

# Generation of Singlet Oxygen from Ozone Catalysed by Phosphinoferrocenes

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**Summary.** A novel chemical source of singlet oxygen based on the conversion of ozone by 1,1'-bis(triphenylphosphino)ferrocene as catalyst was developed into a feasible method for a preparative scale. This is, to our best knowledge, the first application of substituted ferrocenes as oxidation catalysts.

**Keywords.** Ozone; Ozonation; Singlet oxygen; Catalysis; Ferrocenes.

## Introduction

Commonly, singlet oxygen is generated by a photochemical reaction. It is formed by irradiation of gaseous oxygen with ultraviolet light in the presence of sensitizers that absorb the light of a particular wavelength [1]. Rose bengal, tetraphenylporphyrin, and its derivatives, as well as methylene blue are the most well known photosensitizers and are suitable for a large variety of solvents [2]. For industrial use, this method requires substantial investments into special gas/liquid photo-reactors, which do not profit from an economy of scale. In addition, large-scale photo-oxidation comprises hazardous processing conditions because of the combination of light, organic solvents, and dioxygen. As a result of the foregoing disadvantages, industrial use is limited to the manufacture of low-volume, high-value flavor and fragrance compounds [3]. In contrast, chemical sources of <sup>1</sup>O<sub>2</sub>, involving readily available oxidants, such as H<sub>2</sub>O<sub>2</sub>, have proved to be attractive alternatives to the usual photochemical methods. The most attractive one involves the oxidation of hydrogenperoxide by sodium hypochlorite [4–6]. Aubry carried out a screening of most elements of the periodic table or their oxides for their suitability to generate singlet oxygen from hydrogen peroxide [7]. He found that molybdate is

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an active catalyst for the conversion of hydrogen peroxide into singlet oxygen. This method was also developed into an industrial scale application [8, 9].

In 1961, *Thompson* reported the observation of labile intermediates in the low-temperature ozonation of triphenylphosphite, which has oxidizing powers and decomposes above  $-30^{\circ}\text{C}$  with evolution of oxygen and formation of triphenylphosphate [10]. Later on *Murray et al.* have described phosphites as possible auxiliaries for the chemical generation of singlet oxygen [11]. It has been found that phosphite ozonides, formed by low-temperature reaction of phosphites with ozone, can be cleaved into phosphate and singlet oxygen.

*Bartlett et al.* [12, 13] have first derived a dual mechanism for the oxidation reactions of the triphenylphosphite-ozone adducts, one at temperatures below which it decomposes and the other at its decomposition temperature [14, 15]. According to this work and subsequent publications, a direct reaction between the triphenylphosphite-ozone adduct and substrate singlet oxygen seems possible.

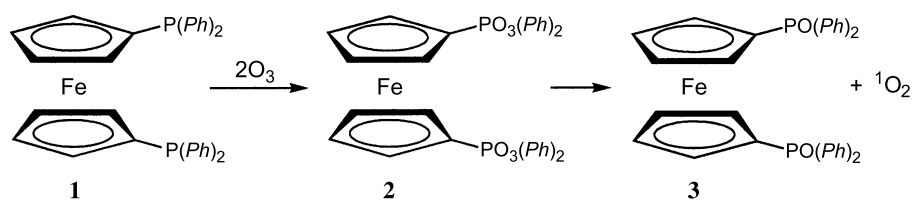
It seemed to us of interest to follow these general lines to develop a novel catalyst system for chemically generated singlet oxygen from ozone, which by means of its physical properties allows an immediate process control detection.

## Results and Discussions

It is known from the literature that the reaction of ferrocene with ozone results in an oxidative decomposition of the Fe–C bond [16]. In contrast to these results preliminary experiments proved that substituted ferrocenes, such as 1,1'-bis(diphenylphosphino)ferrocene (**1**), colored yellow to orange, are stable towards ozone and can even generate singlet oxygen [17]. Therefore, the singlet oxygen activity of **1** was determined by luminescence and trapping experiments. According to the luminescence signal and the ozone uptake observed in this experiment, a stoichiometric conversion of **1** with ozone gave singlet oxygen. The reference used was the 100% singlet oxygen yield of ozone/triphenylphosphite. The luminescence experiments proved that generation of singlet oxygen by the reaction of ozone with **1** was possible in principle. Based on the total ozone uptake of two equivalents ozone the efficiency of singlet oxygen formation ( $\text{mol } ^1\text{O}_2/\text{mol O}_3$ ) amounted to 84%. This high efficiency of singlet oxygen formation can be attributed on the one hand to the reaction of **1** with ozone to form the ozonide **2**, and on the other to a decomposition of **2** or a peroxidic intermediate.

Therefore an experiment was carried out, ozonising **1** at  $-20^{\circ}\text{C}$  while adding continuously the trap  $\alpha$ -terpinene. The slow addition of the trap was necessary in order to favor the reaction of ozone with **1** and suppress a direct oxidation of the organic substrate. Comparative experiments, ozonizing equal amounts of **1** and  $\alpha$ -terpinene at the same time in a “one-pot reaction” proved that a considerable amount of ozone reacted directly with the trap by cleaving it according to a *Criegee* mechanism. The reaction proceeds at first with the formation of the phosphite ozonide **2**, which then decomposes, even at low temperature, into singlet oxygen and the phosphate **3**.

For the preparative use of the ozone/**1** system one has to take into account that most substrates for singlet oxygen are easily attacked by ozone. To avoid this side reaction of ozone with the substrate one way is using the primary reaction of **1** with ozone at low temperatures, stripping off surplus ozone, treating the solution with the



Scheme 1

substrate, and then reacting at elevated temperatures. In our studies we found that no reaction takes place, only the substrate was recovered quantitatively. Analysis of the recovered ferrocene compound showed that the corresponding phosphine oxide **3** was formed, but due to the influence of the ferrocene moiety the ozonide **2** was not stable in contrast to the triphenylphosphite system. This is a main advantage of this system because the ozonide **2** decomposes readily and thus no accumulation of energy-rich ozonides in the reaction mixture occurs. When the reaction was

**Table 1.** Singlet oxygen reactions of four characteristic substrates using the ozone/1 system

Substrate	Conversion %	Selectivity %	Yield %	Product
	64	97	62	
	16	75	12	
	5 <sup>a,b</sup>	8	0.4 <sup>a</sup>	
	84 <sup>c</sup>	43	8/28 <sup>d</sup>	

<sup>a</sup> The primary singlet oxygenation product ( $\beta$ -pinene hydroperoxide) was reduced by triphenylphosphine to myrtenol; <sup>b</sup> 4.6% appeared to be cleavage product of the double bond by ozone, including further decomposition products; <sup>c</sup> 48% appeared to be cleavage product of the conjugated double bonds by ozone, including further decomposition products; <sup>d</sup> *p*-cymene appeared to be the preferred decomposition product of ascaridole, the primary singlet oxygenation product

performed in a semicontinuous way by adding the substrate in solution during the ozonolysis, we obtained the singlet oxygen products in moderate yields. Accordingly, substrates exemplifying the different modes of singlet oxygen reactions were chosen (Table 1) to react under these conditions, namely 1,3-diphenylisobenzofuran to 1,2-dibenzoylbenzene ([2 + 2] cycloaddition followed by cleavage),  $\alpha$ -terpinene to ascaridol and 9,10-dimethylanthracene to its 9,10-peroxide ([2 + 4] cycloaddition), and  $\beta$ -pinene to myrtenol hydroperoxide (*ene*-reaction).

The conversion of the substrates was up to 84%. 1,2-Dibenzoylbenzene was obtained in 62% isolated yield proving a successful [2 + 2] cycloaddition. In the other two cases the obtained yields were 0.4 and 36% of the [2 + 4] cycloaddition and *ene*-reaction products, respectively. In these latter cases it turned out that large amounts of products were formed by cleavage of the double bond by ozone. In the case of ascaridole it should be mentioned that some of the ascaridole formed was rapidly transformed into *p*-cymene by decomposition of the peroxide.

## Conclusion

It was demonstrated that 1,1'-bis(diphenylphosphino)ferrocene (**1**) promotes splitting of ozone to yield the singlet oxygen product. This method is also feasible for large-scale preparations allowing an immediate detection of the catalyst in the process workup. The experimental parameters have to be carefully adjusted in every individual case to reach optimum conditions. The process can be run as batch procedure, or in a semi-continuous way.

Taking into account that the oxidized species of the 1,1'-bis(diphenylphosphino)ferrocene **3** can be captured and reduced by *e.g.* hydrogenation into **1**, a continuous process involving recycling of the catalyst on a large scale is feasible. However, further optimization of the reaction conditions would be necessary to repress ozone based side reactions and to enhance conversion of starting material.

## Experimental

All chemicals were obtained from commercial suppliers and used without purification. Ozone was generated by an air-cooled Fischer OZON 503 and a BMT 803, both operated at a flow between 50 and 165 dm<sup>3</sup> O<sub>2</sub> per hour. The actual flow of O<sub>2</sub> was measured by a rotameter at operation pressure, which was calibrated using a gas meter operating at standard pressure in the off-gas stream. Ozone concentration was monitored by a Fischer OZOTRON 23 using UV/Vis-spectroscopy. A flow of approximately 40 dm<sup>3</sup>/h is required for operation, which was ensured by splitting the off-gas stream by a valve. Ozone was also monitored by the OZONE ANALYZER BMT 963 VENT, BMT Messtechnik Berlin, using UV absorption. The values given are g Ozone/m<sup>3</sup> (0°C, 1 atm) and are corrected for pressure and temperature. The ozone analyzer has to be operated at a flow of 0.1–1 dm<sup>3</sup>/min, which was achieved by installing a rotameter prior to the inlet valve of the ozone analyzer. On a preparative scale the in- and outgoing ozone stream was split prior to the ozone-analyzing unit, to ensure a flux of at most 1 dm<sup>3</sup>/min through the sample cells.

### Caution

All experiments with O<sub>3</sub> should be carried out in a well-vented and closed fume hood. Additionally a safety shield should be placed in front of the reaction apparatus. Peroxide

solutions should not be heated up, stored longer as necessary, or evaporated, otherwise violent detonations could occur!

#### *General Procedure*

A solution of 0.67 g of **1** (1.2 mmol) in 50 cm<sup>3</sup> of CH<sub>2</sub>Cl<sub>2</sub> was prepared. It was subjected to ozonisation at -20°C using a gas flow of 0.06 m<sup>3</sup> O<sub>2</sub>/h and an O<sub>3</sub> concentration of 6 g O<sub>3</sub>/m<sup>3</sup> for 9.5 min. Singlet oxygen substrate (0.6 mmol) dissolved in 15 cm<sup>3</sup> of CH<sub>2</sub>Cl<sub>2</sub> was added continuously *via* a pump (93 cm<sup>3</sup>/h). In all experiments quantitative ozone uptake was observed. After purging gently with Ar the residual weight of the reaction solution was determined. The solution was directly analyzed by HPLC. The singlet oxygenation product of  $\beta$ -pinene, myrtenol hydroperoxide, was reduced to myrtenol by addition of an excess of triphenylphosphine.  $\beta$ -Pinene and myrtenol were quantified by GC. For quantitative determination of  $\alpha$ -terpinene and ascaridole the solvent was evaporated. The residue was weighed and analyzed by quantitative <sup>1</sup>H NMR, using 1,4-dioxane as internal standard. All experiments were carried out twice to ensure reproducibility of the results.

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