Asymmetric Catalysis

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# Asymmetric Epoxidation of Conjugated Olefins with Dioxygen**

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Biological oxygen-atom-transfer reactions, such as C–H oxidation and epoxidation, occur with complete or almost complete stereoselectivity at body temperature.[1] Moreover, these reactions are highly atom efficient because of the use of dioxygen as the stoichiometric oxidant. These reactions are catalyzed by enzymatic oxidation systems that include an oxygenase. For example, cytochrome P450, a typical monooxygenase, catalyzes stereoselective oxygen-atom-transfer reactions. In this biological oxidation, dioxygen, which is taken from air, is activated to an active oxo species by a rather complicated proton and electron transfer (PET), in which multiple enzymes participate; water is coproduced in this oxygen activation process.[1] It is still difficult to implement this activation process by chemical methods. Mukaiyama and co-workers reported a manganese(salen)-catalyzed asymmetric aerobic epoxidation that used an aldehyde as a sacrificial reductant instead of the complicated electron transfer system.[2] On the other hand, in metal-catalyzed oxidation processes, an active high-valent metal species is reduced to a low valent species, and dioxygen can oxidize some low valent metal ions. Thus, dioxygen has also been used as a terminal oxidant for oxygen-atom-transfer reactions.[3,4] Groves et al. reported aerobic epoxidation using a dioxoruthenium(VI)(porphyrin) complex as a catalyst under ambient pressure.[3a] Che and co-workers reported the asymmetric version of this epoxidation with a chiral ruthenium complex under a pressure of 8 atmospheres in oxygen.[3b] Beller and coworkers reported Sharpless asymmetric dihydroxylation using dioxygen as the stoichiometric oxidant at 50 °C.[4] Despite the mechanistic complexity, biological oxygen-atom-transfer reactions are highly attractive for organic synthesis owing to the above-described features. Hence, we investigated the use of a molecular catalyst to activate dioxygen and catalyze the transfer of an oxygen atom enantioselectively in a similar manner to biological oxidation. As discussed above, the oxidation catalyzed by P450 needs two protons and two electrons for oxygen activation and transfers one oxygen atom with coproduction of water. That is, the supplied protons and electrons are consumed for the generation of water. An oxidation reaction is a process in which two electrons are transferred from a substrate to an oxidant. Thus, we inferred that the complicated PET system would be unnecessary for the oxygen activation if the coproduced water could be recycled as a proton source, and another oxidation step could be incorporated into the catalytic cycle for biological oxidation. We have previously discovered asymmetric aerobic alcohol oxidation using ruthenium(NO)(salen) complexes **1** as catalysts under irradiation with visible light.[5] Based on the kinetic study of this oxidation, we proposed that irradiation promotes the dissociation of the apical NO ligand and the resulting alcohol-bound ruthenium(III)(salen) species undergoes single electron transfer (SET) to give a (superoxo)ruthenium(IV) species.[5c] It is well recognized that a (superoxo)metal species is converted into the corresponding hydroperoxo species by proton-coupled electron transfer (PCET)[1] and that metal-bound water is more acidic than water itself.[6] Thus, we hypothesized that an (aqua)-(superoxo)ruthenium(IV) species would undergo PCET to give a (hydroperoxo)(hydroxo)ruthenium(V) species, the hydroperoxo group of which is activated by intramolecular hydrogen bonding, and, in turn, would undergo oxygen atom transfer and give a dihydroxo species. Dihydroxo metal species are known to undergo oxo–hydroxo tautomerization[7] to give (aqua)(oxo) species. Based on these results[5c] and previous reports,[1,6,7] we considered that catalytic aerobic oxygen-atom-transfer reactions, the catalytic cycle of which include two oxidation steps (a and c) and a water-recycling step (b) via the (hydroperoxo)(hydroxo)ruthenium intermediate and the (aqua)(oxo)ruthenium intermediate, could be realized by using complexes **1** as catalyst under irradiation in the presence of water (Scheme 2).[8] Indeed, we have previously achieved highly enantioselective aerobic sulfide oxidation (with **1a**) and epoxidation (with **1b**) at room temperature under irradiation with the visible light without the addition of proton and electron sources (Scheme 1 and Scheme 2).[9] However, biological oxidation proceeds using air as the oxidant[10] and without photoirradiation. Thus, herein we investigate asymmetric aerobic oxygen-atom-transfer reaction without irradiation.

From our previous studies on the aerobic oxidation, we had thought that irradiation is required not only for the dissociation of the nitroso group but also for the SET from **2** to dioxygen.[5c] During the continued study of aerobic alcohol oxidation, we fortunately found that complex **1c** shows the desired aerobic oxidation catalysis, without irradiation, after it is exposed to visible light for a longer time (4 h × 6; Scheme 3). Moreover, hydrogen bonding was recently reported to facilitate SET.[11] Together, this finding and report prompted us to explore asymmetric aerobic epoxidation using **2b** as catalyst without irradiation.

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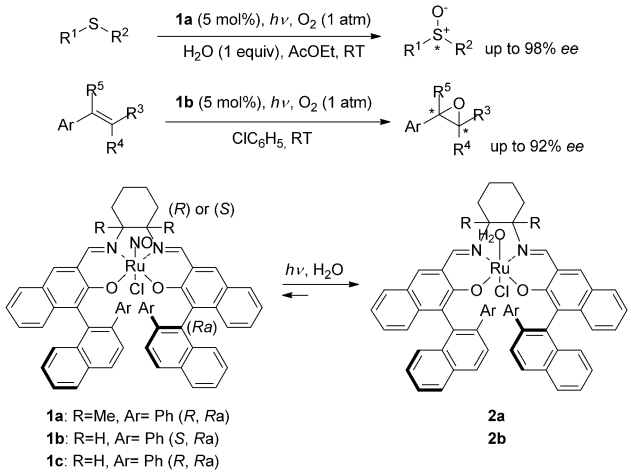
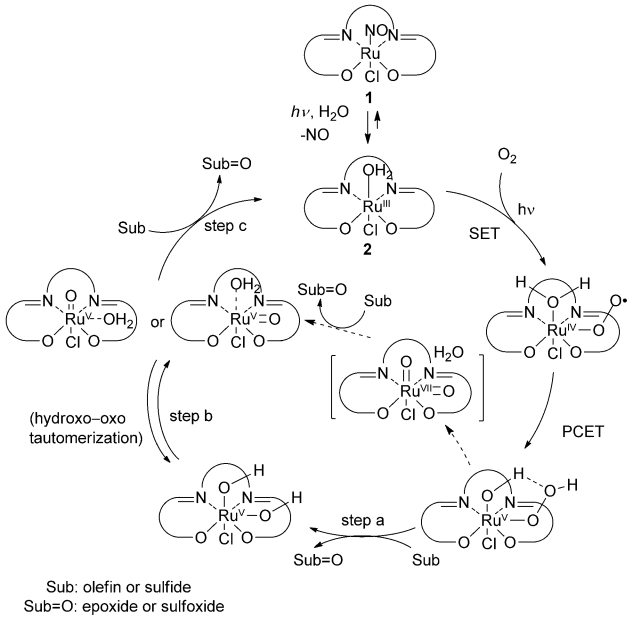
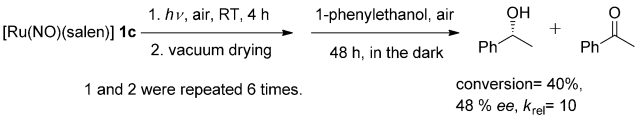



***Scheme 1.*** Asymmetric aerobic sulfide oxidation and epoxidation using ruthenium(NO)(salen) complexes **1** under irradiation conditions.

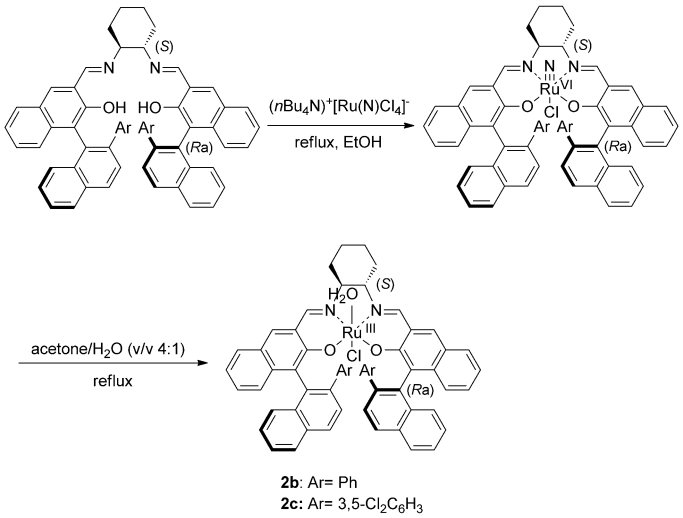



***Scheme 2.*** The proposed mechanism for the aerobic sulfide oxidation and epoxidation using complexes **1** under irradiation conditions. The salen ligand has been simplified for clarity.




***Scheme 3.*** Asymmetric aerobic alcohol oxidation with pre-irradiated ruthenium(NO)(salen) complex **1c**.

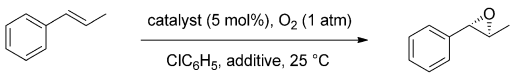
Towards this aim, we prepared complex **2b** by two methods: 1) by heating the ligand and $RuCl_3 \cdot nH_2O$ in ethanol to reflux and 2) by heating the ligand and $(nBu_4N)^+[Ru(N)Cl_4]^-$ in ethanol to reflux and then heating the resulting complex in aqueous acetone to reflux (Scheme 4).[12] The product (**2b**) of both reactions gave




***Scheme 4.*** Preparation of complexes **2b** and **2c**.

identical MS spectra, and in the epoxidation of (*E*)-1-phenyl-1-propene in the dark at room temperature the use of **2b** prepared by method 1 and the use of **2b** prepared by method 2 gave the epoxide with similarly high enantioselectivity (86% *ee* and 87% *ee* (Table 1, entry 1), respectively), albeit in a modest yield. However, the **2b** prepared by method 1 decomposed on standing at room temperature, whereas the **2b** prepared by method 2 was more stable. We synthesized **2c**, which has a robust salen ligand,[13] by method 2. When **2c** was used as the catalyst the yield was increased without any decrease in the enantioselectivity (Table 1, entry 2). Recently, we observed that the yield of the epoxidation catalyzed by a Nb complex in the presence of aqueous hydrogen peroxide was improved by the addition of brine.[14] The present epoxidation is considered to proceed via

***Table 1:*** Asymmetric aerobic epoxidation of (*E*)-1-phenyl-1-propene using ruthenium(salen) complexes **2b** and **2c** as catalysts.[a]




| Entry | Cat. | Additive | *t* [h] | Yield [%][b] | *ee* [%][c] | Configuration[d] |
|---|---|---|---|---|---|---|
| 1 | **2b** | – | 24 | 42 | 87 | (−)-(1*S*,2*S*) |
| 2 | **2c** | – | 24 | 95 | 86 | (−)-(1*S*,2*S*) |
| 3[e] | **2c** | brine | 24 | >99 | 86 | (−)-(1*S*,2*S*) |
| 4[e,f] | **2c** | brine | 48 | 91 | 86 | (−)-(1*S*,2*S*) |
| 5[e,g] | **2c** | brine | 48 | 91 (82)[h] | 91 | (−)-(1*S*,2*S*) |
| 6[i] | **2c** | – | 48 | n.r. | – | – |

[a] Reactions were run with Ru catalyst (5 mol%) at 25°C in chlorobenzene (0.5 mL) on a 0.1 mmol scale under oxygen, unless otherwise stated. [b] Determined by $^1$H NMR analysis using phenanthrene as an internal standard. [c] Determined by GC analysis on a chiral capillary column. See the Supporting Information. [d] Determined by comparison of the optical rotation with the literature value. The sign in parentheses indicates the sign of optical rotation measured in $CHCl_3$. [e] Run on a 0.5 mmol scale in chlorobenzene/brine (*v*/*v* 1:1). [f] Run with air. [g] Run at 0°C. [h] The number in parentheses is the yield of the isolated product. [i] Run in the presence of molecular sieves (4 Å). n.r. = no reaction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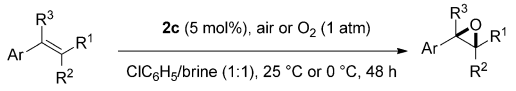
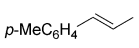
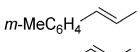
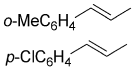
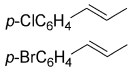
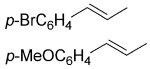
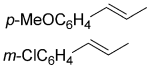
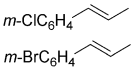
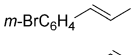
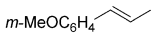
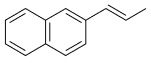
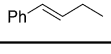
a hydroperoxo species. Thus, we also carried out this reaction in the presence of brine and were able to obtain a higher yield (Table 1, entry 3). Significantly, the epoxidation proceeded with air as the oxidant without any decrease in the enantioselectivity, albeit with reduced yield.[2e] However, when the reaction time was increased an acceptable yield was achieved (Table 1, entry 4). Moreover, the epoxidation using dioxygen could be carried out at 0 °C with an increase of enantioselectivity (to 91 % *ee*; Table 1, entry 5). The reaction was completely suppressed when molecular sieves (4 Å) were added, thus indicating the important role of the ruthenium-bound water (Table 1, entry 6).

Under the optimized reaction conditions, we examined epoxidation of other conjugated olefins with air (Table 2). The epoxidation of (*Z*)-1-phenyl-1-propene proceeded with high enantioselectivity (93 % *ee*) in a good yield (Table 2, entry 1) and no formation of the *E*-configured epoxide was detected. Good enantioselectivity (80 % *ee*) and good yield were obtained in the reaction of (*E*)-2-phenyl-2-butene with air after 24 h (Table 2, entry 2), but a longer reaction time resulted in a slightly decreased yield as a result of epoxide–ketone rearrangement. It has been reported that ruthenium-(salen) complexes catalyze both asymmetric epoxidation and epoxide ring opening but the sense of enantioselectivity of these reactions is opposite.[15] The rearrangement was suppressed by lowering the reaction temperature to 0 °C but the epoxidation reaction became slow. However, the reaction with dioxygen at 0 °C proceeded with a high yield and a better enantioselectivity (84 % *ee*; Table 2, entry 3). The reaction of 2-methyl-1-phenyl-1-propene was rather slow and the enantioselectivity was 76 % *ee* (Table 2, entry 4). The yield was not increased when the reaction was carried out for 72 h at 0 °C under oxygen, but the enantioselectivity was improved to 80 % *ee* (Table 2, entry 5). The effect on enantioselectivity of a substituent on the aryl moiety was examined next. The reaction of (*E*)-1-(*p*-methylphenyl)-1-propene provided the epoxide in 77 % *ee* together with a small amount of the ketone (Table 2, entry 6). Better enantioselectivity (83 % *ee*) and better yield were obtained at 0 °C under oxygen (Table 2, entry 7). The epoxidation of (*E*)-1-(*m*-methylphenyl)-1-propene in air gave the epoxide with 92 % *ee* in 92 % yield (Table 2, entry 8). The epoxidation of (*E*)-1-(*o*-methylphenyl)-1-propene, however, showed only modest enantioselectivity (53 % *ee*) even at 0 °C under oxygen (Table 2, entry 9). Thus, we further examined the effect of *para*- and *meta*-substituents on enantioselectivity. The enantioselectivity of the epoxidations of (*E*)-1-(*p*-chlorophenyl)- and (*p*-bromophenyl)-1-propenes at 0 °C under oxygen was 75 % *ee* (Table 2, entries 10 and 11). The reaction of (*E*)-1-(*p*-methoxyphenyl)-1-propene proceeded with a slightly better enantioselectivity (81 % *ee*) but considerable rearrangement of the epoxide was observed even at 0 °C; this rearrangement is probably due to the high acid sensitivity of the epoxide (Table 2, entry 12). The *meta*-substituted (*E*)-1-phenyl-1-propenes are better substrates for this epoxidation. The reactions of the chloro-, bromo-, and methoxy-substituted compounds gave the epoxides with high enantioselectivity (93, 94, and 82 % *ee*) and good yields (Table 2, entries 13, 14, and 15, respectively). The enantioselectivity of the epoxidation of (*E*)-1-(*m*-methoxyphenyl)-1-propene at 0 °C was 86 % *ee* (Table 2, entry 16). The epoxidation of (*E*)-2-(1-propenyl)-naphthalene proceeded with high enantioselectivity (95 % *ee*) and 91 % yield (Table 2, entry 17). Good enantioselectivity (80 % *ee*) and moderate yield were also obtained for the reaction of (*Z*)-1-phenyl-1-butene (Table 2, entry 18). However, the reaction of (*E*)-1-phenyl-1-butene was slow and modestly enantioselective (Table 2, entry 19). We expected that styrene would also be epoxidized, but neither epoxidation nor aldehyde formation was observed under the optimized reaction conditions. It is likely that the less-bulky styrene is readily coordinated to the ruthenium ion and inhibits an oxygen activation

***Table 2:*** Asymmetric aerobic oxidation of conjugated olefins using ruthenium-(salen) complex **2c** as catalyst.[a]




| Entry | Olefin | *T* [°C] | Air/$O_2$ | Yield [%][b,c] | *ee* [%][d] | Configuration[e] |
|---|---|---|---|---|---|---|
| 1 |  | 25 | air | 62 (77) | 93 | (+)-(1*S*, 2*R*) |
| 2[f] |  | 25 | air | 80 (88) | 80 | (+)-(2*R*, 3*R*) |
| 3 | | 0 | $O_2$ | 89 (>99) | 84 | (+)-(2*R*, 3*R*) |
| 4[f] |  | 25 | air | 49 (51) | 76 | (−)-(*S*) |
| 5[g] | | 0 | $O_2$ | 44 (49) | 80 | (−)-(*S*) |
| 6 |  | 25 | air | 54 (65)[h] | 77 | (−) |
| 7[g] | | 0 | $O_2$ | 80 (83) | 83 | (−) |
| 8 |  | 25 | air | 92 (95) | 92 | (−) |
| 9[g] |  | 0 | $O_2$ | 76 (79) | 53 | (+)-(1*S*, 2*S*) |
| 10[g] |  | 0 | $O_2$ | 85 (90) | 75 | (−) |
| 11[g] |  | 0 | $O_2$ | 71 (73) | 75 | (−) |
| 12[f] |  | 0 | $O_2$ | (35)[i] | 81 | (−) |
| 13 |  | 25 | air | 88 (92) | 93 | (−) |
| 14 |  | 25 | air | 89 (93) | 94 | (−) |
| 15 |  | 25 | air | 92 (94) | 82 | (−) |
| 16[g] | | 0 | $O_2$ | 90 (95) | 86 | (−) |
| 17 |  | 25 | air | 91 (94) | 95 | (−) |
| 18 |  | 25 | $O_2$ | 38 (40) | 80 | (−) |
| 19 |  | 25 | $O_2$ | 25 (36) | 45 | (−) |

[a] Reactions were run at 25 or 0 °C for 48 h in chlorobenzene (2.5 mL) and brine (2.5 mL) with Ru catalyst (5 mol %) on a 0.5 mmol scale under air or $O_2$ atmosphere, unless otherwise mentioned. [b] Yield of the isolated product. [c] The number in parentheses is the yield determined by $^1$H NMR analysis using phenanthrene as an internal standard. [d] Determined by GC on a chiral capillary column or HPLC analysis on a chiral column. See the Supporting Information for details. [e] Determined by comparison of the optical rotation with the literature value. The sign in parentheses indicates the sign of optical rotation measured in $CHCl_3$. [f] Run for 24 h. [g] Run for 72 h. [h] Methyl ketone was obtained in 3 % yield. [i] Methyl ketone was obtained in 8 % yield.

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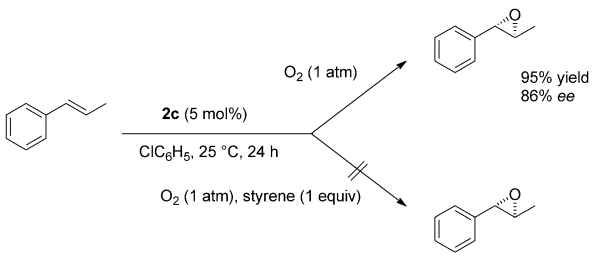
process. Indeed, the epoxidation of (*E*)-1-phenyl-1-propene was blocked by addition of styrene (Scheme 5).[16,17] The epoxidation of *trans*-2-octene did not occur at 25 °C under oxygen.




***Scheme 5.*** Additive effect of styrene.

In summary, we achieved highly enantioselective epoxidation (up to 95 % *ee*) of conjugated olefins using the durable (aqua)ruthenium(salen) complex **2c** as catalyst, at 25 °C under air or at 0 °C under oxygen, without any reductant or photoirradiation. The epoxidation is stereospecific. Further investigations into the mechanism of this epoxidation are in progress.

## *Experimental Section*

General procedure for asymmetric aerobic epoxidation with **2c** (in air): Alkene (0.5 mmol), chlorobenzene (2.5 mL), and brine (2.5 mL) were placed in a test tube under air. Complex **2c** (27.9 mg, 25 μmol) was added to the solution and the mixture was stirred for 48 h at 25 °C. The aqueous layer was separated and extracted with diethyl ether (2 × 2 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$ and concentrated in vacuo. The residue was subjected to chromatography on silica gel with pentane and $Et_2O$ (1:0 to 20:1) to obtain the desired epoxide. The *ee* value of the product was determined by GC or HPLC analysis.

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**Keywords:** aerobic oxidation · asymmetric catalysis · dioxygen · epoxidation · ruthenium

[1] a) F. P. Guengerich, *J. Biochem. Mol. Toxicol.* **2007**, *21*, 163 – 168; b) A. Mahammed, Z. Gross, *J. Am. Chem. Soc.* **2005**, *127*, 2883 – 2887; c) J. T. Groves, *Proc. Natl. Acad. Sci. USA* **2003**, *100*, 3569 – 3574; d) F. van Rantwijk, R. A. Sheldon, *Curr. Opin. Biotechnol.* **2000**, *11*, 554 – 564; e) M. Sono, M. P. Roach, E. D. Coulter, J. H. Dawson, *Chem. Rev.* **1996**, *96*, 2841 – 2888.

[2] a) T. Mukaiyama, T. Yamada, T. Nagata, K. Imagawa, *Chem. Lett.* **1993**, 327 – 330; b) T. Mukaiyama, T. Yamada, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 17 – 35; c) T. Nagata, K. Imagawa, T. Yamada, T. Mukaiyama, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 3241 – 3246; for another asymmetric oxidation using Mukaiyama conditions, see: d) C. Bolm, G. Schlingloff, K. Weickhardt, *Angew. Chem.* **1994**, *106*, 1944 – 1946; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1848 – 1849; a non-enantioselective catalytic epoxidation using air as oxidant in the presence of a β-ketoester was recently reported: e) K. Schröder, B. Join, A. J. Amali, K. Junge, X. Ribas, M. Costas, M. Beller, *Angew. Chem.* **2011**, *123*, 1461 – 1465; *Angew. Chem. Int. Ed.* **2011**, *50*, 1425 – 1429.

[3] a) J. T. Groves, R. Quinn, *J. Am. Chem. Soc.* **1985**, *107*, 5790 – 5792; b) T.-S. Lai, R. Zhang, K.-K. Cheung, H.-L. Kwong, C.-M. Che, *Chem. Commun.* **1998**, 1583 – 1584; recently, aerobic oxidation of alkenes to aldehydes via epoxides under ambient reaction conditions was reported: c) G. Jiang, J. Chen, H.-Y. Thu, J.-S. Huang, N. Zhu, C.-M. Che, *Angew. Chem.* **2008**, *120*, 6740 – 6744; *Angew. Chem. Int. Ed.* **2008**, *47*, 6638 – 6642.

[4] a) C. Döbler, G. Mehltretter, M. Beller, *Angew. Chem.* **1999**, *111*, 3211 – 3212; *Angew. Chem. Int. Ed.* **1999**, *38*, 3026 – 3028; air was used as oxidant at 20 bar and 50 °C: b) C. Döbler, G. M. Mehltretter, U. Sundermeier, M. Beller, *J. Organomet. Chem.* **2001**, *621*, 70 – 76.

[5] a) K. Masutani, T. Uchida, R. Irie, T. Katsuki, *Tetrahedron Lett.* **2000**, *41*, 5119 – 5123; b) R. Irie, K. Masutani, T. Katsuki, *Synlett* **2000**, 1433 – 1436; c) H. Shimizu, S. Onitsuka, H. Egami, T. Katsuki, *J. Am. Chem. Soc.* **2005**, *127*, 5396 – 5413; d) C. F. Works, C. J. Jocher, G. D. Bart, X. Bu, P. C. Ford, *Inorg. Chem.* **2002**, *41*, 3728 – 3739.

[6] E. V. Anslyn, D. A. Dougherty, *Modern physical organic chemistry*, University Science Books, Herndon, **2006**.

[7] For the examples of oxo–hydroxo and oxo–aqua tautomerization, see: a) N. Jin, M. Ibrahim, T. G. Spiro, J. T. Groves, *J. Am. Chem. Soc.* **2007**, *129*, 12416 – 12417; b) K. Chen, M. Costas, J. Kim, A. K. Tipton, L. Que Jr., *J. Am. Chem. Soc.* **2002**, *124*, 3026 – 3035; c) K. A. Lee, W. Nam, *J. Am. Chem. Soc.* **1997**, *119*, 1916 – 1922; d) J. Bernadou, B. Meunier, *Chem. Commun.* **1998**, 2167 – 2173; e) J. Bernadou, A.-S. Fabiano, A. Robert, B. Meunier, *J. Am. Chem. Soc.* **1994**, *116*, 9375 – 9376.

[8] The possibility that the reaction proceeds via a high-valent dioxo ruthenium(VII) species cannot be ruled out (Scheme 2, Ref. [9]). In this pathway, water is regenerated upon the formation of the oxo species.

[9] H. Tanaka, H. Nishikawa, T. Uchida, T. Katsuki, *J. Am. Chem. Soc.* **2010**, *132*, 12034 – 12041.

[10] For the oxidation of aryl methyl sulfides, air could be used as the oxidant: see Ref. [9].

[11] J. Yuasa, S. Yamada, S. Fukuzumi, *J. Am. Chem. Soc.* **2008**, *130*, 5808 – 5820.

[12] **2b** was prepared with a slight modification of the literature procedure: a) W.-L. Man, T.-M. Tang, T.-W. Wong, T.-C. Lau, S.-M. Peng, W.-T. Wong, *J. Am. Chem. Soc.* **2004**, *126*, 478 – 479; b) C.-Y. Wong, W.-L. Man, C. Wang, H.-L. Kwong, W.-Y. Wong, T.-C. Lau, *Organometallics* **2008**, *27*, 324 – 326; c) W.-L. Man, H.-K. Kwong, W. W. Y. Lam, J. Xiang, T.-W. Wong, W.-H. Lam, W.-T. Wong, S.-M. Peng, T.-C. Lau, *Inorg. Chem.* **2008**, *47*, 5936 – 5944.

[13] a) T. Uchida, Y. Tamura, M. Ohba, T. Katsuki, *Tetrahedron Lett.* **2003**, *44*, 7965 – 7968; b) K. Omura, T. Uchida, R. Irie, T. Katsuki, *Chem. Commun.* **2004**, 2060 – 2061; c) H. Kawabata, K. Omura, T. Uchida, T. Katsuki, *Chem. Asian J.* **2007**, *2*, 248 – 256.

[14] H. Egami, T. Oguma, T. Katsuki, *J. Am. Chem. Soc.* **2010**, *132*, 5886 – 5895.

[15] a) J. Mihara, T. Hamada, T. Takeda, R. Irie, T. Katsuki, *Synlett* **1999**, 1160 – 1162; b) T. Takeda, R. Irie, Y. Shinoda, T. Katsuki, *Synlett* **1999**, 1157 – 1159.

[16] The epoxidation was also intercepted by the addition of methyl phenyl sulfide. When (*R*,*R*a)-**2c** or (*S*,*R*a)-**2c** was mixed with methyl phenyl sulfide, a 1:1 complex **2**-sulfide adduct formation was detected by ESI-MS analysis.

[17] See the Supporting Information.

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