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**Breaking the symmetry:
creation and transfer of optical activity via total spontaneous
resolution and stereoselective reactions**

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Abstract

The generation of optical activity from achiral or racemic precursors – absolute asymmetric synthesis – is discussed in relation to the origin of biomolecular homochirality but is also often (incorrectly) regarded as being impossible. One approach to absolute asymmetric synthesis is the use of compounds that form chiral crystals. If the compounds are also stereochemically labile in solution, all crystals in a batch may crystallise as the same enantiomer via total spontaneous resolution. The rare occurrence of conglomerates means that it is advantageous if the optical activity generated during the crystallisation can be transferred via stereoselective reactions to produce several enantiopure products from a single conglomerate phase. For this purpose, organometallic reagents and coordination compounds are well suited, since they combine stereochemical lability in solution with high reactivity.

In this work two indenylzinc complexes were found to undergo total spontaneous resolution. NCS-chlorination of $[\text{Zn}(\text{ind})_2(\text{pic})_2]$ gave 1-chloroindene with up to 89% *ee* for single crystals and 71% *ee* for full crystal batches, while $[\text{Zn}(\text{dcp})(\text{ind})(\text{tmeda})]$ gave 98% *ee* for single-crystals and 95% *ee* for full crystal batches.

Three new octahedral ruthenium complexes with bidentate chelating ligands having at least one prochiral thioether function have been found to undergo total spontaneous resolution. One of the complexes gave optically active crystal batches with up to 97% *ee*. The optical activity of full crystal batches was transferred via oxidation to the corresponding sulfoxide complex with >97% *ee*.

A new method to obtain single-crystals suitable for X-ray diffraction of base-free polymeric $[\text{LiCp}]_n$ and $[\text{Li}(\text{MeCp})]_n$ was developed. In addition, three new complexes of solvated lithocene anions and rare solvated dimer structures were obtained from LiCp and Li(MeCp) in THF at low temperature.

For the first time a tetrahedral silver complex was shown to undergo total spontaneous resolution. Attrition-enhanced (Viedma) deracemisation was used to reproducibly produce enantiopure crystal batches.

Three cases of concomitant crystallisation of conglomerate and racemic phases are reported. Polymorphism of chiral and achiral phases is rare and data on such cases are relevant for crystal structure prediction.

Keywords: absolute asymmetric synthesis, enantioselective reactions, chirality, spontaneous resolution, conglomerate, organometallic chemistry, coordination compounds, attrition-enhanced deracemisation, polymorphism, organolithium compounds, single-crystal X-ray crystallography.

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