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Synthesis of α-iodo β-ketosulfones and α-iodo methylsulfones using iodine monochloride☆

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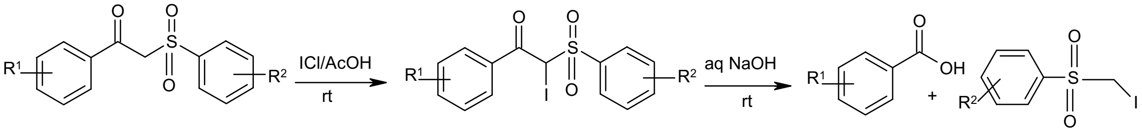
Abstract—The synthesis of α-iodo β-ketosulfones and α-iodo methylsulfones is described. Reaction of β-ketosulfones with iodine monochloride in acetic acid at room temperature gave the corresponding α-iodo β-ketosulfones, which, on treatment with aqueous alkali, underwent base-induced cleavage to afford α-iodo methylsulfones.

1. Introduction

Sulfones are of great importance in organic synthesis[1] and among them β-ketosulfones are important as they are precursors in Michael and Knoevenagel reactions,[2,3] in the preparation of acetylenes, allenes, chalcones,[4–9] vinylsulfones[10] and polyfunctionalized 4*H*-pyrans.[11] β-Ketosulfones are useful for the synthesis of ketones by reductive elimination of the sulfone group[12] as well as optically active β-hydroxysulfones.[13] In addition, β-ketosulfones on halogenation followed by base induced cleavage give α-halo methylsulfones and α,α-dihalo methylsulfones (halogen = Cl, Br)[14] which are excellent α-carbanion stabilizing substituents[15] and precursors for the preparation of alkenes,[16] aziridines[17] and epoxides.[18]

Makosza et al.[19] utilized chloromethyl phenylsulfones and chloromethyl *p*-tolylsulfones in vicarious nucleophilic substitution (VNS) reactions with nitro-arenes to afford VNS adducts. These adducts have been elaborated into both 3-sulfonyl-substituted indoles and indazole derivatives.[20] Haloalkylsulfones are useful in preventing aquatic organisms from attaching to fishing nets and ship hulls,[21] in herbicide compositions,[22] as bactericidal[23] and anti-fungal[24] agents and as algaecides[25] and insecticides.[26] Several methods for the synthesis of α-halo β-ketosulfones[14] and α-halo methylsulfones[27] (halogen = Cl, Br) have been reported in the literature. α-Halo β-ketosulfones and α-halomethylsulfones do not undergo Finklestein reactions[28] due to a strong retardation effect by the sulfone.[29] To the best of our knowledge α-iodo β-ketosulfones and α-iodo methylsulfones are very difficult to prepare.[14,27] We report here an efficient synthesis of α-iodo β-ketosulfones and α-iodo methylsulfones using iodine monochloride as iodine source.

β-Ketosulfones do not react with KI and molecular I_2. It has been reported that the halogenation of β-ketosulfones proceeds by attack of an electropositive halogen atom,[14] which is readily available from iodine monochloride.[30] We reacted several β-ketosulfones[31]



Scheme 1.

Keywords: β-Ketosulfones; α-Iodo β-ketosulfones; α-Iodo methylsulfones.

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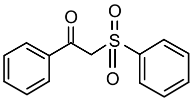
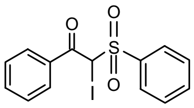
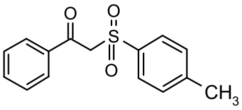
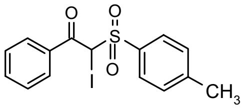
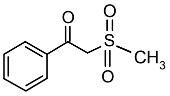
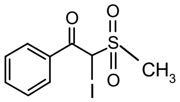
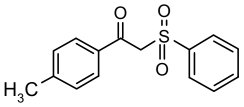
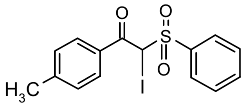
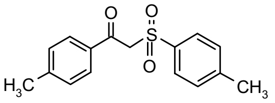
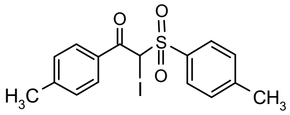
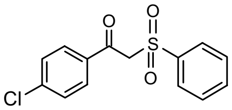
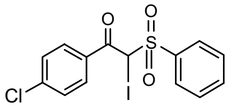
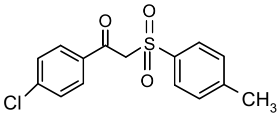
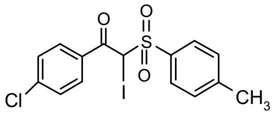
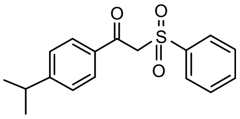
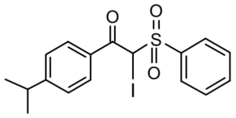
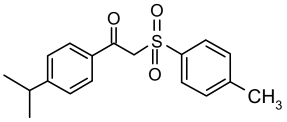
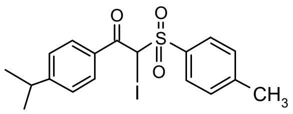
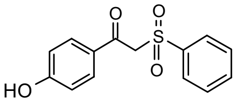
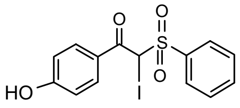
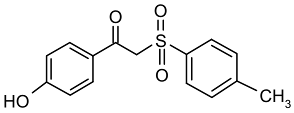
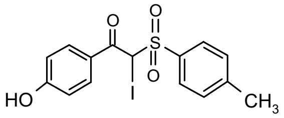
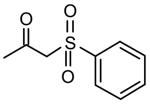
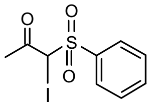
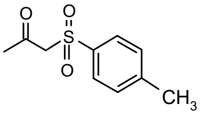
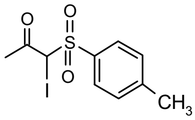
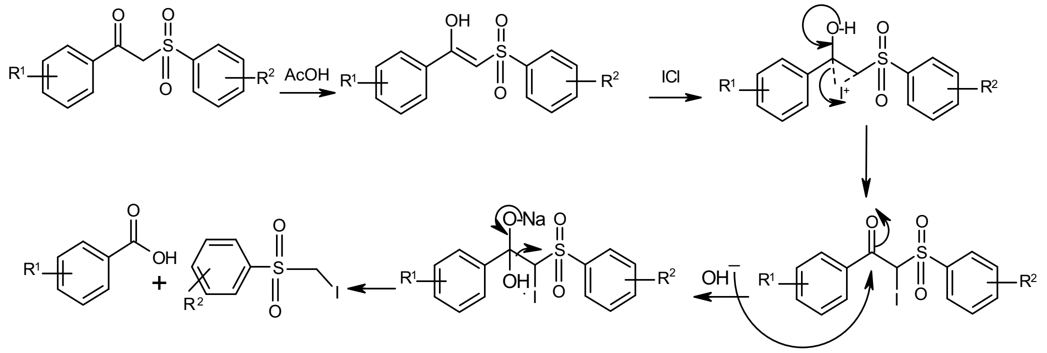
Table 1. Synthesis of α-iodo β-ketosulfones using iodine monochloride in acetic acid

Entry	β-Ketosulfone	Product	Time (h)	Yield[a] (%)
1			12	90
2			12	90
3			24	60
4			12	75
5			15	80
6			12	78
7			14	80
8			15	75
9			18	88
10			15	85
11			12	80
12			12	85
13			12	90

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

with iodine monochloride in acetic acid to yield the corresponding α-iodo β-ketosulfones (Schemes 1, 2 and Table 1). The reaction was attempted in $CHCl_3$, CCl_4, CH_2Cl_2, EtOH and H_2O but without success; acetic acid proved to be the best reaction medium. Further, the α-iodo β-ketosulfones on treatment with aqueous alkali at room temperature underwent base-induced cleavage to give the corresponding α-iodo methylsulfones in 30 min and in excellent yields (Schemes 1, 2 and Table 2).



Scheme 2. Proposed mechanism.

Table 2. Synthesis of α-iodo methylsulfones via base-induced cleavage using aqueous NaOH

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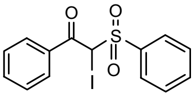
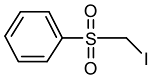
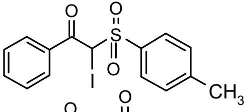
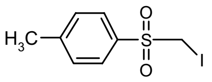
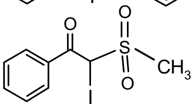
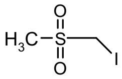
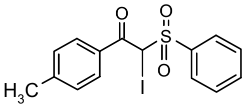
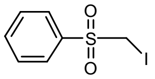
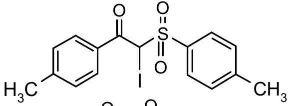
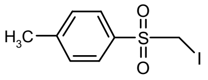
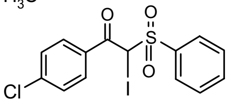
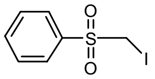
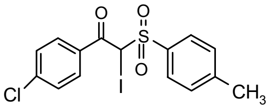
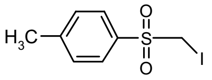
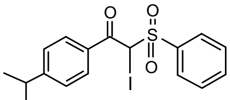
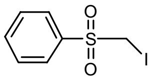
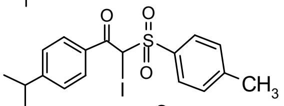
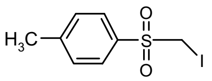
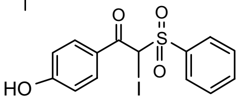
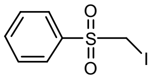
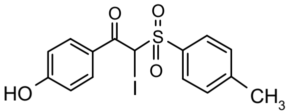
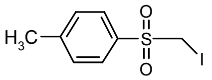
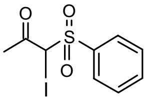
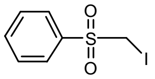
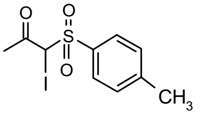
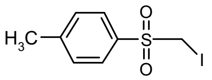
1			95
2			94
3			85
4			90
5			90
6			88
7			89
8			95
9			93
10			92
11			90
12			91
13			95

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

2. Conclusions

We have described an efficient synthesis of various α-iodo β-ketosulfones and α-iodo methylsulfones, by the reaction of β-ketosulfones with iodine monochloride as an iodine source, followed by a base-induced cleavage.

2.1. Synthesis of α-iodo β-ketosulfones

To a solution of β-ketosulfone (10 mmol) in acetic acid (10 mL) was added iodine monochloride (11 mmol) and the mixture stirred at room temperature for the appropriate time (Table 1). After completion of the reaction, as monitored by TLC, the acetic acid was removed under reduced pressure, water was added and product extracted into ethyl acetate (3 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate and evaporated under reduced pressure to give the crude product which was purified by silica column chromatography, eluting with 2:9 ethyl acetate and hexane. Table 1, entry 2. White solid, mp = 149–150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (3H, s), 6.45 (1H, s), 7.40 (2H, d, $J = 8.45$ Hz), 7.45 (2H, d, $J = 8.49$ Hz) 7.49 (1H, t, $J = 2.45$ Hz), 7.75 (2H, d, $J = 8.49$ Hz) 7.85 (2H, d, $J = 8.45$ Hz); EIMS. m/z, $M^+ = 400$.

2.2. Synthesis of α-iodo methylsulfones

To a solution of 10% aqueous NaOH (5 mL) was added the α-iodo β-ketosulfone (5 mmol) at room temperature and the mixture stirred for 30 min. After completion of the reaction as monitored by TLC, the reaction was extracted into diethyl ether, the extract dried over anhydrous sodium sulfate and evaporated to give the corresponding crude α-iodo methylsulfone, which was purified by column chromatography, eluting with 1:9 ethyl acetate and hexane. Table 2, entry 2. White solid, mp = 119–120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (3H, s), 4.41 (2H, s), 7.40 (2H, d, $J = 8.45$ Hz), 7.85 (2H, d, $J = 8.45$ Hz); EIMS m/z $M^+ = 296$.

Acknowledgements

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