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The combination of benzamides/NCS as nitrogen/halogen sources for aminohalogenation of β-nitrostyrenes resulting in dichlorinated haloamides

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The combination of benzamide and NCS was found to be an efficient nitrogen/halogen source for aminohalogenation of β-nitrostyrenes. The reaction was convenient to carry out by using 4-dimethylaminopyridine as the catalyst, resulting in vicinal dichlorinated haloamino nitroalkanes with opposite regiochemistry to that generated from other electron-deficient olefins observed previously. The reaction proceeded smoothly at room temperature with good yields and excellent regioselectivities. A mechanism involving a chloronium intermediate was proposed to explain the resulting regiochemistry. The current system explored a new type of nitrogen sources for aminohalogenation of functionalized olefins.

aminohalogenation, benzamide, β-nitrostyrenes, DMAP, haloamides

1 Introduction

The vicinal haloamines belong to a significant class of building blocks in organic and medicinal chemistry, because they can be easily converted into various synthetic intermediates by the replacement of the halogen in both intramolecular and intermolecular reactions. Among all the methodologies for preparation of vicinal haloamines, aminohalogenation and related reactions of alkenes can be used as the most attractive tools, in which carbon-nitrogen bonds and carbon-halogen bonds were formed at the same time [1–12]. In the last decade, many new aminohalogenation processes have been developed for several functionalized olefins, including α,β-unsaturated carboxylic esters and ketones [13–15], vinylidenecyclopropanes [16], α,β-unsaturated nitriles [17] and β-nitrostyrenes [18, 19]. These aminohalogenation processes are believed to proceed involving aziridinium or chloronium ion intermediates [13–15, 18, 19].

Although several synthetic approaches to vicinal haloamine functionalities have been developed, the nitrogen sources for the catalytic aminohalogenation of functionalized olefins remain great challenges [13–42]. Sulfonamides are usually used as the most suitable nitrogen sources for aminohalogenation of α,β-unsaturated olefins, including $TsNCl_2$ [13–15], $TsNH_2$/NBS [31–35] and $NsNCl_2$ [2, 40–42]. In our continuing study on this reaction, we tried to employ benzamides as nitrogen sources to replace sulfonamides. The benzamides are new nitrogen sources for aminohalogenation of α,β-unsaturated olefins, and the advantage of such a replacement is that the *N*-benzoyl protecting

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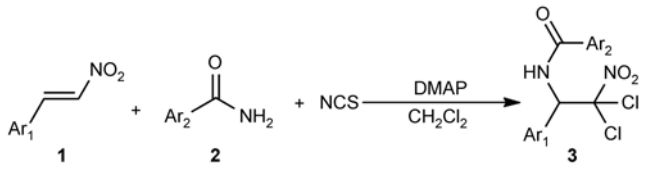
group of the resulting products can be easily cleaved [43–45] compared with the *N*-sulfonyl protecting group. Herein, we report a DMAP catalyzed aminohalogenation reaction of β-nitrostyrenes (**1**) with benzamides as nitrogen sources and *N*-chlorosuccinimide (NCS) as the halogen source, yielding products of 1-aryl-1-arylformamino-2,2-dichloro-2-nitroethanes (**3**) (Scheme 1). The new aminohalogenation system provides an easy access to 1,2-vicinal diamino products that are chemically and biologically significant [46].



Scheme 1 Aminohalogenation with benzamides as nitrogen sources.

2 Experimental

2.1 General methods

All moisture-sensitive reactions were performed under nitrogen in glassware that had been flame-dried. Solvents were dried and distilled prior to use. Flash chromatography was performed on silica gel 60 (F-254) TCL plates (20 cm × 20 cm). Melting points are uncorrected. IR spectra were collected with a Bruker Vector 22 instrument (KBr pellets). ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were acquired in deuterated dimethylsulfoxide (CD_3SOCD_3), deuterated acetone (CD_3COCD_3) and deuterated chloroform ($CDCl_3$). Elemental analyses were performed with a Perkin-Elmer 240 elemental analysis instrument. Mass spectra of new compounds were measured with a Finnigan LCQ Electrospray Mass Spectrometer.

2.2 Starting materials procedure

Starting materials β-Nitrostyrenes (**1a–1h**) were prepared according to the reported methods [47–50].

2.3 General procedure for aminohalogenation

Into a dry vial was added **1** (1.0 mmol), benzamide (3.0 mmol), DMAP (0.2 mmol, 20 mol%) and freshly distilled CH_2Cl_2 (5.0 mL) with nitrogen atmosphere. The mixture was stirred at room temperature for 10 min before NCS (3.0 mmol) was added. The resulting mixture was stirred at room temperature for 48 h in the capped vial nitrogen atmosphere protection and the reaction was then quenched with saturated aqueous Na_2SO_3 (2.0 mL) solution. The solid precipitates were filtered off and washed with EtOAc (3 × 10 mL). The combined organic phases were washed with brine and dried with anhydrous sodium sulfate. The organic solution was concentrated and purified via flash chromatography with EtOAc and petroleum ether (*v*/*v* = 1:4) as the eluent to yield the pure products **3**.

*Benzamido-2,2-dichloro-2-nitro-1-phenylethane (**3a**)*

Colorless solid. mp 130–131 °C. IR (KBr): υ 3400, 1660, 1579, 1511, 1481, 1322 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78–7.81 (m, 2H), 7.43–7.58 (m, 8H), 7.18 (d, J = 9.9 Hz, 1H), 6.53 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 132.8, 132.4, 132.1, 129.5, 128.8, 128.5, 128.5, 126.9, 115.2, 61.9 ppm. ESI-MS *m*/*z*: 361.1 [M+Na]$^+$.

*1-Benzamido-2,2-dichloro-2-nitro-1-(p-tolylethyl)ethane (**3b**)*

Colorless solid. mp 155–156 °C. IR (KBr) υ 3239, 2923, 1644, 1581, 1515, 1315 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78–7.81 (m, 2H), 7.57–7.60 (m, 1H), 7.54–7.57 (m, 2H), 7.45–7.50 (m, 2H), 7.20–7.28 (m, 2H), 7.12 (d, J = 10.2 Hz, 1H), 6.48 (d, J = 10.2 Hz, 1H), 2.37 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 140.0, 133.2, 132.3, 129.7, 129.5, 128.8, 128.7, 127.2, 115.7, 62.1, 21.2 ppm. MS (ESI) *m*/*z*: 375.1 [M+Na]$^+$.

*1-Benzamido-1-(4-chlorophenyl)-2,2-dichloro-2-nitroethane (**3c**)*

Colorless solid. mp 161–162 °C. IR (KBr) υ 3228, 1644, 1583, 1520, 1312, cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76–7.79 (m, 2H), 7.37–7.57 (m, 7H), 7.16 (d, J = 9.9 Hz, 1H), 6.49 (d, J= 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 135.6, 132.5, 132.2, 130.9, 128.7, 128.5, 126.9, 114.9, 61.4 ppm. MS (ESI) *m*/*z*: 394.9 [M+Na]$^+$.

*1-Benzamido-2,2-dichloro-1-(4-fluorophenyl)-2-nitroethane (**3d**)*

Colorless solid. mp 133–134 °C. IR (KBr) υ 3262, 1644, 1590, 1529, 1510, 1336 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.76–7.79 (m, 2H), 7.43–7.56 (m, 5H), 7.03–7.13 (m, 3H), 6.50 (d, J = 10.2 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 165.1, 161.7, 132.9, 132.5, 130.9, 130.8, 128.8, 128.7, 128.6, 127.2, 116.1, 115.8, 115.4, 61.7 ppm. MS (ESI) *m*/*z*: 379.1 [M+Na]$^+$.

*1-Benzamido-1-(4-bromophenyl)-2,2-dichloro-2-nitroethane (**3e**)*

Colorless solid. mp 150–151 °C. IR (KBr) υ 3322, 1649, 1582, 1522, 1329, 1312, 1266 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74–7.77 (m, 2H), 7.52–7.57 (m, 3H), 7.36–7.46 (m, 4H), 7.23 (d, J = 9.9 Hz, 1H), 6.47 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 132.8, 132.6, 132.0, 131.8, 130.5, 128.8, 127.2, 124.3, 115.1, 61.8 ppm. MS (ESI) *m*/*z*: 438.9 [M+Na]$^+$.

*1-Benzamido-2,2-dichloro-1-(2-fluorophenyl)-2-nitroethane (**3f**)*

Colorless solid. mp 145–146 °C. IR (KBr) υ 3268, 1642,

1586, 1525, 1490, 1321 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.79–7.82 (m, 2H), 7.34–7.58(m, 6H), 7.25 (d, J = 9.9 Hz, 1H), 7.25–7.14 (m, 1H), 6.79 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 163.0, 159.6, 132.8, 132.5, 131.9, 131.8, 131.0, 131.0, 128.8, 127.2, 124.7, 127.7, 120.1, 120.0, 116.8, 116.5, 115.3, 59.0 ppm. MS (ESI) *m/z*: 379.1 $[M+Na]^+$.

*1-Benzamido-2,2-dichloro-1-(4-methoxyphenyl)-2-nitroethane (**3g**)*

Colorless solid. mp 124–126 °C. IR (KBr) υ 3406, 1663, 1612, 1580, 1510, 1255, 1188, 1027 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.77–7.80 (m, 2H), 7.40–7.58 (m, 5H), 7.12 (d, J = 10.2 Hz, 1H), 6.90–6.93 (m, 2H), 6.47 (d, J = 10.2 Hz, 1H), 3.82 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 160.6, 133.2, 132.3, 130.1, 128.8, 127.2, 124.6, 115.8, 114.2, 61.8, 55.3 ppm. MS (ESI) *m/z*: 391.0 $[M+Na]^+$.

*1-(4-Chlorobenzamido)-2,2-dichloro-2-nitro-1-phenylethane (**3h**)*

Colorless solid. mp 132–133 °C. IR (KBr) υ 3406, 1668, 1590, 1573, 1506, 1478, 1315, 1249 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.68–7.71 (m, 2H), 7.48–7.52 (m, 2H), 7.39–7.45 (m, 5H), 7.19 (d, J = 10.2 Hz, 1H), 6.49 (d, J = 10.2 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 138.7, 132.5, 131.4, 130.0, 128.9, 128.9, 128.7, 115.5, 62.4 ppm. MS (ESI) *m/z*: 394.9 $[M+Na]^+$.

*2,2-Dichloro-2-nitro-1-(4-nitrobenzamido)-1-phenylethane (**3i**)*

Colorless solid. mp 155–156 °C. IR (KBr) υ 3310, 1661, 1602, 1579, 1342, 1319, 1266 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.31–8.33 (d, J = 8.4 Hz, 2H), 7.93–7.96 (d, J = 8.4 Hz, 2H), 7.43–7.50 (m, 5H), 7.21 (d, J = 9.9 Hz, 1H), 6.49 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 150.0, 138.6, 132.1, 130.2, 129.0, 128.8, 128.5, 124.0, 115.2, 62.5 ppm. MS (ESI) *m/z* 406.1 $[M+Na]^+$.

*1-(4-Chlorobenzamido)-1-(4-chlorophenyl)-2,2-dichloro-2-nitroethane (**3j**)*

Colorless solid. mp 159–160 °C. IR (KBr) υ 3312, 1653, 1580, 1524, 1487, 1328, 1311 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.74–7.70 (m, 2H), 7.38–7.49 (m, 6H), 7.01 (d, J = 9.9 Hz, 1H), 6.45 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, CD_3COCD_3) δ 165.9, 137.5, 135.2, 132.1, 132.0, 131.3, 129.5, 128.6, 128.4, 115.7, 61.8 ppm. MS (ESI) *m/z*: 428.9 $[M+Na]^+$.

*1-(4-Bromobenzamido)-1-(4-chlorophenyl)-2,2-dichloro-2-nitroethane (**3k**)*

Colorless solid. mp 145–146 °C. IR (KBr) υ 3301, 1649, 1587, 1516, 1479, 1343, 1311, 1258 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.60–7.64 (m, 4H), 7.38–7.45 (m, 4H), 7.03 (d, J = 9.9 Hz, 1H), 6.44 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 136.1, 132.0, 131.5, 130.9, 130.1, 129.1, 128.6, 127.3, 114.9, 61.7 ppm. MS (ESI) *m/z*: 472.8 $[M + Na]^+$.

*1-(4-Chlorophenyl)-2,2-dichloro-2-nitro-1-(4-nitrobenzamido) ethane (**3l**)*

Colorless solid. mp 187–189 °C. IR (KBr) υ 3304, 1667, 1581, 1528, 1332, 1291 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.34–8.37 (m, 2H), 7.94–7.97 (m, 2H), 7.43 (m, 4H), 7.11 (d, J = 9.9 Hz, 1H), 6.45 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, d-DMSO) δ 166.5, 149.8, 139.2, 135.1, 132.1, 132.1, 130.0, 129.0, 124.0, 116.0, 62.0 ppm. MS (ESI) *m/z*: 439.9 $[M+Na]^+$.

*1-(2-Bromobenzamido)-1-(4-chlorophenyl)-2,2-dichloro-2-nitroethane (**3m**)*

White solid. mp 170–171 °C. IR (KBr) υ 3300, 1658, 1583, 1519, 1493, 1336, 1317 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.57–7.64 (m, 2H), 7.32–7.48 (m, 6H), 7.22 (d, J = 9.9 Hz, 1H), 6.52 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 136.1, 135.5, 133.6, 132.2, 130.9, 130.5, 130.3, 129.0, 127.7, 119.1, 114.8, 61.8 ppm. MS (ESI) *m/z*: 472.8 $[M+Na]^+$.

*1-(2-Chlorobenzamido)-1-(4-chlorophenyl)-2,2-dichloro-2-nitroethane (**3n**)*

Colorless solid. mp 171–172 °C. IR (KBr) υ 3300, 1657, 1583, 1521, 1493, 1338, 1319 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.72–7.74 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 9.9 Hz, 1H), 7.36–7.47 (m, 7H), 6.53 (d, J = 9.9 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.0, 136.1, 132.6, 132.5, 131.1, 131.0, 130.6, 130.5, 130.4, 129.1, 127.4, 114.8, 61.9 ppm. MS (ESI) *m/z*: 428.9 $[M+Na]^+$.

*1-(4-Bromobenzamido)-2,2-dichloro-2-nitro-1-(p-tolyl) ethane (**3o**)*

Colorless solid. mp 162–163 °C. IR (KBr) υ 3301, 1663, 1602, 1578, 1525, 1338, 1318, 1296 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.29–8.34 (m, 2H), 7.93–7.96 (m, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 9.9 Hz, 1H), 6.44 (d, J = 9.9 Hz, 1H), 2.38 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 149.9, 140.3, 138.5, 129.6, 129.0, 128.5, 128.4, 123.8, 115.2, 62.2, 21.1 ppm. MS (ESI) *m/z*: 452.9 $[M+Na]^+$.

*2,2-Dichloro-1-(4-fluorophenyl)-2-nitro-1-(4-nitrobenzamido) ethane (**3p**)*

Colorless solid. mp 190–192 °C. IR (KBr) υ 3305, 1664, 1605, 1579, 1534, 1338, 1298, 1229 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.32–8.35 (m, 2H), 7.93–7.96 (m, 2H), 7.47–7.57 (m, 2H), 7.11–7.16 (m, 3H), 6.46 (d, J = 9.6 Hz, 1H) ppm. ^{13}C NMR (75 MHz, CD_3COCD_3) δ 165.7, 165.6, 164.9, 161.6, 149.8, 139.8, 139.0, 139.0, 131.9, 131.8,

129.2, 129.1, 123.3, 115.8, 115.5, 115.2, 61.9, 61.8 ppm. MS (ESI) *m/z*: 423.9 $[M+Na]^+$.

*2,2-Dichloro-1-(4-methoxyphenyl)-2-nitro-1-(4-nitrobenzamido)ethane (**3q**)*

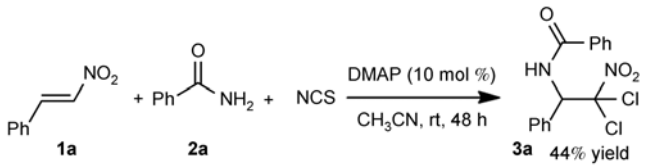
Colorless solid. mp 170–171 °C. IR (KBr) υ 3339, 2971, 1651, 1604, 1582, 1523, 1346, 1311, 1256 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.30–8.33 (m, 2H), 7.92–7.97 (m, 2H), 7.38–7.42 (m, 2H), 7.15 (d, J = 9.6 Hz, 1H), 6.92–6.95 (m, 2H), 6.43 (d, J = 9.6 Hz, 1H), 3.83 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 160.7, 149.9, 138.5, 129.9, 128.3, 123.9, 123.8, 115.3, 114.3, 62.0, 55.3 ppm. MS (ESI) *m/z*: 436.1 $[M+Na]^+$.

*1-(4-Chlorophenyl)-2,2-dichloro-1-(4-methoxybenzamido)-2-nitroethane (**3r**)*

Colorless solid. mp 120–121 °C. IR (KBr) υ 3442, 2963, 1637, 1608, 1580, 1505, 1317, 1252, 1179 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.73–7.77 (m, 2H), 7.36–7.45 (m, 4H), 7.01 (d, J = 10.2 Hz, 1H), 6.93–7.01 (m, 2H), 6.47 (d, J = 10.2 Hz, 1H), 3.87 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 162.9, 135.9, 131.3, 130.1, 129.1, 128.9, 124.8, 115.2, 113.9, 61.6, 55.4 ppm. MS (ESI) *m/z*: 424.9 $[M+Na]^+$.

3 Results and discussion

Initially, β-nitrostyrene (**1a**) was subjected to the reaction as a model substrate. The reaction of **1a** with NCS and benzamide (**2a**) was conducted under our previously reported catalytic aminohalogenation condition with DMAP as the catalyst in the presence of 4 Å molecular sieves in acetonitrile (Scheme 2) [18]. After 48 h, **1a** was partly consumed and the product was detected with 44% chemical yield. The major product was carefully isolated and characterized. ^1H NMR analysis of this isolated product revealed that the β-proton was not present in the ^1H NMR spectrum, which indicated that dichlorinated haloamide formed in the current process.



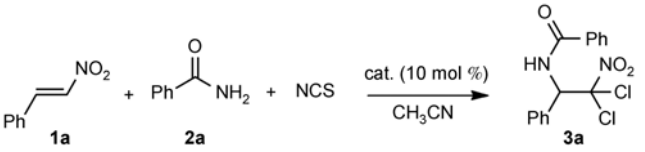
Scheme 2 DMAP catalyzed aminohalogenation reaction.

In order to improve the chemical yields, several catalysts including Ph_3P, 2,2'-bpy, 4,4'-bpy, $MnSO_4$, $Ni(OAc)_2$, $Mn(OAc)_2$, AgOAc, CuOTf, CuI, CuCl and $PdCl_2$ were employed in the current aminohalogenation reaction with benzamide as the nitrogen source. As shown in Table 1, DMAP was the most effective catalyst for the reaction, resulting in product **3a** with 44% chemical yield (Table 1, entry 1). Besides DMAP, CuOTf could also catalyze the reaction and 40% yield was obtained (Table 1, entry 9). Other catalysts either resulted in no product or gave poor chemical yields with most β-nitrostyrene remaining (Table 1, entries 2–8, 10–12).

To further optimize the reaction conditions, several organic solvents were used in the catalytic reaction. As shown in Table 2, the desired products could be observed when CH_3CN, $CHCl_3$, CCl_4 or toluene were used as the solvent. Dichloromethane was found to be the best solvent, and the yield increased to 55% (Table 2, entry 2). No aminohalogenation products were found at all when using DMF or THF as the solvent (Table 2, entries 6 and 7). Increasing the loading amount of NCS did not have much effect on the yield (Table 2, entry 8). However, the use of 3.0 equiv of benzamide could increase the chemical yield to 60% (Table 2, entry 9). The use of 20 mol% DMAP was necessary, and the yield increased to 63% (Table 2, entry 10). Similar to our previous aminohalogenation system, longer reaction time and higher temperature did not show any apparent improvement on the current system (Table 2, entries 12 and 13).

After the reaction conditions have been optimized, a series of β-nitrostyrenes and benzamides were investigated carefully. As listed in Table 3, a wide range of β-nitrostyrenes can be employed as substrates for this reaction and give useful to excellent chemical yields (36%–85%). The reaction of β-nitro-4-methylstyrene gave a high yield, which

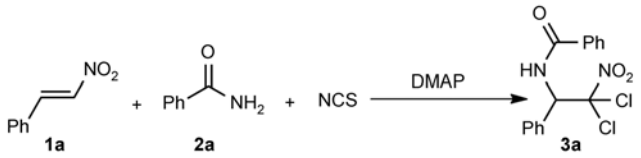
Table 1 Aminohalogenation of β-nitrostyrene using a range of catalysts[a)]



Entry	Cat.	Time (h)	Yield (%) [b)]
1	DMAP	48	44
2	Ph_3P	48	10
3	2,2'-Bpy	48	30
4	4,4'-Bpy	48	35
5	$MnSO_4$	48	10
6	$Ni(OAc)_2$	48	36
7	$Mn(OAc)_2$	48	36
8	AgOAc	48	30
9	CuOTf	48	40
10	CuI	48	10
11	CuCl	48	20
12	$PdCl_2$	48	30

a) Conditions: β-nitrostyrene (1.0 mmol), benzamide (2.0 mmol) and NCS (3.0 mmol), catalysts (10 mol%) and 4 Å molecular sieves (500 mg) in solvent (5.0 mL) under N_2 at room temperature. b) Isolated yields.

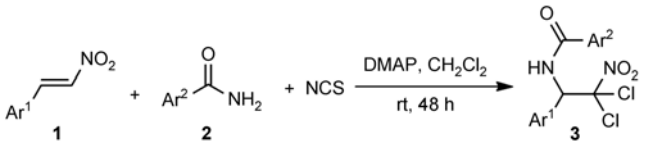
Table 2 Optimization of reaction conditions for aminohalogenation of β-nitrostyrene[a)]



Entry	Solvent	Time (h)	Cat. (mol%)	*T* (°C)	Ratio [b)]	Yield (%) [c)]
1	CH_3CN	48	10	25	1:2:3	44
2	CH_2Cl_2	48	10	25	1:2:3	55
3	$CHCl_3$	48	10	25	1:2:3	40
4	CCl_4	48	10	25	1:2:3	30
5	PhMe	48	10	25	1:2:3	35
6	DMF	48	10	25	1:2:3	N.R.[d)]
7	THF	48	10	25	1:2:3	N.R.[d)]
8	CH_2Cl_2	48	10	25	1:2:4	56
9	CH_2Cl_2	48	10	25	1:3:3	60
10	CH_2Cl_2	48	20	25	1:3:3	63
11	CH_2Cl_2	72	20	25	1:3:3	56
12	CH_2Cl_2	48	10	50	1:3:3	60

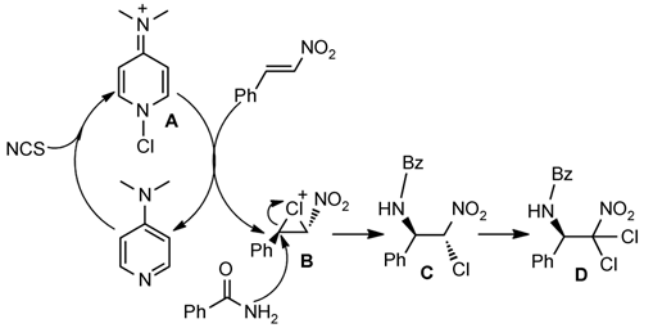
a) Conditions: β-nitrostyrene (1.0 mmol), benzamide and NCS, catalyzed by DMAP, in the presence of 4 Å molecular sieves (500 mg) in solvent (5.0 mL) under N_2. b) The ratio is β-nitrostyrene:benzamide:NCS. c) Isolated yields. d) No reaction was observed.

Table 3 Aminohalogenation of **1** with benzamides/NCS in CH_2Cl_2[a)]



Entry	Ar^1	Ar^2	Time (h)	Product [b)]	Yield (%) [c)]
1	Ph	Ph	48	**3a**	63
2	4-CH_3-Ph	Ph	48	**3b**	70
3	4-Cl-Ph	Ph	48	**3c**	68
4	4-F-Ph	Ph	48	**3d**	63
5	4-Br-Ph	Ph	48	**3e**	67
6	2-F-Ph	Ph	48	**3f**	62
7	4-CH_3O-Ph	Ph	48	**3g**	49
8	Ph	4-Cl-Ph	48	**3h**	68
9	Ph	4-NO_2-Ph	48	**3i**	71
10	4-Cl-Ph	4-Cl-Ph	48	**3j**	70
11	4-Cl-Ph	4-Br-Ph	48	**3k**	75
12	4-Cl-Ph	4-NO_2-Ph	48	**3l**	85
13	4-Cl-Ph	2-Br-Ph	48	**3m**	54
14	4-Cl-Ph	2-Cl-Ph	48	**3n**	51
15	4-CH_3-Ph	4-Br-Ph	48	**3o**	71
16	4-F-Ph	4-NO_2-Ph	48	**3p**	76
17	4-CH_3O-Ph	4-NO_2-Ph	48	**3q**	55
18	4-Cl-Ph	4-CH_3O-Ph	48	**3r**	36

a) Conditions: β-nitrostyrenes (1.0 mmol), DMAP (20 mol%), benzamides (3.0 mmol), NCS (3.0 mmol) and 4 Å molecular sieves (500 mg) in CH_2Cl_2 (5.0 mL) under N_2 at room temperature. b) As shown by 1H NMR spectroscopic analysis of the crude product, there is no regioisomer observed for each case. c) Isolated yields.



Scheme 3 Possible mechanism.

may due to the stabilization of the positively charged intermediate with electron-donating methyl group (Table 3, entry 2). Other substituted groups on the aromatic ring of β-nitrostyrenes did not show apparent effect on the chemical yields. Varieties of benzamides were found to be suitable nitrogen sources for the current system. In the case of the nitrogen source with a strong electron-withdrawing group (NO_2) on the aromatic ring (Table 3, entries 12 and 16), the highest yields of aminochlorination products were obtained. It is possibly due to that the electron-withdrawing nature of nitro groups makes the deprotonation of aryl amide become easier. As expected, the lowest yield was obtained with the nitrogen source substituted by a strong electron-donating group (OCH_3) on the aromatic ring (Table 3, entry 18). The regioselectivities of the reaction were completely controlled, and solely one regio-isomer was observed for all these cases. Careful ^{1}H NMR analysis of the products revealed that the chlorine moiety was attached to the α-carbon position of nitroalkane instead of the β-carbon position as encountered in nearly all of the previous cases where the electron-withdrawing olefins were employed [32–38].

Based on the resulting regiochemistry, the chloronium intermediate is believed to predominantly form during the reaction process (Scheme 3), which is similar to our previous reported aminohalogenation of β-nitrostyrene with $TsNCl_2$ as the nitrogen source [18]. The first step involves the DMAP-promoted dissociation of N–Cl bond of NCS, to form intermediate **A**. The following step is the delivery of 'Cl$^+$' from **A** to the C=C bond of β-nitrostyrenes to give the chloronium intermediate **B**. The positively charged chloronium intermediate **B** is opened by $BzNH_2$ on the β-position of β-nitrostyrenes, and regioselectively forms intermediate **C**, which is a normal monohaloamino product. The final dichlorinated product **D** is formed via deprotonation/electrophilic chlorination of mono-haloamine precursor **C** [47–50].

4 Conclusions

In conclusion, a new regio- and stereoselective aminohalo-

genation of β-nitrostyrenes with DMAP as the catalyst and benzamides/NCS as the nitrogen/halogen sources has been developed. The reaction is convenient to carry out at room temperature, and provides an easy access to vicinal haloamino nitroalkanes with opposite regiochemistry to that of other electron-deficient olefins previously observed. Useful to good chemical yields and excellent regioselectivities have been obtained. The advantage of this new type of nitrogen source lies in that the benzoyl protecting group can be easily removed to give free haloamines.

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