

The Addition of Grignard Reagents to Alkylidenemalonic Esters

IV. The Reactions of Isopropylidenemalonic Esters with Allylmagnesium Bromide and 2-Butenylmagnesium Bromide

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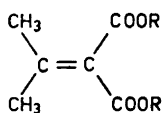
When allylmagnesium bromide reacts with diethyl and diisopropyl isopropylidenemalونات, only the corresponding 1,1-dimethyl-3-butenylmalonates are formed. The two unsaturated malonates react with 2-butenylmagnesium bromide to give diethyl and diisopropyl 1,1,2-trimethyl-3-butenylmalonates. The reactions are thus 1,4-additions of the Grignard reagents to the conjugated double bonds of the malonates, which reactions apparently include allylic rearrangements of the alkenyl groups of the Grignard reagents.

The action of Grignard reagents on α,β -unsaturated malonic esters has previously been examined in this laboratory.¹⁻³ 1,4-Addition of the Grignard reagent to the conjugated double bond system $C=C-C=O$ and reduction of the carbon-to-carbon double bond were shown to be the principal reactions. Only when methylmagnesium iodide reacted with isopropylidenemalonic esters were 1,2-addition products formed.

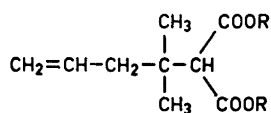
According to Hauser, Yost, and Ringler,⁴ only 1,4-addition products can be isolated when phenylmagnesium bromide reacts with *tert*-butyl cinnamate. Young and Roberts⁵ have, however, shown that 1,4-addition does not occur when 2-butenylmagnesium bromide is substituted for phenylmagnesium bromide. When Munch-Petersen, Møller Jørgensen, and Refn⁶ examined the reactions of β -methylallylmagnesium bromide and butenylmagnesium bromide with the *sec*-butyl esters of crotonic, tiglic, and cinnamic acids, they obtained the corresponding tertiary alcohols as the only products. Substituted allylmagnesium halides consequently seem to give 1,2-addition products exclusively when they react with α,β -unsaturated monocarboxylic esters.

It therefore seemed justified to study the reactions of allylmagnesium bromide and 2-butenylmagnesium bromide with diethyl and diisopropyl isopropylidenemalونات (I). Surprisingly, the results of this investigation showed that only 1,4-addition occurs with the formation of the diethyl and

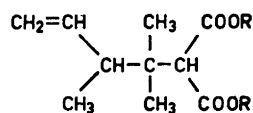
diisopropyl esters of 1,1-dimethyl-3-butenylmalonic acid (II) from allylmagnesium bromide and the diethyl and diisopropyl esters of 1,1,2-trimethyl-3-butenylmalonic acid (III) from 2-butenylmagnesium bromide as the sole products. The second carbalkoxy group of the unsaturated malonates does



I



II

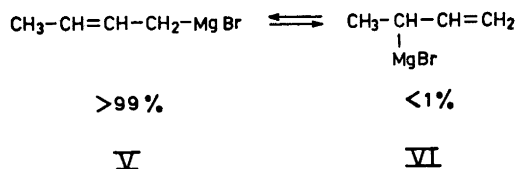


III

a) R = CH₂CH₃b) R = CH(CH₃)₂

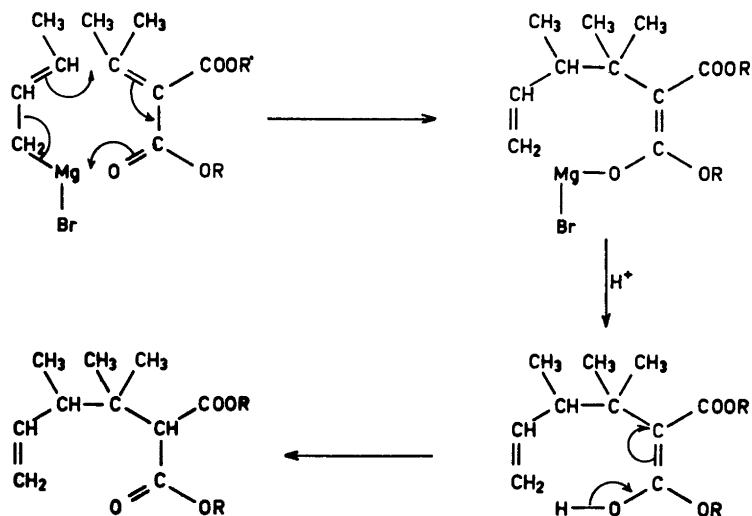
not directly take part in the 1,4-addition, but it contributes by inductively reducing the electron density at the β -carbon atom in such a degree that the alkenyl group of the Grignard reagent becomes attached to this atom rather than to the carbon atom of the carbonyl group.

The Grignard reagent prepared from 1-bromo-2-butene consists almost exclusively of 2-butenylmagnesium bromide (V).^{7,8} Only a small amount of the isomeric compound, 1-methyl-3-propenylmagnesium bromide (VI), is present.

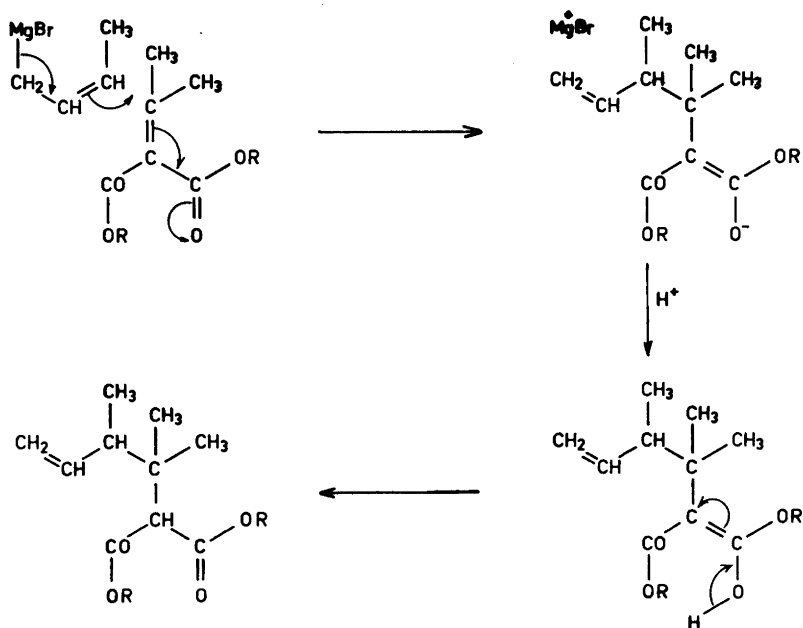


In the reactions of the Grignard reagent with carbon dioxide⁹ and with simple and sterically hindered carbonyl compounds,¹⁰⁻¹² the alkenyl group undergoes allylic rearrangement. The results of the present work show that such rearrangements occur in the reactions with unsaturated malonates.

The results do not give any information about the reaction mechanism. They can be interpreted in terms of a cyclic and an acyclic mechanism. The former (Scheme 1) is a modification of the six center mechanism of Young and Roberts,^{10,11} the latter (Scheme 2) an adaptation of the mechanisms proposed by Felkin and Roussi¹³ for the reactions between allylic Grignard reagents and epoxides and by Felkin, Fraierman, and Gault¹⁴ for the reactions between 1-methyl-2-butenylmagnesium bromide and ketones. The acyclic mechanism does not, of course, exclude the possibility that an initial complex bond is formed between an oxygen atom of the malonate and the magnesium atom of a second molecule of the Grignard reagent.¹⁵



Scheme 1.



Scheme 2.

EXPERIMENTAL

The Grignard reagents. A large excess of magnesium was used in the preparation of the Grignard reagents in order to suppress the Wurtz reactions. The molar ratio of halide to magnesium was 1:2.4 in the case of allylmagnesium bromide and 1:3.0 in the case of 2-butenylmagnesium bromide. Dry ether (17.4 ml/g Mg for the allyl compound and 13.8 ml/g Mg for the 2-butenyl compound) was used as solvent. The halide was added very slowly. The preparation of allylmagnesium bromide took 7 h and that of 2-butenylmagnesium bromide 3.5 h. Each batch was analyzed titrimetrically.²

Table 1. Elemental analyses and mass spectrometric determinations of molecular weights of the reaction products of R-MgBr and dialkyl isopropylidenemalonates.

R in R-MgBr	Ester	Found		Calculated		Mol. weight		
		C	H	for	C	H	Found	Calc.
Allyl	Diethyl	64.24	9.16	C ₁₃ H ₂₂ O ₄	64.44	9.15	242	242
Allyl	Diisopropyl	66.41	9.47	C ₁₅ H ₂₆ O ₄	66.64	9.69	270	270
Butenyl	Diethyl	65.57	9.41	C ₁₄ H ₂₄ O ₄	65.60	9.44	256	256
Butenyl	Diisopropyl	67.83	10.05	C ₁₆ H ₂₈ O ₄	67.57	9.92	284	284

The reactions between the Grignard reagents and diethyl and diisopropyl isopropylidene-malonates were performed as those of the same malonates with saturated Grignard reagents.³

When the reaction products were analysed by gas chromatography, each reaction mixture gave only one main peak (in addition to very small and negligible peaks). The products were isolated and purified in a preparative gas chromatograph. The elemental analyses and mass spectrometrically determined molecular weights (Table 1) show that an allyl group and a hydrogen atom or a butylene group and a hydrogen atom had

Table 2. Chemical shifts (τ) in NMR spectra of the reaction products of R-MgBr and dialkyl isopropylidenemalonates. Signals of 3 vinyl protons (τ 3.85–5.20 ppm) are omitted from all spectra.

R in R-MgBr	Ester	Ppm, multiplicity and intensity					Intensity of methyl signals ^a	Struc- ture
		quartet 4 H	septuplet 2 H	singlet 1 H	quintuplet 1 H	doublet 2 H		
Allyl	Diethyl	5.85	—	6.80	—	7.78	12 H	I a
Allyl	Diisopropyl	—	4.96	6.88	—	7.75	18 H	I b
Butenyl	Diethyl	5.80	—	6.50	7.46	—	15 H	II a
Butenyl	Diisopropyl	—	4.90	6.60	7.48	—	21 H	II b
Structural element due to signal		<i>b</i>	<i>c</i>	<i>d</i>	<i>e</i>	<i>e</i>		

^a Overlapping triplets, doublets, and singlets at τ 8.55–9.10 ppm.

^b Methylene protons of the ethoxy groups.

^c Methine protons of the isopropoxy groups.

^d Central methine proton of the malonic ester.

^e Proton(s) on carbon atom 2 of the substituent.

added to the malonates. This is possible only if 1,4-additions occurred. The constitutions of the reaction products were established by NMR spectrometry (Table 2).

The elemental analyses were performed by Dr. P. Demoen, Janssen Pharmaceutica, Beerse, Belgium. The NMR spectra were taken by Mr. P. Äyräs, Ph. M., University of Turku, Finland. *Statens naturvetenskapliga kommission (Finland)* has supported the work.

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