

Superior Performance of NHPI Cocatalyst in the Autoxidation of Methylbenzenes under Solvent-Free Phase Transfer Conditions

Nimer Taha and Yoel Sasson*

Casali Institute of Applied Chemistry, Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

Abstract:

The novel three-way catalytic system Co(II)/QX/NHPI (QX = lipophilic ammonium salt) is presented as a highly potent promoter for the autoxidation of methylbenzenes to benzoic acids in the absence of a solvent. The key feature of the scheme is the phase transfer of Co(II) and NHPI into the organic phase partially via a hydrogen-bond mechanism. With certain QXs the latter interaction also stabilizes NHPI and prevents its degradation (which is a crucial drawback of this reagent). Ammonium salts that have a tendency to self-assemble in giant multilamellar vesicle (onion) structures, such as DDAB, are particularly effective in this system.

Introduction

N-Hydroxyphthalimide (NHPI) is a well-recognized catalyst for various free radical-mediated reactions, particularly autoxidation of hydrocarbons.¹ This unique organic catalyst is a precursor of the stable free radical phthalimido-*N*-oxyl (PINO) which enhances the initiation and propagation steps in the autoxidation cycle, thus diminishing the impact of the termination step. It was demonstrated that the PINO radical is more reactive than the peroxy counterpart in C–H bond hydrogen abstraction, and it also has the capacity to suppress the peroxy radical which is accountable for the termination step in the standard autoxidation cycle.² The PINO-driven chain propagation is thus essentially “non-terminating”.³ NHPI-catalyzed autoxidation of hydrocarbons normally generates mainly hydroperoxides.⁴ If other oxygenated products are desired (e.g., carboxylic acids, alcohols, or ketones) a cocatalyst should be added. Typical examples are metal (mainly cobalt) salts⁵ or quaternary ammonium salts.⁶

Nonetheless, NHPI as an autoxidation catalyst suffers from two major shortcomings: (1) it has very low solubility in

nonpolar organic medium,⁷ and (2) both NHPI and its product, PINO, are unstable at >80 °C and tend either to decompose to phthalimide or phthalic anhydride⁸ or to form inactive trimers.⁹ Due to (1), polar solvents such as acetonitrile or acetic acid must be used.¹⁰ These solvents (which are hydrogen-bond acceptors) tend to form hydrogen bond complexes with NHPI, resulting in sharp decrease in catalytic activity, particularly when a substantial amount of solvent is present.¹¹ Consequently, [also due to (2)] a large amount of NHPI is typically applied (normally 10–30 mol % relative to the substrate¹²). Despite this excessive quantity, NHPI is a sacrificial catalyst that decomposes in the course of the catalytic reaction and, in most cases, cannot be recovered or recycled.

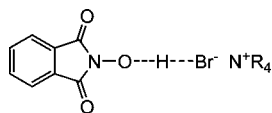
Several potential solutions have been advocated for avoiding the degradation of the NHPI–PINO catalyst. Saha et al. proposed the obvious continuous feed of NHPI solution into the oxidation reactor using a syringe pump.¹³ The same authors proposed another alternative: the protected *N*-acetoxyphthalimide (NAPI) that was shown to be an NHPI precursor and decomposed at a slower rate. Einhorn¹⁴ introduced *N*-hydroxy-3,4,5,6-tetraphenylphthalimide which could be used at low temperature (<35 °C) but decomposed above 50 °C. Tetrahalogenated *N*-hydroxyphthalimide was developed by Xu and co-workers,¹⁵ while Ishii has recently advocated the more thermally stable *N,N',N''*-trihydroxyisocyanuric acid derivative (THICA).¹⁶ Further efforts were made to improve the solubility of NHPI in apolar solvents. Accordingly, 4-lauryloxycarbonyl-*N*-hydroxyphthalimide, which is more lipophilic in nature and could be

* Author for correspondence. E-mail: ysasson@huji.ac.il.

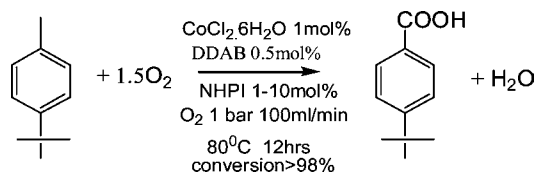
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Scheme 1. Hydrogen bond complex between NHPI and a quaternary ammonium salt



Scheme 2. Autoxidation of PTBT catalyzed by the ternary Co/DDAB/NHPI system



used in neat substrates, was suggested by Ishii.¹⁷ Sheldon introduced *N*-hydroxysaccharin as an alternative to NHPI,¹⁸ and Liu et al. used a pyridine–NHPI derivative in ionic liquids.¹⁹ In another methodology proposed by Hermans,²⁰ NHPI was impregnated on silica which allowed the catalyst's recycle, but the reported conversions were inadequate. Also when NHPI was covalently bonded to a sol–gel-derived silica matrix,²¹ the performance was rather poor.

Results and Discussion

We have now discovered that small amounts of certain lipophilic quaternary ammonium salts (quats) added to NHPI in oxidation reactions, provide an integrated solution to the two drawbacks listed above. First, these ion-pairs function as phase transfer catalysts (PTC) and swiftly solubilize NHPI in apolar solvents or reactants such as toluene or cyclohexane, and second, these ammonium salts stabilize NHPI and inhibit its degradation under autoxidation reaction conditions. Consequently, the reuse of the latter is possible over several consecutive batches of oxidation reactions. Since phase transfer catalysts also effectively extract metal salts into the organic phase, we depict herein a dual function phase transfer system where quaternary salts simultaneously extract (or solubilize) the NHPI and the cobalt chloride cocatalysts into the organic phase.

NHPI is not soluble in toluene; nonetheless, upon mixing 10 mmol of solid NHPI with 100 mL of a 0.1 M solution of didecyltrimethylammonium bromide (DDAB) or didodecyltrimethyl ammonium bromide (DDDAB) in toluene maintained at 70 °C for 1 h, a clear 0.1 M toluene solution of NHPI was generated. We initially presumed that a soluble hydrogen bond complex²² is formed between the DDAB and the NHPI (Scheme 1). The latter complex has a typical UV absorbance peak at 286 nm. Conversely, quaternary ammonium salts of different structure were less effectual in extraction of NHPI. A 0.1 M

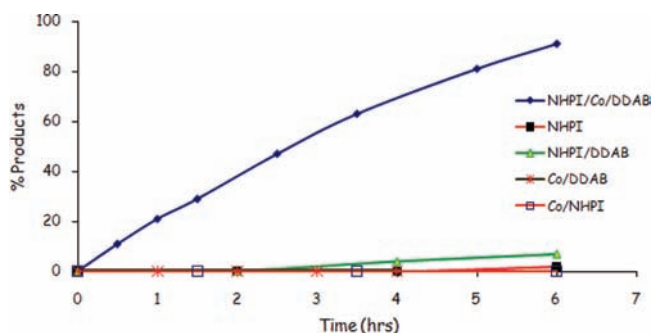


Figure 1. Autoxidation profile of PTBT at 80 °C using various catalyst combinations (for experimental conditions, see Scheme 2).

solution of tetraoctylammonium bromide (TOAB) was able to solubilize 0.08 M of NHPI in toluene (showing a UV peaks at 295 nm). The popular detergent cetyltrimethylammonium bromide (CTAB) showed low activity under identical conditions and extracted a lesser amount of NHPI to create only a 0.02 M solution of the latter in toluene (UV peak at 296 nm). The universal PTC tetrabutylammonium bromide (TBAB) was not effective at all. These observations indicate that hydrogen bond complex is not the only rationale for the extraction of NHPI into the organic phase.

Using these results as guides, we were able to conceive a solvent-free, NHPI-based, autoxidation system. We have established that NHPI has a formidable impact on the autoxidation rate of *p*-*tert*-butyl toluene (PTBT) and other methylbenzenes to the corresponding benzoic acids catalyzed by the DDAB/CoCl₂ system in the absence of solvent (Scheme 2).²³ The effect is particularly pronounced at <95 °C. Above this temperature, the main input of NHPI is not in increasing the reaction rate but, rather, leading to the total elimination of the induction period which is typical in classical autoxidation reactions. Kinetic profiles of several experiments, using different catalyst combinations at 80 °C, are shown in Figure 1. Evidently, the ternary system Co(II)/DDAB/NHPI is by far more reactive than the dual combinations NHPI/Co and DDAB/Co (which were essentially inactive under the specified conditions, Scheme 2), and NHPI/DDAB (which showed slight activity). In practice, a very low concentration of NHPI was found to be satisfactory to promote the autoxidation reaction. Thus, in the presence of 1 mol % of NHPI, 1 mol % of CoCl₂·6H₂O, and 0.5 mol % of DDAB with a continuous flow of oxygen (100 mL/min at ambient pressure), complete conversion of PTBT was measured after 12 h at 90 °C. In the course of the reaction, benzaldehyde was detected as an intermediate in the oxidation process. The aldehyde reached a maximum of 10 mol % after 4 h and then decreased gradually to zero. After completion of the reaction, a second batch of PTBT was added to the final mixture followed by heating to 90 °C and streaming of oxygen. The reaction started again at essentially the same rate as that of the previous batch. The latter experiment clearly demonstrates that NHPI is recyclable under our reaction conditions. Employing the same protocol with toluene, *o*-, *m*- and *p*-xylene, mesitylene, *o*-, *m*-, and *p*-chloro- or -bromotoluene, all resulted in high conversion

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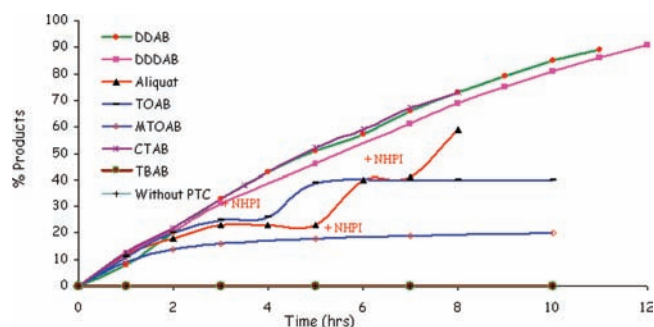


Figure 2. Reaction profiles of Co(II)-/PTC-/NHPI-catalyzed autoxidation of PTBT (experimental conditions see Scheme 2) at 80 °C in the presence of various phase transfer catalysts.

(>95%) and selectivity (>99%) to the corresponding substituted benzoic acid. In the case of xylenes or mesitylene, only one methyl group was oxidized under the above conditions. With *p*-methoxytoluene as substrate, only a 20% conversion occurred, mainly forming anisaldehyde. This was attributed to the formation of a small amount of *p*-cresol via hydrolysis that brought the process to a standstill (phenols are radical scavengers, and as such they act as poisons for free radical chain reactions, see reference 12a). *p*-Nitrotoluene did not react at all. Following the kinetics of the reaction at 60, 80, 90, and 100 °C allowed the calculation of the activation energy of the process, 26.6 kJ/mol, indicating that under our conditions the reaction is, at least partially, mass transfer controlled. The rate-determining step is, most likely, the gas/liquid mass transfer.

Surprisingly, the performance of different quaternary ammonium salts as cocatalysts in the reaction of the aromatic systems listed did not depend exclusively on their phase transfer capacity. Thus, systems containing either TOAB, Aliquat 336, or methyltriocylammonium bromide (MTOAB) combined with NHPI and CoCl₂ in PTBT lost activity after ~3 h with a maximum conversion of 15–25%. The catalytic activity was resumed upon addition of a fresh batch of 10 mol % of NHPI. This is shown in Figure 2 where reaction profiles in the presence of several phase transfer catalysts are shown. In the experiment with Aliquat 336 as PTC, the system is halted again after 40% conversion and restarted a second time with yet another addition of fresh NHPI. These observations evidently suggest that NHPI is decomposing under these experimental conditions. Conversely, in the catalytic systems where either DDAB, DDDAB, or CTAB were used in combination with Co(II) and NHPI, the reaction smoothly continued until complete conversion of PTBT was attained. Addition of a second batch of fresh PTBT to these fully converted mixtures resumed the catalytic process at essentially the original rate. We can therefore safely argue that NHPI is stable in the catalytic system containing either DDAB, DDDAB, or CTAB under the specified reaction conditions. We also verified that the ammonium salts were all resistant to oxidation under the above conditions. It is noteworthy that CTAB, which we found to be a poor extractant for NHPI, performed quite well in protecting it in the course of the process. This unique feature of the latter three ammonium salts cannot be attributed to a greater hydrogen-bond-accepting capacity of these salts. It is quite the opposite, in TOAB or in TBAB. The bromide anion is a stronger hydrogen-bond acceptor as it is substantially more distant from the ammonium cation

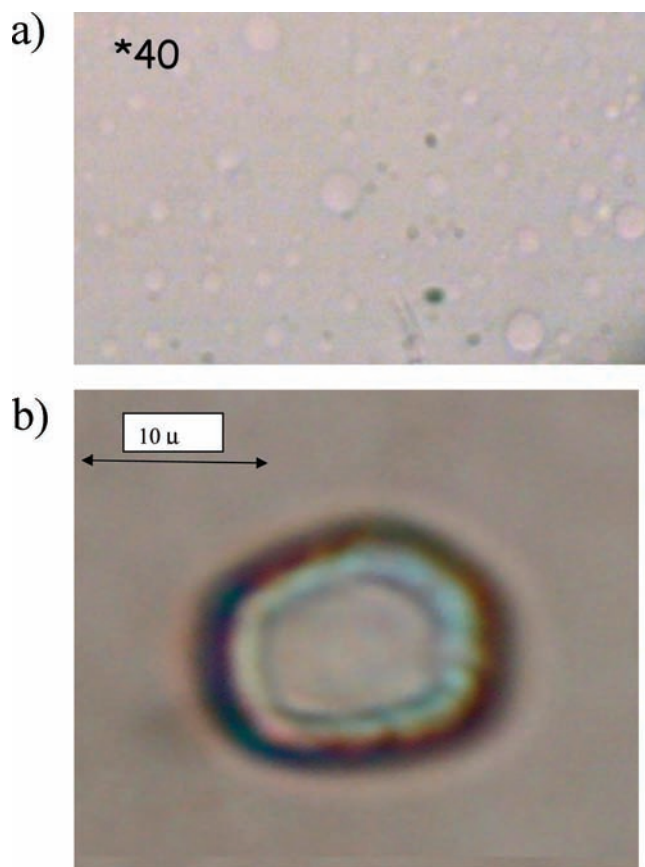


Figure 3. (a) Microscopic (40×) view of CoCl₂/DDAB solution in toluene. Size of the multilamellar vesicles 3–20 μm. (b) Microscopic (1000×) view of a single CoCl₂/DDAB giant multilamellar vesicle in toluene. Size of vesicle 16.5 μm.

and, accordingly, more “naked” than the anion in the nonsymmetrical ammonium salts. Interestingly, when the above procedure was repeated with cobalt acetate instead of cobalt chloride and didecyldimethylammonium tosylate instead of DDAB, essentially the same oxidation rate, final conversion (98%), and selectivity (>99%) were realized under the above standard conditions. This observation again implies that the hydrogen bond complex formation (Scheme 1) is not crucial for the NHPI solubilization/stabilization mechanism. (removal of halides from the reaction mixture is beneficial as it renders these systems much less corrosive).

Consequently, we presume that this remarkable NHPI-stabilizing effect of quats carrying two long and two short alkyl chains can be attributed to the unique propensity of these materials to self-assemble as giant multilamellar vesicles (onion structure). This trait is well recognized in aqueous solutions,²⁴ but as we reported earlier, DDAB in organic solvents spontaneously forms reversed multilamellar vesicles (MLV) which were proposed to function as catalytic microreactors.²⁵ In contrast to normal vesicles, in a reverse vesicle the polar head of the amphiphilic DDAB orients inward, and the inside and outside of the vesicle are a non-polar phase.²⁶ Formation of these reversed MLVs is evidently the source also for the remarkable

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activity of DDAB in standard phase transfer-catalyzed reactions.²⁷ Indeed, microscopic inspection of our reaction mixture prior and after the addition of NHPI exposed the presence of giant spherical vesicles (diameter of 3–20 μm !) with a thick multilayer (onion structure) shell that (based on its color) contains most of the cobalt salt. Panels a and b of Figure 3 show photographs of these vesicles in a typical reaction mixture containing 1 mol % $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ and 0.5 mol % DDAB in toluene. It should be noted that CTAB that performed well as cocatalyst (Figure 2) is a standard surfactant that spontaneously forms reverse micelles in the organic phase. On the other hand, we are not aware of any self-assembly properties of quats such as Aliquat 336, MTOAB, or TOAB which performed poorly in our catalytic system.

Conclusions

The ternary catalytic system Co(II)/PTC/NHPI was verified as highly effective in the autoxidation of methylbenzenes to the corresponding benzoic acids under mild conditions in the absence of a solvent. The major role of the phase transfer catalyst in these systems is the extraction of both Co(II) and NHPI into the apolar organic phase. Exceptional efficacy was realized for the two alkyl long-chain quats such as DDAB and DDDAB. The latter simultaneously extracted and stabilized the

NHPI in the reaction systems. This unique performance was assumed to be related to the self-assembly of giant multilamellar vesicles (MLV) characteristic of these quats.

Experimental Section

Materials. An 80% aqueous solution of DDAB and dry DDDAB were purchased from Alfa Aesar. All other materials were purchased from Sigma-Aldrich.

Typical Procedure. A mixture of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (0.27 mmol, 1 mol %, 0.064 g), DDAB (0.135 mmol, 0.5 mol % 0.068 g), NHPI (2.7 mmol, 10 mol %, 0.44 g), and *p-tert*-butyl toluene (27 mmol, 4 g) was stirred at 80 °C until a blue homogeneous solution was obtained (~20 min). Oxygen was sparged through the solution at 100 mL/min STP for 8 h at 80 °C. Samples were withdrawn from the reaction mixture at regular intervals and analyzed by a gas chromatograph (HP 5890) equipped with a flame ionization detector and a capillary column (5% diphenyl, 95% dimethylpolysiloxane gum, 0.25 mm thickness and 30 m long). After completion of the reaction, the mixture was cooled to room temperature and washed with water (4×25 mL) to remove the DDAB, NHPI, and CoCl_2 catalysts, and the product was vacuum-dried for 5 h. *p-tert*-Butyl benzoic acid (4.57 g, 95% yield) was recovered in 98% purity, mp 164–5 °C.²⁸

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