

acent to the carbonyl. Substitution on the beta carbon had no noticeable effect on the reactions of the carbonyl.

4. Vinyl triethylcarbinyl ketone gave only the addition reaction.

5. Substitution in the active methylene of a beta-diketone decreased the extent of both enolization and addition.

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## Grignard Reactions. XVII.<sup>1</sup> The Reactions of Esters and Acid Chlorides with Grignard Reagents

BY FRANK C. WHITMORE AND W. S. FORSTER<sup>2</sup>

In the course of the preparation of large amounts of diethyl-*t*-butylcarbinol, it was found that while ethylmagnesium bromide reacted with trimethylacetyl chloride to give 26% of this tertiary alcohol and 60% of the secondary alcohol, ethyl-*t*-butylcarbinol, the same reagent reacted with methyl trimethylacetate to give 78.5% of the tertiary alcohol and only 8.6% of the secondary alcohol.

TABLE I  
TRIMETHYLACETYL CHLORIDE-METHYL TRIMETHYL-  
ACETATE

Grignard reagent	Products <sup>a</sup>	Acid chloride	Ester
Ethyl	Ethyl- <i>t</i> -butylcarbinol	60	8.6
	Diethyl- <i>t</i> -butylcarbinol	26.1	76.5
<i>n</i> -Propyl	Neopentyl alcohol	20 <sup>b</sup>	0 <sup>c</sup>
	<i>n</i> -Propyl- <i>t</i> -butylcarbinol	76 <sup>b</sup>	48 <sup>c</sup>
	Di- <i>n</i> -propyl- <i>t</i> -butylcarbinol	0 <sup>b</sup>	40 <sup>c</sup>
Isopropyl	Neopentyl alcohol	23 <sup>b</sup>	0
	Isopropyl- <i>t</i> -butylcarbinol	53 <sup>b</sup>	44.8
<i>n</i> -Butyl	Neopentyl alcohol	28 <sup>b</sup>	0
	<i>n</i> -Butyl- <i>t</i> -butylcarbinol	71 <sup>b</sup>	40 <sup>c</sup>
	Di- <i>n</i> -butyl- <i>t</i> -butylcarbinol	0 <sup>b</sup>	50 <sup>c</sup>
Isobutyl	Neopentyl alcohol	61 <sup>b</sup>	0
	Isobutyl- <i>t</i> -butylcarbinol	26 <sup>b</sup>	25.7
	Isobutyl- <i>t</i> -butyl ketone	0	29.4
<i>t</i> -BUTYLACETYL CHLORIDE-METHYL <i>t</i> -BUTYLACETATE			
Ethyl	Diethylneopentylcarbinol	57.6 <sup>b</sup>	68.5
	Ethyl neopentyl ketone	0 <sup>b</sup>	5
<i>n</i> -Propyl	<i>n</i> -Propylneopentylcarbinol	24.4 <sup>b</sup>	20.4
	Di- <i>n</i> -propylneopentylcarbinol	57 <sup>b</sup>	61.8
	<i>n</i> -Propyl neopentyl ketone		7
Isopropyl	Isopropylneopentylcarbinol	26.7	16.1
	Isopropyl neopentyl ketone	32.7	55.3
<i>n</i> -Butyl	<i>n</i> -Butylneopentylcarbinol	20.5	0
	Di- <i>n</i> -butylneopentylcarbinol	9.9	71.4
	<i>n</i> -Butyl neopentyl ketone		trace
Isobutyl	Isobutylneopentylcarbinol	48.9	9.2
	Diisobutylneopentylcarbinol	13.8	34.2
	Isobutyl neopentyl ketone	20.1	32

<sup>a</sup> The percentage yields of products given by the acid chloride and the ester are listed under the respective headings.

(1) XVI, Whitmore and Lewis, *THIS JOURNAL*, **64**, 2964 (1942).  
(2) Present address: Calco Chemical Div., American Cyanamid Co., Bound Brook, New Jersey.

(3) Whitmore and co-workers, *THIS JOURNAL*, **60**, 2788 (1938).

(4) Leroide, *Ann. chim.*, **16**, 354-410 (1921).

(5) Whitmore and co-workers, *THIS JOURNAL*, **60**, 2462 (1938).

(6) Whitmore and Laughlin, *ibid.*, **56**, 1128 (1934).

(7) Whitmore and Randall, *ibid.*, **64**, 1242 (1942).

(8) Compare Whitmore and co-workers, *ibid.*, **63**, 643 (1941).

These results made desirable a comparison of the reactions of Grignard reagents with esters and with the chlorides of the corresponding acids. The results in Table I include those of this investigation as well as some from other work which completes the comparison.

Although use of the ester in place of the acid chloride decreased the amount of reduction product, it will be seen that structure is also a factor. When a normal Grignard reagent was used, the yield of tertiary alcohol from the ester was greater than from the acid chloride. However, methyl Grignard reagent with the methyl ester of methyl-*t*-butylneopentylacetic acid, beta-Butlerow's acid,<sup>6</sup> gave no reaction at 34° in diethyl ether or at 142° in di-*n*-butyl ether. This is in contrast to the reaction of the corresponding acid chloride which has been shown by Whitmore and Randall<sup>7</sup> to give a 90% yield of methyl methyl-*t*-butylneopentylcarbinyl ketone when treated with the methyl Grignard reagent. With trimethylacetyl chloride only methyl and ethyl Grignard reagents gave tertiary alcohols. With *t*-butylacetyl chloride only the primary reagents gave tertiary alcohols. Reduction to the primary alcohol fails with the primary *t*-butylacetyl chloride as compared with the tertiary trimethylacetyl chloride. It is significant that in no case was any primary alcohol found from the reaction of an ester with a Grignard reagent. This would indicate that aldehydes are not intermediates in the formation of secondary alcohols from esters.<sup>8</sup> This is in sharp contrast to the fact that trimethylacetyl chloride is reduced to neopentyl alcohol even by primary Grignard reagents in yields as high as 60%.<sup>3</sup> *t*-Butylacetyl chloride, however, gave no primary alcohol with the Grignard reagent.<sup>5</sup>

Dimethylethylacetyl chloride reacts with isopropylmagnesium bromide to give products corresponding in structure and yields to those given by trimethylacetyl chloride.<sup>3</sup> This lack of effect of a single ethyl group corresponds to the observations on the related methyl ketones.<sup>1</sup>

We thank Dr. W. A. Mosher of the Hercules Powder Company and R. S. George of this Laboratory for their help.

### Experimental

All Grignard reagents were prepared from the corresponding alkyl bromides in the usual manner.<sup>9</sup> The addition of the ester or acid chloride, unless specified, was carried out at room temperature; the rate of addition was about 1 mole per hour. The products were worked up by shaking with cracked ice, separating the ether and steam distilling the residues. The steam distillates were combined with the respective ether extracts. This method minimized any dehydration of the tertiary alcohols. After stripping off the ether, the products were fractionated through columns of 12-15 theoretical plates.

**Preparation of Materials.**—Trimethylacetic acid was obtained from the oxidation of triisobutylene with sodium dichromate and sulfuric acid.<sup>10</sup> The crude acids from the oxidation were dried and fractionated through a 12-plate column to give material of b. p. 93° (45 mm.). The pure acid was converted to the chloride by treatment with thionyl chloride at steam-bath temperature. The excess thionyl chloride was distilled off, and the crude chloride was fractionated through a 14-plate column to give an 80% yield of material with b. p. 57.6° (150 mm.) and  $n_D^{20}$  1.4121-2. The methyl ester was prepared from the acid chloride, either crude or fractionated, by the addition of methanol and subsequent distillation to give the ester, b. p. 99.5° (731 mm.),  $n_D^{20}$  1.3891-1.3900; the yield of ester was about 50% from the acid.

*t*-Butylacetyl chloride, b. p. 79.5° (165 mm.),  $n_D^{20}$  1.4210-6, was prepared from the acid in 84% yield by treatment with thionyl chloride. The crude acid chloride was refluxed with methanol; the product was washed with water and sodium bicarbonate solution and fractionated to give a 94% yield of ester, b. p. 128° (735 mm.),  $n_D^{20}$  1.3995-9.

Dimethylethylacetic acid was prepared by carbonating *t*-amyl Grignard reagent. The acid chloride, b. p. 129.8° (727 mm.),  $n_D^{20}$  1.4242-8, was obtained in 50% yield by refluxing with thionyl chloride.

**Reaction of Methyl Trimethylacetate with Ethylmagnesium Bromide.**—The reaction of 1.87 moles of methyl trimethylacetate with 4.5 moles of ethylmagnesium bromide gave 18.4 g. or 8.6% of ethyl-*t*-butylcarbinol,<sup>3</sup> b. p. 67° (55 mm.),  $n_D^{20}$  1.4223-32, and 196.2 g. or 76.5% of diethyl-*t*-butylcarbinol, b. p. 84° (40 mm.),  $n_D^{20}$  1.4410-26. No neopentyl alcohol was found.

**Reaction of Methyl Trimethylacetate with Isopropylmagnesium Bromide.**—The reaction of 1.5 moles of ester

with 4.5 moles of the Grignard reagent gave 34.2% of unreacted ester and 87.4 g. or 44.8% of isopropyl-*t*-butylcarbinol; b. p. 75.5° (53 mm.);  $n_D^{20}$  1.4268-92; phenylurethan m. p. and mixed m. p. 88-90°. No neopentyl alcohol could be detected.

**Reaction of Methyl Trimethylacetate with Isobutylmagnesium Bromide.**—The reaction of 0.5 mole of ester with 1.7 moles of the Grignard reagent gave 27.2% of unchanged ketone, 29.4% of isobutyl-*t*-butyl ketone, b. p. 70° (38 mm.),  $n_D^{20}$  1.4128-72, 2,4-dinitrophenylhydrazone m. p. and mixed m. p. 94-95°, and 25.7% of isobutyl-*t*-butylcarbinol, b. p. 74° (23 mm.), phenylurethan m. p. and mixed m. p. 114-115.5°. Isobutyl-*t*-butylcarbinol was oxidized to the corresponding ketone, 2,4-dinitrophenylhydrazone m. p. and mixed m. p. 94-95°, by treatment with sodium dichromate and sulfuric acid. No neopentyl alcohol was found.

**Reaction of Methyl *t*-Butylacetate with Ethylmagnesium Bromide.**—Addition of 1 mole of ester to 4 moles of the Grignard reagent gave 108.4 g. or 68.5% of diethylneopentylcarbinol, b. p. 54° (5 mm.),  $n_D^{20}$  1.4394-1.4403,  $d_{20}$  0.845, mol. ref. calcd. 49.6, found, 49.4; and 7.6 g. or 5% of ethyl neopentyl ketone, b. p. 75-80° (63 mm.),  $n_D^{20}$  1.4158-63, 2,4-dinitrophenylhydrazone m. p. and mixed m. p. 135-7°.

**Reaction of Methyl *t*-Butylacetate with *n*-Propylmagnesium Bromide.**—The reaction of 1 mole of ester with 4 moles of the Grignard reagent gave 10.6 g. or 7% of *n*-propyl neopentyl ketone, b. p. 42° (5 mm.),  $n_D^{20}$  1.4161-70, semicarbazone m. p. and mixed m. p. 93-5°, 29.3 g. or 20.4% of *n*-propylneopentylcarbinol, b. p. 47.5° (5 mm.),  $n_D^{20}$  1.4261-78, phenylurethan m. p. and mixed m. p. 81.5-82°, and 115 g. or 61.8% of di-*n*-propylneopentylcarbinol, b. p. 67° (3 mm.),  $n_D^{20}$  1.4423-8,  $d_{20}$  0.8386, mol. ref. calcd., 58.8; found, 58.9. There was no evidence of neopentylcarbinol.

**Reaction of Methyl *t*-Butylacetate with Isopropylmagnesium Bromide.**—The ester, 1 mole, was added to 4 moles of the Grignard reagent to give 78.6 g. or 55.3% of isopropyl neopentyl ketone, b. p. 107.2° (180 mm.),  $n_D^{20}$  1.4114-29, 2,4-dinitrophenylhydrazone m. p. 128-129°, semicarbazone m. p. and mixed m. p. 168-169° and 23.3 g. or 16.1% of isopropylneopentylcarbinol, b. p. 74.8° (25 mm.),  $n_D^{20}$  1.4286-95,  $d_{20}$  0.825, mol. ref. calcd., 45.0; found, 45.2,  $\alpha$ -naphthylurethan m. p. 88-90°.

*Anal.* Calcd. for C<sub>20</sub>H<sub>27</sub>O<sub>2</sub>N: N, 4.47. Found: N, 4.49.

**Reaction of Methyl *t*-Butylacetate with *n*-Butylmagnesium Bromide.**—The addition of 0.9 mole of ester to 3.6 moles of Grignard reagent gave 137.4 g. or 71.4% of di-*n*-butylneopentylcarbinol, b. p. 83° (3 mm.),  $n_D^{20}$  1.4462-9,  $d_{20}$  0.8403, mol. ref., calcd., 67.96; found, 67.8; a small amount of material believed to be *n*-butyl neopentyl ketone was obtained, semicarbazone m. p. 79-80°, but identification was not conclusive. No *n*-butylneopentylcarbinol was found.

**Reaction of Dimethylethylacetyl Chloride and Isopropylmagnesium Bromide.**—To 4.16 moles of Grignard reagent was added 1 mole of the acid chloride. The products were *t*-amylcarbinol, 30 g., 29.4%, b. p. 34.5° (7 mm.),  $n_D^{20}$  1.4208-12, phenylurethan m. p. and mixed m. p. 65-68°; isopropyl-*t*-amylcarbinol, 76 g., 49.3%, b. p. 52-3° (6.5 mm.),  $n_D^{20}$  1.4395-1.4400,  $d_{20}$  0.8489, mol. ref. calcd.,

(9) Greenwood, Whitmore and Crooks, THIS JOURNAL, 66, 2028 (1938).

(10) Unpublished work by C. S. Miner, Jr., in this Laboratory.

44.9; found, 45.0, phenylurethan m. p. 58–59°,  $\alpha$ -naphthylurethan m. p. 76.5–77.5°.

*Anal.* Calcd. for  $C_{20}H_{27}O_2N$ : N, 4.47. Found: N, 4.52.

**Reaction of Trimethylacetyl Chloride with Ethylmagnesium Bromide.**—The reaction of 2.54 moles of acid chloride with 6.1 moles of the Grignard reagent gave 26.1% of diethyl-*t*-butylcarbinol,<sup>3</sup> b. p. 59.2° (35 mm.),  $n_D^{20}$  1.4230 and 60% of ethyl-*t*-butylcarbinol,<sup>3</sup> b. p. 73° (24 mm.),  $n_D^{20}$  1.4424–6. No neopentyl alcohol was found.

**Reaction of *t*-Butylacetyl Chloride with Isopropylmagnesium Bromide.**—The reaction of 1 mole of acid chloride with 4 moles of Grignard reagent gave 32.7% of isopropyl neopentyl ketone, b. p. 61° (26 mm.),  $n_D^{20}$  1.4120–9, 2,4-dinitrophenylhydrazone m. p. 128–129°, semicarbazone m. p. and mixed m. p. 168–9° and 26.7% of isopropylneopentylcarbinol, b. p. 76.7° (32 mm.),  $n_D^{20}$  1.4283–1.4302,  $d_{20}$  0.825, mol. ref. calcd., 45.0; found, 45.2;  $\alpha$ -naphthylurethan m. p. 88–90°.

*Anal.* Calcd. for  $C_{20}H_{27}O_2N$ : N, 4.47. Found: N, 4.49.

**Attempted Reaction of the Methyl Ester of Methyl-*t*-butylneopentylacetic Acid with Methylmagnesium Bromide.**—The ester was made from methanol and the acid chloride<sup>6</sup> in 88% yield; b. p. 97–8° (13 mm.),  $n_D^{20}$  1.4450–2. The treatment of the ester with the Grignard reagent was carried out in diethyl ether at 34° and in *n*-butyl ether at 142°. The lower temperature gave almost quantitative recovery of unreacted ester. At 142° there were obtained a 70.3% recovery of unchanged ester and a 13% yield of methyl-*t*-butylneopentylacetic acid formed by the splitting of the ester.

**Reaction of *t*-Butylacetyl Chloride with Isobutylmagnesium Bromide.**—The reaction of 0.5 mole of the acid chloride with 1.45 moles of the Grignard reagent gave isobutyl neopentyl ketone, 15.7 g., 0.102 mole, 20.1%, b. p. 65.5° (15 mm.),  $n_D^{20}$  1.4127–91; isobutylneopentylcarbinol, 38.6 g., 0.244 mole, 48.9%, b. p. 75° (15 mm.),  $n_D^{20}$  1.4237–79,  $\alpha$ -naphthylurethan m. p. and mixed m. p.

100–100.5°; diisobutylneopentylcarbinol, 14.7 g., 0.069 mole, 13.8%, b. p. 68.5° (3 mm.),  $n_D^{20}$  1.4395–1.4410,  $d_{20}$  0.8317, mol. ref. calcd., 67.96; found, 68.0.

**Reaction of Methyl *t*-Butylacetate with Isobutylmagnesium Bromide.**—To isobutylmagnesium bromide prepared from 1.7 gram atoms of magnesium and 1.83 moles of isobutyl bromide was added 65 g., 0.5 mole, of the ester. Fractionation gave isobutyl neopentyl ketone, 32.1 g., 0.16 mole, 32%, b. p. 66.4° (15 mm.),  $n_D^{20}$  1.4120–98; isobutylneopentylcarbinol, 15.2 g., 0.046 mole, 9.2%, b. p. 43–44° (3 mm.),  $n_D^{20}$  1.4232–82,  $\alpha$ -naphthylurethan m. p. and mixed m. p. 99–101°; diisobutylneopentylcarbinol, 27.0 g., 0.17 mole, 34.2%, b. p. 69.5° (2 mm.),  $n_D^{20}$  1.4375–1.4411,  $d_{20}$  0.8313, mol. ref. calcd., 67.96; found, 68.0.

*Anal.* Calcd. for  $C_{21}H_{29}O_2N$ : N, 4.26. Found: N, 4.25.

### Summary

1. A comparison of the reactions of trimethylacetyl chloride and methyl trimethylacetate and of *t*-butylacetyl chloride and methyl *t*-butylacetate with ethyl, *n*-propyl, isopropyl, *n*-butyl and isobutyl Grignard reagents has been made. The esters were found to give distinctly less reduction products than the corresponding acid chlorides.

2. The fact that no primary alcohol was found in the reaction of the esters with Grignard reagents indicates that aldehydes are not intermediates in this reaction.

3. The methyl ester of methyl-*t*-butylneopentylacetic acid did not react with methyl Grignard reagent at 34° or at 142°.

4. Isopropylneopentylcarbinol and isopropyl-*t*-amylcarbinol have been prepared.

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## Grignard Reactions. XVIII.<sup>1</sup> Reactions of Benzylmagnesium Chloride

BY FRANK C. WHITMORE AND T. K. SLOAT<sup>2</sup>

The type of rearrangement given by the benzyl Grignard reagent is well known. The first case reported was the reaction of formaldehyde with benzylmagnesium chloride to give *o*-tolylcarbinol instead of the expected benzylcarbinol.<sup>3</sup> The action of a variety of substances with benzylmagnesium chloride has been reported. Not all reactants give rearranged products with this Grignard reagent. The products of rearrangement are

usually *o*-tolyl derivatives. In some cases the *p*-tolyl derivative has been reported.<sup>4</sup> Excellent investigations and reviews of the reactions of benzylmagnesium chloride have been made by Gilman and Kirby<sup>5</sup> and by Austin and Johnson.<sup>6</sup> More recently Coleman and Forrester<sup>7</sup> have investigated the action of benzylmagnesium chloride with monochloramine. No rearranged products were found in this case.

(1) XVII, Whitmore and Forster, *THIS JOURNAL*, **64**, 2966 (1942).

(2) Present address: Research Division, Westinghouse Electric and Manufacturing Co., East Pittsburgh, Pa.

(3) Tiffeneau and Delange, *Compt. rend.*, **137**, 573 (1903).

(4) Gilman and Kirby, *THIS JOURNAL*, **51**, 3475 (1929).

(5) Gilman and Kirby, *ibid.*, **54**, 345 (1932).

(6) Austin and Johnson, *ibid.*, **54**, 647 (1932).

(7) Coleman and Forrester, *ibid.*, **58**, 27 (1936).