

Supramolecular Systems as Microreactors: Control of Product Selectivity in Organic Phototransformation

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ABSTRACT

This Account reviews the developments in microreactor-controlled selectivity in organic phototransformation. Photocycloaddition of α,ω -diaryl compounds with long flexible chains within Y-type zeolite and low-density polyethylene films leads to formation of intramolecular cyclomers to the exclusion of intermolecular products. ZSM-5 zeolite, Nafion membranes, and vesicles as hosts direct photosensitized oxidation of alkenes selectively toward either the energy-transfer-mediated or the electron-transfer-mediated products. Zeolites, Nafion membranes, and microemulsions as microreactors remarkably control chemo-, regio-, and stereoselectivity in the photochemical reaction of phenyl phenylacetates, photocycloaddition of anthracenes, and photocyclization of azobenzene and stilbazole.

Introduction

The development of efficient and highly selective methods for organic synthesis is one of the main topics in organic chemistry, and much effort has been directed toward this goal. Selectivity in ground-state reactions is commonly achieved by developing appropriate catalytic systems. However, the control of photochemical reactions is difficult, because short excited-state lifetimes and low activation energies for reactions in the excited-state(s) leave little room for manipulating the transition states for different reaction pathways. Thus, in molecular organic photochemical reactions (in solution), reaction paths are largely determined by the functional groups in the substrate. However, in the past two decades, it has become apparent that photochemical reactions in microreactors can proceed in a selective manner, and remarkable product

selectivity has been achieved. Microreactors refer to organized and constrained media, which provide cavities and/or surfaces to accommodate the substrate molecules and allow chemical reaction(s) to occur. In this case, the interactions of the substrate with the medium alter the photochemical behavior of the confined substrate and render the possibility to direct the photochemical reaction to the desired product(s). Because various types of microreactors are available in naturally occurring and synthesized materials, organic photochemists can have a choice. It is quite likely that by properly designed microreactors selectivity for more photochemical reactions will be controllable.

There has been a large number of publications on the subject of photophysical and photochemical processes in organized and confined media over the past decades.^{1–8} This Account is mainly limited to the developments in microreactor-controlled selectivity in organic phototransformation made in our own laboratory.

Microreactors

During the last two decades, a growing number of organized assemblies and host systems have been used as microreactors. Among these, molecular-sieve zeolites, Nafion membranes, vesicles, microemulsions, and low-density polyethylene films are outstanding members.

Molecular-sieve zeolites represent a unique class of materials.⁹ 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.

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On the other hand, the structure of Y-type zeolite consists of an interconnecting three-dimensional network of relatively large spherical cavities (supercages) with a diameter of about 13 Å. Each supercage is connected tetrahedrally to 4 other supercages through 7.4 Å diameter windows. As an indication of their volume, each supercage can include 2 molecules of pyrene.

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.¹⁰ The hydrated SO₃⁻ 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 (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.

Vesicles are widely used as simplified models of cell membranes.¹¹ 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.

Low-density polyethylene (LDPE) is a very complex family of materials which consists of crystalline and amorphous regions.¹² A wide variety of organic molecules can be incorporated into LDPE by soaking its films in a swelling solvent containing the guest. The swelling process by which species are introduced "opens" the network of polymethylene chains in the amorphous and interfacial regions; when the swelling liquid is removed, the nearby chains move into van der Waals contact with the reactive guest molecules that have been left behind. It has been established that the principal locations of guest molecules are the amorphous parts and the interfacial regions between crystalline and amorphous domains. Because of its anisotropic nature, LDPE has been used as a reaction medium to control the reaction pathways of a variety of guest molecules.

Water-in-oil (W/O) microemulsions are heterogeneous, thermodynamically stable systems of nanosized domains of water dispersed within an immiscible organic (oil) phase and stabilized by a surfactant shell.¹³ The water microdroplets, often called the "water pool", provide a hydrophilic nanospace, while the organic component forms a hydrophobic continuous phase. These microemulsion systems have the ability to solubilize normally slightly soluble substrates. The hydrophilic substrates are solubilized primarily in the water pool, whereas hydrophobic molecules exist in the organic phase or at the interface of the water pool.

We have used the compounds, whose molecular photochemistry has been well established, as probes to show

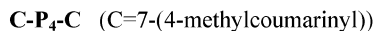
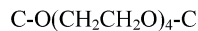
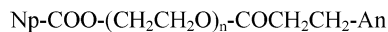
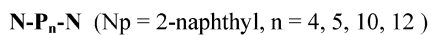
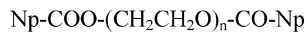
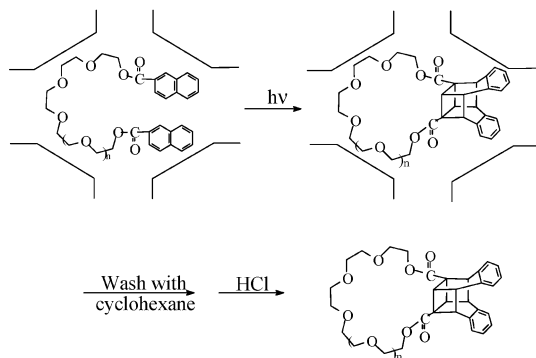
how the zeolite, Nafion, LDPE, vesicle, and W/O microemulsion hosts control the pathways in photochemical reactions.

Zeolites and Low-Density Polyethylene Films as Hosts for Preparation of Large-Ring Compounds: Intramolecular Photocycloaddition of Diaryl Compounds

The construction of macrocyclic compounds continues to be an important topic of synthetic organic chemistry. A bifunctional molecule may undergo either intramolecular or intermolecular reactions. An intramolecular reaction gives macrocyclic ring-closure products, whereas an intermolecular reaction results in dimers, oligomers, and polymers. The rates of the latter are dependent on the concentration of the substrate, whereas those of the former are not. Hence, high substrate concentrations favor polymerization, whereas cyclization proceeds in good chemical yields only at low concentrations. In general, the syntheses of many-membered rings are performed at substrate concentrations as low as 1×10^{-5} M. This corresponds in a batch reaction to 1×10^5 L of solvent for each mole of substrate! The proper choice of solvents and using hydrophobic or lipophobic interactions to induce the flexible linking chains to self-coil, thus increasing the probability of the end-to-end encounters, have proved to be effective for the synthesis of large-ring compounds at high substrate concentrations.¹⁴⁻¹⁸

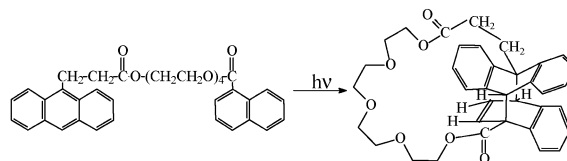
We have devised a new approach to synthesize large-ring compounds in high yields under high substrate concentrations.^{19,20} Our approach involves microporous solids as templates and hosts for the cyclization reactions. The size of the micropore or the cavity has been chosen to permit only 1 substrate molecule to fit within each. Thus, intermolecular reaction is hindered, and cyclization can occur without competition. Because the concentration of the micropores may be very large, we can synthesize large-ring compounds in high yields under conditions of high loadings. We find that the supercages of Y-type zeolite and the "cavities" of LDPE can be used as such microvessels for intramolecular photocycloadditions of diaryl compounds with long flexible chains.

Y-Type Zeolite as the Microreactor. As mentioned above, each supercage of Y-type zeolite can include 2 molecules of pyrene. Thus, one might expect that both aryl parts of a molecule with α,ω -diaryl groups separated by a flexible chain can be included in 1 supercage, and the intramolecular reactions between the 2 aryl groups should be enhanced. On the other hand, according to a Poisson distribution, as long as the loading level is less than 1 substrate molecule per 10 supercages, there is less than a 5% probability to find 2 substrate molecules in 1 supercage, and the intermolecular reactions should be inhibited. A typical NaY zeolite particle of 1 μ m in diameter contains thousands of interconnected supercages, and the concentration of the supercages is ca. 500 μ mol per gram of zeolite.²¹ Assuming that a loading level of 1 substrate molecule per 10 supercages inhibits inter-

Scheme 1. Diaryl Compounds Examined for Intramolecular Photocycloaddition within Y Zeolite and Low-Density Polyethylene

Scheme 2. Intramolecular Photocycloaddition of N-P_n-N within the Supercage of Y Zeolite


molecular reaction completely (*vide infra*) while cyclization still proceeds, only 2×10^4 g of zeolite is needed for each mole of substrate! This corresponds to 40 g of NaY zeolite for each gram of substrate whose molecular weight is 500. This amount of zeolite is more than 10^3 times smaller as compared with that of the solvent in solution-phase reactions that allow cyclization to dominate.

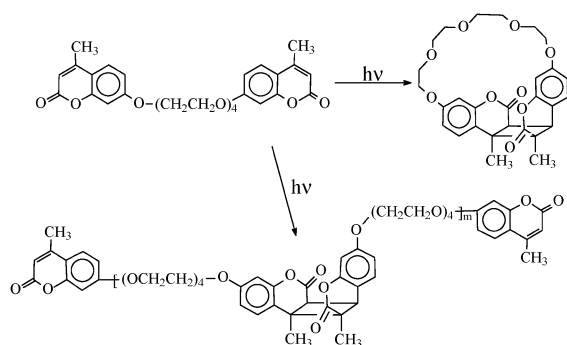
We have investigated the intramolecular photocycloadditions of diaryl compounds as shown in Scheme 1 upon their inclusion in the supercages of NaY zeolite.²⁰ Fluorescence study revealed that at the loading levels below $50 \mu\text{mol/g}$ -zeolite, the diaryl compounds exclusively exhibit either intramolecular excimer fluorescence (for N-P_n-N) or intramolecular exciplex emission (for N-P_n-A). This observation indicates that the 2 terminal aryl groups of 1 molecule of the diaryl compounds are included in 1 supercage of the zeolite. As expected from the analysis above, at these loading levels only intramolecular photocycloaddition is observed. For example, irradiation of alkyl 2-naphthoates is known to yield a "cubane-like" photocyclomer as the unique product (Scheme 2), although six isomeric cyclomers are formally possible.^{17,20,22} Irradiation of N-P_n-N in organic solutions can lead either to intra- or to intermolecular cycloadditions. At concentrations higher than 10^{-3} M, the main product is the intermolecular photocyclomer. By contrast, irradiation of N-P_n-N adsorbed on NaY zeolite results in an intramolecular photocyclomer, as long as the loading level was kept at less than ca. $50 \mu\text{mol}$ of substrate per gram of zeolite (ca. 1 molecule per 10 supercages). In our experimental conditions, after 4 h of irradiation the conversion was near 100%. Similar conversion was obtained in solution after about 1 h of irradiation. Once

Scheme 3. Intramolecular Naphthalene–Anthracene Cross-Photocycloaddition within the Supercage of Y Zeolite


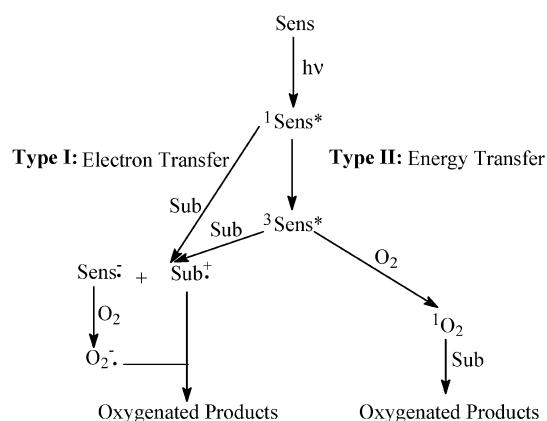
formed, the photocyclomer is trapped inside the supercage of the zeolite, because the 7.4 \AA window is too narrow to allow it to escape (Scheme 2). However, the aluminosilicate framework of Y zeolite can be dissolved in strongly acidic media so that the photocyclomer is released into solution. Thus, first we extracted the unreacted starting material with cyclohexane, and then we isolated the product by dissolving the zeolite framework in concentrated HCl followed by extraction with ether. Generally, the intramolecular ring-closure photocyclomers were obtained in high purity by this procedure, and the mass balance was $>90\%$. By this approach, we also successfully synthesized the cross photocyclomers between an anthracene and a naphthalene moiety from the bichromophoric molecules with anthryl as one chromophore and naphthyl as the other (N-P_n-A), the photoproducts not obtained in homogeneous solution (Scheme 3).^{20,23}

LDPE as the Microreactor. We also investigated the photocycloadditions of diaryl compounds included within LDPE films. The LDPE films used consist of ca. 50% crystalline regions and ca. 50% amorphous regions. As mentioned above, organic molecules can be incorporated into the amorphous parts of LDPE by soaking its film in a swelling solvent containing the guest. In this way, the free volume of the reaction sites can be made sufficiently large to accept a molecule with two reactive groups linked by a flexible chain, yet small enough to force the two terminal groups in proximity. Furthermore, as long as the loading level is less than 1 guest molecule per 10 reaction cavities and the rate of site exchange by guest is slower than that of conformational changes of the guest molecule, intermolecular reaction should be inhibited, while intramolecular reactions still can occur. We found that this indeed is the case for the photocycloadditions of N-P_n-N and C-P₄-C.¹⁹ For example, C-P₄-C can undergo intra- and intermolecular photocycloadditions in an organic solvent, and at concentrations $>1 \times 10^{-3}$ M, a large amount of oligomeric material was formed (Scheme 4). By contrast, irradiation of 1×10^{-2} mol/g-film C-P₄-C in LDPE followed by extraction with chloroform resulted in conversion to intramolecular cyclomer. No intermolecular products were detected. Generally, after 5 h of irradiation, the conversion approached 100%.

Thus, LDPE complements zeolites, which serve a similar role in isolating molecules for intramolecular cyclizations. Each medium has its relative merits; now, it is possible to select the one that is more compatible with a particular reactant and cyclization reaction.

Scheme 4. Photocycloaddition of C-P₄-C

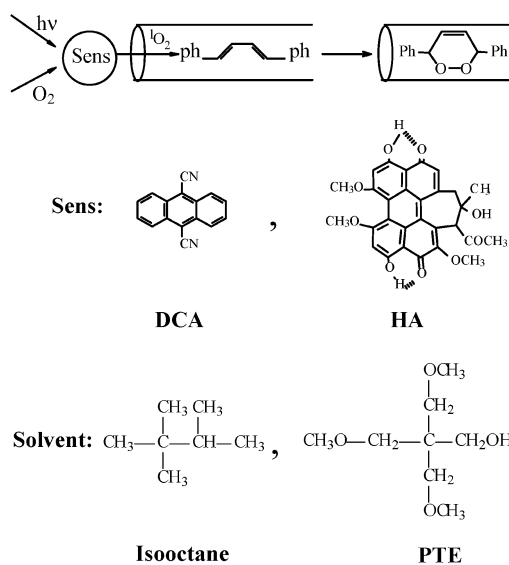
Scheme 5. Scheme for Type I and Type II Photosensitized Oxidation of Alkene



Photosensitized Oxidation of Alkenes Included in Zeolites, Nafion Membranes, and Vesicles: Electron-Transfer Versus Energy-Transfer Pathways

Selective oxidation of small abundant hydrocarbons is the most important type of reaction in organic chemicals production. Among the various oxidizing reagents, oxidation by molecular oxygen is of particular interest, and here photosensitized oxidation holds special promise in achieving the product specificity. There are two well-established types of photooxidations involving molecular oxygen:²⁴ energy-transfer and electron-transfer oxygenations (Scheme 5). Unfortunately, in many cases, the two types occur simultaneously, and the selectivity of the oxidation reactions is poor. 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. Close inspection of Scheme 5 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 singlet oxygen (¹O₂) still can be generated by energy transfer from the triplet-state sensitizer to the ground-state oxygen. The species ¹O₂ has a relatively long lifetime and properties which allow it to diffuse a long distance to meet the

Scheme 6. DCA- and HA-Photosensitized Oxidation of Alkenes under Sensitizer-Excluded Condition

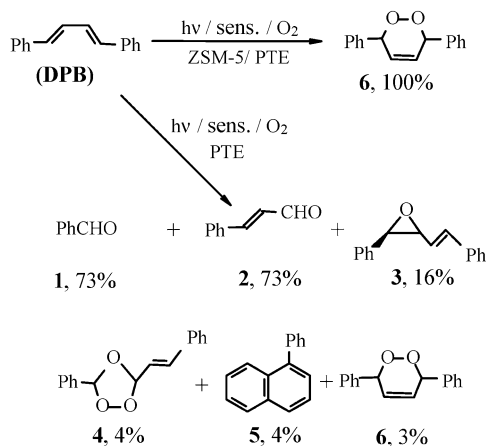


substrate molecules. In this case, only the products derived from the energy-transfer pathway can be produced, and no electron-transfer-mediated products would be generated. On the other hand, if the sensitizer and substrate molecules are incorporated in the same microreactor, the high local concentration 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 ¹O₂ formation. In this case, only the products derived from the electron-transfer pathway will be produced. We have used zeolites, Nafion membranes, and vesicles as the microreactors for such photosensitized oxidation.

ZSM-5 Zeolite as the Microreactor. We used the channels of ZSM-5 zeolite (Si/Al = 25 or 55) as the microreactor to conduct the photosensitized oxidation of alkenes.²⁵ *trans,trans*-1,4-Diphenyl-1,3-butadiene (DPB) and *trans*-stilbene (TS) were selected to represent 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 6). 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 benzalde-

Scheme 7. Photosensitized Oxidation of *trans,trans*-1,4-Diphenyl-1,3-butadiene in Solution and within ZSM-5 Zeolite

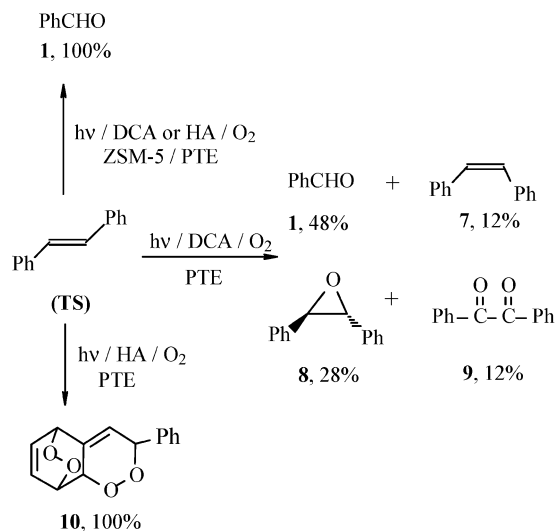


hyde **1**, cinnamaldehyde **2**, epoxide **3**, ozonide **4**, 1-phenylnaphthalene **5**, and endoperoxide **6** (Scheme 7). The product distribution for DCA as the sensitizer is shown in Scheme 7. It has been established that DCA and HA can act both as energy- and as electron-transfer sensitizer. Obviously, **6** is a product of the 1,4-cycloaddition of ¹O₂ to DPB. The other products are derived via the electron-transfer pathway.²⁶ In contrast, the DCA- and HA-sensitized photooxidation of DPB adsorbed on the internal surface of ZSM-5 zeolite gave **6** as the unique product. The yield of this product was close to 100% on the basis of 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.

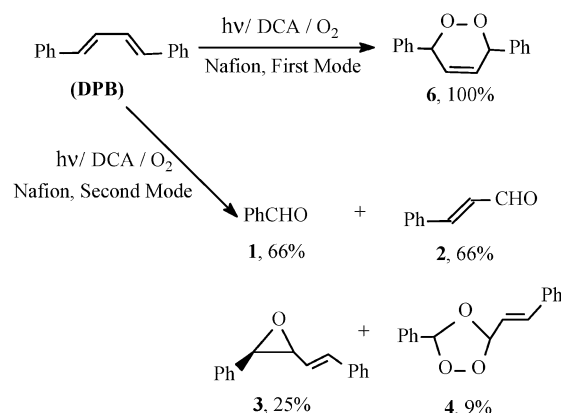
As observed in the case of DPB, the photooxygenation of TS sensitized by DCA or HA differed significantly when included in ZSM-5 zeolite as compared to that in homogeneous solution. In PTE using DCA as the sensitizer, the oxidation products were **1**, *cis*-stilbene **7**, *trans*-2,3-diphenyloxirane **8**, and benzil **9** (Scheme 8). All of 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. This product is proposed to be derived from the 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. The isolation of TS from the sensitizer would prevent electron transfer between the substrate and the sensitizer from occurring. Thus, **1** is derived via the 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 the Microreactor. We extended the study of photosensitized oxidation of alkenes to Nafion

Scheme 8. Photosensitized Oxidation of *trans*-Stilbene in Solution and within ZSM-5 Zeolite



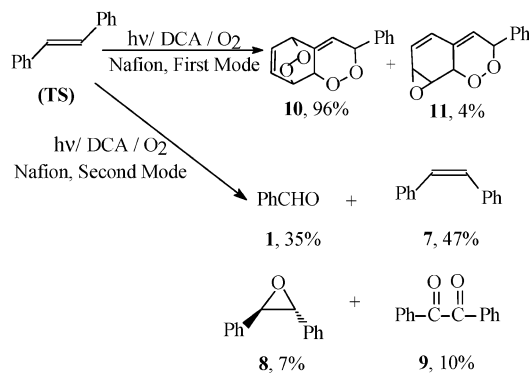
Scheme 9. Photosensitized Oxidation of *trans,trans*-1,4-Diphenyl-1,3-butadiene within Nafion Membranes



membranes to establish the scope of the microreactor-controlled selectivity approach.²⁷ 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. The second mode involves irradiation of the water-swollen Nafion sample which has incorporated both the substrate and the sensitizer.

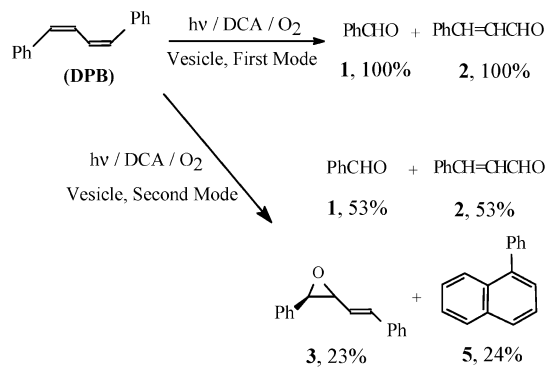
As in the case of the ZSM-5 zeolite sample,²⁵ in the first mode, due to the isolation of the sensitizer in solution from the substrate in Nafion, only the products derived from the energy-transfer pathway were detected. The sensitized photooxidation of DPB gave **6** as the unique product (Scheme 9), while that of TS yielded **10** and **11** (Scheme 10). In contrast, the second mode only resulted in the electron-transfer-mediated products, **1–4** for DPB (Scheme 9) and **1, 7–9** for TS (Scheme 10).

Vesicles as the Microreactor. The above approach to control the reaction pathways in photosensitized oxidation of alkenes has also been demonstrated to be effective in vesicle medium.^{28–30} Again, we performed the photosensitized oxidation in two modes. In the first mode, we incorporated the sensitizer DCA in the bilayer membranes

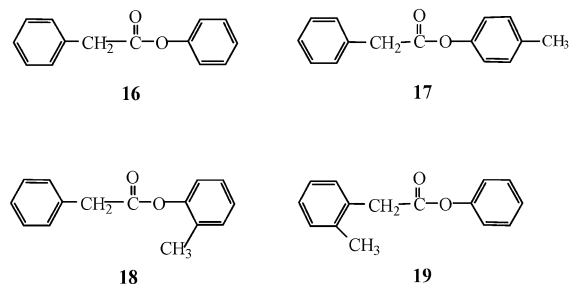
Scheme 10. Photosensitized Oxidation of *trans*-Stilbene within Nafion Membranes

of one set of vesicles and solubilized the substrate in another set of vesicles. Equal volumes of the two sets of vesicle dispersions were then mixed to prepare the samples for irradiation. Thus, the photosensitized oxidation process in this mode involved the generation of $^1\text{O}_2$ 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. We have examined the oxidation of α -pinene (PE) and DPB sensitized by DCA in these vesicles. 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 11. The ene product and the non-ene products have been proposed to be derived from the energy-transfer and electron-transfer pathways, respectively. By contrast, the photosensitized oxidation in vesicles in the first mode exclusively produced the ene product **12**. On the other hand, the photooxidation in the second mode exclusively gave the non-ene products **13–15**.

The photosensitized oxidation of DPB in vesicles in the first mode gave **1** and **2** as the unique products (Scheme 12). We believe that these products are derived from the 1,2-cycloaddition of $^1\text{O}_2$ 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

Scheme 12. Photosensitized Oxidation of *trans,trans*-1,4-Diphenyl-1,3-butadiene in Vesicle Dispersions

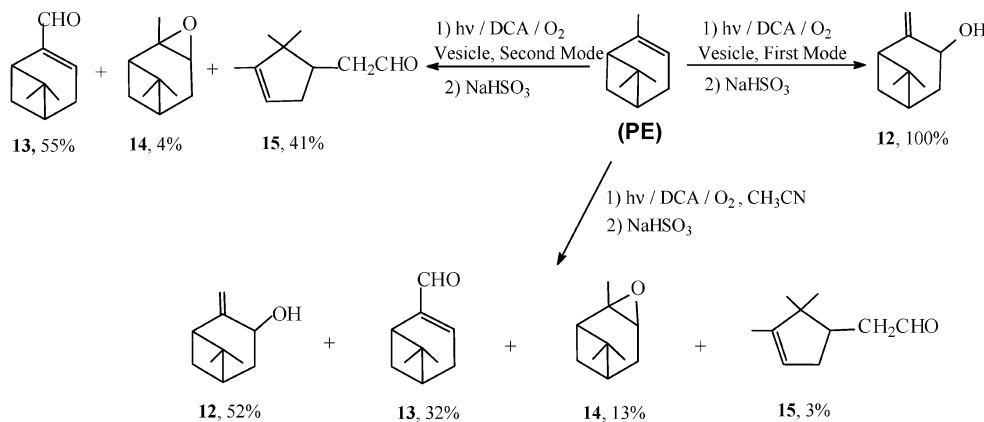
Scheme 13. Phenyl Phenylacetates Examined for Photo-Fries Rearrangement within Zeolites and Nafion Membranes



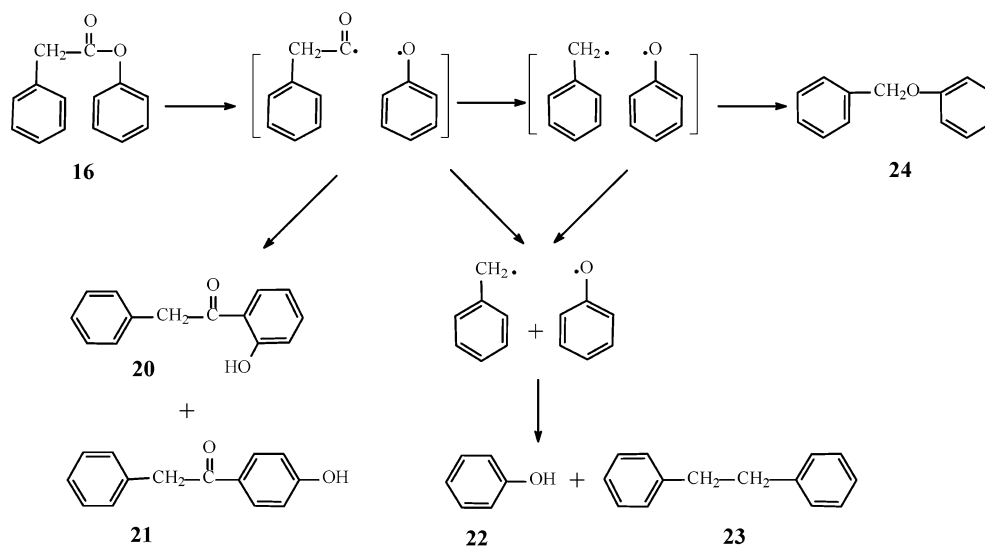
of the greater difficulty of achieving the necessary geometry for 1,4-cycloaddition in this organized medium. In contrast, the photosensitized oxidation in the second mode only produced the electron-transfer-mediated products **1**, **2**, **3**, and **5**.

Zeolites and Nafion Membranes Controlling Radical Pair Reactions: Photochemistry of Phenyl Phenylacetates

The microreactor may impose a restriction on the rotational and translational motions of substrate molecules and reaction intermediates.^{1,4} This would promote, or discourage, specific reactions. The photochemical reaction of phenyl phenylacetates **16–19** (Scheme 13) within zeolites and Nafion membranes provides a good example.^{31,32} Scheme 14 gives the photochemical reaction of these esters with **16** as the example. Photolyses of **16–**

Scheme 11. Photosensitized Oxidation of α -Pinene in CH_3CN and in Vesicle Dispersions

Scheme 14. Intermediacy of Radical Pairs in Photochemical Reactions of Phenyl Phenylacetate



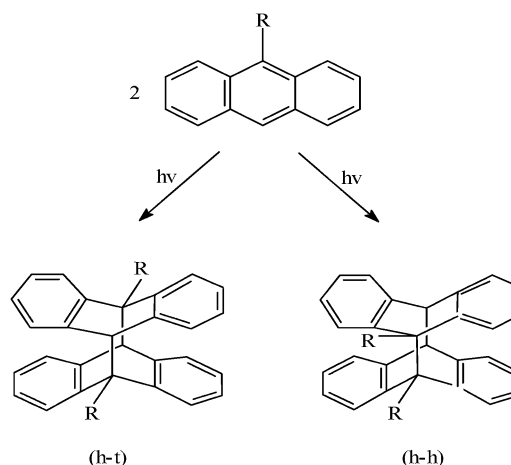
19 in homogeneous solution result in the formation of *ortho*-hydroxyphenones **20** (40–60%), *para*-hydroxyphenones **21** (20–25%), phenols **22** (5–15%), diphenylethanes **23** (5–15%), and phenyl benzyl ethers **24** (3–8%). However, photolyses of all four esters in NaY zeolite and Nafion only produce **20**. Molecular models suggest that esters **16–19** can enter into the NaY zeolite internal surface and the inverse micelle of Nafion. We believe that the preference for formation of *ortho*-hydroxyphenones is a consequence of the restriction on diffusional and rotational motions of the geminate radical pair.

For samples photolyzed on ZSM-5 zeolite, the product distributions of **16** and **17** are dramatically different from those in homogeneous solutions. Only phenols and toluene were detected. In contrast, photolyses of **18** and **19** on ZSM-5 resulted in both photo-Fries rearrangement and decarbonylation products. These results can be understood from consideration of size- and shape-selective sorption combined with restriction on the mobility of the substrates and reaction intermediates imposed by the zeolite pore system. Compounds **16** and **17** are expected to diffuse into and to be adsorbed within the internal surface of the pentasil; both diffusional and rotational motions of the generated radical pair are restricted. In contrast, **18** and **19** possess a size/shape which inhibits them to diffuse into the ZSM-5 channel system. Thus, they are adsorbed on the external surfaces of ZSM-5, and the intermediate radical pairs are expected to experience much less restriction to their diffusional and rotational motions.

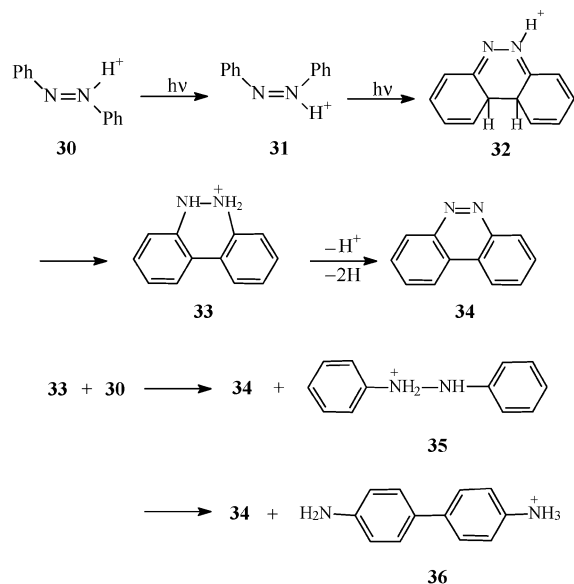
Nafion Membranes and Microemulsions Controlling Regioselectivity of Anthracene Photocyclomers

Photocycloaddition of anthracene and its derivatives continues to be one of the subjects in photochemistry.³³ Irradiation of 9-substituted anthracenes in organic solution typically results in cycloaddition of the aromatic rings at 9,10-positions to yield head-to-tail (h-t) rather than

Scheme 15. Photocycloaddition of 9-Substituted Anthracene



head-to-head (h-h) cyclomers (Scheme 15). We have employed Nafion membranes³⁴ and microemulsions³⁵ as the microreactors to increase the synthetic yields of the h-h photocyclomers. When anthracene bearing an ionic or a polar substituent is incorporated within the inverse micelle of Nafion membranes or microemulsions, one might expect that its molecules would be located in the hydrophobic phase/water interface, and the substituent is directed toward the water pool. This preorientation would favor the formation of a h-h photocyclomer. Irradiation of the solutions of five 9-substituted anthracenes [AnCH₂N⁺(CH₃)₃Br⁻ (**25**), AnCH₂COO⁻Na⁺ (**26**), AnCH₂OH (**27**), AnCOCH₃ (**28**), and AnCH₃ (**29**), An = 9-anthryl] in organic solvents mainly leads to formation of the h-t cyclomers. In contrast, irradiation of **25–28** incorporated within Nafion membranes or microemulsions almost exclusively results in the formation of the h-h cyclomers. On the other hand, under identical conditions, such a regioselectivity for the photocycloaddition of the nonpolar reference substrate **29** was not observed, due to the lack of such a preorientation.

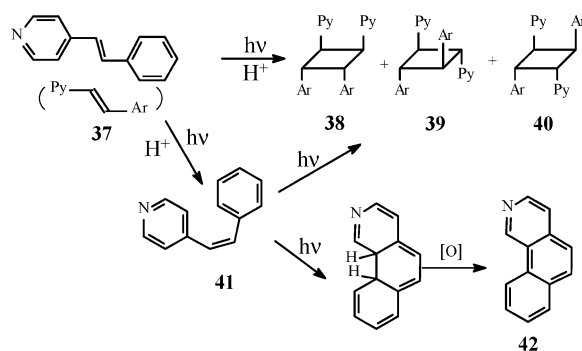
Scheme 16. Mechanism of the Formation of Benzo[*c*]cinnoline and Benzidine

Compartmentalization and Acidity of Nafion Influencing Photochemical Behavior of Azobenzene and Stilbazole

Just like zeolites and LDPE, the inverse micelle-like structure of water-swollen Nafion can compartmentalize the substrate molecules, thus favoring the intramolecular reaction in the competition with the intermolecular reaction. Furthermore, this polymer in its protonated form is a superacid.¹⁰ The acid groups can act as active sites and directly intervene in the chemical process occurring in the water-containing pockets of the polymer. We have shown that the photochemical behaviors of azobenzene³⁶ and stilbazole³⁷ incorporated in Nafion membranes are remarkably altered as compared with those in solution. The azobenzene system follows two different reaction pathways depending on the photolysis condition: *cis*–*trans* isomerization in neutral medium and cyclization to benzo[*c*]cinnoline **34** and benzidine **36** (Scheme 16) in the presence of an acid. Photoirradiation of water-swollen Nafion- H^+ membranes soaking azobenzene results in cyclization to give **34**. Variable amounts of **36** are also produced as shown in Scheme 16. The product distribution was dependent on the occupancy number of azobenzene in the water cluster of the Nafion sample. Photolysis of the sample with an occupancy number greater than 2 leads to the formation of **34** and **36** with a ratio of ca. 50:50. However, for the sample with an occupancy number less than 0.4, we could only isolate the photocyclization product **34** in a quantitative yield.

Similarly, upon irradiation, stilbazole undergoes *cis*–*trans* isomerization in neutral medium. However, in acidic medium it undergoes photochemical cyclization to aza-phenanthrene **42** and dimerization to cyclobutanes **38**–**40**, in addition to *cis*–*trans* isomerization (Scheme 17). Although the photodimerization and *cis*–*trans* photoisomerization have been extensively investigated, the photocyclization product has never been isolated. Further-

Scheme 17. Photochemistry of Stilbazole Salt



more, in the photodimerization the main product is the head-to-tail (h-t) dimer **40**. We were able to use water- and methanol-swollen Nafion membranes as microreactors to direct the photochemical reaction selectively toward either the cyclization or the dimerization, and in the case of dimerization to increase the yield of the h-h dimer **38**. For example, at the occupancy numbers less than 0.5 substrate molecules in each water cluster, the main product was **42**, a product not obtained in homogeneous solution.

Conclusion

We have shown that the photochemical reactions of organic compounds in microreactors usually show a deviation of product distribution from their molecular photochemical reactions in solution and, in some cases, result in the occurrence of reaction pathways that are not otherwise observed. The application of microreactors to synthetic organic photochemistry has already grown out of its infancy and now emerges as an interesting field in photochemical research. In this regard, using microreactors to enhance asymmetric induction in enantioselective photochemical reactions will show promising future achievements.^{6,38} The challenge for the next decade lies not only in developing new experimental and theoretical approaches to better understand the mechanistic and kinetic details of the photochemical processes occurring in microreactors, but also in extending the scope of this methodology and in designing novel microreactors which enhance the selectivity of phototransformations.

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