Pyridine-*N*-oxide: An Efficient Organocatalyst for Ring-Opening Reactions of Aziridines with Aryl Thiols

Yang, Qin[a,b](杨琴) Yin, Zhenlan[a](尹正兰) Yang, Min[a](杨民)
Peng, Yiyuan*[,a,b](彭以元)

[a] *Jiangxi Key Laboratory of Green Chemistry, Department of Chemistry, Jiangxi Normal University, Nanchang, Jiangxi 330027, China*
[b] *Key Laboratory of Functional Small Organic Molecule, Ministry of Education, College of Life Science, Jiangxi Normal University, Nanchang, Jiangxi 330022, China*

Pyridine-*N*-oxide serves as an efficient catalyst for the ring-opening reactions of *N*-tosylaziridines with various aryl thiols under mild conditions. This transformation is highly effective, which gives rise to the corresponding *β*-amino sulfides in good to excellent yields.

Keywords pyridine-*N*-oxide, ring-opening reaction, *N*-tosylaziridine, thiol, *β*-amino sulfide

Introduction

Aziridines have attracted increasing attention as versatile building blocks and important precursors for the synthesis of many nitrogen-containing biologically interesting molecules.[1] Considerable progress has been achieved in the nucleophilic ring-opening reactions of aziridines.[2] They are known to react with various nucleophiles and their properties to undergo regioselective ring opening reactions contribute largely to their synthetic value.[3] Among these reactions, the ring-opening reactions of aziridines with thiols are the most interesting[4] because the resultant *β*-amino sulfides are important for the synthesis of many other biologically interesting molecules such as amino acids,[1b,1h] heterocycles,[5] and alkaloids.[6] However, most of these reactions require a strong base or Lewis acid.[7] Recently, organocatalysts have been successfully employed in such transformation. For instance, phosphine,[2a,2b] tertiary amine,[2c,2d] or DMSO[2e] had been used as catalyst or promoter to facilitate the ring-opening reactions of aziridines with thiols.

It is well-known that the interest in the field of organocatalysis has increased spectacularly in the last few years as result of both the novelty of the concept and, more importantly, the fact that the efficiency and selectivity of many organocatalytic reactions meet the standards of established organic reactions. Besides phophine and tertiaryamine, *N*-oxide is another example of a privileged catalyst class. They are able to mediate an astonishingly wide variety of transformations both as organocatalysts and ligands.[8,9] Prompted by the facts of phophine or tertiary amine as organocatalyst in the ring-opening reactions of aziridines, we envisioned that *N*-oxide might be utilized as an attractive alternative catalyst in the reactions due to its unique characteristics as well as its stability and nucleophilic similarity. To verify the practicability of this projected route, we started to investigate the possibility for *N*-oxide catalyzed ring-opening reactions of aziridines with thiols.

Results and discussion

At the outset, aziridine **1a** and *p*-methylbenzenethiol (**2a**) were utilized as model substrates to optimize the reaction conditions (Table 1). Initially, 10 mol% pyridine-*N*-oxide as catalyst was employed in the reaction. To our delight, we observed the formation of the desired product **3aa** in acetonitrile with 65% yield (Table 1, Entry 1). It is noteworthy that this reaction could be run under the air without loss of efficiency. The *anti*-stereochemistry of the product **3aa** was confirmed by its ^{1}H NOESY NMR coupling constant for two cyclic methine hydrogens at the *trans*-positions.[2a,2d,4f] Further screening of solvents revealed that this reaction also worked well in water, although the yield was low (30% yield) (Table 1, Entry 2). 92% yield of product **3aa** could be obtained when the reaction was performed in THF (Table 1, Entry 6). The same result was observed when methanol was used as a replacement in the reaction (Table 1, Entry 8). In addition, the reaction was completed in 5 h at room temperature. Decreasing the amount of catalyst diminished the product yield with prolonged reaction time (data not shown in Table 1).

* E-mail: yiyuanpeng@yahoo.com
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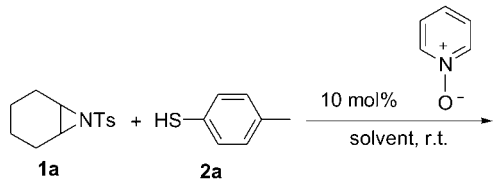
Blank experiment showed that the reaction only gave 25% yield after 10 h in the absence of *N*-oxide (Entry 9), which differs from Lejon's result.[10]

Table 1 Ring-opening reactions of aziridine with *p*-methylbenzenethiol in various solvents



Entry	Solvent	Time/h	Yield[a]/%
1	CH_3CN	25	65
2	H_2O	24	30
3	CH_2Cl_2	16	82
4	$CHCl_3$	18	80
5	CH_3COOEt	24	65
6	THF	16	92
7	C_2H_5OH	5	80
8	CH_3OH	5	92
9[b]	CH_3OH	10	25

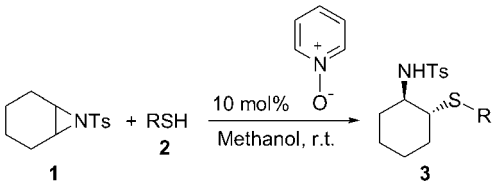
[a] Isolated yield based on the aziridine; [b] pyridine-*N*-oxide was not added.

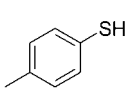
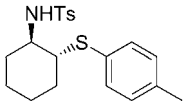
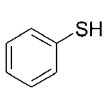
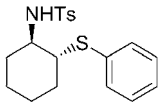
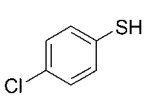
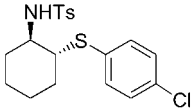
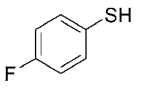
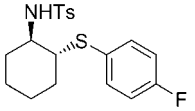
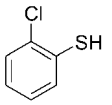
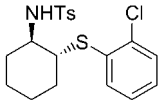
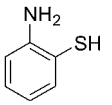
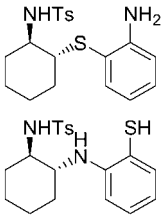
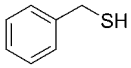
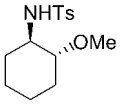
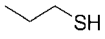
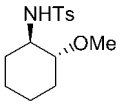
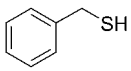
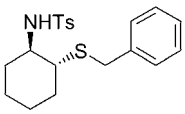
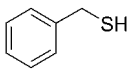
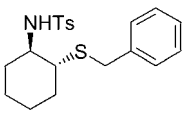
Effects of thios on the ring-opening reactions

We investigated the reaction scope of this *N*-oxide catalytic system and its tolerance of functional groups in the case of other aziridines **1** and thiols **2** under the optimized conditions [pyridine-*N*-oxide (10 mol%), methanol, 25 ℃] (Tables 2 and 3). We rapidly noticed the broad field of application of the process and its remarkable functional group compatibility on both reagents. With respect to the thiophenols, the expected products resulting from reactions of aziridine **1a** were obtained and isolated in good to excellent yields (Table 2, Entris 1—6). It is found that the conditions had proven to be useful for various thiophenols. Aryl thiols, whether the substituent on the benzene ring is electron withdrawing or donating produced in excellent yields (Entries 1—5, yields from 90%—96%). 2-Aminobenzenethiol reacted with aziridine **1a** to afford the mixture of corresponding *S*-nucleophile and *N*-nucleophile ring-opening product in 88% yield with 90/10 ratio (Table 2, Entry 6).

When alkyl thiols were used as the nucleophile under the similar condituion, the expected *S*-nucleophile ring opening products **3** were not obtained, but the methanol (solvent) nucleophile ring-opening product of aziridine **1a** was obtained in low yields (Entries 7—8). When THF or CH_3CN replaced methanol as the solvent,

Table 2 Ring-opening reactions of aziridine **1a** with various thiols in methanol catalyzed by pyridine-*N*-oxide



Entry	RSH	Product **3**	Time/h	Yield[a]/%
1		 (**3aa**)	5	92
2		 (**3ab**)	5	90
3		 (**3ac**)	4.5	92
4		 (**3ad**)	4	90
5		 (**3ae**)	4.5	96
6		 (**3af**) (**3ag**)	8	88 (90∶10)[b]
7		 (**3ah**)	30	25
8		 (**3ah**)	24	23
9[c]		 (**3ai**)	30	10
10[d]		 (**3ai**)	40	12

[a] Isolated yield based on the aziridine. [b] Ratios of the two regioisomers were determined by ^1H NMR. [c] THF was used as the reaction solvent. [d] CH_3CN was used as the reaction solvent.

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the correspound group, were reacted with **1a** and gave the corresponding alkyl thiol nucleophile ring-opening product only obtained in very low yeilds (Entries 9—10).

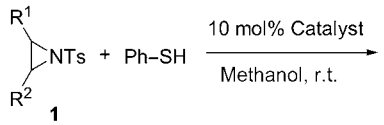
Effects of aziridines on the ring-opening reaction

In a second set of experiments, the scope of the process with respect to aziridines was investigated. All the expected products were generated under our standard experimental conditions, whatever the nature of the substituents was. As shown in Table 3, moderate to excellent yields (71%—96%) were obtained for all aziridines. In the case of the unsymmetric aziridines (**1c** and **1d**), regioselective attack of the thiol on the less substituted aziridine carbon was observed (Entries 3 and 4). When electronic effect participates, such as substrates **1e**, **1f**, **1g** and **1h**, the regioselective attack of the thiol on the benzyl substituted aziridine carbon was observed (Table 3, Entries 5, 6, 7, and 8). These results reflect that the electron effect is the main influence in the reaction.

Mechanism of the ring-opening reaction catalyzed by pyridine-*N*-oxide

For the mechanism, based on the previous reports[2,9i] we reasoned that the pyridine-*N*-oxide would act as a nucleophilic trigger in the reaction process, which attacked the aziridine **1** to form intermediate **A**. Subsequently, deprotonation of thiol **2** would occur to generate RS^-. Then RS^- reacted with aziridine **1** leading to the ring-opened intermediate **C**. Meanwhile another thiol would be involved in the reaction, which gave rise to the corresponding product **3** and regenerated the RS^- to complete the catalytic cycle (Scheme 1). In addition, the product from oxidation process which was described by Hou[9k] was not observed. It might be due to the presence of thiol in the reaction, which inhibited the intramolecular deprotonation process. Furthermore, when alkyl thiols were used as the nucleophile, the nucleophile is not acidic enough to generate RS^-, and the yields are low.

Table 3 Ring-opening reactions of various aziridines with benzenethiol in methanol with 10 mol% pyridine-*N*-oxide



1 **3** **4**

1a: R^1, $R^2 = (CH_2)_4$ **1b:** R^1, $R^2 = (CH_2)_3$
1c: $R^1 = CH_3(CH_2)_3$, R^2 = H **1d:** $R^1 = CH_3(CH_2)_{15}$, R^2 = H
1e: R^1 = Ph, R^2 = H **1f:** R^1 = *p*-Cl-C_6H_4, R^2 = H
1g: R^1 = *p*-Br-C_6H_4, R^2 = H **1h:** R^1 = *o*-Cl-C_6H_4, R^2 = H

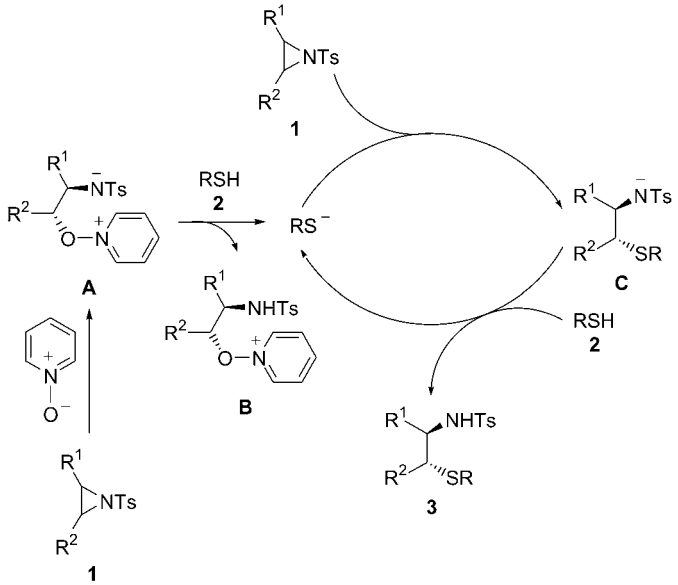
Entry	Reactant	Product	Time/h	Yield[a]/%
1	**1a**	**3ab**	5	89
2	**1b**	**3bb**	4.5	76
3	**1c**	**3cb**/**4cb** (96/4)[b]	5	95
4	**1d**	**3db**/**4db** (80/20)	5	96
5	**1e**	**3eb**/**4eb** (18/82)	4	71
6	**1f**	**3fb**/**4fb** (25/75)	5	75
7	**1g**	**3gb**/**4gb** (10/90)	5	85
8	**1h**	**3hb**/**4hb** (20/80)	10	73

[a] Isolated yield based on the arziridine. [b] Ratio was determined by ^{1}H NMR.

Conclusions

We have developed an efficient method for the ring opening of aziridines with various aryl thiols catalyzed by pyridine-*N*-oxide. The advantages of this method

Scheme 1 Proposed reaction pathway



include the use of air-stable, inexpensive pyridine-*N*-oxide as catalyst under mild conditions, good substrate generality, and experimentally operational ease. Desymmetrization of *meso* aziridines with thiols by using chiral *N*-oxide as catalysts is under investigation in our laboratory.

Experimental section

General procedure for the reactions of aziridines with various thiols

Thiol **2** (0.22 mmol) was added to a solution of aziridine **1** (0.20 mmol) in methanol (2.0 mL). The reaction mixture was stirred at room temperature for time indicated in Tables 2 and 3. After the reaction was completed (as indicated by TLC), the mixture was extracted with CH_2Cl_2. The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification by silica gel column chromatography afforded the corresponding products **3** and **4**. All the products were confirmed by ^{1}H NMR and ^{13}C NMR spectra.

***N*-[2-(4-Methylphenyl)thiocyclohexyl]-4-methylbenzenesulfonamide (3aa)**[2c] White solid; m.p. 94—96 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.15—1.36 (m, 4H), 1.57—1.64 (m, 2H), 1.97—2.01 (m, 1H), 2.27—2.28 (m, 1H), 2.32 (s, 3H), 2.43 (s, 3H), 2.76—2.82 (m, 1H), 2.91—2.95 (m, 1H), 5.31 (brs, 1H), 7.04 (d, ^3J= 8.0 Hz, 2H), 7.14 (d, J=8.0 Hz, 2H), 7.28 (d, J=8.0 Hz, 2H), 7.74 (d, J=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.1, 21.5, 22.7, 23.4, 29.6, 39.7, 51.8, 55.3, 127.3, 128.3, 129.7, 129.9, 133.9, 137.1, 138.0, 143.3.

***N*-[2-(Phenylthio)cyclohexyl]-4-methylbenzenesulfonamide (3ab)**[2a] White solid; m.p. 131—132 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.21—1.35 (m, 4H), 1.47—1.51 (m, 2H), 1.61—1.68 (m, 1H), 1.96—1.97 (m, 1H), 2.37 (s, 3H), 3.04—3.12 (m, 2H), 7.25—7.29 (m, 5H), 7.34 (d, J=7.2 Hz, 2H), 7.63 (d, J=8 Hz, 2H), 7.79 (d, J=7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.4, 22.7, 23.5, 30.5, 31.0, 49.7, 54.5, 126.8, 127.0, 129.4, 129.9, 131.4, 134.9, 139.4, 142.8.

***N*-[2-(4-Chlorophenyl)thiocyclohexyl]-4-methylbenzenesulfonamide (3ac)**[2d] White solid; m.p. 109—111 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.25—1.39 (m, 4H), 1.56—1.62 (m, 2H), 1.97—2.01 (m, 1H), 2.26—2.27 (m, 1H), 2.44 (s, 3H), 2.87—2.97 (m, 2H), 5.03 (brs, 1H), 7.20—7.22 (m, 4H), 7.26—7.30 (m, 2H), 7.73 (d, J=7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.6, 23.1, 24.4, 29.7, 32.0, 51.4, 54.9, 127.2, 129.1, 129.7, 131.2, 133.8, 134.4, 137.2, 143.5.

***N*-[2-(4-Fluorophenylthio)cyclohexyl]-4-methylbenzenesulfonamide (3ad)** White solid; m.p. 102—103 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.24—1.39 (m, 4H), 1.61 (t, J=6.0 Hz, 2H), 1.98—2.01 (m, 1H), 2.26—2.27 (m, 1H), 2.45 (s, 3H), 2.81—2.83 (m, 1H), 2.94—2.95 (m, 1H), 5.29 (br s, 1H), 6.93—6.99 (m, 2H), 7.25—7.33 (m, 4H), 7.76 (d, J=8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.5, 23.2, 24.5, 31.4, 32.1, 51.9, 55.0, 115.9 (d), 127.2 (d), 129.6, 136.0 (d), 137.3, 143.4, 161.4, 163.9; IR (KBr) ν: 3294.4, 3028.8, 2934.7, 2852.6, 1597.2, 1494.9, 1443.9, 1327.0, 1158.4, 1083.8, 817.0, 710.0, 668.0 cm^{-1}; HRMS calcd for $C_{19}H_{22}FNO_2S_2$ 379.1076, found 379.1072.

***N*-[2-(2-Chlorophenyl)thiocyclohexyl]-4-methylbenzenesulfonamide (3ae)**[11] White solid; m.p. 100—101 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.25—1.35 (m, 3H), 1.50—1.53 (m, 1H), 1.58—1.65 (m, 2H), 2.02—2.06 (m, 1H), 2.24—2.37 (m, 1H), 2.43 (s, 3H), 3.12—3.13 (m, 2H), 5.34 (d, J=4.0 Hz, 1H, NH), 7.18—7.20 (m, 2H), 7.27 (d, J=8.0 Hz, 2H), 7.36—7.40 (m, 2H), 7.75 (d, J=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.6, 23.0, 24.0, 31.1, 32.1, 50.0, 55.2, 127.2, 127.3, 128.2, 129.6, 130.0, 132.9, 133.2, 136.2, 137.1, 143.3.

***N*-[2-(2-Aminophenyl)thiocyclohexyl]-4-methylbenzenesulfonamide (3af)** Solid; m.p. 131—133 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18—1.25 (m, 4H), 1.31—1.38 (m, 1H), 1.56—1.62 (m, 1H), 1.91—2.02 (m, 1H), 2.18—2.19 (m, 1H), 2.43 (s, 3H), 2.71—2.72 (m, 1H), 2.98—3.10 (m, 1H), 4.45 (br, 2H), 5.15 (d, J= 5.2 Hz, 1H), 6.61—6.65 (m, 1H), 6.71 (d, J=7.6 Hz, 1H), 7.11—7.16 (m, 2H), 7.28 (d, J=8.4 Hz, 2H), 7.74 (d, J=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.6, 23.7, 24.9, 32.3, 52.0, 56.1, 60.5, 115.2, 115.7, 118.6, 127.2, 129.7, 130.4, 137.4, 137.6, 143.3, 149.1; IR (KBr) ν: 3468.2, 3371.7, 3279.8, 2931.1, 2861.4, 1615.3, 1481.9, 1447.5, 1408.4, 1334.2, 1311.1, 1154.8, 1094.8, 814.0, 749.7, 671.0 cm^{-1}; HRMS calcd for $C_{19}H_{24}N_2O_2S_2$ 376.1279, found 376.1278.

***N*-[2-(2-Mercaptophenylamino)-cyclohexyl]-4-methylbenzenesulfonamide (3ag)** Solid; m.p. 87—90 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.17—1.28 (m, 4H), 1.92—1.93 (m, 2H), 1.94—2.04 (m, 2H), 2.42 (s, 3H), 2.97—3.03 (m, 1H), 3.18—3.23 (m, 1H), 4.67—4.71 (m, 1H), 5.08—5.15 (m, 1H), 6.48—6.56 (m, 2H), 7.06—7.09 (m, 1H), 7.13—7.17 (m, 1H), 7.25—7.27 (m, 3H), 7.73—7.75 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.6, 23.7, 31.2, 33.4, 55.4, 56.2, 111.2, 117.0, 119.7, 127.0, 129.7, 131.6, 137.1, 137.5, 143.3, 147.8; IR (KBr) ν: 3467.8, 3274.8, 2936.1, 2856.5, 1590.2, 1491.0, 1413.1, 1333.6, 1234.5, 1169.9, 1163.0, 1151.9, 1015.7, 834.5, 674.8 cm^{-1}; HRMS calcd for $C_{19}H_{24}N_2O_2S_2$ 376.1279, found 376.1278.

***N*-(2-Methoxycyclohexyl)-4-methylbenzenesulfonamide (3ah)**[12] White solid; m.p. 60—62 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.12—1.25 (m, 4H), 1.58—1.67 (m, 2H), 2.02—2.05 (m, 1H), 2.17—2.20 (m, 1H), 2.42 (s, 3H), 2.84—2.93 (m, 2H), 3.19 (s, 3H), 5.10 (brs, 1H), 7.26—7.30 (m, 2H), 7.74 (d, J=8.0 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, 127.1, 127.2, 129.5, 129.6, 137.3, 143.1.

***N*-(2-Benzylthio-cyclohexyl)-4-methylbenzenesulfonamide (3ai)**[2d] Yellow liquid; ^{1}H NMR ($CDCl_3$) δ: 1.18—1.26 (m, 4H), 1.38—1.39 (m, 1H), 1.59—1.69 (m, 1H), 1.99—2.04 (m, 1H), 2.20—2.24 (m, 1H), 2.39—2.42 (m, 1H), 2.43 (s, 3H), 2.89—2.93 (m, 1H), 4.11 (dd, J=3.2, 14.4 Hz, 2H), 5.11 (d, J=4.0 Hz, 1H), 7.21—7.34 (m, 7H), 7.75 (d, J=8.4 Hz, 2H); ^{13}C NMR

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($CDCl_3$) δ: 21.1, 21.6, 23.7, 25.1, 34.3, 48.2, 55.4, 60.4, 127.2, 127.3, 128.6, 128.8, 129.6, 137.2, 137.9, 143.4.

***N*-[(2-Phenylthio)cyclopentyl]-4-methylbenzenesulfonamide (3bb)**[2a] White solid; m.p. 78—80 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.47—1.59 (m, 2H), 1.64—1.71 (m, 2H), 2.04—2.14 (m, 2H), 2.42 (s, 3H), 3.28—3.31 (m, 1H), 3.33—3.38 (m, 1H), 5.11 (d, J=5.2 Hz, 1H), 7.22—7.26 (m, 7H), 7.65 (d, J=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.5, 21.6, 30.2, 31.5, 52.4, 59.5, 127.1, 127.3, 128.9, 129.7, 132.0, 134.0, 136.8, 143.4.

4-Methyl-*N*-(1-(phenylthio)hexan-2-yl)benzenesulfonamide (3cb)[2e] Liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.74 (t, J=6.0 Hz, 3H), 0.98—1.17 (m, 4H), 1.35—1.44 (m, 1H), 1.58—1.64 (m, 1H), 2.40 (s, 3H), 2.75—2.80 (m, 1H), 3.10—3.14 (m 1H), 3.30—3.35 (m, 1H), 4.76 (d, J=8.0 Hz, 1H), 7.20—7.32 (m, 7H), 7.63 (d, J=7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ: 13.8, 21.5, 22.1, 27.3, 33.4, 39.3, 52.9, 126.5, 127.0, 129.0, 129.6, 129.8, 137.4, 143.3.

4-Methyl-*N*-(1-phenylthiomethylheptadecyl)-benzenesulfonamide (3db) and 4-methyl-*N*-(2-(phenylthio)octadecyl)benzenesulfonamide (4db)[2d] **mixture (80/20)** White solid mixture; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.86 (t, J=6.8 Hz, 3H), 1.04—1.42 (m, 30H), 2.39 (s, 2.4H), 2.43 (s, 0.6H), 2.76—2.81 (m, 0.8H), 3.12—3.19 (m, 1H), 3.31—3.39 (m, 1H), 3.95 (d, J=6.4 Hz, 0.2H), 4.70 (d, J=7.6 Hz, 0.8H), 4.89 (d, J=6.4 Hz, 0.2H), 7.20—7.29 (m, 7H), 7.63 (d, J=8.0 Hz, 1.6H), 7.74 (d, J=8.0 Hz, 0.4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.1, 22.7, 25.2, 29.0, 29.4, 29.5, 29.7, 31.9, 39.3, 52.9, 126.5, 127.1, 129.0, 129.6, 129.8.

4-Methyl-*N*-[1-phenyl-2-(phenylthio)ethyl]-benzenesulfonamide (3eb) and 4-methyl-*N*-[2-phenyl-2-(phenylthio)ethyl]benzenesulfonamide (4eb)[2b] **mixture (18/82)** Colourless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.34 (s, 0.54H), 2.41 (s, 2.46H), 3.18—3.20 (m, 0.36H), 3.35—3.39 (m, 1.64H), 4.15 (t, J=7.2 Hz, 0.82H), 4.28 (d, J=5.6 Hz, 0.18H), 4.83 (t, J=6.4 Hz, 0.82H), 5.4 (d, J=5.2 Hz, 0.18H), 7.05—7.32 (m, 12H), 7.48 (d, J=8.4 Hz, 0.36H), 7.70 (d, J=8.0 Hz, 1.64H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.6, 47.1, 52.4, 126.8, 127.1, 127.8, 127.9, 128.1, 128.9, 129.0, 129.8, 132.6, 136.8, 138.2, 143.6.

***N*-(1-(4-Chlorophenyl)-2-(phenylthio)ethyl)-4-methylbenzenesulfonamide (3fb) and *N*-(2-(4-chlorophenyl)-2-(phenylthio)ethyl)-4-methylbenzenesulfonamide (4fb)**[12,2e] **mixture (25/75)** White solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.37 (s, 0.75H), 2.42 (s, 2.25H), 3.09—3.19 (m, 0.5H), 3.25—3.37 (m, 1.5 H), 4.13 (t, J=7.6 Hz, 0.75H), 4.16—4.19 (m, 0.25H), 4.70 (t, J=6.4 Hz, 0.75H) 5.29 (d, J=9.6 Hz, 0.25H) 6.9—7.04 (m, 2H), 7.12—7.27 (m, 9H), 7.50 (d, J=8.4 Hz, 0.5H), 7.61 (d, J=8.4 Hz,1.5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.6, 46.9, 52.1, 127.0, 128.0, 128.1, 128.9, 129.0, 129.1, 129.2, 129.8, 132.8, 136.7, 136.9, 143.7.

***N*-(1-(4-Bromophenyl)-2-(phenylthio)ethyl)-4-methylbenzenesulfonamide (3gb) and *N*-(2-(4-bromophenyl)-2-(phenylthio)ethyl)-4-methylbenzenesulfonamide**[12] **(4gb) mixture (10/90)** White solid; m.p. 137—139 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.39 (s, 0.3H), 2.44 (s, 2.7H), 3.09—3.15 (m, 0.2H), 3.30—3.35 (m, 1.8H), 4.13 (t, J=7.2 Hz, 0.9H), 4.15 (t, J=7.2 Hz, 0.1H) 4.69 (t, J=6.4 Hz, 0.9H), 5.25 (s, 0.1H) 6.93 (d, J=8.4 Hz, 0.2H), 6.98 (d, J=8.4 Hz, 1.8H), 7.12 (d, J=8.0 Hz, 0.2H), 7.18—7.24 (m, 6.8H), 7.28—7.31 (m, 1.8H), 7.37 (d, J=8.4 Hz, 0.2H), 7.47 (d, J=8.0 Hz, 0.2H), 7.62 (d, J=8.0 Hz, 1.8H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ: 21.5, 46.9, 52.2, 121.9, 127.0, 127.2, 128.0, 128.8, 129.8, 132.3, 132.8, 136.6, 137.4, 138.1, 143.7.

***N*-(1-(2-Chlorophenyl)-2-(phenylthio)ethyl)-4-methylbenzenesulfonamide (3hb) and *N*-(2-(2-chlorophenyl)-2-(phenylthio)ethyl)-4-methylbenzenesulfonamide (4hb) mixture (20/80)** Liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.35 (s, 0.6H), 2.42 (s, 2.4H), 2.89—3.92 (m, 0.2H), 3.26—3.37 (m, 0.8H), 3.42—3.49 (m, 0.8H), 3.57—3.60 (m, 0.2H), 4.62—4.66 (m, 0.8H), 4.67—4.68 (m, 0.2H), 4.87 (t, J=6.0 Hz, 0.8H), 5.30 (t, J=5.6 Hz, 0.2H), 7.09—7.38 (m, 10.6H), 7.53 (d, J=7.6 Hz, 0.4H) 7.64 (d, J=8.0 Hz, 1.6H), 7.73 (d, J=8.0 Hz, 0.4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.6, 45.9, 48.5, 127.1, 127.6, 128.0, 128.5, 129.1, 129.06, 129.9, 132.4, 133.9, 135.6, 136.6, 143.6; IR (KBr) ν: 3287.5, 2926.4, 1598.1, 1439.3, 1331.7, 1265.7, 1160.6, 1092.0, 739.9; HRMS calcd for $C_{21}H_{20}ClNO_2S_2$ 417.0624, found 417.0624.

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