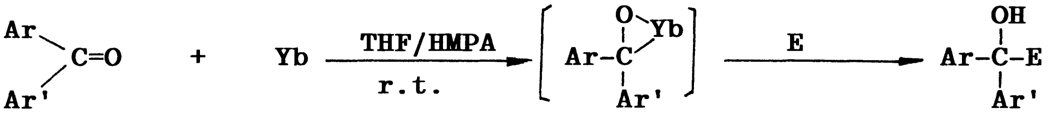
CHEMISTRY LETTERS, pp. 1427-1430, 1990.

Synthesis of Chiral 1,3-Diols from the Reaction of Yb Metal Umpoled Diaryl Ketones with Chiral Epoxides

Ken TAKAKI, Shinji TANAKA, Fumikazu BEPPU,
Yuichiro TSUBAKI, and Yuzo FUJIWARA*
Department of Applied Chemistry, Faculty of Engineering,
Hiroshima University, Saijo, Higashi-Hiroshima 724

The reaction of diaryl ketones such as benzophenone with chiral epoxides in the presence of Yb metal at room temperature has been found to give chiral 1,3-diols in high optical yields.

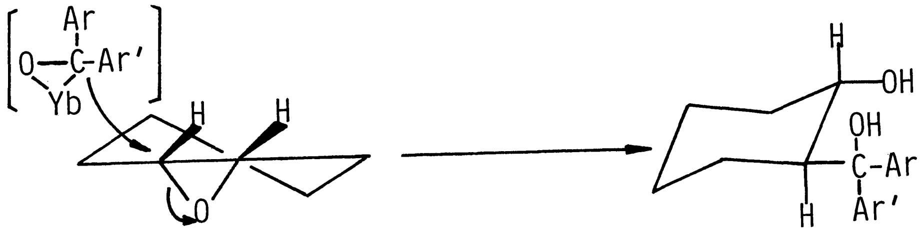
We report here a convenient synthesis of chiral 1,3-diols by the Yb mediated reaction of diaryl ketones with chiral epoxides. Rapid development in application of lanthanoids to organic synthesis has been recently achieved.$^{1)}$ We have found that when treated with 1-2 equiv. of lanthanoid metals, the carbonyl group in diaryl ketones are umpoled from electrophilic to nucleophilic and the reaction intermediate(A) of diaryl ketones and lanthanoid metals can be used as efficient nucleophiles towards a variety of electrophiles to give addition products (Eq. 1).$^{2)}$



A **E:electrophile**

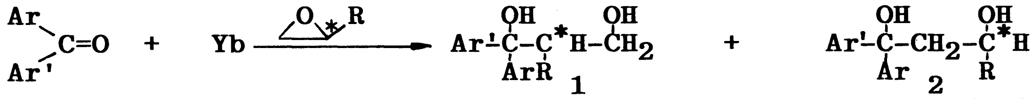
(1)

Since it has been made apparent that intermediate(A) attacks the carbon at the opposite side of oxygen of the epoxide in an SN2 manner in the reaction of intermediate(A) with epoxides,$^{2i,3)}$ chiral 1,3-diols should be obtained if chiral epoxides are allowed to react as an electrophile with diaryl ketones in the presence of Yb metal (Eq. 2).

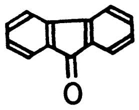
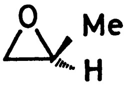
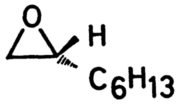
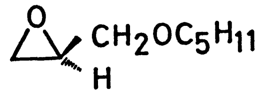
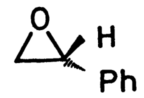
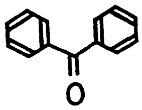
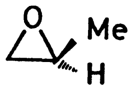
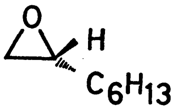
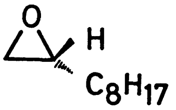
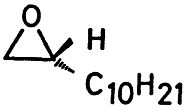
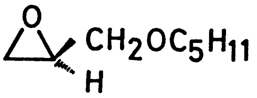
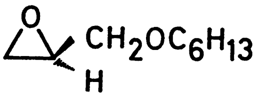
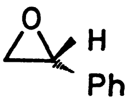


(2)

Table 1. Preparation of Chiral 1,3-Diols from Diaryl Ketones and Chiral Epoxides[a)]



(3)

Educt		Product yield/%[b)]	$[\alpha]_D^{20}$(THF)/° (% ee)		
Ketone	Epoxide	1		2	
		40	-13.5 (99) (c 0.89)	37	-12.5 (90) (c 0.53)
		21	-32.4 (c 0.46)	42	-23.5 (93) (c 0.50)
		10	-4.5	30	+20.5 (c 0.40)
		61	-6.0 (c 0.61)		---
		46	+1.5 (90) (c 0.40)	37	+18.5 (c 0.40)
		24	-1.98 (87) (c 0.59)	50	-4.42 (90) (c 0.52)
		20	-0.90 (c 0.66)	58	+0.96 (c 0.66)
		31	+0.89 (c 0.56)	49	+3.31 (c 0.66)
		23	+14.5 (c 0.39)	62	+6.09 (c 0.67)
		13		57	+7.91 (c 0.68)
		64	+19.3 (67) (c 0.82)		---

---

a) All reactions were carried out using Yb metal (1.0 mmol), ketone (1.0 mmol), and epoxide (1.5 mmol) in THF (4 ml)/HMPA (1 ml) at room temperature for 2-18 h. b) Isolated yields based on Yb.

Thus, the reaction of chiral epoxides with diaryl ketones was carried out at room temperature and the corresponding cross-coupling products, chiral 1,3-diols (**1** and/or **2**) were obtained in good yields.4) Equation 3 and Table 1 summarize the results of the reaction of benzophenone and 9-fluorenone with a variety of chiral epoxides in the presence of Yb metal, to give chiral 1,3-diols (**1** and/or **2**). As shown in Table 1, chiral 1,3-diols are formed in high optical yields.5) For example, reaction of 9-fluorenone with (S)-(-)-propylene oxide gives (-)-1-(9-hydroxy-9-fluorenyl)-1-methyl-2-ethanol(99%ee)5,6) and (-)-1-(9-hydroxy-9-fluorenyl)-2-methyl-2-propanol (90%ee) in 40 and 37% yields, respectively. A mixture of products **1** and **2** derived from attack at both carbon atoms was obtained. In the case of styrene oxide, C-C bond formation occurs predominantly on the more-substituted carbon atom.

Aryl alkyl ketones and dialkyl ketones cannot be used in this reaction because of low stability of the intermediate(A).

The present reaction constitutes the first example of the cross-coupling reaction between ketones and epoxides and should be a good method for synthesis of not only racemic but also chiral 1,3-diols which are important starting materials for synthesis of biologically active macrolides, ionophores, monosaccharides, and various medicines.7)

We thank Professors Koichi Hatada of Osaka University and Yoshio Okamoto of Nagoya University for measurements of optical purity of the products by HPLC using chiral columns. This work was supported in part by a Grant-in-Aid for Scientific Research No. 02231220 from the Ministry of Education, Science, and Culture, Japan.

References

1) H. B. Kagan and J. L. Namy, Tetrahedron, **24**, 6573 (1986) and references therein; W. J. Evans, Polyhedron, **6**, 803 (1987); G. A. Molander and C. Kenny, J. Am. Chem. Soc., **111**, 8236 (1989); T. Imamoto, Yuki Gosei Kagaku Kyokai Shi, **46**, 540 (1988); T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, and Y. Kamiya, J. Am. Chem. Soc., **111**, 4392 (1989); J. Inanaga, Yuki Gosei Kagaku Kyokai Shi, **47**, 200 (1989); M. Murakami, T. Kawano, and Y. Ito, J. Am. Chem. Soc., **112**, 2437 (1990).

2) a) T. Fukagawa, Y. Fujiwara, and H. Taniguchi, Chem. Lett., **1981**, 1771; b) K. Yokoo, Y. Yamanaka, T. Fukagawa, H. Taniguchi, and Y. Fujiwara, ibid., **1983**, 1301; c) Z. Hou, N. Mine, Y. Fujiwara, and H. Taniguchi, J. Chem. Soc., Chem. Commun., **1985**, 1700; d) N. Mine, Y. Fujiwara, and H. Taniguchi, Chem. Lett., **1986**, 357; e) Z. Hou, Y. Fujiwara, T. Jintoku, N. Mine, K. Yokoo, and H. Taniguchi, J. Org. Chem., **52**, 3524 (1987); f) Z. Hou, K. Takamine, Y. Fujiwara, and H. Taniguchi, Chem.

Lett., **1987**, 2061; g) Z. Hou, Y. Fujiwara, and H. Taniguchi, J. Org. Chem., **53**, 3118 (1988); h) Z. Hou, K. Takamine, O. Aoki, H. Shiraishi, Y. Fujiwara, and H. Taniguchi, J. Chem. Soc., Chem. Commun., **1988**, 668; i) Z. Hou, K. Takamine, O. Aoki, H. Shiraishi, Y. Fujiwara, and H. Taniguchi, J. Org. Chem., **53**, 6077 (1988); j) K. Takaki, Y. Tsubaki, S. Tanaka, F. Beppu, and Y. Fujiwara, Chem. Lett., **1990**, 203; k) K. Takaki, F. Beppu, S. Tanaka, Y. Tsubaki, T. Jintoku, and Y. Fujiwara, J. Chem. Soc., Chem. Commun., **1990**, 516.

3) It was further confirmed that reaction of cyclohexene oxide with 2-naphthyl phenyl ketone gives only trans stereoisomer, indicating the back-side attack of the intermediate to the epoxide is operative.
4) A typical reaction was carried out as follows: in a 20-cm^3 flask were placed Yb metal (40 mesh, 1 mmol) and a magnetic stirring bar. The flask was sealed with a serum cap and heated for 30 min by a heat gun under the stream of nitrogen. After cooling, THF (2 cm^3) and HMPA (1 cm^3) were added to the flask by a syringe. Then, MeI (2.5 μl) was added to activate the Yb metal. 9-Fluorenone (1 mmol) in THF (2 cm^3) was then added and the solution immediately turned dark blue. The mixture was stirred for 2 h at room temperature, and then (S)-(-)-propylene oxide (1.5 mmol) was added. The mixture was stirred for 9 h at room temperature. After quenching the reaction with dilute HCl the products were extracted thrice with ether. The combined organic extracts were washed with brine and dried over anhydrous MgSO$_4$. After the solution was evaporated, the products were isolated with medium-pressure liquid chromatography (silica gel) to give (-)-1-(9-hydroxy-9-fluorenyl)-1-methyl-2-ethanol(99%ee)5) and (-)-1-(9-hydroxy-9-fluorenyl)-2-methyl-2-propanol(90%ee) in 40 and 37% yields, respectively which were identified by NMR, IR, mass-spectra, and elemental analysis.
5) Determined by analysis by HPLC using a chiral cellulose tris(3,5-dimethylphenylcarbamate) column.
6) Although X-ray structural analysis of this compounds confirmed the structure, the determination of the absolute configuration (R or S) failed because of lack of heavy atoms in the molecule.
7) S. G. Wilkinson, "Comprehensive Organic Chemistry," ed by D. Barton and W. D. Ollis, Pergamon, New York (1979), Vol. 1, p.662.

(Received May 28, 1990)