Enantioselective epoxidation of *trans*-disubstituted alkenes by D_2-symmetric chiral dioxoruthenium(VI) porphyrins

Rui Zhang, Wing-Yiu Yu, Tat-Shing Lai and Chi-Ming Che*

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong. E-mail: cmche@hkucc.hku.hk

Received (in Cambridge, UK) 10th November 1998, Accepted 4th December 1998

A series of D_2-symmetric chiral *trans*-dioxoruthenium(VI) porphyrins can effect enantioselective epoxidation of *trans*-β-methylstyrene in up to 70% ee, and 76% ee is attained for the oxidation of cinnamyl chloride; the facial selection for the *trans*-alkenes epoxidation is explained by a 'head-on approach' model.

The design of new metal catalysts for highly enantioselective epoxidation of unfunctionalized *trans*-disubstituted alkenes remains a challenge in the field of asymmetric oxidation.[1] A clue to this problem would be to prepare reactive, and yet isolable, chiral metal–oxo complexes which can act upon *trans*-alkenes to give epoxides in better enantioselectivities than the *cis*-counterparts.[2] If such complexes can be obtained, the structure–enantioselectivity relationship established by studying their stoichiometric alkene epoxidations could assist future design for better metal catalysts. Here, we show that a series of *trans*-dioxoruthenium(VI) complexes with D_2 symmetric porphyrins bifacially encumbered by four chiral threitol units (Fig. 1) can react favorably with *trans*-alkenes in exceptional %ee. Also, our findings do not reconcile with the 'side-on approach' model proposed for the oxo-metalloporphyrin-mediated alkene oxidations.

The D_2-symmetric porphyrins $H_2L^{1–3}$* and the [Ru^{II}-$L^{1–3}$*(CO)(EtOH)] precursors were prepared by the literature methods.[3] Treating the ruthenium(II) carbonyl complexes with *m*-chloroperoxybenzoic acid in dichloromethane for 5 min gave [$Ru^{VI}(L^{1–3}*)O_2$] **1a–c**, which were isolated as dark red–purple crystalline solids (80% yield). Complexes **1a–c** are diamagnetic and stable in solid and in solution for hours at room temperature. The oxidation state marker band at 1018 (**1a**), 1019 (**b**,**c**) together with an intense asymmetric O=Ru=O stretch at 818 (**1a**), 821 (**1b**), 819 cm^{-1} (**1c**) observed in their IR spectra are consistent with a Ru(VI) formulation.

At room temperature, complex **1a** in the presence of pyrazole (Hpz) oxidized styrene in a degassed benzene solution to give styrene oxide in 64% yield and 62% ee (Table 1, entry 1). The enantioselectivity was slightly improved (65% ee) when the reaction was carried out at 0 °C, and the %ee is comparable to the best reported value of 69% ee by employing the chiral Mn–porphyrin catalysts.[3] However, the other dioxoruthenium(VI) derivatives bearing *gem*-diethyl (**1b**) and *gem*-cyclopentyl groups (**1c**) at the threitol units afforded slightly lower ee of 60 and 55% respectively. A paramagnetic bis(pyrazolato)ruthenium(IV), [$Ru^{IV}(L^{1–3}*)(pz)_2$] **2** (μ_{eff} = 2.9 μ_B), was isolated by column chromatography at the end of the epoxidation reactions.[4] It is noteworthy that when styrene reacted with **1a** without Hpz; styrene oxide with only 40% ee was obtained and [$Ru^{II}(L^{1}*)(CO)$] was isolated. To account for the ee discrepancy, we propose that a ruthenium(II) species produced by further reduction of the putative Ru(IV) intermediate would racemize the chiral styrene oxide by an epoxide ring opening pathway previously suggested by Groves *et al.* (Scheme 1).[5]

More importantly, **1a** reacted with *trans*-β-methylstyrene in degassed benzene to give the *trans*-epoxide in 67% ee at room temperature, and up to 70% ee was attained when performing the reaction at 0 °C (entry 3). Notably, the oxidation of cinnamyl chloride furnished the corresponding epoxide in 76% ee and 70% yield (entry 4). Indeed, few reported metalloporphyrin-catalyzed asymmetric epoxidation systems are

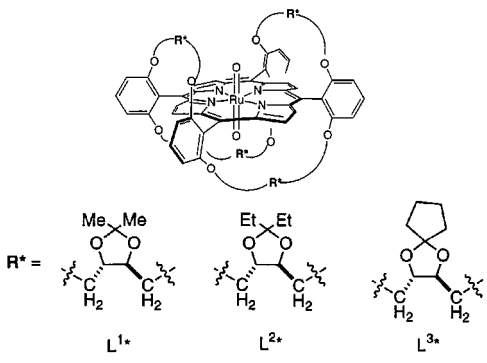
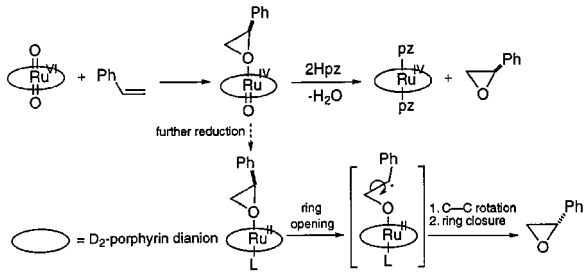


Fig. 1

Table 1 Stoichiometric epoxidation of some aromatic alkenes by [$Ru^{VI}(L^{1}*)O_2$] (1a)

Entry	Alkene	Solvent	Epoxide yield[a] (%)	%ee (abs. config.)[b]
1	Ph	C_6H_6	64[c]	62 (*R*)
		C_6H_6	62	40 (*R*)[d]
		CH_2Cl_2	39	41 (*R*)
		MeCN	13	33 (*R*)
2	Cl	C_6H_6	75	60 (*R*)
3	Ph, Me	C_6H_6	90 (>99 % *trans*)	67 (1*S*,2*R*)
		C_6H_6 (0 °C)	90 (>99 % *trans*)	70 (1*S*,2*R*)
		CH_2Cl_2	58 (>99 % *trans*)	32 (1*S*,2*R*)
		EtOAc	82 (>99 % *trans*)	38 (1*S*,2*R*)
4	Ph, Cl	C_6H_6	70	76 (1*S*,2*R*)
5	Ph, Me	C_6H_6	75 (> 99% *cis*)	40 (1*S*,2*R*)
		CH_2Cl_2	68 (95% *cis*, 5% *trans*)	18 (1*S*,2*R*)
6		C_6H_6	88	20 (1*S*,2*R*)

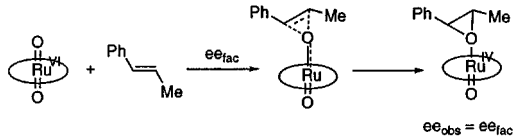
Reaction conditions: to a degassed benzene solution (1 cm^3) containing alkene (1 mmol) and pyrazole (0.3 mmol) was added the dioxoruthenium(VI) complex (0.015–0.03 mmol) under an argon atmosphere. The reaction mixture was stirred at room temperature (or otherwise noted) for 12 h, and the aliquot was analyzed by gas chromatography for product identification and quantification. [a] Yields are based on the amount of the oxidant used. [b] Enantiopurities (%ee) of the epoxides were determined by GC equipped with a chiral capillary column (J & W Scientific cyclodex-B or G-TA). Absolute configuration was determined by comparing with authentic chiral samples. [c] Benzaldehyde (27%) and phenylacetaldehyde (12%) were also detected. [d] Reaction was carried out without pyrazole.



Scheme 1

known to attain >20% ee for the *trans*-β-methylstyrene oxidation.[3,6] We had previously reported that a chiral D_4-symmetric dioxoruthenium(VI) complex can effect epoxidation of *cis*-β-methylstyrene in much higher enantioselectivity of 76% ee *vs*. 20% ee for the *trans*-isomer.[7] In this work, when *cis*-β-methylstyrene (entry 5) and 1,2-dihydronaphthalene (entry 6) reacted with **1a**, the *cis*-epoxides (>99% stereoretention) were produced in only 40 and 20% ee, respectively. Oxidation of *trans*- and *cis*-β-methylstyrene by complexes **1b** and **1c** also resulted similar *trans* preference albeit in lower enantioselectivities, for instance when **1b** was the oxidant, the *trans*- and *cis*-epoxides with 50 and 28% ee resulted respectively.

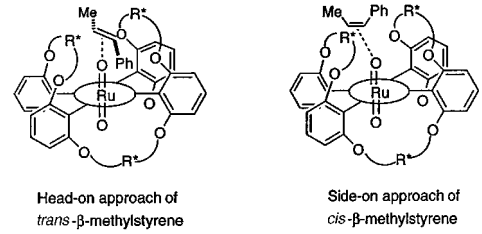
The asymmetric alkene epoxidations by **1a** also exhibit remarkable solvent dependence.[8] The *trans*-β-methylstyrene oxidation by **1a** displays clean pseudo-first-order kinetics: $-d[Ru(VI)]/dt = k_{obs}[Ru(VI)]$, where $k_{obs} = k_2[alkene]$ and k_2 is the second-order rate constant of the reaction. Upon changing solvent from benzene to dichloromethane, the k_2 value halves: 9.04×10^{-4} (C_6H_6), 4.15×10^{-4} dm^3 mol^{-1} s^{-1} (CH_2Cl_2) at 298 K. It is noted that the %ee of the *trans*-epoxide also decreases in a similar fashion: 67% ee (C_6H_6) *vs.* 32% ee (CH_2Cl_2). By contrast, no solvent effect has been observed for the analogous reactions of the D_4-chiral dioxoruthenium(VI) porphyrin. Since the alkene oxidation is highly stereospecific (Table 1, entries 3 and 5), therefore, the %ee of the epoxide should be determined only by facial selectivity at the rate-limiting association of the C=C bond with the Ru=O group (Scheme 2).[9] We suspect that polar solvent may aggregate around the threitol units through dipole–dipole interaction thereby affecting the facial approach of the alkene.



Scheme 2

In literature, *cis–trans* stereoselectivity in the metalloporphyrin-catalyzed alkene epoxidations is generally explained by the 'side-on approach'.[10] Yet, in this case, this model cannot account for the observed *trans* preference. Here, we propose a 'head-on approach' model in which the molecular plane of the C=C bond lies perpendicular to the Ru=O axis (Scheme 3). Since the *cis vs. trans* stereoselectivity should arise from the steric interaction between the incoming alkene and the porphyrin ligand, the 'head-on approach' of a *trans*-alkene molecule to oxo–metalloporphyrins can also be feasible according to previous studies.[11]

The asymmetric epoxidation of *trans*-β-methylstyrene can become catalytic using 2,6-dichloropyridine *N*-oxide (Cl_2pyNO) or O_2 as terminal oxidant. Similarly the catalytic *trans*-alkene oxidation is more enantioselective than that of the analogous *cis*-β-methylstyrene oxidation. For example, with Cl_2pyNO (0.146 mmol) as terminal oxidant and benzene as solvent, the *trans*-β-methylstyrene (1 mmol) oxidation furnished the *trans*-epoxide in 50% ee (70% yield, turnover = 70); whereas the oxidation of the *cis* analogue afforded the *cis*-epoxide in only 7% ee (70% yield, turnover = 66) under the same conditions. On the other hand, **1a** can also effect aerobic asymmetric *trans*-β-methylstyrene epoxidation in benzene (9 atm O_2, 40 h) to give the *trans*-epoxide in 59% ee (turnover = 7).



Scheme 3

We acknowledge support from The University of Hong Kong and The Hong Kong Research Grants Council, ERB003 and HKU7092/98P.

Notes and references

† Characterization data for the dioxoruthenium(VI) and bis(pyrazolato)-ruthenium(IV) porphyrin complexes: [$Ru^{VI}(L^{1*})O_2$ **1a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (d, *J* 4.7 Hz, 4H), 8.55 (d, *J* 4.7 Hz, 4H), 7.77 (t, *J* 6.5 Hz, 4H), 7.22–7.38 (m, *m*-H overlapped with a solvent peak, 8H), 4.91 (d, *J* 10.4 Hz, 4H), 4.62 (d, *J* 9.0 Hz, 4H), 4.43 (t, *J* 9.0 Hz, 4H), 4.22 (d, *J* 10.1 Hz, 4H), 3.76 (d, *J* 9.0 Hz, 4H), 2.60 (t, *J* 8.5 Hz, 4H), 0.77 (s, 12H), −0.78 (s, 12H). UV–VIS (CH_2Cl_2) λ_{max}/nm (log ε/dm^3 mol^{-1} cm^{-1}): 442 (5.12), 536 (4.07). FABMS *m/z*: 1379 (M^+, 18%), 1363 (M^+, 18%), 1363 ($M^+ - O$, 30%), 1347 ($M^+ - 20$, 100%).

[$Ru^{VI}(L^{2*})O_2$] **1b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (d, *J* 4.7 Hz, 4H), 8.53 (d, *J* 4.7 Hz, 4H), 7.74 (m, 4H), 7.37–7.30 (m, *m*-H overlapped with a solvent peak, 8H), 4.98 (d, *J* 10.4 Hz, 4H), 4.60 (d, *J* 8.8 Hz, 4H), 4.44 (t, *J* 8.9 Hz, 4H), 4.23 (d, *J* 10.4 Hz, 4H), 3.74 (d, *J* 8.8 Hz, 4H), 2.63 (t, *J* 8.7 Hz, 4H), 1.02 (m, 8H), 0.53 (t, *J* 7.2 Hz, 12H), −0.25 (m, 8H), −1.37 (t, *J* 7.3 Hz, 12H). UV–VIS (CH_2Cl_2): λ_{max}/nm (log ε/dm^3 mol^{-1} cm^{-1}) 443 (5.15), 534 (4.02). FABMS: *m/z* 1491 (M^+, 9%), 1475 ($M^+ - O$, 20%), 1459 ($M^+ - 2O$, 100%).

[$Ru^{VI}(L^{3*})O_2$] **1c**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, *J* 4.6 Hz, 4H), 8.56 (d, *J* 4.6 Hz, 4H), 7.76 (m, 4H), 7.20–7.37 (m, *m*-H overlapped with a solvent peak, 8H), 4.88 (d, *J* 9.3 Hz, 4H), 4.60 (d, *J* 9.4 Hz, 4H), 4.64 (t, *J* 9.0 Hz, 4H), 4.24 (d, *J* 10.1 Hz, 4H), 3.77 (d, *J* 8.6 Hz, 4H), 2.57 (t, *J* 8.6 Hz, 4H), 0.83 (m, 12H), 0.60 (m, 12H), 0.32 (m, 4H), −1.16 (m, 4H). UV–VIS (CH_2Cl_2) λ_{max}/nm (log ε/dm^3 mol cm^{-1}): 441 (5.03), 535(4.02). FABMS *m/z*: 1483 (M^+, 8%), 1467 ($M^+ - O$, 22%), 1451 ($M^+ - 2O$, 100%).

[$Ru^{IV}(L^{1*})(pz)_2$] **2a**: IR(KBr): 1006 cm^{-1} (oxidation state marker band). FABMS *m/z*: 1483 (M^+, 100%), 1415 ($M^+ -$ pz, 10%), 1347 ($M^+ - 2$ pz, 20%). Anal. Calc. for $C_{78}H_{76}N_8O_{19}Ru \cdot 3H_2O$: C, 60.89; H, 5.33; N, 7.28. Found: C, 60.77; H, 5.31; N, 7.25%. UV–VIS ($CHCl_3$) λ_{max}/nm (logε/dm^3 mol^{-1} cm^{-1}): 425 (5.09), 517 (4.04), 550 (sh).

1 E. N. Jacobsen, in *Comprehensive Organometallic Chemistry II*, ed. G. Wilkinson, F. G. A. Stone, E. W. Abel and L. S. Hegedus, Pergamon, New York, 1995, vol. 12, ch. 11.1; For chiral ruthenium complexes catalyzed asymmetric epoxidation of *trans*-alkenes, see: N. End and A. Pfaltz, *Chem. Commun.*, 1998, 589.
2 Z. Gross, S. Ini, M. Kapon and S. Cohen, *Tetrahedron Lett.*, 1996, **37**, 7325.
3 J. P. Collman, V. J. Lee, C. J. Kellen-Yuen, X. Zhang, J. A. Ibers and J. I. Brauman, *J. Am. Chem. Soc.*, 1995, **117**, 692.
4 C.-J. Liu, W.-Y. Yu, S.-M. Peng, T. C.-W. Mak and C.-M. Che, *J. Chem. Soc., Dalton Trans.*, 1998, 1805.
5 J. T. Groves, K. T. Ahn and R. Quinn, *J. Am. Chem. Soc.*, 1988, **110**, 4217.
6 The best reported ee is 83% for the oxidation of *trans*-β-methylstyrene using chiral Cr–salen catalysts, see: C. Bousquet and D. C. Gilheany, *Tetrahedron Lett.*, 1995, **36**, 7739.
7 T.-S. Lai, R. Zhang, K.-K. Cheung, H.-L. Kwong and C.-M. Che, *Chem. Commun.*, 1998, 1583; T.-S. Lai, H.-L. Kwong, R. Zhang and C.-M. Che, *J. Chem. Soc., Dalton Trans.*, 1998, 3559.
8 Z. Gross and S. Ini, *J. Org. Chem.*, 1997, **62**, 5514.
9 W. Zhang, N. H. Lee and E. N. Jacobson, *J. Am. Chem. Soc.*, 1994, **116**, 425; W.-H. Fung, W.-Y. Yu and C.-M. Che, *J. Org. Chem.*, 1998, **63**, 7715.
10 J. T. Groves and R. S. Myers, *J. Am. Chem. Soc.*, 1983, **105**, 5791.
11 D. Ostovic and T. C. Bruice, *Acc. Chem. Res.*, 1992, **25**, 314.

Communication 8/08776H