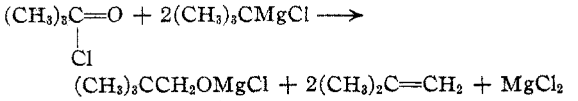
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

The Reducing Action of *t*-Butyl Grignard Reagent on Acyl Chlorides

BY FRED L. GREENWOOD, FRANK C. WHITMORE AND HARRY M. CROOKS

In an attempt to prepare di-*t*-butyl ketone or di-*t*-butylcarbinol by the action of *t*-butylmagnesium chloride on pivalyl (trimethylacetyl) chloride it was found that the chief products are neopentyl alcohol and neopentyl pivalate resulting from the reduction of the acid chloride by the Grignard reagent.



$$(CH_3)_3\underset{\displaystyle Cl}{\underset{|}{C}}{=}O + 2(CH_3)_3CMgCl \longrightarrow (CH_3)_3CCH_2OMgCl + 2(CH_3)_2C{=}CH_2 + MgCl_2$$

The action of *t*-butyl Grignard reagent with pivalyl chloride has been studied by the addition of the Grignard reagent to a large excess of acid chloride at a low temperature, and by the addition of the acid chloride to a large excess of the Grignard reagent at the reflux temperature of ethyl ether. Moreover, we have added isobutyryl and *n*-butyryl chlorides to a large excess of Grignard reagent at ethyl ether reflux temperature. The results are summarized in Table I.

TABLE I

Acid chloride	Ratio of $(CH_3)_3CMgCl$ to acid chloride	Products % addition	Products % reduction
Pivalyl[a]	1/5	32.4	8
Pivalyl[b]	4/1	1.5	94.0
Isobutyryl	5/1	63.0	20.0
n-Butyryl	4/1	71.0	9.0

[a] Grignard reagent added to acid chloride at −10°: addition product hexamethylacetone, reduction product neopentyl pivalate. [b] Acid chloride added to Grignard reagent at about 40°. Addition product was di-*t*-butylcarbinol resulting from addition of 1 mole of Grignard reagent followed by reduction; reduction product was neopentyl alcohol.

In all reactions the isobutylene formed corresponded to two moles of Grignard reagent per mole of acid chloride reduced to primary alcohol plus one mole of Grignard reagent per mole of ketone reduced to secondary alcohol. The alcohols were identified by preparation of derivatives and mixed melting points with known materials. Exception was made in the case of *n*-propyl-*t*-butylcarbinol and isopropyl-*t*-butylcarbinol which were identified by comparison of the physical constants of the substances and of their derivatives with those reported for these compounds by Haller and Bauer,[1] and by Conant, Webb and Mendum.[2] Neopentyl pivalate was identified by hydrolysis and the preparation of known derivatives of the hydrolysis products.

In all cases the Grignard reagent used was filtered and free from particles of magnesium. All attempts to find the aldehyde corresponding to the primary alcohol obtained failed.

Experimental

Preparation of the *t*-Butylmagnesium Chloride Solution.—A calibrated three-liter flask was equipped, by means of a trident, with reflux condenser, separatory funnel and mercury-sealed stirrer. To 121.5 g. of magnesium turnings (5 moles) in the flask was added 5 cc. of tertiary butyl chloride in 30 cc. of dry ether. A few drops of ethyl bromide started the reaction. When vigorous reaction had started, 300 cc. of dry ether was added and followed by the remainder of 460 g. (5 moles) of tertiary butyl chloride (b. p. 50° at 738 mm.; $n^{20}D$ 1.3859) dissolved in 1400 cc. of dry ether. The halide solution was added at such a rate that refluxing was continuous. This required about eighteen hours. Sitrring was continued for an hour after end of addition. The solution was allowed to stand overnight and then titrated by the method of Gilman.[3] The yield of reagent was 75–85%. The clear solution was filtered through two layers of cloth under pressure of dry nitrogen. The filtrate contained no particles of magnesium.

Preparation of Acid Chlorides.—Pivalic acid was prepared by carbonation of *t*-butylmagnesium chloride in 60% yield.[4] Treatment of the acid with thionyl chloride gave an 80% yield of pivalyl chloride, b. p. 70.5–71° at 250 mm., $n^{20}D$ 1.4118.

Isobutyric acid (b. p. 151° at 732 mm., $n^{20}D$ 1.3920) was prepared by alkaline permanganate oxidation of isobutyl alcohol. Isobutyryl chloride was obtained in 75% yield by the use of thionyl chloride, b. p. 90–91°, $n^{20}D$ 1.4070.

n-Butyryl chloride was obtained in 80% yield by treatment of the acid (Eastman Kodak Co.) with thionyl chloride: b. p. 101–101.5° (730 mm.); $n^{20}D$ 1.4117.

Apparatus.—The reactions were carried out in the apparatus used in the preparation of the Grignard reagent except that the system was closed and the exit gases led through the condenser to a gas-collecting carboy.

Three fractionating columns were used, all of the adiabatic, total reflux, variable take off type packed with single-turn glass helices: column 1, 1.5 × 66 cm., 12 theoretical plates; column 2, 1 × 45 cm., 9 plates; column 3, 0.9 × 53 cm., 13 plates.

Addition of *t*-Butylmagnesium Chloride to Pivalyl Chloride.—A solution of 966.5 g. of pivalyl chloride (8.0 moles) in 1 liter of dry ether was placed in the reaction flask and cooled to −10° (thermometer in the solution). To

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[1] Haller and Bauer, *Ann. chim. phys.*, [8] **29**, 313 (1913).

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

[3] Gilman, Wilkinson, Fishel and Meyers, *ibid.*, **45**, 150 (1923).

[4] "Organic Syntheses," Vol. VIII, 104 (1928).

this was added, over a period of seventeen hours, a solution of 1.5 moles of *t*-butylmagnesium chloride in 1 liter of dry ether. During the addition the temperature was kept at −10° or below. After addition was complete the ice-bath was exchanged for a water-bath and the reaction mixture heated to 50° to drive off dissolved gases. The Grignard complex was decomposed by pouring over crushed ice, the layers were separated and the aqueous layer extracted well with ether. The combined ether layers were extracted with an excess of saturated sodium bicarbonate solution which was saved for recovery of the excess pivalic acid. The ether solution was concentrated and fractionated through Column 1. Refractionation through Column 2 yielded the following fractions:

	B. p. (740 mm.)	n^{20}_{D}	Wt., g.	Product
1	151–153	1.4175–83	67.4	Hexamethylacetone
2	153–164	1.4161–40	50.3	Mixture (?)
3	164–165	1.4033–5	14.1	Neopentyl pivalate
4	124(93 mm.)	1.4093	15.3	Pivalic anhydride

Fraction 1 was identified as hexamethylacetone by comparison of the physical constants with a known sample and then by conversion to the carbinol by sodium reduction. The resulting di-*t*-butylcarbinol was identified by means of the phenylurethan, m. p. 120.5–121°, mixed with a known sample (118.5–120°) it melted at 120–121°. Haller and Bauer reported the m. p. as 118–119°.

Fraction 3 was hydrolyzed with 25% KOH, to give an solid alcohol, which was converted to the phenylurethan, m. p. 111.5–112°. Mixed with the known derivative of neopentyl alcohol (112–112.5°) it melted at 112°. Acidification of the alkaline layer yielded an acid which gave an amide of m. p. 153–154°. Mixed with the known amide of pivalic acid (153–153.5°) it melted at 153–154°.

Fraction 4 was hydrolyzed in aqueous potassium hydroxide solution to give a solid acid which gave pivalamide. No non-acidic hydrolysis products were formed.

During the reaction 6.5 l. of isobutylene were collected in the gas carboy, 0.25 mole, a 17% yield based on the Grignard reagent used which is in accordance with the 8% yield of neopentyl trimethylacetate as reduction product.

Addition of Pivalyl Chloride to *t*-Butylmagnesium Chloride.—To a solution of 3.9 moles of *t*-butylmagnesium chloride in 2 liters of ether was added 1.1 moles of pivalyl chloride, undiluted, over a period of four and one-half hours. During this time 90 liters of gas came off consisting of about 40% ether and 55% isobutylene (slightly over two moles of isobutylene measured at 29° and 733 mm.).

After standing overnight the Grignard complex was decomposed by pouring slowly over 2 kg. of crushed ice, the layers separated and the aqueous layer steam distilled until there was no further odor of alcohol in the fresh distillate. The aqueous distillate was saturated with sodium carbonate and thoroughly extracted with ether. All ether solutions were then combined and dried. The ether was removed through Column 3 and the products fractionated through the same column.

	B. p. (737 mm.) °C.	Wt., g.	Product
1	75–100	6.0	Impure hexamethylethane
2	106–112	88.0	M. p. 50°, neopentyl alcohol
3	163–166	1.8	Semisolid, di-*t*-butylcarbinol

The phenylurethan of 2 melted at 112.5–113.5°; mixed with the known derivative of neopentyl alcohol (112–112.5°), it melted 112–113°. The α-naphthylurethan of 2 melted 98.5–99°, mixed with the known (98.5–100.5°) it melted at 98.5–99.5°.

The phenylurethan of 3 melted 120.5–121°; mixed with the known derivative of di-*t*-butylcarbinol (119–121°) it melted at 120–121°.

The yield of neopentyl alcohol was 94% while that of di-*t*-butylcarbinol was 1.5%.

Addition of Isobutyryl Chloride to *t*-Butylmagnesium Chloride.—The addition of 0.84 mole of isobutyryl chloride (89 g.) to 4.2 moles of *t*-butylmagnesium chloride in 2 liters of ether required four hours. During the reaction 1.34 moles of gas was given off which contained 93.5% isobutylene, 1.49 moles, per mole of acid chloride.

The liquid products gave the following

	B. p. (738 mm.) °C.	n^{20}_{D}	Wt., g.	Product
1	79–81	1.3910	7.5	
2	90–103		2.2	Solid, hexamethylethane
3	103–106	1.3950	12.5	Isobutyl alcohol
4	145	1.4281	82.0	*t*-Butylisopropylcarbinol

The phenylurethan of 3 melted at 83–83.5°, mixed with the known derivative of isobutyl alcohol (84–84.5°) it melted at 83–84°. The α-naphthylurethan of 3 melted at 97–97.5°, mixed with the known derivative (98–98.5°) it melted at 97–98°.

The phenylurethan of 4 melted at 86.5–87° and the α-naphthylurethan at 103–104°. Conant gives the melting point of the phenylurethan as 89° and assumes Haller and Bauer's reported value of 79° to be a misprint.

The isobutyl alcohol isolated amounted to a 20% yield based on original acid halide while the secondary alcohol accounted for 63% of the original acid chloride.

Addition of *n*-Butyryl Chloride to *t*-Butylmagnesium Chloride.—The addition of 0.98 mole of *n*-butyryl chloride to 4.0 moles of Grignard reagent dissolved in two liters of ether required five and one-half hours. During the reaction 1.1 moles of gas was given off which contained 84% isobutylene, a yield of 94% isobutylene based on the acid chloride.

The liquid products were worked up as before.

	B. p. (744 mm.) °C.	n^{20}_{D}	Wt., g.	Product
1	79–82	1.3908	7.5	
2	100–106		2	Solid, hexamethylethane
3	115–116.5	1.3993	6.5	1-Butanol
4	152–153	1.4275	90.8	*t*-Butyl-*n*-propylcarbinol

The phenylurethan of 3 melted at 62–62.5°, mixed with the known derivative of 1-butanol (62–62.5°) it melted at 62–62.5°. The α-naphthylurethan melted at 70–71°, mixed with the known derivative (71–72°) it melted at 70–71°.

The phenylurethan of 4 melted at 70.5–71.5° and the α-naphthylurethan at 113–114°. Haller and Bauer report a boiling point of 155–157° for this carbinol and a melting point of 70–71° for the phenylurethan.

The 1-butanol isolated amounted to 9% based on the acid chloride used while the secondary carbinol isolated accounted for 71% of the acid chloride.

All melting points are uncorrected.

Summary

1. The reaction of *t*-butylmagnesium chloride with a large excess of pivalyl chloride at −10° gives a 32% yield of hexamethylacetone and an 8% yield of neopentyl alcohol as its pivalic ester.

2. The reaction of a large excess of *t*-butylmagnesium chloride at about 40° with pivalyl, isobutyryl and *n*-butyryl chlorides results, respectively, in a 1.5, 63 and 71% yield of addition and in a 94, 20 and 9% yield of reduction of the acid chloride to primary alcohol.

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The Action of *t*-Butylmagnesium Chloride on *t*-Butylacetyl Chloride

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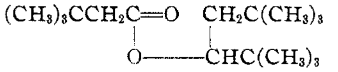
The preparation of *t*-butylneopentylcarbinol in quantity for use in a dehydration study involved the reaction of *t*-butylmagnesium chloride with *t*-butylacetyl chloride. An investigation of the reduction products has proved interesting when compared with the action of the same Grignard compound on trimethylacetyl chloride.[1] The addition of the acid chloride to *t*-butylmagnesium chloride produced *t*-butylneopentylcarbinol in 71% yield together with a 1% yield of neopentylcarbinol. Investigation of the products of this reaction boiling above the secondary carbinol indicates a 5% yield of *t*-butylneopentylcarbinyl *t*-butylacetate as the product of the esterification of the secondary alcohol complex with unreacted acid chloride. However, addition of *t*-butylacetyl chloride to a suitable excess of *t*-butylmagnesium chloride permitted all of the secondary carbinol to be recovered without esterification, thus raising the yield to 76%.

Addition of a slight excess of a filtered solution of *t*-butylmagnesium chloride to an ethereal solution of *t*-butylacetyl chloride, produced *t*-butylneopentyl ketone in 51% yield. In this case all of the secondary carbinol formed as reduction product underwent esterification in the presence of excess acid chloride to yield 17% of pure *t*-butylneopentylcarbinyl *t*-butylacetate. Attempts to saponify this ester by refluxing with alcoholic potassium hydroxide for seventy-one hours or by heating for fifty-six hours in a sealed tube at 90–100° were not successful. However, an authentic sample of the ester obtained from the reaction of *t*-butylneopentylcarbinol and *t*-butylacetyl chloride checked in physical constants with the reduction product and proved equally stable toward saponification under similar conditions.[2]

No reduction was obtained when *t*-butyl neopentyl ketone was treated with a solution of aluminum isopropylate in isopropyl alcohol. This inertness and the inability to form a semicarbazone or an oxime[3] are related to the steric arrangement about the carbonyl group of this ketone. The inertness of the ester is dependent on similar steric conditions.



$$\begin{array}{ll}(CH_3)_3CCH_2C{=}O & CH_2C(CH_3)_3 \\ \qquad\qquad\quad | & \;| \\ \qquad\qquad\quad O\text{———} & CHC(CH_3)_3\end{array}$$

Experimental

Addition of *t*-Butylacetyl Chloride to *t*-Butylmagnesium Chloride.—A solution of 5.4 moles of *t*-butylmagnesium chloride in 2400 cc. of dry ether was prepared by the action of *t*-butyl chloride, b. p. 50° (732 mm.), $n^{20}\text{D}$ 1.3850, on magnesium. *t*-Butylacetyl chloride, b. p. 79° (150 mm.), $n^{20}\text{D}$ 1.4212, was prepared in 86% yield from *t*-butylacetic acid and thionyl chloride.[4] Addition of 336 g. (2.5 moles) of the acid chloride in a liter of ether to the Grignard solution (5.4 moles) was completed in three days and then the thick reaction mixture was refluxed for four days. The complex was decomposed with ice, the products extracted with ether and the solvent removed with an efficient column.[5] Fractionation of the products yielded: Fractions 1–3, 72.9 g., b. p. 34–81° (735 mm.), $n^{20}\text{D}$ 1.3520–1.3880; 4–5, 34.0 g., 81–167°, 1.4081–1.4220; 6–9, 282.3 g., 167–173°, solid; 10–11, 47.9 g., 122–208° (50–45 mm.), 1.4363–1.4450; solid residue, 15.4 g. Fractions 6–9 represent a 71% yield of *t*-butylneopentylcarbinol. A portion of the solid, by a series of fractional crystallizations, gave a pure sample of carbinol, m. p. 49.4° (corr.).

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(1) Greenwood, Whitmore and Crooks, THIS JOURNAL, **60**, 2028 (1938).

(2) Since the completion of this paper, J. S. Whitaker of this Laboratory has succeeded in partially saponifying this ester and identifying *t*-butylacetic acid as the acid fragment.

(3) Bouveault and Locquin, *Bull. soc. chim.*, [3] **35**, 642 (1906).

(4) Homeyer, Whitmore and Wallingford, THIS JOURNAL, **55**, 4209 (1933).

(5) Whitmore and Lux, *ibid.*, **54**, 3451 (1932).