

Fraction B 1 gave dibenzalacetone, m. p. 110°. The m. p. of a mixture with the known substance was 109°. Fraction B 3 gave the 2,4-dinitrophenylhydrazone of trimethylacetaldehyde, m. p. 210°, mixed m. p. 210°. Fraction B 7 gave the amide of trimethylacetic acid, m. p. 153°, mixed m. p. 151°. Most of this acid product was obtained from the acidification of the decomposition mixture. No semicarbazone could be obtained from Fraction B 5.

The high-boiling diisobutylene thus gave yields of acetone, trimethylacetaldehyde and trimethylacetic acid of 81.3, 13.2 and 21.5%, respectively, thus proving it to be 2,4,4-trimethylpentene-2. The absence of formaldehyde and methyl neopentyl ketone among the ozonolysis products showed the completeness of the separation from the low-boiling isomer.

Summary

1. The low-boiling and high-boiling isomers of diisobutylene have been proved to be 2,4,4-trimethylpentene-1 and 2,4,4-trimethylpentene-2, respectively.

2. The completeness of the separation of these isomers is confirmed by the fact that neither gives ozonolysis products which would be expected from the other.

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THE DEHYDRATION OF SECONDARY CARBINOLS CONTAINING A NEOPENTYL SYSTEM. I. ISOPROPYL-*TERT.*-BUTYLCARBINOL. PRELIMINARY PAPER¹

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The dehydration of this carbinol was studied because it presents three possibilities.² (1) Normal dehydration by the removal of the secondary hydroxyl and the tertiary hydrogen, similar to the dehydration of methylisopropylcarbinol to give trimethylethylene, would produce the higher boiling di-isobutylene, 2,4,4-trimethylpentene-2, which has been thoroughly characterized in this Laboratory.³ (2) A shift of the tertiary hydrogen would give an organic "ion"⁴ related to the two di-isobutylenes. This would be expected to lose a proton to give these two substances in the ratio of 4:1, the lower boiling isomer, 2,4,4-trimethylpentene-1, predominant.

¹ Presented by A. L. Houk in partial fulfillment of the requirements for the degree of Ph.D. at the Pennsylvania State College.

² This carbinol was prepared and dehydrated at Northwestern University in 1928 by H. C. Benedict, Jr. No definite knowledge of the resulting olefins was then obtained because of the inadequacy of the distillation equipment available; *cf.* Fenske, Quiggle and Tongberg, *Ind. Eng. Chem.*, **24**, 408 (1932).

³ See preceding article.

⁴ See *ibid.*, p. 3274.

ing.⁵ (3) The shift of a methyl group from the neopentyl system would give an "ion" related to the 2,3,4-trimethylpentenes. Thus at least five different octylenes could be formed from the carbinol by known reactions.

At the time the present study of this carbinol was undertaken (1930), the current conception of alcohol rearrangements in this Laboratory followed the ideas of Meerwein⁶ in regarding a true ionization of an acid derivative as the first step in such processes. It was argued, therefore, that a "dehydration" of the carbinol in the absence of acid and ionizing conditions might prevent rearrangement. The method used was to heat the Grignard complex (alcoholate) obtained from *tert.*-butylmagnesium chloride and isobutyraldehyde. Preliminary experiments showed that olefins could be thus formed by the elimination of XMgOH from similar Grignard products. It was expected, then, that the product would be the higher boiling diisobutylene, 2,4,4-trimethylpentene-2. Such was not the case. Decomposition of the Grignard complex of isopropyl-*tert.*-butylcarbinol by heat gave essentially the same complex mixture of olefins that was obtained from the carbinol by ordinary dehydration with sulfuric acid. None of the normal dehydration product was obtained in either case. It was thus concluded that the organic "ion" first formed was the same in both cases and did not depend on any ordinary process of ionization but was the result of the breaking of the $:\ddot{\text{C}}:\ddot{\text{O}}:$ linkage with the complete octet going with the oxygen atom, thus leaving the carbon with only six electrons.⁷

Isopropyl-*tert.*-butylcarbinol has been prepared by Faworsky⁸ and by Conant and Blatt⁹ from *tert.*-butylmagnesium chloride and isobutyraldehyde and by Haller and Bauer¹⁰ by the reduction of pentamethylacetone with sodium and alcohol.

About two liters of the olefin mixture obtained from the Grignard complex was twice distilled through a 52-ft. adiabatic column using a reflux ratio of about 50:1.¹¹ Most of the material boiled above 105° and consequently could contain none of the di-isobutylenes. Moreover, the refractive indices of the fractions did not correspond to these substances. About 400 cc. distilled below 105° and had n_D^{20} 1.4070 to 1.4118. Repeated distillations through the 90 × 1.2 cm. adiabatic, partial condensation column¹² failed to give any fraction having the properties of 2,4,4-trimethylpentene-2 (b. p. 103.4° (737 mm.), n_D^{20} 1.4158). The only indication of a

⁵ Unpublished results of S. N. Wrenn in this Laboratory.

⁶ See THIS JOURNAL, p. 3277.

⁷ See *ibid.*, p. 3278.

⁸ Faworsky, *J. prakt. Chem.*, [2] **88**, 651 (1913).

⁹ Blatt, THIS JOURNAL, **51**, 1227 (1929).

¹⁰ Haller and Bauer, *Ann. chim. phys.*, [8] **29**, 317 (1913).

¹¹ For description of the column and its operation, see Fenske and co-workers, *Ind. Eng. Chem.*, **24**, 408 (1932).

¹² See THIS JOURNAL, p. 3453.

homogeneous fraction was obtained with b. p. 92–93° (730 mm.) and n_D^{20} 1.4060. Since these properties corresponded to no probable product it was assumed to be an azeotropic mixture. It was mixed with pure tertiary butyl alcohol and fractionated. The main fractions were washed with water to remove the alcohol, dried and distilled. The product had a b. p. of 101.5° (738 mm.) and n_D^{20} 1.4084 corresponding to the properties of the lower di-isobutylene, 2,4,4-trimethylpentene-1 (b. p. 100.1° (737 mm.), n_D^{20} 1.4082). The original two liters of olefin mixture contained less than 150 cc. of this azeotropic mixture which in turn contained less than 100 cc. of the 2,4,4-trimethylpentene-1. The other olefins have not been identified. No trace of the normal dehydration product has been obtained.

Experimental

Preparation of the Grignard Complex, $(\text{CH}_3)_3\text{CCH}(\text{OMgCl})\text{CH}(\text{CH}_3)_2$.—This was done in 6–8 mole runs. A typical 6-mole run was as follows. To 144 g. of freshly turned magnesium in a 3-liter flask equipped with a stirrer, a reflux condenser and a dropping funnel, were added a crystal of iodine and then 20–25 cc. of a solution of 555 g. of *tert.*-butyl chloride in 750 cc. of dry ether. As soon as the reaction began, 300 cc. of dry ether was added, the stirrer was started and 750 cc. of the halide solution was added at such a rate as to maintain gentle refluxing. The remainder of the halide solution was diluted with 450 cc. of dry ether and added similarly. The solution was then heated for one hour on a steam-bath. Titration of a sample showed a yield of 85% of Grignard reagent.¹³ The solution was cooled to 15° and a solution of 327 g. of isobutyraldehyde in an equal volume of dry ether was added at such a rate as to cause gentle refluxing. The mixture was warmed with stirring on a water-bath for three hours.

Decomposition of the Grignard Complex by Heat.—The material from one run was placed in two 1-liter distilling flasks provided with thermometers and heated in baths of copper shot. After gradual heating to remove the ether, the baths were heated slowly to the full heat of a large Méker burner. The baths were then at 350–400°. The highest boiling point registered by the distilling products was 140°. The fraction collected contained much ether. It was highly unsaturated.

Fractionation of the Olefin Mixture.—The combined products from runs starting with a total of 48 moles of *tert.*-butyl chloride were fractionated through the 52 ft. column.¹¹

After the ether had been removed, the following fractions were obtained.

Fraction	Pressure	B. p., °C.	Amt., cc.	n_D^{20}
A 1, 1a, 1b	724	49–94	500	1.3880–1.4077
2–12	728	94–105.4	370	1.4081–1.4118
13–40	735	105.4–129.4	600	1.4120–1.4259
41, 44	740	129.4–135	100	1.4259–1.4140

No cuts were obtained having the boiling point and refractive index for any known octylene. Fractions A 2–4 were distilled through the 90 × 1.2 cm., *partial condensation* column¹⁴ at 730 mm.

¹³ This method of making the *tert.*-butyl Grignard reagent is due to A. R. Lux of this Laboratory. It gives somewhat better yields than the ordinary method.

¹⁴ See THIS JOURNAL, p. 3453.

Fraction	B. p., °C.	Amt., cc.	n_D^{20}
B 1-3	81-91	16	1.4020-1.4061
4-8	91-93	40	1.4052-1.4054
9-16	93-103.2	40	1.4076-1.4112

Fractions B 6-7 were mixed with 20 cc. of *tert.*-butyl alcohol (m. p. 23°) and distilled through a 70 × 1.2 cm. indented, adiabatic, total condensation column¹⁵ at 738 mm.

Fraction	B. p., °C.	After washing with water and drying		B. p. (Cottrell), cc.	n_D^{20}
		Amt., cc.	Amt., cc.		
C 1	72-76	1.5	0		
2-6	78-82	26	11	101.5 (738 mm.)	1.4084
7	82-87	2	1.3		1.4095
8	Residue	6	2		1.4032

Fractions C 2-6 thus had the correct boiling point and refractive index for 2,4,4-trimethylpentene-1,¹⁶ a rearranged product.

Fractions A 8-10 were distilled through the 90 × 1.2 cm. partial condensation column at 727 mm.

Fraction	B. p., °C.	Amt., cc.	n_D^{20}
D 1-4	85-96	21	1.4012-1.4052
5-19	101-104.4	91.	1.4080-1.4120

No fraction having the properties of a diisobutylene was obtained.

Dehydration of Isopropyl-*tert.*-butylcarbinol by Sulfuric Acid.—Two runs of the Grignard product from a total of 12.2 moles of isobutyraldehyde were decomposed with ammonium chloride solution in the usual way. The product consisted of a 35% yield of the carbinol, b. p. 148-150° (740 mm.), n_D^{20} 1.4288, a similar yield of isobutyl alcohol and a 7.5% yield of a solid material which melted at 51-52° after crystallization from petroleum ether. A 1.5% yield of hexamethylethane was also isolated.

A mixture of 117 g. of the carbinol and 5.5 cc. of concd. sulfuric acid was heated under a 40 × 1.8 cm. column until olefin began to distil. The pressure was then reduced slightly and the olefin and water were distilled as fast as formed. When half the calculated amount of water had distilled, the process was stopped, the residue was washed with potassium carbonate solution and added to the distillate. After drying, the product was distilled through the 70 × 1.2 cm. column. The boiling points of 15 fractions ranged from 100 to 148° and the refractive indices from 1.4076 to 1.4288. Two similar dehydrations and distillations were carried out. The average distribution of the products in the three runs was as follows.

Per cent.	B. p., °C.	n_D^{20}
4.5	100-105	1.4076-1.4153
45	105-114	1.4146-1.4254
50	114-148	1.4222-1.4288

As with the product from thermal decomposition of the Grignard complex, no fraction was obtained having the boiling point and refractive index of the normal dehydration product.

Finally, all the remaining fractions boiling up to 120° from the first distillation through the 52 ft. column were combined and distilled once more through that column at 724 mm.

¹⁵ See THIS JOURNAL, p. 3451.

¹⁶ See preceding article.

Fraction	B. p., °C.	Amt., cc.	n_D^{20}
E 1-10	64-90	470	1.3990-1.4066
11-13	94-104.4	185	1.4096-1.4112
14-22	104.4-112.9	335	1.4122-1.4210

Again, no fraction was obtained having the properties of 2,4,4-trimethylpentene-2. This study is being continued.

Summary

1. Isopropyl-*tert.*-butylcarbinol presents a variety of possible dehydrations.
2. None of the normal dehydration product has been obtained either by dehydration of the carbinol or by thermal decomposition of the Grignard complex from which it is prepared.
3. About 5% of 2,4,4-trimethylpentene-1 has been isolated from the complex olefin mixture.
4. The study of the other dehydration products of the carbinol is being continued.

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SOME DERIVATIVES OF DIODOTYROSINE AND THYROXINE. THE ACTION OF ACETIC ANHYDRIDE ON DIODOTYROSINE¹

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The methyl ethers of diiodotyrosine and thyroxine were prepared for a study of their physiologic activity. In general, the procedure used by Karrer³ for the preparation of *O*-methyl-*l*-tyrosine was followed. The color reaction with nitrous acid, described by Kendall,⁴ which depends on the presence of two iodine atoms ortho to a free hydroxyl group, was conveniently used to determine the completion of the methylation. The spontaneous decomposition of acetylthyroxine, observed by Kendall,⁴ which occurs when an aqueous solution of the sodium salt is neutralized, presented some difficulty. This was overcome by performing this step in the procedure in 80% alcohol.

In connection with the synthesis of the methyl ether of diiodotyrosine, it was necessary to establish the identity of *N*-acetyldiiodotyrosine. The levo form of this derivative was obtained by treating the sodium salt of di-

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³ Karrer, *Helv. Chim. Acta*, 5, 469 (1922).

⁴ Kendall, "Thyroxine," Chemical Catalog Co., New York, 1929.