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An approach toward the synthesis of β-hydroxy sulfones on water

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ABSTRACT

Various β-hydroxyl sulfones are prepared by regioselective ring opening of epoxides with sodium salt of sulfinate on water. This is an efficient protocol which avoids hazardous and moisture sensitive catalysts.

Oxirane ring opening with various potential nucleophiles is an important strategy in organic synthesis because nucleophilic addition to the oxirane ring leads to 1,2-bifunctionalized systems which are interesting structural motifs for the synthesis of a wide variety of natural products. The great utility of β-hydroxy sulfones in organic synthesis is due to their use as precursors of d^2 and d^3 reagents[1] via corresponding metallation reaction.[2] The dianions of these β-hydroxy sulfones are subjected to the preparation of lactones[3a–d] and 2,5-disubstituted tetrahydrofurans.[3e] On the other way the anions of these versatile β-hydroxy sulfones react to form vinyl sulfones by β-elimination reaction[4] and olefins by reductive elimination.[5]

The regioselective formation of β-hydroxy sulfones from the epoxides is an important reaction in medicinal and organic chemistries as these are useful intermediates, which can be further derivatized through the coined concept called *Umpolung* (any process by which donor and acceptor reactivity of an atom is interchanged). In the literature sulfonyl group and its inherent properties are well documented.[6] So the chemistry of β-hydroxy sulfones resembles typically that of an anion.

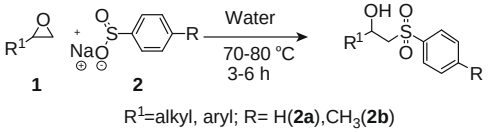
So far there are few reports on the synthesis of β-hydroxy sulfones, by regioselective ring opening of oxiranes with various catalytic systems. Najera and Sansano have reported the synthesis of β-hydroxy sulfones by employing Grignard reagents.[7] Bhattacharyya and Maiti synthesized various β-hydroxy sulfones in presence of PEG as a catalyst.[8] Recently, several methods using promoters or catalysts in different organic solvents[9] have been reported. These methods include use of supercritical carbon dioxide,[10a] microwave irradiation,[10b] hexafluoro-2-propanol,[10c] ionic liquid,[10d] $Bi(OTf)_3$ in water,[10e] and solvent-free conditions.[9]

Although few reagents and catalysts have been reported for efficient opening of epoxide through activation,[11,12] these methodologies have a number of drawbacks such as longer reaction times, low yields, difficulty in preparation and/or storage of reagents or catalysts, tedious workup, and low regioselectivity. Thus in view of these shortcomings there is a need to develop a greener approach for the synthesis of β-hydroxy sulfones.

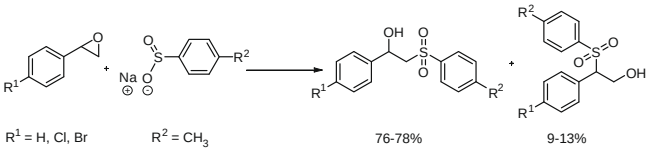
Water is a cheap, nontoxic, and most readily available reaction medium, making it an environmentally benign solvent[13] for green chemistry protocols. To the best of our knowledge there are no reports on regioselective oxirane ring opening with sodium sulfinates on water without using any catalyst. Herein, we wish to report regioselective ring opening of epoxides with sodium sulfinates on water at 80 °C.

The generality of this approach toward the synthesis of β-hydroxy sulfones is established by reacting various epoxides with the sodium salts of sulfinate, on water.[14] Excellent yields of desired β-hydroxy sulfones were obtained. In the case of aliphatic epoxides, attack occurred at the less-hindered site of the epoxide (Scheme 1). In the case of aromatic epoxides, a mixture of regioisomers was obtained (Scheme 2).

Out of these two, the product formed by the attack at the least substituted is the major one (up to 80%), and the attack at the



Scheme 1. Synthesis of β-hydroxy sulfones on water.



Scheme 2.

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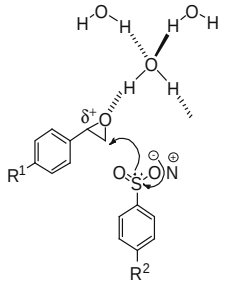


Figure 1. Plausible mechanistic path way.

Table 1
Synthesis of β-hydroxy sulfones on water[a]

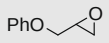
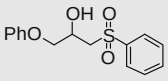
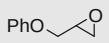
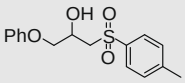
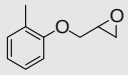
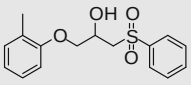
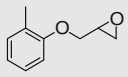
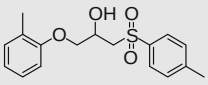
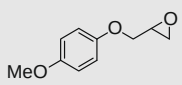
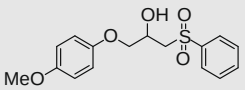
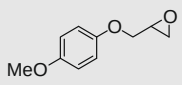
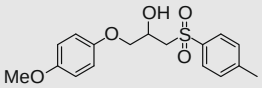
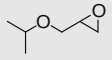
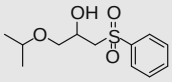
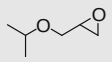
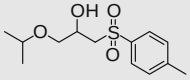
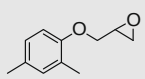
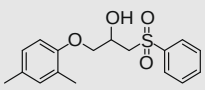
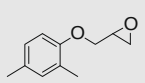
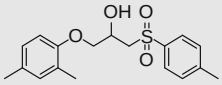
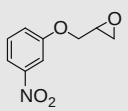
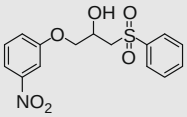
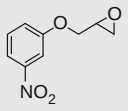
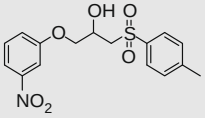
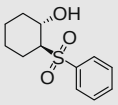
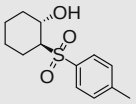
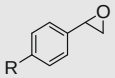
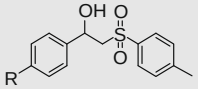
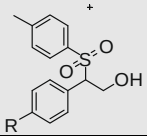
Entry	Epoxide (1)	2	Product[b]	Yield[c] (%)
1		**2a**		89
2		**2b**		92
3		**2a**		86
4		**2b**		91
5		**2a**		85
6		**2b**		89
7		**2a**		84
8		**2b**		87
9		**2a**		84
10		**2b**		87
11		**2a**		78
12		**2b**		84

Table 1 (*continued*)

Entry	Epoxide (1)	2	Product[b]	Yield[c] (%)
13		**2a**		81
14		**2b**		85
15		2b		78 (**2b$_1$**) 76 (**2b$_2$**) 77 (**2b$_3$**)
	R = H (**2b$_1$**), Cl (**2b$_2$**), Br (**2b$_3$**)			13 (**2b$_1$**) 10 (**2b$_2$**) 9 (**2b$_3$**)

[a] Reaction conditions: epoxide (1 equiv), sodium sulfinate (1.1 equiv), and water (20 mL).
[b] Products were confirmed by ^{1}H, ^{13}C NMR, and direct comparison with authentic samples for entries 13–15.
[c] Yields of the isolated product.

benzylic position is the minor one. The probable reason for getting mixture of products in case of styrene oxide is that, the water molecule has a tendency to form hydrogen bonding with the electronegative oxygen of the epoxide resulting in a partial positive charge, this positive charge on oxygen appears to be localized on more substituted benzylic carbon leading to the product, which is minor. Whereas attack from the least-hindered side resulted in the major product (Fig. 1). The product ratio suggests that in case of aliphatic epoxides steric factors predominate over electronic factors, thereby resulting in the attack at the less-hindered carbon atom of the epoxide ring. The results are summarized in (Table 1). The structures of all the products were determined from their analytical and spectral (IR, ^{1}H NMR, and ^{13}C NMR) data[15] and by direct comparison with authentic samples.

In conclusion, we have demonstrated an ecofriendly and catalyst-free protocol for the synthesis of β-hydroxy sulfones under mild conditions on water. This method has several advantages over the existing methods such as high yields, ability to proceed without catalyst or additives, and environmentally friendly conditions. This protocol is an useful addition to the green chemistry in the context of a higher demand for green chemical processes.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.06.078.

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14. *General procedure for the synthesis of β-hydroxy sulfones on water. Typical example: 1-phenoxy-3-(phenylsulfonyl)propan-2-ol* (Table 1, entry 1): To a flask containing the epoxide (0.150 g, 1 mmol) in water (20 mL), sodium sulfinate (0.180 g, 1.1 mmol) was added. The suspension was magnetically stirred at 70–80 °C until reaction was complete (as monitored by TLC) (Table 1). After completion of the reaction, the reaction mixture was extracted with ethyl acetate (4 × 10 mL). The extract was further washed with water and saturated brine solution, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to give β-hydroxy sulfones in 80–94% yields. In case of styrene oxides, the product was further purified by silica gel column chromatography using ethyl acetate and hexane (7:3) as an eluent to afford the corresponding β-hydroxy sulfones (Table 1, entry 1) in 89% yield. Colorless oil; ν_{max} (KBr) 3493, 2929, 1595, 1301, 1243, 1144 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.90 (d, 2H, J = 7.5 Hz, arom.), 7.60 (t, 1H, J = 7.5 Hz, arom.), 7.50 (t, 2H, J = 7.5 Hz, arom.), 7.21 (t, 2H, J = 7.5 Hz, arom.), 6.91 (t, 1H, J = 8.3 Hz, arom.), 6.82 (d, 2H, J = 7.5 Hz, arom.), 4.51 (m, 1H, OCH_2), 3.94 (m, 2H, OCH_2 + CHOH), 3.49 (br s, OH), 3.46 (m, 2H, CH_2SO_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6, 139.5, 133.9, 129.4, 128.1, 121.6, 114.4, 70.0, 64.9, 59.2. Mass (ESI-MS): m/z 293 $(M+H)^+$.
15. *Data for the representative examples of synthesized compounds: 1-(o-tolyloxy)-3-tosylpropan-2-ol* (Table 1, entry 4): Colorless oil; yield 0.291 g (91%); ν_{max} (KBr) 3464, 2933, 1598, 1498, 1293, 1248, 1143 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.79 (d, 2H, J = 8.0 Hz, arom.), 7.29 (d, 2H, J = 8.0 Hz, arom.), 7.06 (t, 2H, J = 7.3 Hz, arom.), 6.82 (t, 1H, J = 7.3 Hz, arom.), 6.67 (d, 1H, J = 8.0 Hz, arom.), 4.46 (m, 1H, OCH_2), 3.91 (m, 2H, OCH_2 + CHOH), 3.43 (m, 2H, CH_2SO_2), 2.40 (s, 3H, CH_3), 2.10 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 155.8, 145.0, 136.3, 130.7, 129.7, 127.7, 126.6, 126.2, 120.8, 110.9, 69.7, 65.0, 59.3, 21.4, 15.9. Mass (ESI-MS): m/z 321 $(M+H)^+$.

L-*Isopropoxy-3-tosylpropan-2-ol* (Table 1, entry 8): Colorless oil; yield 0.236 g (87%); ν_{max} (KBr) 3497, 2973, 1448, 1379, 1303, 1144 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.82 (d, 2H, J = 8.1 Hz, arom.), 7.37 (d, 2H, J = 7.9 Hz, arom.), 4.20 (m, 1H, OCH_2), 3.55 (m, 1H, OCH_2), 3.42 (d, 2H, J = 5.0 Hz, CHOH + CH_2SO_2), 3.28 (m, 2H, CH_2SO_2 + $CH(CH_3)_2$), 2.88 (br s, OH), 2.46 (s, 3H,CH_3), 1.10 (s, 6H, $CH(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 144.5,136.2, 129.4, 127.6, 71.8, 69.9, 65.1, 59.2, 21.5, 21.2. Mass (ESI-MS): m/z 273 $(M+H)^+$.

L-*(2,4-Dimethylphenoxy)-3-tosylpropan-2-ol* (Table 1, entry10): Colorless oil; yield 0.290 g (87%); ν_{max} (KBr) 3511, 2926, 1598, 1505, 1467, 1427, 1380, 1257, 1139 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.81 (d, 2H, J = 8.2 Hz, arom.), 7.35 (d, 2H, J = 7.4 Hz, arom.), 6.84 (d, 2H, J = 8.2 Hz, arom.), 6.58(d, 1H, J_1 = 7.4 Hz, arom.), 4.41 (m, 1H, OCH_2), 3.97 (q, 1H, J_1 = 8.9 Hz, J_2 = 4.4 Hz, OCH_2), 3.87 (q, 1H, J_1 = 9.7 Hz, J_2 = 5.9 Hz, CHOH), 3.46 (dd, 1H, J_1 = 2.9 Hz, J_2 = 2.2 Hz, CH_2SO_2), 3.33 (m, 1H, CH_2SO_2), 2.47 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 2.07(s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 153.6, 144.3, 136.3, 131.1, 129.4, 127.6, 126.5, 125.7,111.0, 69.7, 64.8, 59.2, 21.4, 20.1,15.7. Mass (ESI-MS): m/z 335 $(M+H)^+$.

L-*(3-Nitrophenoxy)-3-(phenylsulfonyl)propan-2-ol* (Table 1, entry 11): Colorless oil; yield 0.262 g (78%);%); υ_{max} (KBr) 3496, 3096, 2931, 1528, 1481, 1449, 1351, 1296, 1247, 1144 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.96 (m, 2H, arom.), 7.82 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.2 Hz, arom.), 7.68 (m, 2H, arom.), 7.60 (m, 2H, arom.), 7.41 (t, 1H, J = 8.3 Hz, arom.), 7.17 (dd, J_1 = 8.3 Hz, J_2 = 2.2 Hz, 1H, arom.), 4.55 (m, 1H, OCH_2), 4.10 (m, 2H, OCH_2 + CHOH), 3.41(m, 2H, CH_2SO_2), 3.38 (br s, OH); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 158.3, 148.9, 134.1, 129.7, 129.1, 127.5, 120.9, 116.1, 108.7, 70.2, 64.5, 58.7. Mass (ESI-MS): m/z 338 $(M+H)^+$.