

Supporting Information

Enantioselective Synthesis of the C₁₀ to C₂₀

Fragment of Fusicoccin

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Determination of the absolute configuration of *ent*-10a^{1,2}

If both esters adopt the preferred *s-trans* configuration of the O-CO bonds and if the trifluoromethyl substituents of the MTPA moieties and the methine protons are in a syn-coplanar arrangement with the carbonyl groups, the conformations illustrated in Figure 1 will result.

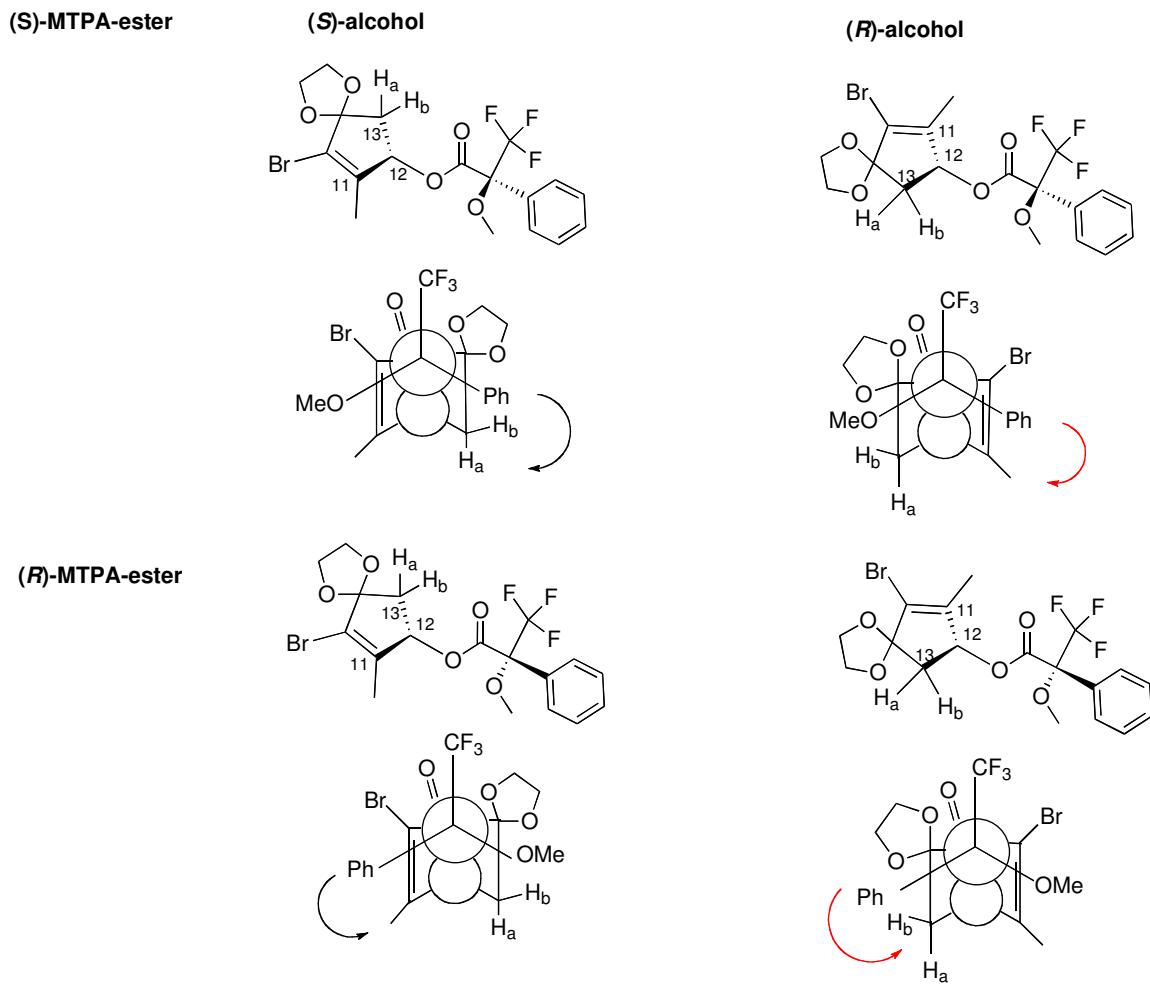


Figure 1: The arrows indicate the expected upfield shifts due to the anisotropic, magnetic shielding effect of the phenyl group, the red marked ones were observed.

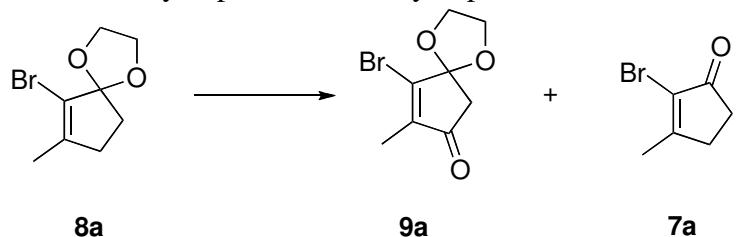
The phenyl substituent of the MTPA moiety induces an anisotropic, magnetic shielding of the protons residing above (or below) the plane of the aryl ring. This results in an upfield chemical shift for the protons close to the phenyl group.

We observed in the spectra for the (*S*)-MTPA ester an upfield shift of the methyl group of the cyclopentyl ring ($\Delta\delta^{SR}$ is calculated to -0.14 ppm), in the (*R*)-MTPA ester an upfield

shift for the proton H_{2a} ($\Delta\delta^{SR}$ is calculated to 0.13 ppm). These results confirm, that **ent-10a** is (*R*)-configured at C(12), which fits with the predicted stereochemical outcome of the CBS reduction using the (*S*)-configured CBS ligand.

Allylic oxidation of **8a**

Table 1: Exploration of different reaction conditions for the allylic oxidation of cyclopentene **8a** to cyclopentenone **9a**.



Reagents	Solvent	T	t	Observation	Yield 9a
1 ³ 10 eq TBHP in decane, 0.7 eq RuCl ₃ , MS 4	C ₂ H ₄ Cl ₂	70 °C	1h	Full conversion, 7a	-
2 ⁴ 5.0 eq TBHP in water, 1.25 eq NaClO ₂	CH ₃ CN/H ₂ O 3:1	50 °C	17 h	Full conversion, 9a/7a 2:1.2	6% ^a
3 5.0 eq TBHP in water, 1.25 eq NaClO ₂	CH ₃ CN/buffer pH = 8, 3:1	50 °C	18 h	8a/9a/7a 1:1:1	-
4 ⁵ 5.0 eq TBHP in water, 1.25 eq NaClO ₂	EtOAc/H ₂ O 3:1	50 °C	20 h	9a/7a 2:1	-
5 2.4 eq TBHP in decane, 0.5 eq Cr(CO) ₆	CH ₃ CN	85 °C	20 h	9a/7a 1:10	-
6 ⁶ 3.9 eq TBHP in decane, 0.1 eq MnOAc ₃ , MS 4, O ₂	EtOAc	r.t.	20 h	No conversion	-

7	7.8 eq TBHP in decane, 0.2 eq MnOAc_3 , MS 4, O_2	EtOAc	50 °C	17 h	Traces of 9a , decomposition	-
8	12 eq TBHP in decane, 0.2 eq MnOAc_3 , MS 4, O_2	$\text{C}_2\text{H}_4\text{Cl}_2$	70 °C	24 h	Traces of 9a , decomposition	9% ^a
9	12 eq TBHP in decane, 0.2 eq MnOAc_3 , MS 4, O_2	$\text{C}_6\text{H}_5\text{Cl}$	75 °C	39 h	Decomposition, traces of 9a	-
10	20 eq TBHP in decane, 0.1 eq MnOAc_3 , MS 4, O_2	$\text{C}_2\text{H}_4\text{Cl}_2$	50 °C	46 h	Traces of 9a , decomposition	-
11	30 eq TBHP in decane, 0.1 eq MnOAc_3 , MS 4, O_2	$\text{C}_2\text{H}_4\text{Cl}_2$	r.t.	60 h	Traces of 9a , decomposition	-
12	10 eq TBHP in $\text{C}_2\text{H}_4\text{Cl}_2$ ^b , 0.05 eq MnOAc_3 , MS 4	-	40 °C	20 h	Full conversion	22% ^a
13	20 eq TBHP in $\text{C}_2\text{H}_4\text{Cl}_2$, 0.5 eq $\text{Cr}(\text{CO})_6$	-	40 °C then r.t.	18 h then 50 h	Full conversion, only 9a	74% ^c

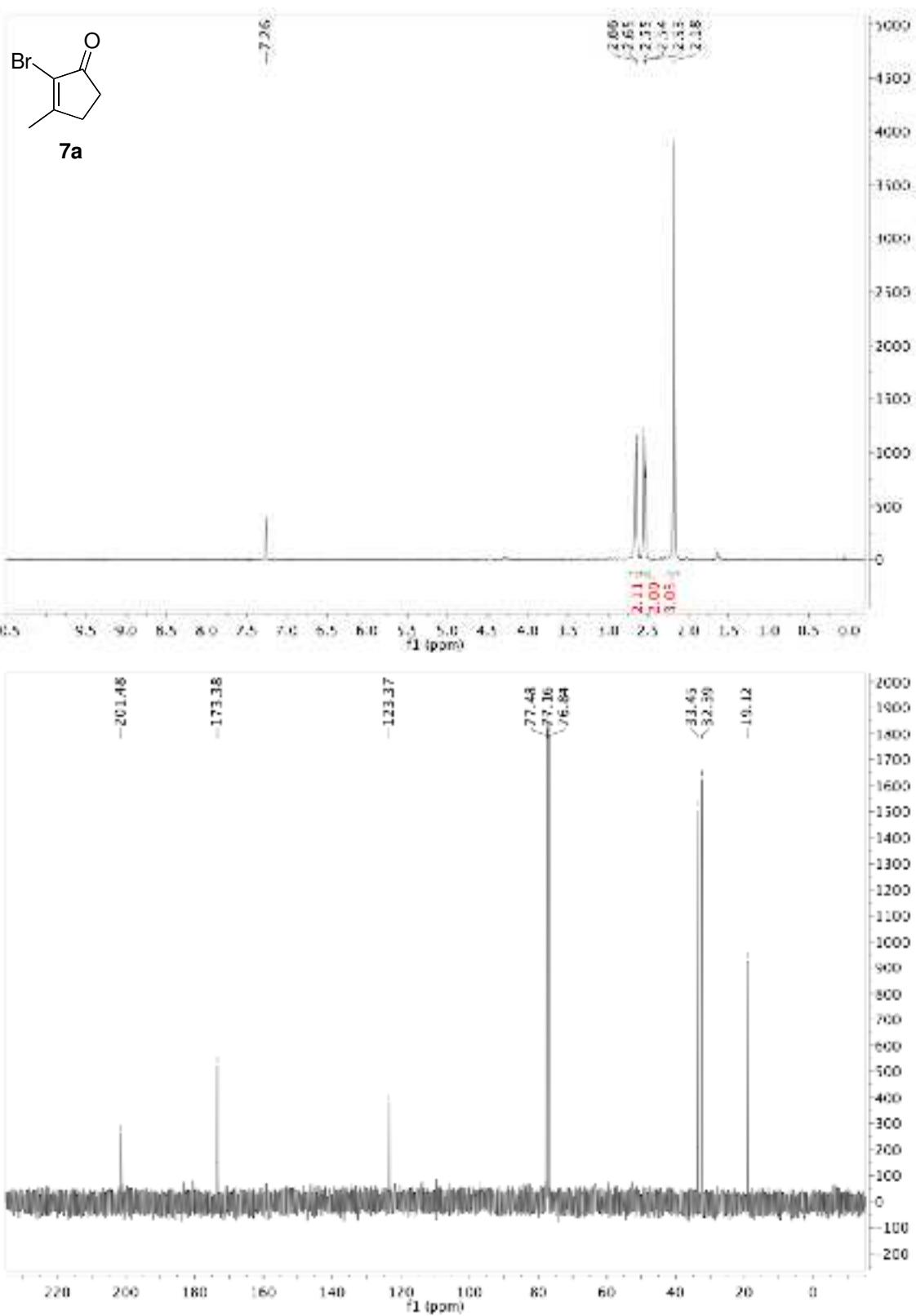
^aPurification by column chromatography over silica gel deactivated with triethylamine.

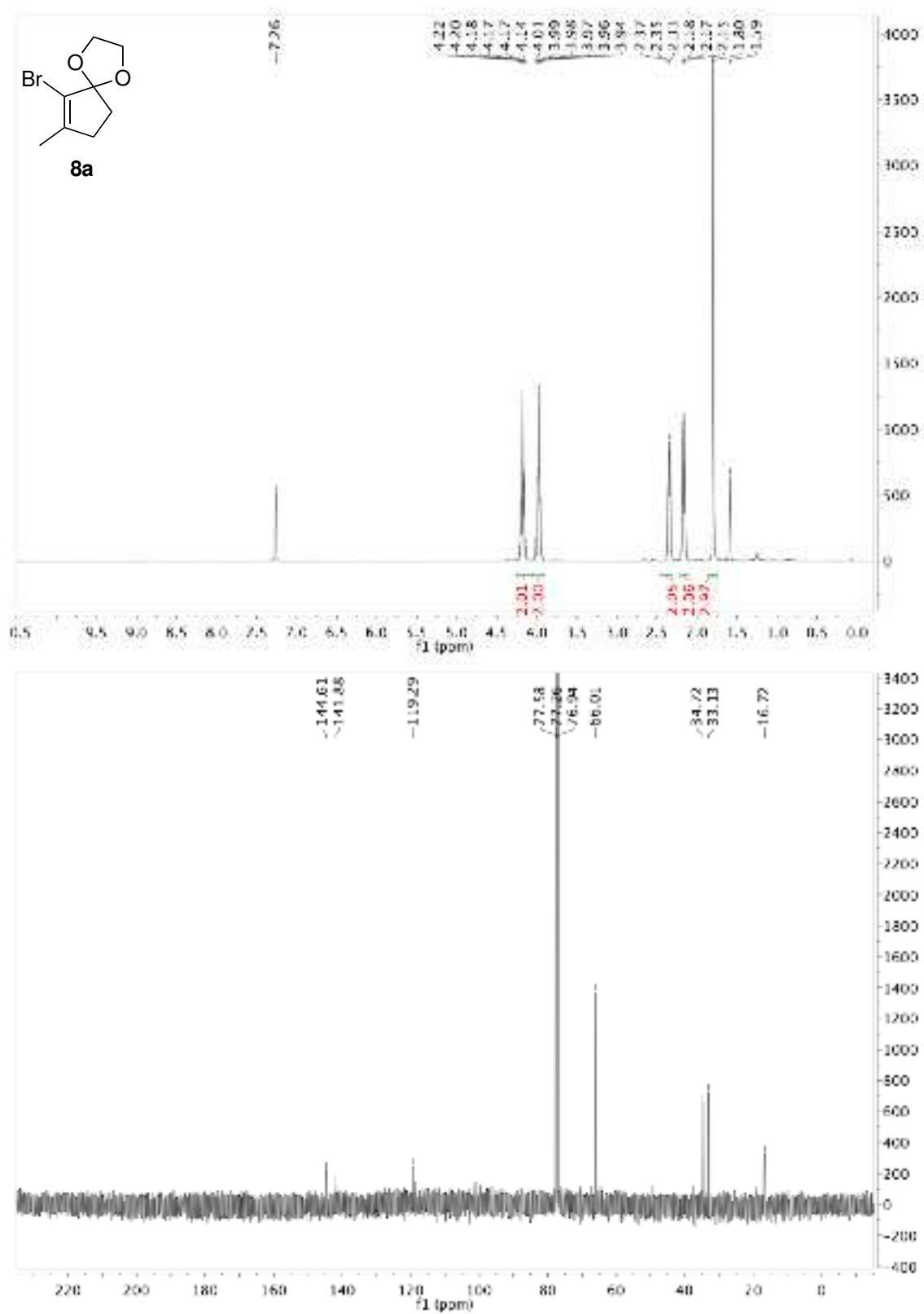
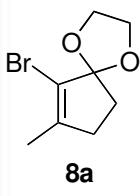
^bTBHP in $\text{C}_2\text{H}_4\text{Cl}_2$ was prepared by extraction of TBHP in water with $\text{C}_2\text{H}_4\text{Cl}_2$.

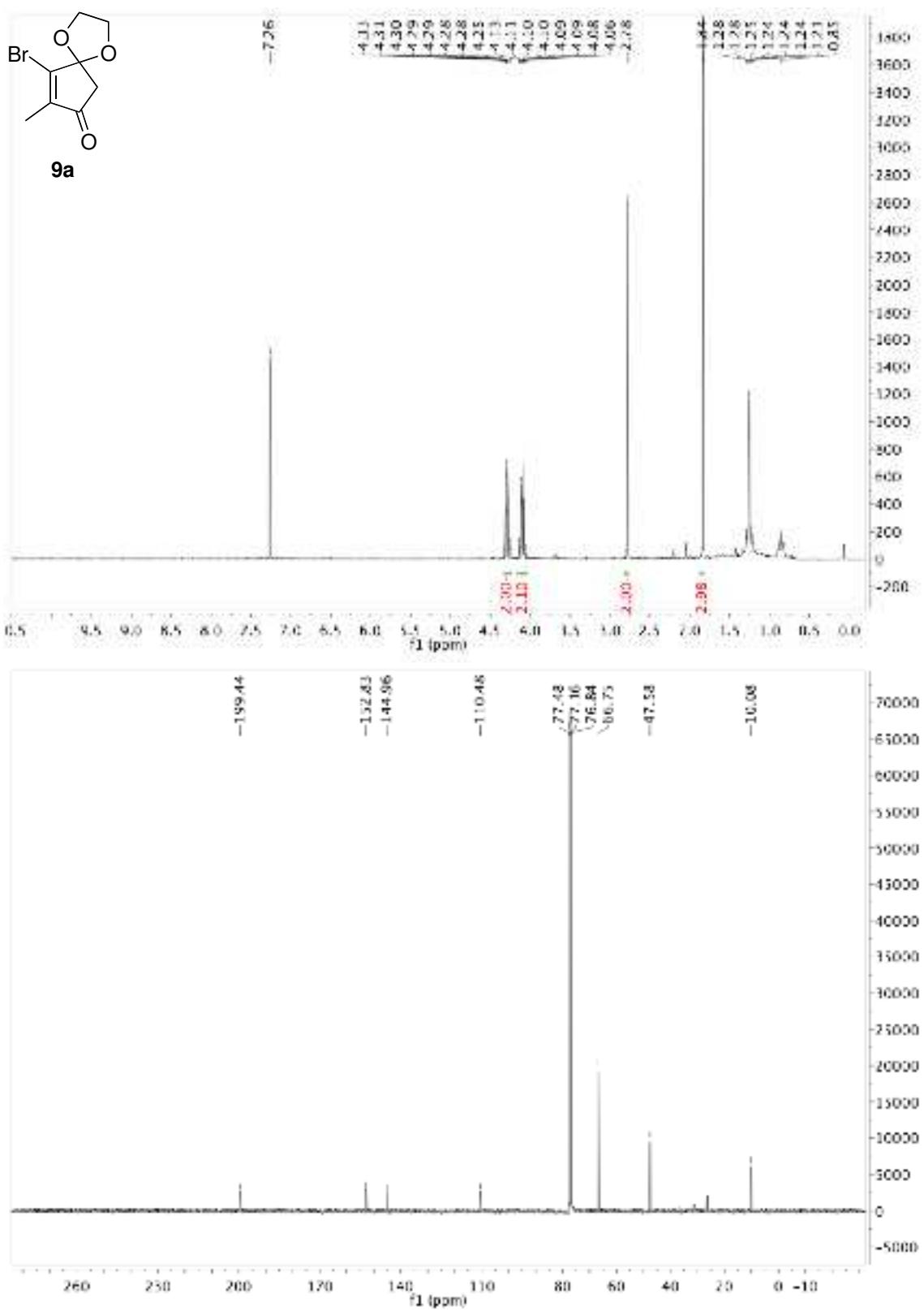
^cCrude yield, **9a** is the only compound detected by GC/MS and TLC, yields varies by purification and reaction scale. Further studies showed that the catalyst loading can be reduced down to 0.1 percent.

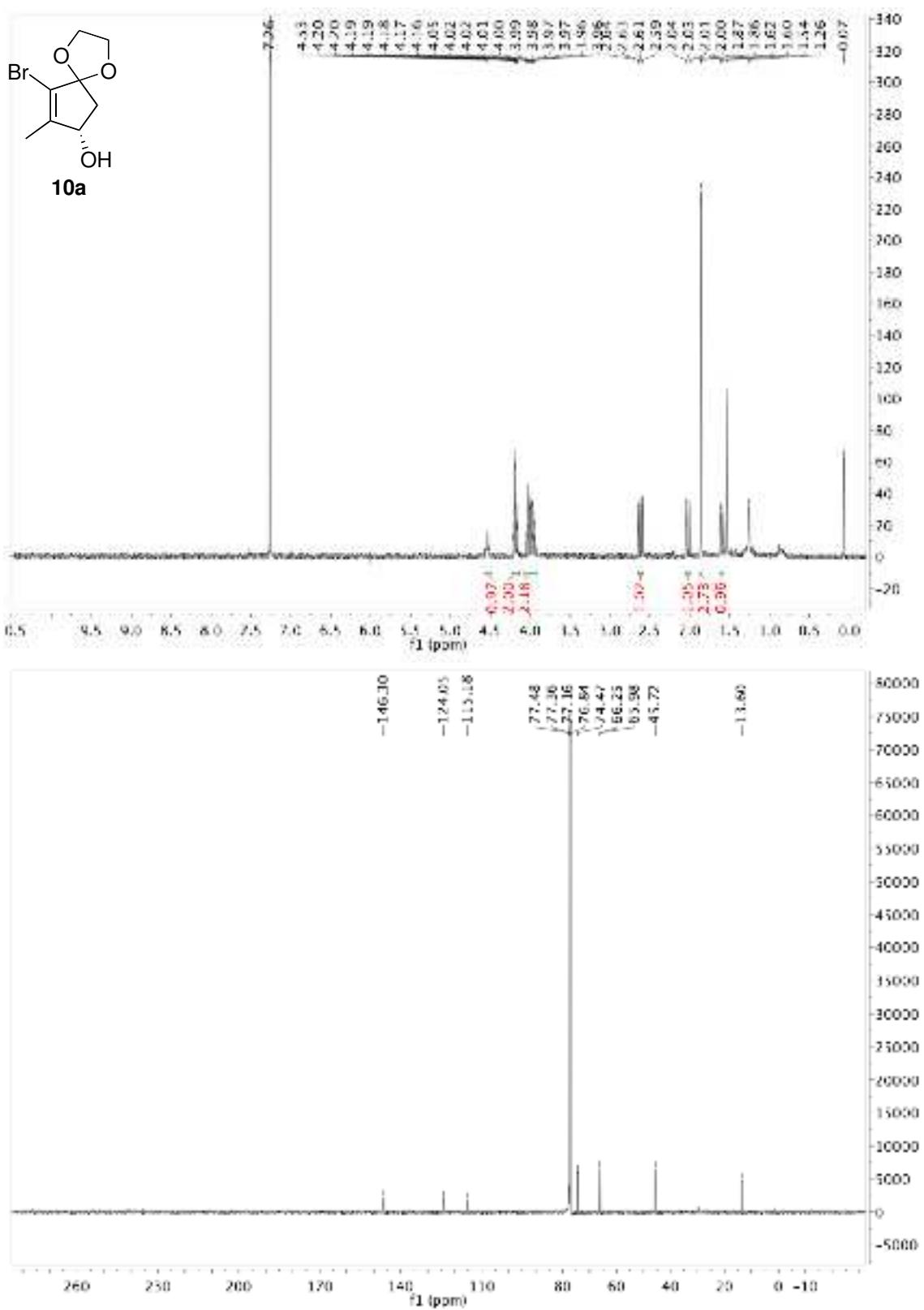
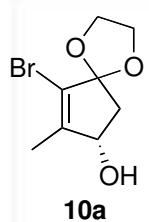
- (1) Hoye, T. R.; Jeffrey, C. S.; Shao, F. *Nat. Protoc.* **2007**, 2, 2451.
- (2) J. M. Seco, E. Quinoá, R. Riguera, *Chem. Rev.* **2004**, 104, 17.
- (3) Miller, R.; Li, W.; Humphrey, G. *Tetrahedron Lett.* **1996**, 37, 3429.
- (4) Silvestre, S. M.; Salvador, J. A. R. *Tetrahedron* **2007**, 63, 2439.
- (5) Pearson, A.; Chen, Y.; Han, G.; Hsu, S.; Ray, T. *J Chem Soc Perk T 1* **1985**, 267.

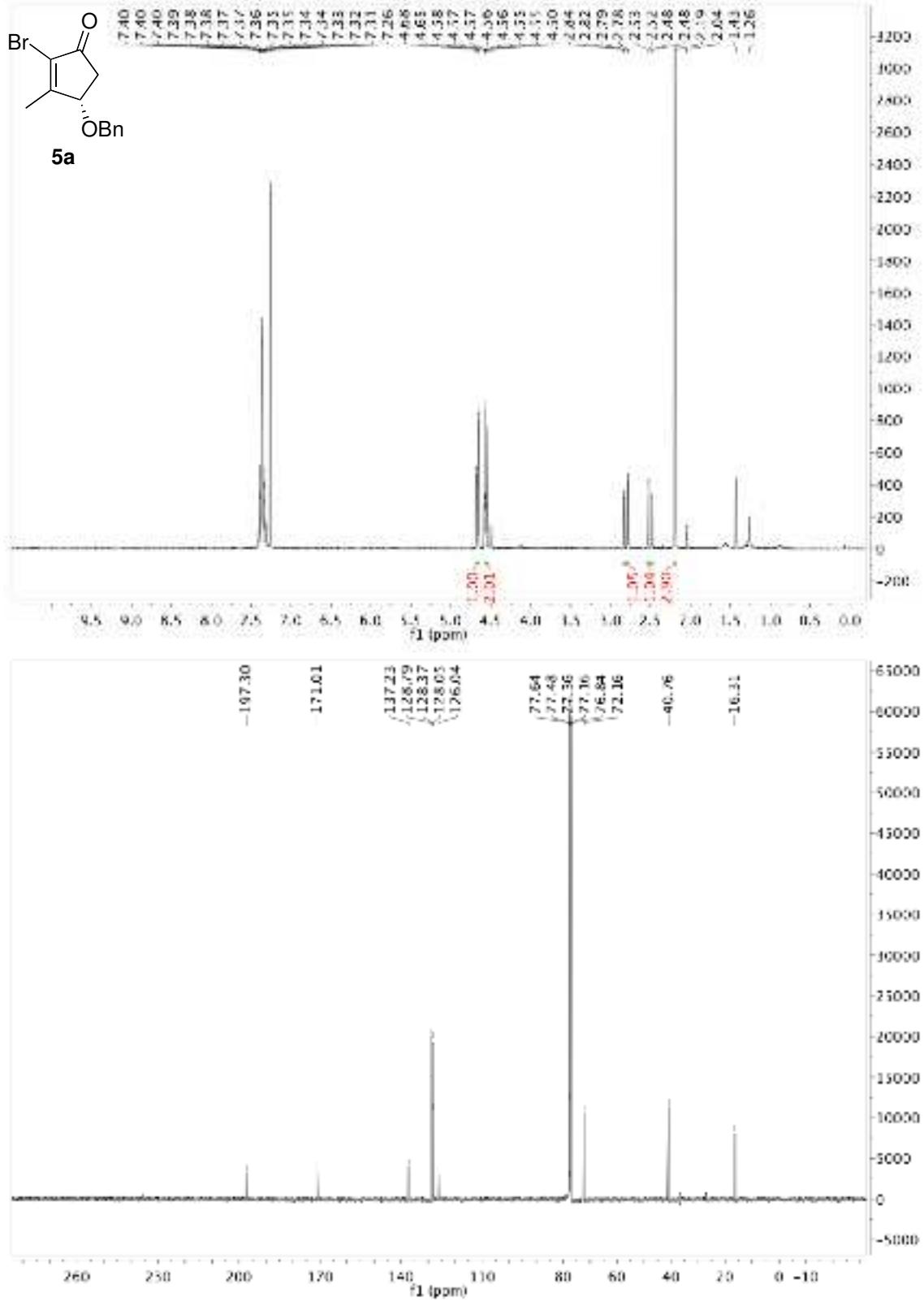
- (6) Shing, T. K. M.; Yeung, Y.-Y.; Su, P. L. *Org. Lett.* **2006**, 8, 3149.

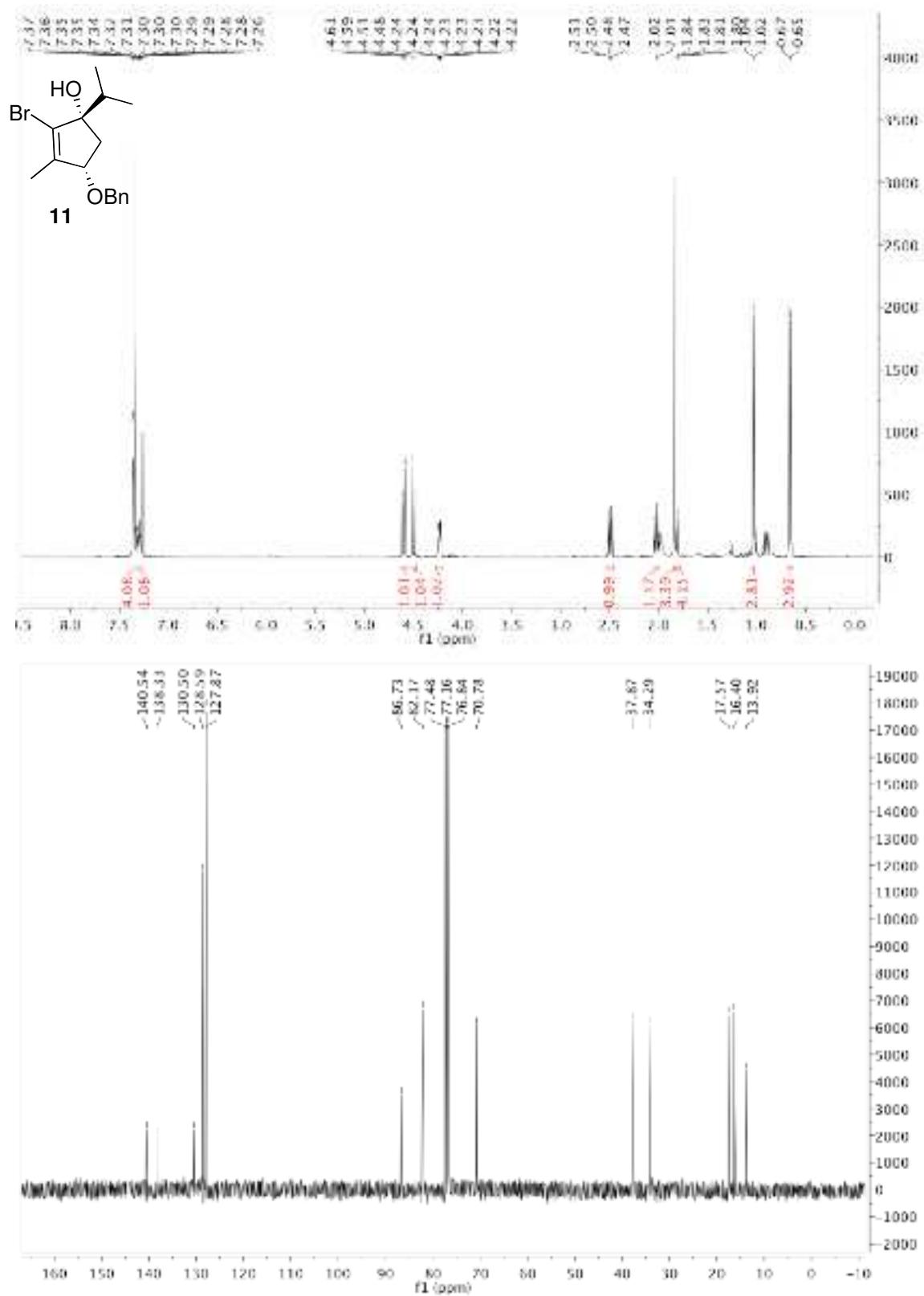


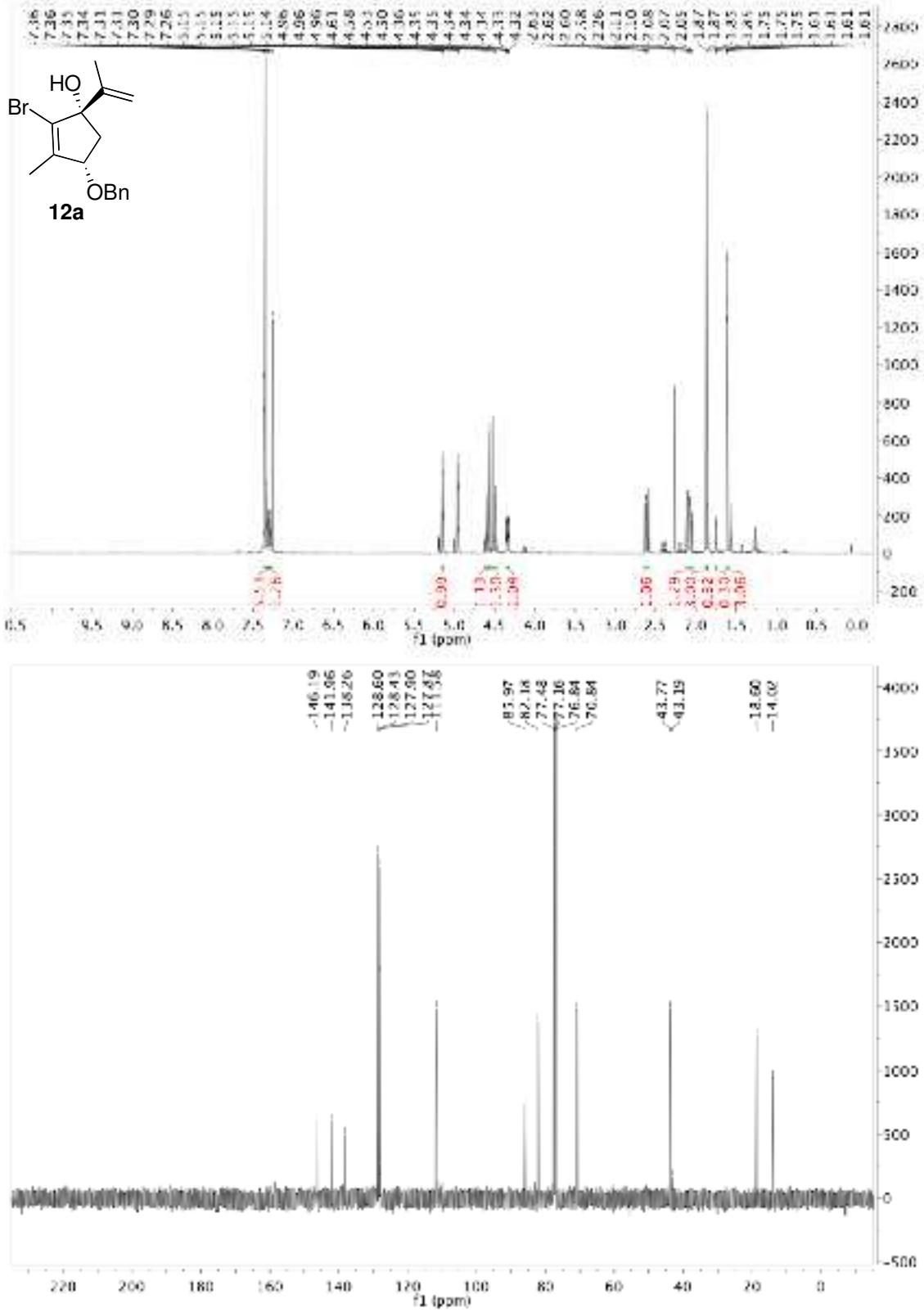


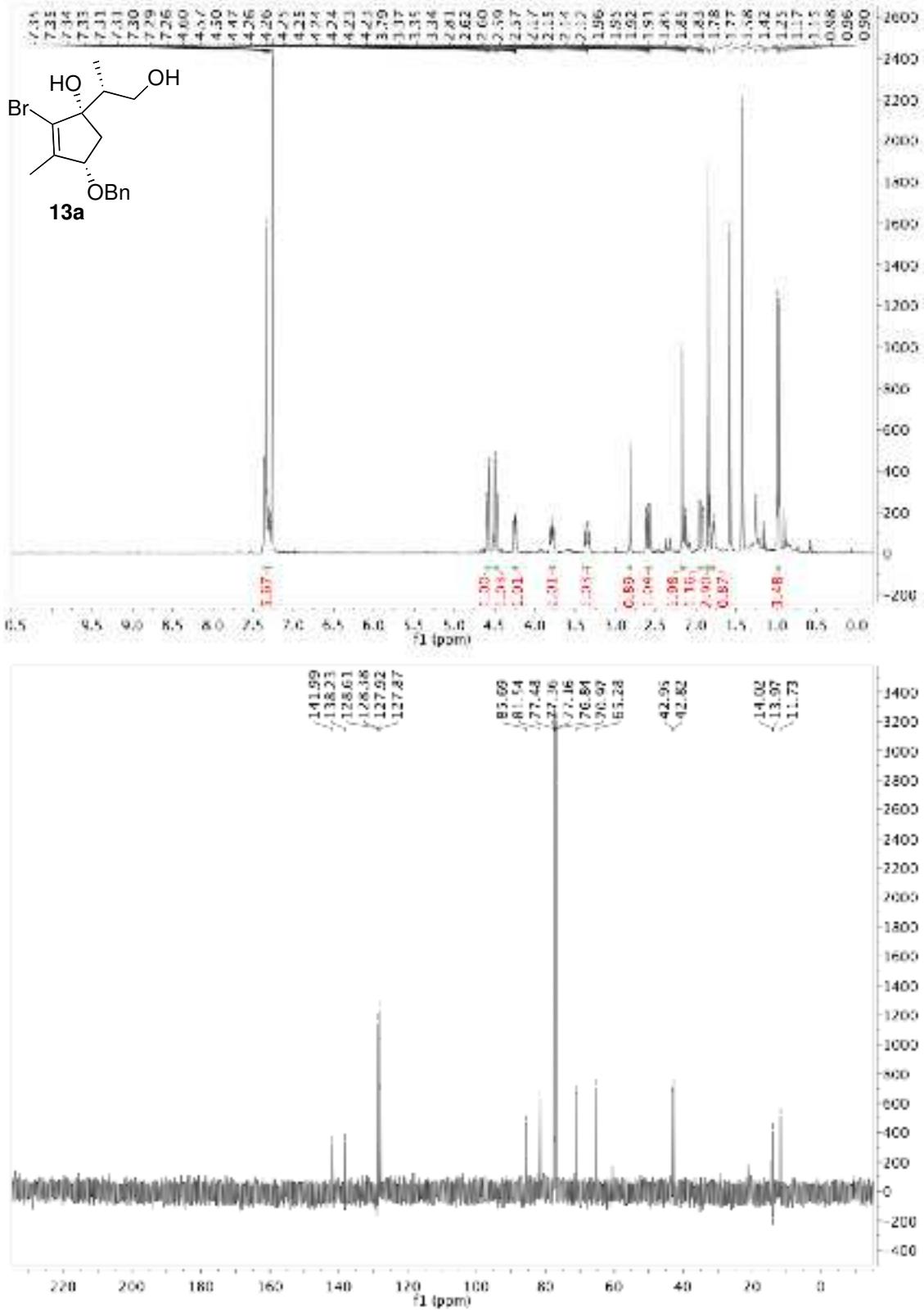


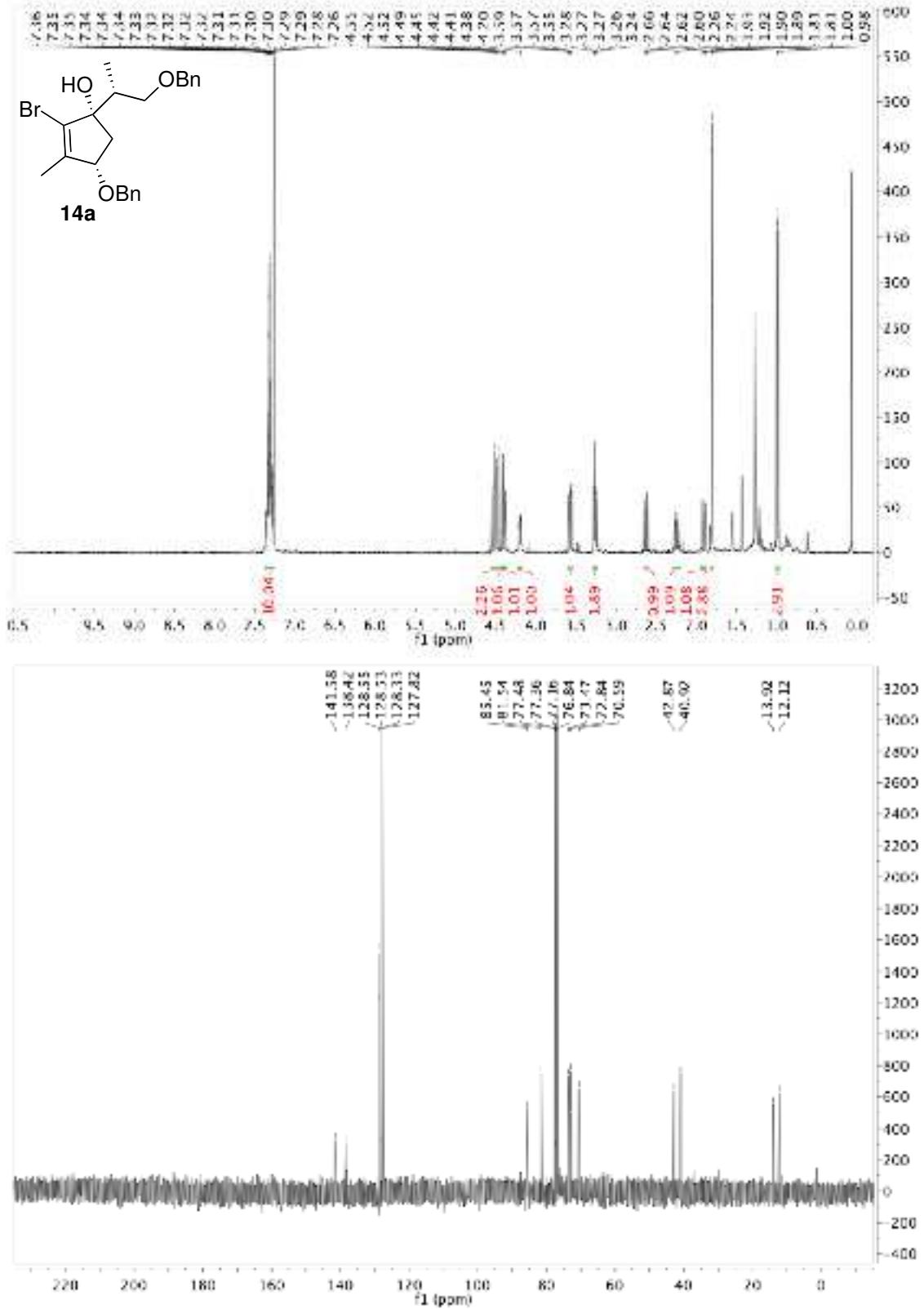


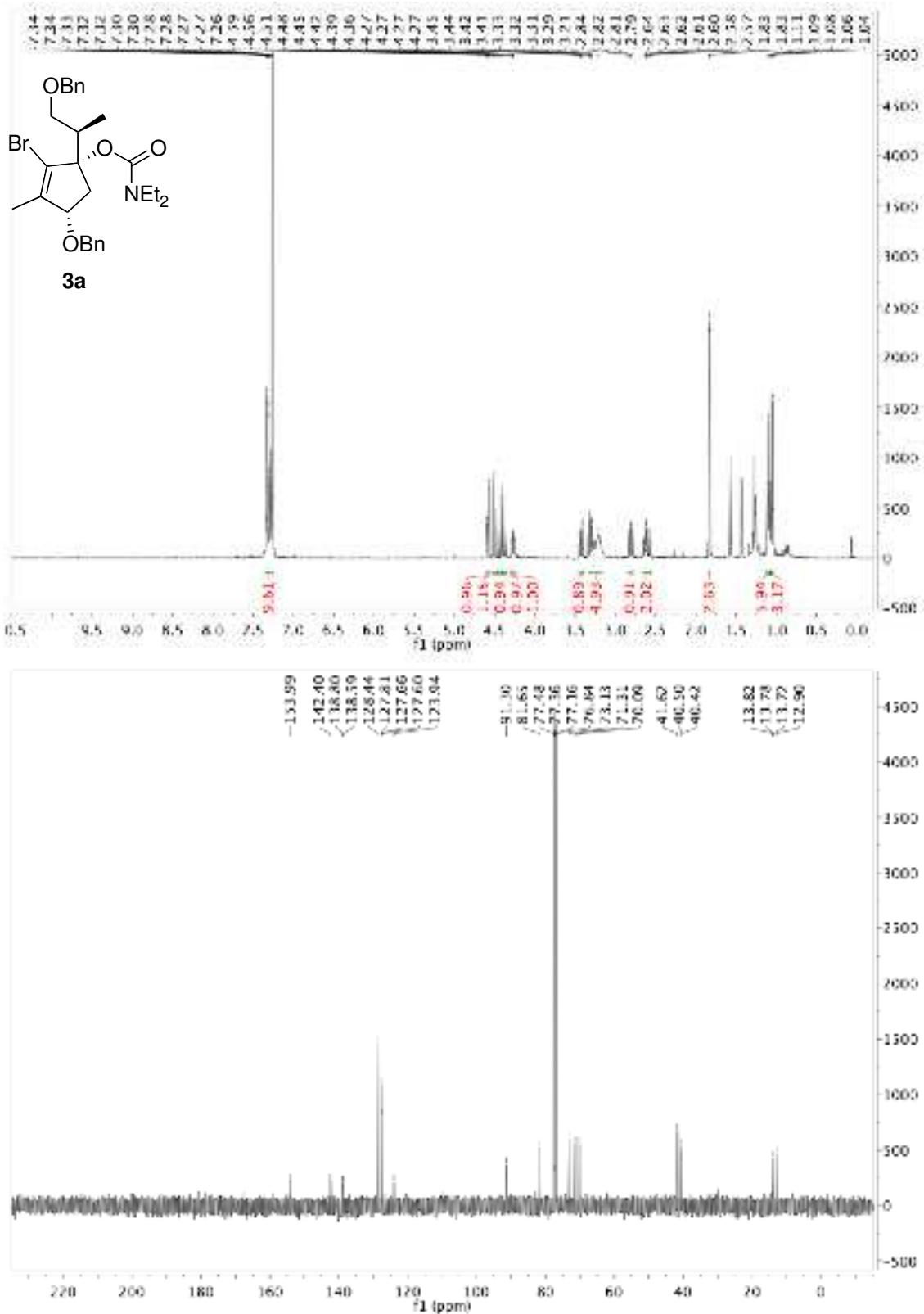


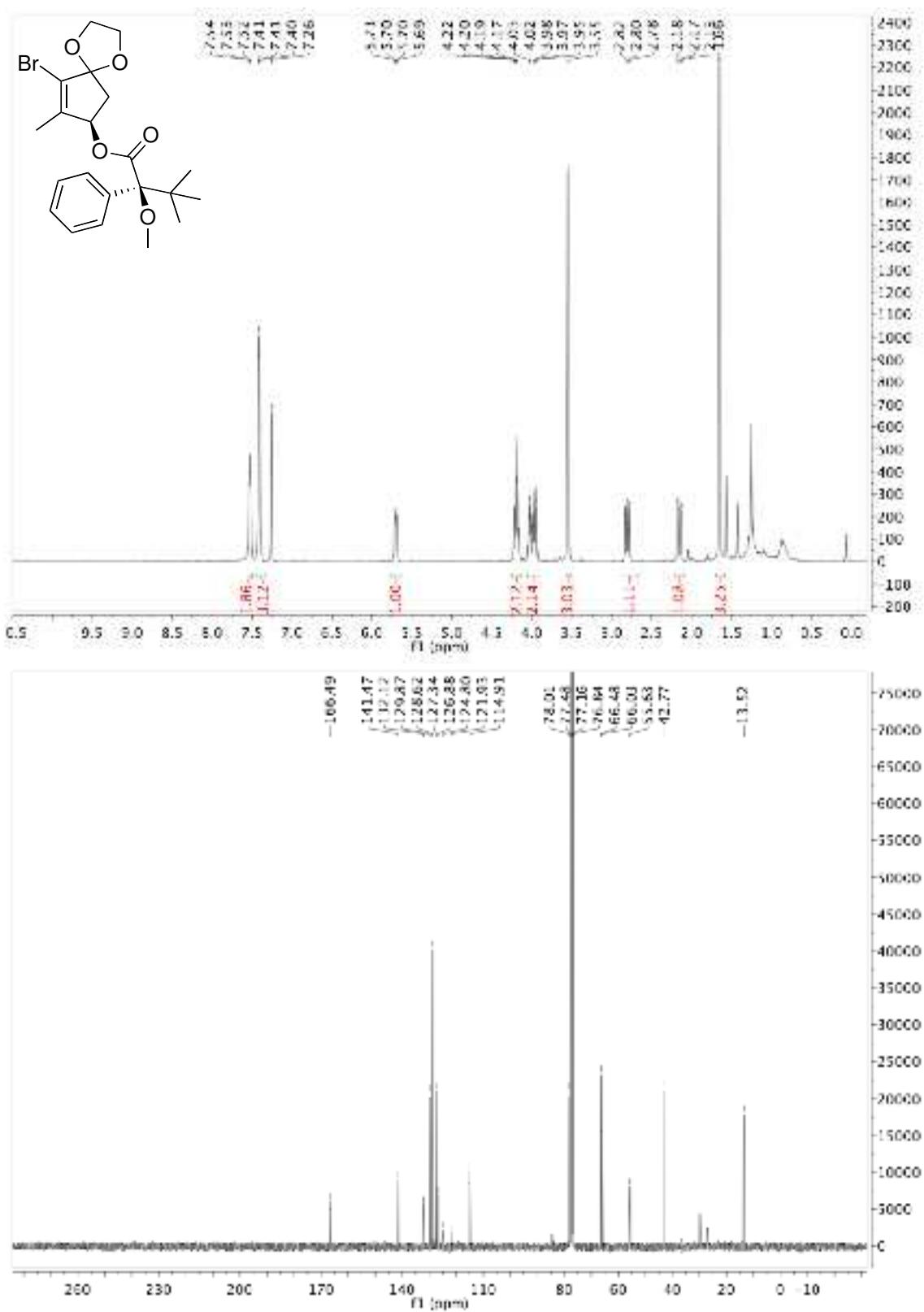
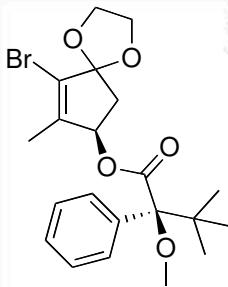


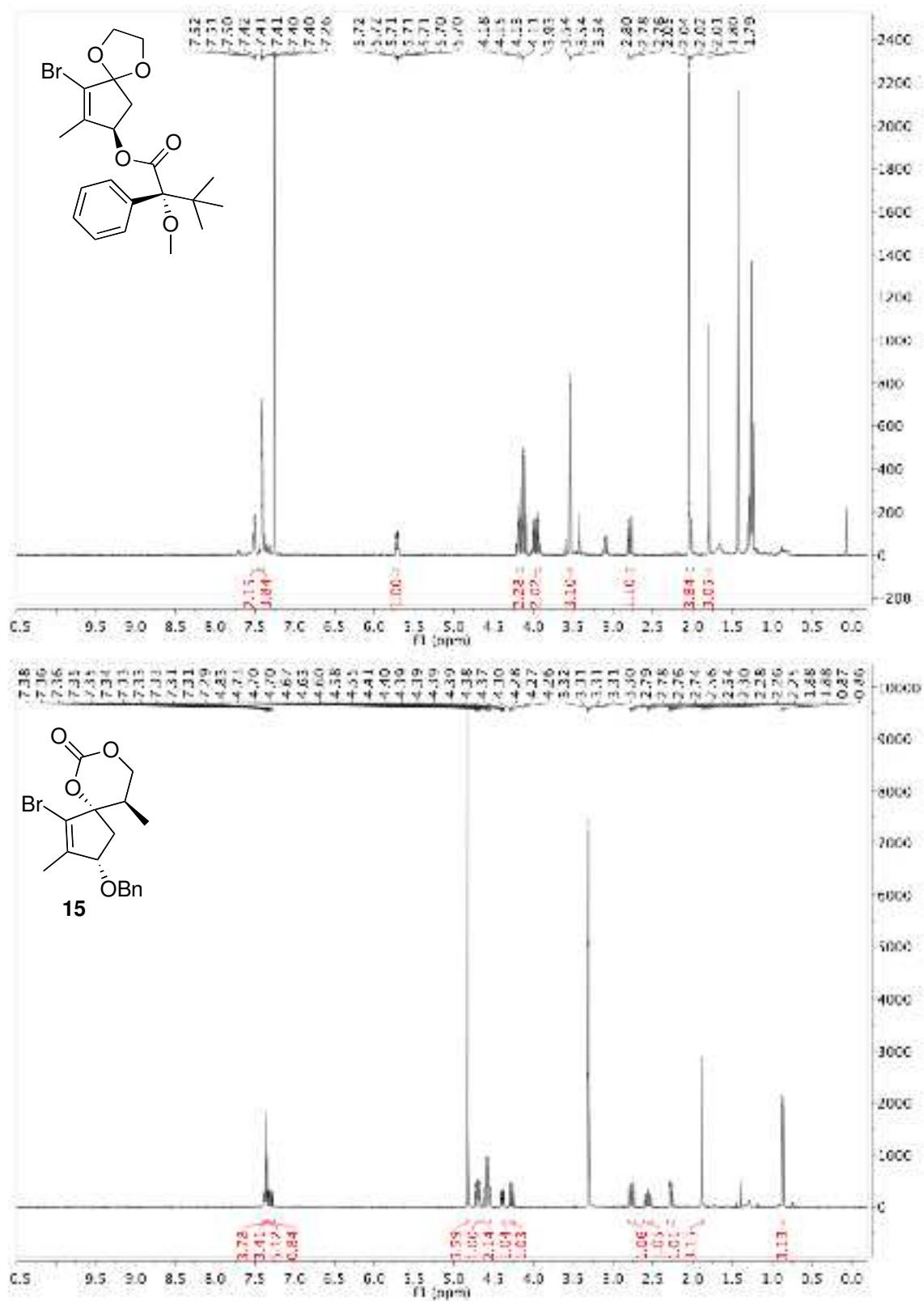


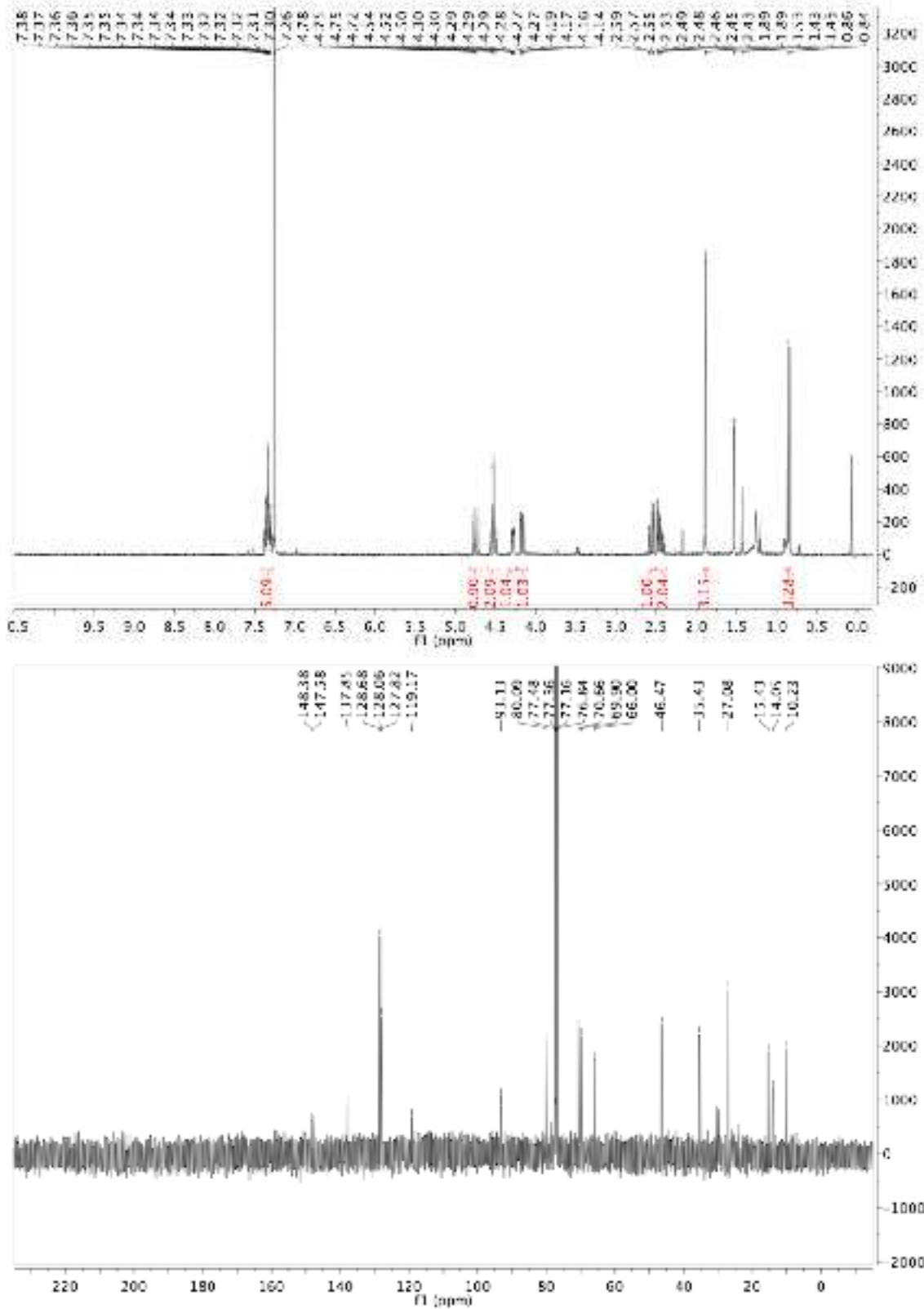


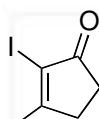




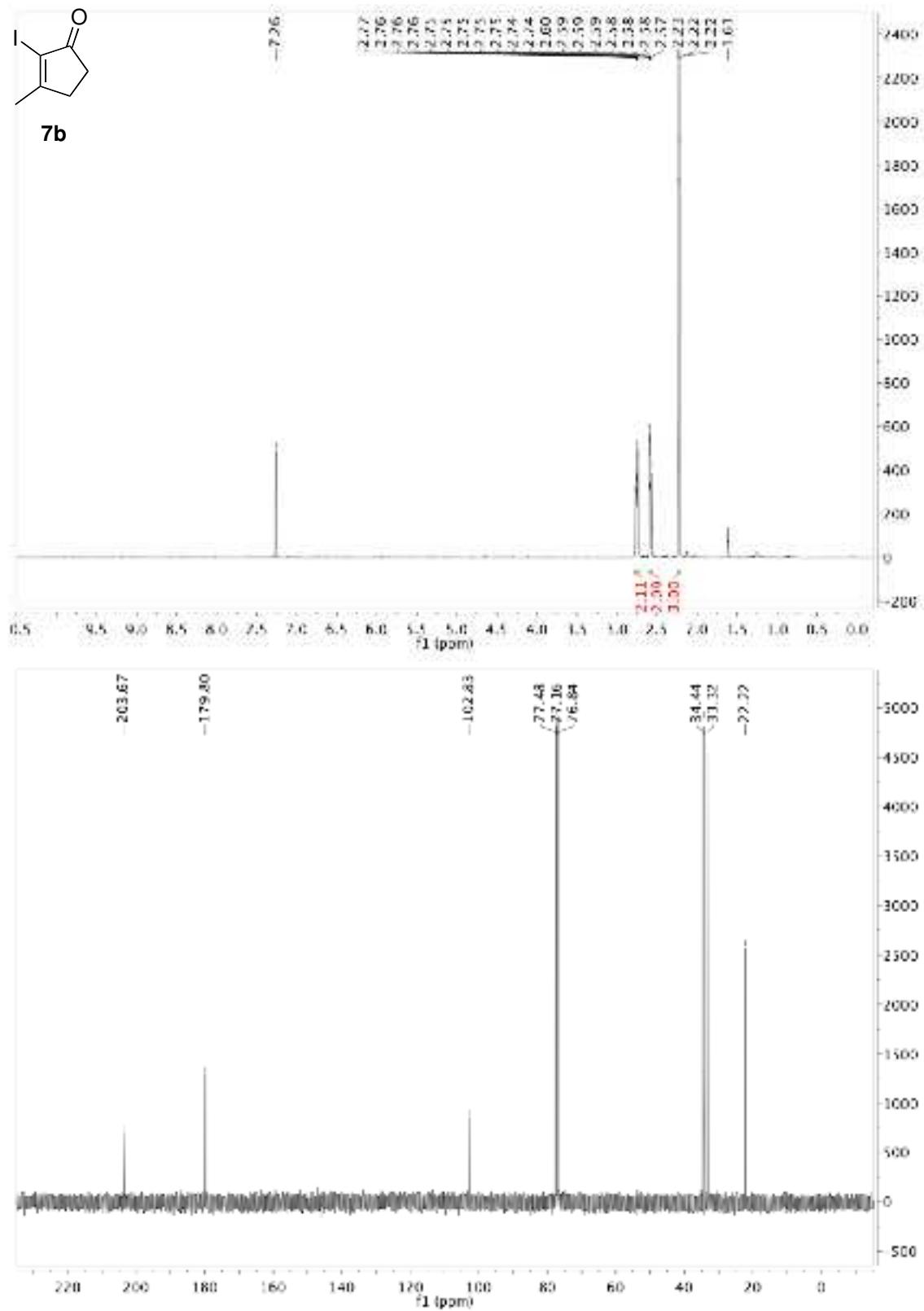


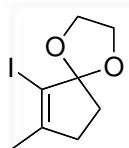






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8b

