JOC Notes

Photooxidations of Alkenes in Fluorinated Constrained Media: Fluoro-organically Modified NaY as Improved Reactors for Singlet Oxygen "Ene" Reactions

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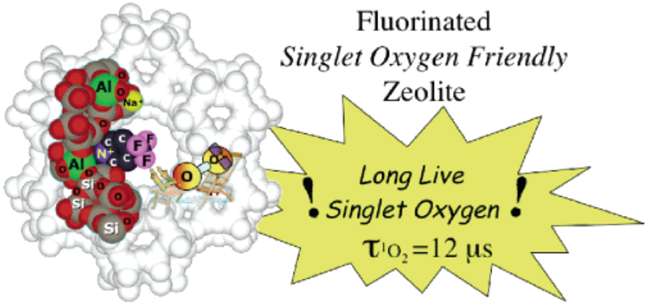

Creating a stationary fluorinated environment inside the zeolite cavity can increase the reactivity observed for intrazeolite photooxidation of alkenes. Exchanging the zeolite with fluorinated organic cations is a much more effective strategy than simply using a fluorinated solvent for slurry irradiations. Use of cations containing C−F bonds is also more efficient than use of deuterated cations for creation of a singlet oxygen friendly environment where the quenching processes are slowed down. Doping the zeolite with fluoro-organic cation **4** resulted in an increase in the singlet oxygen lifetime to 12 μs.

Introduction

Photooxygenations involving singlet oxygen represent a useful tool for the addition of molecular oxygen to organic compounds.[1] Among these photooxidations, the "ene" reaction generates allylic hydroperoxides which can be converted to synthetically valuable allylic alcohols.[1a,2] For valid synthetic applications, the regio- and stereocontrol of this reaction becomes an important issue, particularly when the olefin contains different allylic hydrogens.[3] Since the first intrazeolite photooxidation reported in 1996 by Li and Ramamurthy,[4] use of zeolites as constrained media for supramolecular control of photooxidation processes has been a successful approach to the selectivity problem.[3a,4−6] However, although intrazeolite photooxidation of electron-rich alkenes occurs faster than in solution and with improved selectivity, the reactivity is still low for electron-poor alkenes that react, but only slowly, in solution.[6] According to eq 1, the reaction rate is proportional to (i) the rate constant for alkene consumption, k_T, which is typically low for electron-poor alkenes, (ii) the intrazeolite concentration of the alkene, and (iii) the intrazeolite concentration of singlet oxygen, which depends on its rate of formation and intrazeolite lifetime.[7]

$$-\frac{d[\mathrm{alkene}]}{dt} = k_T[\mathrm{alkene}][^1O_2] \qquad (1)$$

Since k_T is a constant for a given alkene, enhanced reactivity can only be achieved by increasing either the lifetime of singlet oxygen or the amount of loaded substrate (using perfluorocarbons, for example).[7] A first product-based estimate of the intrazeolite singlet oxygen lifetime of 7.5 μs[7] was recently confirmed by direct measurement of $\tau_1O_2 = 7.9\ \mu s$.[8] It is known that the lifetime of $^1O_2$ is much higher in a fluorinated environment than in organic solvents.[7,9] However, in intrazeolite processes it is the zeolite framework (most likely its aluminum tetrahedra AlO_4^-) that is primarily responsible for singlet oxygen deactivation.[7] Therefore, we decided to investigate the effect on the intrazeolite singlet oxygen lifetime caused by introduction of a stationary fluorous phase (created, for example, by exchange with a fluorinated organic cation) in the interior of the zeolite cavity. For this purpose, we compared the reactivity of the electron-poor alkene **1** (Scheme 1) toward photooxidation in different organic cation-exchanged NaY zeolite reactors.

In a typical procedure, zeolite NaY was exchanged with pyridinium cations **4−8** (Chart 1) by suspension in an aqueous solution of their hexafluorophosphate salts. After filtration, the obtained samples of **4−8**<*n*>@NaY were exchanged with

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[1] For recent reviews on this topic, see: (a) Clennan, E. L.; Pace, A. *Tetrahedron* **2005**, *61*, 6665−6691. (b) Schweitzer, C.; Schmidt, R. *Chem. Rev.* **2003**, *103*, 1685−1757. (c) Clennan, E. L. *Tetrahedron* **2000**, *56*, 9151−9179.

[2] Frimer, A. A.; Stephenson, L. M. The Singlet Oxygen Ene Reaction. In *Singlet O_2. Reaction Modes and Products*; Frimer, A. A., Ed.; CRC Press: Boca Raton, FL, 1985; Vol. II, pp 67−91.

[3] (a) Shailaja, J.; Sivaguru, J.; Robbins, R. J.; Ramamurthy, V.; Sunoj, R. B.; Chandrasekhar, J. *Tetrahedron* **2000**, *56*, 6927−6943. (b) Ramamurthy, V.; Prein, M.; Adam, W. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 477.

[4] Li, X.; Ramamurthy, V. *J. Am. Chem. Soc.* **1996**, *118*, 10666−10667.

[5] (a) Stratakis, M.; Kalaitzakis, D.; Stavroulakis, D.; Kosmas, G.; Tsangarakis, C. *Org. Lett.* **2003**, *5*, 3471−3474. (b) Tung, C.-H.; Wang, H.; Ying, Y.-M. *J. Am. Chem. Soc.* **1998**, *120*, 5179−5186.

[6] Clennan, E. L.; Sram, J. P.; Pace, A.; Vincer, K.; White, S. *J. Org. Chem.* **2002**, *67*, 3975−3978.

[7] Pace, A.; Clennan, E. L. *J. Am. Chem. Soc.* **2002**, *124*, 11236−11237.

[8] Jockusch, S.; Sivaguru, J.; Turro, N. J.; Ramamurthy, V. *Photochem. Photobiol. Sci.* **2005**, *4*, 403−405.

[9] Schmidt, R.; Afshari, E. *Ber. Bunsen-Ges. Phys. Chem.* **1992**, *96*, 788−794.

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SCHEME 1. Singlet Oxygen Ene Reaction of Methyl Tiglate 1

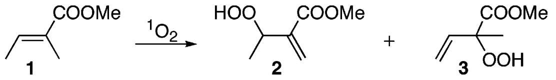
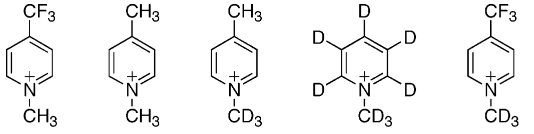


CHART 1



4 5 6 7 8

TABLE 1. Conversions (%) and Conversion Ratios (CR) for the Intrazeolite Singlet Oxygen Photooxydation of Compound 1 as a Function of the Zeolite Reactor and Slurry Solvent

		conversion (%)[a]		CR	
no.	zeolite	C_6F_{14}	C_6H_{14}	C_6F_{14}	C_6H_{14}
1	NaMBY	30 ± 1	27 ± 1	1.00	1.00
2	**4**<0.4>@NaMBY	34 ± 1	37 ± 1	1.13	1.37
3	**4**<0.5>@NaMBY	38 ± 2	38 ± 1	1.27	1.41
4	**4**<0.7>@NaMBY	42 ± 1	44 ± 2	1.40	1.63
5	**4**<0.8>@NaMBY	44 ± 1	46 ± 1	1.47	1.70
6	**4**<1.0>@NaMBY	49 ± 3	48 ± 2	1.63	1.78
7	**5**<1.0>@NaMBY	34 ± 2		1.13	
8	**6**<1.0>@NaMBY	38 ± 1		1.27	
9	**7**<1.0>@NaMBY	46 ± 3		1.53	
10	**8**<1.0>@NaMBY	52 ± 3		1.73	

[a] Average of three independent irradiations.

methylene blue (MB) to obtain a dye loading of one molecule per 100 supercages. These samples of **4**−**8**<*n*>@NaMBY were dried and added to a solution of **1** in either perfluorohexane or *n*-hexane. After quantitative inclusion of the alkene in the zeolite was reached, the slurry was saturated with oxygen and irradiated at $\lambda > 400$ nm under continuous O_2 flow. After irradiation, the solvent was separated and analyzed by HPLC, the zeolite was extracted with THF, and the extracts reduced with Ph_3P and analyzed by HPLC. In all cases, the mass balance was higher than 95% and the product distribution (**2**:**3** = 95:5) reproduced the one previously reported for photooxidation of **1**.[6,7]

The reactivity of **1** was evaluated by comparing the change in substrate conversions upon varying the slurry solvent, the pyridinium cation, and its loading level (Table 1). To better interpret these data, we define CR (eq 2) as the ratio between the substrate conversion observed in a given pyridinium-doped zeolite and the one observed in NaMBY chosen as reference. CR can also be expressed (eq 2) in terms of both the slurry solvent-induced decay rate of singlet oxygen, k_d, and the zeolite-induced decay rate of singlet oxygen, k_q, since under our irradiation conditions the stationary-state approximation is valid for $[^1O_2]$[7] (see Supporting Information).

$$\mathrm{CR} = \frac{\%\ \text{conversion}_{\text{Zeolite}}}{\%\ \textit{conversion}_{\text{NaMBY}}} = \frac{k_T[\text{alkene}] + k_d + k_q^{\text{NaMBY}}}{k_T[\text{alkene}] + k_d + k_q^{\text{Zeolite}}} \qquad (2)$$

CR systematically increases in both perfluorohexane and hexane slurries for photooxidations of **1** as a function of the molecular occupancy <*n*> of the fluorinated pyridinium cation, **4** (Figure 1). Control irradiations of **1** with O_2 in a zeolite containing only the pyridinium cation **4** showed no conversion of the alkene. This excluded any role of the cation **4** as a sensitizer and confirmed that methylene blue is necessary for photooxidation to occur. These results are consistent with decreasing values of k_q^{zeolite} (eq 2) as the fluorous content of the zeolite increases.

Furthermore, for irradiations in the non-fluorinated cation-exchanged zeolite **5**@NaMBY, the reactivity enhancement is much lower (if not absent) in comparison to that observed in the corresponding fluorinated zeolite **4**@NaMBY (see Supporting Information). The lower dependence of CR on cation loading levels in perfluorohexane compared to hexane slurries (i.e., the different slopes in Figure 1) could be interpreted in terms of a leveling effect of the fluorinated solvent in enhancing the intrazeolite lifetime of $^1O_2$.

To provide further confirmation that the observed reactivity enhancement is actually due to an increase of the $^1O_2$ lifetime, we performed irradiations in deuterated systems **6**@NaMBY, **7**@NaMBY, and **8**@NaMBY. It is well established that reduced intermolecular electronic to vibrational energy transfer in deuterated solvents leads to increased lifetimes of singlet oxygen.[10] In fact, by substitution of a CH_3 with CD_3, we observed an increase of reactivity of about 14% in the case of cations **5** and **6** (entries 7 and 8 in Table 1) and 10% in the case of cations **4** and **8** (entries 6 and 10 in Table 1). Furthermore, a reactivity enhancement of about 53% (with respect to NaMBY) was observed when the zeolite was loaded with the octadeuterated cation **7**.

Equation 2 can also be used to conservatively estimate the lifetime of singlet oxygen ($\tau^1O_2 = 1/k_q^{\text{zeolite}}$) in the fluoro-organically modified zeolites. For example, in perfluorohexane slurries of **4**<1.0>@NaMBY, where CR = 1.6 (Table 1), a lifetime of 12 μs for singlet oxygen can be calculated using the literature values of $k_T^1 = 6.1 \times 10^{-3}$ (for an alkene loading level of one molecule per supercage),[7,11] $k_d^{\text{perfluorohexane}} = 1.47 \times 10^1$,[7,9] and $k_q^{\text{NaMBY}} = 1.33 \times 10^5$.[7] This represents a 60% increase in the $^1O_2$ lifetime over that observed in the non-fluoro-organically modified NaMBY.[7,8,12]

The utility of these new fluoro-organically modified zeolites was further demonstrated during intrazeolite photooxidations of three additional alkenes including 2-methyl-2-heptene, which exhibits a dramatic intrazeolite regiochemical change in comparison to solution.[3a] The results (Table 2) show that the reactivity enhancement due to the presence of the fluorinated cation **4** is more pronounced for the less reactive olefins in the series di- < tri- < tetra-alkyl-substituted alkenes. When the intrinsic alkene reactivity increases, k_T values become the more determining factor for the reactivity and the effect of the fluorinated cation is diminished.

In conclusion, a singlet oxygen friendly environment, where the quenching processes are slowed down and the $^1O_2$ lifetime is increased, can enhance the reactivity of intrazeolite photooxidations. The larger CR value for photooxidation of **1** in fluorinated than in deuterated reactors (compare **4**<1.0>@NaMBY and **6**<1.0>@NaMBY; entries 6 and 8 in Table 1) is expected based on the larger singlet oxygen lifetime in C_6D_5F

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(10) (a) Rodgers, M. A. J. *J. Am. Chem. Soc.* **1983**, *105*, 6201−6205. (b) Skovsen, E.; Snyder, J. W.; Lambert, J. D. C.; Ogilby, P. R. *J. Phys. Chem. B* **2005**, *109*, 8570−8573.

(11) Veverbizet, C.; Dellinger, M.; Brault, D.; Rlougee, M.; Bensasson, R.V. *Photochem. Photobiol.* **1989**, *50*, 321−325.

(12) Since the sensitizer (MB) concentration was kept constant at 1 ± 0.02 molecules per 100 supercages in all experiments, such an effect cannot be ascribed to different dye contents which could have affected only the photooxygenation rate but not the lifetime of singlet oxygen.

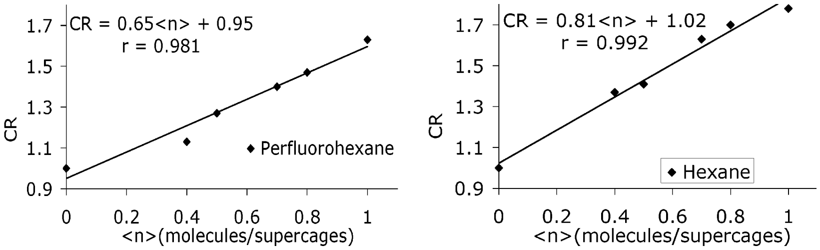

FIGURE 1. Conversion ratios CR as a function of cation loading <*n*> for the intrazeolite photooxidation of methyl tiglate **1** in **4**<*n*>@NaMBY zeolites suspended in perfluorohexane (left) or hexane (right).

TABLE 2. Conversions (%) and Conversion Ratios (CR) for Olefin Photooxidations in NaMBY and in 4<1.0>@NaMBY in C_6F_{14} Slurry

	conversion (%)		
alkene	NaMBY	**4**<1.0>@NaMBY	CR
cyclohexene	24	52	2.17
2-methyl-2-heptene	37	78	2.11
2,3-dimethyl-2-butene	62	97	1.56

(1100 μs) in comparison to C_6D_6 (700 μs).[13] Moreover, creation, by cation exchange, of a stationary fluorinated phase is more effective than a simple change of slurry solvent and has the additional advantage that the fluoro-modified zeolite can be reused after being thoroughly extracted with organic solvents. Despite the fact that rate enhancements from only 1.5 to approximately 2 were observed, this approach appears to be an exciting strategy for the hydroperoxidation of less reactive substrates. Development of zeolites with a higher degree of fluoro-organic modification to improve the rate enhancements is currently in progress.

Experimental Section

General Procedure for the Synthesis of Hexafluorophosphate Salts of Cations 4−8. An excess of iodomethane (2.1 g, 15 mmol) was added to either 4-trifluoromethylpyridine (1.6 g, 11 mmol) or 4-picoline (1.0 g, 11 mmol) in a closed pressure-resistant tube, and the mixture was stirred overnight at 80 °C. A similar procedure was followed for the preparation of deuterated salts by adding an excess of iodomethane-d_3 (2.2 g, 15 mmol) to either 4-trifluoromethylpyridine (1.6 g, 11 mmol), 4-picoline (1.0 g, 11 mmol), or pyridine-d_6 (0.9 g; 11 mmol). The excess iodide was removed by evaporation under reduced pressure. The solid residue was dissolved in water (10 mL) and added dropwise to an aqueous 5 M NH_4PF_6 solution (10 mL). The white precipitate formed from **4**−**8** hexafluorophosphate salts were filtered, washed with water, and recrystallized three times from 1-butanol/acetonitrile 10/1 (vol/vol).

1-Methyl-4-trifluoromethylpyridinium (4) Hexafluorophosphate. Yield 90%; mp 177−178 °C (white crystals, from 1-butanol/acetonitrile 10/1). IR (Nujol, cm^{-1}): 3313, 3148, 3095, 1341, 1184, 1151, 1084, 1060, 829, 753. UV−vis (H_2O, λ_{max} (log ϵ), nm): 265 (3.61), 206 (3.53). ^1H NMR (CD_3CN, δ (ppm), J (Hz)): 4.40 (s, 3H), 8.30 (bs, 2H), 8.88 (d, 2H; $J = 6.3$).

1,4-Dimethylpyridinium (5) Hexafluorophosphate. Yield 78%; mp 211−213 °C (white crystals, from 1-butanol/acetonitrile 10/1). IR (Nujol, cm^{-1}): 3076, 1647, 1579, 841, 811. UV−vis (H_2O, λ_{max} (log ϵ), nm): 255 (3.62), 222 (3.27). ^1H NMR (CD_3CN, δ (ppm), J (Hz)): 2.61 (s, 3H), 4.20 (s, 3H), 7.78 (bd, 2H; $J = 6.5$), 8.41 (d, 2H; $J = 6.5$).

1-Trideuteromethyl-4-methylpyridinium (6) Hexafluorophosphate. Yield 81%; mp 211−212 °C (white crystals, from 1-butanol/acetonitrile 10/1). IR (Nujol, cm^{-1}): 3139, 3066, 1644, 1520, 1194, 839, 801. UV−vis (H_2O, λ_{max} (log ϵ), nm): 254 (3.60), 221 (3.89). ^1H NMR (CD_3CN, δ (ppm), J (Hz)): 2.61 (s, 3H), 7.78 (bd, 2H; $J = 6.5$), 8.41 (d, 2H; $J = 6.5$).

1-Methyl-pyridinium-d_8 (7) Hexafluorophosphate. Yield 65%; mp 207−211 °C (white crystals, from 1-butanol/acetonitrile 10/1). IR (Nujol, cm^{-1}): 2318, 1595, 1279, 1156, 993, 807. UV−vis (H_2O, λ_{max} (log ϵ), nm): 257 (3.65), 206 (3.57). ^{13}C NMR (CD_3CN, δ (ppm)): 48.8, 128.6, 145.8, 146.

1-Trideuteromethyl-4-trifluoromethylpyridinium (8) Hexafluorophosphate. Yield 92%; mp 184−185 °C (white crystals, from 1-butanol/acetonitrile 10/1). IR (Nujol, cm^{-1}): 3313, 3147, 3101, 3080, 1184, 1152, 1084, 1057, 829, 744. UV−vis (H_2O, λ_{max} (log ϵ), nm): 265 (3.63), 205 (3.58). ^1H NMR (CD_3CN, δ (ppm), J (Hz)): 8.24 (bs, 2H), 8.82 (d, 2H; $J = 6.3$).

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Supporting Information Available: Full experimental details, calculation of $k_q^{zeolite}$, ^1H NMR spectra of hexafluorophosphates of cations **4**−**6** and **8**, and ^{13}C NMR spectra of hexafluorophosphate of cation **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[13] Hurst, J. R.; Schuster, G. B. *J. Am. Chem. Soc.* **1983**, *105*, 5756−5760.