Phosphine-Catalyzed Asymmetric Additions of Malonate Esters to γ-Substituted Allenoates and Allenamides

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Supporting Information

Table of Contents

I. General Information

The following reagents were purchased and used as received: toluene (Sigma-Aldrich; anhydrous in a Sure-Seal bottle), diethyl malonate (Alfa), and 2-methoxyphenol (Sigma-Aldrich). Diallyl malonate[1] and phosphepine **1**[2] were synthesized according to literature procedures. HPLC analyses were carried out on an Agilent 1100 Series system with Daicel Chiralpak® columns in hexane/isopropanol mixtures.

II. Preparation of Allenes

General Procedure A: Preparation of Allenes. A 250-mL flask was charged with the olefinating agent (ethyl (triphenylphosphoranylidene)acetate, benzyl

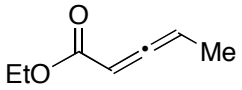
(1) Imao D, Itoi A, Yamazaki A, Shirakura M, Ohtoshi R, Ogata K, Ohmori Y, Ohta T, Ito Y (2007) Easy access to esters with a benzylic quaternary carbon center from diallyl malonates by palladium-catalyzed decarboxylative allylation. *J Org Chem* 72:1652–1658.

(2) Junge K, Hagemann B, Enthaler S, Spannenberg A, Michalik M, Oehme G, Monsees A, Riermeier T, Beller M (2004) Synthesis of chiral monodentate binaphthophosphepine ligands and their application in asymmetric hydrogenations. *Tetrahedron: Asymmetry* 15:2621–2631.

(triphenylphosphoranylidene)acetate, or *N*-methoxy-*N*-methyl(triphenylphosphoranylidene)acetamide) (20.0 mmol), evacuated, and backfilled with argon. CH_2Cl_2 (100 mL) and Et_3N (2.50 mL, 18.0 mmol) were added via syringe, and the solution was cooled to –78 °C. The acid chloride (20.0 mmol) was then added dropwise via syringe over 10 min. The solution was allowed to warm to room temperature over 3-4 h. Then, the reaction mixture was concentrated to one-third of the original volume, and pentane (100 mL) was added. The mixture was stirred for 1 h, and then it was passed through a pad of celite. The filtrate was concentrated on a rotary evaporator, and the residue was purified by flash chromatography (hexanes/Et_2O), which furnished the allene as an oil.

The synthesis of the allenoates depicted in entries 2, 3, 5, and 6 of Table 2 has been described previously.[3]

The yields have not been optimized.



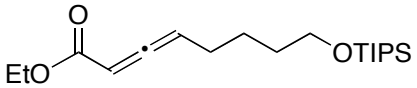
(±)-Ethyl penta-2,3-dienoate. The compound was prepared from propionyl chloride according to General Procedure A (purification by flash chromatography: 10% Et_2O in pentane; 50% yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.61-5.51 (m, 2H), 4.18 (q, J = 7.2 Hz, 2H), 1.77 (dd, J = 3.2 Hz, J = 7.2 Hz, 3H), 1.26 (t, J = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.9, 166.2, 90.2, 87.7, 60.7, 14.2, 12.8.

IR (film) 2983, 2932, 1962, 1721, 1445, 1413, 1253, 1161 cm^{-1}.

LRMS (ES+) calcd for $C_7H_{10}O_2$ (M^+) 126.1, found 126.9.



(±)-Ethyl 8-(triisopropylsilyloxy)octa-2,3-dienoate. The compound was prepared from 6-(triisopropylsilyloxy)hexanoyl chloride according to General Procedure A (purification by flash chromatography: 10% Et_2O in hexanes; 65% yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.64-5.56 (m, 2H), 4.18 (dq, J = 1.6 Hz, J = 7.2 Hz, 2H), 3.69 (t, J = 6.4 Hz, 2H), 2.20-2.14 (m, 2H), 1.64-1.52 (m, 4H), 1.28 (t, J = 7.2 Hz, 3H), 1.13-1.02 (m, 21H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.6, 166.4, 95.4, 88.6, 63.0, 61.0, 32.2, 27.3, 25.1, 18.0, 14.6, 12.0.

IR (film) 2942, 2866, 1962, 1721, 1464, 1255, 1159, 1108 cm^{-1}.

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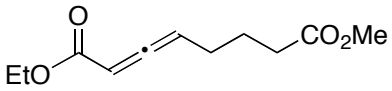
(3) Sun J, Fu GC (2010) Phosphine-catalyzed formation of carbon–sulfur bonds: Catalytic asymmetric synthesis of γ-thioesters. *J Am Chem Soc* 132:4568–4569.

LRMS (ES+) calcd for $C_{19}H_{37}O_3Si$ ($M+H^+$) 341.3, found 341.9.



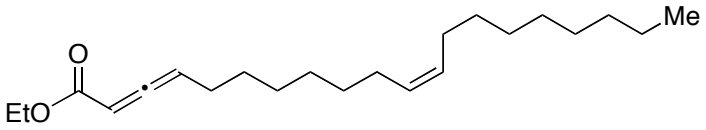
(±)-1-Ethyl 8-methyl octa-2,3-dienedioate. The compound was prepared from methyl 6-chloro-6-oxohexanoate according to General Procedure A (purification by flash chromatography: 10% Et_2O in hexanes; 75% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 5.57-5.54 (m, 2H), 4.17-4.12 (m, 2H), 3.62 (s, 3H), 2.36 (dt, J = 2.0 Hz, J = 7.2 Hz, 2H), 2.18-2.12 (m, 2H), 1.80-1.74 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.2, 173.6, 165.9, 94.3, 88.6, 60.7, 51.4, 32.8, 26.7, 23.6, 14.1.

IR (film) 2983, 2953, 1961, 1717, 1438, 1420, 1254 cm^{-1}.

LRMS (ES+) calcd for $C_{11}H_{16}O_4$ (M^+) 212.1, found 212.9.



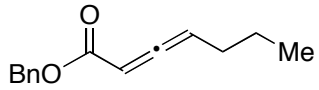
(±)-(*Z*)-Ethyl icosa-2,3,11-trienoate. The compound was prepared from (*Z*)-9-octadecenoyl chloride according to General Procedure A (purification by flash chromatography: 10% Et_2O in hexanes; 71% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 5.63-5.55 (m, 2H), 5.38-5.31 (m, 2H), 4.18 (q, J = 7.2 Hz, 2H), 2.16-2.09 (m, 2H), 2.04-1.99 (m, 4H), 1.47-1.26 (m, 23H), 0.87 (t, J = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.3, 166.3, 130.0, 129.7, 95.3, 88.2, 60.7, 31.9, 29.8, 29.6, 29.5, 29.3 (2), 29.0, 28.8, 28.7, 27.5, 27.2, 27.1, 22.7, 14.2, 14.1.

IR (film) 2927, 2855, 1962, 1720, 1465, 1252, 1157 cm^{-1}.

LRMS (ES+) calcd for $C_{22}H_{39}O_2$ ($M+H^+$) 335.3, found 335.3.



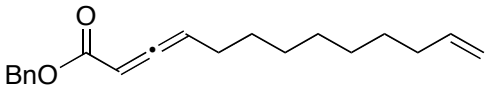
(±)-Benzyl hepta-2,3-dienoate. The compound was prepared from valeryl chloride according to General Procedure A (purification by flash chromatography: 10% Et_2O in hexanes; 67% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.31 (m, 5H), 5.64-5.61 (m, 2H), 5.21 (d, J = 12.4 Hz, 1H), 5.16 (d, J = 12.4 Hz, 1H), 2.15-2.09 (m, 2H), 1.53-1.44 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.7, 166.1, 136.0, 128.5, 128.11, 128.07, 95.3, 88.0, 66.4, 29.5, 22.0, 13.5.

IR (film) 3034, 2961, 2934, 2874, 1960, 1722, 1498, 1456, 1260, 1152 cm^{-1}.

LRMS (ES+) calcd for $C_{14}H_{17}O_2$ ($M+H^+$) 217.1, found 217.8.



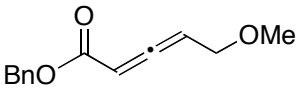
(±)-Benzyl trideca-2,3,12-trienoate. The compound was prepared from undec-10-enoyl chloride according to General Procedure A (purification by flash chromatography: 10% Et_2O in hexanes; 75% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.32 (m, 5H), 5.86-5.76 (m, 1H), 5.66-5.62 (m, 2H), 5.20 (d, J = 12.8 Hz, 1H), 5.16 (d, J = 12.8 Hz, 1H), 5.02-4.92 (m, 2H), 2.16-2.10 (m, 2H), 2.06-2.01 (m, 2H), 1.49-1.27 (m, 10H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.6, 166.1, 139.1, 136.0, 128.5, 128.1, 128.0, 114.2, 95.6, 88.0, 66.4, 33.8, 29.2, 29.0, 28.9, 28.7, 27.4.

IR (film) 3068, 3034, 2928, 2855, 1960, 1723, 1456, 1257, 1150 cm^{-1}.

LRMS (ES+) calcd for $C_{20}H_{26}O_2$ (M^+) 298.2, found 298.9.



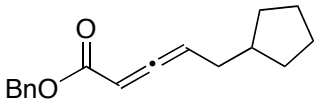
(±)-Benzyl 5-methoxypenta-2,3-dienoate. The compound was prepared from 3-methoxypropanoyl chloride according to General Procedure A (purification by flash chromatography: 15% Et_2O in hexanes; 60% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.28 (m, 5H), 5.74-5.64 (m, 2H), 5.18 (d, J = 12.4 Hz, 1H), 5.14 (d, J = 12.8 Hz, 1H), 4.11-3.99 (m, 2H), 3.30 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.6, 165.3, 135.7, 128.5, 128.23, 128.18, 92.9, 89.0, 68.5, 66.7, 57.8.

IR (film) 3066, 3034, 2989, 1963, 1717, 1456, 1260, 1153 cm^{-1}.

LRMS (ES+) calcd for $C_{13}H_{15}O_3$ ($M+H^+$) 219.1, found 219.9.



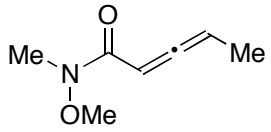
(±)-Benzyl 5-cyclopentylpenta-2,3-dienoate. The compound was prepared from 3-cyclopentylpropanoyl chloride according to General Procedure A (purification by flash chromatography: 10% Et_2O in hexanes; 75% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.26 (m, 5H), 5.63-5.58 (m, 2H), 5.21 (d, J = 12.0 Hz, 1H), 5.16 (d, J = 12.8 Hz, 1H), 2.16-2.12 (m, 2H), 1.97-1.90 (m, 1H), 1.80-1.73 (m, 2H), 1.63-1.44 (m, 4H), 1.20-1.12 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.9, 166.1, 136.0, 128.5, 128.2, 128.1, 94.8, 87.6, 66.4, 39.4, 33.9, 32.3, 25.22, 25.20.

IR (film) 3066, 3034, 2950, 2867, 1960, 1722, 1498, 1257, 1149 cm^{-1}.

LRMS (ES+) calcd for $C_{17}H_{21}O_2$ ($M+H^+$) 257.2, found 257.8.



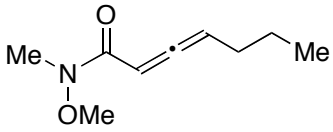
(±)-*N*-Methoxy-*N*-methylpenta-2,3-dienamide. The compound was prepared from propionyl chloride according to General Procedure A (purification by flash chromatography: 50% EtOAc in hexanes; 50% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 6.12-6.10 (m, 1H), 5.62-5.58 (m, 1H), 3.70 (s, 3H), 3.22 (s, 3H), 1.77 (dd, J = 3.2 Hz, J = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.6, 165.9, 90.1, 85.7, 61.6, 32.5, 12.9.

IR (film) 2975, 2937, 1961, 1654, 1422, 1356, 1179 cm^{-1}.

LRMS (ES+) calcd for $C_7H_{11}NO_2$ (M^+) 141.1, found 141.9.



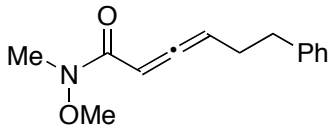
(±)-*N*-Methoxy-*N*-methylhepta-2,3-dienamide. The compound was prepared from valeryl chloride according to General Procedure A [purification by flash chromatography: 1/1 mixture of CH_2Cl_2 and (20%→50% EtOAc in hexanes); 55% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 6.15-6.12 (m, 1H), 5.64-5.59 (m, 1H), 3.69 (s, 3H), 3.21 (s, 3H), 2.13-2.06 (m, 2H), 1.52-1.42 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.1, 166.0, 95.1, 86.1, 61.6, 32.5, 29.6, 22.1, 13.5.

IR (film) 2962, 2874, 1959, 1653, 1425, 1365, 1178 cm^{-1}.

LRMS (ES+) calcd for $C_9H_{16}NO_2$ ($M+H^+$) 170.1, found 170.0.



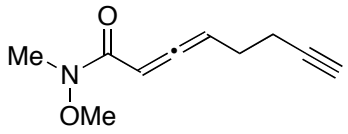
(±)-*N*-Methoxy-*N*-methyl-6-phenylhexa-2,3-dienamide. The compound was prepared from 4-phenylbutanoyl chloride according to General Procedure A (purification by flash chromatography: 50% EtOAc in hexanes; 45% yield).

^1H NMR ($CDCl_3$, 400 MHz) δ 7.27-7.23 (m, 2H), 7.18-7.14 (m, 3H), 6.15-6.12 (m, 1H), 5.69-5.64 (m, 1H), 3.67 (s, 3H), 3.21 (s, 3H), 2.77-2.73 (m, 2H), 2.45-2.39 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.0, 165.9, 141.2, 128.4, 128.3, 126.0, 94.8, 86.7, 61.6, 35.1, 32.6, 29.2.

IR (film) 3027, 2936, 2858, 1959, 1652, 1496, 1425, 1364, 1178 cm^{-1}.

LRMS (ES+) calcd for $C_{14}H_{17}NO_2$ (M^+) 231.1, found 231.9.



***N*-Methoxy-*N*-methylocta-2,3-dien-7-ynamide.** The compound was prepared from hex-5-ynoyl chloride according to General Procedure A (purification by flash chromatography: 1/1 mixture of CH_2Cl_2 and (20%→50% EtOAc in hexanes); 40% yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.23-6.20 (m, 1H), 5.76-5.71 (m, 1H), 3.71 (s, 3H), 3.24 (s, 3H), 2.41-2.32 (m, 4H), 1.99 (t, J = 2.4 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 211.8, 165.6, 93.9, 87.2, 83.1, 69.1, 61.7, 32.6, 26.7, 18.1.

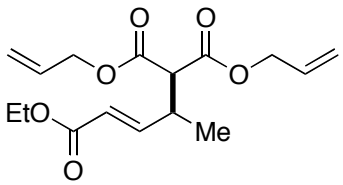
IR (film) 3295, 3243, 2966, 2937, 1962, 1651, 1430, 1367, 1180, 996 cm^{-1}.

LRMS (ES+) calcd for $C_{10}H_{13}NO_2$ (M^+) 179.1, found 179.9.

III. Phosphine-Catalyzed Enantioselective γ Additions

General Procedure B. An oven-dried 4-mL vial was charged with (*S*)-**1** (19.5 mg, 0.050 mmol), anhydrous toluene (0.3 mL), 2-methoxyphenol (5.5 μL, 0.050 mmol), and the 1,3-dicarbonyl compound (0.55 mmol). The vial was capped, purged with nitrogen for 1 min, and cooled to –30 °C. Next, the allene (0.50 mmol) was added via syringe over 2 min. The cap was then sealed with grease, and the mixture was stirred at –30 °C for 48 h. Next, hydrogen peroxide (30% in H_2O; 0.2 mL) was added dropwise, and the mixture was stirred for 30 min. The reaction mixture was then warmed to 0 °C, and a saturated aqueous solution of Na_2SO_3 (2 mL) was added dropwise. The aqueous layer was extracted with Et_2O (3 mL × 3; EtOAc for Weinreb amides), and the combined organic layers were dried over Na_2SO_4 and filtered. The solvent was removed on a rotary evaporator, and the product was purified by flash chromatography.

Notes: 1) A gram-scale reaction was conducted for entry 7 of Table 2 (see below). 2) Phosphepine **1** is relatively stable to oxidation: after exposure to air for two weeks, only a trace of the phosphine oxide was observed by ^{31}P NMR spectroscopy. 3) The course of the reaction *is* concentration-dependent.



(*E*)-1,1-Diallyl 4-ethyl 2-methylbut-3-ene-1,1,4-tricarboxylate (Table 2, entry 1). The compound was prepared according to General Procedure B from (±)-ethyl penta-

2,3-dienoate (64 mg, 0.50 mmol) and diallyl malonate (94 μL, 0.55 mmol). After purification by flash chromatography (2.5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (144 mg, 93% yield) with 94% ee.

$[\alpha]_D^{22} = -15$ (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK IC-H column; 5.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 10.8 min (major), 19.1 min (minor).

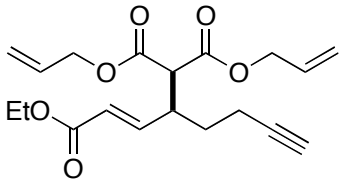
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (147 mg, 95% yield) with 94% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.86 (dd, *J* = 8.0 Hz, *J* = 15.6 Hz, 1H), 5.92-5.82 (m, 3H), 5.35-5.21 (m, 4H), 4.65 (t, *J* = 1.6 Hz, 1H), 4.63 (t, *J* = 1.2 Hz, 1H), 4.61 (t, *J* = 1.6 Hz, 1H), 4.59 (t, *J* = 1.6 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.42 (d, *J* = 8.8 Hz, 1H), 3.16-3.10 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.16 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.30, 167.25, 166.2, 148.7, 131.3, 122.2, 119.01, 118.96, 66.12, 66.09, 60.4, 56.7, 36.3, 17.3, 14.2.

IR (film) 3088, 2982, 1732, 1653, 1450, 1368, 1159 cm^{-1}.

LRMS (ES+) calcd for $C_{16}H_{23}O_6$ ($M+H^+$) 311.2, found 311.1.



(*E*)-1,1-Diallyl 4-ethyl 2-(but-3-yn-1-yl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 2). The compound was prepared according to General Procedure B from (±)-ethyl octa-2,3-dien-7-ynoate (82 mg, 0.50 mmol) and diallyl malonate (94 μL, 0.55 mmol). After purification by flash chromatography (5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (157 mg, 90% yield) with 91% ee.

$[\alpha]_D^{22} = +20$ (c = 1.1, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK OD-H column; 2.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 13.6 min (major), 20.0 min (minor).

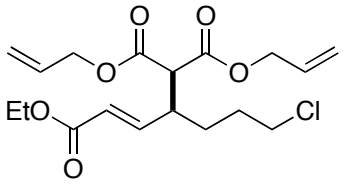
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (150 mg, 86% yield) with 92% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.75 (dd, *J* = 10.0 Hz, *J* = 15.6 Hz, 1H), 5.93 (dd, *J* = 16.0 Hz, *J* = 0.6 Hz, 1H), 5.94-5.81 (m, 2H), 5.36-5.21 (m, 4H), 4.65-4.59 (m, 4H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.51 (d, *J* = 8.0 Hz, 1H), 3.18-3.10 (m, 1H), 2.28-2.20 (m, 1H), 2.15-2.08 (m, 1H), 1.98 (t, *J* = 2.8 Hz, 1H), 1.83-1.78 (m, 1H), 1.69-1.60 (m, 1H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 167.0, 165.8, 145.8, 131.28, 131.26, 124.8, 119.1, 82.6, 69.5, 66.24, 66.17, 60.5, 55.6, 41.0, 30.4, 16.3, 14.2.

IR (film) 3296, 3087, 2984, 2941, 1734, 1653, 1448, 1370, 1159 cm^{-1}.

LRMS (ES+) calcd for $C_{19}H_{25}O_6$ ($M+H^+$) 349.2, found 349.1.



(*E*)-1,1-Diallyl 4-ethyl 2-(3-chloropropyl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 3). The compound was prepared according to General Procedure B from (±)-ethyl 7-chlorohepta-2,3-dienoate (94 mg, 0.50 mmol) and diallyl malonate (94 μL, 0.55 mmol). After purification by flash chromatography (5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (169 mg, 91% yield) with 93% ee.

$[\alpha]_D^{22} = -0.92$ (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 5.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 11.9 min (minor), 13.1 min (major).

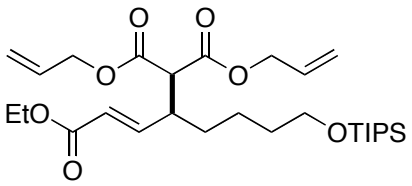
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (167 mg, 90% yield) with 93% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.75 (dd, *J* = 10.0 Hz, *J* = 15.6 Hz, 1H), 5.93-5.80 (m, 3H), 5.35-5.21 (m, 4H), 4.65 (t, *J* = 1.6 Hz, 1H), 4.63 (t, *J* = 1.2 Hz, 1H), 4.60 (t, *J* = 1.6 Hz, 1H), 4.58 (t, *J* = 1.2 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.52-3.46 (m, 3H), 2.96 (qd, *J* = 8.8 Hz, *J* = 2.4 Hz, 1H), 1.82-1.65 (m, 3H), 1.59-1.52 (m, 1H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 167.0, 165.7, 146.5, 131.3, 131.2, 124.4, 119.2, 119.1, 66.3, 66.2, 60.5, 55.9, 44.3, 41.7, 30.1, 29.2, 14.2.

IR (film) 3088, 2984, 2958, 2874, 1733, 1654, 1448, 1369, 1158 cm^{-1}.

LRMS (ES+) calcd for $C_{18}H_{26}ClO_6$ ($M+H^+$) 373.1, found 373.7.



(*E*)-1,1-Diallyl 4-ethyl 2-(4-(triisopropylsilyloxy)butyl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 4). The compound was prepared according to General Procedure B from (±)-ethyl 8-(triisopropylsilyloxy)octa-2,3-dienoate (170 mg, 0.50 mmol) and diallyl malonate (94 μL, 0.55 mmol). After purification by flash chromatography (5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (197 mg, 75% yield) with 88% ee.

$[\alpha]_D^{22} = +1.2$ (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK IC-H column; 2.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 18.0 min (minor), 20.5 min (major).

The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (210 mg, 80% yield) with 86% ee.

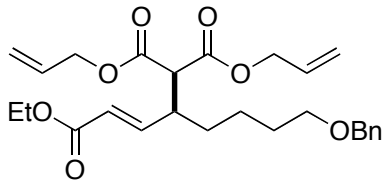
^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.76 (dd, *J* = 9.6 Hz, *J* = 15.6 Hz, 1H), 5.93-5.80 (m, 3H), 5.34-5.20 (m, 4H), 4.64 (t, *J* = 1.6 Hz, 1H), 4.62 (t, *J* = 1.2 Hz, 1H), 4.59 (t, *J* = 1.6 Hz, 1H),

4.57 (t, J = 1.2 Hz, 1H), 4.16 (q, J = 6.8 Hz, 2H), 3.63 (t, J = 6.4 Hz, 2H), 3.47 (d, J = 8.4 Hz, 1H), 2.99-2.91 (m, 1H), 1.59-1.23 (m, 6H), 1.27 (t, J = 7.2 Hz, 3H), 1.10-0.99 (m, 21H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.4, 167.2, 165.9, 147.2, 131.4, 131.3, 123.9, 119.0, 118.9, 66.1, 66.0, 63.0, 60.3, 56.0, 42.3, 32.6, 31.7, 23.4, 18.0, 14.2, 11.9.

IR (film) 3088, 2942, 2866, 1737, 1652, 1463, 1368, 1158 cm^{-1}.

LRMS (ES+) calcd for $C_{28}H_{49}O_7Si$ ($M+H^+$) 525.3, found 525.3.



(*E*)-1,1-Diallyl 4-ethyl 2-(4-(benzyloxy)butyl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 5). The compound was prepared according to General Procedure B from (±)-ethyl 8-(benzyloxy)octa-2,3-dienoate (137 mg, 0.50 mmol) and diallyl malonate (94 μL, 0.55 mmol). After purification by flash chromatography (5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (183 mg, 80% yield) with 90% ee.

$[\alpha]_D^{22}$ = +1.2 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK AS-H column; 3.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 13.9 min (minor), 15.0 min (major).

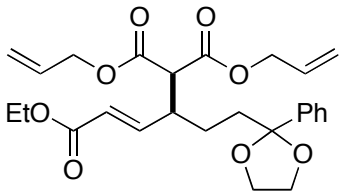
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (174 mg, 76% yield) with 90% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35-7.25 (m, 5H), 6.77 (dd, J = 8.8 Hz, J = 15.6 Hz, 1H), 5.92-5.80 (m, 3H), 5.34-5.20 (m, 4H), 4.63-4.57 (m, 4H), 4.47 (s, 2H), 4.17 (q, J = 7.2 Hz, 2H), 3.47 (d, J = 8.8 Hz, 1H), 3.42 (t, J = 6.4 Hz, 2H), 2.99-2.91 (m, 1H), 1.65-1.22 (m, 6H), 1.27 (t, J = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.3, 167.1, 165.9, 147.2, 138.4, 131.29, 131.26, 128.3, 127.5, 127.4, 123.9, 118.94, 118.91, 72.8, 69.8, 66.1, 66.0, 60.3, 55.9, 42.2, 31.7, 29.3, 23.7, 14.2.

IR (film) 2938, 2860, 1733, 1650, 1454, 1368, 1158 cm^{-1}.

LRMS (ES+) calcd for $C_{26}H_{35}O_7$ ($M+H^+$) 459.2, found 459.2.



(*E*)-1,1-Diallyl 4-ethyl 2-(2-(2-phenyl-1,3-dioxolan-2-yl)ethyl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 6). The compound was prepared according to General Procedure B from (±)-ethyl 6-(2-phenyl-1,3-dioxolan-2-yl)hexa-2,3-dienoate (144 mg,

0.50 mmol) and diallyl malonate (94 μL, 0.55 mmol). After purification by flash chromatography (5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (177 mg, 72% yield) with 94% ee.

$[\alpha]_D^{22}$ = +0.23 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK IA-H column; 3.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 15.7 min (minor), 16.9 min (major).

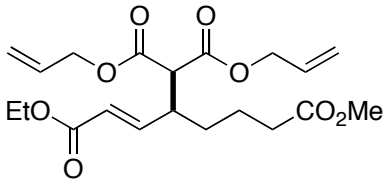
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (165 mg, 70% yield) with 94% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.38 (m, 2H), 7.35-7.27 (m, 3H), 6.73 (dd, *J* = 9.6 Hz, *J* = 15.6 Hz, 1H), 5.89-5.78 (m, 3H), 5.33-5.18 (m, 4H), 4.60-4.55 (m, 4H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.00-3.93 (m, 2H), 3.78-3.71 (m, 2H), 3.46 (d, *J* = 6.8 Hz, 1H), 3.01-2.90 (m, 1H), 1.92-1.76 (m, 2H), 1.71-1.61 (m, 1H), 1.54-1.41 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.3, 167.1, 165.9, 147.0, 142.3, 131.4, 128.1, 127.9, 125.6, 124.2, 118.9, 109.8, 66.1, 66.0, 64.52, 64.46, 60.3, 56.0, 42.1, 37.7, 25.9, 14.2.

IR (film) 2954, 2891, 1734, 1651, 1448, 1369, 1269, 1235, 1157 cm^{-1}.

LRMS (ES+) calcd for $C_{26}H_{33}O_8$ ($M+H^+$) 473.2, found 473.2.



(*E*)-1,1-Diallyl 5-methyl 2-(3-ethoxy-3-oxoprop-1-en-1-yl)pentane-1,1,5-tricarboxylate (Table 2, entry 7). The compound was prepared according to General Procedure B from (±)-1-ethyl 8-methyl octa-2,3-dienedioate (106 mg, 0.50 mmol) and diallyl malonate (94 μL, 0.55 mmol). After purification by flash chromatography (5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (150 mg, 76% yield) with 94% ee.

A gram-scale reaction was carried out according to General Procedure B with (±)-1-ethyl 8-methyl octa-2,3-dienedioate (1.0 g, 4.7 mmol) and diallyl malonate (0.89 mL, 5.2 mmol). After purification by flash chromatography (5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (1.39 g, 75% yield) with 94% ee.

$[\alpha]_D^{22}$ = –2.5 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK OD-H column; 2.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 24.2 min (major), 34.9 min (minor).

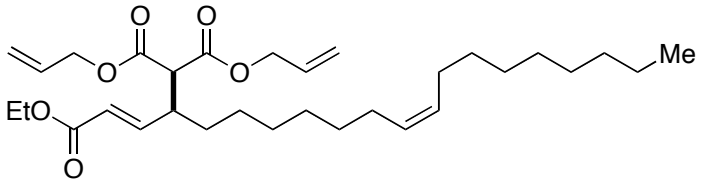
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (154 mg, 78% yield) with 94% ee.

^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.71 (dd, *J* = 9.6 Hz, *J* = 15.6 Hz, 1H), 5.87-5.77 (m, 3H), 5.29-5.17 (m, 4H), 4.59 (d, *J* = 6.0 Hz, 2H), 4.54 (d, *J* = 5.4 Hz, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.61 (s, 3H), 3.44 (d, *J* = 8.4 Hz, 1H), 2.93-2.89 (m, 1H), 2.29-2.19 (m, 2H), 1.61-1.33 (m, 4H), 1.23 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.3, 167.1, 167.0, 165.7, 146.5, 131.18, 131.16, 124.2, 118.94, 118.92, 66.1, 66.0, 60.3, 55.7, 51.4, 41.9, 33.4, 31.1, 22.3, 14.1.

IR (film) 3087, 2953, 1735, 1653, 1438, 1369, 1157 cm^{-1}.

LRMS (ES+) calcd for $C_{20}H_{29}O_8$ ($M+H^+$) 397.2, found 397.2.



(*E*)-1,1-Diallyl 4-ethyl 2-((*Z*)-hexadec-7-en-1-yl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 8). The compound was prepared according to General Procedure B from (±)-(*Z*)-ethyl icosa-2,3,11-trienoate (167 mg, 0.50 mmol) and diallyl malonate (94 μL, 0.55 mmol). After purification by flash chromatography (5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (174 mg, 67% yield) with 87% ee.

$[\alpha]_D^{22}$ = –0.04 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK OD-H column; 1.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 5.8 min (major), 9.3 min (minor).

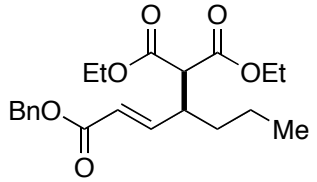
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (192 mg, 74% yield) with 85% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.77 (dd, *J* = 8.8 Hz, *J* = 15.6 Hz, 1H), 5.94-5.80 (m, 3H), 5.35-5.21 (m, 6H), 4.65 (t, *J* = 1.2 Hz, 1H), 4.63 (t, *J* = 1.4 Hz, 1H), 4.59 (t, *J* = 1.4 Hz, 1H), 4.58 (t, *J* = 1.2 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.48 (d, *J* = 8.8 Hz, 1H), 2.96-2.93 (m, 1H), 2.00-1.99 (m, 4H), 1.55-1.14 (m, 25H), 0.87 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.4, 167.2, 166.0, 147.5, 131.4, 131.3, 130.0, 129.7, 123.8, 118.99, 118.96, 66.12, 66.05, 60.4, 56.0, 42.2, 31.92, 31.88, 29.74, 29.66, 29.5, 29.3, 29.2, 29.1, 27.2, 27.1, 27.0, 22.7, 14.2, 14.1.

IR (film) 3087, 2927, 2855, 1737, 1652, 1457, 1368, 1155 cm^{-1}.

LRMS (ES+) calcd for $C_{31}H_{51}O_6$ ($M+H^+$) 519.4, found 519.3.



(*E*)-4-Benzyl 1,1-diethyl 2-propylbut-3-ene-1,1,4-tricarboxylate (Table 2, entry 9). The compound was prepared according to General Procedure B from (±)-benzyl hepta-2,3-dienoate (108 mg, 0.50 mmol) and diethyl malonate (84 μL, 0.55 mmol). After purification by flash chromatography (2.5→20% Et_2O in hexanes), the title compound was isolated as a colorless oil (156 mg, 83% yield) with 93% ee.

$[\alpha]_D^{22} = -4.5$ (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK IC-H column; 5.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 17.8 min (minor), 19.5 min (major).

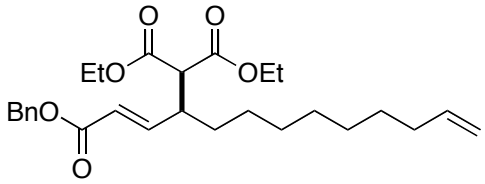
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (160 mg, 85% yield) with 93% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.30 (m, 5H), 6.83 (dd, *J* = 9.6 Hz, *J* = 15.6 Hz, 1H), 5.92 (d, *J* = 15.6 Hz, 1H), 5.16 (s, 2H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.39 (d, *J* = 8.4 Hz, 1H), 3.00-2.92 (m, 1H), 1.52-1.21 (m, 4H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.93 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8, 167.6, 165.8, 148.4, 135.9, 128.5, 128.18, 128.16, 123.2, 66.2, 61.6, 61.4, 56.1, 42.0, 34.0, 20.2, 14.03, 13.98, 13.7.

IR (film) 3034, 2961, 2936, 2874, 1728, 1656, 1456, 1370, 1156 cm^{-1}.

LRMS (ES+) calcd for $C_{21}H_{28}O_6$ (M^+) 376.2, found 376.8.



(*E*)-4-Benzyl 1,1-diethyl 2-(non-8-en-1-yl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 10). The compound was prepared according to General Procedure B from (±)-benzyl trideca-2,3,12-trienoate (149 mg, 0.50 mmol) and diethyl malonate (84 μL, 0.55 mmol). After purification by flash chromatography (2.5→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (149 mg, 65% yield) with 90% ee.

$[\alpha]_D^{22} = +1.1$ (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 2.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 16.8 min (major), 18.0 min (minor).

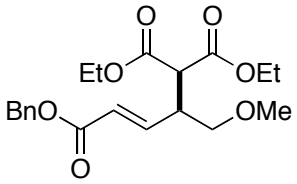
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (147 mg, 64% yield) with 90% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.30 (m, 5H), 6.83 (dd, *J* = 8.4 Hz, *J* = 15.6 Hz, 1H), 5.92 (dd, *J* = 0.8 Hz, *J* = 15.6 Hz, 1H), 5.85-5.74 (m, 1H), 5.17 (s, 2H), 5.01-4.90 (m, 2H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.39 (d, *J* = 8.4 Hz, 1H), 2.98-2.90 (m, 1H), 2.05-1.99 (m, 2H), 1.54-1.18 (m, 12H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8, 167.4, 165.8, 148.5, 139.1, 135.9, 128.5, 128.2, 123.2, 114.1, 66.2, 61.6, 61.4, 56.1, 42.2, 33.7, 31.9, 29.23, 29.19, 29.0, 28.8, 27.0, 14.1, 14.0.

IR (film) 3067, 3034, 2980, 2928, 2856, 1752, 1731, 1656, 1456, 1370, 1305, 1154 cm^{-1}.

LRMS (ES+) calcd for $C_{27}H_{39}O_6$ ($M+H^+$) 459.3, found 459.3.



(*E*)-4-Benzyl 1,1-diethyl 2-(methoxymethyl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 11). The compound was prepared according to General Procedure B from (±)-benzyl 5-methoxypenta-2,3-dienoate (109 mg, 0.50 mmol) and diethyl malonate (84 μL, 0.55 mmol). After purification by flash chromatography (5→10% EtOAc in hexanes), the title compound was isolated as a colorless oil (138 mg, 73% yield) with 93% ee.

$[\alpha]_D^{22} = -20$ (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK OJ-H column; 10.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 14.3 min (minor), 15.7 min (major).

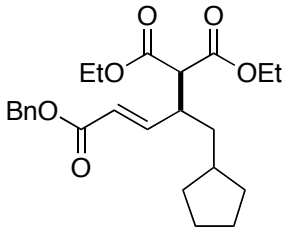
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (142 mg, 75% yield) with 93% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.30 (m, 5H), 6.97 (dd, *J* = 8.8 Hz, *J* = 15.6 Hz, 1H), 5.97 (dd, *J* = 0.8 Hz, *J* = 15.6 Hz, 1H), 5.18 (d, *J* = 12.4 Hz, 1H), 5.14 (d, *J* = 12.4 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.64 (d, *J* = 8.0 Hz, 1H), 3.52-3.45 (m, 2H), 3.29 (s, 3H), 3.27-3.21 (m, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8, 167.6, 165.7, 145.8, 135.9, 128.5, 128.2, 128.1, 123.6, 72.5, 66.2, 61.6, 61.5, 58.9, 52.5, 41.9, 14.0, 13.9.

IR (film) 3067, 3034, 2983, 2934, 1728, 1657, 1456, 1371, 1157, 1029 cm^{-1}.

LRMS (ES+) calcd for $C_{20}H_{27}O_7$ ($M+H^+$) 379.2, found 379.8.



(*E*)-4-Benzyl 1,1-diethyl 2-(cyclopentylmethyl)but-3-ene-1,1,4-tricarboxylate (Table 2, entry 12). The compound was prepared according to General Procedure B, except that 15% of (*S*)-**1** was used, from (±)-benzyl 5-cyclopentylpenta-2,3-dienoate (128 mg, 0.50 mmol) and diethyl malonate (84 μL, 0.55 mmol). After purification by flash chromatography (2→20% EtOAc in hexanes), the title compound was isolated as a colorless oil (146 mg, 70% yield) with 84% ee.

$[\alpha]_D^{22} = +16$ (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK IC-H column; 5.0% *i*-PrOH in hexanes; 0.6 mL/min; retention times: 24.8 min (minor), 26.5 min (major).

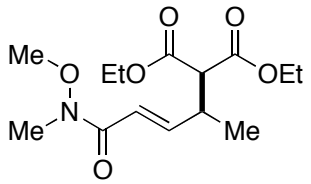
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (148 mg, 71% yield) with 85% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.31 (m, 5H), 6.84 (dd, *J* = 8.8 Hz, *J* = 15.6 Hz, 1H), 5.93 (d, *J* = 15.6 Hz, 1H), 5.17 (s, 2H), 4.23-4.17 (m, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.37 (d, *J* = 8.4 Hz, 1H), 3.03-2.95 (m, 1H), 1.78-1.71 (m, 3H), 1.61-1.46 (m, 5H), 1.43-1.36 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.92 (t, *J* = 7.2 Hz, 3H), 1.17-1.03 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8, 167.7, 165.8, 148.6, 135.9, 128.5, 128.22, 128.19, 123.1, 66.2, 61.6, 61.4, 56.4, 41.6, 38.4, 37.3, 33.3, 31.5, 25.1, 25.0, 14.1, 14.0.

IR (film) 2950, 2869, 1731, 1656, 1455, 1370, 1303, 1150 cm^{-1}.

LRMS (ES+) calcd for $C_{24}H_{33}O_6$ ($M+H^+$) 417.2, found 417.8.



(*E*)-Diethyl 2-(5-(methoxy(methyl)amino)-5-oxopent-3-en-2-yl)malonate (Table 3, entry 1). The compound was prepared according to General Procedure B from (±)-*N*-methoxy-*N*-methylpenta-2,3-dienamide (71 mg, 0.50 mmol) and diethyl malonate (84 μL, 0.55 mmol). After purification by flash chromatography (3% MeOH in 1:1 EtOAc/hexanes), the title compound was isolated as a colorless oil (99 mg, 66% yield) with 95% ee.

$[\alpha]_D^{22}$ = –9.6 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 5.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 22.0 min (major), 25.2 min (minor).

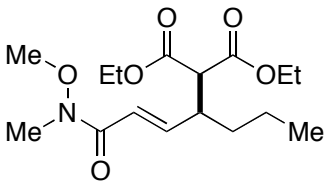
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (114 mg, 76% yield) with 95% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.83 (dd, *J* = 8.4 Hz, *J* = 15.6 Hz, 1H), 6.45 (d, *J* = 15.2 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.67 (s, 3H), 3.33 (d, *J* = 8.8 Hz, 1H), 3.21 (s, 3H), 3.20-3.12 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.54 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.82, 167.76, 166.4, 147.4, 119.5, 61.7, 61.5, 61.4, 57.0, 36.6, 32.3, 17.6, 14.03, 13.98.

IR (film) 2980, 1732, 1666, 1636, 1465, 1371, 1177 cm^{-1}.

LRMS (ES+) calcd for $C_{14}H_{24}NO_6$ ($M+H^+$) 302.2, found 302.8.



(*E*)-Diethyl 2-(1-(methoxy(methyl)amino)-1-oxohept-2-en-4-yl)malonate (Table 3, entry 2). The compound was prepared according to General Procedure B from (±)-*N*-

methoxy-*N*-methylhepta-2,3-dienamide (85 mg, 0.50 mmol) and diethyl malonate (84 μL, 0.55 mmol). After purification by flash chromatography (50→100% Et_2O in hexanes), the title compound was isolated as a colorless oil (115 mg, 70% yield) with 93% ee.

$[\alpha]_D^{22}$ = –0.86 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 5.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 17.8 min (major), 20.1 min (minor).

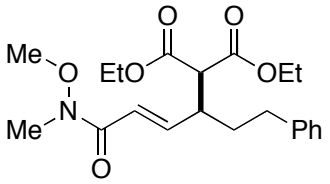
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (102 mg, 62% yield) with 93% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.72 (dd, *J* = 9.6 Hz, *J* = 15.2 Hz, 1H), 6.46 (d, *J* = 15.2 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.67 (s, 3H), 3.39 (d, *J* = 9.2 Hz, 1H), 3.22 (s, 3H), 3.04-2.96 (m, 1H), 1.52-1.18 (m, 4H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.0, 167.8, 166.2, 146.0, 121.2, 61.7, 61.5, 61.3, 56.4, 42.3, 34.2, 32.3, 20.2, 14.1, 14.0, 13.7.

IR (film) 2961, 2937, 2874, 1732, 1666, 1637, 1465, 1382, 1304, 1176 cm^{-1}.

LRMS (ES+) calcd for $C_{16}H_{28}NO_6$ ($M+H^+$) 330.2, found 330.8.



(*E*)-Diethyl 2-(6-(methoxy(methyl)amino)-6-oxo-1-phenylhex-4-en-3-yl)malonate (Table 3, entry 3). The compound was prepared according to General Procedure B from (±)-*N*-methoxy-*N*-methyl-6-phenylhexa-2,3-dienamide (116 mg, 0.50 mmol) and diethyl malonate (84 μL, 0.55 mmol). After purification by flash chromatography (25→50% EtOAc in hexanes), the title compound was isolated as a colorless oil (133 mg, 68% yield) with 94% ee.

$[\alpha]_D^{22}$ = –2.1 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK IC-H column; 20.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 32.6 min (major), 38.1 min (minor).

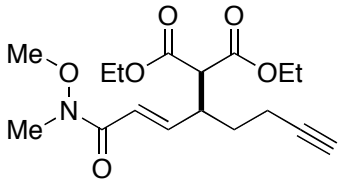
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (123 mg, 63% yield) with 95% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.25-7.21 (m, 2H), 7.16-7.09 (m, 3H), 6.78 (dd, *J* = 10.0 Hz, *J* = 15.6 Hz, 1H), 6.47 (d, *J* = 15.2 Hz, 1H), 4.18-4.06 (m, 4H), 3.66 (s, 3H), 3.40 (d, *J* = 9.2 Hz, 1H), 3.21 (s, 3H), 3.05-3.00 (m, 1H), 2.66-2.60 (m, 1H), 2.51-2.43 (m, 1H), 1.88-1.81 (m, 1H), 1.75-1.68 (m, 1H), 1.23-1.15 (m, 6H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.7, 167.6, 166.1, 145.5, 141.2, 128.34, 128.31, 125.9, 121.8, 61.7, 61.5, 61.4, 56.3, 42.1, 33.7, 33.2, 32.3, 14.00, 13.97.

IR (film) 3063, 3026, 2981, 2937, 1750, 1732, 1665, 1635, 1496, 1302 cm^{-1}.

LRMS (ES+) calcd for $C_{21}H_{29}NO_6$ (M^+) 391.2, found 391.8.



(*E*)-Diethyl 2-(1-(methoxy(methyl)amino)-1-oxooct-2-en-7-yn-4-yl)malonate (Table 3, entry 4). The compound was prepared according to General Procedure B from (±)-*N*-methoxy-*N*-methylocta-2,3-dien-7-ynamide (90 mg, 0.50 mmol) and diethyl malonate (84 μL, 0.55 mmol), except that the reaction time was 72 h. After purification by flash chromatography (1:4:5→2:3:5 EtOAc:hexanes:CH_2Cl_2), the title compound was isolated as a colorless oil (120 mg, 71% yield) with 94% ee.

$[\alpha]_D^{22}$ = +42 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 5% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 47.0 min (major), 53.8 min (minor).

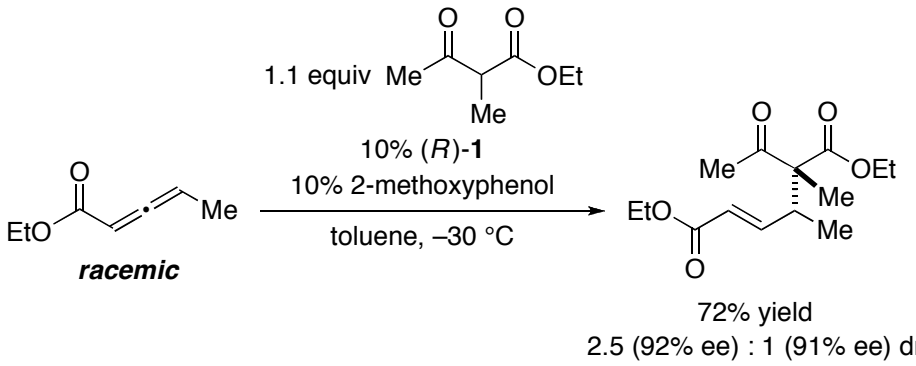
The second run was performed with (*R*)-**1**. The product was isolated as a colorless oil (115 mg, 68% yield) with 94% ee.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.69 (dd, *J* = 10.0 Hz, *J* = 15.6 Hz, 1H), 6.54 (d, *J* = 15.2 Hz, 1H), 4.20 (dq, *J* = 2.0 Hz, *J* = 7.2 Hz, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.68 (s, 3H), 3.42 (d, *J* = 8.8 Hz, 1H), 3.22 (s, 3H), 3.22-3.14 (m, 1H), 2.26-2.19 (m, 1H), 2.14-2.03 (m, 1H), 1.96 (t, *J* = 2.4 Hz, 1H), 1.83-1.75 (m, 1H), 1.68-1.59 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.6, 167.5, 165.9, 144.3, 122.3, 82.9, 69.2, 61.8, 61.6, 61.5, 56.0, 41.3, 32.3, 30.4, 16.2, 14.04, 14.00.

IR (film) 3286, 2959, 2925, 2854, 1732, 1664, 1635, 1464, 1378, 1032 cm^{-1}.

LRMS (ES+) calcd for $C_{17}H_{25}NO_6$ (M^+) 339.2, found 339.8.



(*E*)-Diethyl 5-acetyl-4,5-dimethylhex-2-enedioate (eq 4; relative and absolute stereochemistry to be determined). The compound was prepared according to General Procedure B from (±)-ethyl penta-2,3-dienoate (126 mg, 1.0 mmol) and ethyl 2-methyl-3-oxobutanoate (160 μL, 1.1 mmol), except that catalyst (*R*)-**1** was used and the reaction was run for 72 h. After purification by flash chromatography (20% EtOAc in hexanes), the title compounds were isolated as a colorless oil (194 mg, 72% yield (combined yield

of a 2.5:1 mixture (^{1}H NMR spectroscopy) of diastereomers); 92% (major) ee and 91% ee (minor)).

Analytical data were obtained after HPLC separation of the diastereomers.

Major diastereomer:

$[\alpha]_D^{22}$ = +5.0 (c = 1.0, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK OD-H column; 1.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 13.0 min (minor), 27.5 min (major).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.82 (dd, *J* = 8.4 Hz, *J* = 15.6 Hz, 1H), 5.85 (dd, *J* = 1.2 Hz, *J* = 16.0 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.25-3.21 (m, 1H), 2.14 (s, 3H), 1.31 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.4, 171.2, 166.4, 148.3, 122.8, 62.9, 61.6, 60.4, 39.8, 26.8, 15.9, 15.3, 14.2, 14.0.

IR (film) 2982, 2941, 1716, 1652, 1449, 1367, 1235 cm^{-1}.

LRMS (ES+) calcd for $C_{14}H_{22}O_5$ (M^+) 270.2, found 270.9.

Minor diastereomer:

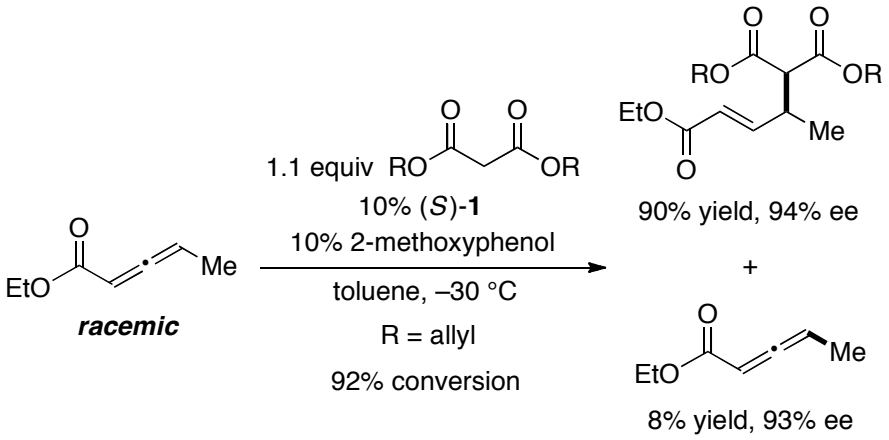
$[\alpha]_D^{22}$ = +64 (c = 0.3, $CHCl_3$). HPLC analysis of the product: Daicel CHIRALPAK OD-H column; 1.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 14.4 min (minor), 32.1 min (major).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.90 (dd, *J* = 8.0 Hz, *J* = 15.6 Hz, 1H), 5.84 (dd, *J* = 1.2 Hz, *J* = 15.6 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.27-3.23 (m, 1H), 2.16 (s, 3H), 1.31 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.01 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.0, 171.3, 166.3, 148.7, 122.6, 63.0, 61.6, 60.3, 39.7, 26.5, 15.2, 14.5, 14.2, 14.0.

IR (film) 2981, 2923, 2851, 1716, 1652, 1449, 1261 cm^{-1}.

LRMS (ES+) calcd for $C_{14}H_{22}O_5$ (M^+) 270.2, found 270.9.



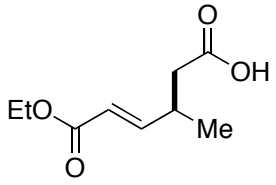
Kinetic resolution (eq 7). An oven-dried 4-mL vial was charged with (*S*)-**1** (19.5 mg, 0.050 mmol), anhydrous toluene (0.3 mL), 2-methoxyphenol (5.5 μL, 0.050 mmol),

diallyl malonate (94 μL, 0.55 mmol), and decane (49 μL, 0.25 mmol). The vial was capped, purged with nitrogen for 1 min, and cooled to –30 °C. Next, the allene (64 mg, 0.50 mmol) was added via syringe over 2 min. The cap was then sealed with grease, and the mixture was stirred at –30 °C. Aliquots were removed, quenched with hydrogen peroxide (30% in H_2O), and then extracted with Et_2O (3 mL × 3). The conversion of the reaction was determined by GC analysis; after 11 h, the conversion was 92%. Hydrogen peroxide (30% in H_2O; 0.4 mL) was added dropwise to the reaction mixture, and the resulting mixture was stirred for 30 min. Next, the mixture was warmed to 0 °C, and a saturated aqueous solution of Na_2SO_3 (2 mL) was added dropwise. The aqueous layer was extracted with Et_2O (3 mL × 3), and the combined organic layers were dried over Na_2SO_4 and filtered. GC analysis showed that the yields of product and starting allene were 90% and 8%, respectively. The solvent was removed by rotary evaporation, and the product and the starting allene were purified by flash chromatography (2.5→10% Et_2O in hexanes followed by 5→20% EtOAc in hexanes).

HPLC analysis of the product showed 94% ee: Daicel CHIRALPAK IC-H column; 5.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 10.8 min (major), 19.1 min (minor).

The starting allene had a positive optical rotation, which corresponds to the (*S*) configuration.[4] HPLC analysis showed 93% ee: Daicel CHIRALPAK AD-H column; 1.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 14.8 min (major), 16.1 min (minor).

IV. Functionalization of the γ-Addition Products



(*R*,*E*)-6-Ethoxy-3-methyl-6-oxohex-4-enoic acid (eq 5). A flask was charged with a solution of (*S*,*E*)-1,1-diallyl 4-ethyl 2-methylbut-3-ene-1,1,4-tricarboxylate (product of Table 2, entry 1; 233 mg, 0.75 mmol), $Pd(OAc)_2$ (16.8 mg, 0.075 mmol), PPh_3 (39.3 mg, 0.15 mmol), and Meldrum's acid (0.55 g, 3.8 mmol) in 1,4-dioxane (7 mL). The flask was purged with nitrogen, and the reaction mixture was refluxed for 3 h. Next, the mixture was cooled to room temperature, the solvent was evaporated, and the residue was purified by flash chromatography (1:1 Et_2O/hexanes→1:1:0.1 EtOAc/hexanes/MeOH), which afforded the title compound as a pale-yellow oil (115 mg, 82% yield).

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(4) Rossi R, Diversi P (1973) Synthesis, absolute configuration, and optical purity of chiral allenes. *Synthesis* 25–36.

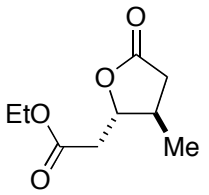
$[\alpha]_D^{22}$ = +20 (c = 1.0, $CHCl_3$). HPLC analysis of the methyl ester of the product, which was prepared by methylation with $TMSCH_2N_2$: Daicel CHIRALPAK AD-H column; 2.0% *i*-PrOH in hexanes; 1.0 mL/min; retention times: 28.1 min (major), 29.9 min (minor).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.4 (br s, 1H), 6.90 (dd, *J* = 7.2 Hz, *J* = 15.6 Hz, 1H), 5.83 (dd, *J* = 1.2 Hz, *J* = 15.6 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.88-2.81 (m, 1H), 2.48 (dd, *J* = 7.2 Hz, *J* = 15.6 Hz, 1H), 2.37 (dd, *J* = 7.6 Hz, *J* = 16.0 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.43 (d, *J* = 6.8 Hz, 3H).

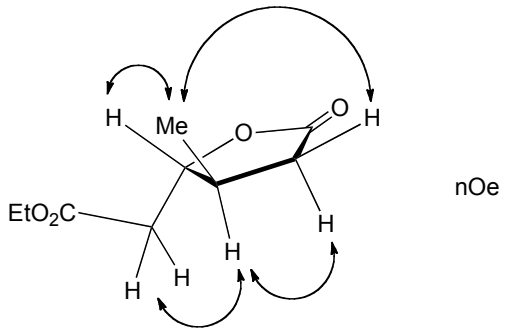
^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.7, 166.6, 151.5, 120.5, 60.4, 40.0, 32.6, 19.0, 14.2.

IR (film) 3200 (br), 2979, 1712, 1654, 1370, 1274, 1181, 1034 cm^{-1}.

LRMS (ES+) calcd for $C_9H_{14}O_4$ (M^+) 186.1, found 186.9.



Ethyl 2-((2*S*,3*R*)-3-methyl-5-oxotetrahydrofuran-2-yl)acetate (eq 6). A flask was charged with a solution of (*S*,*E*)-1,1-diallyl 4-ethyl 2-methylbut-3-ene-1,1,4-tricarboxylate (product of Table 2, entry 1; 142 mg, 0.46 mmol), $Pd(OAc)_2$ (5.3 mg, 0.023 mmol), PPh_3 (24.5 mg, 0.094 mmol), formic acid (44 μL, 1.2 mmol), and Et_3N (0.22 mL, 1.5 mmol) in 1,4-dioxane (2.0 mL). The flask was purged with nitrogen, and the reaction mixture was refluxed for 14 h. Next, the reaction mixture was cooled to room temperature, poured into 1 N HCl (10 mL), and extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (1:1 Et_2O/hexanes), which furnished the title compound as a pale-yellow oil (72 mg, 85% yield (combined yield of a 7:1 mixture (^{1}H NMR spectroscopy) of diastereomers); the cis stereochemistry of the major diastereomer was determined by nOe experiments)).



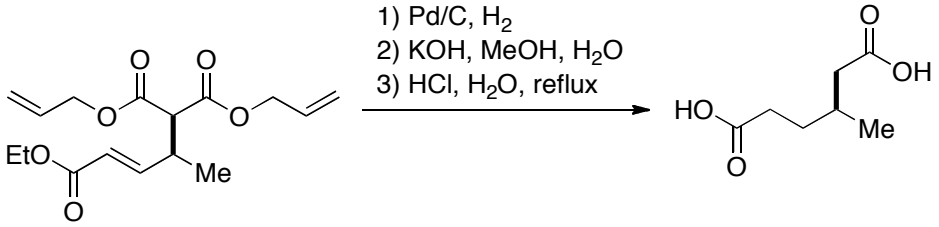
^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.48-4.43 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.72-2.64 (m, 3H), 2.36-2.28 (m, 1H), 2.24-2.17 (m, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.6, 169.6, 82.6, 61.0, 38.7, 36.5, 35.6, 17.3, 14.1.

IR (film) 2978, 2937, 1784, 1735, 1464, 1337, 1188, 1157 cm^{-1}.
LRMS (ES+) calcd for $C_9H_{14}O_4$ (M^+) 186.1, found 186.9.

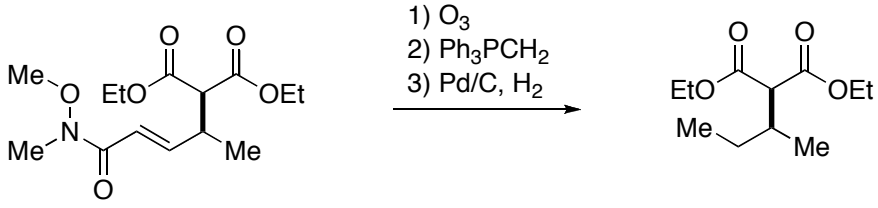
V. Determination of the Absolute Configuration

The absolute configuration of the product of entry 1 of Table 2 (from catalyst (*S*)-**1**) was determined.



(*S*)-3-Methylhexanedioic acid.[5] The product has $[\alpha]_D^{22} = -12$ (c = 1.2, $CHCl_3$; 94% ee).

The absolute configuration of the product of entry 1 of Table 3 (from catalyst (*S*)-**1**) was determined.



(*S*)-Diethyl 2-*sec*-butylmalonate.[6] The product has $[\alpha]_D^{22} = +7.8$ (c = 2.0, $CHCl_3$; 95% ee).

The stereochemistry of the other products has been assigned by analogy.

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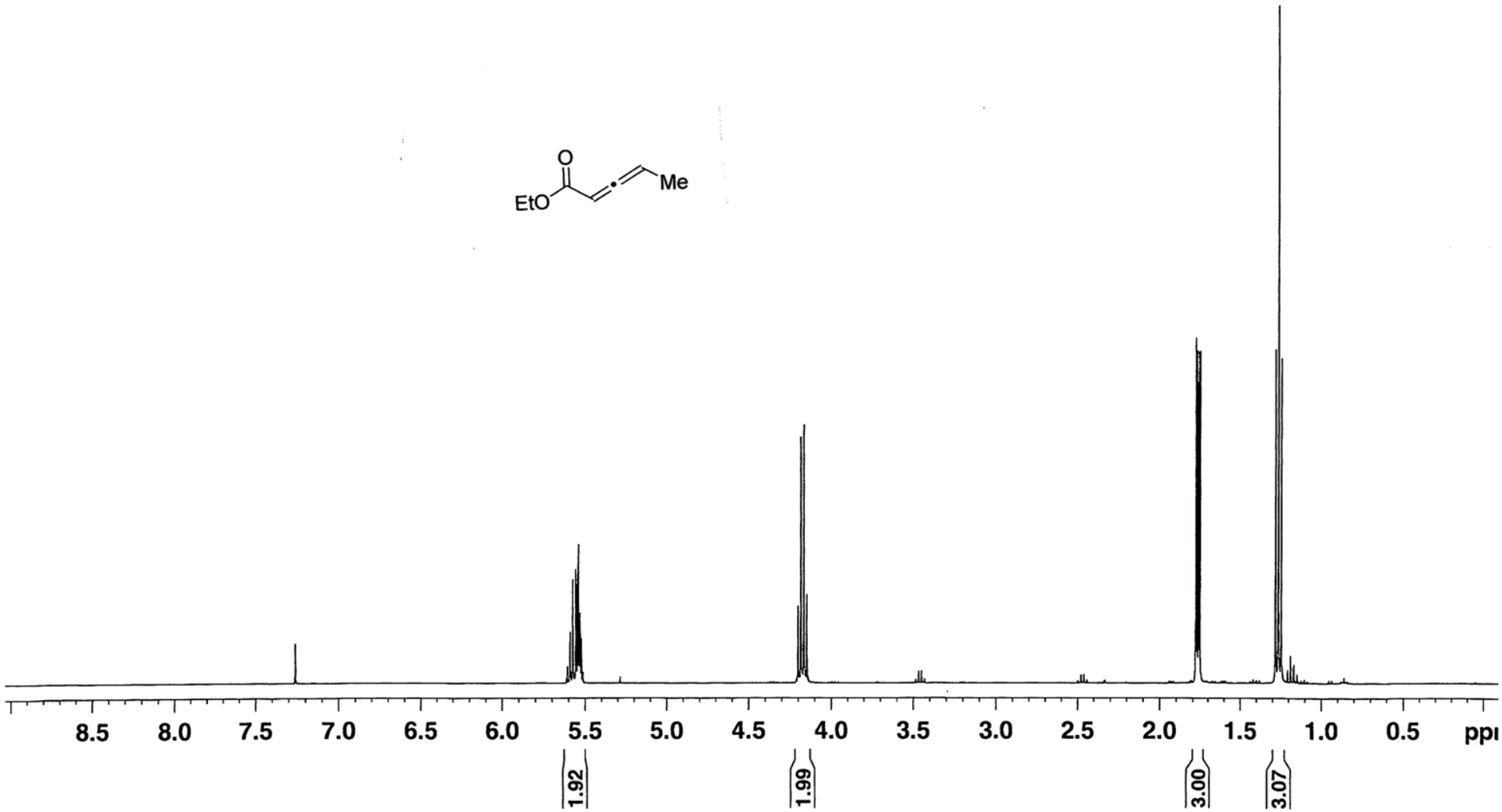
(5) Brown E, Deroye C, Touet J (1998) Synthesis of versatile chiral intermediates by enantioselective conjugate addition of alkenyl Grignard reagents to enamides deriving from (*R*)-(–)- or (*S*)-(+)-2-aminobutan-1-ol. *Tetrahedron: Asymmetry* 9:1605–1614.

(6) Schuppan J, Minnaard AJ, Feringa BL (2004) A catalytic and iterative route to β-substituted esters via highly enantioselective conjugate addition of dimethylzinc to unsaturated malonates. *Chem Commun* 792–793.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Me
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8.0
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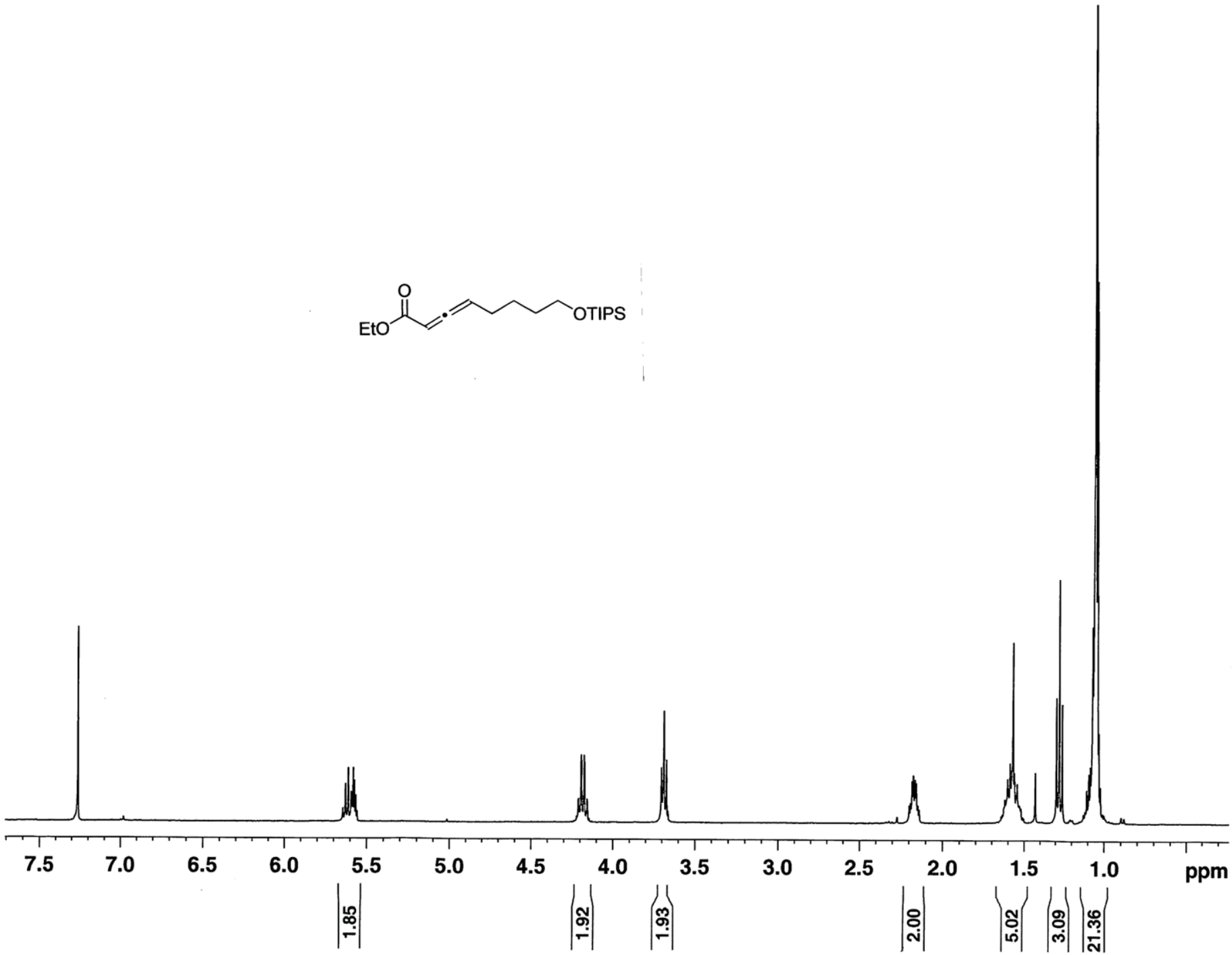
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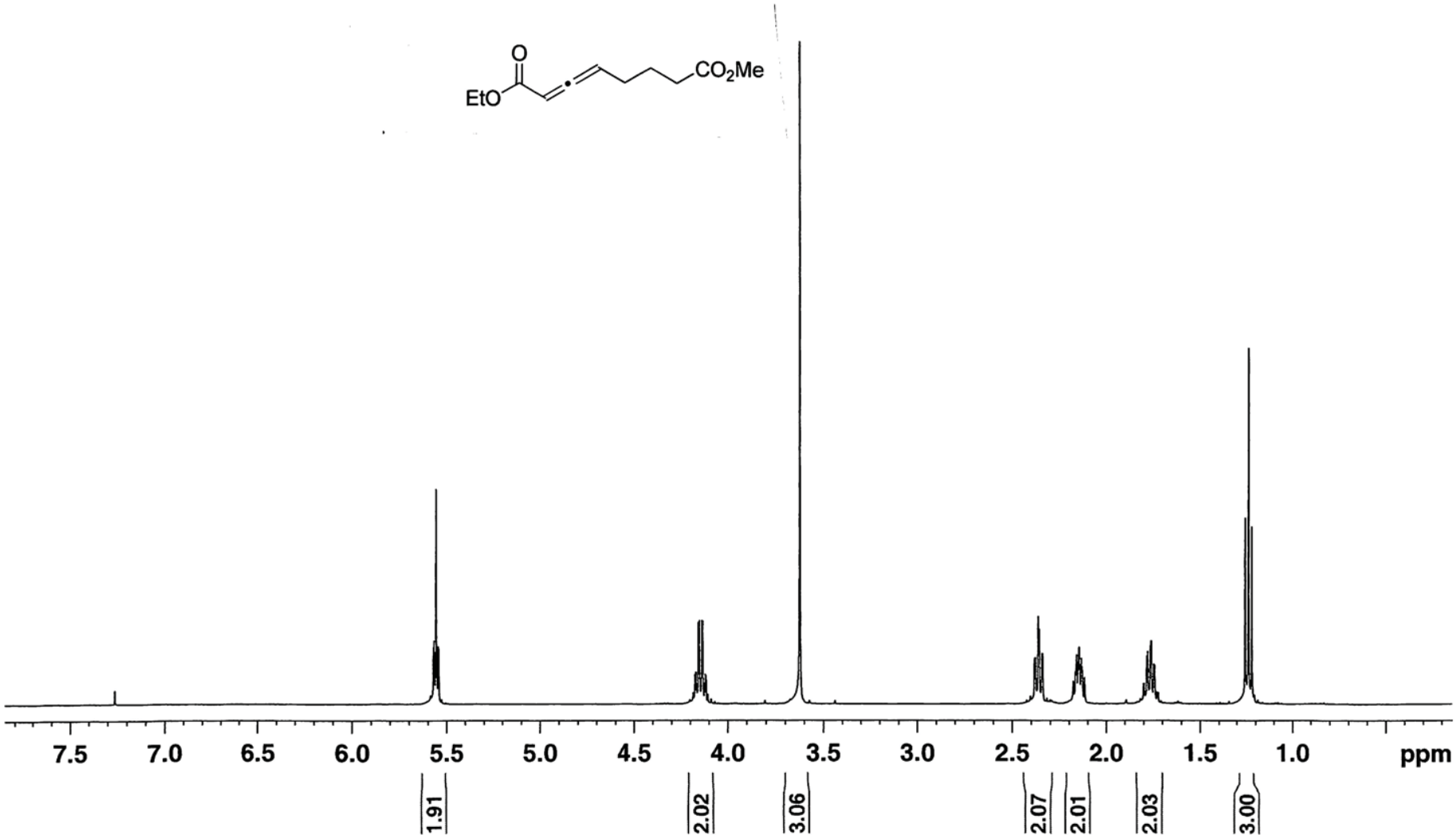
21.36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EtO
CO2Me
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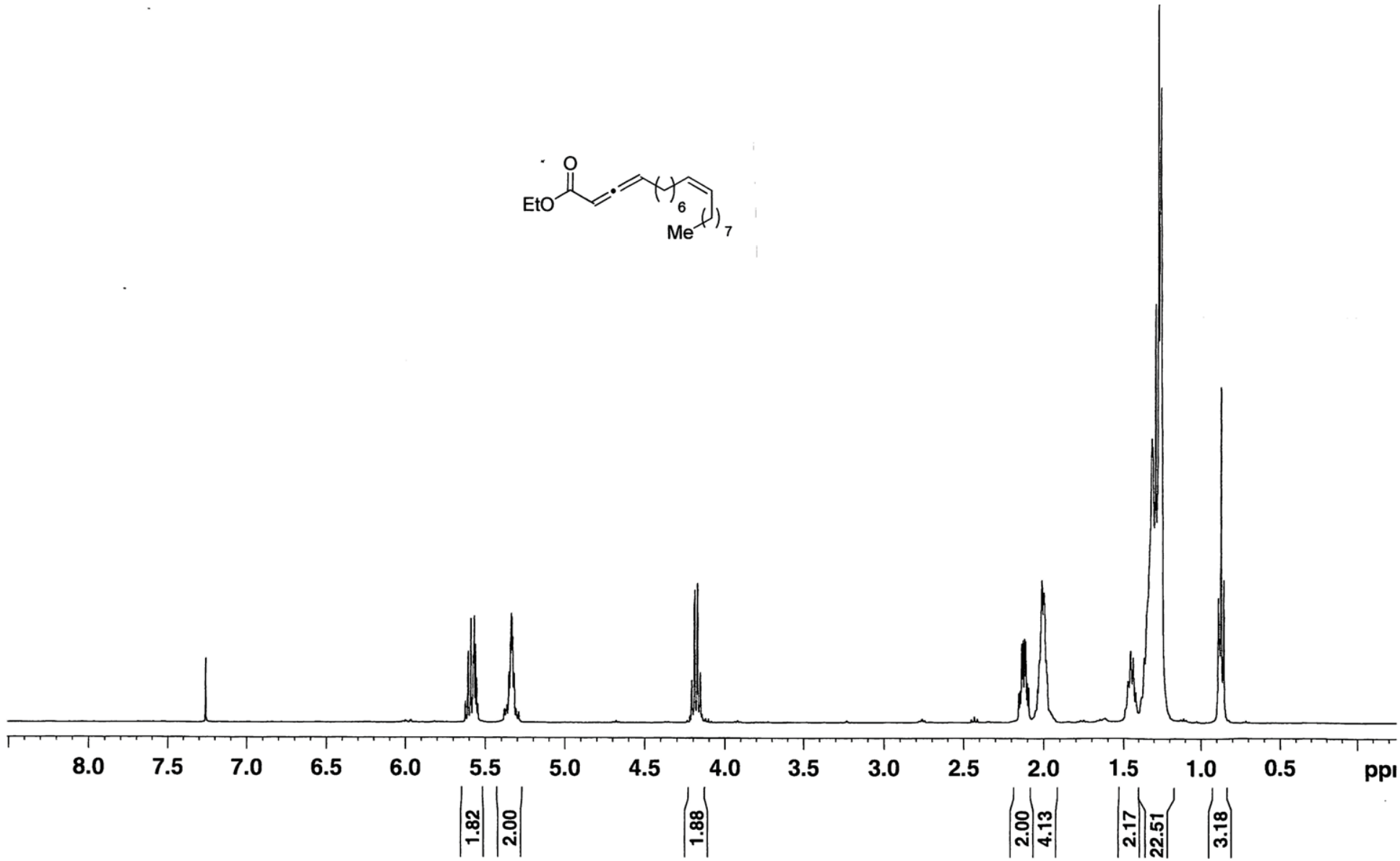
3.00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EtO
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Me
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3.0
2.5
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ppı
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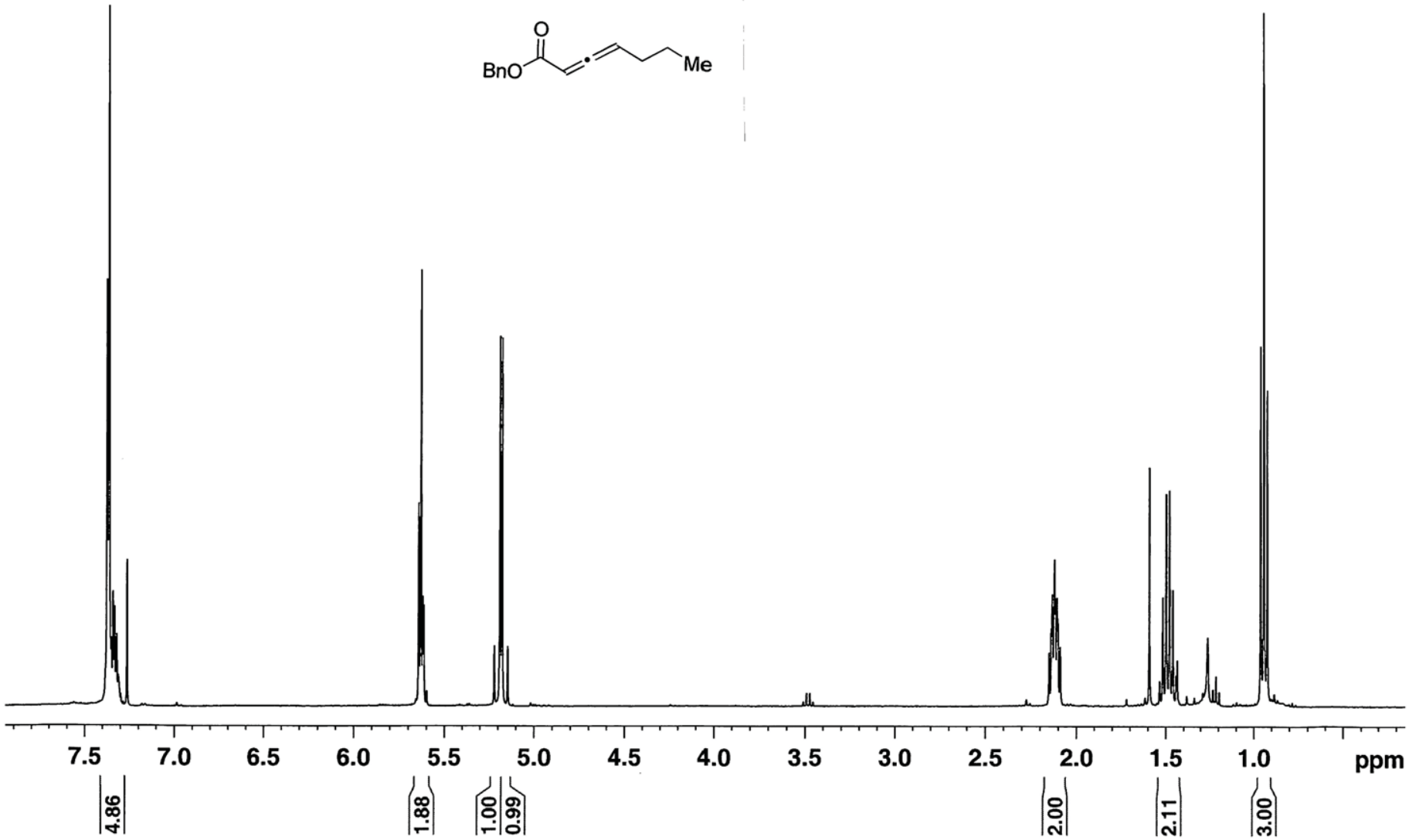
2.17
22.51
3.18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BnO
Me
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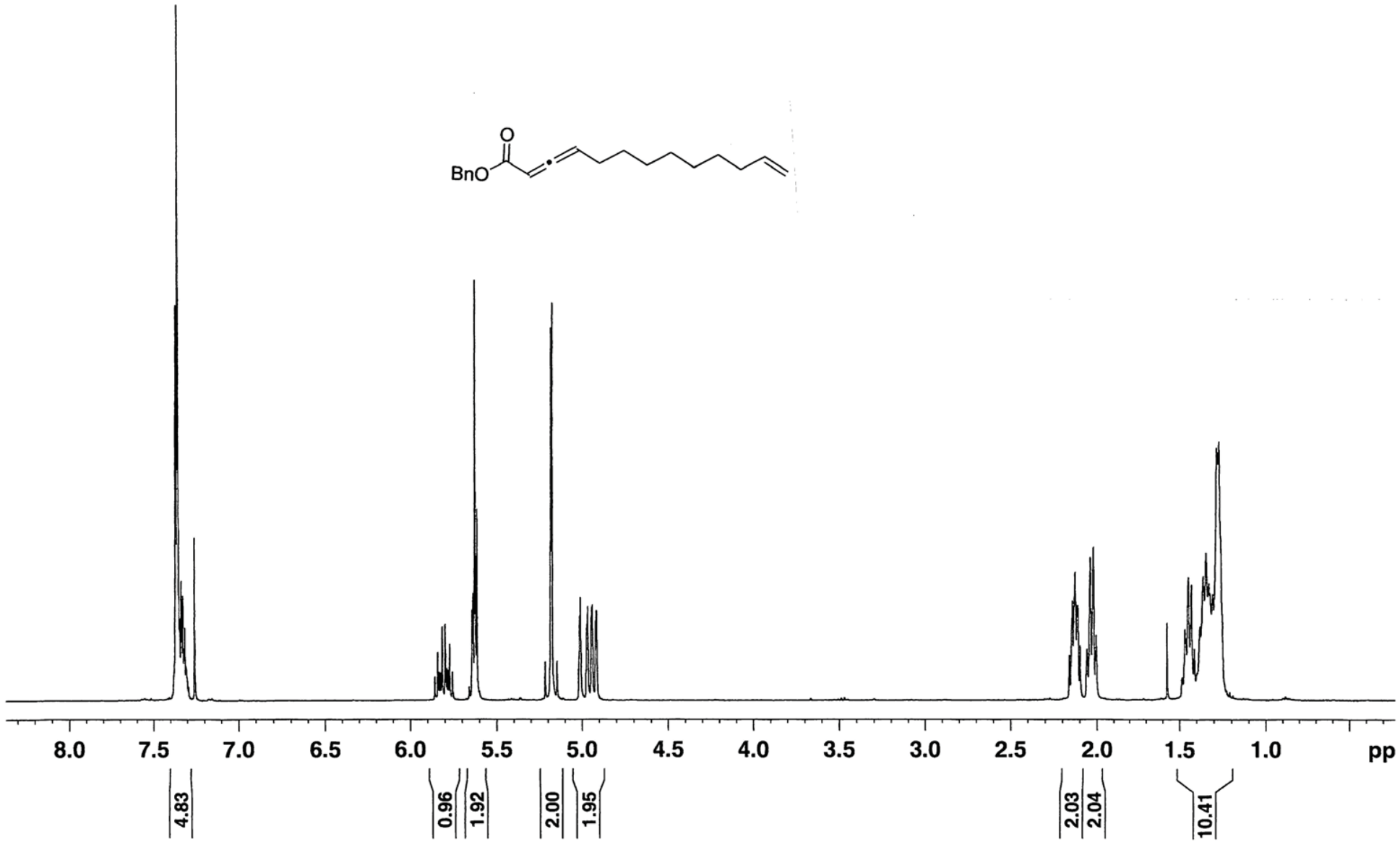
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3.0
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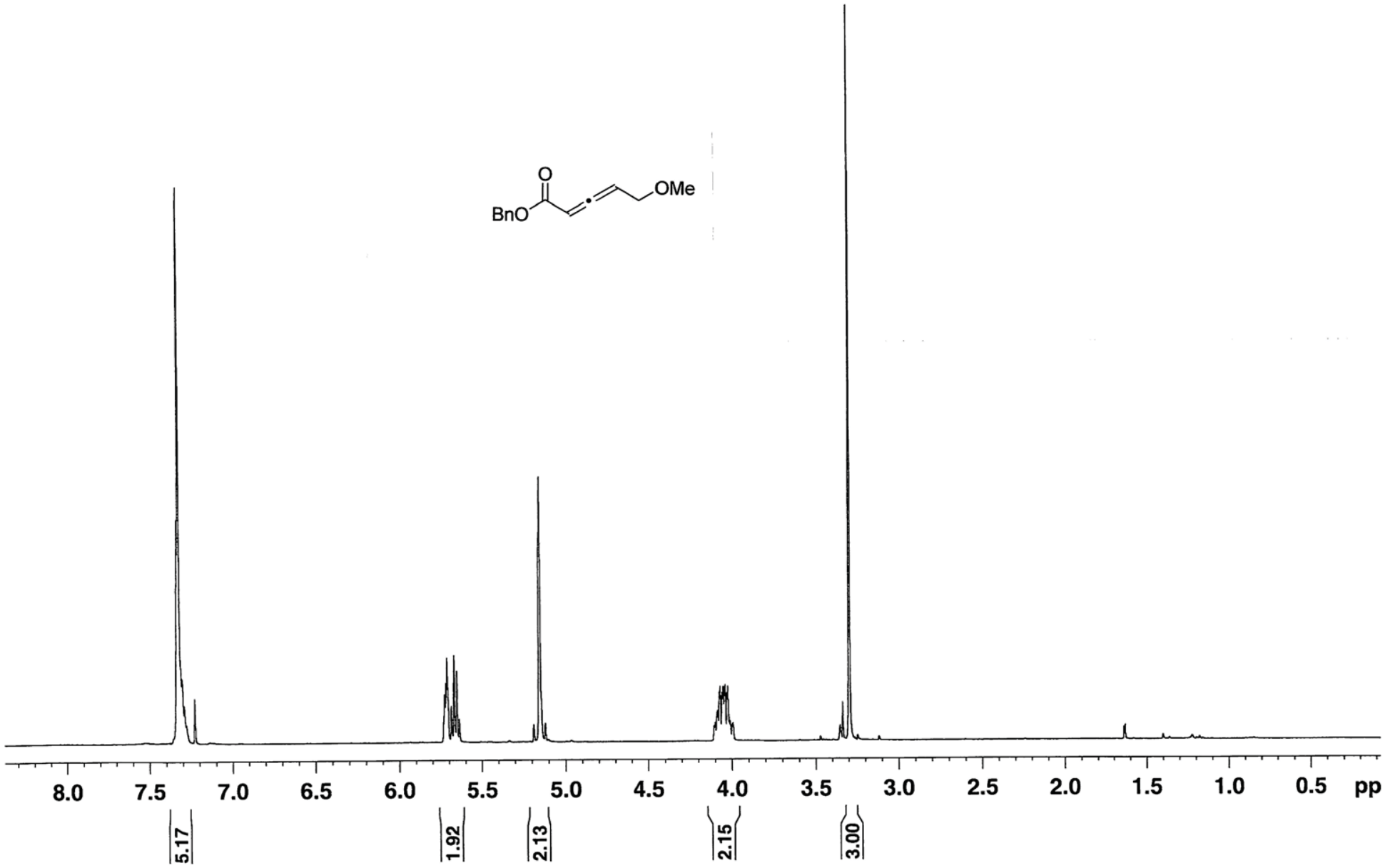
10.41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BnO
OMe
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4.5
4.0
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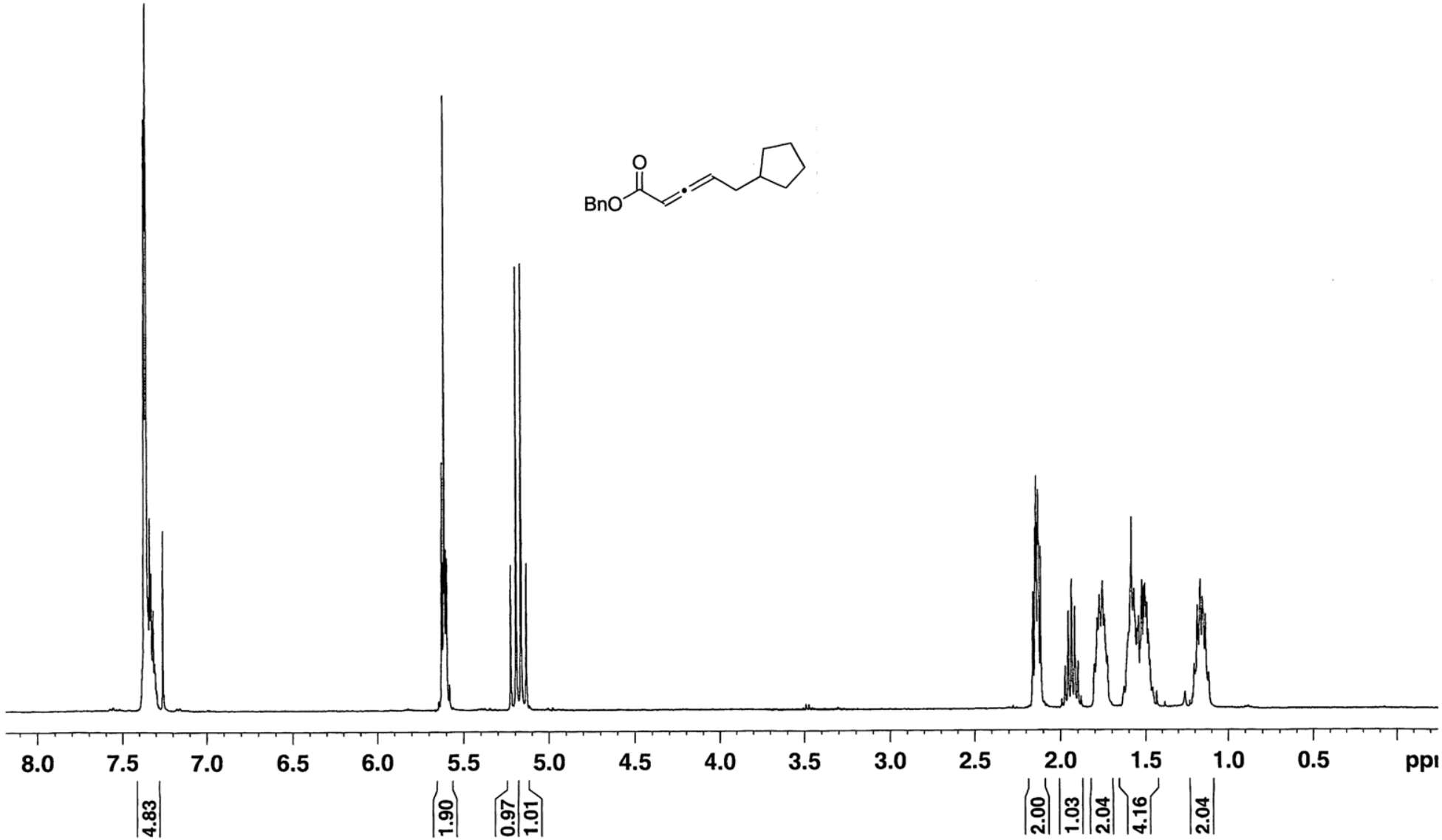
O
BnO
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3.5
3.0
2.5
2.0
1.5
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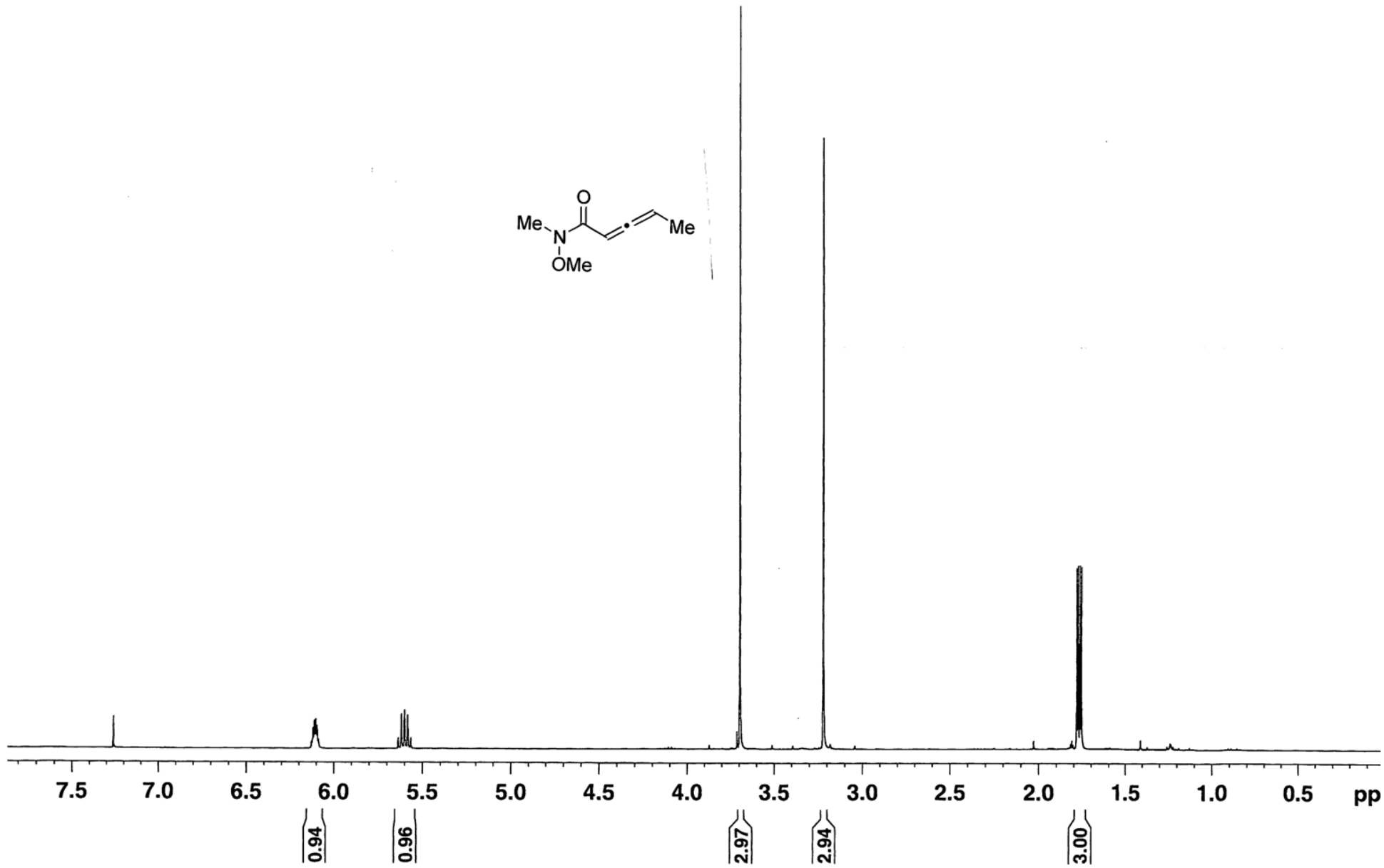
2.00
1.03
2.04
4.16
2.04


Me
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O
OMe
O
Me
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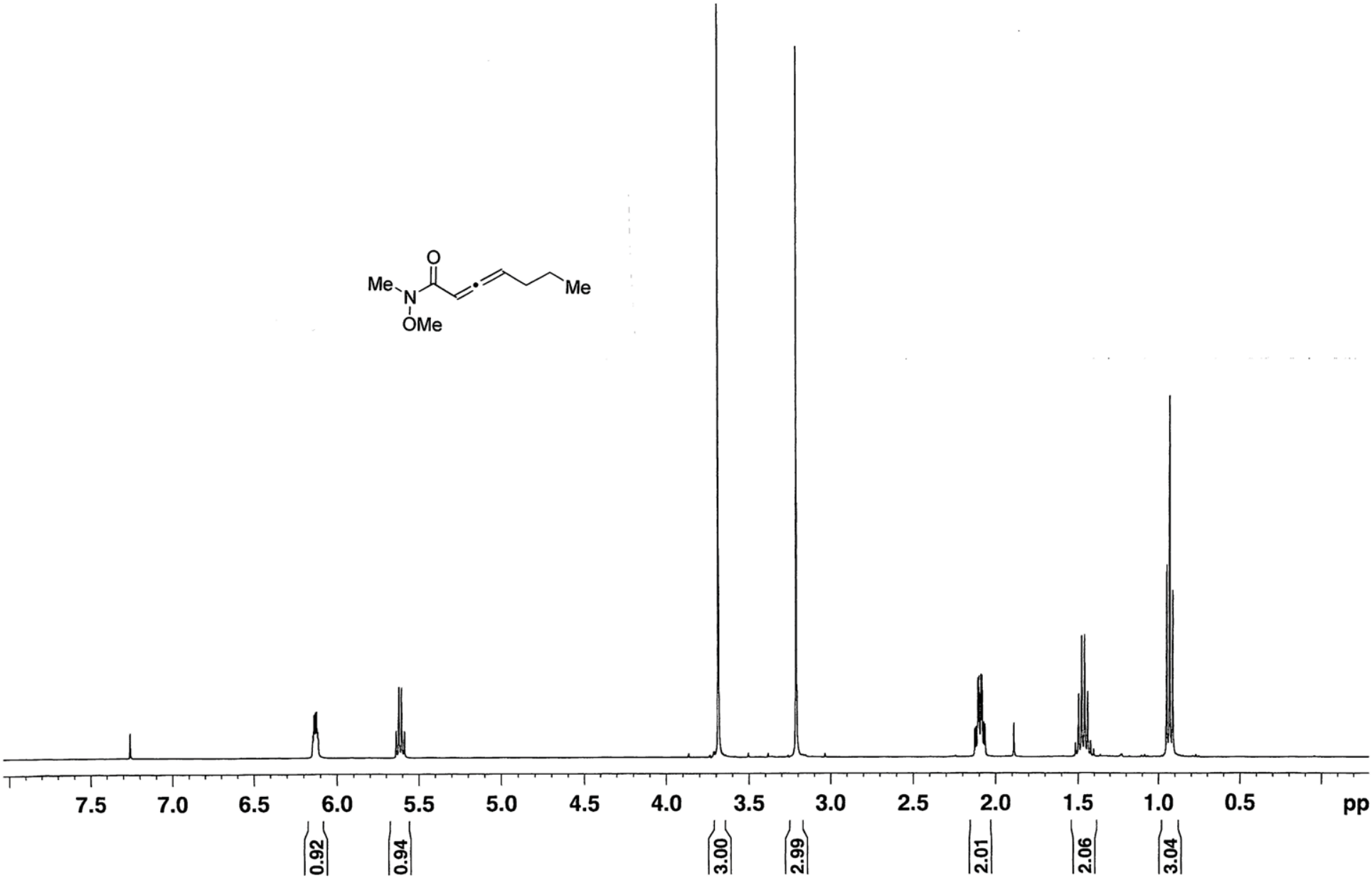
0.96
2.97
2.94
3.00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OMe
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Me
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6.0
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4.5
4.0
3.5
3.0
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pp
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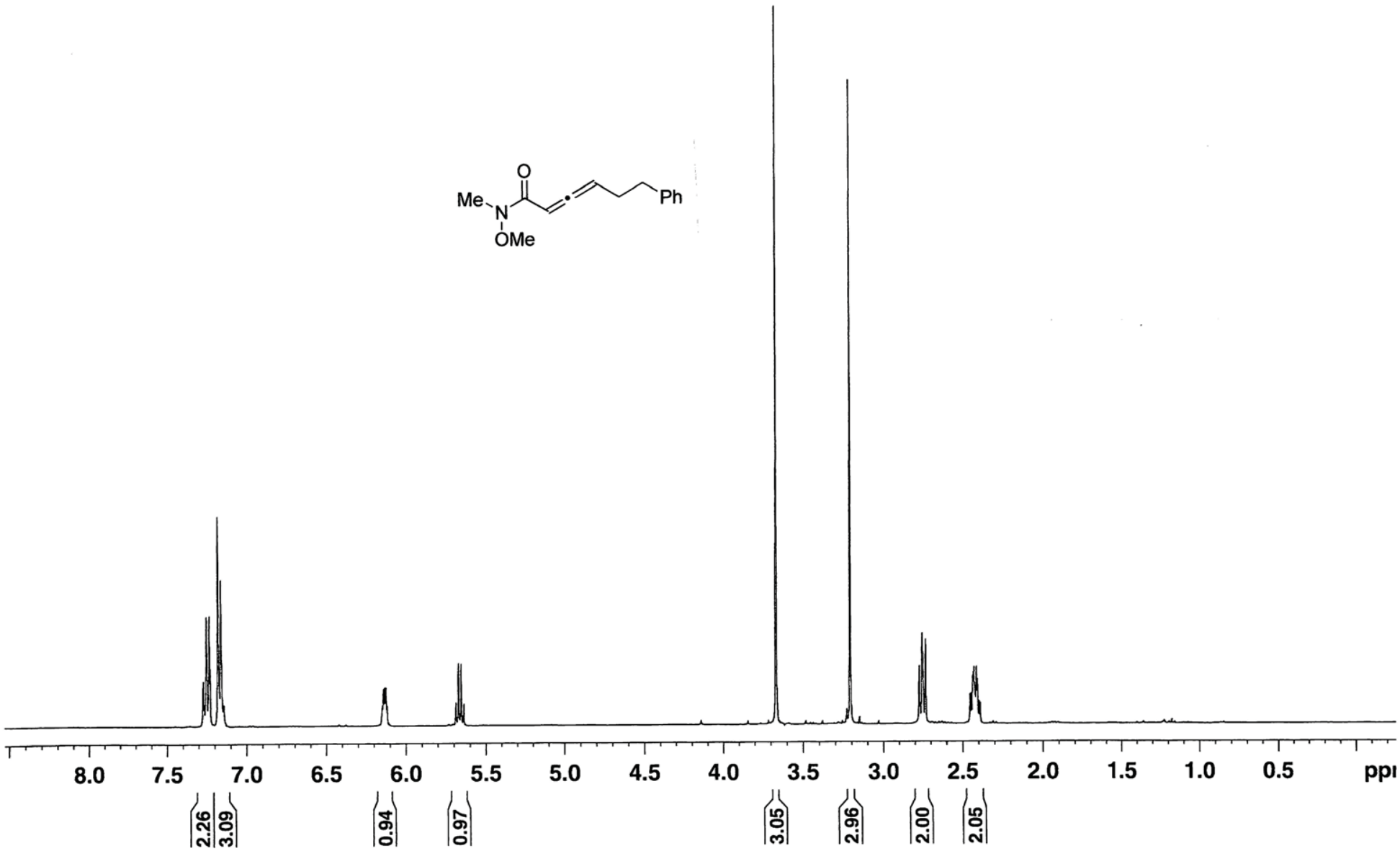
2.01
2.06
3.04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Me
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OMe
Ph
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5.0
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3.5
3.0
2.5
2.0
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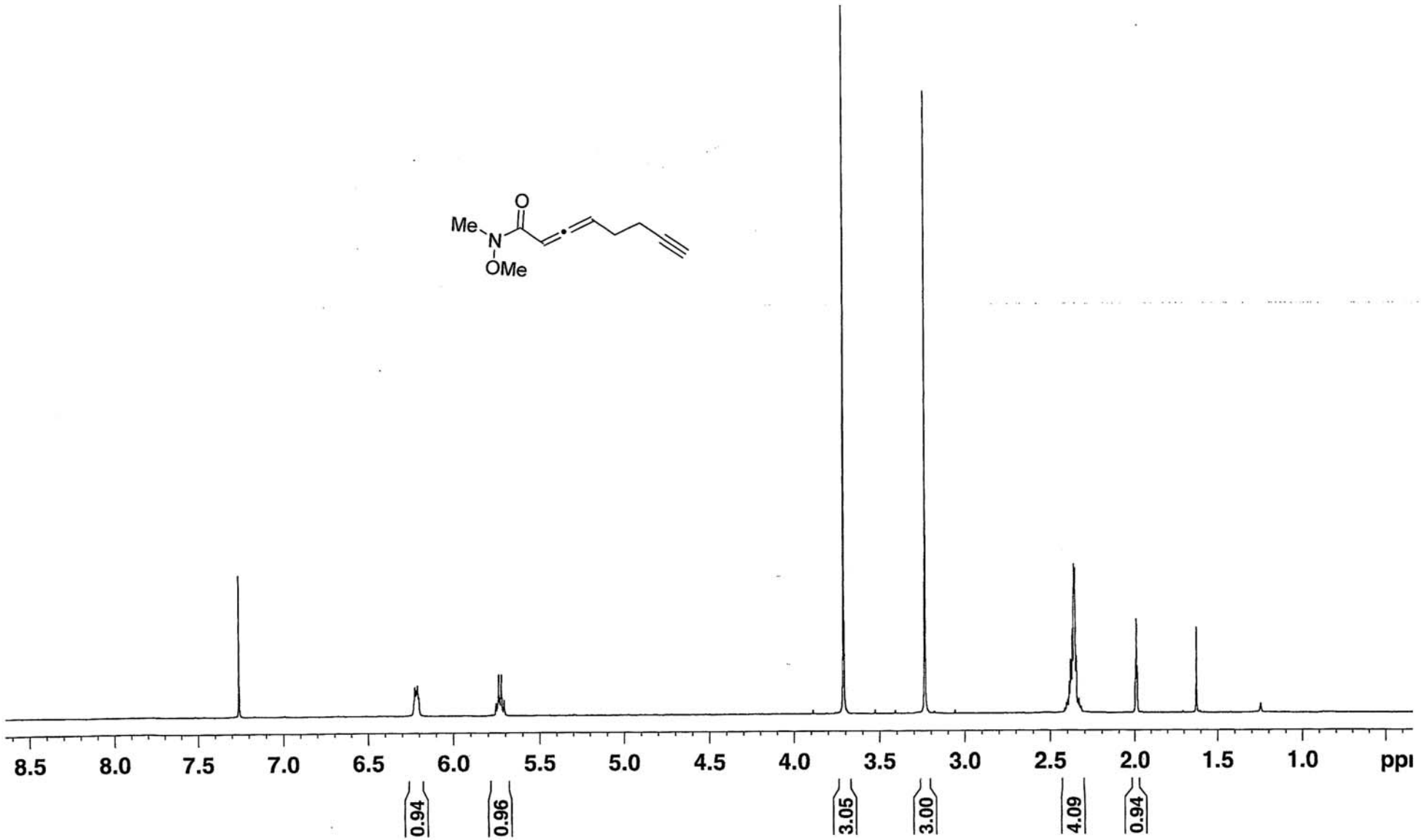
2.00
2.05


Me
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OMe
O
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5.5
5.0
4.5
4.0
3.5
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ppı
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0.96
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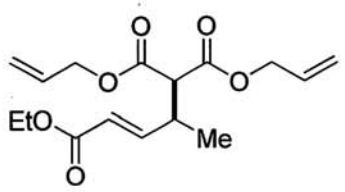
4.09
0.94



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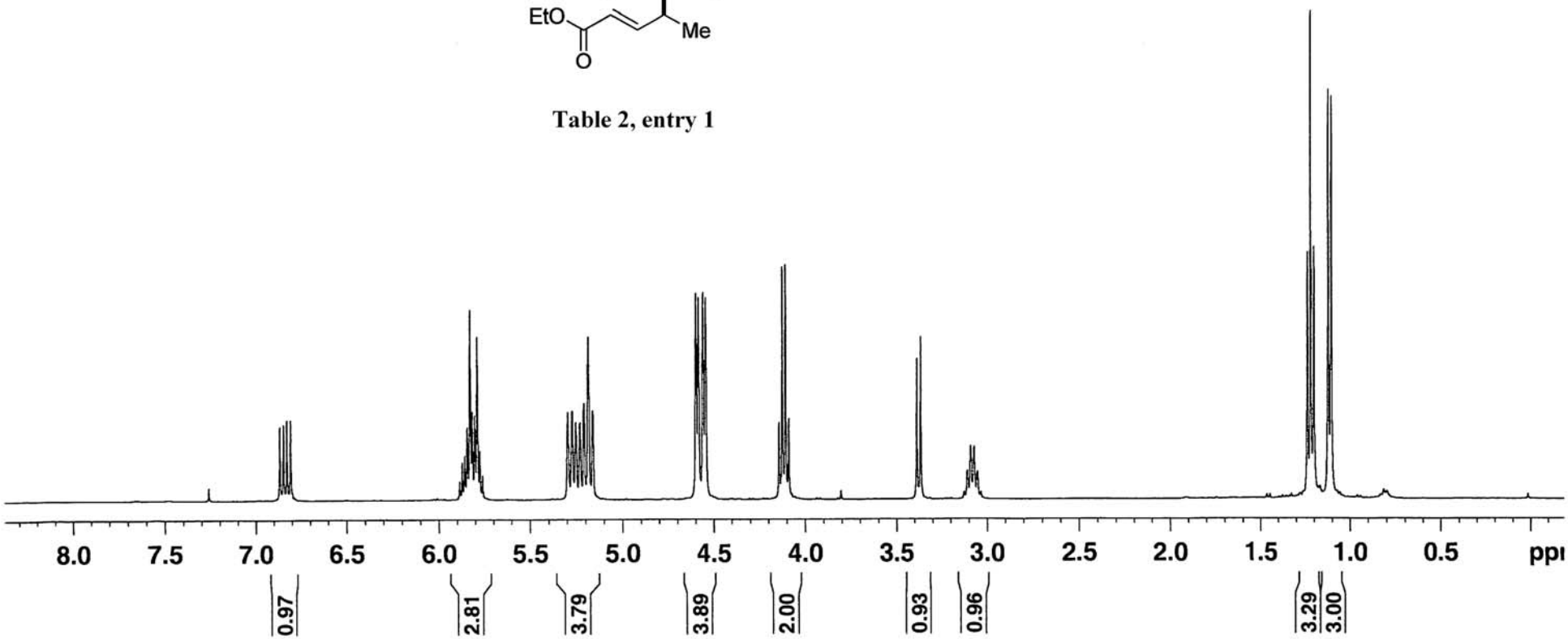

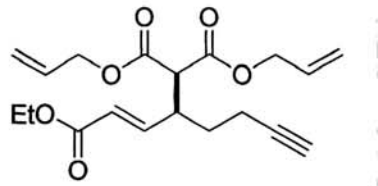

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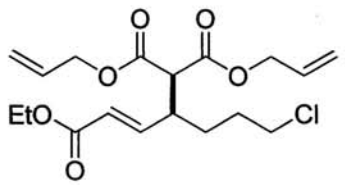

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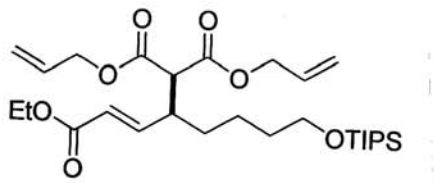

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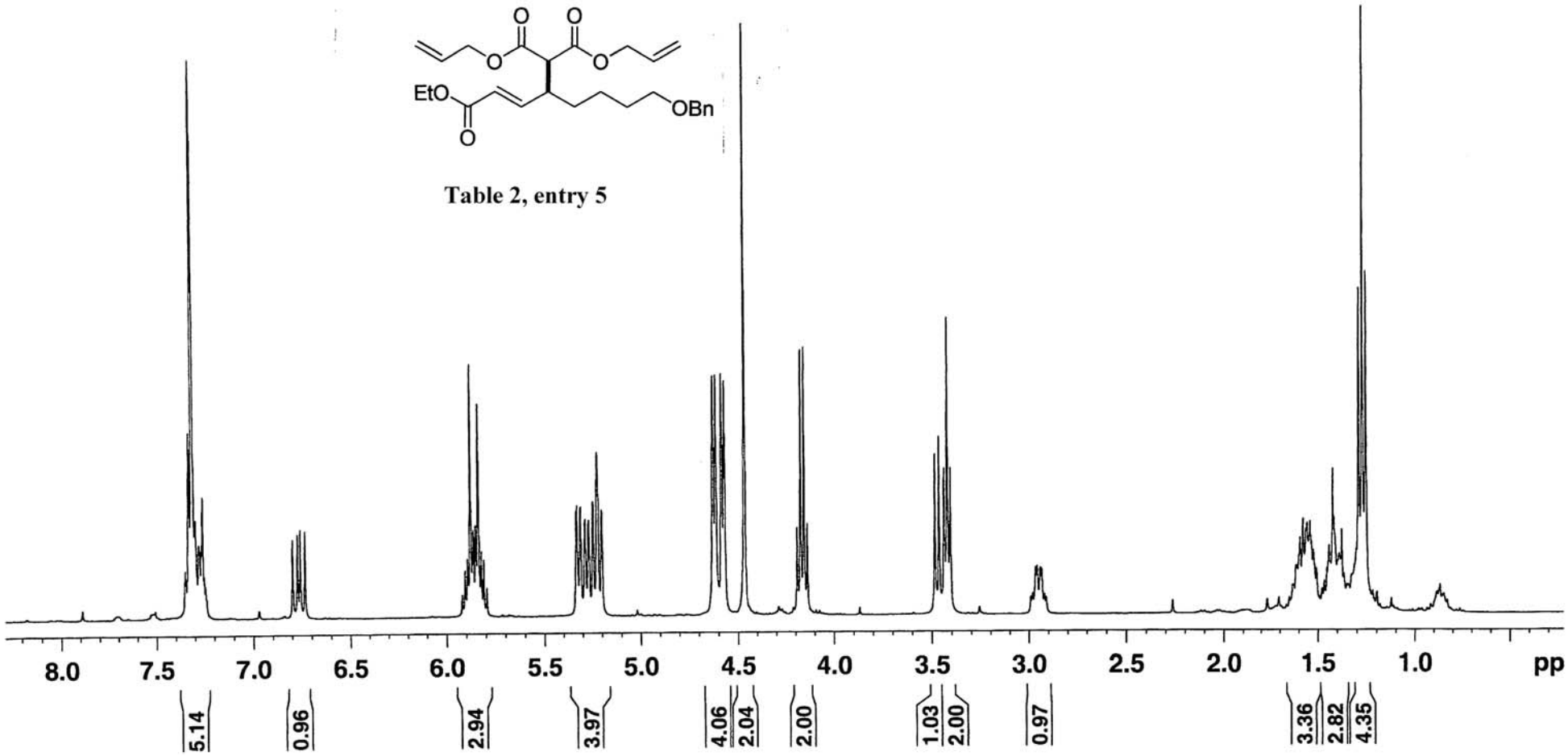
EtO
OBn
Table 2, entry 5
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5.0
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3.5
3.0
2.5
2.0
1.5
1.0
pp
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2.00
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2.00
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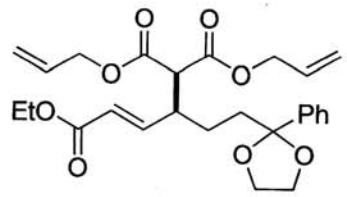
4.35



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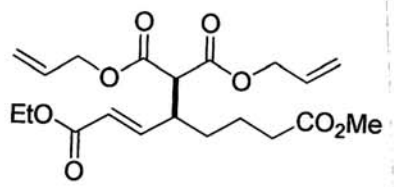

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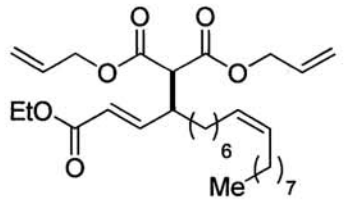

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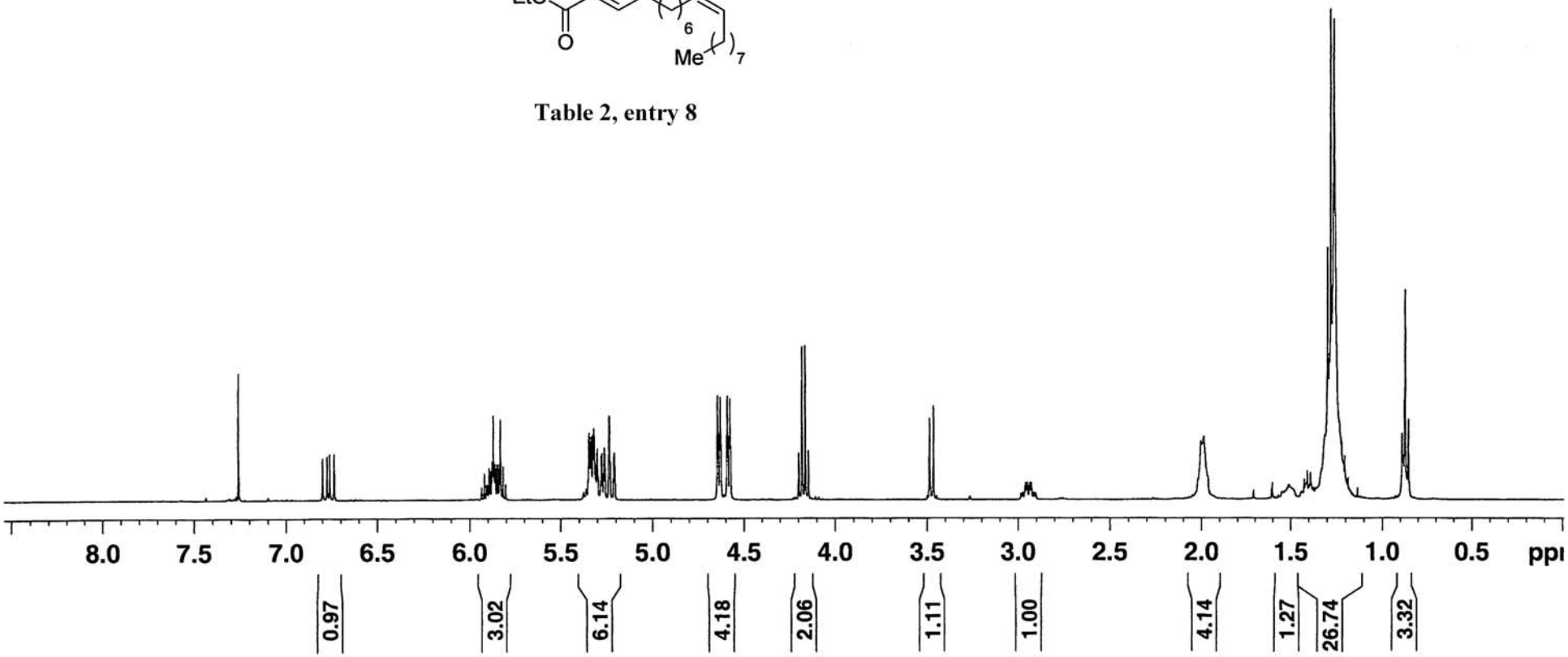

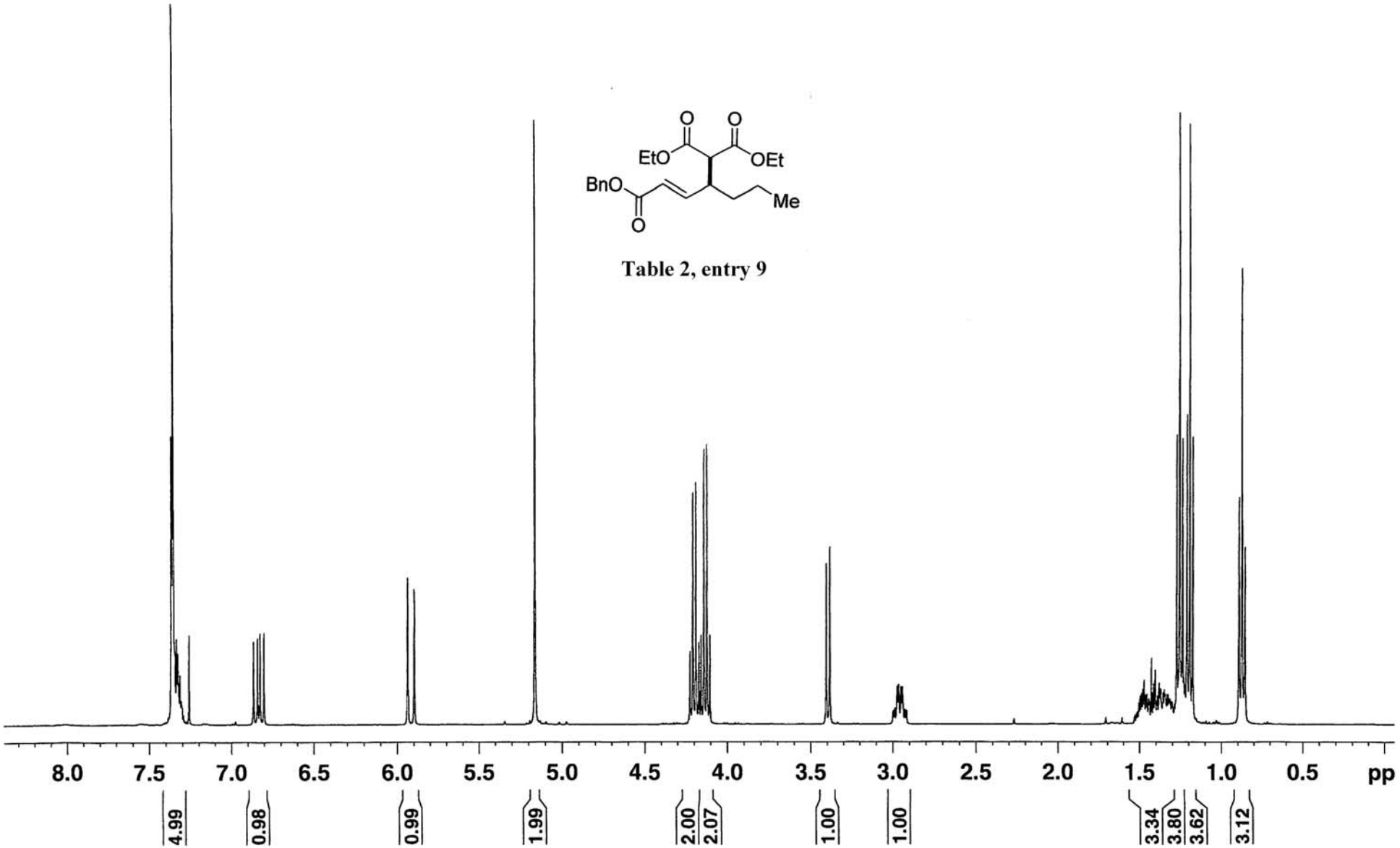

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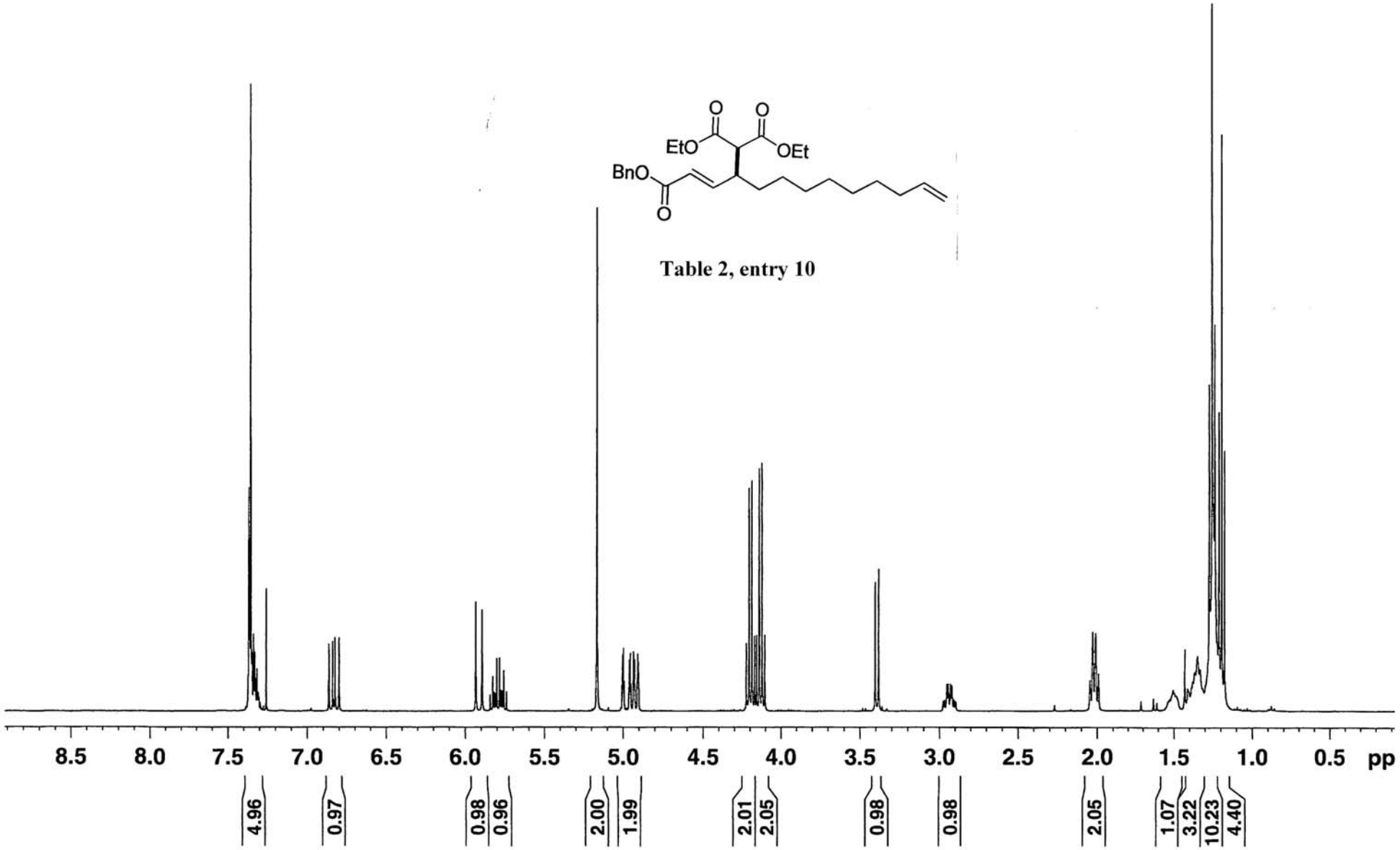

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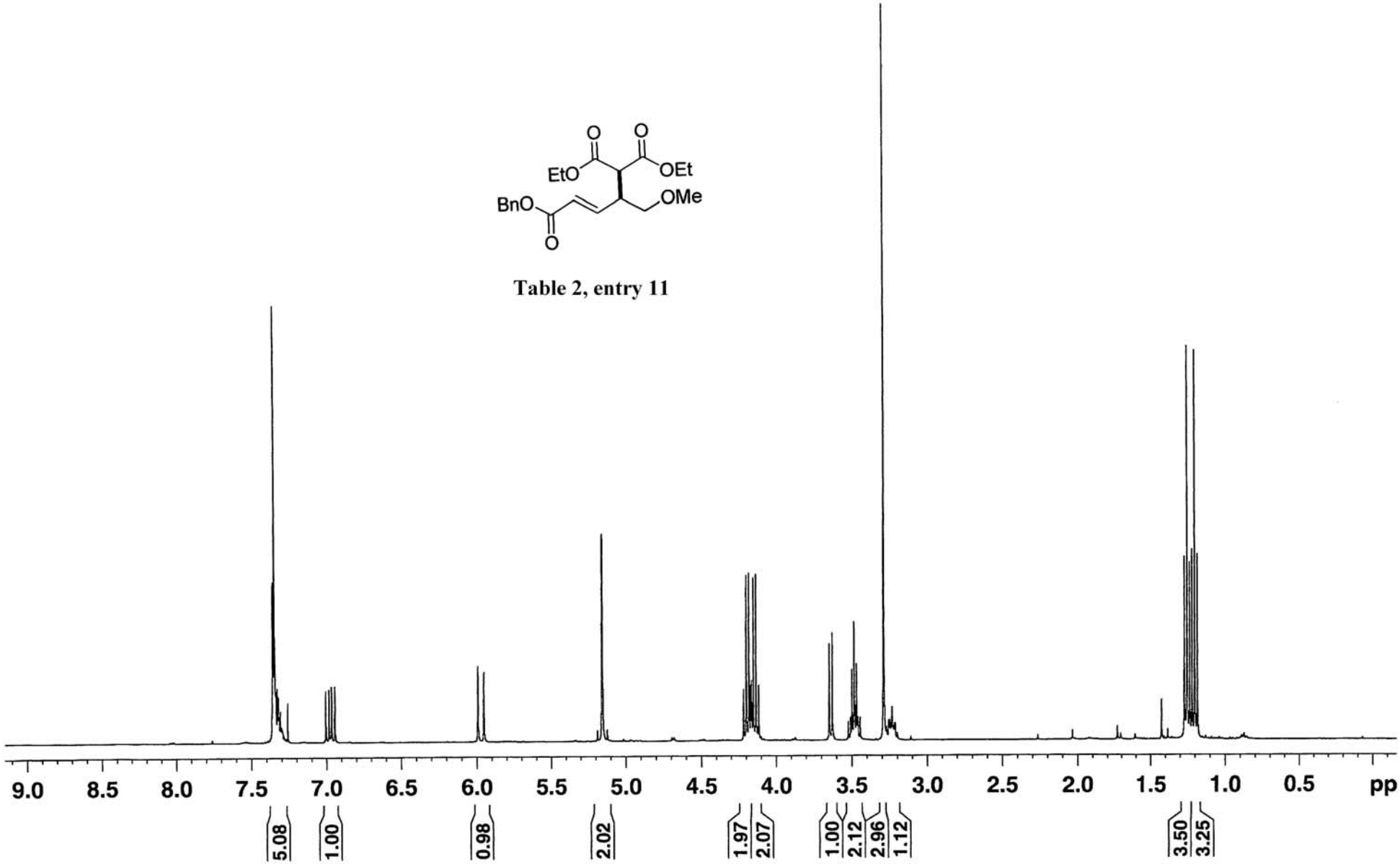

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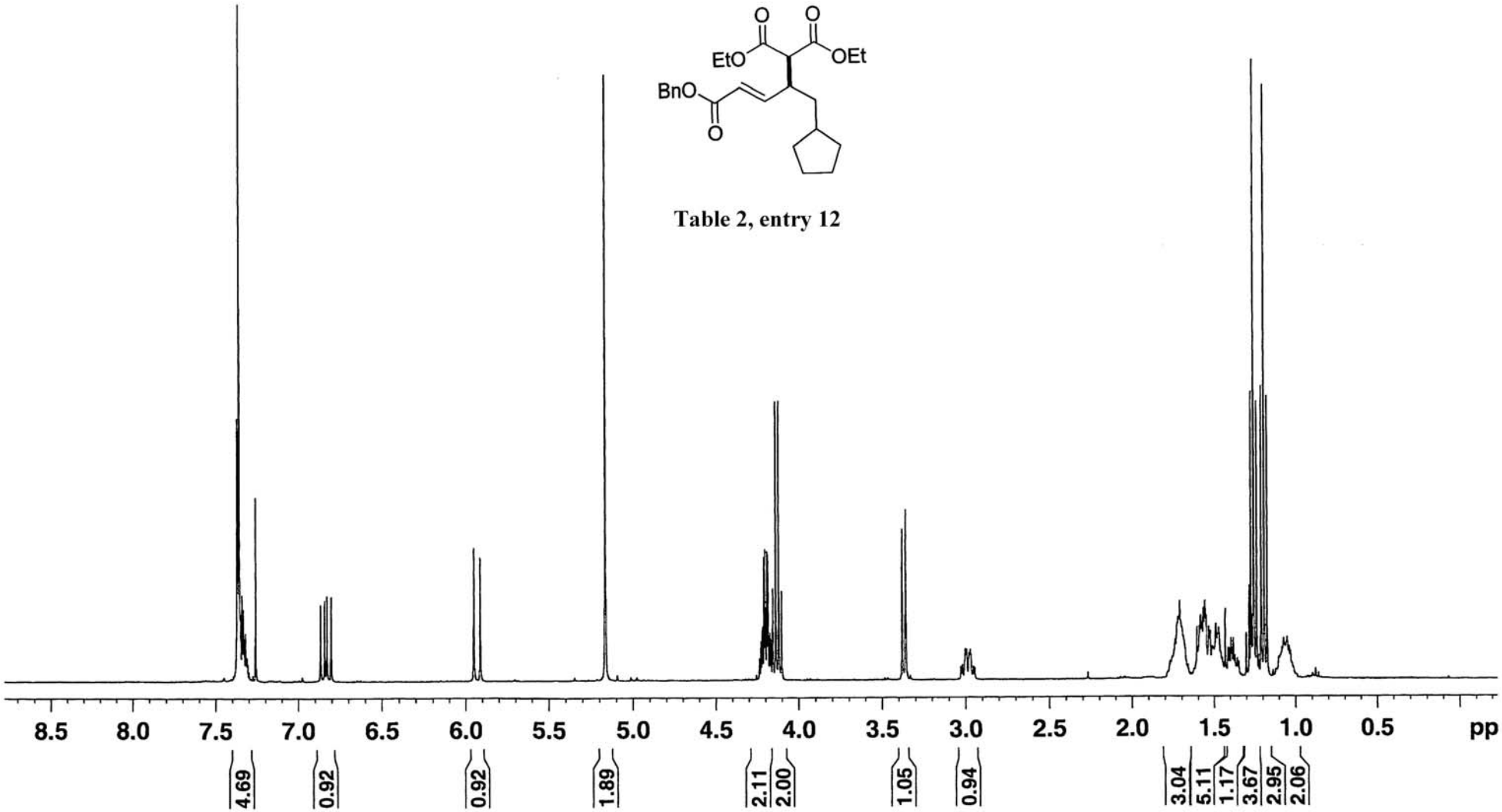

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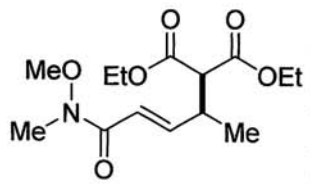

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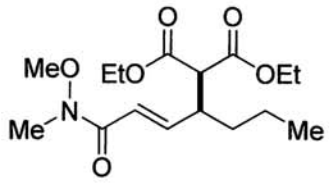

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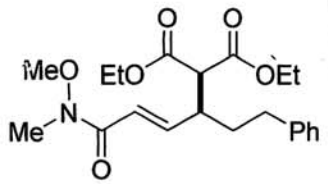

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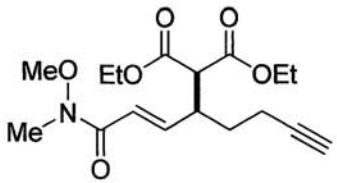

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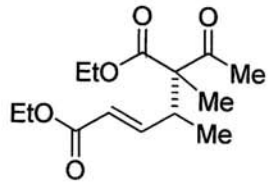
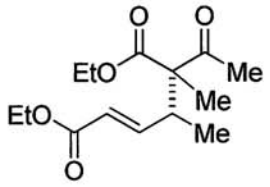
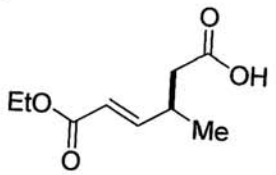


Eq. 4
major diastereomer



Eq. 4
minor diastereomer


O
OH
EtO
Me
O

Eq. 5

12
11
10
9
8
7
6
5
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ppı
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0.93
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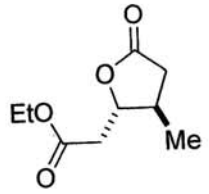
0.97
1.08
3.04
3.04


O
O
EtO
Me
O

Eq. 6

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5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppı
0.90
2.00
0.89
2.13
0.97
1.07
3.07
2.87