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A CONVENIENT PREPARATIVE METHOD OF α-CHLORO KETONES

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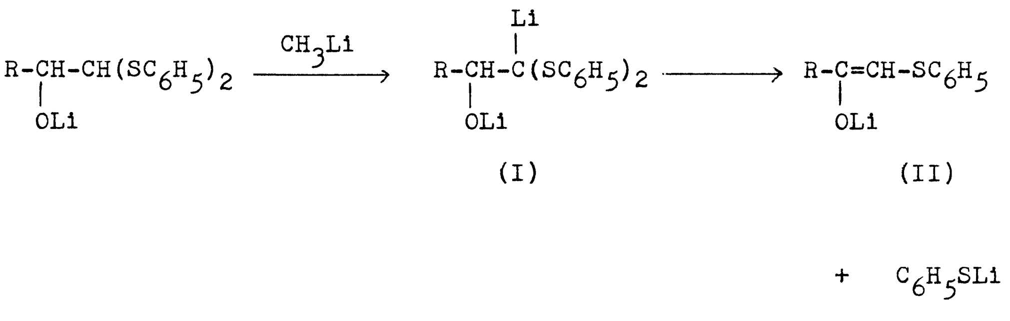
Rearrangement reaction of 1-substituted 2,2-dichloroethanol has been studied and it has been found that the corresponding α-chloro ketone is obtained in good to excellent yield by treating the alcohol with 2~3 equivalents of n-butyllithium in dimethoxyethane.

In the previous paper, we reported that phenylthiomethyl ketones were formed by treating 1-substituted 2,2-bis(phenylthio)ethanol with methyl- or n-butyllithium.[1,2] These results have suggested that the reaction proceeds through an initial formation of the dilithiated intermediate (I), which decomposes, accompanied with removal of phenylthiolate anion and migration of hydride ion to the neighboring carbon atom, into the enolate anion (II) of the corresponding phenylthiomethyl ketone as shown in the following scheme.



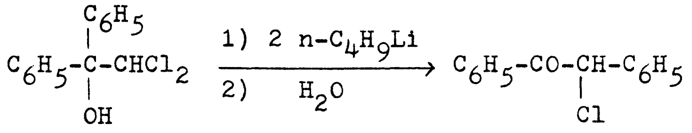
$$\text{R-}\underset{\text{OLi}}{\text{CH}}\text{-CH(SC}_6\text{H}_5)_2 \xrightarrow{\text{CH}_3\text{Li}} \text{R-}\underset{\text{OLi}}{\text{CH}}\text{-}\overset{\text{Li}}{\text{C}}(\text{SC}_6\text{H}_5)_2 \longrightarrow \text{R-}\underset{\text{OLi}}{\text{C}}\text{=CH-SC}_6\text{H}_5 + \text{C}_6\text{H}_5\text{SLi}$$

(I) (II)

As one of the extensions of this type of the rearrangement reaction, we have examined a similar reaction of 1-substituted or 1,1-disubstituted 2,2-dichloroethanol with two equivalents of n-butyllithium and have found that the reaction takes place as expectedly to give the corresponding α-chloro ketone in good to excellent yield in some cases.

Recent publications about a similar reaction by Villieras[3] and Köbrich[4] have prompted us to publish our observation about this rearrangement reaction.

Initially, for synthetic purpose, we have focussed our attention on finding the optimum conditions for the rearrangement reaction and have found that the solvent used and the reaction temperature have serious effects on the formation of the rearrangement product, γ-chloro ketone. Thus, the alcohol (III) derived from the reaction of benzophenone with dichloromethyllithium[5] was shown to lead to the formation of the corresponding rearrangement product (IV) in 85% yield when it was treated with two equivalents of n-butyllithium in dimethoxyethane at 0°C, while (IV) was formed in only 30% yield when the reaction was attempted in tetrahydrofuran at 0°C. In the latter case, formation of the other product was accompanied in appreciable amount---- it was tentatively assigned to be (V), resulted from chlorine-butyl exchange and dehydration reaction, by its nmr and ir spectrum.



$$C_6H_5-\overset{C_6H_5}{\underset{OH}{C}}-CHCl_2 \xrightarrow[2)\ H_2O]{1)\ 2\ n\text{-}C_4H_9Li} C_6H_5-CO-\underset{Cl}{CH}-C_6H_5$$

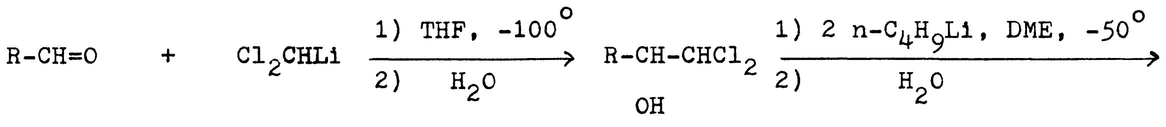
(III) (IV)

$(C_6H_5)_2C=C(C_4H_9)_2$

(V)

On the other hand, in the case of the rearrangement reaction of phenyl group, the reaction temperature effect was found to be not so remarkable as the solvent effect mentioned above. But, decrease of the formation of (IV) was apparently observed along with increase of amounts of the by-products formed when the reaction was carried out in dimethoxyethane at lower temperature such as -20 or -50°C.

Similarly, the rearrangement reaction of hydrogen could also be successfully carried out by using dimethoxyethane as the solvent. Thus, the alcohols (VI) derived from the aldehydes could be converted into the corresponding chloromethyl ketones (VII) in excellent yield by treating it with two equivalents of n-butyllithium in dimethoxyethane at -50~-60°C. Vpc analysis of the products obtained above showed they were practically pure enough for further synthetic purpose without any purification procedure. It was further shown that, contrary to the observation of Villieras,^{3} the product resulted from alkyl group rearrangement (VIII) was little obtained in this case, and better results were usually obtained at lower reaction temperature.



$$\mathrm{R\text{-}CH{=}O} \quad + \quad \mathrm{Cl_2CHLi} \xrightarrow[\mathrm{2)\ \ H_2O}]{\mathrm{1)\ THF,\ -100^{\circ}}} \underset{\mathrm{OH}}{\mathrm{R\text{-}CH}}\mathrm{\text{-}CHCl_2} \xrightarrow[\mathrm{2)\ \ H_2O}]{\mathrm{1)\ 2\ n\text{-}C_4H_9Li,\ DME,\ -50^{\circ}}}$$

(VI)

$\mathrm{R\text{-}CO\text{-}CH_2Cl}$

(VII)

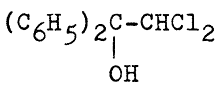
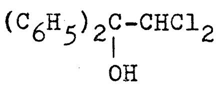
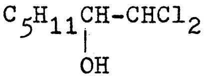
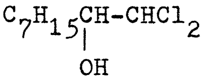
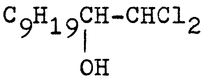
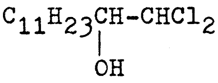
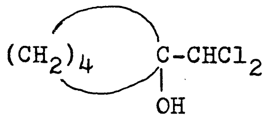
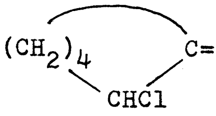
$\mathrm{R\text{-}CHCl\text{-}CH{=}O}$

(VIII)

On the other hand, attempt for a similar rearrangement reaction of the alcohols derived from the reaction of the aliphatic ketones with dichloromethyllithium was shown to lead to complex results. For example, the corresponding alcohol derived from cyclopentanone gave the rearrangement product, 2-chlorocyclohexanone in 92% yield. However, in the cases of the alcohols derived from diethyl ketone, cyclohexanone and methyl t-butyl ketone, the starting materials (the alcohols) or chlorine-butyl exchange products were shown to be major parts and the rearrangement products could not be obtained as the major ones when they were treated with 2∼3 equivalents of n-butyllithium under usual reaction conditions or standing overnight at 0°C.

We are currently investigating a similar rearrangement reaction and a reaction using the products obtained above.

Table. Conversion of 1-Substituted 2,2-Dichloroethanols into α-Chloro Ketones

1-Substituted 2,2-Dichloroethanol	Solvent	Temperature	Time	α-Chloro Ketone (Yield, %)
 $(C_6H_5)_2\underset{OH}{\underset{\mid}{C}}-CHCl_2$	DME	0°	30 min	$C_6H_5-CO-CHCl-C_6H_5$ (85%)
 $(C_6H_5)_2\underset{OH}{\underset{\mid}{C}}-CHCl_2$	THF	0°	30 min	$C_6H_5-CO-CHCl-C_6H_5$ (30%)
 $C_5H_{11}\underset{OH}{\underset{\mid}{CH}}-CHCl_2$	DME	-60°	30 min	$C_5H_{11}-CO-CH_2Cl$ (93%)
 $C_7H_{15}\underset{OH}{\underset{\mid}{CH}}-CHCl_2$	DME	-50°	30 min	$C_7H_{15}-CO-CH_2Cl$ (95%)
 $C_9H_{19}\underset{OH}{\underset{\mid}{CH}}-CHCl_2$	DME	-50°	30 min	$C_9H_{19}-CO-CH_2Cl$ (93%)
 $C_{11}H_{23}\underset{OH}{\underset{\mid}{CH}}-CHCl_2$	DME	-50°	30 min	$C_{11}H_{23}-CO-CH_2Cl$ (94%)
	DME	0°	30 min	 (92%)

References

1) I. Kuwajima and Y. Kurata, Chem. Lett., 291 (1972).

2) I. Kuwajima and T. Kobayashi, Chem. Commun., submitted for publication.

3) J. Villieras, C. Bacquet, and J. F. Normant, J. Organometal. Chem., 40, C1 (1972).

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