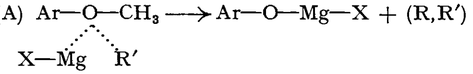
124. (I) *The Mechanism of the Cleavage of Ethers of the Anisole Type by Grignard Mixtures.* (II) *The Action of Grignard Solutions on α-Bromo-ketones.*

By Alexander Schönberg and Radwan Moubasher.

(I) Anisole and related substances undergo scission when heated with Grignard mixtures (*i.e.*, mixtures obtained when ethereal Grignard solutions are evaporated to dryness at about 200°). This cleavage was generally attributed to the action of the organic magnesium compound on the substance concerned (compare scheme A), but it is now suggested that the cleavage is effected by the magnesium halide present in the equilibrium $2RMgI \rightleftarrows MgR_2 + MgI_2$, for the same result is obtained with magnesium iodide or bromide alone under the same conditions (compare scheme B).

(II) α-Bromo-ketones when heated with ethereal Grignard solutions (followed by hydrolysis) yield the corresponding unbrominated ketones [cf. *inter alia* (II) ⟶ (IV)]. We attribute these changes, not to the action of Grignard compounds, as formerly believed, but to that of the magnesium halide present in the Grignard solutions.

(I) *Mode of Action of Grignard Mixtures on Anisole and Related Substances.*—The action of Grignard mixtures (see above) on anisole and related substances has been attributed by many workers to the effect of the organo-magnesium halide, which is supposed to form a derivative of a phenol as in (A), proposed by Grignard and Ritz (*Bull. Soc. chim.*, 1936, **3**, 1181). Here (R, R′) represents various aliphatic by-products.

(A) 

$$Ar{-}\underset{X{-}Mg\quad R'}{O}{-}CH_3 \longrightarrow Ar{-}O{-}Mg{-}X + (R,R')$$

Although this view cannot be disproved, there is no experimental evidence for it, and since we find that magnesium iodide effects cleavage of anisole under the same conditions, and this iodide is known to exist in equilibrium with the Grignard compounds (see above), it seems reasonable to regard this as the active agent, thus :

$$\text{(B)}\quad PhOMe + MgI_2 \longrightarrow [MgI{\cdot}OPhMe]^+\,[I]^- \xrightarrow[\text{decompn.}]{\text{auto-}} Ph{\cdot}O{\cdot}MgI + MeI$$

Application of the New Theory to Special Cases.—(*a*) Grignard and Ritz (*loc. cit.*) found that alkylmagnesium iodides react much more rapidly with anisole than do the bromides. On our theory, therefore, magnesium iodide should be more effective than the bromide, and this deduction was verified.

(*b*) *Action of Grignard solutions on phenyl allyl ether.* Lüttringhaus, von Sääf, and Hauschild (*Ber.*, 1938, **71**, 1673) noted that this ether reacts with *n*-butylmagnesium bromide at 50—70°, whereas scission of anisole requires a temperature of 160—200°, and they proposed the scheme (R = *n*-butyl) :

$$\text{(C)}\quad MgRX + PhO{\cdot}CH_2{\cdot}CH{:}CH_2 \longrightarrow PhO{\cdot}MgX + CH_2R{\cdot}CH{:}CH_2$$

If our theory be true, phenyl allyl ether should be split by magnesium iodide or bromide alone at similarly low temperatures. This deduction, too, has been verified, and we suggest that a scheme analogous to (B) is valid. It is true that the yield with magnesium bromide alone is smaller than with *n*-butylmagnesium bromide, but we attribute this to the effect of the allyl bromide. Under our conditions, this does not escape (at 50—70°) and so tends to reverse the reaction, whereas under the normal Grignard conditions it reacts with the *n*-butylmagnesium bromide (see D) and so cannot suppress the main reaction.

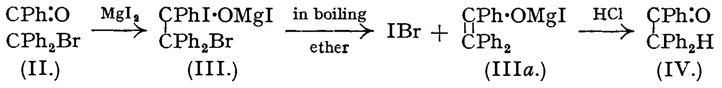
$$\text{(D)}\quad MgRBr + CH_2Br{\cdot}CH{:}CH_2 \longrightarrow MgBr_2 + CH_2R{\cdot}CH{:}CH_2\ \text{(I.)}\quad (R = n\text{-butyl})$$

Confirmation of this view may be found in the fact that Lüttringhaus *et al.* (*ibid.*, p. 1679) stated that *n*-heptene (I) is formed in 37% yield by the action of ethereal butylmagnesium bromide solutions on phenyl allyl ether at 58°.

(II) *The Mode of Action of Grignard Solutions on α-Bromo-ketones.*—It is well known that α-bromo-ketones are converted into the corresponding unbrominated ketones by the action of Grignard reagents followed by hydrolysis. This reaction has been expressed in various forms (see, *e.g.*, Kohler and Johnstin, *Amer. Chem. J.*, 1905, **33**, 45; Umnowa, *Chem. Zentr.*, 1913, **84**, I, 1402; Löwenbein and Schuster, *Annalen*, 1930, **481**, 106; Kohler and Tishler, *J. Amer. Chem. Soc.*, 1932, **54**, 1594), and Löwenbein and Schuster believe that free radicals play a part in it, but all the authors agree in attributing the result to the organo-magnesium compound present in the Grignard reagent.

We believe that there is no experimental evidence for this opinion, and that, as before, the reaction is due to the magnesium halide. Our experiments were carried out with benzoyldiphenylbromomethane (II), which is easily accessible and has been widely used in previous researches on this type of reaction.

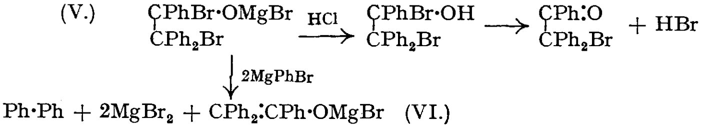
(*a*) *Action of ethereal magnesium iodide on benzoyldiphenylbromomethane* (II). The first product of this reaction is (III); then free halogen is split off to give (III*a*) (autodecomposition), and treatment of the latter with dilute hydrochloric acid yields benzoyldiphenylmethane (IV) quantitatively. The following scheme is proposed :

(E) 

$$\begin{array}{c}CPh{:}O\\ |\\ CPh_2Br\\ \text{(II.)}\end{array} \xrightarrow{MgI_2} \begin{array}{c}CPhI{\cdot}OMgI\\ |\\ CPh_2Br\\ \text{(III.)}\end{array} \xrightarrow[\text{ether}]{\text{in boiling}} IBr + \begin{array}{c}CPh{\cdot}OMgI\\ \|\\ CPh_2\\ \text{(III}a\text{.)}\end{array} \xrightarrow{HCl} \begin{array}{c}CPh{:}O\\ |\\ CPh_2H\\ \text{(IV.)}\end{array}$$

(*b*) *Action of ethereal magnesium bromide on benzoyldiphenylbromomethane* (II). Use of magnesium bromide instead of iodide in the above experiment (with ether as a solvent) afforded unchanged starting material. Nevertheless, we believe the primary reaction to be essentially the same as in (E), but the analogue (V) of (III) to be unaffected by boiling ether; it would then react subsequently as follows :

(V.)



$$\begin{array}{c}\text{CPhBr·OMgBr}\\ |\\ \text{CPh}_2\text{Br}\end{array} \xrightarrow{\text{HCl}} \begin{array}{c}\text{CPhBr·OH}\\ |\\ \text{CPh}_2\text{Br}\end{array} \longrightarrow \begin{array}{c}\text{CPh:O}\\ |\\ \text{CPh}_2\text{Br}\end{array} + \text{HBr}$$

$$\downarrow \text{2MgPhBr}$$

$$\text{Ph·Ph} + 2\text{MgBr}_2 + \text{CPh}_2\text{:CPh·OMgBr}\quad \text{(VI.)}$$

In the presence of Grignard compounds, however, (V) reacts to give (VI), which on acidification affords (IV) (compare the action of phenylmagnesium bromide on dibromostilbene, Kohler and Johnstin, *Chem. Zentr.*, 1905, I, 523 : $\text{CHBrPh·CHBrPh} + 2\text{MgPhBr} \longrightarrow \text{CHPh:CHPh} + \text{Ph·Ph} + 2\text{MgBr}_2$).

(*c*) *Action of magnesium bromide* (*dissolved in warm anisole*) *on benzoyldiphenylbromomethane* (II). If magnesium bromide is allowed to act on (II) (both reagents being dissolved in anisole) at 85°, a product is formed which yields benzoyldiphenylmethane when treated with hydrochloric acid, the reaction being analogous to that in (E). The addition product (V), which is formed in ethereal as well as in anisole solution, is stable at the b. p. of ether, but decomposes at higher temperatures.

EXPERIMENTAL.

(I) *Action of Magnesium Iodide on Anisole.*—This experiment, analogous to that of Simonis and Remmert (*Ber.*, 1914, **47**, 269) using a dried Grignard reagent, was carried out in a vessel fitted with a reflux condenser to which a calcium chloride tube was connected. Magnesium powder (9·7 g.), suspended in 250 c.c. of ether (distilled over sodium), was treated portionwise with iodine (50·8 g.) in the cold; reaction took place immediately, and the mixture was refluxed until almost colourless, excess of magnesium then being filtered off. The ether was evaporated, and during this process anisole (10·8 g.) was added gradually, and the mixture heated, in a vessel fitted with an air condenser, in an oil-bath at 200—220° for one hour. No anisole could then be detected, and the residue was red; after having cooled, it was decomposed with dilute hydrochloric acid, rendered alkaline, and extracted with ether. The aqueous alkaline layer was separated, warmed to expel traces of ether, acidified, and steam-distilled. The distillate was made alkaline and treated with excess of benzoyl chloride in the cold. A crystalline precipitate was formed, and after 15 minutes the reaction mixture was poured into iced water. Phenyl benzoate (11·5 g.) was obtained and crystallised from benzene; m. p. 68°, undepressed on admixture with an authentic specimen. Simonis and Remmert had obtained phenoxymagnesium iodide (see scheme A).

Action of Magnesium Bromide on Anisole.—The magnesium bromide was prepared from bromine (12 g.) and excess of magnesium powder, the conditions and subsequent procedure being as for the iodide (above), except that 20 g. of anisole were used. Phenyl benzoate was obtained in much smaller yield.

Action of Magnesium Bromide on Phenyl Allyl Ether at 95°.—The phenyl allyl ether (Perkin, J., 1896, **69**, 1225) was carefully purified and freed from any traces of phenol. To an ethereal solution of magnesium bromide, prepared as described above (bromine, 32 g.; magnesium, 9·8 g.; ether, 250 c.c.), anisole (30 g.) was added, and the mixture heated to remove the ether. Phenyl allyl ether (13·5 g.) was added, and the mixture heated for 5 hours at 95°, a stream of dry carbon dioxide being passed through it in order to remove the allyl bromide formed. (All these processes were carried out in a dry atmosphere.) The mixture was allowed to cool, and shaken with ammonium chloride solution; aqueous sodium hydroxide solution was then added in excess, and the mixture again shaken and left for several hours. The aqueous layer was separated, acidified, and steam-distilled, and the distillate rendered alkaline and treated with benzoyl chloride. Phenyl benzoate (3·5 g.) was obtained (identified by mixed m. p.).

In two blank experiments, one without magnesium bromide and the other without phenyl allyl ether, phenyl benzoate was not formed.

(II) *Action of Magnesium Iodide on Benzoyldiphenylbromomethane* (II) *in Boiling Ether* (with Miss SOAD BEDEIR).—To a filtered ethereal solution of magnesium iodide, prepared as above from iodine (4 g.) and ether (150 c.c.), benzoyldiphenylbromomethane (0·5 g.) was added, and the solution refluxed for 6 hours. The mixture was then treated with dilute hydrochloric acid and ice, the ethereal layer separated, and dried over sodium sulphate; the ether was distilled off, and the residue crystallised from petrol (b. p. 60—70°), colourless crystals of benzoyldiphenylmethane being obtained, m. p. and mixed m. p. 137°, in almost quantitative yield. In a blank experiment carried out without magnesium iodide, the initial substance was recovered unchanged.

Magnesium Bromide and Benzoyldiphenylbromomethane (II) *in Boiling Ether.*—A solution of magnesium bromide (bromine, 4 g.; magnesium, 1·2 g.; ether, 150 c.c.) was prepared (in diffused light), the bromo-compound added, and the solution refluxed for 9 hours in a dry atmosphere. After treatment with dilute hydrochloric acid and ice, followed by ether extraction as usual and distillation, (II) was recovered unchanged; m. p. and mixed m. p. 97°.

Action of Magnesium Bromide on Benzoyldiphenylbromomethane in the Presence of Warm Anisole.—An ethereal solution of magnesium bromide was prepared as above, and the ether distilled off; during this distillation anisole (10 g.) was added in portions. When all the ether had been driven off, benzoyldiphenylbromomethane (0·5 g.) was added, and the reaction mixture heated under reflux (guard tube) on a water-bath for 9 hours. (The temperature of the mixture did not exceed 85°.) The product was worked up in the usual manner, the ether and most of the anisole being removed in a vacuum on a water-bath. The residue solidified (m. p. 135°), and after recrystallisation from petrol (b. p. 100—150°), had m. p. and mixed m. p. with benzoyldiphenylmethane 136°.

The bromo-compound (II) was heated on the water-bath with anisole for 3 hours, the anisole driven off in a vacuum, and the residue cooled; the initial substance was found to be unchanged.

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