

CHEMISTRY

A European Journal

A Journal of



Accepted Article

Title: Suzuki Cross-Coupling for Post-Complexation Derivatization of Non-Racemic Bis-Cyclometalated Iridium(III) Complexes

Authors: Thomas Mietke, Thomas Cruchter, Erik Winterling, Matthias Tripp, Klaus Harms, and Eric Meggers

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: *Chem. Eur. J.* 10.1002/chem.201701758

Link to VoR: <http://dx.doi.org/10.1002/chem.201701758>

Supported by
ACES

WILEY-VCH

Suzuki Cross-Coupling for Post-Complexation Derivatization of Non-Racemic Bis-Cyclometalated Iridium(III) Complexes

BSc. Thomas Mietke, MSc. Thomas Cruchter, BSc. Erik Winterling, BSc. Matthias Tripp, Dr. Klaus Harms, and Prof. Dr. Eric Meggers*

Fachbereich Chemie, Philipps-Universität Marburg, Hans-Meerwein-Straße 4, 35043 Marburg, Germany

*E-mail: meggers@chemie.uni-marburg.de

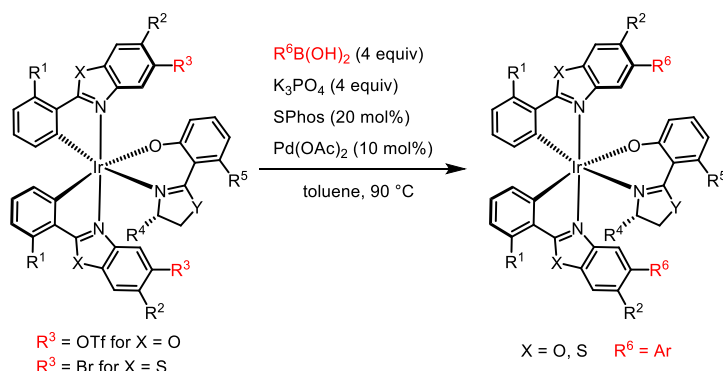
Homepage: <http://www.uni-marburg.de/fb15/ag-meggers>

Accepted Manuscript

Abstract: A straightforward method for post-complexation derivatizations of diastereomerically and enantiomerically pure bis-cyclometalated benzoxazole and benzothiazole iridium(III) complexes is reported. Triflate- and bromine-functionalized iridium(III) dimers, represented as $[\text{Ir}(\mu\text{-Cl})(\text{C}^{\wedge}\text{N})_2]_2$, were converted to the corresponding diastereomeric complexes, represented as $\text{Ir}(\text{C}^{\wedge}\text{N})_2(\text{N}^{\wedge}\text{O})$, using readily available chiral salicyloxazolines and salicylthiazolines as ancillary ligands which are represented as $\text{N}^{\wedge}\text{O}$. The $\text{Ir}(\text{C}^{\wedge}\text{N})_2(\text{N}^{\wedge}\text{O})$ complexes, formed as mixtures of diastereomers, were then resolved via flash chromatography and the diastereomerically pure complexes $\text{Ir}(\text{C}^{\wedge}\text{N})_2(\text{N}^{\wedge}\text{O})$ subjected to Suzuki cross-couplings. The post-complexation cross-couplings proceed without affecting the metal-located stereocenter and hence provide post-complexation derivatized non-racemic iridium(III) complexes, which were not easily accessible with previous methods. This method expands the toolbox to access functionalized non-racemic iridium(III) complexes for diverse applications in the life sciences, materials sciences, and catalysis.

Keywords: Iridium, chiral-at-metal, palladium, Suzuki-Miyaura, cross-coupling.

TOC graphic:



- new easily accessible precursor with high yield
- easy resolution of the resulting precursor diastereomers
- scope of derivatives accessible from one common precursor by simple cross-coupling
- 14 examples for post complexation cross-coupling
- yields up to 94%

Introduction

Cyclometalated iridium(III) complexes have been subject to intensive research due to their photophysical properties which renders them interesting candidates as photo luminescence markers and chemical probes in chemical biology and medicinal chemistry^[1,2] as well as luminophores in organic light emitting diodes (OLEDs).^[3] Recently, we have demonstrated that cyclometalated octahedral chiral-at-metal iridium(III) complexes can serve as versatile catalysts in various asymmetric transformations.^[4-6] In order to obtain the required chiral-at-metal catalysts enantiomerically pure, we rely on acid labile salicyloxazoline and salicylthiazoline ancillary ligands, which typically allow a convenient resolution of the initially formed diastereomeric precursor complexes via standard flash chromatography.^[7,8] Subsequently, the acid labile ancillary ligands are cleaved off to finally provide the desired enantiopure chiral-at-metal catalysts. However, in our efforts to design new catalysts we faced limitations of this approach. We experienced that excessive attachment of bulky hydrophobic groups to the benzoxazole or benzothiazole core structure, often necessary for obtaining catalysts with tailored properties, frequently entails a tedious diastereomer separation as the elution of the diastereomers converges. Other issues involve tailing of the diastereomers, which renders it comparably challenging to isolate the second eluting diastereomer fully separated.^[4,5,8b] Moreover, it is a common approach in the field of cyclometalated iridium(III) complexes referring to the synthesis of libraries to modify the relevant ligands for each derivative before complexation, which accumulates in a lot of steps and work.^[9] To avoid unnecessary steps and a tedious separation, the development of well-resolvable, (non-racemic) precursor complexes, which allow derivatizations after complex formation is desirable. Inspired by the work of other groups on scaffolds like planar chiral [2.2]paracyclophane,^[10] axial chiral binaphthols,^[11] polycyclic aromatic hydrocarbons,^[12] heterocycles,^[12] and others,^[13] we wondered if triflate- or bromine-functionalized bis-cyclometalated iridium(III) complexes could be accessed in a non-racemic fashion and then derivatized by Suzuki cross-coupling *after* diastereomer separation.^[14] Although cross coupling as a method to modify iridium(III) complexes based on cyclometalated phenyl pyridine and phenylated

terpy ligands has already been established,^[15] we did not find examples in the literature where either benzoxazole- / benzothiazole-cyclometalated or diastereomerically pure complexes were subjected to cross-coupling reactions. Therefore, in order to expand the synthetic toolbox for the synthesis of chiral-at-metal complexes we have developed a method for post-complexation derivatizations of diastereomerically and enantiomerically pure benzoxazole- and benzothiazole-cyclometalated iridium(III) complexes by Suzuki cross-couplings (Figure 1).

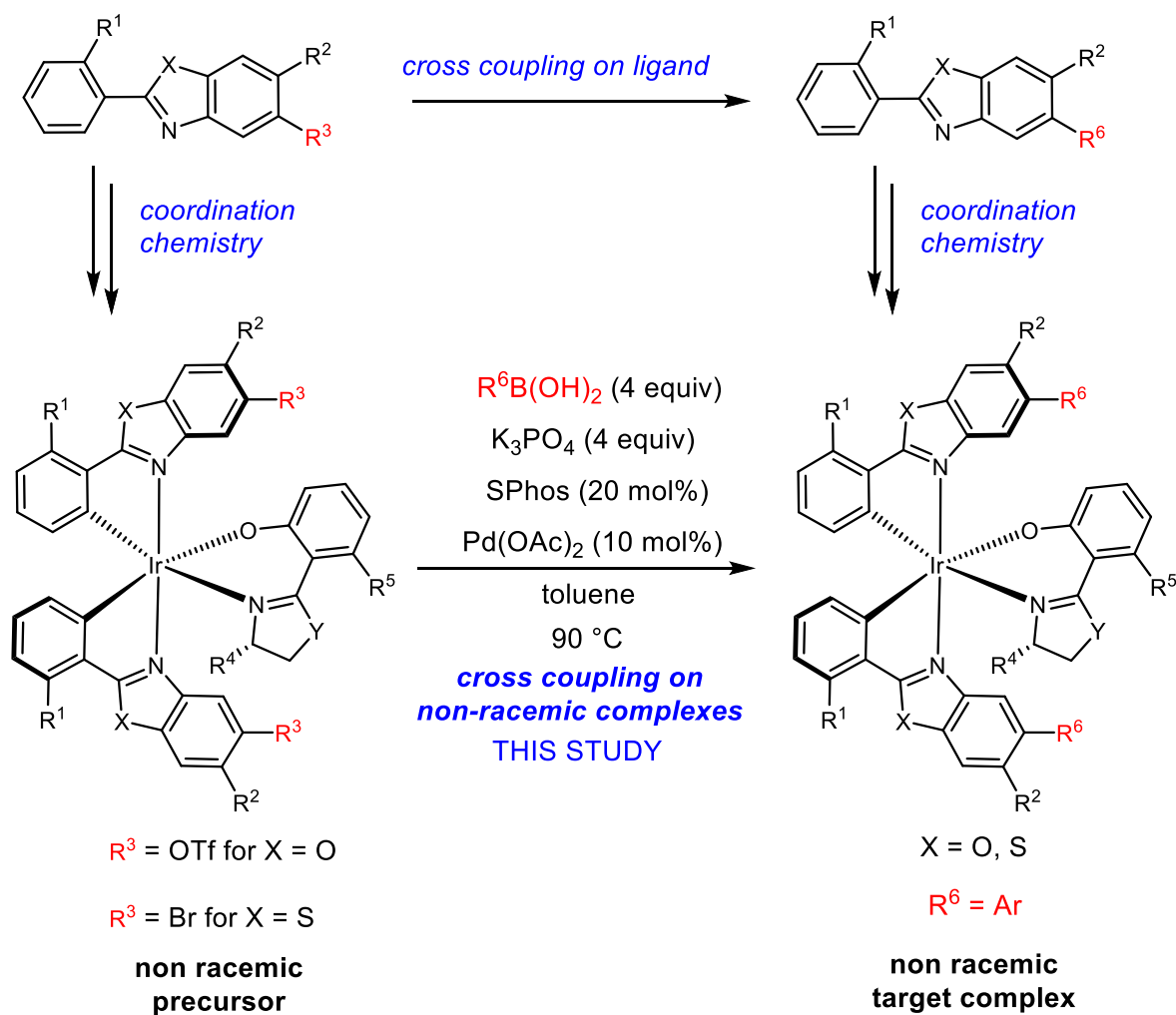
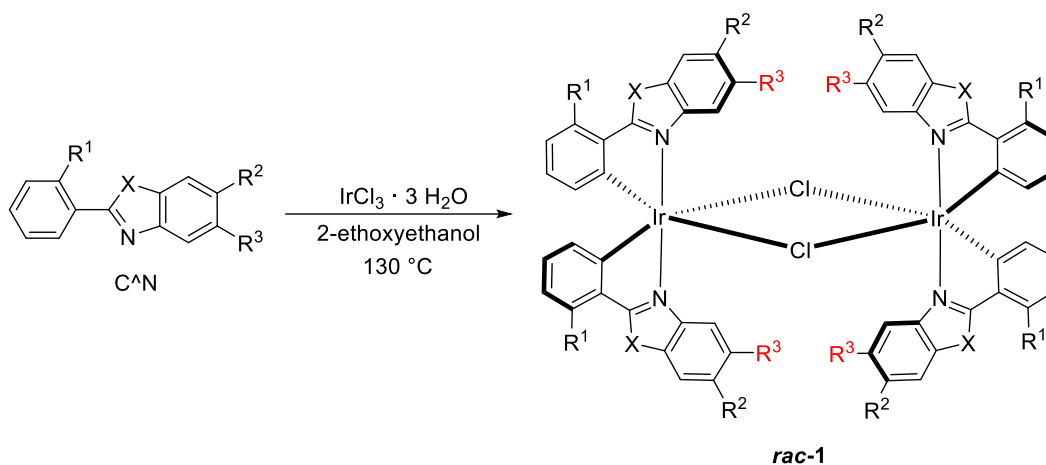


Figure 1. Synthesis of functionalized diastereomerically pure bis-cyclometalated iridium(III) complexes from the corresponding Br- or OTf-functionalized complexes by post-complexation Suzuki cross-coupling (this work).

Results and Discussion

Triflate- and Bromine-functionalized Iridium(III) Precursor Complexes. We started our study with the synthesis of bis-cyclometalated iridium(III) complexes which contain functional groups that can later be modified by Suzuki cross-coupling. At the beginning, we attempted to synthesize OTf-functionalized dimers of the type $[\text{Ir}(\mu\text{-Cl})(\text{C}^{\wedge}\text{N})_2]_2$. For this, we reacted new phenylbenzoxazole ligands **PhboOTf**, **PhboMeOTf** and **XyPhboOTf** bearing a triflate group in the 5-position of the benzoxazole moiety ($\text{R}^3=\text{OTf}$) with iridium(III) chlorate hydrate in ethoxyethanol at 130 °C. To our delight, we were able to obtain iridium(III) dimers **rac-1a-c** with excellent yields of 79 to 89% and triflate functionalization in the 5-position ($\text{R}^3=\text{OTf}$) as orange solids after flash column, using modified literature-known procedures.^[9a] (Table 1, entries 1-3). All complexes formed as racemic single diastereomers with the benzoxazole ligands coordinated trans to each other as illustrated for the crystal structure of **rac-1b** (Figure 2). In contrast to the synthesis of iridium(III) dimers with triflate-functionalized benzoxazole ligands, where a minimum amount of water was leading to better solubility of the ligand and therefore better reaction time and purity, we found that addition of water was crucial to obtain bromine-functionalized **rac-1d** in 70% yield and high purity (Table 1, entry 4).

Table 1. Synthesis of racemic iridium(III) dimer complexes bearing triflate and bromine substituents.^[a]



Entry	Ligand C ^N	Dimer	R ¹	R ²	R ³	X	Yield ^[b]
1	PhboOTf	rac-1a	H	H	OTf	O	87
2	PhboMeOTf	rac-1b	H	Me	OTf	O	89
3	XyPhboOTf	rac-1c	<i>m,m</i> -xylyl	H	OTf	O	79
4	PhbtBr	rac-1d	H	H	Br	S	70

[a] Reaction conditions: Iridium(III) chloride hydrate (1.00 eq.) and C^N ligand (2.00 eq.) in ethoxyethanol (c = 25 – 100 mM based on ligand) at 130 °C under exclusion of light. [b] Isolated yield.

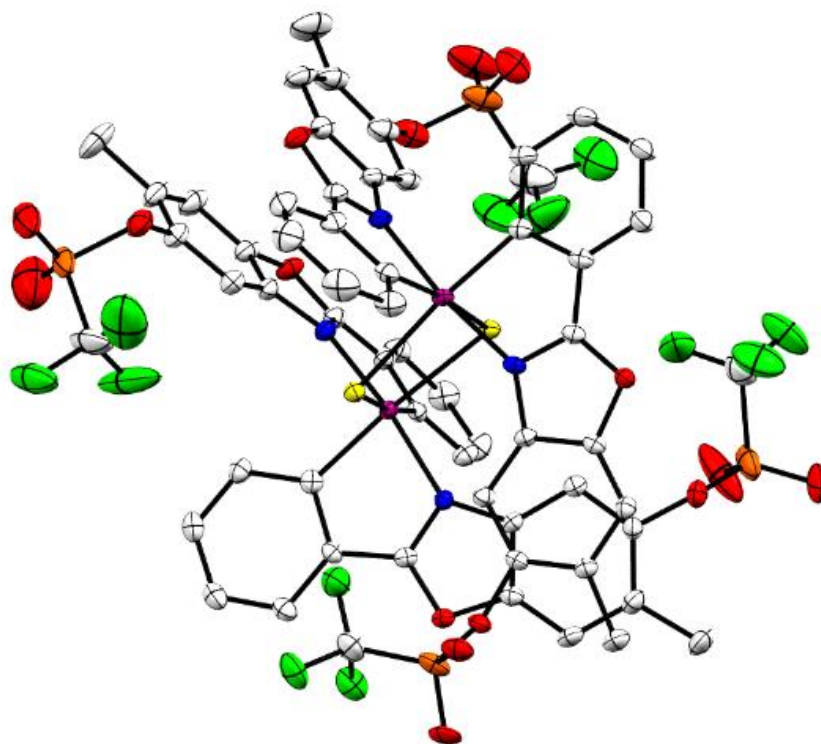
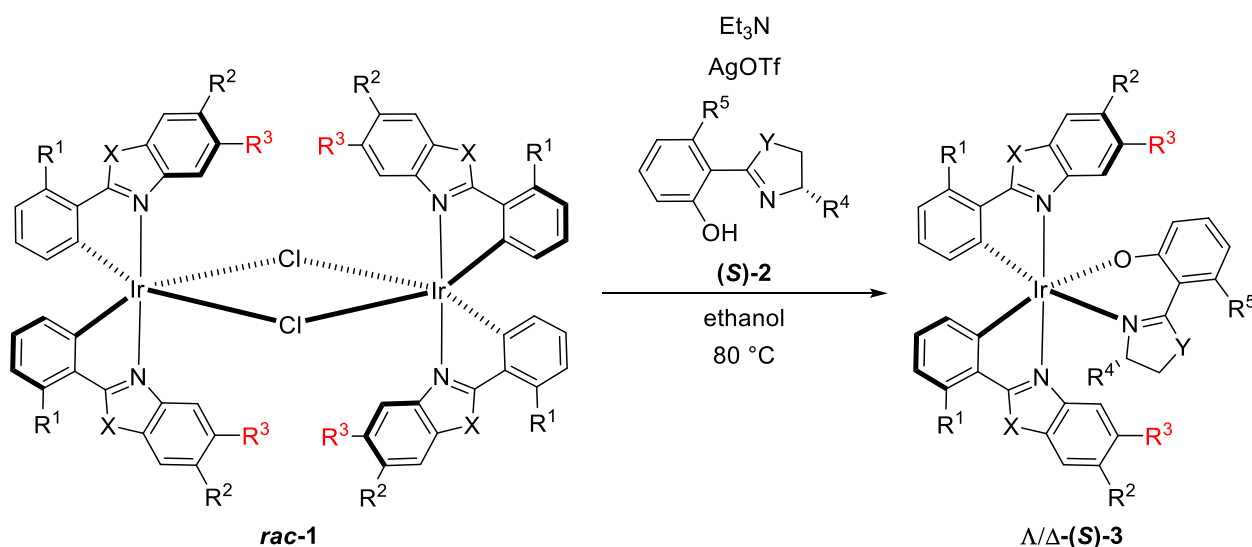


Figure 2. Structure of *rac-1b*. ORTEP drawing with 50% probability of thermal ellipsoids, co-crystallized solvent molecules omitted for clarity.

Auxiliary-mediated generation of single diastereomers. Subsequently, diastereomeric iridium(III) precursor complexes of the general formula $\text{Ir}(\text{C}^{\wedge}\text{N})_2(\text{N}^{\wedge}\text{O})$ were prepared by treating the dimers $[\text{Ir}(\mu\text{-Cl})(\text{C}^{\wedge}\text{N})_2]_2$ with excess ancillary ligand ($\text{N}^{\wedge}\text{O}$) in the presence of silver triflate and triethylamine as shown in Table 2. All diastereomers were obtained as yellow / orange solids and found to be easily resolved by standard silica gel chromatography. Accordingly, the reaction of dimer *rac-1a* with ancillary ligand (*S*)-**2a** afforded diastereomeric complexes Λ -(*S*)-**3a** and Δ -(*S*)-**3a** with an isolated yield of 40% and 38% (Table 2, entry 1). Under similar conditions, dimer *rac-1b* was converted to diastereomeric complexes Λ -(*S*)-**3b** and Δ -(*S*)-**3b** which were obtained in 40% and 37% isolated yield (Table 2, entry 2) using ancillary ligand (*S*)-**2a**. To further demonstrate the scope, salicyloxazoline ligand (*S*)-**2b** was used to convert dimers *rac-1c* and *rac-1d* under otherwise identical conditions, which gave easily separable diastereomer complexes Λ -(*S*)-**3c** (39%), Δ -(*S*)-**3c** (35%), Λ -(*S*)-**3d** (46%), and Δ -(*S*)-**3d** (44%) (Table 2, entries 3 and 4). Similarly, diastereomer

complex Λ -(*S*)-**3e** was synthesized from *rac*-**1d** and ligand (*S*)-**2a** with 35% yield. Single crystal X-ray diffraction was used to determine the metal-centered configuration of the complexes Λ -(*S*)-**3a** and Δ -(*S*)-**3a** (Figure 3 and 4) and all other complexes were assigned by comparison of their circular dichroism spectra (Figure 5). In accordance with our previous results, it turned out that the first eluting diastereomer was always the Λ -(*S*) and the second the Δ -(*S*) diastereomer.^[8c]

Table 2. Synthesis of diastereomeric precursor complexes with salicylthiazolinato (*S*)-**2a** and salicyloxazolinato (*S*)-**2b** ligands.^[a]



Entry	dimer	R ¹	R ²	R ³	X	R ⁴	Y	R ⁵	N ^o O	Λ	Yield	Δ	Yield
<i>rac</i> - 1										complex	[%] ^[b]	complex	[%] ^[b]
1	a	H	H	OTf	O	<i>i</i> Pr	S	H	(<i>S</i>)- 2a	Λ -(<i>S</i>)- 3a	40	Δ -(<i>S</i>)- 3a	38
2	b	H	Me	OTf	O	<i>i</i> Pr	S	H	(<i>S</i>)- 2a	Λ -(<i>S</i>)- 3b	40	Δ -(<i>S</i>)- 3b	37
3	c	xylyl	H	OTf	O	Ph	O	F	(<i>S</i>)- 2b	Λ -(<i>S</i>)- 3c	39	Δ -(<i>S</i>)- 3c	35
4	d	H	H	Br	S	Ph	O	F	(<i>S</i>)- 2b	Λ -(<i>S</i>)- 3d	46	Δ -(<i>S</i>)- 3d	44
5	d	H	H	Br	S	<i>i</i> Pr	O	H	(<i>S</i>)- 2a	Λ -(<i>S</i>)- 3e	35	Δ -(<i>S</i>)- 3e	0 ^[c]

[a] Reaction conditions: Racemic iridium(III) dimer complex *rac*-**1a-d** (1.00 eq.) and ancillary ligand (2.10 eq.) salicylthiazolin (*S*)-**2a** or salicyloxazolin (*S*)-**2b** in the presents of AgOTf (2.10 eq.) and Et₃N (10.0 eq.) in ethanol (15-30 mM) at 80 °C. Resolution of the resulting diastereomeric complexes was achieved by simple flash column.^[8b-c] [b] Isolated yield. [c] Δ -(*S*)-**3e** was found to be not stable on silica and basic aluminiumoxid column.

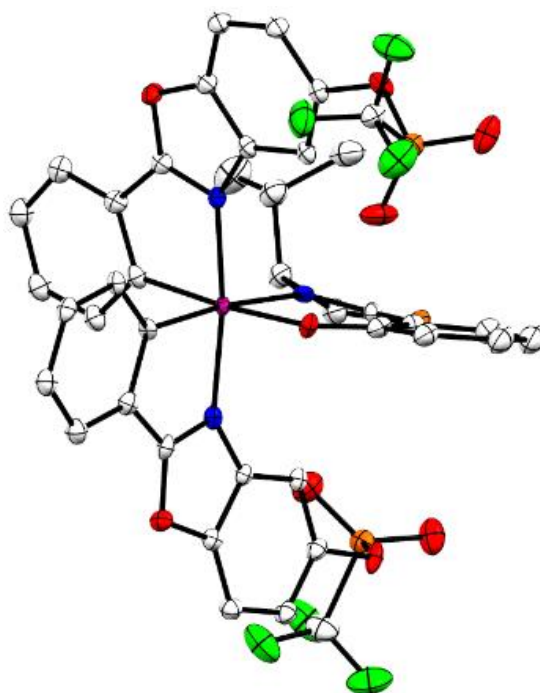


Figure 3. Structure of Δ -(*S*)-3a. ORTEP drawing with 60% probability of thermal ellipsoids, cocrystallized solvent molecules omitted for clarity.

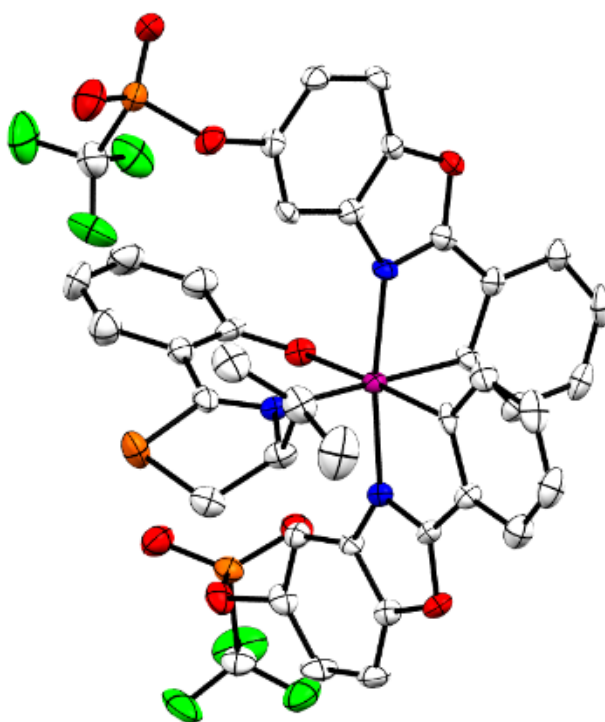


Figure 4. Structure of Δ -(*S*)-3a. ORTEP drawing with 70% probability of thermal ellipsoids, cocrystallized solvent molecules omitted for clarity.

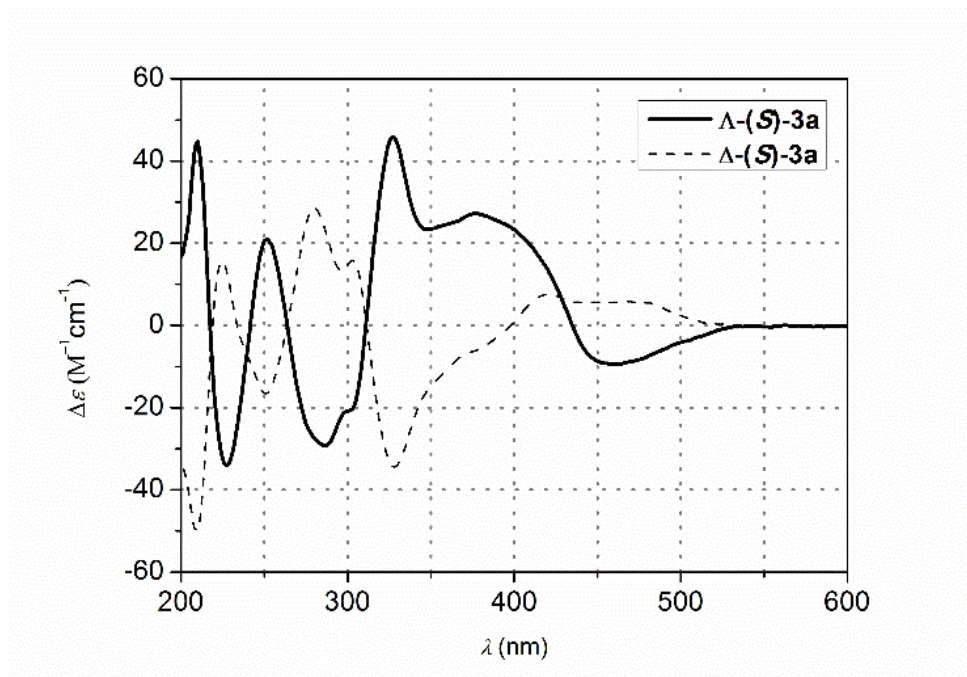


Figure 5. CD spectra of the diastereomers Δ -(S)-3a and Δ -(S)-3a (MeCN; 200 μ M).

Post-complexation Suzuki cross-coupling. From the subsequent post-complexation cross-coupling we expected the following features: (1) Both (pseudo)halides in the complex should take part in the cross-coupling process leading to only a single doubly-derivatized product; (2) the coupling process should require comparably mild reaction conditions to avoid decomposition of the participating complexes; and finally, (3) the cross-coupling should work with a broad range of commercially available reagents and take place under easily reproducible reaction conditions. During our research, we found that a modified version of the SPhos-promoted Suzuki cross-couplings reported by Buckwald *et. al.* fulfill these requirements nicely.^[16,17] Compared to the literature conditions, the catalyst loading was raised to 10 mol% Pd(OAc)₂ and 20 mol% SPhos to decrease the reaction time and to account for the two cross-coupled functional groups in our complexes. In addition, the temperature was lowered to 90 °C to avoid side reactions and complex decomposition. It is important to note that drastically reduced reaction times were observed when the required potassium phosphate was employed finely grounded and thoroughly flame-dried. A 200 mM concentration of (pseudo) halide-functionalized iridium(III) complex in dry and degassed toluene resulted in a good

compromise between reaction time and solubility.^[18] To our satisfaction, these conditions were applicable to a broad scope of iridium(III) complexes. Figure 6 shows the products of the cross-couplings with precursor complexes Λ -(S)-**3a-e** and Λ -(S)-**3b-d**.

At first, Λ -(S)-**3a** of the **PhboOTf** type was investigated under the aforementioned conditions. Iridium(III) complex Λ -(S)-**3a** was therefore combined with phenylboronic acid, powdered potassium phosphate, Pd(OAc)₂, SPhos and set under inert gas atmosphere. The heterogenous mixture was suspended in dry, thoroughly degassed toluene and heated to 90 °C overnight. The reaction vessel was shielded from light to avoid photoinduced side reactions. Subsequently, complex Λ -(S)-**4a** was obtained as orange solid after flash column with a yield of 80%. Consequentially, to increase the scope towards to sterically more demanding functionalization, additional cross-coupling reactions were conducted on iridium(III) complex Λ -(S)-**3a** with different boronic acids under otherwise identical conditions. Utilizing mesitylene-2-boronic acid, complex Λ -(S)-**4b** was obtained as an orange solid with 90% yield. Notably, complex Λ -(S)-**3a** could be functionalized with a considerably bulky 2,4,6-triisopropylphenyl moiety to furnish complex Λ -(S)-**4c** in 60% yield. Thinking along these lines, we felt challenged to introduce an extended polycyclic aromatic functionality using this method. Therefore, we attempted to cross-couple 2-(7-*tert*-butylpyren-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**P1**)^[12e] with iridium(III) complex Λ -(S)-**3a**. To our delight, this cross-coupling proceeded smoothly, which demonstrates that pinacol boronic ester can be applied to this procedure when a slight amount of degassed water is present, yielding complex Λ -(S)-**4d** with 80%.

To extend this concept, experiments with **PhboMeOTf** iridium(III) complexes Λ -(S)-**3b** and Λ -(S)-**3b**, comprising a methyl group ortho to the cross-coupling position, were conducted, and to our surprise, the desired cross-coupling products were obtained in excellent yields. The investigated conditions were applied to complex Λ -(S)-**3b** using mesitylene-2-boronic and 2-(7-*tert*-butylpyren-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**P1**) to receive Λ -(S)-**4e** (94%) and Λ -(S)-**4f** (86%) in excellent yields. Additionally, complex Λ -(S)-**3b** was converted to Λ -(S)-**4g** with 83% yield using

phenylboronic acid. In conclusion, we could demonstrate, that even though the 5-position is sterically less accessible, the cross-coupling still proceeded nicely.

Encouraged by these results, **XyPhboOTf** complexes Λ -(S)-**3c** and Δ -(S)-**3c** were further investigated. Focal point of this experiment was to evaluate the influence of the *m,m*-xylyl groups at the 2' position ($R^1 = \text{xylyl}$) towards cross-coupling reactions. Strikingly, both precursor complexes Λ -(S)-**3c** and Δ -(S)-**3c** could be functionalized with mesitylene-2-boronic acid by cross-coupling with yields comparable to the aforementioned reactions with precursor Λ -(S)-**3a-b**. (Λ -(S)-**4h** 91%; Δ -(S)-**4i** 88%). This results lead to the conclusion that modifications on the metallated phenylring weren't detrimental toward the cross-coupling at the 5-position.

In the context of our previous studies with cyclometalated iridium (III) complexes, we have recognized significant differences in the reactivity of benzothiazole and benzoxazole complexes.^[5c] Hence, benzothiazole **PhbtBr** complexes Λ -(S)-**3d** and Δ -(S)-**3d** were applied to the cross-coupling procedure. Accordingly, Λ -(S)-**3d** and Δ -(S)-**3d** were applied to the cross-coupling method to obtain mesityl functionalized benzothiazole complexes in excellent yields Λ -(S)-**4j** (94%); Δ -(S)-**4k** (92%) applying mesitylene-2-boronic acid. To further extend the scope of the benzothiazole derivatives complex Λ -(S)-**3d** was cross-coupled with 2-(7-*tert*-butylpyren-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**P1**) to obtain Λ -(S)-**4l** with 92% yield. To demonstrate, that both diastereomers undergo cross-coupling, complex Δ -(S)-**3d** was cross-coupled with (3-(dimethylamino)phenyl)boronic acid to receive complex Λ -(S)-**4m** with 55% yield (crystal structure in Figure 7). It is worth mentioning that the quite sensitive complex Λ -(S)-**3e** still undergoes cross coupling yielding complex Λ -(S)-**4n** in 58% yield. Representative CD-spectra of both modified diastereomer complexes Λ -(S)-**4j** and Δ -(S)-**4k** are shown in Figure 8.^[19]

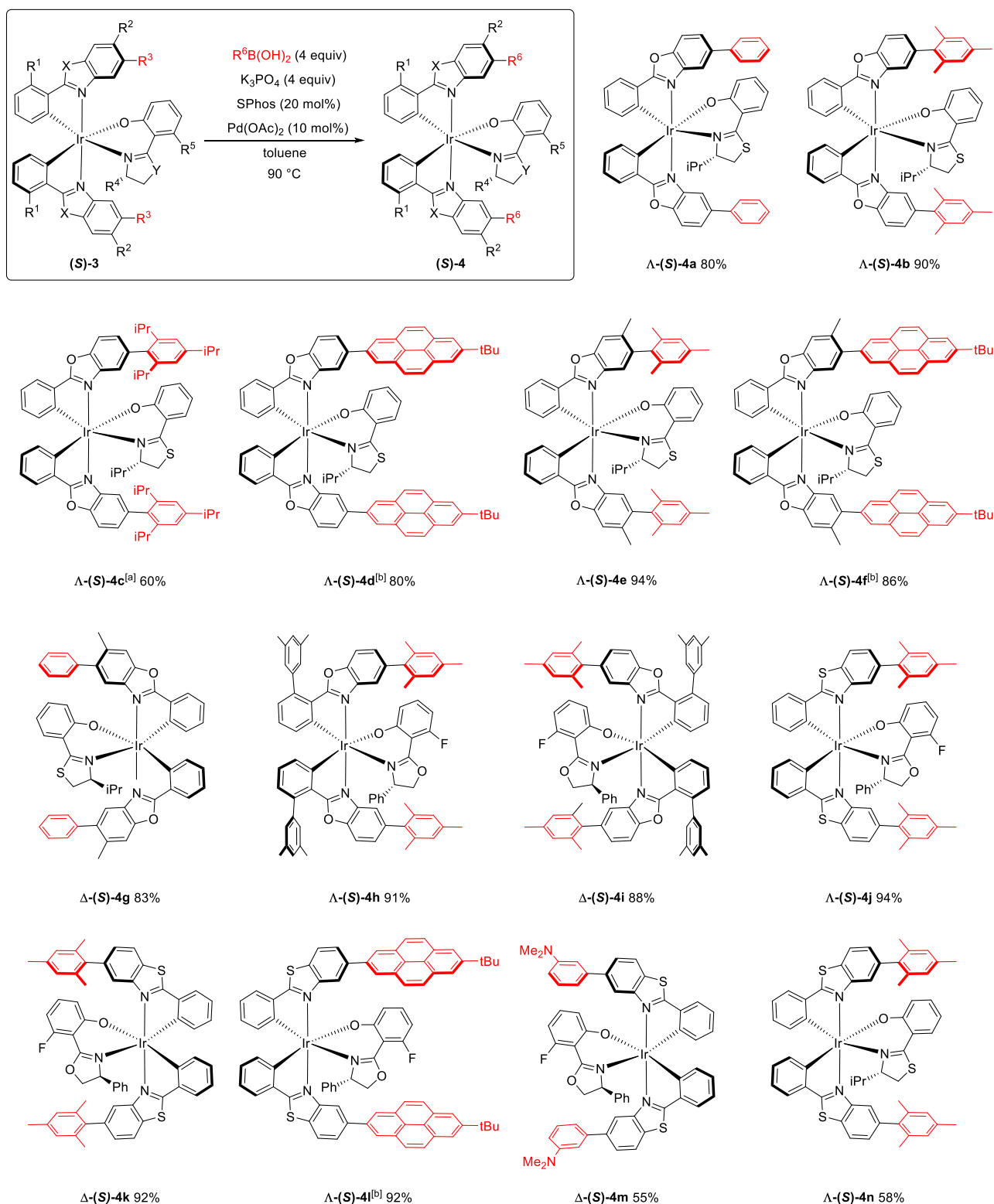


Figure 6. Scope for post-complexation Suzuki cross-couplings on functionalized iridium(III) precursor complexes Λ -(S)-3a-e and Δ -(S)-3b-d. [a] 6 Equivalents of boronic acid were used. [b] Pinacol boronic ester was used instead of free boronic acid. Isolated yields.

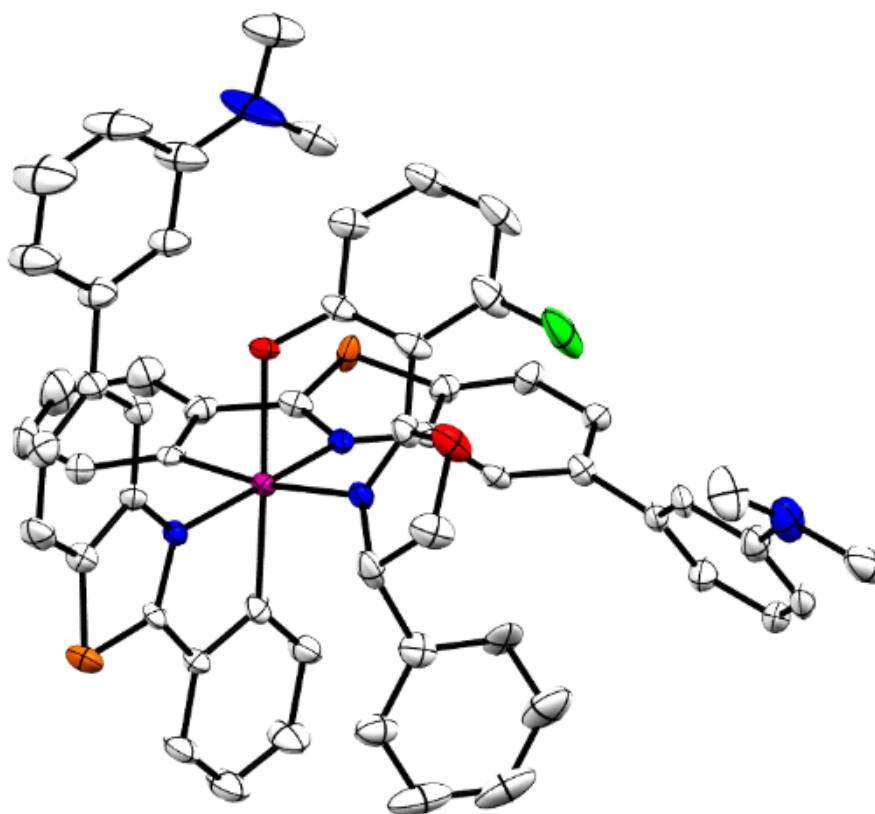


Figure 7. Structure of Δ -(*S*)-4m. ORTEP drawing with 50% probability of thermal ellipsoids; cocrystallized solvent molecules omitted for clarity.

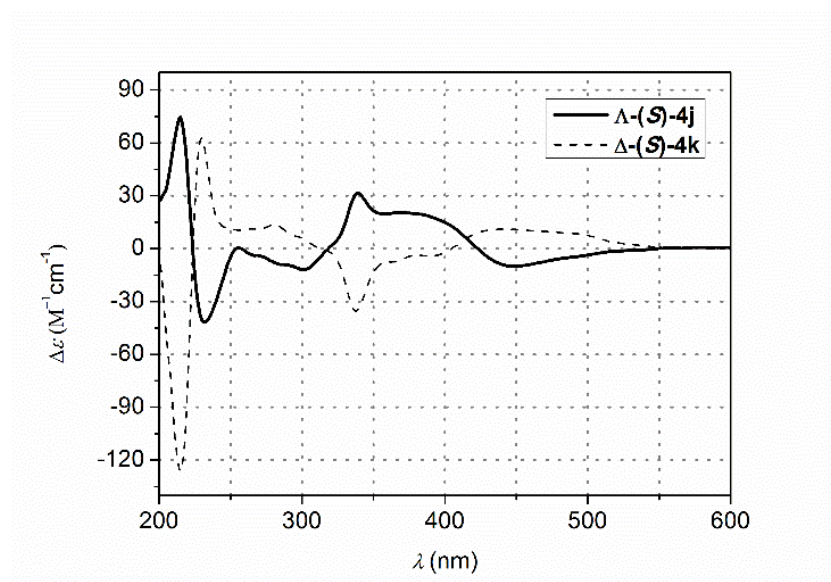
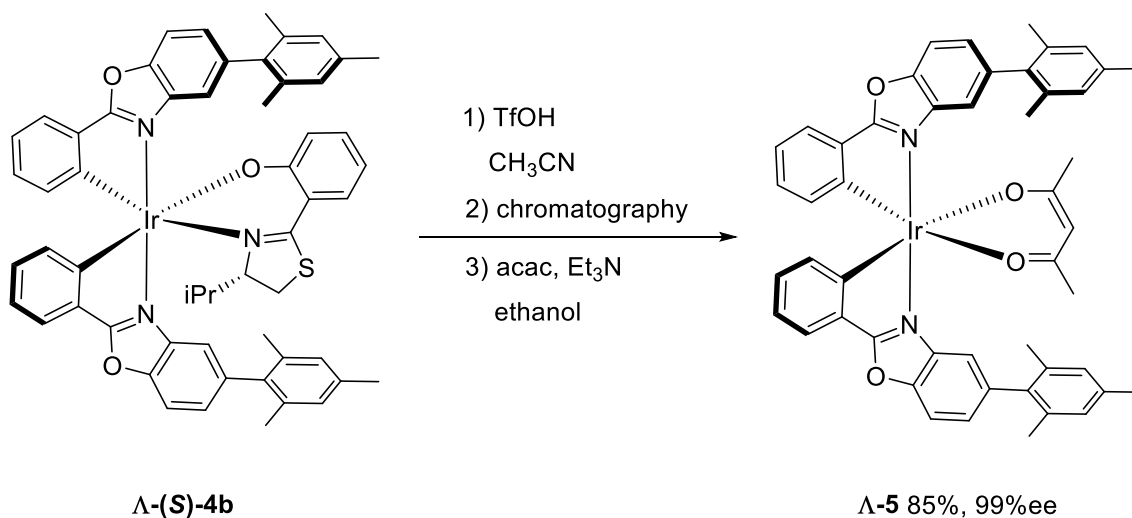


Figure 8. CD spectra of diastereomers Δ -(*S*)-4j and Δ -(*S*)-4k after cross-coupling (MeCN; $c = 200 \mu M$).

A representative HPLC experiment was carried out to proof that the developed post-complexation cross-coupling approach proceeds under retention of the metal centered stereo information and is therefore suited to furnish enantiopure complexes. The chiral ancillary ligand (*S*)-**2a** of diastereomerically pure iridium(III) complex Λ -(*S*)-**4b** was replaced with an achiral acetylacetonate (acac) ligand to obtain the chiral-only-at-metal complex Λ -**5** with 85% yield and 99% ee as determined by HPLC on chiral stationary phase (Scheme 1).^[20]



Scheme 1. Synthesis of the chiral-only-at-metal complex Λ -**5**.

Conclusions

We here reported a strategy to access a variety of diastereomerically and enantiomerically pure bis-cyclometalated iridium(III) complexes via Suzuki cross-coupling reactions with stereochemically defined triflate- and bromide-functionalized iridium(III) complexes. The reported cross-coupling procedure provides a straightforward method to previously difficult to access functionalized bis-cyclometalated iridium(III) complexes which may find applications in the life sciences, materials sciences, and in asymmetric catalysis. In this regard, quite recently we have relied on the reported method to successfully immobilize a chiral-at-metal catalyst on a solid support.^[21] Further examples for applications of this method are currently under investigation in our laboratory.

Experimental section

Remarks: Synthesis and analytical data of the ligands, dimer complexes **rac-1b-d**, diastereomer complexes Λ -(*S*)-**3b-e** and Λ -(*S*)-**3b-d**, cross-coupling products **4b-n**, enantiopure complex Λ -**5** and reference **rac-5**, and boronic acid ester **P1** are provided in the Supporting Information. General experimental remarks, NMR signal assignment remarks, equipment and chemicals used are further detailed in the Supporting Information.

Synthesis of dimer complex rac-1a: The reactions were performed according to a slightly modified reported procedure.^[9a] A flask equipped with nitrogen inlet, condenser and stir bar was charged with the benzoxazole ligand **PhboOTf** (2.00 g, 5.82 mmol, 1.85 eq.) and ethoxyethanol (60 mL). The solution was purged with N₂ for 30 min before iridium(III) chlorate hydrate (1.11 g, 3.17 mmol, 1.00 eq.) was added. The mixture was heated to 130 °C under reflux and exclusion of light overnight. After 12 h, additional iridium(III) chloride hydrate (200 mg) were added and the reaction was prolonged for additional 48 h. The resulting orange solution was filtered through a thin pad of silica gel to remove salts. The filter cake was washed with CH₂Cl₂ thoroughly, the solvent was removed under reduced pressure and the crude product was dried overnight. The crude product was purified with flash chromatography *n*-hexane / MTBE (2:1) as eluent to remove side products. The main product was eluted with CH₂Cl₂/MeOH (75:1). The iridium(III) dimer complex **rac-1a** (2.32 g, 1.27 mmol, 87% based on the amount of starting ligand **PhboOTf**) was obtained as an orange powder. *R*_f = 0.33 (*n*-hexane/CH₂Cl₂ 1:1); ¹H NMR (300 MHz, CD₂Cl₂): δ = 8.22 (d, *J* = 2.5 Hz, 4H), 7.72 (d, *J* = 7.0 Hz, 4H), 7.56 (d, *J* = 9.1 Hz, 4H), 7.17 (dd, *J* = 9.0, 2.6 Hz, 4H), 6.97 (t, *J* = 7.3 Hz, 4H), 6.75 (td, *J* = 7.8, 1.3 Hz, 4H), 6.14 ppm (d, *J* = 7.8 Hz, 4H); ¹³C NMR (75 MHz, CD₂Cl₂): δ = 180.5 (4C), 149.5 (4C), 146.5 (4C), 144.6 (4C), 140.9 (4C), 133.2 (4C), 132.8 (4C), 128.7 (4C), 127.3 (4C), 122.9 (4C), 119.1 (q, *J* = 319.9 Hz, 4C, CF₃), 118.6 (4C), 113.0 (4C), 111.3 (4C) ppm; ¹⁹F NMR (282 MHz, CD₂Cl₂, CFCl₃) δ = -73.4 ppm; IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3077 (w), 1623 (w), 1589 (m), 1513 (w), 1465 (w), 1425 (m), 1339 (w), 1296 (w), 1212 (s), 1135 (m), 1106 (m), 1038 (w), 978 (w), 943 (m), 864

(m), 810 (w), 775 (w), 737 (m), 705 (w), 665 (w), 625 (w), 599 (m), 506 (w), 448 (w); HRMS (ESI): m/z calcd. for $C_{56}H_{28}Cl_2F_{12}Ir_2N_4O_{16}S_4Na_1$ $[M+Na]^+$: 1846.8697, found 1846.8691.

Synthesis of diastereomer complexes Λ -(S)-3a and Δ -(S)-3a: The reaction was performed according to a slightly modified reported procedure.^[8c] A *Schlenk* tube (threaded PTFE plug) equipped with stir a bar was charged with dimer *rac*-1a (1.33 g, 0.73 mmol, 1.00 eq.), ancillary ligand (S)-2a (0.34 g, 1.53 mmol, 2.10 eq.), and ethanol (12.5 mL). This mixture was homogenized by sonication for 10 min before AgOTf (0.39 g, 1.53 mmol, 2.10 eq.) and Et₃N (1.01 mL, 0.74 g, 7.30 mmol, 10.0 eq.) were added. Afterwards, the mixture was further diluted with ethanol (12.5 mL) and again homogenized by sonication. The mixture was heated to 80 °C for 8 h and monitored by TLC. After completion, the flask was cooled to rt, and the mixture filtered through a plug of celite which was rinsed with CH₂Cl₂. The filtrate was concentrated under reduced pressure and the crude product was adsorbed on basic aluminum oxide with CH₂Cl₂ and subjected to silica gel flash column chromatography (CH₂Cl₂/*n*-hexane 13:2 → CH₂Cl₂) to separate the Λ -(S)-3a and Δ -(S)-3a diastereomer iridium(III) complexes. Each complex was further purified by silica gel flash column chromatography (*n*-hexane/EtOAc 5:2) to obtain the first eluting diastereomer Λ -(S)-3a (640 mg, 0.58 mmol, 40%) and the second diastereomer Δ -(S)-3a (608 mg, 0.55 mmol, 38%) as orange solids. Λ -(S)-3a (first eluted isomer): $R_f = 0.29$ (*n*-hexane/EtOAc 5:2), $R_f = 0.09$ (CH₂Cl₂/*n*-hexane 13:2); ¹H NMR (300 MHz, CD₂Cl₂): $\delta = 7.85$ (d, $J = 2.5$ Hz, 1H, H_{Ar}), 7.77–7.68 (m, 2H, H_{Ar}), 7.66–7.58 (m, 2H, H_{Ar}), 7.43 (dd, $J = 8.2, 1.6$ Hz, 1H, H_{Ar}), 7.35–7.32 (m, 2H, H_{Ar}), 7.27 (dd, $J = 9.1, 2.5$ Hz, 1H, H_{Ar}), 7.16–7.07 (m, 1H, H_{Ar}), 6.96–6.73 (m, 4H, H_{Ar}), 6.66 (d, $J = 8.7$ Hz, 1H, H_{Ar}), 6.58 (d, $J = 8.0$ Hz, 1H, H_{Ar}), 6.34–6.24 (m, 2H, H_{Ar}), 4.64–4.55 (m, 1H, CH_{aliph}), 3.33 (dd, $J = 11.9, 9.8$ Hz, 1H, CH_{aliph}), 2.96 (dd, $J = 11.9, 1.7$ Hz, 1H, CH_{aliph}), 0.72–0.55 (m, 1H, CH_{iPr}), 0.19 ppm (t, $J = 6.9$ Hz, 6H, 2xCH₃); ¹³C NMR (75 MHz, CD₂Cl₂): $\delta = 181.2, 180.8, 169.6, 167.5, 151.7, 150.8, 149.9, 149.6, 147.9, 147.4, 140.0, 139.9, 135.2, 134.3, 133.8, 133.2, 132.8, 132.0, 130.3, 129.9, 127.4, 127.0, 124.1, 122.6, 121.7, 119.4, 119.4$ (q, $J = 321.0$ Hz, CF₃), 119.1 (q, $J = 321.4$ Hz, CF₃), 118.6,

118.3, 114.2, 113.4, 113.0, 111.8, 110.2, 85.1, 32.4, 27.3, 19.0, 14.1 ppm; ^{19}F NMR (282 MHz, CD_2Cl_2 , CFCl_3): $\delta = -72.8, -72.9$ ppm; IR (ATR): $\tilde{\nu} = 3054$ (w), 2962 (w), 1592 (m), 1557 (w), 1517 (w), 1463 (m), 1421 (m), 1345 (w), 1297 (w), 1206 (s), 1135 (s), 1104 (m), 1037 (w), 1013 (w), 981 (w), 943 (m), 870 (s), 814 (w), 776 (w), 739 (m), 706 (w), 663 (w), 626 (m), 601 (m), 560 (w), 509 (w), 432 (w) cm^{-1} ; HRMS (ESI): m/z calcd. for $\text{C}_{40}\text{H}_{28}\text{F}_6\text{Ir}_1\text{N}_3\text{O}_9\text{S}_3\text{Na}_1$ $[\text{M}+\text{Na}]^+$: 1120.0411, found 1120.0455; CD (MeCN): λ ($\Delta\epsilon$, $\text{M}^{-1}\cdot\text{cm}^{-1}$) = 210 (+45), 227(-34), 252 (+21), 287 (-29), 327 (+46), 347 (+23), 376 (+27), 458 (-9) nm.

Λ -(S)-3a (second eluted isomer): $R_f = 0.26$ (*n*-hexane/EtOAc 5:2), $R_f = 0.05$ (CH_2Cl_2 /*n*-hexane 13:2); ^1H NMR (300 MHz, CD_2Cl_2): $\delta = 7.86$ – 7.66 (m, 5H, H_{Ar}), 7.44 – 7.37 (m, 2H, H_{Ar}), 7.35 – 7.28 (m, 2H, H_{Ar}), 7.06 – 6.92 (m, 3H, H_{Ar}), 6.89 – 6.75 (m, 2H, H_{Ar}), 6.73 – 6.67 (m, 1H, H_{Ar}), 6.60 – 6.53 (m, 1H, H_{Ar}), 6.40 – 6.26 (m, 2H, H_{Ar}), 3.67 – 3.58 (m, 1H, CH_{aliph}), 2.99 (dd, $J = 11.5, 1.6$ Hz, 1H, CH_{aliph}), 2.82 (dd, $J = 11.3, 10.0$ Hz, 1H, CH_{aliph}), 2.11–1.96 (m, 1H, CH_{iPr}), 1.10 (d, $J = 6.8$ Hz, 3H, CH_3), 0.08 ppm (d, $J = 6.8$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CD_2Cl_2): $\delta = 181.5, 169.5, 167.5, 152.4, 151.1, 150.0, 149.4, 148.0, 147.2, 140.6, 139.7, 136.3, 133.5, 132.7$ (2C), 132.6, 131.8, 129.9, 129.3, 127.6, 127.0, 123.8, 122.5, 121.5, 119.7, 119.5, 119.1 (q, $J = 320.6$ Hz, CF_3), 119.0 (q, $J = 321.4$ Hz, CF_3), 118.7, 114.0, 113.1, 111.5, 110.5, 81.8, 32.4, 30.5, 20.4, 16.5 ppm; ^{19}F NMR (282 MHz, CD_2Cl_2 , CFCl_3): $\delta = -73.0, -73.2$ ppm; IR (ATR): $\tilde{\nu} = 3051$ (w), 2962 (w), 2052 (w), 1593 (m), 1562 (w), 1517 (w), 1463 (m), 1422 (m), 1340 (w), 1297 (w), 1208 (s), 1135 (s), 1105 (m), 1036 (w), 1014 (w), 983 (w), 943 (m), 871 (m), 812 (m), 777 (w), 740 (m), 707 (w), 665 (w), 626 (w), 601 (m), 561 (w), 509 (w), 450 (w) cm^{-1} ; HRMS (ESI): m/z calcd. for $\text{C}_{40}\text{H}_{28}\text{F}_6\text{Ir}_1\text{N}_3\text{O}_9\text{S}_3\text{Na}_1$ $[\text{M}+\text{Na}]^+$: 1120.0411, found 1120.0457; CD (MeCN): λ ($\Delta\epsilon$, $\text{M}^{-1}\cdot\text{cm}^{-1}$) = 210 (-50), 225 (+16), 251 (-17), 280 (+29), 297 (+13), 303 (+16), 328 (-35), 420 (+7) nm.

Synthesis of the cross-coupling product Λ -(S)-4a: A Schlenk tube (10 mL; threaded PTFE plug) equipped with stir a bar was charged with diastereomerically pure iridium(III) complex Λ -(S)-3a (90.0 mg, 82.0 μmol , 1.00 eq.), phenylboronic acid (40.0 mg, 328 μmol , 4.0 eq.), powdered K_3PO_4

(70.0 mg, 328 μmol , 4.00 eq.), $\text{Pd}(\text{OAc})_2$ (1.8 mg, 8.2 μmol , 10 mol%), and SPhos (6.7 mg, 16.4 μmol , 20 mol%). The heterogenous mixture was evacuated and refilled with nitrogen (3x). Toluene (400 μL), thoroughly degassed by freeze-pump-thaw in 5 cycles, was used to suspend the solids. The suspension was sonicated for 10 min and placed in a preheated oilbath (90 $^\circ\text{C}$), stirred for 12 h, and monitored by TLC. The solvent was removed under reduced pressure, the crude product dissolved in CH_2Cl_2 , adsorbed on basic aluminum oxide and purified by silica gel flash chromatography (*n*-hexane/EtOAc 5:1 \rightarrow 5:2) to afford the cross-coupled, diastereomerically pure iridium(III) complex **Λ -(S)-4a** (62.5 mg, 65.6 μmol , 80%) as an orange solid. $R_f = 0.19$ (*n*-hexane/EtOAc 5:1), $R_f = 0.31$ (*n*-hexane/EtOAc 5:2); ^1H NMR (500 MHz, CD_2Cl_2): $\delta = 8.10\text{--}8.06$ (m, 1H, H_{Ar}), 7.79–7.65 (m, 9H, H_{Ar}), 7.56 (dd, $J = 8.1, 1.7$ Hz, 1H, H_{Ar}), 7.52–7.48 (m, 2H, H_{Ar}), 7.45–7.34 (m, 5H, H_{Ar}), 7.33–7.28 (m, 1H, H_{Ar}), 7.25–7.20 (m, 1H, H_{Ar}), 7.00–6.96 (m, 1H, H_{Ar}), 6.95–6.90 (m, 1H, H_{Ar}), 6.89–6.84 (m, 1H, H_{Ar}), 6.82–6.74 (m, 2H, H_{Ar}), 6.72–6.67 (m, 1H, H_{Ar}), 6.43–6.36 (m, 2H, H_{Ar}), 4.92–4.83 (m, 1H, CH_{aliph}), 3.19 (dd, $J = 11.8, 10.0$ Hz, 1H, CH_{aliph}), 2.94 (dd, $J = 11.8, 1.8$ Hz, 1H, CH_{aliph}), 0.92–0.83 (m, 1H, CH_{iPr}), 0.21 (d, $J = 7.2$ Hz, 3H, CH_3), 0.16 ppm (d, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR (125 MHz, CD_2Cl_2): $\delta = 178.9, 178.7, 168.1, 166.8, 150.8, 150.3, 150.1, 149.9, 141.0, 140.4, 140.0, 139.8, 139.6, 139.3, 135.1, 134.0, 133.8, 132.2, 131.8, 131.4, 130.9, 129.3$ (2C), 129.1 (2C), 128.1, 127.9 (3C), 127.7 (2C), 126.5, 126.2, 125.1, 124.5, 124.3, 122.3, 121.2, 118.5, 116.3, 114.4, 113.6, 112.3, 111.7, 86.0, 31.9, 27.9, 18.9, 14.2, 1.2 ppm; IR (ATR): $\tilde{\nu} = 3054$ (w), 2970 (w), 2855 (w), 1593 (m), 1556 (m), 1517 (m), 1442 (s), 1381 (m), 1351 (w), 1296 (m), 1256 (m), 1189 (w), 1154 (m), 1109 (s), 1073 (m), 1034 (m), 1011 (m), 916 (m), 887 (w), 821 (m), 763 (m), 736 (s), 697 (s), 640 (w), 596 (w), 554 (w), 517 (w), 449 (w), 417 (w) cm^{-1} ; HRMS (LIFDI): m/z calcd. for $\text{C}_{50}\text{H}_{38}\text{IrN}_3\text{O}_3\text{S}$ $[\text{M}]^{*+}$: 953.2265, found 953.2289; CD (MeCN): λ ($\Delta\epsilon, \text{M}^{-1}\cdot\text{cm}^{-1}$) = 205 (+11), 218 (+56), 235 (–23), 243 (–12), 257 (–31), 269 (–15), 292 (–53), 336 (+35), 346 (+32), 367 (+36), 463 (–10) nm.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft (ME1805/11-1).

Literature

[1] Reviews on bis-cyclometalated iridium(III) complexes as bioactive complexes and biological probes or sensors: a) J. C. Araya, J. Gajardo, S. A. Moya, P. Aguirre, L. Toupet, J. A. G. Williams, M. Escadeillas, H. Le Bozece, V. Guerschais, *New J. Chem.* **2010**, *34*, 21–24; b) F. L. Thorp-Greenwood, R. G. Balasingham, M. P. Coogan, *J. Organomet. Chem.* **2012**, *714*, 12–21; c) K. K.-W. Lo, A. W.-T. Choi, W. H.-T. Law, *Dalton Trans.* **2012**, *41*, 6021–6047; d) D.-L. Ma, H.-Z. He, K.-H. Leung, D. S.-H. Chan, C.-H. Leung, *Angew. Chem. Int. Ed.* **2013**, *52*, 7666–7682; *Angew. Chem.* **2013**, *125*, 7820–7837; e) C.-H. Leung, H.-J. Zhong, D. S.-H. Chan, D.-L. Ma, *Coord. Chem. Rev.* **2013**, *257*, 1764–1776; f) K. K.-W. Lo, *Acc. Chem. Res.* **2015**, *48*, 2985–2995; g) D.-L. Ma, S. Lin, W. Wang, C. Yang, C.-H. Leung, *Chem. Sci.* **2017**, *8*, 878–889.

[2] For individual studies on using bis-cyclometalated iridium(III) complexes as bioactive compounds and biological probes or sensors, see: a) K. K.-W. Lo, C.-K. Li, J. S.-Y. Lau, *Organometallics* **2005**, *24*, 4594–4601; b) K. K.-W. Lo, J. S.-Y. Lau, *Inorg. Chem.* **2007**, *46*, 700–709; c) F. Shao, B. Elias, W. Lu, J. K. Barton, *Inorg. Chem.* **2007**, *46*, 10187–10199; d) F. Shao, J. K. Barton, *J. Am. Chem. Soc.* **2007**, *129*, 14733–14738; e) D.-L. Ma, W.-L. Wong, W.-H. Chung, F.-Y. Chan, P.-K. So, T.-S. Lai, Z.-Y. Zhou, Y.-C. Leung, K.-Y. Wong, *Angew. Chem. Int. Ed.* **2008**, *47*, 3735–3739; *Angew. Chem.* **2008**, *120*, 3795–3799; f) J. S.-Y. Lau, P.-K. Lee, K. H.-K. Tsang, C. H.-C. Ng, Y.-W. Lam, S.-H. Cheng, K. K.-W. Lo, *Inorg. Chem.* **2009**, *48*, 708–718; g) Q. Zhao, M. Yu, L. Shi, S. Liu, C. Li, M. Shi, Z. Zhou, C. Huang, F. Li, *Organometallics* **2010**, *29*, 1085–1091; h) M. Graf, K. Sünkel, *Inorg. Chim. Acta* **2011**, *379*, 40–43; i) B. Y.-W. Man, H.-M. Chan, C.-H. Leung, D. S.-H. Chan, L.-P. Bai, Z.-H. Jiang, H.-W. Li, D.-L. Ma, *Chem. Sci.* **2011**, *2*, 917–921; j) H.-Y. Shiu, M.-K. Wong, C.-M. Che, *Chem. Commun.* **2011**, *47*, 4367–4369; k) C.-H. Leung, H.-J. Zhong, H. Yang, Z. Cheng, D. S.-H. Chan, V. P.-Y. Ma, R. Abagyan, C.-Y. Wong, D.-L. Ma, *Angew. Chem. Int. Ed.* **2012**, *51*, 9010–9014; *Angew. Chem.* **2012**, *124*, 9144–9148; l) W. H.-T. Law, K.-K.

Leung, L. C.-C. Lee, C.-S. Poon, H.-W. Liu, K. K.-W. Lo, *ChemMedChem* **2014**, *9*, 1316–1329; m) D. Maggioni, M. Galli, L. D'Alfonso, D. Inverso, M. V. Dozzi, L. Sironi, M. Iannacone, M. Collini, P. Ferruti, E. Ranucci, G. D'Alfonso, *Inorg. Chem.* **2015**, *54*, 544–553; n) M. Graf, Y. Gothe, N. Metzler-Nolte, R. Czerwieniec, K. Sünkel, *Z. Anorg. Allg. Chem.* **2015**, *641*, 1798–1802; o) P. Göbel, F. Ritterbusch, M. Helms, M. Bischof, K. Harms, M. Jung, E. Meggers, *Eur. J. Inorg. Chem.* **2015**, 1654–1659.

[3] For applications of bis-cyclometalated iridium(III) complexes in the field of OLED research: a) N. Rehmann, C. Ulbricht, A. Köhnen, P. Zacharias, M. C. Gather, D. Hertel, E. Holder, K. Meerholz, U. S. Schubert, *Adv. Mater.* **2008**, *20*, 129–133; b) C. Ulbricht, N. Rehmann, E. Holder, D. Hertel, K. Meerholz, U. S. Schubert, *Macromol. Chem. Phys.* **2009**, *210*, 531–541; c) N. Tian, A. Thiessen, R. Schiewek, O. J. Schmitz, D. Hertel, K. Meerholz, E. Holder, *J. Org. Chem.* **2009**, *74*, 2718–2725; d) N. Tian, D. Lenkeit, S. Pelz, D. Kourkoulos, D. Hertel, K. Meerholz, E. Holder, *Dalton Trans.* **2011**, 11629–11635; e) H. Xu, R. Chen, Q. Sun, W. Lai, Q. Su, W. Huang, X. Liu, *Chem. Soc. Rev.* **2014**, *43*, 3259–3302; f) J. Jou, S. Kumar, A. Agrawal, T. Lia, S. Sahooa, *J. Mater. Chem. C.* **2015**, *3*, 2974–3002.

[4] Examples for bis-cyclometalated iridium(III) complexes as templates for asymmetric catalysis through the ligand sphere: a) L. Chen, W. Xu, B. Huang, J. Ma, L. Wang, J. Xi, K. Harms, L. Gong, E. Meggers, *J. Am. Chem. Soc.* **2013**, *135*, 10598–10601; b) L. Chen, X. Tang, J. Xi, W. Xu, L. Gong, E. Meggers, *Angew. Chem. Int. Ed.* **2013**, *52*, 14021–14025; *Angew. Chem. Int. Ed.* **2013**, *125*, 14271–14275 c) J. Ma, X. Ding, Y. Hu, Y. Huang, L. Gong, E. Meggers, *Nat. Commun.* **2014**, 4531; d) W. Xu, M. Arieno, H. Löw, K. Huang, X. Xie, T. Cruchter, Q. Ma, J. Xi, B. Huang, O. Wiest, L. Gong, E. Meggers, *J. Am. Chem. Soc.* **2016**, *138*, 8774–8780.

[5] Examples for bis-cyclometalated iridium complexes as (photoactive) chiral Lewis acid catalysts: a) H. Huo, C. Fu, K. Harms, E. Meggers, *J. Am. Chem. Soc.* **2014**, *136*, 2990–2993; b) H. Huo, X. Shen, C. Wang, L. Zhang, P. Röse, L. Chen, K. Harms, M. Marsch, G. Hilt, E. Meggers, *Nature* **2014**, *515*, 100–103; c) X. Shen, H. Huo, C. Wang, B. Zhang, K. Harms, E. Meggers, *Chem. Eur. J.* **2015**,

21, 9720–9726; d) H. Huo, C. Wang, K. Harms, E. Meggers, *J. Am. Chem. Soc.* **2015**, *137*, 9551–9554; e) C. Wang, Y. Zheng, H. Huo, P. Röse, L. Zhang, K. Harms, G. Hilt, E. Meggers, *Chem. Eur. J.* **2015**, *21*, 7355–7359; f) C. Wang, J. Qin, X. Shen, R. Riedel, K. Harms, E. Meggers, *Angew. Chem. Int. Ed.* **2016**, *55*, 685–688; *Angew. Chem.* **2016**, *128*, 695–698; g) G.-Q. Xu, H. Liang, J. Fang, Z.-L. Jia, J.-Q. Chen, P.-F. Xu, *Chem. Asian J.* **2016**, *11*, 3355–3358.

[6] For an overview, see: a) L. Gong, L.-A. Chen, E. Meggers, *Angew. Chem. Int. Ed.* **2014**, *53*, 10868–10874; *Angew. Chem.* **2014**, *126*, 11046–11053; b) Z.-Y. Cao, W. D. G. Brittain, J. S. Fossey, F. Zhou, *Catal. Sci. Technol.* **2015**, *5*, 3441–3451; c) L. Zhang, E. Meggers, *Acc. Chem. Res.* **2017**, *50*, 320–330.

[7] Auxiliary-mediated method for the synthesis of octahedral transition metal complexes: a) E. Meggers, *Chem. Eur. J.* **2010**, *16*, 752–758; b) L. Gong, M. Wenzel, E. Meggers, *Acc. Chem. Res.* **2013**, *46*, 2635–2644.

[8] Auxiliary-mediated strategy for the synthesis of non-racemic, bis-cyclometalated iridium complexes: a) O. Chepelin, J. Ujma, X. Wu, A. M. Z. Slawin, M. B. Pitak, S. J. Coles, J. Michel, A. C. Jones, P. E. Barran, P. J. Lusby, *J. Am. Chem. Soc.* **2012**, *134*, 19334–19337; b) E. Marchi, R. Sinisi, G. Bergamini, M. Tragni, M. Monari, M. Bandini, P. Ceroni, *Chem. Eur. J.* **2012**, *18*, 8765–8773; c) M. Helms, Z. Lin, L. Gong, K. Harms, E. Meggers, *Eur. J. Inorg. Chem.* **2013**, 4164–4172; d) D. L. Davies, K. Singh, S. Singh, B. Villa-Marcos, *Chem. Commun.* **2013**, *49*, 6546–6548; e) M. Helms, C. Wang, B. Orth, K. Harms, E. Meggers, *Eur. J. Inorg. Chem.* **2016**, 2896–2901; f) S.-Y. Yao, Y.-L. Ou, B.-H. Ye, *Inorg. Chem.* **2016**, *55*, 6018–6026. See also ref. [4] and [5].

[9] Selected examples dealing with the racemic synthesis of bis-cyclometalated iridium(III) complexes: a) M. Nonoyama, *Bull. Chem. Soc. Jpn.* **1974**, *47*, 767–768; b) S. Lamansky, P. Djurovich, D. Murphy, F. Abdel-Razzag, H. Lee, C. Adachi, P. E. Burrows, S. R. Forrest, M. E. Thompson, *J. Am. Chem. Soc.* **2001**, *123*, 4304–4312; c) M. S. Lowry, W. R. Hudson, R. A. Pascal, Jr., S. Bernhard, *J. Am. Chem. Soc.* **2004**, *126*, 14129–14135; d) M. Xu, W. Li, Z. An, Q. Zhou, G. Wang, *Appl. Organomet. Chem.* **2005**, *19*, 1225–1231; e) A. S. Ionkin, W. J. Marshall, B. M. Fish,

Organometallics **2006**, *25*, 1461–1471; f) M. Lepeltier, T. Lee, K. Lo, L. Toupet, H. Bozec, V. Guerschais, *Eur. J. Inorg. Chem* **2007**, (18), 2734–2747; g) T. Chen, *J. Organomet. Chem.* **2008**, *693*, 3117–3170; h) J. J. Kim, Y. You, Y. Park, J. Kim, S. Y. Park, *J. Mater. Chem.* **2009**, *19*, 8347–8359; i) E. Baranoff, B. F. E. Curchod, F. Monti, F. Steimer, G. Accorsi, I. Tavernelli, U. Rothlisberger, R. Scopelliti, M. Grätzel, M. K. Nazeeruddin, *Inorg. Chem.* **2012**, *51*, 799–811; j) A. M. Prokhorov, A. Santoro, J. A. G. Williams, D. W. Bruce, *Angew. Chem. Int. Ed.* **2012**, *51*, 95–98; *Angew. Chem.* **2012**, *124*, 99–102; k) J. Dai, K. Zhou, M. Li, H. Sun, Y. Chen, S. Su, X. Pu, Y. Huang, Z. Lu, *Dalton Trans.* **2013**, *42*, 10559–10571; l) B. Liang, S. Hu, Y. Liu, Z. Fan, X. Wang, W. Zhu, H. Wu, Y. Cao, *Dyes and Pigments* **2013**, *99*, 41–51; m) D. R. Whang, K. Sakai, S. Y. Park, *Angew. Chem. Int. Ed.* **2013**, *52*, 11612–11615; *Angew. Chem.* **2013**, *125*, 11826–11829; n) E. Baranoff, B. F. E. Curchod, F. Monti, F. Steimer, G. Accorsi, I. Tavernelli, U. Rothlisberger, R. P. Lanoe, C. M. Tong, R. W. Harrington, M. R. Probert, W. Clegg, J. A. G. Williams, V. N. Kozhevnikov, *Chem. Commun.* **2014**, *50*, 6831–6834; o) Z. Niu, T. Zheng, Y. Su, P. Wang, X. Li, F. Cui, J. Liang, G. Li, *New J. Chem.* **2015**, *39*, 6025–6033; p) C. Pei, P. Cui, C. Mc Cleese, S. Kilina, C. Burda, W. Sun, *Dalton trans.* **2015**, *44*, 2176–2190; q) A. Paul, N. Das, Y. Halpin, J. G. Vos, M. T. Pryce, *Dalton Trans.* **2015**, *44*, 10423–10430; r) J. Kim, K. H. Lee, S. J. Lee, H. W. Lee, Y. K. Kim, Y. S. Kim, S. S. Yoon, *Chem. Eur. J.* **2016**, *22*, 4036–4045.

[10] Examples for cross coupling on planar chiral cyclophanes: a) Y. Morisaki, Y. Chujo, *Macromolecules* **2003**, *36*, 9319–9324; b) Y. Morisaki, Y. Chujo, *Macromolecules* **2004**, *37*, 4099–4103; c) Y. Morisaki, Y. Chujo, *Chem. Lett.* **2012**, *41*, 840–846; d) M. Cakici, Z. Gu, M. Nieger, J. Bürck, L. Heinke, S. Bräse, *Chem. Commun.* **2015**, *51*, 4790–4798; e) D. Enders, M. Ludwig, G. Raabe, *Chirality* **2012**, *24*, 215–222; f) M. Cakici, S. Bräse, *Eur. J. Org. Chem.* **2012**, 6132–6135; g) C. Braun, E. Spurling, N. B. Heine, M. Cakici, M. Nieger, S. Bräse, *Adv. Synth. Catal* **2016**, *358*, 1664–1670.

[11] Examples for cross coupling on axial chiral binaphthol derivatives: a) R. I. Storer, D. E. Carrera, Y. Ni, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2006**, *128*, 84–86; b) M. Yamanaka, J. Itoh, K.

Fuchibe, T Akiyama, *J. Am. Chem. Soc.* **2007**, *129*, 6756–6764; c) X. Cheng, R. Goddard, G. Buth, B. List, *Angew. Chem. Int. Ed.* **2008**, *47*, 5079–5081; *Angew. Chem.* **2008**, *120*, 5157–5159; d) M. Klussmann, L. Ratjen, S. Hoffmann, V. Wakchaure, R. Goddard, B. List, *Synlett* **2010**, (14), 2189–2192; e) B. Li, P. Chiu, *Eur. J. Org.* **2011**, 3932–3937; f) F. Romanov – Michailidis, L. Guénée, A. Alexakis, *Angew. Chem. Int. Ed.* **2013**, *52*, 9266–9270; *Angew. Chem.* **2013**, *125*, 9436–9440; g) D. Parmar, E. Sugiono, S. Raja, M. Rueping, *Chem. Rev.* **2014**, *114*, 9047–9153; h) B. Qu, N. Haddad, S. Rodriguez, J. D. Sieber, J. Desrosiers, N. D. Patel, Y. Zhang, N. Grinberg, H. Lee, S. Ma, U. J. Ries, N. K. Yee, C. H. Senanayake, *J. Org. Chem.* **2016**, *81*, 745–750.

[12] Examples for C-H borylation and cross-coupling on polycyclic aromatic carbohydrates and heterocycles: a) D. N. Coventry, A. S. Batsanov, A. E. Goeta, J. A. K. Howard, T. B. Marder, R. N. Perutz, *Chem. Commun.* **2005**, 2172–2174; b) I. A. I. Mkhalid, D. N. Coventry, D. Albesa-Jove, A. S. Batsanov, J. A. K. Howard, R. N. Perutz, T. B. Marder, *Angew. Chem. Int. Ed.* **2006**, *45*, 489–491; *Angew. Chem.* **2006**, *118*, 503–505; c) P. Harrisson, J. Morris, T. B. Marder, P. G. Steel, *Org. Lett.* **2009**, *11*, 3586–3589; d) A. G. Crawford, A. D. Dwyer, Z. Liu, A. Steffen, A. Beeby, L. Pålsson, D. J. Tozer, T. B. Marder, *J. Am. Chem. Soc.* **2011**, *133*, 13349–13362; e) A. G. Crawford, Z. Liu, I. A. I. Mkhalid, M. Thibault, N. Schwarz, G. Alcaraz, A. Steffen, J. C. Collings, A. S. Batsanov, J. A. K. Howard, T. B. Marder, *Chem. Eur. J.* **2012**, *18*, 5022–5035; f) S. Konishi, S. Kawamorita, T. Iwai, P. G. Steel, T. B. Marder, M. Sawamura, *Chem. Asian J.* **2014**, *9*, 434–438; g) L. Ji, R. M. Edkins, A. Lorbach, I. Krummenacher, C. Brückner, A. Eichhorn, H. Braunschweig, B. Engels, P. J. Low, T. B. Marder, *J. Am. Chem. Soc.* **2015**, *137*, 6750–6753; h) L. Ji, K. Fucke, S. K. Bose, T. B. Marder, *J. Org. Chem.* **2015**, *80*, 661–665; i) L. Ji, A. Lorbach, R. M. Edkins, T. B. Marder, *J. Org. Chem.* **2015**, *80*, 5658–5665; j) S. A. Sadler, A. C. Hones, B. Roberts, D. Blakemore, T. B. Marder, P. G. Steel, *J. Org. Chem.* **2015**, *80*, 5308–5314.

[13] Examples for cross coupling on other scaffolds: a) S. K. Weber, F. Galbrecht, U. Scherf, *Org. Lett.* **2006**, *8*, 4039–4041; b) J. B. Grimm, L. D. Lavis, *Org. Lett.* **2011**, *24*, 6354–6357; c) J. Strueben, P. J. Gates, A. Staubitz, *J. Org. Chem.* **2014**, *79*, 1719–1728.

[14] Examples for oxidative addition steps in cross-coupling with OTf: a) S. E. Denmark, R. F. Sweis, *Org. Lett.* **2002**, *4*, 3771–3774; b) S. Riggleman, P. DeShong, *J. Org. Chem.* **2003**, *68*, 8106–8109; c) M. Bonaterra, R. A. Rossi, S. E. Martin, *Organometallics* **2008**, *28*, 933–936; d) A. He, J. R. Falck, *J. Am. Chem. Soc.* **2009**, *132*, 2524–2525.

[15] For precedence on the cross-coupling at iridium(III) complexes: a) W. Leslie, A. S. Batsanov, J. A. K. Howard, J. A. G. Williams, *Dalton Trans.* **2004**, 623–631; b) J. A. G. Williams, *Chem. Commun.* **2005**, 230–232; c) K. J. Arm, J. A. G. Williams, *Dalton Trans.* **2006**, 2172–2174; d) H. A. Bronstein, C. E. Finlayson, K.R. Kirov, R. H. Friend, C. K. Williams, *Organometallics* **2008**, *27*, 2980–2989; e) J. A. G. Williams, A. J. Wilkinson, V. L. Whittle, *Dalton Trans.* **2008**, 2081–2099; f) K. J. Arm, V. L. Whittle, J. A. G. Williams, *Inorg. Chem.* **2008**, *47*, 6596–6607; g) J. A. G. Williams, *Chem. Soc. Rev.* **2009**, *38*, 1783–1801; h) V. L. Whittle, J. A. G. Williams, *Dalton Trans.* **2009**, 3929–3940; i) N. Akino, R. Okamura, *Metal complex, polymer compound and device containing those*, EP 2128168 A1, **2009**; j) G. Liaptsis, D. Hertel, K. Meerholz, *Angew. Chem. Int. Ed.* **2013**, *52*, 9563–9567; *Angew. Chem.* **2013**, *125*, 9742–9746; k) A. Liang, K Zhang, J. Zhang, F. Huang, X. Zhu, Y. Cao, *Chem. Mater.* **2013**, *25*, 1013–1019; l) M. Lian, Y. Yu, J. Zhao, Z. Huang, X. Yang, G. Zhou, Z. Wu, D. Wang, *J. Mater Chem. C.* **2014**, *2*, 9523–9535; m) J. Pérez-Miqueo, A. Telleria, M. Muñoz-Olasagasti, A. Altube, E. Garcia-Lecina, A. de Cózar, Z. Freixa, *Dalton Trans.* **2015**, 2075–2091; n) A. Telleria, J. Pérez-Miqueo, A. Altube, E. Garcia-Lecina, A. de Cózar, Z. Freixa, *Organometallics* **2015**, *34*, 5513–5529; o) Z. Huang, B. Liu, Y. He, X. Yan, X. Yang, X. Xu, G. Zhou, Y. Ren, Z. Wu, *J. Organomet. Chem.* **2015**, *794*, 1–10; p) R. Muñoz-Rodríguez, E. Buñuel, N. Fuentes, J. A. G. Williams, D. J. Cárdenas, *Dalton Trans.* **2015**, *44*, 8394–8405.

[16] S. D. Walker, T. E. Barder, J. R. Martinelli, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2004**, *43*, 1871–1876; *Angew. Chem.* **2004**, *116*, 1907–1912.

[17] T. E. Barder, S. D. Walker, J. R. Martinelli, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 4685–4696.

[18] More details about the first test reactions are provided in the supporting information.

[19] Further examples of CD spectra of the cross-coupling products are illustrated in the supporting information.

[20] Details about the HPLC experiments and the synthesis of the racemic reference are depicted in the supporting information.

[21] A recent publication from our group relies on such post-complexation cross-coupling. See: V. A. Larionov, T. Cruchter, T. Mietke, E. Meggers, *Organometallics* **2017**, DOI: 10.1021/acs.organomet.7b00016.

Accepted Manuscript