LXIV.—*Syntheses by Means of Magnesium Amyl Halides.*

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ALTHOUGH the magnesium derivatives of *iso*amyl halides have been extensively employed in synthesis, the use of Grignard reagents containing the *n*-amyl radical and, particularly, the β-methylbutyl radical has been rare. Those of the former type have been used by Henry and de Wael (*Rec. trav. chim.*, 1909, **28**, 446), by Pexters (*Bull. Acad. roy. Belg.*, 1906, 796), by Grüttner and Krause (*Ber.*, 1916, **49**, 2666), by Davies, Pearse, and Jones (J., 1929, 1265), and by Dyke, Davies, and Jones (preceding paper); and the Grignard reagent of *dl*-β-methylbutyl bromide was used for the first time by Davies, Pearse, and Jones, and later by Dyke, Davies, and Jones, whilst Klages and Sautter (*Ber.*, 1904, **37**, 653) used that prepared from optically active amyl iodide.

The products of the reactions of certain aldehydes and ketones with magnesium *n*-amyl and *dl*-β-methylbutyl bromides are now described. In these preparations several types of reaction were encountered, although the conditions were so chosen that the addition reaction yielding carbinol should predominate.

In all cases the decanes were produced as by-products. Under the conditions existing in the present experiments the extent of this synthetic action of metallic magnesium on the amyl bromides was such as to yield about 24 c.c. of decane per 24·3 g. of magnesium. The decane was isolated from the fraction, b. p. 70—100°/50 mm., of the product by shaking with concentrated sulphuric acid, washing with water, drying over sodium, and distillation. In this way were obtained *n*-decane, b. p. 169°/760 mm., and *dl*-γζ-dimethyloctane, b. p. 79°/50 mm., 159°/760 mm.; $d_4^{25°}$ 0·7307; $n_D^{25°}$ 1·4106; $[R_L]_D$ 48·33 (Calc., 48·38) (Found: C, 84·6; H, 15·3. Calc. for $C_{10}H_{22}$: C, 84·5; H, 15·5%) (compare Dupont, *Ann. Chim.*, 1913, **30**, 516).

Enolisation of the reacting ketone by the Grignard compound occurred extensively between acetophenone and magnesium *dl*-β-methylbutyl bromide. For instance, purified acetophenone in 52% yield was recovered from the product of reaction, with only 14% yield of the purified tertiary alcohol. In striking contrast thereto was the behaviour of magnesium *n*-amyl bromide with acetophenone, where a 30% yield of purified alcohol was obtained, but no acetophenone was recovered. These results are consonant with the views of Conant and Blatt (*J. Amer. Chem. Soc.*, 1929, **51**, 1236) that the occurrence of subsidiary reactions, such as enolisation, can be correlated with branching of the alkyl groups involved.

In no case in the present work was reduction met with, but condensation appeared to have occurred in the interaction between methyl *n*-nonyl ketone and magnesium *dl*-β-methylbutyl bromide, since an appreciable amount of a substance having a higher b. p. than the carbinol was obtained.

In several cases, details of which are given in the experimental portion, the yield of carbinol was low owing to loss of the elements of water and formation of unsaturated hydrocarbon during the reaction and isolation; and in every case the dehydration was readily effected even on treatment with mild agents.

The preparation of esters of the amylcarbinols, particularly those which contain other higher radicals, is often attended by difficulties. For instance, the acetic ester of *phenylmethyl*-(β-*methylbutyl*)-*carbinol* was obtained in poor yield, but on being distilled even under reduced pressure it continuously decomposed. Again, in an attempt to prepare the bromide of this carbinol, β-*phenyl*-δ-*methyl*-Δ^{β}-*hexylene* was obtained in good yield. In a similar attempt with *phenyl*-(β-*methylbutyl*)*carbinol*, the bromide obtained readily parted with hydrogen bromide, yielding *dl*-α-phenyl-γ-methyl-Δ^{α}-amylene (dibromo-compound, m. p. about 75°), the optically active form of which has been described by Klages and Sautter (*loc. cit.*). In a preparation of the oxalic ester of phenyl-*n*-amylcarbinol, by heating the latter with the anhydrous acid, a considerable amount of unsaturated hydrocarbon was formed, and on distillation the residual oxalate broke down.

The amylcarbinols prepared in the present investigation gave methane with an amyl-ethereal solution of magnesium methyl iodide.

EXPERIMENTAL.

Preparation of Carbinols.—The aldehyde or ketone in ethereal solution was dropped into the filtered Grignard solution, which was kept at 10°. Equivalent weights of the reactants were used. After the addition was complete the mixture was gently boiled for ½ hour, poured on ice, and treated with sufficient mineral acid to dissolve the precipitated magnesium salts. The ethereal layer was washed with sodium bicarbonate solution, with the addition, where necessary, of sodium bisulphite solution. The dried ethereal solution was fractionally distilled under 50 mm. pressure. The carbinol fraction was redistilled.

Preparation of Ketones.—20 C.c. of the secondary alcohol were gradually added with shaking and cooling to 100 c.c. of a saturated solution of potassium dichromate in 20% aqueous sulphuric acid.

The mixture was then mechanically shaken for 5 hours. The resulting ketone was extracted with ether, isolated by fractional distillation, redistilled, and purified by freezing where possible.

All thermometer readings given have been corrected.

Phenyl-n-*amylcarbinol* was prepared by the addition of 106 g. of benzaldehyde in 100 c.c. of ether to a Grignard solution made from 151 g. of *n*-amyl bromide, 24·3 g. of magnesium, and 500 c.c. of ether. The alcoholic fraction distilled at 167—171°/50 mm., and on redistillation yielded 64 g. of pure alcohol, a thick liquid, b. p. 170°/50 mm.; $d_{4^\circ}^{25^\circ}$ 0·9477; $n_D^{25^\circ}$ 1·5042; $[R_L]_D$ 55·65 (Calc. for $C_{12}H_{18}O,3|\!\!=$, 55·54); $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0136 (Calc., 0·0122) (Found : C, 81·1; H, 9·9. $C_{12}H_{18}O$ requires C, 80·9; H, 10·1%). Phenyl *n*-amyl ketone, m. p. 27° (semicarbazone, m. p. 132°) (compare Schroeter, *Ber.*, 1907, **40**, 1603), was obtained on oxidation of the alcohol.

From the products of the interaction between anisaldehyde and magnesium *n*-amyl bromide there was obtained a considerable amount of anisaldehyde, identified by b. p., 164°/50 mm. (literature gives 166°/50 mm.), and by conversion into anisic acid, m. p. 184°. The first fractional distillation of the product also gave p-*methoxyphenyl*-n-*amylcarbinol*, b. p. 207—210°/50 mm. On being redistilled at low pressures this carbinol partly decomposed with elimination of water, a behaviour similar to that observed by Stedman and Stedman (J., 1929, 614) in the case of the corresponding methyl carbinol. On this account the carbinol distillate was saturated with hydrogen chloride and then boiled with excess of pyridine, whereby, after treatment with water, there was obtained α-p-*methoxyphenyl*-Δ^α-*hexylene*, b. p. 187—188°/50 mm.; $d_{4^\circ}^{25^\circ}$ 0·9594; $n_D^{25^\circ}$ 1·5356; $[R_L]_D$ 61·77 (Calc. for $C_{13}H_{18}O,4|\!\!=$, 59·81); $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0213 (Calc., 0·0134) (Found : C, 81·4; H, 9·7. $C_{13}H_{18}O$ requires C, 82·0; H, 9·5%). This compound readily adds on bromine.

Methylethyl-n-*amylcarbinol* was prepared by adding 72 g. of methyl ethyl ketone in 75 c.c. of ether to the Grignard reagent formed by 151 g. of *n*-amyl bromide, 24·3 g. of magnesium, and 500 c.c. of ether. The alcoholic fraction after several redistillations yielded 35 g. of the purified carbinol, b. p. 97·5°/50 mm.; $d_{4^\circ}^{25^\circ}$ 0·8108; $n_D^{25^\circ}$ 1·4257; $[R_L]_D$ 45·52 (Calc., 45·29); $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0077 (Calc., 0·0074) (Found : C, 75·5; H, 13·8. $C_9H_{20}O$ requires C, 74·9; H, 14·0%). The carbinol is a mobile liquid, possessing a characteristic, slightly peppermint-like, smell.

Methyl-n-*amyl*-n-*nonylcarbinol* was obtained from the product of the interaction between 170 g. of methyl *n*-nonyl ketone, dissolved in 100 c.c. of ether, and magnesium *n*-amyl bromide prepared from the equivalent of the amyl bromide. The ketone was obtained by washing oil of rue successively with 20% sulphuric acid, 5% sodium carbonate, and 5% sodium hydroxide solutions, and fractionally distilling it under reduced pressure, and was finally purified by repeated freezing (Sanderson and Jones, *J. Soc. Chem. Ind.*, 1923, **42**, 1). The interaction between the ketone and the Grignard reagent was not vigorous, and, for that reason, the mixture was kept for 12 hours. The usual separation of the magnesium salt-complex was not observed in this case, but the treatment with crushed ice and mineral acid was continued as in the other preparations. The ether having been expelled, the product was repeatedly fractionally distilled under 50 mm. pressure, whereby there were obtained the following main fractions: (1) up to 115°, decane, which on treatment with concentrated sulphuric acid gave 20 c.c. of the hydrocarbon; (2) 143—147°, methyl *n*-nonyl ketone, 50 c.c., identified by its semicarbazone, m. p. 123°; (3) 199—200°, methyl-*n*-amyl-*n*-nonylcarbinol, 80 c.c.; $d_{4^\circ}^{25^\circ}$ 0·8316, $n_D^{25^\circ}$ 1·4446, $[R_L]_D$ 77·50 (Calc., 77·61), $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0079 (Calc., 0·0079) (Found: C, 79·7; H, 14·2. $C_{16}H_{34}O$ requires C, 79·3; H, 14·2%). The large amount of recovered ketone suggests enolisation. It is noteworthy that the only previous application of the Grignard reagent to this ketone was in the preparation of dimethyl-*n*-nonylcarbinol (Houben, *Ber.*, 1902, **35**, 3591).

Phenylmethyl-n-*amylcarbinol* has b. p. 169°/50 mm.; $d_{4^\circ}^{25^\circ}$ 0·9389; $n_D^{25^\circ}$ 1·5028; $[R_L]_D$ 60·47 (Calc. for $C_{13}H_{20}O,3|^{=}$, 60·16); $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0131 (Calc., 0·0119) (Found: C, 80·5; H, 9·8. $C_{13}H_{20}O$ requires C, 81·2; H, 10·5%). It was prepared by the interaction of 120 g. of acetophenone with the magnesium *n*-amyl bromide made from 151 g. of the bromide and 24·3 g. of magnesium. The crude carbinol fraction contained unsaturated hydrocarbon, from which the carbinol was purified by redistillation; yield, 58 g.

Methyl β-methylbutyl ketone has been prepared by Kohler (*Amer. Chem. J.*, 1907, **38**, 527) from ethylideneacetone and magnesium ethyl bromide, and by Clarke (*J. Amer. Chem. Soc.*, 1908, **30**, 1150) by the hydrolysis of ethyl *sec.*-butylacetoacetate. We have now prepared it by treatment of the carbinol fraction, 68—73°/50 mm., obtained from the interaction between acetaldehyde and magnesium *dl*-β-methylbutyl bromide, with a saturated solution of potassium dichromate in 20% sulphuric acid. The ketone was purified through its semicarbazone, 62 c.c. of the crude material being mechanically stirred on the water-bath for 2 hours with 38 g. of semicarbazide hydrochloride, 47 g. of sodium acetate trihydrate, 12 c.c. of ethyl alcohol, and 140 c.c. of water. The solid semicarbazone was recrystallised from aqueous alcohol, and gave 27 g. of pure product.

Methyl β-methylbutyl ketone semicarbazone, m. p. 120—121°

(Found : N, 24·2. $C_8H_{17}ON_3$ requires N, 24·5%), was converted by 1 hour's boiling with 15% hydrochloric acid into the ketone, b. p. 68°/50 mm., 69·5°/57 mm.; $d_{4^\circ}^{25^\circ}$ 0·8085; $n_D^{25^\circ}$ 1·4050; $[R_L]_D$ 34·56 (Calc., 34·54); $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0073 (Calc., 0·0074) (Found : C, 74·0; H, 12·5. Calc. for $C_7H_{14}O$: C, 73·7; H, 12·4%).

Klages and Sautter (*loc. cit.*) state that the product of interaction between benzaldehyde and the magnesium derivative of active amyl iodide consists chiefly of active hexenylbenzene, together with some of the carbinol, which they did not isolate. In the present experiments, however, no difficulty was experienced in isolating the inactive carbinol in pure condition and fair yield. Moreover, no elimination of water from the carbinol during reduced-pressure distillation was noticed (contrast Klages and Sautter, *loc. cit.*). *Phenyl-*(β-*methylbutyl*)*carbinol* (yield, 40 g.), obtained by the addition of 106 g. of benzaldehyde to magnesium *dl*-β-methylbutyl bromide prepared from 151 g. of the *dl*-amyl bromide, has b. p. 163°/50 mm.; $d_{4^\circ}^{25^\circ}$ 0·9523; $n_D^{25^\circ}$ 1·5059; $[R_L]_D$ 55·51 (Calc. for $C_{12}H_{18}O,3|^{=}$, 55·54); $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0143 (Calc., 0·0123) (Found : C, 81·0; H, 10·0; OH, 8·3. $C_{12}H_{18}O$ requires C, 80·9; H, 10·1; OH, 9·5%). On dehydration the carbinol yielded unsaturated hydrocarbon. *Phenyl* β-*methylbutyl ketone* (Found : C, 81·4; H, 9·0. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%) boils at 163°/50 mm.; $d_{4^\circ}^{25^\circ}$ 0·9640; $n_D^{25^\circ}$ 1·5093; $[R_L]_D$ 54·49 (Calc. for $C_{12}H_{16}O,3|^{=}$, 54·03); $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0156 (Calc., 0·0127). The *semicarbazone* (Found : N, 18·3. $C_{13}H_{19}ON_3$ requires N, 18·0%), m. p. 160°, separates as rods from alcohol.

In an attempt to prepare *p*-methoxyphenyl β-methylbutyl ketone, by oxidising the product obtained from the interaction of magnesium *dl*-β-methylbutyl bromide with anisaldehyde, considerable amounts of anisaldehyde and anisic acid were obtained, but no ketone.

Methylethyl-(β-*methylbutyl*)*carbinol*, b. p. 95—97°/50 mm.; $d_{4^\circ}^{25^\circ}$ 0·8177; $n_D^{25^\circ}$ 1·4251; $[R_L]_D$ 45·10 (Calc., 45·29); $n_F^{25^\circ}-n_C^{25^\circ}$ 0·0076 (Calc., 0·0075) (Found : C, 74·6; H, 13·9. $C_9H_{20}O$ requires C, 74·9; H, 14·0%), results (in 25 g. yield) from the interaction of 72 g. of methyl ethyl ketone in 100 c.c. of ether with magnesium *dl*-β-methylbutyl bromide made from 151 g. of the bromide and 24·3 g. of magnesium. The smell of the carbinol resembles that of the corresponding *n*-amyl carbinol, but is more penetrating.

Methyl-(β-*methylbutyl*)-n-*nonylcarbinol* was prepared by treating 170 g. of methyl *n*-nonyl ketone in 100 c.c. of ether with magnesium *dl*-β-methylbutyl bromide prepared from the equivalent of the alkyl bromide, and keeping the reaction mixture for 12 hours. Here also, as in the preparation of methyl-*n*-amyl-*n*-nonylcarbinol, there was no separation of the magnesium salt-complex. After treatment with mineral acid and removal of ether, the resulting oil was repeatedly fractionally distilled at 50 mm. Methyl *n*-nonyl ketone (90 c.c., identified by b. p. and semicarbazone) was recovered. The carbinol fraction (32 c.c.; b. p. 194—202°) was twice redistilled, but yet was not satisfactorily purified. The fraction of b. p. 198—200°/50 mm. (Found : C, 77·4; H, 13·8. $C_{16}H_{34}O$ requires C, 79·3; H, 14·2%) has $d_{4°}^{25°}$ 0·8301; $n_{D}^{25°}$ 1·4438; $[R_L]_D$ 77·50 (Calc., 77·61). The residue, 27 c.c., left after distillation of the carbinol fraction, on being redistilled yielded 11 c.c. of liquid, b. p. 255—265°/50 mm. This *substance* appears to be $CH_3{\cdot}C(C_5H_{11})(C_9H_{19}){\cdot}O{\cdot}C_5H_{11}$ (Found : C, 81·9; H, 13·7; *M*, 295. $C_{21}H_{44}O$ requires C, 80·7; H, 14·2%; *M*, 312); $d_{4°}^{25°}$ 0·8433; $n_{D}^{25°}$ 1·4582; $[R_L]_D$ 103·5 (Calc., 100·8).

Enolisation was encountered in the interaction between equivalents of acetophenone (120 g.) and magnesium *dl*-β-methylbutyl bromide. Fractionation of the crude product gave (1), b. p. 105—140°/50 mm., 72 g., which on redistillation yielded 62 g. of acetophenone, b. p. 115°/50 mm. (Found : C, 80·1; H, 7·0. Calc.: C, 80·0; H, 6·7%), and (2), b. p. 140—170°/50 mm., 48 g., which on redistillation yielded 27 g. of *phenylmethyl*-(β-*methylbutyl*)*carbinol*, b. p. 163·5°/50 mm.; $d_{4°}^{25°}$ 0·9388; $n_{D}^{25°}$ 1·5027; $[R_L]_D$ 60·47 (Calc. for $C_{13}H_{20}O,3|^{=}$, 60·16); $n_{F}^{25°}-n_{C}^{25°}$ 0·0137 (Calc., 0·0119) (Found : C, 81·1; H, 10·2; OH, 8·6. $C_{13}H_{20}O$ requires C, 81·2; H, 10·5; OH, 8·8%). On dehydration, the carbinol yielded β-*phenyl*-δ-*methyl*-Δ^{β}-*hexylene*, b. p. 142°/50 mm.; $d_{4°}^{25°}$ 0·8839; $n_{D}^{25°}$ 1·5117; $[R_L]_D$ 59·10 (Calc. for $C_{13}H_{18},4|^{=}$, 58·16); $n_{F}^{25°}-n_{C}^{25°}$ 0·0167 (Calc., 0·0132) (Found : C, 89·4; H, 10·3. $C_{13}H_{18}$ requires C, 89·6; H, 10·4%).

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