Direct Synthesis of Hydrogen Peroxide from Hydrogen and Oxygen by Using a Water-Soluble Iridium Complex and Flavin Mononucleotide**

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Hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}) is known to be a highly selective and environmentally friendly oxidant and is used in the chemical industry for the manufacture of numerous organic and inorganic compounds.\textsuperscript{[1,2]} However, the current industrial process for H\textsubscript{2}O\textsubscript{2} production by sequential hydrogenation and oxidation of an alkyl anthraquinone is not environmentally benign as a result of a number of disadvantages, such as the requirement for toxic solvents, high energy consumption, and multiple steps.\textsuperscript{[3, 4]} To provide an alternative, extensive efforts have been devoted to achieving the direct synthesis of H\textsubscript{2}O\textsubscript{2} from hydrogen (H\textsubscript{2}) and oxygen (O\textsubscript{2}) by using heterogeneous precious-metal catalysts (mainly Pd, Au, or Au–Pd).\textsuperscript{[3–12]} This direct process suffers from serious problems such as unfavorable high-pressure conditions and relatively low yields owing to undesired side reactions such as formation of H\textsubscript{2}O (H\textsubscript{2} + \textfrac{1}{2}O\textsubscript{2} = H\textsubscript{2}O), decomposition of H\textsubscript{2}O\textsubscript{2} (H\textsubscript{2}O\textsubscript{2} = H\textsubscript{2}O + \textfrac{1}{2}O\textsubscript{2}), and hydrogenation of H\textsubscript{2}O\textsubscript{2} (H\textsubscript{2}O\textsubscript{2} + H\textsubscript{2} = 2H\textsubscript{2}O).\textsuperscript{[3–12]} For this reason, selectivity in the direct synthesis of H\textsubscript{2}O\textsubscript{2} from H\textsubscript{2} and O\textsubscript{2} has been limited. In addition, it has been quite difficult to elucidate the heterogeneous catalytic mechanism as compared with the homogeneous catalytic mechanism, in which intermediates can be detected. However, there has to date been no report of a homogeneous catalytic system for the direct synthesis of H\textsubscript{2}O\textsubscript{2} from H\textsubscript{2} and O\textsubscript{2}.\textsuperscript{[13]}

We report herein the direct synthesis of H\textsubscript{2}O\textsubscript{2} from H\textsubscript{2} and O\textsubscript{2} in water by using a water-soluble iridium aqua complex [Ir\textsuperscript{III}(Cp*)(4-(1\textsubscript{H}-pyrazol-1-yl-N\textsuperscript{2})benzoic acid–k\textsuperscript{C}\textsubscript{3})-(H\textsubscript{2}O)]\textsubscript{2}SO\textsubscript{4} (1\textsuperscript{2}SO\textsubscript{4}), which can react with H\textsubscript{2} to produce an iridium hydride complex (2),\textsuperscript{[14,15]} and flavin mononucleotide (FMN) under normal pressure and at room temperature. The synthesis and characterization of 1 were carried out as reported and are briefly described in the Experimental Section.\textsuperscript{[14]}

At pH 6.0, the carboxylic acid group in 1 is deprotonated to give the carboxylate form 1–H\textsuperscript{+} [Eq. (1)].\textsuperscript{[14]} The Ir\textsuperscript{III}–OH\textsubscript{2} complex 1–H\textsuperscript{+} reacts with H\textsubscript{2} in an aqueous phosphate buffer solution (pH 6.0) to produce the iridium(III) hydride complex 2 (\textlambda\textsubscript{max} = 336 nm; Equation (2) and Figure 1).\textsuperscript{[14]} The reaction of 1–H\textsuperscript{+} with H\textsubscript{2} proceeds rapidly to completion to form 2 within 3 s (Figure S1 in the Supporting Information). For the reaction of 1–H\textsuperscript{+} with O\textsubscript{2}, the formation of 2 was confirmed by changes in the UV/Vis absorption spectrum, which indicates the slower reaction of 2 with O\textsubscript{2} (Figure S2 in the Supporting Information).

![Figure 1. Changes in the UV/Vis absorption spectrum during the reaction of 1 (25 \textmu m) with H\textsubscript{2} (0.82 m \textmu m) in an aqueous phosphate buffer (pH 6.0) at 298 K. An argon-saturated buffer solution of 1 (black line) was bubbled with H\textsubscript{2} (1.0 \times 10\textsuperscript{-3} MPa) for 5 min thus resulting in the formation of 2 (red line).](image-url)

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Complex 2 can efficiently reduce FMN (\(\lambda_{\text{max}} = 373\) and 445 nm) to the 1,5-dihydroflavin (FMNH2; \(\lambda_{\text{max}} = 291\) nm and 390 nm) in aqueous phosphate buffer solution (pH 6.0) under \(\text{N}_2\) [Equation (3) and Figure 2].\(^{[16]}\) FMNH2 was also generated by catalytic reduction of FMN with \(\text{H}_2\) in the presence of 1 (Figure 3). The rise of the absorption band of FMN at \(\lambda_{\text{max}} = 445\) nm obeyed first-order kinetics (Figure S5 in the Supporting Information). From the slope of the first-order plot (inset of Figure S5 in the Supporting Information), a pseudo-first-order rate constant (\(k_{\text{obs}}\)) was obtained, and the second-order rate constant (\(k_c\)) for the reaction of FMNH2 with \(\text{O}_2\) was determined to be \(2.0 \times 10^4\) \(\text{M}^{-1}\) \(\text{s}^{-1}\). FMNH2 can also be independently generated by the reduction of FMN with sodium hydrosulfite (Na2S2O4).\(^{[16a]}\) As the reaction of FMNH2 with \(\text{O}_2\) proceeds, the formation of FMN leads to an increase in the absorbance at \(\lambda_{\text{max}} = 445\) nm, and this increase obeyed first-order kinetics (Figure S6a in the Supporting Information). The pseudo-first-order rate constant (\(k_{\text{obs}}\)) proportionally increased with concentration of \(\text{O}_2\) (Figure S6b in the Supporting Information). From the slope of the linear plot, the second-order rate constant for the reaction of FMNH2 with \(\text{O}_2\) was determined to be \(2.8 \times 10^4\) \(\text{M}^{-1}\) \(\text{s}^{-1}\). This value agrees well with \(k_c\) determined for the reaction in the presence of 1 and \(\text{H}_2\). These values are more or less consistent with the value (5.8 \(\times 10^4\) \(\text{M}^{-1}\) \(\text{s}^{-1}\)) reported for the reaction of a reduced form of a flavoprotein oxidase with \(\text{O}_2\) at pH 7.0.\(^{[17]}\)

The amount of \(\text{H}_2\text{O}_2\) produced was determined by titration with the oxo[5,10,15,20-tetra-(4-pyridyl)porphyrinato]titanium(IV) complex.\(^{[18]}\) In the reaction consisting of the stepwise reduction of FMN by \(\text{H}_2\) to form FMNH2 when using 1 followed by the oxidation of FMNH2 by \(\text{O}_2\) to generate \(\text{H}_2\text{O}_2\), a stoichiometric amount of \(\text{H}_2\text{O}_2\) was produced when the concentration of FMN was varied, thus demonstrating a linear relationship between the concentrations of \(\text{H}_2\text{O}_2\) and FMN with a slope of 1.0 (Figure 4).

Thus, the overall catalytic cycle for the selective direct synthesis of \(\text{H}_2\text{O}_2\) from \(\text{H}_2\) and \(\text{O}_2\) by using 1 and FMN is
expected to proceed according to Scheme 1: the iridium(III) complex $\text{Ir}^{III}$,$\text{H}$ reacts with $\text{H}_2$ to produce the $\text{Ir}^{III}$,$\text{H}$ complex 2, which reduces FMN to FMNH$_2$, followed by oxidation by O$_2$ to produce H$_2$O$_2$, accompanied by the regeneration of FMN.

When the catalytic reduction of FMN (5.0 μm) followed by the oxidation of FMNH$_2$ by O$_2$ was made possible by the presence of 1 (5.0 μm) in an aqueous phosphate buffer solution (pH 6.0), H$_2$O$_2$ was catalytically produced from H$_2$ and O$_2$. The formation of H$_2$O$_2$ stopped within a few minutes at pH 6.0 and 100 min at pH 2.8, when the turnover number (TON) of H$_2$O$_2$ production with respect to 1 and FMN reached 28 at pH 6.0 and 41 at pH 2.8 (Figure 5, black ●). This limited TON stands in sharp contrast to the stepwise catalytic reduction of FMN and the oxidation of FMNH$_2$ by O$_2$ (see above).

When Sc(NO$_3$)$_3$ (100 μm) was added to this system, the amount of H$_2$O$_2$ dramatically increased (Figure 5, red ▲). The TON with respect to 1 and FMN reached 201 at 4 h. When 1 (1.0 μm) and FMN (50 μm) were used, the TON based on 1 reached 847 at 4 h. The product yield of H$_2$O$_2$ based on the total amount of H$_2$ and O$_2$ supplied in the catalytic reaction system was 19.2% at 10 min (Figure S7 in the Supporting Information). This value is more than three times larger than that obtained in the nanocolloidal Pd–Au system under normal pressure of a H$_2$/O$_2$ gas mixture (6.1%).

The rate of catalytic formation of H$_2$O$_2$ is accelerated with [Sc$^{III}$] (Figure 5) and reached a turnover frequency (TOF) of 50 h$^{-1}$, however, the rate remained unchanged on increasing the concentration of Sc$^{III}$ over 50 μm. The limited TOF might be caused by the loss of H$_2$O$_2$ through the catalytic reduction of H$_2$O$_2$ by H$_2$ with 1 to produce H$_2$O (Scheme 2). This was independently confirmed by the reduction of H$_2$O$_2$ by H$_2$ when using 1 in water in the absence and presence of Sc(NO$_3$)$_3$ (Figure S8 in the Supporting Information).

The reduction of H$_2$O$_2$ to H$_2$O by H$_2$ was catalyzed by 1 (Figure S8 in the Supporting Information, black ●). However, this reaction was effectively retarded by the presence of Sc$^{III}$ (Figure S8 in the Supporting Information, red ▲), thus indicating that the further hydrogenation of H$_2$O$_2$ as shown in Scheme 2 could be inhibited by the presence of strong acid; a result consistent with the fact that H$_2$O$_2$ is known to be stabilized under acidic conditions.

In the same manner as in heterogeneous catalytic systems, the decomposition of H$_2$O$_2$ directly synthesized from H$_2$ and O$_2$ in water (pH 2.8) at 298 K in the absence (black ●) or presence of Sc(NO$_3$)$_3$ (25, 50, and 100 μm; green ▲, blue ●, and red ●, respectively). Data shown by ○ were obtained in the absence of FMN but with 1 (5.0 μm) and Sc(NO$_3$)$_3$ (100 μm) under otherwise the same experimental conditions.

![Figure 4](image4.png)

**Figure 4.** Plot of the concentration of H$_2$O$_2$ produced by the catalytic reduction of O$_2$ (1.0 × 10$^{-7}$ MPa) by FMNH$_2$ (generated through the reduction of FMN by 2 under H$_2$) versus the concentration of FMN (25 μm–1.0 mm) loaded at the beginning of the reaction at 298 K. 2 was produced by the reduction of 1 (25 μm) by H$_2$ (1.0 × 10$^{-7}$ MPa) in an aqueous phosphate buffer solution (pH 6.0).

![Scheme 1](image1.png)

**Scheme 1.**

![Scheme 2](image2.png)

**Scheme 2.**
ditions, selective two-electron reduction of O₂ to H₂O₂ occurs without the further reduction of H₂O₂ to H₂O.

In conclusion, the water-soluble iridium(III) complex I can efficiently catalyze the direct synthesis of H₂O₂ from H₂ and O₂ when using a water-soluble flavin (FMN) under normal pressure in aqueous solution at 298 K. The catalytic cycle consists of the reduction of I by H₂ to form the Ir³⁺H complex 2, followed by the reduction of 2 by FMN to FMNH₂, which then reacts with O₂ to produce H₂O₂, accompanied by the regeneration of FMN and I. The addition of Sc(NO₃)₃ led to a high TON (847) and a reasonably high yield of H₂O₂ concentration of H₂ in an aqueous solution was prepared by GB-3C, KOJIMA Instrument Inc.), which can mix two or more gases /C23 2013 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

\[ \text{Keywords:} \quad \text{homogeneous catalysis · hydrogen · hydrogen peroxide · iridium · oxygen} \]


[21] The maximum rate of this reaction step ($r_{\text{B,max}}$) in Scheme 1 under catalytic reaction conditions in the absence of Sc(NO3)3 was determined to be $r_{\text{B,max}} = k_{\text{B}}[\text{FMN}]_{\text{max}}[\text{2}]_{\text{max}} = 1.5 \times 10^{-9} (\text{m}^{-1} \cdot \text{s}^{-1}) \times 5.0 \times 10^{-9} (\mu) \times 5.0 \times 10^{-6} (\mu) = 3.8 \times 10^{-6} \text{ms}^{-1}$. This value is significantly smaller than that for the next catalytic step ($r_{\text{C,max}}$), the reduction of O2 by FMNH2, which was determined to be $r_{\text{C,max}} = k_{\text{C}}[\text{FMNH2}]_{\text{max}}[\text{O2}] = 2.8 \times 10^{-9} (\text{m}^{-1} \cdot \text{s}^{-1}) \times 5.0 \times 10^{-9} (\mu) \times 1.4 \times 10^{-3} (\mu) = 2.0 \times 10^{-9} \text{ms}^{-1}$. The reaction rate of the first catalytic step ($r_{\text{A}}$), the reaction of 1 with H2, can be evaluated based on the data in Figure S1 in the Supporting Information, and was determined to be $r_{\text{A}} > 6.0 \times 10^{-8} \text{ms}^{-1} > r_{\text{B,max}}$. 