

Photosensitized Oxidative Deprotection of Oximes to Their Corresponding Carbonyl Compounds by Platinum(II) Terpyridyl Acetylide Complex

Yue Yang, Dong Zhang, Li-Zhu Wu,* Bin Chen, Li-Ping Zhang, and Chen-Ho Tung*

Technical Institute of Physics and Chemistry, the Chinese Academy of Sciences, Beijing 100101, China

chtung@mail.ipc.ac.cn; lzwu@mail.ipc.ac.cn

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Platinum(II) terpyridyl acetylide complex (**1**) photosensitizes the oxidation of aldoximes **2–4**, aliphatic acyclic and cyclic ketoximes **5–7**, and aromatic ketoximes **8–10** into their corresponding carbonyl compounds with good to excellent yields in acetonitrile solution. This deprotection of oximes proceeds via singlet oxygen ($^1\text{O}_2$) mechanism. The photosensitizer can be easily separated from the product and unreacted starting material by extraction with ethyl acetate and reused for photooxidation without loss of $^1\text{O}_2$ -generation capacity.

Introduction

Oximes are extensively used for group protecting, purification, and characterization of carbonyl compounds.^{1–3} Furthermore, their synthesis from non-carbonyl compounds provides an alternative way for preparation of aldehydes and ketones.⁴ Thus, there has been increasing interest in the development of methods for the conversion of oximes into their corresponding carbonyl compounds, and a number of methods, including hydrolytic,⁵ reductive,^{6,7} and oxidative^{8–11} cleavage reactions, have been explored. However, these methods suffer from one or more disadvantages such as the use of toxic reagents and expensive transition metals, the low yields of the products, and the difficulty in the product isolation. Evidently, it is desirable to develop a method that is environmentally benign and can be applied to a wide range of aldoximes and ketoximes with high selectivity and easy product isolation. Here, photochemical processes hold special promise. Yates and co-worker showed that both aromatic aldoximes and ketoximes in acidic or basic aqueous solution underwent photohydrolysis via their lowest excited singlet state to yield the corresponding

carbonyl compounds.¹² However, the quantum yields for this photochemical deprotection were generally low, and the photohydrolysis for certain oximes could not occur. Furthermore, in this reaction UV light was used to directly excite the substrate, and the yielded carbonyl products also absorbed in this wavelength region. To avoid the secondary photochemical reaction of the products, one has to keep the irradiation time short enough to ensure a low conversion. This in turn results in the difficulty in product isolation. Recently, de Lijser and co-workers reported that chloranil could photoinitiate the deprotection of a variety of oximes via a photoinduced electron-transfer process.¹³ In these reactions, the sensitizer also underwent photochemical reaction and the amount of chloranil used was 2 times of that of the substrate. The product yields were in the range of 5–66% for aldoximes and ketoximes due to the formation of nitriles and polymers during photolysis. Early research carried out by Wamser and co-worker showed that dye (rose bengal) could photosensitize the oxidation of benzophenone oxime derivatives into the ketone with reasonable yield.¹⁴ They proposed that this photosensitized oxidation proceeds via singlet oxygen ($^1\text{O}_2$) mechanism. Curiously, extension of this efficient photochemical deprotection to the oximes of other carbonyl compounds has never been reported. In the present work we report that a variety of oximes of aldehydes, aliphatic acyclic and cyclic ketones, and aromatic ketones undergo the reaction with $^1\text{O}_2$ to yield the corresponding carbonyl compounds in good to excellent yields. We chose platinum(II) terpyridyl acetylide complex (**1**, Chart 1) as the sensitizer, because this complex may photochemically generate $^1\text{O}_2$ with high quantum yield and absorbs light in visible region where the oxime substrates and carbonyl products do not absorb, thus avoiding the secondary photochemical

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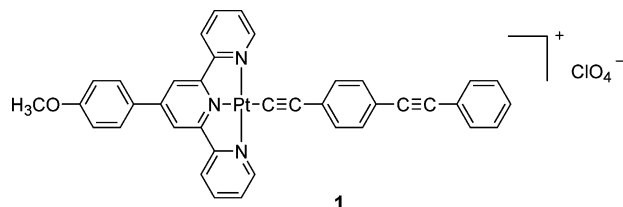
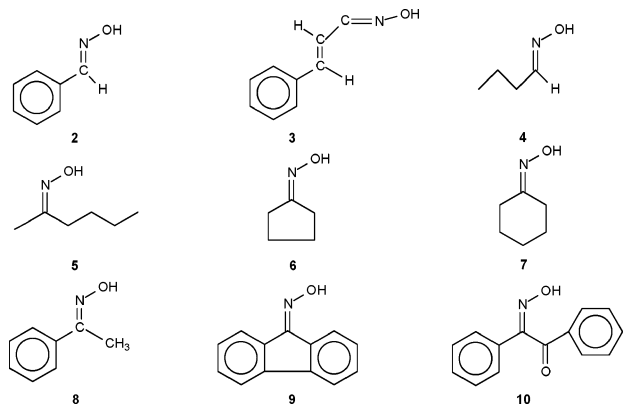
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CHART 1. Structure of Platinum(II) Terpyridyl Acetylide Complex 1**CHART 2. Structure of Oximes**

reactions of the products. The substrates studied involve aldioximes (**2–4**), aliphatic acyclic and cyclic ketoximes (**5–7**), and aromatic ketone oximes (**8–10**), and their structures are shown in Chart 2.

Results and Discussion

Photosensitized Oxidation. **1** in acetonitrile solution exhibits intense vibronic-structured absorption bands at $\lambda < 350$ nm with extinction coefficients (ϵ) on the order of $10^4 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ and a less intense band in the region of 400–520 nm with ϵ on the order of $10^3 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$. The absorption spectral properties were found to follow Beer's Law below saturated concentration in this solvent, suggesting that no significant complex aggregation occurred. The absorption bands at $\lambda < 350$ nm are assigned to the intraligand (IL) transition of terpyridyl and acetylide ligands as well as the charge-transfer transition involved in the Pt–C \equiv CR moiety, while the low-energy absorption band at 400–520 nm is assigned to the $d\pi(\text{Pt}) \rightarrow \pi^*(\text{trpy})$ metal-to-ligand charge transfer (MLCT) transition. In the photosensitized oxidation of the oximes, we selectively excited the MLCT band.

The photosensitized reaction was carried out in oxygen-saturated acetonitrile solution (bubbling with oxygen). Typically, 40 mL of a solution of the substrate (1×10^{-2} M) and the photosensitizer (1×10^{-5} M) in a Pyrex reactor was irradiated by a 500 W high-pressure Hanovia mercury lamp. A glass filter was employed to block light with wavelengths below 400 nm; thus, only the photosensitizer was irradiated. The progress of the reaction was followed by thin-layer chromatography. Generally, after 10 h of irradiation the conversion was close to 100%. The products were purified by flash chromatography and identified by ^1H NMR spectroscopy, MS spectrometry, and on the basis of known retention times of authentic compounds on GC. Table 1 gives the conversions of the oximes and the yields of the isolated carbonyl products

TABLE 1. Conversions and Isolated Product Yields in Photosensitized Oxidation of Oximes by Complex 1 in Acetonitrile Solution after 6 h of Irradiation

oxime	irradiation time (h)	conversion (%) ^a	yield (%) ^b
2	6	75	78
3	6	68	10
4	6	81	78
5	6	70	84
6	6	66	66
7	6	60	67
8	6	95	93
9	1	95	94
10	6	73	57

^a Concentration of **1** is ca. 1×10^{-5} M, and that of the oxime is 0.5×10^{-2} M. ^b Based on consumption of starting materials.

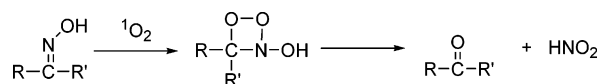
(based on the consumed starting materials) after the samples were irradiated for 6 h. Evidently, aromatic ketoximes underwent the reaction much faster than the other oximes. For example, 1 h irradiation of **9** solution led to 95% conversion. In general the photosensitized oxidative cleavage of all the oximes studied gives the corresponding carbonyl compounds in good to excellent yields except for oxime **3**, where a significant amount of benzaldehyde was produced, suggesting that the olefine C=C band was also oxidized.

The photosensitizer can be easily separated from the reaction mixture and can be reused. For example, after most of the substrate was consumed in the course of irradiation, we evaporated the solvent acetonitrile and used ethyl acetate to extract the product and the unreacted starting material. The residue of **1**, which is insoluble in ethyl acetate, was redissolved in acetonitrile and reused as the sensitizer. After 20 cycles, **1** was still able to photosensitize the deprotection of the oximes without significant loss of $^1\text{O}_2$ -generation capacity.

Mechanism of the Photosensitized Oxidation. de Lijser and co-workers used chloranil to successfully photosensitize the deprotection of a series of oximes to their corresponding carbonyl compounds.¹³ They proposed that the deprotection proceeds via an electron-transfer mechanism. In our case, the photoinduced electron-transfer mechanism can be excluded by the following experiments. First, we have performed the photoluminescence quenching study. Complex **1** in degassed acetonitrile at room temperature displays moderately intense photoluminescence with λ_{max} at 620 nm. This emission is assigned as arising from the $^3\text{MLCT}$ state. None of the oximes studied in the present work can quench the photoluminescence of **1**, suggesting the absence of electron transfer (and energy transfer) between the excited state of **1** and the oxime. Indeed, calculation of the free energy change (ΔG_{ET}) involved in the photostimulated electron-transfer process by the Weller equation reveals that the electron transfer for all the oximes is endothermic and thus impossible.¹⁵ Second, we have performed the photosensitized deprotection of oximes by Nafion-supported photosensitizer. Nafion is a family of polymers that consists of a perfluorinated backbone and short

(15) Triplet energy of **1** is ca. 54.7 kcal/mol as estimated from its photoluminescence spectrum. The reduction potential of **1** is ca. -0.83 eV, and the oxidation potentials of the oximes have been reported by de Lijser.¹³ Calculation by the Weller equation reveals that for all the oximes, the electron transfer from the substrate to the $^3\text{MLCT}$ state of **1** is endothermic.

SCHEME 1



pendant chains terminated by sulfonic groups.¹⁶ When swollen in water or methanol, the structure of Nafion is believed to resemble that of an inverse micelle. The hydrated SO_3^- headgroups are clustered together in a water- or methanol-containing pocket ca. 40 Å in diameter, and the pockets are interconnected with each other by short channels within the perfluorocarbon matrix. Complex **1** can be easily adsorbed into Nafion membranes by immersing the polymer in a well-stirred solution of **1** in methanol. The sample incorporating **1** was removed from the methanol solution, and the methanol adsorbed in the Nafion membranes was evaporated. Then, we used a small amount of D_2O to swell the **1**-incorporated Nafion membranes and immersed them in oxygen-saturated dichloromethane where the oxime substrate was dissolved. Since dichloromethane cannot swell Nafion and is insoluble in water, the water in Nafion cannot be extracted into the solution. On the other hand, the oxime substrate in dichloromethane cannot diffuse into the Nafion because it is insoluble in water. Photoirradiation of the **1**-incorporated Nafion in the manner described above efficiently resulted in the deprotection of the oxime in the outside solution. For example, in the case of **8** as the substrate, 3 h of irradiation led to ca. 20% conversion, and the yield of the acetophenone based on the consumed **8** was ca. 74%. Since the photosensitizer in Nafion is isolated from the oxime in the solution outside, electron transfer between the excited state of **1** and the substrate should be inhibited. The observation of the efficient deprotection suggests that the photosensitization must not proceed via an electron-transfer mechanism.

We believe that our photosensitized deoxime involves singlet oxygen, because in the absence of oxygen the reaction cannot occur. Furthermore, we have demonstrated by EPR spectroscopy that ${}^1\text{O}_2$ was indeed generated upon irradiation of the photosensitizer.¹⁷ It has been established that 2,2,6,6-tetramethylpiperidine (TMP) reacts with ${}^1\text{O}_2$ to give the stable free radical nitroxide (TMPO), which can be readily detected by EPR spectroscopy.¹⁸ We dissolved TMP and **1** in oxygen-saturated acetonitrile and irradiated the solution using light with wavelengths above 400 nm. After 100 s of irradiation of the solution, the nitroxide free radical was clearly detected (see Supporting Information). Obviously, interaction between oxygen and the triplet state of **1** results in energy transfer yielding ${}^1\text{O}_2$. We have determined the quantum yield of the ${}^1\text{O}_2$ for **1** as the sensitizer in acetonitrile by a 9,10-diphenylanthracene bleaching method¹⁹ and found that this quantum yield was close to 1.0. The generated ${}^1\text{O}_2$ would undergo [2 + 2] cycloaddition with the $\text{C}=\text{N}$ double bond of the oximes to give dioxetane analogues (Scheme 1) as in the case of the

cycloaddition with olefins.²⁰ The unstable dioxetane analogues could decompose under the reaction conditions to yield the corresponding carbonyl products and nitrite.¹⁴ Indeed, we detected the formation of nitrite ion by using acidic ferrous sulfate after the reaction was accomplished.²¹

In the case of Nafion-supported **1** as the sensitizer, the oxygen in the outside dichloromethane solution can diffuse into the D_2O -swollen Nafion and undergo energy transfer with the triplet state of sensitizer **1**. The generated ${}^1\text{O}_2$ diffuses back to the outside solution to react with the substrate to form the corresponding carbonyl compound. Thus, although the Nafion-incorporated **1** cannot undergo photoinduced electron transfer with the oxime in solution outside, the photosensitized oxidation for this sensitizer system can efficiently operate.

Conclusion

Singlet oxygen, generated by photosensitization, reacts with aldoximes and ketoximes to produce their corresponding carbonyl compounds. This deprotection of oximes employs molecular oxygen as the oxidant, and the process is environmentally benign. Although the reactions have not been optimized, the yields of the carbonyl compounds are generally good or even excellent. Thus, these reactions may serve as a potential synthetic method for deoximes. Particularly in the case of **1** as the sensitizer, after the reaction is completed, the sensitizer can be easily separated from the products and unreacted starting material and can be reused many times without loss of ${}^1\text{O}_2$ -generation capacity.

Experimental Section

Materials and Instrumentation. Oximes **2–10** were prepared from their corresponding aldehydes or ketones according to a standard oximation method.²² The solvents, acetonitrile and dichloromethane, used in this work were of analytic grade. Nafion membrane 117 in acid form (Nafion- H^+) with an equivalent weight of 1100 and a thickness of 0.0175 cm was a product of DuPont. Prior to use, the membrane was cleaned by boiling in concentrated nitric acid for 4 h and then thoroughly washed with distilled water and finally immersed in water for 24 h. The membrane in sodium form (Nafion- Na^+) was obtained by immersing the pretreated Nafion- H^+ membrane in 1 N NaOH aqueous solution. Excess base was then removed by stirring the sample in water.

Synthesis of Platinum(II) Terpyridyl Acetylde Complex (1). Complex **1** was prepared in two steps. First, the starting material, $[\text{Pt}(4'-(p\text{-methoxyphenyl})\text{-trpy})\text{Cl}]\text{Cl}$ (trpy = 2,2':6',2''-terpyridine), was prepared by a literature method,²³ using 4'-(*p*-methoxyphenyl)-terpyridine and K_2PtCl_4 as the reagents. This starting

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material was then reacted with 2 equiv of $\text{HC}\equiv\text{CC}_6\text{H}_4\text{C}\equiv\text{CC}_6\text{H}_5$ -4 in dimethylformamide in the presence of catalyst CuI and triethylamine at room temperature. After metathesis reaction by NaClO_4 and recrystallization of the crude product by vapor diffusion of diethyl ether into an acetonitrile solution, **1** was obtained as orange crystals with ca. 80% yield. FAB-MS: m/z 735 (M^+). ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 3.92 (s, 3H), 7.22 (d, 2H, $J = 8.85$ Hz), 7.46 (m, 3H), 7.52 (m, 4H), 7.59 (m, 2H), 7.91 (t, 2H, $J = 6.64$ Hz), 8.19 (d, 2H, $J = 8.81$ Hz), 8.53 (t, 2H, $J = 8.13$ Hz), 8.85 (d, 2H, $J = 8.02$ Hz), 8.97 (s, 2H), 9.12 (d, 2H, $J = 5.50$ Hz). Anal. Calcd for $\text{C}_{38}\text{H}_{26}\text{ClN}_3\text{O}_5\text{Pt}\cdot 0.5\text{H}_2\text{O}$: C, 54.07; H, 3.22; N, 4.98; O, 10.42. Found: C, 53.84; H, 2.94; N, 4.81; O, 10.38. UV: $\lambda_{\text{max}} = 460$ nm in CH_3OH ($\epsilon = 7560 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$). Emission: $\lambda_{\text{em}} = 620$ nm in CH_3OH .

Photosensitized Oxidation in Solutions. The photooxidation was carried out in acetonitrile solution in a Pyrex reactor. The light source was a 500 W high-pressure Hanovia mercury lamp with a glass filter to block light with wavelengths below 400 nm, thereby ensuring the absence of direct excitation of the oxime substrate. During irradiation, oxygen was bubbled through the solution. After the oxidative deprotection was completed, the solvent was evaporated, and the residue was extracted with ethyl acetate. The products were analyzed by GC, isolated by column chromatography on silica, and identified by their MS and ^1H NMR spectral properties.

Photooxidation by Nafion-Supported **1.** The weighed Nafion membrane samples were immersed in a solution of **1** in methanol, and the solution was continuously stirred. The amount of the uptake of **1** by the membranes was determined by UV absorbance. The membrane samples were taken off, and the adsorbed

methanol was evaporated under reduced pressure. The dry samples having incorporated **1** were immersed in D_2O to prepare D_2O -swollen samples.

The samples of D_2O -swollen Nafion-supported **1** were immersed in a solution of the oxime substrate in dichloromethane and irradiated under conditions similar to those mentioned above. During irradiation, oxygen was bubbled through the solution. After irradiation, the Nafion-supported sensitizer was removed from the reaction vessel, and the products were analyzed and isolated as in the case of photooxidation in solution.

Detection of Nitrite in the Photooxidation Solution. After the photosensitized oxidative deprotection of oximes was accomplished, to the solution was added a drop of aqueous acidic ferrous sulfate. A dark green-brown color was observed, indicating the presence of nitrite.²¹ A control experiment with the solution including **1** and the substrate in acetonitrile before irradiation showed no color change upon addition of the acidic ferrous sulfate.

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Supporting Information Available: ESR spectrum of nitroxide radical generated by irradiation of the oxygen-saturated TMP solution in acetonitrile in the presence of **1**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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