ORGANIC LETTERS

2003
Vol. 5, No. 18
3221−3224

Versatile Photosensitization System for $^1O_2$-Mediated Oxidation of Alkenes Based on Nafion-Supported Platinum(II) Terpyridyl Acetylide Complex

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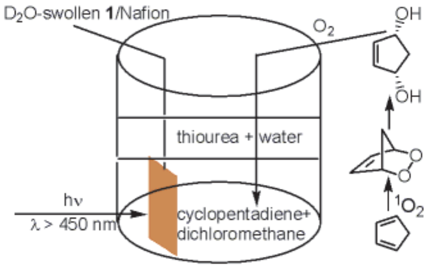
Received June 6, 2003

ABSTRACT



Platinum(II) terpyridyl acetylide complex (1) was incorporated into Nafion membranes as a photosensitizer, and the Nafion was immersed in an aqueous or organic solution of 7-dehydrocholesterol, α-pinene, or cyclopentadiene. This photosensitizer system can generate singlet oxygen ($^1O_2$) in high quantum yield to oxidize the alkenes in the solution outside the Nafion and can be easily removed from the reaction vessel at the end of the photooxidation.

The oxo-functionalization of small abundant hydrocarbons is the most important type of reaction in organic chemical productions.[1,2] For example, essentially almost all building blocks for manufacture of plastics and synthetic fibers are produced by oxidation of hydrocarbons.[1] Among the various oxidizing reagents, oxidation by molecular oxygen (O_2) is of particular interest in realizing economically advantageous and environmentally benign processes.[2−4] However, the reactivity of O_2 toward most organic molecules is inhibited by its spin restriction, and here photoassisted processes hold special promise.[5,6] The most synthetically useful type of hydrocarbon photooxidation is the dye-sensitized reaction involving transient singlet oxygen ($^1O_2$). For example, Diels−Alder reaction of conjugated dienes, “ene” reaction of olefins with allylic hydrogen, and dioxetane reaction of alkenes that do not feature an allylic hydrogen belong to this type of photooxidation.[7,8] However, examples of production of chemicals by this type of photooxidation in industrial scale are still limited. One of the reasons for this is that the separation of the sensitizer from the products and unreacted starting material at the end of the reaction is tedious; thus,

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10.1021/ol035012e CCC: $25.00

the sensitizer cannot be reused. Here we report a versatile and robust Nafion membrane-supported photosensitizer system that is capable of generating $^1O_2$ with high quantum yield and may be easily removed from the reaction vessel and reused for photooxidation without loss of $^1O_2$-generation capacity.

Our photosensitizer system is based on a Nafion membrane-supported transition metal complex. Nafion is a family of polymers that consists of a perfluoronated backbone and short pendant chains terminated by sulfonic groups.[9] 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-containing pocket of ca. 40 Å in diameter, and the pockets are interconnected with each other by short channels within the perfluorocarbon matrix. This water-swollen Nafion can incorporate high concentrations of aromatic hydrocarbons and organic dyes.[10,11] Furthermore, the concentration of oxygen in water-swollen Nafion is more than 10 times greater than in organic solvents.[12,13] Thus, these optically transparent membrane systems are particularly suitable for photooxidation purposes.

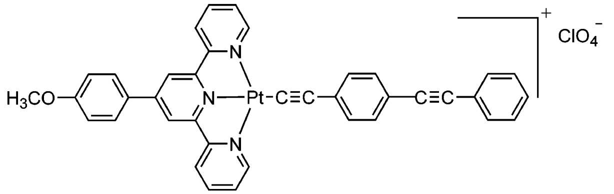

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Figure 1. Structure of the sensitizer.

Platinum(II) terpyridyl acetylide complex (**1**, Figure 1)[14] is chosen as the sensitizer, because this complex absorbs light in the visible region and may photochemically generate $^1O_2$ with high quantum yield (see below). Furthermore, this complex is positively charged and with aromatic ligands. Due to hydrophobic and electrostatic interactions, **1** can be easily adsorbed into Nafion by immersing the polymer into a well-stirred aqueous or methanol solution of the complex and is not leached from the polymer during the photosensitized reaction. Considering the hydrophobicity and the positive charge of the complex, it is likely that the molecules of **1** are located in the fluorocarbon/water interface of the membrane. The Nafion membranes used in the present study were their sodium form (Nafion-Na^+) and had the size of $2 \times 0.4 \times 0.0175$ cm. The loading of the sensitizer was ca. 5 μmol/g Nafion, which allowed the optical density of a single piece of membrane at the λ_{max} of the MLCT transition over 1.0.

The photosensitized oxidations were carried out in oxygen-saturated solution of the substrate in which the sensitizer-incorporated Nafion membranes were immersed. We have demonstrated by EPR spectroscopy that singlet oxygen could be generated in Nafion and could diffuse into the solution to oxidize the substrate. It has been established[15] that 2,2,6,6-tetramethyl-piperidine (TMP) reacts with $^1O_2$ to give the stable free radical nitroxide (TMPO), which can be readily detected by EPR spectroscopy. Thus, we dissolved TMP in oxygen-saturated methanol and immersed the complex-incorporated Nafion membranes in the solution. Figure 2 shows the EPR spectrum obtained after 100 s of irradiation of the solution and clearly demonstrates the formation of the nitroxide free radical. This observation can be interpreted in terms of the fact that methanol can swell the complex-incorporated Nafion membrane, thus enabling oxygen to diffuse into the membrane from the solvent. Interaction between oxygen and the triplet excited state of the complex results in energy transfer to generate singlet oxygen, which diffuses back to the solution to react with TMP resulting in the nitroxide radical.

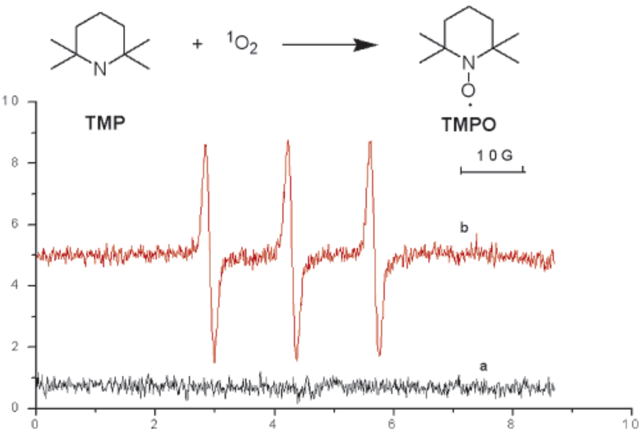

Figure 2. EPR spectrum of nitroxide radical generated by irradiation of the oxygen-saturated TMP methanol solution, where **1**-incorporated Nafion was immersed (a) in the dark and (b) after the sample was irradiated for 100 s.

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(14) Complex **1** was prepared by the reaction of [Pt(trpy)Cl]Cl (trpy = 4′-(4-methoxy-phenyl)-2,2′:6′,2″-terpyridine) with 2 equivalent amounts of $HCCC_6H_4CCC_6H_5$-4, which was synthesized by the literature method (Khatyr, A.; Ziessel, R. *J. Org. Chem.* **2000**, *65*, 3126) in DMF in the presence of catalyst CuI and trimethylamine under nitrogen at room temperature. Recrystallization of the crude product by diffusion of diethyl ether vapor into an acetonitrile solution gave **1** as orange crystals. FAB-MS: *m/z* 835(M^+). ^{1}H NMR (600 MHz, 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. Cacld for $C_{38}H_{26}ClN_3O_5Pt{\cdot}0.5H_2O$: C, 54.07; H, 3.22; N, 4.98; O, 10.42. Found: C, 53.84; H, 2.94; N, 4.81; 0, 10.38. IR: $\nu = 2118$ cm^{-1}. UV: λ_{ab} (CH_3OH) = 460 (ϵ =7560 dm^3 mol^{-1} cm^{-1}). Emission: λ_{em} (CH_3OH) = 620 nm.

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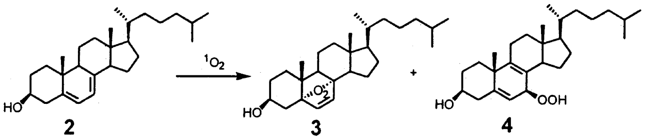
Table 1. Oxidation Products of 7-Dehydrocholesterol (**2**) and α-Pinene (**5**) Photosensitized by **1**-Incorporated in Nafion at Room Temperature

substrate	photosensitizer	solvent	irradiation time (min)	products	conversion (%)	isolated yield (%)
2	TPP (1×10^{-5})[a]	CH_3OH	60	**3**, **4**	90	75:25
2	CH_3OH-swollen **1**/Nafion	CH_3OH	60	**3**, **4**	20	95, minor
2	CD_3OD-swollen **1**/Nafion	CD_3OD	60	**3**, **4**	90	95, minor
2	H_2O-swollen **1**/Nafion	CH_2Cl_2	180	**3**	10	80
2	D_2O-swollen **1**/Nafion	CH_2Cl_2	180	**3**	95	80
5	H_2O-swollen **1**/Nafion	CH_2Cl_2	120	**7**	10	95
5	D_2O-swollen **1**/Nafion	CH_2Cl_2	120	**7**	95	95

[a] Photooxidation sensitized by TPP performed in homogeneous solution.

Scheme 1



The first substrate we studied is 7-dehydrocholesterol (cholesta-5,7-dien-3*β*-ol, **2**, Scheme 1). This substrate is an endogenous compound of the body, involved in a variety of biological processes, and some of its oxidation products possess potent cytotoxic and antitumor activity.[16] It was reported that irradiation of oxygen-saturated solution of **2** in ethanol in the presence of eosin or rose bengal resulted in cholesta-5α,8α-epidioxy-6-ene-3*β*-ol (**3**) and cholesta-5,8-dien-7*β*-hydroperoxide (**4**)[17] as shown in Scheme 1. Both products were derived from $^1O_2$ oxidation and the molar ratio of **3** to **4** was ca. 2.88. We performed the photooxidation by irradiation of **1**-incorporated Nafion membranes that were immersed in oxygen-saturated solution of **2** (2.6×10^{-3} M) in methanol. A glass filter was used to filter out the light with $\lambda < 450$ nm; thus, **1** was selectively excited. After irradiation, the products were isolated by column chromatography on silica eluting with petroleum ether/ethyl acetate and identified by ^{1}H NMR and MS spectroscopy,[18] and the data of the ^{1}HNMR and MS spectroscopy were in agreement with those reported in the literature.[16] The main product was **3**, and only a trace of **4** was obtained. The isolated yield of **3** was greater than 95% on the basis of the consumption of the starting material. However, the quantum yield of the product formation was low. For example, irradiation of oxygen-saturated solution of **2** in methanol in the presence of tetraphenylporphrin (TPP), a typical $^1O_2$ sensitizer, for 60 min resulted in ca. 90% conversion (Table 1). Under identical conditions, irradiation of the sample with **1**-incorporated Nafion as the sensitizer for 60 min only led to ca. 20% conversion. The low quantum yield in the latter case is probably due to the fact that $^1O_2$ was generated within Nafion membrane, and a fraction of the generated $^1O_2$ was quenched by the solvent during its diffusion into the outside solution. To increase the quantum yield of $^1O_2$, which could diffuse into the solution outside Nafion, we used deuterium methanol CD_3OD instead of CH_3OH, because the lifetime of $^1O_2$ in CD_3OD is much longer than in CH_3OH.[19] Indeed, irradiation of **1**-incorporated Nafion membranes immersed in oxygen-saturated solution of **2** in CD_3OD for 60 min gave ca. 90% conversion and the mass balance was greater than 95%. We determined the quantum yield of the $^1O_2$ that had diffused into the solution outside Nafion by 9,10-diphenylanthrancene bleaching method[20] and found that this quantum yield was ca. 0.56 in CD_3OD and ca. 0.21 in CH_3OH. The former value is comparable with the quantum yield of $^1O_2$ formation for TPP sensitizer in benzene ($\Phi = 0.56$).[21]

To save the expensive deuterium solvent, we performed the photooxidation by water-swollen Nafion. We used a small amount of D_2O to swell the complex-incorporated Nafion membranes and immersed them in oxygen-saturated dichloromethane where the 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 substrate cannot diffuse into the Nafion because it is insoluble in water. However, oxygen in the outside solution can diffuse into the Nafion and undergo energy transfer with the triplet state of the sensitizer. The generated $^1O_2$ diffuses back to the outside solution to oxidize the substrate. Irradiation of such a system for 3 h resulted in ca. 95% conversion (Table 1).[22] This photosensitizer system seems to be universal for various substrates because we can change the outside solvent according to the substrate solubility.

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[17] Albro, P. W.; Corbett, J. T.; Schroeder, J. L. *Photochem. Photobiol.* **1994**, *60*, 310.

[18] **Compound 3.** MS: *m/z* 416 (M^+). ^{1}H NMR (400 MHz, CD_3OD) δ: 0.79 (s, 3H, 13-CH_3), 0.89 (s, 3H, 10-CH_3), 3.80 (1H, 3α-H, m), 6.26 (d, $J = 8.5$ Hz, 1H, 6-H) and 6.54 (d, $J = 8.5$ Hz, 1H, 7-H). **4**: MS: *m/z* 416 (M^+). ^{1}H NMR (400 MHz, CD_3OD) δ: 0.66 (s, 3H, 18-CH_3), 1.31 (s, 3H, 19-CH_3), 3.50 (1H, 3α-H, m), 4.57 (H−7, bs), 5.73 (H-6, d, $J = 1.44$ Hz).

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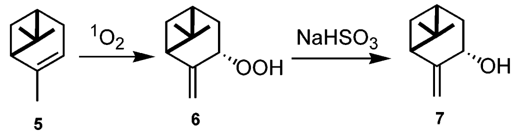
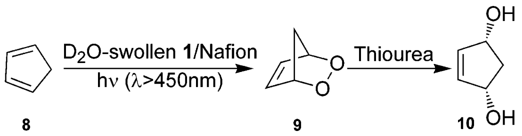
[22] In contrast, under the same conditions, irradiation of the H_2O-swollen sample for 3 h only gave ca. 10% conversion.

Scheme 2



The second substrate we studied is (1*S*,5*S*)-(−)-α-pinene [**5**, Scheme 2]. It was established that the photosensitized oxidation of **5** to form ene product **6** exclusively is a typical example of singlet oxygen oxidation reactions.[23] We conducted this oxidation in the same manner as that for **2**. After reduction of the reaction mixture with sodium sulfite solution, the product was isolated by column chromatography on silica to give (1*S*,3*S*,5*R*)-(+)-*trans*-3-hydroxypin-2(10)-ene [(+)-*trans*-pinocarveol, (+)-**7**]. The data of the ^{1}H NMR spectroscopy of **7** were in agreement with those reported in the literature,[23,24] and the isolated yield of this product is shown in Table 1. Evidently, by using D_2O-swollen **1**-incorporated Nafion as the sensitizer and dichloromethane as the solvent, the oxidation proceeded with relatively high quantum yield and the isolated yield of **7** was greater than 95%.

Scheme 3



The third substrate we studied is cyclopentadiene (**8**, Scheme 3). This diene undergoes [4 + 2] cycloaddition with $^1O_2$ to yield epidioxide (**9**), which can be reduced by thiourea to yield *cis*-2-cyclopentene-1,4-diol (**10**).[25] It has been reported that **10** is an important chemical for synthesis of prostaglandins.[26] We carried out the photooxidation in a glass tube that contained the mixture of dichloromethane and water (1:1 v/v) as shown in the Abstract graphic. The substrate (0.01 M) and thiourea were dissolved in the bottom dichloromethane layer and the top aqueous layer, respectively. A piece of **1**-incorporated Nafion membrane was swollen by D_2O and immersed in the dichloromethane layer. During the irradiation, oxygen was bubbled into the dichloromethane. The generated **9** in dichloromethane reacted with thiourea at the interface between water and dichloromethane to yield the diol **10**. Because **10** is very polar, it moved into the aqueous layer. Thus, at the end of the reaction the unreacted starting material remains in the dichloromethane layer, the product is dissolved in the water layer and the sensitizer is incorporated in the Nafion membrane. These components in the reaction mixture were readily separated. Generally, after 180 min of irradiation, the conversion of the starting material was grater than 95%. Product **10** was obtained with high purity by separation of the aqueous layer followed by evaporation of the water and extraction with chloroform.[27] The isolated yield of **10** was close to 100% on the basis of the consumption of the starting material.

It is of particular interest that in the above outlined photooxidations, the sensitizer system is reusable. For example, in the oxidation of **8**, the D_2O-swollen **1**-incorporated Nafion membranes were reused 20 times without significant loss of $^1O_2$-generation efficiency. We will continue to extend the scope of the application of this sensitizer system.

Acknowledgment. Financial support from the Ministry of Science and Technology of China (Grant Nos. G2000078104 and G2000077502) and the National Science Foundation of China is gratefully acknowledged.

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[26] Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1988**, *110*, 4726.

[27] **Compound 10.** MS: m/z 100 (M^+), 82 $(M - 18)^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.54 (d.t, J = 15 and 4 Hz, 1H), 2.70 (d.t, J = 15 and 7 Hz, 1H), 4.65 (d, d, J = 7 and 4 Hz, 2H), 6.03 (s, 2 H).