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Regioselective Double Kyodai Nitration of Toluene and Chlorobenzene over Zeolites. High Preference for the 2,4-Dinitro Isomer at the Second Nitration Stage

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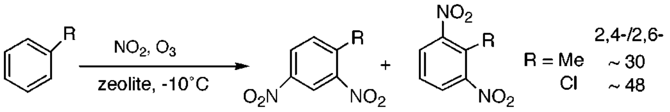
ABSTRACT



The Kyodai nitration of toluene and chlorobenzene has been examined in the presence of a solid inorganic catalyst (montmorillonite K10, zeolite HZSM-5, or HBEA-25). Regioselection was quite low at the mononitration stage, but a considerably high preference for the 2,4-isomer was observed at the dinitration stage.

The nitration of toluene is an important process in the production of various chemical commodities and has long been carried out using nitric and sulfuric acids (mixed acid) on a large-volume scale in developed countries. The reaction is poorly regioselective and usually produces a mixture of 55−60% *ortho*-, 3−4% *meta*-, and 35−40% *para*-nitro isomers.[1] In recent years, however, there has been considerable interest in improving the methodology of this time-honored reaction primarily as a result of increasing environmental concern over chemical wastes and acidic drainage arising therefrom.

The nonacid methodology for aromatic nitration using a NO_2/O_3 system as nitrating agent has demonstrated an excellent conversion of a wide variety of aromatic compounds to the corresponding nitro derivatives under mild conditions (Kyodai nitration).[2] The reaction bears the general appearance of being an electrophilic process and is characterized by some unique features, such as operating under neutral conditions. Inspired by the recent work by Smith and coworkers on the zeolite-promoted *para*-selective nitration of alkylbenzenes and halobenzenes,[3] we also have examined the Kyodai nitration of simple aromatic compounds in the presence of several solid inorganic catalysts. To our disappointment, however, there was observed no significant improvement of regioselectivity. In the case of toluene, for example, the isomer composition of the mononitration product was *ortho* 52−56%, *meta* 1−3%, and *para* 41−45%, the *ortho/para* ratio being in the range 1.2−1.4. These values are not much different from those of traditional nitration based on nitric and sulfuric acids (*ortho/para* ratio, 1.3−1.4) or those of the Kyodai nitration performed in the absence of solid catalyst (*ortho/para* ratio, 1.5).

[†] On leave from Nanjing University of Science and Technology from April 2000 to March 2002.

[1] (a) Harris, G. F. P. In *Industrial and Laboratory Nitrations*; Albright, L. F., Hanson, C., Eds.; American Chemical Society: Washington, DC, 1975; p 313. (b) Hermann, H.; Gebauer, J.; Konieczny, P. In *Nitration. Recent Laboratory and Industrial Developments*; Albright, L. F., Carr, R. V. C., Schmitt, R. J., Eds.; American Chemical Society: Washington, DC, 1995; p 234.

[2] For a survey of the Kyodai nitration, see: (a) Mori, T.; Suzuki, H. *Synlett* **1995**, 383−392. (b) Suzuki, T.; Noyori, R. *Chemtracts* **1997**, *10*, 813−815. (c) Nonoyama, N.; Mori, T.; Suzuki, H. *Zh. Obshch. Khim.* **1998**, *34*, 1591−1601.

[3] (a) Smith, K.; Musson, A.; DeBoos, G. A. *J. Org. Chem.* **1998**, *63*, 8448−8454. (b) Smith, K.; Gibbins, T.; Millar, R. W.; Claridge, R. P. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2753−2758. (c) Smith, K.; Almeer, S.; Black, S. J. *Chem. Commun.* **2000**, 1571−1572.

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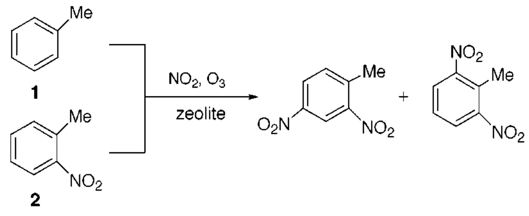
Table 1. Product Composition of the Kyodai Nitration Products of Toluene **1**, Chlorobenzene **3**, and Their *o*-Nitro Derivatives **2** and **4** in the Presence of Clay and Zeolites[a]

		proportion of products at the dinitration stage (%)[b]				isomer distribution at the mononitration stage (%)[e]			
substrate	catalyst	2,4-	2,6-	others[c]	2,4-/2,6- ratio[d]	*ortho*-	*meta*-	*para*-	*ortho*-/*para*- ratio[f]
1		76	17	7.0	4.5	58	2	40	1.5
1	K10[g]	77	13	10	5.9	56	3	41	1.4
1[h]	K10[g]	78	13	9.0	6.0	56	3	41	1.4
1	K10[g]	80	14	6.0	5.7	56	2	42	1.3
1	HZSM−5[j]	77	15	8.0	5.1	52	3	45	1.2
1	HBEA−25[k]	84	9.0	7.0	9.3	56	1	43	1.3
1[l]	HBEA−25[k]	84	8.5	7.5	9.9				
1[j]	HBEA−25[k]	91	5.7	3.3	16	55	2	43	1.3
2		69	30	1.0	2.3				
2	K10[g]	73	24	3.0	3.0				
2	HZSM−5[j]	67	28	5.0	2.4				
2	HBEA−25[k]	88	11	1.0	8.0				
2[l]	HBEA−25[k]	87	11	2.0	7.9				
2[m]	HBEA−25[k]	91	9.0	tr	10				
3		88	3.0	9.0	29	44	1	55	0.8
3	HBEA−25[k]	91	1.9	7.1	48	41	tr	59	0.7
4		91	5.3	3.7	17				
4	HBEA−25[k]	95	2.2	2.8	43				

[a] All reactions of toluene and chlorobenzene were conducted at −10 °C using a given substrate (1.0 mL), liquid NO_2 (1.5−2.0 mL), catalyst (1.0 g), and dichloromethane (30 mL) according to the Kyodai method,[9,10] whereas those of the *o*-nitro derivatives were done using the substrate (5.0−6.0 mmol) in the same solvent (5−10 mL). Conversion of substrate was above 99.5% by GC analysis. [b] Final product composition determined by GC. [c] Other isomeric dinitro compounds. [d] Calculated from GC peak areas. [e] Initial partitioning at the mononitration stage determined by GC. [f] Calculated from GC peak areas. [g] A commercial product from Aldrich, calcined in air at 300 °C for 8 h prior to use. [h] Catalyst amount was increased to 3.0 g. [i] Additional 2.0 g was added 2 h after the start of the reaction. [j] A commercial product from Acros, calcined in air at 500 °C for 8 h prior to use. [k] A gift from the Catalytic Society of Japan, calcined in air at 500 °C for 8 h prior to use. [l] The reaction was carried out at −20 °C. [m] Solvent amount was increased to 50 mL.

Toluene is moderately activated, so the Kyodai nitration of this hydrocarbon is always accompanied by more or less dinitration product. On inspecting the isomer composition of this byproduct, we were very surprised to come upon a considerable preponderance of 2,4-dinitrotoluene over the 2,6-dinitro isomer (2,4-/2,6- = 5.1−9.3). In the classical nitration based on mixed acid or phosphoric-mixed acids, the 2,4-Dinitro and 2,6-dinitro isomers were obtained in about a 4:1 ratio, along with 4% other dinitro isomers.[4]

Scheme 1



2,4-Dinitrotoluene is a basic chemical commodity of great market demand. It is produced annually in many million metric tons scale worldwide and mostly converted to tolylene diisocyanate (TDI), an important precursor to polyurethane resins used for flexible and rigid foams, elastomers, coatings, and fibers. Tolylene 2,4-diisocyanate is preferred to 2,6-diisocyanate for the use in high performance materials, though the mixture of two isomers is frequently employed.

Delighted with this unexpected finding, we have turned our attention to the Kyodai nitration of toluene and *o*-nitrotoluene to give the dinitro compound in the presence of a solid acid catalyst such as montmorillonite K10, zeolite HZSM-5, or HBEA-25. Catalysis by these inorganic solids would provide an opportunity for aromatic nitration to meet environmental economics owing to the easy workup, superior recycling, low price, and noncorrosive nature. Recent literature reports several attempts to obtain the dinitration product of toluene biased in favor of the 2,4-dinitro isomer by using inorganic solids as catalyst. Thus, zirconium and hafnium triflates have been used as an efficient catalyst for the nitration of *o*-nitrotoluene with 69% nitric acid, producing 2,4- and 2,6-dinitrotoluenes in a ratio of 66:34.[5] Dinitration of toluene using Claycop ($Cu(NO_3)_2$ supported on K10), acetic anhydride, and fuming nitric acid in tetrachloromethane leads to a mixture of 2,4- and 2,6-dinitro isomers in a ratio of 9:1.[6] Nitration systems comprising nitric acid,

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(4) A typical isomer distribution of traditional dinitration product of toluene is 2,4- 75%; 2,6- 19%; 3,4- 2.5%; 2,3- 1.0%, and 2,5- 0.5%. Adkins, R. L. In *Kirk-Othmer Encyclopedia of Chemical Technology*, 4th ed.; Wiley: New York, 1996; Vol. 17, pp 150−151.

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trifluoroacetic anhydride (acetic acid or its anhydride), and β zeolite have been used for the two-step dinitration of toluene, giving 2,4- and 2,6-dinitro isomers in a greater ratio of 70:1.[3b] Unfortunately, these nitration methods are still conducted in strong acid media involving inorganic and/or organic acids, so there still remain many problems similar to the conventional method based on mixed acid. In the present work, the inorganic solid assisted conversion of toluene to dinitrotoluenes according to the Kyodai method has been investigated via two different approaches, one involving the straightforward dinitration of toluene and the other involving further nitration of *o*-nitrotoluene.

Clays are assemblies of the tetrahedral layers of SiO_4 silicate units and of the octahedral layers of AlO_6 aluminate units and have interlamellar spacings of less than 1 nm. Organic molecules would be adsorbed onto such limited spaces and/or pores, modifying their reactivity according to the surface properties of inorganic solids. A commercial montmorillonite K10 (Aldrich) was first tested as a catalyst for the regioselective dinitration of toluene. For comparison, we have also carried out the double Kyodai nitration of toluene in dichloromethane in the absence of any solid catalyst and determined the isomer composition of the product. As is apparent from Table 1, the Kyodai method did not affect significantly the isomeric product ratio in comparison to the traditional mixed acid method. Introduction of K10 into the reaction mixture was found to bring only a slight increase in the *para*-selection. Increasing the amount of K10 improved the regioselectivity somewhat toward the 2,4-dinitro isomer.

Zeolites are crystalline aluminosilicates with uniform pore dimension. Zeolite HZSM-5 (Acros) represents a medium-pore material with an elliptical pore size of 0.51−0.55 nm. Table 1 shows the results from the Kyodai nitration of toluene over HZSM-5; the presence or absence of HZSM-5 made only a slight difference under the conditions employed. A minor variation in the composition of the final product probably originated from the mononitration step, where the reaction primarily occurs in a free solution.

Zeolite HBEA-25 (Süd-Chemie AG) with much wider pores than HZSM-5 was then chosen for the study; the results are summarized in Table 1. As can be seen from the table, HBEA-25 is of outstanding catalytic characteristics in the regioselective dinitration of toluene. Judging from the relative variation of the isomer ratios of both mono- and dinitration products, we may well take that HBEA-25 can exert more influence on the dinitration step. It is in the second nitration step that the much higher than normal 2,4-/2,6-dinitro isomer ratio in overall reaction is generated.

The nature of organic solvent was found to exert considerable influence on the regioselectivity of dinitration. As Table 2 shows, of the four different solvents of varied polarity employed, acetonitrile with a high dielectric constant exhibited the best result. The 2,4-/2,6-isomer ratio was enhanced up to 12, along with a 94% combined yield of 2,4- and 2,6-dinitrotoluenes based on toluene.

Table 2. Effect of Solvent Types on the Regioselectivity of Kyodai Dinitration of Toluene in the Presence of Zeolite HBEA-25[a]

		product composition (%)[b]			
substrate	solvent	2,4-	2,6-	others	2,4-/2,6- ratio[c]
1	n-C_6H_{14}	75	15	10	5.0
1	CCl_4	74	18	8.0	4.1
1[d]	CCl_4	78	12	10	6.5
1	CH_2Cl_2	84	9.0	7.0	9.3
1	MeCN	87	7.2	5.8	12
2	n-C_6H_{14}	72	25	3.0	2.9

[a] A gift from the Catalytic Society of Japan; calcined in air at 500 °C for 8 h prior to use. Other conditions excepting the solvent were the same as those given in Table 1. [b] Final product composition determined by GC. [c] Calculated from GC peak areas. [d] Additional 2.0 g was added 2 h after the start of the reaction.

Increasing the amount of solvent and catalyst favored the reaction further toward the 2,4-dinitro isomer up to ca. 97% high selectivity (Table 3), while decreasing the reaction temperature made little difference in regioselectivity.

Table 3. Effect of Catalyst Amount on the Isomer Ratio in the Kyodai Dinitration of Toluene[a]

	product composition (%)[b]			
HBEA-25 (g)	2,4-	2,6-	others	2,4-/2,6- ratio[c]
0.5	83	12	5.0	6.9
1.0	87	7.2	5.8	12
2.0	90	4.7	5.3	19
3.0[d]	93	4.0	3.0	23
4.0	94	3.3	2.7	28

[a] All reactions were carried out in acetonitrile. Other conditions excepting the catalyst amount were the same as those given in Table 1. [b] Final product composition determined by GC. [c] Calculated from GC peak areas. [d] The reaction was started using 1.0 g of catalyst and an additional 2.0 g was added 2 h after the start.

The spent HBEA-25 was easily recovered from the reaction mixture by simple decantation or filtration and could be reused without any loss of original activity. Even after five times usage, there was observed little change in the numerical values as to the yield and relative ratio of 2,4-/2,6-dinitro isomers (Table 4).

As an extension of the present work, we have investigated the double Kyodai nitration of chlorobenzene under similar conditions. 1-Chloro-2,4-dinitrobenzene is of the greatest market demand among the six possible isomers as an intermediate in the manufacture of dyes, fungicides, rubber chemicals, and highly energetic materials. Treatment of chlorobenzene with excess of mixed acid at elevated temperature produces 1-chloro-2,4-dinitrobenzene as the major product, together with about 10% of the 2,6-dinitro isomer.[7]

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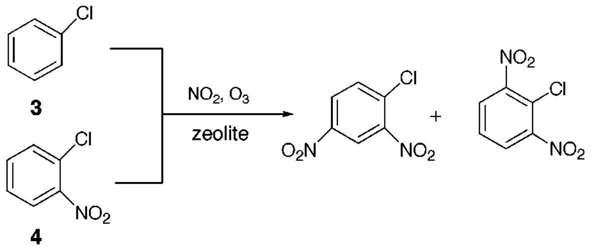
Table 4. Efficacy of Recycled HBEA-25 in the Kyodai Dinitration of Toluene[a]

	product composition (%)[b]			
run	2,4-	2,6-	others	2,4-/2,6- ratio[c]
1	93	3.2	3.8	29
2	94	3.1	2.9	30
3	92	3.1	4.9	30
4	93	3.2	3.8	29
5	94	3.1	2.9	30

[a] All reactions were carried out using 4.0 g of the catalyst in acetonitrile (30 mL). Other conditions were the same as those given in Table 1. [b] Final product composition determined by GC. [c] Calculated from GC peak areas.

When the Kyodai nitration of chlorobenzene was carried out in the presence of zeolites, there was observed only a small change of the isomer composition at the mononitration stage. At the dinitration stage, however, the regioselection was again improved in favor of the 2,4-dinitro isomer (Table 1). Very recently, Moodie and co-workers have performed the nitration of *o*-chloronitrobenzene with dinitrogen pentaoxide in the presence of Faujasite-712, where they obtained a mixture of 1-chloro-2,4-dinitro- and 1-chloro-2,6-dinitrobenzenes in about 30:1 ratio.[8]

Scheme 2



The absence of regioselectivity at the mononitration stage and its appearance at the dinitration stage may be interpreted as follows. The Kyodai nitration involves the nitrogen trioxide (NO_3) generated in situ as an initial electrophile, which is a powerful oxidant and reacts in a dual mode depending on the oxidation potentials of aromatic substrates.[9] Toluene (PhMe) is moderately activated and readily oxidized by NO_3 to generate a radical cation/nitrate anion pair $[PhMe^{+\bullet}/NO_3^{-}]$, which is trapped by NO_2 to give the arenium ion $[PhMe(NO_2)]^+$ and subsequently nitrotoluenes via proton loss. The mononitration of toluene proceeds so rapidly that, as reported previously,[10] the reaction shows no kinetic dependence on the concentration of substrate (diffusion-controlled). Therefore, the initial nitration of toluene would mostly complete in a free solution and the solid catalyst does not play any positive role therein. The resulting nitrotoluenes are deactivated and not readily oxidized to form a radical cation. So they would be adsorbed on the solid surface through the electrostatic interaction, as well as the hydrogen bonding between the nitro function and the Brønsted acid sites, and react further via the ordinary mechanism involving the nitronium ion that arises from NO_2 and NO_3 via dinitrogen pentaoxide (N_2O_5). Thus, further nitration of *p*-nitrotoluene is straightforward to give the 2,4-dinitro derivative, but the regioselection would become important with *o*-nitrotoluene.[11] The vacant position adjacent to the methyl group is subject to the primary *ortho* effect, which in addition is strengthened by the buttressing effect of the solid surface. Then the nitronium ion would preferentially attack the position *para* to the methyl group, leading to the formation of the 2,4-dinitro isomer. Polar solvent systems should work favorably for the generation of this ionic species. Being a weaker Lewis base, the resultant dinitrotoluene is easily evicted from the solid surface by mononitrotoluene, the latter then goes into the next cycle of reaction.

In conclusion, the procedure for the regioselective dinitration of toluene and chlorobenzene described above, which involves the Kyodai nitration in polar organic solvent in the presence of zeolite HBEA-25, is superior to the traditional method based on mixed acid and provides a new efficient route to the 2,4-dinitro derivatives under nonacid conditions. The method is easy to carry out, environmentally benign, and economical.

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Supporting Information Available: Details of analytical procedure, including a typical gas chromatogram. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Suzuki, H.; Murashima, T.; Mori, T. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1591−1597.

(11) On treatment with excess mixed acid, *p*-nitrotoluene gives almost exclusively the 2,4-dinitro isomer (>99%), while *o*-nitrotoluene affords a 67:33 mixture of 2,4- and 2,6-dinitro isomers. Booth, G. In *Ullmann's Encyclopedia of Industrial Chemistry,* 5th ed.; Elvers, B., Hawkins, S., Schulz, G., Eds.; VCH: New York, 1991; Vol. A17, p 421. On similar treatment, *o*-chloronitrobenzene yields 2,4- and 2,6-dinitro compounds in a ratio of 10.6:1. Claridge, R. P.; Lancaster, N. L.; Millar, R. W.; Moodie, R. B.; Sandall, J. P. B. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1815−1818.