418. *Syntheses with Isotopic Tracer Elements. Part III.* The Preparation of Ethylene Oxide and Ethanol labelled with Carbon Isotopes.*

By J. D. Cox and R. J. Warne.

A method is described for the synthesis, on the 2—5 millimol. scale, of carbon-labelled ethylene oxide; reduction of the product with lithium aluminium hydride leads to αβ-labelled ethanol (cf. Part II, *loc. cit.*).

In Parts I and II of this series (*J.*, 1950, 3167, 3176) methods for the preparation of various carbon-labelled intermediates were described. In this and the succeeding Part, methods are given for synthesising two compounds, ethylene oxide and diazomethane, which are particularly valuable intermediates in that they afford means for the ready introduction of isotopic carbon into compounds of many different types.

We have devised a method of preparing ^{14}C-ethylene oxide from barium ^{14}C-carbonate, *via* acetylene, ethylene, and ethylene chlorohydrin, with an 82% recovery of isotope; the method is suitable for the 2—5 millimol. scale. ^{14}C-Acetylene was prepared in 97% isotopic yield by fusing barium ^{14}C-carbonate with excess of barium, followed by treatment of the resulting carbide with water (cf. Monat, Robbins, and Ronzio, U.S.A.E.C.U.—672). Reduction to ^{14}C-ethylene was accomplished by shaking the gas with acid chromous chloride solution (Traube and Passarge, *Ber.*, 1916, **49**, 1692; Arrol and Glascock, *J.*, 1949, S 335); a quantitative yield was secured of a product which contained no unchanged acetylene. Reaction with 2M-hypochlorous acid then afforded an aqueous solution of ^{14}C-ethylene chlorohydrin from which ^{14}C-ethylene oxide was liberated by potassium hydroxide in 85—95% yield (from ethylene).

Part II (*loc. cit.*) contained a description of a method for preparing α- or β-labelled ethanol from labelled barium carbonate, by way of acetic acid, in 78—86% isotopic yield. It has now been found that labelled ethylene oxide may be reduced with lithium aluminium hydride to αβ-labelled ethanol in 93% yield, an overall isotopic recovery of 76% (based on barium carbonate) being realised. Although the lithium aluminium hydride reduction of several complex epoxides has been described (*inter al.*: Trevoy and Brown, *J. Amer. Chem. Soc.*, 1949, **71**, 1675; Plattner, Heusser, and Feurer, *Helv. Chim. Acta*, 1949, **32**, 587), that of ethylene oxide does not seem to have been reported hitherto.

Experimental.

General.—The vacuum apparatus used in the work was as described in Part I (*loc. cit.*). The preparation of ^{14}C-samples for counting was also carried out as described in Part I, and the counting technique has been reported by Audric and Long (Chemical Research Laboratory, Teddington, Scientific Report CRL/AE. 51).† Materials were of "AnalaR" grade where possible. Specific activities (s.a.) are expressed in microcuries (μc.) per mg. of carbon.

Preparation of Acetylene.—$Ba^{14}CO_3$ (58·5 mg.; gross activity 1·74 μc.) was weighed into a thick-walled Pyrex centrifuge tube which contained finely shredded barium metal (1 g.). Inactive barium carbonate (240·3 mg.) was then added, giving a total of 1·515 millimoles of the carbonate (s.a. 0·096), followed by a further layer of shredded barium (1 g.) as shown in Fig. 1. A slow stream of dry carbon dioxide-free argon was passed through the tube, which was warmed to remove traces of water. On being heated with a full Bunsen flame, the reaction mixture suddenly became incandescent and set to a black mass; the tube was allowed to cool in a desiccator.

Next, a file mark was made at *A* (Fig. 1), and a crack started with a hot rod; the bottom of the centrifuge tube could then be broken off inside a round-bottom flask *C* which was quickly fitted to the apparatus illustrated in Fig. 2. When air in the apparatus had been swept out with a current of hydrogen and cooling baths had been placed round traps *E* and *F* (see Fig. 2), water (30 c.c.) from *B* was slowly added. The resulting solution in *C* was brought to the boil during 20 minutes, boiling under reflux being maintained for a further 20 minutes. In experiments during which the water was *rapidly* brought to the boil, evolution of acetylene tended to be so violent that some of the gas escaped condensation in *F*, as shown by precipitation of cuprous acetylide in bubbler *G*. Acetylene could readily be recovered from this cuprous acetylide by treatment with saturated potassium cyanide solution in a closed evacuated system (cf. the generation of carbon dioxide from barium carbonate as described in Part I, *loc. cit.*).

Taps T_{15} and T_{16} were closed, and trap *F* was detached from the train, and, while still immersed in liquid nitrogen, reattached to a vacuum manifold as shown in Fig. 3. Vessel *K* contained pellets

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* Part II, *J.*, 1950, 3176.

† The intention to publish this work as Part III of the present series has been withdrawn.

of activated charcoal which had previously been heated at 200° *in vacuo*; T_1, T_2, T_3, T_9, T_{12}, and T_{16} were opened, all others being shut, and the system was evacuated. As acetylene reacts with mercury mirrors, it was necessary to keep T_5 and T_8 shut while any part of the system was being cooled.

T_2 was shut, the liquid-nitrogen bath removed from *F*, and acetylene condensed into *K* by cooling it to −78°. T_{12} was shut, and *K* was immersed in ice-water. The acetylene was then desorbed from the charcoal and condensed into *H* (at −196°) by slowly opening T_2 followed by continuous pumping for 5 minutes (subsequent experiments showed that a small amount of unidentified material remained adsorbed on the charcoal). T_1 was closed, and the acetylene distilled from *H* into *I*. The product amounted to 1·03 millimoles (137% " yield "), as determined by pressure measurement in a system of known volume (gross activity of product 1·68 μc., 97%; s.a. 0·068).

Preparation of Ethylene.—In a typical experiment, acetylene (4·98 millimoles; inactive) from *I* (Fig. 3) was distilled into an evacuated vessel *J* which contained an acid solution of chromous chloride frozen in liquid nitrogen; the chromous chloride solution had been prepared from chromic chloride hexahydrate (11 g.) as described by Hatfield (" Inorganic Syntheses," Vol. III, McGraw-Hill, New York, 1950; pp. 148—150) and contained concentrated hydrochloric acid (5 ml.).

T_6 and T_{17} were shut; *J* was removed from the manifold, allowed to warm to room temperature, and shaken mechanically for 6 hours. *J* was then reattached to the manifold, the contents of the flask being first frozen in liquid nitrogen. T_2, T_6, and T_{17} were opened, and when the pressure had fallen to 10^{-3} mm., T_2 was closed. The liquid-nitrogen bath around *J* was replaced by a bath at −78° while *I* was immersed in liquid nitrogen. Ethylene thereby condensed in *I*, final traces being removed by allowing the contents of *J* to melt, followed by a second distillation from *J* at −78° to *I* at −196°. The product amounted to 4·96 millimoles (99·8% yield); it gave no colour with ammoniacal cuprous chloride solution and was completely absorbed by a stirred solution of mercuric sulphate in sulphuric acid of the concentration specified by Francis and Lukasiewicz (*Anal. Chem.*, 1945, **17**, 703).

FIG. 1.

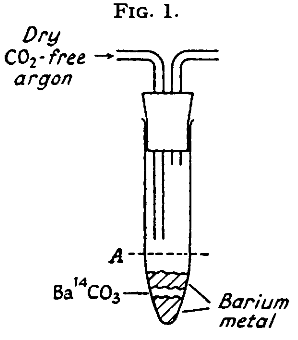
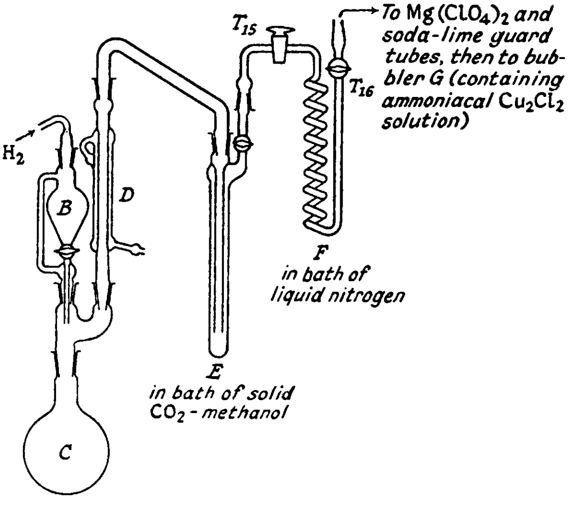


FIG. 2.



In an experiment with ^{14}C-acetylene, the yield of ^{14}C-ethylene was 95%.

Preparation of (a) *Ethylene Chlorohydrin Solution and* (b) *Ethylene Oxide.*—(*a*) To the manifold (see Fig. 4) was attached a flask *L* by way of an adapter *P*. *L* contained a solution of hypochlorous acid (1·8M.; 5 c.c.) prepared by the chlorine–mercuric oxide method (Reformatzky, *J. pr. Chem.*, 1889, **40**, 396) and used immediately after preparation; the use of impure or more dilute solutions of hypochlorous acid gave inferior yields of ethylene chlorohydrin. *L* was immersed in a bath at −78° and evacuated, whereby traces of free chlorine were removed. With T_2 shut, ethylene (4·07 millimoles; gross activity 968 μc.; s.a. 99) contained in *I* was condensed into *L*, now cooled in liquid nitrogen. T_9 and T_{18} were shut; *P*—*L* was removed from the manifold, and shaken mechanically for 2 hours. *P*—*L* was then reattached to the manifold, *L* cooled to −196°, and T_2, T_9, and T_{18} opened. With T_2 shut again, traces of unreacted ethylene and chlorine were distilled from *L* (at −78°) into *I* (at −196°). Finally, T_3 and T_9 were closed, and air admitted to *P*—*L* through T_{10}.

(*b*) While the solution of ethylene chlorohydrin prepared as described in (*a*) was kept frozen (at −78°), a magnetic stirrer capsule and potassium hydroxide pellets (6 g.) were quickly added to flask *L*. The latter was fitted to adapter *O* (Fig. 4), and the whole apparatus evacuated, and T_2 shut. The solid carbon dioxide–methanol bath around *L* was placed around trap *M*, then, as the frozen mass in *L* began to melt, a vigorous evolution of ethylene oxide took place, the product being condensed into *Q* (at −196°) by opening T_6 from time to time; the reaction mixture was stirred magnetically. When the reaction had subsided, the contents of *M* were distilled back into *L* so that the small amount of ethylene chlorohydrin which had distilled into *M* could be caused to react with potassium hydroxide again; finally, the whole process was repeated a third time. The ethylene oxide so obtained amounted to 3·50 millimoles (gross activity 815 μc., 84·2%; s.a. 97). In calculating the number of millimoles of product, allowance was made for the deviation from the ideal-gas laws shown by ethylene oxide. According to Maass and Boomer (*J. Amer. Chem. Soc.*, 1922, **44**, 1709), the deviation was 1·6% at the temperature and pressure of the measurement.

The vapour pressure of the product is compared in the Table with values calculated (by means of the Clausius–Clapeyron equation) from Maass and Boomer's figures (*loc. cit.*) :

Ethylene oxide.	V.p. at 0°, mm.	V.p. at –18·2°, mm.	V.p. at –25·6°, mm.
^{14}C product (see above)	490 ± 4	209 ± 4	138 ± 4
Maass and Boomer	493	211	141

Preparation of Formaldehyde from an Ethylene Oxide Residue.—The alkaline residual solution from a preparation of ethylene oxide (estimated to contain 0·5 millimole of ethylene glycol) was carefully acidified with phosphoric acid. Sodium bismuthate (1 g.) was added, and the reaction mixture slowly distilled (cf. Rigby, *Nature*, 1949, **164**, 185). Formaldehyde was identified in the distillate as its dimedone derivative, m. p. 189°.

FIG. 3.

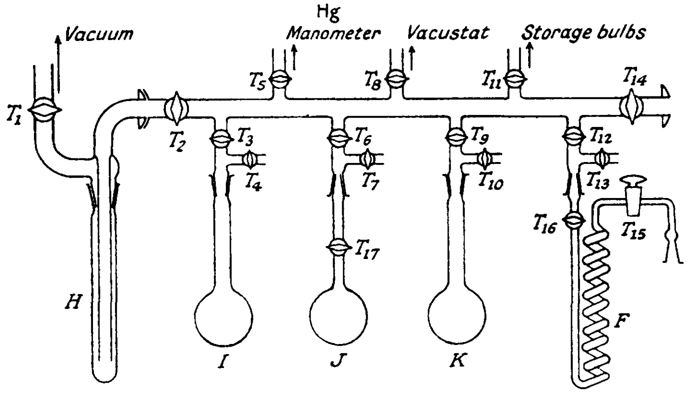
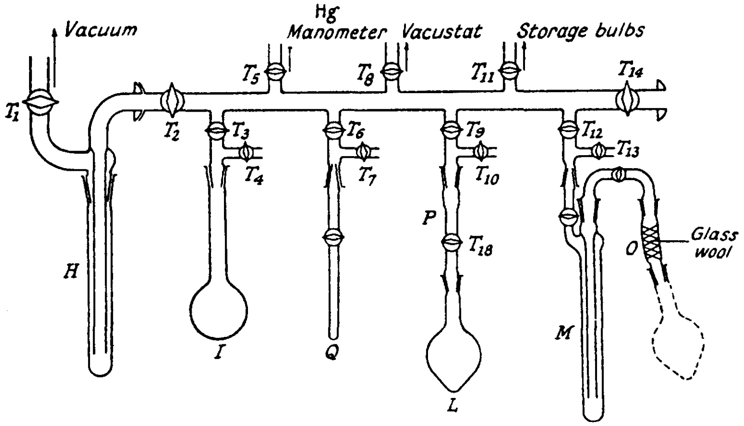


FIG. 4.



Reduction of Ethylene Oxide to Ethanol.—The method was very similar to that described in Part II (*loc. cit.*) for the reduction of acetyl chloride to ethanol. Ethylene oxide (15·95 millimoles; gross activity 0·462 μc.; s.a. 0·00120) was allowed to react at 0° with a stirred solution of lithium aluminium hydride in tetrahydrofurfuryloxytetrahydropyran (0·71M.; 20 c.c., 250% excess). Absorption of the gas was complete within 1 hour. Tetrahydrofurfuryl alcohol (15 c.c.) was then added and ethanol was swept out from the reaction mixture (at 100°), under conditions of partial reflux, by a current of hydrogen during 5 hours. Finally, the crude distillate was subjected to a single-plate distillation (cf. Part II, *loc. cit.*), successive vapour pressure readings (with the liquid reservoir at 20°) being as follows: 39, 38·5, 37, 19·5, 3·5, 0·05 mm. Hg.

The product weighed 0·746 g. and had v.p. (at 0°) of 12·2 mm., n_D^{20} 1·3617, d_4^{20} 0·794 (Found : C, 51·0; H, 13·05. Calc. for C_2H_6O : C, 52·2; H, 13·15%). An analysis by Simmonds's method (*Analyst*, 1912, **37**, 16) showed the presence of *ca.* 3% of methanol (gross activity of product 0·431 μc., 93·3%; s.a. 0·00113).

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