Communication

Synthesis of New C₂-Symmetric Six-Membered NHCs and Their Application for the Asymmetric Diethylzinc Addition of Arylaldehydes

Jie Li 1, Bihui Zhou 1, Yajie Jiang 1 and Xiaoming Liu 2,*

1 School of Medicine, Zhejiang University City College, No. 48, Huzhou Road, Hangzhou 310015, China; lijie@zucc.edu.cn (J.L.); 18868816170@163.com (B.Z.); jjj15858261470@163.com (Y.J.)
2 Department of Dermatology, The Third Affiliated Hospital of Soochow University, No. 185, Juqian Street, Changzhou 213000, China
* Correspondence: xiaomingliu2012@163.com; Tel.: +86-135-1526-7906

Received: 23 December 2017; Accepted: 15 January 2018; Published: 26 January 2018

Abstract: A concise method for the preparation of new 3,4,5,6-tetrahydropyrimidinium salts was presented in this paper. Further application of these salts in asymmetric diethylzinc addition of arylaldehydes was explored, giving the corresponding chiral second alcohols in good yields and moderate enantioselectivities.

Keywords: N-heterocyclic carbene; tetrahydropyrimidinium; enantioselectivity; asymmetric addition; chiral secondary alcohols

1. Introduction

Since Arduengo et al. reported the first isolation of stable N-heterocyclic carbene (NHCs) [1], this kind of ligand has attracted great interest, and tremendous success has been achieved in carbene chemistry [2–12]. Not surprisingly, great effort has been devoted to the design and development of efficient NHC ligands in past decades. These ligands, initially considered as mimics of phosphine [13], are now ubiquitous in organic chemistry because of their outstanding properties such as stronger σ-donor and weaker π-acceptor compared to the corresponding phosphane ligand, and the metal complexes of these ligands usually show better stability to moisture, air, and heat as well [14,15]. Naturally, the development of chiral NHCs and the application of these ligands in stereoselective catalysis are receiving considerable attention as a next step [16–21]. To date, most of the research has employed five-membered NHCs based on imidazole or imidazoline. The so-called “expanded-ring” NHCs with six- [22–37] and seven- [38–49] heterocyclic rings have recently attracted attention, as these “non-standard” NHCs show quite different properties, such as stronger basicity (nucleophilicity) and greater steric demand [50]. Structurally, the larger ring sizes of these unusual NHCs will lead to a comparatively large N–CNHC–N angle and consequential smaller C_NHC–N–C_R angle, which in turn results in better protection of metal centers and subsequently better performance in catalysis. As part of our ongoing interest in ring-expanded NHC chemistry [51,52], we here present the synthesis of C₂-symmetric six-membered NHCs precursors by a smooth three-step method. After deprotonation of the precursor salts in situ, the new six-membered NHCs were tested as catalysts in asymmetric diethylzinc addition of arylaldehydes, giving the corresponding secondary alcohol with good yields and moderate enantioselectivities.

2. Results

Using commercial available amino alcohols as a starting material, we synthesized a series of enantiopure 3,4,5,6-tetrahydropyrimidinium salts (1a–1f) incorporating two hydroxyl groups and
evaluated their efficiency as ligands in palladium-catalyzed deprotonative-cross-coupling processes (DCCP) [52]. However, these salts showed poor enantioselectivities when tested as catalysts in an asymmetric diethylzinc addition to aldehydes (Table 1, entries 1–6). Since a steric functional group around the carbene center may be beneficial for asymmetric catalysis, we were interested in preparing the derivatives of salts (1) by modification of the OH group with bulky silyl groups. As presented in Scheme 1, simple treatment of 1a–1f with tert-butyldimethylsilyle chloride (TBSCI) gave silicification products 2a–2f in good yields (76–94% yield, see Figure S1 in Supplementary Materials for NMR data of 2a–2f).

![Scheme 1. Synthesis of NHC precursors 2a–2f.](image)

The new precursor salts were then tested in enantioselective asymmetric diethylzinc addition to 1-naphthaldehyde (3a). As shown in Table 1, derivatives 2b, 2e, and 2f, as catalysts in this transformation, showed better enantioselectivity than their parent compounds, and 2b gave the best result (92% yield, 45% ee). Three new tetrahydroprimidinium salts (Figure 1, 2g–2i) were further prepared by the same method as shown in Scheme 1, with 1b as a starting material. These salts replaced the OH group with different substituents. However, no improvement of ee values was observed when they were tested in this reaction (Table 1, entries 13–15). Next, we tried a variety of conditions with different solvents and bases. Unfortunately, no combination improved the enantioselectivity either (see Table S1 in Supplementary Materials for details).

**Table 1. Comparison of NHC precursors.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Salts</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>97</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>1b</td>
<td>86</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>1c</td>
<td>95</td>
<td>21</td>
</tr>
<tr>
<td>4</td>
<td>1d</td>
<td>90</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>1e</td>
<td>91</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>1f</td>
<td>77</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>2a</td>
<td>95</td>
<td>2</td>
</tr>
</tbody>
</table>
As indicated in Table 2, the reaction proceeded well in most cases (67–95% yield). Arylaldehydes and moderate enantiomeric excesses. The best enantioselectivity was obtained with nicotinaldehyde (4b).

Figure 1. The structures of 2g–2i.

With 2b as a catalyst precursor, different arylaldehydes were next applied in this transformation. As indicated in Table 2, the reaction proceeded well in most cases (67–95% yield). Arylaldehydes bearing electron-withdrawing (entries 3–9) and electron-donating (entries 10–13) groups, as well as heterocyclic substrates (entries 15–17), were all well-tolerated, giving product 4b–4r in good yields and moderate enantiomeric excesses. The best enantioselectivity was obtained with nicotinaldehyde (3p) as a starting material, giving the product in 54% ee.

Table 1. Cont.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Salts</th>
<th>Yield (%) b</th>
<th>ee (%) c</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>2b</td>
<td>92</td>
<td>45</td>
</tr>
<tr>
<td>9</td>
<td>2c</td>
<td>96</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>2d</td>
<td>95</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>2e</td>
<td>70</td>
<td>24</td>
</tr>
<tr>
<td>12</td>
<td>2f</td>
<td>89</td>
<td>11</td>
</tr>
<tr>
<td>13</td>
<td>2g</td>
<td>95</td>
<td>0</td>
</tr>
<tr>
<td>14</td>
<td>2h</td>
<td>97</td>
<td>6</td>
</tr>
<tr>
<td>15</td>
<td>2i</td>
<td>78</td>
<td>16</td>
</tr>
</tbody>
</table>

a Reaction condition: salt (10 mol %), KN(SiMe3)2 (30 mol %), Et2Zn (2 equiv.), N2, xylene, rt, 24 h. b Isolated yield.

c Determined by chiral HPLC (CHIRALCEL OD Column) analysis.

Table 2. Scope of methodology.

<table>
<thead>
<tr>
<th>Entry a</th>
<th>Ar</th>
<th>Product</th>
<th>Yield (%) b</th>
<th>ee (%) c</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2-Naphthyl</td>
<td>3b</td>
<td>4b</td>
<td>82</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>3c</td>
<td>4c</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td>2-MePh</td>
<td>3d</td>
<td>4d</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>3,4-diMePh</td>
<td>3e</td>
<td>4e</td>
<td>78</td>
</tr>
<tr>
<td>5</td>
<td>2,4,6-triMePh</td>
<td>3f</td>
<td>4f</td>
<td>69</td>
</tr>
<tr>
<td>6</td>
<td>4-EtPh</td>
<td>3g</td>
<td>4g</td>
<td>86</td>
</tr>
<tr>
<td>7</td>
<td>2-MeOPh</td>
<td>3h</td>
<td>4h</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>3-MeOPh</td>
<td>3i</td>
<td>4i</td>
<td>81</td>
</tr>
<tr>
<td>9</td>
<td>4-MeOPh</td>
<td>3j</td>
<td>4j</td>
<td>73</td>
</tr>
<tr>
<td>10</td>
<td>2-FPh</td>
<td>3k</td>
<td>4k</td>
<td>88</td>
</tr>
<tr>
<td>11</td>
<td>4-FPh</td>
<td>3l</td>
<td>4l</td>
<td>79</td>
</tr>
<tr>
<td>12</td>
<td>4-CF3 Ph</td>
<td>3m</td>
<td>4m</td>
<td>95</td>
</tr>
<tr>
<td>13</td>
<td>3,5-diFPh</td>
<td>3n</td>
<td>4n</td>
<td>84</td>
</tr>
<tr>
<td>14</td>
<td>Cinnamyl</td>
<td>3o</td>
<td>4o</td>
<td>81</td>
</tr>
<tr>
<td>15</td>
<td>3-Pyridine</td>
<td>3p</td>
<td>4p</td>
<td>67</td>
</tr>
<tr>
<td>16</td>
<td>2-Thienyl</td>
<td>3q</td>
<td>4q</td>
<td>75</td>
</tr>
<tr>
<td>17</td>
<td>2-Quinolyl</td>
<td>3r</td>
<td>4r</td>
<td>87</td>
</tr>
</tbody>
</table>

a Reaction condition: 2b (10 mol %), KN(SiMe3)2 (30 mol %), Et2Zn (2 equiv.), N2, xylene, rt, 24 h. b Isolated yield.

c Determined by chiral HPLC (CHIRALCEL OD Column) analysis.
3. Materials and Methods

3.1. General

1H- and 13C-NMR spectra were obtained on Bruker AVANCE III 500 MHz and 600 MHz spectrometers (Bruker Co., Billerica, MA, USA) with TMS as the internal standard; MS spectra were measured on a Finnigan LCQDECA XP instrument and a Agilent Q-TOF 1290 LC/6224 MS system (Santa Clara, CA, USA); silica gel GF254 and H (10–40 mm, Qingdao Marine Chemical Factory, Qingdao, China) were used for TLC and CC. Unless otherwise noted, all reactions were carried out under an atmosphere of argon or nitrogen.

3.2. Preparation of Benzimidazolium Salt (2)

A mixture of 1a (824 mg, 2 mmol), tert-butylidimethylsilyl chloride (1.2 g, 8 mmol) (Energy Chemical, Shanghai, China), and imidazole (1.09 g, 8 mmol) was dissolved in dry THF (10 mL). After stirring at room temperature for 12 h, the mixture was poured into water (50 mL) and extracted with dichloromethane (3 × 20 mL). The organic fractions were combined, washed with brine, and dried over Na2SO4 (Energy Chemical, Shanghai, China). The solvent was removed under reduced pressure, and the crude material purified by column chromatography (CH2Cl2/MeOH = 50/1) to give 2a (1.06 g, 83%). 1H-NMR (500 MHz, CDCl3) δ 8.66 (s, 1H), 7.44–7.35 (m, 10H), 4.97 (dd, J = 7.1, 3.9 Hz, 2H), 4.25–4.18 (m, 4H), 3.44–3.36 (m, 2H), 3.31–3.24 (m, 2H), 2.02–1.96 (m, 2H), 0.87 (s, 18H), 0.80 (s, 12H); 13C-NMR (125 MHz, CDCl3) δ 153.6, 133.7, 129.3, 129.2, 127.9, 68.6, 62.2, 41.3, 29.7, 25.8, 19.2, 18.1.

Analogous compounds 2b–2i were prepared according to a procedure similar to that of 2a.

2b: 92% yield; 1H-NMR (500 MHz, CDCl3) δ 8.13 (s, 1H), 7.32 (d, J = 7.4 Hz, 4H), 7.26 (d, J = 7.3 Hz, 2H), 7.18 (d, J = 7.2 Hz, 4H), 4.00 (s, 2H), 3.81–3.78 (m, 4H), 3.29 (m, 4H), 2.96 (dd, J = 7.8, 4.7 Hz, 4H), 1.77–1.70 (m, 2H), 0.90 (d, J = 4.9 Hz, 18H), 0.98 (s, 12H); 13C-NMR (125 MHz, CDCl3) δ 153.1, 136.1, 129.0, 127.2, 67.4, 64.0, 42.2, 34.7, 25.8, 18.9, 18.1. 2c: 76% yield; 1H-NMR (500 MHz, CDCl3) δ 8.20 (s, 1H), 3.87 (m, J = 11.6, 4.8 Hz, 4H), 3.58–3.51 (m, 2H), 3.44–3.35 (m, 4H), 2.13–2.01 (m, 4H), 1.02 (d, J = 6.6 Hz, 6H), 0.96 (d, J = 6.7 Hz, 6H), 0.98 (s, 18H), 0.90 (s, 12H); 13C-NMR (125 MHz, CDCl3) δ 154.0, 72.6, 62.3, 41.0, 26.4, 25.8, 19.8, 19.2, 19.1, 18.2. 2d: 91% yield; 1H-NMR (500 MHz, CDCl3) δ 8.15–8.10 (m, 1H), 3.71 (dd, J = 12.0, 7.5 Hz, 2H), 3.49 (m, 2H), 3.42 (m, 2H), 2.18 (s, 2H), 1.22–1.07 (m, 2H), 1.15–1.45 (m, 4H), 0.98 (dd, J = 6.3, 3.7 Hz, 12H), 0.90 (s, 2H); 13C-NMR (125 MHz, CDCl3) δ 153.4, 64.8, 63.5, 41.6, 36.5, 25.8, 24.8, 22.7, 22.4, 19.1, 18.1. 2e: 86% yield; 1H-NMR (500 MHz, CDCl3) δ 8.17 (s, 1H), 3.92–3.84 (m, 4H), 3.59–3.45 (m, 4H), 3.40–3.33 (m, 4H), 2.10 (dd, J = 11.6, 5.7 Hz, 2H), 1.82 (dt, J = 10.0, 6.6 Hz, 2H), 1.38–1.33 (m, 2H), 1.20–1.17 (m, 2H), 0.97 (d, J = 6.6 Hz, 6H), 0.99 (s, 18H), 0.90 (s, 12H); 13C-NMR (125 MHz, CDCl3) δ 154.1, 71.2, 62.3, 41.0, 32.5, 25.8, 19.1, 18.2, 15.0. 2f: 94% yield; 1H-NMR (500 MHz, CDCl3) δ 8.13 (s, 1H), 3.92 (d, J = 6.8 Hz, 4H), 3.55–3.46 (m, 6H), 2.13 (dd, J = 11.1, 5.5 Hz, 2H), 1.03 (s, 18H), 0.87 (s, 18H), 0.10 (s, 6H), 0.90 (s, 6H). 2g: 73% yield; 1H-NMR (500 MHz, CDCl3) δ 8.19 (s, 1H), 7.32 (d, J = 7.4 Hz, 4H), 7.25 (d, J = 7.0 Hz, 2H), 7.15 (d, J = 7.3 Hz, 4H), 3.97–3.79 (m, 4H), 3.45–3.23 (m, 4H), 3.07–2.85 (m, 4H), 1.79–1.74 (m, 2H), 1.03 (d, J = 6.5 Hz, 36H), 1.00 (m, 6H), 0.64 (m, 2H); 13C-NMR (125 MHz, CDCl3) δ 153.1, 136.0, 129.1, 129.0, 127.3, 67.6, 64.9, 42.2, 34.7, 29.7, 18.0, 11.8. 2h: 84% yield; 1H-NMR (500 MHz, CDCl3) δ 8.10 (s, 1H), 7.32 (t, J = 7.4 Hz, 4H), 7.24 (t, J = 7.1 Hz, 2H), 7.19 (d, J = 7.1 Hz, 4H), 3.98 (tt, J = 8.3, 4.2 Hz, 2H), 3.85–3.73 (m, 4H), 3.37–3.22 (m, 4H), 3.03–2.90 (m, 4H), 1.73 (p, J = 5.7 Hz, 2H), 0.98–0.91 (m, 18H), 0.60 (q, J = 8.0 Hz, 12H); 13C-NMR (125 MHz, CDCl3) δ 153.0, 136.1, 129.1, 129.0, 128.8, 127.2, 67.5, 63.6, 42.3, 34.8, 29.7, 18.9, 6.8, 4.2. 2i: 69% yield; 1H-NMR (500 MHz, CDCl3) δ 8.07 (s, 1H), 7.61–7.56 (m, 8H), 7.47 (m, 4H), 7.41 (td, J = 7.2, 5.0 Hz, 8H), 7.24 (t, J = 7.4 Hz, 4H), 7.16 (t, J = 7.3 Hz, 2H), 7.10 (d, J = 7.1 Hz, 4H), 3.97 (d, J = 11.0 Hz, 2H), 3.88–3.79 (m, 4H), 3.29–3.13 (m, 4H), 2.95–2.83 (m, 4H), 1.70–1.64 (m, 2H), 1.07 (s, 18H); 13C-NMR (125 MHz,
Analogous compounds 4b–4r were prepared according to a procedure similar to that of 4a. 4b: 82% yield, 40% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (minor) = 19.1 min, t<sub>r</sub> (major) = 22.4 min). 4c: 74% yield, 33% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (minor) = 11.3 min, t<sub>r</sub> (major) = 12.2 min). 4d: 89% yield, 26% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (minor) = 11.3 min, t<sub>r</sub> (major) = 12.7 min). 4e: 78% yield, 40% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.4 mL/min, t<sub>r</sub> (major) = 14.5 min, t<sub>r</sub> (minor) = 16.6 min). 4f: 69% yield, 28% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (minor) = 12.2 min, t<sub>r</sub> (major) = 13.1 min). 4g: 86% yield, 37% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.4 mL/min, t<sub>r</sub> (major) = 8.6 min, t<sub>r</sub> (minor) = 9.2 min). 4h: 92% yield, 35% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (major) = 13.6 min, t<sub>r</sub> (minor) = 15.4 min). 4i: 81% yield, 38% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (minor) = 10.6 min, t<sub>r</sub> (major) = 12.4 min). 4j: 88% yield, 14% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (major) = 11.7 min, t<sub>r</sub> (minor) = 15.0 min). 4k: 79% yield, 28% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 93/7, flow rate = 0.5 mL/min, t<sub>r</sub> (major) = 11.1 min, t<sub>r</sub> (minor) = 12.3 min). 4l: 95% yield, 48% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (major) = 7.7 min, t<sub>r</sub> (minor) = 8.6 min). 4m: 84% yield, 44% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 93/7, flow rate = 0.5 mL/min, t<sub>r</sub> (major) = 11.6 min, t<sub>r</sub> (minor) = 14.8 min). 4n: 81% yield, 36% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 93/7, flow rate = 0.5 mL/min, t<sub>r</sub> (major) = 12.8 min, t<sub>r</sub> (minor) = 15.6 min). 4o: 67% yield, 54% ee; the spectral data were comparable to those reported [53]. The ee was determined

3.3. Representative Procedure for the Asymmetric Addition of Diethylzinc to Aldehyde

Under an argon atmosphere, a mixture of salt (2b) (0.01 mmol) and KN (SiMe<sub>3</sub>)<sub>2</sub> (0.03 mmol) in xylene (1 mL) was stirred for 5 min at room temperature. Then diethylzinc (0.2 mmol) was added dropwise, followed by an addition of 1-naphthaldehyde (3a; 14 µL, 0.1 mmol). Upon stirring for 24 h at room temperature, the reaction was quenched by HCl (1 M, 1.0 mL) and extracted with Et<sub>2</sub>O (3 × 2 mL). The combined organic phases were washed with water and dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under vacuum. The residue was further purified by column chromatography (silica gel, hexane/AcOEt) to yield product 4a as a colorless oil (92% yield, 45% ee). The spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/PrOH = 90/10, flow rate = 0.5 mL/min, t<sub>r</sub> (minor) = 15.7 min, t<sub>r</sub> (major) = 28.6 min).

(CDCl<sub>3</sub>) δ 153.2, 135.7, 135.6, 135.5, 132.3, 130.2, 129.0, 128.9, 128.1, 128.0, 127.2, 67.3, 64.3, 41.6, 34.8, 29.7, 27.0, 19.2.
by HPLC analysis with Daicel Chiralcel OD-H (hexane/iPrOH = 93/7, flow rate = 0.5 mL/min, t_r (minor) = 12.9 min, t_r (major) = 14.1 min). 4q: 75% yield, 33% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/iPrOH = 93/7, flow rate = 0.5 mL/min, t_r (minor) = 9.4 min, t_r (major) = 10.7 min). 4r: 87% yield, 29% ee; the spectral data were comparable to those reported [53]. The ee was determined by HPLC analysis with Daicel Chiralcel OD-H (hexane/iPrOH = 90/10, flow rate = 0.5 mL/min, t_r (minor) = 15.6 min, t_r (major) = 29.1 min).

4. Conclusions

The chiral 3,4,5,6-tetrahydropyrimidinium salts with bulky silyl groups were readily synthesized by a three-step method starting with commercial amino alcohols. In situ prepared corresponding carbenes, along with their parent carbenes, were then tested in an asymmetric diethylzinc addition of aryaldehydes, producing the product in good yield and better enantioselectivities. In brief, an example of improvement in performance of catalysts by modification of their OH group with a steric functional group has been shown. Further study of these tetrahydropyrimidinium salts as ligands for metal-mediated asymmetric catalysis are currently underway [54,55].

Supplementary Materials: The following are available online at http://www.mdpi.com/xxx/s1, Figure S1: 1H and 13C NMR Spectra of Compounds 2a–2i, Table S1: Optimization of the reaction conditions.

Acknowledgments: We are grateful to Changzhou High-Level Medical Talents Training Project (2016CZBJ034), the National Natural Science Foundation of China (81302668), and the Hangzhou Science and Technology Information Institute of China (20150633B45).

Author Contributions: Xiaoming Liu and Jie Li conceived and designed the experiments; Bihui Zhou and Yajie Jiang performed the experiments and analyzed the data; Xiaoming Liu and Jie Li wrote the paper.

Conflicts of Interest: The authors declare no conflict of interest.

References


© 2018 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).