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Aminochlorination reaction with *N*-chlorophthalimide as a new nitrogen/chlorine source resulting in α-amino derivatives

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ABSTRACT

A commercial available compound, *N*-chlorophthalimide was reported as an efficient nitrogen/chlorine source for the aminohalogenation of β-nitrostyrenes, which tolerates a wide range of β-nitrostyrenes substrates with good chemical yields, as well as excellent regioselectivities. The resulted vicinal haloamino nitro products have been converted into several other valuable α-amino compounds under simple and mild conditions.

1. Introduction

Aminohalogenation and related reactions of functionalized olefins have been reported as one of the most useful tools for the synthesis of vicinal haloamines,[1,2] by constructing carbon-nitrogen and carbon-halogen bonds in tandem way at the same time.[3–7] The pioneer works about aminohalogenation reaction were found in the 1960s, with simple alkenes as substrates. These reactions have many of the characteristics of a free-radical addition reaction, which resulted in moderate yields and low stereoselectivities.[8] In the past several years, a lot of highly regio- and stereoselective systems have been developed for aminohalogenation of functionalized alkenes, which included α,β-unsaturated carboxylic esters,[9] α,β-unsaturated nitriles,[10] α,β-unsaturated ketones.[11] However, the nitrogen sources for these aminohalogenation reactions were still not well documented until now, and only sulfonamides were efficient for these reaction.[9–11] So, the development of aminohalogenation still remains very difficult and great challenging.

Recently, β-nitrostyrenes, representing a new type of substrates, were reported for the aminohalogenation and attracted many research interests, due to their higher reactivity.[12,13] Furthermore, the resulting haloamino nitro products can be easily converted into corresponding vicinal diamines.[14] We and other groups have reported some nitrogen sources for the aminohalogenation of these electron-deficient alkenes, such as *N*,*N*-dichlorosulfonamide, succinimide/NCS, *N*-bromoacetamide, benzamides/NCS,[12,13] *tert*-butyl *N*,*N*-dichlorocarbamate,[15] benzyl carbamate/NCS,[16] *N*,*N*-dibromourethane[17] and so on. However, the aminohalogenation of β-nitrostyrenes proceeding through chloronium intermediates or Michael adducts, still remained unclear, which seemed to depend on the nitrogen sources.[12–17] So, exploration of more nitrogen sources for the aminohalogenation of β-nitrostyrenes becomes in great need. In our continuous work on this reaction, we found that *N*-chlorophthalimide could reaction with β-nitrostyrenes under simple conditions. Herein, we would like to report an efficient aminochlorination of β-nitrostyrenes with *N*-chlorophthalimide as a new nitrogen source promoted by NaOH (Scheme 1). *N*-Chlorophthalimide was a commercial available compound and with higher thermal stability comparing with the previous reported nitrogen sources, which made the reaction was very facile and practical.

2. Results and discussion

Initially, β-nitrostyrene **2a** was chosen as the substrate for optimizing the aminohalogenation conditions (Table 1). The reaction was carried out under previous catalytic conditions[12b] with dichloromethane as solvent and $Ni(OAc)_2$ as catalyst at room temperature (entry 1, Table 1). No desired haloamide product was observed at all and most of the starting materials remained after 48 h. Then, several other metal catalysts were tried for the reaction,

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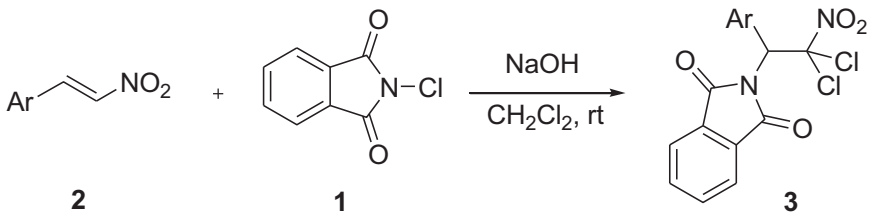
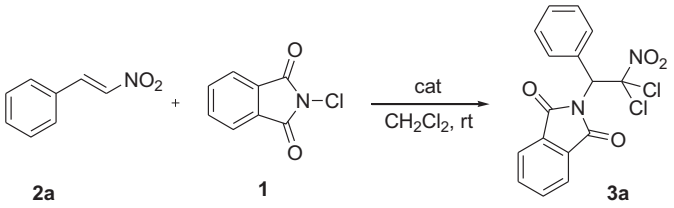


Scheme 1. *N*-Chlorophthalimide as nitrogen source for aminohalogenation reaction.

but giving no obvious improvement on the chemical yields at all (entries 2–11). Fortunately, the desired product was observed with 29% yield in the presence of 20 mol % NaOH (entry 12). Encouraged by this result, the further optimization was carried out by increasing the amount of *N*-chlorophtahlimide, and a slightly higher chemical yield was obtained (35%, entry 13). After careful studies, we found the chemical yield could be increased to 92% when 3 equiv of NaOH was used (entry 17).

Table 1
Aminohalogenation of β-nitrostyrene with various catalysts[a]

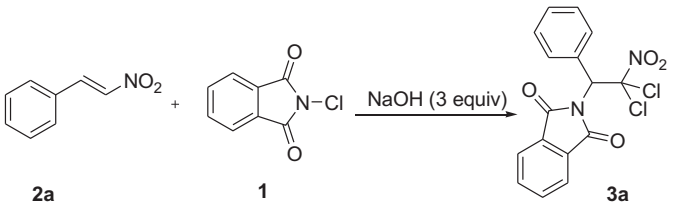


Entry	Catalyst (mol %)	Ratio (**2a**:**1**)	Yields (%)[b]
1	$Ni(OAc)_2$ (20%)	1:2	NR[c]
2	K_2CO_3 (20%)	1:2	13%
3	K_2CO_3/$Ni(OAc)_2$ (20%)	1:2	13%
4	$MgSO_4$ (20%)	1:2	NR[c]
5	$Mn(OAc)_2$ (20%)	1:2	NR[c]
6	KOH (20%)	1:2	15%
7	K_3PO_4 (20%)	1:2	13%
8	NaOAc (20%)	1:2	NR[c]
9	DMAP (20%)	1:2	NR[c]
10	Triethylamine (20%)	1:2	NR[c]
11	$(CH_3)_3CONa$ (20%)	1:2	25%
12	NaOH (20%)	1:2	29%
13	NaOH (20%)	1:3	35%
14	NaOH (50%)	1:3	44%
15	NaOH (150%)	1:3	58%
16	NaOH (200%)	1:3	69%
17	NaOH (300%)	1:3	92%

[a] Conditions: β-nitrostyrene **2a** (0.5 mmol), *N*-chlorophtahlimide, in CH_2Cl_2 (3 mL) at room temperature under N_2.
[b] Isolated yields.
[c] No reaction was observed.

Then, the scan of various organic solvents was carried out in the presence of NaOH to improve the reaction efficiency (Table 2). Solvent was found to play an important role in the current system. No aminohalogenation product was observed at all when DMSO or methanol was used as solvent (entries 4 and 6). The reaction with acetonitrile, THF, DMF or acetone as solvent could also give the desired haloamine products, along with moderate yields (entries 1, 3, 5 and 7). Notably, toluene was also a good choice for the current system, resulting in a good chemical yield (91%, entry 2). The best solvent for the reaction was dichloromethane, giving the desired product with the highest yield (entry 8). After careful studies, we found that 48 h was needed for the reaction to consume all the starting material. Shortening the reaction time resulted in dramatically lower yields (entries 9–12).

Table 2
Aminohalogenation of β-nitrostyrene with various solvents[a]

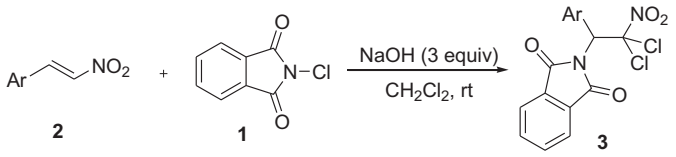


Entry	Solvent	Time (h)	Temperature	Yields (%)[b]
1	CH_3CN	48	rt	55
2	PhMe	48	rt	91
3	DMF	48	rt	25
4	DMSO	48	rt	NR[c]
5	THF	48	rt	47
6	MeOH	48	rt	NR[c]
7	Acetone	48	rt	26
8	CH_2Cl_2	48	rt	92
9	CH_2Cl_2	8	rt	35
10	CH_2Cl_2	12	rt	40
11	CH_2Cl_2	24	rt	61
12	CH_2Cl_2	36	rt	68
13	CH_2Cl_2	72	rt	93

[a] Conditions: β-nitrostyrene **2a** (0.5 mmol), *N*-chlorophtahlimide (1.5 mmol), 3 equiv NaOH, in solvent (3 mL) at room temperature under N_2.
[b] Isolated yields.
[c] No reaction was observed.

After obtaining the optimized reaction conditions, we then examined the scope of the aminohalogenation reaction by using a variety of β-nitrostyrenes (Table 3). The transformation with *N*-chlorophtahlimide as nitrogen/chlorine source can proceed smoothly for a wide range of substrates, giving moderate to excellent chemical yields. The substituent groups on the aromatic ring showed effect on the reaction. Generally, the reaction of electron-rich substrates gave moderate chemical yields, and for the case of methoxyl substituent, only 66% yield was found (entry 10). The electron-deficient substrates were more suitable for the current reaction, resulting in good to excellent chemical yields, even though the substituent groups were fluoro (entries 6 and 7), trifluoromethyl (entry 15). We then examined the substrates with double substituted aromatic ring (**2k** and **2l**), and the results showed that they could also work well, giving the desired products (entries 11 and 12). Notably, 1-naphthyl and 2-naphthyl β-nitrostyrene (**2m** and **2n**) was well tolerated in the reaction along with good chemical yields (entries 13 and 14). Surprisingly, the reaction of the substrates with *ortho*-substituted aromatic ring (**2d**) gave an obvious lower yield (entry 4) than those of the substituents on other positions. It was mainly because that the steric hindrance of the substrate inhibited the addition of nitrogen/chlorine source. Furthermore, excellent regioselectivities were detected for all the cases, and only one regio isomer was obtained from the reaction. The structure of these obtained dichlorinated haloamides has been unambiguously confirmed by the X-ray diffraction analysis of **3d** (Fig. 1).

Table 3
The scope of the aminohalogenation[a]



Entry	Substrate	Ar	Product	Yields (%)[b]
1	**2a**	C_6H_5	**3a**	92%
2	**2b**	2-ClC_6H_4	**3b**	93%
3	**2c**	4-MeC_6H_4	**3c**	76%
4	**2d**	2-$OBnC_6H_4$	**3d**	35%
5	**2e**	4-ClC_6H_4	**3e**	94%
6	**2f**	4-FC_6H_4	**3f**	90%
7	**2g**	3-FC_6H_4	**3g**	74%
8	**2h**	4-BrC_6H_4	**3h**	75%
9	**2i**	3-BrC_6H_4	**3i**	80%
10	**2j**	4-$OMeC_6H_4$	**3j**	66%
11	**2k**	3-Br-4-$OMeC_6H_3$	**3k**	87%
12	**2l**	3-Cl-4-ClC_6H_3	**3l**	67%
13	**2m**	1-Naphthyl	**3m**	80%
14	**2n**	2-Naphthyl	**3n**	71%
15	**2o**	4-$CF_3C_6H_4$	**3o**	72%

[a] Conditions: β-nitrostyrenes **2** (0.5 mmol), *N*-chlorophtahlimide (1.5 mmol), 3 equiv NaOH, in CH_2Cl_2 (3 mL) at room temperature under N_2.
[b] Isolated yields.

According to the previous studies on the aminohalogenation of β-nitrostyrene[12–17] and the resulted regioselectivity from the current aminohalogenation system, a mechanism involving the formation of chloronium intermediate was presented in Scheme 2 for this aminohalogenation reaction with *N*-chlorophtahlimide as nitrogen/chlorine source. In the initial step, *N*-chlorophtahlimide is activated by NaOH,[18] forming the intermediates **A1** and **A2**. Then, **A1** adds to β-nitrostyrene **2a**, generating the chloronium intermediate **B**. The chloronium intermediate **B** undergoes ring-opening process, attacked by **A2** on its α-position, which is more positively charged than its β-position with the aid of NaOH, resulting in intermediate **C**, a normal monohaloamino product. The final step is the formation of dichlorinated compound **3a** via deprotonation/electrophilic chlorination of precursor **C**.

The presence of chloro and nitro functionalities in the resulted vicinal chloroamino nitro products provided an easy access to various other valuable organic blocks by intermolecular or intramolecular reactions. When the product **3a** was stirred in methanol in the presence of Pd/C under the hydrogen atmosphere at room temperature for 16 h, two new compounds were isolated (Scheme 3). One was α-amino acetal **4** with 31% yield, the other was α-amino nitro compounds **5** with 56% yield.

More importantly, when the reaction time was prolonged to 48 h, the nitro group in **5** could undergo the other reduction

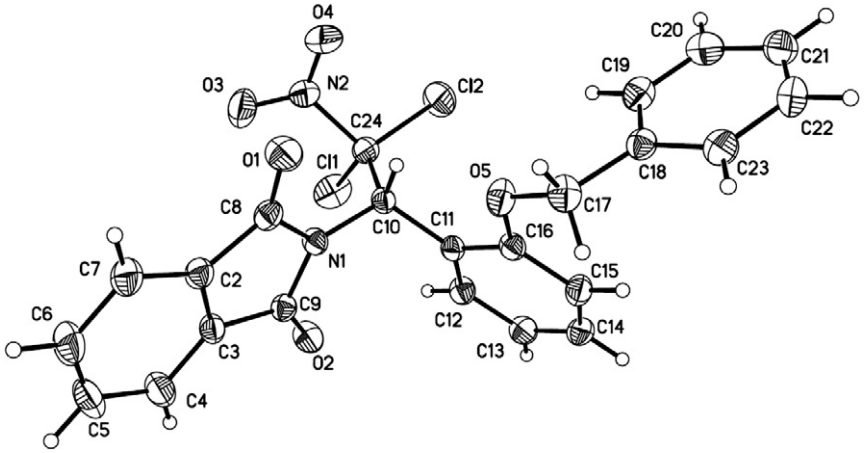
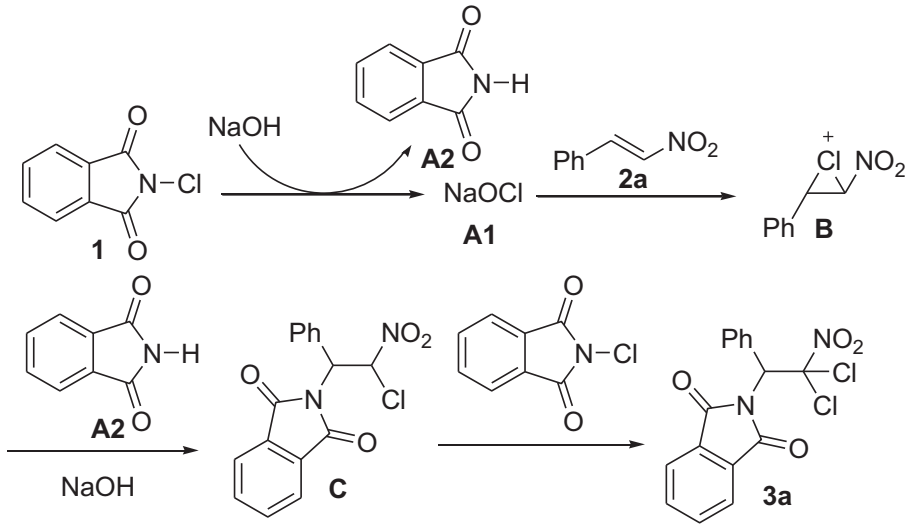
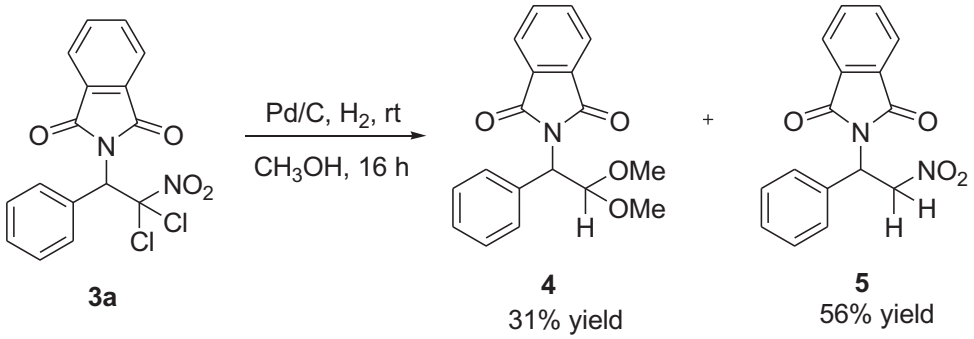


Fig. 1. ORTEP diagram drawing of **3d** (CCDC number: 824479).



Scheme 2. Proposed mechanism for the reaction.

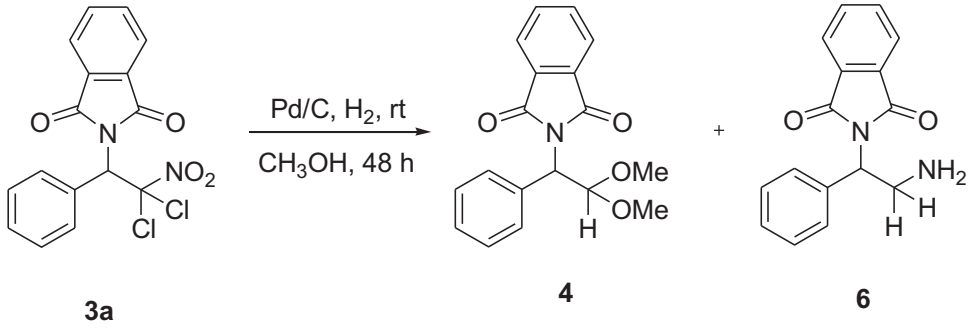


Scheme 3. Conversion of **3a** catalyzed by Pd/C for 16 h.

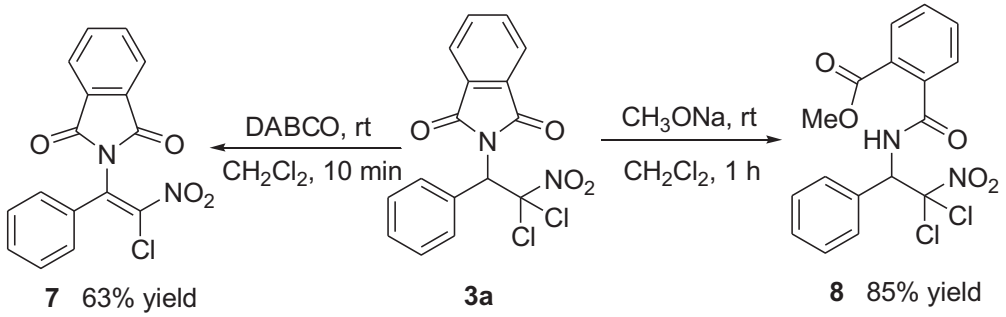
process. Almost all of **5** was converted into vicinal diamine **6** with 48% chemical yield (Scheme 4), and **4** was remained.

Finally, the product **3a** was subjected to DABCO/CH_2Cl_2 system at room temperature for 10 min, α,β-unsaturated vicinal haloamino nitro compound **7** was obtained in 63% yield. **3a** was also easily to be esterified by treatment with sodium methoxide for 1 h, resulting in compound **8** with the yield of 85% (Scheme 5).

temperature with good to excellent yields and high regioselectivities. The resulted chloroamino nitro compounds have been converted into α-amino acetal, α-amino nitro compounds, vicinal diamine, α,β-unsaturated vicinal haloamino nitro compound and so on. Further study on asymmetric aminohalogenation of this new type of nitrogen source is presently under progress.



Scheme 4. Conversion of **3a** catalyzed by Pd/C for 48 h.



Scheme 5. Derivatization reaction of **3a**.

3. Conclusion

In summary, a regioselective aminochlorination of β-nitrostyrenes with *N*-chlorophtahlimide as a new nitrogen/chlorine source under mild conditions has been developed. The system was convenient to carry out in the presence of NaOH at room

4. Experimental section

4.1. General

Reaction progress was monitored by TLC using silica gel 60F-254 with detection by UV. Flash chromatography was performed using

silica gel 60 (200–300mesh) with freshly distilled solvents. Melting points are uncorrected. ^{1}H and ^{13}C NMR (TMS used as internal standard) spectra were recorded with a Bruker ARX300 spectrometer. High resolution mass spectra for all the new compounds were done by Micro mass Q-Tof instrument (ESI). The crystal structure was recorded on a X-ray diffraction spectrometer.

4.2. General procedure for aminohalogenation

Into a dry reaction tube were added the **2** (0.5 mmol), *N*-chlorophtahlimide (1.5 mmol), NaOH (1.5 mmol), and they were mixed with freshly distilled CH_2Cl_2 (3.0 mL) under nitrogen atmosphere. The mixture was stirred at room temperature for 48 h. The reaction was then quenched by saturated aqueous Na_2SO_3 (2.0 mL) solution. The solid precipitates were filtered off and the filtrate was extracted with CH_2Cl_2 three times. Then the combined organic phase was washed with brine and dried with anhydrous Na_2SO_4. After being concentrated, the mixture was purified via column chromatography with ethyl acetate and petroleum ether (v/v=1:4) as eluent to give the product.

4.2.1. ***3a***. White solid. Mp 124–126 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–7.95 (m, 2H), 7.70–7.84 (m, 4H), 7.32–7.45 (m, 3H), 6.67 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.68, 134.82, 131.09, 131.01, 130.73, 130.03, 128.74, 124.05, 114.66, 64.52. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_{10}Cl_2N_2O_4Na$ 386.9915, found 386.9910.

4.2.2. ***3b***. White solid. Mp 131–132 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32–8.42 (m, 1H), 7.73–7.91 (m, 4H), 7.30–7.44 (m, 3H), 7.03 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.27, 134.86, 134.68, 131.64, 130.99, 130.95, 130.11, 128.58, 126.50, 124.04, 114.39, 59.98. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_9Cl_3N_2O_4Na$ 420.9526, found 420.9520.

4.2.3. ***3c***. White solid. Mp 116–117 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.84–8.95 (m, 2H), 7.72–7.83 (m, 2H), 7.65–7.72 (m, 2H), 7.15–7.23 (m, 2H), 6.63 (s, 1H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.74, 140.19, 134.78, 131.14, 130.68, 129.42, 127.91, 124.01, 114.75, 64.37, 21.24. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{17}H_{12}Cl_2N_2O_4Na$ 401.0072, found 401.0066.

4.2.4. ***3d***. White solid. Mp 131–133 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15–8.23 (m,1H), 7.69–7.83 (m, 4H), 7.21–7.38 (m, 6H), 7.15 (s, 1H), 7.00–7.08 (m, 1H), 6.91 (d, J=8.4 Hz, 1H), 4.97–5.10 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.59, 156.06, 135.90, 134.44, 131.23, 130.82, 130.64, 128.53, 128.06, 127.50, 123.83, 120.43, 119.64, 114.81, 112.19, 70.57, 57.14. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{23}H_{16}Cl_2N_2O_5Na$ 493.0334, found 493.0328.

4.2.5. ***3e***. White solid. Mp 112–115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–7.95 (m, 2H), 7.70–7.85 (m, 4H), 7.30–7.40 (m, 2H), 6.62 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.62, 136.30, 134.93, 132.23, 131.01, 129.36, 128.98, 124.14, 114.30, 63.83. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_{14}Cl_2N_2O_4Na$ 420.9526, found 420.9532.

4.2.6. ***3f***. White solid. Mp 133–135 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87–7.95 (m, 2H), 7.75–7.85 (m, 4H), 7.00–7.12 (m, 2H), 6.64 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.68, 165.13, 161.82, 134.89, 133.14, 133.02, 131.03, 126.78, 124.10, 115.93,115.64, 114.53, 63.86. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_9Cl_2FN_2O_4Na$ 404.9821, found 404.9823.

4.2.7. ***3g***. White solid. Mp 97–98 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–7.95 (m, 2H), 7.73–7.85 (m, 2H), 7.60–7.70 (m, 1H), 7.45–7.52 (m, 1H), 7.30–7.42 (m, 1H), 7.05–7.15 (m, 1H), 6.65 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.57, 164.02, 160.75, 134.94, 133.01, 130.99, 130.32, 130.21, 126.56, 126.52, 124.16, 118.11, 117.79, 117.32, 117.05, 114.21, 63.80. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_9Cl_2FN_2O_4Na$ 404.9821, found 404.9836.

4.2.8. ***3h***. White solid. Mp 134–136 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–7.95 (m, 2H), 7.75–7.84 (m, 2H), 7.67 (d, J=8.7 Hz, 2H), 7.50 (d, J=8.4 Hz, 2H), 6.61 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.60, 134.93, 132.44, 131.96, 131.00, 129.89, 124.64, 124.14, 114.21, 63.89. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_9BrCl_2N_2O_4Na$ 464.9020, found 464.9003.

4.2.9. ***3i***. White solid. Mp 100–103 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–8.00 (m, 3H), 7.74–7.84 (m, 3H), 7.48–7.60 (m, 1H), 7.22–7.32 (m, 1H), 6.60 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.55, 134.98, 133.69, 133.23, 132.95, 130.97, 130.20, 129.37, 124.18, 122.61, 114.13, 63.72. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_9BrCl_2N_2O_4Na$ 464.9020, found 464.9031.

4.2.10. ***3j***. White solid. Mp 130–132 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85–7.95 (m, 2H), 7.71–7.81 (m, 4H), 6.87 (d, J=8.7 Hz, 2H), 6.61 (s, 1H), 3.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.79, 160.71, 134.77, 132.47, 131.14, 124.00, 122.67, 114.93, 113.98, 64.25, 55.30. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{17}H_{12}Cl_2N_2O_5Na$ 417.0021, found 417.0015.

4.2.11. ***3k***. White solid. Mp 112–114 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, J=2.1 Hz, 1H), 7.86–7.94 (m, 2H), 7.75–7.84 (m, 3H), 6.86–6.92 (d, J=8.7 Hz, 1H), 6.55 (s, 1H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.66, 157.10, 135.86, 134.91, 131.49, 131.01, 124.11, 123.94, 114.52, 111.62, 111.44, 63.53, 56.32. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{17}H_{11}BrCl_2N_2O_5Na$ 494.9126, found 494.9137.

4.2.12. ***3l***. White solid. Mp 129–131 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87–7.98 (m, 3H), 7.75–7.85 (m, 2H), 7.60–7.71 (m, 1H), 7.37–7.50 (m, 1H), 6.58 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.50, 135.04, 134.84, 132.79, 130.91, 130.81, 130.63, 130.07, 128.33, 124.24, 113.90, 63.29. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_8Cl_4N_2O_4Na$ 456.9106, found 456.9103.

4.2.13. ***3m***. White solid. Mp 186–188 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.55–8.65 (m, 1H), 8.00 (d, J=8.4 Hz, 1H), 7.80–7.96 (m, 4H), 7.70–7.78 (m, 2H), 7.45–7.61 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.72, 134.77, 133.90, 131.39, 130.99, 130.79, 129.58, 128.90, 127.84, 126.03, 125.75, 124.61, 124.02, 121.61, 115.01, 58.76. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{20}H_{12}Cl_2N_2O_4Na$ 437.0072, found 437.0066.

4.2.14. ***3n***. White solid. Mp 171–173 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.73–7.97 (m, 8H), 7.48–7.58 (m, 2H), 6.99 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.78, 134.82, 133.60, 132.77, 131.11, 131.03, 128.60, 128.49, 128.37, 127.62, 127.47, 127.16, 126.73, 124.07, 114.67, 64.66. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{20}H_{12}Cl_2N_2O_4Na$ 437.0072, found 437.0081.

4.2.15. ***3o***. White solid. Mp 41–43 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87–7.98 (m, 4H), 7.75–7.85 (m, 2H), 7.62–7.70 (m, 2H), 6.70 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.54, 135.00, 134.80, 131.19, 130.95, 129.42, 125.69, 125.64, 124.19, 113.97, 63.81, 29.71. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{17}H_9Cl_2F_3N_2O_4Na$ 454.9789, found 454.9780.

4.3. General procedure for reduction reaction of 3a catalyzed by Pd/C

Into a dry reaction vial were added **3a** (0.5 mmol), 10% **Pd/C** (10 mg) and CH_3OH (25 mL). The mixture was stirred at room temperature under hydrogen for the desired reaction time then passed through Celite. The Celite was washed with ether and the organic phase was combined. After evaporation, the crude product was purified by TLC plate.

4.3.1. ***4***. White solid. Mp 123–124 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76–7.85 (m, 2H), 7.66–7.73 (m, 2H), 7.55–7.63 (m, 2H), 7.23–7.38 (m, 3H), 5.73 (d, J=9.3 Hz, 1H), 5.36 (d, J=8.7 Hz, 1H), 3.37 (s, 3H), 3.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.16, 136.89, 133.99, 131.89, 128.98, 128.63, 128.16, 123.34, 101.51, 56.04, 54.73, 53.26. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{18}H_{17}NO_4Na$ 334.1050, found 334.1048.

4.3.2. ***5***. White solid. Mp 129–130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79–7.90 (m, 2H), 7.67–7.78 (m, 2H), 7.47–7.60 (m, 2H), 7.31–7.43 (m, 3H), 6.11–6.17 (m, 1H), 5.79–5.92 (m, 1H), 5.02–5.08 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.71, 134.97, 134.47, 131.49, 129.27, 129.23, 127.98, 123.71, 74.20, 52.24. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_{12}N_2O_4Na$ 319.0689, found 319.0615.

4.3.3. ***6***. White solid. Mp 217–219 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.29 (b, 2H), 7.85–7.91 (m, 4H), 7.31–7.39 (m, 5H), 5.54–5.66 (m, 1H), 4.04–4.11 (m, 1H), 3.52–3.58 (m, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.49, 137.05, 135.10, 132.08, 129.37, 128.80, 127.52, 123.72, 52.26, 39.68. HRMS (ESI/$[M+H]^+$) Calcd. For: $C_{16}H_{15}N_2O_2$ 267.1129, found 267.1128.

4.4. General procedure for conversion of 3a to 7

Into a dry reaction vial were added **3a** (0.5 mmol), DACBO (1.5 mmol) and CH_2Cl_2 (4 mL). The mixture was stirred at room temperature for 10 min. The mixture was directly purified by TLC plate.

4.4.1. ***7***. Yellow solid. Mp 116–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88–7.97(m, 2H), 7.78–7.87 (m, 2H), 7.48–7.58 (m, 2H), 7.26–7.47 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.86, 135.15, 132.05, 131.61, 131.29, 131.25, 129.10, 128.87, 124.52. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{16}H_9ClN_2O_4Na$ 351.0143, found 351.0140.

4.5. General procedure for conversion of 3a to 8

Into a dry reaction vial were added **3a** (0.5 mmol), MeONa (2.5 mmol in 2.5 mL methonal) and CH_2Cl_2 (2 mL). The mixture was stirred at room temperature for 1 h. The mixture was directly purified by TLC plate, giving product **8**.

4.5.1. ***8***. White solid. Mp 150–151 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.87 (d, J=6.9 Hz, 1H), 7.44–7.58 (m, 8H), 7.11 (d, J=9.9 Hz, 1H), 6.47 (d, J=10.5, 1H), 3.51 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.03, 166.92, 136.33, 132.71, 132.23, 130.47, 130.38, 129.88, 129.14, 129.04, 128.80, 127.88, 115.45, 62.11, 52.40. HRMS (ESI/$[M+Na]^+$) Calcd. For: $C_{17}H_{14}Cl_2N_2O_5Na$ 419.0177, found 419.0167.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2012.05.066.

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