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β-Cyclodextrin promoted stereoselective synthesis of β-hydroxysufones from β-keto-sulfones using $NaBH_4$-$CaCl_2$ as an efficient reagent in water

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ABSTRACT

β-Cyclodextrin promoted stereoselective synthesis of β-hydroxysufones from β-keto-sulfones using $NaBH_4$-$CaCl_2$ as an efficient reagent in water is described. Obtained products were purified with column chromatography and crystallization and all products were characterized by ^{1}H NMR and mass spectral data

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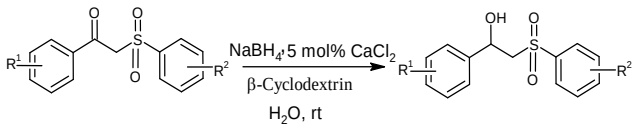
Introduction

Sulfones are very important and fascinating branch of organic chemistry.[1] The presence of the sulfone group, in an organic compound adds variety to its chemical architecture and also enhances the biological activity of the compound. Among sulfones, β-keto-sulfones are very important group of intermediates, as they are precursors in Michael, Knoevenagel reactions,[2-3] in the preparation of acetylenes, allenes, chalcones,[4-9] vinylsulfones,[10] and polyfunctionalized 4H-pyrans.[11] β-Keto-sulfones are useful for the synthesis of ketones by facile reductive elimination of the sulfone group.[12] In addition to this β-keto-sulfones are useful for the synthesis of optically active β-hydroxysulfones,[13] they are also obtained both by chemical methods, for example, via oxidation of chiral β-hydroxysulfoxides, and by the biocatalytic approaches. The latter comprise of baker's yeast-mediated reduction of β-ketosulphones leading to the (S)-enantiomers of the corresponding β-hydroxysulfones and a lipase catalyzed acylation of recemic β-hydroxysulfones, performed under kinetic resolution conditions.[14-20]



Scheme 1.

The optically active β-hydroxysulfones[21] are of great utility in organic synthesis, they have been used as building blocks in the synthesis of a variety of enantio-pure cyclic compound classes such as recemic and non-recemic lactones, tetra hydrofurans and furanones, and in the preparation of other β-hydroxysulfones. Recently, compounds of this class have proved its efficiency as a chiral controller in asymmetric Diels-Alder and alkylation reactions. Although several methods synthesis of β-hydroxysulfones has been reported in literature, but not explored much.[22] We report here our extensive studied developments of new synthetic methodologies on β-keto-sulfones,[23] β-cyclodextrin promoted synthesis of β-hydroxysulfones from β-keto-sulfones, using $NaBH_4$-$CaCl_2$ as an efficient reagent in water.

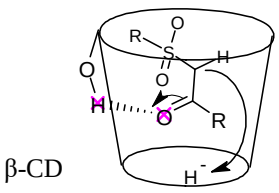


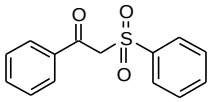
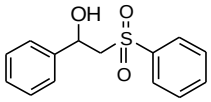
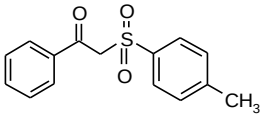
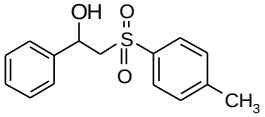
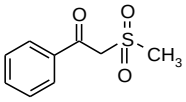
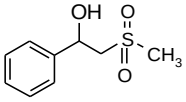
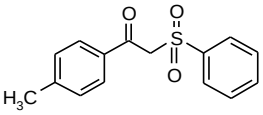
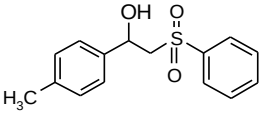
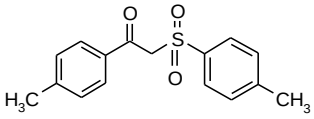
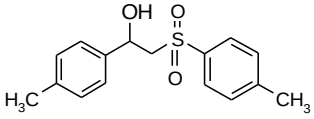
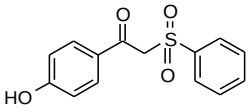
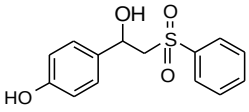
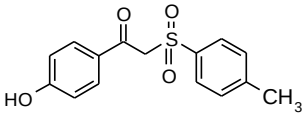
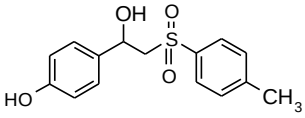
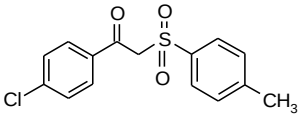
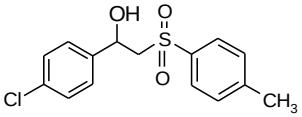
Figure 1.

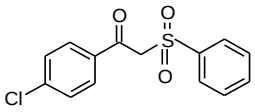
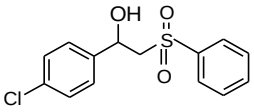
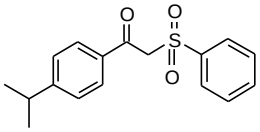
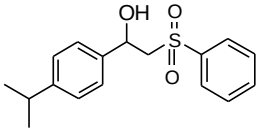
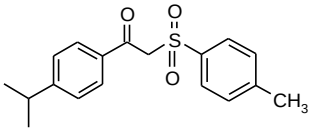
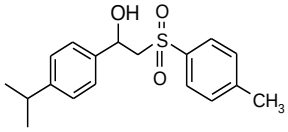
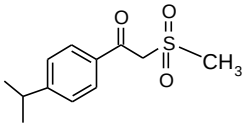
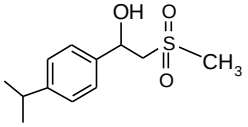
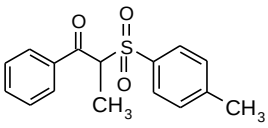
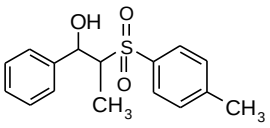
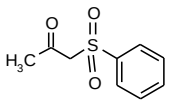
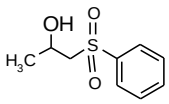
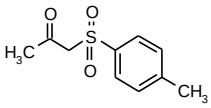
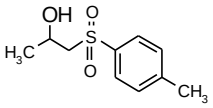
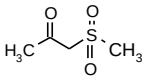
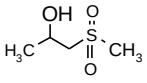
In recent years β-Cyclodextrins[24] have gained very much attention in organic trance formations, they are cyclic oligosaccaharides possessing hydrophobic cavities, which binds

substrates selectively and which catalyze chemical reactions by supramolecular catalysis involving eversible formation of host-guest complexes by non-covalent binding as seen in enzymes. Complexation depends on the size, shape and hydrophobicity of the guest molecules, thus mimicking biochemical selectivity, which is due to the orientation of the substrate by complex formation. This positions only certain regions for attack and can be superior to chemical selectivity, which involves random attack dependent on the intrinsic reactivity of the substrate at different positions.

We first examined the reaction of p-toluene sulfonyl acetophenone with $NaBH_4$-$CaCl_2$ in the presence of catalytic amount of β-cyclodextrin in aqueous medium to yield corresponding β-hydroxysulfones, in excellent yield (>95%) with high enantioselectivity (99%).

Table 1. β-Cyclodextrin promoted synthesis of β-hydroxysulfones from β-keto-sulfones, using $NaBH_4$-$CaCl_2$.

Entry	Product	Product	Time (min)	Yield (%)[a]
1			30	96
2			30	95
3			45	85
4			30	95
5			30	90
6			30	95
7			30	95
8			30	95

9			30	96
10			30	95
11			30	95
12			30	92
13			30	90
14			45	95
15			45	96
16			60	95

[a]Isolated yields after column chromatography/crystallization and all products gave satisfactory spectral data

This result were encouraged us to carry out the reaction in the presence of $NaBH_4$-$CaCl_2$ and β-cyclodextrin, several β-keto-sulfones was reacted to afford corresponding products in excellent yields (Table 1).

The $NaBH_4$ acts as efficient reducing reagent in the presence of catalytic amount of $CaCl_2$. The sodium borohydride first reacts with $CaCl_2$ to give calcium borohydride, which acts as efficient reducing reagent, due to presence of its vacant d-orbitals, more surface area and variable valancy of calcium ion, it stabilizes the hydride ion and act as efficient reducing reagent.

In conclusion we have described β-cyclodextrin promoted synthesis of various β hydroxysulfones from β keto-sulfones using $NaBH_4$-$CaCl_2$ as an efficient reagent.

Typical experimental procedure

To a solution of β-ketosulfone (10 mmol) water (10 mL) was added β-cyclodextrin (5 mol%), $NaBH_4$ (10 mmol) and $CaCl_2$ (5 mol%). The mixture stirred at room temperature for the appropriate time (Table 1). After completion of the reaction, as monitored by TLC, the reaction mass was quenched with aqueous ammoniumchloride and the product was extracted into ethyl acetate (3 x 10 mL). The combined organic extracts were dried over anhydrous sodium sulphate, evaporated under reduced pressure to give crude product, which was purified by silica column chromatography and all products gave satisfactory spectral data.

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