Catalysis Communications 27 (2012) 124–128

Contents lists available at SciVerse ScienceDirect

Catalysis Communications

journal homepage: www.elsevier.com/locate/catcom

Short Communication

Metal free: A novel and efficient aerobic oxidation of toluene derivatives catalyzed by N′, N″, N‴, -trihydroxyisocyanuric acid and dimethylglyoxime in PEG-1000-based dicationic acidic ionic liquid

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A R T I C L E I N F O

Article history:
Received 28 May 2012
Received in revised form 19 July 2012
Accepted 19 July 2012
Available online 28 July 2012

Keywords:
Aerobic oxidation
Alkylaromatics
THICA-DMG
PEG_{1000}–DAIL

A B S T R A C T

A non-metal catalytic system containing of N′, N″, N‴, -trihydroxyisocyanuric acid (THICA) and dimethylglyoxime (DMG) is described for the selective oxidation of toluene derivatives with dioxygen in PEG-1000-based dicationic acidic ionic liquid (PEG_{1000}–DAIL). Several toluene derivatives were efficiently oxidized to corresponding acids under mild conditions. The oxidation followed a radical pathway and a possible mechanism was proposed. Both the catalyst and PEG_{1000}–DAIL could be reused at least eight times without significantly decreasing the catalytic activity.

1. Introduction

The development of new, efficient and sustainable processes for the mild oxidative functionalization of toluene derivatives continues to be a challenging problem of modern chemistry, as evidenced by the increasing number of research publications in this field [1]. Toluene derivatives are known as the abundant carbon raw materials but are inert for selective transformations under mild conditions [2]. Traditional approaches for oxidation were based on metal-catalyzed activation, but the disadvantages of metallic toxicity could not be avoided [3]. N-hydroxyphthalimide (NHPI), which is a valuable carbon radical producing catalyst (CRPC) for the aerobic oxidation, are unstable at >80 °C and has bad performance on the oxidation of electron-withdrawing substituted toluene [4–6]. In recent years, the more thermally stable CRPC N′, N″, N‴, -trihydroxyisocyanuric acid (THICA) is attracting attention due to its highly catalytic efficiencies for the aerobic oxidation of both electron-donating and electron-withdrawing substituted toluene [7–9]. Nonetheless, THICA suffers from two major disadvantages: (1) it usually combines with $Co(OAc)_2$ to complete the catalytic oxidation and employs corrosive acetic acid as solvent. (2) THICA is expensive but no attempt is made on recycling of it [10].

Ionic liquids (ILs), as environmental friendly reaction media or catalysts, have attracted increasing attention over the last decade, and one reason is the expected dissolution or immobilization of the catalyst in the IL that would allow the recycling of the tandem catalyst/solvent [11,12]. Furthermore, ILs have excellent advantages like negligible volatility, thermal stability, remarkable solubility, and a variety of available structures [13]. Recently, the novel PEG-1000-based dicationic acidic ionic liquid (PEG_{1000} -DAIL), which exhibits a temperature-dependent phase behavior with toluene, is widely used in the organic reaction (Scheme 1) [14].

Herein we introduce an efficient, metal-free protocol for the aerobic oxidation of toluene derivatives to the corresponding acids catalyzed by THICA/dimethylglyoxime (DMG) with PEG_{1000}–DAIL as solvent, wherein both the catalyst and PEG_{1000}–DAIL can be successfully recovered and reused.

2. Experimental section

2.1. Materials and methods

All starting materials were purchased from commercial sources and used without further treatment. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) were recorded on a Bruker 500 spectrometer with tetramethylsilane (TMS) as an internal standard. IR spectra were recorded on a Bruker Vector 22 infrared spectrometer, as KBr pellets with absorption in cm^{-1}. EPR spectra were obtained with a Bruker EMX-10/12 spectrometer. High performance liquid chromatography (HPLC) experiments were performed on a liquid chromatograph (Dionex Softron GmbH, America). The conversions of the substrates and the selectivities of products were estimated from the peak areas based on the internal standard technique. The products were determined in some cases by comparison of their HPLC with those of authentic samples.

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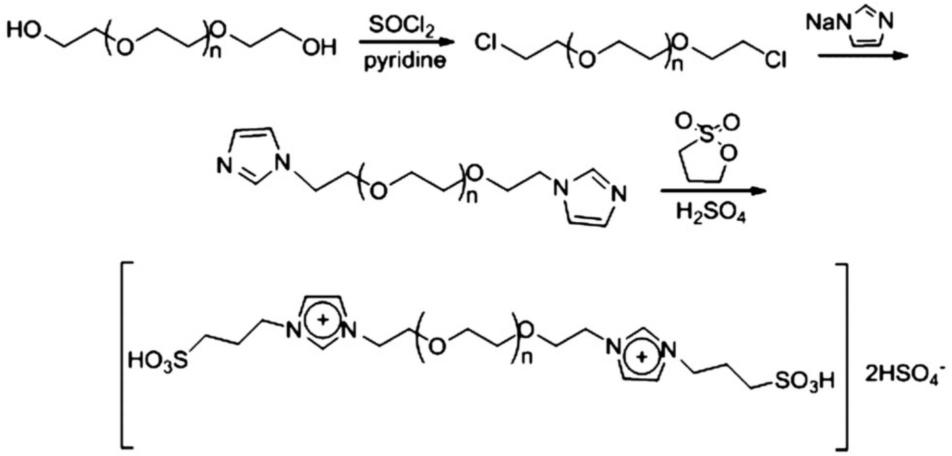
http://dx.doi.org/10.1016/j.catcom.2012.07.019



Scheme 1. The preparation of the PEG-DAIL.

2.2. General procedure for the oxidation

THICA was prepared by the literature procedure [8,15]. ^1H NMR (DMSO-d_6): δ (ppm) 11.03 (s, 3H); ^{13}C NMR (DMSO-d_6): δ (ppm) 146.6; IR (cm^{-1}): 3539, 3166, 2827,1720, 1433, 1211, 1010, 701.

The PEG$_{1000}$–DAIL was prepared by the procedure given in the literature (Scheme 1) [14]. ^1H NMR (D_2O): δ (ppm) 2.15 (t, 4H, $J=7$ Hz, 2×CH_2), 2.77 (m, 4H, 2×CH_2), 3.45–3.66 (m, 90.3H, $(OCH_2CH_2)_n$), 3.74 (4H, 2×CH_2), 4.21–4.30 (8H, 4×NCH_2), 7.41 (s, 4H, 4×CH), 8.71 (s, 2H, 2×CH); ^{13}C NMR (D_2O): δ (ppm) 25.2, 47.7, 47.9, 49.1, 68.6, 68.7, 69.6, 122.3, 123.1, 136.0; IR (cm^{-1}): 3849, 3400, 3020, 2883, 1732, 1591, 1456, 1431, 1377, 1122, 1109, 972, 883, 798, 677, 577.

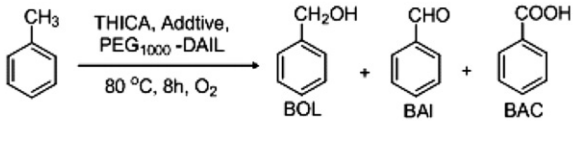
The substrate ($5.0*10^{-3}$ mol), PEG$_{1000}$–DAIL ($2.8*10^{-5}$ mol), THICA ($2.5*10^{-4}$ mol, 5 mol %), and DMG ($2.5*10^{-4}$ mol, 5 mol%) were placed in a three-necked flasks. O_2 was bubbled into the flask at a flow rate of 20 mL min^{-1}. The reaction mixture was stirred at a specific temperature for a specific time, and the reaction progress was monitored by HPLC. After completion of the reaction, the mixture was cooled to room temperature and extracted with ether (10 mL) three times. After concentration of the ether solution, the products were taken for HPLC measurement and the PEG$_{1000}$–DAIL was reused without any treatment.

3. Results and discussions

3.1. Influence of reaction conditions on the oxidation of toluene with THICA

As a representative example, the aerobic oxidation of toluene (Equation 1) was selected to optimize the reaction conditions (Table 1). It is pleasing that the oxidation of toluene with O_2 (1 atm) catalyzed by THICA (5 mol%) combined with DMG (5 mol%) gave benzaldehyde (BAl), benzoic acid (BAC) in 0.7% and 99.0% selectivity, respectively, at 99.5% conversion (Run 1). Several DMG analogues were compared (Runs 2–4) [16]. Substitution by acetoxime, acetaldoxime or cyclohexanoneoxime led to lower conversion with comparable selectivity of BAC. Other non-metallic compounds (like anthraquinone) which also can abstract the hydrogen atom from the hydroxyimide moiety of the NHPI to generate phthalimide N-oxyl were also examined (Runs 5–7). Unsatisfactorily, when anthraquinone [17] or N′, N″-azobisisobutyronitrile [18] (ABIN) was employed, the reaction proceeded in low conversion to result in lots of BAl. And the conversion reached only 9.4% and no benzoic acid appeared in the presence of the HNO_3/THICA [19].

Subsequently, various solvents were screened (Runs 8–14). In contrast to the traditional NHPI/Co(OAc)$_2$ catalyzed oxidation of alkylaromatics where acetic acid or acetonitrile was the appropriate solvent [7], the employment of them in the present oxidation led to a decrease of the conversion and selectivity of BAC. Meanwhile, 1-butyl-3-methylimidazolium tetrafluoroborates ([Bmim]BF$_4$), which had been successfully applied in the nitration of methylbenzenes catalyzed by NHPI [20], did not adapt to oxidation system. The reaction in PEG 1000-based dicationic ionic liquid (PEG$_{1000}$-DIL) resulted in lower conversion due to its lack of acidity. It also shown PEG$_{1000}$–DAIL was



Equation 1. The oxidation of toluene.

Table 1
Oxidation of toluene with O_2 under various conditions.[a]

Run	THICA (mol %)	Additive (mol %)	Solvent[b]	Conversion [%]	Products selectivity [%]		
					BOL	BAl	BAC
1	5	DMG (5)	PEG$_{1000}$-DAIL	99.5	0.7	n.d[c]	99.0
2	5	Acetoxime (5)	PEG$_{1000}$-DAIL	83.0	n.d	2.6	94.6
3	5	acetaldoxime (5)	PEG$_{1000}$-DAIL	73.9	5.2	5.8	84.2
4	5	Cyclohexanone oxime (5)	PEG$_{1000}$-DAIL	75.7	5.7	32.7	60.7
5	5	Anthraquinone (10)	PEG$_{1000}$-DAIL	65.8	n.d.	27.4	69.2
6	5	ABIN (3)	PEG$_{1000}$-DAIL	27.3	0.6	40.4	55.3
7	5	nitric acid[d] (10)	PEG$_{1000}$-DAIL	9.4	n.d.	n.d.	n.d.
8	5	DMG (5)	HOAc	99.0	n.d	0.5	90.3
9	5	DMG (5)	CH_3CN	89.8	n.d	2.7	89.9
10	5	DMG (5)	[Bmim]BF$_4$	10.7	n.d	0.8	30.7
11	5	DMG (5)	PEG$_{1000}$-DIL	90.7	n.d	7.4	85.0
12	5	DMG (5)	PEG$_{400}$-DAIL	97.9	n.d	1.5	98.2
13	5	DMG (5)	PEG$_{600}$-DAIL	98.3	n.d	0.8	98.9
14	5	DMG (5)	PEG$_{2000}$-DAIL	85.5	n.d	5.6	93.1
15	5	DMG (2.5)	PEG$_{1000}$-DAIL	64.4	n.d	5.4	92.3
16	5	DMG (7.5)	PEG$_{1000}$-DAIL	98.9	n.d	0.6	99.1
17	2.5	DMG (5)	PEG$_{1000}$-DAIL	60.5	n.d	7.1	90.7
18	7.5	DMG (5)	PEG$_{1000}$-DAIL	99.6	n.d	0.9	99.0
19	7.5	DMG (7.5)	PEG$_{1000}$-DAIL	99.5	n.d	0.3	99.6
20	5		PEG$_{1000}$-DAIL	47.0	n.d	20.0	58.1
21	0	DMG (5)	PEG$_{1000}$-DAIL	31.1	n.d	28.7	53.1
22	0		PEG$_{1000}$-DAIL	30.2	n.d	27.9	52.4

[a] Toluene (0.05 mol) was allowed to react with O_2 (1 atm) with THICA and additive in solvent at 80 °C for 10 h.

[b] PEG$_{1000}$ -DAIL was $2.8*10^{-5}$ mol and other solvent was 10 ml.

[c] Not detected.

[d] The concentration of nitric acid was 67%.

more suitable than other PEG-based dicationic acidic ionic liquids such as PEG_{400}–DAIL.

Then the catalytic performances of THICA /DMG in PEG_{1000}–DAIL were examined in detail (Runs 14–22). In comparison with the oxidation using 5 mol% THICA and 5 mol% DMG, the conversions markedly decreased when the amount of one component was contracted to 2.5 mol% no matter whether the other component was changed. On the other hand, when the amounts of either one component or both the components were increased to 7.5 mol%, the conversions stayed at 99.5%. These mean that the catalytic ability was not improved obviously by increasing the amounts of the catalysts beyond 5 mol%. Control experiments showed that lower conversion was detected with only THICA added, and the conversion was less than 32% without a catalyst or in the presence of DMG alone.

The influences of time and temperature on the oxidation were also investigated. As illustrated in Fig. 1, the conversion of toluene enhanced with prolonging the reaction time. Simultaneously, the selectivity of BAC continuously increased, and the selectivity of benzyl alcohol (BOL) decreased owing to the continuous oxidation of BOL to BAC. However, after 8 h the conversion changed slowly and became stagnated. As a result, in an 8 h reaction course, 99.5% toluene was oxidized with 99.0% selectivity of BAC. The change of the selectivity of BAl was similar to BOL except the concentrate was always low.

It was also shown that when the temperature was lower than 60 °C, the low conversion was obtained due to incomplete dissolution of toluene in PEG_{1000}–DAIL, and it reached a maximum at 80 °C (Fig. 2). However, the conversion gradually decreased as a result of continuing to elevate the temperature because lots of toluene was exhausted by evaporation at higher temperature. On the contrary, the selectivity of BAC was almost unchanged and almost no side products were found.

3.2. Oxidation of different substrates

With optimized conditions in hand, we then turned our attention to the scope of the reaction (Table 2). First, a variety of toluene with electron-rich substituted group was examined (Runs 1–6). In most cases, they were oxidized to the corresponding products in moderate to excellent conversions. For example, using xylenes as the substrates was obtained the diacids. The sterically hindered p-tert-butyltoluene was also reacted to furnish p-tert-butylbenzoic acid in 80.7% conversion with 95.7% selectivity. Then a series of the electron-withdrawing substituted toluene were tested (Runs 7–14). Toluenes with cyano-, carboxyl- and halo-substituted groups were converted into the corresponding acids with good conversions. P-acetoxytoluene underwent the oxidation with lower conversion. P-Nitrotoluene which had a strong electron-withdrawing substituent gave p-nitrobenzoic acid in fair conversion. Since THICA was stable at high temperature [7], o-nitrotoluene could be oxidized in 54.7% conversions, but the selectivity of o-nitrobenzoic acid was only 29.9%.

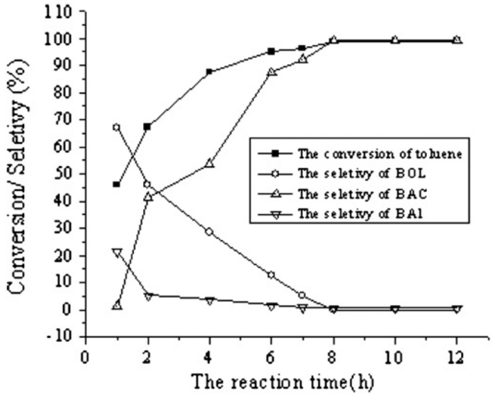


Fig. 1. Time-dependence curves for the aerobic oxidation of toluene[a]. [a]Reaction conditions: $5*10^{-3}$ mol toluene, 5 mol% DMG, 5 mol% THICA, $2.8*10^{-5}$ mol PEG_{1000} -DAIL, O_2, 80 °C.

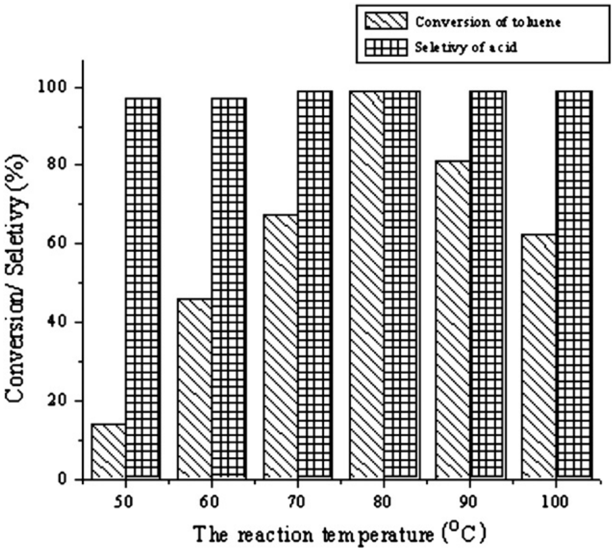
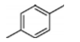
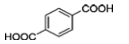
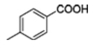
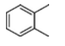
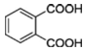
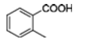
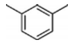
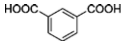
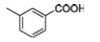
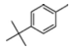
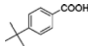
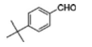
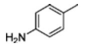
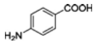
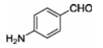
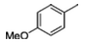
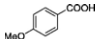
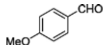
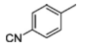
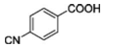
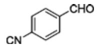
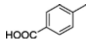
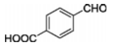
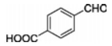
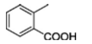
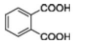
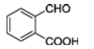
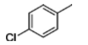
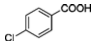
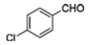
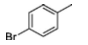
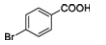
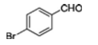
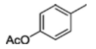
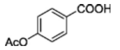
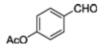
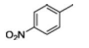
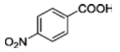
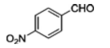
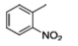
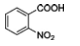
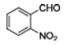


Fig. 2. Temperature-dependence curves for the aerobic oxidation of toluene[a]. [a]Reaction conditions: $5*10^{-3}$ mol toluene, 5 mol% DMG, 5 mol% THICA, $2.8*10^{-5}$ mol PEG_{1000} -DAIL, O_2, 8 h.

3.3. The mechanism of the oxidation

Ishii suggested THICA can generate an N-oxyl radical in higher temperature [7]. The research on the catalytic mechanism of THICA/ HNO_3 system [19] was done and it was suggested the catalytic

Table 2
Aerobic oxidation of various substrates.[a]

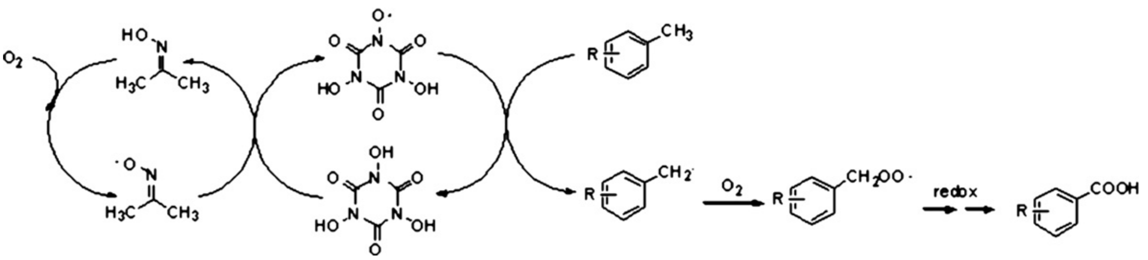
Run	Substrate	Times	Conversion [%]	Main products and selectivity [%]			
1[b]		13	94.3		89.7		10.2
2[b]		13	94.2		85.0		13.9
3[b]		13	90.0		84.7		14.9
4		12	80. 7		95.7		3.2
5		8	95.2		96.0		2.1
6		9	92.0		86.9		12.1
7		10	94.4		96.7		3.0
8		11	91.1		93.4		5.5
9		11	90.9		92.0		7.6
10		9	93.8		94.5		4.8
11		9	94.6		95.0		4.6
12		10	86.8		77.0		22.1
13[c]		16	78.7		86.0		12.5
14[c, d]		16	54.7		29.9		43.7

[a] Reaction conditions: $5*10^{-3}$ mol substrates, 5 mol% DMG, 5 mol% THICA, $2.8*10^{-5}$ mol PEG_{1000}–DAIL, O_2, 80 °C.

[b] Both THICA and DMG were 10 mol%.

[c] Both THICA and DMG were 15 mol%.

[d] The temperature was 140 °C.



Scheme 2. A possible reaction mechanism for the catalytic cycle of the THICA/DMG system.

process was similar with that of NHPI. In order to clarify the mechanism of the THICA/DMG system, following experiments were carried out.

First, p-cresol (5 mol%), a free radical scavenger, was added into the oxidation of toluene catalyzed by THICA/DMG. The result that no reaction occurred indicated that the oxidation followed a radical pathway. Secondly, dimethylglyoxime ester was used to replace DMG in the oxidation of toluene and the conversion was only 47.0%, which was consistent with the result of using THICA alone. This implied that dimethylglyoxime ester had no catalytic effect, and that the N-hydroxy groups of DMG played a key role in the catalytic oxidation. However, it was indicated that the corresponding N-oxyl radical of DMG could not promote the radical aerobic oxidation of hydrocarbons [16], although it was formed in the reaction. We did the similar experiments and found the results were consistent.

A possible catalytic mechanism of THICA/DMG in the aerobic oxidation was proposed in Scheme 2. The first step of the reaction was to involve the corresponding N-oxyl radical of DMG, which was formed by the reaction of DMG and dioxygen. And then this N-oxyl radical abstracted hydrogen from THICA to recover to DMG. Simultaneously, THICA was converted to its radical, which abstracted a hydrogen atom from the toluene derivatives to form benzyl radicals. This benzyl radical was then readily captured by O_2 to give a benzylperoxy radical, followed by a complicated redox process to finally produce the carboxyl acid.

The production of the THICA radical with DMG in PEG_{1000} -DAIL was observed by EPR measurements (Fig. 3). Due to the limits of the analytical condition, the PEG_{1000} –DAIL solution was examined only in room temperature and the signal of THICA was much weaker (The sample was scanned for ten times) than that in nitric acid [19], but the g and $A_{(N)}$ value ($g = 2.00060$, $A_{(N)} = 4.88$ G) of the spectrum in PEG_{1000} –DAIL were similar to them in nitric acid ($g = 2.00075$, $A_{(N)} = 4.86$ G). It was shown THICA was directly abstracted hydrogen atom by N-oxyl radical derived from DMG with oxygen. (The PEG_{1000}–DAIL with only DMG was also examined by EPR and the spectrum was much different from that of THICA.)

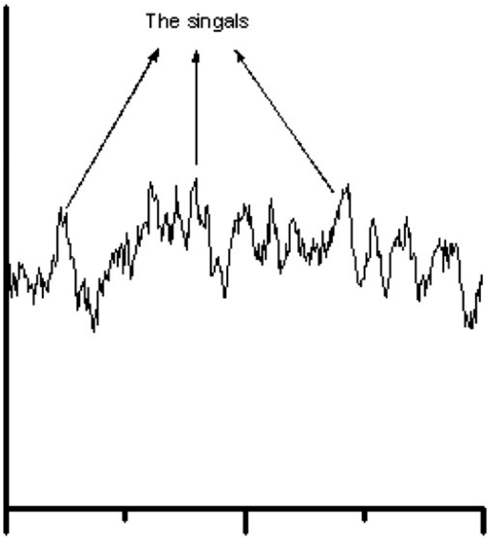


Fig. 3. EPR spectrum of the THICA radical.

3.4. The cycle of catalyst and PEG_{1000}–DAIL

When the final reaction mixture was cooled to room temperature and extracted with ether, the upper layer of ether, containing product, was removed by decantation. Then only fresh substrate was recharged to the residual PEG_{1000} -DAIL and the mixture was heated to react once again. The results from Fig. 4 were shown that the procedure was repeated eight times with no appreciable decrease in conversions. The selectivity of toluene decreased obviously after 7 times.

4. Conclusion

Summarising, we have developed a novel, metal-free catalytic system consisting of THICA and DMG for the aerobic oxidation of alkylaromatics in PEG_{1000}–DAIL, avoiding the use of heavy metals and toxic solvent. By using this catalytic approach, toluene with electron-donating or electron-withdrawing groups can be oxidized to the corresponding acid with high to moderate conversions. This metal-free catalytic oxidation method has an environmentally friendly feature and provides an attractive method which has long been desired in the chemical industry.

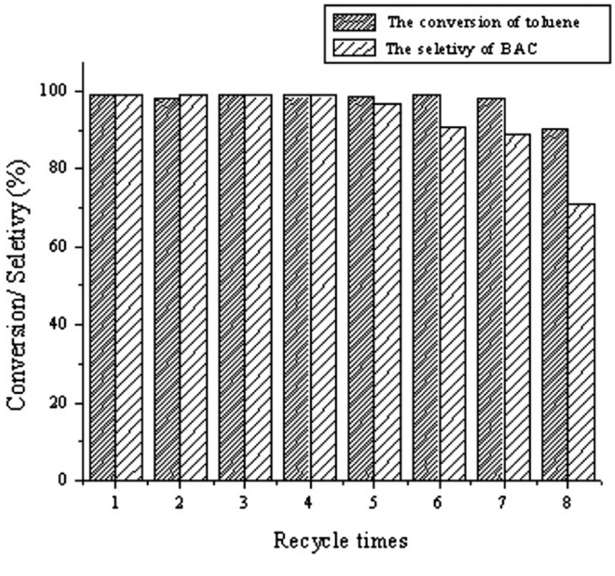


Fig. 4. Repeating reaction using recovered PEG_{1000}–DAIL[a]. [a]The PEG_{1000}–DAIL was used in the further reaction without any disposal.

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