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The Reducing Action of Primary Grignard Reagents with Trimethylacetyl Chloride

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Recent studies have been made of the reducing action of Grignard compounds on acid chlorides.[1]

In the present work, the preparation of a series of secondary carbinols, for use in subsequent rearrangement studies, involved the addition of trimethylacetyl chloride to various primary Grignard reagents. The results, tabulated below, are in accord with previous reduction studies in this Laboratory.

Grignard reagent	% Yield of reduction products $(CH_3)_3CCH_2OH$	$(CH_3)_3CHOHR$
Ethyl[2]	None	69
n-Propyl	20	76
Isopropyl	23	53
n-Butyl[3]	28	71
Isobutyl	61	26
n-Amyl	20	75
Isoamyl[4]	15	71

The reduction of trimethylacetyl chloride to trimethylcarbinol by each of the Grignard reagents except ethyl is in sharp contrast to the failure to reduce *t*-butylacetyl chloride to neopentylcarbinol even by a tertiary Grignard reagent.[1] The obvious explanation that the reduction depends on the attachment of a tertiary group directly to the COCl group is unsound since *n*- and isobutyryl chlorides are reduced to the primary alcohols in 20 and 9% yields by *t*-butylmagnesium chloride.[1]

In these reactions, trimethylacetyl chloride was added to an excess of Grignard reagent. It has since been found that the reverse addition of a primary Grignard reagent to an excess of trimethylacetyl chloride produces carbinols in the form of the corresponding esters, with a marked change in the yield of reduction products. This is being investigated further.

Grignard solutions used in this study were filtered.

Experimental

The columns used were of the total condensation variable take-off type packed with single-turn glass helices. The dimensions (cm.) are of the packed portions: Column I, 45 × 0.9; II, 35 × 1.1; III, 43 × 0.5; IV, 67 × 1.3; V, 75 × 1.2.

Addition of Trimethylacetyl Chloride to Ethylmagnesium Bromide.—The ethylmagnesium bromide was prepared from 545 g. (5 moles) of ethyl bromide, b. p. 36° at 730 mm., n^{20}_{D} 1.4240, 121.5 g. (5 moles) magnesium and 900 cc. of dry ether. Addition of 181.5 g. (1.5 moles) of trimethylacetyl chloride, b. p. 57.6° at 150 mm., n^{20}_{D} 1.4125, prepared in 84% yield from thionyl chloride and trimethylacetic acid, required two and one-half hours for completion. The complex was then decomposed with ice, extracted with ether, and after removal of ether through column IV was fractionated through column I to give fractions: 1–3, 31.9 g. ether, b. p. 34–35° at 732 mm., n^{20}_{D} 1.3532; 4–5, 12.4 g., 50–130.5°, 1.4026–1.4205; 6, 14.6 g., 130.5–133°, 1.4218; 7–11, ethyl-*t*-butylcarbinol, 75.4 g., 133–134° at 732 mm., 1.4223–1.4225; 12, 9.8 g., 85–114° at 150 mm., 1.4292; 13–15, diethyl-*t*-butylcarbinol, 43.5 g., 114.5° at 150 mm., 1.4424–1.4427; residue 10 g.

Cut 4 on refractionation through column III gave: 16, 0.5 g., b. p. 33.5–60° at 735 mm., n^{20}_{D} 1.3696; 17, 1.5 g., 60–75°, 1.4057; 18, 1.1 g., 75–110°, 1.3825; 19, 0.6 g., 110°, 1.4142; residue 0.8 g. No indication of neopentyl alcohol could be found. The identity of fractions 6–13 was proved by m. p. and mixed m. p. of 109–110° for the α-naphthylurethan of ethyl-*t*-butylcarbinol. Fractions 13–15 were diethyl-*t*-butylcarbinol, b. p. 114.5° at 150 mm., n^{20}_{D} 1.4424, d^{20}_{4} 0.8524, in agreement with the constants given by Nasarow.[5]

Fraction 17 contained ethyl alcohol as shown by the m. p. and mixed m. p. of the 3,5-dinitrobenzoate, 93–94°.

Addition of Trimethylacetyl Chloride to *n*-Propylmagnesium Bromide.—The addition of 181.5 g. (1.5 moles) of trimethylacetyl chloride to 4.5 moles of *n*-propylmagnesium bromide in 1900 cc. of dry ether was completed in eighty minutes. The complex was decomposed with ice, extracted with ether, and the solvent removed through column IV. The product was then fractionated through column I to give: fractions 1–4, 59.8 g. ether, b. p. 32.5–42.0° at 739 mm., n^{20}_{D} 1.3529–1.3531; 5–7, 8.9 g., 45.0–107°, 1.3821–1.3953; 8, 3.2 g., 107–110°, 1.4010; 9–12, 24.1 g., 66.5–104° at 150 mm., m. p. 50°; 13–15, 19.0 g., 104–105.5° at 150 mm., 1.4245–1.4260; 16–20, 114.0 g., 105.5–106.5° at 150 mm., 1.4270–1.4276; residue 6.4 g.

Fractions 5–7 contained *n*-propyl alcohol as identified by the 3,5-dinitrobenzoate, m. p. and mixed m. p. 73–74°.

Fractions 8–12 were neopentyl alcohol, phenylurethan, m. p. and mixed m. p. 113–114°.

Fractions 13–20 were *n*-propyl-*t*-butylcarbinol, phenylurethan, m. p. and mixed m. p. 70.5–71.5°.

Addition of Trimethylacetyl Chloride to Isopropylmagnesium Bromide.—The addition of 181.5 g. (1.5 moles) of trimethylacetyl chloride to 4.5 moles of isopropylmagnesium bromide in 900 cc. of dry ether required three

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(1) Greenwood, Whitmore and Crooks, THIS JOURNAL, 60, 2028 (1938); Whitmore and co-workers, *ibid.*, **60**, 2030, 2458, 2462 (1938).

(2) A 20% yield of diethyl-*t*-butylcarbinol was formed as the high boiling fraction.

(3) Yields in this reaction checked with those previously reported.[1]

(4) 7% of olefin, corresponding to the dehydrated tertiary carbinol was also found.

(5) Nasarow, *Ber.*, **69**, 21–24 (1936).

hours. The product was decomposed and extracted in the usual manner and fractionated through column V to give: fractions 1, ether, b. p. 35–36° at 743 mm., n^{20}D 1.3535; 2–7, 9.6 g., 43–99°, 1.3574–1.3840; 8–12, 30.3 g., 111° at 743 mm. and 73–75° at 150 mm., m. p. 50°; 13–14, 5.9 g., 81–96° at 150 mm., 1.4108–1.4212; 15–16, 11.6 g., 98–100° at 150 mm., 1.4277–1.4285; 17–25, 93.5 g., 100° at 150 mm., 1.4290–1.4295; residue 8.2 g.

Fractions 4–6 contained isopropyl alcohol as identified by the phenylurethan, m. p. and mixed m. p. 89–90°.

Fractions 8–12 were neopentyl alcohol, phenylurethan, m. p. and mixed m. p. 113–114°.

Fractions 15–25 were isopropyl-*t*-butylcarbinol, phenylurethan, m. p. and mixed m. p. 86–86.5°.

Addition of Trimethylacetyl Chloride to Isobutylmagnesium Bromide.—Addition of 181.5 g. (1.5 moles) of trimethylacetyl chloride to 4.5 moles of isobutylmagnesium bromide was completed in three hours. The complex was decomposed and extracted in the usual manner and fractionated through column V to give: fractions 1, ether, b. p. 34–35° at 735 mm., n^{20}D 1.3535; 2–9, 13.3 g., 52–104°, 1.3574–1.3952; 9–18, 81.4 g., 106–111 and 76° at 150 mm., m. p. 50°; 19–20, 3.2 g., b. p. 100–109° at 150 mm., 1.4131–1.4212; 21–22, 12.2 g., 110–111° at 150 mm., 1.4270–1.4293; 23–27, 43.2 g., 111–112° at 150 mm., 1.4299–1.4302; residue 5.8 g.

Fractions 5–8, 7.8 g., contained isobutyl alcohol, phenylurethan, m. p. and mixed m. p. 83–84°.

Fractions 9–18 were neopentyl alcohol, phenylurethan, m. p. and mixed m. p. 113–114°.

Fractions 21–27 were isobutyl-*t*-butylcarbinol, phenylurethan, m. p. and mixed m. p. 112–112.5°, α-naphthylurethan, m. p. and mixed m. p. 103.5–104.5°.

Addition of Trimethylacetyl Chloride to *n*-Amylmagnesium Bromide.—The addition of 181.5 g. (1.5 moles) of trimethylacetyl chloride to 4.5 moles of *n*-amylmagnesium bromide in 1900 cc., of dry ether was completed in two hours. The complex obtained was decomposed with ice, extracted with ether, the solvent being removed through column IV and the product on fractionation through column II gave: fraction 1–2, 17.5 g. ether, b. p. 32–55.0° at 741 mm., n^{20}D 1.3535–1.3545; 3–5, 26.9 g., 55–127.0°, solid; 6, 9.6 g., 127.0–176.5°, 1.4171; 7, 4.7 g., 39–61.5° at 18 mm., 1.4340–1.4342; 8–13, 22.1 g., 61.5–86.0° at 18 mm., 1.4176–1.4332; 14–17, 77.7 g., *n*-amyl-*t*-butylcarbinol, 86.0–88.0° at 18 mm., 1.4340–1.4342; 18–19, 62.3 g., b. p. 85–89° at 17 mm., 1.4345–1.4346; 20–23, 10.2 g., 85.0–134.0° at 14 mm., 1.4360–1.4484; residue 6.8 g.

Fractions 3–5 were neopentyl alcohol, identified by the phenylurethan, m. p. and mixed m. p. 113–114°.

Fractions 6–7 failed to produce any evidence of *n*-amyl alcohol. This fraction is probably a mixture of neopentyl alcohol, *n*-amyl alcohol, and the secondary alcohol (*n*-amyl-*t*-butylcarbinol).

Fractions 8–13 and 18–23 on refractionation through column I gave: fractions 24–25, 13.1 g., b. p. 42–67.8° at 7 mm., n^{20}D 1.4199–1.4294; 26–30, 56.4 g., 67.8–72.5° at 7 mm., 1.4336–1.4348; residue 4.4 g.

Fractions 14–17 and 26–30 were *n*-amyl-*t*-butylcarbinol: *MR* found 49.80, calcd. 49.92.

Addition of Trimethylacetyl Chloride to Isoamylmagnesium Bromide.—The addition of 181.5 g. (1.5 moles) of trimethylacetyl chloride to 4.5 moles of isoamylmagnesium bromide required two hours. The complex was decomposed and extracted in the usual manner and fractionated through column I, to give: fractions 1–3, 25.3 g., ether, b. p. 34–35° at 742 mm., n^{20}D 1.3535; 4–7, 26.8 g., 84–113° and 62–81.5° (150 mm.), 1.4000–1.4047; 8–12, 31.6 g., 81.5–128° at 150 mm., 1.4060–1.4130; 13–15, 50 g., 128–133.2° at 150 mm., 1.4284–1.4319; 16–18, isoamyl-*t*-butylcarbinol, 80.3 g., 133.2–133.5° at 150 mm., 1.4320–1.4323; 19–20, 31.9 g., 133.5–134° at 150 mm., 1.4325; 21–22, 24.4 g., 99–108° at 18 mm., 1.4407–1.4410; residue 1.6 g.

Fractions 4–7 were refractionated through column III to give: fractions 23–27, 3.4 g., b. p. 33–107° at 735 mm., n^{20}D 1.3540–1.4080; 28–29, 20.5 g., 107–126°, solid; residue 2.2 g.

Fractions 8–12 were refractionated through column III to give: fractions 30–32, 8.4 g., b. p. 73–101 at 150 mm., n^{20}D 1.4072–1.4080; 33–37, 14.2 g., 101–105.5° at 150 mm., 1.4098–1.4100; residue 1.7 g.

Fractions 30–32 contained isoamyl alcohol, phenylurethan, m. p. and mixed m. p. 54°.

Fractions 28–29 were neopentyl alcohol, phenylurethan, m. p. and mixed m. p. 113–114°.

Fractions 33–37 were olefins formed by the dehydration of isoamyl-*t*-butylcarbinol, d^{20}_4 0.7278; *MR* calcd. 47.43; found 47.37.

Fractions 13–20 were isoamyl-*t*-butylcarbinol d^{20}_4 0.8236; *MR* calcd. 49.92, found 49.74.

Fractions 21–22 were olefins from the dehydration of diisoamyl-*t*-butylcarbinol, d^{20}_4 0.7772; *MR* calcd. 71.03, found 71.34.

Summary

1. The reducing action of Grignard reagents with acid chlorides has been studied further by the addition of trimethylacetyl chloride to the Grignard reagents of ethyl, *n*- and isopropyl, *n*- and isobutyl and *n*- and isoamyl.

2. Neopentyl alcohol was obtained with all except the ethylmagnesium bromide. Even the latter gave reduction as represented by a 68% yield of ethyl-*t*-butylcarbinol.

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