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Ligand Exchange Reaction of Sulfoxides in Organic Synthesis: A New Method for One-Carbon Homologation of Esters to Carboxylic Acids and Esters via α-Chloro α-Sulfinyl Ketones

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Abstract: Reaction of the Carbanion of chloromethyl phenyl sulfoxide with esters gave α-chloro α-sulfinyl ketones, which were treated with KH followed by t-BuLi to afford one-carbon homologated acids and esters in good to excellent yields.

Homologation of carbonyl compounds with carbon-carbon coupling is one of the most useful and reliable methods for obtaining desired carbonyl compounds.[1] We recently reported some new methods for homologation of carbonyl compounds using 1-haloalkyl aryl sulfoxides.[2] Specifically, on treatment with *t*-BuLi, α-chloro sulfoxides gave carbenoids via ligand exchange reaction of the sulfinyl group. These reactions afforded one-carbon homologated ketones[3] and acetylenes[4] from ketones and aldehydes. In continuation of our studies on the ligand exchange reaction of sulfoxides in organic synthesis, here we report a new method for one-carbon homologation of esters **1** to carboxylic acids (**4**; R'=H) and esters (**4**; R'=CH_3)[5] via α-chloro α-sulfinyl ketones **3**.

In a typical experiment, the procedure is reported using methyl benzoate and chloromethyl phenyl sulfoxide. A solution of methyl benzoate in THF was added to a solution of the carbanion **2** (prepared from chloromethyl phenyl sulfoxide with 2.2 equivalents of LDA) in THF at -78 °C to give α-chloro α-sulfinyl ketone (**3**; R=Ph) in 74% yield as a mixture of two diastereomers. First, this ketone was converted to potassium enolate with KH at 0 °C. After 20 min, this solution was cooled to -78 °C and *t*-BuLi (2 equivalents) was added. The reaction mixture was quenched by 5% NaOH after 20 min stirring. The product was obtained in the usual way for isolation of carboxylic acids to give phenylacetic acid (**4**; R=Ph, R'=H) in 85% yield. When the quenching was carried out with methanol, methyl phenylacetate (**4**; R=Ph, R'=CH_3) was obtained in 53% yield.

The table shows the representative results for the procedure. The yields for the preparation of **3** were good. The second step also presented no problem, giving the homologated carboxylic acids in 70-95% yields. However, generally the yields for the esters are always lower than those for the carboxylic acids.

In the second step, it was expected that quenching the reaction with amines would afford amides; however, the reaction with diethylamine gave some complex mixture and the desired amides were obtained in low yields (less than 40% yield).

We are continuing to study the scope and limitations of this procedure and application to synthetic uses.

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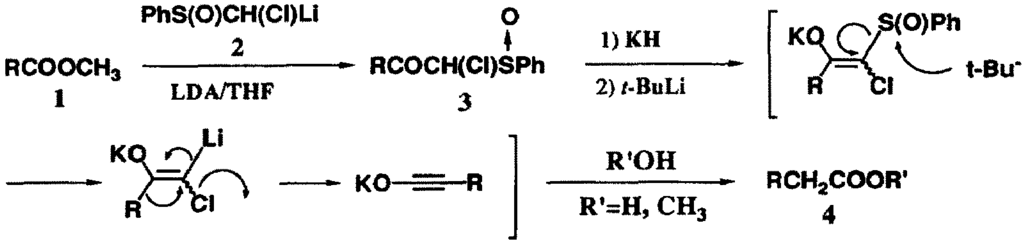
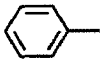
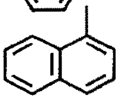
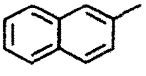
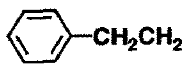


Entry	R	3 Yield/%	Carboxylic Acid Yield/%	Methyl Ester Yield/%
1		74	85	53
2		87	70	50
3		71	95	45
4		77	82	65
5		87	74	42

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