Preparation of C^{14}-Cyanide from C^{14}-Carbonate[1]

BY J. A. MCCARTER

The importance of cyanide in the synthesis of organic compounds labeled with isotopic carbon requires that it be made available in high yields by simple and inexpensive procedures starting with carbonate. Several methods[2-6] have been described for the conversion of carbonate to cyanide but each is somewhat unsatisfactory when judged by the above standards. The procedure used in this Laboratory is based on the finding by Hood and Salamon[7] that sodium cyanide can be obtained by heating a mixture of sodium carbonate and zinc dust in a stream of ammonia gas. Work in this Laboratory has shown that it is likely that a thermal decomposition product of ammonia rather than ammonia itself is involved in the reaction because it has been found necessary to pass the ammonia over hot iron before passing it over the mixture of alkali carbonate and zinc. An average yield of the order of 90% of theory can be obtained by using potassium carbonate instead of sodium carbonate and by following the procedure described in this communication.

Experimental.—Powdered anhydrous C^{14}-potassium carbonate (0.001 mole) was thoroughly mixed with approximately 1 g. of zinc dust (Reagent grade) and the mixture was transferred to a porcelain combustion boat (Coors Size 2). The boat was then placed in a Vycor combustion tube (750 mm. in length and 19 mm. inside diameter) containing 3–4 g. of iron wire (0.01 inch diameter "for standardizing") in the form of a loose ball occupying the mid-portion of the tube. The boat was pushed into the tube until it touched the iron wire.

The end of the tube nearest the iron wire was connected to an apparatus for the preparation of dry ammonia gas. The other end was attached to a glass tube dipping beneath the surface of water in a test-tube in order to serve as an indicator of the rate of flow of the gas. Ammonia was prepared by warming concd. ammonium hydroxide and dried by passing through two towers of calcium oxide and one of sodium hydroxide pellets. A stream of ammonia was allowed to flow through the tube and when the air in the apparatus had been displaced the central portion of the combustion tube (that part occupied by the boat and iron wire) was heated electrically at 650° for 4 hours. During this time the flow of gas was maintained at a rapid rate but not so rapid as to force water out of the test-tube. The flow of ammonia was continued while the tube was allowed to cool to room temperature.

The boat and its contents were then transferred to an apparatus for the distillation of hydrogen cyanide. The boat was placed in a suitable erlenmeyer flask connected to a water-cooled condenser and 25 ml. of water was added. The tip of the condenser dipped below the surface of an excess (20%) of the theoretical amount of 1 *N* sodium or potassium hydroxide. The contents of the flask was then acidified by the addition of 2 *N* sulfuric acid and was heated gently until 15 to 20 ml. of distillate had been collected. The alkaline cyanide solution was then evaporated to dryness *in vacuo*[5] or used directly.

Analysis by the argentimetric method of the distillate obtained in several experiments showed yields of 88–93% of theory with an average yield of 90%. The specific activity of C^{14}-labeled cyanide prepared by this procedure was unchanged from that of potassium carbonate used as the starting material. C^{14}-Labeled potassium carbonate was readily obtained by passing $C^{14}O_2$ into a slight excess of 4 *N* potassium hydroxide and evaporating the solution to dryness.

The yield of cyanide was decreased by heating the reaction mixture below 630° or over 670°. It was found that the conversion could be accomplished in higher yields in an iron tube but the product thus obtained was less pure than that obtained using the procedure described in this communication.

DEPARTMENT OF BIOCHEMISTRY
DALHOUSIE UNIVERSITY
HALIFAX, CANADA

RECEIVED AUGUST 1, 1950

(1) The investigation was supported by research grants from the Medical Research Division, National Research Council of Canada.

(2) Cramer and Kistiakowsky, *J. Biol. Chem.*, **137**, 547 (1941).

(3) Adamson, THIS JOURNAL, **69**, 2564 (1947).

(4) Abrams, *ibid.*, **71**, 3835 (1949).

(5) Belleau and Heard, *ibid.*, **72**, 4268 (1950).

(6) Loftfield, *Nucleonics*, **1**, 54 (1947).

(7) Hood and Salamon, *Chem. Zentr.*, **66**, I, 670 (1895).

N,N-Disubstituted Amidines. IV. Heterocyclic Amidines and Cinnamamidines[1]

BY EMIL LORZ, LEWIS P. ALBRO[2] AND RICHARD BALTZLY

The compounds reported in this note were prepared in the prosecution of leads developed in our earlier work on amidines.[3] Compound LXVII[4] was synthesized in the expectation that it would have antihistaminic properties—an expectation that was not fulfilled. The other substances fall into three classes.

(a) **Cinchoninamidines.**—Compounds LXI–LXIII are variations of a type (Compounds XIV–XX) previously reported.[3a] As compared to N,N-di-*n*-hexylcinchoninamidine (XVIII) the chlorine substitution has little effect on potency; the 2-butoxy group increases toxicity and probably potency, without certain advantage.[5]

(b) **Nicotinamidines.**—Since N,N-di-*n*-butylnicotinamidine (LXIV) showed fair activity as an injection anesthetic (about eight times that of Procaine) though impotent when applied topically, Compounds LXV and LXVI were prepared in the hope of finding increased potency combined with the rather low toxicity of the parent substance. Toxicities remained low but the potencies did not increase.

(c) **Cinnamamidines.**—The unsubstituted cinnamamidine (VIII) first reported[3a] had considerable local anesthetic activity (14 times that of cocaine topically, 13 times that of Procaine by injection). Compounds LXVIII–LXX were synthesized to ascertain the effect of alkoxyl substitution. The results with the three substances were fairly consistent. All were more potent than the parent amidine topically and less active by injection. Compounds VIII and LXIX are about equally toxic (LD_{50}, 24 and 30 mg./kg. in mice) while LXVIII and LXX were considerably less so (LD_{50}, 68 and 124 mg./kg.). Work on this series was discontinued in part because all the methoxy cinnamamidines showed a considerable lag in the onset of anesthesia and in part because the necessary intermediates were relatively expensive to prepare.

(1) The work here reported is part of a joint research carried out in collaboration with a pharmacological group in these laboratories.

(2) Biochemical Research Foundation, Academy St., Newark, Delaware.

(3) Lorz and Baltzly, THIS JOURNAL, (a) **70**, 1904 (1948); (b) **71**, 3992 (1949); (c) **73**, 93 (1951).

(4) The Roman numerals refer to the compounds listed in Table I, numbering being consecutive with that of our earlier papers.

(5) Potencies of several of these substances are indicated in an approximate fashion in Table II. The expressions of potency are the same as those employed in our third paper (ref. 3c) and the remarks made there as to the significance that can be attached to local anesthetic tests on laboratory animals apply also to the compounds of the present paper.