The Bodroux Reaction.

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For the reaction between an aminomagnesium halide and a simple ester, yielding a substituted amide, the mechanism proposed by Bodroux (*Bull. Soc. chim.*, 1905, **33**, 831), involving two molecules of aminomagnesium halide and one molecule of ester in an intermediate complex, has been shown to be incorrect. The complex contains equimolecular proportions of the halide and the ester, the second molecule of aminomagnesium halide acting by decomposing the complex.

An aminomagnesium halide, formed when a primary or secondary amine reacts with a Grignard reagent at room temperature, reacts with a simple aliphatic or aromatic ester to yield a substituted amide.

The reaction has been described by Bodroux (*Bull. Soc. chim.*, 1905, **33**, 831; 1906, **35**, 519; 1907, **1**, 912; *Compt. rend.*, 1904, **138**, 1427; 1905, **140**, 1108; 1906, **142**, 401). He postulated the formation of an intermediate compound involving two molecules of the aminomagnesium halide and one of the ester, because the yield of amide was never more than 50% (based on the ester) when equimolecular quantities of ester and aminomagnesium halide were used, although use of double the quantity of aminomagnesium halide gave an almost theoretical yield.

In this way, with two equivs. of aminomagnesium halide, hexanoanilide, dodecanoanilide and -*m*-toluidide, and *NN*-diphenyl-acetamide and -benzamide have now been prepared in almost theoretical yield (based on the ester).

If Bodroux's mechanism is correct, by using *o*-phenylenediamine as the amine, an intermediate compound should be produced involving the two adjacent groups of the *o*-phenylenebisaminomagnesium dihalide with the ester, and this should give a stable 2-substituted benziminazole as the end-product. No trace of 2-methyl- or 2-phenylbenziminazole was obtained when *o*-phenylenebisaminomagnesium di-iodide was treated with methyl acetate or benzoate respectively, even when more vigorous conditions than usual were used.

Isolation of compounds of type (I) postulated by Bodroux (*loc. cit.*) as intermediates has not been described. However, it has now been found that equimolecular proportions of anilinomagnesium iodide and methyl benzoate give a stable white powder, shown by analysis to be (II). Decomposition of this with dilute acid gave a yield of 32% of benzanilide, whereas refluxing the addition compound with an equimolecular quantity of anilinomagnesium iodide in ether for one hour gave 87% of benzanilide. This compound (II), formed from equimolecular quantities of anilinomagnesium iodide and methyl benzoate, also gave a high yield (96%) of pure benzanilide (free from *NN*-diphenylbenzamide) when refluxed with an equimolecular proportion of diphenylaminomagnesium iodide (prepared from diphenylamine and methylmagnesium iodide). In a similar manner the addition compound formed between equimolecular quantities of diphenylaminomagnesium iodide and methyl benzoate gave a high yield (89%) of pure *NN*-diphenylbenzamide (free from benzanilide) when refluxed with an equimolecular proportion of anilinomagnesium iodide.

(I) $IMg\cdot O\cdot CPh(NHPh)_2$ $IMg\cdot O\cdot CPh(OMe)\cdot NHPh$ (II)

These experiments showed that the second equivalent of aminomagnesium halide does not enter into complex formation, as suggested by Bodroux, but acts by decomposing the addition compound.

Pure *NN*-diphenylbenzamide was also obtained when the diphenylaminomagnesium iodide–methyl benzoate addition compound was allowed to react with aniline (86% yield) and with aqueous sodium hydroxide solution (60% yield).

It thus appears that the reaction between aminomagnesium halides and esters proceeds through an addition compound involving equimolecular quantities of the reactants, and that this addition compound can be broken down by basic reagents to give almost quantitative yields of a substituted amide, although decomposition by acidic reagents gives a much smaller yield of the same compound.

EXPERIMENTAL

The Grignard reagent used in all cases was methylmagnesium iodide, and the aminomagnesium iodides were prepared and used *in situ*. All ethereal extracts were dried over anhydrous potassium carbonate.

General Method.—The amine (0·1 mole) in dry ether (30 ml.) was added slowly to methylmagnesium iodide (0·1 mole) in dry ether (50 ml.). After the vigorous reaction had subsided, the ester (0·05 mole) in ether (*ca.* 20 ml.) was added, and the mixture refluxed on a warm water-bath for 2 hr. It was then decomposed by cautious addition of water (50 ml.), followed by sufficient 2N-hydrochloric acid to dissolve basic magnesium compounds. The separated ethereal extract was dried, and the ether and unchanged amine were distilled off. The residue, when cooled, set to a mass of crystals which were recrystallised.

In this manner the following were prepared : hexanoanilide (from anilinomagnesium iodide and methyl hexanoate), m. p. 52—53° (87%); dodecano-anilide, m. p. 76—77° (80%), and -*m*-toluidide, m. p. 59—60° (89%) (Bowen and Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 3522, give 54—56° as m. p. of this compound), *NN*-diphenyl-acetamide, m. p. 95—98° (85%), and -benzamide, m. p. 178—179° (88%).

Reactions with o-*Phenylenebisaminomagnesium Di-iodide.*—(*a*) The filtered Grignard reagent (0·05 mole) was added dropwise to *o*-phenylenediamine (2·7 g., 0·025 mole) in ether (100 ml.), and then methyl acetate (1·9 g., 0·025 mole) in ether (10 ml.). The mixture was refluxed with stirring for 2 hr., decomposed with water and dilute acid, and worked up as described above. A residue (2·3 g.) was obtained, which crystallised from hot water as brownish plates, m. p. 100—102° (*o*-phenylenediamine, m. p. 102°; 2-methylbenziminazole, m. p. 176°), and were thus unchanged *o*-phenylenediamine.

(*b*) A large excess of methyl acetate (9·3 g., 0·125 mole) was used, and refluxing with stirring continued for 4 hr. Otherwise the experiment was carried out as in (*a*), and the amine recovered (2·3 g., 85%) had m. p. 101—102°.

(*c*) A mixture of *o*-phenylenediamine (2·7 g., 0·025 mole) and methyl benzoate (17·0 g., 0·125 mole) in ether (100 ml.) was added dropwise to the Grignard reagent (0·025 mole), and the mixture refluxed for 4 hr. with stirring. After decomposition and drying of the ethereal layer, this was distilled, giving methyl benzoate (15·8 g., 93%) at 190—200°, and *o*-phenylenediamine (2·3 g., 85%), m. p. 100—102° (2-phenylbenziminazole has m. p. 288°).

The Addition Compound.—A mixture of aniline (9·3 g., 0·1 mole) and methyl benzoate (13·6 g., 0·1 mole) in ether (30 ml.) was added dropwise to methylmagnesium iodide (0·1 mole). The mixture was then filtered through a Büchner funnel, a viscous material being retained on the filter. This was rapidly transferred to a vacuum-desiccator, and dried over concentrated sulphuric acid at 2 mm. After 12 hr., it had changed to a white powder. About 0·5 g. was acidified with dilute nitric acid, the precipitated benzanilide filtered off, and the iodide in the filtrate determined as silver iodide [Found : N, 3·7; I, 33·9. Calc. for $C_{19}H_{17}ON_2MgI$ (I) : N, 6·4; I, 28·8. $C_{14}H_{14}O_2NMgI$ (II) requires N, 3·7; I, 33·5%].

Reactions of the Addition Compound.—(a) *With dilute acid.* The residue of benzanilide from the previous experiment represented a yield of 32%, and had m. p. 161—162° (lit., m. p. 162°).

(b) *With anilinomagnesium iodide.* This reagent (0·025 mole) was prepared in ether, and the addition compound (9·5 g., 0·025 mole) added. The mixture was refluxed for 1 hr. with stirring, and decomposed with dilute hydrochloric acid. Benzanilide (4·3 g., 87% based on the addition compound) was obtained, having m. p. 162° after one crystallisation from aqueous ethanol.

(c) *With diphenylaminomagnesium iodide.* The addition compound (0·025 mole) was added to diphenylaminomagnesium iodide (0·025 mole) in ether, and the reaction carried out as in (b), giving benzanilide (4·7 g., 96% based on the addition compound), m. p. and mixed m. p. 162—163° after one crystallisation from aqueous ethanol.

(d) *Action of anilinomagnesium iodide on the diphenylaminomagnesium iodide–methyl benzoate addition compound.* The addition compound was prepared *in situ* from equimolecular quantities (0·025 mole) of the reagents, and to it was added anilinomagnesium iodide (0·025 mole). The product, worked up as in (*b*), proved to be *NN*-diphenylbenzamide (6·0 g., 89% based on the weight of ester, and hence of addition compound), m. p. and mixed m. p. 178—178·5° after one crystallisation from aqueous ethanol (lit., m. p. 177°, 179°).

(e) *Action of aniline on the addition compound, as in* (d). The addition compound (0·025 mole) was prepared *in situ,* and an equimolecular proportion of aniline added to it. The reaction was then carried out as in (b), and the product shown to be *NN*-diphenylbenzamide (5·8 g., 86%), m. p. and mixed m. p. 178—178·5° after one crystallisation from aqueous ethanol.

(f) *Action of sodium hydroxide on the addition compound, as in* (d). To the addition compound (0·025 mole, *in situ*) was added 10% aqueous sodium hydroxide (10 ml.). After 1 hr.' refluxing with stirring and decomposition with dilute hydrochloric acid, *NN*-diphenylbenzamide (4·1 g., 60%) was obtained, having m. p. and mixed m. p. 178—178·5° after one crystallisation from ethanol.

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