

INTERACTION OF CH_3MgI WITH β -DICARBONYL COMPOUNDS

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Summary

The reaction of CH_3MgI with the ferrocene-containing α -monosubstituted β -dicarbonyl compounds is studied; a general reaction scheme is proposed. The addition reaction to a carbonyl group, the enolization and the C_α – C_β -cleavage prove to be non-specific by D-labelling.

Recently we have shown that the ferrocenyl-containing α -monosubstituted β -dicarbonyl compounds under the action of a Grignard reagent, PhMgBr , form products of C_α – C_β -cleavage along with the well-known addition to the carbonyl group and enolization [1]. In each particular case the ratio of products of the reaction of β -dicarbonyl compounds with PhMgBr is dependent on the activity of the $\text{C}=\text{O}$ group in the addition reaction, the mobility of the α -hydrogen atom, the $\text{p}K_{\text{R}^+}$ value of the α -substituent R, and the stability of the enolate which is formed after C_α – C_β -cleavage. The product ratios are estimated based on the $\text{p}K_{\text{a}}$ value of the corresponding unsubstituted β -dicarbonyl compounds [1].

In our investigation of the interaction of the β -dicarbonyl compounds with CH_3MgI we have shown that these three reactions occur independently. The

TABLE I

YIELDS OF PRODUCTS OF THE REACTIONS OF I–V WITH CH_3MgI

Initial	Products (%)			
	a	b	c	d
I	22	10	28	23
I ^a	16	9	53	7
II	1	11	75	traces
III	traces	49	34	traces
IV	–	32	59	traces
V	–	52	35	traces

^a At -15°C .

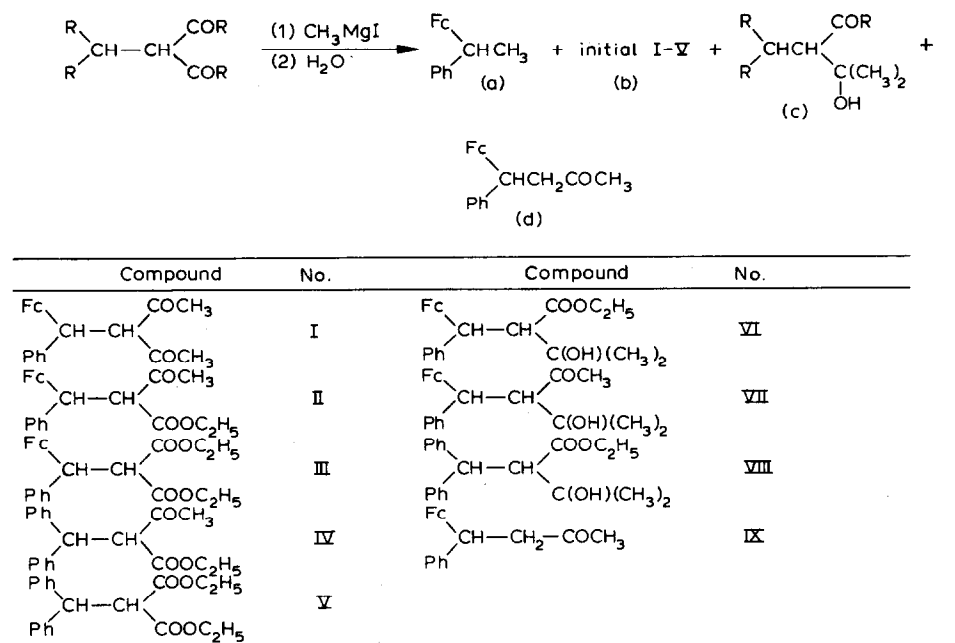
TABLE 2
SPECTRAL DATA AND ELEMENTAL ANALYSIS FOR COMPOUNDS VI-IX

Compound N°	δ (ppm)		H_α	COCH_3	OC_2H_5	$\text{C}(\text{CH}_3)_2$	OH	M.p. (°C)	Formula	Analysis (Found (calcd.)(%))		
	H_β	H_α								C	H	Fe
VI	^a	3.06 ^b			0.83 1.08	0.96 1.08 1.16	3.10 1.92	90	$\text{C}_{24}\text{H}_{28}\text{O}_3\text{Fe}$	68.79 (68.59)	6.95 (6.71)	13.41 (13.27)
VII	^a	3.26	1.70			1.24 0.82	2.56	108	$\text{C}_{23}\text{H}_{26}\text{O}_2\text{Fe}$	70.83 (70.78)	6.92 (6.70)	14.10 (14.31)
VIII	4.50	3.56 ^b			0.88	1.04 1.00 1.22	2.70	60	$\text{C}_{20}\text{H}_{24}\text{O}_3$	76.70 (76.89)	7.42 (7.74)	
IX	3.10	4.30	2.00					96	$\text{C}_{20}\text{H}_{20}\text{OFe}$	72.73 (72.31)	6.11 (6.06)	16.60 (16.80)

^a Assignment difficult. ^b Assigned by deuteration. ¹H NMR spectra recorded with a "Tesla BS-497" and "Bruker-200" with frequencies of 100 and 200 MHz in CDCl_3 , internal standard TMS.

reaction route is shown in Scheme 1

SCHEME 1



The product yields (a-d) are given in Table 1. The results of elemental analysis and some physico-chemical data are given in Table 2.

As can be seen from Table 1, the enolization and the addition reaction to one carbonyl group mainly proceeds under the chosen conditions. The incorporation of a D-label in the initial compound after decomposition of the reaction mixture by D₂O is proof of the enolisation process, which takes place even with a high excess of CH₃MgI. It should be noted that at chromatographic purification of deuterated products of the ferrocenyl derivatives III, II, and particularly I, the loss of D-label is observed.

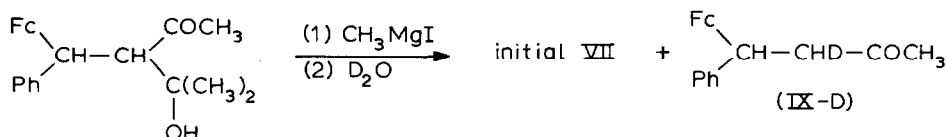
Addition of CH₃MgI to a carbonyl group (c) results in a high yield of β-oxy carbonyl compounds VI-VII. The decrease in yields of carbinols on rearrangement from β-ketonic esters to β-diester is observed both with the derivatives II and III of the ferrocenyl series and for the benzhydryl derivatives IV and V. This decrease in yield is obviously connected with diminishing the carbonyl activity in this series.

It is noteworthy that diastereomeric pairs of carbinols in the ratio 1/2 are formed from β-diester III while β-diketone I gives only one isomer.

There are two chirality centres, C_α- and C_β-, in β-ketonic ester II, II itself being represented by an equimolar mixture of the diastereomers. On the formation of diastereomeric pairs of the carbinols (c) asymmetrical induction is not observed and the ratio remains practically unchanged.

Compounds IX are formed by thermal cleavage (ketonic cleavage) of the corresponding magnesium alcoholate of β-oxyketone VII formed by pathway c. The reaction carried out at low temperature (-15°C) leads in fact to a sharp decrease in

the yield of ketonic cleavage product (d) and correspondingly the yield increase of carbinol VII (see Table 1 and Scheme 1). After the reaction of excess CH_3MgI with carbinol VII and decomposition of the reaction mixture by D_2O the initial VII and deuterated IX-D are obtained with 90% yield:



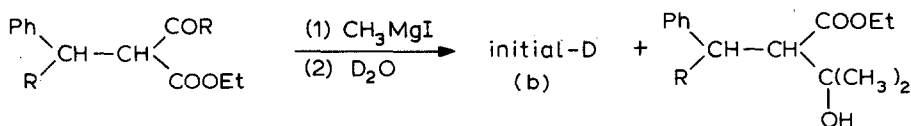
It is noteworthy that $\text{C}_\alpha\text{-C}_\beta$ -cleavage products (a) are not observed and, thus, β -oxyketones (as well as β -oxyesters) and their magnesium alcoholates do not undergo $\text{C}_\alpha\text{-C}_\beta$ -cleavage under the conditions described.

It follows from Table I that only for β -diketone I $\text{C}_\alpha\text{-C}_\beta$ -cleavage proceeds under the action of CH_3MgI with a high yield. In the reaction of CH_3MgI with β -ketonic ester II and β -diester III only traces ($\sim 1\%$) of $\text{C}_\alpha\text{-C}_\beta$ -cleavage products are found while the corresponding benzhydryl derivatives IV and V do not break at all at the $\text{C}_\alpha\text{-C}_\beta$ -bond. We have by dimeric thin-layer chromatography on SiO_2 in benzene shown that β -ketoester II and β -diester III in reactions with CH_3MgI form the ketonic cleavage product IX. Furthermore II forms I with insignificant yield while III (yield 9%) forms II. This explains the appearance of $\text{C}_\alpha\text{-C}_\beta$ -cleavage products in the reaction of excess CH_3MgI with II and III. β -Ketoester II can form product (a) in the reaction with CH_3MgI directly (see [2]) and also as a result of accumulation of I. On the other hand the formation of (a) in the reaction of III with CH_3MgI [2] is caused by formation of II and I as intermediates.

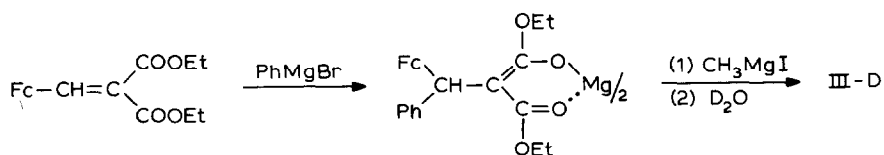
The three courses of the reaction discussed may possibly proceed via two basically different routes, i.e., (1) the interdependence of the three reactions a, b and c or (2) an alternative pathway. Castelli [3] while discussing the interaction of α -methyl-acetoacetic ester with PhMgBr pointed out the possibility of the consecutive course of the enolization and addition reactions.

This conclusion was based on the qualitative analysis of the reaction mixtures, and the data of the intermediate compound reactions with PhMgBr . Yet, the determination of the reaction products does not solve the possibility of the alternative course and therefore cannot serve as a reliable criterium.

To solve this problem we made use of the D-label. We could follow its entrance into the reaction products of compounds I-V with CH_3MgI only by the formation of a C-D bond after decomposition of the reaction mixtures by D_2O . The data of the ^1H NMR and mass spectra unambiguously indicate the independence of these two routes with an accuracy of 90-95%. In fact, if formation of the carbinols by pathway (c) is preceded by the enolization and followed by the 1,2- or 1,4-addition of CH_3MgI to the enolate, then the carbinols (c) labelled by deuterium must be formed after decomposition of the reaction mixture by D_2O and the product of ketonic cleavage (d) must also contain a label. According to our data the product of interaction of I and CH_3MgI does not contain the label whereas only (c) carries it in the molecule, almost quantitatively. The diastereomeric carbinols VI-VII neither contain deuterium irrespective of whether the initial compound was the β -ketoester or the β -diester.



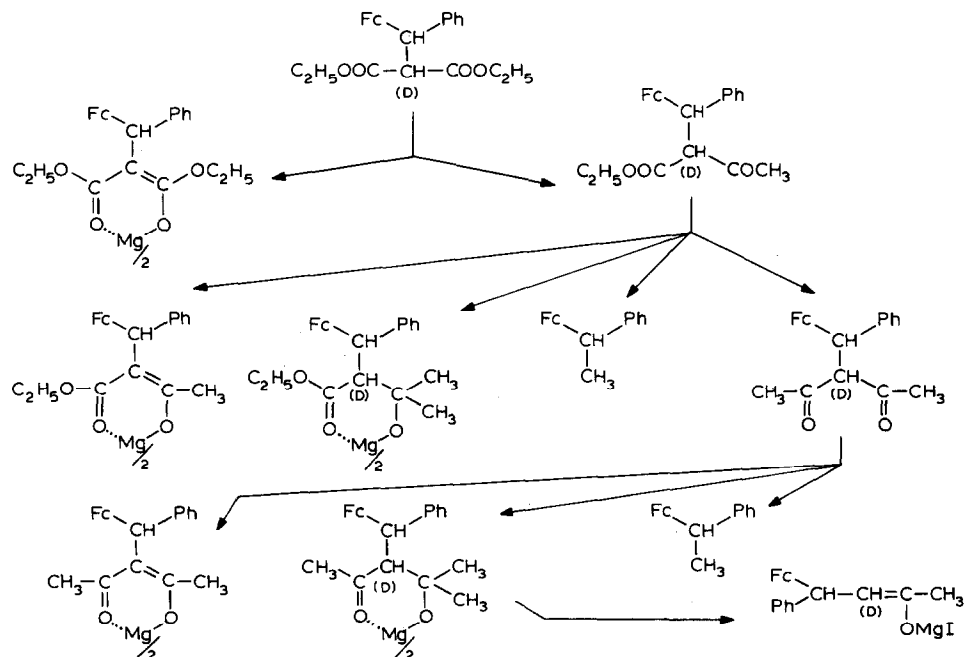
Compounds III and V, if previously deuterated retain the label in carbinols quantitatively after treatment with CH_3MgI and further treatment with H_2O . Thus the initial enolization of the β -ketonic ester with the formation of an intramolecular magnesium compound and further nucleophilic attack is open to discussion [3]; since there are considerable amounts of the initial compounds regenerated from the reaction mixtures, i.e., as enolates not interacted with the excess CH_3MgI . In fact, after addition of excess CH_3MgI to the enolate of β -diester III and the decomposition of the reaction mixture by D_2O the addition product was not formed; the yield of III-D is almost quantitative.



This is the reason why it is possible to detect the formation of II and I upon the action of excess CH_3MgI on III and, correspondingly, to detect I upon the action of CH_3MgI on II.

On the basis of the data obtained the general Scheme 2 for the rearrangements of

SCHEME 2



α -monosubstituted ferrocenyl-containing β -dicarbonyl compounds may be proposed.

According to ^1H NMR and IR spectra the enol form in the initial β -dicarbonyl compounds I—V is nearly absent.

Scheme 2 may be proposed for other monosubstituted β -dicarbonyl compounds and also for other Grignard reagents. Differences may be observed in the ability of $\text{C}_\alpha\text{--C}_\beta$ -cleavage (a) and in the ratio of the products (b–d) taking into account the ketoenol equilibrium in the initial β -dicarbonyl compound.

Experimental

The reactions were carried out in ether/benzene solutions with a 5-fold excess of Grignard reagent at room temperature for 15 min. After decomposition of the reaction mixtures by H_2O or D_2O (99.8%) the reaction products were separated by thin-layer chromatography on SiO_2 by benzene. The total yield is over 80%. The D-content in samples was estimated by mass spectroscopy according to $M^+/M + 1^+$ peak intensities.

References

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