Pergamon

Tetrahedron: Asymmetry Vol. 5, No. 1, pp. 45-48, 1994
Elsevier Science Ltd
Printed in Great Britain
0957-4166/94 $6.00+0.00

0957-4166(93)E0042-U

Enantioselective Catalysis by 1-(1-Isoquinolinyl)-2-naphthalenemethanol: an Atropisomerically Chiral N-O Chelating Ligand

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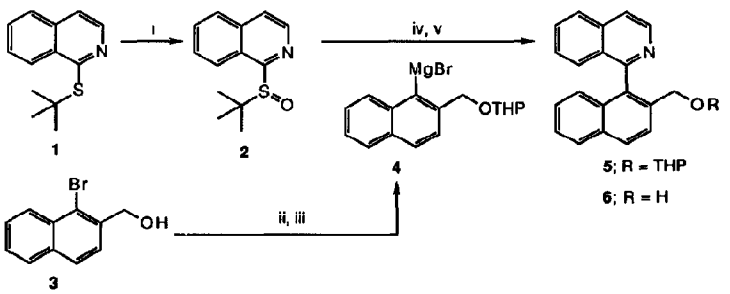
Abstract: Racemic 1-(1-isoquinolinyl)-2-naphthalenemethanol **6** has been prepared through a ligand coupling reaction of racemic 1-(*tert*-butylsulfinyl)isoquinoline **2** with the 1-naphthyl Grignard reagent **4**. Resolution of the ligand **6** was achieved through chromatographic separation of the Noe-lactol® derivatives. The absolute configuration of (*R*)-(-)-**6** was determined by a single crystal X-ray study of the *p*-bromobenzoate derivative **9**. (*R*)-(-)-**6** enantioselectively catalysed the addition of diethylzinc to benzaldehyde, affording (*S*)-(-)-1-phenyl-1-propanol in 68% e.e.

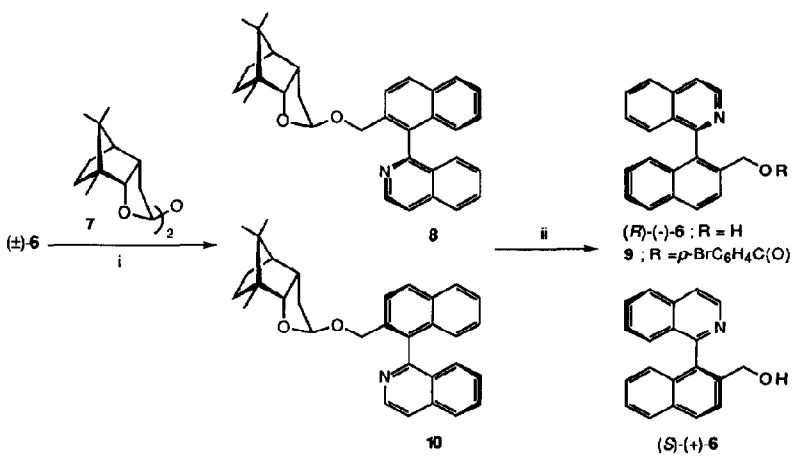
Recently, Alcock *et al.*[2] described the synthesis and resolution of 1-(2-diphenylphosphino-1-naphthyl)isoquinoline, an atropisomerically chiral P-N chelating ligand, which was found to be enantiomerically stable on heating to 65°C for 24h. A related compound, 1-(2-diphenylphosphino-3,6-dimethoxyphenyl)isoquinoline, was found to readily atropisomerise at room temperature.[3] An X-ray crystal structure of a $PdCl_2$ complex of this ligand revealed a Pd-N bond 26° out of the isoquinoline ring plane, this distortion being required to accommodate the constraints of the chelate unit.[3] We were interested in investigating the properties of similar compounds having an additional methylene group within the chelating unit, as molecular modelling suggested that seven-membered chelates involving such compounds should be free from distortion. In this communication, we report the synthesis and resolution of an N-O chelating ligand of this type, and its application in an enantioselective catalytic reaction.

Oae *et al.*[4] have reported that a ligand coupling reaction takes place between 2-(*tert*-butylsulfinyl)pyridine and phenylmagnesium bromide, affording 2-phenylpyridine in 85% yield. This reaction has been successfully adapted to the synthesis of 1-(1-isoquinolinyl)-2-naphthalenemethanol **6** (Scheme 1). Oxidation of 1-(*tert*-butylthio)isoquinoline **1** (prepared from 1-chloroisoquinoline and sodium *tert*-butylthiolate[5]) with *m*-chloroperoxybenzoic acid (*m*-CPBA) furnished 1-(*tert*-butylsulfinyl)isoquinoline **2**[6] in 85% yield. 1-Bromo-2-naphthalenemethanol **3**[7] was protected as the tetrahydropyranyl ether (quantitative yield) and the derived Grignard reagent **4** was prepared in tetrahydrofuran (THF) solution. The sulfoxide **2** was treated with an excess of the Grignard reagent **4** (*ca.* 2 equiv.) in benzene/THF solution at 40-45°C for 48 h, and gave the coupled product **5** in 68% yield. Deprotection then afforded 1-(1-isoquinolinyl)-2-naphthalenemethanol **6** in 93% yield.



Scheme 1. *Reagents and Conditions:* i, *m*-CPBA, CH_2Cl_2, 0°C, 4h; ii, 1.5 equiv. 3,4-dihydro-2*H*-pyran, 0.1 equiv. pyridinium *p*-toluenesulfonate (PPTS), CH_2Cl_2, 25°C, 20 h; iii, Mg, THF, 25°C, 20h; iv, *ca.* 2 equiv. **4**, benzene/THF (2:1), 40-45°C, 48 h; v, 0.6 equiv. PPTS, EtOH, reflux, 4h.

Initial attempts to resolve **6** through fractional crystallisation of the 10-camphorsulfonate or 3-bromocamphor-8-sulfonate salts were unsuccessful. Similarly, the *O*-methylmandelate or camphanate esters were not separable by preparative chromatography or fractional crystallisation. Resolution was finally achieved through the (+)-Noe-lactol® derivatives[8] (Scheme 2). The resulting diastereomers were separable by careful radial chromatography. The earlier eluting fractions, of >99% d.e. by HPLC analysis, consisted of diastereomer **8** {$[\alpha]_D$ +6.5 (*c* 1.33, toluene)}, isolated in 31% yield (based on **7**). Methanolysis of **8** (quantitative yield) gave (*R*)-(-)-**6** in >98% e.e.,[9] $[\alpha]_D$ -325 (*c* 1.44, $CHCl_3$). The *R* absolute configuration was established by a single crystal X-ray diffraction structure determination on the *p*-bromobenzoate



Scheme 2. *Reagents and Conditions:* i, 0.4 equiv. **7**, 1.3 equiv. PPTS, 3A molecular sieves, CH_2Cl_2, reflux, 16h; ii, 1.5 equiv. PPTS, MeOH, 40°C, 24h.

derivative **9**, as depicted in Figure 1.[10] Later eluting fractions, consisting largely of diastereomer **10**, were isolated in 29% yield (based on 7). By HPLC analysis this material was contaminated with 1.5% of **8**. However, methanolysis of **10** (94% yield) gave (*S*)-(+)-**6** in only 90% e.e.,[9] $[\alpha]_D$ +290 (*c* 1.67, $CHCl_3$). The 500 MHz ^1H NMR spectrum of **10** revealed the presence of two additional diastereomers (each present in *ca.* 4%), presumably the β/*endo* anomers of **8** and **10**, which are chromatographically coincident with **10**. Compound **10** was obtained as a gum (as was **8**) and further purification through crystallisation was not possible.

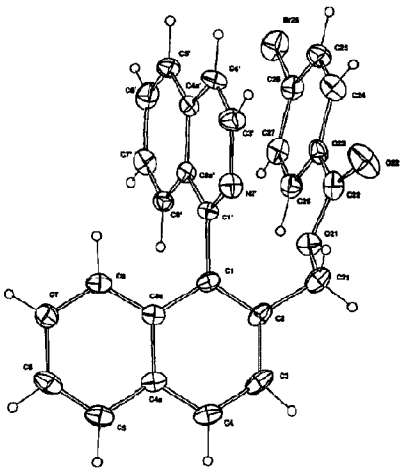


Figure 1. Molecular projection of **9**: 20% thermal ellipsoids are shown for the non-hydrogen atoms; hydrogen atoms have arbitrary radii of 0.1 Å.

Heating the resolved ligand (*R*)-(-)-**6** in benzene solution under reflux for 24 h did not result in any detectable racemisation.[9] The addition of diethylzinc (1.2 equiv.) to benzaldehyde was catalysed by (*R*)-(-)-**6** (0.05 equiv., >98% e.e.,[9] toluene, 25°C, 20 h), providing (*S*)-(-)-1-phenyl-1-propanol in 91% yield and 68% e.e.,[11] $[\alpha]_D$ -32.9 (*c* 5.72, $CHCl_3$). The reaction displayed chiral amplification, typical of amino alcohol promoted alkylation with diorganozincs.[12] Thus, performing the above reaction with (*R*)-(-)-**6** of 53% e.e.,[9] gave (*S*)-(-)-1-phenyl-1-propanol in 53% e.e.,[11] $[\alpha]_D$ -25.5 (*c* 6.54, $CHCl_3$). A proposed transition state for this reaction is depicted in Figure 2. Chelation of Zn with the ligand (*R*)-(-)-**6** leads to the formation of a rigid seven-membered ring. Coordination of Et_2Zn and benzaldehyde occurs from the least hindered face of the chelate ring, opposite the naphthalene nucleus. The addition reaction is illustrated as taking place through a Corey-Hannon type transition state.[13]

We are currently investigating further applications of **6** to asymmetric synthesis and the potential conversion of **6** into additional N-heteroatom ligands through transformation of the hydroxymethyl group. Asymmetric synthesis of **6** through a ligand coupling reaction employing non-racemic **2** is also being explored.[14]

We thank the University of Western Australia for a University Research Fellowship (to R.W.B.), the University of Nijmegen (SNUF) and the Nivard Fund for awards (to E.M.C.S.), and the Australian Research Council for financial support.

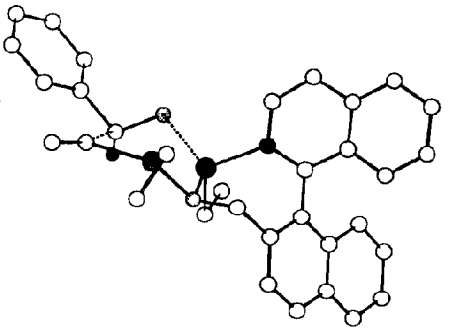
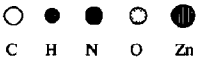


Figure 2. Proposed transition state for the ethylation of benzaldehyde catalysed by (*R*)-(-)-**6**.



References and Notes

1. On leave from the Department of Organic Chemistry, NSR Center for Molecular Structure, Design and Synthesis, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands.
2. N.W. Alcock, J.M. Brown and D.I. Hulmes, *Tetrahedron: Asymmetry*, 1993, **4**, 743.
3. N.W. Alcock, J.M. Brown, M. Pearson and S. Woodward, *Tetrahedron: Asymmetry*, 1992, **3**, 17
4. S. Oae, T. Kawai and N. Furukawa, *Phosphorus and Sulfur*, 1987, **34**, 123.
5. J. Becher and J. Lundsgaard, *Phosphorus and Sulfur*, 1982, **14**, 131.
6. New compounds gave satisfactory elemental analyses or high resolution mass spectral ions and spectra (IR, ^{1}H and ^{13}C NMR) in accord with the assigned structures.
7. S.L. Colletti and R.L. Halterman, *Organometallics*, 1991, **10**, 3438.
8. Noe-lactol® is a registered trademark of Aldrich Chemical Co., Inc.: synthesis, C.R. Noe, *Chem. Ber.*, 1982, **115**, 1576; resolution of chiral alcohols, C.R. Noe, *Chem. Ber.*, 1982, **115**, 1591.
9. Optical purity was estimated by ^{1}H NMR spectroscopy (300 MHz) in the presence of (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol.
10. *Crystal data* for **9**: $C_{27}H_{18}BrNO_2$, M = 468.4, Monoclinic, space group $P2_1$ (No. 4), a = 7.636(8), b = 13.270(3), c = 10.612(2) Å, β = 94.21(5)°. 1970 $hk\pm l$ absorption corrected room temperature diffractometer data ($T \sim 295$K; monochromatic Mo $K\alpha$ radiation, λ = 0.71073 Å, μ_{Mo} = 19.4 cm^{-1}; $A^*_{min,max}$ = 1.27, 1.66), 1380 with $I > 3\sigma(I)$ refining to R, R_w (statistical weights) 0.036, 0.036 (alternative chirality: 0.047, 0.049)(full matrix least squares, anisotropic non-hydrogen atom thermal parameters, (x, y, z, U_{iso})$_H$ constrained estimates), corroborated by independent refinement of $\bar{h}k\pm l$ data. Atomic coordinates, molecular non-hydrogen geometries, thermal parameters and structure factor amplitudes have been deposited at the Cambridge Crystallographic Data Centre.
11. Optical purity was estimated by optical rotation: (*S*)-(-)-1-phenyl-1-propanol, $[\alpha]_D$ -47.6 (*c* 6.11, $CHCl_3$), 98% e.e.; M. Kitamura, S. Suga, K. Kawai and R. Noyori, *J. Am. Chem. Soc.*, 1986, **108**, 6071.
12. R. Noyori and M. Kitamura, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 49.
13. E.J. Corey and F.J. Hannon, *Tetrahedron Lett.*, 1987, **28**, 5237.
14. R.W. Baker, G.R. Pocock and M.V. Sargent, *J. Chem. Soc., Chem. Commun.*, 1993, 1489; R.W. Baker, G.R. Pocock, M.V. Sargent and E. Twiss (née Stanojevic), *Tetrahedron: Asymmetry*, 1993, **4**, 2423.

(*Received in UK* 29 *November* 1993)