Microreactor-Controlled Product Selectivity in Photosensitized Oxidation of Alkenes. Electron Transfer Versus Energy Transfer Pathways

Xiao-Gang Fu, Li-Ping Zhang, Li-Zhu Wu* and Chen-Ho Tung*

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

Zeolite, Nafion membranes and vesicles were used as microreactors to control the pathway of photosensitized oxidation of alkenes and remarkable selectivity was achieved.

INTRODUCTION

Selective oxidation of small abundant hydrocarbons is the most important type of reaction in the production of organic chemicals. For example, essentially 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 is of particular interest [2,3], and here photosensitized oxidation holds special promise in achieving the product specificity. There are two well-established types of photooxidations involving molecular oxygen [4]: energy-transfer oxygenations and electron-transfer oxygenations (Scheme 1). The energy transfer pathway involves energy transfer from the triplet sensitizer to the ground state oxygen to generate singlet oxygen ($^1O_2$), and then the generated singlet oxygen reacts with the substrate. For example, Diels-Alder reaction of conjugated dienes, "ene" reaction of olefins with allylic hydrogen, and dioxetane reaction of olefins that do not feature an allylic hydrogen belong to this type. In electron transfer photosensitized oxidation electron-deficient sensitizers are generally used. Electron transfer from alkene to the sensitizer in its excited states results in an alkene radical cation and a sensitizer radical anion which subsequently reduces O_2 to give superoxide radical anion ($O_2^{-\bullet}$). The generated superoxide radical anion reacts with the alkene radical cation to yield the oxidation products. Unfortunately, in many cases, the two types of photosensitized oxidations occur simultaneously, and the selectivity of the oxidation reactions is poor. To gain the selectivity in such photosensitized oxidation, various efforts have been made in the past decades, and remarkable control of the reaction pathway has been obtained by use of organized and constrained media as microreactors [5]. This paper mainly summarizes the developments in microreactor-controlled selectivity in photosensitized

oxidation of alkenes achieved in our own laboratory.

We are able to direct the photosensitized oxidation of alkenes selectively toward either the energy-transfer-mediated or the electron-transfer-mediated products by controlling the status and location of the substrate and sensitizer molecules in the reaction media [6]. Close inspection of Scheme 1 indicates that in the electron-transfer pathway, the sensitizer and the substrate molecules have to be in close contact for efficient electron transfer, whereas in energy-transfer photosensitized oxidation such a close contact is not a prerequisite. Thus, isolation of the sensitizer from the substrate will prevent them from undergoing electron transfer, whereas $^1O_2$ still can be generated by energy transfer from the triplet state sensitizer to the ground state oxygen. The species $^1O_2$ is small and uncharged and has a relatively long lifetime and properties which allow it to diffuse a long-distance to meet the substrate molecules. In this case only the products derived from the energy-transfer pathway can be produced and no electron-transfer mediated products would be generated. On the other hand, if the sensitizer and substrate molecules are incorporated in the
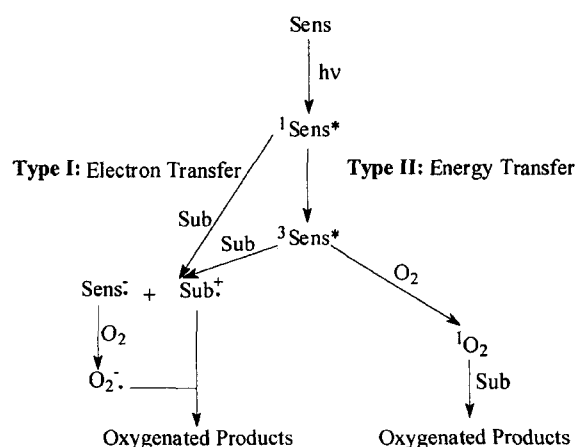
Scheme 1. Scheme for Type I and Type II Photosensitized Oxidation of Alkene.

sample microreactor, the high local concentration of the substrate and the close contact between the sensitizer and the substrate molecules will enhance the electron transfer from the substrate to the singlet excited state of the sensitizer. In this case the intersystem crossing process from the singlet excited state to the triplet state of the sensitizer will not be able to compete with the electron transfer quenching. Thus, no triplet state sensitizer will be generated. This, in turn, results in no $^1O_2$ formation. In this case only the products derived from electron-transfer pathway will be produced. We have used zeolites, Nafion membranes and vesicles as the microreactors and successfully controlled the selectivity in such photosensitized oxidation.

# RESULTS AND DISCUSSION

ZSM-5 Zeolite as Microreactor

Molecular-sieve zeolites represent a unique class of materials [7]. This material may be regarded as open structures of silica in which silicon has been substituted by aluminum in a well-defined fraction of the tetrahedral sites. The frameworks thus obtained contain pores, channels, and cages of different dimensions and shapes. The pores and cages can accommodate, selectively according to size/shape, a variety of organic molecules of photochemical interest, and provide restrictions on the motions of the included guest molecules and reaction intermediates. For example, the internal surface of ZSM-5 consists of two types of channels: one is sinusoidal with a near circular cross section of ca. 5.5 Å, and the other is straight with dimensions of ca. 5.2×5.8 Å. These channels can allow the adsorption of benzene and other molecules of similar molecular size, but prevent molecules with a larger size/shape from being sorbed into the internal framework.

We have used the channels of ZSM-5 zeolite (Si/Al=25 or 55) as the microreactor to conduct the photosensitized oxidation of alkenes [8]. Trans,trans-1,4-diphenyl-1,3-butadiene (DPB) and trans-stilbene (TS) were selected as the represents of alkenes, 9,10-dicyanoanthracene (DCA) and hypocrellin A (HA) were the sensitizers, and isooctane and pentaerythritol trimethyl ether (PTE) were the solvents. The alkenes were trapped in the zeolite channels and the photosensitizers were isolated in the surrounding solution (Scheme 2). The choice of the solvents and sensitizers was motivated by the desire that they were prevented from being sorbed into ZSM-5 channel due to their size and shape characteristics. Thus, the substrate is protected from being extracted to the solution during photolysis. The isolation of the substrate within the zeolite from the sensitizer in the solution outside leads exclusively to the formation of singlet oxygen products.

Irradiation of oxygen-saturated DPB solution in PTE containing DCA or HA with visible light gave benzaldehyde 1, cinnamaldehyde 2, epoxide 3, ozonide 4, 1-phenylnaphthalene 5 and endoperoxide 6 (Scheme 3). The product distribution for DCA as the sensitizer is shown in Scheme 3. In all cases,
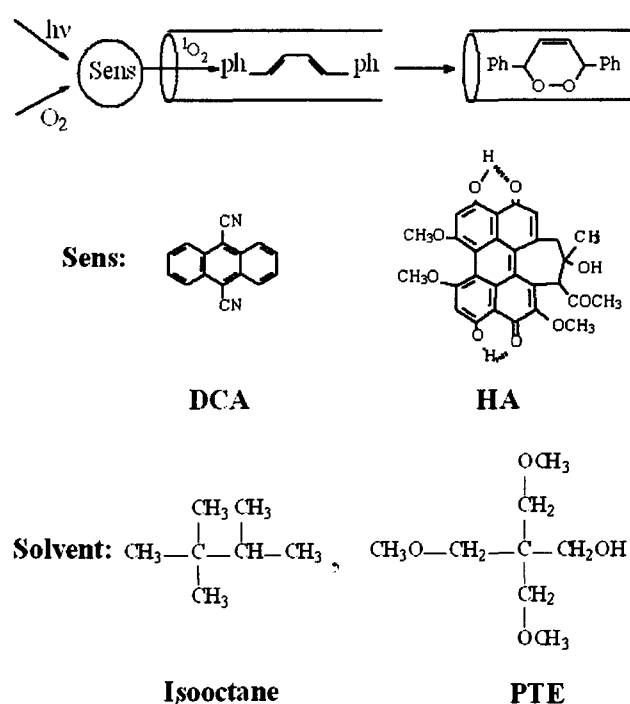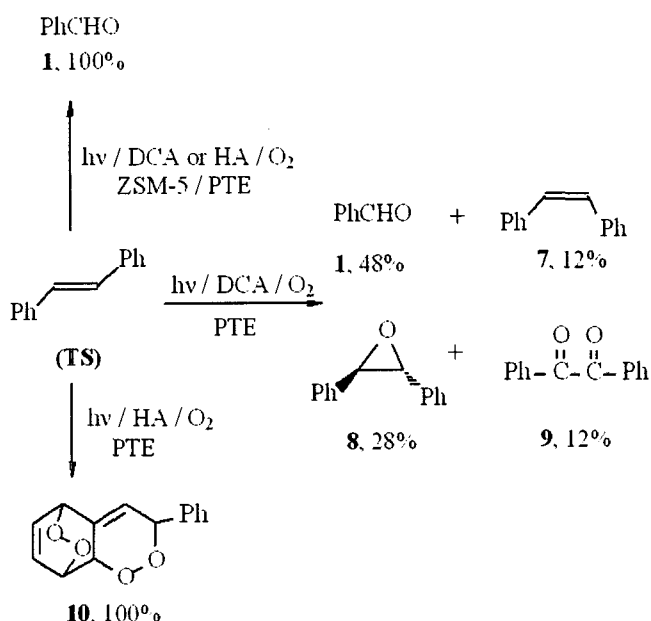

Scheme 2. DCA- and HA-Photosensitized Oxidation of Alkenes under Sensitizer-Excluded Condition.
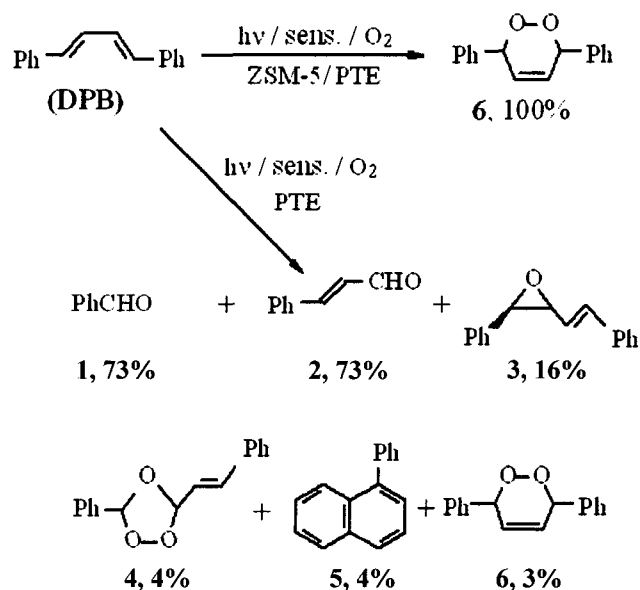
Scheme 3. Photosensitized Oxidation of Trans,trans-1,4-diphenyl-1,3-butadiene in Solution and within ZSM-5 Zeolite.

the main products are 1 and 2. It has been established that DCA [9] and HA [10] can act both as energy and electron transfer sensitizer. Obviously, 6 is a product of 1,4-cycloaddition of $^1O_2$ to DPB. The other products are derived via the electron transfer pathway [9]. In contrast, the DCA- and HA-sensitized photooxidation of DPB adsorbed on the internal surface of

PhCHO

1, 100%

↑

hv / DCA or HA / O₂
ZSM-5 / PTE

PhCHO   +   Ph⎯⎯Ph

1, 48%   **7, 12%**

Ph⎯⎯⎯Ph

hv / DCA / O₂
⎯⎯⎯⎯⎯⎯⎯⎯⎯
PTE

(TS)

hv / HA / O₂
PTE

$$Ph-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-Ph$$

8, 28%   **9, 12%**

10, 100%

Scheme 4. Photosensitized Oxidation of *Trans*-stilbene in Solution and within ZSM-5 Zeolite.

ZSM-5 zeolite gave **6** as the unique product (Scheme 3). The yield of this product was close to 100% based on the consumption of the starting material. Generally after 4 h of photolysis the conversion was near 100%. Similar conversion was obtained in PTE in the absence of ZSM-5 zeolite after about 1 h of irradiation.
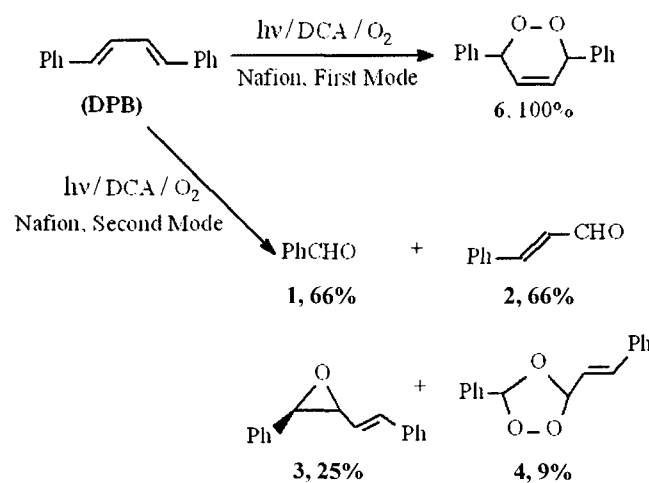
As observed in the case of DPB, the photooxygenation of TS sensitized by DCA or HA differed significantly when included in ZSM-5 zeolite compared to that in homogeneous solution [8]. In PTE using DCA as the sensitizer, the oxidation products were benzaldehyde **1**, *cis*-stilbene **7**, *trans*-2,3-diphenyloxirane **8** and benzil **9** (Scheme 4). All these products were produced via the electron transfer pathway. On the other hand, in the same solvent using HA as the sensitizer, only diendoperoxide **10** was obtained (Scheme 4). This product is proposed to be derived from energy transfer pathway. However, when TS is included within ZSM-5 zeolite and the sensitizer is solubilized in the surrounding solvent PTE, the photooxidation of TS sensitized by DCA or HA yields **1** as the unique product (Scheme 4). The mass balances of this reaction for the two sensitizers are all close to 100%. The isolation of TS from the sensitizer would prevent electron transfer between the substrate and the sensitizer to occur. Thus, **1** is derived via energy transfer pathway. The ¹O₂ generated in solution diffuses into the internal framework of ZSM-5 and reacts with TS to form 1,2-diphenyl-1,2-dioxetane which would decompose to yield **1** under reaction condition. We note that in the HA-sensitized photooxidation **10** was not produced. Probably, the constrained space within ZSM-5 channels is not big enough to accommodate the molecule of **10**.

Nafion Membranes as Microreactors

Nafion is a family of polymers which consists of a perfluorinated backbone and short pendant chains terminated by sulfonic groups. When swollen in water, the structure of Nafion is believed to resemble that of an inverse micelle [11]. The hydrated SO₃⁻ head groups are clustered together in a water-containing pocket of ca. 40 Å in diameter, which are interconnected by short channels (ca. 10 Å in diameter) within the perfluorocarbon matrix. It has been established that water-swollen Nafion can incorporate high concentrations of aromatic hydrocarbons and organic dyes. These optically transparent membrane systems are readily amenable to spectroscopic and photochemical investigations.

We extended the study of photosensitized oxidation of alkenes to Nafion membranes to establish the scope of the microreactor-controlled selectivity approach [12]. The photosensitized oxidation was performed in two modes. The first one involves irradiation of DCA in dichloromethane solution in which the water-swollen Nafion sample incorporating the substrate is immersed. Because dichloromethane can not swell Nafion and is insoluble in water, the substrate and water within Nafion can not be extracted into the solution, and CH₂Cl₂ and DCA in the solution can not diffuse into the Nafion. Thus, the substrate and the sensitizer are isolated from each other during irradiation. The second mode involves irradiation of the water-swollen Nafion sample which has incorporated both the substrate and the sensitizer.

As in the case of ZSM-5 zeolite sample [8], in the first mode, due to the isolation of the sensitizer in solution from the substrate in Nafion, only the products derived from the energy transfer pathway were detected. The sensitized photooxidation of DPB gave **6** as the unique product (Scheme 5), while that of TS yielded **10** and epoxy endoperoxide **11** (Scheme 6). In contrast, irradiation of the water-swollen Nafion sample incorporating both DCA and DPB (the second mode) only

Ph⎯⎯⎯⎯Ph

(DPB)

hv/DCA / O₂
⎯⎯⎯⎯⎯⎯⎯⎯⎯→
Nafion, First Mode

Ph⎯⟨O-O⟩⎯Ph

6, 100%

hv/ DCA / O₂
Nafion, Second Mode

PhCHO   +   Ph⎯⎯CHO

1, 66%   **2, 66%**

3, 25%   **4, 9%**

Scheme 5. Photosensitized Oxidation of *Trans,trans*-1,4-diphenyl-1,3-butadiene within Nafion Membranes.
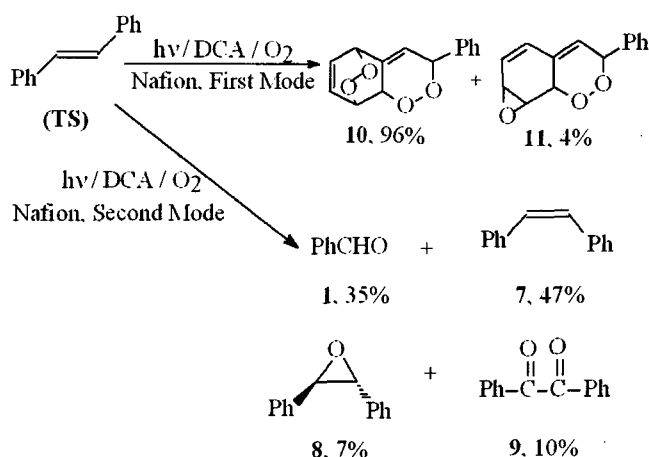
Scheme 6. Photosensitized Oxidation of *Trans*-stilbene within Nafion Membranes.

resulted in the electron-transfer-mediated products, **1-4**. No $^1O_2$ product, **6**, was detected (Scheme 5). Mass balance was near 100%. Similarly, the photosensitized oxidation of TS in the second mode only produced the electron transfer mediated products **1**, **7-9** (Scheme 6).

Vesicles as Microreactor

Vesicles are widely used as simplified models of cell membranes [13]. Generally, vesicles are prepared from double-tailed surfactants. Simple single-tailed surfactants cannot form vesicles due to their relatively large hydrophilic head effect. However, it was established that stable vesicles could be simply produced by mixing commercially available single-tailed cationic and anionic surfactants. These vesicles can accommodate a variety of organic compounds of photochemical interest, and act as microreactors.

The approach to control the reaction pathways in photosensitized oxidation of alkenes by isolation or close contact of the substrate and sensitizer molecules has also been demonstrated to be effect in vesicle medium [14-16]. First, we have shown that singlet oxygen generated in the bilayer or the inner water pool of one vesicle is able to react with the target molecules located in other vesicles. We prepared vesicles by sonicating the equimolar mixture of a cationic surfactant (octyltrimethyl ammonium bromide, ca. 8.2×10^{-2} M) and an anionic surfactant (sodium Laurate, ca. 8.2×10^{-2} M) in buffered solution. The target molecules were *trans*-1,2-dimethoxy-stilbene (DMOS) and the amine 2,2,6,6-tetramethyl-piperidine (TMP). The sensitizer was either a hydrophobic dye, tetraphenylporphyrin (TPP), or a cationic dye, methylene blue (MB). The target molecules were solubilized in the bilayer membranes of one set of vesicles, and the sensitizers were incorporated in the bilayers or the aqueous inner compartments of another set of vesicles. The irradiation samples were prepared by mixing the above two sets of vesicle dispersions. Photo-irradiation of the oxygen-saturated samples resulted in the

oxidation of the target molecules, as evidenced by the isolation of the end products in the olefin oxidation and by the detection of the ESR spectrum of the nitroxide radical in the amine oxidation. The quantum yields for the product formation were enhanced in two to three times in D_2O dispersions compared with those in H_2O medium. All of these observations suggest that singlet oxygen generated in the bilayer or the inner water pool of one vesicle is able to diffuse out and enter into the bilayer of another vesicle through the aqueous dispersion and react with the target molecules. The measurements of the quantum yields revealed a large fraction of the singlet oxygen diffusing from its generated locus to the reaction sites: 8% in H_2O and 15% in D_2O dispersions in the case of singlet oxygen generated in the inner aqueous compartment of the vesicle, and 20% in H_2O and 80% in D_2O dispersions for the singlet oxygen generated in the bilayer of the vesicle. In this context, such easily prepared and inexpensive vesicles were used as the reaction medium to conduct the oxidation of α-pinene (PE) and DPB photosensitized by DCA.

The photosensitized oxidation was performed in two modes. In the first mode, the sensitizer DCA was incorporated in the bilayer membranes of one set of vesicles, and the substrate was solubilized in another set of vesicles. Equal volumes of the two sets of vesicle dispersions were then mixed to prepare the samples for irradiation. Although sonication was carried out during preparation of the component solutions, the final mixture was not sonicated. In this way intermixing of solubilizates was prevented. A control experiment was carried out: The mixed solution prepared from DCA-containing vesicles and substrate-containing vesicles was stored in the dark at room temperature for one day, and then was irradiated. The products and the efficiency of the product formation for the photosensitized oxidation were found to be identical within experimental error limit to those of the sample that was immediately irradiated after the preparation. This observation suggests that the inter-vesicular exchange both of the substrate and the sensitizer indeed did not occur, and the photosensitized oxidation process in this mode involved the generation of $^1O_2$ in one vesicle and reaction with alkene molecules in other vesicles. In the second mode both the sensitizer and the substrate were incorporated in the bilayer of the same set of vesicles. Generally, the concentration of the olefins was ca. 1.0×10^{-3} M corresponding to thousands of substrate molecules in each vesicle, whereas the concentration of the sensitizer was generally ca. 1.0×10^{-4} M.

The photooxidation of PE sensitized by DCA in homogeneous solution followed by reduction of the reaction mixture with sodium sulfite solution gave the ene product pinocarveol **12** and the non-ene products myrtenal **13**, epoxide **14** and aldehyde **15**, as shown in Scheme 7. The ene product and the non-ene products have been proposed to be derived from the energy-transfer and electron-transfer pathways respectively. The product distributions in acetonitrile is given in Scheme 7.

The product distribution of the photosensitized oxidation of PE in vesicles is dramatically altered compared with those in
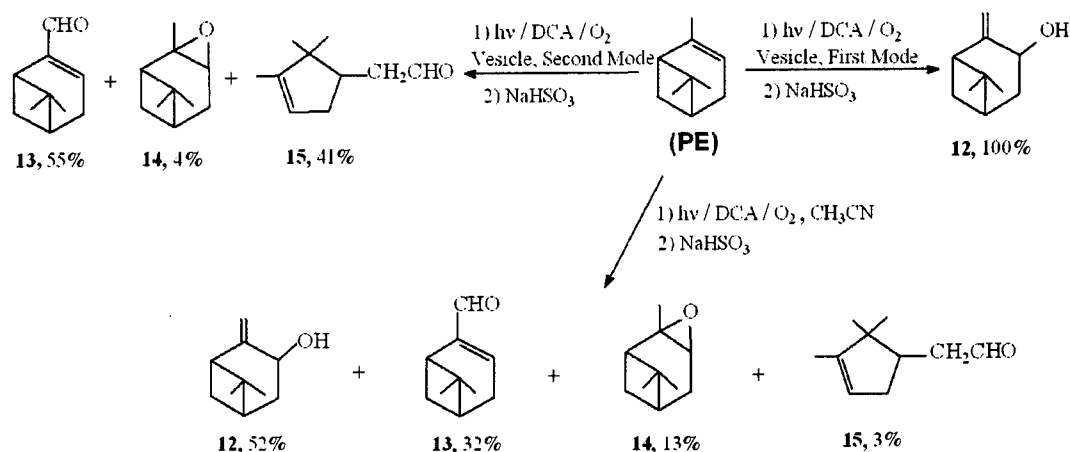
Scheme 7. Photosensitized Oxidation of α-Pinene in CH₃CN and in Vesicle Dispersions.

the above homogeneous solutions and is remarkably dependent on the experimental mode. The photosensitized oxidation in the first mode followed by mixing the sample with a sodium sulfite aqueous solution to reduce the reaction mixture exclusively produced the ene product 12 (Scheme 7). No trace of the non-ene products 13-15 was detected. Evidently, the isolation of PE in the bilayer membranes of one set of vesicles from DCA in another set of vesicles prevents them from undergoing electron transfer. On the other hand, singlet oxygen can be generated in the DCA-containing vesicles by the energy-transfer. The vesicles used in the study have an aggregation number (number of surfactant molecules per vesicle) in the region of 10^5-10^6, and the average aggregation number is ca. $7.2×10^5$, as estimated from the vesicle size and the volume of the surfactant molecule [14]. Thus, at surfactant concentration of $8.2×10^{-2}$ M the vesicle population is equivalent to a molarity of ca. $1.0×10^{-7}$ M, which, in turn, gives the intervesicular distance on average to be ca. 134 nm [17]. On the other hand, the average diffusion length of $^1O_2$ molecule in aqueous solution is estimated to be ca. 780 nm [18]. This diffusion length is much larger than the intervesicular distance estimated above. Thus, the $^1O_2$ generated in DCA-containing vesicles is indeed capable of diffusing into the PE-containing vesicles to react with the alkene molecules to produce the ene product 12.

In contrast, the photooxidation in the second mode followed by mixing the sample with a sodium sulfite aqueous solution to reduce the reaction mixture exclusively gave the non-ene products 13-15 (Scheme 7). No product derived from the energy-transfer pathway was detected. The loading levels used in the study were hundreds of DCA and thousands of PE molecules per vesicle. Thus, each DCA molecule is surrounded by a number of PE molecules. The high "local concentration" of PE in the confined bilayer of vesicles lead to efficient quenching of the singlet excited state of DCA by PE via an electron-transfer process and to inefficient intersystem crossing from the singlet excited state to the triplet state of DCA. Therefore, only the non-ene products 13-15 were produced.
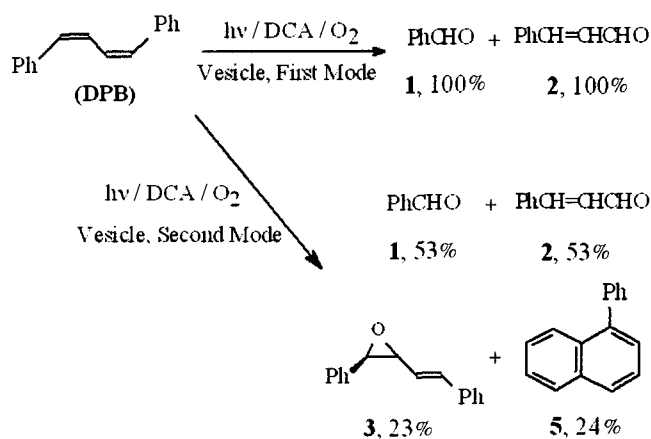
Scheme 8. Photosensitized Oxidation of Trans,trans-1,4-diphenyl-1,3-butadiene in Vesicle Dispersions.

The photosensitized oxidation of DPB in vesicles in the first mode gave 1 and 2 as the unique products (Scheme 8). We believe that these products are derived from the 1,2-cycloaddition of $^1O_2$ to the diene. The preferential formation of the 1,2-cycloaddition products over that of 1,4-cycloaddition (6) is probably best explained in terms of the greater difficulty of achieving the necessary geometry for 1,4-cycloaddition in this organized medium. It has been established that DPB in solution exists in two conformational isomers: cisoid and transoid [19]. At equilibrium the main conformer is the transoid (ca. 99%), and the cisoid is presented only in ca. 1%. The 1,4-cycloaddition of singlet oxygen to 1,3-diene to form endoperoxide is concerted and analogous to the Diels-Alder reaction. This reaction requires a six-membered ring transition state. Only the cisoid conformer can satisfy such a requirement, and in order to undergo 1,4-cycloaddition with singlet oxygen the transoid conformer has to be isomerized to the cisoid one first. Due to the kinetic equilibrium between the two conformers in solution, the cycloaddition can proceed until all of the diene is

converted to the products. Obviously, in vesicles, the organized semirigid environment prevents DPB molecules from conformational change. Thus, only the 1,2-cycloaddition product (dioxetane) was produced which decomposed to yield **1** and **2**. In contrast, the photosensitized oxidation in the second mode only produced the electron-transfer-mediated products **1, 2, 3** and **5**. No singlet oxygen products were detected. These observations demonstrate once again that one can control the selectivity in photosensitized oxidation of alkenes by incorporation of the sensitizer and substrate either in different or in the same sets of vesicles.

CONCLUSION

We have shown that ZSM-5 zeolite, Nafion membranes and vesicles serve as microreactors to direct photosensitized oxidations of alkenes selectively toward either singlet oxygen or superoxide radical anion mediated product formation via control of the status and location of substrate and sensitizer molecules in the reaction media.

REFERENCES

1. Haber, J. (1992) In *Perspectives in Catalysis*; Thomas, J. M.; Zamaraev, K. I., Eds.; IUPAC/Blackwell Scientific Publications: London, pp. 371-385.
2. Parshall, G. W. and Ittel, S. D. (1992) *Homogeneous Catalysis*, 2nd ed., Wiley: New York, pp. 237-268.
3. Sheldon, R. A. and Kochi, J. K. (1981) *Metal-Catalyzed Oxidation of Organic Compounds*; Academic Press: New York.
4. Foote, C. S. (1991) *Photochem. Photobiol.*, **54**, 659.
5. Tung, C. H., Song, K., Wu, L. Z., Li, H. R. and Zhang, L. P. (2001) In *Molecular and Supramolecular Photochemistry*; Ramamurthy, V., Schanze, K. S., Eds.; Marcel Dekker, Inc.: New York, **8**, Chapter 5.
6. Tung, C. H., Wu, L. Z., Zhang, L. P., Li, H. R., Yi, X. Y., Song, K., Xu, M., Yuan, Z. Y., Guan, J. Q., Wang, H. W., Ying, Y. M. and Xu, X. H. (2000) *Pure & Appl. Chem.*, **72**, 2289.
7. Van Bekkum, H., Flanigen, E. M. and Jansen, J. C. (1991) *Introduction to Zeolite Science and Practice*; Elsevier: Amsterdam.
8. Tung, C. H., Wang, H. W. and Ying, Y. M. (1998) *J. Am. Chem. Soc.*, **120**, 5179.
9. Kanner, R. C. and Foote, C. S. (1992) *J. Am. Chem. Soc.*, **114**, 678 and 682.
10. Hu, Y. Z., An, J. Y. and Jiang, L. J. (1993) *J. Photochem. Photobiol. B. Biol.*, **17**, 195.
11. Lee, P. C. and Meisel, D. (1980) *J. Am. Chem. Soc.*, **102**, 5477.
12. Tung, C. H. and Guan, J. Q. (1998) *J. Am. Chem. Soc.*, **120**, 11874.
13. Kaler, E. W., Murthy, A. K., Rodriguez, B. E. and Zasadzinski, J. A. (1989) *Science*, **245**, 1371.
14. Li, H. R., Wu, L. Z. and Tung, C. H. (2000) *J. Am. Chem. Soc.*, **122**, 2446.
15. Li, H. R., Wu, L. Z. and Tung, C. H. (2000) *Chem. Commun.* **12**, 1085.
16. Li, H. R., Wu, L. Z. and Tung, C. H. (2000) *Tetrahedron*, **56**, 7437.
17. Turro, N. J. (1978) In *Modern Molecular Photochemistry*, Benjamin / Cummings. Co., Inc., California, p.319
18. Lissi, E. A., Encinas, M. V., Lemp, E. and Rubio, M. A. (1993) *Chem. Rev.*, **93**, 699.
19. Cao, Y., Zhang, B. W., Ming, Y. F. and Chen, J. X. (1987) *J. Photochem.* **38**, 131.