Design of a well-defined, silica-supported chiral Zn scaffold for enantioselective catalysis[†]

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New compound $Zn[(S,S)-iPr-pybox](Et)_2$ (1) was fully characterized, including by X-ray diffraction structural studies. Its grafting onto partially dehydroxylated silica affords material 2, which bears well-defined chiral (\equiv SiO)Zn[(S,S)*i*Pr-pybox](Et) sites. Hybrid material 2 displays significantly better catalytic performances than 1 in enantioselective silylcyanation, thus demonstrating a beneficial grafting effect.

Since their early discovery, organozinc compounds and their derivatives have been explored as reagents and catalysts in numerous organometallic and organic transformations.¹ In particular, the chemistry of alkyl–zinc derivatives bearing nitrogen-based bi- or tridentate ligands has recently attracted much attention due to their rich structural chemistry,² and the broad scope of their catalytic applications in fine chemicals synthesis and in polymerization.³

Owing to their accessibility, modular nature, and applicability in a wide range of metal-catalyzed transformations, compounds containing a chiral oxazoline ring have become one of the most versatile and commonly used classes of ligands for (asymmetric) catalysis.⁴ An example is the chiral tridentate 2,6-bis(oxazolinyl)pyridine ligand (pybox), which has proved to be a valuable ligand for a variety of asymmetric reactions.^{5,6}

As heterogenization of catalysts is considered beneficial as it eases products/catalyst separation and recycling,⁷ stereoselective chiral supported catalysts have attracted considerable interest.⁸ Dramatic changes in the catalyst's performances in terms of activity and/or selectivity are often observed. If significant efforts have led to some degree of understanding of these phenomena,^{8c} the impact of grafting on the performances of a given supported catalyst is still difficult to rationalize. Progress in this matter is expected from a better understanding of the structure of the surface active sites, which can be achieved by an approach combining controlled synthesis and thorough characterization. Along these lines, we have designed a hybrid material bearing well-defined, chiral zinc centers, by grafting of a new pybox zinc alkyl complex onto a conveniently treated silica surface. Thorough characterization of this supported catalyst is presented, along with preliminary investigations of the reactivity of these new homogeneous and heterogeneous chiral catalysts in aldehyde silylcyanation.

The 1:1 reaction of the tridentate pro-ligand (S,S)-*i*Pr-pybox with ZnEt₂ in toluene at room temperature cleanly affords the diethyl–zinc complex 1 in 90% yield (Scheme 1). Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a saturated hexane solution at room temperature. The molecular structure as well as selected bond lengths and angles are given in Fig. 1. The solid-state structure of 1 features a monomeric molecule with a five-coordinated zinc center, with the pybox ligand



Scheme 1 Synthesis of 1 and 2.



Fig. 1 Solid-state structure of **1**. Selected bond lengths (Å) and angles (°): Zn(1)-C(1), 2.000(3); Zn(1)-C(3), 2.011(3); Zn(1)-N(1), 2.666(2); Zn(1)-N(2) 2.304(2), Zn(1)-N(3), 2.517(2); C(1)-Zn(1)-C(3), 148.31(12); N(1)-Zn(1)-N(3), 137.69(12).

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coordinating in a tridentate fashion. Overall, the structure of **1** is closely related to that of other zinc pybox complexes.⁹ The geometry at Zn(1) could be described as a trigonal bipyramid with N(1) and N(3) as the axial donors, or as a square pyramid with an apical pyridinic N(2). The latter suggestion is favored by the C(1)– Zn(1)–C(3) angle of 148.31°, which is significantly larger than 120°. Furthermore, the geometric parameter τ defined by Addison and Reedijk is 0.18, which implies that the coordination geometry is best described as a square pyramid.¹⁰ The main distortion of the square pyramid is due to the N(1)–Zn–(1)–N(3) angle of 137.69°, which results from the constraints imposed by the ligand.

Comparison of the Zn–N_{oxazolyne} bond lengths reveals a significant discrepancy, as Zn(1)–N(1) is significantly longer than Zn(1)–N(3) (2.666(2) and 2.517(2) Å, respectively). The existence of diverse oxazolinyl bonding modes is reflected in the IR spectrum of **1**, which features two v(C=N) bands at 1670 and 1640 cm⁻¹, the latter value being close to that of the free proligand (1639 cm⁻¹). These observations may be indicative of some degree of fluxionality in the pybox framework. Indeed, as ¹H and ¹³C NMR spectra of complex **1** in C₆D₆ at room temperature show one set of resonances for equivalent (on the NMR timescale) oxazolinyl and Zn–ethyl groups, lowering the temperature caused decoalescence of the pybox's pyridinyl and methyl signals into two species featuring symmetrical pybox frameworks in a 1 : 8 ratio.¹¹†

As zinc alkyls are highly reactive towards protic reagents, complex 1 is well-suited for immobilization by reaction with a silica surface bearing silanol groups. In order to obtain well-defined grafted species, we chose to use silica dehydroxylated at 800 °C, which only bears isolated silanols and which has successfully been used for this purpose.¹² This would lead to the selective formation of $(\equiv SiO)Zn[(S,S)-iPr-pybox](Et)$, that bears a reactive zinc-ethyl moiety available for catalysis or further reactions, thus opening the way to some degree of active site tuning through substitution with electron-attracting ligands, for instance. Grafting of 1 onto non-porous Degussa Aerosil 380 silica heated under vacuum at 800 °C (SiO₂-800, specific area of 350 m² g⁻¹) in toluene proceeds efficiently to afford after work-up a pale orange powder (2).[†] Fast ethane evolution was detected in NMR scale experiments involving 1 and suspended SiO_2 -800 in C_6D_6 . Elemental analysis shows a zinc weight content of 2.18%, which, when combined with the C,H,N analysis results, indicates the formation of a species featuring the expected stoichiometry (N/Zn = 2.94; C/Zn = 19.45, respective theoretical values, 3 and 19). Infrared spectrum of the material shows full consumption of the silanol groups, as evidenced by the disappearance of the sharp SiO-H peak at 3747 cm⁻¹. Accordingly, new sets of signals indicating the presence of grafted species on the surface are observed, more specifically at 2964–2810 ($v(C(sp^3)-H)$), 1662 (v(C=N) from oxazolinyl ring), 1591 and 1469–1446 cm⁻¹ (aromatic ring vibrations). Interestingly, observation of a single v(C=N) band may indicate that the dynamic process observed for 1 in solution is not operative after immobilization. The slight shift in this band's position compared to those of 1 is indicative of electronic and structural modifications of the chiral Zn-pybox fragment after grafting.

Solid-state NMR studies of **2** have been performed on a highfield NMR spectrometer (18.8 T). ¹H NMR data are in agreement with the expected structure, and closely match those of the molecular precursor $1.\dagger$ Indeed, the pybox ligand gives rise to signals accounting for the aromatic (8.1 ppm), oxazolinic ring (4.2 ppm) and aliphatic protons (1.0 ppm). Furthermore, the intense high-field peak comprises shoulders centered at 1.8 and 0.2 ppm. The former may originate from the *i*Pr groups methynic protons, while the latter is characteristic of $ZnCH_2$ protons. The corresponding groups give rise to signals at 1.70 and 0.67 ppm in 1 in C₆D₆ solution, respectively.

The ¹³C CPMAS NMR spectrum of **2** also confirms the formation of the chiral surface zinc complex (\equiv SiO)Zn[(*S*,*S*)-*i*Pr-pybox](Et).† Noteworthy, the α - and β -carbons of the zinc-ethyl moiety resonate at -1.8 and 9.8 ppm, respectively, in good agreement with the corresponding values for **1**, of 3.29 and 14.72 ppm. The observed shielding is rather surprising considering that a donating alkyl ligand was substituted by an electron-attracting siloxide. The pybox ligand gives rise to the expected signals: most particularly, the O–C=N oxazoline sp² carbon resonates at 160.6 ppm (161.4 ppm in **1**), the oxazoline ring CH₂CH fragments at 72.5 ppm (73.14 and 71.68 ppm in **1**), and the *ortho*-pyridyl carbons at 143.2 ppm (145.85 ppm in **1**).

¹H-¹³C CP HETCOR spectrum was recorded using the PMLG sequence during proton evolution to partially cancel homonuclear dipolar couplings (Fig. 2).¹³ ¹H-¹³C correlations are detected at 0.2/–1.8 ppm and 1.0/9.9 ppm, accounting for the zinc–ethyl fragment's CH₂ and CH₃ groups, respectively. Furthermore, a long-distance ¹H-¹³C correlation appears at 1.0/–1.8 (ZnCH₂– CH₃ coupled pair) due to the non-selective property of the CP transfer. The spectrum also features the expected correlations between the ligand framework's H/C pairs: 4.2/72.5 ppm for the (unresolved) CH₂–CH fragments of the oxazolinyl groups, and 1.3/31.7 ppm and 0.9/17.0 ppm for the isopropyl groups' CH and CH₃, respectively. Aromatic C/H pairs are clearly observed on the correlation spectrum obtained under different CP and decoupling conditions: the pairs 8.4/143.2 ppm and 7.7/123.8 ppm account for the pyridyl *meta* and *para* CH, respectively.†



Fig. 2 Aliphatic region of the ¹H-¹³C CP HETCOR NMR spectrum of **2**. (201.21 MHz, 10 kHz spinning speed, relaxation delay of 5 s; contact time was set to 1.5 msec, at a radio-frequency field of 50 kHz. ¹H decoupling at 85 kHz was applied during the acquisition.) The PMLG decoupling was performed at a RF field strength of 50 kHz.

The enantioselective addition of trimethylsilylcyanide to aldehydes catalyzed by chiral metal complexes is a powerful method for the synthesis of enantiomerically pure cyanohydrins, which are versatile synthens for the preparation of various useful synthetic intermediates.¹⁴ If pybox aluminium complexes have been used for this reaction,¹⁵ cheap and environmentally-benign zinc has attracted little attention and has not met much success in this reaction, leaving room for improvement.¹⁶

The catalytic potential of 1 and 2 in benzaldehyde silylcyanation has been probed. Thus, using optimized conditions, \dagger a 5% loading of 1 converts benzaldehyde into silylated mandelonitrile with 18% enantiomeric excess, with a conversion of 20% in 20 h. In comparison, under the same conditions, heterogeneous catalyst 2 gives rise to a significantly improved enantiomeric excess of 66%, while conversion rises to 40% in 20 h.

Indeed, direct anchoring of the poorly active and selective catalyst **1** proved to be most beneficial, as the catalytic performances of the derived material **2** outpace those of its molecular parent compound. The rise in activity may find its origin in the introduction of an electron-withdrawing siloxide group in the Zn coordination sphere. As described by Fraile and Mayoral,⁸^c the selectivity increase may partly originate from the breakdown in symmetry (from C_2 to C_1) upon immobilization. It is also worth mentioning that immobilization prevents the exchange mechanism observed in solutions of complex **1**, and thus contributes to reduce the number of different, potentially catalytically active species in the reaction medium.

Further efforts will be targeted at the tuning of the metal coordination sphere through exchange of the Zn–Et group by anionic, electron-poor ligands, and in the extension of this methodology to other chiral auxiliaries, in order to develop further examples of silica-derived, zinc-containing hybrid materials for enantioselective catalysis.

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