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Cobalt-Catalysed Markovnikov Selective Hydroboration of Vinylarenes

Jingying Peng, Jamie H. Docherty, Andrew. P. Dominey and Stephen P. Thomas

A bipyridiyl-oxazoline cobalt catalyst \( \text{tBuBPOCoCl}_2 \) has been developed for the Markovnikov selective hydroboration of alkenes using pinacolborane and NaO\( \text{tBu} \) as the \textit{in situ} activator with up to >98:2 branched:linear selectivity (24 examples, 45-92% isolated yield).

Metal-catalysed alkene hydroboration has received much attention, as the resulting boronic esters are versatile intermediates in the construction of various C-C and C-heteroatom bonds. The majority of metal-catalysed alkene hydroboration reactions involve complexes of precious metals, such as Rh, Ru and Ir. Although high chemoselectivity, regioselectivity, and enantioselectivity can be achieved, the low abundance and environmental concerns associated with these metals has driven investigations for Earth-abundant metal alternatives.

In recent years, a number of Earth-abundant and base metal complexes have been developed for alkene hydroboration. In most cases, these reactions are either highly anti-Markovnikov selective or give a mixture of both Markovnikov and anti-Markovnikov products. Huang reported that bipyridyl-phosphine cobalt complexes show high activity in the anti-Markovnikov hydroboration of alkenes. Additionally, Chirik developed bis(imino)pyridine cobalt methyl complexes for the anti-Markovnikov selective hydroboration of alkenes (Scheme 1, A). Of direct significance to this advance, Chirik and Hollis have both reported unique cobalt catalysts capable of catalysing the Markovnikov selective hydroboration of styrene in 25:1 and 20:1 branched to linear ratio, respectively (Scheme 1, B). Isomerisation-hydroboration using cobalt catalysis has also been reported by Chirik; this serves as an orthogonal procedure for the generation of branched boronic esters from aliphatic alkenes. However, a general reaction protocol with broad scope using a cobalt catalyst for the direct Markovnikov selective hydroboration of alkenes has not been disclosed.

Herein, we report the preparation of bipyridiyl-oxazoline cobalt(II) complexes and the application of these in cobalt-catalysed alkene hydroboration using NaO\( \text{tBu} \) as the \textit{in situ} pre-catalyst activator. This system presents a new and unique method for the generation of secondary boronic esters from readily available vinylarene starting materials with high regioselectivity, which is divergent from the majority of cobalt-catalysed alkene hydroboration reactions (Scheme 1, C).
A series of cobalt complexes 5a-5d bearing novel bipyridyl-oxazoline ligands were synthesised in four steps (Scheme 2). Reaction of 2,2'-bipyridine with hydrogen peroxide and trifluoroacetic acid gave 2,2'-bipyridine-1-oxide, which was reacted with trimethylsilyl cyanide and benzoyl chloride to give the bipyridyl-carbonitrile compound. Condensation of the bipyridyl-carbonitrile with various amino alcohols in the presence of Zn(OTf)₂ produced the bipyridyl-oxazoline ligands 4a-4c in moderate yields. The neutral bipyridyl-oxazoline cobalt(II) dichloride complexes 5a-5c were formed in high yield by the addition of the corresponding ligand to anhydrous cobalt dichloride in anhydrous tetrahydrofuran (THF). Similarly, terpyridine complex 5d was synthesised in the same way from commercially available terpyridine. These cobalt complexes showed paramagnetically broadened and shifted resonances in the ¹H NMR spectra (see supporting information).

![Scheme 2](image)

Scheme 2. Synthesis of bipyridyl-oxazoline cobalt complexes 5a-5c and terpyridine cobalt complex 5d.

Initial studies focused on the hydroboration of styrene with pinacolborane (1.1 equiv) using a range of cobalt pre-catalysts (1 mol%) and NaO'Bu (2 mol%) as the in situ activator in tetrahydrofuran at room temperature (Table 1). Hydroboration of styrene using [Co]BPOCoCl₂ 5a and [Co]BPOCoCl₂ 5b gave the branched hydroboration product in good yield and with 70:30 and 82:18 branched:linear regioselectivity, respectively (Table 1, entries 1-2). When the more bulky [Co]BPOCoCl₂ 5c was used, hydroboration of styrene proceeded in excellent yield and with the highest selectivity for the Markovnikov regioisomer (97:3) (Table 1, entry 3). Terpyridine cobalt complex 5d gave a moderate yield and good Markovnikov regioselectivity (91:1) (Table 1, entry 4). When the hydroboration of styrene, using [Co]BPOCoCl₂ 5c, was performed in the absence of solvent, good Markovnikov selectivity (91:1 b/l) was also achieved, but with decreased yield (Table 1, entry 5). Hydroboration of styrene proceeded well in ethyl acetate and toluene, albeit in reduced yield and regioselectivity compared to that in THF (Table 1, entries 6-7). Catalyst activation in situ with EtMgBr and NaBHEt₃ gave both lower yields and regioselectivities compared to the activation using NaO'Bu (Table 1, entries 8-9). A control reaction using non-ligated anhydrous CoCl₂ under the optimised reaction conditions, showed no catalytic activity (Table 1, entry 10). Similarly, the reaction did not proceed in the absence of cobalt pre-catalyst or without added NaO'Bu (Table 1, entries 11-12).

Table 1. Reaction optimisation for cobalt-catalysed hydroboration of styrene.²

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Co]</th>
<th>Activator</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>Branched :Linear</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a(1)</td>
<td>NaO'Bu(2)</td>
<td>THF</td>
<td>82</td>
<td>70:30</td>
</tr>
<tr>
<td>2</td>
<td>5b(1)</td>
<td>NaO'Bu(2)</td>
<td>THF</td>
<td>87</td>
<td>82:18</td>
</tr>
<tr>
<td>3</td>
<td>5c(1)</td>
<td>NaO'Bu(2)</td>
<td>THF</td>
<td>&gt;95</td>
<td>97:3</td>
</tr>
<tr>
<td>4</td>
<td>5d(1)</td>
<td>NaO'Bu(2)</td>
<td>THF</td>
<td>69</td>
<td>91:9</td>
</tr>
<tr>
<td>5</td>
<td>5c(1)</td>
<td>Neat</td>
<td>THF</td>
<td>59</td>
<td>91:9</td>
</tr>
<tr>
<td>6</td>
<td>5c(1)</td>
<td>NaO'Bu(2)</td>
<td>EtOAc</td>
<td>77a</td>
<td>96:4</td>
</tr>
<tr>
<td>7</td>
<td>5c(1)</td>
<td>Neat</td>
<td>Toluene</td>
<td>&gt;95</td>
<td>95:5</td>
</tr>
<tr>
<td>8</td>
<td>5c(1)</td>
<td>EtMgBr(2)</td>
<td>THF</td>
<td>85</td>
<td>90:10</td>
</tr>
<tr>
<td>9</td>
<td>5c(1)</td>
<td>NaBHEt₃(2)</td>
<td>THF</td>
<td>63d</td>
<td>86:14</td>
</tr>
<tr>
<td>10º</td>
<td>CoCl₂(1)</td>
<td>NaO'Bu(2)</td>
<td>THF</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>-</td>
<td>NaO'Bu(2)</td>
<td>THF</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>5a(1)</td>
<td>-</td>
<td>THF</td>
<td>3</td>
<td>n.d</td>
</tr>
</tbody>
</table>

[a] Standard reaction conditions: styrene (0.5 mmol), HBpin (1.1 equiv.), [Co] (1.0 mol%) and NaO'Bu (2.0 mol%) in THF (3 ml) at 25 °C. [b] Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard. [c] 2% hydrogenation product observed. [d] 5% hydrogenation product observed. [e] 30% hydrogenation product observed.

Using the optimised reaction conditions, the substrate scope of the Markovnikov selective hydroboration was explored using a range of electronically and sterically differentiated styrene derivatives (Table 2). Hydroboration of styrene gave the secondary boronic ester in excellent isolated yield, and a 97:3 branched:linear selectivity (3a, 90%). Styrene derivatives bearing electron-donating groups such as iso-propyl, tert-butyl and methyl underwent successful hydroboration in excellent yield and regioselectivity (3b-3e, 72-87%). 4-Phenylstyrene gave the secondary boronic ester in good yield and regioselectivity (3f, 88%). Styrene derivatives bearing electron-withdrawing substituents including fluoro-, chloro-, bromo- and trifluoromethyl- also underwent successful hydroboration, giving the secondary boronic esters in moderate to excellent yields, with no cleavage of aryl-halide bond observed (3g-3i, 45-
organo-cobalt species, 22 to generate a cobalt hydride that hydrogenation product observed in the crude reaction mixture. [c] 8% alkene hydrogenation product observed in the crude reaction mixture.

derivatives containing more than one unsaturated group, such as ester and nitrile substituents, were chemoselectively hydroborated at the alkene in excellent yield and regioselectivity, with no observed C–O or C-N bond cleavage, or reduction (3r-3t, 69-80%).21 Styrene derivatives bearing substituents at the β-position, such as trans-β-methylstyrene and indene were also reactive under the developed conditions, giving the product boronic esters with complete control of regioselectivity and in excellent yield (3u-3v, 79-90%). For alkyl alkenes, ketone containing alkene 1w successfully gave the branched boronic ester 3w in good yield with moderate regioselectivity and without ketone reduction. Hydroboration of 2,3-dimethyl-1-butene 1x gave the linear boronic ester 2x in good yield. Presumably the increased steric bulk of the 1,1-disubstituted alkene led to anti-Markovnikov regiosomer. Oxidation of the secondary boronic ester products to the corresponding alcohols, and analysis by chiral HPLC, showed no enantioselectivity, indicating no stereoinduction from the ligand.

In order to gain insight into the mechanism of the Markovnikov selective hydroboration of vinylarenes with HBPin, deuterium labelling experiments were performed. When the hydroboration of styrene was carried out in d5-THF, only the fully protio-boronic ester 3a was obtained, indicating that both H and Bpin originate from pinacolborane (Scheme 3, A). When the hydroboration of d5-styrene with HBPin was performed in THF, the mono-protio-boronic ester d5-3a was formed exclusively with ‘H’ at the terminal methyl group (Scheme 3, B). When DBpin (96% D-content) was used in the hydroboration of styrene, a mixture of mono-deuterated boronic ester d1-3a and fully protio-boronic ester 3a were formed, in a ratio of 88:12 D/H (Scheme 3, C). The presence of (fully) protio-3a presumably arises from either β-hydride elimination of an intermediate organo-cobalt species,22 to generate a cobalt hydride that
serves to add ‘H’ to styrene 1a, or H/D exchange with extraneous water, either present in the reaction medium or on work-up.

In conclusion, we have developed a Markovnikov selective cobalt-catalysed hydroboration of alkenes with pinacolborane at ambient temperature, using a bench-stable cobalt pre-catalyst bearing a bipyridiyl-oxazoline ligand. This strategy has been applied to a variety of electronically and sterically differentiated styrene derivatives, bearing a range of functional groups, to give the secondary boronic esters in both high yield and regioselectivity.

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Notes and references


A bipyridyl-oxazoline cobalt catalyst $t\text{BuBPOCoCl}_2$ has been developed for the Markovnikov selective hydroboration of vinylarenes using pinacolborane and NaO$\text{t}$Bu as the *in situ* activator.