

## Design and Synthesis of Distereogenic Chiral Ionic Liquids and Their Use as Solvents for Asymmetric Baylis-Hillman Reactions

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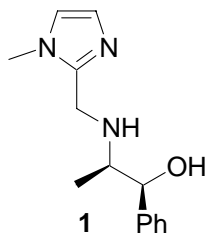
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### Experimental section:

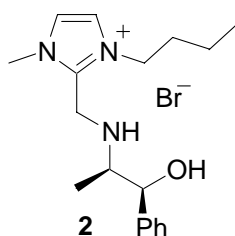
#### (1) Synthesis of compound 1



To a solution of 1-methyl-2-imidazolecarboxaldehyde (0.78g, 7.0 mmol) in methanol (25ml) was added (1S, 2R) norephedrine (1.06g, 7.0 mmol) and 4Å molecular sieves (2.1 g). The reaction mixture was stirred under reflux for 24 h with exclusion of moisture and then cooled to room temperature. To the resulting solution of Schiff base was added NaBH<sub>4</sub> (0.26g, 7.0 mmol) and stirred for 2 h at room temperature. The reduction mixture was quenched by slow and dropwise addition of concentrated HCl (0.4 ml) to the mixture and subsequent neutralization with solid Na<sub>2</sub>CO<sub>3</sub> (1.00 g, 10.0 mmol). The resulting mixture was filtered over celite to remove any solids; the filtrate was evaporated to dryness purified by flash column chromatography on silica gel (CH<sub>2</sub>Cl<sub>2</sub>/ MeOH = 10 : 1)

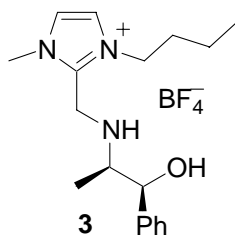
to give pale yellow viscous liquid **1** (1.48 g, 86%).  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  7.32-7.18 (5H, m), 6.94 (1H, d,  $J = 1.2$  Hz), 6.82 (1H, d,  $J = 1.2$  Hz), 4.85 (2H, br), 4.58 (1H, d,  $J = 5.6$  Hz), 3.83 (2H, dd,  $J = 36.8$  and 14.4 Hz), 3.51 (3H, s), 2.85-2.77 (1H, m), 1.00 (3H, d,  $J = 6.4$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  146.6, 141.5, 128.1, 128.0, 127.0, 126.9, 126.1, 121.3, 73.0, 59.0, 43.3, 32.6, 14.5. This compound was used for the next step without further characterization.

## (2) Synthesis of CIL 2



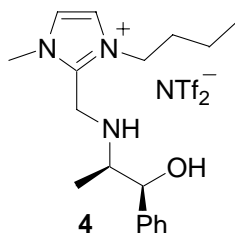
A solution of imidazole compound **1** (1.47 g, 6.0 mmol) and butyl bromide (1.50 g, 6.5 mmol) in toluene (5 mL) was stirred at 85-90  $^\circ\text{C}$  for 24 h. The reaction mixture was then cooled to room temperature, the toluene was removed, and the residue was purified by flash column chromatography on silica gel ( $\text{CH}_2\text{Cl}_2/\text{MeOH} = 10 : 1$ ) to give product **2** (2.17 g, 95%) as a viscous liquid.  $[\alpha]_{\text{D}}^{20} = -15.86^\circ$  ( $c = 0.29$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  7.50-7.17 (7H, m), 5.00 (1H, d,  $J = 2.8$  Hz), 4.57 (1H, d,  $J = 15.2$  Hz), 4.28 (1H, t,  $J = 7.6$  Hz), 4.11 (1H, d,  $J = 14.8$  Hz), 4.02 (3H, s), 3.60-3.10 (2H, br), 3.02-2.95 (1H, m), 1.81-1.68 (2H, m), 1.40-1.28 (2H, m), 0.92 (3H, t,  $J = 7.2$  Hz), 0.87 (3H, d,  $J = 6.8$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ) 144.8, 142.2, 127.8, 126.4, 126.2, 123.2, 121.1, 72.5, 59.9, 48.8, 39.9, 36.5, 32.1, 19.6, 14.3, 13.5. This compound was used for anion exchange and further characterized in the next step.

## (3) Synthesis of CIL 3



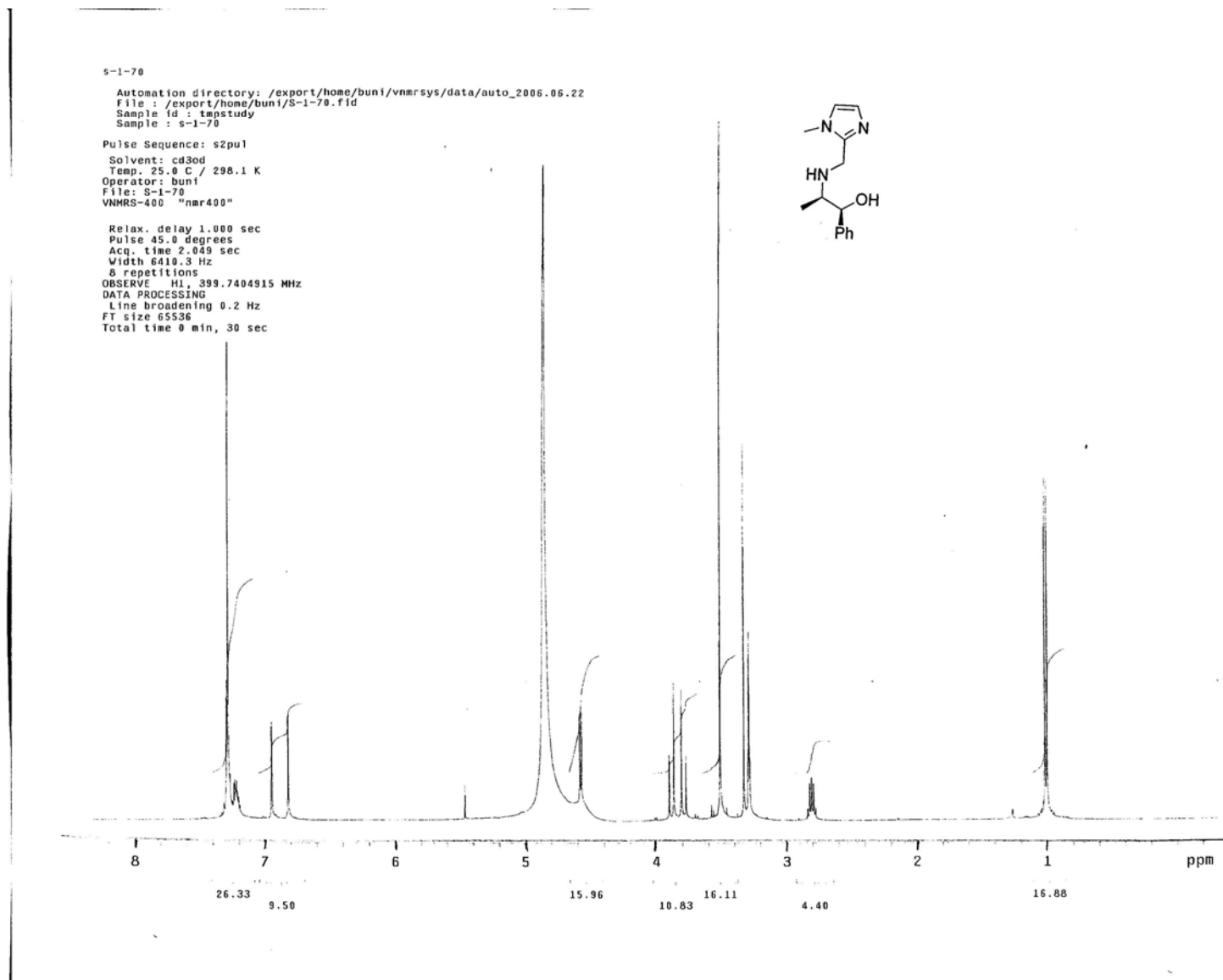
To a solution of imidazolium bromide **2** (550 mg, 1.43 mmol), in MeOH/H<sub>2</sub>O (3 mL, 5:1) was added potassium tetrafluoroborate (252 mg, 2.0 mmol) and allowed to stir at room temperature for 3 days. The reaction mixture was then filtered over celite and concentrated to dryness. The residue was dissolved in dichloromethane and filtered again to give product **3** (472 mg, 85%) as a pale yellow viscous liquid.  $[\alpha]_{\text{D}}^{20} = 7.04^{\circ}$  ( $c = 0.3$ , CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD)  $\delta$  7.41-7.20 (7H, m), 5.00 (1H, d,  $J = 2.8$  Hz), 4.57 (1H, d,  $J = 14.8$  Hz), 4.30 (1H, t,  $J = 7.6$  Hz), 4.15 (1H, d,  $J = 14.8$  Hz), 4.04 (3H, s), 3.04-2.96 (1H, m), 1.82-1.72 (2H, m), 1.40-1.30 (2H, m), 0.93 (3H, t,  $J = 7.2$  Hz), 0.89 (3H, d,  $J = 6.8$  Hz); <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD) 144.8, 142.1, 128.1, 127.9, 126.7, 126.2, 125.9, 123.2, 121.1, 72.8, 59.8, 48.8, 39.9, 36.5, 32.1, 19.6, 14.3, 13.5; HRMS (ESI)  $m/z$  (%) Calcd for C<sub>18</sub>H<sub>28</sub>N<sub>3</sub>O (M<sup>+</sup>): 302.2232, Found: 302.2235.

#### (4) Synthesis of CIL 4

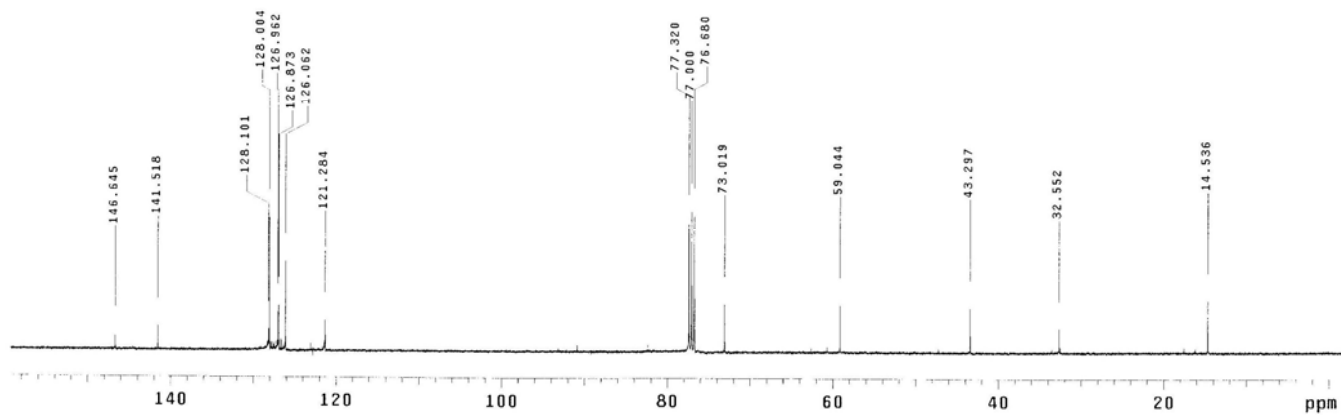
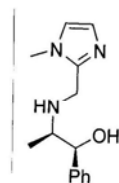


To a solution of imidazolium bromide **2** (550 mg, 1.43 mmol) in water (2 mL) was added lithium bis (trifluoromethanesulfonyl)imide (458 mg, 1.6 mmol) was stirred at room temperature for 2 h. The reaction was extracted with CH<sub>2</sub>Cl<sub>2</sub> (15 mL), and the organic phase was washed with water (3 X 5 mL), then concentrated, and dried in vacuum to give

product **4** (765 mg, 92%) as pale yellow viscous liquid.  $[\alpha]_{\text{D}}^{20} = -3.33^{\circ}$  ( $c = 0.36$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  7.34 -7.20 (5H, m), 7.12 (2H, s), 4.68 (1H, d,  $J = 4.4$  Hz), 4.13-3.95 (3H, m), 3.74 (3H, s), 2.93-2.85 (1H, m), 2.85-2.50 (2H, br), 1.75-1.65 (2H, m), 1.35-1.20 (2H, m), 0.96 (3H, d,  $J = 6.4$  Hz), 0.92 (3H, d,  $J = 7.2$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ) 144.1, 141.4, 128.2, 127.5, 126.3, 123.1, 121.1, 119.7 (q,  $J = 320$  Hz, 2C), 75.5, 58.9, 48.4, 39.2, 35.4, 31.8, 19.5, 14.9, 13.3. HRMS (ESI)  $m/z$  (%) Calcd for  $\text{C}_{18}\text{H}_{28}\text{N}_3\text{O}$  ( $\text{M}^+$ ): 302.2232, Found: 302.2236.



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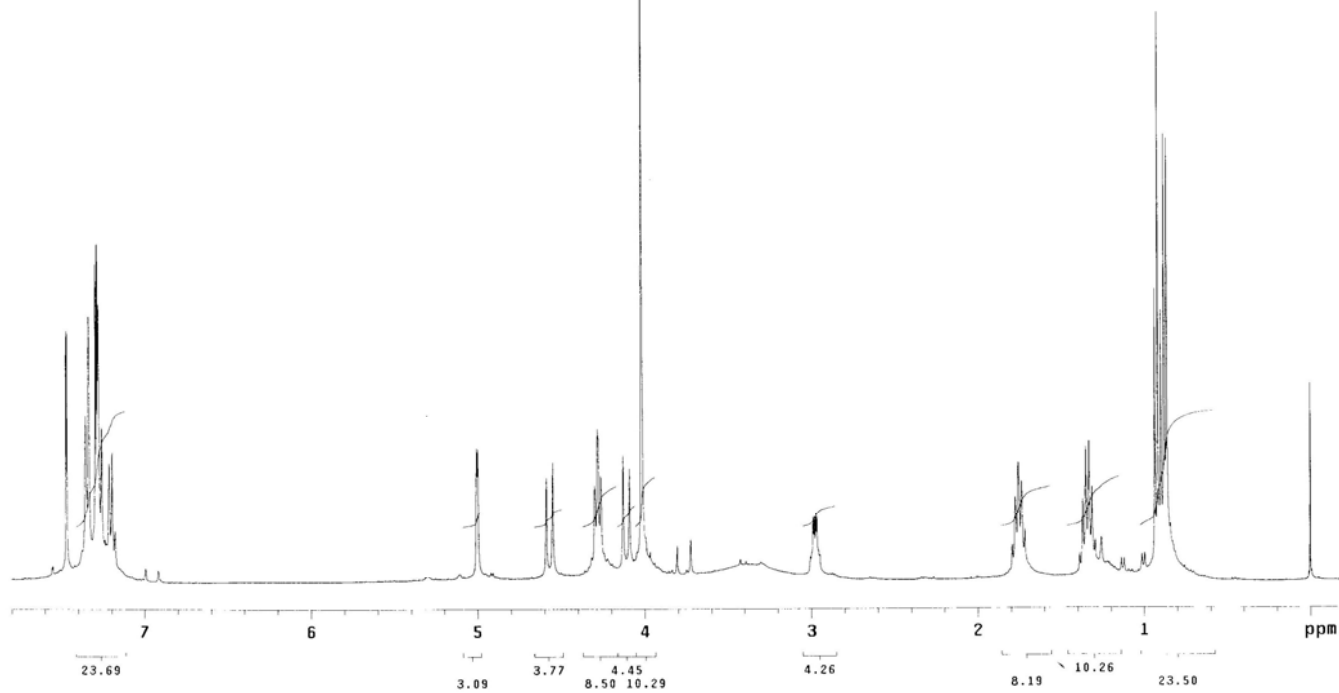
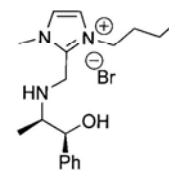


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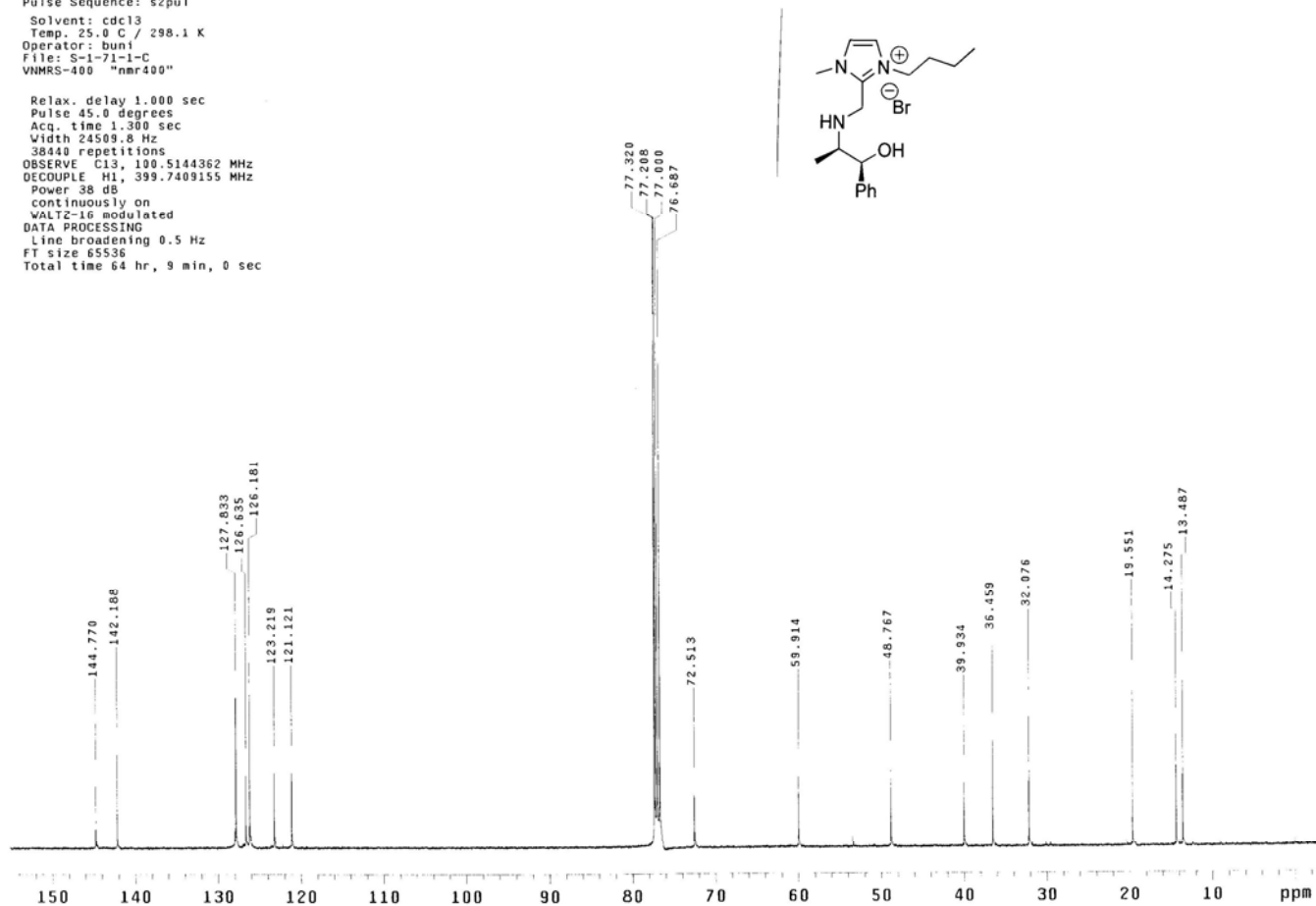


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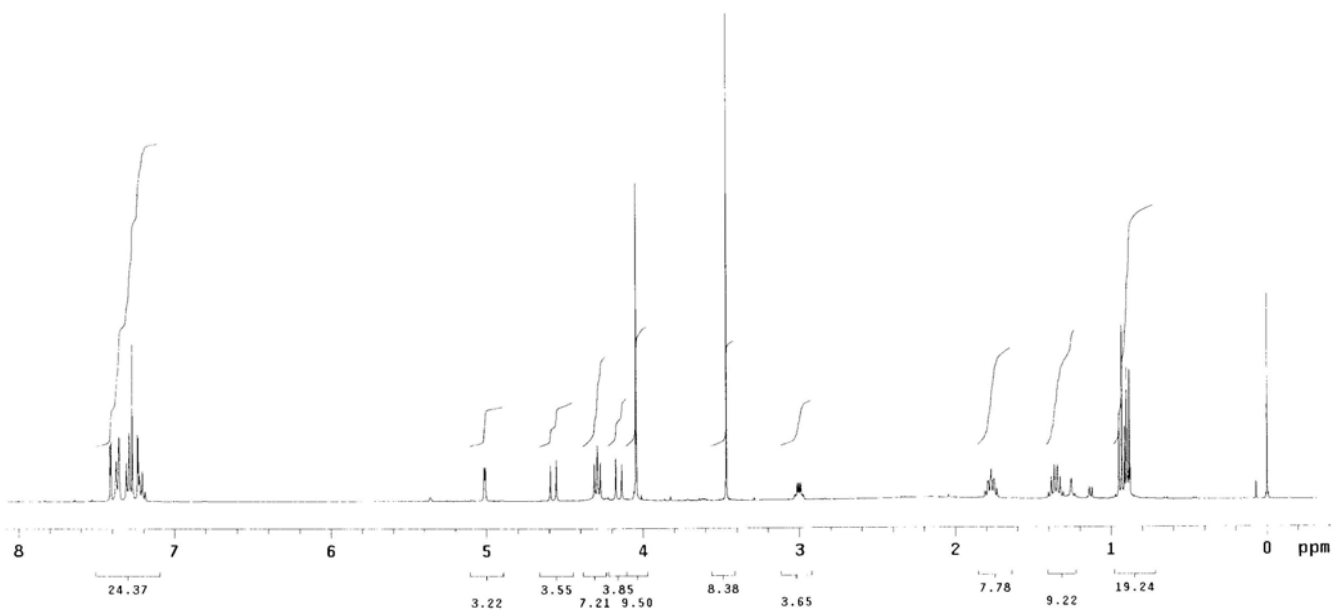
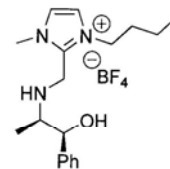
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Pulse 45.0 degrees  
Acq. time 1.300 sec  
Width 24509.8 Hz  
38449 repetitions  
OBSERVE C13, 100.5144362 MHz  
DECOUPLE H1, 399.7409155 MHz  
Power 38 dB  
continuously on  
WALTZ-16 modulated  
DATA PROCESSING  
Line broadening 0.5 Hz  
FT size 65536  
Total time 64 hr, 9 min, 0 sec

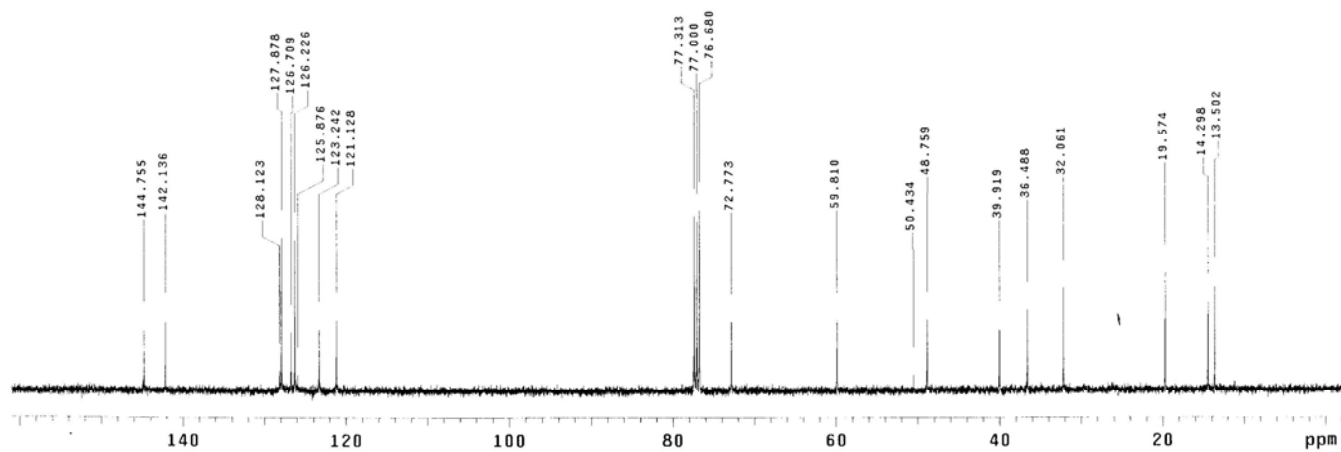
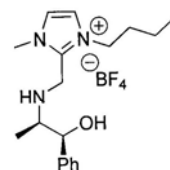




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OBSERVE H1, 399.7389048 MHz  
DATA PROCESSING  
Line broadening 0.2 Hz  
FT size 65536  
Total time 0 min, 30 sec



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WALTZ-16 modulated  
DATA PROCESSING  
Line broadening 0.5 Hz  
FT size 65536  
Total time 64 hr, 9 min, 0 sec



S-1-90-4H

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Operator: buni  
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Acq. time 2.049 sec  
Width 6410.3 Hz  
3 repetitions  
OBSERVE H1, 399.738975 MHz  
DATA PROCESSING  
Line broadening 0.2 Hz  
FT size 65536  
Total time 0 min, 30 sec

