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Polystyrene-Supported 1,5,7-Triazabicyclo[4.4.0]dec-5-ene as an Efficient and Reusable Catalyst for the Thiolysis of 1,2-Epoxides under Solvent-Free Conditions

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Polystyrene-supported 1,5,7-triazabicyclo[4.4.0]dec-5-ene (PS-TBD) is an effective basic catalyst for the thiolysis of the 1,2-epoxides **1a**–**e** by the aryl- and alkyl-substituted thiols **2A**–**E** under solvent-free conditions while its activity is remarkably reduced in MeCN. The reactions are totally *anti*-diastereoselective and generally highly C-β regioselective. The corresponding hydroxy sulfides have been isolated in excellent yields and the catalyst has been easily recovered and reused with no loss in terms of efficiency and selectivity of the process.
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Introduction

Organic catalysts are a very efficient alternative to metal-containing promoters for stereoselective transformations.[1] Their polymer-supported version resolves the problem of their recovery and reuse and simplifies the isolation of the reaction products.[2] Environmental issues are pushing an increasing number of researchers to realize cleaner and more efficient procedures to improve the sustainability of organic synthesis. Accordingly, the use of solid organic catalysts is of particular interest and especially in those reaction media that furnish an alternative to classical organic solvents.[3] Interest is growing rapidly in solvent-free processes, in fact solvent-free condition (SFC) can significantly improve the efficiency of a process while requires simpler equipments and avoids drying procedures.[4]

Our research is focused on the use of water as reaction medium and of SFC to define one-pot procedures for the synthesis of target molecules.[5,6] We have recently found that the efficiency of a Lewis-acid catalyst is increased under SFC allowing the aminolysis and thiolysis of 1,2-epoxides by multidendate nucleophiles and opening the route to the preparation of new heterocyclic nuclei.[6e,6g]

Thiolysis of 1,2-epoxides is a fundamental organic transformation which is used in nature for metabolic detoxification of olefinic xenobiotics.[7] In the laboratory this process has been performed in anhydrous organic solvents (THF, CH_2Cl_2, MeOH, and MeCN) by using stoichiometric amounts of a base to generate a reactive thiolate species.[8] Under these conditions the reactions generally proceed with C-β regioselectivity, furnishing the corresponding hydroxy sulfides in high yields. Alternatively, when thiols are used, milder reaction conditions are usually required, but an activating agent is necessary (onium ions,[9] polyethylene glycols,[10] Lewis acids,[11] solid neutral or acidic catalysts).[12]

We have reported that thiolysis of a variety of 1,2-epoxides can be regio- and stereoselectively performed in water either under acidic[4d] or neutral[4g] conditions by using an In^{III} or Zn^{II} salt, respectively. This reaction can be efficiently performed also under basic aqueous condition at pH 9.0.[4e] Furthermore, we have demonstrated that a catalytic amount of NaOH is sufficient to promote the regio- and stereoselective thiolysis of α,β-epoxy ketones in water.[4i]

According to our interest in the oxirane ring-opening, we have started a study on the base-catalyzed thiolysis of 1,2-epoxides **1a**–**e** by the thiols **2A**–**E** under SFC. Triethylamine (TEA), 4-(dimethylamino)pyridine (DMAP), and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) as well as their polystyrene-supported versions PS-TEA, PS-DMAP, and PS-TBD were chosen as Brønsted-basic catalysts, while triphenylphosphane (TPP) and polystyrene–diphenylphosphane (PS-TPP) were chosen as representative Lewis bases. All the polystyrene-supported bases chosen in this study are commercially available.

Our project is aimed at i) the evaluation of the influence of the anchorage of a basic catalyst on a polystyrene support both under SFC and in organic solvent, ii) the selection of the best polystyrene-supported organic catalyst to promote the thiolysis of 1,2-epoxides.

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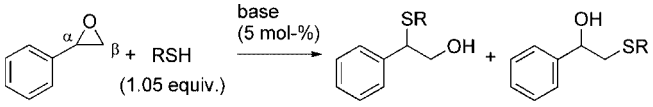
Results and Discussion

We have initially studied the reaction of styrene oxide (**1a**) with a representative aromatic thiol such as benzenethiol (**2A**) and an alkane thiol as 1-butanethiol (**2B**) under SFC in the presence of 5 mol-% of TEA, DMAP, TBD, and TPP (Table 1) and 5 mol-% of the commercially available PS-TEA, PS-DMAP, PS-TBD, and PS-TPP (Table 2). For comparison, the same transformations were also performed in MeCN, which is known to be an efficient organic medium for this process.

Table 1. Thiolysis of **1a** with **2A** and **2B** under SFC and in MeCN at 30 °C catalyzed by organic bases.



1a **2A** R = Ph, **2B** R = *n*-Bu — **3aA** (33%), **3aB** (25%) — **4aA** (67%), **4aB** (75%)

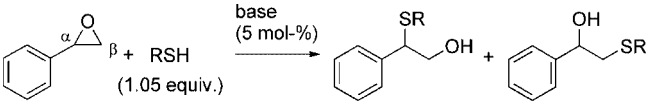
Entry	Thiol	Reaction medium	Base	*t* [h]	Conversion [%][a]
1	**2A**	SFC	TEA	1	> 99
2	**2A**	MeCN	TEA	1	18
3	**2A**	SFC	DMAP	1	> 99
4	**2A**	MeCN	DMAP	24	13
5	**2A**	SFC	TBD	1	> 99[b]
6	**2A**	MeCN	TBD	1	33
7	**2A**	SFC	TPP	24	> 99
8	**2A**	MeCN	TPP	24	11
9	**2B**	SFC	TEA	24	–[c]
10	**2B**	MeCN	TEA	24	–
11	**2B**	SFC	DMAP	20	94
12	**2B**	MeCN	DMAP	70	traces
13	**2B**	SFC	TBD	2	> 99[d]
14	**2B**	MeCN	TBD	2	traces
15	**2B**	SFC	TPP	24	–[e]
16	**2B**	MeCN	TPP	24	–

[a] Conversion measured by GLC analyses. [b] 95% Isolation yield. [c] Complete conversion of **1a** to **3aB/4aB** was obtained by using 1 equiv. of TEA after 6 h at 65 °C. [d] 94% Isolation yield. [e] The same result was obtained at 65 °C and by using 1 equiv. of TPP.

The thiolysis of **1a** by benzenethiol (**2A**) under SFC was efficiently catalyzed by TEA, DMAP, and TBD with complete conversion within 1 h to a 1:2 mixture of the corresponding hydroxy sulfides **3aA** and **4aA** (Table 1, Entries 1, 3, and 5), whereas TPP needed 24 h to promote the complete transformation (Table 1, Entry 7).

In the reaction of **1a** with 1-butanethiol (**2B**) under SFC, the catalytic activity of TEA, DMAP, and TPP was significantly reduced (Table 1, Entries 9, 11, and 15). DMAP gave a 94% conversion of **1a** to a mixture of the products **3aB** and **4aB** after 20 h, while 1.0 equiv. of TEA, 65 °C and 6 h were necessary to obtain the complete conversion of **1a** and TPP was ineffective at all. Only TBD maintained its high catalytic efficiency and promoted the reaction of **1a** with **2B** to completion in only 2 h (Table 1, Entry 13). In all cases the hydroxy sulfides **3aB** and **4aB** were formed in a 1:3 ratio. By performing the base-catalyzed thiolysis of **1a** in MeCN with both thiols **2A** and **2B**, unsatisfactory results were obtained (Table 1, Entries 2, 4, 6, 8, 10, 12, 14, and 16). As expected from our previous experience[6g] the use of a reaction medium (MeCN) reduced the catalytic efficiency of the catalyst while the C-α/C-β ratios remained unchanged (Table 1).

Table 2. Thiolysis of **1a** with **2A** and **2B** under SFC and in MeCN at 30 °C catalyzed by polystyrene-supported organic bases.



1a **2A** R = Ph, **2B** R = *n*-Bu — **3aA** (33%), **3aB** (25%) — **4aA** (67%), **4aB** (75%)

Entry	Thiol	Reaction medium	Base [5 mol-%]	*t* [h]	Conversion [%][a]
1	**2A**	SFC	PS-TEA	5	97
2	**2A**	MeCN	PS-TEA	5	traces
3	**2A**	SFC	PS-DMAP	10	> 99
4	**2A**	MeCN	PS-DMAP	10	10
5	**2A**	SFC	PS-TBD	1.5	> 99[b]
6	**2A**	MeCN	PS-TBD	1.5	50
7	**2A**	SFC	PS-TPP	22	> 99
8	**2A**	MeCN	PS-TPP	24	traces
9	**2B**	SFC	PS-DMAP	21	> 99
10	**2B**	MeCN	PS-DMAP	21	4
11	**2B**	SFC	PS-TBD	2	> 99[c]
12	**2B**	MeCN	PS-TBD	2	15

[a] Conversion measured by GLC analyses. The same reactions performed in DCM gave no conversion at all. [b] Isolated yield: 95%. [c] Isolated yield: 94%.

Under SFC and with PS-supported bases, the regioselectivities of the reactions were the same, and the catalysts showed slightly reduced efficiency (Table 2, Entries 1 and 3) or almost identical catalytic efficiencies (Table 2, Entries 5, 7, 9, and 11) in comparison to their non-supported counterparts.[13] Nevertheless, the slightly reduced catalytic efficiency is fully compensated by the simpler work-up procedure and by the possibility of recovering the solid catalyst thus allowing an environmentally-friendly thiolysis process to be realized.

PS-TBD was shown to be the most efficient supported catalyst, and the processes were complete in 1.5 and 2 h, respectively, affording the hydroxy sulfides in very good yields (95 and 94%, respectively) (Table 2, Entries 5 and 11).

In the presence of MeCN, the supported catalysts were not effective at all, always giving disappointing results (Table 2, Entries 2, 4, 8, 10, and 12), except in the case of PS-TBD, which showed a modest catalytic activity (Table 2, Entry 6). According to the results obtained by using TEA and TPP in the thiolysis of **1a** by **2B** (see Table 1, Entries 9 and 15) PS-TEA and PS-TPP were completely inefficient in promoting this process.

The use of PS-TBD was then extended to a variety of 1,2-epoxides **1b–e** and to functionalized thiols, such as *o*-aminobenzenethiol (**2C**), *o*-hydroxybenzenethiol (**2D**), and 2-propene-1-thiol (**2E**). The results are illustrated in Table 3.

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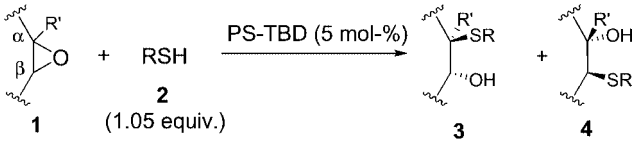
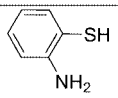
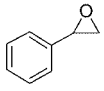
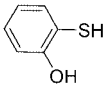
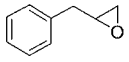
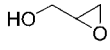
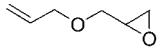
Table 3. PS-TBD-catalyzed thiolysis of **1a**–**e** by the thiols **2A**–**E** under SFC at 30 °C.



1 3 4

Entry	1,2-Epoxide	Thiol	*t* (h)	3/4[a]	Yield (%)[b]
1		 **2C**	1	40/60	92
2	 **1a**	 **2D**	0.25	75/25	94
3		 **2E**[c]	0.5	20/80	90
4	 **1b**	**2C**	0.5	< 1/> 99	98
5		**2E**[c]	0.5	< 1/> 99	90
6	 **1c**	**2C**	0.017	< 1/> 99	90
7		**2E**[c]	0.017	> 99	77
8	 **1d**	**2C**	1.5	< 1/> 99	98
9		**2E**[c]	0.5	< 1/> 99	90
10	 **1e**	**2C**	3	[d]	93
11		**2E**[c]	8	[e]	90

[a] Measured by GLC analyses. [b] Overall isolation yield of both **3** and **4**. [c] 1.2 Equiv. was used. [d] Only *trans*-2-[2′-(amino)phenylthio]cyclohexan-1-ol (**3eC**) was formed. [e] *trans*-2-(Allylthio)cyclohexan-1-ol (**3eE**) was formed.

PS-TBD proved to be a very efficient catalyst, with short reaction times (0.25–8 h) and high yields (90–98%) in all cases, also in the reactions of **1a** with **2C**–**E**. While the thiols **2C** and **2E** attacked preferentially the 1,2-epoxide **1a** at the C-β, giving the hydroxy sulfides **3aC**, **4aC**,and **3aE**, **4aE** in 2:3 and 1:4 ratio, respectively (Table 3, Entries 1 and 3), the 2-hydroxybenzenethiol (**2D**) displayed reversed regioselectivity (**3aD/4aD**, 3:1) (Table 3, Entry 2). This unexpected result can be ascribed to the formation of a hydrogen bond between the hydroxy group of **2D** and the oxirane oxygen of **1a**.

Homostyrene oxide (**1b**), glycidol (**1c**), and *O*-allylglycidol (**1d**) reacted with complete regioselectivity, in very short times (0.017–1.5 h), yielding only the corresponding adducts **4** (Table 3, Entries 4–9). Cyclohexene oxide (**1e**) underwent a completely *anti* stereoselective ring-opening to give in high yields the corresponding hydroxy sulfide **3eC** and **3eE** in 3 h and 8 h, respectively (Table 3, Entries 10 and 11).

When polystyrene-supported catalysts are employed, an important issue is the decrease in their activity after being recovered. PS-TBD used in the reaction of **1a** with **2A** showed a slight decrease in its efficiency only after five consecutive runs (Figure 1). This catalyst could be regenerated by washing it with an ammonia solution at room temperature for 1 h. After filtering the aqueous medium and drying the catalyst, its efficiency was as high as in the first run.

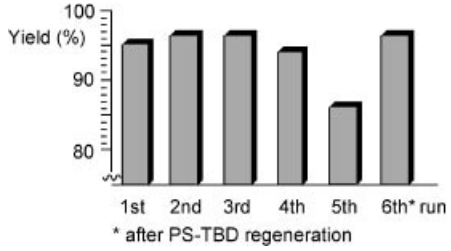


Figure 1. PS-TBD-catalyzed reactions of **1a** and **2A**. Isolated yield of the mixture of **3aA** and **4aA** in the re-use of the catalyst.

Conclusions

In conclusion we have demonstrated that SFC dramatically increased the catalytic efficiency of a polystyrene-supported base, such as PS-TBD, in the nucleophilic ring-opening of oxiranes by thiols. Swelling problems, related to the access to reactive sites of the polymer-supported catalysts, can be overcome under SFC, where, apparently, the reactants are activated as they flow through the polymer network. The polymer-supported catalyst has been recovered and reused, and the products have been isolated in excellent yields by simply filtering the reaction mixture. These results open a new and promising green route to hydroxy sulfides.

Experimental Section

All chemicals were purchased and used without any further purification. All the polystyrene-supported catalysts are commercially available. GC-MS analyses were carried out with 70-eV electron energy. All ^{1}H NMR and ^{13}C NMR spectra were recorded at 200 MHz or 400 MHz, and at 50.3 or 100.6 MHz, respectively, using a convenient deuterated solvent (reported in the characterization data) and the residual peak as internal standard, or TMS in the case of $CDCl_3$. All melting points are uncorrected. Thin-layer chromatography analyses were performed on silica gel on aluminum plates and UV and/or $KMnO_4$ were used as revealing systems. Column chromatography was performed by using silica gel 230–400 mesh and eluting as reported in the following characterization data. Hydroxy sulfides **3aA**,[11e] **3aB**,[14] **4aA**,[15] **4aB**,[16] are known compounds; while **3aC**,[17] **3aD**,[18] **3aE**,[5g] **3eC**,[19] **4aC**,[17,20] **4aD**,[19] **4aE**,[21] have already been prepared, but spectroscopic data have not been reported or are not complete to the best of our knowledge. Compounds **3eE**, **4bC**, **4bE**, **4cC**, **4cE**, **4dC**, **4dE**, are new compounds. Characterization data (^{1}H NMR, ^{13}C NMR, IR, GC-EIMS, R_f) are listed below.

Typical Procedure of the PS-TBD-Catalyzed Thiolysis: A screw-capped vial equipped with a magnetic stirrer was charged with PS-TBD [19 mg, ca. 0.05 mmol (2.6 mmol/g)] and then the thiol (1.05 equiv.) and the 1,2-epoxide (1.0 mmol) were consecutively added. The resulting mixture was left at 30 °C whilst stirring until

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reaction completed (GLC monitoring). EtOAc was then added and the heterogeneous mixture was left whilst stirring for 30 min. Solid PS-TBD was recovered by Büchner filtration of the organic layer, washed with additional EtOAc, dried under vacuum and reused. The organic layer was evaporated under reduced pressure to furnish the almost pure hydroxy sulfide product/s. The mixture of the products was separated by silica gel column chromatography (see below).

2-[2′-(Amino)phenylthio]-2-phenylethan-1-ol (3aC): Oil; chromatography on silica gel, eluent: petroleum ether/EtOAc, 6:4; TLC-R_f: 0.39 (petroleum ether/EtOAc, 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.74 (br. s, 2 H), 3.88 (d, J = 6.4 Hz, 2 H), 4.12 (t, J = 6.5 Hz, 1 H), 6.65–6.74 (m, 2 H), 7.15 (t, J = 7.7 Hz, 1 H), 7.26–7.34 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 55.5, 64.9, 115.3, 116.1, 118.8, 127.6, 127.9, 128.6, 130.6, 137.6, 139.3, 149.0 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3592 (m), 3485 (m), 3370 (m); 3066 (m), 3017 (s), 2877 (w), 2351 (m), 1604 (s), 1478 (s), 1304 (m), 1156 (w), 1057 (m), 1021 (w) cm^{-1}. GC-EIMS (m/z) = 245 (27) [M$^+$], 214 (16), 180 (5), 125 (100), 103 (35), 91 (20), 80 (21). $C_{14}H_{15}NOS$ (245.3): calcd. C 68.54, H 6.16, N 5.71; found C 66.27; H 5.80, N 5.60.

2-[2′-(Hydroxy)phenylthio]-2-phenylethan-1-ol (3aD): Oil; chromatography on silica gel, eluent: petroleum ether/EtOAc/MeOH, 59:40:1; TLC-R_f: 0.39 (petroleum ether/EtOAc, 6:4). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.13 (br. s 1 H), 3.88–3.95 (m, 2 H), 4.01 (dd, J = 6.8, 13.6 Hz, 1 H), 6.79–6.95 (m, 3 H), 7.17–7.31 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 56.4, 64.2, 115.2, 116.8, 120.5, 127.7, 127.9, 128.6, 131.6, 137.2, 138.6, 157.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3597 (m), 3414 (s), 3022 (m), 2938 (w), 1730 (w), 1576 (m), 1470 (s), 1289 (m), 1231 (s), 1208 (s), 1054 (m), 832 (w) cm^{-1}. GC-EIMS (m/z) = 246 (26) [M$^+$], 215 (19), 126 (73), 121 (100), 103 (68), 91 (41), 77 (27). $C_{14}H_{14}O_2S$ (246.3): calcd. C 68.26, H 5.73; found C 68.35, H 5.91.

2-(Allylthio)-2-phenylethan-1-ol (3aE): Oil; chromatography on silica gel, eluent: petroleum ether/EtOAc, 8:2; TLC-R_f: 0.35 (petroleum ether/EtOAc, 7:3). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.99 (dd, J = 7.8, 13.8 Hz, 1 H), 3.12 (dd, J = 6.5, 13.8 Hz, 1 H), 3.83–3.90 (m, 2 H), 3.95 (t, J = 6.9 Hz, 1 H), 5.05–5.12 (m, 2 H), 5.73–5.83 (m, 1 H), 7.27–7.30 (m, 1 H), 7.33–7.37 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 33.9, 51.3, 65.5, 117.5, 127.6, 128.2, 128.6, 134.0, 139.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3592 (m), 3020 (s), 2926 (w), 2632 (w), 1636 (w), 1391 (m), 1220 (m), 1052 (s), 924 (m) cm^{-1}. GC-EIMS (m/z) = 194 (11) [M$^+$], 176 (9), 163 (100), 153 (24), 129 (43), 121 (87), 103 (40), 91 (37), 77 (27). $C_{11}H_{14}OS$ (194.1): calcd. C 68.00, H 7.26; found C 68.10, H 7.35.

***trans*-2-[2′-(Amino)phenylthio]cyclohexan-1-ol (3eC):** Solid; purified by recrystallization from EtOAc/petroleum ether, 1:1; m.p. 82–83 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.21–1.40 (m, 4 H), 1.66–1.68 (m, 2 H), 2.05–2.12 (m, 2 H), 2.64 (dt, J = 3.9, 10.9 Hz, 1 H), 3.28 (dt, J = 4.3, 10.0 Hz, 1 H), 4.13 (m, 2 H), 6.70–6.77 (m, 2 H), 7.14–7.18 (m, 1 H), 7.38–7.41 (1 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 24.3, 26.1, 32.9, 34.2, 56.8, 72.5, 115.4, 115.5, 118.9, 130.4, 138.1, 149.1 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3638 (w), 3491 (w), 3347 (w), 2939 (s), 2862 (m), 1606 (s), 1479 (m), 1448(w), 1305 (w), 1214 (s), 1066 (m), 960 (w), 852 (w) cm^{-1}. GC-EIMS (m/z) = 223 (36) [M$^+$], 162 (20), 125 (100), 93 (12), 80 (18). $C_{12}H_{17}NOS$ (223.3): calcd. C 64.53, H 7.67, N, 6.27; found C 64.44, H 7.58, N 6.30.

***trans*-2-(Allylthio)cyclohexan-1-ol (3eE):** Oil; chromatography on silica gel, eluent: EtOAc/petroleum ether, 2:8. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.25–1.44 (m, 4), 1.71–1.74 (m, 2 H), 2.05–2.08 (m, 2 H), 2.40 (t, J = 10.8 Hz, 1 H), 3.10–3.35 (m, 3 H), 5.07–5.17 (m, 2 H), 5.80–5.87 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 24.0, 25.7, 32.4, 33.3, 33.6, 51.8, 72.1, 116.6, 134.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3518 (m), 3018 (m), 2938 (s), 2862 (m), 1636 (w), 1448 (m), 1272 (m), 1214 (s), 1067 (m), 924 (m) cm^{-1}. GC-EIMS (m/z) = 172 (56) [M$^+$], 113 (17), 98 (62), 81 (100), 69 (28), 57 (20). $C_9H_{16}OS$ (172.3): calcd. C 62.74, H 9.36; found C 62.51, H 9.21.

1-[2′-(Amino)phenylthio]-2-phenylethan-2-ol (4aC): Solid; chromatography on silica gel, eluent: petroleum ether/EtOAc, 6:4; TLC-R_f: 0.30 (petroleum ether/EtOAc, 1:1); m.p. 104–105 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.89 (dd, J = 9.6, 13.7 Hz, 1 H), 3.13 (dd, J = 3.2, 13.7 Hz, 1 H), 4.03 (br. s, 2 H), 4.61 (dd, J = 3.2, 9.6 Hz, 1 H), 6.72–6.77 (m, 2 H), 7.16 (t, J = 7.7 Hz, 1 H), 7.24–7.36 (m, 5 H), 7.44 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 44.5, 71.9, 115.4, 117.0, 119.1, 125.8, 127.7, 128.3, 130.2, 136.3, 142.2, 148.3 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3480 (m), 3369 (m), 3015 (w), 1608 (s), 1480 (m), 1306 (m), 1201 (m), 1056 (m), 996 (w) cm^{-1}. GC-EIMS (m/z) = 245 (33) [M$^+$], 139 (100), 124 (62), 107 (19), 94 (27), 79 (33). $C_{14}H_{15}NOS$ (245.3): C, 68.54, H, 6.16, N, 5.71; found: C, 67.88, H 5.94, N 5.67.

1-[2′-(Hydroxy)phenylthio]-2-phenylethan-2-ol (4aD): Oil; chromatography on silica gel, eluent: petroleum ether/EtOAc/MeOH, 59:40:1; TLC-R_f: 0.34 (petroleum ether/EtOAc, 7:3). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.91 (dd, J = 9.3, 13.7 Hz, 1 H), 3.06 (dd, J = 3.8, 13.7 Hz, 1 H), 4.66 (dd, J = 3.8, 9.3 Hz, 1 H), 7.86–7.01 (m, 2 H), 7.24–7.32 (m, 7 H) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 45.4, 72.2, 115.4, 118.4, 120.8, 125.8, 128.2, 128.6, 131.4, 136.3, 141.9, 157.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3597 (w), 3385 (m), 3069 (w), 2927 (w), 1576 (m), 1472 (s), 1289 (w), 1227 (s), 1212 (s), 1053 (m), 831 (w) cm^{-1}. GC-EIMS (m/z) = 246 (15) [M$^+$], 126 (35), 121 (100), 107 (54), 88 (32), 77 (19). $C_{14}H_{14}O_2S$ (246.3): calcd. C, 68.26, H 5.73; found C 68.10, H 5.57.

1-(Allylthio)-2-phenylethan-2-ol (4aE): Oil; chromatography on silica gel, eluent: petroleum ether/EtOAc, 8:2; Tlc-R_f: 0.31 (petroleum ether/EtOAc, 8:2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.68 (dd, J = 9.3, 13.9 Hz, 1 H), 2.88 (dd, J = 3.7, 14.0 Hz, 1 H), 2.90 (d, J = 2.6 Hz, 1 H), 3.09–3.20 (m, 2 H), 4.74 (td, J = 3.1, 9.3 Hz, 1 H), 5.09–5.15 (m, 2 H), 5.74–5.84 (m, 1 H), 7.27–7.29 (m, 1 H), 7.30–7.37 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 34.5, 40.1, 71.5, 117.7, 125.7, 127.8, 128.4, 133.9, 142.5 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3599 (m), 3508 (s), 3020 (s), 1636 (w), 1409 (m), 1227 (m), 1213 (s), 1202 (s), 1053 (s), 993 (s), 924 (s) cm^{-1}. GC-EIMS (m/z) = 194 (1) [M$^+$], 176 (7), 107 (79), 88 (100), 79 (84), 51 (15). $C_{11}H_{14}OS$ (194.1): calcd. C 68.00, H 7.26; found: C 67.89; H 7.12.

1-[2′-(Amino)phenylthio]-3-phenylpropan-2-ol (4bC): Solid; purified by recrystallization from Et_2O; m.p. 57–59 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.70–2.89 (m, 4 H), 2.95 (dd, J = 3.6, 13.6 Hz, 1 H), 3.80–3.83 (m, 1 H), 4.36 (br. s, 2 H), 6.69–6.74 (m, 2 H), 7.16–7.40 (m, 7 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 42.0, 42.2, 70.8, 115.3, 118.1, 119.0, 126.4, 128.3, 129.3, 130.0, 136.1, 137.9, 148.2 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3580 (w), 3477 (m), 3375 (m), 3020 (s), 2923 (m), 1730 (w), 1608 (s), 1480 (m), 1448 (m), 1305 (w), 1158 (w), 1033 (m), 857 (w) cm^{-1}. GC-EIMS (m/z) = 259 (67) [M$^+$], 150 (41), 139 (24), 124 (100), 117 (65), 91 (53), 80 (35). $C_{15}H_{17}NOS$ (259.1): calcd. C 69.46, H 6.61, N 5.40; found C 69.66, H 6.83, N 5.65.

1-(Allylthio)-3-phenylpropan-2-ol (4bE): Oil; chromatography on silica gel, eluent: petroleum ether/EtOAc, 8:2. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.42 (br. s, 1 H), 2.47 (dd, J = 8.5, 13.7 Hz, 1 H), 2.68 (dd, J = 3.8, 13.7 Hz, 1 H), 2.81 (dd, J = 5.7, 13.4 Hz, 1 H), 2.86 (dd, J = 6.7, 13.3 Hz, 1 H), 3.13 (d, J = 7.2 Hz, 2 H), 3.87–3.89 (m, 1 H), 4.97–5.11 (m, 2 H), 5.69–5.80 (m, 1 H), 7.21–7–23 (m, 3 H), 7.25–7.33 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 34.8, 37.6, 42.6, 70.5, 117.5, 126.5, 128.5, 129.4, 133.9, 137.9

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ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3584 (m), 3083 (w), 3020 (s), 2920 (m), 2362 (w), 1730 (w), 1496 (w), 1428 (w), 1223 (s), 1080 (m), 1032 (m), 923 (m) cm^{-1}. GC-EIMS (*m*/*z*) = 208 (3) [M^+], 190 (39), 148 (36), 117 (97), 103 (45), 91 (100), 73 (25). $C_{11}H_{14}OS$ (208.1): calcd. C 69.19, H 7.74; found C 69.30, H 7.85.

3-[2′-(Amino)phenylthio]propan-1,2-diol (4cC): Oil; chromatography on silica gel, eluent: EtOAc/petroleum ether, 7:3. ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.73 (dd, *J* = 8.3 Hz, 13.6 Hz, 1 H), 2.84 (dd, *J* = 4.3, 13.5 Hz, 1 H), 3.46 (dd, *J* = 6.4, 11.5 Hz, 1 H), 3.56–3.70 (m, 2 H), 4.36 (br. s, 2 H), 6.69–6.72 (m, 2 H), 7.11–7.12 (m, 1 H), 7.37–7.39 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 38.1, 63.3, 70.4, 115.3, 117.3, 118.8, 129.8, 135.8, 148.1 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3440 (m), 3379 (s), 3020 (s), 1730 (s), 1608 (s), 1479 (m), 1305 (w), 1245 (s), 1051 (s), 882 (w) GC-EIMS (*m*/*z*) = 199 (49) [M^+], 199 (52), 150 (13), 136 (28), 125 (100), 94 (29), 80 (38). $C_9H_{13}NO_2S$ (199.3): calcd. C 54.25; H 6.58, N 7.03; found C 54.40, H 6.72, N 7.15.

3-(Allylthio)propane-1,2-diol (4cE): Oil; chromatography on silica gel, eluent: EtOAc/petroleum ether, 7:3; TLC-R_f: 0.35 (EtOAc/MeOH, 98:2); 75% yield. ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.53 (dd, *J* = 8.1, 13.7 Hz, 1 H), 2.62 (dd, *J* = 4.8, 13.8 Hz, 1 H), 2.80 (br. s, 1 H), 3.14 (d, *J* = 7.3 Hz, 2 H), 3.50–3.55 (m, 1 H), 3.70–3.78 (m, 2 H), 5.06–5.12 (m, 2 H), 5.71–5.82 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 33.5, 34.8, 65.1, 70.4, 117.4, 133.8 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3586 (s), 3472 (s), 3017 (m), 2923 (m), 1730 (m), 1635 (w), 1407 (s), 1226 (s), 1057 (s), 924 (m) cm^{-1}. GC-EIMS (*m*/*z*) = 148 (49) [M^+], 117 (11), 99 (42), 87 (37), 74 (100), 61 (42). $C_6H_{12}O_2S$ (148.2): calcd. C 48.62, H 8.16; found C 48.80, H 8.23.

1-(Allyloxy)-3-[2′-(amino)phenylthio]propan-2-ol (4dC): Oil. ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.79 (dd, *J* = 7.7, 13.5 Hz, 1 H), 2.93 (dd, *J* = 4.8, 13.5 Hz, 1 H), 3.13 (br. s, 1 H), 3.38–3.53 (m, 2 H), 3.74–3.84 (m, 1 H), 3.94–3.98 (m, 2), 4.41 (br. s, 2 H), 5.15–5.30 (m, 2 H), 5.91–5.97 (m, 1 H), 6.68–6.73 (m, 2 H), 7.08–7.16 (m, 1 H), 7.37–7.42 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 38.3, 68.7, 71.8, 72.3, 114.9, 116.9, 118.3, 129.5, 135.6, 148.0 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3573 (m), 3479 (s), 3375 (s), 3019 (s), 2920 (m), 2865 (m), 1730 (w), 1608 (s), 1478 (m), 1448 (w), 1306 (m), 1222 (s), 1106 (s), 933 (m) cm^{-1}. GC-EIMS (*m*/*z*) = 239 (60) [M^+], 164 (14), 150 (24), 136 (28), 124 (100), 97 (27), 80 (39). $C_{12}H_{17}NO_2S$ (188.3): calcd. C 60.22, H 7.16, N 5.85; found C 60.07, H 7.03, N 5.74.

1-(Allyloxy)-3-(allylthio)propan-2-ol (4dE): Oil; chromatography on silica gel, eluent: EtOAc/petroleum ether, 3:7; TLC-R_f: 0.33 (EtOAc/MeOH, 98:2). ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.53–2.60 (m, 1 H), 2.61–2.77 (m, 2 H), 3.15 (d, *J* = 7.2 Hz, 2 H), 3.45 (dd, *J* = 6.4, 9.6 Hz, 1 H), 3.53 (dd, *J* = 3.9, 9.6 Hz, 1 H), 3.87–3.88 (m, 1 H), 4.01–4.03 (m, 2 H), 5.07–5.13 (m, 2 H), 5.18–5.29 (m, 2 H), 5.73–5.81 (m, 1 H), 5.85–5.95 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 34.1, 35.0, 69.0, 72.3, 72.7, 117.3, 117.5, 134.0, 138.9 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3573 (m), 3018 (m), 2918 (m), 2864 (w), 1640 (w), 1424 (w), 1213 (s), 1104 (s), 993 (m), 927 (m) cm^{-1}. GC-EIMS (*m*/*z*) = 188 (1) [M^+], 147 (11), 131 (84), 119 (57), 97 (100), 73 (80). $C_9H_{16}O_2S$ (188.3): calcd. C 57.41, H 8.57; found C 57.60, H 8.70.

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