Pergamon

Tetrahedron Letters, Vol. 35, No. 46, pp. 8625-8626, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01813-8

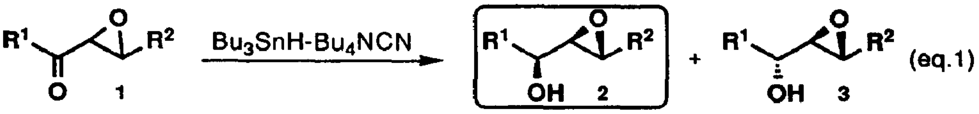
Novel Synthesis of *syn*-α,β-Epoxy Alcohols by Diastereoselective Carbonyl Reduction of α,β-Epoxy Ketones

Takayo Kawakami, Ikuya Shibata,* Akio Baba, Haruo Matsuda,† and Noboru Sonoda

Department of Applied Chemistry, Faculty of Engineering,
Osaka University, 2-1 Yamadaoka, Suita, Osaka 565, Japan.

Abstracts: A novel tin hydride reagent, Bu_3SnH-Bu_4NCN, reduced α,β-epoxy ketones to the corresponding *syn*-α,β-epoxy alcohols in high diastereoselectivities.

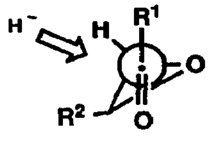
The stereoselective synthesis of α,β-epoxy alcohols is a serious subject of investigations. The most obvious methods of providing *syn*- and *anti*-α,β-epoxy alcohols are the diastereoselective oxidation of allylic alcohols[1] and the diastereoselective carbonyl reduction of α,β-epoxy ketones.[2,3] In particular, the latter method brings to our attention the control of both diastereo- and chemoselectivity, because in which the cleavage of oxirane rings often intervenes. The stereoselective synthesis of *anti*-α,β-epoxy alcohols by the carbonyl reduction of α,β-epoxy ketones is achieved by many groups.[2] In contrast, only a scattering of literatures exist concerning the *syn*-selective reduction[3] because of the disturbance by coordinative effects of the epoxy-oxygen. In this paper, we report a valuable reagent, Bu_3SnH-Bu_4NCN, for the preparation of *syn*-α,β-epoxy alcohols from α,β-epoxy ketones (eq.1).



(eq.1)

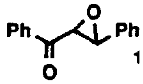
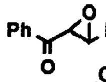
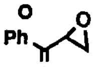
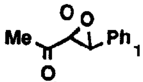
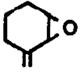
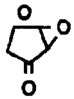
As can be seen from the data in Table 1, Bu_3SnH alone exhibited no reduction activity (entry 1). The addition of HMPA gave higher yields of α,β-epoxy alcohols, **2a** and **3a**, although the ratio of *syn* isomer **2a** was only moderate (entry 2). Instead of HMPA, either of Bu_4NCl and Bu_4NF increased significantly the yields and *syn*-selectivities (entries 3 and 4). Furthermore, tetrabutylammonium cyanide (Bu_4NCN) was found to be the most effective, providing superior *syn*-selectivities (entry 5). Other ammonium salts such as $[Bu_4N]^+[Ph_3SnF_2]^-$,[4] Bu_4NBF_4 and Bu_4NSCN did not have such activity as compared with Bu_4NCN. The dependency of the diastereoselectivity on the donors presented is clearly illustrated. As shown in Scheme 1, the *syn*-selective carbonyl reduction is explained in terms of the Felkin-Ahn model (A).[5] In particular, Bu_3SnH tightly coordinated by an anion like CN^- would react according to the Felkin model more effectively than the other donors. This reduction system, Bu_3SnH-Bu_4NCN, could be applied to various α,β-epoxy ketones **1**. High *syn*-selectivities were exhibited in the case of aromatic ketones, **1b** and **1c** (entries 6 and 7), methyl ketone **1d** (entry 8), and cyclic ones, **1e** and **1f** (entries 9 and 10), whereas in the reduction of **1e** a marginal *syn*-selectivity was

Scheme 1



A

Table 1. *syn*-Selective Carbonyl Reduction of α,β-Epoxy Ketones[a]

Entry	α,β-Epoxy ketone (1)	Tin Hydride	Conditions	Yield (%)	2 : 3
1	 1a	Bu_3SnH	rt, 24 h	trace	–
2		Bu_3SnH–HMPA	rt, 8 h	25	52 : 48[b]
3		Bu_3SnH–Bu_4NCl	0°C, 1 h	69	80 : 20[b]
4		Bu_3SnH–Bu_4NF	0°C, 10 min	80	83 : 17[b]
5	 1b	Bu_3SnH–Bu_4NCN	-78°C ~ -15°C, 10 min	85	87 : 13[b]
6		"	-78°C ~ -15°C, 1 h	90	95 : 5[b]
7	 1c	"	-78°C ~ -15°C, 1 h	37[d]	100 : 0[b]
8	 1d	"	-78°C ~ rt, 4 h	44[d]	78 : 22[b]
9	 1e	"	-78°C ~ rt, 2.5 h	99	82 : 18[c]
10	 1f	"	-78°C ~ rt, 2.5 h	100	100 : 0[c]

[a] α,β-Epoxy ketone (1) 1 mmol, Tin hydride system 1 mmol, THF 1 mL. [b] Determined by ^1H NMR. [c] Determined by GLC. [d] Unreacted starting materials were recovered.

reported with $NaBH_4$.[2a,b,d] Furthermore, in all of these reactions, no by-products derived from the reduction of epoxide ring were detected at all.

Acknowledgment. This work was supported by the JSPS Fellowships for Japanese Junior Scientists and the Grant-in-Aid for Scientific Research on Priority Area of Reactive Organometallics No.05236102 from the Ministry of Education, Science and Culture. Thanks are due to Mrs. Y. Miyaji and Mr. H. Moriguchi, Faculty of Engineering, Osaka University, for assistance in obtaining NMR and HRMS spectra.

References and Note

† Present address: Department of Applied Chemistry, Osaka Institute of Technology, 5-16-1 Omiya, Asahi, Osaka 535, Japan.

1. (a)Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.*,**1973**, *95*, 6136. (b) Tanaka, S.; Yamamoto, H.; Nozaki, H. Sharpless, K. B.; Michaelson, R. C.; Cutting, J. D. *J. Am. Chem. Soc.*,**1974**, *96*, 5254. (c) Mihelich, E. D.*Tetrahedron Lett.*, **1979**, *49*, 4729. (d) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.*, **1979**, *49*, 4733. (e) Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.*, **1980**, *21*, 1657. (f) Tomioka, H.; Suzuki, T.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.*, **1982**, *33*, 3387. (g) Hiyama, T.; Obayashi, M. *Tetrahedron Lett.*, **1983**, *24*, 395.
2. (a) Pierre, J. L.; Chautemps, P. *Tetrahedron Lett.*, **1972**, *42*, 4371. (b) Chautemps, P.; Pierre, J. L. *Tetrahedron*, **1976**, *32*, 549. (c) Weissenberg, M.; Glotter, E. *J. Chem. Soc. PerkinI*, **1978**, 568. (d) Rücker, G.; Hörster, H.; Gajewski, W. *Syn. Commun.*, **1980**, 623. (e) Nakata, T.; Tanaka, T.; Oishi, T. *Tetrahedron Lett.*, **1981**, *22*, 4723. (f) Banfi, S.; Colonna, S.; Molinari, H. *Syn. Commun.*, **1983**, 901. (g) Castaing, M.D.; Rahm, A. *J. Org. Chem.*, **1986**, *51*, 1672. (h) Fujii, H.; Oshima, K.; Utimoto, K. *Chem. Lett.*, **1992**, 967. (i) Kawakami, T.; Shibata, I.; Baba, A.; Matsuda, H. *J. Org.Chem.*, **1993**, *58*, 7608.
3. (a) Fujita, M.; Hiyama, T. *J. Org. Chem.*, **1988**, *53*, 5405. (b) Aoyama, Y.; Urabe, H.; Sato, F. *Tetrahedron Lett.*, **1991**, *32*, 6731.
4. Gingras, M. *Tetrahedron Lett.*, **1991**, *32*, 7381.
5. Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.*, **1968**, *18*, 2199.

(*Received in Japan* 14 *May* 1994; *accepted* 29 *July* 1994)