Anal. Calcd. for $C_{10}H_{15}ON \cdot HCl$: Cl, 17.59; N, 6.95. Found: Cl (as AgCl), 17.49, 17.62; N (Kjeldahl), 7.04.

The free base, isolated as was phenylpropanolamine, melted at 112°.

Anal. Calcd. for $C_{10}H_{15}ON$: N, 8.48. Found: N (Kjeldahl), 8.53, 8.63.

Deamination.—A solution was prepared of 6 g. of *p*-tolylpropanolamine hydrochloride (0.03 mole) in 200 cc. of water and 15 cc. of acetic acid; it was cooled to 7° and to it was slowly added a solution of 6.2 g. of sodium nitrite (0.09 mole) in 35 cc. of water; the mixture was allowed to stand at room temperature for twenty-four hours, was neutralized with sodium carbonate and extracted with ether. From about one-third of the extract the ether was allowed to evaporate spontaneously and the residue was treated in the regular way to form semicarbazone; there was no evidence of its formation. The remainder of the ethereal solution was dried and distilled. The high-boiling product formed a semicarbazone melting at 191°; mixed with known semicarbazone of *p*-tolylethyl ketone there was no change in the melting point.

Phenylpropanolamine was deaminated under similar conditions. From a fourth of the ethereal extract the ether was evaporated on the steam-bath; the residue formed no semicarbazone. From a second fourth the ether was evaporated, the residue heated to boiling but not distilled and treated to form semicarbazone; after standing for ten days a very small yield of crystals was obtained, insufficient to recrystallize. The remainder of the ethereal solution was distilled; that boiling at 210–220° formed a semicarbazone that melted at 177.5°, the semicarbazone of propiophenone.

Thus it appears that the deaminated product must be distilled before it will form a semicarbazone.

Summary

1. Phenylpropanolamine and *p*-tolylpropanolamine have been prepared by reducing the appropriate isonitroso ketones catalytically.

2. The method appears to be of general application and is being extended.

3. The two compounds discussed show physiological activity paralleling that of ephedrine. Further pharmacological studies are being made.

BALTIMORE, MARYLAND

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 30]

THE ALIPHATIC DIOLEFINS. II. THE PREPARATION AND SOME PHYSICAL CONSTANTS OF Δ-1,5-HEXADIENE

BY FRANK CORTESE[1]

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In connection with some previous work on Δ-1,5-hexadiene,[2] it was noticed that great confusion existed among the physical constants recorded in the literature. Accordingly, the hydrocarbon was made from two different sources and the following accurate concordant constants were determined: boiling point, dt/dp, melting point, density and refractive index.

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[2] Cortese, *Ber.*, **62**, 504 (1929).

Δ-1,5-Hexadiene, or diallyl, has been made by the following methods: by the action of sodium,[3] or sodium–tin alloy,[4] on allyl iodide; by the dry distillation of allyl mercuric iodide[5,6]; from allyl bromide, sodium and a few drops of alcohol (anhydrous ether was also a catalyst); from allyl iodide, zinc and a little formic ether[7] or ether;[8] from allyl iodide, aluminum and ether;[9] from 1,2,3-tribromopropane, magnesium and ether.[10] Almost all workers mention that the existing methods give poor yields and a poor quality of product. Undoubtedly this is due to the fact that specific directions are not given, for one worker will get a very low yield with a method which gave a good yield to another worker.

We have adopted the convenient method of causing allyl bromide to react with magnesium in the presence of ether.[11] This is an abnormal Grignard reaction, the magnesium seemingly acting as a coupling agent.[12]

Experimental Part

Preparation of Δ-1,5-Hexadiene from Allyl Bromide.—The allyl bromide was made from allyl alcohol and 48% hydrobromic acid as described in a previous paper[13] from this Laboratory.

Seventy-five grams of magnesium turnings is covered with 150 cc. of dry ether in a 2-liter flask. Six hundred grams of allyl bromide is run in as fast as possible, without stirring. It is best to add about 5 g. and wait until the reaction starts and subsides. The rate of reflux will determine the rate of addition. When the reaction stops, 50 cc. of ether is added and all is refluxed gently for five hours. The mixture of diallyl, unchanged bromide and ether is distilled from an oil-bath whose temperature is gradually raised to 250°. The distillate is dried with sodium and added to 25 g. of magnesium turnings in a one-liter flask. Fifty cc. of ether is added and a small crystal of iodine. If the reaction does not start spontaneously, a *micro burner* is used to induce it. When the reaction subsides, refluxing is continued gently for three hours. After cooling, one cc. is pipetted out and a little magnesium added to it. If there is still a reaction after standing for a few hours, fresh metal is added to the main batch and the refluxing continued. When the indicated test is negative, all is distilled from an oil-bath, gradually raised to 140°. The distillate is shaken with ordinary concentrated hydrochloric acid[14] with cooling under the tap. The layers are separated and the process is repeated five times. Each time a volume of acid equal to that of the hydrocarbon residue is used. Finally, it is washed once with 10% sodium hydroxide and once with water. After a

[3] Berthelot and Luca, *Ann. chim. phys.*, [3] **48**, 294 (1856).

[4] Wurtz, *ibid.*, [4] **3**, 155 (1864).

[5] Linnemann, *Ann.*, **140**, 180 (1866).

[6] Oppenheim, *Ber.*, **4**, 670 (1871).

[7] Sorokin, *J. prakt. Chem.*, [2] **23**, 1 (1881).

[8] Blaise, *Compt. rend.*, **138**, 285 (1904).

[9] Domanizki, *Chem. Zentr.*, I, 982 (1915).

[10] Krestinski, *ibid.*, I, 2056 (1927).

[11] Lespieau, *Ann. chim. phys.*, [8] **27**, 149 (1912).

[12] Gilman and McGlumphy, *Bull. soc. chim.*, [4] **43**, 1322 (1928).

[13] McCullough and Cortese, THIS JOURNAL, **51**, 225 (1929).

[14] Lucas and Dillon, *ibid.*, **50**, 1461 (1928), used aqueous perchloric acid to remove ether from butene-1.

preliminary short shaking with calcium chloride, it is dried over sodium. The amount of this crude hydrocarbon is 70–75% of the theoretical based on the allyl bromide. The rest of the yield is taken up by by-products, a yellowish oil covering the magnesium bromide etherate and a copious evolution of gas when water is added to this etherate residue. These were not investigated. The yield, boiling between 59–60°, is 68%. There are no low- or high-boiling fractions. The yield boiling between 59.4 and 59.6° at 760 mm. is 36%.

From Allyl Chloride.—Exactly analogous procedures were used. The crude yield was 68%. The yield boiling between 59 and 60° was 55%, and the yield boiling between 59.4 and 59.6° was only 27%.

Purification.—The two samples of Δ-1,5-hexadiene were each distilled four times from fresh sodium, through a Widmer[15] column. A distillation curve was made each time and the appropriate cut taken from the flat portion of the curve. The final samples boiled constantly, 30 cc. from the allyl bromide run and 55 cc. from the allyl chloride run. They were halogen free as shown by sodium fusion–silver nitrate tests.

TABLE I

PHYSICAL CONSTANTS OBTAINED FOR Δ-1,5-HEXADIENE

The samples prepared from allyl bromide and allyl chloride are designated A and B, respectively.

Constant	A	B	Mean
B. p., °C.	59.65±0.05° at 762.9±0.1 mm.	59.60±0.05° at 757.6±0.1 mm.	59.57±0.05° at 760.0±0.1 mm.
dt/dp (750–770 mm.)	0.026	0.028	0.027±0.001
M. p. or f. p.[a]	−140.8[5]	−141.1, −141.2	−140.9±0.1
d_4^0	0.7106±0.0002	0.7106±0.0002	0.7106±0.0002
d_4^{25}	0.6863±0.0002	0.6863±0.0002	0.6863±0.0002
n_D^{15}	1.4076±0.0002	.....	1.4076±0.0002
n_D^{20}	1.4044±0.0002	.....	1.4044±0.0002
n_D^{25}	1.4012±0.0002	1.4012±0.0002	1.4012±0.0002

[a] By Dr. E. L. Skau, National Research Fellow.

The determinations of the melting point and freezing point were kindly made by Dr. E. L. Skau[16] in a special apparatus. His remarks were as follows: "Good heating curves were obtained on Sample A, although a cooling curve was not run. On Sample B cooling curves were run which were checked within 0.1° by heating curves. Both cooling and heating curves were reproducible within themselves within 0.04°. The shape of the curves obtained indicated that Sample A was purer than Sample B. From the amount of water and gas observed, when the samples were vacuum distilled, and from the shape of the curves, it was also concluded that the true density of diallyl had probably been determined to at least ±0.0003.

"The methods used and the interpretation of the heating curve as a criterion of purity will be discussed in a forthcoming paper."

[15] Widmer, *Helv. Chim. Acta*, **7**, 59 (1924).

[16] National Research Fellow.

The writer also reached the conclusion that Sample A was the purer one from the distillation characteristics of A and B.

Pure diallyl does not have a sharp odor, as sometimes claimed. It has a very penetrating, highly "unsaturated," nauseating odor, inducing anesthesia easily. It has a sweet taste when highly diluted with water. It must be kept in a sealed bottle as it is very volatile. Ordinary samples develop a sharp odor and deposit a yellow oil on standing; purified material in sealed tubes evidently keeps indefinitely. It can be conveniently identified by the preparation of the cyclic, crystalline, neutral, monosulfuric acid ester of hexane-2,5-diol, which melts at 90° corr.[2]

Summary

1. Detailed directions are given for the preparation of Δ-1,5-hexadiene from allyl halides and magnesium in ether.

2. The boiling point, dt/dp, melting point, density and refractive index of Δ-1,5-hexadiene have been accurately determined.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY, AND FROM THE RESEARCH LABORATORY, ELI LILLY AND COMPANY, INDIANAPOLIS, INDIANA]

SYNTHESIS OF EPHEDRINE AND STRUCTURALLY SIMILAR COMPOUNDS. III. A NEW SYNTHESIS OF ORTHO-DIKETONES

BY HAROLD W. COLES, RICHARD H. F. MANSKE AND TREAT B. JOHNSON

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The synthesis of ephedrine described in Papers I and II[1,2] necessitated the preparation of considerable quantities of 1-phenylpropane-1,2-dione. This substance has been prepared by the decomposition of isonitroso-ethylphenyl ketone by means of dilute sulfuric acid[3] or by means of amyl nitrite.[4] In the first case decomposition is slow and in the second case by-products are formed in large amount so that the yield of diketone in either case is small. In view of the great stability of this oxime it is not surprising that the carbonyl group with which the hydroxylamine is associated displays sufficient affinity to combine readily with primary amines—a reaction upon which the synthesis of ephedrine depends.[5] The formation of a crystalline hydrate of benzoylformaldehyde is another

[1] Manske and Johnson, THIS JOURNAL, **51**, 580 (1929).

[2] Manske and Johnson, *ibid.*, **51**, 1906 (1929).

[3] Pechmann and Müller, *Ber.*, **21**, 2119 (1888); *ibid.*, **22**, 2128 (1889).

[4] Manasse, *ibid.*, **21**, 2176 (1888).

[5] The authors desire to call attention to two errors which occur in the first paper; *ethylbenzyl* (line 18, p. 581) should read *ethylphenyl*, and *specially* (line 2, p. 582) should read *spatially*.