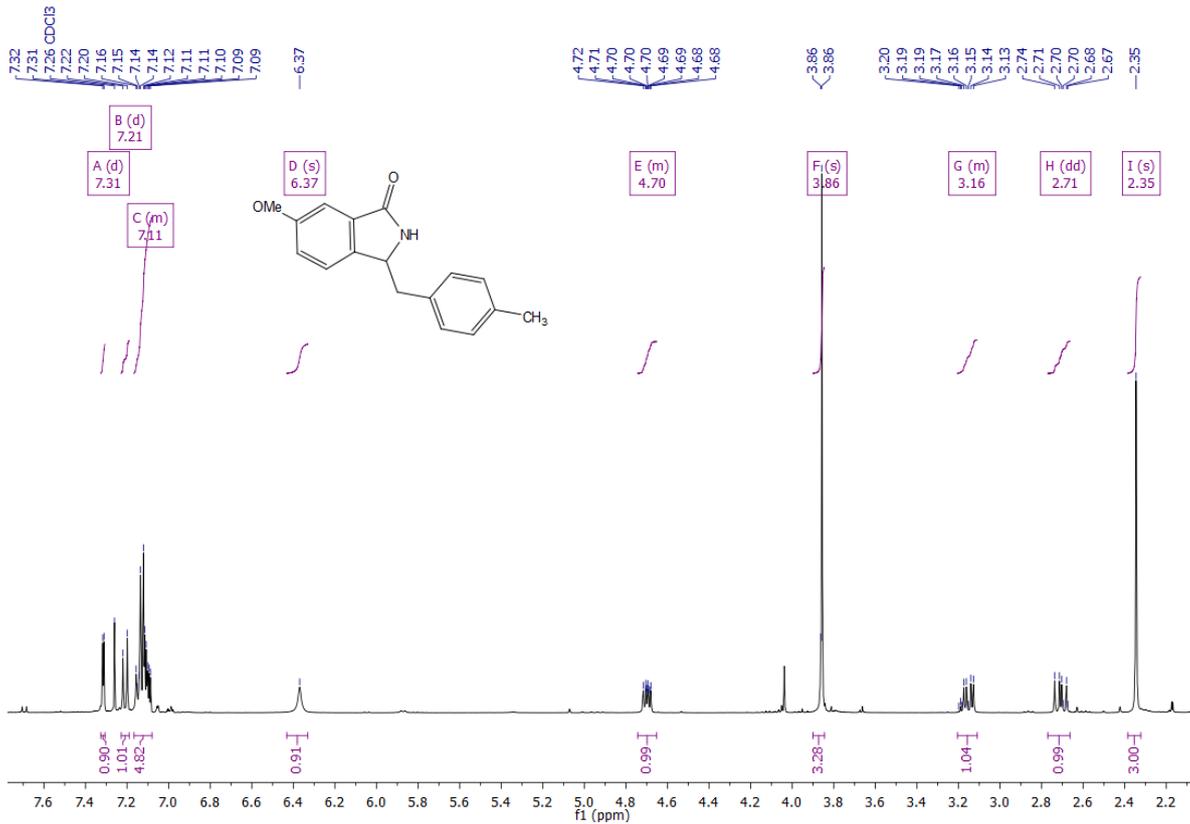
3-Hydroxy-2,5-dimethoxy-3-(4-methylbenzyl)-isoindolin-1-one (4hd)

Supporting Information



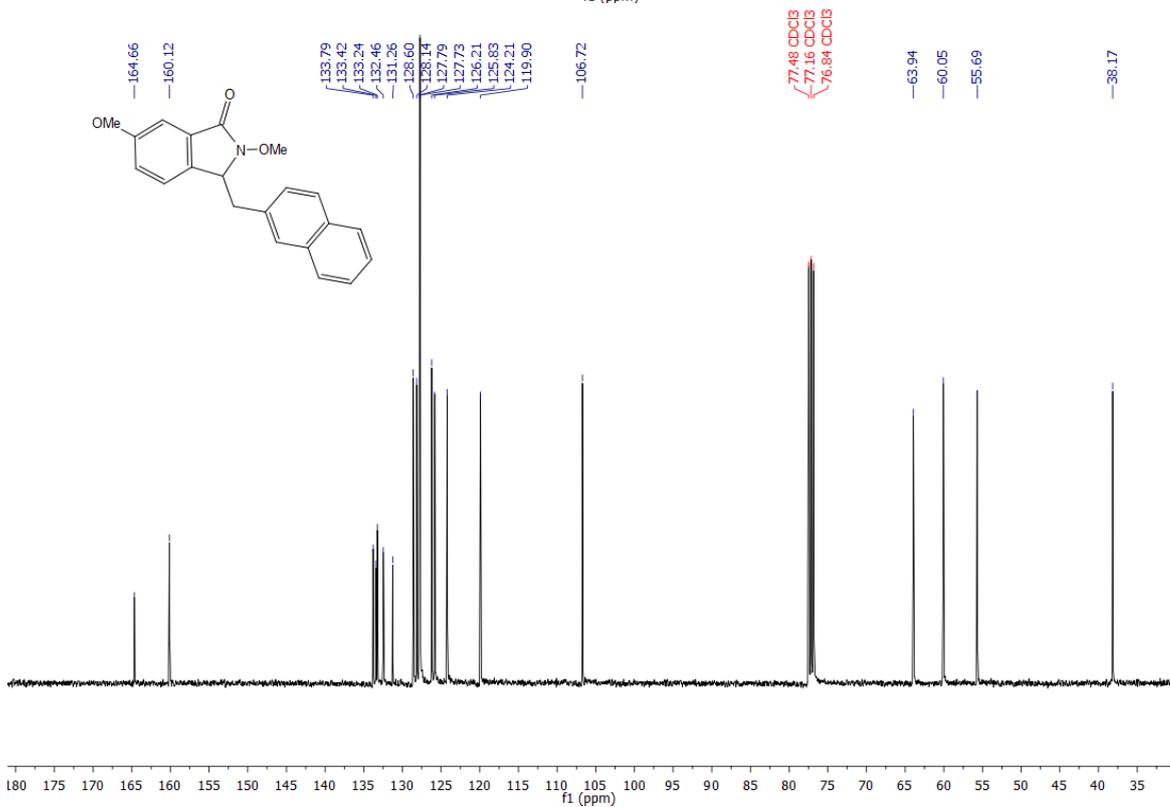
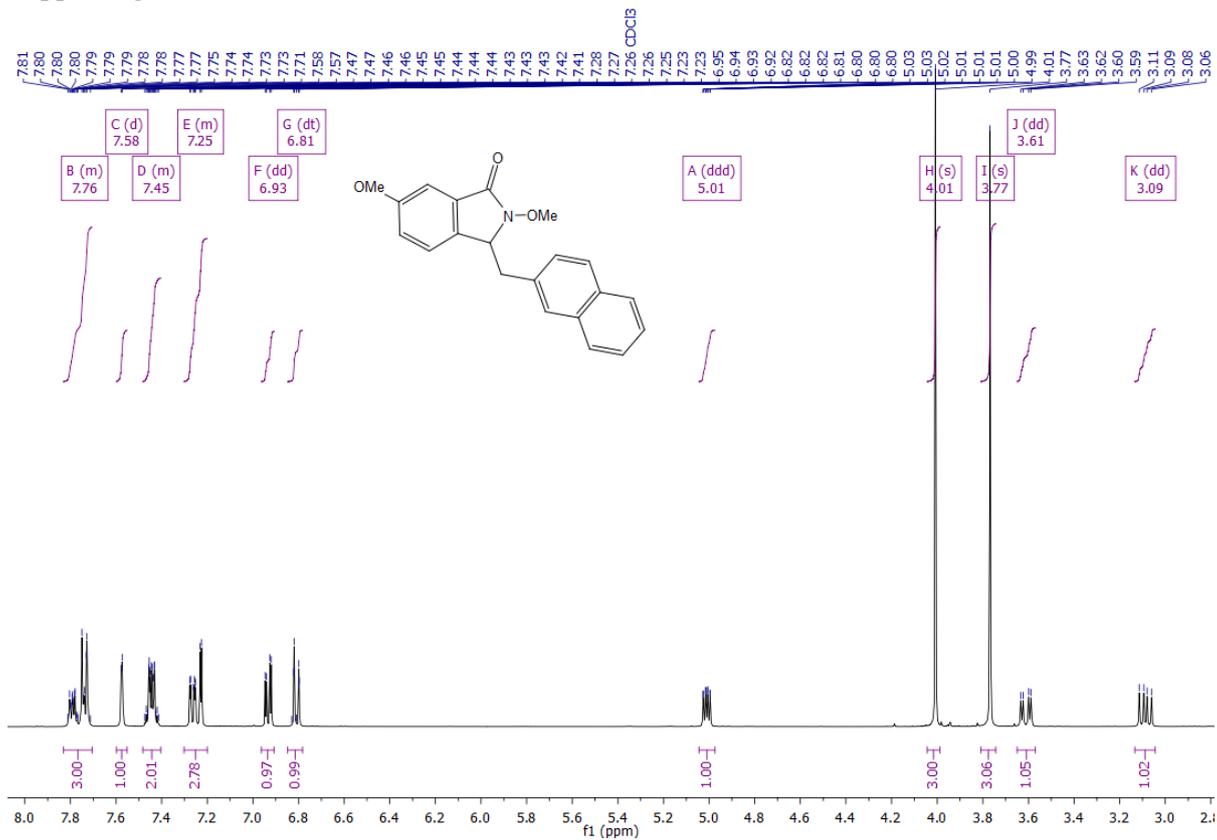
2,3-Dihydro-6-methoxy-3-(4-Methylbenzyl)-isoindolin-1-one (4'hd)

Supporting Information



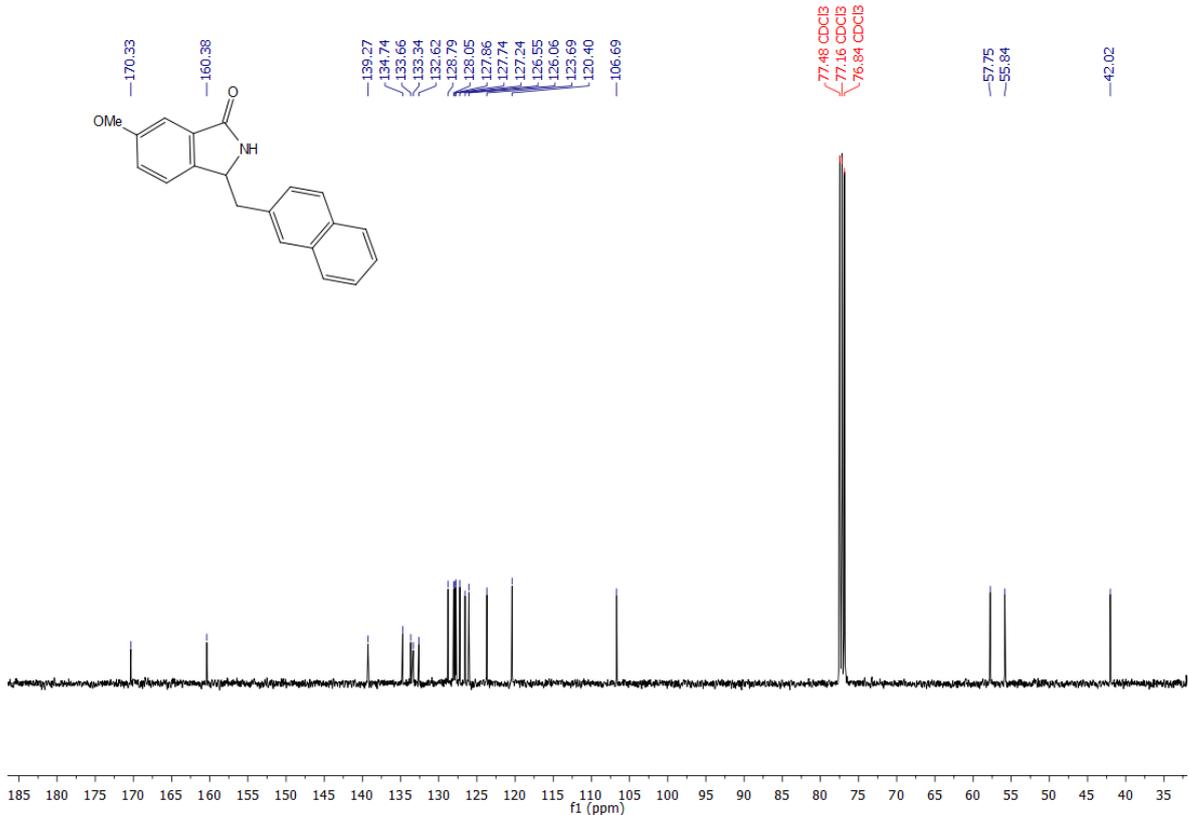
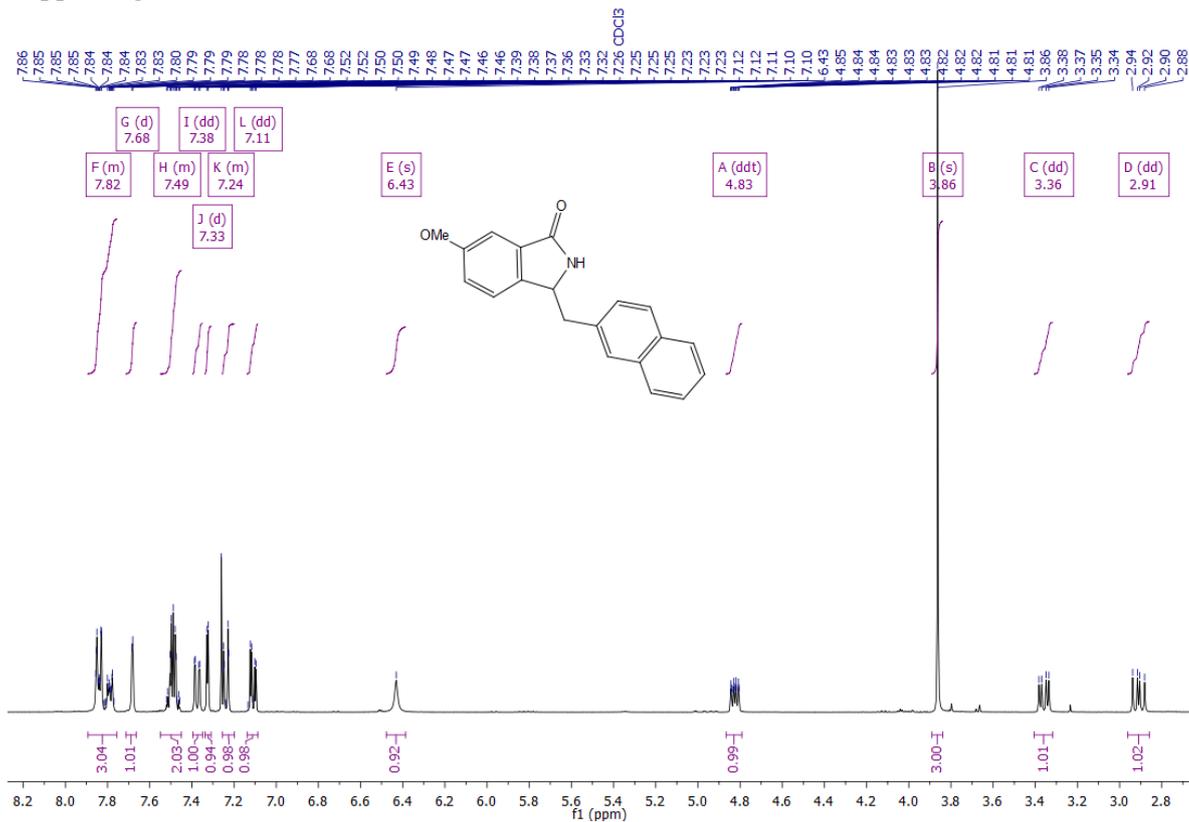
3-Hydro-2,6-dimethoxy-3-(2-naphthylmethyl)-isoindolin-1-one (4he)

Supporting Information



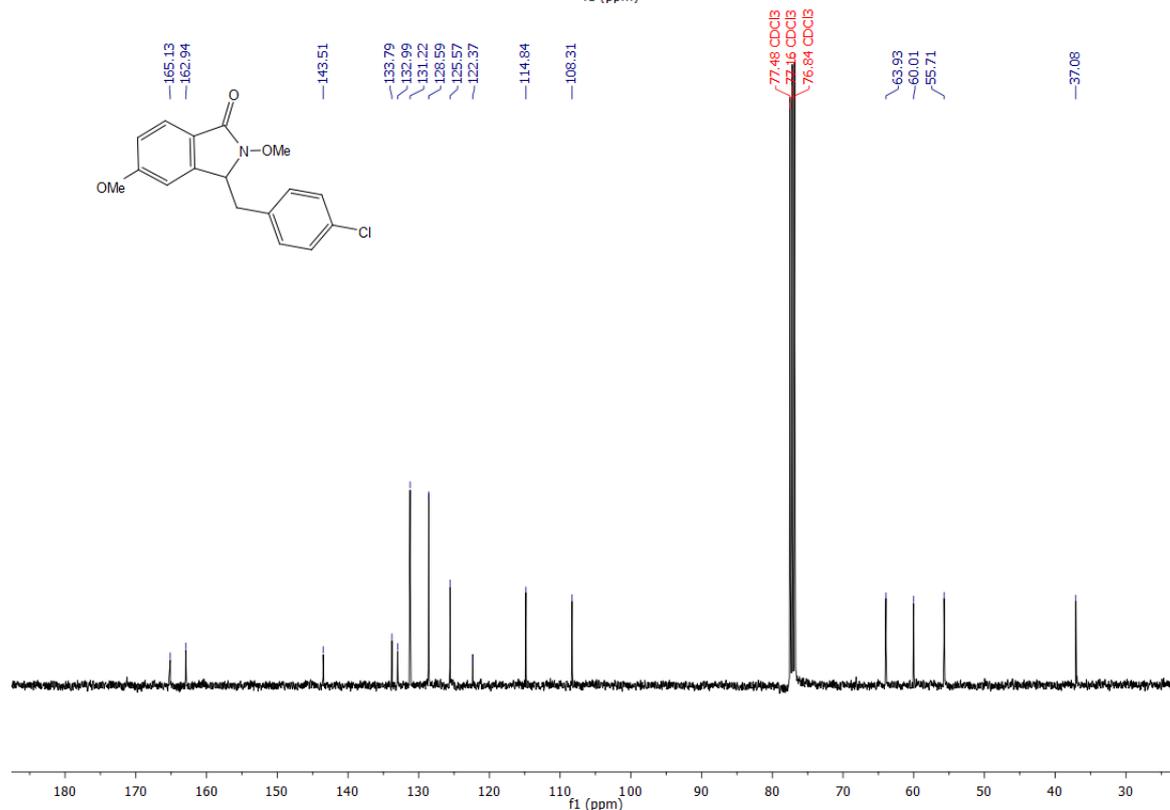
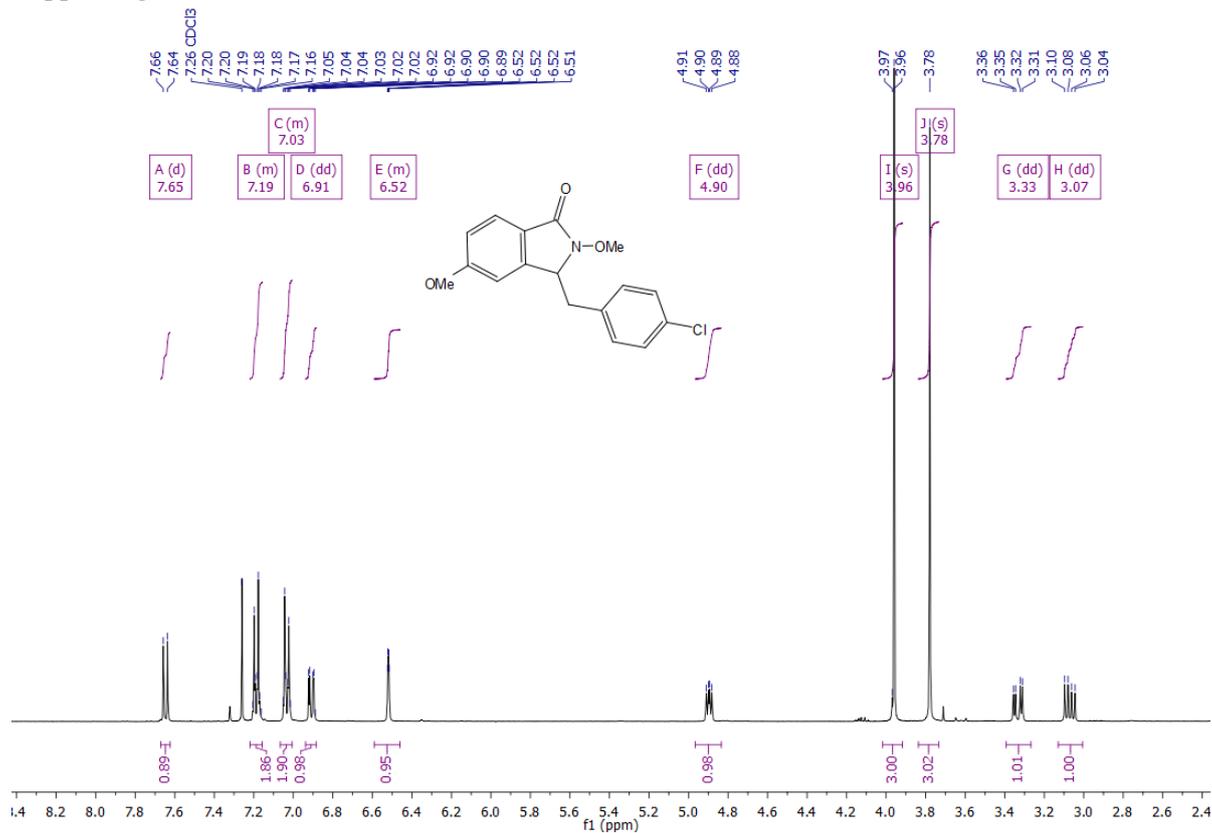
2,3-Dihydro-6-methoxy-3-(2-naphthylmethyl)-isoindolin-1-one (4'he)

Supporting Information



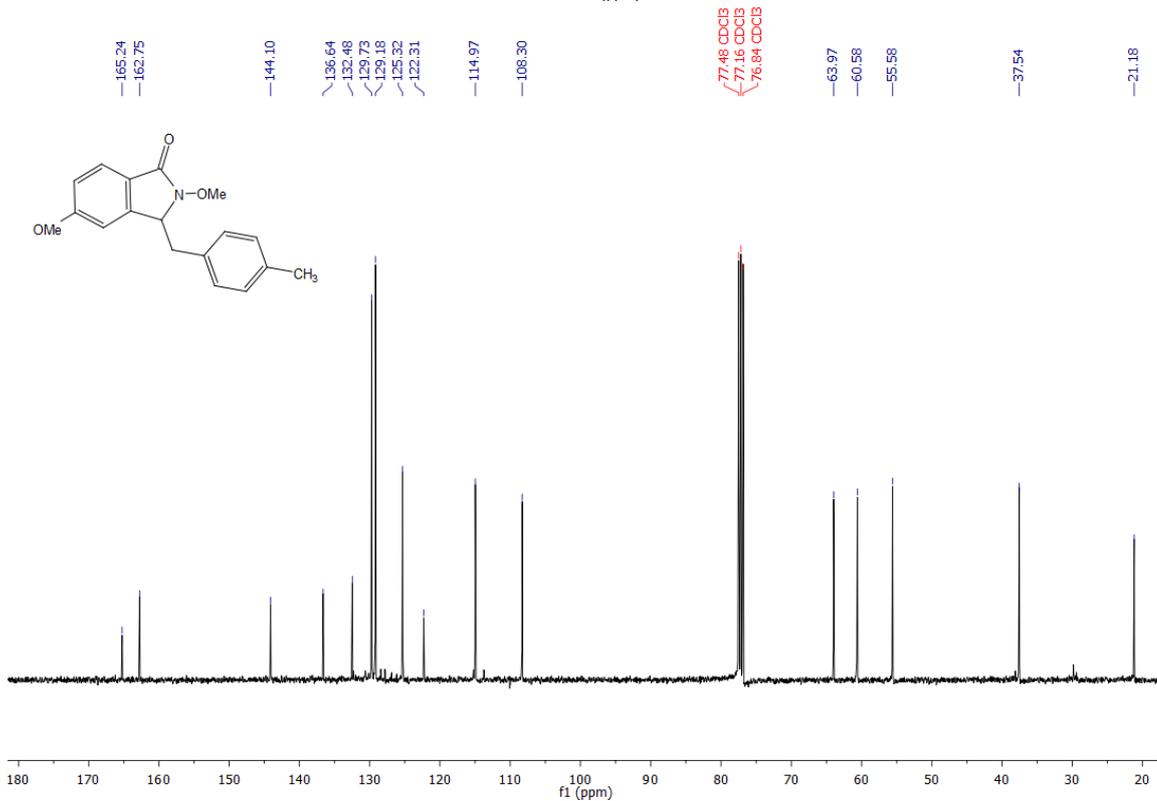
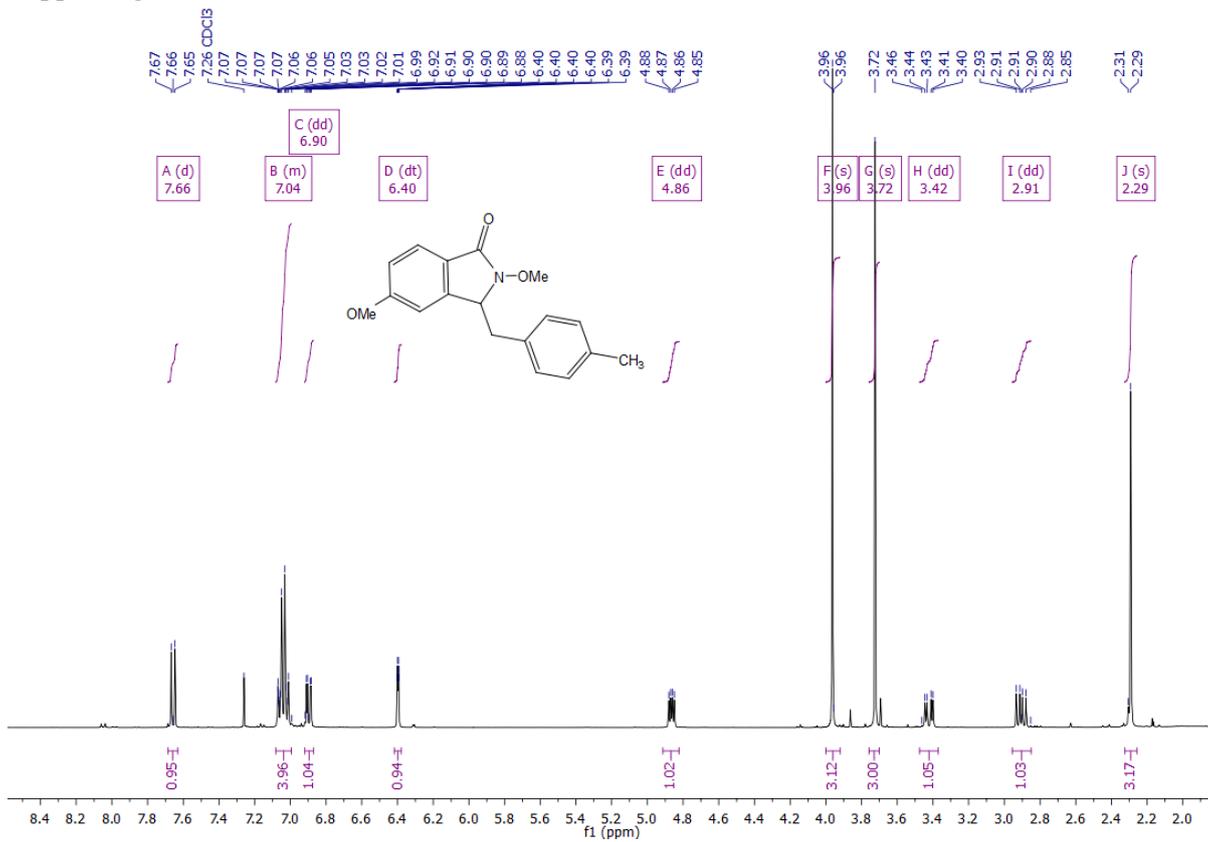
3-(4-Chlorobenzyl)-3-hydro-2,5-dimethoxyisoindolin-1-one (4ib)

Supporting Information



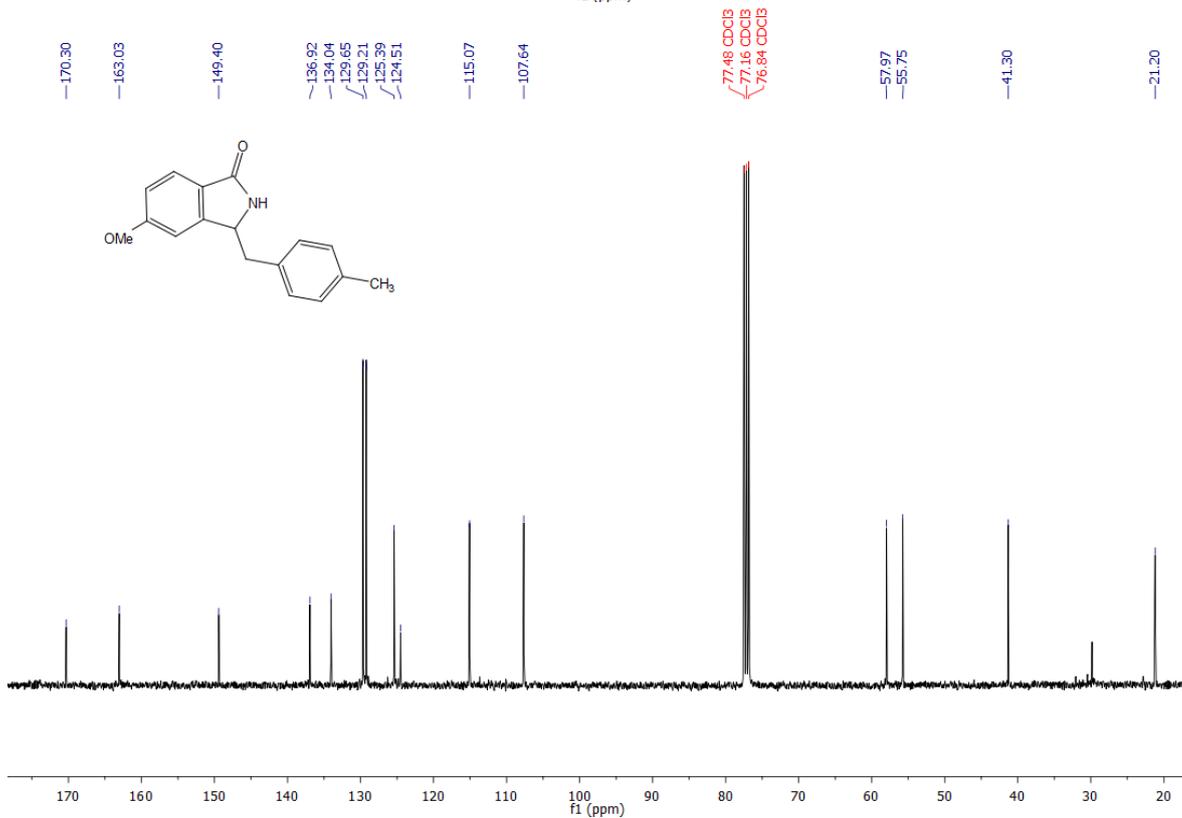
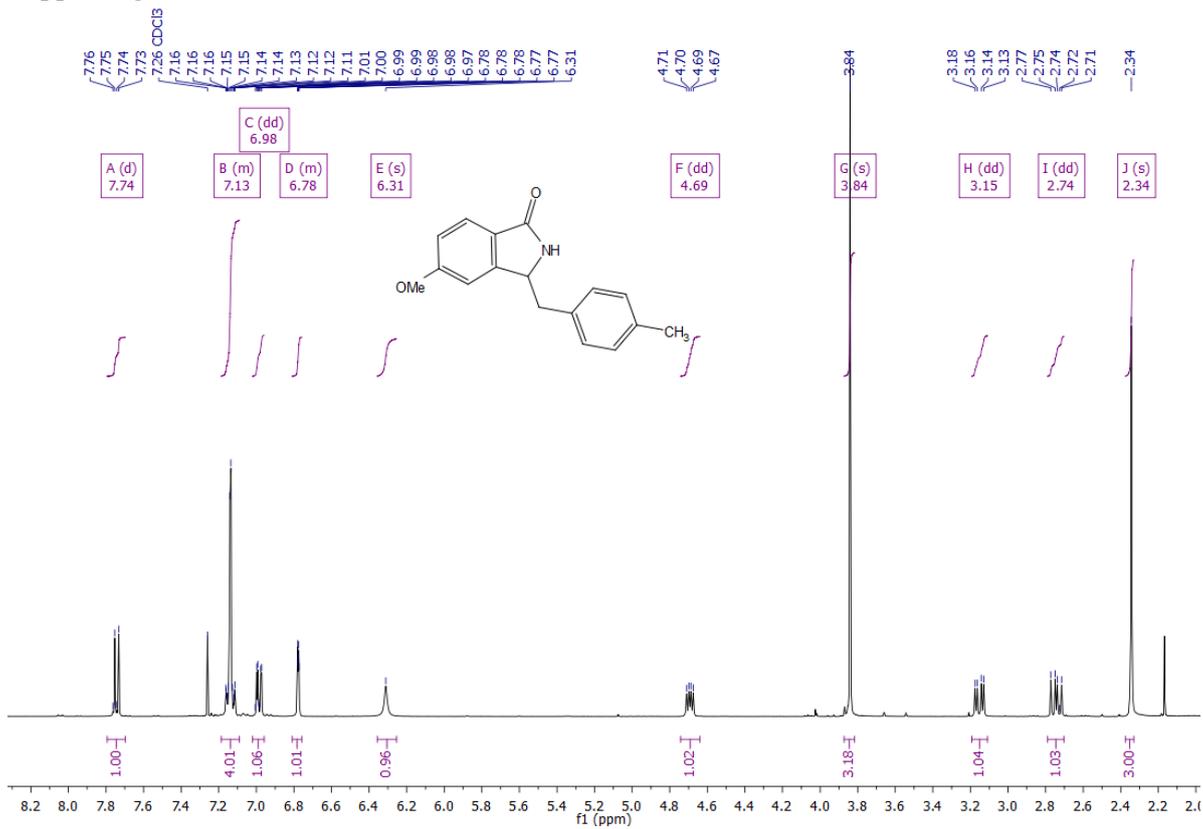
3-Hydro-2,5-dimethoxy-3-(4-methylbenzyl)-isoindolin-1-one (4id)

Supporting Information



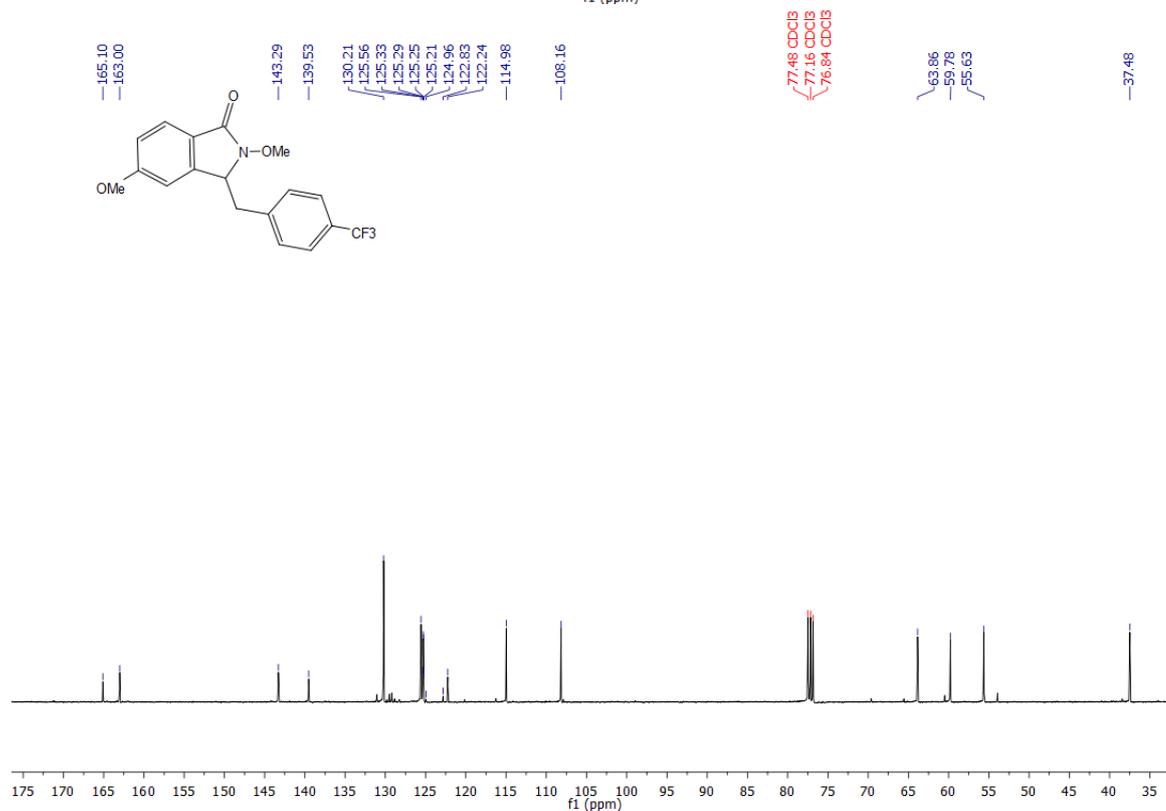
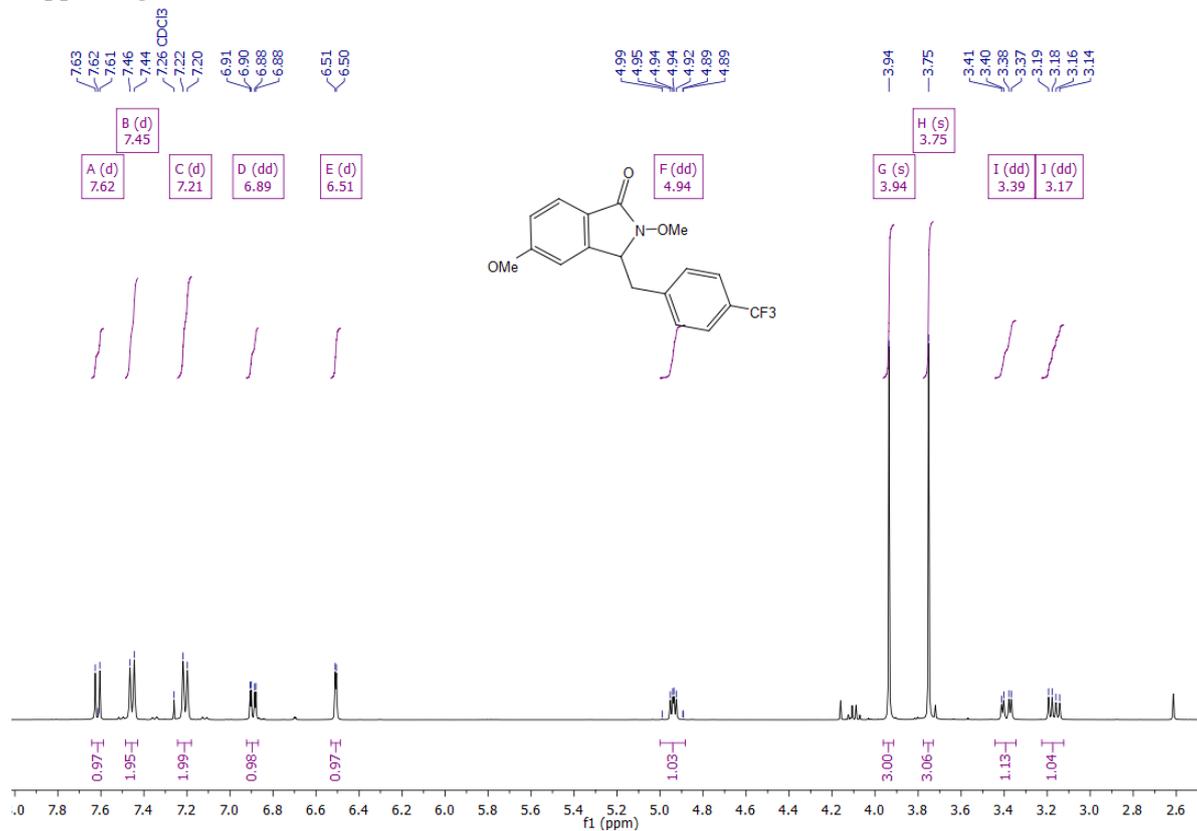
2,3-Dihydro-5-methoxy-3-(4-methylbenzyl)-isoindolin-1-one (4'id)

Supporting Information



3-(4-Trifluoromethyl-benzyl)-3-hydro-2,5-dimethoxy-isoindolin-1-one (4if)

Supporting Information



3-(4-Trifluoromethyl-benzyl)-2,3-dihydro-5-methoxy-isoindolin-1-one (4'if)

Supporting Information

