Supporting information for

A Practical Synthesis of the PDE4 inhibitor, KW-4490

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1. General information

^{1}H NMR spectra were obtained on a JEOL JNM-LA300 spectrometer (300 MHz) or Bruker AVANCE 500 spectrometer (500 MHz). Proton-decoupled ^{13}C NMR spectra were obtained on a JEOL JNM-LA300 spectrometer (75 MHz) or Bruker AVANCE 500 spectrometer (125 MHz).

2. HPLC and GC methods

HPLC analysis were performed on a Hitachi L-4000 system.

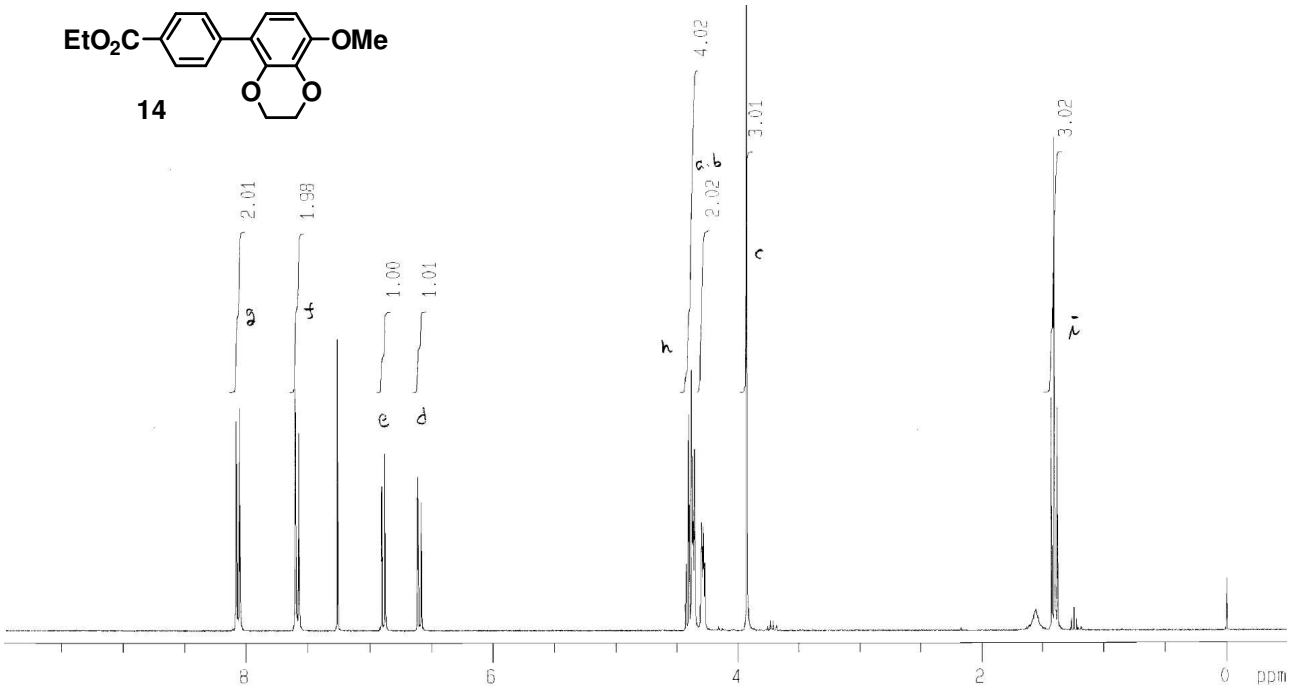
Column: YMC-Pack, C8, 150×60 mm; λ = 230 nm; temperature: 35°C; eluant: phosphate buffer* : methanol = 38 : 62 (*0.01 mol of K_2HPO_4 and 0.01 mol of KH_2PO_4 were dissolved in 1L of water, then pH was adjusted to 3 by H_3PO_4); flow rate: 1mL/min. t_R**: 11** = 4.2 min; **15** = 4.8 min; **1** (KW-4490) = 5.0 min; **16** = 5.6 min; **3** = 8.7 min; **18** = 10.5 min; **cis-8** = 10.6 min; **trans-8** = 12.4 min; **9** = 20.3 min; **19** = 21.0 min; diphenyl (internal standard) = 23.5 min.

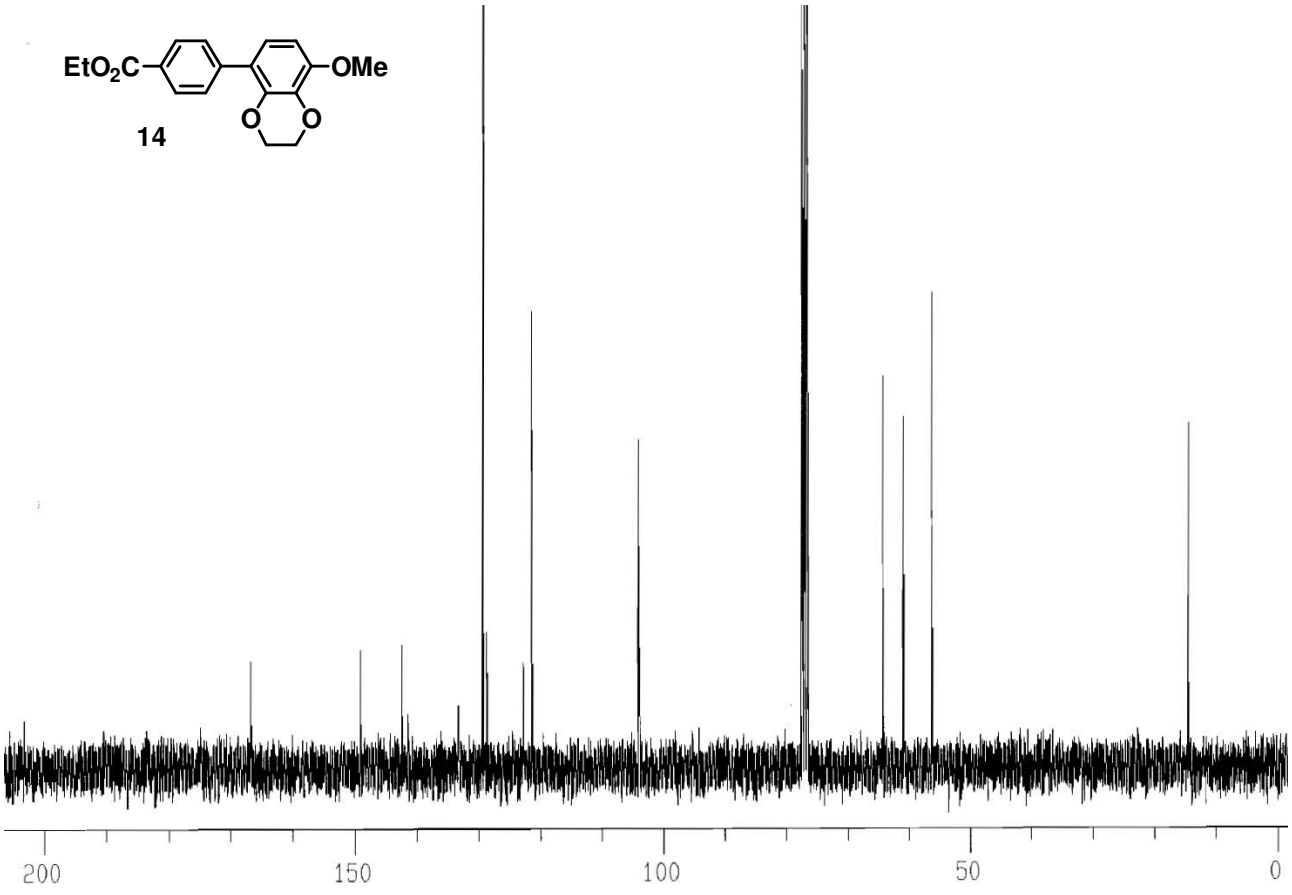
GC analyses were performed on a Shimadzu GC-14A.

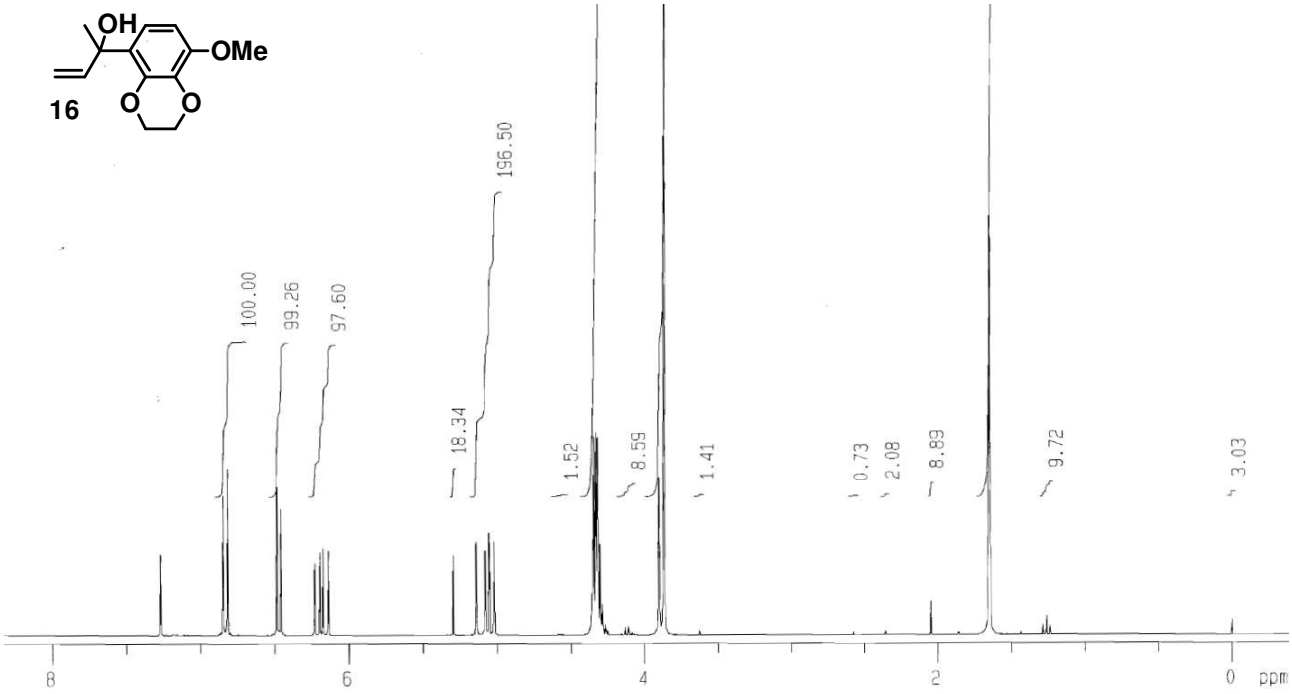
Column: TC-5 30 m×0.25 mm; detection: FID (Flame ionization detector); carrier gas: helium; carrier gas pressure: 1.5 kg/cm^2; injection temp: 250°C; detection temp: 260°C; flow late: split 60.0 mL/min; time program: 5 min at 100°C, 5.0°C/min to 250°C, 210 min at 50°C.

t_R**: 5** 11.5 = min; **12** = 14.9 min.

3. ^{1}H and ^{13}C NMR spectra of new compounds



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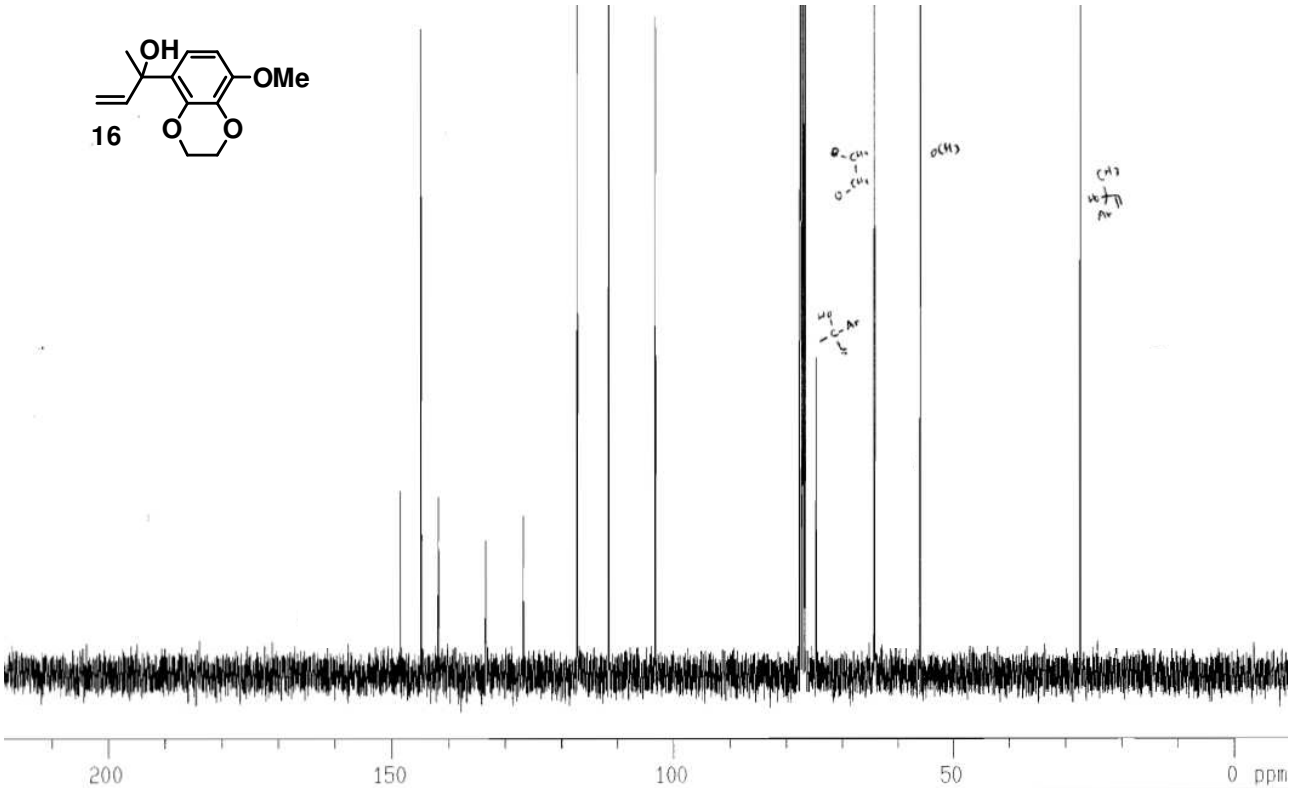
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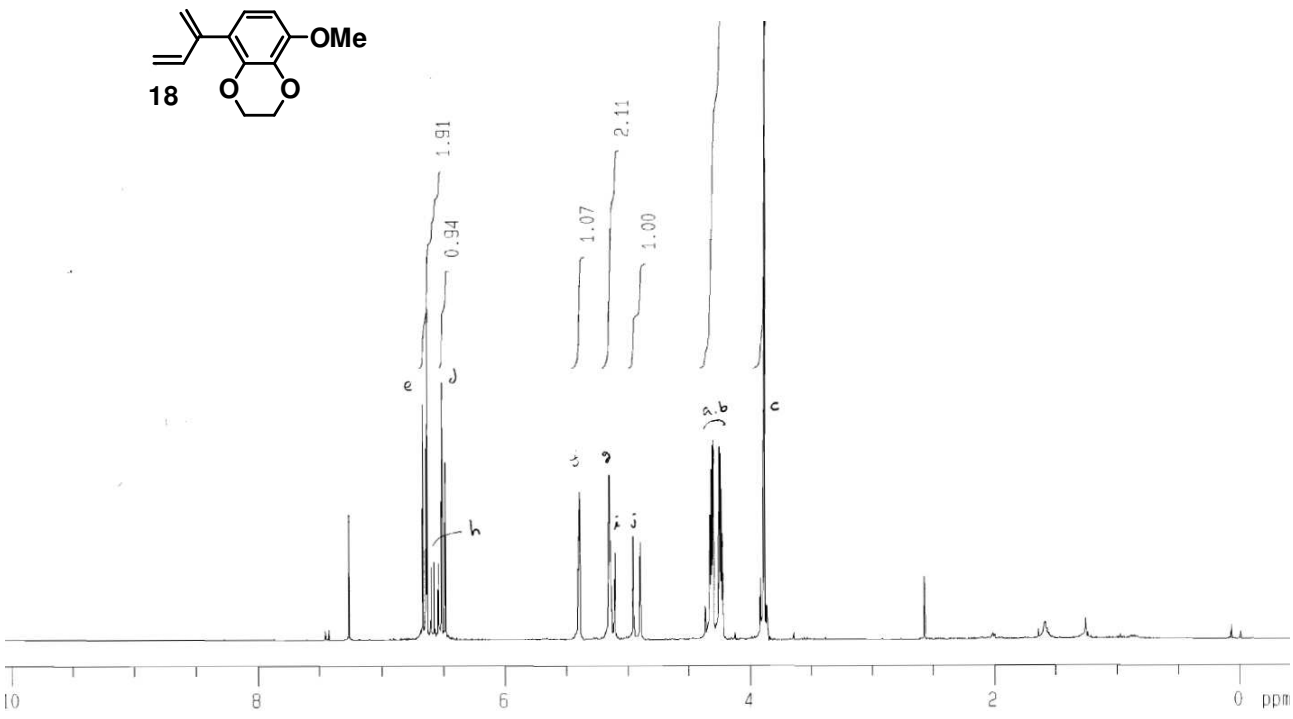
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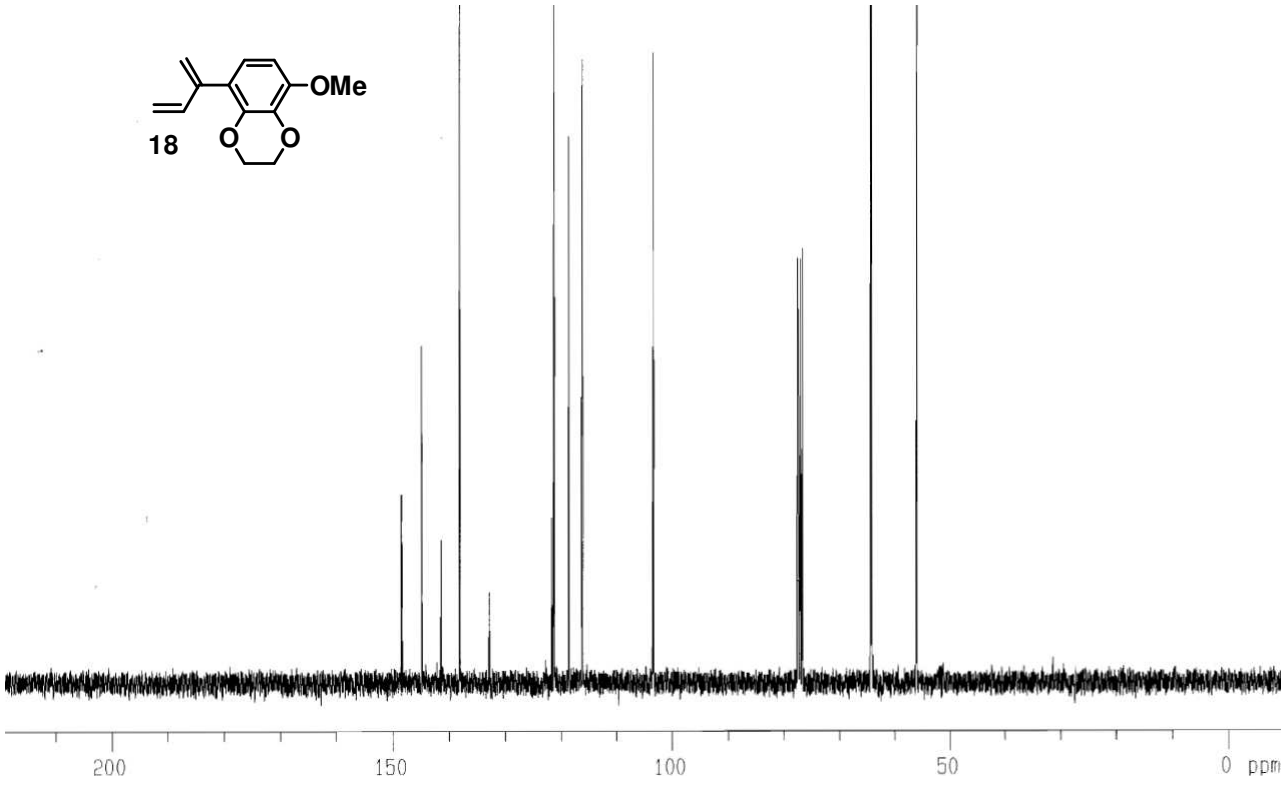
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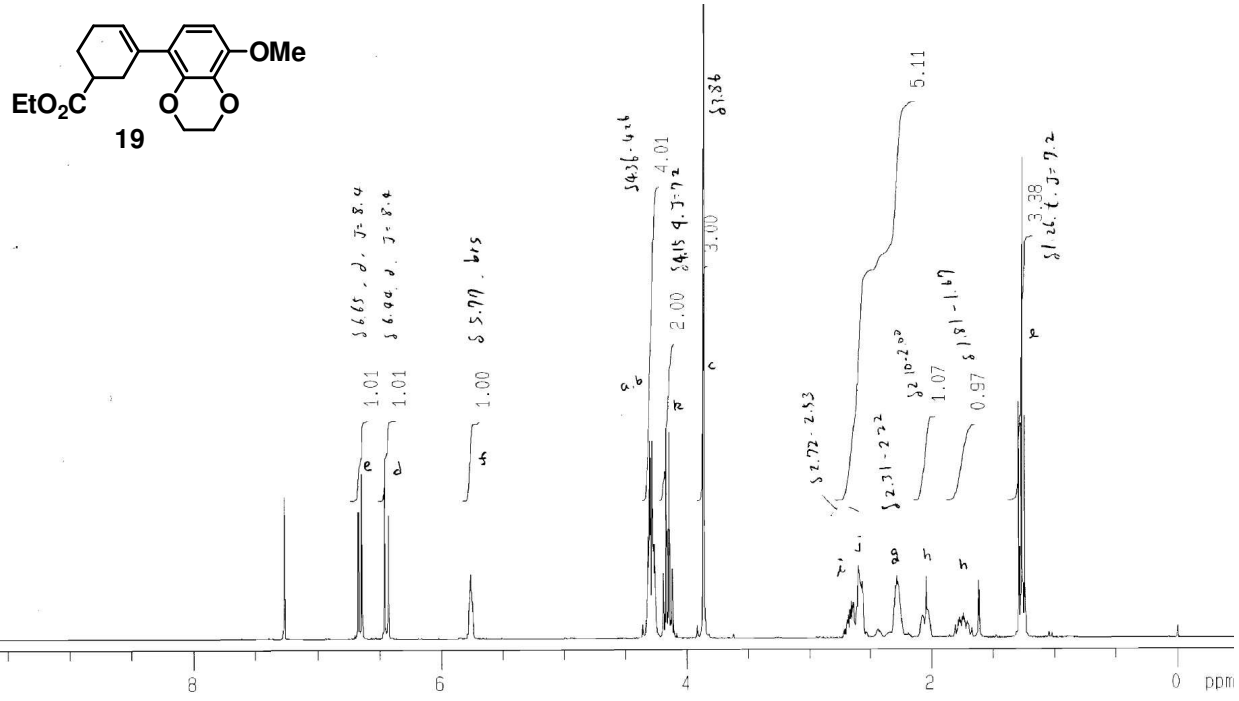
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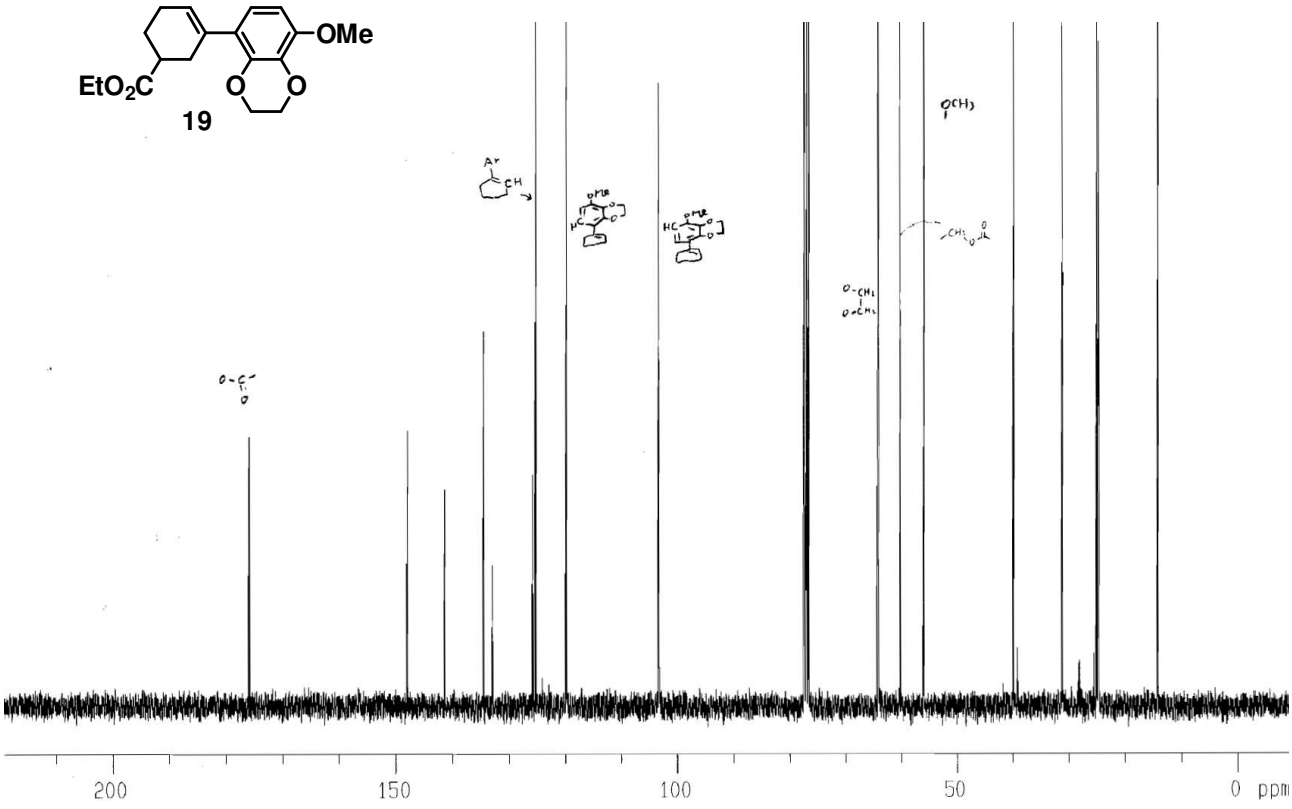
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