

Regioselective Nitration of Inactive 4,4'-Dibromobiphenyl with Nitrogen Dioxide and Molecular Oxygen over Zeolites: An Efficient Preparation of 4,4'-Dibromo-2-nitrobiphenyl

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(Received September 22, 2013; Accepted December 12, 2013)

ABSTRACT. In the presence of zeolites, 4,4'-dibromobiphenyl could be region-selectively nitrated by the action of nitrogen dioxide and molecular oxygen. The ratio of 4,4'-dibromo-2-nitrobiphenyl to 4,4'-dibromo-3-nitrobiphenyl could reach 14 in a high yield of 90%. Zeolites could be easily regenerated by heating and reused four times to give the results similar to those obtained with fresh catalyst. Compared with the classic nitration method, no nitric acid and sulfuric acid were used, which suggested that the method was an environmentally economic process.

Key words: 4,4'-Dibromobiphenyl, 4,4'-Dibromo-2-nitrobiphenyl, Nitration, Nitrogen dioxide, Zeolite

INTRODUCTION

Electrophilic nitration of aromatics is a fundamental reaction in the preparation of intermediates of many compounds including pharmaceuticals, dyestuffs, explosives, pesticides, and so on.¹ The mechanistic and synthetic aspects of nitration chemistry have been studied over these years. However, many traditional processes suffer from serious disadvantages, including low selectivity for the desired product and the requirement for large quantities of mineral or Lewis acids as activators.² Major efforts are therefore being made to develop processes with lower environmental impact.

Among a number of efforts on developing alternative methodologies, the combined use of nitrogen dioxide and molecular oxygen in the place of the classical nitric acid-sulfuric system appears to be the most attractive and promising.³ Suzuki has reported that nitrogen dioxide is activated to react with a wide variety of nonactivated and moderately activated aromatic substrates to afford the corresponding nitro compounds in good yields.⁴ We have reported that 1-nitronaphthalene, naphthonitriles and methylated benzonitriles could be smoothly nitrated in the presence of zeolites by the combined action of nitrogen dioxide and molecular oxygen.⁵ The use of solid acid catalysts is a very attractive alternative to improve regioselectivity because of the ease of separation, recyclability of the catalysts.⁶ 4,4'-Dibromo-2-nitrobiphenyl is an important fine chemical with a constantly increasing world market owing to its

usefulness as synthetic intermediates.⁷ The present work deals with an efficient and high-selective preparation of the nitrated 4,4'-dibromobiphenyl with a nitrogen dioxide/molecular oxygen process.

EXPERIMENTAL

Reagents and Apparatus

Zeolites were purchased from New Materials Research Center of Tianjin in China. Melting points were determined on a WRS-2 apparatus and uncorrected. ¹H NMR and ¹³C NMR spectra were recorded on a Agilent VNMRS-600MHz spectrometer (at 600 and 151MHz, respectively) with TMS as internal standard. Chemical shifts (δ) were expressed and coupling constants *J* were given in Hz. Infrared (IR) spectra were recorded on a Thermo Nicolet 67 Fourier transform (FT)-IR spectrometer as KBr pellets. High resolution mass spectra (HRMS) data were obtained using a Waters ACQUITY UP mass spectrometer with ESI source. TLC was performed with silica gel GF254 percolated on class plates, and spots were visualized with UV. Shimadzu GC-2014C (WONDACAP-1 df=1.5 μ m \times 0.53 mm I.D \times 30 m) was utilized to determine product isomer compositions with 4-nitrotoluene as internal standard. The injector and flame ionization detector were set at 280 °C. The GC column was operated from 140 to 250 °C at a rate of 10 °C/min, and held the final temperature for 3 min. All other chemicals were analytical grade without any further purification.

Typical Experimental Procedure for Zeolite Cation-exchange

The standard procedure for cation-exchange involved stirring a supplied commercial zeolite (2.50 g) in a refluxing aqueous solution of the corresponding metal chloride (0.2 mol/L, 50 mL) for 24 h. The solid was filtrated, washed with deionized water until halide-free and dried at 110 °C for 6 h, and then calcined in air at 550 °C for 6 h.

Nitrate Progress with Nitrogen Dioxide/molecular Oxygen

Quantitative 4,4'-dibromobiphenyl, nitrogen dioxide, zeolite, and dichloromethane were placed in a flask. Oxygen was passed into the system to replace air, and a balloon filled with oxygen was connected. The mixture was stirred at a certain temperature and progress of the reaction was monitored by TLC with pure petroleum ether as eluent. The R_f values of 4,4'-dibromobiphenyl and 4,4'-Dibromo-2-nitrobiphenyl are 0.75 and 0.31, respectively.

When the reaction was complete, excess nitrogen dioxide was removed by blowing air into the solution and collected in a cold trap for reuse. The zeolite was removed by filtration and the filter liquor was washed with water, 5% aqueous solution of sodium bicarbonate followed by water. The organic phase separated was dried with anhydrous sodium sulfate, and concentrated under reduced pressure to give a yellow solid residue. The product was analyzed by GC. The yellow solid with further purifica-

tion was analyzed. The used zeolite was recovered by washing and calcination.

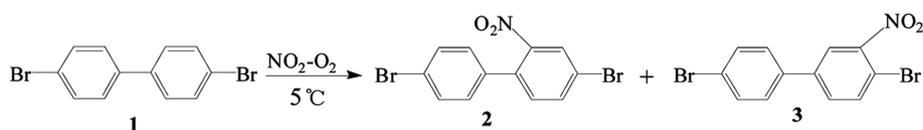
4,4-Dibromo-2-nitrobiphenyl

Yellow solid mp 125.1–125.8 °C (lit.⁸ mp 125–126 °C) IR (KBr) $\nu = 1535$ (NO₂), 785 (C–Br) cm⁻¹. ¹HNMR (CDCl₃, 600 MHz) δ 8.02 (s), 7.55 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H). ¹³CNMR (DMSO, 151 MHz) δ 152.37, 138.91, 138.32, 136.56, 136.15, 134.87, 133.02, 129.90, 125.26, 124.36. HRMS (ESI) for C₁₂H₇Br₂NO₂ calcd 364.8844 found 364.8841.

RESULTS AND DISCUSSION

From *Table 1*, nitration of 4,4'-dibromobiphenyl **1** with traditional nitric acid and nitrosulfuric acids gave a mixture of 4,4'-dibromo-2-nitrobiphenyl **2** and 4,4'-dibromo-3-nitrobiphenyl **3** in the isomer ratio of 2.5 and 3.8 (Entries 1 and 2 in *Table 1*) in yield of 70 and 38%, respectively. Dinitrated products were predominant in nitrosulfuric acids process. However, reaction could be mildly conducted at the combined action of nitrogen dioxide and molecular oxygen. When the amount of nitrogen dioxide increasing, the reaction towards good mononitrated yield in high region-selection up to a ratio of 6.0–9.0 above in **2** to **3** (Entries 5–7 in *Table 1*) and 4,4'-dibromo-2-nitrobiphenyl **2** was efficiently formed in over 70% yield.

It was also found that catalysts played an important role



Scheme 1.

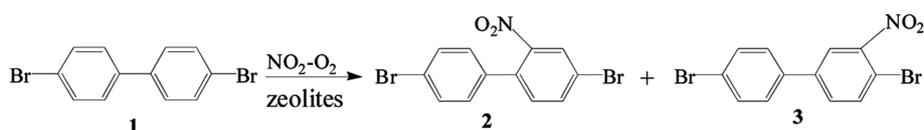
Table 1. Nitration of 4,4'-dibromobiphenyl with acid or NO₂-O₂

Entry	Nitrating agent ^a	Reaction time/h	Conversion (%)	Yield (%)	Isomer proportion		2 : 3 Ratio
					2	3	
1	HNO ₃ ^b	8	75	70	50	20	2.5
2	HNO ₃ -H ₂ SO ₄ ^c	3	100	38	30	8	3.8
3	NO ₂ -O ₂ (1:2)	24	31	28	18	10	1.8
4	NO ₂ -O ₂ (1:4)	12	57	53	35	18	1.9
5	NO ₂ -O ₂ (1:6)	10	78	70	60	10	6.0
6	NO ₂ -O ₂ (1:8)	10	>99	79	71	8	8.9
7	NO ₂ -O ₂ (1:10)	6	100	80	72	8	9.0
8	NO ₂ -O ₂ (1:12)	6	100	81	72	9	8.0
9	NO ₂ -O ₂ (1:14)	6	100	81	73	8	9.1

^aThe data in parentheses meant a molar ratio of nitrogen dioxide to 4,4'-dibromobiphenyl.

^bThere action was carried out in dichloromethane (5.0 mL) using **1** (1.0 mmol), 95% nitric acid (2.0 mmol).

^cThe reaction was conducted in dichloromethane (5.0 mL) using **1** (1.0 mmol), 95% nitric acid (1.5 mmol) and 98% sulfuric acid (1.5 mmol).



Scheme 2.

Table 2. Nitration of 4,4'-dibromobiphenyl with nitrogen dioxide/molecular oxygen in the presence of zeolite catalysts^a

Entry	Catalyst ^b	Reaction time/h	Conversion ^c (%)	Yield ^d (%)	Isomer proportion (%) ^e		2 : 3 Ratio
					2-Nitro 2	3-Nitro 3	
1 ^f	–	10	39	34	27	7	3.9
2 ^f	HBEA-25	10	93	87	78	9	8.7
3 ^g	–	12	53	48	40	8	5.0
4 ^g	–	24	97	89	80	9	8.9
5	–	10	76	70	60	10	6.0
6	HBEA-25	10	100	88	80	8	10
7	BEA-280	10	98	88	82	6	14
8	BEA-500	10	100	89	81	8	10
9	HZSM-5	12	91	80	70	10	7.0
10	Fe-ZSM-5	12	100	90	84	6	14
11	Co-ZSM-5	12	>99	86	78	8	9.8
12	La-ZSM-5	12	>99	84	77	7	11
13	Mg-ZSM-5	12	>99	90	80	10	8.0

^aAll reactions were carried out in dichloromethane (5 mL) using substrate **1** (1.0 mmol), liquid NO₂ (6.0 mmol) and catalyst (0.2 g). Oxygen was passed into the system to replace air, and a balloon filled with oxygen was connected. The mixture was stirred at 5 °C.

^bZeolites were calcined at 550 °C for 2 h in air prior to use.

^cDetermined by GC.

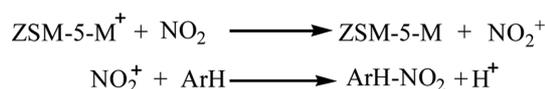
^dA combined yield of **2** and **3** based on consumed **1** was given.

^eCalculated from GC peak areas, excluding other isomers and byproducts.

^fConducted in the air atmosphere.

^g1,2-dichloroethane was used as the solvent.

in improvement of the reaction. Smith and his coworkers had reported that halobenzenes could be nitrated with nitrogen dioxide and molecular oxygen in the presence of zeolite HBEA catalyst can give products of nitration, in which the *para*-nitro isomer predominates over the *ortho*-isomer.⁹ While Suzuki group had reported that ZSM-5 appeared to be better catalytic selective characteristics.¹⁰ In the recent work of the Chun J Shi, superior selectivity for production of 4,4'-dibromo-2-nitrobiphenyl was achieved at low conversion catalyzed by HBEA-500 with nitric acid/acetic anhydride as nitration agent.¹¹ In the hope of improving the selectivity of 4,4'-dibromo-2-nitrobiphenyl in the nitrogen dioxide and molecular oxygen system, hydrogen and its metal ions exchanged BEA and ZSM-5 zeolites were employed. Zeolites facilitated the reaction and gave a high yield as compared with no catalysts. Among H⁺, Co²⁺, Mg²⁺, Fe³⁺ and La³⁺ modified zeolites, FeZSM-5 was observed to give the most excellent yield of 90% with 84% 4,4'-dibromo-2-nitrobiphenyl selectivity (Entries 6-13 in Table 2). The activity of the zeolites may be due to



Scheme 3.

the existence of strong acid sites and metal cations, which could easily prompt the production of NO₂⁺ that appeared to play a positive role in attaining a higher 2 : 3 isomer ratio (Scheme 3).

As considering the prospects for applications, the optimization scale up procedures were investigated. The represented results were summarized in Table 3. From Table 3, the similar yields and isomers ratio had been achieved.

FeZSM-5 could be reused by simple filtration with a little loss of original activity (Table 4). Even after four times usage there was few observed change in nitration selectivity and yield.

Table 3. Scale-up procedures^a

Entry	Amount of substrate (g)	Amount of catalyst (g)	Nitrating agent ^b	Conversion (%)	Yield (%)	Isomer proportion		2 : 3 Ratio
						2	3	
1	0.31	0.2	1:6	100	90	84	6	14
2	0.62	0.3	1:5	94.5	88	82	6	14
3	1.24	0.4	1:4	100	92	86	6	14

^aThe mixture was stirred at 5 °C for 12 h.^bThe ratio in parentheses meant a molar amount in nitrogen dioxide to 4,4'-dibromobiphenyl.**Table 4.** Efficiency of recycled FeZSM-5 in the nitration of 4,4'-dibromobiphenyl^a

Entry	Conversion (%)	Yield (%)	Isomer Production (%)		2 : 3 Ratio
			2-Nitro	3-Nitro	
fresh	100	90	84	6	14.0
1	100	88	82	6	13.7
2	100	87	81	6	13.5
3	100	87	80	7	11.4
4	100	86	80	6	13.3

^aAll conditions were the same to Table 3 (Entry 1).

CONCLUSION

Nitration of 4,4'-dibromobiphenyl with nitrogen dioxide/molecular oxygen system in the presence of zeolites could show excellent selectivity in high yield. Moreover, 4,4'-dibromo-2-nitrobiphenyl could be efficiently prepared using environmentally economic process.

Acknowledgments. The publication cost of this paper was supported by the Korean Chemical Society.

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