Anal. Calcd. for CH_2NSO_3K: K, 26.5; CH_2O, 20.4. Found: K, 26.2; CH_2O, 20.0.

Monoclinic prismatic crystals for goniometric study are best obtained from water–ethanol solution. Rapid cooling produces needles, but thin plates, approximately hexagonal in cross section and developed on the 100 face are obtained by slow cooling. The cleavage of this plate (shown in Fig. 2) is principally parallel to the (001) and (011) faces. Its refractive indices are: α, 1.50 (parallel to the b axis); β, 1.505; γ, 1.515. Density by flotation was found to be 2.127 at 25°.

Unit cell dimensions (Å.) are $a = 14.32 \pm 0.04$, $b = 9.73 \pm 0.03$, $c = 20.11 \pm 0.06$ with $\beta = 102.3 \pm 0.3°$; the cell volume is thus 2737 cu. Å., which accommodates the atomic weight equivalent of 24 molecules of potassium methylenesulfamate. The axial lengths have been checked by the face-diagonal measurements, 001 = 22.30 Å. and 110 = 17.35 Å. Extinctions are consistent with space-group $C^6_{2L}(P_{2_1/n})$, namely, $(h0l)$ when $h + l$ are odd and $(0k0)$ when k is odd.

Spacings and relative intensities from the powder diffraction pattern serve in absence of satisfactory melting point as identification of the salt.

I/I_1	d/n	I/I_1	d/n	I/I_1	d/n	I/I_1	d/n
1.0	3.98	0.4	3.18	0.35	2.00	0.25	3.64
0.9	3.35	.4	3.10	.3	7.05	.25	2.11
.8	3.47	.35	8.71	.3	2.59	.2	6.39
.5	5.27					.2	2.46

The apparent molecular weight of the salt was determined by the freezing-point lowering of aqueous solution at several concentrations as shown in Fig. 1. The *p*H of these aqueous solutions was exactly 7.0.

1,3,5-Trinitro-1,3,5-triazacyclohexane (RDX)

A. From Phosphorus Pentoxide.—Into a 200 ml. three-necked flask equipped with a wide sweep powerful stirrer was placed 34.4 ml. (0.8 mole) of absolute nitric acid. The stirred acid, maintained at 0° was treated with 28.4 g. (0.2 mole) of phosphorus pentoxide over two minutes. This mixture was chilled and stirred while 29.4 g. (0.066 mole) of tripotassium 1,3,5-triazacyclohexane-1,3,5-trisulfonate was added over thirty five minutes so as to maintain a reaction temperature of 25–30°. After one hundred

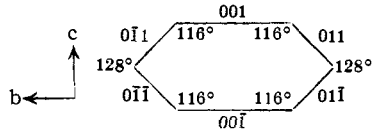


Fig. 2.

fifty minutes more at this temperature the whole was raked into ice (reverse dilution causes decomposition), filtered and washed with dilute ammonia. The vacuum-dried RDX (m. p. 195–197°) weighed 12.4 g. or 84% of theoretical. This was heated cautiously with 50 ml. of 60% nitric acid until by-product decomposition was complete after two minutes, then diluted with 50 ml. of water, cooled and filtered. The product, washed with 3% ammonia and vacuum dried weighed 11.8 g. and melted at 204.3–204.7°.

(b) From Sulfur Trioxide.—The yield was essentially the same as that shown above when 0.01 mole of tripotassium triazacyclohexanetrisulfonate was added to a solution of 0.0225 mole of stabilized liquid sulfur trioxide in 0.11 mole of absolute nitric acid, but the crude (198–201°) and the refined (204.5–204.8°) melting points were slightly better. However the violence of solution of sulfur trioxide in nitric acid (even at −40°) recommends the procedure with phosphorus pentoxide for laboratory use.

Summary

1. Molecular weight determinations by X-ray diffraction studies of the crystal and by freezing point determination of its aqueous solution show that when formaldehyde and potassium sulfamate react they form tripotassium 1,3,5-triazacyclohexane-1,3,5-trisulfonate rather than potassium methylenesulfamate.

2. This trimeric structure is confirmed by nitration studies since only the trimer, 1,3,5-trinitro-1,3,5-triazacyclohexane is produced in absence of 1,3,5,7-tetranitro-1,3,5,7-tetrazacyclooctane.

TORONTO, CANADA RECEIVED FEBRUARY 4, 1950

[CONTRIBUTION FROM THE CHEMISTRY DIVISION OF OAK RIDGE NATIONAL LABORATORY, OAK RIDGE, TENNESSEE]

C¹⁴ Tracer Studies in the Synthesis of Malonic Acid-2-C¹⁴ and Diethyl Malonate-2-C¹⁴ [1]

BY GUS A. ROPP

Although the isotope dilution method for determining the amount of each of several isotopically labeled components in a difficult mixture has been described,[2,3] little attention has been called to its particularly valuable application to determination of successive yields in a series of organic reactions where the scale is so small as to make isolation and identification of the successive products impossible. In the present examples, the syntheses of carbon-14 labeled malonic acid and diethyl malonate by independent methods are described.

In the first and most successful synthesis, a modification of the "Organic Syntheses"[4] procedure was used and the yields of products and of certain intermediates were determined by dilution of appropriate aliquots with the corresponding non-radioactive compounds and radioactive assay of purified derivatives. Potassium acetate-2-C¹⁴ having a millimolar[5] activity of 8 μc. was converted *via* bromoacetic and cyano-

(1) This document is based on work performed under Contract Number W-7405, eng. 26 for the Atomic Energy Project at Oak Ridge National Laboratory.

(2) Calvin, Heidelberger, Reid, Tolbert and Yankwich, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1949, Appendix I.

(3) Keston, Udenfriend and Levy, THIS JOURNAL, **69**, 3151 (1947).

(4) Blatt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, New York, N. Y., 1943, p. 376.

(5) It was suggested by Dr. O. K. Neville that this term be used instead of "molar specific activity of 8 μc. per mmole."

acetic acids to malonic acid-2-C^{14} in 76% yield. That the malonic acid was labeled in only the methylene group was proved by its conversion to 3-(2-furanyl)-propenoic acid-2-C^{14} of identical millimolar activity.

In the second procedure, ethyl acetate-2-C^{14} having a millimolar activity of 25 μc. was converted to diethyl malonate-2-C^{14} in 28.5% yield *via* diethyl oxalacetate which was catalytically decarbonylated in the gas phase[6] at 350°. Intermediate yields were not determined, but a radioactivity balance was obtained; it was therefore possible to determine at which steps the losses in the yield occurred.

Although only tracer levels of radioactivity were used in this work, the processes were designed for use on a 10 mmol. scale with the highest available carbon-14 millimolar activities (approximately 5 millicuries per millimole) and required refined small scale apparatus.

Experimental

The wet combustion and gas counting methods described by Neville[7] were used for all radiochemical assays.

1. **Malonic Acid-2-C^{14} Synthesis: (a) Bromoacetic Acid-2-C^{14}.**—Ten millimoles of potassium acetate-2-C^{14} having a millimolar activity of *ca.* 8 μc. was converted by heating with phosphoric acid to 590 mg. (98% yield) of acetic acid (8.1 μc. per mmole, or a total activity of 79.6 μc.) which was distilled quantitatively into a tared pear-shaped flask in which all subsequent reactions were performed and which could be converted to a continuous extractor for separation of the ultimate product, malonic acid. Two drops of acetic anhydride (equivalent to 0.63 mmols. of acetic acid), 3 mg. red phosphorus, and 0.6 ml. dry bromine were added,[8] and after bromination was completed by heating one hour at 125–135°, hydrogen bromide and excess bromine were removed by bubbling in dry carbon dioxide at 50°. Crude bromoacetic acid (1393 mg.) remained as a clear oil.

Benzylamine Salt.—A sample (13.4 mg.) of the crude bromoacetic acid-2-C^{14} was diluted 79-fold with C. P. bromoacetic acid in ethyl acetate solution, and the benzylamine salt[9] was prepared and crystallized from acetone, m. p. 97–97.5°.

Anal. Calcd. for $C_9H_{12}O_2NBr$: Br, 32.48. Found: Br, 31.4, 31.6.

The millimolar activity was 0.080 μc. corresponding to 6.3 μc. per mmol. for the undiluted bromoacetic acid. The millimolar activity of the acetic acid diluted with acetic anhydride was 79.6/(9.8 + 0.63) = 7.6 μc., and hence the purity of the bromoacetic acid was 6.3/7.6 = 83%. The yield of pure bromoacetic acid was 1393 × 0.83/138.9 (10.0 + 0.63) = 78% based on potassium acetate.

(b) Malonic Acid-2-C^{14} Solution.—The crude bromoacetic acid-2-C^{14} was converted[4] to a solution (total wt. 7.858 g.) of sodium malonate-2-C^{14}.

3-(2-Furanyl)-propenoic Acid-2-C^{14}.—A sample (61.6 mg.) of the solution was diluted 17-fold with C. P. malonic acid and converted to pure 2-furanacrylic acid,[10] millimolar activity 0.048 μc. corresponding to 0.048 × 17/7.6 = 10.7% malonic acid in the solution or a yield of 0.107 × 7.858/104 (10.0 + 0.63) = 76% of malonic acid in solution based on potassium acetate.

(c) Isolation of Malonic Acid-2-C^{14}.—The sodium malonate solution was cooled in ice and acidified to methyl red by bubbling in anhydrous hydrogen chloride. The extractor was set up by attachment of the necessary taper-seal fittings to the reaction bulb, and ether extraction for sixty-six hours separated 820 mg. of tan solid (74% crude yield based on 10.6 mmol. of potassium acetate). After drying at 1 micron pressure one hour, a sample (39.1 mg.) of the crude product was diluted 20-fold and the gross activity was found to be 0.32 μc. per mmol. corresponding to 6.4 μc. per mmol. for the undiluted malonic acid product.

3-(2-Furanyl)-propenoic Acid-2-C^{14}.—A sample (21.2 mg.) of the crude malonic acid-2-C^{14} was diluted 95-fold with C. P. malonic acid and converted to pure 2-furanacrylic acid having a millimolar activity of 0.069 μc. corresponding to 6.5 μc. per mmol. for the undiluted malonic acid. Since the activity present in the malonic acid-2-C^{14} as malonic acid-2-C^{14} was essentially equal to the gross activity, the product was 100% pure radiochemically within experimental error. Comparison of its millimolar activity (6.5 μc.) with that of the acetic acid (7.6 μc.) revealed that the malonic acid was 86% pure chemically, and hence the chemical yield of 100% malonic acid isolated was 0.74 × 0.86 = 64% based on potassium acetate.

β-Phenyl-α-cyanoacrylic Acid.—The product, malonic acid-2-C^{14}, gave only a trace test for halogen and hence contained little if any bromoacetic acid-2-C^{14}. In order to confirm the freedom of the product from activity present as cyanoacetic acid-2-C^{14}, a sample was diluted 4-fold with distilled cyanoacetic acid, and the diluted mixture was converted[11] to pure β-phenyl-α-cyanoacrylic acid which showed only background activity.

2. **Diethyl Malonate-2-C^{14} Synthesis: (a) Conversion of Sodium Acetate-2-C^{14} to Ethyl Acetate-2-C^{14}.**—Anhydrous sodium acetate-2-C^{14} was converted[12] in 93% yield to ethyl acetate-2-C^{14} (286 mg., 3.25 mmol., 25.7 μc. per mmol. or total activity 83.5 μc.).

(b) Diethyl Oxalacetate-2-C^{14}.[13]—The ethyl acetate was condensed at 70° with 3.24 mmols. of diethyl oxalate in the presence of 3.1 mmols. sodium metal dissolved in 2 ml. dry ethanol. The reaction bulb was connected to a vacuum line, and the ethanol containing 22.3 μc. of ethyl acetate-2-C^{14} activity (representing 26.7% of the starting activity) was distilled at 0.1 micron pressure. The dry sodium salt remaining was decomposed by stirring at 0° with 7 ml. benzene and 1.3 ml. 2.85 *N* sulfuric acid, and after separation of the aqueous layer, the benzene solution was washed three times by stirring with 2.5 ml. portions of water. The combined aqueous layers contained 2.8 μc. of activity (3.4% of the starting activity). Crude diethyl oxalacetate-2-C^{14} (309 mg., 51% wt. yield based on ethyl acetate) was obtained by vacuum distillation of the benzene which contained 4.0 μc. (4.8% of the starting activity).

(c) Decarbonylation.—The crude diethyl oxalacetate-2-C^{14} was passed during one hour as vapor at 0.1 to 150 microns pressure up a 7-inch vertical 8-mm. Pyrex tube column filled with glass beads and crushed soft glass and kept at 340–360° by a surrounding electrically heated jacket. The top of the column was sealed to a vacuum line through a U-trap at −190° in which 186 mg. crude diethyl malonate (wt. yield 36% based on ethyl acetate) containing 21.0 μc. activity (25.2% of the starting activity) was condensed. The distillation residue contained 12.2 μc. (representing 14.6% of the starting activity). Thus, a total of 75% of the starting activity was recovered.

Malonic Acid-2-C^{14}.—The yield of 100% diethyl malonate-2-C^{14} was determined by diluting the above crude product 100-fold with C. P. diethyl malonate and saponifying the mixture with cold 20% sodium hydroxide. The resulting malonic acid was purified and found to contain

(6) Altwegg and Maillard, U. S. Patent 1,524,962; *C. A.*, **19**, 991 (1925).

(7) Neville, THIS JOURNAL, **70**, 3501 (1948).

(8) Ward, *J. Chem. Soc.*, 1163 (1922).

(9) Buehler, Carson and Edds, THIS JOURNAL, **57**, 2181 (1935).

(10) Bachman, "Organic Syntheses," Vol. 25, John Wiley and Sons, New York, N. Y., 1945, p. 51.

(11) Gilman, "Organic Syntheses," Coll. Vol. 1, John Wiley and Sons, New York, N. Y., 1941, p. 181.

(12) Ropp, THIS JOURNAL, **72**, 2299 (1950).

(13) J. A. Bassham, Ph.D. Thesis, University of California, Berkeley, 1946.

0.15 μc. per mmol. equivalent to 15 μc. per mmol. for the undiluted diethyl malonate-2-C^{14} product. Hence, the chemical purity of the diethyl malonate-2-C^{14} was 15/25.7 = 58%, and the weight yield of 100% diethyl malonate based on sodium acetate-2-C^{14} was 0.93 × 0.58 × 36% = 19%. The weight yield of 100% diethyl malonate based on unrecovered ethyl acetate-2-C^{14} was 36 × 0.58/(1.00 − 0.267) = 28.5%.

Acknowledgments.—The author wishes to express appreciation to O. K. Neville and W. G. Brown who made helpful suggestions in the course of this work and to B. M. Tolbert and W. L. Johnson who furnished procedures for the preparation of diethyl oxalacetate.

Summary

Potassium acetate-2-C^{14} has been converted in 76% yield to malonic acid-2-C^{14}. Ethyl acetate-2-C^{14} has been converted to diethyl malonate-2-C^{14} in 28.5% yield. Isotope dilution technique has been applied in studying the reactions involved.

OAK RIDGE, TENN. RECEIVED MARCH 6, 1950

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Mechanism of Aromatic Mercuration.[1] I. Orientation Effects

BY WM. J. KLAPPROTH[2] AND F. H. WESTHEIMER

Introduction

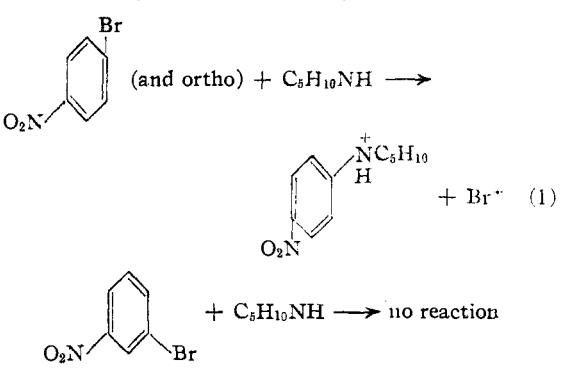
The orientation effects during aromatic substitution are today fairly well understood.[3] During nitration, for example, the OH, NH_2 and CH_3 substituents, present in an aromatic molecule, direct an incoming nitro group to a position ortho or para to the substituent already present, whereas a nitro substituent directs further nitration to the meta position.

It is therefore interesting that mercuration, which occurs quite readily in the aromatic series and which appears (*vide infra*) to be electrophilic substitution, shows a number of anomalies. For although phenol and aniline are mercurated in the ortho and para positions,[4] mercuration of toluene is accompanied by considerable meta substitution,[5] the mercuration of nitrobenzene is reported to be almost random,[6] and mercuration of benzoic acid[7] yields exclusively the compound substituted ortho to the carboxyl group.

It has recently been discovered that mercuration with ionized mercuric salts in strong acid solution[8,9] takes place very much more readily than does the classical mercuration with mercuric acetate in non-polar solvents. It therefore seemed at least possible that the lack of orientation effects in the mercuration of nitrobenzene, etc., was due to the fact that mercuric acetate exists largely, and in non-polar solvents perhaps exclusively, as undissociated molecules, whereas the common electrophilic substituting reagents probably exist either as ions (*e. g.*,[10] NO_2^+) or as highly polarized molecules. The investigations here reported show that mercurations of nitrobenzene and of toluene by mercuric perchlorate in aqueous perchloric acid solutions display the usual orientation effects for electrophilic substitution.

Analytical Methods

The various isomeric mercury compounds obtained on mercuration of nitrobenzene are not readily separable. These compounds were therefore treated with bromine in chloroform solution. This reaction has been shown[11] to lead to replacement, without rearrangement, of the mercury by a bromine atom. The isomeric bromonitrobenzenes can easily be analyzed (for the proportion of meta isomer) by taking advantage of the fact that the halogen atom ortho or para to the nitro group is activated toward replacement reactions, whereas the halogen atom in meta nitrobromobenzene is inert. The reagent chosen for this replacement was piperidine; the sum of the ortho and para isomers was determined by titrating the resulting solution for inorganic bromide ion.



(1) Presented at the Eleventh National Organic Chemistry Symposium, June, 1949, at Madison, Wisconsin.

(2) Atomic Energy Commission Predoctoral Fellow; American Cyanamid Co., Stamford, Conn.

(3) See, for example, G. W. Wheland, "The Theory of Resonance," John Wiley & Sons, Inc., New York, N. Y., 1944, pp. 256-272.

(4) E. Mameli, *Gass. chim. ital.*, **52I**, 352 (1922); O. Dimroth, *Ber.*, **35**, 2032 (1902).

(5) S. Coffey, *J. Chem. Soc.*, **127**, 1029 (1925).

(6) J. Jürgens, *Rec. trav. chim.*, **45**, 61 (1926); S. Coffey, *J. Chem. Soc.*, 3215 (1926).

(7) O. Dimroth, *Ann.*, **446**, 148 (1925).

(8) F. Westheimer, E. Segel and R. Schramm, THIS JOURNAL, **69**, 773 (1947).

(9) R. Schramm, W. Klapproth and F. Westheimer, *J. Phys. Chem.*, in press.

(10) For a good review, see R. Gillespie and D. Millen, *Quart. Rev.*, **2**, 227 (1948).

(11) M. Kharasch and L. Chalkley, Jr., THIS JOURNAL, **43**, 607 (1921).