Stereo- and Enantioselective Alkene Epoxidations: A Comparative Study of D_4- and D_2-Symmetric Homochiral *trans*-Dioxoruthenium(VI) Porphyrins

Rui Zhang,[a] Wing-Yiu Yu,[a] Hong-Zhe Sun,[a] Wei-Sheng Liu,[a] and Chi-Ming Che*[a, b]

Abstract: The mechanism of stoichiometric enantioselective alkene epoxidations by the D_4- and D_2-symmetric homochiral *trans*-dioxoruthenium(VI) porphyrins, [Ru^{VI}(D_4-Por*)O_2] (**1**) and [Ru^{VI}(D_2-Por*)O_2] (**2a**), in the presence of pyrazole (Hpz) was studied by UV/Vis spectrophotometry and analysis of the organic products. The enantioselectivity of styrene oxidations is more susceptible to steric effects than to substituent electronic effects. Up to 72% *ee* was achieved for epoxidation of 3-substituted and *cis*-disubstituted styrenes by employing **1** as the oxidant, whereas entantioselectivities of only 20–40% were obtained in the reactions with 2-substituted and *trans*-disubstituted styrenes. Complex **2a** oxidized 2-substituted styrenes to their epoxides in up to 88% *ee*. Its reactions with *trans*-alkenes are more enantioselective (67% *ee*) than with the *cis*-alkenes (40% *ee*). Based on a two-dimensional NOESY NMR study, **2a** was found to adopt a more open conformation in benzene than in dichloromethane, which explains the observed solvent-dependent enantioselectivity of its reactions with alkenes. The oxidation of aromatic alkenes by the chiral dioxoruthenium(VI) porphyrins proceeds through the rate-limiting formation of a benzylic radical intermediate; the observed enantioselectivity (ee_{obs}) depends on both the facial selectivity of the first C–O bond formation step and the diastereoselectivity of the subsequent epoxide ring closure. To account for the observed facial selection, "side-on" and "top-on" approach transition state models are examined (see: B. D. Brandes, E. N. Jacobsen, *Tetrahedron Lett.* **1995**, *36*, 5123).

Keywords: asymmetric oxidation · epoxidation · kinetics · macrocycles · ruthenium

Introduction

Asymmetric epoxidation of unfunctionalized alkenes is an appealing strategy for the preparation of optically active epoxides,[1] and significant advances in this area have been made with chiral transition-metal complexes[2, 3] and ketones[4] as catalysts. These reactions involve prochiral face recognition of a C=C bond by the chiral catalysts; achievement of a high degree of enantioselectivity based on weak nonbonded interactions constitutes the major challenge in this area. In biomimetic P-450 oxidation chemistry,[5] participation of highly oxidizing M=O reactive intermediates is widely accepted;[6] however, the mechanistic details regarding the reaction of a C=C bond with the M=O moiety in an enantioselective manner remain elusive.[7] Toward this end, our approach is to study the stoichiometric alkene epoxidations by reactive chiral metal–oxo complexes that have tunable structural and electronic properties.[3d,f, 8, 9] We have shown that *trans*-dioxoruthenium(VI) porphyrins are useful models for mechanistic elucidation of organic oxidations by reactive oxometalloporphyrins.[10] These complexes can undergo alkene epoxidation[10a–d] and alkane hydroxylation[10e] under mild conditions. Importantly, their structures can be modified by attaching chiral auxiliaries onto the porphyrin macrocycle leading to reactive chiral M=O oxidants.[3]

In 1996, Gross and co-workers[3a] reported the synthesis of a homochiral ruthenium complex with a D_2-symmetric porphyrin bearing four threitol substituents (D_2-H_2Por*, Fig-

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Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/chemistry/ or from the author. The information includes ^{1}H NMR data of complex **2a** in various solvents, results of the asymmetric alkene epoxidations in various solvents, ^{1}H NMR spectra of **2a** in $CDCl_3$ and C_6D_6, and molecular modeling studies of the transition-state models for the side-on and top-on approach.

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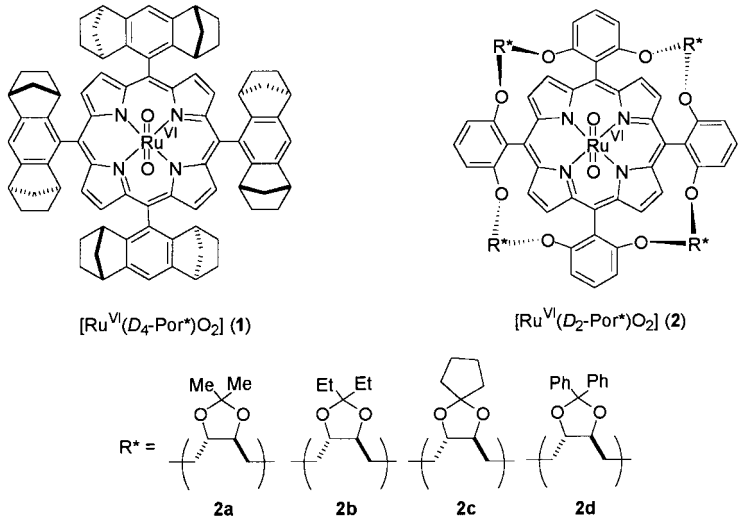

Figure 1. Structures of the D_4- and D_2-symmetric *trans*-dioxoruthenium(VI) porphyrin complexes.

ure 1). Subsequently, both our group and that of Gross found that $[Ru^{VI}(D_2\text{-Por*})O_2]$ (**2a**) and $[Ru^{II}(D_2\text{-Por*})(CO)]$ are active catalysts for enantioselective alkene epoxidations.[3a,b, 3f] Berkessel and our group also reported enantioselective alkene epoxidation[3d,e] and cyclopropanation[11] catalyzed by ruthenium complexes bearing a D_4-symmetric porphyrin [D_4-H_2Por* = 5,10,15,20-tetrakis(1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracen-9-yl)porphyrin], which was first developed by Halterman and co-workers.[2f,12] Similar to other metalloporphyrin-catalyzed asymmetric alkene epoxidations,[2] the stoichiometric epoxidation of *cis*-β-methylstyrene by $[Ru^{VI}(D_4\text{-Por*})O_2]$ (**1**, Figure 1) gave the *cis*-epoxide with good enantioselectivity (72% *ee*), whereas the analogous *trans*-β-methylstyrene epoxidation gave only 20% *ee* under identical conditions.[3d,e] More importantly, complex **2a** and its derivatives (Figure 1) were found to undergo enantioselective epoxidation of *trans*-β-methylstyrene in up to 70% *ee*; however, the related reaction with *cis*-β-methylstyrene achieved only 40% *ee*.[3f] Herein we describe a detailed comparative study on the reactivities of the D_4- and D_2-symmetric homochiral dioxoruthenium(VI) porphyrins toward epoxidation of alkenes. To account for the different enantioselectivities, we propose two transition state models for the oxygen atom transfer reactions involving a "side-on" and/or "top-on" approach of alkene to the Ru=O moiety.

Results

Preparation and characterization of D_4- and D_2-symmetric chiral $[Ru^{VI}(Por*)O_2]$ complexes: The syntheses and characterization of *trans*-dioxoruthenium(VI) porphyrins are well-documented in the literature,[3d,f, 10] and a chiral picket-fence *trans*-dioxoruthenium(VI) porphyrin containing optically active peptide substituents was first reported by Simonneaux and co-workers.[8d,e] Subsequently, we communicated the synthesis of complexes **1** and **2** by oxidation of their ruthenium(II)–carbonyl precursors with either PhIO or *m*-chloroperoxybenzoic acid in dichloromethane.[3d–f] The molecular structure of $[Ru^{VI}(D_4\text{-Por*})O_2]$ (**1**) had been established by X-ray crystallography.[3d] The sterically encumbered D_4- and D_2-symmetric porphyrin ligands disfavor dimerization by Ru-O-Ru formation even in noncoordinating solvents, such as dichloromethane; this eliminates the necessity of alcohol as co-solvent.[10] The dioxoruthenium(VI) complexes were purified by column chromatography on alumina with dichloromethane (**1**) or chloroform (**2**) as the eluant, and pure $[Ru^{VI}(Por*)O_2]$ complexes were obtained in $\approx$70–90% yield. These compounds are air-stable solids and can be stored at $-20\,^{\circ}C$ for months.

All the $[Ru^{VI}(Por*)O_2]$ complexes show a well-resolved ^1H NMR spectrum, consistent with a diamagnetic $(d_{xy})^2$ electronic ground state (the O=Ru=O axis is taken as the z axis). For **1**, all the β-pyrrolic protons are equivalent, showing a singlet absorption at $\delta = 8.96$. In the case of D_2-symmetric complexes **2a–d**, the β-pyrrolic protons are observed as a pair of doublets in $CDCl_3$ ($\delta = 8.66$ and 8.56 for **2a**; 8.64 and 8.53 for **2b**; 8.67 and 8.56 for **2c**; 8.50 and 8.41 for **2d**). This spectral pattern is compatible with a staggered conformational structure, which is characterized by four equivalent pyrrole rings each bearing two nonequivalent β-protons.[2e] Infrared spectra of the $[Ru^{VI}(Por*)O_2]$ complexes show an intense absorption at $\tilde{\nu} = 822-818\ cm^{-1}$ that we assign to the asymmetric O=Ru=O stretches. The oxidation state marker bands are located at $\approx 1018\ cm^{-1}$, in agreement with a Ru^{VI} formulation.[13] The UV/Vis absorption of $[Ru^{VI}(Por*)O_2]$ features an intense Soret band and a less intense Q band.

Stoichiometric enantioselective epoxidation by $[Ru^{VI}(Por*)O_2]$: In a degassed benzene solution containing 2% w/w pyrazole (Hpz), complex **2a** (15–30 μmol) reacted with excess styrene (1 mmol) at room temperature to give styrene oxide in 64% yield and 62% *ee* (Table 1 entry 1); a slightly higher *ee* of 65% was obtained at a lower temperature of $\approx 0\,^{\circ}C$. As reported previously, treatment of styrene with **1** in benzene containing 2% w/w Hpz under ambient conditions produced styrene oxide in 61% yield and 65% *ee*. In both cases, a bis(pyrazolato)ruthenium(IV) porphyrin complex, $[Ru^{IV}(Por*)(pz)_2]$ (**3a**,**b**), was isolated and characterized spectroscopically (see the Experimental Section). Complexes **3a**,**b** are paramagnetic with effective magnetic moments (μ_{eff}) of $\approx 2.9\,\mu_B$, which is consistent with a triplet electronic ground state for a Ru^{IV} formulation.[14] The molecular structure of a related $[Ru^{IV}(dpp)(pz)_2]$ complex (H_2dpp = 2,3,5,7,8,10,12,13,15,17,18,20-dodecaphenylporphyrin), prepared in a similar manner, had previously been established by X-ray crystallography.[10c]

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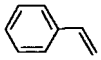
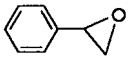
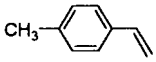
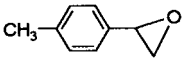
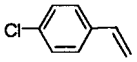
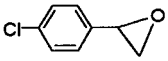
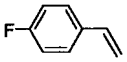
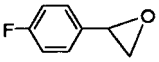
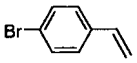
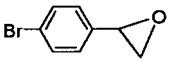
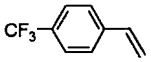
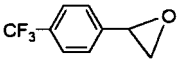
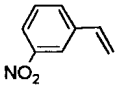
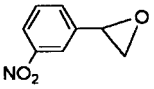
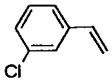
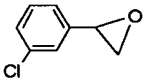
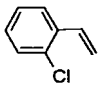
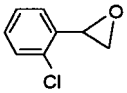
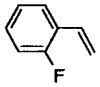
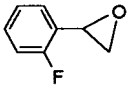
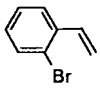
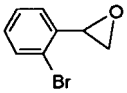
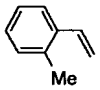
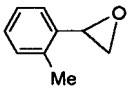
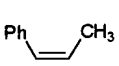
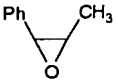
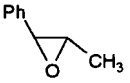
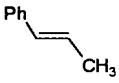
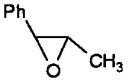
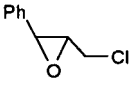
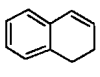
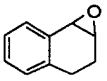
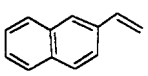
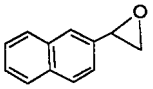
Table 1. Stoichiometric alkene epoxidations by chiral dioxoruthenium(VI) porphyrins.[a]

Entry	Substrate	Product	**1** Yield [%][b]	**1** *ee* [%] (abs. config.)[c, d]	**2a** Yield [%][b]	**2a** *ee* [%] (abs. config.)[c, d]
1			61	65 (*R*)	64 66 (0 °C)	62 (*R*) 65 (*R*)
2			56	64 (*R*)	64	62 (*R*)
3			82	57 (*R*)	75	60 (*R*)
4			86	70 (*R*)	80	68 (*R*)
5			82	54 (*R*)	85	50 (*R*)
6			32	66 (*R*)	25	70 (*R*)
7			78	60 (*R*)	78	49 (*R*)
8			84	72 (*R*)	80	54 (*R*)
9			82	35 (n.d.)[e]	73	14 (*R*)[e]
10			70	44 (*R*)	52	88 (*R*)
11			82	54 (*R*)	68	84 (*R*)
12			48	47 (*R*)	88	80 (*R*)
13			70	50 (*R*)	80	81 (*R*)
14			64	72 (1*R*,2*S*)	75	40 (1*R*,2*S*)
			5	8 (1*R*,2*R*)	1	10 (1*R*,2*R*)
15			66	20 (1*R*,2*R*)	90 90 (0 °C)	67 (1*R*,2*R*) 70 (1*R*,2*R*)
16			60	18 (1*R*,2*R*)	70	76 (1*R*,2*R*)
17			71 78 (−15 °C)	72 (1*R*,2*S*) 82 (1*R*,2*S*)	88	20 (1*R*,2*S*)
18			78	70 (*R*)	< 10	n.d.

[a] Reaction conditions: to a degassed benzene solution (2 mL) containing Hpz (2% w/w) and alkenes (1 mmol) was added [Ru^{VI}(Por*)O_2] (15–30 μmol) under an argon atmosphere. After stirring for 12 h at RT (unless otherwise noted), the reaction mixture was filtered through an alumina column with a hexanes/ethyl acetate (9:1, v/v) mixture as the eluant. The organic products were then analyzed and quantified by GC or ^{1}H NMR by means of the internal standard method. [b] Yields are based on the ruthenium oxidant used. [c] % *ee* determined by chiral GC or ^{1}H NMR with [Eu(hfc)$_3$] as shift reagent. [d] Absolute configuration was assigned by comparison with authentic enantiopure samples. [e] n.d. = not determined.

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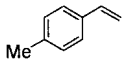
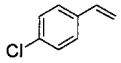
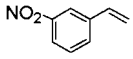
Effect of pyrazole: When the stoichiometric styrene epoxidations were undertaken in benzene without Hpz as an additive, styrene oxide was produced in significantly lower yields (53% (**1**) and 62% (**2a**)) and lower enantioselectivities (6% *ee* (**1**) and 40% *ee* (**2a**)), compared to the same reactions performed in the presence of Hpz (see Table 2). With **1** as the oxidant, the reactions of 4-methylstyrene (40% *ee*) and 4-chlorostyrene (41% *ee*) gave lower *ee* values when no Hpz was added. Notably, without Hpz, 3-nitrostyrene was oxidized to afford racemic epoxide (0% *ee*) in 70% yield (Table 2). Moreover, when enantiopure (*R*)-styrene oxide (3 mmol; >99% *ee*) was stirred in a reaction mixture containing 4-chlorostyrene (300 μmol) and **1** (30 μmol) in benzene at room temperature for 12 h, the initial optically active styrene oxide was recovered (>95% yield) in only 37% *ee*.

Table 2. Effect of pyrazole on the asymmetric alkene epoxidations by $[Ru^{VI}(D_4\text{-Por}^*)O_2]$ (**1**).[a]

Entry	Alkenes	with Hpz		without Hpz	
		Epoxide yield [%]	*ee* [%]	Epoxide yield [%]	*ee* [%]
1		61	65	53	6
2		56	64	41	40
3		82	57	71	41
4		78	60	70	0

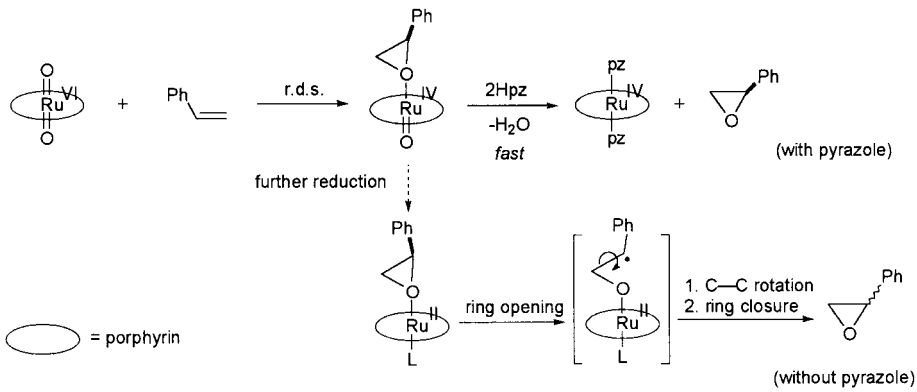
[a] Same reaction conditions as those given in Table 1 were employed, except with/without Hpz as the additive. For complex **2a**, the styrene oxidation achieved only 40% *ee* with 62% epoxide yield in the absence of Hpz, compared with 62% *ee* when 2% w/w Hpz was added.

In the absence of Hpz and with a prolonged reaction time (24 h), **1**/**2a** reacted with an excess of styrene in benzene to form the corresponding $[Ru^{II}(Por^*)(CO)]$ complex, which was isolated (yield >80%) and characterized by IR and ^{1}H NMR spectroscopy and MS. In a previous study by Groves and co-workers, $[Ru^{II}(tmp)(CO)]$ [H_2tmp = *meso*-tetrakis-(mesityl)porphyrin] was also found during the course of the reaction between $[Ru^{VI}(tmp)O_2]$ and styrene.[15] Since ruthenium(II) porphyrin complexes without π-acid axial ligands are known to racemize chiral epoxides (Scheme 1),[16] we propose that the added Hpz reacted spontaneously with the putative oxo–Ru^{IV} intermediate, thereby diverting the reaction pathway away from the undesirable formation of Ru^{II} complexes.

Oxidation of substituted styrenes: In general, *ortho*-, *meta*- and *para*-substituted styrenes are converted by **1** or **2a** to their (*R*)-epoxides in good-to-moderate yields, while arylbenzaldehyde (C=C bond cleavage) and/or 1-arylacetaldehyde (rearrangement) were detected as minor products. An exception to this is *para*-trifluoromethylstyrene, which was found to react with **1** and **2a** to give the epoxide in 32 and 25% yields, respectively, (Table 1, entry 6); *para*-trifluoromethylbenzaldehyde was formed as the major product (60% yield). Stirring the organic epoxide with either $[Ru^{VI}(Por^*)O_2]$ or $[Ru^{IV}(Por^*)(pz)_2]$ in benzene at room temperature did not result in any aldehyde formation; this indicates that the latter side-products should not arise from degradation of the product epoxides.

We have also prepared an enantiomeric D_2-symmetric dioxoruthenium(VI) complex **2a′** by replacing the (*S*,*S*)-threitol substituent in **2a** to give its antipodal (*R*,*R*)-derivative. As anticipated, complex **2a′** reacted with styrene to give the (*S*)-epoxide with a product yield and enantioselectivity identical to that of the (*R*)-epoxide obtained by similar reaction with complex **2a**.

As shown in Table 1, *para*-substitution (*p*-Y-styrene, Y = Me, Cl, F, Br, and CF_3) does not have a significant effect upon the enantioselectivity of styrene epoxidation by **1** or **2a** (≈65% *ee*). Complex **1** oxidized 3-chloro- and 3-nitrostyrenes in 72 and 60% *ee* respectively; however, its reactions with 2-chloro- and 2-bromostyrenes under identical reaction conditions gave the epoxides with much lower enantioselectivities (44 and 47% *ee*). It is noteworthy that the epoxidation of *ortho*-substituted styrenes by **2a** proceeded with enantioselectivities ≥80% *ee* (entries 10–13). The highest *ee* of 88% was attained for the 2-chlorostyrene epoxidation, which is close to some best *ee* values reported for the epoxidation of styrenes.[1–3] On the other hand, *meta*-substituted styrenes reacted with **2a** to furnish the organic epoxides (≈80% yield) in ≈50% *ee* (Table 1, entries 7,8). 2-Vinylnaphthalene underwent facile reaction with **1** to give the corresponding epoxide in 70% *ee* and 78% yield (entry 18). However, the analogous reaction with **2a** was ineffective, 2-vinylnaphthalene oxide was isolated in less than 10% yield, despite the fact that $[Ru^{IV}(D_2\text{-Por}^*)(pz)_2]$ was isolated in 77% yield. Because of the poor product yield, the optical purity of the epoxide was not determined.



Scheme 1. Racemization of chiral epoxides by ruthenium(II) porphyrin complexes with and without pyrazole.

Oxidation of 1,2-disubstituted alkenes: Under the standard reaction conditions (alkene = 1 mmol, Ru = 30 μmol in benzene containing 2% w/w Hpz), epoxidation of *cis*-β-methylstyrene by **2a** afforded predomi-

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nantly *cis*-β-methylstyrene oxide in 40% *ee* (*cis*:*trans* ratio = 75:1; Table 1, entry 14). Yet, the analogous reaction with **1** can afford *cis*-β-methylstyrene oxide in up to 72% *ee* (*cis*:*trans* ratio = 64:5). The optical purity of the *trans*-β-methylstyrene oxide produced from the *cis*-β-methylstyrene epoxidation was determined to be ≤10% *ee*. Stirring a benzene solution of pure *cis*-β-methylstyrene oxide and $[Ru^{IV}(Por^*)(pz)_2]$ at room temperature for 12 h led to full recovery of the starting *cis*-epoxide, and no *trans*-epoxide was detected. This finding indicates that the *trans*-epoxide formation associated with the *cis*-alkene epoxidation is not a consequence of $[Ru^{IV}(Por^*)(pz)_2]$-catalyzed epoxide isomerization.[16]

More importantly, complex **2a** reacted with *trans*-β-methylstyrene to give *trans*-β-methylstyrene oxide in 67% *ee* and 90% yield (Table 1, entry 15), in contrast to the analogous reaction with **1** in which the *trans*-epoxide was afforded in 20% *ee* (Table 1, entry 15). An enantioselectivity of up to 76% *ee* was achieved for the stoichiometric epoxidation of cinnamyl chloride by **2a** (Table 1, entry 16). It should be noted that only few metalloporphyrin-catalyzed enantioselective *trans*-β-methylstyrene epoxidations are known to attain enantioselectivities greater than 20% *ee*.[2] Recently, some chiral chromium/Schiff base[9] and ruthenium–oxalamide/Schiff base complexes[17] were found to catalyze enantioselective *trans*-β-methylstyrene epoxidation with high *ee* values. As with **2a**, complexes **2b**,**c** reacted with *trans*-β-methylstyrene to give the epoxides in higher *ee* values than similar reaction with *cis*-β-methylstyrene, [*cis*-β-methylstyrene oxidation: 28% *ee* (**2b**) and 13% *ee* (**2c**)]. However, we found that the *gem*-diphenyl-substituted complex **2d** oxidized *cis*-β-methylstyrene to give the *cis*-epoxide in 36% *ee*, which is slightly higher than 20% *ee* obtained for the analogous *trans*-alkene oxidation (Table 2, entries 4,5).

Effect of bulky chiral auxiliaries: We have studied the styrene and *trans*-β-methylstyrene epoxidations with several D_2-symmetric dioxoruthenium(VI) porphyrins bearing *gem*-diethyl (**2b**), *gem*-cyclopentyl (**2c**), and *gem*-diphenyl (**2d**) groups at the threitol units, and the results are listed in Table 3. For the styrene epoxidation, the enantioselectivity dropped with increasing bulkiness of the auxiliaries (c.f. 62% *ee* (**2a**), 60% *ee* (**2b**), 55% *ee* (**2c**), and 40% *ee* (**2d**)). A similar trend has also been observed for the *trans*-β-methylstyrene epoxidations (c.f. 67% *ee* (**2a**), 50% *ee* (**2b**), 36% *ee* (**2c**), and 20% *ee* (**2d**)). Indeed, the reaction of **2d** with *trans*-β-methylstyrene required 2 days for completion and the epoxide was obtained in 28% yield with mass balance < 40% (Table 3, entry 1). However, in a related work by Gross and co-workers it was reported that **2d** can catalyze enantioselective *trans*-β-methylstyrene epoxidation with 69% *ee*.[3g]

Kinetic studies: The alkene epoxidations by **1** or **2a** feature isosbestic transformation of $[Ru^{VI}(Por^*)O_2]$ to $[Ru^{IV}(Por^*)(pz)_2]$. Figure 2 depicts the UV/Vis spectral change for the reaction of styrene with **2a** in 1,2-dichloroethane containing

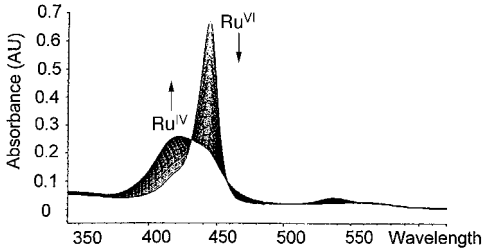
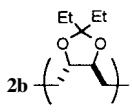
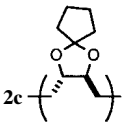
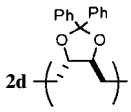
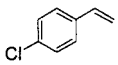


Figure 2. UV/Vis spectral changes during the reaction of **2a** (time scan: 1500 s, 60 s interval) with styrene (1.0 mol dm^{-3}) in 1,2-dichloroethane with 2% w/w Hpz at 298 K.

Hpz (2% w/w). As shown in Figure 2, the conversion of Ru^{VI} to Ru^{IV} is manifested by the decay of the Soret band at λ = 442 nm with concomitant development of a new absorption band at 425 nm. Isosbestic points are located at λ = 414, 440, 479, 560 nm for **1** and 430, 458, 512, 556 nm for **2a**. In the absence of Hpz, the kinetic profile for the Ru^{VI} to Ru^{IV} transformation was influenced by secondary reactions (plau-

Table 3. Effect of bulky auxiliaries on the asymmetric alkene epoxidations by complex **2**.[a]

							
Entry	Alkenes	Epoxide yield [%]	*ee* [%]	Epoxide yield [%]	*ee* [%]	Epoxide yield [%]	*ee* [%]
1		64	60	56	55	28	40
2		78	55	65	46	35	36
3		80	79	74	56	21	33
4		82 (*cis* > 99%)	28	84	13	40	36
5		90 (*trans* > 99%)	50	90	36	34	20

[a] Same reaction conditions as those given in Table 1 were employed. Similar to complex **2a**, the oxidation of styrene (entry 1) and its substituted derivatives (entries 2 and 3) produced (*R*) epoxides preferentially. Oxidations of *cis*- (entry 4) and *trans*-β-methylstyrenes (entry 5) gave (1*R*,2*S*) and (1*R*,2*R*)-epoxides, respectively.

sibly by the formation of Ru^{II} porphyrin) and deviated from first-order exponential decay.

In this work, all of the kinetic studies were conducted in 1,2-dichloroethane and in the presence of 2% w/w Hpz under the condition that $[Ru] \ll [alkene] \leq 2\ mol\ dm^{-3}$. All the reactions exhibited clean pseudo-first-order kinetics and isosbestic spectral changes over four half-lives for the substrates employed. In benzene, toluene, dichloromethane, or 1,2-dichloroethane, the alkenes were oxidized by **1** or **2a** to give epoxides in good yields and with mass balances >90% (see below).

The pseudo-first-order rate constants, k_{obs}, were determined by monitoring the disappearance of the Soret band (λ_{max} = 424 nm for **1** and 442 nm for **2a**) of the dioxoruthenium(VI) complexes; the second-order rate constants, k_2, were evaluated from the linear plots of k_{obs} versus [alkene] (see Table 4). Rate saturation was not observed over the alkene concentrations employed in this work. It should be noted that the k_2 values are unaffected by the Hpz loading (2–10% w/w), and no appreciable reaction between **1** or **2a** with pyrazole was observed within the timescale of the kinetic studies.

Table 4. Second-order rate constants (k_2) for the asymmetric alkene oxidations at 298 K.[a]

Entry	Alkenes	$k_2 \times 10^4$ [$dm^3\ mol^{-1}\ s^{-1}$] (**1**)	(**2a**)
1	styrene	21.9 ± 1.2	7.1 ± 0.2
2	4-methoxystyrene	96.5 ± 5.5	45.6 ± 1.6
3	4-methylstyrene	40.8 ± 1.5	13.8 ± 0.1
4	2-methylstyrene	30.7 ± 0.6	12.9 ± 0.2
5	4-fluorostyrene	26.2 ± 1.0	8.9 ± 0.2
6	4-chlorostyrene	38.4 ± 3.5	12.0 ± 0.4
7	2-chlorostyrene	24.8 ± 0.2	13.5 ± 0.7
8	3-chlorostyrene	26.1 ± 0.1	7.4 ± 0.4
9	4-bromostyrene	72.0 ± 4.0	14.6 ± 0.4
10	*cis*-β-methylstyrene	29.6 ± 1.5	5.8 ± 0.2
11	*trans*-β-methylstyrene	21.5 ± 1.6	8.4 ± 0.1
12	α-deuteriostyrene	21.6 ± 0.6	7.2 ± 0.5
13	β-d_2-styrene	24.9 ± 0.6	8.0 ± 0.3
14	α-methylstyrene	28.0 ± 0.5	8.5 ± 0.5

[a] All the kinetic data was obtained in 1,2-dichloroethane with 2% w/w Hpz as additive.

The effect of temperature on the k_2 values for the epoxidation of some representative alkenes has been studied. The Eyring plots are linear over a temperature range of 293–333 *K*. The activation enthalpies $\Delta H^{\neq}$ and entropies $\Delta S^{\neq}$ for the 2-chlorostyrene, 2-methylstyrene, 3-chlorostyrene, *cis*-β-methylstyrene, and *trans*-β-methylstyrene epoxidations by **1** and **2a** are listed in Table 5.

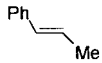
Table 5. Activation parameters for the asymmetric alkene oxidations.[a]

Alkenes	(**1**) $\Delta H^{\neq}$ [kcal mol^{-1}]	(**1**) $\Delta S^{\neq}$ [e.u.]	(**2a**) $\Delta H^{\neq}$ [kcal mol^{-1}]	(**2a**) $\Delta S^{\neq}$ [e.u.]
2-chlorostyrene	11.6 ± 0.4	−(31.6 ± 1.8)	11.6 ± 0.4	−(34.8 ± 2.3)
2-methylstyrene	11.5 ± 0.4	−(31.5 ± 1.5)	11.3 ± 0.5	−(33.9 ± 2.0)
3-chlorostyrene	13.3 ± 1.0	−(25.0 ± 2.2)	11.8 ± 1.0	−(27.6 ± 2.1)
cis-β-methylstyrene	12.1 ± 0.6	−(29.4 ± 2.0)	14.0 ± 0.6	−(26.7 ± 2.8)
trans-β-methylstyrene	12.7 ± 0.6	−(27.8 ± 1.4)	11.1 ± 0.6	−(35.6 ± 2.4)

[a] All the kinetics data were obtained in 1,2-dichloroethane with 2% w/w Hpz as additive.

Solvent effect: The solvent-dependence of the enantioselectivity has been examined. For the reactions with **1**, the solvent shows little influence on the enantioselectivity, and comparable enantioselectivities were obtained with benzene or dichloromethane as the solvent. However, when **2a** was the oxidant, the styrene epoxidation resulted in 62% *ee* with benzene as the solvent (Table 6, entry 2), and dropped to 41% *ee* when the reaction was conducted in dichloromethane

Table 6. Effect of solvent on the asymmetric alkene epoxidations by complex **2a**.[a]

Entry	Solvent	 *ee* [%]	$k_2 \times 10^4$ [$dm^3\ mol^{-1}\ s^{-1}$][b]	 *ee* [%]	$k_2 \times 10^4$ [$dm^3\ mol^{-1}\ s^{-1}$][b]
1	toluene	–	14.1 ± 0.2	62	9.3 ± 0.2
2	benzene	62	13.2 ± 0.1	67	9.2 ± 1.6
3	1,2-dichloroethane	–	7.1 ± 0.2	–	8.4 ± 0.1
4	dichloromethane	41	3.5 ± 0.1	32	4.2 ± 0.1
5	acetonitrile	33	0.97 ± 0.05	26	1.4 ± 0.2
6	ethyl acetate	–	–	38	–

[a] Same reaction conditions as those given in Table 1 were employed. [b] The second-order rate constants were determined at 298 K.

(Table 6, entry 4). Moreover, employing acetonitrile as the solvent led to a low epoxide yield of 13% and enantioselectivity of 33% *ee* (Table 6, entry 5). Similarly, the stoichiometric epoxidations of 4-chlorostyrene, *cis*-/*trans*-β-methylstyrenes, and 1,2-dihydronaphthalene by **2a** afforded the best enantioselectivities only when benzene was the solvent (see the Supporting Information). Gross and co-workers[3b] reported similar solvent dependence for the [Ru^{II}(D_2-Por*)(CO)]-catalyzed styrene epoxidation, and that the use of aromatic solvents, such as benzene and toluene, was found to give the highest enantioselectivity.

The second-order rate constants (k_2) of the reaction of *trans*-β-methylstyrene with **2a** in different solvents were measured (Table 6); the k_2 values decrease in the order: toluene ≈ benzene > 1,2-dichloroethane > dichloromethane > acetonitrile. Parallel with the descending k_2 values, the enantioselectivity also decreases in a similar fashion: 67% (benzene), 32% (CH_2Cl_2), and 26% (CH_3CN) (Table 6). It should be noted that the *trans*-β-methylstyrene epoxidations in the above-mentioned solvents exhibited isosbestic spectral changes and with kinetics conformed to pseudo-first-order decay profile.

In this work, a solvent polarizability parameter (E_T)[18] was employed to correlate the k_2 and enantioselectivity values of the *trans*-β-methylstyrene oxidation in various solvents. The E_T parameter is generally regarded as a better indicator of solvent polarity than the dielectric constant because it is an experimental measure of the molecular interaction between solvent and solute.[18] In this work, we found that the $\log[(100+ee)/(100-ee)]$ values obtained in various solvents do not correlate linearly with the E_T parameter, and a $\log k_2$ versus E_T plot does not establish a linear free-energy relationship. Given that the enantiomeric ratio is directly proportional to the difference in free-energy changes of the diastereomeric transition states ($\Delta\Delta G^{\neq}$).[19] This finding

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suggests that the solvent effect on the enantioselectivity cannot be explained by specific interaction between solvent and $[Ru^{VI}(Por^*)O_2]$ in the transition state.

Compared with complex **1**, the chiral scaffold of the D_2-symmetric complex **2a**, consisting of four staggered chiral threitol units, would be more conformationally flexible through rotation of the *meso*-phenyl groups and the ethereal linkages. Indeed, for **2a**, the use of C_6D_6 or CD_2Cl_2 as the solvent would result in a different ^1H NMR spectral pattern at room temperature; significant chemical shift difference ($\Delta\delta_H$) with magnitude from 0.11–0.47 ppm were found for many of the signals (see Table S1, Supporting Information). Of particular note is that the signals corresponding to the *gem*-methyl groups are shifted considerably downfield from $\delta_H = 0.78$ and -0.64 in CD_2Cl_2 to $\delta_H = 0.93$ and -0.15, respectively, in C_6D_6. In addition, the absorption peaks for the CH^b protons are also shifted downfield from $\delta_H = 2.62$ in $CDCl_3$ to $\delta_H = 3.05$ in C_6D_6 (see Figure 3 for atom labeling). However, the ^1H NMR

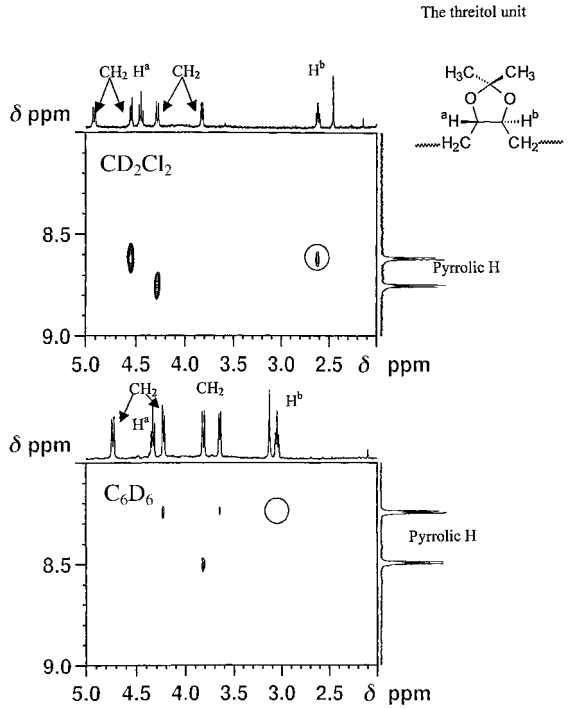
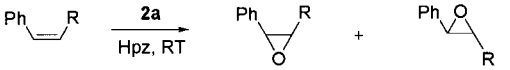


Figure 3. Two-dimensional NOESY ^1H NMR (500 MHz) spectra of **2a** in CD_2Cl_2 and in C_6D_6.

spectra of **1** in C_6D_6 and $CDCl_3$ are almost identical (i.e., no change in chemical shifts). Indeed, the two-dimensional nuclear Overhauser effect (NOESY) NMR spectrum of **2a** recorded in CD_2Cl_2 at room temperature revealed significant NOE between the threitol groups (CH^b and CH_2) and the β-pyrrolic protons (Figure 3). It is noteworthy that this NOE for the threitol groups was completely lost when the NOESY NMR spectrum was recorded in C_6D_6. These findings strongly suggest that in C_6D_6 the threitol substituents of **2a** are slightly displaced from the deshielding porphyrin core, creating a more open chiral cavity than in CD_2Cl_2. Accordingly, the more open chiral cavity for **2a** in aromatic solvents, such as benzene, would result in better resolution of the diastereomeric transition states leading to higher enantioselectivity.

Stereoselectivity in oxidation of aromatic alkenes by chiral *trans*-dioxoruthenium(VI) porphyrins: *cis*-Alkenes, such as stilbene, have been widely employed as a mechanistic probe for concertedness in alkene oxidations by highly reactive metal-oxo complexes. *cis*-Stilbene is particularly prone to *cis*–*trans* isomerization by C–C bond rotation to form *trans*-stilbene oxide, if the epoxidation involves an acyclic intermediate.[20] In this work, the reaction of *cis*-stilbene with **1** or **2a** produced the *cis*-epoxide exclusively, and no *trans*-stilbene oxide was detected (see reaction given in Table 7). This result coincides with our previous findings that the *cis*-stilbene oxidation by sterically congested dioxoruthenium(VI) porphyrins, such as $[Ru^{VI}(tdcpp)O_2]$ and $[Ru^{VI}(tmopp)O_2]$ complexes (H_2tdcpp = *meso*-tetrakis(2,6-dichlorophenyl)porphyrin; H_2tmopp = *meso*-tetrakis(2,4,6-trimethoxyphenyl)-porphyrin), afforded *cis*-stilbene oxide stereoretentively.[10d] However, it should be noted that the analogous reaction with the less hindered $[Ru^{VI}(oep)O_2]$ (H_2oep = 2,3,7,8,12,13,17,18-octaethylporphyrin) gave *trans*-stilbene oxide as the major product with a *trans*:*cis*-oxide ratio = 44:16.[10a]

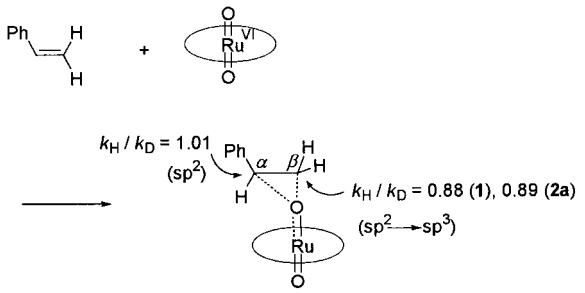
Table 7. Nonstereoselective *cis*-alkene oxidations.



Entry	R	Solvent	Yield [%]	*ee* [%]	Yield [%]	*ee* [%]	*cis*:*trans* Ratio
1	Ph	C_6H_6	75	–	0	–	
2	CH_3	C_6H_6	75	40	1	10	99:1
3	CH_3	CH_2Cl_2	68	18	4	8	95:5
4	D	C_6H_6	52	69	6	10	89:11
5	D	CH_2Cl_2	36	51	12	9	75:25

The stereoselectivity of the epoxidation reaction was further examined by means of *cis*-β-methylstyrene and *cis*-β-deuteriostyrene as mechanistic probes. As depicted in the reaction given in Table 7, the *cis*-β-methylstyrene epoxidations by **1** and **2a** produced the *trans*-epoxide as a minor product: *cis*:*trans* ratios = 93:7 (**1**) and 99:1 (**2a**) in C_6H_6; 90:10 (**1**) and 95:5 (**2a**) in CH_2Cl_2. Moreover, the reaction of *cis*-β-deuteriostyrene with **2a** at room temperature in benzene and dichloromethane are nonstereoselective with *cis*:*trans*-epoxide ratio = 89:11 in C_6H_6 and 75:25 in CH_2Cl_2. The reactions were repeated three times for each ruthenium oxidant, and the *cis*/*trans* selectivities were obtained reproducibly. The purity of the *cis*-alkenes was checked by ^1H NMR spectroscopy, and *trans*-alkenes were not detected at the end of the reactions. A control experiment was performed by stirring a mixture of pure *cis*-β-deuteriostyrene oxide and $[Ru^{IV}(Por^*)(pz)_2]$ in dichloromethane at room temperature for 12 h; the starting *cis*-epoxides were recovered without *trans*-epoxide being detected. This confirms that the formation of *cis*- and *trans*-epoxides did not arise from the $[Ru^{IV}(Por^*)(pz)_2]$-catalyzed epoxide isomerization.[16]

The secondary kinetic H/D isotope effect (KIE) for the reactions of $[Ru^{VI}(Por^*)O_2]$ with α,β-deuteriostyrenes has been measured. As illustrated in Scheme 2, a clear inverse secondary isotope effect[21] was observed only at the β-carbon atom, but not the α-carbon atom. This implies that only the β-carbon atom changes its hybridization from sp^2 to sp^3 [k_H/k_D =



Scheme 2. Secondary KIE for the styrene oxidation by the chiral dioxoruthenium(VI) porphyrins.

0.88(**1**) or 0.89 (**2a**)] upon advancing to the transition state while the α-carbon atom remains essentially sp^2 hybridized [$k_H/k_D = 1.01$ (**1**) or 0.99 (**2a**)]. The inverse secondary KIE result is in accord with a nonsymmetrical transition state, wherein the C–O bond formation is more advanced at the β-carbon atom than at the α-carbon atom. The loss of stereoselectivity and the KIE results are consistent with rate-limiting formation of an acyclic intermediate for the alkene epoxidation.

Linear free-energy relationship for epoxidation of styrenes: To probe the transition state for the asymmetric alkene epoxidations, we have investigated the effect of *para* substituents on the rate of styrene epoxidations. By analogy with previous studies on some other dioxoruthenium(VI) porphyrins,[10] both electron-donating and electron-withdrawing groups moderately accelerate the reactions (1.5-fold for 4-methoxystyrene). For **1** and **2a**, a plot of the $\log k_{rel}$ versus σ^+ [$k_{rel} = k_2$(substituted styrene)/k_2(styrene)] produces concave Hammett curves, which is in contrast to the linear Hammett correlations ($\rho^+ = -1.9$ to -2.1) obtained for the styrene oxidations by [Fe^{IV}(tmp$^{\bullet+}$)O] (H_2tmp = tetramesitylporphyrin),[22] [(Br_8tpp)Cr^V(O)(X)] (H_2Br_8tpp = *meso*-tetrakis(2,6-dibromophenyl)porphyrin)[23] and [$Ru^{VI}(N_4)O_2]^{2+}$ (N_4 = macrocyclic tertiary amines)[24] complexes. The participation of carbocation or alkene-derived carbocation radical is not favored, since the rate-limiting formation of carbocation by electrophilic addition to the C=C bond is usually associated with large and negative ρ^+ values, as exemplified in the hydration ($\rho^+ = -3.5$)[25] and bromination ($\rho^+ = -4.1$)[26] reactions.

If the styrene epoxidation involves rate-limiting formation of a carboradical intermediate, its transition-state energy would be influenced by the polar substituent and spin delocalization effects as spin density is developing at the α-carbon atom upon progressing to the transition state. Considering spin delocalization and polar effects, we employed the $\sigma_{JJ}^{\bullet}$ and σ_{mb} parameters,[27] developed by Jiang and Ji, in a dual-parameter Hammett correlation ($\log k_{rel} = \rho_{JJ}^{\bullet}\sigma_{JJ}^{\bullet} + \rho_{mb}\sigma_{mb}$) for the styrene epoxidations. Two straight lines with slope = 1.00 and $R = 0.99$ [$\log k_{rel} = 1.29\sigma_{JJ}^{\bullet} - 0.44\sigma_{mb}$ (**1**) and $\log k_{rel} = 1.35\sigma_{JJ}^{\bullet} - 0.64\sigma_{mb}$ (**2a**)] were established (Figure 4). The linear free-energy correlation with spin delocalization and polar effects is a good indication of radical character developed at the α-carbon in the transition state. The positive $\rho_{JJ}^{\bullet}$ values suggest that the epoxidation reaction is promoted by the spin delocalization effect, while the negative ρ_{mb} value is consistent with the electrophilic nature of the oxoruthenium complexes. The magnitude of the $|\rho_{JJ}^{\bullet}/\rho_{mb}| = 2.93$ for **1** and 2.10 for **2a** indicates that spin delocalization is more important than the polar effects.[10d,f]

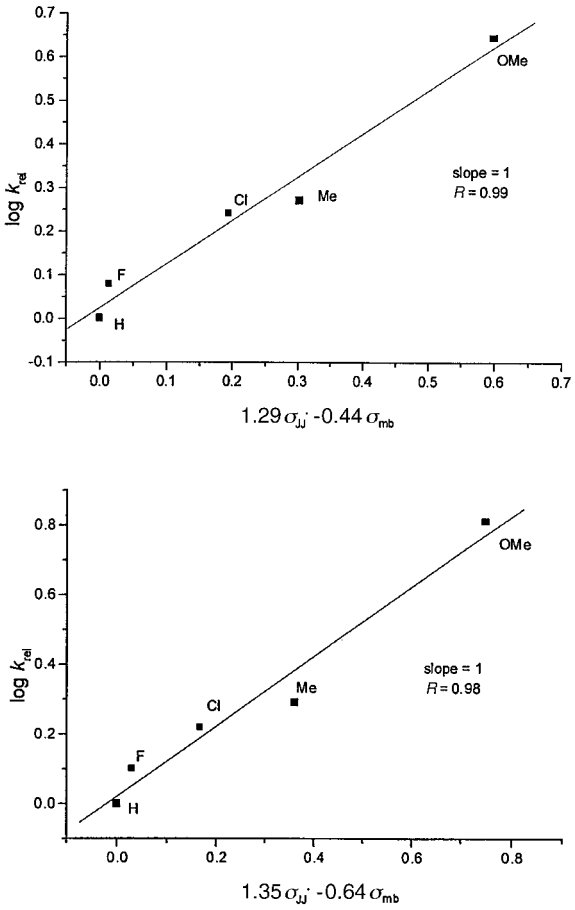


Figure 4. Dual-parameter Hammett correlations for the oxidation of *para*-substituted styrenes by **1** (top) and **2a** (bottom).

Discussion

Based on the results discussed in the previous sections including the secondary kinetic isotope effect (KIE) results, we conclude that the reactions of aromatic alkenes with [Ru^{VI}(Por*)O_2] proceed through the rate-determining formation of a benzylic radical intermediate. The carboradical intermediate would undergo ring closure or C–C bond rotation thereby forming *cis*- and *trans*-epoxides, respectively (Scheme 3). There are several literature reports which propose the participation of carboradical intermediates in alkene oxidations by highly reactive metal–oxo complexes; some notable examples are those involving the [Fe^{IV}(O)(tmp)$^{\bullet+}$],[28b,c] [Mn^V(O)(salen)X],[28d] and [Ru^{IV}(O)(L^1)(L^2)]$^{2+}$ (L^1 and L^2 = polypyridine ligands) complexes.[8c]

With regards to the *cis*-alkene epoxidation, the stereoretention is affected by the bulky substituents on the porphyrin macrocycle. For instance, the *cis*-stilbene oxidations by **1** and **2a** exhibited complete stereoretention, whereas

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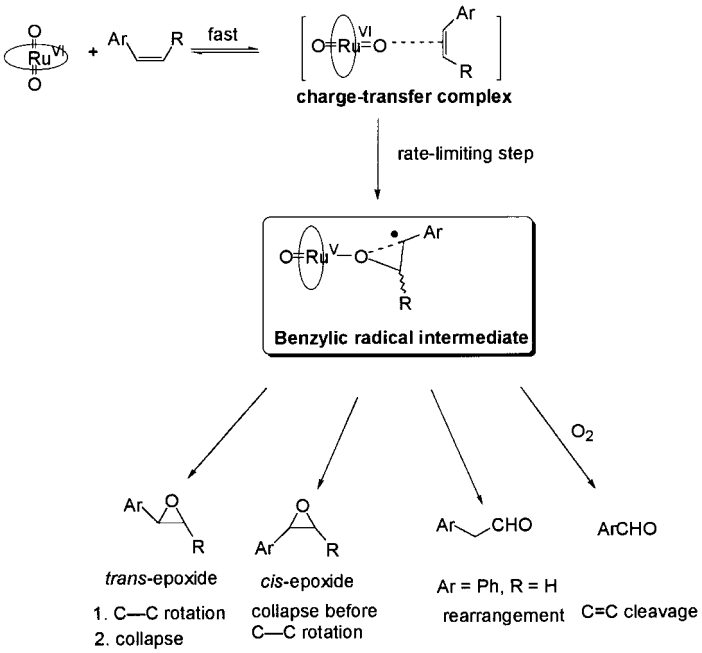


Scheme 3. Proposed mechanism for alkene oxidations by dioxoruthenium(VI) porphyrins.

the analogous reaction with *cis*-β-deuteriostyrene led to substantial formation of the *trans*-epoxide. We reason that bulky groups may hinder the C–C rotation of the benzylic radical intermediate, resulting in stereoretention in the *cis*-stilbene oxidation.

Facial selectivity of the D_4- and D_2-symmetric chiral dioxoruthenium(VI) porphyrins

Side-on approach model: In our earlier attempt to bring about enantioselective styrene epoxidation by chiral metal-oxo complexes, we employed $[Ru^{IV}(terpy)(cxhn)(O)](ClO_4)_2$ [terpy = 2,2′:6′,2″-terpyridine; cxhn = (−)-(1*R*,2*R*)-tetramethyl-1,2-diaminocyclohexane] as the oxidant.[8b] However, this complex failed to effect asymmetric induction upon reaction with styrene. This negative result is ascribed to the undesirable disposition of the terpyridine and chiral diamine ligands, resulting in the lack of enantiofacial discrimination. Prior to this study, Halterman and co-workers reported that the $[Mn^{III}(D_4\text{-Por}^*)Cl]$ complex was an effective catalyst for asymmetric epoxidation of styrene and *cis*-β-methylstyrene with sodium hypochlorite as the oxidant.[2f] We envisioned and established by X-ray crystal structure analysis that the dioxoruthenium group of complex **1** is surrounded by four dinorbanbenzene moieties to create a D_4-symmetric chiral pocket,[3d] which would facilitate prochiral facial recognition of the alkene (Figure 5).

The facial selection for the **1**-mediated asymmetric alkene epoxidation can be rationalized by the "side-on" approach model; (*R*)-styrene oxide in 65% *ee* was obtained for the stoichiometric styrene epoxidation. The formation of the (*S*)-epoxide is less favored because of the steric interaction between the phenyl group and the chiral auxiliaries. We found that complex **1** effectively epoxidized *para*- and *meta*-substituted styrenes with enantioselectivities of 60–70% *ee*.

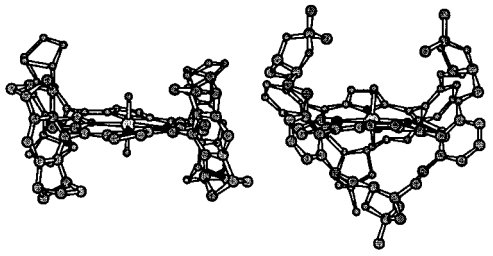
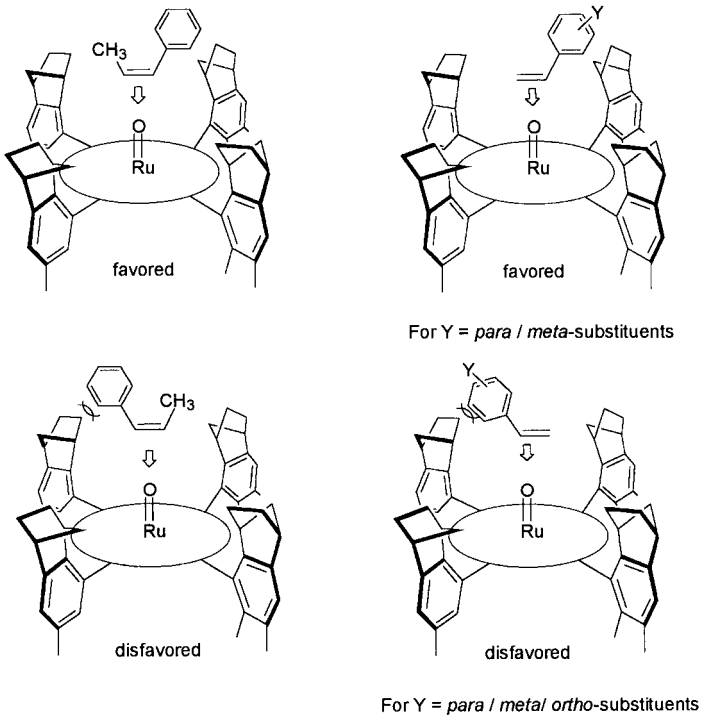


Figure 5. Molecular models of the homochiral complexes **1** and **2a**.

However, with *ortho*-substituted styrenes, such as 2-chloro- and 2-bromostyrenes as substrates, the epoxidations proceeded in considerably lower *ee* of ≈50% (see Table 1). Based on the "side-on approach" model (Scheme 4), it is conceivable that *ortho*-substitution of styrene would intensify steric interaction between the alkene and the chiral auxiliaries in both the pro-*R* and -*S* facial approaches, leading to reduced enantioselectivity.



Scheme 4. Side-on approach model for the D_4-symmetric chiral dioxoruthenium(VI) porphyrin.

Similarly, the reaction of *cis*-β-methylstyrene and 1,2-dihydronaphthalene with **1** preferentially afforded the (1*R*,2*S*)-epoxides in 72 and 82% *ee*, respectively (see Table 1). Analogous to some reported metalloporphyrin-catalyzed alkene epoxidations, reaction of *trans*-β-methylstyrene with **1** gave the *trans*-epoxide in 20% *ee*. Based on the "side-on approach" model, *trans*-alkene epoxidation would be hindered as a result of unfavorable nonbonding interaction of *trans*-alkene with the porphyrin ligand.[2, 3, 5, 29] Indeed, our kinetics studies revealed that the oxidation of *cis*-β-methylstyrene ($k_2 = (29.6 \pm 1.5) \times 10^{-4}\ dm^3 mol^{-1} s^{-1}$) is ≈1.4 times

faster that of its *trans* counterpart ($k_2 = (21.5 \pm 1.6) \times 10^{-4}$ dm^{3}mol^{-1}s^{-1}) at 298 *K* (Table 4).

Groves and co-workers[29] first proposed a side-on approach of the alkene to the putative metal–oxo species to account for the stereoselectivity in the *cis*-alkene oxidation catalyzed by metalloporphyrin complexes. It was suggested that the side-on approach would lead to more effective interaction of the filled π-orbital of the C=C bond with the $d_\pi - p_\pi$ M–O antibonding orbital. The side-on approach model has gained widespread acceptance in the oxidation chemistry of metalloporphyrins and has been used to explain the enantioselectivity of the chiral Mn(salen)-catalyzed asymmetric epoxidation of unfunctionalized alkenes.[1b,c]

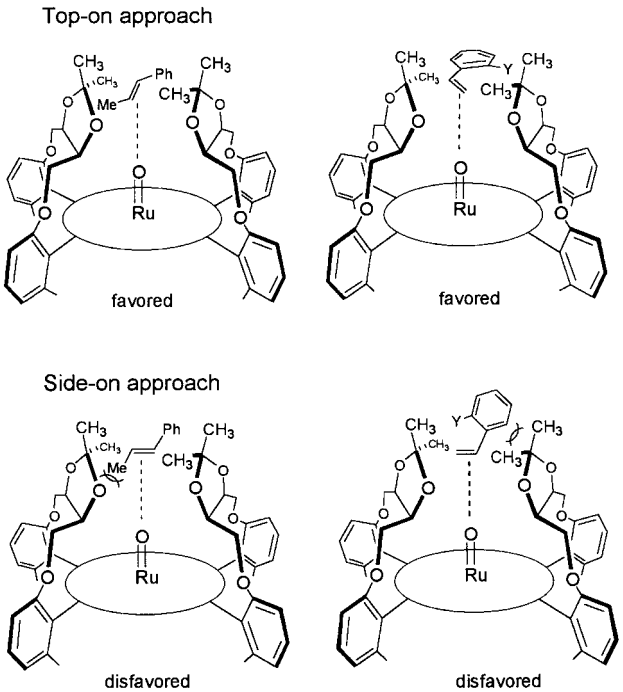
Top-on approach model: Based on the molecular structure of the [Ru^{II}(D_2-Por*)(CO)(EtOH)] complex reported earlier by Gross and co-workers,[3a] we have constructed a molecular model of [Ru^{VI}(D_2-Por*)O$_2$] (**2a**), which reveals that the Ru=O moiety is encased within a chiral pocket containing two C_2-symmetry-related threitol units. As depicted in Figure 5, the model shows that the porphyrin macrocycle exhibits a saddle-shaped distortion. In accord with theoretical calculations by Goddard and co-workers,[30c] complex **2a** shows substantially red-shifted Soret and Q bands (λ_{max} (CH_2Cl_2) = 442, 536 nm), consistent with a smaller HOMO–LUMO gap caused by saddle distortion.[30]

The styrene epoxidation by **2a** afforded the (*R*)-epoxide in 62% *ee*, and the enantioselectivity is somewhat insensitive to the *para*-substituent (≈65% *ee*). As discussed earlier, similar results were found for the stoichiometric epoxidation of *para*-substituted styrenes by **1**. However, **2a** reacted with 3-chlorostyrene to give 3-chlorostyrene oxide in 54% *ee*, which is well below the 72% *ee* value obtained when **1** was used as the oxidant. Based on the side-on approach model described above, *ortho*-substituted styrenes would be expected to react with **2a** with even lower enantioselectivity. However, the reaction of 2-chlorostyrene with **2a** in benzene containing 2% w/w Hpz yielded (*R*)-2-chlorostyrene oxide with an exceptionally high enantioselectivity of 88% *ee* as compared to 44% *ee* achieved with **1** as the oxidant. Other *ortho*-substituted styrenes are also epoxidized effectively by **2a** in ≈80% *ee*; their analogous reactions with **1** have attained only ≈50% *ee* (Table 1, entries 11–13).

Apparently, **2a** exhibits *trans*-preference in contrast to most of the metalloporphyrin-catalyzed alkene epoxidations, and up to 76% *ee* was achieved for its reaction with *trans*-cinnamyl chloride. Notably, the analogous reaction with **1** led to only 18% *ee* under identical reaction conditions (Table 1). Furthermore, the *trans*-β-methylstyrene epoxidation by **2a** proceeded with a larger k_2 value [$(8.4 \pm 0.1) \times 10^{-4}$ dm^{3}mol^{-1}s^{-1} (Table 4)] and higher enantioselectivity (72% *ee*), compared to the related values for the *cis*-β-methylstyrene ($k_2 = (5.8 \pm 0.2) \times 10^{-4}$ dm^{3}mol^{-1}s^{-1} (298 *K*) and 40% *ee*). These findings are inconsistent with the side-on approach model.

We have previously reported the epoxidation of *cis*- and *trans*-β-methylstyrenes by two sterically congested dioxoruthenium(VI) porphyrins, [Ru^{VI}(tdcpp)O$_2$] and [Ru^{VI}(tmopp)O$_2$].[10d] It is expected that the "side-on" approach of the *trans*-alkene to the Ru=O group would be disfavored by the bulky *ortho*-substituents in these complexes. Therefore, if the side-on approach is an obligatory pathway for alkene epoxidation, *trans*-β-methylstyrene should be unreactive toward these two bulky dioxoruthenium(VI) porphyrins. Yet, both *cis*- and *trans*-β-methylstyrenes were oxidized by [Ru^{VI}(tdcpp)O$_2$] and [Ru^{VI}(tmopp)O$_2$] to afford epoxides in good yields. Moreover, the reactions of styrene and *trans*-β-methylstyrene with these two complexes were found to have comparable $\Delta S^{\neq}$ values. To account for these findings, we previously proposed a top-on transition-state model for the *trans*-β-methylstyrene epoxidation.[10d] Based on the docking studies for the oxidation of *trans*-β-methylstyrene and *trans*-stilbene by [Cr^{V}(Br$_8$tpp)(O)(X)] (H_2Br_8tpp = *meso*-tetrakis(2,6-dibromophenyl)porphyrin), Bruice and co-workers had also suggested that the C=C bond is directed preferentially from the top of the Cr^{V}=O group.[31]

As an alternative to the "side-on approach" model, we propose here the "top-on approach" to rationalize the apparent *trans*-preference and facial selectivity of *trans*-β-methylstyrene epoxidation by the D_2-symmetric dioxoruthenium(VI) porphyrins. As shown in Scheme 5, the pro-*R* face of *trans*-β-methylstyrene can fit into the chiral scaffold confined



Scheme 5. Transition-state models for the D_2-symmetric chiral dioxoruthenium(VI) porphyrin.

by the two equatorial methyl groups of the threitol substituents. Consistent with this model, an increase in the size of the *gem*-dialkyl groups reduces the enantioselectivity of the *trans*-alkene epoxidation, since the bulky geminal substituents would hinder both prochiral facial approaches of the alkene. Both the pro-*R* and -*S* faces of *cis*-β-methylstyrene directed side-on to the Ru=O moiety would be disfavored as a result of steric interaction with the chiral auxiliaries. The "top-on approach" model was also proposed by Jacobsen and co-

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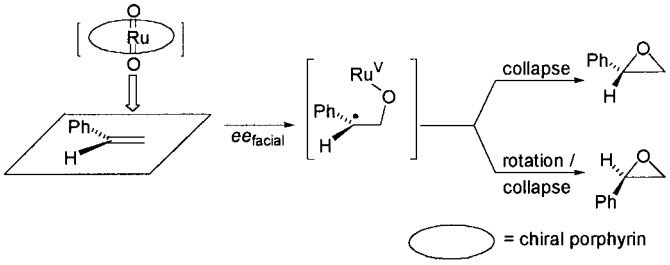
workers for the chiral [Mn(salen)]-catalyzed enantioselective epoxidation of tetrasubstituted alkenes.[32]

Epoxidation of *ortho*-substituted styrenes by **2a** gave the epoxides with exceptional enantioselectivity (≈80% *ee* vs 50% *ee* with **1** as oxidant), which can also be understood if the alkene approaches the Ru=O moiety from a top-on direction.

Facial selectivity and diastereoselectivity of epoxide ring closure: The aromatic alkene epoxidations by $[Ru^{VI}(Por^*)O_2]$ proceed via two nonconcerted C–O bond formation steps; attack of the C=C bond by the Ru=O generates a benzylic radical intermediate which undergoes either collapse (*cis*) or rotation/collapse (*trans*) processes to afford a mixture of *cis*- and *trans*-epoxides. Therefore, the observed enantioselectivity cannot depend solely on the facial selectivity of the initial C–O bond formation, but also upon the extent of *cis*–*trans* isomerization prior to the formation of the second C–O bond. In the case of styrene epoxidation, the α carbon (i.e., the only asymmetric carbon center to be created) remains epimeric; the rotation/collapse pathway tends to reduce the enantioselectivity by generating the opposite enantiomeric epoxide (Scheme 6).



Scheme 6. Nonstereospecific styrene oxidation.

The detrimental effect of the rotation/collapse pathway on the enantioselectivity can be evaluated by the use of *cis*-β-deuteriostyrene as a probe substrate. The epoxidation of *cis*-β-deuteriostyrene by **2a** under the standard reaction conditions (alkene = 1 mmol, **2a** = 15 μmol in degassed benzene containing Hpz (2% w/w) at room temperature) afforded a mixture of *cis*- and *trans*-β-deuteriostyrene oxides (*cis*/*trans* = 89:11, see Table 7). ^{1}H NMR analysis of the product mixture in the presence of the chiral shift reagent [Eu(hfc)$_3$] revealed the enantiomeric composition of the *cis*- (69% *ee*) and *trans*-epoxides (10% *ee*). Since all the steps shown in Scheme 6 are considered to be irreversible, the observed enantioselectivity (ee_{obs}) can be correlated to the *ee* values of the *cis*- and *trans*-β-deuteriostyrene oxides as such: $ee_{obs} = [(ee_{cis}) \times (\%\ cis) - (ee_{trans}) \times (\%\ trans)]$ according to the work of Jacobsen and co-workers.[33] Substituting the data into this equation gives the calculated ee_{obs} value = 63% *ee*, which closely matches the experimental value of 62% *ee*. Because the α-carbon of styrene is the only epimeric/asymmetric center, the facial selectivity (ee_{facial}) at the initial C–O bond formation step should approach the ee_{cis} value when the styrene epoxidation became fully stereospecific, and the rotation/collapse pathway should, therefore, account for approximately 7% *ee* reduction.

As mentioned earlier, the use of dichloromethane for the styrene epoxidation by **2a** results in lower enantioselectivity (40% *ee*) than that obtained with benzene as the solvent. We found that *cis*-β-deuteriostyrene was epoxidized by **2a** to give *cis*- (51% *ee*) and *trans*-epoxides (9% *ee*) with the *cis*:*trans* ratio being 75:25 (Table 7). The reduction in *ee* values is the result of lower facial selectivity (69% *ee* (benzene) vs. 51% *ee* (CH_2Cl_2)) together with the increased *cis*–*trans* isomerization in the epoxide ring closure step (*cis*/*trans*: 89:11 in C_6H_6 vs. 75:25 in CH_2Cl_2).

For the asymmetric epoxidation of 1,2-disubstituted alkenes, such as *cis*-/*trans*-β-methylstyrenes, two diastereomeric carboradical intermediates will be formed at the first C–O bond formation step while creating an asymmetric center at the β-carbon atom. Depending on the ligand asymmetry, the two carboradical intermediates would undergo different degrees of collapse and rotation/collapse processes resulting in their own *cis*–*trans* oxide composition. This situation has been meticulously analyzed by Jacobsen and co-workers in their investigations of asymmetric epoxidation of alkenes;[34] the facial selectivity (ee_{fac}) is given by $[(ee_{cis}) \times (\%\ cis) + (ee_{trans}) \times (\%\ trans)]$, while the diastereoselectivity of the epoxide ring closure is $\{[(1+ee_{cis})/(1-ee_{cis})] \times [1-ee_{trans})/(1+ee_{trans})]\}$. The diastereoselective ring closure would enhance the enantioselectivity of the *cis*-alkene epoxidation.

Experimental Section

General: All the ^{1}H NMR spectra were recorded in $CDCl_3$ at 500 MHz and coupling constants are rounded to 0.5 Hz unless otherwise noted. Gas chromatography was performed on a Hewlett-Packard 5890 Series II system equipped with a HP 5890A flame ionization detector and a HP 3395 integrator. The chiral capillary columns for separation of enantiomers were J&W Scientific Cyclodex-B (30 m), Chiraldex B-PM (30 m), and G-TA (30 m) columns. The *ee*'s were reproducible within ±2% error of the stated values.

Materials: Dichloromethane and 1,2-dichloroethane were refluxed over calcium chloride followed by distillation over calcium hydride. Benzene was distilled over sodium/benzophenone under an argon atmosphere before use. The deuterated solvents, CD_2Cl_2, $CDCl_3$, and C_6D_6 (Aldrich), were used as received. All the alkene substrates were obtained commercially and purified by either vacuum distillation from calcium hydride, or passing through a dry column of activated alumina prior to use. The purity of alkenes was checked by gas chromatography or ^{1}H NMR analysis. *m*-Chloroperoxybenzoic acid (Merck), dodecacarbonyltriruthenium(0) and pyrazole (Aldrich) were used as received. *cis*-β-Methylstyrene,[35] *cis*-β-[D$_1$]styrene,[35] β-[D$_2$]styrene,[36a,b] and α-[D$_1$]styrene[36a,c] were prepared according to the literature procedures. The D_4-[12] and D_2-symmetric[3a] porphyrins were prepared by previously reported procedures. The preparation and characterization of $[Ru^{II}(D_4\text{-}Por^*)(CO)(MeOH)]$[3d,e] and $[Ru^{II}(D_2\text{-}Por^*)(CO)(MeOH)]$[3f] have been reported elsewhere.

General procedure for the preparation of $[Ru^{VI}(Por^*)O_2]$: A solution of $[Ru^{II}(Por^*)(CO)(MeOH)]$ (0.05 mmol) in dichloromethane (5 mL) was added to a well-stirred solution of *m*-chloroperoxybenzoic acid (0.06 mmol) in dichloromethane (15 mL). The mixture was stirred for ≈5 min, and the resultant brown solution was separated by chromatography on a short alumina column. The product was eluted by dichloromethane (for **1**) or chloroform (for **2a–d**). The solution obtained was evaporated to dryness in vacuum, affording a dark purple solid in 70–80% yields.

$[Ru^{VI}(D_4\text{-}Por^*)O_2]$ (1): IR (KBr): $\tilde{\nu}$ = 1019 (oxidation-state marker band), 822 cm^{-1} (Ru=O); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 424 (5.38), 521 nm (4.35); ^{1}H NMR (300 MHz, C_6D_6, TMS): δ = 9.24 (s, 8H), 7.40 (s, 4H), 3.46 (s, 8H), 2.78 (s, 8H), 2.03 (m, 8H), 1.66 (m, 8H), 1.41–1.11 (m, 24H) and

0.96 (m, 8H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 27.18$, 27.56, 42.42, 44.40, 49.34, 113.99, 118.92, 127.91, 130.78, 141.53, 144.27, 148.06; FAB-MS: *m/z*: 1274 [M^+], 1258 [$M^+ - O$], 1242 [$M^+ - 2O$].

[Ru^{VI}(D_2-Por*)O_2] (2a): IR (KBr): $\tilde{\nu} = 1018$ (oxidation-state marker band), 818 cm^{-1} (Ru=O); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 442 (5.12), 536 nm (4.07); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 8.66$ (d, $J = 4.7$ Hz, 4H), 8.56 (d, $J = 4.5$ Hz, 4H), 7.75 (t, $J = 8.5$ Hz, 4H), 7.36 (d, $J = 8.5$ *Hz*, 4H), 7.29 (d, $J = 8.5$ Hz, 4H), 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); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 23.41$, 26.53, 65.33, 68.40, 73.65, 74.42, 75.05, 75.38, 108.22, 111.99, 114.18, 114.68, 121.30, 128.02, 128.57, 129.06, 129.92, 130.00, 130.88, 131.17, 144.52, 144.84, 158.99, 160.90; FAB-MS: *m/z*: 1379 [M^+], 1363 [$M^+ - O$], 1347 [$M^+ - 2O$].

Complex 2b: IR (KBr): $\tilde{\nu} = 1019$ (oxidation-state marker band), 821 cm^{-1} (Ru=O); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 443 (5.15), 534 nm (4.02); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 8.64$ (d, $J = 4.7$ Hz, 4H), 8.53 (d, $J = 4.7$ Hz, 4H), 7.74 (t, $J = 6.5$ Hz, 4H), 7.17–7.30 (m, *m*-phenyl H overlapped with solvent peak, 8H), 4.98 (d, $J = 10.4$ Hz, 4H), 4.60 (d, $J = 8.8$ Hz, 4H), 4.44 (t, $J = 9.0$ Hz, 4H), 4.23 (d, $J = 10.4$ Hz, 4H), 3.74 (d, $J = 9.0$ Hz, 4H), 2.63 (t, $J = 8.5$ 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); FAB-MS: *m/z*: 1491 [M^+], 1475 [$M^+ - O$], 1459 [$M^+ - 2O$].

Complex 2c: IR (KBr): $\tilde{\nu} = 1019$ (oxidation-state marker band), 819 cm^{-1} (Ru=O); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 441 (5.03), 535 nm (4.02); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 8.67$ (d, $J = 4.7$ Hz, 4H), 8.56 (d, $J = 4.7$ Hz, 4H), 7.76 (t, $J = 6.5$ Hz, 4H), 7.20–7.30 (m, *m*-phenyl H overlapped with solvent peak, 8H), 4.88 (d, $J = 10.4$ Hz, 4H), 4.60 (d, $J = 9.4$ Hz, 4H), 4.44 (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); FAB-MS: *m/z*: 1483 [M^+], 1467 [$M^+ - O$], 1451 [$M^+ - 2O$].

Complex 2d: IR (KBr): $\tilde{\nu} = 1021$ (oxidation-state marker band), 818 cm^{-1} (Ru=O); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 443 (5.18), 537 nm (4.05); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 8.50$ (d, $J = 4.7$ Hz, 4H), 8.41 (d, $J = 4.7$ Hz, 4H), 7.73 (d, $J = 8.2$ Hz, 16H), 7.19–7.32 (m, *m*-phenyl H overlapped with solvent peak, 16H), 7.10–6.90 (m, phenyl-H, 10H), 6.07 (t, $J = 7.5$ Hz, 2H), 5.96 (d, $J = 7.0$ Hz, 4H), 5.46 (t, $J = 7.5$ Hz, 4H), 4.65 (dd, $J^1 = 11.0$ Hz, $J^2 = 3.0$ Hz, 2H), 4.46 (d, $J = 7.0$ Hz, 2H), 4.36 (m, 4H), 4.28 (d, $J = 10.5$ Hz, 2H), 4.10 (d, unresolved, 8H), 3.98 (t, $J = 5.0$ Hz, 4H), 3.24 (t, $J = 5.0$ Hz, 2H); FAB-MS: *m/z*: 1876 [M^+], 1860 [$M^+ - O$], 1844 [$M^+ - 2O$).

Stoichiometric oxidation of alkenes by dioxoruthenium(VI) porphyrins: The dioxoruthenium(VI) complex (15–30 μmol) under an argon atmosphere was added to a degassed benzene solution (2 mL) containing alkene (1 mmol) and pyrazole (2% w/w). When the reaction was completed as indicated by the disappearance of the Soret band of the starting complex, the reaction mixture was filtered through a short alumina column with hexane/ethyl acetate (10:1) as the eluant to remove the ruthenium complex. After addition of internal standard, the organic products were then analyzed and quantified by either gas chromatography or ^{1}H NMR spectroscopy.

The bis(pyrazolato)ruthenium(IV) products (**3**) were eluted by dichloromethane, and addition of acetonitrile or *n*-hexanes gave [Ru^{IV}(Por*)$(pz)_2$] as a dark purple solid. Yield: 70–80%.

[Ru^{IV}(D_4-Por*)$(pz)_2$] (3a): Yield: 80%; IR (KBr): $\tilde{\nu} = 1009$ cm^{-1} (oxidation-state marker band); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 408 (5.25), 512 nm (4.12); FAB-MS: *m/z*: 1376 [M^+], 1309 [$M^+ - pz$], 1242 [$M^+ - 2pz$]; elemental analysis calcd (%) for $C_{90}H_{82}N_8Ru \cdot H_2O$: C 77.47, H 6.03, N 8.03; found: C 77.31, H 6.08, N 8.15; μ_{eff} (Evan's method) = 2.9 μ_B (solid, room temperature).

[Ru^{IV}(D_2-Por*)$(pz)_2$] (3b): Yield: 70%; IR (KBr): $\tilde{\nu} = 1006$ cm^{-1} (oxidation-state marker band); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 425 (5.09), 517 (4.04), 550 nm (sh); FAB-MS: *m/z*: 1483 [M^+], 1415 [$M^+ - pz$], 1347 [$M^+ - 2pz$]; elemental analysis calcd (%) 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; μ_{eff} (Evan's method) = 2.9 μ_B (solid, room temperature).

Determination of enantiomeric purities and absolute configurations: The enantiomeric purities of styrene oxide, 4-fluoro-, 4-chloro-, 4-trifluoromethyl-, 4-bromo-styrene oxide, *cis*-β-methylstyrene oxide, and 1,2-dihydronaphthalene oxide were determined by GC with a chiral column (Cyclodex-B). The enantiopurities of 2-chloro-, 2-fluoro-, 2-bromo-, 2-methyl-, and α-methylstyrene oxide were analyzed by GC with a chiral Chiraldex B-PM column. The enantiomeric purities of *trans*-β-methylstyrene oxide, and epoxycinnamyl chloride were determined by chiral GC on a Chiraldex G-TA column. The enantiopurities of 4-methylstyrene oxide, 3-nitrostyrene oxide, 3-chlorostyrene oxide, and 2-vinylnaphthalene oxide were determined by ^{1}H NMR spectroscopy in the presence of a chiral shift reagent [Eu(hfc)$_3$]. The absolute configurations of the epoxides were determined by chiral GC and comparison with the authentic enantiopure samples.

Molecular modeling studies: The three-dimensional computer model of **1** was established directly from its crystal structure with a Silicon Graphics (Indigo 2) computer with a Macromodel software (version 4.5). Construction of the structure of complex **2a** was based on the reported X-ray coordinates for [Ru^{II}(D_2-Por*)(CO)], and the O–Ru bond length was taken to be 1.74 Å, based on the measured distance obtained from the crystal structure of **1**. All alkene structures used in docking experiments were energy minimized prior to use.

Kinetic studies on the reactions of [Ru^{VI}(Por*)O_2] with alkenes: Kinetic measurements were performed on a Hewlett-Packard 8453A Diode Array spectrophotometer interfaced with an IBM-compatible PC and equipped with a Lauda RM6 circulating water bath; standard 1.0 cm quartz cuvettes were employed. The temperature of solutions during kinetic experiments was maintained to within ±0.2 °C.

The pseudo-first-order rate constants (k_{obs}) of the reaction between [Ru^{VI}(Por*)O_2] and alkenes were measured by monitoring the decrease of the Soret band under the condition that the alkene concentration is at least 100-fold in excess of [Ru^{VI}(Por*)O_2]. The k_{obs} values were obtained by nonlinear least-squares fits of ($A_f - A_t$) to time (t) according to the following equation: $(A_f - A_t) = (A_f - A_i)\exp(-k_{obs}t)$, where A_f and A_i are the final and initial absorbances, respectively, and A_t is the absorbance measured at time t. Kinetic data over four half-lives ($t_{1/2}$) were used for the least-squares fitting. Second-order rate constants, k_2, were obtained from the linear fit of k_{obs} values to the concentration of alkenes.

Activation enthalpy ($\Delta H^{\neq}$) and entropy ($\Delta S^{\neq}$) were obtained from the slope and the intercept, respectively, of the plot of $\ln(k_2/T)$ verus ($1/T$) on the basis of the Eyring equation: $\ln(k_2/T) = \ln(R/N\hbar) + \Delta S^{\neq}/R - \Delta H^{\neq}/RT$ where N is Avogadro's number, R is the universal gas constant, ħ is Planck's constant, and T is the temperature in Kelvin. The Eyring plots were fitted by unweighted linear least-squares methods with the software package Origin (Microcal Software, Inc). The cited errors in the activation parameters are the errors of the linear fits.

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