Brønsted Acid Catalyzed Asymmetric Silylation of Biaryl Diols

Jung Tae Han  
Hui Zhou  
Benjamin List*  
Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470, Mülheim an der Ruhr, Germany  
list@kofo.mpg.de  
Published as part of the  
Special Issue Dedicated to Prof. Hisashi Yamamoto

Abstract  We report a Brønsted acid catalyzed enantioselective silylation of biaryl diols with an allylsilane as a silicon source. This process enables facile access to enantioenriched biaryl silyl ethers with an axial stereogenicity. A control experiment supports a mechanism proceeding by desymmetrization followed by kinetic resolution.

Key words  Brønsted acid, imidodiphosphorimidate, silylation, axial chirality, desymmetrization, kinetic resolution

The silylation of alcohols is a commonly used protecting group operation in chemical synthesis.1 Since the first enantioselective variant reported by Ishikawa,2 several catalytic enantioselective approaches have been developed during the past two decades.3 The majority of these methods use a chiral Lewis base catalyst in conjunction with a stoichiometric amount of an achiral base and a silyl chloride (Scheme 1a).4 Transition-metal-catalyzed silylations of alcohols with hydrosilanes via kinetic resolution have also been developed.5 Recently, we reported a Brønsted acid catalyzed enantioselective silylation of phenol derivatives with allylsilanes.6 Inspired by our studies on silicon–hydrogen exchange reactions, we recently found that strong and confined imidodiphosphorimidate (IDPi) Brønsted acids catalyze the enantioselective silylation of phenol derivatives with allylsilanes.7 We envisioned that our silylation strategy could be applied to biaryl diols to yield axially chiral biaryl silyl ethers. Indeed, we herein report a Brønsted acid catalyzed atroposelective silylation of biaryl diols (Scheme 1c).

We commenced our investigation by examining the silylation of biaryl diol 1a in the presence of different IDPi catalysts 4 and allyl(tert-butyl)dimethylsilane (2) (Table 1). Catalyst 4a afforded the desired mono-silylated product, but with poor enantioselectivity (54:46 er; entry 1). While catalysts 4b–e revealed low enantioselectivities (54:46 to 62:38 er; entries 2–5), catalyst 4f resulted in promising enantioselectivity (71:29 er; entry 6). A modification of the m,m-substituents on the 3,3′-phenyl groups of the BINOL backbone from trifluoromethyl to pentafluorosulfanyl further enhanced the enantioselectivity (77:23 er; entry 7). At −50 °C, the reaction proceeded with 86:14 er (entry 8). Finally, high enantioselectivity was achieved by increasing the amount of allylsilane 2 (95:5 er; entry 9).

Scheme 1  Catalytic asymmetric silylation of alcohols
We performed a control experiment that confirmed that a kinetic resolution takes place during a second silylation (Scheme 3). Upon subjecting racemic mono-silylated product 3a to Brønsted acid catalyzed silylation conditions, bis-silylated product 5a was obtained and the remaining 3a showed an er of 68:32. This result is consistent with the desymmetrizing silylation of 1a to initially provide the enantioenriched mono-silylated product 3a, the enantioselectivity of which is further improved in the second silylation via kinetic resolution. Although several catalysts (4b, 4e, and 4f) were further examined for the kinetic resolution, they did not afford the bis-silylated product 5a.

In summary, we have developed a Brønsted acid catalyzed asymmetric silylation of biaryl diols that provides access to axially chiral biaryl silyl ethers. A simple mechanistic investigation has revealed that the reaction proceeds via a desymmetrization–kinetic resolution sequence. Efforts to develop other useful silylation methods are currently underway in our laboratory. During our studies, Professor Martin Oestreich kindly shared a manuscript with us describing his independent and advanced investigation of the same transformation. Our own studies on the asymmetric silylation of biaryl diols have since been terminated at the reported stage.

Conflict of Interest
The authors declare no conflict of interest.

Funding Information
Generous support from the Deutsche Forschungsgemeinschaft (Leibniz Award to B.L. and Germany’s Excellence Strategy–EXC 2033–390677874–RESOLV), and the European Research Council (European Union’s Horizon 2020 research and innovation program ‘Early Stage Organocatalysis, ESOC’) is gratefully acknowledged.

Acknowledgment
We thank the technicians of our group and the members of our mass spectrometry (MS) group for their excellent service.

**Table 1 Optimization of the Reaction Conditions**

<table>
<thead>
<tr>
<th>Entry</th>
<th>IDPi</th>
<th>Temp (°C)</th>
<th>Conv. (%)</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4a</td>
<td>rt</td>
<td>70</td>
<td>54:46</td>
</tr>
<tr>
<td>2</td>
<td>4b</td>
<td>rt</td>
<td>67</td>
<td>54:46</td>
</tr>
<tr>
<td>3</td>
<td>4c</td>
<td>rt</td>
<td>70</td>
<td>61:39</td>
</tr>
<tr>
<td>4</td>
<td>4d</td>
<td>rt</td>
<td>71</td>
<td>56:44</td>
</tr>
<tr>
<td>5</td>
<td>4e</td>
<td>rt</td>
<td>55</td>
<td>62:38</td>
</tr>
<tr>
<td>6</td>
<td>4f</td>
<td>rt</td>
<td>66</td>
<td>71:29</td>
</tr>
<tr>
<td>7</td>
<td>4g</td>
<td>–50</td>
<td>70</td>
<td>77:23</td>
</tr>
<tr>
<td>8b</td>
<td>4g</td>
<td>–50</td>
<td>70</td>
<td>86:14</td>
</tr>
<tr>
<td>9c</td>
<td>4g</td>
<td>full</td>
<td>50</td>
<td>95:5</td>
</tr>
</tbody>
</table>

*Reactions were performed with substrate 1a (0.025 mmol), allylsilane 2 (1.5 equiv.) and IDPi 4 (2.5 mol%) in CHCl3 (0.25 mL); conversions (conv.) were determined by 1H NMR analysis with dibromomethane as an internal standard; enantiomeric ratios (er) were measured by HPLC analysis.

**Scheme 2** Asymmetric silylation of biaryl diols. Reactions were performed on a 0.1 mmol scale. Reaction was conducted with catalyst 4g and allylsilane 2 (2 equiv.) in CHCl3 (0.1 M) at –50 °C for 5 days. Reaction was conducted with catalyst 4b and allylsilane 2 (1.5 equiv.) in CH2Cl2 (0.2 M) at –30 °C for 3 days.

**Scheme 3** Control experiment

In summary, we have developed a Brønsted acid catalyzed asymmetric silylation of biaryl diols that provides access to axially chiral biaryl silyl ethers. A simple mechanistic investigation has revealed that the reaction proceeds via a desymmetrization–kinetic resolution sequence. Efforts to develop other useful silylation methods are currently underway in our laboratory. During our studies, Professor Martin Oestreich kindly shared a manuscript with us describing his independent and advanced investigation of the same transformation. Our own studies on the asymmetric silylation of biaryl diols have since been terminated at the reported stage.

Conflict of Interest
The authors declare no conflict of interest.

Funding Information
Generous support from the Deutsche Forschungsgemeinschaft (Leibniz Award to B.L. and Germany’s Excellence Strategy–EXC 2033–390677874–RESOLV), and the European Research Council (European Union’s Horizon 2020 research and innovation program ‘Early Stage Organocatalysis, ESOC’) is gratefully acknowledged.

Acknowledgment
We thank the technicians of our group and the members of our mass spectrometry (MS) group for their excellent service.
Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-2100-1575.

References and Notes


(9) Silylation of Biaryl Diols; General Procedure
A GC vial equipped with a Teflon-coated magnetic stir bar was charged with catalyst 4 (2.5 mol%), biaryl diol 1 (0.1 mmol) and solvent (CHCl3 or CH2Cl2), and the resulting mixture was cooled to –50 or –30 °C in a cryostat. After 10 min, allylsilane 2 (2 or 1.5 equiv.) was slowly added and the reaction mixture was stirred for 3–5 d at the same temperature. After complete conversion as indicated by TLC, the reaction was quenched with trimethylamine. The solvent was removed in vacuo and the mixture was purified by column chromatography on silica gel to afford the desired silyl ether 3.

(S)-6-((tert-Butyldimethylsilyl)oxy)-2′-methyl-[1,1′-biphenyl]-2-ol [(S)-3a]
Yield: 12.6 mg (40%); white solid; [α]D2525.5 (c 0.53, CHCl3. 1H NMR (501 MHz, CD2Cl2): δ = 7.34–7.24 (m, 3 H), 7.16 (dd, J = 7.4, 1.7 Hz, 1 H), 7.12 (t, J = 8.2 Hz, 1 H), 6.60 (dd, J = 8.2, 1.0 Hz, 1 H), 6.50 (dd, J = 8.1, 1.0 Hz, 1 H), 4.75 (s, 1 H), 2.12 (s, 3 H), 0.65 (s, 9 H), 0.07 (s, 3 H), –0.06 (s, 3 H). 13C NMR (126 MHz, CD 2Cl2): δ = 154.4, 154.0, 139.2, 132.7, 131.5, 130.9, 129.1, 128.8, 126.5, 120.2, 111.7, 108.5, 25.3, 19.8, 18.0, –4.3, –4.6. EI-HRMS: m/z [M]+ calcd for C19H26O2Si: 314.1695; found: 314.1697. HPLC (IA-3, heptane/isopropanol = 95:5, 0.5 mL/min, 298 K, 220 nm): tR1 = 8.6 min, tR2 = 10.8 min; er = 95:5.