Pergamon

Tetrahedron Letters 42 (2001) 8333–8336

TETRAHEDRON LETTERS

Mechanistic consideration of Ti(salen)-catalyzed asymmetric sulfoxidation

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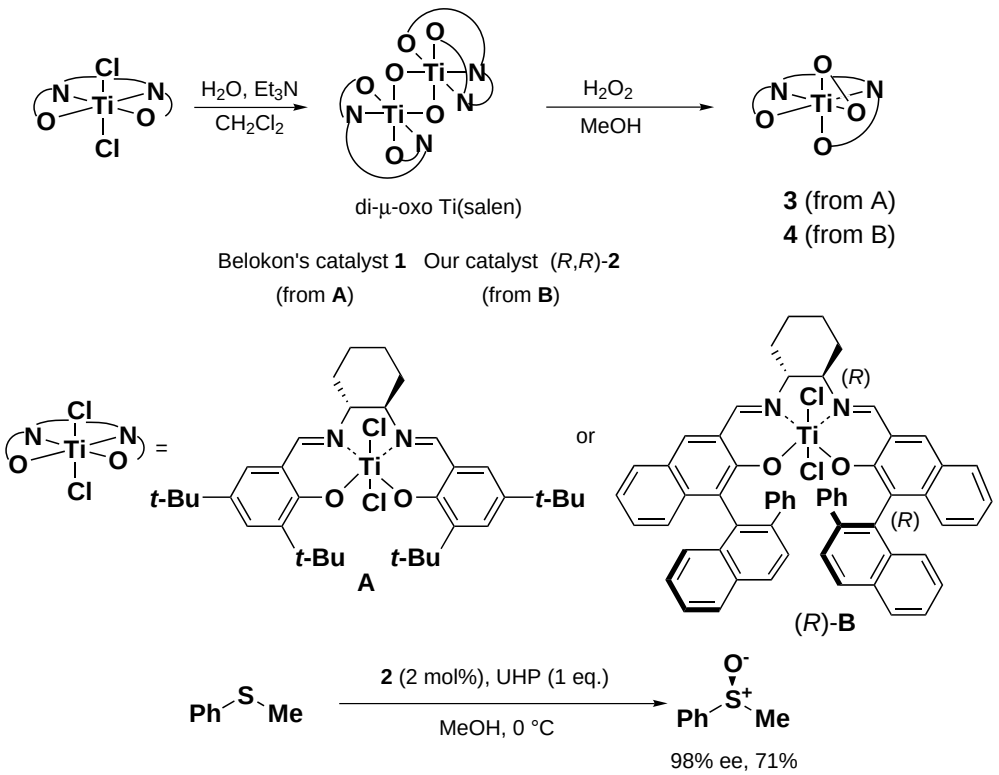
Received 15 August 2001; revised 17 September 2001; accepted 21 September 2001

Abstract—Asymmetric sulfoxidation using di-μ-oxo Ti(salen) complex **2** as the catalyst was revealed to proceed through C_2-symmetric Ti(salen) complex **6** and peroxo Ti(salen) complex **4** in sequence on the basis of MS and NMR studies of the complexes and the observation of positive non-linear effect.

We recently reported a highly enantioselective sulfoxidation using di-μ-oxo Ti(salen) complex **2** in methanol as the catalyst.[1,2] The di-μ-oxo Ti(salen) complex was originally synthesized by Belokon' et al. and successfully used as the catalyst for asymmetric silyl cyanation.[3] The ligand of the di-μ-oxo Ti(salen) complex **1** has been



Scheme 1.

Keywords: asymmetric catalysis; Ti(salen); di-μ-oxo Ti(salen); sulfoxidation; *cis*-β structure; non-linear effect.

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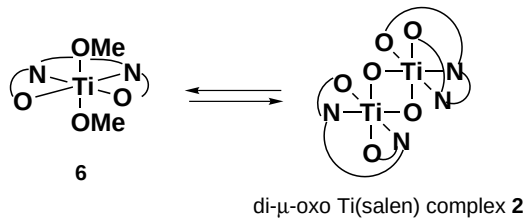
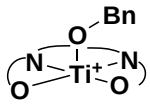
0040-4039/01/$ - see front matter
PII: S0040-4039(01)01789-0

determined to adopt a *cis*-β structure by its X-ray diffraction analysis and the corresponding μ-oxo Ti(salen) species has been proposed to be the real active catalyst for the silyl cyanation.[3a] In its methanolic solution, however, we expected that the di-μ-oxo Ti(salen) complex would be rapidly transformed to a monomeric Ti(salen) species of *cis*-β structure through rapid alkoxide exchange and that hydrogen peroxide or the urea hydrogen peroxide adduct (UHP) would react with the monomeric species to give the corresponding peroxo species (**3** and **4**) which might serve as a good catalyst for asymmetric sulfoxidation. Indeed, high enantioselectivity was realized in the sulfoxidation with complex **2** as the catalyst[1] (Scheme 1). In order to verify this mechanistic proposal for the sulfoxidation, we performed a spectrometrical study of the catalyst and examined the linearity or non-linearity in the relationship between enantiomeric excesses of the catalyst and of the sulfoxide.



Scheme 2.

We first examined FABMS of di-μ-oxo Ti(salen) complex **2** using 2-nitrophenyl octyl ether and *m*-nitrobenzyl alcohol as the matrix. The parent peak (HRFABMS, found: $m/z=1776.5669$, calcd for $[C_{120}H_{88}N_4O_6Ti_2]^+$: $m/z=1776.5663$) of **2** was detected in the analysis using 2-nitrophenyl octyl ether as the matrix, while the analysis with *m*-nitrobenzyl alcohol as the matrix showed the peak (FABMS, $[C_{67}H_{51}N_2O_3Ti_1]^+$: $m/z=1024.3$) corresponding to cationic monomeric Ti(salen) species **5**, suggesting that conversion of the di-μ-oxo Ti(salen) complex to a monomeric Ti(salen) complex in an alcoholic solvent occurs smoothly.



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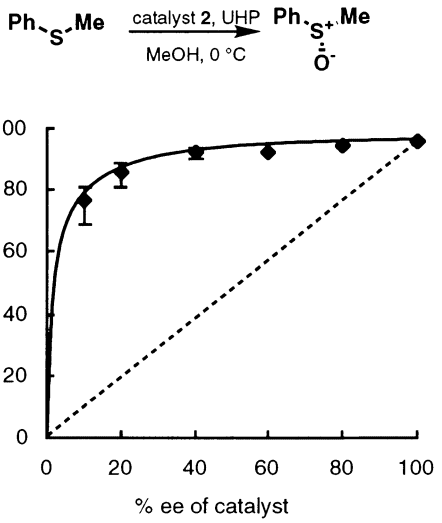
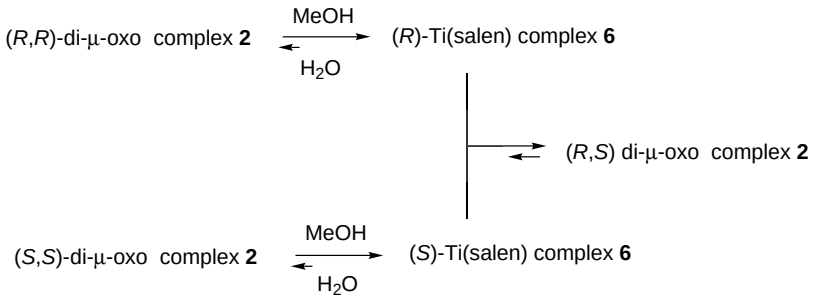


Figure 1.

We next performed NMR measurement of complex **2** in chloroform-*d*. As expected from the *cis*-β structure of **2** which possesses a C_2-symmetric axis, its ^1H NMR (400 MHz) measurement showed the signals of 44 protons. We also measured ^1H NMR of **2** in methanol-d_4, expecting that complex **2** would be transformed into a monomeric Ti(salen) species of *cis*-β structure and show 44 proton signals. Contrary to our expectation, ^1H NMR measurement of **2** in methanol-d_4 showed the signals of 22 protons, strongly suggesting that the species generated in methanol-d_4 was monomeric and adopted not *cis*-β but C_2-symmetric square planar structure **6**. The methanolic-d_4 solution was concentrated in vacuo and the residue was dissolved in chloroform-*d*. Its ^1H NMR spectrum completely agreed with that of **2**, indicating that di-μ-oxo Ti(salen) complex **2** of *cis*-β structure and square planar monomeric Ti(salen) complex **6** were readily interconvertible (Scheme 2).



Scheme 3.

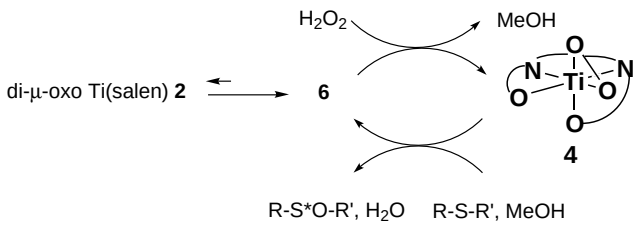
This strongly suggests that the square planar structure of the salen ligand is readily changeable to the *cis*-β structure when a bidentate ligand is coordinated to the titanium ion.

These results also suggested that the sulfoxidation using Ti(salen) complex **2** as the catalyst would show non-linear relationship between the enantiomeric excesses of the catalyst and of sulfoxide.[4,5] Thus, we examined the sulfoxidation of methyl phenyl sulfide with di-μ-oxo complexes **2** of different enantiomeric excesses, which were prepared by mixing (*R*,*R*)- and (*S*,*S*)-di-μ-oxo complex **2** (3.6 mg [(*R*,*R*)+(*S*,*S*)], 2.0 μmol) in methanol (750 ml). Although the mixing caused turbidity, the mixture was used for the sulfoxidation without removing the precipitate. As shown in Fig. 1, a positive non-linear effect was actually observed. We next isolated the precipitate and measured its ^{1}H NMR spectrum that showed 44 proton signals similar to the spectrum of (*R*,*R*)-di-μ-oxo complex **2**. However, the chemical shifts of the protons of the precipitate were slightly different from those of (*R*,*R*)-di-μ-oxo complex **2**, suggesting that the precipitate was not an (*R*,*R*)- but a racemic (*R*,*S*)-di-μ-oxo complex. Indeed, a chloroform solution of the precipitate showed very small optical rotation: $[\alpha]_D^{24} = -0.06$ (*c* 0.038, $CHCl_3$), while the specific optical rotation of (*R*,*R*)-di-μ-oxo complex **2** was $[\alpha]_D^{24} = -372$ (*c* 0.030, $CHCl_3$). FABMS analysis of the precipitate showed the parent peak ($m/z = 1776.5662$) indicating that it was an (*R*,*S*)-di-μ-oxo complex.

The above results meant that (*R*,*R*)- and (*S*,*S*)-di-μ-oxo complexes **2** are readily dissociated in methanol into the corresponding monomeric isomers [(*R*)-**6** and (*S*)-**6**] which are equilibrated with the racemic (*R*,*S*)-di-μ-oxo complex and, due to the low solubility and probably the high stability of the (*R*,*S*)-di-μ-oxo complex, the equilibrium is shifted to the (*R*,*S*)-di-μ-oxo complex and the concentration of (*S*)-**6** in the methanolic solution is reduced, showing the positive non-linear effect as observed (Scheme 3).

From these results, we considered that (*R*,*R*)-di-μ-oxo complex **2** dissolved in methanol rapidly dissociates into a monomeric Ti(salen) complex **6** and reacts with hydrogen peroxide, a bidentate ligand, to give the corresponding peroxo species **4** which undergoes sulfoxidation (Scheme 4).

To prove this consideration, we treated complex (*R*)-**6** with aqueous H_2O_2 (2 equiv.) in $CDCl_3$–MeOH-d_4 (1:1) and performed ^{1}H NMR measurement of the mixture. In the ^{1}H NMR spectrum of (*R*)-**6** which is C_2-symmetric, protons (Ha and Ha′) at the carbons bearing imino group and protons (Hb and Hb′) at the imino carbons show the identical chemical shifts, respectively (Table 1). On the other hand, protons (Ha and Ha′) and (Hb and Hb′) of complex (*R*,*R*)-**2** which are not C_2-symmetric show different chemical shifts. The ^{1}H NMR spectrum of the mixture (**6**+H_2O_2) showed the signals similar to those of complex **2**. This strongly suggested that the complex generated by mixing complex **6** and H_2O_2 is not C_2-symmetric and probably has *cis*-β structure. These results strongly supported the above consideration that complex **6** reacts with hydrogen peroxide to give the corresponding peroxo species **4**.

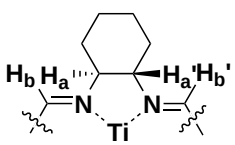


Scheme 4.

Acknowledgements

We are grateful to Ms. Mie Iriguchi, this department, for the measurements of MS spectroscopy.

Table 1. NMR spectra of complexes (**2**, **6**, and **4**): chemical shifts of Ha, Ha′, Hb and Hb′



Complex	Solvent	Chemical shift (ppm)			
		H_a	$H_{a'}$	H_b	$H_{b'}$
2	$CDCl_3$	3.18	4.20	8.43	8.68
6	CD_3OD	3.22	3.22	8.65	8.65
6+H_2O_2 (**4**)	$CDCl_3/CD_3OD$	3.29	4.11	8.55	8.66

References

1. Saito, B.; Katsuki, T. *Tetrahedron Lett*. **2001**, *42*, 3873–3876.
2. For a recent review for asymmetric sulfoxidation, see: Kagan, H. B. In *Catalytic Asymmetric Synthesis*; 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, 2000; Chapter 6c.
3. (a) Belokon', Y. N.; Green, B.; Ikonnikov, N. S.; Larichev, V. S.; Lokshin, B. V.; Moskalenko, M. A.; North, M.; Orizu, C.; Peregudov, A. S.; Timofeeva, G. *Eur. J. Org. Chem*. **2000**, 2655–2661; (b) Belokon', Y. N.; Green, B.; Ikonnikov, N. S.; North, M.; Parsons, T.; Tararov, V. I. *Tetrahedron* **2001**, *57*, 771–779.
4. (a) Puchot, C.; Samuel, O.; Dunach, E.; Zhao, S.; Agami, C.; Kagan, H. B. *J. Am. Chem. Soc*. **1986**, *108*, 2353–2357; (b) Kagan, H. B. *Adv. Synth. Cat*. **2001**, *343*, 227–233; (c) Kitamura, M.; Suga, S.; Oka, H.; Noyori, R. *J. Am. Chem. Soc*. **1998**, *120*, 9800–9809.
5. For examples of positive non-linear effect, see: (a) Oguni, N.; Matsuda, Y.; Kaneko, T. *J. Am. Chem. Soc*. **1988**, *110*, 7877–7878; (b) Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc*. **1989**, *111*, 4028–4036; (c) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc*. **1990**, *112*, 3949–3954; (d) Soai, K.; Niwa, S.; Hori, H. *J. Chem. Soc., Chem. Commun*. **1990**, 982–983; (e) Soai, K.; Shibata, T. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley VCH: New York, 2000; pp. 699–725; (f) Furuno, H.; Hanamoto, T.; Sugimoto, Y.; Inanaga, J. *Org. Lett*. **2000**, *2*, 49–52.