SYNLETT Spotlight 9

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Asymmetric phase transfer catalysts derived from the *cinchona* alkaloids

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I received my B.Sc. degree from the University of Salford in 1997 under the supervision of Dr. Andrew T. Russell. My D.Phil studies in synthetic organic chemistry are currently in progress with Professor Sir Jack E. Baldwin at the University of Oxford, and I am involved in synthesising unnatural substrates as mechanistic probes of the penicillin biosynthetic pathway.

Since the first reported use of asymmetric phase transfer catalysts (PTC) derived from the *cinchona* alkaloids in 1989,¹ the present third generation *N*-9-anthracenylmethyl quaternary salts **1** and **2** have been shown to catalyse a number of reactions, affording optically active products with high ee's.^{2,3} The high enantioselectivity of these salts is due to their well-defined geometries, where three of the four tetrahedron faces around the quaternary nitrogen cation are effectively blocked by the other components of the structure, leaving one relatively open face allowing intimate contact with the counterion of the substrate. This complex can then be attacked enantioselectively. Effective mixing of phases during reaction is necessary, but more recently, catalysts **1(b)** and **2(b)** have been success-

fully employed with Schwesinger bases, in homogeneous solution, yielding similar ee's.⁴

Preparation: The *pseudo*-enantiomers **1** and **2** are easily prepared from the corresponding commercially available enantiomers of cinchonine *via* quaternisation with 9-halomethylanthracene.^{2,3} The 2-hydroxymethylquinuclidine core has also been synthesised asymmetrically from pyridine-4-ethanol.⁸

Abstracts

Enantioselective synthesis of cyclic and functionalised α -amino acids has been achieved *via* asymmetric alkylation of a benzophenone-derived glycine-imine **3** mediated by catalysts **1,2(a)**² or **1,2(b)**.⁵ Tertiary butyl ester **4** of (*S*)-pipecolic acid has been prepared in 99% ee using this methodology.⁵ It has more recently been shown that phosphazene bases allow the reaction to be carried out in homogeneous media.⁴

Enantioselective epoxidation of α,β -unsaturated ketone **5** has been achieved with catalyst **1(c)** and sodium hypochlorite as the stoichiometric oxidant to give **6** in 95% yield and 89% ee.⁶

Alkylation of other enolates allows a variety of chiral functionalised molecules to be prepared. The chiral tetrahydropyran **9** has been synthesised *via* asymmetric alkylation with 1-chloro-3-iodopropane of the α,β -unsaturated ester **7** to give **8** in 95% ee.⁷

References

- (1) O'Donnell, M. J.; Bennett, W. D.; Wu, S. *J. Am. Chem. Soc.* **1989**, *111*, 2353-2355.
- (2) Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.* **1997**, *38*, 8595-8598.
- (3) Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414-12415.
- (4) O'Donnell, M. J.; Delgado, F.; Hostettler, C.; Schwesinger, R. *Tetrahedron Lett.* **1998**, *39*, 8775-8778.
- (5) Corey, E. J.; Noe, M. C.; Xu, F. *Tetrahedron Lett.* **1998**, *39*, 5347-5350.
- (6) Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.* **1998**, *39*, 1599-1602.
- (7) Corey, E. J.; Bo, Y.; Busch-Petersen, J. *J. Am. Chem. Soc.* **1998**, *120*, 13000-13001.
- (8) Lygo, B.; Crosby, J.; Lowdon, T.; Wainwright, P. G. *Tetrahedron* **1999**, *55*, 2795-2810.

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