94. *Grignard Reactions with Ethyl β-Chloropropionate. Part I.*

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For the synthesis of amino-alcohols containing side chains, a method has been devised starting with ethyl β-chloropropionate. This reacts with Grignard compounds, giving β-chloroethyldialkylcarbinols, which condense easily with secondary amines, yielding, *e.g.*, with piperidine, β-piperidinoethyldialkylcarbinols. By treatment with alcoholic potash, hydrogen chloride is split off, with formation of dialkylvinylcarbinols. The *dibenzylvinylcarbinol* thus obtained from *dibenzyl-β-chloroethylcarbinol* gives, on catalytic hydrogenation, *dibenzylethylcarbinol* identical with the carbinol obtained by interaction of dibenzyl ketone and ethylmagnesium bromide.

Dehydration of the carbinols, saturated or unsaturated, could not be effected smoothly. The product of the reaction between ethyl β-chloropropionate and phenylmagnesium bromide, however, underwent spontaneous dehydration, yielding *γγ-diphenylallyl chloride*. When this was treated with phenylmagnesium bromide, it gave αα-diphenyl-β-benzylethylene, the structure of the chloro-compound thus being proved (compare Meisenheimer, *Annalen*, 1927, **456**, 151). Besides γγ-diphenylallyl chloride, a small amount of β-chloropropiophenone was formed in the above Grignard reaction; it could not be isolated in a pure state, but its presence was proved by treatment with phenylmagnesium bromide, which gave β-phenylpropiophenone.

Experimental.

Dibenzyl-β-chloroethylcarbinol.—A Grignard solution prepared from magnesium (16·25 g.) and benzyl chloride (77 c.c.) was added drop by drop to a cold ethereal solution of ethyl β-chloropropionate (42 c.c.). After 2 hours' heating on the water-bath, the mixture was poured into ice-cold dilute sulphuric acid; the ethereal layer was washed with sodium carbonate solution, dried, and evaporated. The residual *carbinol* (35—46 g.) had b. p. 214°/22 mm., 206°/8 mm., 192°/3 mm. (Found: C, 74·2; H, 7·2. $C_{17}H_{19}OCl$ requires C, 74·4; H, 7·0%). After it (10 g.) had been heated with potassium hydrogen sulphate (5 g.) at 180—190° for 2 hours, it was recovered mostly unchanged; only a small amount of a lower-boiling fraction was obtained, which did not give satisfactory analytical figures.

Dibenzylvinylcarbinol.—The preceding chloro-compound (13·7 g.) in methyl alcohol (10 c.c.) was left at the ordinary temperature with 20% methyl-alcoholic potash (14 c.c.) for 12 hours. The liquid was then boiled for 6 hours, the methyl alcohol distilled off, and the residue neutralised with sulphuric acid and treated with water and ether. From the latter, *dibenzylvinylcarbinol* was isolated as a yellowish oil (6 g.), b. p. 145—146°/1 mm. (Found: C, 86·2; H, 7·7. $C_{17}H_{18}O$ requires C, 85·8; H, 7·6%).

Dibenzylethylcarbinol.—(a) The above unsaturated carbinol (5·7 g.) in boiling propyl alcohol (30 c.c.) was treated with hydrogen in presence of palladised barium sulphate (3 g.) for 3 hours. The solution was then filtered and evaporated, and the residue distilled, yielding *dibenzylethylcarbinol*, b. p. 190—192°/12 mm., $n_D^{29°}$ 1·5593 (Found: C, 84·8; H, 8·0. $C_{17}H_{20}O$ requires C, 85·0; H, 8·3%). (b) Dibenzyl ketone (10·5 g.) was treated with ethylmagnesium bromide (ethyl bromide, 6 g., and magnesium, 1·4 g.). The product (7·5 g.) had b. p. 197—200°/17 mm., $n_D^{29°}$ 1·5599 (Found: C, 84·7; H, 8·0%).

Dibenzyl-β-piperidinoethylcarbinol.—A mixture of dibenzyl-β-chloroethylcarbinol (14 g.) and piperidine (10 c.c.) was heated at 100° in a sealed tube for 5 hours, the crystalline mass treated with ether and water, the ethereal solution shaken with dilute hydrochloric acid, and the extract made alkaline and again shaken with ether. The *piperidino-carbinol* (9 g.) was obtained as an oil, b. p. 224—225°/5 mm., which readily solidified; m. p. 45—46° (Found: C, 82·0; H, 9·0. $C_{22}H_{29}ON$ requires C, 81·7; H, 8·9%).

The p-*nitrobenzoate*, prepared by heating the piperidino-carbinol (9 g.) and *p*-nitrobenzoyl chloride (5·2 g.) in benzene (50 c.c.) and pyridine (2·2 c.c.) for 3 hours, crystallised from alcohol in diamond-shaped prisms (8·5 g.), m. p. 138—139° (Found: N, 6·2. $C_{29}H_{32}O_4N_2$ requires N, 5·9%).

The *p*-aminobenzoate was prepared by treating the *p*-nitrobenzoate (7 g.) in hot alcohol with alcoholic sodium hydrosulphide (2 g.), added in small portions, and boiling the whole for 1 hour. The alcohol was evaporated, and the residue treated with water and ether. The product was a resin which crystallised immediately after distillation (b. p. 245—250°/25 mm.). The crystals

were triturated with methyl alcohol and recrystallised from propyl alcohol, forming leaflets, m. p. 147—148°.

β-*Chlorotriethylcarbinol.*—This was prepared by the method described above, ethyl bromide (57·2 c.c.) being used in place of benzyl chloride. It boiled at 118—119°/54 mm. (yield, 19—25 g.), and had a pleasant smell (Found : C, 56·3; H, 9·8. $C_7H_{15}OCl$ requires C, 56·0; H, 10·0%). When it was heated with *p*-nitrobenzoyl chloride in benzene and pyridine, *p*-nitrobenzoic anhydride was obtained, m. p. 187° (from toluene).

β-*Piperidinotriethylcarbinol.*—The preceding carbinol (28 g.) was treated with piperidine (40 c.c.) as described above. The *product* (18 g.) had b. p. 105—106°/3 mm. (Found : C, 72·3; H, 12·5. $C_{12}H_{25}ON$ requires C, 72·4; H, 12·6%).

When the piperidino-carbinol (5·5 g.) was treated with *p*-nitrobenzoyl chloride as described above, a thick crystalline mass of the hydrochloride of the expected compound (thus proved to be more basic than pyridine !) was obtained. It was treated with alkali, and the crystalline product recrystallised from alcohol; it separated with alcohol of crystallisation (m. p. 100°), but lost this even at room temperature (m. p. 148°).

β-*Chloroethyldibutylcarbinol,* prepared from ethyl β-chloropropionate (41 g.), magnesium (11 g.), and butyl bromide (90 g.; 70 c.c.), was a colourless oil (46 g.), b. p. 128—133°/4 mm. (Found : C, 63·9; H, 11·2. $C_{11}H_{23}OCl$ requires C, 64·1; H, 11·2%).

Dibutylvinylcarbinol.—The chloro-compound (17 g.) was left at room temperature with potassium hydroxide (5·1 g.) in methyl alcohol (25 c.c.) for 3 hours; the mixture was then boiled for 5 hours and worked up in the same way as the benzyl compound. The unsaturated *carbinol* (7 g.) had b. p. 125°/34 mm. (Found : C, 77·9; H, 12·7. $C_{11}H_{22}O$ requires C, 77·7; H, 12·9%). It was unchanged after being heated with an equal weight of oxalic acid at 125—135° for 2 hours.

β-*Piperidinoethyldibutylcarbinol* was prepared from the chloro-carbinol (41 g.) and piperidine (36 c.c.) and obtained as a colourless oil (27·5 g.), b. p. 140—143°/5 mm. (Found : C, 75·7; H, 12·9. $C_{16}H_{33}ON$ requires C, 75·3; H, 13·0%). An attempt to prepare the *p*-nitrobenzoate gave a black tar.

γγ-*Diphenylallyl Chloride.*—Phenylmagnesium bromide (from magnesium, 24·3 g., and bromobenzene, 104·6 c.c.) was added to ethyl β-chloropropionate (68 g.) in ether; two layers were formed. On decomposition and distillation, two fractions were obtained : (a) 11 g., b. p. 108—110°/4 mm., 126—129°/14 mm.; (b) 27 g., b. p. 159—161°/4 mm. Fraction (b) was γγ-*diphenylallyl chloride* (Found : C, 78·7; H, 6·4; Cl, 15·0. $C_{15}H_{13}Cl$ requires C, 78·9; H, 6·0; Cl, 15·1%). A portion of it (9·1 g.) was introduced into phenylmagnesium bromide solution (magnesium, 3·1 g.; bromobenzene, 5·3 c.c.) and boiled for 2 hours. The isolated αα-diphenyl-β-benzylethylene boiled at 215°/12 mm. (compare Ziegler, Grabler, and Ulrich, *Ber.*, 1924, **57**, 1989; Schlenk and Bergmann, *Annalen*, 1928, **463**, 50) (Found : C, 92·9; H, 7·1. Calc. for $C_{21}H_{18}$: C, 93·3; H, 6·7%). Fraction (a), despite its constant b. p., was a mixture (Found : C, 72·8, 72·5; H, 7·5, 7·4; Cl, 9·9, 9·8. Calc. for C_9H_9OCl : C, 64·3; H, 5·4; Cl, 21·0%). When treated with phenylmagnesium bromide as fraction (b) was treated, it gave β-phenylpropiophenone, m. p. 72° (Found : C, 85·2; H, 7·3. Calc. for $C_{15}H_{14}O$: C, 85·7; H, 6·7%) (compare Kohler, *Amer. Chem. J.*, 1909, **42**, 390).

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