Enantiospecific synthesis of a planar chiral bidentate indenyl–alkoxide complex of zirconium using an axially chiral indene ligand

Robert W. Baker* and Brian J. Wallace

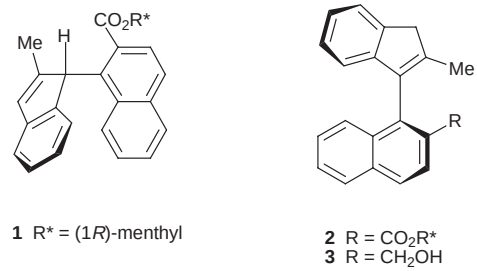
School of Chemistry, The University of Sydney, NSW 2006, Australia. E-mail: r.baker@chem.usyd.edu.au

Received (in Cambridge, UK) 10th May 1999, Accepted 22nd June 1999

The reaction of axially chiral (*M*)-1-(2′-methyl-3′-indenyl)-naphthalene-2-methanol 3 with $Zr(NEt_2)_4$ enantiospecifically provides the planar chiral complex (*P*)-bis(diethylamido)-[1-(2′-methyl-1′-indenyl)naphthalene-2-methoxo]-zirconium 7.

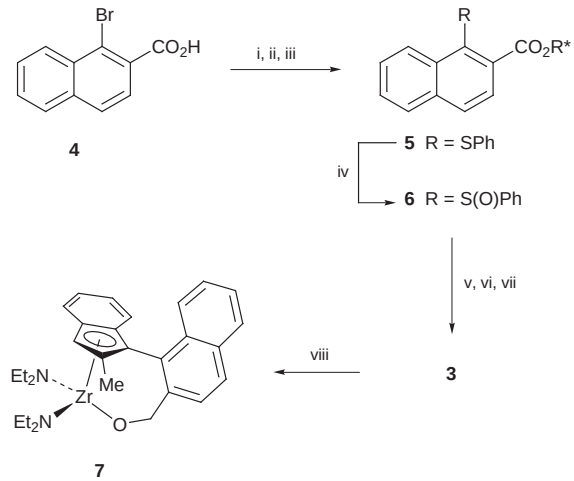
Planar chiral cyclopentadienylmetal complexes feature amongst the more successful stereoselective catalysts. They are usually obtained in enantiomerically pure form through resolution procedures, there being few methodologies allowing asymmetric synthesis. The most common approach[1] designed to avoid resolution utilises cyclopentadienyl ligands containing other stereogenic elements, rendering the faces of the ligand diastereotopic; however, stereoselectivity for the planar chiral element generated during metallation reactions is not guaranteed and separation of diastereoisomers may still be required. An approach extensively employed for 1,2-disubstituted ferrocenes involves the diastereoselective lithiation of complexes containing a chiral *ortho*-directing group.[2] An alternative to this is the enantioselective metallation of ferrocenes with achiral *ortho*-directing groups using a palladium(II) salt with an *N*-protected amino acid,[3] or a chiral lithium amide or an alkyllithium/chiral ligand complex.[2] Two other recently reported methods for the asymmetric synthesis of planar chiral cyclopentadienylmetal complexes are the displacement of chiral auxiliary ligands (L^{ch}) from half-sandwich complexes $Cp^*RuL_2{}^{ch}$ by planar prochiral cyclopentadienylmetals,[4] and the cyclisation of ferrocenyl diazoketones catalysed by chiral rhodium complexes.[5] We have proposed a ligand design whereby a second metal coordination site is constrained to one face of an asymmetrically substituted cyclopentadienyl ring through hindered rotation about the bond between the cyclopentadienyl ring and a naphthalene moiety; formation of chelating complexes using these ligands was anticipated to lead to the enantiospecific generation of a planar chiral cyclopentadienylmetal complex. Towards this objective, we have described approaches to the asymmetric synthesis of precursors to axially chiral chelating fluorene[6,7] and indene[8,9] ligands, employing ligand coupling reactions of sulfoxides. Here we demonstrate the potential of our ligand design with the enantiospecific synthesis of a planar chiral bidentate indenyl–alkoxide complex of zirconium using an axially chiral indene ligand.

We have described previously[9] that the reaction of (1*R*)-menthyl (*R*)-1-(*p*-tolylsulfinyl)naphthalene-2-carboxylate[7] with 2-methylindenyllithium during 30 min at 0 °C provides exclusively the −*ac*-rotamer of (1*R*)-menthyl (*S*)-1-(2′-methyl-1′-indenyl)naphthalene-2-carboxylate **1** in 50% yield and 70% de. The C1–C1′ bond of **1** was shown to be a stable stereogenic element that was conserved during subsequent prototropic shifts to 1-(2′-methyl-3′-indenyl)naphthalenes; thus, treatment of **1** with triethylamine provided **2** in 97% yield and 65% de, while LAH reduction gave **3** in quantitative yield and 70% ee. In order to obtain ligand **3** in enantiomerically pure form, a convenient procedure amenable to operation on a large scale has been developed (Scheme 1). Esterification of 1-bromo-2-naphthoic acid **4** (readily prepared from 2-methylnaphthalene)[10] with (1*R*)-menthol followed by displacement of the bromide with sodium thiophenoxide, furnished the phenylsulfide **5** in 94% overall yield. Oxidation of **5** with dimethyldioxirane, generated *in situ* using OXONE®, provided the sulfoxide **6** as a 58:42 mixture of epimers at sulfur (^{1}H NMR analysis) in 51% yield, accompanied by 46% of recovered **5**.† Reaction of **6** with 2-methylindenyllithium during 40 min at 0 °C furnished **1** and the +*ac*(*R*) isomer of **1**, in a ratio of 44:56, respectively (^{1}H NMR analysis), in 92% combined yield. This mixture was then quantitatively isomerised to a mixture of **2** and the *P*-epimer of **2**, in a ratio of 46:54, respectively,‡ on treatment with triethylamine. Fractional crystallisation, then recrystallisation from hexane solution furnished **2** in > 99% de‡ and 32% yield (maximum theoretical yield 46%). A single-crystal X-ray structure determination on **2**§ establishes the *M* absolute configuration at the chiral axis, which had been previously proposed on the basis of comparisons of CD spectra.[9] The rate of epimerisation of **2** to the *P*-epimer (ultimately affording a 1:1 mixture) has been determined by HPLC analysis in xylenes solution at reflux,‡ providing a barrier to rotation $\Delta G^{\ddagger}_{413}$ = 150.6 kJ mol^{-1}. Reduction of **2** of > 99% de‡ with LAH affords **3** quantitatively with > 99% ee.¶ While the barrier to rotation in **3** has not been determined, it can be anticipated to be higher again than that of **2**.[8]



1 R* = (1*R*)-menthyl

2 R = CO_2R^*
3 R = CH_2OH



Scheme 1 *Reagents and conditions*: i, $SOCl_2$ (15 equiv.), 25 °C, 20 h; ii, (1*R*)-menthol (2 equiv.), pyridine (2 equiv.), CH_2Cl_2, 25 °C, 30 min; iii, PhSNa (1.2 equiv.), DMF, 60 °C, 20 h; iv, OXONE® (3 equiv.), $NaHCO_3$ (5 equiv.), acetone–MeCN–water (20:10:1), 5 °C, 20 h; v, 2-methylindenyllithium (1.3 equiv.), THF, 0 °C, 40 min; vi, NEt_3–toluene (1:1), reflux, 24 h; vii, LAH (5 equiv.), diethyl ether, 25 °C, 1 h; viii, $Zr(NEt_2)_4$ (1 equiv.), toluene, reflux, 16 h.

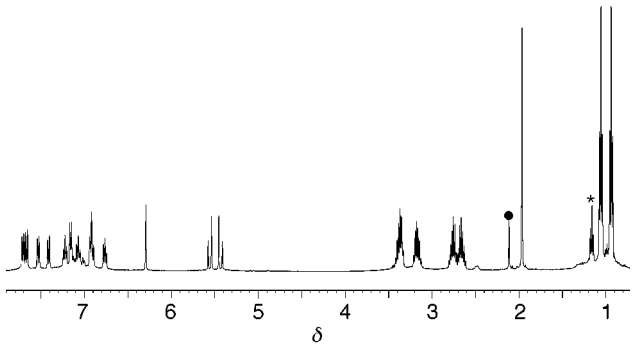


Fig. 1 ^{1}H NMR (400 MHz, C_6D_6) spectrum of complex **7**; unobscured signals of residual toluene and $Zr(NEt_2)_4$ are indicated by • and *, respectively.

With multigram quantities of enantiomerically pure **3** available, we next sought to prepare a bidentate indenyl–alkoxide metal complex[11] in order to demonstrate that the axial chirality of the ligand would indeed translate into planar chirality in the complex without loss of enantiomeric purity.‖ Initial attempts at metallation of **3** through formation of the dilithio species with BuLi, followed by reaction with $ZrCl_4$ in a variety of solvents, failed to produce any of the desired complex. Metallation was readily achieved, however, employing the amine elimination method.[13] Reaction of **3** with 1 equiv. of $Zr(NEt_2)_4$ in toluene solution under reflux for 16 h, followed by removal of the solvent, led to essentially quantitative conversion to the complex **7**,** as evident from inspection of the ^{1}H NMR spectrum of the crude product (Fig. 1).†† In particular, the methylene signal of the indene moiety of **3** (AB pattern centred at δ_H 3.65) is replaced by a singlet at δ_H 6.29 in **7**; the methylene signal of the naphthalenemethanol moiety of **3** (AB pattern centred at δ_H 4.63) is significantly deshielded on formation of **7** (AB pattern centred at δ_H 5.50); and the diastereotopic NEt_2 ligands of **7** appear as two distinct ABX_3 patterns. Consistent with the mononuclear structure proposed for **7**, the high field ^{1}H NMR spectrum of the crude product obtained in the reaction of *rac*-**3** with $Zr(NEt_2)_4$ was identical to that obtained with enantiomerically pure **3**, with additional signals being completely absent. Hydrolysis of complex **7** with dilute HCl solution quantitatively returned ligand **3** with > 99% ee.¶ It follows that complex **7** is also enantiomerically pure and can be assigned *P* absolute configuration (a single descriptor for configuration is used as the atropisomerism of the precursor ligand **3** is considered to be latent in the complex). We are currently examining the expansion of this approach to a wide range of ligands and metal complexes.

Notes and references

† A reaction sequence analogous to that from **4** to **6** was first developed in this laboratory by M. A. Foulkes using the isopropyl esters.

‡ Diastereoisomeric purity was determined by HPLC: a 4.6 × 250 mm column (Zorbax 5 μ silica, Jones) was used with 0.4% ethyl acetate–hexane as eluent at a flow rate of 1.5 ml min^{-1}, detection 254 nm, t_R: 17.4 min for **2** and 20.0 min for the *P*-epimer of **2**.

§ Details of the single-crystal X-ray structure determination of **2** will appear in the full account.

¶ Enantiomeric purity was determined by HPLC: a 4.6 × 250 mm column (Pirkle Type 1A, Regis) was used with 5% propan-2-ol/hexane as eluent at a flow rate of 1.5 ml min^{-1}, detection 254 nm, t_r: 9.5 min for **3** and 10.2 min for *ent*-**3**.

‖ Somewhat related to this work, Pregosin and coworkers[12] have reported that reaction of $Ru(OAc)_2$[(*M*)-6,6′-dimethoxybiphenyl-2,2′-diyl-bis{di(3,5-di-*tert*-butylphenyl)phosphine}] with MeLi affords a planar chiral $RuMe_2$ complex where Ru is coordinated to one phosphine together with an η^6-C_6H_3 moiety from one of the biaryl rings; however, the enantiomeric purity of this complex is not discussed.

** Complex **7** was isolated as an orange viscous oil which, to date, has resisted crystallisation. Consequently, the purity of **7** is dependant on the precision of the stoichiometry of the reaction between **3** and $Zr(NEt_2)_4$, *e.g.* the reaction product shown in Fig. 1 contains *ca.* 5 mol% unreacted $Zr(NEt_2)_4$.

†† *NMR data* for **7**: δ_H (400 MHz, C_6D_6, primed numbers refer to the indenyl moiety) 0.94, 2.65 and 2.74 (10H, ABX_3, *J* 14.0, 6.8, NEt_2), 1.05, 3.17 and 3.38 (10H, ABX_3, *J* 14.0, 6.8, NEt_2), 1.96 (3H, s, 2′-Me), 5.43 and 5.56 (2H, AB, *J* 15.6, CH_2O), 6.29 (1H, s, H-3′), 6.76 (1H, dd, *J* 7.6, 7.6, 6′-H), 6.89–6.94 (2H, m, 5′- and 7′-H), 7.07 (1H, dd, *J* 8.4, 6.8, 7-H), 7.15 (1H, d, *J* 8.4, 3-H), 7.22 (1H, dd, *J* 8.0, 6.8, 6-H), 7.41 (1H, d, *J* 8.4, 8-H), 7.53 (1H, d, *J* 8.4, 4′-H), 7.66 (1H, d, *J* 8.4, 4-H) and 7.71 (1H, d, *J* 8.0, 5-H); δ_C (100 MHz, C_6D_6) 140.3, 134.8, 133.5, 130.9, 128.5 (each C), 128.4, 128.1 (each CH), 127.6 (C), 126.8, 126.6 (each CH), 125.9 (C), 125.6, 125.0, 123.7, 123.5, 123.0, 121.7 (each CH), 110.4 (C), 97.2 (CH), 74.0 (CH_2), 45.02, 44.99 (each 2 × CH_2), 16.2, 15.7 (each 2 × CH_3) and 14.0 (CH_3).

1 R. L. Halterman, *Chem. Rev.*, 1992, **92**, 965 and references cited therein; R. L. Halterman, *Synthesis of Chiral Titanocene and Zirconocene Dichlorides*, in *Metallocenes*, ed. A. Togni and R. L. Halterman, Wiley-VCH, Weinheim, 1998, ch. 8, and references therein.

2 C. J. Richards and A. J. Locke, *Tetrahedron: Asymmetry*, 1998, **9**, 2377 and references therein.

3 V. I. Sokolov, L. L. Troitskaya and O. A. Reutov, *J. Organomet. Chem.*, 1979, **182**, 537.

4 U. Koelle, K. Bücken and U. Englert, *Organometallics*, 1996, **15**, 1376.

5 S. Siegel and H.-G. Schmalz, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2456.

6 R. W. Baker, T. W. Hambley and P. Turner, *J. Chem. Soc., Chem. Commun.*, 1995, 2509.

7 R. W. Baker, M. A. Foulkes and J. A. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1047.

8 R. W. Baker, T. W. Hambley, P. Turner and B. J. Wallace, *Chem. Commun.*, 1996, 2571, (Corrigendum, 1997, 506).

9 R. W. Baker, J. N. H. Reek and B. J. Wallace, *Tetrahedron Lett.*, 1998, **39**, 6573.

10 S. L. Colletti and R. L. Halterman, *Organometallics*, 1991, **10**, 3438.

11 For other examples of bidentate cyclopentadienyl–alkoxide complexes of Group IV metals see: B. Reiger, *J. Organomet. Chem.*, 1991, **420**, C17; Y.-X. Chen, P.-F. Fu, C. L. Stern and T. J. Marks, *Organometallics*, 1997, **16**, 5958; E. E. C. G. Gielens, J. Y. Tiesnitsch, B. Hessen and J. H. Teuben, *Organometallics*, 1998, **17**, 1652; S. D. R. Christie, K. W. Man, R. J. Whitby and A. M. Z. Slawin, *Organometallics*, 1999, **18**, 348.

12 N. Feiken, P. S. Pregosin and G. Trabesinger, *Organometallics*, 1997, **16**, 3735.

13 G. M. Diamond, R. F. Jordan and J. L. Petersen, *J. Am. Chem. Soc.*, 1996, **118**, 8024 and references therein.

Communication 9/03740C