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Singlet oxygen generation from H_2O_2/MoO_4^{2-}: peroxidation of hydrophobic substrates in pure organic solvents

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Abstract—Seventeen organic solvents are screened as reaction media to conduct the molybdate-catalyzed disproportionation of hydrogen peroxide into singlet molecular oxygen, $^1O_2$ ($^1\Delta_g$). The solvents are investigated by resorting to the detection of the infra-red luminescence of $^1O_2$ at 1270 nm. Preparative peroxidations of representative substrates are carried out in the most efficient ones. The latter are protic and polar and constitute a simpler alternative to the well suited but more intricate microemulsion systems for the peroxidation of hydrophobic substrates with chemically generated $^1O_2$. © 2002 Published by Elsevier Science Ltd.

1. Introduction

Singlet molecular oxygen, $^1O_2$ ($^1\Delta_g$), is quantitatively generated in alkaline water through the disproportionation of hydrogen peroxide catalyzed by molybdate ions (Eq. (1)).[1]

$$2H_2O_2 \xrightarrow[\text{pH 9–11}]{MoO_4^{2-}} 2H_2O + {}^1O_2 \ (100\%) \qquad (1)$$

In 1995, the mechanism of this reaction has been elucidated and the different peroxo intermediates formed as a function of pH and $[H_2O_2]$ have all been identified by ^{95}Mo NMR.[2] The oxotriperoxomolybdate, $MoO(O_2)_3^{2-}$, was found to be the main precursor of $^1O_2$ whereas the tetraperoxomolybdate, $Mo(O_2)_4^{2-}$, which is formed with higher concentrations of H_2O_2, does not generate the excited species.

Reaction (1) is usually carried in aqueous medium because of the hydrophilicity of reactants. Such aqueous systems allow the peroxidation of various hydrophilic or low molecular weight organic compounds, such as tiglic acid, 1,4-cyclohexadiene derivatives or allylic alcohols.[3] Unfortunately, the synthetic scope of this aqueous source of $^1O_2$ with regard to the peroxidation of hydrophobic compounds is only very limited. Water-in-oil microemulsions[4] have been developed to overcome this problem: $^1O_2$ is generated into the aqueous microdroplets and then it diffuses before deactivation to the organic phase where it reacts with the substrate. Several drawbacks are, however, associated with these microemulsion systems: (i) these reaction media are relatively intricate since they require water, organic solvent, surfactant and co-surfactant, (ii) all these components have to be mixed in well-defined proportions, (iii) the thermodynamic properties of microemulsions limit the amounts of H_2O_2 that can be added without phase separation, (iv) the recovery of the oxidation products is somewhat tedious.

In order to find a more easily applicable system for the 'dark' singlet oxygenation of lipophilic compounds, the molybdate catalyzed disproportionation of H_2O_2 in various organic solvents was investigated. Preparative peroxidations of typical organic substrates were carried out in organic solvents that were found to be most efficient.

2. Detection of the IR luminescence of $^1O_2$ at 1270 nm

The generation of $^1O_2$ from the system H_2O_2/MoO_4^{2-} was studied in 17 organic solvents by resorting to the detection of the IR luminescence at 1270 nm. This technique constitutes an unambiguous proof of $^1O_2$ formation since the detection of a signal at 1270 nm is specific of this excited species.[5] The solvents were compared in terms of maximal signal intensity (I_{max}), time required to decompose a given amount of H_2O_2 (Δt)

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and yield of cumulated $^1O_2$. The results are listed in Table 1. The concentrations of molybdate ions and hydrogen peroxide were respectively equal to 0.1 and 0.5 mol/L. This molybdate concentration was chosen in order to ensure a significant signal, in other words a relatively high reaction rate, and the amount of H_2O_2 was adjusted in order to favor the formation of the oxotriperoxomolybdate. The temperature was chosen such that the reaction proceeded within a reasonable time in the solvent under study.

The yield of $^1O_2$ generation was determined by addition of a known amount of α-terpinene **1** or furfuryl alcohol **2**, depending on their solubility in the solvent under study. These highly reactive chemical traps are known to react with $^1O_2$ by a pure chemical process.[6] Hence, the missing area in the luminescence signal corresponds to the amount of $^1O_2$ trapped by α-terpinene **1** or furfuryl alcohol **7**. As the total area under the curve is directly related to the cumulated amount of $^1O_2$ generated, the comparison of the two areas provides the yield of $^1O_2$.

Fig. 1 represents the luminescence signal of $^1O_2$ obtained in methanol through the disproportionation of H_2O_2 0.5 M by Na_2MoO_4 0.1 M at 25°C. We can notice that, as soon as H_2O_2 is added in the reaction medium, an important signal with a maximum intensity of about 470 mV is detected. Most of the H_2O_2 is decomposed within 40 min and the process is shown to be catalytic since a second batch of H_2O_2 provides the same luminescence signal. Addition of α-terpinene **1** leads, as expected, to a decrease of the signal. Then, as the substrate is oxidized, the signal rises again to the value measured in the absence of substrate. The missing area corresponds to an amount of $^1O_2$ equal to the initial concentration of α-terpinene **1**, and the cumulated amount of $^1O_2$ is calculated by comparison with the total area.

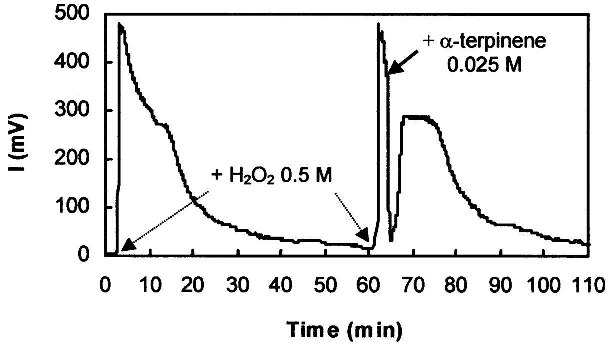


Figure 1. IR luminescence signal of $^1O_2$ generated by a solution containing 0.1 M Na_2MoO_4 and 2×0.5 M H_2O_2 in methanol at $T = 25$°C.

Among the solvents studied, only THF, dichloromethane and ethyl acetate do not lead to a significant formation of $^1O_2$ in the organic phase. Indeed, in these solvents, addition of H_2O_2 (≥ 0.1 M) results in a biphasic medium and the detected signal corresponds to $^1O_2$ generated in the aqueous phase.

Table 1. Luminescence detection of $^1O_2$ generated from the systems H_2O_2/MoO_4^{2-} in various pure organic solvents. $[MoO_4^{2-}] = 0.1$ M, $[H_2O_2] = 0.5$ M, Δt = time corresponding to 5% of I_{max}

Solvents			Chemiluminescence			
Name	$\tau\Delta$ (μs)[7]	Molybdate	T (°C)	I_{max} (mV)	Δt (min)	$^1O_2$ Yield (%)
Water[a,d]	4	Na	25	78	21	100[1]
Ethanol[b]	14	Li	40	502	25	92
		Na	40	80	186	45
Methanol[a,b]	10	Li	25	441	40	81
		Na	25	470	40	71
		K	25	27	42	36
Ethylene glycol[a,d]	7.5	Na	25	410	20	70
N,*N*-Dimethylformamide[a]	19	Na	40	166	71	69
Sulfolane[b]	24[c]	Na	35	930	24	65
N-Methylformamide[a]	12	Na	25	850	20	42
1,2-Dimethoxyethane[b]	–	Li	40	122	172	42
Propylene carbonate[b]	39	Na	50	150	80	27
Formamide[a,d]	11.5	Na	40	221	23	26
Pyridine[b]	15	Na	50	172	61	26
N-Methyl pyrrolidone[b]	12[c]	Na	50	17	21	25
Acetonitrile[b]	67	Li	50	348	180	25
1,4-Dioxane[b]	27	Li	50	48	330	22
Dimethylsulfoxide[b]	19	Na	20	285	2	11
Tetrahydrofuran[b]	22	Li	25	143	43	<5
Ethyl acetate[b]	43	Li	25	166	23	<5
Dichloromethane[b]	97	Li	25	115	28	<5

[a] Homogeneous medium.

[b] Heterogeneous medium.

[c] Our work.

[d] Furfuryl alcohol. $^1O_2$ yields are given at ±5%.

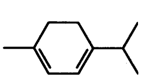
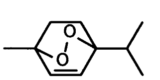
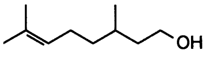
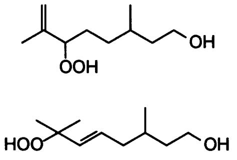
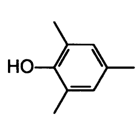
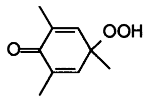
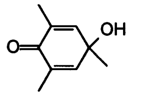
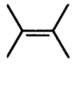
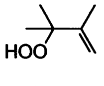
When α-terpinene **1** is added for yield measurement, no decrease of the signal is observed because $^1O_2$ does not interact with the trap located in the organic phase. Therefore, it appears that one required condition for peroxidation of organic substrates by $^1O_2$ chemically generated is that added hydrogen peroxide remains miscible with the organic solvent during the reaction. In acetonitrile, pyridine, propylene carbonate and 1,4-dioxane, the yields of $^1O_2$ are a little bit higher but do not exceed 27%. In these solvents, a biphasic medium is obtained as soon as 0.5 M H_2O_2 is added.

The best solvents are ethanol and methanol, which give, under optimized conditions, 92 and 81% of $^1O_2$, respectively. In the case of MeOH, the $^1O_2$ generation efficiency was found to be influenced by the nature of the cation of the molybdate salt. Thus, when lithium, sodium or potassium molybdates are used as the catalyst, the yields of $^1O_2$ generated are respectively equal to 81, 71 and 36%. Such a result shows that the solubility of the catalyst in the organic solvent, which decreases from lithium to potassium, is a key factor. Na_2MoO_4, which is poorly soluble in MeOH, dissolves in the presence of hydrogen peroxide because of the formation of more soluble peroxymolybdate species. An attractive feature of the Na_2MoO_4 catalyzed 'dark' singlet oxygenation in MeOH is that most of the Na_2MoO_4 precipitates at the end of the reaction when hydrogen peroxide has been consumed completely. This facilitates catalyst recycling by simple filtration.

Besides catalyst solubility, another required factor for efficient $^1O_2$ generation is the amount of H_2O_2 relative to molybdate in the reaction mixture. Care should be taken to avoid a large excess of H_2O_2 since in that case the reaction rate is considerably slowed down because of the formation of the tetraperoxomolybdate, which does not generate $^1O_2$. Therefore, H_2O_2 should be added gradually or batch wise in small portions. As it is commonly observed for molybdate catalyzed H_2O_2 disproportionation, the rate is strongly influenced by temperature. In ethanol, for example, the reaction at 25°C is very slow (more than 12 h to decompose 0.5 M H_2O_2 by 0.1 M Li_2MoO_4), but if the temperature is increased, the reaction time considerably decreases and at 40°C, only 28 min are required to decompose 0.5 M of H_2O_2 by 0.1 M of catalyst.

Other organic solvents such as ethylene glycol, sulfolane, 1,2-dimethoxyethane and formamide derivatives provide fair yields of $^1O_2$ (>40%). In these solvents, the molybdate salt and the peroxides are more or less completely soluble and the nature of the cation has no

Table 2. Preparative peroxidations of typical substrates in organic solvents by the mineral source of $^1O_2$, H_2O_2/MoO_4^{2-}. Conditions: [Substrate] = 0.5 M, [Catalyst] = 0.1 M. [a][**1**] = 0.05 M, [b][**7**] = 0.1 M, Conversion = 100% except for [c]: 80%

Substrates	Products	Solvents	T (°C)/Cata/$[H_2O_2]_{tot}$ (M)/Δt (h)
 α-Terpinene, **1**	 Ascaridole, **2**	EtOH	40 / Li / 1.8 / 2
		MeOH	25 / Li / 2.0 / 3
		CH_3CN[a]	40 / Li / 0.5 / 3
 β-Citronellol, **3**	 Hydroperoxides, **4** (50 %) and **4'** (50 %)	MeOH	25 / Na / 2.0 / 3
		Ethylene glycol	25 / Na / 2.2 / 3
		Sulfolane	40 / Li / 2.5 / 2.5
		DMF[c]	40 / Na / 3.1 / 7
 Mesitol, **5**	 Perquinol, **6** (50 %)  Quinol, **6'** (50 %)	MeOH + 1 eq NaOH	25 / Na / 5.25 / 7
 2,3-Dimethyl-but-2-ene, **7**	 Hydroperoxide, **8**	DME[b]	40 / Li / 0.5 / 3
		Sulfolane	40 / Na / 1.7 / 2

influence on the reaction of $^1O_2$ generation. Nevertheless, such solvents present high boiling points and cannot be removed easily under vacuum. In these cases, the work up of the reaction medium consists in adding a given amount of water and the resulting aqueous phase is extracted with methylene chloride. After drying on Na_2SO_4 and filtration, the organic phase is then rotary evaporated under vacuum providing the oxidation products.

3. Preparative peroxidations

The most efficient solvents providing a good yield for $^1O_2$ generation were applied to the preparative (0.5 M) peroxidation of typical organic compounds of different reactivities: α-terpinene **1**, β-citronellol, **3**, mesitol **5** and 2,3-dimethyl-but-2-ene **7**. H_2O_2 was added in several batches in order to favor the formation of the oxotriperoxomolybdate. The results are listed in Table 2. All the substrates were peroxidized on the preparative scale (0.5 M) providing the expected oxidation products through a straightforward recovery. It is noteworthy that mesitol **5**, which is difficult to oxidize under its phenolic form on account of high physical quenching of $^1O_2$, could be efficiently peroxized into the corresponding perquinol **6** provided that 1 equiv. of NaOH was added in order to form the more chemically reactive phenoxide form.

4. Conclusions

The disproportionation of H_2O_2 by molybdate ions in organic solvents is by far the simplest method to oxidize organic compounds with singlet oxygen. Some molybdate-exchanged layered double hydroxides (LDH) and resin-bound peroxomolybdates have been developed acting as heterogeneous catalysts for H_2O_2 decomposition into $^1O_2$ in organic solvents such as acetone or dioxane but such catalysts need to be prepared.[8,9] Three conditions are required for an efficient reaction: (i) the peroxomolybdates must be soluble in the reaction medium, (ii) the reaction mixture must remain miscible with water generated by H_2O_2 decomposition and (iii) the rate of H_2O_2 addition must be equal to the rate of its decomposition in order to form preferentially the oxotriperoxomolybdate, the precursor of $^1O_2$, since an excess of H_2O_2 leads to the formation of the tetraperoxomolybdate which is very stable in organic solvent. The 'dark' singlet oxygenation proceeds most efficiently in MeOH or EtOH with Li_2MoO_4 as the catalyst.

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