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

The Action of Primary Grignard Reagents with t-Butylacetyl Chloride. II¹

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This is a continuation of the studies in this Laboratory on the reducing action of Grignard reagents.²

In the first paper of this title¹ the acid chloride was added to excess of Grignard solutions. The chief products isolated were tertiary alcohols of the type $(CH_3)_3CCH_2C(OH)R_2$ in which R was ethyl, *n*-propyl, *n*-butyl, or *n*-amyl, and the corresponding olefins $(CH_3)_3CCH=CR_2$ and their isomers. The other products were secondary carbinols of the type $(CH_3)_3CCH_2CHOHR$, in which R was *n*-propyl, *n*-butyl, or *n*-amyl. No reduction product of this type was found when ethylmagnesium bromide was used.

In the present study each of the four Grignard solutions was added to a slight excess of *t*-butylacetyl chloride in anhydrous ether.

Ethylmagnesium bromide gave the largest amount of the primary product, the ketone of the type $(CH_3)_3CCH_2COR$, giving about 51% of neopentyl ethyl ketone. The *n*-propyl, *n*-butyl, and *n*-amyl Grignard reagents gave 37, 34, and 29\%, respectively, of the corresponding ketones.

Reduction by means of the Grignard reagent would convert these ketones to secondary carbinols $(CH_8)_3CCH_2CHOHR$. These would appear as the *t*-butylacetates. About 7% of such reduction took place with the ethyl Grignard solution. This is in contrast to the result of adding the acid chloride to the ethyl Grignard solution which gave no reduction.¹ The other three Grignard solutions gave about 20, 23, and 21%of the corresponding secondary alcohols as the *t*-butylacetates.

It is significant that these yields are nearly the same as those obtained by adding the acid chloride to an excess of the Grignard reagents.¹ As in the earlier experiments no trace of neopentylcarbinol or its ester was found even by extended searches. This is in contrast to the action of trimethylacetyl chloride which gives neopentyl alcohol in about 20% yields with *n*-propyl, *n*-butyl, and *n*-amyl Grignard reagents.²

A small amount of ethyl *t*-butylacetate was (1) No. I, Whitmore, Popkin, Whitaker, Mattil and Zech, THIS found in each of the four reactions. This was due apparently to interaction of the acid chloride with the solvent ether.

The Grignard solutions used were filtered from free magnesium under nitrogen pressure.

Experimental

The t-butylacetyl chloride, b. p. 76-77° at 140 mm., n^{20} D 1.4212, used in these reactions was prepared, in 86% yield, from t-butylacetic acid and thionyl chloride.

The Grignard compounds were prepared from the corresponding alkyl bromides, magnesium, and dry ether in the usual way. They were filtered and titrated.

Addition of Ethylmagnesium Bromide to t-Butylacetyl Chloride.—Ethylmagnesium bromide (1.84 moles in 1 liter of ether) was added to 250 g. (1.86 moles) of t-butylacetyl chloride in 1200 cc. of ether, during fifty minutes. After standing overnight, the complex was decomposed with ice, extracted with ether, and the products after removing most of the solvent using column XII³ were fractionated through column XI, using a solid carbon dioxide trap, to give: nos. 1–5, 71.4 g., b. p. 98–100° at 200 mm., n^{20} p 1.4150–1.4163; residue 130 g.; trap contents 68 g. All fractions contained water, indicating dehydration.

The trap contents with nos. 1–5 were refractionated through column XI to give: 6, 27.5 g., 35° at 736 mm., 1.3580; 7, 1.4 g., 133° , 1.4060; 8–12, 46.5 g., 143° , 1.4150–1.4160. The main residue was added and fractionation continued to give: 13–22, 101.2 g., 62–110° at 23–74 mm., 1.4120–1.4163; 23–24, 14.5 g., 118° at 23 mm., 1.4253–1.4263; 25–27, 15.7 g., 118–135° at 23 mm., 1.4323–1.4500; residue 5 g.

Fractions 6–22, 25–27, and the residue were again refractionated, by parts, through column XI to give: 28– 37, 123.2 g., 92° at 150 mm., 1.4130–1.4160; 38, 4.2 g., 105–134° at 150 mm., 1.4175; 39, 7.0 g., 134° at 150 mm., 1.4130; 40–43, 20.0 g., 124–166° at 90 mm., 1.4152– 1.4500; residue 6.2 g.

Fraction 7, ethyl t-butylacetate, was saponified by aqueous potassium hydroxide to give ethyl alcohol, 3,5-dinitrobenzoate, m. p. and mixed m. p. 92° ; and t-butylacetic acid, anilide, m. p. and mixed m. p. $130-131^{\circ}$.

Fractions 23, 24, and part of 25 represented a 7% yield of neopentylethylcarbinyl *t*-butylacetate. Alcoholic saponification gave neopentylethylcarbinol, previously reported,¹ b. p. 96° at 150 mm., n^{29} D 1.4248, 3,5-dinitrobenzoate, m. p. and mixed m. p. 81–82°; and *t*-butylacetic acid, anilide m. p. and mixed m. p. 130–131°.

Fractions 28–37 represented a 51% yield of ethyl neopentyl ketone, m. p. and mixed m. p. of the dinitrophenylhydrazone 135–136°.

The high index of fraction 38 appeared to be due to the

JOURNAL, **60**, 2462 (1938). (2) Whitmore and co-workers, *ibid.*, **60**, 2028, 2030, 2458, 2462, 2788 (1938).

⁽³⁾ The fractionating columns used have been described: Whitmore, Popkin, Whitaker, Mattil and Zech, *ibid.*, **60**, 2459 (1938).

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presence of diethylneopentylcarbinol or the corresponding olefins.¹

Fraction 39 contained *t*-butylacetic acid, m. p. and mixed m. p. of the anilide $130-131^{\circ}$.

All attempts to find neopentylcarbinol and neopentylcarbinyl *t*-butylacetate failed.

Addition of *n*-PropyImagnesium Bromide to *t*-ButyIacetyl Chloride.—The addition of 1.85 moles of *n*-propyImagnesium bromide, in 1 liter of ether, to 260 g. (1.94 moles) of *t*-butylacetyl chloride in 600 cc. of ether, was completed in forty-five minutes. The complex stood overnight and the products were isolated as above to give: 1-18, 166.3 g., b. p. $20-98^{\circ}$ at 11 mm., n^{20} D 1.4078– 1.4250-1.4147; 19-22, 45 g., $111-112^{\circ}$ at 13 mm., 1.4272-1.4181; 23-25, 7.5 g., $121-128^{\circ}$ at 13 mm., 1.4340-1.4442; residue 3.8 g.; trap contents 37 g.

The trap contents on removal of the ether yielded 5.7 g. of oil, n^{20} D 1.3985. This oil together with 1–18 was fractionated by parts through column X to give: 26–29, 14.9 g., 95–102° at 150 mm., 1.4032–1.4085; 30, 5.9 g., 107° at 150 mm., 1.4100; 31–32, 13.1 g., 109.5°, 1.4132–1.4140; 33, 4.8 g., 99–108°, 1.4105; 34–44, 83.5 g., 108–110°, 1.4132–1.4153; 45–47, 15.2 g., 51–58° at 7 mm., 1.4161–1.4273; 48–49, 7.9 g., 64–74° at 7 mm., 1.4315–1.4228; 50–51, 16.7 g., 78°, 1.4135–1.4122; residue 1 g.

Fractions 26–29 were identified as ethyl *t*-butylacetate. Aqueous saponification gave ethyl alcohol, 3,5-dinitrobenzoate m. p. and mixed m. p. 92°; and *t*-butylacetic acid, anilide m. p. and mixed m. p. 130–131°.

Fractions 31-32 and 34-44 were identified as neopentyl *n*-propyl ketone, semicarbazone m. p. and mixed m. p.⁴ $93-94^{\circ}$, yield 36.7%.

Fractions 47–49 contained dodecenes, as previously reported,¹ obtained by dehydration of the tertiary alcohol.

Fractions 50-51 were *t*-butylacetic acid, anilide m. p. and mixed m. p. $130-131^{\circ}$.

Fractions 19-22 represented a 20% yield of neopentyl*n*-propylcarbinyl *t*-butylacetate. Alcoholic saponification gave neopentyl-*n*-propylcarbinol,¹ b. p. 120-121° at 150 mm., n^{20} D 1.4270, m. p. and mixed m. p. of phenylurethan 80-82°; and *t*-butylacetic acid, m. p. and mixed m. p. of anilide 130-131°.

All attempts to find neopentylcarbinol and neopentylcarbinyl *t*-butylacetate failed.

Addition of *n*-Butylmagnesium Bromide to *t*-Butylacetyl Chloride.—The addition of 2.01 moles of *n*-butylmagnesium bromide, in 1 l. of dry ether, to 292 g. (2.18 moles) of *t*-butylacetyl chloride, in 600 cc. of ether, was completed in eighty minutes. After standing overnight the products were isolated to give: 1–18, 173.6 g., b. p. 34° at 742 mm. to 59° at 4 mm., n^{30} D 1.4070–1.4195; 19–23, 27.6 g., 68–95° at 4 mm., 1.4232–1.4415–1.4365; 24–29, 55.2 g., 98–99° at 4 mm., 1.4300–1.4315; 30, 6.1 g., 109° at 4 mm., 1.4430; residue 5.1 g.; trap contents 18.6 g.

The trap contents, on removal of ether, yielded 8.9 g. of oil. This and 1-18 were fractionated by parts through column X to give: 31-32, 2.7 g., 48-52° at 150 mm., 1.4332-1.4300; 33-38, 22.6 g., 63-102°, 1.4030-1.4098; 39-43, 38.6 g., 127°, 1.4192-1.4195; 44-49, 55.0 g., 126127°, 1.4182-1.4178; 50-53, 39.6 g., 130-134°, 1.4170-1.4150; 54-55, 8.0 g., 134-155° at 150 mm., 1.4270-1.4400; residue 2.0 g.

Fractions 33-38 were ethyl t-butylacetate.

Fractions 39-52 were identified as a mixture of neopentyl *n*-butyl ketone, m. p. and mixed m. p.⁵ of semicarbazone $82-84^{\circ}$, and *t*-butylacetic acid, anilide m. p. and mixed m. p. $130-131^{\circ}$; which contained 105.2 g. of the ketone and 28.0 g. of the acid, as determined from a composition—index of refraction curve. This represented a 34% yield of neopentyl *n*-butyl ketone.

The index of refraction of 20-23 corresponded to tetradecenes.¹

Fractions 24-29 with part of fraction 23 represented a 23% yield of neopentyl-*n*-butylcarbinyl *t*-butylcaretate. Alcoholic saponification gave neopentyl-*n*-butylcarbinol,¹ b. p. 92° at 100 mm., n^{20} D 1.4295-1.4305, phenylurethan m. p. and mixed m. p. 84-85°; and *t*-butylacetic acid, anilide m. p. and mixed m. p. 130-131°.

All attempts to identify neopentylcarbinol and its *t*butylacetate failed.

Addition of *n*-Amylmagnesium Bromide to *t*-Butylacetyl Chloride.—Addition of 1.9 moles of *n*-amyl Grignard solution to 271 g. (2 moles) of *t*-butylacetyl chloride in fifty minutes as above gave: 1-16, 161.7 g., 67-145° at 150 mm., n^{20} D 1.4240-1.4090-1.4235; 17-18, 21.8 g., 128-132° at 20 mm., 1.4342-1.4450; 19-22, 42.3 g., 133-144°, 1.4450; 23-27, 54.1 g., 146-147°, 1.4332-1.4350; 28, 7.1 g., 147°, 1.4412; residue 3 g.; trap contents 91 g.

The trap contents with fractions 1-17 gave: 29-30, 9.8 g., 65-90° at 150 mm., 1.4370-1.4210; 31-34, 45.1 g., 90-103°, 1.4060-1.4080; 35-42, 44.6 g., 103-134°, 1.4160-1.4140; 43-52, 76.3 g., 122-138°, 1.4212-1.4280; residue 1 g.

Fractions 31-34 were identified as ethyl t-butylacetate.

Fractions 35-42 were largely *t*-butylacetic acid, anilide m. p. and mixed m. p. $130-131^{\circ}$. The other component was identified as neopentyl *n*-amyl ketone, semicarbazone m. p. and mixed m. p. $99-102^{\circ}$.¹

Fractions 43-52 were largely neopentyl *n*-amyl ketone. This together with an estimate from fractions 35-42 represented a 29% yield of this ketone.

Fractions 19-22 were hexadecenes.¹

Fractions 23-27 represented a 21% yield of neopentyl*n*-amylcarbinyl *t*-butylacetate. Alcoholic saponification of 26-27 gave neopentyl-*n*-amylcarbinol,¹ b. p. 132° at 100 mm., n^{20} D 1.4340-1.4347, phenylurethan m. p. and mixed m. p. 62-63°; and *t*-butylacetic acid, anilide m. p. and mixed m. p. 130-131°.

All attempts to identify neopentylcarbinol and its *t*-butylacetate failed.

Preparation of Neopentylcarbinyl *t*-Butylacetate.—A solution of 0.8 mole of neopentylmagnesium chloride was prepared from neopentyl chloride, b. p. 82° at 740 mm., n^{29} D 1.4042. An excess of dry formaldehyde, generated by heating dry paraformaldehyde, was passed into the solution during four hours. The complex was decomposed with ice and 30% H₂SO₄ and fractionated through column X to give 48 g. (0.47 mole) of neopentylcarbinol, b. p. 140–146° at 739 mm., n^{29} D 1.4120–1.4034.

(5) Unpublished work of E. Rohrmann, this Laboratory.

⁽⁴⁾ This ketone and the semicarbazone prepared by H. C. Crafton, Jr., of this Laboratory.

Heating 22.2 g. (0.22 mole) of the above carbinol for two hours with 29 g. (0.2 mole) of *t*-butylacetyl chloride, b. p. 79° at 150 mm., n^{20} p 1.4215, and fractionation through column X gave: 1-2, 7.7 g., b. p. 78-140° at 150 mm., n^{20} p 1.4050-1.4190; 3-5, 22.2 g., 104° at 26 mm., 1.4198-1.4202; residue 4.8 g.

Fractions 3-5 represented a 57% yield of neopentylcarbinyl *t*-butylacetate. Saponification of 16.0 g. of this ester with alcoholic potassium hydroxide gave neopentylcarbinol, α -naphthylurethan m. p. and mixed m. p. 81-82°; and *t*-butylacetic acid, anilide m. p. and mixed m. p. 130-130.5°.

Preparation of Ethyl *t*-**Butylacetate**.—A mixture of 57.5 g. (0.54 mole) of *t*-butylacetic acid, n^{20} D 1.4096, 125 cc. of absolute ethyl alcohol, and 25 cc. of concd. sulfuric acid was refluxed fifteen hours. The mixture was dissolved in ether, washed with water and dilute potassium carbonate solution, dried over magnesium sulfate, and fractionated

through column X to give 60.1 g. or a 77% yield of ester of b. p. 102° at 740 mm., n²⁰D 1.4032-1.4040.

Summary

1. Ethyl, *n*-propyl, *n*-butyl, and *n*-amyl Grignard solutions, when added to a slight excess of *t*-butylacetyl chloride, gave ketones of the type $(CH_3)_3CCH_2COR$ in about 51, 37, 34, and 29% yields, respectively. They also gave esters of the type $(CH_3)_3CCH_2CHROCOCH_2C(CH_3)_3$. The latter were obtained in about 7, 20, 23, and 21% yields, respectively, from the four Grignard solutions.

2. Ethyl *t*-butylacetate and neopentylcarbinyl *t*-butylacetate have been prepared.

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Lactone Formation in the Addition Product of Maleic Anhydride and Bicyclohexenyl

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The addition of maleic anhydride to bicyclohexenyl takes place readily with the formation of $\Delta^{4a,5a}$ - dodecahydrophenanthrene - 9,10 - dicarboxylic acid anhydride (I).² During the course of the study of this compound, several reactions were noted which have a general bearing upon lactone formation of γ,δ -unsaturated acids. Linstead has demonstrated³ that the ease and direction of lactonization of aliphatic γ,δ -olefinic acids depend on the substituents on the δ carbon. The formation of a γ -lactone is favored if hydrogens, a δ -lactone if alkyl groups, are present. Lactonization is promoted by mineral acids and in some cases merely by heating the olefinic acids.

$$CH_{2}=CH-CH_{2}CH_{2}COOH \longrightarrow CH_{3}-CH-CH_{2}-CH_{2}-CO \longrightarrow CH_{3}-CH-CH_{2}-CH$$

When I or its anhydride (V) is esterified with absolute ethanol and hydrogen chloride, a monoethyl ester lactone (II) is obtained. Saponification of this compound gives a sodium salt of

(1) Portion of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry. an hydroxy acid (III) which on acidification results not in the hydroxy dibasic acid but in a lactone acid (IV). By the action of heat or acetic anhydride, I forms the anhydride (V) which upon treatment with cold sodium ethylate leads to an ester acid (VI). Hot sodium ethylate, however, results in a complicated reaction, the character of which was not determined. The ester acid (VI) can be hydrolyzed by boiling with dilute alkali to the dibasic acid (I). Heating I alone gives a mixture of anhydride (V) and lactone (IV).

Of significance is the fact that the action of bromine in carbon tetrachloride differentiates between the dibasic acid derivatives and the lactone acid derivatives. Thus, compounds I, V and VI absorb bromine while compounds II and IV do not.

As lactonization of one of the carboxyls results when I or V is esterified and no diethyl ester may be isolated, it is obvious that lactonization of the second carboxyl is the more rapid of the competing reactions. Lactonization also takes place merely by heating the acid (I) in acetone solution in presence of hydrochloric acid; lactone (IV) is formed.

The structures of the lactones obviously may be either those given in II and IV or the isomeric γ -lactones. Stereochemically the γ - or δ -lac-

⁽²⁾ Gruber and Adams, THIS JOURNAL. 57, 2555 (1935).

⁽³⁾ Linstead and others, J. Chem. Soc., 115 (1932); ibid., 557, 561, 568, 577, 580 (1933).