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Expanding the family of bis-cyclometalated chiral-at-metal rhodium(III) catalysts with a benzothiazole derivative†

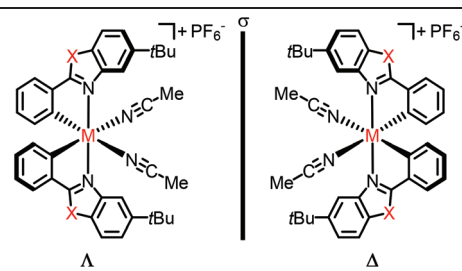
Jiajia Ma,^a Xiaodong Shen,^a Klaus Harms^a and Eric Meggers^{*a,b}

Synthetic access to previously elusive single enantiomers of an octahedral chiral-at-metal rhodium(III) complex containing two cyclometalated 2-phenylbenzothiazoles and two acetonitrile ligands is reported. The complex is a superior chiral Lewis acid catalyst compared to its benzoxazole congener which can be rationalized with a higher steric congestion around the coordination sites.

Chiral Lewis acids play an important role in asymmetric catalysis because many reactions are amenable to Lewis acid activation.¹ Recently, we introduced a new class of chiral Lewis acids based on octahedral iridium(III)^{2–7} and rhodium(III)^{8–11} complexes which draw their chirality exclusively from the metal-centered chirality (metal centrochirality).^{12,13} These chiral-only-at-metal complexes are cyclometalated by two 5-*tert*-butyl-2-phenylbenzoxazoles or the analogous benzothiazole ligands in addition to two exchange-labile acetonitriles, which generates a C₂-symmetric, propeller-type geometry.

Whereas the iridium complexes Λ/Δ -IrO and Λ/Δ -IrS have been demonstrated to be excellent catalysts for visible light induced photoredox reactions,^{3,4,6,7} the rhodium congener Λ/Δ -RhO features advantages for regular Lewis acid catalysis,^{8–10} apparently due to a more rapid ligand exchange kinetics (Table 1). We expected that the related complex Λ/Δ -RhS, in which the coordinating benzoxazole moieties are replaced by benzothiazoles, should provide a higher asymmetric induction due to an increased bond length of C–S over C–O which will position the two *tert*-butyl groups somewhat closer to the substrate coordination site. Here we disclose the previously elusive access to the enantiomerically pure benzothiazole complexes Λ - and Δ -RhS, characterize their structures and configurational

Table 1 Overview of bis-cyclometalated, chiral-only-at-metal iridium and rhodium catalysts^a



Entry	Complex	M	X	Remarks
1	Λ - and Δ -IrO	Ir	O	Ref. 2 and 4
2	Λ - and Δ -IrS	Ir	S	Ref. 3 and 5–7
3	Λ - and Δ -RhO	Rh	O	Ref. 8–11
4	Λ - and Δ -RhS	Rh	S	This study

^a Synthesis by an auxiliary-mediated strategy.

stability, and demonstrate their excellent performance as asymmetric catalysts.

The auxiliary-mediated synthesis^{14–18} starts with rhodium trichloride hydrate which is first converted into *rac*-RhS in a yield of 73% by reaction with 2 equiv. of 5-*tert*-butyl-2-phenylbenzothiazole (**1**), followed by a treatment with 1.2 equiv. of AgPF₆ in MeCN (Fig. 1). The complex *rac*-RhS is then reacted with the monofluorinated salicyloxazoline (*S*)-**2**¹⁹ to provide a diastereomeric mixture of Λ -(*S*)-**3** and Δ -(*S*)-**3** which can be resolved into pure diastereomers (46% each) based on their different solubilities in EtOH or by silica gel chromatography, or a combination thereof depending on the reaction scale. Configurations were assigned based on the crystal structure of Λ -(*S*)-**3** as shown in Fig. 2. Finally, starting with Λ -(*S*)-**3** and Δ -(*S*)-**3**, an acid induced replacement of the coordinated auxiliary ligand with two acetonitriles under retention of the configuration affords the individual enantiomers Λ -RhS (85%) and Δ -RhS (80%). The key aspect of this auxiliary-mediated synthesis is the fluorinated auxiliary (*S*)-**2** which was first

^a Philipps-Universität Marburg, Hans-Meerwein-Strasse 4, 35043 Marburg, Germany. E-mail: meggers@chemie.uni-marburg.de

^b College of Chemistry and Chemical Engineering, Xiamen University, Xiamen 361005, People's Republic of China

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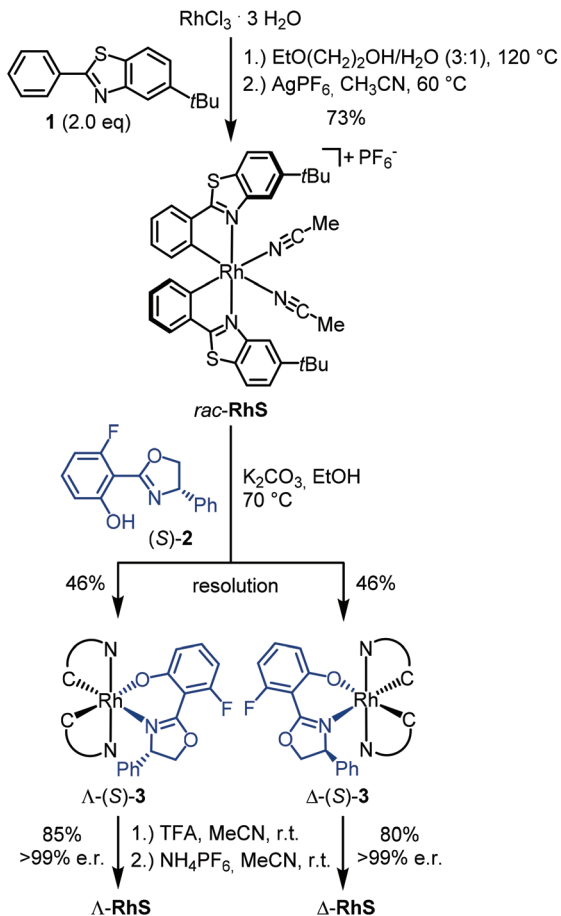


Fig. 1 Auxiliary-mediated synthesis of Λ - and Δ -RhS.

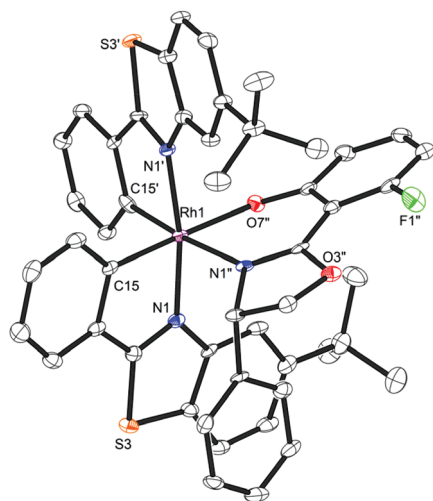


Fig. 2 Crystal structure of the auxiliary complex Λ -(S)-3. ORTEP drawing with 50% thermal ellipsoids. CCDC number 1455732.

introduced by Ceroni and co-workers.¹⁹ All other tested auxiliaries did not provide intermediate rhodium auxiliary complexes with distinct solubilities and were not stable enough for a resolution *via* silica gel chromatography.

The CD spectra of the complexes Λ - and Δ -RhS are shown in Fig. 3, and confirm their mirror-imaged structures. HPLC performed on a chiral stationary phase validates the high enantiomeric purity of the individual enantiomers (Fig. 4).²⁰ For the Δ -enantiomer an er of 99.9 : 0.1 was determined, while peak tailing prevents an accurate validation of the Λ -enantiomer and an er of >99 : 1 was estimated.

Fig. 5 shows the superimposed crystal structures of Λ -RhS and mirror-imaged Δ -RhO, not only confirming the assigned metal-centered configuration of Λ -RhS, but also revealing the differences in how the two *tert*-butyl groups flank the coordination site around the two exchange-labile acetonitrile ligands. In comparison with RhO, the *tert*-butyl groups of RhS are in closer proximity to the labile acetonitriles as quantified by a 0.9 Å shorter intramolecular distance between the quaternary carbons of the two *tert*-butyl groups in RhS (10.5 Å) over RhO (11.4 Å). This is consistent and analogous with a comparison of the related benzoxazole and benzothiazole iridium complexes.^{3,5}

The increased steric hindrance provided by the two *tert*-butyl groups should make RhS an improved asymmetric catalyst for many applications. This is confirmed by the preliminary results shown in Fig. 6. In both enantioselective Michael addition⁸ and a photoinduced enantioselective radical reaction,¹¹ the determined enantioselectivities are appreciably

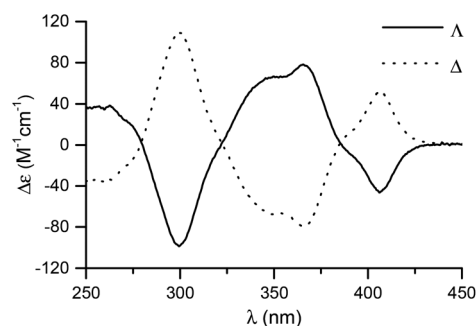


Fig. 3 CD spectra of Λ - and Δ -RhS recorded in $\text{CH}_3\text{OH} : \text{CH}_2\text{Cl}_2$ 4 : 1.

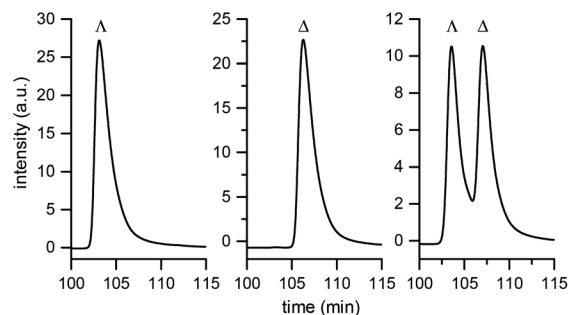


Fig. 4 HPLC traces of racemic, Λ - and Δ -RhS. HPLC conditions: Daicel CHIRALPAK IB, 250 × 4.6 mm, column temp. = 25 °C, λ_{abs} = 254 nm, flow rate = 0.6 mL min⁻¹, solvent A = 0.1% aqueous TFA, solvent B = MeCN, gradient = 40% to 50% B in 180 min.



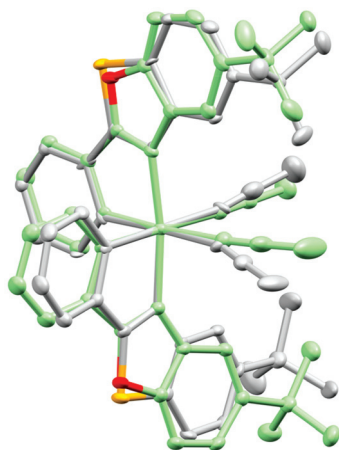


Fig. 5 Superimposed crystal structure of Λ -RhS (grey) with inverted Δ -RhO (green). Fitted is the central metal together with the metal-bound atoms. Atoms are displayed as 50% thermal ellipsoids. CCDC number 1455731 (Λ -RhS).

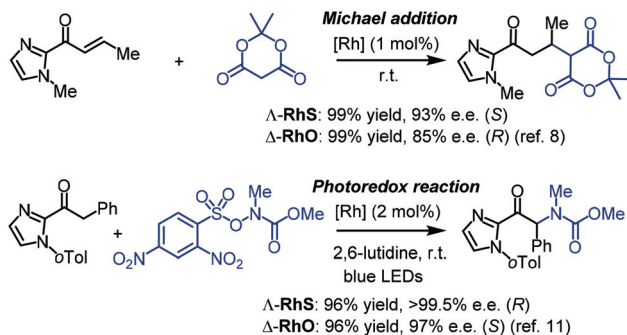


Fig. 6 Comparison of catalytic performances of Λ -RhS and Δ -RhO.

higher for the benzothiazole (**RhS**) over the benzoxazole (**RhO**) catalyst.²¹

In conclusion, here we reported a new chiral-at-metal benzothiazole complex Λ/Δ -RhS which expands the family of bis-cyclometalated rhodium(III) complexes for applications in asymmetric catalysis. Compared to the previously reported benzoxazole complex Λ/Δ -RhO, the benzothiazole ligands in Λ/Δ -RhS provide a higher steric congestion around the labile acetonitrile ligands, thereby making Λ/Δ -RhS a superior asymmetric catalyst. Applications of the new chiral Lewis acid catalyst to challenging asymmetric transformations are underway in our laboratory.

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