Is it possible to implement N-hydroxyphthalimide homogeneous catalysis for industrial applications? A case study of cumene aerobic oxidation

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INTRODUCTION

Following the pioneering works of Ishii and co-workers,[1,2] in the last decade several aerobic oxidations of organic compounds were performed using N-hydroxyphthalimide (NHPI) as free-radical promoter in the presence or absence of metal salt initiators.[3–9] In all these oxidations, the phthalimido-N-oxyl (PINO) radical, generated in situ from NHPI by different initiators, plays a key role in the catalytic process, acting as a more selective and efficient hydrogen-abstracting species with respect to the peroxyl radicals normally involved in autoxidation processes (Scheme 1). This reactivity is related to the bond dissociation energy (BDE) of the O–H group, which we evaluated to be 88.1 kcal/mol.[10–12] This value renders NHPI a good hydrogen donor, trapping peroxyl radicals before they undergo termination, and PINO a good hydrogen abstractor.

In spite of the many results previously disclosed, the industrial use of NHPI as catalyst for aerobic oxidation of organic compounds is still lacking for several reasons.
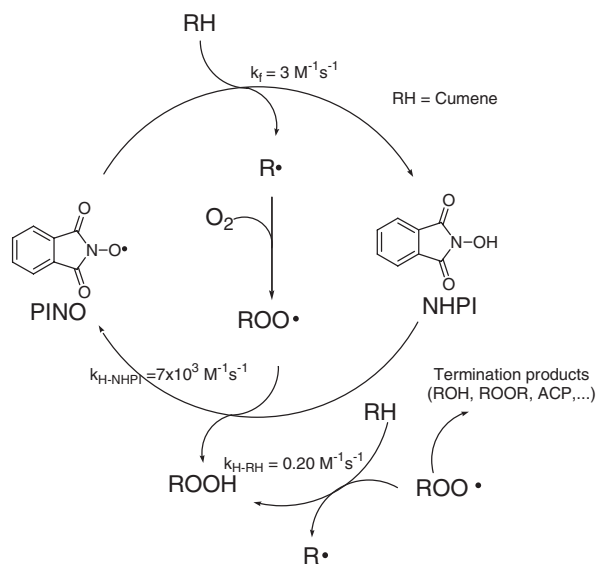
The most important one relies on the fact that, in order to operate under homogeneous conditions, a polar co-solvent is often necessary to provide a sufficiently polar reaction medium to dissolve NHPI, as in the case of hydrocarbons oxidation. Alternatively, NHPI could be functionalized by suitable moieties able to increase the solubility of the catalyst in low polar medium[13] or it should be necessary to operate at high temperatures.[14] All these solutions introduce specific challenges during the scale-up of the process from the laboratory to the industrial plant, also from an economical point of view. In fact, the use of NHPI as homogeneous catalyst is commonly seen as too expensive compared with the consolidated traditional oxidation protocols.

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Scheme 1. Catalytic role of NHPI in the selective oxidation of hydrocarbons.

R_1 = H, Alkyl
R_2 = Alkyl

Scheme 2. Selective aerobic oxidation of alkyl aromatics catalyzed by NHPI/CH$_3$CHO system.
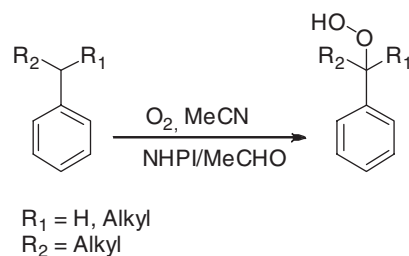
The anchoring of the catalyst on heterogeneous supports could be a valid solution to overcome the above reported drawbacks. Different attempts to immobilize NHPI on a solid support were reported over the last few years.[15−20] These approaches do not guarantee a high selectivity in hydroperoxides, the latter depending on the concentration of the hydrogen donor in solution. As a consequence, homogeneous catalysis should be preferred when selectivity is a specific task of the process.

One more concern regarding the use of NHPI at industrial scale is the necessity for operating in the presence of radical initiators, according to the reference literature. The use of transition metal salts should be avoided, especially when they are detrimental for the selectivity of the protocol (i.e. in hydroperoxides production). On the other side, non-metal sacrificial initiators like α,α'-azobisisobutyronitrile (AIBN)[21−24] or antraquinones[25,26] are perceived as a further cost for the overall economy of the process. Moreover, they are often active at high temperatures, which favour the unimolecular decomposition of the catalyst.[11]

Despite all the challenges that NHPI-based processes pose for their scale-up, the potential and effectiveness of this catalyst as promoter of radical chains in liquid phase aerobic oxidations are now well recognized.

Very recently we have reported a new process, catalysed by NHPI in the presence of tiny amounts of acetaldehyde (MeCHO), for the selective aerobic oxidation of secondary[27] and tertiary[28] alkyl aromatics to the corresponding hydroperoxides (Scheme 2), following two patent applications.[29,30] This reaction, when applied to cumene (CU), represents the first step towards the synthesis of phenol.

In the reported protocols, co-oxidation of acetaldehyde led to the formation of PINO radical by molecule-induced homolysis of NHPI,[31,32] allowing improvement of both conversion and selectivity in the desired product under milder conditions than the classical Hock process[33,34] and to prevent catalyst decomposition. In the present work, which follows a patent application,[35] we treat the oxidation of CU as a case study to demonstrate the potential of NHPI catalysis for industrial applications. First we prove how CU can be converted to the corresponding hydroperoxide under mild conditions via selective aerobic oxidation catalyzed by NHPI, without the addition of initiators. Moreover, we suggest a technological approach for the recovery of the catalyst at the end of the oxidation process by precipitation of NHPI, after removal of the polar co-solvent and cooling at room temperature, and subsequent adsorption of residual catalyst still present in solution on adsorbing solids. The catalyst can then be removed from adsorbing beds by washing with suitable polar solvents, by means of a process described hereunder.

EXPERIMENTAL
Materials

All the reagents were commercially available and were used without further purification. CHP(80%w) was purchased from Sigma-Aldrich. Adsorbent resins Amberlyst® A21, A24, A26(OH), A15 and XAD761 were submitted to specific treatments as detailed in the General Procedure. NHPI measurements were performed by HPLC ($\lambda = 300$ nm) using a reverse phase column Superspher 100 RP-18 (250×4 mm, LiChroCART, Merck) and MeCN/H$_2$O (70/30) as eluent. Conversions and yields were determined by HPLC analysis (reverse phase column; MeCN/MeOH/H$_2$O, 35/5/60), with 2-phenylethanol added as internal standard, and confirmed by ^{1}H NMR.

General procedure
Cumene oxidation

In a typical experiment, 470 mg of NHPI (2.88 mmol – 1% mol) were dispersed in a solution of 40 mL of CU (34.6 g – 288 mmol) in 15 mL of MeCN using a two neck round bottom flask equipped with thermocouple, condenser and magnetic stirrer. The apparatus was connected to an oxygen reservoir (1 atm) by a purpose-designed gas-meter and heated at 70°C in an oil bath. Similar experiments were also performed in the presence of specific initiators like AIBN (0.5%mol) or propionaldeyde (10%mol).

NHPI recovery by precipitation

The experiments were performed dispersing 470 mg of NHPI (2.88 mmol – 1% on molar basis of initial CU) in 40 mL of a CU/CHP solution with a specific CU/CHP molar ratio. Different molar ratios were considered. The mixture was heated under stirring in an oil bath up to homogeneity under N$_2$ atmosphere and then cooled down to room temperature (25°C) by natural convection in air. The temperature was monitored by the thermocouple. The crystalline NHPI precipitated during the cooling process was recovered from the mixture by filtration on a sintered glass filter and extensively washed with hexane in order to remove residual CU and CHP. The material was dried in air and finally weighed.

NHPI recovery by adsorption

Prior to use, Amberlyst A21, A24 and A26(OH) (typically 10 g) were extensively washed with warm methanol (50°C, 5 × 100 mL), warm distilled water (50°C, 5 × 100 mL) and again methanol (50°C, 5 × 100 mL). A26(Cl) was prepared from A26(OH) by treatment with HCl 2 mol L^{-1} (5 × 100 mL), distilled water (5 × 100 mL) and methanol (50°C, 5 × 100 mL). A15(Na) was prepared from the protonated form by treatment with NaOH 2 mol L^{-1} (5 × 100 mL), distilled water (5 × 100 mL) and methanol (50°C, 5 × 100 mL). Amberlyst XAD-761 was washed with methanol (50°C, 5 × 100 mL). After the specific treatments all the resins were dried in air.

Adsorption experiments were performed on model CU/CHP solutions at different molar ratios and with a concentration of NHPI of 2 mg mL^{-1}. In particular two ratios were considered, in order to simulate two solutions with different polarity: CU/CHP ∼ 4.4/1(mol/mol) and CU/CHP ∼ 1.85/1(mol/mol). In particular the latter corresponds to a mixture originated from hypothetical process characterized by a CHP yield of about 35% for which approximately 65% of the original catalyst has been recovered by precipitation. 25mL of each solution were typically put in contact with 1 g of adsorbent resin and kept for 2 h at 25°C under gentle stirring. Preliminary experiments indicated that the adsorption process on the investigated resins was completed in this time. Samples were finally withdrawn and analyzed by HPLC in order to determine the NHPI concentration (C_{eq}, mg mL^{-1}) and verify the stability of CHP. Adsorption isotherms were obtained with the same procedure but changing the mass of adsorbent. The amount of NHPI adsorbed on the resins (Q_e) was calculated by the following equation:

$$Q_e = \frac{V \cdot (C_0 - C_{eq})}{m}$$

where V is the volume of the solution (mL), C_0 is the initial concentration of NHPI (mg mL^{-1}) and m is the mass of adsorbent resin.

The regeneration tests were performed considering only A26(Cl). Practically after adsorption, 1 g of resin previously kept in contact with a CU/CHP solution 1.85:1 (mol/mol) ([NHPI] = 2mg mL^{-1} was gently stirred with MeCN (30 mL) at 30°C for 1 h. The concentration of the released NHPI was then measured and the solvent was replaced with fresh MeCN (30 mL). The procedure was repeated 10 times, until the amount of NHPI released was not capable of

detection by HPLC. To verify whether the resin A26(Cl) was still able to capture NHPI, a new adsorption cycle was performed followed by regeneration as detailed before. The procedure was repeated three times.

RESULTS AND DISCUSSION

The proposed approach consists of four steps as summarized in Fig. 1: (i) the selective aerobic oxidation of CU to cumyl hydroperoxide (CHP) catalyzed by NHPI; (ii) the removal of the solvent by distillation and cooling of the oxidation mixture, followed by partial precipitation and filtration of the catalyst; (iii) the physical adsorption of residual NHPI still present in solution onto selected non-basic adsorbing solids; (iv) the removal of the catalyst from the adsorbing solids by means of the polar co-solvent employed in the oxidative step.

Aerobic oxidation of cumene catalysed by NHPI in the absence of initiators

Under NHPI/MeCHO catalysis the selectivity in CHP did not exceed 84%, the main by-product being cumyl alcohol (CA). This result could not be considered satisfactory from an industrial point of view. We then decided to further investigate the reaction conditions.

It is well known that autoxidation processes carried out in batch conditions and without initiators can have kinetic evolutions characterized by the presence of a random induction period.[36] At industrial scale the liquid phase aerobic autoxidation of hydrocarbons is, instead, performed in continuous mode with gas–liquid reactors where fresh hydrocarbon is fed.[37,38] For this reason, the use of initiators in a process plant should not have the same relevance that it has at laboratory scale. On the basis of this consideration we decided to perform the oxidation of cumene without aldehyde initiator. In classical protocols, the autoxidation of CU[33,34] and other hydrocarbons[39,40] is conducted at temperatures higher than 110°C, both to overcome the thermodynamic barrier of reactivity between oxygen and the alkyl aromatic, and to promote initiation of new radical chains by partial decomposition of the hydroperoxide products. Both these aspects positively influence the kinetic of the process, but negatively affect its selectivity. Nevertheless, when the substrate is sufficiently reactive autoxidation could occur at a lower temperature, generating tiny amounts of peroxyl radicals.
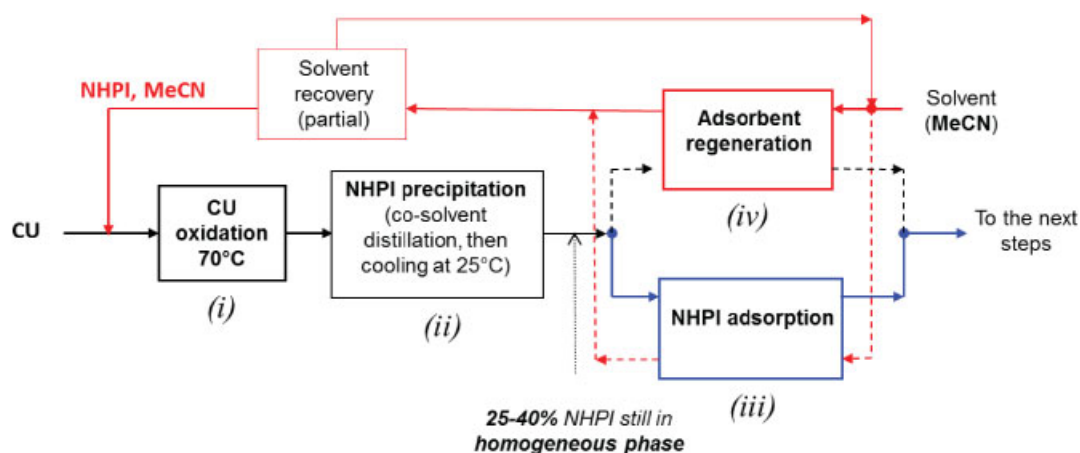

Figure 1. Protocol for the selective oxidation of cumene and recovery of the catalyst NHPI.

Table 1. CU oxidation at 70°C after 6 h. CU/MeCN = 8:3 (v:v); 1% NHPI

		Conv. (%)	Sel. CHP (%)
1	No initiator	31.2	96
2	0.5% AIBN	33.5	92
3	10% EtCHO	34.7	84

If the reaction was carried out in the presence a sufficiently high concentration of NHPI, we would expect to afford good conversions of the tertiary alkyl aromatic in a short time and under mild conditions without using additional initiators.

Data reported in Fig. 2, showing the kinetics of O_2 consumption as well as CU conversion for the aerobic oxidation of CU catalyzed by NHPI, both in the presence and in the absence of initiators, clearly confirmed our assumption. After an induction time of about 30 min, oxidation of CU occurred at 70°C, with a CU/MeCN volume ratio of 8/3, even in the absence of initiator, with a kinetic comparable with that measured when in the presence of α,α'-azobisisobutyronitrile (AIBN) or propionaldehyde (EtCHO) (Table 1). These conditions enabled a conversion of about 31% after 6 h with the corresponding CHP produced with a selectivity higher than 96% in 6 h, CA being the unique by-product.

The high selectivity obtained in this case could be ascribed to the absence of aldehyde as initiator that would give, if used, the formation of carboxylic acid, causing degradation of the alkylaromatic hydroperoxide. The CU/MeCN volumetric ratio adopted during these experiments was a good compromise between the need to completely dissolve the NHPI and the need to operate at high concentration of alkylaromatic.[26] Moreover, it is worth noting that CU reached 20% mol conversion in less than 3 h (Fig. 2), with selectivity in CHP close to 99%. Finally, analogous results in terms of conversions and selectivity were achieved by replacing MeCN with 2-pentanone (data not reported), which was shown to be a good alternative co-solvent characterized by lower environmental and economic impact.

As expected, under the same reaction conditions no conversion was observed for the NHPI-catalyzed oxidation of ethylbenzene (ETB). In fact, the secondary C–H benzylic bond of ETB is less reactive than the tertiary C–H benzylic bond of CU, limiting the effect of the initiation phase.[41] Thus, in this case the presence of tiny amounts of initiators, i.e. MeCHO,[27] is mandatory.

It is important to highlight here that, in the overall economy of the chemical plant, a process characterized by higher selectivity but with a lower conversion degree could be more appealing than a process capable of providing high conversions but with significant formation of by-products. In fact, the formation of secondary derivatives could have a significant impact on the economy of the process

Recovery of the catalyst
NHPI recovery by precipitation and filtration
The low solubility of NHPI in low polar media could be advantageous in the phase of recovery of the catalyst. In fact, the removal of the co-solvent by distillation and the cooling to room temperature of the oxidized mixture containing NHPI favours precipitation of the catalyst due to the reduced polarity of the reaction medium.[42] Both the co-solvent recovered by distillation and the crystalline NHPI recovered by precipitation can be finally recycled by consolidated unit operations of the chemical industry.[43]

Following this approach and in order to investigate the combined effect of the composition of the residual mixture and of the temperature on NHPI precipitation degree, we prepared solutions with variable CU/CHP ratios, all containing 1% mol of NHPI, simulating different conversions of CU in the oxidation reaction and assuming complete selectivity in CHP. This assumption was made in order to simplify the experimental work but creating a mixture in line with the composition results previously discussed. In Fig. 3 we report, respectively, the temperatures of starting precipitation of NHPI (a) and the percentage of NHPI precipitated (b), after cooling the reaction mixture up to 25°C, versus the CU/CHP molar ratio.

Both these plots clearly show the role of CHP in progressively increasing the solution polarity, which is reflected in an increased solubility of NHPI in the reaction medium. Thus, the higher the yield in CHP, the lower the temperature of starting precipitation (Fig. 3(a)) and the lower the amount of NHPI recovered at room temperature (Fig. 3(b)). The NHPI precipitated in white crystals, which were filtered and compared with commercial samples by NMR and MS analysis to confirm the high degree of purity of the recovered material. NHPI was then successfully recycled into the oxidative process, confirming its unchanged catalytic efficiency.

The reported results show the versatility of the oxidation process for its development on industrial scale. It is evident that it could be possible to operate at lower CU conversion and almost complete selectivity in CHP (i.e. 20% CHP molar yield), with the advantage of having a high recovery of the catalyst (up to 75%) by precipitation and filtration. This point could be pursued (in already existing plant) either slowing down the reaction rate by reducing the reactor temperature (at fixed flow rate) or increasing the flow rate feed to the reactor (keeping the temperature constant). The main drawback in the first situation would be reduced productivity. In the second case the handling of higher volumes of unreacted cumene could be an onerous task in terms of equipment (for example the CU/CHP distillation unit) and exercise costs. Alternatively, it could be suitable to push the process towards higher conversion (i.e with a CHP molar yield above 35% in 6 h) but paying for reduced amounts of catalyst recovered by precipitation (~65%). In this case an increment in the cost in the next stage of catalyst recovery could be expected.
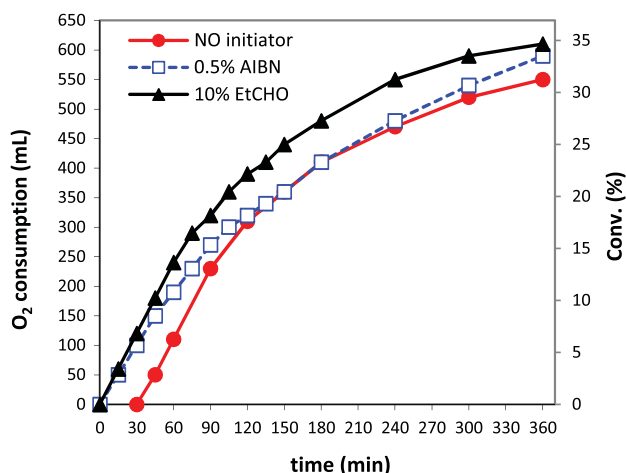

Figure 2. O_2 consumption and conversion versus reaction time for the aerobic oxidation of CU catalyzed by NHPI (1%). CU/MeCN = 8:3 (v:v). $P_{O2} = 1$ atm, $T = 298$ K.
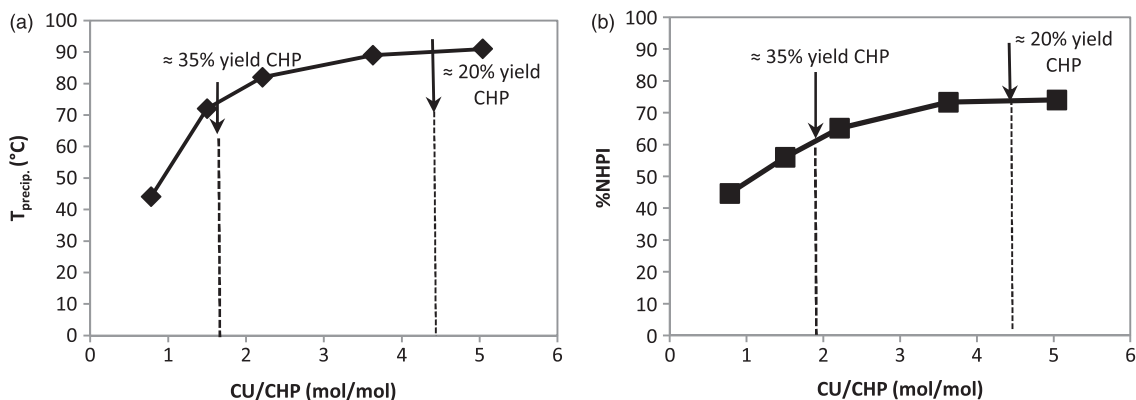
Figure 3. Temperature of precipitation (a) and NHPI recovered by precipitation at 25°C (b) versus CU/CHP molar ratio. Original NHPI content: 1% NHPI on molar basis respect to CU before oxidation.
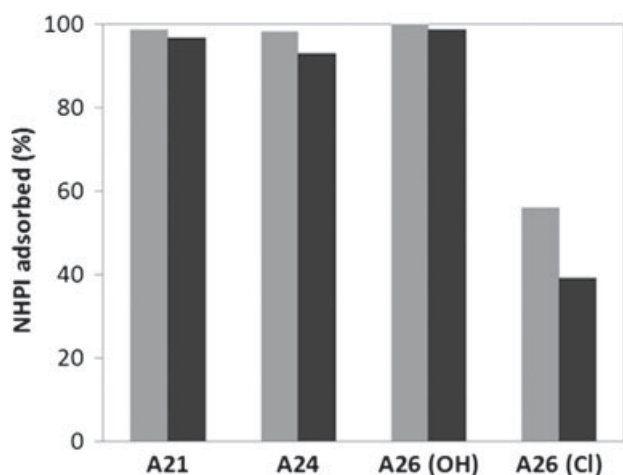

Figure 4. NHPI adsorption onto different Amberlysts from two ideal CU/CHP solutions containing 2 mg mL^{-1} of NHPI. Light grey bars: CU/CHP = 4.4:1(mol/mol); dark grey bars: CU/CHP = 1.85/1(mol/mol).

Figure 5. NHPI adsorption onto A26(OH) and A26(Cl).

In any case, after concentration and cooling, a variable amount of NHPI still remains in solution, requiring a different or additional mechanism for its recovery.

NHPI recovery by means of adsorbing solids

In recent patent applications we have already reported the possibility of recovering the catalyst by means of aqueous extraction.[44,45] Nevertheless, by considering the low solubility of NHPI in aqueous medium, the volumes of water necessary are high and consequently the application of this procedure for large-scale production is not recommended. Moreover, although the solubility of NHPI in water can be increased at basic pH, it is well documented in the literature that NHPI can be hydrolyzed under such conditions.[46,47] In 2009 ExxonMobil claimed the possibility of partially removing the catalyst from the reaction mixture by basic aqueous extraction or, even more important from an industrial application point of view, by treatment of the effluent with a solid adsorbent having basic properties.[48] In this way, the slightly acidic characteristics of the catalyst can be exploited. Metal oxides and ionic exchange basic resins were proposed as suitable adsorbing beds, including in the claims complete NHPI adsorption and total regeneration of the adsorbent bed and NHPI recovery by washing with ethanol.
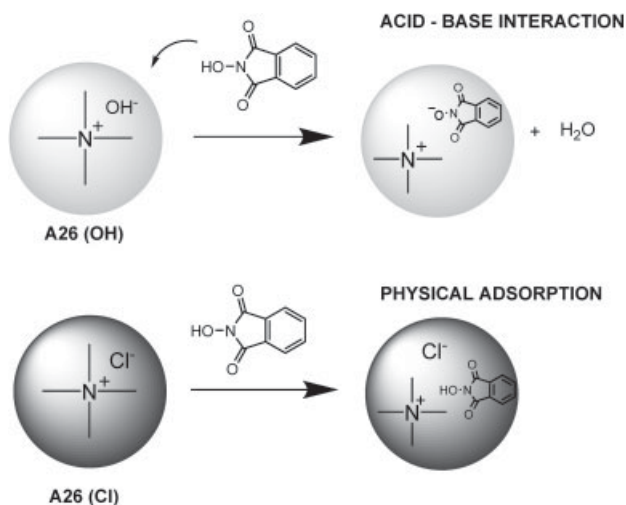
This approach appears to be the ideal solution for catalyst removal from the reaction medium. However, it would also suggest that a simple washing by means of polar solvents is not sufficient for recovery of the catalyst from the adsorbing solid, due to the strong acidic–basic interaction.

We decided to test this hypothesis by performing adsorption experiments in the presence of different basic resins. Among the adsorbing solids we tested A21 (a styrenic macroreticular resin bearing tertiary amino groups), A24 (an acrylic gel resin with tertiary amino groups), and A26(OH) (a styrene-divinylbenzene macroreticular resin with quaternary ammonium groups).

In order to verify the adsorption properties, 1 g of each resin was put into contact at 25°C for 24 h with 25 mL of two different ideal homogeneous solutions of CU/CHP (molar ratio of 4.4:1 and 1.85:1 respectively), both having a NHPI concentration of 2 mg mL^{-1}. The two solutions were chosen in order to simulate two clearly different environments for NHPI in terms of polarity. As expected, all the basic substrates showed very high adsorption efficiency, confirming that this approach is particularly effective in the extraction phase.

Figure 4 clearly shows how more than 95% of the original NHPI content is subtracted from the organic solution by this technique when basic supports are employed (grey bars). Moreover, the increased polarity of the NHPI solution due to the lower CU/CHP

Table 2. Freundlich constants for the adsorption of NHPI onto A26(26) and XAD761 from CU/CHP solutions at different composition at 25°C

	A26(Cl) in CU/CHP = 4.4/1 (mol/mol)	A26(Cl) in CU/CHP = 1.85/1 (mol/mol)	XAD761 in CU/CHP = 1.85/1 (mol/mol)
K_f	56.61	24.59	10.02
n	1.393	0.950	1.036

ratio did not significantly affect the efficiency of removal of the catalyst (Fig. 4, black bars). However, this latter behaviour was the first signal that this approach was not suitable for our purpose. In fact, as expected, washing of resins with high volumes of polar solvents (i.e. MeCN, that is the co-solvent used in the oxidation step) was not sufficiently effective for the removal phase, affording negligible results in terms of catalyst recovery from the adsorbent bed. In this case, NHPI being adsorbed by acid–base interaction, an acid solvent should be used. However, this solution would cause the degradation of residual CHP present on the adsorbent bed. Moreover, adsorbing solids need to be regenerated to their basic form and NHPI has to be re-converted to the unsalified specie to be recycled in the oxidation process. For these reasons, such solutions appear to be complex and expensive for industrial implementation.

Surprisingly, when the non-basic A26(Cl) resin, obtained by substitution the OH⁻ anion with a Cl⁻ one in A26(OH), was used as adsorbing solid, we still observed a good adsorption effect. Moreover, in this case the adsorption efficiency significantly decreased by increasing the polarity of the solution (from 56% to 39%, Fig. 4). This result induced us to think that, despite the reduced capability of the resin to adsorb the NHPI, such limitation could be beneficial during the removal phase from the solid support. We then decided to investigate in depth this different approach, no longer based on acid–base interaction but on physical adsorption of the catalyst on the solid support (Fig. 5).

Besides A26(Cl), an anionic resin, we also tested XAD761 (a non-ionic phenol–formaldehyde resin) and A15(Na) (a cationic styrene–divinylbenzene macroreticular resin with sulphonic groups). The adsorption data were obtained by plotting the adsorbed amount of NHPI per gram of resin (Q_{eq}, mg g^{-1}) versus the equilibrium concentration of the residual catalyst in solution (C_{eq}, mg mL^{-1}). They have been fitted by non-linear regression using the Freundlich model (Equation (1)), where K_f is the Freundlich constant and n is a constant related to the intensity of adsorption (heterogeneity factor): values of $n \geq 1$ are related to a favorable physical adsorption while for values of $n < 1$ the adsorption process is considered to be poor:[49,50]

$$Q_{eq} = K_f C_{eq}^{\frac{1}{n}} \qquad (1)$$

In the range of concentrations investigated Equation (1) was practically linear in particular in the case of data related to A26(Cl) and XAD761 in CU/CHP 1.85:1 solutions. Table 2 reports the parameters calculated according to Equation (1).

In general, it is possible to state that the higher the efficiency of the adsorption phase, the lower the output in the regeneration of the adsorbing bed finalized to the catalyst recovery. In particular,
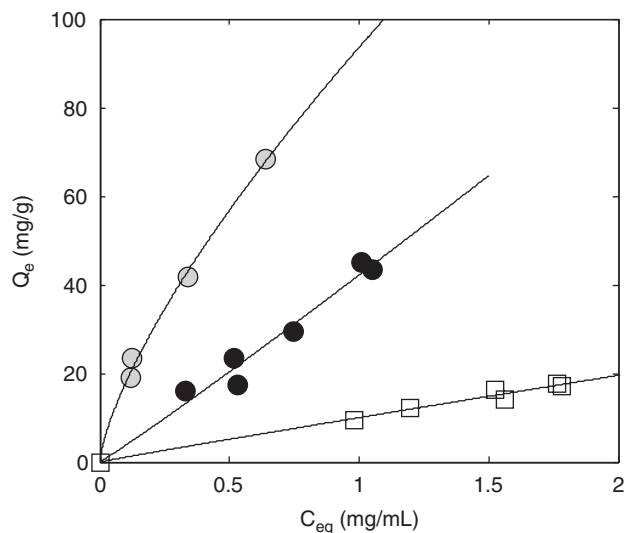

Figure 6. Isotherms of NHPI-adsorption from CU/CHP solutions at 25°C. (⬤ grey): A26(Cl) in CU/CHP = 4.4/1 (mol/mol); (⬤): A26(Cl) in CU/CHP = 1.85/1 (mol/mol); (☐): XAD761 in CU/CHP = 1.85/1 (mol/mol). Continuous lines represent the non-linear fitting of the data according Equation (1)).

we observed how the slope of the isotherms decreased by increasing the solution polarity, this suggesting that regeneration of resins by washing with polar solvents could be a practical solution. Even if this investigation represents a study of feasibility rather than a process optimization, we noticed how A26(Cl) showed higher adsorption capacity with respect to XAD761 (Fig. 6) and A15(Na), the latter having a performance comparable with that of XAD761 (data not shown).

Nevertheless, the decision which, among A26(Cl), XAD761, and A15(Na), would be the more suitable for our purpose is not obvious. Once again, a compromise should be made in choosing a resin having better performances during the adsorption phase and worse during the desorption phase or a solid support characterized by the opposite behavior. We think that, in general, this is the crucial point of all NHPI recovery approaches, whose solution cannot be based uniquely on lab-scale experiments. One more time the economic criteria based on the overall view of the entire process are the guidelines for the most suitable choice. Resins having better adsorbent capacities allow working with reduced volumes of solids and consequently reduced costs. But they pay with a need for high flow rates of solvent for their regeneration.

Our final aim here is to provide a viable solution to demonstrate the sustainability of the proposed approach. We decided to focus our attention on A26(Cl) as adsorbing bed sample to conduct adsorption–desorption cycles. The adsorption protocol was conducted by contacting 1 g of A26(Cl) with 25 mL of a CU/CHP (1.85/1 mol/mol) solution with a concentration of NHPI of 2 mg mL^{-1}. The CU/CHP ratio was chosen in order to simulate an ideal mixture after the oxidation stage corresponding to a CHP yield of about 35% (supposing complete selectivity in CHP). As detailed in Fig. 2 such a composition should give a precipitation of NHPI of about 65% after removing the co-solvent and cooling at room temperature. This means that 35% of NHPI still remains dissolved in the solution. The unrecovered amount of NHPI corresponds to a concentration of NHPI of about 4 mg mL^{-1}. The effective NHPI concentration adopted for the adsorption experiments (2 mg mL^{-1}) was chosen instead in order to simplify the experimental work during the preparation of the solutions. Moreover this choice
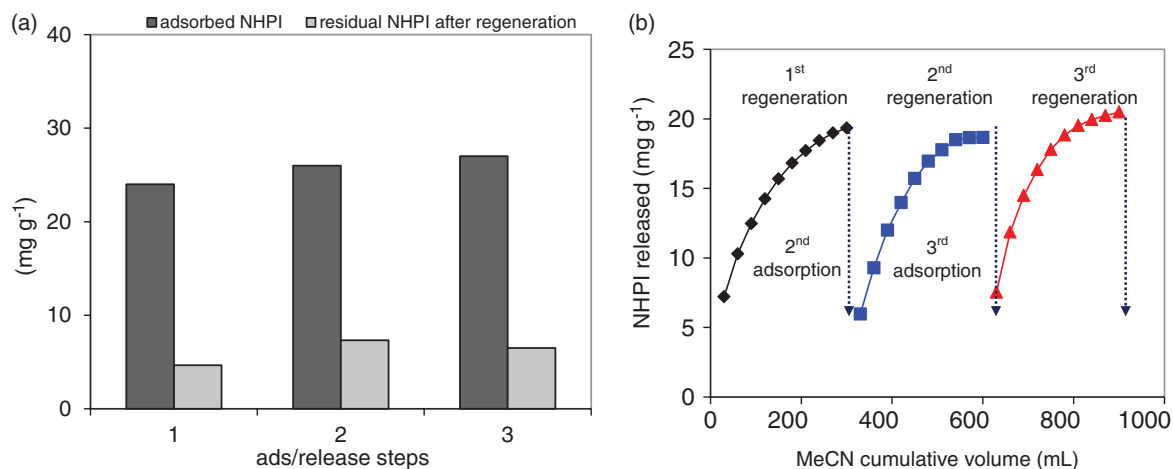
Figure 7. Adsorption of NHPI on A26(Cl) (mg of catalyst adsorbed per gram of A26(Cl) – Fig.7(a)) and regeneration of the adsorbing bed using MeCN. CU/CHP = 1.85/1 (mol/mol) (Fig.7(b)). Initial NHPI concentration: 2 mg mL^{-1}.

allowed preparation of a stable NHPI solution with higher CU/CHP ratio (4.4:1) and used for the data reported in Fig. 7, avoiding further precipitation on the resin and guaranteeing that NHPI removal could be ascribed only to adsorption by the solid bed. On the other side, the higher polarity of the solution with lower amount of catalyst would suggest an underestimation of the adsorption efficiency, which however should not affect evaluation of the effectiveness of the proposed solution.

Figure 7(a) reports the adsorption/desorption cycles of NHPI on A26(Cl), showing the reversibility of the process. In the adsorption phase, 1 g of solid bed kept in contact with 25 mL of CU/CHP solution (1.85:1) having 2 mg mL^{-1} of NHPI was sufficient to remove about 50% of the catalyst ($\approx$ 25 mg) in the first step. The regeneration of the resin was conducted by contacting the resin with 30 mL of MeCN at 50°C for 1 h and measuring the released amount of NHPI in solution by means of HPLC analysis with external standard. This protocol was repeated until about 80% ($\approx$ 20 mg) of the NHPI initially adsorbed on the Amberlyst was recovered (using a total amount of MeCN of about 300 mL – Fig. 7(b), 1st regeneration curve). The NHPI was recovered, characterized and successfully re-utilized in the oxidative process to verify its catalytic activity.

The same resin was used for more adsorption/desorption cycles (three in total), maintaining the same efficiency of catalyst removal (Fig. 7(a) and 7(b)). Moreover, HPLC analysis with an external standard output solution confirmed that CHP did not undergo decomposition after coming into contact with the adsorbent bed.

CONCLUSION

Is it possible to implement the *N*-hydroxyphthalimide homogeneous catalysis for industrial applications? On the basis of our research investigation on CU aerobic oxidation, we should conclude that the answer is still open, even if the route seems to be signed. The key point for the sustainability of the overall process is a valuable technology for the recovery of the catalyst.

Even if strictly economic considerations are out of the purpose of the present work, a few considerations on the costs and benefits of the proposed approach are possible, on the basis of our collaboration with Versalis S.p.A. State-of-the-art technology for the production of phenol via classical CU autoxidation enables a selectivity of 96% by limiting the conversion of CU to 25%.

By maintaining the same selectivity it was possible to increase conversion to values higher than 30%. This result represents savings both in CU demand per ton of phenol produced and also in terms of lower amount of CU to be recovered, that is reflected in reduced energy consumption. This balances in part the costs for solvent handling. Also, CA is the predominant by-product in the proposed process, significantly limiting the COD (chemical oxygen demand) present in waste effluent water. In fact, CA can be re-converted to CU via dehydration to methyl styrene and subsequent hydrogenation.

On the other side, the high cost of NHPI imposes, for the production of derivatives of low added value as phenol, complete recovery of the catalyst.

A possible approach was proposed, consisting of precipitation of the larger amount of NHPI fed (60–80%) after solvent distillation and cooling at room temperature, followed by a reversible adsorption process on adsorbing solids in a second unit. A26(Cl) was not presented as the optimal solution, but as a valuable example of the physical adsorption approach for catalyst removal from the reaction medium. The distilled solvent could be used in the desorption phase from the bed for recycling of the catalyst to be fed back into the oxidation reactor. As previously outlined, the higher the adsorption performance the lower the efficiency in the regeneration of the adsorbing bed. Both these aspects are relevant and need to be considered for the design of the ideal adsorbent bed, in order to find the best compromise between the amount of solid support and the volumes (or flow rates) of the solvent.

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