

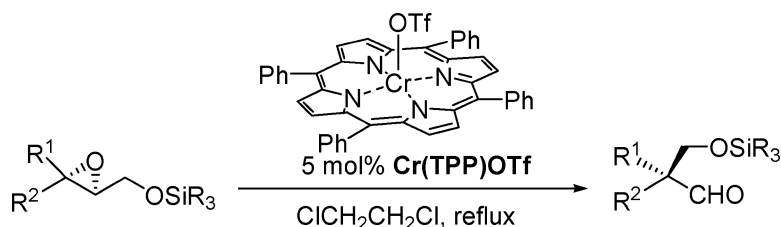
Communication

Highly Regio- and Stereoselective Rearrangement of Epoxides to Aldehydes Catalyzed by High-Valent Metalloporphyrin Complex, Cr(TPP)OTf

Kohji Suda, Taketoshi Kikkawa, Shin-ichiro Nakajima, and Toshikatsu Takanami

J. Am. Chem. Soc., **2004**, 126 (31), 9554-9555 • DOI: 10.1021/ja047104k • Publication Date (Web): 20 July 2004

Downloaded from <http://pubs.acs.org> on April 1, 2009



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 2 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

[View the Full Text HTML](#)

Highly Regio- and Stereoselective Rearrangement of Epoxides to Aldehydes Catalyzed by High-Valent Metalloporphyrin Complex, Cr(TPP)OTf

Kohji Suda,* Taketoshi Kikkawa, Shin-ichiro Nakajima, and Toshikatsu Takanami

Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose, Tokyo 204-8588, Japan

Received May 17, 2004; E-mail: suda@my-pharm.ac.jp

Lewis acid-promoted rearrangement of epoxides into carbonyl compounds is among the most synthetically useful and important functionalization reactions of organic compounds. The rearrangement has widely been applied to the synthesis of various biologically active natural products with unique structural properties,^{1,5} but it is well-known that the yield and regio- and stereoselectivity of these rearrangements markedly vary with the mode of substituents on the ring and the reaction conditions.² Hence, the control of regio- and stereochemistry of the rearrangements still remains an important and fundamental puzzle to be solved in epoxide chemistry.

As illustrated in Scheme 1, the rearrangement of substituted epoxides **1**, in principle, proceeds from a cleavage of the C_β–O bond followed by hydrogen migration (route A) or alkyl (R¹) migration (route B), leading to the corresponding ketones **2** or aldehydes **3**, respectively. Although considerable efforts have recently been made for the development of efficient reagents and catalysts which allow access to ketones **2**,^{3,7a} for the rearrangement to aldehydes **3**, a bulky organoaluminum reagent, methylaluminum bis(4-bromo-2,6-di-*tert*-butyl-phenoxide) (MABR), is still the sole reagent available for this purpose.⁴ MABR is, unfortunately, a reagent rather than a catalyst: more than a stoichiometric amount of the reagent is usually necessary to promote the rearrangement.⁶

We report herein a highly regio- and stereoselective rearrangement of epoxides **1** to aldehydes **3** with a porphyrin-based Lewis acid catalyst, chromium(III) tetraphenylporphyrin triflate, Cr(TPP)-OTf, in low catalyst loading (1–20 mol %) under very mild conditions.^{7,8} This Cr(TPP)OTf-catalyzed reaction is especially appropriate for the synthesis of optically active β-siloxy aldehydes, useful intermediates in natural product synthesis, from 2,3-epoxy silyl ethers which are readily available in enantiomerically enriched forms by the Sharpless epoxidation of allylic alcohols⁹ followed by silylation.^{10,11}

Reaction conditions and regioselectivity for the porphyrin-based catalytic rearrangement of epoxides were investigated with *trans*-2-(*tert*-butyldimethylsiloxy)methyl-3-phenyloxirane, **1a**, as a model substrate in a variety of solvents with a series of high-valent metalloporphyrin catalysts, such as Fe(TPP)ClO₄, Mn(TPP)ClO₄, and Cr(TPP)ClO₄. The representative results are shown in Table 1. As reported previously, an Fe(TPP)ClO₄–dioxane catalyst system exclusively promoted the hydrogen migration of **1a** to give ketone **2a** in a quantitative yield (entry 1).^{7a} On the other hand, the use of Cr(TPP)ClO₄ (1 mol %) in dichloroethane at 83 °C preferentially brought about the alkyl migration of **1a**, affording 87% yield of the desired aldehyde **3a** along with the ketone **2a** in 11% yield (entry 4). Changing the catalyst from Cr(TPP)ClO₄ to Cr(TPP)-OTf further improved the reactivity and regioselectivity of the rearrangement, providing aldehyde **3a** as the sole isolable product in 97% yield under the optimal conditions (entry 5). Attempts for the rearrangement of **1a** with other Lewis acid catalysts, such as B(C₆F₅)₃¹² and chromium and manganese salen complexes,¹³ which have been known to catalyze ring-opening reactions of epoxides,

Scheme 1

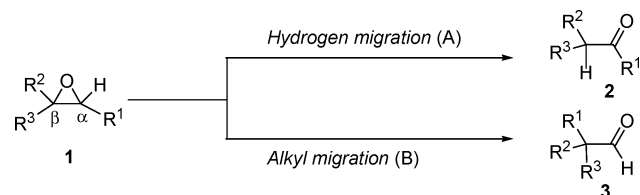


Table 1. Screening of Metalloporphyrin Catalysts and Solvents for the Rearrangement of Epoxides to Aldehydes

The reaction scheme shows the conversion of epoxide **1a** (with a phenyl group and a *tert*-butyldimethylsiloxy group) to ketone **2a** and aldehyde **3a** using a metalloporphyrin catalyst M(TPP)X. The structure of the metalloporphyrin catalyst is shown as a central metal M coordinated to four nitrogen atoms in a porphyrin ring, with phenyl groups at the meso positions and a substituent X at the central metal position.

entry	catalyst (mol %)/solvents/temp.(°C)/time (h)	yield (%) ^a	
		2a	3a
1	Fe(TPP)ClO ₄ (1)/dioxane/100/0.5	>99	0
2	Fe(TPP)ClO ₄ (1)/Cl(CH ₂) ₂ Cl/83/0.5	65	32
3	Mn(TPP)ClO ₄ (1)/Cl(CH ₂) ₂ Cl/83/1	53	45
4	Cr(TPP)ClO ₄ (1)/Cl(CH ₂) ₂ Cl/83/2	11	87
5	Cr(TPP)OTf (1)/Cl(CH ₂) ₂ Cl/83/1	0	97 ^b
6	B(C ₆ F ₅) ₃ (2)/Cl(CH ₂) ₂ Cl/83/40	14	15
7	B(C ₆ F ₅) ₃ (2)/toluene/110/40	no reaction	
8	Cr(salen)OTf (2)/Cl(CH ₂) ₂ Cl/83/40 ^c	16	40
9	Mn(salen)OTf (2)/Cl(CH ₂) ₂ Cl/83/22 ^d	33	34

^a Isolated yield. ^b A trace amount (<2%) of ketone **2a** could be detected in the ¹H NMR spectrum of the crude reaction mixture. ^c Cr(salen)OTf: (S,S)-(+)-N,N'-bis(3,5-di-*tert*-butylsilyl)idene)-1,2-cyclohexanediamino chromium(III) triflate. ^d Mn(salen)OTf: (S,S)-(+)-N,N'-bis(3,5-di-*tert*-butylsilyl)idene)-1,2-cyclohexanediamino manganese(III) triflate.

were, however, unsuccessful under the reaction conditions examined (entries 6–9). The Cr(TPP)OTf-catalyzed rearrangement in dichloroethane can also be applied successfully to a variety of epoxides such as trialkyl-substituted epoxides, spiroepoxides, and bicyclic epoxides (Table 2, entries 1–4), furnishing the corresponding aldehydes in good yields.

We next explored the stereoselectivity of the Cr(TPP)OTf–dichloroethane catalyst system with various optically active epoxy silyl ethers (Table 2, entries 5–10). As a whole, a facile and highly stereoselective migration of the alkyl groups to give the corresponding aldehydes was observed. Optically pure phenyl-substituted epoxy silyl ethers **1b–1d** were converted to the corresponding optically active β-siloxy aldehydes **3b–3d** as the sole isolable products in high yields via highly stereoselective anti migration of the siloxymethyl groups to the C_β of the oxirane moieties. Likewise, stereoselective migration of the siloxymethyl groups took place in the rearrangement of epoxy geraniol and nerol derivatives, **1e** and **1f**, the same aldehyde **3e** being obtained in high yields without any loss of optical purity.

Table 2. Cr(TPP)OTf-Catalyzed Rearrangement of Epoxides to Aldehydes^a

entry	epoxide	time, h	product	yield, % ^b
1		4		89
2		24		63 ^c
3		45		56 ^d
4		1		> 99
5		1		97
	1b (> 99% ee)		3b (> 99% ee)	
6		1		96
	1c (> 99% ee)		3c (> 99% ee)	
7		1		> 99
	1d (96% ee)		3d (96% ee)	
8		5		89
	1e (> 99% ee)		3e (> 99% ee)	
9		6		92
	1f (93% ee)		3e (93% ee)	
10		30		85 ^e
	1g (> 99% ee)		3g (97% ee)	

^a Reaction conditions: 1 mol % Cr(TPP)OTf, CICH₂CH₂Cl, 83 °C; enantiomeric excess was determined by chiral HPLC analysis or 300 MHz ¹H NMR Mosher's ester analysis; The absolute configuration was determined by comparison of the optical rotations with those of authentic samples.^{4b,5c} ^b Isolated yield. ^c Recovery of the starting epoxide, 22%. ^d Recovery of the starting epoxide, 28%. ^e 20 mol % Cr(TPP)OTf was used.

An α,β -disubstituted epoxy alcohol derivative **1g** was also susceptible toward the rearrangement, though an increase of catalyst loading (20 mol %) and a longer reaction time were required to complete the reaction. In this case, the relatively bulky isopropyl group was selectively transferred onto the α -carbon, affording optically active β -siloxy aldehyde **3g**, a key intermediate for the synthesis of L-type calcium channel blockers such as emopamil,^{5c} in 85% yield with minimal racemization.¹⁴

In summary, catalytic and regio- and stereoselective rearrangement of epoxides **1** to aldehydes **3** via alkyl migration (route B in Scheme 1) can now be realized using a high-valent metalloporphyrin complex, Cr(TPP)OTf, in low catalyst loading (1–20 mol %). The yield and regio- and stereoselectivity of the catalytic process are generally good to high and almost fully comparable to those of the corresponding reactions done stoichiometrically in MABR.⁴ This Cr(TPP)OTf-catalyzed reaction is, in combination with the Sharpless epoxidation of allylic alcohols, especially appropriate for the synthesis of optically active β -siloxy aldehydes from 2,3-epoxy silyl ethers. Moreover, the present catalytic method complements our

previously reported Fe(TPP)X (X = OTf or ClO₄)-catalyzed isomerization of epoxides **1** into ketones **2** via hydrogen migration (route A in Scheme 1):^{7a} ketones **2** and aldehydes **3** can selectively be prepared from epoxides **1** in a highly controlled manner by means of a simple choice of Fe(III) and Cr(III) central metal ions of the porphyrin catalysts. Elucidation of the precise mechanism for the present rearrangement and other uses of the Cr(TPP)OTf catalyst in synthetic chemistry are now under active investigation.

Acknowledgment. We thank the Japan Society for the Promotion of Science for financial support, a Grant-in-Aid for Scientific Research (C) (KAKENHI 16590020).

Supporting Information Available: Experimental details, characterization data, NMR spectra, and HPLC traces. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) For a review and some recent examples: (a) Silva, L. F., Jr. *Tetrahedron* **2002**, *58*, 9137–9161. (b) Kita, Y.; Higuchi, K.; Yoshida, Y.; Iio, K.; Kitagaki, S.; Uede, K.; Akai, S.; Fujioka, H. *J. Am. Chem. Soc.* **2001**, *123*, 3214–3222. (c) Grellepois, F.; Chorki, F.; Crousse, B.; Ourévitich, M.; Bonnet-Delpon, D.; Bégue, J. P. *J. Org. Chem.* **2002**, *67*, 1253–1260. (d) Kita, Y.; Futayama, J.; Ohba, Y.; Sawama, Y.; Ganesh, J. K.; Fujioka, H. *J. Org. Chem.* **2003**, *68*, 5917–5924.
- (2) For a review: Rickborn, B. In *Comprehensive Organic Synthesis, Carbon-Carbon σ -Bond Formation*; Patterden, G., Ed.; Pergamon: Oxford, 1991; Vol. 3, Chapter 3.3, pp 733–775.
- (3) (a) Pd(0) catalyst: Kulasegaram, S.; Kulawiec, R. *J. Org. Chem.* **1994**, *59*, 7195–7196. (b) LiClO₄: Sudha, R.; Narashimhan, K. M.; Saraswathy, V. G.; Sankararaman, S. *J. Org. Chem.* **1996**, *61*, 1877–1879. (c) InCl₃: Ranu, B. C.; Jana, U. *J. Org. Chem.* **1998**, *63*, 8212–8216. (d) Bi(OClO₂): Anderson, A. M.; Blazek, J. M.; Garg, P.; Payne, B. J.; Mohan, R. S. *Tetrahedron Lett.* **2000**, *41*, 1527–1530. (e) VO(OEt)Cl₂: Martínez, F.; Campo, C.; Llama, E. F. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1749–1751. (f) SbF₅: see ref 4d.
- (4) (a) Maruoka, K.; Ooi, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1989**, *111*, 6431–6432. (b) Maruoka, K.; Ooi, T.; Nagahara, S.; Yamamoto, H. *Tetrahedron* **1991**, *47*, 6983–6998. (c) Maruoka, K.; Ooi, T.; Yamamoto, H. *Tetrahedron* **1992**, *48*, 3303–3312. (d) Maruoka, K.; Murase, N.; Bureau, R.; Ooi, T.; Yamamoto, H. *Tetrahedron* **1994**, *50*, 3663–3672. (e) Maruoka, K. In *Lewis Acid Reagents*; Yamamoto, H., Ed.; Oxford: New York, 1999; Chapter 2, pp 5–29.
- (5) Applications of MABR-mediated rearrangement of epoxides to natural product synthesis: (a) Bando, T.; Shishido, K. *Chem. Commun.* **1996**, 1357–1358. (b) Matsushita, M.; Maeda, H.; Kodama, M. *Tetrahedron Lett.* **1998**, *39*, 3749–3752. (c) Kimura, T.; Yamamoto, N.; Suzuki, Y.; Kawano, K.; Norimine, Y.; Ito, K.; Nagato, S.; Iimura, Y.; Yonaga, M. *J. Org. Chem.* **2002**, *67*, 6228–6231.
- (6) This requirement sometimes imposes several practical limitations on this valuable reagent, including the need for special workup techniques (see refs 4b and 4e).
- (7) We have previously reported that high-valent metalloporphyrin complexes, such as Fe(TPP)OTf and Fe(TPP)ClO₄, work as useful Lewis acid catalysts for the rearrangement of epoxides to carbonyl compounds: (a) Takanami, T.; Hirabe, R.; Ueno, M.; Hino, F.; Suda, K. *Chem. Lett.* **1996**, 1031–1032. (b) Suda, K.; Baba, K.; Nakajima, S.; Takanami, T. *Tetrahedron Lett.* **1999**, *40*, 7243–7246. (c) Suda, K.; Baba, K.; Nakajima, S.; Takanami, T. *Chem. Commun.* **2002**, 2570–2571.
- (8) Several synthetically useful metalloporphyrin-catalyzed reactions have recently been reported: (a) Chen, Y.; Huang, L.; Zhang, X. P. *Org. Lett.* **2003**, 2493–2496. (b) Li, G.-Y.; Che, C.-M. *Org. Lett.* **2004**, *6*, 1621–1623.
- (9) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974–5976.
- (10) Oshima et al. reported a related rearrangement of 2,3-epoxy alcohols induced by *gem*-dizinc reagents: Matsubara, S.; Yamamoto, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 2837–2840.
- (11) Jung et al. reported R₃SiOTf- and BF₃-mediated stereoselective rearrangements of epoxides: (a) Jung, M. E.; D'Amico, D. C. *J. Am. Chem. Soc.* **1993**, *115*, 12208–12209. (b) Jung, M. E.; Anderson, K. L. *Tetrahedron Lett.* **1997**, *38*, 2605–2608.
- (12) Ishihara, K.; Hanaki, N.; Yamamoto, Y. *Synlett.* **1995**, 721–722.
- (13) Martínez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897–5898.
- (14) Kimura et al. have reported that MAD, methyl aluminum bis(4-methyl-2,6-di-*tert*-butylphenoxide), can induce the rearrangement of epoxide **1g** to aldehyde **3g** (see ref 5c).

JA047104K