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Efficient predetermination of chirality-at-zirconium†

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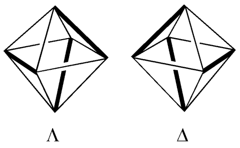
Only one of eight possible diastereomers of the organometallic chiral-at-metal complex [$ZrL_2(CH_2Ph)_2$] (L = a bidentate, chiral non-racemic pyrdine alcoholate) is observed by NMR spectroscopy in the slow exchange regime.

Coordination complexes may contain an element of chirality by virtue of an enantiomeric arrangement of ligands about the metal.[1] It is well known for example that certain tris(chelate) $[M(LL)_3]^{n+}$ complexes of inert metals may be separated into Λ and Δ enantiomers.



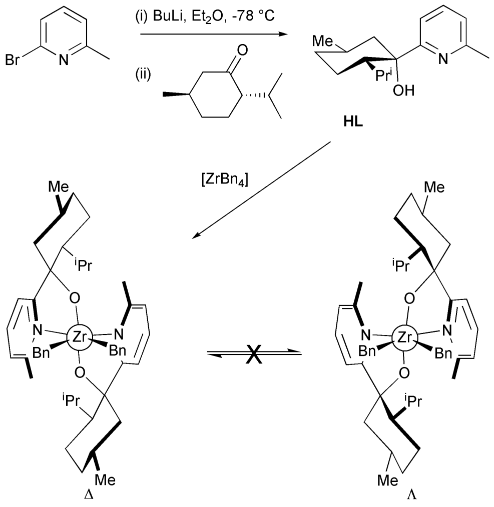
When chiral non-racemic proligands are used, one isomer may be formed preferentially.[2] Excellent diastereoselectivity has been obtained in such processes by von Zelewsky using the Chiragens: multidentate ligands derived from chiral pool sources.[3] With less finely engineered but perhaps more readily accessible proligands, selectivity is frequently far short of ideal.[2] Nevertheless, Brunner, for example, has developed organometallic three-legged piano stool complexes such as [$Ru(\eta^6-C_6H_6)(PPh_3)(ON^*)$] (ON* = a bidentate chiral salicylaldimine) which have very large diastereomer ratios at equilibrium.[4,5]

The above types of complex have potential for application to enantioselective catalysis, not least because the chirality-at-metal should be strongly communicated to prochiral co-ligands.‡ The challenge remains, however, to develop complexes which, by virtue of the presence of one or more catalytically active sites, are inherently suited to this application.[6] We are pursuing a strategy in which complexes with well expressed chiral-at-metal architectures, and most importantly reactive or labile co-ligands, are produced readily from simple chiral-pool ligands.

As part of this programme, the enantiomerically-pure proligand HL was synthesised in high yield by the addition of 2-lithio-6-methylpyridine to (−)-menthone (Scheme 1).[7] The subsequent reaction of two equivalents of HL with [$Zr(CH_2Ph)_4$] gave a single organometallic product [$ZrL_2(CH_2Ph)_2$]. Jordan and coworkers have reported a number of related achiral and racemic pyridine alcoholate complexes.[8,9]

X-Ray crystallography§ revealed the structure Δ-*trans*-,*cis*,*cis*-[$ZrL_2(CH_2Ph)_2$] shown in Fig. 1†¶ and Scheme 1. The geometry about Zr is strongly distorted from octahedral as a result of the ligand bite angles N–Zr–O of *ca.* 70°.

This crystallographically determined structure and the remaining seven possible six-coordinate diastereomers were investigated using DFT calculations.†¶ The minimised structure



Scheme 1 Synthesis of menthone derived ligand HL and the complex [$ZrL_2(CH_2Ph)_2$].

of the Δ-*trans*,*cis*,*cis* isomer (Scheme 1) was essentially superimposable on that observed in the solid state. The Λ-*trans*,*cis*,*cis* diastereomer was found to be *ca.* 36 kJ mol^{-1} less stable than the observed Δ structure. The steric factors responsible for this large energy difference are best appreciated with reference to three-dimensional models of the calculated structures,† but it can be seen from Scheme 1 that in the observed Δ isomer, the mentholyl methyl and *iso*-propyl substituents point into sterically unencumbered regions. In the unstable Λ isomer, the *iso*-propyl groups are necessarily oriented toward the metal at the front of the complex as drawn. The resultant steric compression is partially alleviated by a reduction in the angles between the planes of the 5-membered ligand chelates (*ca.* 120° in the Δ-isomer and 95° in the Λ), but this causes inter-ligand compression in the ″back″ of the complex. Similar steric effects, and no doubt the *trans* influence and other electronic factors, cause the remaining six diaster-

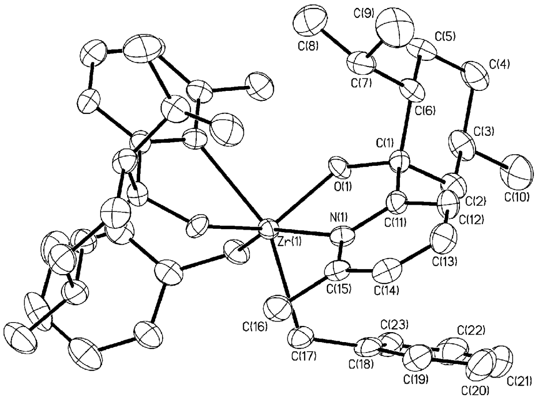


Fig. 1 Molecular structure of Δ-[$ZrL_2(CH_2Ph)_2$].

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† Electronic supplementary information (ESI) available: DFT minimised molecular structures of Δ-[$ZrL_2(CH_2Ph)_2$] (.pdb) and seven further diastereomers. See http://www.rsc.org/suppdata/cc/b2/b205043a/

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eomers to be between 16 and 129 kJ mol^{-1} higher in energy than the observed structure.†

Portions of the variable temperature ^{1}H NMR spectra of a solution of this complex in d$_8$-toluene are shown in Fig. 2. At 273 K a pair of AB doublets centred at *ca*. 2.75 ppm arises from two benzylic CH$_2$ groups in a C_2-symmetric system. The pyridine methyl group resonance is observed at 3.24 ppm. The spectrum corresponds to that of essentially a single diastereomer, which we presume to be Δ-[$\mathrm{ZrL_2(CH_2Ph)_2}$] on the basis of the solid state structure and calculations above. The presence of a small amount of some other species is indicated by a broad resonance at *ca* 2.42 ppm (*vide infra*). Since no major changes were observed in the spectrum below 273 K, we are confident that the system is in the slow exchange regime at these temperatures. Increasing the temperature (313 K) causes broadening of all resonances. By 353 K the spectrum has begun to resharpen with all signals at new (higher field) positions. In the fast exchange regime (above 373 K) the benzyl CH$_2$ resonances appear at *ca*. 2.44 ppm.

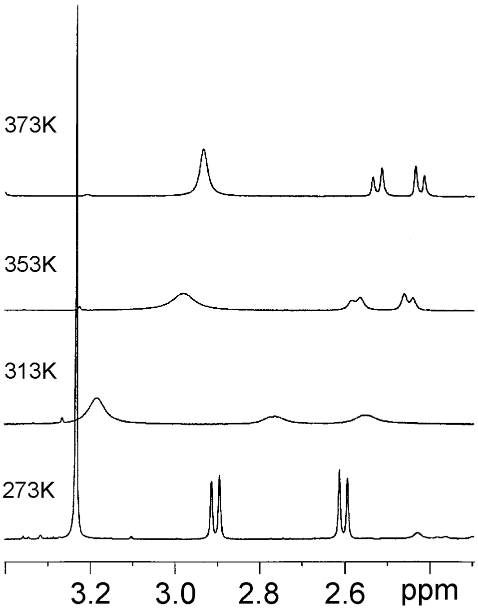

Fig. 2 NMR spectra of [$\mathrm{ZrL_2(CH_2Ph)_2}$].

A topographical exchange mechanism for Δ-[$\mathrm{ZrL_2(CH_2Ph)_2}$] involving an *in situ* twist of the ligands is sterically untenable, and in any event we know from the work of Bickley and Serpone that *N*-dissociation and subsequent Berry pseudorotation is more likely (Fig. 3).[10] Such a mechanism is consistent with the spectra in Fig. 2, most notably in that on increasing the temperature the pyridine methyl group resonance frequency shifts toward that observed for the uncoordinated ligand (2.56 ppm). Also, in the well expressed chiral-at-metal architecture of Δ-*trans*,*cis*,*cis*-[$\mathrm{ZrL_2(CH_2Ph)_2}$] at 273 K, the observed chemical shift difference for the two benzylic hydrogen resonances (*ca*. 0.3 ppm) is rather greater than it is in the fast exchange regime (*ca*. 0.1 ppm), where the diastereotopic appearance results principally from the presence of remote stereogenic centres on the ligands. We speculate that the resonance observed at 2.42 ppm (273 K) may be due to several five-coordinate species in rapid exchange with one-another, but in slow exchange with Δ-[$\mathrm{ZrL_2(CH_2Ph)_2}$] at this temperature.

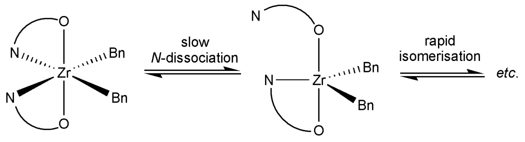

Fig. 3 *N*-dissociative mechanism for topographical exchange in [$\mathrm{ZrL_2(CH_2Ph)_2}$].

The lengthening of one N–Zr bond, as required by this mechanism, necessitates pivoting of the ligand about the cyclic *tert*-alcoholate fulcrum. Models indicate that this will cause severe steric compression between chiral ligands; we believe that this is the origin of the unusually high integrity of the metal-centered chirality in Δ-[$\mathrm{Zr(L)_2(CH_2Ph)_2}$].‖

We are investigating other organometallic systems based on a range of chiral bidentate alkoxido and amido complexes, and are engaged in the application of this readily available type of chiral-at-metal complex to enantioselective catalysis.

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Notes and references

‡ Chiral-at-metal complexes may play a role in several exisiting catalytic reactions, be it by design or otherwise. Noyori and coworkers, for example, have shown that transfer hydrogenation by kinetically labile [Ru(η^6-arene)(chiral-diamine)Cl] occurs *via* diastereomerically-pure chiral-at-metal intermediates, and that this plays an important role in enantioselection.[11]

§ Crystal data: $\mathrm{C_{46}H_{62}N_2O_2Zr}$, M = 766.20, tetragonal, a = 13.5618(2), b = 13.5618(2), c = 22.9202(6) Å, U = 4215.54(14) Å^3 , T = 180(2) K, space group $P4(3)2(1)2$, Z = 4, μ(Mo-Kα) = 0.298 mm^{-1}, 27767 reflections measured, 5390 unique (R_{int} = 0.1428). The final wR_1 was 0.0636 [$I > 2\sigma(I)$]. CCDC reference number 186682. See http://www.rsc.org/suppdata/cc/b2/b205043a/ for crystallographic data in CIF or other electronic format.

¶ All DFT calculations employed the Amsterdam Density Functional (ADF) program version 2000.01. Geometries were optimised in the gas phase at the Local Density Approximation level using a triple-ζ + p STO basis set on Zr (ADF basis IV), double-ζ + polarisation bases on the ligand donor atoms (ADF basis III) and double-ζ bases on all remaining atoms (ADF basis II). Single-point energies were then computed with the Becke88/Perdew86 gradient corrected functional with basis set III for all the non-metal atoms. A 3d frozen core was used for Zr and 1s frozen cores for O, N and C.

‖ Jordan and coworkers found that for a related zircomium benzyl complex based on a racemic acyclic secondary alcohol, the thermodynamic ratio Λ/Δ was *ca*. 3:1 at 183 K, and the coalescence temperature for the benzyl signals was 213 K.[9]

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