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Kinetics and mechanism of PPh₃ oxygenation with $^3$O₂ catalyzed by a 1,3,2-oxazaphosphole as flavin mimic

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An 1,3,2-oxazaphosphole picks up triplet dioxygen in 1:1 stoichiometry like flavin organic co-factors. It catalyzes the oxygenation of triphenylphosphine to triphenyl phosphine oxide. The reaction obeys an overall third order rate equation. In a radical pathway organic hydroperoxide is formed from the catalyst and $^3$O₂, which oxygenates PPh₃ similar as flavin cofactors.

The oxygenation/oxygenation of organic substrates with triplet dioxygen, as a primary oxidant, is a desirable way for economical and environmental reasons. However, spin restriction and thermodynamic burden hampers its reactivity. In order to circumvent these problems transition metal complexes and energy-rich organic compounds (co-factors such as pterins and flavins in biology) are necessary to activate dioxygen for these reactions.

We found earlier that 1,3,2-oxazaphospholes can easily be prepared reacting quinone monoimines with triphenylphosphine in a [4+1] electrocyclic reaction, or quinones with triphenylphosphine in the presence of ammonia in a sealed tube in good yield. Later to our surprise we observed that 1,3,2-oxazaphosphole react with triplet dioxygen in a stoichiometry of 1:1 (Scheme 1). In different solvents of the same amount of $^3$O₂ was taken up with various velocities (SFig. 2). The peroxy form is not stable at room temperature. Iodometric titration of the oxygenated solutions of 3 resulted in peroxy content 10-30% after immediate titration. This $^3$O₂-uptake is very similar to flavin models in which N,N,N-3,5,10-trialkylated flavins (1) were used and it was demonstrated that in their reaction with $^3$O₂ flavin hydroperoxides (2) can be generated. We assumed that 2,2-dihydro-2,2,2-triphenylphosphole[9,10d]1,3,2-oxazaphosphole (3) give in a similar manner alkylhydroperoxides (4) (Scheme 1), which can oxygenate/oxidize various singlet organic compounds.

Kinetic studies resulted in an overall third order rate equation, reaction rate = $k_{obs}$[catalyst][PPh₃][O₂] with a $k_{obs}$ value of 39.10±0.82×10⁻² M⁻²s⁻¹. Time course of the reaction is shown in Fig. 1, which was measured by UV/Vis spectroscopy at 260 nm (SFig. 3). The dependence on the triphenylphosphine and dioxygen concentrations showed also first order using reaction rate vs. initial concentrations of PPh₃, catalyst (3) and O₂ plots (SFig. 4, 5 and 6).

![Scheme 1](image-url)

**Scheme 1.** Similarties in flavin models (1) and 2,2-dihydro-2,2,2-triphenylphosphole[9,10d]1,3,2-oxazaphosphole (3) reactions with $^3$O₂ to give hydroperoxides 2 and the hypothetical hydroperoxide 4.

![Figure 1](image-url)

**Figure 1.** Time course of the oxygenation of PPh₃ catalyzed by 3. Temperature 80°C and 1 bar O₂ pressure, [PPh₃] = 0.5 M, [3] = 2.5×10⁻⁷ M, 20 mL DMF. TON = 160, TOF = 5.7 h⁻¹.
Labeling experiments using $^{18}$O clearly demonstrated that the O-atom of triphenylphosphine oxide originates from O$_2$. The v(P=O) frequencies being 1190 and 1153 cm$^{-1}$ for $^3$OPPh$_3$ and $^3$OPPh$_3$ (SFig. 7). The activation parameters of $E_a$ = 31.6±2.9 kJ mol$^{-1}$, $\Delta H^\ddagger$ = 28.7±2.9 kJ mol$^{-1}$, $\Delta S^\ddagger$ = -174±8 J mol$^{-1}$ K$^{-1}$ of the catalytic reaction suggest that the transition state is very crowded and the small value for the activation energy indicates the easiness of the reaction.

In order to clear some points of the reaction mechanism we measured possible radicals formed during the catalytic reaction. Fig. 2 shows that a well-resolved spectrum of the organic radical could be proved by EPR (Fig. 2) and it reacts with superoxide anion (KO$_2$) to 9 (SFig. 8). The red color changes to greenish indicating the reaction of the radical to the hydroperoxide (4) and to its decomposition products. Similar hydroperoxide have been prepared and characterized also by x-ray measurement from 3,4,6-triisopropylcatechol with di-tert-butylperoxide and dioxygen. The formation of the unstable hydroperoxide 4 is the rate-determining step ($k_{obs}$) involving also the various pre-equilibria and the fast protonation of 9. The course of the catalytic reaction of the hydroperoxide 4 with the substrate PPh$_3$ (Scheme 3) may take two pathways: a) oxygenating the bound phosphorus as part of the iminophosphorane (4), a part of the catalyst, (Pathway a) or that of added PPh$_3$ being oxygenated to the oxide (Pathway b).

Scheme 2. Proposed mechanism of hydroperoxide (10) formation.

Scheme 3. Pathways a and b for the oxygenation of PPh$_3$ by the hydroperoxide 4.

In the reaction path a where the iminophosphorane is oxygenated 9-nitroso-10-hydroxyphenanthrene (10) is formed, which is the tautomeric form of 9,10-phenanthrenequinone oxime. This is also able to transfer an O-atom to PPh$_3$ and gives 9,10-phenanthrenequinone monoimine (SFig. 10), and with additional
triphenylphosphine the iminophosphorane (S) is reformatted. Pathway b starts with the classical oxygenation of PPh₃ and 11 is formed. Triphenylphosphine thereafter abstracts an O-atom from 11 giving triphenylphosphine oxide and the iminophosphorane (S) formed just closing the catalytic cycle.

Conclusions

Although triplet dioxygen does not react with ground state, mostly singlet organic molecules its activation beside transition metal complexes can also be done with some organic molecules, possibly flavin mimics. It has been disclosed that 2,2-dihydro-2,2,2-triphenylpheno[9,10d][1,3,2k²-oxazaphosphole reacts with O₂ under ambient condition and catalyzes the oxygenation of triphenylphosphine to its oxide. Labeling experiments proved that the source of oxygen in triphenylphosphine oxide originates from dioxygen. On the basis of kinetic and spectroscopic data a possible radical mechanism is proposed. The O-transfer to triphenylphosphine from the hydroperoxide differs from the usual H₂O₂ or hydroperoxide oxygenation, since in the present case both O-atoms of the hydroperoxide are transferred to the triphenylphosphine. The scope of the catalytic oxidations/oxygenations however, remains to be elaborated.

Notes and references

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† Electronic Supplementary Information (ESI) available: Method of kinetics, kinetic data, UV-Vis spectra, infrared spectra, and activation parameters of the reaction. See DOI: 10.1039/c000000x/