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STUDIES ON THE GRIGNARD REACTIONS III[1].

COMPETITIVE ADDITION-REDUCTION IN THE REACTION OF 2,4-DIMETHYL-3-PENTANONE WITH THE GRIGNARD REAGENT FROM BROMOPROPANE.

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The competitive addition-reduction of 2,4-dimethyl-3-pentanone with "n.PrMgBr" was studied using the procedure described earlier[1]. The reaction was followed by quantitative vapour phase chromatography[2] analysis of the products. The Grignard reagent was prepared by reaction of n.propylbromide with magnesium in ether; and the excess $MgBr_2$ was determined as being the difference between a Volhard titration and a new method based on the reaction of the Grignard reagent with benzophenone (to be published). Dioxane was added until both analysis methods gave the same result.

When the reagent was in large excess (t $(nPr)_2Mg.MgBr_2$ = 0.579; t ketone = 0.0472) the ratio of addition compound (2-methyl-3-isopropyl-3-hexanol) to reduction compound (2,4-dime-

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[1] Part I. M. Anteunis, J.Org.Chem. 26, 4214 (1961).
Part II. M. Anteunis, J.Org.Chem. 27, 596 (1962).

[2] The instrument used was a A-350-B "Aerograph", equipped with a disc integrator.

thyl-3-pentanol) was constant at different time intervals. This ratio had a value of 10 at -21.6°. At 25°, after completion of the reaction, it was about 4,9. Only small enolization (1-2 %) occurs, while no aldolization could be detected. It is remarkable that we obtained such a high proportion of addition, as other authors[3-6] obtained results with about 35 % addition, 64 % reduction and 1-2 % enolization. This must be caused by a difference in procedure, as in the latter investigations the ketone was slowly added to a stirred solution of the reagent at roomtemperature. As pointed out[7] this can give different results. Indeed, the reaction leads to alcoholates which can rearrange during the prolonged reactiontime[3] and also in certain respect, can act like $MgBr_2$, which is known to favour the addition when present in excess[5]. In any case it follows from our experiments that the order of the reaction, with respect to the ketone, for both reduction and addition is the same, when Grignard reagent is in large excess.

We further made runs at 0,0° under circumstances where ketone was in excess, and the relative yields of addition and reduction are reported in figure 1 as function of the degree of reaction.

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[3] J.Miller, G.Gregoriou, H.Mosher; J.Am.Chem.Soc. **83**, 3966 (1961).

[4] F.Whitmore, S.George; J.Am.Chem.Soc. **64**, 1239 (1942).

[5] S.Swain, H.Boyles; J.Am.Chem.Soc. **73**, 870 (1951).

[6] D.Cowan, H.Mosher; J.Org.Chem. **27**, 1 (1962).

[7] J.Miller, Dr. of Philosophy, Thesis 1960, Stanford University, California, U.S.A.

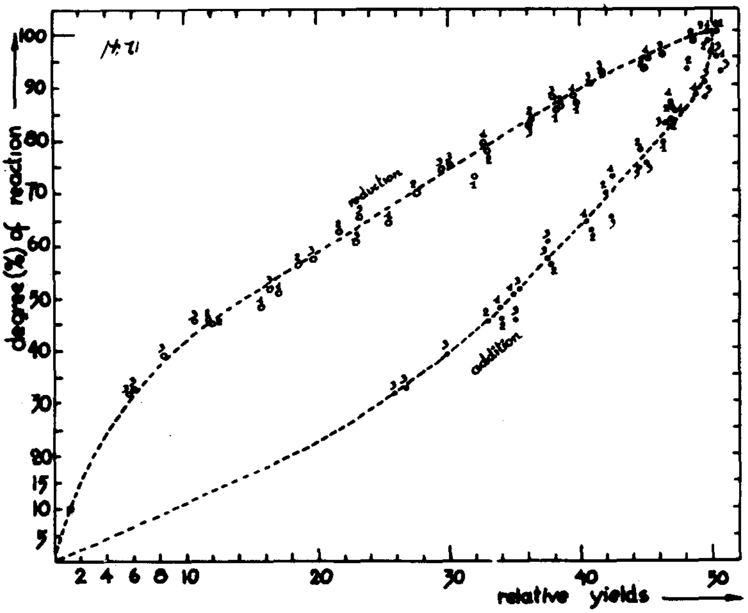


FIG. 1

Relative yields of addition and reduction versus degree of reaction with excess ketone.
Points 1 and 2 : t(Grignard r.) = 0.605; t(2,4-diMe-3-butanone) = 0.787.
3 : t(Grignard r.) = 0.3025; t(ketone) = 0.3935.

Here too no aldolization and very slight enolization (< 1 %) was noted. Now the ratio (addition)/(reduction) changes gradually being 4.34 at 31 % reaction and reaching almost unity at the end of reaction.

The extrapolation at the start of the reaction is based upon a ratio estimation of 7.3, as obtained by linear interpolation of the ratio value at -21.6° and +25°. It is seen that no change in ratio is obtained when the concentrations are halved

(points 3) and while the amount reduction grows linear between 30-90 % reaction, there is a gradual change of the amount addition which seems to remain nearly unchanged towards the end of reaction (85-90 % reaction).

This is perhaps better illustrated by figure 2, where the data of points 3 are reported against time (absolute transformation being used this time).

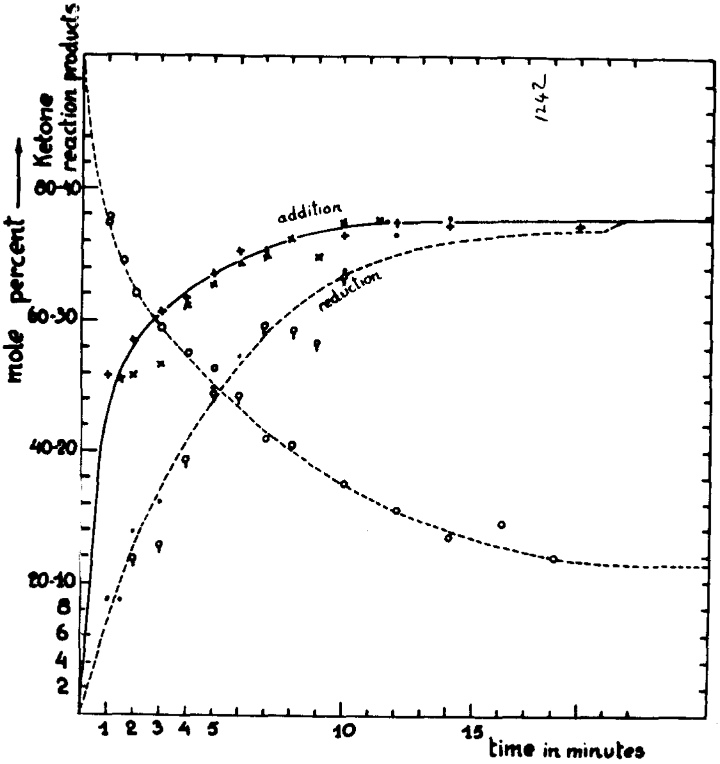
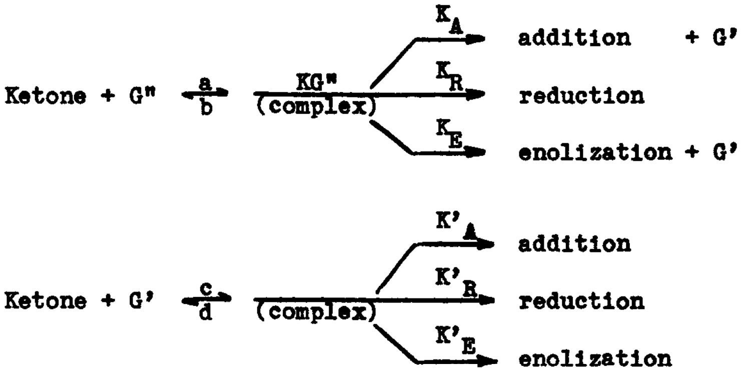


FIG. 2

Here too we observed that reduction is not the principal reaction. A mechanism has been proposed for these reactions, by Miller, Gregoriou and Mosher[3].

These authors assume that the bimolecular architecture of the Grignard reagent (G") is transformed via a complex towards a monomolecular structure (G') which could react, with its own rate, with ketone to give the second possible pathway towards addition, reduction and enolization. Their scheme is then



These assumptions are in contradiction with the kinetics of the reaction of methylmagnesium bromide upon pinacolone and benzophenone[1] which follow an overall third order kinetic (first in ketone, second in reagent).

It is however difficult to accept a third order mechanism for the reduction step, as the only plausible way is the Meisenheimer mechanism[8]. On the other hand there must be a close mechanistic connection between addition and reduction, as varying the absolute concentration of the reaction partners but not their ratio, has practically no influence upon the ratio of the reaction products (see also ref.[2,7]).

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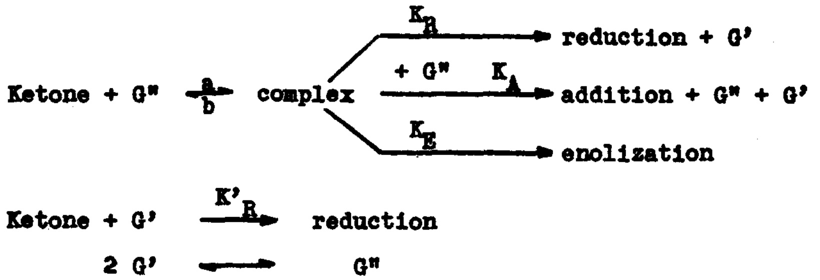
[8] See M.Kharasch, O.Reinmuth in "Grignard Reactions of Nonmetallic substances, Prentice-Hall, New York, 1954.

It is possible that the formed monomeric Grignard reagent G' (which's rate of formation depends upon the velocity of the addition reaction) can either react rapidly with a ketone molecule to give only reduction, or can dimerize to recreate the bimolecular species. When the reduction is fast with regard to the dimerization, it is clear that an end ratio of unity will be reached when ketone is in excess. In this connection it is of importance that with $Et_2Mg.MgBr_2$ the addition reaches 84 % while with ketone in excess this value drops below 50 %[7]. When however the former is hindered or is rendered impossible (f.i. by the use of $Me_2Mg.MgBr_2$) and the latter is fast only addition takes place and this can follow third order kinetics. The scheme is then



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