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Regioselective aminobromination of terminal alkenes☆

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Abstract—The addition of *t*-butyl *N*,*N*-dibromocarbamate (BBC) to a variety of terminal alkenes has been studied. The reaction was spontaneously initiated and proceeded smoothly in refluxing dichloromethane. The *N*-bromo adducts, formed upon addition, could be reduced in situ with aqueous sodium sulfite to give the corresponding 2-bromo-*N*-Boc-amines. Immediate deprotection of these compounds with gaseous HCl or *p*-toluenesulfonic acid afforded 2-bromoamine hydrochlorides or tosylates in pure state and good overall yields. The observed regioselectivity for anti-Markovnikov addition, as proven by NMR and MS, is fully consistent with the radical-chain mechanism proposed for the reaction.

1. Introduction

A plethora of synthetic procedures leading to aziridines has been described.[1] However, there is still a need for a new, simple and economic synthesis of this class of compounds due to their interesting chemistry dominated by ring-opening reactions. Among the methods used for the preparation of aziridines, spontaneous cyclization of 2-bromoamines is practically meaningless because these starting materials are almost inaccessible.

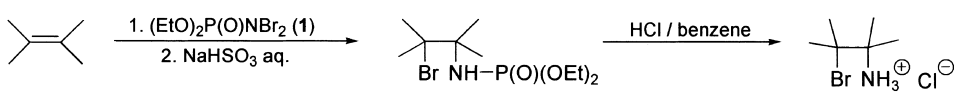
Some years ago we reported[2,3] a simple two-step procedure leading to 2-bromoamine hydrochlorides involving the free-radical or ionic addition of diethyl *N*,*N*-dibromophosphoramidate (DBPA) **1** to alkenes and cycloalkenes followed by degradation of the adducts with gaseous hydrogen chloride (Scheme 1).

This approach to 2-bromoamines remained practically unnoticed by the chemical community possibly due to the necessary use of an organophosphorus reagent of unknown toxicity. Moreover, the addition of DBPA **1** to less reactive alkenes afforded rather low yields of products and often inevitably led to complex and intractable mixtures of compounds containing mainly allylic bromination and/or bromine addition products. All these facts prompted us to investigate a new, phosphorus free reagent, *t*-butyl *N*,*N*-dibromocarbamate (BBC) **3** as a better substitute of DBPA for aminobromination of terminal alkenes.

2. Results and discussion

2.1. Preparation of *t*-butyl *N*,*N*-dibromocarbamate (BBC) 3

The title compound could be readily obtained in high yield by bromination of crude *t*-butyl carbamate **2**[4] contaminated with ca. 10% of an unidentified impurity. The reaction was carried out at room temperature by adding bromine to the aqueous solution of *t*-butyl carbamate **2** containing 10% excess of potassium carbonate. *t*-Butyl *N*,*N*-dibromocarbamate **3**, isolated by extraction with dichloromethane in ca. 90% yield, was an orange solid contaminated with ca. 9% of *t*-butyl *N*-bromocarbamate **3a** as determined by ^{1}H NMR spectroscopy (Scheme 2). Analytically pure samples of **3** (mp 93–95°C) could be prepared by bromination of pure **2** (mp 107–108°C) and washing the product with cold pentane.



Scheme 1.

☆ Preliminary communication: Klepacz, A.; Zwierzak, A. *Tetrahedron Lett.* **2001**, *42*, 4539–4540.

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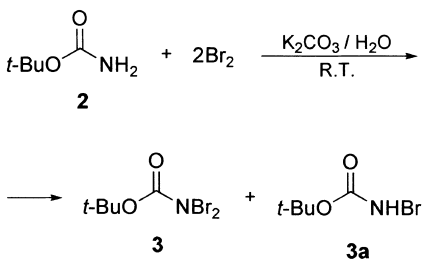
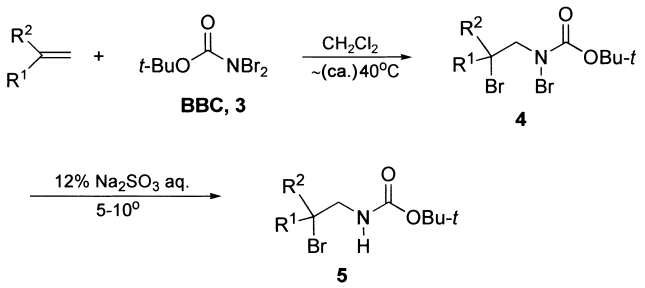
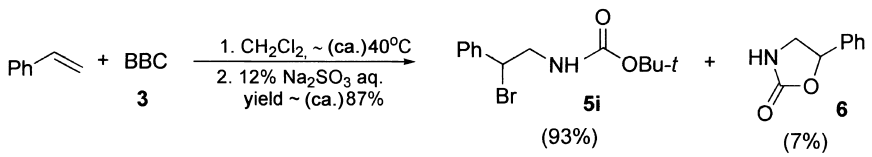


Scheme 2.

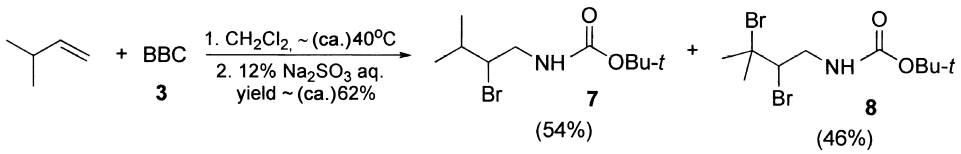


4,5	R^1	R^2	Yield (%)	4,5	R^1	R^2	Yield (%)
a	Ph	Me	—	e	Bu	H	62
b	Me	Me	77	f	C_5H_{11}	H	58
c	Me	Et	87	g	C_6H_{13}	H	65
d	Pr	H	61	h	*neo*-C_5H_{11}	Me	—

Scheme 3.



Scheme 4.



Scheme 5.

t-Butyl *N*,*N*-dibromocarbamate **3** was perfectly stable at +5°C and could be stored when refrigerated for indefinite periods of time without any signs of decomposition. The removal of *t*-butyl *N*-bromocarbamate **3a** from crude **3** before use for addition to alkenes was neither necessary nor desirable because **3a** upon reduction with aqueous sodium sulfite was transformed into *t*-butyl carbamate **2**, easily removable by washing with water.

2.2. Addition of *t*-butyl *N*,*N*-dibromocarbamate (BBC) 3 to terminal alkenes

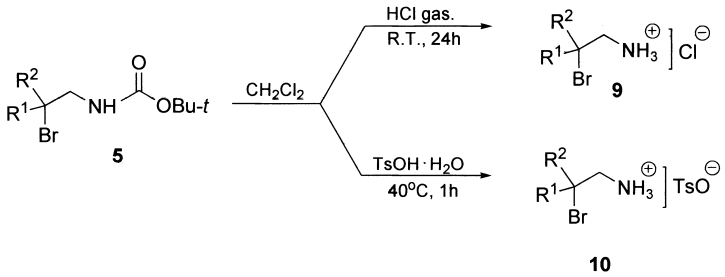
The addition of BBC **3** to several straight and branched-chain terminal alkenes, namely styrene, 2-phenylpropene, isobutylene, 2-methylbut-1-ene, 3-methylbut-1-ene, pent-1-ene, hex-1-ene, hept-1-ene, oct-1-ene, and 2,4,4-trimethylpent-1-ene has been studied.

All reactions were carried out in refluxing dichloromethane by adding dropwise the solution of BBC **3** to an equimolar amount of the alkene. After a short induction period the reaction was practically complete after 20 min in the case of phenylethylenes, isobutylene and 2-methylbut-1-ene. Less reactive alkenes added BBC **3** relatively slowly in refluxing dichloromethane but all reactions were complete after 2 h, which could be tested visually by reduction in the dark-red BBC color. All additions were performed under dispersed light and did not need any UV irradiation. In all cases except styrene and 3-methylbut-1-ene the reactions proceeded according to the same general course outlined in Scheme 3.

The formation of 1:1 adducts was always observed. The reactions proceeded regioselectively in an anti-Markovnikov fashion (see proof of structure below) affording *N*-Boc-*N*-bromo-2-bromoalkylamines **4**. Upon reduction with 12% aqueous sodium sulfite at 5–10°C the initially formed *N*-bromoadducts **4** were quantitatively transformed in situ into *N*-Boc-2-bromoalkylamines **5a**–**i**. Some crude *N*-Boc-2-bromoalkylamines **5b**–**g**,**i** formed in high yields could be easily purified by column chromatography, analyzed, and characterized spectroscopically. Compounds **5a** and **5h** were deprotected by means of hydrogen chloride in dichloromethane to give the corresponding hydrochlorides **9a** and **9h** (vide infra). The adducts of BBC **3** to (*E*)- and (*Z*)-1-phenylpropene were found to be 75:25 diastereomeric mixtures of *erythro*- and *threo*-isomers[†] in both cases (see Section 2.5, stereochemistry of BBC addition).

Addition of BBC **3** to styrene was disturbed by relatively fast consecutive cyclization of the primarily formed *N*-Boc-2-bromo-2-phenylethylamine **5i** to 5-phenyl-oxazolidin-2-one **6** (Scheme 4). This reaction, not observed for other BBC-alkene adducts, involved an intramolecular S_N2 displacement of the benzylic bromine in **5i**. The analogous

[†] *erythro* (*RS* and *SR*) and *threo* (*RR* and *SS*) configurations were ascribed to both racemic diastereomeric adducts on the basis of Cahn, Ingold and Prelog convention.[5]



Scheme 6.

conversion of some 2-mesyloxy-*N*-Boc-amines into oxazolidinones has been reported recently.[6]

Addition of BBC **3** to low-boiling 3-methylbut-1-ene was performed by adding large excess (ca. 4 equiv.) of hydrocarbon dissolved in dichloromethane to the refluxing solution of BBC in this solvent. The reaction (Scheme 5) which was complete in 30 min, afforded ca. 1:1 mixture of *N*-Boc-2-bromo-3-methylbutylamine **7** and *N*-Boc-2,3-dibromo-3-methylbutylamine **8** as determined by ^{1}H NMR spectroscopy of the respective tosylates obtained by deprotection (vide infra).

Compound **8** was probably produced by allylic bromination of the tertiary hydrogen atom in the starting hydrocarbon followed by BBC addition to 3-bromo-3-methylbut-1-ene thus formed.

2.3. Deprotection of *N*-Boc-2-bromoalkylamines (5a–i). Preparation of 2-bromo-alkylamine hydrochlorides (9a–i) and tosylates (10b–i)

All crude BBC adducts to terminal alkenes **5a–i** could be easily and effectively deprotected to the corresponding 2-bromoalkylamine hydrochlorides **9a–i** by treatment with gaseous hydrogen chloride in dichloromethane at room temperature for 24 h. Alternative degradation with *p*-toluenesulfonic acid in boiling dichloromethane was faster (1 h) and more convenient (Scheme 6). The hydrochlorides **9a–i** and tosylates **10b–i** obtained on evaporation of solvent and addition of ether to the residue separated from the solution in pure state leaving all impurities in the mother liquor. Overall yields of 2-bromoalkylamine hydrochlorides **9a–i** and tosylates **10b–i** were within the range 50–85%. All compounds were analytically pure. Their yields are collected in the Table 1. All melting points of 2-bromoalkylamine hydrochlorides **9a–i** were substantially higher than described previously.[2]

Table 1. 2-Bromoalkylamine hydrochlorides (**9a–i**) and tosylates (**10a–i**)

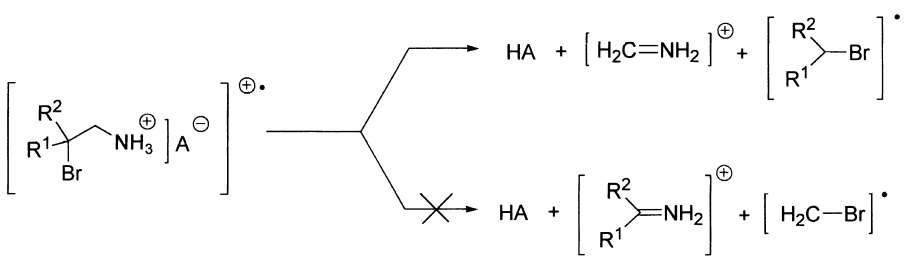
Entry	R^1	R^2	(**9**) Yield (%)[a]	(**10**) Yield (%)[a]
a	Ph	Me	51	–
b	Me	Me	78	76
c	Me	Et	80	75
d	Pr	H	60	66
e	Bu	H	54.5	60
f	C_5H_{11}	H	54	60
g	C_6H_{13}	H	52	58
h	Neo-C_5H_{11}	H	55	44
i	Ph	H	88	86

[a] Yields of crude, analytically pure products.

2.4. Proof of structure of BBC (3) adducts of terminal alkenes

All BBC **3** adducts of terminal alkenes **5a–i** and/or their degradation products **9**,**10b–i** were satisfactorily analyzed for C, H, and N. Regioisomeric purity was evident from ^{1}H NMR spectra examination and could be further confirmed by detailed analysis of these spectra (see Section 4). The anti-Markovnikov orientation of the adducts **5a–i** was unequivocally established by mass spectrometry of 2-bromoalkylamine hydrochlorides **9a–i** and tosylates **10b–i**. The mass spectra of **9a–i** and **10b–i** showed distinct α-cleavage fragmentation giving $[CH_2{=}NH_2]^{\oplus}$ ions, m/z=30, in accord with the regioselectivity shown in Scheme 7.

Such a pattern would not be obtained for the salts **9** and **10** with the amino function at the non-terminal, secondary or tertiary position. The anti-Markovnikov orientation of the adducts **5a–i** could be also corroborated by the absence in MS spectra of **9a–i** and **10b–i** characteristic peaks at m/z=M−CH_2Br, corresponding to the expected preferential α-cleavage fragmentation of the regioisomeric Markovnikov adducts.

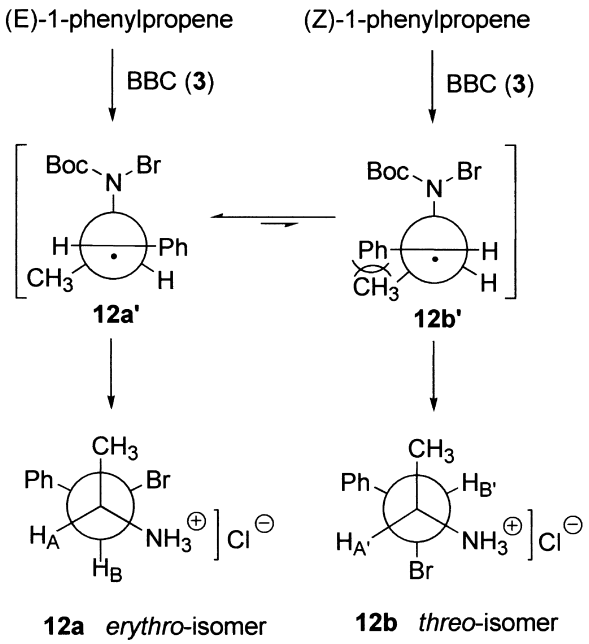


Scheme 7.

2.5. Stereochemistry of BBC (3) addition to 1-phenylpropenes

Diastereomeric (*E*)- and (*Z*)-1-phenylpropenes[7] were selected as model compounds for studying the stereochemical course of BBC **3** addition. Both crude BBC adducts to (*E*)- and (*Z*)-1-phenylpropene **11a** and **11b** have superimposable ^{1}H NMR spectra, suggesting that they are identical mixtures of *erythro*- and *threo*-isomers. The assignment of stereochemistry could not be arrived at by ^{1}H NMR due to the complex multiplicity patterns of the spectra. Detailed analysis was, however, possible for the ^{1}H NMR spectra of the respective 2-bromoamine hydrochlorides **12** obtained upon degradation of the crude adducts **11a** and **11b** with hydrogen chloride in dichloromethane. This treatment does not change the configuration of both chiral centers. The ^{1}H NMR spectrum of the hydrochloride **12** obtained from (*E*)-1-phenylpropene adduct **11a** exhibited the presence of two doublets of different intensities centered at δ=5.53 ppm (J_{HH}=5.0 Hz; higher intensity signal) and δ=5.22 ppm (J_{HH}=10.0 Hz; lower intensity signal) which could be assigned to the benzylic protons H_B and H_B, in both diastereoisomers on the basis of integration, multiplicity and chemical shifts. It is feasible to assume the synclinal arrangement of vicinal protons H_A and H_B in the preferred conformation of *erythro*-isomer **12a**. This would account for a smaller vicinal coupling constant of the lower field doublet according to Karplus relationship. The antiperiplanar arrangement of vicinal protons $H_{A'}$ and H_B, in the preferred conformation of the *threo*-isomer **12b** is in turn fully compatible with a higher value of the respective coupling constant according to Karplus equation (Scheme 8).

Almost identical spectral assignments were found for the mixture of diastereomeric 2-bromoamine hydrochlorides **12** obtained from (*Z*)-1-phenylpropene adduct **11b** (δH_B=5.48 ppm, J_{HH}=5.25 Hz; δH_B=5.19 ppm, J_{HH}=10.25 Hz). Preferential formation of the *erythro*- adduct from both diastereomeric alkenes can be interpreted in terms of the existence of dynamic equilibrium between the intermediately formed benzyl type radicals **12a**′ and **12b**′ (see below). The radical **12a**′ leading to the *erythro*- adduct (**12a**) is more stable and hence more abundant due to lesser crowding between the methyl and phenyl groups.



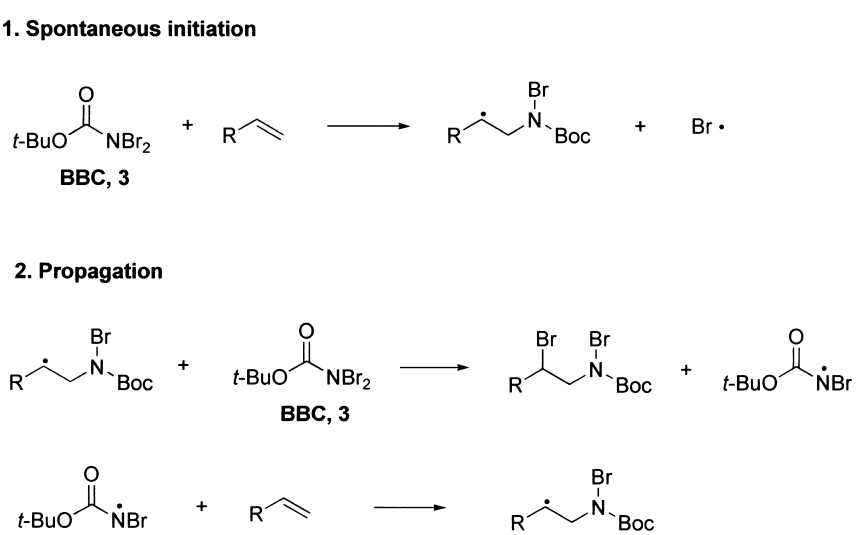
Scheme 8.

2.6. Mechanism of BBC addition to terminal alkenes

All BBC additions to terminal alkenes exhibit characteristic features indicative of spontaneously initiated[8,9] free-radical chain reactions: (i) they follow totally regioselectively affording solely anti-Markovnikov adducts; (ii) they start with a short induction period; (iii) the addition to non-terminal alkenes, e.g. 1-phenylpropene is nonstereospecific. All these phenomena can be plausibly explained by assuming a free-radical reaction pathway presented in Scheme 9.

3. Conclusion

In conclusion we have developed a simple, two-step, and



Scheme 9.

efficient method for regioselective aminobromination of terminal alkenes using the new reagent-*t*-butyl *N*,*N*-dibromocarbamate (**3**). The procedure offers an operationally simple and convenient synthesis of 2-bromoamines. As a potential route to aziridines and *N*-Boc-aziridines it can successfully compete with other available protocols involving activation of the hydroxyl group in 2-amino-alcohols by converting into tosylates or mesylates and subsequent ring closure by means of strong bases.[10]

4. Experimental

4.1. General

Melting points (determined in open capillary tubes) are uncorrected. IR spectra (liquid films or KBr discs) were measured using a specord M 80 (C.Zeiss) instrument. ^{1}H NMR spectra were recorded on a Bruker AVANCE DPX-250 spectrometer operating at 250 MHz, using $CDCl_3$ solutions unless otherwise stated. FAB/MS were measured on an APO Electron (Ukraine) Model MI 12001 mass spectrometer equipped with a FAB ion source (thioglycerol matrix). Xenon was used as ionized gas. The beam energy was set to 5 keV. Column chromatography was performed on silica gel 60 (Baker, 200–400 mesh). All commercially available starting materials were purchased from Fluka and used without additional purification.

4.1.1. Preparation of *t*-butyl *N*,*N*-dibromocarbamate (BBC, 3). Bromine (35.16 g, 0.22 mol) was added dropwise with efficient stirring for 40 min to a solution of crude *t*-butyl carbamate[4] (prepared in CH_2Cl_2, mp 90–93°C, yield ca. 100%, purity ~90%; 12.9 g, 0.11 mol) and K_2CO_3 (15.2 g, 0.11 mol) in water (200 mL) at room temperature. The resulting mixture was stirred for 2 h, CH_2Cl_2 (100 mL) was then added and stirring was continued for further 15 min. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3×30 mL). Combined extracts were washed with water (30 mL), dried ($MgSO_4$), and the solvent evaporated in vacuo to give the title compound **3** (24.6 g, 90%) as an orange solid. Crude **3** was contaminated (^{1}H NMR) with ca. 9% of *t*-butyl *N*-bromocarbamate. Analytically pure sample of **3** (prepared from pure *t*-butyl carbamate, mp 107–108°C and washed with cold pentane) had mp 93–95°C; [Found: C, 21.7; H, 3.4; N, 5.2. $C_5H_9O_2NBr$ requires C, 21.84; H, 3.30; N, 5.09%]; ν_{max} (KBr) 2992, 1696, 1368, 1280, 1264, 1248, 1144, 872, 744 cm^{-1}; δ_H 1.50 (9H, s, C*H*$_3$); δ_C 156.2, 86.2, 27.3; *m*/*z* (CI) 274 (41, M+1), 276 (96, M+3), 278 (40, M+5).

4.2. Addition of BBC (3) to terminal alkenes. General procedure

A solution of BBC (**3**) (1.38 g, 5 mmol) in CH_2Cl_2 (7 mL) was added dropwise with stirring to the solution of terminal alkene (5 mmol) in refluxing CH_2Cl_2 (7 mL) for 20 min. Stirring was then continued if necessary until pale-yellow coloration of the solution was obtained (ca. 2 h for compounds **5d**–**g**). In the case of isobutylene a solution of alkene in CH_2Cl_2 was added to **3** dissolved in CH_2Cl_2 until disappearance of an orange color. The resulting solution was cooled to 5–10°C and 12% aqueous solution of sodium sulphite (5 mL) was added slowly at this temperature. Dichloromethane (15 mL) was then added, the organic layer was separated, washed with water (3×5 mL), dried ($MgSO_4$) and the solvent evaporated in vacuo. The residual crude adducts (**5b**–**g**) were purified by column chromatography using CH_2Cl_2 as eluent. Compounds (**5a**) and (**5h**) decomposed on attempted purification.

4.2.1. *N*-Boc-2-bromo-2-methylpropylamine (5b). Yield 77%, colorless needles, mp 51–53°C; [Found: C, 42.9; H, 7.4; N, 5.7. $C_9H_{18}BrNO_2$ requires C, 42.87; H, 7.20; N, 5.55%]; R_f (CH_2Cl_2) 0.58; ν_{max} (CCl_4 soln) 3336, 2980, 2965, 1716, 1508, 1460, 1392, 1368, 1168, 1128 cm^{-1}; δ_H 5.06 (1H, bs, N*H*), 3.39 (2H, d, *J*=6.25 Hz, C*H*$_2$), 1.74 (6H, s, *Me*$_2$C), 1.46 (9H, s, *Me*$_3$C); FAB/MS: 252 (14, M+1), 250 (14, M−1) 154 (18), 152 (18), 116 (74), 73 (56), 57 (100%).

4.2.2. *N*-Boc-2-bromo-2-methylbutylamine (5c). Yield 87%, colorless solid, mp 30–32°C; [Found: C, 45.0; H, 7.7; N, 5.4. $C_{10}H_{20}BrNO_2$ requires C, 45.12; H, 7.58; N, 5.26%]; R_f (CH_2Cl_2) 0.54; ν_{max} (film) 3300, 2980, 2935, 1708, 1515, 1450, 1400, 1375, 1255, 1175, 1135 cm^{-1}; δ_H 4.99 (1H, bs, N*H*), 3.43 (2H, d, *J*=6.4 Hz, C*H*$_2$NH), 1.91 (1H, q, *J*=7.3 Hz, MeC*H*$_2$), 1.76 (1H, q, *J*=7.3 Hz, MeC*H*$_2$), 1.64 (3H, s, *Me*C(Br), 1.44 (9H, s, *Me*$_3$C), 1.04 (3H, t, *J*=7.3 Hz, *Me*CH$_2$); FAB/MS: 265 (3, M+1), 264 (4, M−1), 168 (21), 166 (26), 136 (38), 69 (47), 57 (100%).

4.2.3. *N*-Boc-2-bromopentylamine (5d). Yield 61%, colorless oil; [Found: C, 45.3; H, 7.6; N, 5.1. $C_{10}H_{20}BrNO_2$ requires C, 45.12; H, 7.58; N, 5.26%]; R_f (CH_2Cl_2) 0.74; ν_{max} (film) 3360, 2990, 2960, 1710, 1520, 1465, 1400, 1380, 1255, 1175 cm^{-1}; δ_H 5.01 (1H, bs, N*H*), 4.06–4.15 (1H, m, C*H*Br), 3.63 (1H, ddd, *J*=14.3, 6.8, 3.8 Hz, CHBr–C*H*$_2$–NH), 3.33 (1H, ddd, *J*=14.3, 7.9, 5.7 Hz, CHBr–C*H*$_2$–NH), 1.79 (2H, q, *J*=7.25 Hz, CH$_2$–C*H*$_2$–CHBr), 1.46 (9H, s, *Me*$_3$C), 1.38–1.63 (2H, m, CH$_3$C*H*$_2$), 0.94 (3H, t, *J*=7.25 Hz, C*H*$_3$–CH$_2$); FAB/MS: 266 (2, M+1), 264 (2, M−1), 168 (65), 166 (71), 57 (56), 41 (74%).

4.2.4. *N*-Boc-2-bromohexylamine (5e). Yield 62%, colorless oil; [Found: C, 47.3; H, 8.1; N, 5.2. $C_{11}H_{22}BrNO_2$ requires C, 47.18; H, 7.91; N, 5.00%]; R_f (CH_2Cl_2) 0.79; ν_{max} (film) 3360, 2980, 2940, 2890, 1700, 1520, 1465, 1400, 1380, 1260, 1180 cm^{-1}; δ_H 4.99 (1H, bs, N*H*), 4.04–4.14 (1H, m, C*H*Br–CH$_2$), 3.63 (1H, ddd, *J*=14.4, 6.6, 3.8 Hz, CHBr–C*H*$_2$–NH), 3.33 (1H, ddd, *J*=14.4, 7.9, 5.5 Hz, CHBr–C*H*$_2$–NH), 1.76–1.86 (2H, m, C*H*$_2$–CHBr–CH$_2$NH), 1.45 (9H, s, *Me*$_3$C), 1.25–1.62 (4H, m, CH$_3$(C*H*$_2$)$_2$), 0.91 (3H, t, *J*=7.1 Hz C*H*$_3$CH$_2$); FAB/MS: 182 (42), 180 (49), 144 (38), 57 (100), 43 (47), 29 (55%).

4.2.5. *N*-Boc-2-bromoheptylamine (5f). Yield 58%, colorless oil; [Found: C, 49.1; H, 8.3; N, 4.0. $C_{12}H_{24}BrNO_2$ requires C, 48.99; H, 8.22; N, 4.76%]; R_f (CH_2Cl_2) 0.60; ν_{max} (film) 3370, 2985, 2950, 2890, 1705, 1520, 1465, 1400, 1380, 1210, 1180 cm^{-1}; δ_H 4.97 (1H, bs, N*H*), 4.08–4.14 (1H, m, C*H*Br–CH$_2$), 3.58–3.68 (1H, m, CHBr–C*H*$_2$–NH), 3.33 (1H, ddd, *J*=14.6, 8.0, 5.4 Hz, CHBr–C*H*$_2$–NH), 1.76–1.85 (2H, m, C*H*$_2$–CHBr–CH$_2$NH), 1.45 (9H, s, *Me*$_3$C), 1.27–1.56 (6H, m, CH$_3$(C*H*$_2$)$_3$), 0.89 (3H, t, *J*=6.25 Hz, C*H*$_3$–CH$_2$); FAB/MS: 296 (3, M+3), 294 (4, M+1), 292 (4, M−1), 196 (82), 194 (84), 73 (32), 57 (100), 29 (43%).

4.2.6. *N*-Boc-2-bromooctylamine (5g). Yield 65%, colorless oil; [Found: C, 50.5; H, 8.6; N, 4.4. $C_{13}H_{26}BrNO_2$ requires C, 50.65; H, 8.50; N, 4.55%]; R_f (CH_2Cl_2) 0.73; ν_{max} (film) 3350, 2960, 2950, 2865, 1725, 1510, 1450, 1400, 1375, 1248, 1170 cm^{-1}; δ_H 4.98 (1H, bs, N*H*), 4.04–4.14 (1H, m, C*H*Br), 3.63 (1H, ddd, *J*=14.4, 6.6, 3.5 Hz, CHBr–CH_2–NH), 3.32 (1H, ddd, *J*=14.4, 7.9, 5.5 Hz, CHBr–CH_2–NH), 1.76–1.82 (2H, m, CH_2–CHBr), 1.45 (9H, s, *Me*$_3$C), 1.28–1.52 (8H, m, $CH_3(CH_2)_4$), 0.88 (3H, t, *J*=6.25 Hz, CH_3–CH_2); FAB/MS: 308 (6, M+1), 306 (4, M−1), 254 (92), 252 (100), 210 (16), 208 (24), 172 (64), 128 (22), 57 (100%).

4.3. Addition of BBC (3) to styrene

The reaction was performed as described above (Section 4.2). Crude adduct was found (^{1}H NMR) to be the mixture containing ca. 93% of *N*-Boc-2-bromo-2-phenylethylamine (**5i**) and 7% of 5-phenyl-oxazolidin-2-one (**6**). Compound (**5i**) was isolated in pure state, by crystallization from pentane. Yield 87%, colorless solid, mp 63–64°C; [Found: C, 51.9; H, 6.2; N, 4.8. $C_{13}H_{18}BrNO_2$ requires C, 52.01; H, 6.04; N, 4.67%]; ν_{max} (KBr) 3430, 3000, 1700, 1525, 1385, 1320, 1280, 1180, 1075, 950, 775, 710, 640, 600 cm^{-1}; δ_H 7.32–7.40 (5H, m, *Ph*), 5.06 (1H, t, *J*=6.75 Hz, C*H*Br–CH_2), 4.91 (1H, bs, N*H*), 3.73 (2H, t, *J*=6.75 Hz, CHBr–CH_2), 1.43 (9H, s, *Me*$_3$C); FAB/MS: 302 (1, M+3), 300 (1.5, M+1), 246 (13), 244 (16), 202 (5), 200 (6), 164 (41), 120 (19), 91 (29), 57 (100%). The residue insoluble in hot pentane afforded pure (**6**) after crystallization from water. Colorless leaflets, mp 87–88°C (Lit.,[11] mp 87–89°C); δ_H 7.37–7.42 (5H, m, *Ph*), 6.56 (1H, bs, N*H*), 5.61 (1H, dd, *J*=8.75, 7.75 Hz, C*H*(O)–CH_2), 3.98 (1H, dt, *J*=8.75, 0.75 Hz, CH(O)–CH_2–NH), 3.54 (1H, ddd, *J*=8.75, 7.75, 0.75 Hz, CH(O)–CH_2–NH).

4.4. Addition of BBC (3) to 3-methylbut-1-ene

The reaction was carried out by adding hydrocarbon (40 mmol) dissolved in CH_2Cl_2 (20 mL) to the solution of BBC (**3**, 2.76 g, 10 mmol) in the same solvent (15 mL) for 20 min at 40°C. Crude adduct obtained after reduction with sodium sulphite was a mixture containing ca. 54% of *N*-Boc-2-bromo-3-methylbutylamine (**7**) and ca. 46% of *N*-Boc-2,3-dibromo-3-methylbutylamine (**8**) as determined by ^{1}H NMR after immediate degradation with *p*-toluenesulfonic acid (vide infra).

4.5. Deprotection of (5a–i) with hydrogen chloride. General procedure

A solution of crude adduct (**5a–i**) prepared as described above (Section 4.2) in CH_2Cl_2 (30 mL) was saturated with gaseous hydrogen chloride at 0°C and then left overnight at room temperature. The solvent was evaporated in vacuo and ether (30 mL) was added to the residue. Colorless crystals of (**9a–i**) obtained on refrigeration for 1 h were filtered off and washed with ether.

4.5.1. 2-Bromo-2-phenylpropylamine hydrochloride (9a). Yield 51%, colorless plates, mp 145–147°C (EtOH–$Et_2$0); [Found: C, 43.3; H, 5.3; N, 5.7. $C_9H_{13}BrClN$ requires C, 43.14; H, 5.23; N, 5.59%]; ν_{max} (KBr) 3264, 3000, 2900, 1500, 1450, 1330, 1260, 1090, 972, 948, 768, 750, 700, 656 cm^{-1}; δ_H (D_2O) 7.33–7.49 (5H, m, *Ph*), 3.82 (1H, d, *J*=9.25 Hz, CH_2–N) 3.77 (1H, d, *J*=9.25 Hz, CH_2–N), 1.79 (3H, s, *Me*); FAB/MS: 216 (6, M_K+2), 214 (18, M_K), 178 (100), 134 (71), 91 (34), 57 (36), 30 (13%).

4.5.2. 2-Bromo-2-methylpropylamine hydrochloride (9b). Yield 78%, colorless solid, mp 157–159°C (dec.) (EtOH–$Et_2$0); [Found: C, 25.7; H, 6.0; N, 7.6. $C_4H_{11}BrClN$ requires C, 25.49; H, 5.88; N, 7.43%]; ν_{max} (KBr) 2960, 2680, 2600, 1590, 1520, 1408, 1165, 1105 cm^{-1}; δ_H (D_2O) 3.35 (2H, s, CH_2–N), 1.84 (6H, s, *Me*); FAB/MS: 154 (41, M_K+2), 152 (44, M_K), 137 (27), 135 (27), 72 (76), 55 (100), 41 (59), 30 (44%).

4.5.3. 2-Bromo-2-methylbutylamine hydrochloride (9c). Yield 80%, colorless solid, mp 149–150°C (dec.) (EtOH–Et_2O); [Found: C, 29.8; H, 6.7; N, 7.1. $C_5H_{13}BrClN$ requires C, 29.65; H, 6.47; N, 6.92%]; ν_{max} (KBr) 2950, 1588, 1514, 1450, 1420, 1395, 1152, 1105, 880 cm^{-1}; δ_H (D_2O) 3.41 (1H, d, *J*=13.8 Hz, CH_2–N), 3.33 (1H, d, *J*=13.8 Hz, H_2, CH_2–N), 2.02 (1H, dq, *J*=15.0, 7.4 Hz, CH_3CH_2), 1.90 (1H, dq, *J*=15.0, 7.4 Hz, CH_3CH_2), 1.06 (3H, t, *J*=7.4 Hz, H_2, CH_3CH_2).

4.5.4. 2-Bromopentylamine hydrochloride (9d). Yield 60%, colorless solid, mp 175–177°C (EtOH–Et_2O); [Found: C, 29.5; H, 6.5; N, 7.1. $C_5H_{13}BrClN$ requires C, 29.65; H, 6.47; N, 6.92%]; ν_{max} (KBr) 3160, 3065, 2010, 1600, 1508, 1410, 630 cm^{-1}; δ_H (D_2O) 4.32 (1H, ddt, *J*=9.6, 7.0, 2.9 Hz, CH_2–C*H*–Br–CH_2), 3.50 (1H, dd, *J*=14.0, 2.9 Hz, C*H*BrCH_2–N), 3.32 (1H, dd, *J*=14.0, 9.6 Hz, CHBr–CH_2–N), 1.86 (2H, q, *J*=7.0 Hz, CH_2CH_2-CHBr), 1.38–1.64 (2H, m, $CH_3CH_2CH_2$), 0.92 (3H, t, *J*=7.4 Hz, CH_3CH_2); FAB/MS: 168 (83, M_K+2), 166 (87, M_K), 69 (68), 41 (100), 30 (70), 27 (50%).

4.5.5. 2-Bromohexylamine hydrochloride (9e). Yield 54.5%, colorless solid, mp 183–185°C (EtOH–Et_2O); [Found: C, 33.4; H, 7.1; N, 6.6. $C_6H_{15}BrClN$ requires C, 33.28; H, 6.98; N, 6.47%]; ν_{max} (KBr) 3160, 2950, 2020, 1600, 1510, 1470, 1415, 1250 cm^{-1}; δ_H (D_2O) 4.29 (1H, ddt, *J*=9.25, 6.9, 3.25 Hz, CH_2CHBrCH$_2$), 3.50 (1H, dd, *J*=14.0, 3.25 Hz, CHBrCH_2–N) 3.32 (1H, dd, *J*=14.0, 9.25 Hz, CHBrCH_2–N), 1.89 (2H, q, *J*=6.9 Hz, CH_2CH_2-CHBr), 1.31–1.53 (4H, m, $CH_3(CH_2)_2CH_2$), 0.89 (3H, t, *J*=7.1 Hz, CH_3CH_2).

4.5.6. 2-Bromoheptylamine hydrochloride (9f). Yield 54%, colorless leaflets, mp 181–183°C (dec.) (Me_2CO); [Found: C, 36.6; H, 7.3; N, 6.2. $C_7H_{17}BrClN$ requires C, 35.46; H, 7.43; N, 6.08%]; ν_{max} (KBr) 2952, 2015, 1600, 1510, 1472, 1404, 1240, 1165, 675 cm^{-1}; δ_H (D_2O) 4.30 (1H, ddt, *J*=9.5, 6.9, 3.0 Hz, CH_2CHBrCH$_2$), 3.49 (1H, dd, *J*=14.0, 3.0 Hz, CHBrCH_2–N), 3.31 (1H, dd, *J*=14.0, 9.5 Hz, CHBrCH_2–N), 1.88 (2H, q, *J*=6.9 Hz, CH_2CH_2-CHBr), 1.30–1.56 (6H, m, $CH_3(CH_2)_3CH_2$), 0.87 (3H, dist.t, *J*=6.0 Hz, CH_3CH_2); FAB/MS: 196 (97, M_K+ 2), 194 (100, M_K), 114 (21), 55 (19), 40 (33), 30 (24), 27 (35%).

4.5.7. 2-Bromooctylamine hydrochloride (9g). Yield 52%, colorless solid, mp 194–196°C (dec.) (EtOH–Et_2O); [Found: C, 39.1; H, 7.7; N, 5.8. $C_8H_{19}BrClN$ requires C,

39.28; H, 7.83; N, 5.73]; ν_{max} (KBr) 3150, 2970, 2020, 1600, 1508, 1468, 1412, 1228, 1164, 620 cm^{-1}; δ_H (D_2O) 4.30 (1H, ddt, J=9.5, 7.2, 3.0 Hz, $CH_2CHBrCH_2$), 3.49 (1H, dd, J=14.0, 3.0 Hz, $CHBrCH_2$–N), 3.31 (1H, dd, J=14.0, 9.5 Hz, $CHBrCH_2$–N), 1.87 (2H, q, J=7.2 Hz, CH_2CH_2-CHBr), 1.28–1.55 (8H, m, $CH_3(CH_2)_4CH_2$), 0.86 (3H, dist.t, J=6.8 Hz, CH_3CH_2).

4.5.8. 2-Bromo-2,4,4-trimethylpentylamine hydrochloride (9h). Yield 55%, colorless solid, mp 110–112°C (EtOH–Et_2O); [Found: C, 39.1; H, 7.6; N, 5.5. $C_8H_{19}BrClN$ requires C, 39.28; H, 7.38; N, 5.73%]; ν_{max} (KBr) 3150, 3070, 2020, 1404, 630 cm^{-1}; δ_H (D_2O) 3.48 (1H, d, J=13.9 Hz, CH_2–N), 3.39 (1H, d, J=13.9 Hz, CH_2–N), 2.19 (1H, d, J=15.5 Hz, Me_3C–CH_2), 2.07 (1H, d, J=15.5 Hz, Me_3C–CH_2), 2.19, 2.07 (2H, 2d, J=15.5 Hz, Me_3C–CH_2), 1.94 (3H, s, CH_3–C(Br)), 1.07 (9H, s, Me_3C); FAB/MS: 210 (2, M_K+2), 208 (2, M_K), 164 (18), 128 (100), 111 (46), 57 (66), 30 (54%).

4.5.9. 2-Bromo-2-phenylethylamine hydrochloride (9i). Yield 88%, colorless plates, mp 165–167°C (dec.) (EtOH–Et_2O); [Found: C, 40.4; H, 4.7; N, 6.1. $C_8H_{11}BrClN$ requires C, 40.62; H, 4.69; N, 5.92%]; ν_{max} (KBr) 2880, 2660, 1610, 1515, 1460, 930, 890, 770, 705, 690 cm^{-1}; δ_H (D_2O) 7.43–7.60 (5H, m, *Ph*), 5.35 (1H, dd, J=9.25, 5.75 Hz, $CHBr$–CH_2–N), 3.80 (1H, dd, J=13.8, 9.25 Hz, CHBr–CH_2–N), 3.69 (1H, dd, J=13.8, 5.75 Hz, $CHBrCH_2$–N); FAB/MS: 202 (34, M_K+2), 200 (35, M_K), 156 (23), 120 (100), 104 (80), 77 (45), 30 (64%).

4.6. Deprotection of BBC adducts (9b–i) with *p*-toluenesulfonic and. Preparation of 2-bromoalkylamine tosylates (10b–i)

A solution of *p*-toluenesulfonic acid monohydrate (0.95 g, 5 mmol) in EtOH (2 mL) was added to the solution of crude BBC adduct (**9b–i**) in CH_2Cl_2 (30 mL) and the mixture was refluxed gently for 1 h. The solvent was evaporated in vacuo and ether (30 mL) was added to the residue. The precipitated tosylates (**10b–i**) were filtered and washed with ether.

4.6.1. 2-Bromo-2-methylpropylamine tosylate (10b). Yield 76%, colorless solid, mp 140–141°C (EtOH–Et_2O); [Found: C, 40.9; H, 5.7; N, 4.4. $C_{11}H_{18}BrNO_3S$ requires C, 40.75; H, 5.60; N, 4.32%]; ν_{max} (KBr) 2950, 2640, 1625, 1540, 1500, 1464, 1408, 1384, 1234, 1172, 1040, 1014, 820, 680, 630, 572 cm^{-1}; δ_H 8.02 (3H, bs, NH_3), 7.17–7.79 (4H, AA′BB′ system, C_6H_4), 3.11 (2H, q, J=5.75 Hz, CH_2–NH_3), 2.36 (3H, s, CH_3–C_6H_4), 1.72 (6H, s, Me_2C); FAB/MS: 326 (13, M+3), 324 (14, M+1) 154 (98, M_K+2), 152 (100, M_K), 137 (19), 135 (19), 72 (95), 55 (46), 30 (27%).

4.6.2. 2-Bromo-2-methylbutylamine tosylate (10c). Yield 75%, colorless solid, mp 140–143°C (EtOH–Et_2O); [Found: C, 42.4; H, 6.0; N, 4.3. $C_{12}H_{20}BrNO_3S$ requires C, 42.61; H, 5.96; N, 4.14%]; ν_{max} (KBr) 3080, 2940, 1630, 1558, 1500, 1475, 1452, 1170, 1136, 1040, 1014, 822, 684, 572 cm^{-1}; δ_H 8.01 (3H, bs, NH_3), 7.18–7.79 (4H, AA′BB′ system, C_6H_4), 3.09 (2H, q, J=5.9 Hz, CH_2–NH_3), 2.36 (3H, s, CH_3–C_6H_4), 1.84, 1.74 (2H, 2q, J=7.25 Hz, CH_3CH_2), 1.68 (3H, s, MeC(Br), 0.94 (3H, t, J=7.25 Hz, CH_3CH_2); FAB/MS: 340 (7, M+3), 338 (8, M+1), 168 (96, M_K+2), 166 (100, M_K), 86 (72), 69 (50), 30 (34%).

4.6.3. 2-Bromopentylamine tosylate (10d). Yield 66%, colorless solid, mp 125–127°C (dec.) (EtOH–Et_2O); [Found: C, 42.4; H, 6.1; N, 4.3. $C_{12}H_{20}BrNO_3S$ requires C, 42.61; H, 5.96; N, 4.14%]; ν_{max} (KBr) 3070, 1604, 1500, 1470, 1450, 1210, 1160, 1132, 1036, 1008, 822, 684, 568 cm^{-1}; δ_H 7.92 (3H, bs, NH_3), 7.16–7.79 (4H, AA′BB′ system, C_6H_4), 4.03–4.19 (1H, m, CHBr–CH_2), 3.24–3.33 (1H, m, CH_2NH_3), 2.95–3.11 (1H, m, CH_2NH_3), 2.36 (3H, s, $CH_3C_6H_4$), 1.61 (2H, q, J=7.2 Hz, CH_2CHBr), 1.41–1.25 (2H, nm, CH_3CH_2); FAB/MS: 340 (4, M+3), 338 (4, M+1), 168 (95, M_K+2), 166 (100, M_K), 86 (68), 69 (71), 41 (64), 30 (69%).

4.6.4. 2-Bromohexylamine tosylate (10e). Yield 60%, colorless solid, mp 129–131°C (EtOH–Et_2O); [Found: C, 44.1; H, 6.5; N, 4.1. $C_{13}H_{22}BrNO_3S$ requires C, 44.32; H, 6.30; N, 3.98%]; ν_{max} (KBr) 3090, 2940, 1604, 1516, 1460, 1220, 1160, 1136, 1038, 1008, 820, 684, 572 cm^{-1}; δ_H 7.95 (3H, bs, NH_3), 7.17–7.80 (4H, AA′BB′ system C_6H_4), 4.02–4.13 (1H, m, $CHBrCH_2$), 3.05–3.33 (2H, m, CH_2NH_3), 2.36 (3H, s, $CH_3C_6H_4$), 1.53–1.73 (2H, m, CH_2CHBr), 1.11–1.42 (4H, m, $CH_3(CH_2)_2$), 0.82 (3H, t, J=7.1 Hz, CH_2); FAB/MS: 254 (9, M+3), 252 (10, M+1), 182 (93, M_K+2), 180 (100, M_K), 100 (31), 30 (19 %).

4.6.5. 2-Bromoheptylamine tosylate (10f). Yield 60%, colorless solid, mp 195–196°C (dec.) (EtOH–Et_2O); [Found: C, 46.1; H, 6.7; N, 3.9. $C_{14}H_{24}BrNO_3S$ requires C, 45.91; H, 6.61; N, 3.82%]; ν_{max} (KBr) 3190, 3088, 2090, 1830, 1600, 1470, 1450, 1164, 1136, 1040, 1012, 816, 684, 572 cm^{-1}; δ_H 7.95 (3H, bs, NH_3), 7.17–7.80 (4H, AA′BB′ system C_6H_4), 4.02–4.13 (1H, m, $CHBrCH_2$), 3.05–3.32 (2H, m, CH_2NH_3), 2.36 (3H, s, $CH_3C_6H_4$), 1.53–1.73 (2H, m, CH_2CHBr), 1.06–1.44 (6H, m, $CH_3(CH_2)_3$), 0.83 (3H, t, J=6.9 Hz, CH_3CH_2); FAB/MS: 368 (5, M+3), 366 (6, M+1), 196 (M_K+2), 194 (100, M_K), 55 (45), 30 (40%).

4.6.6. 2-Bromooctylamine tosylate (10g). Yield 58%, colorless solid, mp 180–181°C (dec.) (EtOH–Et_2O); [Found: C, 47.1; H, 7.0; N, 3.5. $C_{15}H_{26}BrNO_3S$ requires C, 47.37; H, 6.89; N, 3.68%]; ν_{max} (KBr) 3090, 2940, 1618, 1520, 1460, 1230, 1165, 1136, 1038, 1008, 816, 684, 568 cm^{-1}; δ_H 7.95 (3H, bs, NH_3), 7.16–7.79 (4H, AA′BB′ system, C_6H_4), 4.02–4.12 (1H, m, CHBr), 2.93–3.32 (2H, m, $CHBrCH_2$), 2.36 (3H, s, $CH_3C_6H_4$), 1.11–1.53 (2H, m, CH_2CHBr), 1.18–1.39 (8H, m, $CH_3(CH_2)_4$), 0.85 (3H, t, J=6.75 Hz, CH_3CH_2); FAB/MS: 382 (4, M+3), 380 (4, M+1), 210 (93, M_K+2), 208 (100, M_K), 128 (63), 69 (49), 41 (72), 30 (66%).

4.6.7. 2-Bromo-2,4,4-trimethylpentylamine tosylate (10h). Yield 55%, colorless solid, mp 155–156°C (dec.) (EtOH–Et_2O); [Found: C, 47.1; H, 7.0; N, 3.5. $C_{15}H_{26}BrNO_3S$ requires C, 47.37; H, 6.89; N, 3.68%]; ν_{max} (KBr) 3190, 3084, 1646, 1604, 1472, 1454, 1200, 1164, 1136, 1050, 1012, 820, 690, 634, 625, 572 cm^{-1}; δ_H 8.03 (3H, bs, NH_3), 7.17–7.81 (4H, AA′BB′ system, C_6H_4), 3.13–3.20 (2H, m, CH_2NH_3), 2.36 (s, 3H, $CH_3C_6H_4$), 1.99 (1H, d, J=5.55 Hz, *t*-Bu-CH_2), 1.86 (1H, d, J=15.55 Hz,

t-Bu-CH_2), 1.83 (3H, s, CH_3CHBr), 0.96 (9H, s, Me_3C); FAB/MS: 382 (3, M+3), 380 (3, M+1), 210 (76, M_K+2), 208 (73, M_K) 128 (95), 57 (100), 41 (47), 30 (27%).

4.6.8. 2-Bromo-2-phenylethylamine tosylate (10i). Yield 86%, colorless solid, mp 130–132°C (dec.) (EtOH–Et_2O); [Found: C, 48.2; H, 4.9; N, 3.9. $C_{15}H_{18}BrNO_3S$ requires C, 48.40; H, 4.88; N, 3.76%]; ν_{max} (KBr) 3030, 2900, 1604, 1512, 1460, 1220, 1170, 1128, 1040, 1008, 868, 820, 760, 680, 600, 572 cm^{-1}; δ_H 8.04 (3H, bs, NH_3), 7.14–7.78 (4H, AA′BB′ system, C_6H_4, 5.15 (1H, dd, *J*=8.75, 6.0 Hz, $CHBrCH_2$), 3.31–3.37 (2H, m, $CHBrCH_2$), 2.34 (3H, s, $CH_3C_6H_4$); FAB/MS: 374 (8, M+3), 372 (8, M+1), 202 (85, M_K+2), 200 (91, M_K), 185 (26), 183 (25), 120 (100), 104 (79), 91 (24), 30 (41%).

4.7. Addition of BBC (3) to (*E*)-1-phenylpropene followed by deprotection with HCl

Addition and deprotection were carried out as described for other hydrocarbons. Yield 70%, colorless solid, mp 161–165°C (dec.); [Found: C, 43.0; H, 5.3; N, 5.7. $C_9H_{13}BrClN$ requires C, 43.14; H, 5.23; N, 5.59%]; δ_H 8.72 (3H, bs, NH_3), 7.11–7.59 (5H, m, Ph), 5.53 (1H, d, *J*=5.0 Hz, CHBr *erythro*), 5.22 (1H, d, *J*=10.0 Hz, CHBr *threo*), 3.62–3.83, 3.88–4.10 (1H, 2m, $CHCH_3$), 1.33, 1.54 (3H, 2d, *J*=6.5 Hz, CH_3CH).

4.8. Addition of BBC (3) to (*Z*)-1-phenylpropene followed by deprotection with HCl

Addition and deprotection were carried out as described for other hydrocarbons. Yield 57%, colorless solid, mp 168–171°C (dec.); [Found: C, 43.2; H, 5.4; N, 5.8. $C_9H_{13}BrClN$ requires C, 43.14; H, 5.23; N, 5.59%]; δ_H 8.77 (3H, bs, NH_3), 7.26–7.55 (5H, m, Ph), 5.48 (1H, *J*=5.25 Hz, CHBr *erythro*), 5.19 (1H, d, *J*=10.25 Hz, CHBr *threo*), 3.67–3.81, 3.91–4.08 (1H, 2m, $CHCH_3$), 1.33, 1.55 (3H, 2d, *J*=6.5 Hz, CH_3CH).

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