## ETHYLMAGNESIUM BROMIDE MEDIATED DESULFINYLATION OF $\alpha$ -HALO- $\beta$ -KETOSULFOXIDES GIVING $\alpha$ -HALOKETONES, AND TRAPPING OF THE MAGNESIUM ENOLATE INTERMEDIATE

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Summary Treatment of  $\alpha$ -halo- $\beta$ -ketosulfoxides with EtMgBr gives  $\alpha$ -haloketones in high yields after protonation of the magnesium enolates. Trapping of the magnesium enolates with various electrophiles is also carried out.

Since the pioneering work of Trost and others, sulfoxides have been extensively used in modern synthetic organic chemistry.<sup>1</sup> Furukawa,<sup>2</sup> Okamura,<sup>3</sup> and we<sup>4</sup> recently reported the reaction of sulfoxides with alkylmetals to give new alkylmetals or desulfinylated products. These new reactions are thought to be useful for the exploiting the use of sulfoxides in organic synthesis. In continuation of our studies on the use of 1-haloalkyl aryl sulfoxides in organic synthesis, we report here a novel method for synthesizing  $\alpha$ -haloketones 6 from 1-haloalkyl aryl sulfoxides 1 and aldehydes 2 via the EtMgBr mediated desulfinylation of  $\alpha$ -halo- $\beta$ -ketosulfoxides 4. We also report a trapping of the magnesium enolate intermediate 5 with deutrium oxide, ethyl chloroformate, chlorotrimethylsilane, and benzaldehyde as shown in Scheme 1.



## Scheme 1

1-Chlorobutyl p-tolyl sulfoxide<sup>5</sup> (1: Ar=Tol, X=Cl, R<sup>1</sup>=(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>) was treated with LDA at -78 °C in THF followed by 3-phenylpropanal to afford the  $\beta$ -chloroalcohol 3e (Ar=Tol, R<sup>1</sup>=(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, R<sup>2</sup>=CH<sub>2</sub>CH<sub>2</sub>Ph; see Table 1) in 99% yield as a mixture of two diastereomers. Oxidation of this mixture under Swern's condition gave  $\beta$ -ketosulfoxide 4e in 96% yield.  $\beta$ -Ketosulfoxide 4e was treated with 1.1 equivalents of p-BuLi in ether at -78 °C (5 min) and after quenching with water, 4-chloro-1-phenyl-3-heptanone 6e (X=Cl, R<sup>1</sup>= (CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, R<sup>2</sup>=CH<sub>2</sub>CH<sub>2</sub>Ph) was isolated in 86% yield. No product from the reaction with carbonyl group in 4e was detected. This reaction was carried out with other alkylmetals under several conditions, and EtMgBr (1.1 equivalents) in ether at -78 °C was found to be the optimal condition to afford 6e in 91% yield.

The results of the synthesis of  $\alpha$ -fluoro-,  $\alpha$ -chloro-, and  $\alpha$ -bromoketones by this procedure are summarized in Table 1. It is worth noting that  $\alpha$ -fluoroketones<sup>e</sup> (entry a-d) were obtained in high overall yields. Because of the unstable nature of the compounds containing bromine, the yields for the synthesis of  $\alpha$ -bromoketones were somewhat lower than for other  $\alpha$ -haloketones. This desulfinylation reaction was thought to take place through an enolate. Indeed, by quenching the reaction of 4e with EtMgBr with D<sub>2</sub>O instead of water, regioselectively deutrated  $\alpha$ -chloroketone 6 (D) was obtained in 87% yield (Scheme 1). In order to further substantiate the enolate and to clarify the usage of this reaction in new synthetic method, the reaction was carried out with some electrophiles. After the treatment of 4e with EtMgBr in ether at -78 °C, ClCO<sub>2</sub>Et was added and the mixture was stirred at 0 °C (2.5 h) and then at room temperature (1 h) to afford enol carbonate 7 (E= CO<sub>2</sub>Et) in 86% yield (E/Z-mixture).<sup>9</sup> The enolate 5e was treated with ClSiMe<sub>3</sub> in the presence of Et<sub>3</sub>N and HMPA (0 °C 1 h, then room temperature 2 h) to give silyl enol ether 7 (E=SiMe<sub>3</sub>; detected by <sup>1</sup>H NMR) and it was converted to 6e by acid hydrolysis. Quenching the enolate with benzaldehyde at -78 °C afforded cleanly the aldol 8 (syn/anti-mixture) in 80% yield.

	1		2	3	4	6
	х	Ar	R <sup>2</sup>	Yield(%)	Yield(%) <sup>a)</sup>	Yield(%) <sup>b)</sup>
2	Fc)	Dh	ръсн.сн.	27	03	79
b	*	4.11	$CH_3 (CH_2)_8$	95	85	90
с			Ph	94	97	82
d			Cyc-Hex	80	89	85
е	Cl	Tol	PhCH <sub>2</sub> CH <sub>2</sub>	99	96	91
f			CH <sub>3</sub> (CH <sub>2</sub> ) 8	82	92	93
g			Ph	92	83	78
h			Cyc-Hex	91	94	95
i	Br <sup>d)</sup>	Tol	PhCH <sub>2</sub> CH <sub>2</sub>	95	73	68
C			CH <sub>3</sub> (CH <sub>2</sub> ) 8	99	90	70
k			Ph	90	74	56
1			Cyc-Hex	90	72	59

Table 1. Synthesis of  $\alpha$ -Haloketone 6 from 1-Halobutyl Aryl sulfoxide 1 ( $R^1$ =(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>) and Aldehyde 2

a) Conversion yield.
b) Isolated yield.
c) Prepared according to the method by Wunk.<sup>6</sup>
d) Prepared according to the method reported by Iriuchijima.<sup>7</sup>

## References and Notes

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