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LETTERS

A novel method for the synthesis of aryl sulfones

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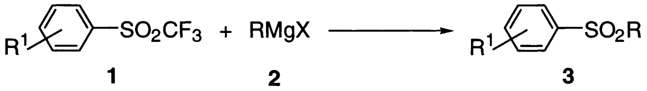
Abstract—New sulfones were produced from aryl trifluoromethyl sulfones and Grignard reagents in good to high yields. The advantage of this transformation over a previous method by which sulfones were prepared from sulfonyl fluorides and organometallic reagents is discussed. © 2001 Published by Elsevier Science Ltd.

Sulfones, by virtue of their diverse chemistry, are valuable intermediates in organic transformations.[1] Most uses of sulfones involve sulfonylcarbanions, which react with a wide range of electrophiles to produce new sulfones that may be further transformed to olefins by reduction, elimination or cyclization by a sulfur dioxide extrusion process. Vinyl sulfones are excellent acceptors in conjugate addition reactions and participate in cycloaddition processes. In addition, alkyl- or aryl-sulfonyl groups can act as leaving groups under promotion by transition metals or Lewis acids.

Although sulfones are commonly obtained by oxidation of the corresponding sulfides,[1c,2–5] preparative methods that involve the direct formation of the C–SO_2 bond are also valuable. These methods include nucleophilic displacements by a sulfinic acid salt,[1e,2,4] Friedel–Crafts reactions of sulfonyl halides with activated aromatic compounds,[6] and reactions of sulfonyl fluorides with organolithium species or Grignard reagents.[7–10] Although the latter process is useful for the synthesis of diaryl sulfones, when an aliphatic organometallic species bearing an alpha proton is treated with a sulfonyl fluoride, 1,1-disulfones tend to arise through further deprotonation and sulfonylation of the initial product.[7,10] In fact, this can be the dominant process, even with Grignard reagents. In this paper, we present an alternative to sulfonyl fluorides that overcomes this limitation.

The general process is shown in Eq. (1) in which an aryl trifluoromethyl sulfone (aryl triflone) reacts with a Grignard reagent to produce a new sulfone.



(1)

Trifluoromethylsulfonylbenzene[6] when treated with various Grignard reagents **2**, either at room temperature or at reflux in tetrahydrofuran (THF), afforded sulfones **3** in good yields. Examples are shown in Table 1. In most cases, the reaction was completed in about 1 hour at room temperature. An aqueous ammonium chloride quench, followed by extractive work-up, afforded sulfones **3** and, in many cases, no further purification was needed.

In general, primary saturated and allylic Grignards (entries a–d) were quite suitable for this reaction. The yields from these reactions ranged from 56 to 83%. Secondary Grignards (entries e and f) also reacted satisfactorily, although elevated temperature was needed in the case of isopropyl magnesium chloride. *tert*-Butyl magnesium chloride did not react with trifluoromethylsulfonylbenzene even after reflux in THF overnight. Treatment of trifluoromethylsulfonylbenzene with aryl Grignards (entries g and h) also produced the corresponding diaryl sulfones in good yields. With vinyl magnesium bromide, consumption of trifluoromethylsulfonylbenzene without formation of the desired sulfone was observed at various temperatures. *para*-Substituted phenyl trifluoromethyl sulfones (entries i–k) were also suitable for this reaction.

No 1,1-disulfones were observed from the reactions of triflones with aliphatic Grignard species bearing alpha protons. Although products **3** were undoubtedly metallated under the reaction conditions,[7,10] the resulting

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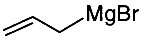
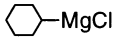
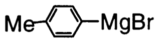
Table 1.

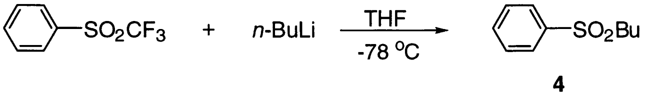
Entry	R^1	RMgX	Temperature	Time (hour)	yield (%)
a	H	MeMgBr	r.t.	1	77
b	H	EtMgBr	r.t.	1	56
c	H	$C_8H_{17}MgBr$	r.t.	1	83
d	H		r.t.	1	77
e	H	*i*-PrMgCl	reflux/THF	16	54
f	H		r.t.	1	67
g	H	PhMgBr	r.t.	1	74
h	H		r.t.	1	56
i	4-Cl	MeMgBr	r.t.	1	47
j	4-Cl	PhMgBr	r.t.	1	50
k	$4\text{-}NH_2$	MeMgBr	r.t.	16	28

Experimental procedure: To a solution of triflone **1** (1 mmol) in anhydrous THF (2 mL) was added Grignard reagent **2** (5 mmol) in THF or diethyl ether at 0°C and the mixture stirred at the temperature and for the time specified in Table 1. The reaction was quenched with ice-cold saturated ammonium chloride and the resulting aqueous mixture extracted with ethyl acetate (3×). The organic portions were combined, washed with saturated sodium bicarbonate and brine, dried over sodium sulfate, filtered, and concentrated to give sulfone **3**. Silica gel column chromatography was applied, when needed.

species were not sulfonylated by aryl triflone, in contrast to their facile sulfonylation by aryl sulfonyl fluoride.

The logical byproduct of the described reaction is a trifluoromethyl magnesium halide, which is quite difficult to obtain.[11] However, attempts to trap this useful Grignard reagent in situ were not successful.

In addition, trifluoromethylsulfonylbenzene also reacted with *n*-BuLi (2 equiv.) to give sulfone **4** in 38% yield. The reaction was conducted at −78°C for 30 minutes and quenched with ammonium chloride solution at the same temperature. No 1,1-disulfone was observed from this reaction either. No additional products were identified from this reaction.



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In summary, we have presented a new and effective procedure for the preparation of aryl–alkyl and diaryl sulfones. This method should serve as a useful addition to the existing methods for the synthesis of sulfones.

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