

Enantioselective Synthesis of Chiral 1-Ferrocenyl Alcohol via CBS-Reduction

Wei Yi CHEN, Jun LU*, Ya Wen ZHANG, Zong Xuan SHEN

Department of Chemistry and Chemical Engineering, Suzhou University, Suzhou 215006

Abstract: Reduction of prochiral ferrocenyl ketones **2a-e** in the presence of 10 mol% of chiral β -amino alcohols **4a-b** provides 1-ferrocenyl alcohols **1a-e** in high yields (>85%) with high optical purity (e.e. up to 96%).

Keywords: β -Amino alcohol, chiral, ferrocene, enantioselective synthesis, borane.

In recent years present interest in the synthesis of chiral ligands has directed attention to the preparation of optically active compounds bearing a ferrocenyl or other organometallic group at the alpha carbon atom. The chirality of all the optically active ferrocenes is due to the ferrocene planar chirality. And many chiral phosphines or amines bearing a ferrocene unit have been used as ligands for transition metal catalyzed asymmetric transportations¹. These complexes have been conveniently prepared through the optically active N,N-dimethyl-1-ferrocenylethylamine, which is obtained by optical resolution of the racemic amine². In the synthesis of many chiral ferrocene compounds, lipases have been successfully utilized as catalysts for the kinetic resolution of a racemic mixture of the alcohol or amine. But the process requires a long time to yield the desired chiral ferrocenes, so this method for preparation of these chiral ferrocenes is limited to use^{2,3,4}.

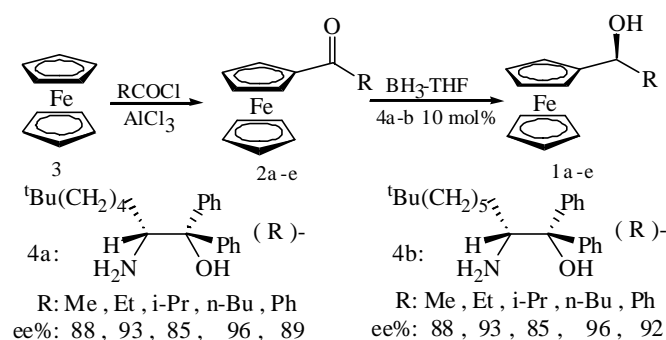
Ferrocene acylation proceeds easily, enantioselective reduction of ferrocenyl ketones is one of the most efficient methods for the preparation of chiral 1-ferrocenyl alcohols, from which many other chiral ferrocene derivatives can be obtained^{5,6}.

In this paper, we report a practical approach to the chiral 1-ferrocenyl alcohols starting from the readily available ferrocenyl ketones using borane reduction in the presence of chiral β -amino alcohols **4a-b**. Prochiral ferrocenyl ketones **2a-e** are easily prepared from Friedel-Crafts reaction with ferrocene **3**. The simultaneous slow addition of BH_3 -THF and a THF solution of the ketone **2** to the catalyst **4** at 0°C provides the desired alcohol **1**. As shown by the data in **Scheme 1**, it can be seen that chiral β -amino alcohols **4a-b** are high efficiency chiral catalysts in borane reduction of prochiral ketones. Under these conditions, ferrocenyl ketones are reduced to the corresponding chiral alcohols, of *S* configuration in each case, in high yields (> 85%) with high optical purity (e.e. up to 96%). Further works on this project, such as the influence of the

* E-mail: organic@suda.edu.cn

structure of catalyst upon its catalytic ability, the relationship of the configuration of the chiral ferrocenyl alcohols with the catalyst, is currently being explored in our lab and all the experimental results will be reported in due course.

Scheme 1



References and Notes

1. C. J. Richards, A. J. Locke, *Tetrahedron: Asymmetry*, **1998**, 9, 2377.
2. D. Marquarding, H. Klusacek, G. Gokel, *J. Am. Chem. Soc.*, **1970**, 92, 5389.
3. G. Nicolo, A. Patti, M. Piattelli, *J. Org. Chem.*, **1994**, 59, 251.
4. N. W. Boaz, *Tetrahedron Lett.*, **1989**, 30, 2061.
5. Y. Matsumoto, A. Ohno, T. Hayashi, *et al.*, *Tetrahedron: Asymmetry*, **1993**, 4, 1763.
6. M. Watanabe, *Tetrahedron Lett.*, **1995**, 36, 8991.
7. **4a**: mp 103-104°C. $[\alpha]_D^{20} +75.6$ (c, 3, CHCl_3). $^1\text{HNMR}$ (DMSO, δ ppm): 0.81 (s, 9H, 3 \times CH₃), 1.03-1.21 (m, 8H, 4 \times CH₂), 3.21 (s, 2H, NH₂), 3.69-3.72 (dd, 1H, J=3.9, 4.1Hz, CH), 5.24 (b, 1H, OH), 7.12-7.60 (m, 10H, 2 \times C₆H₅). Anal. calcd. for C₂₂H₃₁NO: C, 81.18; H, 9.60; N, 4.30. Found: C, 80.82; H, 9.65; N, 4.22.
8. **4b**: mp 100-101°C. $[\alpha]_D^{20} +43.5$ (c, 3, EtOH). $^1\text{HNMR}$ (DMSO, δ ppm): 0.82 (s, 9H, 3 \times CH₃), 1.16-1.40 (m, 10H, 5 \times CH₂), 3.35 (s, 2H, NH₂), 3.71-3.74 (dd, 1H, J=4.3, 4.5Hz, CH), 4.88 (b, 1H, OH), 7.14-7.63 (m, 10H, 2 \times C₆H₅). Anal. calcd. for C₂₃H₃₃NO: C, 81.37; H, 9.80; N, 4.13. Found: C, 81.15; H, 9.80; N, 4.01.

Received 23 April, 2001