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Lewis Acid Catalyzed S_N2-Type Ring Opening of *N*-Activated Aziridines with Electron-Rich Arenes/Heteroarenes

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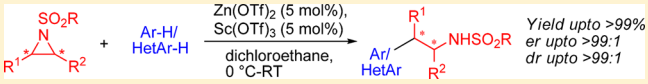
Supporting Information

ABSTRACT: An efficient Lewis acid catalyzed S_N2-type ring opening of substituted aziridines with electron-rich arenes/heteroarenes to provide substituted 2,2-diaryl/heteroarylethylamines in excellent yields and stereoselectivity (er, dr >99:1) is described.



INTRODUCTION

In recent years aziridines have become one of the most useful substrates/building blocks for the generation of a number of nitrogen-containing compounds of contemporary interest.[1] A large variety of heteroatomic and carbon-centered nucleophiles have been used for the nucleophilic ring opening of aziridines.[2,3] Although the ring-opening chemistry of aziridines with heteroatomic nucleophiles is well documented in the literature, the same with the carbon nucleophiles has not been much explored.[4] It is worth mentioning that mostly carbanion-based carbon nucleophiles have been employed for this purpose compared to the neutral carbon nucleophiles such as arenes/heteroarenes.[5] There are very few reports on inter-[5] or intramolecular[6] ring opening of aziridines with arenes/heteroarenes, and most of these methods suffer from poor regioselectivity and/or limited substrate scope. It is noteworthy that the intermolecular ring opening of aziridines with arenes provides an easy access to 2-arylethylamine scaffolds,[7] which are biologically active compounds acting as drug molecules as well, e.g., phenylethylamines and serotonin, venlafaxine (antidepressive), and Salmeterol (antiasthmatic) (Figure 1). Many other synthetic routes are known for the synthesis of substituted 2-arylethylamines.[8,9] Although the ring-opening chemistry of aziridines has been utilized for the synthesis of phenylethylamines,[5] *to the best of our knowledge, there is no report of stereoselective intermolecular ring-opening reactions of aziridines with arenes.*[10,5f] Therefore, the development of an efficient pathway for the stereoselective synthesis of such compounds is highly desirable. In continuation of our research activities in the area of Lewis acid (LA) catalyzed S_N2-type ring opening of activated aziridines/azetidines,[11] we have developed a diastereo- as well as enantioselective route for the synthesis of 2-arylethylamines via intermolecular ring opening of substituted *N*-activated aziridines with electron-rich arenes and heteroarenes. Herein, we report our results in detail.

RESULTS AND DISCUSSION

Our study began with the reaction of 2-phenyl-*N*-nosylaziridine[12] **1a** with 1,3,5-trimethoxybenzene **2a** (1.5 equiv) in the presence of $Sc(OTf)_3$ (20 mol %) as the LA catalyst (Table 1) in dichloromethane to provide the corresponding phenylethylamine **3a** in moderate yield (entry 1, Table 1). In order to find the optimum reaction condition, we screened other Lewis acids as catalysts such as $Cu(OTf)_2$, $Zn(OTf)_2$ and solvents such as dichloroethane, nitromethane, etc. (entries 2−6). When the reaction was carried out in dichloroethane using $Sc(OTf)_3$ (20 mol %) as the LA catalyst, **3a** was obtained in good yield (62%), and even with lesser amount (5 mol %) of the LA catalyst, the reaction was found to be successful (entries 4 and 6). On the basis of a recent report by Wu et al.,[5c] employing $AuCl_3$/AgOTf or Zn/Ag as the dual catalysts for the nucleophilic ring opening of aziridines with arenes, when **1a** was reacted with **2a**, the corresponding product **3a** was produced in very poor yield (entries 8 and 9). On the basis of our success with $Sc(OTf)_3$ in dichloroethane solvent (entry 5), we intended to use a combination of $Sc(OTf)_3$ and another catalyst for this purpose. To our great pleasure, when reaction of **1a** with **2a** was carried out in the presence of catalytic amount of $Sc(OTf)_3$ (5 mol %) and $Zn(OTf)_2$ (5 mol %) in dichloroethane, **3a** was obtained in excellent yield (entry 11). The yield of the product **3a** could not be improved further using other combinations of LA catalysts such as $Sc(OTf)_3$ (5 mol %) and $Cu(OTf)_2$ (5 mol %) (entry 12) or $BF_3{\cdot}OEt_2$ (5 mol %) and $Zn(OTf)_2$ (5 mol %) (entry 13). Unsatisfactory results in terms of yield and the reaction time were obtained with less than 5 mol % of the catalysts.

Using the optimized reaction condition, the strategy was applied for the synthesis of various substituted 2,2-diarylethyl/2,2-aryl/heteroarylethylamines (Table 2). A variety of functionalized 2,2-diarylethylamines **3b−g**, especially, fluoro-substituted product **3d**, could be synthesized in excellent yields from the corresponding aziridines **1b−g** with **2a** following our protocol (entries 2−7). It is worth mentioning that compounds with a fluoro-substituent on the aromatic ring, e.g., **3d**, have found numerous applications in the pharmaceutical industry.[13] When thiophene (**2b**) and 1-methylindole (**2c**) were reacted with **1a**, the corresponding products **3h** and **3i**, respectively, were

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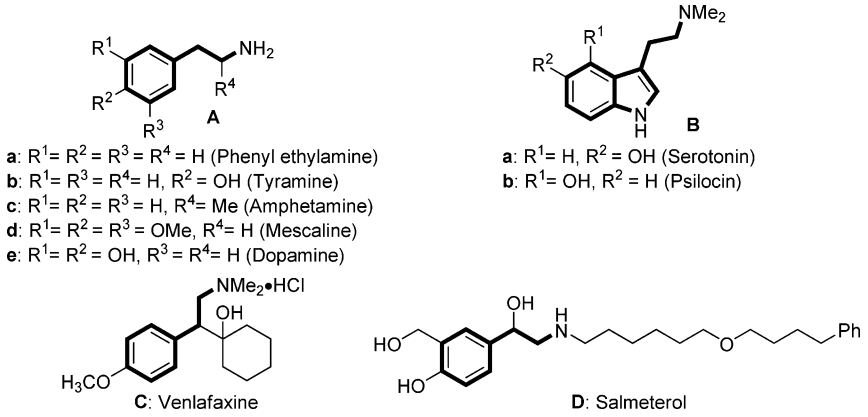
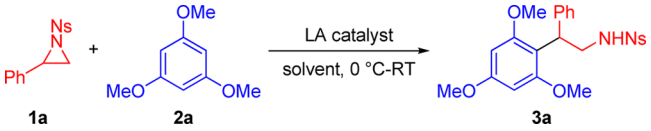


Figure 1. Some biologically active 2-arylethylamine derivatives.

Table 1. Optimization Study[a]



1a 2a 3a

entry	LA catalyst	solvent	time	yield[b] (%)
1	$Sc(OTf)_3$ (20 mol %)	dichloromethane	1.5 h	50
2	$Zn(OTf)_2$ (20 mol %)	dichloromethane	30 h	26
3	$Cu(OTf)_2$ (20 mol %)	dichloromethane	2.5 h	45
4	$BF_3{\cdot}OEt_2$ (20 mol %)	dichloromethane	1.5 h	45
5	$Sc(OTf)_3$ (20 mol %)	dichloroethane	1.5 h	62
6	$Sc(OTf)_3$ (20 mol %)	nitromethane	1.5 h	20
7	$Sc(OTf)_3$ (5 mol %)	dichloroethane	1.5 h	56
8	$AuCl_3$ (5 mol %), AgOTf (15 mol %)	nitromethane	5 min	30
9	$AuCl_3$ (5 mol %), $AgSbF_6$ (15 mol %)	nitromethane	5 min	31
10	$Zn(OTf)_2$ (5 mol %), AgOTf (15 mol %)	nitromethane	5 min	38
11	$Sc(OTf)_3$ (5 mol %), $Zn(OTf)_2$ (5 mol %)	dichloroethane	30 min	85
12	$Sc(OTf)_3$ (5 mol %), $Cu(OTf)_2$ (5 mol %)	dichloroethane	45 min	68
13	$BF_3{\cdot}OEt_2$ (5 mol %), $Zn(OTf)_2$ (5 mol %)	dichloroethane	30 min	70
14	$Sc(OTf)_3$ (5 mol %), $Zn(OTf)_2$ (5 mol %)	dichloromethane	30 min	53
15	$Sc(OTf)_3$ (5 mol %), $Zn(OTf)_2$ (5 mol %)	nitromethane	45 min	25

[a]Reactions were performed using 1.0 equiv of **1a** and 1.5 equiv of **2a**. [b]Products were obtained as a single regioisomer.

obtained in high yields (entries 8 and 9). Product **3h** was obtained as mixture of regioisomers (>3:1) probably due to attack of **2b** on benzylic and less substituted positions of the aziridine ring. It is interesting to note that **3i** bears a tryptamine motif, which is present in pharmaceutical agents and natural products.[14]

Next, we extended the scope of the reaction with other aziridines **1h**–**k** bearing other N-protecting groups, and the results are shown in Table 3.

Reaction of 2-phenyl-*N*-tosylaziridine **1h** with **2a** provided **3j** in quantitative yield as single regioisomer (entry 1, Table 3). Haloaryl-substituted aziridines **1i** and **1j** were also reacted with **2a** in a similar fashion to generate the corresponding products **3k** and **3l**, respectively, in excellent yields (entries 2 and 3). *N*-4-*tert*-Butylphenylsulfonyl-2-phenylaziridine **1k** upon reaction with **2a** produced **3m** in excellent yield. However, the reaction of **1k** with **2b** and **2d** led to the formation of the corresponding products **3n** and **3o**, respectively, with comparatively reduced yields (entries 4–6).

To broaden the scope of our strategy, it was extended further for the synthesis of chiral 2,2-diarylethylamines (Table 4). When chiral aziridine (*R*)-**1h** (ee >99%) was reacted with 1,3,5-trimethoxybenzene **2a** under our optimized condition, to our great pleasure the corresponding product (*R*)-**3j** was produced in excellent yield (97%) and high enantiomeric excess (83%) (entry 2, Table 4). Reduced ee of the products were observed from other chiral aziridines (*R*)-**1a,k** (entries 1 and 3, Table 4).[16]

To investigate the reason behind obtaining reduced enantiomeric excess of the products (*R*)-**3a** and (*R*)-**3m** from the corresponding aziridines (*R*)-**1a** and (*R*)-**1k**, respectively, we performed a time dependent study of reaction of (*R*)-**1a** with **2a** under our developed condition at −30 °C. The aliquots were taken from the reaction at a regular interval of 15 min. After purification, the ee's of both the recovered aziridine (*R*)-**1a** and the product (*R*)-**3a** were determined by chiral HPLC analysis, and the results are shown in Figure 2 (see Supporting Information for details).

From our studies (Figure 2) we could conclude that both the aziridine and the product were racemized during the reaction. Furthermore, the racemization of the product was found to be faster than that of the substrate.

On the basis of our earlier observation that the chiral *trans*-disubstituted aziridines do not undergo racemization in the presence of Lewis acids,[11d] we studied the reaction of chiral *trans* disubstituted aziridines **1l** and **1m** with arenes with a view to obtaining enantiomerically pure products (Table 5). To our great delight, when *trans*-2-phenyl-3-*n*-propyl-*N*-tosylaziridine (2*S*,3*S*)-**1l** was reacted with **2a**, the corresponding ring-opened product (1*S*,2*S*)-**3p** was obtained in excellent yield and in diastereomerically pure form (entry 1, Table 5). A similar result was obtained with aziridine (2*S*,3*S*)-**1m** (entry 2). Racemic *trans* disubstituted aziridine **1n** with a synthetically modifiable appendage (CH_2OTBS) was converted into the corresponding products **3r** and **3s** using **2a** and **2c**, respectively, in excellent yields as single diastereomer (entries 3 and 4). The structure and the relative stereochemistry of **3r** were confirmed by X-ray crystallographic analysis (see Supporting Information for details).

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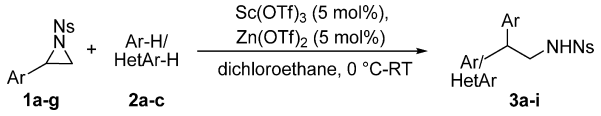
Table 2. Scope of the Reaction with Monosubstituted *N*-Nosylaziridines



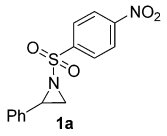
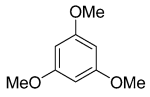
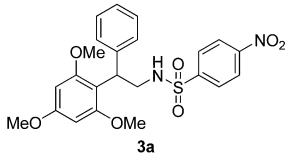
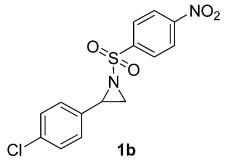
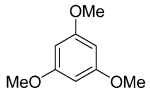
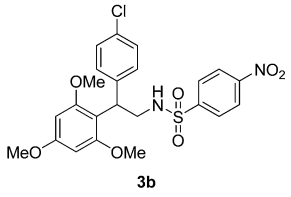
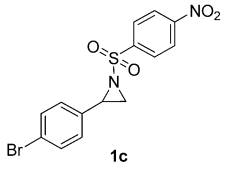
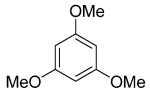
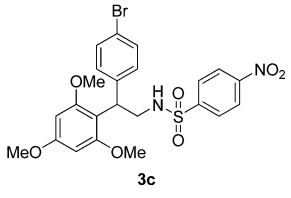
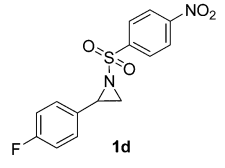
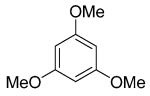
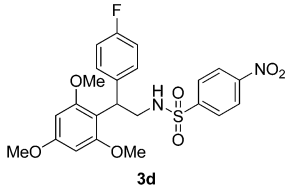
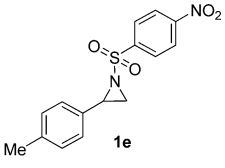
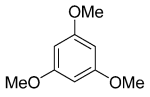
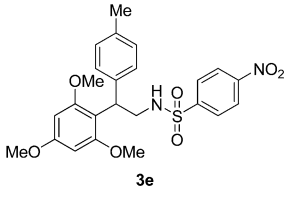
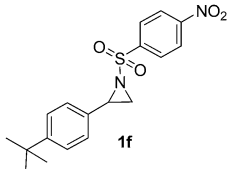
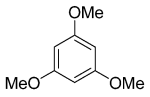
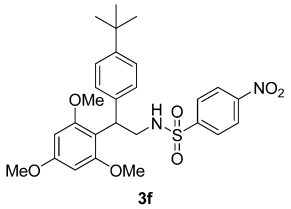
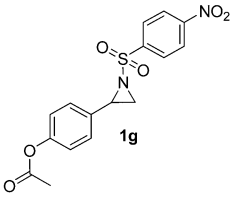
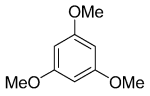
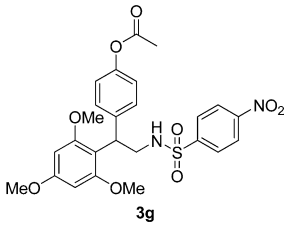
entry	aziridine	nucleophile	product	yield (%)
1	 1a	 2a	 3a	85
2	 1b	 2a	 3b	86
3	 1c	 2a	 3c	92
4	 1d	 2a	 3d	92
5	 1e	 2a	 3e	88
6	 1f	 2a	 3f	87
7	 1g	 2a	 3g	92

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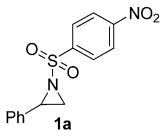
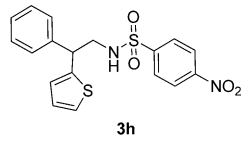
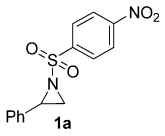
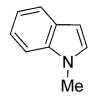
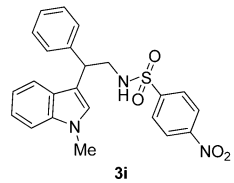
Table 2. continued

entry	aziridine	nucleophile	product	yield (%)
8	 **1a**	 **2b**	 **3h**	75[a]
9	 **1a**	 **2c**	 **3i**	65[b]

[a]Product was obtained as >3:1 mixture of regioisomers (via attack of thiophene on benzylic and unsubstituted position of aziridine[5e]). [b]Some uncharacterized compound was also produced along with **3i**.[15]

CONCLUSION

In conclusion, we have developed an efficient protocol for the synthesis of highly functionalized 2,2-diaryl/heteroarylethylamines from a variety of substituted aziridines. Both enantio- and diastereomerically pure products could be obtained when chiral disubstituted aziridines were employed as the substrates.

EXPERIMENTAL SECTION

General Experimental. Thin layer chromatography (TLC) was used for monitoring progress of the reaction using silica gel 60 F_{254} precoated plates, and the spots were visualized using UV lamp or I_2 stain. Silica gel 230−400 mesh size was used for flash column chromatography using a combination of ethyl acetate and petroleum ether as the eluent. Unless otherwise mentioned, all reactions were carried out in oven-dried glassware under nitrogen atmosphere using anhydrous solvents. Wherever appropriate, all the reagents were purified prior to use following Perrin and Armarego guidelines.[17] Monosubstituted *N*-Ns aziridines,[18] monosubstituted *N*-Ts aziridines,[19] and disubstituted aziridines[11d] were prepared following earlier reports. All the commercial reagents were used as received without further purification unless mentioned. ^{1}H NMR spectra were recorded on 400 or 500 MHz, and the chemical shifts were recorded in parts per million (ppm, δ) using tetramethyl silane (δ 0.00) as the internal standard. Splitting patterns of ^{1}H NMR are mentioned as singlet (s), doublet (d), doublet of doublet (dd), triplet (t), quartet (q), multiplet (m), etc. ^{13}C NMR spectra were recorded on 100 or 125 MHz. HRMS were obtained using (ESI) mass spectrometer (TOF). KBr plates were used for IR spectra of solid compounds, whereas liquid compounds were recorded as neat. Melting point measurements were made using a hot stage apparatus and are uncorrected. Chiral HPLC analysis using Chiralcel OD-H column (detection at 254 nm) was utilized for determining enantiomeric excess (ee). Optical rotations were measured using a 6.0 mL cell with a 1.0 dm path length and are reported as $[\alpha]^{25}_D$ (*c* in g per 100 mL solvent) at 25 °C.

Experimental Procedure. To a suspension of $Zn(OTf)_2$ (5.0 mol %) and $Sc(OTf)_3$ (5.0 mol %) in dichloroethane (2.0 mL) were added arenes/heteroarenes (1.5 equiv) (dissolved in dichloroethane (1.0 mL) if solid) at 0 °C under the nitrogen atmosphere. Subsequently, a solution of *N*-sulfonylaziridine (100 mg, 1.0 equiv) in dichloroethane was added to the reaction mixture. Then the reaction mixture was allowed to stir at room temperature (25 °C) up to completion of the reaction. After complete consumption of the starting compound (monitored by TLC), the reaction was quenched by adding water (2.0 mL). Organic phase was separated, and the aqueous phase was extracted with dichloromethane (3 × 3.0 mL). Combined extracts were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent under the reduced pressure, the crude reaction mixture was purified by flash column chromatography on silica gel (230−400 mesh) using ethyl acetate in petroleum ether as the eluent to give pure 2-aryl/heteroarylethylamines.

4-Nitro-*N*-(2-phenyl-2-(2,4,6-trimethoxyphenyl)ethyl)-benzenesulfonamide (3a). The general method described above was followed when **1a** (100 mg, 0.329 mmol) was reacted with 1,3,5-trimethoxy benzene **2a** (83 mg, 0.494 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 30 min to afford **3a** (132 mg, 0.279 mmol) as a pale yellow solid in 85% yield: mp 108−110 °C; R_f 0.36 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3310, 2949, 1742, 1603, 1494, 1453, 1402, 1335, 1226, 1205, 1165, 1152, 1126, 1062, 1035, 947, 854, 838, 815, 756, 746, 733, 700, 685, 625; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 6H), 3.74−3.88 (m, 2H), 3.77 (s, 3H), 4.57 (dd, *J* = 8.8, 6.8 Hz, 1H), 4.77 (t, *J* = 5.4 Hz, 1H), 6.00 (s, 2H), 7.09−7.21 (m, 5H), 7.87 (d, *J* = 8.8 Hz, 2H), 8.24 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.8, 45.6, 55.4, 55.7, 91.2, 108.9, 124.1, 126.3, 127.6, 128.2 (2C), 141.5, 146.2, 149.8, 159.2, 160.6; HRMS (ESI) calcd for $C_{23}H_{24}N_2O_7S$, $(M + H)^+$ 473.1382, found 473.1385.

For (*R*)-**3a**: $[\alpha]^{25}_D$ = +13.1 (*c* 0.228, $CHCl_3$) for a 43% ee sample, enantiomeric excess was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane−isopropanol 90:10, flow rate = 1.0 mL/min; t_R (1) = 36.34 min (minor), t_R (2) = 57.06 min (major).

***N*-(2-(4-Chlorophenyl)-2-(2,4,6-trimethoxyphenyl)ethyl)-4-nitrobenzenesulfonamide (3b).** The general method described above was followed when **1b** (100 mg, 0.295 mmol) was reacted with 1,3,5-trimethoxy benzene **2a** (74 mg, 0.443 mmol) in the presence of $Zn(OTf)_2$ (5 mg, 0.015 mmol) and $Sc(OTf)_3$ (7 mg, 0.015 mmol) at 25 °C for 30 min to afford **3b** (128 mg, 0.252 mmol) as a pale yellow solid in 86% yield: mp 146−148 °C; R_f 0.33 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^1) 3431, 3279, 2925, 2844, 1608, 1534, 1493, 1471, 1455, 1422, 1347, 1313, 1226, 1206, 1171, 1152, 1119, 1092, 1069, 1037, 1014, 946, 896, 854, 840, 818, 736; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.54 (s, 6H), 3.64−3.72 (m, 2H), 3.70 (s, 3H), 4.48 (dd *J* = 9.0, 6.8 Hz, 1H), 4.66 (t, *J* = 5.5 Hz, 1H), 5.93 (s, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.6 Hz, 2H), 7.79 (d, *J* = 8.8 Hz, 2H), 8.17 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.3, 45.4, 55.4, 55.7, 91.2, 108.4, 124.1, 128.2, 128.3, 129.0, 131.9, 140.1, 146.2, 149.8, 159.1, 160.8; HRMS (ESI) calcd for $C_{23}H_{23}ClN_2O_7S$, $(M - H)^-$ 505.0836, found 505.0837.

***N*-(2-(4-Bromophenyl)-2-(2,4,6-trimethoxyphenyl)ethyl)-4-nitrobenzenesulfonamide (3c).** The general method described above was followed when **1c** (100 mg, 0.261 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (66 mg, 0.392 mmol) in the presence of $Zn(OTf)_2$ (5 mg, 0.013 mmol) and $Sc(OTf)_3$ (6 mg, 0.013 mmol) at 25 °C for 30 min to afford **3c** (139 mg, 0.239 mmol) as a pale yellow solid in 92% yield: mp 90−92 °C; R_f 0.40 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3583, 3272, 2947, 2843, 1605, 1529, 1489, 1459, 1421, 1345, 1223, 1204, 1165, 1123, 1093, 1036, 1009, 948, 890, 836, 812, 738, 684; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 6H), 3.69−3.83 (m, 2H), 3.77 (s, 3H), 4.54 (dd *J* = 9.2, 6.6

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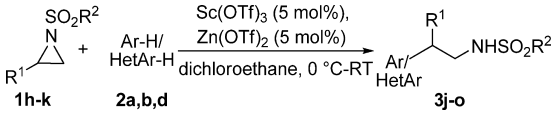
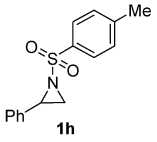
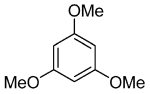
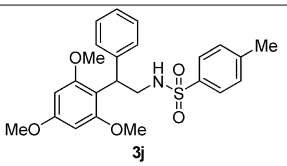
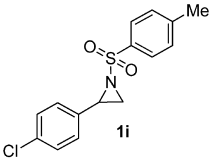
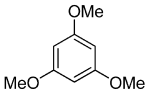
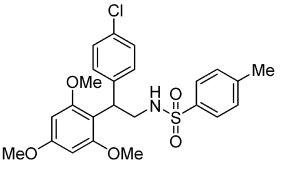
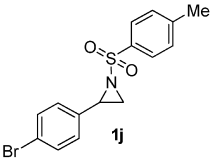
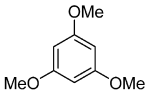
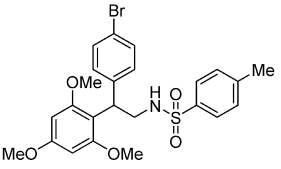
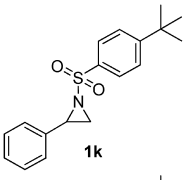
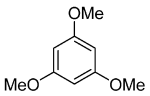
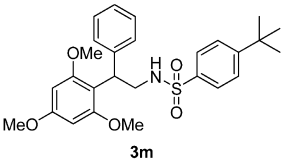
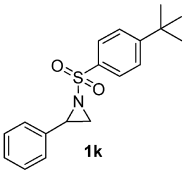
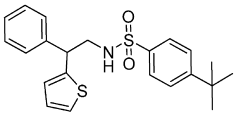
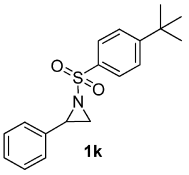
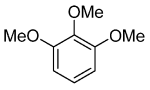
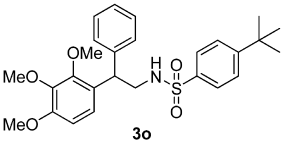
Table 3. Scope of the Reaction with Other *N*-Sulfonylaziridines



entry	aziridine	nucleophile	product	yield (%)
1	 **1h**	 **2a**	 **3j**	97
2	 **1i**	 **2a**	 **3k**	90
3	 **1j**	 **2a**	 **3l**	92
4	 **1k**	 **2a**	 **3m**	90
5	 **1k**	 **2b**	 **3n**	75[a]
6	 **1k**	 **2d**	 **3o**	72

[a]Product was obtained as 4:1 mixture of regioisomers (via attack of thiophene on benzylic and unsubstituted position of aziridine[5e]).

Hz, 1H), 4.78 (dd, *J* = 6.1, 5.3 Hz 1H), 5.99 (s, 2H), 6.99 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 8.8 Hz, 2H), 8.23 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.3, 45.4, 55.4, 55.7, 91.2, 108.3, 120.0, 124.1, 128.2, 129.4, 131.2, 140.7, 146.2, 149.8, 159.1, 160.8; HRMS (ESI) calcd for $C_{23}H_{23}BrN_2O_7S$, $(M - H)^-$ 549.0331, found 549.0339.

***N*-(2-(4-Fluorophenyl)-2-(2,4,6-trimethoxyphenyl)ethyl)-4-nitrobenzenesulfonamide (3d).** The general method described above was followed when **1d** (100 mg, 0.310 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (78 mg, 0.465 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 30 min to afford **3d** (157 mg, 0.285 mmol) as a pale yellow solid in 92% yield: mp 146−148 °C; R_f 0.38 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3270, 2947, 2873, 2843, 1608, 1534, 1506, 1474, 1456, 1424, 1349, 1223, 1171, 1153, 1119, 1038, 947, 903, 845, 820, 737, 682; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 6H), 3.69−3.84 (m, 2H), 3.77 (s, 3H), 4.55 (dd, *J* = 9.5, 6.8 Hz, 1H), 4.76 (t, *J* = 5.8 Hz, 1H), 6.00 (s, 2H), 6.87 (dd, *J* = 8.8, 8.6 Hz, 2H), 7.06−7.09 (m, 2H), 7.87 (d, *J* = 8.8 Hz, 2H), 8.24 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.2, 45.6, 55.4, 55.7, 91.2, 108.6, 114.9, 115.0, 124.1, 128.2, 129.05, 129.11, 137.3, 146.2, 149.8, 159.1, 160.4, 160.7, 162.3; HRMS (ESI) calcd for $C_{23}H_{23}FN_2O_7S$, $(M + H)^+$ 491.1288, found 491.1288.

4-Nitro-*N*-(2-*p*-tolyl-2-(2,4,6-trimethoxyphenyl)ethyl)-benzenesulfonamide (3e). The general method described above was followed when **1e** (100 mg, 0.314 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (79 mg, 0.471 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 45 min to afford **3e** (134 mg, 0.275 mmol) as a pale yellow solid in 88% yield: mp 188−190 °C; R_f 0.44 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3299, 3104, 2925, 2853, 1607, 1529, 1493, 1456, 1437, 1417, 1348, 1311, 1222, 1205, 1164, 1122, 1094, 1064, 1037, 1013, 950, 910, 855, 813, 735, 685; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.61 (s, 6H), 3.71−3.86 (m, 2H), 3.77 (s, 3H), 4.53 (dd, *J* = 9.5, 6.8 Hz, 1H), 4.72 (t, *J* = 5.6 Hz, 1H), 6.00 (s, 2H), 6.98−7.02 (m, 4H), 7.87 (d, *J* = 8.6 Hz, 2H), 8.24 (d, *J* = 8.5

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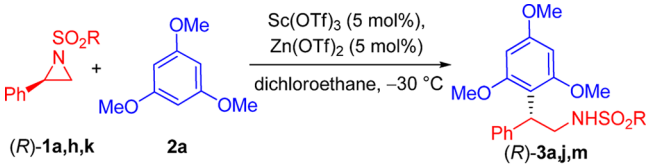
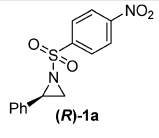
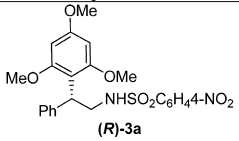
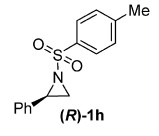
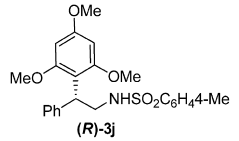
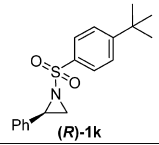
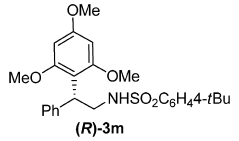
Table 4. Reaction of Chiral Monosubstituted Aziridines with 1,3,5-Trimethoxybenzene 2a



(*R*)-**1a,h,k** (ee >99%) **2a** (*R*)-**3aj,m**

entry	aziridine	product	time (h)	yield (%)	ee (%)
1	 (*R*)-**1a**	 (*R*)-**3a**	1.0	85	43
2	 (*R*)-**1h**	 (*R*)-**3j**	2.5	97	83
3	 (*R*)-**1k**	 (*R*)-**3m**	2.5	88	53

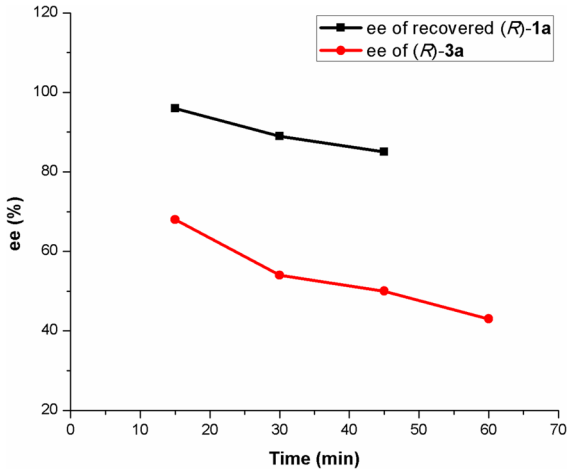


Figure 2. Time dependence study for the racemization process.

Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 39.5, 45.8, 55.4, 55.7, 91.2, 108.9, 124.1, 127.5, 128.2, 128.9, 135.9, 138.4, 146.3, 149.8, 159.2, 160.5; HRMS (ESI) calcd for $C_{24}H_{26}N_2O_7S$, $(M + H)^+$ 487.1539, found 487.1536.

***N*-(2-(4-*tert*-Butylphenyl)-2-(2,4,6-trimethoxyphenyl)ethyl)-4-nitrobenzenesulfonamide (3f).** The general method described above was followed when **1f** (100 mg, 0.277 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (70 mg, 0.416 mmol) in the presence of $Zn(OTf)_2$ (5 mg, 0.014 mmol) and $Sc(OTf)_3$ (7 mg, 0.014 mmol) at 25 °C for 45 min to afford **3f** (127 mg, 0.240 mmol) as a pale yellow solid in 87% yield: mp 78–80 °C; R_f 0.40 (20% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3252, 2962, 2870, 1607, 1531, 1495, 1462, 1420, 1346, 1312, 1268, 1226, 1207, 1168, 1122, 1061, 1036, 952, 910, 850, 810, 736, 684, 612; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 9H), 3.61 (s, 6H), 3.72–3.77 (m, 1H), 3.77 (s, 3H), 3.81–3.89 (m, 1H), 4.54 (dd, J = 9.3, 7.1 Hz, 1H), 4.73 (t, J = 5.6 Hz, 1H), 6.00 (s, 2H), 7.04 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H), 7.88 (d, J = 8.6 Hz, 2H), 8.25 (d, J = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.4, 34.4, 39.5, 45.7, 55.4, 55.7, 91.2, 108.9, 124.1, 125.1, 127.3, 128.3, 138.3, 146.3, 149.1, 149.8, 159.2, 160.5; HRMS (ESI) calcd for $C_{27}H_{32}N_2O_7S$, $(M + Na)^+$ 551.1828, found 551.1827.

4-(2-(4-Nitrophenylsulfonamido)-1-(2,4,6-trimethoxyphenyl)ethyl)phenyl Acetate (3g). The general method described above was followed when **1g** (100 mg, 0.276 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (70 mg, 0.414 mmol) in the presence of $Zn(OTf)_2$ (5 mg, 0.014 mmol) and $Sc(OTf)_3$ (7 mg, 0.014 mmol) at 25 °C for 30 min to afford **3g** (135 mg, 0.254 mmol) as a pale yellow solid in 92% yield: mp 144–146 °C; R_f 0.22 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3287, 2942, 2842, 1753, 1607, 1529, 1506, 1455, 1417, 1350, 1335, 1220, 1201, 1164, 1122, 1097, 1037, 1016, 948, 914, 854, 833, 808, 747, 735; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.61 (s, 6H), 3.70–3.87 (m, 2H), 3.77 (s, 3H), 4.57 (dd, J = 9.0, 6.8 Hz, 1H), 4.78 (t, J = 5.6 Hz, 1H), 6.00 (s, 2H), 6.89 (d, J = 8.8 Hz, 2H), 7.11 (d, J = 8.5 Hz, 2H), 7.86 (d, J = 8.8 Hz, 2H), 8.24 (d, J = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 39.4, 45.7, 55.4, 55.7, 91.2, 108.6, 121.2, 124.1, 128.2, 128.7, 139.1, 146.2, 149.0, 149.8, 159.1, 160.7, 169.7; HRMS (ESI) calcd for $C_{25}H_{26}N_2O_9S$, $(M + H)^+$ 553.1257, found 553.1259.

4-Nitro-*N*-(2-phenyl-2-(thiophen-2-yl)ethyl)-benzenesulfonamide (3h). The general method described above was followed when **1a** (100 mg, 0.329 mmol) was reacted with thiophene **2b** (40 μL, 0.494 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 30 min to afford **3h** (96 mg, 0.247 mmol) as a white solid in 75% yield as regioisomeric mixture (>3:1): R_f 0.44 (20% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3316, 3103, 2925, 1605, 1529, 1496, 1454, 1417, 1351, 1335, 1307, 1159, 1110, 1090, 1076, 1008, 892, 858, 837, 775, 739; ^{1}H NMR (500 MHz, $CDCl_3$) (major regioisomer) δ 3.51–3.66 (m, 2H), 4.33 (dd, J = 8.0, 7.7 Hz, 1H), 4.61–4.63 (m, 1H), 6.80–6.83 (m, 1H), 6.92–6.94 (m, 1H), 7.15–7.17 (m, 2H), 7.26–7.32 (m, 4H), 7.96 (d, J = 8.9 Hz, 2H), 8.33 (d, J = 8.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 46.8, 48.7, 124.5, 125.0, 125.3, 127.2, 127.8, 127.9, 128.4, 129.2, 140.0, 143.8, 145.8, 150.2; HRMS (ESI) calcd for $C_{24}H_{26}N_2O_7S$, $(M + H)^+$ 487.1539, found 487.1536.

***N*-(2-(1-Methyl-1*H*-indol-3-yl)-2-phenylethyl)-4-nitrobenzenesulfonamide (3i).** The general method described above was followed when **1a** (100 mg, 0.329 mmol) was reacted with 1-Methylindole **2c** (62 μL, 0.494 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 30 min to afford **3i** (93 mg, 0.214 mmol) as a thick liquid in 65% yield; R_f 0.38 (25% ethyl acetate in petroleum ether); IR ν_{max} (neat, cm^{-1}) 3301, 3104, 3061, 2925, 1606, 1529, 1472, 1454, 1422, 1348, 1312, 1264, 1164, 1093, 1013, 855, 830, 737, 703, 685; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.56–3.68 (m, 1H), 3.66–3.75 (m, 1H), 3.72 (s, 3H), 4.34 (dd, J = 7.7, 7.3 Hz, 1H), 4.60–4.65 (m, 1H), 6.79 (s, 1H), 6.94–6.98 (m, 1H), 7.14–7.26 (m, 8H), 7.83 (d, J = 8.8 Hz, 2H), 8.21 (d, J = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.9, 42.9, 47.6, 109.6, 113.5, 119.1, 119.4, 122.3, 124.3, 126.7, 126.9, 127.3, 127.9, 128.2, 129.0, 137.3, 140.7, 145.6, 150.0; HRMS (ESI) calcd for $C_{23}H_{21}N_3O_4S$, $(M - H)^-$ 434.1175, found 434.1177.

4-Methyl-*N*-(2-phenyl-2-(2,4,6-trimethoxyphenyl)ethyl)-benzenesulfonamide (3j).[5b,d,i] The general method described above was followed when **1h** (100 mg, 0.366 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (92 mg, 0.549 mmol) in the presence of $Zn(OTf)_2$ (7 mg, 0.018 mmol) and $Sc(OTf)_3$ (9 mg, 0.018 mmol) at 25 °C for 1 h to afford **3j** (157 mg, 0.356 mmol) as a white solid in 97% yield: mp 100–102 °C; R_f 0.42 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3286, 3058, 2924, 2853, 1609, 1590, 1494, 1451, 1407, 1368, 1325, 1290, 1222, 1205, 1184, 1164, 1122, 1094, 1063, 1038, 949, 928, 911, 861, 841, 808, 785, 749, 729; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 3.61 (s, 6H), 3.64–3.76 (m, 2H), 3.79 (s, 3H), 4.37 (dd, J = 6.8, 4.9 Hz, 1H), 4.66 (dd, J = 9.3, 7.3 Hz, 1H), 6.05 (s, 2H), 7.09–7.20 (m, 5H), 7.26 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 39.7, 45.3, 55.4, 55.6, 91.1, 108.9, 126.1, 127.2, 127.8, 128.1, 129.6, 137.1, 141.9, 143.0, 159.4, 160.5; HRMS (ESI) calcd for $C_{24}H_{27}NO_5S$, $(M + H)^+$ 442.1688, found 442.1689. For (*R*)-**3j**: $[\alpha]^{25}_D$ = +16.3 (*c* 0.256, $CHCl_3$) for a 83% ee sample, enantiomeric excess was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane–isopropanol

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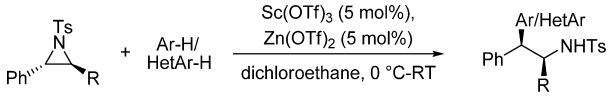
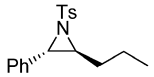
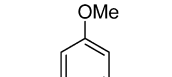
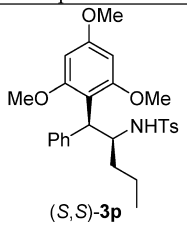
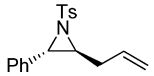
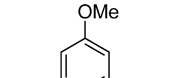
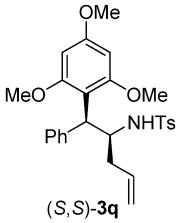
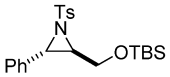
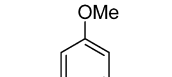
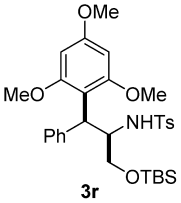
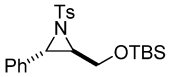
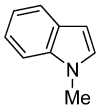
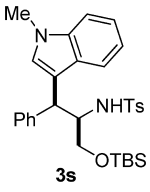
Table 5. Scope of the Reaction with Chiral Disubstituted Aziridines



1l-n 2a,c 3p-s

entry	aziridine	nucleophile	product	yield (%)	dr
1	 (*S*,*S*)-**1l**	 **2a**	 (*S*,*S*)-**3p**	94	>99:1
2	 (*S*,*S*)-**1m**	 **2a**	 (*S*,*S*)-**3q**	92	>99:1
3[a]	 **1n**	 **2a**	 **3r**	95	>99:1
4[a]	 **1n**	 **2c**	 **3s**	76	>99:1

[a]Racemic aziridine was used.

90:10, flow rate = 1.0 mL/min; t_R (1) = 29.27 min (minor), t_R (2) = 34.56 min (major).

***N*-(2-(4-Chlorophenyl)-2-(2,4,6-trimethoxyphenyl)ethyl)-4-methylbenzenesulfonamide (3k).**[5b,i] The general method described above was followed when **1i** (100 mg, 0.325 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (82 mg, 0.488 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 1 h to afford **3k** (139 mg, 0.292 mmol) as a white solid in 90% yield: mp 120−122 °C; R_f 0.31 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3256, 2946, 2871, 2845, 1592, 1492, 1467, 1418, 1327, 1304, 1287, 1222, 1208, 1180, 1157, 1119, 1091, 1070, 1038, 1013, 953, 910, 840, 814, 772, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 3.62 (s, 6H), 3.64−3.69 (m, 2H), 3.79 (s, 3H), 4.35 (dd, J = 6.8, 4.9 Hz, 1H), 4.62 (dd, J = 8.3, 7.8 Hz, 1H), 6.05 (s, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 39.2, 45.2, 55.4, 55.6, 91.1, 108.5, 127.2, 128.2, 129.2, 129.6, 131.8, 137.1, 140.5, 143.1, 159.2, 160.6; HRMS (ESI) calcd for $C_{24}H_{26}ClNO_5S$, $(M + H)^+$ 476.1298, found 476.1292.

***N*-(2-(4-Bromophenyl)-2-(2,4,6-trimethoxyphenyl)ethyl)-4-methylbenzenesulfonamide (3l).** The general method described above was followed when **1j** (100 mg, 0.284 mmol) was reacted with 1,3,5-trimethoxy benzene **2a** (72 mg, 0.426 mmol) in the presence of $Zn(OTf)_2$ (5 mg, 0.014 mmol) and $Sc(OTf)_3$ (7 mg, 0.014 mmol) at 25 °C for 1 h to afford **3l** (136 mg, 0.261 mmol) as a white solid in 92% yield: mp 140−142 °C; R_f 0.31 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3344, 3255, 2946, 2842, 1606, 1488, 1455, 1417, 1325, 1305, 1290, 1220, 1207, 1185, 1162, 1121, 1094, 1070, 1037, 1009, 952, 901, 879, 838, 814, 767, 730, 707, 669, 627; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 3.62 (s, 6H), 3.63−3.68 (m, 2H), 3.79 (s, 3H), 4.35 (dd, J = 6.4, 5.4 Hz, 1H), 4.60 (dd, J = 8.3, 7.8 Hz, 1H), 6.04 (s, 2H), 7.00 (d, J = 8.3 Hz, 2H), 7.25−7.30 (m, 5H), 7.64 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 39.3, 45.1, 55.4, 55.6, 91.1, 108.4, 119.9, 127.2, 129.6 (2C), 131.1, 137.0, 141.0, 143.1, 159.2, 160.6; HRMS (ESI) calcd for $C_{24}H_{26}BrNO_5S$, $(M + H)^+$ 520.0793, found 520.0793.

4-*tert*-Butyl-*N*-(2-phenyl-2-(2,4,6-trimethoxyphenyl)ethyl)-benzenesulfonamide (3m). The general method described above was followed when **1k** (100 mg, 0.317 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (80 mg, 0.476 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 1 h to afford **3m** (138 mg, 0.285 mmol) as a white solid in 90% yield: mp 112−114 °C; R_f 0.31 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3292, 2960, 2926, 2854, 1611, 1591, 1494, 1454, 1405, 1365, 1332, 1267, 1222, 1205, 1166, 1154, 1125, 1088, 1063, 1039, 950, 880, 831, 812, 753, 725, 702; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 9H), 3.60 (s, 6H), 3.62−3.77 (m, 2H), 3.80 (s, 3H), 4.36 (dd, J = 6.6, 4.7 Hz, 1H), 4.71 (dd, J = 9.3, 6.8 Hz, 1H), 6.06 (s, 2H), 7.11−7.20 (m, 5H), 7.47 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.2, 35.2, 39.7, 45.3, 55.4, 55.6,

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91.2, 108.9, 126.0, 126.1, 127.1, 127.8, 128.1, 136.9, 141.9, 156.1, 159.4, 160.5; HRMS (ESI) calcd for $C_{27}H_{33}NO_5S$, $(M + H)^+$484.2158, found 484.2161.

For (*R*)-**3m**: $[\alpha]^{25}_D$ = +10.0 (*c* 0.178, $CHCl_3$) for a 53% ee sample, enantiomeric excess was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane−isopropanol 90:10, flow rate = 1.0 mL/min; t_R (1) = 24.88 min (minor), t_R (2) = 29.60 min (major).

4-*tert*-Butyl-*N*-(2-phenyl-2-(thiophen-2-yl)ethyl)-benzenesulfonamide (3n). The general method described above was followed when **1k** (100 mg, 0.317 mmol) was reacted with thiophene **2b** (38 μL, 0.476 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 1 h to afford **3n** (95 mg, 0.238 mmol) as a white solid in 75% yield as regioisomeric mixture (4:1): R_f 0.38 (15% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3418, 3273, 2963, 2926, 1596, 1494, 1450, 1422, 1366, 1329, 1292, 1268, 1199, 1164, 1113, 1087, 833, 752, 700, 644, 629; ^1H NMR (500 MHz, $CDCl_3$) (major regioisomer) δ 1.36 (s, 9H), 3.48−3.63 (m, 2H), 4.29 (t, *J* = 7.8 Hz, 1H), 4.49 (t, *J* = 6.4 Hz, 1H), 6.79 (d, *J* = 3.4 Hz, 1H), 6.91−6.93 (m, 1H), 7.13−7.32 (m, 6H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.2, 35.3, 46.6, 48.6, 124.8, 125.1, 126.3, 127.0 (2C), 127.7, 127.9, 129.1, 136.8, 140.4, 144.2, 156.7; HRMS (ESI) calcd for $C_{22}H_{25}NO_2S_2$, $(M + H)^+$ 400.1405, found 400.1406.

4-*tert*-Butyl-*N*-(2-phenyl-2-(2,3,4-trimethoxyphenyl)ethyl)-benzenesulfonamide (3o). The general method described above was followed when **1k** (100 mg, 0.317 mmol) was reacted with 1,2,3-trimethoxybenzene **2d** (80 mg, 0.476 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 1 h to afford **3o** (110 mg, 0.227 mmol) as a white solid in 72% yield: mp 90−92 °C; R_f 0.44 (25% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3286, 3062, 3028, 2963, 2872, 1737, 1598, 1495, 1465, 1417, 1364, 1330, 1275, 1199, 1164, 1098, 1015, 884, 832, 797, 752, 730, 700; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 9H), 3.49−3.54 (m, 2H), 3.60 (s, 3H), 3.83 (s, 6H), 4.36 (t, *J* = 7.8 Hz, 1H), 4.42 (t, *J* = 6.1 Hz, 1H), 6.58 (d, *J* = 8.8 Hz, 1H), 6.70 (d, *J* = 8.8 Hz, 1H), 7.08−7.10 (m, 2H), 7.19−7.27 (m, 3H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.72 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.2, 35.2, 43.8, 46.8, 56.0, 60.8, 60.9, 107.2, 122.0, 126.2, 126.9, 127.0, 127.1, 128.1, 128.8, 136.8, 141.3, 142.6, 152.0, 152.9, 156.5; HRMS (ESI) calcd for $C_{27}H_{33}NO_5S$, $(M + H)^+$ 484.2158, found 484.2156.

4-Methyl-*N*-((1*S*,2*S*)-1-phenyl-1-(2,4,6-trimethoxyphenyl)-pentan-2-yl)benzenesulfonamide (3p). The general method described above was followed when (2*S*,3*S*)-**1l** (100 mg, 0.317 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (80 mg, 0.476 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 3 h to afford **3p** (144 mg, 0.298 mmol) as a white solid in 94% yield: mp 174−176 °C; R_f 0.46 (25% ethyl acetate in petroleum ether); $[\alpha]^{25}_D$ = +8.9 (*c* 0.223, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}) 3261, 2951, 2871, 2840, 1607, 1495, 1468, 1455, 1436, 1419, 1378, 1333, 1316, 1287, 1228, 1207, 1158, 1125, 1089, 1060, 1034, 970, 954, 910, 874, 813, 737, 696, 666, 647, 634; ^1H NMR (400 MHz, $CDCl_3$) δ 0.74 (t, *J* = 7.1 Hz, 3H), 1.19−1.44 (m, 3H), 1.69−1.76 (m, 1H), 2.41 (s, 3H), 3.71 (s, 6H), 3.74 (s, 3H), 4.35 (d, *J* = 5.8 Hz, 1H), 4.41 (d, *J* = 10.2 Hz, 1H), 4.45−4.51 (m, 1H), 6.01 (s, 2H), 6.97−7.02 (m, 3H), 7.10−7.14 (m, 4H), 7.41 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 16.7, 21.6, 35.2, 44.3, 55.3 (2C), 55.7, 91.2, 111.2, 126.0, 127.1, 128.1, 128.7, 129.2, 137.5, 141.7, 142.5, 158.5, 159.9; HRMS (ESI) calcd for $C_{27}H_{33}NO_5S$, $(M + H)^+$ 484.2158, found 484.2154.

4-Methyl-*N*-((1*S*,2*S*)-1-phenyl-1-(2,4,6-trimethoxyphenyl)-pent-4-en-2-yl)benzenesulfonamide (3q). The general method described above was followed when (2*S*,3*S*)-**1m** (100 mg, 0.319 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (81 mg, 0.479 mmol) in the presence of $Zn(OTf)_2$ (6 mg, 0.016 mmol) and $Sc(OTf)_3$ (8 mg, 0.016 mmol) at 25 °C for 2 h to afford **3q** (141 mg, 0.293 mmol) as a white solid in 92% yield: mp 156−158 °C; R_f 0.44 (25% ethyl acetate in petroleum ether); $[\alpha]^{25}_D$ = +16.3 (*c* 0.417, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}) 3285, 3063, 3027, 2925, 2852, 1736, 1607, 1494, 1455, 1438, 1419, 1331, 1262, 1225, 1205, 1155, 1123, 1092, 1060, 1034, 953, 914, 810, 736, 699, 663; ^1H NMR (400 MHz, $CDCl_3$) δ 2.10−2.16 (m, 1H), 2.41 (s, 3H), 2.43−2.50 (m, 1H), 3.74 (s, 3H), 3.76 (s, 6H), 4.33−4.36 (m, 2H), 4.64−4.67 (m, 1H), 4.84 (d, *J* = 16.6 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 5.67−5.78 (m, 1H), 6.03 (s, 2H), 6.97−7.05 (m, 3H), 7.11−7.16 (m, 4H), 7.42 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 37.3, 44.3, 54.5, 55.3, 55.7, 91.1, 110.1, 119.4, 126.0, 127.2, 128.1, 128.7, 129.3, 133.0, 137.6, 141.7, 142.6, 158.6, 160.1; HRMS (ESI) calcd for $C_{27}H_{31}NO_5S$, $(M + H)^+$ 482.2001, found 482.2007.

***N*-(3-(*tert*-Butyldimethylsilyloxy)-1-phenyl-1-(2,4,6-trimethoxyphenyl)propan-2-yl)-4-methylbenzenesulfonamide (3r).** The general method described above was followed when **1n** (100 mg, 0.239 mmol) was reacted with 1,3,5-trimethoxybenzene **2a** (60 mg, 0.359 mmol) in the presence of $Zn(OTf)_2$ (4 mg, 0.012 mmol) and $Sc(OTf)_3$ (6 mg, 0.012 mmol) at 25 °C for 3 h to afford **3r** (133 mg, 0.227 mmol) as a white solid in 95% yield: mp 160−162 °C; R_f 0.37 (15% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3486, 3281, 2954, 2927, 2855, 1602, 1495, 1466, 1417, 1361, 1324, 1254, 1219, 1203, 1185, 1158, 1120, 1096, 1081, 1064, 990, 953, 912, 837, 810, 782, 741, 699, 683, 665; ^1H NMR (400 MHz, $CDCl_3$) δ −0.22 (s, 3H), −0.19 (s, 3H), 0.82 (s, 9H), 2.38 (s, 3H), 3.40 (d, *J* = 9.8 Hz, 1H), 3.60 (d, *J* = 9.8 Hz, 1H), 3.74 (s, 9H), 4.60−4.69 (m, 2H), 4.85 (d, *J* = 8.3 Hz, 1H), 6.01 (s, 2H), 7.02−7.03 (m, 3H), 7.08 (d, *J* = 8.3 Hz, 2H), 7.26−7.28 (m, 2H), 7.42 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −6.0, −5.9, 18.3, 21.5, 25.8, 42.4, 55.3, 55.5, 56.4, 63.0, 90.9, 110.9, 125.7, 127.0, 127.9, 128.9, 129.4, 138.2, 142.5 (2C), 158.7, 159.9; HRMS (ESI) calcd for $C_{31}H_{43}NO_6SSi$, $(M + H)^+$ 586.2659, found 586.2656.

***N*-(3-(*tert*-Butyldimethylsilyloxy)-1-(1-methyl-1*H*-indol-3-yl)-1-phenylpropan-2-yl)-4-methylbenzenesulfonamide (3s).** The general method described above was followed when **1n** (100 mg, 0.239 mmol) was reacted with 1-methylindole **2c** (45 μL, 0.359 mmol)) in the presence of $Zn(OTf)_2$ (4 mg, 0.012 mmol) and $Sc(OTf)_3$ (6 mg, 0.012 mmol) at 25 °C for 3.5 h to afford **3s** (100 mg, 0.182 mmol) as a thick liquid in 76% yield: R_f 0.45 (15% ethyl acetate in petroleum ether); IR ν_{max} (neat, cm^{-1}) 3294, 2952, 2927, 2855, 1599, 1470, 1410, 1375, 1330, 1252, 1184, 1160, 1093, 1015, 984, 940, 836, 813, 779, 739, 703, 667; ^1H NMR (400 MHz, $CDCl_3$) δ −0.12 (s, 3H), −0.11 (s, 3H), 0.86 (s, 9H), 2.40 (s, 3H), 3.40 (dd, *J* = 10.0, 6.3 Hz, 1H), 3.60 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.70 (s, 3H), 4.08−4.16 (m, 1H), 4.56 (d, *J* = 9.3 Hz, 1H), 4.62 (d, *J* = 7.3 Hz, 1H), 6.95−7.00 (m, 1H), 7.02 (s, 1H), 7.14−7.35 (m, 12H), 7.53 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.6, −5.5, 18.3, 21.6, 26.0, 32.8, 42.6, 57.8, 62.6, 109.2, 115.0, 118.9, 119.4, 121.7, 126.6, 126.8, 127.1, 127.5, 128.5, 129.1, 129.6, 136.9, 138.3, 140.7, 143.1; HRMS (ESI) calcd for $C_{31}H_{40}N_2O_3SSi$, $(M + H)^+$ 549.2607, found 549.2609.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR spectra for all the new compounds and HPLC chromatograms. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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