JOC Note

pubs.acs.org/joc

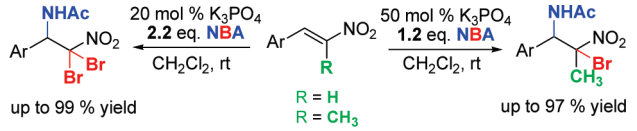
K_3PO_4-Catalyzed Regiospecific Aminobromination of β-Nitrostyrene Derivatives with *N*-Bromoacetamide as Aminobrominating Agent

Zhan-Guo Chen, Yun Wang, Jun-Fa Wei,* Peng-Fei Zhao, and Xian-Ying Shi

School of Chemistry and Materials Science, Shaanxi Normal University, Xi'an, 710062, People's Republic of China, and Key Laboratory for Macromolecular Science of Shaanxi Province, Xi'an, 710062, People's Republic of China

weijf@snnu.edu.cn

Received December 24, 2009



A very simple, efficient, and regiospecific protocol for aminobromination of a wide scope of β-nitrostyrene derivatives with *N*-bromoacetamide (NBA) as nitrogen/bromine sources has been developed by using K_3PO_4 as catalyst. The reaction proceeded smoothly and cleanly to give the bromoamines in good to excellent yields (78−99%) within 24 h in CH_2Cl_2 at room temperature without protection of inert gases. A possible mechanism involving a nucleophilic conjugate addition was proposed.

Aminohalogenation for installing vicinal haloamino moieties of multiply functionalized olefins has become an interesting topic in organic synthesis and medicinal chemistry because the addition products, the vicinal haloamines, are important building blocks to construct numerous derivatives.[1−5] In the past two decades, many aminohalogenation processes have been developed for a variety of simple olefins and electron-deficient olefins, including α,β-unsaturated ketones,[6] cinnamates,[6d,7] and unsaturated nitriles[7d,8] with an array of nitrogen/halogen sources, such as 4-$TsNCl_2$, 2-NsNCl_2,[7b] 2-NsNNaCl,[7b,9a] dichlorocarbamates,[9] $TsNBr_2$,[10] 2-$NsNCl_2$/2-NsNHNa,[6d,7c,9a] or $TsNH_2$/NBS.[6e,11] The effective catalysts cover Lewis acids,[6−11] Brønsted acids,[12] metal and nonmetal powders, and other catalysts.[13,14]

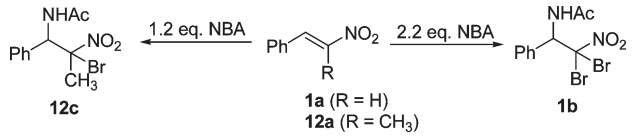
As a expansion of our interest in aminobromination of α,β-unsaturated ketones, cinnamates, and simple olefins,[14] we are also attracted by the aminobromination of β-nitrostyrenes since the products of the reaction can be readily converted into vicinal diamine functionality.[15] An early report involved the aminobromination of nitroolefinic glycosides with *N*-bromoacetamide (NBA) as the nitrogen/bromine sources in the presence of sodium acetate in acetone and in the dark, the yields ranging from 55% to 83%.[16] NBA was also reported by Yoon and co-workers in the aminobromination of unsaturated phosphonates with a highly toxic catalyst ($K_2OsO_2(OH)_4$), which afforded moderate yields even if excess NBA (2.5−3.5 equiv) was used.[17] Only one report concerning the aminobromination of β-nitrostyrenes has been found so far, in which Li and co-workers reported the aminobromination of β-nitrostyrene derivatives with 4-$TsNCl_2$ as nitrogen/halogen sources and copper(I) chloride or 4-dimethylaminopyridine (DMAP) as catalyst. This methodology gave good yields (65−88%) by using excess aminohalogenating agent in the presence of 4 Å MS under N_2 atmosphere.[7d]

Herein, we wish to report a very simple and efficient aminobromination of β-nitrostyrene derivatives with NBA as aminobrominating agent by using commercially available K_3PO_4 as the catalyst. The reaction was performed handily

(1) Kemp, J. E. G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 3, pp 471−513.
(2) For a recent review, see: Li, G.; Saibabu Kotti, S. R. S.; Timmons, C. *Eur. J. Org. Chem.* **2007**, 2745–2758.
(3) (a) Daniher, F. A.; Butler, P. E. *J. Org. Chem.* **1968**, *33*, 4336. (b) Daniher, F. A.; Butler, P. E. *J. Org. Chem.* **1968**, *33*, 2637–2642. (c) Daniher, F. A.; Melchior, M. T.; Butler, P. E. *Chem. Commun.* **1968**, 931–932. (d) Yeung, Y.-Y.; Gao, X.; Corey, E. J. *J. Am. Chem. Soc.* **2006**, *128*, 9644–9645.
(4) (a) Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1991**, *113*, 5863–5864. (b) Driguez, H.; Vermes, J. P.; Lessard, J. *Can. J. Chem.* **1978**, *56*, 119–130. (c) Lessard, J.; Driguez, H.; Vermes, J. P. *Tetrahedron Lett.* **1970**, *11*, 4887–4890. (d) Orlek, B. S.; Stemp, G. *Tetrahedron Lett.* **1991**, *32*, 4045–4048.
(5) Qui, J.; Silverman, R. B. *J. Med. Chem.* **2000**, *43*, 706–720.
(6) (a) Wu, X.-L.; Wang, G.-W. *J. Org. Chem.* **2007**, *72*, 9398–9401. (b) Wu, X.-L.; Xia, J.-J.; Wang, G.-W. *Org. Biomol. Chem.* **2008**, *6*, 548–553. (c) Liu, J.-Y.; Wang, Y.-N.; Li, G. *Eur. J. Org. Chem.* **2006**, 3112–3115. (d) Timmons, C.; Chen, D.-J.; Xu, X.; Li, G. *Eur. J. Org. Chem.* **2003**, 3850–3854. (e) Ma, L.; Du, D.-M.; Xu, J.-X. *J. Org. Chem.* **2005**, *70*, 10155–10158.
(7) (a) Li, G.; Kim, S.-H.; Wei, H.-X. *Tetrahedron Lett.* **2000**, *41*, 8699–8703. (b) Li, G.; Wei, H.-X.; Kim, S.-H. *Tetrahedron* **2001**, *57*, 8407–8411. (c) Li, G.; Wei, H.-X.; Kim, S.-H. *Org. Lett.* **2000**, *2*, 2249–2252. (d) Zhi, S.; Han, J.; Lin, C.; An, G.; Pan, Y.; Li, G. *Synthesis* **2008**, *10*, 1570–1574. (e) Kotti, S. R. S. S.; Xu, X.; Wang, Y.-N.; Headley, A. D.; Li, G. *Tetrahedron Lett.* **2004**, *45*, 7209–7212.
(8) Han, J.-L.; Zhi, S.-J.; Wang, L.-Y.; Pan, Y.; Li, G. *Eur. J. Org. Chem.* **2007**, 1332–1337.
(9) (a) Wang, Y.-N.; Ni, B.; Headley, A. D.; Li, G. *Adv. Synth. Catal.* **2007**, *349*, 319–322. (b) Chen, D.-J.; Guo, L.; Liu, J.-Y.; Kirtane, S.; Cannon, J. F.; Li, G. *Org. Lett.* **2005**, *7*, 921–924. (c) Han, J.-L.; Li, Y.-F.; Zhi, S.-J.; Pan, Y.; Timmons, C.; Li, G. *Tetrahedron Lett.* **2006**, *47*, 7225–7228. (d) Wang, Y.-N.; Kattuboina, A.; Ai, T.; Banerjee, D.; Li, G. *Tetrahetron Lett.* **2007**, *48*, 7894–7898.
(10) Phukan, P.; Chakraborty, P.; Kataki, D. *J. Org. Chem.* **2006**, *71*, 7533–7537.
(11) Thakur, V. V.; Talluri, S. K.; Sudalai, A. *Org. Lett.* **2003**, *5*, 861–864.
(12) Wu, X.-L.; Wang, G.-W. *J. Org. Chem.* **2007**, *72*, 9398–9401.
(13) Minakata, S.; Yoneda, Y.; Oderaotoshi, Y.; Komatsu, M. *Org. Lett.* **2006**, *8*, 967–969.
(14) (a) Chen, Z.-G.; Wei, J.-F.; Li, R.-T.; Shi, X.-Y.; Zhao, P.-F. *J. Org. Chem.* **2009**, *74*, 1371–1373. (b) Wei, J.-F.; Chen, Z.-G.; Lei, W.; Zhang, L.-H.; Wang, M.-Z.; Shi, X.-Y.; Li, R.-T. *Org. Lett.* **2009**, *11*, 4216–4219. (c) Chen, Z.-G.; Wei, J.-F.; Wang, M.-Z.; Zhou, L.-Y.; Zhang, C.-J.; Shi, X.-Y. *Adv. Synth. Catal.* **2009**, *351*, 2358–2368. (d) Wei, J.-F.; Zhang, L.-H.; Chen, Z.-G.; Shi, X.-Y.; Cao, J.-J. *Org. Biomol. Chem.* **2009**, *7*, 3280–3284.
(15) (a) Enders, D.; Wiedemann, J. *Synthesis* **1996**, 1443–1450. (b) Lucet, D.; Toupet, L.; Gall, T. L.; Mioskowski, C. *J. Org. Chem.* **1997**, *62*, 2682–2683.
(16) Rank, W.; Baer, H. H. *Tetrahedran Lett.* **1974**, 1459–1462.
(17) Qi, X.; Lee, S.-H.; Kwon, J. Y.; Kim, Y.; Kim, S.-J.; Lee, Y.-S.; Yoon, J. *J. Org. Chem.* **2003**, *68*, 9140–9143.

DOI: 10.1021/jo9026879 Published on Web 02/19/2010

TABLE 1. Aminohalogenation of β-Nitrostyrenes with Various Catalysts[a]



entry	substrate	catalyst (mol %)	time (h)	yield[b](%)
1	**1a**	no	48	NR
2	**1a**	KOH (20)	24	mixture
3	**1a**	NaOH (20)	24	mixture
4	**1a**	K_3PO_4 (50)	24	**1b**, 97
5	**1a**	K_3PO_4 (20)	24	**1b**, 96
6	**1a**	K_3PO_4 (10)	24	**1b**, 41
7	**1a**	K_2CO_3 (20)	24	**1b**, 89
8	**1a**	NaOAc (20)	48	NR
9	**12a**	no	48	NR
10	**12a**	KOH (20)	24	mixture
11	**12a**	NaOH (20)	24	mixture
12	**12a**	K_3PO_4 (100)	24	**12c**, 94
13	**12a**	K_3PO_4 (50)	24	**12c**, 92
14	**12a**	K_3PO_4 (40)	24	**12c**, 78
15	**12a**	K_3PO_4 (30)	24	**12c**, 65
16	**12a**	K_3PO_4 (20)	24	**12c**, 48
17	**12a**	K_2CO_3 (50)	24	**12c**, 65

[a]Conditions: substrate (0.5 mmol), NBA (1.1 mmol for **1a**, 0.6 mmol for **12a**), CH_2Cl_2 (8 mL), at room temperature. [b]Isolated yields. NR: No reaction was observed.

in CH_2Cl_2 at room temperature without protection of inert gases. The full regiospecificity and excellent yields (up to 99%) can be achieved for a range of β-nitrostyrene derivatives. Besides, it is noteworthy that this base catalyst is cheap, nontoxic, metal-free, and eco-friendly.

According to the electron-deficient feature of β-nitrostyrene, we believed that the aminobromination addition reaction to be studied should occur in a Michael addition fashion. Thus, several bases were initially screened by using β-nitrostyrene (**1a**) as the substrate in CH_2Cl_2, a solvent commonly used for aminohalogenation addition. Strong bases, e.g., solid KOH and NaOH, attracted our attention first. However, no wanted product but a complex mixture was achieved with these caustic alkalis (Table 1, entries 2 and 3). We rationalized the ineffectiveness of these strong bases by Hofmann degradation of the aminobrominating agent, NBA. Therefore, two mild bases, anhydrous K_3PO_4 and anhydrous K_2CO_3, were explored as catalysts for the reaction. To our delight, both bases can efficiently catalyze the aminobromination reaction of β-nitrostyrene with NBA (entries 4−7). Chromatography of the reaction product provided a white solid that showed a simple ^1H NMR spectrum consistent with amino-*gem*-dibromo product (**1b**). This result was rationalized by further deprotonation and subsequent bromination of the aminobrominated product.

To optimize the reaction condition, a systematic study has been carried out with a set of catalyst doses. In addition to β-nitrostyrene (**1a**, R = H, H-type), its methyl homologue, 1-phenyl-2-nitropropene (**12a**, R = CH_3, CH_3-type), was also a substrate to study (Table 1).

With β-nitrostyrene (**1a**, R = H) as the substrate, 41%, 96%, and 97% yields were achieved with the K_3PO_4 doses of 10, 20, and 50 mol % (Table 1, entries 4−6) under air condition. So, a 20 mol % dose of K_3PO_4 was sufficient to ensure the reaction to proceed smoothly, giving the desired product in nearly quantitative yield (96%) within 24 h. K_2CO_3 is less effective than K_3PO_4 (entry 7). Contrarily, the control experiment showed that β-nitrostyrene failed to give any aminobrominated product even if the reaction time was prolonged up to 48 h (entry 1), thus confirming its catalytic role. The weaker base sodium acetate is entirely inactive to the reaction.

TABLE 2. Aminohalogenation of β-Nitrostyrene (1a, 12a) in Various Solvents[a]

			yield (%)[b]	
entry	solvent	time (h)	**1b**	**12c**
1	CH_2Cl_2	24	96	92
2	PhMe	24	88	70
3	acetone	24	80	
4	$CHCl_3$	48	NR	NR
5	THF	48	NR	NR
6	DMF	48	NR	NR
7	MeCN	48	NR	NR

[a]Conditions: substrate (0.5 mmol), NBA (1.1 mmol for **1a**, 0.6 mmol for **12a**), K_3PO_4 (20 mol % for **1a**, 50 mol % for **12a**), solvents (8 mL), at room temperature; [b]Isolated yields. NR: No reaction was observed.

As expected, the normal monobromoamino adduct was produced with β-nitrostyrene of the CH_3-type (**12a**) as the substrate. However, only 48% yield was provided at 20 mol % dose of K_3PO_4. This result is probably due to the steric hindrance and electron-donating effect of R (CH_3). Further studies showed that 50 mol % of K_3PO_4 is sufficient to ensure a smooth reaction and a high yield (92%, entry 13). Similar to β-nitrostyrene, the reaction does not occur in the absence of catalyst (entry 9).

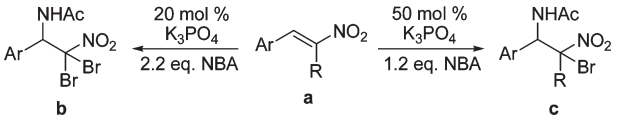
Accordingly, the reasonable loading amount of K_3PO_4 is 20 mol % for the reaction of β-nitrostyrene (**1a**) and 50 mol % for its β-methyl homologue (**12a**).

Solvent affects the reaction dramatically. CH_2Cl_2 was found to be the best solvent for the reaction among the solvents screened (Table 2), such as CH_2Cl_2, toluene, acetone, $CHCl_3$, THF, CH_3CN, and DMF. Toluene and acetone are less effective; the other solvents are entirely inactive.

To explore the scope and generality of the K_3PO_4-catalyzed aminobromination of β-nitrostyrenes and to gain insight into the reaction mechanism, a series of β-nitrostyrene derivatives possessing electron-donating groups (EDG) and/or electron- withdrawing groups (EWG) on the benzene ring have been investigated under the optimal conditions. The results are summarized in Table 3.

As can be seen from Table 3, the reaction of both types of β-nitrostyrene derivatives proceeded successfully to give the corresponding bromoamines in high yields, except for 3,5-dimethoxy-β-nitrostyrene (**11a**). Both EWG and EDG on the phenyl ring are compatible to the reaction. Moreover, the substituents on the benzene ring, especially those situated para to the olefinic bond, affect the reaction to a certain extent. For the β-nitrostyrene derivatives (R = H) which have a EWG on the 4-positon of the benzene ring, the reaction gave the expected adducts in almost quantitative yields (**2b**−**4b**, 95−99%). It is noteworthy that a strong EWG such as NO_2 renders the reaction to complete within 6 h in a quantitative yield (**2b**, 99%). Although the substrates with a strong EDG (OCH_3) incorporated para to

TABLE 3. K_3PO_4-Catalyzed Aminobromiation of Various β-Nitrostyrene Derivatives[a]



subs	Ar	R	prod	time (h)	yield[b] (%)
1a	C_6H_5	H	**1b**	24	96
2a	4-$NO_2C_6H_4$	H	**2b**	6	99
3a	4-ClC_6H_4	H	**3b**	19	97
4a	4-BrC_6H_4	H	**4b**	24	95
5a	4-$CH_3C_6H_4$	H	**5b**	24	95
6a	4-$CH_3OC_6H_4$	H	**6b**	24	80
7a	2-Br-4,5-$(CH_3O)_2C_6H_2$	H	**7b**	24	87
8a	3,4,5-$(CH_3O)_3C_6H_2$	H	**8b**	24	79
9a	1-Naphthyl	H	**9b**	24	97
10a	3-$CH_3OC_6H_4$	H	**10b**	24	81
11a[c]	3,5-$(CH_3O)_2C_6H_3$	H	**11b**	24	25
			11d[d]		6[d]
			11e[e]		27[e]
12a	C_6H_5	CH_3	**12c**	24	92
13a	4-$NO_2C_6H_4$	CH_3	**13c**	24	97
14a	4-ClC_6H_4	CH_3	**14c**	24	94
15a	4-BrC_6H_4	CH_3	**15c**	24	95
16a	4-$CH_3C_6H_4$	CH_3	**16c**	24	90
17a	4-$CH_3OC_6H_4$	CH_3	**17c**	24	88
18a	2-Br-4,5-$(CH_3O)_2C_6H_2$	CH_3	**18c**	24	81
19a	3,4,5-$(CH_3O)_3C_6H_2$	CH_3	**19c**	24	83
20a	3-$CH_3OC_6H_4$	CH_3	**20c**	24	87
21a	3,5-$(CH_3O)_2C_6H_3$	CH_3	**21c**	24	78

[a]Conditions: For **1a**−**10a**, substrate (0.5 mmol), NBA (1.1 mmol), K_3PO_4 (0.1 mmol, 20 mol %), CH_2Cl_2 (8 mL), at room temperature. For **12a-21a,** substrate (0.5 mmol), NBA (0.6 mmol), K_3PO_4 (0.25 mmol, 50 mol %), CH_2Cl_2 (8 mL), at rt. [b]Isolated yields. [c]**11a** (2 mmol), NBA (4.4 mmol), K_3PO_4 (0.4 mmol, 20 mol %), CH_2Cl_2 (8 mL), rt. [d]**11d**, a product of aromatic bromination; [e]**11e**, a product of aromatic bromination and nucleophilic addition.

carbon−carbon double bond underwent the reaction readily and gave the corresponding adducts as the sole products in high yields (**6b**−**8b**, 79−87%), these yields are fairly lower as compared with those of substrates bearing an EWG on the 4-positon of the benzene ring. The substrates with no substituent (**1b** and **9b**, 96% and 97%) or a mild EDG, e.g. CH_3 (**5b**, 95%), also gave excellent yields under the identical conditions.

Parallel trends in reactivity also have been observed in the aminobromination of the CH_3-type β-nitrostyrene derivatives. As shown in Table 3, the yields for the substrates with EWG on the 4-positon of benzene ring (**13c**−**15c**, 94−97%) are higher than those of the substrate without any substituent (**12c**, 92%) and the substrates with a EDG (**16c**−**21c**, 81−90%).

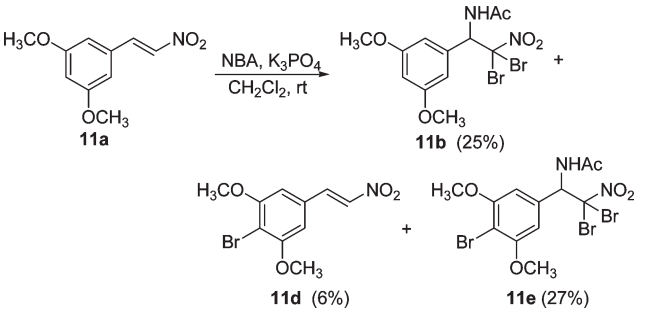
Thus, the effectiveness of the substituents on the reaction yield is in a rough order of:

$$\text{strong EWG} > \text{weak EWG} > \text{H, weak EDG} > \text{strong EDG}$$

i.e., more electron-deficient substrates are more reactive.

3,5-Dimethoxy-β-nitrostyrene (Table 3, **11a** and Scheme 1) gave the expected product (**11b**) in 25% yield and two byproducts (**11d** and **11e**) in 6% and 27% yields. Clearly, the former is the product of electrophilic aromatic substitution and the latter arises from the aminobromiation of the carbon−carbon double bond and the aromatic substitution on the benzene ring. The

SCHEME 1. Aminobromiation Reaction of 3,5-Dimethoxy-β-nitrostyrene



aromatic substitution might be attributed to the high reactivity of the benzene ring activated by the two strong electron-donating groups (OMe).

The substrate **21a**, which has a benzene ring with the same substituted pattern as **11a**, gave the normal addition product (**21c**) only in good yield (78%). No other unexpected product was observed in the reaction.

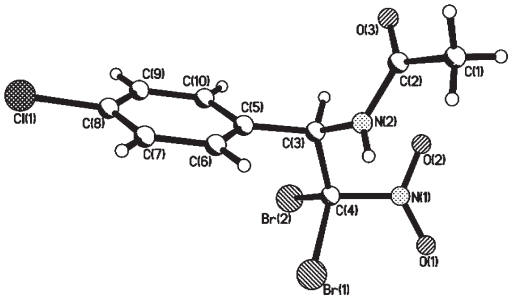
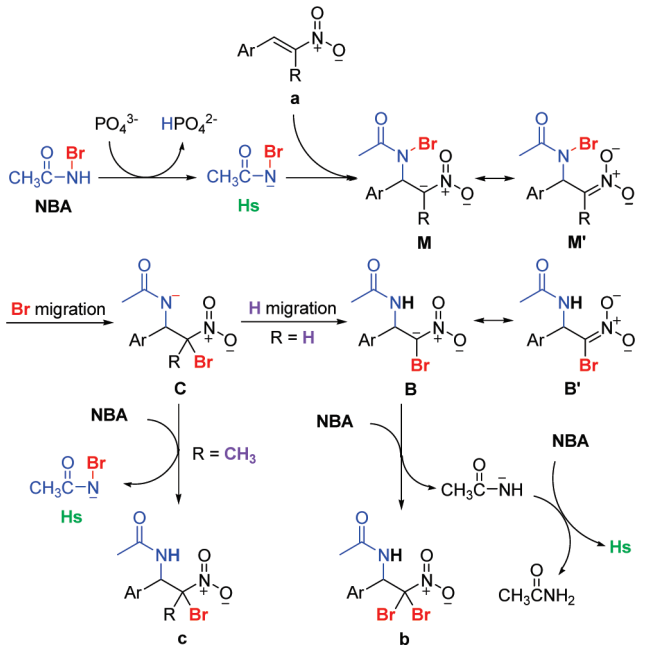


FIGURE 1. X-ray crystal structure of **3b**.

The structure of a typical product, 1-acetylamido-1-(4-chlorophenyl)-2,2-dibromo-2-nitroethane (**3b**), was confirmed by X-ray crystallographic study (Figure 1). It shows that the β-carbon of the substrate is entirely brominated and the nitrogen atom of NBA is added onto the α-carbon. The regiochemistry of the rest of the haloamino products was established by ^1H and ^{13}C NMR spectra in accordance with their chemical shifts and the coupling constants of protons on the carbon atom and the nitrogen atom.

According to the regiochemistry outcomes and the fact that the electron-poorer substrates exhibit higher reactivity, we suggested a possible mechanism involving a Michael addition for this base-catalyzed aminobromination of β-nitrostyrenes of both types (Scheme 2). The first step is a deprotonation of NBA by K_3PO_4 to generate a Hofmann species $AcNBr^-$ (**Hs**), which in turn attacks the benzylic position of β-nitrostyrene (**a**) with the formation of the Michael intermediate (**M**), a carbanion stabilized by the nitro group via resonance with **M′**. In the third step, the Br^+ ion migrates from N−Br of the amide to the negative center in **Hs** and creates an acetamido anion (**C**) in tandem. In this stage, if R = CH_3, **C** accepts a proton from the second NBA molecule and gives the monobrominated product (**c**) and $AcNBr^-$ ion (**Hs**). When R = H, it transfers to the amido **N** atom with the formation of a more stable carbanion (**B**) on the same carbon again. Then **B** is brominated by another NBA molecule at negative center, librating subsequently the dibominated product (**b**) and an $AcNH^-$. The latter, as a stronger base than

SCHEME 2. The Possible Reaction Mechanism



NBA, would convert NBA to the active species $AcNBr^-$ ion (**Hs**) for the next cycle.

Briefly, the present aminobromination of β-nitrostyrenes essentially consists of two key reactions: nucleophilic conjugate addition of electron-deficient olefins and subsequent electrophilic bromination of the formed addition product.[18]

In conclusion, we have developed an easy and efficient method for the aminobromination of β-nitrostyrene derivatives catalyzed by K_3PO_4 with NBA as aminobrominating agent in CH_2Cl_2. The method can conveniently and efficiently convert β-nitrostyrenes into vicinal haloamines at room temperature in good to excellent yields and full regiospecificity. It also has the advantages of low cost, nontoxicity, and elimination of the toxic issue associated with metal-based catalysts. The tendency that more electron-deficient substrates are more reactive indicates the reaction as a nucleophilic conjugate addition. A possible mechanism involving conjugate addition and subsequent bromination was proposed and it explains well the reactivity of substrates and the regiochemistry of products.

Experimental Section

Preparation of *N*-Bromoacetamide. NBA was prepared according to the procedure[19] with a slight modification.

Acetamide (5.0 g, 85 mmol) and liquid bromine (13.5 g, 170 mmol) were added into a 150 mL round-bottomed flask immersed in an ice−water bath and stirred electromagnetically at 0−5 °C until the solid dissolved completely. The ice-cooled 50% KOH solution (10 mL) was dropped while stirring at 0−5 °C and a large amount of light yellow powder precipitated. The mixture was allowed to stand in the ice−water bath for 2−3 h to complete the reaction. Upon addition of 10 g of NaCl and 125 mL of $CHCl_3$, the suspension was heated on a hot-water bath to dissolve the precipitate with vigorous stirring. Then, the organic layer was separated and dried with anhydrous Na_2SO_4. After the solid was filtrated off, 125 mL of hexane was added to the filtrate and the solution was placed in a refrigerator overnight. The white needles were collected by filtration, and dried in vacuum: yield 5.72 g (49.1%); mp 90.5−91.5 °C.

The General Procedure for the Synthesis of 1b−10b Exemplified by 1-Acetamido-2,2-dibromo-1-phenyl-2-nitroethane (1b). Into a dry round-bottomed flask were added the substrate (0.5 mmol), NBA (150.7 mg, 1.1 mmol), anhydrous K_3PO_4 (21.2 mg, 0.1 mmol, 20 mol %), and CH_2Cl_2 (8 mL). The mixture was electromagnetically stirred at room temperature in air until the starting material could not be detected by TLC or to 24 h. Then ethyl acetate (20 mL) was added to the reaction mixture. The resulting solution was washed with brine (3 × 10 mL) and water (3 × 10 mL), then dried with anhydrous Na_2SO_4. Column chromatography with petroleum ether/ethyl acetate as eluent gave the product as a white solid: 175 mg (96% yield); mp 126−127 °C (EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.39 (m, 5H), 6.79 (d, J = 8.40 Hz, 1H), 6.34 (d, J = 9.90 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (75.45 MHz, $CDCl_3$) δ 169.0, 133.4, 129.7, 129.1 (2), 128.7 (2), 93.4, 62.8, 23.2. Anal. Calcd for $C_{10}H_{10}Br_2N_2O_3$: C, 32.82; H, 2.75; N, 7.65. Found: C, 32.79; H, 2.73; N, 7.69.

The General Procedure for the Synthesis of 12c−21c Exemplified by 1-Acetamido-2-bromo-1-phenyl-2-nitropropane (12c). Into a dry round-bottomed flask were added the substrate (0.5 mmol), NBA (0.6 mmol), and anhydrous K_3PO_4 (0.25 mmol, 50 mol %). Then, 8 mL of CH_2Cl_2 was added. The mixture was electromagnetically stirred at room temperature in air until the starting material could not be detected by TLC or to 24 h. The workup was similar to that described above giving a white solid: 138 mg (92% yield); mp 140−140.5 °C (EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, J = 2.40 Hz, 5H), 7.18 (d, J = 8.40 Hz, 1H), 5.78 (d, J = 9.60 Hz, 1H), 2.24 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (75.45 MHz, $CDCl_3$) δ 169.4, 134.3, 129.3, 128.9 (2), 128.2 (2), 96.5, 60.5, 29.4, 23.3. Anal. Calcd for $C_{11}H_{13}BrN_2O_3$: C, 43.87; H, 4.35; N, 9.30. Found: C, 43.83; H, 4.37; N, 9.36.

Acknowledgment. The authors are grateful to the National Foundation of Natural Science in China (Grant Nos. 20572066 and 20906059), the Natural Science Foundation of Shaanxi Province (2009JM2011), and the Innovation Foundation of Postgraduate Cultivation of Shaanxi Normal University (2008CXB009).

Supporting Information Available: Experimental procedures, spectral data, copies of ^{1}H and ^{13}C NMR spectra for all products, and CIF of compound **3b**. This material is available free of charge via the Internet at http://pubs.acs.org.

(18) (a) Bourguignon, J.; Le Nard, G.; Queguiner, G. *Can. J. Chem.* **1985**, *63*, 2354–2361. (b) McAnda, A. F.; Roberts, K. D.; Smallridge, A. J.; Ten, A.; Trewhella, M. A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 501–504. (c) Liu, J.-T.; Yao, C.-F. *Tetrahedron Lett.* **2001**, *42*, 6147–6150. (d) Bowman, R. K.; Johnson, J. S. *J. Org. Chem.* **2004**, *69*, 8537–8540.

(19) Eugene P. O.; Corinne G. *Org. Synth.* **1951**, *31*, 17. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, pp 104.