

Biological evaluation of natural and synthesized homovanillic acid esters as inhibitors of intestinal fatty acid uptake in differentiated Caco-2 cells

Supplemental information

Synthesis of capsiate

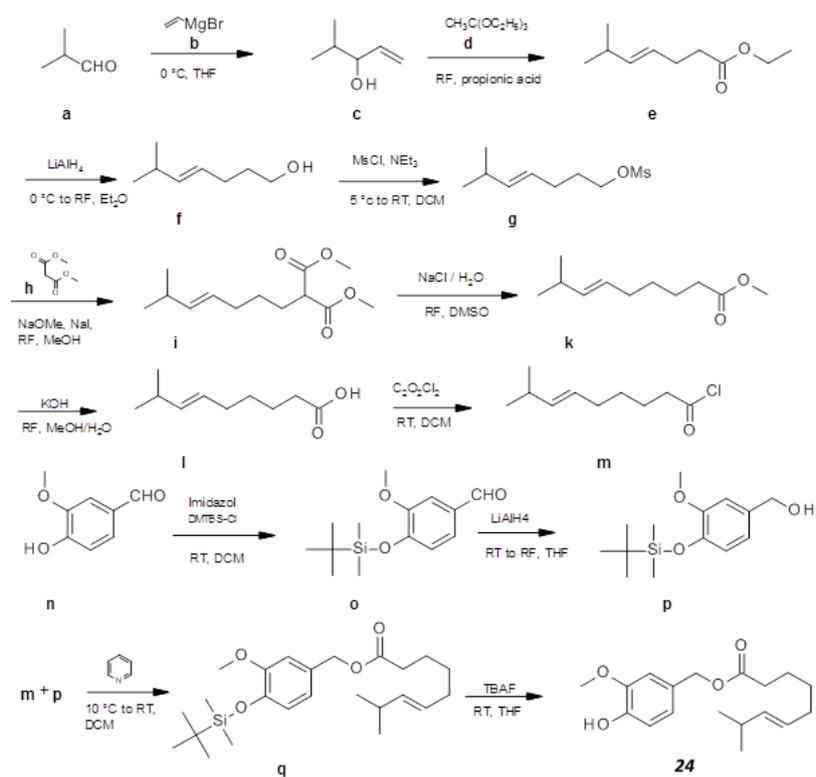
The known substrate Capsiate (**24**) was synthesized according to literature procedures or using common general synthesis methods (scheme **S1**). The used building blocks **m** and **p** were synthesized starting from vanillin (**n**) and isobutyraldehyde (**a**).

Building block **m**: First isobutyraldehyde (**a**) was converted to enol **c** using vinylmagnesium bromide (**b**) in THF. With triethyl orthoacetate **d** in propionic acid the ethyl ester **e** was generated under reflux conditions. This ester **e** was reduced by LiAlH₄ in ether to the corresponding alcohol **f** and mesyl protected to compound **g** [*Tetrahedron* **1996**, *52*, 8451–8470].

Condensation of dimethyl malonate **h** with mesylate **g** in methanol followed by NaCl treatment in DMSO afforded methyl ester **k** which in turn was saponified using potassium hydroxide in MeOH/water (1:1). Acid **l** was converted into its acid chloride **m** by oxalyl chloride in dichloromethane.

Building block **p**: Vanillin (**n**) was TBDMS protected using TBDMS chloride in dichloromethane and the resulting compound **o** was afterwards reduced to the alcohol **p** with LiAlH₄ in THF.

Finally, esterification of acid chloride **m** with alcohol **p** in pyridine followed by TBDMS (*tert*-butyl dimethylsilyl) deprotection using TBAF (tetra-*n*-butylammonium fluoride) in THF afforded the capsiate (**24**).



Scheme S1.

[1] *Tetrahedron* **1996**, *52*, 8451–8470.

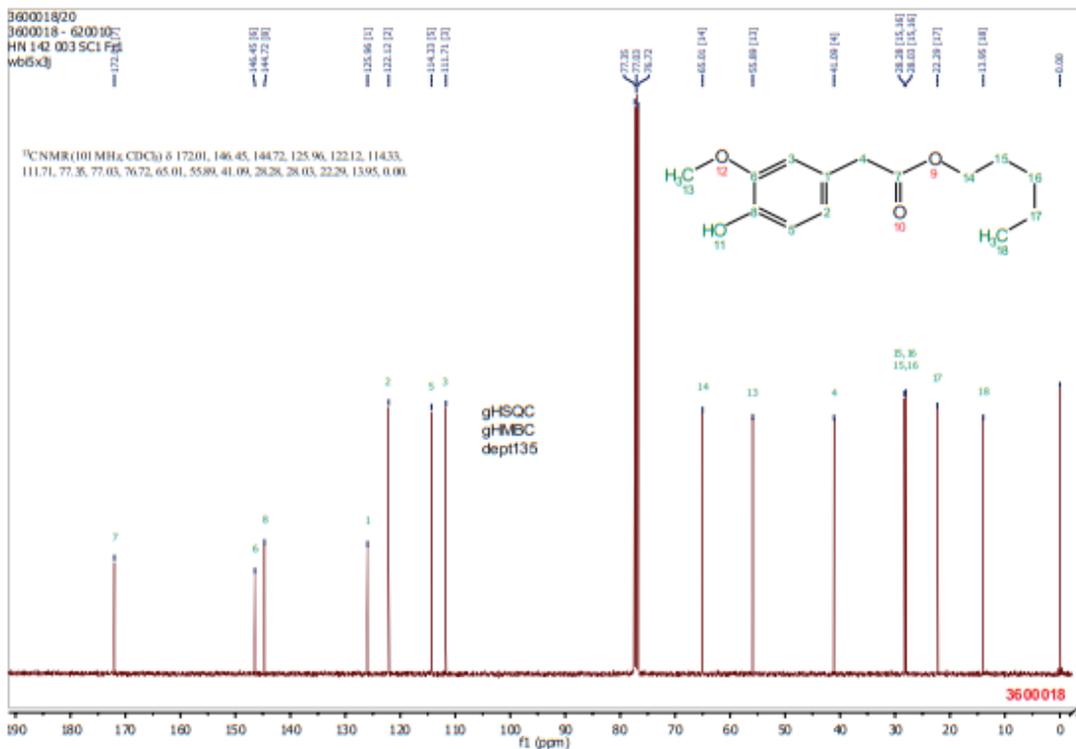
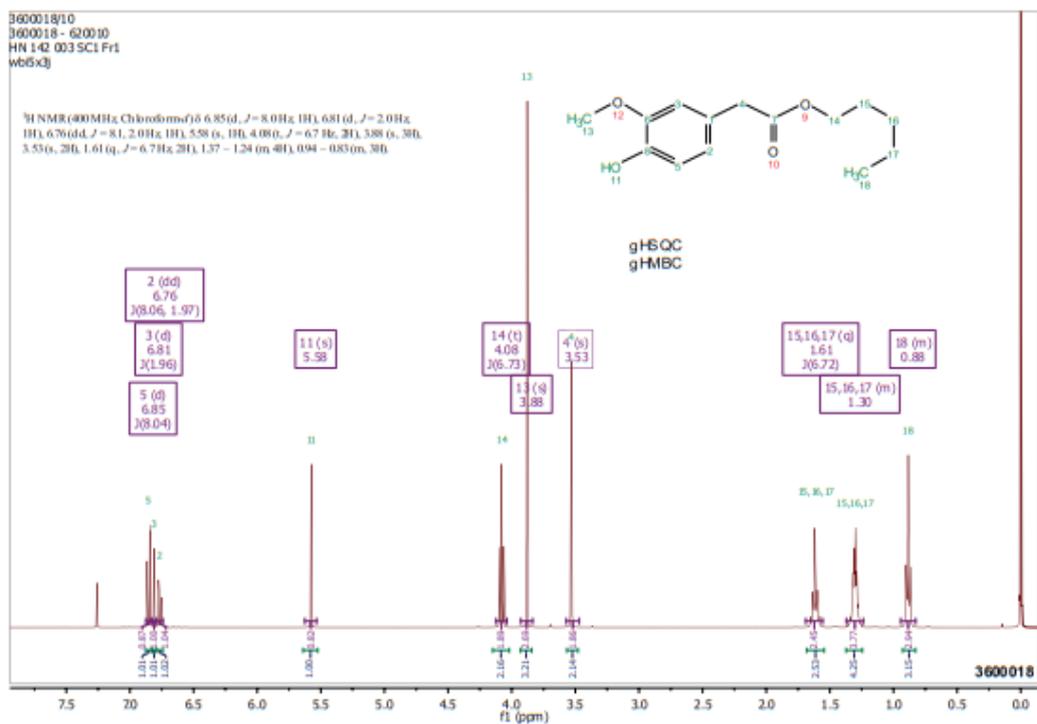


Figure S1: ¹H NMR and ¹³C NMR Compound 5

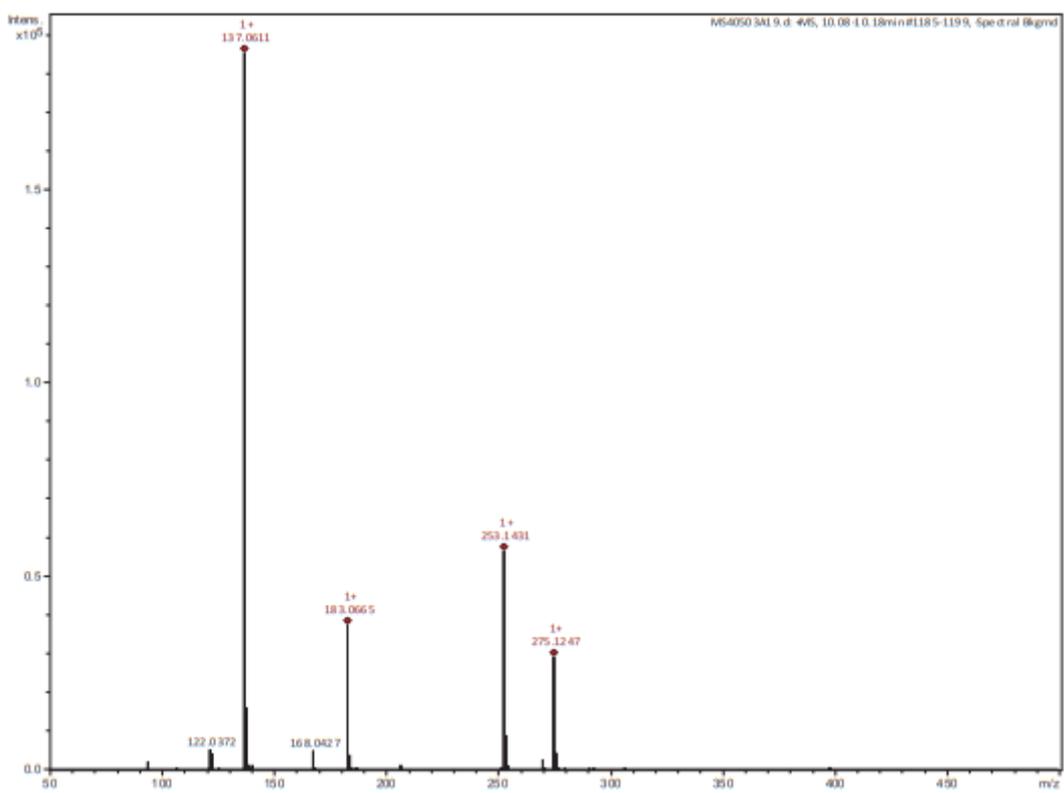


Figure S2: HR-ESIMS Compound 5

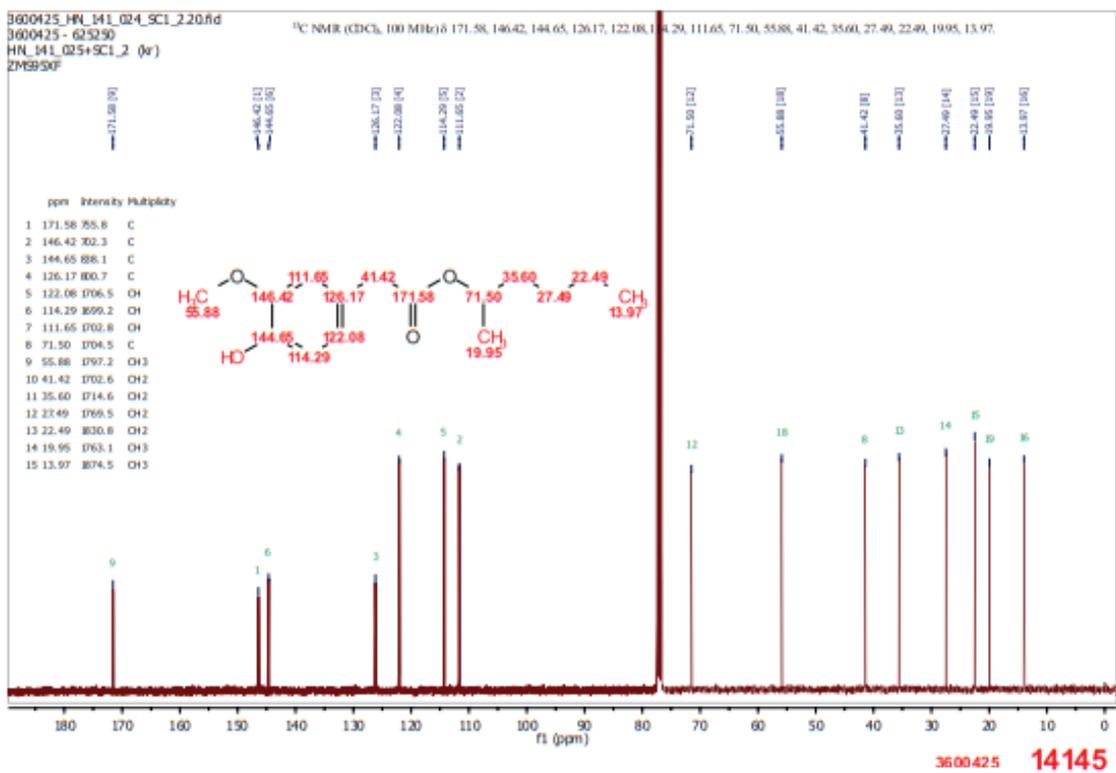


Figure S3: ¹H NMR and ¹³C NMR Compound 12

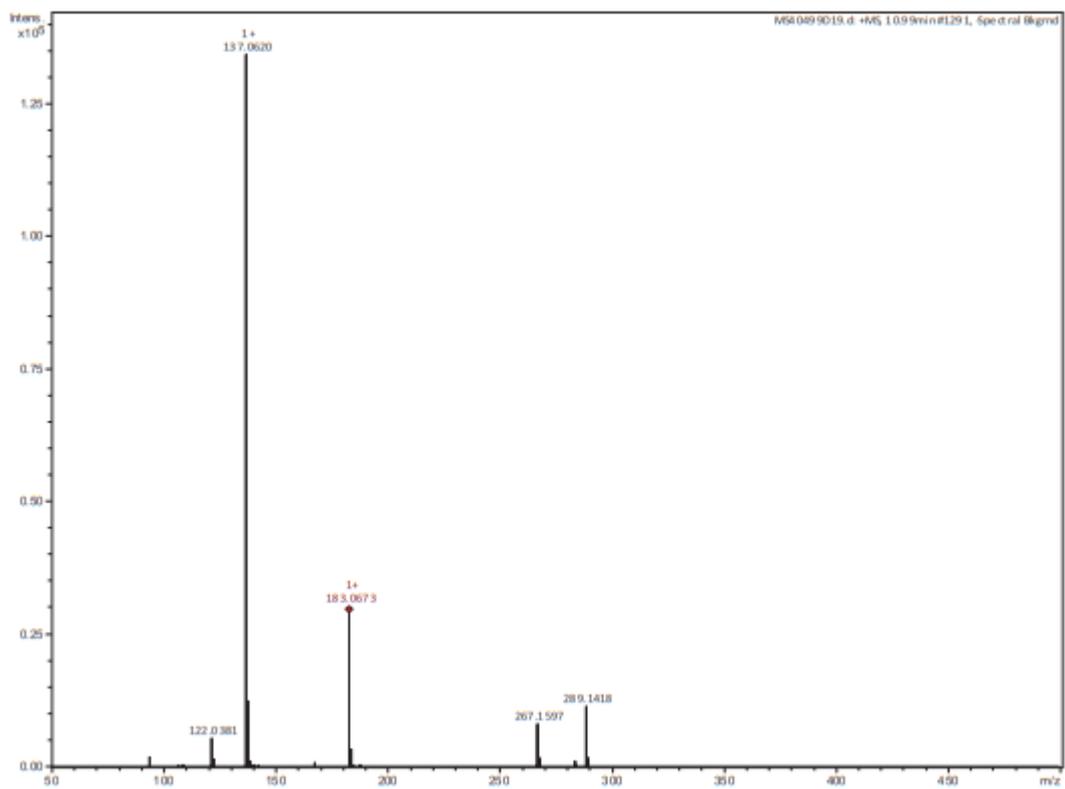


Figure S4: HR-ESIMS Compound 12

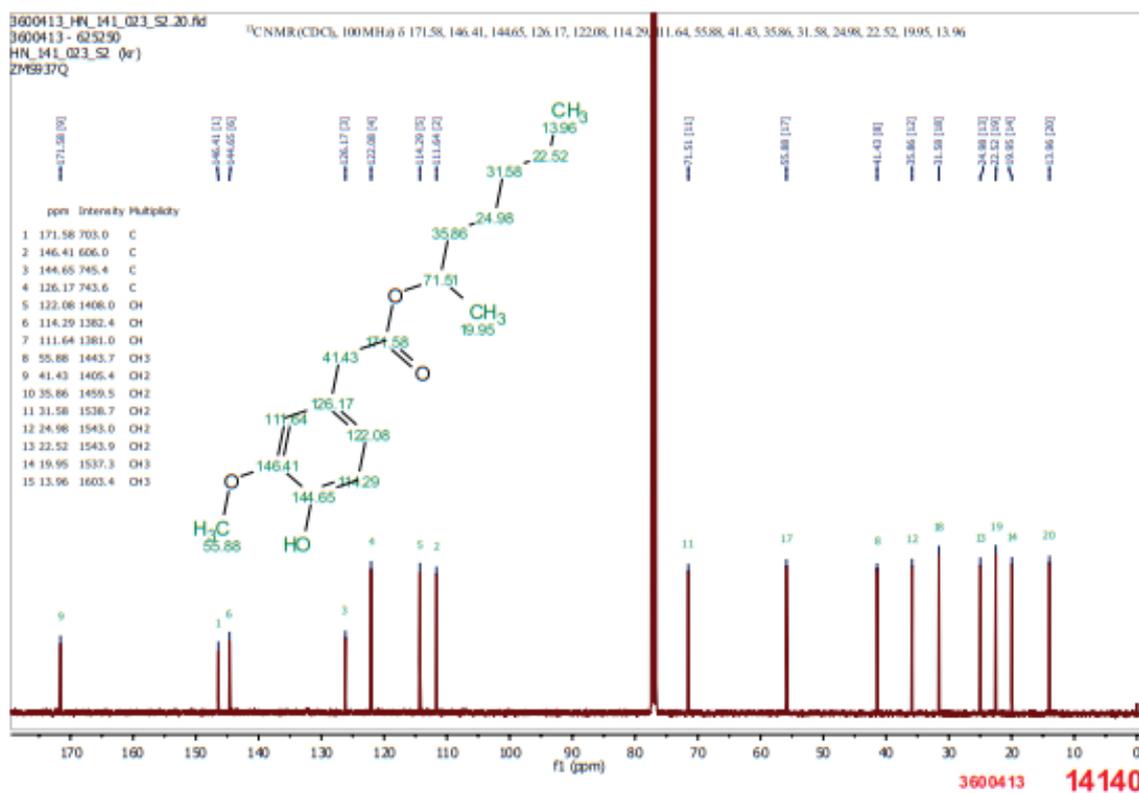
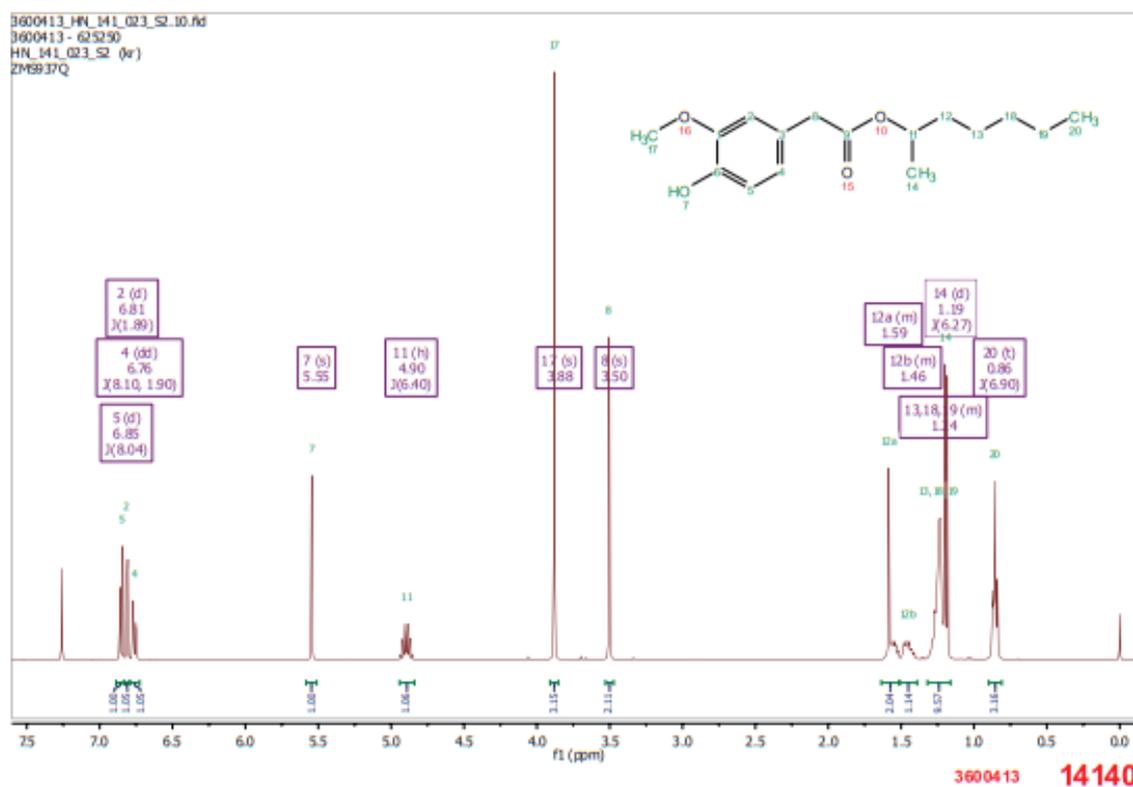


Figure S5: ¹H NMR and ¹³C NMR Compound 13

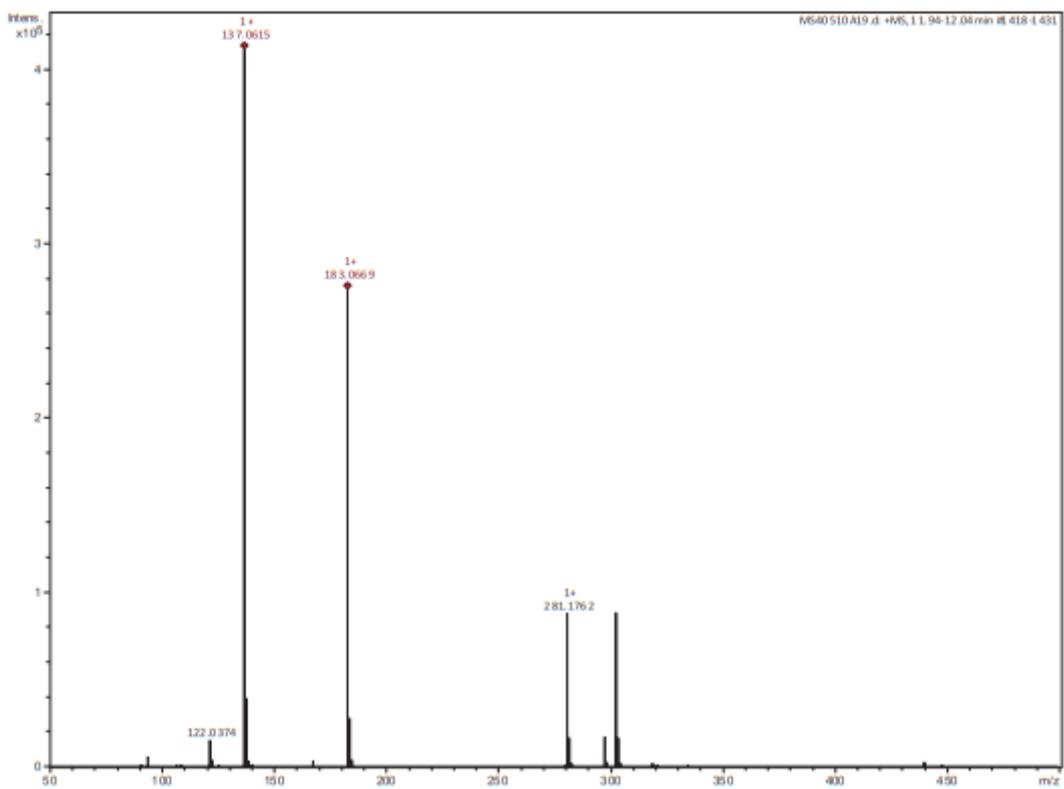


Figure S6: HR-ESIMS Compound 13

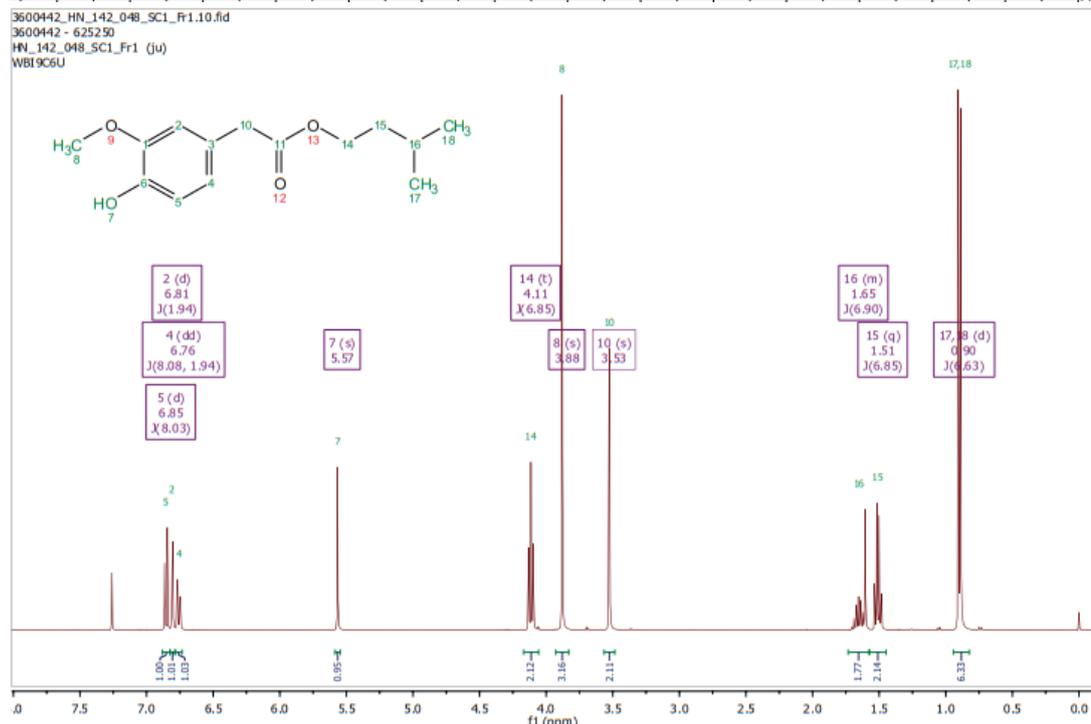
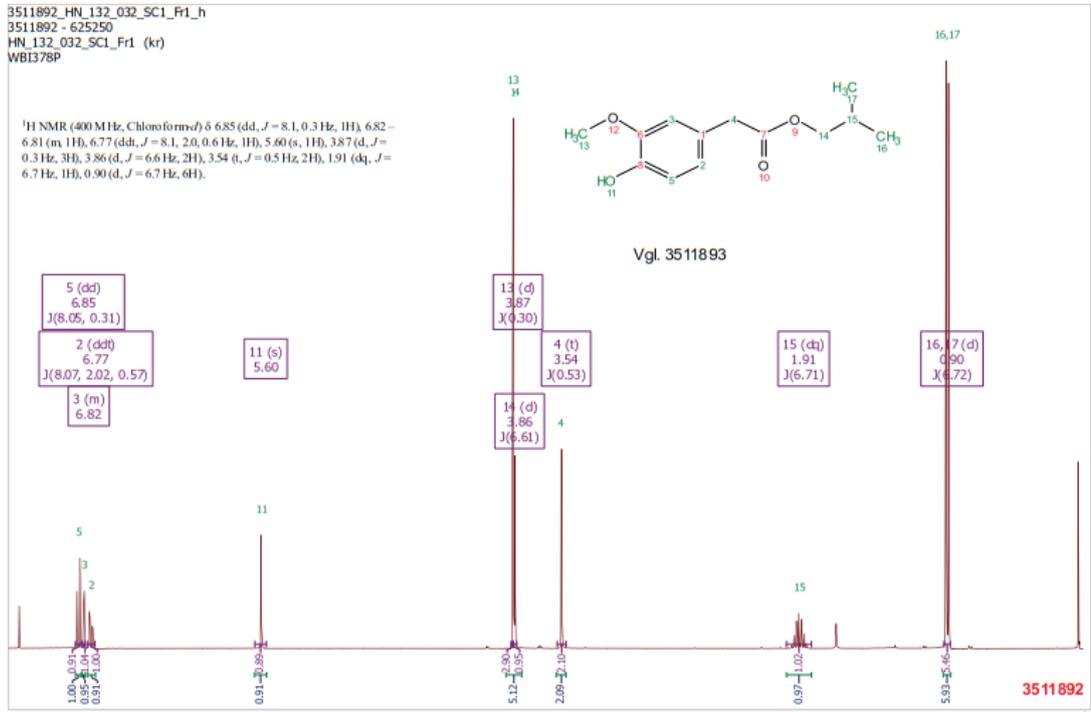


Figure S7: ¹H NMR and ¹³C NMR Compound 14

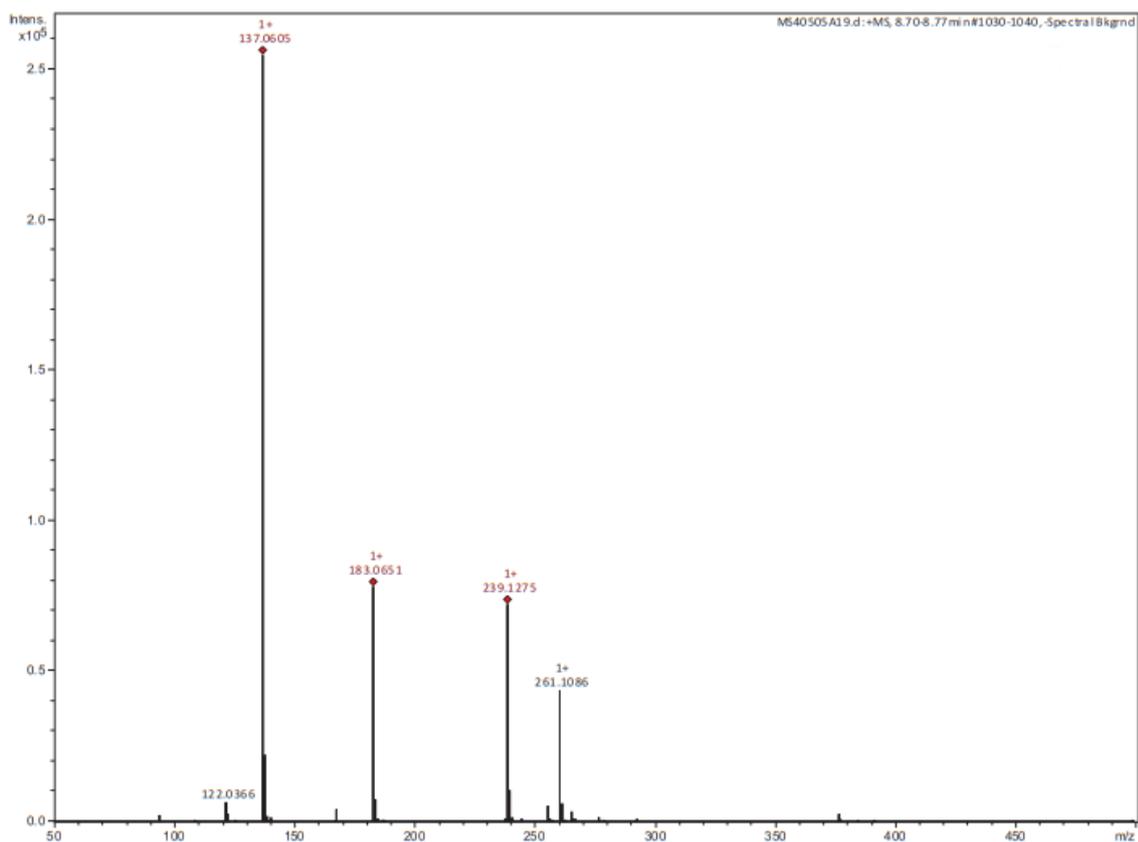


Figure S8: HR-ESIMS Compound 14

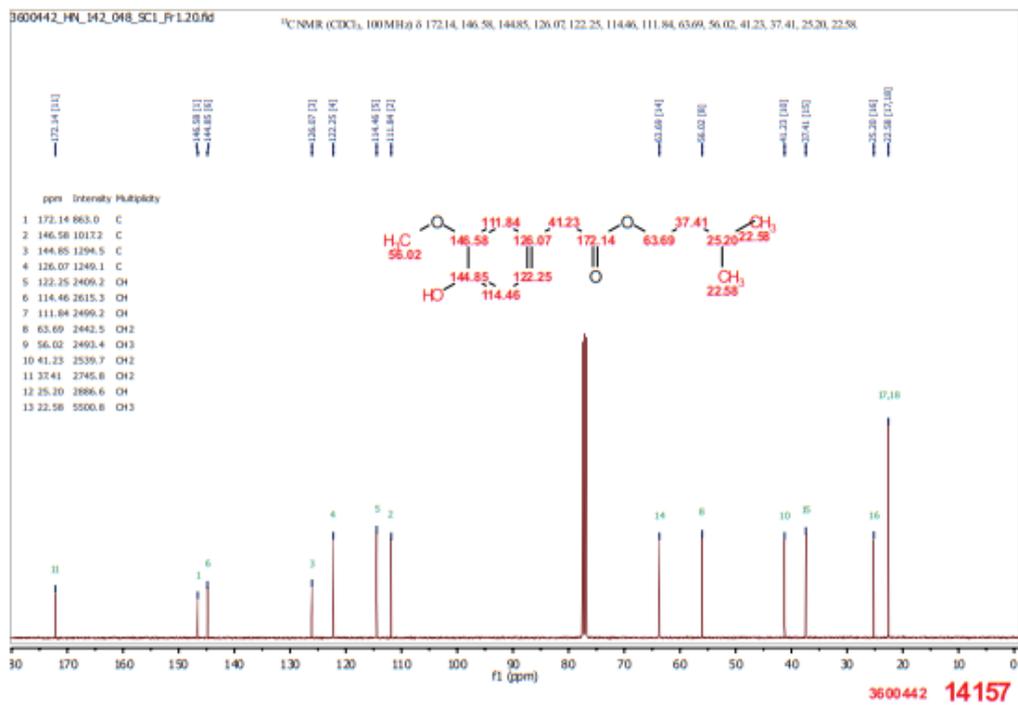
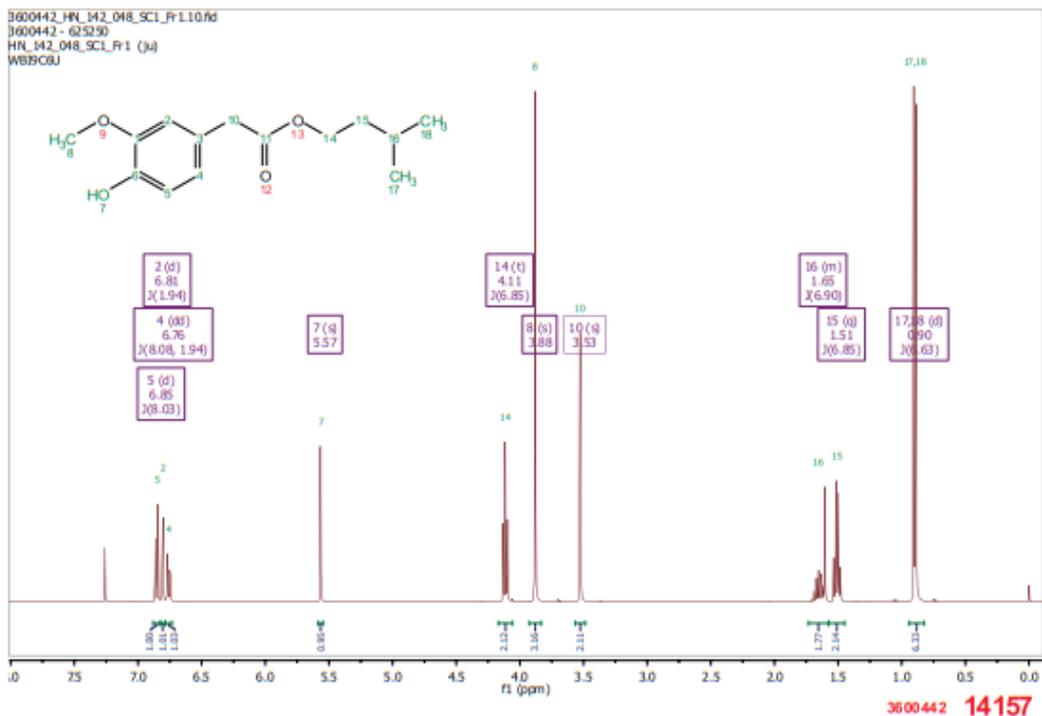


Figure S9: ¹H NMR and ¹³C NMR Compound 15

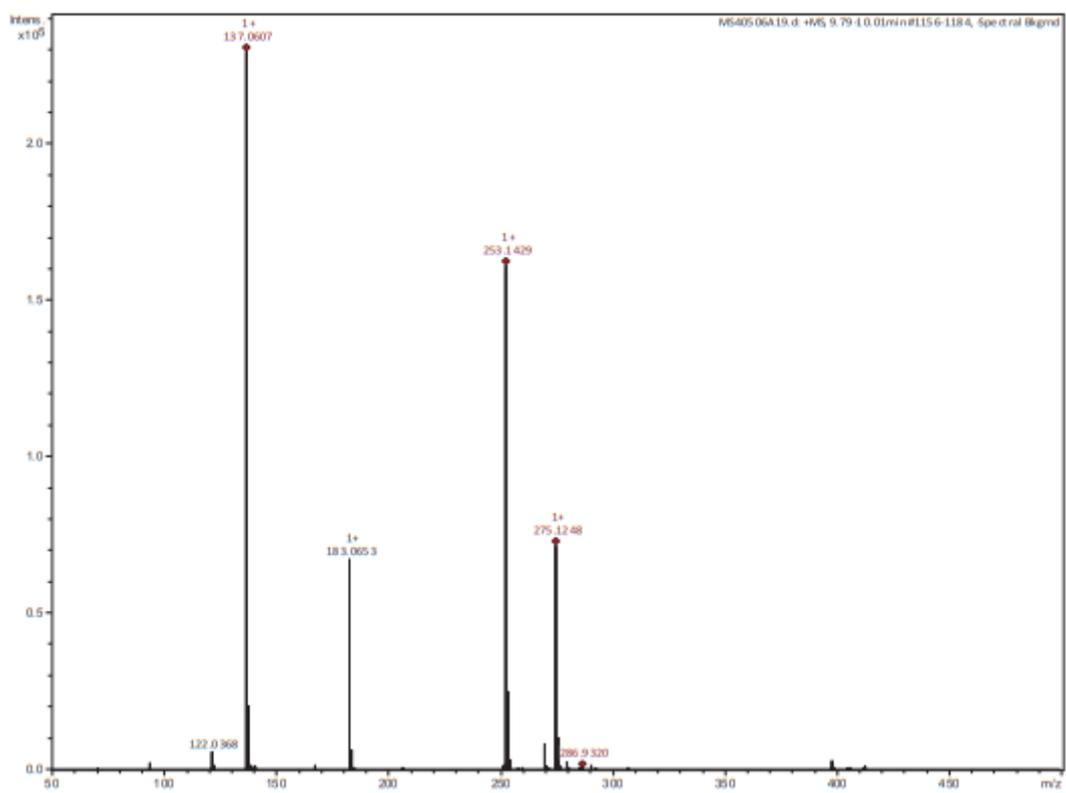


Figure S10: HR-ESIMS Compound 15

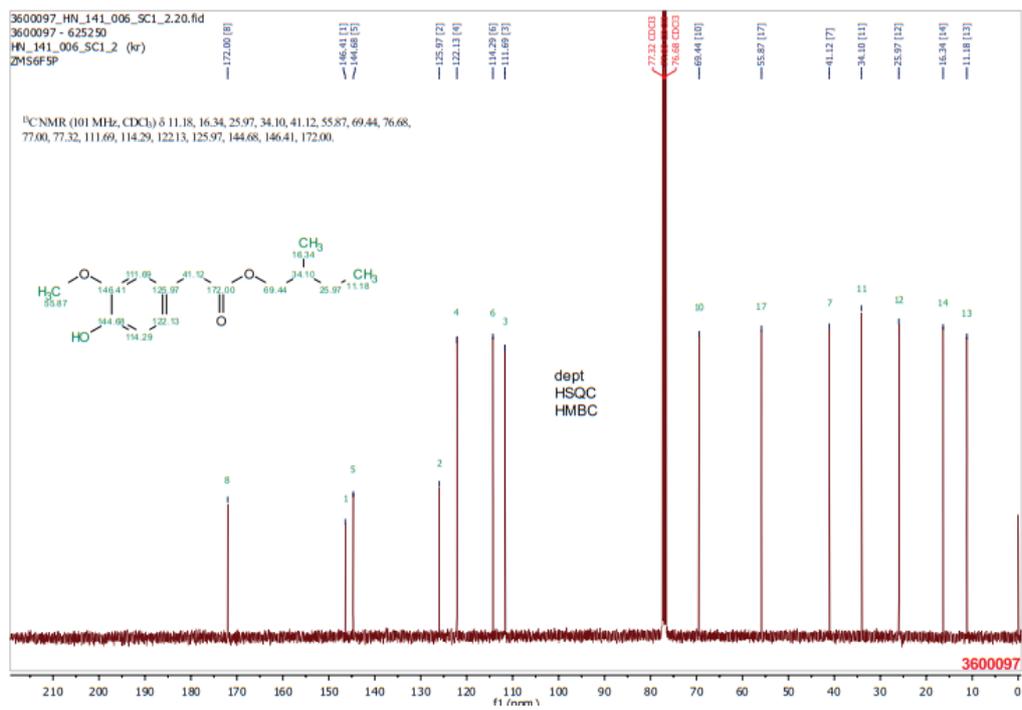
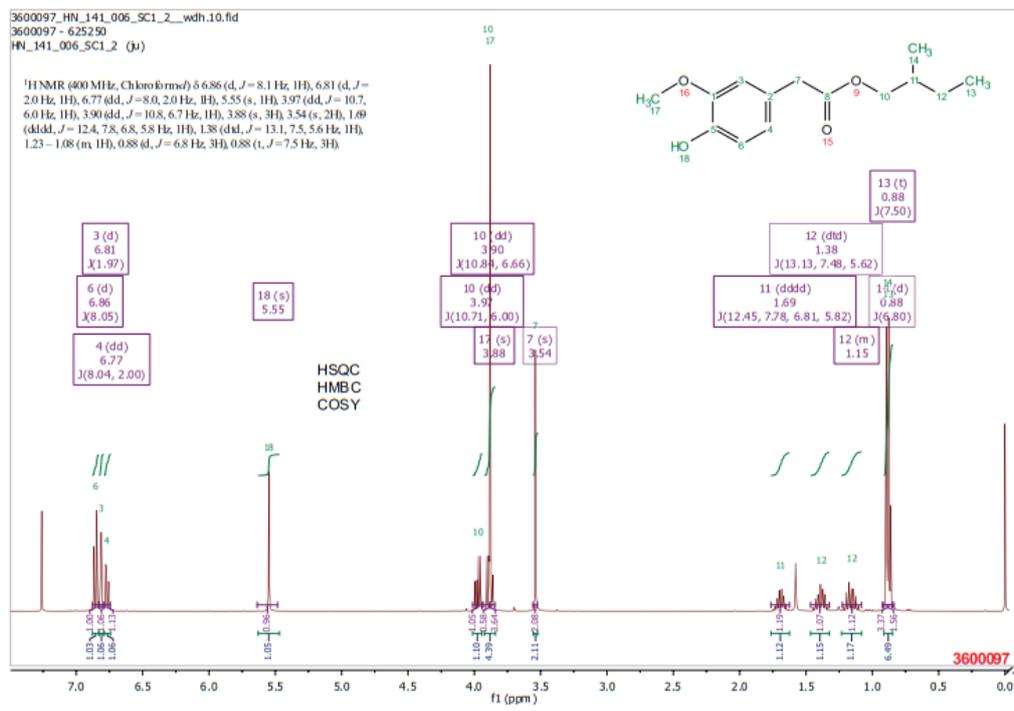


Figure S11: ¹H NMR and ¹³C NMR Compound 16

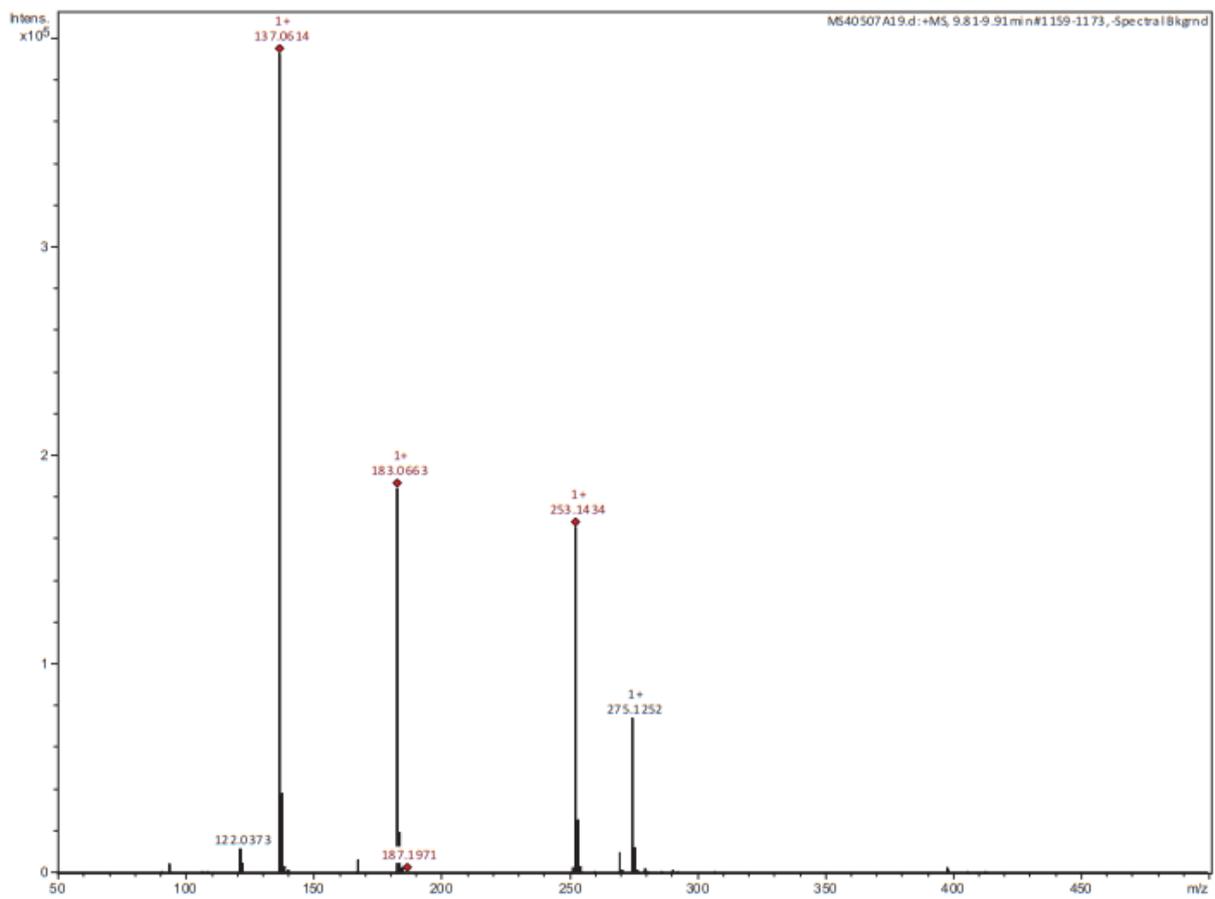


Figure S12: HR-ESIMS Compound 16

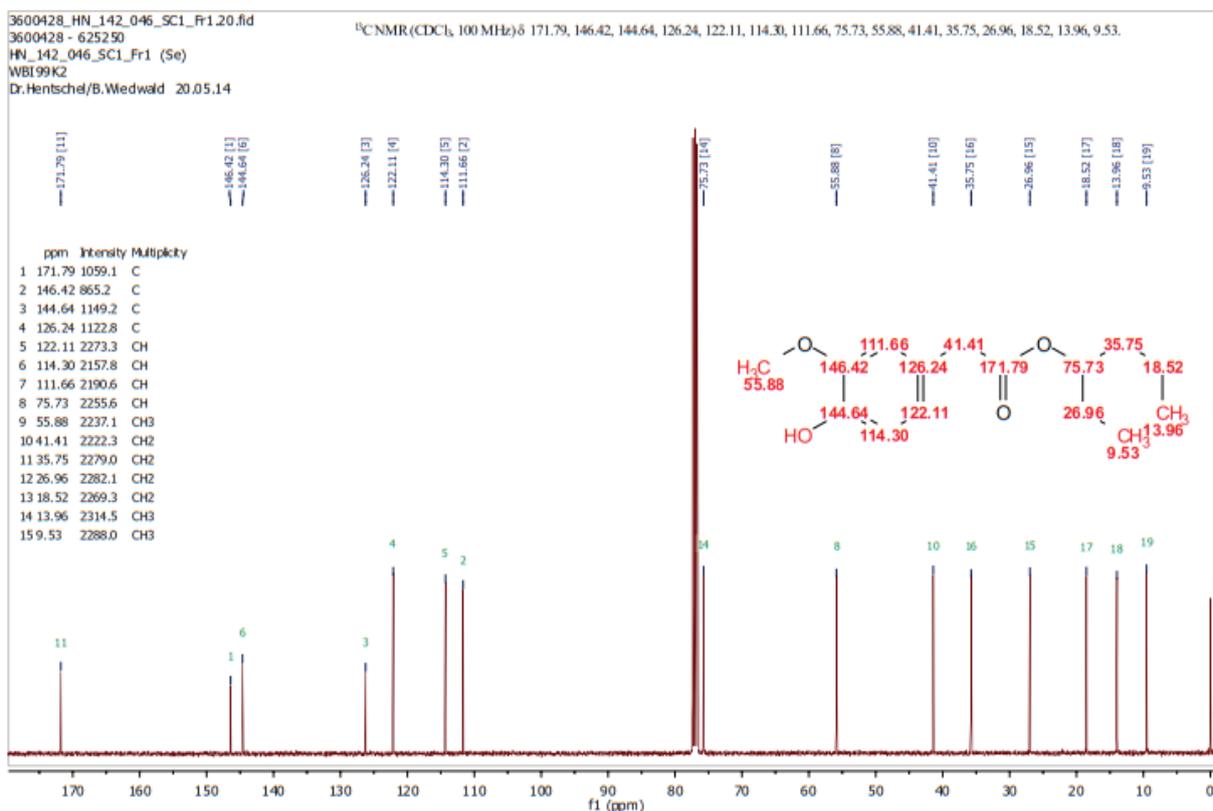
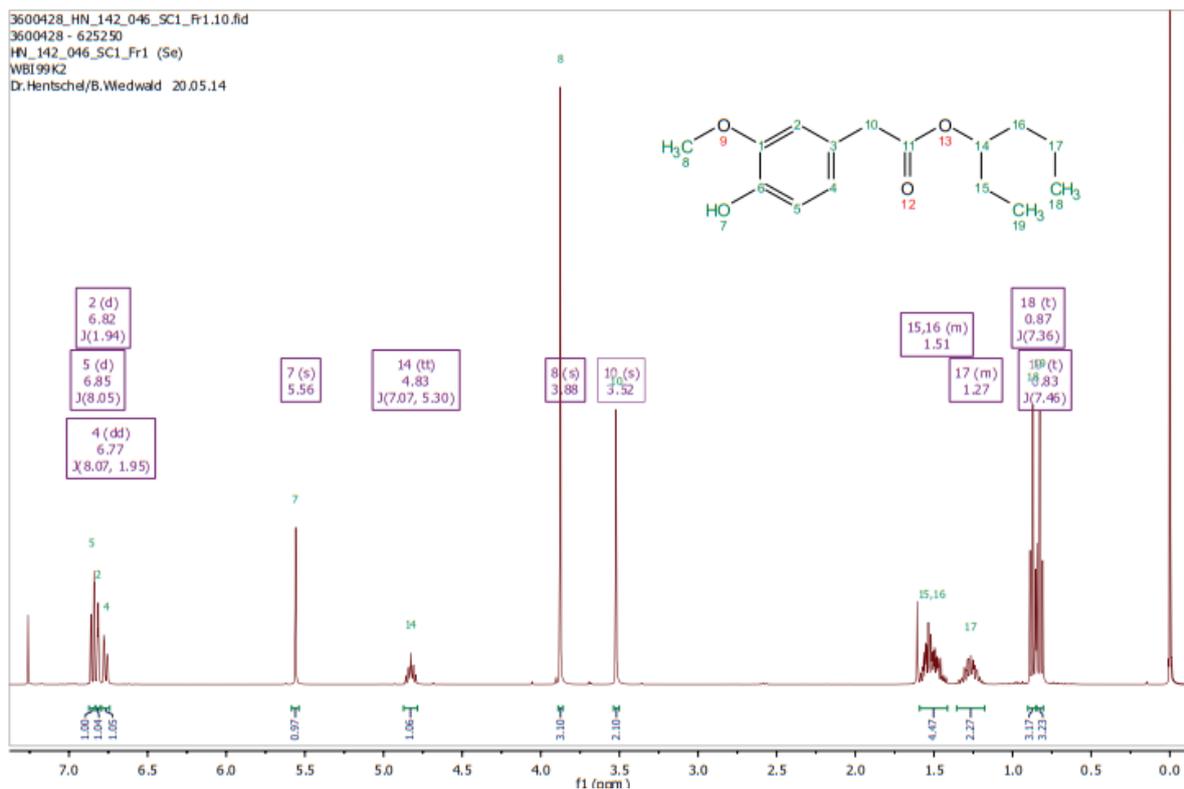


Figure S13: ¹H NMR and ¹³C NMR Compound 17

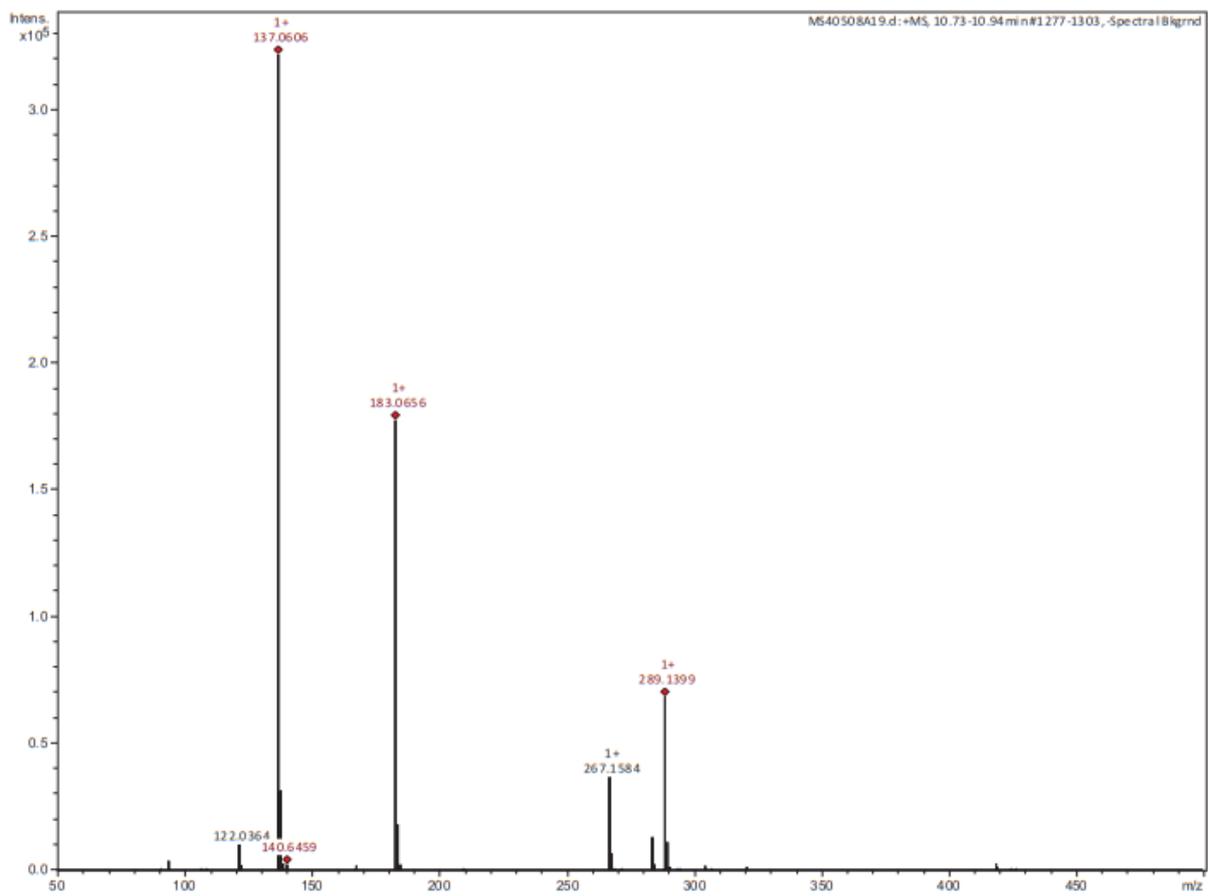


Figure S14: HR-ESIMS Compound 17

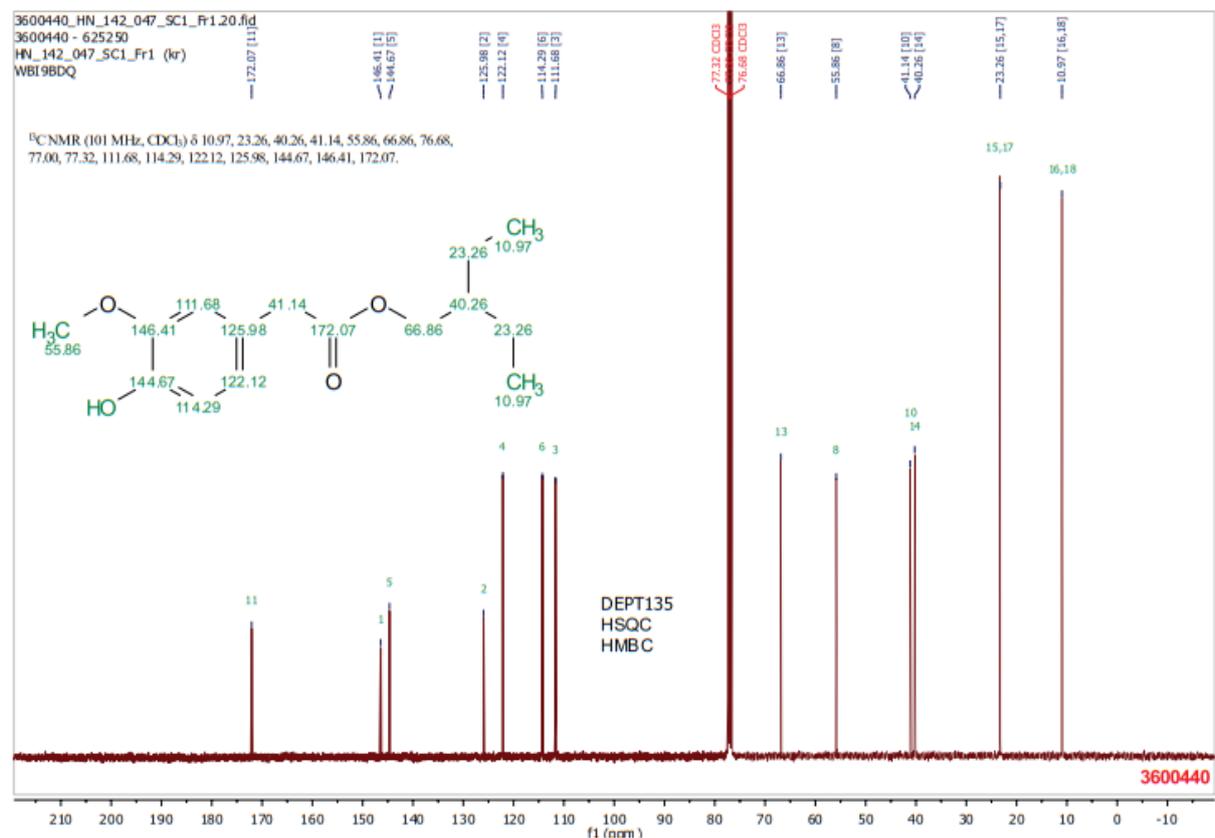
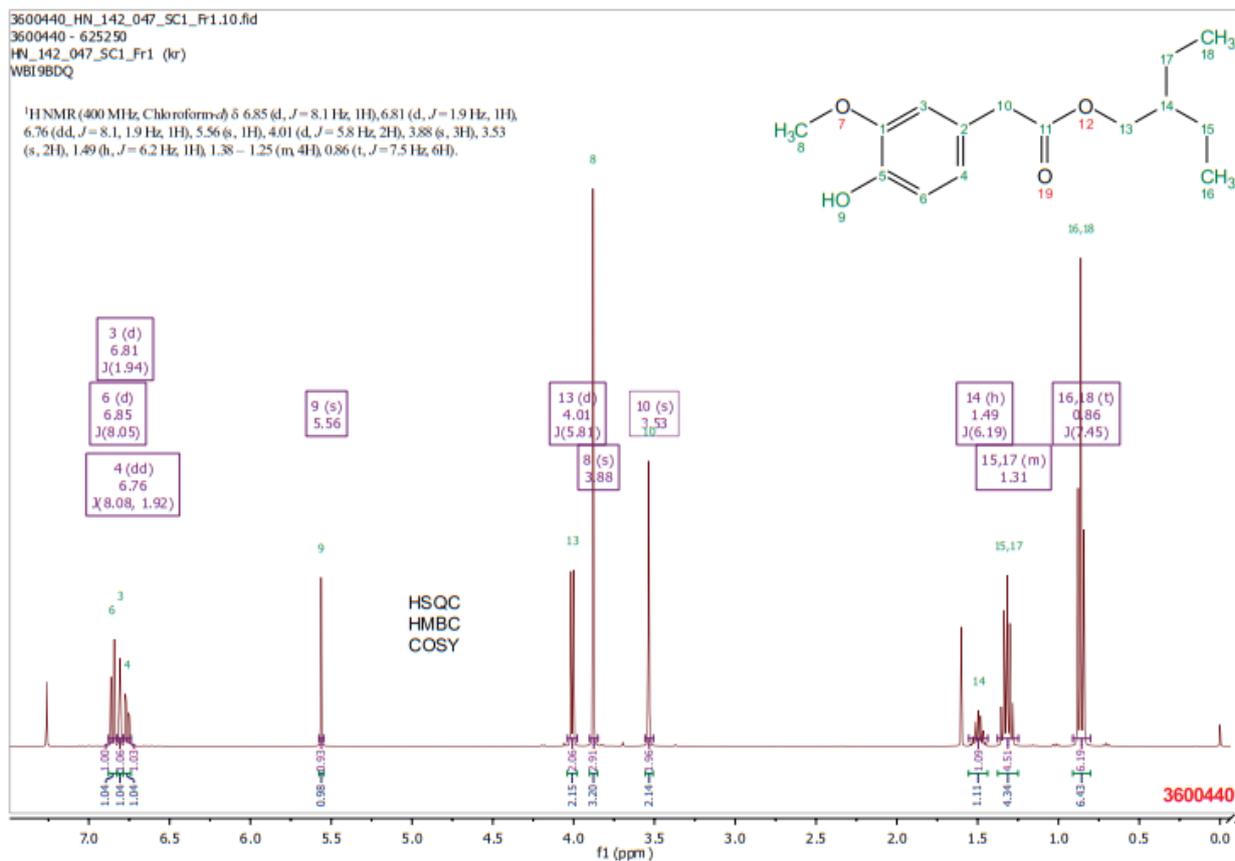


Figure S15: ¹H NMR and ¹³C NMR Compound 18

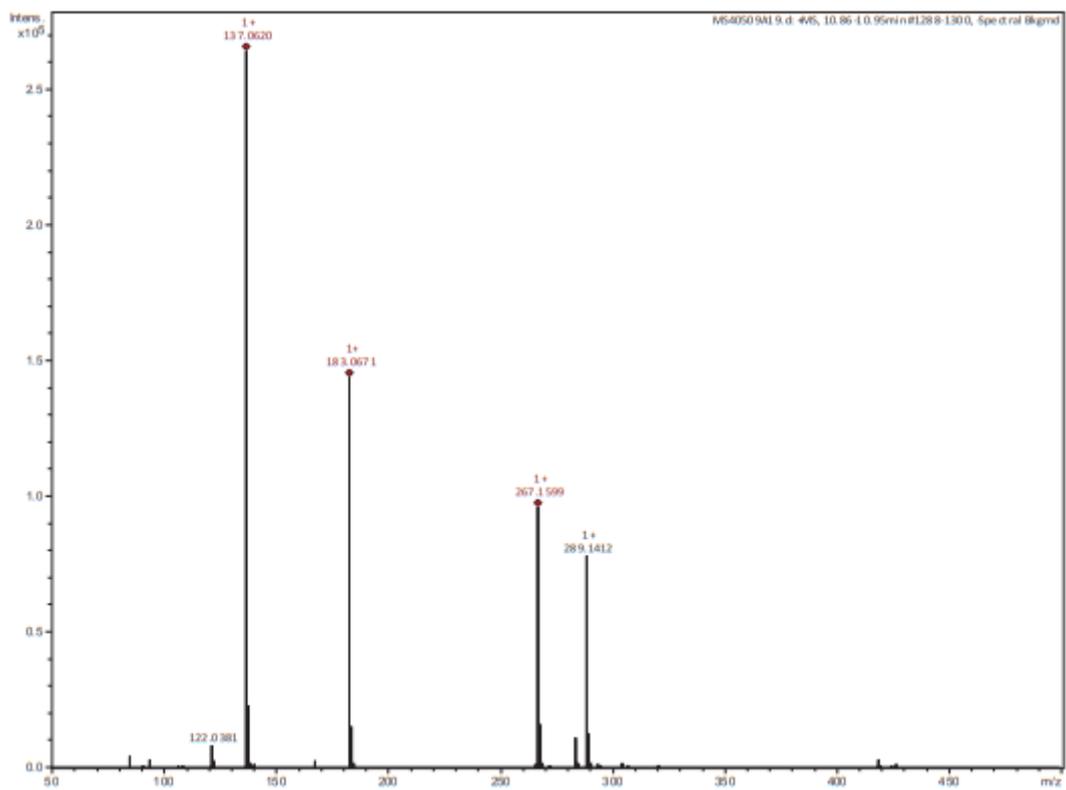


Figure S16: HR-ESIMS Compound 18

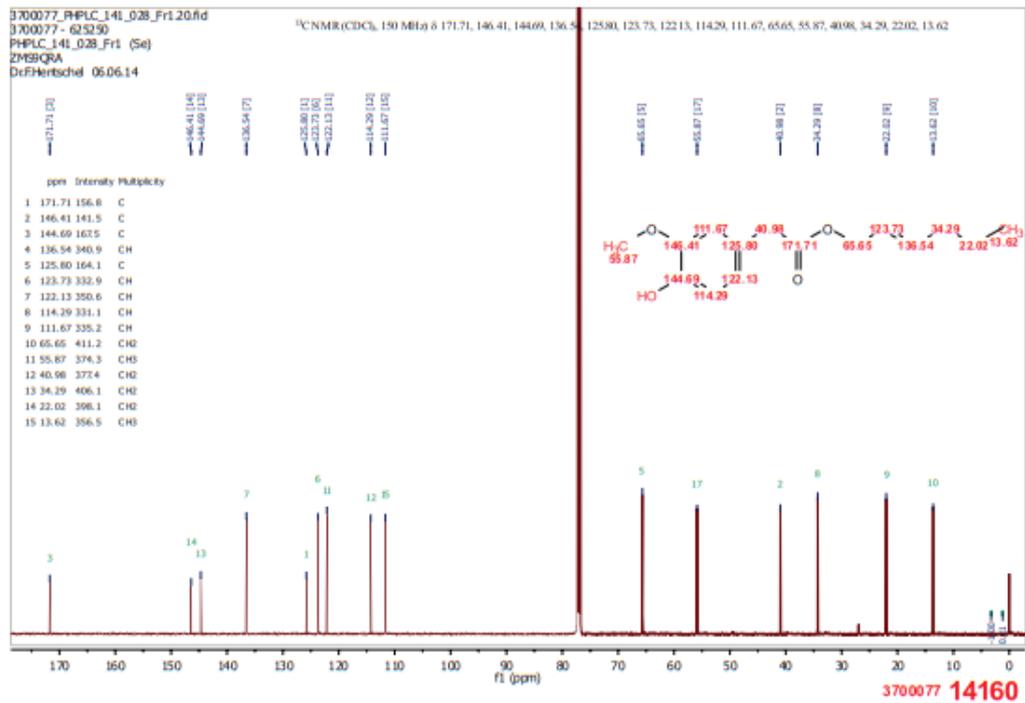
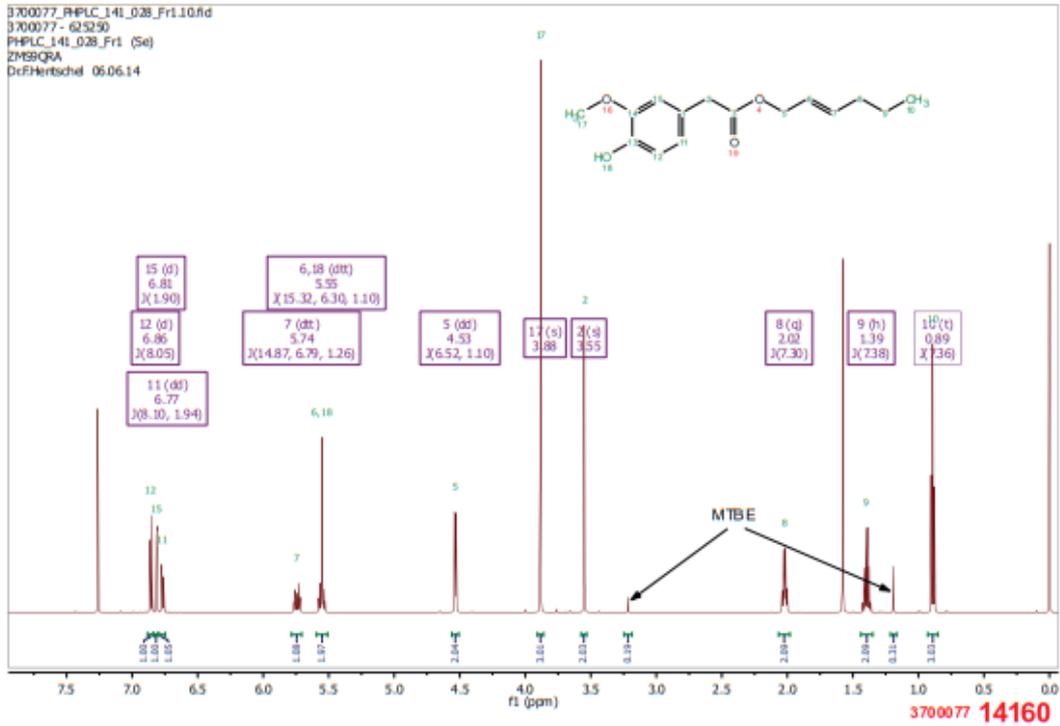


Figure S17: ¹H NMR and ¹³C NMR Compound 19

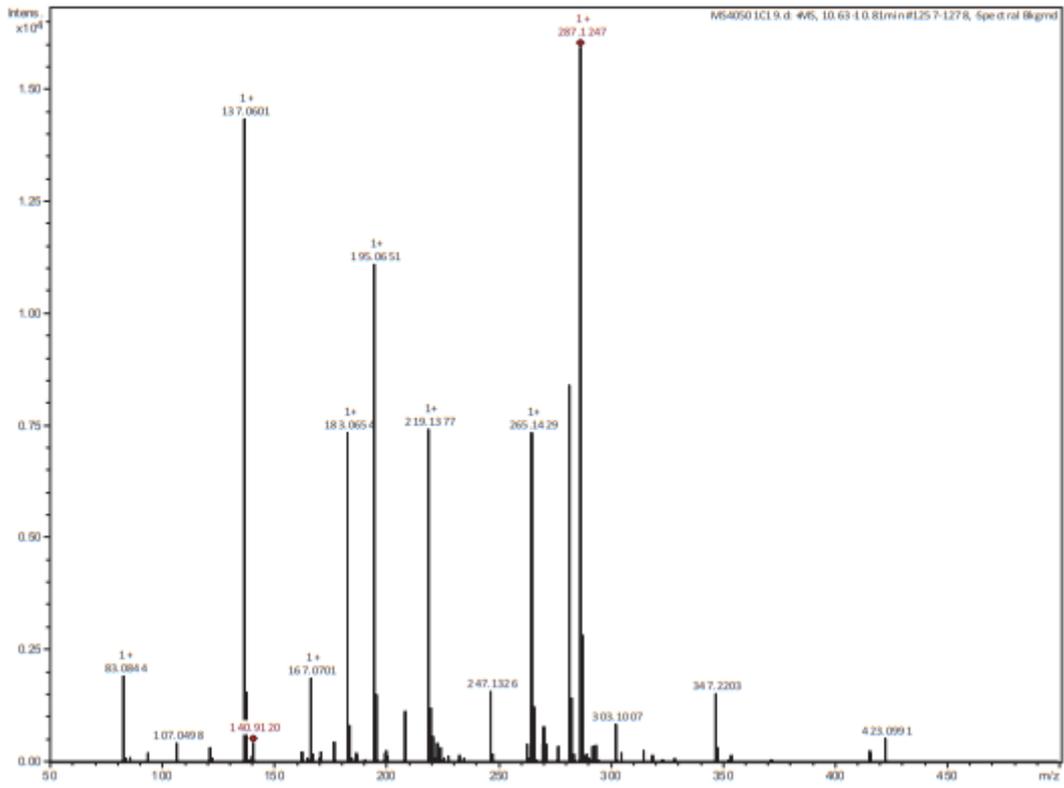


Figure S18: HR-ESIMS Compound 19

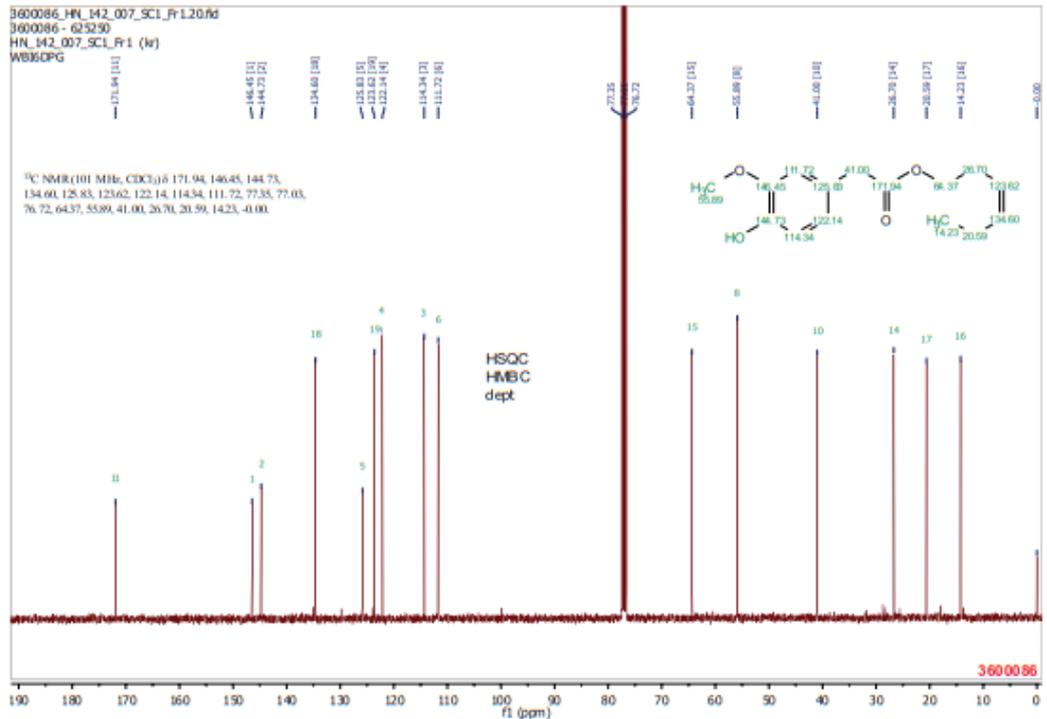
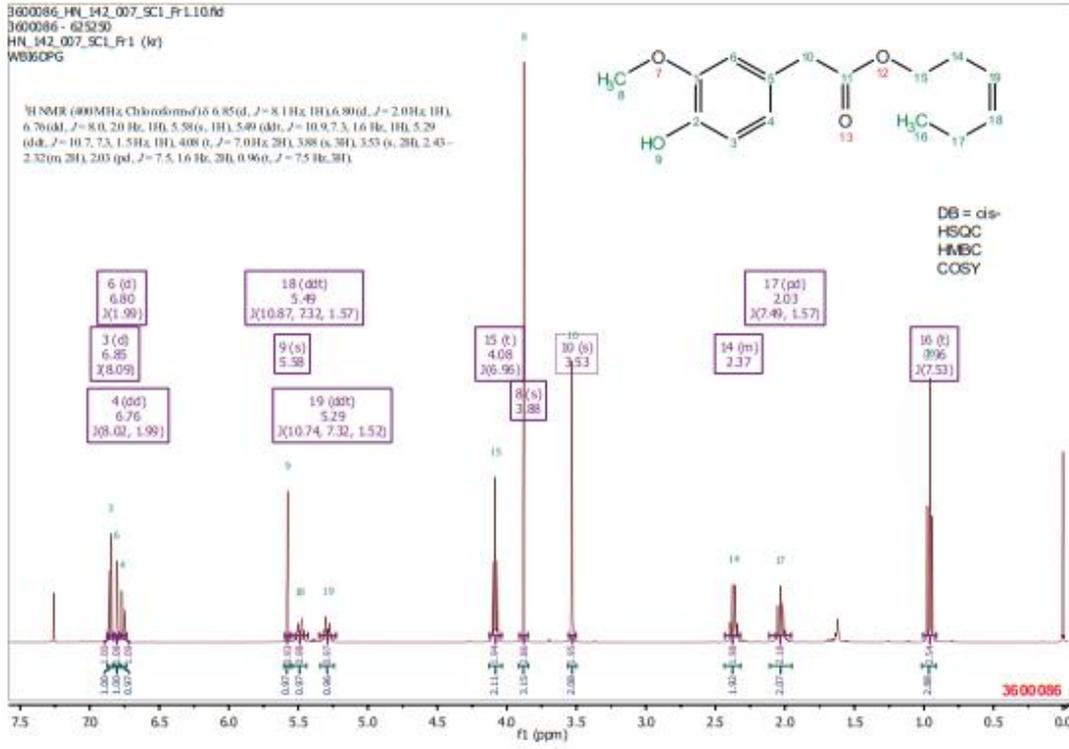


Figure S19: ¹H NMR and ¹³C NMR Compound 20

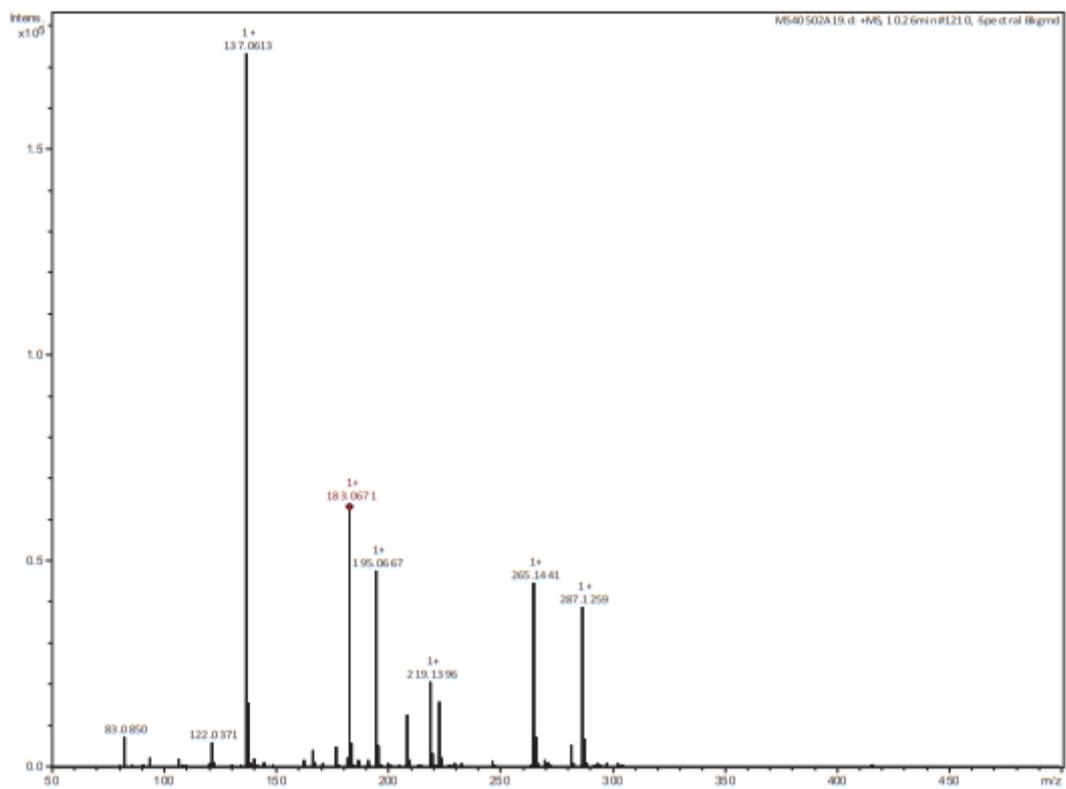


Figure S20: HR-ESIMS Compound 20

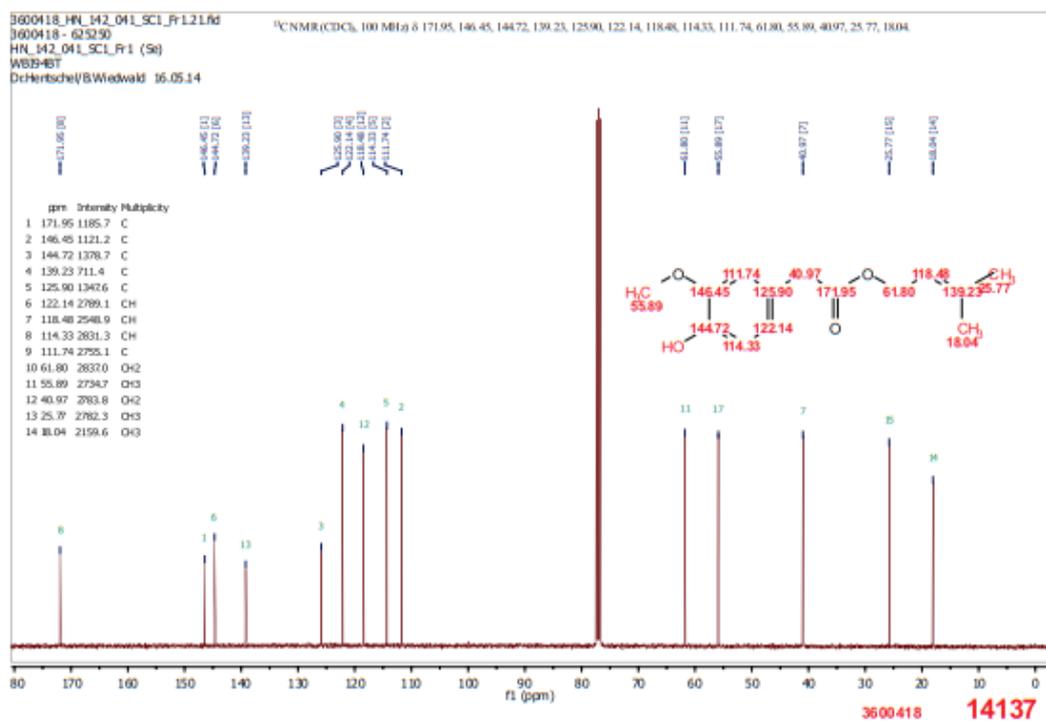
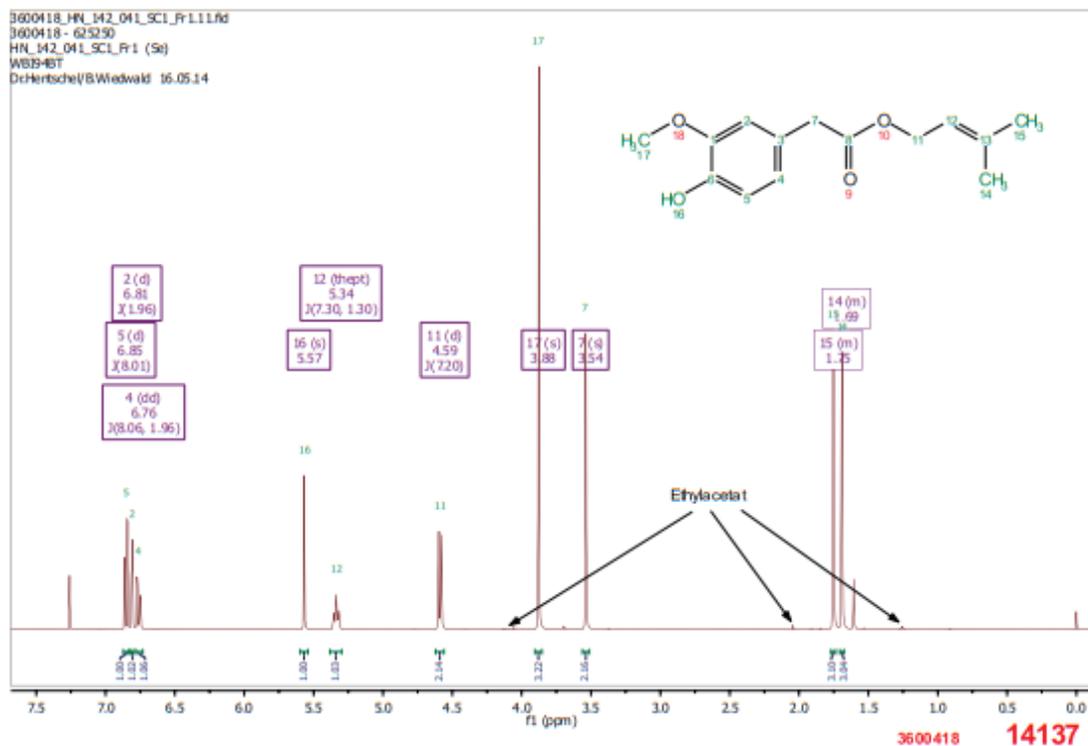


Figure S21: ¹H NMR and ¹³C NMR Compound 21

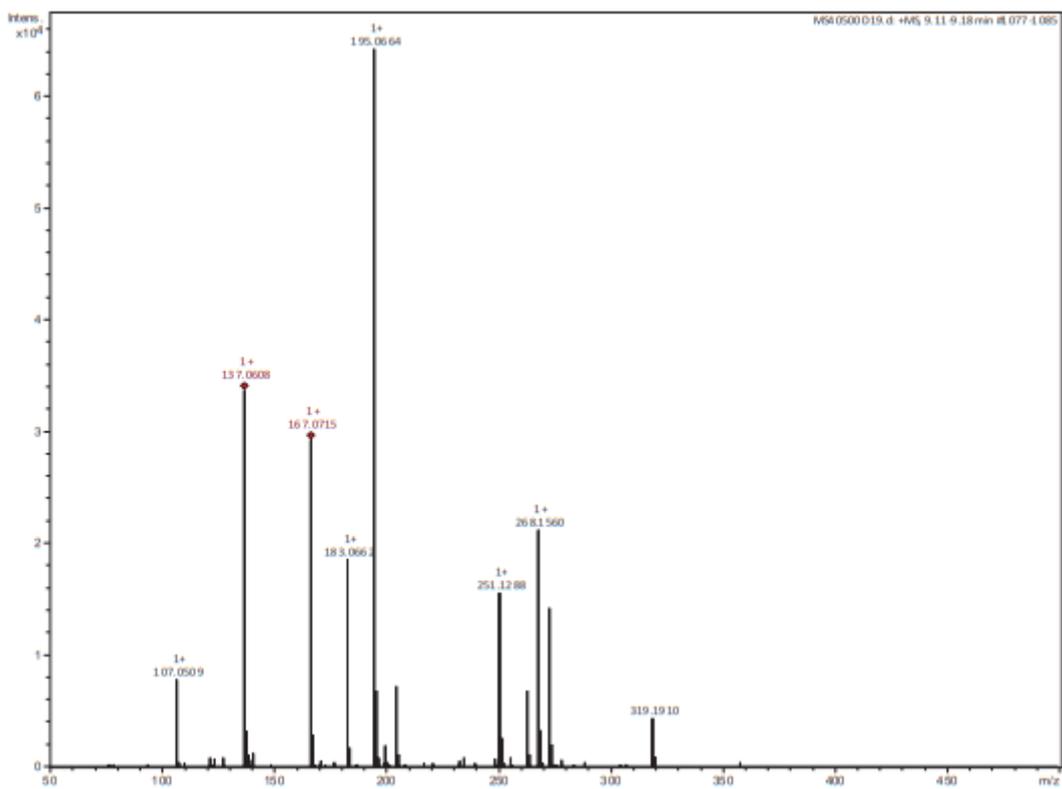


Figure S22: HR-ESIMS Compound 21

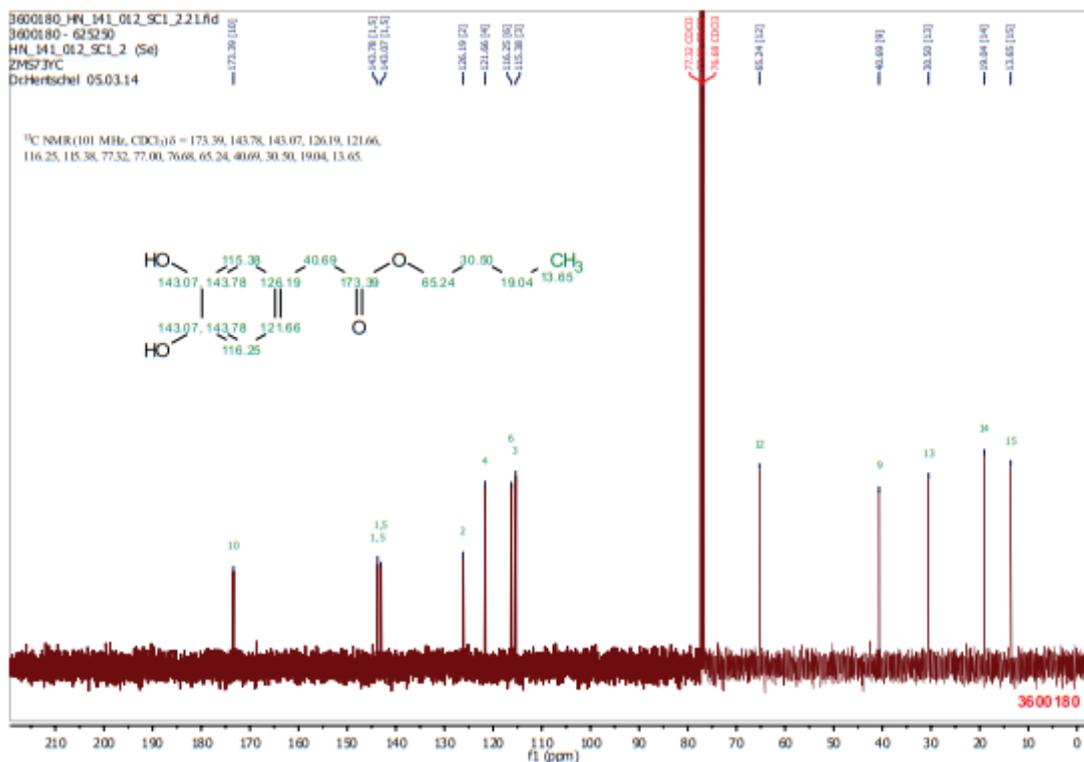
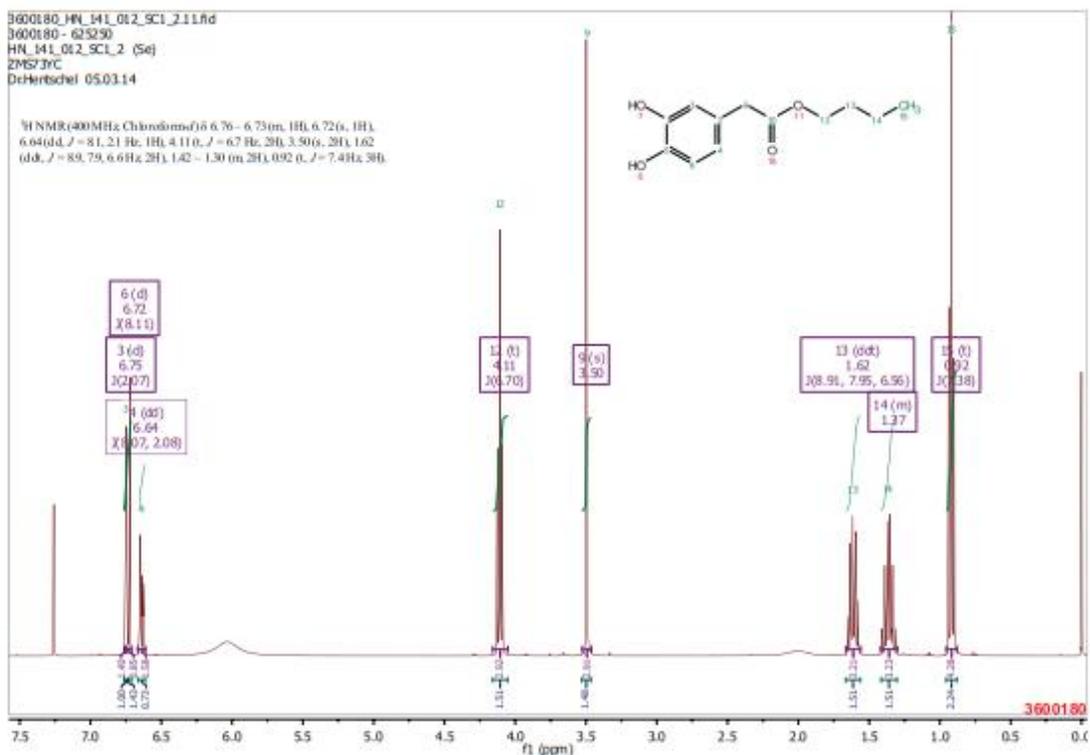


Figure S23: ¹H NMR and ¹³C NMR Compound 23

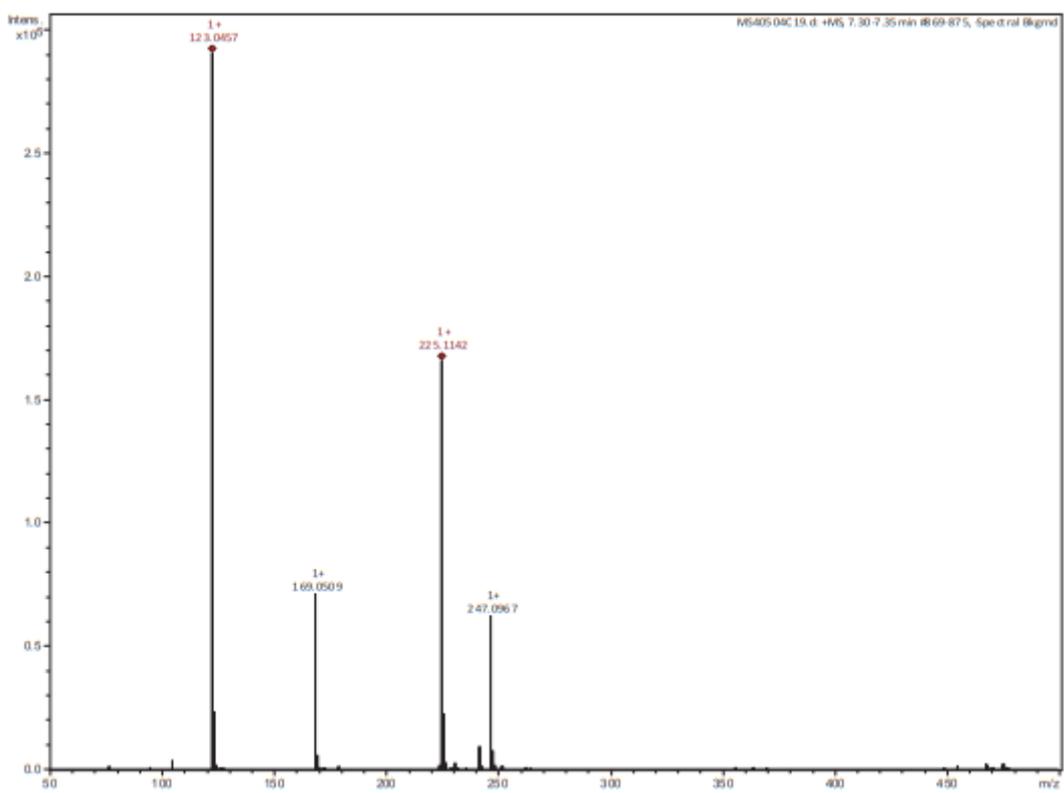


Figure S24: HR-ESIMS Compound 23