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Studies on ring cleavage of aziridines with hydroxyl compounds

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Abstract—Ring cleavage of a variety of *N*-substituted aziridines has been studied with hydroxyl compounds (primary, secondary, allylic and tertiary). It was observed that the cleavage reaction was very facile in the presence of $BF_3{\cdot}OEt_2$ and $Sn(OTf)_2$. Whereas the aziridine opening reaction was facile with primary and secondary alcohols, hindered alcohols took longer (2 days). However, with the help of microwave radiation, the cleavage reaction with hindered alcohols could be achieved in a very short period (15 min). Phenols could only cleave aziridines under microwave irradiation.

Aziridines are nitrogen analogs of epoxides and their ring-opened products are valuable intermediates in organic synthesis.[1] The reactivity of this strained heterocyclic ring system is less than that of epoxides and dependent upon the substitution on the nitrogen atom. The Lewis acid-induced ring-opening of *N*-substituted aziridines with several nucleophiles such as amines[2] and azides[3] has been very well studied, but aziridine opening with hydroxyl compounds was unknown until we recently communicated that less hindered alcohols such as primary and allylic alcohols could easily open aziridines in high yield.[4] In this paper, we describe full details of the work and also report that aziridines can also be opened with hindered alcohols such as secondary and tertiary. We further report the effect of microwave irradiation on the ring cleavage of aziridines.

While working on the $Sn(OTf)_2$ induced cleavage reaction of *N*-tosylcyclohexyl aziridine with TMSCN[5] in MeOH as a solvent, we discovered that the product was β-amino ether **1** resulting from an opening of the aziridine with MeOH. The role of TMSCN in this reaction was ruled out as it also proceeded in its absence. Thus, following a typical procedure, reaction of *N*-tosylcyclohexyl aziridine (1 mmol) with MeOH in the presence of a catalytic amount of $Sn(OTf)_2$ gave the β-amino ether in 99% yield (Table 1, entry 1). The same reaction could be done in a more efficient manner in the presence of $BF_3{\cdot}OEt_2$. The *trans* stereochemistry of the product was deduced from the coupling constants (J=9.0, 9.0, 3.9 Hz) of the peak at δ 2.86 (C*H*–OMe) in the ^{1}H NMR spectrum. We carried out this opening reaction with MeOH in the presence of other Lewis acids such as $CuCl_2$ (24 h, 6% yield), $SnCl_2$ (24 h, 8% yield), $FeCl_3$ (24 h, 32% yield), $LiClO_4$ (24 h, 10% yield), $Cu(OTf)_2$ (24 h, 3% yield), $AlCl_3$ (12 h, 35%) but very poor yields were obtained. Some other Lewis acids such as ZnI_2, $ZnCl_2$, and $CoCl_2$ failed to give any product (12 h, room temperature). Since $Sn(OTf)_2$ and $BF_3{\cdot}OEt_2$ both turned out to be highly effective for aziridine opening with MeOH, the cleavage of *N*-tosylcyclohexyl aziridine was studied using other hydroxyl compounds. The reaction with EtOH in the presence of $Sn(OTf)_2$ took longer time (30 h) whereas the same reaction could be done in 3 h using $BF_3{\cdot}OEt_2$. In both cases, a quantitative yield of the product was obtained (entry 2). The results from allylic and propargyl alcohols were similar (entries 3 and 4). The ring-opening reaction was also carried out with benzyl alcohol and water in CH_2Cl_2 and MeCN, respectively, and the products were obtained in high yields (entries 5 and 6). We had previously reported that aziridines were inert to secondary and tertiary alcohols.[4] On extensive study of these cleavage reactions, we found that activated aziridines were also opened with these hindered alcohols in an efficient manner. Reaction of *N*-tosylcyclohexyl aziridine with *i*-PrOH and *t*-BuOH in the presence of $BF_3{\cdot}OEt_2$ provided the ring-opened products in high yields (entries 7 and 8). It was observed that $Sn(OTf)_2$ was less effective in catalyzing the cleavage of aziridines with hindered alcohols. In fact, it failed to catalyze the opening reaction with *t*-BuOH. The cleavage reaction of *N*-tosylcyclohexyl aziridine by other kinds of hydroxyl groups in the presence of a catalytic amount of $BF_3{\cdot}OEt_2$ was also facile (entries 9–14). In the cases of high boiling hydroxyl compounds such as cyclohexanol, indanol, menthol, etc., the cleavage reaction was performed in CH_2Cl_2. Other solvents such as THF, ether, and acetonitrile gave inferior results. Aziridine opening with chiral alcohols such as (−)-menthol (entry 13) and (*R*)-3-buten-2-ol (entry 14) was efficient, but the diastereoselectivity was poor. Unfortunately, the cleavage of aziridines could not be achieved by other tertiary alcohols. Similarly, α-phenyl substituted hydroxyl compounds such as 1-phenyl ethanol failed to affect the cleavage reaction, possibly due to elimination as a side reaction.[6]

Keywords: aziridines; cleavage; hydroxyl compounds; β-amino ethers.

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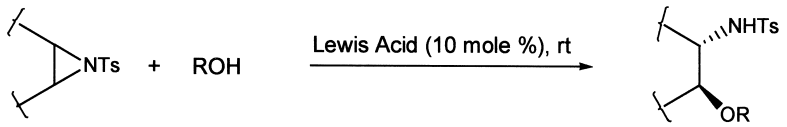
Table 1.



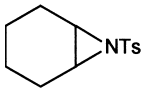
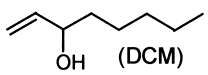
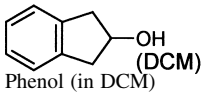
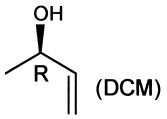
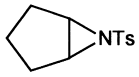
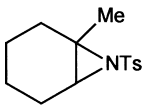
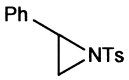
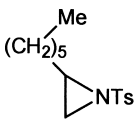
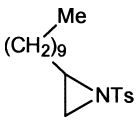
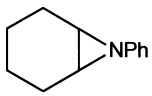
Entry	Aziridine	ROH	Conventional yield, % (time)		Microwave, 70 W, 15 min, yield (%)	
			$Sn(OTf)_2$	$BF_3{\cdot}Et_2O$	$Sn(OTf)_2$	$BF_3{\cdot}Et_2O$
1		MeOH	99 (1 h)	99 (1/2 h)	93	98
2		EtOH	99 (30 h)	99 (3 h)	–	97
3		$CH_2{=}CH{-}CH_2OH$	99 (1 h)	92 (1 h)	–	98
4		$HC{\equiv}C{-}CG_2OH$	99 (1/2 h)	98 (1/2 h)	–	90
5		$PhCH_2OH$ (DCM)	90 (20 h)	94 (2 h)	–	90
6		H_2O (MeCN)	89 (15 h)	90 (2 h)	–	91
7		*i*-PrOH	68 (48 h)	92 (10 h)	61	70
8		*t*-BuOH	Nil (5 d)	72 (48 h)	60	83
9		Cyclohexanol (DCM)	–	72 (3 h)	–	61
10			–	71 (3 h)	–	46
11			–	70 (3 h)	–	50
12		Phenol (in DCM)	–	Nil	–	57
13		(−)-Menthol (DCM)	–	92 (3 h)[a]	–	82[a]
14			–	92 (3 h)[b]	–	80[b]
15		MeOH	99 (5 h)	99 (2 h)	–	97
16		EtOH	98 (65 h)	98 (9 h)	–	97
17		*i*-PrOH	–	67 (48 h)	–	68
18		*t*-BuOH	–	76 (60 h)	–	92
19		PhOH (DCM)	–	Nil	–	40
20		MeOH	–	91[c] (1 h)	–	89[c]
21		EtOH	–	89[c] (3 h)	–	87[c]
22		*i*-PrOH	–	64[c] (60 h)	–	54[c]
23		*t*-BuOH	–	68[c] (60 h)	–	42[c]
24		PhOH (DCM)	–	Nil	–	40[c]
25		MeOH	98[d] (1/2 h)	99[d] (10 min)	–	92[d]
26		EtOH	94[d] (1/2 h)	99[d] (15 min)	–	90[d]
27		*i*-PrOH	–	83[d] (3 h)	–	82[d]
28		*t*-BuOH	–	88[d] (3 h)	–	84[d]
29		PhOH (DCM)	–	Nil	–	54[d]
30		MeOH	96[e] (8 h)	97[f] (3 h)	–	98[f]
31		EtOH	92[g] (24 h)	98[g] (14 h)	–	96[e]
32		*i*-PrOH	–	67[h] (8 h)	–	55[h]
33		*t*-BuOH	–	68[i] (10 h)	–	86[i]
34		MeOH	76[j] (30 h)	96[j] (4 h)	–	–
35		EtOH	74[f] (96 h)	96[f] (20 h)	–	–

Table 1 (*continued*)

Entry	Aziridine	ROH	Conventional yield, % (time)		Microwave, 70 W, 15 min, yield (%)	
			$Sn(OTf)_2$	$BF_3{\cdot}Et_2O$	$Sn(OTf)_2$	$BF_3{\cdot}Et_2O$
36		MeOH	76 (10 min)	92 (10 min)	–	89[k]
37		EtOH	68 (10 min)	94 (10 min)	–	–
38		*n*-PrOH	65 (15 min)	90 (15 min)	–	–
39		$PhCH_2OH$ (DCM)	66 (24 h)	86 (2 h)	–	–
40		$CH_2{=}CH{-}CH_2OH$	86 (15 min)	91 (5 min)	–	–
41		$HC{\equiv}C{-}CH_2OH$	85 (15 min)	93 (5 min)	–	–
42		H_2O (THF)	92 (20 min)	90 (20 min)	–	–
43		*i*-PrOH	–	78 (10 min)	–	74[k]
44		*t* BuOH	–	72 (10 min)	–	70[k]

[a] Diasteromeric ration 1:1.4.
[b] Diastereomeric ration 1:1.6.
[c] Exclusive attack on more substituted carbon.
[d] Exclusive attack on benzylic carbon.
[e] Slight preference for terminal attack; ratio is 60:40.
[f] Slight preference for terminal attack; ratio is 58:42.
[g] Slight preference for terminal attack; ratio is 61:39.
[h] Slight preference for internal attack; ratio is 59:41.
[i] Slight preference for internal attack; ratio is 58:42.
[j] Slight preference for terminal attack; ratio is 63:37.
[k] Time required is 1 min.

Having obtained the success in the opening reaction of *N*-tosylcyclohexyl aziridine with a range of hydroxyl compounds, the reaction was extended to a variety of aziridines and the results are summarized in Table 1. The cleavage reaction of *N*-tosylcyclopentyl aziridine was equally facile (entries 15–18). In the case of a trisubstituted aziridine, the hydroxyl compounds attacked exclusively at the more substituted carbon (entries 20–23). In the case of a phenyl substituted *N*-tosyl aziridine (entries 25–28), only a single product was obtained due to attack of the alcohols at the benzylic carbon (confirmed by ^{1}H NMR spectroscopy and HPLC). In the case of alkyl substituted acyclic *N*-tosyl aziridines, terminal attack was slightly favored for primary alcohols (entries 30, 31, 34, and 35) whereas internal attack was slightly favored for hindered alcohols (entries 32 and 33). *N*-Phenylcyclohexyl aziridine could effectively be cleaved using a variety of hydroxyl compounds in high yield (entries 36–44). The aziridine ring-opening reaction with hydroxyl compounds was much faster with $BF_3{\cdot}OEt_2$ in comparision with $Sn(OTf)_2$. It was also observed that *N*-alkyl substituted azirdines could not be opened under the above conditions. It was also noticed that phenols failed to cleave aziridines under the above conditions.

In view of some of the failures in the above reactions, it was thought to study the same process under microwave irradiation. The application of microwave (MW) irradiation to activate and accelerate organic reactions has experienced exponential growth in the last decade. Microwave mediated organic reactions takes place more rapidly, safely with high yields, and are environmentally friendly. Because of its efficiency and its potential to contribute to clean products, MW chemistry is becoming increasingly popular both in industry and in academia.[7,8] The cleavage of aziridines by hydroxyl compounds was studied in the presence of some Lewis acids under MW irradiation also and the results are compared with the conventional method (Table 1). It was observed that most of reactions were very facile and complete in 15 min. With most of the alcohols, yields were comparable or little less in comparison to conventional methods. However, the noteworthy feature was the cleavage reaction with phenols, which under conventional conditions, failed to open aziridines. Under MW irradiation, the cleavage of aziridines by phenol took place and a modest yield of the products was obtained (entries 12, 19, 24, and 29). Under MW conditions also, we observed the elimination reactions as was found in conventional process for the α-phenyl secondary and tertiary alcohols. Except *t*-BuOH, all other tertiary alcohols underwent dehydration leading to olefins. These microwave reactions were also tried with other Lewis acids such as $Sn(OTf)_2$ and $Cu(OTf)_2$. Whereas moderate yields were obtained with $Sn(OTf)_2$, the reaction did not proceed at all with $Cu(OTf)_2$. Since $BF_3{\cdot}Et_2O$ was more efficient than $Sn(OTf)_2$, we carried out all the microwave reactions with $BF_3{\cdot}Et_2O$ (Table 1).

In summary, we have described a simple and efficient method for cleavage of activated aziridines with a variety of hydroxyl compounds. The noteworthy feature of the reaction is that hindered alcohols can also cleave aziridines in high yield. With the help of microwave irradiations, aziridines can be opened with phenols.

1. Experimental

^{1}H NMR spectra were recorded on Jeol and Bruker, as mentioned in the experimental, using TMS as internal standard. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. IR spectra were recorded on Perkin–Elmer 580 and 1320 spectrometers. Microwave reactions were done in MLS-1200 Mega, Milestone with MDR (MW digestive rotor) technology. MW power frequency 2450 MHz power of mW generating magnetron 1200 W. HPLC was done on a Perkin–Elmer machine.

Routine monitoring of reactions was performed using silica gel-G obtained from Acme. All the chromatographic separations were done by using silica gel (Acme's, 100–200 mesh). Petroleum ether used was of boiling range 60–80°C. Reactions, which needed anhydrous conditions, were run under an atmosphere of dry nitrogen or argon using flame-dried glass wares. The organic layer was washed with brine and stored over anhydrous Na_2SO_4 for 30 min before use. Evaporation of solvents was performed at reduced pressure, using a Büchi rotary evaporator.

1.1. General procedure for cleavage of aziridines with hydroxyl compounds under conventional condition

A solution of a *N*-tosyl aziridine (1 mmol) and a Lewis acid (10 mol%) in an alcohol (1 mL) was stirred at room temperature for 1 h. Most of the alcohol was removed in vacuo and the crude reaction mixture was directly loaded over silica gel for column chromatography. If the hydroxyl compound is high boiling, it (1 mmol) was dissolved in a suitable solvent as mentioned in Table 1.

1.2. General procedure for cleavage of aziridines with hydroxyl compounds under microwave irradiation

A solution of a *N*-tosyl aziridine (1 mmol) and a Lewis acid (10 mol%) in an alcohol (1 mL) was taken in a teflon vessel and irradiated in a microwave oven at 70 W power for 15 min at room temperature. Most of the alcohol was removed in vacuo and the crude reaction mixture was directly loaded over silica gel for column chromatography. If the hydroxyl compound is high boiling, it (1 mmol) was dissolved in a suitable solvent as mentioned in Table 1.

1.2.1. *trans*-*N*-(2-Methoxycyclohexyl)-4-methyl benzenesulfonamide (entry 1). White solid; mp 60–62°C; R_f 0.63 (20% EtOAc in petroleum ether); IR (KBr) 3263, 1317, 1152, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.99–1.18 (m, 4H), 1.52 (m, 1H), 1.61 (m, 1H), 1.96 (m, 1H), 2.12 (m, 1H), 2.35 (s, 3H), 2.78 (ddd, J=9.0, 9.0, 3.9 Hz, 1H), 2.86 (ddd, J=9.0, 9.0, 3.9 Hz, 1H), 3.12 (s, 3H), 5.03 (s, 1H), 7.22 (d, J=8.3 Hz, 2H), 7.69 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 23.4, 23.6, 28.6, 31.0, 55.8, 57.0, 81.3, 127.2, 129.5, 137.3, 143; LCMS (EI, *m*/*z*) 283 (M^+). Anal. calcd for $C_{14}H_{21}NO_3S$: C, 59.57, H, 7.44, N, 4.96. Found: C 59.75, H, 7.46, N, 4.97.

1.2.2. *trans*-*N*-(2-Ethoxycyclohexyl)-4-methyl benzenesulfonamide (entry 2). White powder; mp 94–96°C; R_f 0.54 (20% EtOAc in petroleum ether); IR (KBr) 3582, 3266, 1326, 1162, 1098 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.02 (t, J=6.8 Hz, 3H), 1.02–1.18 (m, 4H), 1.56 (m, 2H), 1.95 (m, 1H), 2.10–2.17 (m, 1H), 2.35 (s, 3H), 2.76 (m, 1H), 2.94 (ddd, J=9.7, 9.5, 3.6 Hz, 1H), 3.19 (m, 1H), 3.46 (m, 1H), 4.93 (s, 1H), 7.22 (d, J=8.5 Hz, 2H), 7.69 (d, J=8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.4, 21.5, 23.6, 23.7, 29.4, 31.3, 57.2, 63.5, 79.7, 127.2, 129.5, 137.1, 143.1; LCMS (EI, *m*/*z*) 297 (M^++1). Anal. calcd for $C_{15}H_{23}NO_3S$: C, 60.81, H, 7.77, N, 4.72. Found: C 60.68, H, 7.81, N, 4.73.

1.2.3. *trans*-*N*-(2-Allyloxycyclohexyl)-4-methyl benzenesulfonamide (entry 3). Viscous liquid; R_f 0.63 (20% EtOAc in petroleum ether); IR (neat) 3180, 1591, 1300, 1062 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.01–1.35 (m, 4H), 1.49–1.61 (m, 2H), 1.92–1.95 (m, 1H), 2.12–2.19 (m, 1H), 2.35 (s, 3H), 2.81 (m, 1H), 3.01 (ddd, J=9.5, 9.3, 3.6 Hz, 1H), 3.69–3.74 (m, 1H), 3.89–3.94 (m, 1H), 4.90 (d, J=2.7 Hz, 1H), 5.05–5.12 (m, 2H), 5.72 (m, 1H), 7.22 (d, J=8.5 Hz, 2H), 7.68 (d, J=8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 23.4, 23.6, 29.3, 31.2, 57.1, 69.1, 79.3, 116.9, 127.2, 129.5, 134.5, 137.8, 143.1; LCMS (EI, *m*/*z*) 309 (M^++1). Anal. calcd for $C_{16}H_{23}NO_3S$: C, 62.33, H, 7.46, N, 4.54. Found: C, 62.45, H, 7.51, N, 4.52.

1.2.4. *trans*-*N*-(2-Prop-2-ynyloxycyclohexyl)-4-methyl benzenesulfonamide (entry 4). Colorless viscous liquid; R_f 0.63 (20% EtOAc in petroleum ether); IR (neat) 3195, 2810, 1595, 1310, 1051 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.07–1.31 (m, 4H), 1.59–1.68 (m, 2H), 2.02 (m, 1H), 2.20 (m, 1H), 2.42 (s, 3H), 2.48 (t, J=2.4 Hz, 1H), 2.87 (ddd, J=9.5, 8.5, 3.9 Hz, 1H), 3.2 (ddd, J=9.5, 9.3, 3.9 Hz, 1H), 4.02 (ABq, J=16.0, 2H), 5.09 (d, J=3.7 Hz, 1H, N*H*), 7.29 (d, J=8.6 Hz, 2H), 7.77 (d, J=8.3 Hz, 2H); LCMS (EI, *m*/*z*) 307 (M^++1), 265. Anal. calcd for $C_{16}H_{21}NO_3S$: C, 62.74, H, 6.86, N, 4.57. Found: C, 62.78, H, 6.80, N, 4.52.

1.2.5. *trans*-*N*-(2-Benzyloxycyclohexyl)-4-methyl benzenesulfonamide (entry 5). White crystalline solid; mp 70–72°C; R_f 0.61 (20% EtOAc in petroleum ether); IR (KBr) 3298, 2932, 1324, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.23–1.28 (m, 4H), 1.73 (m, 2H), 2.10–2.12 (m, 1H), 2.20–2.27 (m, 1H), 2.42 (s, 3H), 2.97 (ddd, J=9.3, 9.8, 3.6 Hz, 1H), 3.19 (ddd, J=9.3, 9.0, 4.2 Hz, 1H), 4.34 (d, J=11.7 Hz, 1H), 4.56 (d, J=11.7 Hz, 1H), 4.89 (d, J=3.16 Hz, 1H), 7.25 (m, 4H), 7.33–7.41 (m, 3H), 7.73 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 23.4, 29.4, 31.5, 56.9, 65.0, 70.1, 79.1, 126.8, 127.5, 128.2, 129.3, 137.1, 138.1, 142.9; LCMS (EI, *m*/*z*) 358 (M^+). Anal. calcd for $C_{20}H_{25}NO_3S$: C, 67.03, H, 6.98, N, 3.91. Found: C, 67.25, H, 6.87, N, 3.98.

1.2.6. *trans*-*N*-(2-Hydroxycyclohexyl)-4-methyl benzenesulfonamide (entry 6). White solid; mp 128–130°C; R_f 0.40 (40% EtOAc in petroleum ether); IR (neat) 3547, 3266, 3047, 1320, 1152 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.11–1.28 (m, 4H), 1.58–1.73 (m, 3H), 2.00–2.05 (m, 1H), 2.43 (s, 3H), 2.68 (bs, 1H), 2.84 (m, 1H), 3.30 (ddd, J=10.10, 4.4 Hz, 1H), 4.95 (d, J=7.1 Hz, 1H), 7.32 (d, J=8.0 Hz, 2H), 7.79 (d, J=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 23.7, 24.6, 31.8, 33.3, 59.6, 73.3, 127.1, 129.8, 137.2, 143.6; LCMS (EI, *m*/*z*) 268 (M^+). Anal. calcd for $C_{13}H_{19}NO_3S$: C, 58.20, H, 7.08, N, 5.22. Found: C, 58.23, H, 7.00, N, 5.28.

1.2.7. *trans*-*N*-(2-Isopropoxycyclohexyl)-4-methyl benzenesulfonamide (entry 7). White solid; mp 89–91°C; R_f 0.65, (20% EtOAc in petroleum ether); IR (KBr) 3236, 3047, 1163, 810 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.05 (d, J=6.1 Hz, 3H), 1.08 (d, J=6.1 Hz, 3H), 1.12–1.28 (m, 4H), 1.56 (m, 1H), 1.66 (m, 1H), 1.95 (m, 1H), 2.20 (m, 1H), 2.42 (s, 3H), 2.79 (ddd, J=9.3, 10.3, 3.7 Hz, 1H), 3.08 (ddd, J=9.5, 9.3, 4.4 Hz, 1H), 3.64 (heptet, J=6.1 Hz, 1H), 4.86 (d, J=4.2 Hz, 1H), 7.29 (d, J=8.3 Hz, 2H), 7.75 (d, J=8.3 Hz, 2H); LCMS (EI, *m*/*z*) 310 (M^+). Anal. calcd for $C_{16}H_{25}NO_3S$: C, 61.93, H, 8.06, N, 4.51. Found: C, 62.15, H, 8.00, N, 4.58.

1.2.8. *trans*-*N*-(2-*tert*-Butoxycyclohexyl)-4-methyl benzenesulfonamide (entry 8). White solid; mp 78–81°C R_f 0.65 (20% EtOAc in petroleum ether); IR (KBr) 3259, 1330, 1084 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.14 (s, 9H), 1.18–1.33 (m, 4H), 1.52 (m, 1H), 1.62 (m, 1H), 1.86 (m, 1H), 2.15 (m, 1H), 2.42 (s, 3H), 2.78 (ddd, J=9.3, 8.3, 4.2 Hz, 1H), 3.24 (ddd, J=8.8, 8.6, 4.2 Hz, 1H), 4.74 (d, J=3.9 Hz, 1H), 7.29 (d, J=8.5 Hz, 2H), 7.75 (d, J=8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 23.4, 28.7, 29.6, 30.9, 33.1, 57.2, 72.3, 74.0, 127.2, 129.5, 137.3, 143.1; LCMS (EI, *m*/*z*) 324 (M^+). Anal. calcd for $C_{17}H_{27}NO_3S$: C, 62.96, H, 8.33, N, 4.32. Found: C, 63.10, H, 8.28, N, 4.25.

1.2.9. *trans*-*N*-(2-Cyclohexyloxycyclohexyl)-4-methyl benzenesulfonamide (entry 9). White solid; mp 74–76°C; R_f 0.55 (20% EtOAc in petroleum ether); IR (KBr) 3240, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.07–1.28 (m, 10H), 1.52–1.70 (m, 5H), 1.83 (m, 1H), 1.95 (m, 1H), 2.21 (m, 1H), 2.42 (s, 3H), 2.79 (ddd, J=10.5, 9.0, 3.2 Hz, 1H), 3.12 (ddd, J=9.5, 9.3, 4.1 Hz, 1H), 3.27 (m, 1H), 4.93 (d, J=2.2 Hz, 1H), 7.29 (d, J=8.3 Hz, 2H), 7.70 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 23.6, 24.0, 24.1, 25.5, 29.6, 30.6, 31.2, 32.0, 33.6, 57.4, 75.0, 77.04, 127.2, 129.5, 137.2, 143.0. Anal. calcd for $C_{19}H_{29}NO_3S$: C, 65.14, H, 8.28, N, 4.0. Found: C, 65.20, H, 8.31, N, 3.94.

1.2.10. *trans*-*N*-[2-(1-Vinylhexyloxy)-cyclohexyl]-4-methyl benzenesulfonamide (entry 10). Viscous liquid; R_f 0.52 (20% EtOAc in petroleum ether); IR (neat) 3230, 1651, 1140 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (m, 3H), 1.03–1.36 (m, 10H), 1.60 (m, 2H), 1.92 (m, 1H), 2.21 (m, 1H), 2.41 (s, 3H), 2.42 (s, 3H), 2.80–2.94 (m, 1H), 3.04–3.11 (m, 1H), 3.60–3.70 (m, 1H), 4.82 (d, J=3.2 Hz, 1H), 4.87 (d, J=3.9 Hz, 1H), 5.02–5.20 (m, 2H), 5.48– 5.66 (m, 1H), 7.29 (m, 2H), 7.75 (m, 2H). Anal. calcd for $C_{21}H_{33}NO_3S$: C, 66.84, H, 8.75, N, 3.71. Found: C, 66.97, H, 8.77, N, 3.68.

1.2.11. *trans*-*N*-[2-(Indan-2-yloxy)-cyclohexyl]-4-methyl benzenesulfonamide (entry 11). White crystalline solid; mp 118–120°C; R_f 0.40 (20% EtOAc in petroleum ether); IR (neat) 3272, 1281, 1153, 1085 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.10–1.31 (m, 4H), 1.58 (m, 1H), 1.66 (m, 1H), 2.02 (m, 1H), 2.22 (m, 1H), 2.36 (s, 3H), 2.71–2.88 (m, 3H), 3.00 (dd, J=16.1, 6.1 Hz, 2H), 3.15 (ddd, J=9.0, 9.0, 3.9 Hz, 1H), 4.36 (m, 1H), 4.84 (d, J=3.4 Hz, 1H), 7.14–7.25 (m, 6H), 7.52 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 23.6, 29.6, 30.1, 31.5, 39.2, 40.5, 57.2, 77.8, 124.5, 124.8, 126.6, 126.7, 127.1, 129.4, 136.9, 140.1, 41.0, 142.9. Anal. calcd for $C_{22}H_{27}NO_3S$: C, 68.75, H, 7.03, N, 3.64. Found: C, 68.89, H, 7.06, N, 3.58.

1.2.12. *trans*-*N*-(2-Phenoxycyclohexyl)-4-methyl benzenesulfonamide (entry 12). White solid; mp 116–118°C; R_f 0.61 (20% EtOAc in petroleum ether); IR (neat) 3286 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.33 (m, 4H), 1.66 (m, 2H), 2.03 (m, 1H), 2.16 (m, 1H), 2.41 (s, 3H), 3.71 (m, 1H), 4.03 (m, 1H), 5.22 (m, 1H), 6.69 (d, J=7.8 Hz, 2H), 6.91 (m, 5H), 7.76 (m, 2H). Anal. calcd for $C_{19}H_{23}NO_3S$: C, 66.27, H, 6.68, N, 4.06. Found: C, 66.34, H, 6.62, N, 4.00.

1.2.13. *trans*-*N*-(−)-[2-(2-Isopropyl-5-methylcyclohexyl)-cyclohexyl]-4-methyl benzenesulfonamide (entry 13). Diastereomeric ratio 1:1.4.

Diastereomer ***I***. Yield 53%; white solid; mp 130–132°C, R_f 0.53 (20% EtOAc in petroleum ether); $[\alpha]_D^{25}=-81.4$ (*c* 0.6, $CHCl_3$); IR (KBr) 3320, 2930, 1152 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.62 (d, J=7.1 Hz, 3H), 0.82 (d, J=7.1 Hz, 3H), 0.91 (d, J=6.6 Hz, 3H), 0.64–1.29 (m, 9H), 1.56–1.68 (m, 5H), 1.88–2.01 (m, 3H), 2.24 (m, 1H), 2.41 (s, 3H), 2.71–2.78 (m, 1H), 3.06 (ddd, J=10.0, 10.0, 3.9 Hz, 1H), 3.15 (ddd, J=9.7, 9.7, 4.1 Hz, 1H), 4.93 (d, J=2.2 Hz, 1H), 7.27 (d, J=8.3 Hz, 2H), 7.74 (d, J=8.3, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.8, 21.1, 21.6, 22.2, 23, 23.6, 23.6, 24.8, 29.6, 31.3, 31.5, 34.4, 40.3, 48.1, 57.5, 73.9, 74.6, 127.3, 129.3, 136.9, 142.9; LCMS (EI, *m*/*z*) 406 (M^+), 268, 154, 113. Anal. calcd for $C_{23}H_{37}NO_3S$: C, 67.98, H, 9.11, N, 3.44. Found: C, 68.01, H, 9.15, N, 3.41.

Diastereomer ***II***. Yield 38%; colorless liquid; R_f 0.50 (20% EtOAc in petroleum ether); $[\alpha]_D^{25}=-27.6$ (*c* 0.5, $CHCl_3$); IR (neat) 3275, 2933, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.79 (d, J=6.8 Hz, 3H), 0.87 (d, J=6.6 Hz, 3H), 0.90 (d, J=7.1 Hz, 3H), 0.72–1.30 (m, 9H), 1.49 (m, 1H), 1.57–1.67 (m, 4H), 1.85 (m, 2H), 2.11 (m, 2H), 2.42 (s, 3H), 2.93 (m, 1H), 3.06 (ddd, J=10.2, 10.3, 4.1 Hz, 1H), 3.15 (m, 1H), 4.92 (d, J=3.9 Hz, 1H), 7.29 (d, J=8.0 Hz, 2H), 7.74 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 21.3, 21.5, 22.3, 22.7, 25.2, 29.7, 31.0, 31.5, 34.2, 42.6, 48.7, 56.1, 77.5, 78.2, 127.2, 127.2, 129.5, 137.2, 143.2. Anal. calcd for $C_{23}H_{37}NO_3S$: C, 67.98, H, 9.11, N, 3.44. Found: C, 67.99, H, 9.09, N, 3.45.

1.2.14. *trans*-*N*-[2-(1-Vinylethoxy)-cyclohexyl]-4-methyl benzenesulfonamide (entry 14). Diastereomeric ratio: 1:1.6.

Diastereomer ***I***. Yield 56%; colorless liquid; R_f 0.52 (20% EtOAc in petroleum ether); $[\alpha]_D^{25}=+6.67$ (*c* 0.5, MeOH); IR (KBr) 3305, 2931, 1564, 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.07 (d, J=6.3 Hz, 3H), 1.08–1.22 (m, 2H), 1.59 (m, 4H), 1.97 (m, 1H), 2.21 (m, 1H), 2.42 (s, 3H), 3.08 (ddd, J=9.8, 9.3, 4.4 Hz, 1H), 3.83–3.90 (m, 1H), 4.81 (s, 1H), 5.10–5.17 (m, 2H), 5.54–5.63 (m, 1H), 7.28 (d, J=8.5 Hz, 2H), 7.75 (d, J=8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 21.8, 23.6, 23.7, 29.6, 31.6, 57.3, 73.9, 76.2, 117.1, 127.2, 129.4, 137.3, 139.9, 143.0. Anal. calcd for $C_{17}H_{25}NO_3S$: C, 63.15, H, 7.73, N, 4.33. Found: C, 63.20, H, 7.71, N, 4.35.

Diastereomer ***II***. Yield 35%; white solid; mp 78–80°C; R_f 0.48 (20% EtOAc in petroleum ether); $[\alpha]_D^{25}=+12.0$ (*c* 0.75, MeOH); IR (neat) 3325, 2932, 1560, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.14 (d, J=6.3 Hz, 3H), 1.15–1.25 (m, 2H), 1.53–1.65 (m, 4H), 1.90 (m, 1H), 2.13 (m, 1H), 2.42 (s, 3H), 2.89 (m, 1H), 3.11 (ddd, J=8.8, 8.8, 4.1 Hz, 1H), 3.91 (m, 1H), 4.81 (s, 1H), 4.99–5.08 (m, 2H), 5.65– 5.73 (m, 1H), 7.29 (d, J=8.3 Hz, 2H), 7.76 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21, 21.5, 23.4, 23.5, 30.9, 31.2, 57.2, 75.6, 77.8, 114.7, 127.2, 129.6, 137.3, 140.8, 143.2. Anal. calcd for $C_{17}H_{25}NO_3S$: C, 63.15, H, 7.73, N, 4.33. Found: C, 63.37, H, 7.70, N, 4.30.

1.2.15. *trans*-*N*-(2-Methoxycyclopentyl)-4-methyl benzenesulfonamide (entry 15). White solid; mp 40–42°C; R_f 0.56 (20% EtOAc in petroleum ether); IR (neat) 3250, 1323, 1152 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.23–1.31 (m, 1H), 1.41–1.56 (m, 3H), 1.70–1.85 (m, 2H), 2.34 (s, 3H), 3.10 (s, 3H), 3.35 (m, 1H), 3.46 (m, 1H), 5.10 (d, J=6.3 Hz, 1H), 7.22 (d, J=8.3 Hz, 2H), 7.72 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.9, 21.4, 29.0, 30.8, 56.8, 59, 86.8, 127.1, 129.6, 137.4, 143.3; LCMS (EI, m/z) 269 (M^++1), 237, 209, 171, 154, 113, 71. Anal. calcd for $C_{13}H_{19}NO_3S$: C, 58.20, H, 7.08, N, 5.22. Found: C, 58.39, H, 7.01, N, 5.17.

1.2.16. *trans*-*N*-(2-Ethoxycyclopentyl)-4-methyl benzenesulfonamide (entry 16). White solid; mp 55–58°C; R_f 0.52 (20% EtOAc in petroleum ether); IR (neat) 3249, 1322, 1077 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.0 (t, J=7.0 Hz, 3H), 1.25–1.32 (m, 1H), 1.40–1.48 (m, 1H), 1.50–1.57 (m, 2H), 1.71–1.85 (m, 2H), 2.35 (s, 3H), 3.24–3.36 (m, 3H), 3.55 (m, 1H), 5.06 (d, J=6.1 Hz, 1H), 7.23 (d, J=8.1 Hz, 2H), 7.71 (d, J=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.3, 20.9, 21.4, 29.5, 30.7, 59.3, 64.6, 84.9, 127.1, 129.5, 137.4, 143.2; LCMS (EI, m/z) 282 (M^+), 232, 155, 131. Anal. calcd for $C_{14}H_{21}NO_3S$: C, 59.57, H, 7.44, N, 4.96. Found: C, 59.71, H, 7.40, N, 5.02.

1.2.17. *trans*-*N*-(2-Isopropoxycyclopentyl)-4-methyl benzenesulfonamide (entry 17). Colorless viscous liquid; R_f 0.61 (20% EtOAc in petroleum ether); IR (neat) 3235, 1377, 1163, 1083 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.95 (d, J=1.4 Hz, 3H), 0.97 (d, J=1.5 Hz, 3H), 1.15–1.61 (m, 4H), 1.78 (m, 2H), 2.35 (s, 3H), 3.27 (quintet, J=6.0 Hz, 1H), 3.47 (heptet, J=6.1 Hz, 1H), 3.63 (dt, J=6.3, 4.6 Hz, 1H), 4.66 (d, J=5.6 Hz, 1H), 7.23 (d, J=8.5 Hz, 2H), 7.71 (d, J=8.3, 2H); LCMS (EI, m/z) 296 (M^+), 236, 141. Anal. calcd for $C_{15}H_{23}NO_3S$: C, 60.81, H, 7.70, N, 4.72. Found: C, 60.77, H, 7.75, N, 4.77.

1.2.18. *trans*-*N*-(2-*tert*-Butoxycyclopentyl)-4-methyl benzenesulfonamide (entry 18). Colorless liquid; R_f 0.61 (20% EtOAc in petroleum ether); IR (neat) 3232, 1165, 815 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.02 (s, 9H), 1.26–1.37 (m, 2H), 1.45–1.63 (m, 2H), 1.75–1.87 (m, 2H), 2.35 (s, 3H), 3.17 (quintet, J=6.6 Hz, 1H), 3.70 (q, J=5.6 Hz, 1H), 5.14 (d, J=6.1 Hz, 1H), 7.22 (d, J=8 Hz, 2H), 7.73 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.2, 21.4, 28.3, 29.7, 31.4, 60.7, 73.4, 77.2, 127.1, 129.4, 137.4, 143. Anal. calcd for $C_{16}H_{25}NO_3S$: C, 61.93, H, 8.06, N, 4.51. Found: C, 62.12, H, 7.99, N, 4.55.

1.2.19. *trans*-*N*-(2-Phenoxycyclopentyl)-4-methyl benzenesulfonamide (entry 19). White crystalline solid; mp 101–104°C; R_f 0.52 (20% EtOAc in petroleum ether); IR (KBr) 3285, 1326, 1084 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.39–1.47 (m, 1H), 1.67–1.81 (m, 3H), 1.97–2.08 (m, 2H), 2.38 (s, 3H), 3.67 (m, 1H), 4.51 (m, 1H), 4.93 (d, J=6.3 Hz, 1H), 6.75 (m, 2H), 6.91 (m, 1H), 7.23 (m, 4H), 7.74 (d, J=8.3 Hz, 2H); LCMS (EI, m/z) 330 (M^+), 237, 171, 154, 91. Anal. calcd for $C_{18}H_{21}NO_3S$: C, 65.45, H, 6.36, N, 4.24. Found: C, 65.38, H, 6.32, N, 4.28.

1.2.20. *trans*-*N*-(2-Methoxy-2-methylcyclohehexyl)-4-methyl benzenesulfonamide (entry 20). White solid; mp 154–156°C; R_f 0.56 (20% EtOAc in petroleum ether); IR (KBr) 3276, 1163 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.09 (s, 3H), 1.20–1.62 (m, 8H), 2.42 (s, 3H), 2.98 (s, 3H), 3.10 (m, 1H), 4.77 (d, J=5.1 Hz, 1H), 7.29 (d, J=8.3 Hz, 2H), 7.76 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.1, 21.5, 21.9, 22.6, 28.3, 33, 48.1, 57.4, 75.8, 127.2, 129.5, 137.5, 143.1. Anal. calcd for $C_{15}H_{23}NO_3S$: C, 60.81, H, 7.77, N, 4.72. Found: C, 60.74, H, 7.70, N, 4.80.

1.2.21. *trans*-*N*-(2-Ethoxy-2-methylcyclohehexyl)-4-methyl benzenesulfonamide (entry 21). White solid; mp 85–87°C; R_f 0.56 (20% EtOAc in petroleum ether); IR (KBr) 3278, 1162 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.01 (t, J=6.8 Hz, 3H), 1.11 (s, 3H), 1.23–1.63 (m, 8H), 2.42 (s, 3H), 3.06 (m, 1H), 3.11–3.20 (m, 1H),3.22–3.30 (m, 1H), 7.29 (d, J=8.3 Hz, 2H), 7.76 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.8, 18.5, 21.5, 22, 22.6, 28.3, 33.8, 55.6, 58.0, 75.6, 127.2, 129.5, 137.4, 143.1. Anal. calcd for $C_{16}H_{25}NO_3S$: C, 61.93, H, 8.06, N, 4.51. Found: C, 62.08, H, 8.13, N, 4.42.

1.2.22. *trans*-*N*-(2-Isopropoxy-2-methylcyclohehexyl)-4-methyl benzenesulfonamide (entry 22). Colorless liquid; R_f 0.56 (20% EtOAc in petroleum ether); IR (neat) 3276, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.96 (d, J=7.3 Hz, 3H), 1.02 (d, J=6.1 Hz, 3H), 1.12 (s, 3H), 1.18–1.28 (m, 4H), 1.32–1.67 (m, 3H), 2.02 (m, 1H), 2.42 (s, 3H), 2.98 (m, 1H), 3.74 (heptet, J=6.1 Hz, 1H), 4.88 (d, J=3.9 Hz, 1H), 7.28 (d, J=8.3 Hz, 2H), 7.76 (d, J=8.3 Hz, 2H); LCMS (EI, m/z) 324 (M^+). Anal. calcd for $C_{17}H_{27}NO_3S$: C, 63.74, H, 8.36, N, 4.30. Found: C, 62.38, H, 8.33, N, 4.32.

1.2.23. *trans*-*N*-(2-*tert*-Butoxy-2-methylcyclohexyl)-4-methyl benzenesulfonamide (entry 23). Colorless liquid; R_f 0.56 (20% EtOAc in petroleum ether); IR (neat) 3275, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.23 (s, 9H), 1.29 (s, 3H), 1.30 (m, 3H), 1.42–1.51 (m, 1H), 1.56–1.70 (m, 3H), 1.80–1.87 (m, 1H), 2.42 (s, 3H), 3.34 (ddd, J=12.7, 8.3, 4.1 Hz, 1H), 5.21 (d, J=8.3 Hz, 1H), 7.29 (d, J=8.5 Hz, 2H), 7.79 (d, J=8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 21.8, 21.9, 29.3, 29.6, 30.1, 31.3, 35.4, 35.6, 94.4, 96.2, 127, 129.5, 137.7, 143.2. Anal. calcd for $C_{18}H_{29}NO_3S$: C, 63.90, H, 8.57, N, 4.14. Found: C, 63.94, H, 8.55, N, 4.10.

1.2.24. *trans*-*N*-(2-Phenoxy-2-methylcyclohexyl)-4-methyl benzenesulfonamide (entry 24). Viscous liquid, R_f 0.55 (20% EtOAc in petroleum ether); IR (neat) 3286, 3030 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.21–1.33 (m, 4H), 1.53–1.64 (m, 3H), 1.60 (s, 3H), 2.13 (m, 1H), 3.36 (m, 1H), 4.98 (d, J=5.4 Hz, 1H), 6.75 (d, J=7.5 Hz, 2H), 7.28 (m, 5H), 7.79 (m, 2H). Anal. calcd for $C_{20}H_{25}NO_3S$: C, 68.82, H, 7.01, N, 3.90. Found: C, 68.68, H, 7.13, N, 3.82.

1.2.25. *trans*-*N*-(2-Methoxy-2-phenylethyl)-4-methyl benzenesulfonamide (entry 25). White solid; mp 63–65°C; R_f 0.56 (20% EtOAc in petroleum ether); IR (KBr) 3456, 1327, 1090 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.34 (s, 3H), 2.87 (m, 1H), 3.09 (s, 3H), 3.09–3.16 (m, 1H), 4.12 (dd, J=9.3, 3.4 Hz, 1H), 4.97 (m, 1H), 7.12 (m, 2H), 7.23 (m, 5H), 7.65 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 49.2, 56.6, 81.9, 126.5, 127, 128.3, 128.6,

129.6, 136.9, 138.2, 143.3; LCMS (EI, *m/z*) 304 (M^+). Anal. calcd for $C_{16}H_{19}NO_3S$: C, 63.15, H, 6.25, N, 4.60. Found: C, 63.20, H, 6.21, N, 4.55.

1.2.26. *trans*-*N*-(2-Ethoxy-2-phenylethyl)-4-methyl benzenesulfonamide (entry 26). White solid; mp 98–101°C; R_f 0.56 (20% EtOAc in petroleum ether); IR (KBr) 3286, 2973, 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.06 (t, J=7.1 Hz, 3H), 2.34 (s, 3H), 2.87 (ddd, J=13.1, 9.3, 3.2 Hz, 1H), 3.13 (ddd, J=13.1, 9.3, 3.9 Hz, 1H), 3.17 (m, 1H), 3.29 (m, 1H), 4.23 (dd, J=9.3, 3.7 Hz, 1H), 4.90 (dd, J=9.3, 2.7 Hz, 1H), 7.12 (d, J=8.3 Hz, 2H), 7.23 (m, 5H), 7.65 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 21.5, 49.3, 64.4, 80.1, 126.4, 127.0, 128.2, 128.6, 129.7, 136.9, 138.9, 143.4; LCMS (EI, *m/z*) 318 (M^+). Anal. calcd for $C_{17}H_{21}NO_3S$: C, 64.15, H, 6.60, N, 4.40. Found: C, 64.20, H, 6.62, N, 4.35.

1.2.27. *trans*-*N*-(2-Isopropoxy-2-phenylethyl)-4-methyl benzenesulfonamide (entry 27). White solid; mp 103–106°C; R_f 0.61 (20% EtOAc in petroleum ether); IR (KBr) 3274, 1358, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.04 (d, J=6.3 Hz, 3H), 1.10 (d, J=5.9 Hz, 3H), 2.42 (s, 3H), 2.91 (ddd, J=12.5, 9.3, 2.9 Hz, 1H), 3.17 (ddd, J=12.9, 9.3, 3.7 Hz, 1H), 3.46 (heptet, J=6.2 Hz, 1H), 4.40 (dd, J=9.5, 3.7 Hz, 1H), 4.87 (dd, J=9.3, 2.4 Hz, 1H), 7.21–7.33 (m, 7H), 7.71 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21, 21.5, 23.3, 49.5, 69.3, 77.4, 126.5, 127.0, 128.1, 128.5, 129.7, 137, 139.6, 143.3; LCMS (EI, *m/z*) 332 (M^+), 273, 148, 106. Anal. calcd for $C_{18}H_{23}NO_3S$: C, 65.06, H, 6.92, N, 4.21. Found: C, 65.20, H, 6.98, N, 4.15.

1.2.28. *trans*-*N*-(2-*tert*-Butoxy-2-phenylethyl)-4-methyl benzenesulfonamide (entry 28). White powder; mp 79–82°C; R_f 0.61 (20% EtOAc in petroleum ether); IR (neat) 3293, 1164 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.10 (s, 9H), 2.4 (s, 3H), 2.84 (ddd, J=12.9, 9.0, 3.9 Hz, 1H), 3.10 (ddd, J=12.9, 9.0, 4.1 Hz, 1H), 4.60 (dd, J=9.0, 4.1 Hz, 1H), 4.74 (dd, J=9.0, 3.4 Hz, 1H), 7.26 (m, 7H), 7.69 (d, J=8.3 Hz, 2H); LCMS (EI, *m/z*) 346 (M^+), 273, 162, 106. Anal. calcd for $C_{19}H_{25}NO_3S$: C, 65.89, H, 7.22, N, 4.04. Found: C, 65.76, H, 7.27, N, 4.00.

1.2.29. *trans*-*N*-(2-Phenoxy-2-phenylethyl)-4-methyl benzenesulfonamide (entry 29). Pale yellow solid; mp 145–146°C; R_f 0.60 (20% EtOAc in petroleum ether); IR (KBr) 3283, 3037 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.41 (s, 3H), 3.54 (m, 2H), 4.52 (t, J=7.8 Hz, 1H), 5.19 (bs, 1H), 6.71 (m, 1H), 6.83 (m, 2H), 7.03 (m, 1H), 7.16 (m, 3H), 7.24 (m, 5H), 7.64 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 115.8, 119.7, 126.5, 126.9, 127.5, 127.7, 128.1, 128.2, 128.3, 129.4, 137.2, 141.0, 142.9, 154.5; LCMS (EI, *m/z*) 366 (M^+). Anal. calcd for $C_{21}H_{21}NO_3S$: C, 68.85, H, 5.73, N, 3.82. Found: C, 68.95, H, 5.81, N, 3.85.

1.2.30. *trans*-*N*-(2-Methoxyoctyl)-4-methyl benzenesulfonamide and *trans*-*N*-(1-methoxymethylheptyl)-4-methyl benzenesulfonamide (entry 30). Viscous oil, R_f 0.63 (20% EtOAc in petroleum ether); IR (neat) 3295, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75–0.81 (m, 3H), 1.06–1.42 (m, 10H), 2.35 (s, 3H), 3.11 (s, $-OCH_3$), 3.19 (s, $-OCH_3$), 3.09–3.30 (m, 3H), 4.81 (m, 1H), 7.22 (m, 4H), 7.68 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 21.4, 22.4, 22.5, 24.9, 25.4, 28.9, 29.2, 29.6, 30.5, 31.0, 31.5, 31.6, 31.9, 32.2, 45.5, 53.4, 56.7, 58.9, 73.8, 79.2, 127, 129.4, 129.6, 136.8, 138.1, 143.1, 143.3; LCMS (EI, *m/z*) 312 (M^+). Anal. calcd for $C_{16}H_{27}NO_3S$: C, 61.53, H, 8.65, N, 4.48. Found: C, 61.58, H, 8.62, N, 4.51.

1.2.31. *trans*-*N*-(2-Ethoxyoctyl)-4-methyl benzenesulfonamide and *trans*-*N*-(1-ethoxymethylheptyl)-4-methyl benzenesulfonamide (entry 31). Viscous oil, R_f 0.63 (20% EtOAc in petroleum ether); IR (neat) 3297, 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75–0.81 (m, 6H), 0.99–1.15 (m, 20H), 2.35 (s, 6H), 2.73 (m, 1H), 3.08 (m, 2H), 3.19–3.27 (m, 6H), 3.36–3.54 (m, 1H), 4.84 (d, J=7.4 Hz, 2H), 7.22 (m, 4H), 7.68 (m, 4H); LCMS (EI, *m/z*) 327 (M^++1), 269, 155. Anal. calcd for $C_{17}H_{29}NO_3S$: C, 62.57, H, 8.89, N, 4.29. Found: C, 62.59, H, 8.91, N, 4.25.

1.2.32. *trans*-*N*-(1-Isopropoxymethylheptyl)-4-methyl benzenesulfonamide and *trans*-*N*-(2-isopropoxyoctyl)-4-methyl benzenesulfonamide (entry 32). Colorless liquid, R_f 0.65 (20% EtOAc in petroleum ether); IR (neat) 3294, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.86 (m, 6H), 1.05 (m, 6H), 1.15–1.47 (m, 20H), 2.42 (s, 6H), 2.78 (heptet, J=6.1 Hz, 1H), 3.06 (heptet, J=6.1 Hz, 1H), 3.17 (m,1H), 3.25 (m, 2H), 3.38 (m, 2H), 3.56 (m, 1H), 4.80 (t, J=7.3 Hz, 1H, N*H*), 4.88 (d, J=7.8 Hz, 1H, N*H*), 7.30 (m, 4H), 7.75 (m, 4H); LCMS (EI, *m/z*) 340 (M^++1), 267, 156, 91. Anal. calcd for $C_{18}H_{31}NO_3S$: C, 63.52, H, 9.11, N, 4.11. Found: C, 63.76, H, 9.06, N, 4.02.

1.2.33. *trans*-*N*-(1-*tert*-Butoxymethylheptyl)-4-methyl benzenesulfonamide and *trans*-*N*-(2-*tert*-butoxyoctyl)-4-methyl benzenesulfonamide (entry 33). Colorless liquid, R_f 0.65 (20% EtOAc in petroleum ether); IR (neat) 3296, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.85 (m, 6H), 1.05 (s, 9H), 1.10 (s, 9H), 1.13–1.46 (m, 20H), 2.69 (m, 1H), 2.84 (m, 1H), 2.94 (m, 1H), 3.13 (m, 1H), 3.22 (m, 1H), 3.54 (m, 1H), 4.85 (t, J=5.8 Hz, 1H, N*H*), 4.94 (d, J=8 Hz, 1H, N*H*), 7.33 (m, 4H), 7.76 (m, 4H); LCMS (EI, *m/z*) 354 (M^+). Anal. calcd for $C_{23}H_{41}NO_3S$: C, 67.11, H, 10.04, N, 3.40. Found: C, 67.28, H, 9.93, N, 3.42.

1.2.34. *trans*-*N*-(2-Methoxydodecyl)-4-methyl benzenesulfonamide and *trans*-*N*-(1-methoxymethylundecyl)-4-methyl benzenesulfonamide (entry 34). White solid; mp 34–36°C; R_f 0.78 (20% EtOAc in petroleum ether); IR (KBr) 3288, 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.81 (m, 6H), 1.07–1.46 (m, 36H), 2.35 (s, 6H), 2.94–3.24 (m, 6H), 3.12 (s, 3H, OCH_3), 3.17 (s, 3H, OCH_3), 4.72 (m, 2H), 7.22 (m, 4H), 7.68 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 21.5, 22.6, 24.9, 25.5, 29.2, 29.3, 29.4, 29.4, 29.4, 29.5, 29.6, 31.0, 31.9, 32.3, 45.5, 53.5, 56.7, 58.9, 73.8, 79.2, 127.0, 129.5, 129.6, 138.0, 143.1, 143.3. Anal. calcd for $C_{20}H_{35}NO_3S$: C, 65.21, H, 9.51, N, 3.80. Found: C, 65.25, H, 9.52, N, 3.83.

1.2.35. *trans*-*N*-(1-Ethoxymethylundecyl)-4-methyl benzenesulfonamide and *trans*-*N*-(2-ethoxydodecyl)-4-methyl benzenesulfonamide (entry 35). Viscous liquid; R_f 0.77 (20% EtOAc in petroleum ether); IR (neat) 3293, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.81 (m, 6H), 1.0–1.13 (m, 36H), 2.35 (s, 3H), 2.36 (s, 3H), 3.02–3.44 (m, 6H), 4.68 (m, 2H), 7.21 (m, 4H), 7.67 (m, 4H); ^{13}C

NMR ($CDCl_3$, 100 MHz) δ 14.1, 14.9, 15.4, 21.5, 22.6, 25.0, 25.6, 29.3, 29.4, 29.51, 29.58, 29.6, 31.7, 31.9, 32.5, 45.9, 53.6, 64.5, 66.6, 71.5, 77.5, 127.02, 127.07, 129.5, 129.6, 138.1, 143.1. Anal. calcd for $C_{21}H_{37}NO_3S$: C, 65.96, H, 9.68, N, 3.66. Found: C, 65.99, H, 9.72, N, 3.71.

1.2.36. *trans*-(2-Methoxycyclohexyl) phenylamine (entry 36). Colorless liquid; R_f 0.40 (2% EtOAc in petroleum ether); IR (neat) 3289, 1565, 1246 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.09–1.32 (m, 4H), 1.55–1.70 (m, 2H), 1.99–2.14 (m, 2H), 3.04 (ddd, J=8.8, 8.7, 3.7 Hz, 1H), 3.15 (ddd, J=8.5, 9.5, 3.9 Hz, 1H), 3.29 (s, 3H), 6.63 (m, 3H), 7.01 (m, 2H); LCMS (EI, m/z) 206 (M^++1), 205 (M^+), 132, 118, 77. Anal. calcd for $C_{13}H_{19}NO$: C, 76.09, H, 9.26, N, 6.82. Found: C, 76.12, H, 9.22, N, 6.85.

1.2.37. *trans*-(2-Ethoxycyclohexyl) phenylamine (entry 37). Colorless liquid; R_f 0.39 (2% EtOAc in petroleum ether); IR (neat) 3295, 1582, 1292, 1080 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.07 (t, J=7.1 Hz, 3H), 1.12–1.36 (m, 4H), 1.58 (m, 1H), 1.68 (m, 1H), 1.98 (m, 1H), 2.12 (m, 1H), 3.05–3.16 (m, 2H), 3.38 (m, 1H), 3.55 (m, 1H), 6.61 (m, 3H), 7.08 (m, 2H); LCMS (EI, m/z) 219 (M^+). Anal. calcd for $C_{14}H_{21}NO$: C, 76.71, H, 9.58, N, 6.39. Found: C, 76.83, H, 9.49, N, 6.38.

1.2.38. *trans*-(2-*n*-Propoxycyclohexyl) phenylamine (entry 38). Colorless viscous liquid; R_f 0.38 (2% EtOAc in petroleum ether); IR (neat) 3401, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (dt, J=7.3, 1.9 Hz, 3H), 1.23–1.53 (m, 4H), 1.66 (m, 1H), 1.76 (m, 1H), 2.04 (m, 1H), 2.22 (m, 1H), 3.17 (m, 2H), 3.37 (m, 1H), 3.57 (m, 1H), 3.89 (bs, 1H), 6.67 (m, 3H), 7.14 (m, 2H). Anal. calcd for $C_{15}H_{23}NO$: C, 77.25, H, 9.87, N, 6.0. Found: C, 77.27, H, 9.89, N, 6.03.

1.2.39. *trans*-(2-Benzyloxycyclohexyl) phenylamine (entry 39). Colorless viscous liquid; R_f 0.39 (2% EtOAc in petroleum ether); IR (neat) 3398, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.18–1.88 (m, 6H), 2.10 (m, 1H), 2.32–2.44 (m, 1H), 3.29 (m, 2H), 4.48 (d, J=11.9 Hz, 1H), 4.65 (d, J=11.9 Hz, 1H), 6.62 (d, J=8.3 Hz, 2H), 6.67 (m, 1H), 7.15 (m, 2H), 7.28 (m, 5H); LCMS (EI, m/z) 281 (M^+), 231, 190, 132. Anal. calcd for $C_{19}H_{23}NO$: C, 81.13, H, 8.18, N, 4.98. Found: C, 81.19, H, 8.21, N, 4.95.

1.2.40. *trans*-(2-Allyloxycyclohexyl) phenylamine (entry 40). Colorless liquid, R_f 0.41 (2% EtOAc in petroleum ether); IR (neat) 3397, 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.25–1.40 (m, 4H), 1.63 (m, 1H), 1.75 (m, 1H), 2.03 (m, 1H), 2.19 (m, 1H), 3.24 (m, 2H), 3.94–4.13 (m, 2H), 5.11–5.25 (m, 2H), 5.88 (m, 1H), 6.68 (m, 3H), 7.15 (m, 2H); LCMS (EI, m/z) 231 (M^+). Anal. calcd for $C_{15}H_{21}NO$: C, 77.92, H, 9.09, N, 6.06. Found: C, 77.95, H, 9.10, N, 6.02.

1.2.41. *trans*-(2-Prop-2-ynyloxycyclohexyl) phenylamine (entry 41). Colorless liquid, R_f 0.4 (2% EtOA in petroleum ether); IR (neat) 3405, 2348 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.15–1.43 (m, 5H), 1.64–1.67 (m, 1H), 1.77 (m, 1H), 2.07 (m, 1H), 2.20 (m, 1H), 2.45 (m, 1H), 3.22 (ddd, J=9.3, 8.8, 4.4 Hz, 1H), 3.44 (ddd, J=8.7, 8.8, 4.1 Hz, 1H), 3.91 (bs, 1H), 4.14–4.31 (m, 2H), 6.68 (m, 3H), 7.16 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.7, 23.7, 29.7, 31.4, 56.1, 56.7, 74.1, 79.6, 80.6, 113.5, 117.2, 119.1, 147.9. Anal. calcd for $C_{15}H_{19}NO$: C, 78.60, H, 8.29, N, 6.11. Found: C, 78.73, H, 8.31, N, 6.04.

1.2.42. *trans*-(2-Hydroxycyclohexyl) phenylamine (entry 42). Viscous liquid; R_f 0.42 (5% EtOAc in petroleum ether); IR (neat) 3393 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.04 (m, 1H), 1.35 (m, 3H), 1.75 (m, 2H), 2.12 (m, 2H), 2.85 (bs, 1H), 3.14 (ddd, J=11.2, 9.5, 3.9 Hz, 1H), 3.34 (ddd, J=9.7, 9.5, 3.9 Hz, 1H), 6.73 (m, 3H), 7.17 (m, 2H); LCMS (EI, m/z) 192 (M^++1), 191 (M^+), 132. Anal. calcd for $C_{12}H_{17}NO$: C, 75.39, H, 9.90, N, 7.32. Found: C, 75.41, H, 8.91, N, 7.31.

1.2.43. *trans*-(2-Isopropoxycyclohexyl) phenylamine (entry 43). Colorless oily liquid, R_f 0.39 (2% EtOAc in petroleum ether); IR (neat) 3397, 1167 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.01 (d, J=6.0 Hz, 3H), 1.05 (d, J=6.4 Hz, 3H), 1.14–1.33 (m, 4H), 1.56 (m, 1H), 1.66 (m, 1H), 1.90 (m, 1H), 2.12 (m, 1H), 3.06–3.17 (m, 2H), 3.64 (heptet, J=6.0 Hz, 1H), 6.60 (m, 3H), 7.07 (m, 2H). Anal. calcd for $C_{15}H_{23}NO$: C, 77.25, H, 9.87, N, 6.0. Found: C, 77.36, H, 9.81, N, 5.77.

1.2.44. *trans*-(2-*tert*-Butoxycyclohexyl) phenylamine (entry 44). Colorless oily liquid, R_f 0.40 (2% EtOAc in petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.49 (s, 9H), 1.22–1.72 (m, 6H), 1.87–2.15 (m, 2H), 3.11 (ddd, J=9.5, 8.3, 3.9 Hz, 1H), 3.30 (ddd, J=9.0, 8.3, 3.9 Hz, 1H), 3.69 (bs, 1H), 6.62 (m, 3H), 7.12 (m, 2H). Anal. calcd for $C_{16}H_{25}NO$: C, 77.73, H, 10.12, N, 5.66. Found: C, 77.79, H, 10.13, N, 5.62.

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