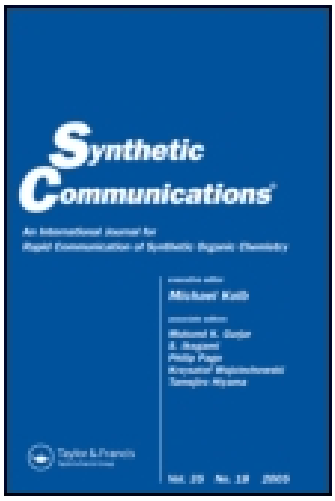

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HYPERVALENT IODINE IN SYNTHESIS. 66. ONE POT PREPARATION OF β-KETO SULFONES BY REACTION OF KETONES, [HYDROXY(TOSYLOXY) IODO] BENZENE, AND SODIUM SULFINATES

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HYPERVALENT IODINE IN SYNTHESIS. 66. ONE POT PREPARATION OF β-KETO SULFONES BY REACTION OF KETONES, [HYDROXY(TOSYLOXY) IODO] BENZENE, AND SODIUM SULFINATES

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ABSTRACT

One pot reactions of ketones, [hydroxy(tosyloxy)iodo] benzene and sodium sulfinates lead to the formation of the corresponding β-keto sulfones under mild conditions and in good yield.

The sulfonyl group is increasingly attracting attention as a useful functionality in organic synthesis. β-Keto sulfones occupy a premier position as derivatives of sulfones and display a broad range of synthetic versatility.[1–5] One particularly well-recognized application of the β-keto

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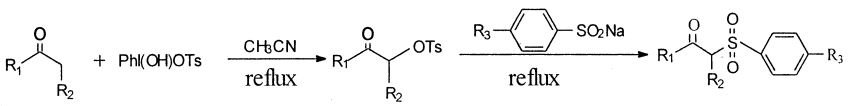
sulfone moiety in synthesis is in α-alkylation with subsequent reductive desulfurization.[6]

According to the importance of β-keto sulfones in organic synthesis, there are many methods available for their synthesis, including Thorpe reaction of cyano Sulfones,[7] oxidation of corresponding β-ketone sulfides or sulfoxides,[8] Claisen condensations of esters with dimethyl sulfone[9] and substitution of α-haloketones with sodium sulfinates.[10] But these methods are deficient in some respects, such as the use of strong base, strict reaction conditions, toxic reagent, and not readily available starting materials. It is necessary to develop a new, effective method for the synthesis of β-keto sulfones.

There is considerable current interest and research activity in hypervalent iodine compounds.[11] It has been demonstrated that the [hydroxy (tosyloxy)iodo] benzene (HTIB, **2**) is a versatile reagent in organic synthesis and especially useful is the reaction of HTIB with ketones leading to tosyloxylketones. This reaction followed by treatment with appropriate nucleophilies *in situ* offers a variety of valuable synthetic methods. It promoted us to examine the α-tosyoxylation of ketones with HTIB followed by treatment with sodium sulfinates. Such reaction would provide a new, effective method for synthesis of β-keto sulfones without use of lachrymatory and toxic α-halohetones.

Here we report a mild, one-pot conversion of ketones to the corresponding β-keto sulfones through treatment of ketones with HTIB and sodium sulfinate successively (Scheme 1).



1 **2** **3** **4**

Scheme 1.

First, ketone reacts with HTIB to produce α-tosyloxy ketone **3** that then reacts with sodium sulfinate to give corresponding β-keto sulfone. The results are summarized in Table 1. Solvent is an important factor for this reaction. In the first step, reaction can complete smoothly in acetonitrile, but in the second step, the reaction proceeds difficultly because of the poor solubility of sodium sulfinate in acetonitrile, so the addition of some water is necessary.

Table 1. Synthesis of β-Keto Sulfones (4)

	R_1	R_2	R_3	Yield[a] (%)	M.P.[b] (°C)	Lit. M.P. (°C)
4a	CH_3	H	H	56	56–57	57[12]
4b	-$(CH_2)_4$-		H	32	83–85	85–86[13]
4c	CH_3CH_2	CH_3	H	80	oil (GC 99.77%)	no report
4d	C_6H_5H	H	73	92–93	96[12]	
4e	p-$CH_3C_6H_4$	H	H	64	121–123	118–119[14]
4f	p-$CH_3OC_6H_4$	H	H	60	108–110	114[15]
4g	p-ClC_6H_4	H	H	65	138–140	141–142[14]
4h	p-FC_6H_4	H	H	62	118–119	116–117.5[16]
4i	m-$NO_2C_6H_4$	H	H	60	126–128	no report
4j	C_6H_5	CH_3	H	66	76–77	77[17]
4k	CH_3	H	CH_3	66	51–52	52[12]
4l	C_6H_5	H	CH_3	80	108–109	110[12]
4m	CH_3	H	Cl	54	81–82	83[12]
4n	C_6H_5	H	Cl	70	133–134	134.5[12]

[a]Isolated yield based on ketone.
[b]Melting points are uncorrected.

The reaction was found to be general and applicable to aliphatic or aromatic ketones. Several aromatic ketones containing various substituents, such as para-chloro, para-methyl, para-methoxy, meta-nitro were successfully reacted. However, this method was not suitable for unsymmetrical aliphatic ketones, since there was not a desirable regioselectivity for them in the α-tosyoxylation process.

In conclusion, we have provided a new, effective method for synthesis of β-keto sulfones. It has some advantages over previous methods, such as simple procedure, mild reaction conditions and good yields.

EXPERIMENTAL SECTION

IR spectra were recorded as KBr pellets on PE-683 Infrared Spectrophotometer. ^{1}H-NMR spectra were recorded on PMK-60 Spectrometer using CCl_4 as the solvent with TMS as an internal standard. MS was recorded on HP-5989B Mass Spectrometer. Elemental analysis was performed on a Carlo Zrba EA 1106 instrument. GC Purity was recorded on Schimadzu GC-16A.

Typical Procedure for Synthesis of 1-Phenyl-2-(Phenylsulfonyl) Ethanone (4d)

Acetophenone (0.12 g, 1 mmol) and HTIB (0.392 g, 1 mmol) were added successively with efficient stirring to acetonitrile (5 mL). The reaction mixture was refluxed for 40 min, then sodium phenylsulfinate (0.4 g, 2 mmol) and water (1 mL) were slowly added. The mixture was refluxed for 2 h. Subsequently, the reaction mixture was poured into water (20 mL) and extracted with dichloromethane (3×10 mL). The combined organic phase was dried with anhydrous magnesium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by preparative TLC (acetate/cyclohexane = 1:3) to obtain 4d (0.19 g, 73% yield) as white solide.

Spectroscopic Data

4a. IR (cm^{-1}) 1740 (C=O), 1295, 1155 (O = S = O). ^{1}H-NMR, ppm: δ 2.40 (s, 3H), 4.07 (s, 2H), 7.57–8.24 (m, 5H).

4b. IR (cm^{-1}) 1719 (C=O), 1309, 1144 (O=S=O). ^{1}H-NMR, ppm: δ 1.35–2.75 (m, 8H), 3.73 (t, 1H), 7.35–7.88 (m, 5H).

4c. IR (cm^{-1}) 1721 (C=O), 1309, 1150 (O=S=O). ^{1}H-NMR, ppm: δ 0.9 (t, 3H), 1.25 (d, 3H), 2.45–2.81 (q, 2H), 4.03–4.40 (q, 1H), 7.41–8.03 (m, 5H). MS *m*/*z* 226 (M^+, 4.97), 85 (5.27), 141 (11.92), 57 (100.00). GC Purity: 99.77%.

4d. IR (cm^{-1}) 1690 (C=O), 1320, 1160 (O=S=O). ^{1}H-NMR, ppm: δ 4.70 (s, 2H), 7.37–8.27 (m, 10H).

4e. IR (cm^{-1}) 1680 (C=O), 1300, 1165 (O=S=O). ^{1}H-NMR, ppm: δ 2.43 (s, 3H), 4.55 (s, 2H), 7.16–8.10 (m, 9H).

4f. IR (cm^{-1}) 1680 (C=O), 1310, 1160 (O=S=O). ^{1}H-NMR, ppm: δ 3.84 (s, 3H), 4.48 (s, 2H), 6.68–8.21 (m, 9H).

4g. IR (cm^{-1}) 1705 (C=O), 1305, 1140 (O=S=O). ^{1}H-NMR, ppm: δ 4.57 (s, 2H), 7.40–8.27 (m, 9H).

4h. IR (cm^{-1}) 1687 (C=O), 1315, 1165 (O=S=O). ^{1}H-NMR, ppm: δ 4.59 (s, 2H), 6.97–8.07 (m, 9H).

4i. IR (cm^{-1}) 1700 (C=O), 1318, 1152 (O=S=O). ^{1}H-NMR, ppm: δ 4.71 (s, 2H), 7.15–8.81 (m, 9H). Elemental Analysis: Calculated C, 55.08; H, 3.63; N, 4.59. Found C, 54.94; H, 3.73; N, 4.65.

4j. IR (cm^{-1}) 1690 (C=O), 1310, 1145 (O=S=O). ^{1}H-NMR, ppm: δ 1.50 (d, 3H), 5.15 (q, 1H), 7.40–8.30 (m, 10H).

4k. IR (cm^{-1}) 1736 (C=O), 1340, 1150 (O=S=O). ^{1}H-NMR, ppm: δ 2.24 (s, 3H), 2.37 (s, 3H), 2.48 (s, 3H), 4.04 (s, 2H), 7.20–7.94 (m, 4H).

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4l. IR (cm^{-1}) 1695 (C=O), 1327, 1156 (O=S=O). ^{1}H-NMR, ppm: δ 2.33 (s, 3H), 4.60 (s, 2H), 7.13–8.20 (m, 9H).

4m. IR (cm^{-1}) 1735 (C=O), 1316, 1150 (O=S=O). ^{1}H-NMR, ppm: δ 2.32 (s, 3H), 4.08 (s, 2H), 7.21–7.97 (m, 4H).

4n. IR (cm^{-1}) 1700 (C=O), 1315, 1146 (O=S=O). ^{1}H-NMR, ppm: δ 4.65 (s, 2H), 7.23–8.10 (m, 9H).

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