Heterogeneous & Homogeneous & Bio- & Nano-
CHEMCATCHEM
CATALYSIS

Accepted Article

Title: Solvent-free Aerobic Oxidation of Ethylbenzene Promoted by NHPI/Co(II) Catalytic System: The Key Role of Ionic Liquids

Authors: Gabriela Dobras, Magdalena Sitko, Manuel Petroselli, Manfredi Caruso, Massimo Cametti, Carlo Punta, and Beata Orlinska

To be cited as: *ChemCatChem* 10.1002/cctc.201901737

Link to VoR: http://dx.doi.org/10.1002/cctc.201901737

A Journal of ChemPubSoc Europe

WILEY-VCH www.chemcatchem.org

Solvent-free Aerobic Oxidation of Ethylbenzene Promoted by NHPI/Co(II) Catalytic System: The Key Role of Ionic Liquids

Gabriela Dobras,[a] Magdalena Sitko,[a] Manuel Petroselli,[b] Manfredi Caruso,[b] Massimo Cametti,[b] Carlo Punta,*[b] and Beata Orlińska*[a]

Abstract: The synergistic action between imidazolium based ionic liquid (IL) [bmim][$OcOSO_3$] and Co(II)/*N*-hydroxyphthalimide (NHPI) systems in the catalytic aerobic oxidation of ethylbenzene under solvent-free conditions have been here demonstrated by reaching a 35% conversion with 83% of selectivity in acetophenone at 80°C. This highly performing catalytic system have been selected after screening several different IL and Co(II) salt combinations, and making sure that the complete solubilization of the polar NHPI in the lipophilic medium, without thus requiring any chemical modification of the organic catalyst, could be attained. This solubilizing effect can be ascribed to a direct interaction between [bmim][$OcOSO_3$] IL and NHPI as revealed by a detailed NMR investigation which also allowed to exclude the formation of higher IL aggregates in the form of micelles or vesicles.

Introduction

Alkyl C-H bond activation by hydrogen atom transfer (HAT) processes is recently attracting a renewed interest. One of the most versatile and effective strategies to reach this goal is undoubtedly the oxidation of C-H bonds to selectively obtain the desired products. In this context, over the past 20 years, the role of *N*-hydroxyphthalimide (NHPI) in the aerobic oxidation of hydrocarbons, and in particular of alkylaromatics, has been highlighted by several studies. The reaction proceeds via a well-established free radical mechanism, where NHPI acts as precursor of the phthalimide–*N*-oxyl radical (PINO) (Fig. 1).[1-6] Compared with the peroxyl radicals involved in autocatalytic reactions, PINO abstracts the substrate's hydrogen at a faster rate (from 2 to 20 times faster)[2] and, at the same time, NHPI favors the propagation of the radical chain at the expense of termination reactions; both factors result in an increase in the oxidation rate of the hydrocarbon. NHPI-catalyzed oxidations of benzylic hydrocarbons are often carried out in the presence of transition metal salts, most commonly of Co(II), as co-catalysts, which play the role of activating molecular oxygen by electron transfer.[2] These species participate in the generation of the PINO radical (Fig. 1, path *i*), but also catalyze the decomposition reaction of initially formed hydroperoxides (Fig. 1, path *v*). Therefore, from a given alkylaromatic substrate, the main products obtained by employing a NHPI/Co(II) catalytic system would be the corresponding alcohol (Fig. 1, path *v*), and the products obtained by further oxidation or termination processes (aldehyde or ketone, and carboxylic acid). For example, oxidation of ethylbenzene (EB) in the presence of 10 mol% NHPI and 0.5 mol% Co(II) in acetic acid leads to acetophenone (AP) and 1-phenylethanol (PEOH).[7]

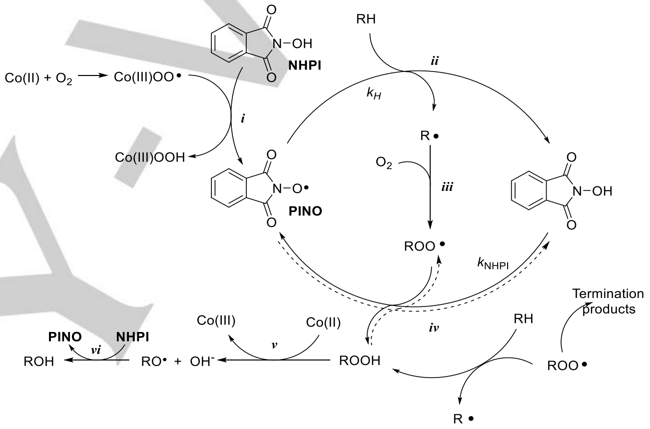


Figure 1. Mechanism of NHPI-catalyzed hydrocarbons oxidation[6]

NHPI-catalyzed oxidation reactions are most often carried out in polar solvents, such as acetic acid, acetonitrile (MeCN), and benzonitrile (PhCN), due to its poor solubility in non-polar hydrocarbons.[7-10] The complete solubilization of NHPI catalyst is essential, as NHPI can exploit its hydrogen atom donating action in the HAT processes shown in Fig. 1 only provided it is under homogeneous conditions. However, the use of polar solvents limits the implementation of the catalytic system in real oxidative processes.[11] As a consequence, given the advantages of operating under solvent-free conditions, especially from an economic point of view, several attempts have been made in order to increase NHPI solubility in apolar or weakly polar hydrocarbons. Main research avenues comprise: i) the structural modification of the NHPI unit to increase its lipophilicity, ii) the formation of solubilizing micelles or higher aggregates; iii) the use of additives into the reaction mixture. The first approach was introduced by Ishii and co-workers[12] and more recently widely explored by our research group.[13-15] It simply consists into the introduction of lipophilic chains on the aromatic ring of NHPI unit trying, at the same time, to avoid any increase of the bond dissociation energy (BDE) of the NO-H group which would consequently negatively affect the HAT process. The second approach was mainly addressed by Sasson and co-workers, and consisted in attaining partial phase transfer of NHPI into the alkylaromatic organic medium by means of formation of multilamellar vesicles made of lipophilic quaternary ammonium salts.[16,17] As to the last alternative, ionic

---

[a] G. Dobras, Dr. M. Sitko, Prof. B. Orlińska
Department of Organic Chemical Technology and Petrochemistry
Silesian University of Technology, Krzywoustego 4, 44-100 Gliwice, Poland
E-mail: beata.orlinska@polsl.pl
[b] Dr. Manuel Petroselli, Mr. Manfredi Caruso, Prof. M. Cametti, Prof. C. Punta.
Department of Chemistry, Materials and Chemical Engineering "G. Natta" Politecnico di Milano, Via Luigi Mancinelli 7, 20131 Milano, Italy
E-mail: carlo.punta@polimi.it

Supporting information for this article is given via a link at the end of the document.

liquids (ILs) have attracted our interest. Considered as alternative green solvents, ILs' advantages include low volatility as well as high polarity and chemical and thermal stability.[18] Several examples have been reported on the use of ILs as solvents for NHPI-mediated oxidations of a wide range of substrates[19,20], including the conversion of alkyl aromatic hydrocarbons, such as *p*-xylene, toluene, EB, cumene and their derivatives, to the corresponding carboxylic acids.[21-23] Among the wide range of ILs commercially available, it was demonstrated that the imidazolium-based ones are particularly suitable for promoting aerobic oxidations, as they can accelerate the electron transfer from metal ions to O_2 by stabilization of the resulting superoxyl radical.[24-27] Recently, some of us reported the oxidation of cumene and other alkylaromatic hydrocarbons to hydroperoxides in the presence of various *N*-hydroxyimides, including NHPI, in a broad range of ILs composed of 1-alkyl-3-methylimidazolium cations and bis(trifluoromethylsulfonyl)imide ($[NTf_2]$), $[PF_6]$, $[BF_4]$, *n*-octylsulfate ($[OcOSO_3]$), and $[CH_3OSO_3]$ anions.[28] However, the replacement of standard polar solvents, such as MeCN, with ILs might not be an improvement in terms of costs and process implementation. Interestingly, ILs have been also used as catalytic additives capable to promote oxidation reactions.[29] In this context, very recently, Mahmood *et al*. reported the beneficial effect of catalytic amounts of different imidazolium-based ILs (5% mol) on the aerobic oxidation of toluene to the corresponding benzoic acid, in the presence of NHPI (10% mol) and $Co(OAc)_2$ (0.5% mol).[30] In this case, the authors observed a behavior quite similar to that reported by Sasson and co-workers[16,17] with lipophilic ammonium salts, that is, the formation of a biphasic water/organic medium with the ILs acting as surfactant and/or phase transfer catalysts.

Here, we report on the aerobic oxidation of EB with NHPI/Co(II) system in the presence of catalytic amounts (0.25-1%) of the imidazolium-based ILs previously investigated as solvents.[28] The full set of experiments here described point to a marked effect of alkylsulfate ILs in the solubilization of NHPI in EB, which in turn allowed to perform substrate oxidation under solvent free conditions, reaching conversion up to 35% with selectivity higher than 82% in AP. Detailed analysis of the outcome of oxidation reactions performed by varying IL species, Co(II) counterions, with and without NHPI, presents a complex scenario with multiple concomitant equilibria which should be taken into account and points to the presence of a specific interaction between IL and NHPI.

Results and Discussion

Our investigation started by considering the effect on the EB oxidation catalyzed by $Co(acac)_2$ of the addition of catalytic amounts of a series of [bmim] ILs (0.5 mol%) under solvent-free conditions (Table 1). All the reactions were conducted at 80°C. As expected, the main products of the oxidation process were AP and PEOH, while ethylbenzene hydroperoxide (EBOOH) was rarely present and only in traces, due to the well-known Co(II)-induced hydroperoxide decomposition into alcohol and ketone. It is quite pertinent to note that while $[bmim][OcOSO_3]$ and $[bmim][C_{12}H_{25}OSO_3]$ ILs dissolve in the system at 80°C within the initial stages of the reaction (ca. 15 minutes), $[bmim][CF_3SO_3]$ and $[bmim][CH_3COO]$ ILs do not. By using $[bmim][BF_4]$, $[bmim][PF_6]$ and $[bmim][NTf_2]$, instead, a brown sediment formed in the flask. Qualitative analysis confirmed the presence of Co(II) in the powder. Keeping aside the data where not optimal dissolution occurred, a positive influence of the addition of ILs $[bmim][OcOSO_3]$ and $[bmim][C_{12}H_{25}OSO_3]$ (Table 1, entries 4 and 5) is evident. Conversion (α) doubles (from ca. 7 to ca. 12), while the AP selectivity slightly diminishes in favor of higher amounts of PEOH or EBOOH.

The reason for this improvement in conversion cannot be simply attributed to a polar effect. Solvent polarity changes would require addition of more significant quantities of polar co-solvent in order to have an observable effect, and this is not the case as demonstrated by entry 6 where PhCN was added (0.5 mol%) and no effect was observed.

Table 1. EB oxidation with oxygen in the presence of $Co(acac)_2$/IL

Entry	Additive	α [%]	S_{AP} [%]	S_{PEOH} [%]	S_{EBOOH} [%]
1[a]	-	0	-	-	-
2[a]	$[bmim][OcOSO_3]$	1.4	68.5	12.8	18.7
3	-	7.8	71.8	23.5	3.7
4	$[bmim][OcOSO_3]$	12.3	61.1	35.8	2.2
5	$[bmim][C_{12}H_{25}OSO_3]$	10.2	64.9	21.2	11.8
6	PhCN	5.3	75.0	20.3	4.2
7	$[bmim][BF_4]$	7.5	72.2	23.3	1.9
8	$[bmim][PF_6]$	6.2	73.1	8.7	16.2
9	$[bmim][CF_3SO_3]$	4.1	69.0	25.3	5.5
10	$[bmim][CH_3COO]$	4.1	62.0	26.5	10.5
11	$[bmim][NTf_2]$	3.6	65.7	18.8	9.2

EB 2 ml, $Co(acac)_2$ 0.1 mol%, additive 0.5 mol%, 0.1 MPa O_2, 80°C, 6 h, 1200 rpm [a] without $Co(acac)_2$

In the following step, we determined the influence of the addition of NHPI to the Co(II)/IL mixture. The results are presented in Table 2. ILs $[bmim][NTf_2]$, $[bmim][OcOSO_3]$, $[bmim][BF_4]$, and, to a minor extent, $[bmim][PF_6]$, led to an increase in conversion in the presence of NHPI (Table 2, entries 5,6,7, and 8, respectively). Again, it must be noted that NHPI (1 mol%) is not soluble by itself in EB at 80 °C, unless significant amounts of co-solvent are added (23% of MeCN in volume was reported to be necessary at 70 °C).[13] In the presence of both $[bmim][OcOSO_3]$ and $[bmim][C_{12}H_{25}OSO_3]$, instead, NHPI dissolved in the reaction mixture within the initial stages of the reaction (within 15 min). On the contrary, in the presence of $[bmim][BF_4]$, $[bmim][PF_6]$, or $[bmim][NTf_2]$, a brown sediment formed similarly to that previously described, and involving Co(II). Nevertheless, the high conversions measured also with these additives suggests a positive effect on NHPI solubilization (vide infra).

Table 2. EB oxidation with oxygen in the presence of NHPI/Co(acac)$_2$/IL

Entry	Additive	α [%]	S_{AP} [%]	S_{PEOH} [%]	S_{EBOOH} [%]
1[a]	-	3.9	58.2	4.1	36.9
2[a]	[bmim][OcOSO$_3$]	5.5	17.0	8.5	73.7
3	-	14.9	74.9	18.9	3.3
4	PhCN	14.1	70.5	22.9	2.0
5	[bmim][NTf$_2$]	21.2	75.5	16.7	3.1
6	[bmim][OcOSO$_3$]	19.2	77.7	15.6	3.3
7	[bmim][BF$_4$]	18.6	73.2	17.4	3.1
8	[bmim][PF$_6$]	15.6	70.9	12.5	7.8
9	[bmim][C$_{12}$H$_{25}$OSO$_3$]	13.5	77.1	18.3	4.4
10	[bmim][CH$_3$COO]	7.0	63.8	32.3	2.1
11	[bmim][CF$_3$SO$_3$]	9.4	62.0	20.1	2.1
12	[bmim][OcOSO$_3$] 0.25mol%	18.5	78.9	15.8	2.5
13	[bmim][OcOSO$_3$] 1mol%	24.5	81.1	13.4	2.3
14	[bmim][OcOSO$_3$] 2 mol%	11.7	40.3	8.8	49.0
15	[bmim][NTf$_2$] 1 mol%	13.9	72.6	20.5	2.3

EB 2 ml, NHPI 1 mol%, Co(acac)$_2$ 0.1 mol%, additive 0.5 mol%, 0.1 MPa O$_2$, 80°C, 6 h, 1200 rpm [a] without Co(acac)$_2$

Oxidation experiments with [bmim][OcOSO$_3$] were conducted also at 0.25, 1, and 2% of IL (Table 2, entries 12,13, and 14). Results showed that the highest conversions were obtained with 1% mol of IL, while the use of 2% mol [bmim][OcOSO$_3$] resulted in the formation of a separate phase, along with a decrease in EB conversion. On the other hand, lower IL content, i.e., 0.25 % mol also decreased the conversion. This indicates once more the crucial role of [bmim][OcOSO$_3$] in dissolving the NHPI/Co(II) system in the medium. Notably, a biphasic system associated to a detrimental effect is also observed with [bmim][NTf$_2$] at 1% mol (Table 2, entry 15). As to the selectivity of the oxidation process by the NHPI/Co(acac)$_2$/IL system, GC-FID and GC-MS analyses showed that the main products were AP and PEOH, with low content of EBOOH (2.0 - 7.8%). GC-MS analysis also showed the presence of (among others) benzoic acid, benzaldehyde, di(1-phenylethyl) ether, and 2.3-diphenylbutane.

Finally, as the oxidation of EB using ILs having [NTf$_2$], [PF$_6$], and [BF$_4$] counteranions, despite the above mentioned „complicating" feature of precipitate formation, contributed to reach a conversion up to 21.2% ([bmim][NTf$_2$]), we decided to explore the effect of differently substituted imidazolium countercations, among those commercially available, aiming at finding a more optimal solution (Table 3). It was shown that, in the case of ILs with [NTf$_2$] and [PF$_6$] anions, the conversion of EB improves along with increasing alkyl chain length, up to a value of 25% (Table 3, entry 5). It seems plausible to assume that the increase in length of the alkyl chain in the IL cation could positively influence the solubility of IL in EB. On the contrary, the increase in length of alkyl group in the IL with the [BF$_4$] anion caused a slight decrease in conversion from 18.6 to 13.3%. GC-FID analysis showed that the presence of [omim][PF$_6$] and [omim][BF$_4$] liquids intensified the side reactions, which led to the production of benzoic acid, di(1-phenylethyl) ether, 2.3-diphenylbutane, and possibly other high-boiling products that are undetectable by gas chromatography.

Table 3. Influence of the length of alkyl group in cation of ILs on EB oxidation with oxygen of in the presence of NHPI/Co(acac)$_2$

Entry	Additive	α [%]	S_{AP} [%]	S_{PEOH} [%]	S_{EBOOH} [%]
1	-	14.9	74.9	18.9	3.3
2	[emim][NTf$_2$]	19.3	70.6	16.2	3.2
3	[bmim][NTf$_2$]	21.2	75.5	16.7	3.1
4	[hmim][NTf$_2$]	22.8	77.3	15.2	3.5
5	[omim][NTf$_2$]	25.0	81.9	11.9	2.6
6	[bmim][PF$_6$]	15.6	70.9	12.5	7.8
7	[omim][PF$_6$]	23.7	71.6	12.1	4.3
8	[bmim][BF$_4$]	18.6	73.2	17.4	3.1
9	[omim][BF$_4$]	13.3	68.0	14.8	4.6

EB 2 ml, NHPI 1 mol%, Co(acac)$_2$ 0.1 mol %, additive 0.5 mol%, 0.1 MPa O$_2$, 80°C, 6 h, 1200 rpm

At this point, our working hypothesis for the interpretation of these data relies on the effect of ILs on the solubility of Co(II) salts, but more importantly, on the NHPI. As said, the effect of alkylammonium salts to NHPI catalytic performances has been already reported.[16,17,31] However, it was concluded that better solubility of NHPI under the tested conditions were due to the formation of vesicles, incorporating and solubilizing the catalyst. In order to better understand the role of ILs in the solubilization of NHPI, we embarked on a more detailed NMR study of the NHPI – IL interaction. Thus, we set out a series of ^{1}H-NMR experiments in toluene-d_8, and we selected [bmim][OcOSO$_3$] as IL of choice for the following tests. We first verified that NHPI becomes indeed soluble at room temperature up to 0.094 M in toluene-d_8 containing 2% IL, up to 0.047 M with IL at 1% and up to 0.023 M in 0.5 % IL conditions. Solubility of NHPI in toluene-d_8 without the addition of ILs is quite low (lower than 0.003 M). Given the narrow set of conditions, in terms of NHPI : IL ratios, which warrant a complete solubilization of both species, a classic titration experiment is impractical. This notwithstanding, it is possible to observe changes in the ^{1}H-NMR spectrum of the IL (2%$_{w/w}$) upon addition of sub-stoichiometric quantities of NHPI (0 – 0.5 equivalents). Indeed, as shown in Fig. 2 (spectra a-f), signals attributed to the imidazolium ion present a progressive upfield shift (of ca. 0.1 ppm for H2 and ca. 0.08 and 0.11 ppm for H4 and H5, respectively).

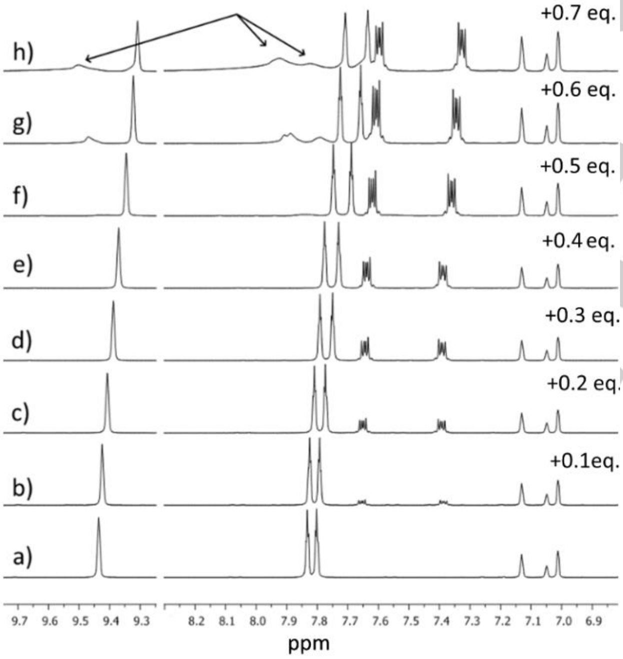


Figure 2. Portions of the ^{1}H-NMR spectra of [bmim][OcOSO3] IL (2%) alone a) and upon addition of increasing quantities of NHPI (from 0.1 to 0.7 equivalents b-h) at 300 K in toluene-d8.

These changes can be attributed to a direct interaction between the IL and the NHPI. Similar behavior was also observed in CDCl$_3$ (Fig. S1). Interestingly, upon further increase of the NHPI added, new, broad signals appear (see spectra g-h), which are consistent with the formation of higher aggregates involving IL and NHPI. A question naturally arises, and it is related to the initial aggregation state of the IL before the addition of NHPI. In other words, are micelle or other aggregates already present in solution, which then further assemble upon addition of NHPI? Or is the IL completely solvated? DOSY-NMR experiments performed with IL samples at 0.25, 1 and 2% w/w concentrations indicate the occurrence of a somewhat intermediate situation.

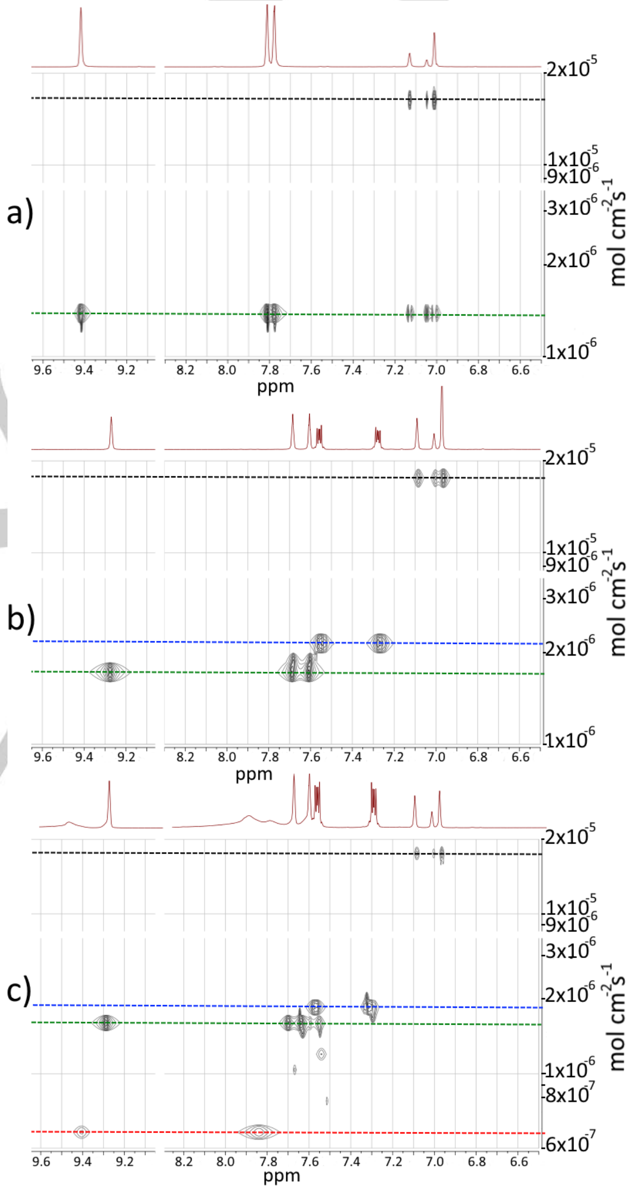


Figure 3. DOSY ^{1}H-NMR spectra of a) 0.25% (w/w) IL solution; b) a mixture of IL (1% w/w) and NHPI (0.5 eq.) and c) a mixture of IL (2% w/w) and NHPI (0.7 eq.), corresponding to the sample described before (see Fig. 2h). Colored dashed lines represent: black=toluene; green=IL; blue=NHPI; red=IL aggregates.

The diffusion coefficient measured for IL within the above range of concentrations change little and is found to be within 1.3 – 2.1

x 10^{-6} mol/cm^{2}s. No discrimination between cation and anion is observed Figure 3a.[32] Within the rough approximation given by the use of the Stokes-Einstein equation, it can be estimated a dynamic radius in the 20-30 Å range, which obviously does not represent a good match with isolated solvated ions, but rather with small ion-pairs aggregates.

However, it must be reminded that in all cases, there is no indication of higher aggregates in the NMR spectra. Thus, the IL in at 0.25 - 2% w/w concentration can be considered to be forming homogeneous solutions in toluene-d_8 with no phase separation or pseudo phases (micelle, vesicles, etc…). The addition of NHPI to IL (1% w/w) does not change much the situation (Fig. 3b) as the IL diffusion coefficient D is unaltered (D = 1.8 x 10^{-6} mol/cm^{2}s). Under these conditions, NHPI can be discriminated, although it features a very similar diffusion (D = 2.1 x 10^{-6} mol/cm^{2}s). A safe assumption would be to consider the two species closely interacting and forming an IL/NHPI associated species. DOSY analysis on the sample IL 2% w/w with NHPI, corresponding to spectrum h in Fig. 2, confirms instead the NHPI induced formation of higher IL aggregates (Fig. 3c). The broad signals appearing indeed correspond to novel diffusing species, whose diffusion coefficient is significantly lower (D = 6.3 x 10^{-7} mol/cm^{2}s), and whose dynamic radius could be estimated around 60 Å.

The above NMR study therefore confirms that NHPI interacts with [bmim][$OcOSO_3$] ionic liquid with the latter most probably in the form of small ion pair aggregates. The system remains homogeneous at r.t. and thus it can be extrapolated that under the oxidation conditions, no phase separation or vesicle formation occurs.

Semi-quantitative information of the efficiency of a given IL in making NHPI soluble in benzene were gathered by ATR FT-IR technique. The height of the peak corresponding to the carbonyl group (1732 cm^{-1}) was measured upon addition of increasing portions of [bmim][$OcOSO_3$] at room temperature (Fig. 4 and Fig. S2).

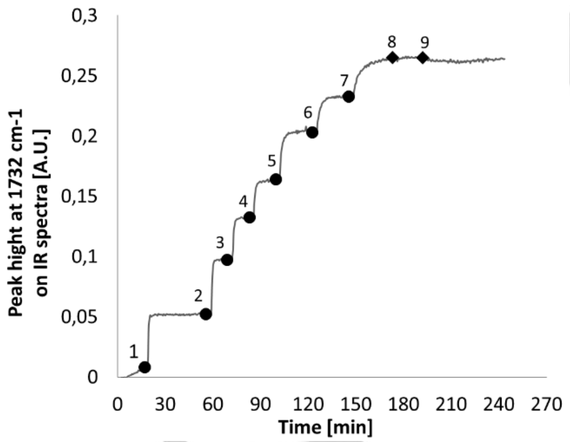


Figure 4. Plot of the intensity of the IR band centered at 1732 cm^{-1} (NHPI carbonyl group) versus time during the addition of [bmim][$OcOSO_3$] IL in portions (black dots represent time of each addition; black rhombus represent clear homogenous solution). Benzene 10 g (128 mmol), NHPI 0.2 g (1.2 mmol, 1 mol% vs benzene), each portion of [bmim][$OcOSO_3$] of about 0.3 mmol

After the addition of more than about 20 mol% [bmim][$OcOSO_3$] (vs NHPI) (Fig. 4, after first portion), the peak height increased significantly. A clear solution was obtained after the reaching of approximately 170 mol% [bmim][$OcOSO_3$] to NHPI (Fig. 4, after 7th portion). The results obtained, in line with the solubility data obtained by NMR, confirmed that the mixture of NHPI and [bmim][$OcOSO_3$] dissolves in a non-polar hydrocarbon much better than NHPI alone. For comparison, the same experiments were carried out with [bmim][NTf_2] and PhCN. Adding over 5000 mol% of [bmim][NTf_2] and 11000 mol% of PhCN to the suspension of NHPI in benzene did not cause the NHPI to dissolve.

Table 4. EB oxidation with oxygen in the presence of Co(II) or NHPI/Co(II) and [bmim][$OcOSO_3$]

Entry	Co(II)	[bmim][$OcOSO_3$] [mol%]	α [%]	S_{AP} [%]	S_{PEOH} [%]	S_{EBOOH} [%]
1[a]	-	-	0	-	-	-
2[a]	-	0.5	1.4	68.5	12.8	18.7
3[a]	$CoCl_2$	-	2.8	nd	nd	81.4
4[a]	$CoCl_2$	0.5	1.8	nd	nd	73.9
5[a]	$Co(C_{17}H_{35}COO)_2$	-	6.4	69.6	22.6	4.5
6[a]	$Co(C_{17}H_{35}COO)_2$	0.5	11.0	69.8	19.7	8.4
7[a]	$Co(acac)_2$	-	7.8	71.8	23.5	3.7
8[a]	$Co(acac)_2$	0.5	12.3	61.1	35.8	2.2
9[a]	$Co(OAc)_2$	-	3.4	34.2	9.3	53.0
10[a]	$Co(OAc)_2$	0.5	8.4	64.8	23.1	9.0
11	-	-	3.9	58.2	4.1	36.9
12	-	0.5	5.5	17.0	8.5	73.7
13	$CoCl_2$	-	6.5	nd	nd	87.5
14	$CoCl_2$	0.5	19.0	39.7	10.0	41.7
15	$Co(C_{17}H_{35}COO)_2$	-	13.8	67.1	24.8	3.6
16	$Co(C_{17}H_{35}COO)_2$	0.5	14.0	73.3	19.5	2.3
17	$Co(acac)_2$	-	14.9	74.9	18.9	3.3
18	$Co(acac)_2$	0.5	19.2	77.7	15.6	3.3
19	$Co(OAc)_2$	-	8.2	15.7	6.4	72.6
20	$Co(OAc)_2$	0.5	30.1	79.7	11.3	5.0
21	$Co(OAc)_2$	1	35.2	82.7	7.4	2.9

EB 2 ml, NHPI 1 mol%, Co(II) 0.1 mol%, 0.1 MPa O_2, 80°C, 6 h, 1200 rpm; [a] without NHPI; nd – not determined

Finally, the recognition of the need to consider the present catalytic mixture as a quite complex, multiple equilibria system led us to study the effect of Co(II) counteranion, seeking the optimal condition for the EB oxidation process. Therefore, the influence of the addition of [bmim][OcOSO$_3$] on the oxidation of EB in the presence of various Co(II) salts, with and without NHPI, was studied. The results are presented in Table 4. Blank experiments testing the activity of various Co(II) salts alone show that conversion remains in the range 2.8 – 6.4 %, probably following the different solubility of the metal salts in EB. Not surprisingly, Co(C$_{17}$H$_{35}$COO)$_2$ presents the highest conversion.

Confirming the overall picture resulting from the previously described data, adding [bmim][OcOSO$_3$] into the reaction mixture caused an increase of EB conversion (Table 4, entries 3-10). The largest enhancement was observed with Co(OAc)$_2$, where this effect was accompanied by a decrease in selectivity towards EBOOH, from 53.0% to 9.0%. Again, we interpret these results in term of increased solubility of Co(II) ions in the presence of IL. Interestingly, the addition of NHPI to the Co(II)/IL systems caused a further increase in the conversion of EB (Table 4, entries 13-20). The biggest effect was observed in the CoCl$_2$ and Co(OAc)$_2$ cases. Notably, highest conversion and selectivity were obtained with the NHPI/Co(OAc)$_2$/[bmim][OcOSO$_3$] system and, to the best of our knowledge, this represents the highest EB conversion ever achieved for the oxidation of EB under mild solvent-free conditions.

As we felt the need to confirm our thesis which attributes the observed improvement on reaction conversion obtained by using catalytic quantities of ILs to their capability to render NHPI soluble in EB, we decided to test lipophilic NHPI derivatives **1** and **2** (Fig. 5) under our experimental conditions (viz. with catalytic ILs present). We reasoned that these derivatives, much more soluble in neat EB regardless the presence of an additive, would respond to the presence of the IL in a way inversely proportional to their lipophilic character. According to previously reported data,[13] **2** is characterized by a much better solubility in non-polar hydrocarbons than NHPI, but lower than that of **1**.

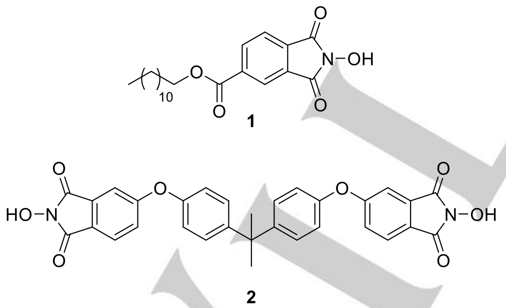


Figure 5. Lipophilic NHPI derivatives **1** and **2**.

In complete agreement with our expectations, the addition of lipophilic [bmim][OcOSO$_3$] to **1** caused a slight increase in EB conversion from 29 to 35% (Table 5, entries 1 and 2), which however is not present with [bmim][C$_{12}$H$_{25}$OSO$_3$] (compare 29.2 vs. 29.3, entries 1 and 5). On the other hand, the IL has a more marked effect when the catalyst used is **2**. In this case, conversion increases from 11.6 to 17.8 % (entries 3 and 4). It was observed that after IL addition, the catalysts were dissolved in the system in the initial stages of the reaction (up to the 15th minute). A negative influence was instead noticed when using ILs composed of the lipophilic cation 1-octyl-3-methylimidazolium and [BF$_4$], [PF$_6$], and [NTf$_2$] anions, despite the fact that **1** as well as the ILs were dissolved in the system, however, this effect is easily interpreted as due to the interaction of these counteranion with the Co(II) salts, as evidenced in the previously described set of experiment. As the solubilizing effect is now negligible, these ILs have only a detrimental effect.

Table 5. EB oxidation with oxygen in the presence of lipophilic derivatives of NHPI, Co(acac)$_2$ and lipophilic ILs

Entry	Additive	Catalyst	α [%]	S_{AP} [%]	S_{PEOH} [%]	S_{EBOOH} [%]
1	-	**1**	29.2	73.9	10.1	12.4
2	[bmim][OcOSO$_3$]	**1**	34.9	87.1	8.4	1.8
3	-	**2**	11.6	27.5	3.3	59.0
4	[bmim][OcOSO$_3$]	**2**	17.8	66.8	14.1	11.5
5	[bmim][C$_{12}$H$_{25}$OSO$_3$]	**1**	29.3	84.6	8.9	1.6
6	[omim][BF$_4$]	**1**	26.9	78.5.	10.9	4.7
7	[omim][NTf$_2$]	**1**	24.9	77.7	5.4	7.2
8	[omim][PF$_6$]	**1**	22.5	74.3	14.0	8.7

EB 2 ml, **1** 1 mol%, **2** 0.5 mol%, Co(acac)$_2$ 0.1 mol%, additive 0.5 mol%, 0.1 MPa O$_2$, 80°C, 6 h, 1200 rpm

Conclusions

In this study, we investigated the role and effect of the addition of tiny amounts of imidazolium based ILs in solvent-free oxidation of EB with oxygen in the presence of NHPI/Co(II) catalytic systems. A positive influence of the IL which is not ascribable to polar effect have been observed. The largest increase in conversion was obtained when the ionic liquid with a lipophilic anion [bmim][OcOSO$_3$] was used. The IL resulted to be able to promote the direct solubilization of NHPI in EB, without thus requiring its chemical modification by introduction of lipophilic chains on the aromatic ring. Among the cobalt(II) salts the highest conversion of EB was attained when the system composed of NHPI (1 mol%), Co(OAc)$_2$ (0.1 mol%), and [bmim][OcOSO$_3$] (1 mol%) was applied: the conversion was equal to 35% (only 8.2% without IL). Such catalytic efficiency can be considered the highest reported to date in terms of conversions of EB under mild conditions. The crucial role of [bmim][OcOSO$_3$] IL in promoting NHPI solubilization in the apolar medium was revealed by FT-IR and ^{1}H-NMR analysis. In particular, the latter technique confirmed the occurrence of a direct interaction between the organocatalyst and small ion-pairs aggregates of IL. The effect of the addition of IL in the reaction medium significantly decreased when operating in the presence of lipophilic catalysts **1** and **2**, which are significantly more soluble in EB than NHPI and for which thus the solubilization effect is neglible. Furthermore, the choice of [bmim][$OcOSO_3$] is particularly beneficial as it is considered a "green" IL,[33] being halogen-free, hydrolysis-stable and all the more so alkylsulfate anions are known to exhibit good rates of biodegradation.[34]

Experimental Section

Ethylbenzene (EB) (Acros 99.8%) was purified by washing with H_2SO_4 and vacuum distillation. Cobalt(II) acetylacetonate ($Co(acac)_2$), cobalt(II) chloride, cobalt(II) acetate tetrahydrate ($Co(OAc)_2{\cdot}4H_2O$), cobalt(II) stearate, *N*-hydroxyphthalimide (NHPI), sodium lauryl sulfate and benzonitrile (PhCN) were purchased from commercial sources and used without purification. 4-Dodecyloxycarbonyl-*N*-hydroxyphthalimide (**1**) and 4,4'-(4,4'-isopropylidenediphenoxy)bis(*N*-hydroxyphthalimide) (**2**) were synthesized according to a previously described procedure.[13,15] Ionic liquids: 1-butyl-3-methylimidazolium chloride [bmim][Cl], 1-ethyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide ([emim][NTf_2]), 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide ([bmim][NTf_2]), 1-hexyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide ([hmim][NTf_2]), 1-butyl-3-methylimidazolium octyl sulfate ([bmim][$OcOSO_3$]), 1-butyl-3-methylimidazolium acetate ([bmim][CH_3COO]), 1-butyl-3-methylimidazolium trifluoromethanesulfonate ([bmim][CF_3SO_3]), 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]), 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]), 1-octyl-3-methylimidazolium hexafluorophosphate ([omim][PF_6]), and 1-octyl-3-methylimidazolium tetrafluoroborate ([omim][BF_4]) were commercial materials and were dried under vacuum before use (50°C, 0.1 bar). 1-Octyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide ([omim][NTf_2]) was prepared according known procedure.[35] 1-Butyl-3-methylimidazolium lauryl sulfate ([bmim][$C_{12}H_{25}OSO_3$]) was prepared according procedure described in literature [33] with small modifications. [Bmim][Cl] (5.00 g, 28.6 mmol) and sodium lauryl sulfate (6.47 g, 22.40 mmol) were dissolved in water (20 ml) and mixed for 6 h at 60°C. The water was slowly removed under vacuum and a white solid precipitated. Dichloromethane (15 ml) was added to extract the product from the mixture and the white solid filtered off. To the clear, slightly yellow filtrate water (20 ml) was added to remove chloride impurities (according procedure described in [33]). After a second addition of 20 ml water, it was observed that the product started to foam and formed a white thick oil. The ionic liquid was then extracted with large portions of CH_2Cl_2 (6x150 ml) which was removed in vacuum to give a colorless oil which crystallized at room temperature. Yield 77%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 9.11 (s, 1 H), 7.77 (s, 1 H), 7.70 (s, 1 H), 4.16 (t, 2 H, *J=8.0 Hz*), 3.85 (s, 3 H), 3.67 (t, 2 H, 6.0 Hz), 1.76 (m, 2 H), 1.47 (m, 2 H), 1.33-1.19 (m, 20 H), 0.81-0.94 (m, 6 H) (Fig. S3). ^{13}C NMR (400 MHz, DMSO-d_6) δ ppm: 136.50, 123.59, 122.25, 65.42, 48.47, 35.71, 31.33, 31.26, 29.14-28.90, 28.75, 28.68, 25.50, 22.06, 18.74, 13.91, 13.23 (Figs. S4 and S5). ESI-HRMS: $[bmim]^+$ found 139.1238 calcd: 139.1237, $[C_{12}H_{25}OSO_3]^-$ found 265.1471 calcd: 265.1502.

The oxidation reactions were performed in a gasometric apparatus as described in ref. [15]. EB, *N*-hydroxyimide, cobalt(II) salt, and the ionic liquid were placed in a 10 ml flask connected to a gas burette filled with oxygen under atmospheric pressure. The reaction was conducted at 80°C for 6 h with magnetic stirring at 1200 rpm. The oxygen uptake (n_{O2}) was measured, recalculated for normal conditions (273 K, 1 atm), and this value was used to calculate the EB conversion (α). The amount of EBOOH was determined iodometrically according to the described method[36], and the result was used for the calculation of the EBOOH selectivity (S_{EBOOH}).

$$n_{O_2} = \frac{V_{O_2} \cdot 273 \cdot p}{101325 \cdot 22.415 \cdot T}[mol]$$

$$\alpha = \frac{n_{O_2}}{n} \cdot 100\%$$

$$S_{EBOOH} = \frac{n_{OOH}}{n_{O_2}} \cdot 100\%$$

n_{O2} –amount of oxygen consumed at normal conditions [mol], V_{O2} – volume of oxygen consumed [dm^3], p - pressure [Pa], T – room temperature [K], α – conversion [%], n – amount of hydrocarbon used [mol], S_{EBOOH} – hydroperoxide selectivity [%], n_{OOH} – amount of EBOOH formed [mol]. EBOOH is thermally unstable and easily decomposes to PEOH and AP. Thus, before GC analysis, the hydroperoxide was quantitatively reduced to PEOH by addition of triethyl phosphite $(EtO)_3P$, which is oxidized to triethyl phosphate $(EtO)_3PO$.[37] The amount of PEOH determined by GC was the sum of the alcohol and hydroperoxide formed. In order to calculate the PEOH selectivity, the amount of EBOOH determined by iodometric analysis was subtracted. The amount of AP was determined based on the GC analysis.

GC analysis was performed using an Agilent Technologies 7890C gas chromatograph (Zebron ZB-5HT capillary column) with an FID detector and *p*-methoxytoluene as the internal standard. GC-MS analysis of the products was performed using an Agilent 7890C gas chromatograph (HP-5ms capillary column, 30 m x 0.25 mm x 0.25 µm, helium 1 ml/min) coupled with an Agilent5975C mass spectrometer with EI (70 eV). The products were identified using the NIST/EPA/NIH Mass Spectral Library. The ^{1}H NMR or ^{13}C NMR spectra were recorded in deuterated chloroform (chloroform-d_1) or dimethyl sulfoxide (DMSO-d_6) with a Varian 600 MHz spectrometer or Agilent 400 MHz NMR. ^{1}H-NMR titration data in Figure 2 and DOSY spectra were recorded with a Bruker Avance 400 MHz spectrometer. DOSY pulse sequence ledbpgp2s was used (LED bipolar gradient), NS=14, DS=4, D1 = 3 s, D16 = 0.2 ms; D20 = 60 ms; D21 = 5ms, P30 = 2.59 ms; data processing were performed with both Topspin and Mestre Nova software. High-resolution electrospray ionisation mass spectroscopy (ESI-HRMS) experiments were performed using a Waters Xevo G2 QTOF instrument equipped with an injection system (cone voltage 50 V; source 120 °C).

The solubility tests for the NHPI were performed on a Mettler-Toledo iC10 FT-IR spectrometer equipped with an ATR probe. The ATR probe was immersed into a suspension of benzene (10 g or 20 g) and NHPI (0.2 or 0.4 g; 1 mol% vs benzene). Then, IL or PhCN was added in portions, and the height of the peak corresponding to the carbonyl groups (1732 cm^{-1}) of NHPI was recorded in real time.

Acknowledgements

Financial support from the National Science Centre of Poland (UMO-2014/13/B/ST8/04256) is gratefully acknowledged. M.C. and C.P. thank MIUR for finacial support (Funds for fundamental research, ANVUR call n. 20/2017, 15-06-2017).

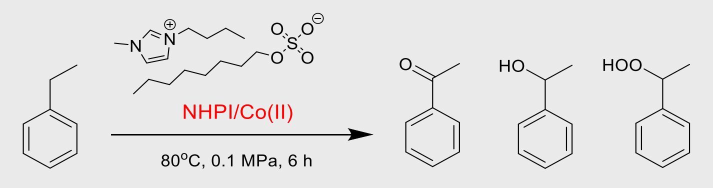
Keywords: ethylbenzene • ionic liquids • *N*-hydroxyphthalimide • oxidation • oxygen

[1] Y. Ishii, S. Sakaguchi, in *Modern Oxidation Methods* (Ed. J.E. Baeckvall), Wiley-VCH, Weinheim, **2004**, pp. 119-163.

[2] F. Recupero, C. Punta, *Chem. Rev.* **2007**, *107*, 3800-3842.

[3] S. Coseri, *Catal. Rev.* **2009**, *51*, 218-292.
[4] L. Melone, C. Punta, *Beilstein J. Org. Chem.* **2013**, *9*, 1296-1310.
[5] K. Chen, P. Zhang, Y. Wang, H. Li, *Green Chem.* **2014**,*16*, 2344-2374.
[6] R. Amorati, M. Lucarini, V. Mugnaini, G.F. Pedulli, F. Minisci, F. Recupero, F. Fontana, P. Astolfi, L. Greci, *J. Org. Chem.* **2003**, *68*, 1747-1754.
[7] Y. Ishii, S. Sakaguchi, *Catal. Surv. Jpn.* **1999**, *3*, 27-35.
[8] Y. Tashiro, T. Iwahama, S. Sakaguchi, Y. Ishii, *Adv. Synth. Catal.* **2001**, *343*, 220-225.
[9] B. Orlińska, J. Zawadiak, *Reac. Kinet. Mech. Cat.* **2013**, *110*, 15–30.
[10] C. Miao, H. Zhao, Q. Zhao, C. Xia, W. Sun, *Catal. Sci. Technol.* **2016**, *6*, 1378-1383.
[11] L. Melone, S. Prosperini, G. Ercole, N. Pastori, C. Punta, *J. Chem. Technol. Biotechnol.* **2014**, *89*, 1370-1378.
[12] N. Sawatari, T. Yokota, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **2001**, *66*, 7889–7891.
[13] M. Petroselli, P. Franchi, M. Lucarini, C. Punta, L. Melone, *ChemSusChem* **2014**, *7*, 2695-2703.
[14] M. Petroselli, L. Melone, M. Cametti, C. Punta, *Chem. Eur. J.* **2017**, *23*, 10616-10625.
[15] K. Kasperczyk, B. Orlińska, J. Zawadiak, *Cent. Eur. J. Chem.* **2014**, *12*, 1176-1182.
[16] N. Taha, Y. Sasson, *Org. Proc. Res. Develop.* **2010**, *14*, 701-704.
[17] R.D. Patil, B. Fuchs, N. Taha, Y. Sasson, *ChemistrySelect*, **2016**, *1*, 3791-3796.
[18] H. Weingärtner, *Angew. Chem. Int. Ed.* **2008**, *47*, 654-670.
[19] J.R. Wang, L. Liu, Y.F. Wang, Y. Zhang, W. Deng, Q.X. Guo, *Tetrahedron Lett.* **2005**, *46*, 4647-4651.
[20] S. Koguchi, T. Kitazume, *Tetrahedron Lett.* **2006**, *47*, 2797-2801.
[21] I. Yavari, E. Karimi, *Synth. Commun.* **2009**, *39*, 3420–3427.
[22] T. Lu, M. Lu, W. Yu, Z. Liu, *Croat. Chem. Acta* **2012**, *85*, 277-282.
[23] Y. Wang, T. Lu, *Chiang Mai J. Sci.* **2014**, *41*, 138-147.
[24] M. Tokunaga, J.F. Larrow, F. Kakiuchi, E.N. Jacobsen, *Science* **1997**, *277*, 936-938.
[25] C.E. Song, W.H. Shim, E.J. Roh, S.-G. Lee, J.H. Choi, *Chem. Commun.* 2001, 1122-1123.
[26] C.E. Song, D.-U. Jung, S.Y. Choung, E.J. Roh, S.-G. Lee, *Angew. Chem. Int. Ed.* **2004**, *43*, 6183-6185.
[27] D.S. Choi, D.H. Kim, U.S. Shin, R.R. Deshmukh, S.-G. Lee, C.E. Song, *Chem. Commun.* **2007**, 3467-3469.
[28] G. Dobras, B. Orlińska, *Appl. Catal., A*, **2018**, *561*, 59-67.
[29] S. Xu, C. Huang, J. Zhang, J. Liu, B. Chen, *Korean J. Chem. Eng.*, **2009**, *26*, 985-989.
[30] S. Mahmood, B.H. Xu, T.L. Ren, Z.B. Zhang, X.M. Liu, S.J. Zhang, *Mol. Catal.* **2018**, *447*, 90-96.
[31] D. Pyszny, B. Orlińska, *Reac. Kinet. Mech. Cat*. **2018**, *124,* 123-138.
[32] M. Zanatta et al., *Phys. Chem Chem. Phys*. **2019**, *21*, 2567-2571.
[33] P. Wasserscheid, R. Hal, A. Bösmann, *Green Chem*. **2002**, *4*, 400-404.
[34] A. Jordan, N. Gathergood, *Chem. Soc. Rev.* **2015**, *44*, 8200-8237.
[35] C. Yao, J.L. Anderson, *Anal. Bioanal. Chem.* **2009**, *395*, 1491-1502.
[36] J. Zawadiak, D. Gilner, Z. Kulicki, S. Baj, *Analyst* **1993**, *118*, 1081-1083.
[37] P. Wiklund, C. Karlsson, M. Levin, *Anal. Sci.* **2009**, *25*, 431-436.

FULL PAPER



The positive effect of the addition of catalytic amounts of [bmim][$OcOSO_3$] in NHPI/Co(II) catalyzed oxidation of ethylbenzene which is not ascribable to polar effect have been reported. The IL promoted the direct solubilization of NHPI in hydrocarbon by means of interaction with small ion-pairs aggregates of IL.

Gabriela Dobras, Magdalena Sitko, Manuel Petroselli, Manfredi Caruso, Massimo Cametti, Carlo Punta, and Beata Orlińska**

Page No. – Page No.

Solvent-free Aerobic Oxidation of Ethylbenzene Promoted by NHPI/Co(II) Catalytic System: The Key Role of Ionic Liquids