

[CONTRIBUTION FROM THE LOS ALAMOS SCIENTIFIC LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Micro-syntheses with Tracer Elements. V. The Synthesis of Formaldehyde-C¹⁴ and of Glyoxylic-1,2-C₂¹⁴ Acid¹

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A micro-synthesis for the preparation of formaldehyde-C¹⁴ from methanol-C¹⁴ has been described. The conditions for the reduction of oxalic acid to glyoxylic acid has been investigated. A method for the reduction of oxalic-1,2-C₂¹⁴ acid to glyoxylic-1,2-C₂¹⁴ acid has been described.

Formaldehyde-C¹⁴ of high specific activity was desired. The commercially available compound has been diluted with inactive formaldehyde. Since no dilution was desired, a method for the catalytic oxidation of high specific activity methanol-C¹⁴ was investigated. A modification of the method described by Arnstein² was adopted and used to prepare formaldehyde-C¹⁴ of high specific activity.

Formaldehyde-C¹⁴ was oxidized to formic-C¹⁴ acid by the method of Blank and Finkenbeiner.³ A basic fusion of the formic acid was used to prepare oxalic-1,2-C₂¹⁴ acid essentially according to the method of Semenov, Yu Shagalov and Astrakhantsev.⁴ A complete investigation of the reduction of oxalic acid to glyoxylic acid using the electrolytic method⁵ and with sodium amalgam⁶ was made. The reduction with sodium amalgam was found to be the most efficient and is reported.

Experimental

Formaldehyde-C¹⁴.—Molybdenum oxide-ferric oxide catalyst was prepared on a -20+40 mesh porous tile carrier. The tile (30 g.), purified by first digesting with aqua regia overnight, then washing and drying, was covered with an aqueous solution of 4.38 g. of Fe(NO₃)₃·9H₂O and boiled briefly. A concentrated solution of 12.28 g. of (NH₄)₂MoO₇·4H₂O in warm ammonium sulfide solution (about 15 ml.) then was added to the mixture. The sirupy mass was evaporated to dryness and ignited. During the heating dense fumes were given off and the dark mass became a very pale greenish-yellow. In order to ensure complete oxidation, the catalyst was placed in a quartz tube and heated for 20-30 minutes at 600-700° in a current of oxygen.

The apparatus used for the oxidation of the methanol is shown in Fig. 1. Compressed air, controlled by a needle valve, was passed through a safety trap, concentrated sulfuric acid, calcium chloride and potassium hydroxide pellets. The air pressure was adjusted by varying the height of mercury in a pressure regulator. A weighed quantity of methanol was admitted to the system in tube G. The oxidation chamber consists of a Pyrex tube 10 cm. long and 12 mm. in diameter, in which was sealed a coarse sintered glass disk H. Thorough mixing of the air and methanol vapor was assured by passing the gases through a section of the tubing 40 mm. long packed with 3 mm. glass beads, I.

A thin mat of asbestos J and a small plug of glass wool L were used to keep the catalyst in place. The bulb of the 500° range thermometer extended into the middle of the catalyst. Five grams of catalyst was enough to fill the reaction tube which was heated electrically. The heating coil consisted of 6.5 feet of No. 30 nichrome wire wrapped over a layer of asbestos paper. Heating was controlled

with a variable auto transformer V. The remainder of the system was heated to approximately 100° in a similar manner using the variable auto transformer W. A 50-ml. round bottomed flask M served as a steam generator. The steam inlet into the apparatus N had an orifice of 2-3 mm. diameter. The surface area of the water cooled condenser O was increased by means of a number of indentations. The receiver inlet tube P was the largest that would pass through joint #19/38 and of such a length that it cleared the liquid surface when 25 ml. of distillate had collected in the receiver. The air outlet was connected to a Mariotte flask through a calcium chloride tube and safety trap. With the apparatus in operation the rate of air flow could be determined at any time by measuring the volume of water displaced per unit time from the Mariotte flask.

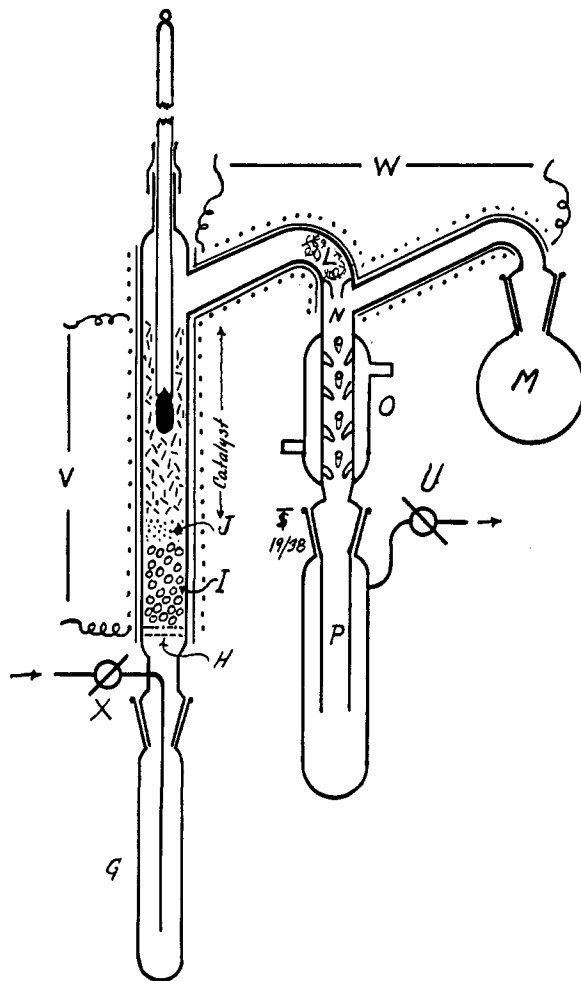


Fig. 1.

The three variables, temperature, rate of air flow and catalyst activity were studied to determine the optimum operating conditions. Our experiments indicated that the temperature of the catalyst was much more critical than the rate of air flow. A different batch of the same catalyst will also have different temperature characteristics. It is also interesting to note that a catalyst prepared by the reverse

(1) Work performed under the auspices of the Atomic Energy Commission.

(2) H. R. V. Arnstein, *Nature*, **164**, 362 (1949). See also V. E. Meharg and H. Adkins, U. S. Patent 1,913,405 (1933).

(3) O. Blank and H. Finkenbeiner, *Ber.*, **31**, 2979 (1898).

(4) V. M. Semenov, A. Yu Shagalov and P. I. Astrakhantsev, *Trans. State Inst. Applied Chem. (U. S. S. R.)*, **31**, 63 (1937); *C. A.*, **33**, 6248 (1939). See also F. Kogl, J. Hulberstadt and T. J. Barendregt, *Rec. trav. chim. Pays-Bas*, **68**, 387 (1949).

(5) J. Tafel and G. Friedrichs, *Ber.*, **37**, 3187 (1904).

(6) W. Mohrschulz, *Z. Elektrochem.*, **32**, 434 (1926).

order than the one described gave the same maximum conversion to formaldehyde when operated at a much higher temperature.

The quantitative estimation of the formaldehyde formed in a given experiment was made by condensing the aldehyde with an excess of 4-hydroxycoumarin to yield the solid derivative "dicumarol" as follows.

An aliquot of the formaldehyde solution containing 0.36–0.56 mM. of aldehyde was added to a filtered, boiling solution of 0.30 g. of the 4-hydroxycoumarin in 100 ml. of water. The solution was refluxed for 15 minutes. The colorless chalky ppt. formed was filtered through a tared medium sintered glass funnel, washed thoroughly with boiling water, dried one hour at 120°, and weighed. Figure 2 shows the yields of formaldehyde, determined as dicumarol, obtained when the temperature of the catalyst was varied.

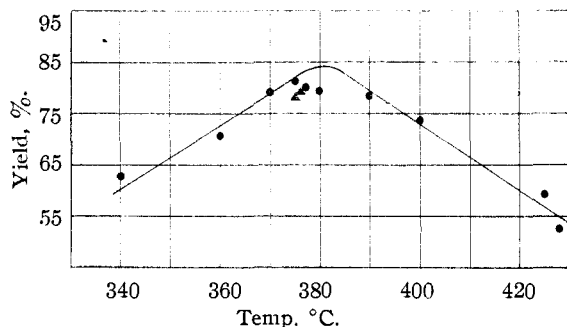


Fig. 2.—● = 210–230 ml./min. air flow; ▲ = 130–145 ml./min. air flow.

Variation of the air flow between 115 to 240 ml./min. did not materially change the yield (see Fig. 2).

In a typical run the catalyst temperature both before and during the experiment was maintained at $375 \pm 2^\circ$. The rate of flow of air passing through the system was 200 ± 25 ml./min. The steam generator *M* was heated and steam was generated for five minutes. The distillate was collected in the receiver which was cooled with Dry Ice chips. Active boiling was discontinued momentarily when the empty tube *G* was replaced with a duplicate containing 0.0392–0.0985 g. of C^{14} methanol (1.22–3.06 mM.). The tube was immersed in a water-bath maintained at 20° and the steam generator was again heated vigorously. The generator required about 30 minutes to boil almost dry. Distillation was then stopped and stopcocks *U* and *X* were closed, thus isolating the system while the frozen formaldehyde solution was allowed to melt. A series of seven runs gave yields varying between 77.5 and 81.2% (av. 79.1%), determined as the dicumarol derivative.

Formic- C^{14} Acid and Oxalic-1,2- C_2^{14} Acid.—Formaldehyde- C^{14} was converted to formic- C^{14} acid by oxidation with 30% hydrogen peroxide.³ The yields varied between 97.7 and 99.5%. Sodium formate- C^{14} was converted in 70–90% yield to oxalic-1,2- C_2^{14} acid by a fusion with sodium hydroxide.^{8,7}

Reduction of Oxalic Acid to Glyoxylic Acid.—The reduction of oxalic acid to glyoxylic by means of sodium amalgam was exhaustively investigated and the effects on the yields of glyoxylic acid caused by varying the duration of reduction, volume of solution, temperature of reduction and acid-

ity of the reduction medium were studied. Since the acidity of the solution appeared to exert a strong influence upon the yield, a series of experiments was undertaken in which the acidity of the solution was followed with a *pH* meter using a glass electrode and was controlled by addition of acid. The results of this series of experiments are shown in Table I.

TABLE I
REDUCTION OF OXALIC ACID UNDER CONTROLLED *pH*

No.	Wt. of oxalic acid, g.	Duration of reduction, min.	Wt. of ^a amalgam used, g.	<i>pH</i>	Yield of glyoxylic acid, %
1	0.150	45	40	3.5–4.0	37.4
2	.150	45	40	2.5–3.0	62.8
3	.150	45	40	1.5–2.0	85.7
4	.150	45	40	1–0.2	85.0
5	.150	55	45	1.5–2.0	85.4
6	.150	55	45	1.5–2.0	80.0
7	.670	55	65	1.5–2.0	84.6

^a 1.2% sodium amalgam.

In an empirical manner the optimum conditions for obtaining useful yields of glyoxylic acid were determined.

Either a solution of 150 mg. of sodium oxalate in 20 ml. of water or the melt from the sodium formate fusion dissolved in 20 ml. of water was transferred to a tall glass beaker (4 cm. \times 10 cm.) containing a short, glass jacketed magnetic stirrer. The beaker was placed in a water-bath maintained at 5° by the periodic addition of ice. Twenty grams of 1.2% sodium amalgam was added to the solution. Stirring was begun, the glass electrode of the *pH* meter⁸ was inserted, and the *pH* of the solution was maintained between *pH* 1.5–2.0 by the dropwise addition of 6 *N* hydrochloric acid. Additional amalgam was added as needed during the course of the experiment. Reduction was considered complete at the end of 1 hour.

The yields of glyoxylic acid were determined by condensing the acid with 4-hydroxycoumarin in acid solution and weighing the condensation product. This method is not quantitative but gives an approximate evaluation of the amount of product that may be obtained.

The water solution of the reduction product was then separated from the mercury and transferred by washing with water (25 ml.) into a boiling solution of 2.0 g. of 4-hydroxycoumarin in 300 ml. of water. The solution was allowed to reflux 20 minutes. Ten milliliters of concd. hydrochloric acid was then added. After heating an additional ten minutes the mixture was filtered while still hot, and washed with 20 ml. of boiling dilute hydrochloric acid (1:20). The yields of di-(4-hydroxycoumarinyl-3)-acetic-1,2- C_2^{14} acid obtained, starting with 0.069 and 0.051 g. (7.5 and 5.5 mc.) of methanol- C^{14} , were 1.1800 g. (58.8%) and 0.6944 g. (46.7%). A solution of 0.687 g. (6 mc.) of sodium formate gave a final yield of 1.195 g. (62.4%) of derivative, m.p. 215–219° (dec.). All yields are based on methanol.

The preparations of high specific activity formaldehyde- C^{14} and glyoxylic-1,2- C_2^{14} acid were used to prepare C^{14} -labeled dicumarol and pelentan (ethyl di-(4-hydroxycoumarino-1)-acetate-1,2- C^{14}). The details of these syntheses will be published elsewhere.

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(7) The details of these syntheses will be published elsewhere.

(8) Beckman *pH* Meter Model G.