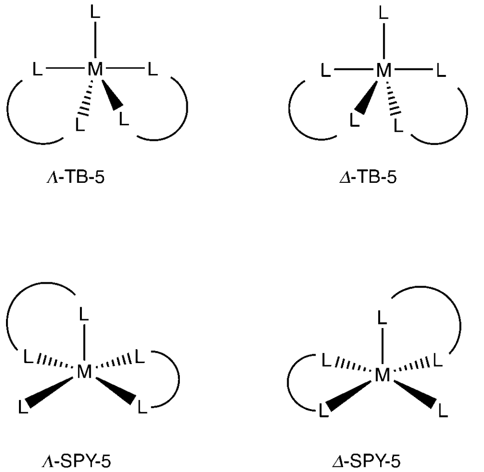
DOI: 10.1002/anie.200902206

Total Spontaneous Resolution of Five-Coordinate Complexes**

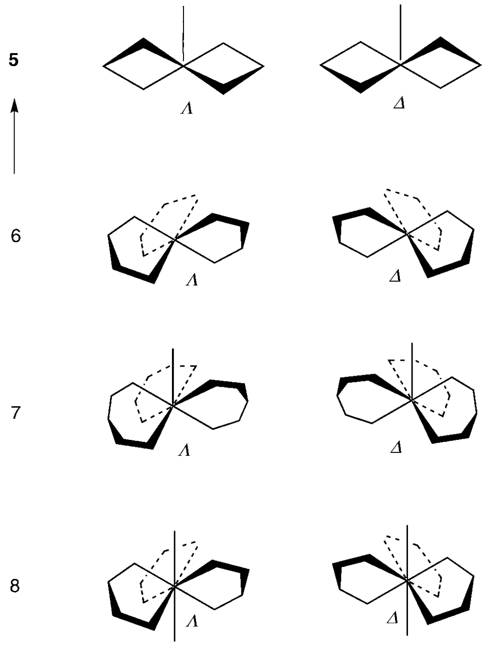
Anders Lennartson and Mikael Håkansson*

Stereoisomerism does generally not occur in five-coordinate complexes with exclusively monodentate ligands owing to rapid interconversion at ambient conditions.[1] Bidentate ligands make five-coordinate complexes more rigid, and both square pyramidal (SPY-5) and trigonal bipyramidal (TB-5) complexes of the $[\mathrm{M}(\widehat{\mathrm{LL}})_2\mathrm{L}]$ type can exhibit chiral configurations.[1] In analogy to the six-coordinate isomers, these should be named Δ and Λ (Scheme 1).



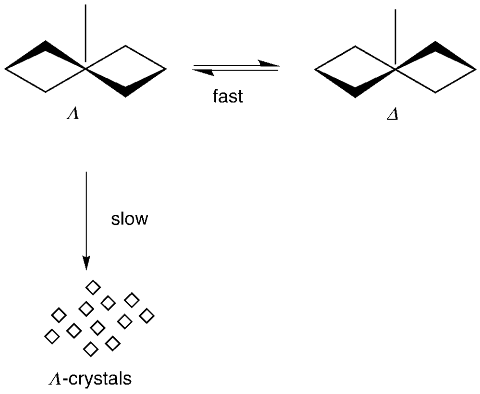
Scheme 1. Chiral configurations for five-coordinate complexes of the $[\mathrm{M}(\widehat{\mathrm{LL}})_2\mathrm{L}]$ type. TB = trigonal bipyramidal, SPY = square pyramidal.

However, the resolution of such enantiomers remains an unanswered challenge. The analogous six-coordinate, octahedral complexes may be substitutionally inert, and Werner reported the first resolution of a six-coordinate complex in 1911.[2] We have reported the synthesis and total spontaneous resolution[3,4] of both seven- and eight-coordinate enantiomers by adding one and two monodentate ligands (Scheme 2), respectively, to a six-coordinate Werner complex of the $[\mathrm{M}(\widehat{\mathrm{LL}})_3]$ type to yield $[\mathrm{M}(\widehat{\mathrm{LL}})_3\mathrm{L}]$ and $[\mathrm{M}(\widehat{\mathrm{LL}})_3\mathrm{L}_2]$ complexes.[5] We now show that the series can be extended in the other direction by replacing one of the bidentate ligands in a $[\mathrm{M}(\widehat{\mathrm{LL}})_3]$ complex with a monodentate ligand. We report the isolation of essentially enantiopure bulk material of five-coordinate enantiomers of the $[\mathrm{M}(\widehat{\mathrm{LL}})_2\mathrm{L}]$ type, namely $[\mathrm{Zn}(\mathrm{S_2CNEt_2})_2\mathrm{L}]$, with the bidentate *N*,*N*-diethyldithiocarbamate ligand. We use total spontaneous resolution (Scheme 3), resulting in high enantiomeric excess (*ee*).



Scheme 2. The resolution of five-coordinate enantiomers presented in this work extends the series of resolved chiral-at-metal complexes. The series now ranges from five- to eight-coordinate complexes.

The stereochemical lability of these five-coordinate complexes, which makes traditional resolution so difficult, has thus been turned into a useful, even instrumental, property. If the crystallization starts without seeding, the overall preparation may be regarded as absolute asymmetric synthesis;[6,7]



Scheme 3. Crystallization-induced asymmetric transformation. The first crystal (obtained from primary nucleation or seeding) determines the handedness of the remaining crystals by secondary nucleation. Both Λ and Δ crystals can be obtained.

---

[*] A. Lennartson, Prof. M. Håkansson
Department of Chemistry, University of Gothenburg
41296 Gothenburg (Sweden)
Fax: (+46) 31-772-3840
E-mail: hson@chem.gu.se

[**] This work was supported by the Swedish Research Council (VR).

that is, the creation of optical activity from achiral (or racemic) precursors without the intervention of molecular optical activity. Absolute asymmetric synthesis and asymmetric autocatalysis[8] are relevant in connection with the origin of biomolecular homochirality.[9]

An additional problem when attempting to resolve stereochemically labile complexes, apart from the actual separation, is that determining the *ee* in a reaction product is non-trivial, as the sample racemizes as soon as it is dissolved. Only solid-state methods are thus viable, and for microcrystalline samples or bulk products, single-crystal analysis, which is normally the most powerful method, is not very helpful. We have, however, recently demonstrated how solid-state circular dichroism (CD) spectroscopy[10] can be used for quantitative determination of *ee* in bulk samples of labile molecules.[4b]

In a quest for new five-coordinate conglomerates,[3] we have synthesized a large number of complexes of the $[\mathrm{M}(\widehat{\mathrm{LL}})_2\mathrm{L}]$ type, using mainly Group 11 or 12 metals with dialkyldithiocarbamates or β-diketonates as bidentate $\widehat{\mathrm{LL}}$ ligands. A wide range of monodentate ligands L, usually containing a nitrogen donor atom, were tested. Most of the complexes gave racemic crystals, but we discovered two cases of spontaneous resolution: $[\mathrm{Zn(S_2CNEt_2)_2(vinim)}]$ (**1**; vinim = 1-vinylimidazole; Figure 1) and $[\mathrm{Cd(S_2CNEt_2)_2(lut)}]$ (**2**; lut = 2,6-lutidine; Figure 2).

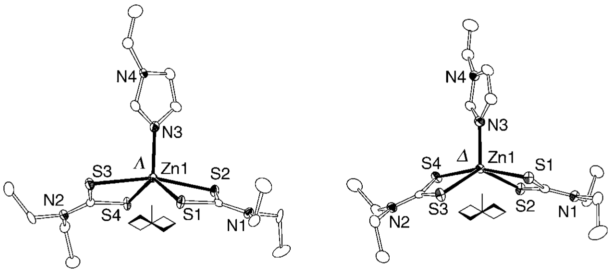


Figure 1. Molecular structures of Λ-$[\mathrm{Zn(S_2CNEt_2)_2(vinim)}]$ (Λ-**1**) and Δ-$[\mathrm{Zn(S_2CNEt_2)_2(vinim)}]$ (Δ-**1**), which can be isolated in separate crystals. Hydrogen atoms omitted for clarity; ellipsoids set at 50 % probability. Selected bond lengths [Å] and angles [°]in Λ-**1**: Zn1–S1 2.6348(7), Zn1–S2 2.3452(7), Zn1–S3 2.3319(6), Zn1–S4 2.5818(6), Zn1–N3 2.036(2); N3-Zn1-S1 99.68(5), N3-Zn1-S2 112.36(5), N3-Zn1-S3 118.18(5), N3-Zn1-S4 97.21(5), S3-Zn1-S1 98.39(2), S3-Zn1-S2 129.46(2), S3-Zn1-S4 73.91(2), S2-Zn1-S1 72.66(2), S2-Zn1-S4 100.28(2), S4-Zn1-S1 163.10(2).

Having designed and synthesized complexes **1** and **2** meant that we now could prepare enantiopure single crystals of five-coordinate complexes by spontaneous resolution. Would it be possible to synthesize entire crystalline batches (i.e. bulk products) comprised of crystals of the same handedness?[11] Such total spontaneous resolution of **1** is indeed possible, as could be proved by the quantitative solid-state CD method.[4a] Microcrystalline samples, which are representative of the bulk product, gave CD spectra (Figure 3) with signals of the same magnitude as signals from enantiopure single crystals, meaning that the bulk product itself was nearly enantiopure. Because the yield was well over 50%, total spontaneous resolution must have occurred, and not merely preferential crystallization of one enantiomer while the other remained in solution. It is noteworthy how readily total spontaneous resolution occurs from solutions of **1**: no stirring[11] or special crystallization conditions are necessary. We suspect that this willingness to undergo total spontaneous resolution is far more common than generally realized.

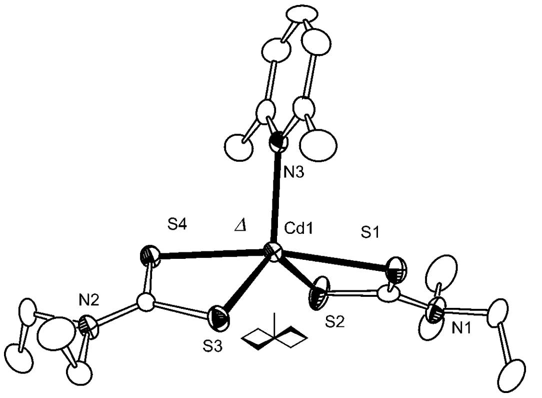


Figure 2. Molecular structure of Δ-$[\mathrm{Cd(S_2CNEt_2)_2(lut)}]$ (Δ-**2**), which exhibits spontaneous resolution (like Λ-**1** and Δ-**1**). The coordination geometry around Cd1 can be described as a distorted trigonal bipyramid with S1 and S4 in axial positions. Hydrogen atoms omitted for clarity; ellipsoids set at 50 % probability. Selected bond lengths [Å] and angles [°]: Cd1–S1 2.6503(8), Cd1–S2 2.5664(8), Cd1–S3 2.5811(8), Cd1–S4 2.6650(8), Cd1–N3 2.345(2); N3-Cd1-S1 95.47(5), N3-Cd1-S2 111.23(6), N3-Cd1-S3 121.85(6), N3-Cd1-S4 95.26(5), S2-Cd1-S1 69.80(2), S2-Cd1-S3 126.91(3), S2-Cd1-S4 106.98(2), S3-Cd1-S1 104.04(2), S3-Cd1-S4 69.25(2), S1-Cd1-S4 169.23(2).

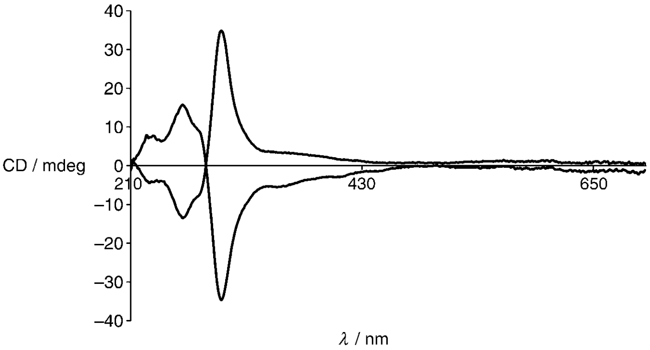


Figure 3. Overlapping solid state CD-spectra of Λ-**1** and Δ-**1**. The Δ-enantiomer exhibits a positive CD-signal around 300 nm.

In conclusion, we have shown how bulk quantities of new types of stereoisomers can be isolated using total spontaneous resolution. The full range of five- to eight-coordinate complexes can now be resolved. The stereochemical outcome can be controlled by seeding with the desired isomer, giving convenient access to either enantiomer in high *ee* and yield.

Experimental Section

All reagents and products are air stable. Commercial reagents were used without further purification. Reflections obtained from a Rigaku

RU/H3R rotating-anode X-ray generator were recorded by a Rigaku R-Axis IIc image-plate system. Solid-state CD spectra were recorded on a Jasco J-175 spectropolarimeter.

$[Zn(S_2CNEt_2)_2(vinim)]$ (**1**): Commercial bis(*N*,*N*-diethyldithiocarbamato)zinc (1.0 g, 2.76 mmol) was gently heated in 1-vinylimidazole (0.8 mL) until complete dissolution occurred. The solution was allowed to cool to ambient temperature, whereupon colorless crystals formed. The mother liquor was removed, and the crystals were washed with hexane (5 × 10 mL) and allowed to air-dry. Yield: 0.88 g (72 %). Powder XRD was used to verify that this bulk material is identical to the crystal-structure material. IR (KBr): $\tilde{\nu} = 3120$(s), 3101(s), 2992(s), 2973(s), 2926(w), 2869(w), 1666(m), 1646(s), 1601(m), 1511(w), 1488(m), 1423(s), 1375(s), 1352(s), 1330(w), 1299(s), 1270(s), 1228(m), 1208(s), 1143(s), 1106(s), 1090(s), 1070(s), 996(s), 962(m), 940(m), 911(s), 844(s), 878(w), 747(s), 660(m), 649(s), 592(m), 567(m), 504(m) cm^{-1}. ^1H NMR($CDCl_3$, 400 MHz): $\delta = 8.18$(s, 1H, $NC\mathit{H}N$), 7.44(s, 1H, Zn-$NC\mathit{H}{=}CHN$), 7.26(s, 1H, Zn-$NCH{=}C\mathit{H}N$), 6.93(dd, 1H, $NC\mathit{H}{=}CH_2$), 5.43(d, 1H, $NCH{=}C\mathit{H}_2$), 5.08(d, 1H, $NCH{=}C\mathit{H}_2$), 3.90(q, 8H, $C\mathit{H}_2CH_3$), 1.32 ppm (t, 12H, $CH_2C\mathit{H}_3$).

$[Cd(S_2CNEt_2)_2(lut)]$ (**2**): Sodium diethylditiocarbamate trihydrate (2.1 g, 10 mmol) was dissolved in water (35 mL) and the solution was filtered. Cadmium chloride (0.91 g, 5 mmol) dissolved in water (20 mL) was added, resulting in a white precipitate. The mixture was filtered, the precipitate washed with water (3 × 15 mL), and allowed to air-dry overnight. The powder was dissolved in boiling 2,6-lutidine (7 mL) and the solution was allowed to cool slowly to ambient temperature, resulting in colorless needles of **2**. The solution was cooled to 0 °C, the mother liquor removed, and the crystals were washed with hexane. Yield: 2.3 g (90 %). Powder XRD was used to verify that this bulk material is identical to the crystal-structure material. IR (KBr): $\tilde{\nu} = 2971$(m), 2930(m), 1597(s), 1575(s), 1494(s), 1455(m), 1422(s), 1371(m), 1350(m), 1293(m), 1270(s), 1203(s), 1141(s), 1093(w), 1075(m), 1063(m), 988(s), 910(s), 841(s), 778(s), 721(w), 602(w), 563(m), 506(w) cm^{-1}. ^1H NMR($CDCl_3$, 400 MHz): $\delta = 7.48$ (t, 1H, *p*-$C\mathit{H}$), 6.97(d, 2H, *m*-$C\mathit{H}$), 3.93(q, 8H, $C\mathit{H}_2CH_3$), 2.55(s, 6H, $CC\mathit{H}_3$), 1.34 ppm (t, 12H, $CH_2C\mathit{H}_3$).

Total spontaneous resolution: In a typical experiment, an entire batch of crystalline **1** (0.105 g), obtained as described above without special precautions or glassware, was carefully ground to a fine powder. To 0.670 mg of the sample, FT-IR grade KBr (1.36099 g) was added in small portions under grinding. From this mixture, 0.12569 g was pressed in to a disc. The CD signal at 297 nm was measured for 20 different disc orientations. The measurements where corrected for different baseline levels (CD at 500 nm was set to 0 mdeg), averaged, and divided by the mass of sample in the disc. A corresponding measurement was performed on a carefully selected single crystal (0.565 mg). The observed CD was 925 $mdeg\,mg^{-1}$ for the single crystal and 813 $mdeg\,mg^{-1}$ for the bulk sample, indicating an enantiomeric excess of approximately 90 %. Correlation between CD spectra and absolute configuration was obtained by single crystal X-ray diffraction analysis followed by a solid state CD analysis on the very same crystal.

Crystal structure data for $ZnS_4N_4C_{15}H_{26}$ (Δ-**1**): crystal size: $0.30 \times 0.20 \times 0.20\ mm^3$, monoclinic, $P2_1$, $a = 8.1345(17)$, $b = 16.270(3)$, $c = 8.2072(17)$ Å, $\beta = 102.124(7)$, $V = 1062.0(4)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.426\ g\,cm^{-3}$, $2\theta_{max} = 54.0°$, $Mo_{K\alpha}$ radiation, $T = 20$ °C, $\mu = 1.555\ mm^{-1}$. Refinement on F^2 for 4007 reflections and 221 parameters gave $R1 = 0.0231$ and $wR2 = 0.0538$ for all data with $-0.29 < \Delta\rho < 0.24$ e Å^{-3}. The absolute structure (Flack) parameter[12] was 0.002(6). $CdS_3N_4C_{17}H_{29}$ (Δ-**2**): crystal size: $0.30 \times 0.25 \times 0.20\ mm^3$, monoclinic, $P2_1$, $a = 10.279(2)$, $b = 9.5297(17)$, $c = 11.832(2)$ Å, $\beta = 103.253(7)$, $V = 1128.1(4)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.519\ g\,cm^{-3}$, $2\theta_{max} = 51.0°$, $Mo_{K\alpha}$ radiation, $T = 20$ °C, $\mu = 1.344\ mm^{-1}$. Refinement on F^2 for 3921 reflections and 226 parameters gave $R1 = 0.0198$ and $wR2 = 0.0486$ for all data with $-0.47 < \Delta\rho < 0.44$ e Å^{-3}. The absolute structure (Flack) parameter[12] was −0.062(16). All non-hydrogen atoms were refined with anisotropic thermal displacement parameters, and the structures were solved and refined using SHELX-97[13] under the WinGX program package.[14a] The figures were drawn using ORTEP3 for Windows.[14b] CCDC 720902 (Δ-**1**), CCDC 720903 (Δ-**2**), and CCDC 720904 (Λ-**1**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Received: April 24, 2009

Keywords: asymmetric synthesis · chiral resolution · circular dichroism · five-coordinate complexes · structure elucidation

---

[1] A. von Zelewsky, Stereochemistry of Coordination Compounds, Wiley, **1996**, pp. 78–101.

[2] A. Werner, *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 1887.

[3] Spontaneous resolution means that the two enantiomers in a racemate crystallize in separate crystals, thus forming a conglomerate. Total spontaneous resolution is possible if the enantiomers racemize in solution during crystallization. See also reference [4].

[4] a) E. L. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds*, Wiley, New York, **1994**, pp. 315–316; b) E. L. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds*, Wiley, New York, **1994**, p. 1207.

[5] a) M. Håkansson, M. Vestergren, B. Gustafsson, G. Hilmersson, *Angew. Chem.* **1999**, *111*, 2336; *Angew. Chem. Int. Ed.* **1999**, *38*, 2199; b) A. Lennartson, M. Vestergren, M. Håkansson, *Chem. Eur. J.* **2005**, *11*, 1757.

[6] a) B. L. Feringa, R. A. Van Delden, *Angew. Chem.* **1999**, *111*, 3624; *Angew. Chem. Int. Ed.* **1999**, *38*, 3418; b) K. Mislow, *Collect. Czech. Chem. Commun.* **2003**, *68*, 849.

[7] a) A. Lennartson, S. Olsson, J. Sundberg, M. Håkansson, *Angew. Chem.* **2009**, *121*, 3183; *Angew. Chem. Int. Ed.* **2009**, *48*, 3137; b) M. Vestergren, J. Eriksson, M. Håkansson, *Chem. Eur. J.* **2003**, *9*, 4678; c) M. Vestergren, B. Gustafsson, O. Davidsson, M. Håkansson, *Angew. Chem.* **2000**, *112*, 3577; *Angew. Chem. Int. Ed.* **2000**, *39*, 3435.

[8] a) K. Soai, I. Sato, T. Shibata, S. Komiya, M. Hayashi, Y. Matsueda, H. Imamura, T. Hayase, H. Morioka, H. Tabira, J. Yamamoto, Y. Kowata, *Tetrahedron: Asymmetry* **2003**, *14*, 185; b) K. Soai, T. Shibata, H. Morioka, K. Choji, *Nature* **1995**, *378*, 767; c) K. Soai, T. Shibata, I. Sato, *Acc. Chem. Res.* **2000**, *33*, 382.

[9] a) A. Saghatelian, Y. Yokobayashi, K. Soltani, M. R. Ghadiri, *Nature* **2001**, *409*, 797; b) G. L. J. A. Rikken, E. Raupach, *Nature* **2000**, *405*, 932; c) M. Avalos, R. Babiano, P. Cintas, J. L. Jimenez, J. C. Palacios, L. D. Barron, *Chem. Rev.* **1998**, *98*, 2391; d) J. S. Siegel, *Nature* **2002**, *419*, 346.

[10] R. Kuroda, T. Honma, *Chirality* **2000**, *12*, 269.

[11] a) D. K. Kondepudi, R. J. Kaufman, N. Singh, *Science* **1990**, *250*, 975; b) D. K. Kondepudi, J. Laudadio, K. Asakura, *J. Am. Chem. Soc.* **1999**, *121*, 1448.

[12] a) H. D. Flack, G. Bernardinelli, *J. Appl. Crystallogr.* **2000**, *33*, 1143; b) H. D. Flack, G. Bernardinelli, *Acta Crystallogr. Sect. A* **1999**, *55*, 908.

[13] G. M. Sheldrick, *Acta Crystallogr. Sect. A* **2008**, *64*, 112.

[14] a) L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837; b) L. J. Farrugia, *J. Appl. Crystallogr.* **1997**, *30*, 565.