Model Reactions of Molybdo-oxidase. Importance of Water on the Air Oxidation of PPh_3 by Catalysis of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (Cys-OR = S-deprotonated Cysteine Ester; R = Me, Et, Pr^i, or CH_2Ph) in *NN*-Dimethylformamide

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Catalytic air oxidation of PPh_3 using $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (Cys-OR = S-deprotonated cysteine ester; R = Me, Et, Pr^i, or CH_2Ph) in *NN*-dimethylformamide was found to require the presence of water. 18-Oxygen of $H_2{}^{18}O$ has been shown to be involved in the oxidation of PPh_3 both stoicheiometrically and catalytically. However, a large excess of water prevents the catalytic redox cycle. The results of e.s.r. and ^1H n.m.r. spectra of the reduced species from $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ indicate that a mononuclear Mo^V complex $[MoO(OH)(Cys\text{-}OR)_2]$ is probably involved in the catalytic cycle, while $[Mo^V{}_2O_3(Cys\text{-}OR)_4]$ is not. An increase in the bulkiness of R increases the turnover numbers of the oxidation.

Chemical activation of the oxo-ligand towards O-atom transfer oxidation of organic compounds has been considered to be important in the catalysis of sulphite oxidase. E.s.r. and extended *X*-ray absorption fine structure investigations of this enzyme during its turnover have been interpreted to indicate the presence of *cis*-dioxomolybdenum(VI) and oxo(hydroxo)-molybdenum(V) species co-ordinated with two or three S-deprotonated cysteinate ligands.[1,2]

Various synthetic models of the dioxomolybdenum(VI) structure have been investigated for O-atom transfer oxidation. The first successful catalysis was observed with $[MoO_2(dtc)_2]$ (dtc = *NN*-diethyldithiocarbamate) which smoothly converted PPh_3 into $P(O)Ph_3$ with dioxygen.[3,4] Molybdenum(VI) complexes of the type $[Mo^{VI}O_2(L\text{-}L)_2]$ (L-L = a bidentate mono-anionic ligand) with O,O or O,N chelates were inactive to the above reaction.[5] Therefore, activation was ascribed to electronic effects of S,S and S,N chelates amongst which dtc seemed to be the most effective.[5] The inactivity of the $[Mo^{VI}O_2(L\text{-}L)_2]$ complexes was attributed to the stability of the corresponding Mo^V state, $[Mo_2O_3(L\text{-}L)_4]$, where the Mo-O-Mo bridge is stable to dissociation into $[Mo^{IV}O(L\text{-}L)_2]$ and $[Mo^{VI}O_2(L\text{-}L)_2]$.

Molybdenum-(VI) and -(V) complexes of cysteine esters have been characterized and examined as a catalyst for the air oxidation of phosphines and phosphites by Speier[6] and Newton and co-workers.[7] Only weak activity was found in *NN*-dimethylformamide (dmf). Since we have been studying various Mo^{IV} and Mo^V complexes of cysteine-containing oligopeptides, we have also examined the catalysis of $[MoO_2(Cys\text{-}OR)_2]$ (Cys-OR = S-deprotonated cysteine ester; R = Me, Et, Pr^i, or CH_2Ph), and found practically no activity in dry dmf.

Interestingly, the addition of water to the catalyst solution remarkably activates the catalyst for air oxidation of PPh_3. We have studied the catalysis in more detail by investigating the structure of the Mo species in dmf-H_2O by ^1H and ^{13}C n.m.r., circular dichroism (c.d.) and e.s.r. spectroscopy. Variations in the structure of the cysteine ester also seemed important in considering the macromolecular character of the peptide ligand in the enzyme. It is also of interest how the R groups of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ effect the catalytic activity of the air oxidation of PPh_3. Although two isomers are possible as shown in Figure 1, both of the R groups are close together according to the Covey-Pauling space-filling atomic models of the Λ and Δ isomers. In this paper, a spectroscopic investigation of the Mo species and the steric effect of the cysteine ester ligand are reported. A new mechanism for the oxidation will be proposed, based on an observation which implies the importance of mononuclear Mo^V species co-ordinated by two cysteinate-*S* ligands.

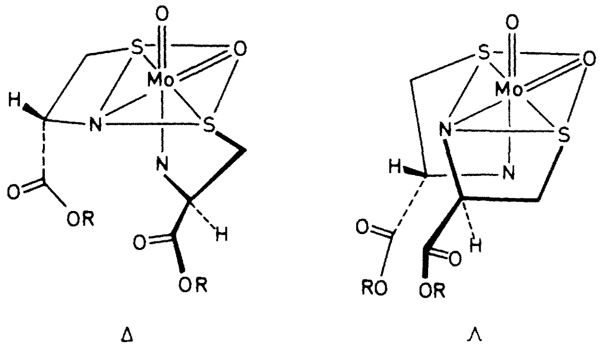


Figure 1. Two possible isomers of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (R = Me, Et, Pr^i, or CH_2Ph)

Experimental

All solvents were purified by distillation under a dinitrogen atmosphere before use.

Complexes.—$[Mo^{VI}O_2(Cys\text{-}OMe)_2]$ and $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ were prepared by the procedure reported by Kay and Mitchell.[8] $[Mo^{VI}O_2(Cys\text{-}OPr^i)_2]$ and $[Mo^{VI}O_2(Cys\text{-}CH_2Ph)_2]$ were synthesized as previously described.[9] $[Mo^V{}_2O_3(Cys\text{-}OMe)_4]$ and $[Mo^V{}_2O_3(Cys\text{-}OEt)_4]$ were prepared by a literature method.[10] Milk xanthine oxidase was extracted by the method reported in the literature.[11,12] Mixtures of $[MoO_4]^{2-}$ and a thiol (see Table 2) were prepared by the addition of an aqueous $Na_2[MoO_4]$ solution to a dmf solution of the thiol under a dinitrogen atmosphere. MeCO-Cys-OH was purchased from Sun-Orient Chemical Co. and the preparations of $PhCH_2OCO$-Cys-His-OMe (His = histidine) and Ala-Cys-OMe (Ala = alanine) will be published elsewhere.

Air Oxidation of PPh_3 *with* Mo^{VI} *Complexes.*—To a solution of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (2.5×10^{-2} mmol) in dmf, a solution of PPh_3 (2.5×10^{-2} mmol) in dmf was added at 30 °C. Part of the reaction mixture was investigated under various conditions by measuring its c.d. spectra. The reaction was also

Table 1. Turnover numbers of the catalytic oxidation of PPh_3; $[PPh_3] = 2.5 \times 10^{-2}$ mol dm^{-3}, $[Mo] = 1.25 \times 10^{-3}$ mol dm^{-3}; $T = 30$ °C

Catalyst	Turnover number (min^{-1})
$[MoO_2(Cys\text{-}OMe)_2]$	0.0025
$[MoO_2(Cys\text{-}OEt)_2]$	0.010
$[MoO_2(Cys\text{-}OPr^i)_2]$	0.018
$[MoO_2(Cys\text{-}OCH_2Ph)_2]$	0.015
$[Mo_2O_3(Cys\text{-}OMe)_4]$	0.0016
$[Mo_2O_3(Cys\text{-}OEt)_4]$	0.0015
Denatured xanthine oxidase *	8.5

* $[PPh_3]/[catalyst] = 4\,000$.

monitored by ^1H n.m.r. to estimate the ratio of $P(O)Ph_3$ formed to unreacted PPh_3.

The rates of catalytic oxidation of PPh_3 were determined by detecting the amounts of PPh_3 or $P(O)Ph_3$ using a Waters HPLC, Microbondapack C_{18} column with $MeOH\text{–}H_2O$ as eluant and calibrated with acenaphthene added as an internal standard. A dmf solution of PPh_3 (2.5×10^{-2} mmol) was added to the dmf–H_2O (1 : 0.15) solution of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (1.25×10^{-3} mmol) at 30 °C with vigorous stirring. After a prescribed time (1—24 h), $P(O)Ph_3$ and unreacted PPh_3 were extracted by dry diethyl ether, filtered off, washed with water, and determined by h.p.l.c.

Incorporation of $H_2{}^{18}O$.—To a solution of $[MoO_2(Cys\text{-}OEt)_2]$ (0.1 mmol) and PPh_3 (0.095 mmol) in dried dmf, 1.1 mmol of ^{18}O-enriched water ($^{18}O : {}^{16}O = 1 : 0.59$, Yeda R & D Co. Ltd) was added at 25 °C under an argon atmosphere. Before the addition of water, no reaction occurs. After 5 h diethyl ether was added to the solution. The ether layer was concentrated and the crystalline mixture obtained washed with n-hexane. The mixture of PPh_3 and $P(O)Ph_3$ was examined directly by mass spectroscopy (JEOL OISG 2 spectrometer). Parent peaks at m/e 277 and 279 were due to $P(^{16}O)Ph_3$ and $P(^{18}O)Ph_3$ respectively.

Catalytic oxidation of PPh_3 was carried out under aerobic conditions. To a dmf solution of $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ (0.01 mmol) and PPh_3 (0.095 mmol), 1.1 mmol of $H_2{}^{18}O$ was added at 25 °C. Unreacted PPh_3 and $P(O)Ph_3$ were extracted by the same method mentioned above.

Physical Measurements.—Proton n.m.r. spectra of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ were recorded on a Varian XL-100 spectrometer. C.d. spectra of the mixture of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ and PPh_3 were obtained with a JASCO J-40 spectrometer. E.s.r. spectra of reduced species of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ with PPh_3 were recorded on a JEOL JES-FE 1X spectrometer at room temperature (298 K) and at 77 K with a field modulation of 100 kHz. The magnetic field was calibrated with Mn^{II}.

Results

Air Oxidation of PPh_3 *catalysed by* $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ *and Denatured Xanthine Oxidase*.—The stoicheiometric oxidation of PPh_3 with $[Mo^{VI}O_2(Cys\text{-}OMe)_2]$ and $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ has been investigated by ^1H n.m.r. in dmf–$CDCl_3$ (1 : 1) at 30 °C. A rate equation was found which involves initial complex formation between the reactants followed by the rate-determining oxygen-atom transfer step, equation (1).[13]

$$PPh_3 + \tfrac{1}{2}O_2 \xrightarrow[Mo^{VI}]{} O{=}PPh_3 \qquad (1)$$

The oxidation of PPh_3 proceeds catalytically under an oxygen atmosphere in the presence of a catalytic amount of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$. The rate of the catalytic reaction in the initial stage was obtained by measuring the amounts of PPh_3 or $P(O)Ph_3$ and was expressed in turnover numbers (min^{-1}). When a small amount of water was present in the solvent system, as discussed below, the time-conversion curves showed no deterioration of the catalysts during the course of the reaction for $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (R = Me, Et, Pr^i or CH_2Ph), which has a first-order dependence on the substrate and the catalyst up to 5 h. Table 1 lists the turnover numbers (min^{-1}) of the air oxidation of PPh_3 by $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (R = Me, Et, Pr^i, or CH_2Ph), $[Mo^V{}_2O_3(Cys\text{-}OR)_4]$ (R = Me or Et), and denatured xanthine oxidase in dmf–H_2O (1 : 0.15). The complexes $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (R = Et, Pr^i, or CH_2Ph) containing bulky R groups exhibit higher activities compared with $[Mo^{VI}O_2(Cys\text{-}OMe)_2]$.

Table 2. Oxidation of PPh_3 with $[MoO_4]^{2-}$–thiol (1 : 2); $[PPh_3] = 2.5 \times 10^{-2}$, $[Mo] = 1.25 \times 10^{-3}$, and $[thiol] = 2.5 \times 10^{-3}$ mol dm^{-3}; $T = 30$ °C

Thiol	Reaction time (h)	Conversion to $O{=}PPh_3$ (%)
MeCO-Cys-OH	3	2
	7	5
	24	51
$PhCH_2OCO$-Cys-His-OMe	3	16
	7	18
	24	17
o-Xylene-α,α′-dithiol	3	1
	7	3
	24	6
Ala-Cys-OMe	3	7
	7	8
	24	17

In order to examine the catalytic activities of mono-μ-oxo-binuclear complexes, two Mo^V complexes, $[Mo^V{}_2O_3(Cys\text{-}OR)_4]$ (R = Me or Et), were studied as shown in Table 1. Both binuclear complexes exhibited extremely weak activities as compared to the $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ complexes. Barral *et al.*,[3] Newton and co-workers,[7] and Garner and co-workers[14] reported that $[Mo^{VI}O_2(dtc)_2]$ reduced by PPh_3 provides $[Mo^V{}_2O_3(dtc)_4]$ and $[Mo^{IV}O(dtc)_2]$. The three species are in equilibrium in solution. They also discussed that $[Mo^V{}_2O_3(dtc)_4]$ is a resting state in the catalytic cycle for the air oxidation of PPh_3. However, our results indicate that the mono-μ-oxo-binuclear complexes such as $[Mo^V{}_2O_3(Cys\text{-}OR)_4]$ do not play a significant role in the catalytic cycle of the oxidation (see Table 1).

It is necessary to evaluate our model systems with reference to the catalytic activity of xanthine oxidase for the air oxidation of PPh_3 in dmf–H_2O (1 : 0.15). This enzyme contains $[M({=}O)({=}S)]^{2+}$, flavin adenine dinucleotide, and 2Fe–2S ferredoxin as cofactors.[15,16] The denatured enzyme prepared under anaerobic conditions still exhibits a high activity with a large turnover (8.5 min^{-1}). The kinetic plot of PPh_3 consumption indicated virtually no substrate binding in the oxidation of PPh_3. Substrate selectivity is thus quite low.

Catalytic oxidations of PPh_3 with $[MoO_4]^{2-}$ in the presence of various thiols were examined and are shown in Table 2. Compared with $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ having a favourable S,N chelate, $[MoO_4]^{2-}$–thiol (1 : 2) systems having a macro-ring S,N chelate such as $PhCH_2OCO$-Cys-His-OMe or Ala-Cys-OMe exhibit weak catalytic activities accompanied with deactivations after 10 h. Isolation of Mo^{VI} complexes of these dipeptides was not successful because of the instability of *cis*-$Mo^{VI}O_2$ complexes. On the other hand, MeCO-Cys-OH provides a 1 : 2 complex as inferred from the c.d. spectra in an aqueous solution, although an attempt at isolation was un-

Table 3. Water-dependent oxidation of PPh_3 by $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$;$[PPh_3] = 2.5 \times 10^{-2}$, $[Mo] = 1.25 \times 10^{-3}$ mol dm^{-3}; $T = 30$ °C

$[H_2O]/[dmf]$	Reaction time (h)	Conversion to $O{=}PPh_3$ (%)
0	1	0
0	8	0
0	25	1
0.15	1	27
0.15	8	65
0.15	25	100
0.26	1	20
0.26	8	56
0.26	25	80

successful. Catalytic activity of the system, $[MoO_4]^{2-}$–MeCO-Cys-OH (1 : 2), for the oxidation was observed which increased gradually with time. The complexation of $[MoO_2]^{2+}$ with MeCO-Cys-OH in 50% dmf–H_2O was determined by Δε values of the c.d. spectra at 305 nm using a method of continuous variation. The results indicated the formation of a 1 : 2 complex. This complex is the most stable at pH 5.5 in aqueous solution. Its structure is not clear at present. Only a slight activity was found with a $[MoO_4]^{2-}$–*o*-xylene-α,α′-dithiol (1 : 2) catalyst. Thus a *cis*-$[Mo^{VI}O_2]^{2+}$ complex surrounded by four thiolato-ligands will be too unstable to maintain the catalytic cycle.

Requirements of Water for the Catalytic System.—By careful examination of the reproducibility of the air oxidation of PPh_3, we found that the catalytic system requires a small amount of water in dmf. Table 3 shows the effect of water added. The addition of a suitable quantity of water to $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ in dmf markedly facilitated the rate of the air oxidation, while its excess diminished the rate. Comparison of the c.d. spectra of $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ with that of the solution reduced by PPh_3 clearly indicates the role of water in the catalytic system. The c.d. spectrum (*iv*) of Figure 2(*a*) indicates that in the presence of water in dmf the air oxidation of the reduced molybdenum species regenerates $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$. In dry dmf, the c.d. maximum at 345 nm (Δε +6.0) in spectrum (*ii*) of Figure 2(*a*) reveals the formation of a binuclear di-μ-oxo-Mo^V complex, $[Mo^V_2O_4(Cys\text{-}OEt)_2]$ which was identified by comparison with the reported value (Δε +35) at 345 nm in dmf.[17] Since such a binuclear di-μ-oxo-Mo^V complex is inert to oxidation to a mononuclear Mo^{VI} state by dioxygen, its formation disrupts the catalytic cycle.

Necessity of water for the oxidation was also supported by an ^{18}O study. The presence of $H_2{}^{18}O$ (^{18}O, 62.5%) in the catalysis results in the formation of $^{18}O{=}PPh_3$. Reaction of $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ with PPh_3 does not occur when water is absent in dmf. Addition of $H_2{}^{18}O$ (^{18}O, 62.5%) starts the stoicheiometric, anaerobic oxidation of PPh_3. The ^{18}O content of the stoicheiometric product $P(O)Ph_3$ was determined by mass spectrometry to be 38.5%. In the case of catalytic air oxidation of PPh_3, the product, $P(O)Ph_3$, had an ^{18}O content of 37.0%.

Formation of Mononuclear Mo^V *Species by Mild Reduction of* $[Mo^{VI}O_2(Cys\text{-}OR)_2]$.—The mild reduction of $[MoO_2(dtc)_2]$ with PPh_3 has been known to give $[Mo^{IV}O(dtc)_2]$ and $[Mo^V_2O_3(dtc)_4]$. An excess of PPh_3 gives $[Mo^{IV}O(dtc)_2]$. A similar reduction of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ was examined by measuring the ^{13}C n.m.r. signals. The ^{13}C n.m.r. spectra $[(CD_3)_2SO]$ of a mixture of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ (R = Me or Et) and excess PPh_3 indicated the formation of a paramagnetic Mo^V species as evidenced by a reduction of the peaks due to cysteine carbons. The presence of the species was confirmed by meas-during the e.s.r. spectra of these complexes. The e.s.r. parameters of $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$–$PPh_3$ (1 : 2) in dmf–H_2O (1 : 0.1) at 77 or 298 K were obtained. Similar $g_{av.}$ values (1.972) at 298 K to $g_{av.} = 1.977$ for xanthine oxidase[18] were obtained for $[Mo^{VI}O_2(Cys\text{-}OR)_2]$–$PPh_3$ (R = Me, Pr^i, or CH_2Ph) in dmf, while the values of $g_x = 1.969$, $g_y = 1.992$, and $g_z = 2.018$ at 77 K correspond to the parameters, $g_x = 1.951$, $g_y = 1.956$, and $g_z = 2.025$ at 77 K characterizing the rapid signal of xanthine oxidase.[1,18] The integration of the Mo^V e.s.r. signal indicated that the content of the mononuclear Mo^V species was 1% of the total Mo. No e.s.r. signal was observed in the dmf or dmf–H_2O (1 : 0.15) solution of $[Mo^V_2O_3(Cys\text{-}OEt)_4]$ prepared according to the procedure of Kay and Mitchell.[8]

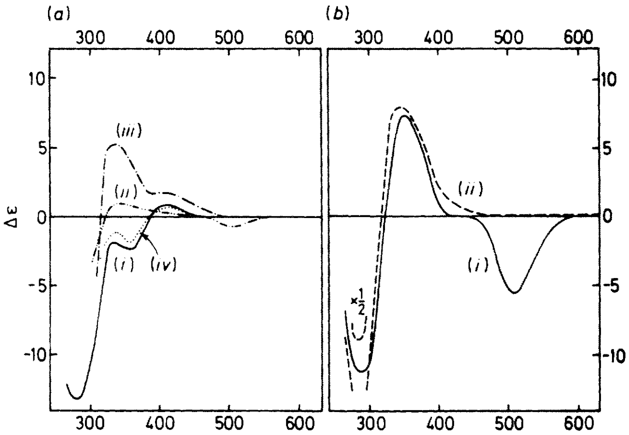


Figure 2. (*a*) Effect of addition of water on the air oxidation of PPh_3 with $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ as catalyst: c.d. spectra of the solutions of (*i*) $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ in dmf, (*ii*) $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ added with 3 mol equiv. of PPh_3 in pure dmf after 30 min under a dinitrogen atmosphere, (*iii*) dioxygen bubbled through a solution of (*ii*) after 5 h, and (*iv*) dioxygen bubbled through a solution of $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ with 3 mol equiv. of PPh_3 in dmf–H_2O (1 : 0.15) after 5 h. (*b*) Air oxidation of a μ-oxo-binuclear complex in fresh dmf: c.d. spectra of (*i*) $[Mo^V_2O_3(Cys\text{-}OEt)_4]$ and (*ii*) $[Mo^V_2O_3(Cys\text{-}OEt)_4]$ after 1 h. Units of Δε are dm^3 mol^{-1} cm^{-1}

Only 15% of the total Mo^V species was the binuclear complex $[Mo^V_2O_3(Cys\text{-}OEt)_4]$ when $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ was reduced by PPh_3 in dmf–H_2O (1 : 0.15) solution, as estimated by the intensity of the typical c.d. maximum for the binuclear complex at 510 nm and also by the i.r. bands at 922 and 426 cm^{-1} due to ν(Mo=O) and ν(Mo–O–Mo).[10] About 85% of the Mo species consist of mononuclear Mo^V, unreacted Mo^{VI} complex, binuclear di-μ-oxo-Mo^V complex, and unknown Mo^{VI} species.

Discussion

Oxidizing Ability of $[MoO_2(L{-}L)_2]$ *Complexes.*—The oxidizing ability of $[Mo^{VI}O_2(L{-}L)_2]$ critically depends on the auxiliary ligands, L–L.[5] Chen *et al.*[7] found that the mild reduction of $[Mo^{VI}O_2(L{-}L)_2]$ [L–L = Cys-OMe, $O_2CCO(OH)$, or acetylacetonate] proceeds to $[Mo^V_2O_3(L{-}L)_4]$, while $[Mo^{VI}O_2(L'{-}L')_2]$ (L′–L′ = S_2CNR_2 or S_2PR_2) were easily reduced to $[Mo^{IV}O(L'{-}L')_2]$.[7] No significant catalytic activity was observed when $[MoO_4]^{2-}$ with large S,N-chelating peptides, *e.g.* $PhCH_2OCO$-Cys-His-OMe or Ala-Cys-OMe, were used. The *cis*-$Mo^{VI}O_2$ complexes of these peptides are found to be quite unstable under ambient conditions. Therefore, the catalytic cycle involving the dioxomolybdenum(VI) stage

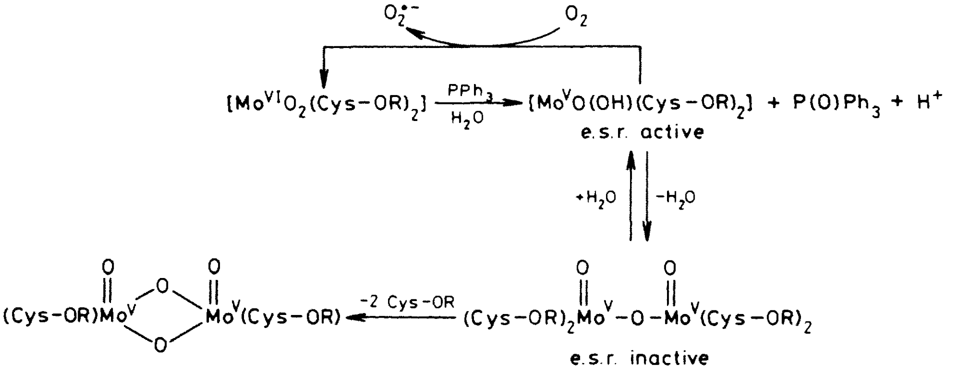


Figure 3. A proposed mechanism of the oxidation of PPh_3

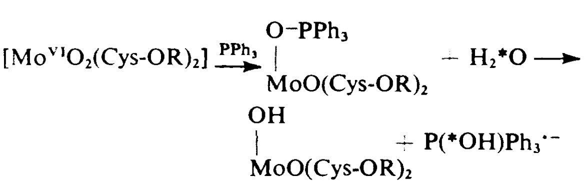
could not be maintained. On the other hand, the Mo^{VI} complex of MeCO-Cys-OH having a stable six-membered S,O chelation exhibited catalysis.

The effect of the bulkiness of the R groups of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ on the catalysis is to be considered. In either the Λ or Δ type of $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ isomers, illustrated in Figure 1, both R groups were relatively close to each other. The two thiolates co-ordinate at *trans* positions and thus both R groups are brought close together owing to the L-configuration of the cysteine alkyl ester. Therefore, we expected that the bulkiness of R would induce distortion from a regular octahedral structure by repulsion. Although the catalytic activities seem to increase with the bulkiness of the R groups, the difference between $\nu_{sym}(Mo{=}O)$ and $\nu_{asym}(Mo{=}O)$ in the Raman spectra of $[MoO_2(Cys\text{-}OR)_2]$ (R = Me, Et, Pr^i, or CH_2Ph) was independent of the bulkiness.[9] It has been suggested that the two Mo=O stretching frequencies of $[Mo^{VI}O_2(L\text{-}L)_2]$ with varying ligands relate to the oxidizing ability of the $[MoO_2]^{2+}$ moiety.[5] Our results suggest that the bulkiness does not contribute to the oxidizing ability of the $[MoO_2]^{2+}$ moiety but suppresses side reactions of the reduced species which will be mentioned later.

Role of Water in the Catalytic Cycle.—Garner *et al.*[14] and Speier[6] have reported that $[MoO_2(Cys\text{-}OEt)_2]$ and $[MoO_2(dtc)_4]$ exhibit weak catalytic activities in dmf. However, $[MoO_2(Cys\text{-}OEt)_2]$ required a large amount of water (300 mol equiv. based on the Mo^{VI} complex). Our results suggest that the dmf used by Speier[6] had been contaminated by a small amount of water. The presence of an excess of water (dmf–H_2O, 1 : 0.26) diminished the catalytic activity. The decomposition of the Mo^{VI} complex caused by an excess of water breaks the catalytic cycle. The changes in solubility of PPh_3 and $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ by dilution with water do not affect the activity. A water-soluble Mo^{VI} complex, $[MoO_2\{Cys\text{-}O(CH_2CH_2O)_nOH\}_2]$ ($n \sim 45$), decomposed rapidly in the presence of excess water giving reduced Mo^{V} species and disulphide compounds.[19]

Our study using ^{18}O-enriched water indicates that $H_2{}^{18}O$ is involved as an oxygen source for $P(O)Ph_3$ both in a stoicheiometric oxidation under anaerobic conditions and in a catalytic oxidation under aerobic conditions. At present it is not clear if water is a direct source of oxygen for $P(O)Ph_3$ because it is difficult to rule out the possibility that, after the oxygen of $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ exchanges with ^{18}O of water, the ^{18}O is incorporated in $P(O)Ph_3$ as shown in equation (2). The exchange rate of oxygen in $[Mo^{VI}O_2(Cys\text{-}OR)_2]$ with water is considered to be slow in dmf. However, the exchange rate of low-valent Mo complexes, such as reduced Mo^{V} species or Mo^{IV} species, should be faster. The rapid exchange of $[Mo^{IV}O(OH)(CN)_4]^{3-}$ with ^{18}O-enriched water was reported by Murmann and Robinson.[20] On the other hand, it is also probable that water hydrolyses a possible complex of PPh_3 with $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ as shown in equation (3).

$$[Mo^{VI}O_2(Cys\text{-}OEt)_2] + H_2{}^{*}O \longrightarrow [Mo^{VI}O^{*}O(Cys\text{-}OEt)_2] \xrightarrow{PPh_3} P(^{*}O)Ph_3 \quad (2)$$



$$[Mo^{VI}O_2(Cys\text{-}OR)_2] \xrightarrow{PPh_3} \begin{array}{c} O\text{-}PPh_3 \\ | \\ MoO(Cys\text{-}OR)_2 \end{array} + H_2{}^{*}O \longrightarrow \begin{array}{c} OH \\ | \\ MoO(Cys\text{-}OR)_2 \end{array} + P(^{*}OH)Ph_3{}^{\bullet -} \quad (3)$$

Further detailed studies are required to clarify the direct role of water for the oxidation.

The c.d. spectra of $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ in dmf or dmf–H_2O (1 : 0.15) provided important information about the role of water. The content of the binuclear di-μ-oxo-Mo^{V} complex or the mono-μ-oxo-Mo^{V} complex (15% of the total Mo species) can be estimated by the analysis of the characteristic c.d. maxima at 345 or 510 nm. Thus, the regeneration of $[Mo^{VI}O_2(Cys\text{-}OEt)_2]$ by the air oxidation of the Mo^{V} species was observed in the presence of water, but not in fresh dmf, where formation of $[Mo^{V}{}_2O_3(Cys\text{-}OR)_4]$ mainly took place. The presence of water prevents the formation of the mono-μ-oxo-binuclear complex. When the requirement of water in the catalytic cycle is considered, the structure of the reduced Mo^{V} species may be $[Mo^{V}O(OH)(Cys\text{-}OR)_2]$. In dmf containing a small amount of water, formation of $[Mo^{V}O(OH)(Cys\text{-}OR)_2]$ should compete with formation of the binuclear complexes. Absence of catalytic activity of $[Mo^{V}{}_2O_3(Cys\text{-}OR)_4]$ for the air oxidation of PPh_3 indicates that formation of the binuclear mono-μ-oxo-Mo^{V} complex is one of the side reactions required to break the catalytic cycle. The complex $[Mo^{V}{}_2O_3(Cys\text{-}OR)_4]$ then gives the binuclear di-μ-oxo-Mo^{V} complex, $[Mo_2O_2(\mu\text{-}O)_2(Cys\text{-}OR)_2]$, by oxidation at the cysteinate anions.

Involvement of a Mononuclear Mo^{V} *Complex in the Catalytic Cycle.*—Absence of ^{1}H n.m.r. signals in a solution of Mo species reduced by PPh_3 indicates the formation of a paramagnetic species, probably a mononuclear Mo^{V} complex. E.s.r. study[21] has shown that part of the reduced species exists as a mononuclear Mo^{V} complex, presumably $[Mo^{V}O(OH)(Cys\text{-}OR)_2]$. Actually, Chen *et al.*[7] reported difficulty in the reduction of $[Mo^{VI}O_2(Cys\text{-}OMe)_2]$ to $[Mo^{IV}O(Cys\text{-}OMe)_2]$ by PPh_3. On the other hand, on mild reduction of $[Mo^{VI}O_2(dtc)_2]$ no e.s.r. signal was observed. Formation of $[Mo^{V}{}_2O_3$-

(dtc)$_4$] and/or [Mo^{IV}O(dtc)$_2$] occurs. Thus, fundamental differences in the catalytic mechanism exist between [Mo^{VI}O$_2$(Cys-OR)$_2$] and [Mo^{VI}O$_2$(dtc)$_2$].

Since air oxidation of PPh$_3$ requires water and a mononuclear Mo^{V} species is involved in the system, we propose that one-electron transfer and protonation occurs to give [Mo^{V}O(OH)(Cys-OR)$_2$] in the oxidation as illustrated in Figure 3. This mechanism is similar to those proposed for desulpho xanthine oxidase,[22] and is different from the oxo-transfer reaction promoted by [Mo^{VI}O$_2$(dtc)$_2$].[4]

Conclusions

The air oxidation of PPh$_3$ catalysed by [Mo^{VI}O$_2$(Cys-OR)$_2$] (R = Me, Et, Pr^i, or CH$_2$Ph) requires an amount of water, which is involved in the formation of P(O)Ph$_3$. In the catalytic cycle, formation of a mononuclear Mo^{V} complex, probably [Mo^{V}O(OH)(Cys-OR)$_2$], was indicated by means of e.s.r. and ^{1}H n.m.r. spectra while the formation of [Mo$^{V}_2$O$_3$(Cys-OR)$_4$] or [Mo$^{V}_2$O$_4$(Cys-OR)$_2$] breaks the catalytic cycle. Bulkiness of the R groups of [Mo^{VI}O$_2$(Cys-OR)$_2$] may enhance the reoxidation of Mo^{V} to Mo^{VI} or prevent the mononuclear Mo^{V} complex from forming the mono- and di-μ-oxo-binuclear complexes, rather than strengthening the oxidation ability of the [Mo^{VI}O$_2$]$^{2+}$ group.

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Received 26*th September* 1983; *Paper* 3/1845