

¹¹C-ACETYLENE

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Acetylene containing carrier carbon which was tagged with 20.4-min ¹¹C first was synthesized more than 30 years ago (1). The carbon oxides labeled with ¹¹C were used which result automatically from hot-atom reactions induced in boron oxide when it is bombarded with protons or deuterons (2). Approximately 3–4 half-lives elapsed during the half dozen main stages involved in the synthesis. Consequently, a maximum of only ~5–10% of the original ¹¹C could have appeared in the product. The overall time soon was shortened (3) by simplifying a major procedural step. However, coupling the carbon atoms from two molecules of ¹¹CO₂ (+ carrier) into the carbon-to-carbon bond of labeled acetylene still required five principal stages.

METHODS

A rapid and direct one-step way to prepare acetylene labeled with ¹¹C in specific activity that is adequate for many purposes is now available. When calcium carbide was bombarded for 12 min with ~2 μA of 15–18-MeV ³He ions in our cyclotron (4), useful amounts of ¹¹C were generated in the ¹²C(³He,⁴He)¹¹C reaction.

Calcium carbide target. About 32 mg (0.5 mmole) of CaC₂ were pressed firmly into a recess milled near an edge of an aluminum target holder. The latter then was attached to the internal cooling probe of our cyclotron (4). The floor of the recess was ~0.45 × 1.15 cm (long axis parallel to the beam edge); its area was ~0.52 cm². Thus the areal density of the CaC₂ target was ~62 mg/cm². The ranges of 15–18-MeV ³He ions in carbon are 31–44 mg/cm² and in calcium are 44–60 mg/cm² (5). Hence, the ³He beam barely was absorbed completely in the target. An excessively thick target was avoided to maximize specific activity.

¹¹C yield. Six minutes after the end of bombardment (EOB) of the CaC₂ with ~2 μA of 15–18-MeV ³He²⁺ ions for 12 min the ¹¹C activity was found to be ~1.0 mCi. Extrapolating to EOB, the

yield was ~1.2 mCi of ¹¹C. Calculations indicate the yield would have been ~1.6 mCi of ¹¹C had a 1-μA beam of 15–18-MeV ³He ions struck the CaC₂ target for 1 hr (~3 half-lives).

¹¹C-acetylene generation. The ¹¹C-acetylene formed automatically and directly when ~4–5 drops of water or of ~5 N H₂SO₄ were added to the bombarded CaC₂ with a long capillary pipet.

The ¹¹C-acetylene (+ carrier) was characterized chemically by the formation of insoluble acetylides of silver or copper when it was bubbled into ammoniacal solutions of salts of these elements. Most of the radioactivity appeared in the precipitates, and it decayed with a half-life of ~20 min. After decay, the dried acetylide precipitates exploded upon ignition.

DISCUSSION

Physics. The cross sections of ¹²C(³He,⁴He)¹¹C are large for a charged-particle reaction. A collection of excitation-function curves of several workers (5, p. 47) reveals substantial agreement that the cross sections exceed ~60 mb in the energy range of ~5–30 MeV, and it has a maximum of 366 ± 26 mb at 8.2 MeV (6). The Q value is +1.85 MeV (5, p. 211); thus there is no threshold although the calculated coulomb barrier is ~2 MeV (5, p. 11).

Although this reaction went well in our cyclotron (4), integration under the excitation-function curves (5, p. 47) indicates the thick-target yields per micro-ampere might become approximately doubled were ¹¹C to be generated in the superior external beams of ³He ions provided by modern biomedical cyclotrons.

The melting point of calcium carbide is given as 2,300°, and its density is listed as 2.22. Its thermal

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conductivity appears to be good since there was little evidence the ^3He beam altered the CaC_2 . Assuming our target were to withstand bombardment with 50 μA of $\sim 30\text{-MeV}$ ^3He ions for 1 hr, the calculated yield becomes ~ 150 mCi of ^{11}C , and the specific activity might exceed ~ 300 mCi/mole (~ 12 mCi/mg of ^{11}C -acetylene).

Generation of 10-min ^{13}N . By the time the bombarded target reached our laboratory in the hospital, any 10-min ^{13}N largely had decayed and no attempt was made to study it. The $^{12}\text{C}(^3\text{He},\text{d})^{13}\text{N}$ reaction has cross sections of $\sim 40\text{--}120$ mb in the $7\text{--}30\text{-MeV}$ range (5, p. 48). Thus, a modern cyclotron might furnish thick-target yields of ^{13}N comparable with those of ^{11}C . We plan to pursue studies near a machine providing a highly energetic external beam of ^3He ions to ascertain whether no-carrier-added $^{13}\text{N-NH}_3$ might be generated (7,8) simultaneously and conveniently in the strong reducing conditions accompanying release of ^{11}C -acetylene.

Chemistry. The reaction $\text{CaC}_2^* + 2 \text{HOH} = \text{HC}^*\text{CH} + \text{Ca}(\text{OH})_2$ is strongly exothermic and the ^{11}C -acetylene spontaneously evolves rapidly when water falls on the target in the dry process for obtaining acetylene from calcium carbide. The $\text{HC}^*\text{CH}^\dagger$ is of course randomly labeled, and it is diluted with relatively large amounts of nonradioactive acetylene. Because water dissolves approximately equal volumes of acetylene, only $\sim 4\text{--}5$ drops were used.

Alternatively, $\sim 4\text{--}5$ drops of $\sim 5 \text{ N H}_2\text{SO}_4$ were added so that precipitation of CaSO_4 forced the reaction rapidly to completion. A slight excess of H_2SO_4 served two purposes: (A) to displace the weakly acidic ^{11}C -acetylene even more completely, and (B) to trap any ^{13}N -ammonia.

BIOMEDICAL POTENTIAL

Inhalation of acetylene in $\sim 10\%$ concentration has been used in measurements of cardiac output and in $\sim 35\text{--}40\%$ concentration in surgical anesthesia. Additionally, HC^*CH may be applicable as such in dynamic studies since blood dissolves almost equal volumes of acetylene. Here the paired 511-keV annihilation \pm γ -rays emitted at 180 deg to each other provide high inherent directionality when they interact simultaneously with detectors which are coupled by coincidence circuitry and which lie on opposite sides of a volume of interest as a labeled bolus traverses it.

\dagger The asterisk (*) is used here to symbolize the randomly alternative positions the ^{11}C atom may be expected to take in compounds into which the carbon atoms of HC^*CH become incorporated.

Of primary interest because of the 20-min half-life of ^{11}C is the ready availability of the HC^*CH to serve as a labeled highly reactive *two-carbon* starting reagent for rapid and facile syntheses of vital substrate or precursor ^{11}C -biomolecules. A few examples suffice to illustrate some of this potential of HC^*CH .

^{11}C -acetaldehyde, ^{11}C -acetate, and ^{11}C -ethanol. $\text{C}^*\text{H}_3\text{C}^*\text{HO}$ is made rapidly and in good yield (1) simply by catalytic hydration of HC^*CH . In turn, the $\text{C}^*\text{H}_3\text{C}^*\text{HO}$ is readily oxidizable to randomly labeled acetate, $\text{C}^*\text{H}_3\text{C}^*\text{OO}^-$, or reducible to ethanol, $\text{C}^*\text{H}_3\text{C}^*\text{H}_2\text{OH}$.

^{11}C -alanine and ^{11}C -lactate. The reaction between $\text{C}^*\text{H}_3\text{C}^*\text{HO}$ and cyanide, in the presence of ammonia, forms the aminonitrile, $\text{C}^*\text{H}_3\text{C}^*\text{H}(\text{NH}_2)\text{CN}$, which is hydrolyzed to alanine, $\text{C}^*\text{H}_3\text{C}^*\text{H}(\text{NH}_2)\text{COOH}$ (Strecker synthesis). In the presence of alkali, the reaction between $\text{C}^*\text{H}_3\text{C}^*\text{HO}$ and cyanide very rapidly forms the cyanohydrin $\text{C}^*\text{H}_3\text{C}^*\text{H}(\text{OH})\text{CN}$, α -hydroxypropionitrile (1). Hydrolysis of the latter gives the corresponding lactate, $\text{C}^*\text{H}_3\text{C}^*\text{HOHCOO}^-$ (1).

Temporal localizations of ^{11}C atoms in this lactate, which are revealed in situ by modern imaging instruments (9), may be found to be different than when ^{11}C -lactate is administered which carries the ^{11}C in the carboxyl position (3).

^{11}C -succinate. A method is available (10) for rapid synthesis of this important intermediary metabolite in which, presumably, the ^{11}C atoms of HC^*CH will locate in the two central positions of the succinate, $-\text{OOC}^*\text{H}_2\text{C}^*\text{H}_2\text{COO}^-$.

Carbon-11 labeling of any of the acids above in positions other than carboxyl may be advantageous in impeding rapid loss of the label.

^{11}C -carbon dioxide. The compactness of the CaC_2 target and its holder simplifies shielding after bombardment. The easy release of ^{11}C -acetylene and its ready combustibility provide a convenient alternative route to $^{11}\text{CO}_2$ at the site of usage over that involved in the discovery of ^{11}C in 1934 (2).

SUMMARY

^{11}C -acetylene formed directly and rapidly in a one-step synthesis when water or $\sim 5 \text{ N H}_2\text{SO}_4$ dropped on calcium carbide, following bombardment of it with ^3He ions. After $\sim 2 \mu\text{A}$ of $\sim 15\text{--}18\text{-MeV}$ $^3\text{He}^{2+}$ had struck ~ 0.5 mmole of CaC_2 for 12 min, the yield of ^{11}C was 1.2 mCi. The calculated yield per microampere for 60 min (~ 3 half-lives) is 1.6 mCi, and the specific activity is 3.2 mCi/mole.

The cross sections of the $^{12}\text{C}(^3\text{He},^4\text{He})^{11}\text{C}$ reaction are sufficiently large at the energies of ^3He ions

provided by modern biomedical cyclotrons that bombardment of CaC₂ with 50 μ A for 1 hr might provide as much as \sim 150 mCi of ¹¹C-acetylene, with specific activity as great as \sim 300 mCi/mole (\sim 12 mCi/mg of ¹¹C-HCCH).

The ready availability of the highly reactive two-carbon reagent, ¹¹C-acetylene, provides new opportunities to exploit the usefulness of 20-min ¹¹C. Projections are made for facile syntheses of randomly labeled two-carbon ¹¹C molecules of potential interest in biomedicine, e.g., acetaldehyde, acetate, and ethanol. Using ¹¹C-acetylene for random labeling of vital acids such as alanine, lactate, and succinate in positions other than carboxyl may be advantageous for applications in nuclear medicine.

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The First World Congress of Nuclear Medicine and Biology will be held in Tokyo and Kyoto, Japan, from September 30 to October 5, 1974, under the auspices of the World Federation of Nuclear Medicine and Biology (WFNMB).

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The Organizing Committee for the Congress is now making extensive preparations and has selected a meeting date that will not conflict with other international congresses in related fields scheduled for that time of year. Since a large number of participants from all over the world are expected, the Organizing Committee would appreciate information from every country on the number of persons who might attend.

A second progress report on the meeting will be mailed out soon. If you have any questions concerning the congress, please contact:

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