Chinese Chemical Letters Vol. 15, No. 2, pp 167 – 168, 2004
http://www.imm.ac.cn/journal/ccl.html

New Chiral Pyridine Prolinol Derivatives and Preliminary Study on Asymmetric Catalytic Reaction

Xiao CHEN[1], Yong Xin ZHANG[1, 2], Da Ming DU[1], Wen Ting HUA[1] *

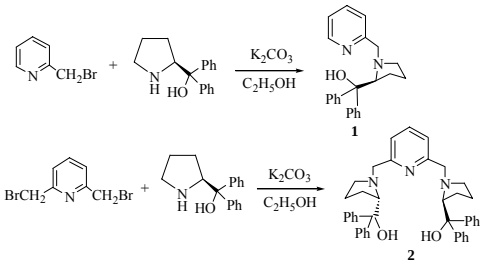
[1]Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871
[2]Shangqiu normal University, Shangqiu 476000

Abstract: Two new chiral pyridine prolinol derivatives have been synthesized from *N*-alkylation of (*S*)-α,α-diphenyl-2-pyrrolidinemethanol with 2-bromomethylpyridine and 2, 6-dibromo-methyl-pyridine. The catalytic asymmetric borane reduction of prochiral ketones and the asymmetric addition of diethylzinc to benzaldehyde were investigated.

Keywords: Prolinol, pyridine, enantioselective reaction, borane.

The enantioselective reduction of prochiral ketones with borane and the addition of diethylzinc to aldehydes in the presence of chiral ligand leading to enantiomerically pure secondary alcohols have received considerable attention in recent years[1,2]. Enantiomerically pure secondary alcohols are important intermediates for the synthesis of various other organic compounds and many new ligands have been prepared for the purpose of more effective catalysts[3,4].

Scheme 1 Synthesis of new pyridine prolinol derivatives **1** and **2**



In this paper, two new chiral pyridine prolinol derivatives **1** and **2** have been synthesized from *N*-alkylation of (*S*)-α, α-diphenyl-2-pyrrolidinemethanol with 2-bromomethylpyridine and 2, 6-dibromomethylpyridine in yields of 75.5% and 80.4% respectively[5].

In order to evaluate the efficiency of these new ligands in the catalyzed asymmetric reaction, we first carried out the enantioselective reduction of ketone with borane.

* E-mail: huawt@pku.edu.cn

When the reaction was carried out at room temperature for 2 h, the reduction of acetophenone by the complex prepared *in situ* from ligands **1** and **2** with borane afforded the corresponding *R*-α-phenylethanol in 62% ee (91% yield)[6] and 8.1% ee (85% yield) respectively. When the reaction was carried out at refluxing temperature for 1 h, the corresponding *R*-α-phenylethanol was obtained in 97% ee (80% yield) and 81% ee (80% yield) respectively. The reduction of β-acetonaphthalene by the complex prepared *in situ* from ligands **1** and **2** with borane afford the corresponding *R*-α-2-naphthylethanol in 98% ee (95% yield) and 80% ee (95% yield) respectively. From above results, we can see higher temperature will enhance the enantioselectivty and pyridine prolinol **1** with one side-arm is more effective than C_2-symmetric ligand **2**.

The enantioselective addition reaction of diethylzinc to benzaldehyde was further investigated. When the reaction was carried out at room temperature for 36 h, the addition of diethylzinc to benzaldehyde catalyzed by ligands **1** and **2** (8% mol) afforded the corresponding *R*-α-phenylethanol in 32% ee (76% yield) and 9.8% ee (62% yield) respectively. Although moderate enantioselectivity was obtained preliminarily, there exists potential to further optimize the enantioselectivity.

Acknowledgment

Project supported by the National Natural Science Foundation of China (Grant No. 20172001).

References and Notes

1. E. J. Corey, C. J. Helal, *Angew*. *Chem*. *Int*. *Ed*. *Engl*., **1998**, *37*, 1986.
2. L. Pu, H. B. Yu, *Chem*. *Rev*., **2001**, *101*, 757.
3. S. Sato, H. Watanabe, M. Asami, *Tetrahedron*: *Asymmetry*, **2000**, *11*, 4329.
4. M. Schinnerl, M. Seitz, A. Kaiser, O. Reiser, *Org. Lett.*, **2001**, *3(26)*, 4259.
m.p. 111-113°C; $[\alpha]_D^{20}$ = -69.0 (c = 0.98, $CHCl_3$), 99% ee; MS (FAB): *m/z* 345 $(M+H)^+$; IR (KBr): ν 3415, 2951, 2864, 1639, 1590, 1442, 1375, 1309, 1188 cm^{-1}; ^{1}HNMR ($CDCl_3$): δ ppm 8.43-8.40 (m, 1H), 7.71-7.54 (m, 5H), 7.33-7.04 (m, 8H), 4.11-4.04 (q, 1H), 3.35 (s, 2H), 2.99-2.95 (m, 1H), 2.54-2.49 (q, 1H), 1.96-1.61 (m, 4H); Anal. Calcd. for $C_{23}H_{24}N_2O$: C, 80.20%; H, 7.02%; N, 8.13%; Found: C, 80.34%; H, 7.13%; N, 8.19%。 **2**. m.p.210-212°C (Dec.); $[\alpha]_D^{20}$ = +45.0 (c = 0.1, CH_2Cl_2), 97.5% ee; MS (FAB): *m/z* 610 $(M+H)^+$; IR (KBr): ν 3344, 3030, 2942, 1589, 1448, 1376, 1300, 1170, 1112 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.67-6.84 (m, 23H), 4.12-4.05 (q, 2H), 3.30 (s, 4H), 2.95-2.90 (q, 2H), 2.54-2.41 (q, 2H), 2.01-1.62 (m, 10H); Anal. Calcd. for $C_{41}H_{43}N_3O_2$: C, 80.75%; H, 7.11%; N, 6.89%; Found: C, 80.91%; H, 7.18%; N, 6.79%。
5. All *ee* values were determined by HPLC with the chiral Diacel OB column.

Received 11 February, 2003