$Sc(OTf)_3$-Catalysed ring-opening of aziridines with phenol derivatives under solvent-free conditions

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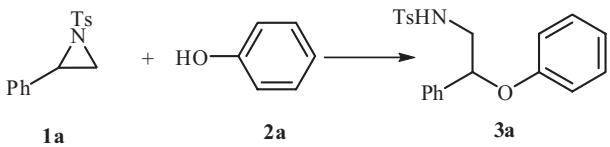
Scandium(III) triflate-catalysed ring opening of aziridines with phenol derivatives affords various 2-amino ethers **3** (eg 4-methyl-*N*-(2-phenoxy-2-phenylethyl) benzenesulfonamide) with high regioselectivity and high yields under solvent-free conditions. The unexpectedly rearranged product **4** (e.g. 4-methyl-N-(3-methyl-3-phenoxy butyl) benzene sulfonamide) was obtained when 2-isopropyl-*N*-tosylaziridine was the substrate.

Keywords: scandium(III) triflate, ring opening, aziridines, 2-amino ethers, regioselectivity, solvent-free

Aziridines and epoxides are valuable building blocks in ring-opening reactions.[1-5] Recently, we have reported the thiolysis reaction of epoxides in ionic liquids without any catalyst[6] and the ring opening of epoxides catalysed by gallium (III) triflate to afford β-hydroxy sulfides with high regioselectivity under solvent-free conditions.[7] Aziridines are nitrogen analogues of epoxides and their corresponding ring-opening products are valuable intermediates in organic synthesis,[8-12] but trisubstituted and tetrasubstituted aziridines exhibit diminished reactivity due to increased steric hindrance. Ring-opening of aziridines is primary and secondary alcohols is facile, catalysed by $BF_3{\cdot}OEt_2$,[13] $Sn(OTf)_2$[13] or $H_3PMo_{12}O_{40}/SiO_2$,[14] but hindered alcohols and phenols afford poor yields under similar conditions.[13] So far, ring opening reaction of aziridines with phenols have been investigated, promoted by *n*-Bu_3P in toluene[15] or H_2O,[16] or catalysed by CuOAc/DBU.[17] The main disadvantages of these methods are poor stereoselectivity[15,16] or low yields.[17] As water tolerant, recyclable catalysts, rare earth metal triflates have efficiently promoted several carbon–carbon or carbon–heteroatom bond forming reactions.[18-20] Here we describe a simple and practical method for the ring opening catalysed by $Sc(OTf)_3$.

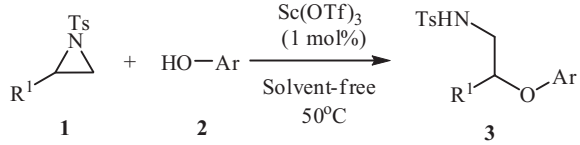
Initially, the opening reaction of 2-phenyl-N-tosylaziridine **1a** with phenol **2a** was carried out in the presence of different catalysts (Scheme 1). Several Lewis acids, $AlCl_3$, $Zn(OTf)_2$, $Yb(OTf)_3$, and $Y(OTf)_3$, were used, but very poor yields were obtained (Table 1). Fortunately, catalysed by $Sc(OTf)_3$, the reaction proceeded smoothly in different solvents such as CH_3NO_2 (6 h, 50%), THF (6 h, 70%), CH_2Cl_2 (2 h, 83%). Moreover, in the case of solvent-free conditions, the product **3a** could be obtained with high regioselectivity in 95% yield when 1 mol% $Sc(OTf)_3$ was used (Table 1, Entry 9).

It was found that phenol **2a** attacks at the more substituted carbon of the aziridine, which affords the desired product **3a**



1a **2a** **3a**

Scheme 1



1 **2** **3**

Scheme 2

with high regioselectivity. The structure of **3** was confirmed by ^1H NMR, ^{13}C NMR, MS and IR. Encouraged by this excellent result, we explored the scope of the reaction with various aziridines **1** and phenols **2** (Scheme 2) and the results are summarised in Table 2. It was found that the phenols with electron-donating groups reacted with aziridines to afford the corresponding products with good yields, while those with electron-withdrawing groups gave relatively low yields (entries 1–11). In the case of 2-acetophenol (**2g**), no product **3** was detected under similar conditions due to the intramolecular hydrogen bonding. According to previous literature,[21] the full mechanistic scheme for the ring opening of 2-substituted-*N*-tosylaziridine **1** with phenols *via* an S_N2-like pathway is given by Scheme 3.

To our surprise, when 2-isopropyl-*N*-tosylaziridine **1d** was reacted with **2** under the given conditions, no product was obtained. When the reaction time was prolonged to 6 h, the main product was **4** instead of **3** (Scheme 4). This may be

Table 1 The ring-opening of **1a** with **2a** under different conditions

Entry	Catalyst	Loading/mol%	Solvent	Temperature/°C	Time/h	Yield/%[a]
1	$AlCl_3$	100	CH_2Cl_2	Reflux	12	ND
2	$Zn(OTf)_2$	10	CH_2Cl_2	Reflux	12	10
3	$Yb(OTf)_3$	10	CH_2Cl_2	Reflux	12	30
4	$Y(OTf)_3$	10	CH_2Cl_2	Reflux	12	35
5	$Sc(OTf)_3$	1	CH_3NO_2	25/50/reflux	6	ND/52/55[b]
6	$Sc(OTf)_3$	1	THF	25/50/reflux	6	ND/70/72[b]
7	$Sc(OTf)_3$	1	CH_2Cl_2	25	6	ND
8	$Sc(OTf)_3$	1	CH_2Cl_2	Reflux	2	83[b]
9	$Sc(OTf)_3$	1	Solvent-free	50	1	95

ND, not determined
[a]Isolated yields based on **1a**.
[b]Isolated yields based on different temperature.

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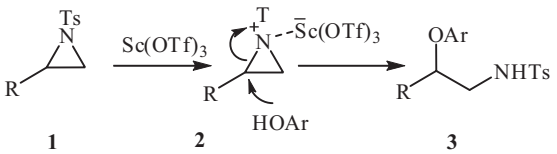
Table 2 The ring-opening reaction of aziridines **1** with phenol derivatives **2** in the presence of $Sc(OTf)_3$

Entry	R^1	Ar	Product	Time/h	Yield of **3**/%[a]
1	Ph (**1a**)	C_6H_5 (**2a**)	**3a**	1	95
2	Ph (**1a**)	*m*-$CH_3C_6H_4$ (**2b**)	**3b**	1	94
3	Ph (**1a**)	*p*-ClC_6H_4 (**2c**)	**3c**	2	85
4	Ph (**1a**)	*p*-$NO_2C_6H_4$ (**2d**)	**3d**	2	82
5	CH_3 (**1b**)	C_6H_5 (**2a**)	**3e**	1	94
6	CH_3 (**1b**)	*m*-$CH_3C_6H_4$ (**2b**)	**3f**	1	93
7	CH_3 (**1b**)	*p*-ClC_6H_4 (**2c**)	**3g**	2	81
8	CH_3 (**1b**)	*p*-$NO_2C_6H_4$ (**2d**)	**3h**	2	78
9	$PhCH_2$ (**1c**)	C_6H_5 (**2a**)	**3i**	1	82
10	$PhCH_2$ (**1c**)	*m*-$CH_3C_6H_4$ (**2b**)	**3j**	1	78
11	$PhCH_2$ (**1c**)	*p*-ClC_6H_4 (**2c**)	**3k**	2	75
12	Ph (**1a**)	*o*-$CH_3COC_6H_4$ (**2g**)	–	4	0

[a]Isolated yields based on **1**, the regioselectivity was determined by NMR.



Scheme 3

ascribed the formation of the more stable carbonium in **B**, by rearrangement of the species **A**. Phenols attack the more stable cation to afford the unexpected product **4** in moderate yield. Other phenols reacted with substrate **1d** and similar results were obtained (**Table 3**). In view of these experimental facts, a possible mechanism for the formation of **4** can be proposed (Scheme 4).

In summary, $Sc(OTf)_3$-catalysed regioselective ring-opening of aziridines with phenols is described, which provides a convenient approach to the synthesis of tertiary alkyl–aryl ethers. Further investigations of the scope of the reaction are currently underway.

Experimental

Melting points were determined on a Büchi B-540 melting apparatus and are uncorrected. The NMR spectra were measured with a Bruker Advance III 500 or Varian Mercury Plus-400 instrument using $CDCl_3$ as the solvent with TMS as internal standard. IR spectra were recorded using KBr pellets on a Nicolet Aviatar-370 instrument. Mass spectra were measured with Thermo Finnigan LCQ-Advantage instrument. Elemental analysis was performed on a VarioEL-III instrument. High resolution mass spectrometric (HRMS) analyses were measured on an APEX (Bruker) mass III spectrometer using ESI (electrospray ionisation) techniques. All spectroscopic data of the products were identical to those of authentic samples.

General procedure

To a mixture of 2-phenyl-1-tosylaziridine **1a** (1 mmol, 0.27 g) and phenol **2a** (1.05 mmol, 0.10 g), scandium triflate (0.01 mmol, 4.9 mg) was added. The reaction mixture was stirred at 50°C and the reaction monitored by TLC. After completion the reaction mixture was quenched with water (10 ml) and extracted with CH_2Cl_2 (10 ml). The organic phase was washed with brine and dried over sodium sulfate. After concentration under reduced pressure, the residue was purified by silica gel column chromatography using petroleum ether–ethyl acetate (10 : 1) as eluent to afford **3a** (0.35 g, yield: 95%).

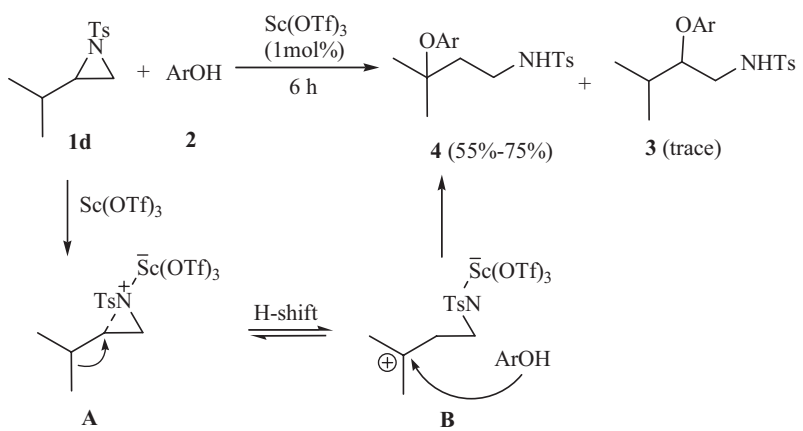
The synthetic procedure for **4a** was the same as for product **3a**.

Spectroscopic data for obtained compounds (for **3c***,* **3g***,* **3k** *and* **4c** *M^+ is given for ^{35}Cl)*

4-methyl-N-*(2-phenoxy-2-phenylethyl)benzenesulfonamide* (**3a**): White solid; m.p. 108.5–109.5°C. [lit.(13): 145–146°C]. MS (ESI): *m/z* (%) = 367 (M^+, 2), 274 (100). IR (KBr) ν_{max}: 3145, 1401, 1321, 1154, 1104 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.72 (d, 2H, *J* = 8.0 Hz), 7.23–7.30 (m, 7H), 7.14 (t, 2H, *J* = 8.0 Hz), 6.88 (t, 1H, *J* = 7.2 Hz), 6.71 (d, 2H, *J* = 8.0 Hz), 5.11 (d, 1H, *J* = 6.0 Hz), 5.03 (d, 1H, *J* = 4.4 Hz), 3.38–3.45 (m, 1H), 3.22–3.28 (m, 1H), 2.40 (s, 3H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.2, 143.5, 137.9, 137.1, 129.8 (CH × 2), 129.3 (CH × 2), 128.8 (CH × 2), 128.4, 127.0 (CH × 2), 126.0 (CH × 2), 121.4, 115.8 (CH × 2), 78.5, 49.5, 21.5.

4-methyl-N-*(2-phenyl-2-(*m-*tolyloxy)ethyl)benzenesulfonamide* (**3b**): White solid; m.p. 95.5–97.5°C. MS (ESI): *m/z* (%) = 381 (M^+, 3), 274 (100). Anal. Calcd for $C_{22}H_{23}NO_3S$: C, 69.26; H, 6.08; N, 3.67; Found: C, 69.15; H, 6.1; N, 3.55. IR (KBr) ν_{max}: 3145, 1400, 1320, 1157, 1091 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.72 (d, 2H, *J* = 8.0 Hz), 7.25–7.32 (m, 7H), 7.01 (d, 1H, *J* = 8.0 Hz), 6.70 (d, 1H, *J* = 8.0 Hz), 6.56 (s, 1H), 6.49 (d, 1H, *J* = 8.0 Hz), 5.10 (dd, 1H, *J* = 3.6, 9.2 Hz), 5.02 (brs, 1H), 3.42 (ddd, 1H, *J* = 3.6, 8.8, 12.8 Hz), 3.23 (ddd, 1H, *J* = 3.6, 8.8, 12.8 Hz), 2.41 (s, 3H), 2.23 (s, 3H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.2, 143.5, 139.4, 138.1, 137.2, 129.8 (CH × 2), 129.1, 128.8 (CH × 2), 128.3, 127.0 (CH × 2), 126.0 (CH × 2), 122.3, 116.7, 112.6, 78.4, 49.5, 21.5, 21.4.

N-*(2-(4-chlorophenoxy)-2-phenylethyl)-4-methylbenzene-sulfonamide* (**3c**): White solid; m.p. 129.5–130.5°C. MS (ESI): *m/z* (%) = 403 ([M + 2]$^+$, 1), 401 (M^+, 3), 274 (100). Anal. Calcd for $C_{21}H_{20}ClNO_3S$: C,



Scheme 4

Table 3 The reaction of **1d** with **2**

Entry	ArOH	Yield/%
1	C_6H_5 (**2a**)	55 (**4a**)
2	*m*-$CH_3C_6H_4$ (**2b**)	56 (**4b**)
3	*p*-ClC_6H_4 (**2c**)	70 (**4c**)
4	ß-$C_{10}H_7$ (**2e**)	75 (**4d**)

62.76; H, 5.02; N, 3.49; Found: C, 62.6; H, 5.1; N, 3.4. IR (KBr) ν_{max}: 3134, 1400, 1317, 1155, 1105 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.72 (d, 2H, *J* = 8.4 Hz), 7.23–7.34 (m, 7H), 7.09 (d, 2H, *J* = 9.2 Hz), 6.63 (d, 2H, *J* = 9.2 Hz), 5.06 (dd, 1H, *J* = 3.6, 9.2 Hz), 4.97–5.02 (m, 1H), 3.42 (ddd, 1H, *J* = 3.6, 8.8, 12.8 Hz), 3.26 (ddd, 1H, *J* = 3.6, 8.8, 12.8 Hz), 2.41 (s, 3H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.2, 143.5, 137.9, 137.1, 129.8 (CH × 2), 129.3 (CH × 2), 128.8 (CH × 2), 128.4, 127.0 (CH × 2), 126.0 (CH × 2), 121.4, 115.8 (CH × 2), 78.5, 49.5, 21.5.

4-methyl-N-*(2-(4-nitrophenoxy)-2-phenylethyl)benzenesulfonamide* (**3d**): White solid; m.p. 185.5–187.0°C. MS (ESI): *m/z* (%) = 412 (M^+, 1), 367 (4), 274 (30), 155 (100). Anal. Calcd for $C_{21}H_{20}N_2O_5S$: C, 61.15; H, 4.89; N, 6.79; Found: C, 60.9; H, 5.0; N, 6.7. IR (KBr) ν_{max}: 3313, 2932, 1593, 1315, 1161, 1109 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.05 (d, 2H, *J* = 9.2 Hz), 7.72 (d, 2H, *J* = 8.0 Hz), 7.31–7.37 (m, 3H), 7.25–7.29 (m, 4H), 6.79 (d, 2H, *J* = 9.2 Hz), 5.27 (dd, 1H, *J* = 3.6, 8.8 Hz), 5.06 (brs, 1H), 3.45 (ddd, 1H, *J* = 4.0, 8.8, 13.6 Hz), 3.34 (ddd, 1H, *J* = 4.8, 8.8, 13.6 Hz), 2.40 (s, 3H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.2, 143.8, 141.8, 137.0, 136.4, 129.8 (CH × 2), 129.2 (CH × 2), 129.0, 127.0 (CH × 2), 126.0 (CH × 2), 125.7 (CH × 2), 115.3 (CH × 2), 73.5, 47.8, 21.5.

4-methyl-N-*(2-phenoxypropyl)benzenesulfonamide* (**3e**): White solid; m.p. 80.1–82.5°C. MS (ESI): *m/z* (%) = 305 (M^+, 20), 212 (100). Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59; Found: C, 62.7; H, 6.35; N, 4.5. IR (KBr) ν_{max}: 3293, 2917, 1325, 1155, 1089 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.73 (d, 2H, *J* = 7.6 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.23 (d, 2H, *J* = 8.0 Hz), 6.95 (t, 1H, *J* = 7.2 Hz), 6.78 (d, 2H, *J* = 8.4 Hz), 4.98 (dd, 1H, *J* = 4.4, 7.6 Hz), 4.39–4.43 (m, 1H), 3.26 (ddd, 1H, *J* = 3.6, 8.0, 12.4 Hz), 3.06 (ddd, 1H, *J* = 4.8, 7.6, 12.8 Hz), 2.42 (s, 3H), 1.22 (d, 3H, *J* = 6.0 Hz), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.0, 143.5, 137.0, 129.8 (CH × 2), 129.6 (CH × 2), 127.0 (CH × 2), 121.5, 116.0 (CH × 2), 72.4, 48.0, 21.5, 17.1.

4-methyl-N-*(2-(m-tolyloxy)propyl)benzenesulfonamide* (**3f**): White solid; m.p. 76.5–78.1°C. MS (ESI): *m/z* (%) = 319 (M^+, 30), 212 (100). Anal. Calcd for $C_{17}H_{21}NO_3S$: C, 63.92; H, 6.63; N, 4.39; Found: C, 63.8; H, 6.7; N, 4.25. IR (KBr) ν_{max}: 3131, 2978, 2925, 1401, 1160, 1091 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.72 (d, 2H, *J* = 8.4 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.12 (t, 1H, *J* = 7.6 Hz), 6.77 (d, 1H, *J* = 7.6 Hz), 6.59 (s, 1H), 6.58 (d, 1H, *J* = 8.8 Hz), 4.93 (brs, 1H), 4.36–4.40 (m, 1H), 3.25 (ddd, 1H, *J* = 3.6, 8.0, 12.8 Hz), 3.05 (ddd, 1H, *J* = 4.4, 7.6, 12.4 Hz), 2.42 (s, 3H), 2.29 (s, 3H), 1.21 (d, 3H, *J* = 6.0 Hz), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.0, 143.4, 139.6, 137.1, 129.7 (CH × 2), 129.3, 127.0 (CH × 2), 122.3, 116.9, 112.9, 72.4, 48.0, 21.5, 21.4, 14.1.

N-*(2-(4-chlorophenoxy)propyl)-4-methylbenzenesulfonamide* (**3g**): White solid; m.p. 77.5–79.0°C. MS (ESI): *m/z* (%) = 341 ([M + 2]$^+$, 5), 339 (M^+, 15), 212 (95), 155 (100). Anal. Calcd for $C_{16}H_{18}ClNO_3S$: C, 56.55; H, 5.34; N, 4.12; Found: C, 56.4; H, 5.4; N, 4.0. IR (KBr) ν_{max}: 3266, 2924, 1320, 1150, 1086 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.72 (d, 2H, *J* = 8.0 Hz), 7.26 (d, 2H, *J* = 8.4 Hz), 7.17 (d, 2H, *J* = 8.8 Hz), 6.71 (d, 2H, *J* = 9.2 Hz), 5.02 (dd, 1H, *J* = 4.4, 7.2 Hz), 4.32–4.37 (m, 1H), 3.24 (ddd, 1H, *J* = 3.6, 8.0, 12.4 Hz), 3.06 (ddd, 1H, *J* = 4.8, 7.2, 12.8 Hz), 2.42 (s, 3H), 1.21 (d, 3H, *J* = 6.4 Hz), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.6, 143.6, 137.0, 129.8 (CH × 2), 129.7 (CH × 2), 127.0 (CH × 2), 126.4, 117.3 (CH × 2), 73.0, 47.9, 21.5, 17.0.

4-methyl-N-*(2-(4-nitrophenoxy)propyl)benzenesulfonamide* (**3h**): White solid; m.p. 126.2–128.1°C. MS (ESI): *m/z* (%) = 350 (M^+, 10), 212 (40), 155 (100). Anal. Calcd for $C_{16}H_{18}N_2O_5S$: C, 54.85; H, 5.18; N, 7.99; Found: C, 54.7; H, 5.3; N, 7.85. IR (KBr) ν_{max}: 3266, 1593, 1318, 1149, 1088 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.16 (d, 2H, *J* = 9.2 Hz), 7.73 (d, 2H, *J* = 8.0 Hz), 7.28 (d, 2H, *J* = 8.4 Hz), 6.85 (d, 2H, *J* = 9.2 Hz), 4.90 (t, 1H, *J* = 6.0 Hz), 4.55–4.59 (dd, 1H, *J* = 6.8, 10.4 Hz), 3.29 (ddd, 1H, *J* = 3.6, 8.0, 12.4 Hz), 3.14 (ddd, 1H, *J* = 4.0, 7.6, 12.8 Hz), 2.42 (s, 3H), 1.29 (d, 3H, *J* = 6.0 Hz), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.2, 143.8, 141.8, 137.1, 129.8 (CH × 2), 127.0 (CH × 2), 126.0 (CH × 2), 115.3 (CH × 2), 73.5, 47.8, 21.5, 16.9.

4-methyl-N-*(2-phenoxy-3-phenylpropyl)benzenesulfonamide* (**3i**): White solid; m.p. 94–96°C. MS (ESI): *m/z* (%) = 381 (M^+, 23), 380 ([M-1]$^+$, 100), 286 (18). Anal. Calcd for $C_{22}H_{23}NO_3S$: C, 69.26; H, 6.08; N, 3.67; Found: C, 69.2; H, 6.15; N, 3.6. IR (KBr) ν_{max}: 3272, 2925, 1598, 1494, 1150, 1086 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (d, 2H, *J* = 8.0 Hz), 7.20–7.29 (m, 7H), 7.13 (t, 2H, *J* = 6.0 Hz), 6.95 (t, 1H, *J* = 6.0 Hz), 6.79 (d, 2H, *J* = 8.0 Hz), 4.87 (brs, 1H), 4.43 (d, 1H, *J* = 4.0 Hz), 3.19 (dd, 1H, *J* = 4.0, 8.0 Hz), 3.10 (dd, 1H, *J* = 4.0, 12.0 Hz), 2.97 (dd, 1H, *J* = 4.0, 12.0 Hz), 2.84 (dd, 1H, *J* = 8.0, 12.0 Hz), 2.41 (s, 3H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.1, 143.5, 136.8, 136.5, 129.8 (CH × 2), 129.7 (CH × 2), 129.4 (CH × 2), 128.7 (CH × 2), 127.1 (CH × 2), 127.0, 121.8, 116.2 (CH × 2), 77.3, 45.3, 37.5, 21.5.

4-methyl-N-*(3-phenyl-2-(*m-*tolyloxy)propyl)benzenesulfonamide* (**3j**): White solid; m.p. 86–88°C. MS (ESI): *m/z* (%) = 395 (M^+, 21), 394 ([M-1]$^+$, 100), 332 (68). Anal. Calcd for $C_{23}H_{25}NO_3S$: C, 69.84; H, 6.37; N, 3.54; Found: C, 69.75; H, 6.5; N, 3.3. IR (KBr) ν_{max}: 3271, 2976, 2919, 1597, 1489, 1152, 1084 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (d, 2H, *J* = 8.0 Hz), 7.25–7.32 (m, 7H), 7.01 (d, 1H, *J* = 8.0 Hz), 6.77 (d, 1H, *J* = 8.0 Hz), 6.60 (s, 1H), 6.59 (d, 1H, *J* = 8.0 Hz), 4.87 (brs, 1H), 4.40 (d, 1H, *J* = 4.0 Hz), 3.18 (dd, 1H, *J* = 4.0, 8.0 Hz), 3.09 (dd, 1H, *J* = 4.0, 12.0 Hz), 2.98 (dd, 1H, *J* = 4.0, 12.0 Hz), 2.84 (dd, 1H, *J* = 8.0, 12.0 Hz), 2.41 (s, 3H), 2.30 (s, 3H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.1, 143.5, 139.8, 136.8, 136.6, 129.8, 129.7 (CH × 2), 129.4 (CH × 2), 128.7 (CH × 2), 127.1 (CH × 2), 127.0, 122.6, 117.1, 113.0, 77.3, 45.3, 37.6, 21.5 (CH × 2).

N-*(2-(4-chlorophenoxy)-3-phenylpropyl)-4-methylbenzene sulfonamide* (**3k**): White solid; m.p. 95–97°C. MS (ESI): *m/z* (%) = 417 ([M + 2]$^+$, 6), 415 (M^+, 18), 414 (100). Anal. Calcd for $C_{22}H_{22}ClNO_3S$: C, 63.53; H, 5.33; N, 3.37; Found: C, 63.45; H, 5.6; N, 3.2. IR (KBr) ν_{max}: 3264, 2922, 1596, 1490, 1149, 1092 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (d, 2H, *J* = 8.0 Hz), 7.19–7.28 (m, 5H), 7.15 (d, 2H, *J* = 8.0 Hz), 7.11 (d, 2H, *J* = 8.0 Hz), 6.68 (d, 2H, *J* = 8.0 Hz), 4.96 (brs, 1H), 4.39 (dd, 1H, *J* = 4.0 Hz), 3.18 (dd, 1H, *J* = 4.0, 8.0 Hz), 3.10 (dd, 1H, *J* = 4.0, 12.0 Hz), 2.94 (dd, 1H, *J* = 4.0, 12.0 Hz), 2.84 (dd, 1H, *J* = 8.0, 12.0 Hz), 2.41 (s, 3H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.1, 143.6, 136.7, 136.2, 129.8 (CH × 2), 129.7 (CH × 2), 129.4 (CH × 2), 128.8 (CH × 2), 127.1 (CH × 2), 127.0, 126.5, 117.5 (CH × 2), 77.8, 45.3, 37.5, 21.5.

4-methyl-N-*(3-methyl-3-phenoxybutyl)benzenesulfonamide* (**4a**): Light yellow liquid. MS (ESI): *m/z* (%) = 334 ([M + 1]$^+$, 13), 240 (92), 184 (100). HRMS (ESI) Calcd for $C_{18}H_{23}NO_3S$ (M + 1)$^+$, 334.1471. Found: (M + 1)$^+$, 334.1472. IR (KBr) ν_{max}: 3131, 2978, 1401, 1160, 1094 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.77 (d, 2H, *J* = 8.0 Hz), 7.31 (d, 2H, *J* = 8.0 Hz), 7.25 (t, 2H, *J* = 7.6 Hz), 7.10 (t, 1H, *J* = 7.6 Hz), 6.86 (d, 2H, *J* = 7.8 Hz), 5.29 (brs, 1H), 3.23 (dd, 2H, *J* = 6.4, 12.0 Hz), 2.44 (s, 3H), 1.84 (t, 2H, *J* = 6.8 Hz), 1.18 (s, 6H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.1, 143.3, 136.9, 129.7 (CH × 2), 129.0 (CH × 2), 127.2 (CH × 2), 124.1 (CH × 2), 124.0, 80.4, 41.0, 39.6, 26.3 (CH × 2), 21.5.

4-methyl-N-*(3-methyl-3-(m-tolyloxy)butyl)benzenesulfonamide* (**4b**): Light yellow liquid. MS (ESI): *m/z* (%) = 370 ([M + Na]$^+$, 100). HRMS (ESI) Calcd for $C_{19}H_{25}NO_3S$ (M + 1)$^+$, 348.1628. Found: (M + 1)$^+$, 348.1624. IR (KBr) ν_{max}: 3285, 2977, 2928, 1600, 1485, 1160, 1094 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.77 (d, 2H, *J* = 8.0 Hz), 7.31 (d, 2H, *J* = 8.0 Hz), 7.12 (t, 1H, *J* = 7.5 Hz), 6.91 (d, 1H, *J* = 7.5 Hz), 6.67 (s, 1H), 6.66 (m, 1H, *J* = 8.0 Hz), 5.34 (d, 1H, *J* = 5.0 Hz), 3.22 (dd, 2H, *J* = 6.0, 12.0 Hz), 2.44 (s, 3H), 2.31 (s, 3H), 1.83 (t, 2H, *J* = 6.5 Hz), 1.17 (s, 6H), ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 154.1, 143.2, 139.0, 137.0, 129.7 (CH × 2), 128.7, 127.2 (CH × 2), 124.8, 124.7, 121.0, 80.3, 41.0, 39.6, 26.3 (CH × 2), 21.5, 21.4.

N-*(3-(4-chlorophenoxy)-3-methylbutyl)-4-methylbenzene-sulfonamide* (**4c**): Light yellow liquid. MS (ESI): *m/z* (%) = 370 ([M + 3]$^+$, 33), 368 ([M + 1]$^+$, 100). HRMS (ESI) Calcd for $C_{18}H_{22}ClNO_3S$ (M + 1)$^+$, 368.1082. Found: (M + 1)$^+$, 368.1076. IR (KBr) ν_{max}: 3286, 2977, 2928, 1488, 1160, 1093 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.76 (d, 2H, *J* = 8.0 Hz), 7.32 (d, 2H, *J* = 8.0 Hz), 7.20 (dd, 2H, *J* = 2.0, 7.0 Hz), 6.79 (dd, 2H, *J* = 2.0, 7.0 Hz), 5.26 (t, 1H, *J* = 5.5 Hz), 3.20 (dd, 2H, *J* = 6.5, 12.5 Hz), 2.44 (s, 3H), 1.83 (t, 2H, *J* = 7.0 Hz), 1.16 (s, 6H), ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 152.8, 143.4, 136.9, 129.7 (CH × 2), 129.2, 129.1 (CH × 2), 127.2 (CH × 2), 125.4 (CH × 2), 80.8, 41.0, 39.4, 26.3 (CH × 2), 21.6.

4-methyl-N-*(3-methyl-3-(naphthalen-2-yloxy)butyl)benzenesulfonamide* (**4d**): White solid; m.p. 95.0–96.7°C. MS (ESI): *m/z* (%) = 407 ([M + Na]$^+$, 100). Anal. Calcd for $C_{22}H_{25}NO_3S$: C, 68.90; H, 6.57; N, 3.65; Found: C, 68.85; H, 6.6; N, 3.6. IR (KBr) ν_{max}: 3246, 2972, 1401, 1151, 1095 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.81 (d, 1H, *J* = 8.0 Hz), 7.78 (d, 2H, *J* = 8.0 Hz), 7.72–7.75 (m, 2H), 7.47 (ddd, 1H, *J* = 1.0, 6.5, 8.0 Hz), 7.42 (ddd, 1H, *J* = 1.0, 6.5, 8.0 Hz), 7.32

(d, 2H, J = 8.0 Hz), 7.27 (d, 1H, J = 2.5 Hz), 7.05 (d, 1H, J = 2.5, 9.0 Hz), 5.28 (t, 1H, J = 5.5 Hz), 3.28 (dd, 2H, 6.5, 10.5 Hz), 2.45 (s, 3H), 1.91 (t, 2H, J = 6.5 Hz), 1.25 (s, 6H), ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 151.9, 143.3, 136.9, 134.0, 130.5, 129.7 (CH × 2), 128.9 (CH × 2), 127.6, 127.2 (CH × 2), 126.3, 124.9, 124.5, 120.0, 81.0, 41.1, 39.6, 26.4 (CH × 2), 21.6.

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