



Regioselectivity nitration of aromatics with N_2O_5 in PEG-based dicationic ionic liquid

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ABSTRACT

Regioselective mononitration of simple aromatic compounds has been investigated with N_2O_5 as nitrating agent and a new PEG₂₀₀-based dicationic acidic ionic liquid (PEG₂₀₀-DAIL) as catalyst. The results of experiments show that this nitration system can significantly improve the *para*-selectivity of alkyl-benzenes and the *ortho*-selectivity of halogenated-benzenes. The PEG₂₀₀-DAIL exhibits recyclable temperature-dependant phase behavior in CCl_4 solvent, and it can be recycled without apparent loss of catalytic activity, and only 5% loss of weight is observed after six times recycling.

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1. Introduction

Nitration of aromatic compounds is a ubiquitous reaction to realize organic intermediates required in large tonnages for the fine chemical industry. However, most of these reactions, employing a nitrating mixture of nitric and sulfuric acid, are facing the problems of waste acid cauterization and poor selectivity.¹ So, finding green catalysts and nitrating reagents to selective synthesis of the desired isomer in the nitration of substituted aromatic compounds is of topical interest, with the purpose to reduce environment pollution and specifically to respond to market demand. Strategies for improving this notoriously 'ungreen' reaction had included the use of clays^{2,3} or zeolites^{4–6} as solid supports or perfluorocarbons⁷ as solvents.

In the past few years, a growing interest had been witnessed in ionic liquids as solvents or catalysts for aromatic nitration. Laali and Gettewert⁸ first reported 1-ethyl-3-methylimidazolium salts [emim] [X] with $X = OTf^-$ and CF_3COO^- as ionic liquids for electrophilic nitration of aromatics. Smith et al.⁹ reported that [bmim] [X] with $X = BF_4^-$ and PF_6^- performed better than CCl_4 in reaction rate. Later researchers mainly focused on the modified methods of former ionic liquids. Qiao et al.^{10,11} immobilized ionic liquids to modified silica gel and got an excellent *ortho/para* ratio. Rajagopal and Srinivasan¹² reported that ultrasound promoted *para*-selective nitration of phenols in ionic liquid. Fang et al.¹³ reported that halogen-free SO_3H -functional Brønsted-acidic ILs that bear an alkane

sulfonic acid group in an acyclic trialkanylammonium cation could efficiently catalyze the nitration of aromatic compounds. Nevertheless, the traditional mixed acid systems as HNO_3/Ac_2O and HNO_3/H_2SO_4 were still widely applied.

N_2O_5 employed as a green nitrating reagent had been studied for several years. Millar and Philbin¹⁴ introduced N_2O_5 in an inert solvent into syntheses of nitramines and nitrate esters. Talawar et al.¹⁵ succeed in finding several N_2O_5 -inert solvents as green and moderate systems. Qian et al.¹⁶ reported that HZSM-5 solid acid with N_2O_5 promoted an excellent *para*-selective nitration of chlorobenzene.

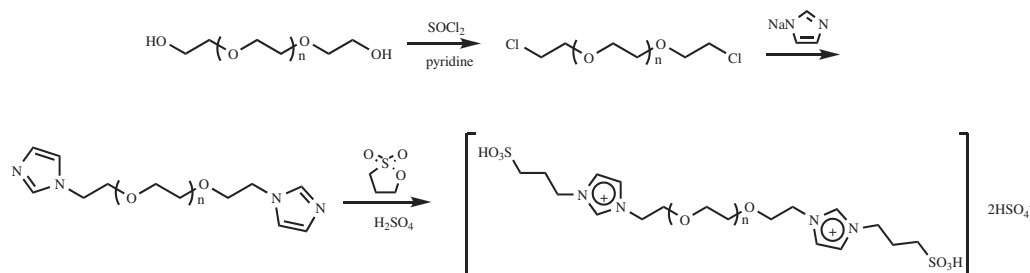
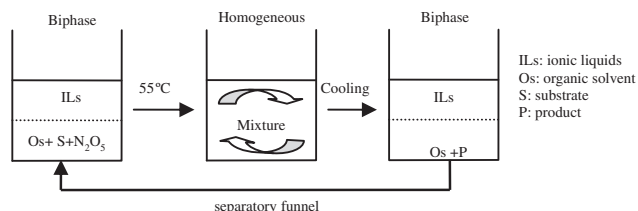
Here we combined a novel polyethylene glycol (PEG)-200-based dicationic acidic ionic liquid (PEG₂₀₀-DAIL)¹⁷ with N_2O_5 (Scheme 1). Nitration in ionic liquids was surveyed using a host of aromatic substrates with similar reactivity. And ionic liquid recycling procedures had also been devised. The easily recovered ionic liquid opened up the possibility of a more economic process.

2. Results and discussion

Our initial effort aimed to use PEG₂₀₀-DAIL as catalyst and N_2O_5 as the nitrating agent (Fig. 1). The typical reaction with toluene was investigated to optimize the reaction conditions (Fig. 2, Table 1). It was observed that the variation in the amount of PEG₂₀₀-DAIL had an effective influence. When the amount of catalyst was increased to 3 g (5.6 mmol) at 50 °C, the conversion and the *para*-selectivity of the nitrotoluene got the best result. And then the effect would glissade in both sides with conditions changed. We supposed that an increasing of by-products as 2,4-dinitrobenzene and

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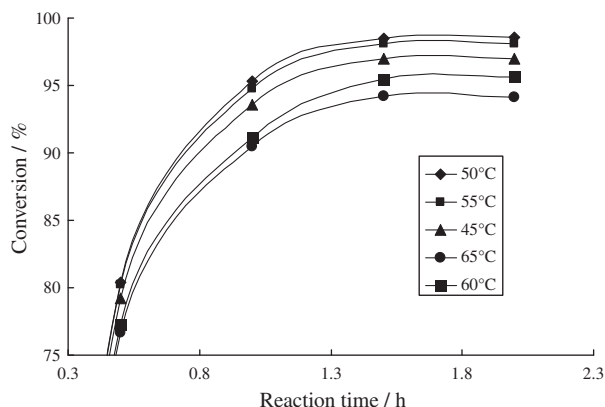
Scheme 1. Synthesis of PEG₂₀₀-DAIL.Figure 1. Reaction process with N₂O₅ in PEG₂₀₀-DAIL.

2,6-dinitrobenzene might be the major factor of this phenomenon. Temperature was another important factor. The conversion increased to 98.5% until 50 °C with temperature rising, but then decreased rapidly for the decomposition of N₂O₅.

Then the reaction was compared with several reported IL systems in the nitration of toluene, and the results were summarized in Table 2. As can be seen from Table 2, PEG₂₀₀-DAIL successfully decreased the ratio of *o/p* to 1.09, while the conversion was still kept at 98.5%. But the traditional ILs could not remain competitive both in terms of conversion and selectivity. The IL of highest selectivity was [emim] CF₃COO[−]; a pity that its conversion was only 65%.

But the nitration of chlorobenzene was out of our expectation: the result was significantly opposed with toluene in selectivity (Table 3). It showed a strongly *ortho*-selectivity and the *p/o* ratio decreased to 1.04.

In order to investigate the roles of different constituents, such as PEG₂₀₀-DAIL and N₂O₅ each played in reaction, a comparison of the results obtained by five various nitration systems was carried. Toluene and chlorobenzene were chosen as the typical compounds for activated and deactivated substituent benzenes separately (Figs. 3 and 4). As can be seen in the nitration of toluene,

Figure 2. Nitration of toluene at different temperatures. Reaction condition: toluene (0.48 mmol), N₂O₅ (1 equiv), PEG₂₀₀-DAIL (3 g), CCl₄ (15 ml).Table 1
Effect of catalyst's amount in toluene nitration^a

PEG ₂₀₀ -DAIL (g)	Conv. (%)	<i>m</i> -MNT (%)	<i>o</i> -MNT (%)	<i>p</i> -MNT (%)	<i>o/p</i> ^b
1	97.1	2.0	54.2	43.8	1.24
2	97.7	2.0	52.5	45.5	1.15
3	98.5	1.9	51.2	46.9	1.09
4	97.2	1.9	53.7	44.4	1.21
5	97.9	2	54.6	43.4	1.26

^a Toluene (0.48 mmol), N₂O₅ (1 equiv), CCl₄ (15 ml), 50 °C, 2 h.^b Ratio of *para/ortho* calculated from original GC data.Table 2
Regioselective nitration of toluene in various IL

IL	Conv. (%)	<i>m</i> -MNT (%)	<i>o</i> -MNT (%)	<i>p</i> -MNT (%)	<i>o/p</i>
HNO ₃ /H ₂ SO ₄	92.2	4.6	61.3	34.1	1.79
[emim]OTf ^a	60.0	3.5	57.2	39.3	1.45
[emim] CF ₃ COO ^{−a}	65.0	3.1	48.9	48.0	1.02
[MIMPS]HSO ₄ ^b	90.0	5.5	53.1	41.4	1.28
[<i>p</i> -SABPy]HSO ₄ ^b	97.4	5.1	53.3	41.6	1.28
[TEPSA]HSO ₄ ^b	94.8	5.3	53.9	40.8	1.32
PEG ₂₀₀ -DAIL	98.5	1.9	51.2	46.9	1.09

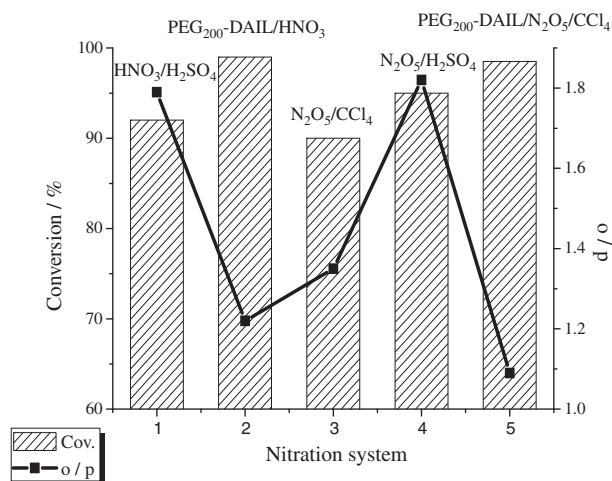
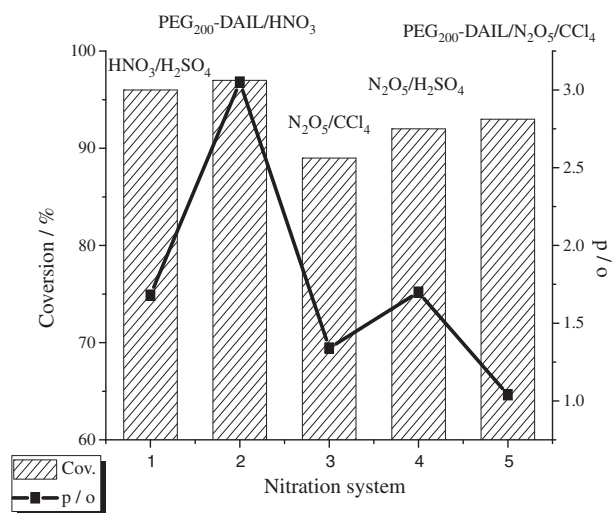
^a Ref. 8.^b Ref. 9.

two main phenomena were attractive: first, mixed acid systems both HNO₃/H₂SO₄ and N₂O₅/H₂SO₄ were poor in selectivity (*o/p* ratio is 1.79 and 1.8), they are very close to the theoretical value (*o/p* ratio is 2); second, the effect of *para*-selectivity would be obviously increased with an existence of PEG₂₀₀-DAIL (*o/p* ratio is 1.22 and 1.09). While in nitration of chlorobenzene, the *p/o* ratio increased to 3.09 with the existence of PEG₂₀₀-DAIL in PEG₂₀₀-DAIL/ HNO₃ system, but *p/o* ratio decreased to 1.04 in N₂O₅/CCl₄ system for this system was facilitated in producing *o*-MNCB. The causation of complicated diversification could be explained with two different nitration mechanisms. In mixed acid systems, NO₂⁺ would generate quickly, NO₂⁺ was the main body attacking benzene ring (Eq. (1)); in organic solvent system, the dissociation of N₂O₅ became so slight that the main body attacking benzene ring was N₂O₅ itself (Eqs. (2)–(4)). And PEG₂₀₀-DAIL per-

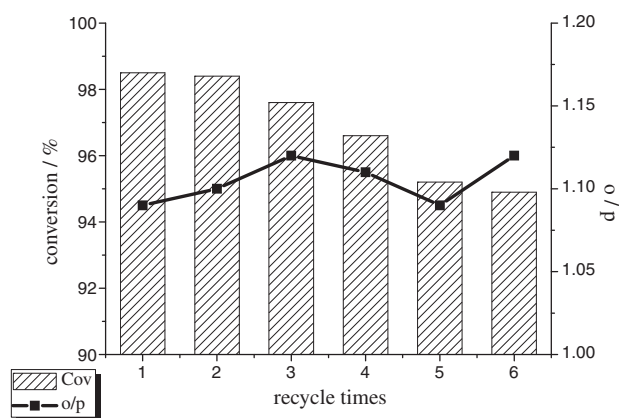
Table 3
Effect of catalyst's amount in chlorobenzene nitration^a

PEG ₂₀₀ -DAIL/g	Conv. (%)	<i>m</i> -MNCB (%)	<i>o</i> -MNCB (%)	<i>p</i> -MNCB (%)	<i>p/o</i> ^b
1	91.1	0.7	42.8	56.5	1.32
2	91.7	0.5	46.7	52.8	1.13
3	92.8	0.4	48.8	50.8	1.04
4	91.3	0.4	47.2	52.4	1.11
5	90.9	0.6	46.8	52.6	1.12

^a Chlorobenzene (0.48 mmol), N₂O₅ (1 equiv), CCl₄ (15 ml), 50 °C, 2 h.^b Ratio of *para/ortho* calculated from original GC data.

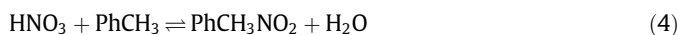
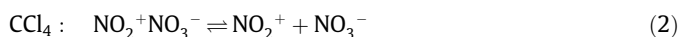
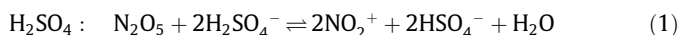
Figure 3. Nitration of toluene in different systems.¹⁸Figure 4. Nitration of chlorobenzene in different systems.¹⁹Table 4
Selectivity on nitration of various aromatic with amides²⁰

Substrate	Products	Selectivity	Conv. (%)
Ethylbenzene	2-Nitroethylbenzene	39.15	97.16
	3-Nitroethylbenzene	4.99	
	4-Nitroethylbenzene	55.86	
<i>tert</i> -Butylbenzene	1- <i>tert</i> -Butyl-2-nitrobenzene	8.12	89.9
	1- <i>tert</i> -Butyl-3-nitrobenzene	6.85	
	1- <i>tert</i> -Butyl-4-nitrobenzene	85.03	
Bromobenzene	2-Nitrobromobenzene	52.45	91.96
	3-Nitrobromobenzene	0.70	
	4-Nitrobromobenzene	46.85	
Fluorobenzene	2-Nitrofluorobenzene	88.97	95.77
	3-Nitrofluorobenzene	0.24	
	4-Nitrofluorobenzene	10.79	
Benzoic acid	3-Nitrobenzoic acid	100	87.35
Nitrobenzene	1,3-Dinitrobenzene	89.26	78.36
	1,2-Dinitrobenzene	10.13	
	1,4-Dinitrobenzene	0.61	
<i>p</i> -Nitrotoluene	2,4-Dinitrotoluene	100	86.27
<i>m</i> -Toluic acid	3-Me-6-nitrobenzoic acid	44.96	89.87
	3-Me-2-nitrobenzoic acid	44.58	
	3-Me-4-nitrobenzoic acid	10.46	
<i>o</i> -Toluic acid	2-Me-5-nitrobenzoic acid	74.58	93.32
	2-Me-3-nitrobenzoic acid	23.32	
	3,5-Dinitro- <i>o</i> -toluic acid	2.10	

Figure 5. Repeating reaction using recovered PEG₂₀₀-DAIL.

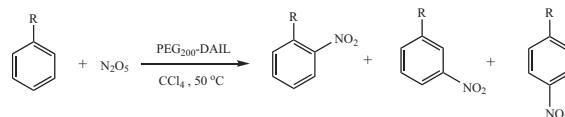
formed excellent in processing nitration. It accelerated the reaction, in the case of not changing the trend of selectivity. Simultaneously, dissimilarity in conversion was also observed. When N₂O₅ was added, its oxidation and decomposition made the conversion decreased by about 2%. But with respect to its significant selectivity, this shortcoming could be ignored. According to the marvelous effects, the use of N₂O₅ and PEG₂₀₀-DAIL in nitration was attractive.

Equations: Suggested mechanism for aromatics nitration.



Encouraged by the remarkable results obtained with the above reaction conditions, and in order to show the generality and scope of this new protocol, we used various substituted aromatics. The results obtained were summarized in Table 4. In the nitration of activated substrates, they showed the same phenomenon of toluene: higher conversion and *para*-selectivity than mixed acid. A lit-

tle difference was that the product of *para*-position increased significantly with the steric effect of the substituted group. The nitration of deactivated substrates showed greater impact of using the ionic liquid and N₂O₅. As is shown in the table, under the reaction conditions employed, the conversion of bromobenzene was 91.96%. And the rare *ortho*-selectivity gave a possible approach to meet the industry need of several *ortho*-products. For some substituted aromatics which had no other products, their conversions were improved in this nitration system more or less. Another praiseworthy advantage was that the mononitro-products were predominant in this N₂O₅/PEG₂₀₀-DAIL system. Dinitration and multinitation made up only about 1% in conversion.



The procedure was repeated six times and the results indicated that PEG₂₀₀-DAIL could be recycled without the apparent loss of catalytic activity (Fig. 5) and only 5% loss of weight was observed after six times of recycling. With the recycle times increased, the

color of ionic liquid turned from brown to yellow at room temperature. It was surmised that a few NO_3^- generated in the reaction replaced the HSO_4^- as anionic group. We prepared this NO_3^- -based ionic liquid, and its character was the same with the ionic liquid after numerous recycle.

Supplementary data

Supplementary data (experimental details for the synthesis and characteristic data for key intermediates are provided. ^1H NMR spectra of PEG₂₀₀-DAIL and GC/LC of aromatic compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.01.053.

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- Reaction conditions of five systems in toluene nitration. $\text{HNO}_3/\text{H}_2\text{SO}_4$ system: toluene (0.48 mmol), HNO_3 (65%, 1 equiv), H_2SO_4 (98%, 5 equiv), 60 °C, 4 h. PEG₂₀₀-DAIL/ HNO_3 system: toluene (0.48 mmol), HNO_3 (65%, 1 equiv), PEG₂₀₀-DAIL (3 g), H_2SO_4 (98%, 5 equiv), 50 °C, 3 h. $\text{N}_2\text{O}_5/\text{CCl}_4$ system: toluene (0.48 mmol), N_2O_5 (1 equiv), CCl_4 (15 ml), 0 °C, 3 h. $\text{N}_2\text{O}_5/\text{H}_2\text{SO}_4$ system: toluene (0.48 mmol), N_2O_5 (1 equiv), H_2SO_4 (98%, 3 equiv), 0 °C, 3 h. PEG₂₀₀-DAIL/ $\text{N}_2\text{O}_5/\text{CCl}_4$ system: toluene (0.48 mmol), N_2O_5 (1 equiv), PEG₂₀₀-DAIL (3 g), CCl_4 (15 ml), 50 °C, 2 h.
- Reaction conditions of five systems in chlorobenzene nitration. $\text{HNO}_3/\text{H}_2\text{SO}_4$ system: chlorobenzene (0.48 mmol), HNO_3 (65%, 1 equiv), H_2SO_4 (98%, 5 equiv), 70 °C, 4 h. PEG₂₀₀-DAIL/ HNO_3 system: chlorobenzene (0.48 mmol), HNO_3 (65%, 1 equiv), PEG₂₀₀-DAIL (3 g), H_2SO_4 (98%, 5 equiv), 50 °C, 3 h. $\text{N}_2\text{O}_5/\text{CCl}_4$ system: chlorobenzene (0.48 mmol), N_2O_5 (1 equiv), CCl_4 (15 ml), 0 °C, 3 h. $\text{N}_2\text{O}_5/\text{H}_2\text{SO}_4$ system: chlorobenzene (0.48 mmol), N_2O_5 (1 equiv), H_2SO_4 (98%, 3 equiv), 0 °C, 3 h. PEG₂₀₀-DAIL/ $\text{N}_2\text{O}_5/\text{CCl}_4$ system: chlorobenzene (0.48 mmol), N_2O_5 (1 equiv), PEG₂₀₀-DAIL (3 g), CCl_4 (15 ml), 50 °C, 2 h.
- All chemicals were purchased from Sinopharm Chemical Reagent Co. Ltd and used without further purification, N_2O_5 was prepared with Ref. 14 *General procedure*: In a typical reaction protocol, 15 ml CCl_4 , 0.48 mmol aromatic compound and PEG₂₀₀-DAIL were placed in a 50 ml three-necked flask. Then the flask was put in a constant temperature water bath and N_2O_5 was added with stirring. After adding, temperature was raised to 50 °C and kept for 2 h. The final solution was cooled to room temperature and separated. Then the organic phase was washed once with 10%M sodium bicarbonate solution (50 ml) and twice with distilled water (50 ml). After dried over magnesium sulfate, the solvent was evaporated to spontaneously crystallize after several hours. The constituents were confirmed based on GC or LC analysis (comparison with an authentic sample).