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Synthesis of chiral β-chalcogen amine derivatives and Gram-positive bacteria activity

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ABSTRACT

Efficient ring opening reaction between aziridines and diphenyl dichalogenides using HCl, Zn° in ionic liquid is disclosed, affording chiral β-chalcogen amines derivatives in good yields under mild reaction condition. The ionic liquid was further reused four times without the loss of its efficiency. The chiral chalcogenoamines showed antimicrobial activity against Gram-positive bacteria strains.

1. Introduction

Development of methods for stereocontrolled synthesis of chiral β-chalcogen amine derivative continues to receive significant attention. They have generally targeted as compounds with antioxidant, antitumour, and antimicrobial activities and many of these compounds are competitive inhibitors for target proteins.[1] In addition to the interesting properties of thio- and seleno-proteins, simple organosulfur and organoselenium compounds exhibit several useful biological and medicinal applications.[2] Besides, synthetic methods for preparation of seleno-cysteine,[3] selenium-based peptides,[4] selenoglycosides,[5] seleno-nucleosides[6] and other important natural compounds[7] is an intensive current research area. Moreover, chiral selenide and diselenides containing ligands offer attractive and practical options in the development of asymmetric transformations.[8]

The development of new methods for the introduction of sulfur- and selenium-containing groups into organic molecules, remains a significant challenge. In this context, ring opening reaction of aziridines with chalcogen nucleophiles provides an useful protocol to synthesize chiral β-chalcogen amine derivatives using organic solvents.[9]

Substantial number of reports have been appearing in the literature describing the reductive cleavage of S–S/Se–Se bonds, employing $NaBH_4$,[10] Zn,[11] $Zn/InCl_3$,[12] InI[13] and others,[14] which generate chalcogen nucleophiles upon further reaction with aziridines afford the corresponding chiral β-chalcogen amine derivatives.

However, these methods all possess one or more of the following disadvantages, including prolonged reaction time, suffered from the fact that a Lewis acid or strong base was necessary to effect the reaction, or the requirement for costly, air-sensitive substances.

Keeping in mind the wide range of applications of these analogues, general and recyclable synthetic methodologies to prepare sulfur- and selenium-containing derivatives of amino acids in a simple, efficient, stereo-regulated manner is greatly appreciated and remains as a highly challenging and desiring endeavour.

Room-temperature ionic liquids are currently attracting considerable scientific interest on several fronts. Ionic liquids (ILs) are low melting organic salts composed solely of cations and anions, which make them highly tunable for specific applications.[15] Ionic liquids are noted to have a number of unique properties[16] and these behaviours have been shown to have a large number of applications. Moreover, ionic liquids have received considerable attention due to their ability to serve as effective reaction media for a wide range of organic reactions and other applications in chemistry.[17] By modifying the structure of the cations or anions of ionic liquids, it has been shown that their properties can be altered in order to influence the outcomes of reactions. On other hand, Gram-positive infections are associated to high rates of morbidity and mortality.[18] For instance, *Listeria monocytogenes* causes serious localized and generalized infections in humans and a variety of other vertebrates, including domesticated and wild birds as well mammals.[19] *Bacillus cereus* is also a Gram-positive, rod-shaped, spore-forming aerobe commonly found in soil and many other sources, is a cause of food

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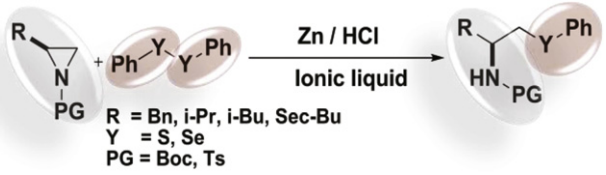
poisoning and can occasionally be responsible for surgical wound infection, pneumonia and meningitis in compromised patients. In this context, the development of new and modulate compounds for antimicrobial activity could afford an important point for biological applications and this way we reported the synthesis of chiral β-organochalcogen amines and the Gram-positive bacteria evaluation.

2. Results and discussion

In the course of our ongoing research towards the synthesis and application of organochalcogen compounds in organic synthesis and searching for the biological and synthetic importance of chiral β-organochalcogen amine and their derivatives, it is reported in this paper a simple and efficient methodology for the synthesis of chiral β-organochalcogen amine derivatives from the ring opening reaction of aziridines with diphenyl dichalcogenides using HCl (1 M), Zn in ionic liquid and the biological evaluation of the synthesized compounds as antimicrobial agent, as depicted in Scheme 1.

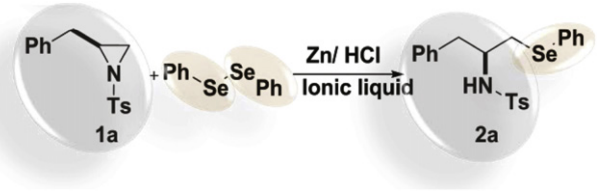


Scheme 1. Synthesis of chiral β-organochalcogen amines.

In order to identify the optimal reaction conditions, *N*-Ts protected aziridine **1a** derived from L-phenyl alanine, diphenyl diselenide and HCl (1 M) was chosen as a test substrate.

We carried out the reaction employing *N*-Ts protected aziridine **1a**, with PhSeSePh, 0.5 equiv of zinc dust and 10 μL HCl in ionic liquid (0.5 mL) under different conditions to get the desired chiral β-seleno amine **2a**, as summarized in Table 1. Firstly, it was performed a series of experiments with four different ionic liquids (Fig. 1) in order to check the influence of these in the reaction course.

Table 1
Screening of reaction conditions



Entry	Ionic liquid[a]	Temp (°C)	Time (h)	Yield[b] (%)
1	[bmim]BF_4	rt	2	—
2	[bmim]BF_4	80	2	90
3[c]	[bmim]BF_4	80	2	—
4	[bmim]PF_6	80	4	76
5	[bpy]BF_4	80	4	50
6	[bmmim]BF_4	80	4	64
7[d]	[bmim]BF_4	80	2	92
8	THF	Reflux	12	56
9	CH_2Cl_2	Reflux	12	38
10	CH_3CN	Reflux	12	44

[a] Ionic liquids were prepared by the available literature procedure[17h,l] and were subjected to vacuum before use (except [bmim]BF_4, which was acquired from ALDRICH).
[b] Yields refer to pure isolated products and characterized by ^1H and ^{13}C NMR.
[c] Without HCl.
[d] Zn dust (0.6 equiv).

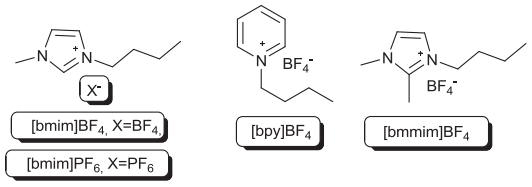
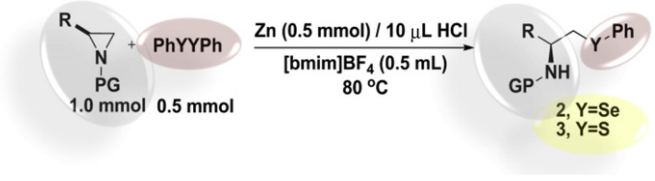


Fig. 1. Room-temperature ionic liquids.

Analyzing Table 1, the desired β-seleno amine **2a** was obtained in a good yield using [bmim]BF_4 at 80 °C. When [bmim]BF_4 was used at room temperature, the desired product was not observed (Table 1, entries 1 and 2), the same was observed when the reaction was conducted without HCl (Table 1, entry 3). While other ionic liquids such as [bmim]PF_6, [bmmim]BF_4, [bpy]BF_4 were effective for the transformation, they were less efficient than [bmim]BF_4 (Table 1, entries 4–6). The amount of zinc required to promote the completion of the reaction was also evaluated. The reaction with 0.6 equiv of zinc showed similar results, leading to the desired product **2a** in excellent yields as well (Table 1, entry 7). In addition, ionic liquids could increase the aziridine ring opening due to the Lewis acid ability of these compounds. This could be observed, comparing the more effectivity of the [bmim]BF_4 compared to [bmmim]BF_4 (Table 1, entries 2 and 6) and additionally, HCl also appears as an important catalyst for this aziridine ring opening. Lower yield was observed by using conventional organic solvents such as THF, CH_2Cl_2 and CH_3CN under reflux temperature as compared to [bmim]BF_4 (Table 1, entries 1, 8–10). Hence, the optimal conditions for the ring opening of aziridines using diphenyl diselenide with 0.5 equiv of Zn related to diselenide, 10 μL HCl in [bmim]BF_4 (0.5 mL) at 80 °C affording the chiral β-seleno amine derivatives. In order to demonstrate the generality of this method, it was investigated the scope of this reaction to prepare a variety of chiral β-seleno amine derivatives from *N*-protected aziridines **1a**–**g** derived from L-phenyl alanine, L-valine, L-leucine and L-isoleucine as depicted in Table 2.

Table 2
Synthesis of chiral β-chalcogenoamine derivatives



Entry	R	Reactant	PG[a]	Product	Yield[b] (%)
1	Bn	**1a**	Ts	**2a**	90
2			Ts	**3a**	78
3	Bn	**1b**	Boc	**2b**	88
4			Boc	**3b**	70
5	*i*-Pr	**1c**	Boc	**2c**	73
6			Boc	**3c**	75
7	*i*-Pr	**1d**	Ts	**2d**	85
8			Ts	**3d**	70
9	*i*-Bu	**1e**	Ts	**2e**	76
10			Ts	**3e**	66
11	*s*-Bu	**1f**	Ts	**2f**	62
12			Ts	**3f**	60
13	*s*-Bu	**1g**	Boc	**2g**	67

[a] Reaction time for PG=Boc, 120 min; PG=Ts, 90 min.
[b] Yields refer to pure isolated products and characterized by ^1H and ^{13}C NMR.

As shown in Table 2, it was possible to verify that the respective chiral β-seleno amine derivatives were obtained in good to excellent yields from different *N*-protected aziridines. In general, *N*-Ts afforded better yields than the *N*-Boc protected aziridines (for

instance, see Table 2, entries 2 and 4). The R group derived from the aminoacid side showed a small steric effect, allowing slightly better yields to the small groups. As a further extension of our protocol, it was applied the same reaction conditions employed for the preparation of chiral β-seleno amino derivatives to prepare a series of chiral β-sulfur amino derivatives.

The reaction of aziridines **1a**–**f** with diphenyl disulfide mediated by zinc in ionic liquid and HCl resulted to the formation of the corresponding chiral β-amino sulfides **3a**–**f** in good to excellent yield (Table 2, entries 1–12), showing a similar behaviour for the selenide aziridine ring opening.

Continuing our efforts to provide synthetic methods that are more benign at an environmental point of view, it was attempted to reuse the ionic liquid/[bmim]BF_4, which was one of the prime objectives in our quest. In this regard, it was performed a set of experiments aiming to reuse the reaction medium, Fig. 2. After completion of the reaction, ionic liquid/[bmim]BF_4 was recovered (see Supplementary data) and subjected to another run, affording the corresponding product in good yield. This process was repeated four more times affording the desired product in a close range of yield.

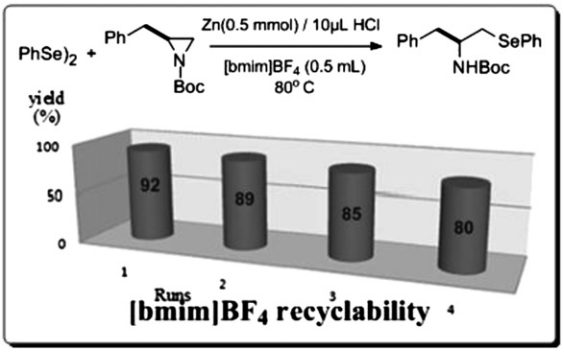


Fig. 2. Reuse of ionic liquid/[bmim]BF_4.

In connection with the synthetic approach, compounds **2f** and **3f** were evaluated for their efficacy as antimicrobial agents (Table 3). From the results of disc diffusion and microdilution method[20,21] (see Supplementary data), was observed an activity against Gram-positive bacteria strains, especially *L. monocytogenes*, *B. cereus* and *Paenibacillus* species (Table 3). Comparing these results to those obtained with standard antibiotics, compounds **2f** and **3f** produced a lower inhibition to that produced by Amikacin (see Supplementary data).

Table 3
Antimicrobial activities of **2f** and **3f**

Microorganisms	Source	MIC compounds (μg/mL)	
		2f	**3f**
Bacillus cereus	ATCC9634	1100	1100
Listeria monocytogenes	ATCC7644	1100	1100
Paenibacillus alginolyticus	Environmental isolate	1100	1100
Paenibacillus azotofixans	Environmental isolate	550	1100
Paenibacillus gluconolyticus	Environmental isolate	550	1100
Paenibacillus thiaminolyticus	Environmental isolate	550	1100

Despite the moderate activity, the structural simplicity, easy preparation and modulate character of the synthesis may allow this methodology as an alternative basis for the preparation of new antimicrobial agents class and the results illustrate, up to our knowledge, for the first time an antimicrobial effect of chiral chalcogenoamines.

3. Conclusion

In summary, reductive cleavage of diphenyl disulfides and diselenides mediated by zinc and HCl in ionic liquid followed by the ring opening of aziridines provides an easy access to chiral β-amino sulfides and β-amino selenides in a stereospecific and regioselective manner under mild conditions with good skeletal diversity in a *one-pot* process. The methodology would be of interest due to the cost-effective, mild reaction conditions and good to excellent yields were obtained in a short time. We believe that this method reported in this study would greatly contribute to environmentally greener protocol since the solvent/ionic liquid would be reused up to four successive runs besides safer processes. Current efforts are directed at gaining a deeper understanding of some of the fundamental principles dictating the reactivity of these systems, as well as extending their utility by expanding the substrate scope.

4. Experimental

4.1. General procedure for the synthesis of chiral β-chalcogen amine derivatives (2a–g and 3a–f)

In a Schlenk flask, under argon atmosphere, diphenyl dichalcogenide (0.5 mmol) and zinc dust (0.5 mmol) were added to [bmim]BF_4 (0.5 mL) at 80 °C. The reaction mixture was allowed to stir for 10 min to solubilize the diphenyl dichalcogenide and afterwards 10 μL HCl (1 M) was added. Then, the mixture was allowed to stir for 5 min and aziridine (1 mmol) was slowly added. The reaction mixture was allowed to stir for suitable reaction time (monitored by TLC and assisted by visual observation). The mixture was then extracted with ether (3×20 mL), and the combined ether extract was washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product. Purification by column chromatography over silica gel (hexane/ethyl acetate 95:5), furnished the pure chiral β-chalcogen amino derivatives **2a**–**g** and **3a**–**f**.

*4.1.1. (S)-4-Methyl-N-(1-phenyl-3-(phenylselanyl)propan-2-yl) benzenesulfonamide (**2a**).*[22] Yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.43–7.39 (m, 4H), 7.27–7.09 (m, 9H), 6.93–6.91 (m, 2H), 4,72 (d, J=7.2 Hz, 1H), 3.55–3.48 (m, 1H), 3.12 (dd, ^1J=12.83 Hz, ^2J=4.54 Hz, 1H), 2.95 (dd, ^1J=14.42 Hz, ^2J=6.48 Hz, 1H), 2.82 (dd, ^1J=12.83 Hz, ^2J=7.21 Hz, 1H), 2.74 (dd, ^1J=14.42 Hz, ^2J=7.21 Hz, 1H), 2.37 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=143.13, 136.68, 136.45, 132.92, 129.51, 129.24, 128.61, 127.29, 126.96, 126.72, 54.49, 40.29, 32.87, 21.47 ppm.

*4.1.2. (S)-tert-Butyl 1-phenyl-3-(phenylselanyl) propan-2-ylcarbamate (**2b**).*[9c] Yield 88%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.51–7.48 (m, 2H), 7.29–7.12 (m, 8H), 4.70–4.66 (m, 1H), 4.09–4.06 (m, 1H), 3.04–3.01 (m, 2H), 2.87–2.82 (m, 2H), 1.38 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=154.96, 137.48, 132.74, 129.29, 129.09, 128.68, 128.40, 126.99, 126.44, 80.98, 38.21, 32.77, 28.24, 27.81 ppm.

*4.1.3. (S)-tert-Butyl 3-methyl-1-(phenylselanyl)butan-2-ylcarbamate (**2c**).*[22] Yield 73%; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.55–7.50 (m, 2H), 7.26–7.23 (m, 3H), 4.60–4.55 (m, 1H), 3.69–3.59 (m, 1H), 3.07 (d, J=5.6 Hz, 2H), 1.94–1.77 (m, 1H), 1.42 (s, 9H), 0.91–0.87 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=155.54, 132.93, 129.05, 126.99, 79.10, 55.64, 32.41, 31.69, 28.33, 19.43, 17.97 ppm.

*4.1.4. (S)-4-Methyl-N-(3-methyl-1-(phenylselanyl)butan-2-yl)benzenesulfonamide (**2d**).*[14d] Yield 85%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.62 (d, J=8.4 Hz, 2H), 7.37–7.35 (m, 2H), 7.26–7.17 (m, 5H), 4.82 (d, J=6.4 Hz, 1H), 3.23–3.17 (m, 1H), 3.06 (dd, ^1J=12.8 Hz, ^2J=4.8 Hz, 1H), 2.74 (dd, ^1J=12.8 Hz, ^2J=6.6 Hz, 1H), 2.38 (s, 3H), 2.01–1.93 (m, 1H), 0.81 (d, J=6.8 Hz, 3H), 0.76 (d, J=6.8 Hz, 3H) ppm; ^{13}C NMR

(100 MHz, $CDCl_3$): δ=143.19, 137.65, 133.07, 129.54, 129.15, 127.29, 127.05, 58.57, 31.64, 30.68, 21.49, 19.01, 17.44 ppm.

*4.1.5. (S)-4-Methyl-N-(4-methyl-1-(phenylselanyl)pentan-2-yl)benzenesulfonamide (**2e**).*[23] Yield 76% ; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.60 (d, *J*=8.4 Hz, 2H), 7.42–7.40 (m, 2H), 7.29–7.21 (m, 3H), 7.18 (d, *J*=8.4 Hz, 2H), 4.86 (d, *J*=8.4 Hz, 1H), 3.46–3.38 (m, 1H), 3.10 (dd, ^1J=12.2 Hz, ^2J=3.6 Hz, 1H), 2.73 (dd, ^1J=12.2 Hz, ^2J=6.8 Hz, 1H), 2.38 (s, 3H), 1.48–1.36 (m, 2H), 1.29–1.23 (m, 1H), 0.77 (d, *J*=6.4 Hz, 3H), 0.59 (d, *J*=6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=142.19, 137.65, 133.19, 129.52, 129.08, 127.23, 126.98, 51.54, 43.82, 34.65, 24.30, 22.76, 21.52, 21.43 ppm.

*4.1.6. 4-Methyl-N-((2S,3S)-3-methyl-1-(phenylselanyl)pentan-2-yl) benzenesulfonamide (**2f**).*[23] Yield 62%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.64 (d, *J*=8.0 Hz, 2H), 7.34–7.32 (m, 2H), 7.26–7.18 (m, 5H), 4.88 (d, *J*=8.4 Hz, 1H), 3.30–3.24 (m, 1H), 2.99 (dd, ^1J=5.6 Hz, ^2J=12.8 Hz, 1H), 2.77 (dd, ^1J=6 Hz, ^2J=12.4 Hz, 1H), 2.39 (s, 3H), 1.74–1.68 (m, 1H), 1.45–1.36 (m, 1H), 1.04–0.98 (m, 1H), 0.80–0.76 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ=143.6, 137.58, 133.04, 129.51, 129.35, 129.08, 127.24, 127.06, 57.52, 37.52, 31.10, 24.44, 21.47, 14.96, 11.38 ppm.

*4.1.7. tert-Butyl-(2S,3S)-3-methyl-1-(phenylselanyl)pentan-2-ylcarbamate (**2g**).*[23] Yield 67% ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ=7.54–7.50 (m, 2H), 7.26–7.21 (m, 3H), 4.6–4.5 (m, 1H), 3.75–3.7 (m, 1H), 3.1–3.0 (m, 1H), 1.67–1.57 (m, 2H), 1.42 (s, 9H), 1.17–0.95 (m, 2H), 0.9–0.84 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ=155.49, 133.12, 129.06, 129.05, 127.07, 71.88, 38.44, 32.1, 28.38, 27.76, 15.43, 11.37 ppm.

*4.1.8. (S)-4-Methyl-N-(1-phenyl-3-(phenylthio)propan-2-yl)benzenesulfonamide (**3a**).*[24] Yield 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.44 (d, *J*=8 Hz, 2H), 7.29–7.16 (m, 8H), 7.10 (d, *J*=8 Hz, 2H), 6.97–6.94 (m, 2H), 4.66 (d, *J*=6.8 Hz, 1H), 3.52–3.47 (m, 1H), 3.15 (dd, ^1J=6.4 Hz, ^2J=13.6 Hz, 1H), 2.98 (dd, ^1J=6.4 Hz, ^2J=13.8 Hz, 1H), 2.87–2.75 (m, 2H), 2.38 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ=143.16, 136.67, 136.35, 134.97, 129.68, 129.51, 129.26, 129.03, 128.62, 126.96, 126.74, 126.48, 53.91, 39.43, 38.02, 21.46 ppm.

*4.1.9. (S)-tert-Butyl 1-phenyl-3-(phenylthio)propan-2-ylcarbamate (**3b**).*[25] Yield 70%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.35–7.33 (m, 2H), 7.30–7.15 (m, 8H), 4.68–4.66 (m, 1H), 4.10–4.04 (m, 1H), 3.09–3.01 (m, 2H), 2.91–2.86 (m, 2H), 1.39 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ=155.16, 138.0, 136.35, 129.26, 128.79, 128.81, 128.16, 126.62, 125.19, 79.5, 57.2, 40.08, 39.61, 28.40 ppm.

*4.1.10. (S)-tert-Butyl 3-methyl-1-(phenylthio)butan-2-ylcarbamate (**3c**).*[26] Yield 75%; ^{1}H NMR ($CDCl_3$, 200 MHz) δ=7.41–7.18 (m, 5H), 4.61–4.56 (m, 1H), 3.70–3.67 (m, 1H), 3.08 (d, *J*=6.0 Hz, 2H), 1.97–1.87 (m, 1H), 1.43 (s, 9H), 1.01–0.88 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ=155.79, 130.84, 129.70, 128.93, 126.21, 68.96, 37.57, 30.83, 28.35, 22.44, 19.13 ppm.

*4.1.11. (S)-4-Methyl-N-(3-methyl-1-(phenylthio)butan-2-yl)benzenesulfonamide (**3d**).*[27] Yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.66 (d, *J*=8.4 Hz, 2H), 7.27–7.19 (m, 7H), 4.87 (d, *J*=8.4 Hz, 1H), 3.23–3.17 (m, 1H), 3.06 (dd, ^1J=4.8 Hz, ^2J=13.6 Hz, 1H), 2.78 (dd, ^1J=6.8 Hz, ^2J=13.2 Hz, 1H), 2.38 (s, 3H), 2.09–2.02 (m, 1H), 0.83 (d, *J*=7.2 Hz, 3H), 0.77 (d, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ=143.23, 137.63, 135.29, 129.75, 129.52, 128.94, 127.09, 126.43, 57.95, 36.62, 29.62, 21.47, 18.89, 17.11 ppm.

*4.1.12. (S)-4-Methyl-N-(4-methyl-1-(phenylthio)pentan-2-yl)benzenesulfonamide (**3e**).* Yield 66%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.63 (d, *J*=8.0 Hz, 2H), 7.23–7.19 (m, 7H), 4.74 (d, *J*=7.6 Hz, 1H), 3.44–3.33 (m, 1H), 3.14 (dd, ^1J=4.0 Hz, ^2J=13.6 Hz, 1H), 2.75 (dd, ^1J=6.8 Hz, ^2J=13.2 Hz, 1H), 2.39 (s, 3H), 1.49–1.40 (m, 2H), 1.34–1.26 (m, 1H), 0.79 (d, *J*=6.4 Hz, 3H), 0.59 (d, *J*=6.0 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ=143.38, 137.57, 135.39, 130.18, 129.55, 128.95, 127.07, 126.56, 51.22, 43.37, 39.94, 24.33, 22.88, 21.51, 21.46 ppm; $[\alpha]_D^{20}$ −47 (*c* 1.0, ethyl acetate). ESI-HRMS calcd for $C_{19}H_{25}NO_2S_2$ 364.1413 (M^++H), found, *m*/*z* 364.1394.

*4.1.13. 4-Methyl-N-((2S,3S)-3-methyl-1-(phenylthio)pentan-2-yl) benzenesulfonamide (**3f**).* Yield 60%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.66 (d, *J*=8.4 Hz, 2H), 7.28–7.15 (m, 7H), 4.86 (d, *J*=8.0 Hz, 1H), 3.29–3.21 (m, 1H), 2.98 (dd, ^1J=6.0 Hz, ^2J=13.6 Hz, 1H), 2.83 (dd, ^1J=6.0 Hz, ^2J=13.6 Hz, 1H), 2.38 (s, 3H), 1.84–1.73 (m, 1H), 1.46–1.37 (m, 1H), 1.09–0.97 (m, 1H), 0.82–0.76 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ=143.20, 137.50, 135.23, 129.81, 129.49, 128.91, 127.10, 126.44, 56.98, 36.74, 36.14, 24.40, 21.46, 14.87, 11.64 ppm; $[\alpha]_D^{20}$ +24 (*c* 1.0, ethyl acetate). ESI-HRMS calcd for $C_{19}H_{25}NO_2S_2$ 364.1399 (M^++H), found, *m*/*z* 364.1394.

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Supplementary data

Synthetic procedures and compounds characterization data. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.09.049.

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