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Abstract

Full Text

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On the Interaction of Acid Esters with Lithium Alkyls

In our previous investigations ($^{1-3}$), we studied chiefly the influence of temperature on the direction of reactions of lithium alkyls with acid esters. It was shown that at −35° the reaction proceeds according to the normal scheme, with formation of tertiary alcohols. At +35° and above, the reaction proceeds anomalously, with formation of a ketone bearing the radicals of the initial acid ester.

However, β-keto esters remained unisolated (the Claisen-condensation product of the initial ester), the decomposition of which is the most probable route for formation of ketones of the indicated type. A β-keto ester was isolated by Zook (^{4}) in the interaction of tert-C_4H_9MgCl with the ester of propionic acid; however, its hydrolysis was carried out with an alcoholic solution of KOH at 95° for three hours, i.e., under conditions absent in Grignard syntheses.

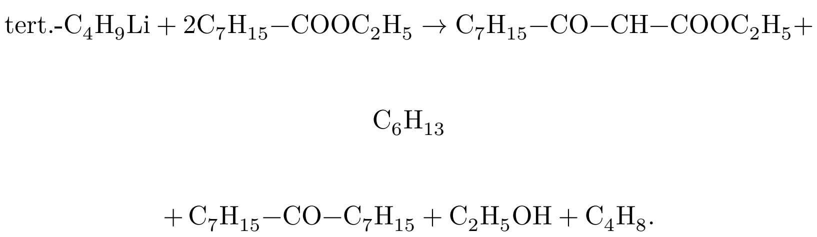
From the work of Gilman and co-workers (^{5,6}) it is known that organolithium compounds are thermally unstable and readily decompose to an olefin and lithium hydride (^{7}). The latter, apparently, may bring about a Claisen condensation.

Since the stability of lithium alkyls decreases in the series:

$$\text{iso-}C_3H_7Li > \text{sec.-}C_4H_9Li > \text{tert.-}C_4H_9Li > \text{tert.-}C_5H_{11}Li,$$

different temperature conditions are also required for the formation of the anomalous products—the β-keto ester and ketone. This is in good agreement with our experimental data (^{1}), which showed that diethyl ketone is obtained in the reaction of tert-$C_5H_{11}Li$ with ethyl caprylate even at −30°, whereas with iso-C_3H_7Li only at $+35, +70°$. The possibility of the anomalous reaction is also influenced by the nature of the acid ester. Thus, for example, we did not observe formation of the ketone R−CO−R from the ester of phenylacetic acid, evidently because here the β-keto ester is formed at a temperature considerably higher than that at which lithium alkyls decompose. Indeed, from the ester of phenylacetic acid the keto ester is formed upon heating with sodium ethylate for 6 hours at 95° (^{8}). In the case of esters of aromatic acids (benzoic, naphthoic), where Claisen condensation is impossible, the reaction proceeds according to the acyloin-condensation type, with formation of ketols (^{2}).

In the present investigation, wishing to stop the reaction at the stage of the intermediate product, the β-keto ester, we slowed its course by replacing the polar solvents ether and tetrahydrofuran (THF) with n-hexane. This same replacement excluded the possibility of formation of lithium alkoxide, obtained in the interaction of alkyl lithium with ether and acting as a strong condensing agent. Under these conditions we obtained, in 30% yield, ethyl 2-n-hexyldecan-3-oate and a small amount of diheptyl ketone:



$$\text{tert.-}C_4H_9Li + 2C_7H_{15}{-}COOC_2H_5 \rightarrow C_7H_{15}{-}CO{-}\underset{C_6H_{13}}{CH}{-}COOC_2H_5 + C_7H_{15}{-}CO{-}C_7H_{15} + C_2H_5OH + C_4H_8.$$

Unsaturated β-keto esters, as was shown by Nazarov and co-workers (^{9}), are hydrolyzed to ketones even in an aqueous medium with 10% KOH content. In our case, hydrolysis in aqueous solution proceeded with 5% LiOH.

We observed for the first time the formation of anomalous products also in the interaction of the ester of caprylic acid with a primary normal lithium alkyl—butyllithium. The reaction proceeded in THF at 40—50° for 8 hours with a yield of 20%, whereas secondary and tertiary lithium alkyls under milder conditions gave a yield of diheptyl ketone of 60-70%.

Experimental Part

Reaction of tert-C_4H_9Li with caprylic acid ester. The synthesis was carried out in a stream of nitrogen in a flask equipped with a reflux condenser, stirrer, dropping funnel, and thermometer. Into the flask were placed 7 g of finely cut lithium, 200 ml of hexane, and 46 g of tert-C_4H_9Cl was added dropwise at room temperature. To accelerate the formation of tert-C_4H_9Li, 1 ml of THF was added. After 5 hr of stirring, the lithium that had not entered into the reaction was filtered off. To the tert-C_4H_9Li was added a solution of 43 g of ethyl caprylate in 50 ml of hexane. The first portion of the ester was added at a temperature of 20°; then the reaction proceeded vigorously, and the temperature rose to 55-60°. After decomposition at a temperature of 10-15° and distillation of the product, the following fractions were obtained:

60-85°/4 mm —4 g of the initial ethyl caprylate.
120-165°/4 mm —6 g of liquid, which crystallized.
By recrystallization from alcohol, 3 g of diheptyl ketone with m.p. 39° was

obtained.
171-175°/4 mm —10 g of ethyl ester of 2-hexyldecan-3-oic acid, n_D^{20} 1.4460.

Found, %: C 73.01, 73.27; H 11.30, 11.51
$C_{18}H_{34}O_3$. Calculated, %: C 72.44; H 11.46

IR spectra were recorded: on an IKS-14 with a NaCl prism in the region 2000-1600 cm^{-1}, in CCl_4 solution, $d = 1$ mm, and on an IKS with a LiF prism in the region 3600-3000 cm^{-1}, in CCl_4 solution, $d = 1$ mm. Bands were found: an intense band at 1740 cm^{-1}, assigned to $C=O$ in the ester group, and a weak band at 1730 cm^{-1}, corresponding to $C=O$ in ketones.

Hydrolysis of the keto ester. A mixture of 7 g of ethyl ester of 2-hexyldecan-3-oic acid and 25 ml of a 5% aqueous solution of LiOH was stirred for 1 hr at a temperature of 5-10°. Then 10% hydrochloric acid was added. The product was extracted with ether, washed with water, and dried. After fractionation, two fractions were obtained. The first, 150-165° —3 g, rapidly crystallized. From it was isolated diheptyl ketone with m.p. 39° (from alcohol); a mixed-melting-point test with diheptyl ketone gave no depression. The second, 170° —2.5 g, was the initial keto ester.

Reaction of n-C_4H_9Li with caprylic acid ester. n-Butyllithium was prepared from 7 g of lithium and 47 g of n-C_4H_9Cl in 200 ml of THF. The lithium that had not entered into the reaction was filtered off. To the n-butyllithium, at room temperature, 41 g of ethyl caprylate was added. Then the reaction mixture was stirred for another 8 hr at 40-50°, after which it was hydrolyzed with 5% HCl at 5-10°. Obtained: 145-146°/3 mm —8 g of dodecanone-5, n_D^{20} 1.4546.

3 g of diheptyl ketone, m.p. 40°. 160-161°/3 mm —3 g of heptyl-di-n-butylcarbinol, n_D^{20} 1.4508.

Found, %: C 80.08, 80.07; H 14.12, 14.04
$C_{16}H_{34}O$. Calculated, %: C 79.40; H 14.20

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