

REDUCTION OF ESTERS WITH "HMgBr"

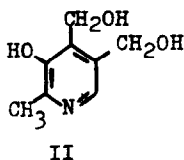
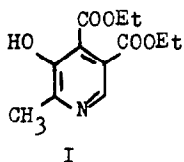
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Esters are generally much less reactive toward complex hydride reducing agents than are aldehydes and ketones, and reports (1) of their reduction by simple hydrides are few. A need for a new reducing agent for the ester I prompted us to consider unusual substances. Grignard reagents RMgX easily reduce esters to alcohols but dialkylate them at the same time; if, however, R = H, primary alcohols would be obtained. Therefore, the synthesis of



HMgBr, magnesium bromohydride, was investigated.

In the literature was found a description of one especially promising reagent, a gray powder prepared by pyrolyzing EtMgBr in vacuo at 220° for 4 hours, whose composition was HMgBr and which reduced benzophenone to benzhydrol (2). This report has aroused little attention, probably because ketones are so easily reduced by other means.

We have found that the Grignard pyrolysate does indeed reduce esters to primary alcohols. For example, 8½ mmoles of EtMgBr was heated at 235° for 2½ hours under 0.5 mm. pressure. The resulting gray powder was stirred overnight under N₂ with 0.5 mmole of I in ether, affording II (pyridoxine) in 30% yield,

after suitable workup. Identification was by IR, UV, paper chromatography and bioassay.

Ethyl benzoate is reduced to benzyl alcohol (35%), and ethyl butyrate to n-butyl alcohol (10%). One amide was also tried, N,N-dimethylbenzamide, which was reduced to N,N-dimethylbenzylamine (32%). The products were identified by VPC comparison, and yields are only approximate. The chromatograms were quite clean, showing little other than products and recovered starting materials.

As for the structure of the reagent, there is good evidence that it actually consists of a finely divided mixture of MgH_2 and $MgBr_2$ (3), although an earlier opinion that $HMgBr$ is also present may be noted (4). Pertinent to this question is the observation that, in the reductions of the three mono-functional compounds described above, the yields varied widely (10-35%) but so did the ratios of reagent to substrate (1.6-5.0). If the reagent is really a mixture of active and inert components, the amount of active material turns out to be surprisingly constant for the three runs, varying from about 6 to 9 percent. Whether any $HMgBr$ is actually present in the Grignard pyrolysate is still conjectural, however.

The preparation of authentic $HMgBr$ was next attempted. It seemed desirable to use the traditional method, treating magnesium with HBr in ether. The problem, of course, is that our "alkyl halide" happens also to be a strong protic acid, which should instantly destroy the Grignard compound, forming H_2 and $MgBr_2$. This reaction was tried, and as expected, the clear solution of $MgBr_2$ etherate which remained after the vigorous gas evolution subsided had no reducing properties toward ethyl benzoate. No reduction was observed even when ester was present during the $Mg-HBr$ reaction.

Clearly, if any $HMgBr$ is ever to be detected from this system, it must be whisked away from its progenitor, HBr , before they can mix. Accordingly, a solution of HBr in ether was trickled slowly down a column of magnesium turnings. With short columns, the effluents were strongly acidic, denoting incomplete reaction, but when the columns were long enough, ca. 12-14", the

clear, colorless effluents now gave strongly alkaline solutions with water, and with careful observation tiny bubbles could be seen to form at the interface on mixing with water or alcohols.

Ether solutions prepared in this way reduce ethyl benzoate to benzyl alcohol; benzonitrile and benzamide to benzylamine; and N,N-dimethylbenzamide to N,N-dimethylbenzylamine. The yields are, not surprisingly, very small (<1%), and detectable only by VPC, but identifications are secure. In a control experiment, no benzyl alcohol whatever could be detected from a reaction of ethyl benzoate with EtMgBr; this was important because some EtBr was present in the ether-HBr solution owing to cleavage of the ether, and this would form EtMgBr which might escape the HBr along with the HMgBr.

We believe, therefore, that magnesium bromohydride does exist in these solutions, although perforce in very low concentration. The possibility exists that other metal-acid reductions also involve intermediates of this type.

REFERENCES

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