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ARTICLE

# Synthesis of α-Tribromomethylamines via Mg-Mediated Addition of Bromoform to Imines

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Mg-mediated addition of bromoform to electron deficient imines such as N-sulfonylimines affords α-tribromomethylated N-sulfonylamines in good to excellent yield. The procedure could be further simplified by transforming the imine precursors, α-sulfonyl-N-tosyl- and Boc-amines, in one-pot to the corresponding α-tribromomethyl derivatives. Facile removal of the Boc protecting group in nearly quantitative yield and a silver carbonate mediated monodebromination have also been demonstrated.

## Introduction

Organohalogens constitute many drug candidates and other bioactive compounds, including natural products.[1] Among numerous bioactive trihalomethylated compounds,[2] TaFlu **1a**, TaClo **1b** and TaBro **2** belong to a new class of tetrahydro-β-carboline based neurotoxins of which the most potent one is TaBro **2**.[3]

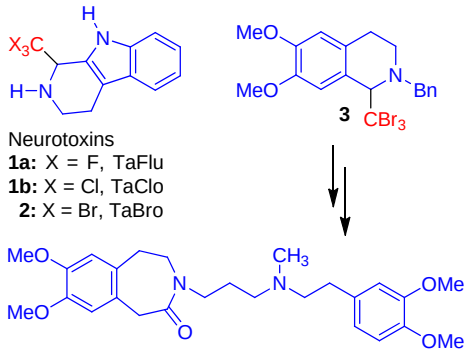


**Figure 1.** Selected Potentially Bioactive Compounds and Synthetic Intermediates with a Key Tribromomethyl Group

From synthetic perspective, the tribromomethylated compounds are versatile intermediates for the synthesis of many biological agents, for example, the anti-anginal agent zatebradine **4**.[4] The tribromomethyl group has the ability to take part in key ring enlargement steps for the synthesis of complex molecules.[4-5] It is also amenable for facile transformation to a variety of functional groups such as carboxylic acid/ester, aldehyde, alkyne, cyclopropane and aziridine.[6-7]

Although trihalomethylation can be effected by $CX_3$-$CO_2H$,[8] $CX_3$-TMS[9] and other miscellaneous electrophilic and nucleophilic reagents,[10] $CHX_3$ is a simple and convenient reagent, but employed in conjunction with a strong Bronsted base or Lewis acid.[11] However, addition of bromoform to activated imines just in the presence of a metal such as Mg remains unreported.

As part of our interest in the application of Mg-$CHBr_3$ as a reagent system for the facile introduction of $CBr_3$ group, we have reported conjugate addition of bromoform to nitroalkenes[12] and enones.[13-14] In the case of α-substituted enones, especially cyclic ones, the Michael adducts spontaneously cyclized to afford dibromocyclopropanation products.[14-15] Herein we report the addition of bromoform to an electron deficient carbon-heteroatom bond as in *N*-tosylimine and *N*-Boc-imine for the first time.[16]

## Results and discussion

Treatment of N-tosylimines **5** with Mg-$CHBr_3$ under our previous optimized conditions,[12-14] viz 8 equiv of Mg and 22 equiv of $CHBr_3$, afforded the tribromomethylated sulfonamides in good to excellent yield in 2 h (Table 1). N-Tosylimines with strongly electron donating aryl groups **5b-d** and heteroaryl groups **5g-h** afforded the adducts **6b-d** and **6g-h**, respectively, in excellent yield (79-82%, entries 2-4 and 7-8). On the other hand, slighly lower yields (69-75%) of the adducts **6a** and **6e-f** were encountered in the case of N-tosylimines with weakly electron donating and electron withdrawing aryl groups, **5a** and **5e-f**, respectively (entries 1 and 5-6).

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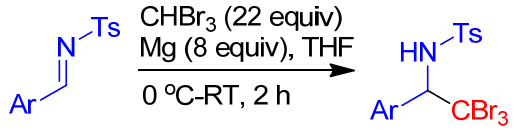
† Electronic supplementary information (ESI) available: NMR and X-ray data tables, complete characterization data and copies NMR spectra. CCDC reference number 984737. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/ x0xx00000x.

**Table 1.** Mg-mediated addition of bromoform to N-tosylimines **5**



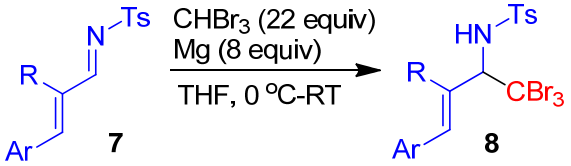

**5** **6**

| Entry | 5 | Ar | 6 | % Yield[a] |
|---|---|---|---|---|
| 1 | **5a** | 4-$MeC_6H_4$ | **6a** | 69 |
| 2 | **5b** | 4-$OMeC_6H_4$ | **6b** | 82 |
| 3 | **5c** | 3, 4-$(OMe)_2C_6H_3$ | **6c** | 80 |
| 4 | **5d** | 4-$NMe_2C_6H_4$ | **6d** | 79 |
| 5 | **5e** | 4-$FC_6H_4$ | **6e** | 75 |
| 6 | **5f** | 4-$NO_2C_6H_4$ | **6f** | 75 |
| 7 | **5g** | 2-furyl | **6g** | 80 |
| 8 | **5h** | 2-thienyl | **6h** | 82 |

[a] After purification by silica gel column chromatography

Having successfully added bromoform to imines **5** under our optimized conditions, we investigated the possible addition of bromoform to electron deficient azadienes such as **7** (Table 2). This too proceeded well with azadienes containining electroneutral and electron rich aryl groups, **7a** and **7b**, to provide exclusively the 1,2-adducts **8a** and **8b** in 59 and 63% yields, respectively (entries 1-2). Azadiene **7c**, possessing an alkyl group in the chain, delivered the adduct **8c** in much higher yield (76%), though the reaction required slightly longer time (5 h, entry 3).

**Table 2.** Mg-Mediated addition of bromoform to N-tosylazadienes **7**



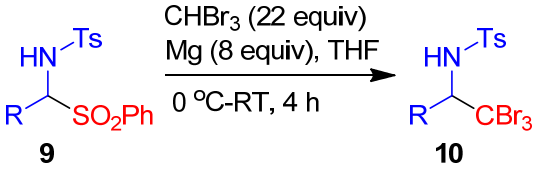

**7** **8**

| Entry | 7 | Ar | R | Time (h) | 8 | % Yield[a] |
|---|---|---|---|---|---|---|
| 1 | **7a** | $C_6H_5$ | H | 3.5 | **8a** | 59 |
| 2 | **7b** | 2-$OMeC_6H_4$ | H | 4 | **8b** | 63 |
| 3 | **7c** | $C_6H_5$ | Me | 5 | **8c** | 76 |

[a] After purification by silica gel column chromatography

At this juncture, it was felt that the Mg-$CHBr_3$ conditions would be suitable not only for the addition of bromoform to imines **5** and **7**, but for the in situ generation of N-tosylimine **5** from its precursor **9** as well.[17] Thus we were pleased to isolate α-tribromomethyl N-sulfonamides **10** in high yields by treating α-sulfonyl N-sulfonamides **9** with Mg-$CHBr_3$ under standard conditions (Table 3). α-Sulfonyl N-sulfonamides with aryl groups **9a** and **9b** underwent smooth transformation to tribromomethyl N-sulfonamides **10a** and **10b**, respectively, in 75 and 81% yields (entries 1-2). The scope of the reaction was further investigated using sulfonamides **9c-f** with R as aralkyl (benzyl), cycloalkyl, *n*-alkyl and H to afford tribromomethyl N-sulfonamides **10c-f** in high (79-86%) yields (entries 3-6).

**Table 3.** One-pot transformation of α-sulfonyl tosylamines **9** to α-tribromomethyl tosyl-amines **10**



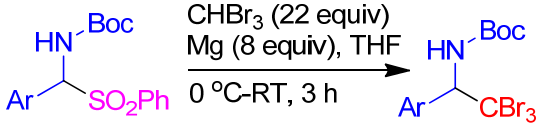

**9** **10**

| Entry | 9 | R | 10 | % Yield[a] |
|---|---|---|---|---|
| 1 | **9a** | $C_6H_5$ | **10a** | 75 |
| 2 | **9b** | 3,4-$Me_2C_6H_3$ | **10b** | 81 |
| 3 | **9c** | $C_6H_4CH_2$ | **10c** | 86 |
| 4 | **9d** | cyclohexyl | **10d** | 84 |
| 5 | **9e** | *n*-butyl | **10e** | 79 |
| 6 | **9f** | H | **10f** | 85 |

[a] After purification by silica gel column chromatography

The successful transformation of sulfonyl sulfonamides **9** to tribromomethyl sulfonamides **10** in one-pot encouraged us to investigate the scope of the electron withdrawing group on N. Therefore, the corresponding Boc derivatives **11** were subjected to the standard conditions of tribromomethylation (Table 4). Again, we were pleased to isolate tribromomethylated Boc-amines **12** in high yield. Sulfonyl Boc-amines with diverse substituents, viz. electroneutral **11a**, electron donating **11b-d** and electron withdrawing **11e-f** reacted with bromoform in the presence of Mg over 3 h to provide tribromomethyl Boc-amines **12a-f** in 75-84% yield. No appreciable substituent effect was discernible in these transformations.

**Table 4.** One-Pot transformation of α-sulfonyl Boc-amines **11** to α-tribromomethyl Boc-amines **12**




**11** **12**

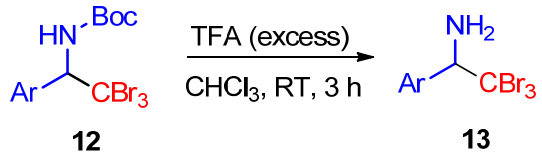
| Entry | 11 | Ar | 12 | % Yield[a] |
|---|---|---|---|---|
| 1 | **11a** | $C_6H_5$ | **12a** | 75 |
| 2 | **11b** | 4-$MeC_6H_4$ | **12b** | 83 |
| 3 | **11c** | 4-$OMeC_6H_4$ | **12c** | 78 |
| 4 | **11d** | 4-$SMeC_6H_4$ | **12d** | 84 |
| 5 | **11e** | 4-$FC_6H_4$ | **12e** | 81 |
| 6 | **11f** | 3-$NO_2C_6H_4$ | **12f** | 80 |

[a] After purification by silica gel column chromatography

Finally, generation of tribromomethylated free amine **13** by removal of the protecting group was explored. Boc-amines **12** underwent smooth deprotection with TFA in chloroform at

room temperature to provide free amines **13** in nearly quantitative yield (90-97%).

**Table 5.** Boc deprotection of α-tribromomethyl Boc-amines **12**




**12** **13**

| Entry | 12 | R | 13 | % Yield[a] |
|---|---|---|---|---|
| 1 | **12a** | $C_6H_5$ | **13a** | 90 |
| 2 | **12b** | 4-$MeC_6H_4$ | **13b** | 97 |
| 3 | **12c** | 4-$OMeC_6H_4$ | **13c** | 91 |
| 4 | **12d** | 4-$SMeC_6H_4$ | **13d** | 90 |
| 5 | **12e** | 4-$FC_6H_4$ | **13e** | 95 |

[a] After purification by silica gel column chromatography

The structure and the stereochemistry of the products were confirmed by detailed analysis of $^1$H, $^{13}$C and $^1$H-$^1$H COSY NMR data. In the $^1$H NMR of protected amines **6**, **8**, **10** and **12**, in general, NH appeared as a doublet in the range of δ 5.50-6.50 with a *J* value of 9.0-10.5 Hz due to coupling with the vicinal CH which appeared in the range of δ 4.50-5.50. The $CBr_3$ carbons in the protected amines **6**, **8**, **10** and **12**, appeared in the range of δ 45-51 whereas in the free amine **13**, it was deshielded to δ 59-61. The *E* geometry for the double bond in **8** was evident from a *J* value of 15.7-15.9 Hz for the olefinic protons in **8a-b**. Finally, the structure was unambiguously established by single crystal X-ray analysis of a representative compound **8b** (Figure 2).

A *J* value of 9.0-10.5 Hz for the CH-NH vicinal protons is indicative of their anti-periplanar relationship which in turn suggests that the bulky $CBr_3$ group and Ts (Boc) group prefer to be anti to each other. That the same conformer is favored in solid state as well is evident from the X-ray data (a dihedral angle of 160.5° for $Br_3C$-C-C-N-S in **8b**, Figure 2).

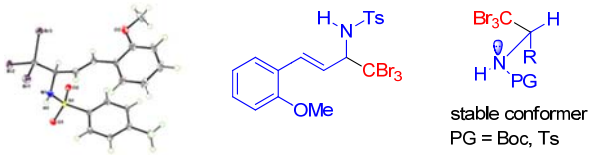
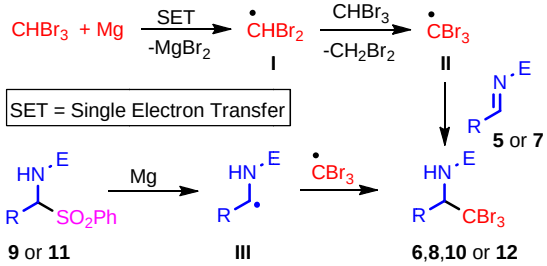


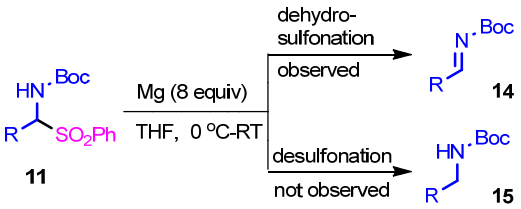

**Figure 2.** X-ray crystal structure of **8b**

As for the mechanism of the reaction, both radical and anionic pathways were considered (Schemes 1-3). In the direct tribromomethylation of imine **5** or **7**, Mg mediated formation of $CBr_3$ radical via single electron transfer (SET) and its addition to imine **5** or **7** appeared feasible (Scheme 1). In the one-pot transformation of sulfonyl *N*-tosylamine or *N*-Boc-amine **9** or **11**, formation of aminoalkyl radical **III** via Mg mediated desulfonation of **9** or **11** and its coupling with $CBr_3$ radical was a possibility.



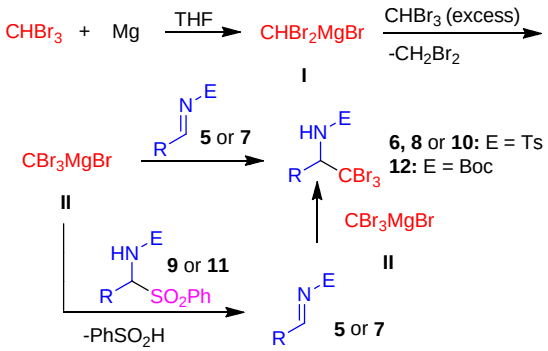

**Scheme 1**

In order to verify whether the Mg mediated desulfonation took place in the one-pot process, a control experiment was conducted with sulfonyl *N*-Boc-amine **11** by excluding bromoform from the reaction (Scheme 2). Interestingly, the only product isolated was the dehydrosulfonation product, imine **14**, suggesting that Mg acted as a base. There was no evidence for the formation of desulfonation product **15** ruling out any radical intermediacy. Furthermore, when *N*-Boc-amine **11a** was subjected to Mg-mediated bromoform addition in the presence of 50 mol % TEMPO, there was no appreciable change in the reaction time or isolated yield of the product **12a**, thus ruling out the radical pathway.



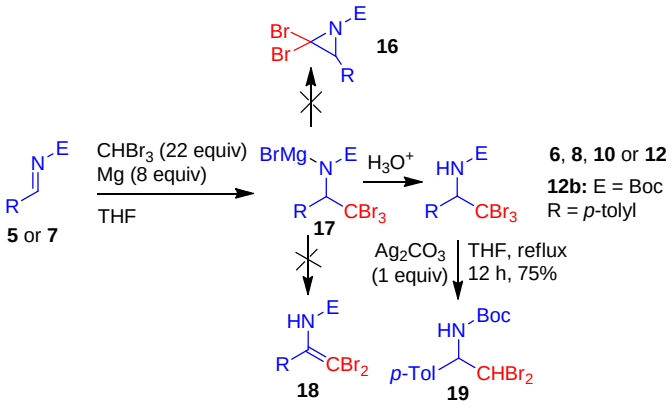

**Scheme 2**

In view of the above results, an anionic mechanism is proposed for the tribromomethylation of imines **5** and **7** and their precursors **9** and **11** (Scheme 3). Initial oxidative addition of Mg to bromoform generates dibromomethylmagnesium bromide **I** which acts as a base and deprotonates bromoform to generate tribromomethylmagnesium bromide **II**. 1,2-Addition of **II** to imine **5** or **7** generates tribromomethylated amine **6**, **8**, **10** or **12**. In the one-pot reaction, imine **5** or **7** could be generated either by Mg or by reagents **I** or **II** via dehydrosulfonation.




**Scheme 3**

Addition of α-dihalocarbanion to imine was reported to give a mixture of products, aziridine being the major one.[18] However, in our case, formation of aziridine **16** or vicarious elimination product **18** was not observed presumably due to the strong co-ordination of Mg with N and stabilization of the intermediate as in **17** (Scheme 4). Such co-ordination of Mg ion with the imine N also had a rate accelerating effect in that the reaction which was initially sluggish proceeded at a faster rate after 30 min. However, our attempts to cyclize a representative tribromomethylated amine **12b** using a halophilic salt such as silver carbonate led to monodebromination to afford dibromide **19**.




**Scheme 4.** Diverse pathways after addition of $CHBr_3$ to N-tosyl- and *N*-Boc-imines

## Conclusions

In conclusion, a simple and convenient method for the 1,2-addition of tribromomethyl group to electron deficient imines has been developed using bromoform and Mg. This reagent system could be employed for the α-tribromomethylation of *N*-tosylimines and *N*-Boc-imines. A one-pot transformation of imine precursors, α-sulfonyl derivatives, via dehydrosulfonation and tribromomethylation to tribromomethylated adducts could be carried out using the same reagent system thus demonstrating its simplicity, efficiency and dual reactivity. Further, selected transformations of tribromomethylated *N*-Boc-amines to free α-tribromomethylamines and monodebromination products highlight the synthetic potential of our methodology.

## Experimental Section

**General.** The melting points recorded are uncorrected. The $^1H$ NMR spectra were recorded at 400 MHz and the $^1H$ decoupled $^{13}C$ NMR spectra were recorded at 100 MHz or 75 MHz with TMS as the internal standard. The coupling constants (*J* values) are given in Hz. The high resolution mass spectra were recorded under ESI Q-TOF conditions. X-ray data were collected on a diffractometer equipped with Mo Kα radiation. The structure was solved by direct methods shelxs97 and refined by full-matrix least squares against $F^2$ using shelxl97 software.

**General Procedure for Tribromomethylation.** To a stirred solution of magnesium (97 mg, 4 atom g) and imines **5** or **7**, or α-sulfonylamines **9** or **11** (0.5 mmol) in THF (10 mL) was added bromoform (2.7 g, 1 mL, 11 mmol) dropwise over a period of 10 min at 0 °C. The reaction mixture was gradually brought to room temperature over a period of 2 h during which the solution turned dark brown. The reaction mixture was subsequently quenched with saturated solution of $NH_4Cl$ (10 mL). The aqueous layer was extracted with ethyl acetate (5 × 20 mL) and the combined organic layers were washed with $H_2O$ (3 × 10 mL), dried (anhyd $Na_2SO_4$), and concentrated in vacuo to afford the crude product, which was subjected to silica gel column chromatography (ethyl acetate/hexane mixture, gradient elution) to afford the product **6**, **8**, **10** or **12**.

**4-Methyl *N*-(2,2,2-tribromo-1-(p-tolyl)ethyl)benzene-sulfonamide (6a).** Colorless solid; Yield 181 mg, 69%; mp 178-180 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3271brs, 1335s, 1162vs, 744s; $\delta_H$ (400 MHz, $CDCl_3$) 7.52 (2H, d, *J* 8.3 Hz), 7.22 (2H, d, *J* 8.1 Hz), 7.04 (2H, d, *J* 8.3 Hz), 6.96 (2H, d, *J* 8.1 Hz), 5.95 (1H, d, *J* 9.7 Hz), 5.12 (1H, d, *J* 9.7 Hz), 2.32 (3H, s), 2.28 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 143.6, 139.2, 136.7, 131.6, 129.6, 129.4, 128.6, 127.4, 73.1, 48.1, 21.6, 21.3; MS (ES$^+$, Ar) m/z (rel intensity) 552 ([M+6]Na$^+$, 3), 550 ([M+4]Na$^+$, 9), 548 ([M+2]Na$^+$, 9), 546 (MNa$^+$, 3), 530 ([MH+6]$^+$, 3), 528 ([MH+4]$^+$, 9), 526 ([MH+2]$^+$, 9), 524 (MH$^+$, 3), 359 (28), 357 (100), 355 (90), 353 (25); HRMS (ES$^+$, Ar) calcd for $C_{16}H_{17}NO_2SBr_3$ (MH$^+$) 523.8525, found 523.8504.

**4-Methyl-*N*-(2,2,2-tribromo-1-(4-methoxyphenyl)ethyl)-benzenesulfonamide (6b).** Colorless solid; Yield 222 mg, 82%; mp 178-180 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3255brm, 1331s, 1164s, 669m; $\delta_H$ (400 MHz, $CDCl_3$) 7.54 (2H, d, *J* 8.2 Hz), 7.26 (2H, d, *J* 8.7 Hz), 7.05 (2H, d, *J* 8.2 Hz), 6.67 (2H, d, *J* 8.7 Hz), 6.13 (1H, d, *J* 9.7 Hz), 5.12 (1H, d, *J* 9.7 Hz), 3.75 (3H, s), 2.34 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 160.2, 143.6, 136.8, 131.0, 129.4, 127.4, 126.5, 113.3, 72.9, 55.4, 48.9, 21.6; MS (ES$^+$, Ar) m/z (rel intensity) 568 ([MNa+6]$^+$, 15), 566 ([MNa+4]$^+$, 46), 564 ([MNa+2]$^+$, 50), 562 ([MNa]$^+$, 15), 462 (100), 377 (95); HRMS (ES$^+$, Ar) calcd for $C_{16}H_{16}NO_3SBr_3Na$ (MNa$^+$) 561.8293, found 561.8279.

**4-Methyl-*N*-(2,2,2-tribromo-1-(3,4-dimethoxyphenyl)-ethyl)benzenesulfonamide (6c).** Colorless solid; Yield 228 mg, 80%; mp 174-176 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3270brm, 1335s, 1270s, 1161vs, 693m, 668m; $\delta_H$ (400 MHz, $CDCl_3$) 7.56 (2H, d, *J* 8.2 Hz), 7.04 (2H, d, *J* 8.2 Hz), 6.88 (1H, s), 6.85 (1H, d, *J* 10 Hz), 6.61 (2H, d, *J* 9.1 Hz), 5.10 (1H, d, *J* 10.0 Hz), 3.82 (3H, s), 3.76 (3H, s), 2.31 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 149.6, 148.2, 143.6, 136.6, 129.3, 127.4, 126.7, 123.1, 112.3, 110.1, 73.2, 56.0, 55.9, 48.7, 21.5; MS (ES$^+$, Ar) m/z (rel intensity) 1173 ([2MNa+12]$^+$, 7), 1171 ([2MNa+10]$^+$, 35), 1169 ([2MNa+8]$^+$, 91), 1167 ([2MNa+6]$^+$, 100), 1165

([2MNa+4]$^+$, 75), 1163 ([2MNa+2]$^+$, 34), 1161 ([2MNa]$^+$, 6); HRMS (ES$^+$, Ar) calcd for $C_{34}H_{36}N_2O_8S_2Br_6Na$ (2MNa$^+$) 1160.6906, found 1160.6963.

**4-Methyl-*N*-(2,2,2-tribromo-1-(4-(dimethylamino)phenyl)-ethyl)benzenesulfonamide (6d).** Colorless solid; Yield 219 mg, 79%; mp 136-138 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3261brw, 1333s, 1162vs, 670w; $\delta_H$ (400 MHz, $CDCl_3$) 7.54 (2H, d, *J* 8.2 Hz), 7.17 (2H, d, *J* 8.7 Hz), 7.06 (2H, d, *J* 8.2 Hz), 6.47 (2H, d, *J* 8.7 Hz), 5.89 (1H, d, *J* 9.6 Hz), 5.08 (1H, d, *J* 9.6 Hz), 2.94 (6H, s), 2.33 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 150.3, 143.2, 136.8, 130.7, 129.3, 127.4, 121.5, 111.7, 73.2, 50.4, 40.7, 21.6; MS (ES$^+$, Ar) m/z (rel intensity) 559 ([MH+6]$^+$, 13), 557 ([MH+4]$^+$, 34), 555 ([MH+2]$^+$, 34), 553 ([MH]$^+$, 13), 413 (100), 301 (55); HRMS (ES$^+$, Ar) calcd for $C_{17}H_{20}N_2O_2SBr_3$ (MH$^+$) 552.8790, found 552.8783.

**4-Methyl-*N*-(2,2,2-tribromo-1-(4-fluorophenyl)ethyl)-benzenesulfonamide (6e).** Colorless solid; Yield 198 mg, 75%; mp 200-202 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3258brm, 1334s,1162vs, 663s; $\delta_H$ (400 MHz, $CDCl_3$) 7.53 (2H, d, *J* 8.1 Hz), 7.34 (2H, dd, *J* 8.7, 5.2 Hz), 7.08 (2H, d, *J* 8.1 Hz), 6.86 (2H, t, *J* 8.7 Hz), 6.06 (1H, d, *J* 9.4 Hz), 5.16 (1H, d, *J* 9.4 Hz), 2.34 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 163.1 (d, *J* 240.0 Hz), 144.0, 136.7, 131.7 (d, *J* 7.0 Hz), 130.5, 129.5, 127.3, 115.0 (d, *J* 21.0 Hz), 72.6, 47.3, 21.6; $\delta_F$ (470 MHz, $CDCl_3$) -111.9; MS (ES$^+$, Ar) m/z (rel intensity) 534 ([MH+6]$^+$, 36), 532 ([MH+4]$^+$, 100), 530 ([MH+2]$^+$, 95), 528 ([MH]$^+$, 35); HRMS (ES$^+$, Ar) calcd for $C_{15}H_{14}NO_2FSBr_3$ (MH$^+$) 527.8279, found 527.8290.

**4-Methyl-*N*-(2,2,2-tribromo-1-(4-nitrophenyl)ethyl)-benzenesulfonamide (6f).** Pale yellow solid; Yield 208 mg, 75%; mp 204-206 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3271brm, 1523s, 1437m, 1347vs, 1163s, 564m, 541m; $\delta_H$ (400 MHz, $CDCl_3$) 8.04 (2H, d, *J* 8.8 Hz), 7.60 (2H, d, *J* 8.8 Hz), 7.55 (2H, d, *J* 8.2 Hz), 7.10 (2H, d, *J* 8.2 Hz), 6.04 (1H, d, *J* 9.0 Hz), 5.26 (1H, d, *J* 9.0 Hz), 2.32 (3H s); $\delta_C$ (100 MHz, acetone-$d_6$) 148.6, 144.3, 142.7, 138.4, 132.5, 130.0, 128.0, 123.2, 73.4, 46.5, 21.2; MS (ES$^+$, Ar) m/z (rel intensity) 599 ([MK+6]$^+$, 31), 597 ([MK+4]$^+$, 80), 595 ([MK+2]$^+$, 78), 593 ([MK]$^+$, 22), 413 (100); HRMS (ES$^+$, Ar) calcd for $C_{15}H_{13}N_2O_4SBr_3K$ (MK$^+$) 592.7778, found 592.7781.

**4-Methyl-*N*-(2,2,2-tribromo-1-(furan-2-yl)ethyl)benzene-sulfonamide (6g).** Colorless solid; Yield 200 mg, 80%; mp 174-176 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3247brm, 1329vs, 1165vs, 699m, 528m; $\delta_H$ (400 MHz, $CDCl_3$) 7.62 (2H, d, *J* 8.2 Hz), 7.22 (1H, d, *J* 1.4 Hz), 7.16 (2H, d, *J* 8.2 Hz), 6.35 (1H, d, *J* 3.3 Hz), 6.18 (1H, dd, *J* 3.3, 1.4 Hz), 5.95 (1H, d, *J* 10.4 Hz), 5.29 (1H, d, *J* 10.5 Hz), 2.36 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 147.3, 143.8, 142.8, 136.8, 129.6, 127.2, 112.0, 110.7, 67.8, 45.8, 21.7; MS (ES$^+$, Ar) m/z (rel intensity) 528 ([MNa+6]$^+$, 30), 526 ([MNa+4]$^+$, 100), 524 ([MNa+2]$^+$, 100), 522 ([MNa]$^+$, 33), 422 (5), 343 (5); HRMS (ES$^+$, Ar) calcd for $C_{13}H_{12}NO_3SBr_3Na$ (MNa$^+$) 521.7980, found 521.7986.

**4-Methyl-*N*-(2,2,2-tribromo-1-(thiophen-2-yl)ethyl)-benzenesulfonamide (6h).** Colorless solid; Yield 212 mg, 82%; mp 178-180 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3243brm, 1328s, 1162s, 730m; $\delta_H$ (400 MHz, $CDCl_3$) 7.56 (2H, d, *J* 8.3 Hz), 7.20 (1H, d, *J* 5.1 Hz), 7.11 (2H, d, *J* 8.3 Hz), 7.00 (1H, d, *J* 3.6 Hz), 6.78 (1H, dd, *J* 5.1, 3.6 Hz), 5.75–5.62 (1H, br unresolved), 5.47 (1H, d, *J* 9.9 Hz), 2.35 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 143.8, 137.3, 136.9, 130.4, 129.5, 127.3, 127.2, 126.1, 70.1, 47.6, 21.7; MS (ES$^+$, Ar) m/z (rel intensity) 544 ([MNa+6]$^+$, 35), 542 ([MNa+4]$^+$, 100), 540 ([MNa+2]$^+$, 94), 538 ([MNa]$^+$, 32), 438 (22); HRMS (ES$^+$, Ar) calcd for $C_{13}H_{12}NO_2S_2Br_3Na$ (MNa$^+$) 537.7752, found 537.7749.

**(*E*)-4-Methyl-*N*-(1,1,1-tribromo-4-phenylbut-3-en-2-yl)-benzenesulfonamide (8a).** Colorless solid; Yield 158 mg, 59%; mp 144-146 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3365brvs, 1651br, s, 1335m, 1165s, 789m, 752m; $\delta_H$ (400 MHz, $CDCl_3$) 7.81 (2H, d, *J* 7.4 Hz), 7.30-7.22 (3H, m), 7.20-7.10 (4H, m), 6.33 (1H, d, *J* 15.7 Hz), 6.00 (1H, dd, *J* 15.7, 8.0 Hz), 5.52 (1H, d, *J* 9.7 Hz), 4.68 (1H, t, *J* 8.0 Hz), 2.22 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 144.1, 137.4, 137.3, 135.5, 129.8, 128.8, 128.7, 127.6, 126.9, 122.3, 72.3, 48.3, 21.6; MS (ES$^+$, Ar) m/z (rel intensity) 564 ([MNa+6]$^+$, 36), 562 ([MNa+4]$^+$, 100), 560 ([MNa+2]$^+$, 100), 558 ([MNa]$^+$, 35), 458 (55), 378 (50), 301 (22); HRMS (ES$^+$, Ar) calcd for $C_{17}H_{16}NO_2SBr_3Na$ (MNa$^+$) 557.8344, found 557.8347.

**(*E*)-4-Methyl-*N*-(1,1,1-tribromo-4-(2-methoxyphenyl)but-3-en-2-yl)benzenesulfonamide (8b).** Colorless solid; Yield 178 mg, 63%; mp 146-148 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3396brvs, 1651vs, 1337m, 1167s, 856m, 746m; $\delta_H$(400 MHz, $CDCl_3$) 7.80 (2H, d, *J* 8.2 Hz), 7.26-7.21 (1H, m), 7.17-7.15 (1H, m), 7.13 (2H, d, *J* 8.2 Hz), 6.88-6.81 (2H, m), 6.76 (1H, d, *J* 15.9 Hz), 6.06 (1H, dd, *J* 15.9, 7.7 Hz), 5.55 (1H, d, *J* 9.7 Hz), 4.71 (1H, dd, *J* 9.7, 7.7 Hz), 3.84 (3H, s), 2.23 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 157.1, 143.8, 137.4, 132.6, 129.8, 129.7, 127.6, 127.5, 124.4, 122.5, 120.6, 111.0, 72.9, 55.6, 49.1, 21.5; MS (ES$^+$, Ar) m/z (rel intensity) 594 ([MNa+6]$^+$, 34), 592 ([MNa+4]$^+$, 100), 590 ([MNa+2]$^+$, 100), 588 ([MNa]$^+$, 31), 408 (20); HRMS (ES$^+$, Ar) calcd for $C_{18}H_{18}NO_3SBr_3Na$ (MNa$^+$) 587.8450, found 587.8457. Selected X-ray data for **8b:** $C_{18}H_{18}Br_3NO_3S$, *M* = 568.12, Monoclinic, space group *P 21/n*, *a* = 10.212(3) Å, *b* = 11.258(3) Å, *c* = 17.747(4) Å, $\alpha$ = 90.00 °, $\beta$ = 98.985(4) °, $\gamma$ = 90.00 °, *V* = 2015.3(9) Å$^3$, $D_c$ = 1.872 Mg/m$^3$, *Z* = 4, F(000) = 1112, $\lambda$ = 0.71073 Å, $\mu$ = 6.127 mm$^{-1}$, Total/ unique reflections = 15300 / 3677 [R(int) = 0.0658], *T* = 100(2) K, $\theta$ range = 3.07 to 25.34 °, Final *R* [I>2$\sigma$(I)]: R1 = 0.0286, wR2 = 0.0584, *R* (all data): R1 = 0.0351, wR2 = 0.0600.

**(*E*)-4-methyl-*N*-(1,1,1-tribromo-3-methyl-4-phenylbut-3-en-2-yl)benzenesulfonamide (8c).** Colorless solid; Yield 210 mg, 76%; mp 164-165 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 3263m, 1334s, 1163vs, 723m, 669m; $\delta_H$ (400 MHz, $CDCl_3$) 7.78 (2H, d, *J* 8.1 Hz), 7.31–7.23 (3H, m), 7.20 (2H, d, *J* 8.1 Hz), 7.03-6.98 (2H, m), 6.49 (1H, d, *J* 0.7 Hz), 6.01 (1H, d, *J* 9.9 Hz), 4.79 (1H, d, *J* 9.9 Hz), 2.32 (3H, s), 1.75 (3H, d, *J* 0.7 Hz); $\delta_C$ (100

MHz, $CDCl_3$) 143.9, 137.3, 136.2, 136.0, 131.4, 129.7, 129.1, 128.2, 127.5 (× 2), 77.0, 46.1, 21.6, 15.1; MS ($ES^+$, Ar) m/z (rel intensity) 578 ($[MNa+6]^+$, 15), 576 ($[MNa+4]^+$, 50), 574 ($[MNa+2]^+$, 48), 572 ($MNa^+$, 15), 573 ($[M+H_2O+6]^+$, 27), 571 ($[M+H_2O+4]^+$, 100), 569 ($[M+H_2O+2]^+$, 97), 567 ($[M+H_2O]^+$, 27); HRMS ($ES^+$, Ar) calcd for $C_{18}H_{18}NO_2SBr_3Na$ ($MNa^+$) 571.8501, found 571.8505.

**4-Methyl-*N*-(2,2,2-tribromo-1-phenylethyl)benzene-sulfonamide (10a).** Colorless solid; Yield 192 mg, 75%; mp 232-233 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3254brm, 1644 brs, 1332s, 1162vs, 708w; $\delta_H$ (400 MHz, $CDCl_3$) 7.50 (2H, d, *J* 8.2 Hz), 7.34 (2H, d, *J* 7.4 Hz), 7.29–7.24 (1H, m), 7.16 (2H, t, *J* 7.4 Hz), 7.03 (2H, d, *J* 8.2 Hz), 5.83 (1H, d, *J* 9.6 Hz), 5.16 (1H, d, *J* 9.6 Hz), 2.30 (3H, s); $\delta_C$ (125 MHz, DMSO-$d_6$) 142.2, 137.6, 134.4, 129.9, 128.8, 128.1, 127.1, 126.4, 72.9, 50.0, 20.8; MS ($ES^+$, Ar) m/z (rel intensity) 538 ($[MNa+6]^+$, 34), 536 ($[MNa+4]^+$, 97), 534 ($[MNa+2]^+$, 100), 532 ($[MNa]^+$, 34), 432 (95); HRMS ($ES^+$, Ar) calcd for $C_{15}H_{14}NO_2SBr_3Na$ ($MNa^+$) 531.8188, found 531.8189.

**4-Methyl-*N*-(2,2,2-tribromo-1-(3,4-dimethylphenyl)ethyl)-benzenesulfonamide (10b).** Colorless solid; Yield 219 mg, 81%; mp 181-182 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3253brs, 1645brm, 1330vs, 1160vs, 663s; $\delta_H$ (400 MHz, $CDCl_3$) 7.54 (2H, d, *J* 8.2 Hz), 7.12 (1H, dd, *J* 7.8, 1.7 Hz), 7.00 (2H, d, *J* 8.2 Hz), 6.97 (1H, d, *J* 1.7 Hz), 6.90 (1H, d, *J* 7.8 Hz), 6.43 (1H, d, *J* 10.1 Hz), 5.10 (1H, d, *J* 10.1 Hz), 2.30 (3H, s), 2.15 (3H, s), 2.09 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 143.3, 137.5, 136.6, 135.9, 131.7, 131.0, 129.1 (× 2), 127.3, 127.2, 73.3, 48.3, 21.5, 19.7, 19.6; MS ($ES^+$, Ar) m/z (rel intensity) 566 ($[MNa+6]^+$, 40), 564 ($[MNa+4]^+$, 100), 562 ($[MNa+2]^+$, 100), 560 ($[MNa]^+$, 35), 460 (75), 405 (25), 379 (30); HRMS ($ES^+$, Ar) calcd for $C_{17}H_{18}NO_2SBr_3Na$ ($MNa^+$) 559.8501, found 559.8506.

**4-Methyl-*N*-(1,1,1-tribromo-3-phenylpropan-2-yl)-benzenesulfonamide (10c).** Colorless solid; Yield 226 mg, 86%; mp 199-201 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3281m, 1333s, 1158vs, 668m; $\delta_H$ (400 MHz, $CDCl_3$) 7.36 (2H, d, *J* 8.2 Hz), 7.22–7.15 (3H, m), 7.13–7.10 (2H, m), 7.05 (2H, d, *J* 8.2 Hz), 5.05 (1H, d, *J* 9.7 Hz), 4.53 (1H, td, *J* 9.7, 2.5 Hz), 3.78 (1H, dd, *J* 14.3, 2.5 Hz), 2.76 (1H, dd, *J* 14.3, 9.7 Hz), 2.36 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 143.0, 138.5, 135.7, 129.7, 129.5, 128.8, 127.1, 126.8, 72.8, 50.7, 40.6, 21.7; MS ($ES^+$, Ar) m/z (rel intensity) 552 ($[MNa+6]^+$, 34), 550 ($[MNa+4]^+$, 100), 548 ($[MNa+2]^+$, 97), 546 ($[MNa]^+$, 34); HRMS ($ES^+$, Ar) calcd for $C_{16}H_{16}NO_2SBr_3Na$ ($MNa^+$) 545.8344, found 545.8337.

**4-Methyl-*N*-(2,2,2-tribromo-1-cyclohexylethyl)benzene-sulfonamide (10d).** Colorless solid; Yield 217 mg, 84%; mp 199-200 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3274brvs, 1337s, 1162s, 925w; $\delta_H$ (400 MHz, $CDCl_3$) 7.82 (2H, d, *J* 8.2 Hz), 7.29 (2H, d, *J* 8.2 Hz), 5.40 (1H, d, *J* 10.5 Hz), 3.95 (1H, dd, *J* 10.5, 1.9 Hz), 2.41 (3H, s), 2.01-1.98 (1H, m), 1.93-1.55 (5H, m), 1.35-1.18 (3H, m), 1.08-0.07 (2H, m); $\delta_C$ (100 MHz, $CDCl_3$) 143.8, 138.3, 129.6, 127.6, 74.4, 50.6, 41.4, 34.0, 29.5, 26.7, 26.2, 25.9, 21.7; MS ($ES^+$, Ar) m/z (rel intensity) 544 ($[MNa+6]^+$, 36), 542 ($[MNa+4]^+$, 96), 540 ($[MNa+2]^+$, 100), 538 ($[MNa]^+$, 35); HRMS ($ES^+$, Ar) calcd for $C_{15}H_{20}NO_2SBr_3Na$ ($MNa^+$) 537.8657, found 537.8655.

**4-Methyl-*N*-(1,1,1-tribromohexan-2-yl)benzene-sulfonamide (10e).** Colorless solid; Yield 195 mg, 79%; mp 144-145 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3255s, 1332vs, 1158vs, 559s, 546s; $\delta_H$ (400 MHz, $CDCl_3$) 7.81 (2H, d, *J* 8.2 Hz), 7.26 (2H, d, *J* 8.2 Hz), 5.51 (1H, d, *J* 9.7 Hz), 4.07 (1H, td, *J* 9.7, 2.2 Hz), 2.39 (3H, s), 2.33-2.25 (1H, m), 1.65-1.55 (1H, m), 1.34-1.18 (4H, m), 0.80 (3H, t, *J* 6.9 Hz); $\delta_C$ (100 MHz, $CDCl_3$) 143.6, 138.8, 129.5, 127.3, 71.1, 51.4, 34.2, 28.3, 22.4, 21.7, 13.9; MS ($ES^+$, Ar) m/z (rel intensity) 518 ($[MNa+6]^+$, 36), 516 ($[MNa+4]^+$, 82), 514 ($[MNa+2]^+$, 100), 512 ($[MNa]^+$, 32), 496 ($[MH+6]^+$, 7), 494 ($[MH+4]^+$, 27), 492 ($[MH+2]^+$, 27), 490 ($MH^+$, 9), 462 (5); HRMS ($ES^+$, Ar) calcd for $C_{13}H_{18}NO_2SBr_3Na$ ($MNa^+$) 511.8501, found 513.8484.

**4-Methyl-*N*-(2,2,2-tribromoethyl)benzenesulfonamide (10f).** Colorless solid; Yield 185 mg, 85%; mp 117-118 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3278vs, 1320vs, 1161vs, 727w; $\delta_H$ (400 MHz, $CDCl_3$) 7.81 (2H, d, *J* 8.2 Hz), 7.31 (2H, d, *J* 8.2 Hz), 6.00 (1H, t, *J* 7.0 Hz), 4.13 (2H, d, *J* 7.0 Hz), 2.42 (3H, s); $\delta_C$ (100 MHz, $CDCl_3$) 144.2, 137.3, 130.0, 127.2, 64.3, 40.2, 21.7; MS ($ES^+$, Ar) m/z (rel intensity) 462 ($[MNa+6]^+$, 38), 460 ($[MNa+4]^+$, 100), 458 ($[MNa+2]^+$, 87), 456 ($[MNa]^+$, 33), 440 ($[MH+6]^+$, 11), 438 ($[MH+4]^+$, 35), 436 ($[MH+2]^+$, 33), 434 ($[MH]^+$, 9), 413 (75), 389 (10; HRMS ($ES^+$, Ar) calcd for $C_9H_{10}NO_2SBr_3Na$ ($MNa^+$) 455.7875, found 455.7861.

***tert*-Butyl (2,2,2-tribromo-1-phenylethyl)carbamate (12a).** Colorless solid; Yield 171 mg, 75%; mp 172-174 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3307m, 1695vs, 1521vs, 1497vs, 1248s, 1167vs, 706s; $\delta_H$ (400 MHz, $CDCl_3$) 7.62-7.58 (2H, m), 7.42-7.35 (3H, m), 5.74 (1H, br d, *J* 9.3 Hz), 5.63 (1H, br d, *J* 9.3 Hz), 1.45 (9H, s); $\delta_C$ (100 MHz, $CDCl_3$) 154.4, 135.9, 129.9, 129.2, 128.1, 81.0, 70.0, 51.0, 28.5; MS ($ES^+$, Ar) m/z (rel intensity) 484 ($[MNa+6]^+$, 32), 482 ($[MNa+4]^+$, 100), 480 ($[MNa+2]^+$, 96), 478 ($[MNa]^+$, 30); HRMS ($ES^+$, Ar) calcd for $C_{13}H_{16}NO_2Br_3Na$ ($MNa^+$) 477.8629, found 477.8642.

***tert*-Butyl (2,2,2-tribromo-1-(p-tolyl)ethyl)carbamate (12b).** Colorless solid; Yield 195 mg, 83%; mp 160-162 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3305w, 1702vs, 1511vs, 1497vs, 1166vs, 680w, 578w; $\delta_H$ (400 MHz, $CDCl_3$) 7.48 (2H, d, *J* 8.0 Hz), 7.19 (2H, d, *J* 8.0 Hz), 5.68 (1H, br d, *J* 9.7 Hz), 5.59 (1H, br d, *J* 9.7 Hz), 2.36 (3H, s), 1.45 (9H, s); $\delta_C$ (100 MHz, $CDCl_3$) 154.3, 139.1, 132.9, 129.7, 128.8, 80.9, 69.8, 51.4, 29.4, 21.4; MS ($ES^+$, Ar) m/z (rel intensity) 498 ($[MNa+6]^+$, 33), 496 ($[MNa+4]^+$, 83), 494 ($[MNa+2]^+$, 100), 492 ($[MNa]^+$, 33); HRMS ($ES^+$, Ar) calcd for $C_{14}H_{18}NO_2Br_3Na$ ($MNa^+$) 491.8785, found 491.8790.

***tert*-Butyl (2,2,2-tribromo-1-(4-methoxyphenyl)ethyl)-carbamate (12c).** Colorless solid; Yield 190 mg, 78%; mp 143-145 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3424brs, 1699s, 1513s, 1246s,

1166s, 747m; $\delta_H$ (400 MHz, $CDCl_3$) 7.51 (2H, d, *J* 8.8 Hz), 6.89 (2H, d, *J* 8.8 Hz), 5.69 (1H, br d, *J* 9.3 Hz), 5.57 (1H, br d, *J* 9.3 Hz), 3.81 (3H, s), 1.44 (9H, s); $\delta_C$ (100 MHz, $CDCl_3$) 160.1, 154.3, 131.1, 127.9, 113.4, 80.9, 69.6, 55.4, 52.0, 28.4; MS ($ES^+$, Ar) m/z (rel intensity) 514 ($[MNa+6]^+$, 20), 512 ($[MNa+4]^+$, 76), 510 ($[MNa+2]^+$, 100), 508 ($[MNa]^+$, 35); HRMS ($ES^+$, Ar) calcd for $C_{14}H_{18}NO_3Br_3Na$ ($MNa^+$) 507.8734, found 507.8729.

***tert*-Butyl (2,2,2-tribromo-1-(4-(methylthio)phenyl)ethyl)-carbamate (12d).** Colorless solid; Yield 212 mg, 84%; mp 136-137 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3305w, 1699vs, 1494vs, 1163vs, 741m; $\delta_H$ (400 MHz, $CDCl_3$) 7.49 (2H, d, *J* 8.2 Hz), 7.23 (2H, d, *J* 8.2 Hz), 5.66 (1H, br d, *J* 8.9 Hz), 5.58 (1H, br d, *J* 8.9 Hz), 2.49 (3H, s), 1.45 (9H, s); $\delta_C$ (100 MHz, $CDCl_3$) 154.3, 140.1, 132.3, 130.2, 125.5, 81.0, 69.7, 50.9, 28.4, 15.5; MS ($ES^+$, Ar) m/z (rel intensity) 530 ($[MNa+6]^+$, 35), 528 ($[MNa+4]^+$, 100), 526 ($[MNa+2]^+$, 100), 524 ($[MNa]^+$, 35); HRMS ($ES^+$, Ar) calcd for $C_{14}H_{18}NO_2Br_3SNa$ ($MNa^+$) 523.8501, found 523.8498.

***tert*-Butyl (2,2,2-tribromo-1-(4-fluorophenyl)ethyl)-carbamate (12e).** Colorless solid; Yield 192 mg, 81%; mp 128-130 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3420brvs, 3308brvs, 1688vs, 1605m, 1510s, 1229m, 1167s, 747m; $\delta_H$ (400 MHz, $CDCl_3$) 7.57 (2H, dd, *J* 8.6, 5.2 Hz), 7.07 (2H, t, *J* 8.6 Hz), 5.62 (2H, br unresolved), 1.45 (9H, s); $\delta_C$ (100 MHz, $CDCl_3$) 163.1 (d, $J_{C-F}$ 250.0 Hz), 154.3, 131.8, 131.7 (d, $J_{C-F}$ 7.0 Hz), 115.1 (d, $J_{C-F}$ 9.0 Hz), 81.2, 69.4, 50.5, 28.4; $\delta_F$ (470 MHz, $CDCl_3$) -112.2; MS ($ES^+$, Ar) m/z (rel intensity) 502 ($[MNa+6]^+$, 36), 500 ($[MNa+4]^+$, 98), 498 ($[MNa+2]^+$, 100), 496 ($[MNa]^+$, 36); HRMS ($ES^+$, Ar) calcd for $C_{13}H_{15}NO_2Br_3FNa$ ($MNa^+$) 495.8535, found 495.8551.

***tert*-Butyl (2,2,2-tribromo-1-(3-nitrophenyl)ethyl)-carbamate (12f).** Colorless solid; Yield 200 mg, 80%; mp 173-175 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3369brs, 1715s, 1520s, 1353m, 1245m, 1152m; $\delta_H$ (400 MHz, $CDCl_3$) 8.50 (1H, t, *J* 2.1 Hz), 8.26 (1H, ddd, *J* 8.3, 2.1, 1.0 Hz), 7.95 (1H, dd, *J* 8.3, 2.1 Hz), 7.57 (1H, t, *J* 8.3 Hz), 5.78 (1H, br d, *J* 9.2 Hz), 5.74 (1H, br d, *J* 9.2 Hz), 1.45 (9H, s); $\delta_C$ (100 MHz, $CDCl_3$) 154.2, 147.9, 138.0, 136.5, 129.0, 124.5, 124.1, 81.6, 69.3, 47.8, 28.4; MS ($ES^+$, Ar) m/z (rel intensity) 529 ($[MNa+6]^+$, 22), 527 ($[MNa+4]^+$, 79), 525 ($[MNa+2]^+$, 73), 523 ($[MNa]^+$, 27), 451 (30), 449 (98), 447 (100), 445 (25), 367 (45); HRMS ($ES^+$, Ar) calcd for $C_{13}H_{15}N_2O_4Br_3Na$ ($MNa^+$) 522.8480, found 522.8464.

**General Procedure for Boc Deprotection of 12.** To a stirred solution of the Boc protected amine **12** (0.1 mmol) in chloroform (5 mL), trifluoroacetic acid (1.6 mL, excess) was added. The reaction mixture was maintained at room temperature for 3 h. Chloroform was evaporated and the crude residue was neutralized with 5% aqueous sodium hydroxide. The aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layer was dried (anhyd $Na_2SO_4$), and concentrated in vacuo to afford the crude product, which was subjected to silica gel column chromatography (ethyl acetate/hexane mixture, gradient elution) to afford product **13**.

**2,2,2-Tribromo-1-phenylethan-1-amine (13a).** Yellow solid; Yield 32 mg, 90%; mp 103-105 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3317brs, 1615m, 1297m, 726vs, 708m, 692m; $\delta_H$ (400 MHz, $CDCl_3$) 7.62–7.60 (2H, m), 7.40–7.35 (3H, m), 4.60 (1H, s), 2.45 (2H, br s); $\delta_C$ (100 MHz, $CDCl_3$) 137.1, 129.6, 129.1, 128.0, 73.9, 59.7; MS ($ES^+$, Ar) m/z (rel intensity) 345 ($[M-NH_2+6]^+$, 30), 343 ($[M-NH_2+4]$, 76), 341 ($[M-NH_2+2]^+$, 100), 339 ($[M-NH_2]^+$, 36); HRMS ($ES^+$, Ar) calcd for $C_8H_6Br_3$ ($[M-NH_2]^+$) 338.8020, found 338.8028.

**2,2,2-Tribromo-1-(p-tolyl)ethanamine (13b).** White solid; Yield 36 mg, 97%; mp 130-132 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3395brm, 1616m, 1496m, 1453m, 1265m, 736vs, 705s, 694s; $\delta_H$ (400 MHz, $CDCl_3$) δ 7.50 (2H, d, *J* 8.0 Hz), 7.18 (2H, d, *J* 8.0 Hz), 4.56 (1H, s), 2.39 (2H, br s), 2.36 (3H, s); $\delta_C$ (100 MHz; $CDCl_3$) 139.0, 134.1, 129.5, 128.7, 73.7, 60.2, 21.4; MS ($ES^+$, Ar) m/z (rel intensity) 376 ($[MH+6]^+$, 19), 374 ($[MH+4]^+$, 47), 372 ($[MH+2]^+$, 48), 370 ($MH^+$, 20), 359 ($[M-NH_2+6]^+$, 45), 357 ($[M-NH_2+4]^+$, 100), 355 ($[M-NH_2]+2]^+$, 84), 354 ($[M-NH_2]^+$, 50); HRMS ($ES^+$, Ar) calcd for $C_9H_{11}NBr_3$ ($MH^+$) 369.8442, found 369.8435.

**2,2,2-Tribromo-1-(4-methoxyphenyl)ethanamine (13c).** White solid; Yield 35 mg, 91%; mp 98-100 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3404brw, 1609m, 1515s, 1254s, 1182m, 1032m, 737vs; $\delta_H$ (400 MHz, $CDCl_3$) 7.53 (2H, d, *J* 8.7 Hz), 6.89 (2H, d, *J* 8.7 Hz), 4.55 (1H, s), 3.81 (3H, s), 2.30 (2H, br s); $\delta_C$ (100 MHz, $CDCl_3$) 160.1, 130.8, 129.1, 113.3, 73.4, 60.8, 55.4; MS ($ES^+$, Ar) m/z (rel intensity) 375 ($[M-NH_2+6]^+$, 35), 373 ($[M-NH_2+4]^+$, 95), 371 ($[M-NH_2]+2]^+$, 100), 369 ($[M-NH_2]^+$, 35), 311 (10), 292 (25); HRMS ($ES^+$, Ar) calcd for $C_9H_8OBr_3$ ($[M-NH_2]^+$) 368.8125, found 368.8116.

**2,2,2-Tribromo-1-(4-(methylthio)phenyl)ethan-1-amine (13d).** Colorless solid; Yield 36 mg, 90%; mp 180-181 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3320w, 1597m, 738s, 704m, 560m; $\delta_H$ (400 MHz, $CDCl_3$) 7.52 (2H, d, *J* 8.4 Hz), 7.22 (2H, d, *J* 8.4 Hz), 4.55 (1H, s), 2.49 (3H, s), 2.15 (2H, br s); $\delta_C$ (100 MHz, $CDCl_3$) 139.8, 133.5, 129.9, 125.4, 73.4, 59.8, 15.5; MS ($ES^+$, Ar) m/z (rel intensity) 391 ($[(M-NH_2)+6]^+$, 29), 389 ($[(M-NH_2)+4]^+$, 86), 387 ($[(M-NH_2)+2]^+$, 77), 385 ($[(M-NH_2)]^+$, 24), 325 (36), 310 (54), 308 (100), 305 (47); HRMS ($ES^+$, Ar) calcd for $C_9H_8Br_3S$ $[M-NH_2]^+$ 384.7891, found 384.7878.

**2,2,2-Tribromo-1-(4-fluorophenyl)ethanamine (13e).** White solid; Yield 36 mg, 95%; mp 174-176 °C; $\nu_{max}$(KBr)/$cm^{-1}$ 3387brm, 1605m, 1512vs, 1233s, 1162m, 837s, 783m, 733m, 553m, 500m; $\delta_H$ (400 MHz, $CDCl_3$) 7.64–7.55 (2H, m), 7.10–7.01 (2H, m), 4.59 (1H, s), 2.41 (2H, br s); $\delta_C$ (100 MHz, $CDCl_3$) 163.1 (d, *J* 247.0 Hz), 133.0, 131.4 (d, *J* 8.0 Hz), 115.0 (d, *J* 22.0 Hz), 73.2, 59.5; $\delta_F$ (470 MHz, $CDCl_3$) -112.3; MS ($ES^+$, Ar) m/z (rel intensity) 380

([MH+6]$^+$, 13), 378 ([MH+4]$^+$, 47), 376 ([MH+2]$^+$, 45), 374 (MH$^+$, 13), 363 ([M-$NH_2$+6]$^+$, 34), 361 ([M-$NH_2$+4]$^+$, 96), 359 ([M-$NH_2$+2]$^+$, 100), 357 ([M-$NH_2$]$^+$, 34), 311 (18); HRMS (ES$^+$, Ar) calcd for $C_9H_{11}NBr_3$ (MH$^+$) 373.8191, found 373.8207.

**General Procedure for the Monodebromination of 12.** To a stirred solution of the Boc protected amine **12b** (47 mg, 0.1 mmol) in THF (5 mL), silver carbonate (28 mg, 0.1 mmol, 1 equiv) and water (1 mL) were added. The reaction mixture was refluxed overnight. THF was evaporated in vacuo and the crude residue was subjected to silica gel column chromatography (ethyl acetate/hexane mixture, gradient elution) to afford pure **18**.

**Tert-butyl (2,2-dibromo-1-(p-tolyl)ethyl)carbamate (18).** Yellow solid; Yield 31 mg, 75%; mp 112-114 $^oC$; $\nu_{max}$(KBr)/cm$^{-1}$ 3333brw, 1714vs, 1495vs, 1368m, 1248m, 1165vs, 820m, 737m, 561m; $\delta_H$ (400 MHz, $CDCl_3$) 7.25, 7.18 (4H, ABq, *J* 8.1 Hz), 5.96 (1H, br unresolved), 5.47 (1H, br unresolved), 5.28 (1H, br d, *J* 6.7 Hz), 2.35 (3H, s), 1.47 (9H, s); $\delta_C$ (100 MHz, $CDCl_3$) 155.1, 138.6, 134.4, 129.4, 127.3, 80.7, 61.4, 50.6, 28.5, 21.3; MS (ES$^+$, Ar) m/z (rel intensity) 418 ([MNa+4]$^+$, 51), 416 ([MNa+2]$^+$, 100), 414 ([MNa]$^+$, 56), 396 ([MH+4]$^+$, 17), 394 ([MH+2]$^+$, 27), 392 ([MH]$^+$, 13); HRMS (ES$^+$, Ar) calcd for $C_{14}H_{20}NO_2Br_2$ (MH$^+$) 391.9861, found 391.9868.

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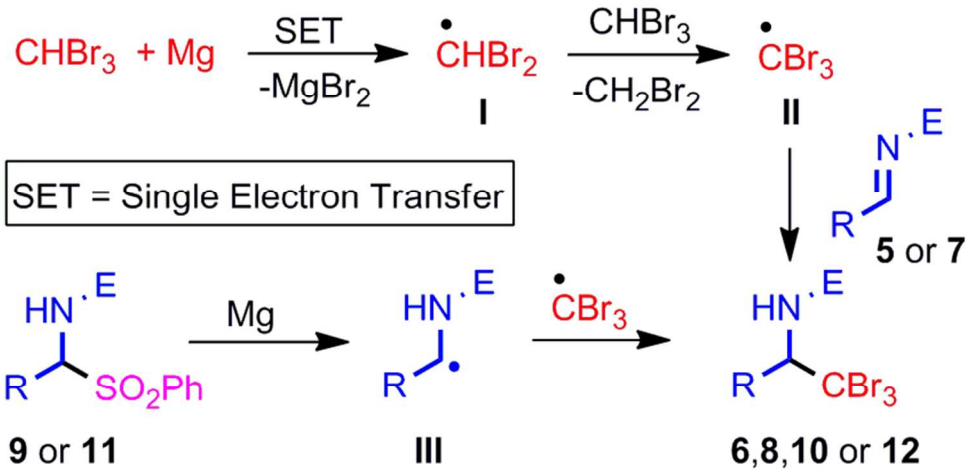


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