

# Dearomative [2,3] sigmatropic rearrangement of ammonium ylides followed by 1,4-elimination to form $\alpha$ -(*ortho*-vinylphenyl)amino acid esters

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## Electronic Supplementary Information

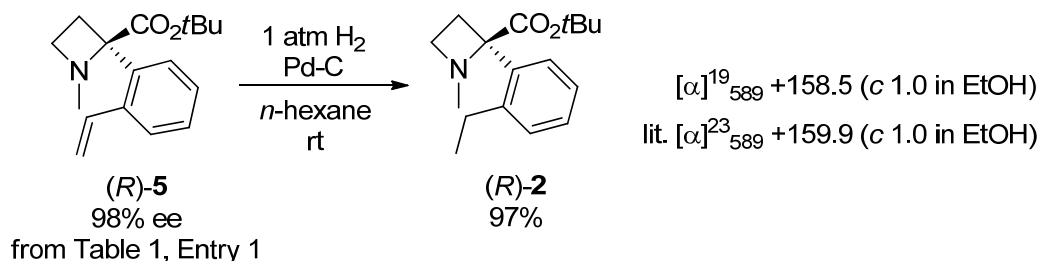
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## 1. Determination of absolute stereochemistry

### 1-1. (*R*)-*tert*-Butyl 1-methyl-2-(2-vinylphenyl)azetidine-2-carboxylate [(*R*)-5]

The absolute configuration of **5** was determined by the specific rotation value after conversion into (*R*)-*tert*-butyl 2-(2-ethylphenyl)-1-methylazetidine-2-carboxylate [(*R*)-2].<sup>1</sup>

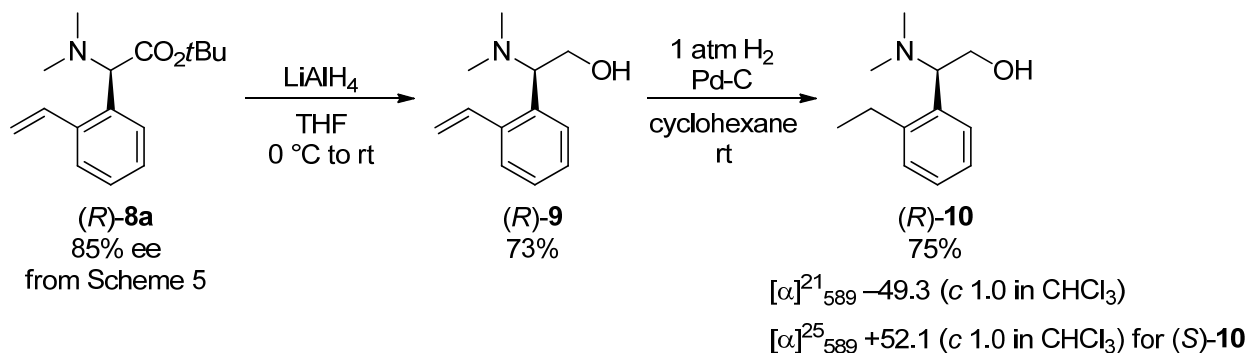


A mixture of (*R*)-**5** (29.2 mg, 0.107 mmol, 98% ee) and Pd-C (loading: 10 wt.%, 2 mg) in *n*-hexane (1.1 mL) was stirred for 1 h at room temperature under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was evaporated. The crude (*R*)-**2** (28.5 mg, 97% yield) was obtained as a colourless oil and sufficiently pure without purification.  $[\alpha]_{589}^{19} +158.5$  (c 1.0 in EtOH); IR (film)  $\nu_{\max}/\text{cm}^{-1}$  3065, 2971, 2931, 2852, 2782, 1714, 1481, 1454, 1391, 1367, 1253, 1196, 1164, 1121, 1086, 1045, 1029, 975, 952, 908, 845, 822, 760; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.54-7.48 (1H, m, ArH), 7.23-7.14 (3H, m, ArH), 3.48 (1H, ddd, *J* = 8.5, 6.0, 2.4 Hz, 4-H), 3.34 (1H, ddd, *J* = 8.9, 8.2, 6.0 Hz, 4-H), 2.93 (1H, ddd, *J* = 10.5, 8.2, 2.4 Hz, 3-H), 2.49 (3H, s, NCH<sub>3</sub>), 2.355 (1H, q, *J* = 7.4 Hz, CH<sub>2</sub>CH<sub>3</sub>), 2.351 (1H, q, *J* = 7.4 Hz, CH<sub>2</sub>CH<sub>3</sub>), 2.19 (1H, ddd, *J* = 10.5, 8.9, 8.5 Hz, 3-H), 1.42 (9H, s, *t*Bu), 1.19 (3H, dd, *J* = 7.4, 7.4 Hz, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.8, 142.0, 139.3, 127.6, 126.7, 125.4, 125.1, 81.6, 75.7, 52.2, 39.9, 29.8, 28.1, 24.3, 14.5; HRMS (ESI): calcd for C<sub>17</sub>H<sub>26</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 276.1958, found 276.1949.

### 1-2. (*R*)-*tert*-Butyl 2-(dimethylamino)-2-(2-vinylphenyl)acetate [(*R*)-8a]

The absolute configuration of **8a** was determined by the specific rotation value after conversion into (*R*)-2-(dimethylamino)-2-(2-ethylphenyl)ethanol [(*R*)-10].

#### 1-2-1 Conversion of (*R*)-**8a** into (*R*)-10

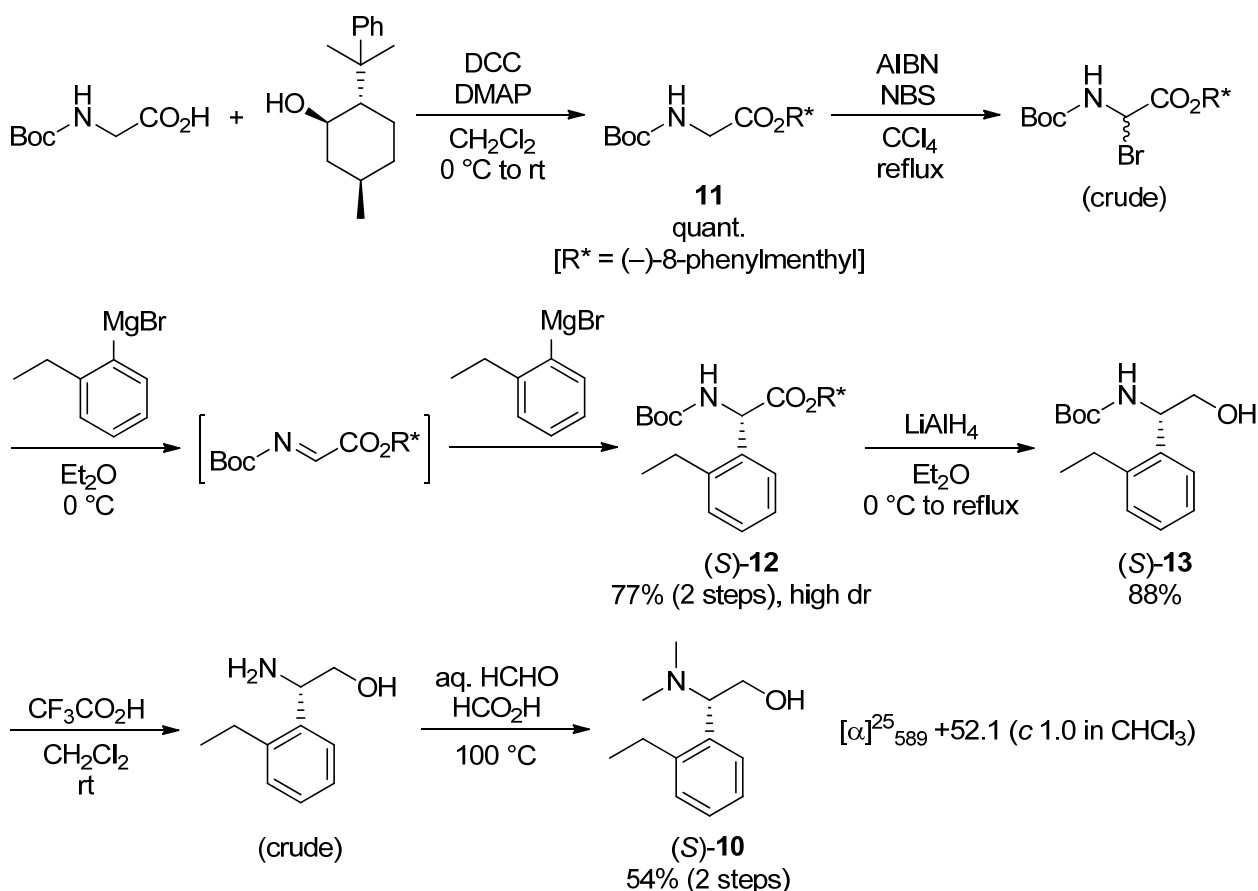


<sup>1</sup> (a) E. Tayama, K. Watanabe and S. Sotome, *Org. Biomol. Chem.*, 2017, **15**, 6668; (b) E. Tayama, K. Watanabe and Y. Matano, *Eur. J. Org. Chem.*, 2016, 3631.

(Step 1) A solution of (*R*)-**8a** (71.0 mg, 0.272 mmol, 85% ee) in THF (1.4 mL) was added to a suspension of LiAlH<sub>4</sub> (15 mg, 0.40 mmol) in THF (1.4 mL) at 0 °C and the mixture was stirred for 3 h at room temperature under an argon atmosphere. The resulting mixture was cooled to 0 °C, diluted with Et<sub>2</sub>O and quenched with H<sub>2</sub>O. The mixture was extracted with EtOAc and the combined extracts were washed with brine. The organic solution was dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 6/1 to 4/1 as the eluent) gave (*R*)-2-(dimethylamino)-2-(2-vinylphenyl)ethanol [(*R*)-**9**] (37.8 mg, 73% yield) as a colourless oil. (Step 2) A mixture of (*R*)-**9** (37.8 mg, 0.198 mmol) and Pd-C (loading: 10 wt.%, 4 mg) in cyclohexane (2.0 mL) was stirred for 1 h at room temperature under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was evaporated. The residue was purified by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 6/1 to 4/1 as the eluent) to obtain (*R*)-**10** (28.8 mg, 75% yield) as a colourless oil.  $[\alpha]_{589}^{21} -49.3$  (*c* 1.0 in CHCl<sub>3</sub>); IR (film)  $\nu_{\max}/\text{cm}^{-1}$  3401, 3062, 3017, 2963, 2872, 2820, 2775, 1487, 1466, 1404, 1374, 1346, 1279, 1258, 1207, 1178, 1158, 1097, 1052, 1039, 953, 885, 851, 799, 757; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.35-7.30 (1H, m, ArH), 7.24-7.16 (3H, m, ArH), 3.87 (1H, dd, *J* = 10.3, 6.9 Hz, 1-H), 3.81 (1H, dd, *J* = 6.9, 5.2 Hz, 2-H), 3.71 (1H, dd, *J* = 10.3, 5.2 Hz, 1-H), 2.79 (1H, dq, *J* = 14.4, 7.6 Hz, CH<sub>2</sub>CH<sub>3</sub>), 2.69 (1H, dq, *J* = 14.4, 7.6 Hz, CH<sub>2</sub>CH<sub>3</sub>), 2.56 (1H, br, OH), 2.26 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.21 (3H, dd, *J* = 7.6, 7.6 Hz, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  143.3, 135.2, 129.1, 127.8, 127.4, 125.7, 64.7, 63.0, 42.6, 26.0, 16.0; HRMS (ESI): calcd for C<sub>12</sub>H<sub>20</sub>NO [M + H]<sup>+</sup> 194.1539, found 194.1538.

## 1-2-2 Preparation of authentic sample (S)-10

The authentic (S)-10 was prepared via diastereoselective addition of 2-ethylphenylmagnesium bromide to *N*-Boc-iminoacetate of (–)-8-phenylmenthol.<sup>2,3</sup>



(Step 1) A solution of DCC (0.50 g, 2.4 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5.0 mL) was added to a mixture of Boc-glycine (0.42 g, 2.4 mmol), (–)-8-phenylmenthol<sup>4</sup> (465 mg, 2.00 mmol), and DMAP (49 mg, 0.40 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5.0 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and for 12 h at room temperature. The resulting mixture was filtered and the filtrate was evaporated. The residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 7/1 to 5/1 as the eluent) to obtain *N*-Boc-glycine (–)-8-phenylmenthol ester (**11**) (783 mg, quant.) as a colourless gum. (Step 2) A mixture of **11** (783 mg, 2.01 mmol), NBS (356 mg, 2.00 mmol), AIBN (16 mg, 0.097 mmol) in CCl<sub>4</sub> (4.0 mL) was refluxed for 15 min. The resulting mixture was cooled to room temperature and filtered. The filtrate was evaporated and the residue was dissolved in Et<sub>2</sub>O (6.0 mL). The solution was added to a solution of 2-ethylphenylmagnesium bromide in Et<sub>2</sub>O (ca. 1 M, 6.0 mL, 6.0 mmol, prepared from Mg turnings and 1-bromo-2-ethylbenzene) at 0 °C under an argon atmosphere. After stirring for 5 min at 0 °C, the mixture was quenched with saturated NH<sub>4</sub>Cl aq. and extracted with EtOAc. The

<sup>2</sup> P. Ermert, J. Meyer, C. Stucki, J. Schneebeli and J. -P. Obrecht, *Tetrahedron Lett.*, 1988, **29**, 1265.

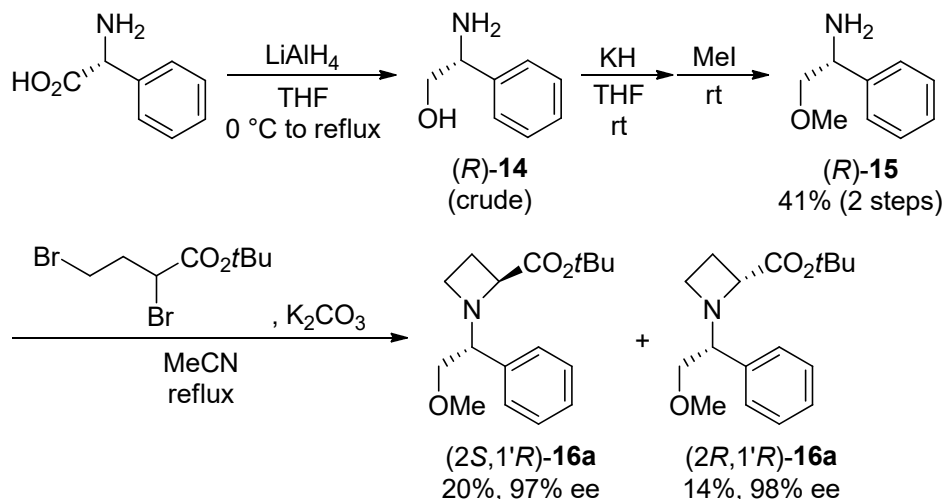
<sup>3</sup> Previously, we reported that the reaction of 2-methylphenylmagnesium bromide to *N*-Boc-iminoacetate of (–)-8-phenylmenthol gave (S)-isomer with high diastereoselectivity, see: E. Tayama and H. Kimura, *Angew. Chem. Int. Ed.*, 2007, **46**, 8869.

<sup>4</sup> O. Ort, *Org. Syn.*, 1987, **65**, 203.

combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 15/1 to 10/1 as eluent) to give (2*S*,1*R*',2*S*',5*R*')-5'-methyl-2'-(2''-phenylpropan-2''-yl)cyclohexyl 2-((*tert*-butoxycarbonyl)amino)-2-(2-ethylphenyl)acetate [(*S*)-**12**] (760 mg, 77% yield) as a pale yellow solid. <sup>1</sup>H NMR of the product (*S*)-**12** showed that the diastereomer ratio was high (ca. 9/1). (Step 3) A solution of (*S*)-**12** (359 mg, 0.727 mmol) in Et<sub>2</sub>O (3.6 mL) was added to a suspension of LiAlH<sub>4</sub> (42 mg, 1.1 mmol) in Et<sub>2</sub>O (3.6 mL) at 0 °C under an argon atmosphere. The mixture was refluxed for 30 min and the reactant was quenched with H<sub>2</sub>O at 0 °C. The mixture was treated with 1 M KHSO<sub>4</sub> aq. and extracted with EtOAc. The combined extracts were washed with saturated NaHCO<sub>3</sub> aq. and brine. The solution was dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The residue was purified by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 50/1 to 20/1 as the eluent) to obtain (*S*)-*tert*-butyl (1-(2-ethylphenyl)-2-hydroxyethyl)carbamate [(*S*)-**13**] (169 mg, 88% yield) as a white solid. (Step 4) A solution of (*S*)-**13** (56.9 mg, 0.214 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2.0 mL) was treated with CF<sub>3</sub>CO<sub>2</sub>H (1.0 mL) at room temperature. After stirring for 1 h at the same temperature, the resulting mixture was evaporated. The residue was treated with 2 M NaOH aq. and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined extracts were washed with H<sub>2</sub>O, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The residue was treated with 37 wt.% HCHO aq. (33 μL, 0.45 mmol) and HCO<sub>2</sub>H (33 μL, 0.87 mmol). The mixture was stirred for 1 h at 100 °C and cooled to room temperature. The residue was treated with 2 M NaOH aq. and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined extracts were washed with H<sub>2</sub>O, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 10/1 to 5/1 as the eluent) gave (*S*)-2-(dimethylamino)-2-(2-ethylphenyl)ethanol [(*S*)-**10**] (22.3 mg, 54% yield) as a colourless oil.  $[\alpha]_{589}^{25} +52.1$  (*c* 1.0 in CHCl<sub>3</sub>).

## 2. Preparation of substrates

**(2*S*,1'*R*)- and (2*R*,1'*R*)-*tert*-Butyl 1'-(2'-methoxy-1'-phenylethyl)azetidine-2-carboxylate [(2*S*,1'*R*)-16a and (2*R*,1'*R*)-16a]**

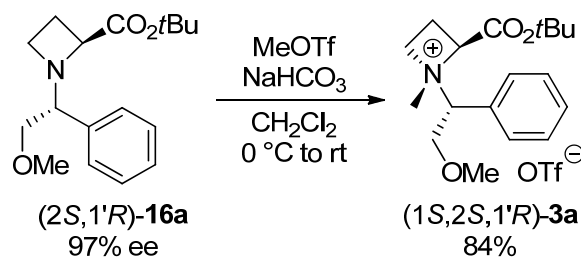


(Step 1) D-2-phenylglycine (2.27 g, 15.0 mmol) was added to a suspension of LiAlH<sub>4</sub> (0.85 g, 22.4 mmol) in THF (30 mL) at 0 °C and the mixture was refluxed for 18 h under an argon atmosphere. The resulting mixture was cooled to 0 °C, diluted with Et<sub>2</sub>O and quenched with H<sub>2</sub>O (0.85 mL). The mixture was treated with 15 wt.% NaOH aq. (0.85 mL) followed by H<sub>2</sub>O (2.55 mL) and stirred for over 30 min at room temperature. The mixture was filtered through a pad of Celite and the filtrate was evaporated to obtain crude (*R*)-2-amino-2-phenylethanol [(*R*)-14] as yellow crystals (1.94 g). (Step 2)<sup>5</sup> A solution of crude (*R*)-14 (1.94 g) in THF (28 mL) was added to a suspension of KH (30 wt.% in oil, 2.30 g, 17 mmol) in THF (28 mL) at room temperature under an argon atmosphere. The mixture was stirred for 6 h and treated with MeI (834 μL, 13.4 mmol) at the same temperature. After stirring for 40 h, the resulting mixture was quenched with H<sub>2</sub>O at 0 °C and extracted with toluene. The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 15/1 to 10/1 as the eluent) gave (*R*)-2-methoxy-1-phenylethylamine [(*R*)-15] (839 mg, 41% yield) as a yellow oil. (Step 3) A mixture of (*R*)-15 (835 mg, 5.52 mmol), *tert*-butyl 2,4-dibromobutanoate (1.67 g, 5.53 mmol), and K<sub>2</sub>CO<sub>3</sub> (2.29 g, 16.6 mmol) in MeCN (28 mL) was refluxed for 12 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel [*n*-hexane/EtOAc = 10/1 to 2/1 as the eluent, *R*<sub>f</sub>: (2*S*,1'*R*) > (2*R*,1'*R*)] to obtain (2*S*,1'*R*)-16a (314 mg, 20% yield, 97% ee) as a pale yellow oil and (2*R*,1'*R*)-16a (227 mg, 14% yield, 98% ee) as a pale yellow oil. The stereochemistry of (2*S*,1'*R*)-16a and (2*R*,1'*R*)-16a were determined by analogy with analogous derivatives reported previously.<sup>1</sup> (2*S*,1'*R*)-16a: [α]<sub>D</sub><sup>22</sup><sub>589</sub> −120.3 (*c* 1.0 in EtOH); 97% ee [determined by HPLC analysis: Daicel Chiralcel OJ-H column (25 cm), *n*-hexane/EtOH = 98/2 as the eluent, flow rate = 0.50 mL/min, *t*<sub>R</sub> = 8.9 min for (2*R*,1'*S*)-16a (1.5%) and 10.4 min for (2*S*,1'*R*)-16a (98.5%)]; IR (film) ν<sub>max</sub>/cm<sup>−1</sup> 3061, 3027, 3002, 2976, 2930, 2888, 2826,

<sup>5</sup> A. B. Smith III, K. M. Yager, B. W. Phillips and C. M. Taylor, *Org. Syn.*, 1998, **75**, 19.

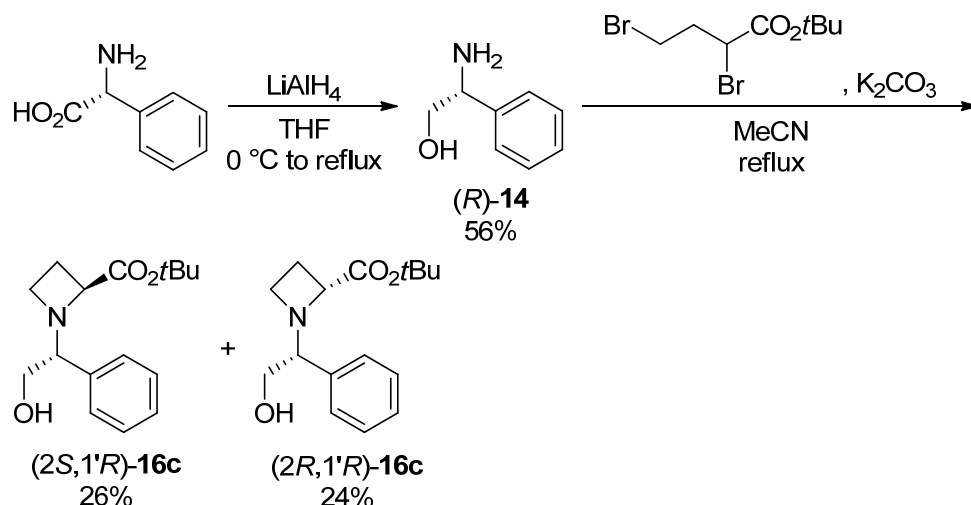
1745, 1719, 1494, 1473, 1453, 1390, 1366, 1345, 1315, 1291, 1235, 1222, 1212, 1195, 1155, 1117, 1100, 1069, 1041, 1031, 992, 971, 947, 851, 764, 702; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.42-7.34 (2H, m, Ph), 7.34-7.22 (3H, m, Ph), 3.89 (1H, t, *J* = 8.6 Hz, 2-H), 3.62 (1H, dd, *J* = 9.0, 8.1 Hz, 2'-H), 3.53 (1H, dd, *J* = 8.1, 3.7 Hz, 1'-H), 3.34 (1H, dd, *J* = 9.0, 3.7 Hz, 2'-H), 3.21 (3H, s, OCH<sub>3</sub>), 3.09-2.99 (1H, m, 4-H), 2.73 (1H, ddd, *J* = 8.7, 8.4, 7.0 Hz, 4-H), 2.19 (2H, ddd, *J* = 8.6, 8.4, 5.6 Hz, 3-H), 1.49 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.4, 138.7, 128.24, 128.21, 127.5, 80.0, 77.6, 71.1, 65.5, 58.7, 49.6, 28.1, 22.7; HRMS (ESI): calcd for C<sub>17</sub>H<sub>26</sub>NO<sub>3</sub> [M + H]<sup>+</sup> 292.1907, found 292.1897. (*2R,1'R*)-**16a**: [α]<sub>D</sub><sup>23</sup><sub>589</sub> +43.2 (*c* 1.0 in EtOH); 98% ee [determined by HPLC analysis: Daicel Chiralpak AD-H column (25 cm), *n*-hexane/EtOH = 98/2 as the eluent, flow rate = 0.50 mL/min, *t*<sub>R</sub> = 12.7 min for (*2R,1'R*)-**16a** (99.1%) and 14.3 min for (*2S,1'S*)-**16a** (0.9%)]; IR (film) *v*<sub>max</sub>/cm<sup>-1</sup> 3061, 3029, 2976, 2930, 2877, 2827, 1739, 1494, 1477, 1454, 1391, 1366, 1302, 1233, 1195, 1153, 1122, 1102, 1050, 1030, 983, 973, 949, 848, 761, 701; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.34-7.20 (5H, m, Ph), 3.65 (1H, dd, *J* = 9.0, 6.2 Hz, 2'-H), 3.61-3.53 (3H, m, 2-H, 4-H, and 1'-H), 3.48 (1H, dd, *J* = 9.0, 5.8 Hz, 2'-H), 3.27 (3H, s, OCH<sub>3</sub>), 3.16 (1H, ddd, *J* = 8.6, 8.6, 7.2 Hz, 4-H), 2.28-2.10 (2H, m, 3-H), 1.19 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 171.5, 138.1, 129.0, 128.2, 127.7, 80.1, 76.1, 71.6, 65.0, 59.0, 52.0, 27.7, 22.1; HRMS (ESI): calcd for C<sub>17</sub>H<sub>26</sub>NO<sub>3</sub> [M + H]<sup>+</sup> 292.1907, found 292.1898.

**(1*S*,2*S*,1'*R*')-2-(*tert*-Butoxycarbonyl)-1-(2'-methoxy-1'-phenylethyl)-1-methylazetidinium trifluoromethanesulfonate [(1*S*,2*S*,1'*R*')-**3a**]**



A mixture of (*2S,1'R*)-**16a** (311 mg, 1.07 mmol) and NaHCO<sub>3</sub> (0.27 g, 3.2 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5.4 mL) was treated with MeOTf (242 μL, 2.14 mmol) at 0 °C and stirred for 1 h at room temperature. The resulting mixture was evaporated to ca. 1/2 to 1/3 volume and the residue was purified by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 30/1 to 15/1 as the eluent) to obtain (*1S,2S,1'R*)-**3a** (408 mg, 84% yield) as a colourless gum. The relative stereochemistry was determined by analogy with (*1S,2S,1'S*)-**1a** and analogous derivatives reported previously.<sup>1</sup> [α]<sub>D</sub><sup>24</sup><sub>589</sub> -37.5 (*c* 1.0 in EtOH); IR (film) *v*<sub>max</sub>/cm<sup>-1</sup> 3056, 2983, 2937, 2822, 1743, 1459, 1396, 1371, 1259, 1224, 1155, 1125, 1093, 1066, 1031, 990, 973, 934, 884, 841, 772, 755, 709; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.60 (2H, d, *J* = 7.0 Hz, Ph), 7.52-7.42 (3H, m, Ph), 5.66 (1H, dd, *J* = 10.0, 10.0 Hz, 2-H), 5.21 (1H, dd, *J* = 7.7, 3.1 Hz, 1'-H), 5.01 (1H, ddd, *J* = 10.0, 10.0, 9.6 Hz, 4-H), 4.13 (1H, dd, *J* = 11.8, 7.7 Hz, 2'-H), 3.94 (1H, dd, *J* = 11.8, 3.1 Hz, 2'-H), 3.37 (3H, s, NCH<sub>3</sub> or OCH<sub>3</sub>), 3.34-3.25 (1H, m, 4-H), 3.24 (3H, s, NCH<sub>3</sub> or OCH<sub>3</sub>), 2.95-2.80 (2H, m, 3-H), 1.52 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 164.1, 131.0, 130.8, 129.5, 128.7, 120.7 (q, *J* = 319 Hz), 85.1, 75.1, 71.0, 69.8, 62.4, 59.2, 41.6, 27.8, 20.0; HRMS (ESI): calcd for C<sub>18</sub>H<sub>28</sub>NO<sub>3</sub> [M - OTf]<sup>+</sup> 306.2064, found 306.2054.

**(2*S*,1'*R*)- and (2*R*,1'*R*)-*tert*-Butyl 1-(2'-hydroxy-1'-phenylethyl)azetidine-2-carboxylate [(2*S*,1'*R*)-16c and (2*R*,1'*R*)-16c]**

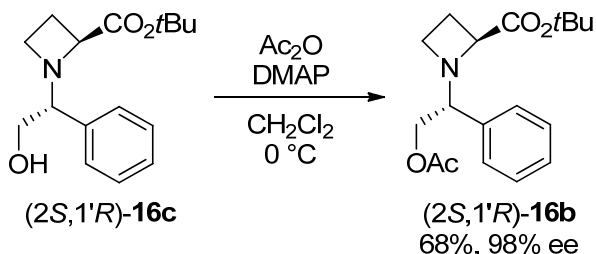


(Step 1) D-2-phenylglycine (2.27 g, 15.0 mmol) was added to a suspension of LiAlH<sub>4</sub> (0.85 g, 22.4 mmol) in THF (30 mL) at 0 °C and the mixture was refluxed for 18 h under an argon atmosphere. The resulting mixture was cooled to 0 °C, diluted with Et<sub>2</sub>O and quenched with H<sub>2</sub>O (0.85 mL). The mixture was treated with 15 wt.% NaOH aq. (0.85 mL) followed by H<sub>2</sub>O (2.55 mL) and stirred for over 30 min at room temperature. The mixture was filtered through a pad of Celite and the filtrate was evaporated. The residue was diluted with toluene to crystallize. The crystals were isolated by filtration and dried under reduced pressure to obtain (R)-14 (1.15 g, 56% yield) as yellow crystals. (Step 2) A mixture of (R)-14 (823 mg, 6.0 mmol), *tert*-butyl 2,4-dibromobutanoate (1.81 g, 5.99 mmol), and K<sub>2</sub>CO<sub>3</sub> (2.49 g, 18.0 mmol) in MeCN (30 mL) was refluxed for 12 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel [*n*-hexane/EtOAc = 3/1 to 1/2 as the eluent, *R<sub>f</sub>*: (2*S*,1'*R*) > (2*R*,1'*R*)] to obtain (2*S*,1'*R*)-16c (438 mg, 26% yield) as pale yellow crystals and (2*R*,1'*R*)-16c (393 mg, 24% yield) as pale yellow crystals. The stereochemistry of (2*S*,1'*R*)- and (2*R*,1'*R*)-16c were determined by analogy with analogous derivatives reported previously.<sup>1</sup> (2*S*,1'*R*)-16c: mp 74–77 °C; [α]<sub>589</sub><sup>22</sup> –117.9 (*c* 1.0 in EtOH); IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$  3483, 2967, 2867, 2843, 1748, 1717, 1494, 1455, 1420, 1383, 1367, 1289, 1245, 1223, 1160, 1097, 1077, 1050, 1031, 945, 931, 847, 827, 779, 761, 702; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.41–7.22 (5H, m, Ph), 3.87–3.65 (2H, m, 2'-H), 3.81 (1H, dd, *J* = 8.8, 8.8 Hz, 2-H), 3.61–3.49 (1H, m, 1'-H), 3.37 (1H, t, *J* = 3.2 Hz, OH), 3.12 (1H, ddd, *J* = 7.0, 5.6, 5.6 Hz, 4-H), 2.76 (1H, ddd, *J* = 8.6, 8.6, 7.0 Hz, 4-H), 2.32–2.19 (2H, m, 3-H), 1.50 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  174.1, 138.7, 128.4, 128.1, 127.4, 81.8, 73.4, 64.3, 64.1, 49.1, 28.0, 21.5; HRMS (ESI): calcd for C<sub>16</sub>H<sub>24</sub>NO<sub>3</sub> [*M* + *H*]<sup>+</sup> 278.1751, found 278.1742. (2*R*,1'*R*)-16c: mp 95–99 °C; [α]<sub>589</sub><sup>22</sup> +62.1 (*c* 1.0 in EtOH); IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$  3446, 3011, 2975, 2939, 2913, 2882, 2833, 1733, 1496, 1479, 1455, 1394, 1369, 1307, 1270, 1246, 1234, 1209, 1153, 1104, 1082, 1060, 1045, 1034, 981, 955, 943, 919, 844, 779, 752, 702; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.40–7.27 (3H, m, Ph), 7.27–7.22 (2H, m, Ph), 3.76 (1H, dd, *J* = 11.2, 7.7 Hz, 2'-H), 3.71–3.64 (1H, m, 2'-H), 3.67 (1H, dd, *J* = 8.4, 8.4 Hz, 2-H), 3.56 (1H, dd, *J* = 7.7, 5.4 Hz, 1'-H), 3.42 (1H, ddd, *J* = 8.6, 6.4, 2.8 Hz, 4-H), 3.09 (1H, ddd, *J* = 8.8, 8.4, 6.4 Hz, 4-H), 2.99 (1H, br, OH), 2.22 (1H, dddd, *J* = 10.4, 8.8, 8.6,



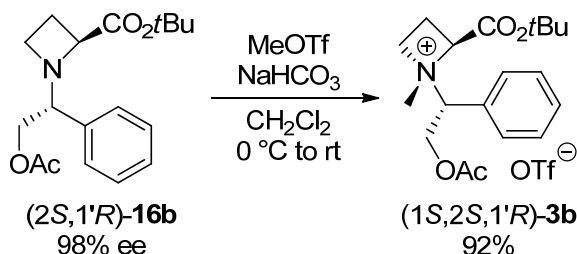
8.4 Hz, 3-H), 2.06 (1H, dddd,  $J = 10.4, 8.4, 8.4, 2.8$  Hz, 3-H), 1.35 (9H, s, *t*Bu);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  172.6, 136.3, 129.2, 128.4, 128.0, 81.0, 70.5, 63.1, 61.7, 49.1, 27.8, 21.9; HRMS (ESI): calcd for  $\text{C}_{16}\text{H}_{24}\text{NO}_3$   $[\text{M} + \text{H}]^+$  278.1751, found 278.1742.

**(2*S*,1'*R*)-*tert*-Butyl 1-(2'-acetoxy-1'-phenylethyl)azetidine-2-carboxylate [(2*S*,1'*R*)-16b]**



A solution of (2*S*,1'*R*)-**16c** (102 mg, 0.368 mmol) in  $\text{CH}_2\text{Cl}_2$  (1.8 mL) was treated with  $\text{Ac}_2\text{O}$  (52  $\mu\text{L}$ , 0.55 mmol) followed by DMAP (9 mg, 0.07 mmol) at 0 °C and stirred for 30 min. The resulting mixture was treated with saturated  $\text{NaHCO}_3$  aq. and extracted with EtOAc. The combined extracts were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 5/1 to 3/1 as the eluent) afforded (2*S*,1'*R*)-**16b** (80.3 mg, 68% yield, 98% ee) as a colourless oil. (2*S*,1'*R*)-**16b**:  $[\alpha]_{589}^{21} -103.4$  ( $c$  1.0 in EtOH) for 98% ee [determined by HPLC analysis: Daicel Chiralpak AD-H column (25 cm), *n*-hexane/*i*PrOH = 99/1 as the eluent, flow rate = 0.50 mL/min,  $t_R = 13.6$  min for (2*S*,1'*R*)-**16b** (99.1%) and 15.9 min for (2*R*,1'*S*)-**16b** (0.9%)]; IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$  3060, 3031, 2966, 2937, 2843, 1739, 1493, 1475, 1454, 1367, 1295, 1236, 1158, 1096, 1071, 1035, 994, 962, 944, 850, 822, 791, 761, 703;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39-7.25 (5H, m, Ph), 4.21 (1H, dd,  $J = 11.2, 7.2$  Hz, 2'-H), 4.15 (1H, dd,  $J = 11.2, 4.8$  Hz, 2'-H), 3.85 (1H, dd,  $J = 8.4, 8.4$  Hz, 2-H), 3.62 (1H, dd,  $J = 7.2, 4.8$  Hz, 1'-H), 3.09 (1H, dddd,  $J = 7.0, 7.0, 4.0, 0.6$  Hz, 4-H), 2.77 (1H, ddd,  $J = 8.5, 8.5, 7.0$  Hz, 4-H), 2.30-2.16 (2H, m, 3-H), 2.00 (3H, s,  $\text{COCH}_3$ ), 1.49 (9H, s, *t*Bu);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  172.4, 170.6, 137.8, 128.4, 128.3, 127.9, 80.7, 69.8, 67.9, 65.3, 49.7, 28.0, 22.2, 21.0; HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{26}\text{NO}_4$   $[\text{M} + \text{H}]^+$  320.1856, found 320.1847.

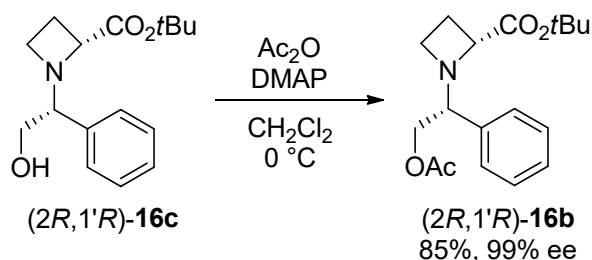
**(1*S*,2*S*,1'*R*)-1-(2'-Acetoxy-1'-phenylethyl)-2-(*tert*-butoxycarbonyl)-1-methylazetidin-1-ium trifluoromethanesulfonate [(1*S*,2*S*,1'*R*)-3b]**



A mixture of (2*S*,1'*R*)-**16b** (325 mg, 1.02 mmol, 98% ee) and  $\text{NaHCO}_3$  (0.26 g, 3.1 mmol) in  $\text{CH}_2\text{Cl}_2$  (5.1 mL) was treated with MeOTf (231  $\mu\text{L}$ , 2.04 mmol) at 0 °C and stirred for 1 h at room temperature. The resulting mixture was evaporated to ca. 1/2 to 1/3 volume and the residue was purified by chromatography on silica gel ( $\text{CH}_2\text{Cl}_2/\text{MeOH} = 15/1$  to 8/1 as the eluent) to obtain (1*S*,2*S*,1'*R*)-**3b** (453 mg, 92% yield) as a white solid. The relative stereochemistry was determined by analogy with (1*S*,2*S*,1'*S*)-**1a**.<sup>1</sup>  $[\alpha]_{589}^{19} -24.9$  ( $c$  1.0

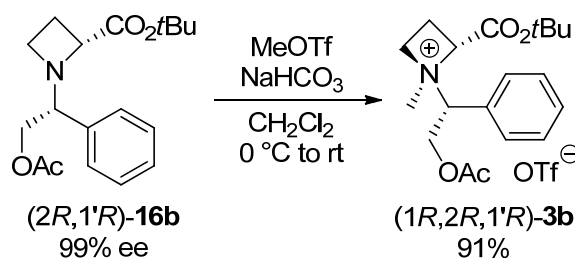
in EtOH); IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$  3058, 2983, 1743, 1459, 1397, 1372, 1259, 1225, 1154, 1030, 995, 925, 885, 838, 772, 756, 709;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57-7.43 (5H, m, Ph), 5.94 (1H, dd,  $J = 10.0, 10.0$  Hz, 2-H), 5.47 (1H, dd,  $J = 7.6, 4.4$  Hz, 1'-H), 5.06 (1H, ddd,  $J = 10.0, 10.0, 10.0$  Hz, 4-H), 4.84 (1H, dd,  $J = 12.9, 7.6$  Hz, 2'-H), 4.64 (1H, dd,  $J = 12.9, 4.4$  Hz, 2'-H), 3.32 (1H, ddd,  $J = 10.0, 7.0, 5.2$  Hz, 4-H), 3.15 (3H, s,  $\text{NCH}_3$ ), 2.99-2.84 (2H, m, 3-H), 2.05 (3H, s,  $\text{COCH}_3$ ), 1.53 (9H, s,  $t\text{Bu}$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  169.8, 164.2, 131.3, 130.4, 129.7, 128.0, 120.7 (q,  $J = 319$  Hz), 86.0, 74.1, 71.5, 62.6, 60.7, 41.0, 27.8, 20.5, 19.5; HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{28}\text{NO}_4$   $[\text{M} - \text{OTf}]^+$  334.2013, found 334.2004.

**(2*R*,1'*R*)-tert-Butyl 1-(2'-acetoxy-1'-phenylethyl)azetidide-2-carboxylate [(2*R*,1'*R*)-16b]**



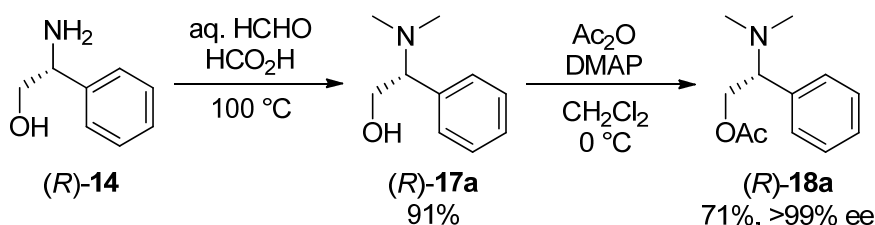
A solution of (2*R*,1'*R*)-**16c** (267 mg, 0.963 mmol) in  $\text{CH}_2\text{Cl}_2$  (4.8 mL) was treated with  $\text{Ac}_2\text{O}$  (136  $\mu\text{L}$ , 1.44 mmol) followed by DMAP (23 mg, 0.19 mmol) at 0  $^\circ\text{C}$  and stirred for 30 min. The resulting mixture was treated with saturated  $\text{NaHCO}_3$  aq. and extracted with EtOAc. The combined extracts were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and evaporated. Purification of the residue by chromatography on silica gel ( $n$ -hexane/EtOAc = 3/1 to 1.5/1 as the eluent) gave (2*R*,1'*R*)-**16b** (260 mg, 85% yield, 99% ee) as a pale yellow oil.  $[\alpha]_{589}^{21} +53.6$  ( $c$  1.0 in EtOH) for 99% ee [determined by HPLC analysis: Daicel Chiralpak AD-H column (25 cm),  $n$ -hexane/ $i$ PrOH = 98/2 as the eluent, flow rate = 0.50 mL/min,  $t_R = 20.9$  min for (2*R*,1'*R*)-**16b** (99.7%) and 22.9 min for (2*S*,1'*S*)-**16b** (0.3%)]; IR (film)  $\nu_{\max}/\text{cm}^{-1}$  3062, 3029, 3003, 2976, 2934, 2863, 1742, 1494, 1477, 1455, 1389, 1366, 1297, 1232, 1153, 1082, 1052, 1038, 979, 949, 915, 846, 764, 733, 701;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36-7.23 (5H, m, Ph), 4.29 (1H, dd,  $J = 11.2, 6.4$  Hz, 2'-H), 4.16 (1H, dd,  $J = 11.2, 6.4$  Hz, 2'-H), 3.65-3.58 (2H, m, 4-H and 1'-H), 3.57 (1H, dd,  $J = 8.4, 8.0$  Hz, 2-H), 3.17 (1H, ddd,  $J = 8.8, 8.4, 7.0$  Hz, 4-H), 2.25 (1H, dddd,  $J = 10.6, 8.8, 8.8, 8.4$  Hz, 3-H), 2.17 (1H, dddd,  $J = 10.6, 8.4, 8.0, 2.8$  Hz, 3-H), 1.99 (3H, s,  $\text{COCH}_3$ ), 1.20 (9H, s,  $t\text{Bu}$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  171.4, 170.7, 137.0, 129.1, 128.3, 128.0, 80.3, 70.4, 66.8, 64.9, 52.1, 27.7, 21.9, 20.9; HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{26}\text{NO}_4$   $[\text{M} + \text{H}]^+$  320.1856, found 320.1848.

**(1*R*,2*R*,1'*R*)-1-(2'-Acetoxy-1'-phenylethyl)-2-(tert-butoxycarbonyl)-1-methylazetidide-1-ium trifluoromethanesulfonate [(1*R*,2*R*,1'*R*)-3b]**



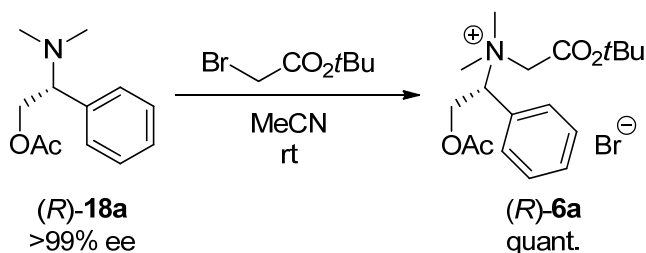
A mixture of (*2R,1'R*)-**16b** (283 mg, 0.886 mmol, 99% ee) and NaHCO<sub>3</sub> (0.22 g, 2.6 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (4.4 mL) was treated with MeOTf (200 μL, 1.77 mmol) at 0 °C and stirred for 1 h at room temperature. The resulting mixture was evaporated to ca. 1/2 to 1/3 volume and the residue was purified by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 20/1 to 8/1 as the eluent) to obtain (*1R,2R,1'R*)-**3b** (389 mg, 91% yield) as a colourless gum. The relative stereochemistry was determined by analogy with (*1R,2R,1'S*)-**1a**.<sup>1</sup> [ $\alpha$ ]<sub>589</sub><sup>21</sup> +14.0 (*c* 1.0 in EtOH); IR (KBr)  $\nu_{\text{max}}$ /cm<sup>-1</sup> 3058, 2983, 2935, 1749, 1458, 1396, 1371, 1259, 1225, 1155, 1030, 926, 884, 835, 771, 708; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.64-7.59 (2H, m, Ph), 7.55-7.44 (3H, m, Ph), 5.65 (1H, dd, *J* = 10.0, 9.6 Hz, 2-H), 5.42 (1H, dd, *J* = 10.0, 4.4 Hz, 1'-H), 5.15 (1H, ddd, *J* = 10.2, 10.0, 10.0 Hz, 4-H), 4.81 (1H, dd, *J* = 13.2, 10.0 Hz, 2'-H), 4.59 (1H, dd, *J* = 13.2, 4.4 Hz, 2'-H), 4.15 (1H, ddd, *J* = 10.2, 7.5, 4.8 Hz, 4-H), 3.34 (3H, s, NCH<sub>3</sub>), 2.97-2.85 (2H, m, 3-H), 2.13 (3H, s, COCH<sub>3</sub>), 1.18 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.7, 162.9, 131.3, 130.4, 129.7, 127.9, 120.7 (q, *J* = 318 Hz), 85.0, 74.1, 69.5, 66.0, 60.5, 40.1, 27.4, 20.6, 20.1; HRMS (ESI): calcd for C<sub>19</sub>H<sub>28</sub>NO<sub>4</sub> [M - OTf]<sup>+</sup> 334.2013, found 334.2001.

**(*R*)-2-(Dimethylamino)-2-phenylethyl acetate [(*R*)-**18a**]**



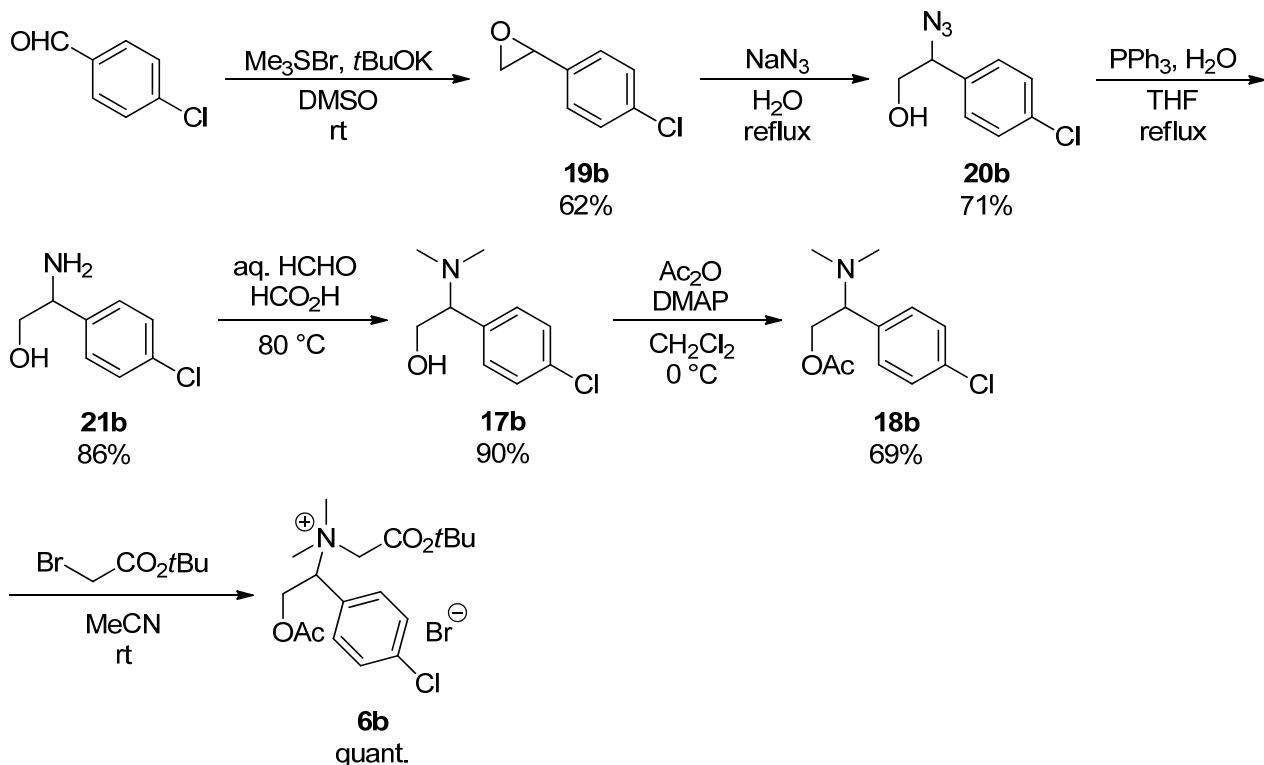
(Step 1) A mixture of (*R*)-**14** (1.14 g, 8.31 mmol), 37 wt.% HCHO aq. (1.3 mL, ca. 18 mmol) and HCO<sub>2</sub>H (1.3 mL, 34 mmol) was stirred at 100 °C for 2 h. The resulting mixture was treated with 2 M NaOH aq. and extracted with toluene. The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The residue was purified by bulb-to-bulb distillation under reduced pressure (3 to 5 mmHg, 150 to 160 °C) to afford (*R*)-2-(dimethylamino)-2-phenylethanol [(*R*)-**17a**] (1.25 g, 91% yield) as a pale yellow oil. (Step 2) A solution of (*R*)-**17a** (1.25 g, 7.57 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (38 mL) was treated with Ac<sub>2</sub>O (1.08 mL, 11.4 mmol) followed by DMAP (184 mg, 1.51 mmol) at 0 °C and stirred for 30 min. The resulting mixture was treated with saturated NaHCO<sub>3</sub> aq. and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined extracts were washed with saturated NaHCO<sub>3</sub> aq., dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 1.5/1 to 1/1 as the eluent) gave (*R*)-**18a** (1.11 g, 71% yield, >99% ee) as a colourless oil. [ $\alpha$ ]<sub>589</sub><sup>20</sup> -26.0 (*c* 1.0 in EtOH); >99% ee [determined by HPLC analysis: Daicel Chiralcel OJ-H column (25 cm), *n*-hexane/EtOH = 90/10 as the eluent, flow rate = 0.50 mL/min, *t*<sub>R</sub> = 18.9 min for (*R*)-**18a** (99.8%) and 30.5 min for (*S*)-**18a** (0.2%)]; IR (film)  $\nu_{\text{max}}$ /cm<sup>-1</sup> 3084, 3061, 3028, 2954, 2901, 2865, 2823, 2777, 1738, 1493, 1454, 1436, 1406, 1382, 1365, 1231, 1153, 1100, 1071, 1041, 982, 961, 922, 881, 848, 781, 758, 744, 703; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.37-7.24 (5H, m, Ph), 4.43 (1H, dd, *J* = 11.6, 6.0 Hz, 1-H), 4.34 (1H, dd, *J* = 11.6, 6.0 Hz, 1-H), 3.49 (1H, dd, *J* = 6.0, 6.0 Hz, 2-H), 2.24 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 2.01 (3H, s, COCH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  171.0, 138.3, 128.4, 128.2, 127.6, 68.9, 65.4, 43.1, 21.0; HRMS (ESI): calcd for C<sub>12</sub>H<sub>18</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 208.1332, found 208.1327.

**(R)-2-Acetoxy-N-(2'-(tert-butoxy)-2'-oxoethyl)-N,N-dimethyl-1-phenylethanaminium bromide [(R)-6a]**



A solution of (*R*)-**18a** (981 mg, 4.73 mmol, >99% ee) and *tert*-butyl bromoacetate (1.05 mL, 7.11 mmol) in MeCN (4.7 mL) was stirred for 15 h at room temperature. The resulting mixture was evaporated and the residue was purified by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 15/1 to 5/1 as the eluent) to give (*R*)-**6a** (1.91 g, quant.) as a white solid.  $[\alpha]_{589}^{21} -31.1$  (*c* 1.0 in EtOH); IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$  2979, 2928, 1741, 1636, 1473, 1458, 1415, 1396, 1370, 1249, 1228, 1155, 1045, 984, 929, 909, 871, 844, 777, 759, 711; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.59-7.47 (5H, m, Ph), 5.68 (1H, dd, *J* = 7.6, 4.4 Hz, 1-H), 5.13 (1H, dd, *J* = 13.9, 7.6 Hz, 2-H), 4.88 (1H, d, *J* = 17.2 Hz, NCH<sub>2</sub>CO), 4.83 (1H, dd, *J* = 13.9, 4.4 Hz, 2-H), 4.50 (1H, d, *J* = 17.2 Hz, NCH<sub>2</sub>CO), 3.81 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 3.56 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 2.10 (3H, s, COCH<sub>3</sub>), 1.52 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.6, 164.1, 131.5, 130.9 (br), 129.7, 129.0, 85.6, 73.3, 62.2, 61.3, 50.4, 50.0, 28.0, 20.9; HRMS (ESI): calcd for C<sub>18</sub>H<sub>28</sub>NO<sub>4</sub> [M – Br]<sup>+</sup> 322.2013, found 322.2003.

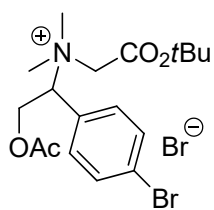
**2-Acetoxy-N-(2'-(tert-butoxy)-2'-oxoethyl)-1-(4'-chlorophenyl)-N,N-dimethylethanaminium bromide (**6b**)**



(Step 1) A solution of 4-chlorobenzaldehyde (774 mg, 5.51 mmol) and trimethylsulfonium bromide (1.40 g, 8.91 mmol) in DMSO (8.2 mL) was treated with a solution of *t*BuOK (0.93 g, 8.3 mmol) in DMSO (8.2 mL)

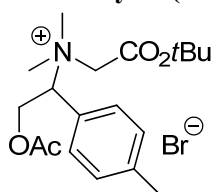
at room temperature under an argon atmosphere and stirred for 24 h. The mixture was diluted with H<sub>2</sub>O and extracted with toluene. The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 40/1 to 20/1 as the eluent) afforded 2-(4-chlorophenyl)oxirane (**19b**) (530 mg, 62% yield) as a colourless oil. (Step 2) A mixture of **19b** (515 mg, 3.33 mmol) and NaN<sub>3</sub> (0.68 g, 10.5 mmol) in H<sub>2</sub>O (16.7 mL) was refluxed for 7 h. The mixture was cooled to room temperature, diluted with H<sub>2</sub>O and extracted with EtOAc. The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 5/1 to 1/1 as the eluent) to obtain 2-azido-2-(4-chlorophenyl)ethanol (**20b**) (465 mg, 71% yield) as a white solid. (Step 3) A mixture of **20b** (442 mg, 2.24 mmol), PPh<sub>3</sub> (0.88 g, 3.4 mmol) and H<sub>2</sub>O (0.8 mL) in THF (11.2 mL) was refluxed for 17 h. The mixture was evaporated and the residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub>. The solution was dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 10/1 to 1/1 as the eluent) gave 2-amino-2-(4-chlorophenyl)ethanol (**21b**) (332 mg, 86% yield) as a white solid. (Step 4) A mixture of **21b** (322 mg, 1.88 mmol), 37 wt.% HCHO aq. (0.28 mL, ca. 3.8 mmol) and HCO<sub>2</sub>H (0.28 mL, 7.4 mmol) was stirred at 80 °C for 30 h. The resulting mixture was treated with 28 wt.% NH<sub>3</sub> aq. and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined extracts were washed with saturated NaHCO<sub>3</sub> aq. followed by brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. Purification of the residue by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 20/1 to 10/1 as the eluent) gave 2-(4-chlorophenyl)-2-(dimethylamino)ethanol (**17b**) (338 mg, 90% yield) as a pale yellow oil. (Step 5) A solution of **17b** (343 mg, 1.72 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (8.6 mL) was treated with Ac<sub>2</sub>O (0.24 mL, 2.5 mmol) followed by DMAP (50 mg, 0.41 mmol) at 0 °C and stirred for 30 min. The resulting mixture was treated with saturated NaHCO<sub>3</sub> aq. and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined extracts were washed with saturated NaHCO<sub>3</sub> aq. followed by brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 1/1 to 1/4 as the eluent) gave 2-(4-chlorophenyl)-2-(dimethylamino)ethyl acetate (**18b**) (286 mg, 69% yield) as a colourless oil. (Step 6) A solution of **18b** (280 mg, 1.16 mmol) and *tert*-butyl bromoacetate (0.25 mL, 1.7 mmol) in MeCN (1.2 mL) was stirred for 15 h at room temperature. The resulting mixture was evaporated and purified by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 20/1 to 5/1 as the eluent) to give **6b** (505 mg, quant.) as a colourless gum. IR (film)  $\nu_{\max}/\text{cm}^{-1}$  2981, 2933, 2774, 1738, 1596, 1479, 1420, 1396, 1369, 1227, 1153, 1094, 1044, 1014, 983, 923, 837, 731; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.65 (2H, d, *J* = 8.4 Hz, ArH), 7.50 (2H, d, *J* = 8.4 Hz, ArH), 5.76 (1H, dd, *J* = 7.2, 4.4 Hz, 1-H), 5.23 (1H, dd, *J* = 13.5, 7.2 Hz, 2-H), 4.84 (1H, dd, *J* = 13.5, 4.4 Hz, 2-H), 4.82 (1H, d, *J* = 17.2 Hz, NCH<sub>2</sub>CO), 4.55 (1H, d, *J* = 17.2 Hz, NCH<sub>2</sub>CO), 3.78 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 3.56 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 2.09 (3H, s, COCH<sub>3</sub>), 1.51 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.5, 163.7, 137.5, 132.4 (br), 129.8, 127.4, 85.5, 72.9, 61.8, 61.1, 50.2, 49.7, 27.8, 20.8; HRMS (ESI): calcd for C<sub>18</sub>H<sub>27</sub>ClNO<sub>4</sub> [M – Br]<sup>+</sup> 356.1623, found 356.1613.

**2-Acetoxy-1-(4''-bromophenyl)-N-(2'-(tert-butoxy)-2'-oxoethyl)-N,N-dimethylethanaminium bromide**



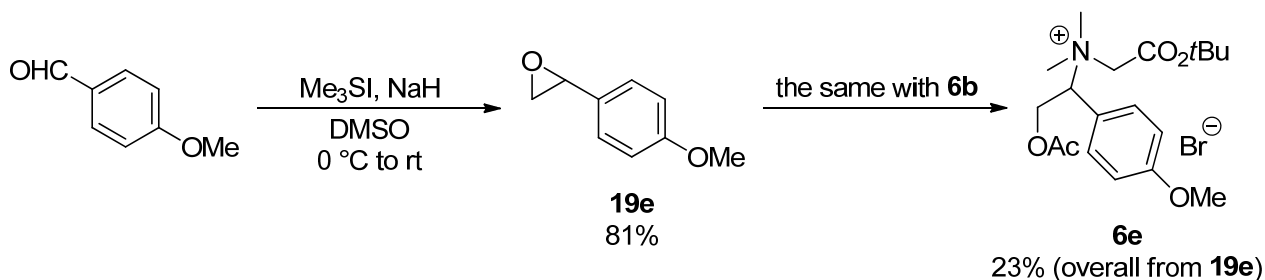
**(6c):** Prepared from 4-bromobenzaldehyde by the same procedure with **6b** in 27% overall yield; colourless gum; IR (film)  $\nu_{\max}/\text{cm}^{-1}$  2979, 2928, 1743, 1591, 1484, 1452, 1415, 1394, 1368, 1223, 1151, 1068, 1042, 1009, 980, 905, 868, 830, 786, 756, 731;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66 (2H, d,  $J = 8.4$  Hz, ArH), 7.57 (2H, d,  $J = 8.4$  Hz, ArH), 5.74 (1H, dd,  $J = 7.2, 4.4$  Hz, 1-H), 5.21 (1H, dd,  $J = 13.6, 7.2$  Hz, 2-H), 4.83 (1H, dd,  $J = 13.6, 4.4$  Hz, 2-H), 4.82 (1H, d,  $J = 17.2$  Hz,  $\text{NCH}_2\text{CO}$ ), 4.55 (1H, d,  $J = 17.2$  Hz,  $\text{NCH}_2\text{CO}$ ), 3.79 (3H, s,  $\text{N}(\text{CH}_3)_2$ ), 3.56 (3H, s,  $\text{N}(\text{CH}_3)_2$ ), 2.09 (3H, s,  $\text{COCH}_3$ ), 1.51 (9H, s,  $t\text{Bu}$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  169.5, 163.8, 132.8, 132.7 (br), 127.9, 126.0, 85.6, 72.9, 61.8, 61.1, 50.2, 49.8, 27.9, 20.8; HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{27}\text{BrNO}_4$  [ $\text{M} - \text{Br}$ ] $^+$  400.1118, found 400.1108.

**2-Acetoxy-N-(2'-(tert-butoxy)-2'-oxoethyl)-N,N-dimethyl-1-(p-tolyl)ethanaminium bromide (6d):**



Prepared from *p*-tolubenzaldehyde by the same procedure with **6b** in 28% overall yield; colourless gum; IR (film)  $\nu_{\max}/\text{cm}^{-1}$  2980, 2930, 2764, 1735, 1614, 1516, 1473, 1456, 1396, 1369, 1222, 1153, 1082, 1044, 983, 924, 868, 826, 784, 759, 729;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (2H, d,  $J = 7.6$  Hz, ArH), 7.30 (2H, d,  $J = 7.6$  Hz, ArH), 5.62 (1H, dd,  $J = 7.3, 4.1$  Hz, 1-H), 5.20 (1H, dd,  $J = 13.4, 7.3$  Hz, 2-H), 4.85 (1H, d,  $J = 17.2$  Hz,  $\text{NCH}_2\text{CO}$ ), 4.82 (1H, dd,  $J = 13.4, 4.1$  Hz, 2-H), 4.47 (1H, d,  $J = 17.2$  Hz,  $\text{NCH}_2\text{CO}$ ), 3.78 (3H, s,  $\text{N}(\text{CH}_3)_2$ ), 3.54 (3H, s,  $\text{N}(\text{CH}_3)_2$ ), 2.40 (3H, s, ArCH<sub>3</sub>), 2.09 (3H, s,  $\text{COCH}_3$ ), 1.52 (9H, s,  $t\text{Bu}$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  169.2, 163.5, 141.2, 130.4 (br), 129.8, 125.5, 84.8, 73.2, 61.5, 61.1, 49.7, 49.3, 27.5, 20.8, 20.5; HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{30}\text{NO}_4$  [ $\text{M} - \text{Br}$ ] $^+$  336.2169, found 336.2159.

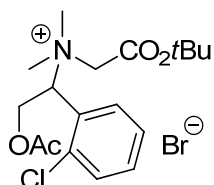
**2-Acetoxy-N-(2'-(tert-butoxy)-2'-oxoethyl)-1-(4''-methoxyphenyl)-N,N-dimethylethanaminium bromide (6e)**



A solution of trimethylsulfonium iodide (1.26 g, 6.17 mmol) in DMSO (8.0 mL) was treated with NaH (0.25 g, 6.3 mmol) at 0 °C under an argon atmosphere and stirred for 30 min at the same temperature. A solution of *p*-anisaldehyde (0.61 mL, 5.0 mmol) in DMSO (1.5 mL) was added to the mixture and stirred for 16.5 h at room temperature. The resulting mixture was diluted with  $\text{H}_2\text{O}$  and extracted with toluene. The combined extracts were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and evaporated. The residue was purified by bulb-to-bulb distillation under reduced pressure (3 to 5 mmHg, 150 to 160 °C) to obtain 2-(4-methoxyphenyl)oxirane (**19e**) (610 mg, 81% yield) as a colourless oil. The following procedure was the same with **6b**. The compound **6e** was prepared from **19e** in 23% overall yield. Colourless gum; IR (film)  $\nu_{\max}/\text{cm}^{-1}$  2977, 2928, 2839, 2764, 1736, 1610, 1582, 1516, 1460, 1396, 1369, 1311, 1222, 1186, 1152, 1082, 1029, 983, 924, 839, 780, 759, 729;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (2H, d,  $J = 6.4$  Hz, ArH), 7.00 (2H, d,  $J = 6.4$  Hz, ArH),

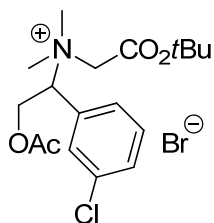
5.67-5.58 (1H, m, 1-H), 5.16 (1H, dd,  $J = 13.6, 7.6$  Hz, 2-H), 4.87-4.74 (1H, m, 2-H), 4.81 (1H, d,  $J = 17.2$  Hz, NCH<sub>2</sub>CO), 4.47 (1H, d,  $J = 17.2$  Hz, NCH<sub>2</sub>CO), 3.85 (3H, s, OCH<sub>3</sub>), 3.76 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 3.52 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 2.10 (3H, s, COCH<sub>3</sub>), 1.52 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.3, 163.7, 161.2, 132.2 (br), 120.3, 114.6, 85.0, 73.2, 61.5, 61.2, 55.2, 49.7, 49.3, 27.7, 20.7; HRMS (ESI): calcd for C<sub>19</sub>H<sub>30</sub>NO<sub>5</sub> [M – Br]<sup>+</sup> 352.2118, found 352.2108.

**2-Acetoxy-*N*-(2'-(*tert*-butoxy)-2'-oxoethyl)-1-(2''-chlorophenyl)-*N,N*-dimethylethanaminium bromide**



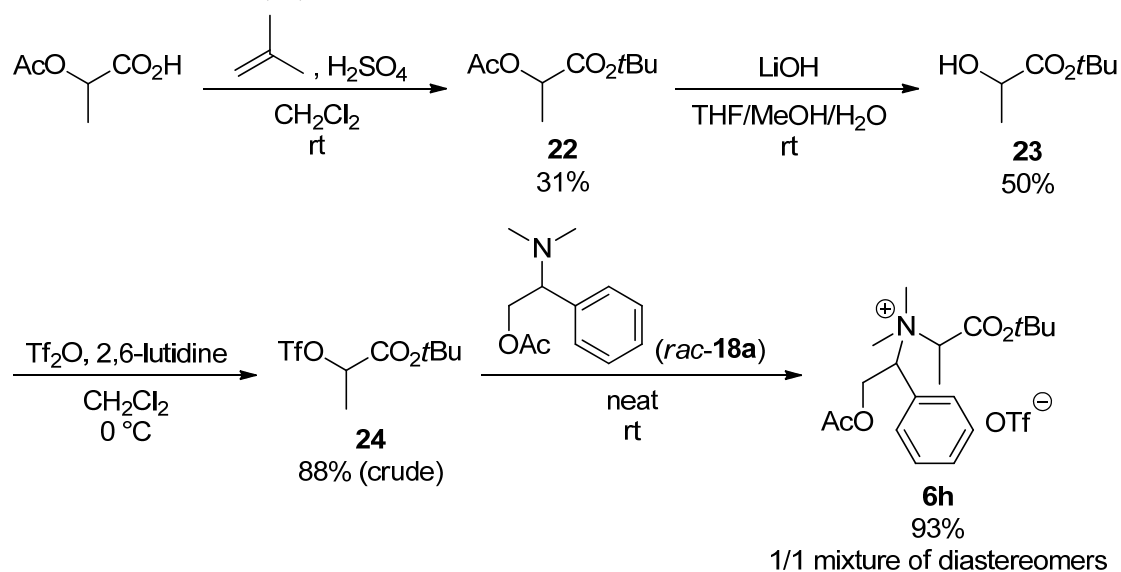
**(6f):** Prepared from 2-chlorobenzaldehyde by the same procedure with **6b** in 30% overall yield; colourless gum; IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$  2979, 2928, 2771, 1741, 1636, 1591, 1478, 1418, 1396, 1367, 1243, 1150, 1042, 982, 924, 870, 842, 763, 732; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.84-7.78 (1H, m, ArH), 7.59-7.53 (1H, m, ArH), 7.53-7.46 (2H, m, ArH), 6.17 (1H, dd,  $J = 8.0, 3.3$  Hz, 1-H), 5.40 (1H, dd,  $J = 13.9, 8.0$  Hz, 2-H), 5.03 (1H, d,  $J = 17.4$  Hz, NCH<sub>2</sub>CO), 4.88 (1H, d,  $J = 17.4$  Hz, NCH<sub>2</sub>CO), 4.75 (1H, dd,  $J = 13.9, 3.3$  Hz, 2-H), 3.88 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 3.54 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 2.10 (3H, s, COCH<sub>3</sub>), 1.55 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.3, 163.6, 136.0, 132.1, 132.0, 130.6, 127.8, 127.0, 85.0, 67.9, 61.9, 61.7, 50.6, 49.6, 27.7, 20.6; HRMS (ESI): calcd for C<sub>18</sub>H<sub>27</sub>ClNO<sub>4</sub> [M – Br]<sup>+</sup> 356.1623, found 356.1613.

**2-Acetoxy-*N*-(2'-(*tert*-butoxy)-2'-oxoethyl)-1-(3''-chlorophenyl)-*N,N*-dimethylethanaminium bromide**



**(6g):** Prepared from 3-chlorobenzaldehyde by the same procedure with **6b** in 21% overall yield; colourless gum; IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$  2981, 2933, 2774, 1738, 1627, 1596, 1573, 1477, 1396, 1369, 1222, 1152, 1088, 1045, 982, 922, 873, 841, 828, 801, 761, 728; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.61 (1H, d,  $J = 7.2$  Hz, ArH), 7.57-7.46 (3H, m, ArH), 5.68 (1H, br, 1-H), 5.22 (1H, dd,  $J = 13.6, 7.2$  Hz, 2-H), 4.96 (1H, d,  $J = 17.2$  Hz, NCH<sub>2</sub>CO), 4.83 (1H, dd,  $J = 13.6, 4.4$  Hz, 2-H), 4.44 (1H, br d,  $J = 17.2$  Hz, NCH<sub>2</sub>CO), 3.86 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 3.61 (3H, s, N(CH<sub>3</sub>)<sub>2</sub>), 2.11 (3H, s, COCH<sub>3</sub>), 1.53 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.5, 163.7, 135.1, 131.3, 130.93, 130.89, 85.4, 72.8, 61.9, 61.1, 50.2, 49.9, 27.8, 20.7; HRMS (ESI): calcd for C<sub>18</sub>H<sub>27</sub>ClNO<sub>4</sub> [M – Br]<sup>+</sup> 356.1623, found 356.1616.

***N*-(2'-Acetoxy-1'-phenylethyl)-1-(*tert*-butoxy)-*N,N*-dimethyl-1-oxopropan-2-aminium trifluoromethanesulfonate (**6h**)**



(Step 1) A mixture of the ( $\pm$ )-2-acetoxypropionic acid (1.94 g, 14.7 mmol), conc. H<sub>2</sub>SO<sub>4</sub> (0.15 mL) and isobutene (excess) in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) was stirred for 18 h at room temperature. The resulting mixture was treated with saturated NaHCO<sub>3</sub> aq. and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined extracts were washed brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 15/1 to 10/1 as the eluent) gave *tert*-butyl 2-acetoxypropanoate (**22**) (868 mg, 31% yield) as a colourless oil. (Step 2)<sup>6</sup> LiOH·H<sub>2</sub>O (193 mg, 4.60 mmol) was added to a solution of **22** (864 mg, 4.59 mmol) in THF (2.3 mL), MeOH (4.6 mL) and H<sub>2</sub>O (4.6 mL) at room temperature and the mixture was stirred for 2 h. The resulting mixture was treated with saturated NH<sub>4</sub>Cl aq. and extracted with EtOAc. The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 6/1 to 4/1 as the eluent) to give *tert*-butyl 2-hydroxypropanoate (**23**) (333 mg, 50% yield) as a colourless oil. (Step 3)<sup>7</sup> A solution of **23** (323 mg, 2.21 mmol) and 2,6-lutidine (0.38 mL, 3.3 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (11 mL) was treated with Tf<sub>2</sub>O (0.52 mL, 3.1 mmol) at 0 °C under an argon atmosphere and stirred for 1 h at the same temperature. The resulting mixture was diluted with *n*-hexane followed by 1 M HCl aq. and the mixture was extracted with *n*-hexane. The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated to afford *tert*-butyl 2-(((trifluoromethyl)sulfonyl)oxy)propanoate (**24**) (541 mg, 88% yield) as a brown oil which was used without purification. (Step 4) A mixture of **24** (541 mg, 1.94 mmol) and *rac*-**18a** (402 mg, 1.94 mmol, prepared by the same procedure with (*R*)-**18a** from DL-2-phenylglycine) was stirred for 36 h at room temperature. The resulting mixture (pale brown gum) was dissolved with CH<sub>2</sub>Cl<sub>2</sub> and purified by chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 20/1 to 10/1 as the eluent) to obtain **6h** (876 mg, 93% yield, 1/1 mixture of diastereomers) as a pale brown gum. IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$  3058, 2985, 2935, 1738, 1476, 1461, 1397, 1371, 1262, 1225, 1154,

<sup>6</sup> C.-N. Hsiao and T. Kolasa, *Tetrahedron Lett.*, 1992, **33**, 2629.

<sup>7</sup> A. M. Haydl and B. Breit, *Chem. Eur. J.*, 2017, **23**, 541.

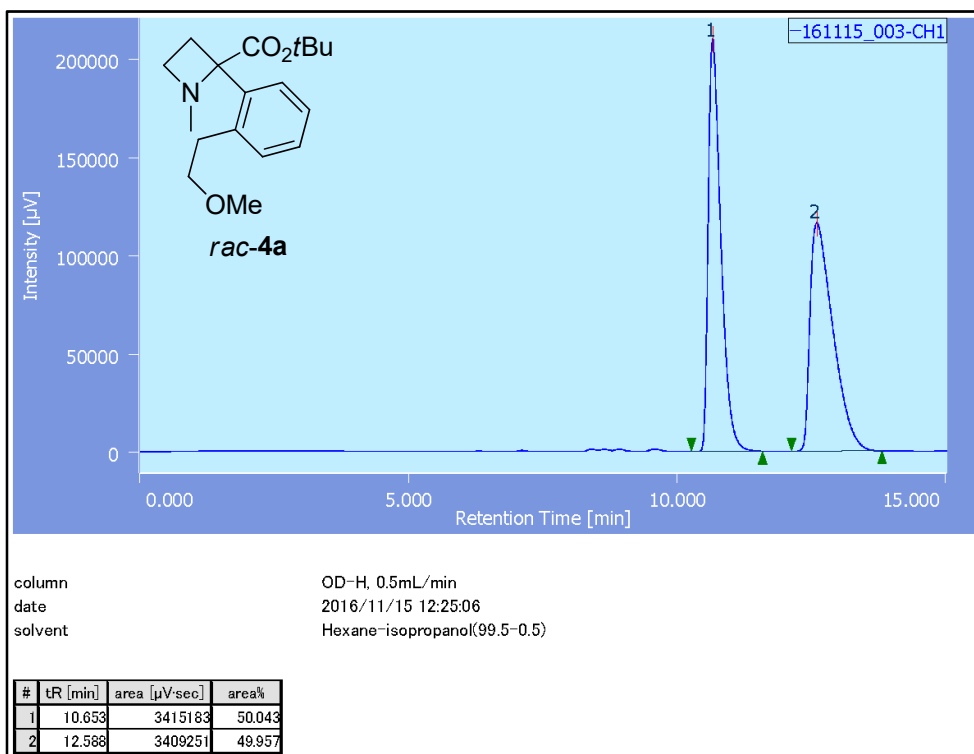
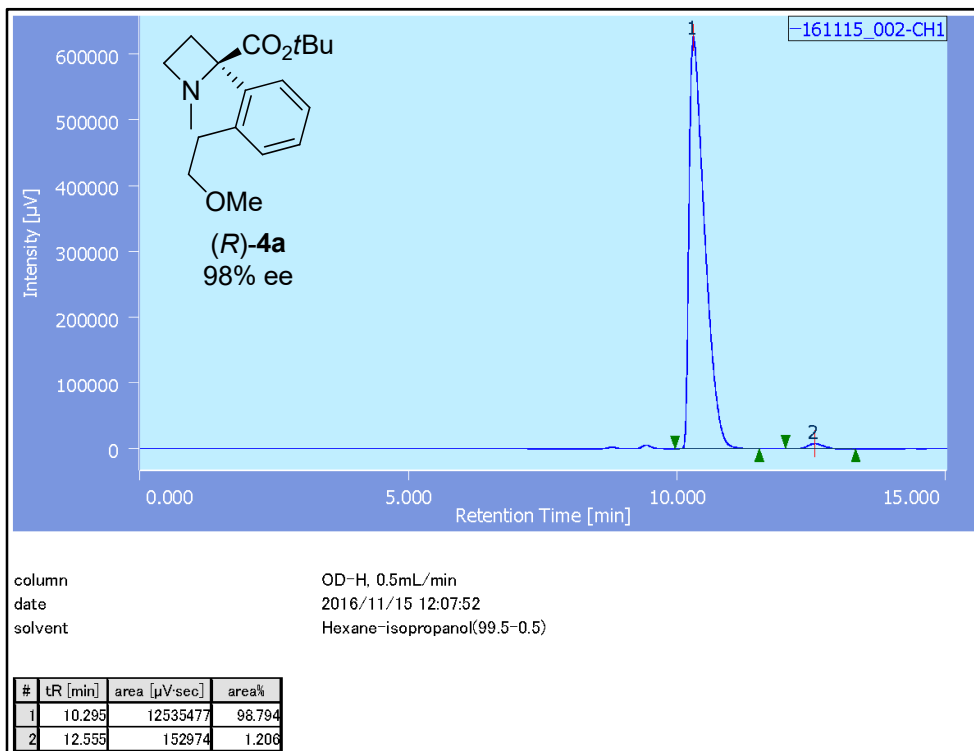


1095, 1079, 1031, 924, 840, 775, 755, 710;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60-7.45 (4.5H, m, Ph), 7.40-7.30 (0.5H, m, Ph), 5.30 (0.5H, dd,  $J = 7.1, 4.6$  Hz, 1'-H), 5.23 (0.5H, dd,  $J = 7.1, 4.6$  Hz, 1'-H), 5.00 (0.5H, dd,  $J = 13.6, 7.1$  Hz, 2'-H), 4.96 (0.5H, dd,  $J = 13.6, 7.1$  Hz, 2'-H), 4.80 (0.5H, dd,  $J = 10.7, 4.6$  Hz, 2'-H), 4.77 (0.5H, dd,  $J = 10.7, 4.6$  Hz, 2'-H), 4.44 (0.5H, q,  $J = 7.0$  Hz, NCHCO), 3.95 (0.5H, q,  $J = 7.0$  Hz, NCHCO), 3.49 (1.5H, s,  $\text{N}(\text{CH}_3)_2$ ), 3.39 (1.5H, s,  $\text{N}(\text{CH}_3)_2$ ), 3.22 (1.5H, s,  $\text{N}(\text{CH}_3)_2$ ), 3.12 (1.5H, s,  $\text{N}(\text{CH}_3)_2$ ), 2.08 (1.5H, s,  $\text{COCH}_3$ ), 2.07 (1.5H, s,  $\text{COCH}_3$ ), 1.80 (1.5H, d,  $J = 7.0$  Hz, 1- $\text{CH}_3$ ), 1.74 (1.5H, d,  $J = 7.0$  Hz, 1- $\text{CH}_3$ ), 1.53 (4.5H, s, *t*Bu), 1.52 (4.5H, s, *t*Bu);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  169.8, 169.7, 167.4, 167.0, 131.44, 131.41, 131.1 (br), 129.7, 129.0, 128.7, 128.5, 128.4, 120.7 (q,  $J = 319$  Hz), 85.73, 85.70, 74.9, 74.0, 68.6, 68.4, 61.5, 61.0, 46.9, 46.7, 46.3, 46.1, 27.73, 27.67, 20.7, 20.6, 13.6, 13.1; HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{30}\text{NO}_4$  [ $\text{M} - \text{OTf}$ ] $^+$  336.2169, found 336.2164.

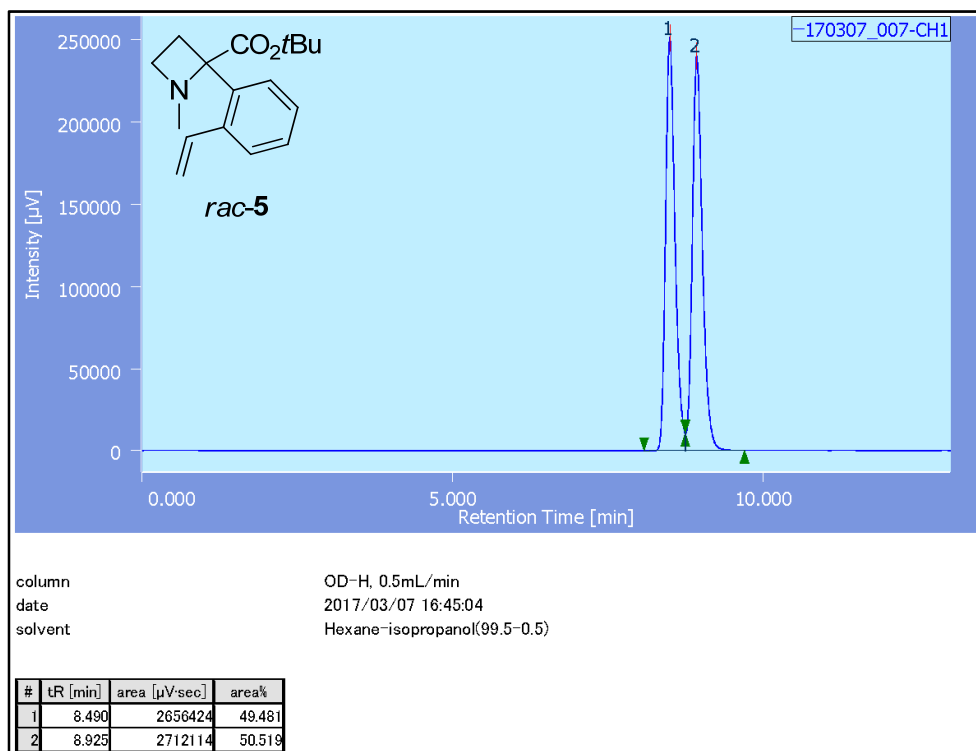
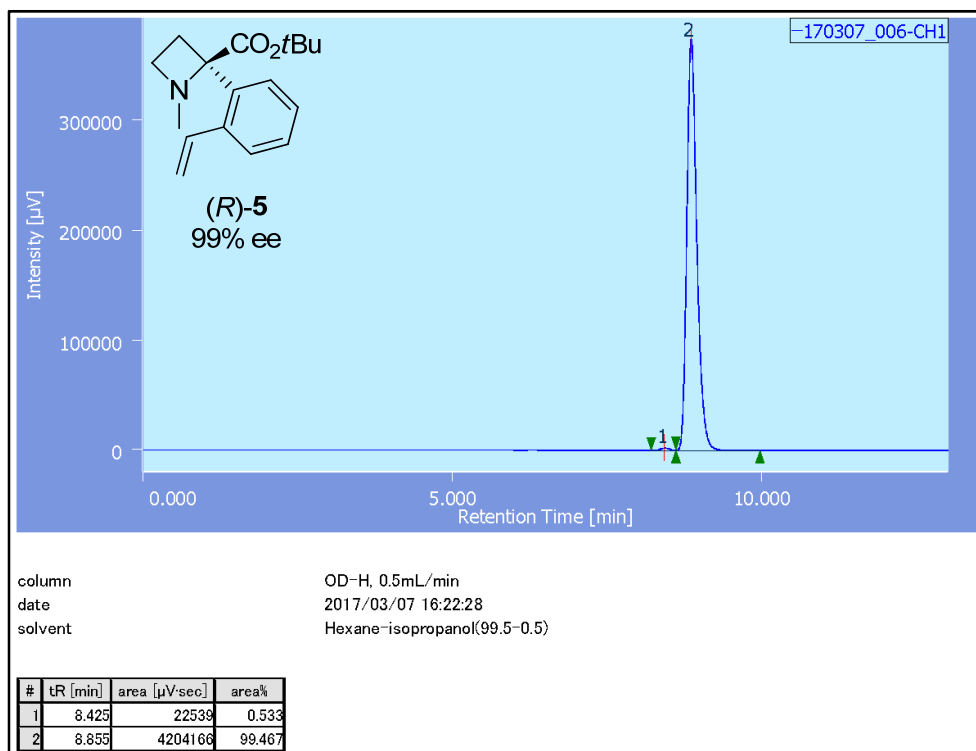
### 3. HPLC chromatogram for determination of ee

The ee were determined by HPLC analysis using chiral column in comparison with the racemic compounds.

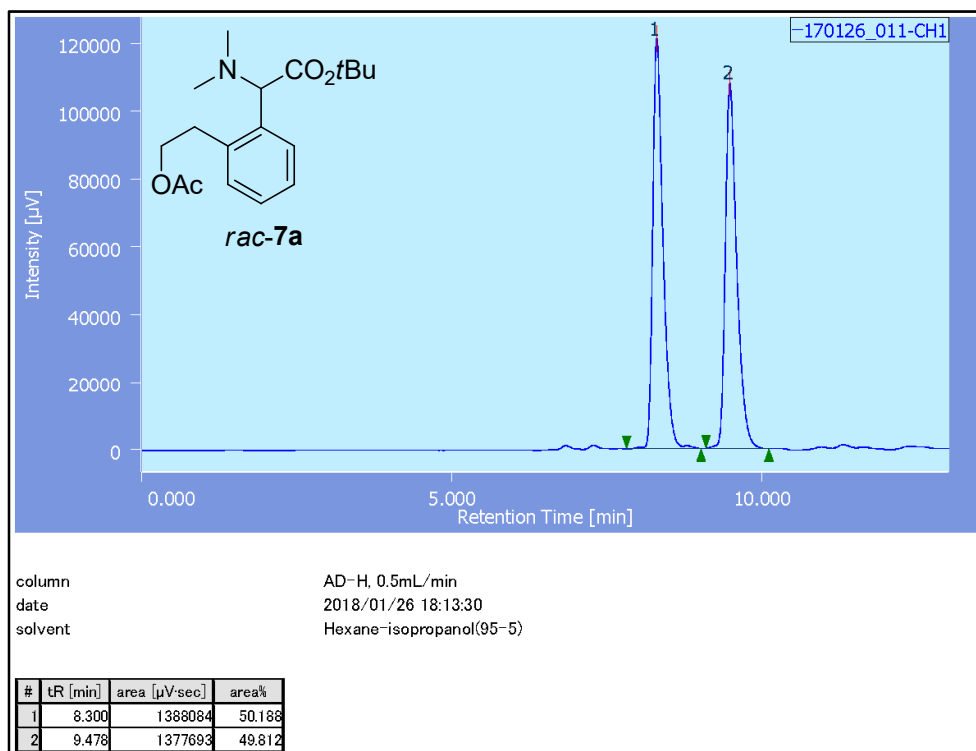
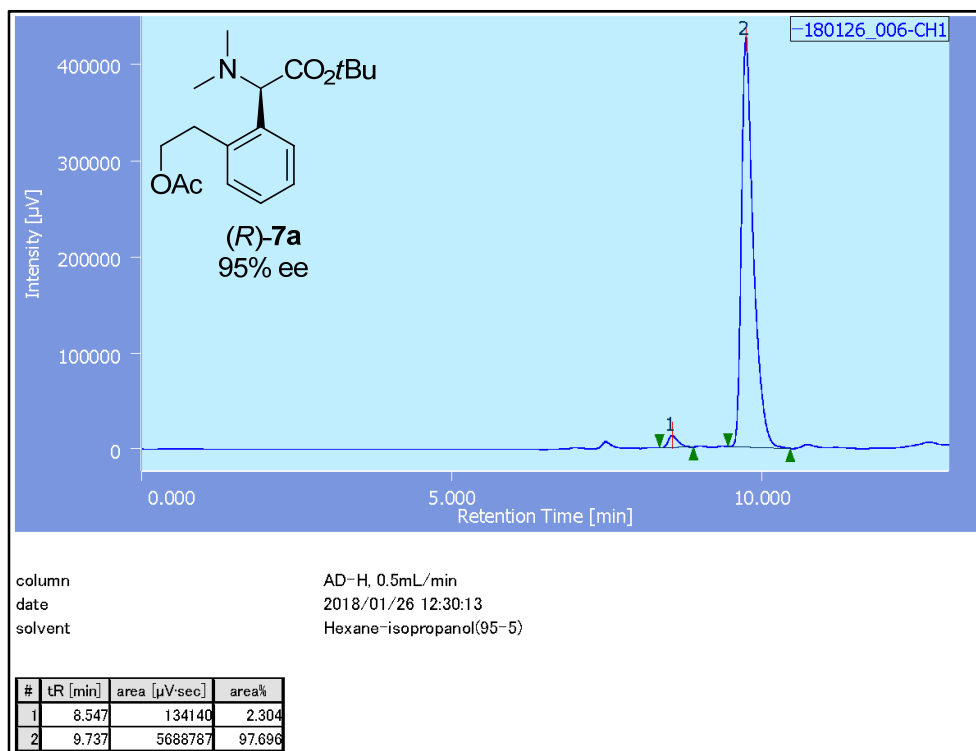
(*R*)-**4a** (98% ee): Daicel Chiralcel OD-H column (25 cm), *n*-hexane/*i*PrOH = 99.5/0.5 as the eluent, flow rate = 0.50 mL/min,  $t_R$  = 10.3 min for (*R*)-**4a** (98.8%) and 12.6 min for (*S*)-**4a** (1.2%)



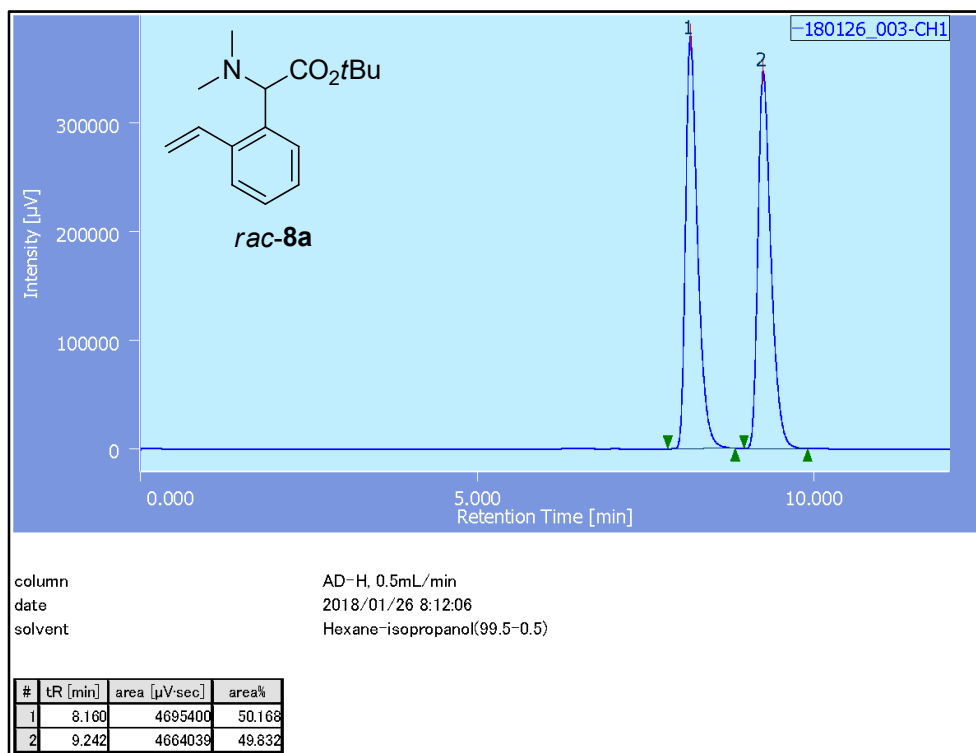
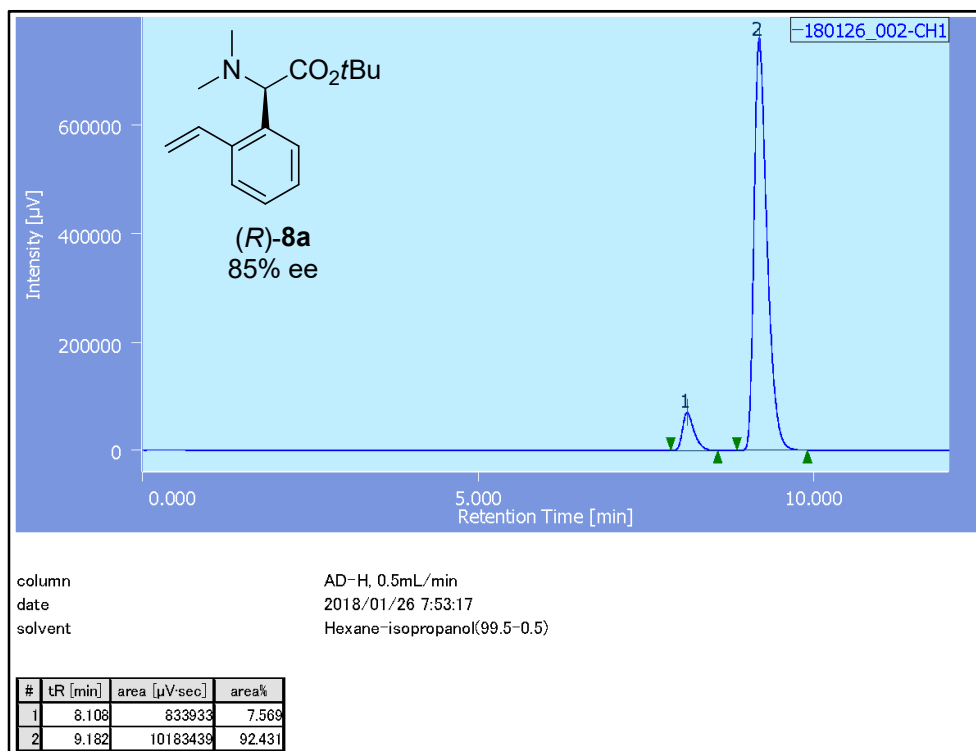
(*R*)-**5** (99% ee): Daicel Chiralcel OD-H column (25 cm), *n*-hexane/*i*PrOH = 99.5/0.5 as the eluent, flow rate = 0.50 mL/min,  $t_R = 8.4$  min for (*S*)-**5** (0.5%) and 8.9 min for (*R*)-**5** (99.5%)]



(*R*)-**7a**: 95% ee [determined by HPLC analysis: Daicel Chiralpak AD-H column (25 cm), *n*-hexane/*i*PrOH = 95/5 as the eluent, flow rate = 0.50 mL/min,  $t_R$  = 8.5 min for (*S*)-**7a** (2.3%) and 9.7 min for (*R*)-**7a** (97.7%)]

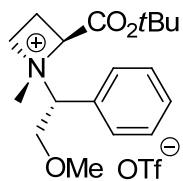


(*R*)-**8a** (85% ee): Daicel Chiralpak AD-H column (25 cm), *n*-hexane/*i*PrOH = 99.5/0.5 as the eluent, flow rate = 0.50 mL/min,  $t_R$  = 8.1 min for (*S*)-**8a** (7.6%) and 9.2 min for (*R*)-**8a** (92.4%)



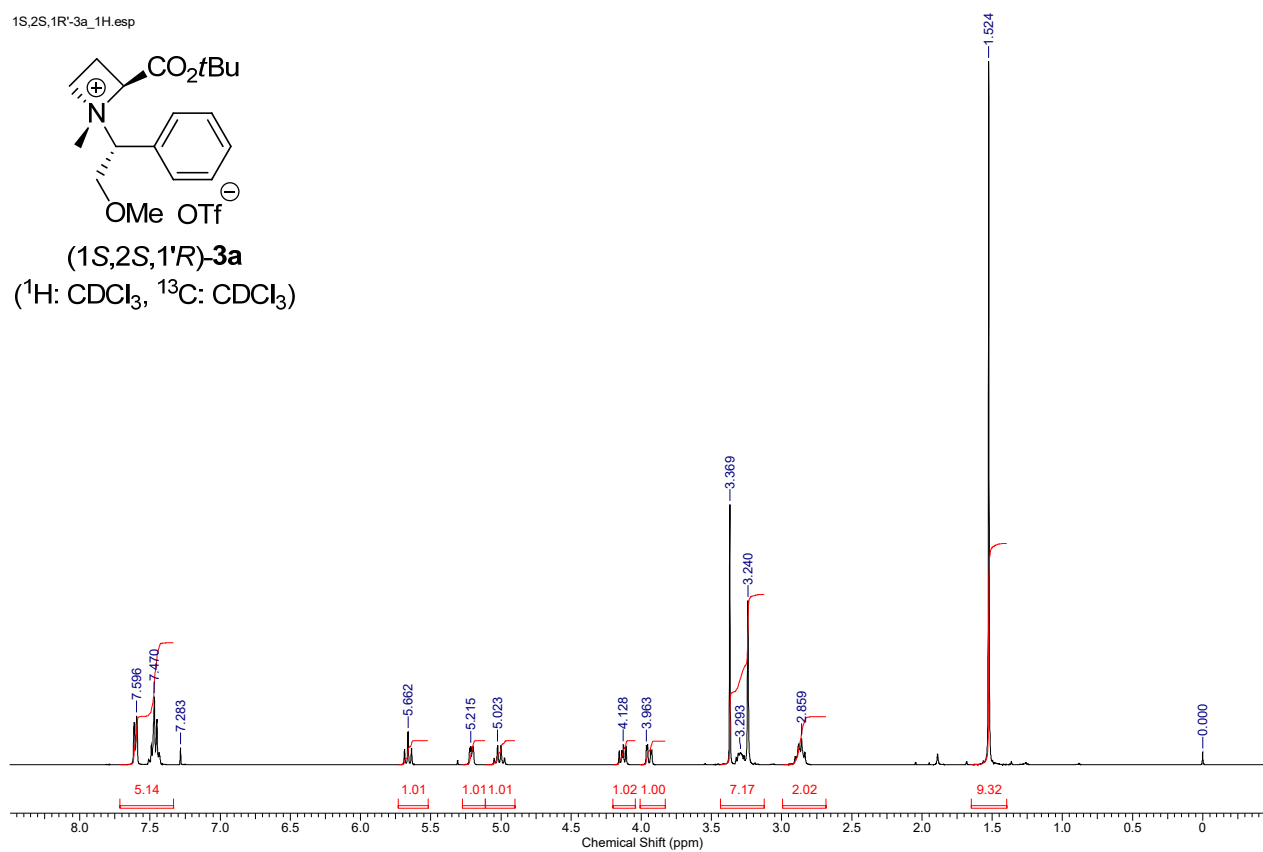
## 4. Copies of $^1\text{H}$ and $^{13}\text{C}$ NMR spectra

1S,2S,1R'-3a\_1H.esp

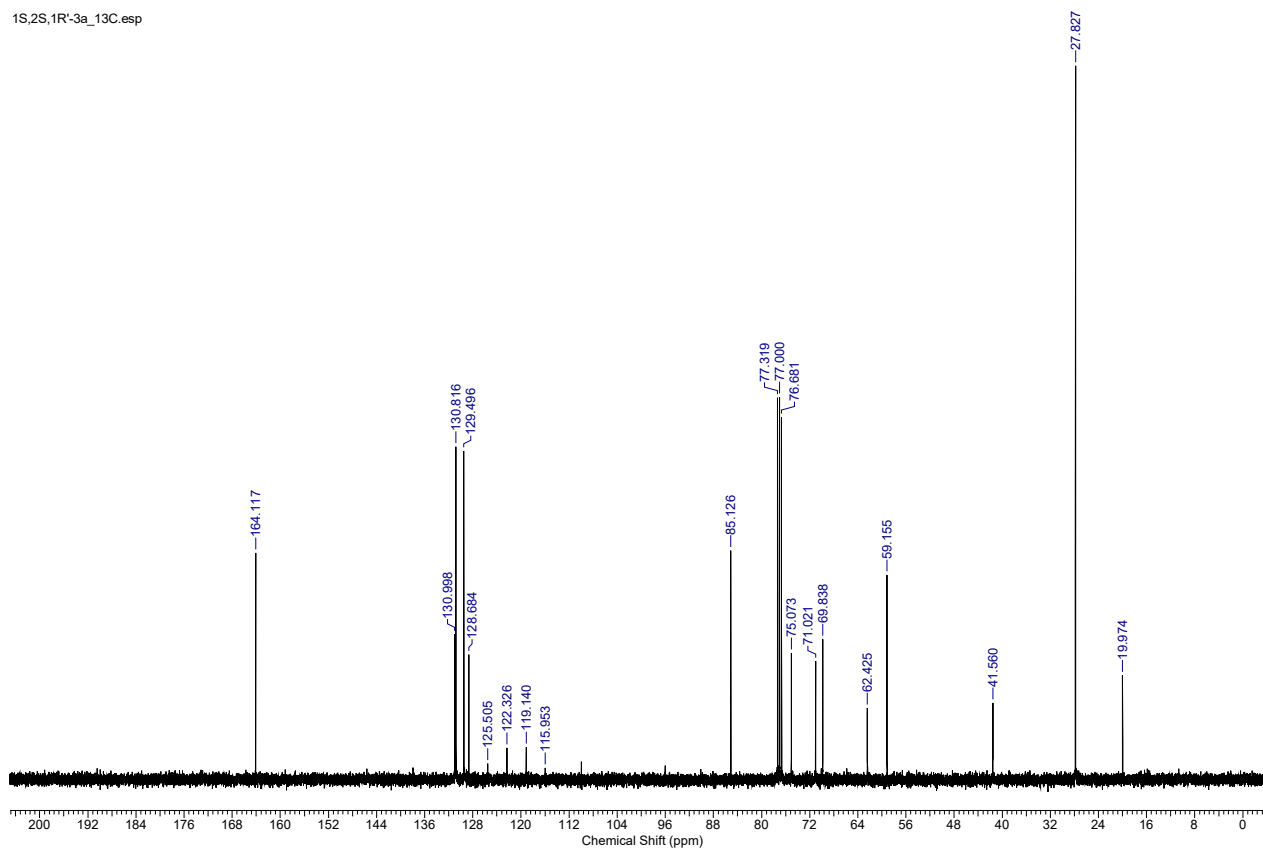


(1S,2S,1'R)-3a

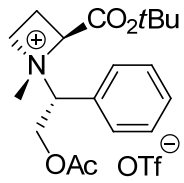
( $^1\text{H}$ :  $\text{CDCl}_3$ ,  $^{13}\text{C}$ :  $\text{CDCl}_3$ )



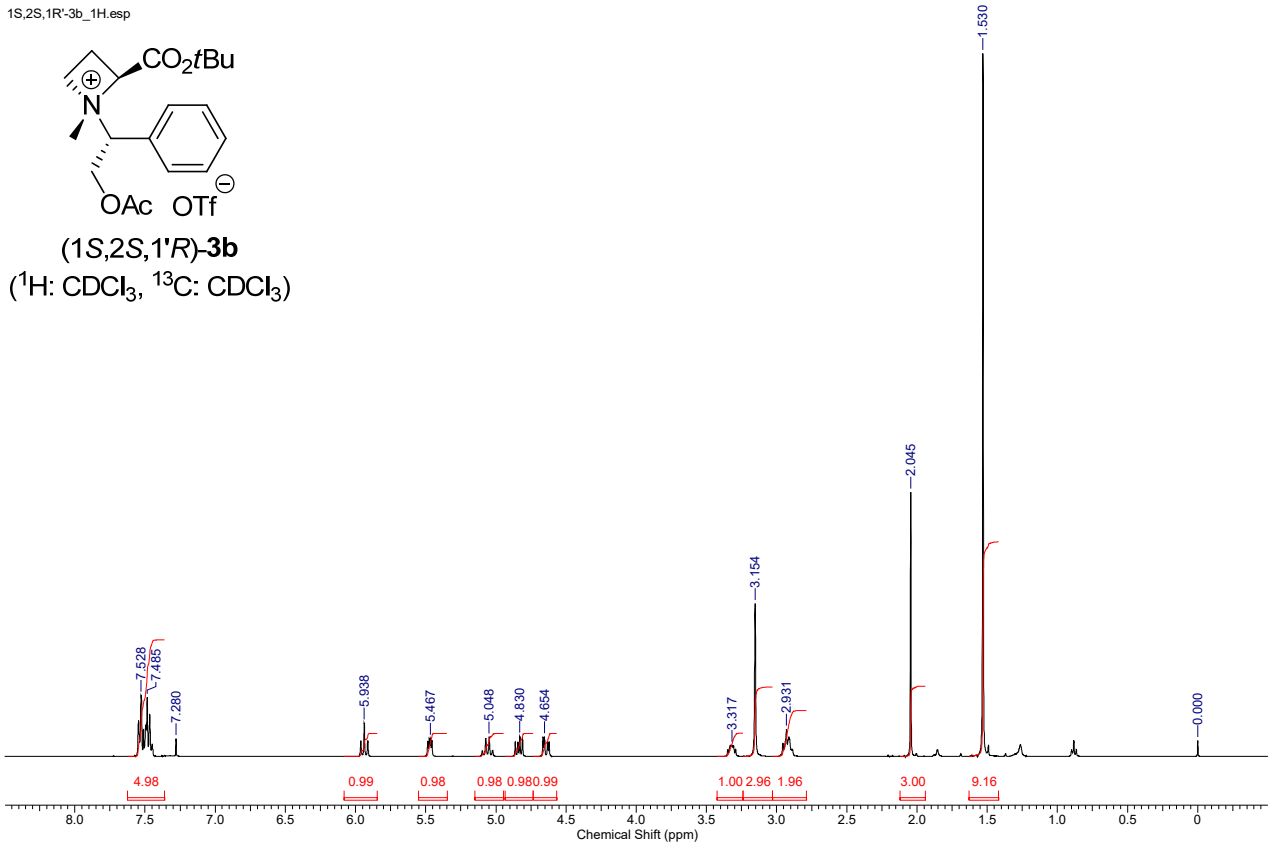
1S,2S,1R'-3a\_13C.esp



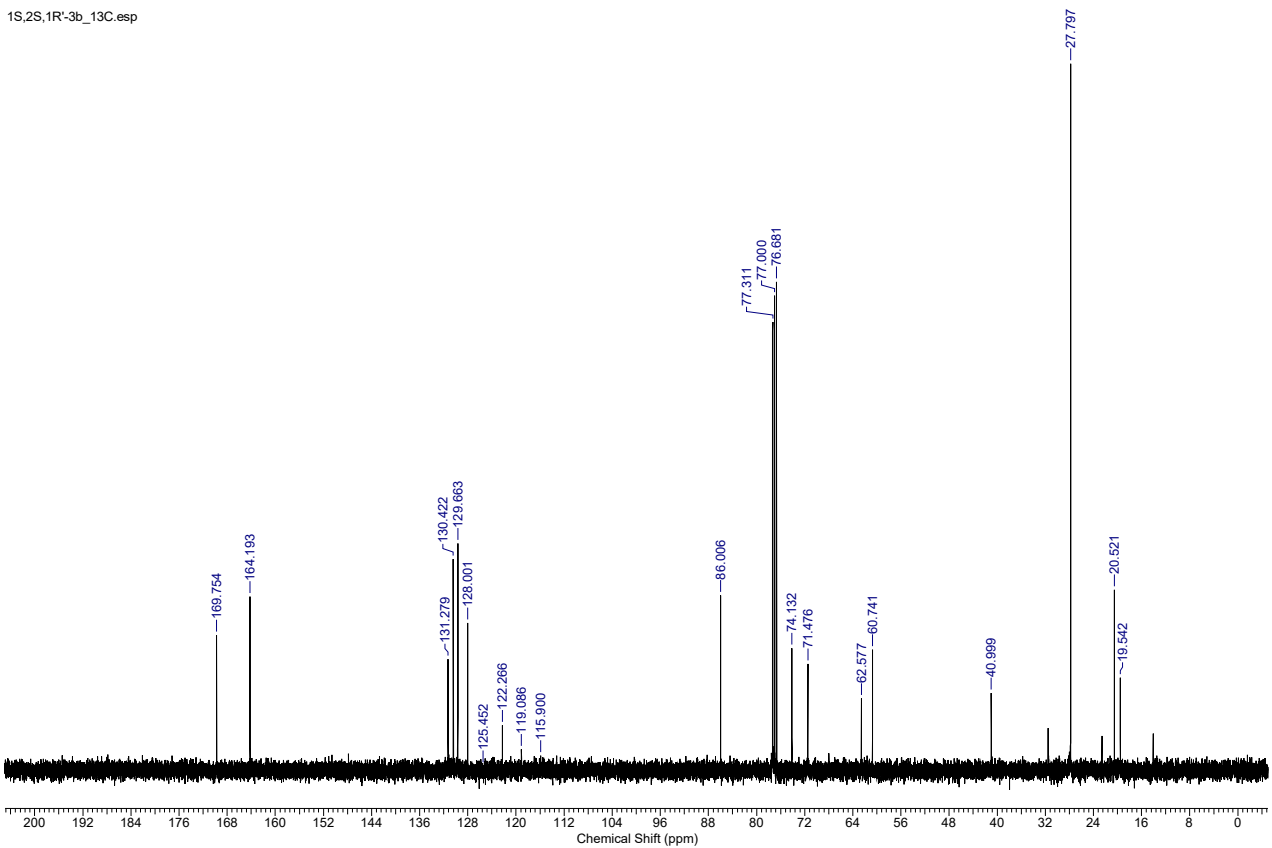
1S,2S,1R'-3b\_1H.esp



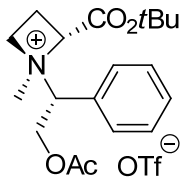
(1S,2S,1'R)-**3b**  
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



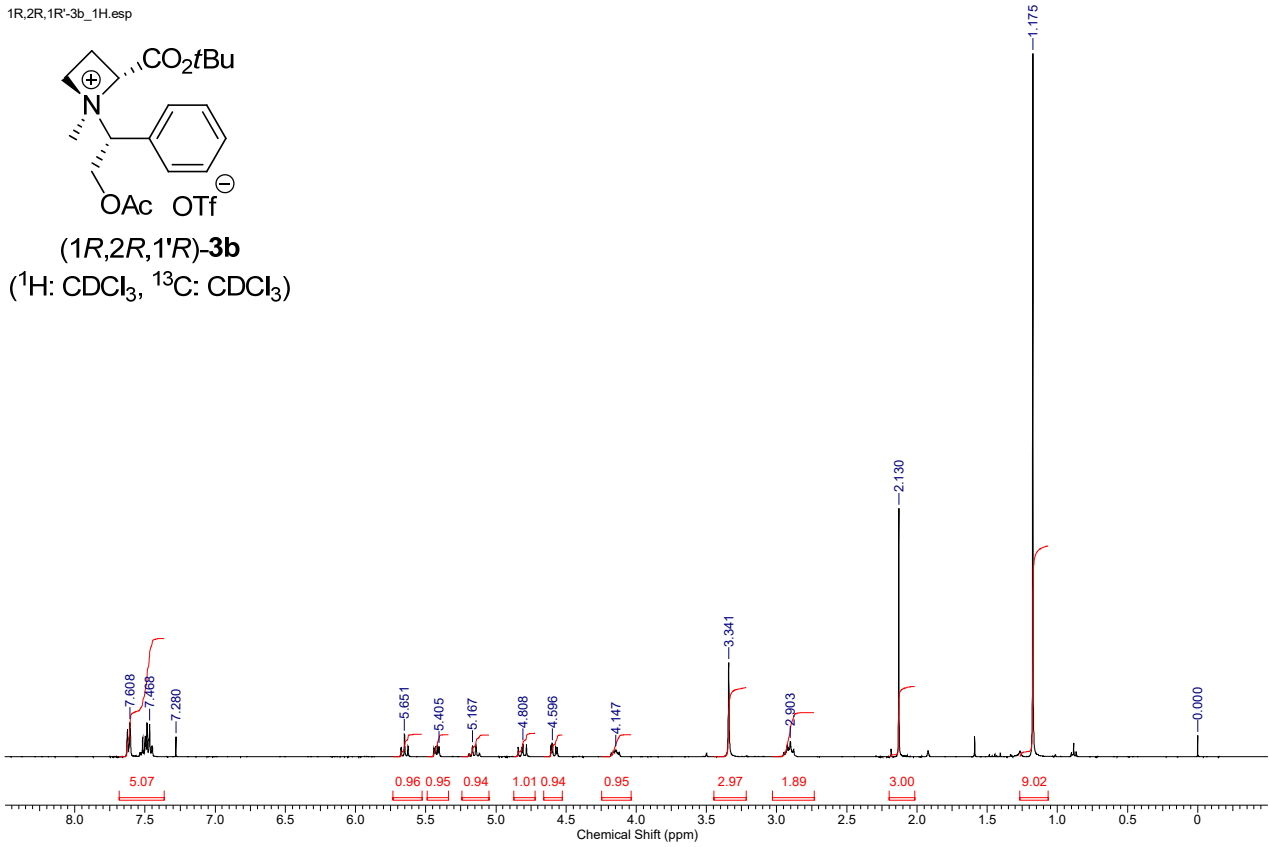
1S,2S,1R'-3b\_13C.esp



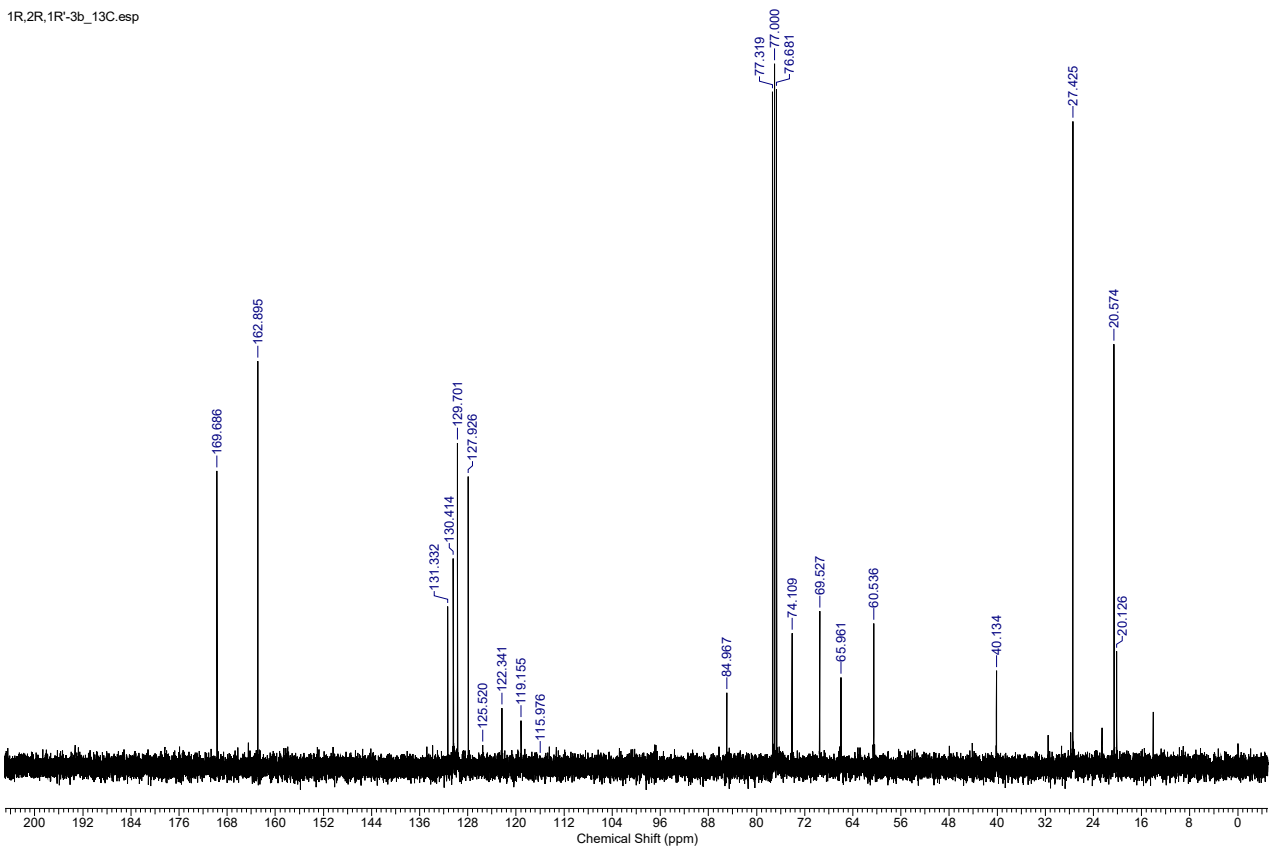
1R,2R,1R'-3b\_1H.esp



(1R,2R,1'R)-3b  
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)

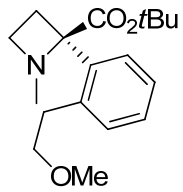


1R,2R,1R'-3b\_13C.esp



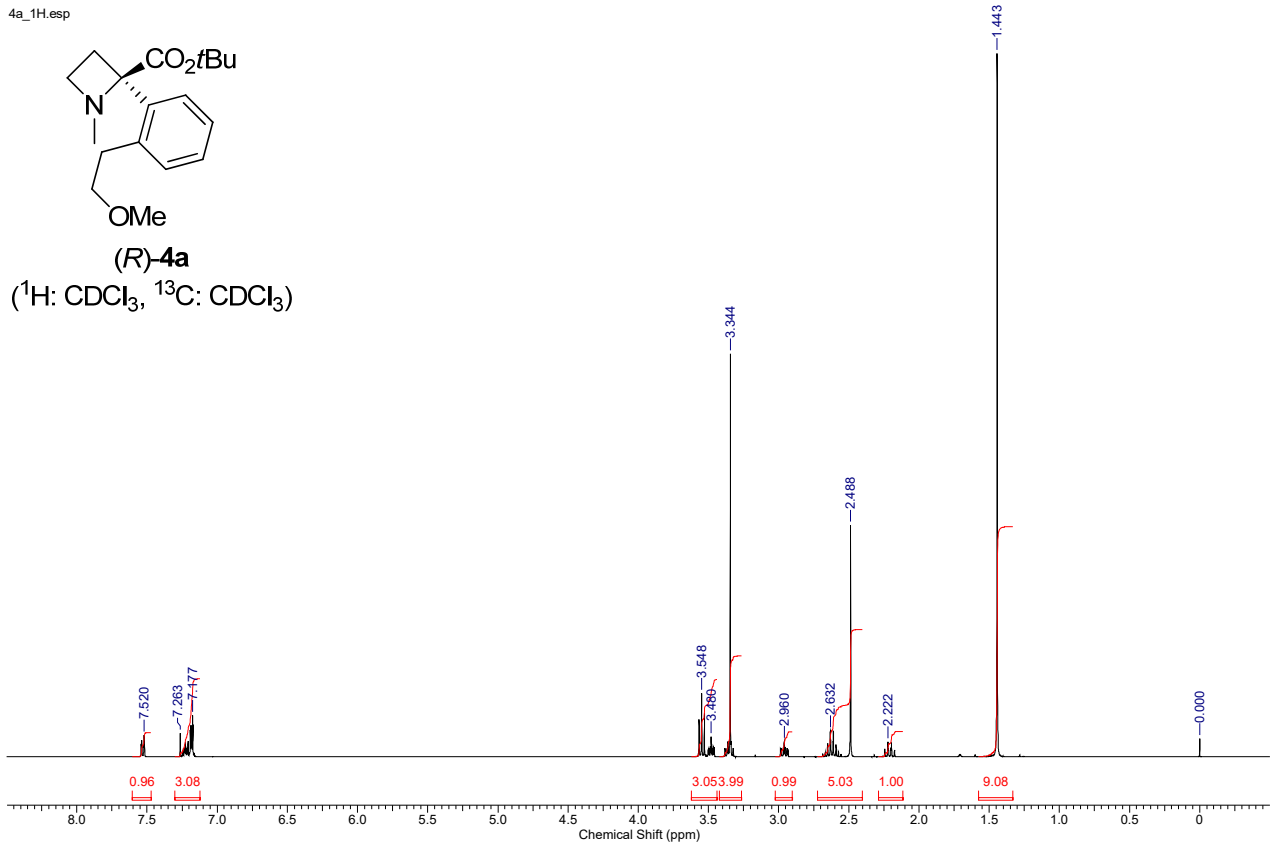


4a\_1H.esp

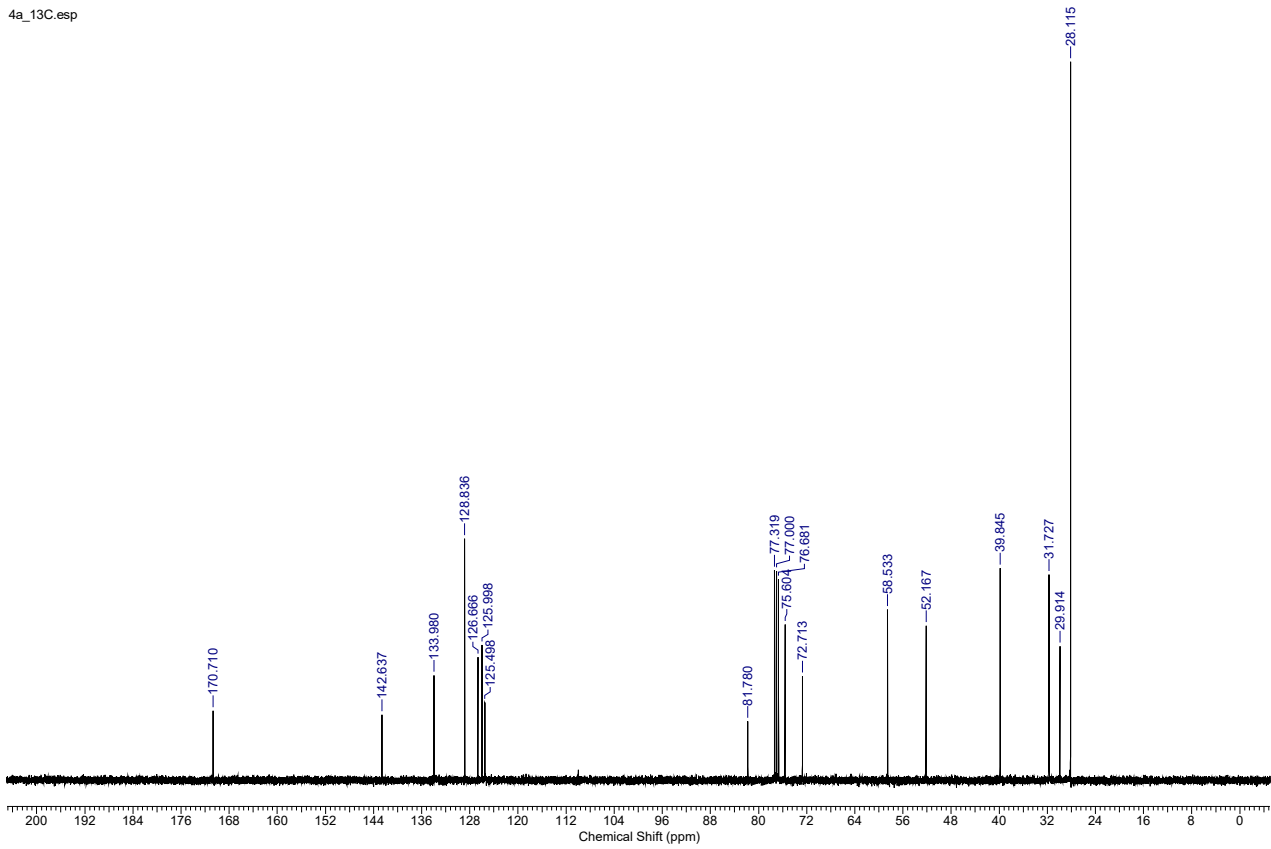


(R)-4a

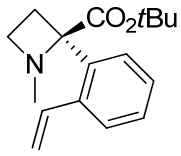
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



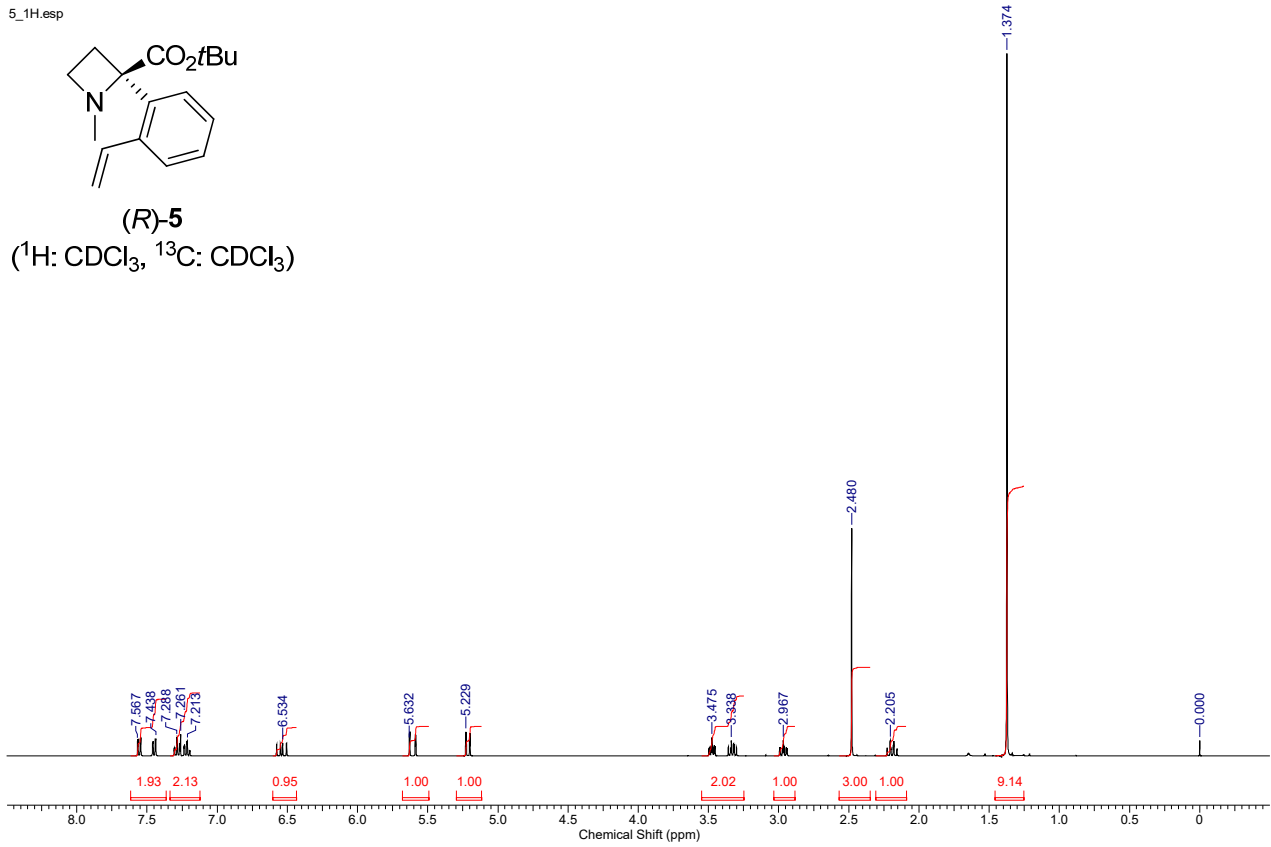
4a\_13C.esp



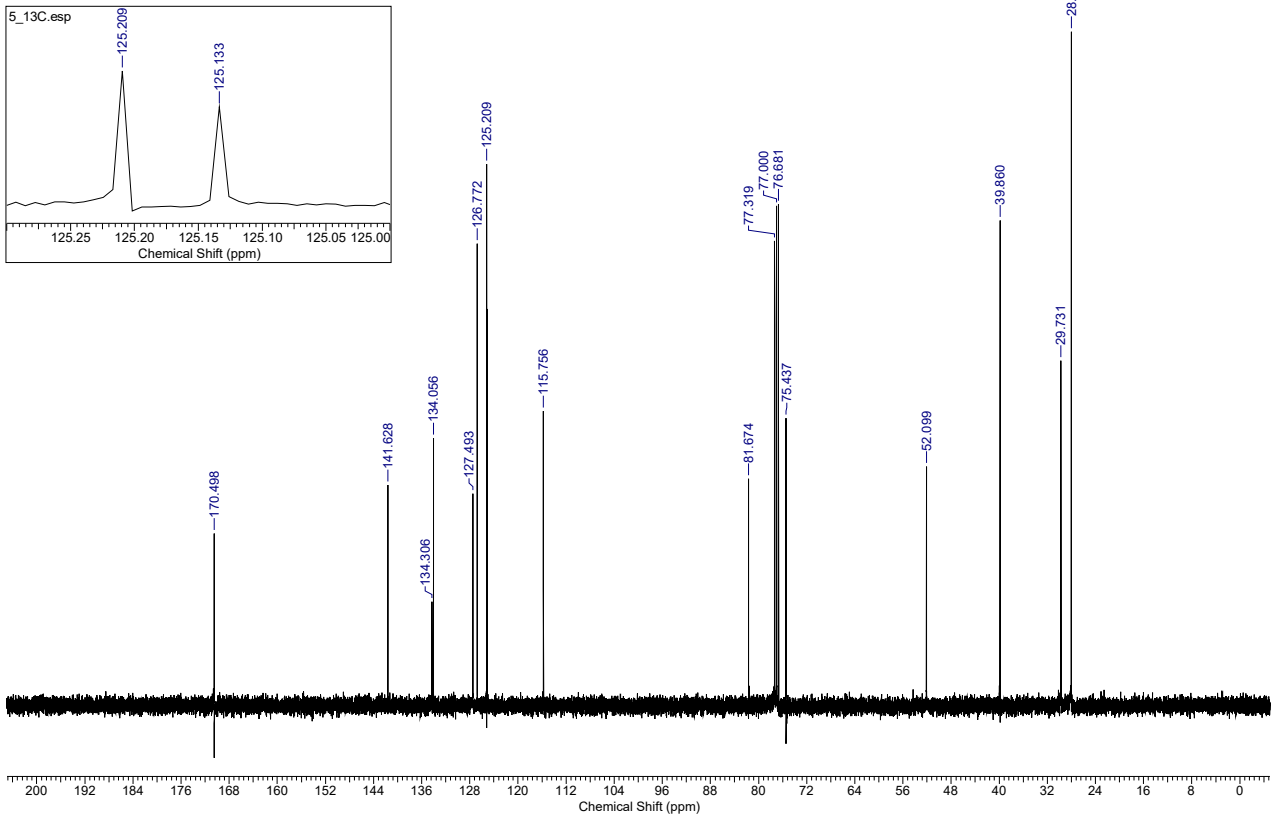
5\_1H.esp



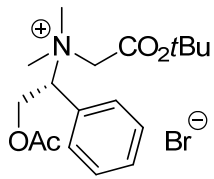
(R)-5  
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



5\_13C.esp

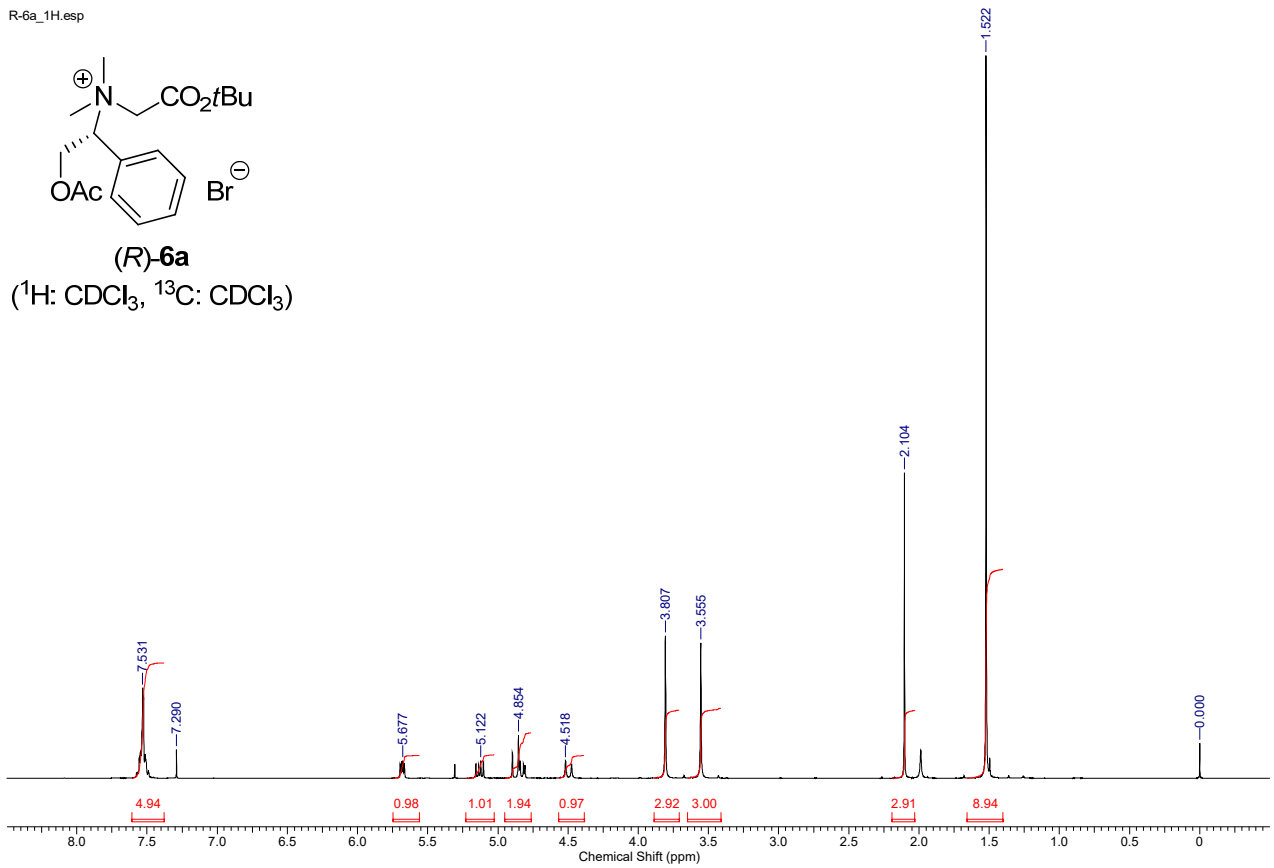


R-6a\_1H.esp



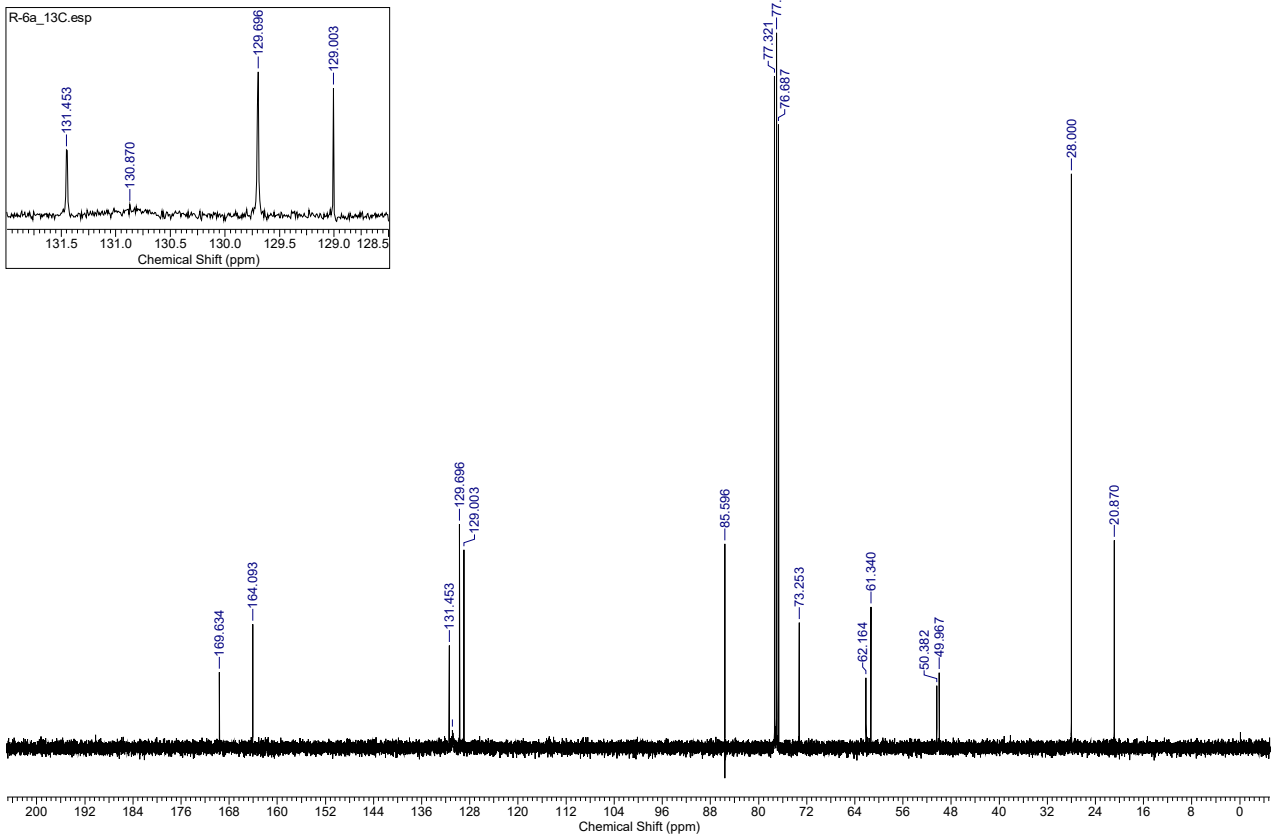
(R)-6a

(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)

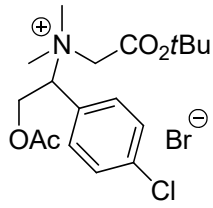


R-6a\_13C.esp

R-6a\_13C.esp

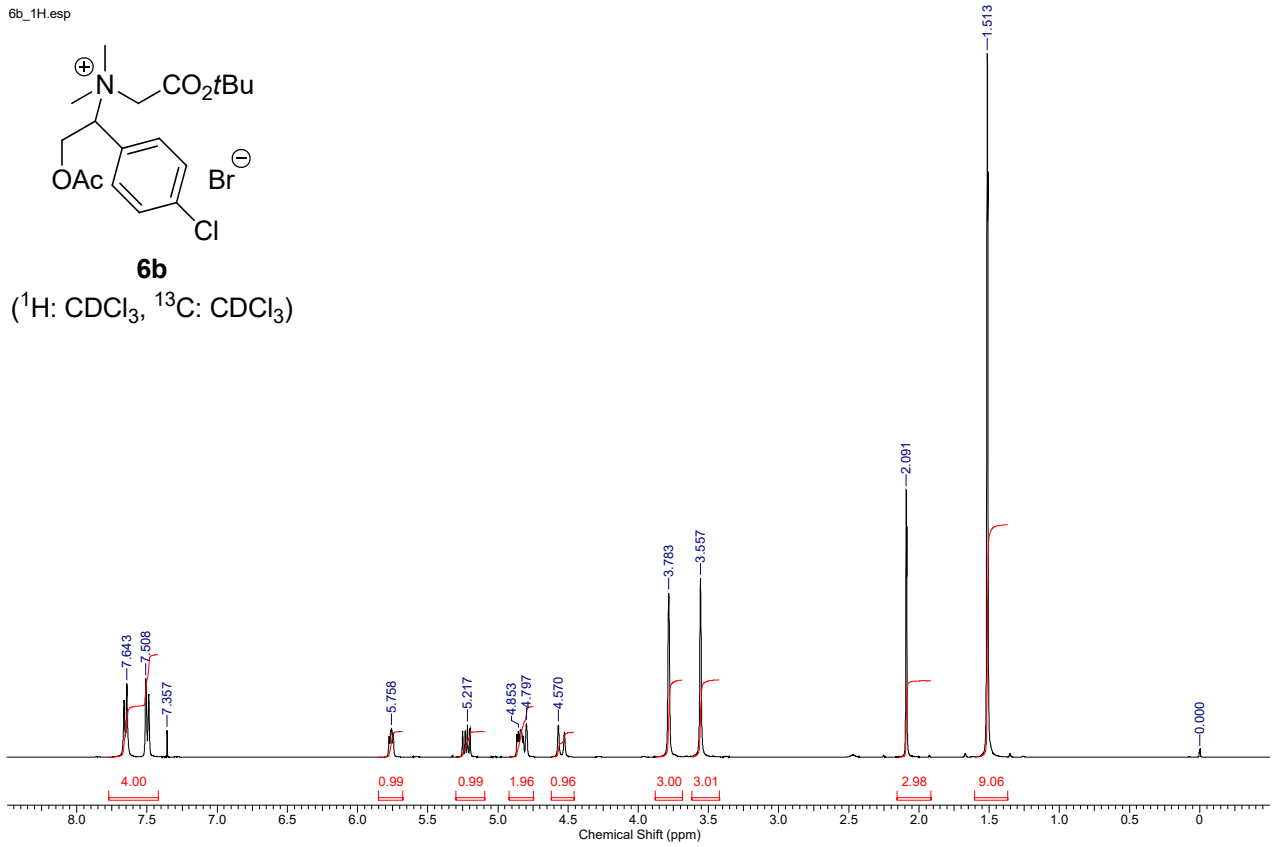


6b\_1H.esp

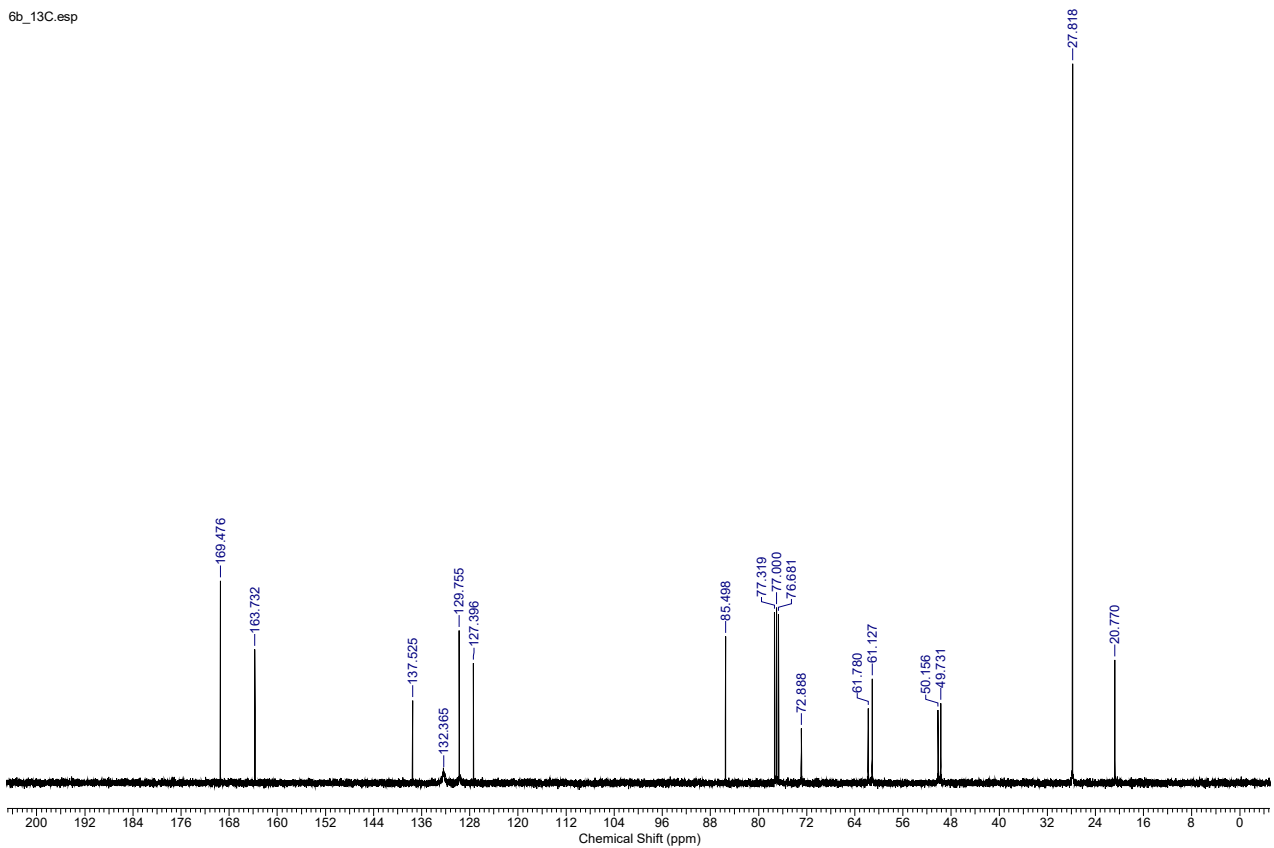


**6b**

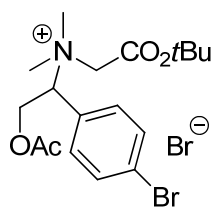
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



6b\_13C.esp

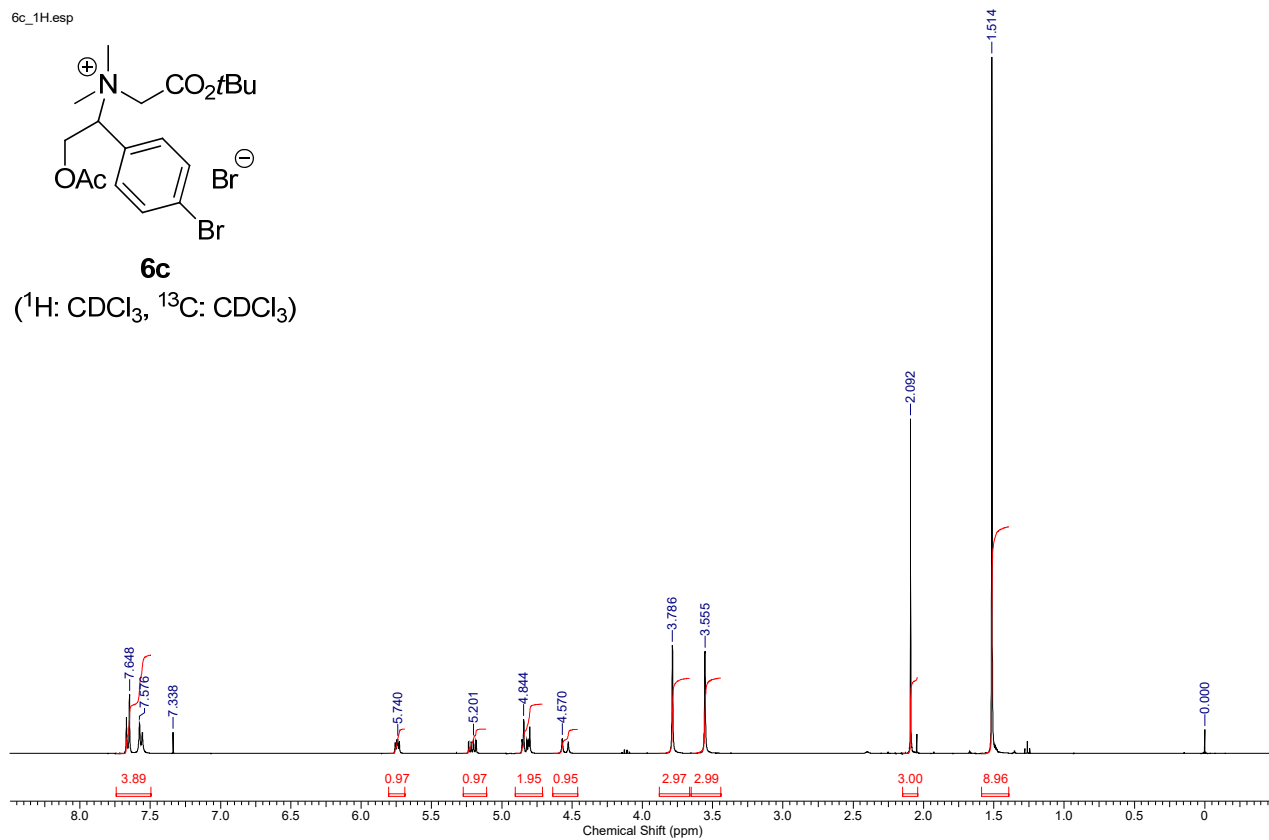


6c\_1H.esp

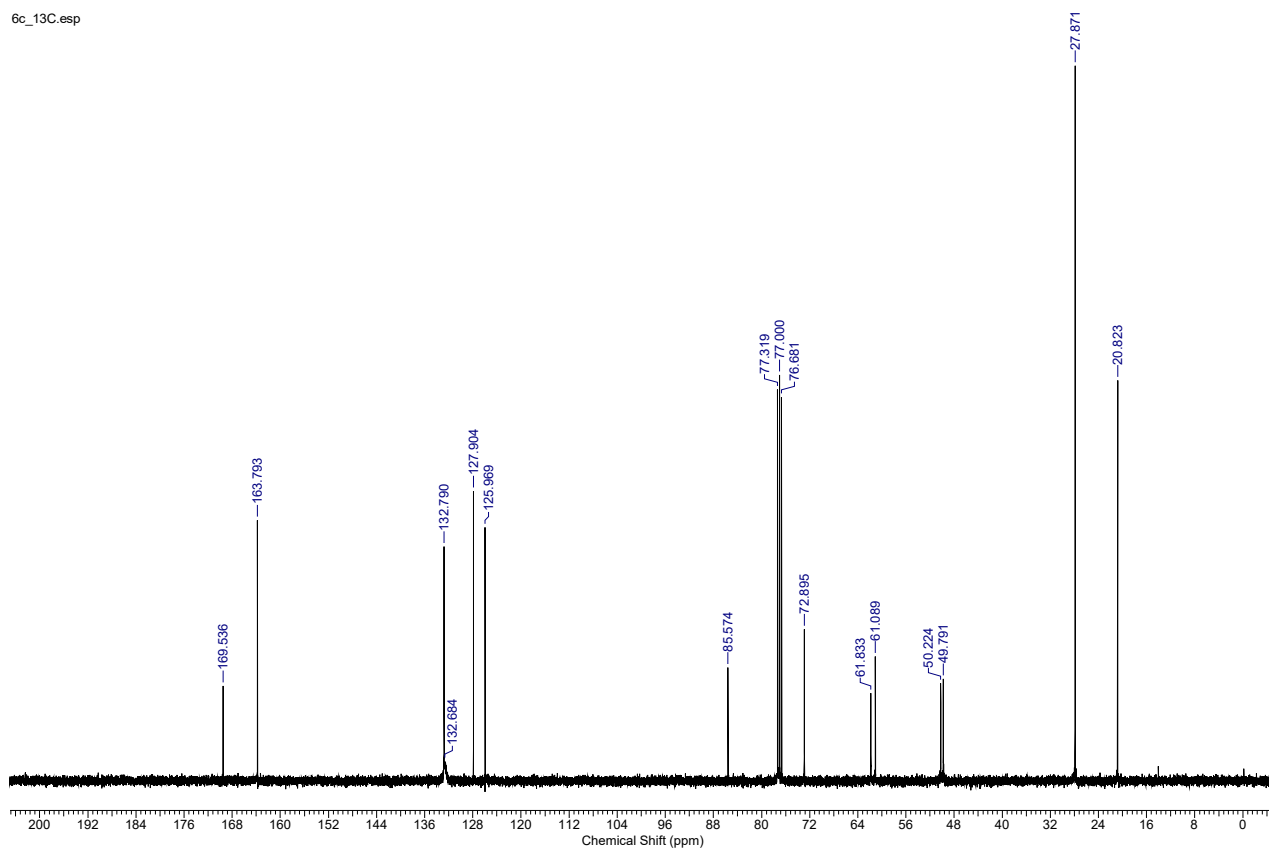


**6c**

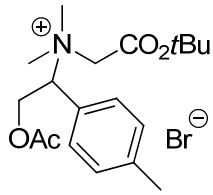
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



6c\_13C.esp

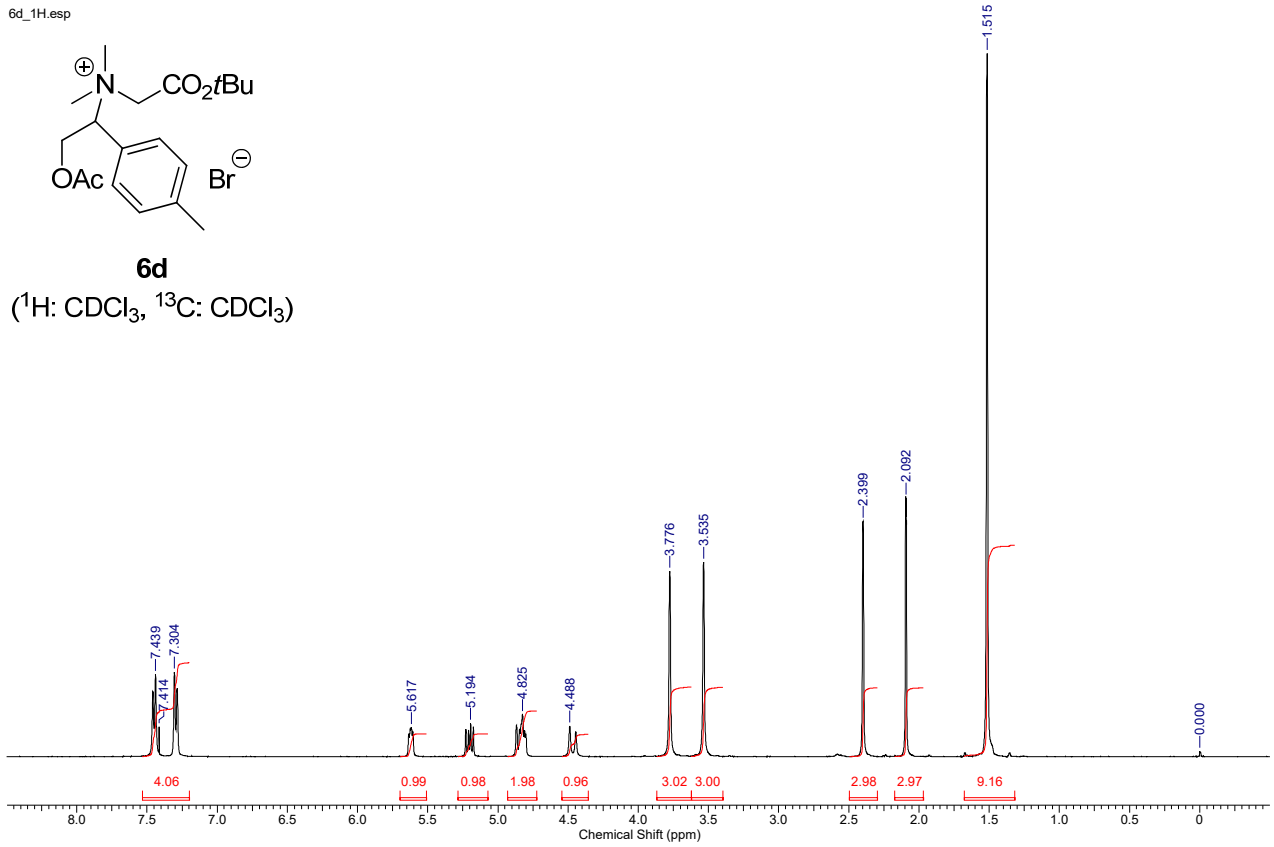


6d\_1H.esp

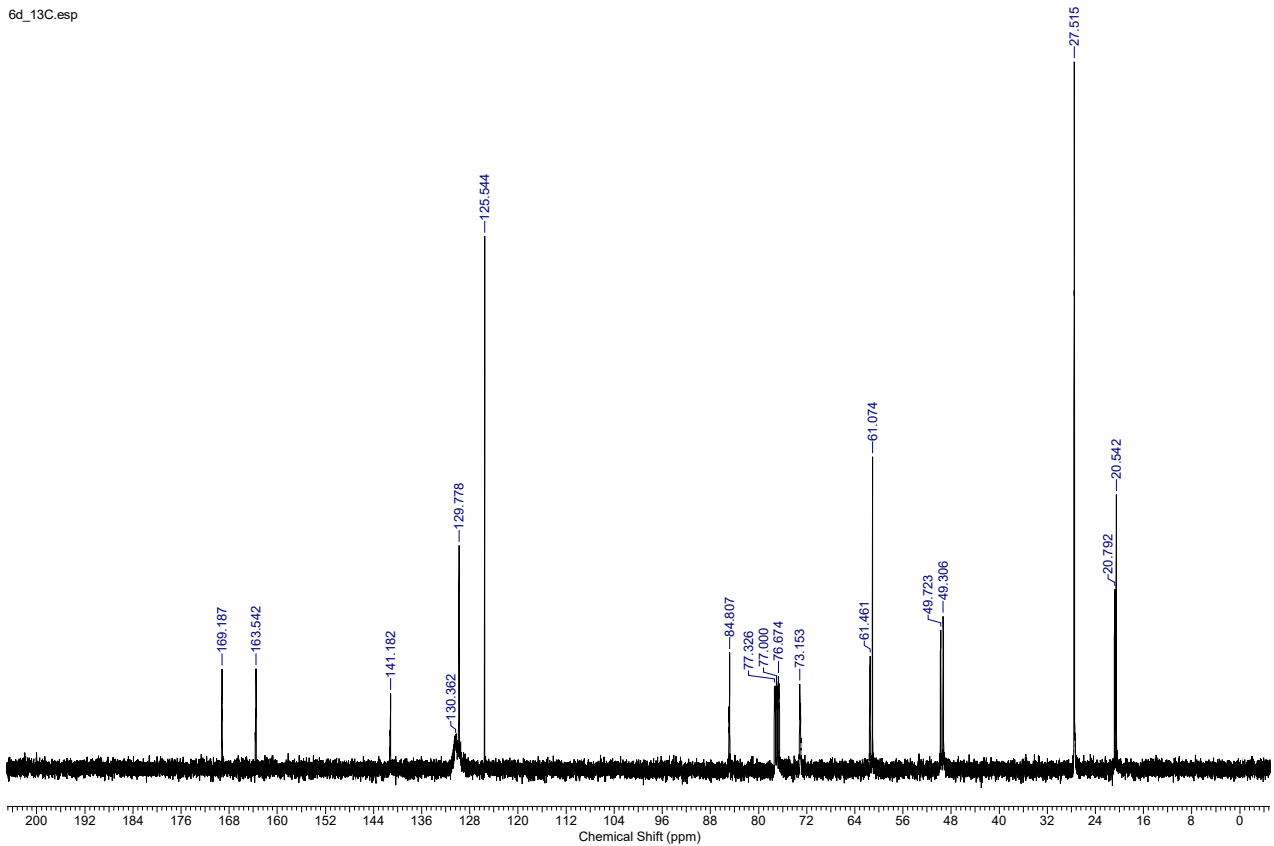


**6d**

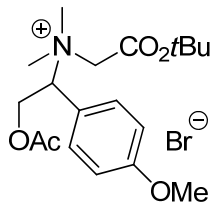
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



6d\_13C.esp

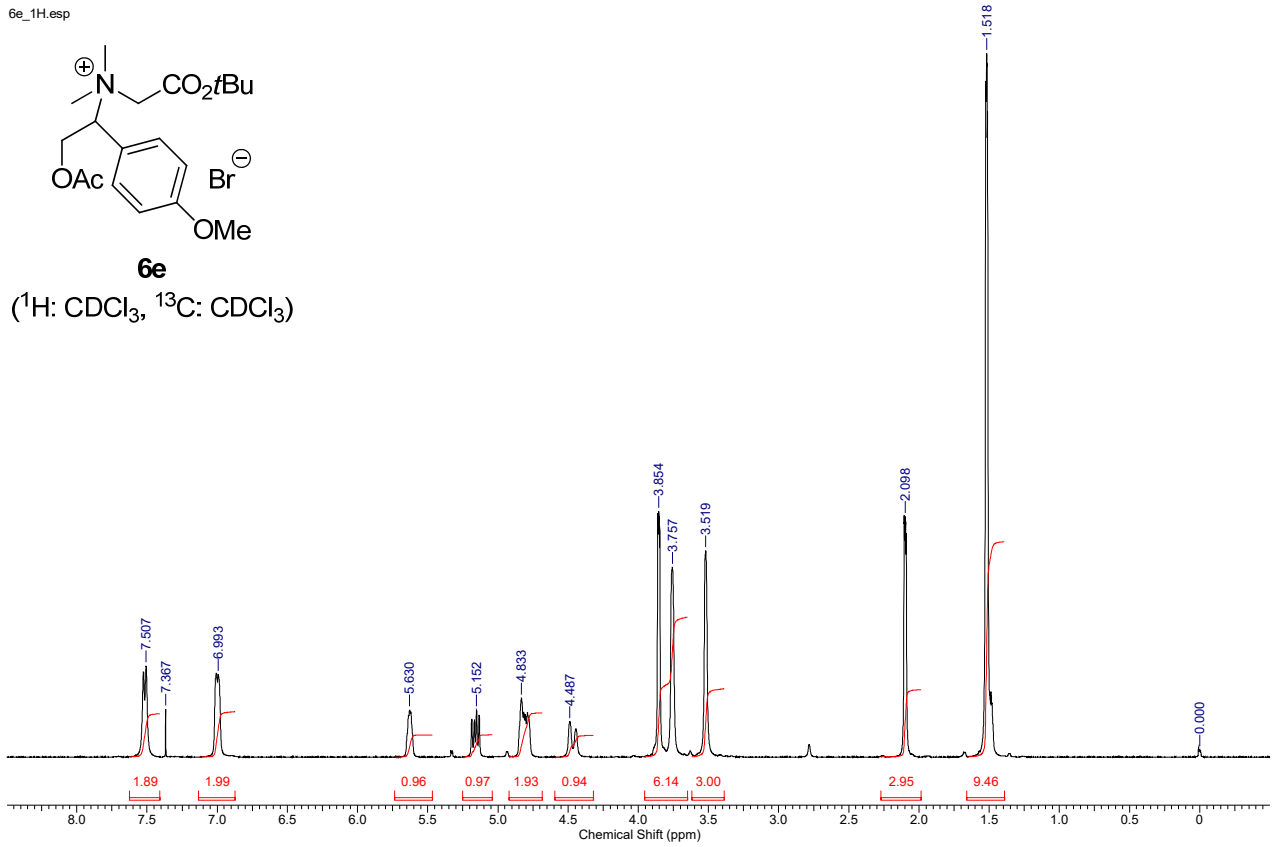


6e\_1H.esp

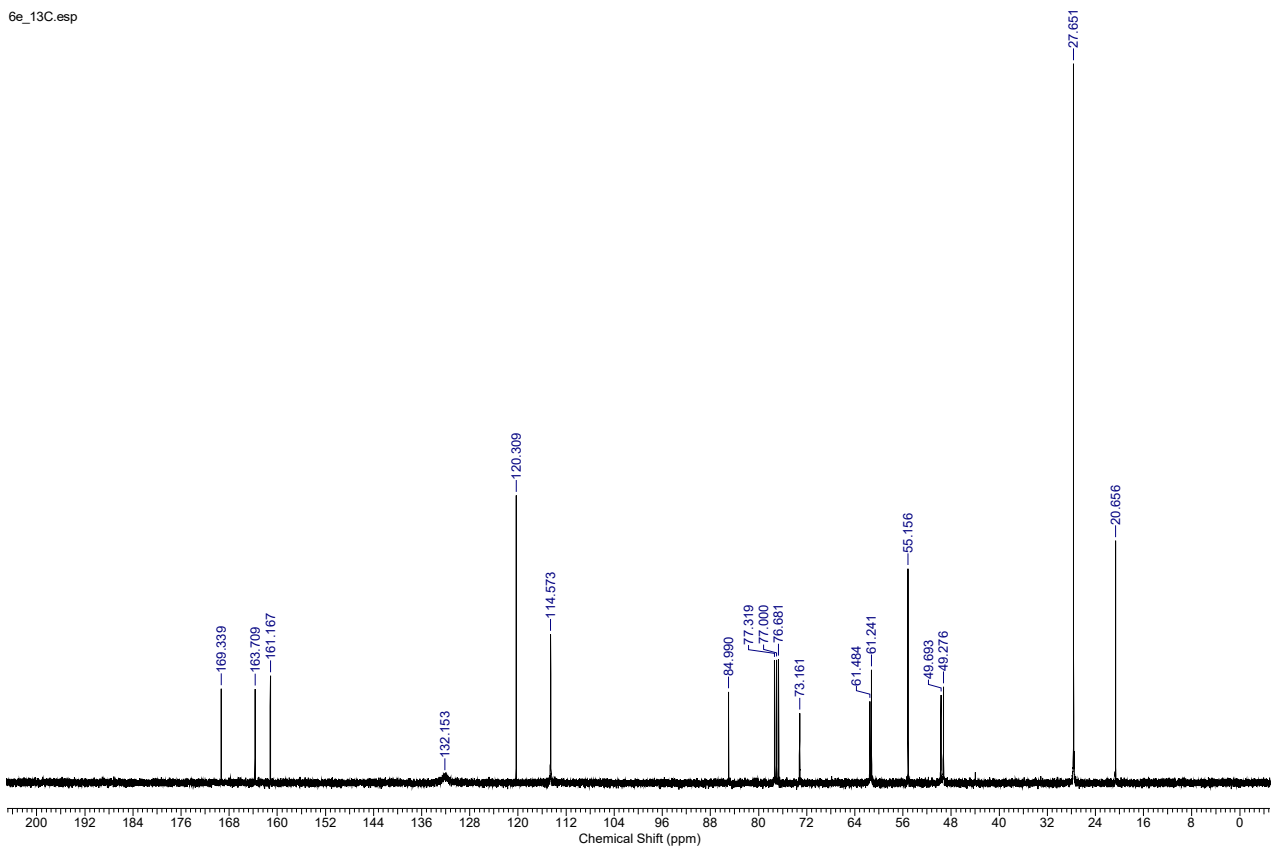


**6e**

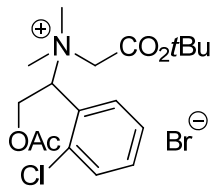
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



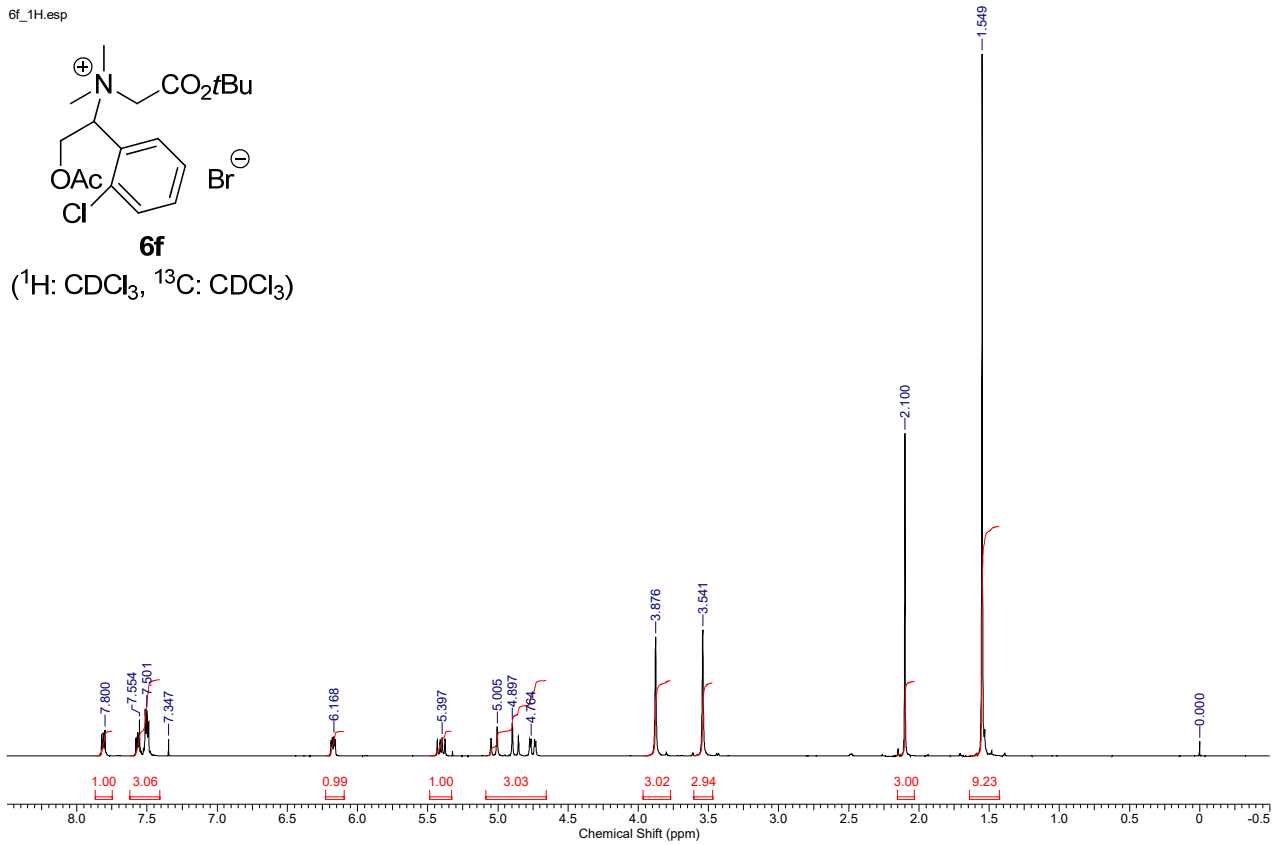
6e\_13C.esp



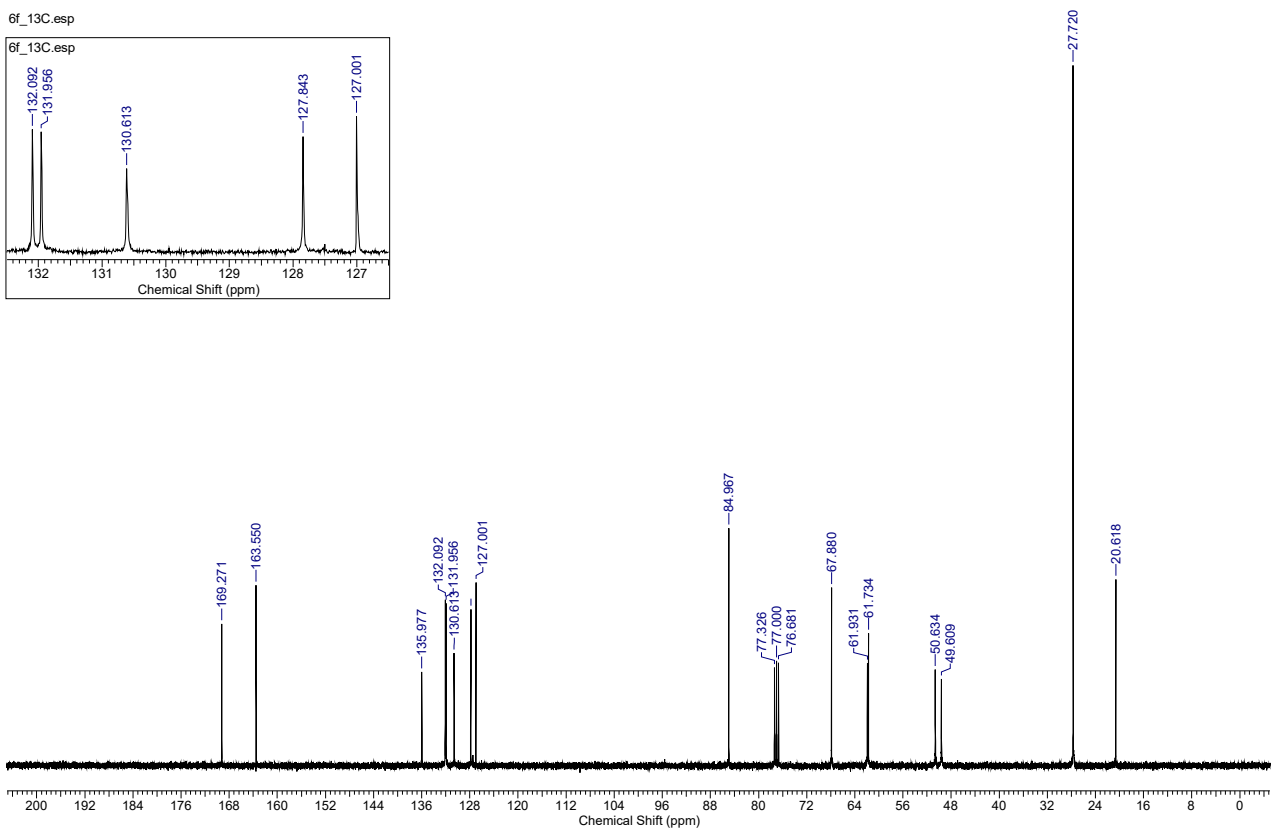
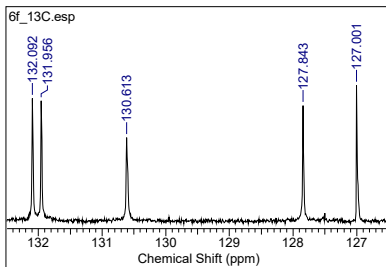
6f\_1H.esp



(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)

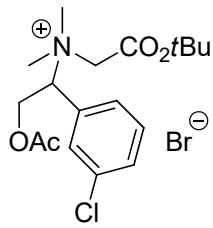


6f\_13C.esp



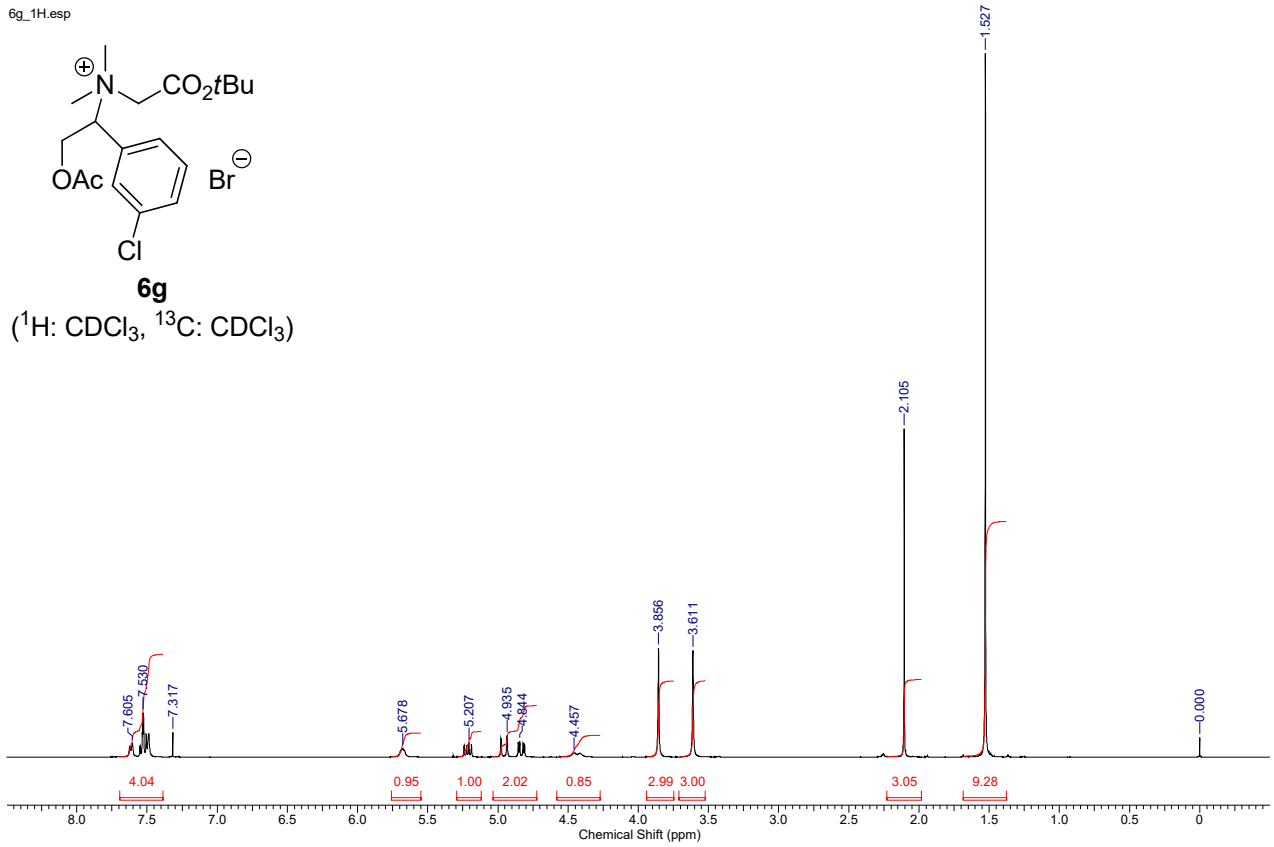


6g\_1H.esp

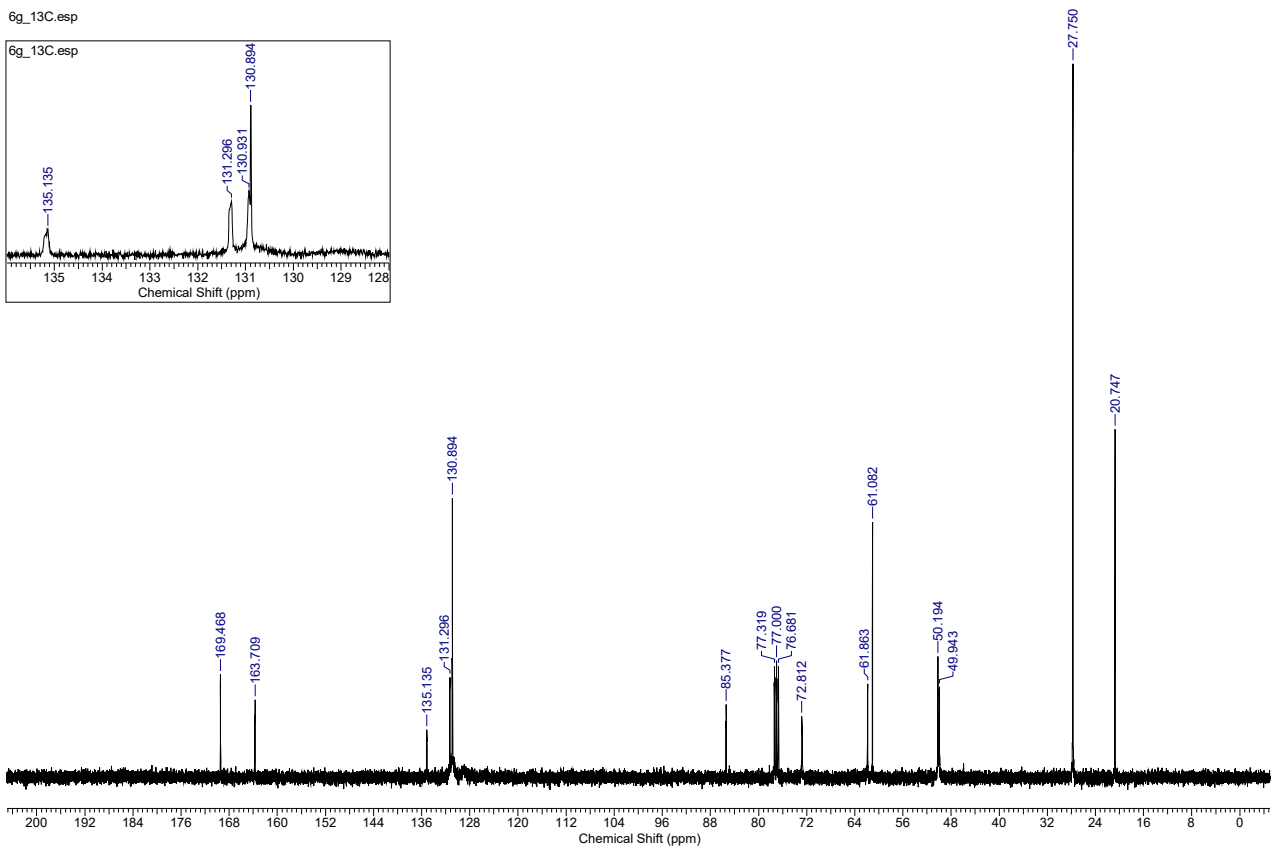
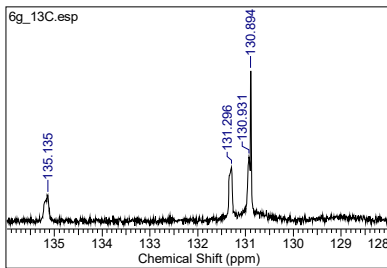


**6g**

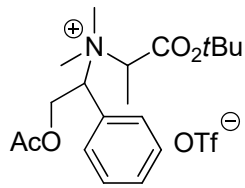
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



6g\_13C.esp

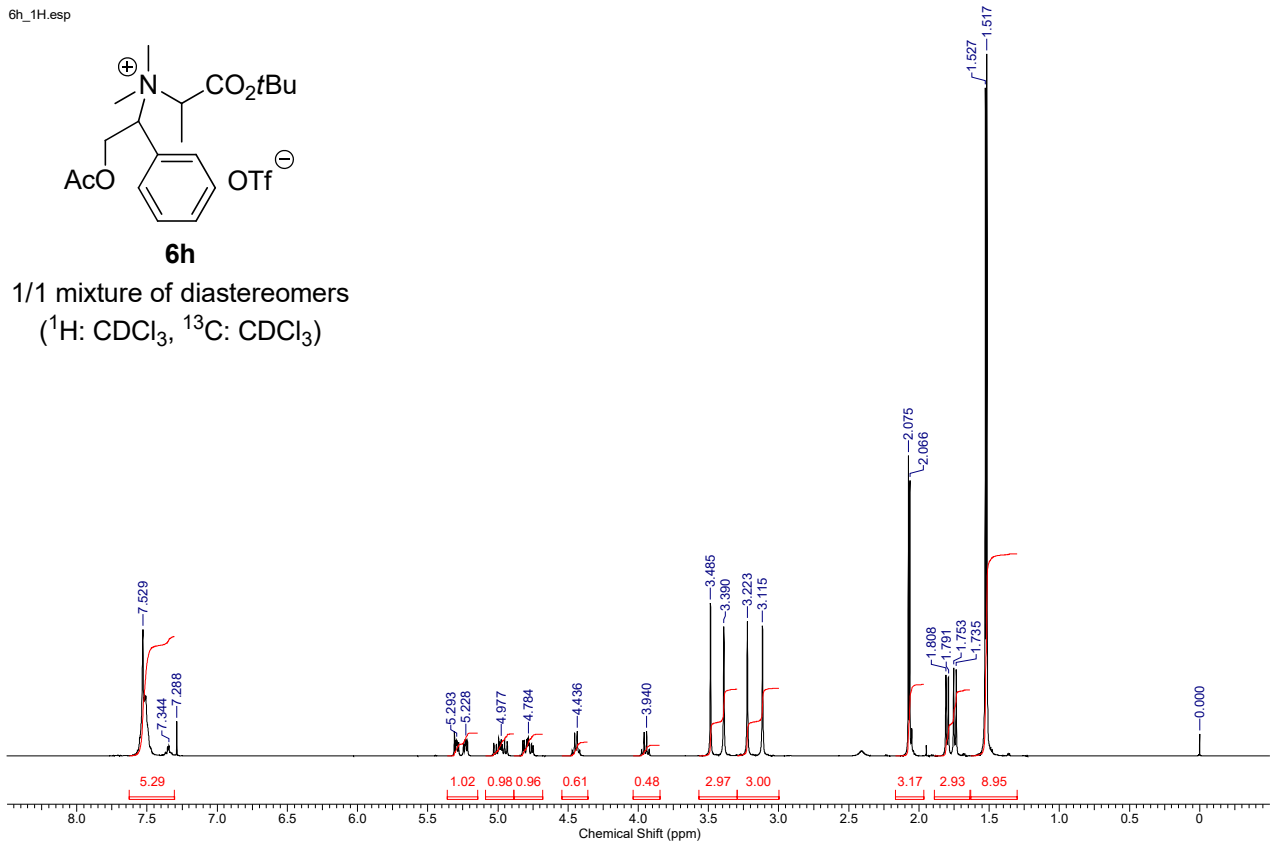


6h\_1H.esp

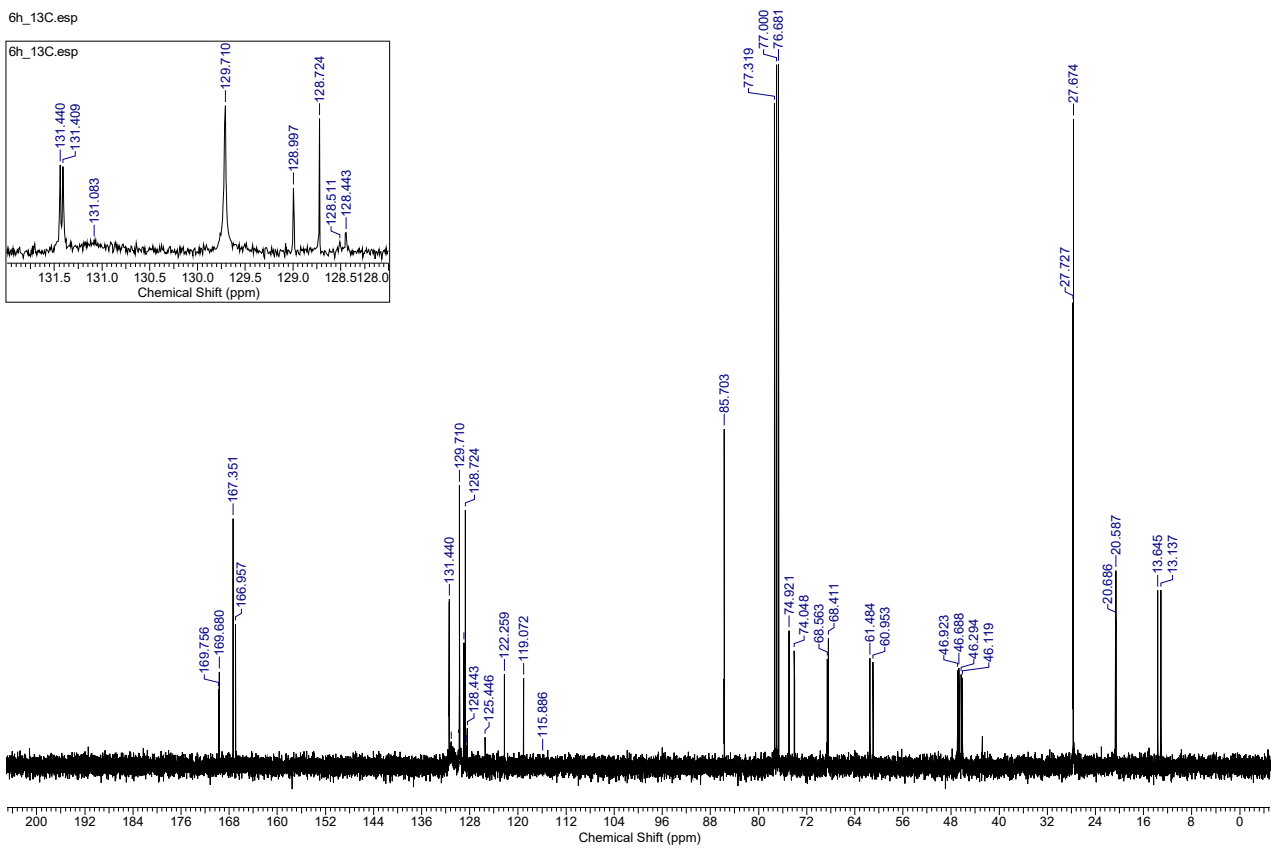
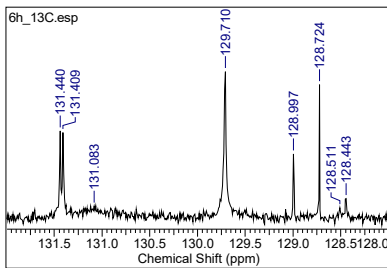


**6h**

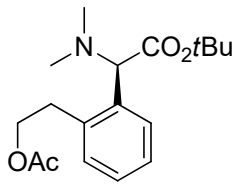
1/1 mixture of diastereomers  
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



6h\_13C.esp

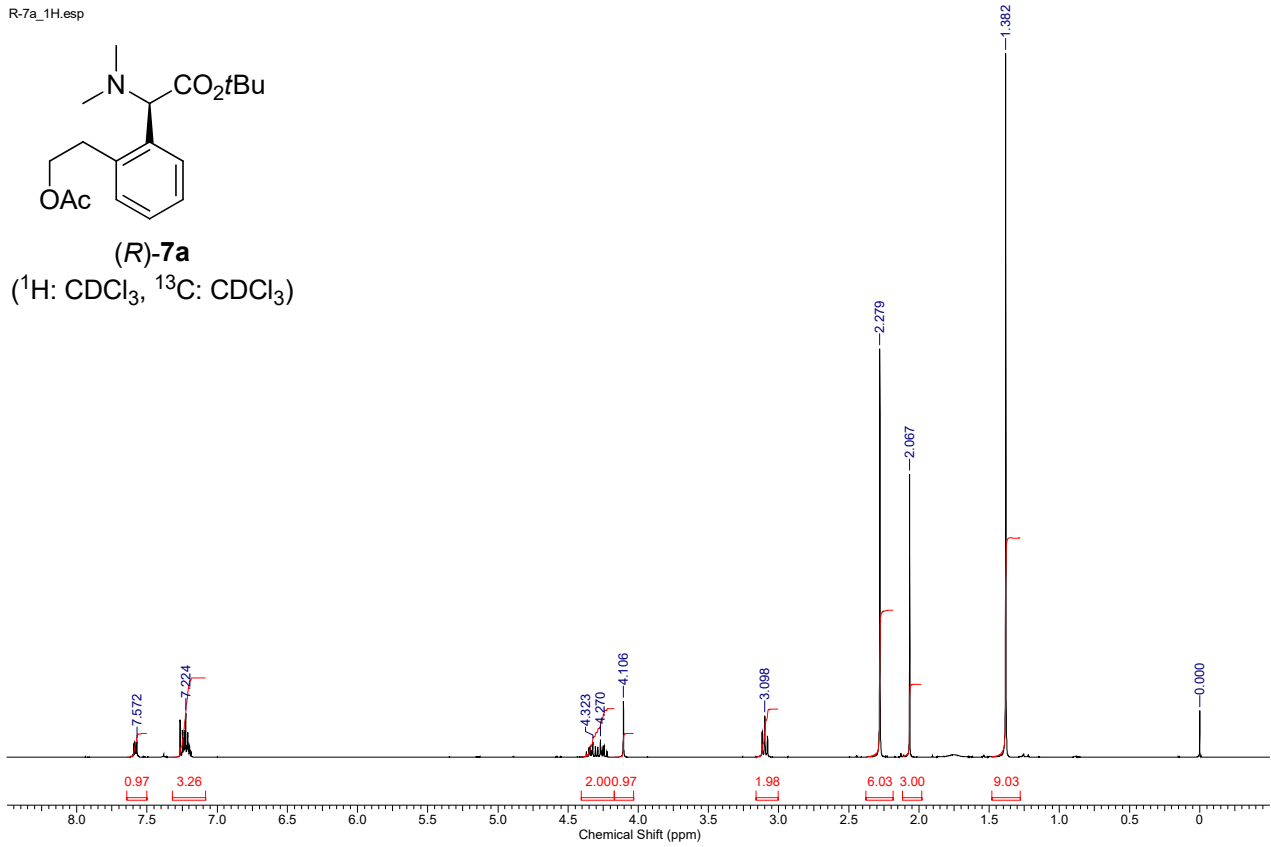


R-7a\_1H.esp



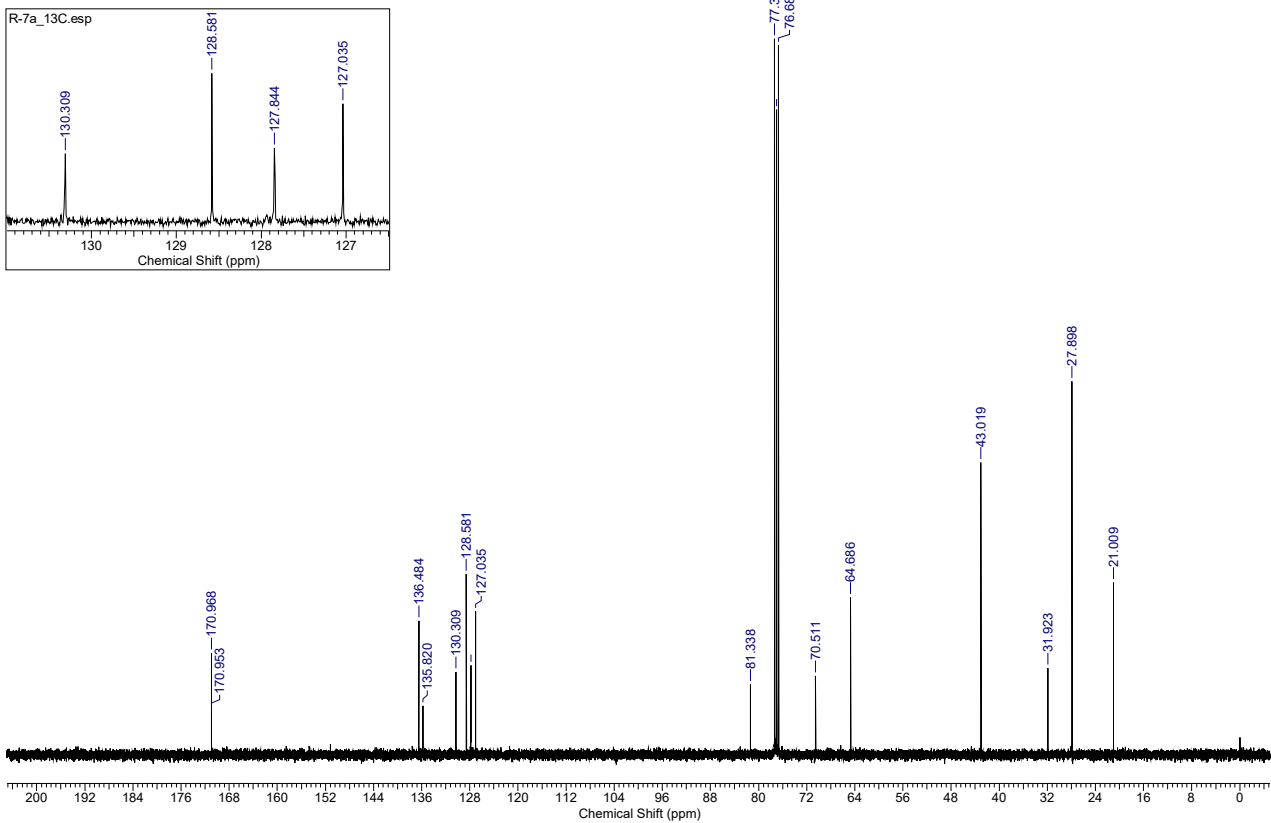
**(R)-7a**

(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)

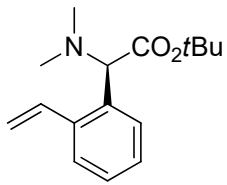


R-7a\_13C.esp

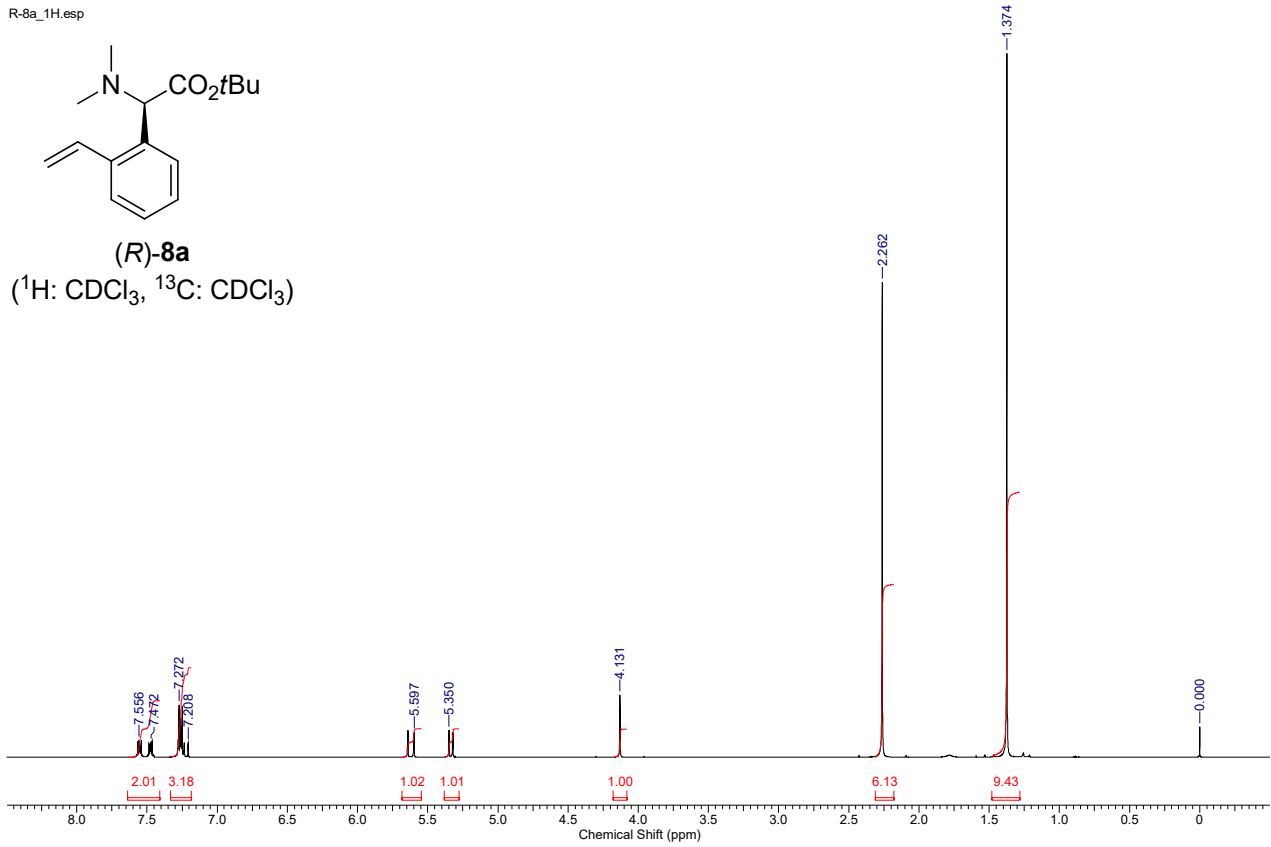
R-7a\_13C.esp



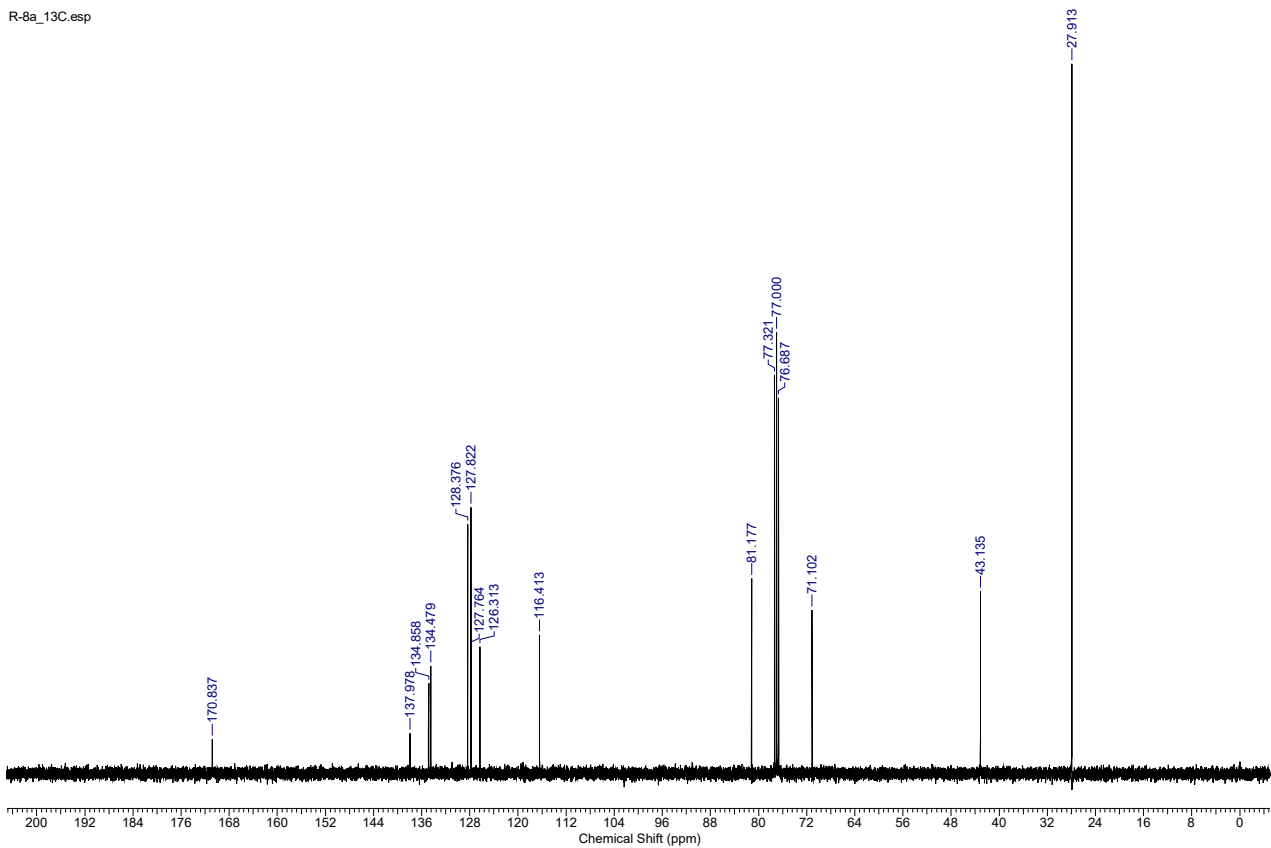
R-8a\_1H.esp



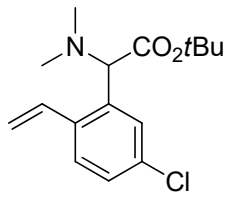
**(R)-8a**  
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



R-8a\_13C.esp

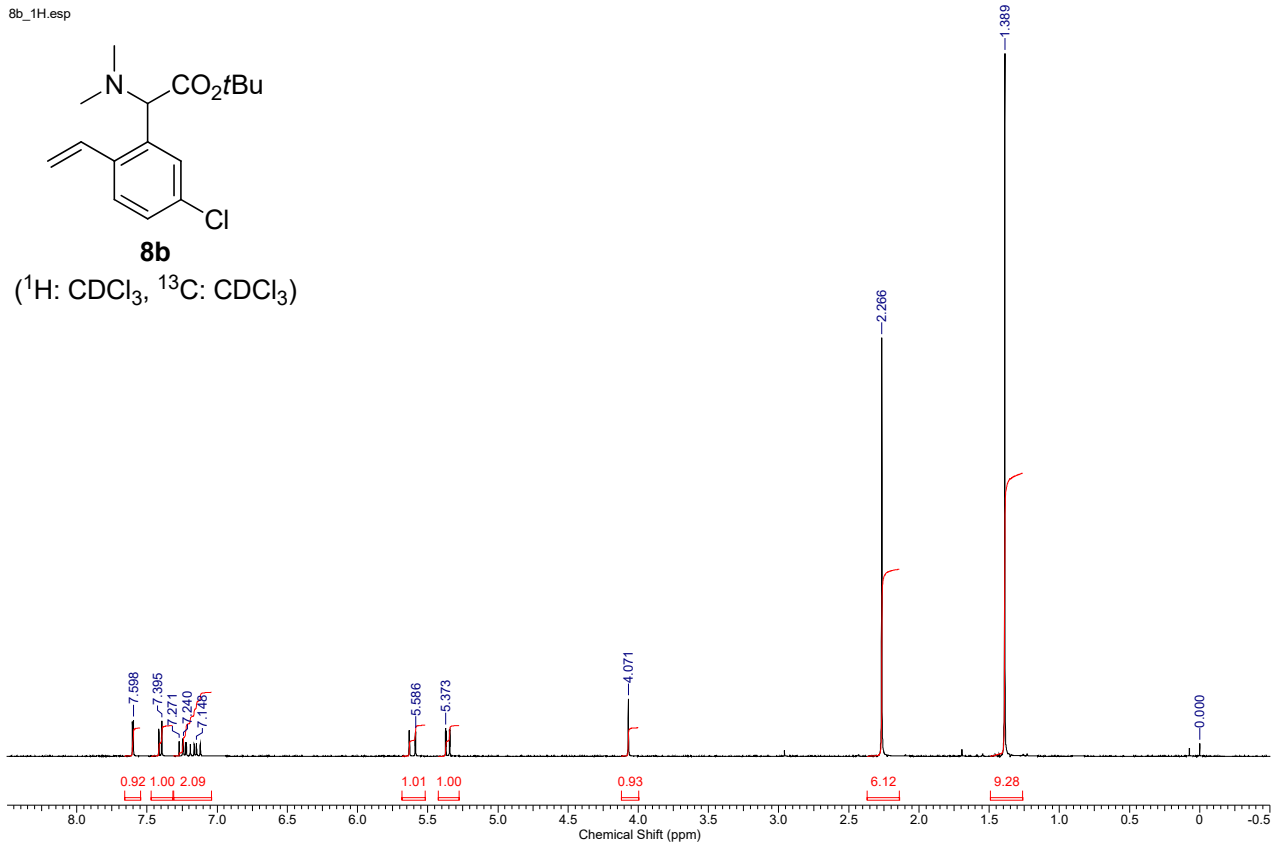


8b\_1H.esp

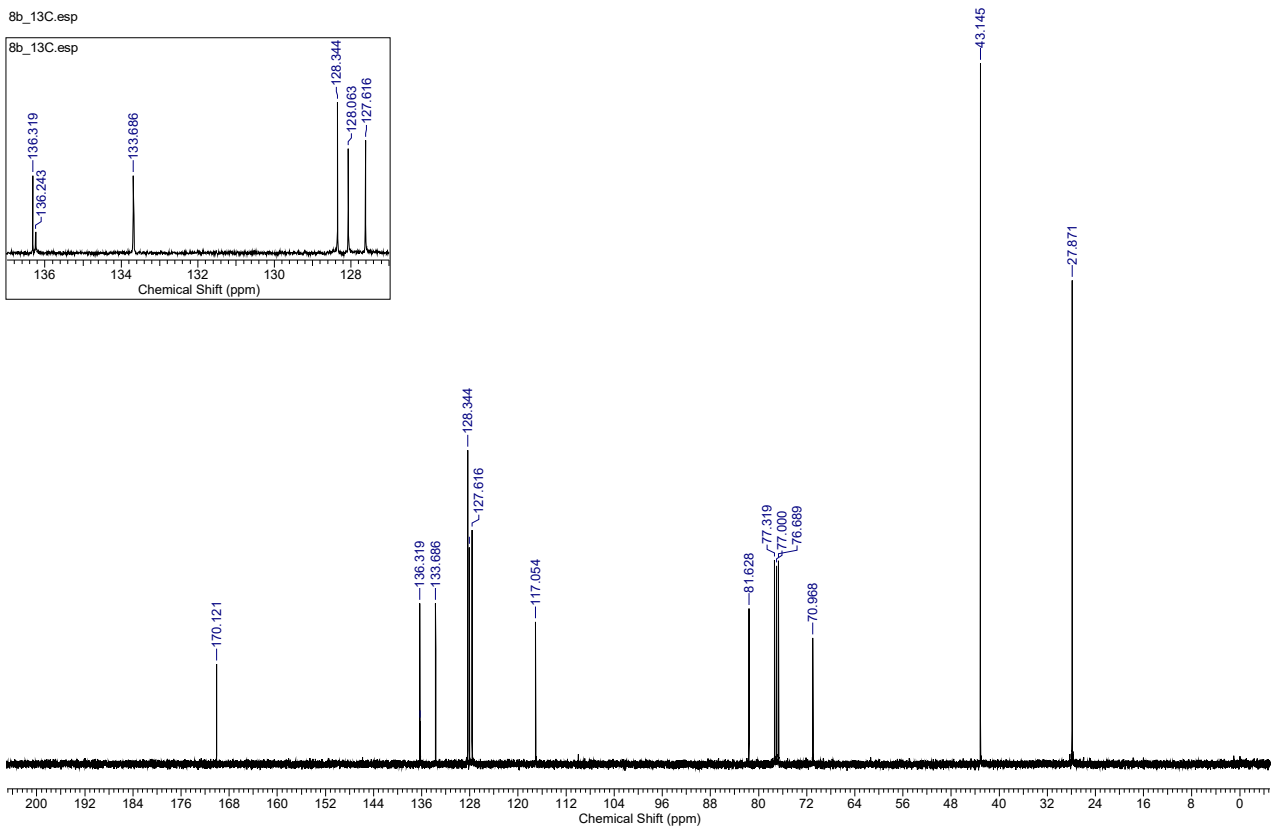
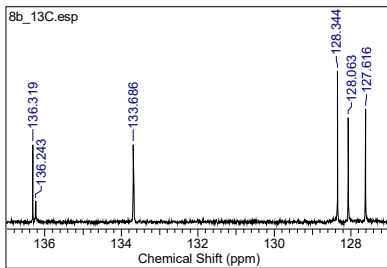


**8b**

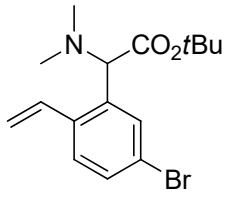
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



8b\_13C.esp

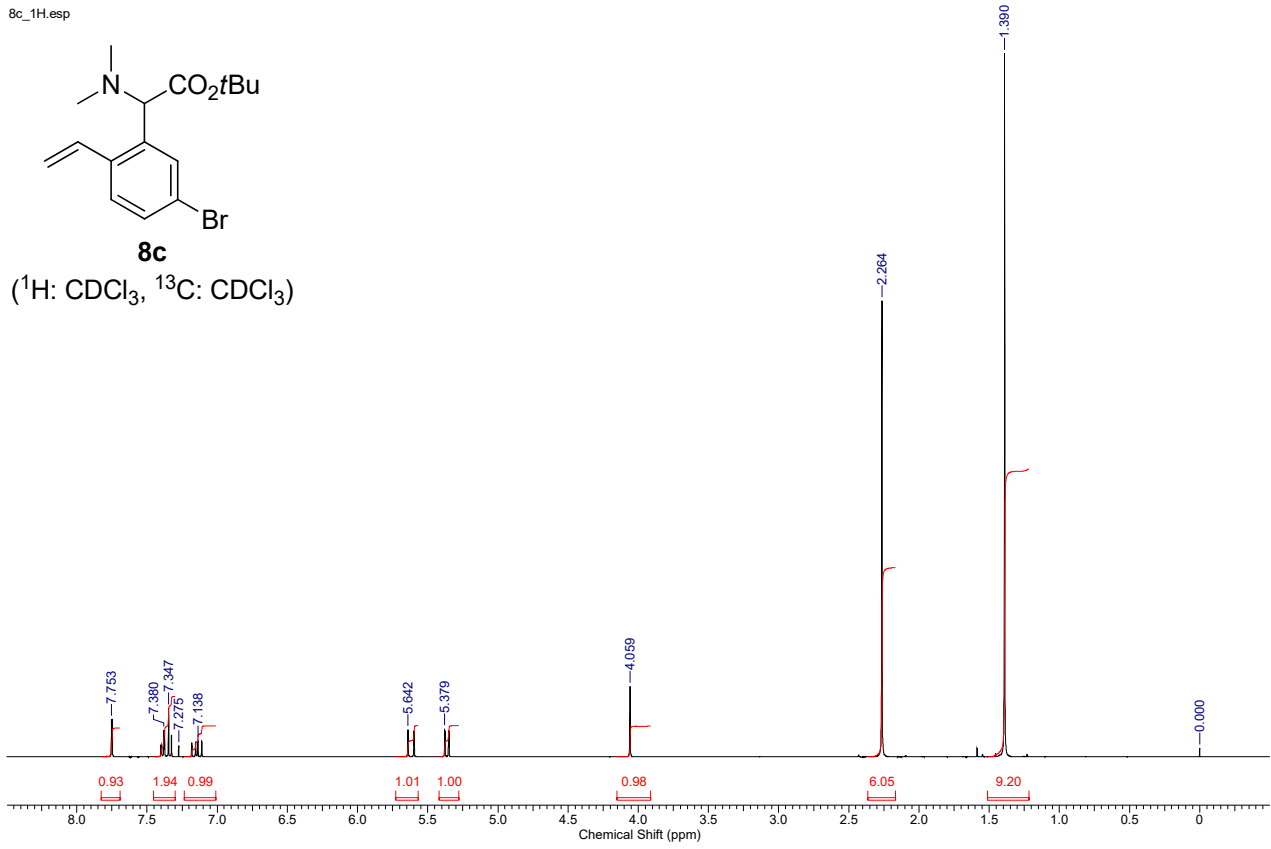


8c\_1H.esp

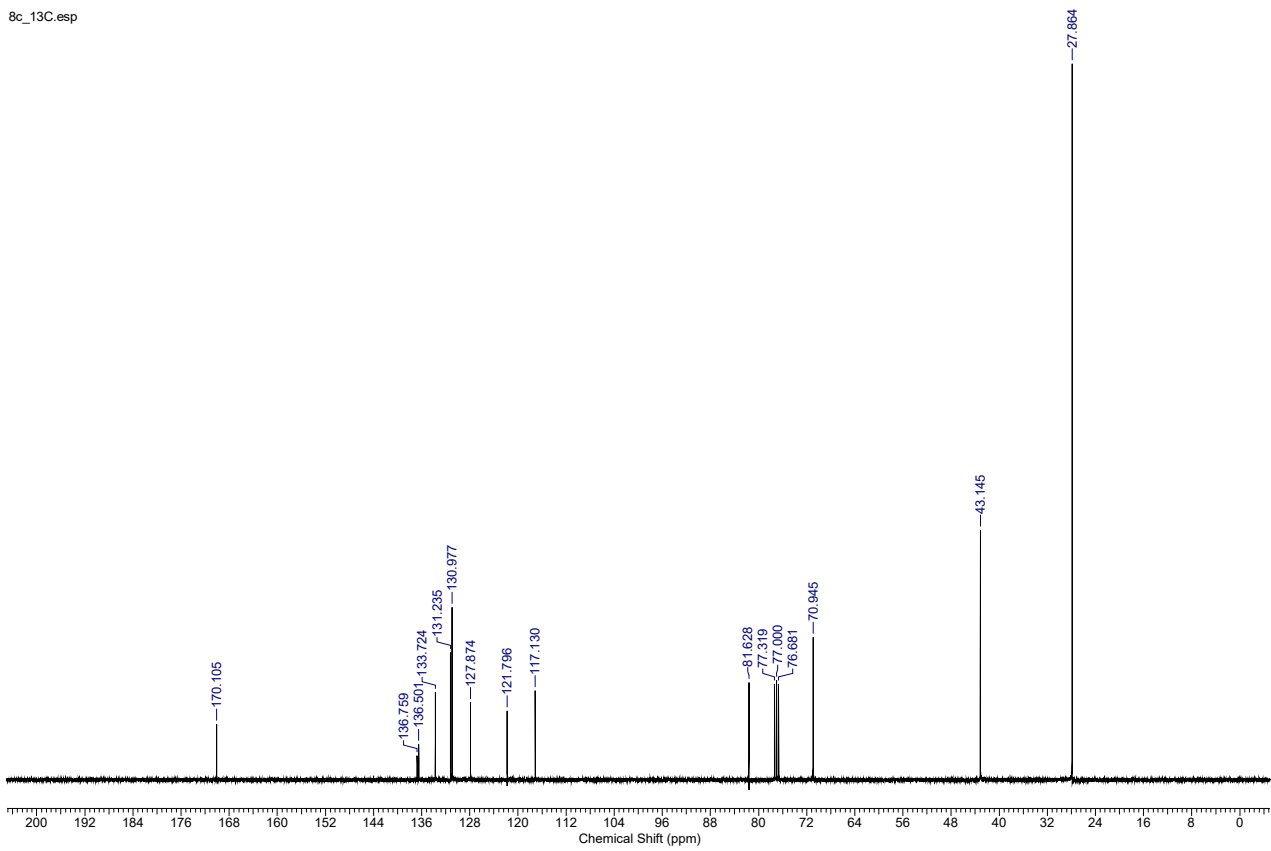


**8c**

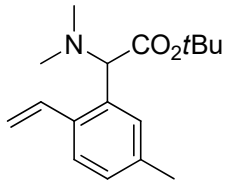
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



8c\_13C.esp

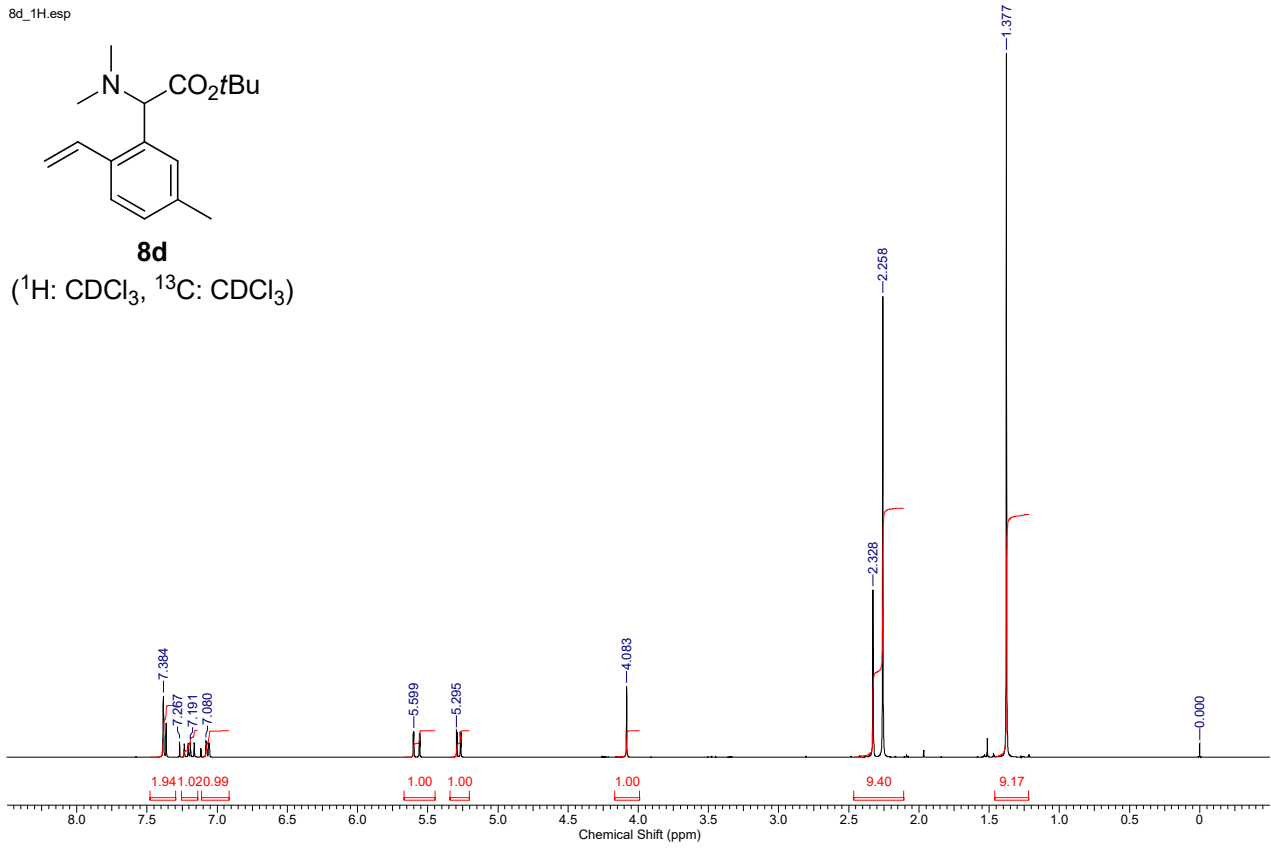


8d\_1H.esp



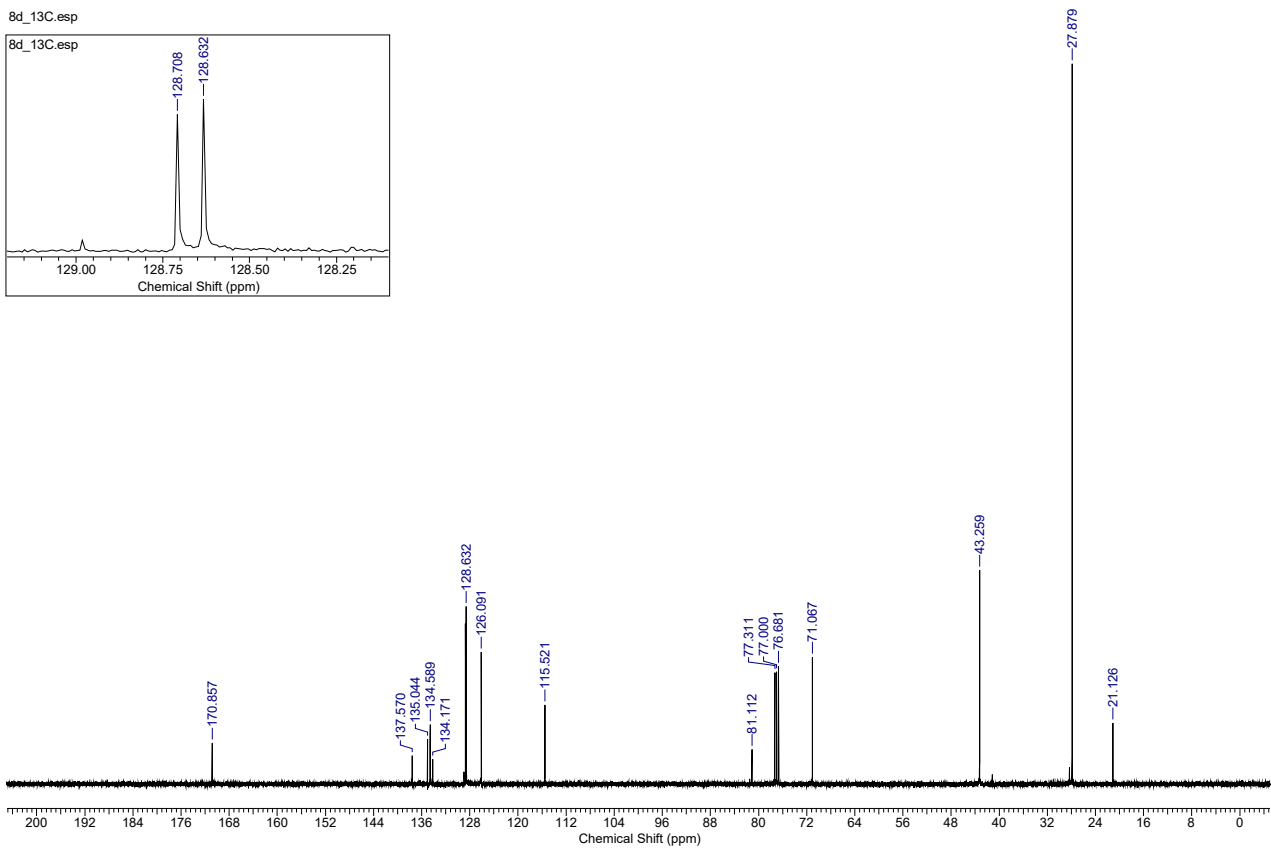
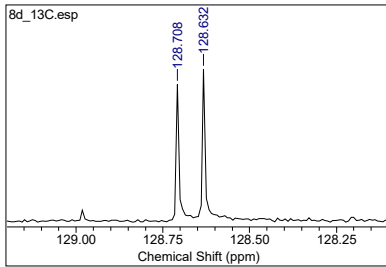
**8d**

(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)

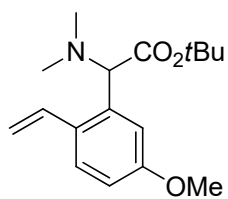


8d\_13C.esp

8d\_13C.esp

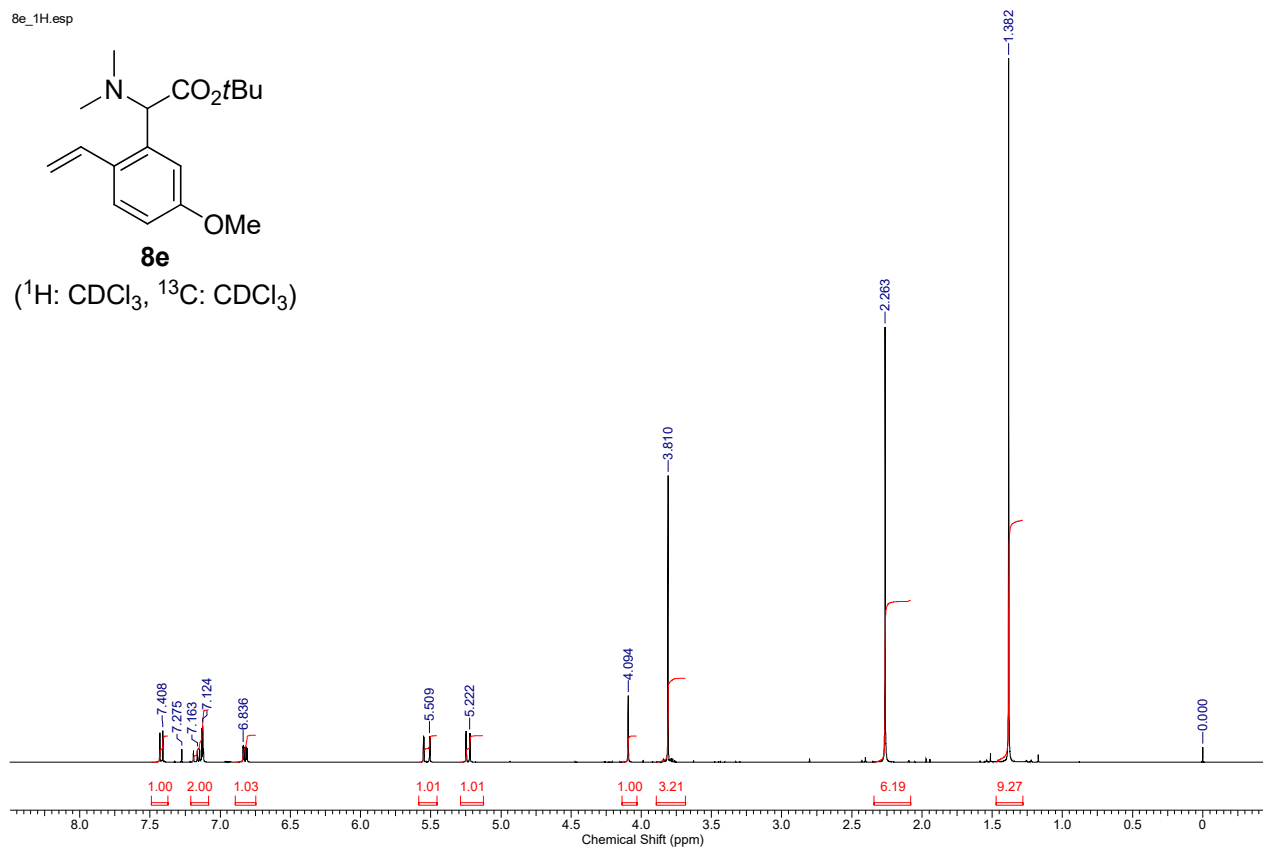


8e\_1H.esp



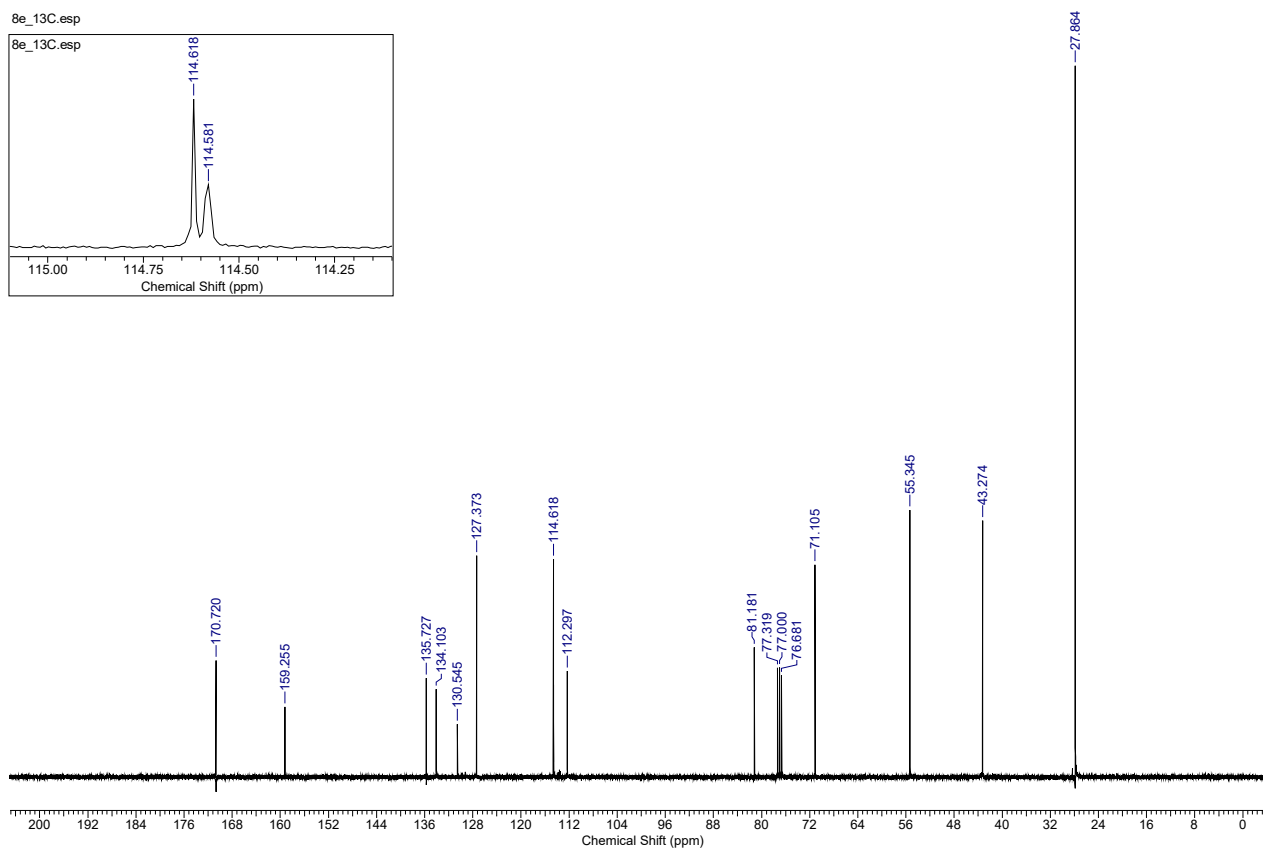
**8e**

(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



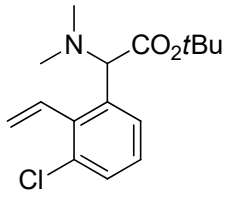
8e\_13C.esp

8e\_13C.esp



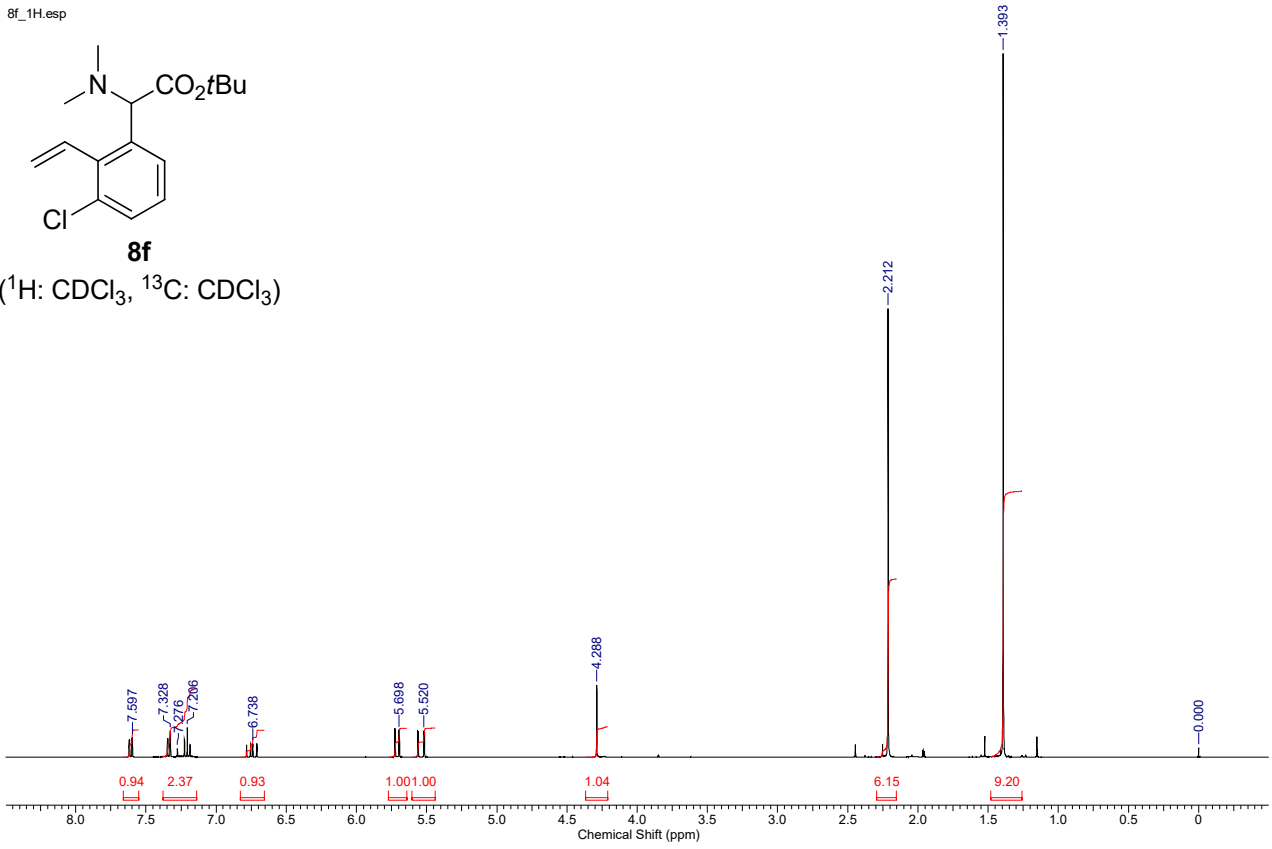


8f\_1H.esp

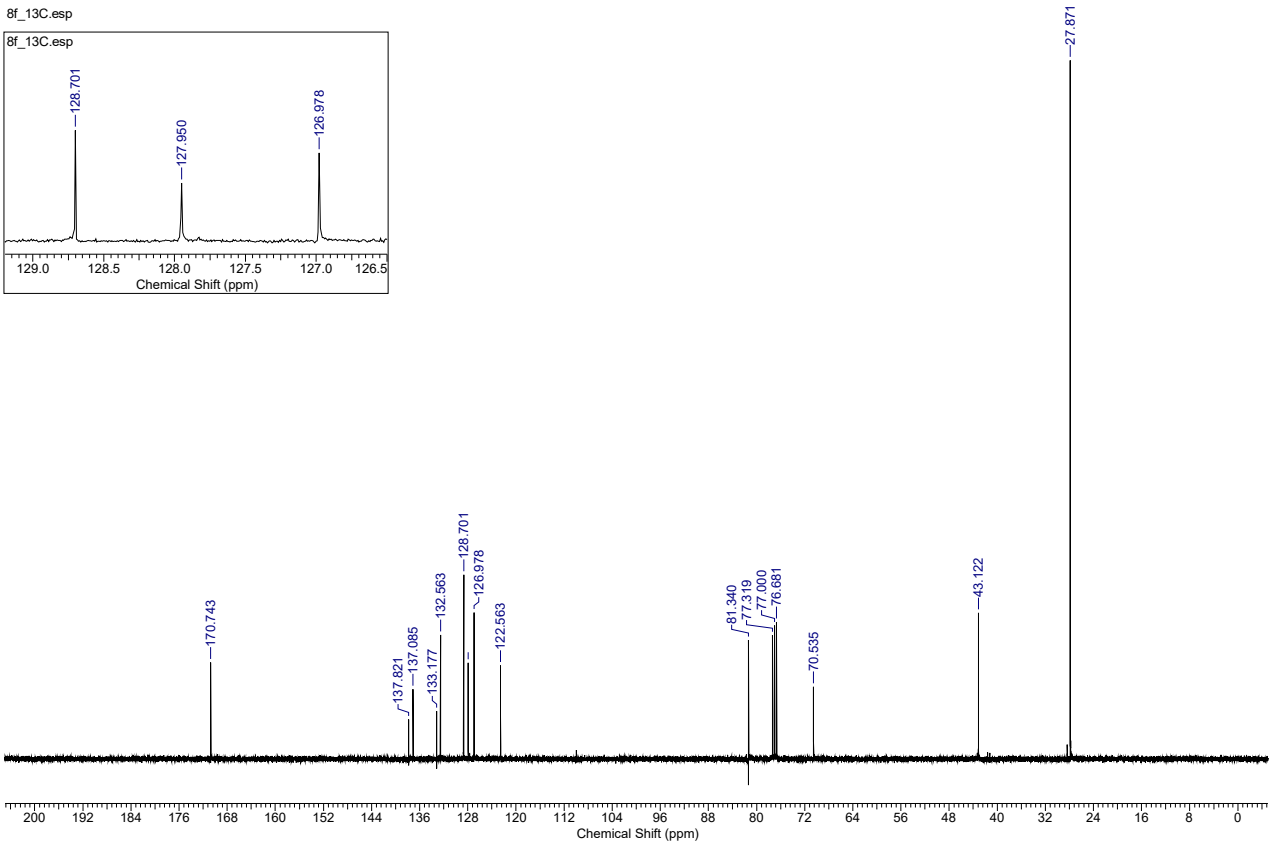
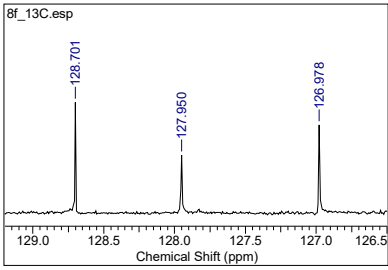


**8f**

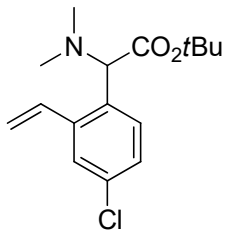
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



8f\_13C.esp

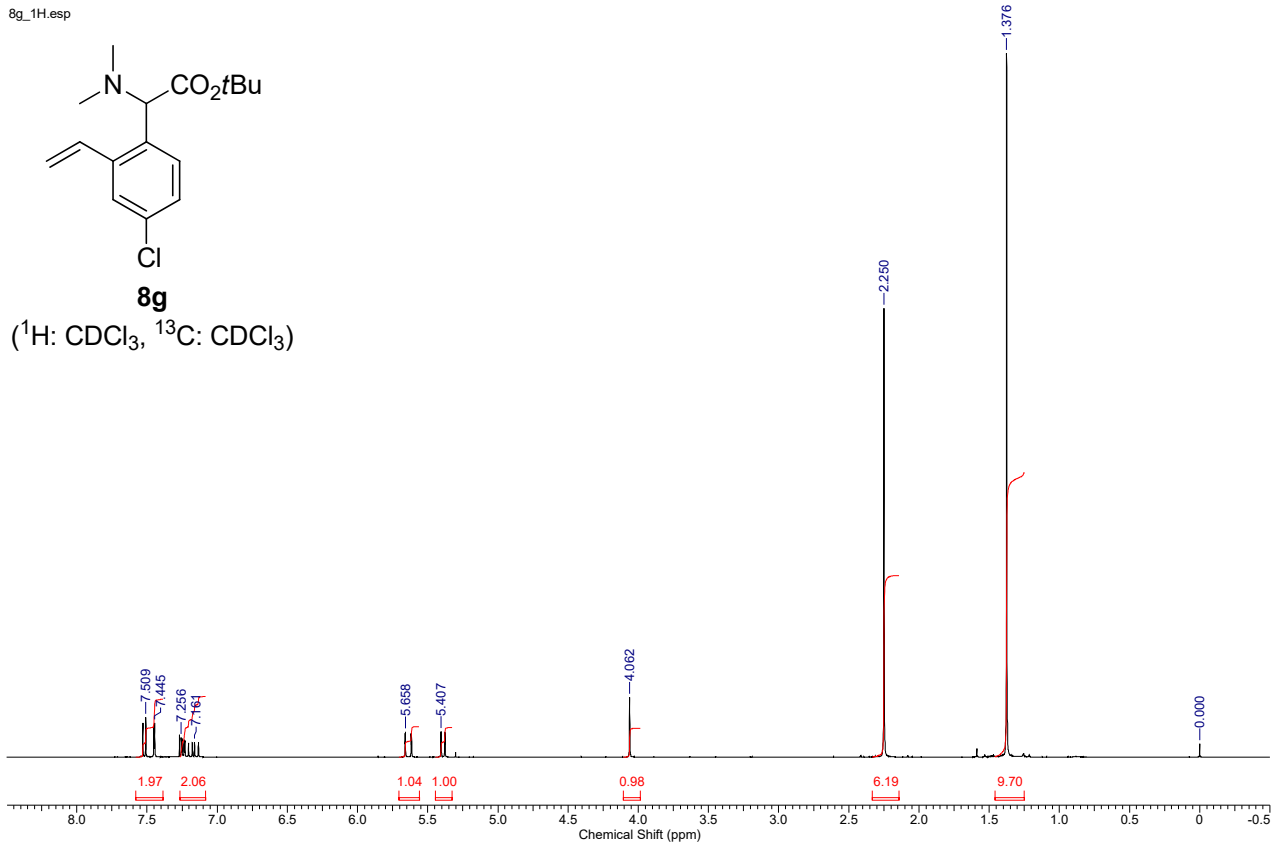


8g\_1H.esp



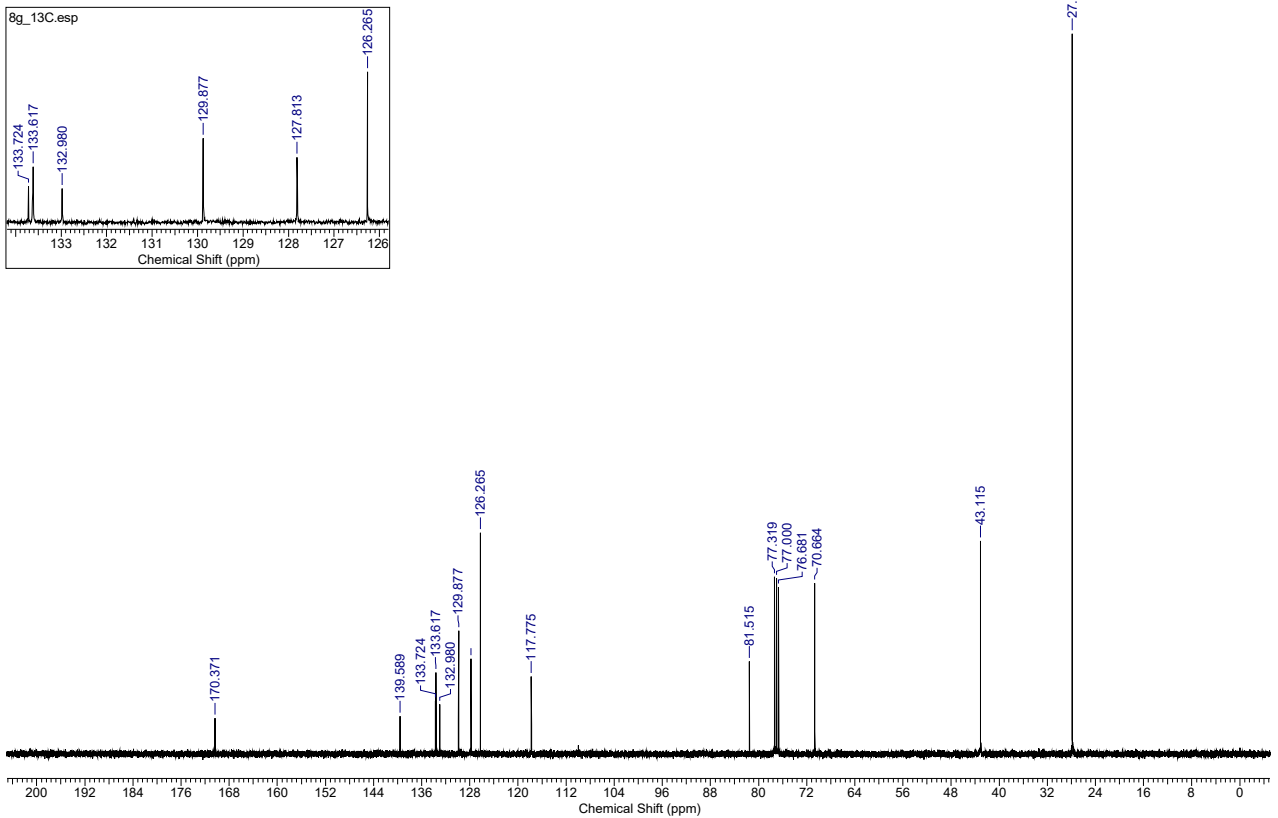
**8g**

(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)

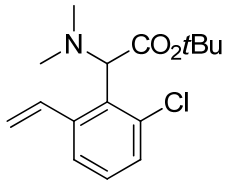


8g\_13C.esp

8g\_13C.esp

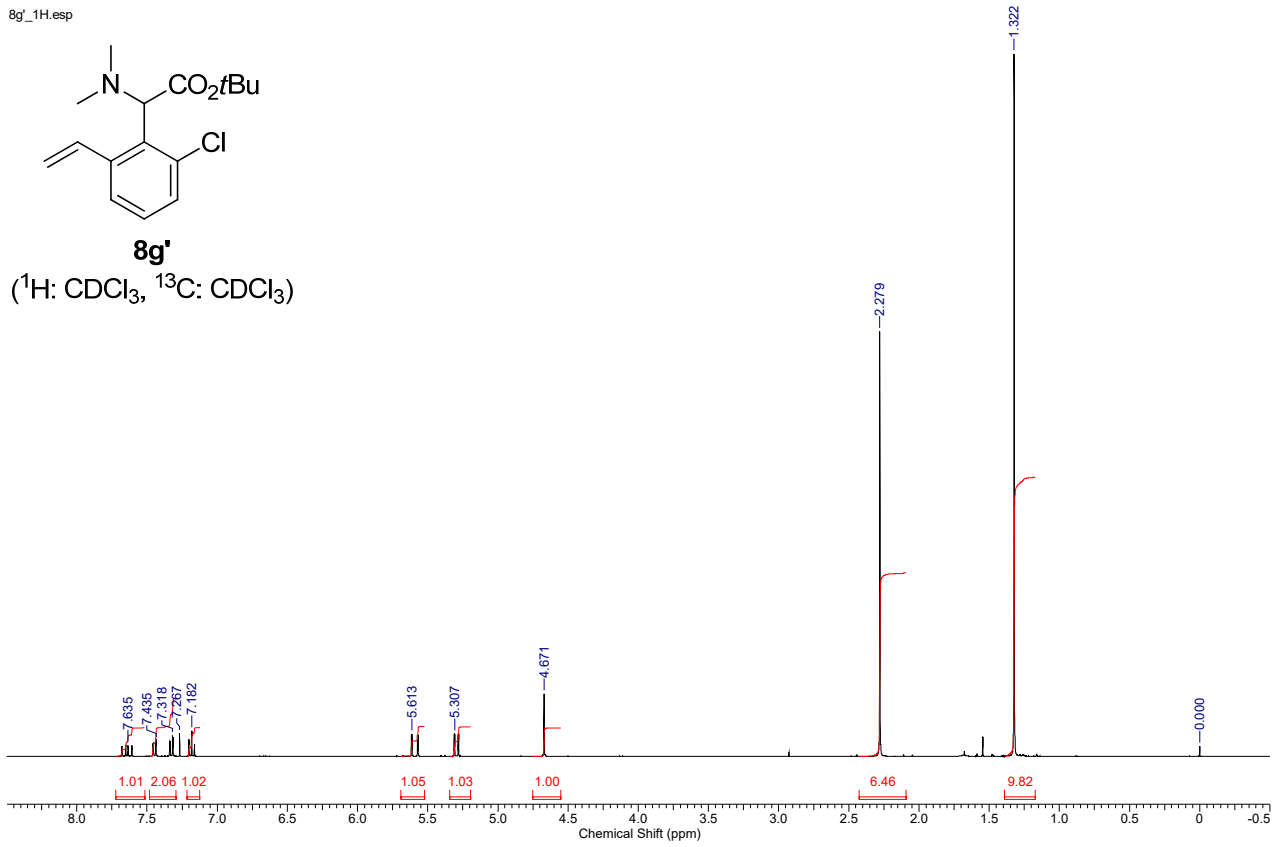


8g'\_1H.esp

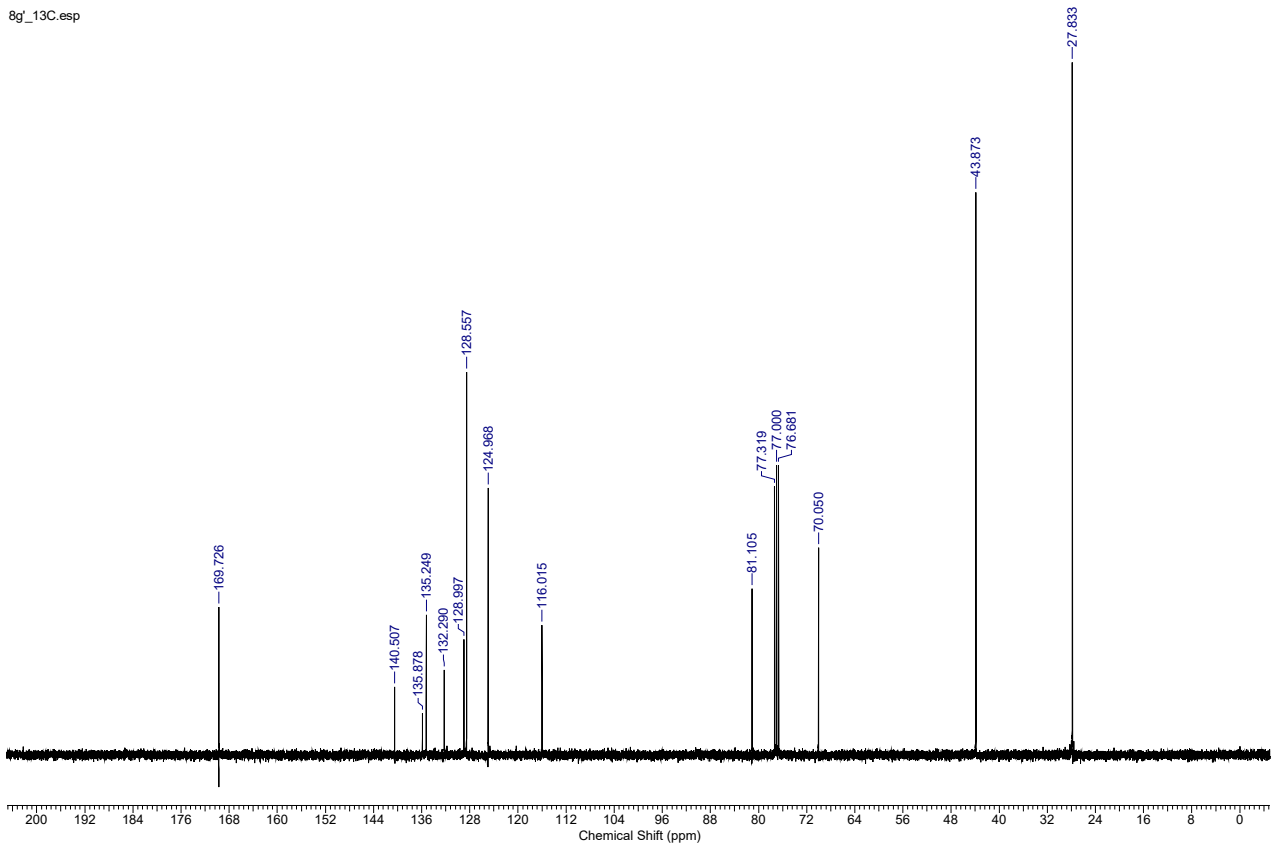


**8g'**

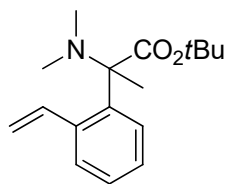
(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



8g'\_13C.esp

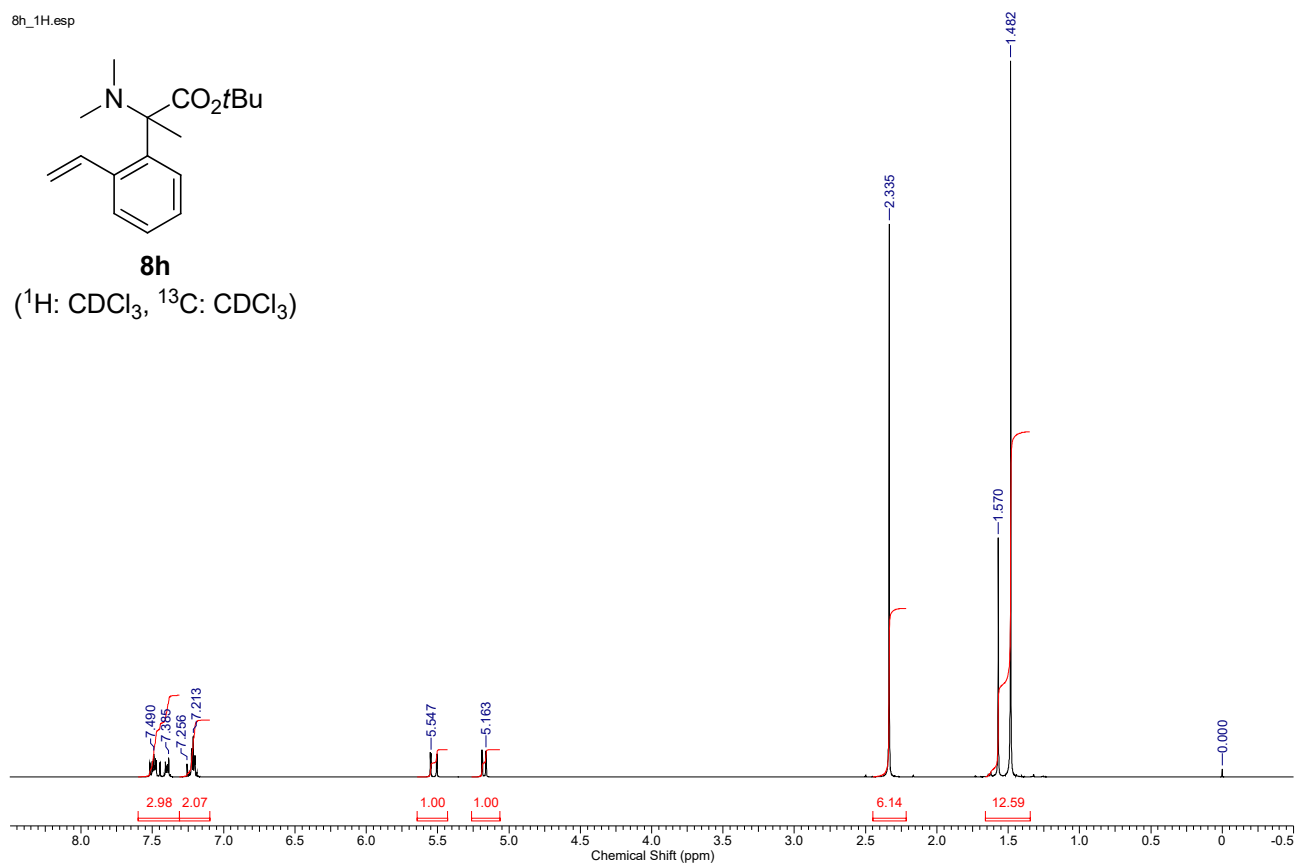


8h\_1H.esp



**8h**

(<sup>1</sup>H: CDCl<sub>3</sub>, <sup>13</sup>C: CDCl<sub>3</sub>)



8h\_13C.esp

