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THE REACTION OF ALKYL LITHIUM COMPOUNDS WITH β-KETO ESTERS

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A recent report on the generation and alkylation of dianions from β-keto-esters with n-butyl-lithium(1), leads us to communicate substantially different results.

We were interested in determining whether carbonyl addition reactions could become competitive with active hydrogen abstraction, to , for instance β-hydroxy esters. To our surprise, the principal products, even in the presence of excess organolithium reagent, were ketones. Thus the reaction of n-butyl lithium (3 mols.) with ethyl α-n-butyl acetoacetate (1 mole) gave as a principal product 5-decanone (24.3%). In a related reaction, ethyl 2-cyclohexanone carboxylate (1 mole) reacted with n-butyl-lithium (3 moles) to give cyclohexanone (27.9%) and 5-nonanone (43.5%).

In order to derive further information on this unexpected result, we examined the reaction products of the latter reaction for two plausible intermediates, 2-valeryl cyclohexanone and ethyl valerate.

Careful examination of the reaction products from ethyl 2-cyclohexanone carboxylate indicated the presence of 2-valeryl cyclohexanone. No evidence was found for the presence of ethyl valerate.

We may conclude then that, in the case of β-keto esters, the ester carbonyl group is attacked preferentially, with formation of a β-diketone. This diketone reacts further to give the final product ketones by cleavage of the intermediate addition product. This conclusion is also supported by the isolation of 2-hexanone (18%), 2-heptanone (6%), and 5-nonanone (8%) from the reaction of n-butyl lithium and ethyl α-n-butyl acetoacetate. Presumably the higher reaction temperature and longer reaction time accounts for the difference between our results and those reported by Weiler (1).

As this route seemed potentially interesting as a means of synthesis for long-chain ketones, we studied the reaction of several additional keto-esters and organolithium reagents. The results are summarized in Table 1.

Table 1[a]

Starting Material	RLi	Product	Yield[b]
n-butyl EEA	n-butyl	5-decanone (2)	24.3%[c]
n-butyl EEA	n-octyl	6-tetradecanone (3)	11.5%
n-octyl EEA	n-butyl	5-tetradecanone (4)	22.5%
n-decyl EEA	n-octyl	9-eicosanone (5)	8.8%

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[a] All reactions run in THF-hexane, organolithium added at 0°, followed by 1 hr. reflux.

[b] Yields determined gas-chromatographically except as noted.

[c] Preparative yield.

Since the first mole of alkyl-lithium compound is presumably consumed by abstraction of the most acidic hydrogen, lithium hydride was used to generate the monoanion. Subsequent treatment with alkyl-lithium considerably improved the yield of ketones.

Thus 5-decanone was obtained in 50% yield from ethyl α-n-butyl acetoacetate, and 5-hexadecanone (68%) from ethyl α-n-decyl acetoacetate.

This method then represents a versatile alternate means for the synthesis of long-chain ketones (6).

Acknowledgement

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