

One-pot synthesis of ketones and lactones by oxidation of the parent hydrocarbons with KHSO_5 catalyzed by manganese(III) porphyrins in a biphasic, solid–liquid, system

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Abstract

The oxidation of alkanes to ketones and lactones by Oxone[®] ($\text{KHSO}_4 \times \text{K}_2\text{SO}_4 \times 2\text{KHSO}_5$) catalyzed by manganese porphyrins has been studied in an anhydrous two-phase (solid Oxone[®]/DCE solution) catalytic system. Under the experimental conditions adopted, i.e., an excess of Oxone[®] over the organic substrate and catalytic amount of $\text{Mn}(\text{TDCPP})\text{Cl}$, almost complete hydrocarbon conversions are obtained. Acyclic alkanes give ketones as main oxygenated product whereas cyclic alkanes give mainly lactones together with minor amounts of alcohols and ketones. The overall process leading to lactones involves two subsequent manganese porphyrin catalyzed oxidative steps and a stoichiometric reaction involving monopersulfate and the intermediate ketone. The lack of a water phase and of strong acids prevents the hydrolysis of the lactones formed. The products are obtained in yields ranging from low to fair depending on the nature of substrate, catalyst, and on phase transfer agent concentration. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Baeyer–Villiger; Oxidation; Peroxomonosulfate; Manganese; Porphyrins

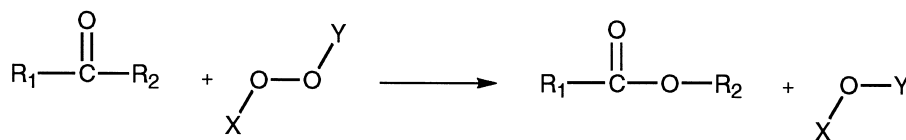
1. Introduction

The Baeyer–Villiger (BV) oxidation of ketones to esters [1–3] with peroxidic compounds, Scheme 1, stoichiometrically amounts to an oxygen transfer from the oxidant to the substrate akin to other oxidative transformations such as olefins epoxidation, heteroatoms (N, P, S) oxygenation and alkanes hydroxylation.

While for most of the oxidations mentioned above, several catalytic procedures based on the use of transition metal derivatives have been developed, the BV reaction is, with few exceptions, still carried out under stoichiometric conditions by employing strong oxidants such as trifluoroacetic acid under rather drastic conditions [4–8]. The exceptions are catalytic procedures in which the oxidant is a nucleophilic peroxocomplex of Pt and Pd [9–12] as expected for a process involving, as first step, the nucleophilic addition of the peroxidic oxidant to the

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Scheme 1.

carbonyl carbon. Accordingly, peroxocomplexes of d^0 transition metal ions such as V(V), Mo(VI) or W(VI), which are typical electrophilic oxidants, do not carry out any BV oxidation [13]. There have also been recent reports on examples of BV oxidation promoted by d^0 transition metals such as Ti(IV) [14,15] and Re(VI) [16,17]. In particular, methyltrioxorenum originates, in presence of hydrogen peroxide, an oxidiperoxocomplex exhibiting both electrophilic and nucleophilic character, and reacts either with olefins or ketones. Aerobic oxidations of ketones to esters in the presence of a metal catalyst and an aldehyde as reductant have also been accomplished [18–23]. However, these procedures still involve an organic peracid, formed in situ by aldehyde autooxidation.

In the course of our mechanistic investigation on the oxygenation of alkanes by Ph_4PHSO_5 , a derivative of Caro's acid soluble in 1,2-dichloroethane (DCE) [24–26], catalyzed by Mn(III)-porphyrins, e.g., 5,10,15,20-tetrakis(2',4',6'-trimethylphenyl)manganese porphyrinate (Mn(TMP)Cl), we observed that in many cases the main product of the reaction is the corresponding ketone [27,28]. For example, in ethylbenzene oxidation, acetophenone/1-phenylethanol ratios ranging from 6 to 20 are obtained even employing an excess of substrate respect to the oxidant. These unusual high ketone/alcohol ratios are likely related to the scarcity of nucleophilic species in solution which could compete with the alcohol intermediate for the catalyst thus preventing a further oxidation to ketone. In our kinetic experiments, a large excess of the substrate over the oxidant was used so that a possible further BV oxidation of the ketone could not have been observed. Moreover, the

BV reaction proceeds much faster with cyclic ketones than with acyclic ones. Therefore, we checked by direct experiments that a model cyclic ketone, such as cyclohexanone, was oxidized to ϵ -caprolactone by Ph_4PHSO_5 in DCE at 30°C. In particular, by reacting 1.1 mmol of Ph_4PHSO_5 with 1.0 mmol of cyclohexanone in 10 ml of DCE, 0.33 mmol of ϵ -caprolactone in 160 h is obtained. This result suggested the development of a one-pot procedure for obtaining lactones by oxidizing the parent cyclic hydrocarbon.

2. Experimental

2.1. Reagents and solvents

1,2-Dichloroethane (DCE) was purified by distillation over P_2O_5 . Spectrophotometric grade methanol (99.9%) from Aldrich was used without further purification. 5,10,15,20-tetrakis(2',4',6'-trimethylphenyl)porphyrin (TMPH_2) and 5,10,15,20-tetrakis(2',6'-dichlorophenyl)porphyrin (TDCPPH_2) were synthesized following a slightly modified Lindsay Smith method [29,30]. 5,10,15,20-tetrakis(2',4',6'-trimethylphenyl)- β -octabromoporphyrin (Br_8TMPH_2) and 5,10,15,20-tetrakis(3'-chloro-2',4',6'-trimethylphenyl)- β -octachloroporphyrin ($\text{Cl}_{12}\text{TMPH}_2$) were obtained by alogenation of TMPH_2 , respectively, with *N*-bromosuccinimide and *N*-chlorosuccinimide in methanol as solvent [31]. The metallation of free base porphyrin ligands with Mn(II)(OAc) $_2$ was performed by conventional methods [32,33]. Ph_4PHSO_5 was prepared and purified as previously reported [24]. Oxone[®], tetraphenylphosphonium chloride, Aliquat 336, 4-*tert*-butyl-

pyridine, bromobenzene (GLC internal standard), ethylbenzene, diphenylmethane, cyclooctane, cyclohexane, cyclopentane, cyclohexanone, cyclopentanone, acetophenone, 1-phenylethanol, diphenylcarbinol, cyclohexanol, ϵ -caprolactone and γ -valerolactone (authentic samples of reaction products) were all commercially available, high purity products (Aldrich) and used as received.

2.2. Oxidation procedures and product analysis

Typically, the reactions were initiated by suspending under magnetic stirring 1.3 g of Oxone[®] (2.0 mmol) in a DCE solution containing the substrate (0.8 mmol), the manganese porphyrin (0.001 mmol), the 4-*tert*-butylpyridine acting as axial ligand of the catalyst (0.27 mmol), the phase transfer agent (PTA) (0–0.3 mmol) and an appropriate GLC internal standard (0.5 mmol), in a jacketed reactor thermostated at 30°C. At appropriate time intervals, the stirring was suspended and 0.1 ml of the supernatant solution were withdrawn, quenched with an equivalent volume of a 0.4 M solution of PPh₃ in DCE and analyzed by GL-Chromatography on a 10% Carbowax 20 M stationary phase adsorbed on Chromosorb WAW-DMCS (1.8 m packed column). The concentration of the oxygenation products was measured on the basis of previously determined response factors.

3. Results and discussion

The oxidation of a series of alkanes was carried out in DCE by employing an excess of oxidant respect to the substrate. In view of the potential synthetic relevance of such a procedure, the simplest experimental conditions and the cheapest reagents were selected. Thus, 2.0 mmol of Oxone[®] (KHSO₄ × K₂SO₄ × 2KHSO₅) were suspended under stirring in 10 ml of DCE in which 0.8 mmol of alkane, catalytic amount of a manganese porphyrin, 4-*tert*-butylpyridine, which acts as axial ligand of

the catalyst, and a phase transfer agent were dissolved at 30°C. Tables 1 and 2 collect a series of data which illustrate the scope of the reaction, providing, at the same time, useful hints on the role played by the various parameters. Ethylbenzene has been used in the experiments whose results are reported in Table 1 in order to select the best catalyst for ketone production. In fact, the negligible reactivity of acetophenone toward BV oxidation in this system, allows the contribution of such uncatalyzed reaction to be neglected (see Scheme 2).

In the anhydrous system reported here, the presence of an aromatic nitrogen base, i.e., 4-*tert*-butylpyridine, is a necessary requisite for the formation of an *oxo*-manganese species and it is therefore even more important for alkane oxidation. On the other hand, nitrogen derivatives are oxidizable substrates and consume part of the monopersulfate thus reducing the efficiency of the process leading to ketone formation. Therefore, it is probable that the efficiency of the overall oxidative process can be improved by tuning basicity and concentration of the base acting as catalyst's axial ligand. To this aim, further work is now in progress in our laboratory.

On the basis of the results of Table 1, it is clear that among the porphyrins tested, the best

Table 1
Oxidation of ethylbenzene (0.8 mmol) by Oxone[®] (KHSO₄ × K₂SO₄ × 2KHSO₅) (2.0 mmol) catalyzed by various manganese-porphyrins (0.001 mmol) in the presence of 4-*tert*-butylpyridine (0.27 mmol) and of Ph₄PCl (PTA, 0.03 mmol), in 10 ml of DCE, at 30°C

Entry	Mn(Porphyrin)	Time (h) ^a	Products, yields (%) ^b
1	Mn(TMP)Cl	48	acetophenone, 15; 1-phenylethanol, 2
2	Mn(Br ₈ TMP)Cl	115	acetophenone, 12; 1-phenylethanol, 2
3	Mn(Cl ₁₂ TMP)Cl	240	acetophenone, 15; 1-phenylethanol, 10
4	Mn(TDCPP)Cl	210	acetophenone, 60; 1-phenylethanol, 6

^aTimes corresponding to the maximum products concentration reached.

^bYields are calculated with respect to the organic substrate.

Table 2

Oxidation of various substrates (0.8 mmol) by Oxone[®] ($\text{KHSO}_4 \times \text{K}_2\text{SO}_4 \times 2\text{KHSO}_5$) (2.0 mmol) catalyzed by $\text{Mn}(\text{TDCPP})\text{Cl}$ (0.001 mmol) in the presence of 4-*tert*-butylpyridine (0.27 mmol) and of a phase transfer agent (PTA) in 10 ml of DCE, at 30°C

Entry	Substrate	PTA (mmol)	Time (h) ^a	Products, yields (%) ^b
5	ethylbenzene	—	70	acetophenone, 52; 1-phenylethanol, 0
6	ethylbenzene	Ph_4PCI , 0.033	210	acetophenone, 60; 1-phenylethanol, 6
7	ethylbenzene	Ph_4PCI , 0.33	180	acetophenone, 22; 1-phenylethanol, 4
8	ethylbenzene	Aliquat 336, 0.033	180	acetophenone, 47; 1-phenylethanol, 1
9	ethylbenzene	Aliquat 336, 0.33	180	acetophenone, 24; 1-phenylethanol, 5
10	diphenylmethane	Aliquat 336, 0.033	100	benzophenone, 35; diphenylcarbinol, 4
11	cyclooctane	Aliquat 336, 0.033	160	cyclooctanone, 47; cyclooctanol, 27; octanocyclactone, 3
12	cyclohexane	Aliquat 336, 0.033	160	cyclohexanone, 2; cyclohexanol, 12; ϵ -caprolactone, 29
13	cyclopentane	Aliquat 336, 0.033	120	cyclopentanone, 14; γ -valerolactone, 14
14	cyclohexanone	Aliquat 336, 0.033	110	ϵ -caprolactone, 33
15 ^c	cyclohexanone	Aliquat 336, 0.033	110	ϵ -caprolactone, 97
16 ^c	cyclopentanone	Aliquat 336, 0.033	160	γ -valerolactone, 100

^aTimes corresponding to the maximum products concentration reached.

^bYields are calculated with respect to the organic substrate.

^cIn absence of $\text{Mn}(\text{TDCPP})\text{Cl}$.

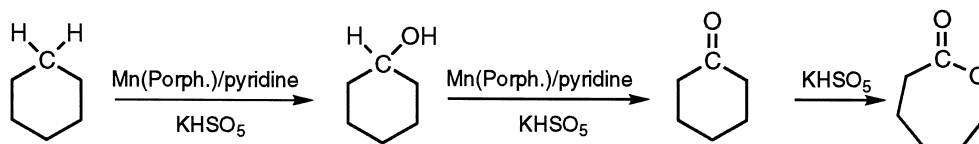
one for the oxidation of the model hydrocarbon ethylbenzene is $\text{Mn}(\text{TDCPP})\text{Cl}$ (entry 4). In fact, with this catalyst up to ca. 1500 turnovers are reached and, along with near complete hydrocarbon conversion, up to 60% acetophenone yield is obtained. The final concentration of 1-phenylethanol produced is low (6%) confirming the peculiar chemoselectivity of such anhydrous oxidizing system. The other catalysts tested (entries 1–3) undergo bleaching before substantial hydrocarbon conversions have been reached, thus limiting products yield.

Entries 5–9 of Table 2 indicate that the addition and the nature of species capable of acting as phase-transfer agent helps the dissolution of solid KHSO_5 in DCE, but it has a relatively minor effect on hydrocarbon oxidation. In fact, the oxidative process takes place even in the absence of PT agent (entry 5). Moreover, by adding 0.03 mmol of either Ph_4PCI (entry 6) or

Aliquat 336 (entry 8), the reaction yields do not increase significantly. Interestingly, a further increase in the PT agent concentration (entries 7,9) provides lower acetophenone yields, thus suggesting a faster catalyst bleaching in the presence of higher monopersulfate concentrations.

Diphenylmethane (entry 10) and cyclooctane (entry 11) oxidation still leads to the corresponding ketone as main oxygenated product. When cyclooctane is the substrate, an almost quantitative total yield is observed, indicating that parallel processes, involving either the starting material or intermediate products, do not have relevance.

The subsequent oxidation of the ketone initially formed to lactone takes place, under our conditions, only for small or medium-size cyclic alkanones, i.e., cyclopentanone and cyclohexanone (entries 12,13). This agrees with the well



Scheme 2.

known behavior of BV oxidation which proceeds much smoothly when cyclic ketones are the substrates. Note that for the latter, the yield of the corresponding lactone is acceptable (29%), particularly in the light of the fact that the parent hydrocarbon is the starting material. Curiously, the presence of the porphyrin catalyst, which is essential for the oxidation of the cycloalkanes to ketones, decreases the yield of the subsequent oxidation of the ketones to lactones. In fact, carrying on cycloalkanones oxidation with Oxone[®] (entries 15,16), quantitative yields in the corresponding lactones are obtained. On the other hand, when the catalyst is also present (entry 14) the lactone yield drops to 33%. This outcome is likely related to the concomitant catalase-like activity of the manganese porphyrin promoting the catalytic decomposition of monopersulfate.

It must be recalled that in the procedure developed, the oxidation of the hydrocarbon to alcohol, and subsequently to the corresponding ketone, is catalytically carried on by a manganese ipervalent oxospecies generated by oxidation of the manganese porphyrin with monopersulfate. On the contrary, the last oxygen atom transfer leading to lactone is directly effected by monopersulfate in a stoichiometric reaction with the ketone. Therefore, the synthetic relevance of the procedure described is tightly connected with an accurate choice of the type and the concentration of the porphyrin used. Other investigations along this line aimed at optimizing the experimental conditions are currently being carried out in our laboratory.

4. Conclusions

We have established the feasibility and generality of a catalytic procedure that allows the transformation of a methylenic function into a carbonyl compound in fair yields. The oxidative process is carried out in an anhydrous and heterogeneous system based on Oxone[®] and a suitable manganese porphyrin as catalyst. When

small or medium-size cycloalkanes are the substrates, the process provides moderate yields of the corresponding lactones. The synthetic value stems mainly from the possibility of preparing valuable chemicals as ketones and lactones by direct oxidation of the parent saturated hydrocarbon.

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