Silver Catalyzed Bromination of Aromatics with *N*-bromosuccinimide

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Abstract A heterogeneous silver catalyst was prepared and applied efficiently for the selective bromination of aromatics with NBS. The silver nanoparticles combined with the acidic support HMB can activate both the aromatic ring and NBS, and the synergistic effects between the silver nanoparticles and the HMB highly enhanced the efficiency of the bromination reaction.

Keywords Silver · Aryl bromides · Bromination · Aromatics · *N*-bromosuccinimide

1 Introduction

Aryl bromides are useful intermediates for the synthesis of pharmaceuticals, agrochemicals and functional materials through cross-coupling reactions [1–4]. A variety of brominating agents have been developed and reported for the bromination of aromatic compounds [5, 6]. Among these reagents, *N*-bromosuccinimide (NBS) is a useful brominating reagent in laboratory synthesis, since only inert succinimide by-product formed in the process. A lot of methods have been developed for the preparation of aryl bromides from electron-rich aromatics, but the bromination of unactivated aromatics with NBS proceeded only in the presence of stoichiometric amounts of strong Lewis acids or protic acids as catalysts [7–10]. Moreover, harsh experimental conditions were required for the bromination

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of deactivated aromatics, such as high temperature and high acidic solutions [11, 12]. Recently, efficient catalyst systems were reported for the bromination reactions under mild conditions, but high catalyst loading required, and only electron-rich aromatics were applicable [13–17]. Thereafter, the development of green and efficient catalysts for the bromination of aromatics remains important.

Mesoporous molecular sieves are versatile catalysts and catalytic supports as they are thermal stable, strong acidic, with high surface area and large pore volume, which are highly beneficial to catalytic reactions [18–21]. For example, Kumar et al. [22] reported a mesoporous catalyst Ag-MCM-41 applied for ozone decomposition at ambient temperature. In addition, a SBA-15 supported silver nanocatalyst was developed for the three-component reaction of aldehydes, alkynes and amines [23]. Herein, we reported a silver nanocatalyst on mesoporous beta molecular sieve (Ag/HMB) for the selective bromination of aromatics with NBS, and the catalyst was efficient and reusable (Scheme 1).

2 Experimental

2.1 Reagents

All the reagents were purchased from Aladdin Reagent, Sigma-Aldrich Company and Alfa-Aesar Company without further purification.

2.2 Analytical Methods

Gas chromatograph (GC) analysis was performed on a Hewlett Packard 5890 instrument with a FID detector and Hewlett Packard 24 m \times 0.2 mm i.d. HP-5 capillary

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column. ¹H-NMR spectra were recorded on a Bruker 500 MHz instrument with chemical shifts reported in ppm relative to the residual deuterated solvent or the internal standard tetramethylsilane. The inductively coupled plasma optical emission spectroscopy (ICP-OES) analysis was performed with a Perkin Elmer OPTIMA 2000DV. Transmission electron microscopy (TEM) images were obtained on a JEM-2010URH with an accelerating voltage of 200 kV. The specific surface areas and the average pore sizes of the materials were measured on a Belsorp II physical adsorption apparatus by BET and BJH methods, and scanning electron microscope (SEM) images were taken using a HITACHI S4800 operated at an accelerating voltage of 10-20 kV. X-ray powder diffraction (XRD) analysis was carried out using a D8 Diffractometer (advance superspeed, Bruker-AXS Company).

2.3 General Procedure for Synthesis of HMB

Tetraethyl ammonium hydroxide (20% aqueous solution, 5 mL, 6.7 mmol), sodium aluminate (0.1255 g, 1.0 mmol), and silicon dioxide (2 g, 33.3 mmol) were added in 22.87 mL water at 40 °C. The mixture was stirred at 40 °C for 2 h, and then aged at 100 °C for 18 h. After the mixture was cooled to room temperature, cetyltrimethyl ammonium bromide (1.58 g, 4.33 mmol) was added with stirring, and the mixture was aged again at 150 °C for 2 days. When the mixture was cooled, the solid was filtered and washed with water until the filtrate was neutral (pH = 7). The solid was dried under vacuum and then heated to 580 °C (with a heating rate of 1 °C min⁻¹) and calcined at 580 °C for 5 h to give NaMB (the Na⁺ form). The NaMB (1.0 g) was treated with NH₄Cl solution (3.75 g NH₄Cl contained) at 60 °C for 12 h to form the NH₄MB (the NH₄⁺ form), and then the NH₄MB was calcined at 500 °C for 4 h to afford HMB (the H^+ form).

Molecular sieve beta was synthesized as following: Tetraethyl ammonium hydroxide (20% aqueous solution, 5 mL, 6.7 mmol), sodium aluminate (0.1255 g, 1.0 mmol), and silicon dioxide (2 g, 33.3 mmol) were added in 22.87 mL water at 40 °C. The mixture was stirred at 40 °C for 2 h, and then aged at 100 °C for 18 h. After the mixture was cooled to room temperature, the solid was filtered, washed with water until the filtrate was neutral (pH = 7). The solid was dried under vacuum and then calcined at

580 °C. And then the solid was treated with NH₄Cl solution and calcined again to give the molecular sieve beta (the H^+ form).

2.4 Synthesis of the Supported Metal Catalysts

Ag/HMB and Ag/Beta were prepared by cation-exchange/ reduction method, and the procedure was as following: The HMB (0.5 g) was added into 20 mL AgNO₃ (0.02 g) aqueous solution in a round bottom flask. After stirring for 10 h at room temperature, the solid was filtered off, washed with water, dried under vacuum, and then reduced with H₂ at 180 °C for 5 h to afford brown powder Ag/HMB catalyst (0.5 g, Ag 2.15 wt%). Ag/Beta (Ag supported on molecular sieve beta) was prepared in the similar way (Ag 2.09 wt%). Au/HMB was prepared as follows: the HMB (0.5 g) was added into 20 mL HAuCl₄ (0.025 g) aqueous solution in a round bottom flask with vigorously stirring at room temperature. After stirring for 10 h at room temperature, the solid was filtered off, washed with water, dried under vacuum, and then reduced with H₂ at 180 °C for 5 h to afford violet powder Au/HMB catalyst (Au 2.10 wt%).

Other Ag catalysts were prepared as follows: the support (0.5 g) was added into 20 mL AgNO₃ (0.016 g) solution in a round bottom flask. After stirring for 10 h at room temperature, the solid was dried under vacuum, and then reduced with H₂ at 180 °C for 5 h to afford Ag/TiO₂ (Ag/anatase, Ag 2.05 wt%), Ag/CeO₂ (Ag/ceria, Ag 2.09 wt%), Ag/C (Ag 2.07 wt%), Ag/HT (Ag/hydrotalcite, Ag 2.07 wt%), Ag/HAP (Ag/hydroxyapatite, Ag 2.03 wt%) respectively. The content of Ag/Au was determined by ICP-OES.

2.5 Typical Procedure for the Bromination of Aromatics with NBS

An aromatic compound (1.0 mmol), Ag/HMB (Ag: 2–4 mol%), NBS (1.1 mmol), and dichloroethane (DCE) (2.0 mL) were added in a pressure tube with a magnetic stir bar, and the tube was kept at 25–100 °C for 16 h (see Table 2 for the detailed reaction conditions). After the reaction was completed, the reaction mixture was added 100 μ L hexadecane (internal standard), and the Ag/HMB was separated by filtration. The conversions and yields were determined by GC with an internal standard (C₁₆H₃₄).

The products were isolated by flash column chromatography (eluting with ethyl acetate/hexane mixture) characterized by ¹H-NMR. All prepared products are commercial available and identified by comparison (GC/MS) with authentic samples (purchased from Aldrich Company).

2.6 Reusability of the Ag/HMB

When the reaction completed and the reaction mixture was cooled, the used catalyst Ag/HMB was collected by filtration, and washed with ether, and then dried by vacuum at 25 °C for 12 h. The recycled catalyst was used again for the bromination of p-xylene under the same condition described in Table 1.

3 Results and Discussion

From the SEM image, the HMB was a mesoporous structured material (Fig. 1). On the basis of the nitrogen

Table 1 Bromination of *p*-xylene with NBS in DCE

adsorption-desorption analysis, the BET surface area and the BJH pore volume of HMB were $832 \text{ m}^2 \text{ g}^{-1}$ and $1.017 \text{ cm}^3 \text{g}^{-1}$ respectively, which indicated that HMB was highly porous. On the other hand, the BET surface area and BJH pore volume of the Ag/HMB were 767 m² g⁻¹ and $0.976 \text{ cm}^3 \text{ g}^{-1}$ respectively, which were slightly reduced in contrast of the original HMB material (Fig. 2). The average pore diameter of Ag/HMB was 4.9 nm, which was similar to that of the original HMB material (4.7 nm). The TEM image of the catalyst showed that Ag nanoparticles were dispersed well on the HMB, and the average diameter of the Ag particles was about 3-5 nm (Fig. 3). The diffraction wide peaks of Ag (111) (38.12°) and Ag (200) (44.28°) were found in the X-ray diffraction spectra of Ag/HMB (Fig. 4). Wide peaks of the Ag/HMB implied small size of the Ag particles, which was in consistent with the results from TEM image.

In order to estimate the strength of acid sites, Ag/HMB and Ag/Beta were characterized by means of NH_3 -TPD. The Ag/Beta was strongly acidic, and a strong desorption peak of

	$+ \qquad \begin{array}{c} 0 \\ N-Br \\ 0 \end{array} \qquad \begin{array}{c} Ca \\ solv \end{array}$	ent Br +	O N-H O
Entry	Catalyst	T (°C)	Conv./yield (%)
1	Ag/HMB	25	45/44
2	Ag/HMB	40	70/69
3	Ag/HMB	60	98/96
4	Ag/HMB	80	99/95
5 ^a	Ag/HMB	60	80/77
6	Ag/TiO ₂	60	93/45
7	Ag/CeO ₂	60	97/3
8	Ag/C	60	72/18
9	Ag/HT	60	10/trace
10	Ag/HAP	60	17/trace
11	Ag/Beta	60	30/11
12	Au/HMB	60	70/62
13 ^b	Ag/HMB	60	97/94
14	AgBr	60	5/trace
15	AgNO ₃	60	5/2
16	HMB	60	27/10
17	No	60	Trace/trace

Reaction conditions Ag/Au catalyst, 2 mol%; p-xylene, 1.0 mmol; NBS 1.1 equiv.; DCE 2.0 mL as solvent; 16 h; conversions and yields were determined by GC using hexadecane as the internal standard

^a 2.0 mL acetonitrile as solvent

^b Recycled Ag/HMB as catalyst



Fig. 1 SEM image of the HMB



Fig. 2 Nitrogen adsorption-desorption isotherms of the HMB (up); Ag/HMB (down)



Fig. 3 TEM images of the Ag catalyst Ag/HMB (scale bar 100 nm)



Fig. 4 XRD of the Ag/HMB

ammonia at high temperature (at about 507 °C) was found (Fig. 5). In addition, two small desorption peaks of ammonia at about 360 °C and at about 507 °C assigned to the medium-strong acidic center and strong acidic center respectively were observed from the Ag/HMB catalyst, which suggesting that the Ag/HMB was medium-strong acidic.

3.1 Bromination of p-Xylene with NBS in DCE

The bromination of *p*-xylene with NBS was studied as a model reaction for reaction condition screening (Table 1). The bromination of *p*-xylene gave 2,5-dimethylbromobenzene in excellent yield with NBS in DCE solution at 60 °C (96%, Table 1, entry 3), and no benzyl bromide byproduct formed. Acetonitrile was a good solvent also for the



Fig. 5 NH₃-TPD of Ag/Beta and Ag/HMB

reaction, and the reaction gave 2,5-dimethylbromobenzene in 77% yield in acetonitrile (Table 1, entry 5). Benzylic bromination occurred when Ag/TiO2, Ag/CeO2, Ag/C were used as catalyst in place of Ag/HMB, and 4-methylbenzyl bromide was formed as the main product (Table 1, entries 6-8). Only trace 2,5-dimethylbromobenzene was detected with Ag/HT and Ag/HAP as catalysts (Table 1, entries 9 and 10). For comparison, molecular sieve beta was tested as the support for the silver catalyst, the Ag/Beta showed low activity and low selectivity for the bromination of *p*-xylene (Table 1, entry 11). As Au catalyst was reported recently for the bromination of aromatics [17], Au/HMB was tested also for the model reactions, and 2,5-dimethylbromobenzene was obtained in lower yield (Table 1, entry 12). The Ag/ HMB was recovered easily by filtration, and no Ag was detected in the filtrate analyzed by ICP-OES (below the detection limit 7 ppb). The recovered Ag/HMB catalyst was used again for the bromination of *p*-xylene and quantitative yield of 2,5-dimethylbromobenzene was obtained (Table 1, entry 13). The AgNO₃, AgBr and the parent HMB were also tested as catalyst for the bromination of *p*-xylene under similar reaction conditions, only trace 2,5-dimethylbromobenzene was obtained (Table 1, entries 14-16). No bromination took place without catalysts (Table 1, entry 17).

Acidic supports are important for the selectivity of the bromination reaction with NBS, as the Ag catalysts on neutral supports were not selective enough, and the main product were the benzylic bromides (Table 1, entries 6–8). Moreover, the Ag catalysts on basic supports (such as hydrotalcite and hydroxyapatite) were not efficient catalysts for the bromination reaction (Table 1, entries 9 and 10). The Ag/Beta was not as active as the Ag/HMB although the beta molecular sieve is stronger acidic than the HMB from the spectra of NH₃-TPD. The beta molecular sieve is microporous and not accessible conveniently

for the substrates, which showed the advantage of the mesoporous Ag/HMB catalyst.

Arylsilver complexes were known well for decades [24-27], which suggested that Ag or Ag⁺ can activate aromatic rings through the aryl-Ag intermediates. At the same time, the activation of NBS by acid was studied extensively, and a dual activation of both aromatic rings and NXS by Au was proposed recently [17, 28]. A dual activation mechanism was proposed for the bromination of aromatic rings by the Ag/HMB (Scheme 2). The HMB support was a mesoporous acidic solid, which can activate NBS efficiently through the protonation of the carbonyl oxygen atom of NBS (Scheme 2). In addition, the aromatic ring was activated by the Ag catalyst and the arylsilver intermediates formed, and then the arylsilver reacted with the acid-activated NBS to afford the brominated products (Scheme 2). Thereafter, the dual activation of both aromatic ring by Ag and the NBS by the HMB greatly enhanced the efficiency of the bromination process. Moreover, the Ag/HMB was reusable easily, which was highly favorable for the bromination process.

3.2 Ag/HMB-Catalyzed Bromination of Aromatics with NBS in DCE

With optimized reaction conditions, we investigated the application scope of the bromination reaction. Several aromatics were examined for the bromination with Ag/HMB catalyst in DCE (Table 2), and the corresponding monobromination products were obtained in good yields without benzyl bromination (Table 2, entries 1, 2 and 4). The bromination of p-xylene and m-xylene gave 2,5-dimethylbromobenzene (95%) and 2,4-dimethylbromobenzene (97%) in good yields respectively (Table 2, entries 1 and 2), and trace dibrominated compounds were detected as the by-products. The transformation of toluene afforded p-bromotoluene in 95% yield with small amount of (5%) o-bromotoluene (Table 2, entry 4). The bromination of benzene and fluorobenzene gave bromobenzene and p-bromofluobenzene in good yields respectively at higher temperature (80 °C), which was due to no activating group and a deactivating (F) group with benzene rings (Table 2, entries 5 and



Scheme 2 Aromatics halogenation through dual activation by Ag/ HMB catalyst

 Table 2
 Ag/HMB-catalyzed bromination of aromatic rings by NBS

	Ar-H +	Br <u>Ag</u> /H DC	MB → Ar−Br + E	O N-H O
Entry	ArH	T (°C)	ArBr	Yield (%)
1		60	Br	96 (84)
2		60	Br	99 (91)
3	\bigcirc	80	Br	98 (93)
4 ^a	\bigcirc	60	Br	99 (34 ^b) <i>o/p</i> =1:18
5 ^a	\bigcirc	80	Br	95 (23 ^b)
6 ^a	F	80	Br	92 (19 ^b)
7 ^a	CF3	100	Br U CF3	81(16 ^{b, c}) m/p=4:1
8	OMe	25	Br	100 (95)
9	ОН	25	Br	100 (90°) <i>o/p</i> =1:14
10	NH ₂	25	Br	95 <i>o/p</i> =1:3 (85°)

Reaction conditions Ag/HMB, 2 mol %; substrate, 1.0 mmol; NBS 1.1 equiv.; DCE 2.0 mL as solvent; 16 h; conversions and yields were determined by GC using hexadecane as the internal standard; isolated yield in parentheses

- ^a Ag/HMB, 4 mol%; substrates 4.0 mL used without solvent; NBS 1.0 mmol
- ^b Volatile compounds
- ^c Mixture of the isomers

6). Moreover, benzene with an electron-withdrawing group (CF₃), benzotrifluoride was transformed into the mixture of 3-bromobenzotrifluoride (65%) and 4-bromobenzotrifluoride (16%) at 100 °C (Table 2, entry 7). The aromatics with electron-donating groups, such as phenol, aniline and anisole were converted to the monobrominated products in good yields at room temperature. The bromination of anisole and phenol showed high selectivity to the corresponding *para*-substituted products (Table 2, entries 8 and 9). The transformation of aniline afforded *o*- and *p*-bromoaniline in 24 and 71% yields respectively (Table 2, entry 10).

4 Conclusion

In summary, we have demonstrated a reusable silver nanocatalyst for the selective bromination of aromatic compounds. A dual activation of aromatic ring and NBS was proposed, and the synergistic effects between the silver nanoparticles and the acidic HMB enhanced the activity and selectivity for the bromination reaction. The silver catalyst is heterogeneous and reusable, which is important for the green and sustainable chemistry. Moreover, the activation of aromatic rings by silver nanocatalyst may be applicable for other reactions in aromatic rings.

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