distillation. The *p*H titrations were carried out as described for pyridine bases.[3]

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[3] A. Gero and J. J. Markham, *J. Org. Chem.*, **16**, 1835 (1951).

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The Preparation of Vinylacetylene

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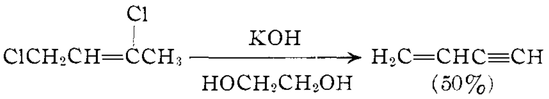
RECEIVED MAY 13, 1954

Several methods for the preparation of vinylacetylene have been reported. Perhaps the best known of these methods is the dimerization of acetylene discovered by Nieuwland.[2]

$$HC{\equiv}CH \xrightarrow{\text{Cat.}} H_2C{=}CHC{\equiv}CH + H_2C{=}CHC{\equiv}CCH{=}CH_2\ (+\ H_2C{=}CHCl)$$

Not only is this method inconvenient as a laboratory procedure, but it also suffers from the difficulty that appreciable amounts of divinylacetylene, formed as a by-product, must be eliminated before the vinylacetylene may be safely employed. It is also difficult to remove small amounts of vinyl chloride contaminating the product. Other methods reported[3a,b] are also not readily adapted to laboratory synthesis.

We have found that the preparation of vinylacetylene by the dehydrohalogenation of 1,3-dichloro-2-butene using potassium hydroxide in ethylene glycol offers a number of advantages for a laboratory scale preparation since it is a one-step process, all the starting materials are readily available, the yields of pure vinylacetylene are better than 50% and there are no hazardous or difficulty-removed by-products.



$$ClCH_2CH{=}\overset{\overset{\displaystyle Cl}{|}}{C}CH_3 \xrightarrow[HOCH_2CH_2OH]{KOH} \underset{(50\%)}{H_2C{=}CHC{\equiv}CH}$$

The apparatus for the dehydrohalogenation is arranged as follows. A 2-l., three-necked flask, heated by means of a Carbowax bath, is equipped with a motor-driven, oil-sealed stirrer, a bulb reflux condenser and a 250-ml. dropping funnel. The dropping funnel is connected to the flask by means of a side-arm test-tube with the end removed. This side-arm is connected through a calcium chloride drying tube and a bubbler to a nitrogen tank.

The top of the condenser is connected to a horizontal tube (*ca.* 2 × 25 cm.) partially filled with calcium chloride. This in turn is connected to a 100-ml. graduated cylinder immersed in an acetone–Dry Ice mixture. The cylinder is also equipped with an escape tube which is protected by a calcium chloride drying tube.

A typical preparation of vinylacetylene is carried out as follows. Four hundred grams of powdered technical potassium hydroxide flakes is placed in the flask and 500 ml. of ethylene glycol is added. This mixture is stirred vigorously while adding 100 ml. of *n*-butyl cellosolve. The system is swept with a rapid stream of nitrogen for 15–20 minutes while the temperature of the wax-bath is raised to 165–170°. The flow of nitrogen is then reduced to a rate just sufficient to maintain an atmosphere of nitrogen in the system.

One hundred twenty-five grams (1.0 mole) of 1,3-dichloro-2-butene is then added from the dropping funnel at a rate of about three drops per second. The addition should be complete in less than an hour. During the addition the temperature of the wax-bath is maintained at 165–170° and the reaction mixture is stirred vigorously. Heating is continued for one hour after the addition of dichlorobutene is complete.

The yields of crude product obtained in typical runs were 39–42 ml. (31.2–33.6 g.,[4] 60–64.7%). The product was purified by distillation through a Davis low temperature column to yield 37–40 ml. (56.9–61.6%) of vinylacetylene, b.p. 0–6°.

The vinylacetylene was identified by formation of the silver salt, using ammoniacal silver nitrate, and by conversion to ethylvinylacetylene, b.p. 83–84°, n^{20}_D 1.4515, d^{20}_{20} 0.7536, 35% yield, using the method of Jacobson and Carothers,[5] lit.[4] n^{20}_D 1.4522, d^{20}_4 0.7492.

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[1] General Tire and Rubber Co. Fellow, 1952–1954.

[2] J. A. Nieuwland, W. S. Calcott, F. B. Downing and A. S. Carter, THIS JOURNAL, **53**, 4197 (1931).

[3] (a) R. Willstätter and T. Wirth, *Ber.*, **46**, 535 (1913); (b) W. J. Croxall and J. O. Van Hook, U. S. Patent 2,623,077 (Dec. 23, 1952, to Rohm & Haas Co.); THIS JOURNAL, **76**, 1700 (1954).

[4] Calculated on basis of d^{-80} 0.80, extrapolated from data at higher temperatures; K. Kuchinskaya and Anitima, *Khim. Referat. Zhur.*, **2**, 65 (1939) (*C. A.*, **34**, 2783[7] (1940)).

[5] R. A. Jacobson and W. H. Carothers, THIS JOURNAL, **55**, 1622 (1933).

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The Preparation of 1-C^{14}-Labeled Glucose, Mannose and Fructose[1]

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RECEIVED JUNE 1, 1954

As no convenient method has been described for the direct synthesis of 1-C^{14}-labeled fructose, the authors have used a procedure, based upon the cyanohydrin method of Isbell, *et al.*,[4] to prepare this sugar on a millimole scale in addition to 1-labeled glucose and mannose. This was achieved by epimerization of a mixture of the labeled aldoses in phosphate buffer. As no carrier was added at any stage of the reaction or purification the specific activity of the hexoses was equal to that of the starting cyanide.

The procedure of Isbell, *et al.*, was simplified by omitting the separation of the epimeric gluconic acid and γ-mannolactone, thus obtaining, after reduction, a mixture of glucose and mannose instead of the individual sugars. Such a mixture is suitable for epimerization as it theoretically yields the same ratio of glucose, mannose and fructose as does any one of the pure sugars. After epimerization the products were separated and purified chromatographically.

Experimental

C^{14}-Labeled $BaCO_3$ was converted to $KC^{14}N$,[5] and then to $NaC^{14}N$ by distillation of the regenerated $HC^{14}N$ into NaOH. The reaction between D-arabinose and $NaC^{14}N$ was carried out in the presence of $CaCl_2$ by the procedure of Isbell, *et al.* The resultant mixture of epimeric hexonic acids was converted by slow concentration in methyl cellosolve to the corresponding lactone mixture, and this sirup was reduced directly by sodium amalgam in oxalate buffer to yield glucose and mannose. Isbell's procedure was then followed until the deionized sugar solution was collected from the

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[1] This work was supported in part by a research contract with the U. S. Atomic Energy Commission.

[2] Rockefeller Foundation Research Fellow.

[3] Chercheur qualifié F.N.R.S.

[4] H. S. Isbell, J. V. Karabinos, H. L. Frush, N. B. Holt, A. Schwebel and T. T. Galkowski, *J. Research Natl. Bur. Standards*, **48**, 163 (1952).

[5] J. A. McCarter, THIS JOURNAL, **73**, 483 (1951).

mixed resin column. Unreacted hexonic acid was eluted from the column with 2 N NH_4OH and treated as before; this second treatment contributed about 20% of the final yield of sugar. The sugar mixture was dissolved in 0.2 molar Na phosphate buffer pH 7.5 (2.5% hexose w./v.) and epimerization effected by heating the solution on a steam-bath for 90 minutes. Glucose, mannose and fructose were partially separated by paper chromatography on four sheets of Whatman No. 1 filter paper (57 × 47 cm.) using phenol-water as solvent,[6] and the sugars located by exposing the dried sheets to X-ray film. After elution from the paper the sugars were further purified by paper chromatography in butanol–acetic acid–water.[6] The final products were shown by two-dimensional chromatography in phenol–water and butanol–ethanol–water[6] to contain no significant quantity of radioactive contaminants.

The yields of hexoses from 2.7 millimoles of starting NaC^{14}N were: glucose 0.496, fructose 0.055 and mannose 0.077 millimole. The total hexose obtained (0.628 millimole) was 23% of the theoretical yield.

Degradation of glucose by heterolactic fermentation[7] after its isolation from the epimeric mixture showed that carbon atom 1 contained 100% of the total radioactivity in the molecule. Carbon atoms 2 to 6 contained no significant activity.

Acknowledgment.—We wish to thank Dr. W. Z. Hassid for his interest in this work.

(6) S. M. Partridge, *Biochem. J.*, **42**, 238 (1948).

(7) I. C. Gunsalus and M. Gibbs, *J. Biol. Chem.*, **194**, 871 (1952).

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Reaction of Methylal with Some Acid Anhydrides

BY W. B. HUGHES AND R. D. KLEENE

RECEIVED MAY 26, 1954

Claisen[1] reported that the reaction of diethylacetal with acetic anhydride gave a good yield of α-ethoxyethyl acetate. He found it necessary to conduct the reaction in a sealed tube at 150°.

Recently we have studied this reaction with methylal and acetic, propionic and n-butyric anhydrides and find that it proceeds smoothly in the presence of an acid catalyst to give good yields of the corresponding methoxymethyl esters. Moreover, the use of a catalyst permits the reaction to take place merely by refluxing the mixture under atmospheric pressure. The products of the reaction are the methyl and methoxymethyl esters of the acid anhydride used and these can be separated readily by fractionation. The methoxymethyl esters have been prepared previously from monochloromethyl ether and the sodium salts of the corresponding acids.[2]

TABLE I

PROPERTIES OF METHOXYMETHYL ESTERS PREPARED

	This investigation	Literature[2]
	Methoxymethyl acetate	
B.p., °C.	117–118	117–118
Mol. wt.	102.4	104 (calcd.)
n^{25}_D	1.3917	1.3980
d^{20}_4	1.018	0.989
M_R	23.21	23.97 (calcd.)
	Methoxymethyl propionate	
B.p., °C.	133	133
Mol. wt.	117	118 (calcd.)
n^{20}_4	0.9886	0.9872
	Methoxymethyl n-butyrate	
B.p., °C.	152	151–152
Mol. wt.	131	132 (calcd.)
d^{20}_4	0.9740	0.9747

Attempts to extend the reaction to benzoic and phthalic anhydrides were not successful.

Experimental

Methoxymethyl Acetate.—The methylal used in this work was prepared from the methylal–methanol azeotrope by refluxing the latter over calcium chloride to remove most of the methanol and then distilling the product over sodium. The presence of methanol or moisture in the methylal results in decreased yield of the desired esters.

Acetic anhydride (102 g., 1 mole), methylal (76 g., 1 mole) and 1 g. of p-toluenesulfonic acid were refluxed gently for six hours. The mixture was then distilled through a 30-plate Oldershaw column and the cut boiling at 100–125° was collected. Redistillation gave 81 g. of a fraction boiling at 117–118° which was the desired product; n^{25}_D 1.3917, d^{20}_4 1.018. From the residue 14.5 g. of acetic anhydride was recovered. The yield of methoxymethyl acetate based on acetic anhydride consumed was 95%.

Methoxymethyl Propionate and n-Butyrate.—Methoxymethyl propionate was prepared as described above, using an equivalent amount of propionic anhydride. The cut boiling at 130–135° was washed with 10% sodium bicarbonate followed by water, dried over magnesium sulfate and refractionated. The product boiled at 133°, d^{20}_4 0.9886. Thirty-one per cent. of the propionic anhydride was recovered and the yield of ester based on anhydride consumed was 94%.

Methoxymethyl n-butyrate was similarly prepared. The ester boiled at 155°, d^{20}_4 0.9740. Of the n-butyric anhydride taken, 27.6% was recovered and the yield of ester on this basis was 86%.

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The Reduction of Streptomycin with Sodium Borohydride

BY MURRAY A. KAPLAN, OLIVER B. FARDIG AND IRVING R. HOOPER

RECEIVED JUNE 7, 1954

The generally accepted procedure for the reduction of the aldehyde group of streptomycin involves a catalytic hydrogenation with platinum or other metals as catalyst.[1–3] An electrochemical procedure for the reduction of streptomycin has also been reported.[4] Chaikin and Brown[5] demonstrated the reduction of organic aldehydes in aqueous solution with sodium borohydride. We have found sodium borohydride to be a very effective reagent with which to convert the aldehyde group of streptomycin and hydroxystreptomycin to their respective derivatives.

The completeness of the reduction of streptomycin by sodium borohydride was investigated with variations in time of reaction, temperature, pH of the solution, quantity of sodium borohydride, and purity of the streptomycin.

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(5) S. W. Chaikin and W. G. Brown, THIS JOURNAL, **71**, 122 (1949).