Epoxidation

Chemoselective Epoxidation of Allyloxybenzene by Hydrogen Peroxide Over MFI-Type Titanosilicate

Yoshihiro Kon,*[a] Takuya Nakashima,[a] Dachao Hong,[a] Xinyi Ji,[b] Ryota Osuga,[b] Satoru Ito,[a,c] Tadahiro Fujitani,[a] Kazuhiko Sato,[a] and Toshiyuki Yokoi*[b]

Abstract: The chemoselective synthesis of 2-(phenoxymethyl)oxirane from allyloxybenzene is achieved with over 90 % yield in a sustainable reaction system using titanium-substituted silicalite-1 (TS-1) as a catalyst, hydrogen peroxide (H_2O_2) as an oxidant, and a mixture of MeOH/MeCN as a solvent at 40 °C. No acid-catalyzed side reactions prompted by the Lewis acidity of the Ti active site in TS-1 are observed. The TS-1 catalyst can also promote the formation of oxiranes from various p-substituted allyloxybenzenes in good yields. The reaction mechanism is investigated through the reaction with other allyloxy compounds. The results, which are supported by DFT calculations, indicate that an active species of Ti peroxides formed from the reaction of TS-1 with H_2O_2 selectively oxidizes the allyloxybenzene to 2-(phenoxymethyl)oxirane.

Selective oxidation of alkenes to epoxides is a fundamental transformation in organic synthesis, and is one of the most frequently utilized processes in chemical industries.[1] Especially, 2-(phenoxymethyl)oxiranes (**1**) are major constituents of epoxy resins,[2] which are known as versatile materials used in lamination of circuit boards and encapsulation of electronic components owing to their excellent thermal and chemical resistances as well as their workability and durability.[2,3] Several catalysts have been reported to selectively oxidize allyloxybenzenes (**2**) to produce **1** in high yields. For example, 2-(phenoxymethyl)oxirane (**1a**) was reported to be produced from allyloxybenzene (**2a**) by using phosphotungstic acid-immobilized catalysts and Oxone® or tert-butyl hydroperoxide (tBuOOH) as an oxidant.[4] However, these reactions inevitably lead to the formation of wastes such as acids and tBuOH.

The use of H_2O_2 as an oxidant for the epoxidation of **2a** to produce **1a** is one of the most promising approaches because water is the only by-product.[5–8] Sheldon's group showed that the H_2O_2 oxidation of **2a** gave **1a** when catalyzed by $HReO_4$/Ph_2AsMe in trifluoroethanol solutions.[6] Strukul and co-workers reported the green H_2O_2 oxidation of **2a** to **1a** by a Pt^{II} complex catalyst.[7] Unfortunately, these reactions did not give **1a** in

good yields (26 % and 5 %, respectively) because **2a** generally suffers from ether bond cleavage to form phenol under acidic conditions.[9] The Claisen rearrangement of **2a** can occur as a side reaction under acidic conditions (Scheme 1).[10] Moreover, the obtained product **1a** can decompose to form 1-methoxy-3-phenoxypropan-2-ol (**3a**),[6] resulting in low yields. Since hydrophobic fields in zeolites have been reported to inhibit the formation of by-products in oxidation reactions,[8b] the utilization of "hydrophobic pockets" in zeolites[1,11,12] can be expected to suppress the side reactions observed in the epoxidation of **2a**. In this work, we describe the design and preparation of different types of zeolites containing Ti active sites for the chemoselective epoxidation of allyloxybenzene.
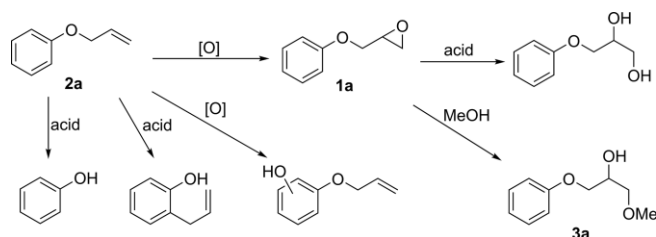
Scheme 1. Possible reaction scheme from **2a**.

We found that the chemoselective oxidation of **2** to produce **1** proceeded in high yields with good selectivity using a titanium-substituted silicalite-1 (TS-1) catalyst and H_2O_2 as an oxidant. This reaction system was applicable to the production of various kinds of allyloxy compounds. The TS-1 catalyst could be reused for the epoxidation of **2a** for at least five cycles with 99 % selectivity. We also successfully obtained **1a** from the chemoselective oxidation of **2a** on a gram-scale under optimized conditions; 5.30 g of **2a** was oxidized by TS-1 to produce
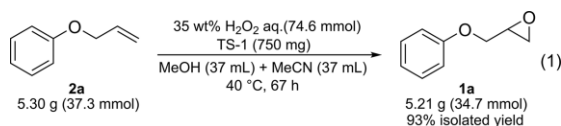
[a] Interdisciplinary Research Center for Catalytic Chemistry, National Institute of Advanced Industrial Science and Technology (AIST),
Central 5, 1-1-1 Higashi, Tsukuba 305-8565, Japan
E-mail: y-kon@aist.go.jp
[b] Nanospace Catalysis Unit, Institute of Innovative Research, Tokyo Institute of Technology
4259 Nagatsuta, Midori-ku, Yokohama 226-8503, Japan
E-mail: yokoi@cat.res.titech.ac.jp
http://www.nc.iir.titech.ac.jp/
[c] Institute for Energy and Material/Food Resources, Technology Innovation Division, Panasonic Corporation
3-4 Hikaridai, Seika-cho, Soraku-gun, Kyoto 619-0237, Japan
Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under https://doi.org/10.1002/ejoc.202000249.

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5.21 g of **1a** in 93 % isolated yield [Equation (1), see the detailed procedure in Supporting Information (SI)].

(1)

2a
5.30 g (37.3 mmol)

35 wt% H_2O_2 aq.(74.6 mmol)
TS-1 (750 mg)
MeOH (37 mL) + MeCN (37 mL)
40 °C, 67 h

1a
5.21 g (34.7 mmol)
93% isolated yield

The TS-1 catalyst, which was prepared by the YNU method (see, SI), is known to catalyze the epoxidation of small and simple alkenes.[13] We characterized its crystal structure by XRD, DR-UV, FT-IR, ^{29}Si MAS NMR, and pyridine-adsorbed FT-IR spectroscopy (Figures S1–S5).[13] The screening of the catalyst and the reaction conditions for the oxidation of **2a** to **1a** with H_2O_2 were investigated, and the results are summarized in Table 1.

Table 1. Screening of conditions for the oxidation of allyloxybenzene (**2a**) with H_2O_2.[a]

Catalyst [mg]	Si/Ti ratio	Conversion of **2a** [%][b]	Yield of **1a** [%][b]	Selectivity [%][c]
none	–	0	0	0
TS-1 (10)	59	73	73	> 99
TS-1 (20)	59	91	90	99
TS-1 (30)	59	93	91	98
TS-1 (20)[d]	59	63	62	98
TS-1 (20)[e]	59	99	91	92
TS-1 (20)[f]	59	97	86	89
H-ZSM-5 (20)	–	0	0	0
Ti-MWW (20)	77	7	4	57
Ti-β (20)	270	11	3	27
Ti-MCM-41 (20)	50	3	0	0
TiO₂ (20)	–	5	1	20
TS-1 + TiO₂[g]	–	86	77	90

[a] Reaction conditions: catalyst, 40 °C, 67 h, mixture of MeOH (1 mL) and MeCN (1 mL) as solvent, 1.0 mmol of **2a**, 2.0 mmol of 35 wt.-% H_2O_2 aqueous solution (aq). [b] Determined by GC analysis based on **2a**. [c] Selectivity = yield/conversion × 100. [d] Using 1.0 mmol of 35 wt.-% H_2O_2 aq. [e] Reaction at 50 °C. [f] Using MeOH (2 mL) without MeCN. [g] Using TS-1 (18 mg) with TiO₂ (2 mg).

The yield of **1a** at 67 h was increased from 73 % to 91 % by increasing the amount of TS-1 catalyst from 10 to 30 mg (see also Tables S1 and S2), suggesting that TS-1 can stabilize the steady state of an intermediate generated in the oxidation of **2a**. The turnover numbers (TONs) were calculated to be 260 (10 mg), 160 (20 mg), and 110 (30 mg) for TS-1.[14] Since the use of large amounts of TS-1 (30 mg) also induced the formation of **3a**, we employed 20 mg of TS-1 for further screenings. The reaction requires double molar amount of H_2O_2 to reach a 90 % yield of **1a** due to partial decomposition of H_2O_2 induced by TS-1 (Table S3). The efficiency of H_2O_2 consumption for the epoxidation was measured to be 64 %, and unavoidable decomposition occurred by using 2 equiv. of. H_2O_2. When using 10 mg of TS-1, the efficiency was increased to 96 %; however, the yield of **1a** was decreased to 73 % (Table S2).[15] The optimal reaction temperature is important to obtain **1a** with good selectivity (Table S4) because decomposition of **1a** to **3a** occurred above 40 °C (Table S5). The TS-1 catalyst used in the reaction exhibited few defects and low OH density on its surface (Figures S2–S4), which might suppress the acid-catalyzed side reaction at 40 °C.

Solvents are known to affect the accessibility of the alkene to TS-1.[12,16,17] Accordingly, we observed that the conversion of

2a and the selectivity of **1a** were strongly correlated with the MeOH:MeCN ratio (Figure 1).
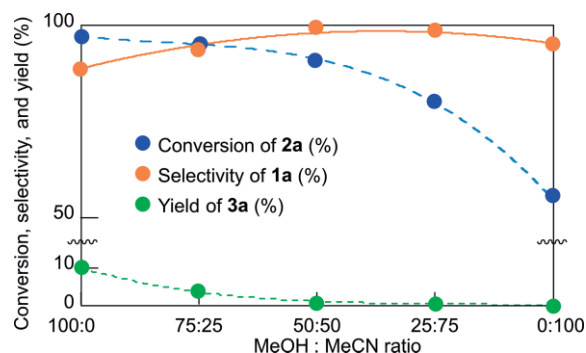

Figure 1. Correlation between MeOH/MeCN ratio and reactivity of **2a**.

The addition of MeOH resulted in higher conversion of **2a** and higher yield of **1a**. The yield of **1a** decreased as the solvent alcohol size increased in the order MeOH < EtOH < *i*PrOH < *t*BuOH (86 %, 43 %, 19 %, and 20 % yield, respectively; Table S6). The alcohol size dependence of the yield of **1a** is consistent with that previously reported for propene epoxidation in a gas flow reaction.[11,12] Considering this, a five-membered ring Ti–OOH active species would be the most plausible Ti active site because MeOH enhanced the conversion of **2a**.[11,18] On the other hand, **3a** was obtained in 10 % yield as a by-product when using net MeOH as solvent, which was suppressed by adding MeCN into MeOH. The MeCN solvent is known to form hydrogen bonding with MeOH;[19] therefore, the addition of MeCN would reduce the Brønsted acidity of the solution through hydrogen bonding between MeOH and MeCN, thereby inhibiting the formation of **3a**.

The H-ZSM-5 catalyst, which contains Al instead of Ti, showed no reactivity in the H_2O_2 oxidation of **2a**. Ti-MWW gave **1a** in 4 % yield despite having almost the same Si/Ti ratio and BET surface area as TS-1. The low yield for Ti-MWW can be ascribed to be the less accessibility of **1a** to the catalytic sites due to the lower hydrophobicity of Ti-MWW compared to that of TS-1.[20] Meanwhile, Ti-β[21] and Ti-MCM-41,[22] which are known as catalysts for the oxidation of small alkenes, gave **1a** in negligible yields (3 % and 0 %, respectively), due to their lower partition coefficient in MeOH as compared to that of TS-1.[16] Besides, Ti-MCM-41 was decomposed by H_2O_2 during the reaction. Control experiments using Ti-containing solid catalysts were performed by employing a physical mixture of TS-1 and TiO₂ (TS-1/TiO₂ = 9:1) or pristine TiO₂ as catalysts to examine the function of internal Ti atoms. In the case of the TS-1/TiO₂ mixture, the yield of **1a** decreased to 77 %, and pristine TiO₂ yielded only 1 % of **1a** (Table 1). The TS-1 catalyst was easily separated from the reaction solution and could be reused after calcination at 500 °C for 3 h. Thus, the yield of **1a** was maintained as high as 90–95 % with 99 % selectivity even after five cycles (Figure 2 and Table S7). The oxidation reaction of **2a** with H_2O_2 took place on the surface of TS-1 as evidenced by a hot-filtration test, in which the epoxidation of **2a** ceased after TS-1 was separated from the reaction solutions at 6 h reaction time (Table S8).

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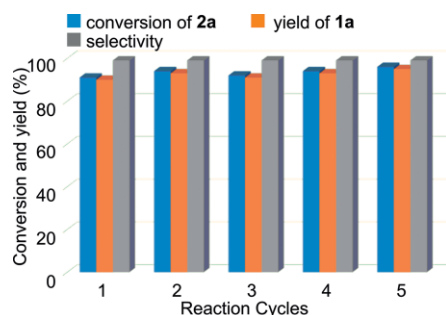of Organic Chemistry

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Figure 2. Conversions and yields of the production of **1a** catalyzed by TS-1 in the repeated experiments.

Oxidation of various allyloxy *p*-substituted benzenes (**2b**–**2i**) was effectively achieved by the TS-1 catalyst, producing the corresponding epoxides (**1b**–**1i**) in up to 93 % isolated yields (Table 2).

The reactivities for aryl halide derivatives **2d**–**2f** were similar to that for **2a**, and **1d**–**1f** were obtained in 85–93 % isolated yields. Both electron-rich and electron-poor alkenes (**2b**, **2c**, and **2g**–**2i**) afforded the corresponding epoxides in 56 %–77 % isolated yields. In the case of 1-(allyloxy)-3-chlorobenzene (**2j**) and 1-(allyloxy)-2-chlorobenzene (**2k**), the corresponding oxiranes were obtained in 32 % and 0 % yields, respectively. The reaction of [(3-methylbut-2-en-1-yl)oxy]benzene (**2l**) having a bulky allyl moiety showed a low conversion (31 %) and a 22 % yield of the corresponding oxirane **1l**. The steric hindrance of substrates has been reported to prevent the oxidation of the alkene in the presence of TS-1 catalysts.[11] Accordingly, the drastic decrease of the yield in the order of allyloxy 4-, 3-, and 2-chlorosubstituted benzenes suggests the effect of steric hindrance between **2** and TS-1. In pyridine-adsorbed FT-IR measurements, the characteristic band of pyridine adsorbed on the Brønsted acid site at 1545 cm^{-1} was not observed, and a Lewis acid site at 1445 cm^{-1} was detected (Figure S5).[17] The Brønsted acid sites, which facilitated Claisen rearrangement of **1** or hydrolysis of **2**, were not observed on the surface of TS-1.

In the case of other ethers such as 1-(allyloxy)octane (**4**) and [(allyloxy)methyl]benzene (**5**), TS-1 also showed good reactivity to give the corresponding oxiranes **6** and **7** in 62 % and 49 % yields, respectively, together with the formation of 1-octanol and benzyl alcohol in 11 % and 10 % yields (Scheme 2).

The use of TS-1 catalysts has been reported to oxidize aryl compounds,[23,24] which could be a potential side reaction in the reaction of **2** by TS-1. DFT calculations showed that the HOMO (–6.41 eV), HOMO-1 (–6.47 eV), and HOMO-2 (–6.69 eV) orbitals of **2a** were distributed in the aryl moiety, and the HOMO-3 orbital was located on the allyl moiety (–7.57 eV) (Table S9 and Figure S6). The van der Waals radius of the allyl moiety and the benzene ring in **2a** were calculated to be 4.25 and 6.53 Å, respectively (Figure S7). Thus, the steric repulsion between the bulky benzene ring of **2a** and TS-1 can prohibit the access of the benzene ring of **2a** to the Ti active sites in TS-1. These results are consistent with those previously reported for a bulky alkoxide-substituted benzene ring whose contact with the Ti active sites in TS-1 was inhibited.[11,23]

Table 2. TS-1-catalyzed oxidation of allyloxybenzenes (**2**) with H$_2$O$_2$.[a]

Reactant	Product	Conversion (%)[b]	Yield (%)[c]	Selectivity (%)[d]
2b	**1b**	48 / 58[e]	47 / 56[e]	99 / 97
2c	**1c**	46 / 76[e]	46 / 69[e]	>99 / 91
2d	**1d**	61 / 92[e]	60 / 86[e]	99 / 93
2e	**1e**	94	93	99
2f	**1f**	91	85	93
2g	**1g**	53 / 72[e]	53 / 68[e]	>99 / 94
2h	**1h**	53 / 77[e]	48 / 73[e]	91 / 95
2i	**1i**	51 / 79[e]	51 / 77[e]	>99 / 97
2j	**1j**	32	32	>99
2k	**1k**	0	0	0
2l	**1l**	31	22	71

[a] Reaction conditions: 20 mg of TS-1 (Si/Ti = 59), 40 °C, 67 h, mixture of 1 mL of MeOH and 1 mL of MeCN as solvent, 1.0 mmol of **2**, 2.0 mmol of H$_2$O$_2$ (35 % in aqueous solution). [b] Determined by GC analysis based on **2a**. [c] Isolated yield. [d] Selectivity = yield/conversion × 100. [e] 40 mg of TS-1, 90 h.
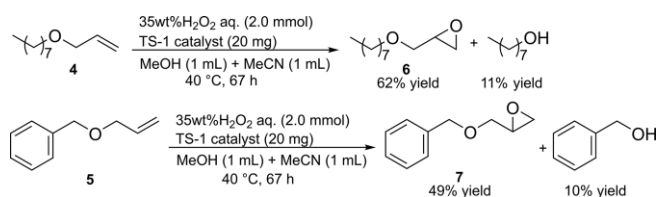
Scheme 2. TS-1-catalyzed epoxidation of allyloxy compounds to oxiranes.

In summary, we have demonstrated the selective H_2O_2 oxidation of **2** to **1** in over 90 % yield with excellent selectivity notwithstanding the multifunctionality of **2**. The Brønsted acid sites of TS-1 was not observed in pyridine-adsorbed FT-IR, and the side reactions such as the Claisen rearrangement and hydrolysis were inhibited. Furthermore, the acid-catalyzed ether bond cleavage at **2** was not observed in the reaction because Ti Lewis acidic sites were present only in the framework. The Lewis acidity enabled the formation of Ti–OOH as active sites for the epoxidation of **2** at 40 °C.

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[14] The turnover numbers (TONs) per Ti sites were defined as [mol of **1a**]/ [mol of Ti in the zeolite].

[15] Efficiency of H_2O_2 (%) = 2 × (yield of **1a** [mmol]) / (initial H_2O_2 [mmol] – remaining H_2O_2 [mmol]) × 100.

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Epoxidation

Y. Kon,* T. Nakashima, D. Hong,
X. Ji, R. Osuga, S. Ito, T. Fujitani,
K. Sato, T. Yokoi* 1–5

Catalyst:
TS-1 zeolite
35wt% H$_2$O$_2$ aq.
MeOH, MeCN

Up to 95% yield
10 examples

A H$_2$O$_2$ chemoselective epoxidation of allyloxybenzene was developed using titanium-substituted silicalite-1 (TS-1) as catalyst. The gram-scale synthesis of 2-(phenoxymethyl)oxirane was performed using 5.30 g of allyloxybenzene to produce 5.21 g of 2-(phenoxymethyl)oxirane in 93 % isolated yield. MeOH/MeCN as mixed solvent facilitated the desired epoxidation even at 40 °C. The developed TS-1 catalyst is reusable, productive, and has a broad substrate scope.

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