



Photocatalytic deracemisation of cobalt(III) complexes with fourfold stereogenicity†

Tanno A. Schmidt and Christof Sparr *

Cite this: *Chem. Commun.*, 2022, 58, 12172

Received 21st September 2022,
Accepted 5th October 2022

DOI: 10.1039/d2cc05196f

rsc.li/chemcomm

The deracemisation of fourfold stereogenic cobalt(III) diketonates with a chiral photocatalyst is described. With only 0.5 mol% menthyl Ru(bpy)₃²⁺ photocatalyst, an enantiomeric enrichment of up to 88 : 12 e.r. was obtained for the major meridional diastereomers. Moreover, a distribution of configurationally stable diastereomers distinct from the thermodynamic ratio was observed upon reaching the photostationary state.

Carbon stereocentres are found in a nearly endless number of organic molecules, rendering the efficient control of their configuration an important topic of research.¹ Besides the prototypical carbon-based stereogenic centres, tri- and tetra-coordinated silicon, sulfur and phosphorus stereocentres were stereoselectively prepared by auxiliary and catalytic methods.² However, catalyst stereocontrol over high-valent stereocentres (Fig. 1A) that lead to more than two stereoisomers per stereocentre remained a fascinating challenge to be addressed. Notably, the foundations of high-valent stereoisomerism have already been laid over 100 years ago by Alfred Werner³ and the stereochemistry of coordination compounds is now well established.⁴ For instance, while the octahedral complex Co(acac)₃ (acac = acetylacetonate) exists in two C₃ symmetric enantiomeric forms Λ and Δ , the homoleptic Co(tfac)₃ (tfac = 1,1,1-trifluoroacetylacetonate) with a reduced symmetry of the ligand gives rise to four stereoisomers, the two enantiomeric pairs (Λ and Δ) of C₃ and C_s symmetric diastereomers (*mer* = meridional and *fac* = facial isomers; Fig. 1B). These complexes are hence characterised by irreducible stereogenic units with higher-order stereogenicity, each giving rise to more than two stereoisomers (s₁ⁿ¹ × s₂ⁿ², ...).⁵ Moreover, the stereochemical complexity can be further increased in heteroleptic complexes, for example in Co(acac)(tfac)₂ with six stereoisomers.⁶

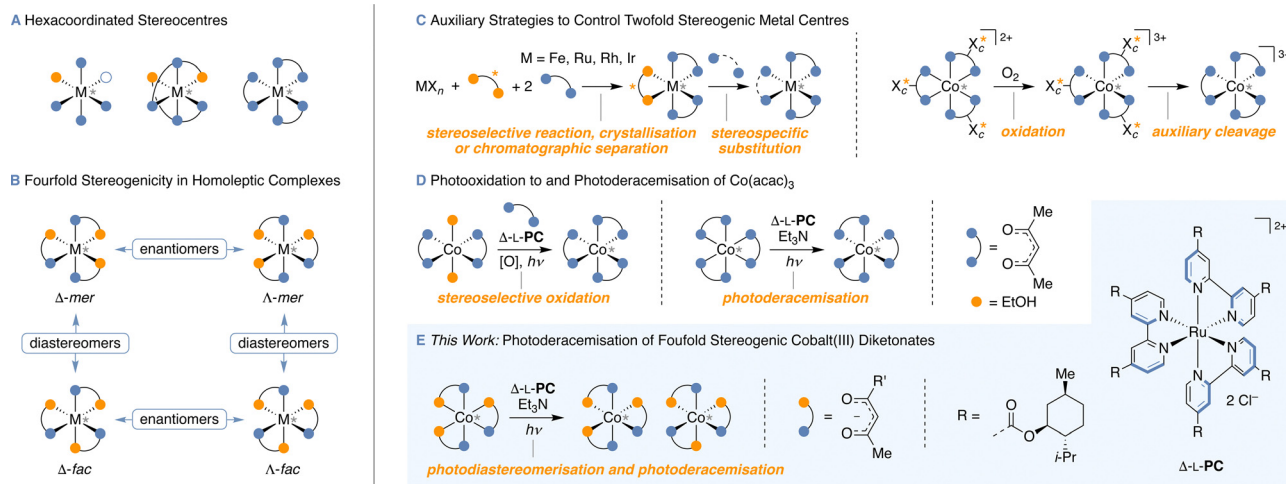
To control the absolute configuration of metal stereocentres, various methods were developed tailored to specific metal–ligand

combinations. Aside from complexes where the configuration of the metal atom is directly controlled by configurationally well-defined stereogenic units in the ligands,⁷ complexes with the metal centre as the only stereogenic element are of particular interest and their application as efficient catalysts was demonstrated with impressive versatility in stereoselective synthesis.⁸ The use of chiral counterions has been long-known as a viable method to obtain cationic complexes in enantioenriched form by crystallisation.^{3,9} While the use of chiral auxiliaries, which thermodynamically or kinetically control the configuration of an intermediate¹⁰ or allow for the separation of diastereomers by column chromatography,¹¹ has over the last years become a practical method to isolate isomers with stereogenic Fe-, Ru-, Rh- and Ir-centres, this strategy not only requires the introduction of an auxiliary, but also the subsequent stereospecific substitution by an achiral ligand (Fig. 1C). Progress has been made towards a more direct kinetic resolution, which in turn still requires the half-stoichiometric use of a chiral additive.¹² These methods allow for enantiocontrol over a range of hexavalent stereocentres and pioneering examples of a catalytic process were established for stereocentres with twofold stereogenicity (enantiomers).¹³ Interestingly, the Shinkai group¹⁴ examined the interconversion between stereodynamic cobalt(II) and configurationally stable cobalt(III) species as promising concept for controlling the configuration of cobalt(III) with C_{2v} symmetric ligands to differentiate enantiomers with boronate-bound saccharides as auxiliaries, providing [Co(bpy)₃](NO₃)₃ (bpy = 2,2′-bipyridine) with up to 89 : 11 e.r. (Fig. 1C). After equilibrating the respective cobalt(II) complexes by auxiliary control to diastereomerically enriched mixtures, the cobalt(II) complexes were oxidised to the configurationally stable cobalt(III) analogues, followed by an auxiliary cleavage to yield complexes with the metal centre as only stereogenic element. Remarkably, Ohkubo *et al.* developed a photocatalytic strategy by the stereoselective oxidation of Co(acac)₂, making use of auxiliary-supported chiral-at-metal Δ -[Ru(*l*-menbpy)₃]Cl₂ (Δ -*l*-PC) to yield Co(acac)₃ with up to 55 : 45 e.r. (Fig. 1D).¹⁵ A related copper(I) catalysed photooxidation provided [Co(EDTA)][−] (EDTA = ethylenediaminetetraacetate)

Department of Chemistry, University of Basel, St. Johannis-Ring 19, Basel CH-4056, Switzerland. E-mail: christof.sparr@unibas.ch

† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d2cc05196f>





with up to 54 : 46 e.r.¹⁶ The former process was later coupled with the photoreduction/kinetic resolution of Co(acac)₃,¹⁷ eventually resulting in the photoderacemisation of Co(acac)₃ giving rise to an e.r. of up to 75 : 25.¹⁸ It was proposed that enantioinduction of this process results from different stabilities of diastereomeric cobalt(II)–ruthenium(III) contact ion pairs, in which the cobalt centre is stereodynamic allowing for the equilibration between its Δ- and Λ-enantiomers.¹⁸ When the ruthenium(III) re-oxidises the cobalt(II), the equilibrium constant of the Δ-Ru^{III}–Δ/Λ-Co^{II} pair is reflected by the enantioenrichment of the resulting cobalt(III) complex. However, the application of this highly efficient and elegant method to complexes other than Co(acac)₃ was yet to be explored and the intricate stereocontrol for systems with higher-order stereogenicity remained unprecedented.

As the use of photocatalysts in diastereomerisation,¹⁹ racemisation²⁰ and deracemisation reactions²¹ has drawn the attention of many organic chemists, we anticipated that photocatalytic reactions allow to control the configuration of high-valent stereocentres with more than two states, such as fourfold stereogenic cobalt centres (Fig. 1E). Furthermore, a photoderacemisation would grant most direct access to stereoisomerically enriched material from a racemate. Our interest in catalyst stereocontrol over higher-order stereogenicity^{5,22} ultimately motivated us to investigate the possibility of photocatalysts to stereoisomerise fourfold stereogenic cobalt(III) diketonate complexes. Strikingly, governing the stereocentre configuration of $\text{Co}(\text{tfac})_3$ and related coordination compounds requires catalytic stereoselectivity for both the photoderacemisation and the diastereoisomerisation.

We thus initiated our studies of the photocatalytic stereoisomerisation of cobalt(III) diketonates with the homoleptic $\text{Co}(\text{tfac})_3$ (**1a**). To our delight, the determination of its thermal stereoisomerisation barriers at 90 °C in heptane revealed that the cobalt(III) complex is particularly configurationally stable, with all macroscopically observable stereoisomerisation processes having activation barriers greater than 113 kJ mol⁻¹

(see ESI†). In accord with the proposed mechanisms for the stereoisomerisation of octahedral complexes with bidentate ligands,²³ no interconversion between Λ -*mer*-**1a** and Δ -*fac*-**1a** nor Δ -*mer*-**1a** and Λ -*fac*-**1a** was found. The thermal stereoisomerisation reached its endpoint in a racemic mixture of *mer*- and *fac*-**1a** within 3.5 hours at 90 °C. As the high stereoisomerisation barriers suggest that thermal isomerisation is not to be expected under ambient conditions, we turned our attention to other factors potentially impacting the stereoisomer interconversion of **1a**. Since additional diketone ligand and organic bases have been employed in the photoderacemisation of Co(acac)₃,¹⁸ we studied their impact on the thermal stereoisomerisation. At room temperature, neither the presence of ligand and base nor ligand or base alone led to significant stereoisomerisation within 24 h (see ESI†). Also, no significant acceleration of the *mer*/*fac*-diastereomerisation in the presence of 1,1,1-trifluoroacetylacetone (tfacH) was observed after irradiating CHCl₃ solutions of *mer*-**1a** with blue light for 10 h, further substantiating the feasibility of a catalytic deracemisation of **1a**.

Aiming at the most direct access to single stereoisomers of cobalt(III) diketonates, racemic *mer*-Co(tfac)₃ (*rac-mer-1a*) was subjected to deracemisation conditions. Irradiating **1a** in presence of Δ -L-**PC**,¹⁸ tfacH and Et₃N with blue LED light resulted in complete decomposition of the cobalt(III) complex, possibly because the re-oxidation of the cobalt(II) intermediate is hampered by the electron-withdrawing CF₃ groups as reflected by the high reduction potential of Co(tfac)₃ (**1a**).²⁴ A similar outcome was observed for phenyl substituted **1b** (Table 1, entries 1 and 2). However, to our delight, introducing a cyclohexyl moiety to the diketonate ligand yielded the Λ -*mer*-stereoisomer of **1c** with 79:21 d.r. and an e.r. of 84:16 (entry 3), while the minor *fac*-isomer showed reduced enantiocontrol with an e.r. value of 69:31 (Λ/Δ). In contrast, cobalt(III) complex **1d** bearing a sterically demanding *tert*-butyl group provided higher enantioselectivity for the *fac*- than for the *mer*-isomer (entry 4). Surprisingly, the

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endeavour for which photocatalysts need yet to be designed, but also to unveil further intricacies of the mechanism.

In conclusion, we describe the feasibility of photocatalytic stereocontrol over fourfold stereogenic metal centres of cobalt(III) diketonates. The deracemisation allowed an enantioenrichment of up to 88 : 12 e.r. with 0.5 mol% of a chiral photocatalyst under irradiation with blue LED light. A notable impact of steric factors on the enantioenrichment for either the *mer*- or *fac*-diastereomer was thereby revealed. Moreover, configurationally stable cobalt(III) complexes with a diastereomeric distribution distinct from the thermodynamic ratio were isolated.

We gratefully acknowledge the Swiss National Science Foundation (175746), the University of Basel and the NCCR Molecular Systems Engineering (182895) for financial support. This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No. 101002471). We thank Prof. Dr Oliver Wenger for helpful discussions.

Conflicts of interest

There are no conflicts to declare.

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