

A CONVENIENT PREPARATIVE METHOD OF γ, δ -UNSATURATED ESTERS

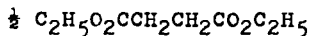
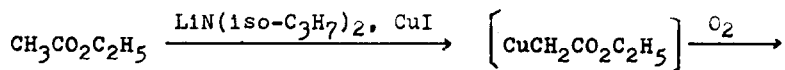
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(Received in Japan 2 February 1972; received in UK for publication 16 February 1972)

The reactions of organocopper compounds with organic halides have been reported,¹ and their utility has been shown in the field of synthetic chemistry.

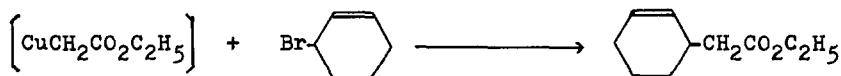
We wish to report here a convenient method for the preparation of γ, δ -unsaturated ester from allylic halide by means of the reagent, designated herein ethoxycarbonylmethylcopper. When lithium di-isopropylamide was added to an equimolar amount of ethyl acetate in the presence of cuprous iodide at -110° under nitrogen atmosphere, followed by warming up gradually to -30° , light brown homogeneous solution was obtained. The resulting solution was treated with dry oxygen at -50° for identification of the formation of ethoxycarbonylmethylcopper, which resulted in the formation of diethyl succinate in 73% yield along with a trace amount of ethyl acetoacetate.² From this result, the copper compound could be estimated to be formed in the yield above, at least.



The condition cited above was quite critical for efficient formation of ethoxycarbonylmethylcopper. For example, treatment of ethyl acetate with lithium di-

isopropylamide at -78° , followed by the similar procedure, was found to lead to considerable decrease of the formation of diethyl succinate (17% yield). The fact that the formation of the copper compound is seen to be remarkably sensitive to temperature is probably attributable to the preferable formation of copper di-isopropylamide ($\text{CuN}(\text{iso-C}_3\text{H}_7)_2$) at higher temperature which is inert toward ethyl acetate.


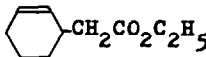
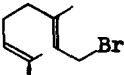
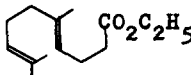
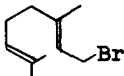
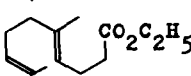
It is known that copper compounds such as methylcopper have only poor reactivity and fail to react with alkyl halides or non-conjugated carbonyl compounds. Only exceptional case is that with allylic halides and it is reported that phenylthiomethylcopper³ and cyanomethylcopper⁴ react with allylic bromides to give the corresponding coupling products. Similar to the cases above, attempt to react with butyl bromide, butyraldehyde, or butyl tosylate all failed, but it was found that ethoxycarbonylmethylcopper reacted smoothly with allylic halides to yield the corresponding coupling products. Thus, treatment of ethoxycarbonylmethylcopper (1.5 times excess) with 1-bromo-2-cyclohexene at -30° for 1 hr led to the formation of ethyl cyclohexenylacetate in 69% yield.



Similarly as shown in the Table I, all of the allylic halides attempted gave the corresponding coupling products in high yields. A trace amount of ethyl acetate and of diethyl succinate were also usually formed in this reaction, but the formation of the latter could be practically avoided by quenching the reaction mixture under nitrogen atmosphere.

The synthetic potential of ethoxycarbonylmethylcopper is indicated by its reaction with allylic halides having another functional groups such as methyl bromocrotonate. Large difference of reactivities between allylic halogen atom and other functional groups toward the copper compound is shown to make this reaction much selective.⁵ A typical procedure for the coupling reaction is as follows; a solution of lithium di-isopropylamide (4 mmoles) in tetrahydrofuran (5 ml) was slowly added to a solution of ethyl acetate (352 mg, 4 mmoles) and cuprous iodide (1.52 g, 8 mmoles) in tetrahydrofuran (15 ml) at -110° under

Table I. Reactions of Ethoxycarbonylmethylcopper with Allylic Halides.

Allylic Halides	Reaction Temperature	Product (Yield ^a)
$\text{CH}_2=\text{CBr}-\text{CH}_2\text{Br}$	$-110\sim-30^\circ(\text{b}), -30^\circ(\text{c})$	$\text{CH}_2=\text{CBr}-\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (83)
$\text{CH}_2=\text{CBr}-\text{CH}_2\text{Br}$	$-78\sim-30^\circ(\text{b}), -30^\circ(\text{c})$	$\text{CH}_2=\text{CBr}-\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (17)
	$-110\sim-30^\circ(\text{b}), -30^\circ(\text{c})$	 (69)
	$-110\sim-30^\circ(\text{b}), -30^\circ(\text{c})$	 (94 ^d)
	$-78\sim-30^\circ(\text{b}), -30^\circ(\text{c})$	 (19)
$\text{CH}_3\text{O}_2\text{C}-\text{CH}=\text{CH}-\text{CH}_2\text{Br}$	$-110\sim-30^\circ(\text{b}), -30^\circ(\text{c})$	$\text{CH}_3\text{O}_2\text{C}-\text{CH}=\text{CH}-\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (89)
$\text{C}_6\text{H}_5\text{CH}_2\text{Br}$	$-110\sim-30^\circ(\text{b}), -30^\circ(\text{c})$	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (62)

a) Satisfactory analytical and spectral data have been obtained for all of the products. Isolated yield. b) Reaction temperature on treating ethyl acetate with lithium di-isopropylamide and cuprous iodide. c) Reaction temperature on treating ethoxycarbonylmethylcopper with allylic halides. d) An another isomer was formed in less than 2% by vpc analysis.

nitrogen atmosphere. After it kept stirring until the cooling bath was warmed up to -30° , a solution of 2,3-dibromopropene (328 mg, 2 mmoles) in tetrahydrofuran (5 ml) was added at that temperature and it kept stirring for 1 hr. Then, the reaction mixture was worked up with aqueous ammonium chloride and the crude product was purified by tlc procedure, giving ethyl 4-bromo-4-pentenoate in 83 % yield. The infrared spectrum of the product (in CCl_4) manifested peaks due to ester at 1735 cm^{-1} and $\text{CH}_2=\text{C}$ at 1630 and 885 cm^{-1} ; the nmr spectrum (CCl_4) showed peaks at 1.32δ (triplet 3H, $\text{CH}_3-\text{C}-\text{O}$), $2.54-2.93\delta$ (multiplet 4H, $-\text{C}=\text{C}-\text{CH}_2\text{CH}_2\text{CO}-$), 4.15δ (quartet 2H, $-\text{CH}_2-\text{O}-$), 5.42δ (doublet 1H, olefinic proton) and 5.64δ (doublet 1H, olefinic proton).

References

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- 5) It has been reported that lithio ethyl acetate has higher reactivity toward carbonyl group than organic halide; M. W. Rathke, J. Am. Chem. Soc., 92, 3222 (1970); M. W. Rathke and A. Lindert, ibid., 93, 2318 (1971).