Regioselective synthesis of oxepinones and azepinones by gold-catalyzed cycloisomerizations of functionalyzed cyclopropyl alkynes

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Electronic Supplementary Information

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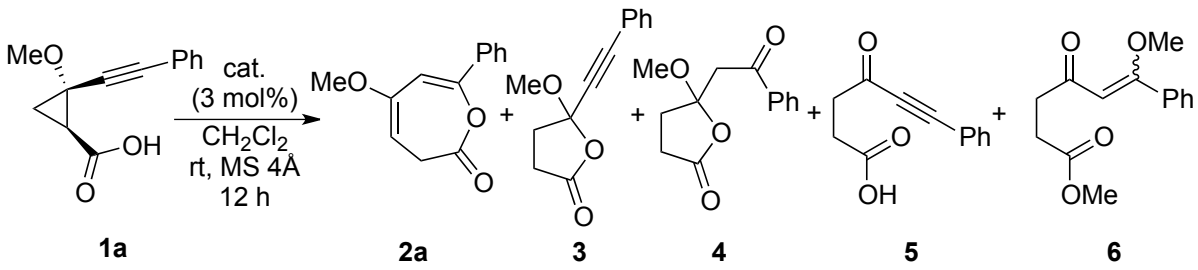
1. Optimization of the Reaction Conditions

A selected set of the tested conditions is displayed on table ESI-1.

Table ESI-1 Optimization of the reaction conditions (I)



Entry[a]	cat.	**2a**	**3**	**4**	**5**	**6**
1	$Ph_3PAuCl/AgSbF_6$		54		7	
2	$Ph_3P_3AuNTf_2$	55				15
3	$AgSbF_6$				80	
4	$(p\text{-}CF_3C_6H_4)_3PAuNTf_2$	27				
5	JohnphosAuNTf$_2$	38		<10		
6	IPrAuNTf$_2$	54		11[b]		3[b]
7	IPrAuNTf$_2$[c]	69				13[b]
8	$Ph_3PAuCl/AgOTs$[c]	65		9		6
9	IPrAuCl/AgOTs[c]	90				
10	IPrAuCl/AgOTs[d]	86				
11	AgOTs	<10				

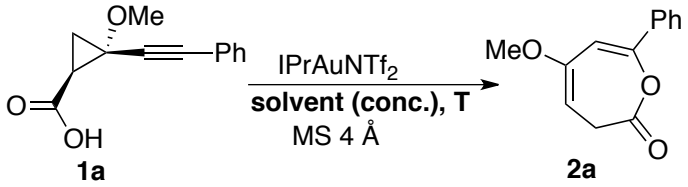
[a] Isolated yields. [b] Estimated by ^{1}H-NMR using hexamethylbenzene as internal standard. [c] The catalyst system was lyophilized prior to carrying out the reaction. [d] Only the silver salt was lyophilized prior to carrying out the reaction.

First essays using $Ph_3PAuCl/AgSbF_6$ as catalyst system did not lead to the expected oxepinone; instead they caused the opening of the cyclopropane ring leaving the triple bond unaltered and giving rise mainly to five-membered lactone **3**, with 4-oxo-6-phenyloct-5-ynoic acid **5** as byproduct (entry 1). Gratifyingly, when we switched to $Ph_3PAuNTf_2$ as catalyst[1] we obtained the desired seven-membered heterocycle **2a** as major product accompanied with the acyclic ester derivative **6** (entry 2). To determine whether this variation in the selectivity was caused by the change in the counterion or by the presence/absence of silver in the reaction mixture, we treated **1a** with catalytic amounts of $AgSbF_6$ and we observed complete and selective conversion to **5** (entry 3). This result shows how silver hexafluoroantimonate is able to catalyze the transformation of **1a** into **5** and, therefore, its presence should be avoided in order to get selective formation of oxepinone **2a**. As a consequence, preformed cationic gold catalysts were employed for evaluating the influence of different ligands. A considerable improvement in the isolated yield of the oxepin-2-one was achieved by modifying the

electronic properties of the ligand, by moving from an electron-deficient phosphine ligand to an electron-rich phosphine ligand and, then, to a NHC carbene ligand (entries 4-6). However, a five-membered lactone with concomitant hydration of the triple bond **4** as well as previously observed ester derivative **6** appeared as minor byproducts. A great advance was achieved when the catalyst was lyophilized (see below) prior to carrying out the reaction, which improved both the yield and the selectivity of the reaction (entries 6 vs 7). On the other hand, slightly lower yield of **2a** and selectivity were reached when the Ph_3PAuCl/AgOTs system was tested (entry 8). A final survey revealed that the combination IPrAuCl/AgOTs led to a remarkable 90% isolated yield of **2a** (entry 9). As suggested by one of the referees, considering that lyophilisation only removes water from the catalyst and gold complexes are usually not hygroscopic, it seems therefore essential to remove water from the hygroscopic silver salt by lyophilisation (otherwise the amount of wet silver salt contains less silver, not all the gold catalyst is activated, the conversion becomes slower and incomplete). A test carried out with lyophilised AgOTs and non-lyophilised gold complex led to a similar result, within the experimental error (86% isolated yield of **2a**, entry 10). In these cases the presence of silver was not detrimental for the selectivity, as AgOTs turned out to be almost inert (entry 11).

During the catalyst optimization, the reactivity of carboxylic acids **1** was tested under very different conditions. Optimization of the reaction conditions is indeed a dynamic process where different reaction parameters are analysed, occasionally in a simultaneous manner. Thus, an extensive optimization of temperature, solvent and substrate concentration was carried out with lyophilized $IPrAuNTf_2$, which was the best catalyst system that we had found so far. The main results are listed in Table ESI-2. It is worth to notice that with such catalyst compound **2a** was isolated in 27% yield (entry 10) when the reaction was carried out at 0 ºC and no by-products could be identified.

Table ESI-2 Optimization of the reaction conditions (II)



Entry	Solvent[a]	Conc.	T	Yield[b]
1	DCM	0.05 M	rt	69
2	DCE	0.05 M	rt	67
3	THF	0.05 M	rt	Traces
4	Hexane	0.05 M	rt	Traces
5	MeCN	0.05 M	rt	Traces
6	Toluene	0.05 M	rt	-
7	DMF	0.05 M	rt	-
8	DCM	0.025 M	rt	21
9	DCM	0.1 M	rt	26
10	DCE	0.05 M	0 ºC	27
11	DCE	0.05 M	40 ºC	42
12	DCE	0.05 M	60 ºC	33
13	DCE	0.05 M	80 ºC	31

[a] DCM= CH_2Cl_2; DCE = $ClCH_2CH_2Cl$. [b] Isolated yield of **2a**.

However, after establishing the system IPrAuCl/AgOTs as the best catalyst, we had not carried out lower temperature experiments. Therefore, attending at a request made by one of the referees, we decided to carry out two experiments at 0 ºC and at –20 ºC. Both reactions led to **2a** as major product (42-73% yield) and no traces of products of type **II** were observed neither in the crude nor after purification. In both cases, compound **4** was observed, but not isolated (10-25%, estimated yield).

On the other hand, it is also worth to remark that molecular sieves are necessary; during our initial tests for the optimization of the reaction conditions the formation of higher amounts of compounds **4** (which results from hydration of the triple bond), **5** or **6** (both of them come from hydrolysis of the quaternary cyclopropyl carbon) was observed. The amount of such by-products was reduced or suppressed by the employment of molecular sieves. A reaction carried out recently (at request of one referee) with model compound **1a** under the optimized reaction conditions but without the presence of molecular sieves resulted in 38% of **2a** and a 58% of **4**.

A commentary about the remarkable effect of the silver salt seems also required. There are precedents for counter-ion effects in Au/Ag catalysis[2] and it is usually explained on the basis of the different coordinating properties of the anion. Also, the long-overlooked "silver effect" in gold(I) catalysis has been recently confirmed as crucial and real[3]. Thus, we have observed that, depending on the reaction analysed, the effect of the counter-ion in the selectivity may be almost negligible,[4] minor,[5] or play a crucial role.[6] On the other hand, counter-ion effects in silver catalysis are also known.[7] In our case, an exhaustive study of the counter-ion effect has not been carried out and the fact that non-previously-lyophilized $AgSbF_6$ led exclusively to compound **5** (which was probably formed by hydrolysis of the acetal moiety in **3**), while the starting material is almost quantitatively recovered in the presence of AgOTs seems to indicate that the different hygroscopic character of both catalysts may have played also some role in the reaction outcome.

2. Proposal to Explain the Lack of Reactivity of *trans*-DA Alkynylcyclopropanes

As stated in the experimental part (see below), the cyclopropanation reaction, carried out to prepare alkynylcyclopropanecarboxylic esters **18** (which are later hydrolysed to the corresponding alkynylcyclopropanecarboxylic acids **1**, used as starting materials), takes place diastereoselectively leading to the desired *cis*-isomer as major component while the *trans*-isomer is the minor component.[8]

For compound **1a**, the separation of the diastereomers was carried at the ester stage (compound **18a**).

It was found that the *trans*-isomer **1a** remains inert under the optimized reaction conditions (listed in Table ESI-1, entry 9), being recovered once the reaction has ended. Two conclusions were reached from this observation:

1) A mechanistic conclusion: The lack of reactivity of the *trans*-isomers is probably due to the fact that the carboxylic group is not close enough to the triple bond because of the rigidity imposed by the cyclopropane ring, which inhibits the nucleophilic attack of the carboxylic group to the activated triple bond. This fact also suggests that, under the optimized conditions, the nucleophilic attack should take place prior to the cyclopropane ring opening, thus supporting *Via A* pathway; on the contrary, if the opening of the cyclopropane ring takes place prior to the nucleophilic attack (*Via B*), the loss of the rigidity should also allow the transformation of the *trans*-isomer into oxepinone **2a**, which does not occur.

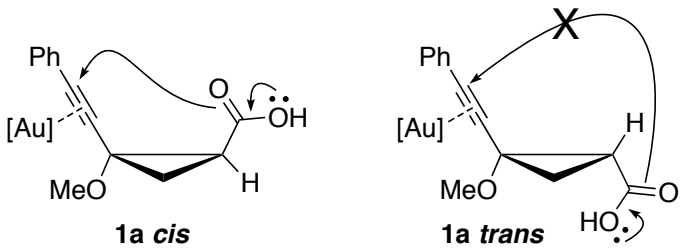


Figure S1. Proposal to explain the lack of reactivity of *trans*-DA alkynylcyclopropanecarboxylic acid **1a**

2) A practical conclusion: Separation of the diastereomers was unnecessary, as only one of them reacted. Therefore, once the optimized conditions were reached, the reactions to establish the scope of the transformation were carried out with the mixture of both diastereomers. The reported yields in Table 1 and Scheme 3 were determined taking into account this lack of reactivity of the *trans*-isomers.

3. Experimental Part

3.1. General Considerations:

All reactions involving air sensitive compounds were carried out under inert atmosphere (Ar or N_2, ≥ 99.99%). All glassware was oven-dried (120 °C), evacuated and purged with nitrogen. All common reagents and solvents were obtained from commercial suppliers and used without any further purification unless otherwise indicated. Gold catalysts $Ph_3PAuNTf_2$,[1] (*p*-$CF_3C_6H_4)_3PAuNTf_2$,[1] JohnphosAuNTf$_2$,[9] IPrAuNTf$_2$,[10] IPrAuCl[11] were prepared following previously reported literature procedures, and some of them were lyophilized prior to use (see Table ESI-1 for each case; see below for lyophilisation procedure). AgOTs was purchased from commercial supplies and, in some cases, lyophilized prior to use. Solvents were dried by standard methods.[12] Hexane (HxH), ethyl acetate and triethylamine were purchased as extra pure grade reagents and used as received. TLC was performed on aluminium-backed plates coated with silica gel 60 with F_{254} indicator; the chromatograms were visualized under ultraviolet light and by staining with $KMnO_4$ reagent and subsequent heating. R_f values are reported on silica gel. Column chromatography was carried out on silica gel 60, 230-240 mesh. Routine NMR measurements were recorded on Bruker AV-400 or DPX-300 spectrometers. The values of δ are expressed in ppm and referred to the residual signal of the solvent ($CDCl_3$). The coupling constants values *J* are expressed in Hz. ^{1}H NMR: splitting pattern abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; sext, sextet; at, apparent triplet; dd, double doublet; ddd, double doublet of doublet; m, multiplet. ^{13}C NMR: multiplicities were determined by DEPT, abbreviations are: q, CH_3; t, CH_2; d, CH; s quaternary carbons, except for compounds bearing fluorine atoms **1g** and **2g** (see below). For these compounds, the abbreviation (q) regarding the carbon multiplicity refers to the F-C coupling and there will be no abbreviation if there is no F-C coupling; the number of hydrogen atoms linked to a determined carbon atom is indicated as C, CH, CH_2 or CH_3. In the cases where a mixture of

two diastereomers was observed, the abbreviation "min" refers to the signals assigned to the minor diastereomer and the abbreviation "maj" to the signals belonging to the major one; in the cases where nothing is specified, either it hasn't been possible to assign the signal to any of the diastereomers or it belongs to both of them. COSY, HSQC, HMBC and NOESY experiments were carried out on a Bruker AV-400 spectrometer. Standard pulse sequences were employed for the DEPT experiments. FT-IR experiments were performed with a Varian 1000 FT-IR spectrometer using sodium chloride plates; samples were measured as films from dichloromethane. Mass spectra were determined by Universidad de Vigo (CACTI) with a VG AutoSpec M and Universidad de Burgos with a Micromass Autospec mass spectrometers respectively for high resolution mass spectra (HRMS); low resolution mass spectra were obtained on a gas chromatograph mass spectrometer Shimadzu QP2010 Plus with auto injector AOC-20i. Electron ionization (70 eV) or electrospray ionization (ESI) were employed.

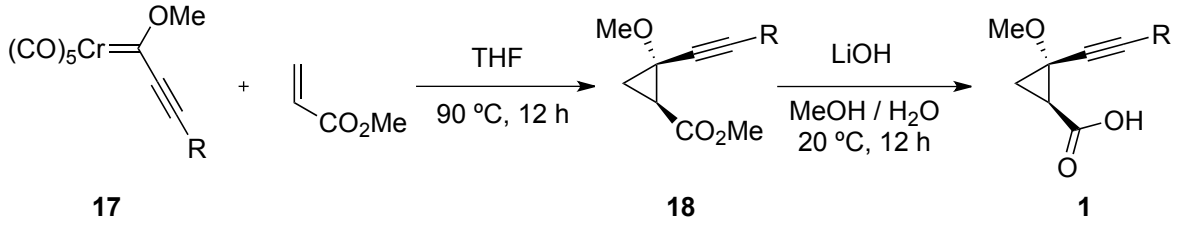
3.2. Catalyst Lyophilisation Procedure.

Some catalysts were lyophilized prior to their use (see manuscript Table 1) by placing them into an Alpha 2-4 LSC (Christ) lyophilisation (freeze-drying) apparatus, and following a three-step procedure: (1) *manual freezing* + *warm up*, for 20 min.; (2) *main drying*, for 2 hours and (3) *final drying* for 12 hours.

The lyophilisation is essential to remove water from hygroscopic silver salts.

3.3. Synthetic Procedures and Compounds Characterization Data.

Table ESI-3 Synthesis of Alkynylcyclopropanecarboxylic Acids **1**



17 **18** **1**

Entry	R	**18**	Yield[a]	dr[b]	**1**	Yield[a]	Yield[c]
1	Ph	**18a**	48	5:1	**1a**	96	46
2	*p*-$MeOC_6H_4$	**18b**	50	5:1	**1b**	90	45
3	*p*-Me-*o*-$MeOC_6H_3$	**18c**	54	4:1	**1c**	95	51
4	*p*-MeC_6H_4	**18d**	42	5:1	**1d**	98	41
5	*o*-MeC_6H_4	**18e**	56	6.7:1	**1e**	96	54
6	*p*-ClC_6H_4	**18f**	48	4:1	**1f**	94	45
7	*p*-$CF_3C_6H_4$	**18g**	57	4.5:1	**1g**	97	55
8	2-Thiophenyl	**18h**	55	5:1	**1h**	100	55
9	(*E*)-1-Methylstyryl	**18i**	44	4:1	**1i**	100	44
10	Bu	**18j**	38	4:1	**1j**	98	37
11	Cyclopentyl	**18k**	41	5:1	**1k**	96	39
12	^{t}Bu	**18l**	58	5:1	**1l**	98	57
13	(*E*)-Styryl	**18m**	50	3:1	**1m**	90	45
14	TMS	**18n**	60	10:1	**1n**[d]	96	58

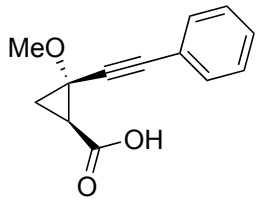
[a] Isolated yield. [b] Diastereomeric ratio: the major isomer has a *cis* relationship between alkynyl and ester substituents. [c] Isolated yield for the two-step sequence from Fischer carbene complexes **17**.[d] The TMS group is lost in the basic hydrolysis step (**1n** R= H).

General procedure for the synthesis of alkynylcyclopropanecarboxylic acids 1:

In a sealed tube methyl acrylate (15 equiv) was added to a solution of the corresponding Fischer alkoxy alkynylcarbene complex[13] **17** (1 equiv, 5 mmol) in dry THF (100 mL). The mixture was stirred at 90º C until complete disappearance of the carbene complex was observed by TLC (~12 h). Solvent was removed under reduced pressure, and the residue was purified by flash chromatography (hexane/AcOEt); the corresponding alkynylcyclopropane ester **18** was isolated. Alkenes, resulting from the opening of the cyclopropane ring, were obtained as minor byproducts[2] and, in general, they could not be separated from alkynylcyclopropane esters **18**. In particular cases (for instance, for model compound **18a**), chromatographic separation of both

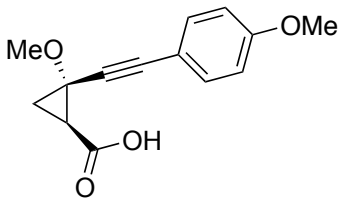
diastereomers was achieved at this stage. Isolated yields and diastereomeric ratios of alkynylcyclopropane esters are listed in previous table ESI-3.

$LiOH \cdot H_2O$ (6 equiv, 18 mmol, 755 mg) was added to a solution of the corresponding alkynylcyclopropanecarboxylic ester **18** (3 mmol) in $MeOH/H_2O$ 1:1 mixture (50 mL) in a 250 mL flask. The mixture was stirred during 12 hr at room temperature, the final of the reaction was verified by TLC. The solution was cleaned with ether (2 x 25 mL), the resulting aqueous layer was neutralized with HCl 1N and was extracted employing ether (3 x 25 mL). In most cases the resulting alkynylcyclopropanecarboxylic acid **1** did not require further purification; when needed, the crude was purified by flash chromatography employing hexane/AcOEt/formic acid mixtures of variable composition. Epimerization was not observed during basic hydrolysis.



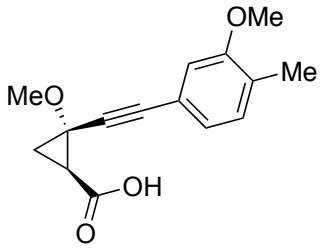
1a

(1*S,2*S**)-2-methoxy-2-(phenylethynyl)cyclopropanecarboxylic acid (1a).** Yellow oil; isolated yield for the two-step sequence = 46 %; the major *cis*-diastereomer could be separated by column chromatography at the ester stage (after the first reaction of the synthesis). The following data correspond to the major *cis*-diastereomer: R_f = 0.00 (HxH/AcOEt, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 11.2 (bs, 1 H), 7.47-7.41 (m, 2 H), 7.32- 7.26 (m, 3 H), 3.50 (s, 3 H), 2.18-2.09 (m, 1 H), 1.73 (dd, *J* = 7.2, 5.7 Hz, 1 H), 1.58 (dd, *J* = 9.3, 5.7 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 175.3 (s), 132.2 (d, 2 CH), 128.8 (d), 128.7 (d, 2 CH), 122.8 (s), 86.9 (s), 84.0 (s), 60.0 (s), 56.4 (q), 30.6 (d), 22.9 (t); LRMS: (EI) *m/z* (%) = 216 ($[M]^+$, 6), 171 (72), 141 (33), 129 (100), 115 (32); HRMS: (EI) calculated for $C_{13}H_{12}O_3$ $[M]^+$: 216.0781, found: 216.0781.



1b

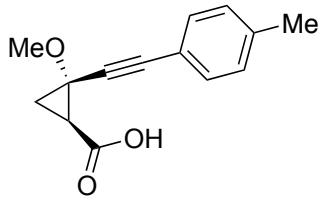
(1*S,2*S**)-2-methoxy-2-[(4-methoxyphenyl)ethynyl]cyclopropanecarboxylic acid (1b).** Yellow liquid; isolated yield for the two-step sequence = 46 %, of a 5:1 mixture of diasteroisomers (a 7 % of alkene carboxylic acid remains after purification); R_f = 0.20 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.43 (bs, 2 H, min + maj), 7.38 (d, *J* = 8.9 Hz, 2 H, min), 7.35 (d, *J* = 8.8 Hz, 2 H, maj), 6.84 (d, *J* = 8.9 Hz, 2 H, min), 6.80 (d, *J* = 8.8 Hz, 2 H, maj), 3.81 (s, 3 H, min), 3.78 (s, 3 H, maj), 3.50 (s, 3 H, maj), 3.46 (s, 3 H, min), 2.22 (dd, *J* = 8.7, 7.4 Hz, 1 H, min), 2.17 (dd, *J* = 9.2, 7.4 Hz, 1 H, maj), 1.95 (dd, *J* = 7.4, 6.0 Hz, 1 H, min), 1.79 (dd, *J* = 7.4, 5.9 Hz, 1 H, maj), 1.68 (dd, *J* = 9.2, 5.9 Hz, 1 H, maj), 1.59 (dd, *J* = 8.7, 6.0 Hz, 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.5 (s, maj), 174.6 (s, min), 160.0 (s, min), 159.8 (s, maj), 133.4 (d, 2 CH, min), 133.3 (d, 2 CH, maj), 114.4 (s, min), 114.3 (s, maj), 114.0 (d, 2 CH min), 113.9 (d, 2 CH, maj), 86.7 (s, maj), 84.7 (s, min), 84.3 (s, min), 81.4 (s, maj), 60.2 (s, maj), 59.3 (s, min), 56.3 (q, min), 56.0 (q, maj), 55.3 (q, min), 55.2 (q, maj), 29.7 (d, min), 29.5 (d, maj), 22.7 (t, maj), 22.2 (t, min); LRMS: (EI) *m/z* (%) = 246 ([M]$^+$, 15), 201 (69), 173 (25), 159 (100), 144 (26); HRMS: (EI) calculated for $C_{14}H_{14}O_4$ [M]$^+$: 246.0892, found: 246.0895.



1c

(1*S,2*S**)-2-methoxy-2-[(3-methoxy-4-methylphenyl)ethynyl]cyclopropanecarboxylic acid (1c).** Yellow liquid; isolated yield for the two-step sequence = 51 % of a 4:1 mixture of

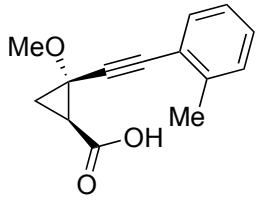
diastereoisomers; R_f = 0.25 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.12 (bs, 2 H, min + maj), 7.08 (d, *J* = 7.8 Hz, 1 H, min), 7.03 (d, *J* = 7.7 Hz, 1 H, maj), 6.98 (d, *J* = 7.8 Hz, 1 H, min), 6.95 (d, *J* = 7.7 Hz, 1 H, maj), 6.90 (s, 1 H, min), 6.85 (s, 1 H, maj), 3.84 (s, 3 H, min), 3.81 (s, 3 H, maj), 3.52 (s, 3 H, maj), 3.47 (s, 3 H, min), 2.26 – 2.15 (m + s, 8 H, min + maj), 1.96 (at, *J* = 6.4 Hz, 1 H, min), 1.81 (at, *J* = 6.6 Hz, 1 H, maj), 1.70 (dd, *J* = 9.3, 5.8 Hz, 1 H, maj), 1.61 (dd, *J* = 8.7, 5.9 Hz, 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.9 (s, maj), 174.8 (s, min), 157.4 (s, min), 157.3 (s, maj), 130.6 (d, min), 130.4 (d, maj), 128.3 (s, min), 127.9 (s, maj), 124.2 (d, min), 124.0 (d, maj), 120.4 (s, maj), 120.1 (s, min), 113.0 (d, min), 112.9 (d, maj), 87.1 (s, maj), 85.1 (s, min), 84.7 (s, min), 81.9 (s, maj), 60.2 (s, maj), 59.2 (s, min), 56.4 (q, min), 56.1 (q, maj), 55.3 (q, min), 55.2 (q, maj), 29.6 (d, maj), 28.1 (d, min), 22.8 (t, maj), 22.1 (t, min), 16.3 (q, min), 16.2 (q, maj); LRMS: (EI) *m/z* (%) = 260 ($[M]^+$, 5), 215 (30), 173 (100), 158 (19); HRMS: (EI) calculated for $C_{15}H_{16}O_4$ $[M]^+$: 260.1049, found: 260.1056.



1d

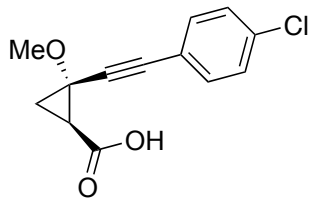
(1*S, 2*S**)-2-methoxy-2-(*p*-tolylethynyl)cyclopropanecarboxylic acid (1d).** Yellow liquid; isolated yield for the two-step sequence = 41 % of a 5:1 mixture of diasteroisomers (a 6 % of alkene carboxylic acid remains after purification); R_f = 0.22 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.17 (bs, 2 H, min + maj), 7.36 (d, *J* = 7.8 Hz, 2 H, min), 7.33 (d, *J* = 7.8 Hz, 2 H, maj), 7.14 (d, *J* = 7.8 Hz, 2 H, min), 7.09 (d, *J* = 7.8 Hz, 2 H, maj), 3.53 (s, 3 H, maj), 3.48 (s, 3 H, min), 2.37 (s, 3 H, min), 2.34 (s, 3 H, maj), 2.28 – 2.23 (m, 1 H, min), 2.23 – 2.17 (m, 1 H, maj), 2.00 – 1.97 (m, 1 H, min), 1.84 – 1.81 (m, 1 H, maj), 1.71 (dd, *J* = 9.1, 5.8 Hz, 1 H, maj), 1.61 (dd, *J* = 8.3, 6.1 Hz, 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.7 (s, maj), 174.8 (s, min), 139.0 (s, min), 138.6 (s, maj), 131.8 (d, 2 CH, min), 131.7 (d, 2

CH, maj), 129.2 (d, 2 CH, min), 129.0 (d, 2 CH, maj), 119.2 (s, maj), 118.9 (s, min), 86.9 (s, maj), 85.4 (s, min), 84.5 (s, min), 82.2 (s, maj), 60.2 (s, maj), 59.3 (s, min), 56.4 (q, min), 56.1 (q, maj), 29.7 (d, min), 29.6 (d, maj), 22.8 (t, maj), 22.2 (t, min), 21.53 (q, min), 21.47 (q, maj); LRMS: (EI) *m/z* (%) = 230 ($[M]^+$, 14), 197 (23), 185 (40), 169 (52), 143 (100), 114 (9); HRMS: (EI) calculated for $C_{14}H_{14}O_3$ $[M]^+$: 230.0943, found: 230.0943.



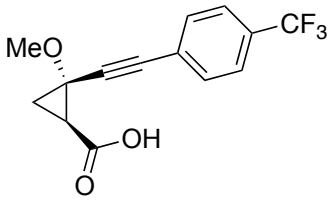
1e

(1*S, 2*S**)-2-methoxy-2-(*o*-tolylethynyl)cyclopropanecarboxylic acid (1e).** Yellow liquid; isolated yield for the two-step sequence = 54 % of a 6.7:1 mixture of diasteroisomers (a 4 % of alkene carboxylic acid remains after purification); R_f = 0.24 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.52 (bs, 2 H, min + maj), 7.42 (dd, *J* = 7.6, 1.0 Hz, 1 H, maj + 1 H, min), 7.29 – 7.10 (m, 6 H, min + maj), 3.56 (s, 3 H, maj), 3.51 (s, 3 H, min), 2.46 (s, 3 H, min), 2.41 (s, 3 H, maj), 2.27 (dd, *J* = 8.6, 7.2 Hz, 1 H, min), 2.23 (dd, *J* = 9.3, 7.5 Hz, 1 H, maj), 2.02 (dd, *J* = 7.2, 5.9 Hz, 1 H, min), 1.85 (dd, *J* = 7.5, 5.8 Hz, 1 H, maj), 1.73 (dd, *J* = 9.3, 5.8 Hz, 1 H, maj), 1.63 (dd, *J* = 8.8, 5.9 Hz, 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.8 (s, maj), 174.8 (s, min), 140.4 (s, min), 140,3 (s, maj), 132.12 (d, maj), 132.08 (d, min), 129.5 (d, min), 129.4 (d, maj), 128.8 (d, min), 128.5 (d, maj), 125.7 (d, min), 125.5 (d, maj), 122.1 (s, maj), 121.8 (s, min), 90.1 (s, min), 86.7 (s, maj), 85.7 (s, maj), 83.3 (s, min), 60.3 (s, maj), 59.4 (s, min), 56.4 (q, min), 56.1 (q, maj), 29.9 (d, min), 29.7 (d, maj), 22.9 (t, maj), 22.4 (t, min), 20.7 (q, min), 20.5 (q, maj); LRMS: (EI) *m/z* (%) = 230 ($[M]^+$, 5), 185 (37), 169 (22), 143 (100), 115 (98); HRMS: (EI) calculated for $C_{14}H_{14}O_3$ $[M]^+$: 230.0943, found: 230.0944.



1f

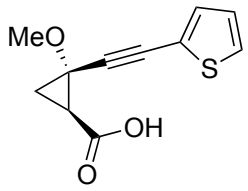
(1*S, 2*S**)-2-[(4-chlorophenyl)ethynyl]-2-methoxycyclopropanecarboxylic acid (1f).** Yellow liquid; isolated yield for the two-step sequence = 45 % of a 4:1 mixture of diasteroisomers (a 3 % of alkene carboxylic acid remains after purification); R_f = 0.27 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.46 (bs, 2 H, min + maj), 7.37 (d, *J* = 8.3 Hz, 2 H, min), 7.32 (d, *J* = 8.3 Hz, 2 H, maj), 7.24 (d, *J* = 8.3, 2 H, maj + 2 H, min), 3.50 (s, 3 H, maj), 3.46 (s, 3 H, min), 2.28 – 2.20 (m, 1 H, min), 2.23 – 2.17 (m, 1 H, maj), 2.01 – 1.94 (m, 1 H, min), 1.86 – 1.79 (m, 1 H, maj), 1.71 (dd, *J* = 9.2, 5.9 Hz, 1 H, maj), 1.60 (dd, *J* = 8.7, 6.1 Hz, 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.6 (s, maj), 174.5 (s, min), 134.9 (s, min), 134.6 (s, maj), 133.1 (d, 2 CH, min), 132.9 (d, 2 CH, maj), 128.7 (d, 2 CH, min), 128.6 (d, 2 CH, maj), 120.7 (s, maj), 120.4 (s, min), 87.0 (s, min), 85.6 (s, maj), 84.0 (s, maj), 83.2 (s, min), 60.1 (s, maj), 59.0 (s, min), 56.5 (q, min), 56.2 (q, maj), 29.7 (d, min), 29.6 (d, maj), 22.8 (t, maj), 22.1 (t, min); LRMS: (EI) *m/z* (%) = 250 ($[M]^+$, 1), 236 (4), 205 (23), 165 (30), 163 (100); HRMS: (EI) calculated for $C_{13}H_{11}ClO_3$ $[M]^+$: 250.0397, found: 250.0406.



1g

(1*S, 2*S**)-2-methoxy-2-{[4-(trifluoromethyl)phenyl]ethynyl}cyclopropanecarboxylic acid (1g).** Yellow liquid; isolated yield for the two-step sequence = 55 % of a 4.5:1 mixture of diasteroisomers (a 3 % of alkene carboxylic acid remains after purification); R_f = 0.21

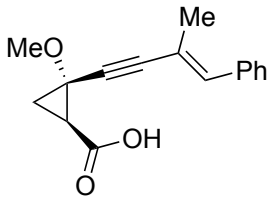
(HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (401 MHz, $CDCl_3$) δ = 10.53 (bs, 2 H, min + maj), 7.61 – 7.45 (m, 8 H, maj + min), 3.50 (s, 3 H, maj), 3.46 (s, 3 H, min), 2.27 – 2.17 (m, 2 H, min + maj), 2.00 – 1.96 (m, 1 H, min), 1.86 – 1.80 (m, 1 H, maj), 1.71 (dd, *J* = 9.2, 6.0 Hz, 1 H, maj), 1.60 (dd, *J* = 8.6, 6.1 Hz, 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.0 (C, maj), 173.8 (C, min), 132.0 (2 CH, min), 131.8 (2 CH, maj), 130.1 (q, $^{2}J_{C\text{-}F}$ = 32.7 Hz, C, maj), 126.0 (C, maj), 125.8 (C, min), 125.3 (q, $^{3}J_{C\text{-}F}$= 3.6 Hz, C, min), 125.1 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz, C, maj), 124.6 (q, $^{1}J_{C\text{-}F}$ = 271.4 Hz, C, maj), 88.6 (C, min), 85.8 (C, maj), 85.2 (C, maj), 82.9 (C, min), 59.9 (C, maj), 58.8 (C, min), 56.4 (CH_3, min), 56.2 (CH_3, maj), 29.7 (CH, min), 29.6 (CH, maj), 22.7 (CH_2, maj), 21.9 (CH_2, min) [two signals corresponding to -CF_3 and to F_3C-C- of the minor isomer were not observed]; LRMS: (EI) *m/z* (%) = 284 ([M]$^{+}$, 3), 239 (83), 209 (24), 197 (100); HRMS: (EI) calculated for $C_{14}H_{11}O_3F_3$ [M]$^{+}$: 284.0660, found: 284.0664.



1h

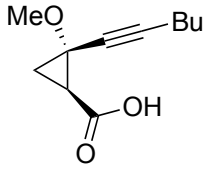
(1*S, 2*S**)-2-methoxy-2-(thiophen-2-ylethynyl)cyclopropanecarboxylic acid (1h).** Yellow liquid; isolated yield for the two-step sequence = 55 % of a 5:1 mixture of diasteroisomers; R_f = 0.17 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.83 (bs, 2 H, min + maj), 7.29 (dd, *J* = 5.1, 1.1 Hz, 1 H, min), 7.24 (dd, *J* = 5.1, 1.1 Hz, 1 H, maj + 1 H min), 7.20 (dd, *J* = 3.6, 1.1 Hz, 1 H, maj), 6.98 (dd, *J* = 5.1, 3.7 Hz, 1 H, min), 6.95 (dd, *J* = 5.1, 3.6 Hz, 1 H, maj), 3.49 (s, 3 H, maj), 3.46 (s, 3 H, min), 2.24 (dd, *J* = 8.9, 7.4 Hz, 1 H, min), 2.19 (dd, *J* = 9.3, 7.4 Hz, 1 H, maj), 1.96 (dd, *J* = 7.4, 6.0 Hz, 1 H, min), 1.80 (dd, *J* = 7.4, 5.9 Hz, 1 H, maj), 1.70 (dd, *J* = 9.3, 5.9 Hz, 1 H, maj), 1.60 (dd, *J* = 8.9, 6.0 Hz, 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.1 (s, min), 175.0 (s, maj), 133.0 (d, min), 132.7 (d, maj), 127.9 (d, min), 127.6 (d, maj), 127.0 (d, min), 126.9 (d, maj), 122.3 (s, min), 122.2 (s, maj), 86.9 (s, maj), 80.0 (s, maj), 60.1 (s, maj), 59.4 (s, min), 56.5 (q, min), 56.2 (q, maj), 29.64 (d, min), 29.60 (d, maj),

22.9 (t, maj), 22.2 (t, min) [the signals corresponding to *sp* carbons belonging to the minor isomer were not observed]; LRMS: (ESI) *m/z* (%) = 223 ($[M+1]^+$, 25), 209 (100), 191 (17); HRMS: (ESI) calculated for $C_{11}H_{11}O_3S$ $[M+1]^+$: 223.0423, found: 223.0434.



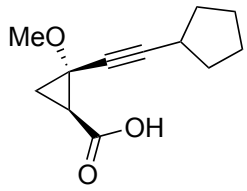
1i

(1*S, 2*S**)-(*E*)-2-methoxy-2-(3-methyl-4-phenylbut-3-en-1-yn-1-yl)cyclopropane-carboxylic acid (1i).** Yellow liquid; isolated yield for the two-step sequence = 44 % of a 4:1 mixture of diasteroisomers (a 8 % of alkene carboxylic acid remains after purification); R_f = 0.30 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.60 (bs, 2 H, min + maj), 7.40 – 7.23 (m, 10 H, min + maj), 6.87 (s, 1 H, min), 6.84 (s, 1 H, maj), 3.49 (s, 3 H, maj), 3.47 (s, 3 H, min), 2.18 (dd, *J* = 9.2, 7.5 Hz, 1 H, maj + 1 H, min), 2.08 (s, 3 H, min), 2.05 (s, 3 H, maj), 1.95 (dd, *J* = 7.5, 5.9 Hz, 1 H, min), 1.79 (dd, *J* = 7.5, 5.8 Hz, 1 H, maj), 1.68 (dd, *J* = 9.2, 5.8 Hz, 1 H, maj), 1.58 (dd, *J* = 8.8, 5.9 Hz, 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.5 (s, maj), 174.5 (s, min), 137.0 (d, min), 136.6 (d, maj), 129.1 (d, 2 CH, min), 129.0 (d, 2 CH, maj), 128.44 (s, min) 128.36 (d, 2 CH, min), 128.3 (d, 2 CH, maj), 128.2 (s, maj), 127.5 (d, min), 127.3 (d, maj), 118.9 (s, maj), 118.7 (s, min), 90.5 (s, maj), 88.1 (s, min), 85.0 (s, min), 81.9 (s, maj), 60.2 (s, maj), 59.3 (s, min), 56.3 (q, min), 56.0 (q, maj), 29.7 (d, maj), 25.6 (d, min), 22.8 (t, maj), 22.2 (t, min), 19.1 (q, min), 19.0 (q, maj). LRMS: (EI) *m/z* (%) = 256 ($[M]^+$, 3), 224 (12), 181 (20), 169 (43), 141 (76), 115 (100); HRMS: (EI) calculated for $C_{16}H_{16}O_3$ $[M]^+$: 256.1099, found: 256.1093.



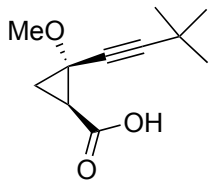
1j

(1*S,2*S**)-2-(hex-1-yn-1-yl)-2-methoxycyclopropanecarboxylic acid (1j).** Yellow liquid; isolated yield for the two-step sequence = 37 % of a 4:1 mixture of diasteroisomers; R_f = 0.28 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.36 (bs, 2 H, min + maj), 3.39 (s, 3 H, maj), 3.38 (s, 3 H, min), 2.36 (t, *J* = 7.1 Hz, 2 H, min), 2.22 (t, *J* = 6.8 Hz, 2 H, maj), 2.10 – 1.97 (m, 2 H, maj + min), 1.89 – 1.76 (m, 1 H, min), 1.66 – 1.58 (m, 2 H, maj + min), 1.53 (dd, *J* = 9.1, 6.0 Hz, 1 H maj + 1 H min), 1.49 – 1.32 (m, 8 H, maj + min), 0.98 – 0.79 (m, 6 H, maj + min); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.9 (s, maj), 174.9 (s, min), 87.7 (s, maj), 85.3 (s, min), 80.3 (s, min), 73.5 (s, maj), 60.0 (s, maj), 59.1 (s, min), 56.0 (q, min), 55.6 (q, maj), 30.5 (d, maj), 29.6 (t, min), 29.3 (d, min), 29.1 (t, maj), 22.3 (t, maj), 22.0 (t, min), 21.9 (t, min), 21.8 (t, maj), 18.4 (t, maj), 18.3 (t, min), 13.5 (q, maj), 13.4 (q, min); LRMS: (ESI) *m/z* (%) = 197 ($[M+1]^+$, 32), 183 (71), 165 (100); HRMS: (ESI) calculated for $C_{11}H_{17}O_3$ $[M+1]^+$: 197.1178, found: 197.1167.



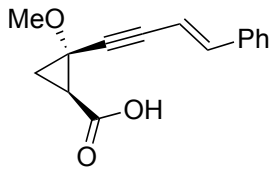
1k

(1*S,2*S**)-2-(cyclopentylethynyl)-2-methoxycyclopropanecarboxylic acid (1k).** Pale yellow liquid; isolated yield for the two-step sequence = 39 % of a 5:1 mixture of diasteroisomers; the following data correspond to the major diastereomer, which was separated by column chromatography. R_f = 0.23 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.06 (bs, 1 H), 3.41 (s, 3 H), 2.66 (p, *J* = 7.2 Hz, 1 H), 2.04 (dd, *J* = 9.2, 7.3 Hz, 1 H), 1.94 – 1.83 (m, 2 H), 1.73 - 1.69 (m, 2 H), 1.64 (dd, *J* = 7.3, 5.8 Hz, 1 H), 1.66 – 1.51 (m, 4 H), 1.55 (dd, *J* = 9.2, 5.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.9 (s), 92.0 (s), 73.0 (s), 60.0 (s), 55.7 (q), 33.74 (t), 33.67 (t), 30.1 (d), 29.2 (d), 24.91 (t), 24.89 (t), 22.4 (t).



1l

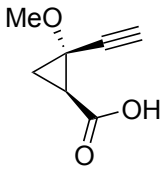
1*S,2*S**)-2-(3,3-dimethylbut-1-yn-1-yl)-2-methoxycyclopropanecarboxylic acid (1l).** Colourless liquid; isolated yield for the two-step sequence = 57 % of a 5:1 mixture of diasteroisomers (a 5 % of alkene carboxylic acid remains after purification); R_f = 0.34 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.81 (bs, 2 H, min + maj), 3.34 (s, 3 H, maj), 3.32 (s, 3 H, min), 1.98 (dd, *J* = 9.2, 7.3 Hz, 1 H, maj + 1 H, min), 1.77 (dd, *J* = 7.2, 5.9 Hz, 1 H, min), 1.57 (dd, *J* = 7.3, 5.8 Hz, 1 H, maj), 1.48 (dd, *J* = 9.2, 5.8 Hz, 1 H, maj), 1.36 (dd, *J* = 8.7, 5.9 Hz, 1 H, min), 1.17 (s, 9 H, min), 1.15 (s, 9 H, maj); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.5 (s, maj), 174.6 (s, min), 95.6 (s, maj), 93.3 (s, min), 75.5 (s, maj), 72.0 (s, maj), 59.8 (s, maj), 58.9 (s, min), 55.7 (q, min), 55.4 (q, maj), 30.73 (q, 3 CH_3, min), 30.69 (q, 3 CH_3, maj), 29.3 (d, min), 29.2 (d, maj), 27.4 (s, maj), 27.3 (s, min), 22.2 (t, maj), 22.0 (t, min); LRMS: (EI) *m/z* (%) = 196 ([M]$^+$, 2), 181 (100), 151 (88), 109 (88), 93 (87), 91 (93), 79 (97); HRMS: (EI) Calculated for $C_{11}H_{16}O_3$ [M]$^+$: 196.1099, found: 196.1093.



1m

(1S*,2S*)-2-methoxy-2-[(*E*)-4-phenylbut-3-en-1-yn-1-yl]cyclopropanecarboxylic acid (1m). Yellow liquid; isolated yield for the two-step sequence = 45 % of a 3:1 mixture of diasteroisomers (a 10 % of alkene carboxylic acid remains after purification); R_f = 0.23 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (401 MHz, $CDCl_3$) δ = 10.95 (bs, 2 H, min + maj), 7.43 – 7.24 (m, 10 H, min + maj), 6.99 (d, *J* = 16.3 Hz, 1 H, min), 6.98 (d, *J* = 16.3 Hz, 1 H, maj), 6.31 (d, *J* = 16.3 Hz, 1 H, min), 6.18 (d, *J* = 16.3 Hz, 1 H, maj), 3.49 (s, 3 H, maj), 3.47 (s, 3 H, min), 2.24 – 2.20 (m, 1 H, min), 2.21 – 2.17 (m, 1 H, maj), 1.99 – 1.95 (m, 1 H, min),

1.81 – 1.78 (m, 1 H, maj), 1.69 (dd, *J* = 9.2, 5.9 Hz, 1 H, maj), 1.57 (dd, *J* = 8.8, 6.0 Hz, 1 H, min); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.7 (s, maj), 174.7 (min), 142.5 (d, min), 142.3 (d, maj), 136.1 (s, maj), 135.9 (s, min), 129.1 (d, min), 129.0 (d, 2 CH, min), 128.8 (d, maj), 128.7 (d, 2 CH, maj), 126.5 (d, 2 CH, min), 126.4 (d, 2 CH, maj), 107.1 (d, maj), 106.8 (d, min), 88.2 (s, min), 86.1 (s, maj), 85.0 (s, maj), 83.7 (s, min), 60.3 (s, maj), 59.3 (s, min), 56.4 (q, min), 56.1 (q, maj), 29.8 (d, min), 29.7 (d, maj), 22.9 (t, maj), 22.2 (t, min); LRMS: (EI) *m/z* (%) = 242 ([M]$^+$, 11), 209 (19), 197 (45), 181 (37), 165 (85), 153 (85), 127 (100); HRMS: (EI) calculated for $C_{15}H_{14}O_3$ [M]$^+$: 242.0943, found: 242.0945.

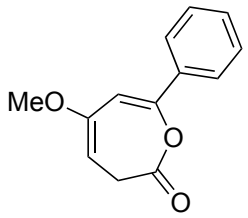


1n

(1*S,2*S**)-2-ethynyl-2-methoxycyclopropanecarboxylic acid (1n).** Obtained according to the general procedure by employing the corresponding silylated carbene complex **17n** (R = Me_3Si). Desilylation takes place during basic hydrolysis. Colourless liquid; isolated yield for the two-step sequence = 58 % of a 10:1 mixture of diasteroisomers; R_f = 0.32 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.66 (bs, 2 H, min + maj), 3.42 (s, 3 H, maj), 3.41 (s, 3 H, min), 2.56 (s, 1 H, maj), 2.50 (s, 1 H, min), 2.12 (dd, *J* = 8.8, 7.4 Hz, 1 H, min), 2.08 (dd, *J* = 9.3, 7.4 Hz, 1 H, maj), 1.85 (dd, *J* = 7.4, 6.0 Hz, 1 H, min), 1.68 (dd, *J* = 7.4, 5.9, 1 H, maj), 1.59 (dd, *J* = 9.3, 5.9 Hz, 1 H, maj), 1.49 (dd, *J* = 8.8, 6.0 Hz, 1 H, min); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.3 (s, maj), 174.3 (s, min), 80.7 (s, min), 77.4 (s, maj), 75.2 (d, maj), 74.5 (d, min), 59.4 (s, maj), 56.6 (s, min), 56.0 (q, maj), 55.3 (q, min), 29.07 (d, min), 29.03 (d, maj), 22.3 (t, maj), 21.6 (t, min). LRMS: (EI) *m/z* (%) = 140 ([M]$^+$, 8), 125 (36), 115 (100), 95 (63), 83 (83); HRMS: (EI) calculated for $C_7H_8O_3$ [M]$^+$: 140.0473, found: 140.0479.

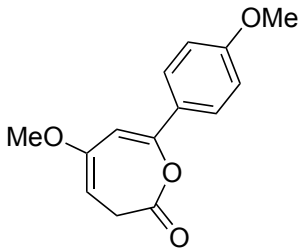
General procedure for the synthesis of oxepin-2-ones 2:

A solution of freshly lyophilized IPrAuCl (3 mol%, 0.015 mmol, 9.3 mg) and AgOTs (3 mol%, 0.015 mmol, 4.2 mg) in CH_2Cl_2 (5 mL) was placed in a carrousel tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of the corresponding alkynylcyclopropanecarboxylic acid **1** (0.5 mmol) in CH_2Cl_2 (5 mL) was then added; stirring was maintained for 12 h. End of reaction was monitored by TLC; solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give the corresponding oxepinone **2** in the yield indicated in Scheme 1 or in Table 1.



2a

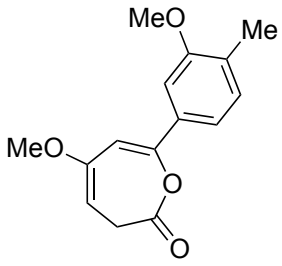
5-methoxy-7-phenyloxepin-2(3*H*)-one (2a). Yellow liquid; yield = 90 %; R_f = 0.65 (HxH/AcOEt, 3/1); FT-IR (film, cm^{-1}): ν = 1760, 1643; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.70-7.65 (m, 2 H), 7.41-7.37 (m, 3 H), 6.42 (s, 1 H), 4.85 (t, *J* = 6.8 Hz, 1 H), 3.65 (s, 3 H), 3.00 (d, *J* = 6.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.9 (s), 155.8 (s), 150.3 (s), 133.5 (s), 129.5 (d), 128.5 (d, 2 CH), 125.4 (d, 2 CH), 106.2 (d), 89.7 (d), 55.5 (q), 32.0 (t). LRMS: (EI) *m/z* (%) = 216 ($[M]^+$, 10), 187 (14), 147 (22), 111 (17), 105 (100), 77 (97); HRMS: (EI) calculated for $C_{13}H_{12}O_3$ $[M]^+$: 216.0781, found: 216.0780.



2b

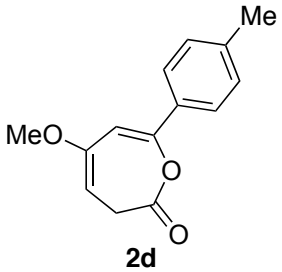
5-methoxy-7-(4-methoxyphenyl)oxepin-2(3*H*)-one (2b). Pale yellow liquid; yield = 78 %; R_f = 0.33 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61 (d, *J* = 8.8 Hz, 2 H), 6.90 (d, *J*

= 8.8 Hz, 2 H), 6.30 (s, 1 H), 4.81 (t, *J* = 7.0 Hz, 1 H), 3.83 (s, 3 H), 3.64 (s, 3 H), 2.99 (d, *J* = 7.0 Hz, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.1 (s), 160.8 (s), 156.1 (s), 150.5 (s), 127.0 (d, 2 CH), 126.1 (s), 114.0 (d, 2 CH), 104.6 (d), 89.2 (d), 55.5 (q), 55.4 (q), 32.2 (t); LRMS: (EI) *m/z* (%)= 246 ([M]$^+$, 11), 218 (9), 135 (100), 92 (9); HRMS: (EI) calculated for $C_{14}H_{14}O_4$ [M]$^+$: 246.0892, found: 246.0894.



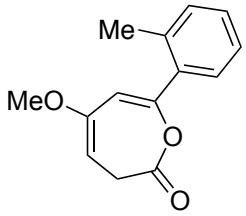
2c

5-methoxy-7-(3-methoxy-4-methylphenyl)oxepin-2(3*H*)-one (2c). Pale yellow liquid; yield = 84 %; R_f = 0.27 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27 – 7.11 (m, 3 H), 6.39 (s, 1 H), 4.84 (t, *J* = 7.0 Hz, 1 H), 3.87 (s, 3 H), 3.65 (s, 3 H), 3.00 (d, *J* = 7.0 Hz, 2 H), 2.23 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.1 (s), 157.8 (s), 156.1 (s), 150.8 (s), 132.5 (s), 130.7 (d), 128.8 (s), 117.7 (d), 106.9 (d), 105.6 (d), 89.6 (d), 55.6 (q), 55.4 (q), 32.2 (t), 16.1 (q).



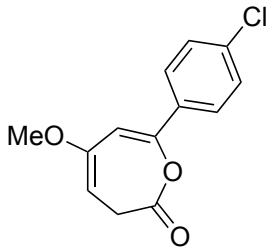
2d

5-methoxy-7-(*p*-tolyl)oxepin-2(3*H*)-one (2d). Colourless liquid; yield = 92 %; R_f = 0.35 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, *J* = 8.3 Hz, 2 H), 7.19 (d, *J* = 8.3 Hz, 2 H), 6.38 (s, 1 H), 4.83 (t, *J* = 7.0 Hz, 1 H), 3.63 (s, 3 H), 2.99 (d, *J* = 7.0 Hz, 2 H), 2.37 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.1 (s), 156.1 (s), 150.7 (s), 139.8 (s), 130.8 (s), 129.4 (d, 2 CH), 125.5 (d, 2 CH), 105.5 (d), 89.6 (d), 55.5 (q), 32.1 (t), 21.2 (q).



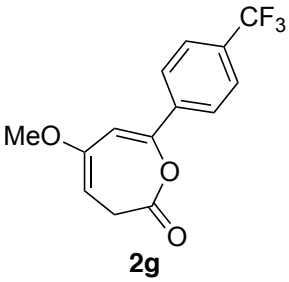
2e

5-methoxy-7-(*o*-tolyl)oxepin-2(3*H*)-one (2e). Colourless liquid; yield = 72 %; R_f = 0.35 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 (d, *J* = 7.8 Hz, 1 H), 7.34 – 7.19 (m, 3 H), 6.01 (s, 1 H), 4.84 (t, *J* = 7.0 Hz, 1 H), 3.65 (s, 3 H), 3.08 (d, *J* = 7.0 Hz, 2 H), 2.41 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.9 (s), 155.7 (s), 152.9 (s), 136.2 (s), 134.8 (s), 130.8 (d), 129.5 (d), 129.4 (d), 125.9 (d), 110.3 (d), 89.5 (d), 55.5 (q), 32.3 (t), 20.6 (q); LRMS: (EI) *m/z* (%)= 230 ([M]$^+$, 8), 161 (84), 119 (100), 115 (18), 91 (40); HRMS: (EI) calculated for $C_{14}H_{14}O_3$ [M]$^+$: 230.0943, found: 230.0948.



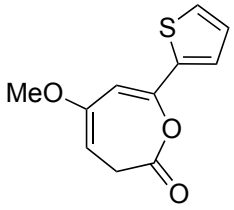
2f

7-(4-chlorophenyl)-5-methoxyoxepin-2(3*H*)-one (2f). Colourless liquid; yield = 75 %; R_f = 0.38 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61 (d, *J* = 8.7 Hz, 2 H), 7.37 (d, *J* = 8.7 Hz, 2 H), 6.39 (s, 1 H), 4.86 (t, *J* = 7.0 Hz, 1 H), 3.65 (s, 3 H), 3.00 (d, *J* = 7.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.7 (s), 155.8 (s), 149.5 (s), 135.7 (s), 132.1 (s), 128.9 (d, 2 CH), 126.8 (d, 2 CH), 106.6 (d), 90.1 (d), 55.6 (q), 32.1 (t).



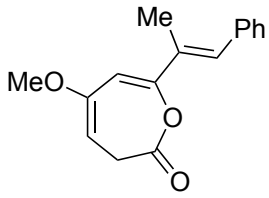
2g

5-methoxy-7-[4-(trifluoromethyl)phenyl]oxepin-2(3*H*)-one (2g). Colourless liquid; yield = 86 %; R_f = 0.39 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.79 (d, *J* = 8.1 Hz, 2 H), 7.65 (d, *J* = 8.2 Hz, 2 H), 6.49 (s, 1 H), 4.90 (t, *J* = 6.9 Hz, 1 H), 3.66 (s, 3 H), 3.02 (d, *J* = 6.9 Hz, 2 H); for this compound, the abbreviation (q) regarding the carbon multiplicity refers to the F-C coupling and there will be no abbreviation if there is no F-C coupling; the number of hydrogen atoms linked to a determined carbon atom is indicated as C, CH, CH_2 or CH_3: ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.5 (C), 155.7 (C), 149.0 (C), 137.0 (C), 131.3 (q, $^2J_{C\text{-}F}$ = 32.7 Hz, C), 125.8 (2 CH), 125.7 (q, $^3J_{C\text{-}F}$ = 3.6 Hz, 2 CH), 123.8 (q, $^1J_{C\text{-}F}$ = 272.1 Hz, C), 108.1 (CH), 90.6 (CH), 55.6 (CH_3), 32.1 (CH_2).



2h

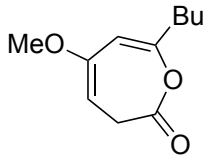
5-methoxy-7-(thiophen-2-yl)oxepin-2(3*H*)-one (2h). Colourless liquid; yield = 62 %; R_f = 0.43 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 (dd, *J* = 3.7 and 1.1 Hz, 1 H), 7.32 (dd, *J* = 5.1 and 1.1 Hz, 1 H), 7.04 (dd, *J* = 5.1 and 3.7 Hz, 1 H), 6.31 (s, 1 H), 4.82 (t, *J* = 7.0 Hz, 1 H), 3.64 (s, 3 H), 3.03 (d, *J* = 7.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.6 (s), 155.8 (s), 146.3 (s), 137.6 (s), 127.9 (d), 127.0 (d), 126.0 (d), 105.0 (d), 89.6 (d), 55.6 (q), 32.1 (t).



2i

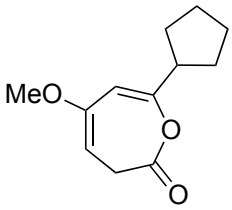
(*E*)-5-methoxy-7-(1-phenylprop-1-en-2-yl)oxepin-2(3*H*)-one (2i). Colourless liquid; yield = 82 %; R_f = 0.50 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 –7.26 (m, 6 H), 6.09

(s, 1 H), 4.84 (t, *J* = 6.9 Hz, 1 H), 3.63 (s, 3 H), 2.97 (d, *J* = 6.9 Hz, 2 H), 2.07 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.6 (s), 156.0 (s), 152.3 (s), 136.9 (s), 130.3 (d), 129.5 (d, 2 CH), 129.3 (s), 128.2 (d, 2 CH), 127.3 (d), 107.2 (d), 90.2 (d), 55.5 (q), 32.0 (t), 14.7 (q); LRMS: (EI) *m/z* (%) = 256 ([M]$^+$, 4), 187 (17), 159 (29), 145 (49), 117 (56), 115 (100); HRMS: (EI) calculated for $C_{16}H_{16}O_3$ [M]$^+$: 256.1099, found: 256.1096.



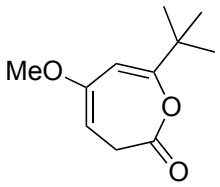
2j

7-butyl-5-methoxyoxepin-2(3*H*)-one (2j). Colourless liquid; yield = 89 %; R_f = 0.55 (HxH/AcOEt, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.64 (s, 1 H), 4.68 (t, *J* = 7.0 Hz, 1 H), 3.57 (s, 3 H), 2.88 (d, *J* = 7.0 Hz, 2 H), 2.31 (t, *J* = 7.2 Hz, 2 H), 1.55 (p, *J* = 7.2 Hz, 2 H), 1.36 (sext, *J* = 7.2 Hz, 2 H), 0.92 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.5 (s), 156.0 (s), 155.4 (s), 106.7 (d), 88.8 (d), 55.7 (q), 35.2 (t), 32.3 (t), 29.7 (t), 22.4 (t), 14.1 (q).



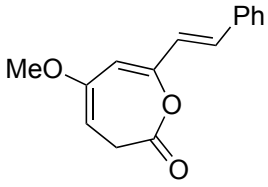
2k

7-cyclopentyl-5-methoxyoxepin-2(3*H*)-one (2k). Colourless liquid; yield = 87 %; R_f = 0.50 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.69 (s, 1 H), 4.68 (t, *J* = 6.9 Hz, 1 H), 3.57 (s, 3 H), 2.86 (d, *J* = 6.9 Hz, 2 H), 2.71 (p, *J* = 8.2 Hz, 1 H); 1.91 – 1.88 (m, 2 H), 1.74 – 1.70 (m, 2 H), 1.65 – 1.60 (m, 4 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.3 (s), 157.9 (s), 155.6 (s), 105.0 (d), 88.4 (d), 55.3 (q), 45.0 (d), 32.0 (t), 31.2 (t, 2 CH_2), 25.4 (t, 2 CH_2); LRMS: (EI) *m/z* (%) = 208 ([M]$^+$, 2), 167 (100), 163 (61), 121 (70), 91 (86), 79 (65), 77 (56); HRMS: (EI) calculated for $C_{12}H_{16}O_3$ [M]$^+$: 208.1099, found: 208.1096.



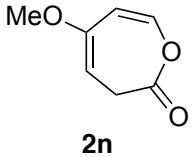
2l

7-(*tert*-butyl)-5-methoxyoxepin-2(3*H*)-one (2l). Colourless liquid; yield = 74 %; R_f = 0.53 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.74 (s, 1 H), 4.70 (t, *J* = 6.9 Hz, 1 H), 3.58 (s, 3 H), 2.83 (d, *J* = 6.9 Hz, 2 H), 1.20 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.7 (s), 162.5 (s), 155.6 (s), 103.7 (d), 88.7 (d), 55.3 (q), 36.7 (s), 31.8 (t), 28.2 (q, 3 CH_3).



2m

(*E*)-5-methoxy-7-styryloxepin-2(3*H*)-one (2m). Colourless liquid; yield = 30 %; R_f = 0.80 (HxH/AcOEt, 1/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.49 – 7.27 (m, 5 H), 7.14 (d, *J* = 15.8 Hz, 1 H), 6.60 (d, *J* = 15.8 Hz, 1 H), 5.92 (s, 1 H), 4.83 (t, *J* = 7.0 Hz, 1 H), 3.64 (s, 3 H), 3.01 (d, *J* = 7.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.4 (s), 156.4 (s), 150.2 (s), 136.2 (s), 132.7 (d), 129.2 (d, 2 CH), 129.1 (d), 127.5 (d, 2 CH), 122.4 (d), 110.4 (d), 90.5 (d), 55.9 (q), 32.5 (t); LRMS: (EI) *m/z* (%) = 242 ([M]$^+$, 3), 173 (60), 131 (100), 103 (62); HRMS: (EI) calculated for $C_{15}H_{14}O_3$ [M]$^+$: 242.0943, found: 242.0943



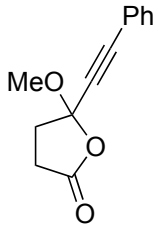
2n

5-methoxyoxepin-2(3*H*)-one (2n). Not isolated. Data retrieved from a mixture of **2n**:**8** (54:46). Colourless liquid; combined yield (**2n** + **8**) in the reaction carried out at rt, according to the general procedure = 30 %; combined yield (**2n** + **8**) in the reaction carried out in refluxing

dichloromethane = 71 %; R_f = 0.53 (HxH/AcOEt, 5/1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.57 (d, *J* = 7.2 Hz, 1 H), 5.79 (d, *J* = 7.2 Hz, 1 H), 4.77 (t, *J*= 7.0 Hz, 1 H), 3.60 (s, 3 H), 2.93 (d, *J* = 7.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.0 (s), 155.3 (s), 141.1 (d), 110.5 (d), 90.1 (d), 55.4 (q), 32.0 (t).

Procedure for the synthesis of oxepin-2-ones 2m or 2n in refluxing dichloromethane:

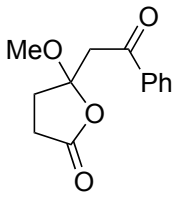
A solution of freshly lyophilized IPrAuCl (3 mol%, 0.015 mmol, 9.3 mg) and AgOTs (3 mol%, 0.015 mmol, 4.2 mg) in CH_2Cl_2 (5 mL) was placed in a carrousel tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of the corresponding alkynylcyclopropanecarboxylic acid **1m** or **1n** (0.5 mmol) in CH_2Cl_2 (5 mL) was then added. The reaction tube was placed in an oil bath at 40 ºC, and stirring was maintained for 12 h. End of reaction was monitored by TLC; solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give the corresponding oxepinone **2m** or a mixture of oxepinone **2n** and (1*S**,5*S**)-5-methoxy-4-methylen-3-oxabicyclo[3.1.0]hexan-2-one **8** (ratio 52/48) in the yields indicated in Table 1 (entries 13 or 15).



3

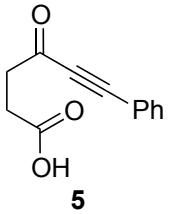
5-Methoxy-5-(phenylethynyl)dihydrofuran-2(3*H*)-one (3). Obtained as a byproduct in some of the reactions during the optimization process (see Table ESI-1) and as major product when $Ph_3PAuCl/AgSbF_6$ was used as catalyst system. A solution of Ph_3PAuCl (3 mol%, 0.015 mmol, 7.4 mg) and $AgSbF_6$ (3 mol%, 0.015 mmol, 5.2 mg) in CH_2Cl_2 (5 mL) was put in a carrousel tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of alkynylcyclopropanecarboxylic acid **1a** (0.5 mmol, 108 mg) in CH_2Cl_2 (5 mL)

was then added; stirring was maintained for 12 h. The end of the reaction was monitored by TLC, solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give 5-methoxy-5-(phenylethynyl)dihydrofuran-2(3*H*)-one **3** in 54% yield (58 mg). Yellow liquid; R_f = 0.55 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50-7.48 (m, 2 H), 7.39-7.33 (m, 3 H), 3.60 (s, 3 H), 2.79-2.53 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.1 (s), 131.9 (d, 2 CH), 129.5 (d), 128.5 (d, 2 CH), 120.9 (s), 102.9 (s), 87.5 (s), 82.8 (s), 53.2 (q), 36.5 (t), 28.0 (t).



4

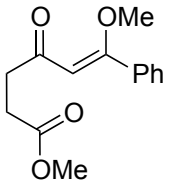
Dihydro-5-benzoylmethyl-5-methoxyfuran-2(3*H*)-one (4). Obtained as a byproduct in some of the reactions during the optimization process (see Table ESI-1). Isolated in 9% yield under the conditions reported in table ESI-1, entry 8. Yellow oil; R_f = 0.26 (HxH/AcOEt, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 – 7.95 (m, 2 H), 7.67 – 7.60 (m, 1 H), 7.56 – 7.48 (m, 2 H), 3.73 (d, *J* = 17.1 Hz, 1 H), 3.61 (d, *J* = 17.1 Hz, 1 H), 3.42 (s, 3 H), 2.89 – 2.65 (m, 2 H), 2.63-2.43 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 195.2 (s), 175.9 (s), 136.8 (s), 133.7 (d), 128.8 (d, 2 CH), 128.1 (d, 2 CH), 108.7 (s), 50.2 (q), 43.4 (t), 31.5 (t), 28.8 (t). LRMS: (EI) *m/z* (%) = 234 ([M]$^+$, 5), 202 (23), 115 (81), 105 (100), 77 (97); HRMS: (EI) calculated for $C_{13}H_{14}O_4$ [M]$^+$: 234.0892, found: 234.0895.



5

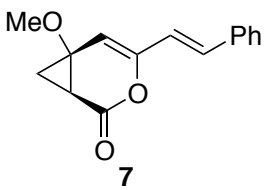
4-Oxo-6-phenylhex-5-ynoic acid (5). Obtained as a byproduct in some of the reactions during the optimization process (see Table ESI-1) and as major product when $AgSbF_6$ was used as catalyst. A solution of $AgSbF_6$ (3 mol%, 0.015 mmol, 5.2 mg) in CH_2Cl_2 (5 mL) was put in a

carrousel tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of alkynylcyclopropanecarboxylic acid **1a** (0.5 mmol, 108 mg) in CH_2Cl_2 (5 mL) was then added; stirring was maintained for 12 h. The end of the reaction was monitored by TLC, solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give 4-oxo-6-phenylhex-5-ynoic acid **5** in 80% yield (162 mg). Yellow liquid; R_f = 0.05 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61 – 7.58 (m, 2 H), 7.48 – 7.39 (m, 3 H), 3.04 (t, *J* = 6.6 Hz, 2 H), 2.78 (t, *J* = 6.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 185.1 (s), 177.6 (s), 133.1 (d, 2 CH), 130.9 (d), 128.7 (d, 2 CH), 119.7 (s), 91.7 (s), 87.3 (s), 39.7 (t), 27.8 (t).



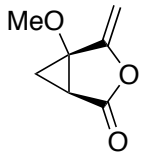
6

Methyl (Z)-6-methoxy-4-oxo-6-phenylhex-5-enoate (6). Obtained as a byproduct in some of the reactions during the optimization process (see Table ESI-1). Isolated in 15% yield under the conditions reported in Table ESI-1, entry 2. Yellow oil; R_f = 0.10 (HxH/AcOEt, 20/1); FT-IR (pure, cm^{-1}): ν = 1732, 1651; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 – 7.88 (m, 2 H), 7.55 – 7.42 (m, 3 H), 6.17 (s, 1 H), 3.78 (s, 3 H), 3.69 (s, 3 H), 3.20 (t, *J* = 7.6 Hz, 2 H), 2.65 (t, *J* = 7.6 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189.9 (s), 175.7 (s), 173.2 (s), 140.2 (s), 131.9 (d), 128.4 (d, 2 CH), 127.7 (d, 2 CH), 96.3 (d), 55.8 (q), 51.7 (q), 31.3 (t), 28.7 (t). LRMS: (EI) *m/z* (%) = 248 ([M]$^+$, 1), 217 (4), 189 (9), 174 (100), 105 (83), 77 (26); HRMS: (EI) calculated for $C_{14}H_{16}O_4$ [M]$^+$: 248.1043, found: 248.1044.



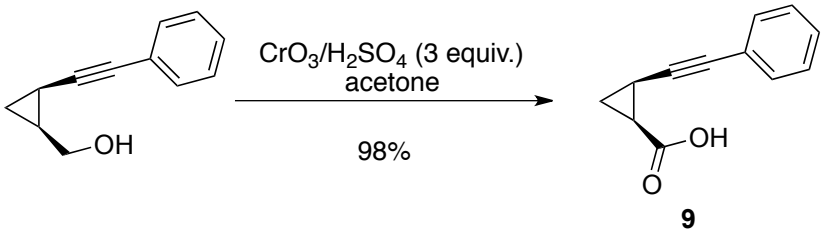
7

(1S*,6R*)-6-Methoxy-4-[(*E*)-styryl]-3-oxabicyclo[4.1.0]hept-4-en-2-one (7). Pale yellow liquid; isolated yield = 30 % (from alkynylcyclopropanecarboxylic acid **1m** under the reaction conditions reported in the general procedure); R_f= 0.74 (HxH/AcOEt, 1/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.44 – 7.27 (m, 5 H), 7.08 (d, *J* = 15.9 Hz, 1 H), 6.42 (d, *J* = 15.9 Hz, 1 H), 5.77 (bs, 1 H), 3.39 (s, 3 H), 2.36 (ddd, *J* = 11.2, 5.4, 1.4 Hz, 1 H), 2.01 (dd, *J* = 11.2, 5.4 Hz, 1 H), 1.17 (t, *J* = 5.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.9 (s), 147.1 (s), 135.9 (s), 131.0 (d), 128.8 (d, 2 CH), 128.5 (d), 126.9 (d, 2 CH), 119.4 (d), 106.1 (d), 64.6 (s), 56.7 (q), 24.9 (d), 23.2 (t); LRMS: (EI) *m/z* (%)= 242 ($[M]^+$, 1), 134 (22), 131 (100), 103 (61); HRMS: (EI) calculated for $C_{15}H_{14}O_3$ $[M]^+$: 242.0943, found: 242.0954.



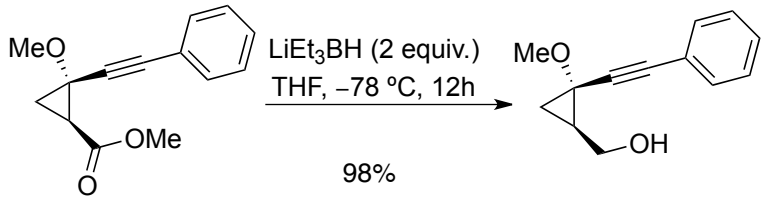
8

(1S*,5S*)-5-Methoxy-4-methylen-3-oxabicyclo[3.1.0]hexan-2-one (8). Not isolated. Data retrieved from a mixture of **2n**:**8** (54:46). Colourless liquid; combined yield (**2n** + **8**) in the reaction carried out at rt, according to the general procedure = 30 %; combined yield (**2n** + **8**) in the reaction carried out in refluxing dichloromethane = 71 %; R_f = 0.53 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.90 (d, *J* = 2.5 Hz, 1 H), 4.64 (d, *J* = 2.5 Hz, 1 H), 3.45 (s, 3 H), 2.48 (dd, *J* = 10.0, 3.5 Hz, 1 H), 1.86 (dd, *J* = 10.0, 5.5 Hz, 1 H), 1.45 (dd, *J* = 5.5, 3.5 Hz, 1 H); ^{13}C NMR (100 MHz, CDCl3) δ = 170.2 (s), 153.1 (s), 88.4 (t), 69.3 (s), 57.0 (q), 22.9 (d), 22.1 (t).



9

(1*S,2*R**)-2-(phenylethynyl)cyclopropanecarboxylic acid (9).** Jones reagent ($CrO_3/H_2SO_4/H_2O$) was dropwise added to a solution of (1*S**,2*R**)-2-(phenylethynyl)cyclopropylmethanol[14] (1 mmol, 172 mg) at 0 ºC till the orange colour persists in the solution. The reaction was stirred until disappearance of starting material was observed by TLC. Then, isopropanol was added till the orange colour vanished, and water (50 mL) was added. The reaction mixture was transferred to a separatory funnel and extracted with dichloromethane (2 x 20 mL). The combined organic layer was placed again in the separatory funnel and treated with 2% NaOH (2 x 20 mL). The combined basic aqueous layers are treated with concentrated HCl; cloudiness was observed. After dichloromethane extraction (2 x 15 mL), the combined organic layer was dried over sodium sulphate. Solvent was removed under vacuum. (1*S**,2*R**)-2-(phenylethynyl)cyclopropanecarboxylic acid **9** was isolated as a yellow liquid (182 mg, 98%), which did not require further purification. R_f = 0.22 (HxH/AcOEt/HCOOH, 5/1/0.01); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39 – 7.36 (m, 2 H), 7.27 – 7.23 (m, 3 H), 2.16 – 2.03 (m, 2 H), 1.57 (td, *J* = 6.5, 4.8 Hz, 1 H), 1.38 (td, *J* = 8.3, 4.8 Hz, 1 H), the signal corresponding to the carboxylic acid proton was not observed. ^{13}C NMR (75 MHz, CDCl3) δ = 176.7 (s), 132.2 (d, 2 CH), 128.6 (d, 2 CH), 128.3 (d), 123.6 (s), 86.9 (s), 80.6 (s), 21.7 (d), 15.9 (t), 11.5 (d).

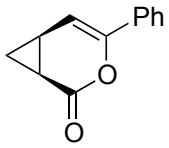


18a **10**

(1*R,2*S**)-[2-methoxy-2-(phenylethynyl)cyclopropyl]methanol (10).** Ester **18a** [1 mmol, 230 mg, (used as a 6.7:1 mixture of diastereomers)] was dissolved in THF (10 mL) in a 50 mL round bottomed flask under inert atmosphere. Then $LiBEt_3H$ (2 equiv) was added at –78 ºC and the mixture was stirred for 12 hr. When end of reaction was observed by TLC, NaOH 1M (25

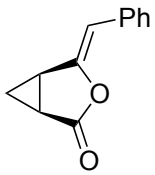
mL) was added. THF was removed by evaporation under reduced pressure, the crude was extracted with ether (2 x 25 mL) and the combined organic layer was dried with Na_2SO_4. The ether was removed by evaporation under reduced pressure leading to the final alcohol **10** as a colourless liquid (98 % yield, 198 mg of a 6.7:1 mixture of diastereomers), which was used without further purification. R_f = 0.10 (HxH/AcOEt, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.48 – 7.44 (m, 4 H, min + maj), 7.37 – 7.31 (m, 6 H, min + maj), 4.04 – 3.95 (m, 1 H, min), 3.93 – 3.84 (m, 1 H, maj), 3.73 – 3.64 (m, 1 H, min), 3.58 (dd, *J* = 11.9, 9.0 Hz, 1 H, maj), 3.53 (s, 3 H, min), 3.48 (s, 3 H, maj), 1.93 (bs, 1 H, min), 1.83 (bs, 1 H, maj), 1.79 – 1.65 (m, 2 H, min + maj), 1.36 (dd, *J* = 10.0, 5.7 Hz, 1 H, maj), 1.21 (dd, *J* = 9.6, 5.6 Hz, 1 H, min), 1.02 (dd, *J* = 7.1, 5.6 Hz, 1 H, min), 0.97 (dd, *J* = 7.0, 5.7 Hz, 1 H, maj); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 131.73 (d, 2 CH, maj), 131.70 (d, 2 CH, min), 128.8 (d, min), 128.5 (d, maj), 128.4 (d, 2 CH, maj), 128.3 (d, 2 CH, min), 122.7 (s, min), 122.4 (s, maj), 88.3 (s, min), 85.9 (s, maj), 85.7 (s, maj), 83.8 (s, min), 63.4 (t, maj), 62.6 (s, min), 61.4 (t, min), 57.1 (s, maj), 56.1 (q, min), 55.7 (q, maj), 29.9 (d, min), 29.0 (d, maj), 20.3 (t, maj), 18.7 (t, min).

Cycloisomerization of (1*S,2*R**)-2-(phenylethynyl)cyclopropanecarboxylic acid 9: Formation of (1*R**,6*S**)-4-phenyl-3-oxabicyclo[4.1.0]hept-4-en-2-one (11) and (1*S**,5*R**,*Z*)-2-benzylidene-3-oxabicyclo[3.1.0]hexan-2-one (12).** This cycloisomerization was carried out following the general procedure at 50 ºC in 1,2-dichloroethane, by employing (1*S**,2*R**)-2-(phenylethynyl)cyclopropanecarboxylic acid **9** (0.5 mmol, 93 mg) as starting material. Once the reaction was concluded (checked by TLC), solvents were removed under vacuum to give a crude reaction mixture formed by (1*R**,6*S**)-4-phenyl-3-oxabicyclo[4.1.0]hept-4-en-2-one **11** and (1*S**,5*R**,*Z*)-2-benzylidene-3-oxabicyclo[3.1.0]hexan-2-one **12**, in 58/42 ratio. Separation of regiosiomers by column chromatography was not possible; a 54% yield of the mixture of **11** and **12** [containing some IPrAu(OH)] was recovered after column chromatography.



11

(1*R,6*S**)-4-phenyl-3-oxabicyclo[4.1.0]hept-4-en-2-one (11).** Not isolated; data retrieved form a mixture of **11**/**12** in 57/43 ratio, containing also some IPrAu(OH) (not quantified). R_f = 0.70 (HxH/AcOEt, 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.58 – 7.56 (m, 2 H), 7.38 – 7.27 (m, 3 H), 6.03 (d, *J* = 5.1 Hz, 1 H), 2.21 – 2.17 (m, 1 H), 2.08 – 2.04 (m, 1 H), 1.71 – 1.55 (m, 1 H), 0.97 – 0.94 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.1 (s), 148.3 (s), 132.4 (s), 128.9 (d), 128.5 (d, 2 CH), 124.4 (d), 101.2 (d), 17.9 (d), 17.0 (d), 15.1 (t); LRMS: (EI) *m/z* (%) = 186 ($[M]^+$, 9), 158 (100), 105 (66), 77 (61).

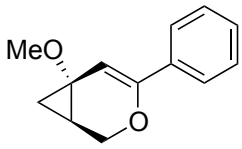


12

(1*S,5*R**,*Z*)-2-benzylidene-3-oxabicyclo[3.1.0]hexan-2-one (12).** Not isolated; data retrieved form a mixture of **11**/**12** in 57/43 ratio, containing also some IPrAu(OH) (not quantified). R_f = 0.70 (HxH/AcOEt, 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54 – 7.51 (m, 2 H), 7.38 – 7.29 (m, 2 H), 7.22 – 7.17 (m, 1 H), 5.62 (s, 1H), 2.84 – 2.80 (m, 1 H), 2.44 – 2.40 (m, 1 H), 1.45 – 1.39 (m, 1 H), 1.20 – 1.17 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.6 (s), 147.7 (s), 133.7 (s), 128.5 (d, 4 CH), 126.8 (d), 104.1 (d), 22.4 (d), 18.3 (d), 15.0 (t); LRMS: (EI) *m/z* (%) = 186 ($[M]^+$, 65), 158 (25), 129 (22), 118 (100), 90 (51).

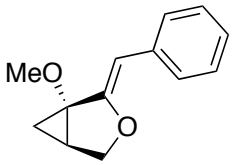
Cycloisomerization of (1*R,2*S**)-[2-methoxy-2-(phenylethynyl)cyclopropyl]methanol 10: Formation of (1*R**,6*S**)-6-methoxy-4-phenyl-3-oxabicyclo[4.1.0]hept-4-ene (13) and (1*S**,5*R**,*Z*)-2-benzylidene-1-methoxy-3-oxabicyclo[3.1.0]hexane (14).** This cycloisomerization was carried out following the general procedure at room temperature, by

employing alkynylcyclopropane alcohol **10** (0.5 mmol, 101 mg) as starting material. Once the reaction was concluded (as checked by TLC), solvents were removed under vacuum to give a crude reaction mixture formed by oxabicyclo[4.1.0]hept-4-ene **13** and oxabicyclo[3.1.0]hexane **14**, in 95% combined yield and 80/20 ratio.



13

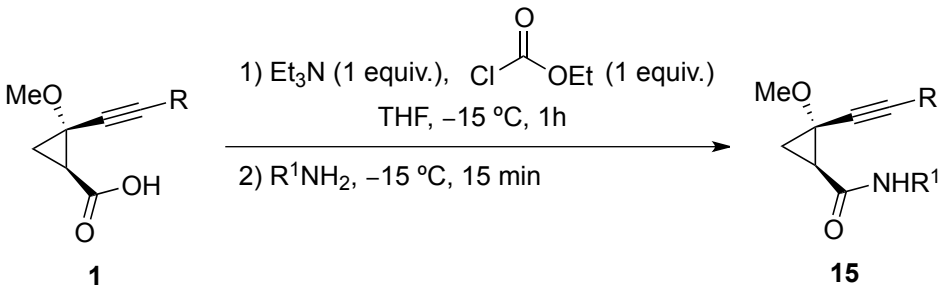
(1*R,6*S**)-6-methoxy-4-phenyl-3-oxabicyclo[4.1.0]hept-4-ene (13).** Chromatographic purification using hexane/AcOEt (5:1) as eluent allowed the partial isolation of oxabicyclo[4.1.0]hept-4-ene **13** as colourless liquid. R_f = 0.56 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, *J* = 7.2 Hz, 2 H), 7.47 – 7.21 (m, 3 H), 6.09 (s, 1 H), 4.28 (dd, *J* = 10.3, 0.9 Hz, 1 H), 3.99 (dd, *J* = 10.3, 1.8 Hz, 1 H), 3.41 (s, 3 H), 1.82 – 1.75 (m, 1 H), 1.33 (dd, *J* = 9.9, 5.1 Hz, 1 H), 1.10 (at, *J* = 5.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.4 (s), 135.0 (s), 128.2 (d , 2 CH), 128.1 (d), 124.3 (d, 2 CH), 103.0 (d), 63.9 (t), 57.6 (s), 55.5 (q), 24.8 (t), 19.7 (d); HRMS: (ESI) Calculated for $C_{13}H_{15}O_2$ $[M+1]^+$: 203.1067, found: 203.1070.



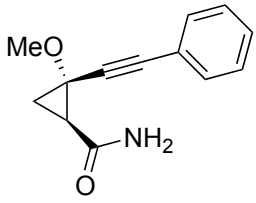
14

(1*S,5*R**,*Z*)-2-benzylidene-1-methoxy-3-oxabicyclo[3.1.0]hexane (14).** Colourless liquid; spectral data obtained from an enriched mixture containing **13** (ratio **14**/**13** = 3:2); R_f= 0.58 (Hexane/AcOEt, 5/1); ^{1}H NMR (401 MHz, $CDCl_3$) δ = 7.60 – 7.53 (m, 2 H), 7.35 – 7.26 (m, 2 H), 7.12 (d, *J* = 7.4 Hz, 1 H), 5.50 (s, 1 H), 4.41 (dd, *J* = 8.9, 4.3 Hz, 1 H), 4.07 (d, *J* = 8.9 Hz, 1 H), 3.46 (s, 3 H), 2.12 – 2.06 (m, 1 H), 1.60 (dd, *J* = 9.1, 5.3 Hz, 1 H), 0.96 (at, *J* = 5.3 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 153.4 (s), 136.2 (s), 128.2 (d, 2 CH), 127.4 (d, 2 CH), 125.1 (d), 97.3 (d), 72.6 (t), 71.0 (s), 56.8 (q), 21.4 (d), 21.9 (t).

General procedure for the synthesis of alkynylcyclopropanecarboxamides 15:



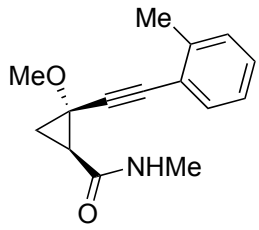
A solution of alkynylcyclopropane acid **1** (1 mmol) in THF (15 mL) under inert atmosphere was cooled to –15 ºC with stirring. Et_3N (1 equiv, 1 mmol, 0.14 mL) and ethyl chloroformate (1 equiv, 1 mmol, 0,96 mL) were sequentially added; a white precipitate was formed. Stirring was maintained for 1h at that temperature and, then, the corresponding amine (or ammonium hydroxide) was added. Stirring was continued for 15 min at –15 ºC, before removing the cooling bath and allowing the mixture to reach room temperature. Solvent was evaporated under vacuum; ethyl acetate (25 mL) and 5% sodium bicarbonate solution (15 mL) were added. Following shaking and separation, the ethyl acetate layer was sequentially washed with water (15 mL), 1*N* hydrochloric acid (15 mL), and finally, water (15 mL). After drying over anhydrous sodium sulphate, evaporation of the ethyl acetate solution led to amides **15**, which were used without further purification. No epimerization was observed under the reaction conditions.



15a

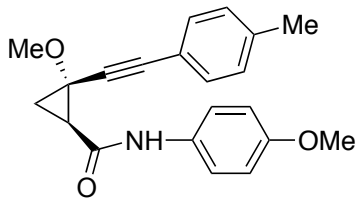
(1*S, 2*S**)-2-methoxy-2-(phenylethynyl)cyclopropanecarboxamide (15a).** Colourless liquid; yield = 98 % (of a 5:1 mixture of diasteroisomers); R_f = 0.05 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 – 7.39 (m, 4 H, min + maj), 7.31 – 7.24 (m, 6 H, min + maj), 6.29 (bs, 4

H, min + maj), 3.48 (s, 3 H, min), 3.45 (s, 3 H, maj), 2.13 – 2.07 (m, 2 H, min + maj), 1.73 – 1.64 (m, 2 H, min + maj), 1.53 – 1.46 (m, 2 H, min + maj); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.1 (s, min), 170.7 (s, maj), 131.9 (d, 2 CH, maj), 131.8 (d, 2 CH, min), 128.7 (d, min), 128.5 (d, maj), 128.4 (d, 2 CH, min), 128.2 (d, 2 CH, maj), 122.3 (s, maj), 122.0 (s, min), 86.7 (s, maj), 86.4 (s, min), 84.2 (s, min), 83.8 (s, maj), 58.6 (s, maj), 57.7 (s, min), 56.3 (q, min), 55.8 (q, maj), 31.1 (t, min), 31.0 (t, maj), 21.6 (d, min), 21.0 (d, maj).



15b

(1*S, 2*S**)-2-methoxy-*N*-methyl-2-(*o*-tolylethynyl)cyclopropanecarboxamide (15b).** Colourless liquid; yield = 97% (of a 6.7:1 mixture of diasteroisomers); R_f = 0.21 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 – 7.36 (m, 2 H, min + maj), 7.23 – 7.07 (m, 6 H, min + maj), 6.25 (bs, 1 H, min), 6.11 (bs, 1 H, maj), 3.51 (s, 3 H, min), 3.48 (s, 3 H, maj), 2.82 (d, *J* = 4.8 Hz, 3 H, maj + 3 H min), 2.41 (s, 6 H, min + maj), 2.12 (dd, *J* = 9.8, 7.6 Hz, 1H, min), 2.08 (dd, *J* = 9.7, 7.4 Hz, 1 H, maj), 1.72 (dd, *J* = 7.4, 5.7 Hz, 1 H, maj + 1 H min), 1.49 (dd, *J* = 9.7, 5.7 Hz, 1 H, maj + 1 H min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.9 (s, min), 168.4 (s, maj), 140.3 (s, maj), 140.2 (s, min), 132.1 (s, maj), 131.9 (d, min), 129.5 (d, min), 129.4 (d, maj), 128.6 (d, min), 128.4 (d, maj), 125.6 (d, min), 125.4 (d, maj), 122.3 (s, maj), 121.9 (s, min), 90.6 (s, min), 87.8 (s, maj), 85.5 (s, maj), 82.9 (s, min), 58.4 (s, maj), 57.4 (s, min) 56.3 (q, min), 55.7 (q, maj), 31.7 (t, min), 31.5 (t, maj), 26.6 (q, min), 26.5 (q, maj), 21.3 (d, min), 20.73 (d, maj), 20.66 (q, min), 20.60 (q, maj); LRMS: (EI) *m/z* (%) = 243 ($[M]^+$, 19), 228 (33), 185 (99), 115 (100), 112 (57); HRMS: (EI) calculated for $C_{15}H_{17}NO_2$ $[M]^+$: 243.1259, found: 243.1257.



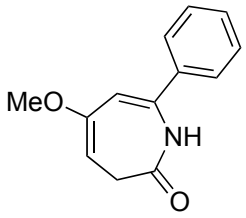
15c

(1*S,2*S**)-2-methoxy-*N*-(4-methoxyphenyl)-2-(*p*-tolylethynyl)cyclopropanecarboxamide (15c).** Colourless liquid; yield = 90% (of a 5:1 mixture of diasteroisomers); R_f = 0.18 (HxH/AcOEt, 5/1); ^{1}H NMR (401 MHz, $CDCl_3$) δ = 7.85 (bs, 1 H, min), 7.57 (bs, 1 H, maj), 7.42 (d, *J* = 8.9 Hz, 2 H, min), 7.40 (d, *J* = 8.9 Hz, 2 H, maj), 7.34 (d, *J* = 8.0 Hz, 2 H, min), 7.30 (d, *J* = 7.9 Hz, 2 H, maj), 7.14 (d, *J* = 8.0 Hz, 2 H, min), 7.08 (d, *J* = 7.9, 2 H, maj), 6.85 (d, *J* = 8.9 Hz, 2 H, min), 6.82 (d, *J* = 8.9 Hz, 2 H, maj), 3.79 (s, 3 H, min), 3.77 (s, 3 H, maj), 3.56 (s, 3 H, min), 3.51 (s, 3 H, maj), 2.36 (s, 3 H, min), 2.33 (s, 3 H, maj), 2.20 (dd, *J* = 9.2, 7.6 Hz, 1 H, maj + 1 H, min), 1.81 – 1.76 (m, 2 H, min + maj), 1.60 (dd, *J* = 9.4, 5.8 Hz, 1 H, maj + 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.3 (s, min), 166.2 (s, maj), 156.3 (s, min), 156.2 (s, maj), 138.9 (s, min), 138.6 (s, maj), 131.8 (d, 2 CH, maj), 131.7 (d, 2 CH, min), 131.3 (s, maj), 131.2 (s, min), 129.2 (d, 2 CH, min), 129.0 (d, 2 CH, maj), 121.9 (d, 2 CH, maj), 121.8 (d, 2 CH, min), 119.2 (s, maj), 119.0 (s, min), 114.2 (d, 2 CH, min), 114.0 (d, 2 CH, maj), 87.2 (s, maj), 85.8 (s, min), 84.4 (s, min), 83.1 (s, maj), 58.8 (s, maj), 57.8 (s, min), 56.4 (q, min), 55.8 (q, maj), 55.5 (q, min), 55.4 (q, maj), 32.2 (t, 2 CH_2, min + maj), 21.49 (d, min), 21.45 (d, maj), 21.3 (q, min), 20.9 (q, maj); LRMS: (EI) *m/z* (%) = 335 ($[M]^+$, 34), 302 (51), 185 (100), 143 (52), 115 (39); HRMS: (EI) calculated for $C_{21}H_{21}NO_3$ $[M]^+$: 335.1521, found: 335.1527.

General procedure for the synthesis of azepinones 16:

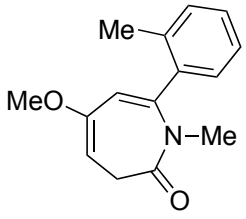
A solution of freshly lyophilized IPrAuCl (3 mol%, 0.015 mmol, 9.3 mg) and AgOTs (3 mol%, 0.015 mmol, 4.2 mg) in CH_2Cl_2 (5 mL) was placed in a sealed tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of the

corresponding alkynylcyclopropanecarbamide **15** (0.5 mmol) in CH_2Cl_2 (5 mL) was then added; stirring was maintained for 12 h at 110 ºC. End of reaction was monitored by TLC; solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give the corresponding azepinone **16** in the yield indicated in Scheme 4.



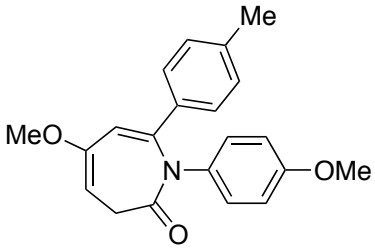
16a

5-methoxy-7-phenyl-1*H*-azepin-2(3*H*)-one (16a). Colourless liquid; yield = 85 %; R_f = 0.25 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56 – 7.53 (m, 2 H), 7.44 – 7.38 (m, 3 H), 7.26 (bs, 1 H), 6.12 (s, 1 H), 4.76 (t, *J* = 7.1 Hz, 1 H), 3.63 (s, 3 H), 2.91 (d, *J* = 7.1 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.3 (s), 156.1 (s), 138.9 (s), 136.9 (s), 129.6 (d), 129.0 (d, 2 CH), 126.6 (d, 2 CH), 109.8 (d), 90.8 (d), 55.6 (q), 32.9 (t). LRMS: (EI) *m/z* (%) = 215 ($[M]^+$, 100), 201 (82), 186 (82), 146 (94), 104 (90); HRMS: (EI) calculated for $C_{13}H_{13}NO_2$ $[M]^+$: 215.0946, found: 215.0948.



16b

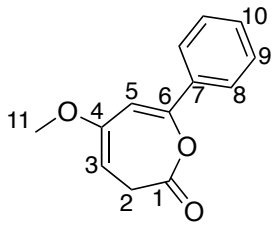
5-Methoxy-1-methyl-7-(*o*-tolyl)-1*H*-azepin-2(3*H*)-one (16b). Colourless liquid; yield = 76 %; R_f = 0.36 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 – 7.17 (m, 4 H), 5.90 (s, 1 H), 4.83 (t, *J* = 7.0 Hz, 1 H), 3.62 (s, 3 H), 3.01 (bs, 2 H), 2.77 (s, 3 H), 2.23 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.6 (s), 161.8 (s), 155.3 (s), 137.4 (s), 135.5 (s), 130.6 (d), 129.7 (d), 128.9 (d), 126.5 (d), 115.4 (d), 92.5 (d), 55.5 (q), 34.0 (q), 33.3 (d), 19.5 (q).



16c

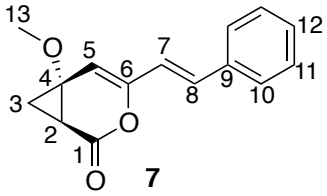
5-methoxy-1-(4-methoxyphenyl)-7-(*p*-tolyl)-1*H*-azepin-2(3*H*)-one (16c). Colourless liquid; yield = 62 %; R_f = 0.38 (HxH/AcOEt, 5/1); ^{1}H NMR (401 MHz, $CDCl_3$) δ = 7.22 (d, *J* = 7.9 Hz, 2 H), 7.06 (d, *J* = 8.9 Hz, 2 H), 6.99 (d, *J* = 7.9 Hz, 2 H), 6.70 (d, *J* = 8.9 Hz, 2 H), 6.27 (s, 1 H), 4.93 (t, *J* = 6.8 Hz, 1 H), 3.69 (s, 3 H), 3.67 (s, 3 H), 3.12 (bs, 2 H), 2.24 (s, 3 H); ^{13}C NMR (1010 MHz, $CDCl_3$) δ = 169.1 (s), 157.7 (s), 155.6 (s), 144.3 (s), 138.2 (s), 134.9 (s), 132.9 (s), 129.0 (d, 2 CH), 128.8 (d, 2 CH), 127.7 (d, 2 CH), 116.1 (d), 113.6 (d, 2 CH), 93.7 (d), 55.6 (q), 55.2 (q), 34.3 (t), 21.1 (q). LRMS: (EI) *m/z* (%) = 335 ($[M]^+$, 63), 320 (15), 306 (100), 292 (14), 224 (32); HRMS: (EI) calculated for $C_{21}H_{21}NO_3$ $[M]^+$: 335.1521, found: 335.1515.

4 . Tables with the 2D-NMR (HSQC, COSY, HMBC and NOESY) Experiments for Selected Compounds [400 MHz ($CDCl_3$)]



2a

Site	^{13}C RMN	DEPT	^{1}H RMN	COSY	HMBC	NOESY
1	166.9	C				
2	32.0	CH_2	**3.00 (d, *J* = 6.8 Hz, 2 H)**	3	1, 3, 4, 6	3
3	89.7	CH	**4.85 (t, *J* = 6.8 Hz, 1 H)**	2	2, 5, 6, 1	2, 11
4	155.8	C				
5	106.2	CH	**6.42 (s, 1 H)**		3,4, 6, 7,	8, 11
6	150.3	C				
7	133.5	C				
8	125.4	CH	**7.70-7.65 (m, 2 H)**	9, 10	6, 8, 10	5
9	128.5	CH	**7.41-7.37 (m, 2 H)**	8, 10	7, 9, 10	
10	129.5	CH	**7.41-7.37 (m, 1 H)**	8, 9	8	
11	55.5	CH_3	**3.65 (s, 3 H)**		4	3, 5



7

Site	^{13}C RMN	DEPT	^{1}H RMN	COSY	HMBC	NOESY
1	166.9	C				
2	24.9	CH	**2.36 (ddd, *J* = 11.2, 5.4, 1.4 Hz, 1 H)**	3, 5	3,4	
3	23.2	CH_2	**1.17 (t, *J* = 5.4 Hz, 1 H),** **2.01 (dd, *J* = 11.2, 5.4 Hz, 1 H)**	2, 3	1, 3, 4, 5	
4	64.6	C				
5	106.1	CH	**5.77 (s, 1 H)**		3, 6, 7	7, 13
6	147.1	C				
7	119.4	CH	**6.42 (d, *J* = 15.9 Hz, 1 H)**	7	1, 5, 6, 8, 9,	5, 10
8	131.0	CH	**7.08 (d, *J* = 15.9 Hz, 1 H)**	8	5, 6, 7,9, 10	10
9	135.9	C				
10	126.9	CH	**7.44-7.27 (m, 2 H)**	11, 12	8, 10, 12	7, 8
11	128.8	CH	**7.44-7.27 (m, 2 H)**	10, 12	9, 11	
12	128.5	CH	**7.44-7.27 (m, 1 H)**	10, 11	10	
13	56.7	CH_3	**3.39 (s, 3 H)**		4	5

5. References and notes.

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[12] D. D. Perrin, W. L. F. Armarego, D. R. Perrin, *Purification of Laboratory Chemicals*, Pergamon Press., 3h Ed., 1998.
[13] For the preparation of Fischer alkoxy alkynylcarbene complexes see ref. 8 and references cited therein.
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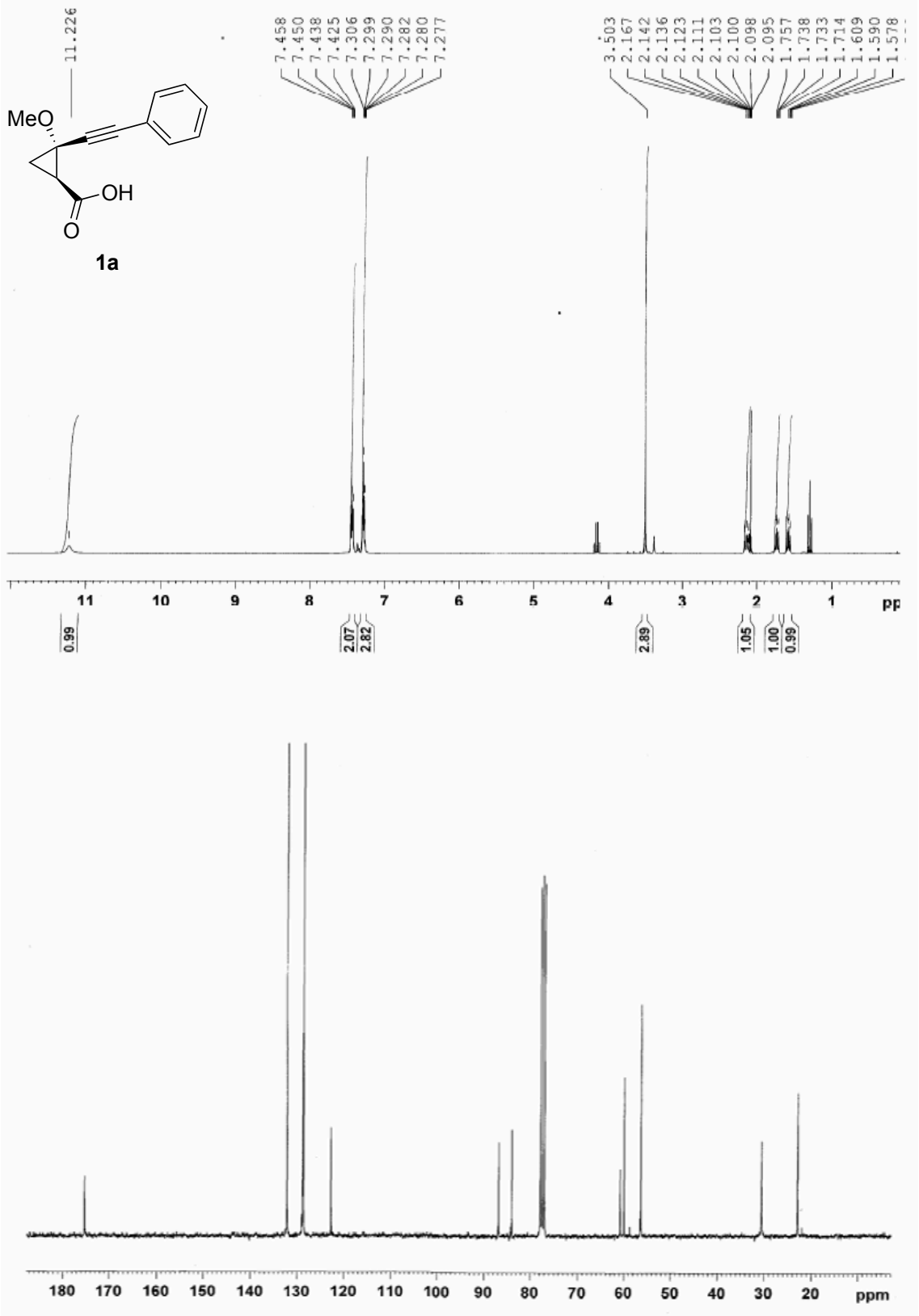
6. Copies of ^{1}H- and ^{13}C-NMR Spectra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2.142
2.136
2.123
2.111
2.103
2.100
2.098
2.095
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1.738
1.733
1.714
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1.590
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OH
O
1a
11
10
9
8
7
6
5
4
3
2
1
ppm
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2.82
2.89
1.05
1.00
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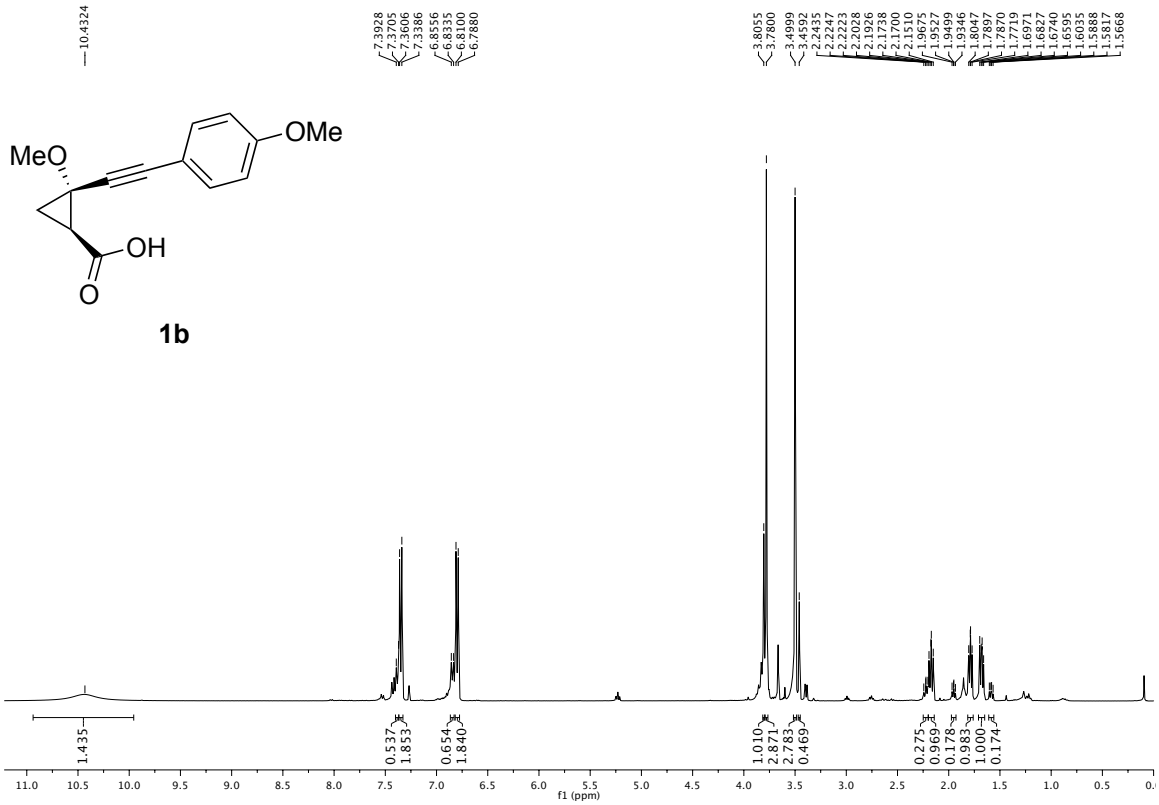
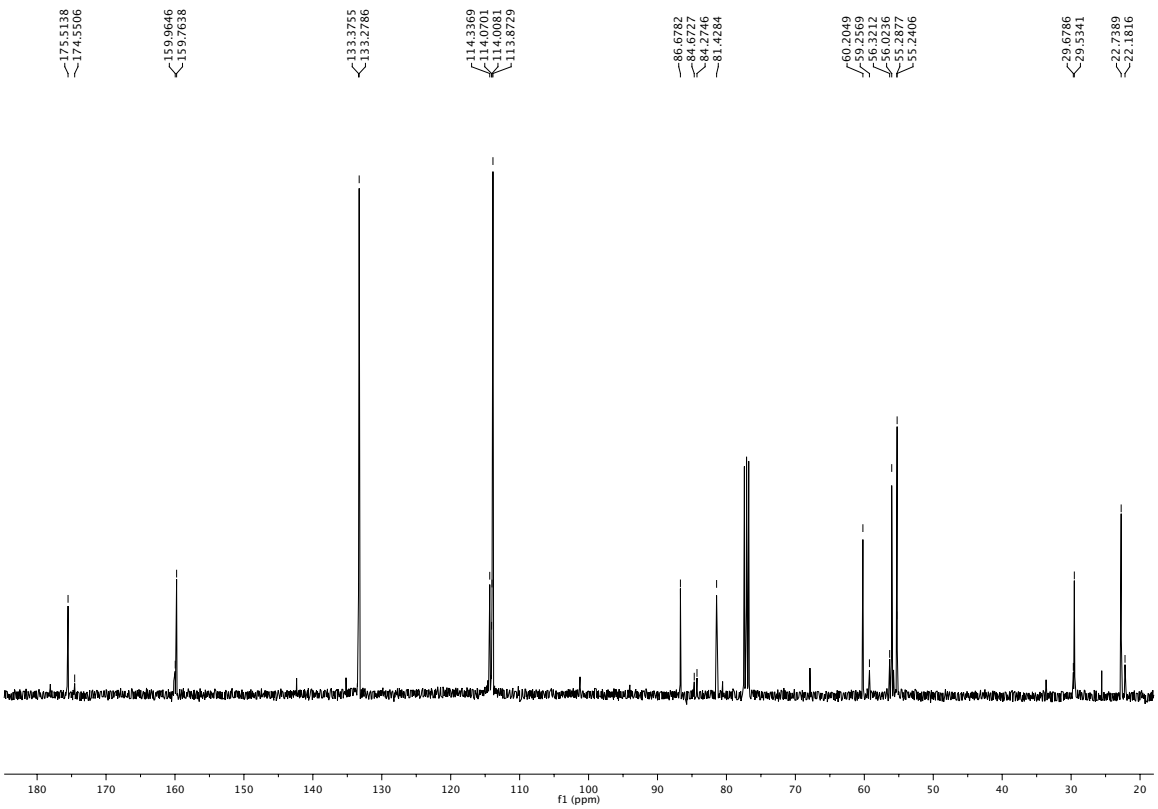
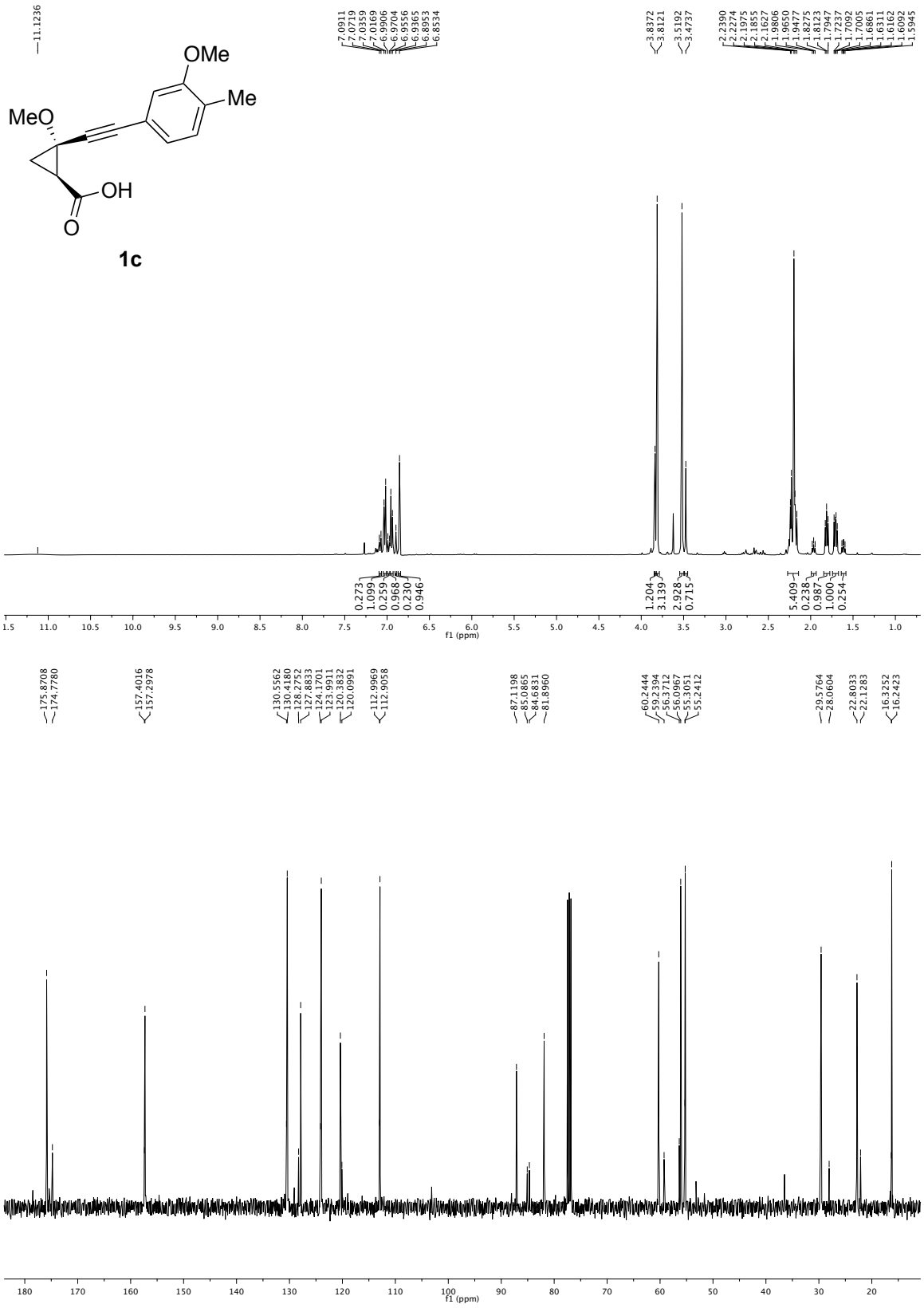
20
ppm



1b

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84.6831
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56.3712
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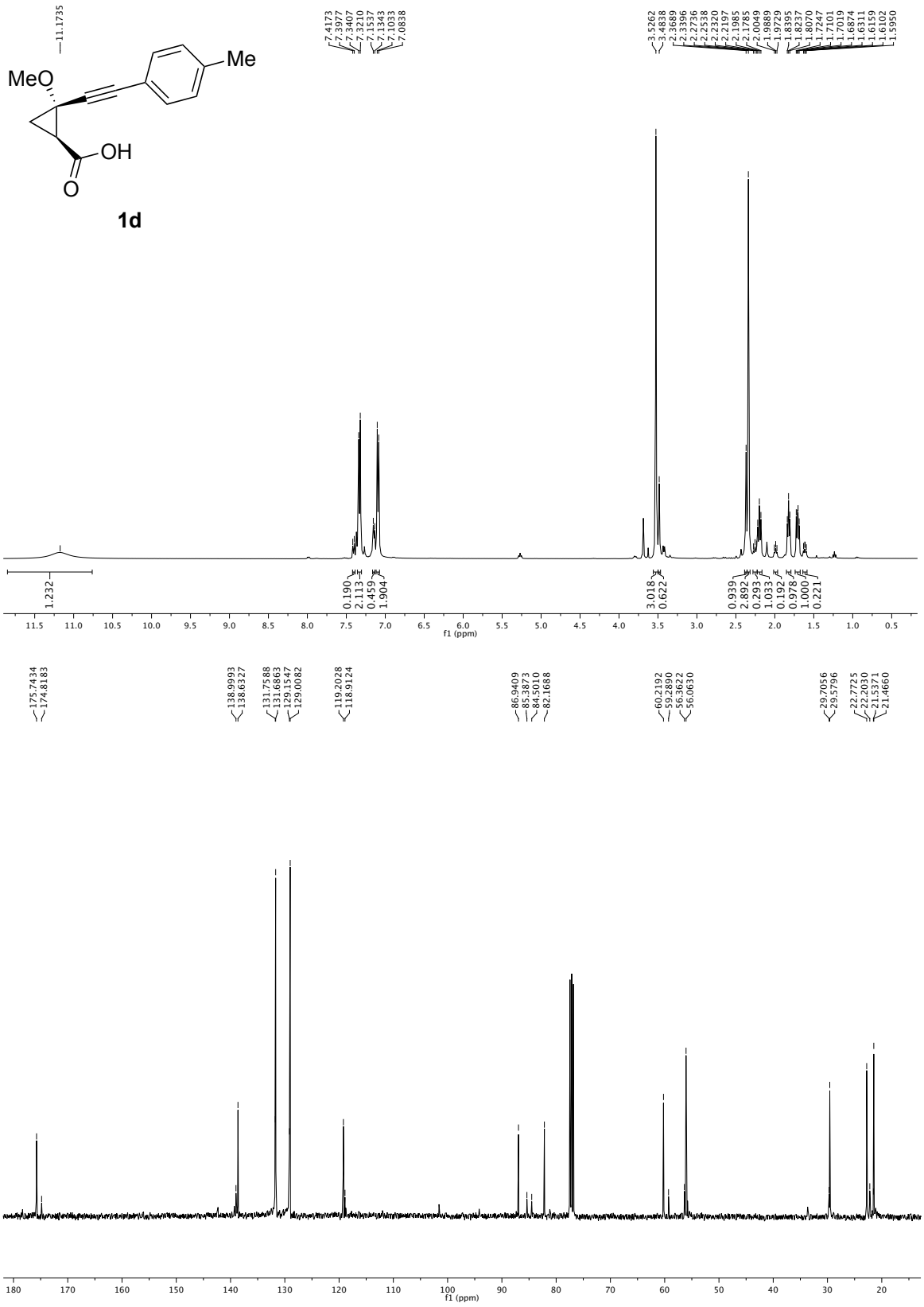
f1 (ppm)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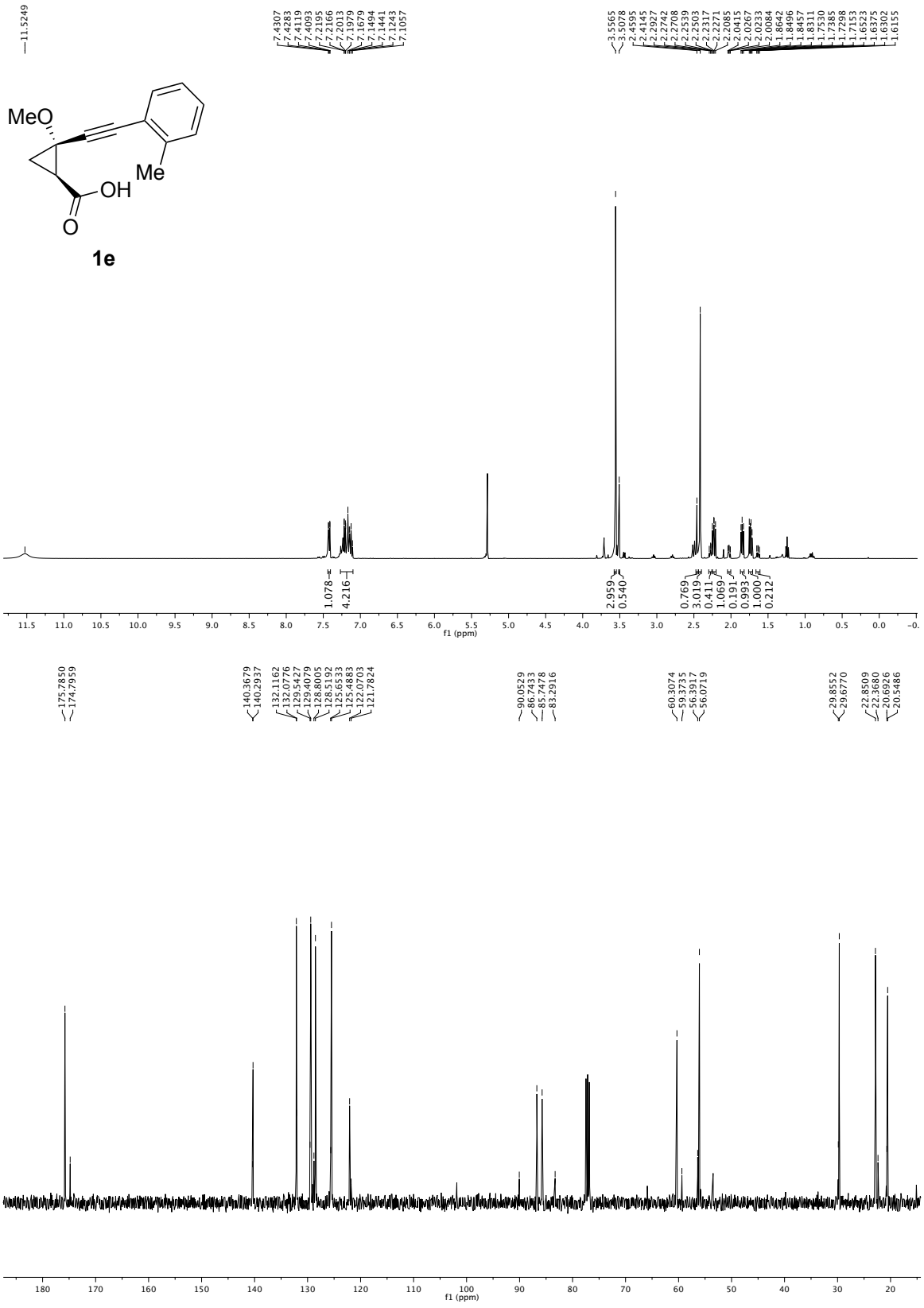
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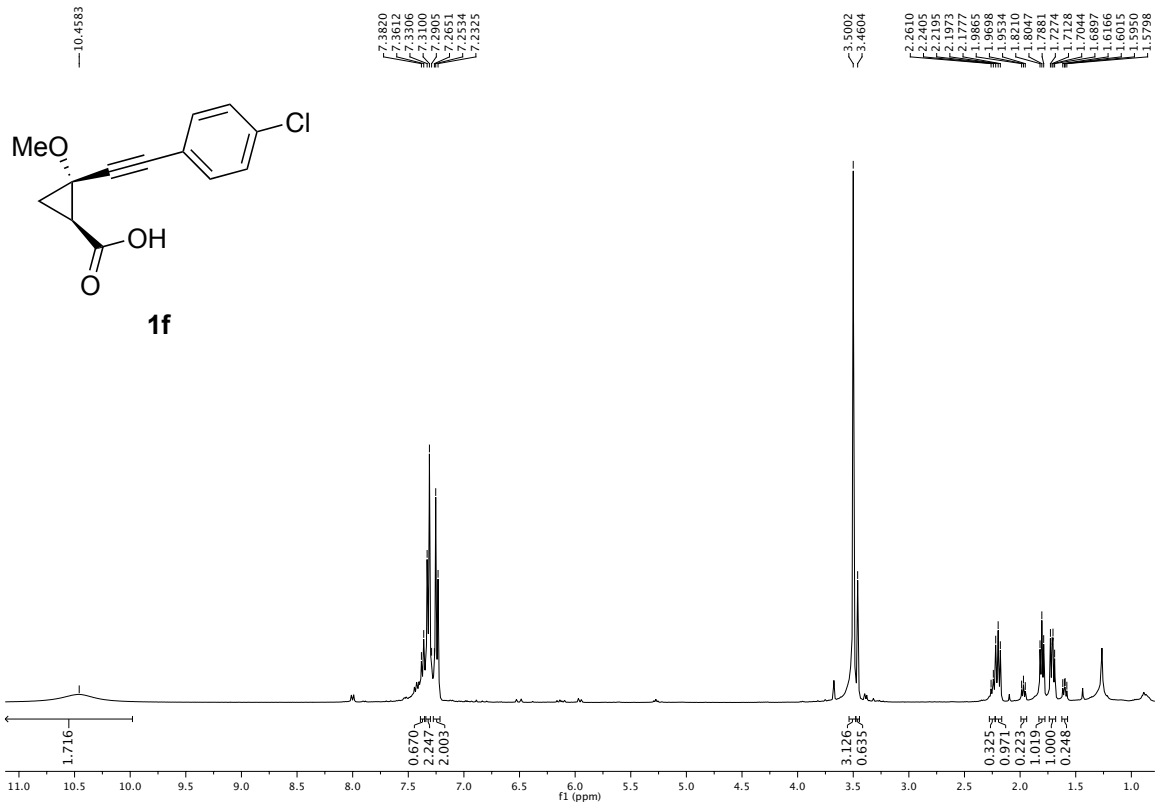
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O
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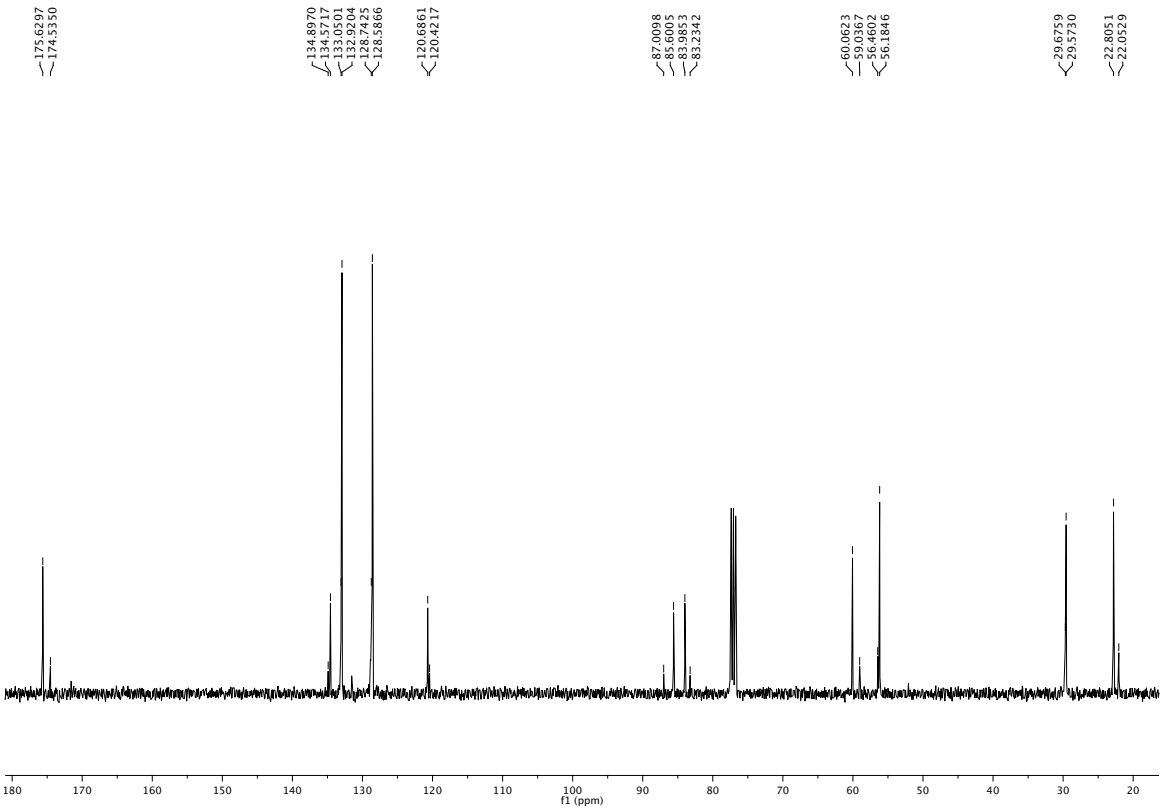
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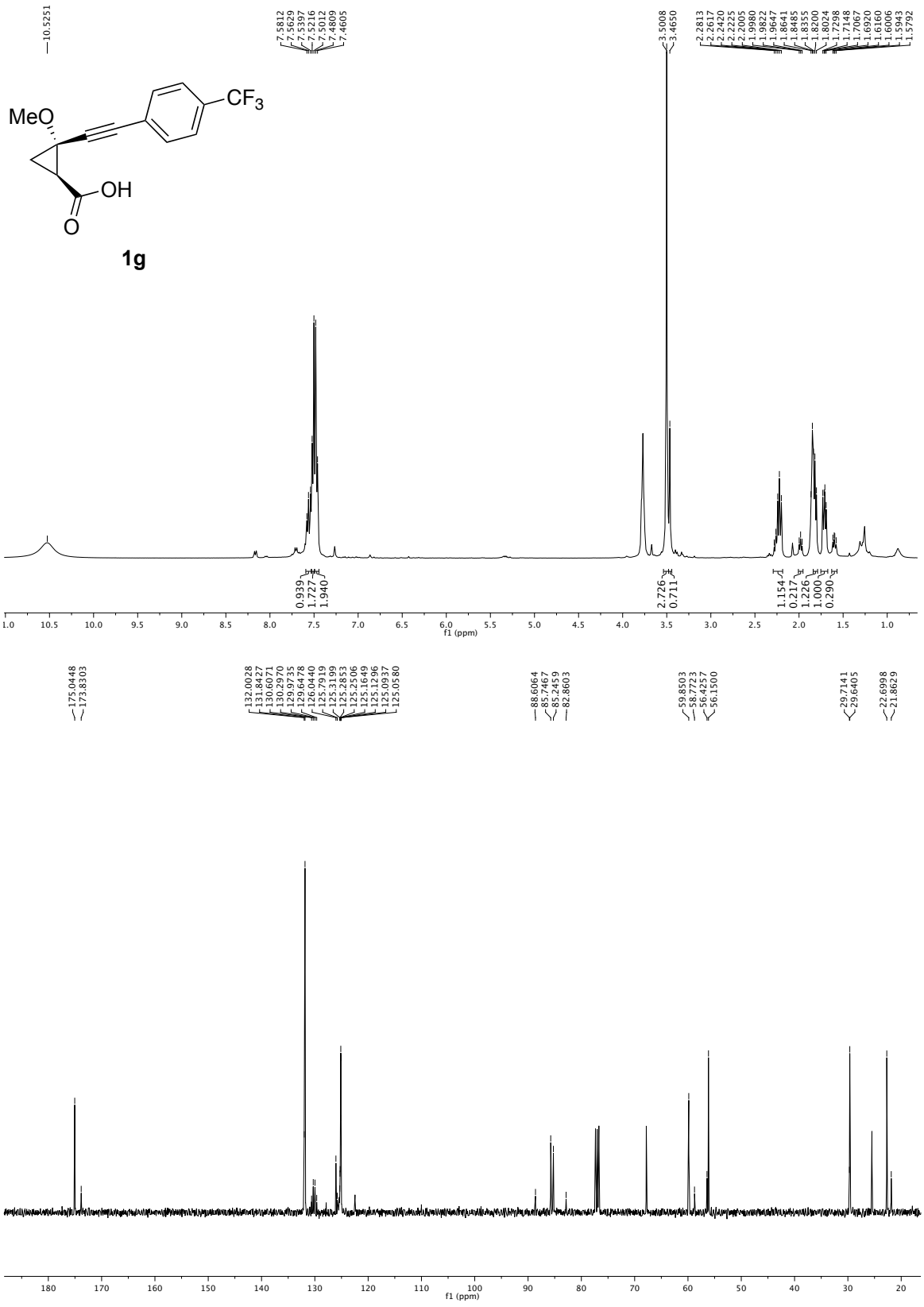
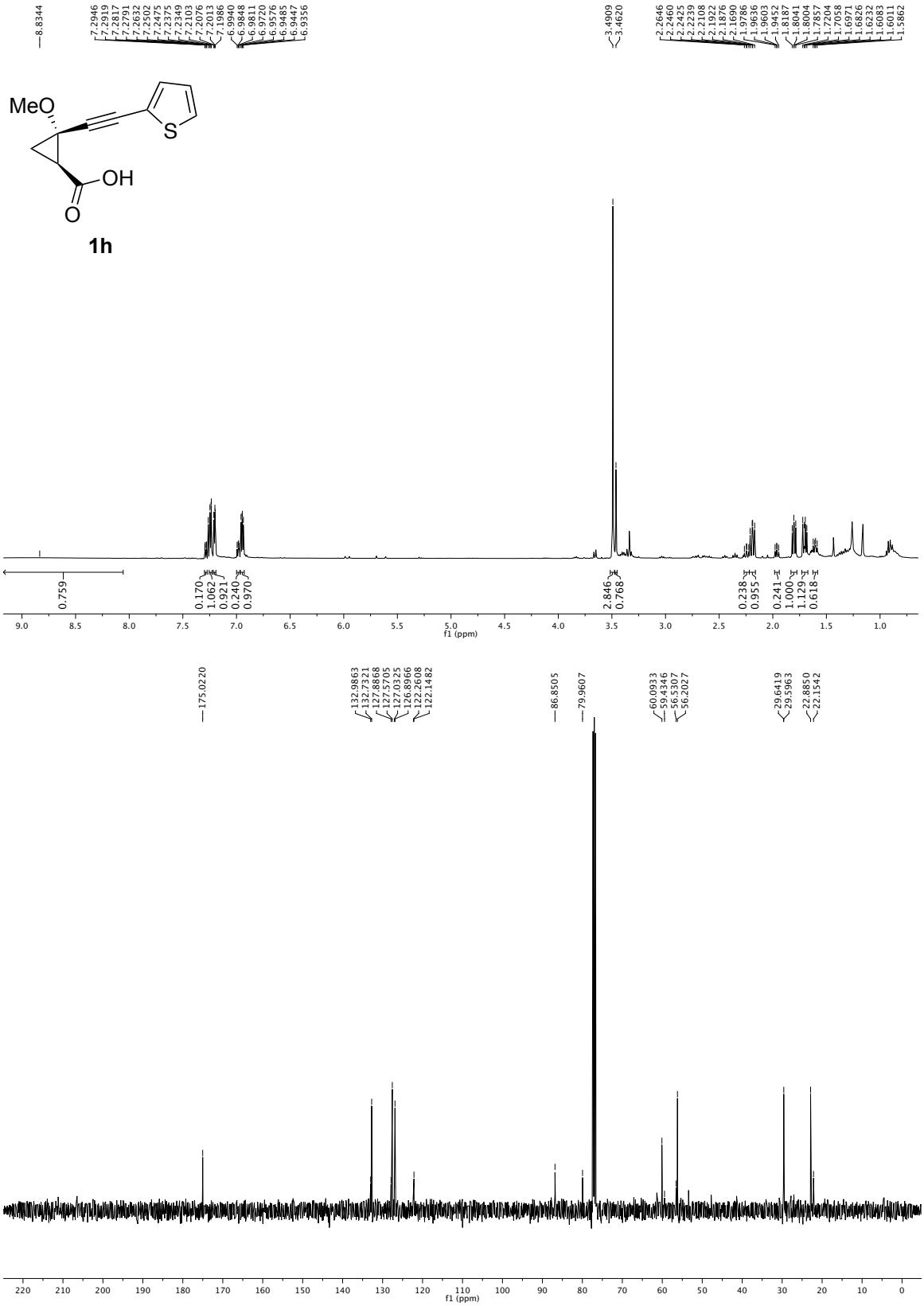
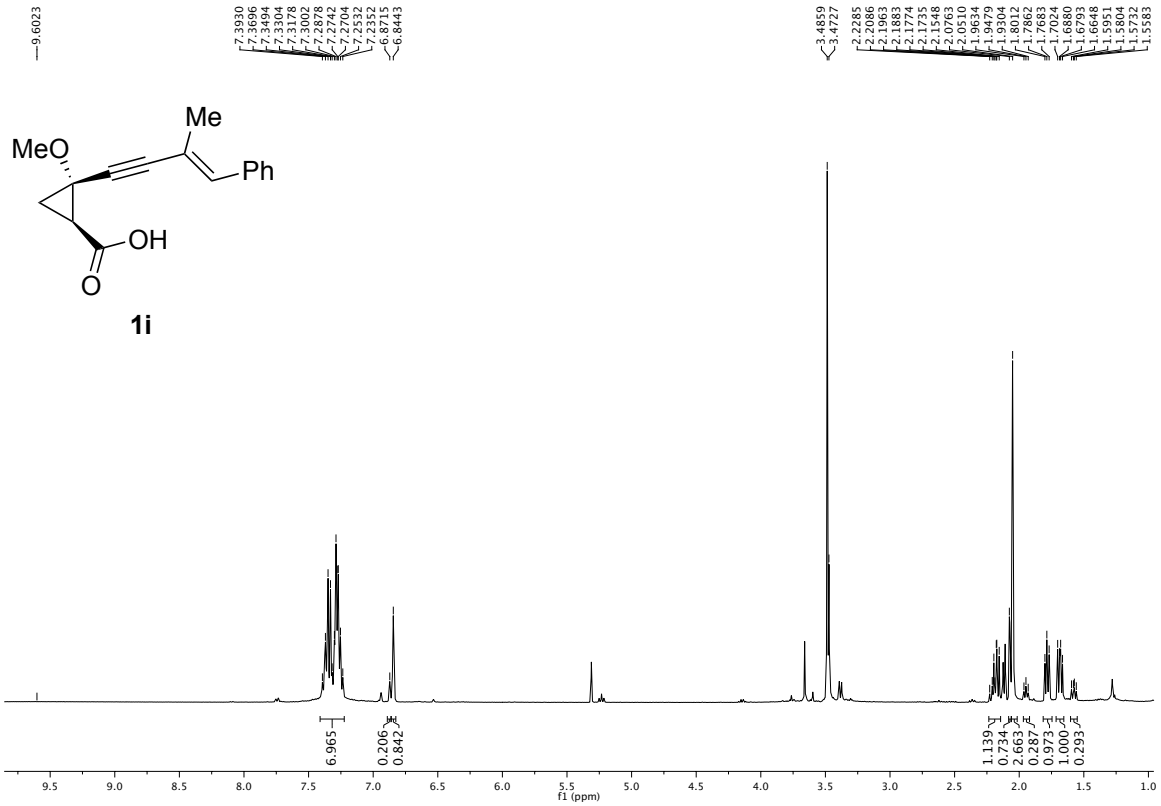
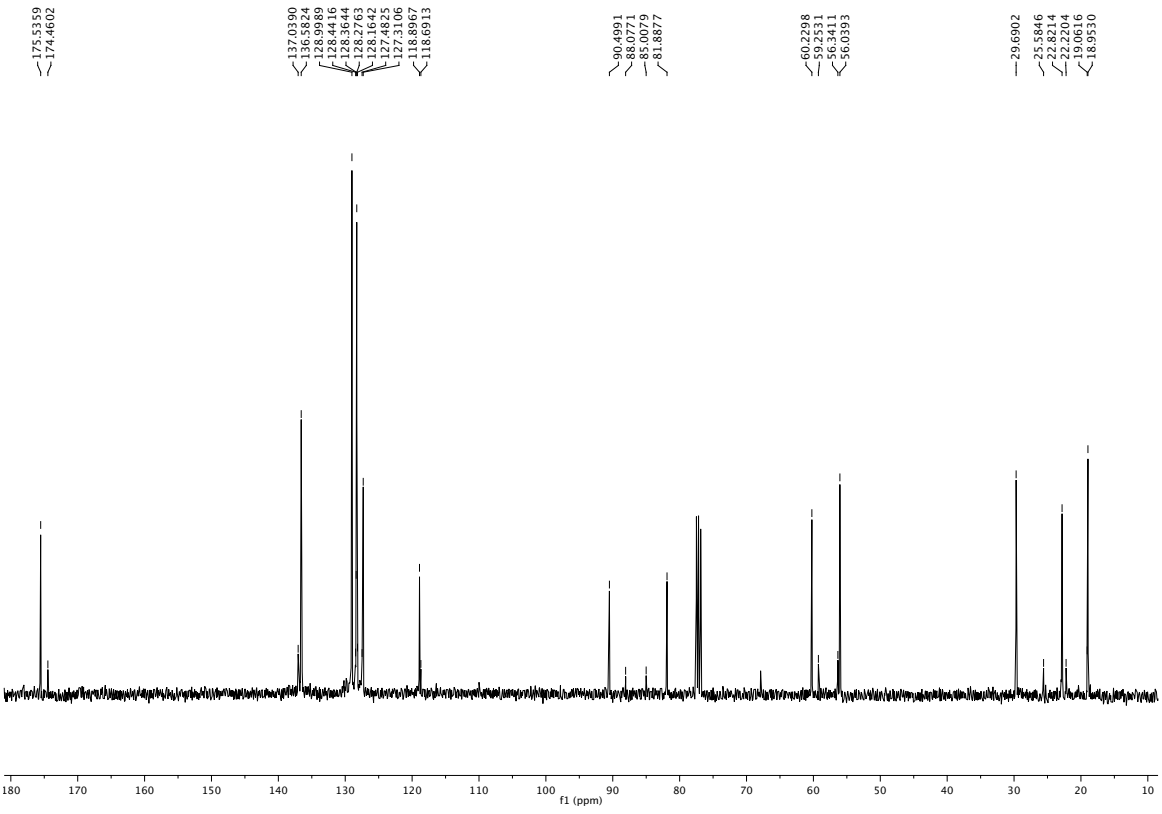
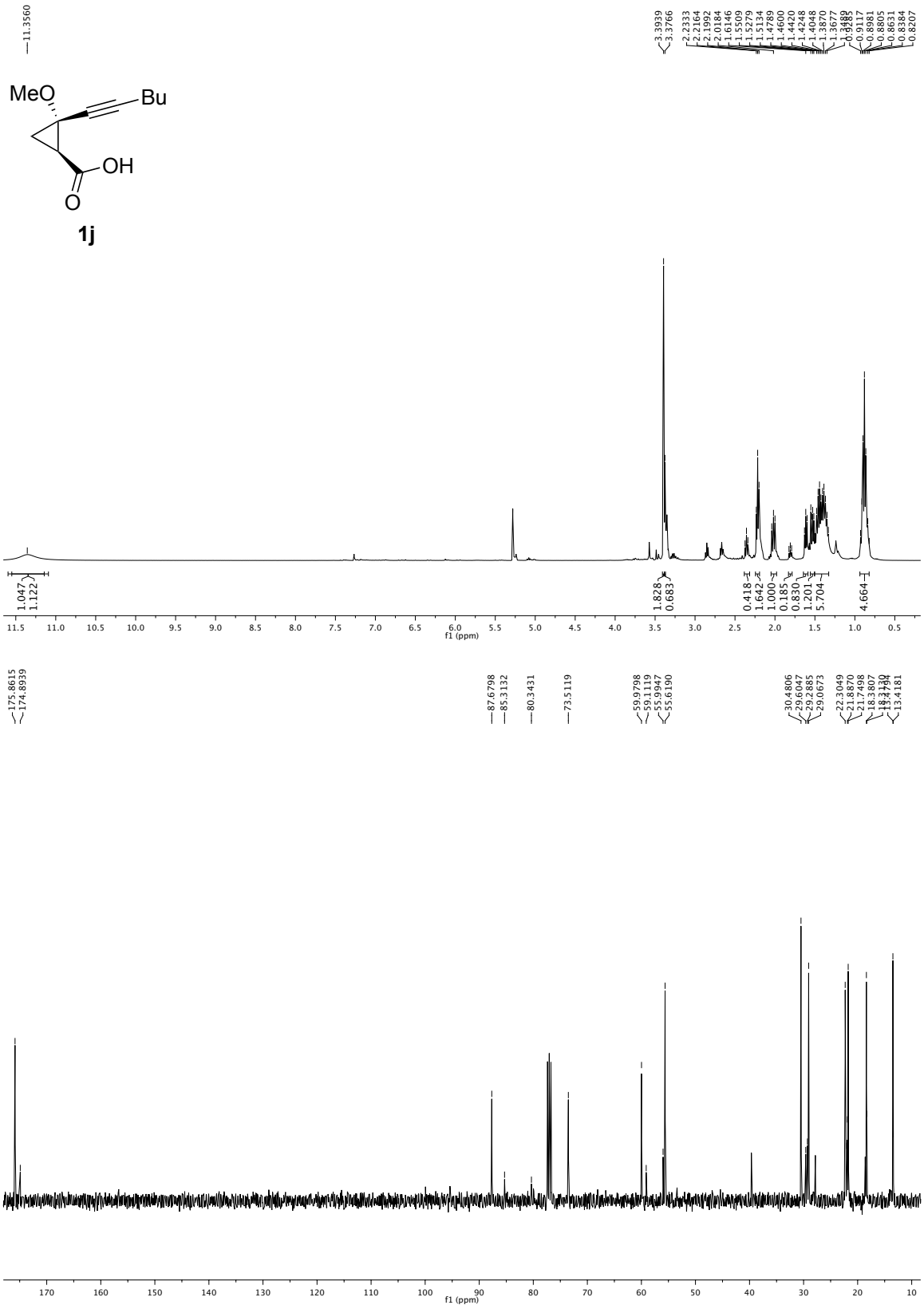
22.0529
f1 (ppm)

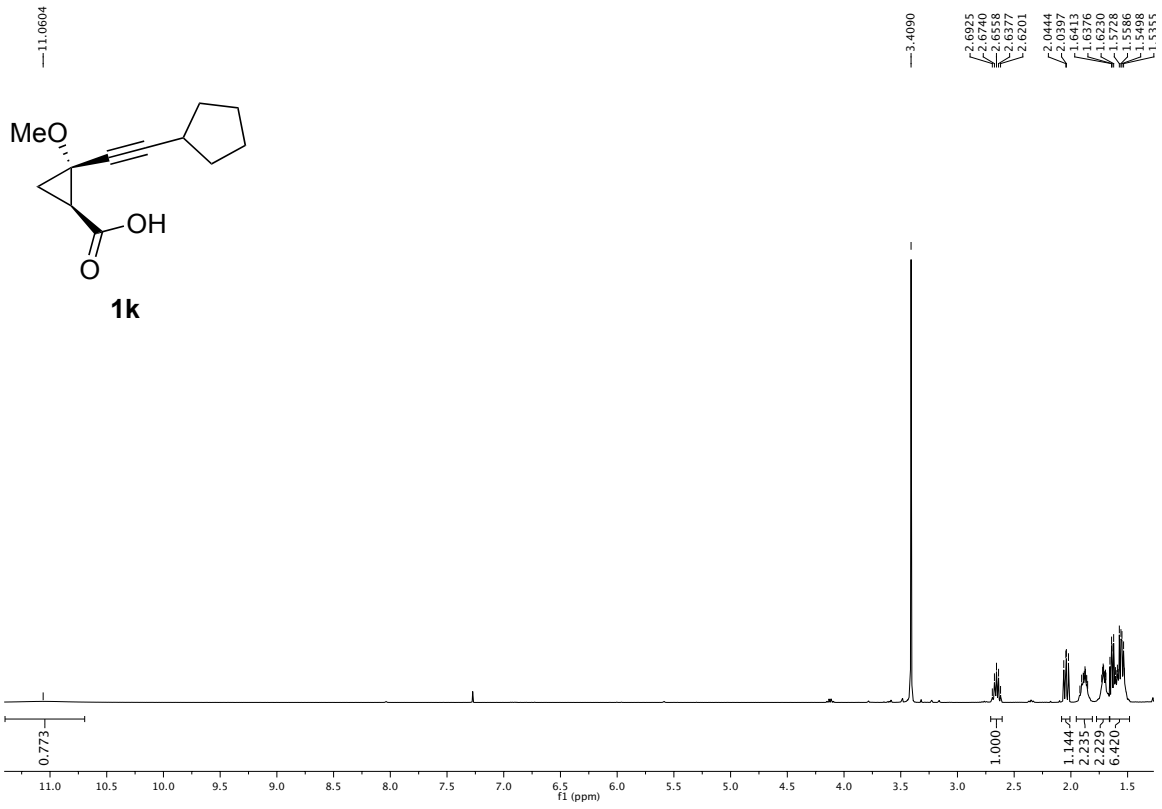

MeO
CF3
OH
O
1g
f1 (ppm)
f1 (ppm)


MeO
S
OH
O
1h
f1 (ppm)
f1 (ppm)

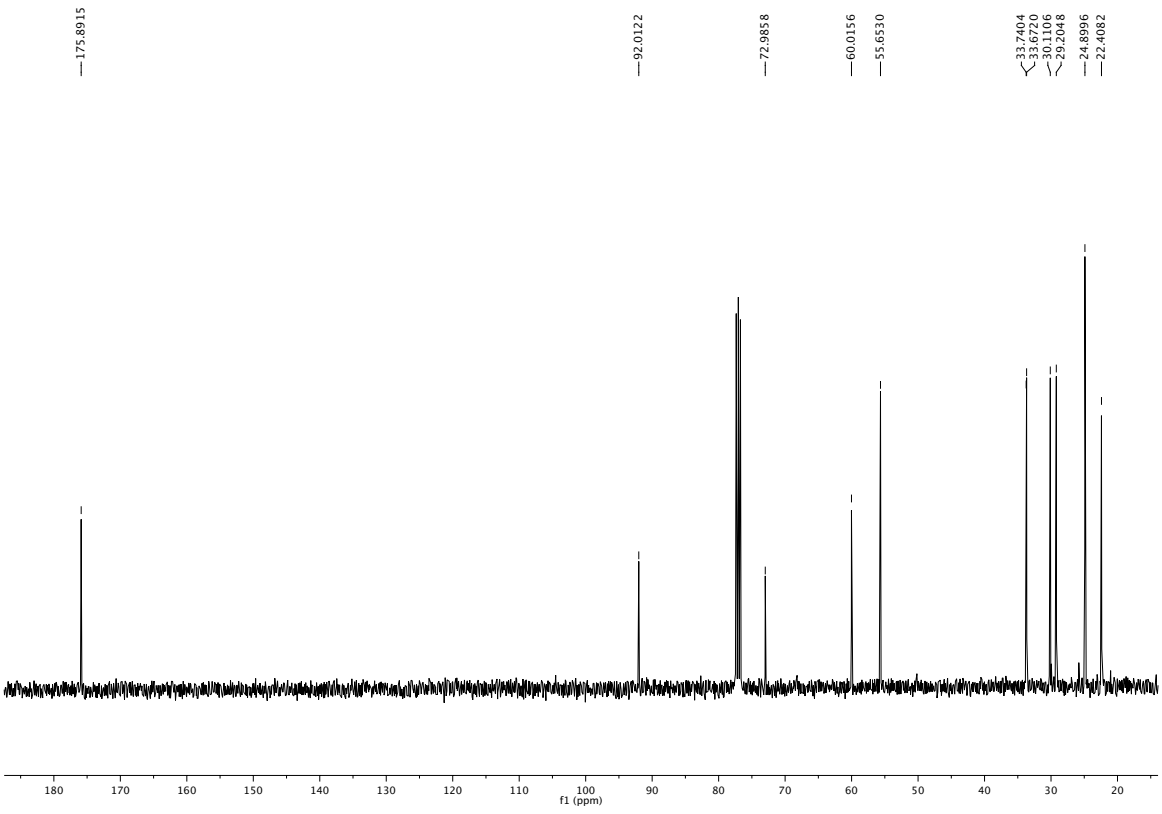

9.6023
7.3930
7.3696
7.3494
7.3304
7.3178
7.3002
7.2878
7.2742
7.2704
7.2532
7.2352
6.8715
6.8443
3.4859
3.4727
2.2285
2.2086
2.1963
2.1883
2.1774
2.1735
2.1548
2.0763
2.0510
1.9634
1.9479
1.9304
1.8012
1.7862
1.7683
1.7024
1.6880
1.6793
1.6648
1.5951
1.5804
1.5732
1.5583
Me
MeO
Ph
OH
O
1i
6.965
0.206
0.842
1.139
0.734
2.663
0.287
0.973
1.000
0.293
f1 (ppm)

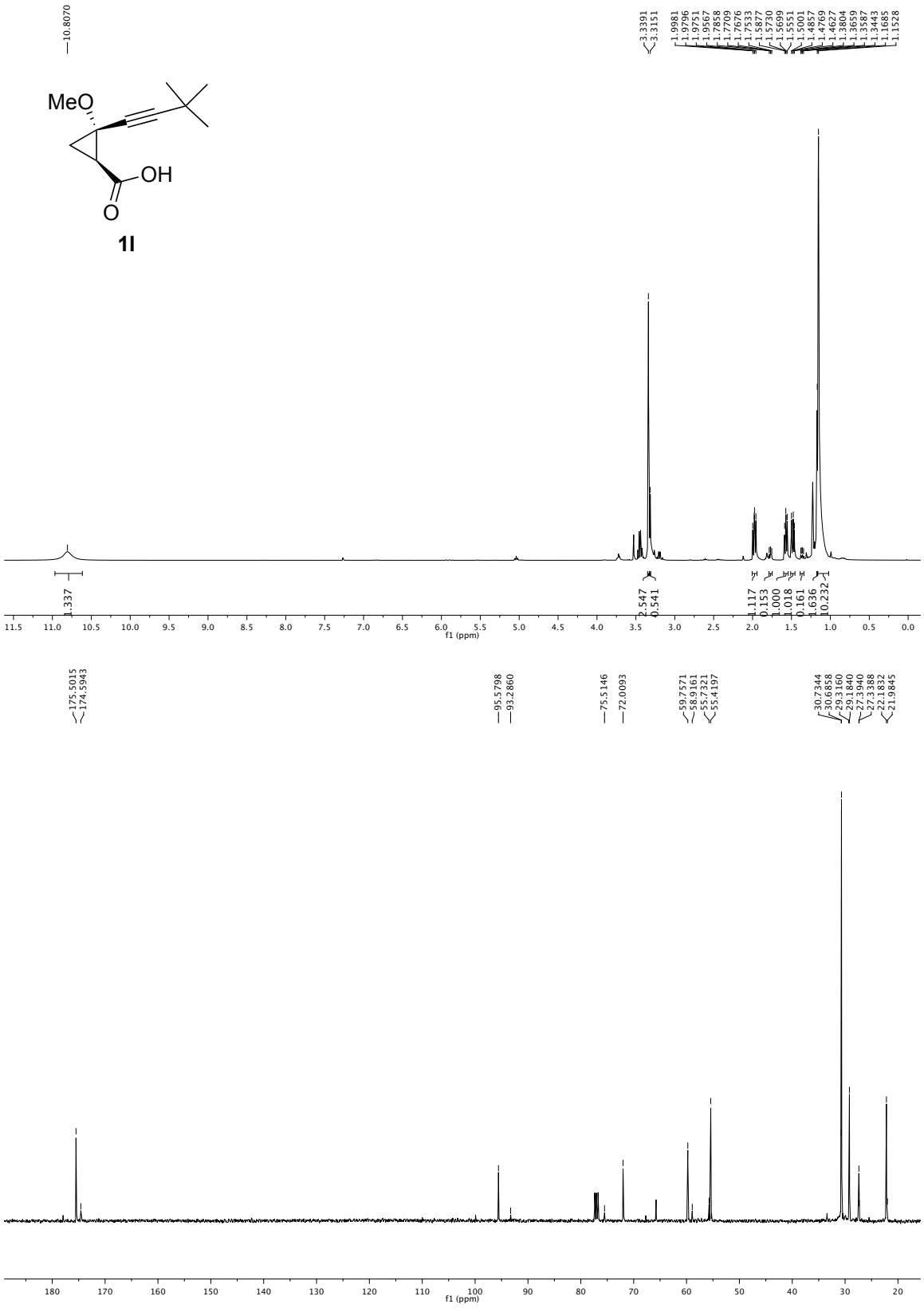

175.5359
174.4602
137.0390
136.5824
128.9989
128.4416
128.3644
128.2763
128.1642
127.4825
127.3106
118.8967
118.6913
90.4991
90.0771
85.0079
81.8877
60.2298
59.2531
56.3411
56.0393
29.6902
25.5846
22.8214
22.2214
19.2216
18.9530
f1 (ppm)

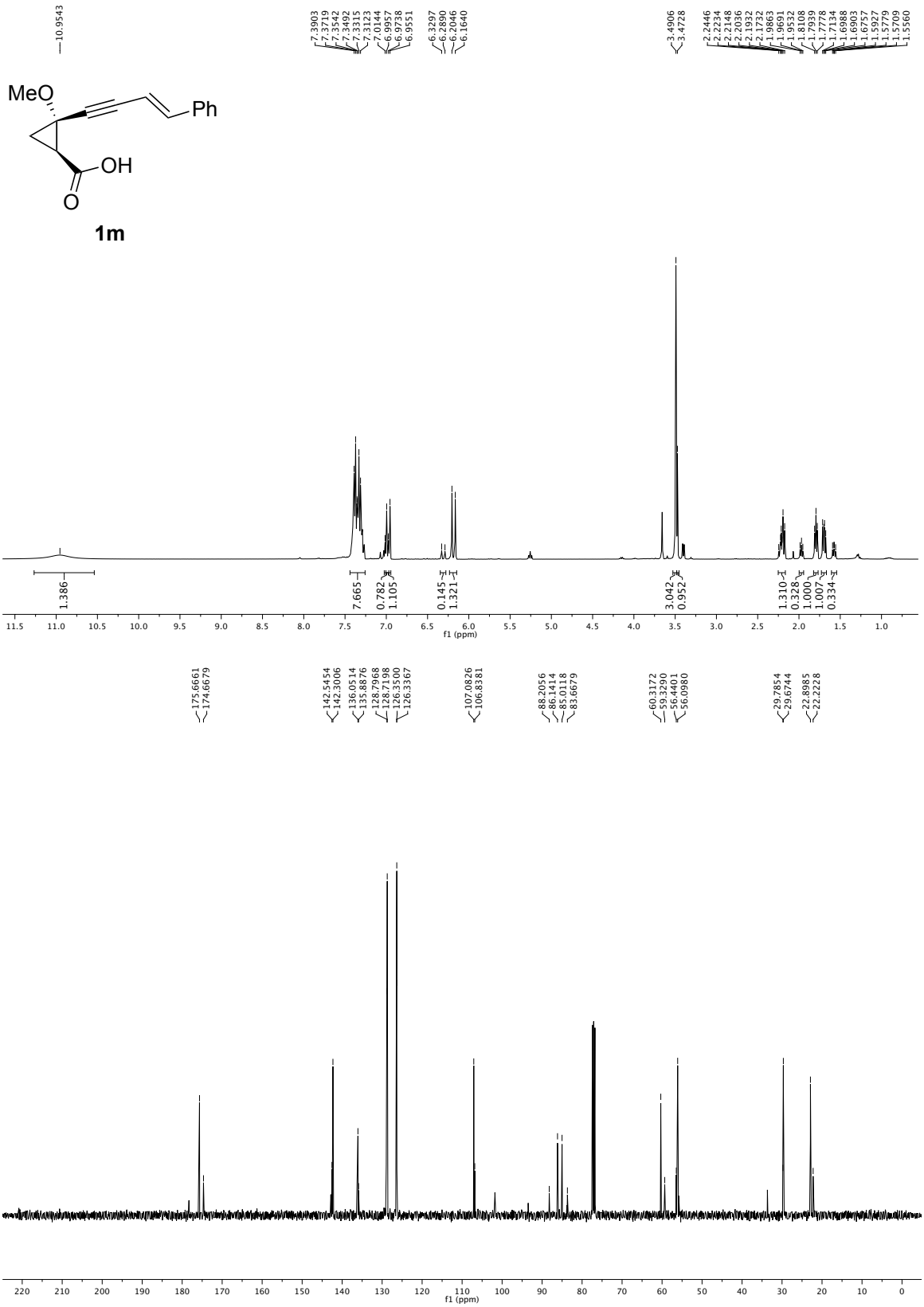

MeO
Bu
OH
O
1j
f1 (ppm)

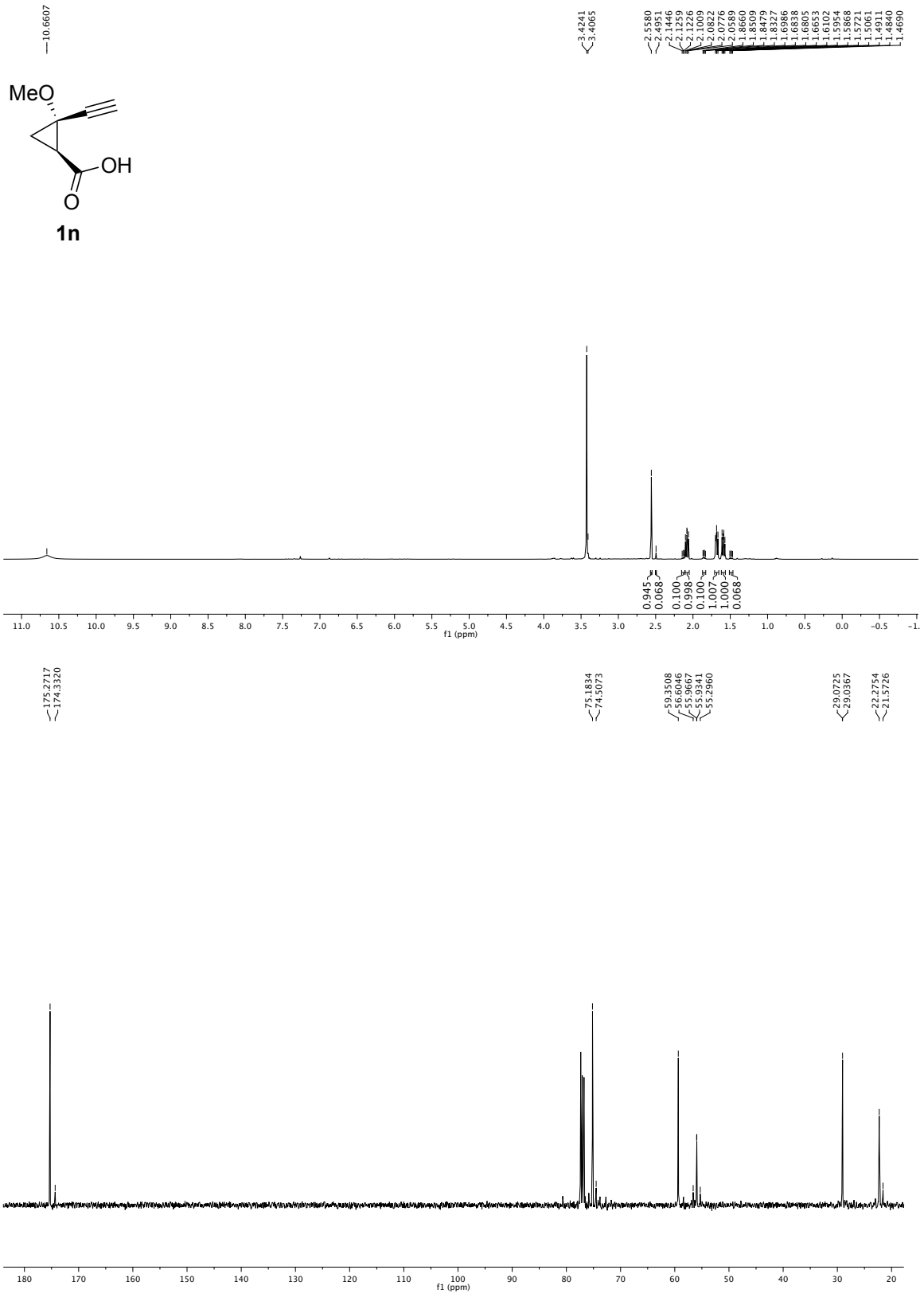

11.0604
3.4090
2.6925
2.6740
2.6558
2.6377
2.6201
2.0444
2.0397
1.6413
1.6376
1.6230
1.5728
1.5586
1.5498
MeO
OH
O
0.773
1.000
1.144
2.235
2.229
6.420
f1 (ppm)

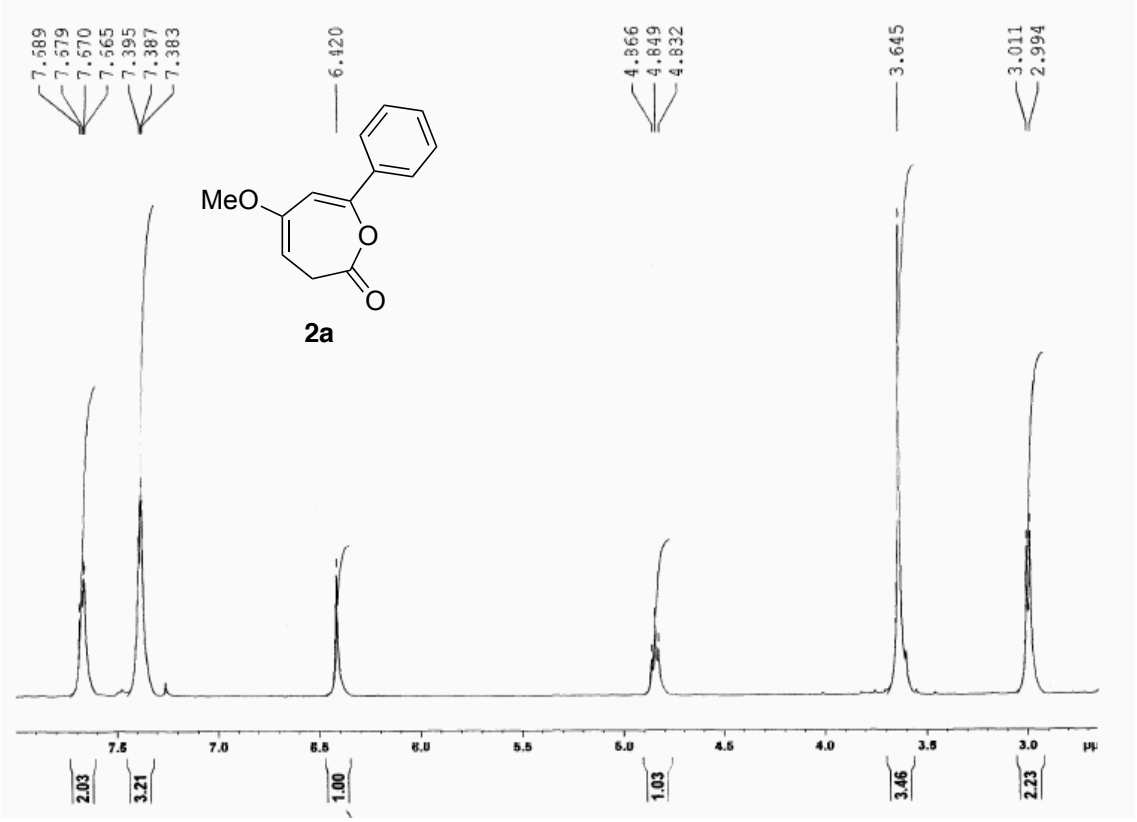
1k

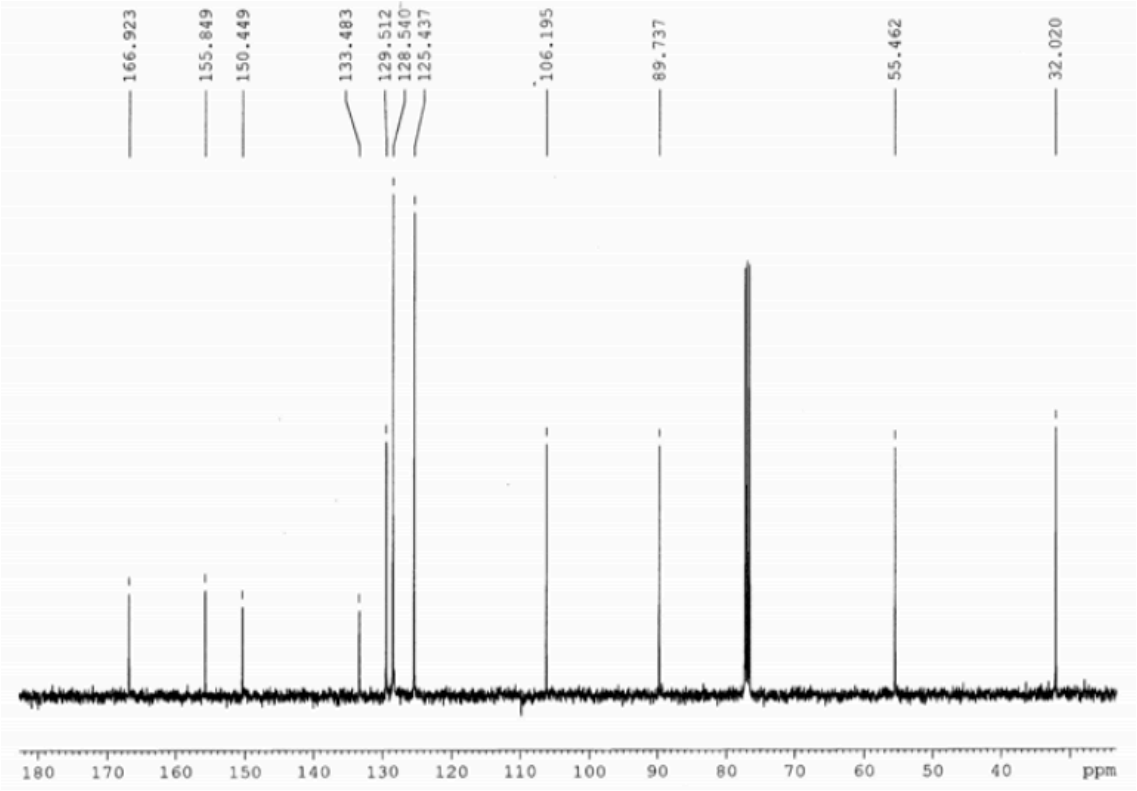

175.8915
92.0122
72.9858
60.0156
55.6530
33.7404
33.6720
30.1106
29.2048
24.8996
22.4082
f1 (ppm)

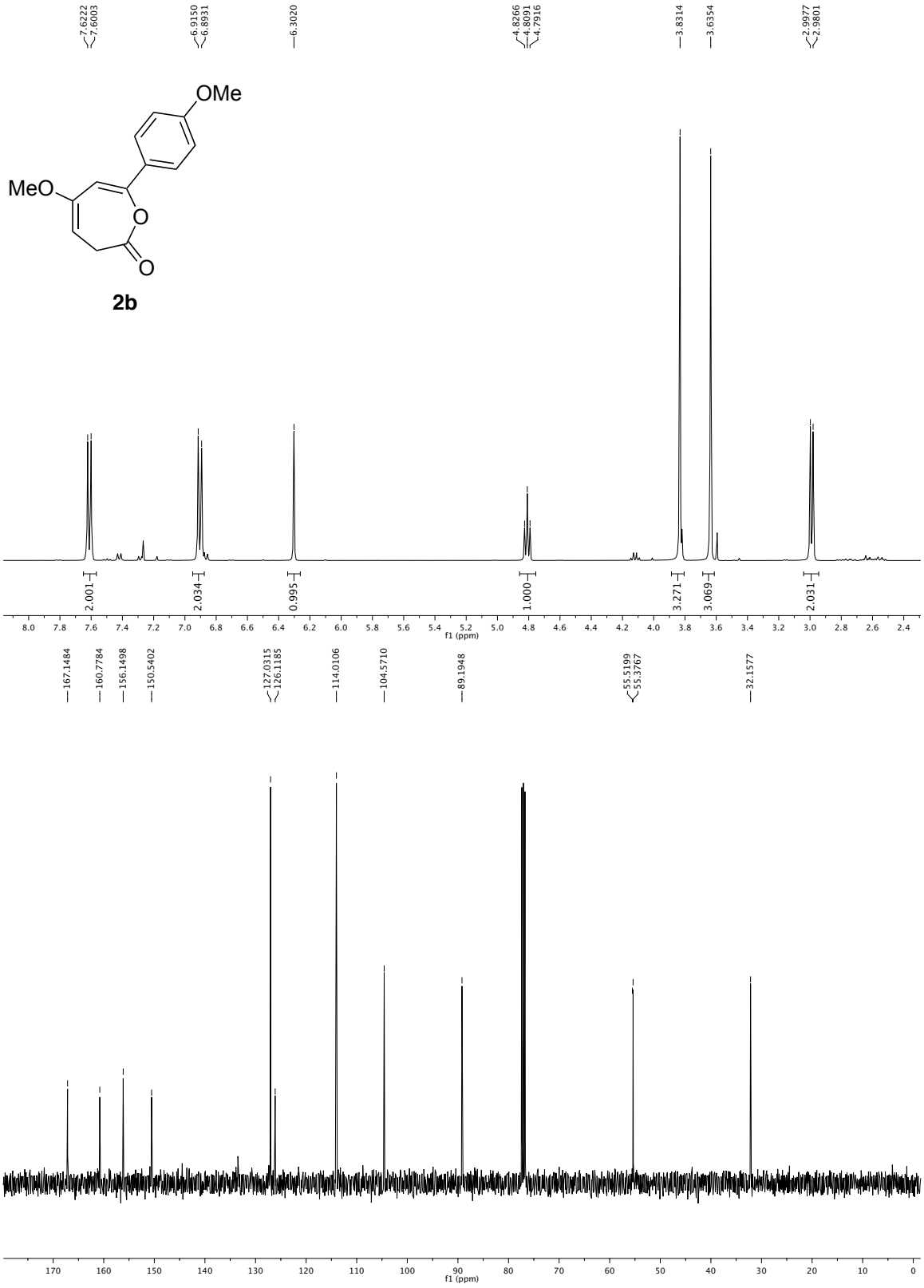

10.8070
MeO
OH
O
1l
3.3391
3.3151
1.9981
1.9796
1.9751
1.9567
1.7858
1.7709
1.7656
1.7533
1.5877
1.5730
1.5699
1.5551
1.5001
1.4857
1.4769
1.4627
1.3804
1.3659
1.3587
1.3443
1.1685
1.1528
1.337
2.547
0.541
1.117
0.153
1.000
1.018
0.161
1.636
10.232
f1 (ppm)
175.5015
174.5943
95.5798
93.2860
75.5146
72.0093
59.7571
58.0161
56.7321
55.4197
30.7344
30.6858
29.3160
29.3140
27.3940
27.3388
22.1832
21.9845
f1 (ppm)

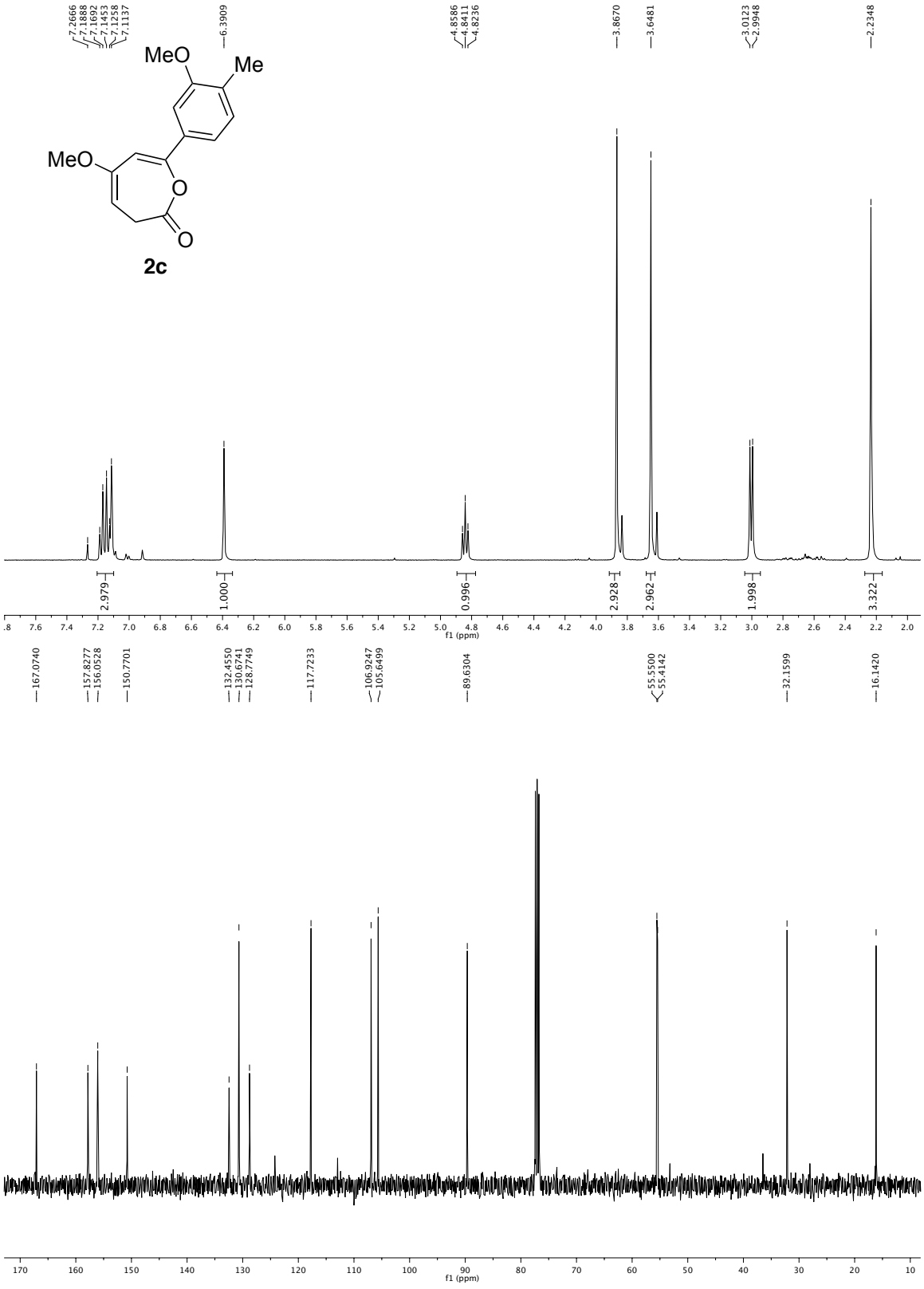

10.9543
7.3903
7.3719
7.3542
7.3492
7.3315
7.3123
7.0144
6.9957
6.9738
6.9551
6.3297
6.2890
6.2046
6.1640
3.4906
3.4728
2.2446
2.2234
2.2148
2.2036
2.1932
2.1732
2.1663
1.9691
1.9532
1.8108
1.7939
1.7778
1.7134
1.6988
1.6903
1.6757
1.5927
1.5779
1.5709
1.5560
MeO
Ph
OH
O
1m
1.386
7.665
0.782
1.105
0.145
1.321
3.042
0.952
1.310
0.328
1.000
1.007
0.334
f1 (ppm)
175.6661
174.6679
142.5454
142.3006
136.0514
135.8876
128.7968
128.7198
126.3500
126.3367
107.0826
106.8381
88.2056
86.1414
85.0118
83.6679
60.3172
59.3290
56.4401
56.0980
29.7854
29.6744
22.8985
22.2228
f1 (ppm)

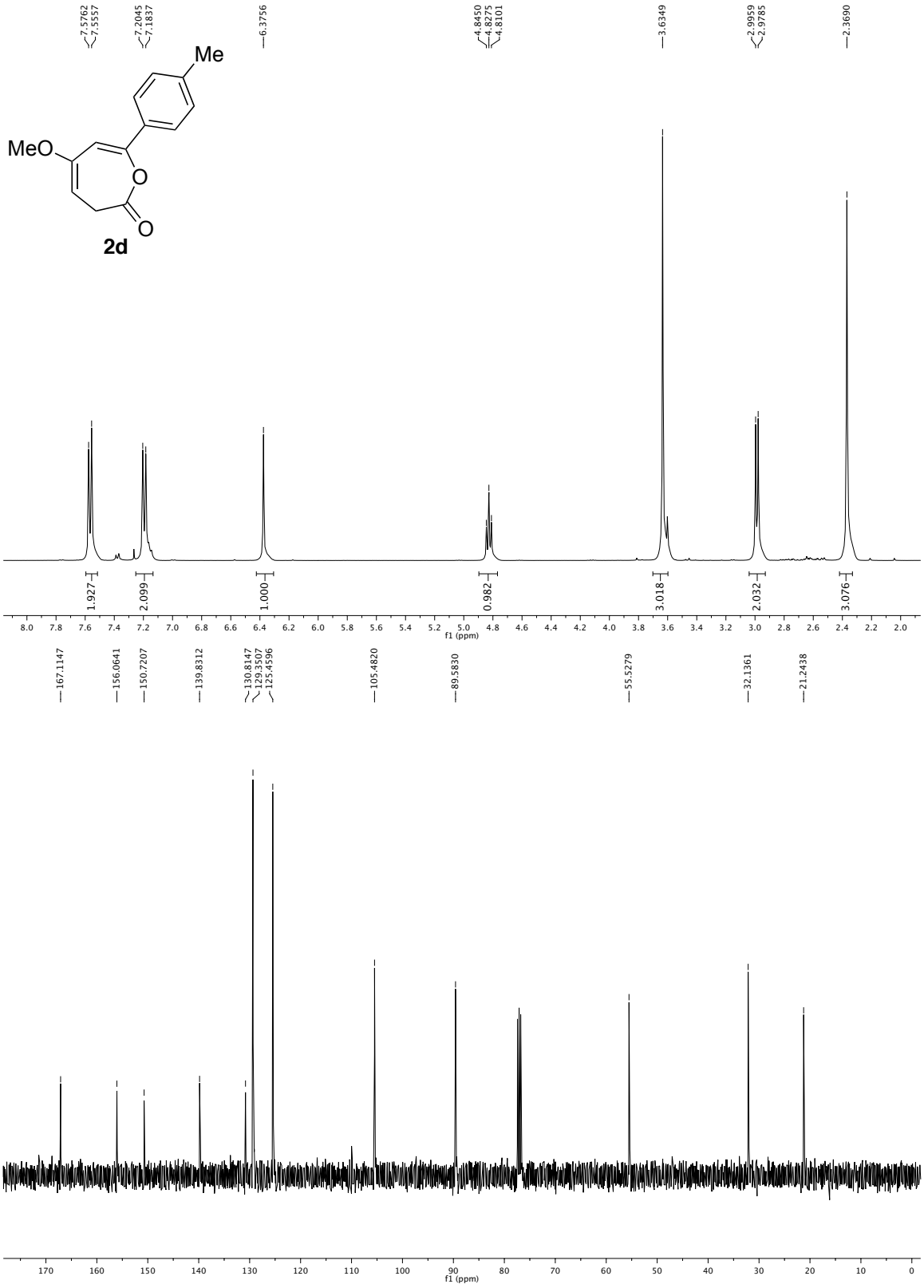

10.6607
3.4241
3.4065
2.5580
2.4951
2.1446
2.1259
2.1226
2.1009
2.0822
2.0776
2.0589
1.8660
1.8509
1.8479
1.8327
1.6986
1.6838
1.6805
1.6653
1.6102
1.5954
1.5868
1.5721
1.5061
1.4911
1.4840
1.4690
MeO
OH
O
1n
0.945
0.068
0.100
0.998
0.100
1.007
1.000
0.068
f1 (ppm)
175.2717
174.3320
75.1834
74.5073
59.3508
56.6046
55.9667
55.9341
55.2960
29.0725
29.0367
22.2754
21.5726
f1 (ppm)

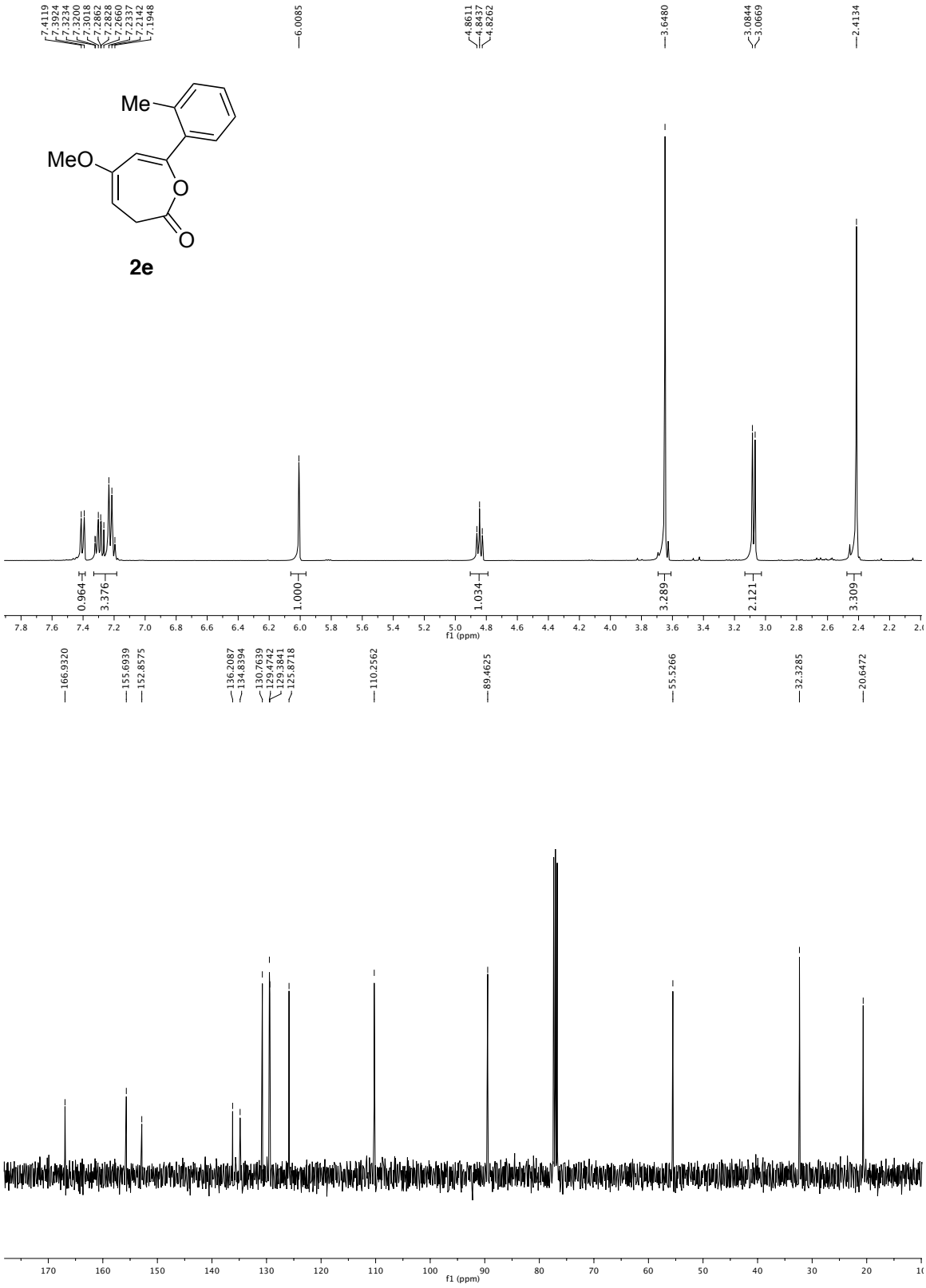

7.689
7.679
7.670
7.665
7.395
7.387
7.383
6.420
4.866
4.849
4.832
3.645
3.011
2.994
MeO
O
O
2a
2.03
3.21
1.00
1.03
3.46
2.23

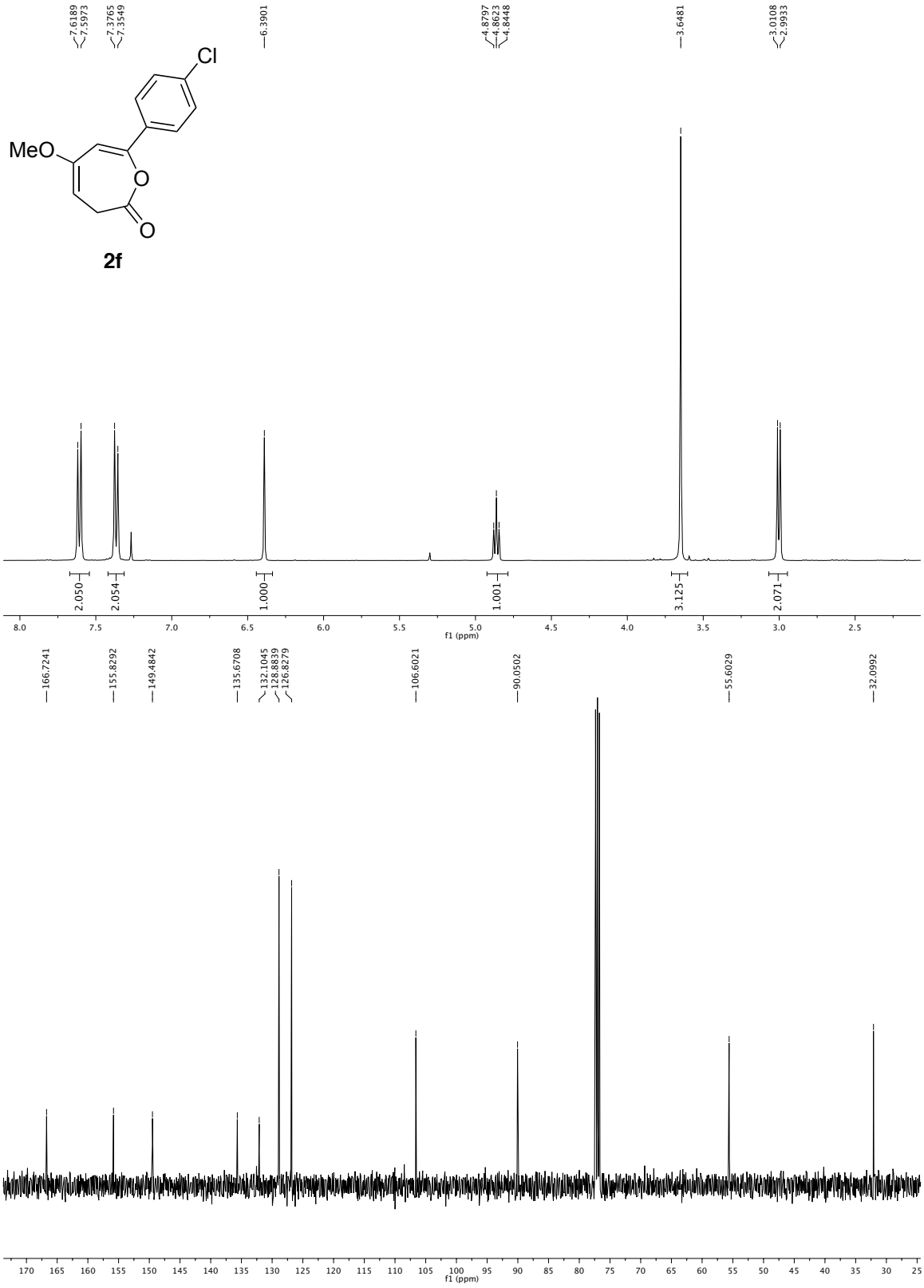

166.923
155.849
150.449
133.483
129.512
128.540
125.437
106.195
89.737
55.462
32.020
ppm

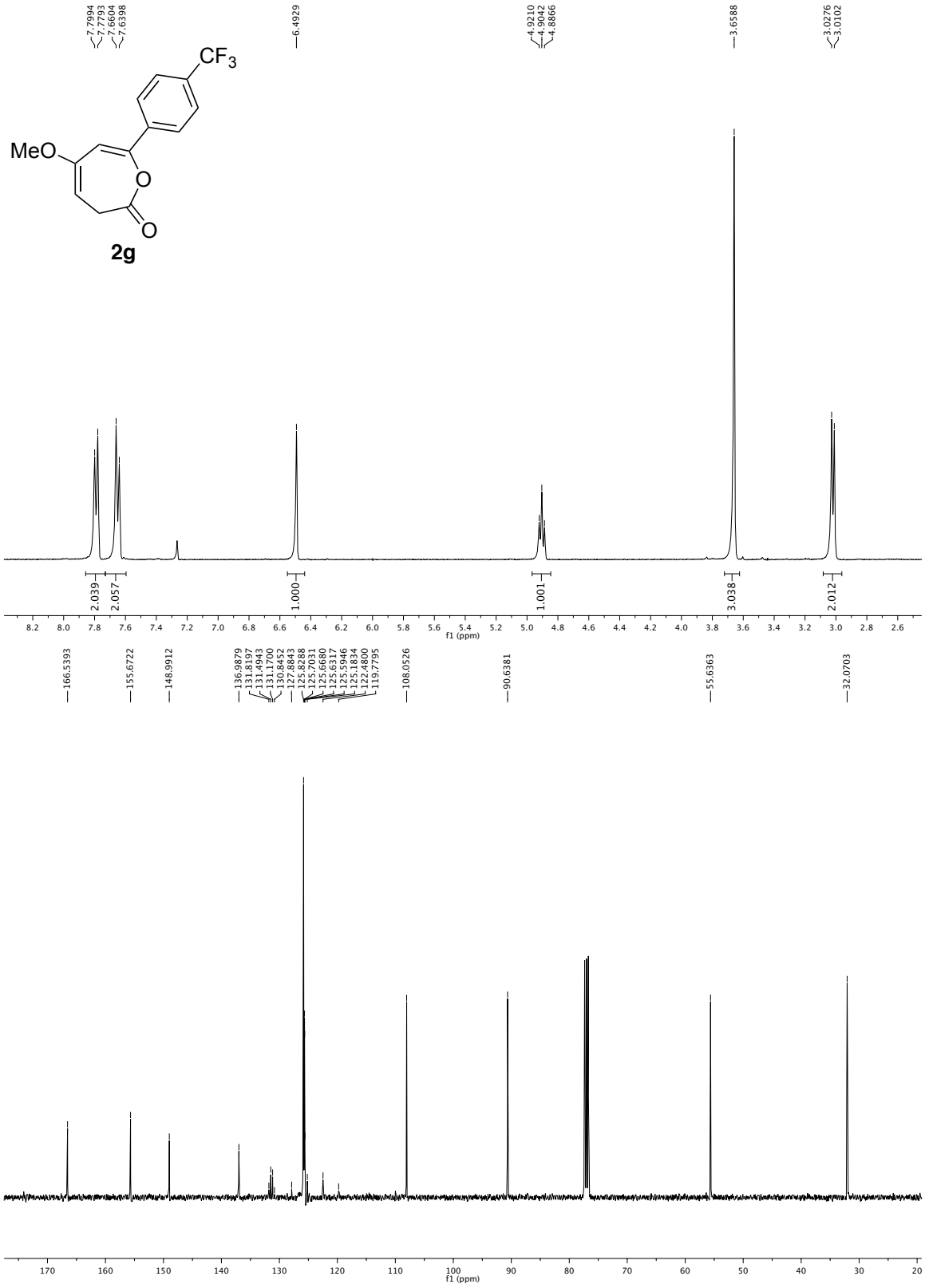

7.6222
7.6003
6.9150
6.8931
6.3020
4.8266
4.8091
4.7916
3.8314
3.6354
2.9977
2.9801
OMe
MeO
O
O
2b
2.001
2.034
0.995
1.000
3.271
3.069
2.031
f1 (ppm)
167.1484
160.7784
156.1498
150.5402
127.0315
126.1185
114.0106
104.5710
89.1948
55.5199
55.3767
32.1577
f1 (ppm)

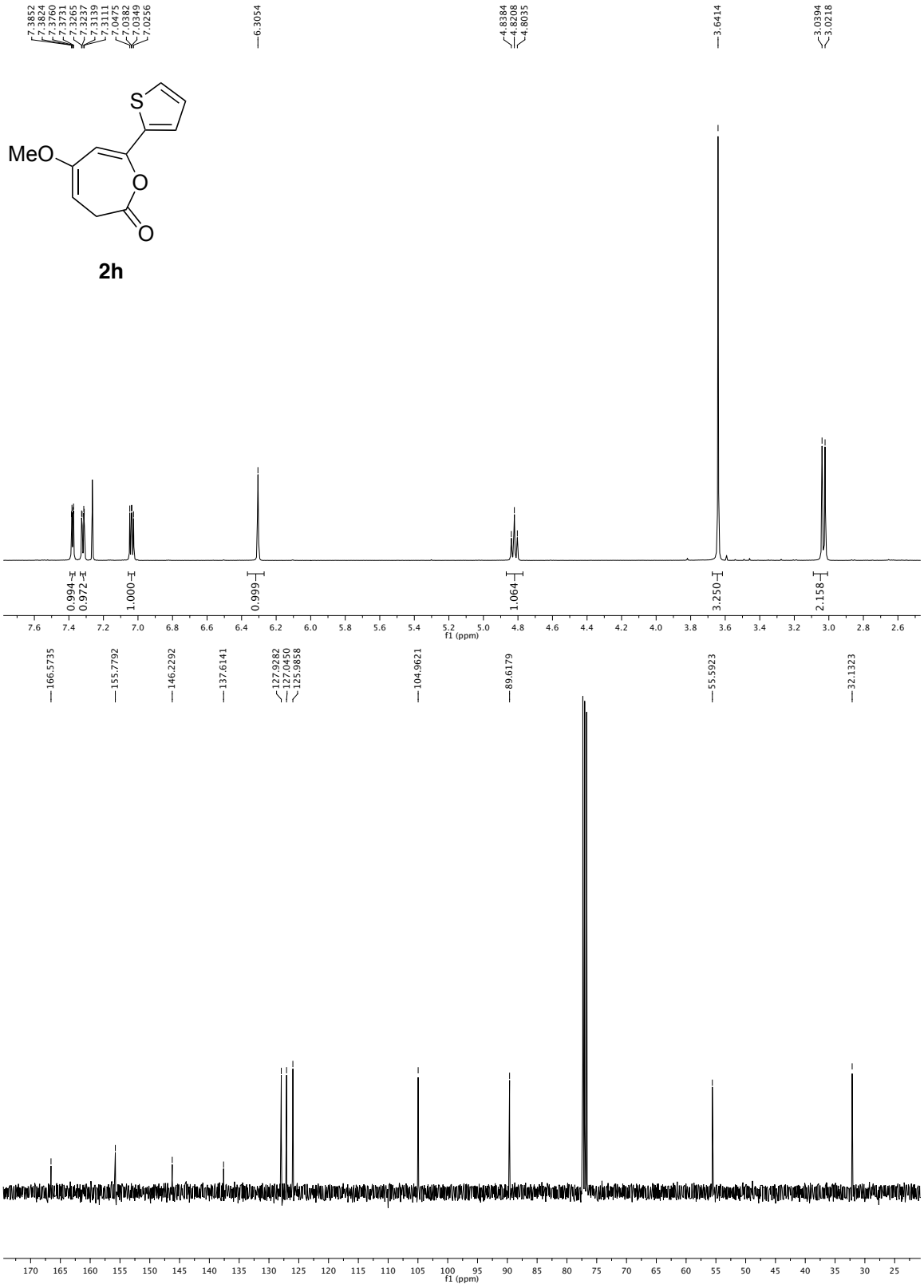

7.2666
7.1888
7.1692
7.1453
7.1258
7.1137
6.3909
4.8586
4.8411
4.8236
3.8670
3.6481
3.0123
2.9948
2.2348
MeO
Me
MeO
O
O
2c
2.979
1.000
0.996
2.928
2.962
1.998
3.322
f1 (ppm)
167.0740
157.8277
156.0528
150.7701
132.4550
130.6741
128.7749
117.7233
106.9247
105.6499
89.6304
55.5500
55.4142
32.1599
16.1420
f1 (ppm)


7.5762
7.5557
7.2045
7.1837
6.3756
4.8450
4.8275
4.8101
3.6349
2.9959
2.9785
2.3690
Me
MeO
O
O
2d
1.927
2.099
1.000
0.982
3.018
2.032
3.076
f1 (ppm)
167.1147
156.0641
150.7207
139.8312
130.8147
129.3507
125.4596
105.4820
89.5830
55.5279
32.1361
21.2438
f1 (ppm)

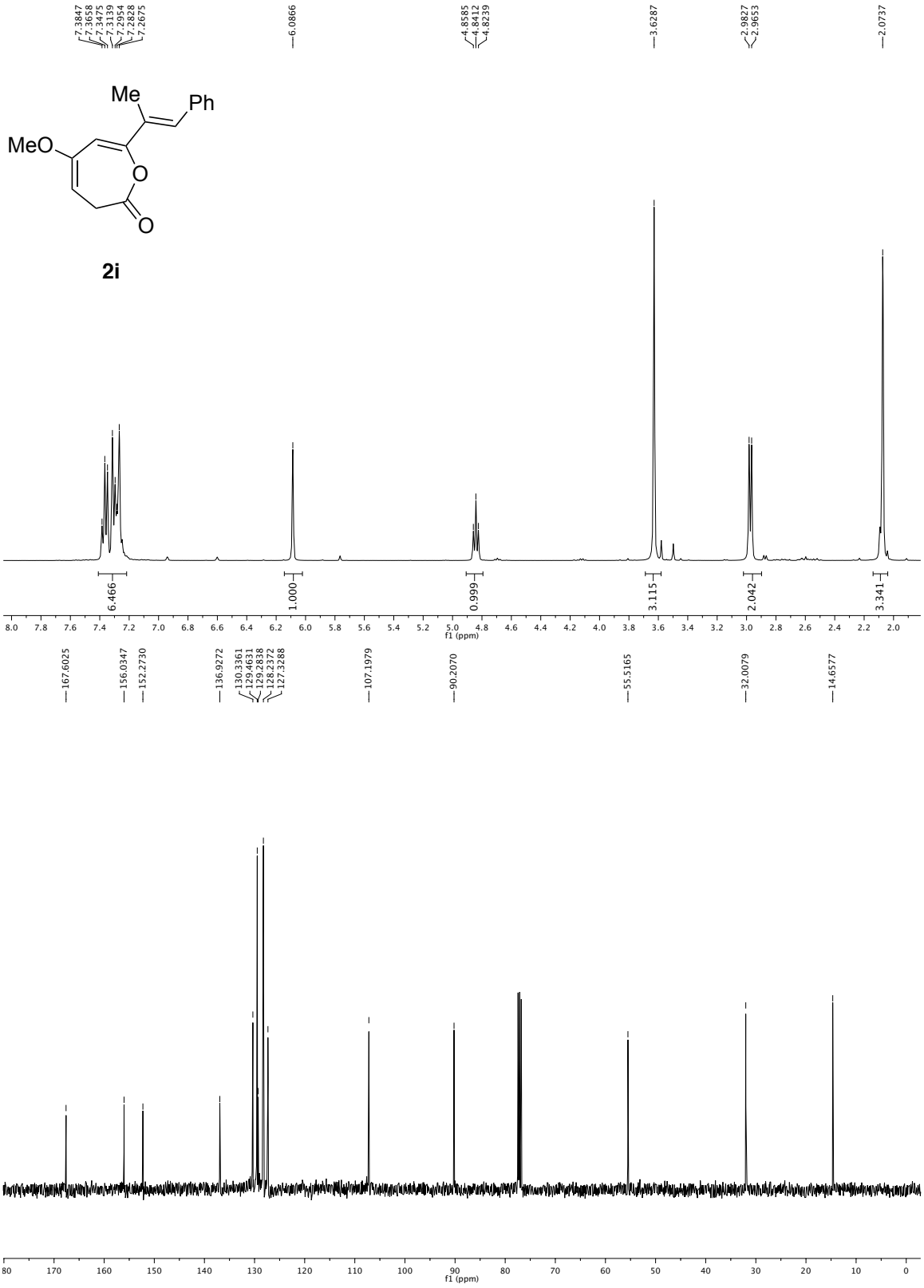

7.4119
7.3924
7.3234
7.3200
7.3018
7.2862
7.2828
7.2660
7.2337
7.2142
7.1948
6.0085
4.8611
4.8437
4.8262
3.6480
3.0844
3.0669
2.4134
Me
MeO
O
O
2e
0.964
3.376
1.000
1.034
3.289
2.121
3.309
f1 (ppm)
166.9320
155.6939
152.8575
136.2087
134.8394
130.7639
130.4742
129.3841
125.8718
110.2562
89.4625
55.5266
32.3285
20.6472
f1 (ppm)


7.6189
7.5973
7.3765
7.3549
6.3901
4.8797
4.8623
4.8448
3.6481
3.0108
2.9933
Cl
MeO
O
O
2f
2.050
2.054
1.000
1.001
3.125
2.071
f1 (ppm)
166.7241
155.8292
149.4842
135.6708
132.1045
128.8839
126.8279
106.6021
90.0502
55.6029
32.0992
f1 (ppm)

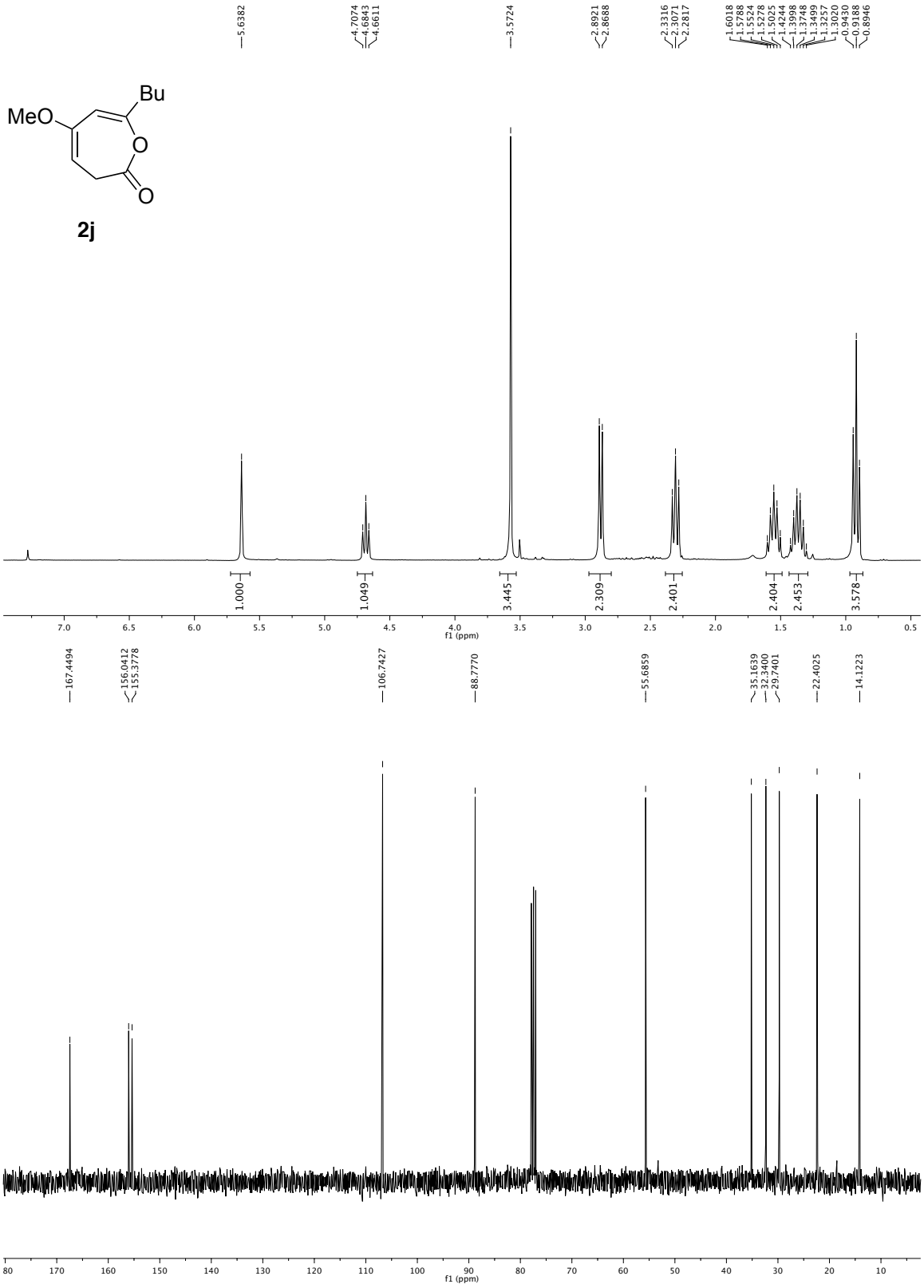

7.7994
7.7793
7.6604
7.6398
6.4929
4.9210
4.9042
4.8866
3.6588
3.0276
3.0102
CF3
MeO
O
O
2g
2.039
2.057
1.000
1.001
3.038
2.012
f1 (ppm)
166.5393
155.6722
148.9912
136.9879
131.8197
131.4943
131.1700
130.8453
127.8843
125.8288
125.7031
125.6680
125.6317
125.5946
125.1834
122.4800
119.7795
108.0526
90.6381
55.6363
32.0703
f1 (ppm)

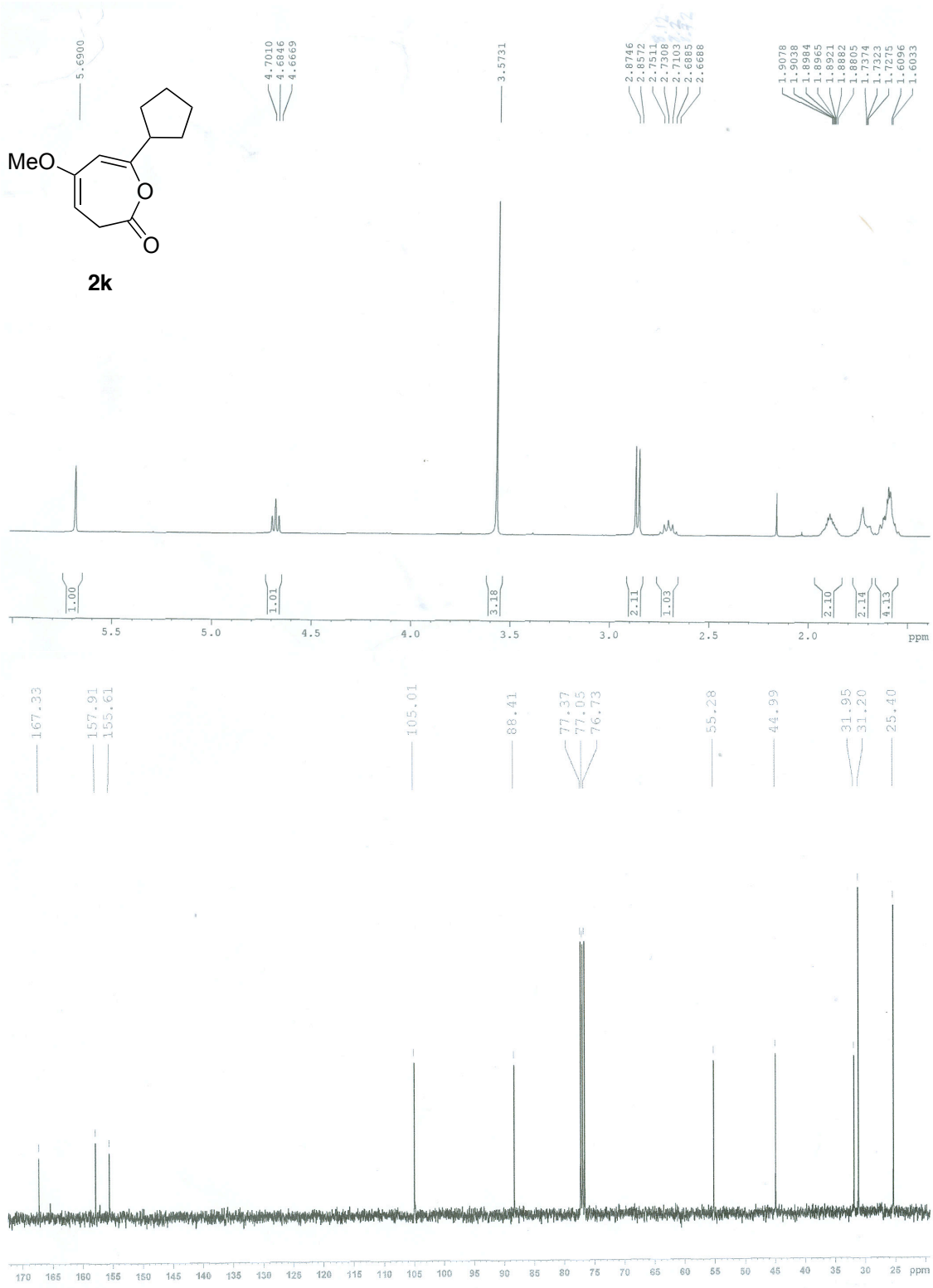

7.3852
7.3824
7.3760
7.3731
7.3265
7.3237
7.3139
7.3111
7.0475
7.0382
7.0349
7.0256
6.3054
4.8384
4.8208
4.8035
3.6414
3.0394
3.0218
S
MeO
O
O
0.994
0.972
1.000
0.999
1.064
3.250
2.158
f1 (ppm)
166.5735
155.7792
146.2292
137.6141
127.9282
127.0450
125.9858
104.9621
89.6179
55.5923
32.1323
f1 (ppm)

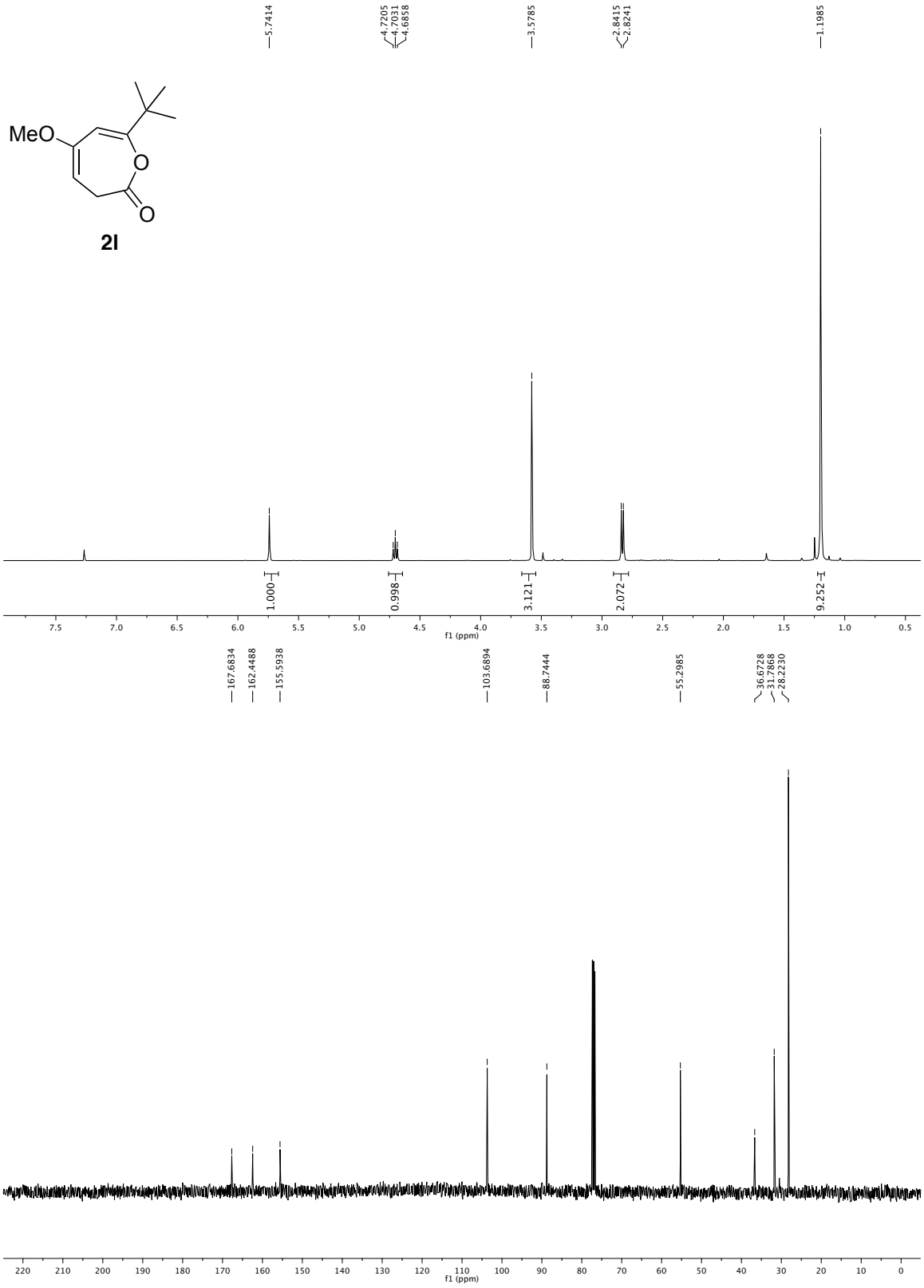
2h

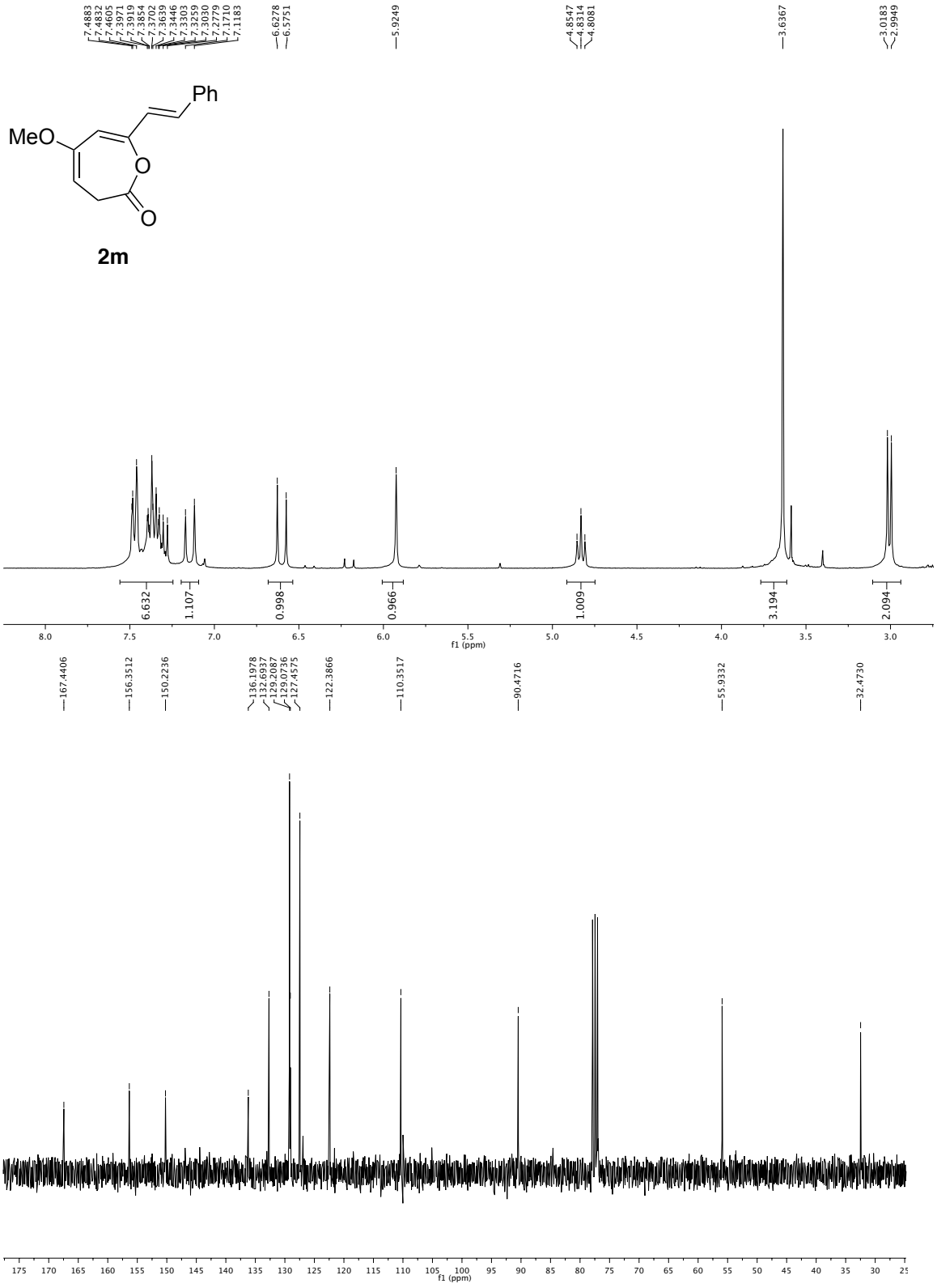

7.3847
7.3658
7.3475
7.3139
7.2954
7.2828
7.2675
6.0866
4.8585
4.8412
4.8239
3.6287
2.9827
2.9653
2.0737
Me
Ph
MeO
O
O
6.466
1.000
0.999
3.115
2.042
3.341
f1 (ppm)
167.6025
156.0347
152.2730
136.9272
130.3361
129.4631
129.2838
128.2372
127.3288
107.1979
90.2070
55.5165
32.0079
14.6577
f1 (ppm)

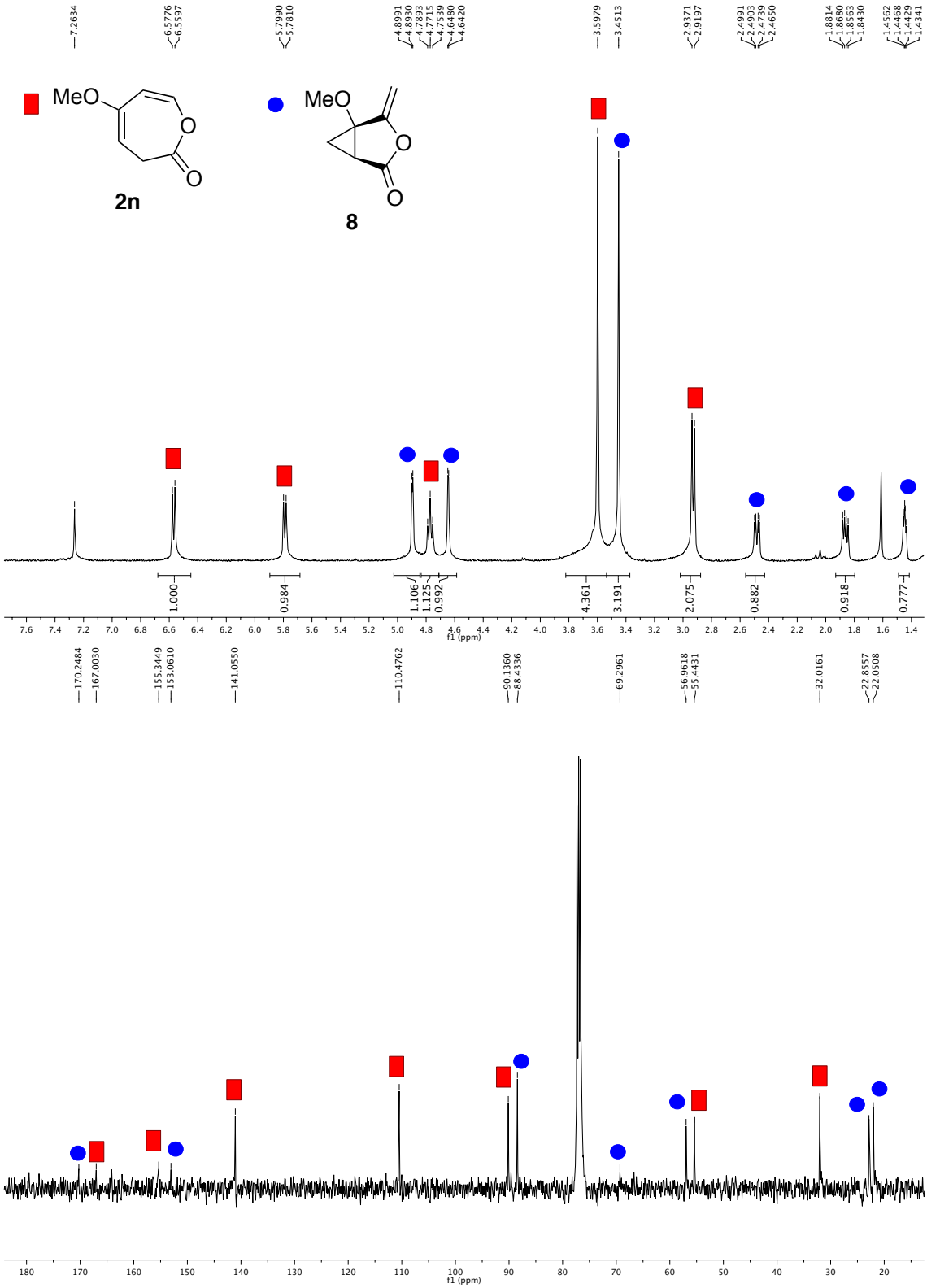
2i


5.6382
4.7074
4.6843
4.6611
3.5724
2.8921
2.8688
2.3316
2.3071
2.2817
1.6018
1.5788
1.5524
1.5278
1.5025
1.4744
1.3998
1.3748
1.3499
1.3257
1.3020
0.9430
0.9188
0.8946
Bu
MeO
O
O
2j
1.000
1.049
3.445
2.309
2.401
2.404
2.453
3.578
f1 (ppm)
167.4494
156.0412
155.3778
106.7427
88.7770
55.6859
35.1639
32.3400
29.7401
22.4025
14.1223
f1 (ppm)


MeO
O
O
2k
5.6900
4.7010
4.6846
4.6669
3.5731
2.8746
2.8572
2.7511
2.7308
2.7103
2.6885
2.6688
1.9078
1.9038
1.8984
1.8965
1.8921
1.8882
1.8805
1.7374
1.7323
1.7275
1.6096
1.6033
1.00
1.01
3.18
2.11
1.03
2.10
2.14
4.13
ppm
167.33
157.91
155.61
105.01
88.41
77.37
77.05
76.73
55.28
44.99
31.95
31.20
25.40
ppm


5.7414
4.7205
4.7031
4.6858
3.5785
2.8415
2.8241
1.1985
MeO
O
O
2l
1.000
0.998
3.121
2.072
9.252
f1 (ppm)
167.6834
162.4488
155.5938
103.6894
88.7444
55.2985
36.6728
31.7868
28.2230
f1 (ppm)


7.4883
7.4832
7.4605
7.3971
7.3919
7.3854
7.3702
7.3639
7.3446
7.3303
7.3259
7.3090
7.2779
7.1710
7.1183
6.6278
6.5751
5.9249
4.8547
4.8314
4.8081
3.6367
3.0183
2.9949
Ph
MeO
O
O
2m
6.632
1.107
0.998
0.966
1.009
3.194
2.094
f1 (ppm)
167.4406
156.3512
150.2236
136.1978
132.6937
129.2087
128.0726
127.4575
122.3866
110.3517
90.4716
55.9332
32.4730
f1 (ppm)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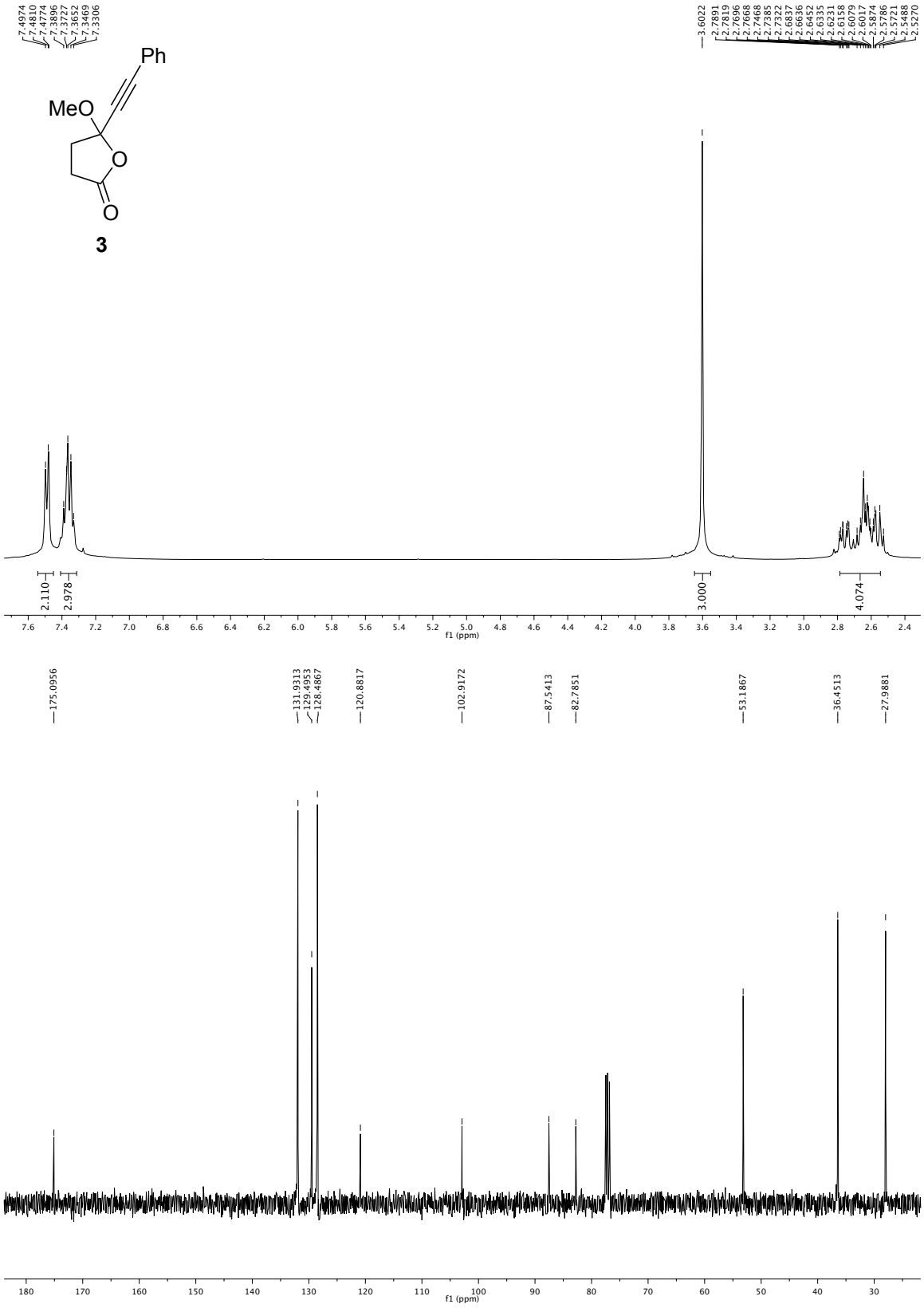
6.5776
6.5597
5.7990
5.7810
4.8991
4.8930
4.7893
4.7715
4.7539
4.6480
4.6420
3.5979
3.4513
2.9371
2.9197
2.4991
2.4903
2.4739
2.4650
1.8814
1.8680
1.8563
1.8430
1.4562
1.4468
1.4429
1.4341
MeO
O
O
2n
MeO
O
O
8
1.000
0.984
1.106
1.125
0.992
4.361
3.191
2.075
0.882
0.918
0.777
f1 (ppm)
170.2484
167.0030
155.3449
153.0610
141.0550
110.4762
90.1360
88.4336
69.2961
56.9618
55.4431
32.0161
22.8557
22.0508
f1 (ppm)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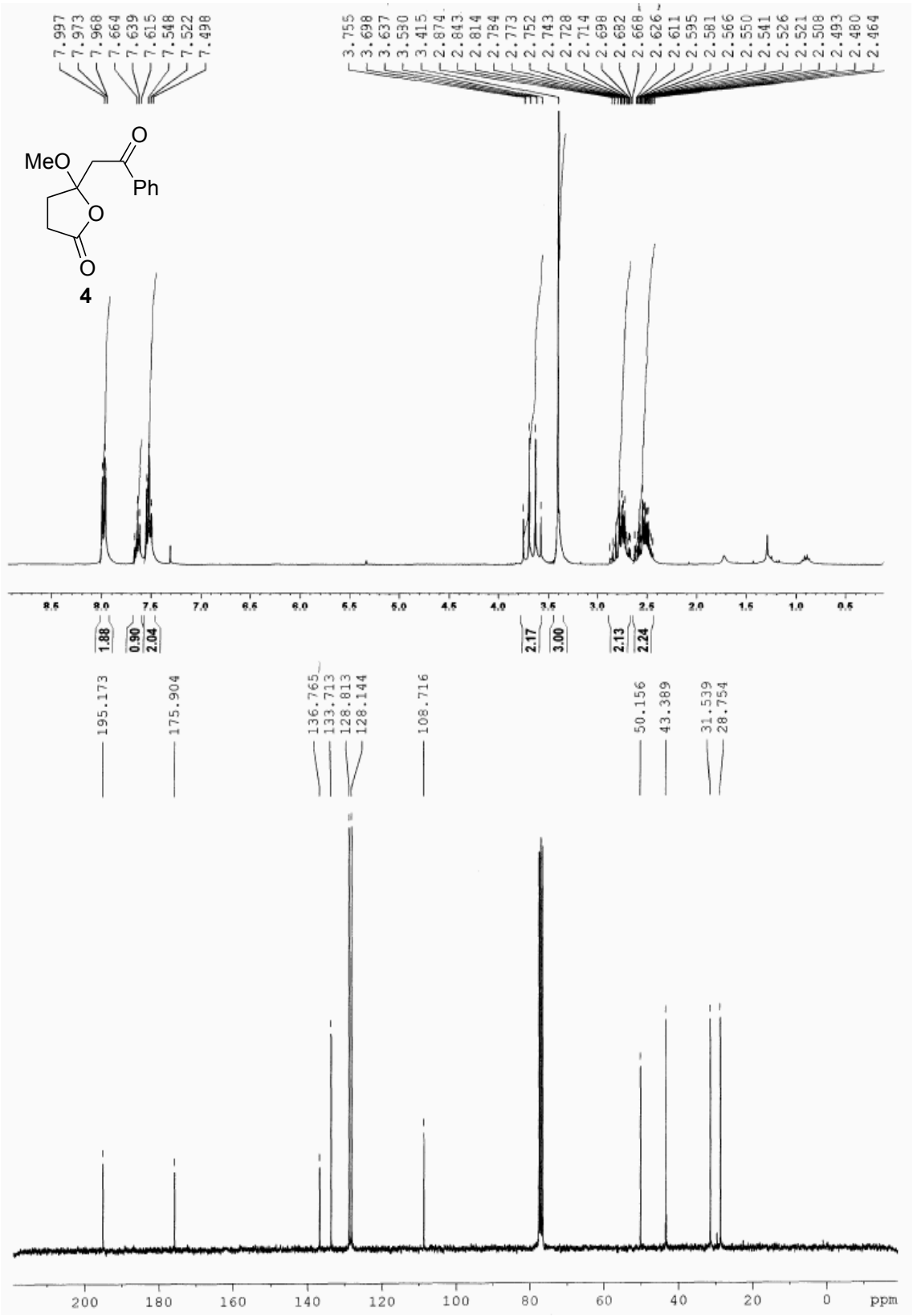
7.4810
7.4774
7.3896
7.3727
7.3652
7.3469
7.3306
3.6022
2.7891
2.7819
2.7696
2.7668
2.7468
2.7385
2.7322
2.6837
2.6636
2.6452
2.6335
2.6231
2.6158
2.6079
2.6017
2.5874
2.5726
2.5571
2.5488
2.5270
Ph
MeO
O
O
3
2.110
2.978
3.000
4.074
f1 (ppm)
175.0956
131.9313
129.4953
128.4867
120.8817
102.9172
87.5413
82.7851
53.1867
36.4513
27.9881
f1 (ppm)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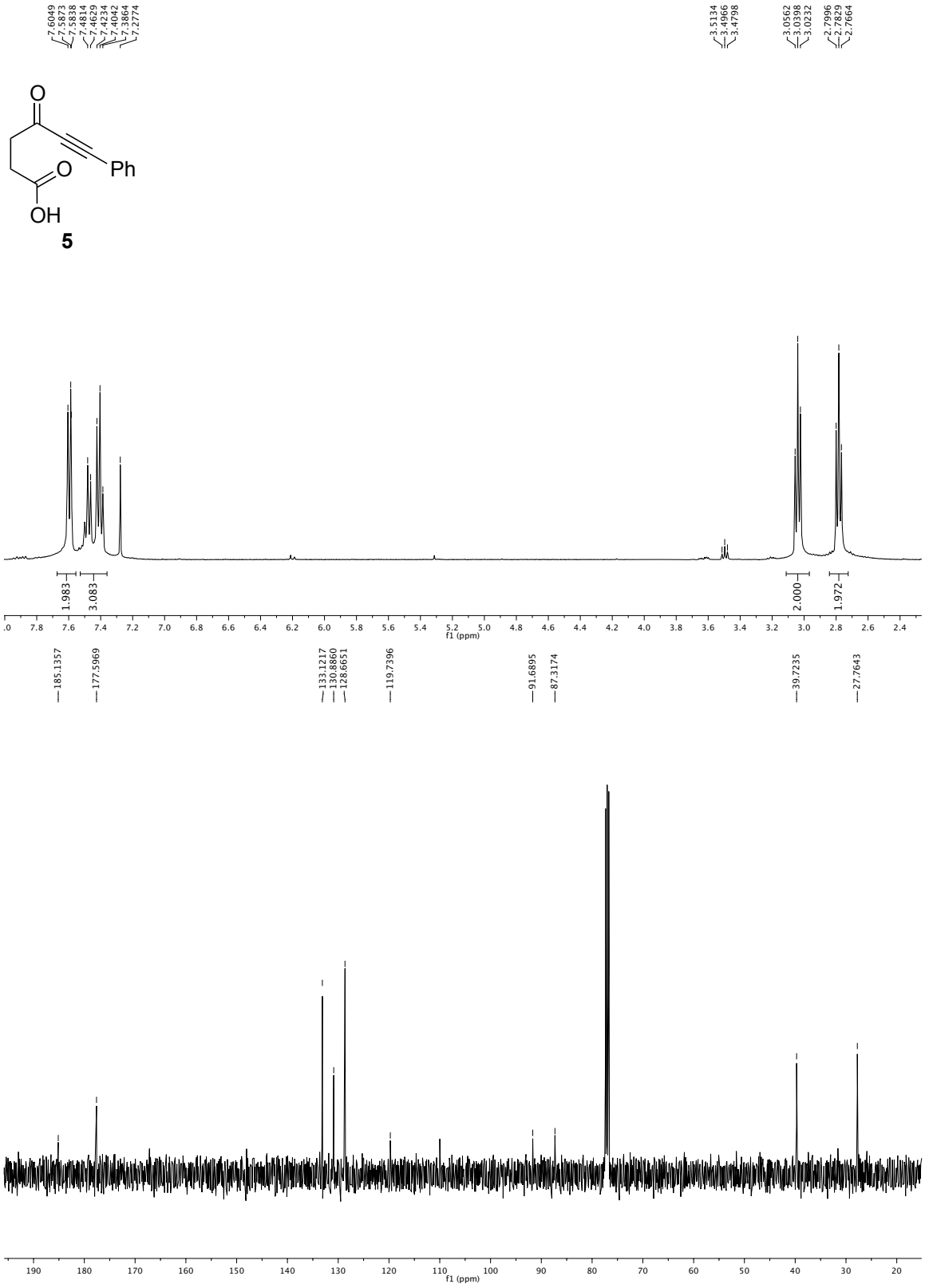
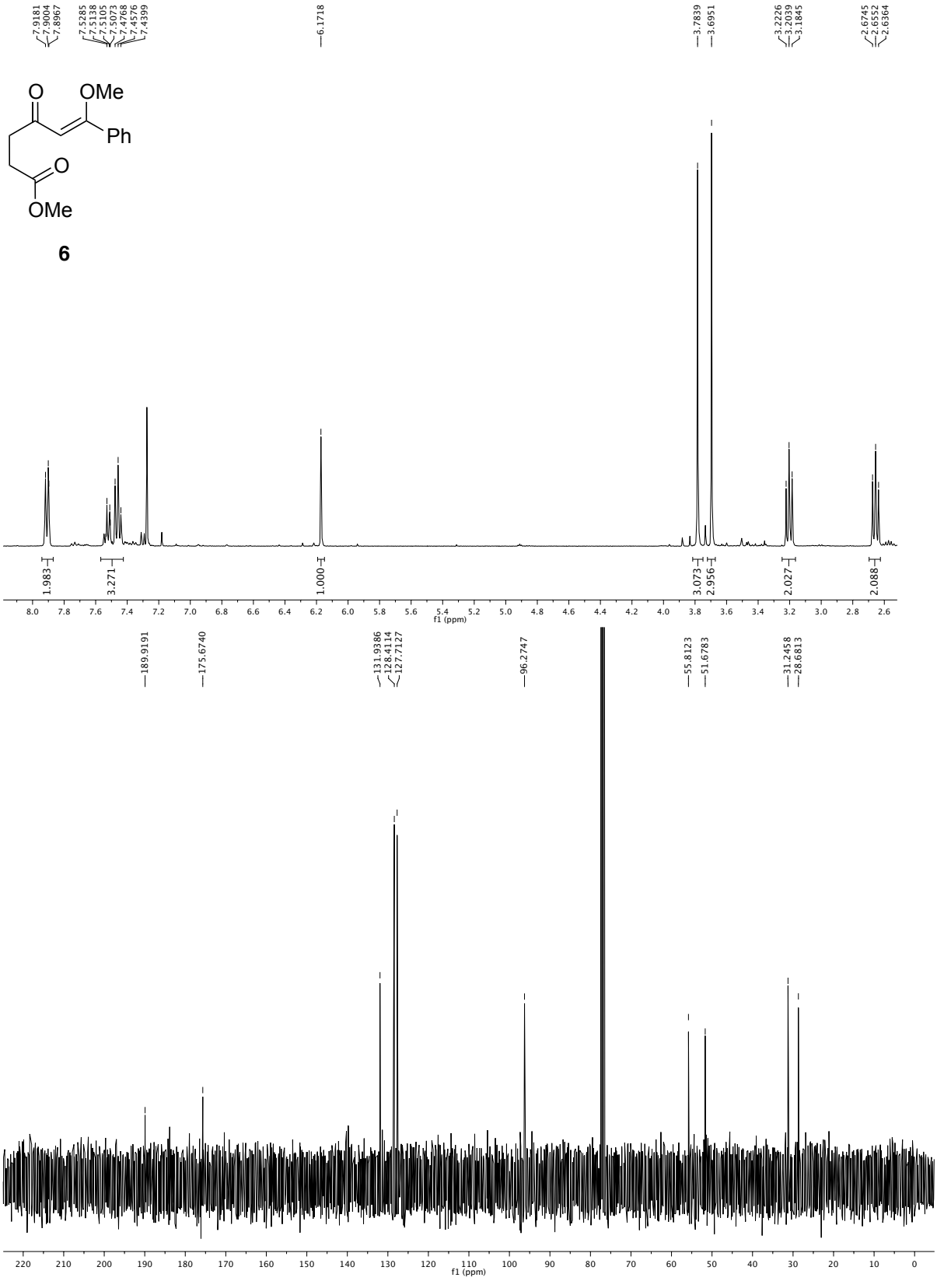
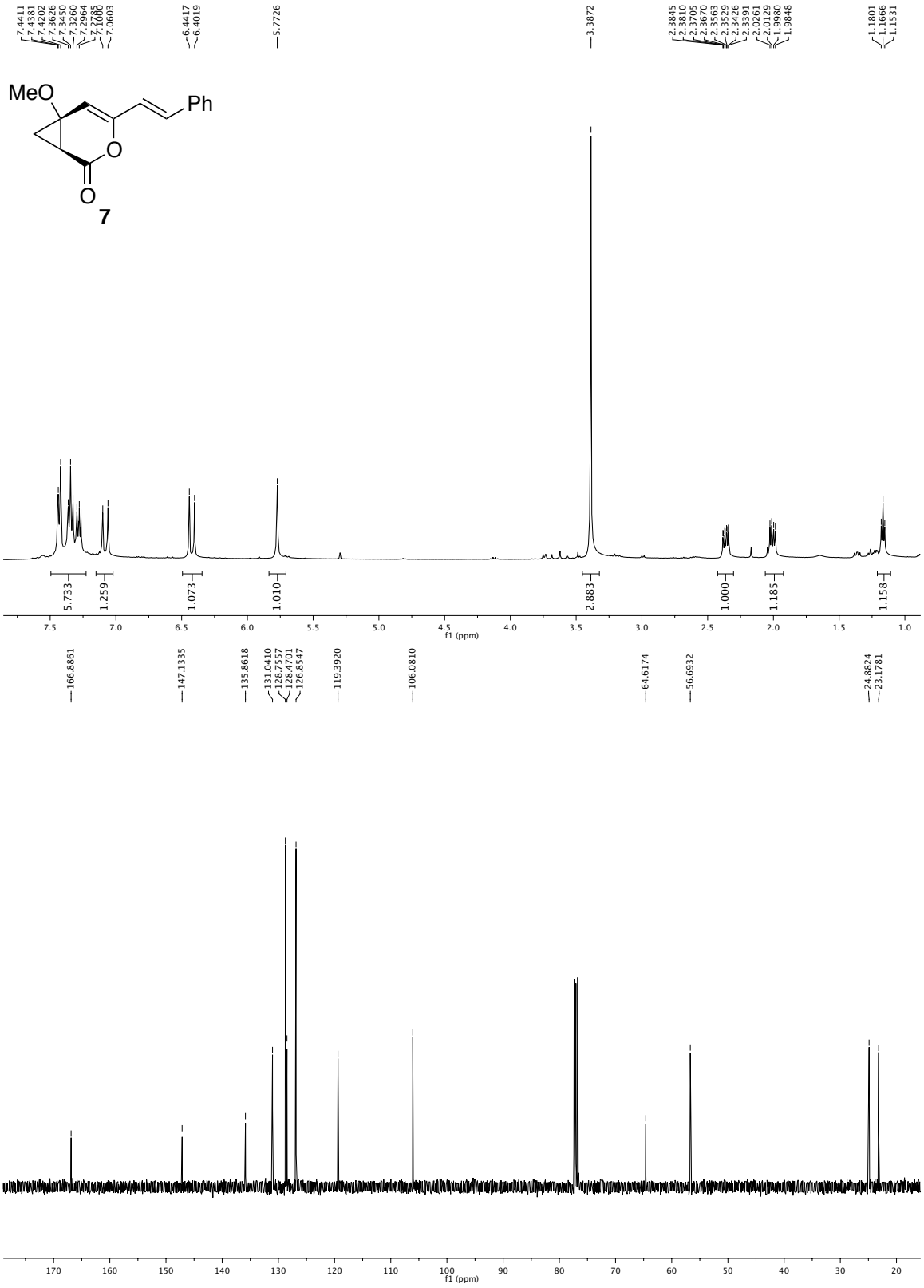
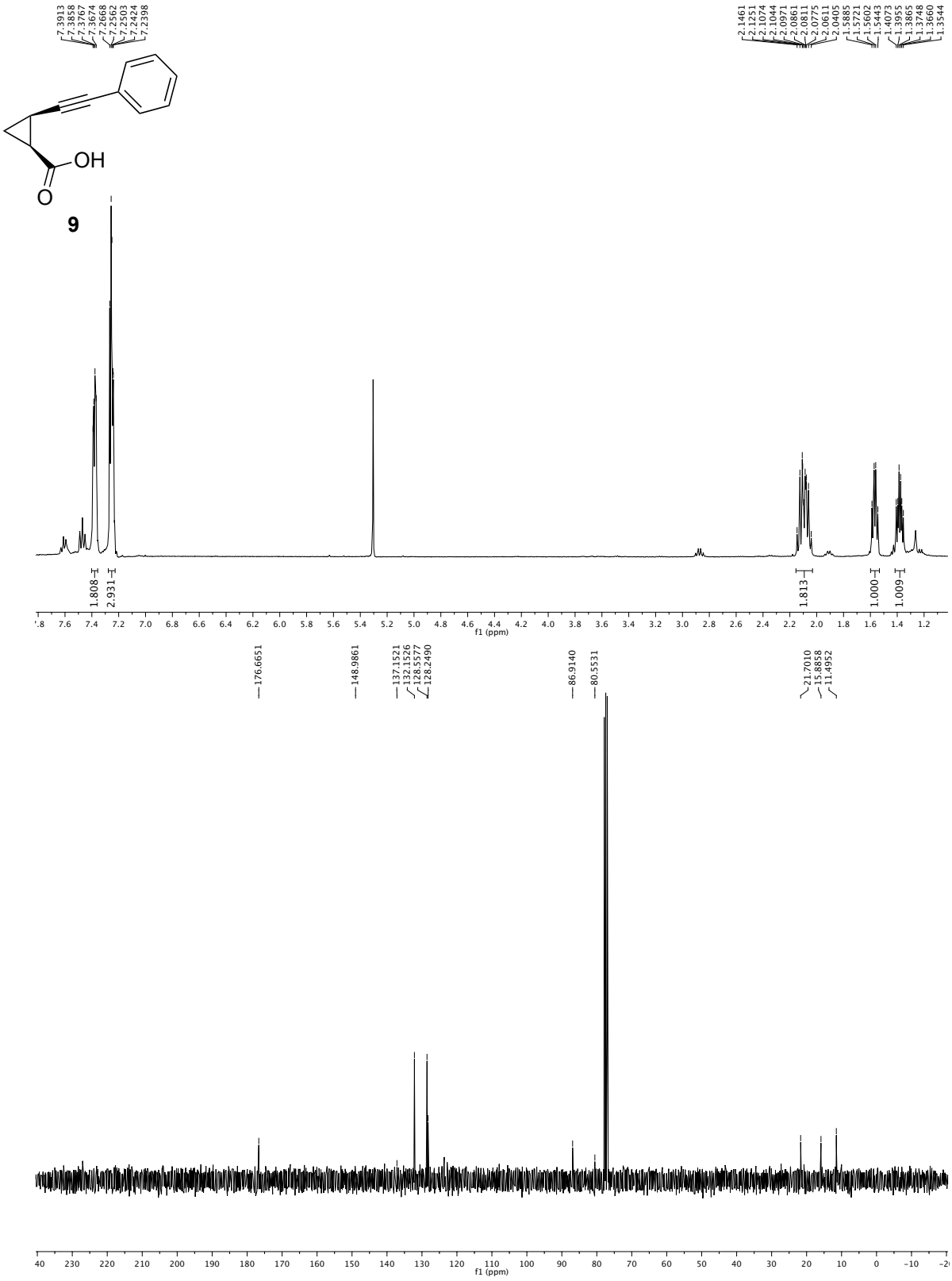
7.973
7.968
7.664
7.639
7.615
7.548
7.522
7.498
3.755
3.698
3.637
3.530
3.415
2.874
2.843
2.814
2.784
2.773
2.752
2.743
2.728
2.714
2.698
2.682
2.668
2.626
2.611
2.595
2.581
2.566
2.550
2.541
2.526
2.521
2.508
2.493
2.480
2.464
MeO
O
Ph
O
O
4
1.88
0.90
2.04
2.17
3.00
2.13
2.24
195.173
175.904
136.765
133.713
128.813
128.144
108.716
50.156
43.389
31.539
28.754
ppm


7.6049
7.5873
7.5838
7.4814
7.4629
7.4234
7.4042
7.3864
7.2774
3.5134
3.4966
3.4798
3.0562
3.0398
3.0232
2.7996
2.7829
2.7664
O
O
Ph
OH
5
1.983
3.083
2.000
1.972
f1 (ppm)
185.1357
177.5969
133.1217
130.8860
128.6651
119.7396
91.6895
87.3174
39.7235
27.7643
f1 (ppm)


7.9181
7.9004
7.8967
7.5285
7.5138
7.5105
7.5073
7.4768
7.4576
7.4399
6.1718
3.7839
3.6951
3.2226
3.2039
3.1845
2.6745
2.6552
2.6364
O
OMe
Ph
O
OMe
6
1.983
3.271
1.000
3.073
2.956
2.027
2.088
f1 (ppm)
189.9191
175.6740
131.9386
128.4114
127.7127
96.2747
55.8123
51.6783
31.2458
28.6813
f1 (ppm)


7.4411
7.4381
7.4202
7.3626
7.3450
7.3260
7.2964
7.1788
7.1600
7.0603
6.4417
6.4019
5.7726
3.3872
2.3845
2.3810
2.3705
2.3670
2.3563
2.3529
2.3426
2.3391
2.0261
2.0129
1.9980
1.9848
1.1801
1.1666
1.1531
MeO
Ph
O
O
7
5.733
1.259
1.073
1.010
2.883
1.000
1.185
1.158
f1 (ppm)
166.8861
147.1335
135.8618
131.0410
128.7557
128.4701
126.8547
119.3920
106.0810
64.6174
56.6932
24.8824
23.1781
f1 (ppm)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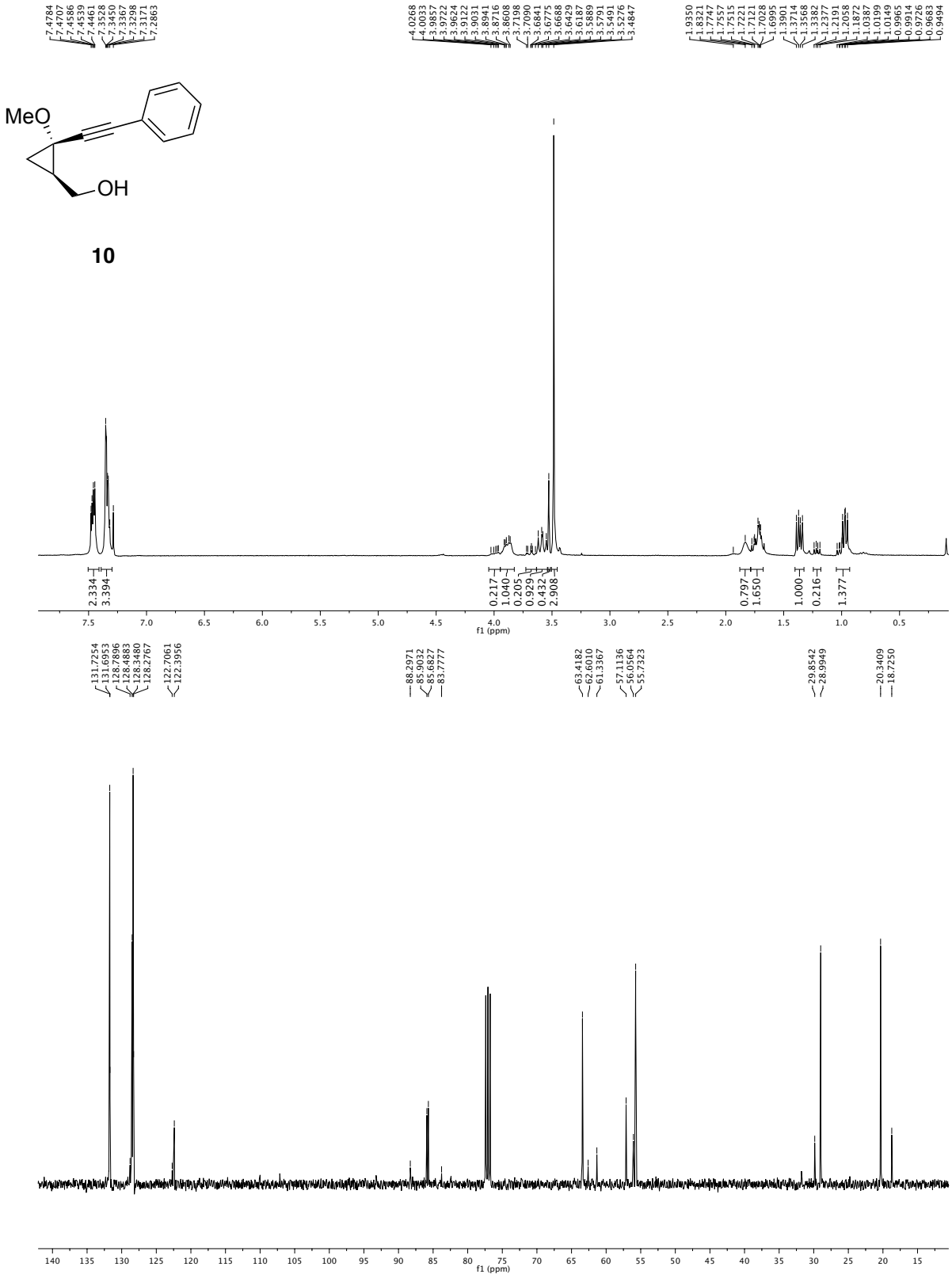
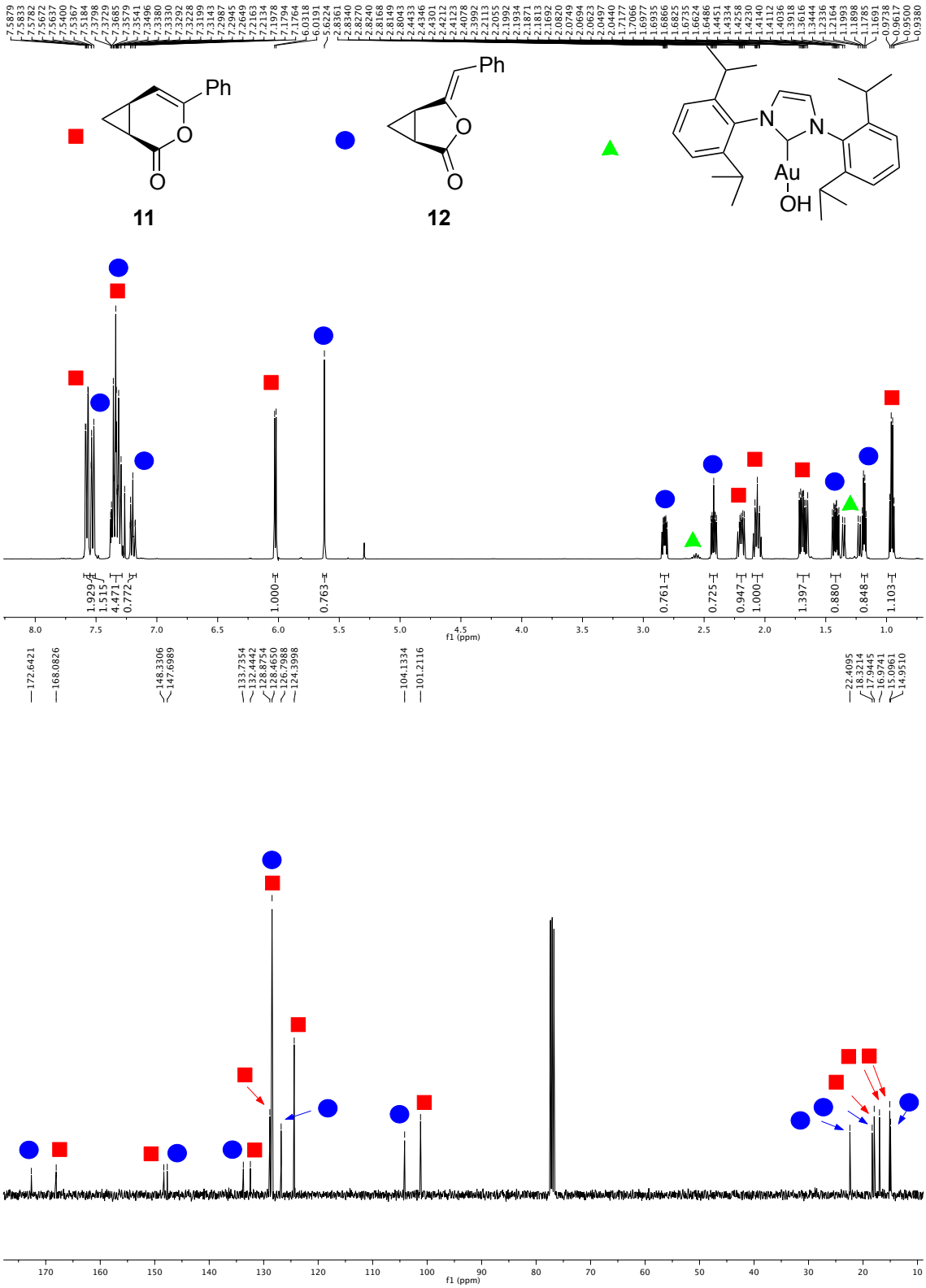
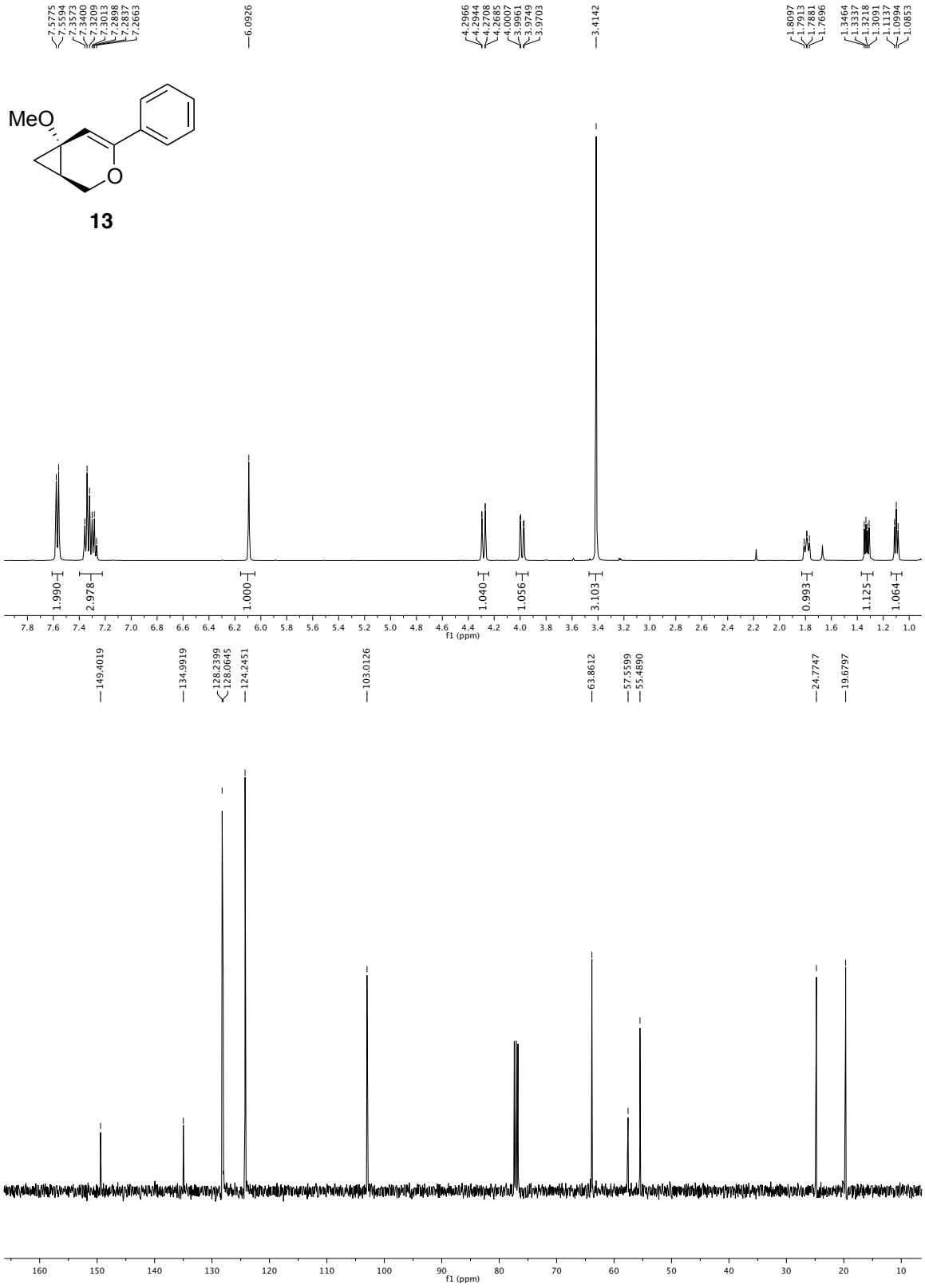
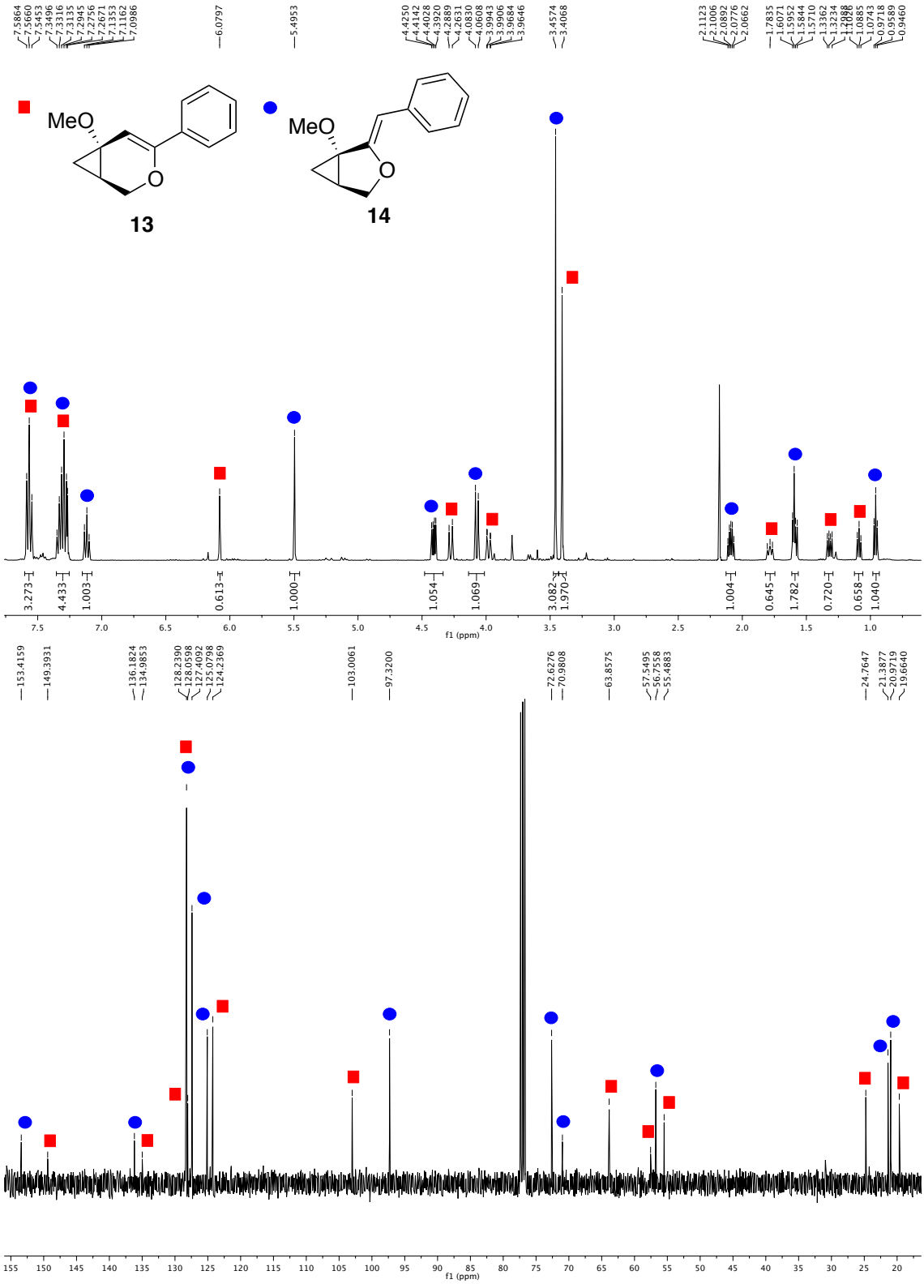
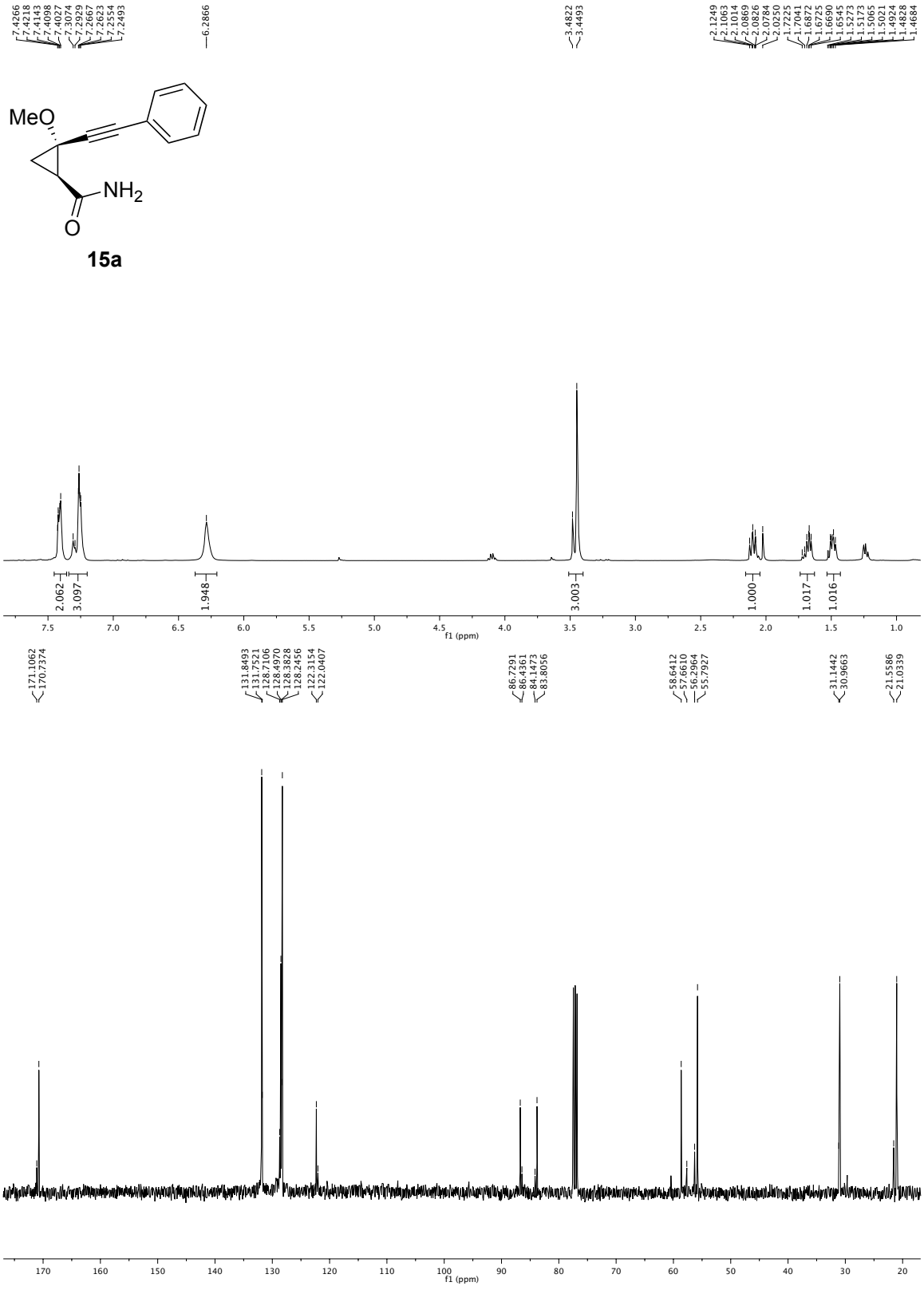
7.3858
7.3767
7.3674
7.2668
7.2562
7.2503
7.2424
7.2398
2.1461
2.1251
2.1074
2.1044
2.0971
2.0861
2.0811
2.0775
2.0611
2.0405
1.5885
1.5721
1.5602
1.5443
1.4073
1.3955
1.3865
1.3748
1.3660
1.3544
OH
O
9
1.808
2.931
1.813
1.000
1.009
f1 (ppm)
176.6651
148.9861
137.1521
132.1526
128.5577
128.2490
86.9140
80.5531
21.7010
15.8858
11.4952
f1 (ppm)

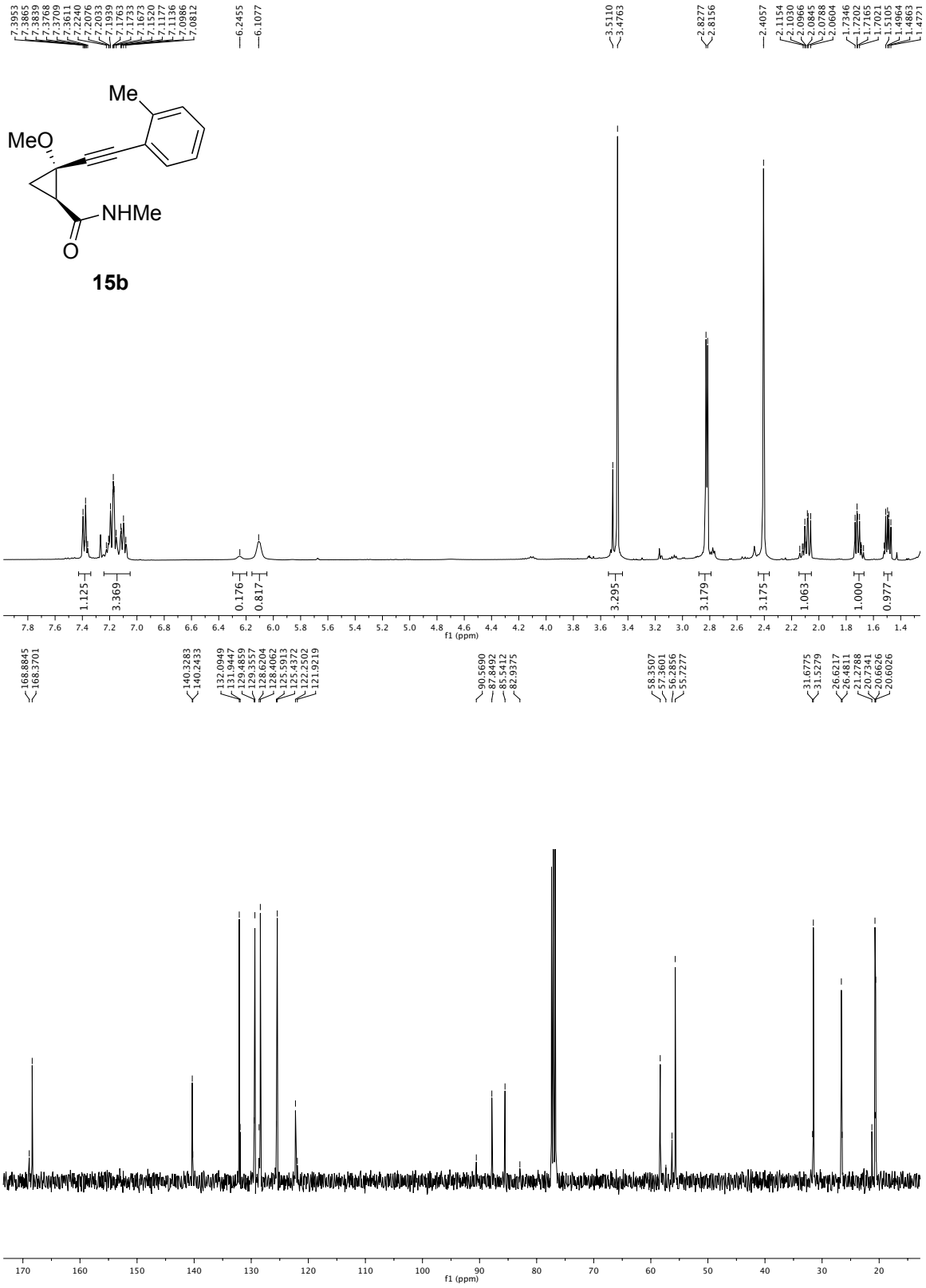

MeO
OH
10
f1 (ppm)
f1 (ppm)

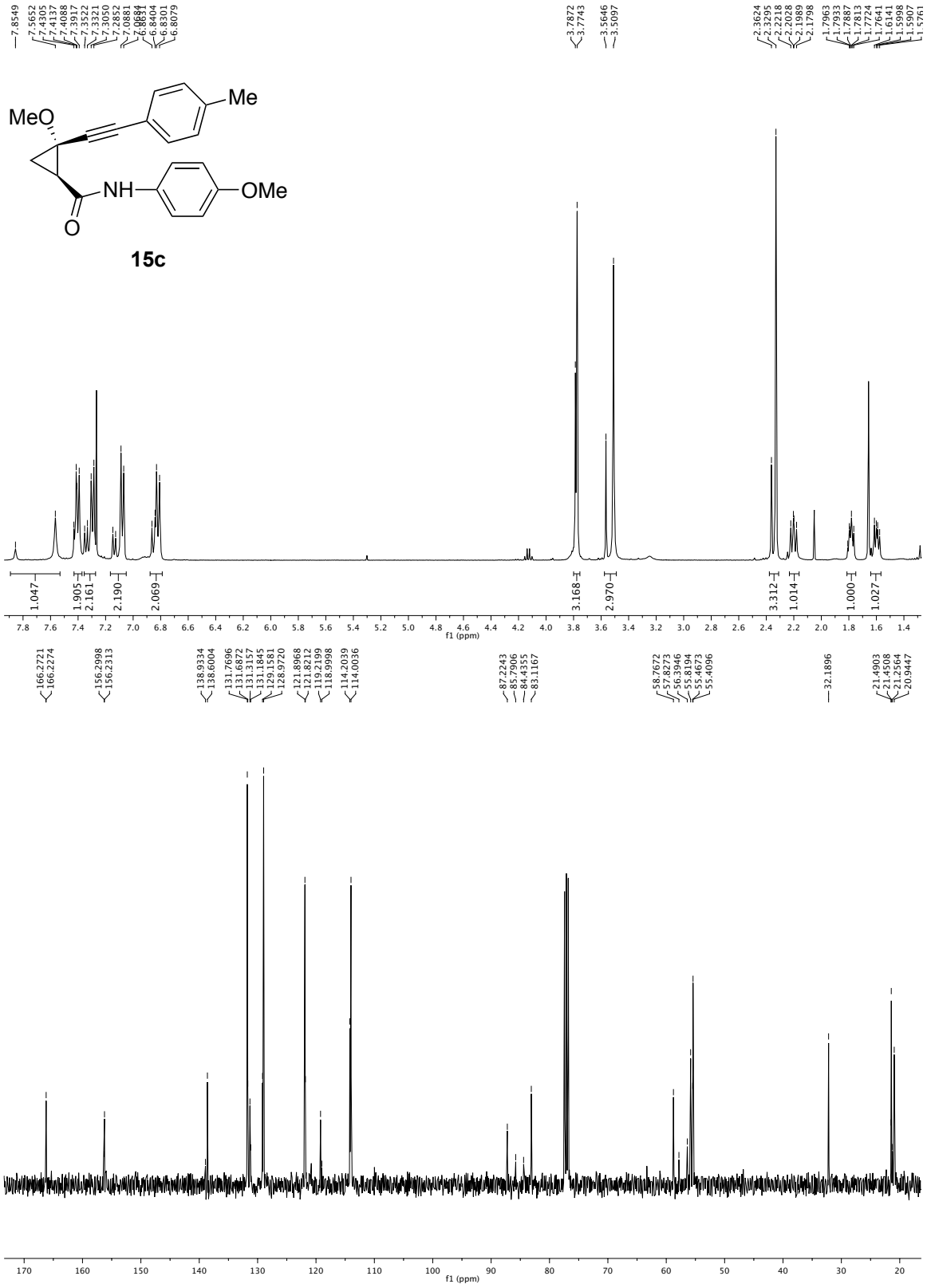

Ph
O
O
11
Ph
O
O
12
N
N
Au
OH
f1 (ppm)
f1 (ppm)

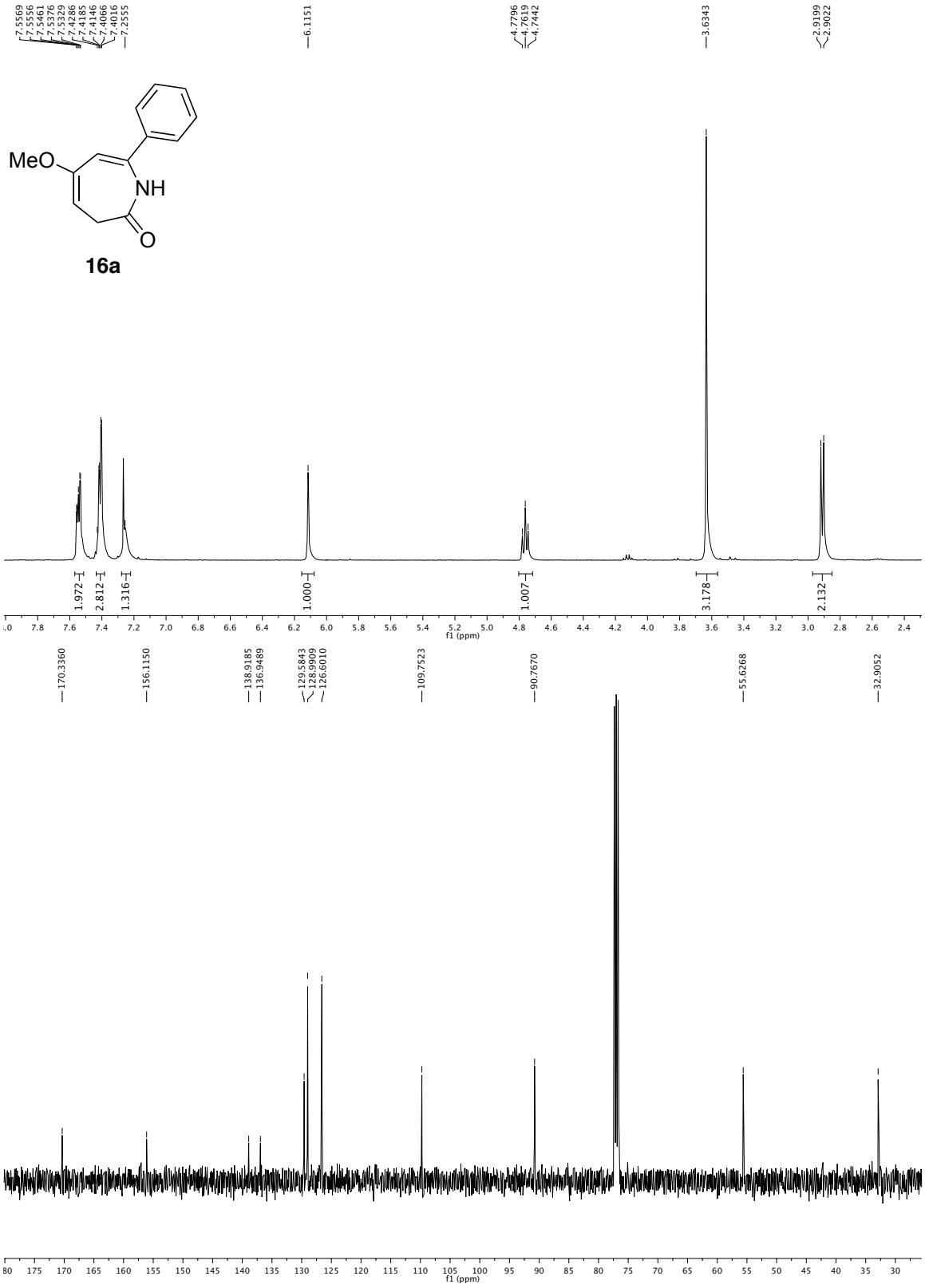

7.5775
7.5594
7.3573
7.3400
7.3209
7.3013
7.2898
7.2837
7.2663
6.0926
4.2966
4.2944
4.2708
4.2685
4.0007
3.9961
3.9749
3.9703
3.4142
1.8097
1.7913
1.7881
1.7696
1.3464
1.3337
1.3218
1.3091
1.1137
1.0994
1.0853
MeO
O
13
1.990
2.978
1.000
1.040
1.056
3.103
0.993
1.125
1.064
f1 (ppm)
149.4019
134.9919
128.2399
128.0645
124.2451
103.0126
63.8612
57.5599
55.4890
24.7747
19.6797
f1 (ppm)

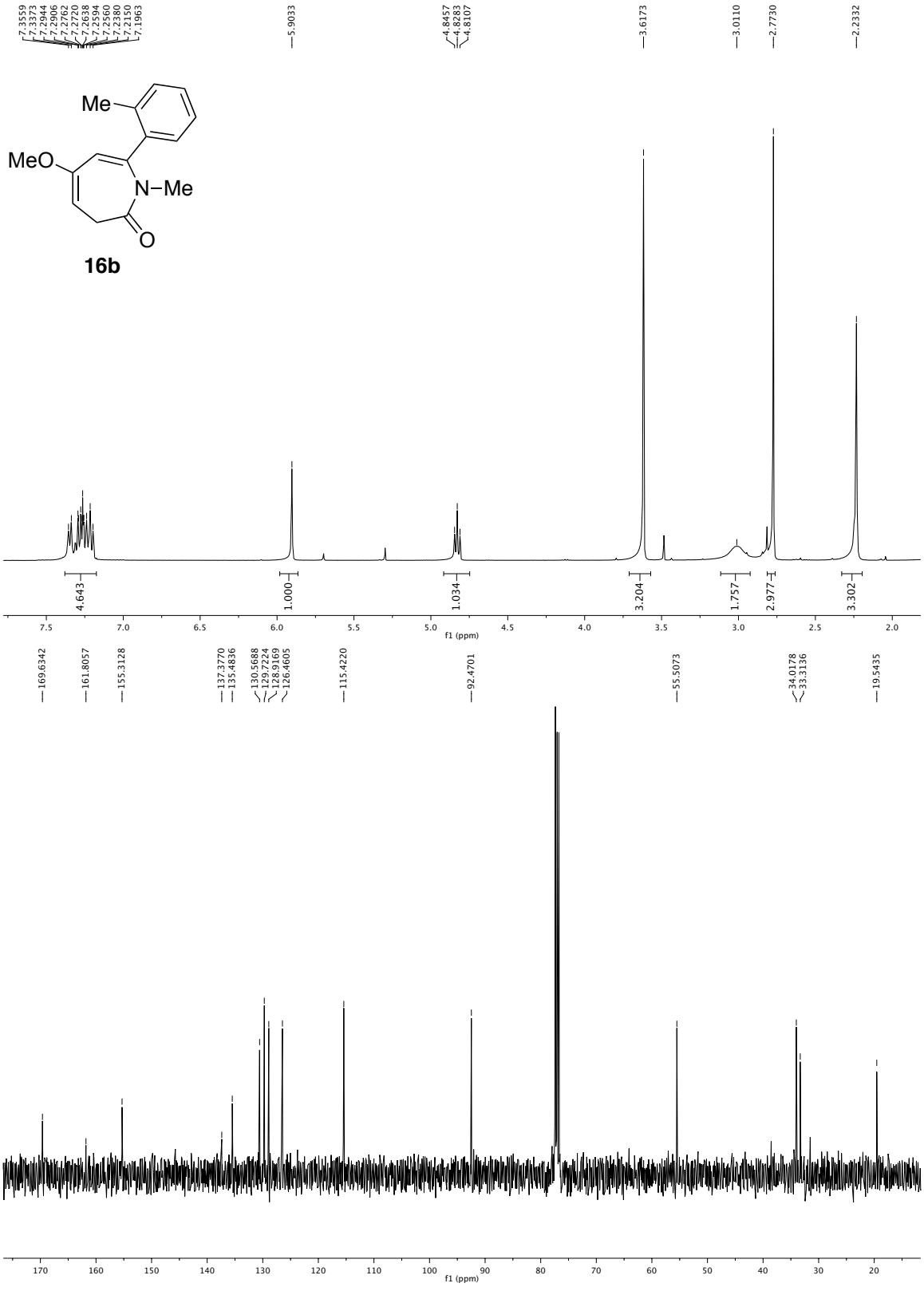

MeO
O
13
MeO
O
14
f1 (ppm)
f1 (ppm)

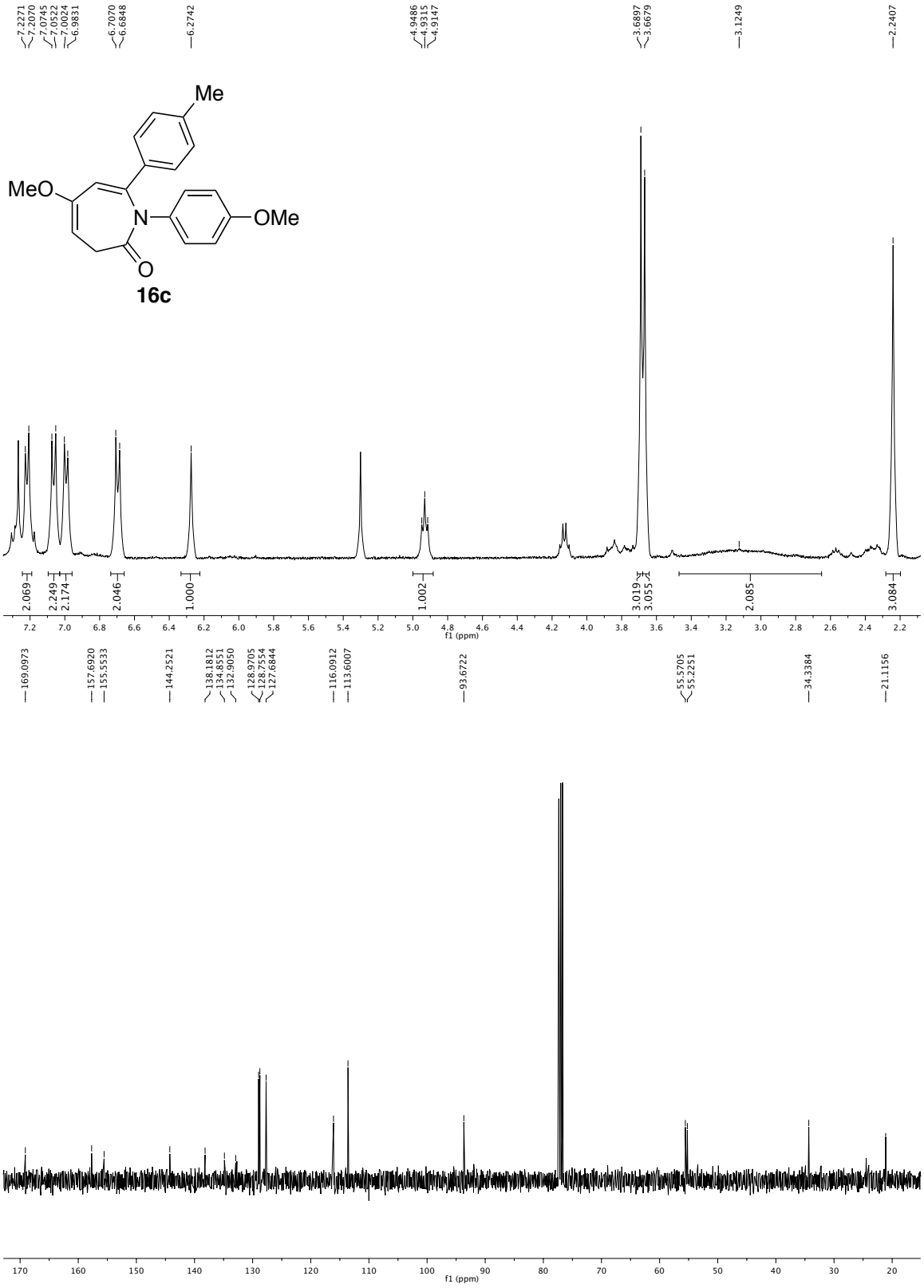

7.4266
7.4218
7.4143
7.4098
7.4027
7.3074
7.3029
7.2667
7.2623
7.2554
7.2493
6.2866
3.4822
3.4493
2.1249
2.1063
2.1014
2.0869
2.0826
2.0784
2.0250
1.7225
1.7041
1.6872
1.6725
1.6690
1.6545
1.5273
1.5173
1.5065
1.5021
1.4924
1.4828
1.4684
MeO
NH2
O
15a
2.062
3.097
1.948
3.003
1.000
1.017
1.016
f1 (ppm)
171.1062
170.7374
131.8493
131.7521
128.7106
128.4970
128.3828
128.2456
122.3154
122.0407
86.7291
86.4361
84.1473
83.8056
58.6412
57.6610
56.2964
55.7927
31.1442
30.9663
21.5586
21.0339
f1 (ppm)


Me
MeO
NHMe
O
15b
f1 (ppm)


MeO
Me
NH
OMe
O
15c
f1 (ppm)


7.5569
7.5556
7.5461
7.5376
7.5329
7.4286
7.4185
7.4146
7.4066
7.4016
7.2555
6.1151
4.7796
4.7619
4.7442
3.6343
2.9199
2.9022
MeO
NH
O
16a
1.972
2.812
1.316
1.000
1.007
3.178
2.132
f1 (ppm)
170.3360
156.1150
138.9185
136.9489
129.5843
128.9909
126.6010
109.7523
90.7670
55.6268
32.9052
f1 (ppm)


7.3559
7.3373
7.2944
7.2906
7.2762
7.2720
7.2638
7.2594
7.2560
7.2380
7.2150
7.1963
5.9033
4.8457
4.8283
4.8107
3.6173
3.0110
2.7730
2.2332
Me
MeO
N−Me
O
16b
4.643
1.000
1.034
3.204
1.757
2.977
3.302
f1 (ppm)
169.6342
161.8057
155.3128
137.3770
135.4836
130.5688
129.7224
128.9169
126.4605
115.4220
92.4701
55.5073
34.0178
33.3136
19.5435
f1 (ppm)


Me
MeO
N
OMe
O
16c
7.2271
7.2070
7.0745
7.0522
7.0024
6.9831
6.7070
6.6848
6.2742
4.9486
4.9315
4.9147
3.6897
3.6679
3.1249
2.2407
2.069
2.249
2.174
2.046
1.000
1.002
3.019
3.055
2.085
3.084
f1 (ppm)
169.0973
157.6920
155.5533
144.2521
138.1812
134.8551
132.9050
128.9705
128.7554
127.6844
116.0912
113.6007
93.6722
55.5705
55.2251
34.3384
21.1156
f1 (ppm)