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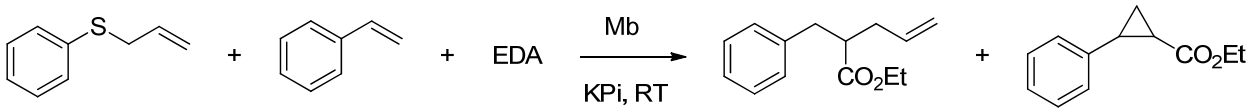
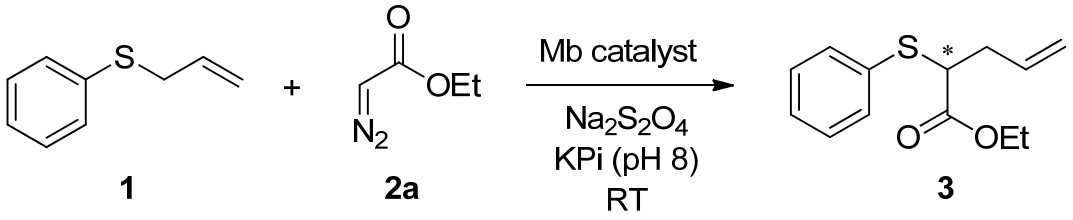
Supplementary Table S1. Co-substrate experiments for Mb-catalyzed reaction of EDA with allyl phenyl sulfide (A), to give the Doyle-Kirmse product (DK product), and/or with styrene (B) to give the cyclopropanation product (CP product), in the presence and in the absence of reductant ($Na_2S_2O_4$). See section "**Doyle-Kirmse reactions with ferric myoglobin**" for more detailed discussion of these results and those reported in **Figure S2**.



A **B** **C** **DK product** **CP product**

Entry	Enzyme	$Na_2S_2O_4$	A	B	C	DK product (TON)	CP product (TON)
1	-	-	1 mM	10 mM	10 mM	0	0
2	-	10 mM	1 mM	10 mM	10 mM	0	0
3	10 μM	-	-	10 mM	10 mM	0	<5
4	10 μM	-	10 mM	-	10 mM	91	0
5	10 μM	10 mM	1 mM	10 mM	10 mM	39	29
6	10 μM	-	1 mM	10 mM	10 mM	29	8

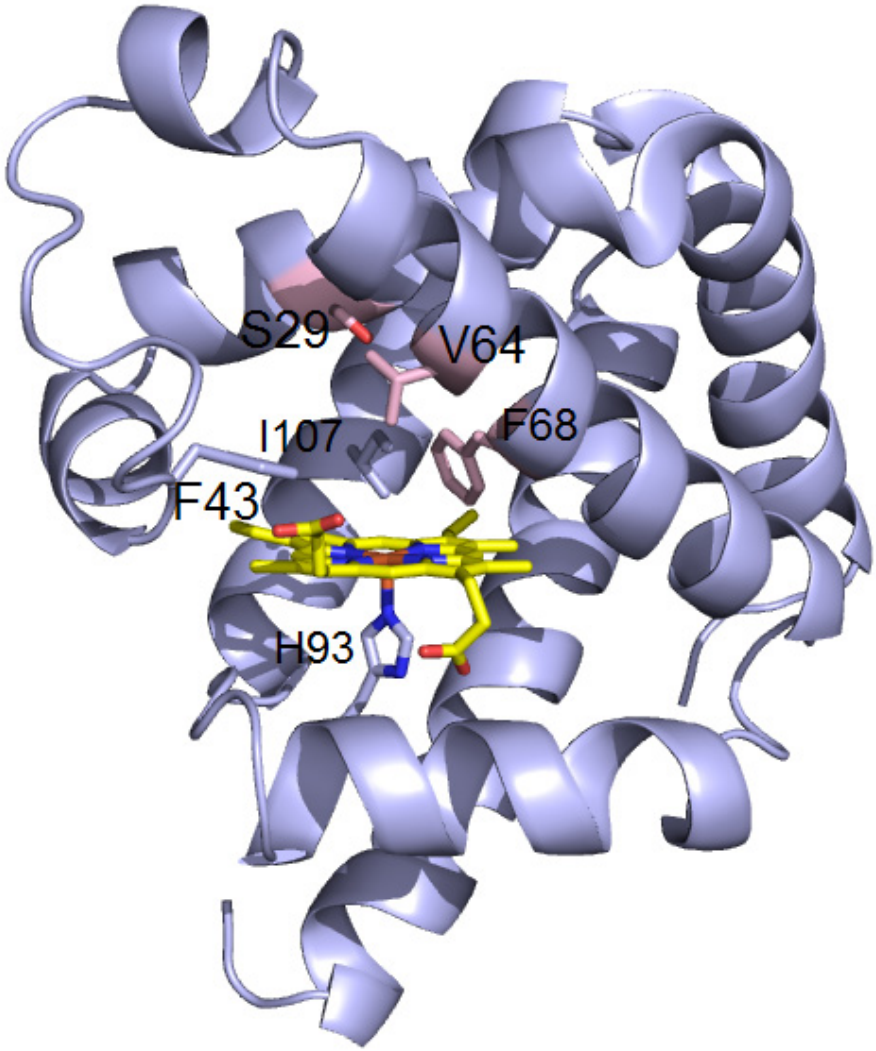
Supplementary Table S2. Total turnovers (TTN), rate, and enantioselectivity of Mb, Mb(L29S,H64V,V68F), and its reversion variants, in the synthesis of 3. Reaction conditions for total turnovers (TTN) determination: 10 mM **1**, 20 mM **2a**, 1 μM Mb catalyst (0.01 mol%), 10 mM $Na_2S_2O_4$ in oxygen-free potassium phosphate buffer (50 mM, pH 8) at room temperature for 12 hours. Reaction conditions for initial rate determination: 10 mM **1**, 20 mM **2a**, 5 μM Mb catalyst (0.05 mol%), 10 mM $Na_2S_2O_4$ in oxygen-free potassium phosphate buffer (50 mM, pH 8) at room temperature for 10 minutes. Enantiomeric excess was determined by chiral GC. Standard errors are within 15%.



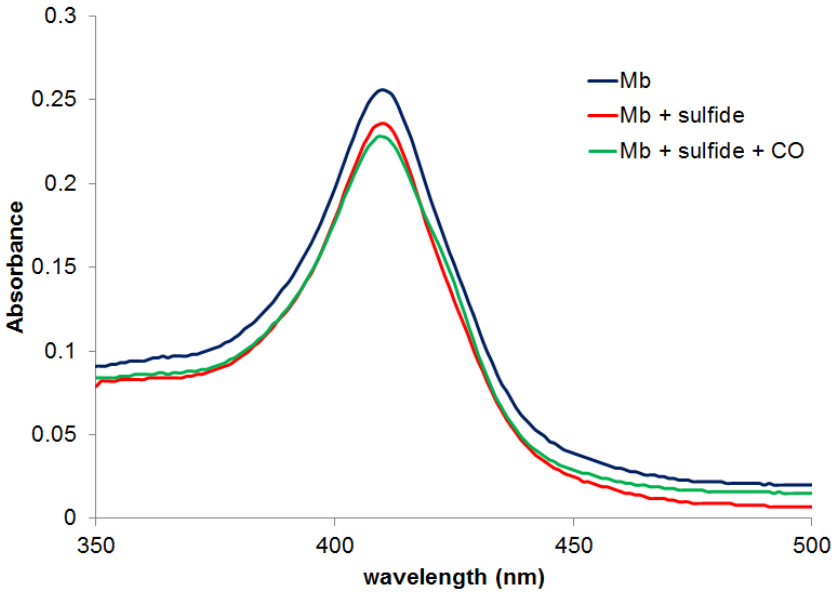
1 **2a** **3**

Mb variant	Total turnovers (TTN)	Rate (min^{-1})	*Enantiomeric excess (e.e.)*
WT Mb	1,620	79	**0%**
Mb(H64V)	2,230	121	**5%**
Mb(V68F)	560	43	**1%**
Mb(L29S,H64V)	3,085	118	**-1%**
Mb(H64V,V68F)	1,360	33	**4%**
Mb(L29S,H64V,V68F)	6,280	167	**71%**

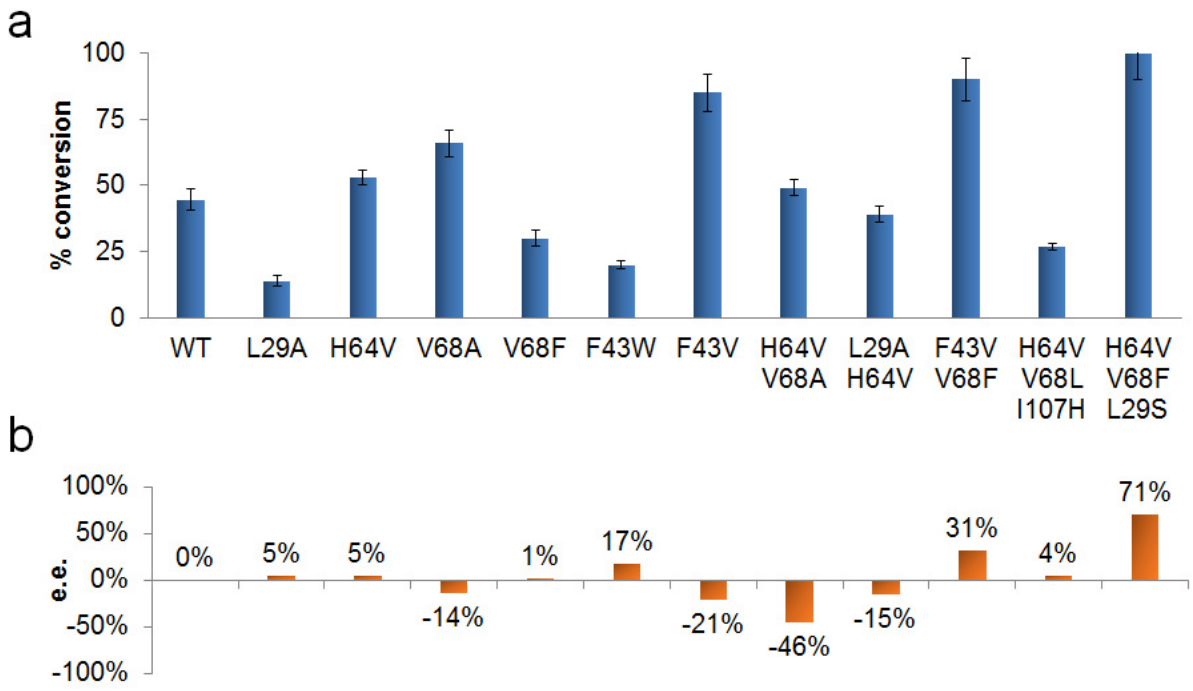
Supplementary Figure S1. Model of Mb(L29S, H64V,V68F) variant. Active site residues and heme bound histidine are shown as stick models. The heme and the mutated active site residues are colored in yellow and pink, respectively.



Supplementary Figure S2. UV-vis spectra of wild type myoglobin as measured before and after addition of allyl phenyl sulfide **1**, and after addition of **1** and carbon monoxide. In each case, the spectrum is consistent with that of ferric myoglobin ($\lambda_{max} \approx 409$ nm), indicating that no ferrous myoglobin is formed through a reaction with the sulfide reactant. See section "**Doyle-Kirmse reactions with ferric myoglobin**" for more detailed discussion of these results and those reported in **Table S1**.

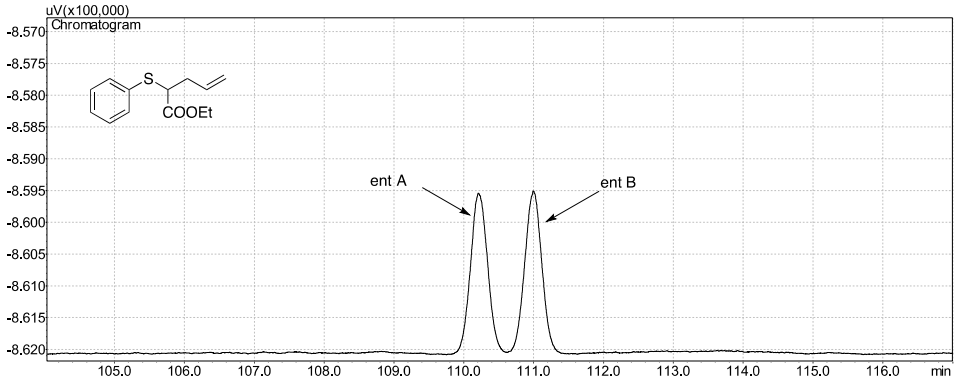


Supplementary Figure S3. Product conversion (a) and enantioselectivity (b) for the synthesis of **3** from phenyl allyl sulfide (**1**) and EDA (**2a**) as catalyzed by different active site variants of myoglobin under standard reaction conditions (=10 mM **1**, 20 mM **2a**, 10 μM Mb catalyst (0.1 mol%), 10 mM $Na_2S_2O_4$ in oxygen-free potassium phosphate buffer (pH 8) at room temperature).

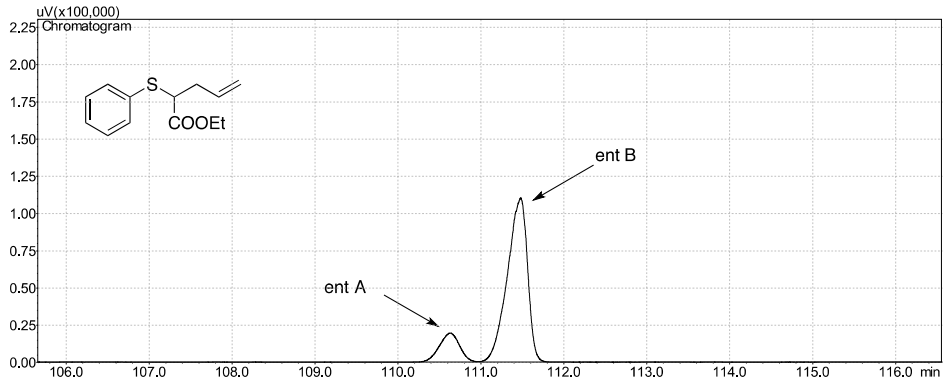


Supplementary Figure S4. Representative chiral GC chromatograms corresponding to product **3** (a) as authentic racemic standard synthesized using $Rh_2(OAc)_4$ catalyst, (b) as produced from the reaction with Mb(L29S, H64V, V68F), (c) as produced from the reaction with Mb(H64V, V68A). The two enantiomers of **3** are labeled **ent-A** and **ent-B**.

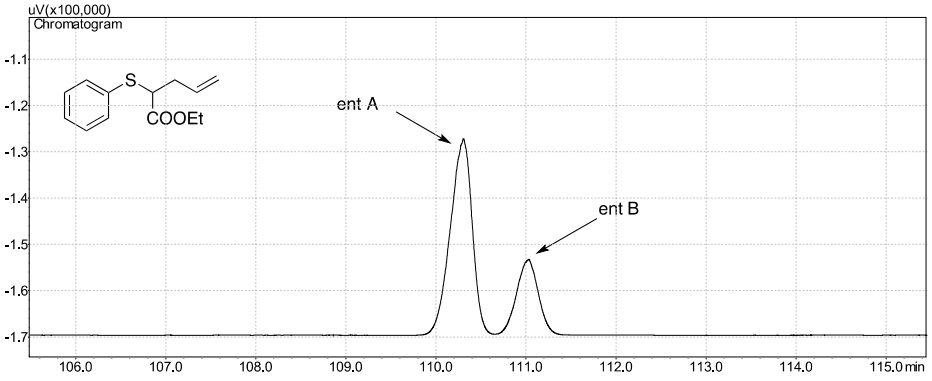
(a)



(b)



(c)



Experimental Procedures

Reagents. All the chemicals and reagents were purchased from commercial suppliers (Sigma-Aldrich, Alfa Aesar) and used without any further purification, unless otherwise stated. All dry reactions were carried out under argon atmosphere in oven-dried glassware with magnetic stirring using standard gas-tight syringes, cannulae and septa. ^{1}H and ^{13}C NMR spectra were measured on Bruker DPX-400 (operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C) or Bruker DPX-500 (operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C). Tetramethylsilane (TMS) served as the internal standard (0 ppm) for ^{1}H NMR and $CDCl_3$ was used as the internal standard (77.0 ppm) for ^{13}C NMR. Silica gel chromatography purifications were carried out using AMD Silica Gel 60 230-400 mesh.

Analytical Methods. Gas chromatography (GC) analyses were carried out using a Shimadzu GC-2010 gas chromatograph equipped with a FID detector and a chiral Cyclosil-B column (30 m x 0.25 mm x 0.25 μm). GC method for measurement of TON and TTN values: 1 μL injection, injector temp.: 200 ºC, detector temp: 300 ºC. Gradient: column temperature set at 140 ºC for 3 min, then to 160 ºC at 1.8 ºC/min, then to 165 ºC at 1 ºC/min, then to 245 ºC at 25 ºC/min. Total run time was 28.31 min.

Enantiomeric excess for product **3**, **16**, **19**, **22**, and **24** was determined using a Shimadzu GC-2010 gas chromatograph equipped with a FID detector and chiral Cyclosil-B column (30 m x 0.25 mm x 0.25 μm), with the following separation method: 1 μL injection, injector temp.: 200 ºC, detector temp: 300 ºC. Gradient: column temperature set at 80 ºC for 3 min, then to 180 ºC at 0.50 ºC/min, then to 200 ºC at 2 ºC/min, then to 245 ºC at 25 ºC/min for 6 min. Total run time was 220.80 min.

Product	t_R (min) for ent A	t_R (min) for entB
3	110.64	111.46
16	146.90	147.48
19	117.68, 118.36	118.94, 119.58
22	22.39	23.37
24	105.03	105.63

Enantiomeric excess for products **13**, **14**, **15**, **17**, **18**, **20**, **21**, **23**, **28**, **29**, and **30** was determined by Supercritical Fluid Chromatography (SFC) analysis, using a Jasco Analytical and Semi-Preparative SFC instrument equipped with a column oven (35 °C), photodiode array detector, a backpressure regulator (12.0 MPa), and a carbon dioxide pump. Daicel Chiralpak IA, IB, IC, or IF columns (0.46 cm ID × 25 cm L) were used for separation of enantiomers. All samples were eluted using an isocratic solvent system of 5% modifier (see below) in liquid CO_2 at an elution rate of 4 mL/min and detected at $\lambda = 220$ nm. Total run time was 10.2 min.

Product	Column	Modifier Solvent	t_R (min) for ent A	t_R (min) for ent B
13	IA	2% EtOH in Hexanes	2.72	3.28
14	IB	2% EtOH in Hexanes	4.20	4.62
15	IB	2% EtOH in Hexanes	7.08	7.48
17	IA	2% EtOH in Hexanes	2.33	2.50
18	IF	10% EtOAc in Hexanes	1.98	2.08
20	IC	20% EtOH in Hexanes	3.56	4.21
21	IC	20% EtOH in Hexanes	4.46	5.33
28	IF	2% EtOH in Hexanes	6.10	6.36
29	IF	10% EtOH in Hexanes	8.17	8.76
30	IF	2% EtOH in Hexanes	6.68	6.92

Protein expression and purification. Wild-type Mb and the engineered Mb variants were expressed in *E. coli* BL21(DE3) cells as described previously (Bordeaux et al., Angew. Chem. Int. Ed. 2015, 54, 1744–1748). Briefly, cells were grown in TB medium (ampicillin, 100 mg L^{-1}) at 37 °C (150 rpm) until OD_{600} reached 0.6. Cells were then induced with 0.25 mM β-D-1-thiogalactopyranoside (IPTG) and 0.3 mM δ-aminolevulinic acid (ALA). After induction, cultures were shaken at 150 rpm and 27 °C and harvested after 20 h by centrifugation at 4000 rpm at 4 °C. After cell lysis by sonication, the proteins were purified by Ni-affinity chromatography using the following buffers: loading buffer (50 mM KPi, 800 mM NaCl, pH 7.0), wash buffer 1 (50 mM KPi, 800 mM NaCl, pH 6.2), wash buffer 2 (50 mM KPi, 800 mM NaCl, 250 mM glycine, pH 7.0) and elution buffer (50 mM KPi, 800 mM NaCl, 300 mM L-histidine, pH 7.0). After buffer exchange (50 mM KPi, pH 7.0), the proteins were stored at 4 °C. Myoglobin concentration was determined using an extinction coefficient $\varepsilon_{410} = 157\ mM^{-1}\ cm^{-1}$ (Redaelli et al., Chembiochem 2002, 3, 226-233).

Biocatalytic Doyle-Kirmse reactions: Under standard reaction conditions (**Table 1**, Entry 1), reactions were carried out at a 400 μL scale using 10 μM myoglobin (or Mb variant), 10 mM allyl phenyl sulfide, 20 mM EDA, and 10 mM sodium dithionite. In a typical procedure, a solution containing sodium dithionate (100 mM stock solution) in potassium phosphate buffer (50 mM, pH 8.0) was degassed by bubbling argon into the mixture for 4 min in a sealed vial. A buffered solution containing myoglobin was carefully degassed in a similar manner in a separate vial. The two solutions were then mixed together via cannula. Reactions were initiated by addition of 10 μL of allyl phenyl sulfide (from a 0.4 M stock solution in ethanol), followed by the addition of 10 μL of EDA (from a 0.8 M stock solution in ethanol) with a syringe, and the

reaction mixture was stirred for 12 hours at room temperature, under positive argon pressure. For the optimization of the allyl phenyl sulfide : EDA ratio (**Table 1**), reactions were performed according to the general procedure described above, using 10 μM of protein, 10 mM of allyl phenyl sulfide and variable amounts of EDA (2.5 mM EDA to 10 mM EDA). Reactions at varying catalyst loadings (**Table 1**) were carried according to the general procedure but varying the enzyme concentration from 10 μM to 1 μM of Mb(L29S, H64V, V68F). Reactions for TTN determination were carried out according to the general procedure described above using 1 μM Mb(L29S, H64V, V68F), 10 mM allyl phenyl sulfide (10 μL of 0.4 M stock solution in ethanol), and 20 mM EDA (10 μL of 0.8 M stock solution in ethanol).

Preparative-scale reactions. A solution containing 10 mM sodium dithionate (1 mL from 100 mM stock solution) was mixed with 8 mL potassium phosphate buffer (50 mM, pH 8.0) and degassed by bubbling argon into the mixture for 10 min in a sealed vial. A buffered solution containing 10 μM Mb(H64V,V68F,L29S) (394 μL of 241 μM stock solution) was carefully degassed in a similar manner in a separate vial. The two solutions were then mixed together via cannula. Reactions were initiated by addition of 14.8 μL of allyl phenyl sulfide (**1**) in 250 μL of ethanol, followed by the addition of 24 μL of EDA (**2a**) in 250 μL of ethanol with a syringe. The reaction mixture was stirred for 12 hours at room temperature, under positive argon pressure. The reaction mixture was then extracted with ethyl acetate (3 x 10 mL). The organic layer evaporated under reduced pressure and the residue was purified by flash chromatography (10% ethyl acetate in hexanes) to yield the desired product **3** as colorless liquid (19.5 mg, 84% isolated yield).

Product analysis: The reactions were analyzed by adding 20 μL of internal standard (benzodioxole, 50 mM in ethanol) to the reaction mixture, followed by extraction with 400 μL of dichloromethane and analysis by GC-FID or SFC (see **Analytical Methods** section for details on GC and SFC analyses). Samples for SFC analyses were prepared in a similar manner (i.e., via extraction with dichlorometane) and injected at a concentration of ~ 0.5 mg/mL. Calibration curves for quantification of the different [2,3]-sigmatropic rearrangement products were constructed using authentic (racemic) standards prepared synthetically as described in **Synthetic Procedures**. All measurements were performed at least in duplicate. For each experiment, negative control samples containing either no enzyme or no reductant were included.

Doyle-Kirmse reactions with ferric myoglobin. The ability of myoglobin to catalyze Doyle-Kirmse reactions in the absence of reductant (**Table 1**, Entry 3) is unlike previously investigated myoglobin-catalyzed carbene transfer reactions, which were only catalyzed by ferrous Mb.[3d, 7, 9a] To verify that ferric Mb is a competent catalyst in Doyle-Kirmse reactions, the control experiments described in **Figure S2** and **Table S1** were carried out. As shown in **Figure S2**, UV-vis spectra were acquired before and after addition of allyl phenyl sulfide (**1**) to ferric Mb. In each case, the measured spectrum is consistent with that of ferric myoglobin (λ_{max} = 409 nm vs. λ_{max} = 434 nm for ferrous Mb). Similarly, no formation of a CO-ferrous Mb complex (λ_{max} = 424 nm) was observed upon incubation of ferric Mb with the sulfide and CO (**Figure S2**). These results rule out that ferrous Mb is formed upon reaction with the sulfide reactant. To further confirm the reactivity of ferric Mb in Doyle-Kirmse transformations, reactions were carried out in the presence of EDA as the carbene donor, allyl phenyl sulfide (**1**) and/or styrene as the substrate(s), and in the presence or in the absence of reductant (**Table S1**). These experiments

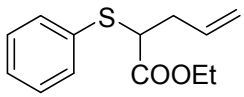
show that, in the absence of reductant, the Mb-catalyzed Doyle-Kirmse reaction proceeds efficiently (91 TON, Entry 4), whereas negligible cyclopropanation activity is observed (<5 TON, Entry 3), which is consistent with the dependence of the latter reactivity on ferrous Mb.[3d] Similarly, cyclopropanation reactivity is observed in the presence of both substrates only when the reductant is added (Entry 5 vs. 6). These results indicate that ferrous Mb is not generated upon reaction with EDA and support the notion that ferric Mb is a competent catalyst for Doyle-Kirmse reactions but not cyclopropanation reactions. In line with these conclusions, hemin (= iron(III)-protoporphyrin IX) is also catalytically active in the transformation of **1** and EDA into **3** in the absence of reductant (100 TON)**.**

Synthetic Procedures:

General procedure for synthesis of authentic standards in racemic form:

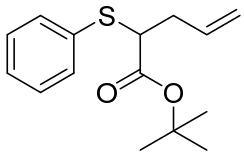
To a flame dried round bottom flask under argon, equipped with a stir bar was added sulfide (1.2 equiv.) and $Rh_2(OAC)_4$ (5 mol%) in dichloromethane (2-3 mL). To this solution was added a solution of diazo reagent (1 equiv.) in dichloromethane (1-2 mL) over 15-20 minutes at 0°C. The resulting mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure and the crude mixture was purified using flash chromatography and a 9:1 mixture of hexanes and diethyl ether.

Ethyl 2-(phenylthio)pent-4-enoate (3):



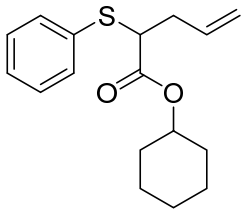
Following the standard procedure, 86% yield, GC-MS m/z (% relative intensity): 236(61.9), 195(81.5), 163(88.1), 149(98.1), 121 (93.7), 109 (100); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.47 (d, J = 5.5 Hz, 2H), 7.30-7.26 (m, 3H), 5.85-5.76 (m, 1H), 5.15-5.08 (m, 2H), 4.18-4.09 (m, 2H), 3.71-3.67 (m, 1H), 2.66-2.60 (m, 1H), 2.54-2.49 (m, 1H), 1.18-1.14 (m, 3H) ppm, ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.6, 133.9, 133.1, 128.9, 128.0, 118.0, 61.1, 50.3, 35.8, 14.1 ppm.

***tert*-Butyl 2-(phenylthio)pent-4-enoate (13):**



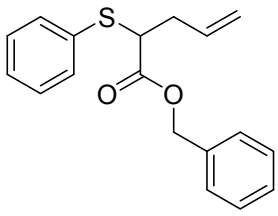
Following the standard procedure, 82% yield, GC-MS m/z (% relative intensity): 264(26.7), 208(22.5), 163(78.8), 135(36.9), 109(26.8), 57(100); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.47 (d, J = 7.2 Hz, 2H), 7.29-7.26 (m, 3H), 5.85-5.75 (m, 1H), 5.14-5.06 (m, 2H), 3.64 (t, *J* = 7.6 Hz, 1H), 2.61-2.54 (m, 1H), 2.49-2.42 (m, 1H), 1.34 (s, 9H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.7, 134.0, 133.6, 132.8, 128.8, 127.7, 117.8, 81.5, 50.8, 35.9, 27.8 ppm.

Cyclohexyl 2-(phenylthio)pent-4-enoate (14):



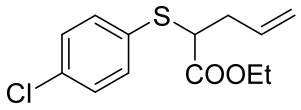
Following the standard procedure, 76% yield, GC-MS m/z (% relative intensity): 290(63.8), 163(100), 135(60.2), 99(65.8), 83(90.4), 55(94.6); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.46 (d, *J* = 6.5 Hz, 2H), 7.30-7.26 (m, 3H), 5.83-5.78 (m, 1H), 5.14-5.07 (m, 2H), 4.76-4.73 (m, 1H), 3.70 (t, *J* = 6.0 Hz, 1H), 2.63-2.59 (m, 1H), 2.54-2.49 (m, 1H), 1.75-1.64 (m, 5H), 1.36-1.22 (m, 5H) ppm, ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.1, 133.9, 133.4, 132.7, 128.9, 127.8, 117.9, 73.4, 50.3, 35.9, 31.5, 31.4, 31.3, 25.3, 23.5 ppm.

Benzyl 2-(phenylthio)pent-4-enoate (15)



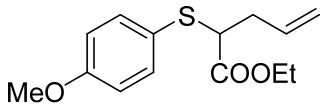
Following the standard procedure, 76% yield, GC-MS m/z (% relative intensity): 298(23.5), 163(33.5), 135(39.4), 109(37.5), 91(100), 65(26.4); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.45-7.43 (m, 2H), 7.36-7.35 (m, 3H), 7.29-7.28 (m, 5H), 5.87-5.79 (m, 1H), 5.16-5.09 (m, 4H), 3.80-3.77 (m, 1H), 2.71-2.65(m, 1H), 2.59-2.54 (m, 1H) ppm, ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.5, 135.5, 133.8, 133.3, 132.9, 129.0, 128.5, 128.4, 128.3, 128.1, 118.2, 66.9, 50.3, 35.8 ppm.

Ethyl 2-((4-chlorophenyl)thio)pent-4-enoate (16):



Following the standard procedure, 80% yield, GC-MS m/z (% relative intensity): 270(81.4), 229(48.5), 197(84.9), 183(100), 155(74.2), 143(49.6), 108(69.0); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38-7.36 (m, 2H), 7.26-7.24 (m, 2H), 5.82-5.72 (m, 1H), 5.13-5.07 (m, 2H), 4.12 (q, J = 6.8 Hz, 2H), 3.65-3.61 (m, 1H), 2.62-2.55 (m, 1H), 2.50-2.43 (m, 1H), 1.18 (t, J = 7.2 Hz, 3H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 134.5, 134.3, 133.6, 131.5, 129.1, 118.2, 61.2, 50.3, 50.2, 35.6, 14.1 ppm.

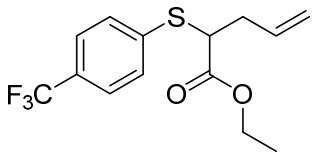
Ethyl 2-((4-methoxyphenyl)thio)pent-4-enoate (17):



Following the standard procedure, 74% yield, GC-MS m/z (% relative intensity): 266(100), 193(27.4), 179(94.7), 151(57.6), 139(93.0); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41 (d, J =8.8 Hz, 2H), 6.84 (d, J= 8.4 Hz, 2H), 5.83-5.73 (m, 1H), 5.12-5.05 (m, 2H), 4.11 (q, J = 6.8 Hz, 2H), 3.78 (s, 3H), 3.53-3.50 (m, 1H), 2.58-2.51 (m, 1H), 2.47-2.40 (m, 1H), 1.19 (t, J = 7.2 Hz, 3H)

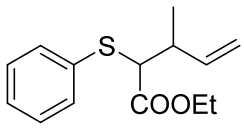
ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.7, 160.2, 136.5, 134.1, 122.7, 117.8, 114.4, 61.0, 55.3, 50.9, 35.6, 14.1 ppm.

Ethyl 2-((4-(trifluoromethyl)phenyl)thio)pent-4-enoate (18):



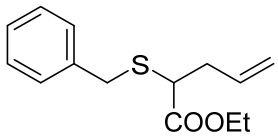
Following the standard procedure, 61% yield, GC-MS m/z (% relative intensity): 304(57.2), 263(41.3), 231(56.2), 189(100), 127(51.2), 99(50.0); ^1H NMR ($CDCl_3$, 500 MHz): δ 7.55-7.51 (m, 4H), 5.84-5.76 (m, 1H), 5.17-5.11 (m, 2H), 4.17-4.10 (m, 2H), 3.82 (t, J = 7.0 Hz, 1H), 2.70-2.64 (m, 1H), 2.57-2.52 (m, 1H), 1.19 (t, J = 7.0 Hz, 3H) ppm, ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.2, 139.0, 133.3, 131.1, 129.4, 129.2, 125. 7, 125.6, 125.0, 122.8, 118.5, 61.4, 49.3, 35.7, 14.0 ppm.

Ethyl 3-methyl-2-(phenylthio)pent-4-enoate (19):



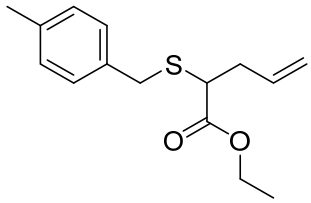
Following the standard procedure, 82% yield, GC-MS m/z (% relative intensity): 250(36), 195(41.4), 177(26.9), 149(100), 121(93.2); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.46-7.43 (m, 2H), 7.28-7.25 (m, 3H), 5.88-5.72 (m, 1H), 5.16-5.01 (m, 2H), 4.10-4.05 (m, 2H), 3.58-3.51 (m, 1H), 2.75-2.62 (m, 1H), 1.25-1.12 (m, 6H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.6, 139.6, 132.6, 128.9, 128.8, 127.7, 116.0, 61.1, 57.3, 56.8, 39.8, 14.1 ppm.

Ethyl 2-(benzylthio)pent-4-enoate (20):



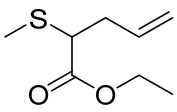
Following the standard procedure, 86% yield, GC-MS m/z (% relative intensity): 250(4.61), 204(4.8), 128(23.1), 123(46.4), 100(15.9), 91(100);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32-7.24 (m, 5H), 5.75-5.64 (m, 1H), 5.07-5.01 (m, 2H), 4.19-4.13 (m, 2H), 3.85-3.77 (m, 2H), 3.23-3.20 (m, 1H), 2.61-2.54 (m, 1H), 2.40-2.34 (m, 1H), 1.29-1.26 (m, 3H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.1, 137.4, 134.0, 129.1, 128.5, 127.2, 117.6, 61.1, 45.5, 35.8, 35.3, 14.2 ppm

Ethyl 2-((4-methylbenzyl)thio)pent-4-enoate (21):



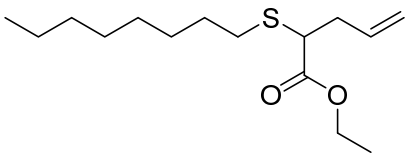
Following the standard procedure, 84% yield, GC-MS m/z (% relative intensity): 264(1.0), 191(5.4), 137(97.9), 105(100), 85(12.8), 77(17.5);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.22-7.21 (d, *J*= 7.2 Hz, 2H), 7.12-7.10 (d, *J* = 7.6 Hz, 2H), 5.76-5.66 (m, 1H), 5.08-5.02 (m, 2H), 4.19-4.15 (m, 2H), 3.83-3.74 (m, 2H), 3.25 (t, *J* = 8.4 Hz, 1H), 2.62-2.54 (m, 1H), 2.41-2.36 (m, 1H), 2.32 (s, 3H), 1.30 (t, *J*= 7.2 Hz, 3H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.0, 136.8, 134.3, 134.1, 129.2, 128.9, 117.5, 61.1, 45.5, 35.6, 35.4, 21.1, 14.2 ppm.

Ethyl 2-(methylthio)pent-4-enoate (22):



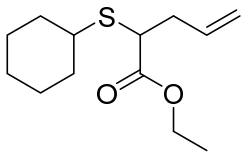
Following the standard procedure, 52% yield, GC-MS m/z (% relative intensity): 174 (64.2), 133(48.8), 101(100), 61(58.7), 55(99.3); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.80-5.75 (m, 1H), 5.13-5.06 (m, 2H), 4.21-4.16 (m, 2H), 3.24 (t, *J* = 6.2 Hz, 1H), 2.63-2.60 (m, 1H), 2.43-2.40 (m, 1H), 2.13 (s, 3H), 1.28 9 (t, *J* = 7.5 Hz, 3H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.7, 134.2, 117.6, 61.0, 46.8, 34.9, 14.2, 13.8 ppm.

Ethyl 2-(octylthio)pent-4-enoate (23)



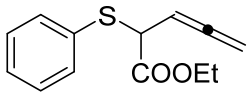
Following the standard procedure, 49% yield, GC-MS m/z (% relative intensity): 272(1.0), 199(19.2), 160(44.3), 128(100), 100(40.7), 87(47.0), 69(63.0), 55(62.5);^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.82-5.72 (m, 1H), 5.11-5.04 (m, 2H), 4.18 (q, *J* = 6.8 Hz, 2H), 3.29 (t, *J* = 8.0 Hz, 1H), 2.64-2.56 (m, 3H), 2.43-2.37 (m, 1H), 1.57-1.53 (m, 2H), 1.25-1.24 (m, 13H), 0.86 (t, *J* = 6.8 Hz, 3H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.2, 134.1, 117.5, 60.9, 46.2, 35.7, 31.7, 31.3, 29.3, 29.1, 28.8, 22.6, 14.2, 14.0 ppm.

Ethyl 2-(cyclohexylthio)pent-4-enoate (24):



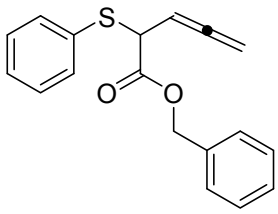
Following the standard procedure, 58% yield, GC-MS m/z (% relative intensity): 242(5.0), 169(11.3), 115(100), 87(41.2), 55(58.1);^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.81-5.71(m, 1H), 5.11-5.03 (m, 2H), 4.23-4.10 (m, 2H), 3.37 (t, *J* = 8.4 Hz, 1H), 2.78 (brs, 1H), 2.61-2.54 (m, 1H), 2.42-2.35 (m, 1H), 2.02-1.99 (m, 1H), 1.88 (brs, 1H), 1.72 (brs, 2H), 1.60-1.56 (m, 1H), 1.30-1.24 (m, 8H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.7, 134.3, 117.5, 60.9, 45.1, 43.9, 36.3, 33.7, 33.5, 26.0, 25.9, 25.6, 14.2 ppm.

Ethyl 2-(phenylthio)penta-3,4-dienoate (28):



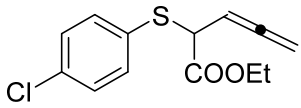
Following the standard procedure, 59% yield, GC-MS m/z (% relative intensity): 205(19.3), 161(78.6), 128(38.3), 97(100);^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.47-7.46 (m, 2H), 7.30 (m, 3H), 5.38-5.33 (m, 1H), 4.83-4.79 (m, 1H), 4.75-4.70 (m, 1H), 4.31 (d, *J* = 8.8 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 1.20 (t, *J* = 6.8 Hz, 3H) ppm, ^{13}C NMR ($CDCl_3$, 100 MHz): δ 209.0, 169.9, 133.9, 132.6, 128.9, 128.3, 87.3, 77.4, 61.6, 50.8, 14.1 ppm.

Benzyl 2-(phenylthio)penta-3,4-dienoate (29):



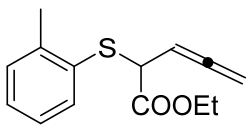
Following the standard procedure, 51% yield, GC-MS m/z (% relative intensity): 296(10), 177(21.2), 128(37.6), 91(100), 65(26.9);^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.47-7.46 (m, 2H), 7.45-7.24 (m, 8H), 5.45-5.41 (m, 1H), 5.15-5.14 (m, 2H), 4.86-4.75 (m, 2H), 4.41-4.40 (m, 1H) ppm, 13C NMR ($CDCl_3$, 125 MHz): δ 209.1, 169.8, 135.1, 134.0, 132.5, 129.1, 128.9, 128.6, 128.4, 128.4, 87.1, 77.6, 67.3, 50.8 ppm,

Ethyl 2-((4-chlorophenyl)thio)penta-3,4-dienoate (30):



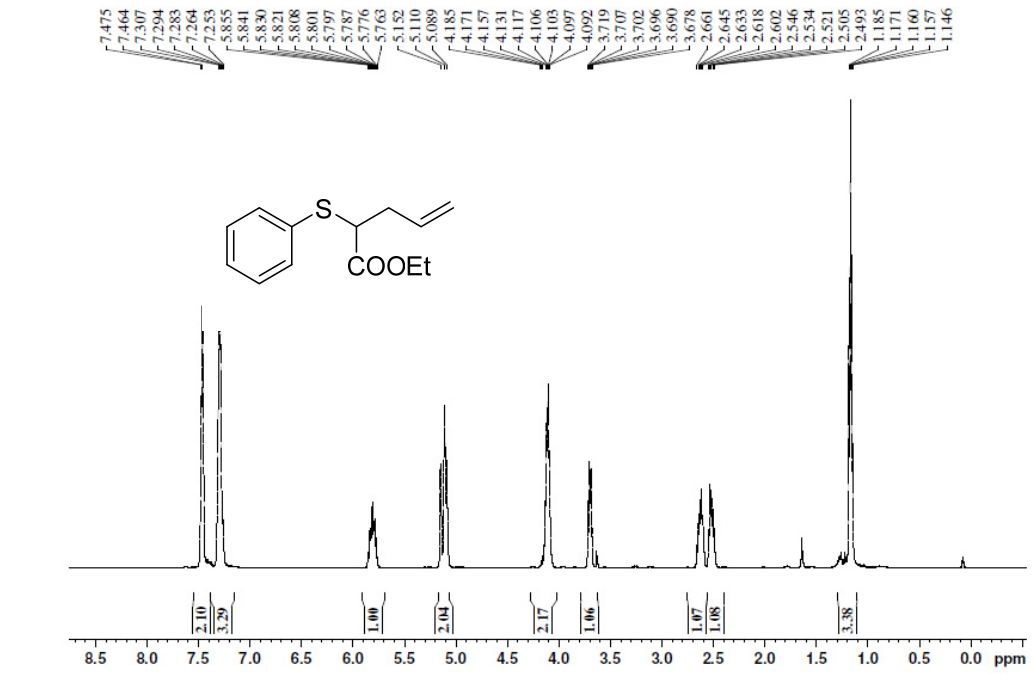
Following the standard procedure, 41% yield, GC-MS m/z (% relative intensity): 268(58.2), 195(100), 181(48.0), 160(28.4), 115(30.8); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.39 (d, J= 8.5 Hz, 2H), 7.27 (d, J = 8.5 Hz, 2H), 5.35-5.31 (m, 1H), 4.84-4.80 (m, 1H), 4.76-4.73 (m,1H), 4.26 (d, J = 9.0 Hz, 1H), 4.15-4.11(m, 2H), 1.21(t, J= 7.0 Hz, 3H), ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.1, 169.6, 135.2, 134.7, 131.1, 129.0, 87.1, 77.6, 61.7, 50.8, 14.1 ppm.

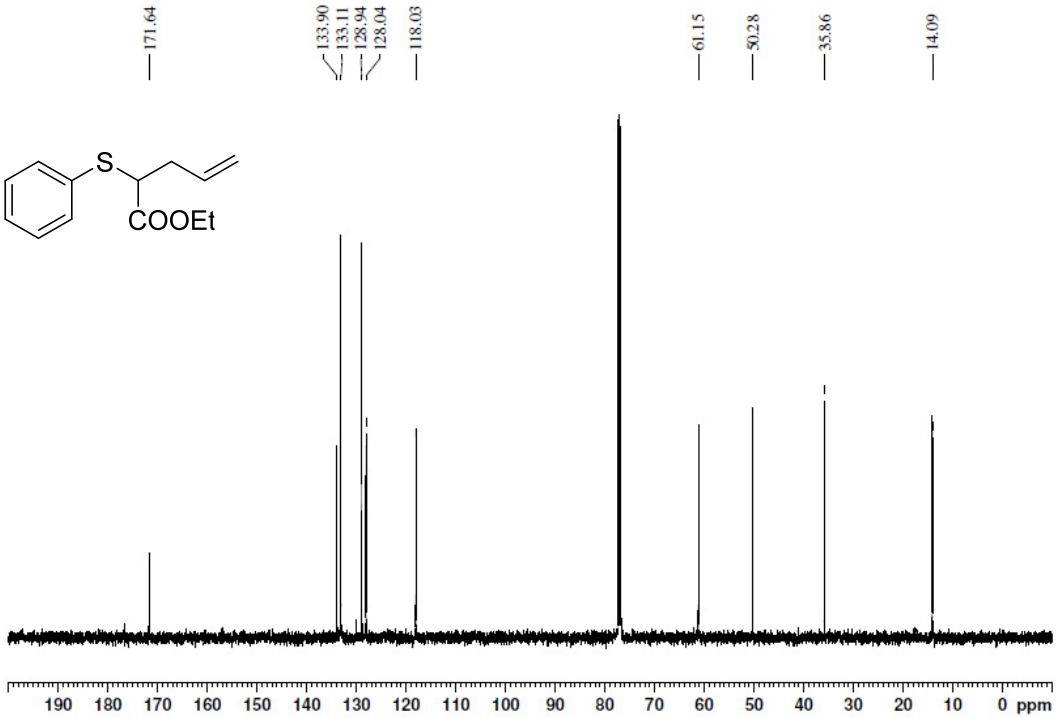
Ethyl 2-(o-tolylthio)penta-3,4-dienoate (31):

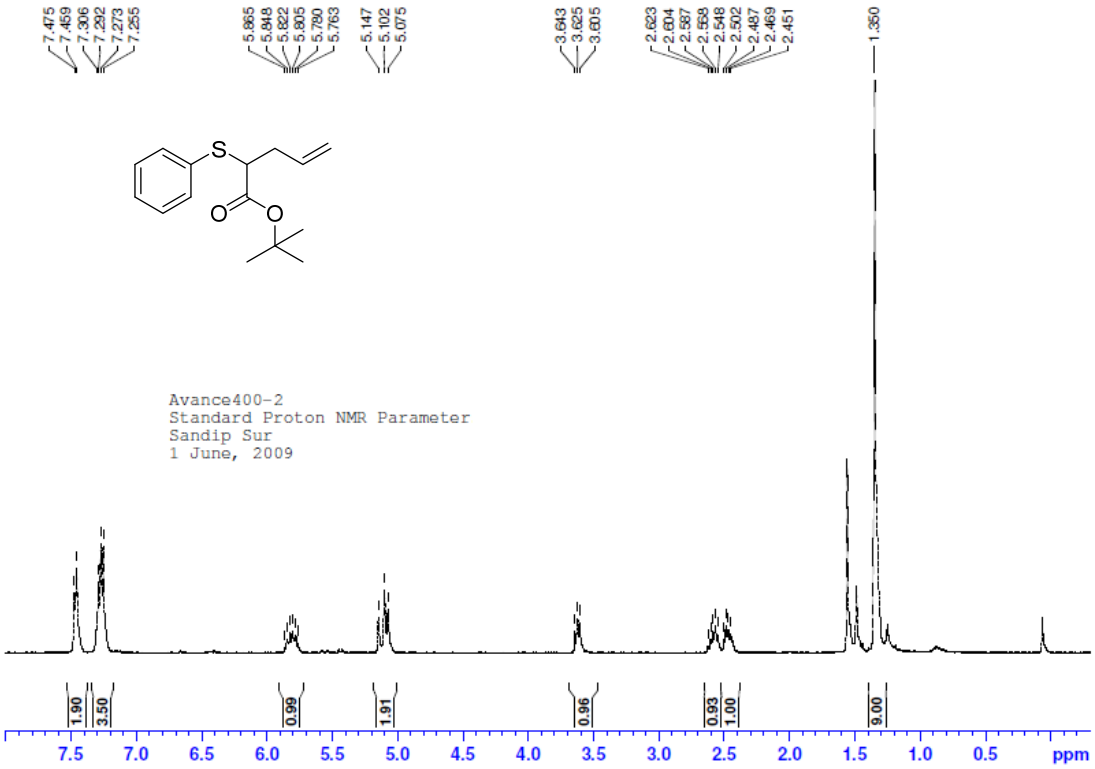


Following the standard procedure, 49% yield, GC-MS m/z (% relative intensity): 248(28.9), 175(100), 161(24.4), 115(2.5), 97(39.3);^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.46 (d, J = 7.5 Hz, 1H), 7.21-7.20 (m, 2H), 7.15-7.11 (m, 1H), 5.40 (q, J= 6.5 Hz, 1H), 4.82-4.79 (m, 1H), 4.73-4.69 (m, 1H), 4.28 (d, J = 7.5 Hz, 1H), 4.13-4.07 (m, 2H), 2.46 (s, 3H), 1.19 (t, J = 7.5 Hz, 3H) ppm, ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.0, 169.9, 141.3, 134.7, 132.1, 130.1, 128.6, 126.3, 87.3,77.4, 61.6, 50.2, 20.8, 14.0 ppm.

^{1}H and ^{13}C NMR spectra:



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5.102
5.075
3.643
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3.605
2.623
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2.587
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2.469
2.451
1.350
S
O
O
Avance400-2
Standard Proton NMR Parameter
Sandip Sur
1 June, 2009
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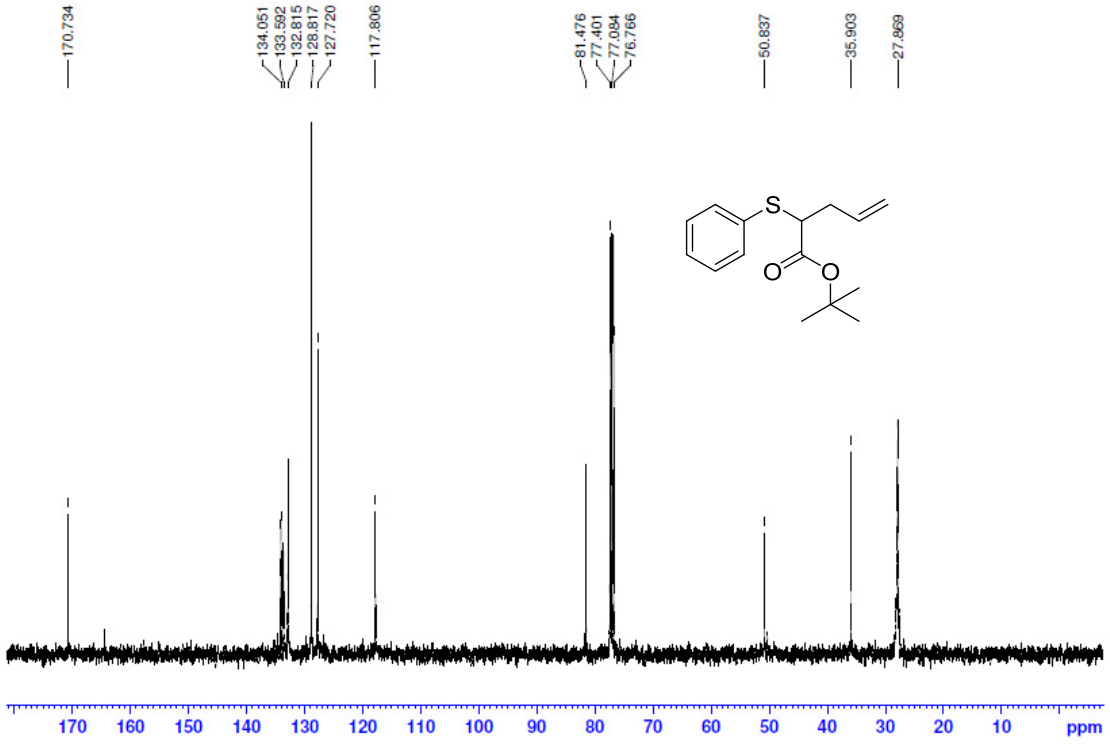
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127.720
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81.476
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35.903
27.869
S
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150
140
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110
100
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70
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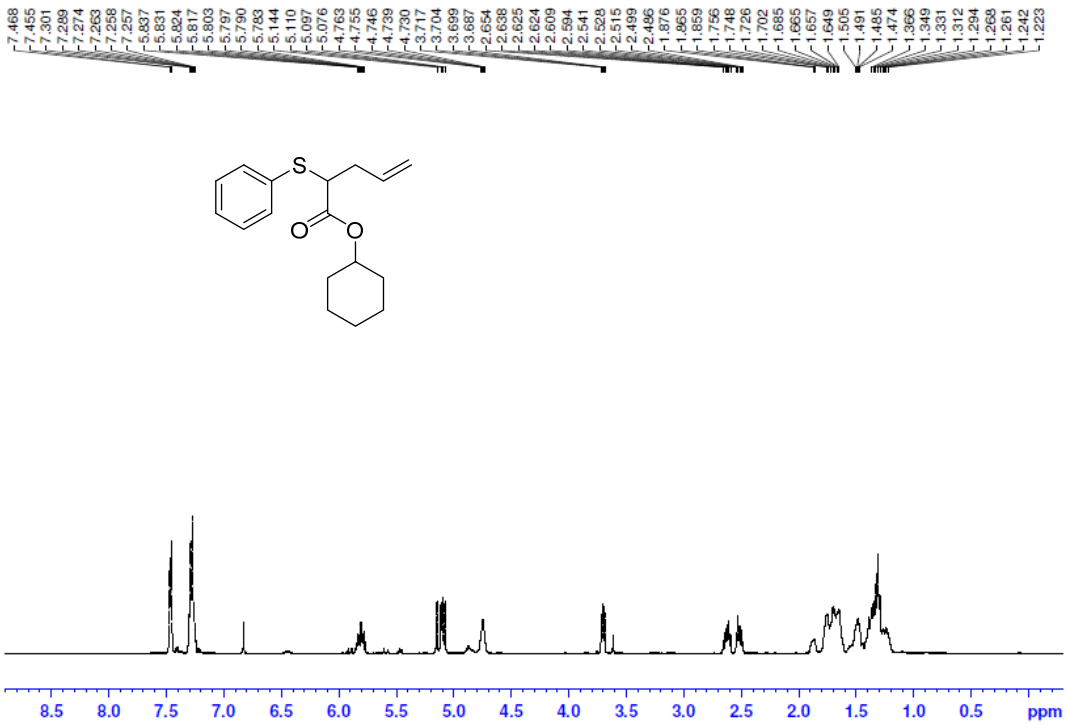
30
20
10
ppm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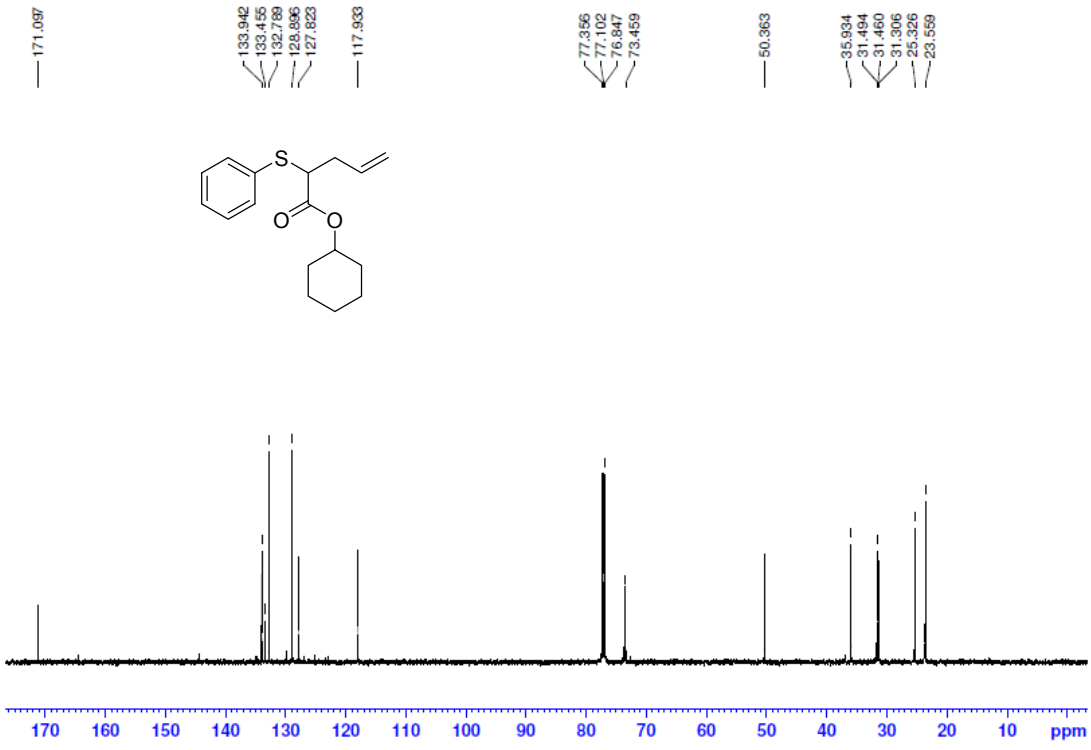
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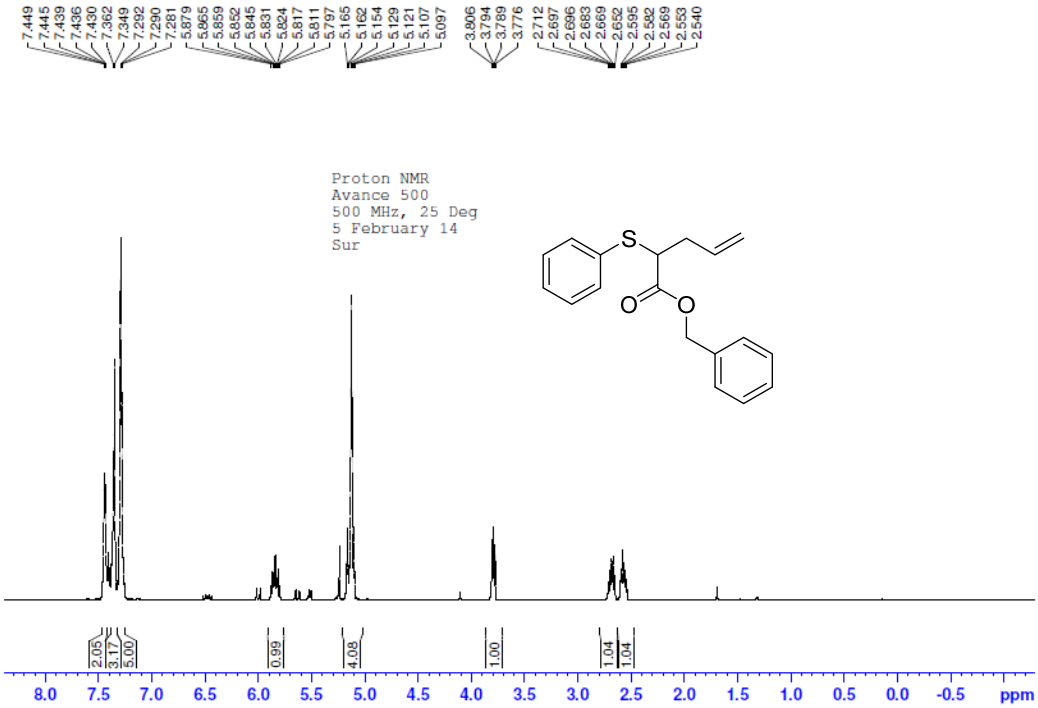
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3.794
3.789
3.776
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2.697
2.696
2.683
2.669
2.652
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2.540
Proton NMR
Avance 500
500 MHz, 25 Deg
5 February 14
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1.04
1.04
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6.0
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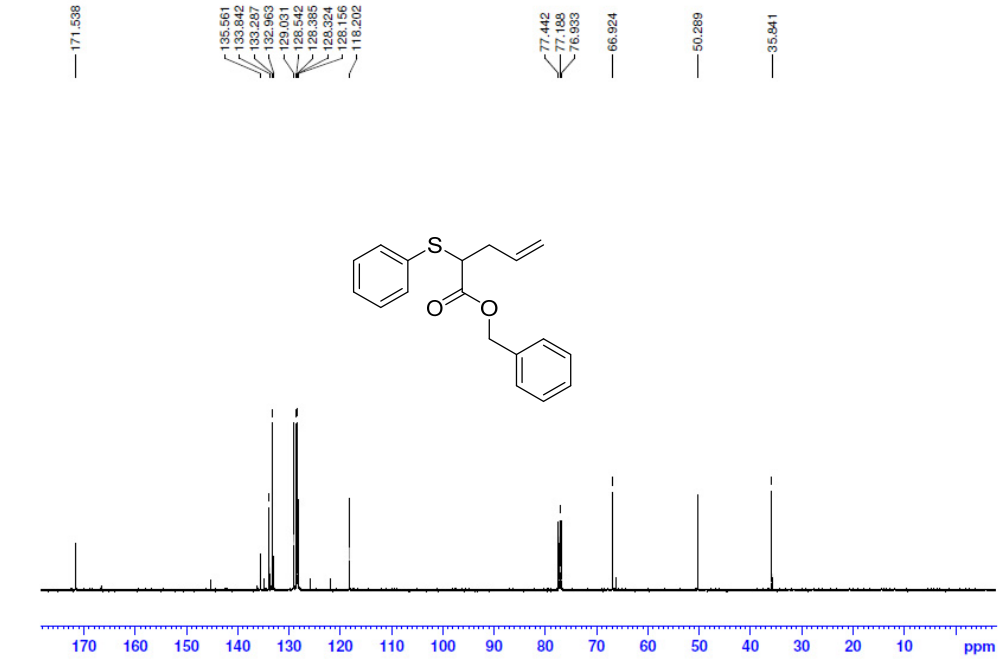
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35.841
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70
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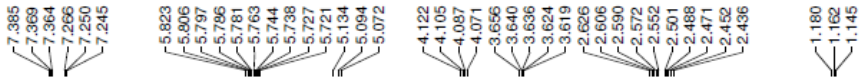
ppm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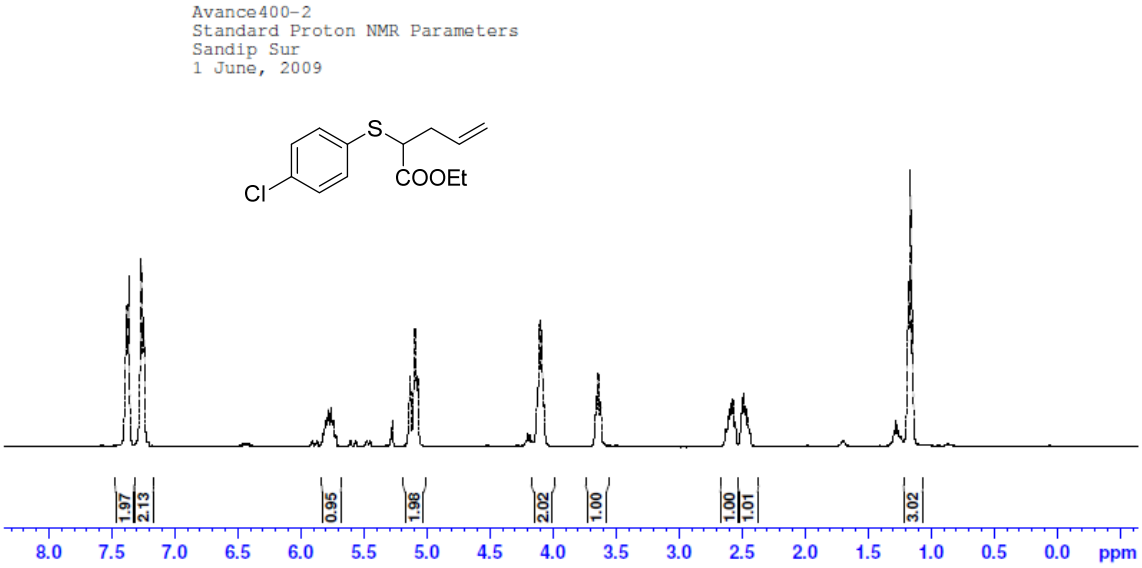
Avance400-2
Standard Proton NMR Parameters
Sandip Sur
1 June, 2009
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6.0
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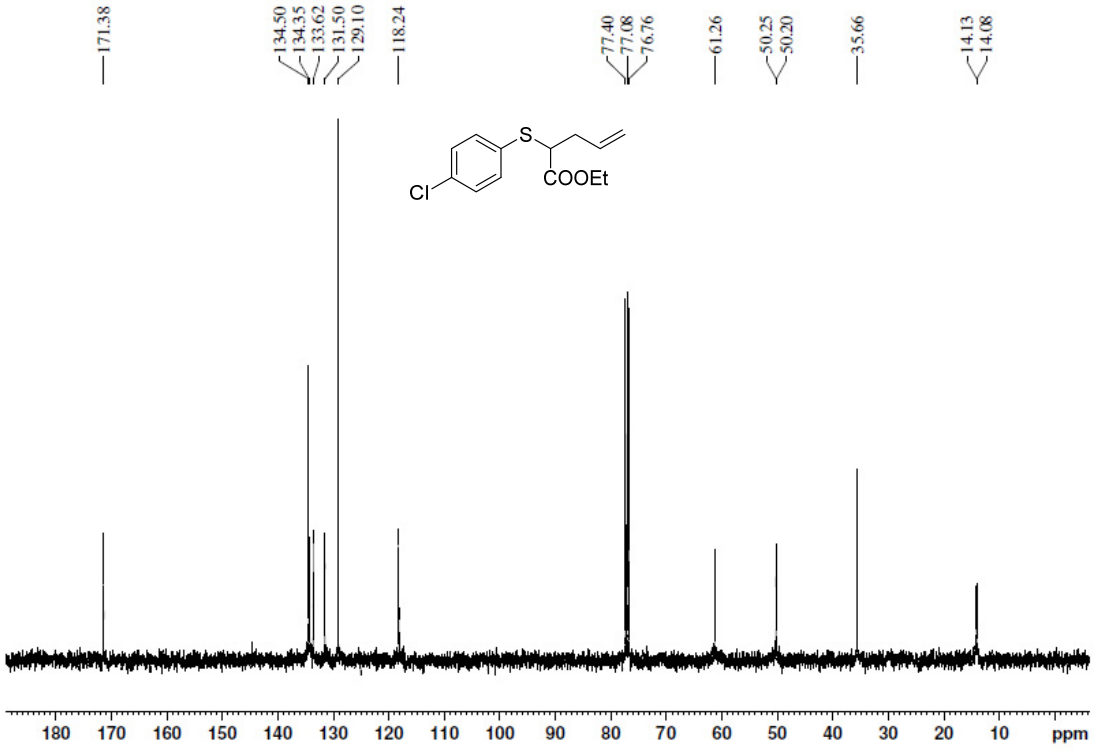
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COOEt
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110
100
90
80
70
60
50
40
30
20
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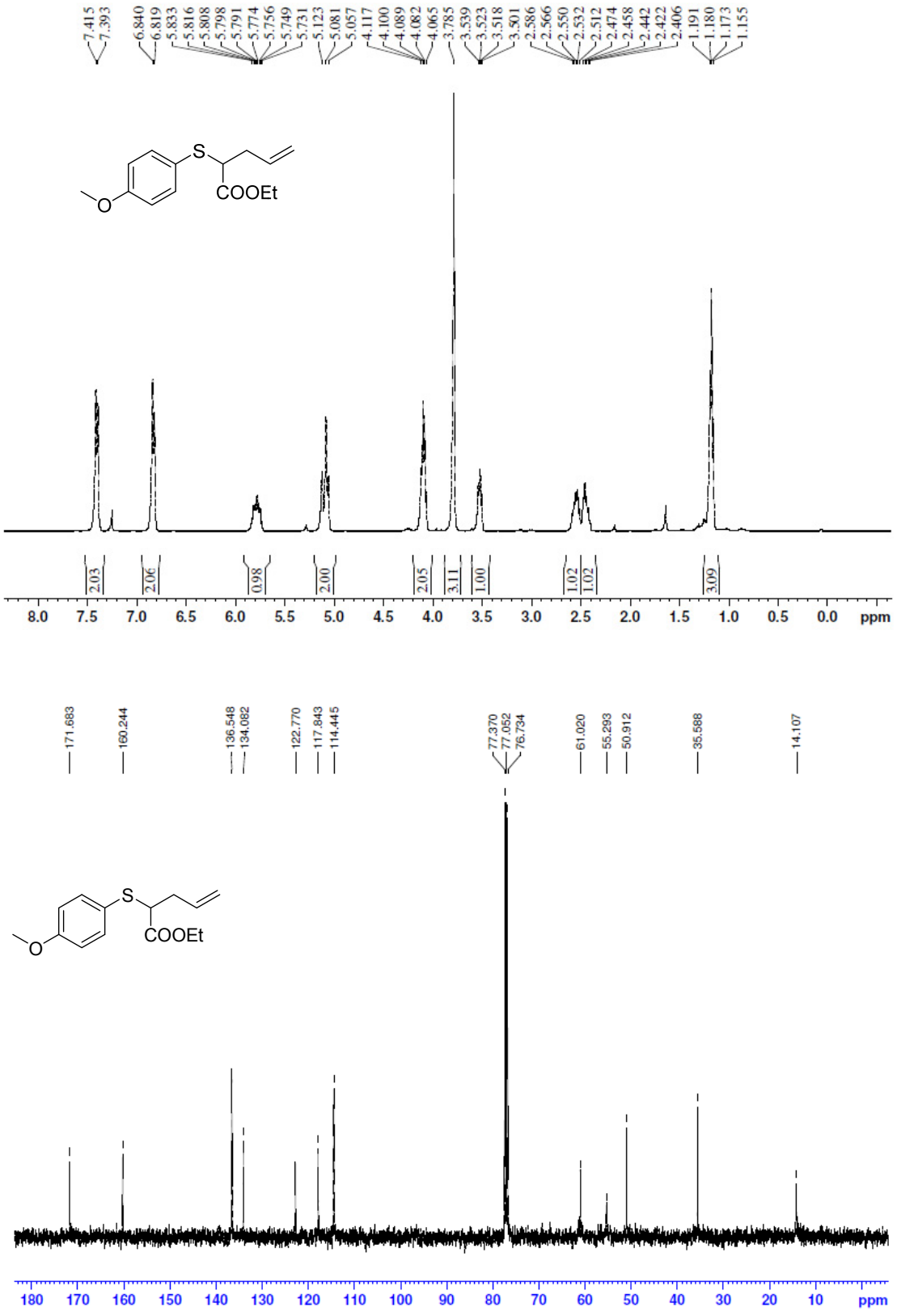
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5.731
5.123
5.081
5.057
4.117
4.100
4.089
4.082
4.065
3.785
3.539
3.523
3.518
3.501
2.586
2.566
2.550
2.532
2.512
2.474
2.458
2.442
2.422
2.406
1.191
1.180
1.173
1.155
S
COOEt
O
2.03
2.06
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2.00
2.05
3.11
1.00
1.02
1.02
3.09
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
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3.0
2.5
2.0
1.5
1.0
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61.020
55.293
50.912
35.588
14.107
S
COOEt
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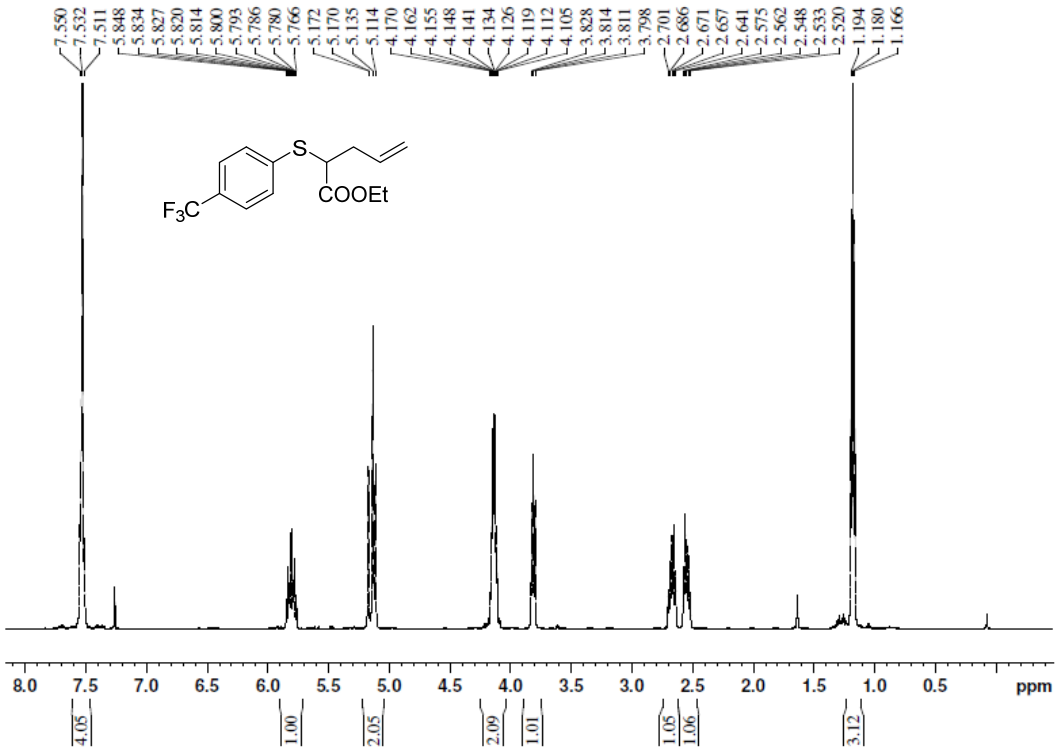
ppm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5.800
5.793
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5.780
5.766
5.172
5.170
5.135
5.114
4.170
4.162
4.155
4.148
4.141
4.134
4.126
4.119
4.112
4.105
3.828
3.814
3.811
3.798
2.701
2.686
2.671
2.657
2.641
2.575
2.562
2.548
2.533
2.520
1.194
1.180
1.166
S
COOEt
F3C
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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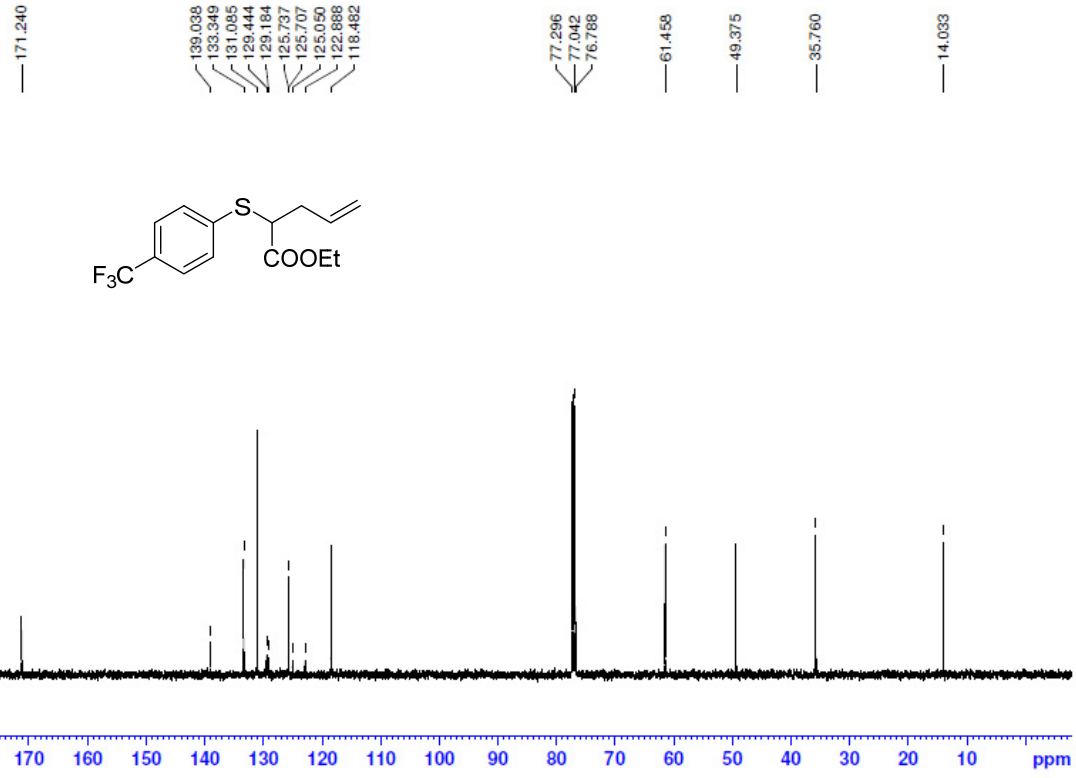
2.05
2.09
1.01
1.05
1.06
3.12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125.707
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77.296
77.042
76.788
61.458
49.375
35.760
14.033
S
COOEt
F3C
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150
140
130
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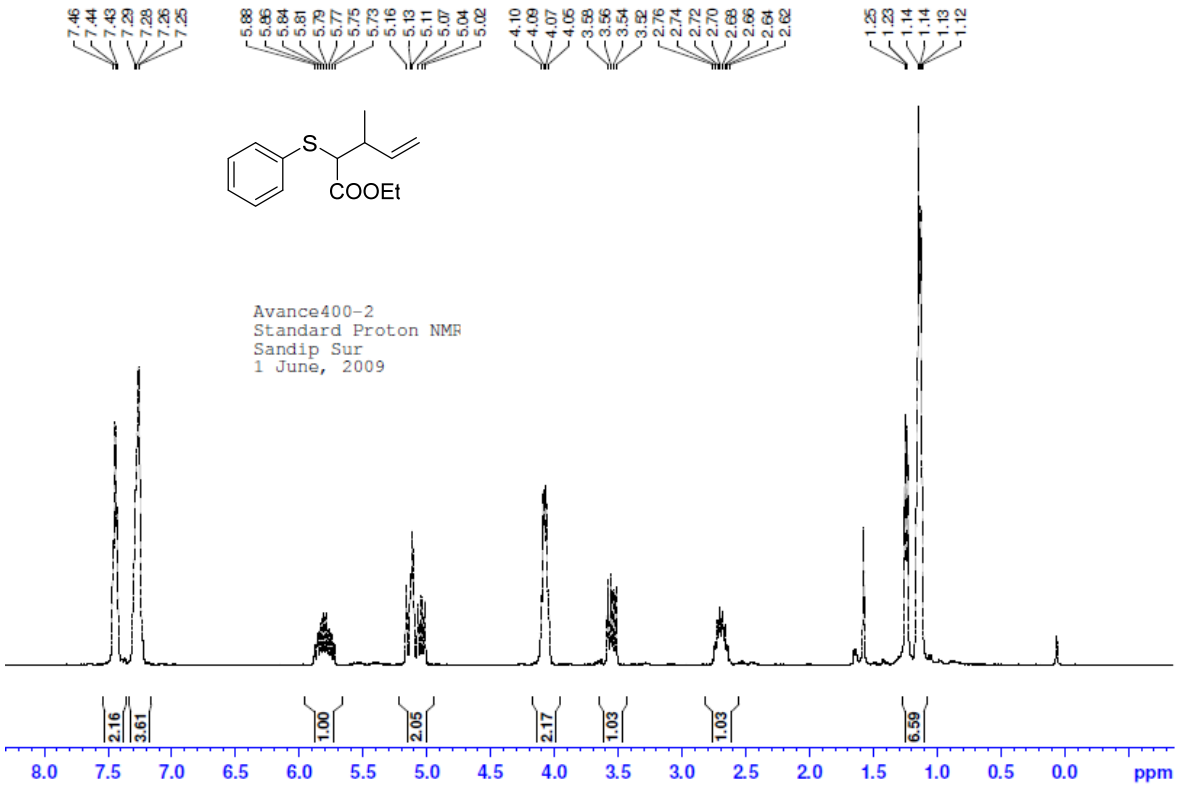
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5.77
5.75
5.73
5.16
5.13
5.11
5.07
5.04
5.02
4.10
4.09
4.07
4.05
3.58
3.56
3.54
3.52
2.76
2.74
2.72
2.70
2.68
2.66
2.64
2.62
1.25
1.23
1.14
1.14
1.13
1.12
S
COOEt
Avance400-2
Standard Proton NMR
Sandip Sur
1 June, 2009
2.16
3.61
1.00
2.05
2.17
1.03
1.03
6.59
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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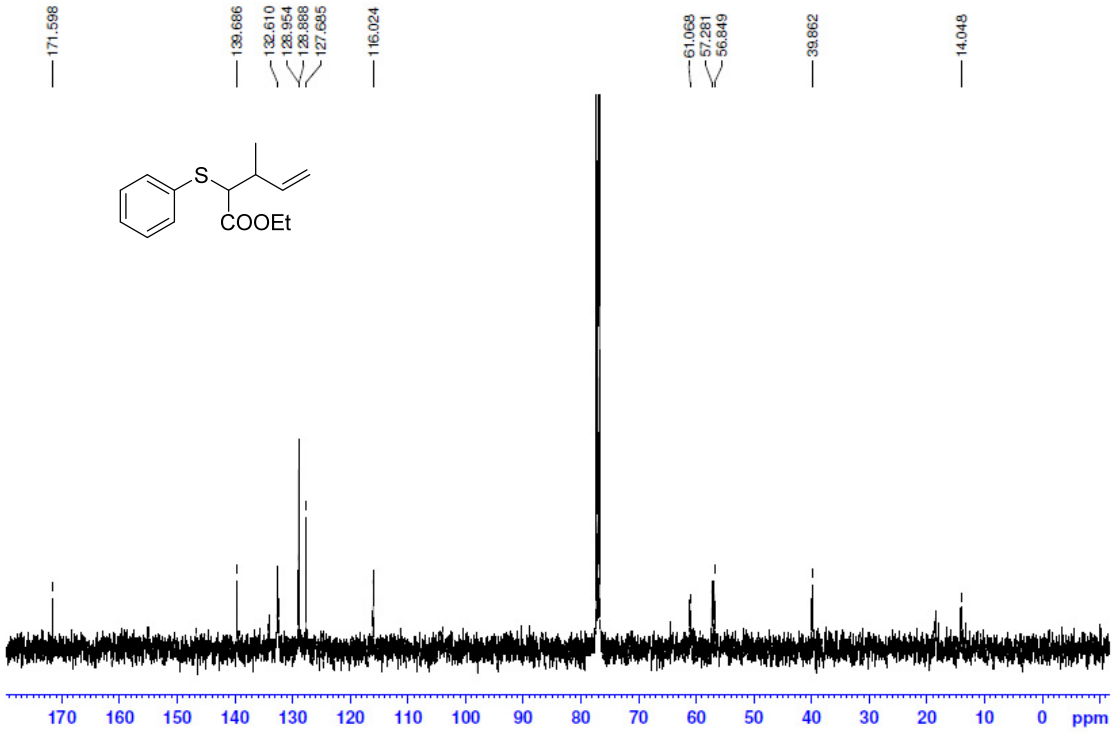
ppm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56.849
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S
COOEt
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150
140
130
120
110
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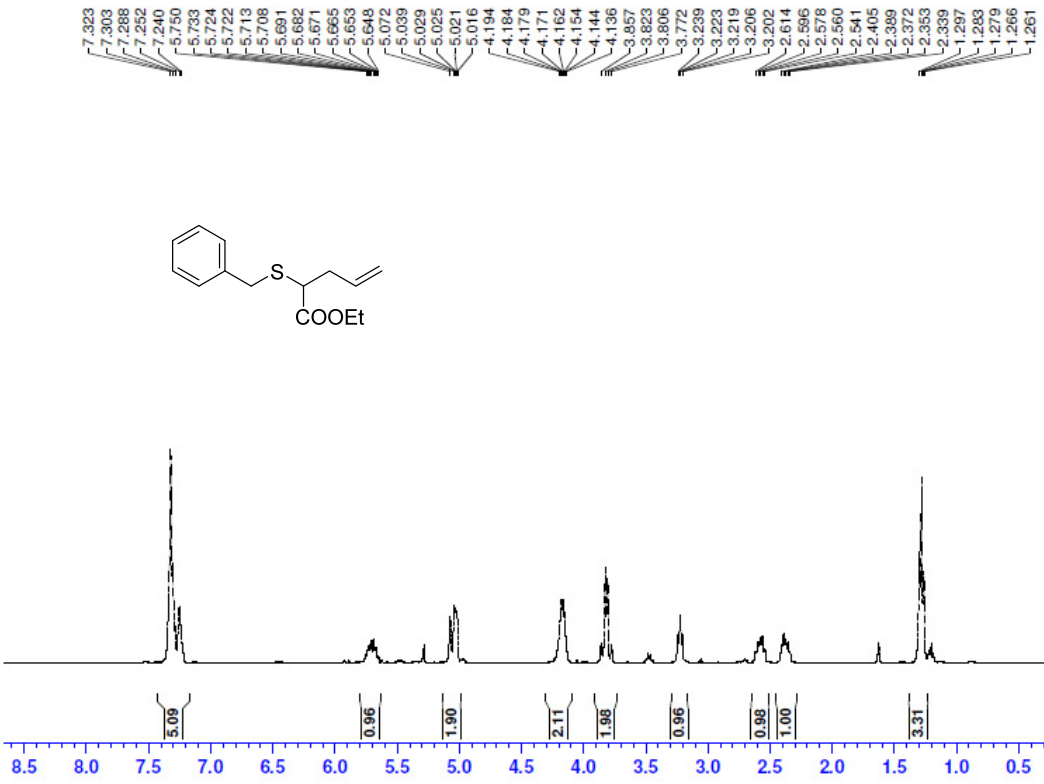
0
ppm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7.303
7.288
7.252
7.240
5.750
5.733
5.724
5.722
5.713
5.708
5.691
5.682
5.671
5.665
5.653
5.648
5.072
5.039
5.029
5.025
5.021
5.016
4.194
4.184
4.179
4.171
4.162
4.154
4.144
4.136
3.857
3.823
3.806
3.772
3.239
3.223
3.219
3.206
3.202
2.614
2.596
2.578
2.560
2.541
2.405
2.389
2.372
2.353
2.339
1.297
1.283
1.279
1.266
1.261
S
COOEt
5.09
0.96
1.90
2.11
1.98
0.96
0.98
1.00
3.31
8.5
8.0
7.5
7.0
6.5
6.0
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4.5
4.0
3.5
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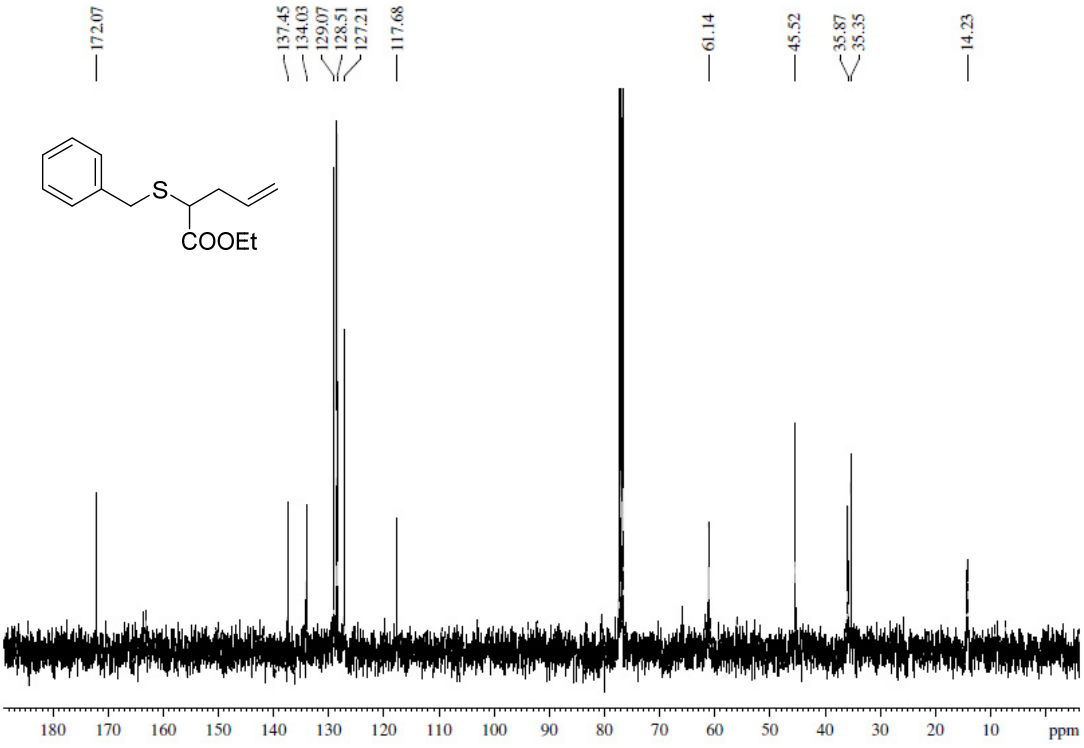
2.0
1.5
1.0
0.5
ppm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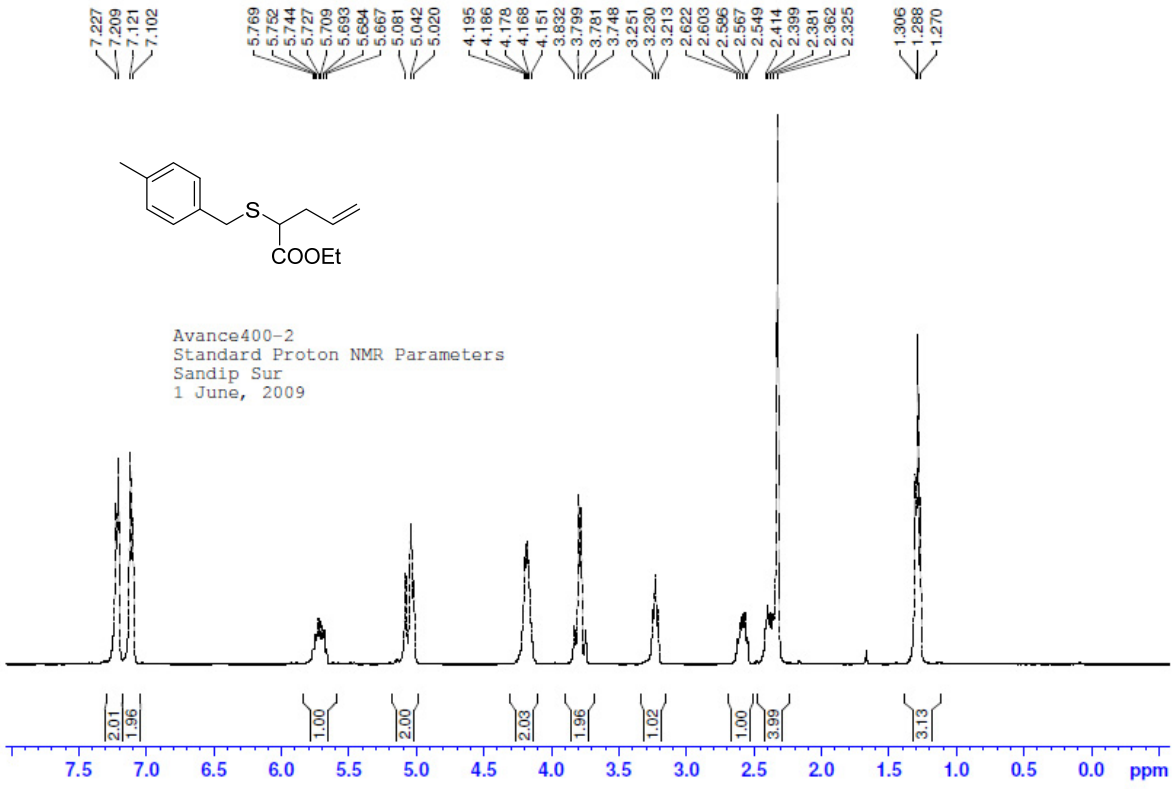
127.21
117.68
61.14
45.52
35.87
35.35
14.23
S
COOEt
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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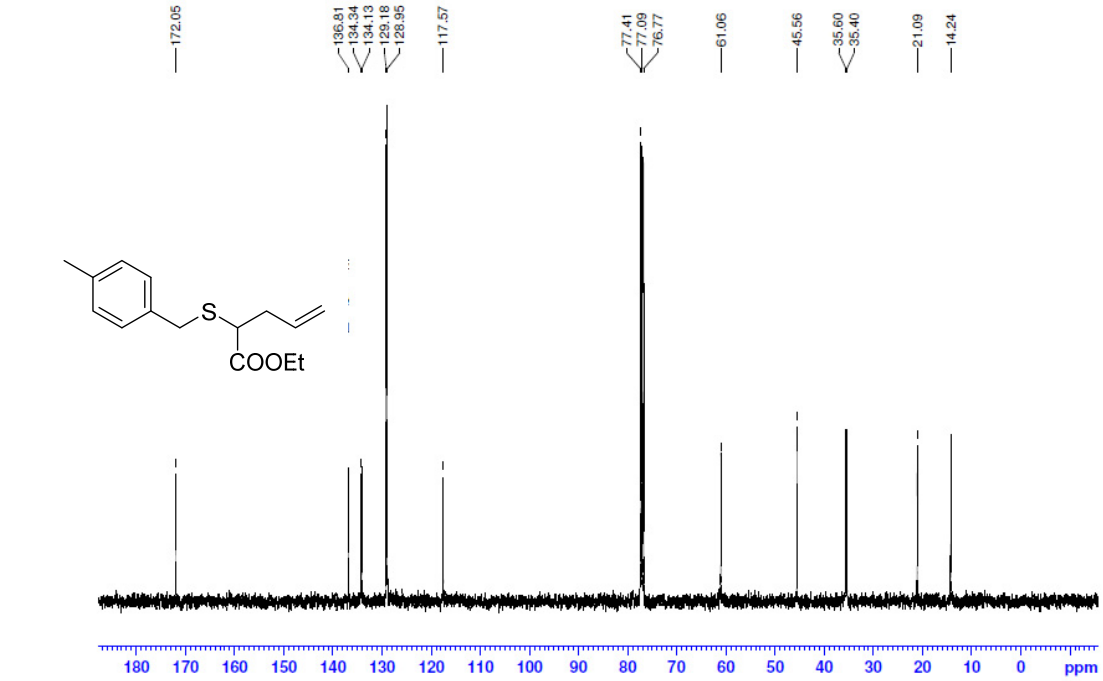
5.752
5.744
5.727
5.709
5.693
5.684
5.667
5.081
5.042
5.020
4.195
4.186
4.178
4.168
4.151
3.832
3.799
3.781
3.748
3.251
3.230
3.213
2.622
2.603
2.596
2.567
2.549
2.414
2.399
2.381
2.362
2.325
1.306
1.288
1.270
S
COOEt
Avance400-2
Standard Proton NMR Parameters
Sandip Sur
1 June, 2009
2.01
1.96
1.00
2.00
2.03
1.96
1.02
1.00
3.99
3.13
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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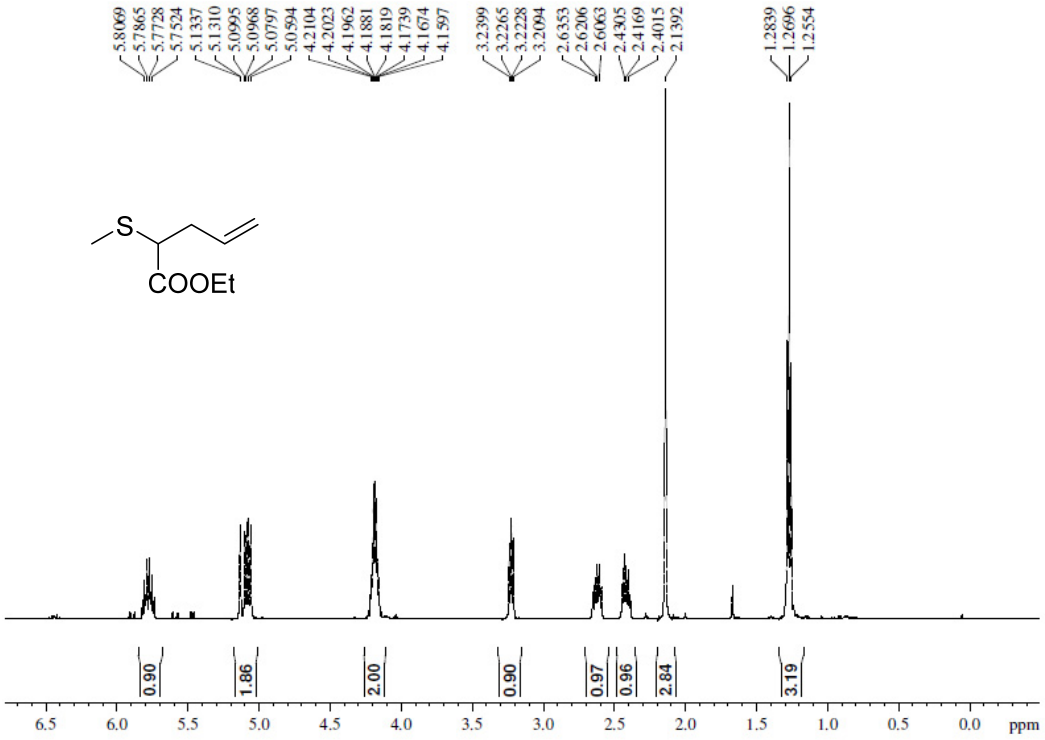
117.57
77.41
77.09
76.77
61.06
45.56
35.60
35.40
21.09
14.24
S
COOEt
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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5.1310
5.0995
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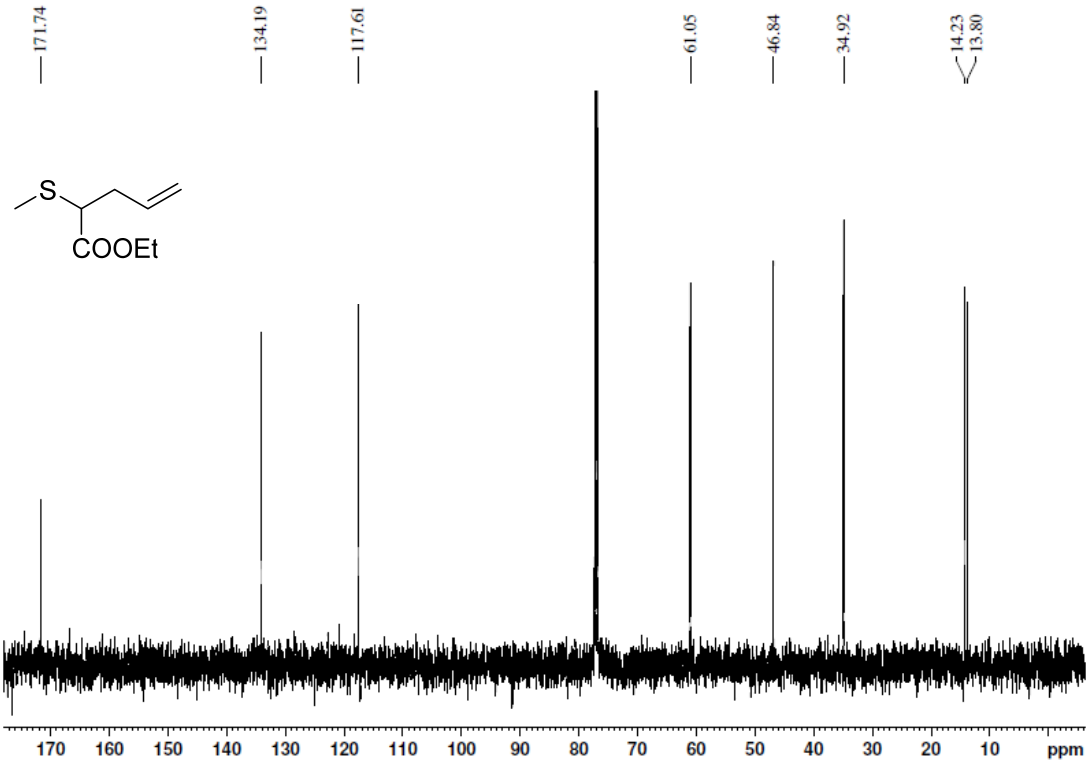
5.0797
5.0594
4.2104
4.2023
4.1962
4.1881
4.1819
4.1739
4.1674
4.1597
3.2399
3.2265
3.2228
3.2094
2.6353
2.6206
2.6063
2.4305
2.4169
2.4015
2.1392
1.2839
1.2696
1.2554
S
COOEt
0.90
1.86
2.00
0.90
0.97
0.96
2.84
3.19
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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110
100
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70
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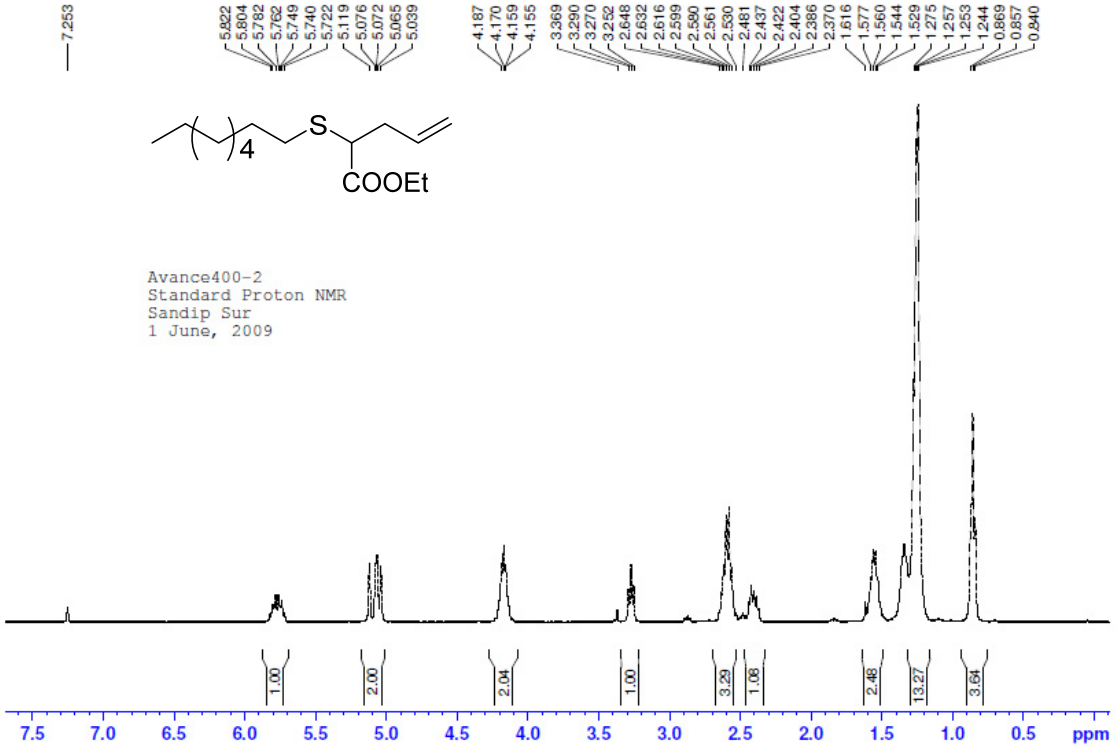
50
40
30
20
10
ppm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5.072
5.065
5.039
4.187
4.170
4.159
4.155
3.369
3.290
3.270
3.252
2.648
2.632
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2.599
2.590
2.561
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2.370
1.616
1.577
1.560
1.544
1.529
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1.257
1.253
1.244
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0.857
0.840
S
4
COOEt
Avance400-2
Standard Proton NMR
Sandip Sur
1 June, 2009
1.00
2.00
2.04
1.00
3.29
1.08
2.48
13.27
3.64
7.5
7.0
6.5
6.0
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
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1.0
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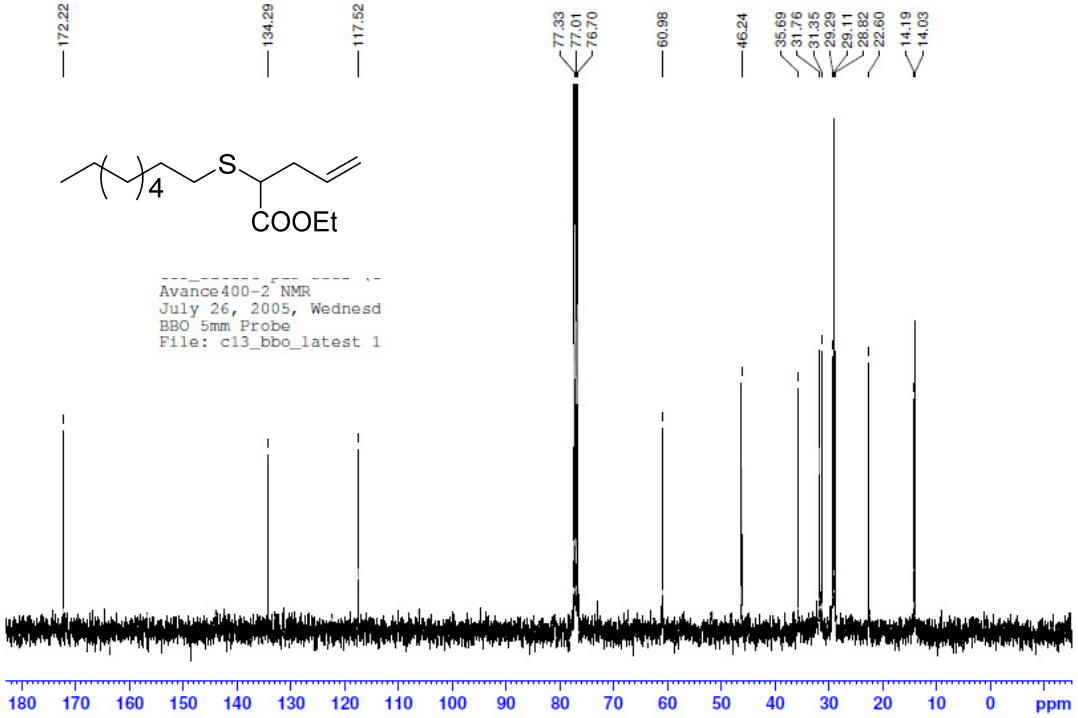
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76.70
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31.76
31.35
29.29
29.11
28.82
22.60
14.19
14.03
S
4
COOEt
Avance400-2 NMR
July 26, 2005, Wednesd
BBO 5mm Probe
File: c13_bbo_latest 1
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170
160
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140
130
120
110
100
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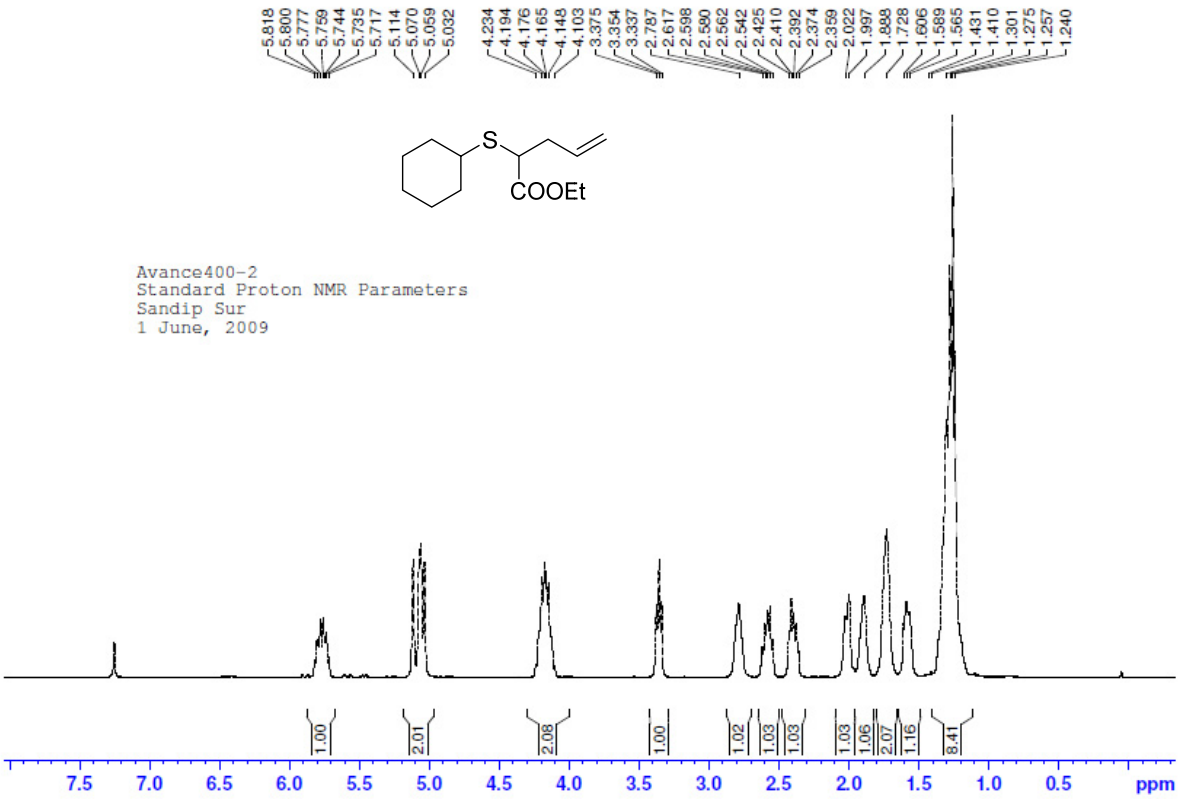
80
70
60
50
40
30
20
10
0
ppm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5.735
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5.114
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5.059
5.032
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4.194
4.176
4.165
4.148
4.103
3.375
3.354
3.337
2.787
2.617
2.598
2.590
2.562
2.542
2.425
2.410
2.392
2.374
2.359
2.022
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1.888
1.728
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1.589
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1.431
1.410
1.301
1.275
1.257
1.240
S
COOEt
Avance400-2
Standard Proton NMR Parameters
Sandip Sur
1 June, 2009
1.00
2.01
2.08
1.00
1.02
1.03
1.03
1.03
1.06
2.07
1.16
8.41
7.5
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6.5
6.0
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4.0
3.5
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2.0
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1.0
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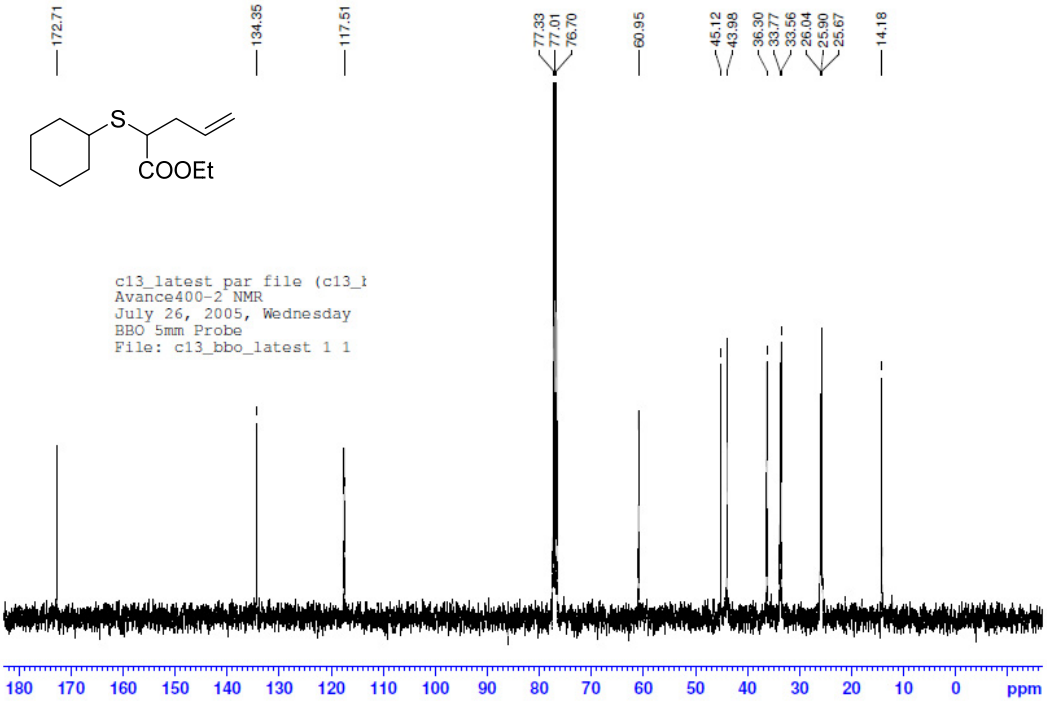
ppm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36.30
33.77
33.56
26.04
25.90
25.67
14.18
S
COOEt
c13_latest par file (c13_l
Avance400-2 NMR
July 26, 2005, Wednesday
BBO 5mm Probe
File: c13_bbo_latest 1 1
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140
130
120
110
100
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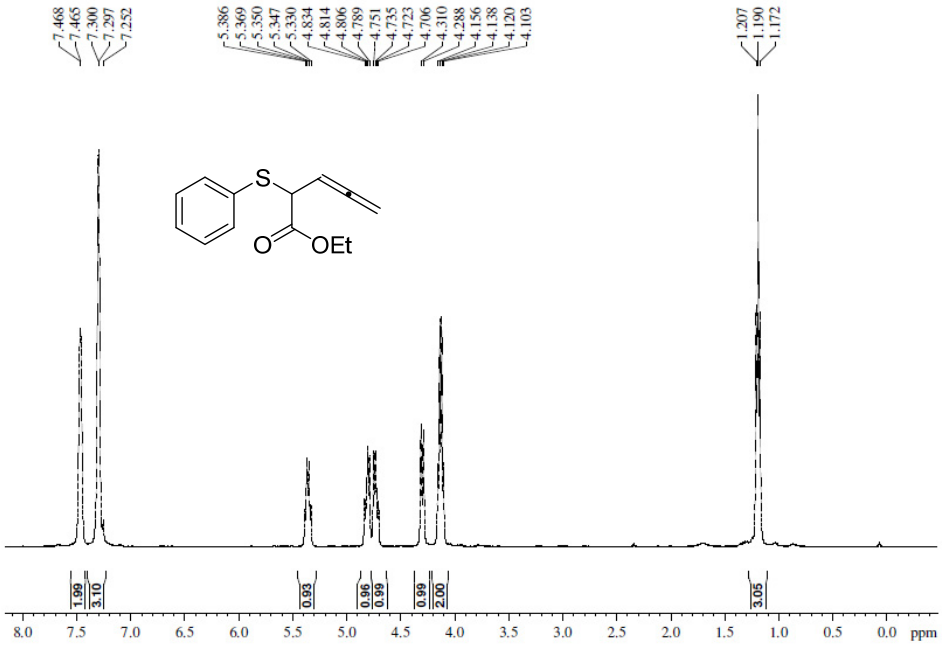
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4.814
4.806
4.789
4.751
4.735
4.723
4.706
4.310
4.288
4.156
4.138
4.120
4.103
1.207
1.190
1.172
S
O
OEt
1.99
3.10
0.93
0.96
0.99
0.99
2.00
3.05
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
3.0
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2.0
1.5
1.0
0.5
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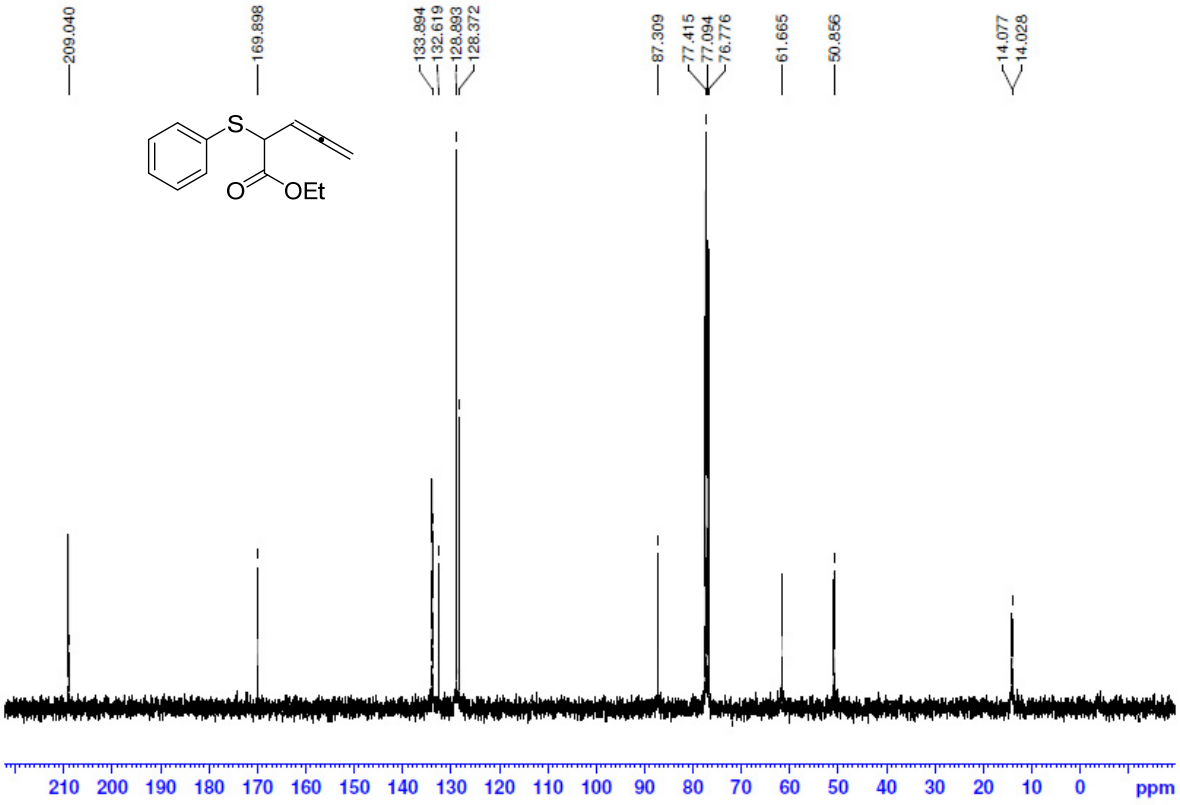
ppm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128.372
87.309
77.415
77.094
76.776
61.665
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14.077
14.028
S
O
OEt
210
200
190
180
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140
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120
110
100
90
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70
60
50
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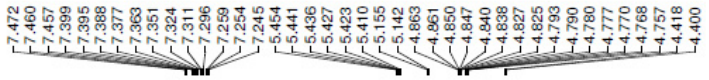
30
20
10
0
ppm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7.259
7.254
7.245
5.454
5.441
5.436
5.427
5.423
5.410
5.155
5.142
4.863
4.861
4.850
4.847
4.840
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4.827
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4.790
4.780
4.777
4.770
4.768
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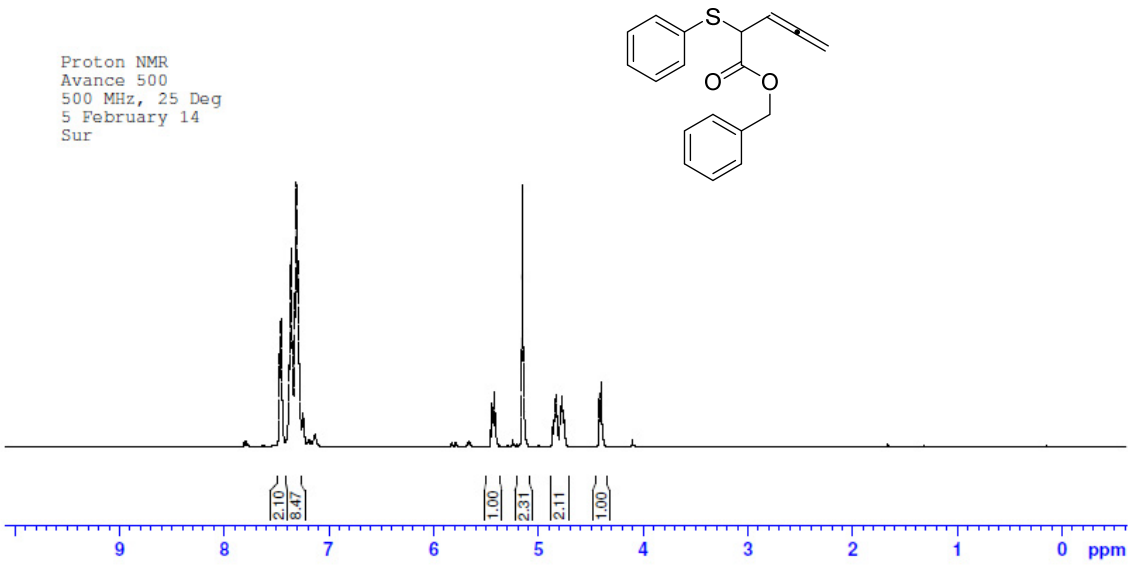
4.418
4.400


Proton NMR
Avance 500
500 MHz, 25 Deg
5 February 14
Sur
S
O
O
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2.31
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1.00
9
8
7
6
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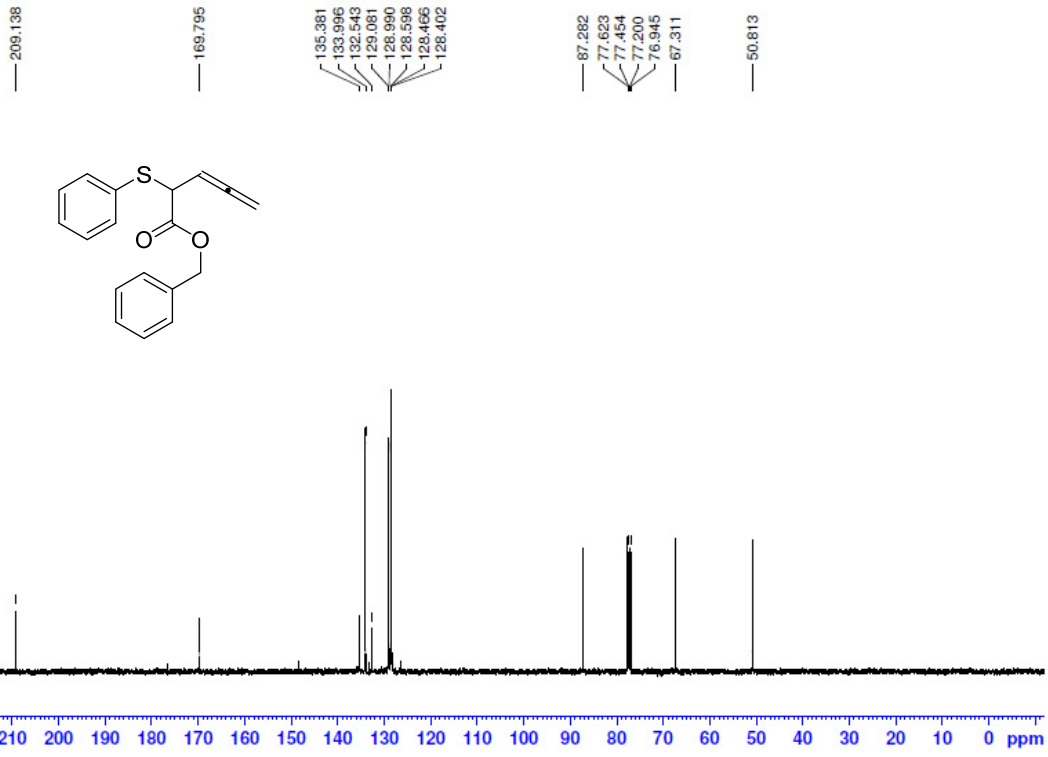
ppm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128.402
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77.623
77.454
77.200
76.945
67.311
50.813
S
O
O
220
210
200
190
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140
130
120
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60
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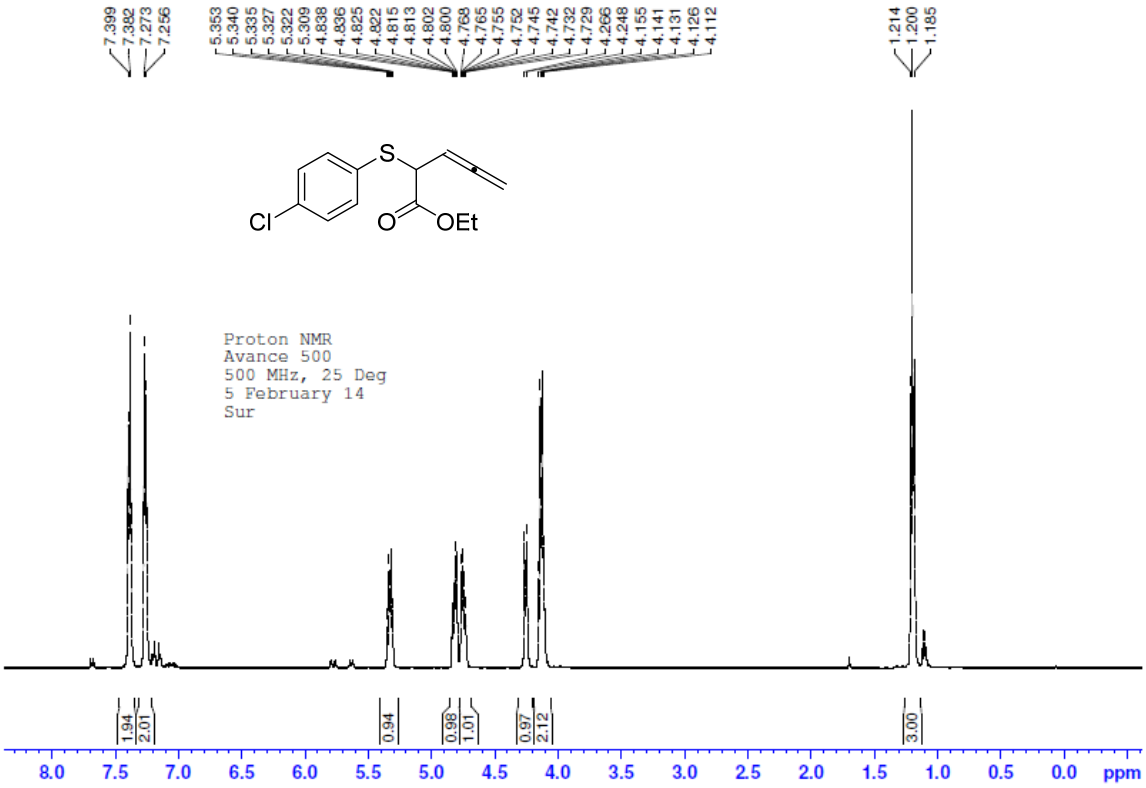
ppm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5.309
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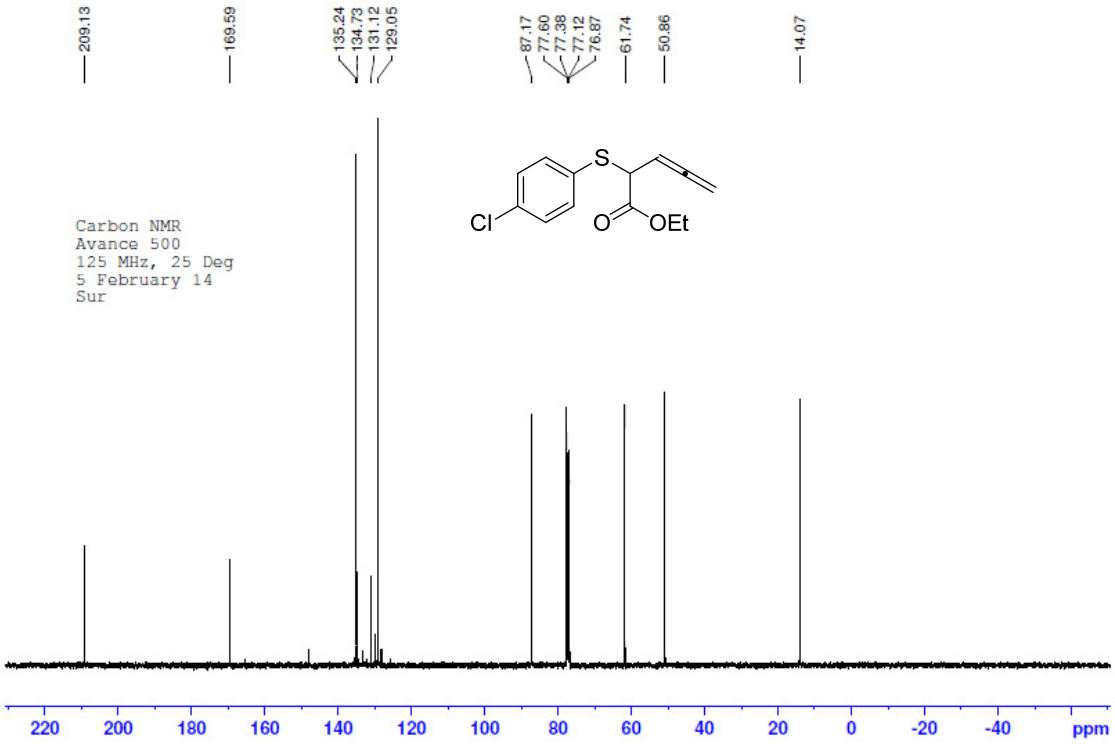
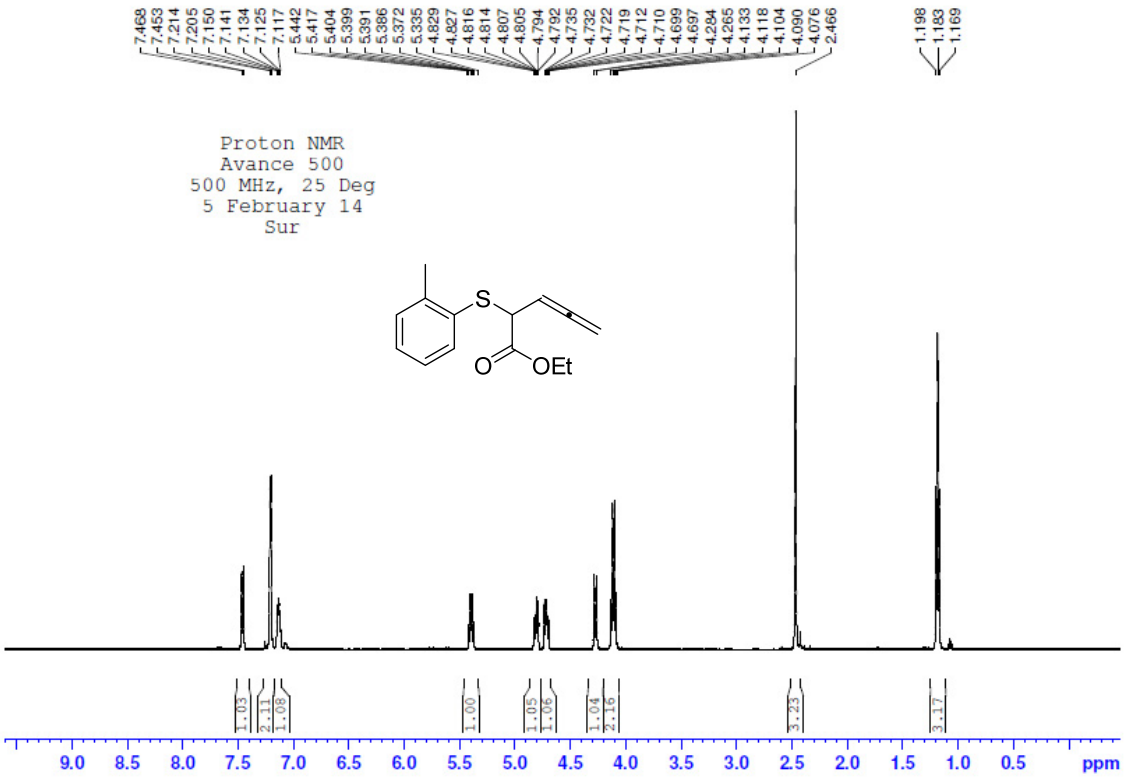
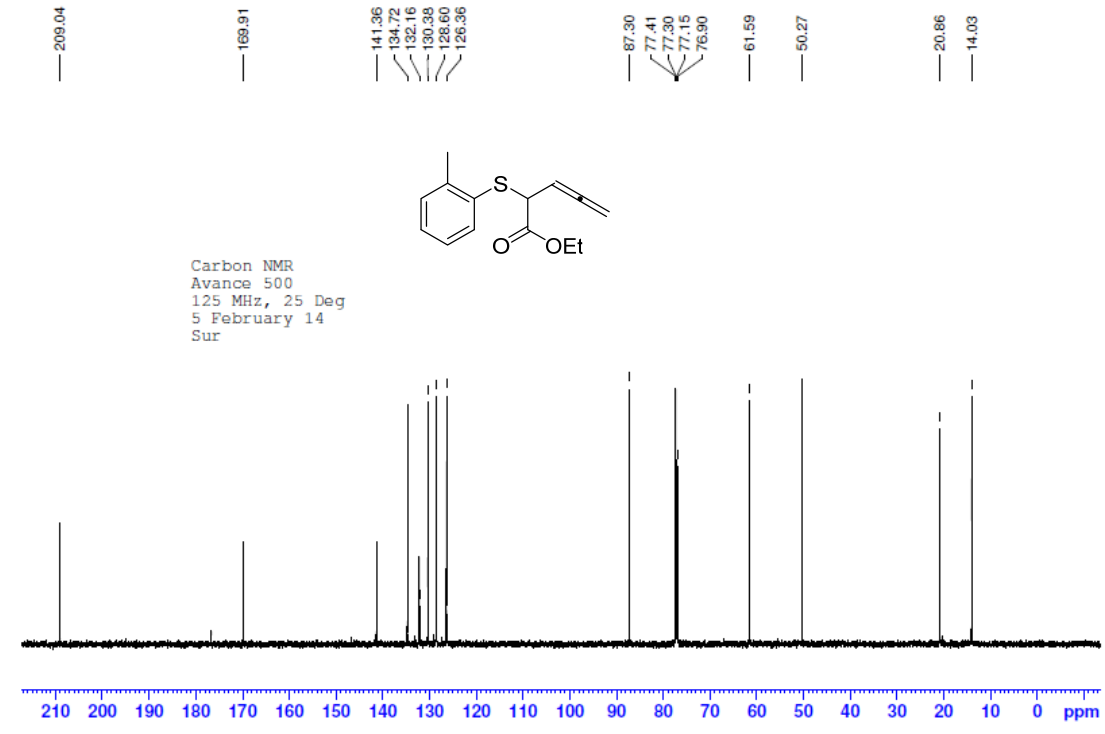
4.825
4.822
4.815
4.813
4.802
4.800
4.768
4.765
4.755
4.752
4.745
4.742
4.732
4.729
4.266
4.248
4.155
4.141
4.131
4.126
4.112
1.214
1.200
1.185
S
Cl
O
OEt
Proton NMR
Avance 500
500 MHz, 25 Deg
5 February 14
Sur
1.94
2.01
0.94
0.98
1.01
0.97
2.12
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


209.13
169.59
135.24
134.73
131.12
129.05
87.17
77.60
77.38
77.12
76.87
61.74
50.86
14.07
S
Cl
O
OEt
Carbon NMR
Avance 500
125 MHz, 25 Deg
5 February 14
Sur
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
ppm


7.468
7.453
7.214
7.205
7.150
7.141
7.134
7.125
7.117
5.442
5.417
5.404
5.399
5.391
5.386
5.372
5.335
4.829
4.827
4.816
4.814
4.807
4.805
4.794
4.792
4.735
4.732
4.722
4.719
4.712
4.710
4.699
4.697
4.284
4.265
4.133
4.118
4.104
4.090
4.076
2.466
1.198
1.183
1.169
Proton NMR
Avance 500
500 MHz, 25 Deg
5 February 14
Sur
S
O
OEt
1.03
2.11
1.08
1.00
1.05
1.06
1.04
2.16
3.25
3.17
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


209.04
169.91
141.36
134.72
132.16
130.38
128.60
126.36
87.30
77.41
77.30
77.15
76.90
61.59
50.27
20.86
14.03
S
O
OEt
Carbon NMR
Avance 500
125 MHz, 25 Deg
5 February 14
Sur
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm