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A NOVEL METHOD FOR THE PREPARATION OF PHENYLTHIOMETHYL KETONES

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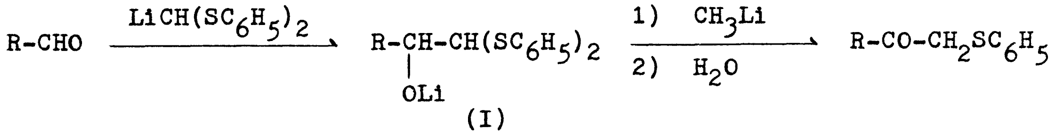
It has been found that the reaction of bis(phenylthio)methyllithium with various aldehydes, followed by treatment with methyllithium leads to the formation of the corresponding phenylthiomethyl ketones, accompanied with liberation of phenylthiolate anion, in high yields.

We have recently reported the elimination reaction of phenylmercapto group from α-hydroxyaldehydes diphenyl mercaptal by means of trivalent phosphorus compound.[1] We wish to report here an another reaction of this type of compound, which is outstandingly useful for the preparation of phenylthiomethyl ketones.

It is reported that bis(phenylthio)methyllithium reacts with aldehydes to yield the corresponding addition product (I).[2] Treatment of this addition product (I) with methyllithium at 0° was found to lead to the formation of the corresponding phenylthiomethyl ketone in high yield, accompanied with liberation of phenylthiolate anion, as shown in the following equation.



$$\text{R-CHO} \xrightarrow{\text{LiCH(SC}_6\text{H}_5)_2} \underset{\text{OLi}}{\underset{|}{\text{R-CH}}}\text{-CH(SC}_6\text{H}_5)_2 \xrightarrow[2)\ \text{H}_2\text{O}]{1)\ \text{CH}_3\text{Li}} \text{R-CO-CH}_2\text{SC}_6\text{H}_5$$

(I)

Only exceptional case is that with the addition product (I; $R=C_6H_5CH=CH-$) derived from cinnamaldehyde and the corresponding α-hydroxyaldehyde diphenyl mercaptal was recovered under such a reaction condition (0° for 30 min).

Advantages over the conventional process involving direct introduction of phenylmercapto group into active methyl or methylene group of ketones[3] include operational simplicity, and avoidance of the formation of the other isomers such as phenylthioalkyl methyl ketone, $RCH(SC_6H_5)-CO-CH_3$, and highly substituted products. A typical procedure is as follows; bis(phenylthio)methyllithium was treated with an equimolar amount of n-hexanal in tetrahydrofuran for 1 hr at 0°.[2] To the resulting solution was added an equimolar amount of methyllithium in situ at 0° and it kept stirring for 30 min at 0°. Then, the reaction mixture was worked up with aqueous ammonium chloride and the crude product was purified by tlc, which gave phenylthiomethyl n-pentyl ketone in 81% yield. The infrared spectrum of the product (in CCl_4) manifested peaks due to carbonyl at 1710 cm^{-1} and phenylmercapto group at 1580, 1475 and 690 cm^{-1}; the nmr spectrum (CCl_4) showed peaks at 0.80-1.85 δ (multiplet 9H, $CH_3CH_2CH_2CH_2-$), 2.58 δ (triplet 2H, $-CH_2-CO-$), 3.57 δ (singlet 2H, $-CO-CH_2-S-$), 7.20-7.43 δ (multiplet 5H, aromatic protons).

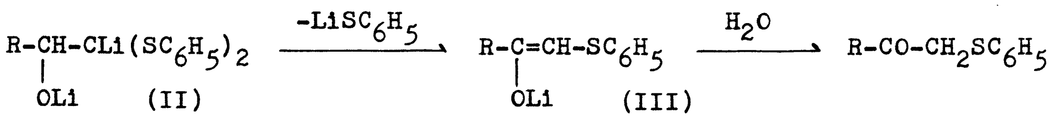
Table I. Yields of Phenylthiomethyl Ketones[a]

R-CHO	Yield (%)[b]
$n-C_3H_7CHO$	69
$n-C_5H_{11}CHO$	81
$n-C_7H_{15}CHO$	83
$n-C_9H_{19}CHO$	90
C_6H_5CHO	86

a) All of the products gave the satisfactory analytical and spectral data.

b) Isolated yields based on the aldehydes.

Now, we have only a few data for discussing the reaction mechanism, but the reaction is considered to proceed through the initial formation of a dilithiated intermediate (II), which changes into the enolate anion (III), by trapping them through their reactions with carbonyl compound under suitable reaction conditions. The reactions of (II) and (III) will be described in a separate note.



$$\underset{\text{OLi}}{\underset{|}{\text{R-CH}}}\text{-CLi}(SC_6H_5)_2\ \text{(II)} \xrightarrow{-LiSC_6H_5} \underset{\text{OLi}}{\underset{|}{\text{R-C}}}\text{=CH-}SC_6H_5\ \text{(III)} \xrightarrow{H_2O} R\text{-CO-}CH_2SC_6H_5$$

References

1) I. Kuwajima, S. Sato and Y. Kurata, Tetrahedron Lett., submitted to publication.

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