Dehydrogenation versus Oxygenation in Two-Electron and Four-Electron Reduction of Dioxygen by 9-Alkyl-10-methyl-9,10-dihydroacridines Catalyzed by Monomeric Cobalt Porphyrins and Cofacial Dicobalt Porphyrins in the Presence of Perchloric Acid

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Abstract: Dehydrogenation of 10-methyl-9,10-dihydroacridine (AcrH$_2$) by dioxygen (O$_2$) proceeds efficiently, accompanied by the two-electron and four-electron reduction of O$_2$ to produce H$_2$O$_2$ and H$_2$O, which are effectively catalyzed by monomeric cobalt porphyrins and cofacial dicobalt porphyrins in the presence of perchloric acid (HClO$_4$) in acetonitrile (MeCN) and benzonitrile (PhCN), respectively. The cobalt porphyrin catalyzed two-electron reduction of O$_2$ also occurs efficiently by 9-alkyl-10-methyl-9,10-dihydroacridines (AcrHR; R = Me, Et, and CH$_2$COOEt) to yield 9-alkyl-10-methylacridinium ion (AcrR$^+$) and H$_2$O$_2$. In the case of R = Bu^t and CMe$_2$COOMe, however, the catalytic two-electron and four-electron reduction of O$_2$ by AcrHR results in oxygenation of the alkyl group of AcrHR rather than dehydrogenation to yield 10-methylacridinium ion (AcrH$^+$) and the oxygenated products of the alkyl groups, i.e., the corresponding hydroperoxides (ROOH) and the alcohol (ROH), respectively. The catalytic mechanisms of the dehydrogenation vs the oxygenation of AcrHR in the two-electron and four-electron reduction of O$_2$, catalyzed by monomeric cobalt porphyrins and cofacial dicobalt porphyrins, respectively, are discussed in relation to the C(9)−H or C(9)−C bond cleavage of AcrHR radical cations produced in the electron-transfer oxidation of AcrHR.

Introduction

Most organic compounds that have singlet ground states are unreactive toward dioxygen, which has a triplet ground state, because the reactions of triplet dioxygen (^{3}O$_2$) with singlet molecules to produce singlet products are spin-forbidden.[1] In contrast, electron transfer from organic donors to O$_2$ to produce the radical cations of organic donors and the radical anion of O$_2$ (O$_2$$^{•−}$) is spin-allowed.[2] In the respiratory chain, reduced nicotinamide adenine dinucleotide (NADH) acts as the electron source for the four-electron reduction of O$_2$ to H$_2$O via stepwise electron transport, coupled to membrane-spanning proton transport for ATP synthesis.[3−6] NADH itself is stable against O$_2$, and thus, either dioxygen or NADH should be activated to undergo the reduction of O$_2$ by NADH.[7] In the former case, activated dioxygen species such as singlet oxygen can oxidize NADH to yield the two-electron oxidized form, i.e., NAD$^+$.[8−11] Photoinduced electron transfer from the singlet excited states of NADH analogues to O$_2$ also leads to the two-electron reduction of O$_2$.[12] In the presence of acids, the thermal electron-transfer reduction of O$_2$ becomes energetically much more

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favorable than that in the absence of acids.[13] Thus, the thermal reduction of O_2 is made possible by an acid-stable NADH analogue, i.e., 10-methyl-9,10-dihydroacridine (AcrH$_2$)[14-16] in the presence of perchloric acid (HClO$_4$) in acetonitrile (MeCN) to yield H_2O_2 and the corresponding NAD$^+$ analogue, 10-methylacridinium ion (AcrH$^+$).[17] The thermal two-electron reduction of O_2 by AcrH$_2$ has been reported to be catalyzed efficiently by metalloporphyrins such as Co(TPP)$^+$ (TPP^{2-} = tetraphenylporphyrin dianion) in the presence of HClO$_4$ in MeCN.[18,19] In the respiratory chain, NADH is used as the electron source in the terminal enzymes of the respiratory chains, i.e., cytochrome c oxidases (CcO's), which consist of the bimetallic Fe/Cu core located in the inner mitochondrial membrane and catalyze the four-electron reduction of O_2 to H_2O by the soluble one-electron carrier, cytochrome c, without formation of H_2O_2.[3-6] In this context, we have recently reported four-electron reduction of O_2 by one-electron reductants such as ferrocene derivatives, which is efficiently catalyzed by cofacial dicobalt porphyrins in the presence of perchloric acid (HClO$_4$) in benzonitrile (PhCN).[20] A number of synthetic models of CcO's have so far been synthesized to mimic the coordination environment of the Fe/Cu core as well as the catalytic function of the four-electron reduction of O_2.[21-24] Electrocatalytic four-electron reduction has so far been studied extensively because not only it is of great biological interest, but also it is of technological significance such as in fuel cells.[25-28] However,

Scheme 1

Cat. Dicobalt Porphyrins
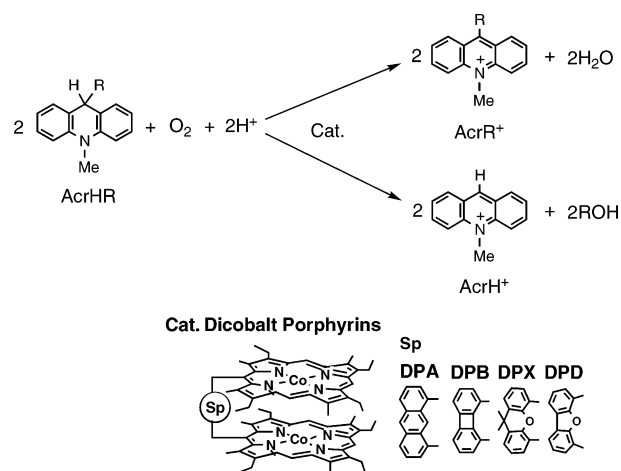
the catalytic four-electron reduction of O_2 by an NADH analogue without formation of H_2O_2 has yet to be achieved.

We report herein that the four-electron reduction of O_2 by an acid-stable NADH analogue (AcrH$_2$) occurs efficiently using cofacial dicobalt porphyrins as effective catalysts in the presence of HClO$_4$ in benzonitrile (PhCN), as shown in Scheme 1, but only the two-electron reduction of O_2 by AcrH$_2$ takes place using monomeric cobalt porphyrins under otherwise identical experimental conditions. When AcrH$_2$ is replaced by 9-alkyl-10-methyl-9,10-dihydroacridine (AcrHR),[29,30] the monomeric cobalt porphyrins catalyze two-electron reduction of O_2 by AcrHR in the presence of HClO$_4$, resulting in oxygenation of the alkyl group via the C(9)−C bond cleavage of AcrHR to yield AcrH$^+$ and the dioxygenated product, i.e., alkyl hydroperoxide (ROOH), instead of dehydration of AcrHR via the C(9)−H cleavage to yield H_2O_2 depending on the type of R group. Similar selectivity in the dehydration vs oxygenation of AcrHR by O_2 is observed for the cofacial dicobalt porphyrin catalyzed four-electron reduction of O_2 by AcrHR, in which the dehydration of AcrHR yields H_2O and AcrR$^+$ whereas the oxygenation yields ROH and AcrH$^+$ (Scheme 1). The selectivities of the C−H vs C−C bond cleavage as well as the reactivities of AcrHR in the monomeric and dimeric cobalt porphyrin catalyzed reduction of O_2 are compared to those in the electron-transfer oxidation of AcrHR with one-electron oxidants.[29] Such comparison provides valuable insight into the catalytic mechanism of the dehydration vs oxygenation pathways in the monomeric and dimeric cobalt porphyrin-catalyzed two-electron and four-electron reductions of O_2 by AcrHR.

Experimental Section

Materials. Cobalt(II) tetraphenylporphyrin [Co(TPP)] was prepared according to the literature.[31] Co(TPP) was oxidized by O_2 in the presence of HCl in methanol to obtain Co(TPP)Cl,[32] which was purified by recrystallization from methanol. Co(TPP)ClO$_4$ was obtained by the

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metathesis of the corresponding chloride salt with AgClO₄ and recrystallized from toluene.[33] Cobalt(II) octaethylporphyrin [Co(OEP)] was purchased by Aldrich Co., USA. Details of the synthesis and characterization of each cofacial dicobalt porphyrin [Co₂(DPB), Co₂-(DPA), Co₂(DPX), and Co₂(DPD)] have been reported elsewhere.[34–37] Acetonitrile (MeCN) and benzonitrile (PhCN) were purchased from Tokyo Kasei Organic Chemicals, Japan, and distilled over P₂O₅ prior to use.[38] Perchloric acid (70%) and hydrogen peroxide were obtained from Wako Pure Chemicals. 10-Methyl-9,10-dihydroacridine (AcrH₂) was prepared from 10-methylacridinium iodide (AcrH⁺I⁻) by reduction with NaBH₄ in methanol, and purified by recrystallization from ethanol.[39] 10-Methylacridinium iodide was prepared by the reaction of acridine with methyl iodide in acetone, and it was converted to the perchlorate salt (AcrH⁺ClO₄⁻) by the addition of magnesium perchlorate to the iodide salt and purified by recrystallization from methanol.[14] 9-Alkyl-10-methyl-9,10-dihydroacridines (AcrHR; R = Me, Et, CH₂-Ph) were prepared by the reduction of AcrH⁺I⁻ with the corresponding Grignard reagents (RMgX).[29] AcrHR (R = Buᵗ) was prepared by the photoreduction of AcrH⁺ClO₄⁻ with RCOOH in the presence of NaOH in H₂O−MeCN.[40] AcrHR's (R = CH₂COOEt and CMe₂COOMe) were prepared by the reduction of AcrH⁺ClO₄⁻ with the corresponding ketene silyl acetals (CH₂=C(OEt)OSiEt₃ and Me₂C=C(OMe)OSiMe₃, respectively).[41] 9-Substituted 10-methylacridinium perchlorate (AcrR⁺ClO₄⁻; R = Me, Et, Buᵗ) was prepared by the reaction of 10-methylacridone in dichloromethane with RMgX and purified by recrystallization from ethanol−diethyl ether.[29]

Reaction Procedure. Typically, an O₂-saturated acetonitrile or chloroform (CD₃CN or CDCl₃, 0.7 mL) solution containing HClO₄ (5.0 × 10⁻² M) was added to an NMR tube which contained AcrHR (5.6 × 10⁻³ mmol) and a catalyst (7.0 × 10⁻⁵ mmol). The oxidized products were identified by comparing the ¹H NMR spectra of the resulting solution with those of the authentic samples, which were obtained independently. ¹H NMR (CD₃CN): AcrH⁺ClO₄⁻ δ 4.76 (s, 3H), 7.9−8.8 (m, 8H); AcrMe⁺ClO₄⁻ δ 3.48 (s, 3H), 4.74 (s, 3H), 7.9−8.9 (m, 8H); AcrEt⁺ClO₄⁻ δ 1.52 (t, 3H), 3.95 (q, 2H), 4.71 (s, 3H), 7.9−8.9 (m, 8H); AcrCH₂Ph⁺ClO₄⁻ δ [4.79 (s, 3H), 5.35 (s, 2H), 7.5−8.6 (m, 13H)]; AcrCH₂COOEt⁺ClO₄⁻ δ 1.09 (t, 3H), 2.41 (q, 2H), 4.76 (s, 3H), 5.02 (s, 2H), 7.7−8.7 (m, 8H); BuᵗOOH δ 1.18 (s, 9H); BuᵗOH δ 1.16 (s, 9H); HOOCMe₂COOMe δ 1.37 (s, 6H), 3.70 (s, 3H). The ¹H NMR measurements were performed using Japan Electron Optics JEOL JNM-AL300 (300 MHz) and JNM-GSX-400 (400 MHz) NMR spectrometers. The amount of hydrogen peroxide (H₂O₂) was determined by titration by iodide ion.[42] The aliquots of the product mixture in MeCN or PhCN were treated with excess NaI, and the amount of I₃⁻ formed was determined by the UV−visible spectrum (λ_{max} = 365 nm, ϵ_{max} = 28 000 M⁻¹ cm⁻¹)[42] using a Hewlett-Packard 8453 diode array spectrophotometer with a quartz cuvette (path length = 10 mm) at 298 K. Electronic absorption spectra during the cobalt porphyrin-catalyzed oxidation of AcrHR by O₂ in the presence of HClO₄ in MeCN or PhCN were recorded on a Shimadzu UV-2200 or UV-3100PC spectrophotometer with a quartz cell (1 mm or 1 cm i.d.), which was
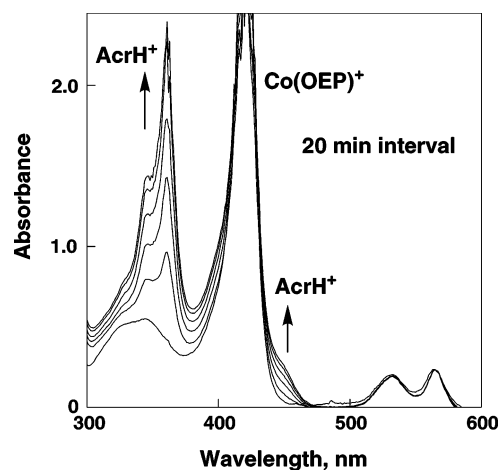

Figure 1. Spectral change observed in the oxidation of AcrH₂ (1.2 × 10⁻⁴ M) with O₂ (8.5 × 10⁻³ M), catalyzed by Co(OEP) (2.0 × 10⁻⁵ M) in the presence of HClO₄ (3.0 × 10⁻² M) in PhCN.

placed in a thermostated compartment at 298 K. An air-saturated PhCN solution was used for the catalytic reduction of O₂ by AcrHR. The O₂ concentrations in an air-saturated PhCN solution (1.7 × 10⁻³ M) and an air-saturated MeCN solution (2.6 × 10⁻³ M) were determined by spectroscopic titration for the photooxidation of AcrH₂ by O₂ as reported previously.[12,20] Larger concentrations of AcrHR than those of O₂ were used for the catalytic reduction of O₂ by AcrHR, when dioxygen was the limiting reagent in the reaction cell which was filled with the reactant solution.

Kinetic Measurements. All kinetic measurements were performed on a Shimadzu UV-2200 or UV-3100PC spectrophotometer at 298 K. Rates of the oxidation of AcrHR were monitored by the rise of the absorption band due to AcrH⁺ and AcrR⁺ (λ_{max} = 358 nm, ϵ_{max} = 1.8 × 10⁴ M⁻¹ cm⁻¹)[18,29] in MeCN or (λ_{max} = 361 nm, ϵ_{max} = 1.7 × 10⁴ M⁻¹ cm⁻¹; λ_{max} = 460 nm, ϵ_{max} = 650 M⁻¹ cm⁻¹) in PhCN at 298 K. The kinetic measurements were carried out under pseudo-first-order conditions, where dioxygen concentrations were maintained at more than 10 times excess the concentrations of AcrHR.

Cyclic Voltammetry. Cyclic voltammetric measurements were performed at 298 K on a BAS 100 W electrochemical analyzer in deaerated PhCN containing 0.1 M tetra-*n*-butylammonium phosphate (TBAPF₆) as supporting electrolyte. A conventional three-electrode cell was used with a platinum working electrode (surface area of 0.3 mm²) and a platinum wire as the counter electrode. The Pt working electrode (BAS) was routinely polished with a BAS polishing alumina suspension and rinsed with acetone before use. The measured potentials were recorded with respect to the Ag/AgNO₃ (0.01 M) reference electrode. All potentials (vs Ag/Ag⁺) were converted to values vs SCE by adding 0.29 V.[43]

Results and Discussion

Catalytic Two-Electron vs Four-Electron Reduction of O₂ by AcrH₂. No reduction of O₂ by AcrH₂ occurs in PhCN at 298 K. In the absence of HClO₄, no catalytic oxidation of AcrH₂ by O₂ in the presence of Co(TPP)⁺ in MeCN is observed.[18a] In the presence of a catalytic amount of Co(OEP) and more than stoichiometric amount of HClO₄, however, AcrH₂ is readily oxidized by O₂ to yield AcrH⁺ (λ_{max} = 361 nm) as shown in Figure 1, where Co(OEP) is oxidized to Co(OEP)⁺ (λ_{max} = 420 nm), the concentration of which remains the same during the reaction. To determine the stoichiometry of the reaction, the O₂ concentration is fixed at 1.7 × 10⁻³ M and the catalytic

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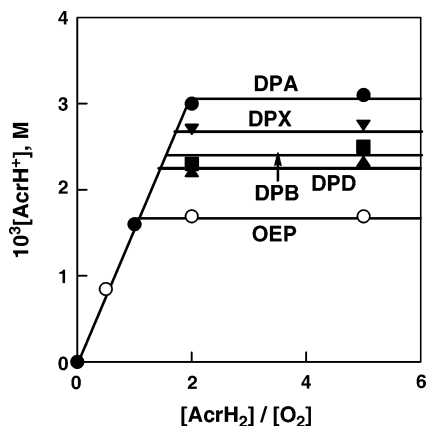(43) DeSimone, R. E.; Drago, R. S. *J. Am. Chem. Soc.* **1970**, *92*, 2343.

Figure 2. Plots of the concentration of AcrH$^+$ formed in the oxidation of AcrH$_2$ (3.0 × 10^{-3} M) by O$_2$ (1.7 × 10^{-3} M), catalyzed by Co$_2$(DPA), Co$_2$(DPX), Co$_2$(DPB), Co$_2$(DPD) (1.0 × 10^{-5} M), and Co(OEP) (2.0 × 10^{-5} M) in PhCN, vs the ration of the concentration of AcrH$_2$ to the initial concentration of O$_2$ in the presence of HClO$_4$ (3.0 × 10^{-2} M).

reduction of O$_2$ is examined by changing the concentration of AcrH$_2$. The results of such spectral titration are shown in Figure 2 (○), which indicates that AcrH$_2$ reacts with 1 equiv of O$_2$ to produce AcrH$^+$ and H$_2$O$_2$ (eq 1). The stoichiometric formation
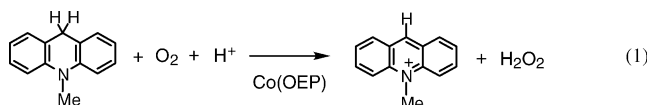
of H$_2$O$_2$ (1.6 × 10^{-3} M) was confirmed by the iodometric titration (see Experimental Section). Such catalytic two-electron reduction of O$_2$ by AcrH$_2$ has previously been reported for the Co(TPP)$^+$-catalyzed reduction of O$_2$ by AcrH$_2$ in the presence of HClO$_4$ in MeCN.[18]

When Co(TPP)$^+$ is replaced by a cofacial dicobalt porphyrin [Co$_2$(DPA)], the concentration of AcrH$^+$ formed in the Co$_2$-(DPA)-catalyzed reduction of O$_2$ by AcrH$_2$ becomes 2 times the O$_2$ concentration (1.7 × 10^{-3} M), as shown in Figure 2 (●). Thus, the four-electron reduction of O$_2$ by AcrH$_2$ occurs efficiently in the presence of a catalytic amount of Co$_2$(DPA) and HClO$_4$ (2.0 × 10^{-2} M) in PhCN (eq 2). In this case, it was
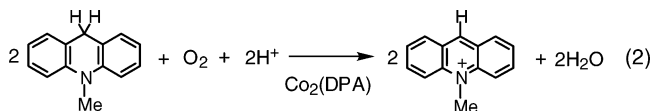
confirmed that no H$_2$O$_2$ was formed by iodometric titration in the catalytic reduction of O$_2$ by AcrH$_2$.

The other cofacial dicobalt porphyrins also catalyze the four-electron reduction of O$_2$ by AcrH$_2$. However, the concentration of AcrH$^+$ formed in the catalytic reduction of O$_2$ by AcrH$_2$ in Figure 2 decreases following the sequence Co$_2$(DPX), Co$_2$-(DPB), and Co$_2$(DPD), indicating that the contribution of the two-electron-reduction pathway of O$_2$ increases in this order.

Catalytic Dehydration vs Oxygenation of AcrHR by O$_2$. The catalytic two-electron reduction of O$_2$ by 9-alkyl-10-methyl-9,10-dihydroacridines (AcrHR) also proceeds efficiently using Co(TPP)$^+$ or Co(OEP) as a catalyst. The oxidized products of AcrHR were examined by ^{1}H NMR. The results are summarized in Table 1. In the case of R = H, Me, Et, and CH$_2$COOEt, the oxidized product in the Co(TPP)$^+$-catalyzed reduction of AcrHR by O$_2$ in CD$_3$CN is solely AcrR$^+$ and the reduced product of

O$_2$ is H$_2$O$_2$ (Table 1). The smaller H$_2$O$_2$ yields than AcrR$^+$ yields shown in Table 1 suggest that H$_2$O$_2$ decomposes partially during the Co(TPP)$^+$-catalyzed reactions. The Co(OEP)-catalyzed reduction of O$_2$ by AcrHR affords virtually the same products (Table 1). This indicates that the dehydration of AcrHR (R = H, Me, Et, and CH$_2$COOEt) occurs exclusively via the C(9)−H bond cleavage (Scheme 2a). In contrast, the oxygenation of R occurs selectively in the case of R = Bu^t and CMe$_2$-COOMe to yield AcrH$^+$ and ROOH via the C(9)−C bond cleavage (Table 1). Thus, the dehydration pathway via the C(9)−H bond cleavage of AcrHR (R = H, Me, Et, and CH$_2$-COOEt) in Scheme 2a is changed to the oxygenation pathway via the C(9)−C bond cleavage of AcrHR (R = Bu^t and CMe$_2$-COOMe) in Scheme 2b. In the case of R = CH$_2$Ph, both the dehydration and the oxygenation pathway occur to yield AcrCH$_2$Ph$^+$ and AcrH$^+$ together with the oxygenated product, PhCHO, which may be formed via the decomposition of Ph$_2$-CHOOH.
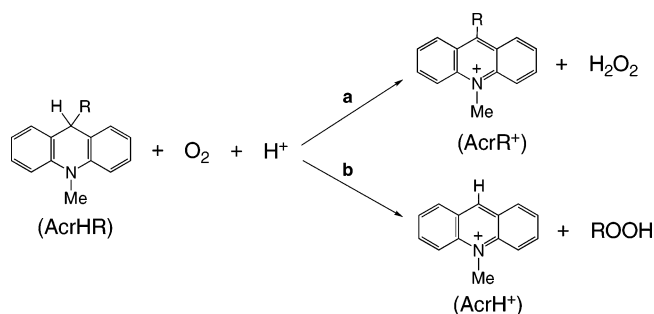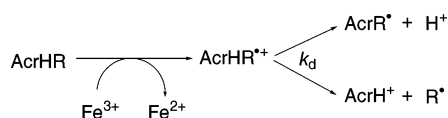
The observed selectivities for the C(9)−H vs C(9)−C bond cleavage in Table 1 agree with those reported for the C(9)−H vs C(9)−C bond cleavage of radical cations of AcrHR (AcrHR$^{•+}$) produced in the electron-transfer oxidation of AcrHR with Fe-(phen)$_3^{3+}$ (phen = 1,10-phenanthroline) depending on the type of R substituent (Scheme 3).[29] In the case of R = Me, Et, and CH$_2$COOEt, the C(9)−H bond of AcrHR$^{•+}$ is heterolytically cleaved to produce AcrR$^•$ and H$^+$ exclusively.[29,44] AcrR$^•$ is further oxidized by Fe(phen)$_3^{3+}$ to yield AcrR$^+$. Such a deprotonation pathway is disfavored in the case of R = Bu^t and CMe$_2$COOMe, when the C(9)−C bond of AcrHR$^{•+}$ is homolytically cleaved to produce AcrH$^+$ and R$^•$ exclusively.[29,45,46] In the case of CH$_2$Ph, both the C(9)−H and C(9)−C bonds are cleaved to yield AcrCH$_2$Ph$^+$ and AcrH$^+$.[29] Such agreement in the competition of C(9)−H vs C(9)−C bond cleavage indicates that the dehydrogenation vs oxygenation of AcrHR depending on R in the cobalt porphyrin-catalyzed reduction of O$_2$ by AcrHR (Scheme 2) is determined by the selectivities for C−H and C−C bond cleavages in the radical cation (AcrHR$^{•+}$), which may be produced by electron transfer from AcrHR to cobalt(III) porphyrins as discussed in more detail later.

When the monomeric cobalt porphyrin is replaced by a cofacial dicobalt porphyrin in the reduction of O$_2$ by AcrHBu^t, the yield of the two-electron-reduced product of O$_2$, i.e., Bu^t-OOH, decreases in the order Co$_2$(DPB)$_2$, Co$_2$(DPX), and Co$_2$-(DPA), accompanied by the formation of the four-electron-reduced product of O$_2$, Bu^{t}OH, as shown in Table 1.[47] In the case of Co$_2$(DPA), a significant amount of acetone is formed with methanol. Such a change in the stoichiometry from the

(44) Hapiot, P.; Moiroux, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1990**, *112*, 1337.
(45) (a) Anne, A.; Fraoua, S.; Moiroux, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1996**, *118*, 3938. (b) Anne, A.; Fraoua, S.; Moiroux, J.; Savéant, J.-M. *J. Phys. Org. Chem.* **1998**, *11*, 774.
(46) For C−C bond cleavage of radical cations of other NADH analogues, see: (a) Anne, A.; Moiroux, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1993**, *115*, 10224. (b) Takada, N.; Itoh, S.; Fukuzumi, S. *Chem. Lett.* **1996**, *25*, 1103. (c) Fukuzumi, S.; Suenobu, T.; Patz, M.; Hirasaka, T.; Itoh, S.; Fujitsuka, M.; Ito, O. *J. Am. Chem. Soc.* **1998**, *120*, 8060.
(47) In the presence of 1.0 × 10^{-4} M Co(OEP) as well as in the absence of Co(OEP) or Co$_2$(DPA), no decomposition of Bu^{t}OOH (5 × 10^{-3} M) was observed in the presence of 5.0 × 10^{-2} M HClO$_4$ in air-saturated CDCl$_3$ in 1.5 h. In the presence of 1.0 × 10^{-4} M Co$_2$(DPA), only 9% Bu^{t}OH was formed by the catalytic decomposition of Bu^{t}OOH (5 × 10^{-3} M) in the presence of 5.0 × 10^{-2} M HClO$_4$ in air-saturated CDCl$_3$ in 1.5 h. Thus, the catalytic decomposition pathway of Bu^{t}OOH is negligible in the results of Table 1.

Table 1. Monocobalt Porphyrin or Dicobalt Porphyrin-Catalyzed Reduction of O_2 by AcrHR (8.0×10^{-3} M) in the Presence of Cobalt Porphyrins (1.0×10^{-4} M) and $HClO_4$ (5.0×10^{-2} M) in O_2-Saturated CD_3CN and $CDCl_3$ at 298 K

| catalyst	AcrHR	time, h	product (yield, %)	$[Bu^tOH]/[Bu^tOOH]$
$Co(TPP)^+$	R = H	1	$AcrH^+$ (100), H_2O_2 (90)	
	Me	2	$AcrMe^+$ (100), H_2O_2 (61)	
	Et	2	$AcrEt^+$ (100), H_2O_2 (59)	
	CH_2COOEt	4	$AcrCH_2COOEt^+$ (100), H_2O_2 (53)	
	CH_2Ph	2	$AcrCH_2Ph^+$ (43), $AcrH^+$ (57), PhCHO (34)	
	CMe_2COOMe	1	$AcrH^+$ (100), $HOOCMe_2COOMe$ (83), Me_2CO (8)	
	Bu^t	1	$AcrH^+$ (100), Bu^tOOH (99)	0
$Co(OEP)$	R = H	1	$AcrH^+$ (100), H_2O_2 (98)	
	Et	2	$AcrEt^+$ (100), H_2O_2 (85)	
	CMe_2COOMe	1	$AcrH^+$ (100), $HOOCMe_2COOMe$ (48), Me_2CO (33)	
	Bu^t	1.5	$AcrH^+$ (100), Bu^tOOH (85)	0
$Co_2(DPA)$	R = CMe_2COOMe	1	$AcrH^+$ (100), $HOOCMe_2COOMe$ (50), Me_2CO (40)	
	Bu^t	1.5	$AcrH^+$ (100), Bu^tOOH (31), Bu^tOH (19), Me_2CO (47), MeOH (6), HCHO (2)	0.61
$Co_2(DPX)$	Bu^t	1.5	$AcrH^+$ (100), Bu^tOOH (67), Bu^tOH (32), Me_2CO (1)	0.48
$Co_2(DPB)$	Bu^t	1.5	$AcrH^+$ (100), Bu^tOOH (73), Bu^tOH (26), Me_2CO (1)	0.36

Scheme 2

Scheme 3

two-electron reduction of O_2 in the case of Co(OEP) to the four-electron reduction of O_2 in the case of cofacial dicobalt porphyrins is shown in Figure 3. The contribution of the four-electron-reduction pathway increases in the order $Co_2(DPB)$, $Co_2(DPX)$, and $Co_2(DPA)$, in agreement with the order in the case of the catalytic reduction of O_2 by $AcrH_2$ (Figure 2).

Kinetic Comparison of Catalytic Reactivity in Oxidation of AcrHR by O_2 with Reactivity of $AcrHR^{\bullet+}$. Rates of the catalytic oxidation of AcrHR with an excess amount of O_2 and $HClO_4$ in the presence of a catalytic amount of $Co(TPP)^+$ obey pseudo-first-order kinetics. The observed pseudo-first-order rate constant (k_{obs}, s^{-1}) increases linearly with an increase in the $Co(TPP)^+$ concentration as shown in Figure 4, which confirms that $Co(TPP)^+$ acts as an efficient catalyst in the oxidation of AcrHR by O_2 in the presence of $HClO_4$ in MeCN. The rate of the oxidation of AcrHR by O_2 in the presence of $HClO_4$ without $Co(TPP)^+$ is negligible as compared with the rates in the presence of $Co(TPP)^+$ (Figure 4). Thus, the rate of formation of $AcrR^+$ is given by eq 3

$$d[AcrR^+]/dt = k_{cat}[AcrHR][Co(TPP)^+] \qquad (3)$$

where k_{cat} is the second-order rate constant for the $Co(TPP)^+$-catalyzed oxidation of AcrHR by O_2. When Co(II)(TPP) was used as the catalyst instead of $Co(III)(TPP)^+$, the same k_{cat} value was obtained for the Co(TPP)-catalyzed oxidation of $AcrH_2$ by O_2. This indicates that Co(II)(TPP) is immediately converted
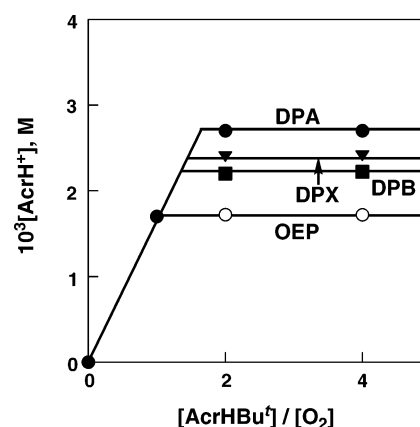
Figure 3. Plots of the concentration of $AcrH^+$ formed in the oxidation of $AcrHBu^t$ (3.0×10^{-3} M) by O_2 (1.7×10^{-3} M), catalyzed by $Co_2(DPA)$, $Co_2(DPX)$, $Co_2(DPB)$, $Co_2(DPD)$ (1.0×10^{-5} M), and Co(OEP) (2.0×10^{-5} M) in PhCN, vs the ration of the concentration of AcrHR to the initial concentration of O_2 in the presence of $HClO_4$ (3.0×10^{-2} M).
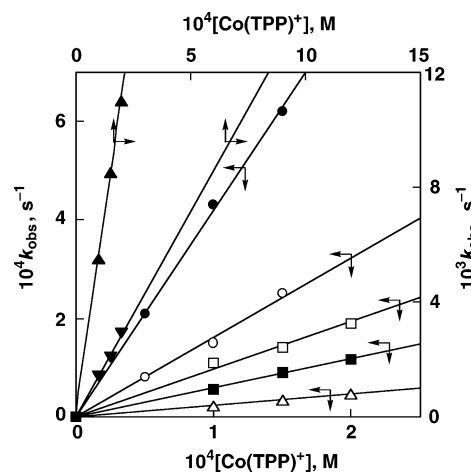
Figure 4. Plots of k_{obs} vs $[Co(TPP)^+]$ for the $Co(TPP)^+$-catalyzed reduction of O_2 (2.6×10^{-3} M) by AcrHR (1.0×10^{-4} M) in the presence of $HClO_4$ (2.0×10^{-3} M) in MeCN at 298 K; R = CMe_2COOMe (▲), Bu^t (▼) H (●), Me (○), Et (□), CH_2COOEt (△), and $AcrD_2$ (■).

to $Co(III)(TPP)^+$, the concentration of which remains the same during the catalytic oxidation of AcrHR with O_2 as indicated in Figure 1 in the case of $AcrH_2$. The same kinetic formation (eq 3) is applied to the oxidation of AcrHR by O_2 catalyzed by Co(OEP) and $Co_2(DPA)$. The k_{obs} values of the cobalt porphyrin catalyzed oxidation of $AcrH_2$ by O_2 are rather independent of
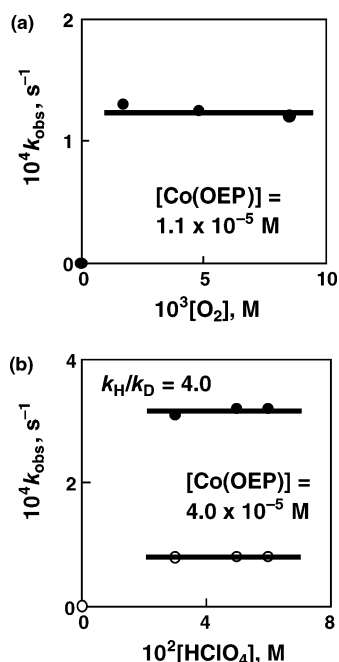
Figure 5. (a) Plot of k_{obs} vs $[O_2]$ for the oxidation of $AcrH_2$ (1.0×10^{-4} M) with O_2 catalyzed by Co(OEP) (1.1×10^{-5} M) in the presence of $HClO_4$ (5.0×10^{-2} M) in PhCN at 298 K. (b) Plots of k_{obs} vs $[HClO_4]$ for the oxidation of $AcrH_2$ (1.0×10^{-4} M) and $AcrD_2$ (1.0×10^{-4} M) with O_2 (8.5×10^{-3} M), catalyzed by Co(OEP) (4.0×10^{-5} M) in PhCN at 298 K.

Table 2. Rate Constants (k_{cat}) of Cobalt Porphyrin-Catalyzed Reduction of O_2 by AcrHR in the Presence of $HClO_4$ in MeCN and PhCN and Decay Rate Constants (k_d) of AcrHR$^{•+}$ Formed by the One-Electron Oxidation with Fe^{3+} in MeCN at 298 K

	k_{cat}, M^{-1} s^{-1}			
AcrHR	Co(TPP)$^{+ a}$	Co(OEP)^b	Co$_2$(DPA)^b	k_d,^{c} s^{-1}
$AcrH_2$	4.2	7.1	740	6.4
$AcrD_2$	0.59	1.8	180	0.71
R = Me	1.6			1.1
R = Et	1.0	2.4		0.49
R = CH_2COOEt	0.23			0.37
R = CMe_2COOMe	55	97	5000	72
R = Bu^t	15	27	4600	14

^{a} $[HClO_4] = 2.0 \times 10^{-2}$ M; $[O_2] = 2.6 \times 10^{-3}$ M in MeCN. ^{b} $[HClO_4] = 5.0 \times 10^{-2}$ M; $[O_2] = 8.5 \times 10^{-3}$ M in PhCN. ^{c} Taken from ref 29.

concentrations of O_2 and $HClO_4$ as shown in parts a and b, respectively, of Figure 5. This indicates that the steps affected by O_2 and $HClO_4$ in the catalytic cycle of O_2 reduction are not involved in the catalytic rate-determining step. When $AcrH_2$ is replaced by the dideuterated compound ($AcrD_2$), a significant kinetic deuterium isotope effect ($k_H/k_D = 4.0$) is observed (Figure 5b) in Co(OEP). This indicates that the C(9)−H bond cleavage (deprotonation from $AcrH_2^{•+}$) is involved in the catalytic rate-determining step for the reduction of O_2 by $AcrH_2$. The k_{cat} values of the oxidation of various AcrHR's by O_2, catalyzed by Co(TPP)$^+$, Co(OEP), and Co$_2$(DPA) at the fixed concentrations of O_2 and $HClO_4$, are listed in Table 2.

We have previously reported the decay rate constants (k_d) of AcrHR$^{•+}$ with various alkyl substituents, formed by the one-electron oxidation of Fe(phen)$_3^{3+}$ in MeCN, which were determined directly by monitoring the decay of the transient absorption due to AcrHR$^{•+}$ using a stopped-flow spectrophotometer.[29] The k_d values of AcrHR$^{•+}$ are also listed in Table 2, indicating that the reactivity of the C(9)−H or C(9)−C bond
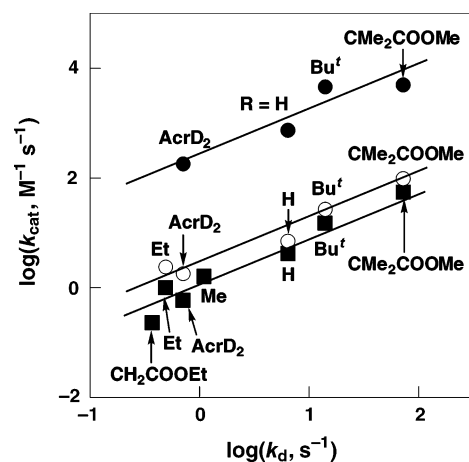
Figure 6. Plots of log k_{cat} for the cobalt porphyrin-catalyzed oxidation of AcrHR or $AcrD_2$ by O_2 vs log k_d for the deprotonation of AcrHR$^{•+}$ or $AcrD_2^{•+}$ in MeCN and PhCN; Co$_2$(DPA) (●), Co(OEP) (○), and Co(TPP)$^+$ (■).

cleavage of AcrHR$^{•+}$ varies significantly depending on the type of R in parallel with the variation of the k_{cat} values.[29]

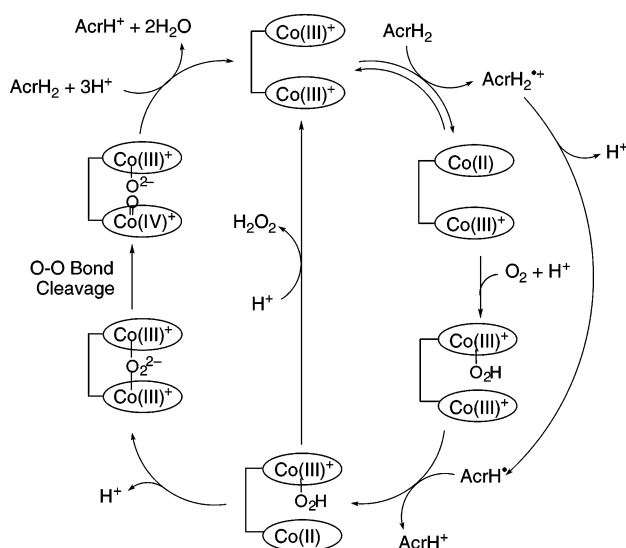The log k_{cat} values are compared with the log k_d values in Figure 6, where a good linear correlation between them is obtained for each catalyst. In addition, the slope of the linear correlation is virtually the same irrespective of different catalysts Co(TPP)$^+$, Co(OEP), and Co$_2$(DPA). Such a linear correlation with the same slope irrespective of different catalysts indicates that the C(9)−H and/or C(9)−C bond cleavage of AcrHR$^{•+}$ is involved in the rate-determining step in each catalytic oxidation of AcrHR by O_2. AcrHR$^{•+}$ may be produced by electron transfer from AcrHR to cobalt(III) porphyrins. Since the one-electron-oxidation potential of AcrHR (e.g., 0.81 V vs SCE for $AcrH_2$)[29] is higher than the one-electron-reduction potential of Co(TPP)$^+$ (0.37 V vs SCE),[18] the electron transfer from AcrHR to Co-(TPP)$^+$ is endergonic.[48] In such a case, the oxidation of AcrHR by Co(TPP)$^+$ proceeds via the slow electron transfer from AcrHR to Co(TPP)$^+$, followed by the C(9)−H and/or C(9)−C bond cleavage in competition with the back electron transfer from Co(TPP) to AcrHR$^{•+}$.[15] Since the one-electron-oxidation potential of AcrHR is rather constant irrespective of the type of R,[29,49] the difference in the oxidation reactivity of AcrHR is mainly determined by the rate of the C(9)−H and/or C(9)−C bond cleavage (k_d). This may be the reason there is a good linear correlation between log k_{cat} and log k_d in Figure 6.

Catalytic Mechanism of Four-Electron Reduction of O_2 by AcrHR. When the catalytic rate-determining step is the slow electron transfer from AcrHR to cobalt(III) porphyrins, followed by the C(9)−H and/or C(9)−C bond cleavage in competition with the back electron transfer from cobalt(II) porphyrins to AcrHR$^{•+}$, the kinetic analysis provides no information about the subsequent catalytic cycle. However, we have previously proposed the mechanism of four-electron reduction of O_2 by ferrocene derivatives in which the catalytic rate-determining step is changed depending on the electron-donor ability of ferrocene derivatives.[20] Virtually the same mechanism may be applied for the catalytic four-electron reduction of O_2 by $AcrH_2$ via the

(48) Electron transfer from a series of AcrHR's to all the cobalt porphyrins employed in this study is endergonic judging from their one-electron redox potentials; see refs 16 and 22.
(49) Anne, A.; Fraoua, S.; Hapiot, P.; Moiroux, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1995**, *117*, 7412.

Scheme 4

AcrH$^+$ + 2H$_2$O

AcrH$_2$ + 3H$^+$

Co(III)$^+$ Co(III)$^+$

AcrH$_2$

AcrH$_2$$^{\bullet+}$

Co(III)$^+$ O^{2-} O Co(IV)$^+$

H$_2$O$_2$

Co(II) Co(III)$^+$

H$^+$

O-O Bond Cleavage

H$^+$

O$_2$ + H$^+$

Co(III)$^+$ O$_2^{2-}$ Co(III)$^+$

H$^+$

Co(III)$^+$ O$_2$H Co(III)$^+$

Co(III)$^+$ O$_2$H Co(II)

AcrH$^\bullet$

AcrH$^+$

Scheme 5

AcrH$^+$ + 2Bu^{t}OH

AcrHBu^t + 2H$^+$ + Bu^{t+}

Co(III)$^+$ Co(III)$^+$

AcrHBu^t

AcrHBu$^{t\bullet+}$

Co(III)$^+$ O^{2-} Co(IV)$^+$

AcrH$^+$

+ H$^+$

Co(II) Co(III)$^+$

O-O Bond Cleavage

Bu^{t}OOH

Co(III)$^+$ O$_2^{2-}$ Co(III)$^+$

Bu^{t}OO$^\bullet$

O$_2$ + H$^+$

Co(III)$^+$ O$_2$H Co(III)$^+$

O$_2$

Bu^{t+}

H$^+$

Co(III)$^+$ O$_2$H Co(II)

Bu$^{t\bullet}$

C(9)—H bond cleavage, as shown in Scheme 4. It has been shown that the initial electron reduction of the Co(III)$_2$ complex by ferrocene derivatives gives the Co(III)Co(II) complex.[20] In the case of AcrH$_2$, the initial slow electron transfer from AcrH$_2$ to the Co(III)$_2$ complex is followed by the C(9)—H and/or C(9)—C bond cleavage in competition with the back electron transfer from the Co(III)Co(II) complex to AcrH$_2$$^{\bullet+}$ to produce AcrH$^\bullet$. Since the catalytic rate-determining step is deprotonation of AcrH$_2$$^{\bullet+}$ rather than the steps affected by O$_2$ and HClO$_4$ (vide supra), the Co(III)Co(II) complex may react rapidly with O$_2$ and H$^+$ to give the Co(III)Co(III)O$_2$H complex, followed by electron transfer from AcrH$^\bullet$ to the Co(III)Co(III)O$_2$H complex to produce AcrH$^+$ and the Co(II)Co(III)O$_2$H complex. After deprotonation, the μ-peroxo Co(III)—O$_2$—Co(III) complex is formed as the case of the catalytic four-electron reduction of O$_2$ by ferrocene derivatives.[20] The heterolytic O—O bond cleavage of the Co(III)—O$_2$—Co(III) complex affords the high-valent Co(IV) oxo porphyrin π-radical cation which is reduced by AcrH$_2$ in the presence of proton to yield H$_2$O, accompanied by formation of AcrH$^+$ (Scheme 4). When a strong electron donor such as decamethylferrocene (Fe(C$_5$Me$_5$)$_2$) is employed as an electron source in the catalytic four-electron reduction of O$_2$, the catalytic rate-determining step changes from the electron-transfer step to the O—O bond cleavage of the Co(III)—O$_2$—Co(III) complex which becomes independent of concentration of Fe(C$_5$Me$_5$)$_2$, thus affording the zero-order kinetics with respect to formation of Fe(C$_5$Me$_5$)$_2$.[20] In the case of AcrH$_2$, which is a weaker electron donor than ferrocene, the catalytic rate-determining step is the initial electron transfer followed by the deprotonation of AcrH$_2$$^{\bullet+}$, affording first-order kinetics with respect to the formation of AcrH$^+$ (vide supra).

The critical point to distinguish between the two-electron and four-electron-reduction pathways is formation of the μ-peroxo Co(III)—O$_2$—Co(III) complex, which requires an appropriate Co—Co distance in the cofacial dicobalt complex. The Co—Co distance in Co$_2$(DPB) (3.73 Å)[34a] may be too short whereas the separation in Co$_2$(DPD)(2MeOH) (8.62 Å)[50] is too long to
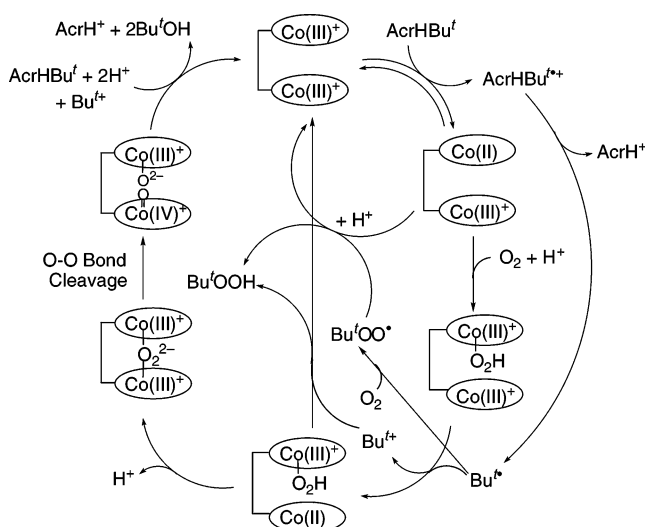
accommodate O$_2$ between two cobalt atoms. On the other hand, the Co—Co distance in Co$_2$(DPA) (4.53 Å)[51] and that in Co$_2$-(DPX) (4.58 Å)[50] may be suitable for formation of the μ-peroxo Co(III)—O$_2$—Co(III) complex, resulting in the catalytic four-electron reduction of O$_2$ by AcrH$_2$.[52] In the case of monomeric cobalt porphyrins such as Co(TPP)$^+$ and Co(OEP), there is no way to form the μ-peroxo Co(III)—O$_2$—Co(III) complex. In such a case, the protonation of the Co(III)O$_2$H complex yields H$_2$O$_2$, resulting in only two-electron reduction of O$_2$ by AcrH$_2$.

In the case of AcrHBu^t, the mechanism of the catalytic four-electron reduction of O$_2$, accompanied by the oxygenation of Bu^t, is modified as shown in Scheme 5. The initial electron transfer from AcrHBu^t to the Co(III)$_2$ complex results in the homolytic C(9)—C bond cleavage to produce Bu$^{t\bullet}$ and AcrH$^+$ (vide supra). Since the homolytic C(9)—C bond cleavage is also the catalytic rate-determining step (vide supra), the Co(III)Co-(III)O$_2$H complex is formed by the reaction of O$_2$ and H$^+$, followed by electron transfer from Bu$^{t\bullet}$ (E^0_{ox} = 0.09 V vs SCE)[53] to the Co(III)Co(III)O$_2$H complex to produce Bu^{t+} and the Co-(II)Co(III)O$_2$H complex. The subsequent step may be the same as the case of the four-electron reduction of O$_2$ by AcrH$_2$ in Scheme 4. The high-valent Co(IV) oxo porphyrin π-radical cation, which is produced by the heterolytic O—O bond cleavage of the Co(III)—O$_2$—Co(III) complex, is reduced by AcrHBu^t in the presence of proton to yield Bu^{t}OH, accompanied by formation of AcrH$^+$ (Scheme 5). However, Bu$^{t\bullet}$ produced in the initial electron transfer from AcrHBu^t to the Co(III)$_2$ complex is known to be readily trapped by O$_2$ to give the peroxyl radical Bu^{t}OO$^\bullet$.[54] Such alkylperoxyl radicals (ROO$^\bullet$)

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(52) Co$_2$(DPX) acts as the most selective catalyst for the four-electron reduction of O$_2$ by ferrocene derivatives,[20] whereas Co$_2$(DPA) is the most selective for the four-electron reduction of O$_2$ by AcrHR. This difference depending on the type of reductants, i.e., one-electron reductants (ferrocene derivatives) vs two-electron reductants (AcrHR) may result from the contribution of the direct reaction of AcrH$^\bullet$ with O$_2$ and H$^+$ in the catalytic cycle.[12] Such a reaction can compete with electron transfer from AcrH$^\bullet$ to the Co(III)-Co(III)O$_2$H complex, which may be faster in the case of Co$_2$(DPA) than the case of Co$_2$(DPX) because of the more positive reduction potential of Co(III)$_2$(DPX) (0.53 V vs SCE) than Co(III)$_2$(DPA) (0.43 V vs SCE). This may lead to the more selective four-electron reduction of O$_2$ by AcrH$_2$ in the case of Co$_2$(DPA) as compared with the case of Co$_2$(DPX). However, the difference in the catalytic selectivity for four- vs two-electron reduction of O$_2$ depending on the type of reductants has yet to be fully clarified.

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are regarded as rather strong one-electron oxidants judging from the highly positive one-electron-reduction potentials.[55,56] There have been reports on electron-transfer reactions from a variety of electron donors to alkylperoxyl radicals.[56–58] Thus, the initial electron transfer from AcrHBu^t to the Co(III)$_2$ complex may also be followed by the subsequent electron transfer from the Co(III)Co(II) complex to Bu^{t}OO$^•$ to produce Bu^{t}OOH after protonation, accompanied by regeneration of the Co(III)$_2$ complex (Scheme 5). This may be the reason the two-electron-reduction pathway to yield Bu^{t}OOH is competing even in the case of the cofacial dicobalt porphyrin catalyzed reduction of O$_2$ by AcrHBu^t (Table 1), in contrast with the case of AcrH$_2$

which undergoes clean four-electron reduction of O$_2$. In the case of monomeric cobalt porphyrins, the reaction of the Co(III)-O$_2$H complex with Bu^{t+} yields Bu^{t}OOH (Scheme 5), resulting in only the two-electron reduction of O$_2$ by AcrHBu^t.

In conclusion, the four-electron reduction of O$_2$ by AcrHR catalyzed by cofacial dicobalt porphyrins occurs efficiently via the electron transfer from AcrHR to cofacial dicobalt porphyrins, followed by the C(9)−H and/or C(9)−C bond cleavage of AcrHR$^{•+}$, depending on the type of R, as the catalytic rate-determining step, leading to the dehydration and oxygenation of AcrHR, respectively. In each case, the formation of the μ-peroxo Co(III)−O$_2$−Co(III) complex, which requires an appropriate Co−Co distance in the cofacial dicobalt complex, is essential for the four-electron reduction of O$_2$ by AcrHR.

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