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Tetrahedron Letters 47 (2006) 3853–3856
Tetrahedron Letters

Facile polyethylene glycol (PEG-400) promoted synthesis of β-ketosulfones☆

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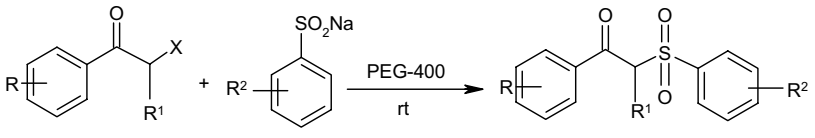
Received 22 February 2006; revised 22 March 2006; accepted 29 March 2006
Available online 27 April 2006

Abstract—An efficient and convenient synthesis of β-ketosulfones is described. Reaction of an α-haloketone with sodium alkyl/aryl sulphinate yields the corresponding β-ketosulfone promoted by polyethylene glycol (PEG-400) as an efficient reaction medium.

Among sulfur containing compounds, β-ketosulfones are an important group of intermediates[1] in Michael and Knoevenagel reactions,[2,3] and are valuable precursors in the synthesis of acetylenes, allenes, chalcones,[4–9] vinylsulfones[10] and polyfunctionalized 4*H*-pyrans.[11] β-Ketosulfones are useful for the synthesis of ketones by facile reductive elimination of the sulfone group[12] and also in the preparation of epoxy sulfones.[13] In addition, β-ketosulfones are precursors for optically active β-hydoxysulfones.[14] Although several methods for their synthesis[15–24] and their chemical reactions[25,26] have been reported in the literature, most are associated with long reaction times, tedious reaction conditions and low yields. Hence, there is a need for a rapid and efficient method for the synthesis of β-ketosulfones.

Polyethylene glycol promoted reactions[27] have attracted the attention of organic chemists due to their ease of workup, the ability to act as phase transfer catalysts and their inexpensive and eco-friendly nature. In this connection, we report a synthesis of β-ketosulfones in the presence of polyethylene glycol (PEG-400) as an efficient reaction medium.

Reaction of sodium *p*-toluenesulphinate with a phenacyl bromide/phenacyl chloride in refluxing ethanol for 10–12 h resulted in the formation of the corresponding β-ketosulfone in 50% yield. However, when we carried out the reaction in polyethylene glycol (PEG-400), the formation of *p*-toluenesulfonylacetophenone, that is, β-ketosulfone **3** (Scheme 1), was complete in 10 min in 96% yield. Encouraged by the speed of the reaction, various α-haloketones were reacted with sodium alkyl/aryl sulphinates in PEG-400 to yield β-ketosulphones **3** in excellent yields. The reaction is facile even with hindered α-haloketones, such as those in entries 13 and 17 in Table 2. In order to compare the rate of the reaction in PEG-400, we carried out the reaction in different solvents (Table 1). The poor



1 X = Cl, Br **2** **3**

Scheme 1.

Keywords: Polyethylene glycol (PEG-400); β-ketosulfones; α-haloketone; Sodium alkyl/aryl sulphinate.
☆ IICT Communication No. 060318.
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doi:10.1016/j.tetlet.2006.03.181

Table 1. Solvent effect on the reaction of phenacyl bromide with sodium *p*-toluenesulphinate at room temperature

Entry	Solvent	Time	Yield (%)
1	PEG	10 min	96
2	PEG/CH_3CN (1:1)	10 min	95
3	EtOH	24 h	50
4	CH_3CN	24 h	49
5	IPA	24 h	40
6	C_6H_6	24 h	Nil
7	$CHCl_3$	24 h	Nil
8	DCM	24 h	Nil

yields in hydroxylic and less polar solvents are probably due to the lower solubilities of the sulphinate salt in these solvents, coupled with the fact that the nucleophile ($PhSO_2^-$) is solvated in hydroxylic solvents, thereby reducing its effective nucleophilicity. It was observed that in PEG-400 the reaction was complete with very fast times and in excellent yields (Scheme 1, Table 2).

In conclusion, we have disclosed an inexpensive, fast and efficient synthesis of β-ketosulfones using polyethyl ethlylene glycol 400 as the reaction medium.

Typical experimental procedure (Scheme 1): A mixture of the sodium alkyl/aryl sulphinate (1.1 mmol) and the α-haloketone (1 mmol) was taken in 10 ml of polyethylene glycol, and stirred at rt for the appropriate time (see Table 2). After completion of the reaction, as monitored by TLC, the reaction mass was poured into water and extracted into ethyl acetate. The organic layer was removed under reduced pressure, and the crude product was purified by column chromatography or crystallized from methanol. The PEG was recovered from the aqueous layer and reused without loss of activity.

Table 2. Synthesis of β-ketosulfones by using polyethylene glycol (PEG-400) as an efficient reaction medium at room temperature

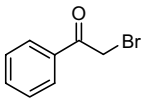
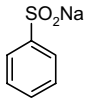
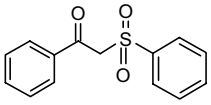
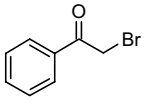
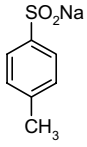
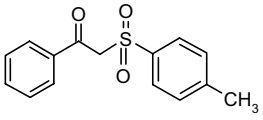
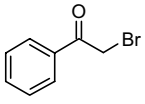
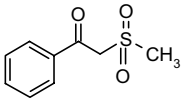
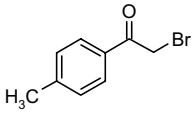
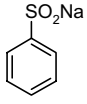
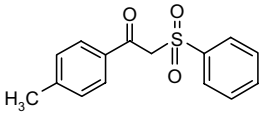
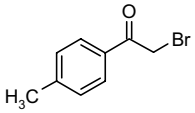
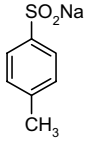
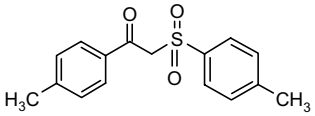
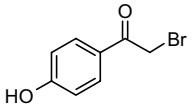
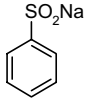
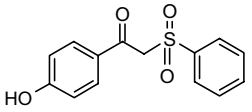
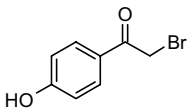
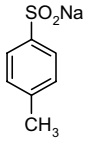
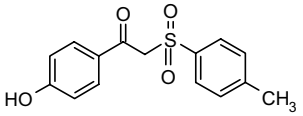
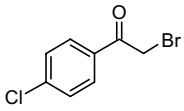
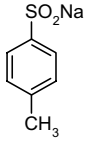
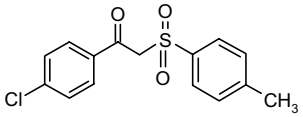
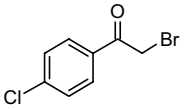
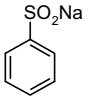
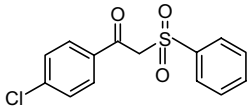
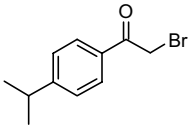
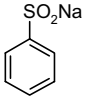
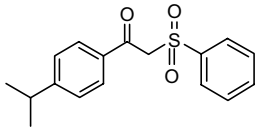
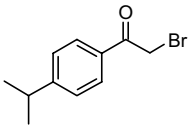
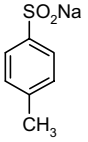
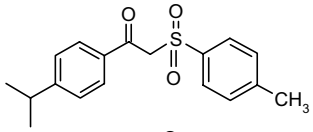
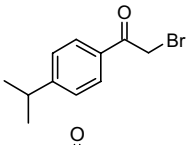
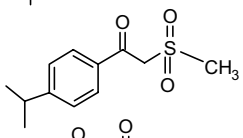
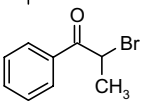
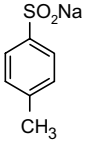
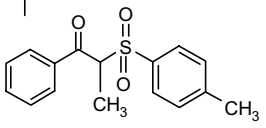
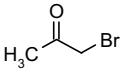
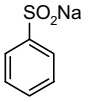
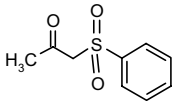
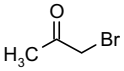
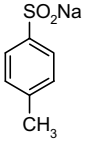
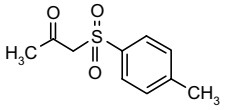
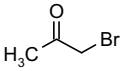
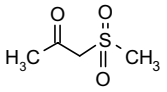
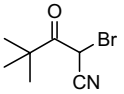
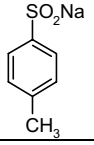
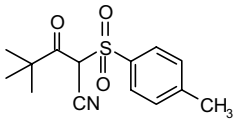
Entry	α-Haloketone	Sodium alkyl/aryl sulphinate	Product	Time (min)	Yield[a] (%)
1				10	96
2				10	95
3		CH_3SO_2Na		30	80
4				10	95
5				10	90
6				10	95
7				10	93
8				10	93

Table 2 (*continued*)

Entry	α-Haloketone	Sodium alkyl/aryl sulphinate	Product	Time (min)	Yield[a] (%)
9				10	94
10				10	95
11				10	90
12		CH_3SO_2Na		10	92
13				10	90
14				10	95
15				10	95
16		CH_3SO_2Na		10	95
17				30	90

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

Acknowledgements

The authors thank Director IICT and CSIR for the financial support.

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