New chiral bis(oxazolinyl)bipyridine ligands and application in the iron catalyzed asymmetric hydrosilylation of ketones

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$C_2$ symmetrical $6,6'$-bis(oxazolinyl)-2,2'-bipyridine ($bipybox$) chiral ligands have been synthesized from readily available 2,2'-bipyridine. Catalytic asymmetric hydrosilylation of ketones was studied using this family of ligands in the presence of iron(II) acetate.

Introduction

The reduction of unsaturated compounds containing C=C, C=N and C=O bonds is among the most studied and probably the most diversified reactions. There is a large variety of methods to perform the reduction of double bonds.[1] Our work focuses on the asymmetric reduction of the C=O carbonyl group using the hydrosilylation reaction.[2] There is a large interest to develop procedures affording enantiomerically pure secondary alcohols. Their preparation is essential because they are important building blocks in the synthesis of biologically important products. Especially, chiral secondary alcohols are suitable key intermediates for the synthesis of biologically active components and hence have emerged as important targets in the pharmaceutical industry.[3] Iron is one of the most abundant metals on Earth; it is inexpensive, environmentally benign, and relatively nontoxic in comparison with other metals. From a green chemistry point of view, the development of new Fe-catalyzed methods is of great excitement.[4]

Many catalysts are derived from rare metals, and their price or toxicity prevents their use on an industrial scale. Iron, which is ubiquitous, is thus becoming one of the most versatile transition metals. Various reviews have been published in the field of asymmetric catalysis using iron.[1c,5]

The asymmetric hydrosilylation of ketones was investigated by Nishiyama using Fe(OAc)$_2$ with chiral tridentate bis(oxazoline) ligands, such as pyridine bis(oxazoline) ($pybox$-$bn$), or bis(oxazolinephenyl)amine ($bopa$) and bis(oxazolinyl)phenyl ($phebox$) ligands.[6] The synthesis and structural characterization of the first chiral iron complexes prepared from
bis(oxadizonyl)phenyl ligands resulting from the oxidative addition of Fe₂(CO)₉ to 2-bromo-substituted ligands phebox was also disclosed. The corresponding Feᴵᴵ phebox complex was used in the enantioselective hydrosilylation of ketones. The enantioselectivity of the hydrosilylation of ketones was further improved by ligand design. Bulky substituents on the oxazoline ring led to a higher enantioselectivity (up to 88% ee). Gade described the synthesis of well-defined iron complexes containing a bidentate ligand and new enantiopure tridentate N–N–N donor ligands, and used the obtained Fe complex in the asymmetric hydrosilylation of ketones. More recently, Gade also developed chiral Feᴵᴵ alkyl and Feᴵᴵ alkoxide complexes bearing bis(oxadizonyl-methylidene)isoindoline (boxmi) pincers as stereodirecting ligands, which have been employed as catalysts for enantioselective hydrosilylation reactions with unprecedented activity and selectivity. Chirik studied pybox and box ligands for the hydrosilylation reaction of ketones. Following the same synthetic protocol used for the bis(imino)pyridine Feᴵᴵ dialkyl derivatives, the corresponding pybox and box Feᴵᴵ dialkyl complexes have been also isolated and characterized. Although high conversions were reported for the hydrosilylation of various ketones, the chiral induction of these systems was rather poor (up to 54% ee). Togni synthesized novel diamine ligands and used them in association with Fe(acac)₂ to promote the asymmetric reduction of acetophenone using phenylsilane. Beller developed a highly enantioselective reduction of ketones by selecting (S,S)-Meduphos among a series of phosphine ligands. Hunang developed a series of Feᴵᴵ complexes of chiral iminopyridine-oxazoline (IPO) ligands. The most sterically hindered FeᴵІ catalyst exhibits excellent activity (up to 99% yield) and high enantioselectivity (up to 93% ee) in the asymmetric hydrosilylation of aryl ketones.

**Results and discussion**

Three novel 6,6’-bis(oxadizonyl)-2,2’-bipyridine ligands 1b-d and already known bipybox-i-Pr 1a ligand were prepared from 2,2’-

![Scheme 1](image-url)

**Scheme 1. Synthesis of bipybox ligand**

bipyridine 2 via a seven-step synthesis
2,2′-Bipyridine 2 was oxidized to bis-N-oxide 3 using hydrogen peroxide in glacial acetic acid. α-Bis-cyanation of bis-N-oxide 3 with KCN and benzyol chloride yielded dinitrile 4 in excellent yield. Conversion of 4 into the corresponding 6,6′-bis(ethoxycarbonyl)-2,2′-bipyridine 5 was performed by stirring 4 in ethanol and sulfuric acid. After two days, 5 was afforded as a white solid. The resulting dicarboxylic acid was treated with SOCl₂ at reflux to give acid chloride 7 in excellent yield. Condensation of 7 with 2 equivalents of various amino alcohols followed after two days by the addition of SOCl₂ at room temperature afforded the corresponding bis-amidochloride 8a-d. The previously described cyclization procedure (NaOH/MeOH) was employed successfully to prepare 1a in an excellent yield (Table 1).

Table 1 Conditions for the synthesis of bipybox ligands

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Base</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>i-Pr</td>
<td>NaOH</td>
<td>MeOH</td>
<td>92</td>
</tr>
<tr>
<td>2b</td>
<td>Bn</td>
<td>NaOH</td>
<td>CH₂Cl₂</td>
<td>91</td>
</tr>
<tr>
<td>3c</td>
<td>i-Bu</td>
<td>NaH</td>
<td>THF</td>
<td>80</td>
</tr>
<tr>
<td>4d</td>
<td>s-Bu</td>
<td>NaH</td>
<td>THF</td>
<td>85</td>
</tr>
</tbody>
</table>

Condition: a) 8a, 6 N NaOH, MeOH, 40 °C, 2 days; b) 8b, 6 N NaOH, CH₂Cl₂, 40 °C, 7 days; c) 8c8d, NaH (3.8–4.1 equiv.), THF, rt, 7 days.

Treatment of 8b-d with NaOH in MeOH was ineffective, and the starting bis-amidochloride 8b-d was quantitatively recovered. This is probably explained by the low solubility of 8b-d in methanol. However, bipybox-Bn 1b was obtained by cyclization of corresponding bis-amidochloride 8b by using 6 N NaOH as a base in CH₂Cl₂ giving an excellent yield after recrystallization. The change in the conditions by using the NaH in THF gave the bipybox-i-Bu 1c, bipybox-s-Bu 1d in a good yield after 7 days at room temperature.

Following our studies in iron catalyzed asymmetric catalysis, we want to disclose our preliminary results using iron(II) acetate conjointly with the aforementioned new series of chiral ligands for the study of the asymmetric hydrosilylation of ketones.

Initially, several chiral bipybox ligands were tested for the reduction of acetophenone 9 to 1-phenylethanol 10 by using a given set of conditions. Structurally derived bipybox ligands, such as bipybox-i-Pr 1a, bipybox-Bn 1b, bipybox-i-Bu 1c, and bipybox-s-Bu 1d, have been used (Table 2) for the asymmetric hydrosilylation of acetophenone in the presence of Fe(OAc)₂ as a catalyst and PhSiH₃ as a reducing agent in THF as a solvent to give good to excellent yields of corresponding alcohol 10 (80–90%), but poor enantioselectivities. No reaction was observed using either FeCl₂, FeBr₂, Fe(Otf)₂ or Fe(ClO₄)₂·6H₂O as a catalyst. Among the salts tested, Fe(OAc)₂ was found to be optimal in terms of conversion.

Using these ligands and Fe(OAc)₂, different hydride sources, such as (EtO)₂MeSiH, Ph₂SiH₂ and poly(methylhydroxysilane)
(PMHS), were surveyed, but PhSiH\textsubscript{3} showed better reactivity and selectivity. We also observed a small temperature effect on the selectivity of catalyst. Typically, when the reaction was carried out at room temperature the conversion was slightly lowered and no enantioselectivity was observed. Various organic solvents such as diethyl ether, dichloromethane, and toluene have been studied but the best results have been obtained using THF as solvent.

**Table 2** Ligand screening for the asymmetric hydrosilylation of acetophenone using Fe(OAc)\textsubscript{2}-ligand.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Yield (%)</th>
<th>ee</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>bipybox-i-Pr</td>
<td>85</td>
<td>40:60</td>
</tr>
<tr>
<td>2</td>
<td>bipybox-Bn</td>
<td>90</td>
<td>55:45</td>
</tr>
<tr>
<td>3</td>
<td>bipybox-i-Bu</td>
<td>85</td>
<td>52:48</td>
</tr>
<tr>
<td>4</td>
<td>bipybox-s-Bu</td>
<td>80</td>
<td>52:48</td>
</tr>
</tbody>
</table>

Conditions: Fe(OAc)\textsubscript{2} (5 mol %), ligand (6 mol %), acetophenone, PhSiH\textsubscript{3} (2 equiv.), THF, 65 °C, 24 h.

The pre-catalyst prepared from FeCl\textsubscript{2} (5 mol %) and *bipybox*-\textit{i}-Pr 1a (6 mol %) was also tentatively activated using NaBEt\textsubscript{3}H (10 mol %).\textsuperscript{14} The resulting catalytic system was active for the hydrosilylation of acetophenone 9 using several common silanes. After 24 h, the hydrosilylation product was converted to 1-phenylethanol 10 after acidic work up. Ph\textsubscript{2}SiH\textsubscript{2} (2 equiv.) and PhSiH\textsubscript{3} (2 equiv.) showed good reactivity, giving 75% and 65% yield, respectively, but no enantioselectivity was observed. We have also checked the effect of AgBF\textsubscript{4} (20 mol %) as an additive,\textsuperscript{15a} used in the presence of FeCl\textsubscript{2} (10 mol %) and *bipybox*-\textit{i}-Pr 1a (12 mol %), using Ph\textsubscript{3}SiH\textsubscript{2} (2 equiv.) and PhSiH\textsubscript{3} (2 equiv.) as silane sources (65 °C, 24 h), but no conversion was observed and the unreacted product was recovered.

**Conclusions**

We have presented efficient protocols for the synthesis of three new chiral bis(oxazolinyl)bipyridine ligands starting from 2,2'-bipyridine in seven steps. We have used the newly synthesized ligands, such as *bipybox*-\textit{i}-Bu, *bipybox*-\textit{s}-Bu, *bipybox*-Bn and *bipybox*-\textit{i}-Pr, in the presence of Fe(OAc)\textsubscript{2} as a catalyst in the enantioselective hydrosilylation of acetophenone using PhSiH\textsubscript{3} as reducing agent. The enantioselectivities of the reactions were not yet satisfactory using *bipybox*-\textit{i}-Bu, *bipybox*-\textit{s}-Bu, *bipybox*-Bn, but it was demonstrated that a promising enantioselectivity was obtained with *bipybox*-\textit{i}-Pr ligand used with Fe(OAc)\textsubscript{2}, together with PhSiH\textsubscript{3} as the hydride source, in the hydrosilylation of acetophenone. Our method has the advantage of using a cheap and environmentally benign Lewis acid. The use of these new chiral ligands, complexed \textit{in situ} with various Fe\textsuperscript{II} sources, either under organic or aqueous conditions, is now under investigation for the asymmetric hydrosilylation of various ketones. Further studies to expand the scope and generality of our method are in progress.
Experimental part

General information. All chemicals were commercially available. The bipybox ligand 1a was synthesized according to known procedures. The amino alcohols were prepared from corresponding commercially available amino acids by using already known procedures. Solvents (THF, CH₂Cl₂, Et₂O, CHCl₃) were distilled prior to use. Thin-layer chromatography (TLC) was carried out on 250 µm commercial silica gel plates and compounds were visualized using UV absorbance and/or aqueous KMnO₄. Flash column chromatography was performed on silica gel (230–400 mesh). ¹H and ¹³C NMR spectra were recorded on a Varian Inova 400 MHz, Varian Inova 500 MHz spectrometer in CDCl₃, D₂O or DMSO-d₆. For ¹H NMR (400 MHz), chemical shift were reported in ppm downfield from tetramethylsilane (TMS) used as internal standard (δ = 0 ppm), and coupling constant and integration (in Hz). For ¹³C NMR (500 MHz), CDCl₃ was used as internal standard (δ = 77.23 ppm) and spectra were obtained with complete proton decoupling. Chiral HPLC was performed using Daicel Chiracel OD-H chiral column, eluting with n-hexanes and i-propanol. IR spectra were recorded on a NICOLET 380 FT-IR spectrometer with ZnSn ATR accessory and are reported in reciprocal centimeter (cm⁻¹). Melting points (mp) are uncorrected and were recorded on a MEL-TEMP® melting point apparatus.

Reduction of acetophenone. In a glass tube, Fe(OAc)₂ (4.4 mg, 0.025 mmol) and bipybox-i-Pr (11.4 mg, 0.03 mmol) were added to distilled THF (1 mL). The mixture was stirred for 1 h in a preheated oil bath at 65 ºC under argon. After removal of the oil bath, acetophenone (60.1 mg, 0.5 mmol) and PhSiH₃ (120 µL, 1 mmol) were added with a syringe under argon. The mixture was stirred for 20 h at 65 ºC and the reaction was monitored by TLC; hexane: ethyl acetate (9:1). At 0 ºC, aq. HCl (2N, 2 mL) was added to quench the reaction. After stirred for 1 h, the mixture was extracted with ethyl acetate (3 x 10 mL). The combined organic phases were washed with brine and aq. NaHCO₃ and dried over MgSO₄. After concentration, the residue was purified by silica gel column chromatography to give the desired alcohol as colorless oil (51.9 mg, 0.43 mmol) in a 85% yield and 20% ee.

¹H NMR (400 MHz, CDCl₃): δ 7.33–7.40 ppm (m, 2H); 7.25–7.30 (m, 3H), 4.89–4.92 (m, 1H), 1.49–1.56 (d, 3J = 6.5 Hz, 3H). HPLC conditions: Chiralcel OD-H column, n-hexane/i-PrOH = 95:5, flow rate = 0.8 mL/min, wavelength = 254 nm, tᵣ = 9.8 min (S), tᵣ = 11.6 min (R).

2,2’-Bipyridine-N,N’-dioxide (3).[15b] A solution of 30% aqueous hydrogen peroxide (68 mL) was added dropwise to 2,2’-bipyridine 2 (15.1 g, 96.0 mmol) in glacial acetic acid (90 mL) at a rate that maintained the temperature between 70 and 80 ºC. This mixture was stirred at 75 ºC for 15 h. The colorless solution was then cooled to room temperature, and acetone (330 mL) was
added to precipitate the product as a white solid, which was collected by filtration and air-dried (15.8 g, 87% yield). mp: 298 °C (lit. 296–298 °C).[18] 1H NMR (400 MHz, D_{2}O): δ 8.27–8.32 (m, 2H), 7.68 (dd, ^3J = 8.0, 7.3 Hz, 2H), 7.54–7.62 (m, 4H) ppm. 13C NMR (150 MHz, D_{2}O): δ 141.68, 139.59, 131.36, 128.77, 128.35 ppm. IR (ZnSn): 3037, 1473, 1426, 1297, 1248 cm\(^{-1}\).

6,6'-Dicyano-2,2'-bipyridine (4). Using a variation of a known procedure,[15c] 2,2'-bipyridine-N,N'-dioxide 3 (5.0 g, 26.6 mmol) and potassium cyanide (10.4 g, 159.3 mmol) were dissolved in water (53 mL). To this solution cooled at 0 °C, benzoyl chloride (19.2 g, 136.4 mmol) in dichloromethane (27 mL) were added dropwise. The reaction mixture was stirred for 16 h at room temperature. The precipitate was filtered, washed with ethanol and dried at room temperature. The product was obtained as a white solid (5.5 g, 99% yield). mp: 257 °C (lit. 255 °C).[19] 1H NMR (400 MHz, CDCl\(_3\)): δ 8.73 (d, ^3J = 8.0 Hz, 2H), 8.02 (dd, ^3J = 7.9, 7.9 Hz, 2H), 7.78 (d, ^3J = 7.9 Hz, 2H) ppm. 13C NMR (150 MHz, CDCl\(_3\)): δ 155.51, 138.41, 131.36, 128.77, 128.35 ppm. IR (ZnSn): 165.16, 155.40, 147.72, 138.00, 125.38, 124.70, 61.92, 14.31 ppm. IR (ZnSn): 2974, 1732, 1699, 1578, 1472 cm\(^{-1}\).

6,6'-Dicarboxy-2,2'-bipyridine acid (6).[15c] To a solution of 6,6'-bis(ethoxycarbonyl-2,2'-bipyridine 5 (5.7 g, 19.0 mmol), ethanol (196 mL) and sodium hydroxide (3.6 g, 89.0 mmol) was added. The reaction mixture was heated and refluxed for 1 day, after which the solution was poured into water (140 mL) and acidified with aqueous 6 N HCl until pH = 1~2. The white precipitate was filtered, washed with ethanol and air-dried to afford a white solid (4.4 g, 96% yield). mp: 288–289 °C (lit. dec. 286 °C; 288 °C).[19–20] 1H NMR (400 MHz, DMSO-\(d_{6}\)): δ 8.70 (dd, ^3J = 7.7, 1.3 Hz, 2H), 8.14 (dd, ^3J = 7.7, 7.7 Hz, 2H), 8.09 (dd, ^3J = 7.7, 1.3 Hz, 2H) ppm. 13C NMR (150 MHz, DMSO-\(d_{6}\)): δ 166.30, 154.82, 148.44, 139.35, 125.67, 124.50 ppm. IR (ZnSn): 2837, 2551, 1690, 1581, 1421 cm\(^{-1}\).

2,2'-Bipyridine-6,6'-dicarboxyl chloride (7).[15a] 2,2'-Bipyridine-6,6'-dicarboxylic acid 6 (6.1 g, 24.9 mmol) was treated with distilled SOCl\(_2\) (120 mL) at reflux for 17 h. Excess of
SOCl₂ was removed under reduced pressure to afford the acid chloride as a white solid (6.8 g, 97% yield). mp: 182–184 °C (lit. 177–178 °C). 1H NMR (400 MHz, CDCl₃): δ 8.93 (d, J = 7.8 Hz, 2H), 8.19 (d, J = 7.7 Hz, 2H), 8.11 (dd, J = 7.7, 7.7 Hz, 2H) ppm. 13C NMR (150 MHz, CDCl₃): δ 216.70, 155.14, 148.25, 138.77, 126.31, 125.78 ppm. IR (ZnSn): 3279, 2961, 1655, 1579, 1562, 1517 cm⁻¹.

**General procedure to prepare 2,2’-bipyridine-6,6’-dicarboxamide (8).** To a solution of amino alcohol (5.34 mmol) and triethylamine (1.5 mL, 10.7 mmol) in distilled CHCl₃ (15 mL), the acid chloride 7 (0.5 g, 1.8 mmol) was added at 0 °C. The mixture was stirred for 2 days at room temperature and then distilled SOCl₂ (3.4 mL) was added dropwise. After stirring for 12 h excess of SOCl₂ was removed under reduced pressure to give a black oil, which was extracted with CH₂Cl₂ (3 x 80 mL). The combined organic phases were washed with brine and dried over MgSO₄. Concentration gave black solid product which was purified by silica gel column to give the product (CH₂Cl₂/MeOH = 98:2).

**N₆,N₆’-bis((S)-1-chloro-3-phenylpropan-2-yl)-2,2’-bipyridine-6,6’-dicarboxamide (8a).**

White solid (4.6 g, 78% yield). mp 210 °C (lit. 210 °C). 1H NMR (400 MHz, CDCl₃): δ 8.52 (d, J = 7.8 Hz, 2H), 8.35 (d, J = 9.4 Hz, 2H), 8.28 (d, J = 7.7 Hz, 2H), 8.06 (dd, J = 7.8, 7.8 Hz, 2H), 4.17–4.26 (m, 2H), 3.89 (dd, J = 11.3 Hz, J = 3.7 Hz, 2H), 3.80 (dd, J = 11.3 Hz, J = 3.7 Hz, 2H), 2.12–2.24 (m, 2H), 1.09 (d, J = 6.8 Hz, 6H), 1.06 (d, J = 6.8 Hz, 6H). 13C NMR (150 MHz, CDCl₃): δ 163.82, 153.68, 149.18, 138.72, 123.57, 122.89, 55.02, 46.84, 29.56, 19.46, 18.89 ppm. IR (ZnSn): 3279, 2961, 1655, 1579, 1517, 1469 cm⁻¹.

**N₆,N₆’-bis((S)-1-chloro-4-methylpentan-2-yl)-2,2’-bipyridine-6,6’-dicarboxamide (8c).**

White solid (1.7 g, 78% yield). mp: 184–185 °C. 1H NMR (400 MHz, CDCl₃): δ 8.53 (dd, J = 7.9, 1.1 Hz, 2H), 8.27 (dd, J = 7.7, 1.1 Hz, 2H), 8.24 (d, J = 9.1 Hz, 2H), 8.06 (dd, J = 7.8, 7.8 Hz, 2H), 4.55–4.63 (m, 2H), 3.87 (dd, J = 11.1 Hz, J = 3.6 Hz, 2H), 3.76 (dd, J = 11.2 Hz, J = 3.6 Hz, 2H), 1.68–1.77 (m, 4H), 1.56–1.68 (m, 2H), 1.01 (d, J = 6.3 Hz, 6H), 0.99 (d, J = 6.2 Hz,
To a solution of the product was obtained as a white solid. After recrystallization (ethyl acetate/hexane) the product was obtained as a white solid (1.6 g, 96% yield). mp: 184 °C.

Yellow solid (0.5 g, 62% yield). mp: 148 °C. 

$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 163.56, 153.62, 138.61, 123.60, 122.85, 122.79, 48.75, 47.65, 41.06, 24.88, 22.84, 22.38 ppm. IR (ZnSn): 3305, 2954, 1722, 1650, 1566, 1465 cm$^{-1}$.

$N_{6,6'}$-bis(2S,3R)-1-chloro-3-methylpentan-2-yl)-2,2'-bipyridine-6,6'-dicarboxamide (8d).

$N_{6,6'}$-bis(2S,3R)-1-chloro-3-methylpentan-2-yl)-2,2'-bipyridine-6,6'-dicarboxamide (8d). Yellow solid (0.5 g, 62% yield). mp: 148 °C. 

$^{1}$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.53 (d, $^3$J = 7.9 Hz, 2H), 8.35 (d, $^3$J = 9.8 Hz, 2H), 8.28 (d, $^3$J = 7.7 Hz, 2H), 8.06 (dd, $^3$J = 7.8, 7.8 Hz, 2H), 4.23–4.33 (m, 2H), 3.90 (dd, $^2$J = 11.5 Hz, $^3$J = 3.8 Hz, 2H), 3.83 (dd, $^2$J = 11.5 Hz, $^3$J = 3.8 Hz, 2H), 1.85–2.03 (m, 2H), 1.56–1.71 (m, 2H), 1.18–1.35 (m, 2H), 1.05 (d, $^3$J = 6.7 Hz, 6H), 0.95 (t, $^3$J = 7.4 Hz, 6H) ppm. $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 163.66, 153.56, 149.10, 138.61, 123.50, 122.77, 53.61, 46.95, 35.77, 25.17, 15.38, 11.04 ppm. IR (ZnSn): 3313, 2962, 2874, 1722, 1652, 1579, 1462 cm$^{-1}$.

6,6'-Bis(4-(S)-isopropyloxazolin-2-yl)-2,2'-bipyridine (1a).$^{[15a]}$ To a solution of the $N_{6,6'}$-bis((S)-1-chloro-3-phenylpropan-2-yl)-2,2'-bipyridine-6,6'-dicarboxamide 8a (2 g, 4.4 mmol) in MeOH (110 mL), aqueous NaOH (6 N, 35 mL) was added. The mixture was then stirred 2 days at 40 °C. The reaction was monitored by TLC (CH$_2$Cl$_2$/MeOH 9:1). The mixture was extracted with CH$_2$Cl$_2$, dried over MgSO$_4$, and concentrated in vacuo to give a white solid. After recrystallization (ethyl acetate/hexane) the product was obtained as a yellow solid (1.5 g, 91% yield). mp: 206–208 °C. 

$^{1}$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.68 (dd, $^3$J = 7.8, 1.1 Hz, 2H), 8.12 (dd, $^3$J = 7.8, 1.1 Hz, 2H), 7.94 (dd, $^3$J = 7.8, 7.8 Hz, 2H), 7.32–7.36 (m, 4H), 7.24–7.30 (m, 6H), 4.66–4.75 (m, 2H), 4.49 (dd, $^3$J = 9.4 Hz, $^2$J = 8.5 Hz, 2H), 4.29 (dd, $^2$J = 8.5 Hz, $^3$J = 7.6 Hz, 2H), 3.35 (dd, $^2$J = 13.8 Hz, $^3$J = 5.0 Hz, 2H), 2.80 (dd, $^2$J = 13.8 Hz, $^3$J = 9.2 Hz, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 163.12, 155.34, 146.17, 137.76, 137.62, 129.17, 128.54, 126.53, 124.40, 123.55, 72.39, 68.09, 41.64 ppm. IR
6,6'-Bis(4-(S)-isobutyloxazolin-2-yl)-2,2'-bipyridine (1c). To a solution of the N6,N6'-bis((S)-1-chloro-4-methylpentan-2-yl)-2,2'-bipyridine-6,6'-dicarboxamide 8c (0.5 g, 1.1 mmol) in THF (11 mL, 0.1 M), NaH (0.1 g, 4.24 mmol) was added. The mixture was then stirred 7 days at room temperature under argon atmosphere. The reaction was monitored by TLC (CH2Cl2/MeOH 9:1). The mixture was extracted with CH2Cl2, dried over MgSO4, and concentrated to give a brownish solid. After recrystallization (ethyl acetate/hexane) the product was obtained as a white solid (0.35 g, 80% yield). mp: 150–152 °C. 1H NMR (500 MHz, CDCl3): δ 8.66 (d, 3J = 7.9 Hz, 2H), 8.10 (dd, 3J = 7.8, 1.1 Hz, 2H), 7.92 (dd, 3J = 7.8, 7.8 Hz, 2H), 4.65 (dd, 3J = 9.5 Hz, 2J = 8.1 Hz, 2H), 4.41–4.48 (m, 2H), 4.14 (dd, 3J = 8.1 Hz, 3J = 8.1 Hz, 2J = 8.1 Hz, 2H), 1.84–1.92 (m, 2H), 1.78–1.84 (m, 2H), 1.42–1.48 (m, 2H), 1.02 (d, 3J = 6.6 Hz, 6H), 1.00 (d, 3J = 6.5 Hz, 6H). 13C NMR (100 MHz, CDCl3): δ 162.08, 154.95, 146.06, 137.10, 129.00, 123.02, 73.22, 65.09, 45.15, 25.13, 22.82, 22.61 ppm. IR (ZnSn): 2959, 2876, 1657, 1577, 1445, 1381 cm−1.

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References


