of Fluorothene 1 × 1 × 9 inches. The block was machined to a diameter of 0.75 inch with exception of a flange at top of rod to fit a $^3/_4$ inch flare nut. The rod was then drilled with a $^5/_8$ inch drill to within 0.50 inch of the bottom. The reaction vessel assembly consisted of the reaction vessel, a $^3/_4$ inch male to $^3/_8$ inch female adapter and a Kerotest valve.

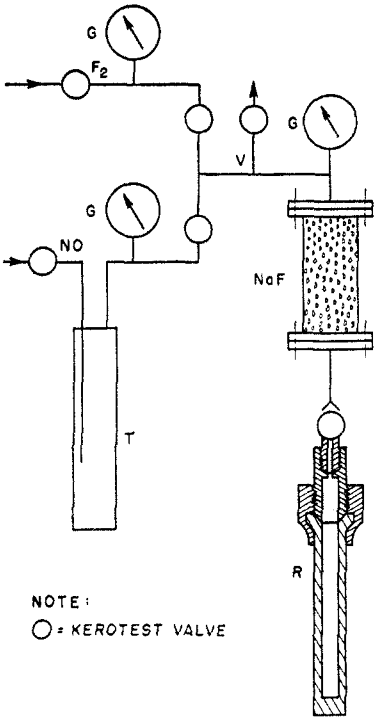

Fig. 1

All connecting lines were of $^3/_8$ inch copper tubing. A vacuum line (V) was used to evacuate the system before and after runs were completed. Brass $^3/_8$ inch S. A. E. flare Kerotest valves with Fluorothene seats were used as indicated.

The nitric oxide (NO) used in the preparation of nitrosyl fluoride was passed through a cold trap (T) cooled to 163°K. to remove any nitrogen dioxide present as an impurity. An isopentane–liquid nitrogen-bath was used to cool the cold trap.

A tower filled with sodium fluoride (NaF) was used to remove any hydrogen fluoride present in the fluorine (F_2).

Vacuum-pressure gages (G) with bronze Bourdon tubes were used as indicated. All gages were of the range 30″ to 60 p.s.i.

Nitrosyl Fluoride.—The system was evacuated and commercial nitric oxide was passed through the cold trap at 163°K. and into the Fluorothene reaction vessel which was cooled in liquid nitrogen. The liquid nitrogen was removed and the nitric oxide was allowed to warm to just above its melting point. Fluorine was then passed through the sodium fluoride tower and allowed to react with the liquid nitric oxide in the reactor. A small yellow flame appeared momentarily upon contact. As this procedure was repeated, the liquid became progressively lighter in color until a colorless liquid product was obtained. The product was frozen down and evacuated to remove any excess fluorine which might be present. The observed molecular weight by the vapor density method was 48.6, calculated for NOF, 49.0. The boiling range at atmospheric pressure was 213–214°K. A yield of better than 90% was obtained.

Nitryl Fluoride.—Nitrogen dioxide used for this preparation was prepared by bubbling oxygen into liquid nitric oxide. As in the preparation of nitrosyl fluoride, the sequence of fluorination steps was continued until a colorless liquid product was obtained. The product was frozen down and evacuated to remove any excess fluorine present. The observed molecular weight was 64.7, calculated for NO_2F, 65.0. The product had a boiling range of 200–201°K. The yield obtained was greater than 90%.

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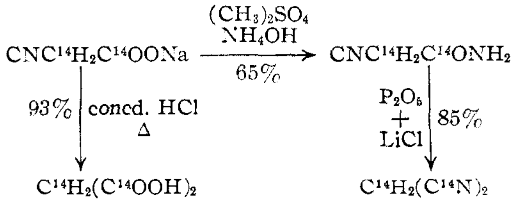
Improved Syntheses of C^{14}-Labeled Malonic Acid and Malononitrile[1]

BY EMERY M. GAL[2] AND ALEXANDER T. SHULGIN

It has been found that the methods published for the preparation of malonic acid rely on the alkaline hydrolysis of cyanoacetic acid, followed either by a several day liquid–liquid extraction of the acidified solution of the isolated calcium malonate with ether[3a,b] or by the liberation of malonic acid from its calcium salt with oxalic acid.[4] One of the methods[3a] gave a crude tan product in 75% yield (from acetate). The other method[3b] described a crude malonic acid of unknown purity in 64% yield (from acetate). The above methods were checked by us in a series of experiments and they led to inconsistent yields, always below that reported in this paper. Conrad's method was found to be unsuited for isotopic work.

The references of the literature employing the acid hydrolysis of cyanoacetic acid to malonic acid were brief and were used only as a method of identification of the former.[5a,b] We have, therefore, undertaken the study of the optimum conditions of this acid hydrolysis and have developed a fast and dependable method of high yield for the preparation of malonic acid. Further verification of our malonic acid was obtained by its conversion, with crotonic acid as intermediate, to DL-threonine (activity 3.1 μc./mg.).

Malononitrile was prepared from cyanoacetamide according to the method of Henry[6] which seemed to be the most suitable. It was found that the introduction of finely ground lithium chloride (10% of the weight of the phosphorus pentoxide used) increased the average yield to 85%. The flow sheet shows the efficiency of the operations.



$$\begin{tikzcd}
CNC^{14}H_2C^{14}OONa \arrow[r, "{(CH_3)_2SO_4 \atop NH_4OH}", "65\%"'] \arrow[d, "93\%"', "{\text{concd. HCl} \atop \Delta}"] & CNC^{14}H_2C^{14}ONH_2 \arrow[d, "{P_2O_5 \atop + \atop LiCl}"', "85\%"] \\
C^{14}H_2(C^{14}OOH)_2 & C^{14}H_2(C^{14}N)_2
\end{tikzcd}$$

Experimental

Preparation of Malonic Acid $C^{14}H_2(C^{14}OOH)_2$.—Chloroacetic acid 4.1 g. (5.9 μc/mg.) prepared according to the procedure of Hughes and Tolbert[7] was dissolved in 8 ml. of

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[1] This work was supported by a grant from the National Cancer Institute, U. S. Public Health Service, to David M. Greenberg.

[2] U. S. Public Health Special Fellow 1948–1950.

[3] (a) Ropp, THIS JOURNAL, **72**, 4459 (1950); (b) Calvin, *et al.*, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 191.

[4] Conrad, *Ann.*, **131**, 349 (1880).

[5] (a) Van't Hoff, *Ber.*, **7**, 1383 (1874); (b) Meisenheimer and Schwarz, *ibid.*, **39**, 2551 (1906).

[6] Henry, *Compt. rend.*, **102**, 1396 (1886).

[7] Hughes and Tolbert, UCRL-256 (University of California Radiation Laboratory).

water and sodium carbonate was added to bring the solution to *p*H 8 (about 2.2 g. of carbonate was required). The solution was then cooled slightly, and 4.2 g. of KCN was added portionwise, with care, to prevent the temperature of the exothermic reaction from exceeding 90°. After the reaction had subsided, the mixture was warmed on a steam-bath for an hour. The solution containing the salt of cyanoacetate was evaporated to dryness *in vacuo* and to the solid sufficient concentrated HCl was added to bring it to *p*H 1. It was then evaporated to dryness *in vacuo* and the solid was transferred with 30 ml. of concentrated hydrochloric acid into a pressure-stopcock bomb-tube which was placed in boiling water-bath for two hours. After cooling the bomb, the solution was transferred into a distillation apparatus and evaporated to dryness *in vacuo* at 70°. The flask containing the solid residue was placed on a high vacuum line (the flask immersed in a dewar flask containing hot water) and left for six hours on the line which was usually sufficient time to complete drying of the solid. The flask was then removed from the line and the solid was extracted three times with 50 ml. of absolute ether. The ether extracts were pooled and filtered. On evaporating the solvent white crystalline malonic acid separated out; yield 3.8 g. (84% based on chloroacetic acid); melting point 130°; activity 556 μc./mM.

Preparation of $C^{14}H_2(C^{14}N)_2$.—1.00 g. of cyanoacetamide (activity 6.6 μc.mg.), 2.5 g. of phosphorus pentoxide and 0.1 g. lithium chloride were thoroughly mixed. This mixture was heated over an open flame, and the malononitrile thus formed was distilled under vacuum (1 m/m) without delay into a Dry Ice cooled receiver. At the end of the distillation, which should not be allowed to exceed five minutes, the receiver must be returned to room temperature before re-admitting air to preclude the condensation of moisture on the malononitrile; average yield 0.672 g. (85.7%); melting point 32°; activity 8.3 μc./mg. (As determined indirectly from a stable malononitrile derivative.)

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The Lithium Aluminum Hydride Test for Aromatic Nitro and Nitroso Groups

BY HENRY GILMAN AND THEODORE N. GOREAU

It has previously been reported, in some highly suggestive work, that "the immediate appearance of the azo color upon adding an aromatic nitro compound to lithium aluminum hydride solution at room temperature constitutes a simple and positive test for the nitro group."[1] However, in extending that orienting work it has been found that some aromatic nitro compounds do not give this test when treated in the above manner.

A procedure has been worked out and tested on acids, amides, amines, aldehydes, ketones, phenols, picrates, esters, hydrazines, benzyl halides, salts, ethers and nitriles containing at least one aromatic nitro or nitroso group. In all, sixty-five different compounds were tested, and the presence of the aromatic nitro or nitroso group was detected in each case, except with potassium 2,4-dinitrobenzenesulfonate.[2]

The test was run by making a saturated solution of lithium aluminum hydride in dry ether or ethylene glycol diethyl ether. A saturated solution of the compound to be tested was made using dry ether or dry ethylene glycol diethyl ether as the solvent.[3] The lithium aluminum hydride reagent was added drop by drop to the solution to be tested until an excess of the reagent had been added. The appearance of any definite color or color change in the solution (or in the precipitate, if one is formed) was judged to constitute a positive test. The colors formed were usually various shades of brown, yellow, orange or red.

The color test was confirmed by pouring the reaction mixture into three ml. of water. Aqueous 50% sulfuric acid was added until all of the salts and hydroxides were dissolved, then two ml. of acid was added in excess. A colored solution, other than the color of the original solution of the compound being tested, was taken as confirmatory evidence for a positive test. A definite change of color was shown by comparing the acidified mixture to a blank. The blank was prepared by using the same quantity of test compound and following the same procedure, except that no lithium aluminum hydride reagent was used.

Experimental

4-Nitrophenylacetonitrile.—One ml. of dry ether was saturated with 4-nitrophenylacetonitrile. A saturated solution of lithium aluminum hydride in ether was added drop by drop to the test solution. A bright red color immediately appeared in the solution; it quickly turned very dark, almost black. The reaction mixture was poured into three ml. of water. Aqueous 50% sulfuric acid was added until all of the solid had dissolved, then two ml. of acid was added in excess. The lower, aqueous, layer was colored red.

Lithium 2,4-Dinitrobenzenesulfonate.—One ml. of boiling dry ethylene glycol diethyl ether was saturated with lithium 2,4-dinitrobenzenesulfonate. A saturated solution of lithium aluminum hydride in dry ethylene glycol diethyl ether was added drop by drop until an excess of reagent was added. A very fine precipitate, which gave the solution a muddy appearance, was formed. Fifteen minutes after the addition of the reagent the mixture was poured into three ml. of water. Aqueous 50% sulfuric acid was added until all of the solid had dissolved, then two ml. of acid was added in excess. The lower, aqueous, layer was colored orange-red.

Potassium 2,4-Dinitrobenzenesulfonate.—Since it is known that mixtures of lithium aluminum hydride and certain aromatic nitro compounds darken when exposed to air and that the yields of azo compounds are diminished,[4] a run was made with potassium 2,4-dinitrobenzenesulfonate using increased amounts of reactants in an inert atmosphere. Hydrolysis and acidification subsequent to a two-hour reaction period showed that a definite color change had taken place. When the reaction described above was run without the benefit of an inert atmosphere it was necessary to use a blank in order to confirm the color change.

Approximately 50 mg. of potassium 2,4-dinitrobenzenesulfonate was suspended in 30 ml. of dry ethylene glycol diethyl ether in a dry three-necked flask equipped with a stirrer, a reflux condenser, and a gas inlet tube. The gas inlet tube was connected to a supply of pure, dry nitrogen. The solution was heated to boiling, then the inlet tube was removed momentarily while 10 ml. of a saturated solution of lithium aluminum hydride was rapidly added. After stirring the reaction mixture for two hours a one-ml. aliquot was removed and hydrolyzed with three ml. of water. Aqueous 50% sulfuric acid was added until all of the solid had dissolved, then two ml. of acid was added in excess. The lower, aqueous, layer was dark red-brown.

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(1) R. F. Nystrom and W. G. Brown, THIS JOURNAL, **70**, 3738 (1948).

(2) It is thought that the failure of this compound to give a positive test is due to its insolubility, since the free acid and the lithium salt of the acid do give a positive test (see, also, Experimental part).

(3) Ethylene glycol diethyl ether seems to be the better solvent due to the increased solubility of some nitro compounds in this solvent. Lithium aluminum hydride is also more soluble in the glycol ether. The approximate molarities of saturated solutions of our lithium aluminum hydride in diethyl ether and ethylene glycol diethyl ether were found to be 0.83 and 1.1, respectively. Tetrahydrofuran is also a good solvent for this test.

(4) Private communication from Dr. Weldon G. Brown.