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Mechanistic study on regioselective oxygenation reaction of 1,2-quinones with peroxybenzoic acids: Relevant to mechanisms of catecholdioxygenases

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Abstract

The reaction of 1,2-quinone with peroxybenzoic acid affords two types of oxygenated products, muconic anhydride and 7-membered α-ketolactone, via a Criegee intermediate analogous to the proximal peroxy intermediate proposed for catecholdioxygenases. We examined factors that determine the regioselectivity of the oxygenation reaction of 1,2-quinone in order to provide mechanistic insights into the regioselective cleavage of catechols catalysed by the enzymes. Polar solvents, acid catalysts and electron-withdrawing groups on peroxybenzoic acids were found to enhance the selectivity for the formation of 7-membered α-ketolactone. These data indicate that 7-membered α-ketolactone is formed via a heterolytic O–O lysis in the Criegee intermediate. In addition, oxygen-18 labelling experiment revealed that a homolytic O–O lysis in the Criegee intermediate yields muconic anhydride. These results suggest that the cleavage fashion of the O–O bond in the Criegee intermediate determines the regioselectivity of the reaction of not only 1,2-quinones with peroxybenzoic acids, but also the catecholate ligand with molecular oxygen in the enzymatic intermediate.

Keywords: Catecholdioxygenase; Oxygenation; Heterolysis; Homolysis; Quinone

1. Introduction

Catecholdioxygenases found in a wide range of soil bacteria are mononuclear nonheme enzymes, which play a key role in the biodegradation of aromatic compounds in the environments [1–8]. These enzymes catalyse the oxidative cleavage of an aromatic C–C bond in catechol derivatives with concomitant insertion of both oxygen atoms of molecular oxygen into acyclic aliphatic products. Depending on the position of the cleaved C–C bond, catecholdioxygenases have been subclassified into two types; intradiol and extradiol enzymes. Intradiol enzymes contain an iron(III) centre that is ligated by 2 His and 2 Tyr residues [9,10], while extradiol enzymes utilise an iron(II) centre, or rarely manganese(II), that is coordinated by 2 His and 1 Glu residues [11–13]. Each enzyme performs selective cleavage at the strict position in a catechol substrate as depicted in Scheme 1.

To account for the two modes of cleavage, two types of peroxy intermediates were proposed as a reaction intermediate in the oxidative cleavage of catechols; i.e., a proximal peroxy intermediate that leads to intradiol products and a distal peroxy intermediate that yields extradiol products (Scheme 2) [1,14]. This mechanism is based on the idea that the acyl migration to the O–O group affords oxygenated products in both cases. However, there is another possibility, as discussed before [1,14], that the intra- and extradiol oxygen insertions proceed via a common intermediate (proximal peroxy intermediate) through either the acyl or alkenyl migration, respectively. The former mechanism had been supported by us and others until X-ray crystal structures of the enzymes were reported. The structures of extradiol catecholdioxygenases indicated that the distal peroxy intermediate is hard to be formed without a drastic motion of the catechol substrate in the active site because of its highly constrained conformation [11,12]. By using carba-analogs of the proximal and distal peroxy intermediates as inhibitors, Bugg and co-workers elegantly demonstrated that the proximal peroxy intermediate is involved in the reaction mechanism of extradiol enzymes, similarly to intradiol enzymes [1,14,15]. However, further investigations are necessary to clarify how the regioselective oxygen insertion can take place through the common proximal peroxy intermediate.

Previously we have reported that the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone (3,5-DTBQ) with *m*-chlorobenzoic peracid (*m*CPBA) affords muconic acid anhydride (**1**), 7-

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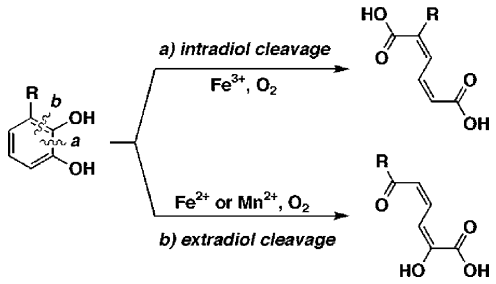
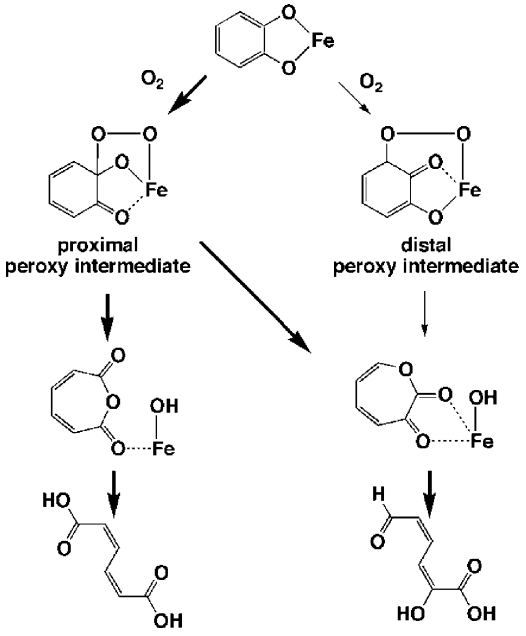
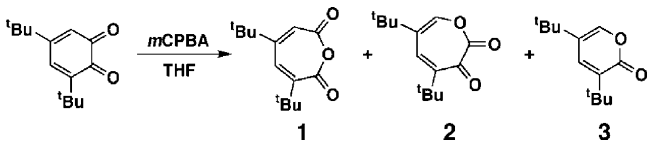


Scheme 1. Two modes of catechol cleavage catalysed by intradiol and extradiol catecholdioxygenases.

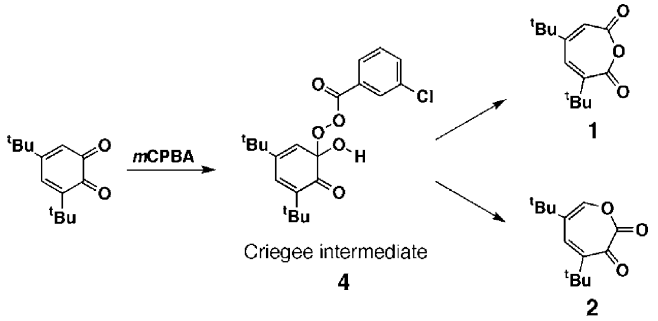


Scheme 2. Proposed mechanisms for the intra- and extradiol cleavages of a catecholate ligand by catecholdioxygenases.

membered α-ketolactone (**2**), and 3,5-di-*tert*-butyl-2-pyrone (**3**) (Scheme 3) [14]. Compound **3** is a decomposed product of **2** through decarbonylation. Both **1** and **2** correspond to the intra- and extradiol cleavage products of 3,5-di-*tert*-butylcatechol, respectively. During this reaction, *m*CPBA attacks a carbonyl group of 3,5-DTBQ to produce a Criegee intermediate (**4**) (Scheme 4). Considering that the structure of the intermediate is analogous to the proximal peroxy intermediate proposed for the reactions catalysed by catecholdioxygenases, it is expected that clarification of factors controlling the product ratio of **1** and **2** provide mechanistic insights into the two oxygen insertion pathways from the Criegee intermediate. Thus, we have performed the reaction of 1,2-quinones with peroxybenzoic acids



Scheme 3. Reaction of 3,5-DTBQ with *m*CPBA.



Scheme 4. Criegee intermediate giving two oxygenated products.

Table 1
Product ratios of **1** and **2** in a series of solvents[a]

Solvent	1	2
Toluene	90	10
Benzene	84	16
Diethyl ether	94	6
Tetrahydrofuran	90	10
Chloroform-*d*	71	29
Dichloromethane	67	33
Acetonitrile	54	46

[a] At room temperature.

under various reaction conditions. As a result, it was revealed that homolytic and heterolytic cleavages of the O–O bond in the Criegee intermediate lead to **1** and **2**, respectively. Assuming that the same oxygen insertion processes are operative in both enzymatic and model systems, the effects of the protein environments on the fashion of the O–O bond cleavage in the intermediates are discussed.

2. Results

2.1. Solvent effects on the product ratios

We performed the reaction of 3,5-DTBQ with *m*CPBA in a variety of solvents. Progress of the reaction in $CDCl_3$ monitored by ^1H NMR spectroscopy showed that 3,5-DTBQ was converted to **1** and **2** with a constant ratio throughout the reaction without forming detectable intermediates. Since **2** was readily converted to **3** during isolation by silica column chromatography or by heating a solution of **2**, we quantified the ratio of **1** and **2** by NMR spectroscopy after evaporation of solvents at low temperatures. As shown in Table 1, the product ratio was found to be dependent on solvents, with enhancement of the extra-type products in polar solvents.

2.2. Substituent effects of peroxybenzoic acids on the product ratios

Substituent effects of peroxybenzoic acids on the product ratios of **1** and **2** were examined in THF or $CDCl_3$ by using a series of peroxybenzoic acids; *p*-nitrobenzoic peracid, benzoic peracid, *p*-methoxybenzoic peracid, and *m*CPBA. Product

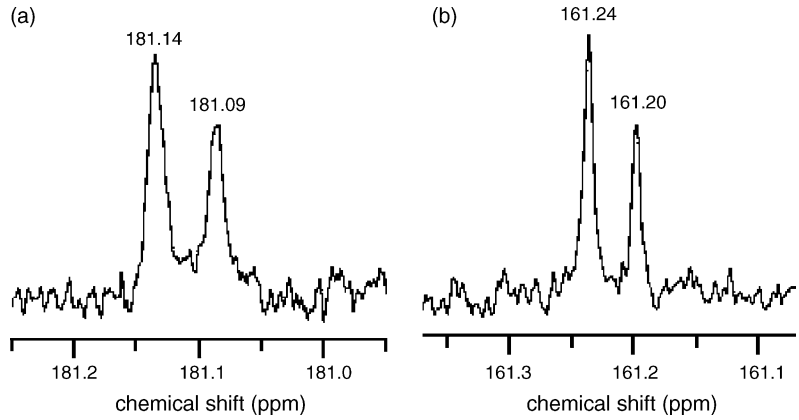


Fig. 1. ^{13}C NMR spectra of (a) ^{18}O-labelled 3,6-DTBQ and (b) ^{18}O-labelled muconic anhydride.

1 was preferentially obtained in these solvents, but the ratio of **2** to **1** varied depending on the substituent groups of peroxybenzoic acids as shown in Table 2. A plot of the logarithms of the product ratios against Hammett σ-values gave a slope with $\rho = 0.22$ and 0.32 in THF and $CDCl_3$, respectively (Figure S1).

2.3. Effects of acid additives on the product ratios

Since the presence of acid may accelerate the heterolysis of the O–O bond, a catalytic amount of acids (5 mol%) was added to the reaction solution. As shown in Table 3, formation of the extra-type products (**2** and **3**) was greatly enhanced. Not only Lewis acids but also strong Brønsted acid were effective for enhancement of the selectivity for the formation of **2** and **3**.

Table 2
Substituent effects on product ratios of **1** and **2**[a]

Substituent group	**2**/**1** in THF	**2**/**1** in $CDCl_3$
*p*MeO	0.10	0.27
H	0.11	0.29
*m*Cl	0.13	0.41
pNO_2	0.17	0.56

[a] In tetrahydrofuran or chloroform-*d* at room temperature.

Table 3
Effect of acid additives (5 mol%) on product ratios of **1** and **2**

Additive	**1**	**2**	**3**
None[a]	90	10	0
$Sc(OTf)_3$[a]	3	44	19
TfOH[a]	14	4	21
None[b]	94	6	0
$BF_3{\cdot}Et_2O$[b]	0	44	11
$Sc(OTf)_3$[b]	7	39	20

[a] In tetrahydrofuran.
[b] In Et_2O.

2.4. Oxygen-18 labelling studies on the oxygen insertion

To determine the position of the incorporated oxygen from *m*CPBA in muconic anhydride, we synthesised ^{18}O-labelled 3,6-di-*tert*-butyl-1,2-benzoquinone (3,6-DTBQ) by using $H_2{}^{18}O$. Because 3,6-DTBQ has a higher symmetric structure than 3,5-DTBQ, it is easy to identify the ^{18}O-labelled carbonyl group.

^{13}C NMR spectra of ^{18}O-labelled 3,6-DTBQ exhibited a new signal that appears upfield (0.05 ppm) with respect to unlabelled 3,6-DTBQ (Fig. 1a). Since an ^{18}O atom adjacent to a carbon atom causes a small upfield shift (0.01–0.05 ppm) in its ^{13}C NMR spectrum [16–18], the result indicates the formation of 3,6-DTBQ with partially ^{18}O-labelled carbonyl groups [18]. Ratio of two signals was estimated to be 60:40 by Lorentzian peak fitting.

The ^{18}O-labelled 3,6-DTBQ was oxidised with *m*CPBA in THF. ^{13}C NMR spectrum of the products showed an additional signal that is shifted upfield 0.04 ppm with respect to the unlabelled muconic anhydride (Fig. 1b). The observed large magnitude of ^{18}O-isotope-induced upfield shift clearly indicates that ^{18}O atoms place in the carbonyl groups in muconic anhydride [17]. The ratio of unlabelled and labelled carbonyl groups was 62:38. Based on this value, the ratio of unlabelled, mono-, and di-^{18}O-labelled muconic anhydrides is estimated to be 38:47:14.

Mass spectrum of the ^{18}O-labelled muconic anhydrides showed three peaks at 236, 238, 240 m/z, which correspond to unlabelled, mono- and di-^{18}O-labelled muconic anhydrides, respectively (Fig. 2a). The peak intensity pattern was well simulated by assuming 38% ^{18}O-labelling of carbonyl groups in

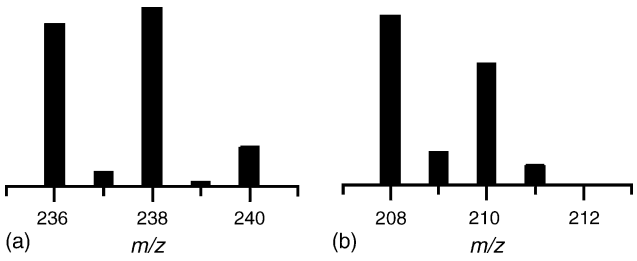


Fig. 2. Mass spectra of ^{18}O-labelled 3,6-di-*tert*-butylmuconic anhydride. (a) M^+ and (b) M^+–CO.

muconic anhydride (Figure S2a), which is very close to the ratio of 40% that is estimated from ^{13}C NMR data. Fig. 2b shows peaks of decarbonylated species of muconic anhydride. Peaks at 208 *m/z* and 210 *m/z* correspond to the unlabelled and mono-^{18}O-labelled M–CO species, respectively. The peak corresponding to di-^{18}O-labelled M–CO species was not observed at 212 *m/z*. The peak pattern for M–CO was also simulated by assuming 38% ^{18}O-labelling of carbonyl groups in M–CO species (Figure S2b). These results indicate that the oxygen atom derived from *m*CPBA places in a ring of muconic anhydride.

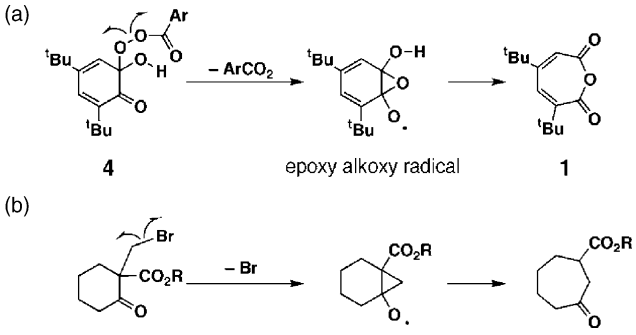
3. Discussion

Reaction of 3,5-DTBQ with peroxybenzoic acids gave a mixture of **1** and **2** (**2** was converted to **3** thermally or by acid). In the course of the reaction, the **2/1** ratio held constant and no reaction intermediate was detected. These results indicate that the formation of the Criegee intermediate **4** is a rate limiting step, and that intra- and extradiol oxygen insertions competitively take pace via the Criegee intermediate **4**.

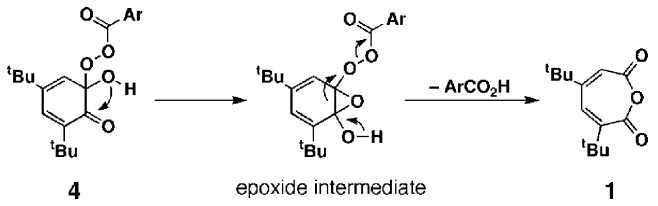
Solvent polarity shows a clear correlation with the product ratio (Table 1, Figure S3) [19]. The higher selectivity for **2** in polar solvents such as acetonitrile indicates that **4** is converted to **2** through the transition state with more polar structure than the transition state from **4** to **1**. Addition of catalytic amount of strong acids greatly enhanced formation of **2** compared with **1**. These results suggest that the transform from **4** to **2** involves the heterolytic O–O bond cleavage through an ionic transition state.

Electron-withdrawing groups on peroxybenzoic acids have been reported to facilitate the heterolytic O–O bond cleavage due to the good leaving ability of the corresponding benzoate group [20,21]. As shown in Table 2, the **2/1** ratio increases as the ring substituents become more electron-withdrawing. The positive ρ values (0.22 in THF and 0.32 in $CDCl_3$) obtained for the **2/1** ratio demonstrate that the reaction pathway yielding **2** involves a heterolytic O–O bond cleavage (Figure S1). If **1** is also formed via a heterolytic O–O bond cleavage, the **2/1** ratio should depend only on the relative migratory aptitude of alkenyl and acyl groups regardless of reaction conditions such as the substituent groups of peroxybenzoic acids. Thus, the present results also indicate that the decomposition from **4** to **1** does not proceed via the Criegee rearrangement by the heterolytic O–O bond cleavage and the alkenyl migration.

Homolytic cleavage is another mode of the O–O bond cleavage in the peroxy group (Scheme 5a). Although there is only one report on the homolytic cleavage in Criegee rearrangement to our knowledge [22], it has been well documented in the field of heme model chemistry that the two cleavage modes (homolytic and heterolytic) of the O–O bond are modulated by solvent polarity, acid catalyst, and substituent groups on the peroxy group [21,23,24]. When we apply the O–O bond cleavage to model reactions, one of the oxy radicals formed could attack the adjacent carbonyl group and form muconic anhydride via an epoxy alkoxy radical intermediate. This reaction is very similar to the Dowd–Beckwith ring-expansion reaction, which is known in the Vitamin B_{12} model reaction. The reaction involves an addition of a carbon atom to a carbonyl carbon, followed by the decomposition the formed cyclopentane ring as shown in Scheme 5b [25,26]. It seems probable that in place of a carbon atom an oxy radical formed by homolytic O–O lysis attacks the carbonyl carbon to form muconic anhydride.

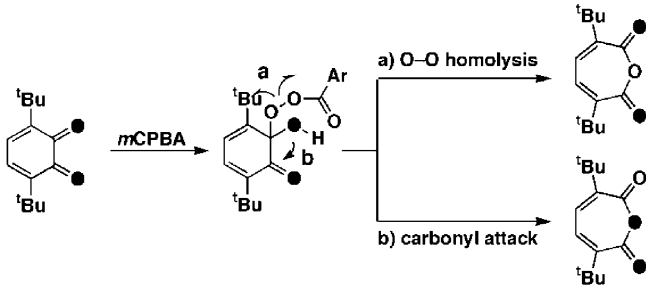


Scheme 5. (a) The O—O homolysis mechanism involving an epoxy alkoxy radical intermediate and (b) the Dowd–Beckwith ring expansion reaction.

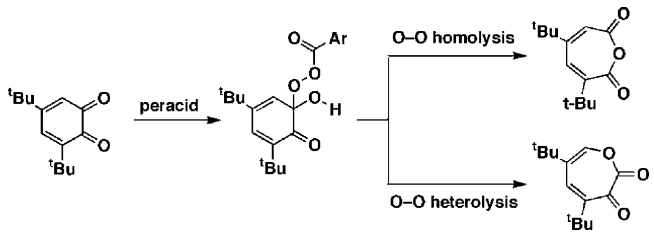


Scheme 6. The carbonyl attack process yielding muconic anhydride through an epoxide intermediate.

There is another possible pathway yielding muconic acid from the Criegee intermediate, in which the alkoxy group attacks the adjacent acyl carbon atom to form an epoxide intermediate (carbonyl attack process), as depicted in Scheme 6. The similar mechanism was proposed for Baeyer–Villiger oxidation of 1,2-diketone [27]. It is of importance to distinguish the two possible pathways for the intra-type oxygen insertion to 1,2-quinones. As shown in Scheme 7, each path inserts the oxygen atom of peroxybenzoic acids to the distinct positions in muconic anhydride. The ^{18}O-labelling studies revealed that the oxygen atom derived from peroxybenzoic acids places in muconic anhydride at the ring oxygen atom rather than the carbonyl oxygen atom. This result clearly indicates that the formation of muconic anhydride proceeds via the homolytic O–O lysis. Further support for the homolytic O–O lysis was obtained by the reaction of 3,5-DTBQ with phenylperacetic acid (PPAA), which has been utilised as a probe of homolytic cleavage [28–30]. We have detected toluene,



Scheme 7. Two possible reaction pathways yielding muconic anhydride via the homolytic O—O bond cleavage or the carbonyl attack process.



Scheme 8. Two reaction pathways yielding muconic anhydride (**1**) and α-ketolactone (**2**) via homolytic and heterolytic O—O bond cleavages in the Criegee intermediate (**4**).

which is derived from a benzyl radical formed by decarboxylation of phenylacetoxy radical, indicating the homolytic O–O bond cleavage of PPAA.

3.1. Implications for mechanisms of catecholdioxygenases

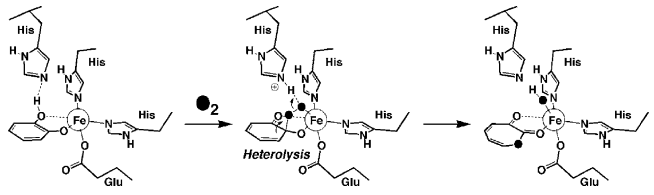
We have demonstrated here that the reaction of 1,2-quinones with peroxybenzoic acids yields two types of oxygenated products via a common intermediate by two distinct mechanisms; i.e., homolytic O–O bond fission to afford muconic anhydride and heterolytic O–O bond cleavage to give 7-membered α-ketolactone (Scheme 8). This important result is highly worthy to be applied for discussion on the regioselective oxygenation of catechols by iron(III) complexes and enzymes with O_2.

In the present model reaction, catalytic amount of acids dramatically shifted the selectivity from intra- to extra-type products. The result suggests that an acid catalyst play an important role to facilitate the extradiol oxygen insertion performed by the extradiol enzymes. Based on X-ray crystal structures of the extradiol enzymes [13,31], the ferrous centre and a conserved His residue (His200 for homoprotocatechuate 2,3-dioxygenase (2,3-HPCD), His194 for 2,3-dihydroxydiphenyl 1,2-dioxygenase (BphC)) can be considered to assist the O–O heterolysis to produce 7-membered α-ketolactone. Recently, Lipscomb and co-workers reported that a H200F mutant of the extradiol 2,3-HPCD exhibits the intradiol activity [32], which indicates that His200 might be more crucial to promote the O–O heterolysis rather than the ferrous centre. In the extradiol enzyme, when catechol substrates bind to the ferrous centre as a monoanion [12,33,34], the remaining phenolic proton acts as a acid catalyt as shown in Scheme 9 [13,31]. The importance of such a proton-assisted heterolytic O–O lysis to afford 7-membered α-ketolactone has been also pointed out by DFT calculations [35].

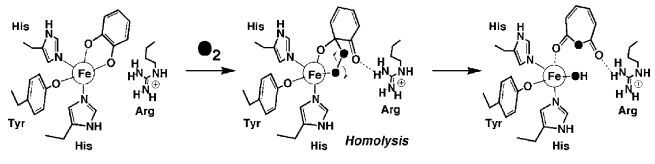
The present study has shown that the Criegee rearrangement involving the O–O bond heterolysis affords extradiol products. Since the Criegee rearrangement strictly requires the correct alignment of the O–O bond and the migration group, which is termed the primary stereoelectronic effect [36–38], the extradiol cleavage of the catecholate ligand via the Criegee rearrangement should satisfy such a conformational requirement in the enzymatic active sites. A plausible structure of the Criegee intermediate, which is generated based on X-ray crystal structures of the extradiol enzymes, is favourable for the alkenyl group migration to a peroxide moiety without a significant movement of a catechol substrate (Scheme 9) [13,31].

In contrast to ferrous ions, a ferric centre itself may have the ability to assist the heterolytic O–O lysis, because some iron(III) model complexes have been known to yield extradiol products without external acid catalysts [39–43]. In this context, iron(III)-containing enzymes are expected to exhibit the extradiol cleavage activity if the alignment of the O–O bond and the alkenyl group satisfies the conformational requirement for the Criegee rearrangement. This consideration leads us to the idea that the protein environments of the intradiol enzymes play a role in suppressing the alkenyl migration. X-ray crystal structures of the intradiol enzymes suggest that the carbonyl group of the peroxy intermediate swings out from the ferric centre through the interaction with a highly conserved Arg residue as shown in Scheme 10 [44]. Such a conformation is incompatible with the heterolytic O–O bond cleavage, and consequently allows homolytic O–O bond cleavage. This parallels the recent proposal that the O–O bond of iron(III)–alkylperoxo species tends to be broken in the homolytic fashion [45]. In addition, our study on the oxygen insertion into the catecholate ligand by DFT quantum chemical calculations has shown that muconic anhydride is formed via an epoxide intermediate after the homolytic splitting of the O–O bond [46]. It is to be noted that an unnatural substrate, 3-methylcatechol, is known to be cleaved in the extradiol fashion by the intradiol enzymes [47]. The methyl group might prevent the proper conformational change required for the homolytic O–O lysis probably due to steric repulsions.

These two types of mechanisms may be applied to the reaction of the biomimetic catecholatoiron(III) complexes with O_2, which also proceeds via the proximal peroxy intermediate. As for the selectivity control in the model systems, ligands play a key role, i.e., tetradentate and facial-capping tridentate ligands induce the intra- and extradiol cleaving activities, respectively [8,14,48,49]. This selectivity should be correlated with the conformation of the proximal peroxy intermediate, similarly to the enzymatic system. In the case of tetradentate ligands, the carbonyl group of the proximal peroxy intermediate should swing out from the iron centre due to the unstable 7-coordination



Scheme 9. Proposed mechanism for the extradiol cleavage of catechol by the enzymes.



Scheme 10. Proposed mechanism for the intradiol cleavage of catechol by the enzymes.

geometry in the similar way to the intradiol enzymes. The resulting conformation prevents the heterolytic O–O lysis but induce the homolytic O–O lysis. On the other hand, the facial-capping tridentate ligands allow the coordination of the carbonyl group, forming a conformation suitable for the heterolytic O–O lysis and the alkenyl migration.

4. Conclusion

We have demonstrated that the cleavage fashion of the O–O bond determines the position of oxygen insertion into 1,2-quinones; i.e., homolytic and heterolytic cleavages of the O–O bond lead to muconic anhydride and 7-membered α-ketolactone, respectively. The mechanisms should be operative in both reactions performed by the enzymes and their functional model complexes. In the enzymatic systems, the protein environments play important roles in controlling the fashion of the O–O bond cleavage in the proximal iron-peroxy intermediate towards insertion of an oxygen atom at the specific positions of catechol substrates.

5. Experimental

5.1. General

Nuclear magnetic resonance spectra were recorded on a JEOL EX270KS Fourier transform spectrometer (270 MHz for ^{1}H, and 100 MHz for ^{13}C). Mass spectra were recorded on a JOEL GCmate (BU 20/25) mass spectrometer in electron impact mode. 3,6-DTBQ was prepared according to a published procedure [50]. Oxygen-18 labelled water (normalised 95 at.% ^{18}O) was purchased from Isotec Co. *m*CPBA was purchased from Aldrich Chemical Co. All other peroxybenzoic acids and PPA were prepared according to a published procedure [51]. Peroxybenzoic acids were purified by washing with a phosphate buffer (pH7.4) prior to use. All other chemicals were purchased from Aldrich or Wako Chemical Co.

5.2. Oxidation of 3,5-DTBQ with mCPBA

The reaction was conducted in a series of solvents; diethyl ether, toluene, tetrahydrofuran, benzene, chloroform, dichloromethane, acetonitrile. A solution of *m*CPBA (4.6 mg, 0.027 mmol) was added to a solution of 3,5-DTBQ (5.9 mg, 0.027 mmol) under N_2. The mixture was stirred at 298 K under N_2 for 15 min. The solvents were evaporated in vacuo and dried. The residue was dissolved in $CDCl_3$, and analysed by ^{1}H NMR measurement.

5.2.1. 3,5-Di-tert-butyl-1,2-benzoquinone

δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.23 (9H, s), 1.27 (9H, s), 6.22 (1H, d), 6.94 (1H, d). δ_H (270 MHz; acetone-d_6; Me_4Si) 1.26 (9H, s), 1.27 (9H, s), 6.10 (1H, d), 7.10 (1H, d).

5.2.2. 3,5-Di-tert-butyl-1-oxacyclohepta-3,5-diene-2,7-dione (**1**)

δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.16 (9H, s), 1.28 (9H, s), 6.14 (1H, d), 6.45 (1H, d). δ_H (270 MHz; acetone-d_6; Me_4Si) 1.21 (9H, s), 1.29 (9H, s), 6.22 (1H, d), 6.70 (1H, d).

5.2.3. 3,5-Di-tert-butyl-2-pyrone (**3**)

δ_H (270 MHz; acetone-d_6; Me_4Si) 1.20 (9H, s), 1.32 (9H, s), 7.23 (1H, d).

5.3. Oxidation of 3,5-DTBQ with mCPBA in the presence of acids

The reaction was conducted in diethyl ether or tetrahydrofuran in the presence of acids; $Sc(OTf)_3$, BF_3etherato, TfOH, TFA. A solution of *m*CPBA (22.4 mg, 0.10 mmol) was added to a solution of 3,5-DTBQ (17.7 mg, 0.10 mmol) under N_2. 5 or 10 mol% of acid was added to the mixture, and then the solution was stirred at 0 °C under N_2 for 1 h. The solvent was evaporated in vacuo and dried. The residue was dissolved in acetone-d_6, and analysed by ^{1}H NMR measurement.

5.4. Purification and characterisation of **2**

*m*CPBA (2.4 mmol) was added to a solution of 3,5-DTBQ (2.0 mmol) in MeCN (7.6 mL) under N_2. BF_3etherato (0.3 mmol) was added to the mixture, and then the solution was stirred at 0 °C under N_2 for 1 h. The white precipitate was filtered off. The filtrate was washed with $NaHCO_3$ aq., and evaporated in vacuo and dried. The residue was purified through a Sephadex LH-20 gel column using $CHCl_3$ as eluent.

5.4.1. 4,6-Di-tert-butyl-1-oxacyclohepta-4,6-diene-2,3-dione (**2**)

δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.14 (9H, s), 1.26 (9H, s), 6.44 (2H, d). δ_H (270 MHz; acetone-d_6; Me_4Si) 1.18 (9H, s), 1.26 (9H, s), 6.64 (2H, d).

5.5. Oxidation of 3,5-DTBQ with a series of peroxybenzoic acids

The reaction was conducted in chloroform-*d* or tetrahydrofuran. 3,5-DTBQ (0.030 mmol) was dissolved in 1 mL of solvent, and peroxybenzoic acid (0.030 mmol) was dissolved in 1 mL of solvent. The mixed solution was stirred at 298 K under N_2 for 15 min (1 h for PPAA). The solvent was evaporated in vacuo and dried. The residue was analysed by ^{1}H NMR measurement.

5.6. Oxygen-18 labelling experiment

^{18}O-labelled 3,6-DTBQ (22 mg, 0.1 mmol) was dissolved in THF. *m*CPBA (0.36 g, 2.1 mmol) was added to the mixture. The solution was stirred at 298 K under N_2 for 2 h. The solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2, washed with sat. $NaHCO_3$ aq. The organic layer was dried over Na_2SO_4, and dried in vacuo.

5.6.1. 3,6-Di-tert-butyl-1,2-benzoquinone

δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.23 (18H, s), 6.77 (2H, s). δ_H (270 MHz; dioxane-d_8; Me_4Si) 1.21 (18H, s), 6.78 (2H, s). δ_C (100 MHz; $CDCl_3$; Me_4Si) 29.14, 34.98, 133.85, 149.65, 180.85.

5.6.2. 3,6-Di-tert-butyl-1-oxacyclohepta-3,5-diene-2,7-dione

δ_H (270 MHz; $CDCl_3$; Me_4Si) 1.26 (18H, s), 6.40 (2H, s). δ_C (100 MHz; $CDCl_3$; Me_4Si) 29.30, 36.16, 125.60, 146.46, 161.21.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2006.02.002.

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