Odorless regioselctive ring opening of epoxides with *S*-alkylisothiouronium salts as masked thiols in water

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Abstract

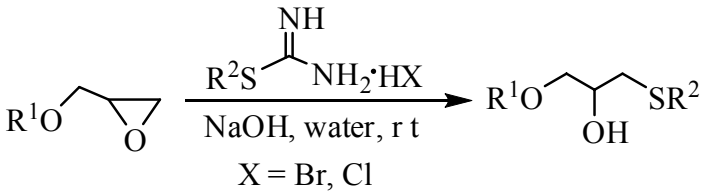
Opening of epoxides with various *S*-alkylisothiouronium salts as thiol equivalent in water has been carried out in excellent yield following an environmentally benign odorless reaction condition. Yields were excellent in every case.

Keywords: Epoxides, thiolysis, alkylisothiouronium salts, β-Hydroxy sulfides, water

Introduction

β-Hydroxy sulfides serve as important intermediates for the synthesis of several bioactive and medicinally important natural products.[1] Most often, they can be synthesized by the ring opening of epoxides with thiols in the presence of a base[2] or a homogeneous and heterogeneous acidic catalysts [3] in organic solvents. A number of special reaction conditions have also been reported in the literature. These conditions include microwave irradiation[4] and use of complex Lewis acids for the enantioselective ring opening.[5] Opening of epoxides with thiols have also been reported in water in the presence of some catalysts.[6] Despite their synthetic utilities most of the reaction conditions suffer from a number of drawbacks, which include the use of obnoxious thiols, strong and non-selective acidic catalysts, expensive and toxic reagents, organic solvents, low yield and long reaction time. Recently, we required a diverse range of β-hydroxy sulfides for their use in the synthesis of several medicinally active molecules. For this purpose, we were looking for a method through which the above-mentioned drawbacks could be avoided and large quantities of β-hydroxy sulfides could be obtained in an environmentally benign way. Recently we noted a report on the thia-Michael reaction in water using *S*-alkylisothiouronium salts as thiol equivalent.[7] Prompted by this, we envisioned that *S*-alkylisothiouronium salts could be used as masked thiols for the regioselective opening of epoxides in water following a green chemistry approach, avoiding the use of malodorous thiols and organic solvents. Earlier, a series of reports appeared in the literature for the epoxide ring opening with amines[8] and aza, thia-Michael

reactions using water as reaction media.[9] We herein report a simple and practical method for the synthesis of β-hydroxy sulfides by opening of oxiranes with *in situ* generated thiolate ions using *S*-alkylisothiouronium salts[10] catalyzed by sodium hydroxide in water (Scheme 1). To the best of our knowledge, there is no report of the thiolysis of epoxides using *S*-alkylisothiouronium salts in water.



Scheme 1. Regioselective thiolysis of epoxide in water using *S*-alkylisothiouronium salts.

Table 1. Opening of epoxides with S-alkylisothiouronium salts in the presence of NaOH in water

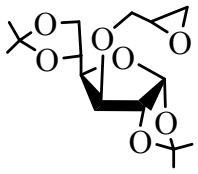
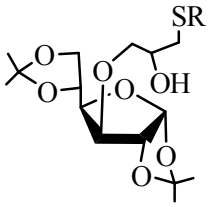
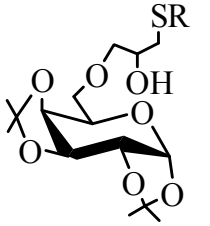
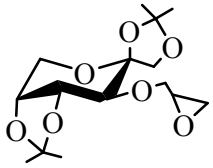
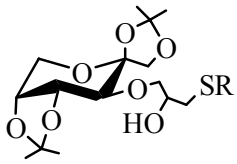
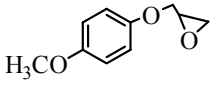
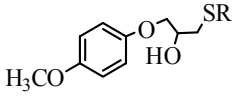
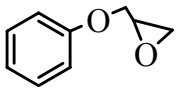
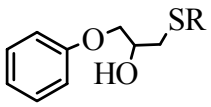
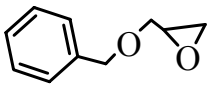
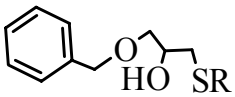
Entry	Epoxide	Product		Time (min)	Yield (%)
1	 **1**		**7**: R = Benzyl	30	92
			8: R = $C_{14}H_{29}$	45	90
			9: R = methyl	30	88
			10: R = 4-methoxybenzyl	40	90
			11: R = 3,4-dimethylbenzyl	45	85
2	 **2**		**12**: R = Benzyl	30	95
			13: R = Allyl	30	92
			14: R = methyl	30	88
			15: R = 4-methoxybenzyl	40	85
			16: R = 3,4-dimethylbenzyl	40	80
3	 **3**		**17**: R = Allyl	30	90
			18: R = $C_{14}H_{29}$	40	92
4	 **4**		**19**: R = Allyl	30	92
			20: R = methyl	30	90
			21: R = 4-methoxybenzyl	30	92

Table 1. Continued

Entry	Epoxide	Product		Time (min)	Yield (%)
5	 **5**		**22**: R = Benzyl	30	87
			23: R = $C_{14}H_{29}$	45	90
			24: R = allyl	30	92
			25: R = methyl	30	88
			26: R = 4-methoxybenzyl	30	90
			27: R = 3,4-dimethylbenzyl	40	85
7	 **6**		**28**: R = Benzyl	30	90
			29: R = $C_{14}H_{29}$	40	85
			30: R = allyl	30	92
			31: R = methyl	30	85
			32: R = 4-methoxybenzyl	30	90
			33: R = 3,4-dimethylbenzyl	30	88

Results and Discussion

In order to study the thiolysis of epoxide derivatives a series of oxirane derivatives were prepared from carbohydrate and phenolic precursors. For this purpose, a series of hydroxy group containing carbohydrate derivatives, phenols and benzyl alcohol were treated with epichlorohydrine in the presence of a base to furnish oxirane derivatives in excellent yield. After considerable experimentation, we found that treatment of epoxides with 1.5 equiv of *S*-alkylisothiouronium salts in the presence of NaOH (2.5 equiv.) in water at room temperature resulted in formation of β-hydroxy sulfides (Table 1). The synthesis of a series of β-hydroxy sulfides was achieved using a variety of epoxides and *S*-alkylisothiouronium salts by stirring the reaction mixture in water at room temperature in the presence of NaOH. It was observed that the quantity of water does not have a significant role in the rate of reaction. However, stirring has an important role in the reaction rate, which was confirmed from a comparative study. Only ~50% conversion took place by keeping a mixture of epoxide, *S*-alkylisothiouronium salts and NaOH in water at room temperature without stirring even after 24 h. *S*-alkylisothiouronium salts can easily be prepared from the corresponding alkyl halide on treatment with thiourea and used without purification. The reaction can be carried out in a large scale without the requirement of

organic solvent and obnoxious thiols. Most of the reactions are highly regioselective. All products were characterized by their NMR and mass spectral data.

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 using *S*-alkylisothiouronium salts as masked thiols, avoiding the use of obnoxious thiols. Operational simplicity, high yields, high regioselectivity makes this protocol superior to the existing methods.

Experimental Section

General Procedures. All 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 on a hot plate. Silica gel 230-400 mesh was used for column chromatography. ^1H and ^{13}C NMR spectra were recorded on Brucker Advance DPX 300 MHz using $CDCl_3$ as solvents and TMS as internal reference unless stated otherwise. Chemical shift values are expressed in δ ppm. ESI-MS were recorded on a MICROMASS QUTTRO II triple quadrupole mass spectrometer. Elementary analysis was carried out on Carlo ERBA-1108 analyzer. Commercially available grades of organic solvents of adequate purity are used in many reactions.

Preparation of oxirane substrates

To a solution of sugar alcohol or phenol (2 mmol) in THF (5 mL) was added epichlorohydrine (2.5 mmol) at 0 °C and the reaction mixture was allowed to stir at room temperature for 3 h. The reaction mixture was poured into water and extracted with CH_2Cl_2 (50 mL). The organic layer was washed with aq. $NaHCO_3$, water, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified over SiO_2 using hexane-EtOAc (10:1) as eluant to give pure oxirane derivatives.

Compound 1. Yellow oil; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.87-5.83 (m, 1 H), 4.55 (dd, *J* = 14.7, 3.7 Hz, 1 H), 4.30-4.25 (m, 1 H), 4.11-4.03 (m, 2 H), 4.00-3.86 (m, 3 H), 3.67-3.43 (m, 1 H), 3.16-3.10 (m, 1 H), 2.82-2.76 (m, 1 H), 2.65-2.60 (m, 1 H), 1.72, 1.49, 1.42, 1.30 (4 s, 12 H); ^{13}C ($CDCl_3$, 75 MHz): δ 111.7, 108.9, 105.1, 82.8, 81.0, 72.2, 70.5, 67.3, 67.0, 50.5, 44.2, 26.1 (2 C), 25.4, 25.3; ESI-MS ($C_{15}H_{24}O_7$): 339.1 $[M+Na]^+$; Anal. Calcd. for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65; found: C, 56.80; H, 7.92.

Compound 2. Yellow oil; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.54 (d, *J* = 5.0 Hz, 1 H), 4.63 (dd, *J* = 8.0, 2.5 Hz, 1 H), 4.30 (dd, *J* = 8.0, 2.4 Hz, 1 H), 4.27 (dd, *J* = 5.2, 2.5 Hz, 1 H), 4.25 (dd, *J* = 11.6, 4.8 Hz, 1 H), 4.20 (dd, *J* = 11.6, 7.6 Hz, 1 H), 4.04-4.00 (m, 1 H), 3.48-3.30 (m, 2 H), 3.16-3.10 (m, 1 H), 2.78-2.60 (m, 2 H), 1.52, 1.45, 1.34, 1.33 (4 s, 12 H); ^{13}C ($CDCl_3$, 75 MHz): δ

109.5, 108.6, 96.2, 71.0, 70.6, 70.3, 69.0, 63.9, 63.3, 50.0, 44.2, 26.0 (2 C), 24.8, 24.6; ESI-MS ($C_{15}H_{24}O_7$): 339.1 $[M+Na]^+$; Anal. Calcd. for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65; found: C, 56.77; H, 7.90.

Compound 3. Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.59-4.56 (m, 1 H), 4.38-4.36 (m, 1 H), 4.22-4.19 (m, 1 H), 3.91-3.65 (m, 3 H), 3.61-3.56 (m, 2 H), 3.46-3.40 (m, 1 H), 3.15-3.11 (m, 1 H), 2.78-2.75 (m, 1 H), 2.63-2.57 (m, 1 H), 1.52, 1.45, 1.42, 1.33 (4 s, 12 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 109.3, 108.9, 102.9, 73.2, 72.7, 71.4, 70.6, 70.4, 61.4, 50.9, 44.5, 26.9, 26.3, 25.7, 24.5; ESI-MS ($C_{15}H_{24}O_7$): 339.0 $[M+Na]^+$; Anal. Calcd. for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65; found: C, 56.77; H, 7.90.

Compound 4. Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.85-6.78 (m, 4 H), 4.14-4.10 (m, 1 H), 3.94-3.88 (m, 1 H), 3.75 (s, 3 H), 3.31-3.28 (m, 1 H), 2.88-2.85 (m, 1 H), 2.72-2.70 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 154.0, 152.5, 115.5 (2 C), 114.5 (2 C), 69.4, 55.4, 50.0, 44.5; ESI-MS ($C_{10}H_{12}O_3$): 181.1 $[M+1]^+$; Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; found: C, 66.53; H, 6.85.

Compound 5. Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.42-7.10 (m, 5 H), 4.26-3.98 (m, 2 H), 3.11-3.0 (m, 1 H), 2.77-2.43 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.7, 127.3 (2 C), 126.1, 117.2 (2 C), 70.3, 51.0, 44.0; ESI-MS ($C_9H_{10}O_2$): 151.1 $[M+1]^+$; Anal. Calcd. for $C_9H_{10}O_2$: C, 71.98; H, 6.71; found: C, 71.84; H, 6.87.

Compound 6. Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.56-7.40 (m, 5 H), 4.72 (br s, 2 H), 3.71-3.42 (m, 2 H), 2.90-2.82 (m, 1 H), 2.70-2.42 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.9, 127.1 (2 C), 127.0, 126.8 (2 C), 71.9, 70.8, 50.1, 44.8; ESI-MS ($C_{10}H_{12}O_2$): 165.1 $[M+1]^+$; Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37; found: C, 73.0; H, 7.50.

Typical experimental procedure for the opening of epoxide

To a suspension of epoxide (1.0 mmol) in water (3 mL) was added appropriate *S*-alkylisothiouronium salts (1.5 mmol) and NaOH (2.5 mmol) and the reaction mixture was allowed to stir briskly at room temperature for appropriate time (Table 1). After completion of the reaction (TLC), the reaction mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The pure product was obtained by passing the crude product through a short pad of SiO_2.

Spectral data of β-hydroxy sulfides

Compound 7. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.32-7.24 (m, 5 H, Ar-H), 5.88 (d, J = 3.5 Hz, 1 H), 4.52-4.51 (m, 1 H), 4.31-4.23 (m, 1 H), 4.16-4.04 (m, 2 H), 4.01-3.96 (m, 2 H), 3.86-3.82 (m, 1 H), 3.76-3.72 (m, 3 H), 3.59-3.56 (m, 1 H), 2.58-2.50 (m, 2 H), 1.50, 1.44, 1.34, 1.33 (4 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.6-127.5 (Ar-C), 112.2, 109.6, 105.9, 84.6, 82.9, 81.6, 73.2, 72.8, 69.2, 68.2, 37.2, 34.5, 27.3 (2 C), 26.7 (2 C); ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$; Anal. Calcd. for $C_{22}H_{32}O_7S$: C, 59.98; H, 7.32; found: C, 59.80; H, 7.48.

Compound 8. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.88 (d, J = 3.4 Hz, 1 H), 4.54-4.53 (m, 1 H), 4.31-4.28 (m, 1 H), 4.26-3.99 (m, 3 H), 3.77-3.65 (m, 2 H), 3.60-3.57 (m, 1 H), 2.62-

2.49 (m, 3 H), 1.60-1.53 (m, 2 H), 1.48, 1.41, 1.36, 1.31 (4 s, 12 H), 1.30-1.24 (m, 22 H), 0.88 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 112.2, 109.7, 105.9, 84.7, 82.9, 81.7, 73.2, 69.3, 68.2, 35.5, 32.3, 30.0-23.0 (16 C), 14.5; ESI-MS ($C_{29}H_{54}O_7S$): *m/z* 569.3 $[M+Na]^+$; Anal. Calcd. for $C_{29}H_{54}O_7S$: C, 63.70; H, 9.95; found: C, 63.50; H, 10.10.

Compound 9. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.89 (d, *J* = 3.5 Hz, 1 H), 4.55 (d, *J* = 3.6 Hz, 1 H), 4.34-4.28 (m, 1 H), 4.17-3.97 (m, 3 H), 3.94-3.79 (m, 2 H), 3.63-3.58 (m, 2 H), 2.62-2.57 (m, 2 H), 2.16 (s, 3 H), 1.50, 1.44, 1.37, 1.32 (4 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 112.2, 109.7, 105.9, 84.6, 82.9, 81.7, 73.1, 72.7, 68.9, 68.2, 37.3, 27.3 (2 C), 26.6 (2 C), 16.6; ESI-MS ($C_{16}H_{28}O_7S$): *m/z* 387.2 $[M+Na]^+$; Anal. Calcd. for $C_{16}H_{28}O_7S$: C, 52.73; H, 7.74; found: C, 52.57; H, 7.90.

Compound 10. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.24 (d, *J* = 8.6 Hz, 2 H), 6.84 (d, *J* = 8.6 Hz, 2 H), 5.88 (d, *J* = 3.8 Hz, 1 H), 4.53 (d, *J* = 3.5 Hz, 1 H), 4.33-4.23 (m, 1 H), 4.16-4.04 (m, 2 H), 4.01-3.97 (m, 2 H), 3.89-3.82 (m, 1 H), 3.81 (s, 3 H), 3.77-3.68 (m, 3 H), 3.59-3.54 (m, 1 H), 2.57-2.46 (m, 2 H), 1.50, 1.43, 1.34, 1.32 (4 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 159.1-114.3 (Ar-C), 112.3, 109.7, 105.9, 84.7, 83.0, 81.7, 73.2, 72.7, 69.2, 68.2, 55.5, 36.6, 34.0, 27.3 (2 C), 26.6 (2 C) ; ESI-MS ($C_{23}H_{34}O_8S$): *m/z* 493.2 $[M+Na]^+$; Anal. Calcd. for $C_{23}H_{34}O_8S$: C, 58.70; H, 7.28; found: C, 58.52; H, 7.50.

Compound 11. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.05-6.98 (m, 3 H), 5.85 (d, *J* = 3.4 Hz, 1 H), 4.49-4.48 (m, 1 H), 4.32-4.18 (m, 1 H), 4.11-3.98 (m, 2 H), 3.96-3.93 (m, 2 H), 3.84-3.65 (m, 4 H), 3.54-3.53 (m, 2 H), 2.54-2.49 (m, 2 H), 2.22 (s, 3 H), 1.47, 1.41, 1.31, 1.30 (4 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 130.1-125.9 (Ar-C), 112.3, 109.8, 106.0, 84.7, 83.0, 81.7, 73.2, 72.8, 69.1, 68.2, 36.9, 34.5, 27.3 (2 C), 26.7 (2 C), 21.0, 19.8; ESI-MS ($C_{24}H_{36}O_7S$): *m/z* 491.0 $[M+Na]^+$; Anal. Calcd. for $C_{24}H_{36}O_7S$: C, 61.51; H, 7.74; found: C, 61.30; H, 7.90.

Compound 12. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.32-7.23 (m, 5 H, Ar-H), 5.53 (d, *J* = 1.2 Hz, 1 H), 4.62-4.58 (m, 1 H), 4.32-4.30 (m, 1 H), 4.24-4.21 (m, 1 H), 3.98-3.93 (m, 1 H), 3.88-3.85 (m, 1 H), 3.75 (brs, 2 H), 3.67-3.59 (m, 3 H), 3.55-3.53 (m, 1 H), 2.55-2.53 (m, 2 H), 1.54, 1.45, 1.34 (3 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.6-127.4 (Ar-C), 109.7, 108.9, 96.6, 74.8, 71.5, 70.8, 70.7, 70.1, 69.5, 66.9, 37.0, 30.1, 26.5 (2 C), 25.3, 24.9; ESI-MS ($C_{22}H_{32}O_7S$): *m/z* 463.2 $[M+Na]^+$; Anal. Calcd. for $C_{22}H_{32}O_7S$: C, 59.98; H, 7.32; found: C, 59.80; H, 7.46.

Compound 13. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.90-5.75 (m, 1 H), 5.53 (d, *J* = 4.9 Hz, 1 H), 5.15-5.09 (m, 2H), 4.62-4.59 (m, 1 H), 4.33-4.22 (m, 2 H), 3.99-3.75 (m, 2 H), 3.69-3.47 (m, 4 H), 3.35-3.15 (m, 2 H), 2.60-2.56 (m, 2 H), 1.54, 1.45, 1.34 (3 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 134.5, 117.7, 109.7, 108.9, 96.6, 74.5, 71.5, 70.8, 70.7, 70.2, 69.6, 67.2, 35.6, 34.2, 26.5 (2 C), 25.3, 24.9; ESI-MS ($C_{18}H_{30}O_7S$): *m/z* 413.2 $[M+Na]^+$; Anal. Calcd. for $C_{18}H_{30}O_7S$: C, 55.36; H, 7.74; found: C, 55.20; H, 7.86.

Compound 14. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.53 (d, *J* = 4.9 Hz, 1 H), 4.62-4.59 (m, 1 H), 4.32-4.22 (m, 2 H), 3.99-3.90 (m, 2 H), 3.71-3.65 (m, 3 H), 3.62-3.48 (m, 2 H), 2.66-2.59 (m, 2 H), 2.15 (s, 3 H), 1.54, 1.45, 1.34 (3 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 109.9, 108.9, 96.6, 74.7, 71.0, 70.8, 70.6, 70.2, 69.4, 67.0, 37.9, 26.3 (2 C), 25.3, 24.9, 16.5; ESI-MS

($C_{16}H_{28}O_7S$): *m/z* 387.1 $[M+Na]^+$; Anal. Calcd. for $C_{16}H_{28}O_7S$: C, 52.73; H, 7.74; found: C, 52.57; H, 7.90.

Compound 15. Yellow oil; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.22 (d, *J* = 8.6 Hz, 2 H), 6.83 (d, *J* = 8.5 Hz, 2 H), 5.52-5.50 (m, 1 H), 4.61-4.57 (m, 1 H), 4.31-4.21 (m, 2 H), 3.97-3.93 (m, 1 H), 3.87-3.84 (m, 1 H), 3.79 (s, 3 H), 3.70 (brs, 2 H), 3.66-3.53 (m, 2 H), 3.48-3.44 (m, 1 H), 2.54-2.51 (m, 2 H), 1.54, 1.44, 1.34 (3 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 159.1-114.3 (Ar-C), 109.7, 108.9, 96.5, 74.8, 71.6, 70.8, 70.6, 70.2, 69.5, 67.2, 55.5, 36.5, 34.7, 26.5 (2 C), 25.3, 24.9; ESI-MS ($C_{23}H_{34}O_8S$): *m/z* 493.2 $[M+Na]^+$; Anal. Calcd. for $C_{23}H_{34}O_8S$: C, 58.70; H, 7.28; found: C, 58.54; H, 7.50.

Compound 16. Yellow oil; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.08-7.03 (m, 3 H), 5.52 (d, J = 4.8 Hz, 1 H), 4.61-4.58 (m, 1 H), 4.32-4.22 (m, 2 H), 3.98-3.87 (m, 2 H), 3.78-3.48 (m, 6 H), 2.61-2.53 (m, 2 H), 2.30, 2.26 (2 s, 6 H), 1.54, 1.45, 1.34 (3 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 136.9-125.6 (Ar-C), 109.7, 108.9, 96.6, 74.8, 71.5, 70.9, 70.0, 69.6, 69.3, 67.2, 36.8, 34.9, 26.5 (2 C), 25.3, 24.9, 20.1, 19.8; ESI-MS ($C_{24}H_{36}O_7S$): *m/z* 491.2 $[M+Na]^+$; Anal. Calcd. for $C_{24}H_{36}O_7S$: C, 61.51; H, 7.74; found: C, 61.35; H, 7.52.

Compound 17. Yellow oil; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.92-5.70 (m, 1 H), 5.22-5.09 (m, 2 H), 4.60-4.57 (m, 1 H), 4.36-4.34 (m, 1 H), 4.24-4.21 (m, 1 H), 3.92-3.76 (m, 2 H), 3.75-3.52 (m, 6 H), 3.18-3.15 (m, 1 H), 2.87-2.80 (m, 1 H), 2.62-2.55 (m, 2 H), 1.54, 1.48, 1.41, 1.35 (4 s, 12 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 134.5, 117.7, 109.3, 108.7, 102.8, 75.5, 73.3, 71.3, 71.2, 70.5, 69.5, 61.4, 35.6, 34.5, 26.9, 26.3, 25.7, 24.4; ESI-MS ($C_{18}H_{30}O_7S$): *m/z* 413.2 $[M+Na]^+$; Anal. Calcd. for $C_{18}H_{30}O_7S$: C, 55.36; H, 7.74; found: C, 55.20; H, 7.88.

Compound 18. Yellow oil; ^1H NMR ($CDCl_3$, 200 MHz): δ 4.59-4.56 (m, 1 H), 4.35-4.33 (m, 1 H), 4.22-4.19 (m, 1 H), 3.91-3.85 (m, 2 H), 3.75-3.48 (m, 5 H), 2.71-2.50 (m, 4 H), 1.62-1.54 (m, 2 H), 1.53, 1.47, 1.40, 1.34 (4 s, 12 H), 1.28-1.24 (m, 22 H), 0.88 (t, *J* = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 109.3, 108.8, 102.9, 75.5, 73.4, 71.3, 70.8, 70.6, 69.5, 61.4, 36.2, 33.1, 30.1-29.6 (12 C), 26.9, 26.3, 25.8, 24.4, 14.5; ESI-MS ($C_{29}H_{54}O_7S$): *m/z* 569.3 $[M+Na]^+$; Anal. Calcd. for $C_{29}H_{54}O_7S$: C, 63.70; H, 9.95; found: C, 63.52; H, 10.14.

Compound 19. Yellow oil; ^1H NMR ($CDCl_3$, 200 MHz): δ 6.87-6.80 (m, 4 H), 5.88-5.74 (m, 1 H), 5.17-5.11 (m, 2 H), 4.07-3.99 (m, 1 H), 3.98-3.94 (m, 2 H), 3.78 (s, 3 H), 3.20-3.18 (m, 2 H), 2.83-2.64 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 154.6-115.0 (Ar-C and $CH=CH_2$), 71.6, 69.1, 55.9, 35.5, 34.5; ESI-MS ($C_{13}H_{18}O_3S$): *m/z* 255.1 $[M+1]^+$; Anal. Calcd. for $C_{13}H_{18}O_3S$: C, 61.39; H, 7.13; found: C, 61.22; H, 7.30.

Compound 20. Yellow oil; ^1H NMR ($CDCl_3$, 200 MHz): δ 6.87-6.80 (m, 4 H), 4.17-4.05 (m, 1 H), 4.03-3.95 (m, 2 H), 3.77 (s, 3 H), 2.88 (brs, 1 H), 2.84-2.66 (m, 2 H), 2.16 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 154.6-115.0 (Ar-C), 71.5, 68.7, 55.9, 38.3, 16.4; ESI-MS ($C_{11}H_{16}O_3S$): *m/z* 229.1 $[M+1]^+$; Anal. Calcd. for $C_{11}H_{16}O_3S$: C, 57.87; H, 7.06; found: C, 57.72; H, 7.25.

Compound 21. Yellow oil; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.28-6.82 (m, 8 H), 4.06-3.99 (m, 1 H), 3.94-3.92 (m, 2 H), 3.81 (s, 3 H), 3.78 (s, 3 H), 3.72 (s, 2 H), 2.76-2.58 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 159.2-130.2 (Ar-C), 71.5, 69.2, 55.9, 55.6, 36.4, 35.0; ESI-MS

($C_{18}H_{22}O_4S$): *m/z* 335.1 $[M+1]^+$; Anal. Calcd. for $C_{18}H_{22}O_4S$: C, 64.65; H, 6.63; found: C, 64.50; H, 6.78.

Compound 22. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.33-6.90 (m, 10 H), 4.11-4.0 (m, 1 H), 4.01-3.99 (m, 2 H), 3.78 (br s, 2 H), 2.80-2.62 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 158.8-115.0 (Ar-C), 70.8, 69.2, 37.0, 35.2; ESI-MS ($C_{16}H_{18}O_2S$): *m/z* 275.1 $[M+1]^+$; Anal. Calcd. for $C_{16}H_{18}O_2S$: C, 70.04; H, 6.61; found: C, 69.90; H, 6.77.

Compound 23. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.32-6.91 (m, 5 H), 4.15-4.09 (m, 1 H), 4.06-4.05 (m, 2 H), 2.90-2.69 (m, 3 H), 2.60-2.55 (m, 2 H), 1.67-1.57 (m, 2 H), 1.42-1.26 (m, 22 H), 0.91 (t, *J* = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 158.2-114.9 (Ar-C), 70.4, 69.0, 36.3, 33.1, 32.3-23.1 (12 C), 14.6; ESI-MS ($C_{23}H_{40}O_2S$): *m/z* 381.3 $[M+1]^+$; Anal. Calcd. for $C_{23}H_{40}O_2S$: C, 72.58; H, 10.59; found: C, 72.45; H, 10.74.

Compound 24. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.32-6.90 (m, 5 H), 5.88-5.74 (m, 1 H), 5.17-5.11 (m, 2 H), 4.13-4.07 (m, 1 H), 4.05-4.03 (m, 2 H), 3.20-3.18 (m, 2 H), 2.85-2.65 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 158.8-121.6 (Ar-C), 118.1, 114.9, 70.5, 69.3, 35.5, 34.6; ESI-MS ($C_{12}H_{16}O_2S$): *m/z* 225.1 $[M+1]^+$; Anal. Calcd. for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19; found: C, 64.10; H, 7.37.

Compound 25. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.32-6.91 (m, 5 H), 4.19-4.08 (m, 1 H), 4.06-4.04 (m, 2 H), 2.97 (br s, 1 H), 2.86-2.68 (m, 2 H), 2.17 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 158.8-114.9 (Ar-C), 70.7, 68.7, 38.3, 16.4; ESI-MS ($C_{10}H_{14}O_2S$): *m/z* 199.1 $[M+1]^+$; Anal. Calcd. for $C_{10}H_{14}O_2S$: C, 60.57; H, 7.12; found: C, 60.44; H, 7.27.

Compound 26. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.25-6.80 (m, 9 H), 4.07-3.98 (m, 1 H), 3.96-3.95 (m, 2 H), 3.78 (s, 3 H), 3.70 (br s, 2 H), 2.74-2.56 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 159.2-114.4 (Ar-C), 70.7, 69.0, 55.5, 36.4, 35.0; ESI-MS ($C_{17}H_{20}O_3S$): *m/z* 305.1 $[M+1]^+$; Anal. Calcd. for $C_{17}H_{20}O_3S$: C, 67.08; H, 6.62; found: C, 67.0; H, 6.75.

Compound 27. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.30-6.89 (m, 8 H), 4.19-4.07 (m, 1 H), 4.02-3.99 (m, 2 H), 3.82-3.72 (m, 2 H), 2.85-2.62 (m, 3 H), 2.33, 2.28 (2 s, 6 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 158.8-114.9 (Ar-C), 70.7, 69.2, 36.7, 35.2, 20.2, 19.8; ESI-MS ($C_{18}H_{22}O_2S$): *m/z* 303.2 $[M+1]^+$; Anal. Calcd. for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33; found: C, 71.32; H, 7.48.

Compound 28. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.39-7.22 (m, 5 H, Ar-H), 4.55 (brs, 2 H, PhCH_2), 3.96-3.86 (m, 1 H, C*H*), 3.75 (brs, 2 H, SCH_2Ph), 3.56-3.46 (m, 2 H, OCH_2), 2.66-2.51 (m, 3 H, O*H* and SCH_2); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.6-127.5 (Ar-C), 73.8 (Ph*C*H_2), 73.3 (O*C*H_2), 69.7 (*C*H), 37.0 (S*C*H_2), 35.2 (S*C*H_2); ESI-MS ($C_{17}H_{20}O_2S$): *m/z* 289.1 $[M+1]^+$; Anal. Calcd. for $C_{17}H_{20}O_2S$: C, 70.80; H, 6.99; found: C, 70.67; H, 7.16.

Compound 29. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.40-7.29 (m, 5 H, Ar-H), 4.58 (brs, 2 H, PhCH_2), 3.95-3.88 (m, 1 H, C*H*), 3.60-3.50 (m, 2 H, OCH_2), 2.76-2.60 (m, 2 H, SCH_2), 2.58-2.51 (m, 3 H, O*H* and SCH_2), 1.64-1.54 (m, 2 H, CH_2), 1.38-1.25 (m, 22 H, $(CH_2)_{11}$), 0.91 (t, *J* = 6.3 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.3-128.1 (Ar-C), 73.8 (Ph*C*H_2), 73.3 (O*C*H_2), 69.6 (*C*H), 36.4 (S*C*H_2), 33.0 (S*C*H_2), 32.3-23.1 $(CH_2)_{12}$), 14.6 (CH_3); ESI-MS

($C_{24}H_{42}O_2S$): *m/z* 395.3 $[M+1]^+$; Anal. Calcd. for $C_{24}H_{42}O_2S$: C, 73.04; H, 10.73; found: C, 72.90; H, 10.86.

Compound 30. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.39-7.28 (m, 5 H, Ar-H), 5.86-5.72 (m, 1 H, C*H*=CH_2), 5.25-5.10 (m, 2 H, CH=CH_2), 4.57 (brs, 2 H, PhCH_2), 3.96-3.88 (m, 1 H, C*H*), 3.62-3.48 (m, 2 H, OCH_2), 3.17-3.15 (m, 2 H, SCH_2), 2.71-2.54 (m, 3 H, O*H* and SCH_2); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.2-128.1 (Ar-C), 117.8, 73.8 (Ph*C*H_2), 73.3 (O*C*H_2), 69.6 (*C*H), 35.5 (S*C*H_2), 34.7 (S*C*H_2); ESI-MS ($C_{13}H_{18}O_2S$): *m/z* 239.1 $[M+1]^+$; Anal. Calcd. for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61; found: C, 65.38; H, 7.74.

Compound 31. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.38-7.28 (m, 5 H, Ar-H), 4.57 (brs, 2 H, PhCH_2), 3.94-3.88 (m, 1 H, C*H*), 3.59-3.49 (m, 2 H, OCH_2), 2.87 (brs, 1 H, O*H*), 2.71-2.55 (m, 2 H, SCH_2), 2.12 (CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.3-128.1 (Ar-C), 73.8 (Ph*C*H_2), 73.3 (O*C*H_2), 69.2 (*C*H), 38.3 (S*C*H_2), 16.4 (*C*H_3); ESI-MS ($C_{11}H_{16}O_2S$): *m/z* 213.1 $[M+1]^+$; Anal. Calcd. for $C_{11}H_{16}O_2S$: C, 62.23; H, 7.60; found: C, 62.05; H, 7.75.

Compound 32. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.35-7.28 (m, 5 H), 7.22 (d, *J* = 8.6 Hz, 2 H), 6.82 (d, *J* = 8.6 Hz, 2 H), 4.55 (br s, 2 H), 3.94-3.84 (m, 1 H), 3.80 (s, 3 H), 3.70 (s, 2 H), 3.56-3.46 (m, 2 H), 2.65-2.49 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 159.1-114.3 (Ar-C), 73.8, 73.2, 69.5, 55.5, 36.3, 35.1; ESI-MS ($C_{18}H_{22}O_3S$): *m/z* 319.1 $[M+1]^+$; Anal. Calcd. for $C_{18}H_{22}O_3S$: C, 67.89; H, 6.96; found: C, 67.74; H, 7.15.

Compound 33. Yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.36-7.30 (m, 5 H, Ar-H), 7.08-7.01 (m, 3 H, Ar-H), 4.57 (brs, 2 H, PhCH_2), 3.95-3.86 (m, 1 H,C*H*), 3.78-3.69 (m, 2 H, OCH_2), 3.58 (m, 2 H, SCH_2), 2.72-2.52 (m, 3 H, O*H* and SCH_2), 2.32, 2.27 (2 s, 6 H, 2 CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.3-125.7 (Ar-C), 73.8 (Ph*C*H_2), 73.3 (O*C*H_2), 69.7 (*C*H), 36.7 (S*C*H_2) 35.6 (S*C*H_2), 20.2, 19.8 (2 C, 2 *C*H_3); ESI-MS ($C_{19}H_{24}O_2S$): *m/z* 317.1 $[M+1]^+$; Anal. Calcd. for $C_{19}H_{24}O_2S$: C, 72.11; H, 7.64; found: C, 72.0; H, 7.78.

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