"Dark" Singlet Oxygenation of Hydrophobic Substrates in Environmentally Friendly Microemulsions

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Abstract: The molybdate-catalyzed "dark" singlet oxygenation of hydrophobic compounds with hydrogen peroxide proceeds efficiently with low catalyst loadings (10^{-3} mol %) in chlorine-free w/o microemulsions. These micro-heterogeneous systems are composed of sodium dodecyl sulfate (SDS)/*n*-butanol/water/organic phase, the latter being either a "green" solvent such as ethyl acetate or a liquid substrate, such as α-terpinene or β-citronellol. Very high reactor yields with improved product/SDS ratio can be obtained for the "dark" singlet oxygenation of such liquid substrates.

Keywords: hydrogen peroxide; microemulsion; oxidation; simplex; singlet oxygen; sodium molybdate.

Introduction

Singlet molecular oxygen, $^1O_2$ (^1A_g), is a powerful oxidizing agent that reacts selectively with various electron-rich compounds. Industrially, singlet oxygenation is carried out by classical dye-sensitized photo-oxidation based on molecular oxygen.[1-4] This method requires substantial investments in dedicated gas/liquid photo-reactors, which do not profit from an economy of scale. Moreover, large-scale photo-oxidation entails hazardous processing conditions because of the combination of light, organic solvents, and dioxygen. As a result of the foregoing disadvantages, industrial use of photo-oxidation is mainly limited to the manufacture of low-volume (1 – 5 tons/year), high-value flavour and fragrance compounds. "Dark" singlet oxygenation by catalytic disproportionation of hydrogen peroxide provides a safe and potentially inexpensive alternative to photo-oxidation that can be carried out in ordinary multi-purpose plant stirred-tank reactors.[5] It is now well established that the disproportionation of hydrogen peroxide catalyzed by molybdate ions leads quantitatively to singlet molecular oxygen, $^1O_2$ (^1A_g), in alkaline medium, Equation (1).[6]

$$2\,H_2O_2 \xrightarrow[pH = 9\text{–}12]{MoO_4^{2-}} 2\,H_2O + {}^1O_2\ (100\ \%) \qquad (1)$$

However, most hydrophobic organic substrates cannot be readily oxidized with the chemical source H_2O_2/MoO_4^{2-} since the generation of $^1O_2$ regularly proceeds efficiently in pure water or in aqueous mixtures such as methanol/water.[7] To overcome this problem, water-in-oil (w/o) microemulsions have been proposed as reaction media to carry out the "dark" singlet oxygenation of hydrophobic substrates (Figure 1).[8]

Such media are able to dissolve both huge amounts of hydrophilic compounds (Na_2MoO_4, H_2O_2), which are confined in the aqueous droplets, as well as non-polar organic molecules, which are localized in the organic continuous phase. In addition, the typical size of the microdroplets (≈10 nm) is much smaller than the mean travel distance of $^1O_2$ in water (≈200 nm).[8a,9] Hence, in spite of its short lifetime in H_2O ($\tau_{\Delta} = 4.4$ μs), $^1O_2$ can diffuse freely, before deactivation, from the aqueous droplets to the organic phase, where it can react with the substrate.

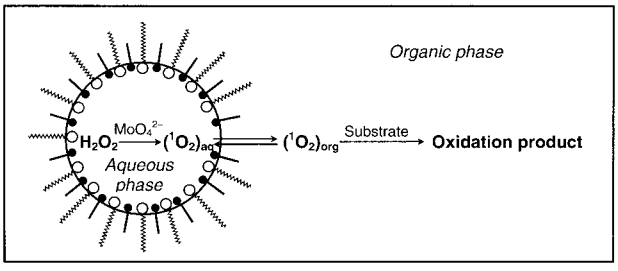


Figure 1. Schematic representation of the w/o microemulsion used to oxidize organic substrates with $^1O_2$ chemically generated by the system H_2O_2/MoO_4^{2-} (—● *n*-butanol, ∿∿○ SDS).

We have shown previously that a microemulsion based on sodium dodecyl sulfate (SDS) as the surfactant, *n*-butanol as the cosurfactant, and methylene chloride as the oil meets all the requirements in order to be a preparatively useful medium: (i) no phase separation during storage and during the oxidation process, (ii) high solubility of the reactants, (iii) chemical inertness of the microemulsion components towards H_2O_2, Na_2MoO_4 or the intermediates derived thereof ($^1O_2$ and peroxomolybdates), (iv) relatively high lifetime of $^1O_2$ ($\tau_\Delta \approx 96$ μs),[10] and (v) simple recovery of the oxidized products, surfactant and catalyst at the end of the reaction. In spite of its demonstrated synthetic usefulness, however, industrial use of this SDS/*n*-BuOH/CH_2Cl_2-based microemulsion is hampered for several reasons: (i) environmental legislation aims at reducing the use of chlorinated solvents, (ii) large-scale handling of CH_2Cl_2, which also includes measures to avoid emission of its vapour, is not straightforward because of its volatility, (iii) a large amount of SDS relative to the substrate is required in order to obtain a stable microemulsion.

This work describes our attempts to develop new microemulsions suitable for large-scale "dark" singlet oxygenation. The development of such new microemulsion media that meet all the demands from a preparative and industrial point of view is not straightforward. In particular, a major challenge is finding a substitute for CH_2Cl_2, in which $^1O_2$ has a relatively long lifetime, thus reducing the required amount of aqueous H_2O_2 and the risk of phase separation. By resorting to the simplex method, suitable compositions for stable microemulsions based on ethyl acetate as organic solvent in the highly complex, seven-component system (organic solvent, H_2O, SDS, BuOH, substrate, Na_2MoO_4 and H_2O_2) have been found that allow "dark" singlet oxygenation of lipophilic substrates. For two liquid substrates, i.e., α-terpinene (α-Terp) **1** and β-citronellol (β-Cit) **3**, solvent-free microemulsion conditions were developed that are compatible with both the preparative as well as the industrial demands. β-Citronellol **3** is particularly relevant as a model since this substrate is industrially photooxidized with $^1O_2$ for the synthesis of rose oxide.[4]

Results and Discussion

Kinetic Study by Laser Flash Photolysis

Influence of the Nature of the Solvent on the Lifetime of $^1O_2$

The organic solvent, which constitutes the continuous phase of the w/o microemulsion, must meet several requirements: (i) to be non-chlorinated and non-toxic, (ii) to solubilize high amounts of hydrophobic substrates, (iii) to have a boiling point lower than 120 °C and (iv) to have a relatively low physical quenching constant (k_d) towards $^1O_2$ ($\tau_\Delta > 20$ μs). Based on the first three criteria, four solvents have been selected: toluene (bp = 111 °C), cyclohexane (bp = 81 °C), ethyl acetate (bp = 77 °C) and dipropyl ether (bp = 90 °C). The influence of the nature of the solvent on the lifetime of $^1O_2$ in the corresponding microemulsions was investigated by resorting to laser flash photolysis,[11b,12] using (w/o) microemulsions of identical compositions (71.2% of organic solvent, 15.2% of BuOH, 7.6% of SDS, and 6.0% H_2O). For comparison, CH_2Cl_2- and CCl_4-based microemulsions were also studied and lifetimes of $^1O_2$ were measured in the pure solvents as well. It has previously been shown that, in microemulsions, $^1O_2$ behaves kinetically in the same way as in homogeneous media.[8a]

The lifetimes of $^1O_2$ (τ_Δ) measured in the different solvents and in the corresponding microemulsions are given in Table 1.

The lifetime of $^1O_2$ strongly depends on the nature of the solvent. As expected, the highest values for the lifetime of $^1O_2$ are obtained in the chlorinated solvents CH_2Cl_2 and CCl_4.[13] It is also noteworthy that the lifetimes of $^1O_2$ in the microemulsions are longer than expected if the media were considered as homogene-

Table 1. Lifetimes of $^1O_2$, overall rate constants ($k_r + k_q$) and Foote reactivity index $k_d/(k_r + k_q)$ of β-citronellol **3** in pure solvents and in the corresponding w/o microemulsions constituted of solvent 71.2%/BuOH 15.2%/SDS 7.6%/H_2O 6.0%.

Organic phases	Pure solvents			w/o Microemulsions		
	τ_Δ (μs)	$k_r + k_q$ ($mol^{-1} \cdot L \cdot s^{-1}$)	$k_d/(k_r + k_q)$ ($mol \cdot L^{-1}$)	τ_Δ (μs)	$k_r + k_q$ ($mol^{-1} \cdot L \cdot s^{-1}$)	$k_d/(k_r + k_q)$ ($mol \times L^{-1}$)
Toluene	23	4.4×10^5	0.10	25	4.0×10^5	0.10
Cyclohexane	23	1.6×10^5	0.27	23	1.7×10^5	0.25
Ethyl acetate	38	5.8×10^5	0.05	30	4.4×10^5	0.07
Propyl ether	21	2.1×10^5	0.23	19	2.4×10^5	0.22
Methylene chloride	97	9.2×10^5	0.01	41	5.1×10^5	0.05
Carbon tetrachloride	1300	2.5×10^5	0.003	59	3.4×10^5	0.05

ous.[8a] Except for CCl_4, the lifetimes measured in the pure solvents are of the same order of magnitude than those measured in the microemulsions. Actually, once generated in the aqueous droplet, $^1O_2$ can either be quenched by water or diffuse out the droplet into the organic continuous phase where it can either be deactivated by the molecules of solvent or enter back into the aqueous micelle. The equilibrium reaction of $^1O_2$ between the two phases is much faster than the decay processes. Therefore, the w/o microemulsion behaves kinetically as an ordinary solvent. In particular, the $^1O_2$ lifetime in the AcOEt-based microemulsion is only slightly lower than the $^1O_2$ lifetime in the CH_2Cl_2 microemulsion. Because the latter has already proved to be useful for preparative "dark" singlet oxygenations, AcOEt may also be a suitable solvent, provided that stable AcOEt-based microemulsions could be prepared.

Influence of the Solvent on the Reactivity of β-Citronellol (β-Cit) ***3***

In order to quantitatively assess the reactivity of β-citronellol **3** towards $^1O_2$ in different media, Table 1 lists the Foote's reactivity index $\beta = k_d/(k_r + k_q)$ of β-Cit **3**.[14] This useful parameter provides the minimal concentration of substrate required so that the interaction of $^1O_2$ with the substrate becomes predominant over the deactivation process by the solvent. Thus, it is preferable to use an initial concentration of the substrate higher than the β value in order to avoid the wasting of the major part of available $^1O_2$ by physical quenching by the solvent (k_d). We can notice that the values of $(k_r + k_q)$ of β-Cit **3** depend on the polarity of the solvent. Actually, the lowest overall rate constants are obtained in strictly apolar solvents such as cyclohexane or CCl_4 in agreement with the polar character of the perepoxide intermediate formed in the ene reaction.[2b,15] On the other hand, they do not change a lot if the solvent is pure or in microemulsion suggesting that, under our chosen conditions, β-Cit **3** is mainly located in the continuous organic phase. The β values reported in the last column of Table 1 show that AcOEt is the best candidate as a substitute for chlorinated solvents.

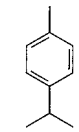
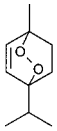
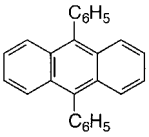
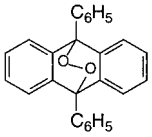
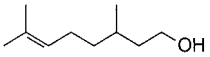
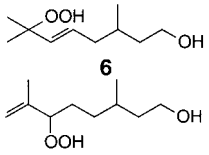
Design of an Ethyl Acetate-Based w/o Microemulsion for Preparative Peroxidation of Organic Substrates

Since more than 20 years, microemulsions have been employed as reaction media for various organic reactions.[16] Actually, such thermodynamically stable microdispersed media allow one to solve the problem of reacting water-soluble inorganic reactants with water-insoluble organic compounds. However, in most reported studies, the oil phase of the microemulsions is based on a limited range of hydrocarbons, such as heptane, cyclohexane, or toluene. This choice results from their first large-scale application, i.e., the enhanced oil recovery and also from the fact that physico-chemists prefer to use simple apolar solvents to investigate the properties of microemulsions.[16-18] Hence, few microdispersed reaction media based on polar solvents have been described in the literature.[8,16,18-20] In particular, only very few publications describe ethyl acetate-based microemulsions and, in most cases, they concern biochemical reactions involving enzymes, amino acids and proteins.[16a,19] The formulation of microemulsions based on polar solvents is critical because polar molecules are likely to interact with the interfacial film impeding a straightforward formation of the microdispersed medium. In addition, most reported reactions cannot be considered as really preparative. Actually, the concentrations of substrates are generally limited to 0.1 mol × L^{-1} in order to maintain the stability of the microemulsion throughout the reaction. Only Menger has described the oxidation of 1 mol × L^{-1} of mustard oils with hypochlorites.[20] This high concentration could nevertheless be achieved by compensating the influence of the reactants on the stability of the microemulsion by high surfactant concentration. In Table 2, we have reported the chosen substrates for performing preparative peroxidation in chlorine-free microemulsions. For each of them, the main physical and chemical features of the substrate and the formulas of the expected oxidation products are given.

To be used as a reaction medium for preparative peroxidations, a microemulsion should allow the simultaneous solubilization of high concentrations of reactants (H_2O_2, MoO_4^{2-}, substrate) without demixing during the process. Every constituent present in the reaction medium considerably influences the stability of the microemulsion. For instance, the introduction of an electrolyte such as sodium molybdate strongly restricts the microemulsion domain owing to the interaction between the anionic head R-SO_4^- of the surfactant SDS with the cations Na^+ of the electrolyte, which makes the surfactant less hydrophilic. The determination of the composition of the optimal microemulsion is then tedious on account of the high number of interacting parameters.

In order to localize rapidly the optimal microemulsion in the quaternary phase diagram (oil, surfactant, cosurfactant, water), we resorted to a simplex technique.[21] This stepwise method of optimization allows us to determine the best compromise between conflicting aims by varying simultaneously several parameters. A similar approach has already been applied to the optimization of the preparative peroxidation of β-citronellol **3** in a microemulsion SDS/BuOH/CH_2Cl_2/H_2O.[8c] The progression of the simplex was carried out in a pseudo-ternary phase diagram in which the ratio BuOH/SDS was maintained at a constant value. In the present work, the amounts of SDS, AcOEt, BuOH and

Table 2. Substrates peroxidized in chlorine-free microemulsions.

Substrates	Features	Products	$\log(k_r + k_q)$[8a]	$k_r/(k_r + k_q)$[8a]
 **α-Terp, 1**	liquid hydrophobic very reactive [4 + 2] cycloaddition	 **Ascaridole, 4**	8.0	1.0
 **DPA, 2**	solid very hydrophobic moderately reactive [4 + 2] cycloaddition	 **$DPAO_2$, 5**	6.2	0.34
 **β-Cit, 3**	liquid polar moderately reactive ene reaction	 **6** **7** **Hydroperoxides**	6.0	0.87

water were all changed but the concentration of the model substrate, α-terpinene **1**, was maintained at 1 mol × kg^{-1} in order to ensure preparative conditions. Thus, four starting mixtures A, B, C and D (Table 3), delimit the initial simplex, i.e., a small regular tetrahedron within the quaternary phase diagram (Figure 2).

This initial simplex was chosen on the basis of the following requirements: (i) low amount of surfactant (SDS), (ii) high proportion of organic solvent (AcOEt) and (iii) no demixing of the microemulsion. The mixtures were then compared according to their ability to solubilize simultaneously maximal amounts of catalyst and water without phase separation. The amount of catalyst present in the microemulsion is directly related to the reaction time whereas the amount of added water, resulting from H_2O_2 decomposition limits the maximal amount of $^1O_2$ that can be produced in the microemulsion through reaction (1). Based on these criteria, the "worst" point (mixture C) was identified, discarded and replaced by its symmetric (mixture E) in relation to the centre of gravity of the three remaining points (mixtures A, B and D).[21] This method of simplex progression was applied until no better conditions could be obtained. For all studied points (A to L), proportions of components and maximal amounts of sodium molybdate and added water are given in Table 3. Thus, the microemulsions J and L were those for which the highest amounts of water and sodium molybdate could simultaneously be added.

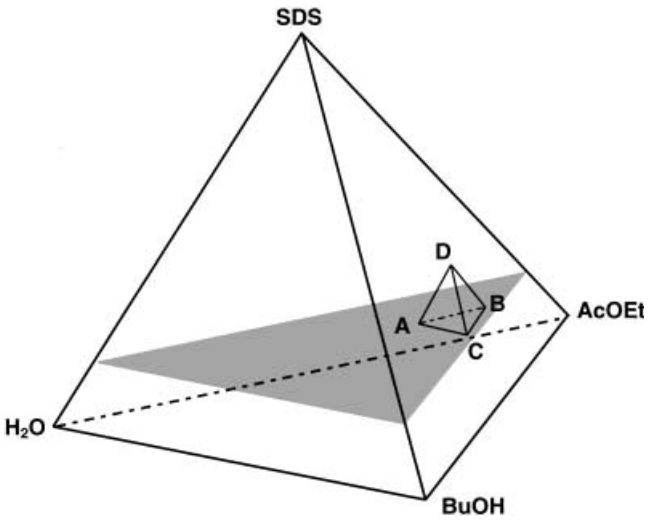


Figure 2. Quaternary phase diagram and initial simplex used to optimize microemulsion.

During the oxidation process, hydrogen peroxide is added in batches to the microemulsion in order to promote the formation of $MoO(O_2)_3^{2-}$, the precursor of $^1O_2$.[6a] The total amount of H_2O_2 that can be added is limited by the demixing of the microemulsion due to the accumulation of H_2O coming from H_2O_2 (disproportionation and water of dilution). By using 50% H_2O_2, the oxidation of 1 mol × kg^{-1} of α-terpinene **1** requires at least 2 mol × kg^{-1} of H_2O_2 which generate 5.8 mol × kg^{-1} of H_2O as by-product. It is noteworthy that the most useful microemulsions are those containing high concentrations of the catalyst MoO_4^{2-}, in order to minimize reaction time. Although the rate of $^1O_2$ formation is rather intricate since it depends on the temperature, pH,

Table 3. Compositions (% in weight) of w/o microemulsions SDS/BuOH/AcOEt/H_2O containing 1 mol × kg^{-1} of α-terpinene **1** and the maximum amount of sodium molybdate and H_2O. Mixtures F, H, K and M do not form stable microemulsions.

Mixtures	SDS [%]	BuOH [%]	AcOEt [%]	H_2O [%]	$[H_2O]_{max}$ [mol × kg^{-1}]	$[MoO_4^{2-}]$'(mol × kg^{-1})
A	7.5	7.5	70.0	15.0	2.70	0.030
B	7.5	7.5	75.0	10.0	5.20	0.030
C	7.5	12.5	70.0	10.0	6.70	0.000
D	12.5	7.5	70.0	10.0	11.70	0.060
E	10.8	2.5	73.5	13.2	3.70	0.080
G	13.1	4.2	67.2	15.5	6.40	0.110
I	11.2	10.3	64.8	13.7	10.80	0.040
J	17.0	7.1	64.7	11.2	14.50	0.045
L	15.0	6.9	61.1	17.0	10.40	0.070
O	17.6	5.9	62.3	14.2	13.75	0.085
P	14.4	8.1	63.5	14.0	13.00	0.055

$[MoO_4^{2-}]$ and $[H_2O_2]$,[6b] the reaction time (Δt) can be predicted as pH is constant and $[H_2O_2]$ is adjusted so that the triperoxomolybdate, main precursor of $^1O_2$, is always the prevalent species in solution, Equation (2):

$$\Delta t = \frac{[^1O_2]_t}{10 \times [MoO_4^{2-}]} = \frac{[H_2O_2]_o}{2 \times 10 \times [MoO_4^{2-}]} \approx \frac{[\alpha\text{-terpinene}]_o}{10 \times [MoO_4^{2-}]} \quad (2)$$

According to Equation (2) where Δt is expressed in hours, we can predict that for $[MoO_4^{2-}] = 10^{-2}$ M, 10^{-1} M or 1 M, the peroxidation of 1 mol × kg^{-1} of α-Terp **1** will require 10 h, 1 h or 6 min, respectively.

Finally, for a further optimization, we investigated two other microemulsions, O and P, localized at the same distance between J and L (see Table 3). For both microemulsions, the amounts of H_2O that could be added before demixing were higher than the one required (5.8 mol × kg^{-1}) for the peroxidation of 1 mol × kg^{-1} of α-Terp **1.** However, the reaction time, which is inversely proportional to $[MoO_4^{2-}]$, must also be considered as an important factor in the determination of the optimal microemulsion. Therefore, according to this secondary criterion, the microemulsion O, would be the best one since 13.85 mol × kg^{-1} of H_2O could be added before demixing for a concentration of MoO_4^{2-} equal to 0.085 mol × kg^{-1}. Under these conditions, a predicted reaction time of 1.2 h can be calculated instead of 2.5 h for the microemulsion J.

Such an approach allows us to define two other interesting microemulsions, B and D (see Table 3). The first one contains the highest amount of organic phase (75%) and the lowest amount of SDS (7.5%). Such a composition is particularly favourable to solubilize high amounts of substrate and to make easier the recovery of the oxidation product since elimination of SDS and BuOH is troublesome. However, this microemulsion B would be more suitable for highly reactive substrates, with no physical quenching of $^1O_2$, since the amount of H_2O and catalyst that can be added are only of 5.2 and 0.03 mol × kg^{-1}, respectively. The microemulsion D is also of some interest since it contains 70% of AcOEt, 12.5% of SDS and only 7.5% of BuOH. In addition, the amount of water that can be added is relatively high (11.7 mol × kg^{-1}) for a concentration of catalyst equal to 0.06 mol × kg^{-1}. This formulation provides a good compromise between the conditions of oxidation (reaction time and amount of substrate) and the treatment of the reaction medium for the recovery of the products.

In order to validate the optimal ethyl acetate-based microemulsion, O, the peroxidation of 1 mol × kg^{-1} of α-terpinene **1** was performed. The reaction was carried out at 25 °C and the disappearance of the substrate was monitored by HPLC at 266 nm after dilution of the reaction medium in MeOH. The peroxidation of α-Terp **1** was completed in 1.5 h with addition of a total amount of H_2O_2 equal to 2.2 mol × kg^{-1}. Thus, 91% of the $^1O_2$ formed in the reaction medium was trapped chemically by the substrate. The NMR analysis confirmed the formation of pure ascaridole **4**, the expected oxidation product.

Finally, the microemulsion O was applied to the oxidation of 9,10-diphenylanthracene (DPA) **2**, which is about 100 times less reactive than α-terpinene **1** and much less soluble in polar solvents. The concentration of **2** was equal to 0.1 mol × kg^{-1}, which is higher than its solubility in the reaction medium. Under such conditions, a yellow suspension of **2** was present at the beginning of the reaction. The disappearance of DPA **2** and the appearance of its endoperoxide $DPAO_2$ **5** were followed by HPLC at 392 nm and 220 nm, respectively. The peroxidation of DPA **2** was completed in 2.0 h with addition of a total amount of H_2O_2 equal to 3.3 mol × kg^{-1}. This result shows that 36% of the $^1O_2$ formed in the reaction medium was trapped chemically by the substrate. The NMR analysis confirmed the formation of pure $DPAO_2$ **5**, the expected oxidation product. It is noteworthy that, at the end of the reaction, the reaction medium is still a microemulsion, with a white suspension of $DPAO_2$, suggesting that a higher amount of starting material could have been oxidized. This result clearly shows that the oxidation can well be performed even when the substrate is not completely solubilized in the

microemulsion. Such a procedure presents a tremendous advantage in terms of oxidation product recovery since it requires a simple filtration of solid products.

Design of Solvent-Free w/o Microemulsions for Preparative Peroxidations of Liquid Organic Substrates

The concept of "solvent-free" microemulsions has already been applied to some reactions involving the copolymerization of vinyl acetate,[22a] the catalytic oxidation of alkanes with H_2O_2 and iron salts[22b,22c] and the oxidation of olefins and styrene by the Wacker process.[22d,22e] For all these systems, the reacting substrate, which is always an unpolar compound, constitutes the organic continuous phase of the microemulsion. For singlet oxygen peroxidations of organic hydrophobic substrates, such solvent-free microemulsions exhibit several advantages: (i) huge amounts of reacting substrate, (ii) no toxicity problem arising from the solvent and (iii) maximum chemical trapping of $^1O_2$ since no physical quenching of $^1O_2$ by the solvent (k_d) takes place. The only requirement is that both substrate and product have to be liquid. In order to apply this concept to $^1O_2$ oxidations, α-terpinene **1** and β-citronellol **3** were chosen as models since they illustrate nicely the typical [4 + 2] cycloaddition and the ene reaction. The first substrate, which is very reactive towards $^1O_2$, should rather be considered as a hydrophobic oil whereas the second one is polar through the presence of the hydroxy group and presents a moderate reactivity towards the excited species (see Table 1).

The composition of the solvent-free microemulsions was defined from the composition of the optimized ethyl acetate-based microemulsion O, previously determined with the simplex method. According to the amount of water that could be added to these microemulsions before demixing, the proportions of BuOH and of the oil were consequently adjusted. The amount of SDS was maintained in the range 16 – 17%. On the other hand, in order to add a sufficient amount of sodium molybdate likely to provide an acceptable reaction time in comparison to the high concentration of substrate, the proportion of the oil should be decreased to 57% for β-Cit **3** (i.e., 3.6 mol × kg^{-1}) and 59% for α-Terp **1** (i.e. 4.3 mol × kg^{-1}), respectively. In the same way, microemulsions could be obtained by addition of much higher amounts of BuOH, 16 and 13% for α-Terp **1** and β-Cit **3**, respectively, instead of 5.8% for the AcOEt-based microemulsion.

The quantitative peroxidation of 4.3 mol × kg^{-1} α-Terp **1** in the solvent-free microemulsion was limited by the demixing of the reaction medium which was observed when 4.1 mol × kg^{-1} of H_2O_2 were added. Under these conditions, 45% of the starting material could be oxidized providing 1.94 mol × kg^{-1} of ascaridole **4**. After treatment of the final reaction medium, a mixture of α-terpinene **1** and ascaridole **4** remains that can be readily separated by distillation under vacuum. On the other hand, 3.6 mol × kg^{-1} of β-Cit **3** could be completely oxidized with 8.6 mol × kg^{-1} of H_2O_2 without demixing of the microemulsion, leading to equal amounts of the two expected hydroperoxides **6** and **7.** Such a result provides a fixation rate of $^1O_2$ equal to 84%. In order to bring out the usefulness and the efficiency of environmentally friendly microemulsions, we have summarized in Table 4 all the peroxidations of α-terpinene **1** and β-citronellol **3** described in the literature and carried out in microemulsion systems by using chemically generated $^1O_2$.

This table reveals two important results: (i) the replacement of CH_2Cl_2 by the more environmentally friendly AcOEt allows α-terpinene **1** to be quantita-

Table 4. Peroxidations of α-terpinene **1** and β-citronellol **3** performed in microemulsions.

α-Terpinene **1**						
Oil	$[\alpha\text{-Terp}]_0$ [mol × kg^{-1}]	$[MoO_4^{2-}]$/[prod]	$[H_2O_2]$/[prod]	[SDS]/[prod]	Conversion [%]	Ref.
CH_2Cl_2	0.32	0.047	2.44	1.30	100	[5b]
CH_2Cl_2	0.49	0.098	2.25	1.03	100	[8a]
AcOEt	1.0	0.085	2.20	0.94	100	this work
α-Terp	4.3	0.0049	2.12	0.44	45	this work
β-Citronellol **3**						
Oil	$[\beta\text{-Cit}]_0$ [mol × kg^{-1}]	$[MoO_4^{2-}]$/[prod]	$[H_2O_2]$/[prod]	[SDS]/[prod]	Conversion [%]	Ref
CH_2Cl_2	0.29	0.052	2.96	1.08	100	[5b]
CH_2Cl_2	0.39	0.039	4.70	1.58	82	[8a]
CH_2Cl_2	1.5	0.023	3.33	0.47	100	[8c]
β-Cit	3.6	0.0036	2.39	0.25	100	this work

tively converted at a higher concentration (twice more) and with less SDS and H_2O_2 per product, thus significantly increasing efficiency and utility of microemulsions as media for "dark" singlet oxygenation, (ii) solvent-free microemulsions allow the preparative peroxidation of liquid substrates at very high concentration ($\simeq$4 mol/kg) with low amounts of SDS and molybdate catalyst per product. However, with some substrates such as α-terpinene **1**, the conversion is incomplete and the product must be separated from the substrate at the end of the reaction.

Conclusion

When a liquid substrate has to be peroxidized with chemically generated $^1O_2$, solvent-free microemulsions are the most convenient media. They allow one to convert huge amounts of starting materials using low SDS/product and MoO_4^{2-}/product ratios with minimum loss of $^1O_2$ through physical quenching. For solid substrates, the alternative solution is to resort to ethyl acetate-based microemulsions which also provide high substrate conversions on the preparative scale. In addition, such media do not require complete solubilization of the substrate and permit a straightforward recovery of poorly soluble products such as $DPAO_2$ by a simple filtration.

Experimental Section

Chemicals

Sodium molybdate dihydrate (99%), α-terpinene (α-Terp, **1**, 98%) 9,10-diphenylanthracene (DPA, **2**, 98%), β-citronellol (β-Cit, **3**, 95 %), methylene chloride (99.9%), toluene (99%), cyclohexane (99%), ethyl acetate (99.5%), dipropyl ether (99%), 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine (TPP, 98%) and 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine-*p, p′,p″,p‴*-tetrasulfonic acid, tetrasodium salt dodecahydrate (TPPS, 98%) were purchased from Aldrich Chemie and used as received. Carbon tetrachloride (Rectapur), *n*-butanol (BuOH) (Normapur), sodium dodecyl sulfate (SDS, 98%), hydrogen peroxide (Rectapur, 50%) were obtained from Prolabo.

Instrumentation

Flash Photolysis: (PICR, Manchester). The photosensitized generation of $^1O_2$ was carried out by energy transfer from a photosensitizer (TPP or TPPS) to $^3O_2$. In a quartz cell, a 2-mL sample of an air-saturated solvent or microemulsion containing the photosensitizer (TPP for organic solvent, TPPS for microemulsions) was irradiated with a short (6 ns) flash of light at 532 nm, emitted by a Nd-YAG laser. Infrared phosphorescence of $^1O_2$ at 1270 nm was detected perpendicularly with a germanium photodiode (Judson J16) and the signal was recorded with an oscilloscope and analyzed according to a first-order decay.[11]

HPLC: High-performance liquid chromatography analyses were carried out with a reversed-phase column (Nova-pack C18, 4 μm, 4.6 × 250 mm) using a 600 controller pump from Waters, a mixture of $CH_3OH/H_2O/H_3PO_4$ as the eluent, and UV detection with a Waters 490E programmable multiwavelength detector.

^{1}H and ^{13}C NMR Spectroscopy: Spectra were recorded in $CDCl_3$ at 300 MHz for the ^{1}H and 75.46 MHz for the ^{13}C by using a Bruker AC 300P FT spectrometer. All chemical shifts are relative to the TMS signal ($\delta = 0$ ppm) as reference.

General Procedure for Preparative Peroxidations in Microemulsion

Microemulsions were prepared in a thermostatted bath at 25 °C by adding dropwise an aqueous solution of sodium molybdate to a magnetically stirred slurry of SDS, *n*-BuOH, and organic phase (AcOEt or liquid substrate). The transparent, mobile and isotropic medium was obtained after 5 min of mixing and can be kept unchanged in a capped flask for several weeks. To this system was added the substrate for AcOEt-based microemulsions. At the initial time, a fraction of 50% H_2O_2 was introduced and the red-brown reaction medium was stirred at 25 °C until the colour faded to yellow. Several other fractions of H_2O_2 were then allowed to react in the same way until complete conversion of the substrate or demixing of the microemulsion. The solvents (BuOH, water and AcOEt) were rotary evaporated at 40 °C under vacuum. The residue was stirred vigorously in 100 mL of toluene for 15 min and the suspension was filtered to recover sodium molybdate and sodium dodecyl sulfate. It is noteworthy that, if an environmentally friendly process has to be investigated, toluene can readily be replaced by any other solvent like cyclohexane, able to dissolve the oxidation products and to leave as precipitates both sodium molybdate and SDS. The resulting organic phase was dried with Na_2SO_4 and passed through a silica layer in

Table 5. Compositions of chlorine-free microemulsions and amounts of reactants used for the preparative peroxidation of organic compounds.

Microemulsion compositions						Substrates		H_2O_2 (50%)	Conversion [%]
Solvent		SDS	BuOH	H_2O	MoO_4^{2-}				
AcOEt	31.2 g	8.8 g	2.9 g	7.1 g	1.03 g	α-Terp **1**	6.85 g	8 × 0.8 mL	100
AcOEt	31.2 g	8.8 g	2.9 g	7.1 g	1.03 g	DPA **2**	1.7 g	12 × 0.8 mL	100
α-Terp **1**	17.7 g	4.8 g	4.8 g	2.7 g	0.069 g	α-Terp **1**	–	70 × 0.1 mL	45
β-Cit **3**	17.0 g	5.25 g	4.0 g	3.75 g	0.097 g	β-Cit **3**	–	150 × 0.1 mL	100

order to eliminate traces of SDS and catalyst. Finally, toluene was rotary evaporated under vacuum at yielding the oxidation products. Compositions of the microemulsions and amounts of reactants are listed in Table 5.

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