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Ionic addition of *t*-butyl *N*,*N*-dibromocarbamate (BBC) to alkenes and cycloalkenes

Anna Śliwińska and Andrzej Zwierzak*

Institute of Organic Chemistry, Technical University (Politechnika), Żeromskiego 116, 90-924 Łódź, Poland

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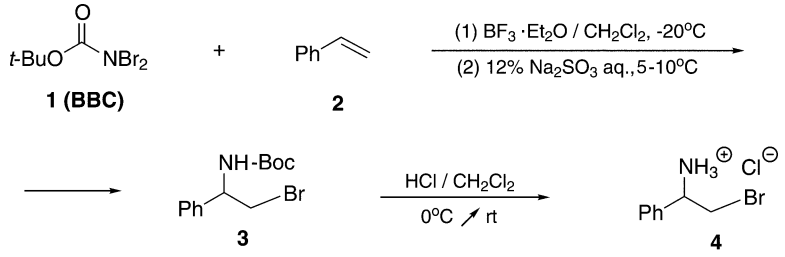
Abstract—The addition of *t*-butyl *N*,*N*-dibromocarbamate (BBC) to alkenes and cycloalkenes in the presence of $BF_3{\cdot}Et_2O$ proceeds smoothly at −20°C in CH_2Cl_2 affording upon reduction with aqueous Na_2SO_3 the corresponding β-bromo-*N*-Boc-amines. Immediate deprotection of these adducts with gaseous HCl yields β-bromoamine hydrochlorides in moderate yields. The regioselectivity typical for Markovnikov addition was observed for styrene. Stereospecific *anti*-addition of BBC to cyclohexene and (*E*)-hex-3-ene, as proven by ^1H NMR evidence, is compatible with an ionic addition pathway and can be rationalized by assuming the intermediate complex formation between BBC and BF_3.

While free-radical addition of various *N*,*N*-dihaloamides to carbon–carbon double bonds has been extensively studied,[1] the available information regarding ionic reactions of such systems with unsaturated compounds still remains scarce.[2]

We have recently proved the efficiency of *t*-butyl *N*,*N*-dibromocarbamate (BBC) **1** for free-radical regioselective aminobromination of terminal alkenes.[3] Homolytic addition of BBC **1** to non-terminal alkenes and cycloalkenes occurs, however, sluggishly leading inevitably to complex and often intractable mixtures of compounds. This observation prompted us to investigate the possibility of heterolytic addition of BBC to double bonds with the hope of extending the preparative applicability of this reagent.

It was found that clean heterolytic addition of BBC **1** to styrene **2** could be accomplished in the presence of a stoichiometric amount of $BF_3{\cdot}Et_2O$ using the preformed BBC-BF_3 complex (vide infra) as a source of electropositive bromine. The reaction was carried out in CH_2Cl_2 by dropwise addition of the hydrocarbon to an equimolar mixture of BBC **1** and $BF_3{\cdot}Et_2O$ at −20°C. The reaction was rapid and was virtually complete within 1 h. Upon reduction with 12% aqueous Na_2SO_3 at 5–10°C the initially formed *N*-bromo adduct was reduced into *N*-Boc-2-bromo-1-phenylethylamine **3** (Scheme 1). The Markovnikov orientation of this compound was confirmed by comparing its mp and spectral data with those of the regioisomer prepared by free-radical addition of BBC **1** to styrene.[4] The addition procedure elaborated for styrene could be then extended to other unsaturated hydrocarbons.[5] Cycloalkenes **5a**–**c** added BBC **1** easily and cleanly affording the corresponding *N*-Boc-β-bromocycloalkylamines **6a**–**c** in moderate yields (Scheme 2).[6] In contrast to free-radical additions the reactions of BBC-BF_3



Scheme 1.

Keywords: alkenes; amines; cycloalkenes; ionic addition.
* Corresponding author. Tel.: +48-42-6313146; fax: +48-42-6365540.

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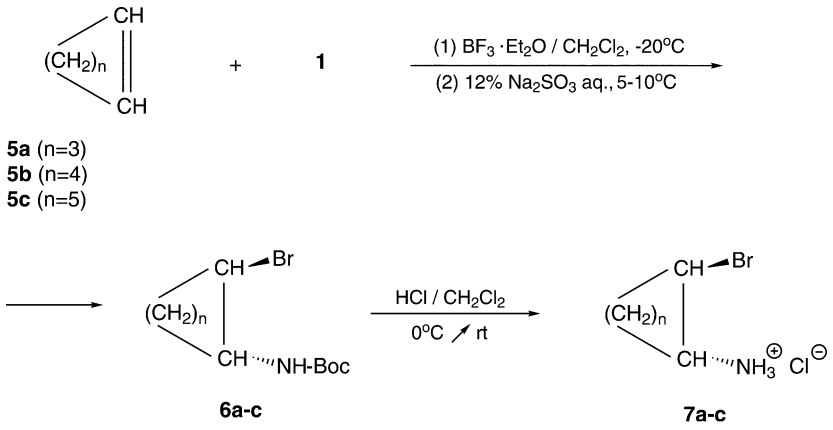
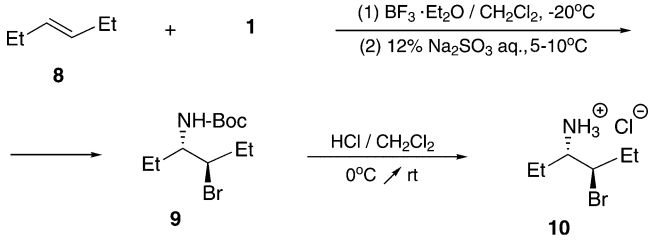


Scheme 2.



Scheme 3.

with terminal alkenes, such as pent-1-ene and hex-1-ene were not regioselective affording ca. 1:1 mixtures of both regioisomers as determined by ^{1}H NMR. All *N*-Boc-adducts **3**, **6a**–**c**, and **9** could be immediately deprotected without purification to the corresponding β-bromoamine hydrochlorides **4**, **7a**–**c**, and **10** by means of gaseous HCl in CH_2Cl_2 at 0°C (1 h) and then at room temperature (24 h).[3]

(*E*)-Hex-3-ene **8** was used as a model compound for studying the stereochemistry of the BBC-BF_3 addition. Pure *erythro* diastereoisomer **9** was obtained by stereospecific *anti*-addition under heterolytic conditions (Scheme 3).[7] The stereochemical assignment could be arrived at by ^{1}H NMR after deprotection of **9** into the β-bromoamine hydrochloride **10**. The synclinal arrangement of vicinal methine protons in the preferred conformation of the *erythro*-isomer **10**[8] is fully compatible with the low value ($J = 2.9$ Hz) of the respective coupling constant according to Karplus equation. The anti-addition of BBC-BF_3 to cyclohexene **5b** could be corroborated by detailed analysis of the ^{1}H NMR spectra of **6b** and **7b**.[9] The configurations and conformations of these compounds follow from the splitting patterns and the large vicinal methine proton coupling constants ($J = 10.1$ and 11.1 Hz, respectively) which are typical for the axial arrangement.

The ionic mechanism of BBC-BF_3 addition can be rationalized by assuming formation of the BBC-BF_3 intermediate complex **11a**–**c** (Scheme 4) leading to subsequent ionization of the BBC molecule. It was found that addition of an equimolar amount of $BF_3{\cdot}Et_2O$ to the solution of BBC in CH_2Cl_2 changes the IR spectrum of the reagent. The C=O absorption band at 1724 cm^{-1} is shifted to 1655 and 1630 cm^{-1} suggesting a considerably diminished bond order of the carbonyl group consistent with the two contributing structures **11b** and **11c**.

In conclusion we have demonstrated the possibilities of heterolytic BBC **1** addition to alkenes and cycloalkenes as a convenient route to some *N*-Boc-β-bromoamines and β-bromoamine hydrochlorides (Table 1).

Acknowledgements

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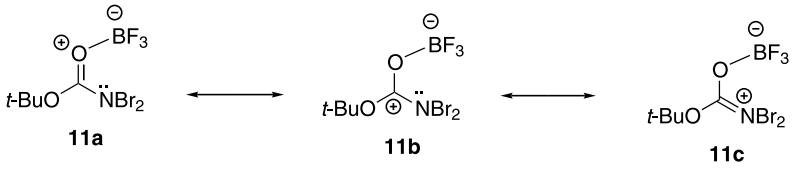

Scheme 4.

Table 1. Preparation of β-bromo-*N*-Boc-amines (**3**, **6a**–**c**, **9**) and β-bromoamine hydrochlorides (**4**, **7a**–**c**, **10**)[a]

Compound no	Yield (%)	Mp (°C)	Lit.[10] mp (°C)
3	70	106–108[c]	[e]
6a	63	73–74[c]	[e]
6b	55	98–99[c]	[e]
6c	48	79–81[c]	[e]
9	63	–	[e]
4	65[b]	178–180[d]	176–178
7a	65[b]	192–194[d]	182–184
7b	60[b]	198–200[d]	187–189
7c	50[b]	164–166[d]	152–154
10	57[b]	178–180[d]	157–159

[a] All new compounds were fully characterized by MS, IR, and ^{1}H NMR spectroscopy.
[b] Overall yield after immediate deprotection of the crude adduct.
[c] Crystallized from hexane.
[d] Crystallized from ethanol–ether.
[e] Not reported previously.

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4. Selected data for the compound **3**: IR (KBr), ν_{max} 3400, 2990, 1680, 1512, 1392, 1368, 1280, 1248, 1168, 1048, 1024, 700, 660, 640 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): 7.28–7.41 (5H, m, Ph), 5.13 (1H, bs, N*H*), 5.01 (1H, bs, C*H*-NH), 3.63–3.75 (2H, m, CH_2Br), 1.44 (9H, s, *Me*$_3$C). MS/CI: 302 (49, M+3), 300 (51, M+1), 246 (98), 244 (100). [Found: C, 52.0; H, 6.1; N, 4.7. $C_{13}H_{18}BrNO_2$ requires C, 52.01; H, 6.04; N, 4.67%].
5. General procedure for the preparation of compounds **3**, **6**, and **9**: To a solution of crude *t*-butyl *N*,*N*-dibromocarbamate[3] (BBC, **1**, 2.75 g, 10 mmol) in CH_2Cl_2 (28 mL), $BF_3{\cdot}Et_2O$ (1.40 g, 10 mmol) dissolved in CH_2Cl_2 (6 mL) was added with stirring and cooling at −20°C. After 15 min the solution of hydrocarbon (10 mmol) in CH_2Cl_2 (6 mL) was added over 15 min at −20°C and stirring was continued at this temperature for 1 h. The resulting pale yellow solution was warmed to 5–10°C and a 12% aqueous solution of Na_2SO_3 (10 mL) was added slowly at this temperature. Dichloromethane (20 mL) was then added, the organic layer was separated and washed with water (3×10 mL). After drying ($MgSO_4$) the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using $CHCl_3$ as eluent to give the pure isolated products **3**, **6**, and **9**. Compounds **3** and **6** were recrystallized from hexane.
6. Selected data for compounds **6a**–**c**. Compounds **6a**: ^{1}H NMR (250 MHz, $CDCl_3$): 4.58 (1H, bs, CH-N*H*), 4.11–4.17 (2H, m, C*H*NH and C*H*Br); 2.17–2.36 (2H, m, CH_2), 1.67–2.11 (4H, m, CH_2), 1.46 (9H, s, *Me*$_3$C). Compound **6b**: ^{1}H NMR (250 MHz, $CDCl_3$): 4.63 (1H, bs, N*H*), 3.87 (1H, dt, J=10.1, 4.25 Hz, C*H*Br), 3.61 (1H, ddt, J=10.1, 8.5, 3.75 Hz, C*H*-NH), 2.31–2.41 (2H, m, CH_2), 2.17–2.24 (2H, m, CH_2), 1.81–1.97 (2H, m, CH_2), 1.65–1.76 (2H, m, CH_2), 1.46 (9H, s, *Me*$_3$C). MS/CI: 280 (60, M+3), 278 (63, M+1), 224 (95), 222 (100). Compound **6c**: ^{1}H NMR (250 MHz, $CDCl_3$): 4.76 (bs, 1H, N*H*), 4.12 (1H, ddd, J=8.5, 8.25, 4.0 Hz, C*H*Br), 3.78–3.88 (1H, m, C*H*NH), 1.99–2.42 (3H, m, CH_2), 1.45–1.82 (7H, m, CH_2), 1.45 (9H, s, *Me*$_3$C).
7. Selected data for compound **9**: ^{1}H NMR (250 MHz, $CDCl_3$): 4.68 (1H, d, J=9.0 Hz, N*H*), 4.14 (1H, dt, J=7.1, 3.0 Hz, C*H*Br), 3.50–3.60 (1H, m, C*H*NH), 1.85 (2H, qt, J=7.1 Hz, CH_2-CHBr), 1.60–1.77 (2H, m, CH_2-CHNH), 1.45 (9H, s, *Me*$_3$C), 1.07 (3H, t, J=7.1 Hz, CH_3-CH$_2$-CHBr), 0.97 (3H, t, J=7.3 Hz, CH_3-CH$_2$-CHNH). MS/CI: 226 (1.1, M+4-C_4H_9), 224 (1.6, M+2-C_4H_9), 182 (92, M+4-Boc), 180 (100, M+2-Boc).
8. Selected data for compound **10**: IR (KBr) ν_{max} 3460, 2980, 2950, 1592, 1520, 1465, 1390, 1312, 1200, 1150, 792, 630, 620 cm^{-1}. ^{1}H NMR (250 MHz, D_2O): 4.32 (1H, ddd, J=9.6, 4.5, 2.9 Hz, C*H*-Br), 3.48 (1H, ddd, J=9.25, 4.5, 2.9 Hz, C*H*-NH$_3$), 1.65–1.98 (4H, m, 2×CH_2), 1.06 (3H, t, J=6.9 Hz, CH_3), 1.03 (3H, t, J=7.1 Hz, CH_3).
9. Selected data for compound **7b**: ^{1}H NMR (250 MHz, D_2O), 4.10 (1H, dt, J=11.1, 4.4 Hz, C*H*-Br), 3.41 (1H, dt, J=11.1, 4.2 Hz, C*H*-NH$_3$), 2.39–2.46 (1H, m, CH_2), 2.10–2.21 (1H, m, CH_2), 1.66–1.97 (3H, m, CH_2), 1.26–1.59 (3H, m, CH_2).
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