Potassium Carbonate Catalyzed Regioselective Aminohalogenation of β-Nitrostyrenes by Using Benzyl Carbamate/*N*-Chlorosuccinimide as a New Nitrogen/Chlorine Source

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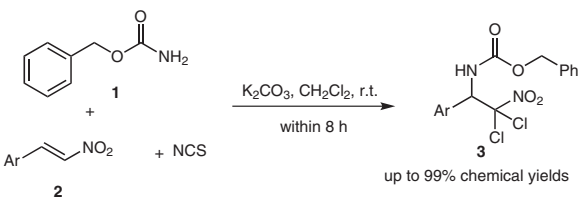
Abstract: A combination of benzyl carbamate and *N*-chlorosuccinimide was developed as a new system for aminohalogenation of β-nitrostyrenes catalyzed by potassium carbonate in dichloromethane at room temperature. The reaction tolerates a wide range of substituents on the β-nitrostyrene, and proceeds smoothly in good-to-excellent chemical yields (77–99%). The new system shows a high efficiency and it markedly shortens the reaction time for aminochlorination. *N*,*N*-Dichlorobenzyl carbamate was also found to be a highly efficient source of both nitrogen and chlorine for the aminohalogenation reaction.

Key words: aminations, chlorinations, alkenes, carbamates, amides

Aminohalogenations and related reactions of functionalized olefins are becoming increasingly useful as tools for the simultaneous construction of C–N and C–halogen bonds in a tandem fashion.[1–4] The resulting vicinal haloamines belong to an important class of building blocks in both organic synthesis and medicinal chemistry.[5] The products can also be readily converted into numerous other valuable derivatives by replacing the halogen atoms through either intramolecular or intermolecular substitution reactions.[6] In the past decade, many new catalytic systems have been developed for the aminohalogenation of a range of functionalized alkenes, such as α,β-unsaturated carboxylic esters,[7] α,β-unsaturated nitriles,[8] or α,β-unsaturated ketones.[9] However, the sources of nitrogen for these aminohalogenation reactions lack diversity, as sulfonamides are used in most cases.[7–9] Recently, β-nitrostyrenes, which are a particularly important class of substrates, were reported to undergo aminohalogenation and, as a result, they have attracted a great deal of research interest.[10,11] Furthermore, the resulting haloamine products can be easily converted into the corresponding vicinal diamines.[12]

In the 1960s, *N*,*N*-dichlorocarbamates were used for aminohalogenation of simple or electron-deficient olefins.[13] This pioneering work showed that the reaction has many of the characteristics of a free-radical addition reaction.[13a] In subsequent decades, very few reports on these types of reaction appeared,[3f] mainly because of their moderate chemical yields and low regioselectivities. Although, recent studies on aminohalogenation of β-nitrostyrenes with similar nitrogen sources have reported marked improvements in regio- and stereoselectivities, the transformations usually suffer from long reaction times of more than 24 hours.[10a–d,11] The efficient and selective aminohalogenation of β-nitrostyrenes, therefore, still remains an important and challenging problem. In our work on the aminohalogenation reaction, we found that benzyl carbamate can be used as an efficient source of nitrogen for the aminohalogenation of β-nitrostyrenes. Here, we would like to report a simple and highly efficient aminochlorination of β-nitrostyrenes with benzyl carbamate ($CbzNH_2$, **1**) as a new source of nitrogen in the presence of potassium carbonate as a catalyst (Scheme 1). This new reaction can be complete within eight hours, which greatly shortens the reaction time. It also gives higher yields than the previous methods.[7–11]



Scheme 1 Aminohalogenation with benzyl carbamate as a nitrogen source

In the initial study, we used β-nitrostyrene (**2a**) as the starting material under the previous aminochlorination conditions.[10] The reaction was carried out at room temperature with benzyl carbamate as a nitrogen source and *N*-chlorosuccinimide (NCS) as a source of chlorine with 4-(*N*,*N*-dimethylamino)pyridine as the catalyst in dichloromethane without protection by an inert atmosphere. No reaction was detected and most of the starting materials remained even with a prolonged reaction time (Table 1, entry 1). We then examined triphenylphosphine as an alternative organocatalyst (entry 2) and several metal catalysts (entries 3–5), but almost none of the desired haloamine products were obtained. Further optimization of the catalyst showed that the transformation proceeds

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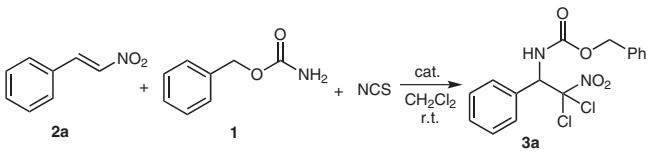
Table 1 Aminohalogenation of **2a** with Various Catalysts



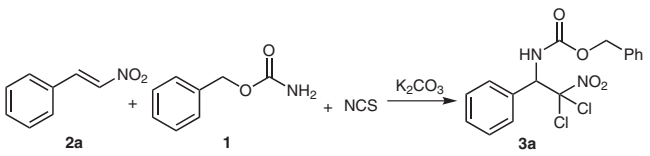
Entry[a]	Catalyst (mol%)	Time (h)	Yield (%)[b]
1	DMAP (20%)	24	NR[c]
2	Ph_3P (20%)	24	NR
3	CuCl (20%)	24	NR
4	$Ni(OAc)_2$ (20%)	24	NR
5	$Mn(OAc)_2$ (20%)	24	NR
6	K_2CO_3 (20%)	10	94
7	K_2CO_3 (10%)	10	63
8	K_2CO_3 (15%)	10	85
9	K_2CO_3 (30%)	10	94
10	KOH (20%)	24	88

[a] Conditions: **2a** (0.5 mmol), NCS (1.5 mmol), $CbzNH_2$ (1.5 mmol), CH_2Cl_2 (3 mL), r.t.
[b] Isolated yield.
[c] NR = no reaction was observed.

smoothly in the presence of 20 mol% of potassium carbonate, giving the desired product **3a** in 94% yield, with the reaction going to completion within ten hours (entry 6). The amount of catalyst was found to be critical for the reaction, and lower chemical yields were obtained when 10 or 15 mol% of potassium carbonate was used (entries 7 and 8). Although potassium hydroxide was also found to work well as a catalyst in the reaction, giving a good chemical yield (88%), 24 hours were needed before the starting material was completely consumed (entry 10).

We then examined various solvents with potassium carbonate as catalyst to improve the efficiency of the reaction (Table 2). The solvent was found to play an important role in the system and the choice of solvent had a marked effect on the yield. No aminohalogenation product was obtained when *N*,*N*-dimethylformamide or dimethyl sulfoxide was used (entries 4 and 7). The reaction in tetrahydrofuran or acetonitrile as solvent was also complete within ten hours, but the yields were slightly lower (entries 3 and 6). Dichloromethane was the best choice of solvent, giving the highest yield (94%; entry 1). After careful studies, we found that the reaction time could even be reduced to eight hours with an excellent yield (93%; entry 9), whereas a shorter reaction time resulted in a lower yield (65%; entry 8). Increasing the temperature did not have much effect on the efficiency of the reaction, although it was complete within a slightly shorter time (entries 11–13). The use of three equivalents each of benzyl carbamate and NCS was necessary for the reaction, and

Table 2 Optimization of Conditions for Aminohalogenation of **2a**



Entry[a]	**2a**/$CbzNH_2$/NCS (equiv)	Temp (°C)	Solvent	Time (h)	Yield (%)[b]
1	1:3:3	r.t.	CH_2Cl_2	10	94
2	1:3:3	r.t.	toluene	10	61
3	1:3:3	r.t.	THF	10	89
4	1:3:3	r.t.	DMSO	10	NR[c]
5	1:3:3	r.t.	MeOH	10	29
6	1:3:3	r.t.	MeCN	10	88
7	1:3:3	r.t.	DMF	10	NR
8	1:3:3	r.t.	CH_2Cl_2	7	65
9	1:3:3	r.t.	CH_2Cl_2	8	93
10	1:3:3	r.t.	CH_2Cl_2	9	94
11	1:3:3	45	CH_2Cl_2	3	35
12	1:3:3	45	CH_2Cl_2	5	88
13	1:3:3	45	CH_2Cl_2	7	95
14	1:1:2	r.t.	CH_2Cl_2	8	46
15	1:2:2	r.t.	CH_2Cl_2	8	70
16	1:1:3	r.t.	CH_2Cl_2	8	31
17	1:2:3	r.t.	CH_2Cl_2	8	79

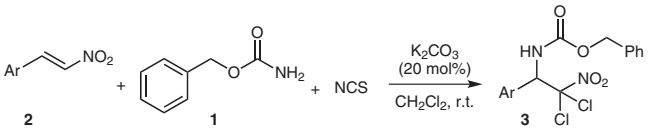
[a] Conditions: **2a** (0.5 mmol), K_2CO_3 (20 mol%), solvent (3 mL).
[b] Isolated yield.
[c] NR = no reaction was observed.

decreasing the amount of any one of them resulted in a lower yield (entries 14–17).

Having optimized the conditions for the aminohalogenation reaction, we examined its scope by using a variety of β-nitrostyrenes (Table 3). The reaction proceeded smoothly with a wide range of substrates, resulting in good-to-excellent chemical yields (77–99%). The substituent groups on the aromatic rings did not have much effect on the reaction. Both electron-rich and electron-deficient substrates were suitable for the reaction, and excellent yields were obtained with fluoro (entries 7 and 10), trifluoromethyl (entry 11), or methoxy (entries 17 and 18) substituents. Surprisingly, in the case of the 4-chloro derivative **2d** and the 3-bromo derivative **2e**, the reaction needed a longer time before all the starting materials were consumed (entries 4 and 5). We then examined a substrate with a disubstituted aromatic ring **2h**, and we found it also worked well, giving an excellent yield of the corresponding product (99%; entry 8). Note also that the 1-naphthyl

analogue **2l** also gave a high chemical yield (99%; entry 12). Furthermore, excellent regioselectivities were detected in all the cases, and a single regioisomer was obtained from each reaction.

Table 3 Scope of the Aminohalogenation Reaction



Entry[a]	Substrate	Ar	Time (h)	Product	Yield (%)[b]
1	**2a**	Ph	8	**3a**	94
2	**2b**	2-ClC_6H_4	8	**3b**	99
3	**2c**	3-ClC_6H_4	8	**3c**	99
4	**2d**	4-ClC_6H_4	20	**3d**	87
5	**2e**	3-BrC_6H_4	32	**3e**	90
6	**2f**	2-BrC_6H_4	8	**3f**	99
7	**2g**	4-FC_6H_4	8	**3g**	99
8	**2h**	3-Br-4-$MeOC_6H_3$	8	**3h**	99
9	**2i**	4-BrC_6H_4	8	**3i**	87
10	**2j**	3-FC_6H_4	8	**3j**	93
11	**2k**	4-$F_3CC_6H_4$	8	**3k**	89
12	**2l**	1-naphthyl	8	**3l**	99
13	**2m**	4-NCC_6H_4	8	**3m**	91
14	**2n**	2-MeC_6H_4	8	**3n**	79
15	**2o**	3-MeC_6H_4	8	**3o**	77
16	**2p**	4-MeC_6H_4	8	**3p**	93
17	**2q**	2-$MeOC_6H_4$	8	**3q**	97
18	**2r**	4-$MeOC_6H_4$	8	**3r**	97
19	**2s**	2-$BnOC_6H_4$	8	**3s**	91

[a] Conditions: substrate (0.5 mmol), NCS (1.5 mmol), $CbzNH_2$ (1.5 mmol), K_2CO_3 (20 mol%), CH_2Cl_2 (3 mL), r.t.
[b] Isolated yield.

The structure of the resulting dichlorinated halo amides was unambiguously confirmed by X-ray diffraction analysis of the phenyl derivative **3a** (Figure 1).

Next we tried to develop a better system for the aminohalogenation of β-nitrostyrenes (Table 4) by using *N*,*N*-dichlorobenzyl carbamate ($CbzNCl_2$) as the source of nitrogen and chlorine instead of a combination of benzyl carbamate and NCS. As shown in Table 4, the reaction was complete within eight hours for all the substrates examined, and the desired halo amide products were obtained in high chemical yields. In the cases of **2a**, **2k**, and **2n**, the yields were higher than those from the benzyl carbamate/NCS system. Furthermore, this system also gave excellent regioselectivities, and only one regioisomer was obtained from each of the β-nitrostyrenes that we examined.

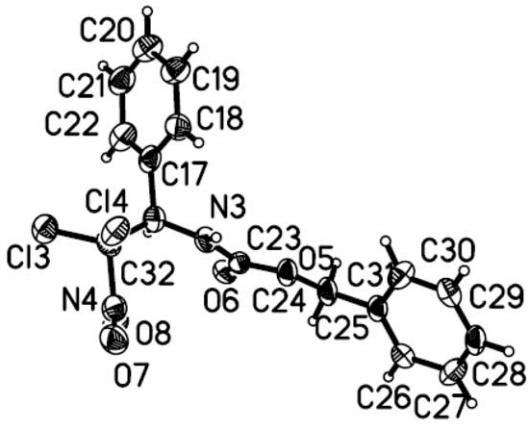
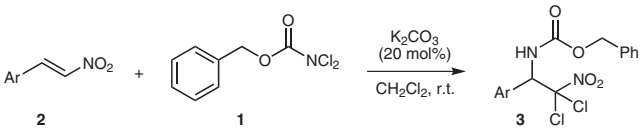


Figure 1 ORTEP diagram for compound **3a**

On the basis of a previous report on the aminohalogenation of β-nitrostyrene,[10] and the regioselectivity that we obtained with the current aminohalogenation system, we propose that the reaction proceeds by a pathway involving a Michael addition (Scheme 2).

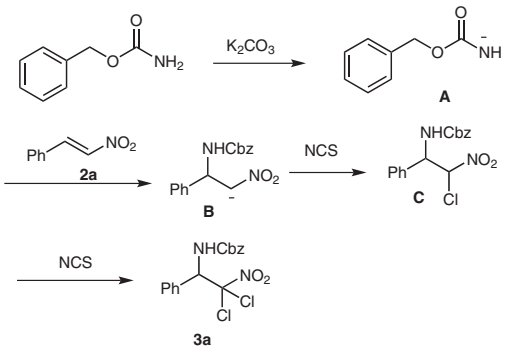
In the initial step, potassium carbonate reacts with benzyl carbamate to give the intermediate **A**, which adds to the α-position of β-nitrostyrene (**2a**), giving the Michael intermediate **B**. The Cl^+ cation derived from NCS adds to the negatively charged intermediate **B**, giving the monohalo amine intermediate **C**. The final step is the formation of the dichlorinated compound **3a** by deprotonation/electrophilic chlorination of precursor **D**.[14] The reaction with the *N*,*N*-dichlorobenzyl carbamate as the nitrogen/chlorine

Table 4 Aminochlorination of β-Nitrostyrene Derivatives with *N*,*N*-Dichlorobenzyl Carbamate



Entry[a]	Substrate	Ar	Time (h)	Product	Yield (%)[b]
1	**2a**	Ph	8	**3a**	99
2	**2c**	3-ClC_6H_4	8	**3c**	99
3	**2f**	2-BrC_6H_4	8	**3f**	99
4	**2g**	4-FC_6H_4	8	**3g**	89
5	**2k**	4-$F_3CC_6H_4$	8	**3k**	95
6	**2l**	1-naphthyl	8	**3l**	99
7	**2n**	2-MeC_6H_4	8	**3n**	91

[a] Conditions: substrate (0.5 mmol), $CbzNCl_2$ (1 mmol), K_2CO_3 (20 mol%), CH_2Cl_2 (3 mL), at r.t.
[b] Isolated yield.



Scheme 2 Proposed mechanism for the reaction

source is presumably to proceed through a previously reported chloronium process.[10a]

In summary, the regioselective aminochlorination of β-nitrostyrenes with a combination of benzyl carbamate as a nitrogen source and NCS as a source of chlorine under mild catalytic conditions has been developed. The synthesis is convenient to perform because it is catalyzed by potassium carbonate at room temperature and does not require protection by an inert gas. The new process is highly efficient, and only eight hours is needed to complete the reaction. Good chemical yields and excellent regioselectivities can be achieved with a wide range of β-nitrostyrenes. Further studies on this new system will focus on the aminohalogenation of α,β-unsaturated carboxylic ester and ketones.

Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. $CbzNCl_2$ was prepared according to the literature.[15] The progress of the reactions was monitored by TLC on silica gel 60F-254 with detection by UV. Flash chromatography was performed using silica gel 60 (200–300 mesh) with freshly distilled solvents. Melting points are uncorrected. IR spectra were recorded on a Bruker Vector 22 spectrometer in KBr pellets. ^1H and ^{13}C NMR spectra were recorded on a Bruker ARX300 spectrometer with TMS as the internal standard. High-resolution mass spectra for all the new compounds were obtained by using a MicroMass Q-Tof instrument in the ESI mode. The crystal structure was recorded on an X-ray diffraction spectrometer.

Aminohalogenation of β-Nitrostyrenes with $CbzNH_2$/NCS; Typical Procedure

A dry round-bottomed flask was charged with the β-nitrostyrene (0.5 mmol), NCS (1.5 mmol), $CbzNH_2$ (1.5 mmol), and anhyd K_2CO_3 (0.1 mmol). CH_2Cl_2 (3 mL) was then added and the soln was stirred at r.t., with no protection by inert gas, until the reaction was complete (TLC). Sat. aq Na_2SO_3 (3 mL) was added to quench the reaction. The aqueous phase was extracted with EtOAc (3 × 25 mL) and the combined organic phase was dried (Na_2SO_4). The solvent was removed to give a crude product that was purified by TLC (PE–EtOAc, 4:1).

Aminohalogenation of β-Nitrostyrenes with *N*,*N*-Dichlorobenzyl Carbamate; Typical Procedure

A dry round-bottomed flask was charged with the β-nitrostyrene (0.5 mmol), $CbzNCl_2$ (1 mmol), and anhyd K_2CO_3 (0.1 mmol). CH_2Cl_2 (3 mL) was then added and the soln was stirred at r.t. with no protection by inert gas until the reaction was complete (TLC). Sat. aq Na_2SO_3 (3 mL) was added to quench the reaction. The aqueous phase was extracted with EtOAc (3 × 25 mL) and the combined organic phase was dried (Na_2SO_4). The solvent was removed to give a crude product that was purified by TLC (PE–EtOAc, 4:1).

Benzyl (2,2-Dichloro-2-nitro-1-phenylethyl)carbamate (3a)

White solid; yield: 98%; mp 85–87 °C.

IR (KBr): 3418, 3290, 3034, 2927, 1603, 1694, 1583, 1249, 1050 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.50 (m, 10 H), 6.02 (d, *J* = 10.2 Hz, 1 H), 5.76 (d, *J* = 9.7 Hz, 1 H), 5.01–5.19 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.26, 135.59, 132.88, 129.93, 128.99, 128.83, 128.69, 128.54, 128.36, 115.81, 68.01, 64.46.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{14}Cl_2N_2NaO_4$: 391.0223; found: 360.0225.

Crystallographic data for compound **3a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 825669; copies can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336033 or email: deposit@ccdc.cam.ac.uk].

Benzyl [2,2-Dichloro-1-(2-chlorophenyl)-2-nitroethyl]carbamate (3b)

White solid; yield: 99%; mp 83–85 °C.

IR (KBr): 3413, 3304, 3035, 2973, 1710, 1587, 1526, 1235, 1060 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.66–7.13 (m, 9 H), 6.81 (d, *J* = 10.2 Hz, 1 H), 5.83 (d, *J* = 10.1 Hz, 1 H), 5.17–4.92 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.63, 135.60, 135.32, 131.88, 130.93, 130.36, 129.71, 128.63, 128.53, 128.43, 127.35, 115.19, 68.09, 59.54.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{13}Cl_3N_2NaO_4$: 424.9833; found: 424.9836.

Benzyl [2,2-Dichloro-1-(3-chlorophenyl)-2-nitroethyl]carbamate (3c)

White solid; yield: 99%; mp 104–105 °C.

IR (KBr): 3415, 3314, 3066, 2961, 1716, 1587, 1506, 1330, 1229, 1050 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.15 (m, 9 H), 6.04 (d, *J* = 10.4 Hz, 1 H), 5.80 (d, *J* = 9.9 Hz, 1 H), 5.06–5.13 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.74, 135.26, 134.76, 130.12, 130.00 (2 C), 128.94, 128.68, 128.62, 128.41, 127.16, 114.94, 68.17, 63.68.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{13}Cl_3N_2NaO_4$: 424.9833; found: 424.9835.

Benzyl [2,2-Dichloro-1-(4-chlorophenyl)-2-nitro]ethylcarbamate (3d)

White solid; yield: 87%; mp 70–71 °C.

IR (KBr): 3420, 3319, 3065, 2961, 1717, 1587, 1493, 1332, 1228, 1094, 1050 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.38 (m, 9 H), 6.03 (d, *J* = 9.8 Hz, 1 H), 5.80 (d, *J* = 9.2 Hz, 1 H), 5.05–5.13 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.75, 136.13, 135.30, 131.30, 130.15, 129.04, 128.68, 128.62, 128.39, 115.10, 68.13, 63.66.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{13}Cl_3N_2NaO_4$: 424.9833; found: 424.9836.

Benzyl [1-(3-Bromophenyl)-2,2-dichloro-2-nitroethyl]carbamate (3e)

White solid; yield: 90%; mp 87–89 °C.

IR (KBr): 3408, 3305, 3034, 2961, 1706, 1586, 1331, 1233, 1050 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.78–7.17 (m, 9 H), 5.93–6.03 (m, 2 H), 5.03–5.11 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.89, 135.31, 135.06, 133.04, 131.88, 130.27, 128.69, 128.61, 128.38, 127.71, 122.77, 115.05, 68.19, 63.70.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{13}BrCl_2N_2NaO_4$: 468.9328; found: 468.9343.

Benzyl [1-(2-Bromophenyl)-2,2-dichloro-2-nitroethyl]carbamate (3f)

White solid; yield: 99%; mp 62–63 °C.

IR (KBr): 3413, 3308, 3065, 2966, 1714, 1587, 1507, 1335, 1231, 1054 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 7.6 Hz, 1 H), 7.51 (d, *J* = 7.1 Hz, 1 H), 7.45–7.20 (m, 7 H), 6.86 (d, *J* = 10.0 Hz, 1 H), 5.77 (d, *J* = 10.0 Hz, 1 H), 5.28–4.93 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.61, 135.31, 133.75 (2 C), 131.15, 128.62, 128.55, 128.47, 127.97, 126.47, 115.23, 68.11, 61.86.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{13}BrCl_2N_2NaO_4$: 468.9328; found: 468.9326.

Benzyl [2,2-Dichloro-1-(4-fluorophenyl)-2-nitroethyl]carbamate (3g)

White solid; yield: 99%; mp 73–75 °C.

IR (KBr): 3420, 3314, 3035, 2963, 1713, 1585, 1511, 1329, 1228, 1166, 1051 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.29 (m, 7 H), 7.21–6.96 (m, 2 H), 6.04 (d, *J* = 10.1 Hz, 1 H), 5.80 (d, *J* = 10.1 Hz, 1 H), 5.23–5.03 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.44 (d, $^1J_{CF}$ = 250.3 Hz), 154.89, 135.38, 130.77 (d, $^3J_{CF}$ = 8.6 Hz), 128.75, 128.67, 128.59, 128.36, 115.89 (d, $^2J_{CF}$ = 21.8 Hz), 115.38, 68.09, 63.66.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{13}Cl_2FN_2NaO_4$: 409.0129; found: 409.0123.

Benzyl [1-(3-Bromo-4-methoxyphenyl)-2,2-dichloro-2-nitroethyl]carbamate (3h)

Colorless oil; yield: 99%.

IR (KBr): 3405, 3314, 3033, 2961, 1713, 1585, 1498, 1293, 1259, 1230, 1056 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 2.2 Hz, 1 H), 7.45–7.28 (m, 6 H), 6.90 (t, *J* = 7.5 Hz, 1 H), 6.00 (d, *J* = 10.1 Hz, 1 H), 5.88 (d, *J* = 9.5 Hz, 1 H), 5.24–5.01 (m, 2 H), 3.92 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.01, 154.86, 135.36, 133.42, 129.45, 128.67, 128.57, 128.36, 126.15, 115.37, 111.96, 111.63, 68.09, 63.32, 56.35.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{15}BrCl_2N_2O_5Na$: 498.9434; found: 498.9438.

Benzyl [1-(4-Bromophenyl)-2,2-dichloro-2-nitroethyl]carbamate (3i)

White solid; yield: 87%; mp 70–72 °C.

IR (KBr): 3405, 3311, 3065, 2962, 1713, 1585, 1515, 1491, 1330, 1233, 1076 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.4 Hz, 2 H), 7.32 (m, 7 H), 6.04 (d, *J* = 10.1 Hz, 1 H), 5.84–5.88 (b, 1 H), 5.04–5.12 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.80, 135.31, 132.00, 131.85, 130.44, 128.68, 128.61, 128.37, 124.36, 115.03, 68.13, 63.76.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{13}BrCl_2N_2NaO_4$: 468.9328; found: 468.9324.

Benzyl [2,2-Dichloro-1-(3-fluorophenyl)-2-nitroethyl]carbamate (3j)

White solid; yield: 93%; mp 96–98 °C.

IR (KBr): 3419, 3317, 3035, 2962, 1716, 1587, 1506, 1336, 1233, 1049 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.01 (m, 9 H), 6.09 (d, *J* = 9.3 Hz, 1 H), 5.89 (d, *J* = 9.3 Hz, 1 H), 5.14 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.54 (d, $^1J_{CF}$ = 248.1 Hz), 154.91, 135.34, 135.13 (d, $^3J_{CF}$ = 6.6 Hz), 130.38 (d, $^3J_{CF}$ = 7.9 Hz), 128.67, 128.60, 128.37, 124.84, 116.98 (d, $^2J_{CF}$ = 21.2 Hz), 116.04 (d, $^2J_{CF}$ = 22.8 Hz), 115.9, 68.09, 63.66.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{13}Cl_2FN_2NaO_4$: 409.0129; found: 409.0123.

Benzyl {2,2-Dichloro-2-nitro-1-[4-(trifluoromethyl)phenyl]ethyl}carbamate (3k)

Colorless oil; yield: 89%.

IR (KBr): 3408, 3308, 3036, 2964, 1711, 1587, 1533, 1327, 1237, 1130, 1070 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.2 Hz, 2 H), 7.58 (d, *J* = 8.1 Hz, 2 H), 7.32–7.35 (m, 5 H), 6.12 (d, *J* = 10.1 Hz, 1 H), 5.95 (d, *J* = 10.0 Hz, 1 H), 5.22–5.04 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.85, 136.77, 135.27, 131.99 (q, $^2J_{CF}$ = 32.8 Hz), 129.45, 128.68, 128.64, 128.35, 125.72 (q, $^3J_{CF}$ = 3.0 Hz), 123.64 (q, $^1J_{CF}$ = 272.3 Hz), 114.84, 68.20, 63.83.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{13}Cl_2F_3N_2NaO_4$: 459.0097; found: 459.0094.

Benzyl [2,2-Dichloro-1-(naphth-1-yl)-2-nitroethyl]carbamate (3l)

White solid; yield: 99%; mp 96–98 °C.

IR (KBr): 3413, 3315, 3035, 2958, 1713, 1503, 1326, 1232, 1057 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 8.1 Hz, 1 H), 7.87–7.93 (m, 2 H), 7.47–7.67 (m, 4 H), 7.24–7.30 (m, 5 H), 7.08–7.11 (m, 1 H), 5.85 (d, *J* = 9.6 Hz, 1 H), 5.07–5.10 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.09, 135.39, 133.75, 131.96, 130.63, 130.33, 129.05, 128.63, 128.52, 128.38, 127.48, 126.42, 125.40, 124.95, 123.17, 116.14, 68.05, 57.98.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{16}Cl_2N_2NaO_4$: 441.0379; found: 441.0382.

Benzyl [2,2-Dichloro-1-(4-cyanophenyl)-2-nitroethyl]carbamate (3m)

Colorless oil; yield: 91%.

IR (KBr): 3320, 3065, 2961, 2232, 1732, 1586, 1509, 1231, 1051 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.1 Hz, 2 H), 7.54 (d, *J* = 8.2 Hz, 2 H), 7.24–7.32 (m, 5 H), 6.11 (d, *J* = 9.4 Hz, 1 H), 5.97 (d, *J* = 9.2 Hz, 1 H), 5.05–5.09 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.77, 137.87, 135.19, 132.44, 129.79, 128.69, 128.33, 117.90, 114.51, 113.91, 68.26, 63.83.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{13}Cl_2N_3NaO_4$: 416.0175; found: 416.0213.

Benzyl [2,2-Dichloro-2-nitro-1-(2-tolyl)ethyl]carbamate (3n)
Colorless oil; yield: 79%.

IR (KBr): 3406, 3304, 3032, 2964, 1768, 1704, 1584, 1507, 1230, 1044 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 7.4 Hz, 1 H), 7.21–7.29 (m, 8 H), 6.43 (d, *J* = 10.0 Hz, 1 H), 5.78 (d, *J* = 9.7 Hz, 1 H), 4.97–5.08 (m, 2 H), 2.58 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.01, 138.17, 135.43, 132.63, 131.20, 129.64, 128.65, 128.53, 128.36, 126.62, 126.46, 115.97, 67.98, 59.14, 20.29.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{16}Cl_2N_2NaO_4$: 405.0379; found: 405.0377.

Benzyl [2,2-Dichloro-2-nitro-1-(3-tolyl)ethyl]carbamate (3o)
White solid; yield: 77%; mp 106–108 °C.

IR (KBr): 3416, 3315, 3034, 2962, 1715, 1585, 1501, 1334, 1230, 1053 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.18–7.32 (m, 9 H), 5.97 (d, *J* = 10.4 Hz, 1 H), 5.80–5.84 (m, 1 H), 5.03–5.12 (m, 2 H), 2.35 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.96, 138.59, 135.48, 132.70, 130.63, 129.57, 128.65 (2 C), 128.53, 128.39, 125.79, 115.66, 67.98, 64.29, 21.46.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{16}Cl_2N_2NaO_4$: 405.0379; found: 405.0374.

Benzyl [2,2-Dichloro-2-nitro-1-(4-tolyl)ethyl]carbamate (3p)
Colorless oil; yield: 93%.

IR (KBr): 3415, 3316, 3034, 2961, 1713, 1585, 1513, 1336, 1233, 1051 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.14 (m, 9 H), 5.97 (d, *J* = 9.9 Hz, 1 H), 5.87 (d, *J* = 9.6 Hz, 1 H), 5.11–5.01 (m, 2 H), 2.33 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.02, 139.99, 135.53, 129.80, 129.47, 128.70, 128.66, 128.51, 128.37, 115.80, 67.95, 64.14, 21.23.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{16}Cl_2N_2NaO_4$: 405.0379; found: 405.0381.

Benzyl [2,2-dichloro-1-(2-methoxyphenyl)-2-nitroethyl]carbamate (3q)
Colorless oil; yield: 97%.

IR (KBr): 3419, 3320, 3034, 2964, 2842, 1732, 1712, 1584, 1495, 1337, 1251, 1027 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.38 (m, 7 H), 6.89–6.99 (m, 2 H), 6.42 (d, *J* = 10.2 Hz, 1 H), 6.28 (d, *J* = 10.2 Hz, 1 H), 5.03–5.13 (m, 2 H), 3.79 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.73, 155.38, 135.76, 131.14, 130.84 (2 C), 128.62, 128.43 (2 C), 120.92, 116.16, 111.74, 67.77, 61.95, 55.61.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{16}Cl_2N_2NaO_5$: 421.0328; found: 421.0324.

Benzyl 2,2-[dichloro-1-(4-methoxyphenyl)-2-nitroethylcarbamate (3r)
Colorless oil; yield: 97%.

IR (KBr): 3410, 3315, 3035, 2961, 2839, 1709, 1611, 1585, 1514, 1251, 1031 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.29–7.33 (m, 7 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.95 (d, *J* = 10.0 Hz, 1 H), 5.77 (d, *J* = 10.3 Hz, 1 H), 5.24–5.02 (m, 2 H), 3.79 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.63, 154.95, 135.50, 130.05, 128.64, 128.52, 128.37, 124.63, 115.82, 114.14, 67.95, 63.87, 55.34.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{16}Cl_2N_2NaO_5$: 421.0328; found: 421.0325.

Benzyl {1-[2-(Benzyloxy)phenyl]-2,2-dichloro-2-nitroethyl}carbamate (3s)
Colorless oil; yield: 91%.

IR (KBr): 3416, 3319, 3065, 3034, 2953, 2888, 1732, 1585, 1498, 1228, 1045 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.29 (m, 12 H), 6.95–7.00 (m, 2 H), 6.38–6.46 (m, 2 H), 5.07–5.09 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.95, 155.23, 136.06, 135.78, 131.11, 130.89, 128.85, 128.60, 128.36, 128.32, 128.23, 127.40 (2 C), 121.16, 116.21, 112.94, 70.76, 67.68, 61.69.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{23}H_{20}Cl_2N_2O_5Na$: 497.0641; found: 497.0642.

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References

(1) Kemp, J. E. In *Comprehensive Organic Synthesis*, Vol. 3; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, **1991**, 469.
(2) (a) Yeung, Y. Y.; Gao, X.; Corey, E. J. *J. Am. Chem. Soc.* **2006**, *128*, 9644. (b) Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1991**, *113*, 5863. (c) Lessard, J.; Driguez, H.; Vermes, J. P. *Tetrahedron Lett.* **1970**, *11*, 4887.
(3) (a) Lessard, J.; Driguez, H.; Vermes, J. P. *Tetrahedron Lett.* **1970**, *11*, 4887. (b) Driguez, H.; Vermes, J. P.; Lessard, J. *Can. J. Chem.* **1978**, *56*, 119. (c) Daniher, F. A.; Butler, P. E. *J. Org. Chem.* **1968**, *33*, 4336. (d) Daniher, F. A.; Melchior, M. T.; Butler, P. E. *Chem. Commun.* **1968**, 931. (e) Orlek, B. S.; Stemp, G. *Tetrahedron Lett.* **1991**, *32*, 4045.
(4) For a recent review on aminohalogenation, see: Li, G.; Saibabu Kotti, S. R. S.; Timmons, C. *Eur. J. Org. Chem.* **2007**, 2745.
(5) Qui, J.; Silverman, R. B. *J. Med. Chem.* **2000**, *43*, 706.
(6) (a) Chen, D.; Timmons, C.; Guo, L.; Xu, X.; Li, G. *Synthesis* **2004**, 2749. (b) Chen, D.; Guo, L.; Liu, J.; Kirtane, S.; Cannon, J. F.; Li, G. *Org. Lett.* **2005**, *7*, 921. (c) Mei, H. B.; Yan, L. J.; Han, J. L.; Li, G.; Pan, Y. *Chem. Biol. Drug Des.* **2010**, *76*, 392. (d) Han, J. L.; Li, Y. F.; Zhi, S. J.; Pan, Y.; Timmons, C.; Li, G. *Tetrahedron Lett.* **2006**, *47*, 7225.

(7) (a) Li, G.; Wei, H. X.; Kim, S. H.; Neighbors, M. *Org. Lett.* **1999**, *1*, 395. (b) Wei, H. X.; Kim, S. H.; Li, G. *Tetrahedron* **2001**, *57*, 3869. (c) Li, G.; Wei, H. X.; Kim, S. H. *Tetrahedron* **2001**, *57*, 8407. (d) Saibabu Kotti, S. R. S.; Xu, X.; Wang, Y. N.; Headley, A. D.; Li, G. G. *Tetrahedron Lett.* **2004**, *35*, 7209. (e) Li, G.; Wei, H. X.; Kim, S. H. *Org. Lett.* **2000**, *2*, 2249. (f) Chen, Z. G.; Wei, J. F.; Wang, M. Z.; Zhou, L. Y.; Zhang, C. J.; Shi, X. Y. *Adv. Synth. Catal.* **2009**, *351*, 2358.

(8) Han, J. L.; Zhi, S. J.; Wang, L. Y.; Pan, Y.; Li, G. *Eur. J. Org. Chem.* **2007**, 1332.

(9) (a) Sun, H.; Zhang, G. Q.; Zhi, S. J.; Han, J. L.; Li, G.; Pan, Y. *Org. Biomol. Chem.* **2010**, *8*, 4236. (b) Chen, D.; Timmons, C.; Chao, S.; Li, G. *Eur. J. Org. Chem.* **2004**, 3097. (c) Chen, Z. G.; Wei, J. F.; Li, R. T.; Shi, X. Y.; Zhao, P. F. *J. Org. Chem.* **2009**, *74*, 1371. (d) Wei, J. F.; Zhang, L. H.; Chen, Z. G.; Shi, X. Y.; Cao, J. J. *Org. Biomol. Chem.* **2009**, *7*, 3280. (e) Wu, X. L.; Xia, J. J.; Wang, G. W. *Org. Biomol. Chem.* **2008**, *6*, 548. (f) Thakur, V. V.; Talluri, S. K.; Sudalai, A. *Org. Lett.* **2003**, *5*, 861. (g) Wu, X. L.; Wang, G. W. *Eur. J. Org. Chem.* **2008**, 6239. (h) Liu, J. Y.; Wang, Y. N.; Li, G. *Eur. J. Org. Chem.* **2006**, 3112. (i) Shaikh, T. M.; Karabal, P. U.; Suryavanshi, G.; Sudalai, A. *Tetrahedron Lett.* **2009**, *50*, 2815. (j) 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.

(10) (a) Zhi, S. J.; Han, J. L.; Lin, C.; An, G. H.; Pan, Y.; Li, G. *Synthesis* **2008**, 1570. (b) Zhi, S. J.; Sun, H.; Lin, C.; Zhang, G. Q.; Li, G.; Pan, Y. *Sci. China Chem.* **2010**, *53*, 140. (c) Chen, Z. G.; Wang, Y.; Wei, J. F.; Zhao, P. F.; Shi, X. Y. *J. Org. Chem.* **2010**, *75*, 2085. (d) Zhi, S. J.; Mei, H. B.; Zhang, G. Q.; Sun, H.; Han, J. L.; Li, G.; Pan, Y. *Sci. China Chem.* **2010**, *53*, 1946. (e) Mei, H.; Han, J.; Li, G.; Pan, Y. *RSC Adv.* **2011**, *1*, 429.

(11) (a) Zhi, S. J.; Sun, H.; Zhang, G. Q.; Li, G. G.; Pan, Y. *Org. Biomol. Chem.* **2010**, *8*, 628. (b) Zhi, S. J.; An, G. H.; Sun, H.; Han, J. L.; Li, G. G.; Pan, Y. *Tetrahedron Lett.* **2010**, *51*, 2745.

(12) (a) Enders, D.; Wiedemann, J. *Synthesis* **1996**, 1443. (b) Lucet, D.; Toupet, L.; Gall, T. L.; Mioskowski, G. *J. Org. Chem.* **1997**, *62*, 2682.

(13) (a) Foglia, T. A.; Swern, D. *J. Org. Chem.* **1966**, *31*, 3625. (b) Foglia, T. A.; Swern, D. *J. Org. Chem.* **1968**, *33*, 766. (c) Crookes, B.; Seden, T. P.; Turner, R. W. *Chem. Commun.* **1968**, 324.

(14) (a) Bourguignon, J.; Le Nard, G.; Queguiner, G. *Can. J. Chem.* **1985**, *63*, 2354. (b) Liu, J.; Yao, C. F. *Tetrahedron Lett.* **2001**, *42*, 6147. (c) Bowman, R. K.; Johnson, J. S. *J. Org. Chem.* **2004**, *69*, 8537.

(15) White, R. E.; Kovacic, P. *J. Am. Chem. Soc.* **1975**, *97*, 1180.