ber of the acids were prepared. The esters were prepared by modification of a method previously described,[4] and the amides were, in general, made from the corresponding esters by reaction with alcoholic ammonia.

Experimental

Benzoyl-DL-valine Ethyl Ester (I).—A solution of 7.25 g. (0.04 mole) of DL-valine ethyl ester hydrochloride in 19 ml. of water was stirred with 90 ml. of 2 *N* sodium carbonate (0.09 mole) and 200 ml. of chloroform. The mixture was cooled in an ice-bath and a solution of 6.5 g. of benzoyl chloride (0.046 mole, 15% excess) in dry chloroform was added with stirring over a 30-minute period. The ice-bath was removed and the stirring continued for an additional 30 minutes. The chloroform layer was separated and the aqueous layer was extracted twice with chloroform (25 ml.) and twice with ether (25 ml.). All extracts were combined and dried over sodium sulfate. After evaporation of the solvent a yellow sirup was obtained. This was dissolved in 25 ml. of benzene and treated with 275 ml. of hexane. A seed, obtained by pre-treating a small quantity of benzene solution, was introduced and the mixture set aside to crystallize in the cold. Filtration gave 8.2 g. (82%) of I; m.p. 65–68°.

Anal. Calcd. for $C_{14}H_{19}O_3N$: N, 5.62. Found: N, 5.42.

Carbobenzoxy-DL-valine Ethyl Ester (II).—Treatment of 5.5 g. (0.03 mole) of DL-valine ethyl ester hydrochloride with a 15% excess of carbobenzoxy chloride,[5] as described for the benzoyl derivative, yielded an oil which was soluble in benzene–hexane and crystallized on long standing at −12°. Recrystallization from benzene–hexane gave 2.7 g. (32%) of II; m.p. 32–33°.

Anal. Calcd. for $C_{15}H_{21}O_4N$: N, 5.02. Found: N, 5.04.

Carbobenzoxy-DL-leucine Ethyl Ester (III).—This derivative was prepared by treating 5.9 g. (0.03 mole) of DL-leucine ethyl ester hydrochloride with 5.9 g. (0.034 mole) of carbobenzoxy chloride by the same general procedure. The residue obtained after evaporation of the extraction solvent was crystallized from benzene–hexane. The solid was filtered off in the cold; a second crop was obtained from the filtrate; yield 6.9 g. (78%); m.p. 18.5–19°.

Anal. Calcd. for $C_{16}H_{23}O_4N$: N, 4.78. Found: N, 4.79.

Carboallyloxy-DL-valine Ethyl Ester (IV).—Treatment of 5.4 g. (0.03 mole) of DL-valine ethyl ester hydrochloride with 4.2 g. (0.034 mole) of allylchloroformate,[6] according to the general acylating procedure, yielded an oil which showed no tendency to crystallize from benzene–hexane at −12°. Removal of the solvents yielded solid after chilling at −12°. This was washed with cold hexane. The total yield was 2.5 g. (36%); m.p. 9–11°.

Anal. Calcd. for $C_{11}H_{19}O_4N$: N, 6.11. Found: N, 5.94.

Carbobenzoxyglycinamide (V).—Carbobenzoxyglycyl chloride was synthesized according to the method of Bergmann and Zervas. Addition of the acid chloride, obtained from 4.2 g. (0.02 mole) of carbobenzoxyglycine, to 50 ml. of anhydrous ether previously saturated with ammonia, gave a white precipitate. Ammonia was passed through the mixture for 15 minutes. After cooling overnight, the solid was filtered off. This material was extracted with 40 ml. of boiling ethyl acetate and the residue remaining after the extraction was extracted continuously for 7 hours with ethyl acetate, in a Butt extractor. The ethyl acetate extracts were combined, heated to boiling and filtered hot. The filtrate was evaporated until, upon cooling, crystallization occurred. An additional crop was obtained by adding hexane to the filtrate. The combined yield was 2.4 g. (58%); m.p. 133–136°.

Anal. Calcd. for $C_{10}H_{12}O_3N_2$: N, 13.4. Found: N, 13.3.

A second preparation of V was obtained by treating 1.8 g. (0.0075 mole) of carbobenzoxyglycine ethyl ester, in 20 ml. of absolute alcohol, with a stream of ammonia for 45 minutes. After 4 days at room temperature, crystals appeared. The alcohol was removed under reduced pressure and the solid residue was recrystallized from 15 ml. of boiling water. Filtration gave 1.1 g. (71%) of V, m.p. 136–137.5°. A mixed m.p., run with the above preparation, gave 135–136.5°.

Carboallyloxyglycinamide (VI).—Carboallyloxyglycine ethyl ester was prepared by treating 5.6 g. (0.04 mole) of glycine ethyl ester hydrochloride with 5.6 g. (0.046 mole) of allylchloroformate in 25 ml. of carbon tetrachloride. The general procedure described for benzoyl-DL-valine ethyl ester was used. An oil (7.3 g.) was obtained.

The oil dissolved in 50 ml. of absolute alcohol, and dry ammonia gas was passed into the solution for 15 minutes. The flask was stoppered and after 6 weeks (this period was unnecessarily long) at room temperature the alcohol was distilled off under reduced pressure. The solid residue was dissolved in a small quantity of ethyl acetate, and on the addition of hexane, the material crystallized. The yield of VI was 5.5 g. (87%) based on the 0.04 mole of glycine ethyl ester hydrochloride used in the preparation of the intermediate acylamino acid ester; m.p. 107–107.5°.

Anal. Calcd. for $C_6H_{10}O_3N_2$: N, 17.7. Found: N, 17.2.

Carboallyloxy-DL-leucinamide (VII).—Attempts to prepare the corresponding ester from 5.9 g. (0.03 mole) of DL-leucine ethyl ester hydrochloride, according to the general acylating procedure, yielded an oil (7.1 g.).

The oil was dissolved in 50 ml. of absolute alcohol and treated with gaseous ammonia as described above. The sirupy residue which remained after evaporation of the alcohol was dissolved in 25 ml. of hot ethyl acetate. One hundred ml. of hexane was added and after 4 hours at −12°, crystallization commenced. After filtering, washing with hexane, and drying, 1.5 g. (23%) of VII, m.p. 83–85°, was obtained.

Anal. Calcd. for $C_{10}H_{18}O_3N_2$: N, 13.1. Found: N, 13.1.

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(4) S. W. FOX, THIS JOURNAL, **68**, 194 (1946).

(5) M. Bergmann and L. Zervas, *Ber.*, **65**, 1192 (1932).

(6) A generous sample of this compound was furnished by the Columbia Chemical Division, Pittsburgh Plate Glass Co., Pittsburgh, Pa. It was redistilled and stored at −12°.

The Preparation of Nitrosyl Fluoride and Nitryl Fluoride[1]

BY ALBERT V. FALOON AND WILLIAM B. KENNA

The compounds nitrosyl fluoride and nitryl fluoride have been prepared by Ruff, Menzel and Neumann.[2] The method consisted of the vapor-phase fluorination of nitric oxide and nitrogen dioxide with the reaction products being trapped in a quartz vessel. Since these fluorides attack quartz, silicon tetrafluoride and nitrogen sesquioxide were obtained as impurities.

This investigation has shown that a vapor–liquid fluorination carried out in a Fluorothene[3] reaction vessel proceeds very smoothly and without the formation of the above impurities. The fluorinations were carried out at temperatures just above the melting points of the respective oxides.

Experimental

The apparatus used in this investigation is shown in Fig. 1. The reaction vessel (R) was constructed from a block

(1) This document is based on work performed for the Atomic Energy Commission by Carbide and Carbon Chemicals Division, Union Carbide and Carbon Corporation, at Oak Ridge, Tennessee.

(2) Otto Ruff, W. Menzel and W. Neumann, *Z. anorg. allgem. Chem.*, **208**, 293 (1932).

(3) Chlorotrifluoroethylene plastic polymer produced by Carbide and Carbon Chemicals Division, Union Carbide and Carbon Corporation.

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.

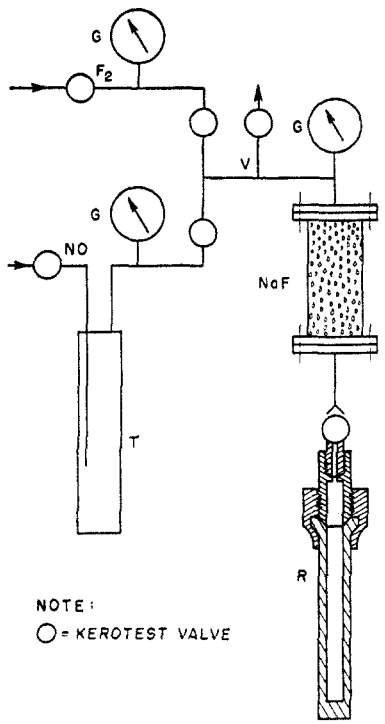

Fig. 1

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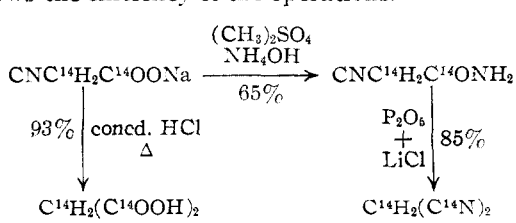
Improved Syntheses of C^{14}-Labeled Malonic Acid and Malononitrile[1]

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.



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

(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).