[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE ACTION OF THE GRIGNARD REAGENT ON HIGHLY BRANCHED CARBONYL COMPOUNDS[1]

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While a great variety of straight-chain aliphatic compounds of large molecular weight are known, the information in regard to many groups of branched aliphatic compounds is relatively meager. For example, of the 38 tertiary alcohols listed in the new edition of Beilstein's "Handbuch" (which covers the literature to 1910), 32 contain only primary alkyl groups. Of the remaining 6, four contain one secondary group and two primary groups, while only two contain a tertiary group; none contains more than one secondary or tertiary group. Although a great deal of work in aliphatic chemistry has been published in the last eighteen years, our information concerning branched compounds has not materially increased. Purely aliphatic carbinols of the type[4] $(R^3)_3COH$, $(R^2)_2R^3$-COH and $(R^2)_3COH$ appear to be still unknown.[5] In regard to the hydrocarbons our information is even more restricted. The only hexa-alkylethanes, (R_3C–CR_3), that have been prepared are hexamethylethane[6] and tetramethyldiethylethane.[7] Hexa-alkylethanes containing branched alkyl groups are entirely unknown.

The facts which are available regarding branched aliphatic compounds indicate that these compounds possess highly interesting properties, and indicate further that predictions as to the behavior of branched compounds based on the behavior of their primary straight-chain analogs are likely to be quite misleading. For example, the reaction of *iso*propyl alcohol with the halogen acids to form the *iso*propyl halides is often given as a typical reaction of secondary alcohols. Now there are six

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[1] This paper contains results obtained in an investigation on "Isolation and Investigation of Thermo-Labile Hydrocarbons Present in Petroleum," listed as Project 16 of American Petroleum Institute Research. Financial assistance in this work has been received from a research fund of the American Petroleum Institute donated by the Universal Oil Products Company. This fund is being administered by the Institute with the coöperation of the Central Petroleum Committee of the National Research Council.

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[4] We shall use R^1, R^2 and R^3 to represent primary, secondary and tertiary groups, respectively.

[5] A few alicyclic compounds are known of the type $(R^2)_3COH$; thus Murat and Amouroux, *Bull. soc. chim.*, [4] **15**, 159 (1914) prepared di-*iso*propylcyclohexylcarbinol, while Zelinsky, *Ber.*, **60**, 713 (1927), has recently prepared tri-cyclohexylcarbinol.

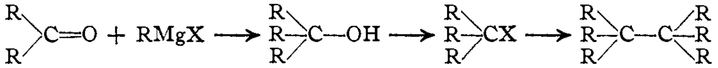
[6] Richards, *Ann. chim. phys.*, **21**, 323 (1910); Henry, *Bull. acad. roy. belg.*, **1906**, 256, 352; *Compt. rend.*, **142**, 1075 (1906).

[7] Späth, *Monatsh.*, **34**, 1982 (1913).

different classes of secondary alcohols possible, according to whether the alkyl groups are primary, secondary or tertiary and alike or different. Examples of each of these classes are known. With members of five of these classes the behavior when treated with halogen acids has been studied and for *only one class*, that where both alkyl groups are primary is the behavior similar to that of *iso*propyl alcohol. The members of the other classes yield halides formed as a result of rearrangement, or yield oxonium salts and no halides.

In still another respect do branched alkyl groups differ from straight-chain groups, for recent work has shown that with the tetra-aryldialkylethanes[8] and the dialkyldixanthyls,[9] secondary alkyl groups are markedly more effective than primary in promoting the dissociation of carbon–carbon linkages.

Since the information regarding highly-branched aliphatic compounds, in particular tertiary alcohols and hexa-alkylethanes, is thus extremely meager, we have attempted to prepare complex tertiary alcohols and from them hexa-alkylethanes by the following general procedure



$$R_2C{=}O + RMgX \longrightarrow R_3C{-}OH \longrightarrow R_3CX \longrightarrow R_3C{-}CR_3$$

The peculiarities of highly-branched compounds became apparent earlier than expected and blocked the project at the first step. It was found that the typical addition reaction between ketones and the Grignard reagent ceases to be the main reaction as soon as highly-branched compounds are employed. We have studied a variety of branched compounds in this reaction and from our results and the data available in the literature it is possible to state the limits of usefulness of the Grignard reaction as a method of preparing secondary and tertiary alcohols (employing the procedures now available).

Besides the normal addition of Grignard reagents to carbonyl compounds three other important reactions have been noted. These are reduction, enolization and condensation. Which of these four reactions will predominate in a given case depends largely on the nature of the alkyl groups present in the Grignard reagent and in the carbonyl compound. When primary alkyl groups are present the addition reaction appears to prevail to such an extent that satisfactory yields of the desired carbinols may always be expected. Complications arise, however, when branched alkyl groups are present in the carbonyl compound or the reagent or in both. The following table gives a general summary of the phenomena. In it the letters A, R, E and C refer, respectively, to addition, reduction,

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[8] Conant and Bigelow, THIS JOURNAL, **50**, 2041 (1928); Ziegler and Schnell, *Ann.*, **437**, 237 (1924).

[9] Conant, Small and Sloan, *ibid.*, **48**, 1743 (1926).

enolization and condensation. Yields are not given in exact figures because the results, taken from data of several workers, are not strictly comparable, but an approximate idea of the extent of the reaction is denoted by doubling the letter for yields greater than 50%.

TABLE I

SUMMARY OF RESULTS

	CH_3MgI	n-C_3H_7MgBr or n-C_4H_9MgBr	$(CH_3)_2CHMgBr$	$(CH_3)_3CMgCl$
CH_3CHO	AA[a]	....	A[b]	AA[c]
$(CH_3)_2CHCHO$	A[b]	....	AA	AR
$(CH_3)_3CCHO$	...	n-C_3H_7MgBr AA[d]	AR[d]	RR[d]
CH_3COCH_3	AA[a]	....	AA[e]	A[f]
$C_2H_5COC_2H_5$	AA[g]	n-C_4H_9MgBr AA	AA[g]	C
$CH_3COCH(CH_3)_2$	AA[g]	....	AA (R)[g]	...
$CH_3COC(CH_3)_3$	AA[f]	n-C_4H_9MgBr AR	EC	EC
$(CH_3)_2CHCOCH(CH_3)_2$	AA[g]	n-C_4H_9MgBr	RR	RR
$(CH_3)_2CHCOC(CH_3)_3$	AA	....	RR	RR
$(CH_3)_3CCOC(CH_3)_3$	AA	(No reaction with C_6H_5MgBr)	R	RR
$(CH_3)_2CHCO_2C_2H_5$	...	....	RR[g]	...
$(CH_3)_3CCO_2C_2H_5$	...	....	...	No reaction
$C_6H_5CH_2CO_2C_2H_5$	...	....	EE, CC	...

[a] Grignard, *Ann. chim. phys.*, [7] **24**, 464 (1901).

[b] Pickard and Kenyon, *J. Chem. Soc.*, **101**, 628 (1912).

[c] All facts given in this table and elsewhere in this article for which no reference is given are based on the experimental part of this work.

[d] Conant, Webb and Mendum, THIS JOURNAL, **51**, 1246 (1929).

[e] Ziegler, *Ann.*, **437**, 244 (1924).

[f] Henry, *Bull. acad. roy. belg.*, 352 (1906).

[g] Stas, *Bull. soc. chim. belg.*, **35**, 379 (1926).

The first and most striking fact shown by this table is that it has not been possible to prepare tertiary alcohols containing more than two secondary or tertiary groups. For when the simplest ketone containing two secondary groups, *iso*butyrone, is treated with the reagent from *iso*propyl bromide or *tert.*-butyl chloride the product, formed in an 80% yield, is di-*iso*propylcarbinol. There is no evidence of addition. When *iso*propyl *tert.*-butyl ketone or di-*tert.*-butyl ketone is treated with these same reagents reduction again occurs, the corresponding secondary alcohols being formed. Even in the case of aldehydes the reduction reaction is very evident when a secondary Grignard reagent acts on trimethylacetaldehyde and no addition occurs when *tert.*-butylmagnesium chloride is employed.

The special behavior of the methyl and benzyl reagents, a fact not shown in Table I, should be emphasized. Thus with *iso*butyrone and methylmagnesium iodide, addition to the extent of 78% takes place. In the course of some other work we found that this same ketone will add benzylmagnesium chloride, giving an 80% yield of tertiary alcohol. If now *iso*butyrone is treated with ethylmagnesium bromide[10] the yield of tertiary alcohol drops to 54% and is accompanied by 23% of reduction; with *n*-propylmagnesium bromide there is 30% of addition and 30% of reduction, while butylmagnesium bromide gives 40% of addition and 13% of reduction.

If we attempt to correlate structure and amount of reduction the facts of the preceding paragraph give a first clue that for a given carbonyl compound the amount of reduction increases with the size of the alkyl groups in the reagent. This same effect is also shown by pinacolone. With methylmagnesium iodide,[11] there is no reduction; with propylmagnesium chloride[12] there is 20% of reduction, and with butylmagnesium bromide over 30% of reduction. Much more important than the size of the alkyl group in the reagent is its complexity. The reduction of *iso*butyrone by *n*-butylmagnesium bromide amounts to 13%; with *tert.*-butylmagnesium chloride there is 80% reduction and no evidence of addition.

Just as an increase in the size and complexity of the alkyl group in the reagent promotes reduction, so also does an increase in the size and complexity of the alkyl groups in the carbonyl compound. Leroide[13] showed that while ethyl *iso*butyrate on treatment with *n*-propylmagnesium bromide gave a tertiary alcohol, ethyl pelargonate with the same reagent yielded a secondary alcohol. The effect of branching the carbon chain is shown by the behavior of diethyl ketone, *iso*butyrone and pinacolone toward *n*-butylmagnesium bromide. With the first ketone addition only is observed, with the second there is 13% of reduction and with the third 30% of reduction.

This effect of branching the alkyl groups in the carbonyl compound and reagent limits the usefulness of the Grignard reaction in preparing tertiary alcohols but it furnishes a convenient method for the reduction of highly branched ketones to the corresponding secondary alcohols. Thus *iso*butyrone, pentamethyl acetone and hexamethyl acetone are reduced by *tert.*-butylmagnesium chloride with excellent yields; the reduction is easily carried out and should be of use in working with branched compounds.

Besides reduction we have also encountered enolization and condensation. These two reactions seem to be limited to methyl ketones or to carbonyl compounds with a CH_2 group adjacent to the functional group, for they were encountered only with pinacolone and diethyl ketone.

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[10] Stas, *Bull. soc. chim. belg.*, **35**, 379 (1926).

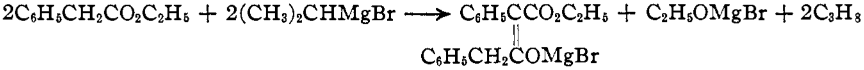
[11] Henry, *Bull. acad. roy. belg.*, 352, (1906).

[12] Leroide, *Ann. chim. phys.*, [9] **16**, 361 (1921).

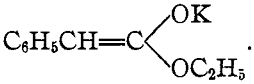
[13] Leroide, ref. **12**, p. 354.

Our evidence for enolization was the recovery of the ketone from reactions where an excess of the reagent was present, coupled with the known enolizing effect of the Grignard reagent which has recently been pointed out by Grignard[14] and by Kohler.[15] By condensation in the above cases we refer to the formation of material of high boiling point.

Our most striking illustration of enolization and condensation is furnished by phenylacetic ester. When this ester is added to *iso*propylmagnesium bromide there is a steady evolution of gas (a saturated hydrocarbon) and on decomposing the reaction mixture the product is α,γ-diphenylacetoacetic ester, the acetoacetic ester condensation product of the original ester; the yield is over 90%.

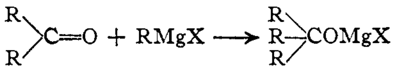


$$2C_6H_5CH_2CO_2C_2H_5 + 2(CH_3)_2CHMgBr \longrightarrow C_6H_5\underset{\underset{\displaystyle C_6H_5CH_2COMgBr}{\|}}{C}CO_2C_2H_5 + C_2H_5OMgBr + 2C_3H_8$$

This condensation, effected only with difficulty by using dry sodium ethylate,[16] can also be carried out using metallic potassium and in this case Scheibler[17] has advanced evidence to show that the intermediate product is  $C_6H_5CH{=}C\begin{smallmatrix}\diagup OK\\ \diagdown OC_2H_5\end{smallmatrix}$.

One more Grignard reaction may be mentioned as illustrating the limiting case of the effect of branched alkyl groups. When ethyl trimethylacetate was treated with *tert.*-butylmagnesium chloride no reaction could be observed even after boiling the reaction mixture for ten hours; the ester was recovered unattacked.

Any discussion of the mechanism of these abnormal reactions must be at present largely a restatement of the experimental facts. The following seems to be the most satisfactory. With simple, straight-chain compounds the normal addition reaction takes place very rapidly



$$R_2C{=}O + RMgX \longrightarrow R_3COMgX$$

As the alkyl groups present are increased in size and complexity, there is a decrease in the rate of this addition reaction. This would be expected in view of the known effect on the rate of bisulfite addition to carbonyl compounds of increasing the size and complexity of the alkyl groups in these compounds. When the normal addition reaction is slowed down sufficiently, other reactions, ordinarily too slow to be observed, and which are less subject to hindrance, become predominant. This is illustrated by the reduction of *iso*butyrone, pentamethyl acetone and hexamethyl

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[14] Grignard and Savard, (a) *Compt. rend.*, **179**, 1573 (1924); (b) *Bull. soc. chim. belg.*, **36**, 97 (1927).

[15] Kohler, Stone and Fuson, THIS JOURNAL, **49**, 3181 (1927).

[16] (a) Newbauer, "Dissertation," Leipzig, **1889**; (b) Volhard, *Ann.*, **296**, 1 (1897).

[17] Scheibler and Mahboub, *Ber.*, **60**, 564 (1927).

acetone and by the enolization and condensation of pinacolone when branched reagents are used. The limiting case, when all reactions are slowed down to such an extent as to be negligible in rate, is that of trimethylacetic ester and *tert.*-butylmagnesium chloride where no reaction takes place. When the hindrance to addition is great but reduction and enolization are not possible because of the structure of the ketone and reagent, there is no reaction; this is the case with phenylmagnesium bromide and hexamethyl acetone. The assumption that the rate of the enolization and reduction reactions is less affected than the addition reaction by what we may call steric factors is in accord with many rate measurements on a variety of organic reactions.

Experimental

Since essentially the same procedure was employed in all the Grignard reactions it will be economical of space to give here a general description of this procedure; then in the individual cases any variations used will be noted. The reagent was prepared in the usual apparatus, a flask fitted with a trident adapter in which were placed a condenser, dropping funnel and mercury-seal stirrer. Five hundred cc. of ether was used per mole of alkyl halide and magnesium. The average yields with the various reagents were as follows: *n*-butylmagnesium bromide, 80%; *iso*propylmagnesium bromide, 70–75%; *tert.*-butylmagnesium chloride, 50–55%. In preparing *tert.*-butylmagnesium chloride a solution of 5 cc. of *tert.*-butyl chloride and 50 cc. of ether was added to the magnesium plus a crystal of iodine. After the reaction had started (two or three minutes) an additional 75 cc. of ether was added at once and then the remainder of the ether and alkyl halide mixed and added slowly. After the reagents had been prepared they were chilled, then decanted into a second flask in order to separate any excess magnesium. The second flask was surrounded by an ice-bath and then the carbonyl compound, dissolved in dry ether, was added slowly. The ice-bath was removed, the mixture stirred at room temperature for several hours or left overnight and then boiled for one hour. Finally it was cooled, decomposed with ice and a bare excess of sulfuric acid[18] and the ether layer separated. The aqueous layer was extracted once with ether and the combined ether layers washed with water, sodium carbonate solution and water and then dried over sodium sulfate. The final working up of the products varied, of course, according to their properties. The practical distillations were carried out using a Widmer special column which was found very efficient.

The reagents in general were not analyzed, but knowing the yields to be expected, a large excess of the reagent was used. In the one case,

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[18] If hydrochloric acid is used for the decomposition there is danger, with *tert.*-alcohols, of forming the ether-soluble chlorides.

tert.-butylmagnesium chloride, where the yield of reagent may vary within wide limits it is, fortunately, quite easy to detect poor preparations, for the magnesium chloride etherate formed in such cases is very slightly soluble in ether and the reagent is pasty. Well-conducted preparations of this reagent, which contained but little precipitate, when analyzed showed that about 50% of the magnesium had been converted into a Grignard reagent.

A. Grignard Reagents and Aldehydes

Acetaldehyde and *Tert.*-butylmagnesium Chloride.—Eleven grams (0.25 mole) of freshly distilled acetaldehyde dissolved in 50 cc. of ether was added to a theoretical 8 moles of *tert.*-butylmagnesium chloride. After working up, the ether was removed on the steam-bath and the residual material fractionated. There was obtained 1.3 g. of low-boiling material (85–115°), then 20.5 g. boiling at 115–119°, mostly at 116–118°, a yield of 80%. The residue was less than 1 cc. The main fraction, methyl-*tert.*-butylcarbinol, gave with phenyl *iso*cyanate the well-known phenylurethan,[19] m. p. 75–76°.

***Iso*butyraldehyde and *Iso*propylmagnesium Bromide.**—Four-tenths of a mole (28.8 g.) of freshly distilled *iso*butyraldehyde in 50 cc. of ether was added to a theoretical 0.7 mole of *iso*propylmagnesium bromide. After removing the ether the residue, on fractionation, yielded 3 g. of low-boiling material (80–133°) and 36 g. of di-*iso*propylcarbinol, 134–138°; yield, 78%.

With phenyl isocyanate the di-*iso*propylcarbinol set to a solid mass. This phenylurethan crystallized from ether and petroleum ether in splendid long needles melting at 96–99°.

Anal. Calcd. for $C_{14}H_{21}O_2N$: C, 71.5; H, 8.9. Found: C, 71.6; H, 9.0.

***Iso*butyraldehyde and *Tert.*-butylmagnesium Chloride.**[20]—Sixty-five grams (0.9 mole) of freshly distilled *iso*butyraldehyde in 100 cc. of ether was added to a theoretical 2.2 moles of *tert.*-butylmagnesium chloride. After removing the ether on the steam-bath the residual material was fractionated. On the fourth fractionation the following fractions were obtained: (1) 50–100°, 4.5 g.; (2) 106–114°, 13 g.; (3) 115–145°, 2.4 g.; (4) 148–152°, 57 g. The residue was less than 1 cc.

Fraction 2 consisted of *iso*butyl alcohol for with phenyl isocyanate it yielded within five minutes a solid cake of the phenylurethan of that alcohol.[21] The melting point of the phenylurethan and the mixed melting point with a known specimen was 85–86°; yield of reduction product, 20%.

Fraction 4 consisted of *iso*propyl-*tert.*-butylcarbinol. With phenyl isocyanate it yielded the phenylurethan, m. p. 89°. This melting point, confirmed with other specimens, is exactly 10° higher than that given by Haller and Bauer,[22] yield of addition product, 44%. We could find none of the glycol which previously was reported to be formed in this reaction.

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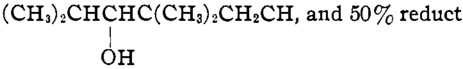
[19] Delacre, *Bull. soc. chim.*, [4] **1**, 460 (1907).

[20] Faworsky, *J. prakt. Chem.*, [2] **88**, 652 (1913), carrying out this same reaction, obtained 25% addition, 25% condensation and reduction to yield the glycol, (CH₃)₂CHCHC(CH₃)₂CH₂CH, and 50% reduction to *iso*butyl alcohol.



$$(CH_3)_2CH\underset{\displaystyle OH}{\underset{|}{C}}HC(CH_3)_2CH_2CH$$

[21] Mylius, *Ber.*, **5**, 973 (1872); Blaise and Piccard, *Ann. chim. phys.*, [8] **26**, 279 (1912).

[22] Haller and Bauer, *ibid.*, [8] **29**, 317 (1913).

B. Grignard Reagents and Ketones

Diethyl Ketone and *n*-Butylmagnesium Bromide.—Forty-three grams (0.5 mole) of diethyl ketone in 100 cc. of ether was added to a theoretical 1.0 mole of *n*-butylmagnesium bromide. The reaction mixture yielded on fractionation 6 g. of material boiling from 106–113°, 2.5 g. boiling from 113–115° and 46 g. boiling at 119–121° at 110 mm. and 116–118° at 105 mm. This last fraction consisted of *diethyl-n-butyl carbinol*, yield, 60%; d_4^{20}, 0.8409; n_D^{20}, 1.4360; M_D, calcd. for n^2 formula, 45.05; n formula, 74.44. Found: n^2 formula, 44.79; n formula, 74.65.

Anal. Calcd. for $C_9H_{20}O$: C, 75.0; H, 13.9. Found: C, 74.7; H, 14.2.

The fraction boiling at 113–115° was heated with 3,5-dinitrobenzoyl chloride and pyridine. No dinitrobenzoate of diethylcarbinol was formed.

In order to secure a solid derivative of diethylcarbinol for identification we had previously treated a known sample of this carbinol with phenyl isocyanate. A solid phenylurethan was not formed. Consequently we had recourse to 3,5-dinitrobenzoyl chloride and pyridine. These yielded the 3,5-dinitrobenzoate of diethylcarbinol which melted, after crystallization from methyl or ethyl alcohol, at 101°.

Anal. Calcd. for $C_{12}H_{14}O_6N_2$: C, 51.1; H, 5.0. Found: C, 50.5; H, 5.1.

Diethyl Ketone and *Tert.*-butylmagnesium Chloride.—Four-tenths of a mole (34.4 g.) of diethyl ketone in 100 cc. of ether was added to a theoretical 1.0 mole of *tert.*-butylmagnesium chloride. On fractionation, the reaction mixture yielded 1.3 g. of material boiling from 70–105°, 10 g. boiling from 105–120° and 20 g. boiling from 30–100° at 5 mm. From this material no definite products could be isolated.

Pinacolone and *n*-Butylmagnesium Bromide.—Fifty grams (0.5 mole) of pinacolone was added to a theoretical 1.0 mole of *n*-butylmagnesium bromide. On fractionating the reaction product there was obtained 5.5 g. of material boiling from 95–117°, 16 g. boiling from 117–119° and 20 g. boiling from 84–87° at 13 mm. This last fraction was *methyl-n-butyl-tert.-butylcarbinol*, yield, 25%; d_4^{20}, 0.8487; n_D^{20}, 1.4409; M_D, calcd. from n^2 formula, 49.65; from n formula, 82.09. Found: n^2 formula, 49.16; n formula, 82.09.

Anal. Calcd. for $C_{10}H_{22}O$: C, 75.9; H, 13.9. Found: C, 75.6; H, 14.1.

The fraction boiling at 117–119° was shown to be the reduction product of pinacolone, pinacoline alcohol, by conversion to the phenylurethan, m. p. 79°, and a mixed melting point with a known specimen. The yield of reduction product was 30%.

Pinacolone and *Iso*propylmagnesium Bromide.—Twenty-five grams (0.25 mole) of pinacolone was added to a theoretical 0.5 mole of *iso*propylmagnesium bromide. Much gas was evolved. On fractionation there was obtained 13 g. of material boiling from 105–115° and 8 g. of high-boiling material. The low-boiling material yielded no phenylurethan, but with hydroxylamine gave an oxime, m. p. 75°, which was identified as pinacolone oxime by comparison with an authentic specimen,[23] yield of recovered pinacolone, 50%. The high-boiling material on distilling *in vacuo* boiled at 60–95° at 3 mm. and evidently consisted of condensation products, for methyl-*iso*propyl-*tert.*-butylcarbinol (see later) boils at 56° at 6 mm.

Pinacolone and *Tert.*-butylmagnesium Chloride.—Thirty-five grams (0.35 mole) of pinacolone was added to a theoretical 1 mole of *tert.*-butylmagnesium chloride and the product fractionated twice. There was obtained 22 g. of material boiling at 100–117°, and 9.4 g. of high-boiling material. This latter consisted of condensation products, for on distillation *in vacuo* it boiled over a wide range, 65–100° at 5 mm. The material boiling at 100–117° was shown to be recovered pinacolone by the preparation from it of benzalpinacolone, m. p. 41–42°.[24]

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[23] Janny, *Ber.*, **15**, 2780 (1882).

[24] "Organic Syntheses," John Wiley and Sons, Inc., New York, **5**, 15 (1926).

Iso**butyrone and *n*-Butylmagnesium Bromide.**—From 57 g. (0.5 mole) of *iso*butyrone and a theoretical mole of reagent there was obtained on fractionation a small amount of low-boiling material, then 3 g. boiling from 128–137°, 8 g. boiling from 137–140° and 34 g. boiling at 115–118° at 45 mm. This last fraction, consisting of *di-isopropyl-n-butyl carbinol,* which was obtained in a yield of 40%; d_4^{20}, 0.8487; and n_D^{20}, 1.4435; M_D, calcd. from n^2 formula, 54.26; from n formula, 89.64. Found: n^2 formula, 53.78; n formula, 89.86.

Anal. Calcd. for $C_{11}H_{24}O$: C, 76.7; H, 14.0. Found: C, 76.6; H, 14.2.

The material boiling at 137–140° was shown to be di-*iso*propylcarbinol by conversion to the phenylurethan and mixed melting point with a known sample. The yield of this reduction product was 13%.

Iso**butyrone and *Iso*propylmagnesium Bromide.**[25]—From 28.5 g. (0.25 mole) of *iso*butyrone and a theoretical 0.5 mole of *iso*propylmagnesium bromide, there was obtained 2.4 g. of material boiling from 80–134°, then 22.5 g. boiling at 135–138° and 3 g. boiling from 138–143°. The residue amounted to 2 cc. The fractions boiling at 135–138° and 138–143° consisted of di-*iso*propylcarbinol, for with phenyl isocyanate they set to a solid mass of phenylurethan, m. p. 95°. The identity of this phenylurethan was established by a mixed melting point. The yield of reduction product was 78%.

Iso**butyrone and *Tert.*-butylmagnesium Chloride.**—From 28.5 g. (0.25 mole) of *iso*butyrone and a theoretical 0.8 mole of *tert.*-butylmagnesium chloride there was obtained 3 g. of material boiling at 70–110°, 2.1 g. boiling at 110–130° and 21.8 g. boiling at 136–138°. The residue amounted to 1 cc. The two latter fractions consisted of the reduction product, di-*iso*propylcarbinol, for with phenyl isocyanate they yielded the known phenylurethan (melting point and mixed melting point). The yield of reduction product was 80%.

Pentamethylacetone and Methylmagnesium Iodide.—From 26 g. of pentamethylacetone and a theoretical 0.3 mole of methylmagnesium iodide there was obtained 4 g. of low-boiling material and then 18 g. of *methyl-isopropyl-tert-butylcarbinol,* b. p. 56–57° at 6 mm., a yield of 60%. This carbinol has d_4^{20}, 0.8564; n_D^{20}, 1.4430. M_D, calcd. from n^2 formula, 45.05; from n formula, 74.44. Found: n^2 formula, 44.59; n formula, 74.49.

Anal. Calcd. for $C_9H_{20}O$: C, 75.0; H, 13.9. Found: C, 75.2; H, 13.9.

In this reaction the intermediate magnesium compound separates as splendid colorless crystals.

Pentamethylacetone and *Iso*propylmagnesium Bromide.—From 19.2 g. (0.15 mole) of ketone and a theoretical 0.29 mole of reagent there was obtained 0.8 g. of low-boiling material, to 149°, then 17.1 g. of reduction product boiling at 149–151°. The *iso*propyl-*tert.*-butylcarbinol, identified through its phenylurethan, was obtained in an 88% yield.

Pentamethylacetone and *Tert.*-butylmagnesium Chloride.—From 19.2 g. (0.15 mole) of ketone and a theoretical 0.5 mole of reagent there was obtained 1.3 g. of material boiling up to 149°, then 17.6 g. of reduction product, boiling at 149–151°. The reduction product, *iso*propyl-*tert.*-butylcarbinol, yield 90%, was identified as the phenylurethan.

Hexamethylacetone and Methylmagnesium Iodide.—From 13 g. of hexamethylacetone and the Grignard reagent prepared from 4 g. of magnesium and 23 g. of methyl

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[25] This reaction, already carried out by Stas, *Bull. soc. chim. belg.*, **34,** **188** (1925); **35,** 379 (1926), was repeated because from the experimental data given in his article the yield of reduction product (50%) was not as large as we expected in view of our results with *tert.*-butylmagnesium chloride.

iodide there was obtained 11.4 g. of solid *di-tert.-butyl-methylcarbinol*, b. p. 184–191°, m. p. 39–41° and 0.9 g. of low-boiling material; yield, 78%. (The period of refluxing was four hours.)

Anal. Calcd. for $C_{10}H_{22}O$: C, 75.8; H, 14.0. Found: C, 75.4; H, 13.7.

Hexamethylacetone and *Iso*propylmagnesium Chloride.—From 13 g. of the ketone and the Grignard reagent from 4 g. of magnesium and 13 g. of *iso*propyl chloride (period of refluxing three and one-half hours) there was obtained 6 g. of unchanged ketone (b. p. 150–159°), 1.5 g. of b. p. 159–161° and 1.2 g. of b. p. 163–167°. The last fractions solidified and were identified as di-*tert.*-butylcarbinol.

Hexamethylacetone and *Tert.*-butylmagnesium Chloride.—From 14 g. of the ketone and the Grignard reagent from 6 g. of magnesium and 23 g. of *tert.*-butyl chloride there was obtained (after four hours of refluxing) 9.9 g. of solid di-*tert.*-butylcarbinol, b. p. 159–167°; yield, 69%.

C. Grignard Reagents and Esters

Trimethylacetic Ester and *Tert.*-butylmagnesium Chloride.—One-tenth mole (12 g.) of trimethylacetic ester was added to a theoretical 0.6 mole of reagent and the mixture boiled for ten hours. On working up the products there was obtained 9 g. of recovered ester boiling at 116–119°. No hexamethylacetone or *tert.*-butylcarbinol could be found.

Phenylacetic Ester and Isopropylmagnesium Bromide.—Three-tenths of a mole (49.2 g.) of phenylacetic ester was added to a theoretical 0.5 mole of *iso*propylmagnesium bromide chilled in an ice-bath. There was a steady evolution of saturated gas and the separation of a light gray magnesium compound. After standing overnight the reaction mixture was decomposed and the ether layer on evaporation gave 39.5 g. of crude diphenylacetoacetic ester; yield, 94%. The crude ester melted at 72–75°. After it was triturated in a mortar with cold alcohol, filtered and dried, it melted at 78°. This product may be recrystallized from alcohol with only slight loss.

The ester was identified by a mixed melting point and by the preparation of the pyrazolone on treatment with phenylhydrazine.[16b]

Summary

1. Besides the normal addition of the Grignard reagent to carbonyl compounds, three other reactions—reduction, enolization and condensation—may take place. The occurrence of these reactions has been correlated with the lengthening and branching of the alkyl groups in the carbonyl compound and reagent. The limits of usefulness of the Grignard reaction for synthesizing secondary and tertiary alcohols have been pointed out. The extreme case where no reaction at all takes place has been illustrated.

2. It is shown that ketones containing two secondary groups or one secondary and one tertiary group may be easily and conveniently reduced to the corresponding secondary alcohols with *iso*propylmagnesium bromide or *tert.*-butylmagnesium chloride.

3. A synthesis of α,γ-diphenylacetoacetic ester based on the enolizing and condensing action of *iso*propylmagnesium bromide is described.

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