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Supporting Information

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Catalytic Asymmetric C–N Bond Formation: Phosphine-Catalyzed Intra- and Intermolecular γ-Addition of Nitrogen Nucleophiles to Allenoates and Alkynoates**

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Table of Contents

I. General

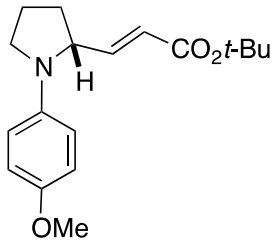
The following reagents were purchased and used as received: CPME (Aldrich, anhydrous), TBME (Aldrich, anhydrous), 2,4-dimethoxyphenol (available from Matrix Scientific), and 2-fluoro-6-methoxylphenol (Aldrich). Catalyst **1** is commercially available from Strem Chemicals and Abblis Chemicals.

HPLC analyses were carried out on an Agilent 1100 Series system, using Daicel CHIRALCEL® columns or Daicel CHIRALPAK® columns (internal diameter 4.6 mm, column length 250 mm, particle size 5 μm).

II. Catalytic Asymmetric γ-Additions of Nitrogen Nucleophiles: *Intra*molecular Reactions

General Procedure. In a nitrogen-filled glovebox (a glovebox is *not* necessary: see the next paragraph), catalyst (*S*)-**1** (0.10 equiv), the phenol (2,4-dimethoxyphenol: 0.50 equiv; 2-fluoro-6-methoxyphenol: 0.20 equiv), and a solution of the substrate (1.0 equiv) in CPME (1 mL) were added in turn to an oven-dried 4-mL vial. Additional CPME was added to generate a 0.125 M solution of the substrate. The vial was capped, the cap was wrapped with electrical tape, and the vial was removed from the glovebox and stirred at 60 °C for 48 h. Next, the mixture was allowed to cool, the reaction mixture was concentrated, and the residue was purified by column chromatography (visualization with $KMnO_4$).

Glovebox-free procedure. Catalyst (*R*)-**1** (24.4 mg, 0.0690 mmol) and 2,4-dimethoxyphenol (53.8 mg, 0.350 mmol) were weighed in air and transferred to a 20-mL vial, which was capped with a PTFE-lined septum cap and then wrapped with electrical tape. The vial was evacuated and back-filled with nitrogen (three cycles). Anhydrous CPME (3 mL) was added via syringe, and the reaction mixture was stirred for 5 min. Next, the substrate (178 mg, 0.682 mmol) was added via syringe as a solution in CPME (2.5 mL), and the reaction mixture was heated to 60 °C. After 48 h, the reaction mixture was cooled and then concentrated, and the product was purified by column chromatography. Table 1, entry 3: 95% ee and 67% yield.



(*R*,*E*)-*tert*-Butyl 3-(1-(4-methoxyphenyl)pyrrolidin-2-yl)acrylate (Table 1, entry 1). The title compound was prepared according to the General Procedure from *tert*-butyl 7-((4-methoxyphenyl)amino)hept-2-ynoate (103 mg, 0.34 mmol). After purification by flash chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless solid (69 mg, 67% yield) in 92% ee.

HPLC analysis of the product: Diacel CHIRALCEL OD-H column; 1% 2-propanol in hexanes; retention times: 15.5 min (minor), 19.2 min (major).

The second run was performed with the (*R*)-catalyst. The product was isolated as a colorless solid (67 mg, 68% yield) in 89% ee.

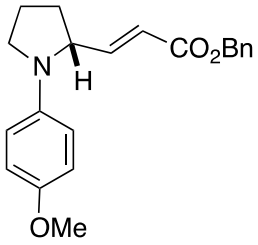
^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.89-6.82 (m, 3H), 6.53-6.48 (m, 2H), 5.81 (dd, *J* = 1.6, 15.6 Hz, 1H), 4.22-4.15 (m, 1H), 3.75 (s, 3H), 3.55-3.47 (m, 1H), 3.20 (q, *J* = 8.4 Hz, 1H), 2.20-2.08 (m, 1H), 2.05-1.95 (m, 2H), 1.90-1.85 (m, 1H), 1.47 (s, 9H);

^{13}C NMR ($CDCl_3$, 101 MHz) δ 166.2, 151.3, 148.8, 142.2, 122.8, 115.1, 113.0, 80.5, 60.3, 56.1, 49.4, 32.0, 28.3, 23.6;

IR (film) 2974, 2831, 1710, 1651, 1618, 1457, 1365, 1241, 1151, 1040, 985, 866, 848, 811, 784 cm^{-1};

LRMS (LCMS EI): calcd for $C_{18}H_{26}NO_3$ (M+H) 304.2, found 304.2;

$[\alpha]^{25}_D$ = +137° (c = 1.00, $CHCl_3$).



(*R*,*E*)-Benzyl 3-(1-(4-methoxyphenyl)pyrrolidin-2-yl)acrylate (Table 1, entry 2). The title compound was prepared according to the General Procedure from benzyl 7-((4-methoxyphenyl)amino)hept-2-ynoate (150 mg, 0.45 mmol). After purification by flash chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a light-yellow oil (109 mg, 73% yield) in 95% ee.

HPLC analysis of the product: Diacel CHIRALCEL OD-H column; 5% 2-propanol in hexanes; retention times: 13.9 min (minor), 16.0 min (major).

The second run was performed with the (*R*)-catalyst. The product was isolated as a light-yellow oil (99 mg, 67% yield) in 95% ee.

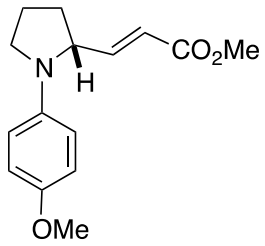
^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39-7.34 (m, 5H), 7.04 (dd, *J* = 5.0, 15.5 Hz, 1H), 6.83 (dt, *J* = 3.5, 9.0 Hz, 2H), 6.50 (dt, *J* = 4.0, 9.0 Hz, 2H), 5.96 (dd, *J* = 1.5, 15.5 Hz, 1H), 5.19 (d, *J* = 12.5 Hz, 1H), 5.14 (d, *J* = 12.5 Hz, 1H), 4.26-4.21 (m, 1H), 3.77 (s, 3H), 3.55-3.50 (m, 1H), 3.22 (q, *J* = 8.5 Hz, 1H), 2.22-2.14 (m, 1H), 2.02-1.98 (m, 2H), 1.94-1.88 (m, 1H);

^{13}C NMR ($CDCl_3$, 126 MHz) δ 166.5, 151.2, 150.6, 141.8, 135.9, 128.6, 128.4, 128.3, 120.7, 114.9, 112.9, 66.3, 60.2, 55.9, 49.3, 31.8, 23.4;

IR (film) 2947, 2831, 1715, 1649, 1618, 1509, 1454, 1367, 1243, 1159, 1038, 816, 740 cm^{-1};

LRMS (LCMS EI): calcd for $C_{21}H_{24}NO_3$ (M+H) 338.2, found 338.2;

$[\alpha]^{25}_D$ = +96° (c = 1.00, $CHCl_3$).



(*R*,*E*)-Methyl 3-(1-(4-methoxyphenyl)pyrrolidin-2-yl)acrylate (Table 1, entry 3). The title compound was prepared according to the General Procedure from methyl 7-((4-methoxyphenyl)amino)hept-2-ynoate (130 mg, 0.50 mmol). After purification by flash chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a light-yellow oil (99 mg, 76% yield) in 94% ee.

HPLC analysis of the product: Diacel CHIRALCEL OD-H column; 1% 2-propanol in hexanes; retention times: 18.9 min (minor), 21.5 min (major).

The second run was performed with the (*R*)-catalyst. The product was isolated as a light-yellow oil (106 mg, 80% yield) in 94% ee.

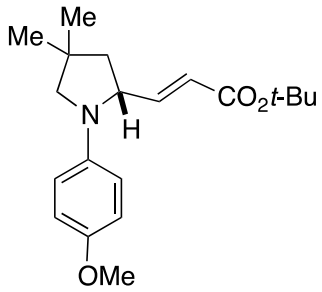
^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.00 (dd, *J* = 5.0, 15.5 Hz, 1H), 6.83 (dt, *J* = 3.5, 9.5 Hz, 2H), 6.51 (dt, *J* = 4.0, 9.0 Hz, 2H), 5.91 (dd, *J* = 1.5, 15.5 Hz, 1H), 4.25-4.20 (m, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.55-3.50 (m, 1H), 3.23 (q, *J* = 8.5 Hz, 1H), 2.22-2.14 (m, 1H), 2.02-1.98 (m, 2H), 1.94-1.86 (m, 1H);

^{13}C NMR ($CDCl_3$, 126 MHz) δ 167.1, 151.2, 150.2, 141.8, 120.6, 114.9, 112.9, 60.1, 55.9, 51.5, 49.2, 31.8, 23.4;

IR (film) 2958, 2836, 1723, 1655, 1512, 1436, 1241, 1177, 1042, 982, 813 cm^{-1};

LRMS (LCMS EI): calcd for $C_{15}H_{20}NO_3$ (M+H) 262.1, found 262.2;

$[\alpha]^{25}_D$ = +109° (c = 1.00, $CHCl_3$).



(*R*,*E*)-*tert*-Butyl 3-(1-(4-methoxyphenyl)-4,4-dimethylpyrrolidin-2-yl)acrylate (Table 1, entry 4). The title compound was prepared according to the General Procedure from *tert*-butyl 7-((4-methoxyphenyl)amino)-6,6-dimethylhept-2-ynoate (120 mg, 0.36 mmol). After purification by flash chromatography (10:1→4:1 hexanes/ethyl acetate), the title compound was isolated as a pale-yellow oil (71 mg, 59% yield) in 93% ee.

HPLC analysis of the product: Diacel CHIRALCEL OD-H column; 1% 2-propanol in hexanes; retention times: 8.5 min (minor), 12.6 min (major).

The second run was performed with the (*R*)-catalyst. The product was isolated as a pale-yellow oil (72 mg, 60% yield) in 94% ee.

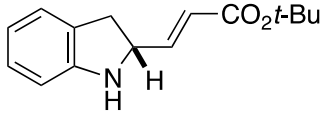
^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.88 (dd, *J* = 6.0, 15.6 Hz, 1H), 6.90-6.80 (m, 2H), 6.54-6.46 (m, 2H), 5.87 (dd, *J* = 1.6, 15.6 Hz, 1H), 4.28-4.23 (m, 1H), 3.76 (s, 3H), 3.37 (d, *J* = 8.8 Hz, 1H), 3.07 (d, *J* = 8.8 Hz 1H), 2.06 (dd, *J* = 8.4, 12.4 Hz, 1H), 1.72 (dd, *J* = 6.4, 12.4 Hz, 1H), 1.47 (s, 9H), 1.19 (s, 3H), 1.07 (s, 3H);

^{13}C NMR ($CDCl_3$, 101 MHz) δ 166.2, 151.4, 150.4, 143.0, 122.5, 114.8, 113.7, 80.5, 64.1, 60.7, 56.0, 46.9, 37.9, 28.3, 27.6, 27.5;

IR (film) 2952, 2868, 2825, 1707, 1649, 1462, 1391, 1365, 1246, 1146, 1042, 982, 813 cm^{-1};

LRMS (LCMS EI): calcd for $C_{20}H_{30}NO_3$ (M+H) 332.2, found 332.2;

$[\alpha]^{25}_D$ = +96° (c = 1.00, $CHCl_3$).



(*R*,*E*)-*tert*-Butyl 3-(indolin-2-yl)acrylate (Table 1, entry 5). The title compound was prepared according to the General Procedure from *tert*-butyl 5-(2-aminophenyl)pent-2-ynoate (115 mg, 0.47 mmol). After purification by flash chromatography (10:1→2:1 hexanes/ethyl acetate), the title compound was isolated as a colorless solid (66 mg, 57% yield) in 89% ee.

HPLC analysis of the product: Diacel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 18.3 min (minor), 26.6 min (major).

The second run was performed with the (*R*)-catalyst. The product was isolated as a colorless solid (60 mg, 52% yield) in 90% ee.

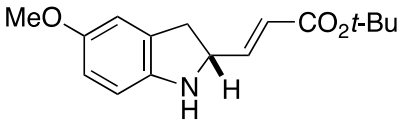
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.08-7.00 (m, 2H), 6.92 (dd, *J* = 6.8, 15.6 Hz, 1H), 6.72 (td, *J* = 1.2, 7.6 Hz, 1H), 6.60-6.52 (m, 1H), 5.93 (dd, *J* = 1.2, 15.6 Hz, 1H), 4.47 (q, *J* = 8.0 Hz, 1H), 3.91 (br s, 1H), 3.26 (dd, *J* = 9.2, 15.6 Hz, 1H), 2.86 (dd, *J* = 8.0, 15.6 Hz, 1H), 1.48 (s, 9H);

^{13}C NMR ($CDCl_3$, 101 MHz) δ 165.9, 150.4, 147.7, 127.8, 127.7, 124.9, 123.1, 119.3, 109.5, 80.7, 60.4, 36.3, 28.3;

IR (film) 2931, 1710, 1604, 1483, 1467, 1309, 1248, 1148, 742 cm^{-1};

LRMS (LCMS EI): calcd for $C_{15}H_{20}NO_2$ (M+H) 246.1, found 246.2;

$[\alpha]^{25}_D$ = –29° (c = 1.00, $CHCl_3$).



(*R*,*E*)-*tert*-Butyl 3-(5-methoxyindolin-2-yl)acrylate (Table 1, entry 6). The title compound was prepared according to the General Procedure from *tert*-butyl 5-(2-amino-5-methoxyphenyl)pent-2-ynoate (85 mg, 0.31 mmol). After purification by flash chromatography (10:1→4:1 hexanes/ethyl acetate), the title compound was isolated as a pale-yellow solid (39 mg, 46% yield) in 90% ee.

HPLC analysis of the product: Diacel CHIRALPAK AD-H column; 5% 2-propanol in hexanes; retention times: 14.8 min (minor), 21.7 min (major).

The second run was performed with the (*R*)-catalyst. The product was isolated as a pale-yellow solid (50 mg, 42% yield) in 88% ee.

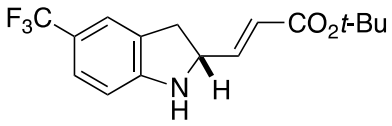
^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.91 (dd, *J* = 7.2, 15.6 Hz, 1H), 6.71 (s, 1H), 6.62-6.56 (m, 2H), 5.92 (d, *J* = 15.6 Hz, 1H), 4.47-4.42 (m, 1H), 3.74 (s, 4H), 3.24 (dd, *J* = 9.0, 15.6 Hz, 1H), 2.84 (dd, *J* = 7.8, 15.6 Hz, 1H), 1.47 (s, 9H);

^{13}C NMR ($CDCl_3$, 151 MHz) δ 165.9, 153.7, 147.7, 144.0, 129.4, 123.0, 112.5, 111.6, 110.0, 80.7, 60.8, 56.0, 36.6, 28.2;

IR (film) 2979, 2942, 2836, 1808, 1731, 1620, 1504, 1370, 1248, 1154, 1037, 840, 734 cm^{-1};

LRMS (LCMS EI): calcd for $C_{16}H_{22}NO_3$ (M+H) 276.2, found 276.2;

$[\alpha]^{25}_D = -19°$ (c = 2.00, $CHCl_3$).



(*R*,*E*)-*tert*-Butyl 3-(5-(trifluoromethyl)indolin-2-yl)acrylate (Table 1, entry 7). The title compound was prepared according to the General Procedure from *tert*-butyl 5-(2-amino-5-(trifluoromethyl)phenyl)pent-2-ynoate (81 mg, 0.26 mmol). After purification by flash chromatography (10:1→4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless solid (35 mg, 43% yield) in 88% ee.

HPLC analysis of the product: Diacel CHIRALPAK AD-H column; 3% 2-propanol in hexanes; retention times: 16.7 min (minor), 23.7 min (major).

The second run was performed with the (*R*)-catalyst. The product was isolated as a colorless solid (54 mg, 45% yield) in 87% ee.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32-7.26 (m, 2H), 6.88 (dd, *J* = 7.2, 15.6 Hz, 1H), 6.61 (d, *J* = 8.8 Hz, 1H), 5.93 (d, *J* = 1.2, 15.6 Hz, 1H), 4.60-4.54 (m, 1H), 4.17 (s, 1H), 3.31 (dd, *J* = 9.6, 16.0 Hz, 1H), 2.89 (dd, *J* = 7.6, 16.0 Hz, 1H), 1.48 (s, 9H);

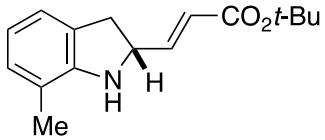
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.5, 153.0, 146.6, 127.7, 124.9 (q, *J* = 271 Hz), 125.6 (q, *J* = 4 Hz), 123.8, 123.3 (*J* = 4 Hz), 120.7 (q, *J* = 32 Hz), 108.0, 80.8, 60.2, 35.6, 28.1;

^{19}F NMR ($CDCl_3$, 376 MHz) δ –61.1;

IR (film) 3317, 2979, 2942, 1691, 1623, 1367, 1328, 1156, 1117, 1053, 977, 813 cm^{-1};

LRMS (LCMS EI): calcd for $C_{16}H_{19}F_3NO_2$ (M+H) 314.1, found 314.1;

$[\alpha]^{25}_D = -11°$ (c = 1.00, $CHCl_3$).



(*R*,*E*)-*tert*-Butyl 3-(7-methylindolin-2-yl)acrylate (Table 1, entry 8). The title compound was prepared according to the General Procedure from *tert*-butyl 5-(2-amino-3-methylphenyl)pent-2-ynoate (96 mg, 0.37 mmol). After purification by flash chromatography

(10:1→4:1 hexanes/ethyl acetate), the title compound was isolated as a pale-yellow solid (60 mg, 62% yield) in 89% ee.

HPLC analysis of the product: Diacel CHIRALPAK AD-H column; 3% 2-propanol in hexanes; retention times: 10.0 min (minor), 12.4 min (major).

The second run was performed with the (*R*)-catalyst. The product was isolated as a pale-yellow solid (81 mg, 72% yield) in 87% ee.

^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.00-6.92 (m, 2H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.68 (t, *J* = 7.2 Hz, 1H), 5.95 (dd, *J* = 0.6, 15.0 Hz, 1H), 4.49 (q, *J* = 7.8 Hz, 1H), 3.75 (s, 1H), 3.29 (dd, *J* = 9.0, 15.6 Hz, 1H), 2.89 (dd, *J* = 7.8, 15.0 Hz, 1H), 2.14 (s, 3H), 1.48 (s, 9H);

^{13}C NMR ($CDCl_3$, 151 MHz) δ 165.9, 148.9, 147.8, 128.7, 127.1, 123.0, 122.3, 119.4, 119.0, 80.8, 60.3, 36.5, 28.3, 17.0;

IR (film) 3354, 2973, 2921, 2851, 1707, 1657, 1599, 1467, 1391, 1365, 1304, 1259, 1154, 1072, 980, 866, 845, 753 cm^{-1};

LRMS (LCMS EI): calcd for $C_{16}H_{22}NO_2$ (M+H) 260.2, found 260.2;

$[\alpha]^{25}_D = -8°$ (c = 1.00, $CHCl_3$).

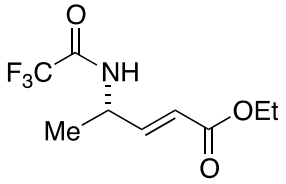
III. Catalytic Asymmetric γ-Additions of Nitrogen Nucleophiles: *Inter*molecular Reactions

General Procedure. In a nitrogen-filled glovebox (a glovebox is *not* necessary: see the next paragraph), 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol), TBME (6.0 mL), a stir bar, and catalyst (*R*)-**1** (17.7 mg, 0.0500 mmol; in 2.0 mL of TBME) were added in turn to an oven-dried 20-mL vial. The solution was stirred for 5 min, and then the allenoate (1.00 mmol) was added (in 2.0 mL of TBME). The vial was capped (the cap was wrapped with electrical tape) and then removed immediately from the glovebox. The reaction mixture was stirred at 10 °C for 36 h. The mixture was then concentrated, and the product was purified by column chromatography (visualization with $KMnO_4$).

Note: For the γ-addition illustrated in Table 3, entry 2: in the presence of 0.10 equiv of water, the product was formed in 89% ee and 93% yield; in the presence of 0.50 equiv of water, the product was formed in 89% ee and >95% yield.

Glovebox-free procedure. Catalyst (*R*)-**1** (17.7 mg, 0.0500 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol) were weighed in air and transferred to a 20-mL vial, which was capped with a PTFE-lined septum cap and then wrapped with electrical tape. The vial was evacuated and back-filled with nitrogen (three cycles). Anhydrous TBME (10 mL) was added via syringe, and the reaction mixture was stirred for 5 min. Next, the allenoate (1.00 mmol) was added via syringe, and the vial was cooled to 10 °C. After 36 hours, the reaction mixture was concentrated, and the product was purified by column chromatography. Table 3, entry 4: 89% ee and 78% yield (run 1); 86% ee and 83% yield (run 2).

Note: For the γ-addition illustrated in Table 3, entry 4: when this reaction was conducted in a capped vial under air, the product was formed in 89% ee and 68% yield (run 1); 87% ee and 72% yield (run 2).



(*S*,*E*)-Ethyl 4-(2,2,2-trifluoroacetamido)pent-2-enoate (Table 3, entry 1). The title compound was prepared according to the General Procedure from (±)-ethyl penta-2,3-dienoate (126 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol). After purification by column chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless oil (108 mg, 90% yield) in 87% ee.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 12.1 min (major), 18.6 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless oil (104 mg, 87% yield) in 85% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.86 (dd, *J* = 5.4, 15.8 Hz, 1H), 6.42 (br s, 1H), 5.95 (dd, *J* = 1.7, 15.8 Hz, 1H), 4.83-4.72 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.42 (d, *J* = 7.0 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H);

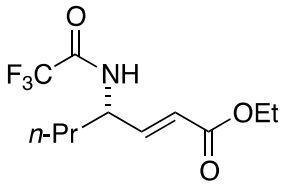
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.8, 156.5 (q, *J* = 38 Hz), 145.6, 122.0, 115.7 (q, *J* = 289 Hz), 60.8, 46.5, 19.6, 14.2;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.7;

IR (film) 3308, 3088, 2985, 1732, 1660, 1552, 1454, 1371, 1196, 1033, 979, 867, 624 cm^{-1};

LRMS (LCMS EI): calcd for $C_9H_{13}F_3NO_3$ (M+H) 240.1, found 240.1;

$[\alpha]^{25}_D = -27°$ (c = 1.00, $CHCl_3$).



(*S*,*E*)-Ethyl 4-(2,2,2-trifluoroacetamido)hept-2-enoate (Table 3, entry 2). The title compound was prepared according to the General Procedure from (±)-ethyl hepta-2,3-dienoate (154 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol). After purification by column chromatography (10:1→4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless oil (118 mg, 88% yield) in 88% ee.

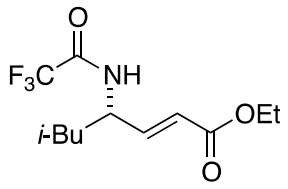
HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 10.6 min (major), 22.6 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless oil (122 mg, 91% yield) in 85% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.82 (dd, *J* = 6.1, 15.8 Hz, 1H), 6.36 (br d, *J* = 7.9 Hz, 1H), 5.94 (dd, *J* = 1.5, 15.7 Hz, 1H), 4.71-4.62 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.72-1.64 (m, 2H), 1.47-1.37 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 7.3 Hz, 3H);

^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.8, 156.7 (q, *J* = 38 Hz), 144.9, 122.4, 115.7 (q, *J* = 289 Hz), 60.8, 50.7, 36.0, 18.8, 14.2, 13.6;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.7;
IR (film) 3308, 3090, 2965, 2877, 1718, 1663, 1559, 1466, 1370, 1184, 1041, 981, 864, 724 cm^{-1};
LRMS (LCMS EI): calcd for $C_{11}H_{17}F_3NO_3$ (M+H) 268.1, found 268.2;
$[\alpha]^{25}_D = -17°$ (c = 1.00, $CHCl_3$).

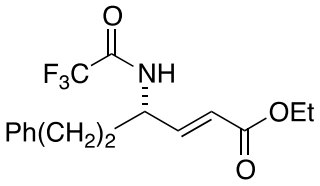


(*S*,*E*)-Ethyl 6-methyl-4-(2,2,2-trifluoroacetamido)hept-2-enoate (Table 3, entry 3). The title compound was prepared according to the General Procedure from (±)-ethyl 6-methylhepta-2,3-dienoate (168 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol). After purification by column chromatography (10:1→4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless oil (131 mg, 93% yield) in 86% ee.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 9.6 min (major), 19.1 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless oil (127 mg, 90% yield) in 89% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.81 (dd, *J* = 6.2, 15.8 Hz, 1H), 6.37 (br d, 8.2 Hz, 1H), 5.95 (dd, *J* = 1.5, 15.7 Hz, 1H), 4.76-4.68 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.70-1.64 (m, 1H), 1.55 (t, *J* = 7.6 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 3.4 Hz, 3H), 0.96 (d, *J* = 3.3 Hz, 3H);
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.9, 156.6 (q, *J* = 37 Hz), 145.2, 122.2, 115.7 (q, *J* = 289 Hz), 60.8, 49.2, 43.0, 24.7, 22.5, 22.1, 14.2;
^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.7;
IR (film) 3306, 3091, 2961, 1713, 1661, 1557, 1471, 1370, 1182, 1096, 1042, 980, 873, 726 cm^{-1};
LRMS (LCMS EI): calcd for $C_{12}H_{19}F_3NO_3$ (M+H) 282.1, found 282.2;
$[\alpha]^{25}_D = -53°$ (c = 1.00, $CHCl_3$).



(*S*,*E*)-Ethyl 6-phenyl-4-(2,2,2-trifluoroacetamido)hex-2-enoate (Table 3, entry 4). The title compound was prepared according to the General Procedure from (±)-ethyl 6-phenylhexa-2,3-dienoate (216 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol). After purification by column chromatography (10:1→4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless oil (158 mg, 96% yield) in 88% ee.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 3% 2-propanol in hexanes; retention times: 17.8 min (major), 22.6 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless oil (149 mg, 91% yield) in 87% ee.

Gram-scale reaction (4.0 mmol): 1.25 g (95%), 87% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.31 (m, 2H), 7.26-7.22 (m, 1H), 7.20-7.16 (m, 2H), 6.85 (dd, *J* = 6.0, 15.8 Hz, 1H), 6.37 (br d, 8.3 Hz, 1H), 5.95 (dd, *J* = 1.2, 15.8 Hz, 1H), 4.72-4.64 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.74-2.70 (m, 2H), 2.10-1.95 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H);

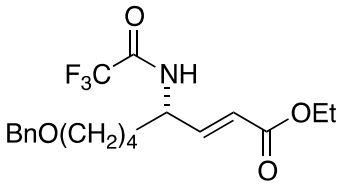
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.7, 156.7 (q, *J* = 37 Hz), 144.5, 139.9, 128.8, 128.3, 126.6, 122.8, 115.7 (q, *J* = 289 Hz), 60.9, 50.7, 35.3, 31.8, 14.2;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.8;

IR (film) 3306, 3087, 3028, 2932, 2864, 1713, 1604, 1552, 1495, 1455, 1372, 1200, 1034, 978, 875 cm^{-1};

LRMS (LCMS EI): calcd for $C_{16}H_{19}F_3NO_3$ (M+H) 330.1, found 330.2;

$[\alpha]^{25}_D$ = +31° (c = 1.00, $CHCl_3$).



(*S*,*E*)-Ethyl 8-(benzyloxy)-4-(2,2,2-trifluoroacetamido)oct-2-enoate (Table 3, entry 5). The title compound was prepared according to the General Procedure from (±)-ethyl 8-(benzyloxy)octa-2,3-dienoate (274 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol). After purification by column chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless oil (170 mg, 88% yield) in 88% ee.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 17.5 min (major), 39.9 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless oil (165 mg, 85% yield) in 90% ee.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35-7.26 (m, 5H), 6.78 (dd, *J* = 6.0, 15.7 Hz, 1H), 6.61 (br d, *J* = 7.7 Hz, 1H), 5.90 (dd, *J* = 1.4, 15.7 Hz, 1H), 4.73-4.67 (m, 1H), 4.49 (s, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.48 (t, *J* = 6.0 Hz, 2H), 1.75-1.60 (m, 4H), 1.53-1.42 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H);

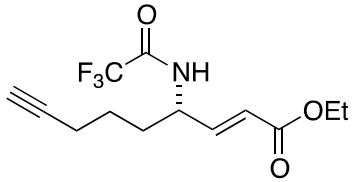
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.8, 156.7 (q, *J* = 37 Hz), 144.9, 138.2, 128.4, 127.8, 127.7, 122.4, 115.7 (q, *J* = 289 Hz), 73.1, 69.7, 60.8, 51.1, 33.4, 29.0, 22.7, 14.2;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.7;

IR (film) 3309, 3088, 2941, 2864, 1719, 1660, 1555, 1454, 1369, 1182, 1041, 980, 868, 736 cm^{-1};

LRMS (LCMS EI): calcd for $C_{19}H_{25}F_3NO_4$ (M+H) 388.2, found 388.2;

$[\alpha]^{25}_D$ = +18° (c = 1.00, $CHCl_3$).



(*S*,*E*)-Ethyl 4-(2,2,2-trifluoroacetamido)non-2-en-8-ynoate (Table 3, entry 6). The title compound was prepared according to the General Procedure from (±)-ethyl nona-2,3-dien-8-ynoate (178 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol). After purification by column chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless waxy solid (127 mg, 87% yield) in 89% ee.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 17.5 min (major), 39.9 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless waxy solid (123 mg, 84% yield) in 89% ee.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.81 (dd, *J* = 6.1, 15.7 Hz, 1H), 6.43 (br s, 1H), 5.95 (dd, *J* = 1.5, 15.7 Hz, 1H), 4.70-4.62 (m, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 2.26 (td, *J* = 2.6, 6.8 Hz, 2H), 2.00 (t, *J* = 2.6 Hz, 1H), 1.90-1.70 (m, 2H), 1.64-1.55 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H);

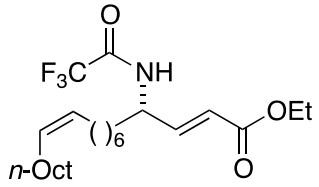
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.7, 156.8 (q, *J* = 38 Hz), 144.4, 122.8, 115.7 (q, *J* = 289 Hz), 83.0, 69.6, 60.9, 50.6, 32.7, 24.3, 18.0, 14.2;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.7;

IR (film) 3307, 3089, 2942, 1713, 1661, 1557, 1456, 1372, 1180, 1038, 978, 868, 725 cm^{-1};

LRMS (LCMS EI): calcd for $C_{13}H_{17}F_3NO_3$ (M+H) 292.1, found 292.2;

$[\alpha]^{25}_D = -60°$ (c = 1.00, $CHCl_3$).



(*S*,2*E*,11*Z*)-Ethyl 4-(2,2,2-trifluoroacetamido)icosa-2,11-dienoate (Table 3, entry 7). The title compound was prepared according to the General Procedure from (±)-(*Z*)-ethyl icosa-2,3,11-trienoate (167 mg, 0.500 mmol) and 2,2,2-trifluoroacetamide (28.3 mg, 0.250 mmol). After purification by column chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless oil (95 mg, 86% yield) in 87% ee.

HPLC analysis of the product: Diacel CHIRALPAK AD-H column; 1% 2-propanol in hexanes; retention times: 8.1 min (major), 24.3 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless oil (100 mg, 90% yield) in 87% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.82 (dd, *J* = 6.1, 15.7, Hz, 1H), 6.31 (d, *J* = 8.5 Hz, 1H), 5.94 (dd, *J* = 1.5, 15.7 Hz, 1H), 5.43-5.30 (m, 2H), 4.69-4.60 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.02 (d, *J* = 6.9 Hz, 4H), 1.76-1.62 (m, 2H), 1.39-1.22 (m, 23H), 0.94-0.87 (m, 3H).

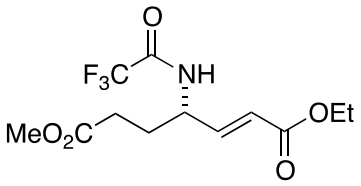
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.8, 156.7 (q, *J* = 37 Hz), 144.9, 130.2, 129.5, 122.5, 115.7 (q, *J* = 289 Hz), 60.8, 50.9, 34.0, 31.9, 29.8, 29.6, 29.5, 29.33, 29.32, 29.1, 29.0, 27.2, 27.1, 25.5, 22.7, 14.2, 14.1.

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.7;

IR (film) 3305, 2926, 2855, 1703, 1660, 1551, 1466, 1370, 1275, 1182, 1041, 978, 866, 723 cm^{-1};

LRMS (LCMS EI): calcd for $C_{24}H_{40}F_3NNaO_3$ (M+Na) 470.3, found 470.3;

$[\alpha]^{25}_D$ = –35° (c = 1.00, $CHCl_3$).



(*S*,*E*)-Ethyl 7-methyl 4-(2,2,2-trifluoroacetamido)hept-2-enedioate (Table 3, entry 8). The title compound was prepared according to the General Procedure from (±)-ethyl 7-methyl hepta-2,3-dienedioate (119 mg, 0.600 mmol) and 2,2,2-trifluoroacetamide (33.9 mg, 0.300 mmol). After purification by column chromatography (4:1→2:1 hexanes/ethyl acetate), the title compound was isolated as a colorless oil (63 mg, 68% yield) in 83% ee.

HPLC analysis of the product: Diacel CHIRALPAK AD-H column; 7% 2-propanol in hexanes; retention times: 9.1 min (major), 11.1 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless oil (62 mg, 67% yield) in 81% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.50 (d, *J* = 6.6 Hz, 1H), 6.81 (dd, *J* = 5.7, 15.7 Hz, 1H), 5.95 (dd, *J* = 1.6, 15.7, 1H), 4.77-4.62 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.72 (s, 3H), 2.56-2.42 (m, 2H), 2.11-2.02 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H);

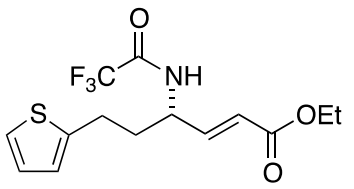
^{13}C NMR ($CDCl_3$, 126 MHz) δ 174.2, 165.6, 157.0 (d, *J* = 38 Hz), 144.0, 122.9, 115.7 (d, *J* = 289 Hz), 60.9, 52.3, 50.7, 30.1, 27.9, 14.2;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.7;

IR (film) 3315, 3085, 2985, 2956, 1720, 1661, 1551, 1440, 1371, 1310, 1270, 1179, 1037, 981, 867, 724 cm^{-1};

LRMS (LCMS EI): calcd for $C_{12}H_{17}F_3NO_5$ (M+H) 312.1, found 312.1;

$[\alpha]^{25}_D$ = –45° (c = 1.00, $CHCl_3$).



(*S*,*E*)-Ethyl 6-(thiophen-2-yl)-4-(2,2,2-trifluoroacetamido)hex-2-enoate (Table 3, entry 9). The title compound was prepared according to the General Procedure from (±)-ethyl 6-(thiophen-2-yl)hexa-2,3-dienoate (236 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg,

0.500 mmol). After purification by column chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless oil (148 mg, 88% yield) in 86% ee.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 17.4 min (major), 21.6 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless oil (143 mg, 86% yield) in 85% ee.

^{1}H NMR ($CDCl_3$, 300 MHz) δ (dd, *J* = 1.2, 5.2 Hz, 1H), 6.93 (dd, *J* = 3.4, 5.1 Hz, 1H), 6.88-6.76 (m, 2H), 6.42 (d, *J* = 8.1 Hz, 1H), 5.93 (dd, *J* = 1.5, 15.7 Hz, 1H), 4.74-4.68 (m, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.93 (t, *J* = 7.4 Hz, 2H), 2.14-1.98 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H);

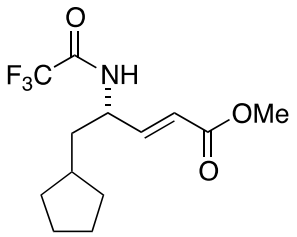
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.7, 156.7 (q, *J* = 38 Hz), 144.2, 142.4, 127.1, 125.0, 123.9, 123.0, 115.6 (q, *J* = 289 Hz), 60.9, 50.5, 35.5, 26.1, 14.2;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.7;

IR (film) 3304, 3087, 2983, 2938, 1703, 1659, 1552, 1444, 1370, 1279, 1181, 1036, 978, 850 cm^{-1};

LRMS (LCMS EI): calcd for $C_{14}H_{17}F_3NO_3S$ (M+H) 336.2, found 336.2;

$[\alpha]^{25}_D$ = +43 (c = 1.00, $CHCl_3$).



(*S*,*E*)-Methyl 5-cyclopentyl-4-(2,2,2-trifluoroacetamido)pent-2-enoate (eq 3). The title compound was prepared according to the General Procedure from (±)-methyl 5-cyclopentylpenta-2,3-dienoate (180 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol). After purification by column chromatography (4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless waxy solid (117 mg, 80% yield) in 91% ee.

HPLC analysis of the product: Diacel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 15.0 min (major), 29.2 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless waxy solid (112 mg, 76% yield) in 91% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.82 (dd, *J* = 6.3, 15.7 Hz, 1H), 6.60 (br s, 1H), 5.93 (d, *J* = 15.7 Hz, 1H), 4.70-4.56 (m, 1H), 3.74 (s, 3H), 1.87-1.72 (m, 3H), 1.72-1.45 (m, 6H), 1.12 (dd, *J* = 7.4, 3.8 Hz, 2H);

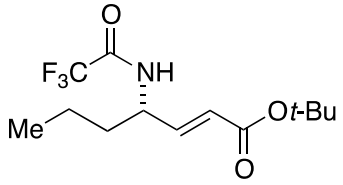
^{13}C NMR ($CDCl_3$, 126 MHz) δ 166.4, 156.6 (q, *J* = 37 Hz), 145.6, 121.7, 115.7 (q, *J* = 289 Hz), 51.8, 50.6, 40.2, 36.5, 32.7, 32.5, 25.1, 24.9;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.8;

IR (film) 3306, 3092, 2953, 2870, 1713, 1661, 1557, 1439, 1180 cm^{-1};

LRMS (LCMS EI): calcd for $C_{13}H_{19}F_3NO_3$ (M+H) 294.1, found 294.1;

$[\alpha]^{25}_D$ = –57° (c = 1.00, $CHCl_3$).



(*S*,*E*)-*tert*-Butyl 4-(2,2,2-trifluoroacetamido)hept-2-enoate (eq 3). The title compound was prepared according to the General Procedure from (±)-*tert*-butyl hepta-2,3-dienoate (109 mg, 0.600 mmol) and 2,2,2-trifluoroacetamide (33.9 mg, 0.300 mmol). After purification by column chromatography (10:1→4:1 hexanes/ethyl acetate), the title compound was isolated as a colorless waxy solid (82 mg, 93% yield) in 90% ee.

HPLC analysis of the product: Diacel CHIRALPAK AD-H column; 2% 2-propanol in hexanes; retention times: 8.6 min (major), 19.3 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless waxy solid (80 mg, 91% yield) in 88% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.69 (dd, *J* = 6.1, 15.7 Hz, 1H), 6.44 (s, 1 H), 5.84 (dd, *J* = 1.5, 15.7, 1H), 4.65-4.59 (m, 1H), 1.70-1.57 (m, 2H), 1.48 (s, 9 H), 1.43-1.34 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H);

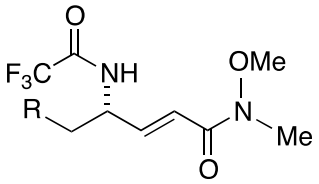
^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.1, 156.6 (q, *J* = 37 Hz) 143.8, 124.1, 115.7 (q, *J* = 289 Hz) 81.1, 50.6, 36.0, 28.0, 18.8, 13.6;

^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.8;

IR (film) 3301, 3092, 2966, 1703, 1659, 1554, 1459, 1369, 1315, 1161, 980, 846, 723 cm^{-1};

LRMS (LCMS EI): calcd for $C_{13}H_{20}F_3NNaO_3$ (M+Na) 318.1, found 318.1;

$[\alpha]^{25}_D$ = –55° (c = 1.00, $CHCl_3$).



R = cyclopentyl

(*S*,*E*)-5-Cyclopentyl-*N*-methoxy-*N*-methyl-4-(2,2,2-trifluoroacetamido)pent-2-enamide (eq 4). The title compound was prepared according to the General Procedure (except 15% catalyst was used) from (±)-5-cyclopentyl-*N*-methoxy-*N*-methylpenta-2,3-dienamide (207 mg, 1.00 mmol) and 2,2,2-trifluoroacetamide (56.5 mg, 0.500 mmol). After purification by column chromatography (4:1→2:1 hexanes/ethyl acetate), the title compound was isolated as a colorless waxy solid (96 mg, 60% yield) in 91% ee.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 15% 2-propanol in hexanes; retention times: 4.8 min (major), 7.7 min (minor).

The second run was performed with (*S*)-catalyst. The product was isolated as a colorless waxy solid (97 mg, 60% yield) in 88% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.83 (br s, 1H), 6.82 (dd, *J* = 7.2, 15.5 Hz, 1H), 6.57 (d, *J* = 15.5 Hz, 1H), 4.74-4.68 (m, 1H), 3.72 (s, 3H), 3.26 (s, 3H), 1.85-1.80 (m, 3H), 1.72-1.65 (m, 2H), 1.65-1.60 (m, 2H), 1.60-1.50 (m, 2H), 1.18-1.12 (m, 2H);

^{13}C NMR ($CDCl_3$, 126 MHz) δ 156.5 (q, J = 37 Hz), 143.7, 120.2, 115.8 (q, J = 289 Hz), 61.9, 51.0, 40.6, 36.5, 32.8, 32.5, 25.1, 25.0;

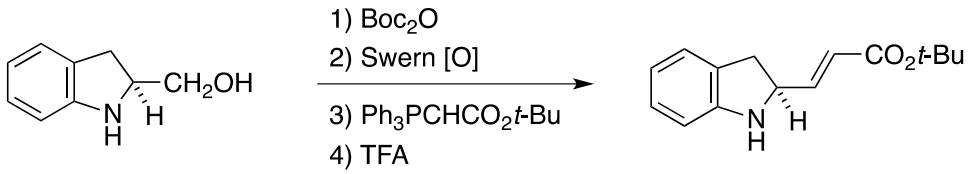
^{19}F NMR ($CDCl_3$, 282 MHz) δ –75.8;

IR (film) 3263, 3079, 2948, 2870, 1716, 1665, 1626, 1553, 1428, 1387, 1182, 999, 874, 726 cm^{-1};

LRMS (LCMS EI): calcd for $C_{14}H_{22}F_3N_2O_3$ (M+H) 323.2, found 323.2;

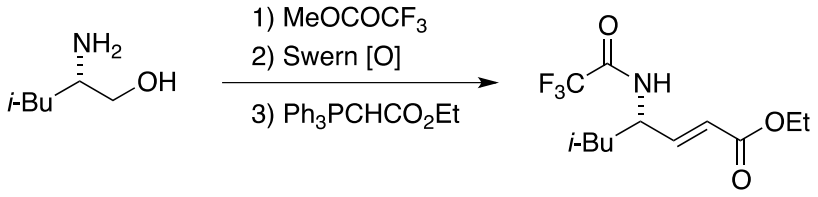
$[\alpha]^{25}_D$ = –16° (c = 1.00, $CHCl_3$).

IV. Determination of Absolute Stereochemistry



Identical with material generated from a γ addition with catalyst (*R*)-**1**

The absolute stereochemistry of the product in entry 5 of Table 1 (generated with catalyst (*R*)-**1**) was determined by converting the illustrated commercially available enantioenriched aminoalcohol into the corresponding γ-addition product, and then comparing the HPLC data. The other intramolecular γ-addition products were assigned by analogy.



Identical with material generated from a γ addition with catalyst (*R*)-**1**

The absolute stereochemistry of the product in entry 3 of Table 3 (generated with catalyst (*R*)-**1**) was determined by converting the commercially available (*S*)-leucinol into the corresponding γ-addition product, and then comparing the HPLC data. The other intermolecular γ-addition products were assigned by analogy.

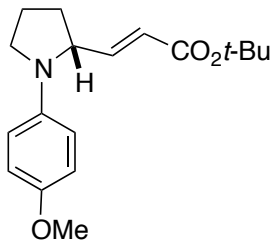


Table 1, entry 1

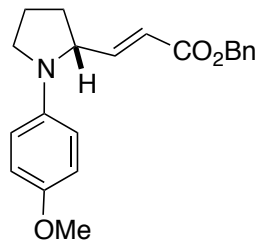
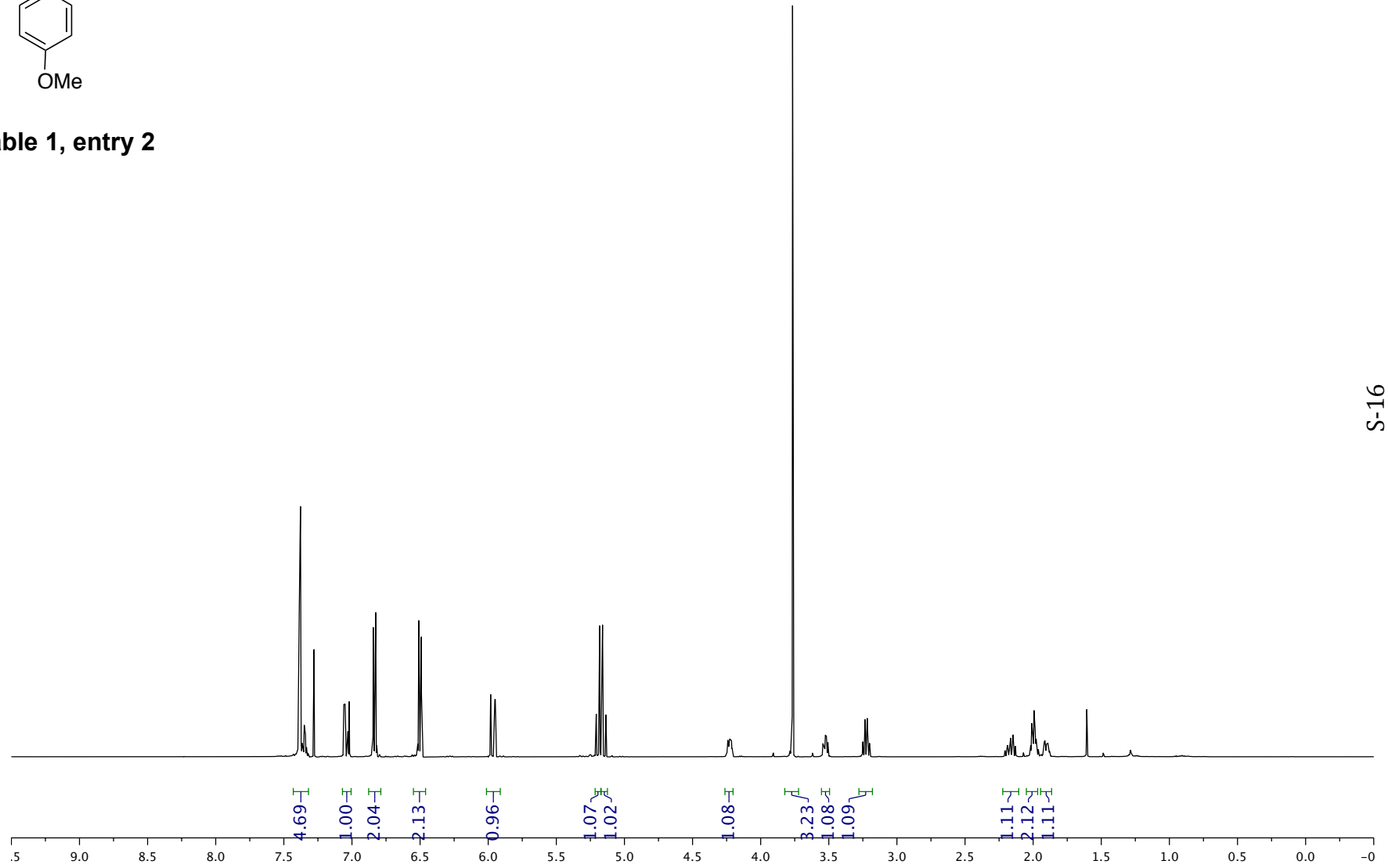


Table 1, entry 2



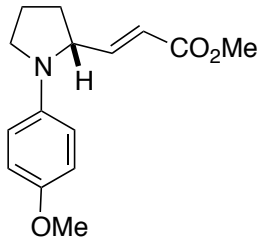


Table 1, entry 3

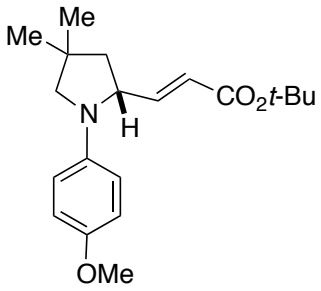


Table 1, entry 4

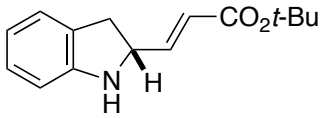
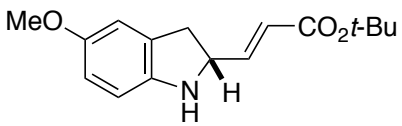


Table 1, entry 5



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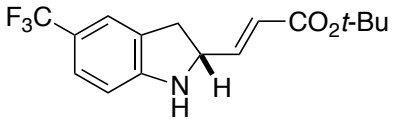


Table 1, entry 7

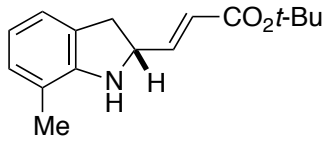


Table 1, entry 8

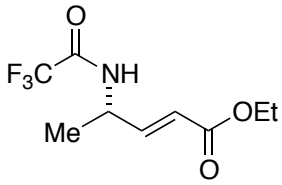
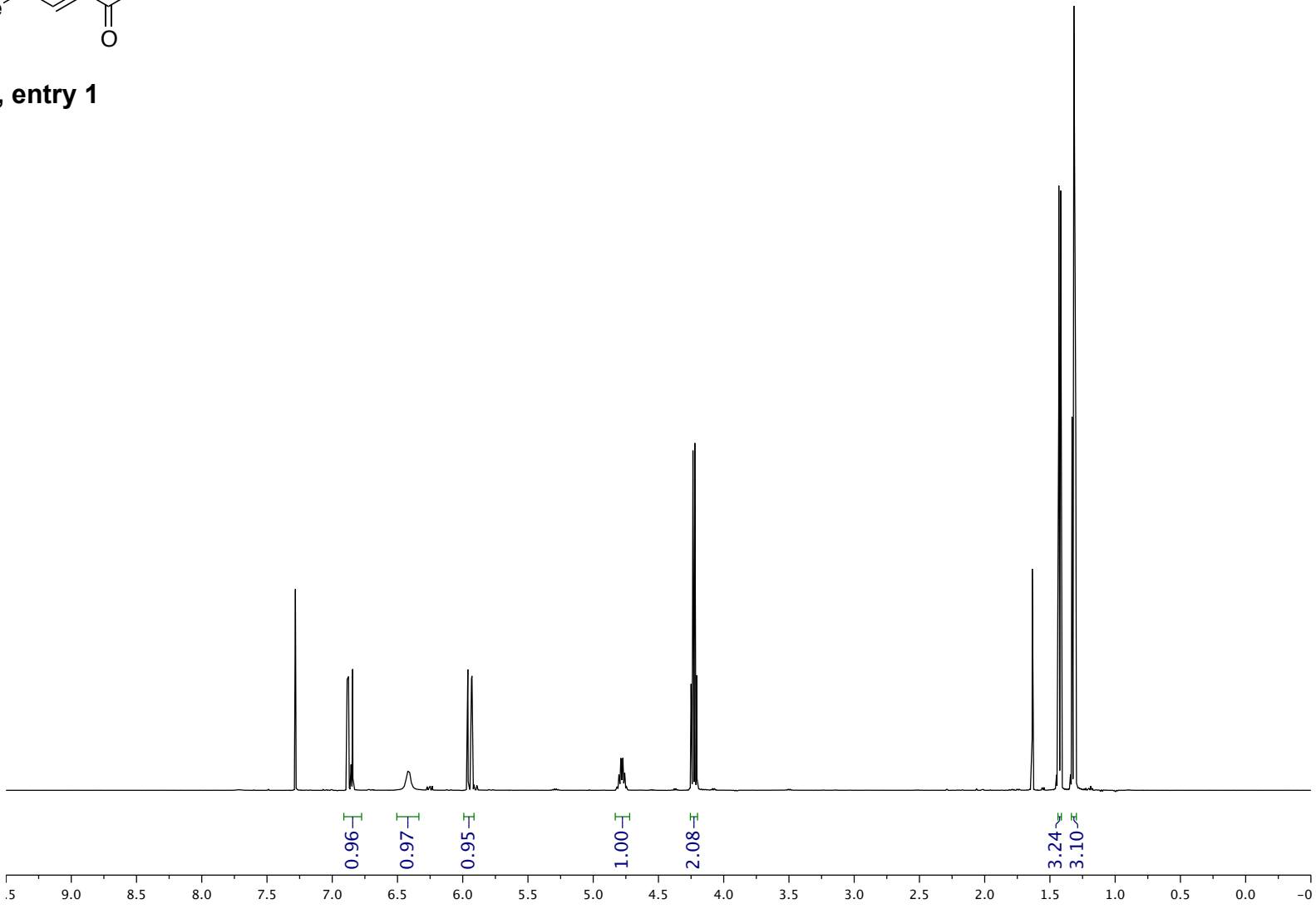


Table 3, entry 1



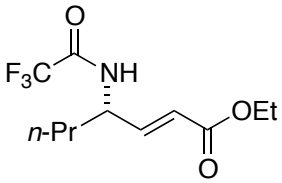


Table 3, entry 2

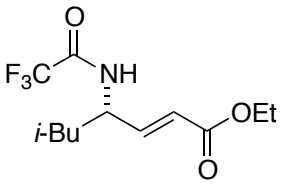
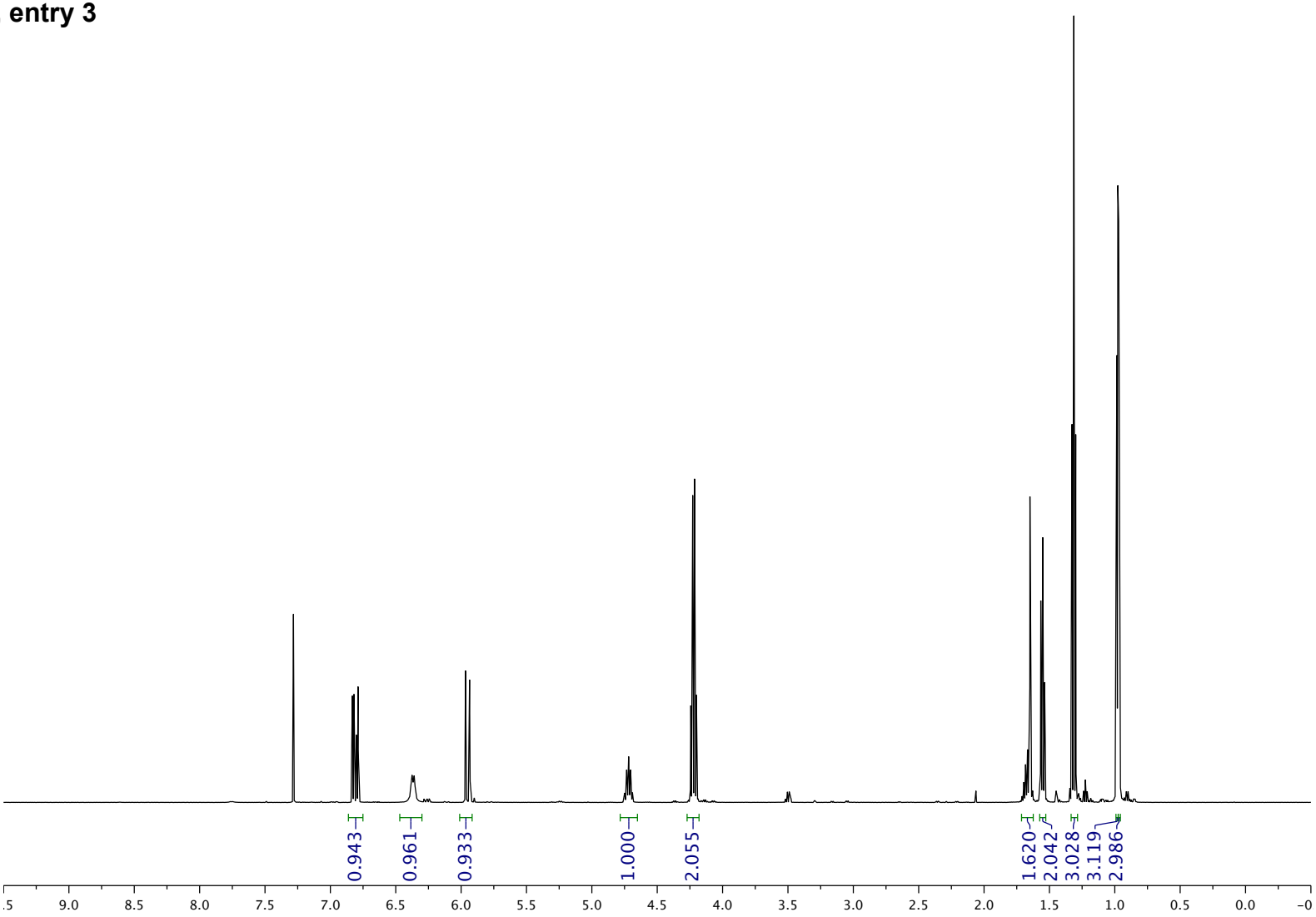


Table 3, entry 3



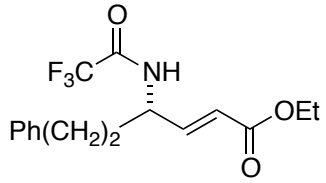
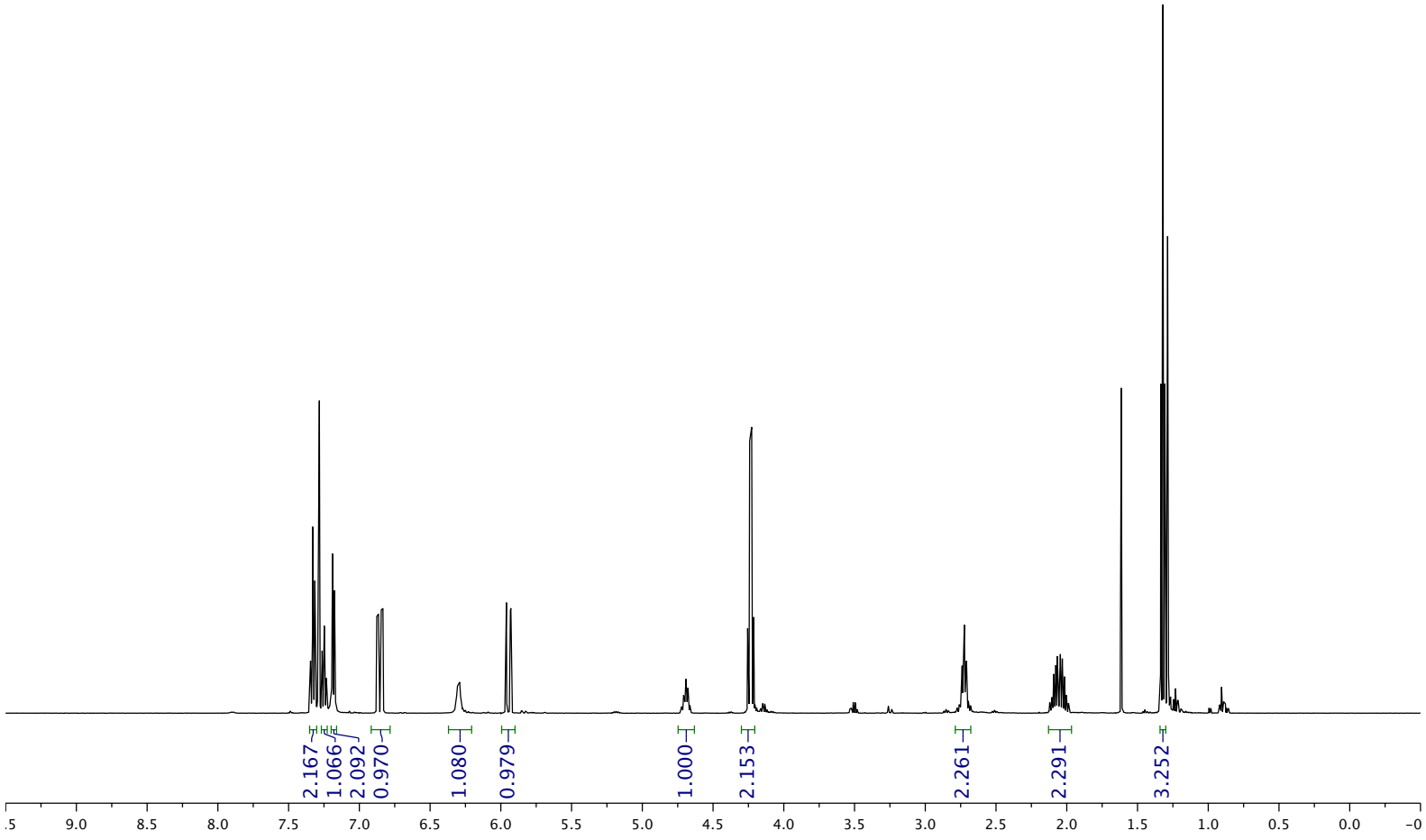


Table 3, entry 4



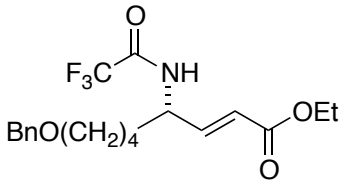
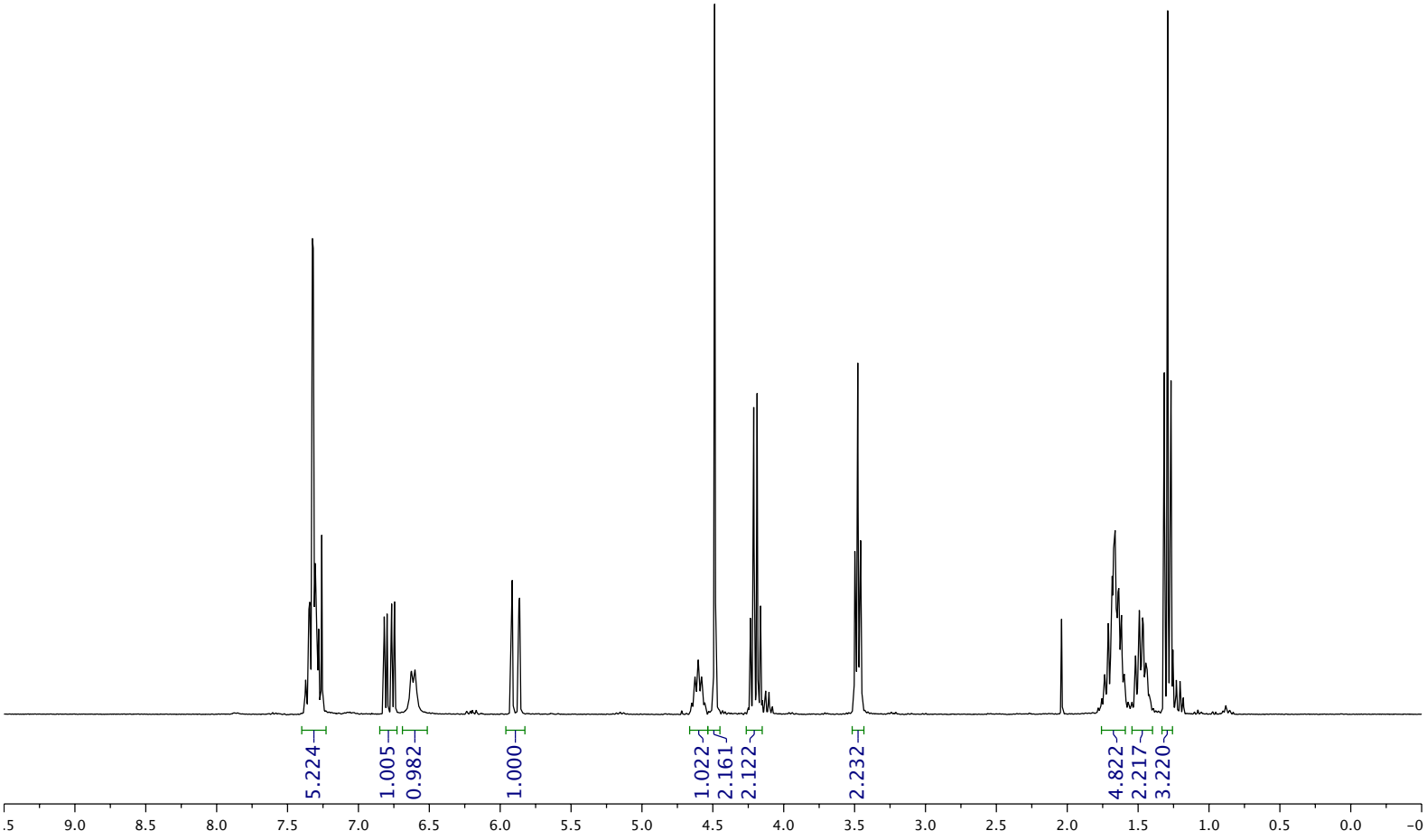


Table 3, entry 5



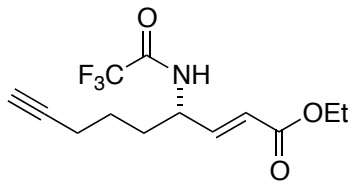
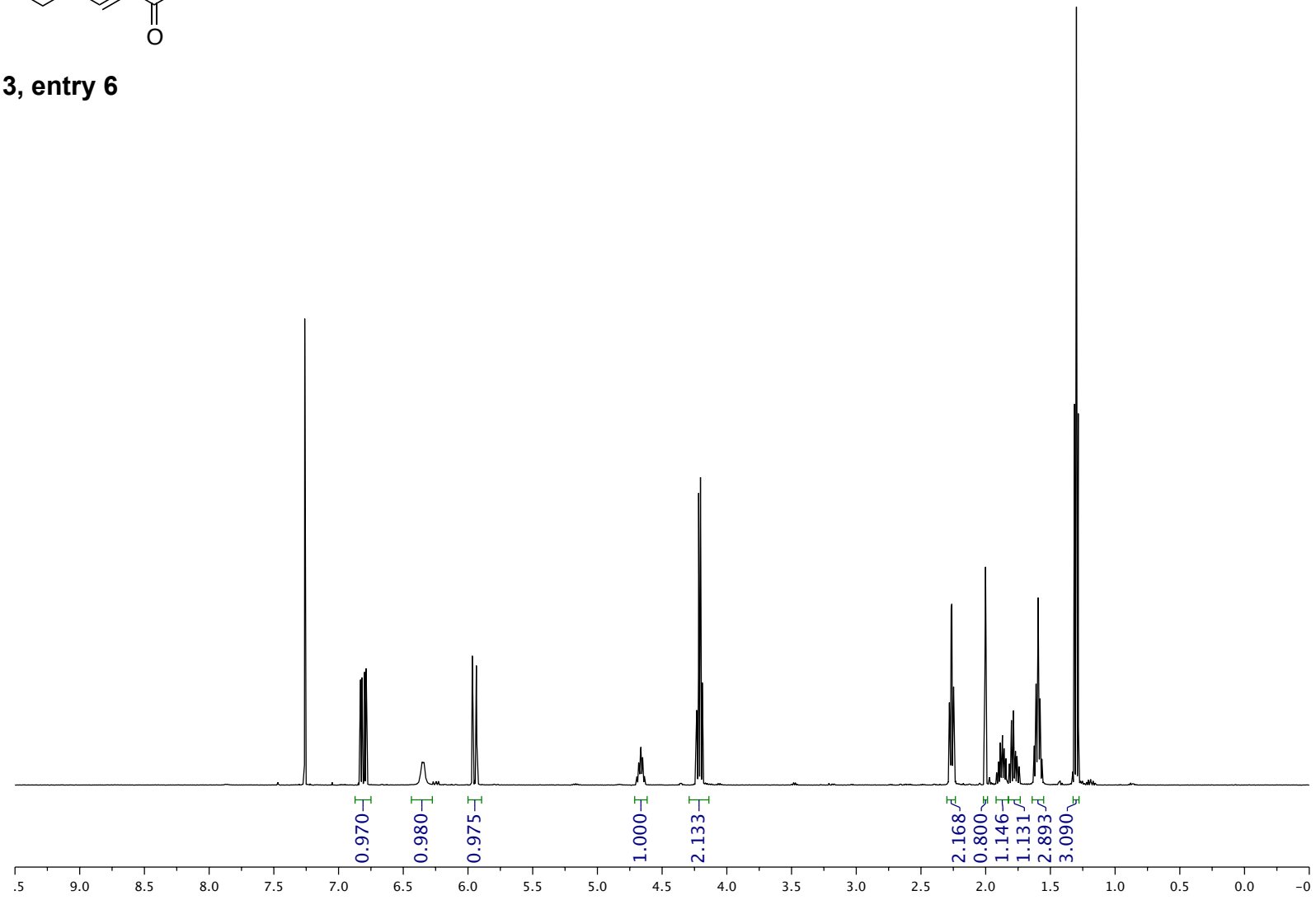


Table 3, entry 6



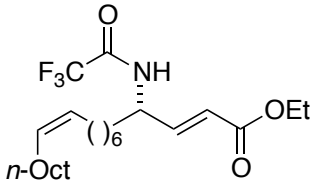
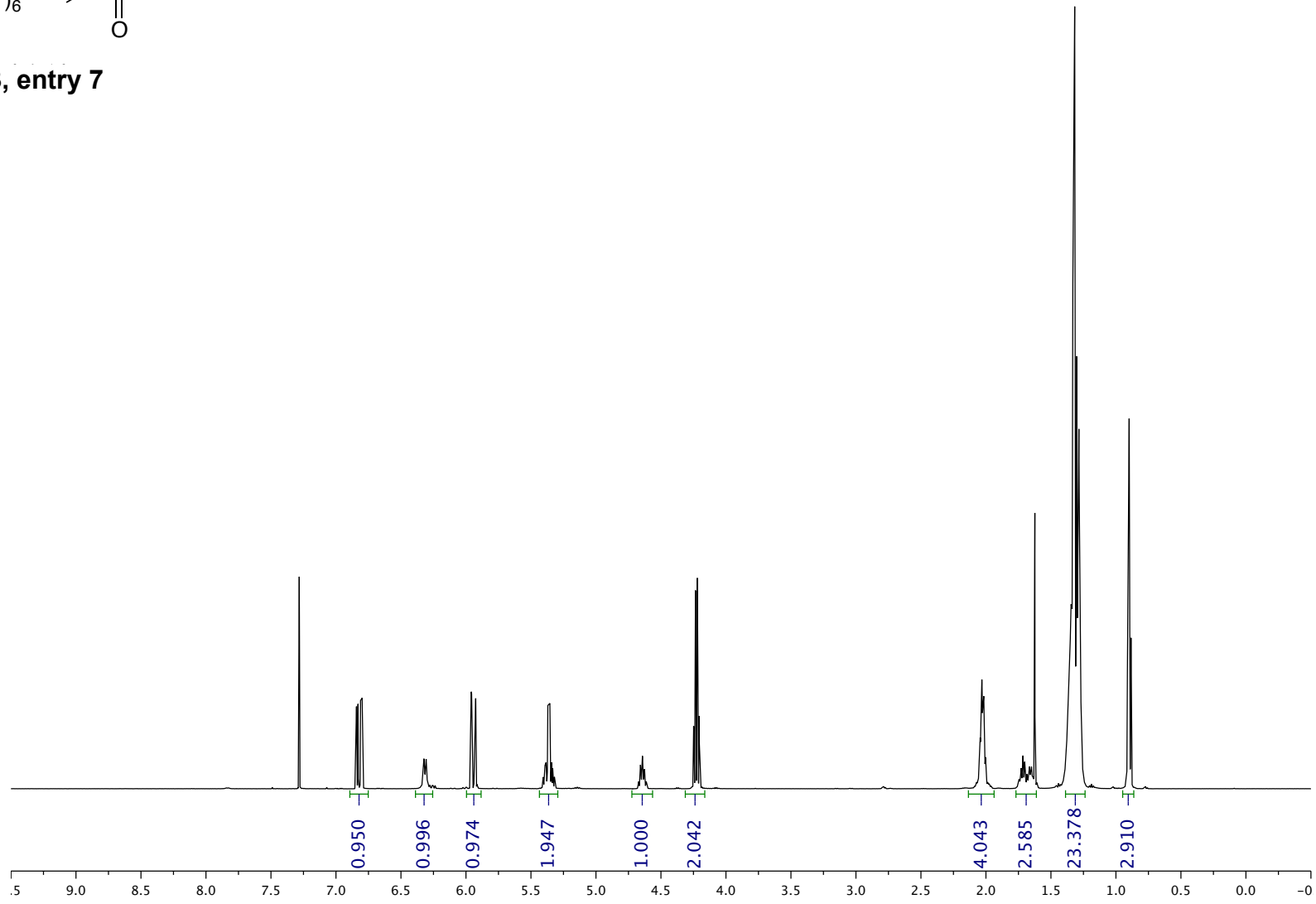


Table 3, entry 7



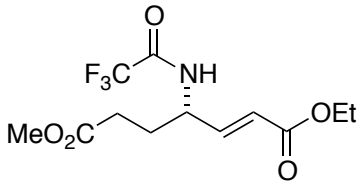
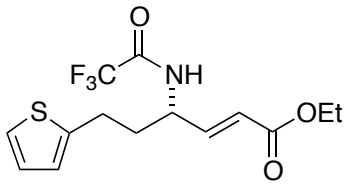


Table 3, entry 8



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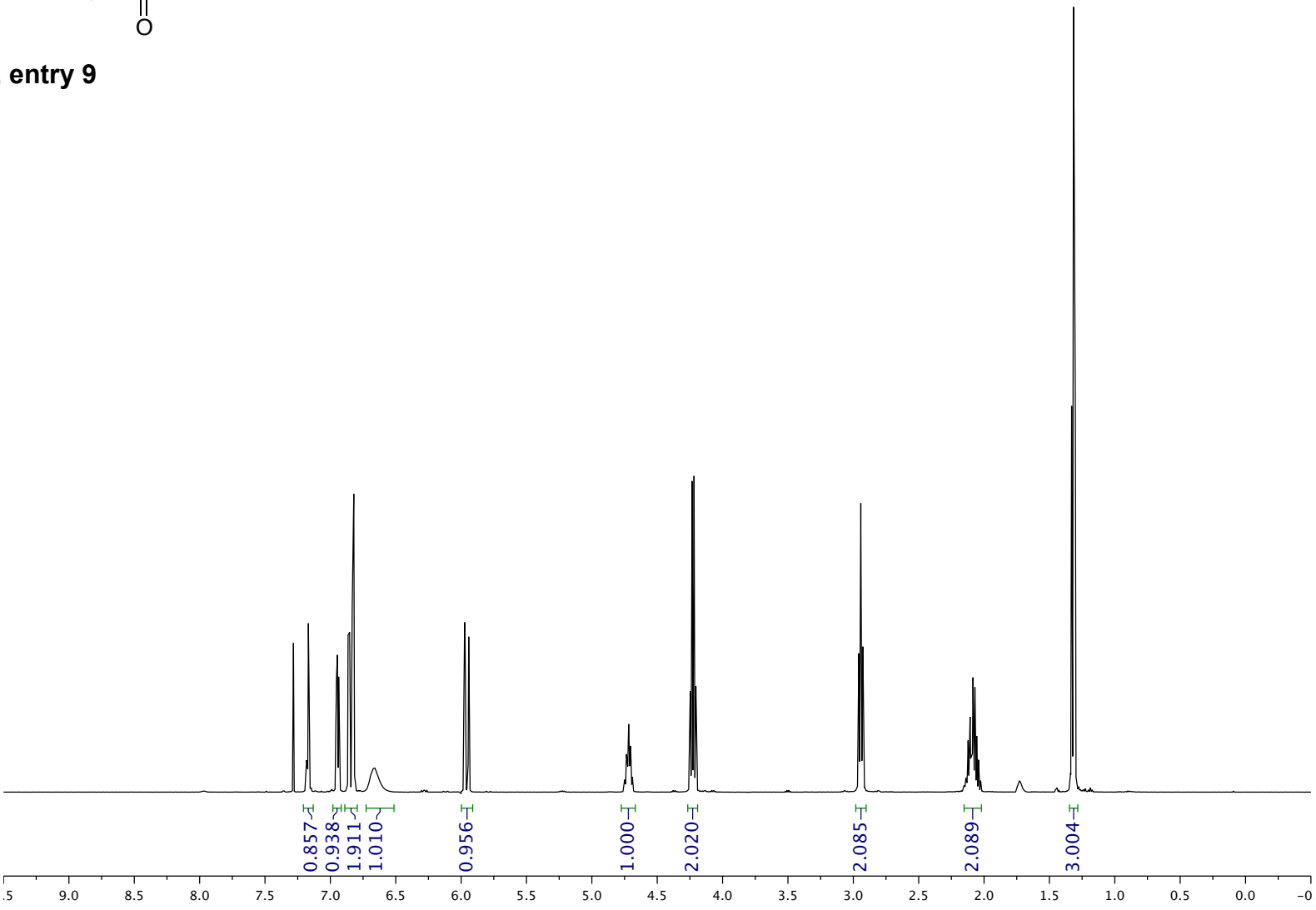

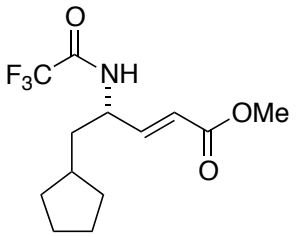
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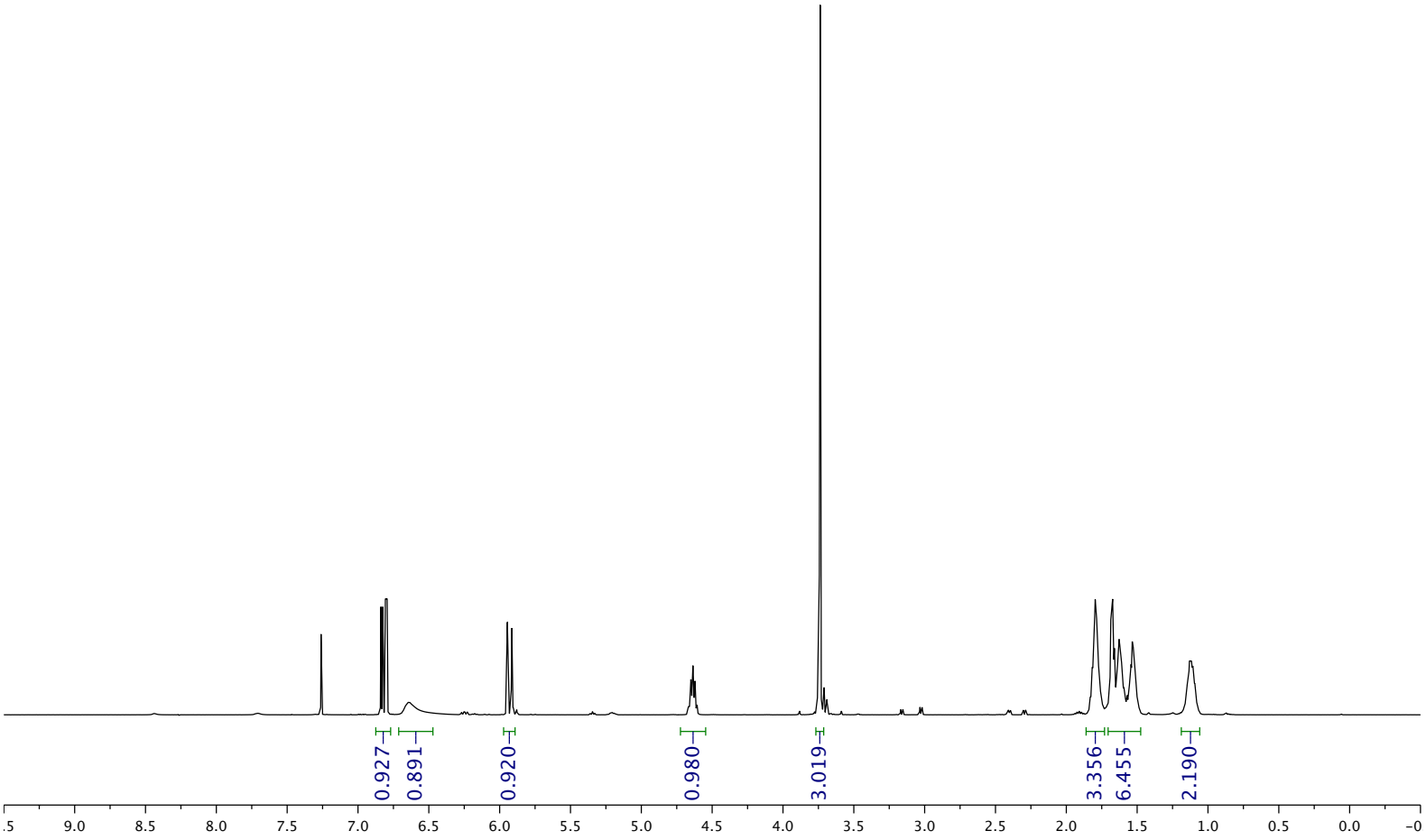
F3C
NH
OMe
O

eq 3a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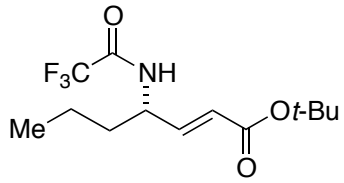
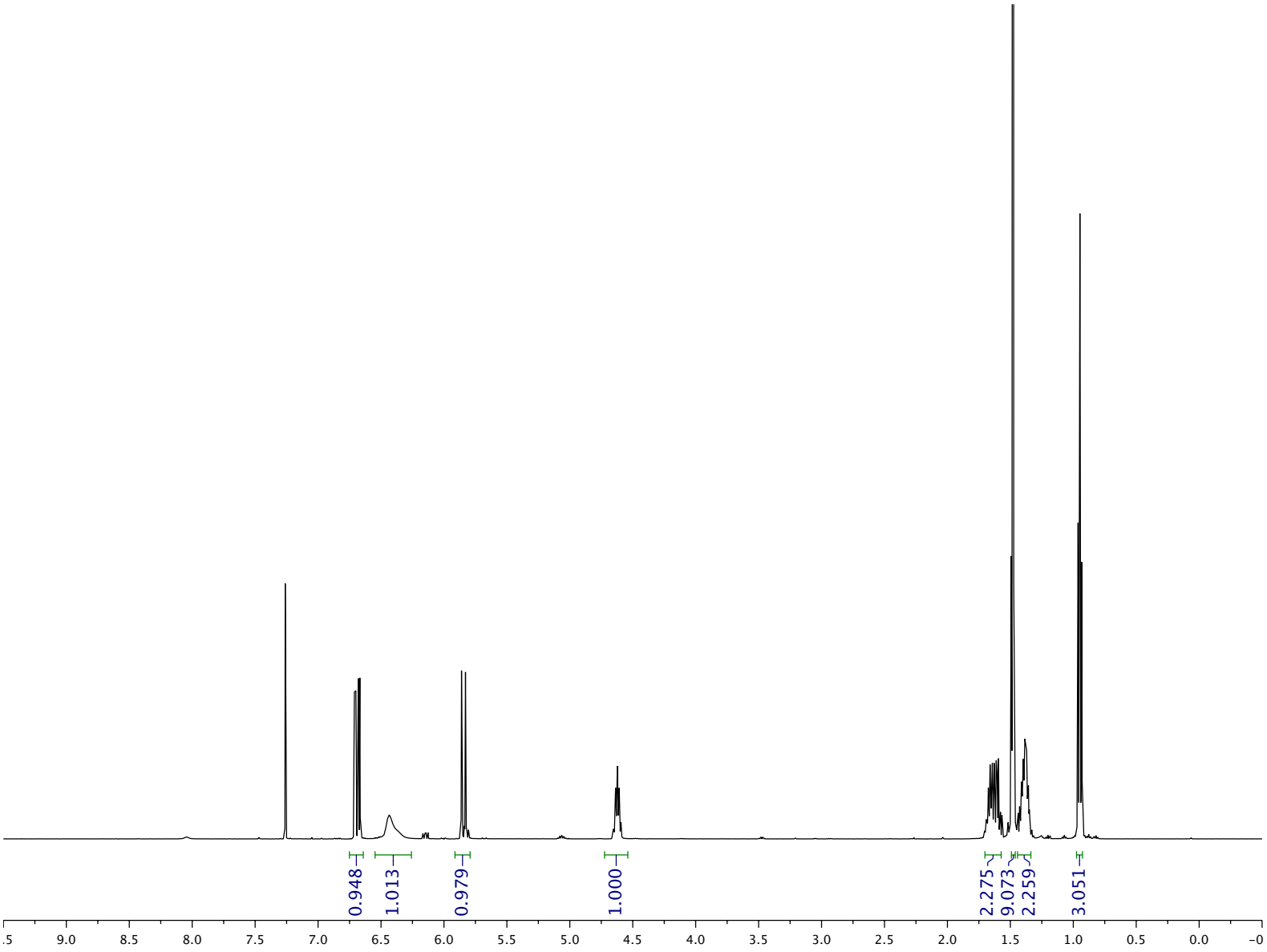

O
F3C
NH
Me
Ot-Bu
O

eq 3b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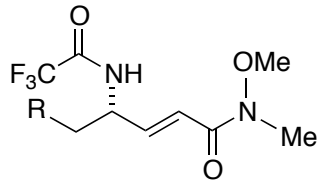
0.0



R = cyclopentyl

eq 4