

The following preliminary data relative to the pharmacological tests were kindly furnished me by my associate, Mr. L. W. Rowe:

"Neither the butyric nor the propionic ester of brometone appears to possess anesthetic properties. The propionic ester is the more readily absorbed following hypodermic injection and is much less irritating than the butyric ester. Neither ester exerts a very appreciable action upon the heart or general circulation as the intravenous injection of a rather large dose of each into an anesthetized dog caused only a very slight fall in blood pressure. They are both comparatively inactive pharmacologically due to the probable fact that they are not decomposed into soluble constituents having a typical physiological action and are rather slowly absorbed. In this respect they are similar to other esters of this series."

DETROIT, MICHIGAN.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS.]

ORGANIC CHEMICAL REAGENTS. II.¹ AMYLENE, TERTIARY AMYL ALCOHOL.

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Amylene is a substance which is used at one time or another in most organic chemical laboratories either as a reagent or as a substance from which to prepare certain organic compounds such as tertiary amyl alcohol. In spite of its comparatively simple nature, it is in general considered not only an expensive substance but also one rather troublesome to prepare. For this reason we have studied the various methods for its production, and two which have proved satisfactory are described in detail below. One of these may be used if only small amounts, the other if large amounts of amylene are required.

Tertiary alcohols in general can be dehydrated with the production of unsaturated hydrocarbons far more readily than secondary or primary alcohols. Hence it is not surprising that oxalic acid serves as a convenient reagent for the preparation of trimethyl ethylene from tertiary amyl alcohol.² Tertiary amyl alcohol is, however, usually prepared from isoamylene and hence the reverse reaction becomes of less practical importance except as a method for the preparation of pure trimethyl ethylene from a mixture of isoamylenes.

Dehydration of primary alcohols for the preparation of alkylene hydrocarbons encounters increased difficulties as one goes higher in a given

¹ This publication is the second in the series of those describing the results of the investigations at the University of Illinois on various organic chemical reagents. The first publication appeared in *THIS JOURNAL*, 40, 1281 (1918).

² *Friedlaender*, 3, 980; D. R. P. 66,866.

homologous series. This is particularly noticeable when sulfuric acid is used as a dehydrating agent. In the preparation of ethylene from alcohol and conc. sulfuric acid fair results are obtained, although the yield may be considerably improved by the addition of a small quantity of amorphous silica¹ which serves to lower the temperature required for the decomposition of ethyl sulfuric acid. Nevertheless, this method of preparation cannot compete with either the phosphoric acid method² or still less with the catalytic method.³ In the preparation of propylene from normal propyl alcohol by the sulfuric acid method, considerably more charring takes place but fair yields are nevertheless obtained if the proportion of sulfuric acid is decreased. For the preparation of isobutylene from isobutyl alcohol, however, it is advisable to use more dilute sulfuric acid.⁴ No satisfactory method has yet been described for the production of amylene from amyl alcohol and sulfuric acid, the chief difficulty being the excessive carbonization which always takes place.

Several attempts were first made therefore to dehydrate amyl alcohol with zinc chloride.⁵ The method, however, results in the formation of very considerable quantities of high boiling polymerized products together with only very poor yields of amylene, and for this reason it has been discarded in this laboratory as being prohibitive in cost.

The preparation of amylene by the sulfuric acid method was then thoroughly studied until satisfactory results were developed for the production. The method involves merely the action of sulfuric acid upon a large excess of amyl alcohol under conditions modified considerably from those maintained in the usual preparation of an alkylene of lower molecular weight. It is quite satisfactory when amylene is required in small amounts and especially when the by-product, isoamyl ether, may be desired. The directions may also serve as a convenient laboratory experiment for student use. A search through the literature has shown that a method for the dehydration of amyl alcohol somewhat analogous to this one has previously been proposed for the preparation of isoamyl ether,⁶ and, indeed, a small quantity (2-4%) of amylene was obtained as a by-product.

The dehydration of amyl alcohol by means of phosphoric acid at a temperature of about 240-260° has also been used in this laboratory, and possesses the advantage of yielding less isoamyl ether as a by-product. In this connection the superiority of Pyrex flasks as compared with glassware obtainable before the war for reactions of this type should

¹ *Compt. rend.*, 151, 392 (1910).

² *J. Chem. Soc.*, 79, 916 (1901).

³ *Ber.*, 35, 1047, 1057 (1902); 36, 190 (1903); *Compt. rend.*, 144, 1109 (1907).

⁴ *J. Chem. Soc.*, 37, 237 (1880).

⁵ *Bull. soc. chim.*, 5, 301 (1863).

⁶ *Friedlaender*, 9, 32; D. R. P. 200,150.

be pointed out. On the whole, however, the sulfuric acid method is considered the better.

For producing larger quantities of amylene, the pyrogenic-catalytic method has been found much more satisfactory. Five pounds or more of amylene a day may easily be prepared in the apparatus described below. The method possesses the further advantage of yielding no isoamyl ether. The pyrogenic-catalytic dehydration of amyl alcohol has been described by Ipatiew¹ and his general directions have been followed with very satisfactory results. The additional details given in this communication concerning the electrically heated furnace and the application of the catalyst will aid those who may desire to prepare large amounts of amylene.

Preparation of Amylene by the Sulfuric Acid Method.

Into a 3 liter Pyrex flask connected with a reflux condenser there is placed a 1.5 liter portion of amyl alcohol (128–131° fraction from fusel oil). A 100 cc. portion of conc. sulfuric acid is then added, after which the mixture is *vigorously* refluxed. The reflux condenser used should be inclined at an angle of at least 20 degrees from the perpendicular so as to insure an even return flow of the condensed vapors. For the same reason, the lower end of the condenser tube should not be constricted. The water in the upright condenser should be maintained at such a temperature (60 to 90°) as to permit a considerable amount of vapor to distill out of the apparatus. The top of the condenser is connected with a second, efficiently cooled condenser, best of the spiral type, attached so as to permit downward distillation. In this manner low-boiling products are removed as they are formed.

Heating of the reaction mixture usually requires a maximum time of about 8 hours. During the first hour a considerable quantity of water and amyl alcohol with only traces of amylene are obtained in the distillate. Soon, however, a regular flow of liquid consisting primarily of amylene is obtained which usually continues until one-half or more of the material in the flask has been distilled over into the receiver. At the same time, and particularly near the end of the reaction, a considerable quantity of sulfur dioxide is evolved. The end is indicated by a let-up in the flow of amylene and also by increased carbonization.

The distillate, which usually measures 900 cc., consists of two layers. The lower, water layer is separated and the remaining product is washed once with dil. sodium hydroxide solution to remove sulfur dioxide. The amylene layer is then, without drying, subjected to distillation, and a fraction (350 cc.) boiling up to 100° collected. The residue in the flask is used as amyl alcohol in the next run.

The amylene distillate is separated from the small quantity of water

¹ Ber., 36, 2000 (1903).

present, dried over a small quantity of solid sodium hydroxide and fractionated. A fraction boiling at from 32 to 42° and usually measuring 250 cc. is obtained. Refractionation will yield a product boiling over a range of only 4°. Titration of the 10° product with a standard solution of bromine in carbon tetrachloride shows it to be free from saturated hydrocarbons. A further test of the purity of the product is shown below in its conversion into tertiary amyl alcohol. Both unsymmetrical methylethyl ethylene and trimethyl ethylene yield tertiary amyl alcohol and this product is no doubt a mixture of these two amylenes, with the latter predominating. Methylethyl ethylene boils at 31-32° and trimethyl ethylene boils at 36°.

In this preparation there is obtained apparently only a negligible amount of isopropyl ethylene (b. p. 20 to 21°). The preparation is also characterized by the absence of the large quantities of polymerization products produced when zinc chloride is used for the dehydration of amyl alcohol. High boiling by-products are found to consist primarily of isoamyl ether and of unchanged alcohol.

The material remaining in the original reaction flask consists of a mixture of isoamyl ether, amyl alcohol, and sulfuric acid, together with carbonization products. It is subjected to steam distillation, thus removing amyl alcohol and isoamyl ether. Upon fractionation the total quantity of isoamyl ether obtained is usually 400 cc. The quantity of amyl alcohol both from the original distillate and from the residue which may be used again for the preparation of amylene, measures about 500 cc.

For the preparation of pure trimethyl ethylene, the mixture must of course be converted into tertiary amyl alcohol and the latter compound dehydrated by the usual methods. For most purposes, however, the isoamylene fraction may be used directly. A student may prepare two to three pounds of amylene a day by this method provided he have 6 to 8 sets of apparatus to use for refluxing the amyl alcohol sulfuric acid mixture.

The Preparation of Amylene by the Pyrogenic-Catalytic Method.

The apparatus¹ to be described below can be made up cheaply and easily by any plumber or pipe-fitter, and can be used not only for the catalytic production of amylene but also for many other catalytic processes.

The furnace consists of a 5-ft. iron pipe two inches in diameter, which is covered with a quarter-inch layer of alundum cement. After the insulating cement has hardened, a 4-ft. section of the pipe (leaving 6 in. at each end) is wound with two 65-ft. lengths of No. 18 Chromel C. wire.

¹ A diagram and somewhat more detailed description of the apparatus will be given in the proposed bulletin on the preparation of organic chemical reagents to be published by the University of Illinois.

These two lengths are arranged so that one is wound between the coils of the other. Another layer of cement is then applied and thoroughly dried by passing a current of not over 10 amp. through one of the coils. The furnace is then packed in a galvanized iron jacket 4 ft. in length and 10 in. in diameter, using 30 lbs. of light weight infusorial earth as a heat insulating material.¹

To one end of the pipe is fitted a screw cap holding a half-inch well which extends half way through the furnace. This is to hold the pyrometer, a Hoskin's thermo-electric pyrometer being used for temperature readings in these experiments. Next to the cap holding the well and extending vertically from the top of the iron tube, a one-ft. iron pipe (one in. in diameter) is screwed in. A rubber stopper with a separatory funnel, inserted in the top of this small pipe, serves for the introduction of the alcohol. At the other end of the main tube, a flange connection (using a litharge-glycerine cement) is made with a small iron pipe ($1/2$ in. diam.) which is attached directly to an efficient set of condensers.

Ipatiew has suggested the use of aluminum oxide as a catalyst but has not given details for the application of the material. We employed small pieces of pumice thoroughly soaked in a thick paste of aluminum oxide and water. The moist lumps of pumice were introduced into the furnace and dried out when the furnace was heated.

The two coils were connected in parallel to a 110 volt, alternating current circuit, 2.5 hours being required to bring the furnace to a temperature of 540°. A switch and carbon resistance in the circuit with the coils allows for easy temperature control.

The best temperature for the decomposition of amyl alcohol to amylene was found to be 500 to 540°, which agrees with the data given by Ipatiew. Amyl alcohol may be introduced at the rate of one liter per hour and possibly the rate might be increased. The capacity of the furnace is thus 4 times that used by Ipatiew, and yet practically no unchanged amyl alcohol is found in the distillate. The yield of isoamylene boiling over a range of about 10° averages from 450 to 500 g. which corresponds to a yield of 70 to 80% of the theoretical. The amyl alcohol used was a product obtained in the laboratory merely by one distillation of technical fusel oil and boiled over a range of 125 to 130°. A purer product would probably produce even a better yield of amylene.

The length of time during which the catalyst will remain effective has not yet been determined but after decomposition of 25 liters of amyl alcohol in the apparatus just described, it was just as effective as at the beginning.

The amylene by this method is about 98 to 99% pentene as indicated by titration with a standard carbon tetrachloride solution of bromine.

¹ The technical product sold as "Sil-o-cel" is very satisfactory.

Moreover, the amylene contains a somewhat larger percentage of isopropyl ethylene than that prepared by the sulfuric acid method.

Isoamyl ether may be run through the furnace under exactly the same conditions as the alcohol and amylene is produced in the same yields as from alcohol.

Using amyl alcohol, 5 lbs. of amylene may readily be prepared in a day's time by this method and the cost, considering carefully all the necessary charges, is much below Kahlbaum's pre-war price. Since the present cost of amyl alcohol is many times the pre-war price, there is no reason why amylene, tertiary amyl alcohol or trimethyl ethylene should not be produced in normal times at a very low figure.

Tertiary Amyl Alcohol.

$\frac{1}{2}$ kilo of cracked ice is placed in a 5-liter round-bottom flask and $\frac{1}{2}$ liter of conc. sulfuric acid is added. The mixture is cooled to 0° and through a dropping funnel $\frac{1}{2}$ liter of amylene (prepared by the sulfuric acid method) is run in. The mixture is vigorously agitated by means of a mechanical stirrer during the addition of the amylene and the stirring is then continued for one hour longer. After this time most of the amylene has gone into solution, although a small quantity of unchanged hydrocarbon (50 cc.) is separated by means of a separatory funnel and is recovered. The sulfuric acid solution is then run into a mixture of two kilos of cracked ice and water after which a concentrated solution of 720 g. of sodium hydroxide is added gradually. The mixture is distilled until from the distillate no more alcohol may be salted out by the addition of potassium carbonate; the tertiary amyl alcohol is very volatile and distills rapidly. The product is finally dried over calcined potassium carbonate¹ and then fractionated. 275–300 g. of a product boiling at 100 to 103° may be obtained from 325 g. of amylene.

URBANA, ILLINOIS.

CORRECTION.

The Identification of the Cinchona Alkaloids by Optical-crystallographic Measurements.—In the July number of THIS JOURNAL, through oversight two references were omitted from footnote 2, page 1063: Kley, *Z. anal. Chem.*, **43**, 160 (1904), and Bolland, *Monatsh.*, **29**, 991 (1908); **31**, 387 (1910); it may be noted that the data on alkaloids given by these authors are apparently only rough approximations. On making up pages some shifting of the figures occurred, and it is not clearly

¹ The cost of potassium carbonate for salting out and for efficient drying of organic preparations is no longer prohibitive; in fact, a good grade of 90% calcined potassium carbonate may now be obtained at a very reasonable cost and the market is reported to be over-supplied. When considerable quantities are used, the material is readily recovered and may be used repeatedly.