

Title	Access to some C5-cyclised 2 pyrones and 2-pyridones via direct arylation; retention of chloride as a synthetic handle
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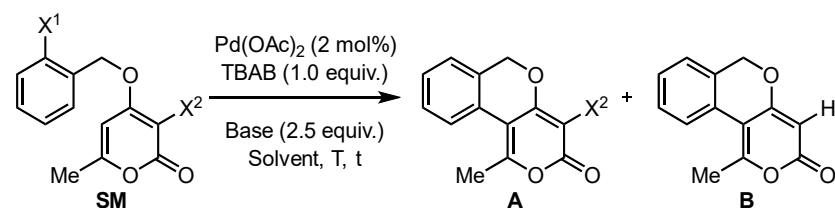
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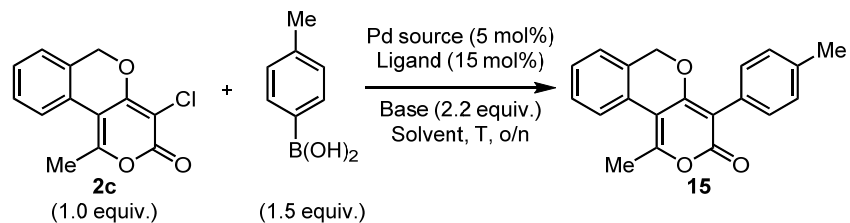
Table S1. Optimisation of the Direct Arylation Reaction



X ¹	X ²	TBAB	Base	Solvent	T (°C)	Time (h)	Product ^{a)}
I	I	1.0	KOAc	DMF	100	4.5	degradation
I	Br	1.0	KOAc	DMF	100	6	B (90%)
I	Br	1.0	KOAc	Toluene	127	4	B
I	Br	1.0	KOAc	THF	76	6	B
Br	Br	1.0	KOAc	DMF	100	4.5	B (78%)
Br	I	1.0	KOAc	DMF	100	4	A (11%) B (5%)
Br	Cl	1.0	KOAc	THF	76	8	SM:A^{b)} 61:39
I	Cl	1.0	Na ₂ CO ₃	THF	76	8	mixture
I	Cl	0.5	KOAc	THF	76	8	SM
I	Cl	0.2	KOAc	THF	76	8	SM
I	Cl	—	Na ₂ CO ₃ ^{c)}	NMP	60	16	A 40%

^{a)} Isolated yields. Yields calculated using quantitative ¹H NMR in parenthesis. ^{b)} Conversion calculated from the ¹H NMR spectrum of the crude reaction mixture. ^{c)} Reaction conditions: Pd₂(dba)₃ (2 mol%), PPh₃ (4 mol%), PivOH (30 mol%), Na₂CO₃ (3.0 equiv.).

Table S2. Optimisation of the Suzuki-Miyaura Cross-Coupling Reaction



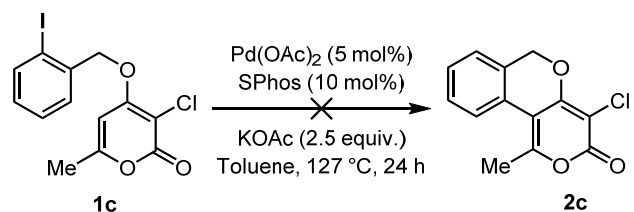
Pd Source	Ligand	Base	Solvent	T (°C)	Conversion ^{a)}
Pd ₂ (dba) ₃ (1.5 mol%)	P(^t Bu) ₃ .HBF ₄ (3.6 mol%)	KF (3.3 equiv.)	THF	60	0
Pd(OAc) ₂ (2 mol%)	DavePhos (3 mol%)	CsF (3.0 equiv.)	Dioxane	110	0
Pd(OAc) ₂	SPhos ^{b)}	K ₂ CO ₃	Toluene	110	60
Pd(OAc) ₂	SPhos ^{b)}	Cs ₂ CO ₃	Toluene	110	degradation
Pd(OAc) ₂	SPhos ^{b)}	KOAc	Toluene	110	70
Pd(OAc) ₂	SPhos ^{b)}	KOAc	Toluene	127	22
Pd(OAc) ₂	SPhos ^{b)}	KOAc	THF	76	71
Pd(OAc) ₂	XPhos	KOAc	THF	76	29
Pd(OAc) ₂	RuPhos	KOAc	THF	76	64
Pd ₂ (dba) ₃	SPhos	KOAc	THF	76	6
Pd(OAc) ₂	SPhos	KOAc	2-MeTHF	90	69
Pd(OAc) ₂	SPhos	KOAc	1,4-Dioxane	110	44
Pd(OAc) ₂	SPhos	KOAc	THF	50	9
Pd(OAc) ₂	SPhos	KOAc	THF	76	93 (92)

^{a)} Conversion calculated from the ¹H NMR spectrum of the crude reaction mixture. Isolated yields in parenthesis. ^{b)} 10 mol%.

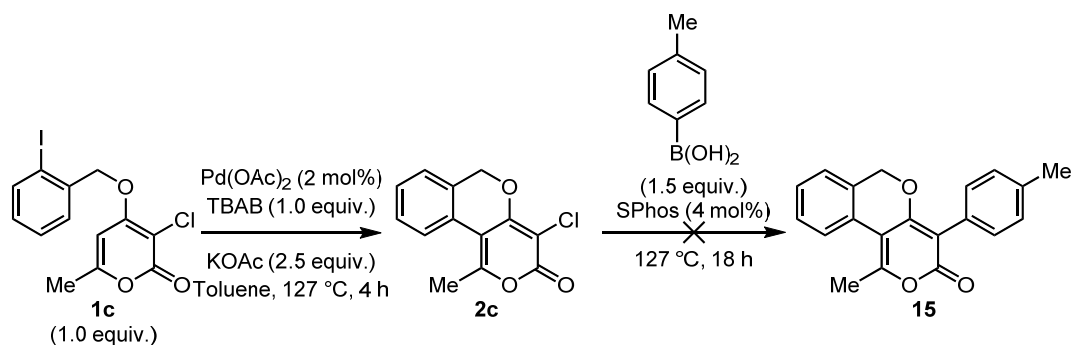
Investigation of a one-pot direct arylation/Suzuki-Miyaura cross-coupling

It was anticipated that due to the similarity of the reaction conditions ($\text{Pd}(\text{OAc})_2$, KOAc, THF, 76 °C), a one pot direct arylation/Suzuki-Miyaura cross-coupling could be performed on these substrates. Unfortunately, all attempts to do so were unsuccessful. In summary:

The Suzuki-Miyaura conditions do not catalyse the direct arylation reaction.



It was also attempted to add in the SPhos ligand and boronic acid after the direct arylation reaction had proceeded to completion, but this was also unsuccessful at providing the final product.

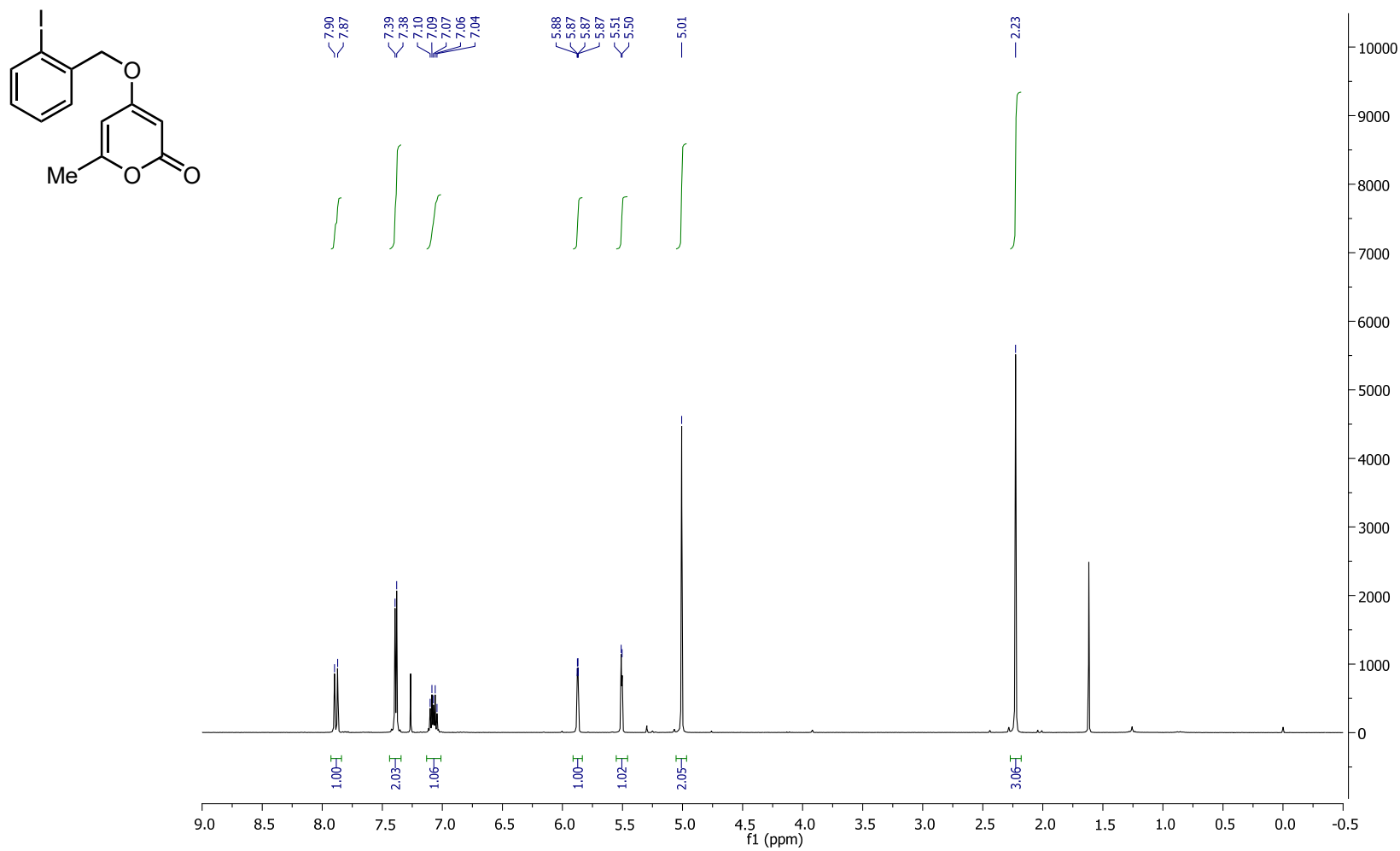


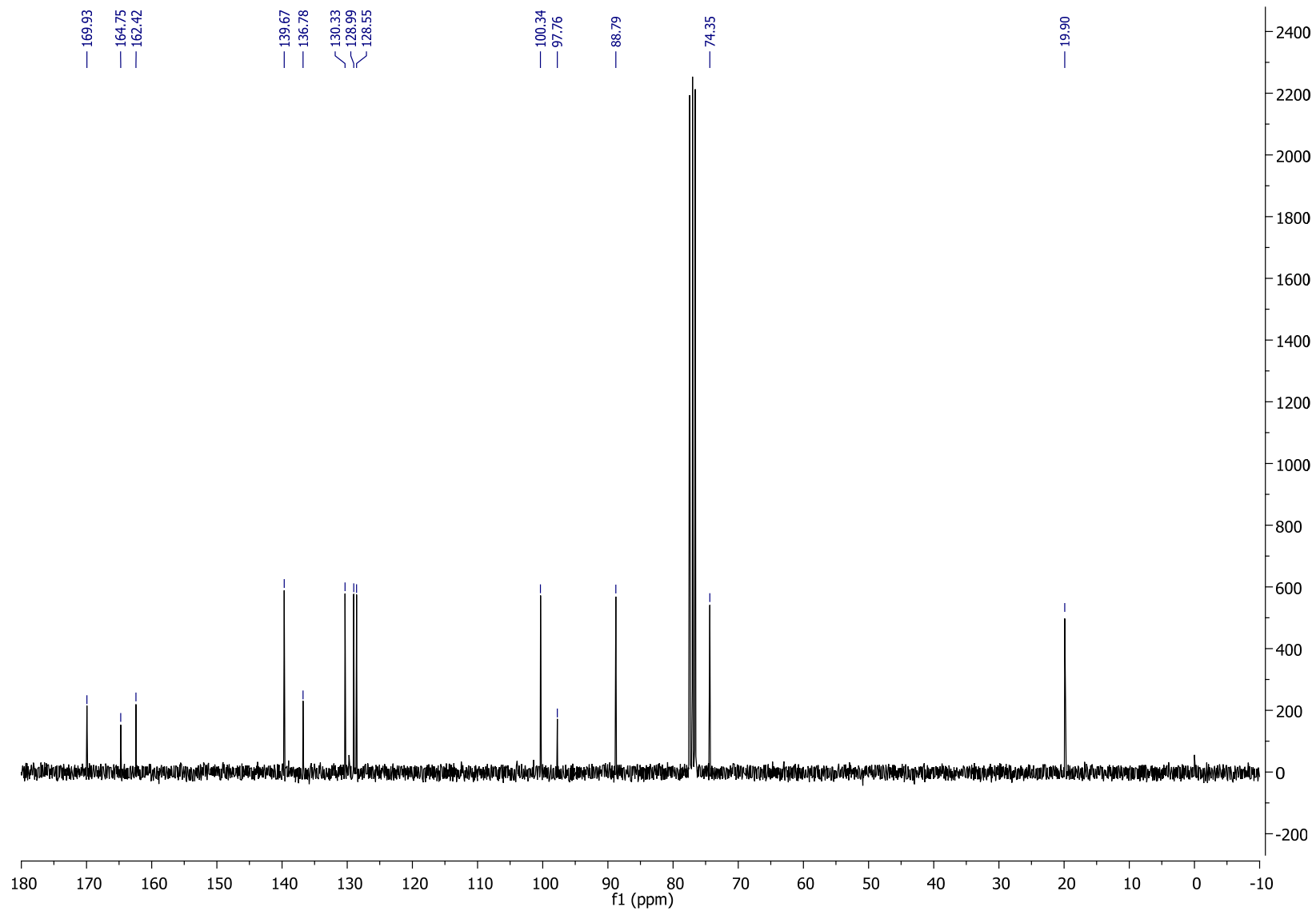
This demonstrates the difficulty in using one precatalyst for two mechanistically distinct transformations, and the exquisitely precise conditions which are required for each transformation.

Spectra

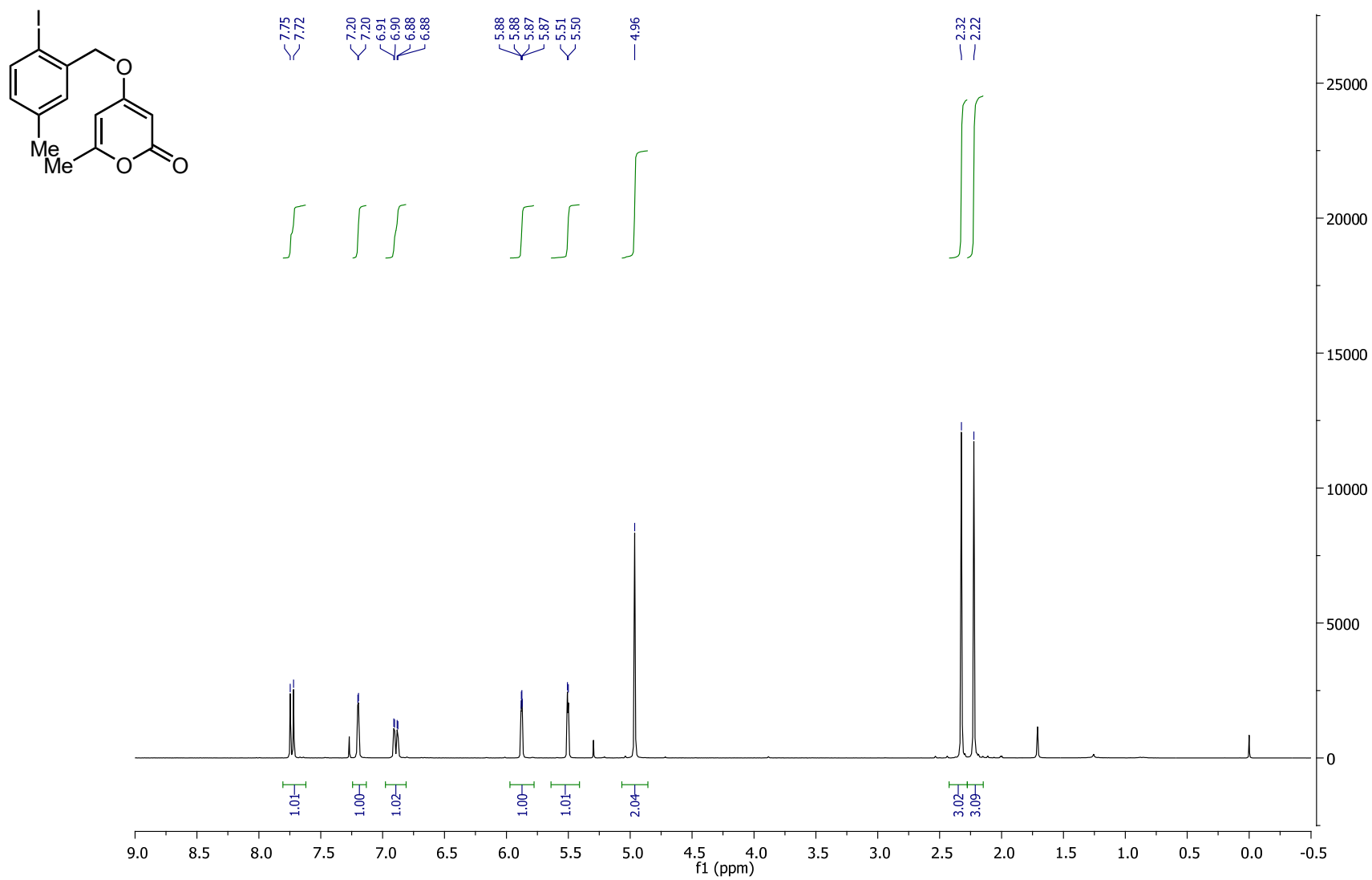
4-Benzyloxy-2-pyrones and 2-pyridones

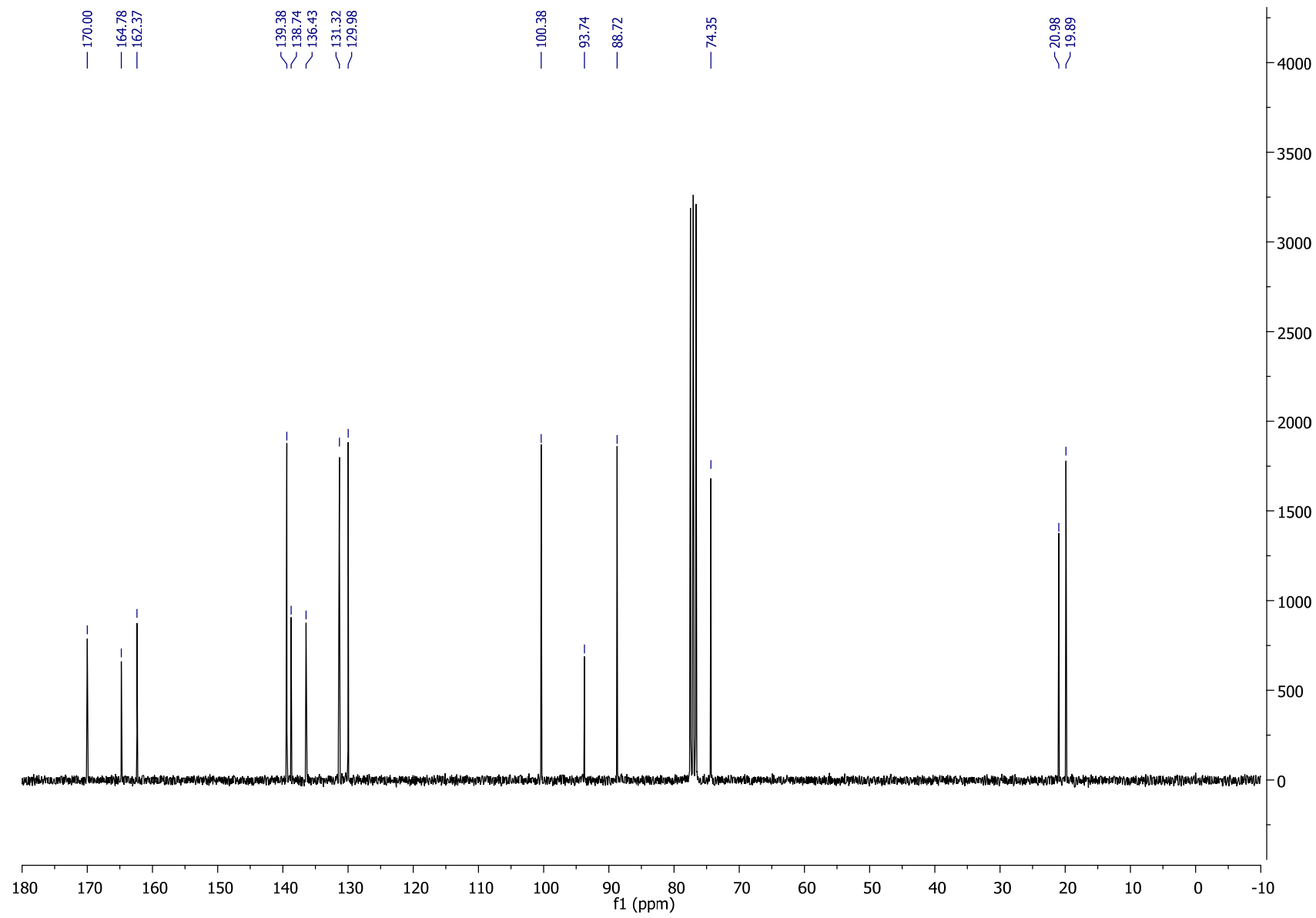
4-((2-Iodobenzyl)oxy)-6-methyl-2H-pyran-2-one





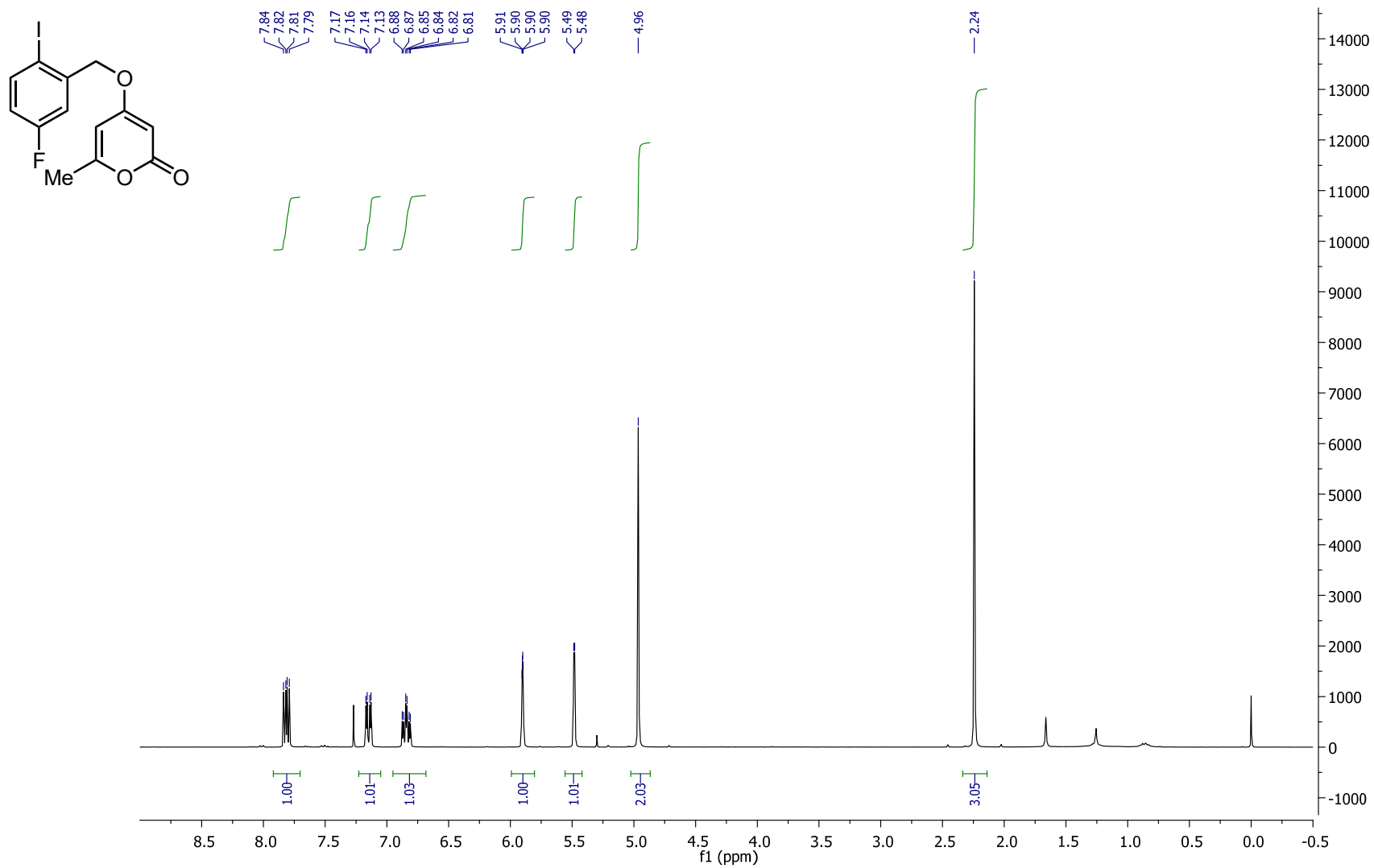
4-((2-Iodo-5-methylbenzyl)oxy)-6-methyl-2H-pyran-2-one

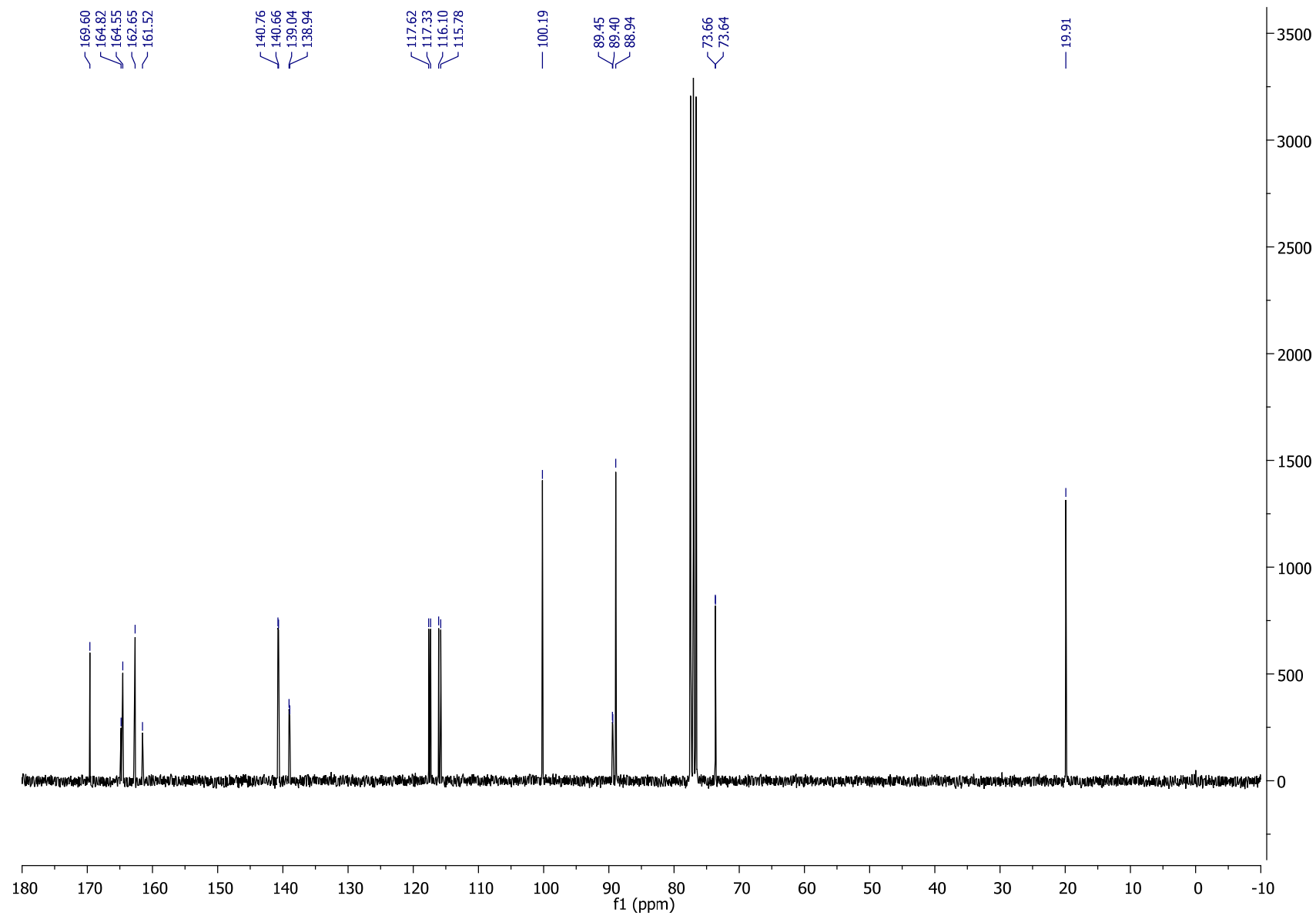




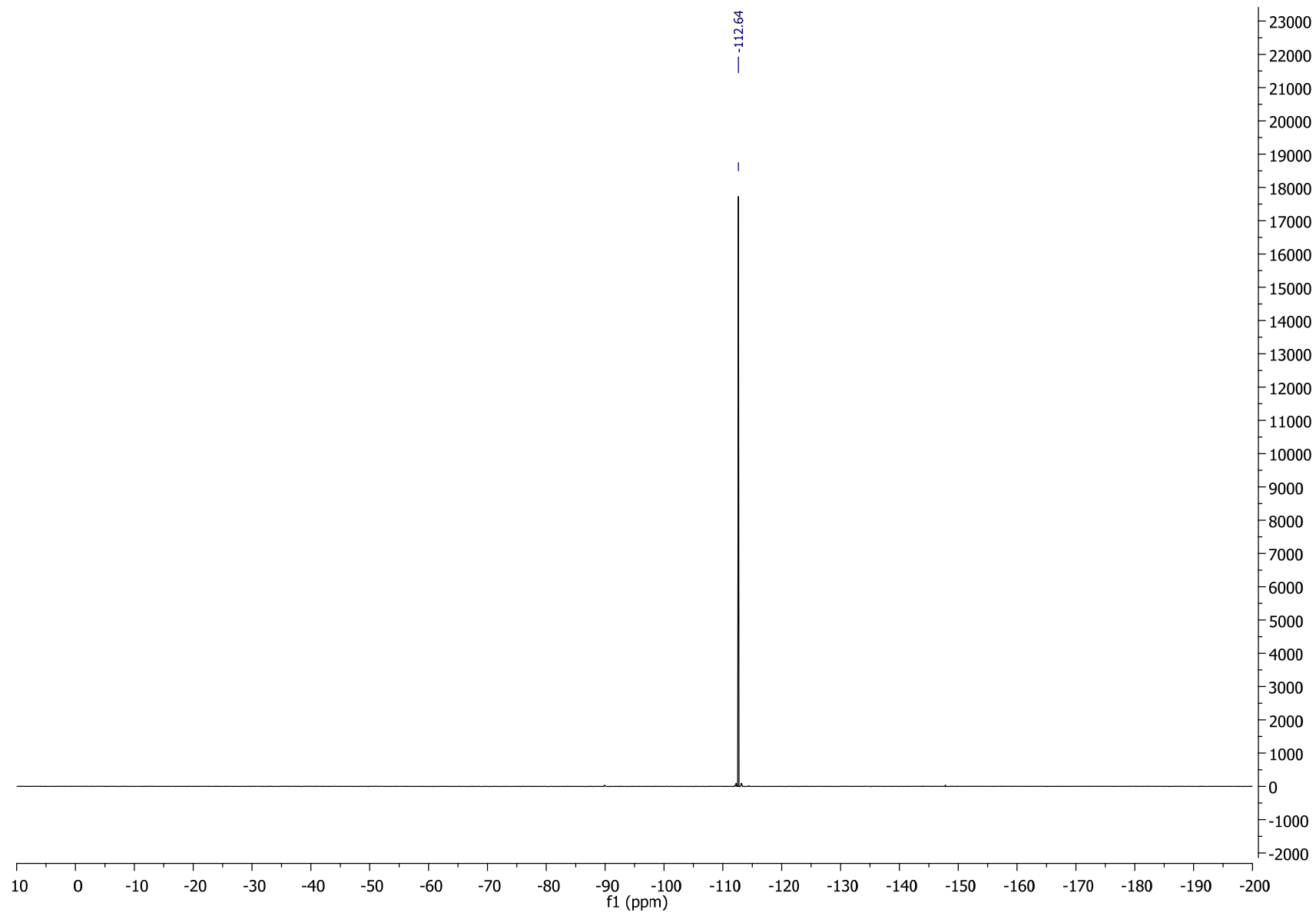
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4-((5-Fluoro-2-iodobenzyl)oxy)-6-methyl-2H-pyran-2-one



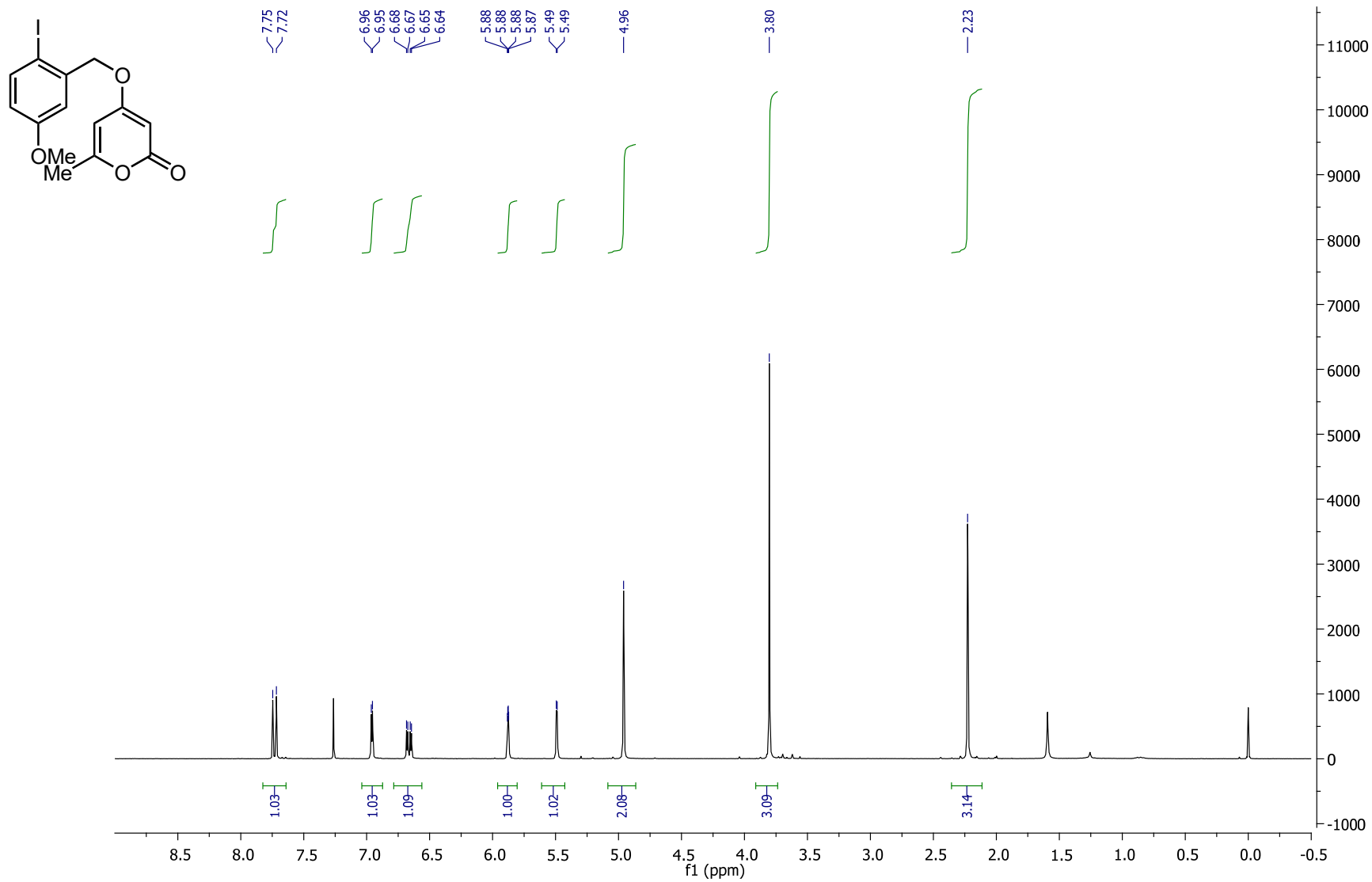


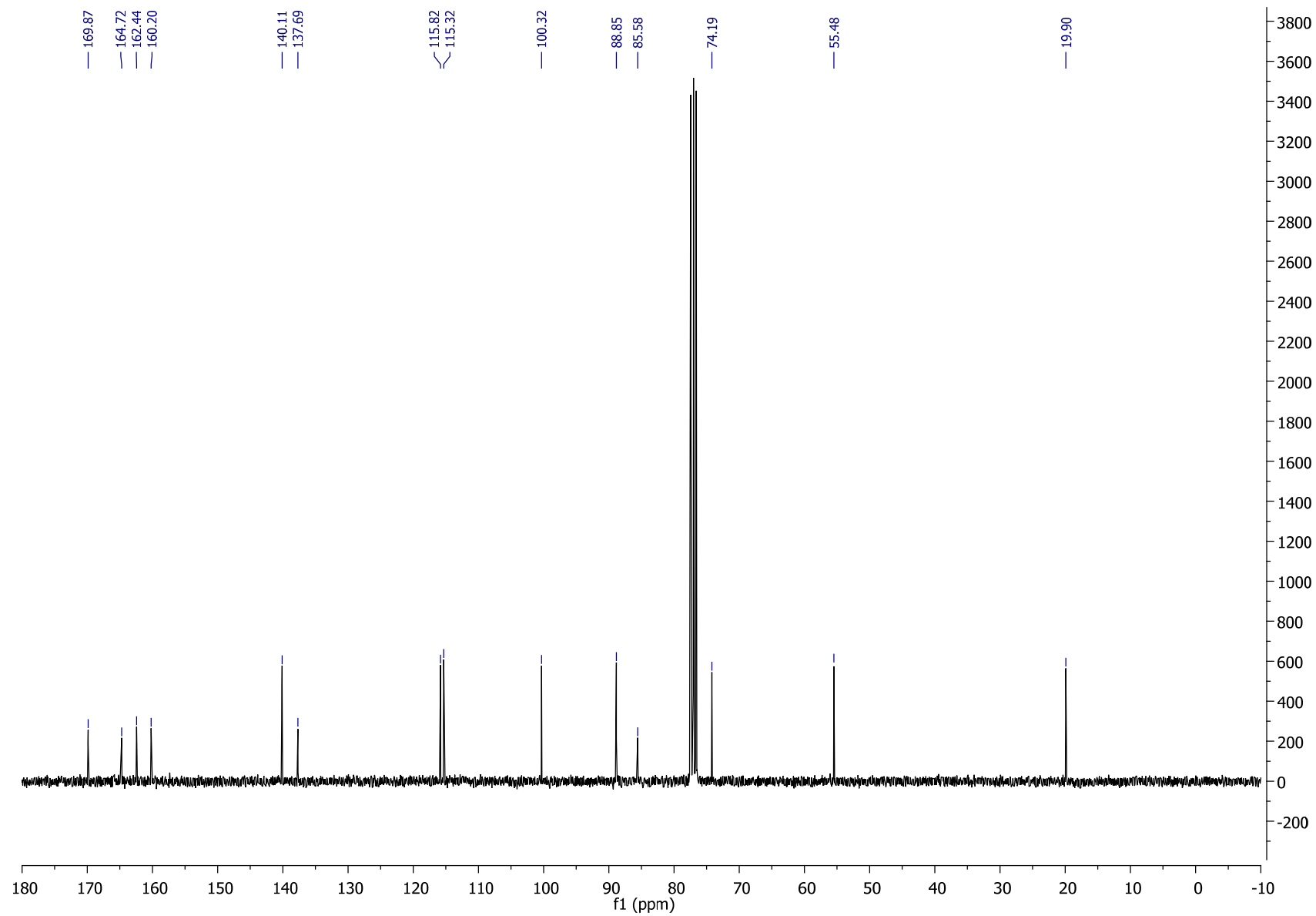
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S11

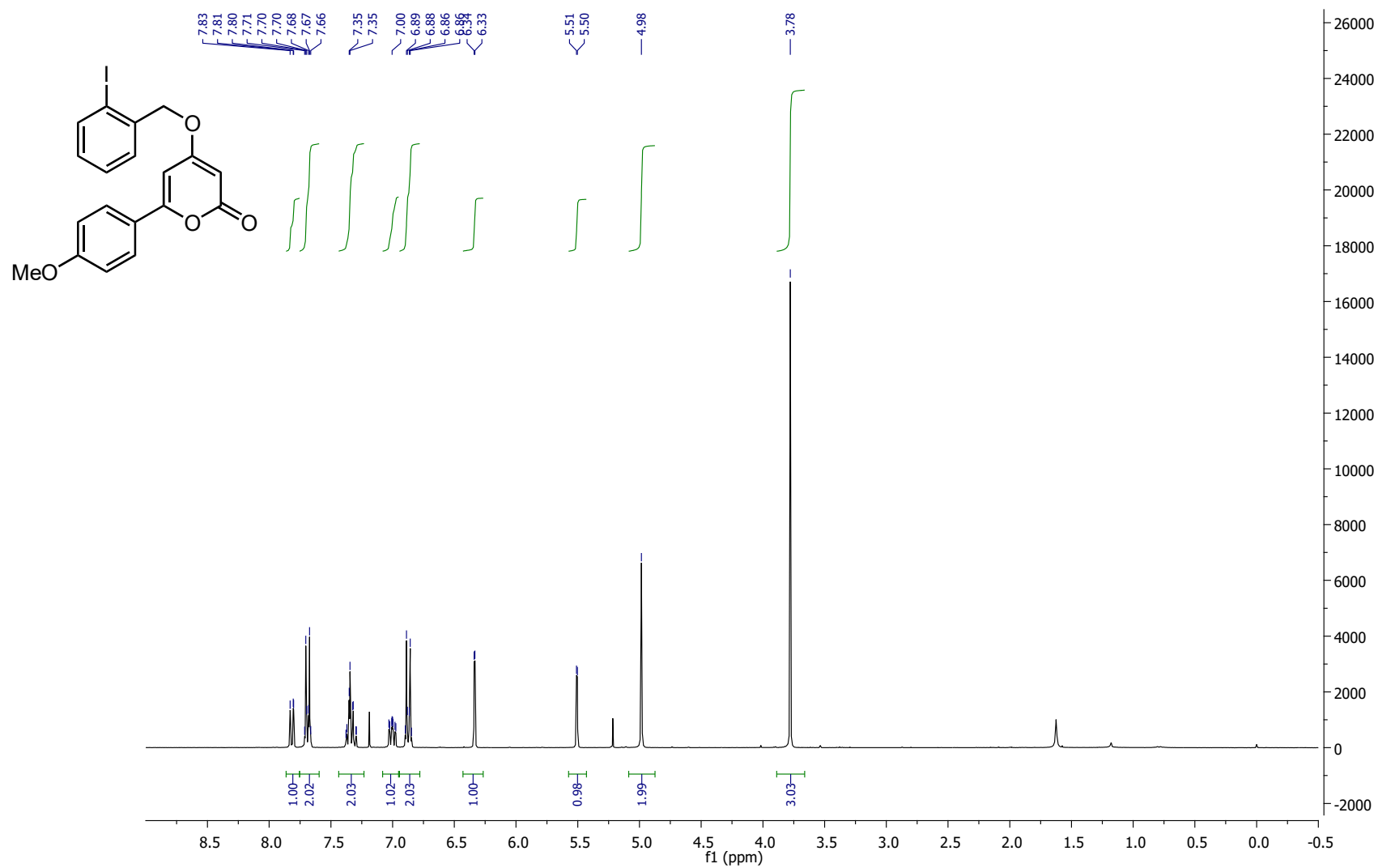
4-((2-Iodo-5-methoxybenzyl)oxy)-6-methyl-2H-pyran-2-one

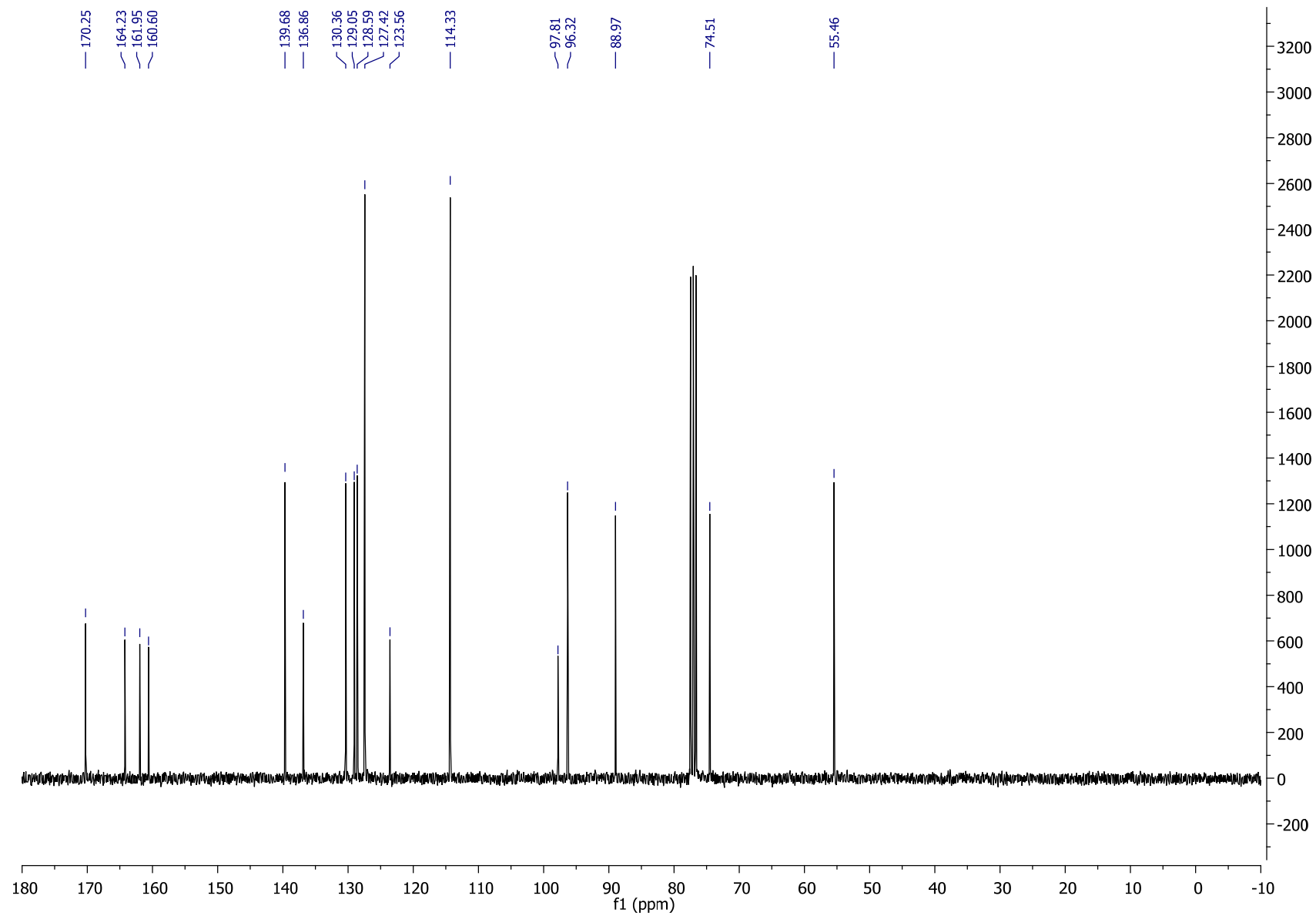




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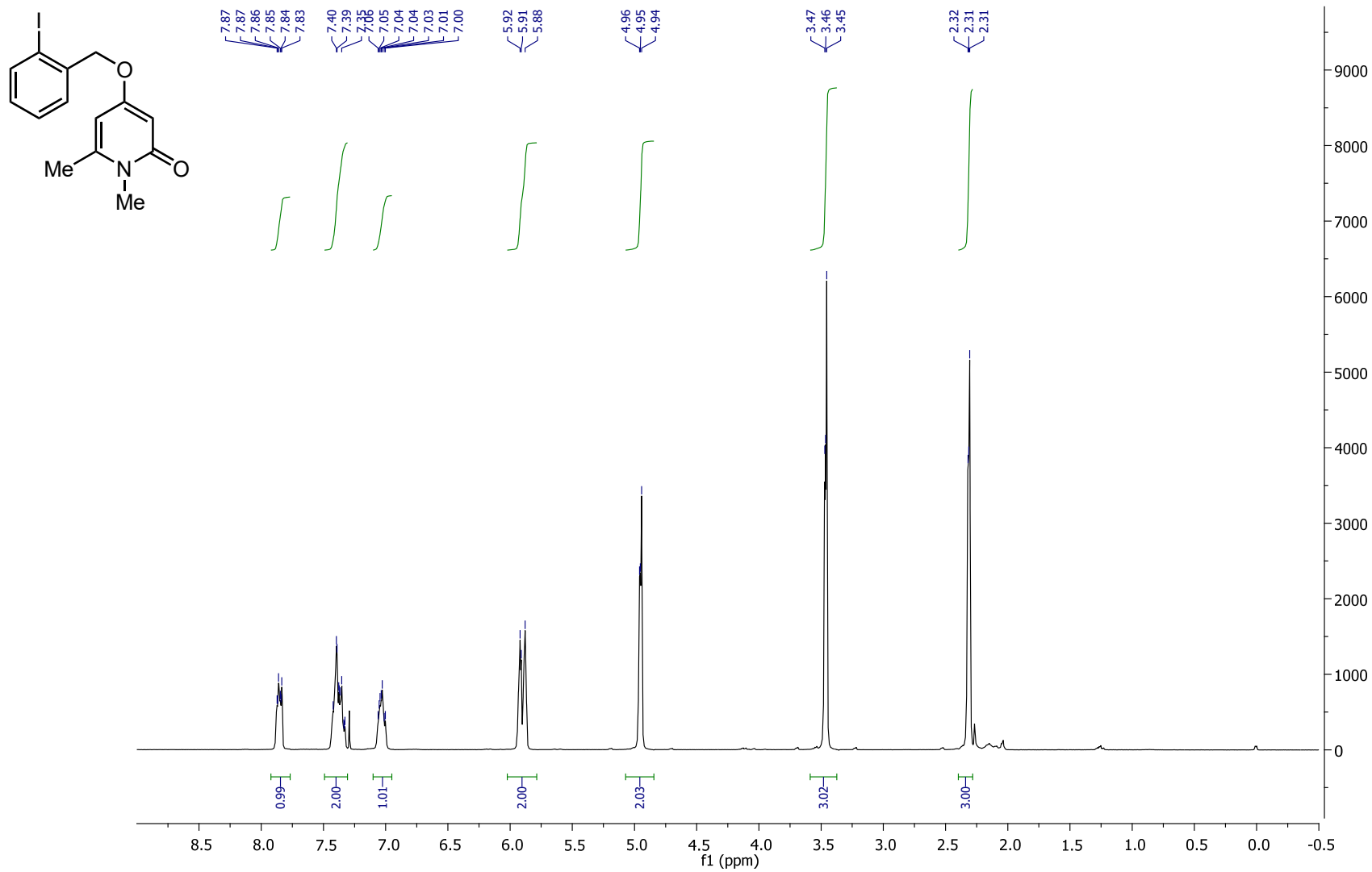
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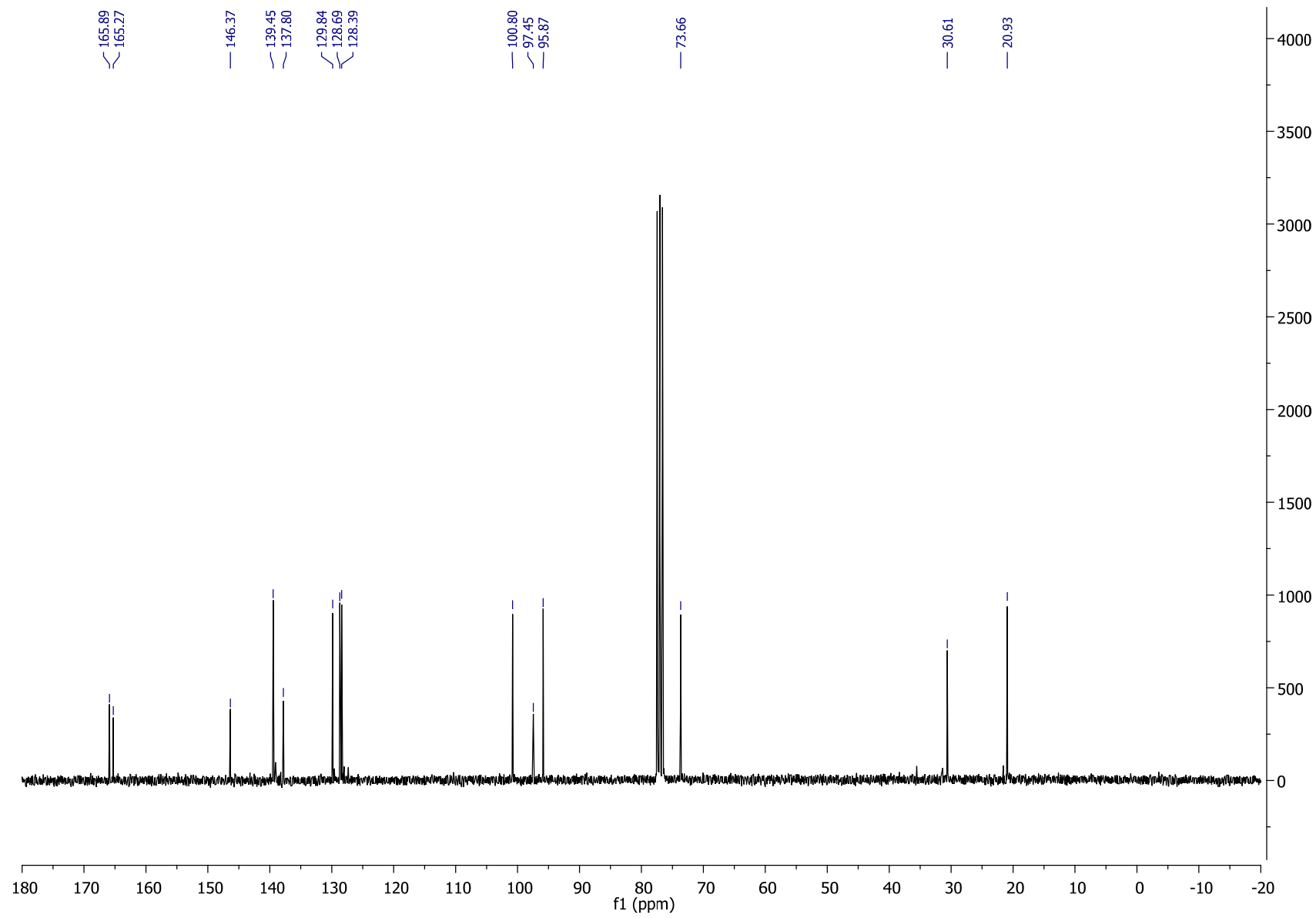




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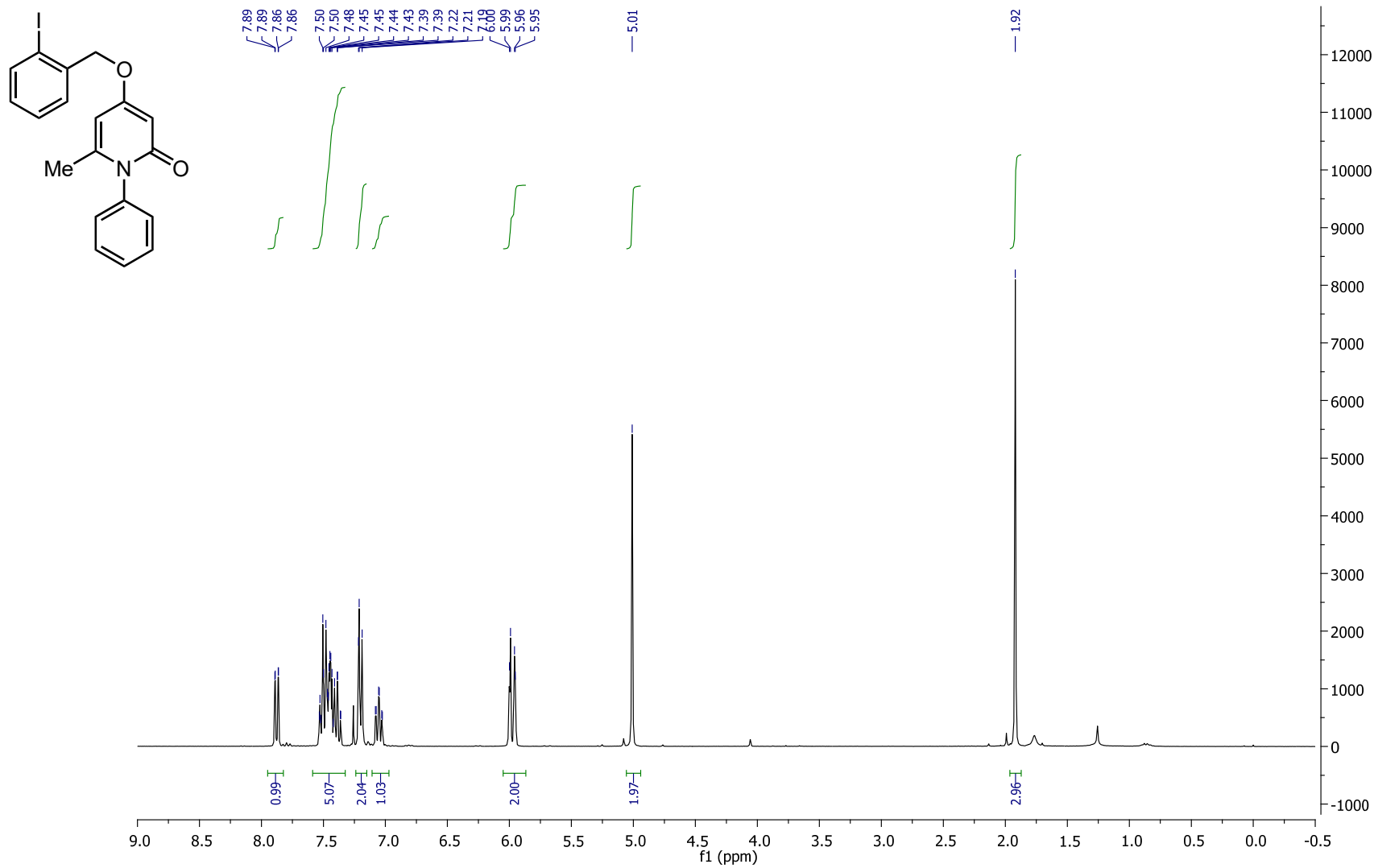
4-((2-Iodobenzyl)oxy)-1,6-dimethylpyridin-2(1H)-one

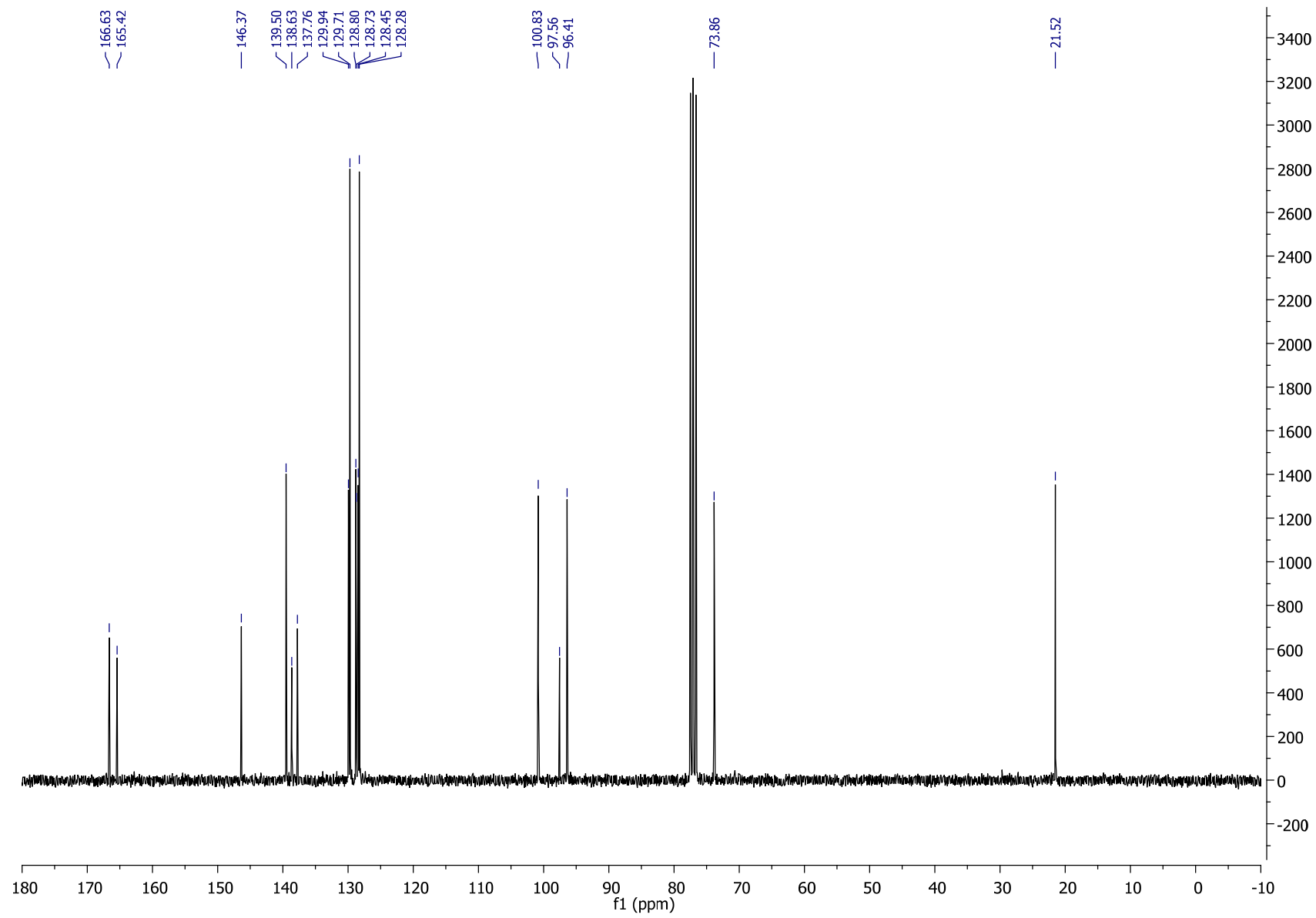




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4-((2-iodobenzyl)oxy)-6-methyl-1-phenylpyridin-2(1H)-one

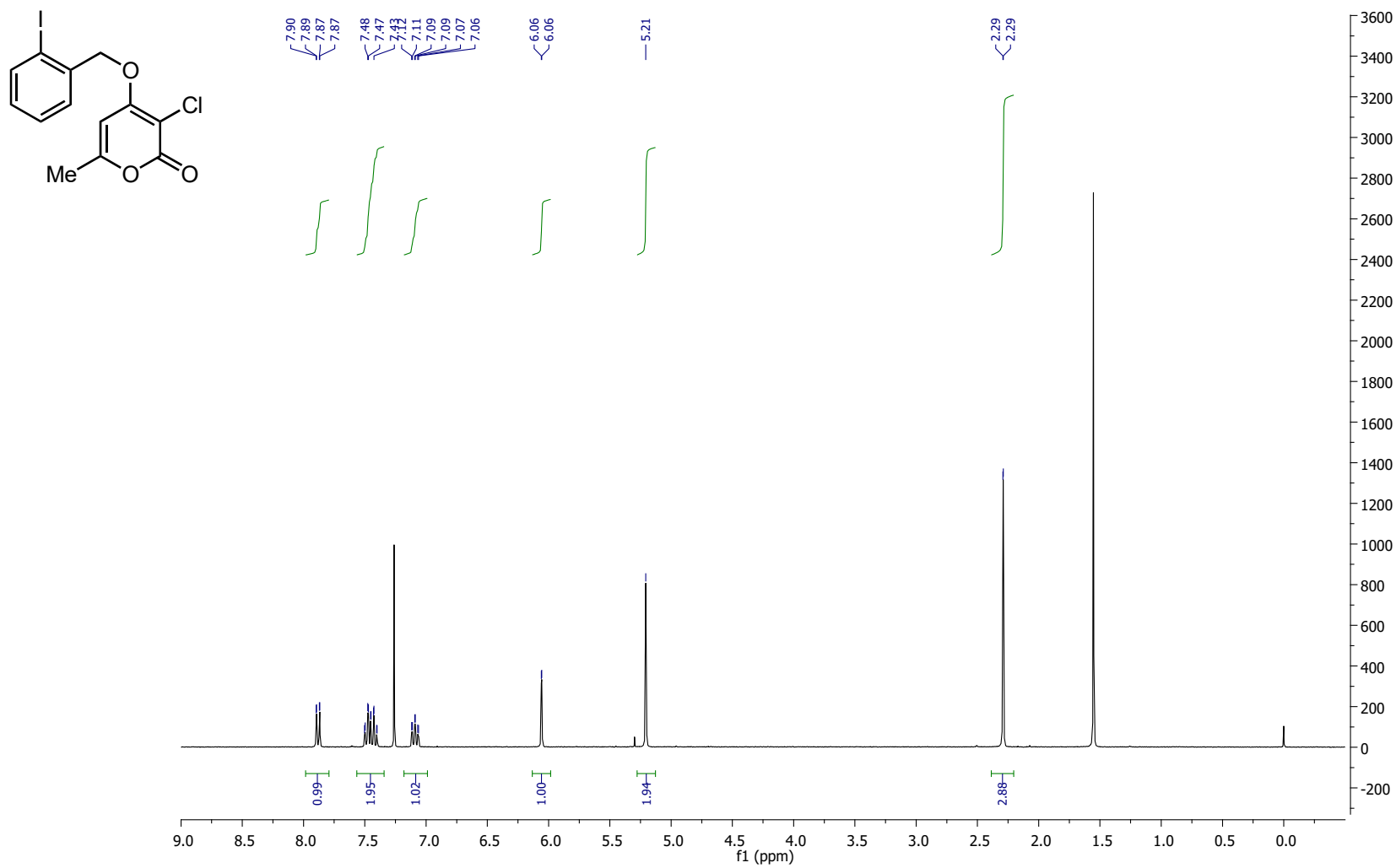


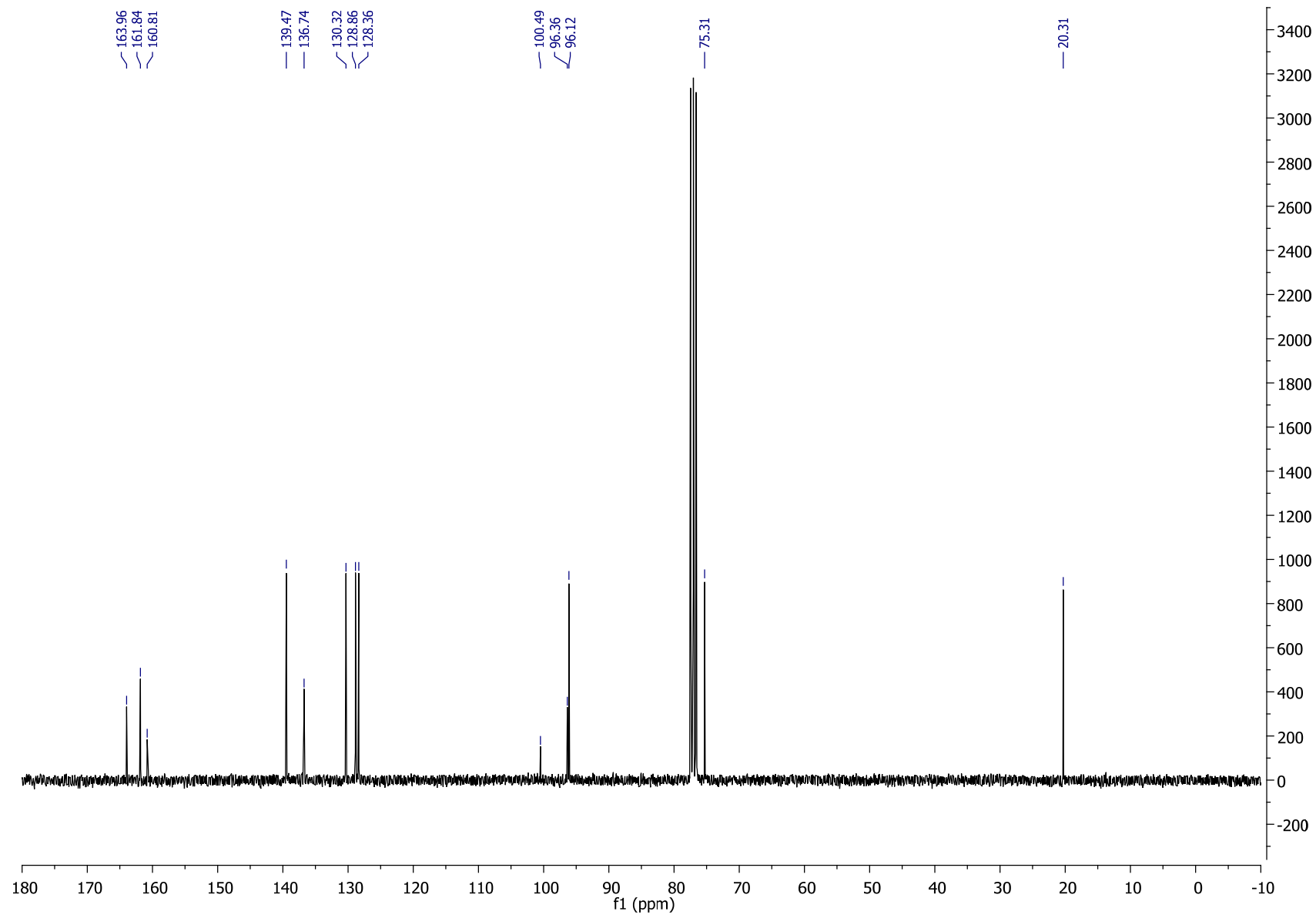


S19

3-Chloro-4-benzyloxy-2-pyrones and 2-pyridones (1c, 3-8)

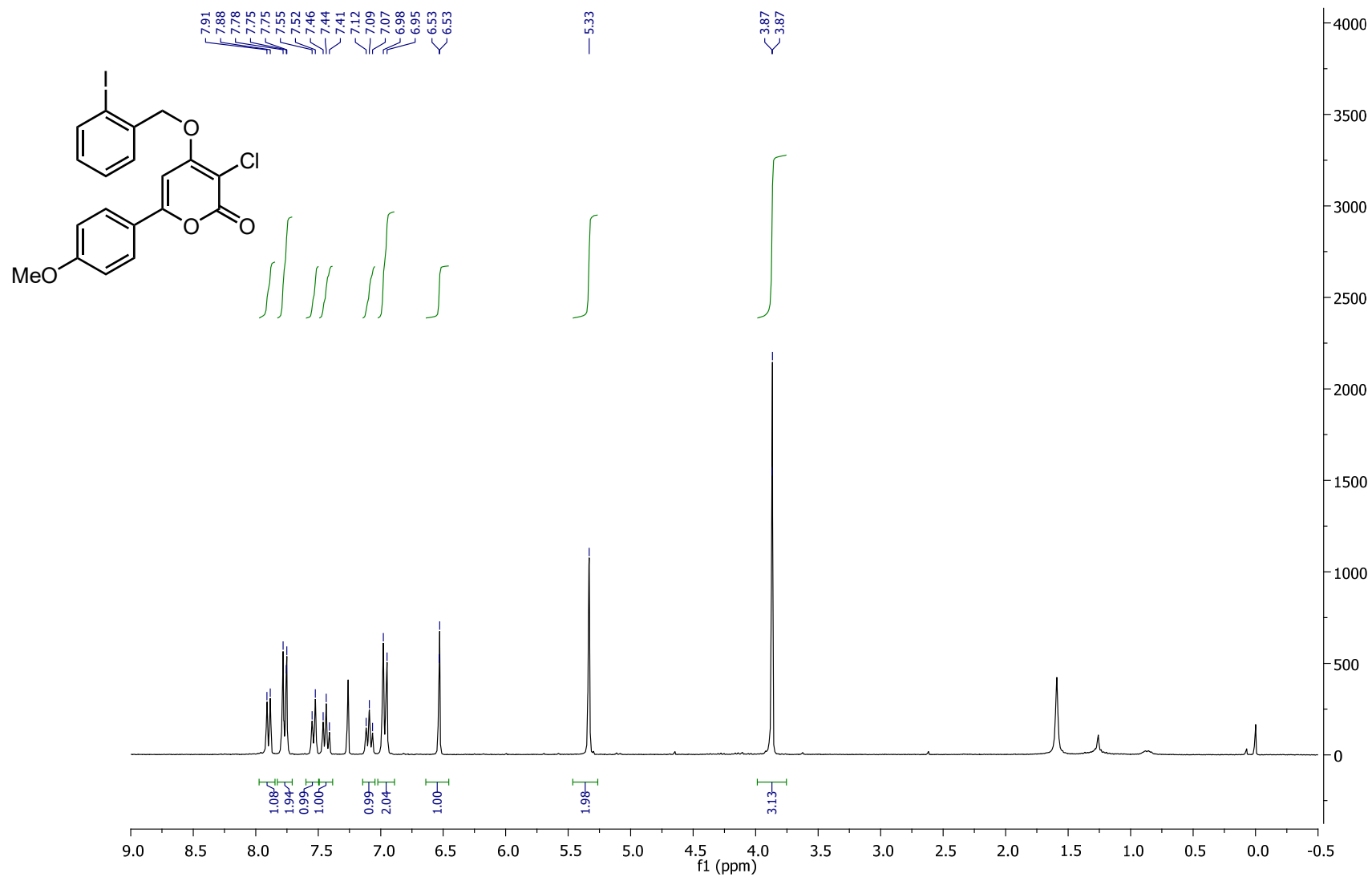
3-Chloro- 4-((2-iodobenzyl)oxy)-6-methyl-2H-pyran-2-one, 1c

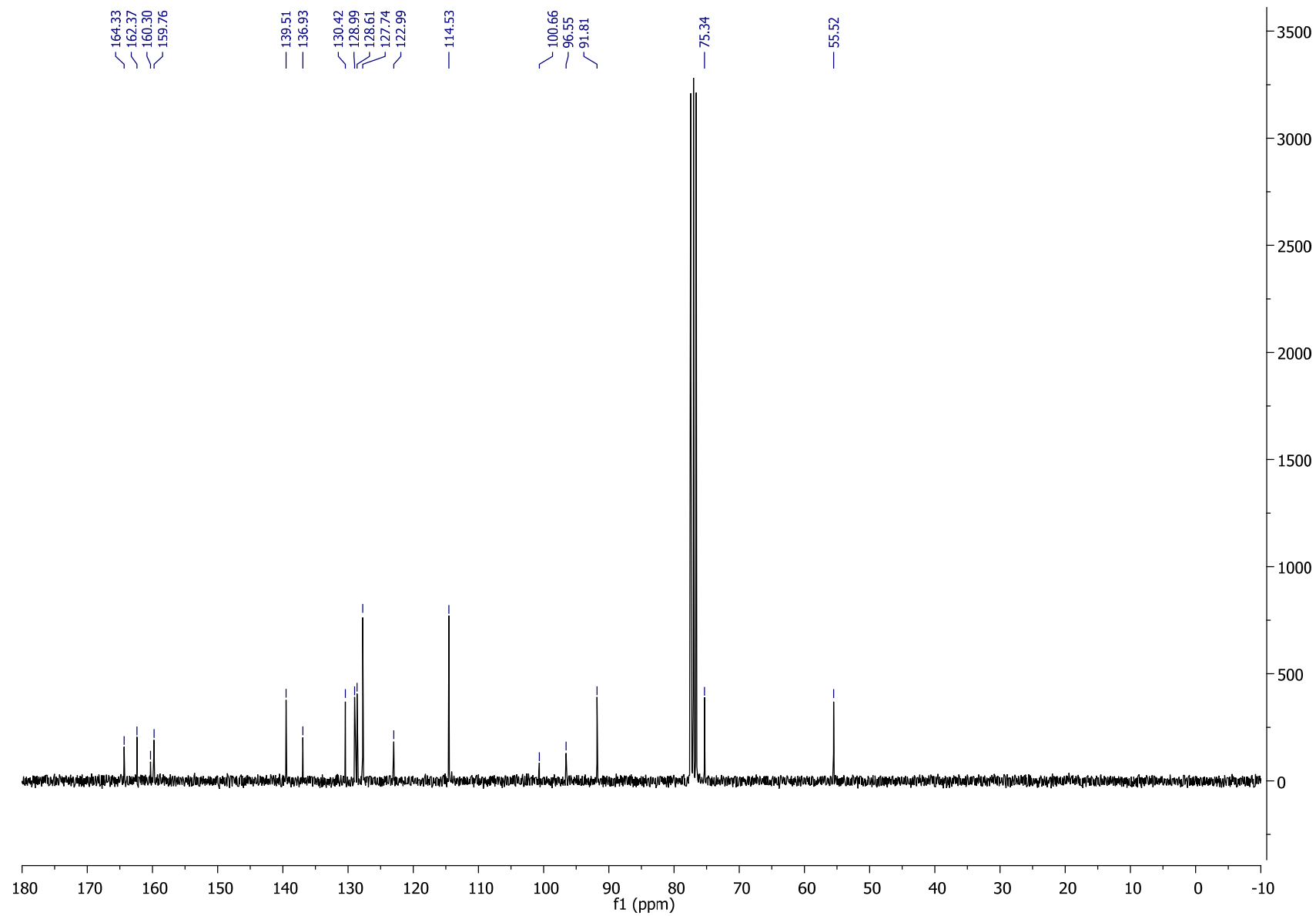




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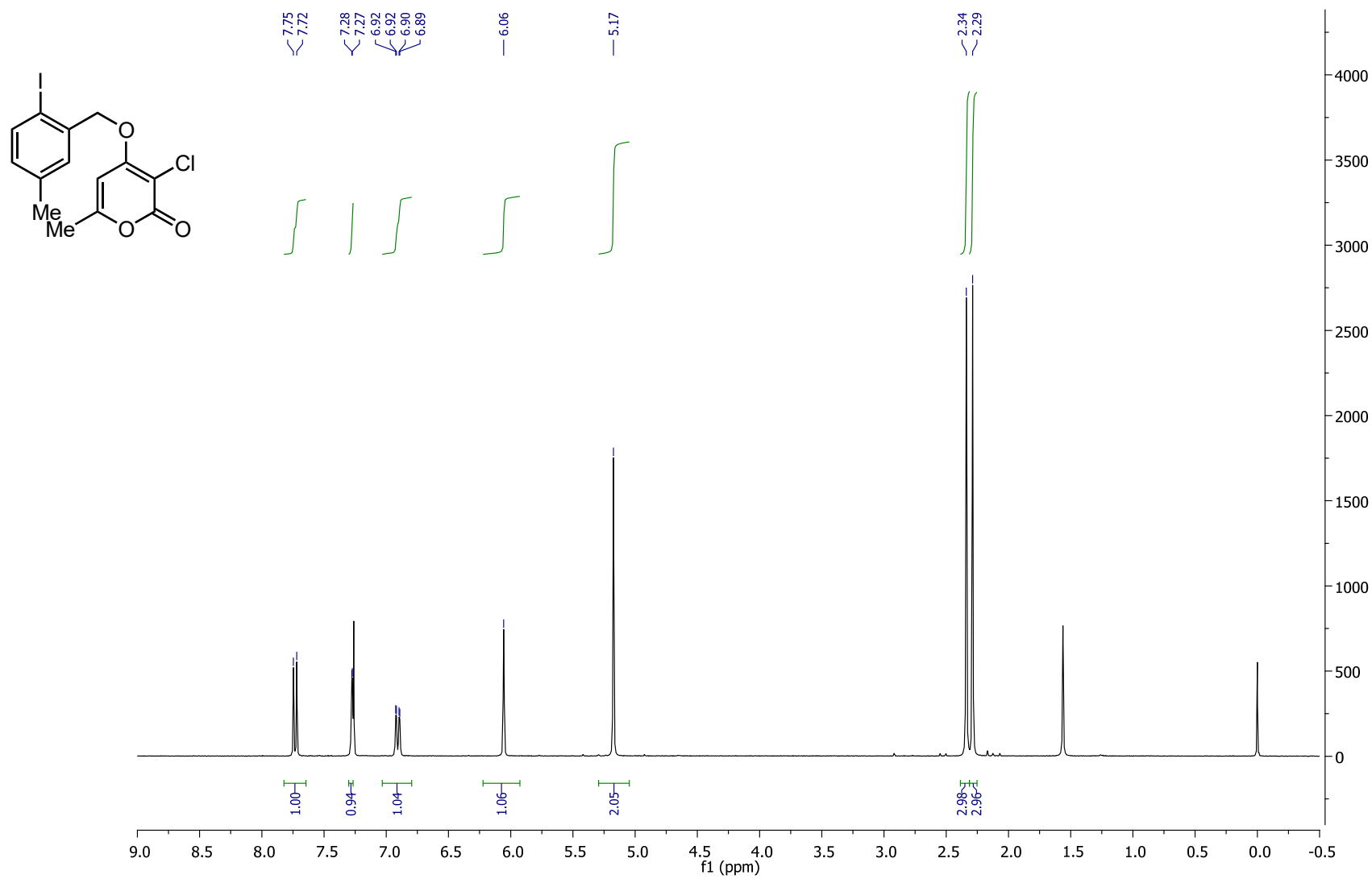
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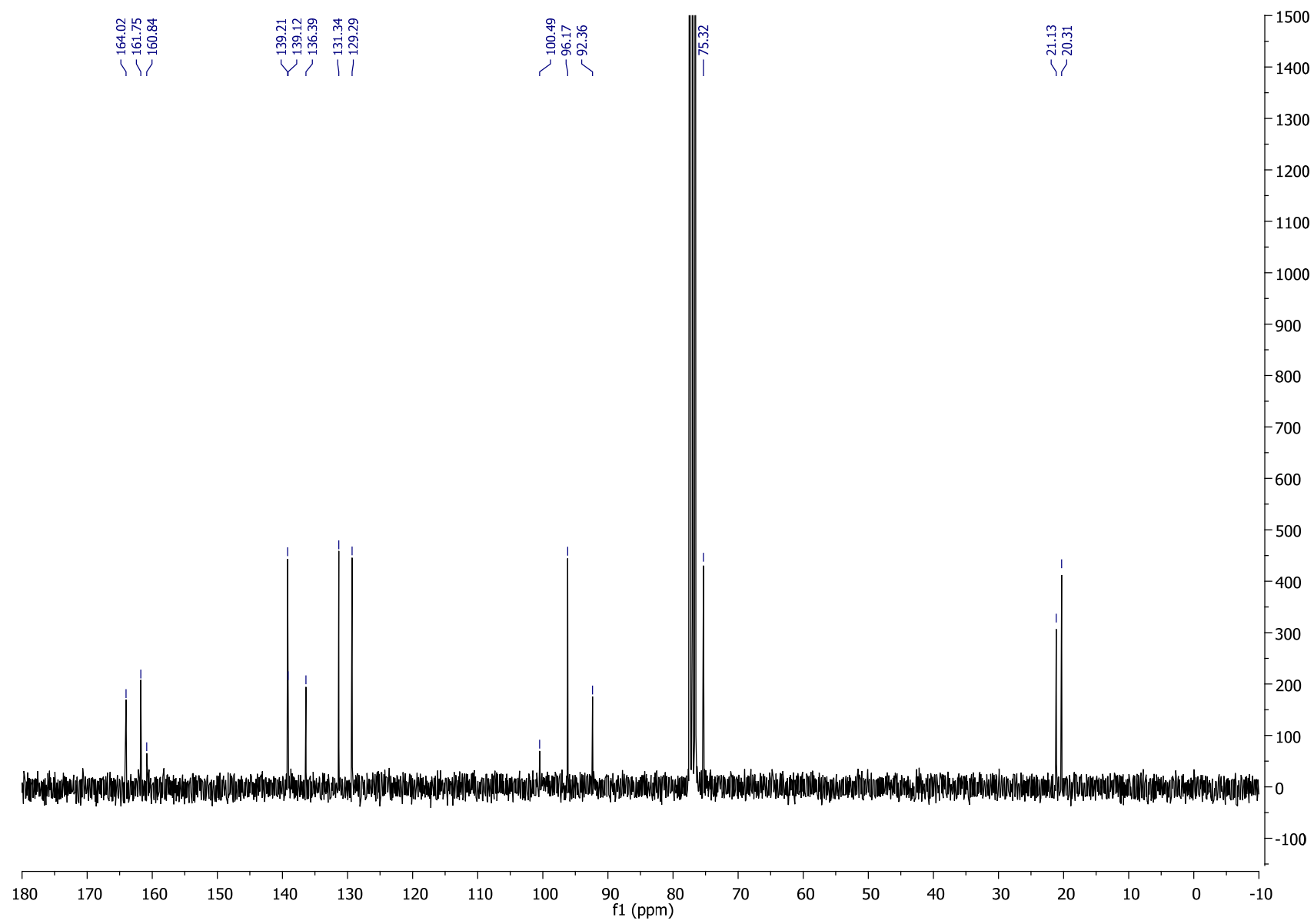




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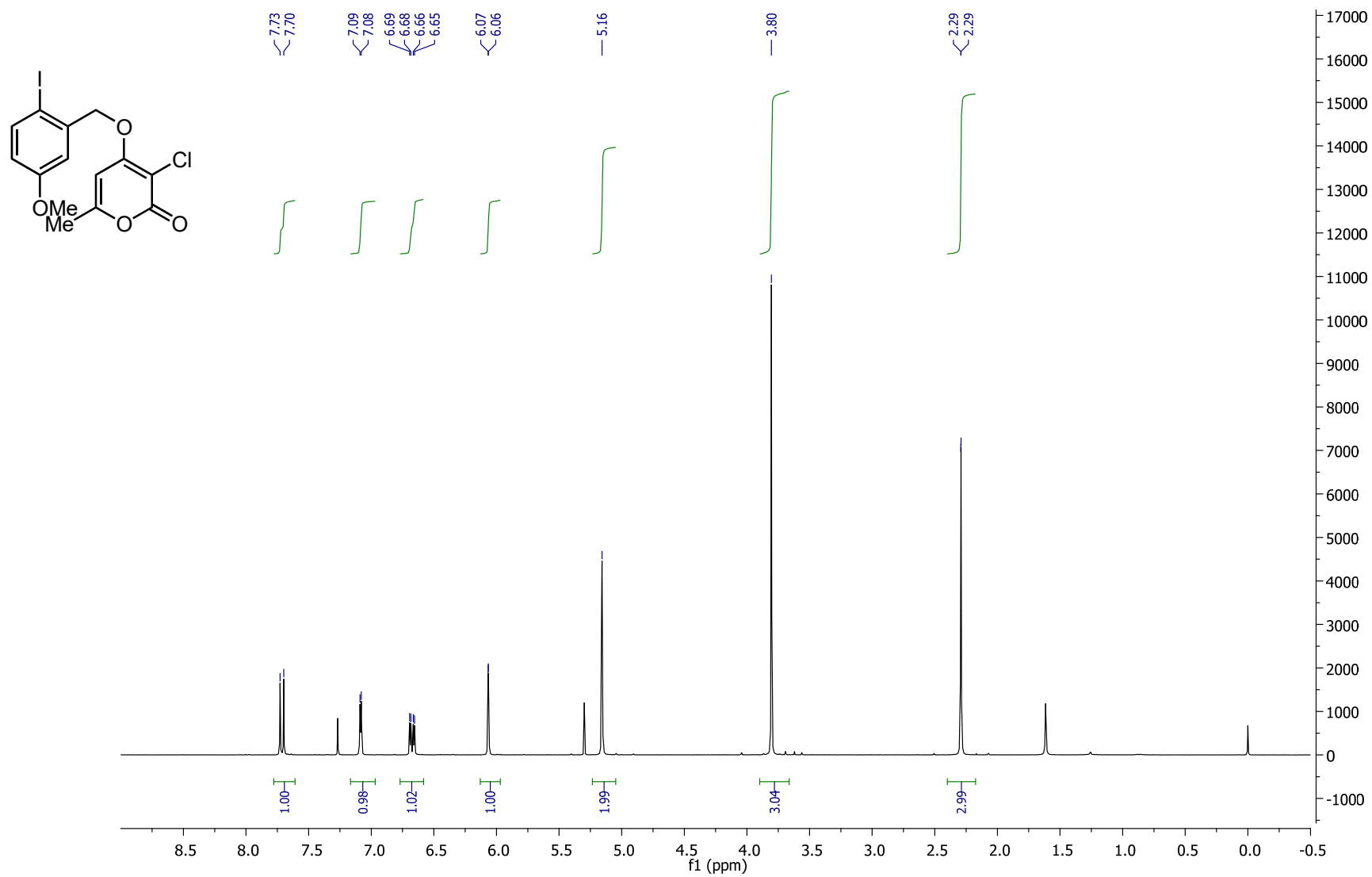
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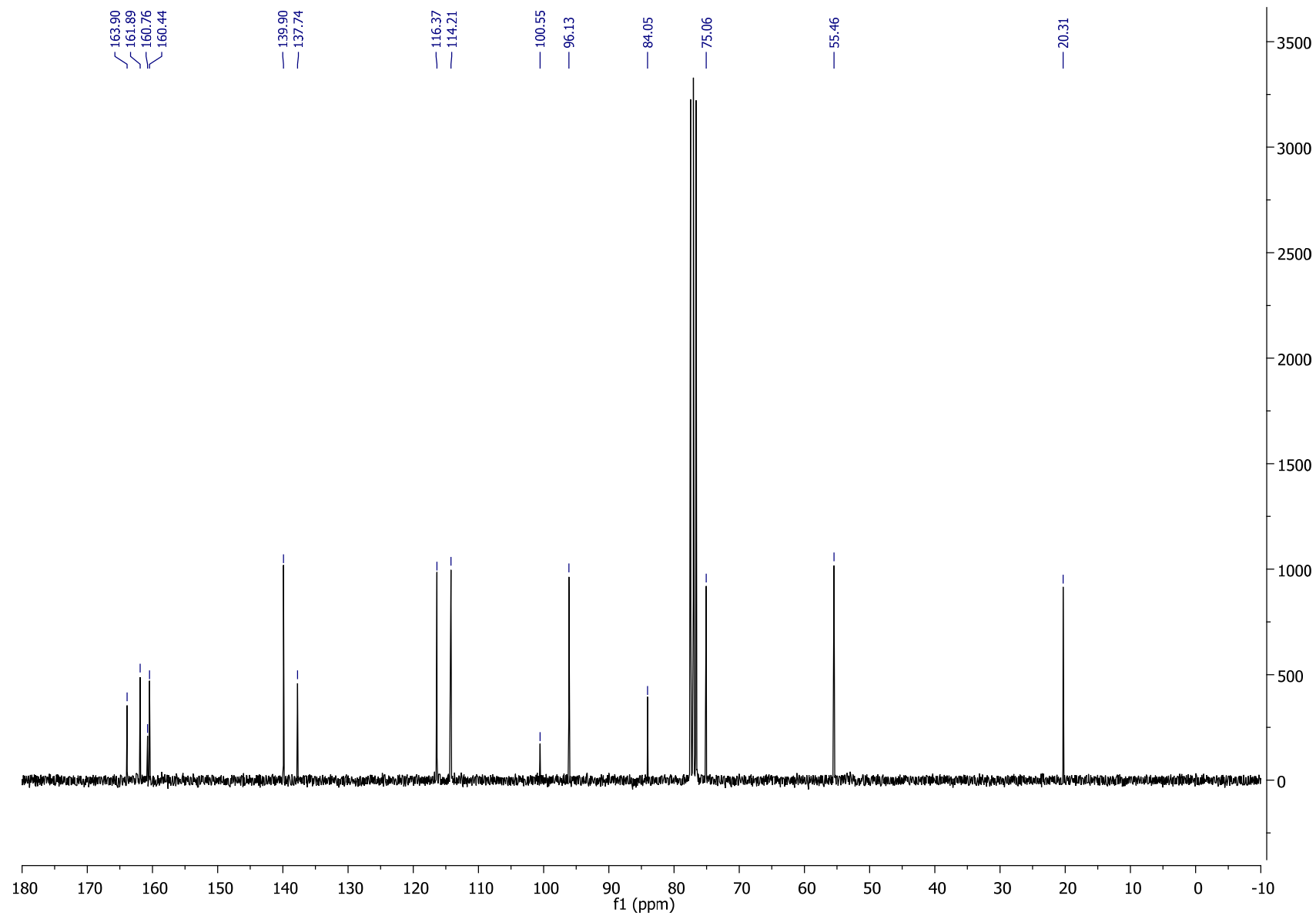




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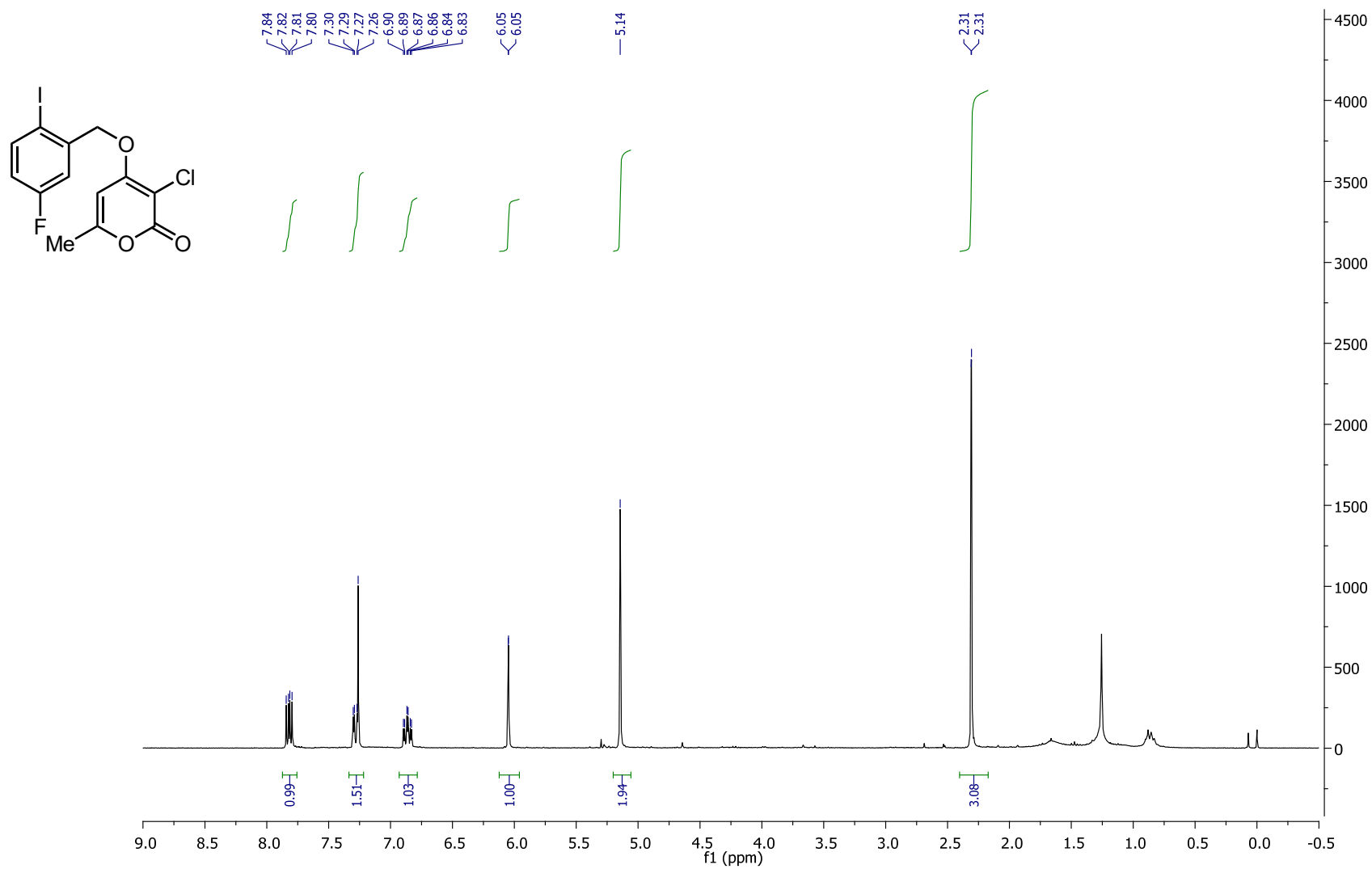
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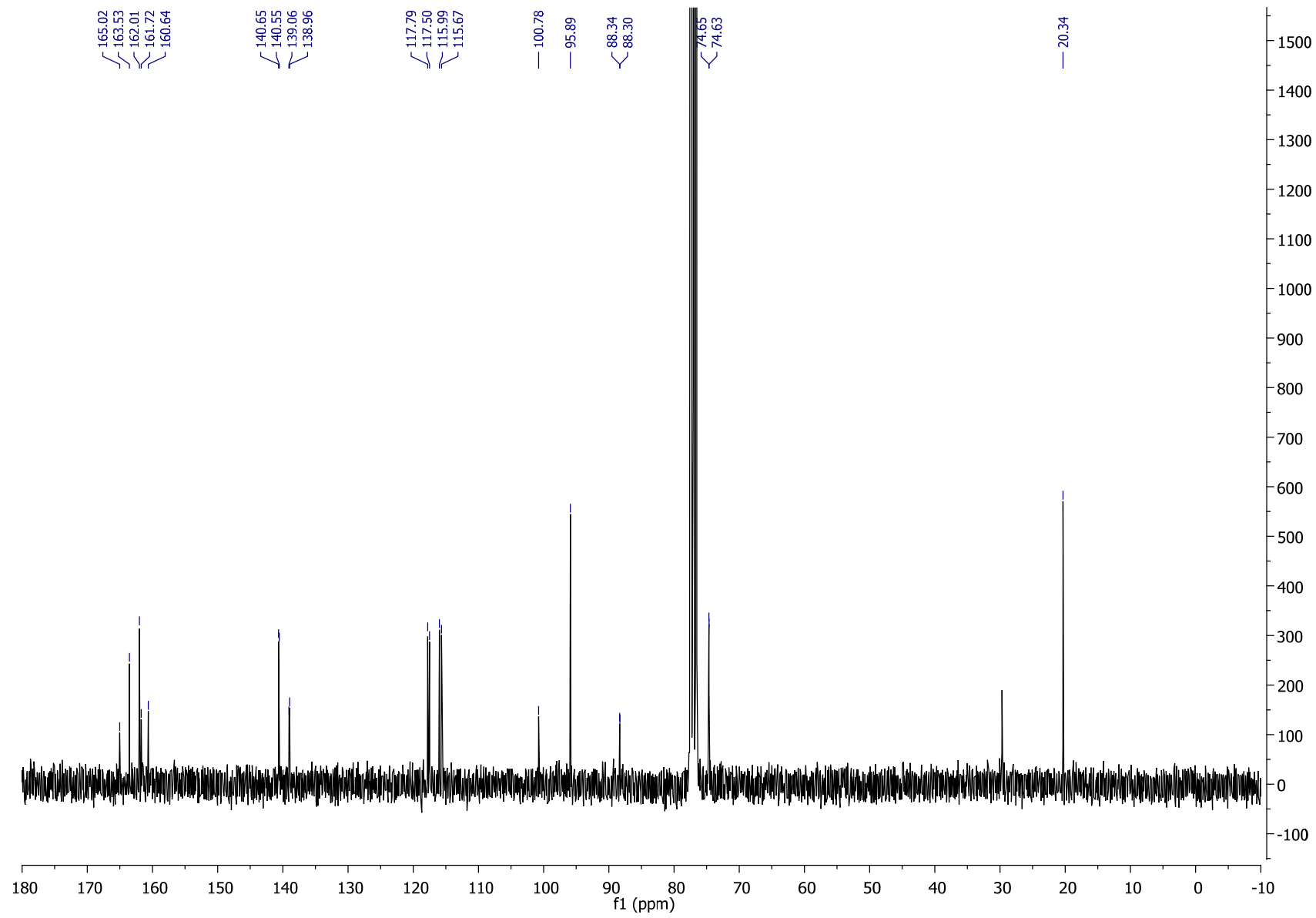




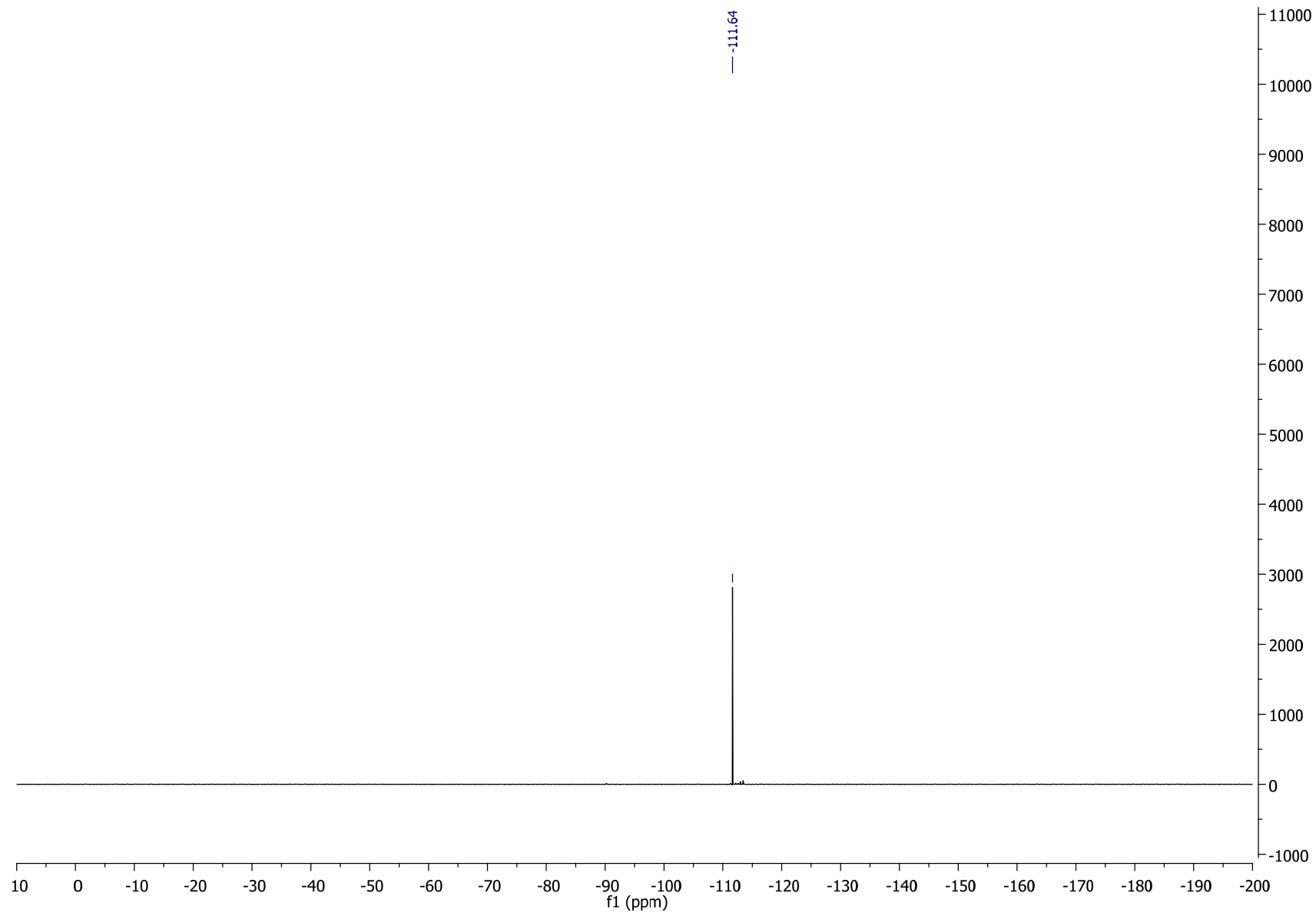
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3-Chloro-4-((5-fluoro-2-iodobenzyl)oxy)-6-methyl-2H-pyran-2-one, 6



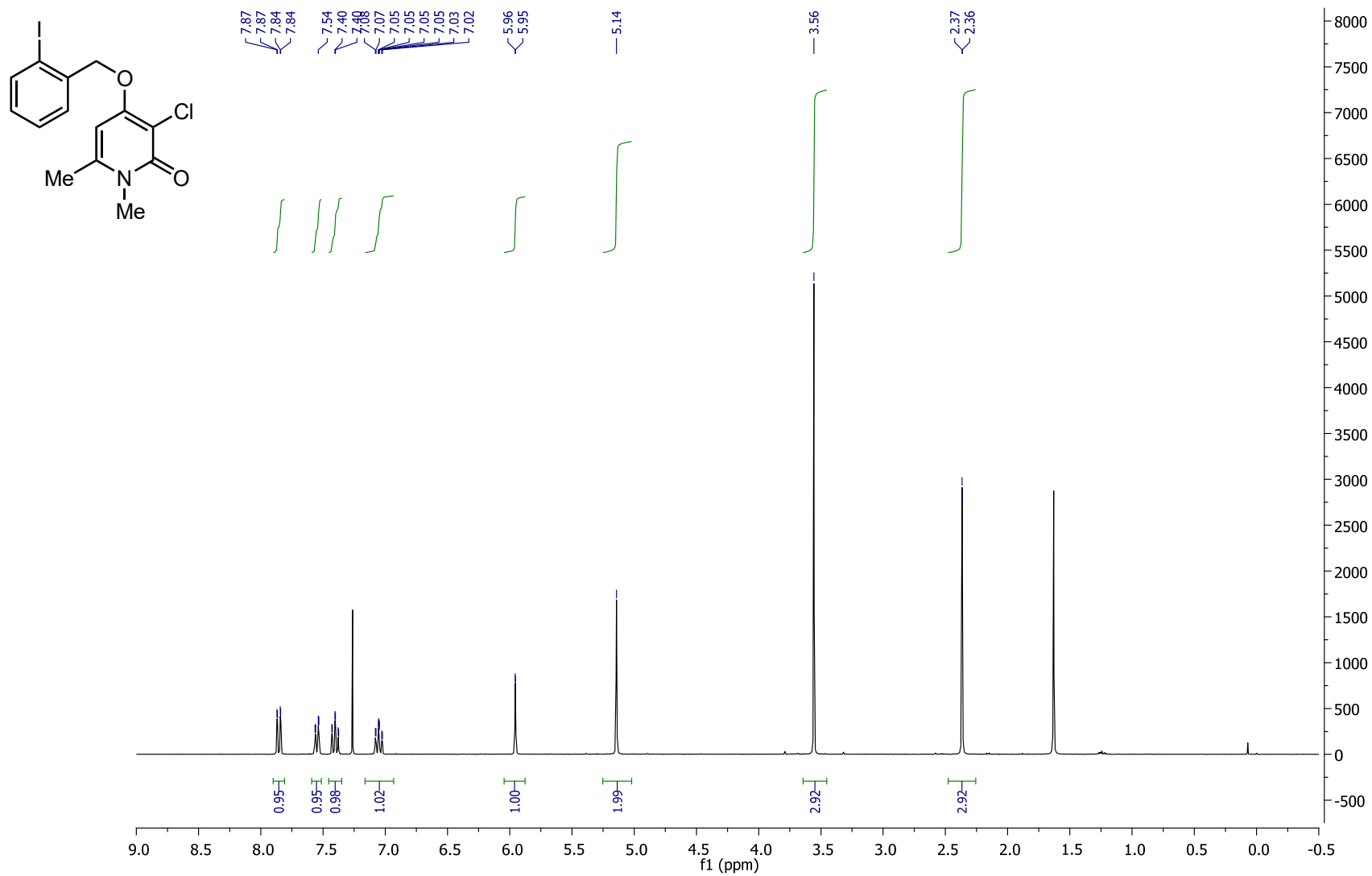


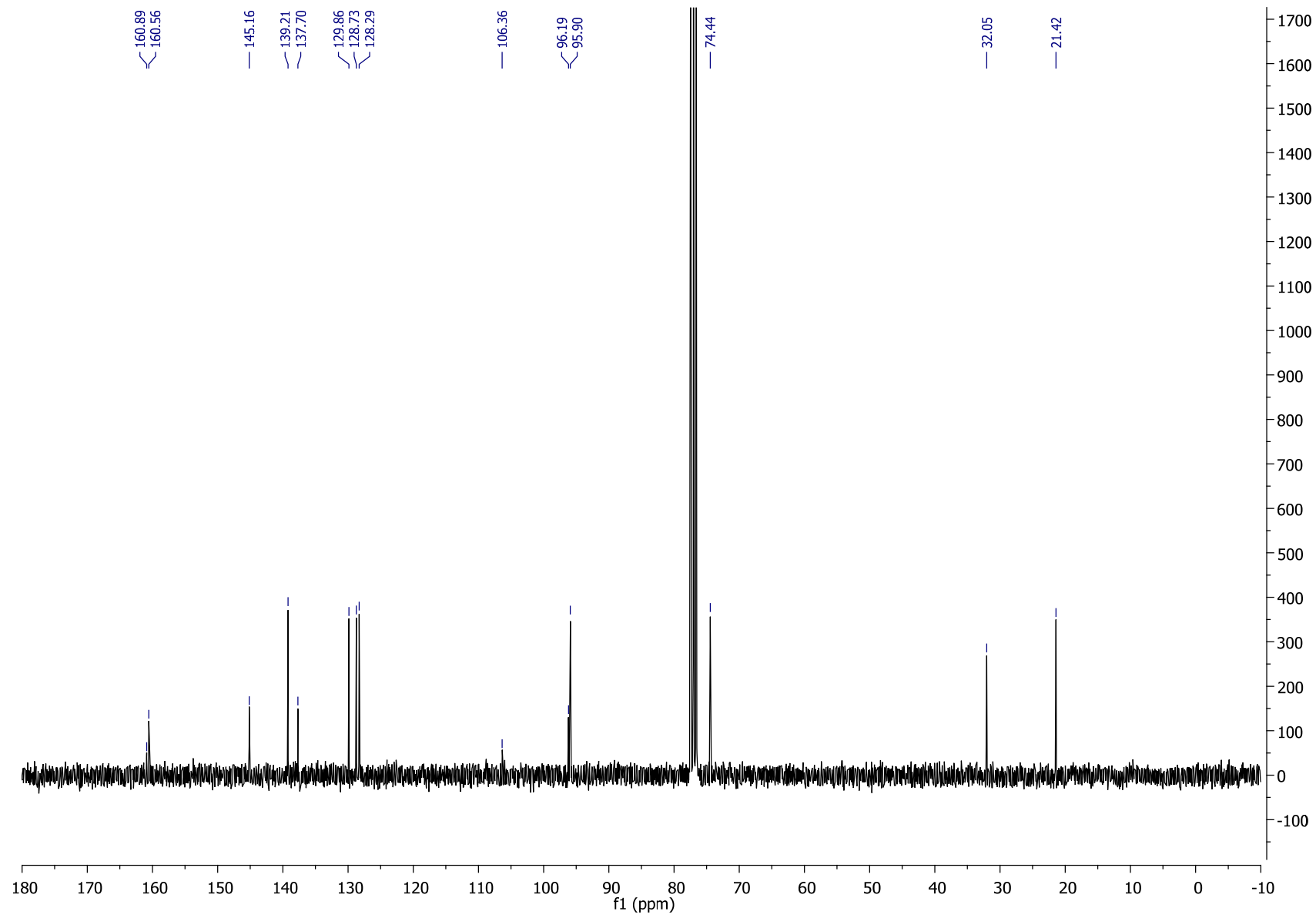
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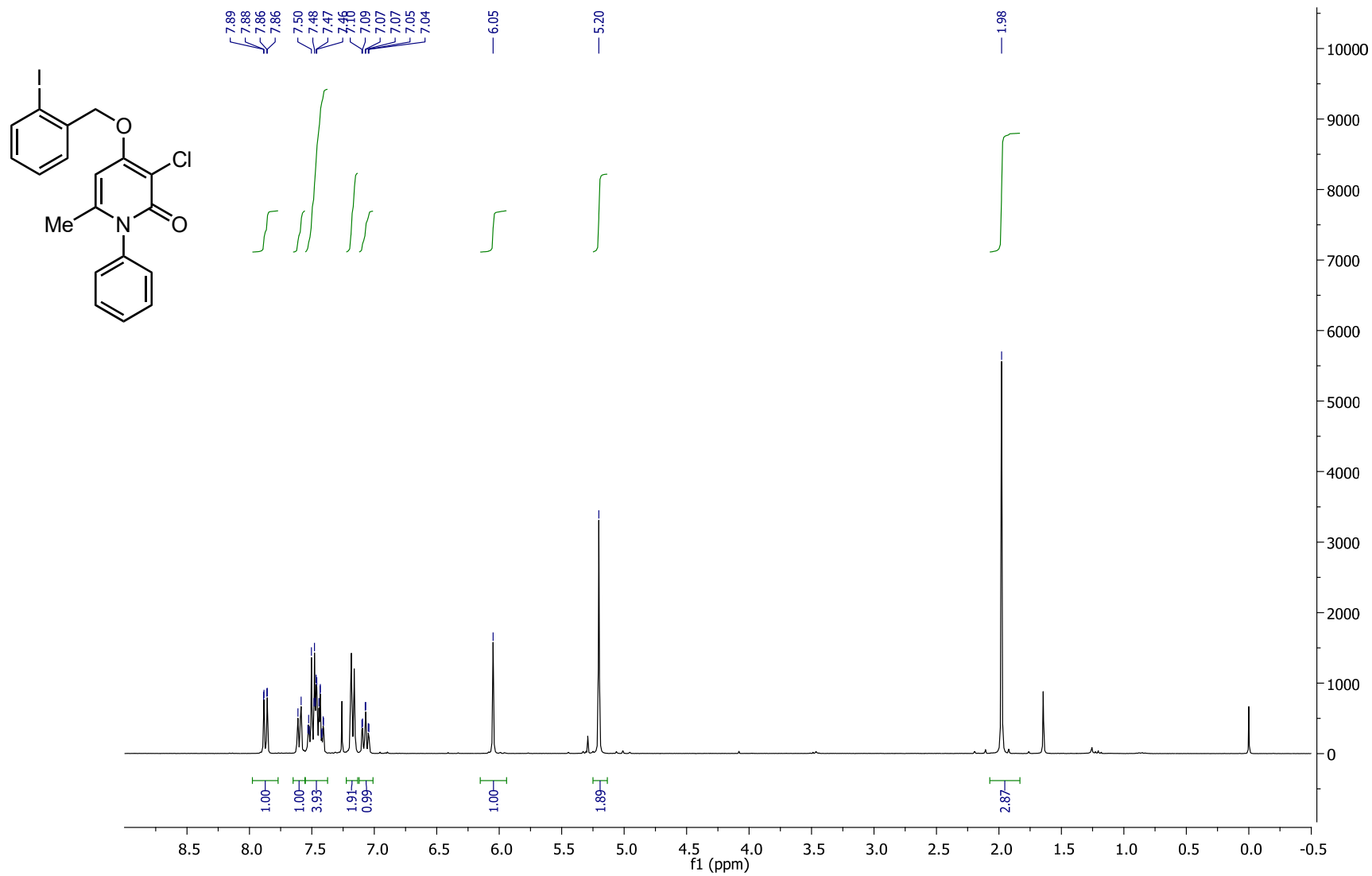
3-Chloro-4-((2-iodobenzyl)oxy)-1,6-dimethylpyridin-2(1H)-one, 7

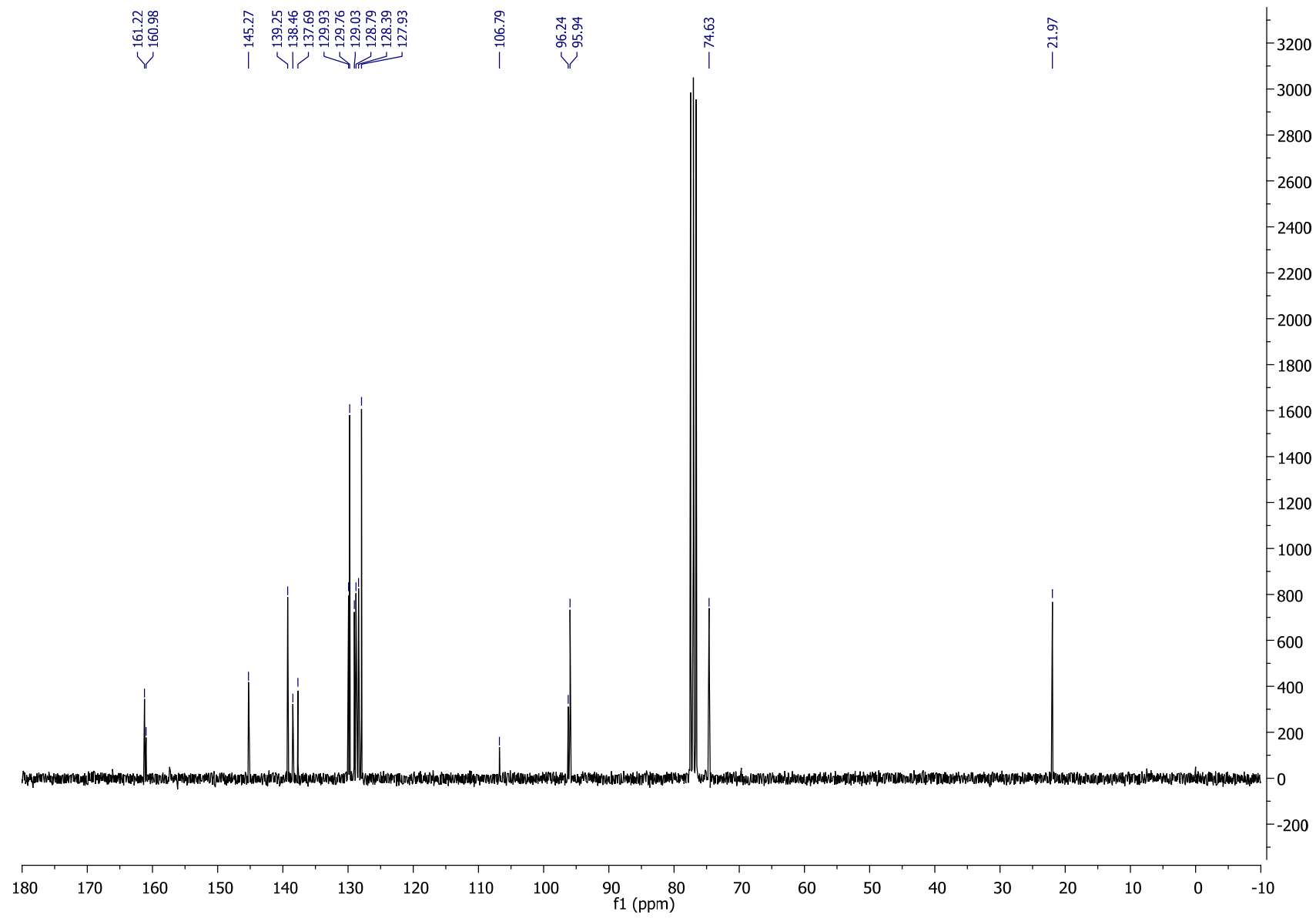




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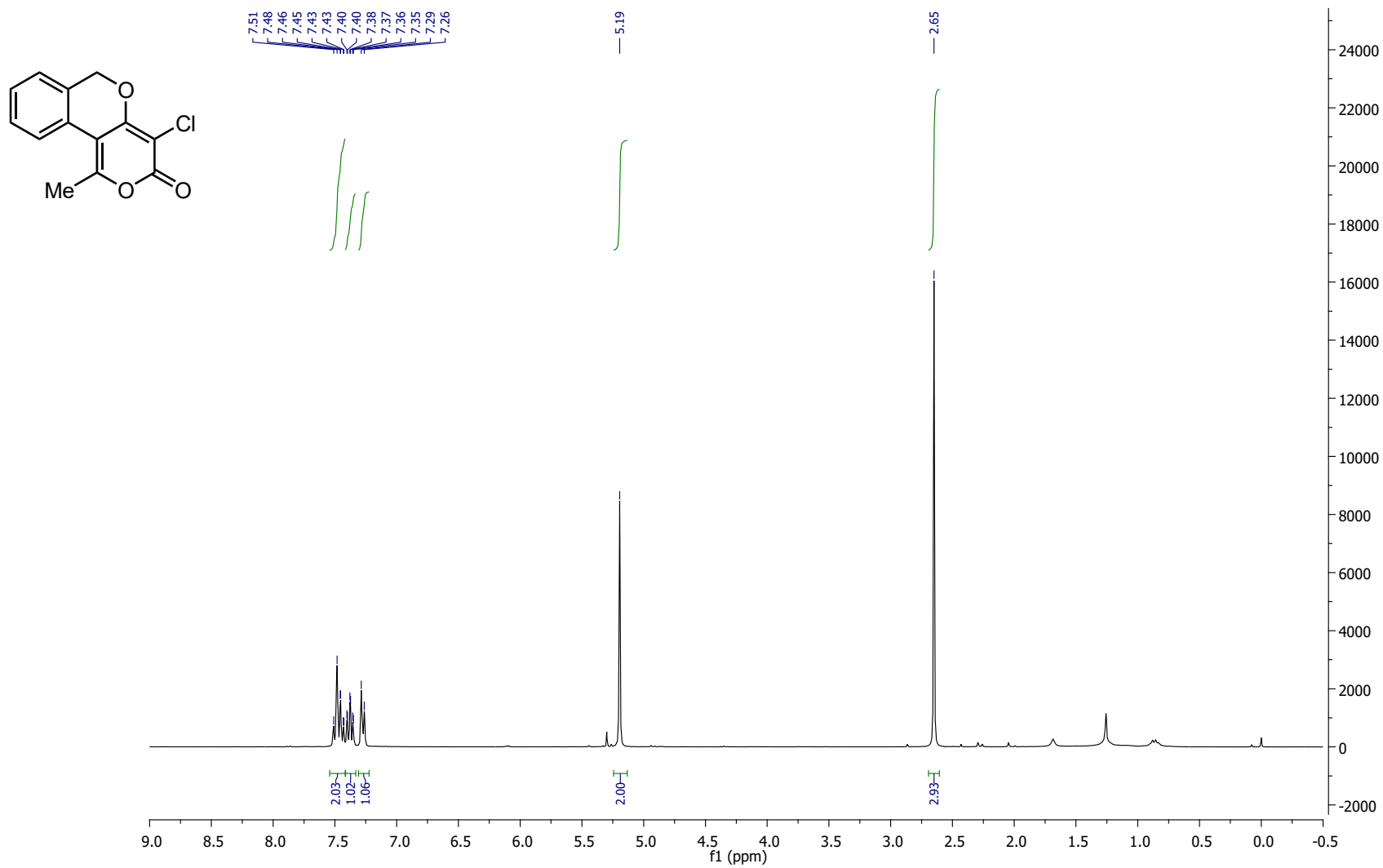


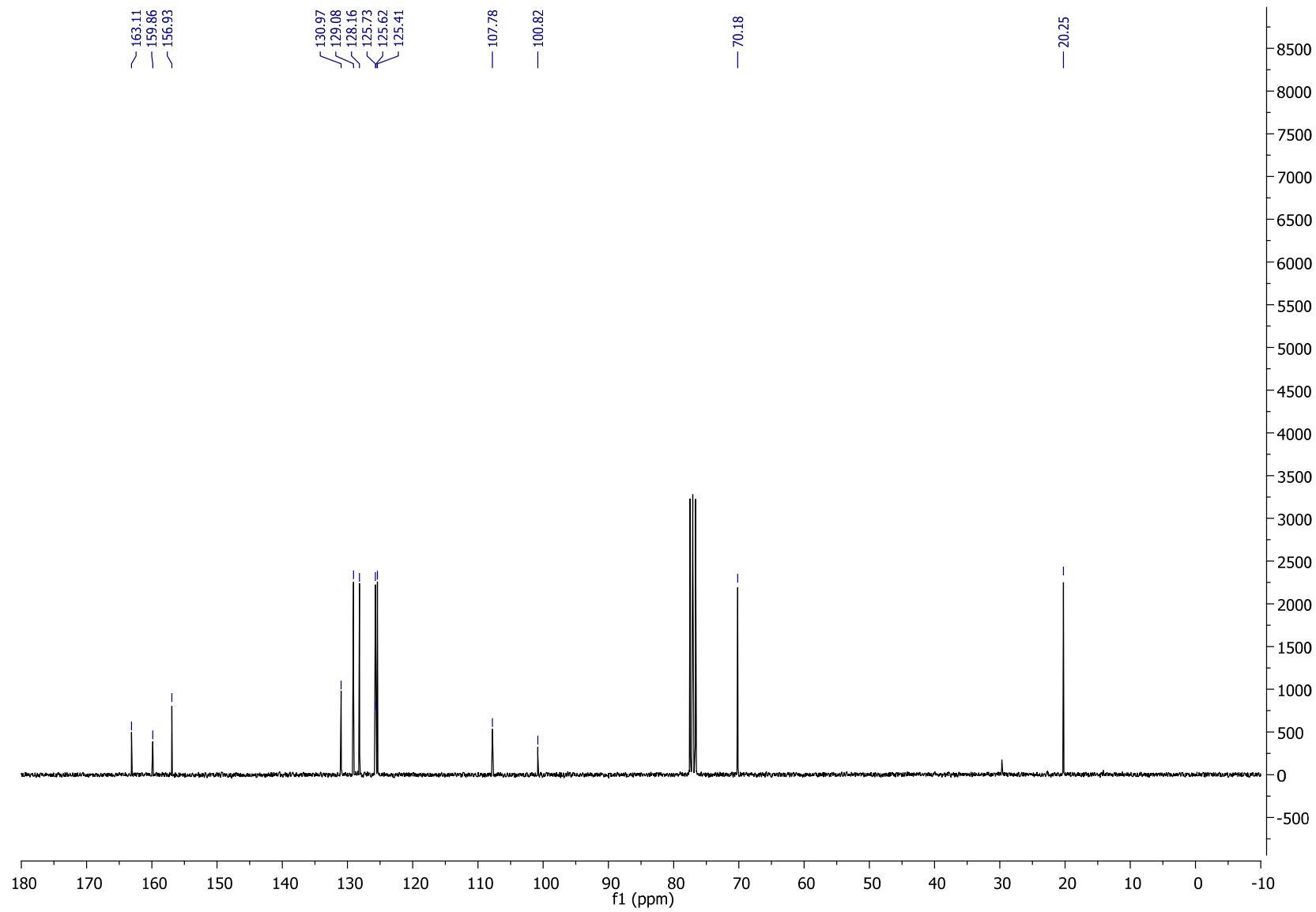


S34

Direct Arylation Products (2c, 9-14)

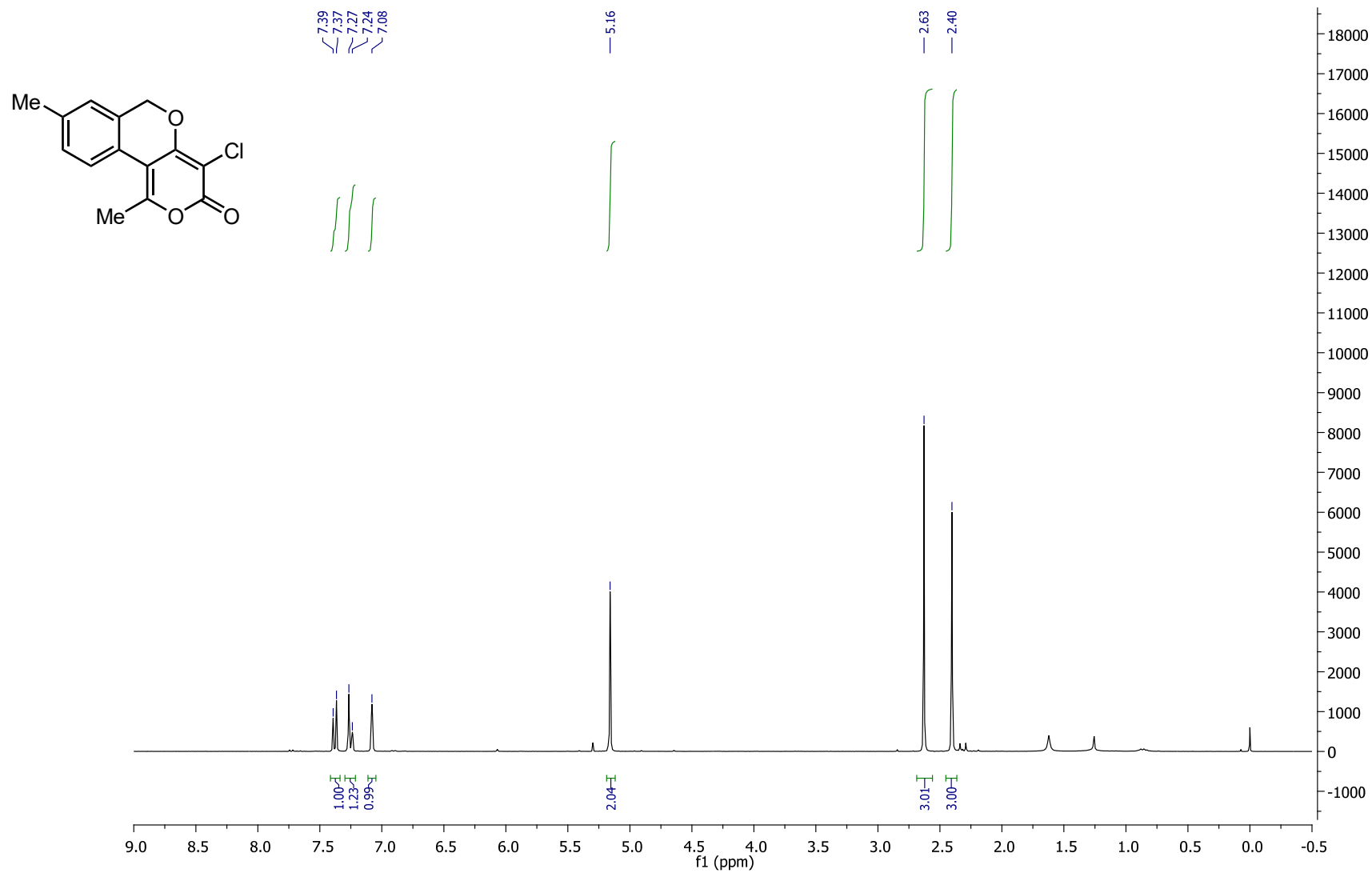
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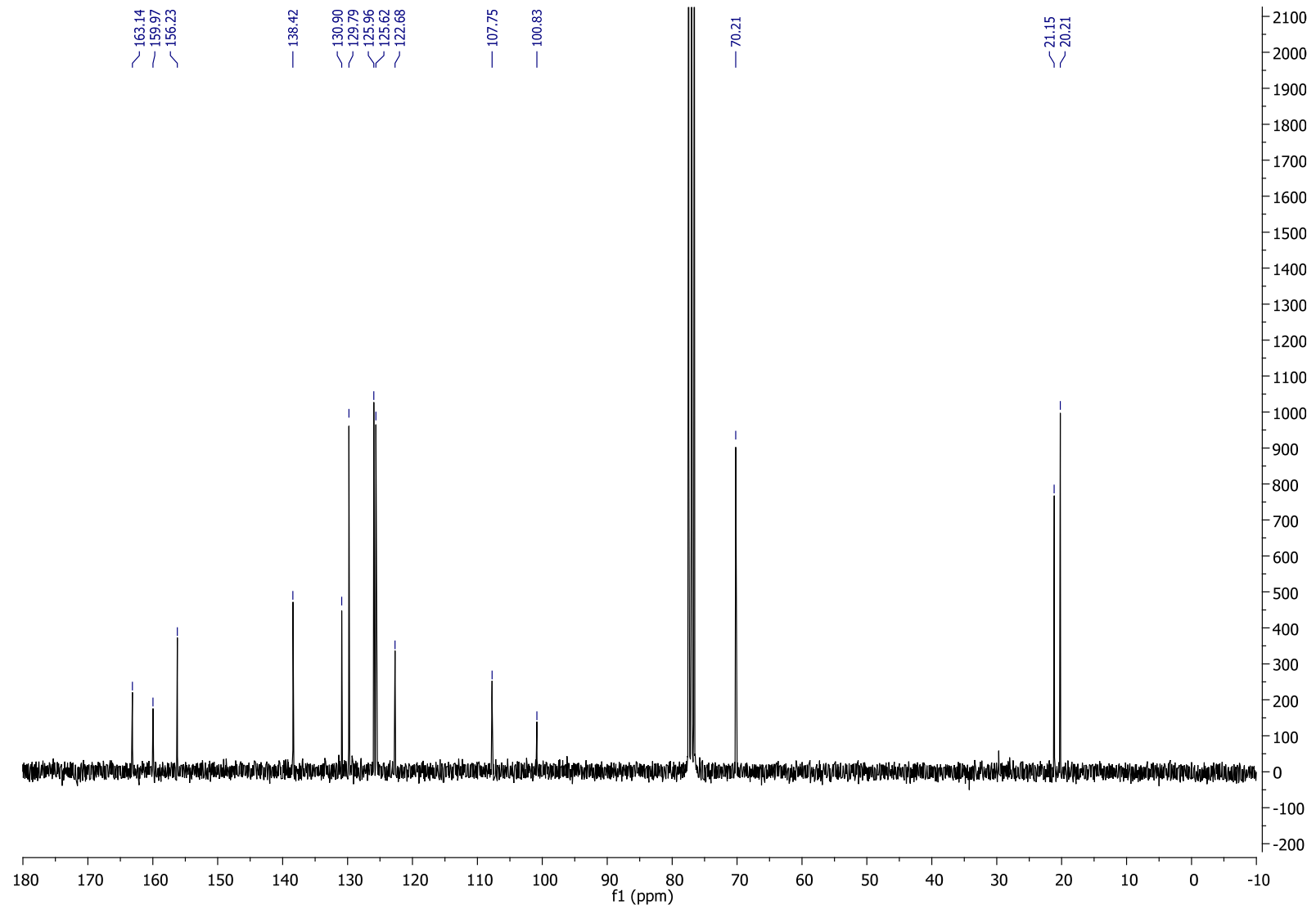




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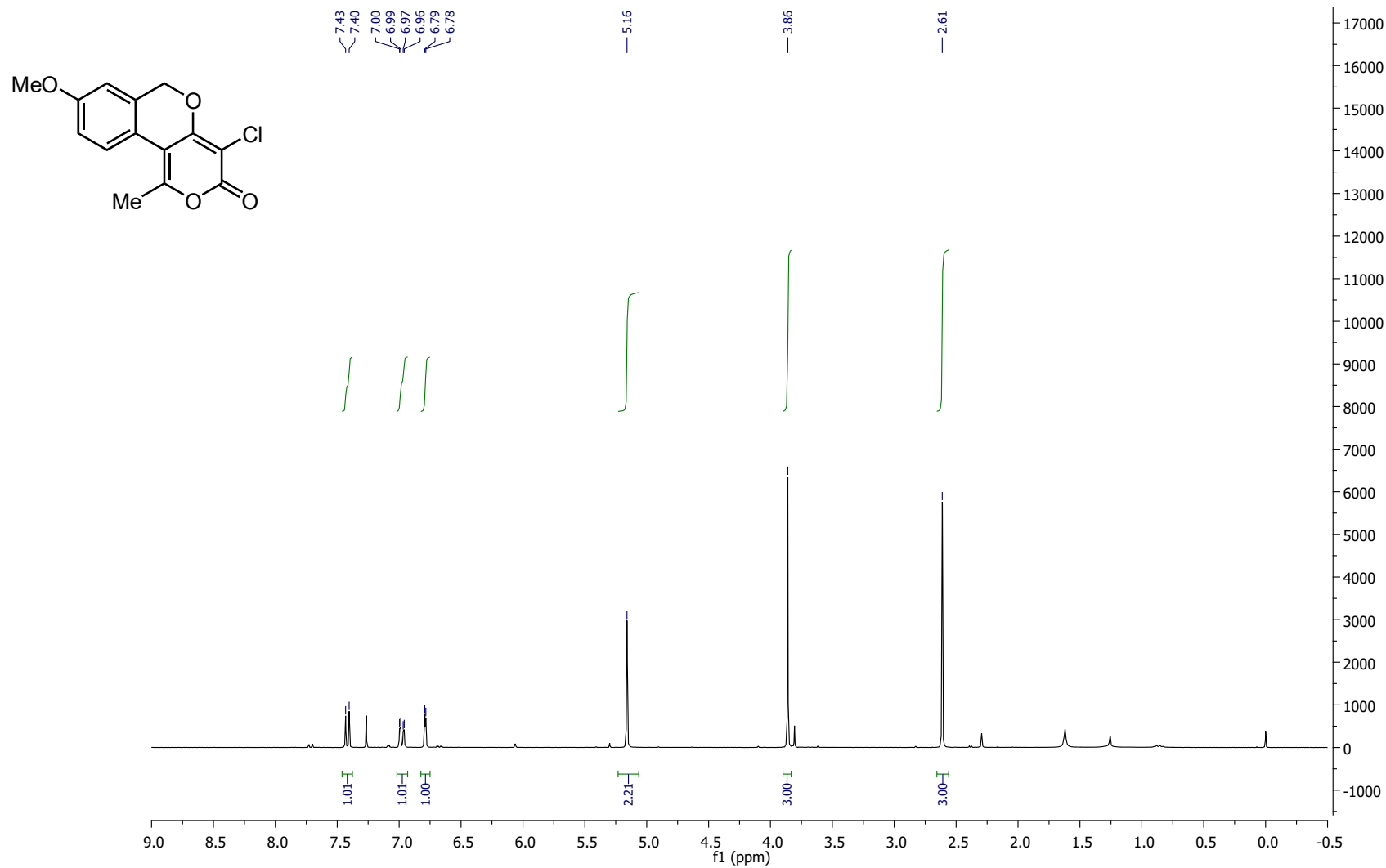
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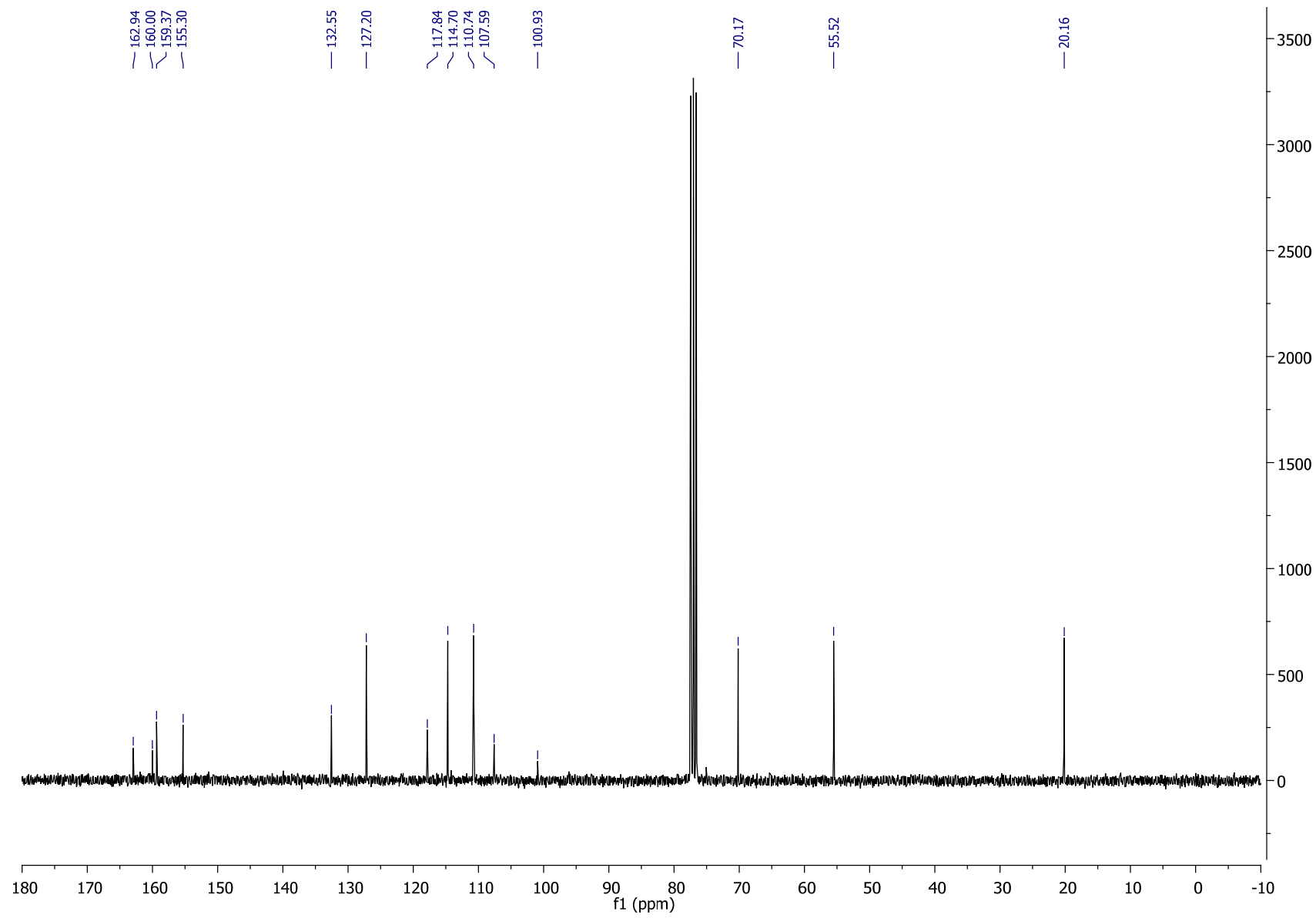




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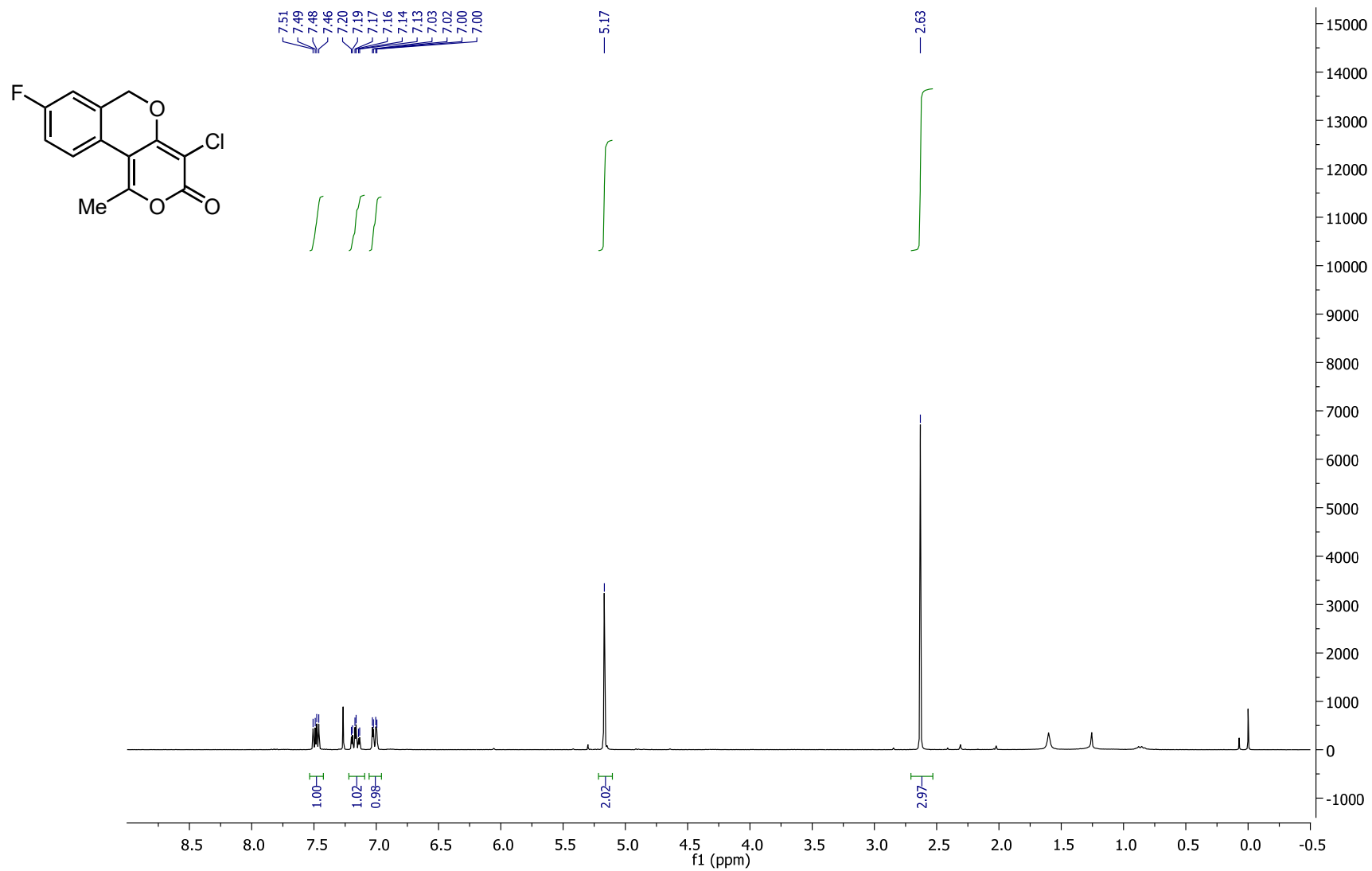
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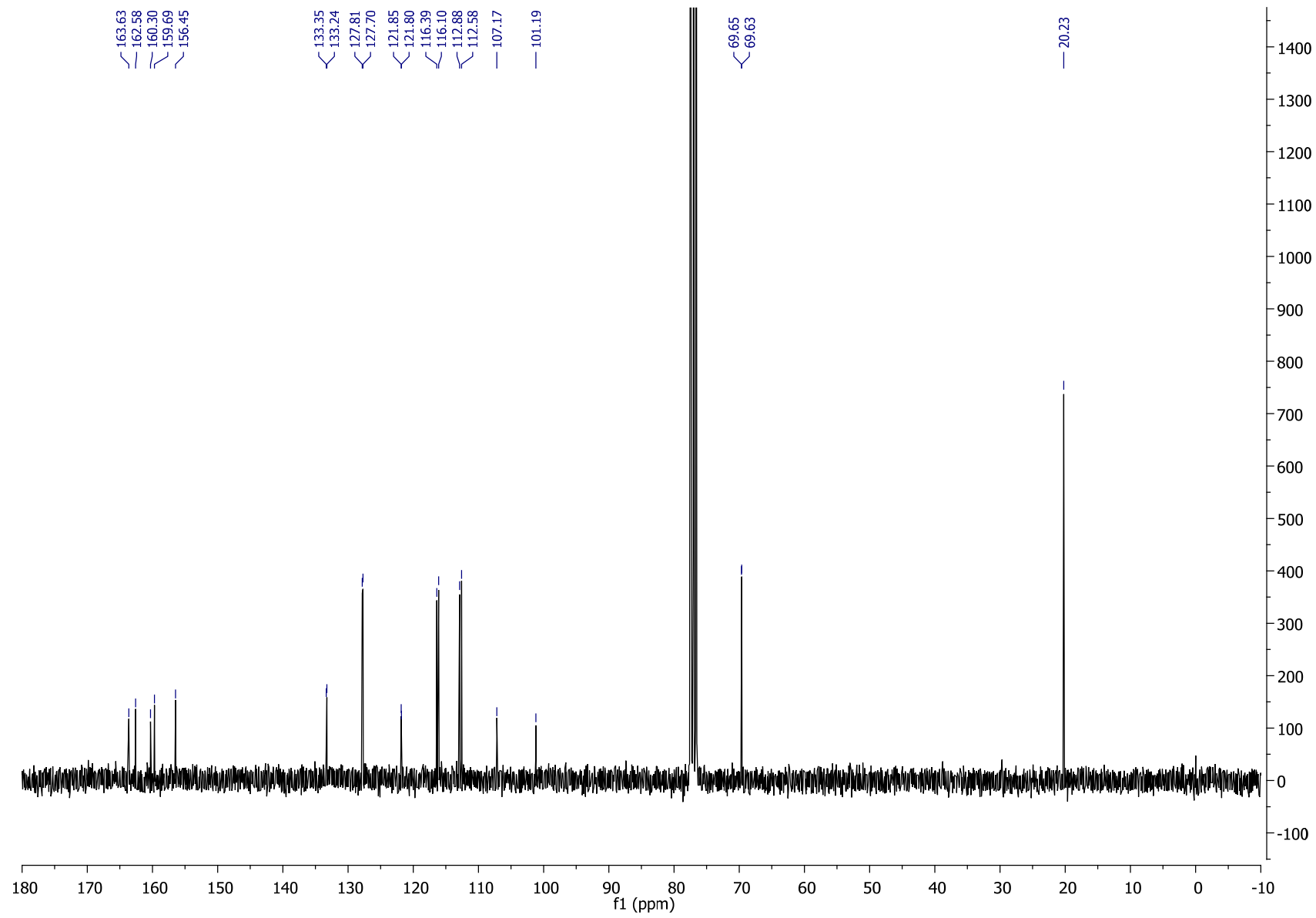




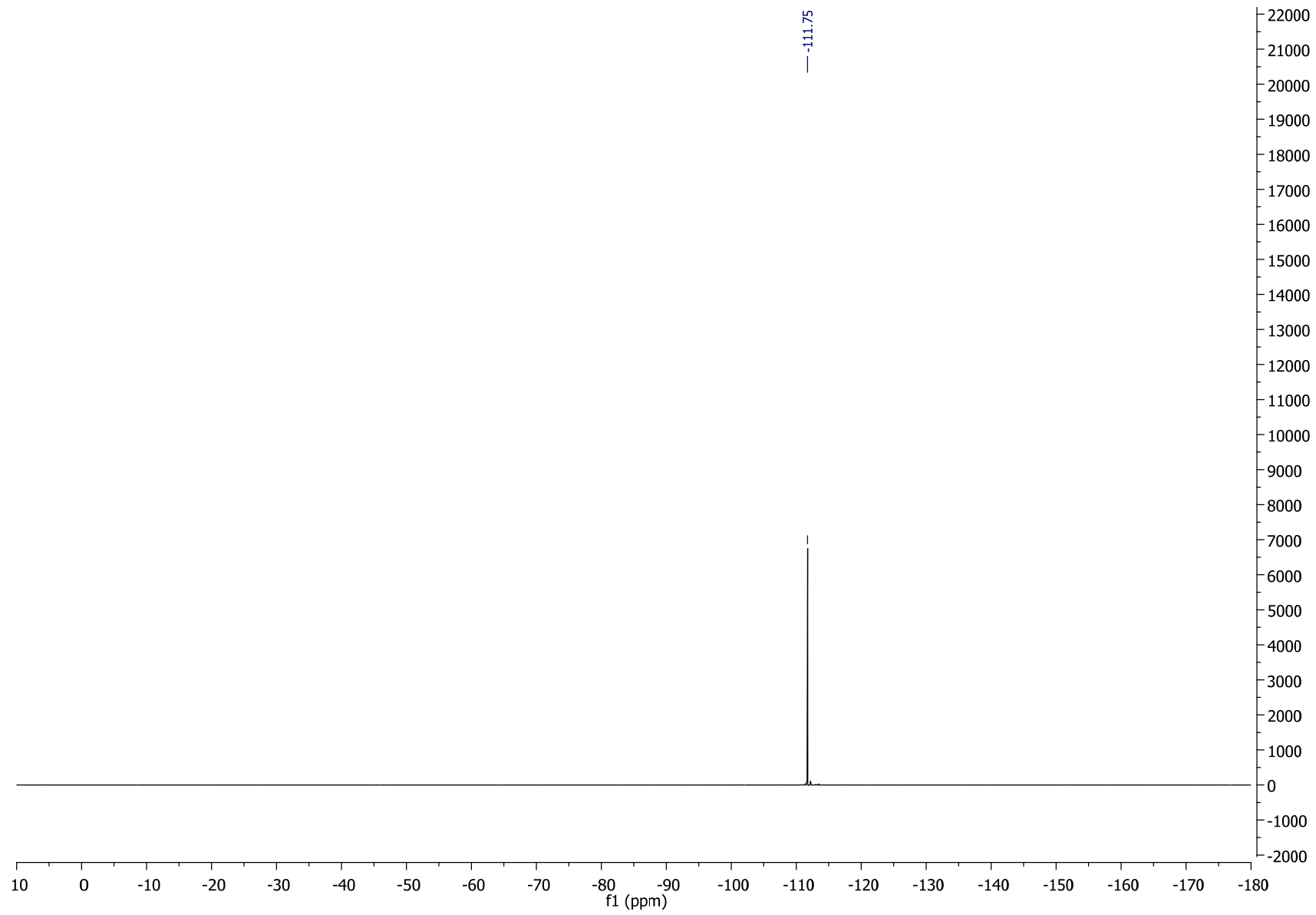
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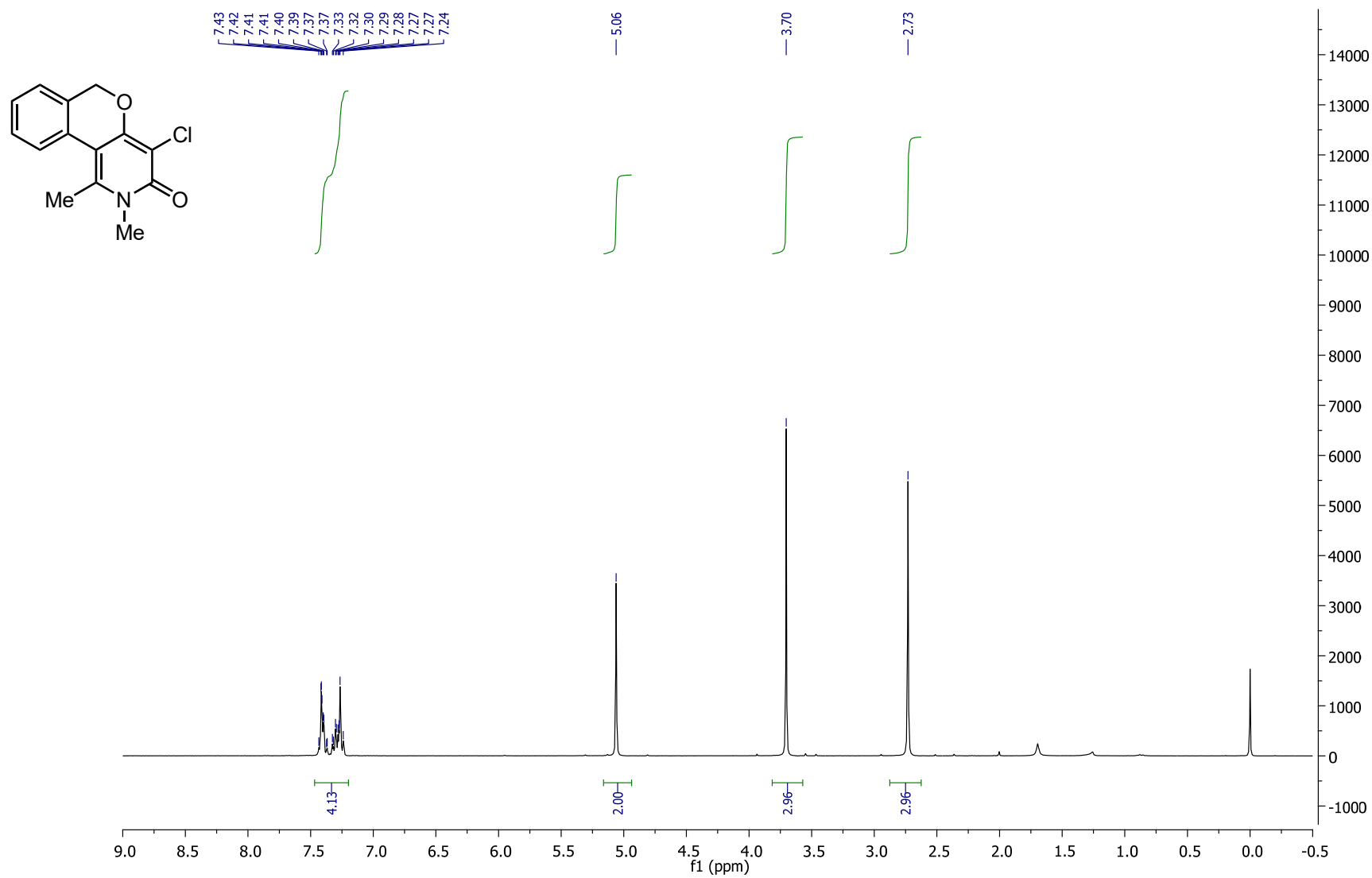


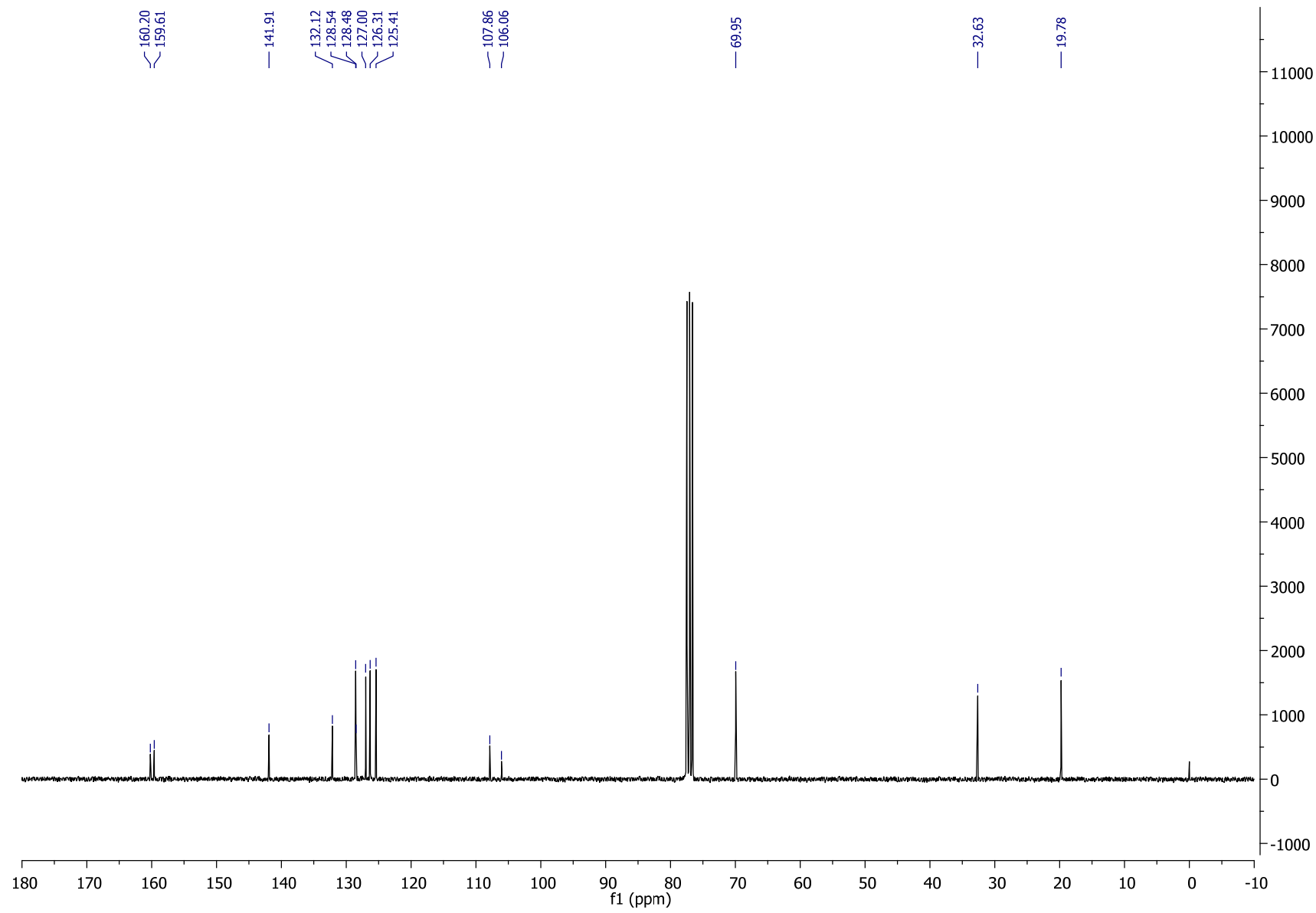
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S43

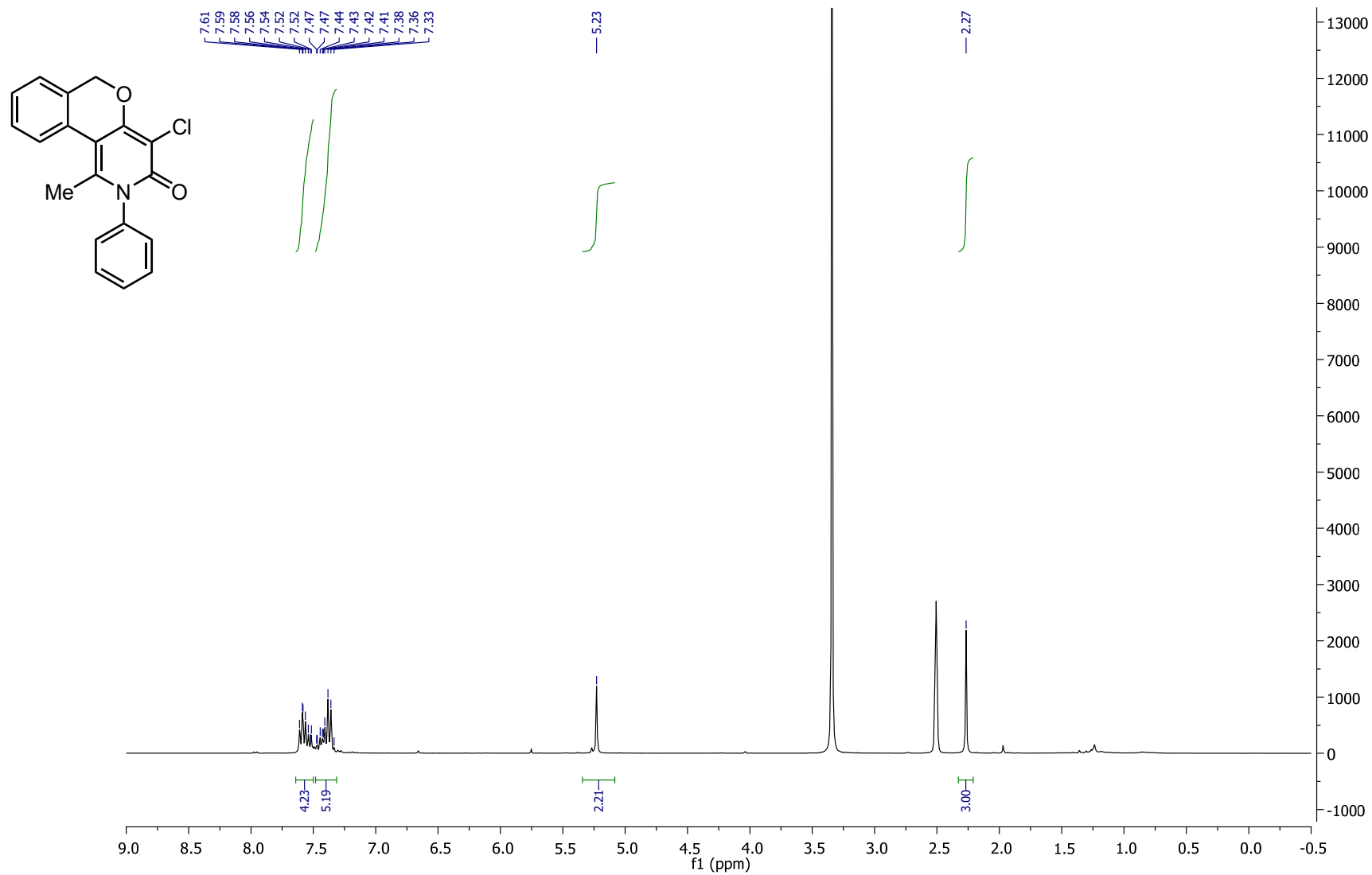
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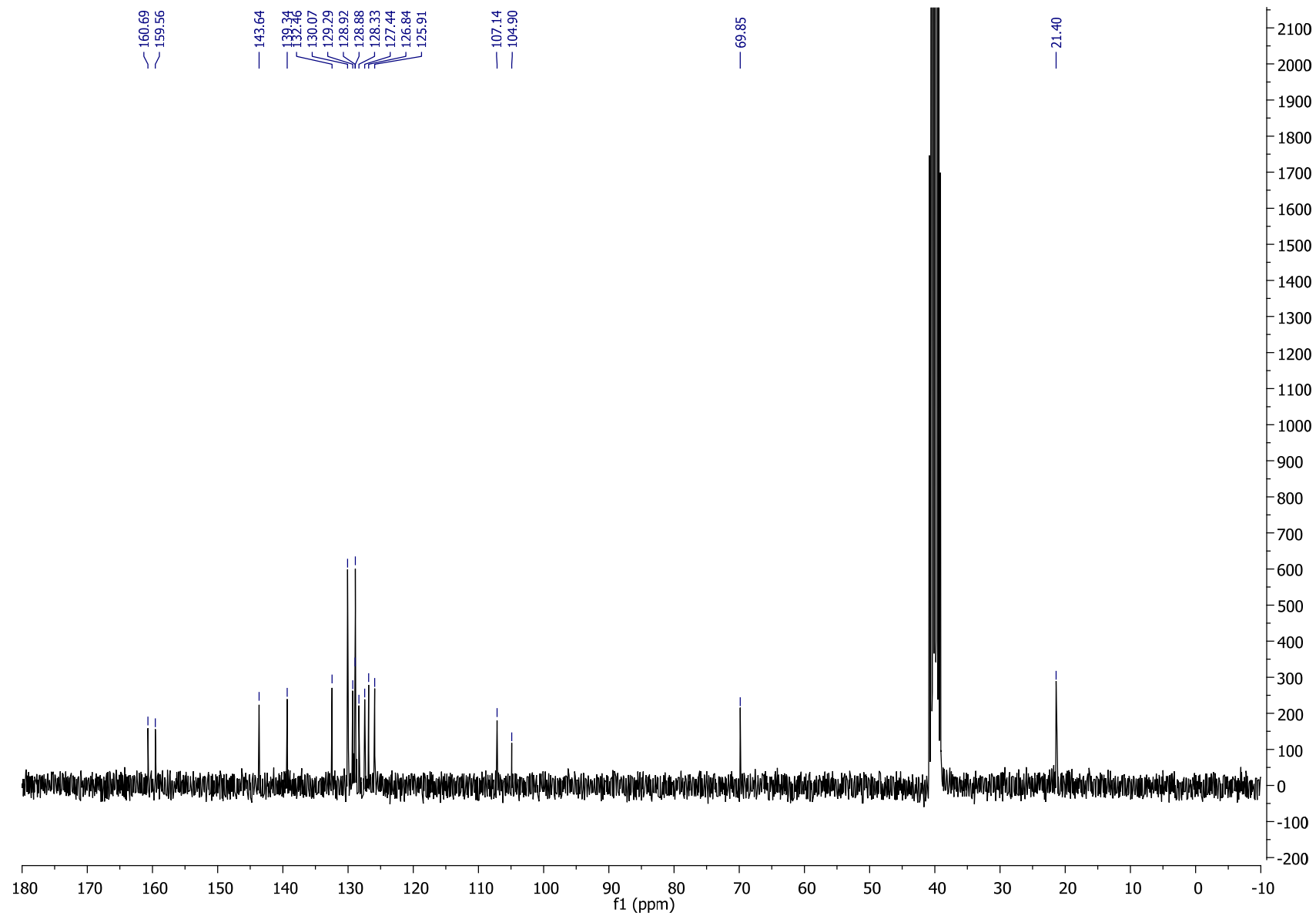




S45

4-Chloro-1-methyl-2-phenyl-2,6-dihydro-3H-isochromeno[4,3-c]pyridin-3-one, 14

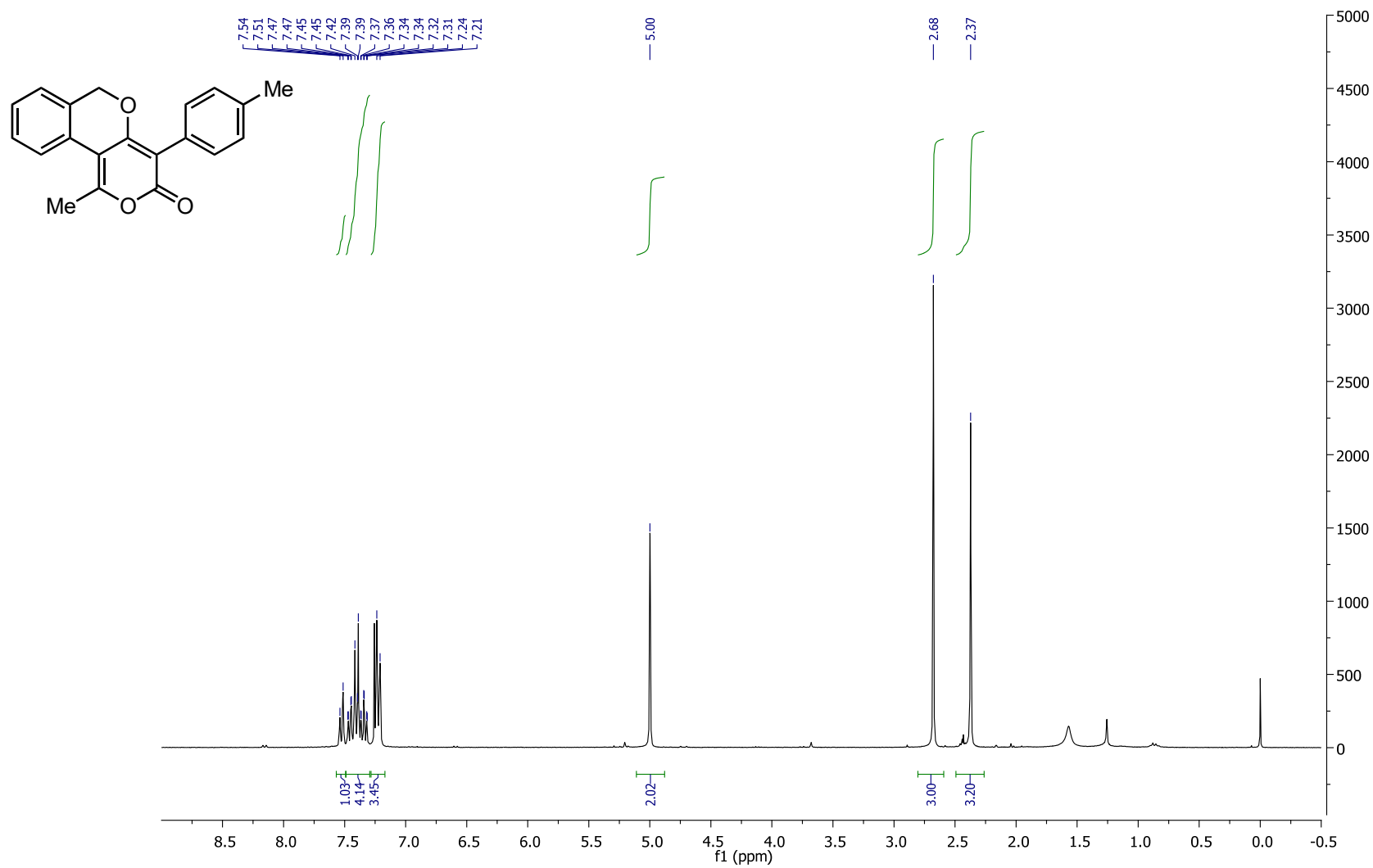


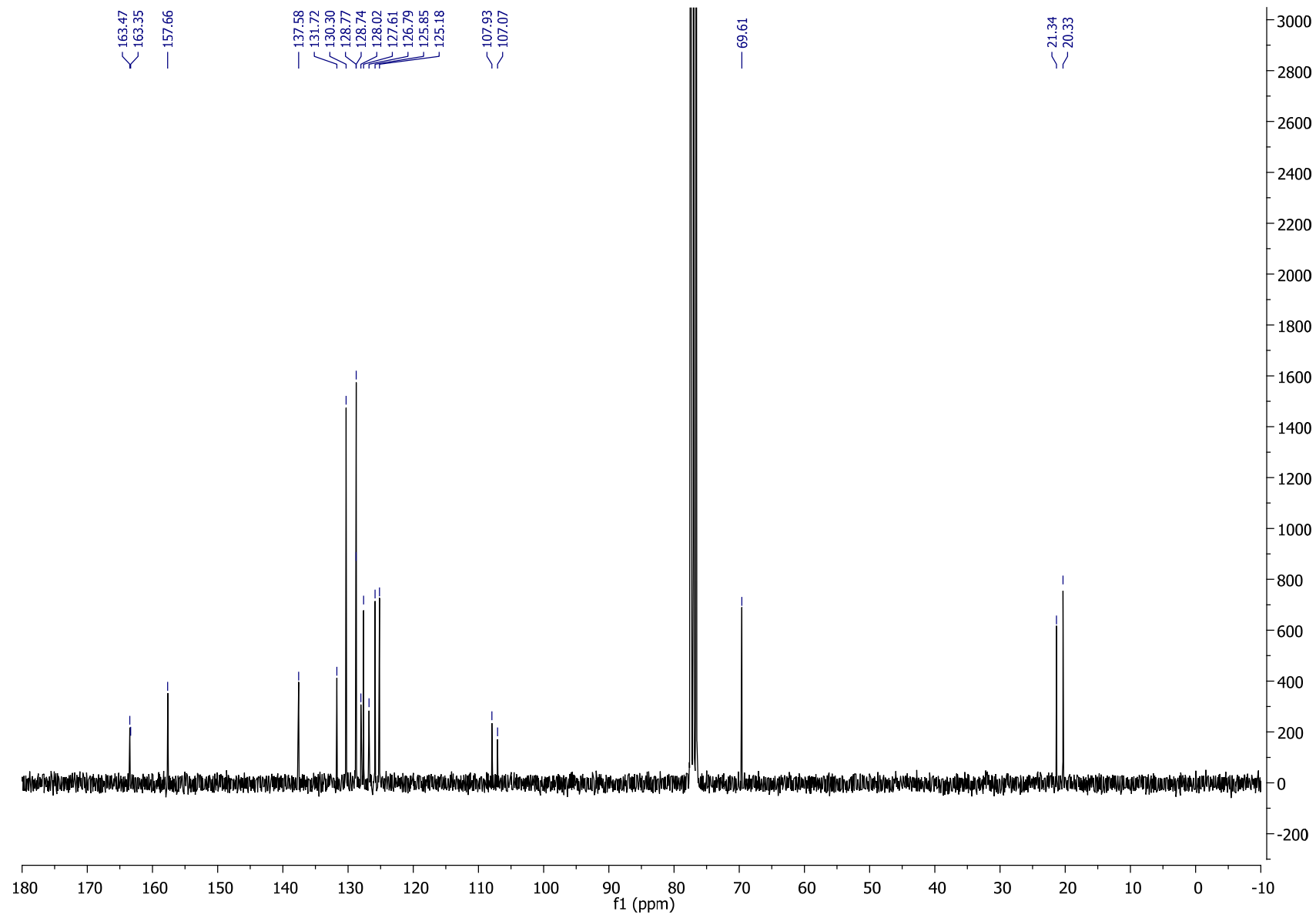


S47

Suzuki-Miyaura Cross-Coupling Products (15-16)

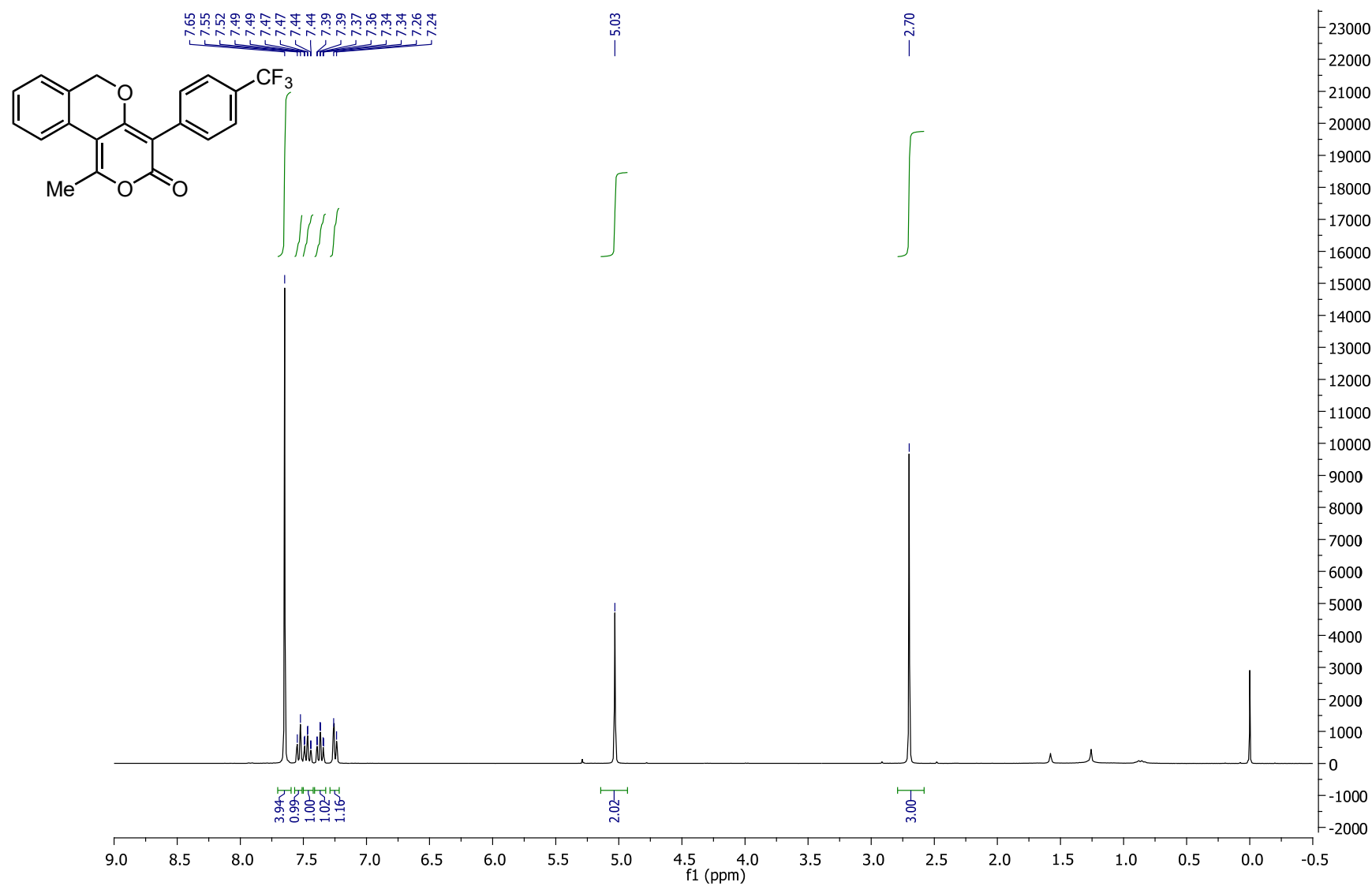
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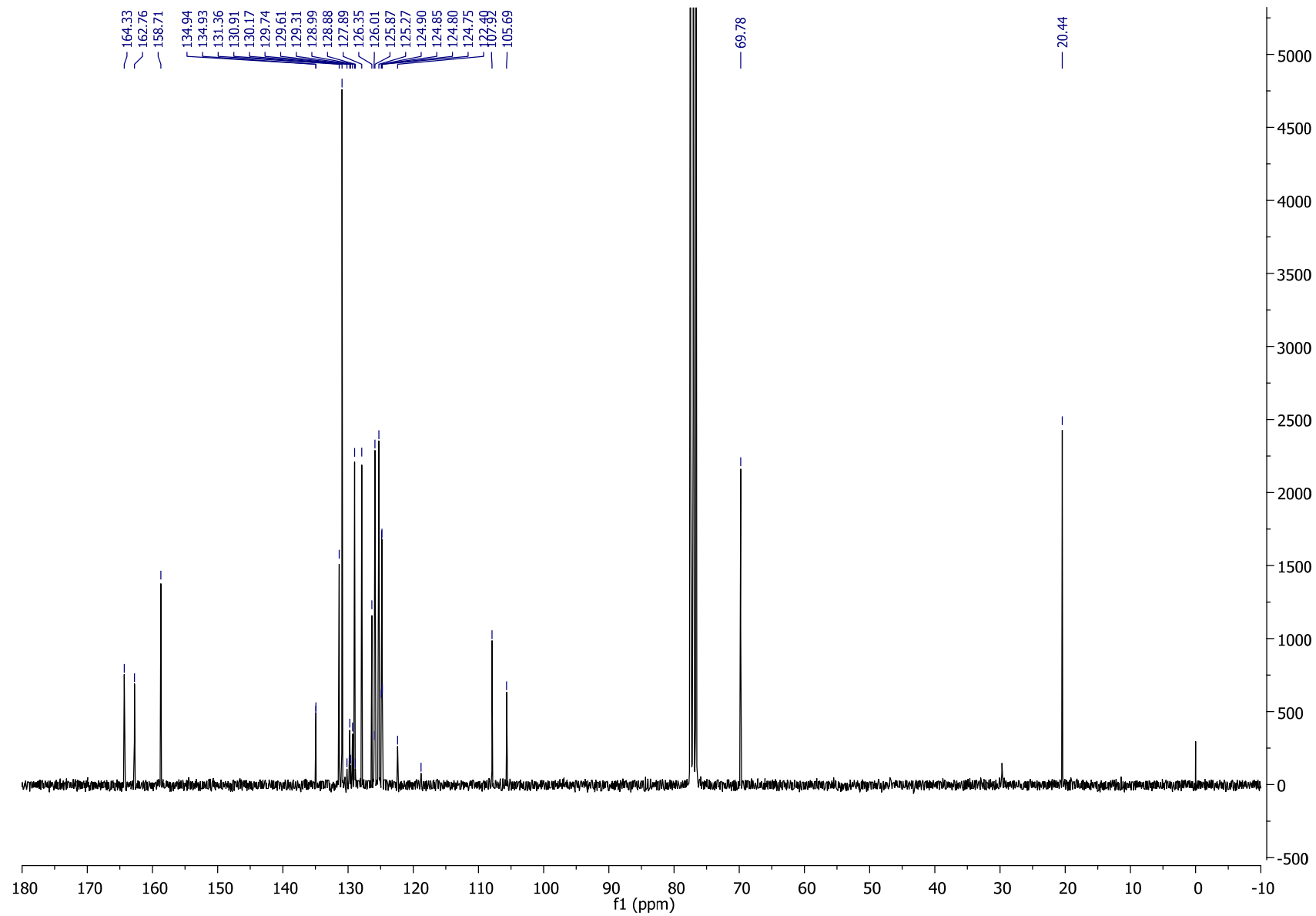




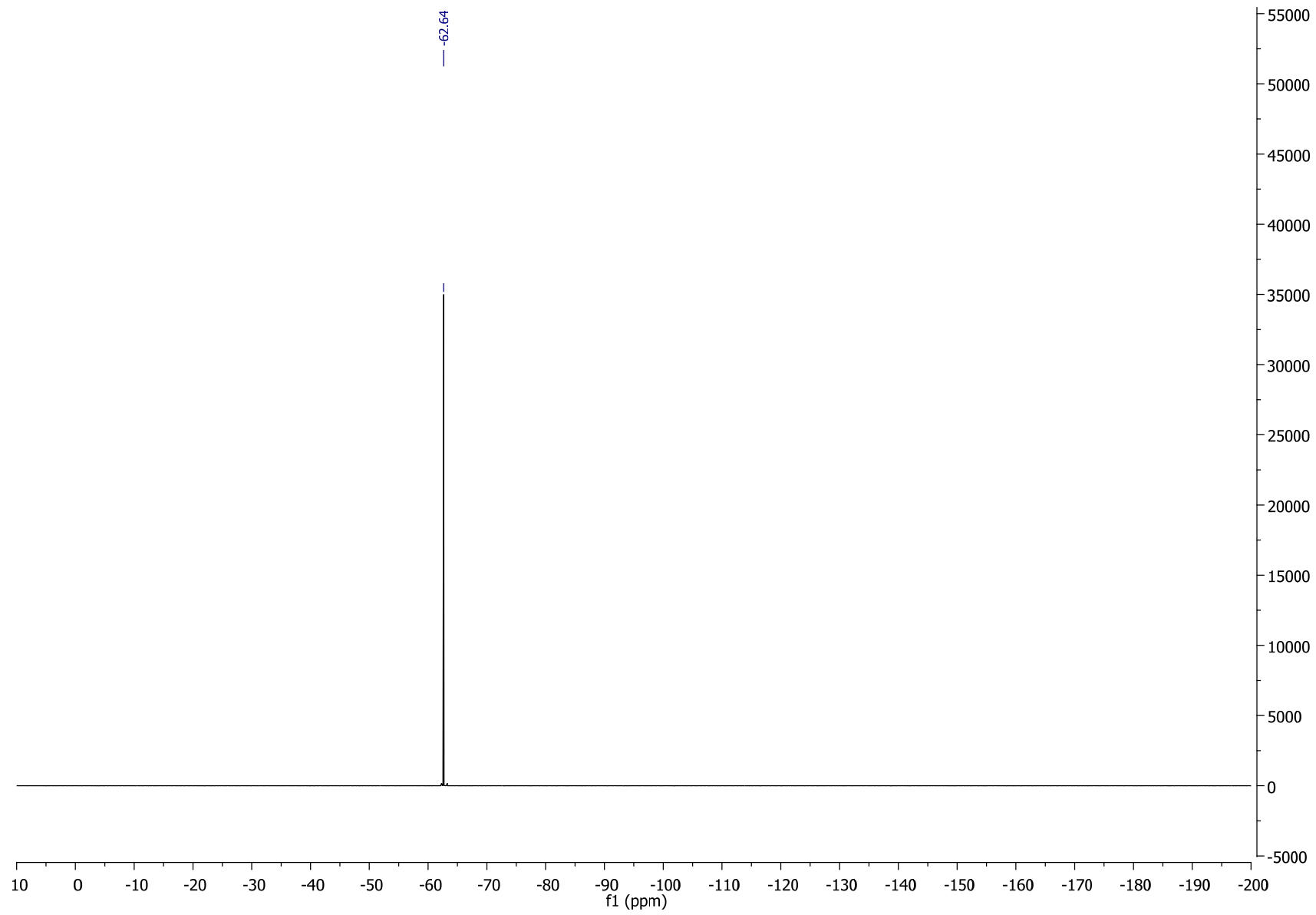
S49

1-Methyl-4-(4-(trifluoromethyl)phenyl)-3H,6H-pyrano[4,3-c]isochromen-3-one, 16





S51



S52