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Stereoselectivity in Ene Reactions with ¹O₂: Matrix Effects in Polymer Supports, Photo-oxygenation of Organic Salts and Asymmetric Synthesis

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ABSTRACT

The ene reaction of chiral allylic alcohols is applied as a tool for the investigation of intrapolymer effects by means of the stereoselectivity of the singlet-oxygen addition. The diastereo selectivity strongly depends on the structure of the polymer, the substrate loading degree and also on the degree of conversion demonstrating additional supramolecular effects evolving during the reaction. The efficiency and the stability of polymer-bound sensitizers were evaluated by the ene reaction of singlet oxygen with citronellol. The ene reaction with chiral ammonium salts of tiglic acid was conducted under solution phase conditions. The products thus obtained precipitate during the photoreaction as ammonium salts. Moderate asymmetric induction was observed for this procedure for the first time.

INTRODUCTION

Singlet oxygen is a versatile reagent in organic oxidation chemistry. Because this molecule can be generated by numerous thermal methods, singlet-oxygen chemistry is often not considered per se as a photochemical topic. The most practical method to generate singlet oxygen in solution, however, is triplet sensitization by use of electronically excited triplet states of dye molecules. Furthermore, singlet oxygen is an electronically excited molecule and can decay to its ground state by radiationless or radiative processes in addition to chemical reactions. The chemical process that leads to the oxidation of organic substrates by transfer of both oxygen atoms is termed Type-II photooxygenation (1-3). The atom economy of such a process is 100%, a major advantage over other oxidants, such as hydrogen peroxide, that can only reach an atom economy of 48%, if calculated for the formation of epoxides from alkenes (4). The primary peroxidic products from Type-II photo-oxygenation can be reduced to numerous polyoxygenated derivatives either with loss of the original oxygen content (allylic alcohols from allylic

hydroperoxides) or with conservation of the oxygen content (1,2and 1,4-diols from dioxetanes and endoperoxides, respectively, or epoxy-alcohols from allylic hydroperoxides by means of titanium[IV]-catalyzed oxygen transfer).

Singlet-oxygen reaction media

In the last decade, the area of polymer-supported organic reactions (5-7) and polymer-supported catalysts (8,9) has impressively increased. This is obvious for solid-phase synthetic chemistry, where reactions are carried out in resins and/or catalyzed by supported catalysts. Photo-oxygenation in solution with the use of insoluble polymer-bound sensitizers facilitates the problem of dve recovery. The first polymer-bound sensitizer was the now commercially available polystyrene-bound Rose Bengal developed by Schaap et al. (10) followed by a series of immobilized sensitizers, e.g. the immobilized fullerene C_{60} (11,12), ionic porphyrins immobilized on cationically functionalized polystyrene (13), tetrakis(4-hydroxyphenyl)porphyrin supported to polyethylene glycol (14), aluminum(III) tetracarboxyphthalocyanine bound to poly(styrene-co-chloromethylstyrene) (15), polystyrene-bound benzophenones (16), immobilized pyrylium salts on Merrifield resins (17), sensitizer-incorporated nation membranes (18), or ionexchange resins ionically bound to photosensitizers (19). Other heterogeneous catalysts using clay (20), silica (21), and zeolites (22,23) as support materials were also recently developed. From the viewpoint of solution photochemistry, the use of nonpolar solvents enhances dye oxidation and bleeding, especially if long reaction times are needed, which decreases the singlet-oxygen quantum yield and hence the reaction efficiency. On the other hand, photo-oxygenation reactions carried out in aqueous solutions are also not favored, due to low solubility of most organic substrates, the low singlet-oxygen lifetime, and hydrophobic aggregations of nonpolar sensitizers (leading to self quenching), which as a consequence reduces the triplet lifetime (24,25). We have recently reported a solution to circumvent some of the mentioned technical problems: Under solvent-free reaction conditions, in which the substrates are embedded in a porphyrin-loaded polystyrene polymer matrix, irradiation and product isolation accompanied by complete sensitizer separation by extraction with ethanol offers a shortcut to green photo-oxygenation reactions (26),

Two major problems in photo-oxygenation chemistry appeared unsolved until recently: (a) altering the regio- and diastereoselectivity

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Scheme 1. The singlet-oxygen ene reaction.

of singlet-oxygen ene or [4+2]-cycloadditions by optimizing the reaction media, and (b) making singlet oxygen chiral, *i.e.* introducing high enantioselectivity into singlet-oxygen ene or [4+2]-cycloaddition reactions by catalytic methods.

The singlet-oxygen ene reaction

The singlet-oxygen ene reaction was discovered in 1943 by G. O. Schenck (27,28). In the course of this reaction, ${}^{1}O_{2}$ attacks one center of a CC double bond with abstraction of an allylic hydrogen atom and shift of the double bond (Scheme 1). As a result of this reaction, allylic hydroperoxides are formed, compounds that are versatile intermediates for the synthesis of allylic alcohols, epoxides, epoxyalcohols, 1,2-diols, and 1,2,3-triols. Several mechanisms have been postulated for this reaction, most recently the two-step no-intermediate mechanism involving a bifurcating transition state with perepoxide structure (29), as well as 1,4-biradicals (30), 1,4-zwitterions (31), perepoxide (32), dioxetane or exciplex intermediates.

The results of inter- and intramolecular isotope experiments (33) with isotopically labeled tetramethylethylenes provided evidence for the suprafacial ${}^{1}O_{2}$ attack and for a perepoxide intermediate. Also, the small negative activation enthalpies and highly negative activation entropies observed for the singlet-oxygen ene reaction argue for the participation of a reversibly formed exciplex as an intermediate (34). The regiochemistry of the ene reaction with substrates with multiple sites for allylic hydrogen transfer was extensively studied and several general effects can predict the regioselective introduction of the hydroperoxy group: (a) the ciseffect (syn-effect) in the reaction of ${}^{1}O_{2}$ with trisubstituted alkenes (35-37) (b) the gem effect that leads to highly selective abstraction of an allylic hydrogen atom from a CHX-substituent in α position of an α , β -unsaturated carbonyl compound (38,39), and (c) the large-group effect (40,41) that leads to selective (moderate) abstraction of an allylic hydrogen from the substituent geminal to a large group. Several factors that control the π facial selectivity of singlet-oxygen ene reaction are known: (1) steric factors, mostly in rigid cyclic and polycyclic substrates (42,43); (2) conformational effects, based on the optimal position of reactive allylic hydrogens perpendicular to the alkene plane (44); and (3) hydrogen bonding effects, which have been used for control of the diastereoselectivity in the ene reaction of allylic alcohols and other substrates (45).

Enantioselectivity of the singlet-oxygen ene reaction

In contrast to the high diastereoselective control of the singletoxygen ene reaction, enantioselective reactions are still rare. Several attempts to control the enantioselectivity were reported. The use of β -cyclodextrins covalently bound to porphyrin sensitizers in the photo-oxygenation of linoleic acid resulted in



Scheme 2. Enantioselective singlet-oxygen ene reactions.



Figure 1. Singlet-oxygen sensitizers used in polymer matrices.

low ee values (10–20%) (46,47). The photo-oxygenation of 2methyl-4-phenyl-2-butene in NaY zeolite in presence of (+)ephedrine as chiral inductor also resulted in 15% ee hydroperoxide formation (48). Recently, Córdova et al. published a fundamental report on the amino-acid–catalyzed asymmetric incorporation of molecular oxygen into the α position of a series of aldehydes and ketones (49,50). The mechanism is assumed to proceed through an ene reaction of singlet oxygen with the intermediate enamines to give the corresponding hydroperoxides which are *in situ* reduced to afford vicinal diols in high ee values (Scheme 2).

MATERIALS AND METHODS

General aspects and methods. Protoporphyrin IX (PP-IX), meso-tetraphenylporphyrin (TPP), and meso-tetrakis-4-methylphenyl-porphyrin (TTP) were purchased from Porphyrin Systems. Fullerene C_{60} was purchased from Dynamic Enterprises. Polystyrene beads (1% divinylbenzene copolymer, 100–200 mesh) were purchased from Acros Organics. The solvents for solution photo-oxygenation were puriss. and used as purchased. NMR spectra were recorded on Bruker AC 250 and DPX 300 spectrometers, CP-MAS spectra were run on a Bruker DRX 500 spectrometer, carbon multiplicities were determined by DEPT; melting points were determined with a Büchi melting-point apparatus (Type 535) and are uncorrected.

Photo-oxygenation of citronellol (1) and the allylic alcohol 4methylpent-3-en-2-ol (4). A slurry of 5 g of polystyrene beads with a solution of 2 mg (3×10^{-3} mmol) of TPP (or the equivalent amount of TTP) and citronellol in 30 mL of dichloromethane was dispensed on a petri dish (\emptyset 19 cm). The excess solvent was evaporated by leaving the petri dish for a few minutes in a well-ventilated hood. The sandy solid obtained was irradiated for 5 h in the loosely covered petri dish by a sodium street lamp or a halogen lamp without external cooling and without external oxygen purging. The polymer beads were subsequently rinsed with 3×20 mL of ethanol and filtered. After evaporation of the solvent, the product was collected as a 1.1:1 mixture of the two regioisomers (2, 3). The residual polystyrene beads were used for five additional photo-oxygenations with ethyl acetate applied instead of dichloromethane for swelling.



Scheme 3. Photo-oxygenation of (S)-citronellol (1).



cycle number

Figure 2. Photo-oxygenation of citronellol (1) with different sensitizer/ polymer systems after constant reaction time: blue and red: tetraphenylporphyrine (TPP) in polystyrene (PS) with different substrate amounts (black: 1.0 mmol/g support; dark grey: 0.4 mmol/g support); light grey: polymerbound PP-IX; white: fullerene C_{60} in PS.

6-hydroperoxy-3,7-dimethyl-oct-7-en-1-ol (2) and (*E*)-7-hydroperoxy-3,7-dimethyl-oct-5-en-1-ol (3): 1.2:1 mixture of regioisomers; 3 consists of a 1:1 mixture of diastereoisomers independent of the reaction conditions. ¹H NMR (CDCl₃) characteristic signals for 2: δ 1.65 (s, 3 H, C₄CH₃), 1.95 (m, 2 H, COOHCH₂), 4.24 (m, 1 H, CHOOH), 4.95 (s, 2 H, C₄=CH₂); characteristic signals for 3: δ 1.29 (s, 6 H, COOH(CH=3)₂), 5.51 (d, *J* = 15.8 Hz, 1 H, COOHCH=CH), 5.63 (m, 1 H, COOHCH=CH). ¹³C NMR (CDCl₃) characteristic signals for 2: δ 16.9/17.0 (q, 1 C, CqCH₃) 19.4/19.5 (q, 1 C, CHCH₃), 24.2/24.3 (t, 1 C, COOHCH₂) 28.3/29.2 (d, 1 C, CHCH₃), 32.5/32.7 (t, 1 C, COOHCH₂CH₂), 39.3/39.5 (t, 1 C, CH₂CH₂OH), 60.8 (t, 1 C, CH₂OH), 89.4/89.8 (d, 1 C, CHOOH), 113.8/114.2 (t, 1 C, Cq=CH₂), 143.7/143.9 (s, 1 C, Cq); characteristic signals for 3: δ 19.7 (q, 1 C, CHCH₃), 28.0 (d, 1 C, CH₃CH), 29.5 (q, 2 C, CH(CH₃)₂), 38.9 (t, 1 C, CH=CHCH₂), 199.7 (t, 1 C, COOHCH=CH), 06.8 (t, 1 C, CH₂OH), 81.9 (s, 1 C, COOH), 129.8 (d, 1 C, COOHCH=CH), 135.0 (d, 1 C, COOHCH=CH).

The corresponding process with the allylic alcohol 4-methyl-pent-3-en-2-ol (4) resulted in mixtures of diastereoisomeric hydroperoxides *syn*-5 and *anti*-5.

(R*,R*)-3-hydroperoxy-4-methyl-pent-4-en-2-ol (*syn*-5). ¹H-NMR (CDCl₃): δ 1.12 (d, J = 6.3 Hz, 3 H, CHC<u>H₃</u>), 1.72 (dd, J = 1.3 Hz, 1.0 Hz, 3 H, C_qC<u>H₃</u>), 2.7 (br s, O<u>H</u>, 1 H), 3.84 (dq, J = 6.3 Hz, 8.4 Hz, 1 H, C<u>H</u>CH₃), 4.12 (d, J = 8.4Hz, C<u>H</u>OOH, 1 H), 5.06-5.08 (m, 2 H, C=C<u>H₂</u>). ¹³C-NMR (CDCl₃): δ 18.2 (q, 1 C, C_qC<u>H₃</u>), 18.8 (q, 1 C, CHC<u>H₃</u>), 67.3 (d, 1 C, C<u>H</u>OH), 94.8 (d, 1 C, CHOOH), 116.7 (t, 1 C, C<u>H₂=C_q</u>), 141.1 (s, 1 C, CH₂=<u>C_q</u>); (R*,S*)-3hydroperoxy-4-methyl-pent-4-en-2-ol (*anti*-5). ¹H-NMR (CDCl₃): δ 1.2 (d, J = 6.5 Hz, 3 H, CHC<u>H₃</u>), 1.8 (dd, J = 1.3 Hz, 1.0 Hz, 3 H, C_qC<u>H₃</u>), 3.93 (dq, J = 6.5 Hz, 8.3 Hz, 1 H, C<u>H</u>CH₃), 4.26 (d, J = 8.3 Hz, C<u>H</u>OOH, 1 H), 5.10–5.12 (m, 2 H, C=C<u>H₂</u>). ¹³C-NMR (CDCl₃): δ 18.3 (q, 1 C, C_qC<u>H₃</u>), 19.5 (q, 1 C, CHC<u>H₃</u>), 65.1 (d, 1 C, C<u>H</u>OH), 92.2 (d, 1 C, C<u>H</u>OOH), 115.4 (t, 1 C, C<u>H₂=C_q</u>), 140.9 (s, 1 C, CH₂=<u>C_q</u>).

Photo-oxygenation of tiglic acid ammonium salts (6).

- L-phenylethylammonium tiglate ([6] PEA). To a solution of 2.0 g (20 mmol) of tiglic acid in 20 mL of acetone 2.42 g (20 mmol) of L-phenyl-ethylamine was added over 5 min and slightly warmed in a water bath until complete dissolution. After 10–20 min at room temperature, the salt precipitated and was filtered off and washed twice with cold acetone to give 3.04 g of the product as white needles (68%), m.p. 112–115°C. ¹H NMR (CDCl₃) δ 1.55 (d, 3H, CH₃CHNH₃⁺, J = 6.8 Hz), 1.66 (d, 3H, =CHCH₃, J = 6.8 Hz), 1.67 (s, 3H, =CCH₃), 4.26 (q, 1H, CHNH₃⁺, J = 6.8 Hz), 6.45 (q, 1H, =CH, J = 6.8 Hz), 7.39 (m, 5H, Ar). ¹³C NMR (CDCl₃) δ 12.6 (CH₃), 14.1 (CH₃), 22.3 (CH₃), 50.9 (CHNH₃⁺), 126.3 (C_{ar}), 127.7 (C_{ar}), 128.6 (C_{ar}), 132.8 (=C_q), 132.9 (C_{ar}), 139.7 (=CH), 174.9 (C=O).
- 2. 3-hydroperoxy-2-methylenebutanoic acid, phenylethylammonium salt ([7] xPEA).
 - (i) In solution: A sample of 100 mg of **6** was dissolved in 30 mL of a 10^{-4} M TPP solution in CCl₄ and was irradiated with a 150 W high-pressure mercury lamp (cut-off filter at 300 nm)



Scheme 4. Photo-oxygenation of the allylic alcohol (4)—NMR-characteristic hydrogens.

at 10°C in an oxygen-uptake apparatus. After no more oxygen was consumed (ca. 7 h) the solvent was removed on a rotary evaporator. The NMR of the raw product indicated complete conversion of the substrate. The resulting oil was crystallized from EtOH to give 120 mg of the product as white needles (80%), m.p. 91–94°C (decomp).

(ii) In polystyrene: A sample of 100 mg of 6 and 2 mg of TTP were dissolved in 20 ml of CH₂Cl₂. This solution was combined on a petri dish with 500 mg of polystyrene beads and the solvent was allowed to evaporate. The open dish was placed under a 150-W sodium street lamp for 7 h. Subsequently, the beads were treated with 20 mL of EtOH, filtered off and washed twice with EtOH. The combined organic phases were concentrated under reduced pressure resulting in 115 mg of the product as white needles (76%). ¹H-NMR (CDCl₃) $\delta = 1.31$ (d, 3H, 1.diast. CHOOHCH₃, J = 6.5 Hz), 1.38 (d, 3H, 2.diast. CHOOHCH₃, J = 6.5 Hz), 1.55 (d, 1H, CH₃NH₃⁺, J = 6.8 Hz), 4.26 (q, 1H, $CHNH_3^+$, J = 6.8 Hz), 4.77 (m, 1H, CHOOH), 5.35 (d, 1H, =CH, J = 3.6 Hz), 5.73 (d, 1H, =CH, J = 4.1 Hz), 7.39 (m, 5H, Ar). ¹³C-NMR (CDCl₃) $\delta = 17.4$ (1.diast. CH₃), 17.5 (CH₃), 22.3 (CH₃), 50.9 (CHNH₃⁺), 80.8 (1.diast. C-OOH), 80.2 (2.diast. C-OOH), 121.7 (1.diast. =CH₂), 121.8 (2.diast. =CH₂), 126.3 (Car), 127.7 (Car), 128.6 (Car), 139.7 (Car), 146.4 (Cq), 173.8 (C=O).

RESULTS AND DISCUSSION

In the focus of our current investigation is the search for solventfree photo-oxygenation procedures in polymer matrices that on the one hand satisfy the requirements for sustainable applications of photochemistry in organic synthesis, and on the other hand might serve as framework for the improvement of diastereoselectivity and the induction of enantioselectivity in singlet-oxygen ene reactions.

Dyes adsorbed in polymer frameworks: Citronellol as a monitor

A set of efficient singlet-oxygen sensitizers for solution-phase Type-II chemistry were chosen as dyes for incorporation into the polymer framework (Fig. 1). These included the porphyrine dyes meso-tetraphenyl- and meso-tetrakis-4-methyl-tetraphenylporphyrin (TPP, TTP), fullerene C₆₀ as well as the polymerizable dyes mesotetrakis-4-vinyl-tetraphenylporphyrin (TSP) and protoporphyrine IX (PP-IX). The first three sensitizers were adsorbed by swelling the polymer with a methylene chloride solution of the dye and subsequent drying and washing with ethyl acetate; the two vinylfunctionalized dyes were cross-polymerized into a polystyrene matrix by emulsion polymerization (51). The morphology of the polymers was investigated by means of optical microscopy, TEM, SEM, and AFM measurements. The commercial polystyrene beads can be reversibly swollen with organic substrates (see Materials and Methods) or solvents reaching maximum uptake of 120% in weight. The spheroid space structure does not change during the

Table 1. syn/anti ratio: $^{1}O_{2}$ ene reaction with 4: Different degrees of loading

Loading ^a	0.1	1.0	4.0
syn/anti	6.6 : 1	3.8 : 1	2.9 : 1

^ammol allylic alcohol (4)/g support (PS-DVB-TPP).

loading process; however, solvent- or substrate-filled channels of 40–60-nm diameters are generated that can be visualized in TEM and probably explain the efficient mass transport throughout the polymer beads. The polymer particles that were synthesized by emulsion polymerization are translucent in color and polyhedral in shape with sizes ranging from 200–500 nm (51). These particles are characterized by high surface areas accounting for their high substrate loading capacity. In the course of synthetic photooxygenation studies, gram scale reactions were carried out applying a loading degree of about 100% by wt. for PP IX and TSP-containing polymer beads.

In order to characterize the stability of these dye-polymer systems, the standard ene reaction with citronellol (1) as substrate (Scheme 3) was performed and compared with the solution phase reaction using the same amount of substrate. The polymer particles were deloaded after irradiation by washing with ethanol and reloaded with identical amounts of starting material without the use of additional solvent. The best results were obtained with the TPP/TTP-doped polystyrene beads, whereas the fullerene-doped and the covalently linked PP-IX-polystyrene beads lost their catalytic activities after three cycles and showed already strong activity decrease after the first cycle (Fig. 2).

In the two latter cases, the oxidative instability of the sensitizers is responsible for this behavior, as already described for protoporphyrine IX and fullerenes in solution (52,53). In all cases,



Figure 3. Change in diastereoselectivities in the photoxygenation of 4 in polystyrene matrix at high (upper trace, 4.0 mmol/g support) and medium substrate loading degree (second trace, 0.1 mmol/g support); CH(OOH) indicated in boxes; SM = starting material. Change in diastereoselectivities at medium substrate loading (0.1 mmol/g support) with increasing conversion.

Table 2. syn/anti ratio: ${}^{1}O_{2}$ ene reaction with 4^{a} : Conversion dependence

Conversion ^b	10	30	50	80	100	
syn/anti	8.5 : 1	8.3 : 1	7.2 : 1	6.6 : 1	6.0 : 1	
					1.	

^a0.4 mmol allylic alcohol (**4**)/g support (PS-DVB-TPP). ^bIn percent versus the standard toluene.

the regioisomer distribution (1.1:1 for 2, 3) as well as the diastereoselectivity observed for the secondary hydroperoxide (2) were independent of the reaction conditions applied; thus the citronellol photo-oxygenation is a convenient Type-II characteristic monitor for the investigation of the efficiency of polymer-bound sensitizers.

Diastereoselectivity as a probe for intrapolymer environment: Mesitylol as a monitor (Scheme 4). The addition of ${}^{1}O_{2}$ to the chiral allylic alcohol 4-methyl-pent-3-en-2-ol (4, mesitylol) has evolved as a reliable probe for solvent effects on the diastereoselectivity of the singlet-oxygen ene reaction (54). Whether the environment in the polymer network in the course of an intrapolymer photo-oxygenation is more nonpolar or polar, protic or nonprotic, is reflected in the syn/anti ratio of the allylic hydroperoxides. In the extreme case of CCl₄, the syn isomer dominated at approximately 92%; in methanol, the syn/anti ratio drops to 2:1. In our hands, different polymers resulted in characteristic stereoisomer composition of the allylic hydroperoxides (5): Low diastereoselectivities were observed for polar polymers like polyhydroxybutyrate (PHB), polylactic acid (PLA) or in cellulose acetate films (55). In the current investigation, we have monitored the diastereoselectivity of the ene reaction of 4 in polystyrene beads as a function of the initial concentration of the substrate and its degree of conversion. In contrast to solution conditions (nonpolar or polar), where both factors did not notably alter the product composition, strong effects were detected for intrapolymer reactions. Dilution of the substrate 4 by the polystyrene network (Table 1) with adsorbed TPP leads to a doubling in diastereoselectivity. Figure 3 shows the drop in selectivity when increasing the amount of substrate in the polymer to maximum loading.

The values for the diastereoselectivity in Table 1 were determined after complete substrate conversion. However, when the reaction is monitored before completion, higher selectivities are observed (Table 2). At very low conversions, the diastereoselectivity reached the value observed for tetrachloromethane and decreased with increasing product formation. This unusual effect of



Scheme 5. Mechanistic model for the diastereoselectivity change during ${}^{1}O_{2}$ reaction with an allylic alcohol.



Scheme 6. Ene reaction of ${}^{1}O_{2}$ with tiglic acid (6): Products and secondary reactions.

product selectivity inhibition can be understood when considering the established reaction mechanism and the solvent effects on the diastereotopic differentiation as shown in Scheme 5 (54). Conformer **B**, with an allylic hydroxyl group oriented nearly perpendicular to the C=C plane, is preferred over conformer A because of reduced allylic strain. The diastereotopic faces of the double bond are differentiated by the size of the substituents on one hand and by hydrogen bonding on the other hand. Hydrogen bonding between the incoming ${}^{1}O_{2}$ and the allylic hydroxyl group in B favors the syn-attack. Under solution conditions, competing hydrogen bonding with solvent molecules reduces this stereodirecting effect (independent of concentration of the substrate or degree of conversion). Under polymer-phase driven photooxygenation, however, higher concentrations of the starting material can lead to substrate aggregation that consumes part of the hydrogen-bonding capability of the substrate. Likewise, increasing amounts of product molecules with the additional hydrogen-bonding functional group OOH shield the allylic hydroxyl group and lead to a decrease in diastereotopic control.

Enantioselective singlet-oxygen transfer: Tiglate salts as monitor. The photo-oxygenation of tiglic acid (6) and its deri-

Table 3. Crystal structure analyses data of the phenylethylammonium salts 6 and 7

Crystal data	6 (xPEA)	7 (xPEA)	
Empirical formula	C13H10NO2	C13H19NO4	
Formula weight	221.29	253.29	
Temperature [K]	100(2)	100(2)	
Crystal system	Orthorhombic	Monoclinic	
Space group	P212121	P21	
a [Å]	6.1651(9)	9.617(2)	
b [Å]	13.333(3)	5.7185(7)	
c [Å]	16.042(4)	12.822(3)	
α [°]	90	90	
β[°]	90	108.170(7)	
γ [°]	90	90	
Volume [Å ³]	1318.6(5)	670.0(2)	
Z	4	2	
d_{calcd} [g cm ⁻³]	1.115	1.256	
Crystal size [mm]	$0.3 \times 0.09 \times 0.06$	$0.1 \times 0.1 \times 0.03$	
No. refl. collected	4876	3368	
No. unique refl.	1606	1534	
No. obs. refl.	801	867	
R1	0.0595	0.0466	
wR2	0.1074	0.0859	
Largest diff.			
peak/hole[e/Å-3]	0.186/-0.219	0.225/-0.251	



Scheme 7. Ene reaction of ${}^{1}O_{2}$ with chiral ammonium tiglates.

vatives, especially alkyl tiglates and amides, proceeds with high regiocontrol to give the secondary hydroperoxides (38,39). A change in regioselectivity has been reported for sodium tiglate under aqueous conditions (56). The initial product, the hydroxperoxy acrylate (7), can be dehydrated to the peroxylactone (8) or reduced to the corresponding 1,3-diol (9) (Scheme 6) (see Table 3).

Using the chiral oxazolidinone auxiliary, diastereoselective ene reactions of the corresponding tiglic amides have been achieved (57). A more advanced procedure using ephedrine-doped zeolite conditions resulted in a maximum enantiomeric excess for the ene reaction with 2-methyl-4-phenyl-2-butene of 15% (48). Two other concepts in organic photochemistry that have been proven to be successful for inducing high enantiomeric excess are the ionic chiral auxiliary concept by Scheffer et al. (58) and the frozen chirality concept by Sakamoto et al. (59) We tried to adopt the ionic chiral auxiliary idea to the tiglate system and investigated the ene reaction of chiral tiglate ammonium salts (6) xPEA in the solid state (for the crystal structure of the starting material see Fig. 4).

The photo-oxygenation of a solid sample, however, did not proceed to useful conversions and thus, the salt was dissolved in a nonpolar solvent and irradiated at low temperatures. During photo-oxygenation in CCl₄ at 10°C, the product precipitated as the phenylethylammonium salt (7) xPEA. In an analogous procedure, the chiral tiglate salt was dissolved in methylene chloride and incorporated into polystyrene beads. In order to avoid the reaction of nonadsorbed substrate, the beads were thoroughly washed with methylene chloride and dried. By means of solid-state NMR, the binding states of the substrate can be distinguished (Fig. 5): free and polymer adsorbed (R)-phenylethylammonium tiglate (6) xPEA appear in the initial spectra after swelling of the polymer beads with a methylene chloride solution of (6) xPEA, see Scheme 7.



Figure 4. Structure of (R)-phenylethylammonium tiglate (6) xPEA in the crystal.



Figure 5. CP-MAS solid state NMR (¹H, 500 MHz) traces—from bottom to top—of (a) polystyrene beads, dye loaded, treated with a solution of (*R*)-phenylethylammonium tiglate ([6] xPEA) in methylene chloride, subsequently dried; (b) after subsequent washing with solvent; (c) solution phase from the washing procedure (corresponds to ethyltiglate); (d) pure polystyrene beads, dye loaded.

After subsequent washing with solvent, only signals for the polymer-bound substrate were detected, free (6) xPEA was observed in the solution. The photo-oxygenation of (6) xPEA in polystyrene resulted in the hydroperoxide (7) xPEA in 76% yield. From the NMR spectra of the salt in CDCl₃, an ee value lower than 5% was estimated which corresponds to the results from chiral GC analysis of the diol (9) obtained by reduction of the secondary hydroperoxide with LiAlH₄. From the experiment in CCl₄, 80% of the (7) xPEA was obtained with low but detectable enantiomeric excess. Further increase in enantioselectivity was observed for the analogous reaction in CFCl₃ at low temperatures. The X-ray structure of the (R,R) compound (7) xPEA is shown in Fig. 6 (for the hydrogen bonding network see Fig. 7).



Figure 6. Structure of the (R)-allylic hydroperoxide (7) xPEA from the singlet-oxygen ene reaction with (R)-phenylethylammonium tiglate in the crystal.



Figure 7. Hydrogen-bonding network of the allylic hydroperoxide from the singlet-oxygen ene reaction with (R)-phenylethylammonium tiglate (6) xPEA in the crystal.

SUMMARY

Three molecular probes have been described for the investigation of the reaction efficiency of the singlet-oxygen ene reaction in polymer network (citronellol [1]), the diastereoselectivity of the ene reaction with chiral substrates (allylic alcohol [4]), and the enantioselectivity of the ene reaction of chiral salts (tiglate [6]). Whereas strong intrapolymer effects were detected for the diastereoselectivity of the ${}^{1}O_{2}$ addition to 4, the enantioselectivity of the photo-oxygenation of 6 in polystyrene is neglectable and increases under solution phase conditions at low temperatures. These results serve as starting point for the improvement of reaction conditions, the polymer structure, as well as noncovalent interactions between the polymer and the substrate for the singlet oxygenation.

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