## Regioselective Preparation of 4-Nitro-o-xylene Using Nitrogen Dioxide/Molecular Oxygen over Zeolite Catalysts. Remarkable Enhancement of para-Selectivity

Hongtao Liu, Cheng Ji, Xiongzi Dong, Xinhua Peng,\* and Chunjie Shi School of Chemical Engineering, Hefei University of Technology, Hefei 230009, P. R. China

(E-mail: xinhpeng@mail.njust.edu.cn)

In the presence of molecular oxygen and zeolite H- $\beta$  with Si/  $Al_2 = 500$ , *o*-xylene reacted regioselectively with liquid nitrogen dioxide at 35 °C to yield mononitro-o-xylenes as the main product, where the 4-nitro-o-xylene isomer predominated up to 89% and the 4-nitro-/3-nitro-o-xylene isomer ratio improved to 7.8. The process is eco-friendly, less expensive, and the zeolite could be easily regenerated by a simple workup to afford results similar to those obtained with the fresh catalyst.

4-Nitro-o-xylene is an industrially important intermediate for the manufacture of pharmaceuticals, agrochemicals, fragrances, and dyestuffs.<sup>1</sup> Industrial preparation employs nitric and sulfuric acids to produce approximately equal amount of isomer mixtures involving 3-nitro-o-xylene and 4-nitro-o-xylene. However, this time-honored reaction suffers from several disadvantages such as corrosiveness, potential danger of explosion, poor selectivity, overnitration, oxidative degradation by-products, and waste acids.<sup>2</sup> Thus, it is urgent to develop an environmentally friendly, commercially viable process for the selective preparation of nitro compounds.

In recent years, some clean approaches are employed with the aim to use nitrating agents such as nitrogen dioxide,<sup>3,4</sup> dinitrogen tetraoxide,<sup>5</sup> and dinitrogen pentaoxide.<sup>6</sup> Various catalysts and supports promote the nitrating activity and regioselectivity.<sup>7,8</sup> The Kyodai nitration<sup>9-11</sup> using lower nitrogen oxides/ozone system has demonstrated an excellent conversion of various aromatic compounds into the corresponding nitro derivatives.<sup>12</sup> It is noted that zeolites are very appealing catalysts to make positive contributions to the desirable selectivity in the nitration processes. In our sustained attempt, we achieved an efficient and highly selective preparation of 4-nitro-o-xylene with nitrogen dioxide as a nitrating agent over catalysts toward industrialization.

The current trends in the preparation of nitro compounds emphasize minimizing the by-product formation and spent-acid amount. Moreover, regioselective nitration of the desired product involving lower nitrogen dioxide of atom economy was improved by using various zeolite catalysts.13,14 Suzuki and co-workers have reported that ZSM-5 zeolites appear to have good catalytic selectivity toward monosubstituted benzenes,<sup>3</sup> while Smith et al.<sup>5,15</sup> have found that *para*-nitro isomer predominated over the ortho-isomer over β-zeolites with dinitrogen tetroxide nitration. Generally, o-xylene (1) is commercially nitrated to afford a mixture of 3-nitro-o-xylene (2) and 4-nitro-o-xylene (3). The traditional process using mixed acids formed mixtures with the isomer ratio of approximately 0.8 and 1.1 (Entries 1 and 2 in Table 1). However, we found that the formation of 3 was highly favored when the substrate was subjected to the combined action of nitrogen dioxide and molecular oxygen in the presence of aluminosilicate zeolites, leading to the substantive reversal of the 3-nitro-/4-nitro-oxylene isomer ratios. Some typical results are shown in Table 1.

Table 1. Regioselectivity in the preparation of nitro-o-xylene using nitrogen dioxide and molecular oxygen over various zeolite catalysts<sup>a</sup>

$\overset{CH_3}{\underset{NO_2}{\overset{CH_3}{\underset{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{\underset{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{\underset{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{\atop{NO_2}{\overset{H_{NO_2}{\overset{H}{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{\overset{H_{NO_2}{&H}{NO_2}{\overset{H_{NO_2}{&H}{NO_2}{\overset{H_{NO_2}{&H}{NO_2}{&H}{NO_2}{H}{H}{H_{NO_2}{H}{H}{H_{NO_2}{H}{H}{H_{NO_2}{H}{H}{H_{NO_2}{H}{H}{H_{NO_2}{H}{H}{H_{NO_2}{H}{H}{H_{NO_2}{H}{H}{H_{NO_2}{H}{H}{H}{H}{H}{H}{H}{H}{H}{H}{H}{H$						
Factor	Nitrating	Cut tu	Z 0.	Isomer p	oroportion <sup>d</sup> /%	2.2
Entry	agent	Catalyst	Yield <sup>e</sup> /%	3	2	3:2 ratio
1	HNO <sub>3</sub>	_	67	45	55	0.8
2	HNO <sub>3</sub>	$H_2SO_4$	81	52	48	1.1
3	NO <sub>2</sub> -O <sub>2</sub>	_	64	66	34	1.9
4	NO <sub>2</sub>	_	61	60	40	1.5
5	$NO_2-O_2$	HZSM-5	63	66	34	1.9
6	$NO_2 - O_2$	Y-type	70	67	33	2.0
7	$NO_2-O_2$	HBEA30	76	76	24	3.1
8	NO <sub>2</sub> -O <sub>2</sub>	HBEA60	75	66	34	2.9
9	$NO_2-O_2$	HBEA130	72	73	27	2.7
10	NO <sub>2</sub> -O <sub>2</sub>	HBEA260	75	75	25	3.0
11	$NO_2 - O_2$	HBEA500	77	78	22	3.5

<sup>a</sup>Reactions conditions: *o*-xylene:acetic anhydride = 0.6:5 (v/v), *o*-xylene: nitrogen dioxide = 1:5 ratio, catalyst (0.11 g, 20 wt % based on o-xylene) at room temperature for 12 h under oxygen atmosphere. <sup>b</sup>Zeolites were calcined at 550 °C for 2 h in air prior to use. °Combined yield of 2 and 3 based on consumed 1 was given. <sup>d</sup>Proportion of products was determined by GC with 4-nitrotoluene as internal standard.

Various zeolites were screened in the nitration of o-xylene with lower nitrogen dioxide. ZSM-5, Y-type zeolites could slightly promote regioselectivity toward the 4-nitro isomer in the 4-nitro/3-nitro isomer ratio of 1.9-2.0 (Entries 5 and 6 in Table 1) compared with those of mineral acids (Entries 1 and 2 in Table 1). Sengupta and co-workers reported that the HY zeolite showed para-positional orientation in the nitration of o-xylene with fuming nitric and polyphosphoric acids.<sup>16</sup> By using nitrogen dioxide process, we found that zeolite HBEA appear to be encouraging 4-nitro selectivity (Entries 7-11 in Table 1). Further studies were extended to the BEA catalysts of various Si/Al<sub>2</sub> ratios. It was found that HBEA500 of higher Si/Al2 ratio due to the dealumination had excellent catalytic para-selectivity up to the ratios 2.7-3.5 in moderate yields (Entries 7-11 in Table 1).

Moreover, in the hope of improving further reactivity, the amount of nitrogen dioxide and o-xylene substrate was discussed. The representative results are summarized in Table 2.

To optimize the reaction temperature for maximum mononitration yield and selectivity, the samples were analyzed at temperatures ranging from -5 to  $35 \,^{\circ}$ C (Table 3). At  $35 \,^{\circ}$ C, a higher yield of nitro-o-xylene and a higher selectivity of 4-nitroo-xylene were observed. The results showed that the selectivity for the 4-nitro isomer increased with increasing temperature. Higher temperatures were preferable because of the faster

 Table 2. Effect of nitrogen dioxide/o-xylene molar ratios in the preparation of nitro-o-xylene<sup>a</sup>

Enter	Niturting	Yield <sup>c</sup> /%	Isomer proportion <sup>d</sup> /%		2.2
Епиу	Nitrating agent		3	2	3.2 ratio
1	NO <sub>2</sub> -O <sub>2</sub> (1:2)	68	80	20	4.0
2	NO <sub>2</sub> -O <sub>2</sub> (1:3)	76	86	14	6.3
3	$NO_2 - O_2$ (1:4)	78	88	12	7.2
4	NO <sub>2</sub> -O <sub>2</sub> (1:5)	77	86	14	6.4
5	$NO_2 - O_2$ (1:6)	63	85	15	5.7

<sup>a</sup>All reactions were carried out in acetic anhydride (5.0 mL) using substrate **1** (5.0 mmol), HBEA500 (0.53 g, 100 wt% based on *o*-xylene) at room temperature for 12 h under oxygen atmosphere. Zeolite was calcined at 550 °C for 2 h in air prior to use. <sup>b</sup>The ratio data in parentheses mean a molar amount in nitrogen dioxide to *o*-xylene. <sup>c</sup>Combined yield of **2** and **3** based on consumed **1** was given. <sup>d</sup>Proportion of products was determined by GC with 4-nitrotoluene as internal standard.

Table 3. Effect of temperature and amount of HBEA500 in the preparation of nitro-o-xylene<sup>a</sup>

Town /°C	Amount of	Yield <sup>b</sup> /%	Isomer pro	2.7 ratio	
remp./ C	HBEA500/g		3	2	3.2 Tatio
RT	0.21	75	83	17	5.0
RT	0.32	77	86	14	6.1
RT	0.42	79	87	13	6.9
RT	0.53	79	88	12	7.2
RT	0.64	78	88	12	7.5
35	0.53	81	89	11	7.8
15	0.53	76	78	22	3.5
5	0.53	72	67	33	2.0
-5	0.53	64	58	42	1.4

<sup>a</sup>Reaction conditions: *o*-xylene:acetic anhydride = 0.6:5 (v/v), *o*-xylene: nitrogen dioxide = 1:4 ratio, reaction time: 12 h, under oxygen atmosphere. <sup>b</sup>Combined yield of **2** and **3** based on consumed **1** was given. <sup>c</sup>Proportion of products was determined by GC with 4-nitrotoluene as internal standard.

diffusion of 4-nitro-*o*-xylene, and simply raising the temperature to 35 °C in the sealed system could dramatically reduce the required reaction time. However, if the temperature was too low, then a decrease in the mononitration yield was observed. The lower yield can be explained by formation of a by-product, which was detected by GC in the reaction at -5 °C. This could be ascribed to the low reaction rate. Hence, the optimal temperature was 35 °C. The effect of the HBEA500 catalyst quantity on the selectivity was also investigated (Figure 1a and Table 3). Increasing the amount of the catalyst improved the regioselectivity of 4-nitro-*o*-xylene and the yield of isomer products. These could be due to the three-dimensional interconnecting channel system, in which the accessible amount of the pores of the catalyst increased.

Nitration reaction is accompanied with the release of water that will adversely affect the activity of the zeolite. Therefore, the hydrophobic and hydrophilic character of zeolites must be taken into account. This is controlled by the Si/Al<sub>2</sub> ratio. Zeolites containing large amounts of alumina show high hydrophilicity, whereas zeolites containing large amounts of silica tend to be more hydrophobic. Because of the need to remove water from the catalyst in this system, hydrophobic zeolites are preferred. Hydrophobic zeolites generally have greater Si/Al<sub>2</sub> ratios, and hydrophobicity generally increases with increasing Si/Al<sub>2</sub> ratios. Hence, HBEA500 zeolite catalyst with a high Si/Al<sub>2</sub> ratio showed better activity with the release of water in the reaction. In practice, it has been observed that very small



Figure 1. SEM images: (a) fresh HBEA500 and (b) HBEA500 used 4 cycles.



Figure 2. FT-IR spectra of (a) fresh, (b) used, and (c) regenerated HBEA500.

decreases in the ring dimensions can effectively hinder or block the movement of particular molecular species through the zeolite structure. The effective pore dimensions that control the access to the interior of the zeolites are determined not only by the geometric dimensions of the tetrahedra forming the pore opening, but also by the presence or absence of ions in or near the pore. The approximate molecular dimensions of the reactant o-xylene,  $3.6 \times 7.1 \times 8.1 \text{ Å}^3$ , result in very slow diffusion into the medium-pore-type zeolites such as HZSM-5 (5.6  $\times$  $5.4 \text{ Å}^2$ );<sup>16</sup> both the selectivity and yield were unsatisfactory (Entry 5, Table 1). This may be attributed to the mediumpore-sized structure, which would place more restriction on the transport of a substrate through the pores. The 4-nitro-o-xylene to 3-nitro-o-xylene ratio was marginally higher (7.8) over HBEA500 zeolite as compared to the other zeolites, probably owing to the large pores (pore size:  $7.6 \times 6.4 \text{ Å}^2$ ) of HBEA500 and its open framework structure leading to the faster diffusion of 4-nitro-o-xylene than 3-nitro-o-xylene because of the difference in the kinetic diameter. Zeolites possess both the Lewis and Brønsted acid sites, which are catalytically active sites.<sup>17</sup> The IR spectrum at 3610 and 3740 cm<sup>-1</sup> are assigned to the acidic bridged OH of Si(OH)Al and isolated silanol group (Figure 2a).<sup>18,19</sup> Highly conspicuous decreases in the number of acid sites have been observed with the increase in the Si/Al<sub>2</sub> ratios (Table 4). Catalytic results showed that zeolites with high Si/Al<sub>2</sub> ratios improved the yields of isomer products. Zeolites with lower Si/Al<sub>2</sub> ratios, which have stronger acid strength, are sufficiently strong to catalyze the substrate to produce by-side as well, restricting the increase in the yield. Therefore, it could be expected that HBEA500 with  $Si/Al_2 = 500$  is a milder catalyst,

Table 4. Characteristics of zeolites with different Si/Al<sub>2</sub> molar ratios

Catalyst	Si/Al <sub>2</sub>	Acid amount $/\text{mmol}\text{g}^{-1\text{a}}$	H <sub>o</sub>	$\begin{array}{c} BET \ surface \\ area/m^2 \ g^{-1} \end{array}$	Pore volume $/cm^3g^{-1}$
HZSM-5	30	0.58	$H_{\rm o} < -8.2$	399	0.20
Y-type	4	0.37	$-0.2 < H_0 < +0.8$	782	0.23
HBEA30	31	0.66	$-4.4 < H_o < -0.2$	615	0.27
HBEA60	58	0.35	$-0.2 < H_0 < +0.8$	599	0.27
HBEA130	127	0.15	$+3.3 < H_0 < +4.8$	594	0.26
HBEA260	256	0.09	$+3.3 < H_0 < +4.8$	587	0.28
HBEA500	503	0.05	$+3.3 < H_0 < +4.8$	583	0.29

<sup>a</sup>Acid amount and acid strength ( $H_0$ ) were determined by Hammett indicator method.



Figure 3. XRD patterns of (a) fresh and (b) 4 cycles HBEA500.

Table 5. Efficiency of recycled HBEA500 in the preparation of nitro-oxylene<sup>a</sup>

Recycle	Vialdb/0	Isomer pro	2.2 ratio	
number	riela / %	3	2	- 3.2 Tatio
Fresh	81	89	11	7.8
1	79	88	12	7.3
2	77	88	12	7.1
3	76	87	13	6.8

<sup>a</sup>Reaction conditions: *o*-xylene:acetic anhydride = 0.6:5 (v/v), *o*-xylene: nitrogen dioxide = 1:4 ratio, HBEA500 0.53 g (100 wt % based on oxylene), reaction temperature: 35 °C, reaction time: 12 h, under oxygen atmosphere. <sup>b</sup>Combined yield of 2 and 3 based on consumed 1 was given. Proportion of products was determined by GC with 4-nitrotoluene as internal standard.

which showed good yield and selectivity for the nitration reaction and produced less polynitration and oxidation products.

HBEA500 was easily recovered from the reaction mixture by simple filtration for reuse. The XRD patterns of fresh catalysts and catalysts used for four cycles displayed two typical peaks located at  $2\theta = 22.5$  and 7.4, respectively (Figure 3), exhibiting that the structure of HBEA500 is similar to that of the BEA zeolite. SEM and FT-IR showed the same results (Figure 1b, Figure 2b, and Figure 2c). Even after using HBEA500 four times, only a slight change was observed in the selectivity and vield with a minor loss of the original activity (Table 5).

A comparative analysis of the nitration aromatic compounds under similar conditions was also described. The results are summarized in Table 6. The catalyst was very effective toward activities aromatic compounds (Entries 1-3, Table 6) and the corresponding nitro products were readily obtained in good to excellent yields. It is notable that polyaromatic hydrocarbon

Table 6. Nitration of various substrates with nitrogen dioxide and HBEA 500<sup>a</sup>

Entry	Substrate	Conversion <sup>b</sup> /%	Yield <sup>c</sup> /%	Distribution <sup>d</sup> /%
1 <sup>e</sup>	CH3	99.7	87.2	$\bigcup_{i=1}^{CH_3} \overset{CH_3}{\underset{i=1}{\overset{CH_3}{\overset{CH_3}}}} 3.4 \qquad \bigcup_{i=1}^{CH_3} 70.6$
2	CH3 CH3	100	98.5	CH <sub>3</sub> CH <sub>3</sub> CH <sub>3</sub> NO <sub>2</sub> KO <sub>2</sub> KO <sub>2</sub> CH <sub>3</sub> KO <sub>2</sub> CH <sub>3</sub> KO <sub>2</sub>
3	CH3	100	86.0	CH <sub>3</sub> NO <sub>2</sub>
4		99.8	93.2	$\bigcirc^{O_2N}_{P_2N}$ 35.4 $\bigcirc$ NO <sub>2</sub> 64.6
5 Br-		-Br 99.9	91.9	Br-C-Br 91.0 Br-C-Br 9.0

<sup>a</sup>Reaction conditions: substrate:nitrogen dioxide = 1:4 (mole ratio), reaction time: 12 h, reaction temperature: 35 °C, acetic anhydride as the solvent, under oxygen atmosphere. Amount of HBEA500 was 0.53 g. <sup>b</sup>Determined by GC. Combined yield of products based on consumed substrate. 4-Nitrotoluene was used as an internal standard. <sup>d</sup>Proportion of products was determined by GC with 4-nitrotoluene an internal standard. <sup>e</sup>Nitrobenzene was used as an internal standard.

biphenyl (Entry 4, Table 6) and 4,4'-dibromobiphenyl (Entry 5, Table 6) underwent regioselective nitration under the same reaction conditions. In the nitration of biphenyl (Entry 4, Table 6) and 4,4'-dibromobiphenyl (Entry 5, Table 6), an unprecedented conversion was shown by this nitration system.

In conclusion, 4-nitro-o-xylene was highly selectively prepared in moderate yield with a nitrogen dioxide/molecular oxygen system in the presence of zeolites. Furthermore, the reaction is environmentally friendly because of atom economy and easy workup of HBEA500. Moreover, the present process could be promising for clean and highly selective preparation of nitro aromatic compounds.20

## **References and Notes**

- G. A. Olah, R. Malhotra, S. C. Narang, Nitration: Methods and Mechanisms, VCH, New York, 1989
- Tasneema, M. M. Ali, K. C. Rajanna, P. K. Saiparakash, Synth. Commun. 2 2001, 31, 1123.
- X. Peng, H. Suzuki, C. Lu, Tetrahedron Lett. 2001, 42, 4357.
- M. V. Landau, S. B. Kogan, D. Tavor, M. Herskowitz, J. E. Koresh, Catal. 4 Todav 1997, 36, 497.
- 5 K. Smith, S. Almeer, C. Peters, Chem. Commun. 2001, 2748.
- X. Ma, B. Li, M. Lu, C. Lv, Chin. Chem. Lett. 2012, 23, 73. 6
- K. Smith, G. A. El-Hiti, Curr. Org. Chem. 2006, 10, 1603.
- 8 P.-C. Wang, M. Lu, Tetrahedron Lett. 2011, 52, 1452.
- X. Peng, X. Dong, Y. Tai, Curr. Org. Chem. 2012, 16, 1549.
- 10 T. Suzuki, R. Noyori, Chemtracts 1997, 10, 813.
- 11
- T. Mori, H. Suzuki, Synlett 1995, 383. 12
- X. Peng, H. Suzuki, Org. Lett. 2001, 3, 3431.
- B. M. Choudary, M. Sateesh, M. L. Kantam, K. K. Rao, K. V. R. Prasad, 13 K. V. Raghavan, J. A. R. P. Sarma, Chem. Commun. 2000, 25.
- 14 S. Bernasconi, G. D. Pirngruber, A. Kogelbauer, R. Prins, J. Catal. 2003, 219. 231.
- 15 K. Smith, A. Musson, G. A. DeBoos, J. Org. Chem. 1998, 63, 8448.
- S. K. Sengupta, J. A. Schultz, K. R. Walck, D. R. Corbin, J. C. Ritter, Top. 16 Catal. 2012, 55, 601.
- V. N. Sheemol, B. Tyagi, R. V. Jasra, J. Mol. Catal. A: Chem. 2006, 252, 17 194
- 18 Y. Miyamoto, N. Katada, M. Niwa, Microporous Mesoporous Mater. 2000, 40, 271.
- 19 I. Kiricsi, C. Flego, G. Pazzuconi, W. O. Parker, Jr., R. Millini, C. Perego, G. Bellussi, J. Phys. Chem. 1994, 98, 4627
- 20 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.