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An Approach to Vicinal *t*-Boc-Amino Dibromides *via* Catalytic Aminobromination of Nitrostyrenes without using Chromatography and Recrystallization

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Abstract

1.0 % Mol of K₃PO₄·3H₂O was found to catalyze aminohalogenation reaction of nitrostyrenes with *N,N*-dibromo-*tert*-butylcarbamate (*t*-Boc-NBr₂) in *dichloroethane* system. Good to excellent yields and complete regioselectivity have been achieved by taking advantage of the GAP work-up without using traditional purification techniques such as column chromatography and recrystallization. *New mechanism* was proposed involving radical and ionic catalytic cycles and an intramolecular migration.

Keywords

Aminohalogenation; bromoamine; Group-Assistant-Purification (GAP) chemistry; *N,N*-dibromo-*tert*-butylcarbamate; nitrostyrenes

Introduction

Aminohalogenation reaction has become an important tool for the synthesis of vicinal haloamine compounds that are versatile building blocks in organic and medicinal chemistry.^{1–6} For example, they can be readily converted into many other synthetic precursors, such as aziridines and enamines. In the past one decade, many efforts have been devoted to this reaction under a series of metal-catalyzed and organocatalytic conditions. Functionalized substrates, such as α,β -unsaturated carboxylic esters,^{4,5} α,β -unsaturated nitriles,⁷ α,β -unsaturated ketones,⁸ β -nitrostyrenes⁹ and other substrates^{5,10}, have been proven to be suitable for aminohalogenation reaction. In the meanwhile, several nitrogen/halogen sources including *N,N*-dichlorotoluenesulfonamide (TsNCl₂),^{4,5} NsNCl₂/NsNHNa,⁴ *N*-bromoacetamide,¹¹ Chloramine-T,¹¹ *p*TsNH₂/NBS,¹² NsNCl₂/NsNH₂,¹³ *tert*-butyl-*N,N*-dibromo- and dichlorocarbamates¹⁴ have been found to be efficient for aminohalogenation reaction with very well controlled regio and stereoselectivity. The reaction is believed to go through the formation of aziridinium intermediates, halonium (bromonium or chloronium) intermediates or radicals. Aziridinium intermediate-based

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Supporting Information Available. ¹H and ¹³C NMR spectra of all pure products are available free of charge via the Internet at <http://pubs.acs.org>.

mechanism has been confirmed by the direct formation of imidazoline products that serve as a new protocol for the synthesis of diamino compounds.^{1b, 14}

Very recently, we established a new concept called the GAP chemistry (Group-Assistant-Purification chemistry). This chemistry can avoid the use of traditional purification method such as chromatography or recrystallization and the pure products can be obtained simply by washing the solid crude products with organic solvents.¹⁵⁻¹⁷ This new concept is attributed to the discovery of achiral/chiral *N*-phosphonyl and chiral *N*-phosphinyl imine reagents and their reactions. The characteristics of GAP chemistry requires the functional groups of starting materials should enable the resulting products to have adequate solubility, *i.e.*, the products must be dissolved some solvents (*e.g.*, THF, DCM, etc.) for further transformations, but should not be readily dissolved in others (*e.g.*, hexane, petroleum ether, their mixtures with EtOAc, etc.); the functional groups should enable their attached substrates to have efficient chemical reactivity toward various species; For asymmetric reactions, the functional groups should be able to show efficient asymmetric induction and control; the functional groups should have great flexibility for structural modifications so that both physical (*e.g.*, solubility) and chemical properties (tolerable to further transformations) of resulting products can be readily adjusted; the functional group-attached auxiliaries can be cleavable under various conditions and recycled for re-use. So far, controlling solubility of organic products *via* designing auxiliaries has been very challenging in chemical synthesis. The *N*-phosphonyl and *N*-phosphinyl functional group-based GAP chemistry has been proven to meet this purpose due to the special polarity of P=O bonds in which adequate amount of negative charge and positive charge localized on oxygen and phosphorous, respectively. We are pleased to find that this concept can be extended to other reactions such as aminohalogenation of olefins as shown in this article.

Results and Discussion

The present aminobromination reaction is based on the use of β -nitrostyrenes as the substrates due to their high flexibility for further transformations. The reaction was performed in 1,2-dichloroethane at room temperature without using inert gas protection (Scheme 1). The loading of 1.0 mol % $K_3PO_4 \cdot 3H_2O$ was able to efficiently catalyze the reaction to completion within one hour affording vicinal bromoamine products in good to excellent yields (up to 99 %). Since several polar functional groups, nitro, t-Boc and two bromo moieties, exist in the structures of resulting products, they can lower the solubility of product in organic solvents and enable GAP purification to be performed. Small amounts of impurities are either dissolved in liqueur or washed away simply by washing with some organic solvents.

At the beginning, we did the reaction according to the literature procedure.¹³ As anticipated that nitrostyrene as a difficult for aminobromination substrate did not result in any products when it was subjected to the reaction with *tert*-butyl-*N,N*-dibromocarbamate for up to 16 hours in dichloromethane at room temperature. Screening of a series of organic bases, inorganic bases and salts was carried out. Several organic bases include DMAP, DIPEA, triethylamine, triphenylphosphine. We found these common organic bases afforded no or trace amounts of products as monitored by TLC. Inorganic salts such as sodium fluoride, NaOAc, $KHCO_3$, $NaHCO_3$, K_2HPO_4 were also proven to be ineffective giving no product either. 10 mol% of Na_2CO_3 , K_2CO_3 , anhydrous Na_3PO_4 ¹³ and $Ca(OH)_2$ resulted in less than 49% of vicinal aminobromides within 1 hour as monitored by TLC determination. Two stronger bases, sodium and potassium hydroxide give good yields of 86% and 81%, respectively. Pleasantly, when anhydrous K_3PO_4 ¹⁸ and $K_3PO_4 \cdot 3H_2O$ were employed as the catalyst, more than 90% chemical yield was achieved under the same condition; similar results were obtained by decreasing the catalyst loading to 5.0 mol % and 2.5 mol%,

respectively. The above reaction was performed by reacting 1.0 mmol of nitrostyrene with 1.2 mmol of *tert*-butyl-*N,N*-dibromocarbamate in 2.5 mL of dichloromethane at room temperature. However, when the catalyst loading was decreased to 1.0 mol%, no product was observed. However, then the volume of solvent was changed from 2.5 to 1.0 mL, > 90% of chemical yield was obtained.

To explore further improvements, we next examined a series of solvents. Three solvents, ethyl acetate, acetonitrile and acetone gave very poor yields (5-37%); three other solvents, THF, DMF and ethanol did not show any products. However, 1,2-dichloroethane was found to be even more effective and resulted in a almost quantitative yield when the reaction was performed by using 1.2 equiv of *tert*-butyl-*N,N*-dibromocarbamate in the presence 1.0 mol% of $K_3PO_4 \cdot 3H_2O$ in 1.0 mL of solvent within one hour. The actual loading of K_3PO_4 is lower than 1.0 mol% if water is excluded from the above stoichiometric calculation.

Since $K_3PO_4 \cdot 3H_2O$ was used in a tiny amount (1.0 mol%), after it was added into reaction mixture containing *tert*-butyl-*N,N*-dibromocarbamate and nitrostyrene in 1,2-dichloroethane, it can be dissolved well. At the beginning, the color of reaction mixture was yellow; it gradually became light greenish as the reaction proceeds for 20-30 min.

The preparation of *tert*-butyl-*N,N*-dibromocarbamate was performed by following the literature procedure.¹³ In its synthesis, a modification was made by replacing potassium carbonate with KOH to give a quantitative yield. Essentially, there is no need for further purification of the crude *tert*-butyl-*N,N*-dibromocarbamate after work-up was performed; it was directly subjected to the aminobromination reaction with nitrostyrene. It should be pointed out that as compared with the known procedure by Zwierzak and coworkers in which crude product was contaminated with about 9% of *tert*-butyl *N*bromocarbamate, the present modification would provide an alternative and more efficient approach to *tert*-butyl-*N,N*-dibromocarbamate on large scale. In addition, this synthesis belongs to our GAP chemistry in which the products were purified without using chromatography and recrystallization.

After the catalytic system was established, we investigated the substrate scope of this aminobromination reaction by using a variety of nitrostyrene derivatives with substituents on their aromatic rings. As shown in Table 1, this reaction showed a great substrate scope in which twenty substrates were proven to be suitable for this system. There is no particular trend for these substrates. Most electron-withdrawing group (EWG)-attached substrates gave nearly quantitatively chemical yields (entries 2,4,7,13 & 15, Table 1); only 4- CF_3 and two dichloro substituted ones (entries 6, 11 & 12, Table 1) gave slightly lower yields of 91%, 92% and 88%, respectively. Interestingly, strong-electron-donating group (EDG)-attached substrates usually give lower chemical yields as compared with those with neutral and EWG-attached ones, but in this catalytic system, 2-MeO-Ph and 3,4-(MeO)₂-Ph cases also afforded the vicinal aminobromide products in quantitatively yields (entries 18 & 19, Table 1). Two other EDG cases, 4-MeO-Ph and 2-BnO-Ph, also showed excellent yields of 94% and 95%, respectively (entries 3 and 10, Table 1). There are no side-products generated from bromination on phenyl rings observed as at all. It is not clear why two neutral cases, 1-naphthyl and 4-butyl-Ph (entries 9 and 20, Table 1), resulted in lowest chemical yields of 82% and 83%, respectively. As mentioned that this reaction resulted in vicinal aminobromide products which can be purified *via* GAP process without the use of traditional column chromatography and recrystallization, *i.e.*, after work-up is done, the pure product can be readily obtained simply by washing the crude product with organic solvents (in this case, hexane). We also conducted the reaction of nitrostyrene on a scale of 3.0 g (20 mmol) and obtained product **1b** in almost quantitative yield (Scheme 2), which indicates that the present reaction is promising for large scale production. The vicinal aminobromide

products have been fully determined by NMR spectroscopic, HR-MS analysis, etc.; and the product of **3a** has been unambiguously analyzed by X-ray diffractive analysis with the ORTEP diagram presented in Figure 1 (see SI).

This reaction is suggested to proceed through free-radical chain stage and ionic catalytic cycle (Scheme 3). The first stage of radical mechanism has been proposed for the reaction of *t*-Boc-NBr₂ with styrene in literature.¹³ This catalytic cycle involves the common spontaneous initiation, propagation and radical termination to generate the monobromide intermediate (**A**). The deprotonation of **A** by PO₄³⁻ leads to the formation of intermediate **B** and P(OH)O₃²⁻. The intramolecular migration of bromine from amide nitrogen onto carboanion to give intermediate **C** in which the negative charge can be shifted onto oxygen of *t*-Boc group. Two contributing structures exist for this negative charge shifting. The protonation of **C** by P(OH)O₃²⁻ affords the final product **3a**, and concurrently gives the catalytic species, PO₄³⁻, back for continuing cycles of stage 2. This mechanistic hypothesis can account for the following observations: (1) several common bases, such as KOH, NaOH, Ca(OH)₂, K₂CO₃, etc, can also serve as the catalysts for this reaction, albeit they are not as efficient as K₃PO₄; (2) Only 1.2 equiv. of *t*-Boc-NBr₂ (no need for 2.0 equiv) is needed for the complete consumption of the starting material of nitrostyrene.

It should be noted that the present work represents the first GAP chemistry example of non-imine-based reactions in our labs. It can encourage synthetic chemists to find more GAP preparations so as to reduce the consumption of organic solvents and silica gels for column chromatography. Therefore, the use of nature's energy resources and manpower can be minimized due to the fast synthesis GAP chemistry. If GAP is employed for pharmaceutical and industrial productions on large scales, the environmental contaminations can also be reduced substantially.

In conclusion, we have demonstrated a concise and efficient aminobromination of β -nitrostyrene derivatives with *N,N*-dibromocarbamate as nitrogen/bromine sources in the presence of 1.0 mol% of K₃PO₄·3H₂O as catalyst. This reaction proceeded smoothly and environmentally friendly to give the β,β -dibromo Boc-protected amines in complete regioselectivity and good to excellent yields (82 ~ 99%). By using 1.2 equiv of nitrogen/bromine sources, the reaction can occur to completion within one hour at room temperature without using protection of inert gases. The GAP chemistry was found to be suitable for simple purifying the products without using traditional purification techniques of column chromatography and recrystallization. A mechanism involving spontaneously initiated free-radical chain and ionic catalytic cycles was proposed to account for experimental observations. Finally, this reaction showed promising result for practical scale up synthesis.

Experimental Section

General

Commercial chemicals and solvents were used without any further purification. Melting points were uncorrected. IR spectra were collected in KBr pellets. ¹H-NMR, ¹³C-NMR (TMS used as internal standard) spectra were collected in CDCl₃. High-resolution mass spectra for all the new compounds were collected on Q-TOF instrument (ESI).

Procedure for preparing BocNBr₂

To a stirred solution of BocNH₂ (5.86 g, 50 mmol) and NaOH (4.0 g, 0.1 mol) in water (50 mL) was added bromine Br₂ (19 g, 0.12 mol) dropwise at room temperature and stirred another 2 h. When the reaction completed, lot of orange solid was formed, which was filtered to get the crude product. The residue was dissolved in CH₂Cl₂, washed with brine,

dried with anhydrous Na₂SO₄, and concentrated to get the pure product (13.7g, quant). Mp = 93–94 °C (lit^{13a} 93–95 °C). ¹H-NMR (300 MHz, CDCl₃) δ 1.49 (s, 9H).

Typical procedure for the aminobromination reaction

Into a vial was added **1a** (149 mg, 1 mmol), BocNBr₂ (330 mg, 1.2 mol), K₃PO₄·3H₂O (2.7 mg, 1 mol %), (CH₂Cl)₂ (1.0 mL) and stirred 60 min at room temperature. The reaction completion was indicated by TLC and the color change which turned from yellow to light green. The reaction mixture was washed with brine, and the aqueous phase extracted with DCM. The organic layer was dried with anhydrous Na₂SO₄, concentrated to nearly dryness to give a solid/oil mixture. A tiny amount of oil was washed away by hexane; if more oil stuck on solid product appeared, 10 mL of hexane was added into the above mixture which was heated to give a solution mixture containing white solids. After cooling to room temperature, solution was filtrated off to afford pure product **3a**.

1-tert-Butoxyl-formamido-2,2-dibromo-1-phenyl-2-nitroethane (3a)

White solids (415 mg, 98 %). Mp = 122–124 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.45–7.35 (m, 5H), 5.97 (d, *J* = 10.20 Hz, 1H), 5.60 (d, *J* = 9.60 Hz, 1H), 1.44 (s, 9H) ppm. ¹³C NMR (75.45 MHz, CDCl₃) δ 153.8, 133.5, 129.4, 129.0 (2), 128.4 (2), 94.5, 81.1, 64.4, 28.0 (3) ppm. IR (KBr): ν = 3313, 2976, 1693, 1572, 1520, 1456, 1367, 1319, 1248, 1167, 837, 700 cm⁻¹. MS (ESMS/[M+Na]⁺): calcd for C₁₃H₁₆Br₂N₂O₄Na: 446.9349; found 446.9331.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(4-chlorophenyl)-2-nitroethane (3b)

White solids (449 mg, 98 %). Mp = 121–123 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.39 (d, *J* = 9.00 Hz, 2H), 7.35 (d, *J* = 8.70 Hz, 2H), 5.95 (d, *J* = 9.30 Hz, 1H), 5.55 (d, *J* = 9.90 Hz, 1H), 1.43 (s, 9H) ppm. ¹³C NMR (75.45 MHz, CDCl₃) δ 153.7, 135.6, 132.1, 130.4 (2), 128.6 (2), 93.8, 81.3, 63.9, 28.0 (3) ppm. MS (ESMS/[M+Na]⁺): calcd for C₁₃H₁₅Br₂ClN₂O₄Na: 480.8958; found 480.8944. IR (KBr): ν = 3278, 2978, 1687, 1577, 1514, 1369, 1323, 1250, 1163, 831 cm⁻¹.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(4-methoxyphenyl)-2-nitroethane (3c)

White solids (427 mg, 94 %). Mp = 129–131 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.34 (d, *J* = 9.00 Hz, 2H), 6.89 (d, *J* = 9.00 Hz, 2H), 5.91 (d, *J* = 10.20 Hz, 1H), 5.54 (d, *J* = 9.60 Hz, 1H), 3.81 (s, 3H), 1.44 (s, 9H) ppm. ¹³C NMR (75.45 MHz, CDCl₃) δ 160.2, 153.9, 130.2 (2), 125.4, 113.7 (2), 95.0, 81.0, 64.0, 55.1, 28.0 (3) ppm. MS (ESMS/[M+Na]⁺): calcd for C₁₄H₁₈Br₂N₂O₅Na: 476.9455; found 476.9453. IR (KBr): ν = 3313, 2976, 1689, 1576, 1508, 1302, 1244, 1169, 1034, 837 cm⁻¹.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(2-chlorophenyl)-2-nitroethane (3d)

White solids (454 mg, 99 %). Mp = 164–166 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.60 (br, 1H), 7.49–7.45 (m, 1H), 7.38–7.34 (m, 2H), 6.70 (d, *J* = 10.20 Hz, 1H), 5.56 (br, 1H), 1.42 (s, 9H) ppm. ¹³C NMR (75.45 MHz, CDCl₃) δ 153.4, 135.6, 133.1, 130.6, 130.1, 128.4, 127.1, 93.1, 81.6, 59.8, 28.1 (3) ppm. MS (ESMS/[M+Na]⁺): calcd for C₁₃H₁₅Br₂ClN₂O₄Na: 480.8958; found 480.8941. IR (KBr): ν = 3357, 2987, 1709, 1577, 1473, 1365, 1155, 1045, 843 cm⁻¹.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(p-tolyl)-2-nitroethane (3e)

White solids (416 mg, 95 %). Mp = 108–110 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.31 (d, *J* = 8.10 Hz, 2H), 7.18 (d, *J* = 8.10 Hz, 2H), 5.93 (d, *J* = 9.30 Hz, 1H), 5.56 (d, *J* = 9.00 Hz, 1H), 2.35 (s, 3H), 1.44 (s, 9H) ppm. ¹³C NMR (75.45 MHz, CDCl₃) δ 153.8, 139.4, 130.5, 129.0 (2), 128.8 (2), 94.8, 81.0, 64.3, 28.0, 21.0 (3) ppm. MS (ESMS/[M+Na]⁺): calcd for

$C_{14}H_{18}Br_2N_2O_4Na$: 460.9506; found 460.9479. IR (KBr): $\nu = 3292, 2978, 1687, 1577, 1509, 1323, 1250, 1161, 1022, 845\text{cm}^{-1}$.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(4-(trifluoromethyl)phenyl)-2-nitroethane (3f)

White solids (448 mg, 91 %). Mp = 113–115 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.65 (d, $J = 8.70$ Hz, 2H), 7.59 (d, $J = 8.10$ Hz, 2H), 6.04 (d, $J = 10.20$ Hz, 1H), 5.60 (d, $J = 10.50$ Hz, 1H), 1.43 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 153.8, 137.7, 131.6 (q, $J = 32.82$ Hz), 129.6 (2), 125.4, 125.3, 121.8, 93.2, 81.6, 64.1, 28.0 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $C_{14}H_{15}Br_2F_3N_2O_4Na$: 514.9223; found 514.9231. IR (KBr): $\nu = 3319, 2981, 1687, 1579, 1510, 1327, 1250, 1132, 1070, 839\text{cm}^{-1}$.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(4-cyanophenyl)-2-nitroethane (3g)

White solids (435 mg, 97 %). Mp = 146–148 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.69 (d, $J = 8.40$ Hz, 2H), 7.59 (d, $J = 8.40$ Hz, 2H), 6.03 (d, $J = 10.20$ Hz, 1H), 5.58 (d, $J = 9.60$ Hz, 1H), 1.43 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 153.6, 138.7, 131.9 (2), 129.9 (2), 117.8, 113.2, 92.6, 81.4, 63.9, 27.8 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $C_{14}H_{15}Br_2N_3O_4Na$: 471.9302; found 471.9315. IR (KBr): $\nu = 3315, 2979, 2239, 1730, 1576, 1502, 1327, 1244, 1159, 833\text{cm}^{-1}$.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(naphthalen-2-yl)-2-nitroethane (3h)

White solids (431 mg, 91 %). Mp = 139–141 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.91–7.84 (m, 4H), 7.55–7.52 (m, 3H), 6.16 (d, $J = 9.60$ Hz, 1H), 5.72 (d, $J = 10.20$ Hz, 1H), 1.44 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 153.9, 133.3, 132.5, 130.8, 129.3, 128.2, 128.1, 127.5, 127.0, 126.6, 125.5, 94.4, 81.2, 64.6, 28.0 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $C_{17}H_{18}Br_2N_2O_4Na$: 496.9506; found 496.9549. IR (KBr): $\nu = 3261, 3149, 2983, 1709, 1574, 1506, 1363, 1254, 1159, 1018\text{cm}^{-1}$.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(naphthalen-1-yl)-2-nitroethane (3i)

White solids (389 mg, 82 %). Mp = 201–203 °C. ^1H NMR (300 MHz, CDCl_3) δ 8.42 (d, $J = 7.50$ Hz, 1H), 7.91 (t, $J = 8.40$ Hz, 2H), 7.78 (d, $J = 6.60$ Hz, 1H), 7.65 (t, $J = 7.20$ Hz, 1H), 7.56 (d, $J = 8.10$ Hz, 1H), 7.51 (d, $J = 8.10$ Hz, 1H), 7.00 (d, $J = 9.00$ Hz, 1H), 5.71 (d, $J = 8.40$ Hz, 1H), 1.40 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, $\text{DMSO}-d_6$) δ 154.8, 133.1, 131.5, 131.4, 129.8, 128.9, 127.3, 126.9, 125.9, 125.0, 123.0, 94.4, 79.7, 57.8, 27.9 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $C_{17}H_{18}Br_2N_2O_4Na$: 496.9506; found 496.9505. IR (KBr): $\nu = 3240, 3134, 2977, 1693, 1577, 1361, 1257, 1159, 1049, 775\text{cm}^{-1}$.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(2-(benzyloxy)phenyl)-2-nitroethane (13j)

White solids (504 mg, 95 %). Mp = 120–122 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.50–7.32 (m, 7H), 6.99 (d, $J = 8.10$ Hz, 2H), 6.39 (d, $J = 9.60$ Hz, 1H), 6.15 (d, $J = 7.20$ Hz, 1H), 5.15 (s, 2H), 1.43 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, $\text{DMSO}-d_6$) δ 155.6, 154.4, 136.8, 130.4, 129.8, 128.3 (2), 127.7 (2), 127.2, 123.8, 120.4, 112.4, 95.0, 79.4, 69.6, 56.7, 28.0 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $C_{20}H_{22}Br_2N_2O_5Na$: 552.9769; found 552.9737. IR (KBr): $\nu = 3246, 3141, 2978, 1699, 1574, 1493, 1367, 1252, 1161, 1020, 748\text{cm}^{-1}$.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(2,6-dichlorophenyl)-2-nitroethane (3k)

White solids (454 mg, 92 %). Mp = 104–106 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.45 (d, $J = 7.80$ Hz, 1H), 7.35–7.24 (m, 2H), 7.12 (d, $J = 10.50$ Hz, 1H), 6.43 (d, $J = 9.30$ Hz, 1H), 1.45 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 153.8, 138.6, 134.4, 130.7, 130.6, 130.0, 129.1, 91.6, 81.4, 62.3, 28.0 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $C_{13}H_{14}Br_2Cl_2N_2O_4Na$: 514.8567; found 514.8554. IR (KBr): $\nu = 3323, 2976, 1703, 1577, 1439, 1348, 1254, 1155, 1014, 769\text{cm}^{-1}$.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(3,4-dichlorophenyl)-2-nitroethane (3l)

White solids (434 mg, 88 %). Mp = 156–158 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.57 (s, 1H), 7.46 (d, J = 8.40 Hz, 1H), 7.29 (d, J = 8.40 Hz, 1H), 5.94 (d, J = 9.60 Hz, 1H), 5.55 (br, 1H), 1.44 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 153.7, 134.0, 133.9, 132.7, 131.0, 130.4, 128.5, 93.0, 81.7, 63.5, 28.1 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $\text{C}_{13}\text{H}_{14}\text{Br}_2\text{Cl}_2\text{N}_2\text{O}_4\text{Na}$: 514.8567; found 514.8557. IR (KBr): ν = 3353, 3151, 2976, 1705, 1572, 1473, 1369, 1254, 1159, 1022, 777 cm^{-1} .

1-tert-Butoxyl-formamido-2,2-dibromo-1-(4-fluorophenyl)-2-nitroethane (3m)

White solids (438 mg, 99 %). Mp = 118–120 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.42 (dd, J_1 = 8.70 Hz, J_2 = 5.10 Hz, 2H), 7.07 (t, J = 8.70 Hz, 2H), 5.96 (d, J = 9.00 Hz, 1H), 5.55 (br, 1H), 1.44 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 163.1 (d, J = 249 Hz), 153.8, 130.9 (d, J = 7.50 Hz), 129.5, 115.4 (d, J = 21.50 Hz), 94.2, 81.3, 63.8, 28.0 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $\text{C}_{13}\text{H}_{15}\text{Br}_2\text{FN}_2\text{O}_4\text{Na}$: 464.9255; found 464.9247. IR (KBr): ν = 3398, 2985, 1697, 1577, 1506, 1369, 1321, 1232, 1167, 850 cm^{-1} .

1-tert-Butoxyl-formamido-2,2-dibromo-1-(4-bromophenyl)-2-nitroethane (3n)

White solids (483 mg, 96 %). Mp = 129–131 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.52 (d, J = 8.40 Hz, 2H), 7.32 (d, J = 8.40 Hz, 2H), 5.93 (d, J = 10.20 Hz, 1H), 5.54 (d, J = 10.20 Hz, 1H), 1.43 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 153.7, 132.7, 131.5 (2), 130.6 (2), 123.8, 93.7, 81.4, 63.9, 28.0 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $\text{C}_{13}\text{H}_{15}\text{Br}_3\text{N}_2\text{O}_4\text{Na}$: 524.8454; found 524.8455. IR (KBr): ν = 3280, 2978, 1687, 1577, 1512, 1369, 1321, 1250, 1163, 837 cm^{-1} .

1-tert-Butoxyl-formamido-2,2-dibromo-1-(3-fluorophenyl)-2-nitroethane (3o)

White solids (433 mg, 98 %). Mp = 135–137 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.36 (dd, J_1 = 7.80 Hz, J_2 = 13.80 Hz, 1H), 7.22 (d, J = 8.40 Hz, 1H), 7.13 (d, J = 9.60 Hz, 1H), 7.11 (t, J = 8.10 Hz, 1H), 5.97 (d, J = 9.00 Hz, 1H), 5.56 (d, J = 9.90 Hz, 1H), 1.44 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 162.2 (d, J = 247 Hz), 153.8, 136.0, 129.9 (d, J = 7.50 Hz), 125.0 (d, J = 3.20 Hz), 116.4 (d, J = 28.20 Hz), 116.1 (d, J = 30.20 Hz), 93.6, 81.4, 63.9, 28.0 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $\text{C}_{13}\text{H}_{15}\text{Br}_2\text{FN}_2\text{O}_4\text{Na}$: 464.9255; found 464.9253. IR (KBr): ν = 3253, 3141, 2985, 1695, 1576, 1452, 1379, 1232, 1161, 1018, 775 cm^{-1} .

1-tert-Butoxyl-formamido-2,2-dibromo-1-(3-bromophenyl)-2-nitroethane (3p)

White solids (433 mg, 86 %). Mp = 155–157 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.61 (s, 1H), 7.54 (d, J = 8.10 Hz, 1H), 7.37 (d, J = 7.80 Hz, 1H), 7.25 (t, J = 7.80 Hz, 1H), 5.94 (d, J = 10.20 Hz, 1H), 5.56 (d, J = 10.20 Hz, 1H), 1.44 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, $\text{DMSO}-d_6$) δ 154.5, 136.8, 132.1(2), 130.0, 129.0, 121.4, 93.8, 79.7, 64.0, 27.9 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $\text{C}_{13}\text{H}_{15}\text{Br}_3\text{N}_2\text{O}_4\text{Na}$: 524.8454; found 524.8464. IR (KBr): ν = 3244, 3143, 2985, 1698, 1576, 1477, 1369, 1255, 1155, 1018, 847 cm^{-1} .

1-tert-Butoxyl-formamido-2,2-dibromo-1-(3-bromo-4-methoxyphenyl)-2-nitroethane (3q)

White solids (469 mg, 88 %). Mp = 157–159 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.63 (d, J = 2.10 Hz, 1H), 7.33 (dd, J_1 = 8.80 Hz, J_2 = 2.10 Hz, 1H), 6.87 (d, J = 8.80 Hz, 1H), 5.88 (d, J = 9.90 Hz, 1H), 5.50 (d, J = 9.90 Hz, 1H), 3.90 (s, 3H), 1.44 (s, 9H) ppm. ^{13}C NMR (75.45 MHz, CDCl_3) δ 155.9, 154.5, 133.7, 130.7, 127.7, 111.7, 110.3, 94.5, 79.6, 63.6, 56.2, 27.9 (3) ppm. MS (ESMS/[M+Na] $^+$): calcd for $\text{C}_{14}\text{H}_{17}\text{Br}_3\text{N}_2\text{O}_5\text{Na}$: 554.8560; found 554.8564. IR (KBr): ν = 3269, 3153, 2983, 1695, 1576, 1506, 1369, 1271, 1161, 1022, 845 cm^{-1} .

1-tert-Butoxyl-formamido-2,2-dibromo-1-(2-methoxyphenyl)-2-nitroethane (3r)

White solids (445 mg, 98 %). Mp = 153–155 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.37 (t, *J* = 6.90 Hz, 2H), 7.00–6.91 (m, 2H), 6.29 (d, *J* = 10.20 Hz, 1H), 6.05 (s, 1H), 3.85 (s, 3H), 1.44 (s, 9H) ppm. ¹³C NMR (75.45 MHz, CDCl₃) δ 157.4, 154.1, 133.3, 130.7, 130.3, 120.5, 111.3, 80.8, 94.6, 61.2, 55.3, 28.1 (3) ppm. MS (ESMS/[M+Na]⁺): calcd for C₁₄H₁₈Br₂N₂O₅Na: 476.9455; found 476.9447. IR (KBr): ν = 3251, 3138, 2976, 1693, 1576, 1493, 1361, 1248, 1159, 1022, 754 cm⁻¹.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(3,4-dimethoxyphenyl)-2-nitroethane (3s)

White solids (474 mg, 98 %). Mp = 139–141 °C. ¹H NMR (300 MHz, CDCl₃) δ 6.98 (dd, *J*₁ = 8.10 Hz, *J*₂ = 2.10 Hz, 1H), 6.89 (d, *J* = 2.10 Hz, 1H), 6.84 (d, *J* = 8.10 Hz, 1H), 5.89 (d, *J* = 9.90 Hz, 1H), 5.54 (d, *J* = 10.20 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 1.44 (s, 9H) ppm. ¹³C NMR (75.45 MHz, DMSO-*d*₆) δ 154.7, 149.4, 148.2, 126.1, 122.6, 113.2, 110.8, 95.4, 79.5, 64.5, 55.7, 55.4, 28.0 (3) ppm. MS (ESMS/[M+Na]⁺): calcd for C₁₅H₂₀Br₂N₂O₆Na: 506.9561; found 506.9587. IR (KBr): ν = 3359, 2972, 1693, 1574, 1502, 1352, 1315, 1246, 1155, 1024, 845 cm⁻¹.

1-tert-Butoxyl-formamido-2,2-dibromo-1-(4-(tert-butyl)phenyl)-2-nitroethane (3t)

White solids (398 mg, 83 %). Mp = 123–125 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.39–7.32 (m, 4H), 5.95 (d, *J* = 8.70 Hz, 1H), 5.58 (d, *J* = 8.70 Hz, 1H), 1.44 (s, 9H), 1.31 (s, 9H) ppm. ¹³C NMR (75.45 MHz, CDCl₃) δ 153.9, 152.5, 130.5, 128.7 (2), 125.4 (2), 94.7, 81.1, 64.2, 34.6, 31.1 (3), 28.1 (3) ppm. MS (ESMS/[M+Na]⁺): calcd for C₁₇H₂₄Br₂N₂O₆Na: 502.9976; found 502.9997. IR (KBr): ν = 3253, 3145, 2962, 1705, 1577, 1477, 1365, 1257, 1159, 1016, 837, 775 cm⁻¹.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Scheme 2.

Scheme 3.

Table 1K₃PO₄·3H₂O-catalyzed aminobromination of nitrostyrenes^[a]

Entry	Ar	Product	Yield (%) ^[b]
1	Ph	3a	98
2	4-Cl-C ₆ H ₄	3b	98
3	4-MeO-C ₆ H ₄	3c	94
4	2-Cl-C ₆ H ₄	3d	99
5	4-Me-C ₆ H ₄	3e	95
6	4-CF ₃ -C ₆ H ₄	3f	91
7	4-CN-C ₆ H ₄	3g	97
8	2-naphthyl	3h	91
9	1-naphthyl	3i	82
10	2-BnO-C ₆ H ₄	3j	95
11	2, 6-Cl ₂ -C ₆ H ₃	3k	92
12	3, 4-Cl ₂ -C ₆ H ₃	3l	88
13	4-F-C ₆ H ₄	3m	99
14	4-Br-C ₆ H ₄	3n	96
15	3-F-C ₆ H ₄	3o	98
16	3-Br-C ₆ H ₄	3p	86
17	3-Br-4-MeO-C ₆ H ₃	3q	88
18	2-MeO-C ₆ H ₄	3r	98
19	3, 4-(CH ₃ O) ₂ -C ₆ H ₃	3s	98
20	4-Butyl-C ₆ H ₄	3t	83

^[a] Conditions: **1a** (1.0 mmol), BocNBr₂ (1.2 mmol), with K₃PO₄·3H₂O (0.01 mmol) in (CH₂Cl)₂ (1 ml) at room temperature for 60 min.

^[b] Isolated yields.