

A Case of Reduction in the Reactions between Phenylmagnesium Bromide and Ethyl Chromone-2-carboxylate

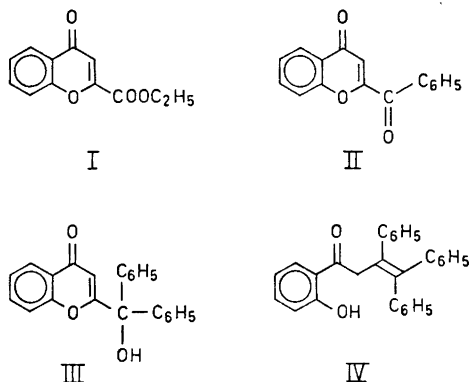
GUST.-AD. HOLMBERG and RAINER SJÖHOLM

Institutionen för organisk kemi, Åbo Akademi, SF-20500 Åbo, Finland

When phenylmagnesium bromide reacts with ethyl chromone-2-carboxylate, 2-benzoylchromone and 2-(diphenylhydroxymethyl)chromone were formed as primary and secondary products. A large excess of the Grignard reagent causes the formation of 1-(*o*-hydroxyphenyl)-3,4,4-triphenyl-3-buten-1-one. A reductive fission of the ether bond between the atoms in the positions 1 and 2 or a direct or indirect reduction of the double bond of the chromone nucleus is apparently involved in the reactions.

The reaction between arylmagnesium bromides and ethyl 3-phenylchromone-2-carboxylate has previously been examined in this laboratory.¹ It was then established that the primary reaction was a 1,2-addition to the carbonyl group of the carbethoxy portion of the molecule. The order, and in part even the nature of the subsequent reactions were not easy to elucidate in detail. Nevertheless, it seemed apparent that either a reductive fission of the ether bond between the atoms in the positions 1 and 2 or a reduction of the double bond between the atoms in the positions 2 and 3 occurred.

Because no reduction had been observed in the reactions between phenylmagnesium bromide and ethyl chromone-2-carboxylate (I),² investigations of these reactions were resumed. It was again established that the first reactions were 1,2-additions of the Grignard reagent to the carbonyl group of the carbethoxy portion, and the primary and secondary products, 2-benzoylchromone (II) and 2-(diphenylhydroxymethyl)chromone (III), were isolated when the molar ratio of the ester and the Grignard reagent was 1:2.5. If the excess of phenylmagnesium bromide was increased until the ratio was 1:5, 1-(*o*-hydroxyphenyl)-3,4,4-triphenyl-3-buten-1-one (IV) was formed and isolated. The quantities of the reaction products, evaluated from gas chromatograms of the reaction mixtures, clearly showed that the latter substance had formed from 2-(diphenylhydroxymethyl)chromone. One reaction sequence for this transformation would be a reductive fission of the ether bond between the atoms in the positions 1 and 2, followed by a 1,4-addition of phenylmagnesium bromide to the conjugated double bond system C=C-C=O. The double bond



in the butene chain is formed by elimination of water upon treatment with hydrochloric acid. Several equally possible reaction sequences can be constructed for the transformation. Either a reductive fission of the ether bond or a direct or indirect reduction of the ethylenic double bond of the chromone nucleus is included in all these sequences. The mechanisms and the reducing agents have to some extent been discussed previously.¹

EXPERIMENTAL

Experiment 1 (molar ratio of ethyl chromone-2-carboxylate and phenylmagnesium bromide 1:2.5, inverse addition). A Grignard reagent, prepared from magnesium (0.60 g), bromobenzene (3.92 g), and dry ether (30 ml), was gradually added to a solution of ethyl chromone-2-carboxylate (2.18 g) in dry ether (30 ml). The temperature of the reaction mixture was kept at 0° during the addition (1 h). The reaction mixture was poured into a mixture of hydrochloric acid, water, and ice. The ether phase was separated and washed with water and 5% potassium hydrogen carbonate solution. After drying with sodium sulphate, the solvent was evaporated. When cold ether was added to the remaining oil, a small quantity of 2-(diphenylhydroxymethyl)chromone (III) crystallized. The solvent was evaporated from the mother-liquor, the remaining oil dissolved in a small quantity of ethanol, and the solution placed in a refrigerator. After some days, a substance had crystallized. It was repeatedly recrystallized from ethanol. The pure compound, 2-benzoylchromone (II), melted at 92–93°. (Found: C 76.72; H 3.93. Calc. for $C_{16}H_{10}O_3$: C 76.79; H 4.03.) MS: $M^{+\cdot}$ at m/e 250, calc. 250, r.a. 16.5%; $(M+1)^+$ at m/e 251, r.a. 2.8%, calc. 2.9%; $(M-CO)^{+\cdot}$ at m/e 222, r.a. 15.1%; benzoyl ion at m/e 105, r.a. 100%; phenyl ion at m/e 77, r.a. 54.3%. NMR spectrum: aromatic protons at τ 1.6–2.7; methine proton at τ 3.14; ratio of the intensities 9:1. Gas chromatographic analysis of the original reaction product oil revealed that 2-benzoylchromone was the main product but that considerable amounts of 2-(diphenylhydroxymethyl)chromone were also present.

Experiment 2 (molar ratio of ethyl chromone-2-carboxylate and phenylmagnesium bromide 1:5). A solution of ethyl chromone-2-carboxylate (2.18 g) in dry ether (30 ml) was gradually added to a Grignard reagent, prepared from magnesium (1.21 g), bromobenzene (7.90 g), and dry ether (30 ml). After the reaction mixture had been held at 40° for 1 h, it was worked up as described above. The oil obtained was dissolved in ethanol and, after some days in a refrigerator, a substance crystallized. The pure product, obtained by recrystallisation from chloroform, melted at 183–184°. Analytical and spectroscopical data showed it to be 1-(*o*-hydroxyphenyl)-3,4,4-triphenyl-3-buten-1-one. (Found: C 86.05; H 5.59. Calc. for $C_{26}H_{22}O_2$: C 86.13; H 5.68.) IR spectrum: CO absorption at 1645 cm^{-1} . MS: $M^{+\cdot}$ at m/e 390, calc. 390, r.a. 28.3%; $(M+1)^+$ at m/e 391, r.a. 8.9%, calc. 8.7%; $(M-HOC_6H_4CO)^+$ at m/e 269, r.a. 24.8%; unknown ions at m/e 223, r.a.

9.6 %, and 191, r.a. 21.7 %; $(\text{HO}_6\text{H}_4\text{CO})^+$ at m/e 121, r.a. 100 %; self-explanatory ions at m/e 105, 91, 77, and 65 with r.a. less than 20 %. NMR spectrum: hydroxyl proton at τ - 2.12; aromatic protons at τ 2.3 - 3.1; uncoupled methylene protons at τ 5.74; ratio of intensities 1:19:2. Gas chromatographic analysis showed that the isolated compound was the main product.

Experiment 3 (molar ratio of ethyl chromone-2-carboxylate and phenylmagnesium bromide 1:3.5). The above experiment was repeated with a Grignard reagent prepared from magnesium (0.84 g) and bromobenzene (5.50 g). Gas chromatographic analysis revealed that the amounts of 2-benzoylchromone, 2-(diphenylhydroxymethyl)chromone, and 1-(*o*-hydroxyphenyl)-3,4,4-triphenyl-3-buten-1-one were almost equal.

The elemental analyses were performed by Janssen Pharmaceutica, Analytical Department, Beerse, Belgium.

Statens naturvetenskapliga kommission (Finland) has supported the work.

REFERENCES

1. Holmberg, G.-A. and Jalander, L. *Acta Acad. Aboensis, Ser. B* **30** (1970) No. 14.
2. Holmberg, G.-A., Malmström, F. and Blom, U. Å. *Acta Chem. Scand.* **22** (1968) 1375.

Received January 19, 1973.