Aminobromination of olefins with $TsNH_2$ and NBS as the nitrogen and bromine sources mediated by hypervalent iodine in a ball mill

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A series of olefins including α,β-unsaturated ketones, cinnamates, cinnamides and styrenes have been aminobrominated with good yields and excellent diastereoselectivities under mechanical milling conditions, using $TsNH_2$ and NBS as the nitrogen and bromine sources, promoted by (diacetoxyiodo)benzene.

Introduction

Aminohalogenation of olefins is a powerful method for installing vicinal haloamino moieties, which are extremely versatile building blocks because of their relevance to organic synthesis by replacement of halogen with multifarious nucleophiles.[1] A number of synthetic strategies have been developed to furnish this functionality since the discovery of the aminohalogenation reaction several decades ago. Various reagent systems such as *N*,*N*-dihalosulfonamides,[2] *N*,*N*-dihalocarbamates,[3] *N*-halocarbamates,[4] cyanamide–NBS[5] and *S*,*S*-dimethyl-*N*-(*p*-toluenesulfonyl)sulfilimine–NBS[6] have been developed to effect this transformation of olefins. Corey and co-workers have illustrated a versatile methodology for the aminobromination of a broad scope of olefins involving *N*-bromoacetamide and Lewis acid in acetonitrile.[7] However, the preparation of vicinal haloamine derivatives still confronts significant limitations such as low yield, tedious procedure and using large quantities of heavy metal salts.

Despite the fact that the resulting vicinal haloaminated carbonyl compounds are synthetically important intermediates, the aminohalogenation of α,β-unsaturated ketones and esters was not well tackled until very recently[8] when various new systems for the aminohalogenation of electron-deficient olefins were successfully established by Li[9,10] and others.[11] A series of α,β-unsaturated ketones,[9g,10] esters[9a–e] and nitriles[9j] have been easily aminochlorinated with good yields and excellent diastereoselectivities by the use of several different nitrogen/chlorine sources such as 4-$TsNCl_2$,[9a,c,e–h,j,k] 2-$NsNCl_2$,[10] 2-NsNNaCl,[9d] or the combination of 2-$NsNCl_2$ and 2-NsNHNa[9b,9i] with[9] or without[10] metal catalysts. We also disclosed a ball-milling[12] aminochlorination process of electron-deficient olefins with Chloramine-T[13] promoted by 50 mol% of (diacetoxyiodo)benzene ($PhI(OAc)_2$).[14a] Very recently, we revealed the possibility of using water as a reaction medium in the aminochlorination process promoted by Brønsted acids.[14b]

The aminobromination reactions of a large range of olefins using the combination of *p*-tosylsulfonamide ($TsNH_2$) and NBS catalyzed by transition metals have been realized by Sudalai and co-workers.[15] Huang and Fu also reported the aminobromination of methylenecyclopropanes using $TsNH_2$ and NBS as the nitrogen and bromine sources, respectively.[16] Very recently, Fan and co-workers reported a highly efficient oxidative bromocyclization of homoallylic sulfonamides utilizing KBr as the bromine source induced by stoichiometric $PhI(OAc)_2$ without a metal catalyst.[17] Based on these excellent discoveries, we reasoned that it was possible to perform the aminobromination of olefins with a $TsNH_2$–NBS system mediated by $PhI(OAc)_2$. Herein we present the metal-free aminobromination of olefins using $TsNH_2$ and NBS as the nitrogen and bromine sources under mechanical milling conditions.

Results and discussion

In our initial study, we chose chalcone **1a** as a model compound to examine the feasibility of our hypothesis. The results are summarized in Table 1. Much to our delight, bromoamine **2a** was obtained in fairly good yield (63%) and high diastereoselectivity (91 : 9 *anti* : *syn*) accompanied by dibrominated product **3** in 25% yield by simply mixing the reactants with 25 mol% of $PhI(OAc)_2$ in a ball mill (entry 1).[18] This result indicated that $PhI(OAc)_2$ could be used in a catalytic amount in our system. We can conclude that $PhI(OAc)_2$ acted as more than an oxidant here. Then, the Lewis acids employed in Sudalai's procedure were examined.[15] Surprisingly, CuI failed to give any bromoamine **2a**. Instead, dibrominated product **3** was isolated in 57% yield (entry 2). $MnSO_4 \cdot H_2O$ only furnished **2a** in 7% isolated yield along with 20% yield of **3** (entry 3). Other Lewis acids such as $FeCl_3 \cdot 6H_2O$ and $InCl_3 \cdot 4H_2O$ were also screened, however, only dibromination reaction was observed (entries 4–5). The side reaction was obviously suppressed to give the desired product in high yield when the $PhI(OAc)_2$ loading was increased to 50 mol%, affording **2a** in 75% yield along with 10% yield of **3** (entry 6). The dibromination reaction was totally invisible by further increasing $PhI(OAc)_2$ loading to 75 mol%, giving bromoamine **2a** in 83% yield (entry 7). Decreasing the loading of either $TsNH_2$ or NBS was harmful to the reaction yield, yet high diastereoselectivity was observed (entries 8–9).

With the optimized conditions in hand, we next investigated the substrate generality of the reaction. The results are shown in Table 2. Reactions of various chalcones bearing either electron-donating groups or electron-withdrawing groups on the phenyl

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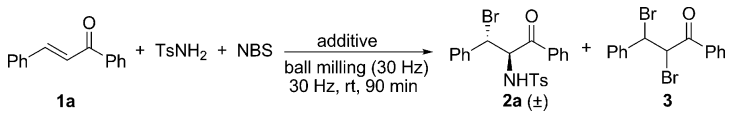
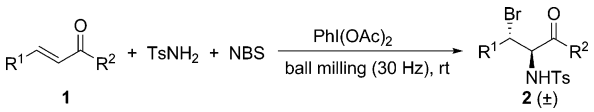
Table 1 Aminobromination of chalcone **1a** with various additives under mechanical milling conditions



Entry	Additive	Additive loading	Yield (%)[b] 2a	Yield (%)[b] 3	Dr (*anti* : *syn*) of **2a**[c]
1	$PhI(OAc)_2$	25 mol%	63	25	91 : 9
2	CuI	25 mol%	0	57	—
3	$MnSO_4·H_2O$	25 mol%	7	20	92 : 8
4	$FeCl_3·6H_2O$	25 mol%	0	38	—
5	$InCl_3·4H_2O$	25 mol%	0	62	—
6	$PhI(OAc)_2$	50 mol%	75	10	92 : 8
7	$PhI(OAc)_2$	75 mol%	83	trace	92 : 8
8[d]	$PhI(OAc)_2$	75 mol%	69	trace	92 : 8
9[e]	$PhI(OAc)_2$	75 mol%	67	11	92 : 8

[a] Unless otherwise specified, all reactions were performed with chalcone **1a** (0.1 mmol), $TsNH_2$ (0.2 mmol), NBS (0.15 mmol) and a given amount of additives. [b] Isolated yields by flash column chromatography. [c] Determined by the analysis of ^1H NMR. [d] 0.1 mmol of NBS was employed. [e] 0.15 mmol of $TsNH_2$ was employed.

Table 2 Aminobromination of electron-deficient olefins promoted by $PhI(OAc)_2$ under mechanical milling conditions[a]



Entry	R^1	R^2	Products	Time (h)	Yield (%)[b]	Dr (*anti* : *syn*)[c]
1	C_6H_5	C_6H_5	**2a**	1.5	83	92 : 8
2	4-CH_3–C_6H_4	C_6H_5	**2b**	1.5	61	92 : 8
3	4-Cl–C_6H_4	C_6H_5	**2c**	1.5	73	94 : 6
4	2-Cl–C_6H_4	C_6H_5	**2d**	1.5	79	94 : 6
5[d]	3,4-Cl_2–C_6H_3	C_6H_5	**2e**	1.5	76	93 : 7
6[e]	4-NO_2–C_6H_4	C_6H_5	**2f**	3.0	73	95 : 5
7	C_6H_5	4-Cl–C_6H_4	**2g**	1.5	76	96 : 4
8[d]	4-Cl–C_6H_4	4-Cl–C_6H_4	**2h**	1.5	71	94 : 6
9	C_6H_5	4-CH_3O–C_6H_4	**2i**	1.5	83	92 : 8
10	4-Cl–C_6H_4	4-CH_3O–C_6H_4	**2j**	1.5	81	92 : 8
11	C_6H_5	CH_3	**2k**	1.5	70	92 : 8
12	C_6H_5	OCH_3	**2l**	1.5	66	91 : 9
13	4-Cl–C_6H_4	OCH_3	**2m**	1.5	52	91 : 9
14	4-Cl–C_6H_4	OEt	**2n**	1.5	57	89 : 11
15	C_6H_5	$N(C_2H_5)_2$	**2o**	1.5	69	>99 : 1
16	4-Cl–C_6H_4	$N(C_2H_5)_2$	**2p**	1.5	48	>99 : 1
17	Et	Ph	**2q**	3.0	0	—
18	^{t}Bu	Me	**2r**	3.0	0	—

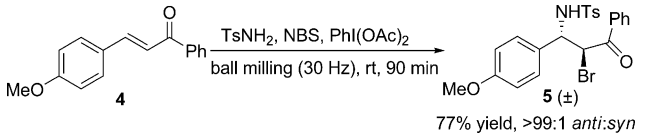
[a] Unless otherwise specified, all reactions were performed with olefin (0.1 mmol), $TsNH_2$ (0.2 mmol), NBS (0.15 mmol) and $PhI(OAc)_2$ (0.075 mmol). [b] Isolated yields by flash column chromatography. [c] Determined by the analysis of ^1H NMR. [d] 0.1 mmol of $PhI(OAc)_2$ was employed. [e] 0.4 mmol of $TsNH_2$, 0.3 mmol of NBS, and 0.15 mmol of $PhI(OAc)_2$ were employed.

rings afforded the corresponding vicinal bromoamines in good yields (up to 83%) and excellent diastereoselectivities (up to 96 : 4 *anti* : *syn*, entries 1–10). However, it was obvious that the electron-donating group on the phenyl ring attached to the double bond of the chalcone reduced the yield (entry 2). We were pleased to find that the yield of the bromoaminoketone decreased only slightly when the R^2 group of the enones was an alkyl substituent, along with good diastereoselectivity (entry 11).

Our methodology could be applied to the aminobromination of α,β-unsaturated esters and amides. Cinnamates **1l–n** and cinnamides **1o–p** were employed as the selected examples to show the scope. All of them were successfully aminobrominated with moderate to good yields and excellent diastereoselectivities (entries 12–16). However, we were cornered by the inextricable failure in the aminobromination of enones where R^1 was an alkyl group (entries 17–18). This limitation could also be found in our previously reported methodology for the aminochlorination of olefins[14] that may be ascribed to the electronic factor of the substrates.

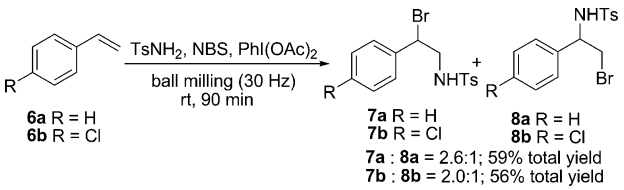
When chalcone **4**, with a strong electron-donating group substituted on the phenyl ring of the double bond, was employed in the reaction, a reversed regioselectivity was observed.[15] Vicinal

bromoamine **5** was isolated with 77% yield exclusively in the *anti*-configuration (Scheme 1).



Scheme 1 Reversed regioselectivity of the aminobromination reaction.

Simple olefins were also examined in our reaction system. Much to our pleasure, the aminobrominated product of styrene could be obtained in 59% total yield, and existed as two regioisomers with a ratio of 2.6 : 1, while 4-chlorostyrene gave a slightly reduced yield and isomer ratio (Scheme 2).

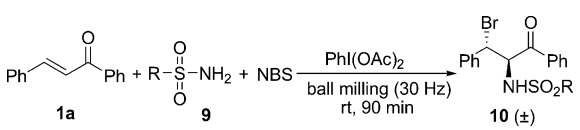


Scheme 2 Aminobromination of styrenes promoted by $PhI(OAc)_2$.

Extension to other sulfonamides was explored, and the results are listed in Table 3. The substituted group on the phenyl ring of the sulfonamides notably influenced the reaction (entries 1–2 *vs.* entry 3). An electron-withdrawing group could reduce the yield dramatically, only giving **10b** in 37% yield (entry 3). However, the alkyl sulfonamide **9c** reacted smoothly, affording **10c** with a slightly decreased yield and diastereoselectivity (entry 4).

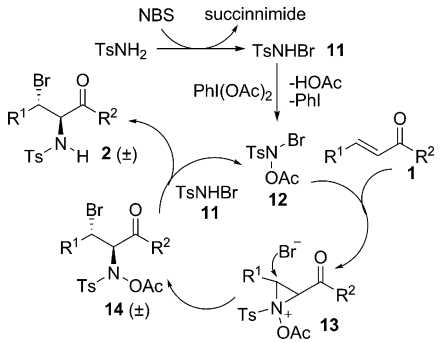
Although the role of $PhI(OAc)_2$ and the exact mechanism of the reaction are not quite clear right now, a tentative pathway (Scheme 3) is proposed according to experimental results. NBS could react with $TsNH_2$ to generate *N*-bromo-*p*-toluenesulfonamide (TsNHBr, **11**).[19] Then, TsNHBr was oxidized by $PhI(OAc)_2$ to yield *N*-acetoxy-*N*-bromo-*p*-toluenesulfonamide **12** by releasing acetic acid and iodobenzene.[14a] Compound **12** was then attacked by olefin **1** to generate aziridinium intermediate **13** and bromide anion. Aziridinium cation **13** was immediately attacked by the nearby bromide anion *via* an S_N2 pathway to produce intermediate **14** in high regio- and diastereoselectivity.[9,14]

Table 3 Aminobromination of chalcone **1a** with various sulfonamides[a]



Entry	R	Products	Yield (%)[b]	Dr (*anti* : *syn*)[c]
1	4-CH_3–C_6H_4	**2a**	83	92 : 8
2	C_6H_5	**10a**	85	92 : 8
3	4-NO_2–C_6H_4	**10b**	37	89 : 11
4	CH_3	**10c**	69	89 : 11

[a] All reactions were performed with chalcone **1a** (0.1 mmol), sulfonamide (0.2 mmol), NBS (0.15 mmol) and $PhI(OAc)_2$ (0.075 mmol). [b] Isolated yields by flash column chromatography. [c] Determined by the analysis of ^1H NMR spectra.



Scheme 3 Possible pathway of the aminobromination process.

Finally, **14** reacted with TsNHBr **11** to furnish the final product **2** and regenerate **12**. The excellent regio- and diastereoselectivity sufficiently supported this process. A bridged bromonium ion mechanism can be excluded because a reversed regiostereoselectivity should be observed by attacking the bromonium intermediate with the nitrogen nucleophile.

Conclusion

In summary, we have demonstrated the aminobromination reaction of olefins with $TsNH_2$ and NBS as the nitrogen and bromine sources mediated by $PhI(OAc)_2$ under mechanical milling conditions. This metal-free and solvent-free methodology was broadly applicable for the aminobromination of various olefins including α,β-unsaturated ketones, cinnamates, cinnamides and styrenes in reasonable yields. $PhI(OAc)_2$ exhibited a unique accelerating property here compared with metal salts, and was used in substoichiometric loading, while its role remains for further exploration.

Experimental

General

Reagents and solvents were obtained from commercial sources and were used without further purification. Solvent compositions reported for all chromatographic seperations are on a volume/volume (v/v) basis. All melting points were reported uncorrected. Infrared spectra were recorded in KBr pellets and reported in cm^{-1}. ^1H NMR spectra were recorded at 300 MHz and are reported in parts per million (ppm) on the δ scale relative to tetramethylsilane (δ 0.00) as an internal standard. ^{13}C NMR spectra were recorded at 75 MHz and are reported in parts per million (ppm) on the δ scale relative to $CDCl_3$ (δ 77.0), High-resolution mass spectra (HRMS) were recorded in EI mode. Analytical TLC and column chromatography were performed on silica gel GF254, and silica gel H60, respectively.

General procedure for the aminobromination of olefins 1a–p, 4, 6a and 6b in a ball mill. To a mixture of olefin **1a** (**1b–p**, **4**, **6a** and **6b**, 0.1 mmol), $TsNH_2$ (34.2 mg, 0.2 mmol) and NBS (26.7 mg, 0.15 mmol) in a stainless steel jar (5 mL) was added $PhI(OAc)_2$ (24.2 mg, 0.075 mmol). The same mixture was introduced into another parallel jar. The two reaction vessels were closed and fixed on the vibration arms of MM200 (Retsch GmbH, Haan,

Germany) and were milled vigorously (30 Hz) at room temperature for the indicated time. The resulting mixture was extracted with ethyl acetate twice (10 mL × 2). The solvent was evaporated to dryness *in vacuo*. The residue was separated on a silica gel column with petroleum ether–ethyl acetate 7 : 1 as the eluent to get the desired product **2a** (**2b–p**, **5**, **7a–b** and **8a–b**).

Replacing $TsNH_2$ with **9a–c**, the same procedure afforded products **10a–c** respectively.

The identities of known compounds **2a**, **2c**, **2l**, **2n**, **5**, **7a** and **8a** were confirmed by comparison of their spectral data with the reported ones.[15] Physical and spectroscopic data of the newly synthesized compounds are given below.

3-Bromo-3-(4-methylphenyl)-1-phenyl-2-(tosylamino)propan-1-one (2b). White solid, mp = 172–174 °C. IR (KBr) *ν* 3234, 2925, 1683, 1595, 1449, 1433, 1332, 1158, 1092, 914, 808, 681, 552, 512 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.80 (d, *J* = 8.1 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.48–7.41 (m, 4H), 7.14 (d, *J* = 8.1 Hz, 2H), 7.05–7.00 (m, 4H), 5.53–5.48 (m, 2H), 5.08 (d, *J* = 5.7 Hz, 1H), 2.31 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 196.7, 143.6, 139.1, 136.9, 135.3, 134.2, 133.6, 129.5 (2C), 129.4 (2C), 129.0 (2C), 128.8 (2C), 128.5 (2C), 127.2 (2C), 61.0, 51.6, 21.5, 21.3; HRMS (EI–TOF): *m/z* [M^+ − HBr] calcd for $C_{23}H_{21}NO_3S$, 391.1242; found, 391.1241.

3-Bromo-3-(2-chlorophenyl)-1-phenyl-2-(tosylamino)propan-1-one (2d). White solid, mp = 139–141 °C. IR (KBr) *ν* 3234, 2926, 1686, 1595, 1448, 1333, 1158, 1069, 914, 814, 766, 685, 569, 552 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.75 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.28–7.26 (m, 1H), 7.18–7.14 (m, 2H), 6.98 (d, *J* = 7.8 Hz, 2H), 5.63–5.58 (m, 3H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 196.6, 143.7, 136.7, 135.5, 134.3, 134.2, 133.4, 131.4, 130.1, 129.7, 129.5 (2C), 128.9 (2C), 128.6 (2C), 127.4, 127.2 (2C), 60.5, 47.4, 21.5; HRMS (EI–TOF): *m/z* [M^+ − HBr] calcd for $C_{22}H_{18}NO_3S^{35}Cl$, 411.0696; found, 411.0703.

3-Bromo-3-(3,4-dichlorophenyl)-1-phenyl-2-(tosylamino)propan-1-one (2e). White solid, mp = 155–157 °C. IR (KBr) *ν* 3174, 2924, 1671, 1595, 1449, 1335, 1250, 1160, 1083, 972, 913, 812, 791, 672, 659, 570, 545 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.95 (d, *J* = 8.7 Hz, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.57–7.47 (m, 4H), 7.31–7.25 (m, 2H), 7.12 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.04 (d, *J* = 8.1 Hz, 2H), 5.56 (d, *J* = 9.6 Hz, 1H), 5.44 (dd, *J* = 9.6, 8.4 Hz, 1H), 4.94 (d, *J* = 8.4 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 197.1, 143.9, 137.3, 136.7, 135.3, 134.6, 133.3, 132.7, 130.7, 130.5, 129.5 (2C), 129.2 (2C), 128.9 (2C), 128.0, 126.8 (2C), 60.1, 49.3, 21.6; HRMS (EI–TOF): *m/z* [M^+ − HBr] calcd for $C_{22}H_{17}NO_3S^{35}Cl_2$, 445.0306; found, 445.0302.

3-Bromo-3-(4-nitrophenyl)-1-phenyl-2-(tosylamino)propan-1-one (2f). White solid, mp = 159–161 °C. IR (KBr) *ν* 3256, 2925, 1683, 1526, 1349, 1161, 1073, 920, 806, 684, 553 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 8.06 (d, *J* = 8.7 Hz, 2H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.50–7.41 (m, 6H), 6.98 (d, *J* = 7.5 Hz, 2H), 5.53–5.47 (m, 2H), 5.08 (d, *J* = 7.2 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 196.7, 148.0, 144.1, 143.9, 136.7, 135.1, 134.7, 129.8 (2C), 129.6 (2C), 129.2 (2C), 129.0 (2C), 127.0 (2C), 123.8 (2C), 60.2, 49.2, 21.4; HRMS (EI–TOF): *m/z* [M^+ − HBr] calcd for $C_{22}H_{18}N_2O_5S$, 422.0936; found, 422.0939.

3-Bromo-1-(4-chlorophenyl)-3-phenyl-2-(tosylamino)propan-1-one (2g). White solid, mp = 123–125 °C. IR (KBr) *ν* 3234, 2923, 1683, 1589, 1333, 1156, 1090, 846, 810, 698, 672, 551 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.72 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 2H), 7.28–7.21 (m, 5H), 7.02 (d, *J* = 8.1 Hz, 2H), 5.46–5.42 (m, 2H), 5.06 (d, *J* = 6.9 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 195.9, 143.9, 141.0, 136.7, 136.6, 133.8, 130.4 (2C), 129.6 (2C), 129.2, 129.1 (2C), 128.8 (2C), 128.7 (2C), 127.2 (2C), 60.5, 51.7, 21.5; HRMS (EI–TOF): *m/z* [M^+ − HBr] calcd for $C_{22}H_{18}NO_3S^{35}Cl$, 411.0696; found, 411.0698.

3-Bromo-1,3-bis(4-chlorophenyl)-2-(tosylamino)propan-1-one (2h). White solid, mp = 156–158 °C. IR (KBr) *ν* 3222, 2924, 1684, 1588, 1492, 1335, 1162, 1091, 832, 808, 796, 676, 553 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.82 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 9.0 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 9.0 Hz, 2H), 7.16 (d, *J* = 9.0 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 2H), 5.47–5.36 (m, 2H), 4.96 (d, *J* = 8.4 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 196.3, 144.0, 141.2, 136.7, 135.4, 135.2, 133.8, 130.5 (2C), 130.0 (2C), 129.6 (2C), 129.2 (2C), 128.9 (2C), 127.0 (2C), 60.1, 50.2, 21.6; HRMS (EI–TOF): *m/z* [M^+ − HBr] calcd for $C_{22}H_{17}NO_3S^{35}Cl_2$, 445.0306; found, 445.0314.

3-Bromo-1-(4-methoxyphenyl)-3-phenyl-2-(tosylamino)propan-1-one (2i). White solid, mp = 142–144 °C. IR (KBr) *ν* 3252, 2920, 1653, 1599, 1571, 1250, 1164, 1088, 844, 812, 663, 549, 524 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.77 (d, *J* = 9.0 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.30–7.24 (m, 5H), 7.01 (d, *J* = 8.1 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 5.46–5.45 (m, 2H), 5.11–5.09 (m, 1H), 3.90 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 194.5, 164.6, 143.6, 136.9, 136.7, 131.5 (2C), 129.5 (2C), 129.1, 128.7 (2C), 128.6 (2C), 128.2, 127.2 (2C), 114.1 (2C), 60.6, 55.8, 51.9, 21.5; HRMS (EI–TOF): *m/z* [M^+ − HBr] calcd for $C_{23}H_{21}NO_4S$, 407.1191; found, 407.1186.

3-Bromo-3-(4-chlorophenyl)-1-(4-methoxyphenyl)-2-(tosylamino)-propan-1-one (2j). White solid, mp = 143–145 °C. IR (KBr) *ν* 3279, 2924, 1676, 1599, 1321, 1266, 1178, 1154, 1091, 815, 666, 609, 548, 534 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.83 (d, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.21–7.15 (m, 4H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 5.50–5.39 (m, 2H), 5.02 (d, *J* = 7.5 Hz, 1H), 3.91 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 194.8, 164.8, 143.7, 136.9, 135.6, 134.9, 131.6 (2C), 130.0 (2C), 129.5 (2C), 128.8 (2C), 128.2, 127.0 (2C), 114.2 (2C), 60.2, 55.8, 50.6, 21.5; HRMS (EI–TOF): *m/z* [M^+ − HBr] calcd for $C_{23}H_{20}NO_4S^{35}Cl$, 441.0802; found, 441.0801.

4-Bromo-4-phenyl-3-(tosylamino)butan-2-one (2k). White solid, mp = 123–125 °C. IR (KBr) *ν* 3251, 1720, 1454, 1338, 1160, 1090, 882, 813, 765, 700, 665, 546 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.53 (d, *J* = 8.1 Hz, 2H), 7.27–7.20 (m, 7H), 5.26 (d, *J* = 8.4 Hz, 1H), 5.01 (d, *J* = 7.6 Hz, 1H), 4.46 (dd, *J* = 8.4, 7.6 Hz, 1H), 2.41 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) *δ* 204.7, 144.0, 136.5 (2C), 129.8 (2C), 129.1, 128.9 (2C), 128.3 (2C), 127.3 (2C), 65.7, 51.1, 30.2, 21.7; HRMS

(EI–TOF): m/z [M^+ − HBr] calcd for $C_{17}H_{17}NO_3S$, 315.0929; found, 315.0923.

3-Bromo-3-(4-chlorophenyl)-2-(tosylamino)propionic acid methyl ester (2m). White solid, mp = 111–113 °C. IR (KBr) ν 3246, 1725, 1435, 1337, 1162, 1092, 1015, 911, 814, 665, 551, 525 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 8.1 Hz, 2H), 7.31–7.22 (m, 6H), 5.17 (d, J = 9.9 Hz, 1H), 5.02 (d, J = 7.2 Hz, 1H), 4.44 (dd, J = 9.9, 7.2 Hz, 1H), 3.56 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) δ 169.6, 144.1, 136.5, 135.2, 135.1, 129.7 (4C), 128.9 (2C), 127.3 (2C), 61.9, 52.9, 50.4, 21.7; HRMS (EI–TOF): m/z [M^+ − HBr] calcd for $C_{17}H_{16}NO_4S^{35}Cl$, 365.0489; found, 365.0483.

3-Bromo-*N*,*N*-diethyl-3-phenyl-2-(tosylamino)propionamide (2o). White solid, mp = 185–187 °C. IR (KBr) ν 3196, 1628, 1486, 1445, 1339, 1160, 1086, 922, 809, 668, 556 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 8.4 Hz, 2H), 7.38–7.29 (m, 5H), 7.15 (d, J = 8.4 Hz, 2H), 5.65 (d, J = 9.6 Hz, 1H), 5.05 (d, J = 9.3 Hz, 1H), 4.96–4.90 (m, 1H), 3.54–3.42 (m, 3H), 3.25–3.18 (m, 1H), 2.42 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H), 1.10 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) δ 168.9, 143.1, 137.8, 137.7, 129.4 (2C), 128.8 (3C), 128.6 (2C), 126.9 (2C), 56.9, 52.8, 42.8, 40.9, 21.5, 14.0, 12.3; HRMS (EI–TOF): m/z [M^+ − HBr] calcd for $C_{20}H_{24}N_2O_3S$, 372.1508; found, 372.1504.

3-Bromo-3-(4-chlorophenyl)-*N*,*N*-diethyl-2-(tosylamino)propionamide (2p). White solid, mp = 145–147 °C. IR (KBr) ν 3134, 1626, 1463, 1330, 1158, 1092, 919, 811, 664, 544 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, J = 8.4 Hz, 2H), 7.20–7.09 (m, 6H), 5.69 (d, J = 9.3 Hz, 1H), 4.94 (d, J = 9.9 Hz, 1H), 4.84 (t, J = 9.6 Hz, 1H), 3.58–3.44 (m, 3H), 3.25–3.18 (m, 1H), 2.40 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H), 1.10 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) δ 169.1, 143.3, 137.8, 136.5, 134.8, 130.1 (2C), 129.4 (2C), 128.7 (2C), 126.6 (2C), 57.2, 51.6, 43.0, 41.1, 21.6, 14.1, 12.4; HRMS (EI–TOF): m/z [M^+ − HBr] calcd for $C_{20}H_{23}N_2O_3S^{35}Cl$, 406.1118; found, 406.1117.

1-Bromo-1-(4-chlorophenyl)-2-(tosylamino)ethane (7b) and 2-bromo-1-(4-chlorophenyl)-1-(tosylamino)ethane (8b). ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 8.4 Hz, 2H (**7b**)), 7.60 (d, J = 8.1 Hz, 2H (**8b**)), 7.34–7.05 (m, 6H (**7b**) + 6H (**8b**)), 5.20 (d, J = 6.0 Hz, 1H (**8b**)), 4.90 (t, J = 6.9 Hz, 1H (**7b**)), 4.81 (t, J = 6.3 Hz, 1H (**7b**)), 4.56 (dd, J = 12.0, 6.3 Hz, 1H (**8b**)), 3.57–3.50 (m, 2H (**7b**) + 2H (**8b**)), 2.47 (s, 3H (**7b**)), 2.45 (s, 3H (**8b**)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0 (**7b**), 143.9 (**8b**), 136.9, 136.4, 135.0, 134.2, 130.0, 129.7, 129.2, 128.8, 128.3, 127.2, 127.1, 57.6, 51.4, 50.1, 36.3, 21.6; HRMS (EI–TOF): m/z [M^+ − HBr] calcd for $C_{15}H_{14}NO_2S^{35}Cl$, 307.0434; found, 307.0432.

2-(Benzenesulfonylamino)-3-bromo-1,3-diphenylpropan-1-one (10a). White solid, mp = 121–123 °C. IR (KBr) ν 3240, 3061, 1683, 1595, 1449, 1331, 1167, 1091, 1069, 908, 874, 803, 774, 753, 724, 683, 583, 561 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 8.1 Hz, 2H), 7.62–7.57 (m, 3H), 7.47–7.34 (m, 3H), 7.27–7.22 (m, 7H), 5.53–5.52 (m, 2H), 5.13 (d, J = 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) δ 196.3, 139.7, 136.4, 135.2, 134.4, 132.8, 129.2, 129.0 (6C), 128.7 (2C), 128.6 (2C), 127.1 (2C), 61.0, 51.6; HRMS (EI–TOF): m/z [M^+ − HBr] calcd for $C_{21}H_{17}NO_3S$, 363.0929; found, 363.0934.

3-Bromo-2-(4-nitrobenzenesulfonylamino)-1,3-diphenylpropan-1-one (10b). White solid, mp = 194–196 °C. IR (KBr) ν 3303, 2927, 1675, 1528, 1350, 1159, 1079, 850, 675, 541, 497 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 8.7 Hz, 2H), 7.88 (d, J = 7.5 Hz, 2H), 7.74 (d, J = 8.7 Hz, 2H), 7.65 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.26–7.24 (m, 5H), 5.85 (d, J = 9.9 Hz, 1H), 5.59 (dd, J = 9.9, 7.2 Hz, 1H), 5.13 (d, J = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) δ 196.0, 150.0, 145.7, 136.3, 135.0, 134.9, 129.4, 129.2 (2C), 129.1 (2C), 128.9 (2C), 128.7 (2C), 128.3 (2C), 124.2 (2C), 61.4, 51.0; HRMS (EI–TOF): m/z [M^+ − HBr] calcd for $C_{21}H_{16}N_2O_5S$, 408.0780; found, 408.0779.

3-Bromo-2-(methanesulfonylamino)-1,3-diphenylpropan-1-one (10c). White solid, mp = 120–122 °C. IR (KBr) ν 3283, 1666, 1596, 1448, 1328, 1286, 1217, 1146, 1086, 967, 778, 749, 700, 541, 519 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, J = 7.5 Hz, 2H), 7.68 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.2 Hz, 2H), 7.37–7.32 (m, 5H), 5.70 (dd, J = 9.0, 7.6 Hz, 1H), 5.24 (d, J = 9.0 Hz, 1H), 5.18 (d, J = 7.6 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated) δ 196.5, 137.1, 135.1, 134.7, 129.5, 129.3 (4C), 129.0 (2C), 128.9 (2C), 61.7, 51.3, 42.1; HRMS (EI–TOF): m/z [M^+ − HBr] calcd for $C_{16}H_{15}NO_3S$, 301.0773; found, 301.0767.

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