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**RESEARCH ARTICLE**

# Efficient synthesis of β-hydroxy-sulfones via opening of epoxides with sodium sulfinates in ionic liquid [TPA][Pro]

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An efficient synthesis of β-hydroxy-sulfones is described by the reaction of sodium sulfinates with epoxides in ionic liquid [TPA][Pro] as an efficient reaction medium to afford the corresponding β-hydroxy-sulfones in excellent yields.

*Keywords*: β-Hydroxy-sulfones; Sodium sulfinates; Epoxides; Ionic liquid [TPA][Pro]



## 1. Introduction

Sulfones are a very important and fascinating branch of chemistry [1, 2]. Among sulfones, β-hydroxy-sulfones are very important group of intermediates as they are important key constituents in organic synthesis [3, 4]. The optically active β-hydroxy-sulfones are of great utility in organic synthesis, as they have been used as building blocks in the synthesis of variety of compounds such as racemic and non-racemic lactones [5–7], tetra hydro furans and furanones [8–10]. Recently, compounds of this class have proved its efficiency as a chiral controller in asymmetric Diels–Alder and alkylation reactions [11]. Despite their importance, comparatively few methods for the preparation of β-hydroxy-sulfones have been reported in literature, which includes by chemical reduction of β-keto-sulfones [11–14], by bio reduction using baker's yeast [15] and using fungus *Curvularia lunata* [16]. The optically active β-hydroxy-sulfones can be achieved by a lipase promoted kinetic resolution methods [17, 18]. However, the preparation of β-hydroxy-sulfones by the opening of epoxides with sulfinate salts has been much less thoroughly investigated [19–26], because the generation of basic alkoxide adducts leads to a progressive increase in the basisity of the reaction medium. This in turn, promotes side reactions involving the starting epoxides. Very recently, the synthesis of β-hydroxy-sulfones via opening of epoxides with zinc sulfinates have been reported [27].

In recent years, the use of ionic liquids (ILs) as green solvents in organic synthetic processes has gained considerable importance due to their solvating ability, negligible vapor pressure,

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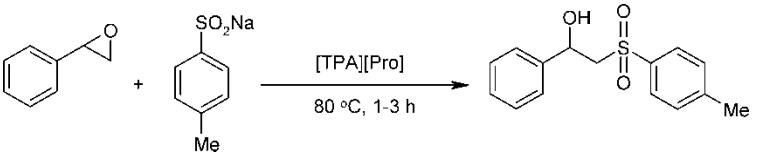
easy recyclability and reusability [28–32]. Maschmeyer *et al.* [33], have reported the synthesis of ionic liquids using quaternary ammonium hydroxide and carboxylic acids, which are inexpensive and can be prepared easily. Recently, we reported the facile synthesis of β-keto-sulfones in ionic liquid [TPA][Pro] [34]. In continuation of our work, we envisaged the synthesis of β-hydroxy-sulfones.




SCHEME 1

## 2. Results and discussion

In this report (scheme 1), we describe an efficient method for the synthesis of β-hydroxy-sulfones in ionic liquid [TPA][Pro]. This method does not need expensive reagents or special care to exclude the moisture from the reaction medium. We prepared ionic liquid [TPA][Pro] using tetrapropyl ammonium hydroxide and L-proline in aqueous medium at 60 °C. Tetrapropyl ammonium hydroxide is a strong base, which readily deprotanates the carboxylic acid moiety of amino acid like L-proline to form a carboxylic acid salt and water, the

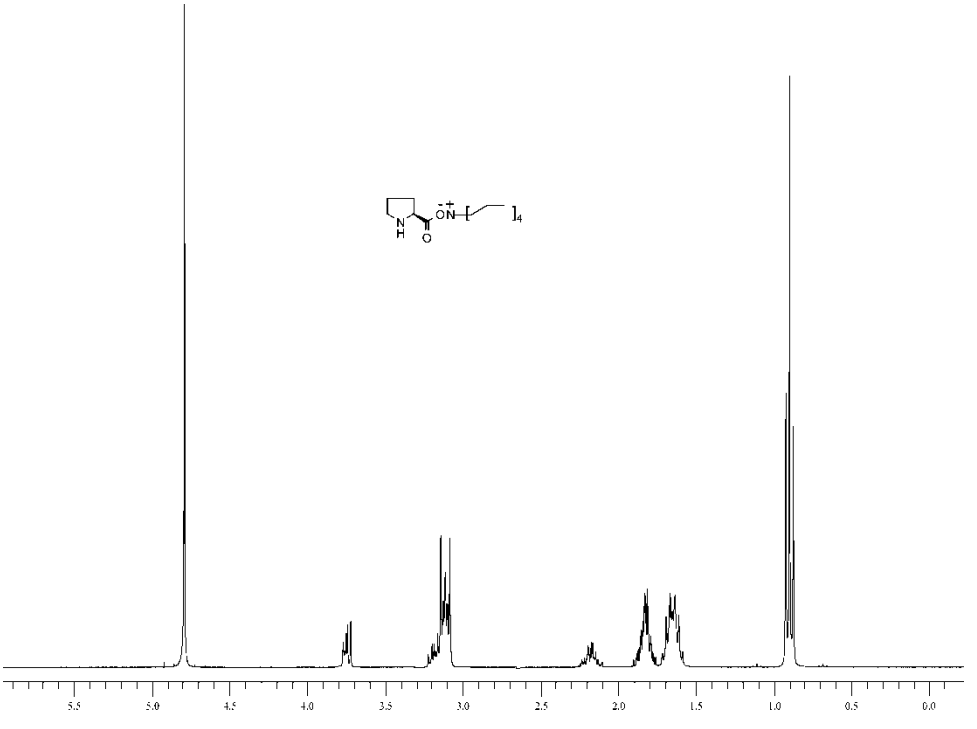
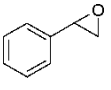
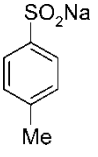
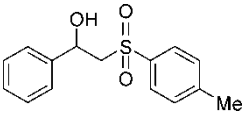
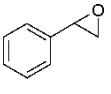
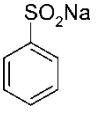
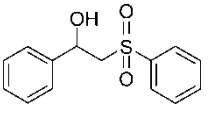
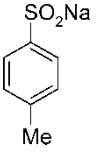
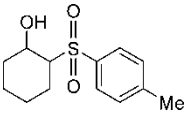
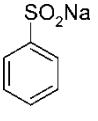
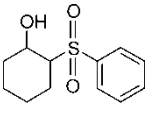
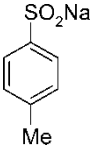
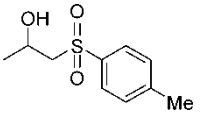
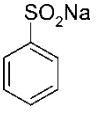
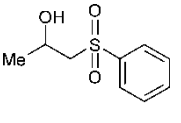



Figure 1. $^{1}$H NMR (300 MHz, $D_2O$) of ionic liquid [TPA][Pro].

Table 1. Screening of different solvents on the reaction of styrene oxide with *p*-toluenesulfinate at 80 °C.

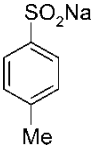
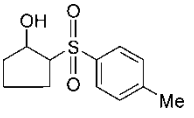
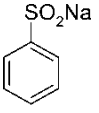
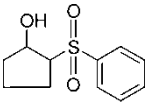
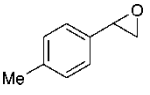
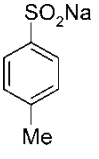
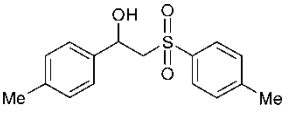
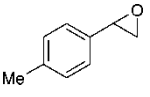
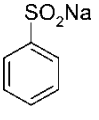
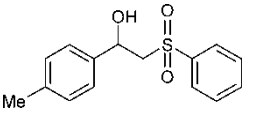
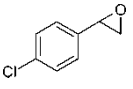
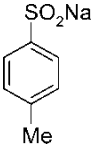
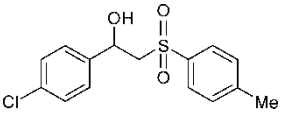
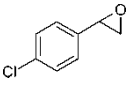
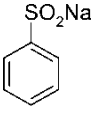
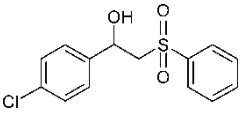
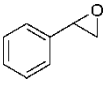
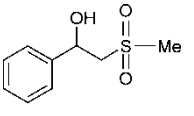
| Entry | Solvent | Time | Yield (%) |
|---|---|---|---|
| 1 | EtOH | 12 h | Nil |
| 2 | 1,4 Dioxane | 12 h | Nil |
| 3 | Isopropanol | 12 h | Trace |
| 4 | $CH_3CN$ | 12 h | 10 |
| 5 | PEG-400 | 4 h | 90 |
| 6 | Water | 6 h | 60 |
| 7 | Neat | 4 h | 50 |
| 8 | [TPA][Pro] | 1 h | 92 |

Table 2. Synthesis of β-hydroxy-sulfones via opening of epoxides with sodium sulfinates in ionic liquid [TPA][Pro].

| Entry | Epoxide | Sodium sulfinate | Product | Time (h) | Yield (%)† [Ref.] |
|---|---|---|---|---|---|
| 1 |  |  |  | 1 | 92 [14] |
| 2 |  |  |  | 1 | 90 [13] |
| 3 |  |  |  | 2 | 89 |
| 4 |  |  |  | 2 | 90 |
| 5 |  |  |  | 3 | 89 [26] |
| 6 |  |  |  | 3 | 90 [4] |

(*continued*)

Table 2. Continued.

| Entry | Epoxide | Sodium sulfinate | Product | Time (h) | Yield (%)† [Ref.] |
|---|---|---|---|---|---|
| 7 |  |  |  | 2 | 90 |
| 8 |  |  |  | 2 | 90 |
| 9 |  |  |  | 1 | 90 [14] |
| 10 |  |  |  | 2 | 92 [13] |
| 11 |  |  |  | 3 | 95 [14] |
| 12 |  |  |  | 3 | 94 [13] |
| 13 |  | $MeSO_2Na$ |  | 3 | 90 |

†Isolated yields after column chromatography. All products gave satisfactory spectral data.

resulting salt being a liquid at room temperature. The formation of ionic liquid [TPA][Pro] has been confirmed by its $^1$H NMR spectrum (figure 1). We first examined the reaction of styrene oxide with sodium *p*-toluenesulfinate in ionic liquid [TPA][Pro] at 80 °C to give the corresponding β-hydroxy-sulfone in 92% in 1 h. In order to optimize the reaction conditions, we carried out the above reaction in various organic solvents such as, EtOH, 1,4 Dioxane, IPA, $CH_3CN$, PEG-400 and water. The poor yields in protic solvents and less polar solvents are probably due to the lower solubility of the sulfinate salt in these solvents, coupled with the fact that the nucleophile ($p$-$C_6H_4SO_2^-$) is solvated in protic solvents, thereby, reducing its effective nucleophilicity. It was observed that in ionic liquid [TPA][Pro], the reaction was complete in excellent yields (scheme 1, table 1). Further, it has been found that, the sulfinate sulfur nucleophile preferentially attacked from less hindered side to yield the corresponding β-hydroxy-sulfone (scheme 1) and no trace of formation of sulfinate esters was observed. Encouraged by the above reaction conditions, we extended the generality of the reaction by reacting different sodium sulfinates with various epoxides in ionic liquid [TPA][Pro] to yield the corresponding β-hydroxy-sulfones in excellent yields (table 2).

## 3. Conclusion

In conclusion, we have described an efficient and facile synthesis of β-hydroxy-sulfones via opening of epoxides with sodium sulfinates using ionic liquid [TPA][Pro] as an efficient reaction medium.



## 4. Experimental section

### 4.1 *Typical experimental procedure for the preparation of ionic liquid [TPA][Pro]*

An aqueous solution of tetrapropylammonium hydroxide (40% w/w, 20 mmol) was added to an aqueous suspension of the L-proline (21 mmol). The resulting reaction mixture was stirred at 60 °C for 2 h. The water was removed in vacuum (8 milli bar) at 60 °C. The resulting reaction mass was dissolved in $CH_3CN$ (50 mL) and filtered to remove the unreacted L-proline. The filtrate was dried over anhydrous sodium sulfate, solvent was evaporated under reduced pressure to afford the ionic liquid [TPA][Pro].

### 4.2 *Typical experimental procedure for synthesis of* β*-hydroxy Sulfones*

To a mixture of epoxide (1 mmol), sodium sulfinate (1.1 mmol) was taken in ionic liquid [TPA][Pro] (1 mL). The mixture stirred at 80 °C for an appropriate time (table 2). After completion of the reaction, as monitored by TLC, water (10 mL) was added to the reaction mass, the product was extracted into ethyl acetate (3 × 20 mL). The combined organic extract was dried over anhydrous sodium sulphate, evaporated under reduced pressure to give crude product, which was purified by silica gel column chromatography. Table 2, Entry 1, $^1$H NMR (300 MHz, $CDCl_3$) $\delta = 2.41$ (s, 3H), 3.20–3.40 (m, 2H), 3.69 (brs, 1H), 5.20 (dd, 1H, $J = 1.6$ and 10.1 Hz), 7.20–7.30 (m, 7H), 7.80 (d, 2H, $J = 7.8$ Hz); EIMS: $m/z$ 277 ($M^{+\cdot} + 1$). $^{13}$C NMR (75 MHz, CDCl3) $\delta = 21.67$, 63.99, 68.44, 125.63, 128.00, 128.30, 128.74, 130.10, 136.11, 140.64, 145.27. Anal. calcd for $C_{15}H_{16}O_3S$: C, 65.19; H, 5.84; S, 11.60. Found: C, 65.14; H, 5.90; S, 11.63. Entry 3, $^1$H NMR (300 MHz, $CDCl_3$) $\delta = 1.96$–2.10 (m, 8H), 2.41 (s, 3H), 3.10–3.20 (m, 1H), 3.80 (brs, 1H), 4.27–4.33 (m, 1H), 7.25 (d, 2H, $J = 7.9$ Hz),

7.80 (d, 2H, $J = 7.9$ Hz); EIMS: $m/z$ 239 ($M^{+\cdot}+1$). Entry 4, $^1$H NMR (300 MHz, $CDCl_3$) $\delta = 1.97$–$2.09$ (m, 8H), 3.11–3.19 (m, 1H), 3.85 (brs, 1H), 4.47–4.33 (m, 1H), 7.47–7.71 (m, 3H), 7.93–7.98 (m, 2H); EIMS: $m/z$ 226 ($M^{+\cdot} + 1$). Entry 7, $^1$H NMR (300 MHz, $CDCl_3$) $\delta = 1.90$–$2.05$ (m, 6H), 2.40 (s, 3H), 3.11–3.21 (m, 1H), 3.90 (brs, 1H), 4.25–4.30 (m, 1H), 7.26 (d, 2H, $J = 8.1$ Hz), 7.85 (d, 2H, $J = 8.1$ Hz); EIMS: $m/z$ 225 ($M^{+\cdot} + 1$). Entry 8, $^1$H NMR (300 MHz, $CDCl_3$) $\delta = 1.96$–$2.05$ (m, 6H), 3.10–3.20 (m, 1H), 3.95 (brs, 1H), 4.45–4.35 (m, 1H), 7.46–7.70 (m, 3H), 7.92–7.99 (m, 2H); EIMS: $m/z$ 211 ($M^{+\cdot} + 1$). Entry 13, $^1$H NMR (300 MHz, $CDCl_3$) $\delta = 3.14$ (s, 3H), 3.15–3.30 (m, 2H), 3.60 (brs, 1H), 5.18 (dd, 1H, $J = 1.6$ and 10.1 Hz), 7.20–7.30 (m, 5H); EIMS: $m/z$ 201 ($M^{+\cdot} + 1$).

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