was collected in one of three ways: (1) in a saturated solution of 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid, (2) in Dry Ice traps, (3) in liquid air traps. The yield of acetone by any of these procedures was in the neighborhood of 80% as determined by precipitation of the 2,4-dinitrophenylhydrazone.

Methods of Activity Measurement.—All samples were converted to carbon dioxide by combustion; the carbon dioxide was collected in an ionization chamber and the activity measured using a Vibrating Reed Electrometer (Model 30, Applied Physics Corporation, Pasadena). Activities are expressed in terms of millivolts per second per millimole. One microcurie of activity corresponds to approximately 350 mv./sec./mmole. An ionization chamber containing a small piece of radioactive polystyrene was used as a standard to eliminate small daily fluctuations of the Reed.

The lithium acetate was assayed by wet combustion of weighed samples with Van Slyke–Folch[12] oxidizing mixture; the carbon dioxide produced was either led directly into the ionization chamber, or collected in carbonate-free base, precipitated as barium carbonate, and the barium carbonate acidified, the liberated carbon dioxide then being led to an ionization chamber as before. The two methods gave results agreeing closely. The activity in Table I is the average of twenty determinations.

The acetone was best assayed by collecting in Dry Ice or liquid air traps, and oxidizing with Van Slyke mixture; attempts to assay the 2,4-dinitrophenylhydrazone gave less satisfactory results. The activity in Table I is the average of nine determinations.

The lithium carbonate was decomposed by acid and converted to barium carbonate which was in turn acidified and the carbon dioxide measured as before. The activity value in Table I is the average of sixteen determinations.

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[12] D. D. Van Slyke, J. Folch and J. Plazin, *J. Biol. Chem.*, **136**, 509 (1940).

DEPARTMENT OF CHEMISTRY AND
RADIOISOTOPE LABORATORY
UNIVERSITY OF NORTH CAROLINA
CHAPEL HILL, N. C.

Friedel–Crafts Synthesis of Functionally Labeled Ketones

BY ROBERT J. SPEER AND J. K. JEANES

This Laboratory, under the auspices of Atomic Energy Contract AT-(40-1)-274, has undertaken to develop suitable methods for the synthesis of functionally labeled ketones from carboxylic acids and their derivatives. Shantz and Rittenberg[1] have reported the preparation of acetophenone-carbonyl-C^{14} from sodium acetate through the intermediate acetic anhydride. Brown and Neville[2] have secured this same product directly from acetic acid. In addition, benzophenone-carbonyl-C^{14} was obtained as an intermediate in a synthesis reported by Fleming and Rieveschl.[3] Despite these investigations, information is unavailable relative to the generality of the methods employed, and in many cases experimental details are lacking. This study had as its primary purpose an evaluation of the generality of the Friedel–Crafts method for production of functionally labeled ketones from carboxylic acids. It has proven feasible to extend this synthetic method to include alkyl–aryl, diaryl and alicyclic ketones. As specific examples, acetophenone-C^{14}, propiophenone-C^{14}, stearophenone-C^{14}, *p*-methylbenzophenone-C^{14}, benzophenone-C^{14}, *p*-methoxybenzophenone-C^{14}, *p*-chlorobenzophenone-C^{14}, acenaphthenone-C^{14} and 1-indanone-C^{14} have been prepared in yields ranging from 71 to 89% of theory. In many cases, existing procedures have been simplified and isotopic conversion efficiencies improved.[4]

In the course of this study, acetophenone and propiophenone have been prepared directly from the corresponding potassium salts of acetic and propionic acid. Eliminating as it does, the necessity for isolation of the free anhydrous acids or the preparation of the volatile acid chlorides and anhydrides, this innovation constitutes a very practical advantage in the handling of isotopic materials.

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[1] E. M. Shantz and D. Rittenberg, THIS JOURNAL, **68**, 2109 (1946).

[2] W. G. Brown and O. K. Neville, Atomic Energy Commission, MDDC-1168.

[3] R. W. Fleming and G. Rieveschl, Jr., Abstract of paper presented before American Chemical Society, New York, September, 1947.

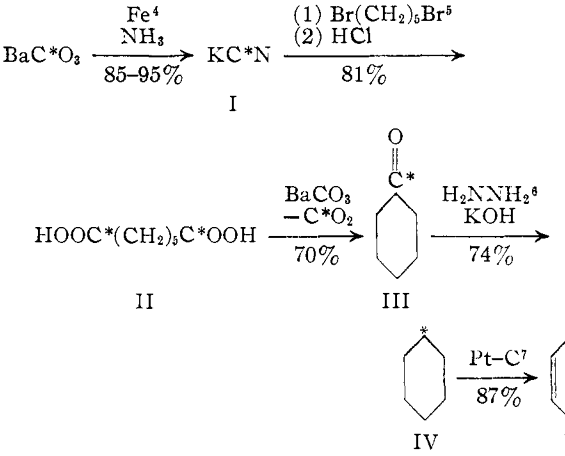
[4] For full experimental details order Document 3501 from American Documentation Institute, 1719 N Street, N. W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35-mm. motion picture film) or $1.00 for photocopies (6 × 8 inches) readable without optical aid.

RADIOCHEMICAL DIVISION
TEXAS RESEARCH FOUNDATION
RENNER, TEXAS
RECEIVED NOVEMBER 30, 1951

A Method for the Synthesis of High Specific Activity Benzene-C^{14} [1,2]

BY ROBERT J. SPEER, MARY L. HUMPHRIES AND AMMARETTE ROBERTS

A semimicro method for the synthesis of high specific activity benzene-C^{14} has been developed. Potassium cyanide-^{14}, pimelic acid-1,7-C^{14}, cyclohexanone-C^{14} and cyclohexane-C^{14} were employed as intermediates in the sequence of reactions[3] as follows:



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[1] This work was done under Atomic Energy Commission Contract AT-(40-1)-274.

[2] Presented at Southwest Regional Meeting of the American Chemical Society, Austin, Texas, December, 1951.

[3] For full experimental details order Document 3500 from American Documentation Institute 1719 N Street, N. W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35-mm. motion picture film) or $1.00 for photocopies (6 × 8 inches) readable without optical aid.

[4] J. A. McCarter, THIS JOURNAL, **73**, 483 (1951).

[5] J. Cason, L. Wallcave and C. N. Whiteside, *J. Org. Chem.*, **14**, 37 (1949).

[6] Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).

[7] R. P. Linstead and S. L. S. Thomas (with K. A. O. Michaelis), *J. Chem. Soc.*, 1127 (1940).

An over-all isotopic conversion efficiency of 22% from $\mathrm{BaC^{14}O_3}$ was achieved.

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Synthesis for Carbon-14 Labeled *dl*-Glutamic Acid

BY ROBERT J. SPEER, AMMARETTE ROBERTS, MARGARET MALONEY AND HENRY R. MAHLER

Under the auspices of the Atomic Energy Commission, Contract AT-(40-1)-274, synthetic methods for *dl*-glutamic acid-5-$\mathrm{C^{14}}$ and *dl*-glutamic acid-1,2-$\mathrm{C^{14}}$ have been developed. *dl*-Glutamic acid-5-$\mathrm{C^{14}}$ has been successfully prepared by modification of the method of Marvel and Stoddard[1] through the sequence of reactions[2,3]

$$\mathrm{BaC^*O_3} \xrightarrow[85\text{–}95\%]{\substack{\mathrm{NH_3}^{4} \\ \mathrm{Fe}}} \underset{\text{I}}{\mathrm{KC^*N}} \xrightarrow[80\%]{\mathrm{ClCH_2CH_2OH}^{5}}$$

$$\underset{\text{II}}{\mathrm{HOCH_2CH_2C^*N}} \xrightarrow[92\%]{\mathrm{HBr}^{5}} \underset{\text{III}}{\mathrm{BrCH_2CH_2C^*OOH}} \xrightarrow[88\%]{\mathrm{C_2H_5OH}^{1}}$$

$$\underset{\text{IV}}{\mathrm{BrCH_2CH_2C^*OOC_2H_5}} + [\mathrm{C_6H_4(CO)_2}]\mathrm{NCH(COOC_2H_5)_2} \xrightarrow[70\text{–}75\%]{\substack{(1)\ \mathrm{NaOH}^{1} \\ (2)\ \mathrm{HCl}}} \underset{\text{V}}{\mathrm{HOOCCH(NH_2)CH_2CH_2C^*OOH}}$$

By this procedure, an over-all isotopic conversion efficiency of 47% on the basis of potassium cyanide was achieved.

The synthesis of *dl*-glutamic acid-1,2-$\mathrm{C^{14}}$, reported by Koegl, *et al.*,[2] during the course of this work, was achieved as follows

$$\mathrm{C^*O_2} \xrightarrow[80\%]{\mathrm{C_2H_5MgBr}^{6}} \underset{\text{VI}}{\mathrm{CH_3CH_2C^*OOH}} \xrightarrow[80\%]{\substack{(1)\ \mathrm{KMnO_4}^{7,8} \\ \mathrm{NaOH} \\ (2)\ \mathrm{Ca^{++}}}}$$

$$\underset{\text{VII}}{\mathrm{(C^*OO)_2Ca}} \xrightarrow[92\%]{\substack{(1)\ \text{IR-100-H} \\ (2)\ \mathrm{Ag^+}}} \underset{\text{VIII}}{\mathrm{(C^*OOAg)_2}} \xrightarrow[70\%]{\mathrm{CH_3I}^{2}}$$

$$\underset{\text{IX}}{\mathrm{(C^*OOCH_3)_2}} \xrightarrow[60\text{–}70\%]{\substack{(1)\ \mathrm{(CH_2COOC_2H_5)_2}^{9} \\ \mathrm{KOCH_3} \\ (2)\ \mathrm{HCl}}}$$

$$\underset{\text{X}}{\mathrm{HOOCCH_2CH_2C^*OC^*OOH}} \xrightarrow[64\%]{\substack{\text{Pd–C}^{2} \\ \mathrm{NH_3\text{–}H_2}}} \underset{\text{XI}}{\mathrm{HOOCCH_2CH_2C^*H(NH_2)C^*OOH}}$$

Utilization of the techniques developed by these investigators, together with modifications from this Laboratory, served to attain an over-all isotopic yield of 20.4% from the starting propionic acid-1-$\mathrm{C^{14}}$.

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(1) C. S. Marvel and M. P. Stoddard, *J. Org. Chem.*, **3**, 198 (1938).

(2) F. Koegl, J. Halberstadt and T. J. Barendregt, *Rec. trav. chim.*, **68**, 387 (1949).

(3) For full experimental details order Document 3502 from American Documentation Institute, 1719 N Street, N. W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35-mm. motion picture film) or $1.00 for photocopies (6 × 8 inches) readable without optical aid.

(4) J. A. McCarter, THIS JOURNAL, **73**, 483 (1951).

(5) W. A. Jacobs and M. Heidelberger, *ibid.*, **39**, 1465 (1917).

(6) M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert and P. F. Yankwich, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 171.

(7) P. Nahinsky and S. Ruben, THIS JOURNAL, **63**, 2275 (1941).

(8) P. Nahinsky, C. N. Rice, S. Ruben and M. D. Kamen, *ibid.*, **64**, 2299 (1942).

(9) *Org. Syntheses*, **26**, 42 (1946).

Yeast Biosynthesis of Radioactive Sulfur Compounds

BY JOHN L. WOOD[1] AND JESSE D. PERKINSON, JR.

RECEIVED AUGUST 30, 1951

The possibility of synthesis of isotope labeled compounds by microörganisms is often dismissed by the organic chemist for lack of special equipment and because of the complexity of the mixtures of products obtained. These problems are minimized in sulfur labeling, due to the distribution of the isotope among relatively few compounds, and by the utilization of yeast culture in ordinary glassware. Moreover, the yeast itself is well established as a dietary supplement and source of protein. Radioactive yeast may be fed for introduction of labels into body sulfur compounds.

The production of yeast labeled with radioactive sulfur has been carried out by use of a synthetic medium[2] containing only the small amount of sulfur furnished by the impurities in C.P. chemicals.[3] Carrier-free $\mathrm{S^{35}}$ sulfate, furnished by the Oak Ridge National Laboratory, was quantitatively incorporated by the yeast which was grown in 500-ml. erlenmeyers on a shaker. The labeled yeast was produced with a high specific radioactivity to permit dilution as desired before use.

Yeast prepared in separate runs of this procedure has been found to vary little in composition. It contained 6% nitrogen which was 50% non-protein. The protein fraction, however, contained 95% of the radioactivity labeled compounds. The biological availability of the sulfur was demonstrated by feeding the yeast as part of the diet of 3 rats. Radioactivity determinations done on blood, liver, kidney, muscle and urine showed an active metabolism of the sulfur compounds had occurred. The direct isolation of radioactive L-methionine and L-cystine from hydrolyzed yeast has been described.[4] Specific activities of the order of one microcurie per microgram of sulfur were obtained after a preliminary dilution of the product, with no indication that this was a limiting value. Analyses showed a moisture content of 5.3%, ash, 6%. Corrected percentage values

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(1) Department of Chemistry, University of Tennessee, Memphis.

(2) A. S. Schultz and D. K. McManus, *Archiv. Biochem.*, **25**, 401 (1950).

(3) For complete experimental details order Document 3482 from American Documentation Institute, 1719 N St., N. W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35-mm. motion picture film) or $1.95 for photocopies (6 × 8 inches) readable without optical aid.

(4) J. L. Wood and G. C. Mills, THIS JOURNAL, **74**, 2445 (1952).