The Isotope Effect. II. Pyrolysis of Lithium Acetate-1-C^{14}

BY ARTHUR ROE AND J. B. FINLAY

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Several recent investigations have established the fact that an appreciable isotope effect may occur in reactions involving carbon-14. Yankwich and Calvin[1] reported a 12% effect in the decarboxylation of malonic-1-C^{14} acid; this work was repeated by Roe and Hellmann[2] who found a 6% effect in the same reaction. Stevens and Attree[3] found a 16% effect in the hydrolysis of carboxy-labeled ethyl benzoate, and Stranks and Harris[4] reported an 11% effect in the absorption of CO_2-C^{14} by a cobaltamine complex. Ropp, Weinberger and Neville[5] found an 8.6% effect at 25° in the dehydration of labeled formic acid. Theoretical discussions of the isotope effect have recently appeared.[6,7]

The pyrolysis of an acid salt yielding a ketone and carbon dioxide (or a carbonate) has been used frequently as a degradative procedure in organic tracer work as a means of determining the amount of isotopic carbon in the carboxyl group of the acid; each of the two products was assumed to contain the same molar concentration of isotopic carbon that was originally present in the carboxyl group. This assumption has been shown to be valid enough under certain conditions for most purposes[8]; however, except for a study of barium adipate in which no fractionation of ordinary carbon containing 1.06% C^{13} was found,[9] no report appeared to be sufficiently exact to preclude the possibility that an over-all isotope effect might be taking place in the reaction where carbon-14 was involved.

A careful study of the pyrolysis of lithium acetate-1-C^{14} was therefore undertaken to determine if an isotope effect did occur; no isotope effect was found. Lithium acetate was chosen because it is reported[10] that pyrolysis of it gave an excellent yield of acetone. The reactions which take place are indicated in the accompanying equations.

$$\left.\begin{matrix}\mathrm{CH_3C^{14}OOLi}\\ \mathrm{CH_3C^{12}OOLi}\end{matrix}\right\} \xrightarrow{490^\circ} \left\{\begin{matrix}\mathrm{CH_3—C^{14}O—CH_3 + Li_2C^{12}O_3} & (1)\\ \mathrm{CH_3—C^{12}O—CH_3 + Li_2C^{14}O_3} & (2)\end{matrix}\right.$$

$$\mathrm{2CH_3C^{14}OOLi} \xrightarrow{490^\circ} \mathrm{CH_3—C^{14}O—CH_3 + Li_2C^{14}O_3} \quad (3)$$

$$\mathrm{2CH_3C^{12}OOLi} \xrightarrow{490^\circ} \mathrm{CH_3—C^{12}O\text{-}CH_3 + Li_2C^{12}O_3} \quad (4)$$

If equations 1 and 2 proceed at different rates, then the molar concentrations of carbon-14 in the acetone and carbonate will differ from each other and from that of the lithium acetate. Reaction 3 is unimportant because of the relatively small amount of tracer material present.

The results of the work are summarized in Table I in which the activities (expressed in millivolts per millimole per second) are compared. Since the activities of the acetone and acetate are identical within limits of experimental error, it is evident that there is no over-all isotope effect. The low value for the activity of the lithium carbonate is attributed to dilution resulting from contamination with $C^{12}O_2$ arising from a certain amount of decomposition which always takes place during the reaction. This was expected in view of the reports[8a,8b] that a certain amount of activity was found in barium carbonate from pyrolysis of *methyl*-labeled barium acetate. (In this Laboratory, Mr. E. L. Albenesius has found that on pyrolysis of methyl-labeled lithium acetate, approximately 2% of the activity was detected in the lithium carbonate formed.)

TABLE I

ACTIVITIES OF REACTANT AND PRODUCTS IN THE PYROLYSIS OF LITHIUM ACETATE-1-C^{14}

Compound	Activity, mv./sec./mmole	Av. deviation from mean
Lithium acetate	49.1	±0.1
Acetone	49.0	± .1
Lithium carbonate	48.2	± .1

It has been pointed out[9] that whether or not an isotope effect will be observed in disproportionation reactions depends on whether or not the labeled atom is involved in the bond rupture (or formation) when the symmetry of the molecule is destroyed. The fact that no isotope effect was found in the present pyrolysis indicates that neither the cleavage nor the formation of a C^{12}–C^{14} bond is involved in a step in which the symmetry of the molecule is altered.

Further work on the isotope effect is in progress in this Laboratory.

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Experimental

Preparation of Lithium Acetate-1-C^{14}.—Acetic acid-1-C^{14} was prepared by carbonation of methylmagnesium iodide with $C^{14}O_2$ at −70° in a manner and in an apparatus somewhat like that previously described.[11] After steam distillation, the acetic acid was neutralized with carbonate-free lithium hydroxide solution, after which a drop of acetic acid in excess was added, and the solution evaporated to dryness. The lithium acetate was recrystallized from ethanol and dried at 110°. Activity measurements taken from time to time over a period of eight months showed no change. Approximately 6 g. of acid having an activity of 150 mv./sec./mmole was prepared; this was diluted 2–3 times with inactive material for the reactions.

Pyrolysis of Lithium Acetate-1-C^{14}.—Ten pyrolyses were carried out as follows: approximately 2.5 mmoles of lithium acetate was weighed into a platinum boat five inches long. The boat was inserted into a platinum sleeve of equal length and the assembly inserted into a Pyrex combustion tube maintained at 490° with an electric furnace. The acetone produced was swept out by means of a nitrogen stream and

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(1) Yankwich and Calvin, *J. Chem. Phys.*, **17**, 109 (1949).

(2) A. Roe and M. Hellmann, *ibid.*, **19**, 660 (1951).

(3) W. Stevens and R. Attree, *Can. J. Research*, **B27**, 807 (1949).

(4) D. R. Stranks and G. M. Harris, *J. Chem. Phys.*, **19**, 257 (1951).

(5) G. A. Ropp, A. J. Weinberger and O. K. Neville, Cleveland Meeting of the Am. Chem. Soc., before the Division of Physical Chemistry, THIS JOURNAL, **73**, 5573 (1951).

(6) J. Bigeleisen, *J. Chem. Phys.*, **17**, 425 (1949).

(7) K. Pitzer, *ibid.*, **17**, 1341 (1949).

(8) (a) H. G. Wood, *et al.*, THIS JOURNAL, **63**, 2140 (1941); (b) M. Calvin, *et al.*, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 248; (c) S. Aronoff, V. A. Haas and B. Fries, *Science*, **110**, 476 (1948).

(9) A. A. Bothner-By, L. Friedman and J. Bigeleisen, Brookhaven Conference Report, BNL 44 (C-10), pp. 39–49.

(10) W. Kronig, *Z. angew. Chem.*, **37**, 667 (1924).

(11) Reference 8b, p. 175, and following.

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
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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

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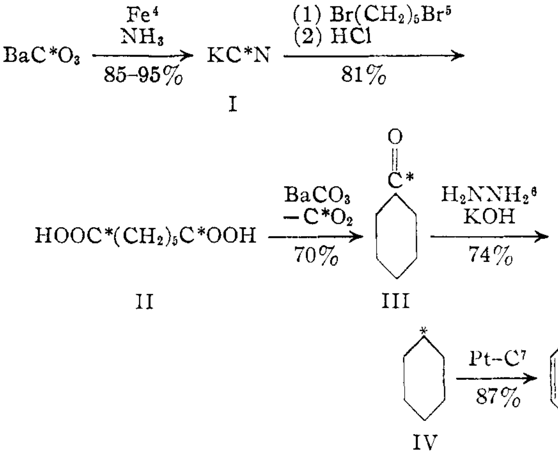
A Method for the Synthesis of High Specific Activity Benzene-C^{14} [1,2]

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).