# Regioselective ring opening of epoxides with thiols in water

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**Abstract**
A convenient reaction condition for the regioselective thiolysis of epoxides using a series of thiols in water without applying any catalyst has been demonstrated with excellent yields.

**Keywords:** Epoxide, thiolysis, *β*-hydroxy sulfides, regioselective, water

## Introduction

Ring opening of epoxides with thiols is one of the most practically used protocols for the synthesis of *β*-hydroxy sulfides for use in organic synthesis.[1] *β*-Hydroxy sulfides serve as important intermediates for the synthesis of several molecules of biological interest and natural products.[2] Conventionally, thiolysis of epoxides or oxiranes can be carried out in the presence of a base[3] or a Lewis acid,[4] or in the presence of a heterogeneous catalysts.[5] A number of reports have appeared for the thiolysis of epoxides using microwave irradiation[6] or complex Lewis acids.[7] But most of them have some limitations such as: use of strong and non-selective catalysts, toxic and expensive reagents, low yield, lack of regioselectivity and long reaction times. Because of the importance of these compounds in organic synthesis, the development of environmentally friendly, high yielding, and clean approaches for the synthesis of *β*-hydroxy sulfides are always welcome.

As a part of our medicinal chemistry research, we needed to prepare a series of *β*-hydroxy sulfides in large quantities for their use in developing some bioactive molecules. Recently, a number of reports appeared for the thia-Michael[8] and aza-Michael[9] reaction and ring opening of epoxides with amines[10] in water without using any catalyst. Prompted by these reports, we were interested to perform the thiolysis of epoxides using water as a solvent avoiding the use of a catalyst and organic solvents. Although, the opening of epoxides with thiols has been reported in water using indium chloride or $ZnCl_2$ or NaOH,[11] to the best of our knowledge, thiolysis of

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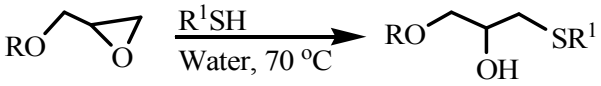
epoxides for the preparation of β-hydroxy sulfides in water without using any catalyst has not been attempted before. Very recently opening of epoxides by nucleophiles has been carried out in water under simultaneous ultrasound/microwave irradiation.[12] We report herein a practical methodology for the preparation of *β*-hydroxy sulfides by thiolysis of epoxides in water without using any catalyst or special technical requirement (Scheme 1).



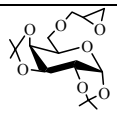
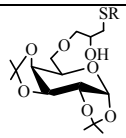
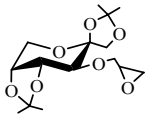
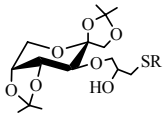
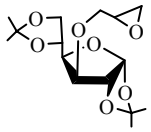
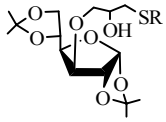
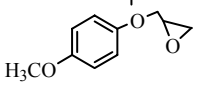
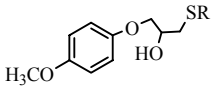
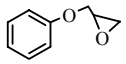
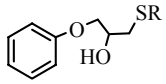
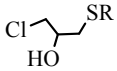
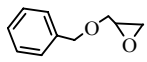
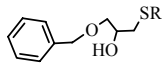
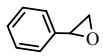
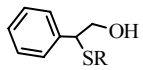

**Scheme 1.** Regioselective thiolysis of epoxide in water.

## Results and Discussion

In a set of initial experiments, a mixture of fructose derived terminal epoxide (Table 1, entry 2) and a varied quantity of thiophenol in water was allowed to stir at different temperatures ranging from room temperature to 80 °C. It was observed that use of 2.5 equiv. of thiol and water (3 mL/mmol of substrate) under vigorous stirring at 70 °C furnished a clean formation of *β*-hydroxy sulfide derivatives in excellent yield in 5 h. Following similar reaction condition a series of *β*-hydroxy sulfide derivatives have been prepared using different thiols in excellent yield (Table 1). In general, all reactions are very clean and high yielding. Variation of the quantity of water used did not show any significant change in the reaction rate. However, stirring plays an important role on the reaction time. In a comparative study, only ~40% conversion took place by keeping a mixture of epoxide and thiol in water at 70 °C without stirring even after 24 h. The reaction does not require any organic solvent as co-solvent. Carrying out the reaction without using water in a neat reaction condition did not give satisfactory yield of the product. All products were characterized by NMR and mass spectral analysis. Most of the reactions are highly regioselective except in the case of styrene epoxide (Table 1, entry 8) in which a mixture of both regioisomers were obtained due to the addition of thiols to the benzylic carbon to give the major product. It is presumed that water forms hydrogen bonding with the oxygen atom of the epoxide ring as well as with the thiol making them closely associated, which enhances the attack of thiol to the epoxide towards the formation of *β*-hydroxy sulfides. In another approach, it can be explained by considering the acidic thiol acts as its own Lewis acid, which forms an ion pair of a protonated epoxide and a thiolate and thus enhances the ring opening. Although the aromatic thiols furnished excellent yield of the *β*-hydroxy sulfides, aliphatic thiols did not give satisfactory results may be due to their less acidic nature. In the case of aliphatic thiols, no ring opened product of the epoxide was observed after a longer reaction time. To further prove the efficacy of the present protocol, a comparison study has been carried out to the previously reported methods for thiolysis of epoxides using water as reaction medium, which are presented in Table 2. From

the comparison in Table 2, it is clear that the present protocol has many aspects to be considered as effective over the previously reported methods.

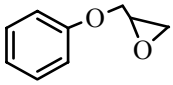
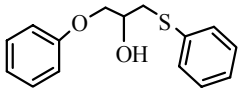
**Table 1.** Regioselective opening of oxiranes with thiols in water

| Entry | Epoxide (1) | | | Time (h) | Yield (%) | Ref |
|---|---|---|---|---|---|---|
| 1 |  |  | **2a**: R = Phenyl | 5.0 | 95 | -- |
| | | | **2b**: R = o-tolyl | 5.0 | 92 | |
| | | | **2c**: R = m-tolyl | 5.0 | 95 | |
| | | | **2d**: R = p-tolyl | 5.0 | 90 | |
| | | | **2e**: R = 2-naphthyl | 6.0 | 90 | |
| | | | **2f**: R=2-thiobenzothiazolyl | 7.0 | 88 | |
| 2 |  |  | **2g**: R = Phenyl | 5.0 | 95 | -- |
| | | | **2h**: R = o-tolyl | 5.0 | 95 | |
| | | | **2i**: R = m-tolyl | 5.0 | 92 | |
| | | | **2j**: R = p-tolyl | 5.5 | 88 | |
| | | | **2k**: R = 2-thiobenzothiazolyl | 6.5 | 82 | |
| 3 |  |  | **2l**: R = Phenyl | 5.0 | 95 | -- |
| | | | **2m**: R = p-tolyl | 5.0 | 92 | |
| 4 |  |  | **2n**: R = Phenyl | 4.5 | 92 | -- |
| | | | **2o**: R = 2-thiobenzothiazolyl | 6.0 | 90 | |
| 5 |  |  | **2p**: R = Phenyl | 5.0 | 87 | 4i |
| | | | **2q**: R = o-tolyl | 6.0 | 90 | |
| | | | **2r**: R = 2-naphthyl | | | |
| 6 |  |  | **2s**: R = Phenyl | 4.5 | 91 | 4j |
| | | | **2t**: R = p-tolyl | 4.5 | 92 | 4i |
| | | | **2u**: R = 2-naphthyl | 5.0 | 85 | |
| 7 |  |  | **2v**: R = Phenyl | 5.0 | 95 | -- |
| | | | **2w**: R = 2-naphthyl | 5.5 | 90 | |
| 8 |  |  | **2x**: R = Phenyl | 5.0 | 86[a] | 4i |
| | | | **2y**: R = p-tolyl | 5.0 | 85[b] | |
| | | | **2z**: R = 2-naphthyl | 6.5 | 80[c] | |

[a]Ratio of regioisomers (4:1). [b]Ratio of regioisomers (3.5:1). [c]Ratio of regioisomers (3:1) (determined from the $^1$H NMR spectra).

**Table 2.** Comparative reaction conditions for the thiolysis of epoxides in water

| Substrate | Product | Reaction condition | Temp. (°C) | Time (h) | Yield (%) |
|---|---|---|---|---|---|
|  |  | $InCl_3/H_2O$ | 30 | 5 | 75 |
| | | $ZnCl_2/H_2O$ | 30 | 5 | 80 |
| | | $NaOH/H_2O$ | 30 | 3 | 90 |
| | | $H_2O$/MW | -- | 4 min | 70 |
| | | $H_2O$ | 70 | 5 | 87 |

MW: Domestic microwave (450 W).

## Conclusions

In summary, we have demonstrated an economical and practical environmentally benign methodology for the synthesis of a wide range of *β*-hydroxy sulfides in water. Operational simplicity, high yields, regioselectivity, no requirement of a catalyst in aqueous reaction condition makes this protocol superior to the existing methods.

## Experimental Section

**General Procedure.** All the reactions were monitored by thin layer chromatography over silica gel coated TLC plates. The spots on TLC were visualized by warming ceric sulphate (2% $Ce(SO_4)_2$ in 2N $H_2SO_4$) sprayed plates in hot plate. Silica gel 230-400 mesh was used for column chromatography. $^1H$ and $^{13}C$ NMR was recorded on Brucker Advance DPX 300 MHz using TMS as internal reference. Chemical shift value is expressed in δ ppm. ESI-MS were recorded on a MICROMASS QUTTRO II triple quadrupole mass spectrometer. Optical rotations were measured at 25°C on a Rudolf Autopol III polarimeter. Commercially available grades of organic solvents of adequate purity are used in many reactions.

**General reaction conditions**

A mixture of epoxide (1 mmol) and thiol (2.5 mmol) in water (3 mL) was allowed to stir vigorously at 70 °C for appropriate time (Table 1). The reaction mixture was extracted with EtOAc (20 mL) and washed with dilute aq. bleach solution. The organic layer was dried ($Na_2SO_4$ (5 g) and concentrated under reduced pressure to give the β-hydroxy sulfide derivative, which was purified through a short pad of $SiO_2$ using hexane-EtOAc (5:1) to furnish pure product (Table 1). Following similar reaction condition a series of β-hydroxy sulfide derivatives were prepared in excellent yield.

Spectral data of *β*-hydroxysulfides, which are not reported earlier:

**Compound 2a.** Colourless oil; $[\alpha]_D^{25}$ –61.8 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.38-7.16 (m, 5 H), 5.50 (d, *J* = 5.0 Hz, 1 H), 4.62-4.56 (m, 1 H), 4.32-4.28 (m, 1 H), 4.26-4.19 (m, 1 H), 3.98-3.85 (m, 2 H), 3.71-3.48 (m, 4 H), 3.05 (d, *J* = 6.4 Hz, 2 H), 1.53, 1.43, 1.33, 1.33 (4 s, 12 H, $CCH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 135.9, 129.3, 129.2 (2 C), 128.9, 126.1, 109.3, 108.6, 96.2, 73.9, 71.1, 70.6, 70.4, 70.3, 69.0, 66.8, 36.9, 26.0, 25.9, 24.9, 24.4; ESI-MS ($C_{21}H_{30}O_7S$): *m/z* 449.2 $[M+Na]^+$.

**Compound 2b.** Colourless oil; $[\alpha]_D^{25}$ –50.1 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.33-7.07 (m, 4 H, Ar-H), 5.51 (d, *J* = 5.0 Hz, 1 H), 4.61-4.57 (m, 1 H), 4.32-4.28 (m, 1 H), 4.26-4.20 (m, 1 H), 3.96-3.88 (m, 2 H), 3.72-3.49 (m, 4 H), 3.02 (d, *J* = 6.4 Hz, 2 H), 2.38 (s, 3 H, $CH_3$), 1.53, 1.44, 1.33, 1.33 (4 s, 12 H, 4 $CCH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 137.6, 135.1, 130.1, 128.2, 126.5, 125.9, 109.3, 108.6, 96.2, 74.1, 71.1, 70.6, 70.4, 70.3, 69.1, 66.9, 36.2, 26.1, 26.0, 24.9, 24.5, 20.4; ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$.

**Compound 2c.** Colourless oil; $[\alpha]_D^{25}$ –54.0 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.18-7.14 (m, 3 H, Ar-H), 6.99-6.97 (m, 1 H, Ar-H), 5.51 (d, *J* = 5.0 Hz, 1 H), 4.62-4.57 (m, 1 H), 4.32-4.28 (m, 1 H), 4.26-4.18 (m, 1 H), 3.97-3.86 (m, 2 H), 3.71-3.48 (m, 4 H), 3.03 (d, *J* = 6.3 Hz, 2 H), 2.32 (s, 3 H, $CH_3$), 1.53, 1.44, 1.33, 1.33 (4 s, 12 H, 4 $CCH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 138.6, 135.6, 130.0, 128.8, 127.1, 126.4, 109.3, 108.6, 96.2, 74.0, 71.1, 70.6, 70.5, 70.4, 69.1, 66.8, 37.0, 26.1, 26.0, 24.9, 24.5, 21.3; ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$.

**Compound 2d.** Colourless oil; $[\alpha]_D^{25}$ –54.0 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.08 (d, *J* = 8.0 Hz, 2 H, Ar-H), 5.50 (d, *J* = 5.0 Hz, 1 H), 4.60-4.56 (m, 1 H), 4.31-4.28 (m, 1 H), 4.25-4.19 (m, 1 H), 3.98-3.82 (m, 2 H), 3.70-3.44 (m, 4 H), 2.99 (d, *J* = 6.3 Hz, 2 H), 2.31 (s, 3 H, $CH_3$), 1.53, 1.43, 1.33, 1.33 (4 s, 12 H, 4 $CCH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 136.3, 132.0, 130.3, 130.2, 129.7 (2 C), 109.3, 108.6, 96.2, 74.0, 71.1, 70.6, 70.5, 70.3, 69.0, 66.8, 37.7, 26.1, 26.0, 24.9, 24.5, 21.0; ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$.

**Compound 2e.** Colourless oil; $[\alpha]_D^{25}$ –51.0 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.79-7.71 (m, 4 H), 7.48-7.41 (m, 3 H), 5.50 (d, *J* = 4.9 Hz, 1 H), 4.61-4.55 (m, 1 H), 4.32-4.27 (m, 1 H), 4.19 (ddd, *J* = 13.2, 7.9 and 1.6 Hz, 1 H), 4.00-3.92 (m, 2 H), 3.73-3.52 (m, 4 H), 3.15 (d, *J* = 6.3 Hz, 2 H), 1.52, 1.42, 1.32, 1.32 (4 s, 12 H, 4 $CCH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$): δ 133.8, 133.4, 131.8, 128.5, 127.7, 127.3, 127.1, 127.0, 126.5, 125.7, 109.3, 108.6, 96.2, 74.0, 71.1 (2 C), 70.6, 70.4, 69.2, 66.9, 36.8, 26.0, 25.9, 24.9, 24.5; ESI-MS ($C_{25}H_{32}O_7S$): *m/z* 499.2 $[M+Na]^+$.

**Compound 2f.** Colourless oil; $[\alpha]_D^{25}$ –45.3 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.72 (d, *J* = 7.9 Hz, 1 H, Ar-H), 7.40-7.36 (m, 1 H, Ar-H), 7.31-7.26 (m, 1 H, Ar-H), 5.51 (d, *J* = 5.0 Hz, 1 H), 4.61-4.56 (m, 1 H), 4.30 (dd, *J* = 4.9 and 2.3 Hz, 1 H), 4.27-4.18 (m, 2 H), 4.00-3.94 (m, 1 H), 3.73-3.43 (m, 6 H), 1.54, 1.44, 1.33, 1.32 (4 s, 12 H, 4 $CCH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 167.7, 152.5, 135.3, 126.0, 124.3, 121.3, 120.9, 109.2, 108.5, 96.2, 73.8, 71.1, 70.6, 70.4, 70.2, 69.8, 66.7, 37.0, 26.0, 25.9, 24.9, 24.4; ESI-MS ($C_{22}H_{29}NO_7S_2$): *m/z* 506.2 $[M+Na]^+$.

**Compound 2g.** Colourless oil; $[\alpha]_D^{25}$ –24.3 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.38-7.17 (m, 5 H), 4.57 (dd, *J* = 7.9 and 2.5 Hz, 1 H), 4.32 (dd, *J* = 6.3 and 2.5 Hz, 1 H), 4.20 (dd, *J*

= 7.9 and 0.9 Hz, 1 H), 3.94-3.84 (m, 2 H), 3.76-3.49 (m, 5 H), 3.08-2.99 (m, 2 H), 1.52, 1.46, 1.37, 1.33 (4 s, 12 H, $CCH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$): δ 136.0, 129.5 (2 C), 129.0 (2 C), 126.3, 108.9, 108.4, 102.4, 74.8, 73.5, 70.9, 70.5, 70.3, 68.7, 61.0, 37.4, 26.5, 25.9, 25.8, 24.0; ESI-MS ($C_{21}H_{30}O_7S$): *m/z* 449.2 $[M+Na]^+$.

**Compound 2h.** Colourless oil; $[\alpha]_D^{25}$ –25.8 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.33-7.26 (m, 1 H, Ar-H), 7.17-7.08 (m, 3 H, Ar-H), 4.57 (dd, *J* = 7.9 and 2.5 Hz, 1 H), 4.32 (dd, *J* = 6.1 and 2.5 Hz, 1 H), 4.21 (d, *J* = 7.9 Hz, 1 H), 3.95-3.92 (m, 1 H), 3.88 (dd, *J* = 13.0 and 1.5 Hz, 1 H), 3.76-3.50 (m, 5 H), 3.04-3.00 (m, 2 H), 2.39 (s, 3 H, $CH_3$), 1.53, 1.46, 1.38, 1.34 (4 s, 12 H, $CCH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$): δ137.6, 134.8, 130.1, 128.3, 126.4, 125.9, 108.8, 108.3, 102.3, 74.8, 73.4, 70.8, 70.4, 70.2, 68.7, 60.9, 36.5, 26.4, 25.8, 25.3, 23.9, 20.3; ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$.

**Compound 2i.** Colourless oil; $[\alpha]_D^{25}$ –19.8 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.18-7.14 (m, 3 H, Ar-H), 6.98 (brs, 1 H, Ar-H), 4.57 (dd, *J* = 7.9 and 2.5 Hz, 1 H), 4.32 (dd, *J* = 6.6 and 2.5 Hz, 1 H), 4.21 (dd, *J* = 7.8 and 0.7 Hz, 1 H), 3.94-3.84 (m, 2 H), 3.76-3.48 (m, 5 H), 3.06-2.97 (m, 2 H), 2.32 (s, 3 H, $CH_3$), 1.52, 1.46, 1.37, 1.33 (4 s, 12 H, $CCH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 138.7, 135.3, 130.3, 128.9, 127.3, 126.7, 109.0, 108.5, 102.5, 74.9, 73.6, 70.9, 70.6, 70.2 (2 C), 61.1, 37.5, 26.5, 25.9, 25.4, 24.1, 21.4; ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$.

**Compound 2j.** Colourless oil; $[\alpha]_D^{25}$ –20.7 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.27 (d, J = 8.0 Hz, 2 H, Ar-H), 7.08 (d, *J* = 8.0 Hz, 2 H, Ar-H), 4.57 (dd, *J* = 7.9 and 2.5 Hz, 1 H), 4.31 (dd, *J* = 6.4 and 2.5 Hz, 1 H), 4.20 (dd, *J* = 7.9 and 0.9 Hz, 1 H), 3.88 (dd, *J* = 13.0 and 1.7 Hz, 1 H), 3.87-3.83 (m, 1 H), 3.75-3.47 (m, 5 H), 3.07-2.93 (m, 2 H), 2.32 (s, 3 H, $CH_3$), 1.52, 1.46, 1.37, 1.33 (4 s, 12 H, 4 $CCH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$): δ 136.4, 131.8, 130.4 (2 C), 129.7 (2 C), 108.9, 108.4, 102.4, 74.8, 73.4, 70.9, 70.5, 70.2, 68.7, 61.0, 38.2, 26.5, 25.9, 25.4, 24.0, 21.0; ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$.

**Compound 2k.** Colourless oil; $[\alpha]_D^{25}$ –28.2 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.73 (d, *J* =7.7 Hz, 1 H, Ar-H), 7.40 (t, *J* = 8.2 Hz, 1 H, Ar-H), 7.29 (t, *J* = 8.0 Hz, 1 H, Ar-H), 4.60-4.55 (m, 1 H), 4.35 (t, *J* = 2.8 Hz, 1 H), 4.21 (d, *J* = 7.2 Hz, 2 H), 3.89 (dd, *J* = 12.9 and 1.8 Hz, 1 H), 3.75-3.55 (m, 6 H), 3.51-3.43 (m, 1 H), 1.53, 1.47, 1.41, 1.33 (4 s, 12 H, 4 $CCH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$): δ 167.6, 152.5, 135.4, 126.1, 124.5, 121.3, 120.9, 108.9, 108.4, 102.5, 74.6, 73.3, 70.9, 70.3, 70.2, 69.8, 61.0, 37.3, 26.5, 25.9, 25.4, 24.0; ESI-MS ($C_{22}H_{29}NO_7S_2$): *m/z* 506.2 $[M+Na]^+$.

**Compound 2l.** Colourless oil; $[\alpha]_D^{25}$ –31.8 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.37-7.17 (m, 5 H), 4.48 (dd, *J* = 15.8 and 3.6 Hz, 1 H), 4.31-4.24 (m, 1 H), 4.18-3.55 (m, 7 H), 3.40 (dd, *J* = 10.2 and 7.5 Hz, 1 H), 3.11-2.93 (m, 2 H), 1.48, 1.43, 1.35, 1.30 (4 s, 12 H, 4 $CCH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$): δ 135.8, 129.3, 128.9 (2 C), 126.2, 126.1, 111.8, 109.3, 105.6, 84.3, 83.2, 81.3, 74.2, 72.8, 69.6, 67.8, 36.4, 26.9, 26.8, 26.2, 25.2; ESI-MS ($C_{21}H_{30}O_7S$): *m/z* 449.2 $[M+Na]^+$.

**Compound 2m.** Colourless oil; $[\alpha]_D^{25}$ –34.5 (*c* 1.5, $CHCl_3$), $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.09 (d, *J* = 8.0 Hz, 2 H, Ar-H), 4.48 (dd, *J* = 15.9 and 3.6 Hz, 1 H),

4.32-4.23 (m, 1 H), 4.17-3.53 (m, 7 H), 3.38 (dd, *J* = 10.2 and 7.7 Hz, 1 H), 3.06-2.86 (m, 2 H), 2.32 (s, 3 H, $CH_3$), 1.48, 1.42, 1.35, 1.30 (4 s, 12 H, 4 $CCH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 136.4, 132.0, 130.2, 130.1, 129.7 (2 C), 111.8, 109.3, 105.6, 84.2, 82.5, 81.3, 74.1, 72.8, 69.6, 67.8, 37.2, 26.9, 26.7, 26.2, 25.2, 21.0; ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$.

**Compound 2n.** Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.40-7.17 (m, 5 H, Ar-H), 6.78 (brs, 4 H, Ar-H), 4.05-4.01 (m, 1 H, CHOH), 3.98 (brs, 2 H, $OCH_2$), 3.74 (s, 3 H, $OCH_3$), 3.22 (dd, *J* = 13.8 and 5.6 Hz, 1 H, $SCH_2$), 3.11 (dd, *J* = 14.0 and 6.7 Hz, 1 H, $SCH_2$), 2.71 (brs, 1 H, CHOH); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 154.1, 152.5, 135.3, 129.6, 129.4, 129.0 (2 C), 126.4, 115.5 (2 C), 114.9, 114.6, 70.9 ($OCH_2$), 68.6 (CHOH), 55.5 ($OCH_3$), 37.5 ($SCH_2$); ESI-MS ($C_{16}H_{18}O_3S$): *m/z* 291.1 $[M+1]^+$.

**Compound 2o.** Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.1 Hz, 1 H, Ar-H), 7.72 (d, *J* = 7.9 Hz, 1 H, Ar-H), 7.43-7.24 (m, 2 H, Ar-H), 6.86-6.78 (m, 4 H, Ar-H), 4.46-4.38 (m, 1 H, CHOH), 4.10-3.98 (m, 2 H, $OCH_2$), 3.75 (s, 3 H, $OCH_3$), 3.69 (dd, *J* = 14.7 and 3.3 Hz, 1 H, SC$H_2$), 3.57 (dd, *J* = 14.5 and 6.5 Hz, 1 H, SC$H_2$); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 167.9, 154.1, 152.6, 152.3, 135.4, 126.2, 124.6, 121.3, 121.0, 115.5 (2 C), 114.7 (2 C), 70.7 ($OCH_2$), 69.8 (CHOH), 55.6 ($OCH_3$), 37.5 ($SCH_2$); ESI-MS ($C_{17}H_{17}NO_3S_2$): *m/z* 348.1 $[M+1]^+$.

**Compound 2q.** Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.38-7.05 (m, 6 H, Ar-H), 6.94 (t, *J* = 7.4 Hz, 1 H, Ar-H), 6.87 (d, *J* = 7.9 Hz, 2 H, Ar-H), 4.15-3.97 (m, 3 H, CHOH and $OCH_2$), 3.21 (dd, *J* = 13.7 and 5.4 Hz, 1 H, $SCH_2$), 3.08 (dd, *J* = 13.7 and 6.6 Hz, 1 H, $SCH_2$), 2.64 (d, *J* = 3.9 Hz, 1 H, CHOH), 2.41 (s, 3 H, $CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 158.4, 138.0, 136.7, 130.6, 130.3, 129.8, 129.5, 128.8, 126.6, 126.3, 121.2, 114.6, 70.2 ($OCH_2$), 68.6 (CHOH), 37.5 ($SCH_2$), 21.0 ($CH_3$); ESI-MS ($C_{16}H_{18}O_2S$): *m/z* 275.1 $[M+1]^+$.

**Compound 2r.** Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.84-7.65 (m, 4 H, Ar-H), 7.49-7.38 (m, 3 H, Ar-H), 7.27-7.18 (m, 2 H, Ar-H), 6.92 (t, *J* = 7.4 Hz, 1 H, Ar-H), 6.84 (d, *J* = 7.9 Hz, 2 H, Ar-H), 4.17-4.08 (m, 1 H, CHOH), 4.07-4.00 (m, 2 H, $OCH_2$), 3.33 (dd, *J* = 13.9 and 5.6 Hz, 1 H, $SCH_2$), 3.23 (dd, *J* = 13.9 and 6.8 Hz, 1 H, SC$H_2$), 2.72 (brs, 1 H, CHOH); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 158.3, 133.7-114.5 (15 C), 70.0 (O*C*$H_2$), 68.6 (*C*HOH), 37.3 (S*C*$H_2$); ESI-MS ($C_{19}H_{18}O_2S$): *m/z* 311.1 $[M+1]^+$.

**Compound 2t.** Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.10 (d, *J* = 8.0 Hz, 2 H, Ar-H), 3.92-3.82 (m, 1 H, CHOH), 3.69-3.60 (m, 2 H, Cl$CH_2$), 3.11 (dd, *J* = 13.9 and 5.6 Hz, 1 H, SC$H_2$), 3.00 (dd, *J* = 13.9 and 7.0 Hz, 1 H, SC$H_2$), 2.61 (d, *J* = 4.8 Hz, 1 H, CHOH), 2.32 (s, 3 H, C$H_3$); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 137.0, 130.9, 130.8 (2 C), 129.9 (2 C), 69.5 (*C*HOH), 47.8 (Cl*C*$H_2$), 38.8 (S*C*$H_2$), 21.0 (*C*$H_3$); ESI-MS ($C_{10}H_{13}ClOS$): *m/z* 217.2 $[M+1]^+$.

**Compound 2u.** Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.79-7.71 (m, 4 H, Ar-H), 7.50-7.40 (m, 3 H, Ar-H), 4.00-3.91 (m, 1 H, CHOH), 3.67 (d, *J* = 4.9 Hz, 2 H, Cl$CH_2$), 3.25 (dd, *J* = 13.9 and 5.7 Hz, 1 H, SC$H_2$), 3.15 (dd, *J* = 13.9 and 6.8 Hz, 1 H, SC$H_2$); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 133.6, 132.1, 132.0, 128.7, 128.1, 127.7, 127.5, 127.1, 126.7, 126.0, 69.6 (CHOH), 47.9 (Cl$CH_2$), 37.9 ($SCH_2$); ESI-MS ($C_{13}H_{13}ClOS$): *m/z* 253.0 $[M+1]^+$.

**Compound 2v.** Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.33-7.14 (m, 10 H, Ar-H), 4.50 (s, 2 H, PhCH2), 3.91-3.89 (m, 1 H, CHOH), 3.59-3.48 (m, 2 H, $OCH_2$), 3.11 (dd, *J* = 13.8 and 5.9 Hz, 1 H, S*CH*$_2$), 3.02 (dd, *J* = 13.7 and 6.8 Hz, 1 H, S*CH*$_2$), 2.62 (m, 1 H, C*H*OH); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 137.7, 135.6, 129.5, 129.3, 128.9, 128.4 (2 C), 127.7, 127.6, 126.3 (2 C), 123.9, 73.3 (Ph*C*H$_2$), 72.4 (O*C*H$_2$), 69.0 (*C*HOH), 37.4 (SCH$_2$); ESI-MS ($C_{16}H_{18}O_2S$): *m/z* 275.1 $[M+1]^+$.

**Compound 2w.** Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.80-7.66 (m, 4 H, Ar-H), 7.49-7.38 (m, 3 H, Ar-H), 7.34-7.23 (m, 5 H, Ar-H), 4.50 (s, 2 H, PhCH$_2$), 3.99-3.90 (m, 1 H, C*H*OH), 3.62-3.50 (m, 2 H, OC*H*$_2$), 3.21 (dd, *J* = 13.8 and 5.9 Hz, 1 H, S*CH*$_2$), 3.12 (dd, *J* = 13.8 and 6.8 Hz, 1 H, S*CH*$_2$); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 137.7, 133.7, 133.1, 131.8, 128.5-125.7 (Ar-C), 73.3 (Ph*C*H$_2$), 72.5 (O*C*H$_2$), 69.0 (*C*HOH), 37.3 (S*C*H$_2$); ESI-MS ($C_{20}H_{20}O_2S$): *m/z* 325.3 $[M+1]^+$.

**Compound 2y.** *α-isomer*: Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.36-7.23 (m, 7 H, Ar-H), 7.11 (d, *J* = 7.9 Hz, 2 H, Ar-H), 4.64 (dd, *J* = 9.6 and 3.3 Hz, 1 H, C*H*OH), 3.25 (dd, *J* = 13.8 and 3.4 Hz, 1 H, S*CH*$_2$), 2.98 (dd, *J* = 13.8 and 9.7 Hz, 1 H, S*CH*$_2$), 2.99-2.90 (m, 1 H, C*H*OH); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 142.2, 137.0, 131.1 (2 C), 131.0, 129.9 (2 C), 128.5 (2 C), 127.9, 125.9 (2 C), 71.4 (CHOH), 45.0 ($CH_2S$), 21.1 ($CH_3$); *β-isomer:* Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.35-7.18 (m, 7 H, Ar-H), 7.03 (d, *J* = 7.9 Hz, 2 H, Ar-H), 4.20 (t, *J* = 6.9 Hz, 1 H, PhCH), 3.85 (dd, *J* = 7.0 and 2.6 Hz, 2 H, C*H*$_2$), 2.30 (s, 3 H, C*H*$_3$); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 139.2, 137.8, 133.3 (2 C), 129.9, 129.7 (2 C), 128.6 (2 C), 128.1 (2 C), 127.7, 65.0 (*C*H$_2$O), 56.6 (Ph*C*H), 21.2 (*C*H$_3$); ESI-MS ($C_{15}H_{16}OS$): *m/z* 245.1 $[M+1]^+$.

**Compound 2z.** *α-isomer:* Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.85-7.70 (m, 4 H, Ar-H), 7.50-7.41 (m, 3 H, Ar-H), 7.37-7.23 (m, 5 H, Ar-H), 4.75 (dd, *J* = 9.4 and 3.5 Hz, 1 H, C*H*OH), 3.40 (dd, *J* = 13.8 and 3.6 Hz, 1 H, S*CH*$_2$), 3.16 (dd, *J* = 13.8 and 9.4 Hz, 1 H, S*CH*$_2$), 2.86 (brs, 1 H, C*H*OH); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 142.2, 133.8, 132.3, 132.2, 128.8, 128.6 (3 C), 128.0, 127.9, 127.8, 127.3, 126.7, 126.1, 125.9 (2 C), 71.8 (*C*HOH), 44.1 (S*C*H$_2$); *β-isomer*: Colourless oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.79-7.63 (m, 4 H, Ar-H), 7.46-7.20 (m, 8 H, Ar-H), 4.38 (t, *J* = 6.9 Hz, 1 H, PhC*H*), 3.91 (dd, *J* = 6.7 and 1.7 Hz, 2 H, C*H*$_2$); $^{13}$C NMR (50 MHz, $CDCl_3$): δ 139.0, 133.6, 132.4, 131.3, 131.2, 129.6, 128.7 (2 C), 128.4, 128.1 (2 C), 127.8, 127.6, 127.4, 126.5, 126.2, 65.3 (*C*H$_2$OH), 56.0 (Ph*C*H); ESI-MS ($C_{18}H_{16}OS$): *m/z* 281.1 $[M+1]^+$.

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