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Oxidation of Sulfides and Epoxidation of Olefins Caused by the Reaction of Pd–Peroxo or Co–Superoxo Complex with Carboxylic Acid Derivatives

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The Pd–peroxo complex (dioxygen)bis(triphenylphosphine)palladium [$Pd(Ph_3P)_2O_2$] caused epoxidation of olefins and oxidations of sulfides and sulfoxides in the presence of carboxylic acid derivatives. The Co–superoxo complex cobalt bis(salicylaldehyde)-3,3′-diamino-di-*n*-propylamine [Co(Salpr)O_2] also oxidized sulfides to sulfoxides during the reaction with carboxylic acid derivatives. These oxidations were dependent upon the presence of a metal–dioxygen complex and an electrophile such as acyl cation. Metal–acylperoxide, generated *in situ* by the reaction of metal–dioxygen complex with a carboxylic acid derivative, could promote heterolytic cleavage of the O–O bond of dioxygen coordinated to metal to form a metal–oxo complex, which seems to be the ultimate species mediating the oxidations.

Keywords——(dioxygen)bis(triphenylphosphine)palladium; S-oxidation; epoxidation; cobalt bis(salicylaldehyde)-3,3′-diamino-di-*n*-propylamine; metal–oxo; oxene transfer

Introduction

In cytochrome P-450 monooxygenations, the metalloporphyrin–oxenoid complex is considered to be the ultimate reactive species which is responsible for the oxidation of substrates,[1] although the conversion mechanism of the metalloporphyrin–dioxygen complex to the oxenoid species is still not clear. Groves *et al.* reported the formation of a metalloporphyrin–oxenoid species by decomposition of the acylperoxy metalloporphyrin complex, using the Mn(III)–porphyrin complex as a P-450 monooxygenase model system.[2] The formation of the metalloporphyrin–oxenoid *via* acylperoxy metalloporphyrin was proposed. Sligar *et al.* also obtained evidence that dioxygen of ferrous oxygenated *Pseudomonas* cytochrome P-450 attacks dihydrolipoic acid, which is essential for the P-450 activity, to form a transient iron–acylperoxy intermediate.[3] Decomposition of the iron–acylperoxy intermediate should give an active oxidant such as an iron–oxenoid species.

On the other hand, Chen and Kochi found that transfer of an oxygen atom from the Pt–peroxo complex to an unactivated olefin can be promoted by acyl halides.[4] That is, an acyl halide reacts with the Pt–dioxygen complex to afford the acylperoxy Pt complex, whose O–O bond should be more easily cleaved than that of the Pt–peroxo complex.[5] However, they reported only epoxidations of norbornene and cyclohexene by the complex.[4]

Considerable interest has been focused on the reactivities of metal–oxenoid complexes formed *via* acylperoxy metal complexes.[6] In previous papers,[7] we have reported that electrophiles, *i.e.* acyl cation, activate the reactivities of superoxide due to the formation of acylperoxy radical (RC(O)OO$^{\bullet}$) and/or acylperoxy anion (RC(O)OO^{-}). In this paper, we describe oxygen atom transfer reactions to some substrates from the Pd– or Co–oxo complex induced by the reaction of Pd–peroxo or Co–superoxo complex with an electrophile. The mechanism of these reactions can be considered to be P-450 mimetic.

Results and Discussion

Oxidation by Pd–Peroxo Complex (1) in the Presence of Carboxylic Acid Derivatives

$Pd(Ph_3P)_4$ is known to react with dioxygen to form the Pd–peroxo complex $[Pd(Ph_3P)_2O_2]$ (**1**).[8] Localization of electronic charge on metal-coordinated dioxygen suggested that the complex (**1**) would react readily with an acyl cation to produce an active oxidant (Pd–oxo complex) *via* formation of an acylperoxy Pd complex.[9] We found that the reaction of Pd–peroxo complex (**1**) with an electrophile such as benzoyl chloride caused co-oxidations of sulfides, sulfoxides and olefins to sulfoxides, sulfone and olefin oxides, respectively (Chart 1).

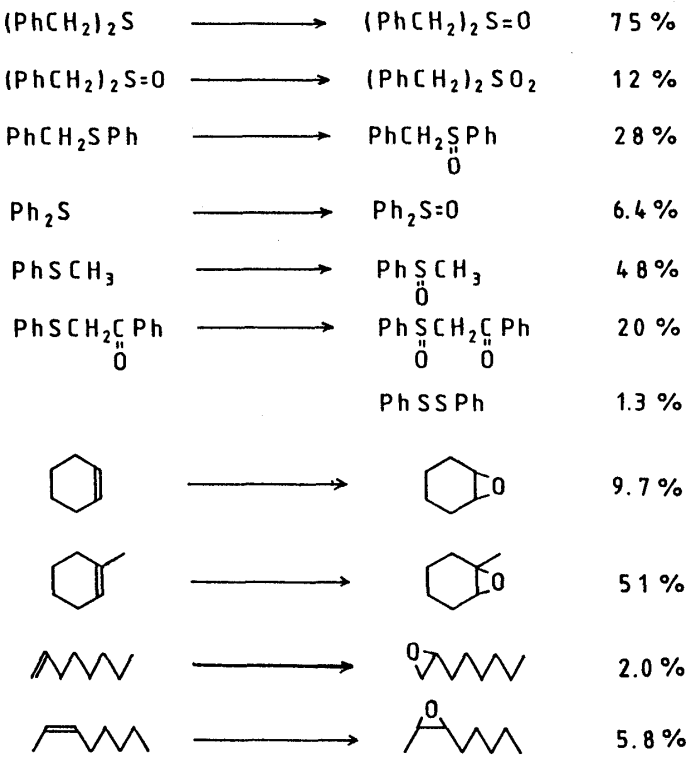


Chart 1. Oxidations by $Pd(Ph_3P)_2O_2$ (**1**) in the Presence of Benzoyl Chloride

In a general procedure, the complex (**1**) (0.1 mmol) and benzoyl chloride (0.1 mmol) were dissolved in CH_2Cl_2 (10 ml) at -70 to -76 °C with stirring for 30 min. Dibenzyl sulfide (1.0 mmol) was added to the reaction mixture and dibenzyl sulfoxide was obtained in 75% yield after stirring for 2 h (Chart 1). Under an N_2 atmosphere, the sulfoxide was also produced by **1** with benzoyl chloride in the same yield. Sulfide was more easily oxidized than sulfoxide. Phenacyl phenyl sulfide gave the corresponding sulfoxide (yield: 20%) and diphenyl disulfide (yield: 1.3%). The poor yield of diphenyl disulfide may indicate that the reaction did not involve one-electron oxidation. If it had, phenacyl phenyl sulfide, which has an electron-withdrawing substituent at the α-position, would have facilitated the α-proton removal to form the α-sulfenyl radical intermediate, followed by hydroxylation to afford the aldehyde and thiophenol, which can be readily oxidized to diphenyl disulfide.[10] The relative reactivities of *p*-substituted thioanisole derivatives were correlated with Hammett σ_p-values as shown in Fig. 1. The oxidation of dibenzyl sulfide by **1** and benzoyl chloride was inhibited by addition of dimethylformamide (DMF), which acts as an inhibitor of the formation of Pt ozonide in the reaction of the Pt–peroxo complex with some ketone compounds (Fig. 2).[11] DMF may compete with benzoyl chloride for coordination to Pd to cause the inhibition. These results indicate that oxene transfer is the most probable mechanism in the oxidation of sulfides. Pd-

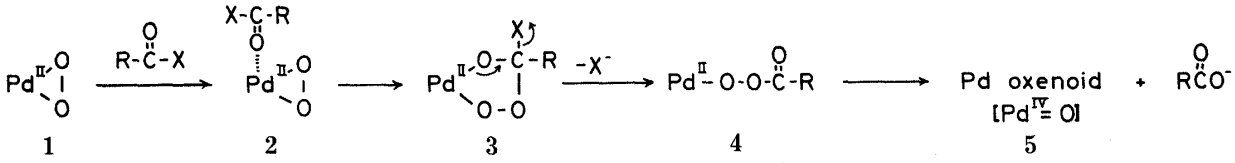
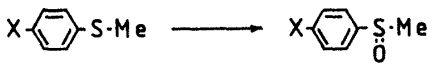


Chart 2. Proposed Reaction Mechanism of $Pd(Ph_3P)_2O_2$ (**1**) with a Carboxylic Acid Derivative



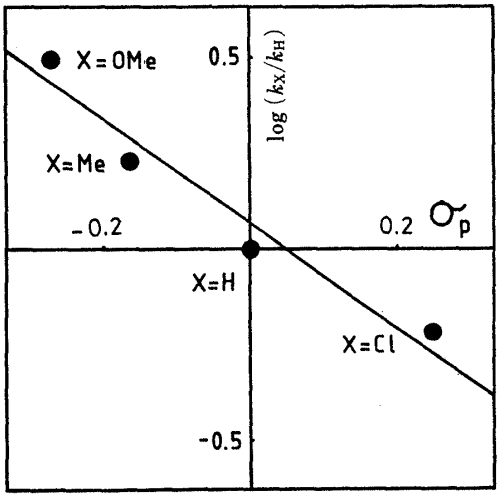


Fig. 1. Relationships between the Relative Reactivities in the Oxidation of *p*-Substituted Thioanisoles to the Corresponding Sulfoxides and Hammett Values (σ_p)

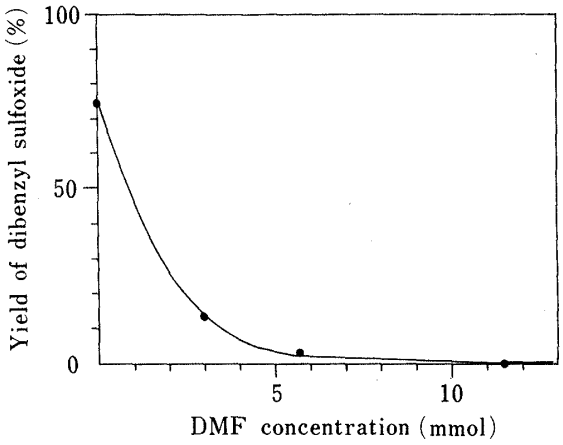


Fig. 2. Effects of DMF on the Oxidation of Dibenzyl Sulfide by $Pd(Ph_3P)_2O_2$ (**1**) and Benzoyl Chloride

coordinated dioxygen first attacks the carbonyl carbon as a nucleophile to form Pd–ozonide (**3**), as shown in Chart 2. Pd–acylperoxide (**4**) can be easily formed by elimination of the group X^-. Such a metal–acylperoxide has been proposed to be involved in the reaction of the oxygenated Mn–porphyrin with *m*-chlorobenzoyl chloride by Groves *et al.*[2] Compound **4** could be decomposed to Pd–oxenoid (**5**), which should be the ultimate reactive species. The O–O bond cleavage of dioxygen coordinated to Pd could be promoted by the formation of Pd–acylperoxide.

Table I shows the effects of various additives instead of benzoyl chloride on the oxidation yields of dibenzyl sulfide to dibenzyl sulfoxide by the Pd–peroxo complex (**1**). Acyl chloride, sulfonyl chloride, phosphoryl chloride and acid anhydride were effective. These additives with good leaving groups (X) should also form a Pd–acyl, –sulfonyl or –phosphoryl peroxide complex which can act as an intermediate in the oxidation of sulfides.

Olefins were also oxidized by **1** in the presence of benzoyl chloride (Chart 1). 1-Methylcyclohexene gave its epoxide in 51% yield, while cyclohexene was epoxidized in 9.7% yield. Since *cis*-2-octene afforded only *cis*-2-octene oxide, the epoxidation was stereospecific. These facts show that the reaction mechanism includes oxene transfer. Acylperoxy radical or acylperoxy anion, generated *in situ* by the reaction of acyl chloride with superoxide, has been reported to oxidize olefins and polycyclic aromatic compounds to the corresponding epoxides.[7] However, these active species can not be formed in the reaction mixture including Pd–peroxo complex (**1**) and acyl halide, because the reaction of the complex (**1**) with acyl

TABLE I. Yields of Dibenzyl Sulfoxide Obtained with $Pd(Ph_3P)_2O_2$ (**1**) or $Co(Salpr)O_2$ (**6**) in the Presence of Various Additives

$$(C_6H_5CH_2)_2S \xrightarrow[\text{additive}]{Pd(Ph_3P)_2O_2 \text{ or } Co(Salpr)O_2} (C_6H_5CH_2)_2SO$$

Run	Additive	Yield (%)	
		$Pd(Ph_3P)_2O_2$	$Co(Salpr)O_2$
1	C_6H_5COCl	75	24
2	CH_3COCl	62	36
3	$C_6H_5SO_2Cl$	66	27
4	$(EtO)_2POCl$	15	14
5	$(CH_3CO)_2O$	69	2
6	$(CF_3CO)_2O$	23	26
7	CH_3COO-(p-NO_2-C_6H_4)	21	0
8	C_6H_5COO-(p-NO_2-C_6H_4)	13	0
9	None	0	0

Reaction conditions are described in Experimental.

TABLE II. Oxidation of Sulfides by $Co(Salpr)O_2$ (**6**) in the Presence of Benzoyl Chloride

$$R^1\text{-}S\text{-}R^2 \xrightarrow[PhCOCl]{Co(Salpr),\ O_2} R^1\text{-}\overset{\overset{O}{\|}}{S}\text{-}R^2$$

R^1	R^2	Yield (%)
$PhCH_2$	$PhCH_2$	24
$PhCH_2$	Ph	16
Ph	Ph	1
Ph	CH_3	32

Reaction conditions are described in Experimental.

halide did not cause the co-oxidation of polycyclic aromatic compounds to the corresponding epoxides. When $PdCl_2$ or $Pd(CH_3CN)_2$, which can not form the Pd–peroxo complex, was used in place of $Pd(Ph_3P)_2O_2$, neither oxidation of sulfides nor that of olefins occurred. These oxidations were clearly dependent upon the presence of the additives from the results shown in Table I, run 9.

Oxidation by Co–Superoxo Complex (6) in the Presence of Carboxylic Acid Derivatives

Co(Salpr) also reacts with dioxygen to form Co–superoxo complex [$Co(Salpr)O_2$] (**6**).[12] Kamiya *et al.* reported that **6** reacts with benzoyl bromide or benzoyl cyanide to give benzoic acid.[13] Thus, it is of great interest to know whether the Co–superoxo complex is effective for the oxidations in the presence of acyl halide. Under an O_2 atmosphere, sulfides were converted to sulfoxides during the reaction of Co(Salpr) with benzoyl chloride (Table II).

$CoCl_2$ had no effect, which indicates that the formation of a Co–superoxo complex is essential for the oxidations. Furthermore, acyl chloride, sulfonyl chloride, phosphoryl chloride or $(CF_3CO)_2O$ could act as an effector in the oxidation of dibenzyl sulfide (Table I). However, in contrast with $Pd(Ph_3P)_2O_2$, Co(Salpr) could not form the Co–oxo complex when $(CH_3CO)_2O$ or p-nitrophenol esters were used (runs 5, 7 and 8 in Table I). The difference between the reactivities of **1** and **6** may arise from the nucleophilicities of Pd– and Co–

coordinated dioxygens, though the detailed reaction mechanism is still not clear. Since the coordination sites of **6** are occupied, the Co–oxo complex may be produced without direct coordination of a carboxylic acid derivative to Co, followed by the formation of Co–ozonide.

Generally, most of the metal–dioxygen complexes may form a metal–acylperoxy intermediate with carboxylic acid derivatives to yield the corresponding metal–oxenoid species. The Pd–peroxo or Co–superoxo complex is more stable than the Fe–peroxo complex, and should be favorable for studies of the activation mechanism of dioxygen at the active site of cytochrome P-450.

Experimental

(Dioxygen)bis(triphenylphosphine)palladium [Pd(Ph_3P)$_2O_2$] (1)——Tetrakis(triphenylphosphine)palladium (Pd(Ph_3P)$_4$) was prepared by Corlson's method.[8] Pd(Ph_3P)$_4$ (900 mg, 0.78 mmol) was dissolved in dry benzene (25 ml), and the reaction solution was stirred for 20 min at 10 °C under an O_2 atmosphere. After the yellow reaction solution turned green, **1** precipitated. It was collected by filtration then washed with dry benzene.[14] Yield, 420 mg (83%). mp 114—116 °C.

General Procedure for the Reaction of 1 in the Presence of a Carboxylic Acid Derivative——**1** (76 mg, 0.1 mmol) and a carboxylic acid derivative (0.1 mmol) were dissolved in CH_2Cl_2 (10 ml) at −70 to −76 °C. The mixture was stirred for 30 min, then a substrate (1.0 mmol) was added. Stirring was continued for 2 h and the yields were determined by high performance liquid chromatography (HPLC) or gas-liquid chromatography (GLC). All yields were based on **1**.

Determination of the Relative Reactivities of *p*-Substituted Thioanisol Derivatives——**1** (76 mg, 0.1 mmol) and benzoyl chloride (14 mg, 0.1 mmol) were dissolved in CH_2Cl_2 (10 ml) at −70 to −76 °C, and then the mixture was stirred for 30 min. A mixture of thioanisole (124 mg, 1.0 mmol) and *p*-substituted thioanisole derivative (1.0 mmol) was added to the reaction solution. Stirring was continued for 2 h, then the yields were obtained by HPLC or GLC. The relative reactivities were approximated by the ratios of the product yields.

Cobalt Bis(salicylaldehyde)-3,3′-diamino-di-*n*-propylamine [Co(Salpr)]——The complex was prepared according to Bailes and Calvin.[12] 3,3′-Diamino-di-*n*-propylamine (2.62 g, 20 mmol) was dissolved in 95% ethanol (40 ml), and salicylaldehyde (4.9 g, 46 mmol) was added. The color of the solution changed to yellow with the exothermic process. Aqueous NaOH solution was added to the reaction mixture, followed by addition of a heated aqueous solution of cobaltous acetate tetrahydrate (5.0 g, 24 mmol). The reaction mixture was concentrated on a steambath until yellow-brown crystals precipitated. The mixture was cooled and filtered, and the filtrate was washed with H_2O and dried. Yield 4.34 g (64%).

General Reaction Procedure for 6 in the Presence of Carboxylic Acid Derivatives——Co(Salpr) (0.25 mmol) was dissolved in DMF (25 ml) with stirring for 10 min under an O_2 atmosphere at 10 to 15 °C. After the substrate (2.5 mmol) and the carboxylic acid derivative (0.25 mmol) had been added, the reaction solution was stirred for 2 h under an O_2 atmosphere. The yields, based on Co(Salpr), were determined by HPLC or GLC.

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