Conjugate Additions of Grignard Reagents to alpha,beta-Unsaturated Esters

## VI. The Course of Reactions with Allylic Grignard Reagents

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In contrast to ordinary Grignard reagents, allylic Grignard reagents with *sec*-butyl esters of crotonic, tiglic and cinnamic acids give exclusively and in high yields tertiary alcohols as a result of additions to the carbonyl group (1,2-addition). Benzylmagnesium chloride, on the other hand, adds to the carbon-carbon double bonds in crotonic and cinnamic esters (1,4-addition), whereas tiglic ester with this Grignard reagent gives, in low yields, mixtures of both 1,2- and 1,4-additions products. Cuprous chloride has no effect in the reactions here described.

Grignard reagents from allylic halides differ in several respects from ordinary alkyl- and arylmagnesium halides. Not only must special measures usually be applied by their preparation (*cf.* below, experimental part) in order to prevent nucleophilic attack by the reagent on unreacted halide leading to hydrocarbons of the type biallyl, bibenzyl *etc.*, but also the Grignard reagent itself in its reactions may show a reactivity different from that of other Grignard reagents *. Thus, with allylic Grignard reagents very often the formation of "inverted" products (involving an allylic "rearrangement") is encountered and furthermore, many reactions, which take one course with ordinary Grignard reagents, give rise to other reaction products or to different yields with allylic Grignard reagents. Particularly the reactions of the so-called butenyl Grignard reagent (prepared from crotyl bromide) were thoroughly studied by Young, Roberts and co-workers [2]. These authors give extensive evidence that allylic Grignard reagents react by a cyclic mechanism, involving a synchronous electron shift, resulting in inversion of the allylic group:

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* Reactions of allylic Grignard reagents, especially the work of Young, Roberts *et al.* (*e. g.* Ref.[2]), are discussed in several advanced treatises of organic chemistry [1].
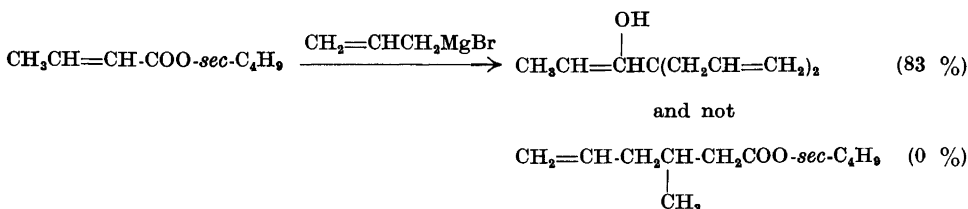
$$(1)$$
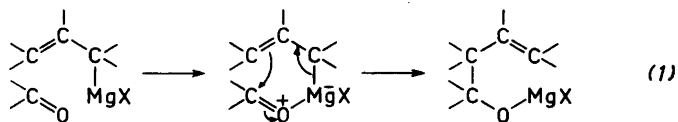
Consistent with this mechanism are the facts that addition of allylic Grignard reagents to the carbonyl group of sterically hindered ketones is facilitated, compared to the addition of other Grignard reagents, and that the allylic grouping is inverted during the addition process.

The present paper describes the reaction between sec-butyl esters of certain α,β-unsaturated acids and some allylic Grignard reagents under conditions which have previously been found favourable for conjugate addition (to the carbon-carbon double bond) of ordinary Grignard reagents [3]. As model substances have been used crotonic, tiglic and cinnamic esters, and as allylic halides: allyl, methallyl and crotyl (butenyl) bromides and benzyl chloride. The results are given in Table 1. They are seen to be in agreement with the findings of Young and Roberts [2], that 1,2-addition to the carbonyl group is greatly favoured. In contrast to the corresponding reactions with n-butyl-magnesium bromide and other Grignard reagents, the reactions with allyl-, methallyl- and crotylmagnesium bromides all give tertiary alcohols in high yields. Benzylmagnesium chloride, on the other hand, gives 1,4-addition (ester) with crotonic and cinnamic esters, whereas it gives low yields and mixtures of ester and impure tertiary alcohol with tiglic ester *.

In the conjugate addition of Grignard reagents to α,β-unsaturated carbonyl compounds a different cyclic mechanism is generally believed to operate [4]:

$$(2)$$
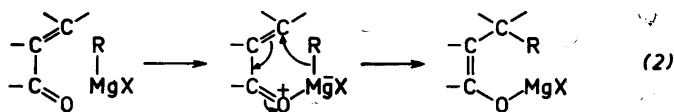
but in the case of allylic Grignard reagents the above-mentioned cyclic electron shift (1) competes successfully with (2), unsaturated ketones and tertiary alcohols being formed in stead of "saturated" esters, e. g.

$$CH_3CH=CH\cdot COO\text{-}sec\text{-}C_4H_9 \xrightarrow{\quad CH_2=CHCH_2MgBr \quad} CH_3CH=\overset{\overset{\displaystyle OH}{\displaystyle |}}{C}HC(CH_2CH=CH_2)_2 \quad (83\ \%)$$

and not

$$CH_2=CH\cdot CH_2CH\cdot CH_2COO\text{-}sec\text{-}C_4H_9 \quad (0\ \%)$$
$$\overset{\displaystyle |}{CH_3}$$

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* The tertiary alcohols formed by these reactions are presumably rather unstable, eliminating water easily. Many of them, after standing for a few weeks, turned into viscous polymers, insoluble in most solvents.

Table 1. Products and yields from reactions of *sec*-butyl esters of α,β-unsaturated acids with allylic Grignard reagents (RMgX).

| Ester \ R	Allyl	Methallyl	Crotyl	Benzyl
Crotonic	tert. alcohol [a] 83 %	tert. alcohol [b] 85 %	tert. alcohol [c] 87 %	ester [d] (53 %)
Tiglic	tert. alcohol [e] 70 %	tert. alcohol [f] 94 %	tert. alcohol [g] 91 %	ester[h], 10—20 % tert. alcohol [i], (25—35 %)
Cinnamic	tert. alcohol [j] 65 %	tert. alcohol [k] 48 %	tert. alcohol [l] 67 %	ester [m] 63 %

[a] Propenyldiallylcarbinol, b. p. 93.5°/35 mm, n_D^{20} 1.4707; calc. for $C_{10}H_{16}O$ (152.23): C 78.89; H 10.60. Found: C 78.90; H 10.64. [b] Propenyldimethallylcarbinol, b. p. 89°/12 mm, n_D^{20} 1.4695. Calc. for $C_{12}H_{20}O$ (180.28): C 79.94; H 11.18. Found: C 79.85; H 10.90. [c] Propenyldibutenyl-carbinol, b. p. 87°/13 mm, n_D^{25} 1.4674. Calc. for $C_{12}H_{20}O$ (180.28): C 79.94; H 11.18. Found: C 79.40; H 11.33. [d] *sec*-Butyl β-methyl-γ-phenylbutyrate, b. p. 95—96°/0.5 mm. The product is not pure; by saponification was obtained a 70 % yield of β-methyl-γ-phenylbutyric acid, b. p. 124—125°/0.8 mm, n_D^{20} 1.5132. Calc. for $C_{11}H_{14}O_2$ (178.22): C 74.13; H 7.92. Found: C 74.20; H 7.92. [e] 1-Methylpropenyl-diallylcarbinol, b. p. 81—82°/11 mm, n_D^{20} 1.4765. Calc. for $C_{11}H_{18}O$ (166.25): C 79.46; H 10.92. Found: C 78.95; H 10.84. [f] 1-Methylpropenyl-dimethallylcarbinol, b. p. 105°/15 mm, n_D^{20} 1.4770. Calc. for $C_{13}H_{22}O$ (194.31): C 80.35; H 11.41. Found: C 80.25; H 11.39. [g] 1-Methylpropenyl-dibutenylcarbinol, b. p. 96°/12 mm, n_D^{20} 1.4810. Calc. for $C_{13}H_{22}O$ (194.31): C 80.35; H 11.41. Found: C 79.70; H 11.44. [h] *sec*-Butyl α,β-dimethyl-γ-phenylbutyrate, b. p. 102—103°/0.8 mm, n_D^{20} 1.4866. Calc. for $C_{16}H_{24}O_2$ (248.35): C 77.37; H 9.74. Found: C 77.72; H 9.83. [i] The product, b. p. 141—142°/0.8 mm, n_D^{25} 1.5621, was not obtained pure. According to the infra-red spectrum, it is essentially alcohol: 1-methylpropenyl-dibenzylcarbinol. [j] Styryl-diallylcarbinol b. p. 117—118°/0.9 mm, n_D^{20} 1.5770. Calc. for $C_{15}H_{18}O$ (214.29): C 84.07; H 8.47. Found: C 83.90; H 8.96. [k] Styryldimethallylcarbinol, b. p. 123°/1 mm, n_D^{20} 1.5597. Calc. for $C_{17}H_{22}O$ (242.35): C 84.25; H 9.15. Found: C 83.60; H 8.25. [l] Styryldibutenylcarbinol, b. p. 119°/0.7 mm, n_D^{20} 1.5479. Calc. for $C_{17}H_{22}O$ (242.35): C 84.25; H 9.15. Found: C 84.50; H 9.16. [m] *sec*-Butyl β,γ-diphenylbutyrate, b. p. 157°/1 mm, n_D^{20} 1.5333. Calc. for $C_{20}H_{24}O_2$ (296.39): C 81.04; H 8.16. Found: C 81.00; H 8.05.

These results constitute further evidence, that the enhanced reactivity of allylic Grignard reagents towards carbonyl groups is caused by a special mechanism operating and is not merely due to a generally greater reactivity of these Grignard reagents as compared to others. Thus, they lend support to the cyclic mechanism of Young and Roberts *.

The fact that benzylmagnesium chloride does give the "normal" conjugate addition product (*i. e.* not reacting as an allylic reagent) is not incompatible

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* In fact, Young and Roberts have themselves tried the reaction between butenylmagnesium bromide and *tert*-butyl cinnamate [5]. Very little 1,4-addition product was found, but the main reaction product was not identified.

with these considerations. As pointed out above, the Young-Roberts mechanism involves the inversion of the allylic system, which is well known to occur also in the case of the benzyl grouping, e.g. the formation of o-methylbenzyl-alcohol from benzylmagnesium chloride and formaldehyde [7]. However, this inversion must imply a transitory loss of the aromaticity of the ring and, consequently, require a rather high energy of activation:

(3)
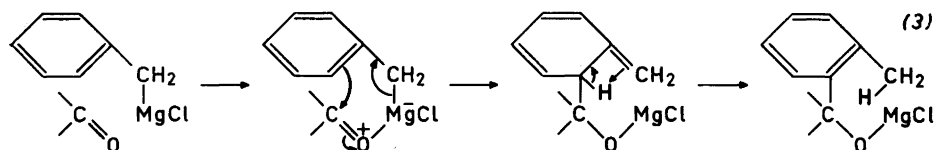
In this case, therefore, the conjugate addition process (2) is the one mostly favoured. Indeed, the results with the benzyl reagent may thus be considered to be consistent with the Young-Roberts mechanism.

Cuprous chloride, which is known to catalyze 1,4-addition of Grignard reagents in competion with 1,2-addition [8], has been found to have no effect in the cases of allylic Grignard reagents here described.

During this work no attempt was made to determine the structure of the butenyl group in the tertiary alcohols formed. According to Young and Roberts [2], they are assumed to have the α-methylallyl structure.

EXPERIMENTAL

Microanalyses are by Mr. Preben Hansen, Microanalytical Division, The Chemical Laboratory, The University of Copenhagen. Fractional distillations were through a simple 45 cm × 8 mm Podbielniak-type column with a tantalum wire spiral, a heated jacket and a partial reflux head.

sec-Butyl esters were prepared as previously described [9]. Allyl bromide was obtained according to Organic Syntheses [10]. Methallyl (β-methylallyl) bromide, b. p. 95—96°, n_D^{20} 1.4718, was synthesized from the alcohol (Fluka, pract.) according to Jones et al.[11] Crotyl bromide, b. p. 102—105°, n_D^{20} 1.4775, was the Fluka, purum, product, which was purified by washing with sodium bicarbonate solution, drying and destillation. Benzyl chloride was the commercial product (Fluka, purum), which was redistilled, b. p. 64°/14 mm, n_D^{20} 1.5398. The magnesium turnings used were those from May & Baker; this product is much more finely cut than ordinary Grignard magnesium, and it has been found particularly suitable for the preparation of allylic Grignard reagents (below).

The Grignard reagents were prepared according to the general procedure of Gilman and McGlumphy [12], which consists in using a great excess of magnesium, effective stirring and slow addition of the halide.

The reactions between the Grignard reagents and the α,β-unsaturated esters and the isolation of the products were carried out as previously described [3]. The products are given in Table 1.

The identities of the reaction products were further checked by infra-red spectroscopy. The spectra were measured with a Beckman IR2 spectrophotometer with sodium chloride prisms, using 5 % solutions in carbon tetrachloride. The alcohols were identified by their hydroxyl band in the 3 μ region and by the absence of a carbonyl absorption. The spectra of the esters (from benzylmagnesium chloride) showed — besides a carbonyl band — the

group of absorption bands (around 1 111 cm⁻¹), which has previously been found to be characteristic for *sec*-butyl esters [13].

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