Supporting Information for

Highly diastereoselective synthesis of quaternary α-trifluoromethyl α-amino acids from chiral imines of trifluoropyruvate

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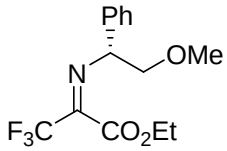
General information: Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). For ^{19}F NMR, $CFCl_3$ was used as outside standard and low field is positive The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. NMR yield was determined by ^{19}F NMR using benzotrifluoride as an internal standard before working up the reaction.

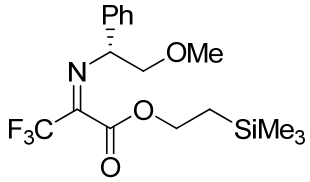
Materials: All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature. All reagents were weighed and handled in air, and refilled with an inert atmosphere of N_2 at room temperature. THF was distilled from sodium and benzophenone immediately before use.

Preparation of Chiral Imino Ester 1a.



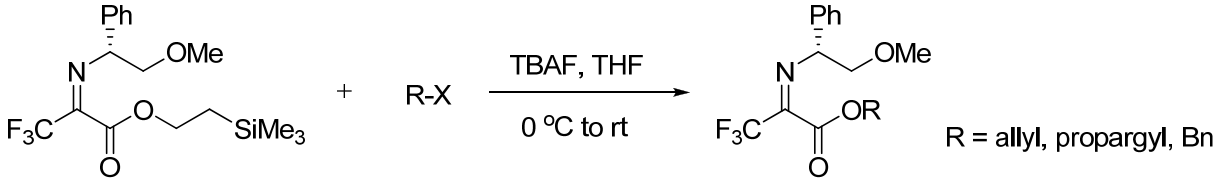
***(R)*-Ethyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate (1a).** To a stirred solution of ethyl trifluoropyruvate (2.806 g, 16.5 mmol, 1.1 equiv) in toluene (150 mL) was slowly added the (*R*)-2-methoxy-1-phenylethanamine (2.268 g, 15 mmol, 1.0 equiv) at room temperature, followed by pyridinium p-toluenesulfonate (378 mg, 1.5 mmol, 0.1 equiv). After stirring for 2.0 h at room temperature, the reaction mixture was heated to reflux with a Dean-Stark apparatus for 20 h. Then the reaction mixture was cooled to 0 ^{o}C with an ice-bath, and toluene was evaporated. The residue was isolated with silica gel by flash chromatography (Petroleum ether /Ethyl Acetate = 80:1) to give **1a** (4.0 g, 88% yield) as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.37-7.22 (m, 5H), 5.20 (dd, *J* = 8.7 Hz, 4.5 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.57-3.48 (m, 2H), 3.23 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 149.3 (q, *J* = 36.4 Hz), 138.2, 128.7, 128.0, 127.2, 118.3 (q, *J* = 276.8 Hz), 76.7, 66.5, 62.4, 59.0, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$) δ -70.5 (s, 3F). IR (thin film): ν_{max} 3034, 1743, 1682 cm^{-1}. MS (EI): *m/z* (%) 258 (M^+ -C_2H_5O, 100), 135, 91. HRMS: Calculated for $C_{14}H_{16}NO_3F_3$ (M^+): 303.1082; Found: 303. 1077.

Preparation of Chiral Imino Ester 1b.

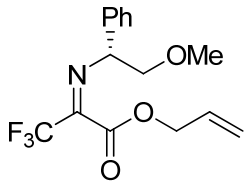


***(R)*-2-(Trimethylsilyl)ethyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate(1b).** According to Uneyama's procedure,[1] imino ester **1b** (2.62 g) was prepared from TFA (1.43 g, 12.5 mmol) in 56% overall yield (3 steps) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.20 (m, 5H), 5.19 (dd, *J* = 8.1 Hz, 4.5 Hz, 1H), 4.30 (m ,2H), 3.55-3.48 (m, 2H), 3.22 (s, 3H), 1.03-0.97 (m, 2H), -0.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 149.5 (q, *J* = 35.6 Hz), 138.2, 128.6, 128.0, 127.3, 118.3 (q, *J* = 276.8 Hz), 76.7, 66.5, 65.1, 59.0, 17.3, -1.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -70.2 (s, 3F). IR (thin film): ν_{max} 3035, 1740, 1683, 1604 cm^{-1}. MS (ESI): *m/z* (%) 398 ($M^+ + Na^+$), 376 ($M^+ + H^+$), 348. HRMS: Calculated for $C_{17}H_{24}F_3NO_3SiNa$ (M^++Na^+): 398.13698; Found: 398.13732.

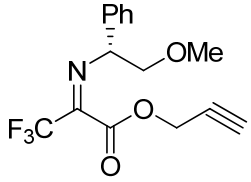
General procedure for the preparation of imino esters 1c-e.



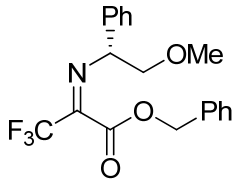
The preparation of imino esters **1c-e** was according to literature.[2] To a stirred solution of silylated imino ester **1b** (1 mmol) in THF (10 mL) were added corresponding electrophile R-X (2 mmol), followed by dropwise TBAF (1 M in THF, 1.1 mL, 1.1 mmol) at 0 °C. The reaction mixture was then warmed to room temperature and stirred until the starting material was consumed. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography.



***(R)*-Allyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate(1c).** Imino ester **1c** (220 mg, 70% yield) was prepared as above described from **1b** (375 mg) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 50:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.24 (m, 5H), 5.99-5.88 (m, 1H), 5.44-5.28 (m, 3H), 4.79 (d, *J* = 5.4 Hz, 2H), 3.67-3.56 (m, 2H), 3.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 148.9 (q, *J* = 36.4 Hz), 138.1, 130.4, 128.7, 128.1, 127.3, 119.7, 118.2 (q, *J* = 276.8 Hz), 76.6, 66.6, 59.0. ^{19}F NMR (282 MHz, $CDCl_3$) δ -70.2 (s, 3F). IR (thin film): ν_{max} 3090, 1745, 1683, 1604 cm^{-1}. MS (ESI): *m/z* (%) 316 ($M^+ + H^+$). HRMS: Calculated for $C_{15}H_{16}NO_3F_3Na$ ($M^+ + Na^+$): 338.09745; Found: 338.09810.



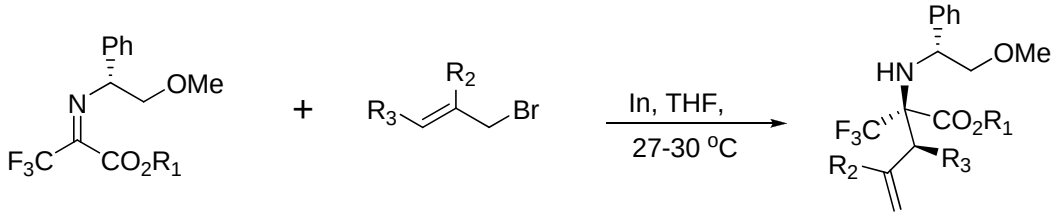
***(R)*-prop-2-ynyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate(1d).** Imino ester **1d** (330 mg, 52% yield) was prepared as above described from **1b** (750 mg) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 50:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.33 (m, 5H), 5.33 (dd, *J* = 9.3 Hz, 4.2 Hz, 1H), 4.90 (d, *J* = 2.4 Hz, 2H), 3.69-3.55 (m, 2H), 3.34 (s, 3H), 2.60 (t, *J* = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 148.2 (q, *J* = 36.4 Hz), 137.9, 128.7, 128.1, 127.3, 118.1 (q, *J* = 268.0 Hz), 76.5, 76.3, 75.9, 66.6, 59.0, 53.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ -69.9 (s, 3F). IR (thin film): ν_{max} 2964, 1749, 1261 cm^{-1}. MS (ESI): *m/z* (%) 314 ($M^+ + H^+$). HRMS: Calculated for $C_{15}H_{14}NO_3F_3$ (M^+): 313.0926; Found: 313.0923.



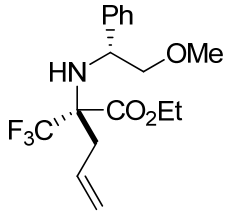
***(R)*-benzyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate (1e).** Imino ester **1e** (245 mg, 67% yield) was prepared as above described from **1b** (375 mg) as a yellow oil. The

product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 50:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.28 (m, 10H), 5.32 (d, *J* = 5.1 Hz, 2H), 5.25 (m, 1H), 3.56 (m, 2H), 3.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 148.9 (q, *J* = 35.6 Hz), 138.0, 134.2, 128.8, 128.6, 128.5, 128.4, 128.0, 127.2, 118.2 (q, *J* = 276.9 Hz), 76.5, 67.9, 66.5, 58.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -70.1 (s, 3F). IR (thin film): ν_{max} 3068, 1745, 1682, 1604 cm^{-1}. MS (ESI): *m/z* (%) 366 ($M^+ + H^+$). HRMS: Calculated for $C_{19}H_{18}NO_3F_3Na$ ($M^+ + Na^+$): 388.11310; Found: 388.11420.

General procedure for the preparation of α-allyl α-Tfm α-amino acids 3.

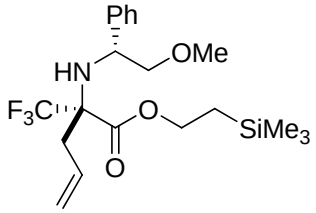


To a 10 mL of Schlenk tube were added chiral imino ester **1** (0.3 mmol) and In powder (69 mg, 0.6 mmol) under N_2 at room temperature. After standing for 5 min, THF (3 mL) was added. The resulting mixture was stirred for 15 min at 27-30 °C, and then fresh distilled allyl bromide **2** (0.66 mmol) was added. The reaction mixture was stirred at the same temperature until the starting material was totally consumed, as confirmed by means of TLC. The reaction mixture was quenched with HCl (1 M, 2 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic layers were washed with brine (3 x 7 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography.

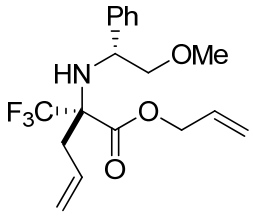


***(R)*-Ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3a).** Compound **3a** (104 mg, 98% yield) was prepared as above described from **1a** (91 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 50:1). $[\alpha]_D^{25}$ = -49.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.22 (m, 5H),

5.80-5.71 (m, 1H), 5.11-5.06 (m, 2H), 4.18-4.07 (m, 2H), 4.05-3.95 (m, 1H), 3.38 (d, *J* = 6.6 Hz, 2H), 3.33 (s, 3H), 2.83 (br, 1H), 2.65 (dd, *J* = 14.7 Hz, 6.6 Hz, 1H), 2.45 (dd, *J* = 14.7 Hz, 7.8 Hz, 1H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 141.6, 131.2, 128.2, 127.5, 124.9 (q, *J* = 286.0 Hz), 119.4, 77.5, 67.9 (q, *J* = 25.0 Hz), 61.7, 58.6, 56.9, 36.7, 13.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.5 (s, 3F). IR (thin film): ν_{max} 3339, 3084, 1740, 1642, 1603 cm^{-1}. MS (EI): *m/z* (%) 300 (M^+-C_2H_5O, 100), 135, 131, 91. HRMS: Calculated for $C_{15}H_{17}NO_2F_3$ (M^+-C_2H_5O): 300.1211; Found: 300.1217.

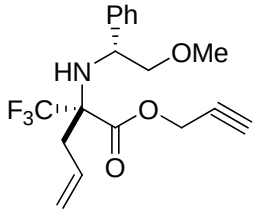


***(R)*-2-(Trimethylsilyl)ethyl 2-(*(R)*-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3b).** Compound **3b** (118 mg, 94% yield) was prepared as above described from **1b** (113 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). $[\alpha]_D^{25}$ = -38.6 (*c* 1.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.21 (m, 5H), 5.71 (m, 1H), 5.07-5.03 (m, 2H), 4.15-3.94 (m, 3H), 3.34 (d, *J* = 6.3 Hz, 2H), 3.30 (s, 3H), 2.80 (br, 1H), 2.61 (dd, *J* = 15.0 Hz, 6.5 Hz, 1H), 2.41 (dd, *J* = 15.0 Hz, 7.5 Hz, 1H), 0.91 (t, *J* = 8.1 Hz, 2H), -0.03 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 168.2, 141.7, 131.3, 128.1, 127.3, 124.9 (q, *J* = 286.9 Hz), 119.3, 77.6, 67.9 (q, *J* = 25.3 Hz), 64.3, 58.7, 56.9, 36.7, 17.0, -1.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.1 (s, 3F). IR (thin film): ν_{max} 3343, 3085, 1739, 1643 cm^{-1} MS (ESI): *m/z* (%) 418 ($M^+ + H^+$). HRMS: Calculated for $C_{20}H_{31}NO_3F_3Si$ ($M^+ + H^+$): 418.20198; Found: 418.20255.

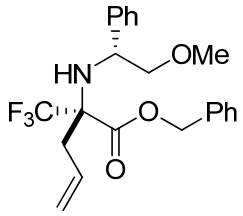


***(R)*-Allyl 2-(*(R)*-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3c).** Compound **3c** (104 mg, 97% yield) was prepared as above described from **1c** (95 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). $[\alpha]_D^{25}$ = -54.7 (*c* 0.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.23 (m, 5H),

5.82-5.75 (m, 2H), 5.33-5.21 (m, 2H), 5.11-5.06 (m, 2H), 4.49 (dd, *J* = 13.2 Hz, 5.3 Hz, 1H), 4.37 (dd, *J* = 13.2 Hz, 5.4 Hz, 1H), 4.16 (t, *J* = 6.3 Hz, 1H), 3.37 (d, *J* = 6.9 Hz, 2H), 3.32 (s, 3H), 2.66 (br, 1H), 2.65 (dd, *J* = 14.3 Hz, 6.2 Hz, 1H), 2.45 (dd, *J* = 14.3 Hz, 7.4 Hz, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 167.7, 141.6, 131.2, 128.2, 127.3, 124.8 (q, *J* = 287.7 Hz), 119.7, 118.7, 77.4, 68.0 (q, *J* = 25.6 Hz), 66.2, 58.6, 57.0, 36.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.1 (s, 3F). IR (thin film): ν_{max} 3340, 3086, 1744, 1644, 1604 cm^{-1}. MS (ESI): *m/z* (%) 358 ($M^+ + H^+$). HRMS: Calculated for $C_{18}H_{22}NO_3F_3Na$ ($M^+ + Na^+$): 380.14440; Found: 380.14610.

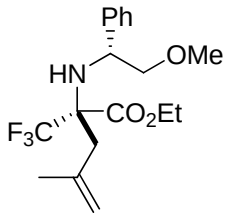


***(R)*-Prop-2-ynyl 2-(*(R)*-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3d).** Compound **3d** (104 mg, 98% yield) was prepared as above described from **1d** (94 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). $[\alpha]_D^{25}$ = -51.7 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.25 (m, 5H), 5.74 (m, 1H), 5.15-5.09 (m, 2H), 4.53 (dd, *J* = 15.6 Hz, 2.1 Hz, 1H), 4.36 (dd, *J* = 15.6 Hz, 2.7 Hz, 1H), 4.18 (t, *J* = 6.6 Hz, 1H), 3.38 (d, *J* = 6.6 Hz, 2H), 3.34 (s, 3H), 2.81 (br, 1H), 2.66 (dd, *J* = 14.4 Hz, 6.6 Hz, 1H), 2.57 (br, 1H), 2.50-2.44 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 141.1, 130.7, 128.2, 127.4, 124.7 (q, *J* = 288.4 Hz), 120.0, 77.5, 75.5, 67.9 (q, *J* = 25.2 Hz), 58.7, 56.9, 52.9, 37.0. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.7 (s, 3F). IR (thin film): ν_{max} 3306, 3034, 2136, 1750, 1642 cm^{-1}. MS (ESI): *m/z* (%) 378 ($M^+ + Na^+$), 356 ($M^+ + H^+$). HRMS: Calculated for $C_{18}H_{20}NO_3F_3Na$ ($M^+ + Na^+$): 378.12875; Found: 378.12982.

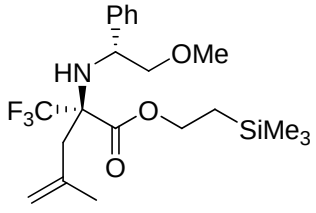


***(R)*-Benzyl 2-(*(R)*-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3e).** Compound **3e** (55 mg, 45% yield) was prepared as above described from **1e** (110 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). $[\alpha]_D^{25}$ = -50.4 (c 2.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.21 (m, 10H),

5.70 (m, 1H), 5.07-4.99 (m, 3H), 4.91 (d, *J* = 12.9 Hz, 1H), 4.15 (t, *J* = 6.3 Hz, 1H), 3.34 (d, *J* = 6.6 Hz, 2H), 3.27 (s, 3H), 2.86 (br, 1H), 2.64 (dd, *J* = 15.0 Hz, 6.6 Hz, 1H), 2.44 (dd, *J* = 15.0 Hz, 8.1 Hz, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 168.0, 141.4, 134.9, 131.0, 128.5, 128.3, 128.2, 128.0, 127.3, 124.8 (q, *J* = 288.0 Hz), 119.6, 77.4, 68.1 (q, *J* = 25.6 Hz), 67.4, 58.6, 57.0, 36.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.0 (s, 3F). IR (thin film): ν_{max} 3340, 3036, 1743 cm^{-1}. MS (ESI): *m/z* (%) 408 ($M^+ + H^+$). HRMS: Calculated for $C_{22}H_{24}NO_3F_3Na$ ($M^+ + Na^+$): 430.16005; Found: 430.16018.

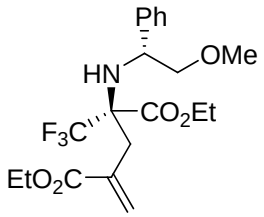


***(R)*-Ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-4-methyl-2-(trifluoromethyl)pent-4-enoate (3f).** Compound **3f** (103 mg, 96% yield) was prepared as above described from **1a** (91 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). $[\alpha]_D^{25}$ = -36.3 (*c* 1.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.20 (m, 5H), 4.88 (s, 1H), 4.84 (s, 1H), 4.23 (t, *J* = 6.0 Hz, 2H), 4.09-4.04 (m, 1H), 3.94-3.88 (m, 1H), 3.42-3.38 (m, 2H), 3.30 (s, 3H), 2.79 (br, 1H), 2.63 (d, *J* =15.0 Hz, 1H), 2.54 (d, *J* =15.0 Hz, 1H), 1.70 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 142.2, 139.4, 128.0, 127.3, 127.1, 125.0 (q, *J* = 289.0 Hz), 115.6, 77.6, 67.5 (q, *J* = 25.5 Hz), 61.8, 58.8, 56.8, 39.8, 23.5, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.5 (s, 3F). IR (thin film): ν_{max} 3370, 1742 cm^{-1}. MS (ESI): *m/z* (%) 360 ($M^+ + H^+$). HRMS: Calculated for $C_{18}H_{24}NO_3F_3Na$ ($M^+ + Na^+$): 382.16005; Found: 382.15994.

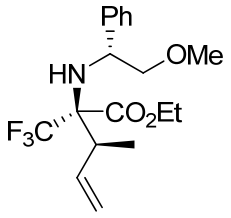


***(R)*-2-(Trimethylsilyl)ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-4-methyl-2-(trifluoromethyl)pent-4-enoate (3g).** Compound **3g** (110 mg, 85% yield) was prepared as above described from **1b** (113 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). $[\alpha]_D^{25}$ = -45.7 (*c* 3.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.19 (m, 5H), 4.86 (s, 1H), 4.81 (s, 1H), 4.23 (t, *J* = 5.7 Hz, 1H), 4.08-4.05 (m, 1H),

3.92-3.89 (m, 1H), 3.39-3.35 (m, 2H), 3.30 (s, 3H), 2.81 (br, 1H), 2.60 (d, J = 14.9 Hz, 1H), 2.51 (d, J = 14.9 Hz, 1H), 1.67 (s, 3H), 0.88-0.81 (m, 2H), -0.02 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 168.5, 142.2, 139.4, 128.0, 127.3, 127.1, 125.0 (q, J = 288.0 Hz), 115.5, 77.5, 67.3 (q, J = 25.6 Hz), 64.4, 58.7, 56.7, 39.5, 23.5, 16.9, -1.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.5 (s, 3F). IR (thin film): ν_{max} 3344, 3031, 1739, 1651 cm^{-1}. MS (ESI): *m/z* (%) 432 (M^+ + H^+). HRMS: Calculated for $C_{21}H_{32}NO_3F_3SiNa$ (M^+ + Na^+): 454.19958; Found: 454.20001.

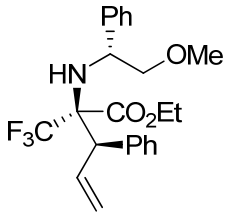


***(R)*-Diethyl 2-(*(R)*-2-methoxy-1-phenylethylamino)-4-methylene-2-(trifluoromethyl)pentane Dioate (3h).** Compound **3h** (110 mg, 88% yield) was prepared as above described from **1a** (91 mg, 0.3 mmol) as a yellow oil (Note: The reaction was quenched with water instead of HCl (1 M, 2 mL)) . The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). $[\alpha]_D^{25}$ = -38.3 (*c* 5.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.20 (m, 5H), 6.28 (s, 1H), 5.68 (s, 1H), 4.25-4.17 (m, 3H), 3.95-3.89 (m, 1H), 3.78-3.72 (m, 1H), 3.42 (d, J = 6.3 Hz, 2H), 3.29 (s, 3H), 2.95 (s, 2H), 2.88 (br, 1H), 1.30 (t, J = 7.2 Hz, 3H), 0.99 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 167.6, 167.0, 142.3, 134.9, 128.7, 127.8, 127.1, 126.9, 125.1 (q, J = 289.6 Hz), 77.4, 68.2 (q, J = 25.3 Hz), 61.6, 61.0, 58.7, 57.0, 33.8, 14.0, 13.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ -71.9 (s, 3F). IR (thin film): ν_{max} 3350, 2986, 1744 cm^{-1}. MS (EI): *m/z* (%) 372 (M^+ -C_2H_5O, 100), 157, 135, 131, 91. HRMS: Calculated for $C_{20}H_{26}NO_5F_3$ (M^+): 417.1763; Found: 417.1754.

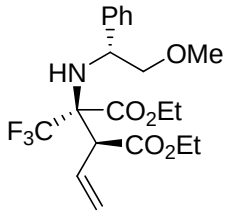


***(2R,3S)*-Ethyl 2-(*(R)*-2-methoxy-1-phenylethylamino)-3-methyl-2-(trifluoromethyl)pent-4-Enoate (3i).** Compound **3i** (90 mg, 82% yield) was prepared as above described from **1a** (91 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.19 (m, 5H), 5.90 (m, 1H), 5.20-5.15 (m, 2H), 4.17 (t, J = 5.4 Hz, 1H), 3.94-3.88 (m, 1H), 3.65-3.60 (m, 1H), 3.59-3.43 (m,

2H), 3.28 (s, 3H), 2.92 (t, *J* = 7.5 Hz, 1H), 2.61 (br, 1H), 1.13 (d, *J* = 6.6 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 142.6, 137.5, 127.8, 127.3, 126.8, 125.7 (q, *J* = 289.0 Hz), 117.7, 77.4, 70.4 (q, *J* = 24.3 Hz), 61.2, 58.9, 57.1, 43.1, 15.2, 13.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ -67.1 (s, 3F). IR (thin film): ν_{max} 3360, 2985, 1743 cm^{-1}. MS (ESI): *m/z* (%) 360 (M^+ + H^+). HRMS: Calculated for $C_{18}H_{24}NO_3F_3Na$ (M^+ + Na^+): 382.16005; Found: 382.15987.



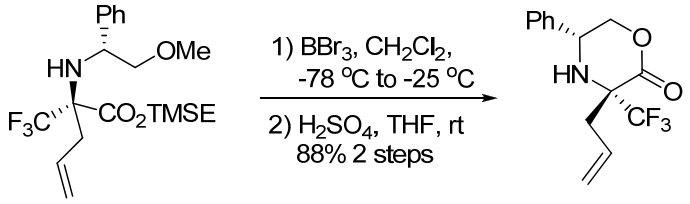
***(2R,3R)*-Ethyl 2-(*(R)*-2-methoxy-1-phenylethylamino)-3-phenyl-2-(trifluoromethyl)pent-4-enoate (3j).** Compound **3j** (110 mg, 92% yield) was prepared as above described from **1a** (91 mg, 0.3 mmol) as a yellow oil. The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 100:1). $[\alpha]_D^{25}$ = -48.1 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.17 (m, 10H), 6.37 (m, 1H), 5.29-5.16 (m, 2H), 4.11 (t, *J* = 5.1 Hz, 1H), 4.03 (d, *J* = 9.6 Hz, 1H), 3.69-3.63 (m, 1H), 3.58-3.41 (m, 3H), 3.26 (s, 3H), 2.81 (d, *J* = 5.1 Hz 1H), 0.69 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 142.4, 137.3, 134.6, 129.4, 127.9, 127.6, 127.3, 127.1, 126.6, 125.3 (q, *J* = 291.0 Hz), 119.5, 76.5 71.7 (q, *J* = 23.0 Hz), 61.1, 58.7, 57.2, 54.9, 12.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -65.2 (s, 3F). IR (thin film): ν_{max} 3375, 3088, 1740, 1638, 1603 cm^{-1}. MS (ESI): *m/z* (%) 422 (M^+ + H^+). HRMS: Calculated for $C_{23}H_{27}NO_3F_3$ (M^+ + H^+): 422.19375; Found: 422.19471.



***(2R,3S)*-Diethyl 2-(*(R)*-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)-3-vinylsuccinate (3k).** Compound **3k** (75 mg, 60% yield) as a yellow oil was prepared as above described with utilization of In powder (96 mg, 0.84 mmol) and allyl bromide **2f** (0.96 mmol) from **1a** (91 mg, 0.3 mmol) The product was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 80:1). (Note: The reaction was quenched with water instead of HCl (1 M, 2 mL)). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.23 (m, 5H), 6.11 (m, 1H), 5.34-5.26 (m, 2H), 4.18-4.10 (m, 3H), 3.88-3.82

(m, 1H), 3.66 (d, *J* = 9.6 Hz, 2H), 3.56-3.49 (m, 2H), 3.46-3.40 (m, 1H), 3.30 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.5, 166.6, 141.4, 130.7, 127.9, 127.4, 127.2, 124.8 (q, *J* = 290.2 Hz), 121.7, 77.4, 69.0 (q, *J* = 24.7 Hz), 61.5, 58.8, 57.3, 54.7, 13.7, 13.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ -68.8 (s, 3F). IR (thin film): ν_{max} 3360, 3034, 1747, 1637 cm^{-1}. MS (EI): *m/z* (%) 372 (M^+ -C_2H_5O, 100), 135, 58, 43. HRMS: Calculated for $C_{18}H_{21}NO_4F_3$ (M^+ -C_2H_5O): 372.1423; Found: 372.1422.

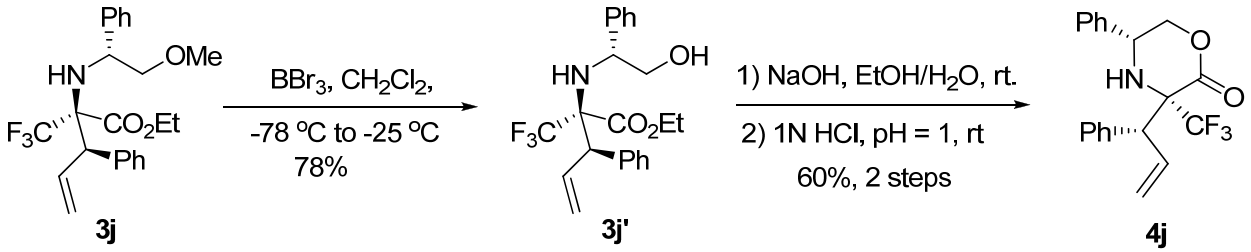
Preparation of (3*R*, 5*R*)-4b.



3b dr (>20:1) (3*R*, 5*R*)-**4b**

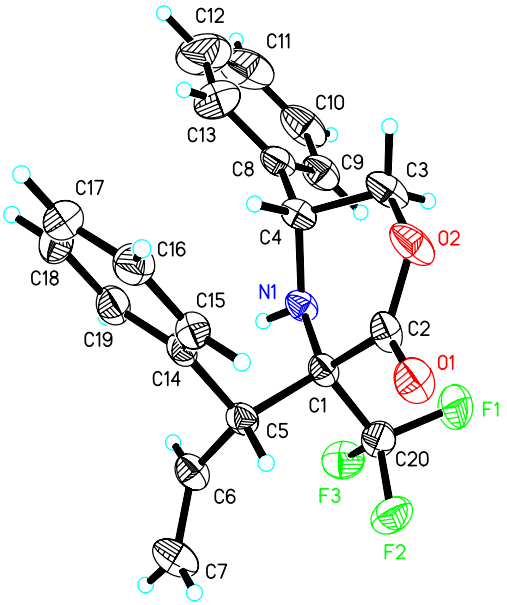
(3*R*,5*R*)-3-allyl-5-phenyl-3-(trifluoromethyl)morpholin-2-one (4b). To a solution of **3b** (84 mg, 0.2 mmol) in CH_2Cl_2 (2 mL) was added dropwise BBr_3 (2 M in CH_2Cl_2, 0.5 mL, 1 mmol) at -78 °C. After stirring for 1 h at the same temperature, the reaction mixture was warmed to -25 °C and stirred for 4 h. The reaction was quenched with brine, extracted with CH_2Cl_2, washed with water, dried over anhydrous Na_2SO_4, filtered, and concentrated to provide crude amino alcohol which was used to do the next step without further purification. The crude amino alcohol was dissolved in anhydrous THF (4 mL) under N_2. Concentrated H_2SO_4 (15 μL) was added, and the resulting mixture was stirred at room temperature for 3 days. The reaction mixture was diluted with ethyl acetate, washed with saturated $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 50:1) to give (3*R*,5*R*)-**4b** 50 mg (88% overall yield, 2 steps) as a white solid. This compound is known.[3] $[\alpha]_D^{25}$ = 13.7 (*c* 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.37 (m, 5H), 5.82 (m, 1H), 5.33-5.25 (m, 2H), 4.37-4.26 (m, 3H), 3.16 (dd, *J* = 13.6 Hz, 6.6 Hz, 1H), 2.54 (dd, *J* = 13.6 Hz, 7.8 Hz, 1H), 2.08 (br, 1H).. ^{19}F NMR (282 MHz, $CDCl_3$) δ -76.9 (s, 3F).

Preparation of optically pure 4j.



***(3R,5R)*-5-phenyl-3-(*(R)*-1-phenylallyl)-3-(trifluoromethyl)morpholin-2-one (4j).** To a solution of **3j** (66 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) was added dropwise BBr_3 (4 M in CH_2Cl_2, 0.2 mL, 0.8 mmol) at -78 ^oC. After stirring for 2 h at the same temperature, the reaction mixture was warmed to -25 ^oC and stirred for 4 h. The reaction was quenched with brine at same temperature, extracted with CH_2Cl_2, washed with water, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified with silica gel chromatography ((Petroleum ether /Ethyl Acetate = 20:1) to give **3j′** (51 mg, 78%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.34-7.25 (m, 10H), 6.42 (m, 1H), 5.33-5.23 (m, 2H), 4.08-4.00 (m, 2H), 3.80-3.64 (m, 3H), 3.54-3.44 (m,1H), 2.32 (br, 2H), 0.73 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -65.5 (s, 3F).

3j′ (20 mg, 0.05 mmol) was dissolved in THF (2 mL), a solution of NaOH (3 mg, 0.075 mmol) in H_2O (2 mL) was added. The resulting mixture was stirred at room temperature for 36 h. The reaction was quenched with 1N HCl and adjusted pH value to 1-2. The resulting mixture was extracted with EtOAc, dried over Na_2SO_4, filtered, and concentrated. The residue was purified with silica gel chromatography (Petroleum ether /Ethyl Acetate = 50:1) to give (3*R*,5*R*)-**4j** 11 mg (60% yield) as a white solid. $[\alpha]_D^{25}$ = -49.6 (*c* 0.91, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 8H), 7.24 (m, 2H), 6.24 (m, 1H), 5.40-5.30 (m, 2H), 4.65 (d, *J* = 9.9 Hz, 1H), 4.22 (t, *J* = 10.8 Hz, 1H), 3.95 (dd, *J* = 10.5 Hz, 3.0 Hz, 1H), 3.29 (dd, *J* = 10.5 Hz, 2.4 Hz, 1H), 2.43 (br, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 164.7, 137.5, 136.5, 131.5, 129.3, 129.1, 129.0, 128.0, 127.3, 124.0 (q, *J* = 285.7 Hz), 120.4, 73.9, 70.4 (q, *J* = 24.1 Hz), 54.1, 53.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.8 (s, 3F). IR (thin film): ν_{max} 3350, 1735 cm^{-1}. MS (ESI): *m/z* (%) 384 ($M^+ + Na^+$), 362 ($M^+ + H^+$). HRMS: Calculated for $C_{20}H_{19}NO_2F_3$ ($M^+ + H^+$): 362.13624; Found: 362.13701.


C12
C11
C10
C13
C8
C9
C3
C17
C4
O2
C16
C18
N1
C15
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C19
O1
C14
C1
F1
C5
C20
C6
F3
F2
C7

4j

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Bond precision:      C-C = 0.0051 A              Wavelength=0.71073
Cell:        a=7.8902(10)   b=12.4068(16)  c=9.9490(12)
             alpha=90       beta=113.018    gamma=90
                            (2)
Temperature: 293 K
                   Calculated                      Reported
Volume             896.4(2)                        896.39(19)
Space group        P 21                            P2(1)
Hall group         P 2yb                           ?
Moiety formula     C20 H18 F3 N O2                 ?
Sum formula        C20 H18 F3 N O2                 C20 H18 F3 N O2
Mr                 361.35                          361.35
Dx,g cm-3          1.339                           1.339
Z                  2                               2
Mu (mm-1)          0.107                           0.107
F000               376.0                           376.0
F000'              376.24
h,k,lmax           9,15,12                         9,15,12
Nref               1752[ 3335]                     1749
Tmin,Tmax          0.960,0.976                     0.392,1.000
Tmin'              0.959
Correction method= EMPIRICAL
Data completeness= 1.00/0.52   Theta(max)= 25.500
R(reflections)= 0.0374( 1592)     wR2(reflections)= 0.0926( 1749)
S = 1.022             Npar= 240
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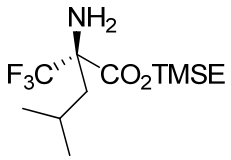
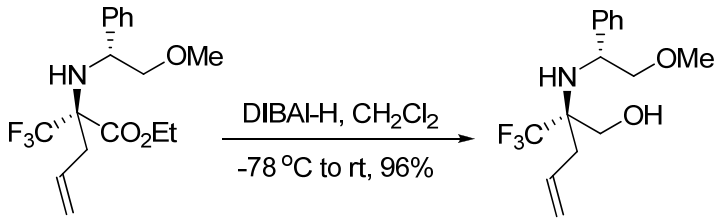
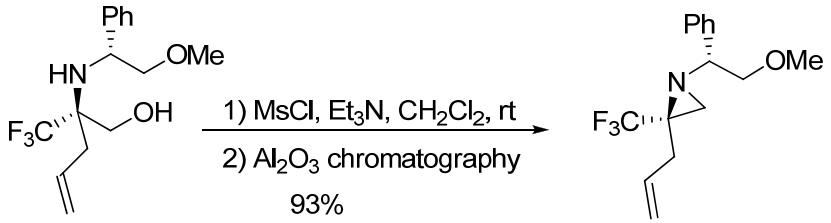


***(R)*-2-(Trimethylsilyl)ethyl 2-amino-4-methyl-2-(trifluoromethyl)pentanoate (5).** To a solution of **3g** (50 mg, 0.116 mmol) in MeOH (5 mL) was added $Pd(OH)_2/C$ (20%, 21.5 mg). The resulting mixture was stirred under H_2 (5 atm) for 24 h at room temperature. The mixture was filtered with celite and the filtrate was concentrated without further purification to give (*R*)-α-Tfm-Leu **5** 28 mg (80% yield) as a light yellow oil. $[\alpha]_D^{25}$ = -4.85 (*c* 0.75, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.29 (m, 2H), 2.03 (dd, *J* = 13.8 Hz, 7.8 Hz, 1H), 1.82 (m, 2H), 1.65 (dd, *J* = 13.8 Hz, 5.4 Hz, 1H), 1.05 (dd, *J* = 10.8 Hz, 7.2 Hz, 2H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.06 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.6, 125.2 (q, *J* = 285.9 Hz), 64.9, 64.3 (q, *J* = 26.1 Hz), 40.0, 24.4, 23.7, 22.4, 17.1, -1.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -78.3 (s, 3F). IR (thin film): ν_{max} 2959, 1747, 1253 cm^{-1}. MS (ESI): *m/z* (%) 256 (M^+ - C_3H_7), 154, 73 (100). HRMS: Calculated for $C_9H_{17}NO_2F_3Si$ (M^+ - C_3H_7): 256.0981; Found: 256.0976.



3a (dr >20:1) **6** (dr > 20:1)

(*R*)-2-((*R*)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-en-1-ol (6). To a solution of **3a** (103 mg, 0.3 mmol) in CH_2Cl_2 (3 mL) was added dropwise DIBAl-H (1 M in toluene, 0.9 mL, 0.9 mmol) at – 78 °C. After stirring for 1 h at the same temperature, the reaction mixture was warmed to room temperature and stirred for 1.5 h. The reaction was quenched with 1N HCl, and extracted with CH_2Cl_2, dried over Na_2SO_4, filtered and concentrated. The residue was purified with Al_2O_3 chromatography (CH_2Cl_2/MeOH = 60:1) to give **6** 87 mg (96% yield). $[\alpha]_D^{25}$ = -59.8 (*c* 1.56). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.28 (m, 5H), 5.76 (m, 1H), 5.12-5.06 (m, 2H), 4.23 (dd, *J* = 8.7 Hz, 3.6 Hz, 1H), 3.49 (d, *J* = 6.3 Hz, 2H), 3.44-3.31 (m, 5H), 2.43 (t, *J* = 7.4 Hz, 1H), 2.39 (dd, *J* = 14.7 Hz, 8.1 Hz), 2.29 (dd, *J* = 14.7 Hz, 7.5 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 142.2, 131.6, 128.6, 127.8, 127.1 (q, *J* = 288.8 Hz), 126.9, 119.4, 77.7, 63.2 (q, *J* = 22.7 Hz), 61.1, 58.7, 55.7, 36.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -71.8 (s, 3F). IR (thin film): ν_{max} 3450, 3355, 1640 cm^{-1}. MS (ESI): *m/z* (%) 304 ($M^+ + H^+$), 326 ($M^+ + Na^+$). HRMS: Calculated for $C_{15}H_{20}NO_2F_3Na$ ($M^+ + Na^+$): 326.13383; Found: 326.13403.



6 **7** (dr > 20:1)

(*R*)-2-allyl-1-((*R*)-2-methoxy-1-phenylethyl)-2-(trifluoromethyl)aziridine (7). To a solution of **6** (45 mg, 0.15 mmol) in CH_2Cl_2 (1.5 mL) was added Et_3N (56 μL, 0.30 mmol), followed by MsCl (18 μL, 0.225 mmol) at 0 °C. The resulting mixture was then warmed to room temperature and stirred for 12 h. The reaction mixture was directly purified with Al_2O_3 chromatography (pure CH_2Cl_2) to give **7** 40 mg (93% yield). $[\alpha]_D^{25}$ = -100.0 (*c* 1.6). ^{1}H NMR (300 MHz, $CDCl_3$) δ

7.42-7.27 (m, 5H), 5.56 (m, 1H), 5.03-4.97 (m, 2H), 3.68 (dd, *J* = 9.6 Hz, 8.1 Hz, 1H), 3.50 (dd, *J* = 9.6 Hz, 3.9 Hz, 1H), 3.37 (m, 1H), 3.35 (s, 3H), 2.42 (s, 1H), 2.34 (dd, *J* = 15.6 Hz, 6.3 Hz, 1H), 2.20 (dd, *J* = 15.6 Hz, 7.5 Hz, 1H), 1.83 (s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 139.7, 133.8, 128.4, 127.6, 127.2, 125.2 (q, J = 276.9 Hz), 117.6, 78.9, 66.1, 59.1, 35.1, 28.9. ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.2 (s, 3F). IR (thin film): ν_{max} 1643, 1454, 1123 cm^{-1}. MS (ESI): *m/z* (%) 286 ($M^+ + H^+$). HRMS: Calculated for $C_{15}H_{19}NOF_3$ ($M^+ + H^+$): 286.14133; Found: 286.14184.

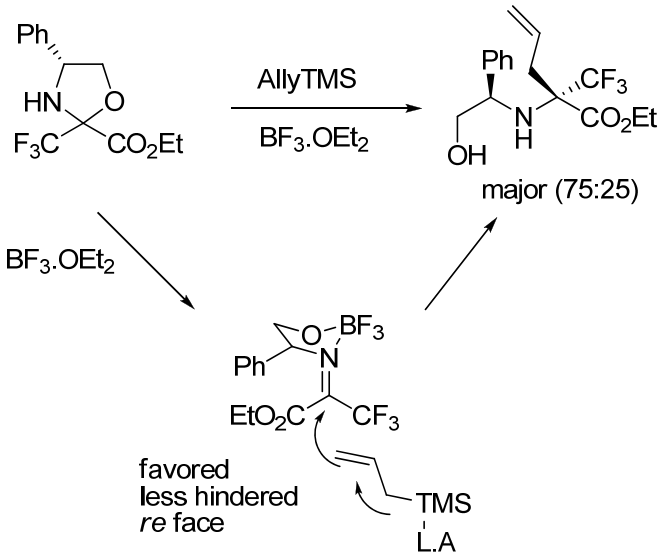
References:

(1) (a) Uneyama, K.; Tamura, K.; Mizukami, H.; Maeda, K.; Watanabe, H. *J. Org. Chem.* **1993**, *58*, 32-35. (b) Watanabe, H.; Hashizume, Y.; Uneyama, K. *Tetrahedron Lett.* **1992**, *33*, 4333-4336. (c) Amii, H.; Kishikawa,Y.; Kageyama, K.; Uneyama, K. *J. Org. Chem.* **2000**, *63*, 3404-3408.

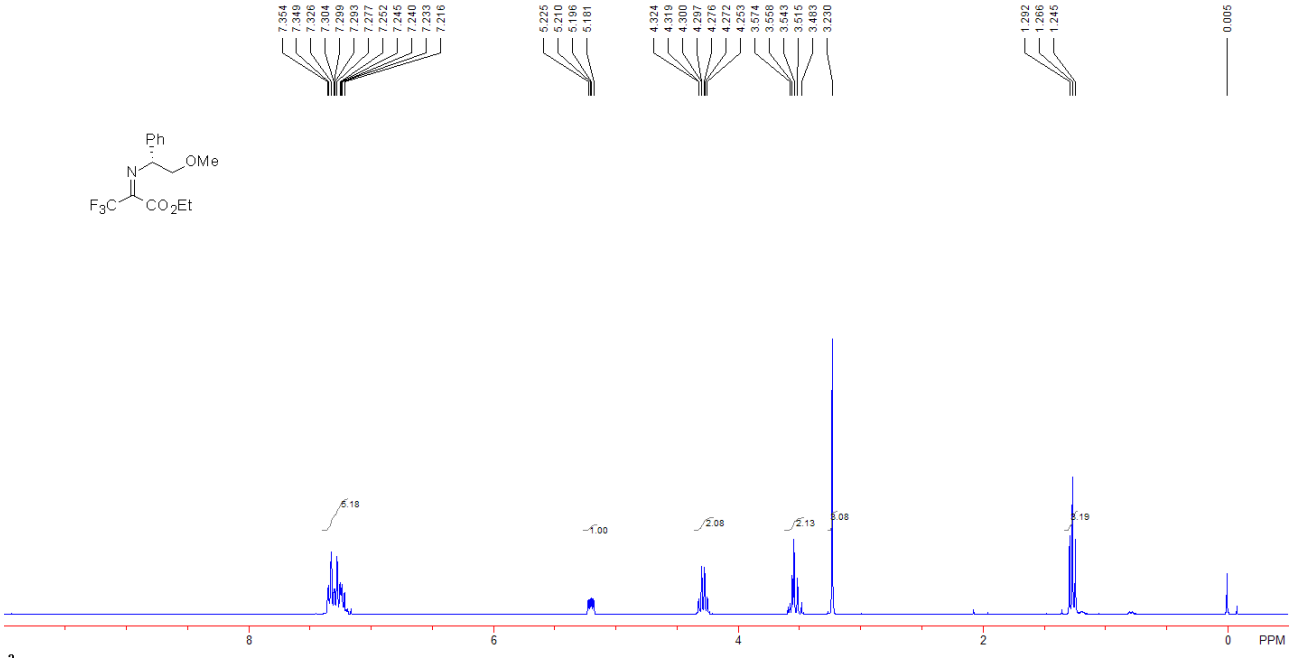
(2) Fustero, S.; Sanchez-Rosello, M.; Rodrigo, V.; Pozo, C.; Sanz-Cervera, J. F.; Simon, A. *Org. Lett.* **2006**, *8*, 4129.

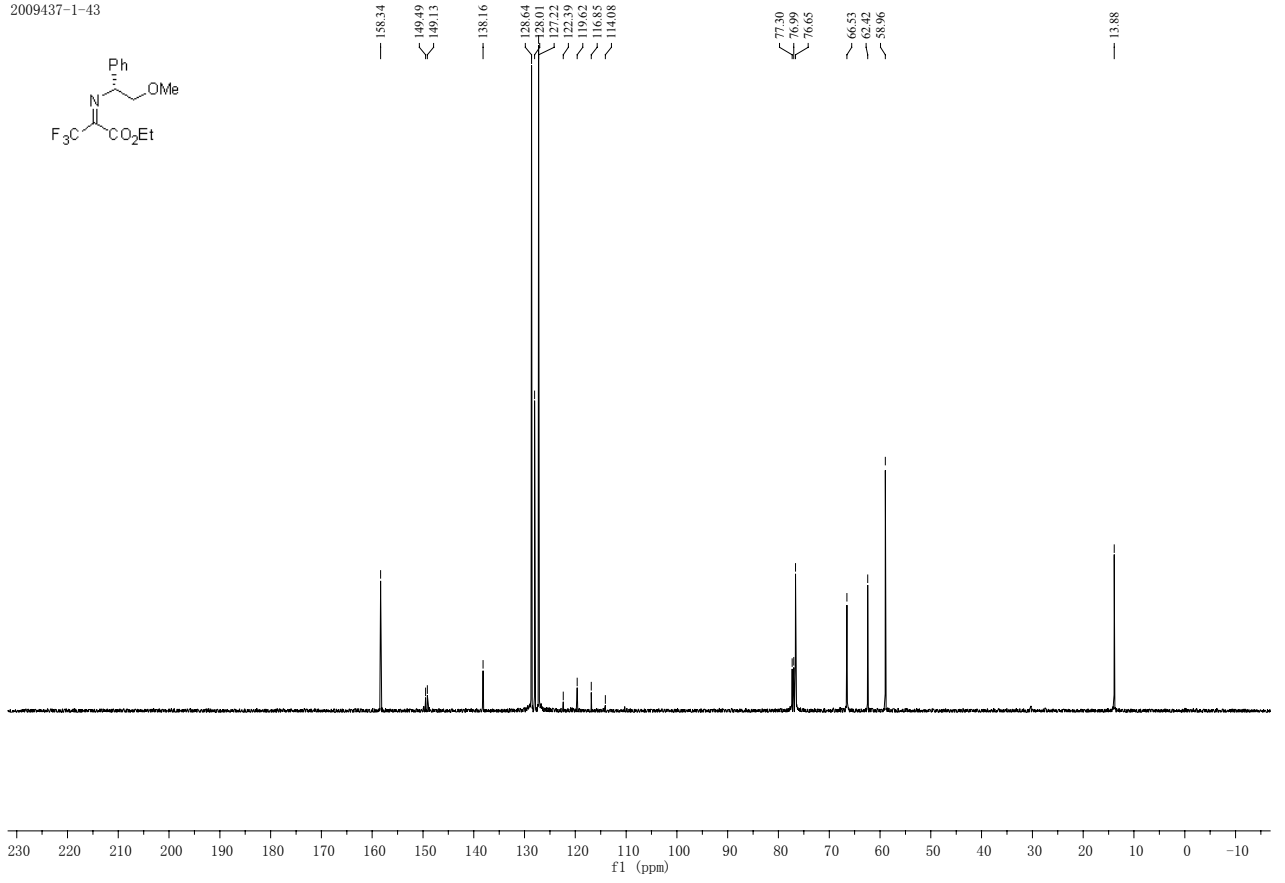
(3) Chaume, G.; Van Severen, M.-C.; Marinkovic, S.; Brigaud, T. *Org. Lett.* **2006**, *8*, 6123.

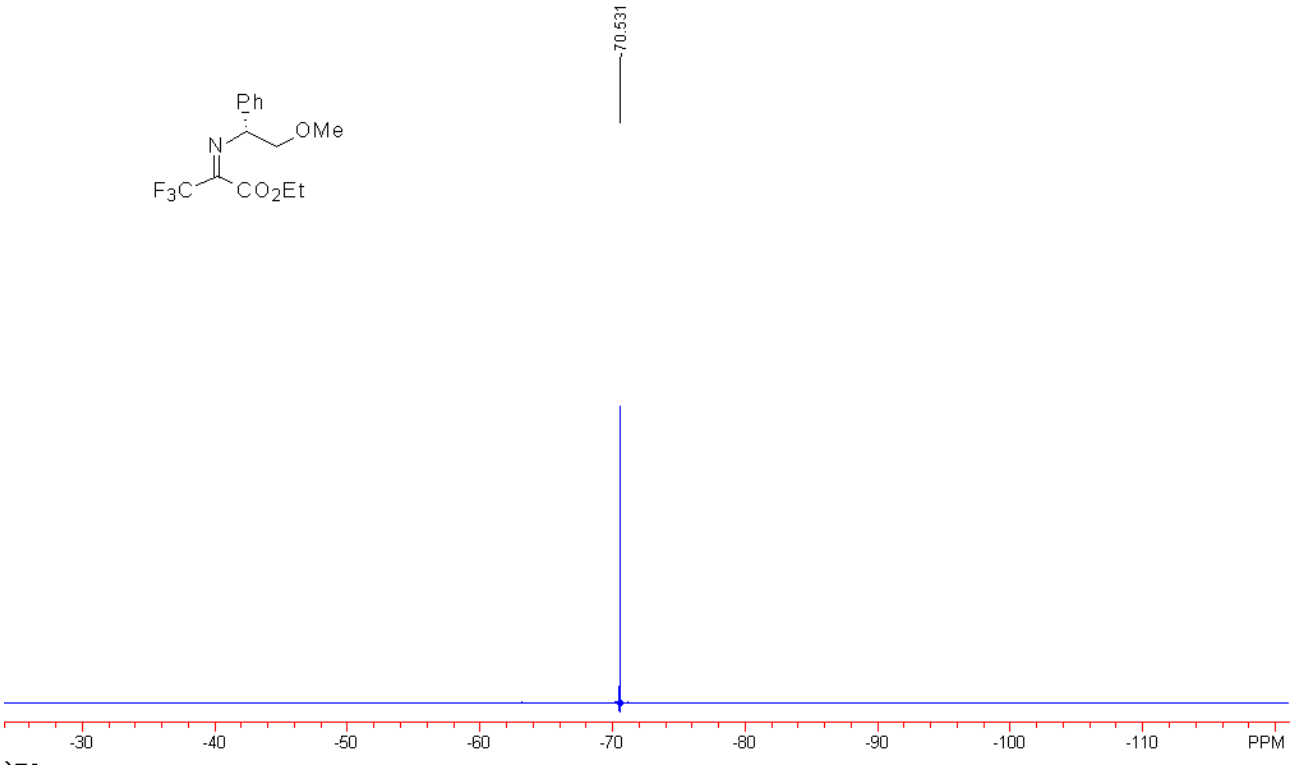
Proposed transition state for Brigaud's method



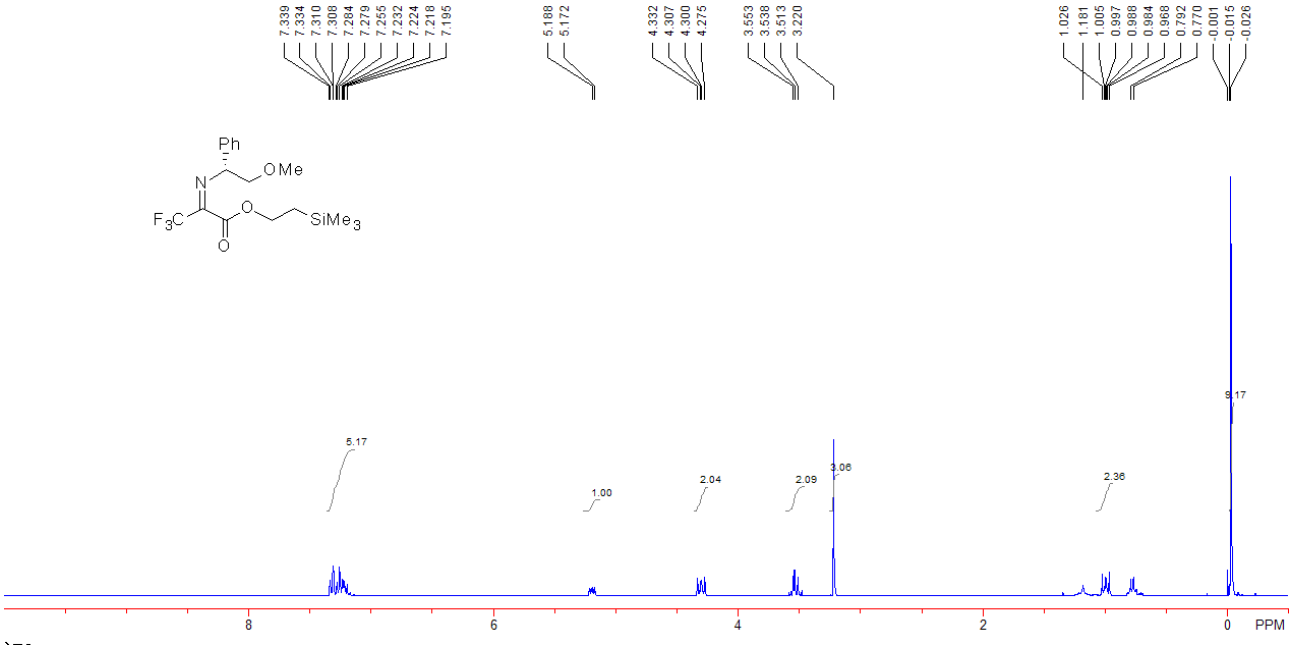
_(R)_-Ethyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate (1a).

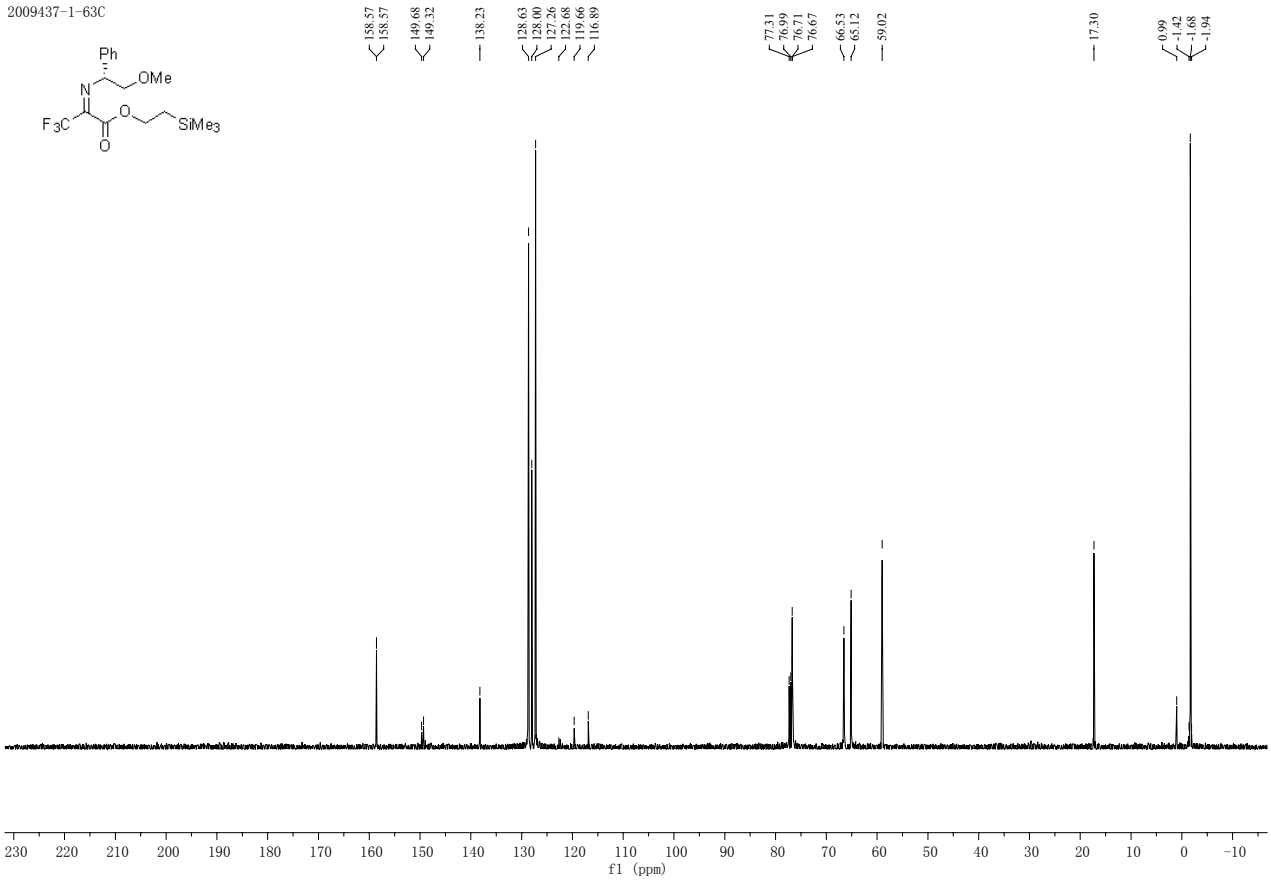


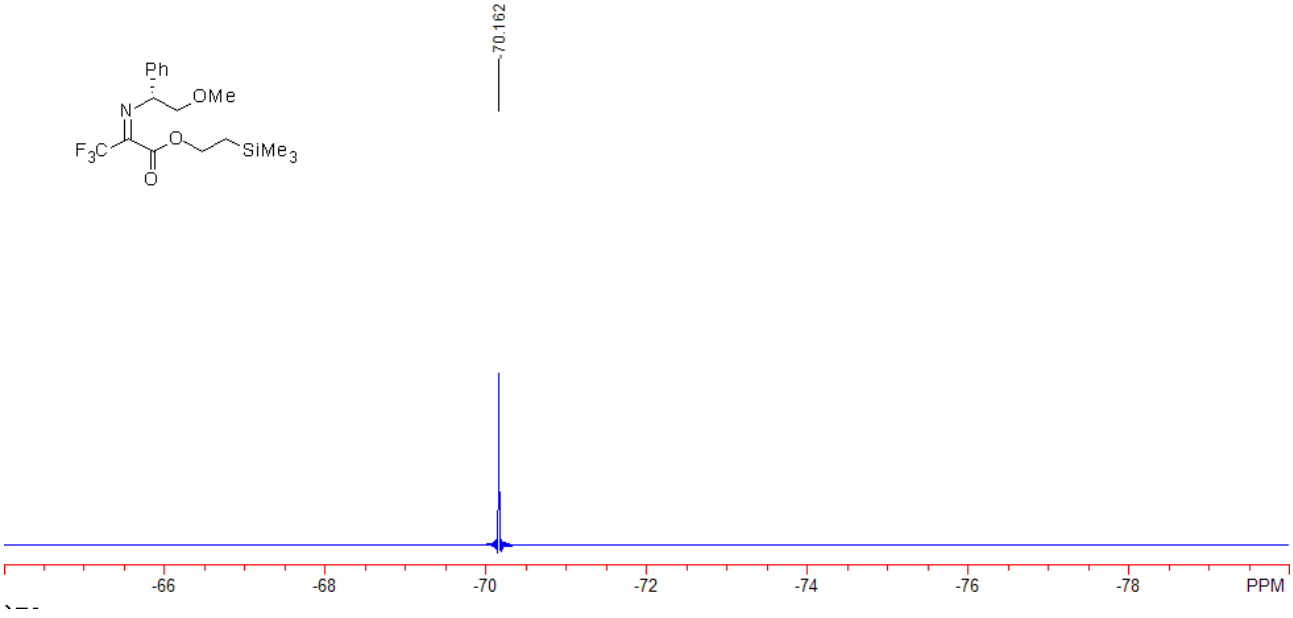




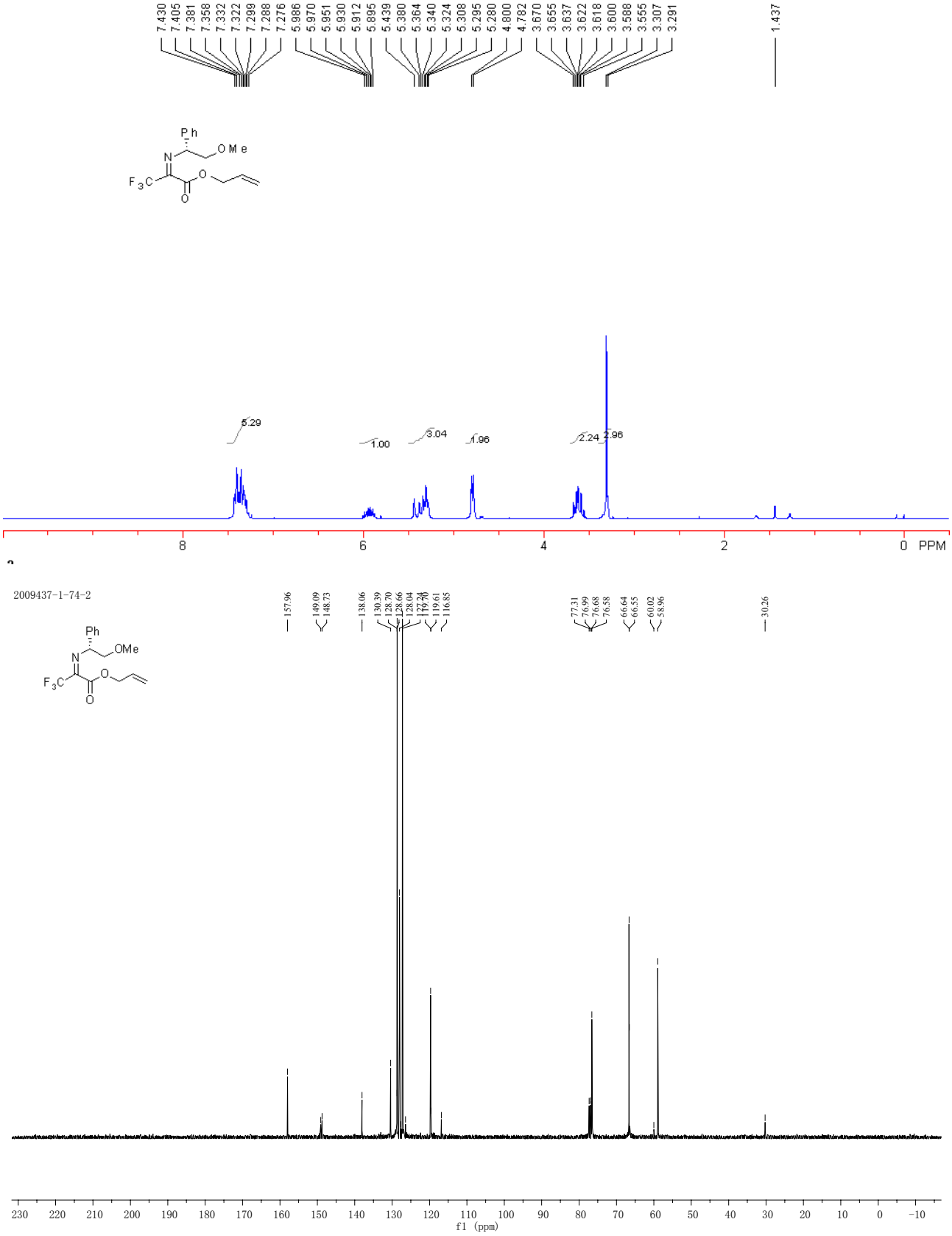
***(R)*-2-(Trimethylsilyl)ethyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate (1b).**

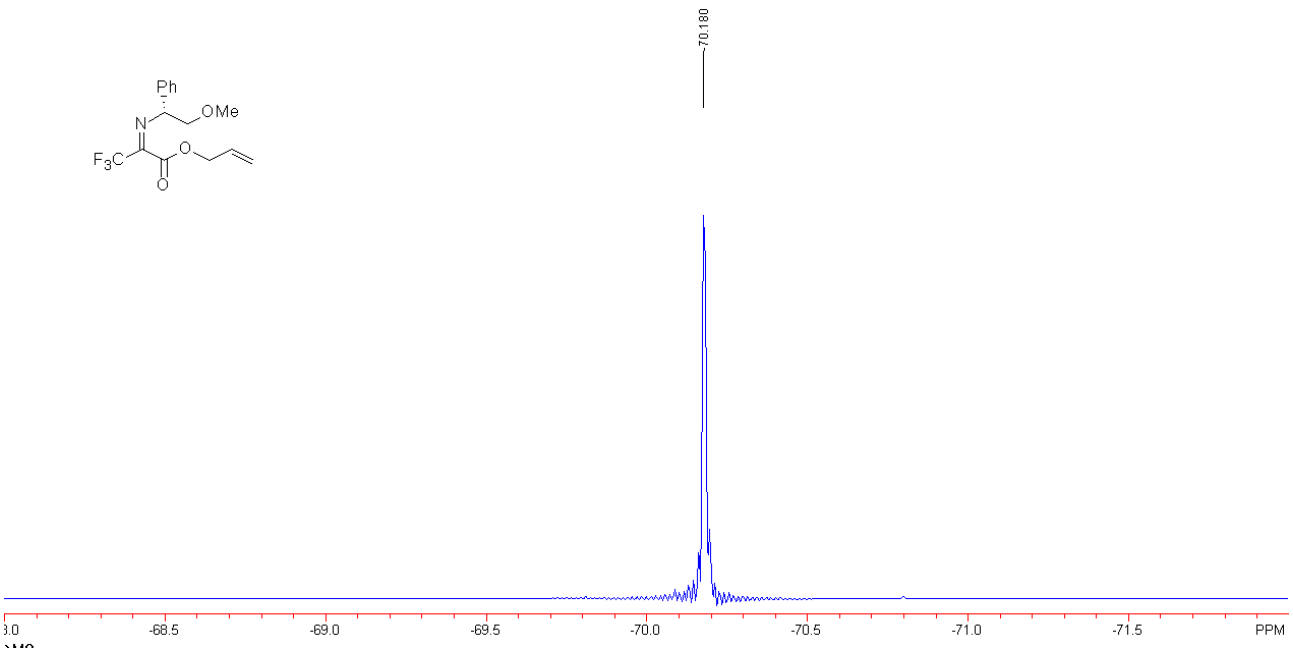



2009437-1-63C
158.57
158.57
149.68
149.32
138.23
128.63
128.00
127.26
122.68
119.66
116.89
77.31
76.99
76.71
76.67
66.53
65.12
59.02
17.30
0.99
-1.42
-1.68
-1.94
Ph
OMe
N
F3C
O
O
SiMe3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

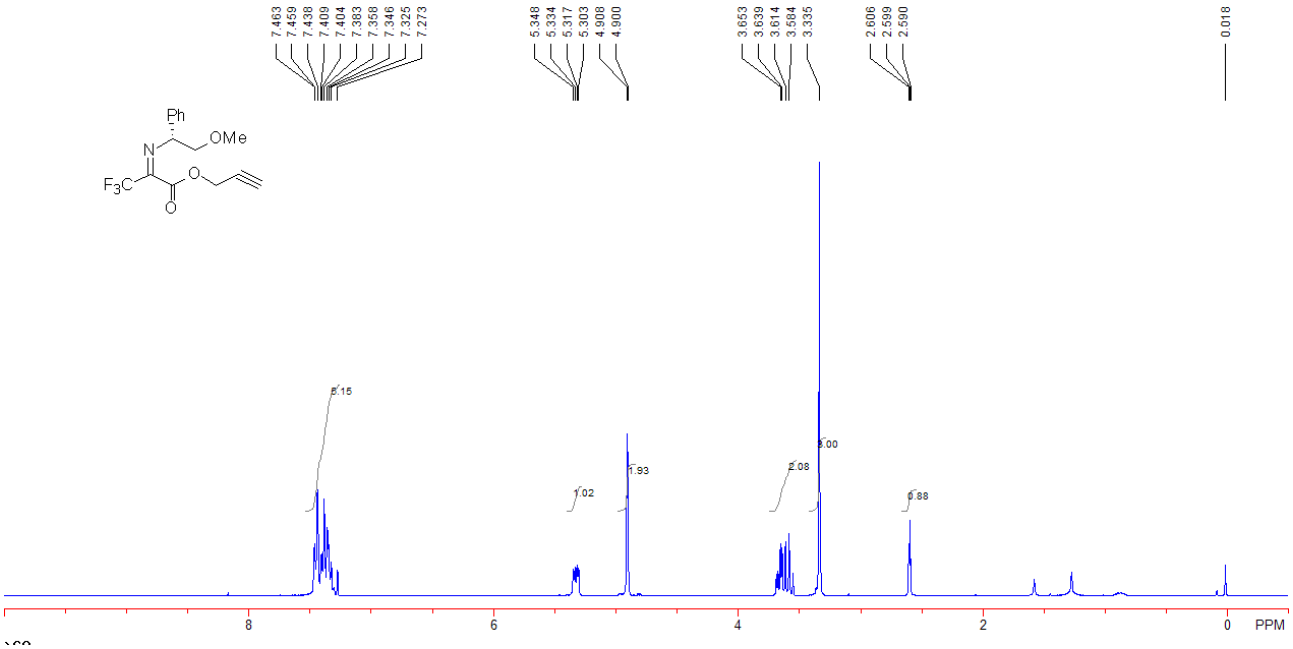

70.162
Ph
OMe
N
F3C
O
O
SiMe3
-66
-68
-70
-72
-74
-76
-78
PPM

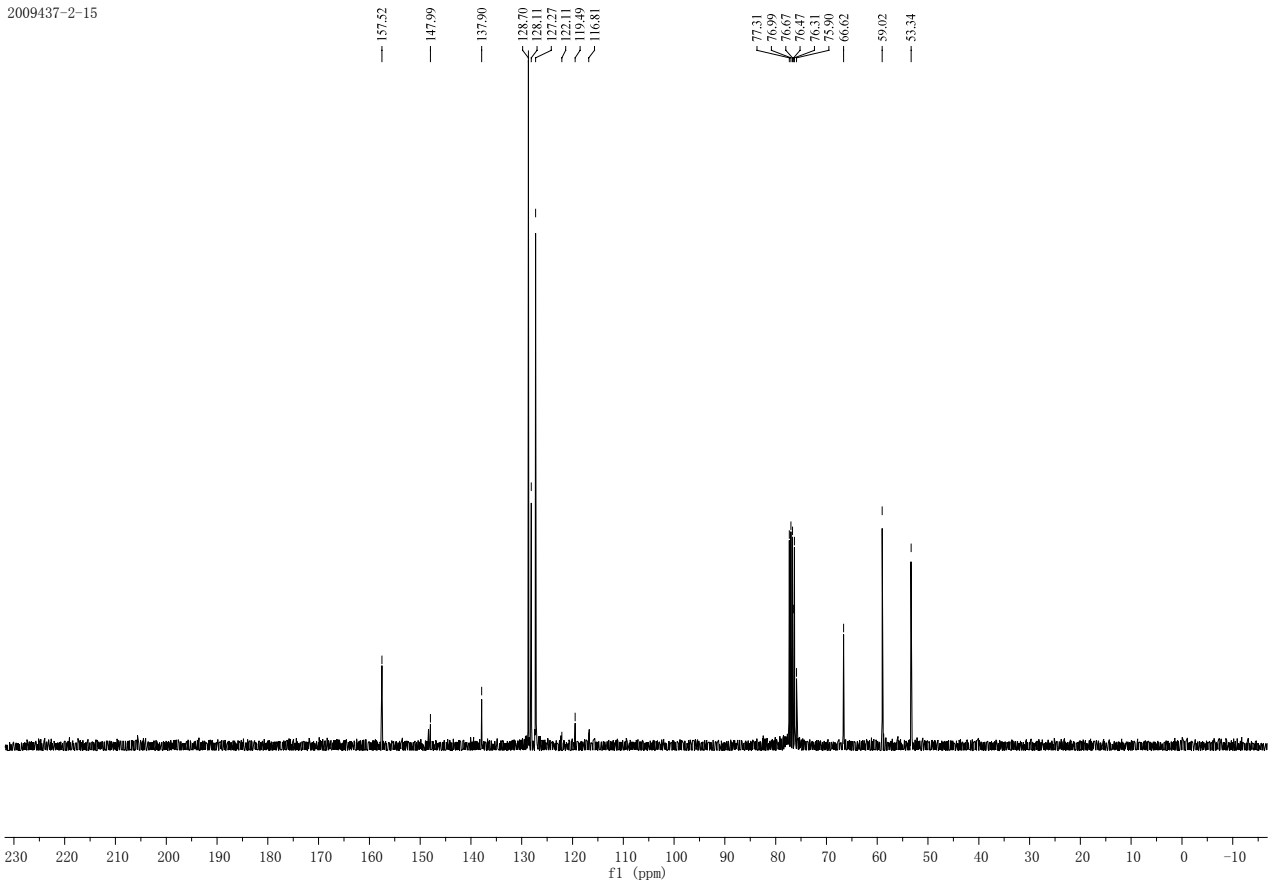
***(R)*-Allyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate(1c).**

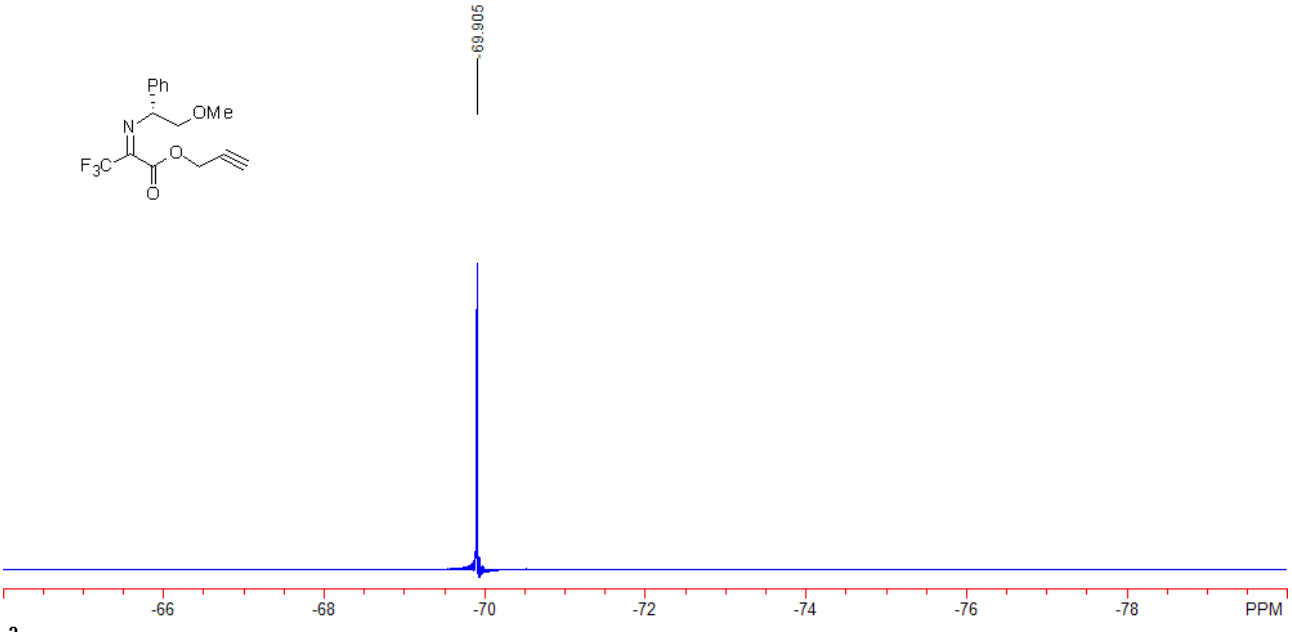




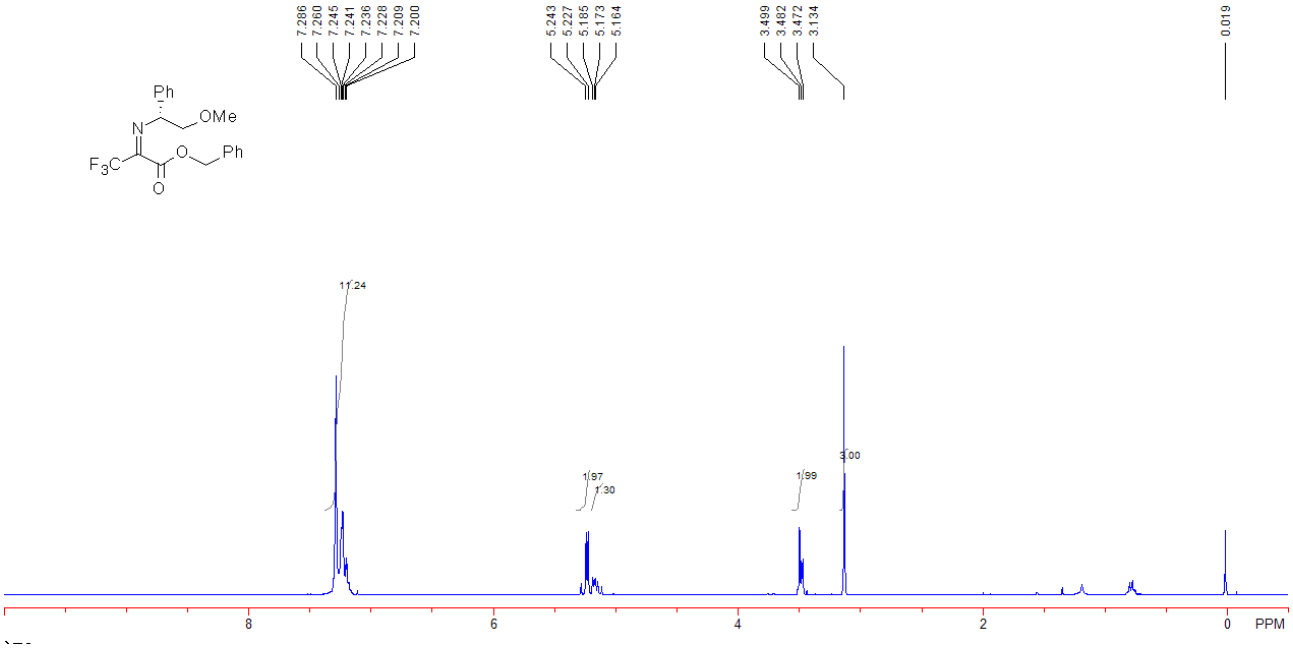
***(R)*-prop-2-ynyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate (1d).**

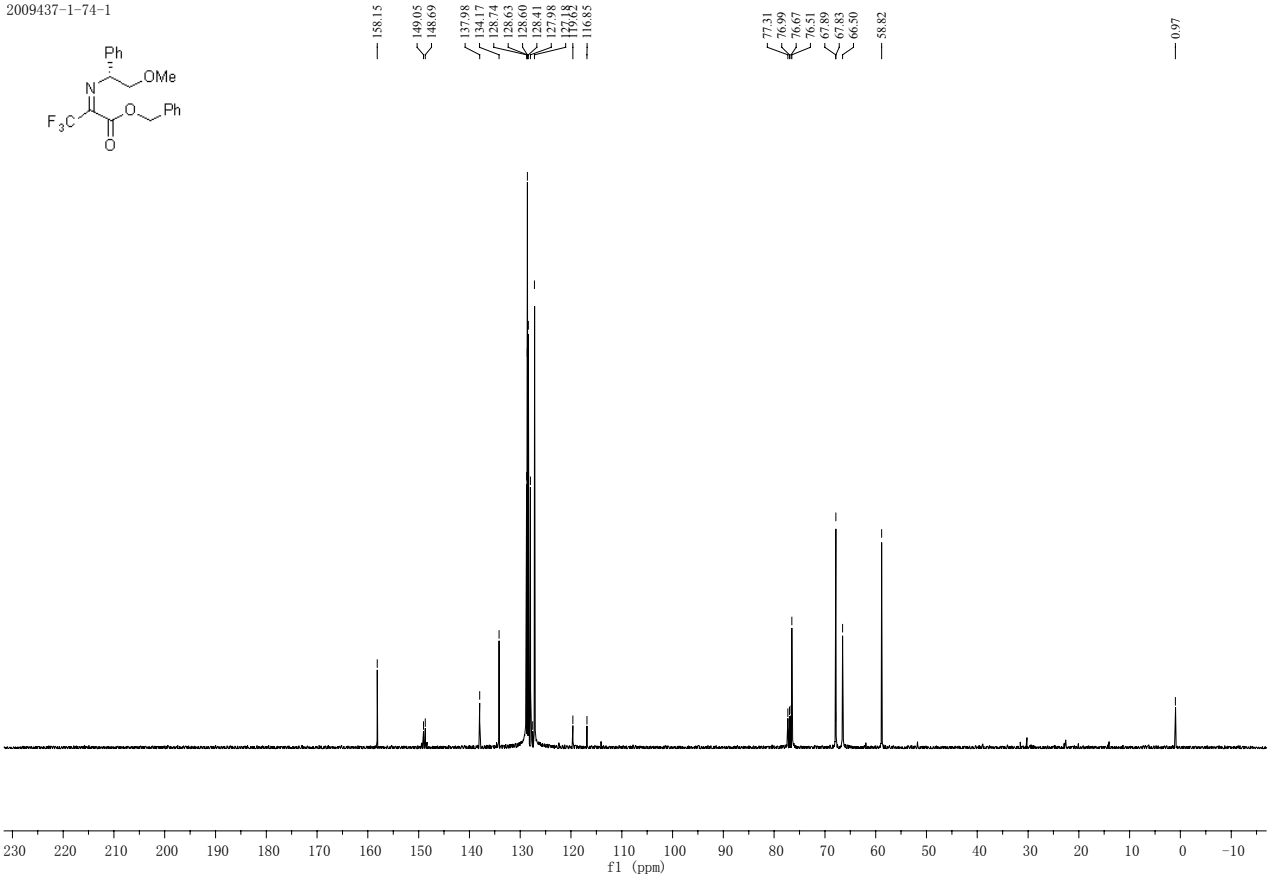


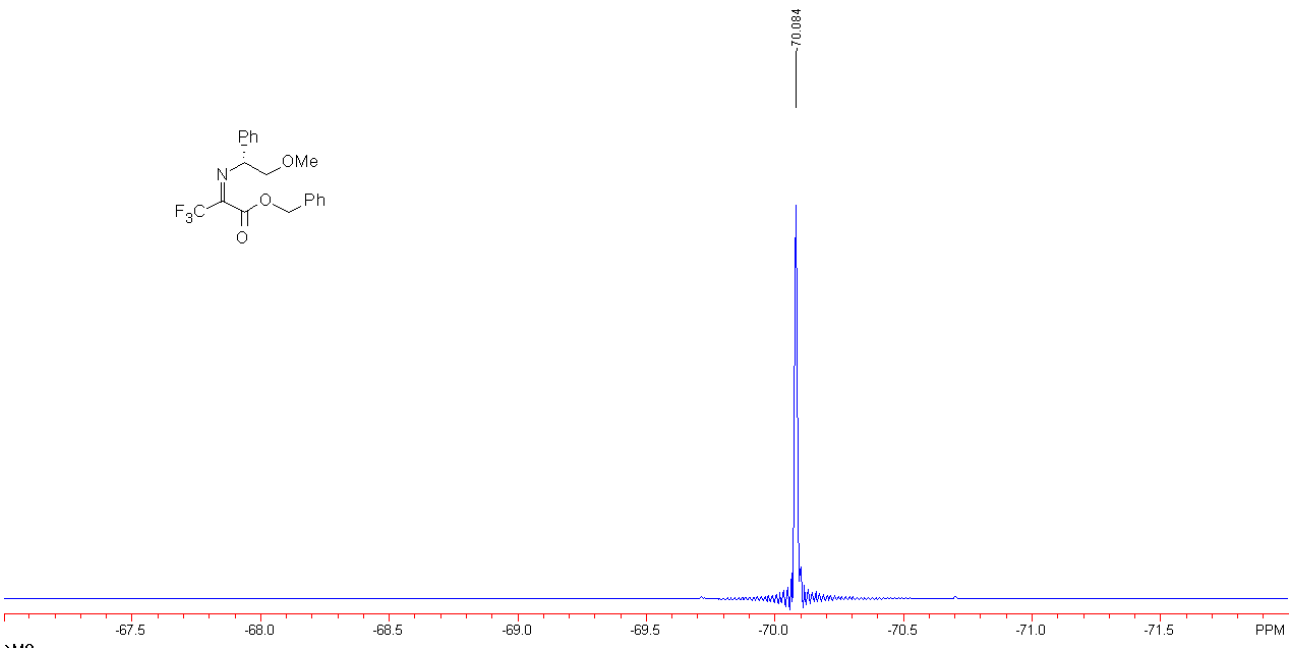

2009437-2-15
157.52
147.99
137.90
128.70
128.11
127.27
122.11
119.49
116.81
77.31
76.99
76.67
76.47
76.31
75.90
66.62
59.02
53.34
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-69.905
Ph
OMe
N
F3C
O
O
-66 -68 -70 -72 -74 -76 -78 PPM

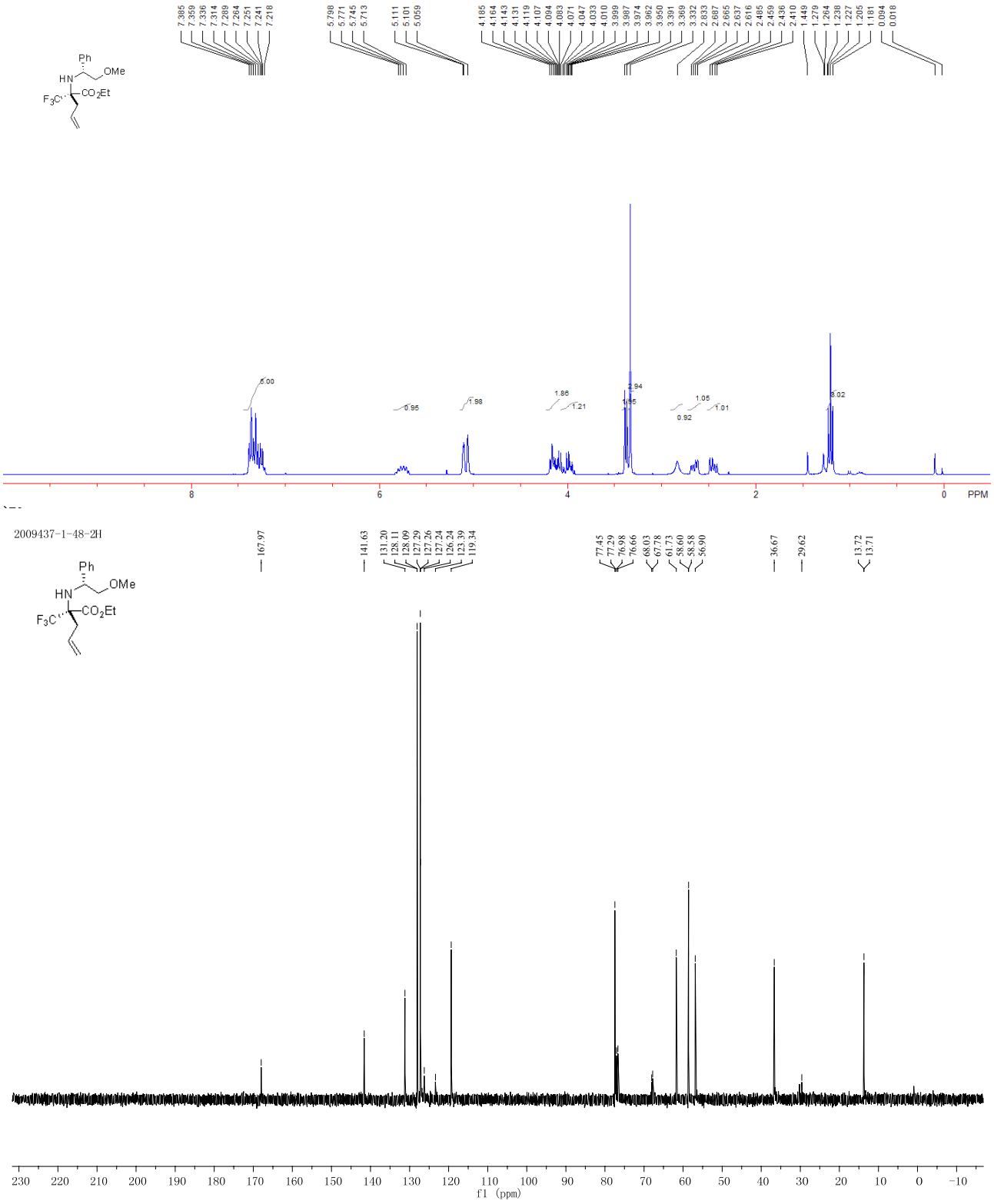
***(R)*-benzyl 3,3,3-trifluoro-2-(2-methoxy-1-phenylethylimino)propanoate (1e).**

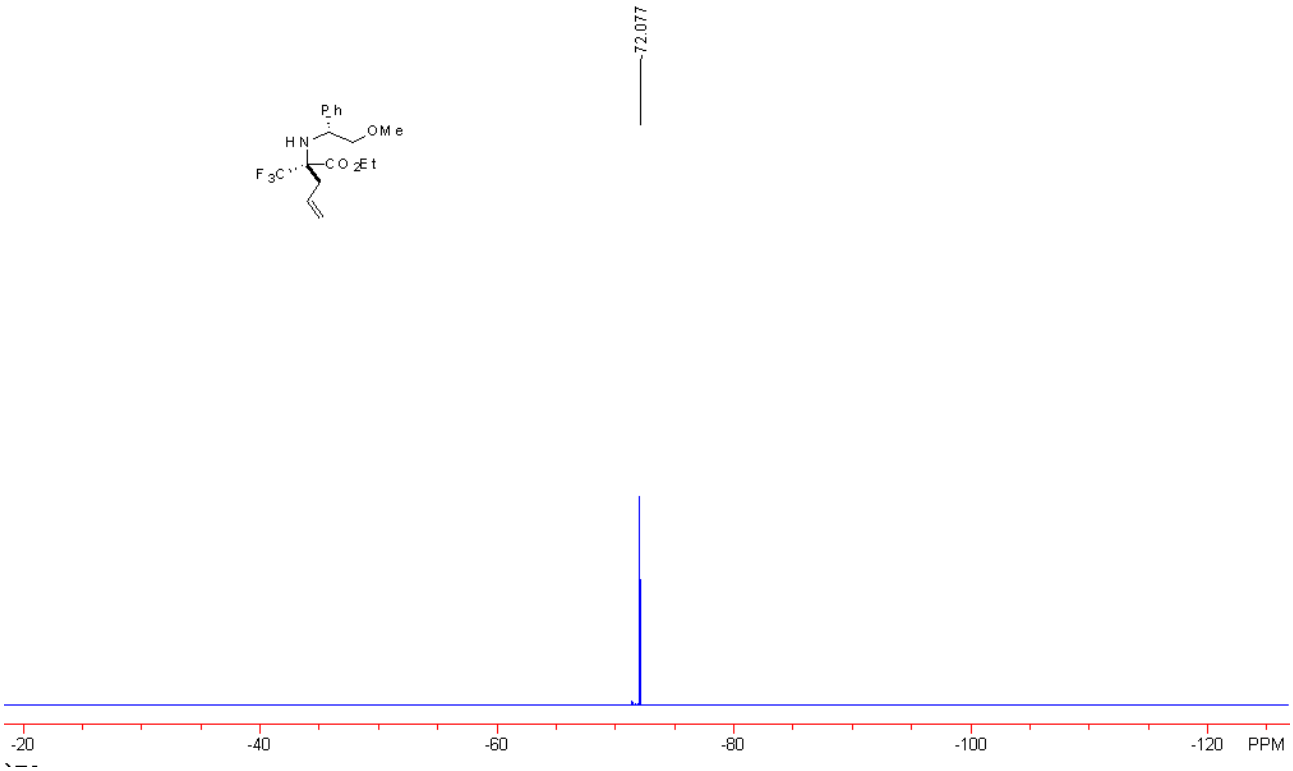




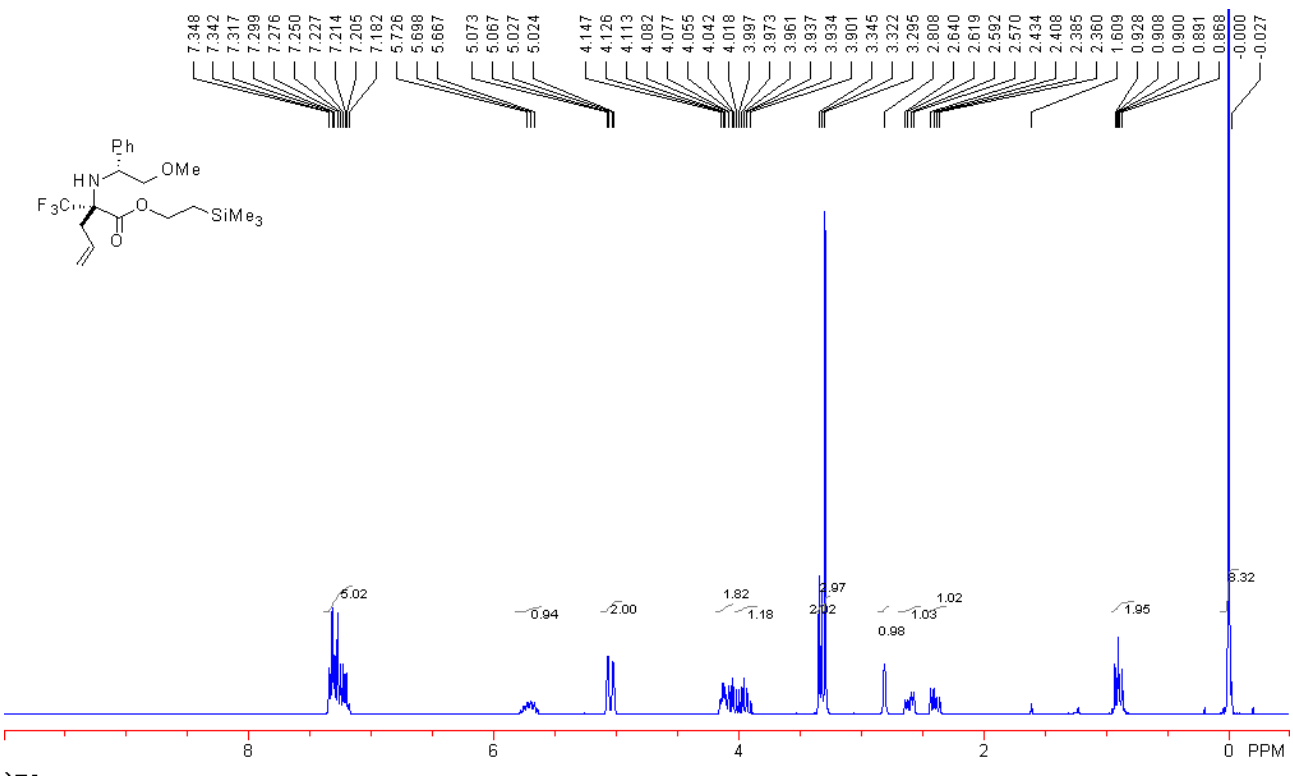

-70.084
Ph
N
OMe
F3C
O
O
Ph
-67.5
-68.0
-68.5
-69.0
-69.5
-70.0
-70.5
-71.0
-71.5
PPM

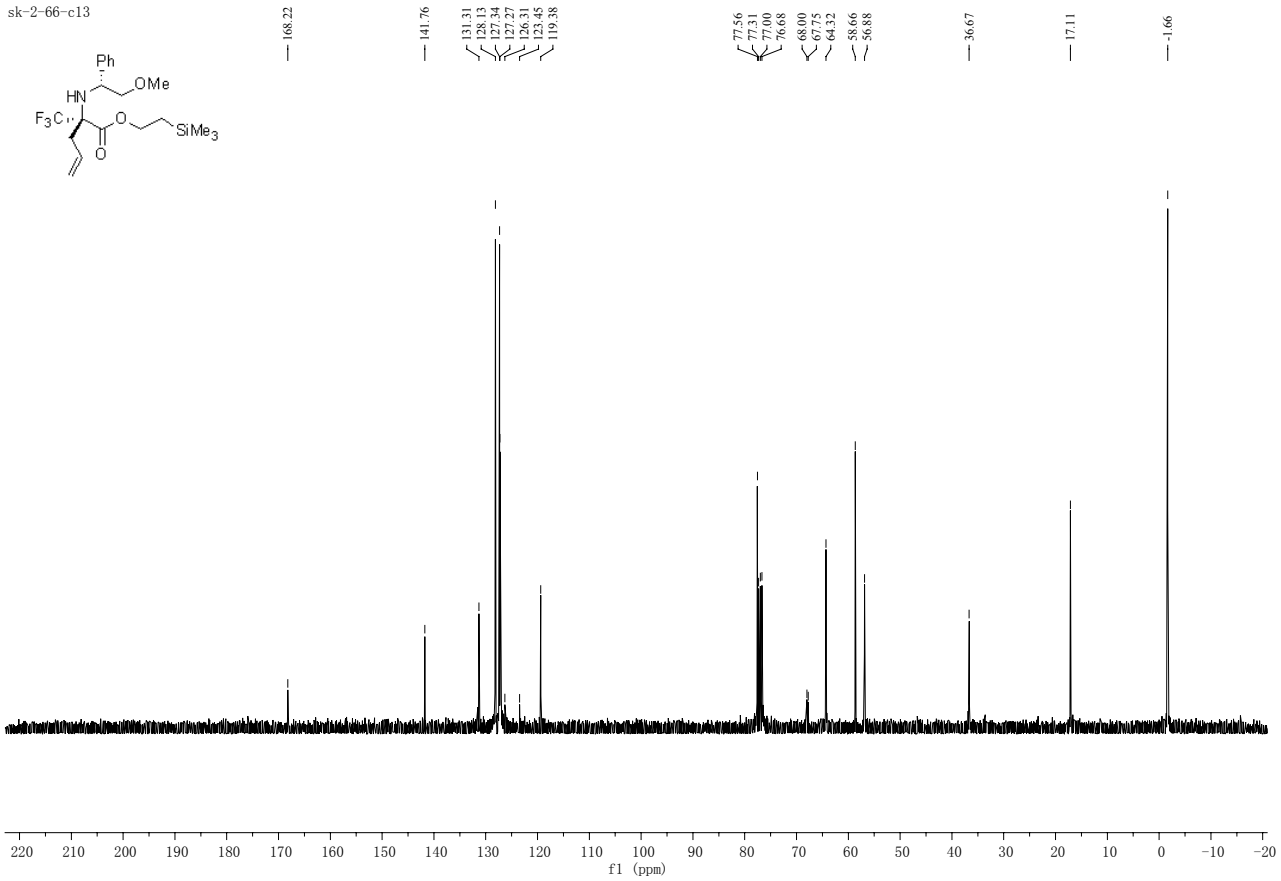
(*R*)-Ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3a).

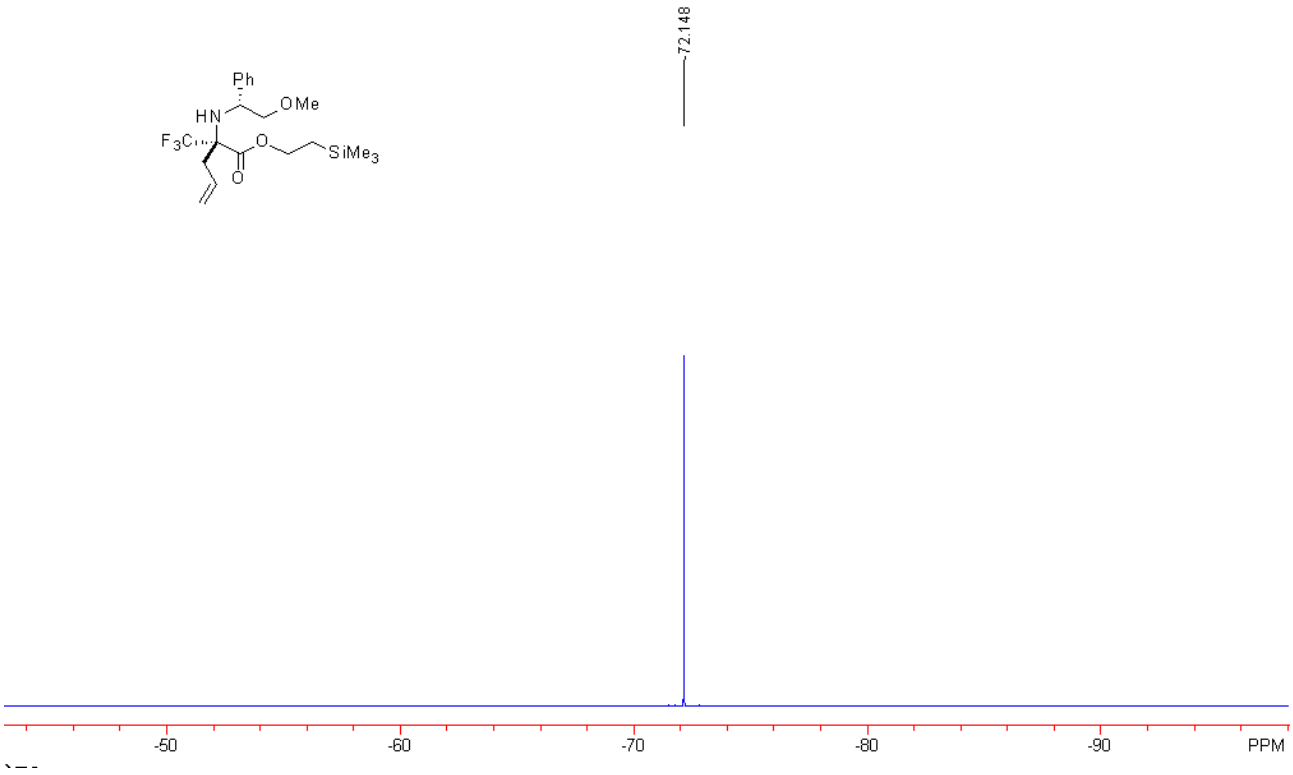




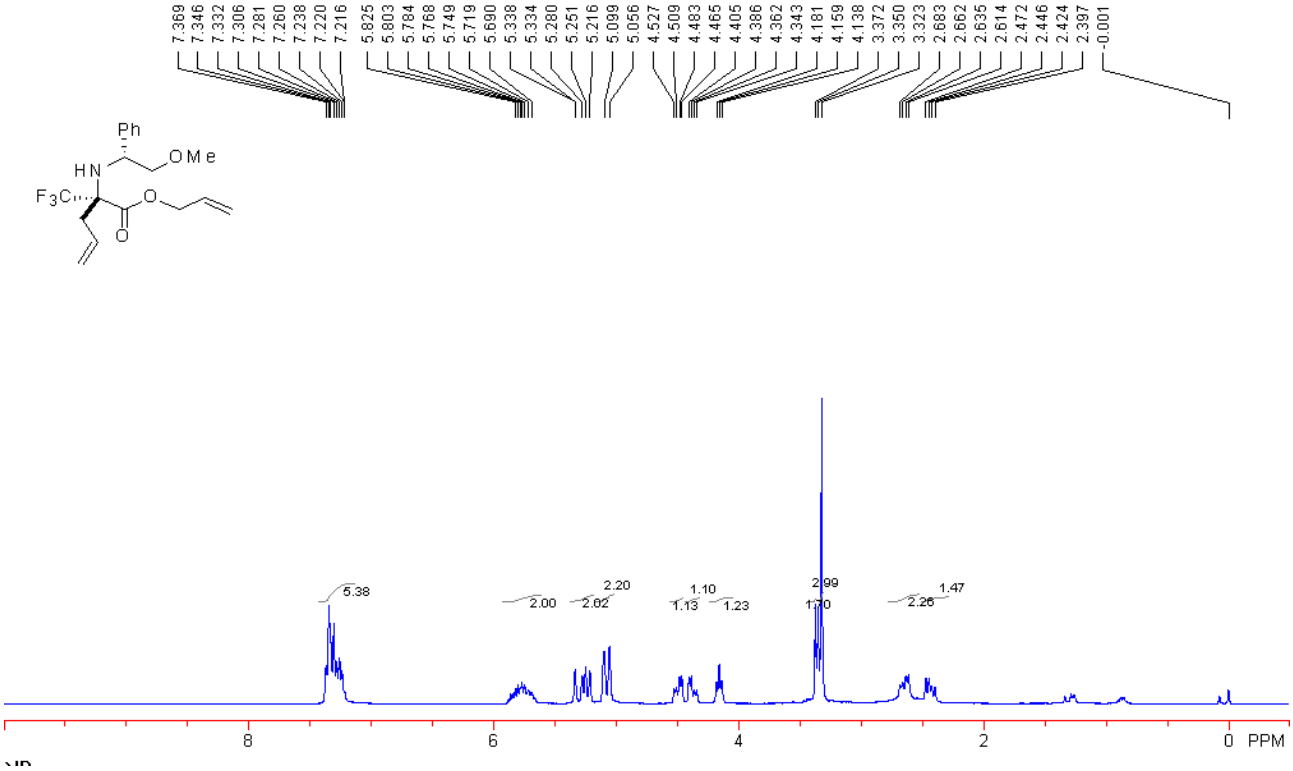
***(R)*-2-(Trimethylsilyl)ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3b).**

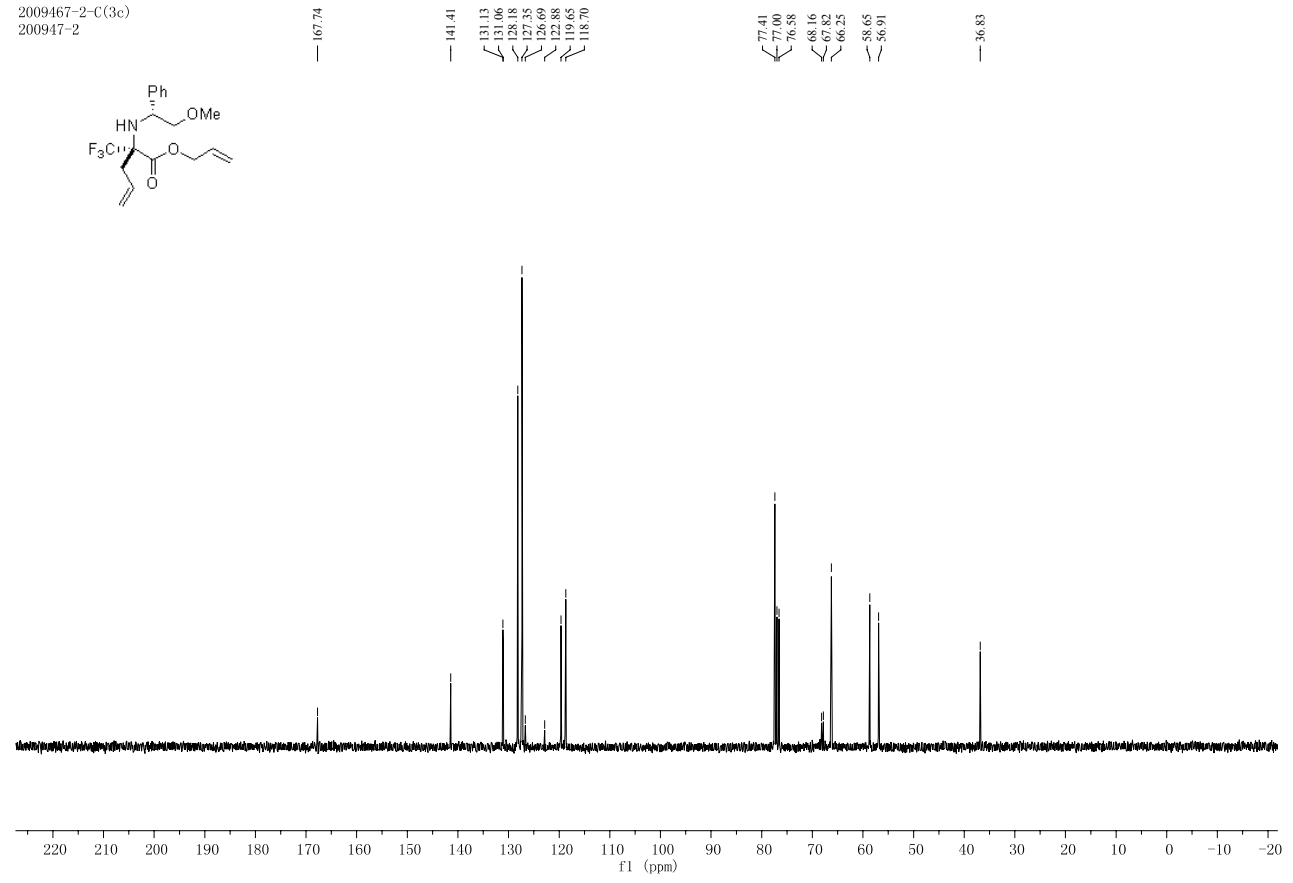


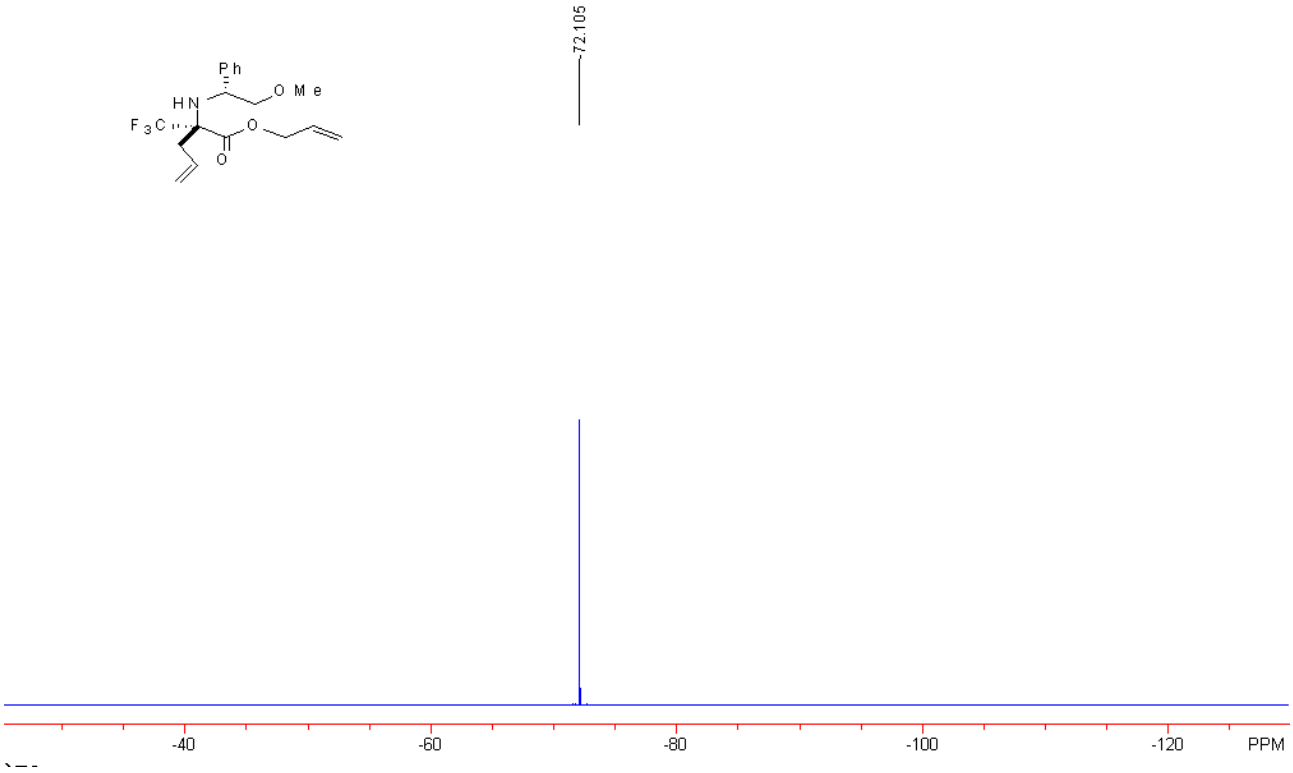

sk-2-66-c13
168.22
141.76
131.31
128.13
127.34
127.27
126.31
123.45
119.38
77.56
77.31
77.00
76.68
68.00
67.75
64.32
58.66
56.88
36.67
17.11
-1.66
Ph
OMe
HN
F3C
O
O
SiMe3
O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


72.148
Ph
OMe
HN
F3C
O
O
SiMe3
O
-50
-60
-70
-80
-90
PPM

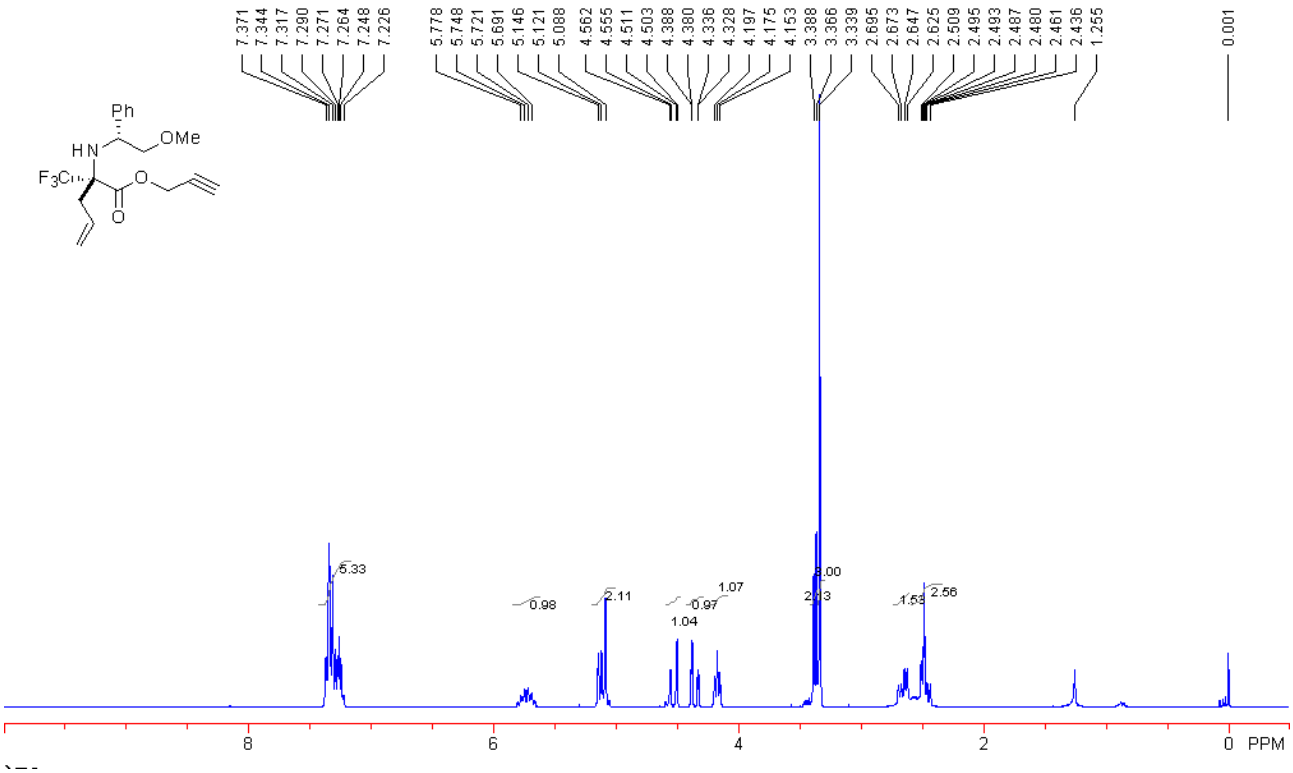
(*R*)-Allyl 2-((*R*)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3c).

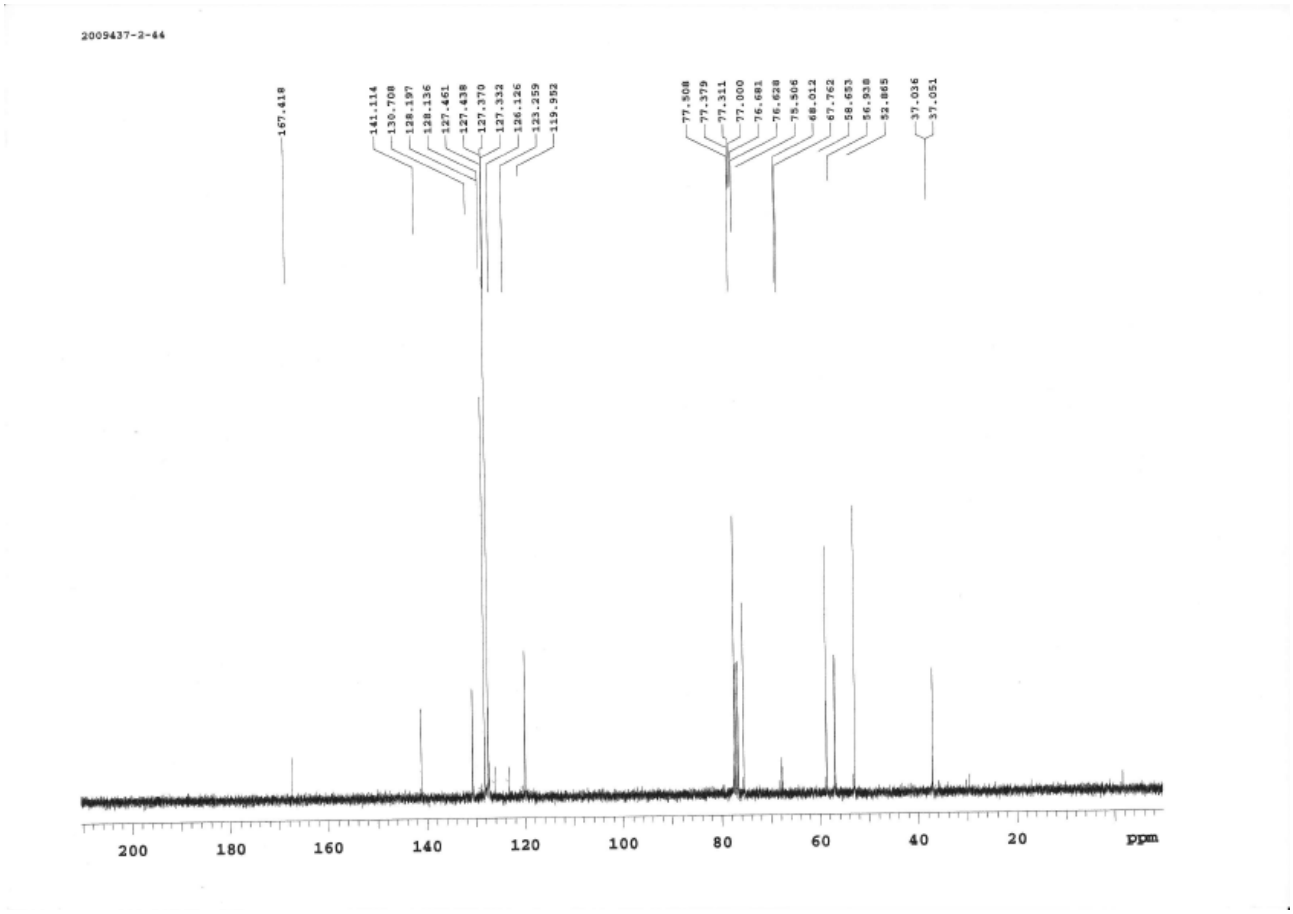


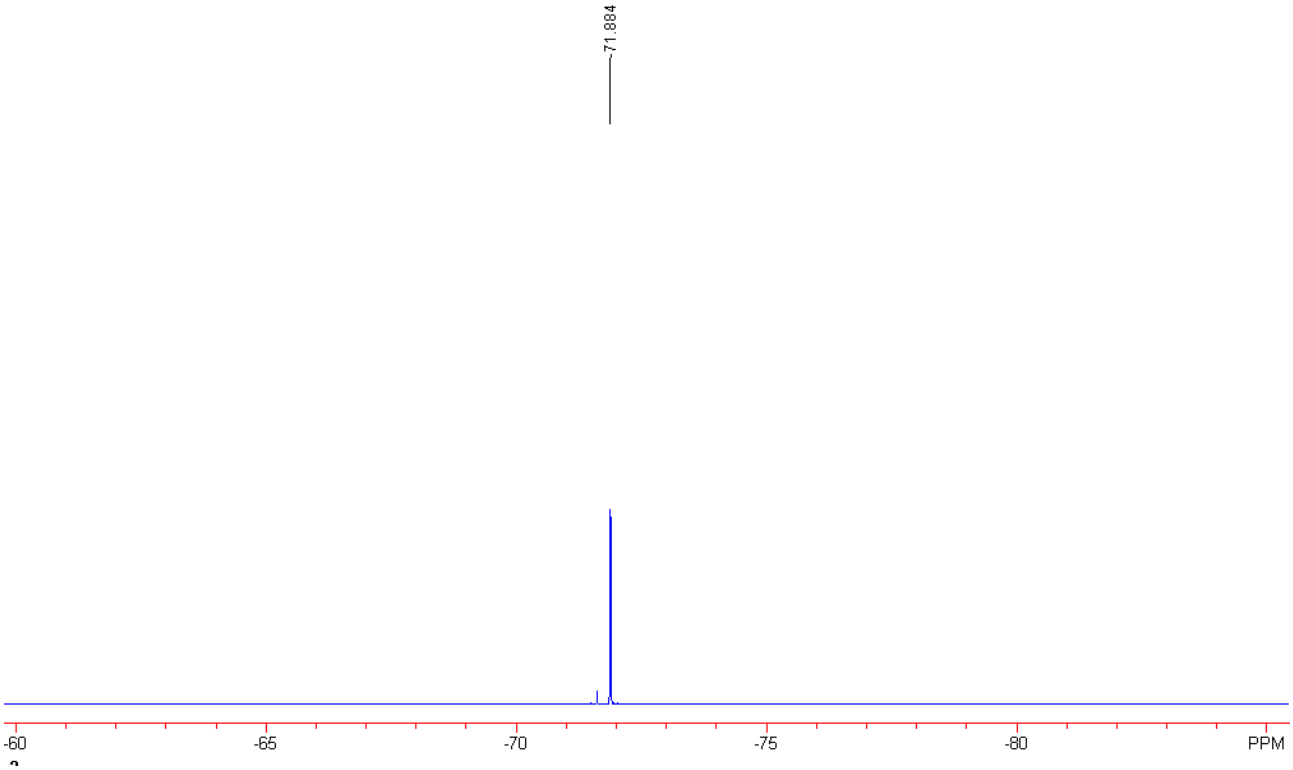




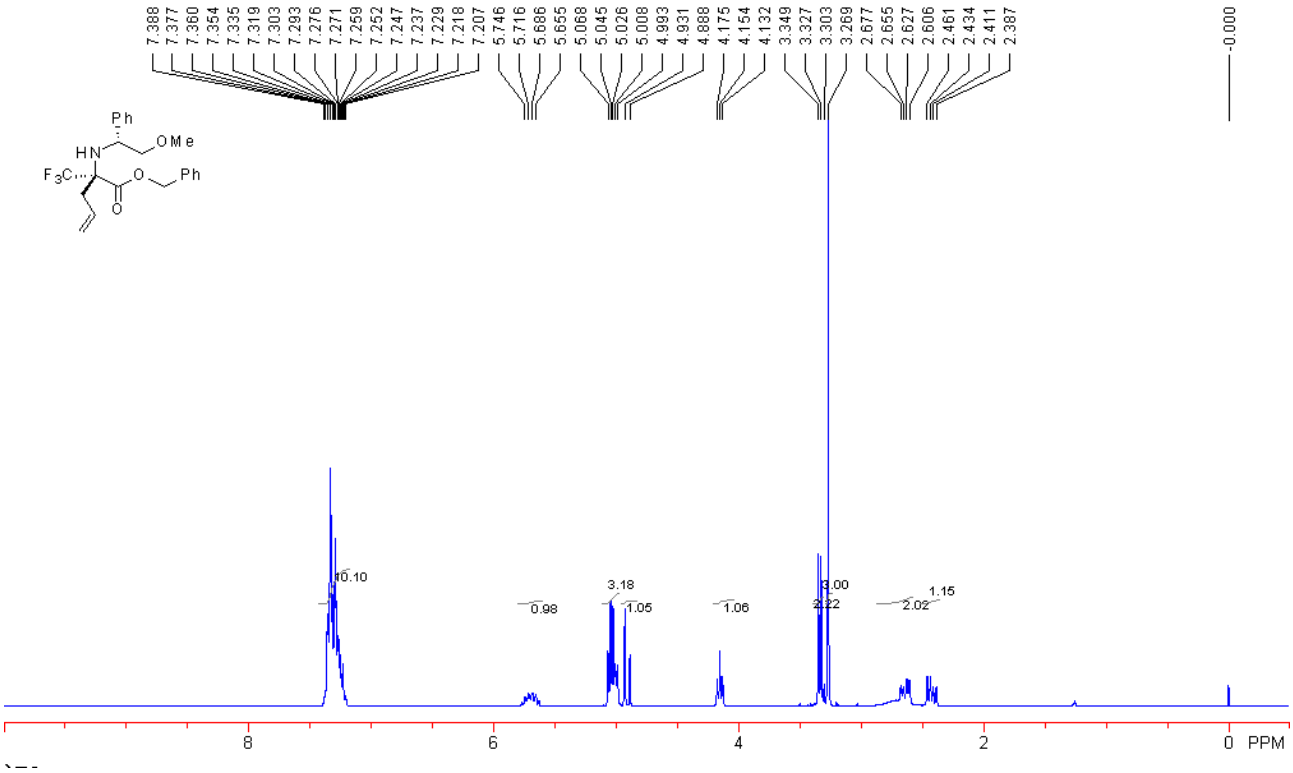
***(R)*-Prop-2-ynyl 2-((*R*)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3d).**

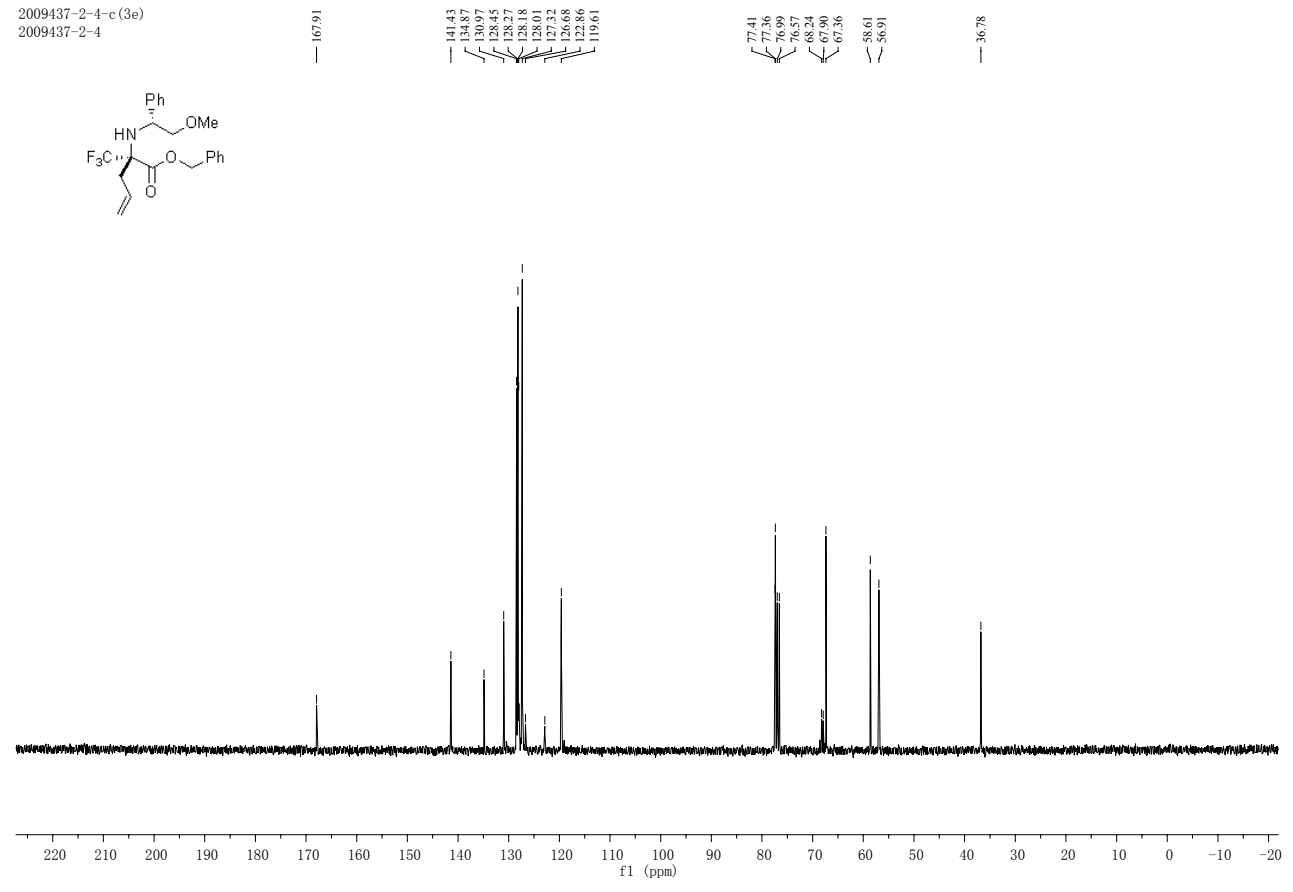


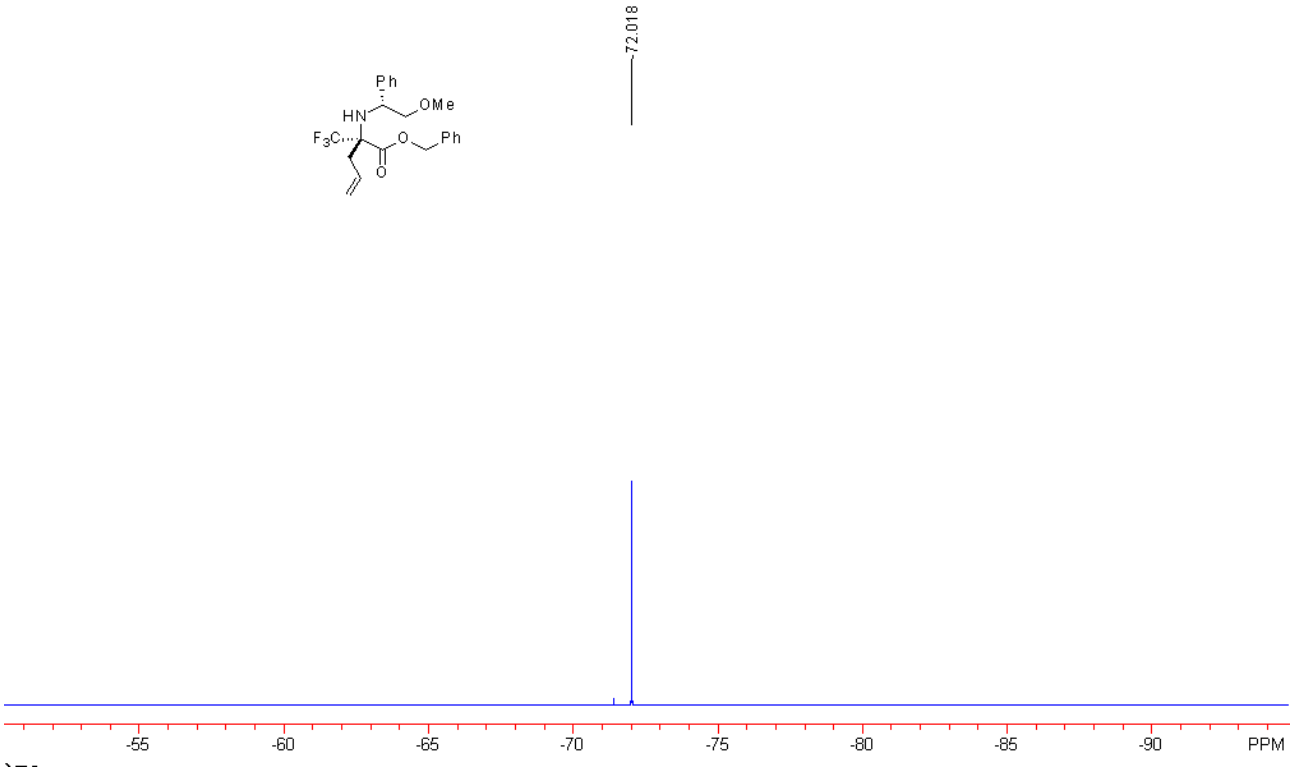

2009437-2-44
167.418
141.114
130.708
128.197
128.136
127.461
127.438
127.370
127.332
126.126
123.259
119.952
77.508
77.379
77.311
77.000
76.681
76.628
75.506
68.012
67.762
58.693
56.938
52.865
37.036
37.051
200
180
160
140
120
100
80
60
40
20
ppm


-71.884
-60
-65
-70
-75
-80
PPM

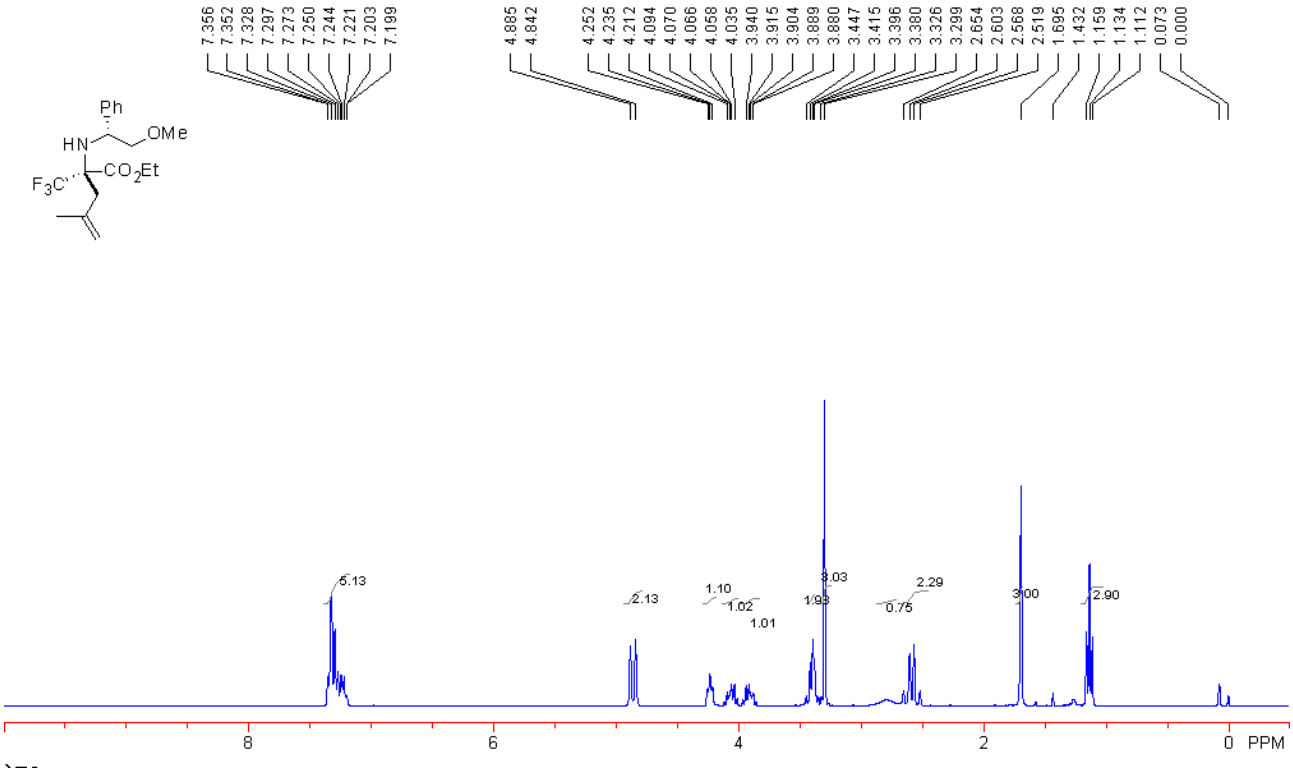
_(R)_-Benzyl 2-((_R_)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-enoate (3e).

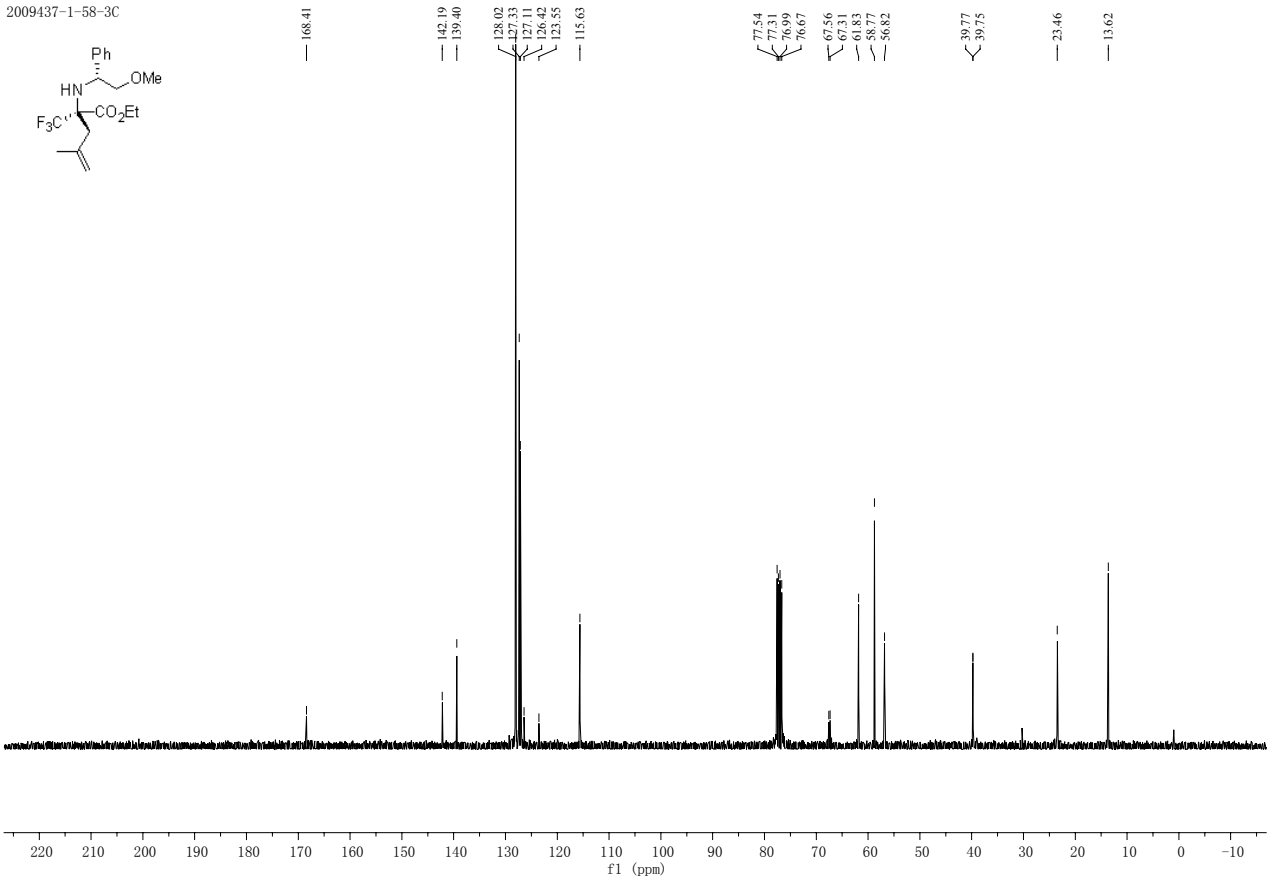


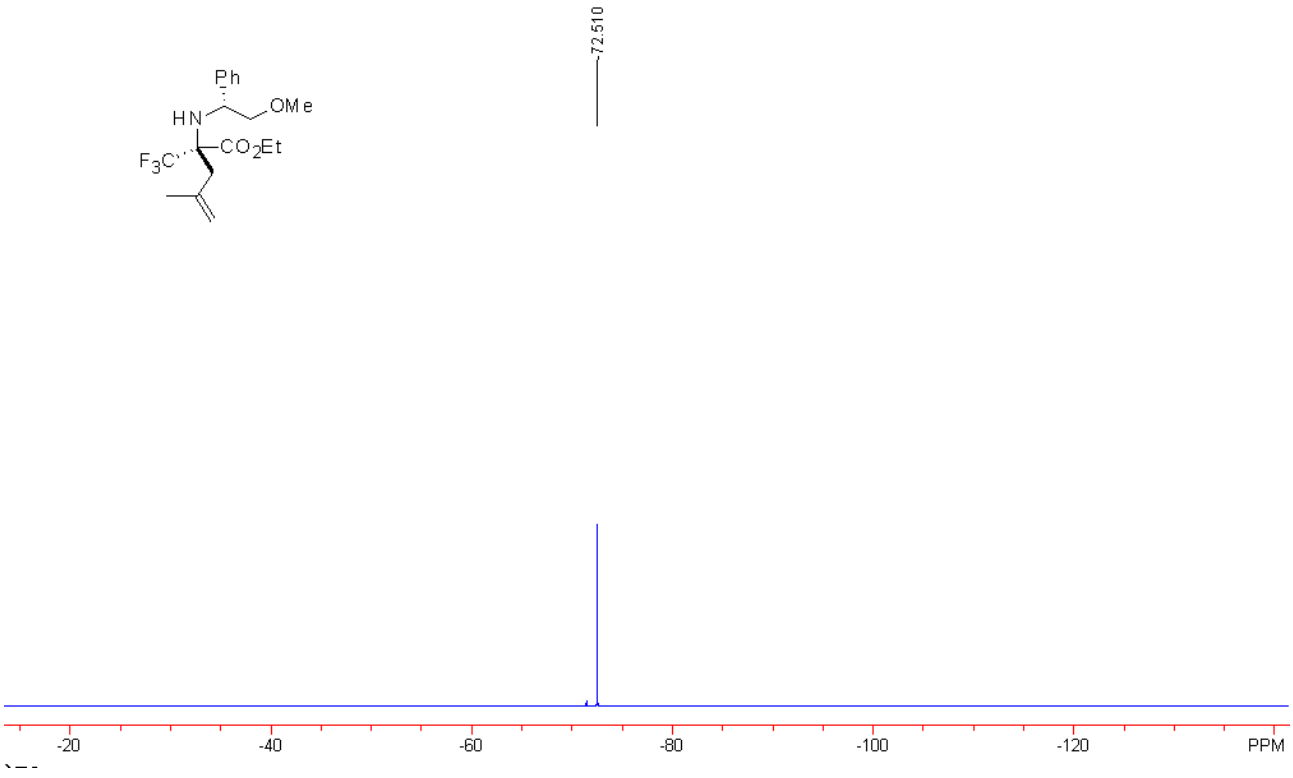




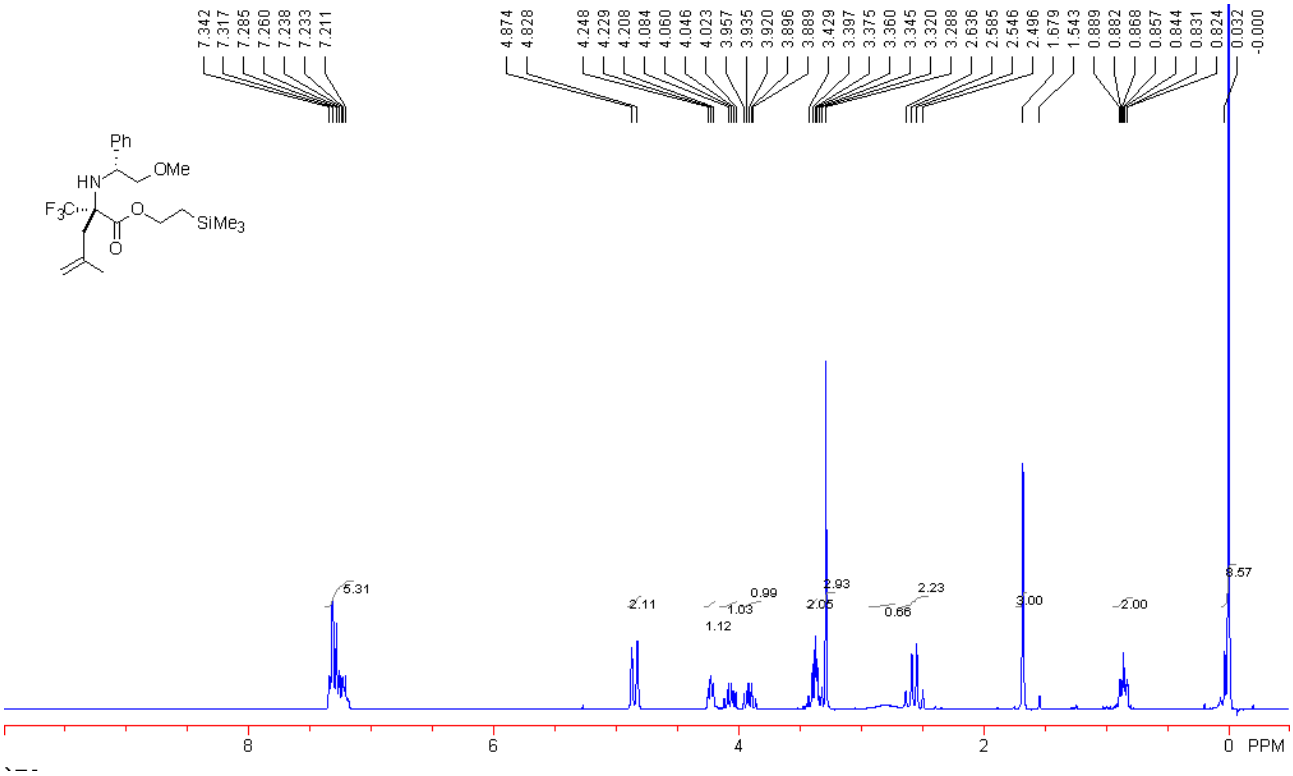
(*R*)-Ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-4-methyl-2-(trifluoromethyl)pent-4-enoate (3f).

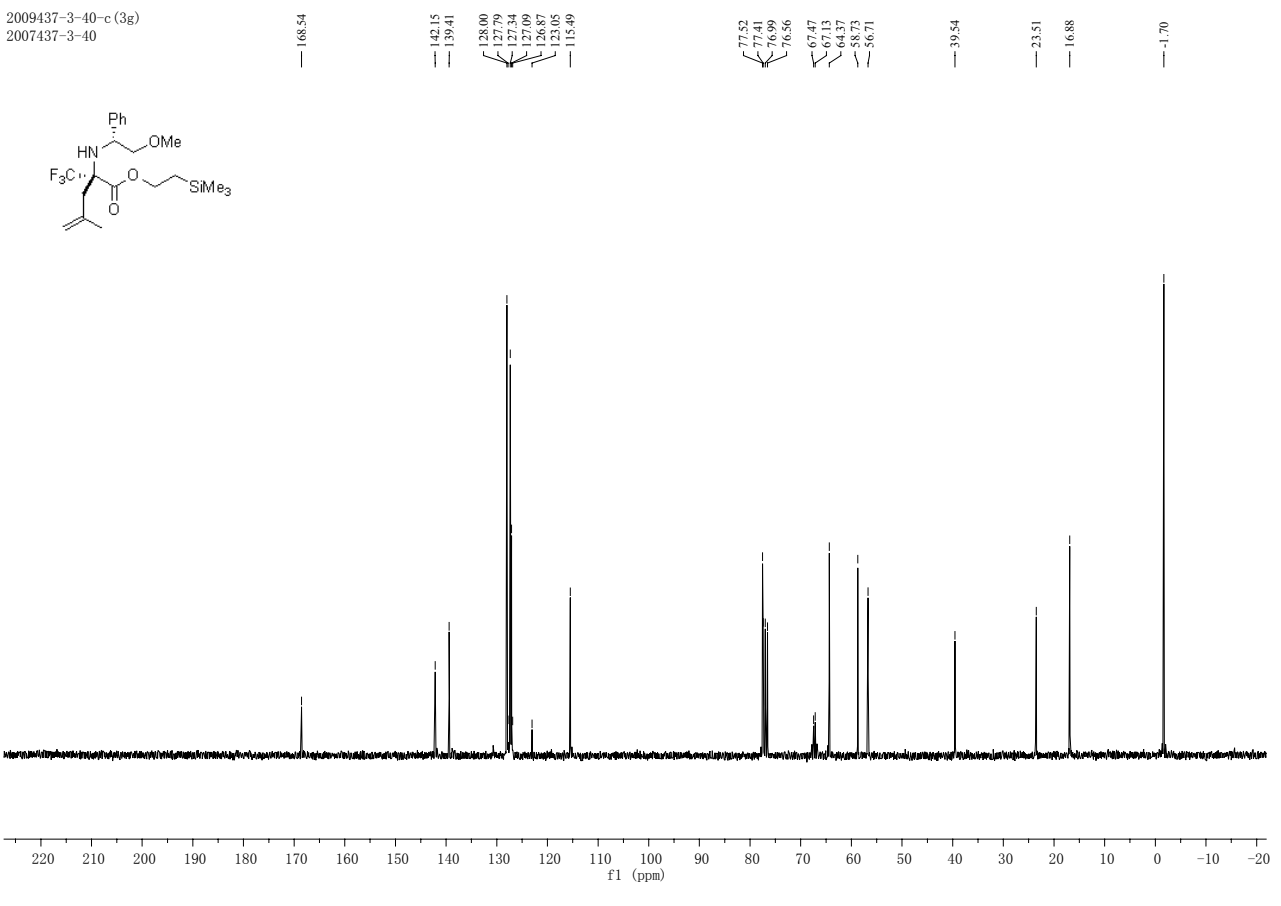


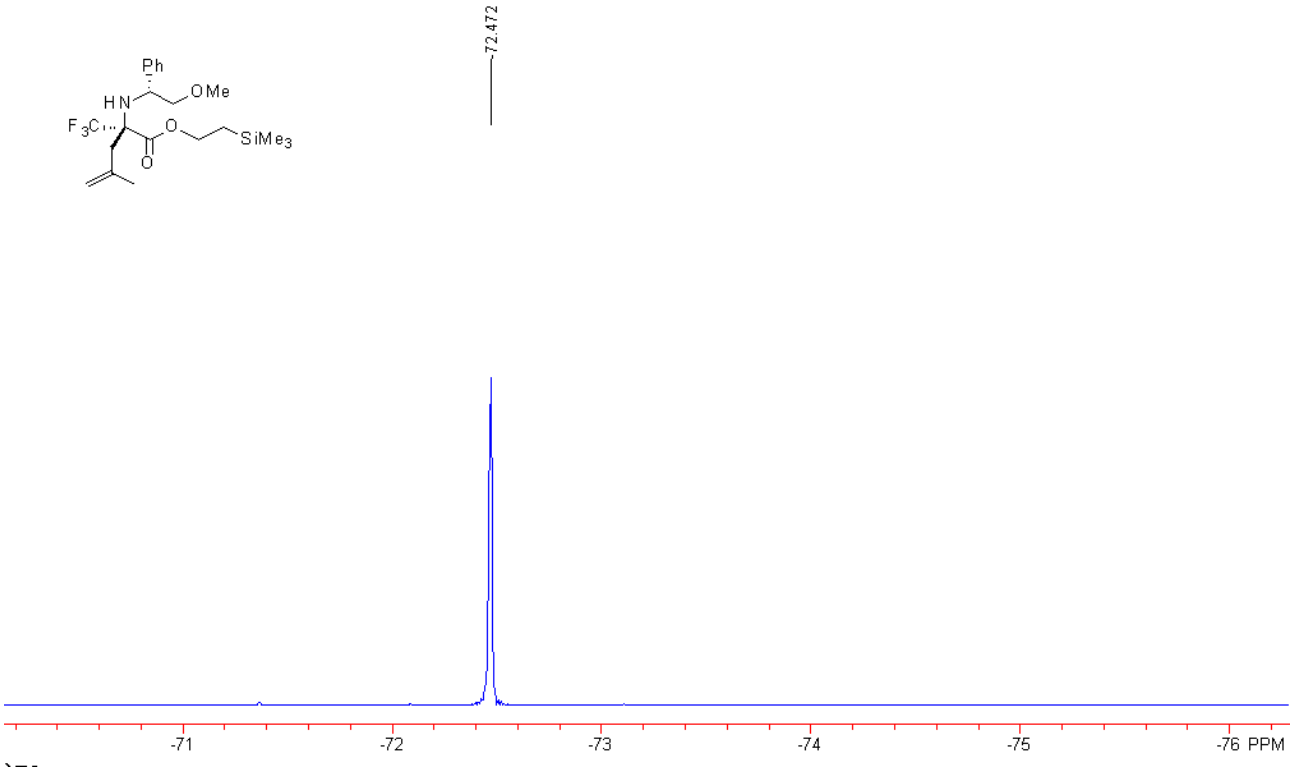

2009437-1-58-3C
Ph
HN
OMe
F3C
CO2Et
168.41
142.19
139.40
128.02
127.33
127.11
126.42
125.55
115.63
77.54
77.31
76.99
76.67
67.56
67.31
61.83
58.77
56.82
39.77
39.75
23.46
13.62
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
HN
OMe
F3C
CO2Et
72.510
-20 -40 -60 -80 -100 -120 PPM

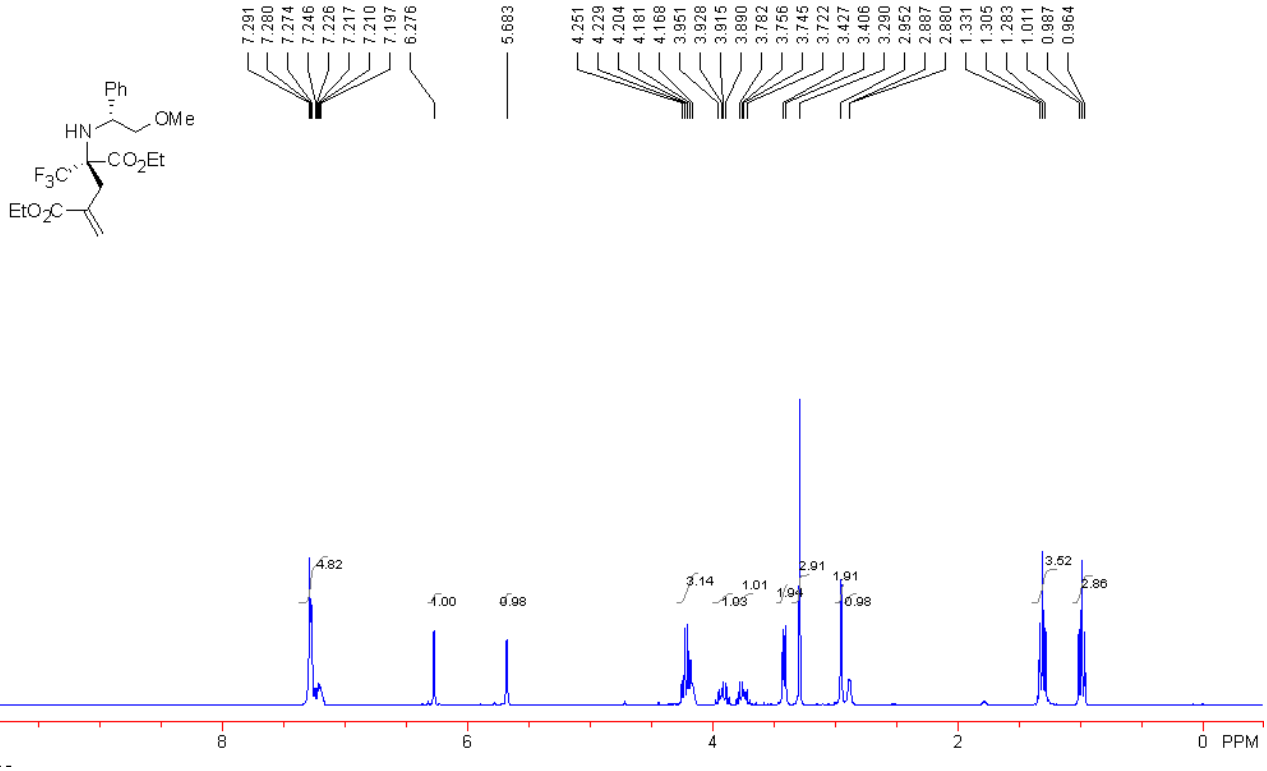
(*R*)-2-(Trimethylsilyl)ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-4-methyl-2-(trifluoromethyl)pent-4-enoate (3g).

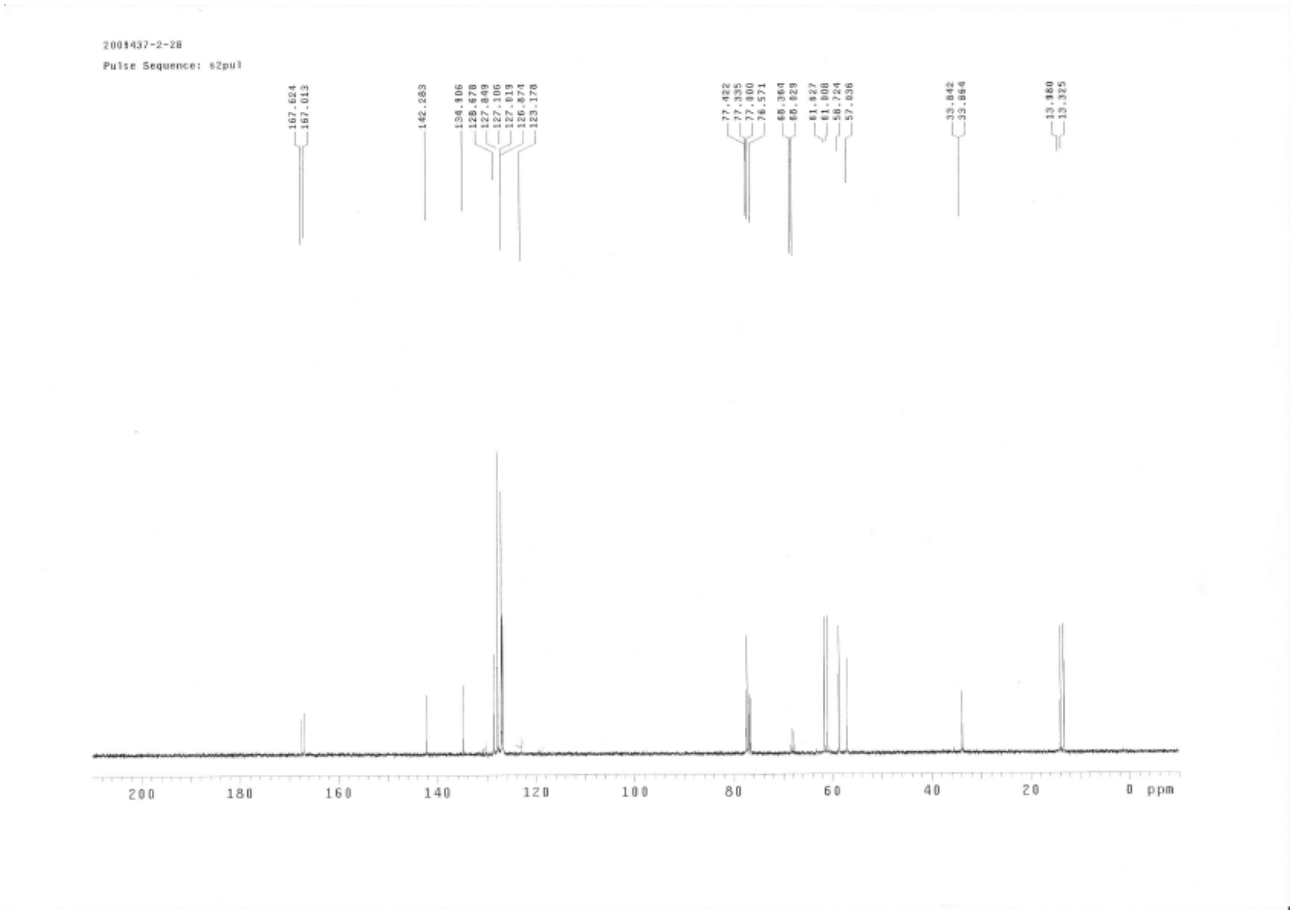


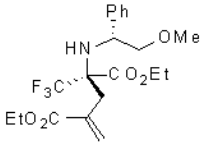




_(R)_-Diethyl 2-((_R_)-2-methoxy-1-phenylethylamino)-4-methylene-2-(trifluoromethyl)pentane Dioate (3h).

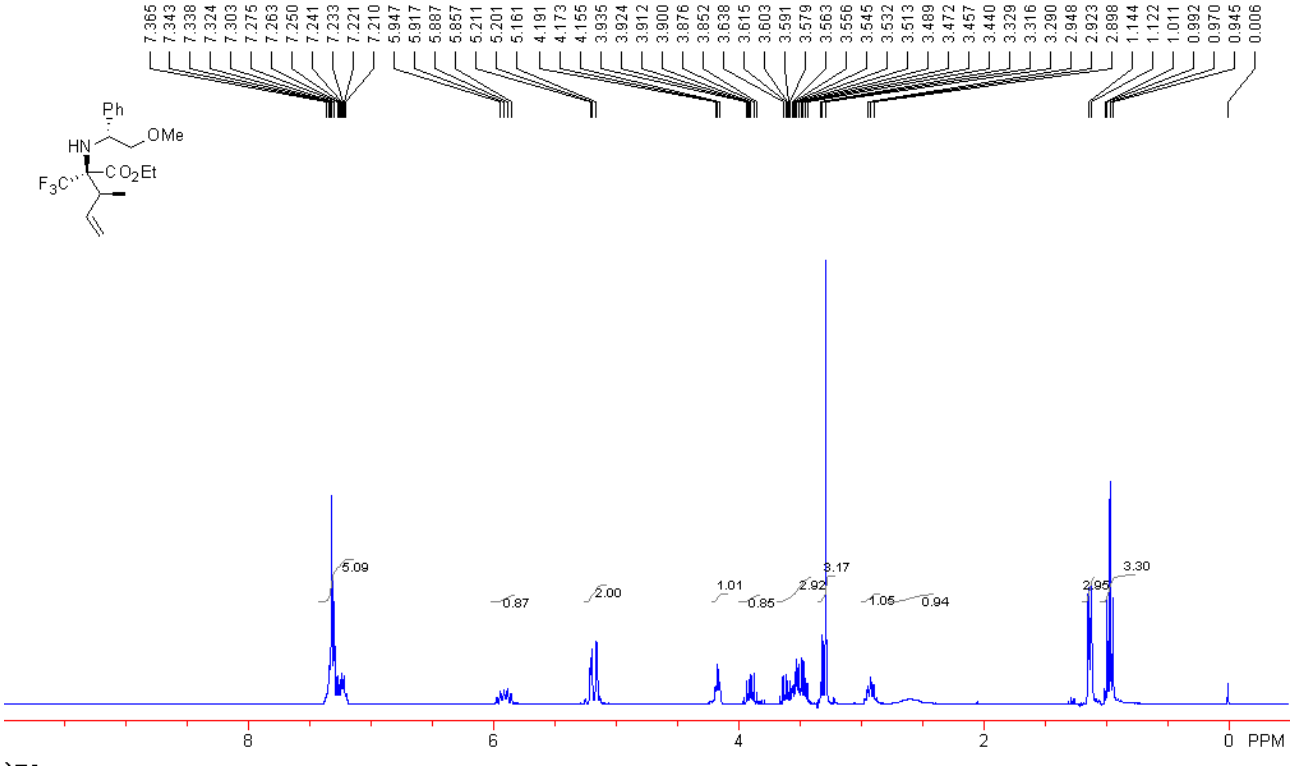


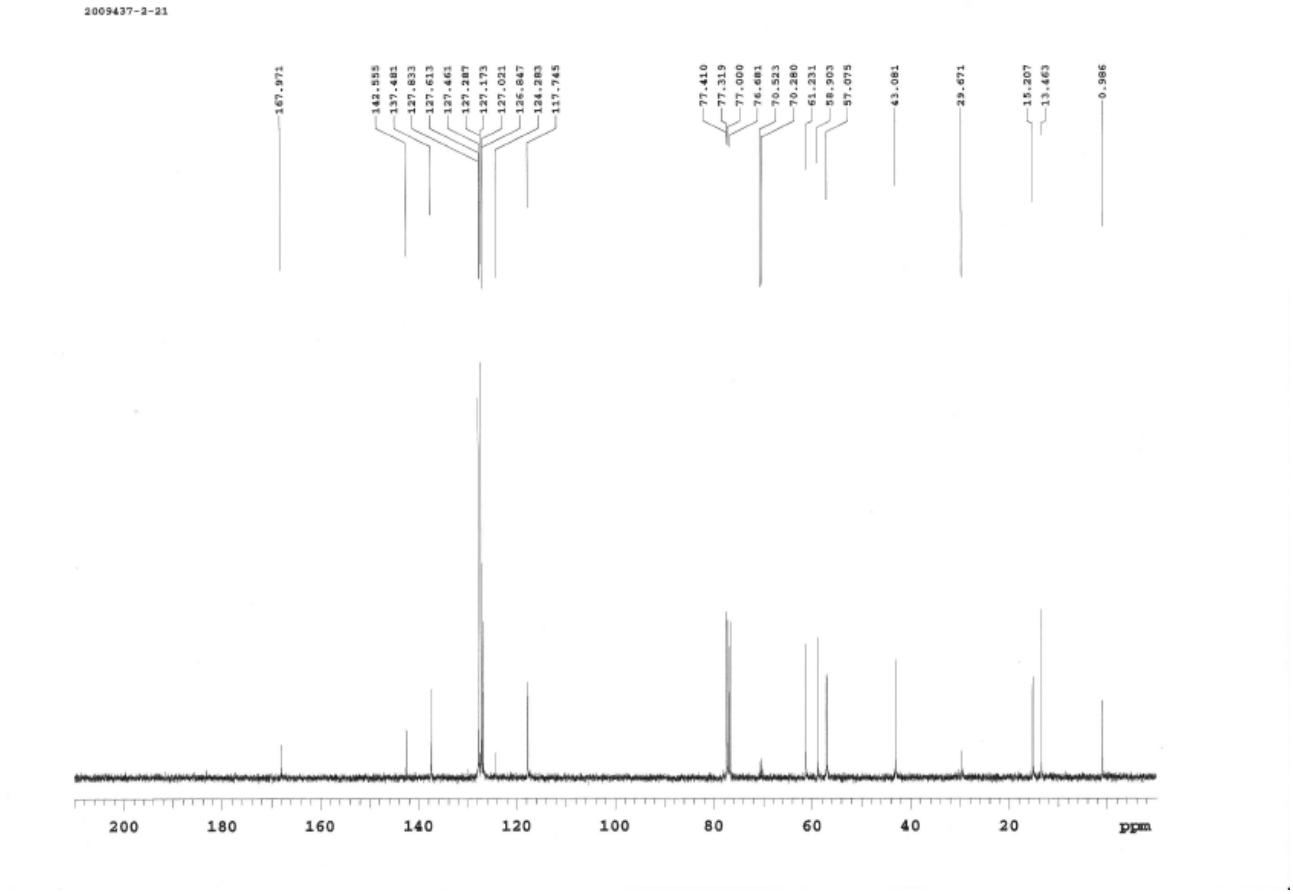

2001437-2-28
Pulse Sequence: s2pul
167.624
167.013
142.283
134.806
128.678
127.449
127.106
127.010
126.474
123.170
77.422
77.335
77.000
76.571
60.860
60.629
61.427
61.008
58.724
57.636
33.842
33.864
13.480
13.325
200
180
160
140
120
100
80
60
40
20
0 ppm

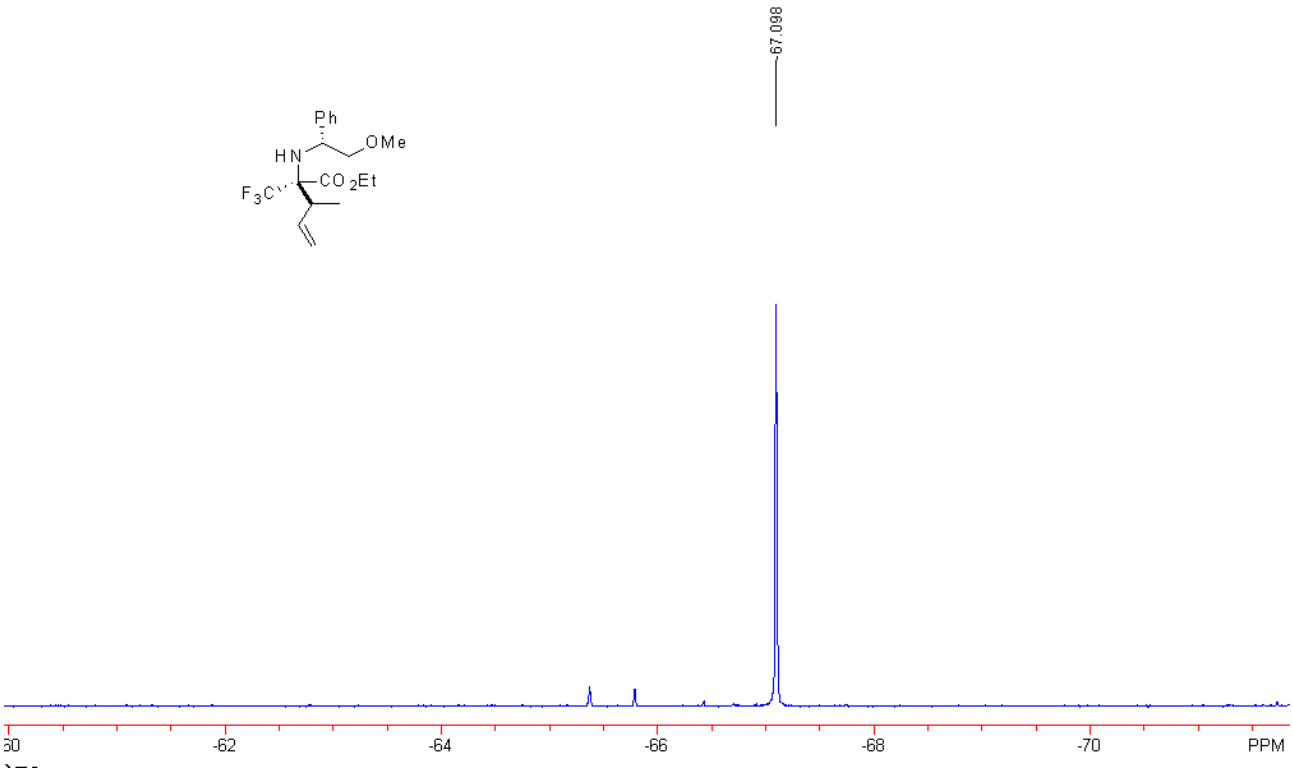

Ph
HN
OMe
C O2Et
F3C
EtO2C

-71.933
-64
-66
-68
-70
-72
-74
-76
PPM

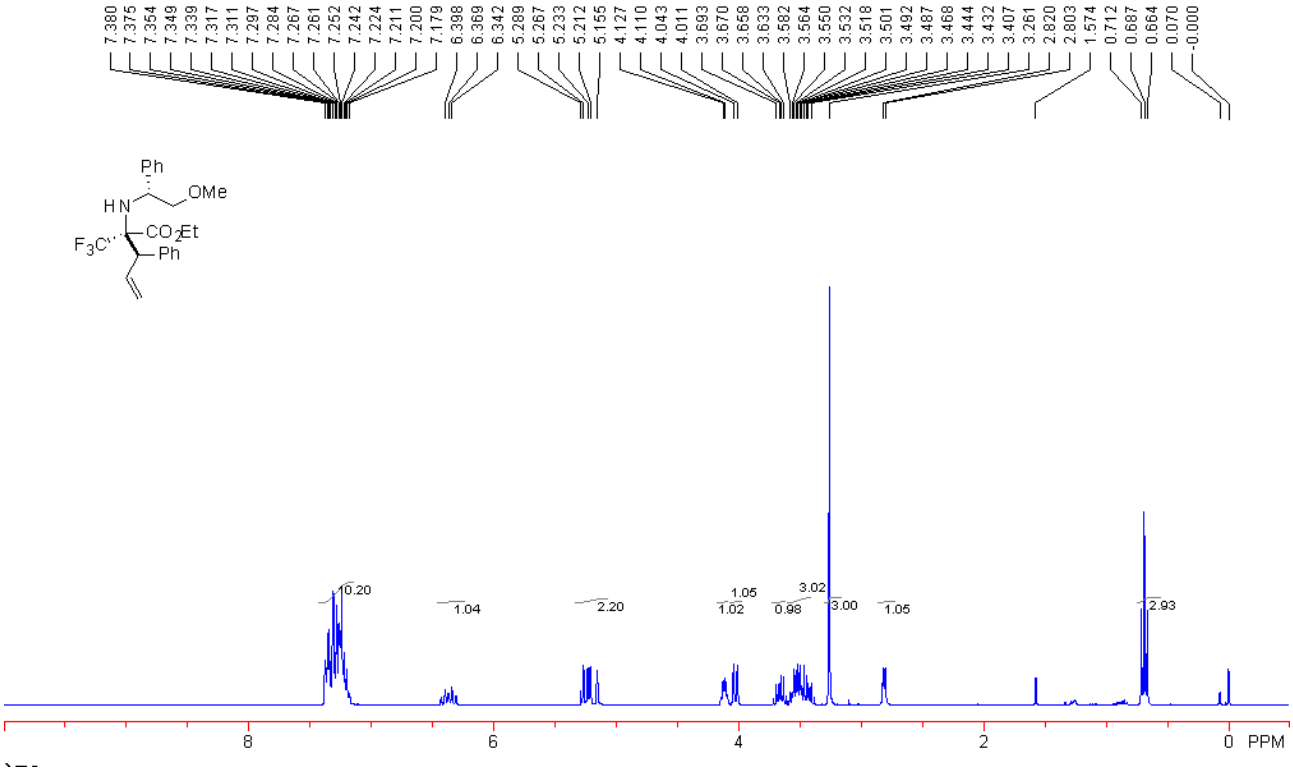
***(2R,3S)*-Ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-3-methyl-2-(trifluoromethyl)pent-4-Enoate (3i).**

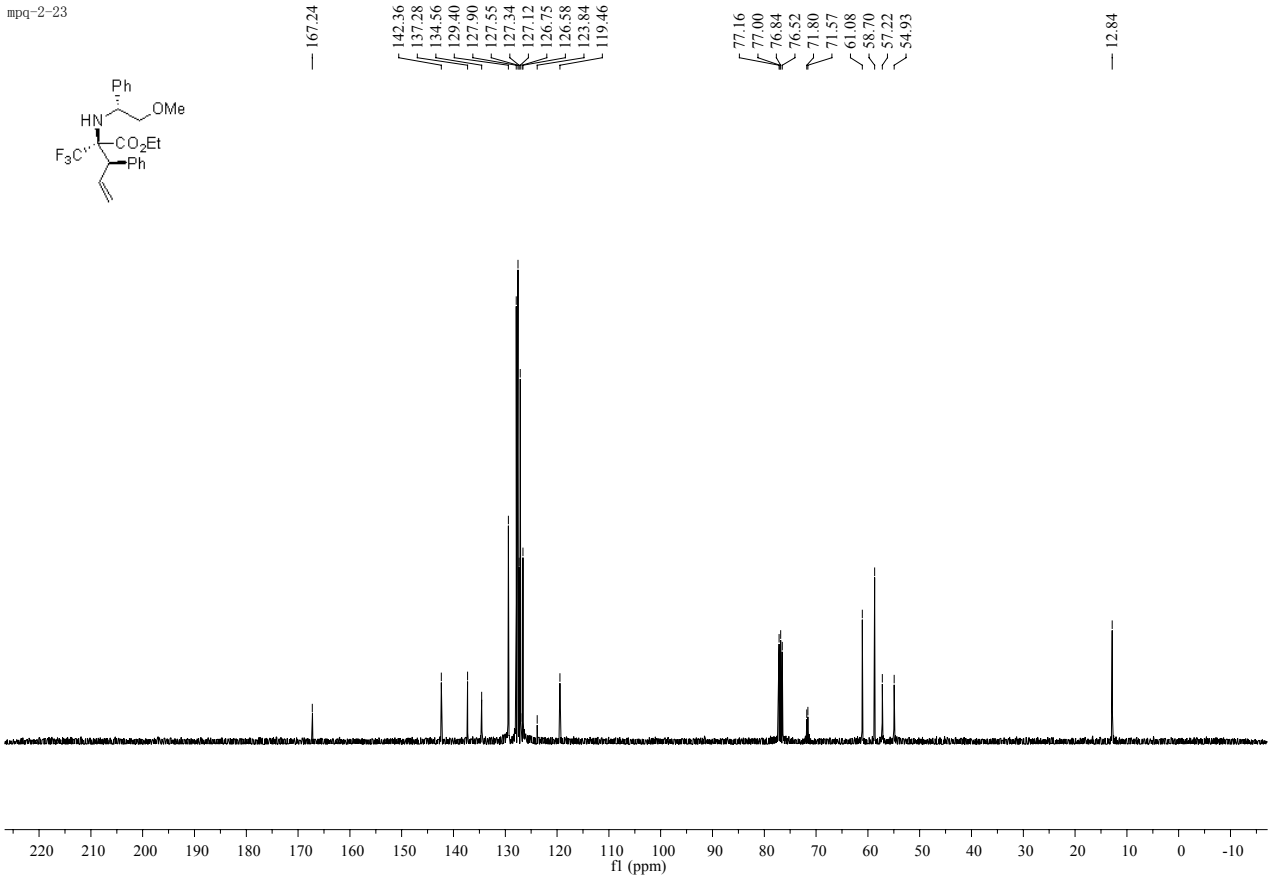


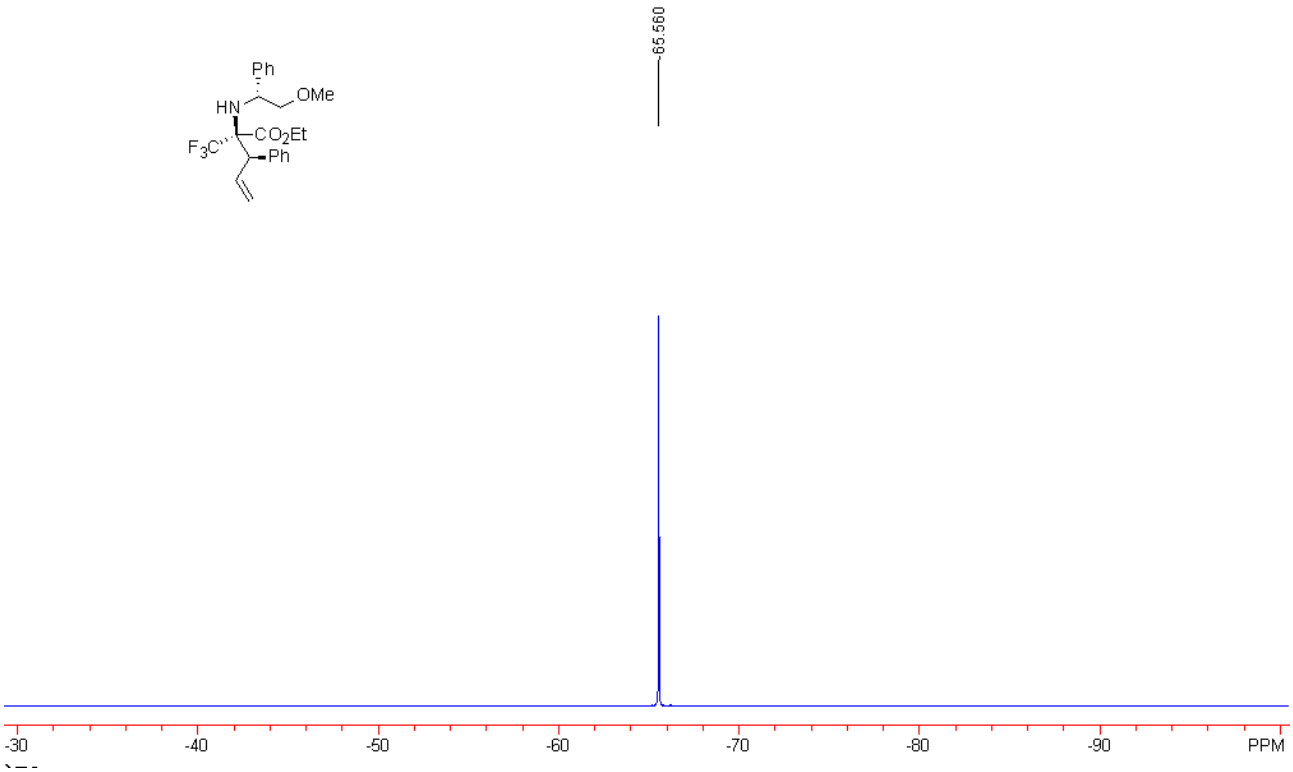




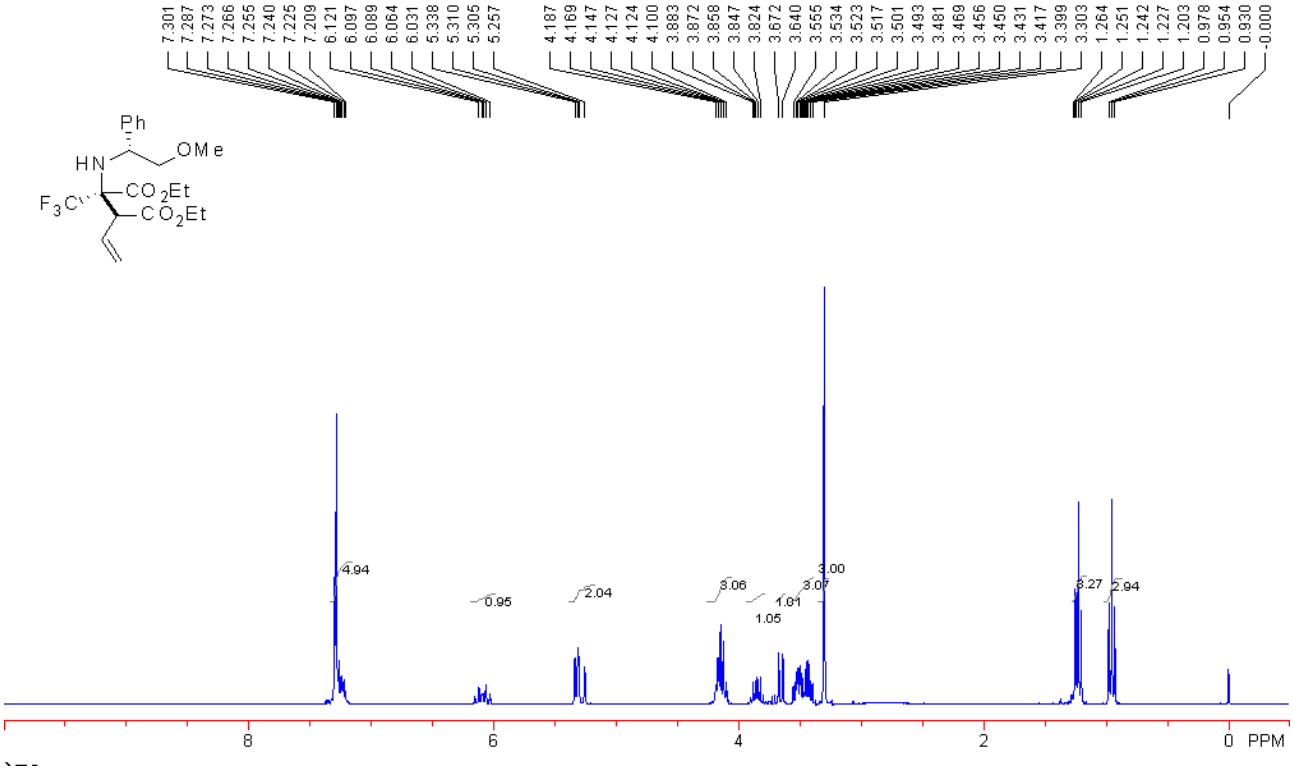
***(2R,3R)*-Ethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-3-phenyl-2-(trifluoromethyl)pent-4-enoate (3j).**

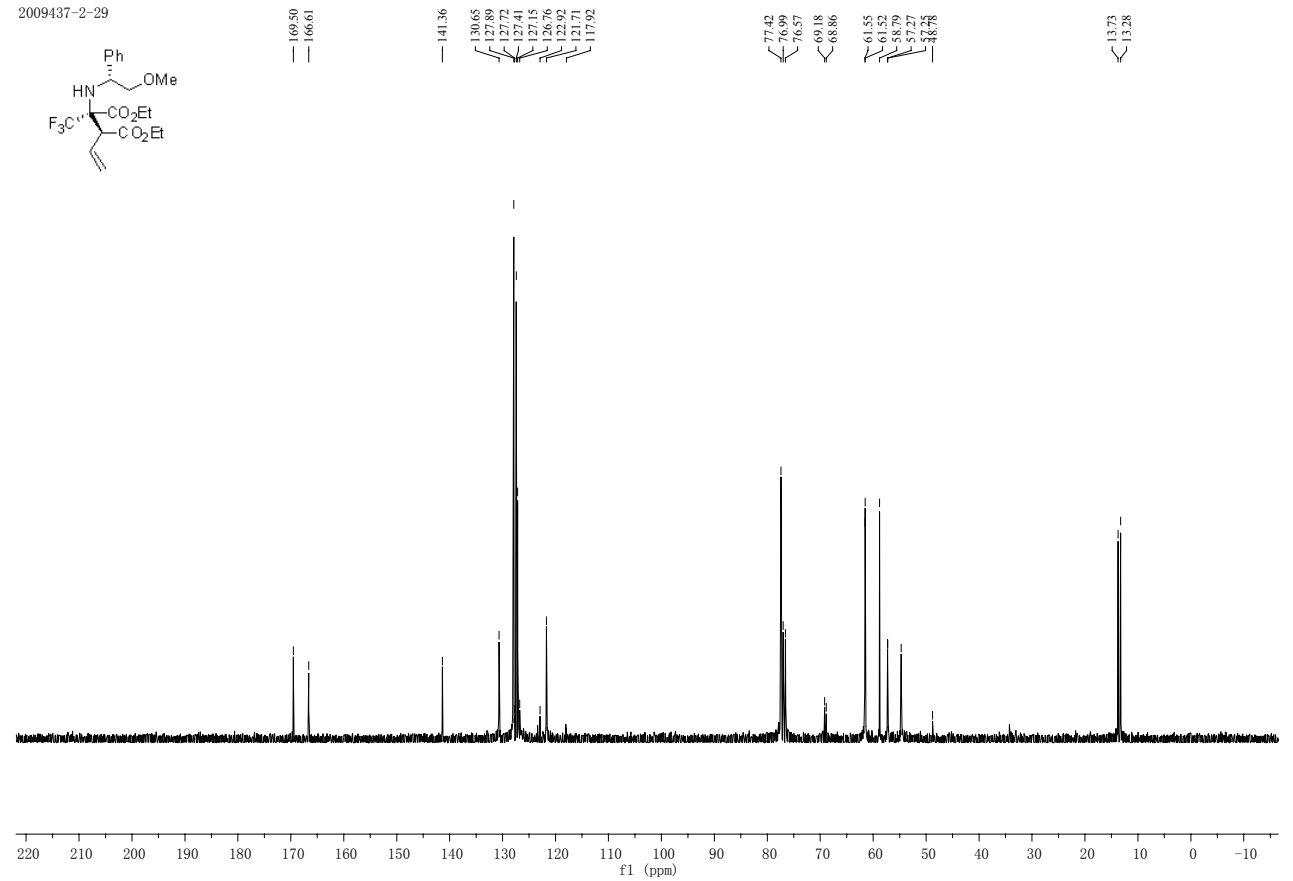


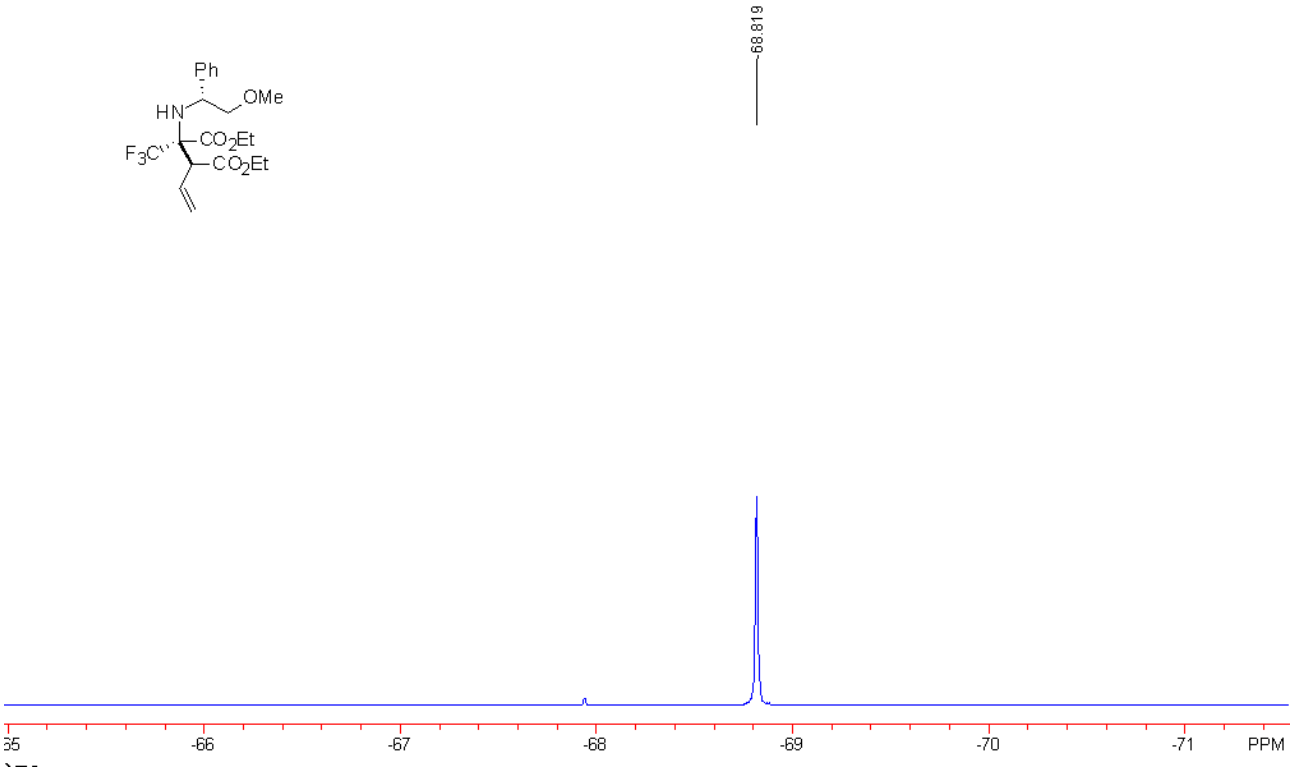

mpq-2-23
167.24
142.36
137.28
134.56
129.40
127.90
127.55
127.34
127.12
126.75
126.58
123.84
119.46
77.16
77.00
76.84
76.52
71.80
71.57
61.08
58.70
57.22
54.93
12.84
Ph
HN
OMe
F3C
CO2Et
Ph
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-65.560
Ph
HN
OMe
F3C
CO2Et
Ph
-30 -40 -50 -60 -70 -80 -90 PPM

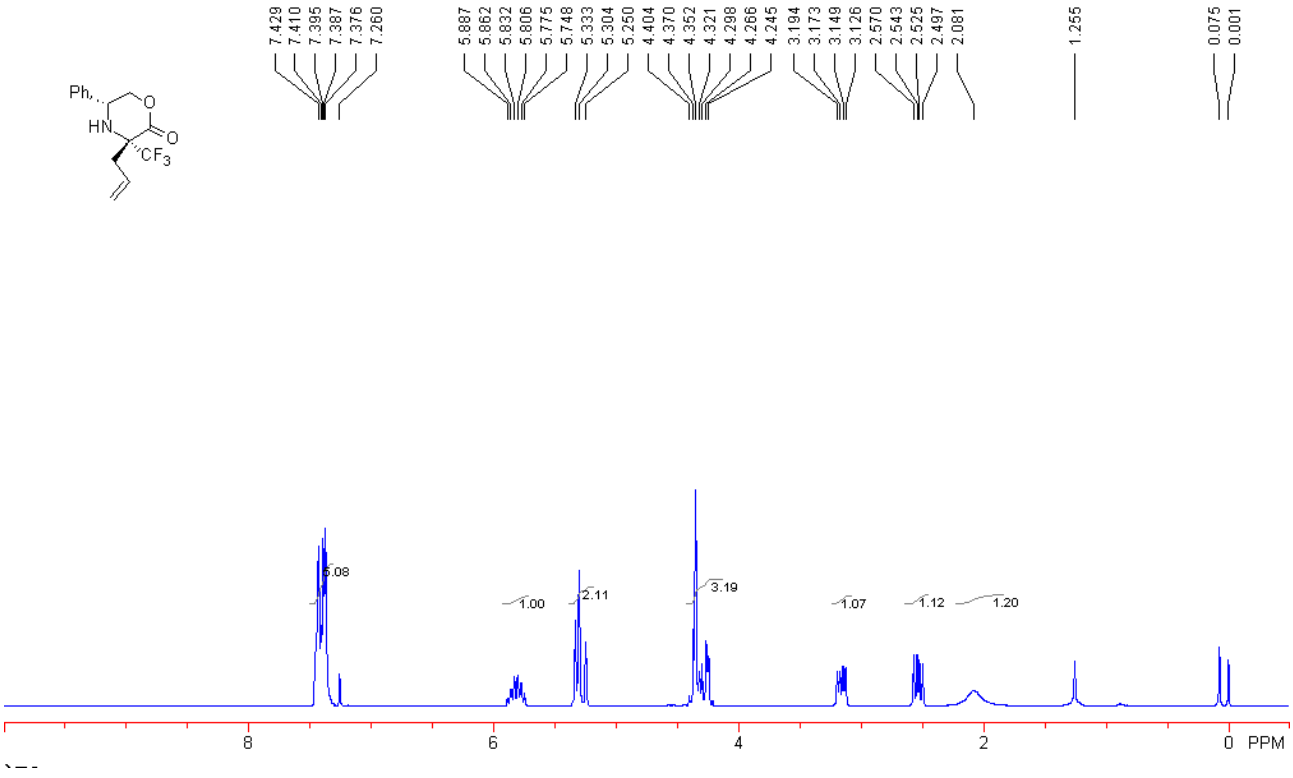
(2*R*,3*S*)-Diethyl 2-((*R*)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)-3-vinylsuccinate (3k).



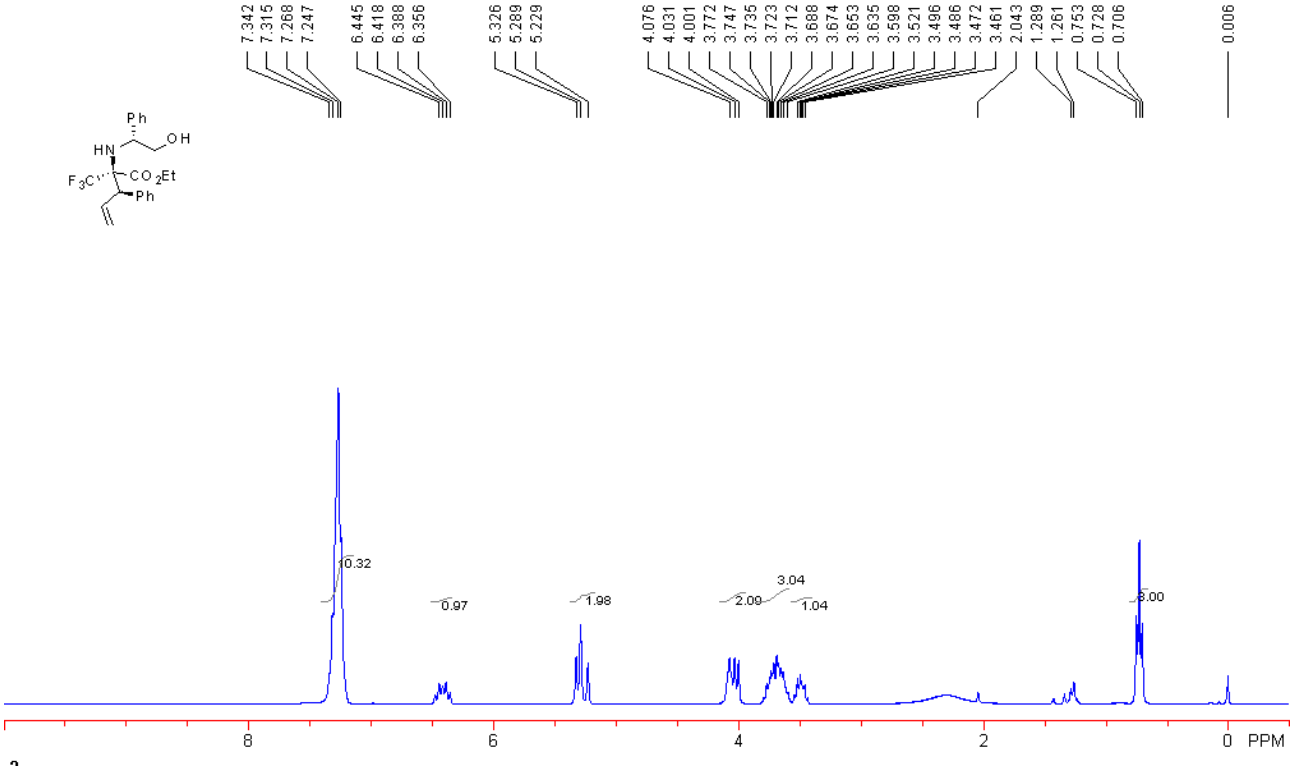


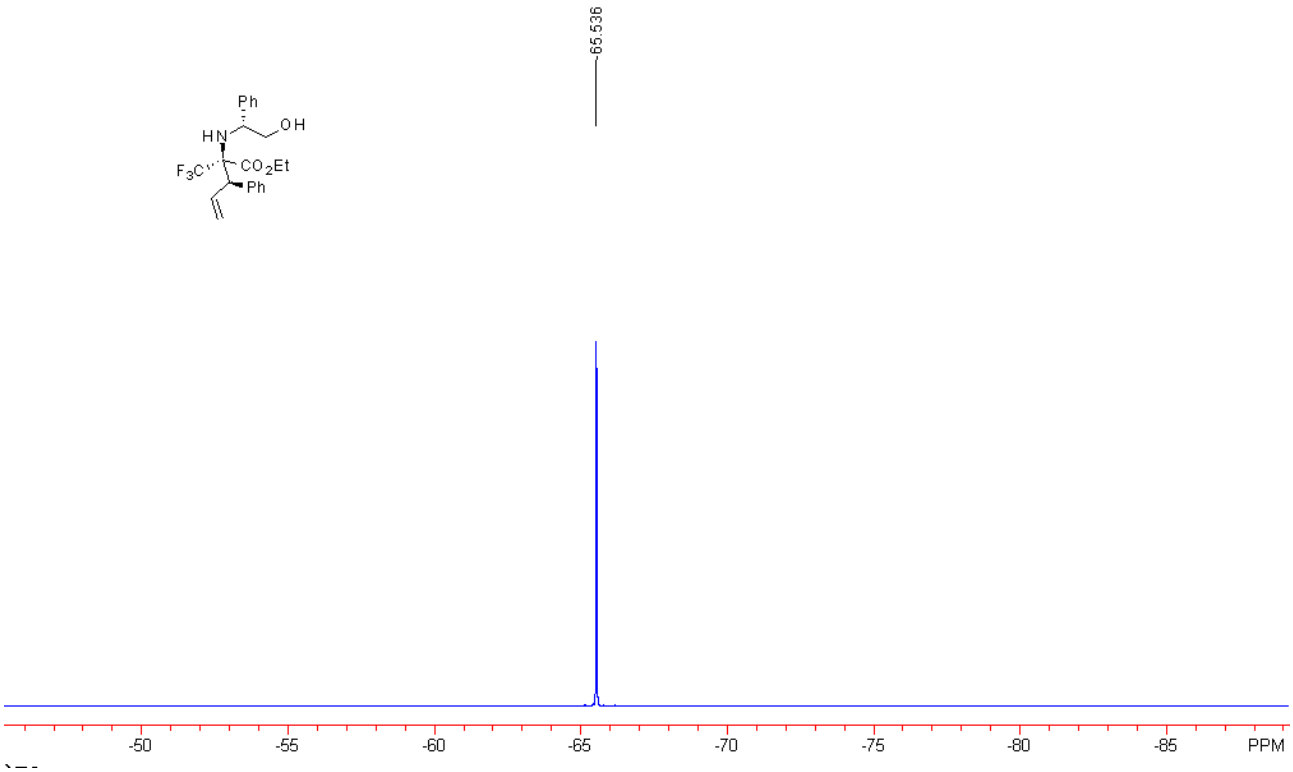


(3*R*,5*R*)-3-allyl-5-phenyl-3-(trifluoromethyl)morpholin-2-one (4b).

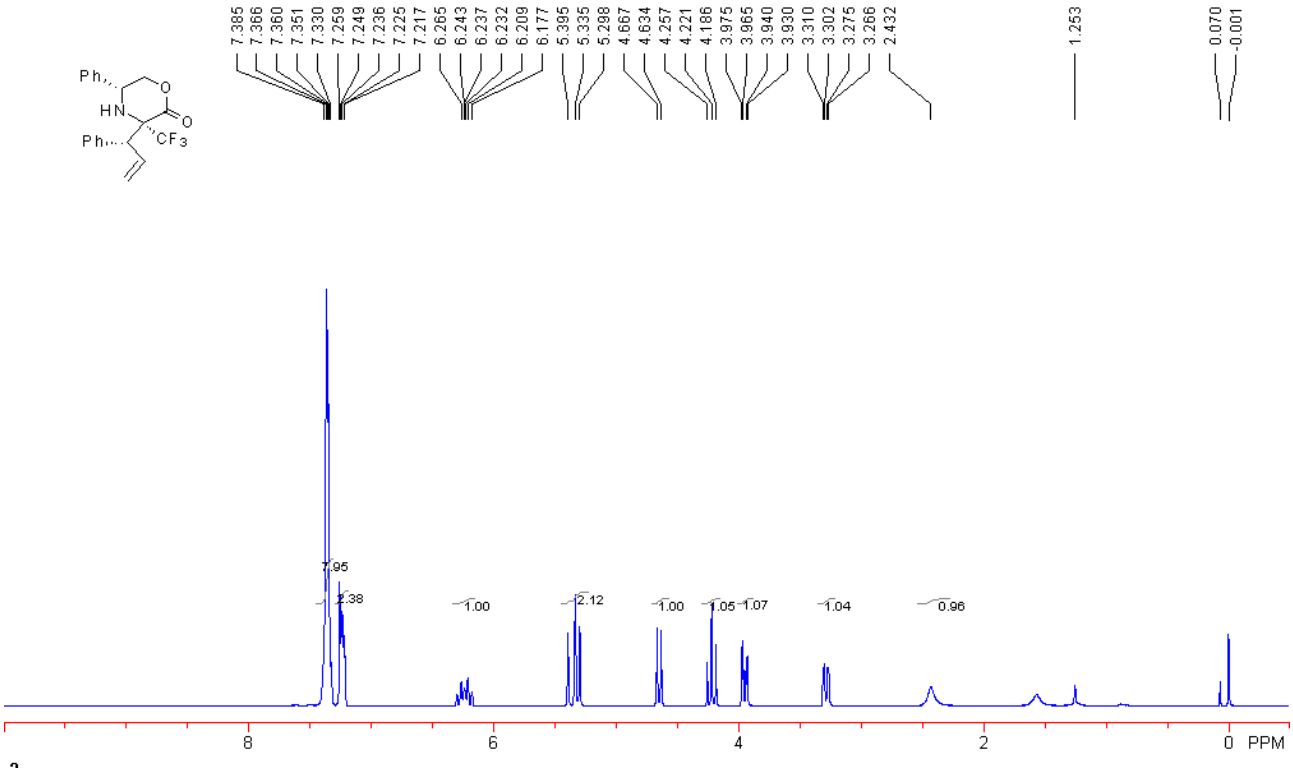


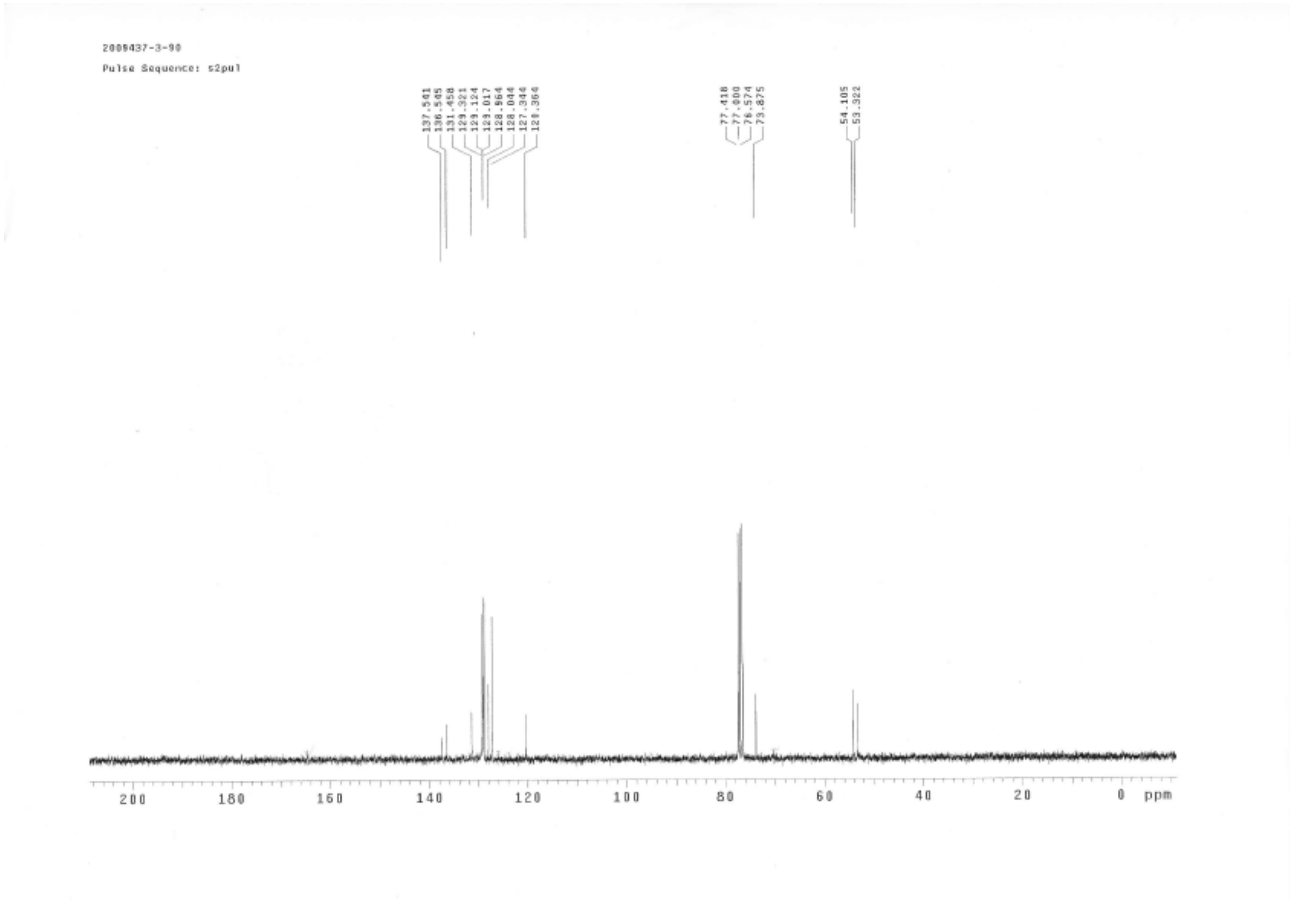
(2R,3R)-ethyl 2-((*R*)-2-hydroxy-1-phenylethylamino)-3-phenyl-2-(trifluoromethyl)pent-4-enoate (3j′)

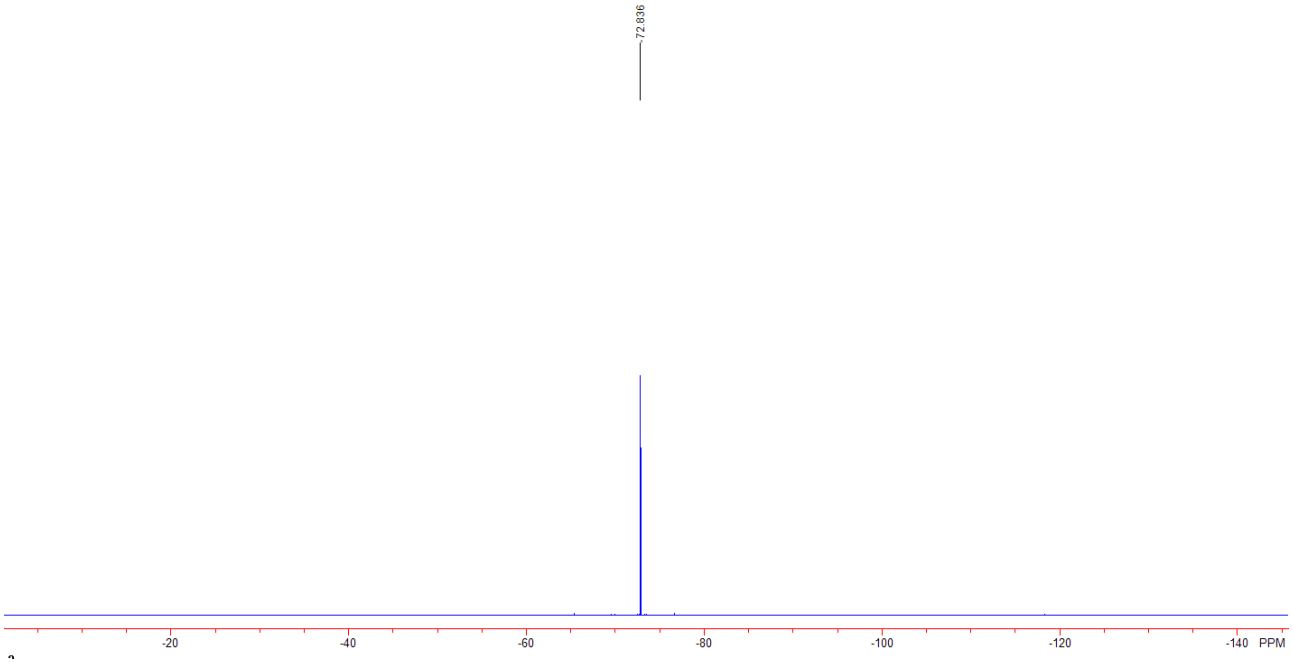




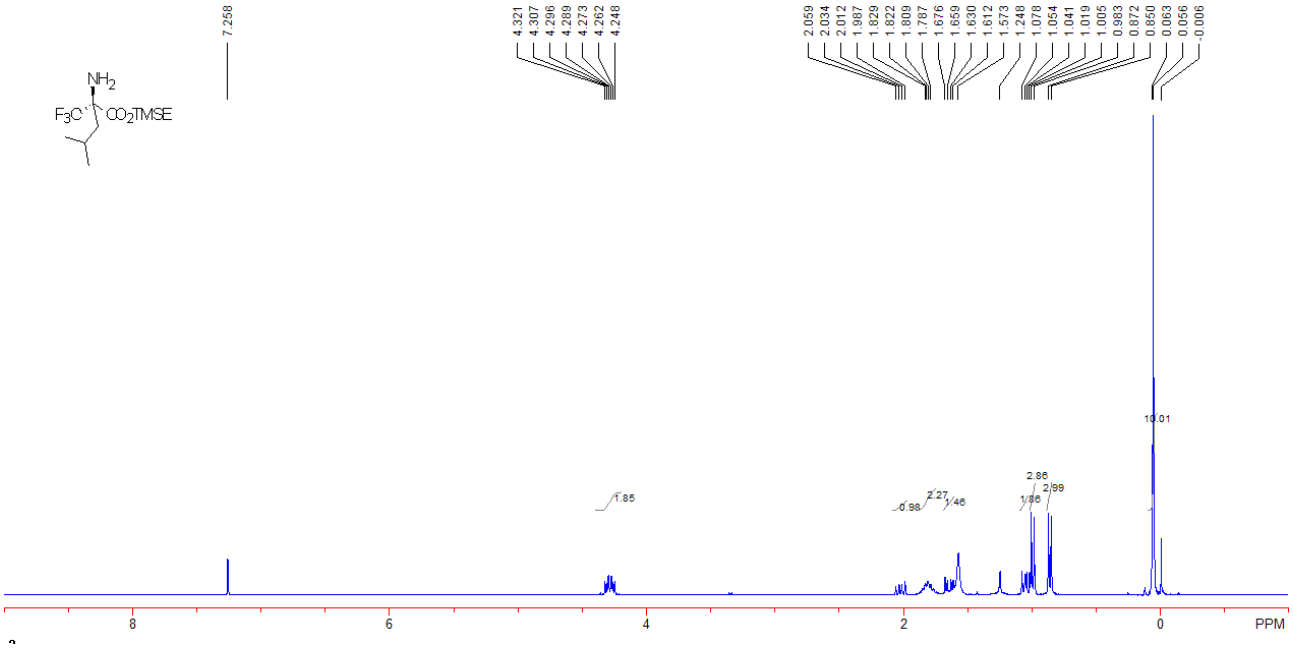
***(3R,5R)*-5-phenyl-3-((*R*)-1-phenylallyl)-3-(trifluoromethyl)morpholin-2-one (4j).**

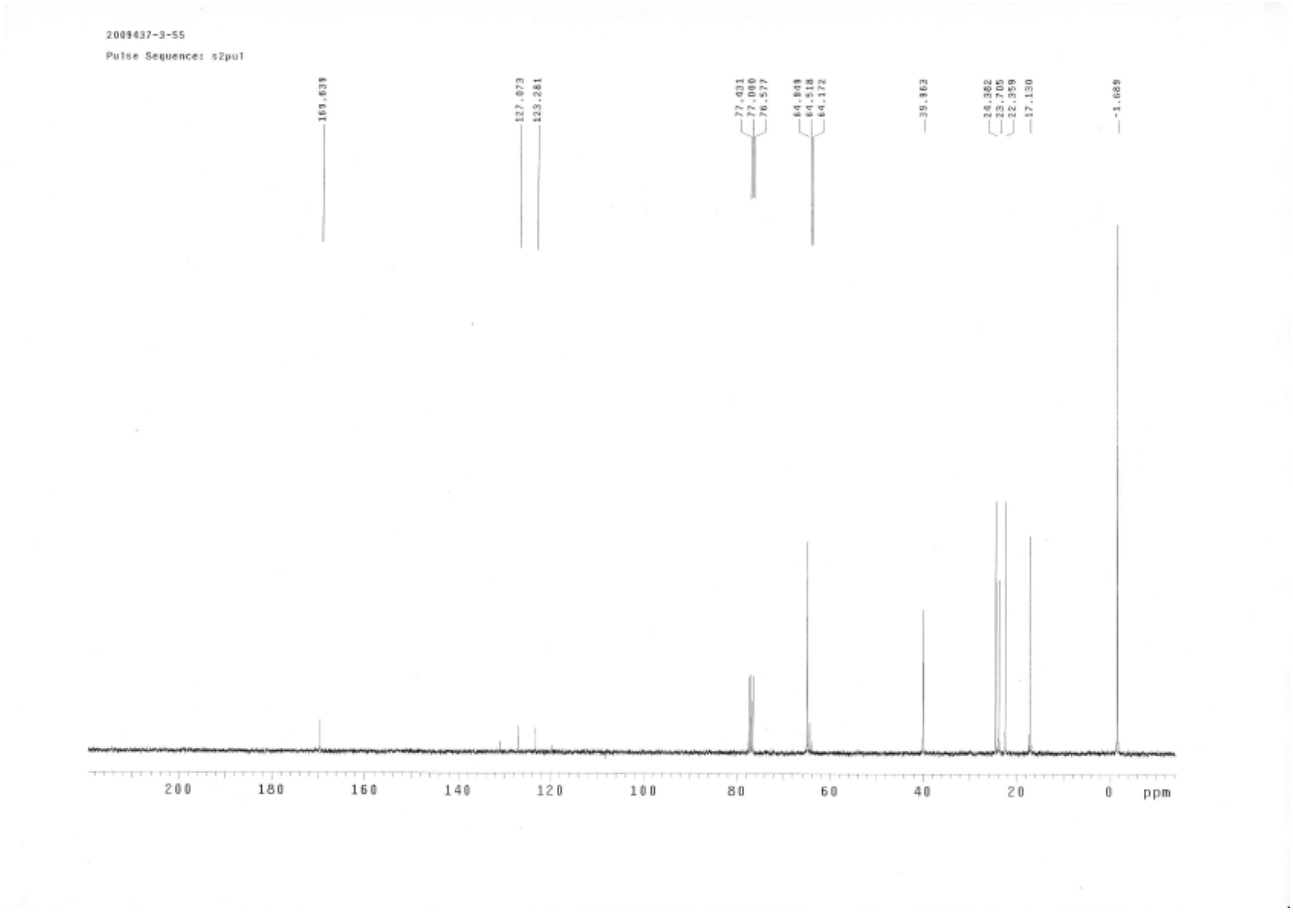


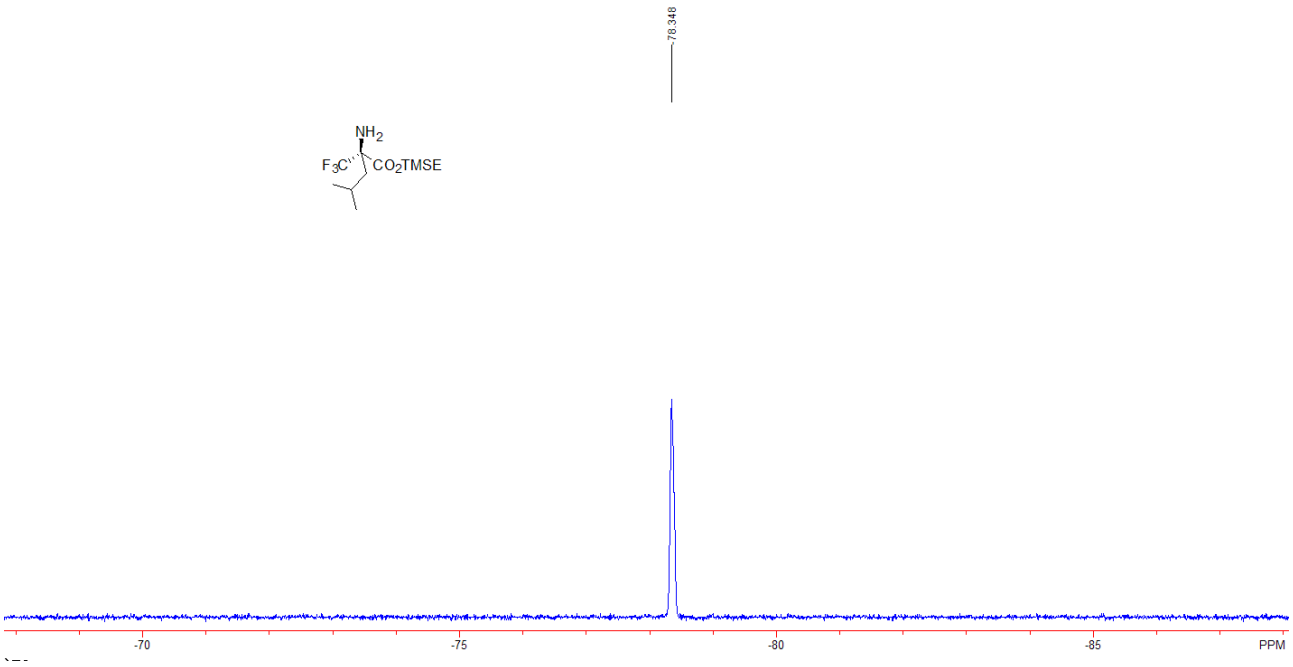



-72.836
-20
-40
-60
-80
-100
-120
-140
PPM

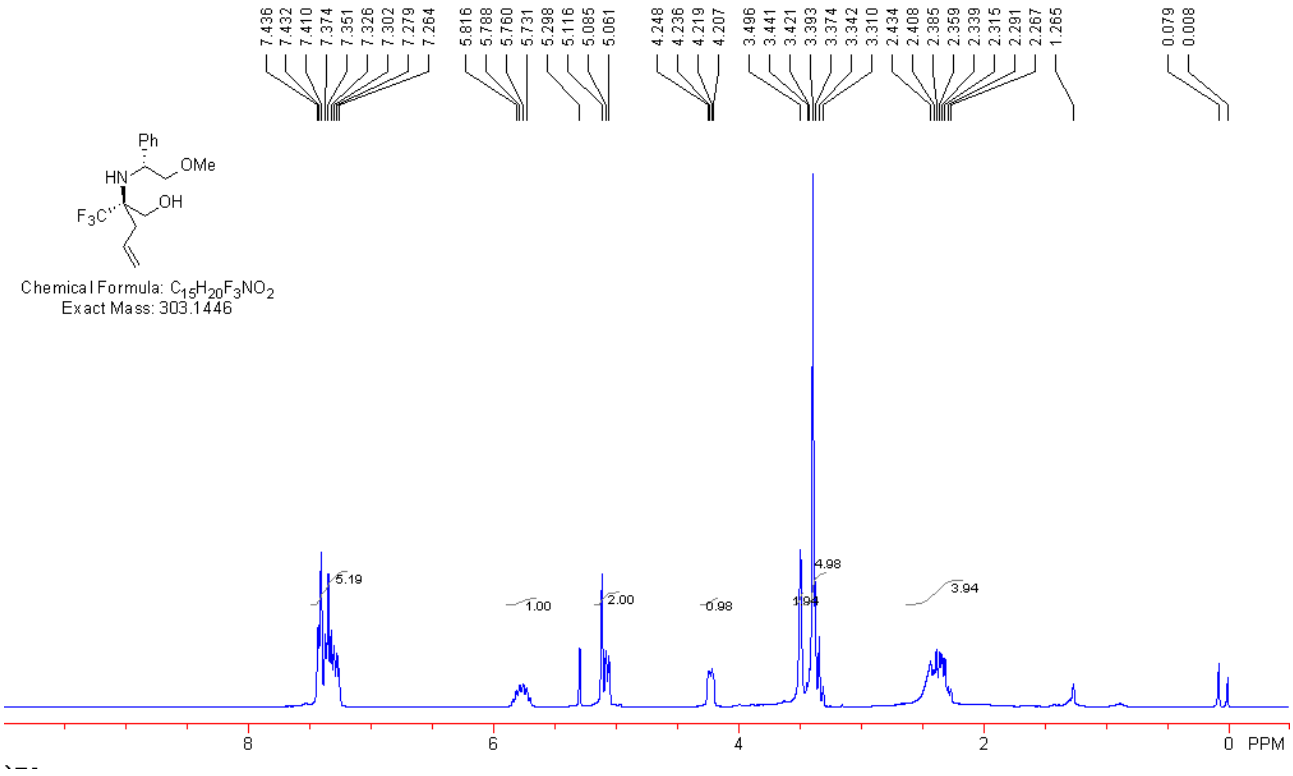
***(R)*-2-(Trimethylsilyl)ethyl 2-amino-4-methyl-2-(trifluoromethyl)pentanoate (5).**

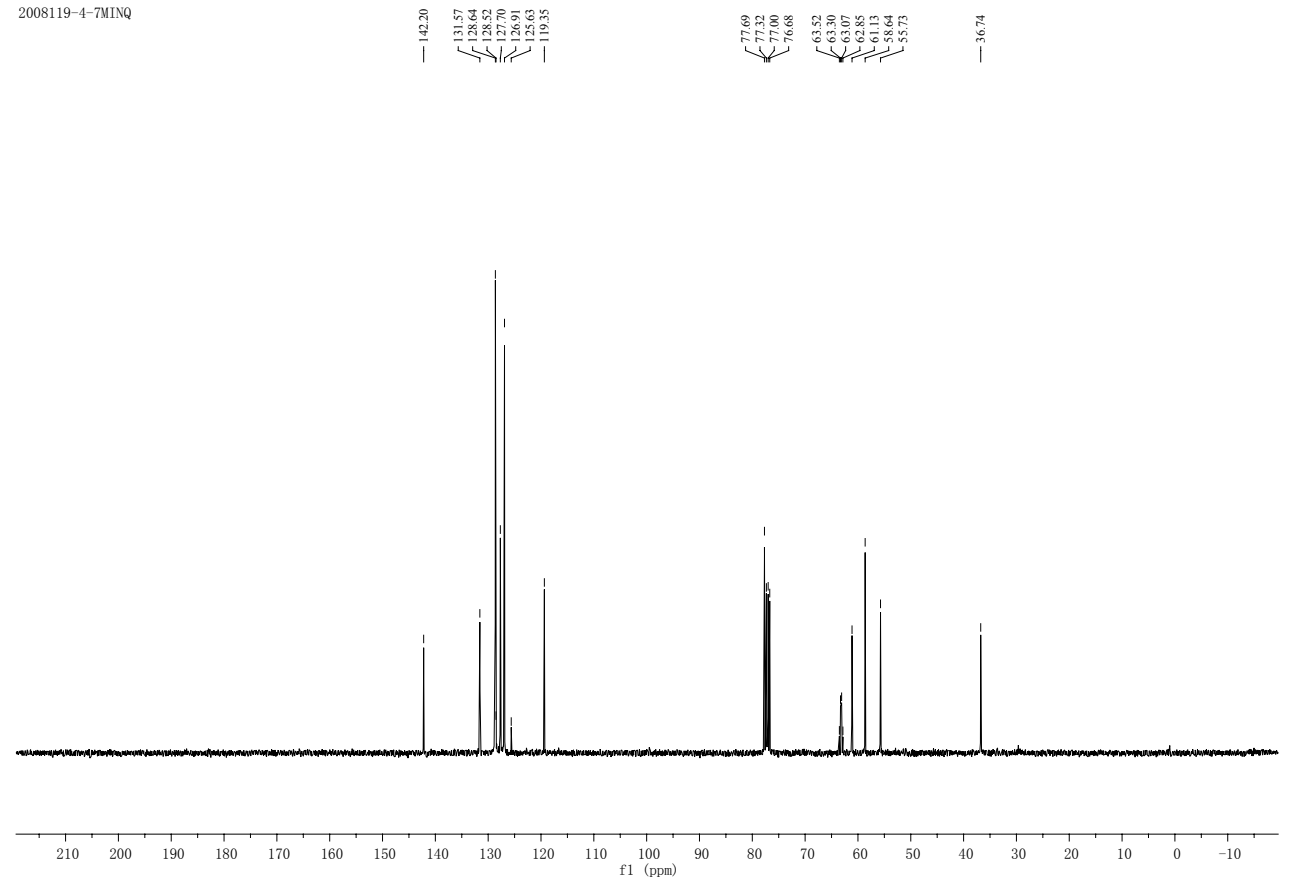


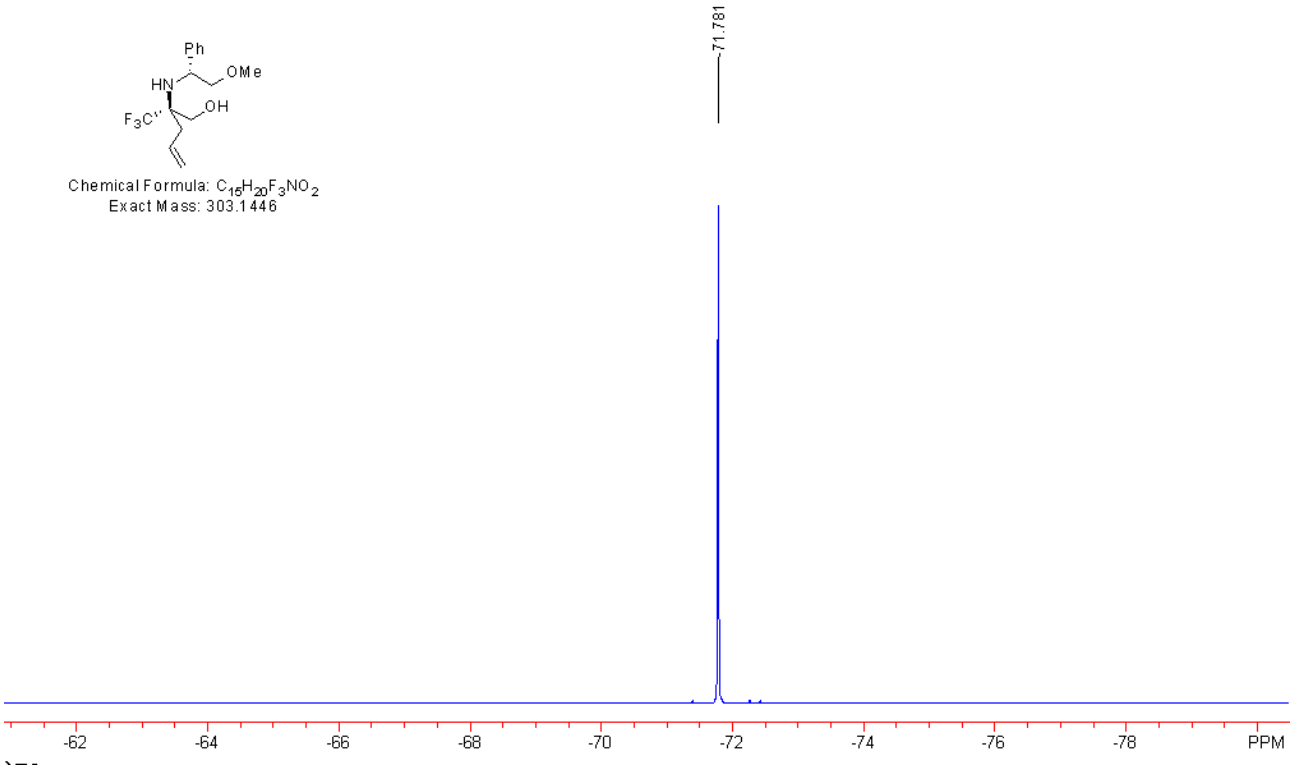



-78.348
NH2
F3C
CO2TMSE
-70
-75
-80
-85
PPM

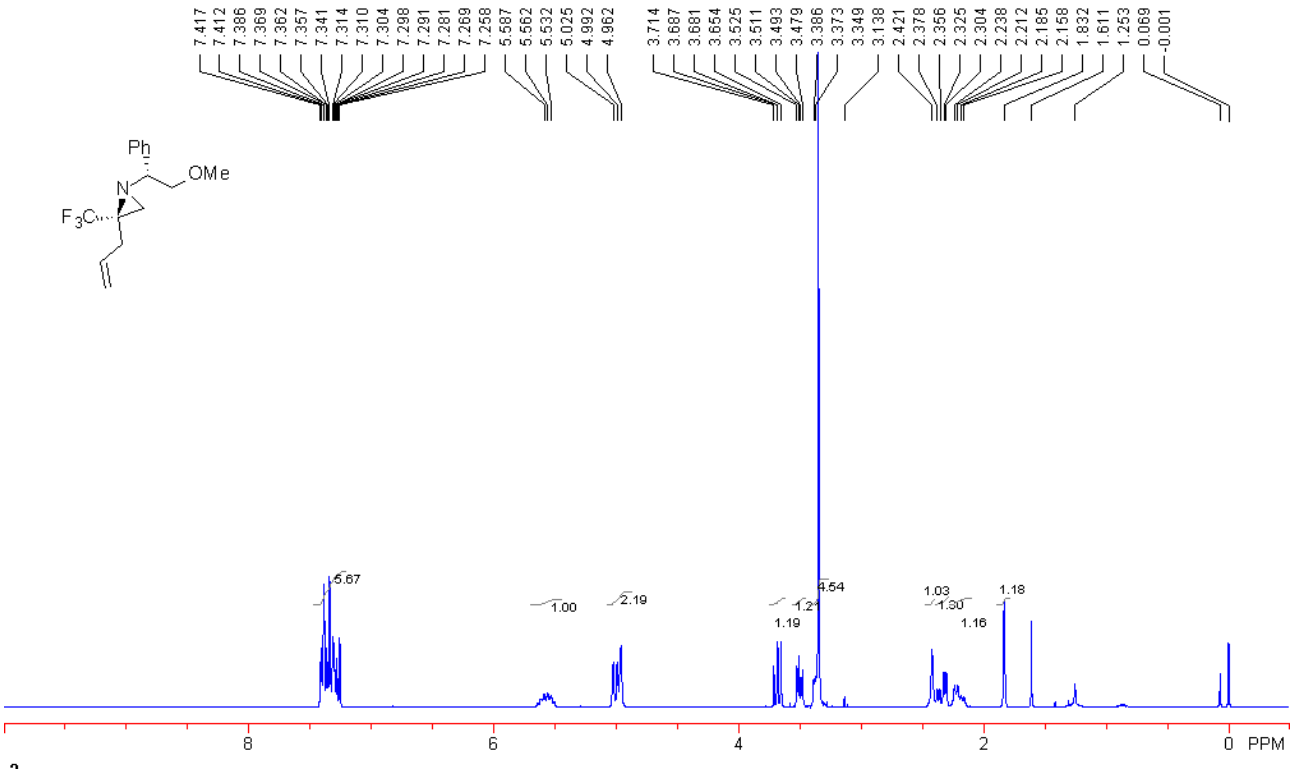
(*R*)-2-((*R*)-2-methoxy-1-phenylethylamino)-2-(trifluoromethyl)pent-4-en-1-ol (6).

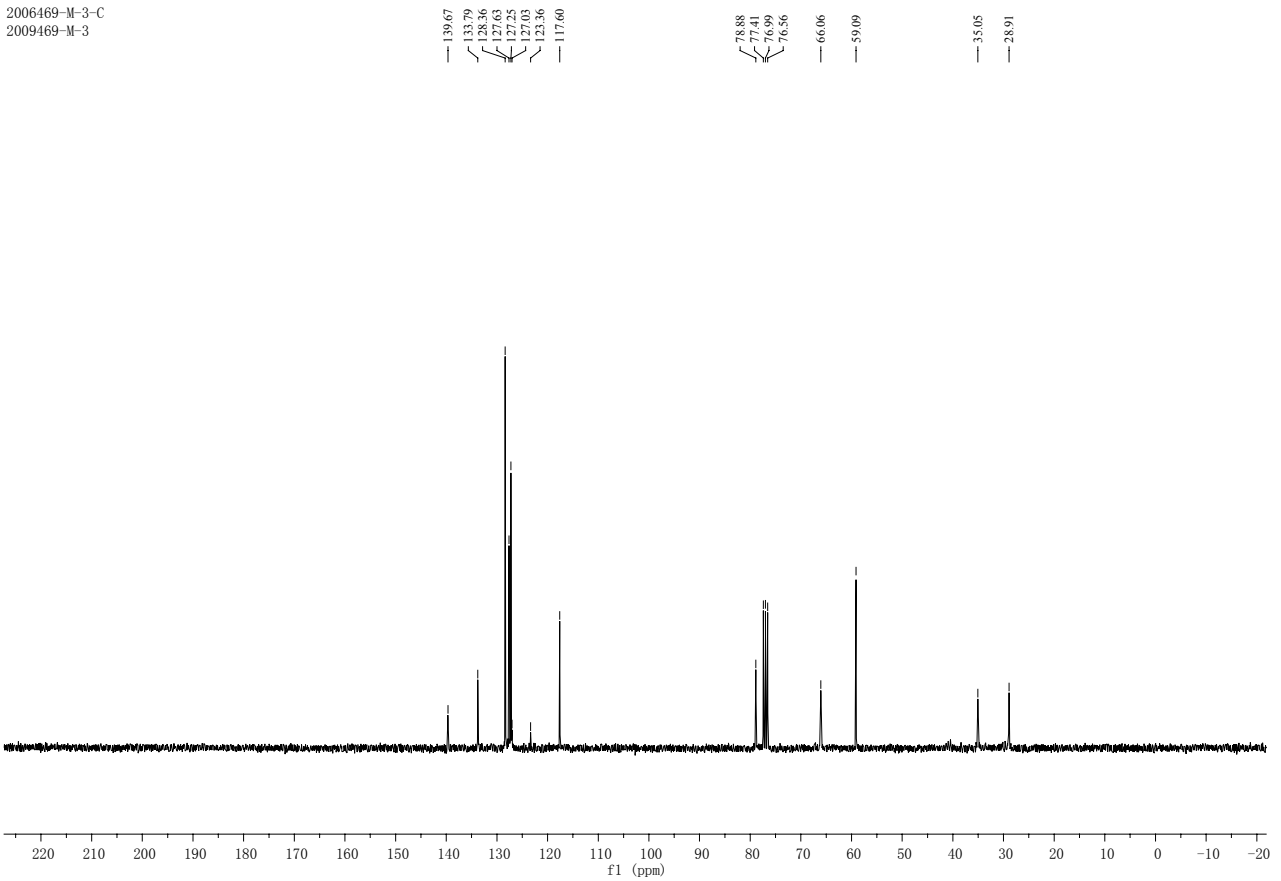


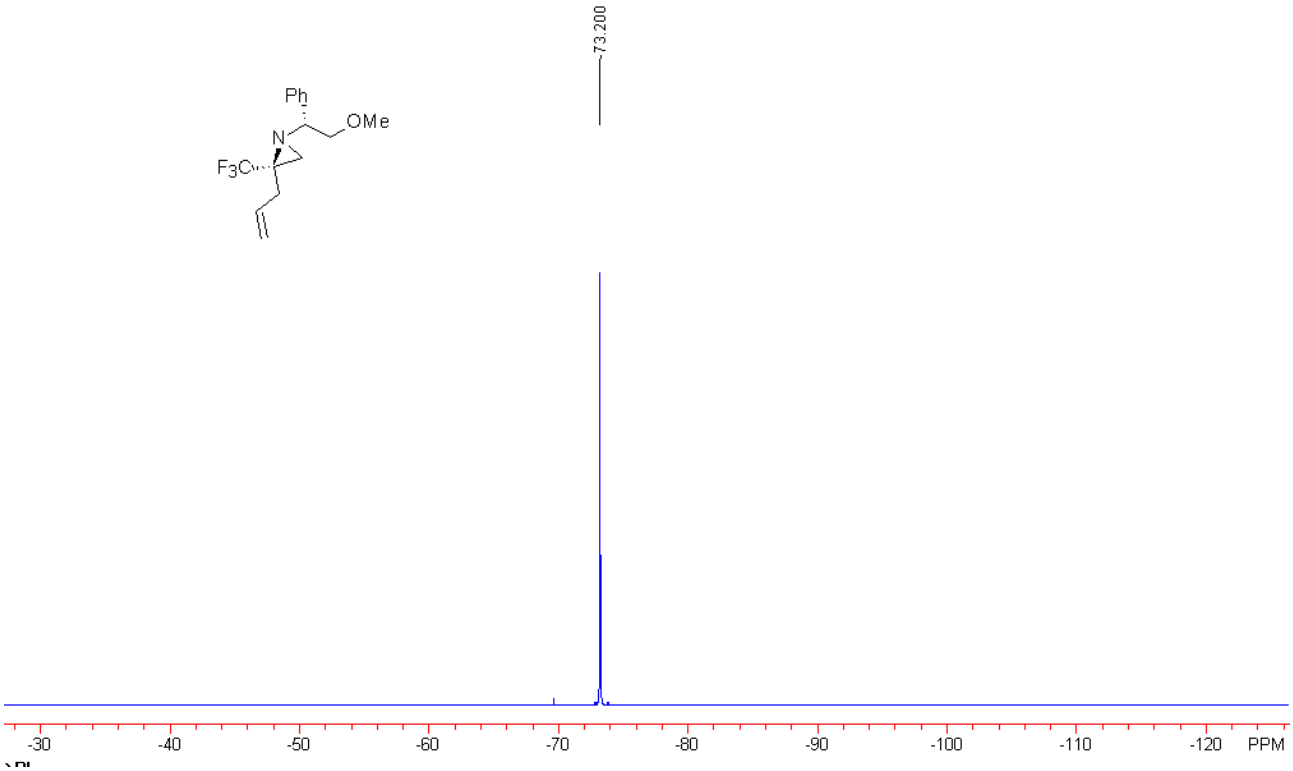



Ph
OMe
HN
OH
F3C
Chemical Formula: C15H20F3NO2
Exact Mass: 303.1446
-71.781
-62
-64
-66
-68
-70
-72
-74
-76
-78
PPM

(*R*)-2-allyl-1-((*R*)-2-methoxy-1-phenylethyl)-2-(trifluoromethyl)aziridine (7).






73.200
Ph
OMe
N
F3C
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
PPM