Pergamon

Tetrahedron Letters, Vol. 36, No. 24, pp. 4265-4268, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)00728-8

Asymmetric Catalytic Reduction of *meso*-Imides

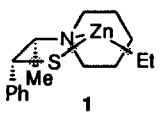
Jahyo Kang*, Jun Won Lee, Joo In Kim and Chongsuh Pyun

Department of Chemistry, Sogang University, Seoul 121-742, Korea

Abstract: A thiazazincolidine complex, **1**, was shown to be an excellent catalyst for enantioselective reduction with bis(2,6-dimethylphenoxy)borane (BDMPB) of *meso N*-phenylimides in high ee to the corresponding hydroxy lactams, which were eventually converted to the corresponding lactones of high optical purity.

Chiralization of *meso* compounds is interesting in that all the compounds are enantioselectively converted without waste to optically active compounds with correct stereochemistry.[1] In this regard, enantioselective reduction of *meso* dicarboxylic acids to the corresponding enantiopure lactones would certainly be one of such targets. Chiral lactones as building blocks for synthesis[2] have been prepared by enzymatic oxidation of *meso* diols.[3] Alternatively, Matsuki reported the enantioselective reduction of *meso* carboxylic acid derivatives which has been achieved by reduction of cyclic *meso* anhydrides and imides with BINAL-H, a stoichiometric reagent.[4] Recently, Speckamp reported an enantioselective reduction of *meso N*-benzyl imides with borane in the presence of an oxazaborolidine catalyst.[5] However, the enantioselectivities were only moderate (60~72%) even with a large amount of the catalyst (50 mol %).

Previously, a thiazazincolidine complex, **1**, prepared *in situ* from (1*R*, 2*S*)-(-)-1-phenyl-2-(1-piperidino)-1-propanethiol and diethylzinc, was shown to be an excellent catalyst for enantioselective addition of dialkylzinc to aldehydes through enantioselective blocking of a specific prochiral face of coordinated aldehyde.[6] Thus, efforts were made to utilize such a enantiodiscriminative coordination of carbonyl groups for enantioselective reduction of cyclic *meso* imides with a reducing agent in the presence of the thiazazincolidine complex **1** as a catalyst.



1

Enantioselective reduction of the *meso N*-alkylimide **2**[7,8] even with excess of the reducing reagents gave the monoreduction product **3**, which was further reduced to the corresponding hydroxy amide with $NaBH_4$ followed by acid-catalyzed lactonization[9] to give the lactone **4** (Scheme 1). Among the various *N*-alkyl groups of the imides examined, it was found that, with [bis(2,6-dimethyphenoxy)borane)],

BDMPB[10], the best *N*-alkyl group was phenyl group: 48% ee (68% yield of lactone **4**: 1*R*, 2*S*) with R = $PhCH_2$, 86% ee (65% yield) with R = Ph, 84% ee (72% yield) with R = 2-MeC_6H_4, 73% ee (50% yield) with R = 2,6-$Me_2C_6H_3$, and 50% ee (64% yield) with R = 2,6-$Cl_2C_6H_3$. Consequently, it was thought that the conformation of the substrates at the transition state was such that the two rings bisected each other (Figure 1), which might facilitate enantioselective coordination of a Lewis acid to a specific enantiotopic carbonyl oxygen.

SCHEME 1

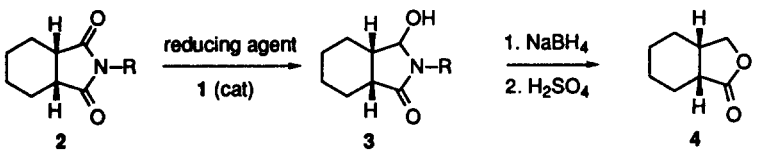
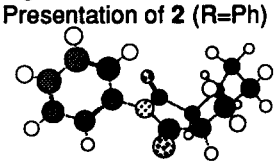


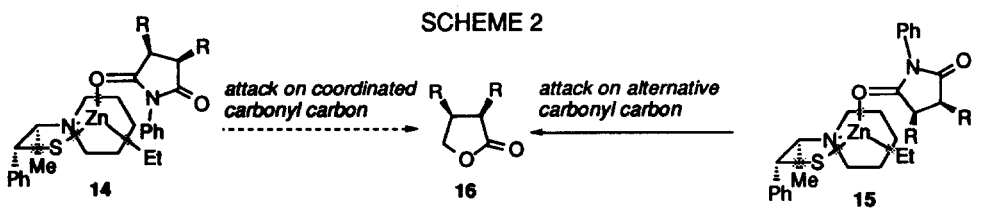
Figure 1. Chem-3D Presentation of **2** (R=Ph)



Among various reducing agents examined such as borane•THF, catechol borane *etc.*, BDMPB, [bis(2,6-dimethylphenoxy)borane)],[10] gave best enantioselectivity with good yields in toluene: 81% ee (72% yield of the lactone **4**) in the presence of 10 mol % of the catalyst **1**; 84% ee (69% yield) in the presence of 20 mol % of the catalyst; 86% ee (77% yield) in the presence of 30 mol % of the catalyst; and 86% ee (65% yield) in the presence of 50 mol % of the catalyst. Thus, while the yields were almost the same with decrease in the amount of the catalyst **1**, enantioselectivity decreased only slightly. Consequently, 20 mole % of catalyst seemed to be appropriate in normal cases without much sacrifice in enantioselectivity. Under this standard condition [BDMPB (2 equiv.), toluene, 20 mol % of **1**], various cyclic *meso* imides[7] were reduced enantioselectively to the corresponding lactones *via* the 3-step sequence shown in Scheme 1.[11] The results are summarized in Table 1.

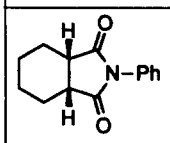
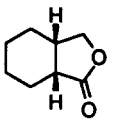
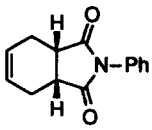
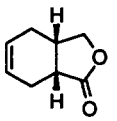
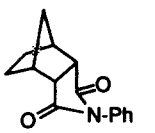
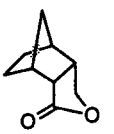
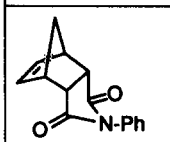
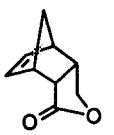
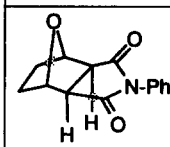
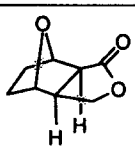
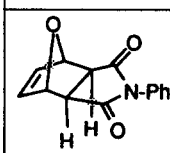
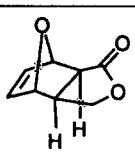
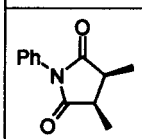
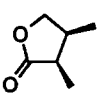
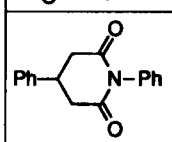
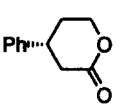
Between the two possible transition states **14** and **15**, the complex **15** with *anti* arrangement of donor (N of imide) and acceptor (Zn) atoms and with the phenyl group stretching away from the sterically congested space must be more stable both electronically and sterically (Scheme 2). Moreover, the bulky nucleophile should attack selectively the indirectly activated carbonyl carbon rather than the directly coordinated carbonyl group, leading to the lactone **16**, even though the latter has been claimed to be more reactive than the alternative carbonyl group in literature.[13]

SCHEME 2



ACKNOWLEDGMENTS: The financial support by OCRC-KOSEF and Korea Research Foundation is gratefully acknowledged.

Table 1. Reduction of *N*-Phenylimides with BDMPB in the Presence of the Catalyst **1**.

Starting Material	Reaction Temp(℃)	Product (Lactone)				
		Structure	Ee[a]	Yield[b]	Config.	Optical Rotation, $[\alpha]^{25}_D$
 (**2**)	-10		84%	69%	(1*R*, 2*S*)	-46.6 (c 0.56, $CHCl_3$)[c]
 (**6**)	-10		96%	72%	(1*R*, 6*S*)	+45.1 (c 1.1, $CHCl_3$)[d]
 (**7**)	-10		95%	61%	(2*R*, 3*S*)	-120.5 (c 0.9, $CHCl_3$)[e]
 (**8**)[f]	-10		82%	69%	(2*R*, 3*S*)	-124.4 (c 5.2, $CHCl_3$)[g]
 (**9**)	0~rt		70%	50%	(2*S*, 3*R*)	-78.5 (c 1.0, $CHCl_3$)[h]
 (**10**)	0~rt		83%	56%	(2*S*, 3*R*)	-128.9 (c 1.0, $CHCl_3$)[i]
 (**11**)	-10		82%	92%	(2*R*, 3*S*)	-33.0 (c 11.0, $CHCl_3$)[j]
 (**12**)	-10		99%	83%	(3*R*)	-3.8 (c 1.0, $CHCl_3$)[k]

[a]By GC with a Chiraldex G-TA chiral column. [b]Isolated yield. [c]Lit. for (1S, 2R) isomer of 100% ee $[\alpha]^{25}_D$ +48.8 (c 0.5, $CHCl_3$).[3c] [d]Lit. for (1*S*, 6*R*) isomer of 100% ee $[\alpha]^{25}_D$ -67.1 (c 1, $CHCl_3$).[3c] [e]Lit. for (2*S*, 3*R*) isomer of >97% ee $[\alpha]^{25}_D$ +123.7 (c 0.84, $CHCl_3$).[3d] [f]With 50 mol % of catalyst 1. [g]Lit. for (2*S*, 3*R*) isomer of >97% ee $[\alpha]^{25}_D$ +143.2 (c 5.2, $CHCl_3$).[3d,h] [h]Lit. for (2*R*, 3*S*) isomer of >98% ee $[\alpha]^{25}_D$ +111 (c 1, $CHCl_3$).[12] [i]Lit. for (2*S*, 3*R*) isomer of >98% ee $[\alpha]^{25}_D$ -153.5 (c 1, $CHCl_3$).[12] [j]Lit. for (2*S*, 3*R*) isomer of 100% ee $[\alpha]^{25}_D$ +39.9 (c 11.3, $CHCl_3$).[3e] [k]Lit. for (3*S*) isomer of 16% ee $[\alpha]^{25}_D$ +0.8 (c 1, $CHCl_3$).[38]

REFERENCES AND NOTES

1. For example, see Seebach, D. Angew. *Chem. Int. Ed. Engl.* **1990**, *29*, 1320.
2. a) Jones, G.; Raphael, R. A.; Wright, S. *J. Chem. Soc., Perkin I,* **1974**, 1676. b) Gerecke, von M.; Zimmerman, J. P.; Aschwanden, W. *Helv. Chim. Acta,* **1970**, *53*, 991. c) Takano, S.; Inomata, K.; Kuntaki, A.; Ohkawa, T.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1987**, 1720. d) Arai, Y.; Kawanami, S.; Koizumi, T. *J. Chem. Soc., Perkin Trans. I,* **1991**, 2969. e) Arai, Y.; Kontani, T.; Koizumi, T. *Tetrahedron; Asymmetry* **1992**, *3*, 535. f) Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367.
3. a) Jakovac, I. J.; Ng, G.; Lok, K. P.; Jones, J. B. *J. Chem. Soc., Chem. Commun.* **1977**, 469. b) Jones J. B.; Lok, K. P. *Can. J. Chem.* **1979**, *57*, 1025. c) Jakovac, I. J.; Goodbrand, H. B.; Lok, K. P.; Jones, J. B. *J. Am. Chem. Soc.* **1982**, *104*, 4659. d) Lok, K. P.; Jakovac, I. J.; Jones, J. B. *J. Am. Chem. Soc.* **1985**, *107*, 2521.
4. a) Matsuki, K.; Inoue, H.; Takeda, M.*Tetrahedron Lett.* **1993**, *34*, 1167. b) Matsuki, K.; Inoue, H.; Ishida, A.; Takeda, M. *Heterocycles*, **1993**, *36*, 937.
5. Romagnoli, R.; Roos, E. C.; Hiemstra, H.; Moolenaar, M. J.; Speckamp, W. N.; Kaptein, B.; Schoemaker, H. E. *Tetrahedron Lett*, **1994**, *35*, 1087.
6. a) Kang, J.; Lee, J. W.; Kim, J. I. *J. Chem. Soc., Chem. Commun.* **1994**, 2009. b) Kang, J.; Kim, D. S.; Kim, J. I. *Synlett*, **1994**, 842. (c) Kang, J.; Kim, J. W.; Lee, J. W.; Kim, D. S.; Kim, J. I., manuscript in preparation.
7. Imides were prepared from the corresponding anhydrides by the method of Cava, M. P.; Deana, A. A.; Muth, K.; Mitchell, M. J. *Org. Syn.* **1975**, Coll. Vol. *4*, 944.
8. Reduction of anhydrides gave moderate ee's with the present technology. J. W. Lee, and J. I. Kim, unpublished results.
9. Mukaiyama, T.; Yamashita, H.; Asami, M. *Chem. Lett.* **1983**, 385.
10. BDMPB can be prepared easily: A stoichiometric mixture of 2,6-dimethylphenol and BMS was stirred until no more hydrogen gas evolved and then the product was directly distilled out (bp 134 ℃/1.5 mmHg). ^{11}B NMR (THF-$CDCl_3$) δ 27.2 (d, $J_{^{11}B\text{-}H}$=149). MS m/e 254(M). BDMPB is stable. The reactivity of BDMPB was very low (aldehyde with $t_{1/2}$ 1.5 h), virtually inert (ketone, alkyne, acid chloride, and sulfoxide) and inert (alkene, ester, epoxide, disulfide, and nitrile) at a concentration of 0.25 M in THF at 23 °C. Park, H. Ph. D. Thesis, Sogang University, **1986**.
11. The procedure for reduction of *N*-Phenylhexahydrophthalimide to the corresponding lactone is representative: To a solution of the *N*-phenyl imide **2** (0.50 g, 2.18 mmol) and the preformed catalyst **1**, prepared by stirring a mixture of (1*R*, 2*S*)-1-phenyl-2-(1-piperidinyl)propan-1-thiol (103 mg, 0.44 mmol) and diethylzinc (1.1 M in toluene, 0.40 mL, 0.44 mmol) in toluene (5 mL) at 0 ℃ for 10 min under nitrogen, was added dropwise BDMPB (1.0 M in toluene, 4.4 mL, 4.4 mmol) -78 °C. The mixture was allowed to warm up to -10 °C and stirred for 5 h. The reaction mixture was quenched with 1 *N* HCl, and extracted with methylene chloride three times. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was chromatographed to give the hydroxy lactam **3**, which was converted to the lactone **4** (212 mg, 69%) by the established method.[9]
12. Bloch, R.; Guibe-Jampel, E.; Girard, C. *Tetrahedron Lett.* **1985**, *26*, 4087.
13. Parish, R. C.; Stock, L. M. *J. Org. Chem.* **1965**, *30*, 927.

(*Received in Japan* 22 *February* 1995; *revised* 5 *April* 1995; *accepted* 12 *April* 1995)