Samples were degassed at −190°. Alcohols were generally reagent grade or 99+ mol % pure. Commercial grade toluene, *t*-butyl alcohol, *n*-butyl alcohol, and neopentyl alcohol were used as received. Deuterated 2-propanol, $(CD_3)_2CHOH$, >99% D was prepared by a standard procedure[45] from lithium aluminum hydride and acetone-d_6 (Stohler Isotopic Chemicals, >99.5% D). Methanol-O-*d* (>99%) was obtained as a gift from Professor C. Djerassi.

Preparation of Samples. All samples were prepared as gases or gas mixtures (22–28°) directly on a vacuum line, degassed by using 3–5 freeze–pump–thaw cycles, and trap distilled (−190°) directly into a 250-ml gas-sample bulb. The glass-sample bulb was fitted with a high-vacuum stopcock and ground-glass joint for direct introduction of the sample into the unheated inlet of the icr spectrometer. During the course of this study the single inlet of the icr instrument was replaced with a dual inlet which greatly facilitated the introduction of samples into the icr cell. In general the compound which was used as the source of negative ions (*e.g.*, water) was introduced through one inlet, and the other one or two components were introduced through the other inlet. The partial pressures of the neutrals in the icr cell usually were comparable and never exceeded a 5:1 ratio for any two species. The composition of the mixture could be determined by observing the positive ion mass spectrum at the same pressure at which the negative ion reactions were studied. In experiments where no double resonance signal was observed, care was taken to make sure that a sufficient partial pressure of neutral was present for collisions with the ion in question. The total pressure was generally maintained within the range $1–5 \times 10^{-5}$ Torr measured at the Vac-Ion pump.

Instrumentation. The basic icr instrument used was the Syratron mass spectrometer (V-5900) (Serial No. 105) obtained commercially from Varian Associates, Palo Alto, Calif. Auxiliary equipment included a Princeton Applied Research lock-in amplifier (Model JB-4) for phase-sensitive detection, a Hewlett-Packard test oscillator (Model 650A) used as an auxiliary double resonance oscillator, the Varian Associates double resonance oscillator (Model V5918, Serial No. 110), a F. L. Moseley Model 7030A X–Y recorded, a Tetronix type RM 504 oscilloscope, a Hewlett-Packard 5321 B electronic counter, and a Hewlett-Packard 410 C voltmeter.

Single-resonance spectra were obtained by fixing the marginal oscillator frequency (153.5 kHz) and sweeping the magnetic field using, for the most part, a field-modulation phase-sensitive detection scheme. The pulsed double resonance technique[8c,e] was used for all reaction studies. For double resonance, irradiating radio-frequency amplitudes were kept to a minimum, and reactions were studied near the threshold for a double resonance signal. Typical amplitudes were 0.02–0.10 V (peak-to-peak measured externally at the base of the cell). Trapping voltages in the range 0.7–2.5 V were used. Analyzer drift voltages <0.10 V for both analyzer plates were typical. Source drift voltages <1.0 V for both source plates were typical. Trapping and drift voltages were measured at the console (peak-to-peak). The cross-sectional dimensions of the cell in this instrument are 2.54 × 2.54 cm. No special modification in cell design or instrumentation was made for observing negative ions.

Acknowledgment. We thank Dr. J. D. Baldeschwieler for helpful discussions and J. V. Garcia for technical assistance. We gratefully acknowledge support from the National Science Foundation (GP-6736, GP-10621, GP-4924-X), the National Institutes of Health (GP-145652-02), the donors of the Petroleum Research Fund administered by the American Chemical Society (2917-A4), the National Aeronautics and Space Administration (NGR-05-020-250), and the Center for Materials Research, Stanford University.

(45) A. I. Vogel, "Practical Organic Chemistry," 3rd ed, Wiley, New York, N. Y., 1966, p 877.

Protonated Cyclopropanes. V. The Treatment of 1-^{14}C-1-Chloropropane with Aluminum Chloride[1]

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Received February 24, 1970

Abstract: The isotopic scrambling during partial isomerization of 1-^{14}C-1-chloropropane (I-Cl-1-^{14}C) to 2-chloropropane (IV-Cl-^{14}C) induced by treatment with $AlCl_3$ at 0° has been investigated. When the isomerization to IV-Cl-^{14}C was 90%, the recovered I-Cl-^{14}C showed about 7 and 22% rearrangements of the label from C-1 to C-2 and C-3, respectively. Since some conversion of IV-Cl to I-Cl was found to take place under the conditions employed, reversible isomerizations between I-Cl and IV-Cl would contribute to some of the isotope position rearrangements from C-1 to C-3. To account for the scrambling to C-2, it is proposed that equilibrating protonated cyclopropane intermediates were involved, and these would collapse to I-Cl with the ^{14}C-label rearranging to both C-2 and C-3. Small amounts of ^{14}C activity (1.4–3.0%) were found at the C-2 position of the IV-Cl-^{14}C obtained in these experiments. It is suggested that the IV-Cl-2-^{14}C could have arisen from isomerizations involving isotopically scrambled I-Cl-2-^{14}C.

In reactions involving protonated cyclopropane as an intermediate, there is general agreement that the face-protonated structure is not the stable species[2] and that equilibrating edge-protonated cyclopropanes might be preferred over corner protonation.[2,3] Recently, Collins[4] has pointed out that in reactions with 1-propyl derivatives labeled with isotopic carbon at C-1 (*e.g.*, I-X-1-^{14}C), a differentiation between corner and edge protonation may be possible from isotopic scrambling data. If products were formed before equilibrium has

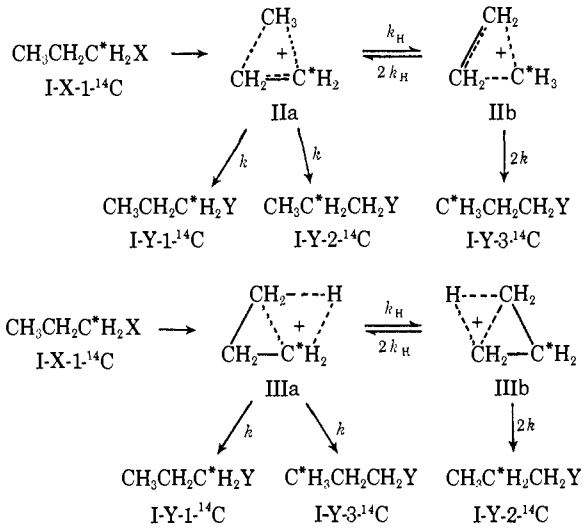
(1) (a) Supported by a grant from The National Research Council of Canada; (b) paper IV, C. C. Lee and W. K.-Y. Chwang, *Can. J. Chem*, **48**, 1025 (1970).

(2) (a) R. Hoffmann, *J. Chem. Phys.*, **40**, 2480 (1964); J. D. Petke and J. L. Whitten, *J. Amer. Chem. Soc.*, **90**, 3338 (1968); (b) C. C. Lee, *Progr. Phys. Org. Chem.*, 7, 129 (1970).

(3) (a) R. L. Baird and A. A. Aboderin, *J. Amer. Chem. Soc.*, **86**, 252 (1964); (b) C. C. Lee and J. E. Kruger, *Tetrahedron*, **23**, 2539 (1967).

(4) C. J. Collins, *Chem. Rev.*, 543 (1969), and private communications from Professor Collins.

been established, from processes involving corner protonation (IIa ⇄ IIb), I-Y-3-^{14}C *can never be* greater than I-Y-2-^{14}C, while from processes involving edge protonation (IIIa ⇄ IIIb), I-Y-3-^{14}C *can be* greater than I-Y-2-^{14}C. It was noted[4] that the formolysis of 1-^{14}C-1-propyl tosylate (I-OTs-1-^{14}C),[5] which gave



0.68 and 0.15% rearrangements of the ^{14}C-label to C-3 and C-2, respectively, in the resulting 1-propyl formate, and the treatment of 1-^{13}C-1-bromopropane (I-Br-1-^{13}C) with $AlBr_3$,[6] which resulted in 10.6 and 3.7% rearrangements of the ^{13}C label to C-3 and C-2, respectively, in the recovered 1-bromopropane, are examples in the literature which gave support to processes involving edge protonation. The present paper reports on studies of the $AlCl_3$-induced partial isomerization of 1-^{14}C-1-chloropropane (I-Cl-1-^{14}C) to isotopically scrambled 1-chloropropane and 2-chloropropane with the view of possibly providing further data in support of edge protonation.

Results and Discussion

I-Cl-1-^{14}C was prepared from I-OTs-1-^{14}C[5] by a displacement reaction as described in the analogous preparation of I-Cl-1-*t*.[7] All the treatments with $AlCl_3$ were carried out by stirring 10.0 g of I-Cl-1-^{14}C with 1.0 g of anhydrous $AlCl_3$ at 0° for 20 min followed by quenching the reaction with ice–water. In preliminary trials with inactive I-Cl, such treatments gave about 80% isomerization to 2-chloropropane (IV-Cl). However, in the initial experiments (expt 1 and 2) with I-Cl-1-^{14}C, isomerization to IV-Cl-^{14}C occurred only to the extent of 65–70% and the reproducibility of the data on isotopic scrambling in the recovered I-Cl-^{14}C (*vide infra*) was not good. It was subsequently noted that the I-Cl-1-^{14}C used in expt 1 and 2 contained traces of diethyl ether, and possibly, the ether may have caused some deactivation of the $AlCl_3$ catalyst. In expt 3 and 4, rigorously purified I-Cl-1-^{14}C and a new batch of anhydrous $AlCl_3$ were utilized. The isomerization to IV-Cl-^{14}C in expt 3 and 4 was found to be 90%. The fact that none of the four experiments with active material could reproduce the preliminary result of 80% isomerization of I-Cl to IV-Cl suggested that such partial isomerization reactions, induced by aluminum halide, would be very susceptible to changes in reaction conditions. This conclusion is in accord with the data of Karabatsos, *et al.*,[6] from similar studies with I-Br-1-d_2 and I-Br-2-d_2, since slight variations in reaction conditions in these experiments gave substantially different results in respect to the extents of isomerization and isotopic scrambling.

The mixture of chlorides, I-Cl-^{14}C and IV-Cl-^{14}C, obtained from the partial isomerization reactions, were converted to the mixed alcohols, I-OH-^{14}C and IV-OH-^{14}C, which were purified and separated by preparative vpc.[8] The extents of isotopic scrambling from C-1 to C-2 and C-3 in the I-OH-^{14}C were determined by degradation through conversions to propionic acid, to acetic acid, and to methylamine as previously described.[3b] The results are summarized in Table I.

Table I. Isotopic Scrambling Data from Degradation of the Recovered ^{14}C-1-Chloropropane (I-Cl-^{14}C) after Treatment of 1-^{14}C-1-Chloropropane (I-Cl-1-^{14}C) with $AlCl_3$ at 0° for 20 Min

	Specific activity,[a] cpm/mmol			—^{14}C distribution, %—		
Expt	CH_3CH_2-COOH[b]	CH_3-COOH[b]	CH_3-NH_2[c]	C-1	C-2	C-3
1[d]	2,341,000	111,800	63,300	95.2	2.1 (1.8)[e]	2.7
2[d]	623,000	49,600	30,500	92.0	3.1 (3.0)[e]	4.9
3	83,600	25,300	18,900	69.7	7.7	22.6
4	65,500	18,500	14,500	71.8	6.1	22.1

[a] Measured by a liquid scintillation counter. [b] Assayed as the *p*-bromophenacyl esters. [c] Assayed as N-methyl-*p*-toluenesulfonamide. [d] The I-Cl-1-^{14}C used in these experiments contained traces of diethyl ether. [e] Measured directly by the activity of the benzoic acid obtained from oxidation of the acetophenone derived from reaction of the active acetyl chloride with benzene.

In the above degradation procedure, the ^{14}C content at C-2 was determined by difference from the activities of the acetic acid and methylamine. Since the presence of ^{14}C at both the C-2 and C-3 positions of the 1-propyl products from reactions of 1-^{14}C-1-propyl substrates is of primary importance in implicating the involvement of protonated cyclopropane intermediates,[3b] Reutov[9] has indicated that it would be desirable to have a direct measurement of the radioactivity at C-2. In the present work, part of the acetic acid obtained from the degradation in expt 1 and 2 was converted to acetyl chloride which was used to acylate benzene to give acetophenone. Oxidation of the latter gave benzoic acid whose radioactivity measured the ^{14}C content at C-2. The results, also given in Table I, are in fairly good agreement with those obtained by the method that was usually employed.

The IV-OH-^{14}C derived from the IV-Cl-^{14}C obtained in the present experiments was also degraded. This was done by conversion to acetone, treatment with phenylmagnesium bromide to give dimethylphenylcarbinol, and then oxidation of the latter to benzoic acid. The activity of the benzoic acid thus is a measure of the amount of isotopic scrambling to C-2 in the IV-Cl-^{14}C obtained from the treatment of I-Cl-1-^{14}C with $AlCl_3$. The results are given in Table II.

(5) C. C. Lee and J. E. Kruger, *Can. J. Chem.*, 44, 2343 (1966).
(6) G. J. Karabatsos, J. L. Fry, and S. Meyerson, *Tetrahedron Lett.*, 38, 3735 (1967).
(7) C. C. Lee, B.-S. Hahn, K.-M. Wan, and D. J. Woodcock, *J. Org. Chem.*, 34, 3210 (1969).
(8) C. C. Lee, W. K.-Y. Chwang, and K. M. Wan, *J. Amer. Chem. Soc.*, 90, 3778 (1968).
(9) O. A. Reutov, private communications.

Table II. Isotopic Scrambling Data from Degradation of the ^{14}C-2-Chloropropane (IV-Cl-^{14}C) Obtained from Treatment of 1-^{14}C-1-Chloropropane (I-Cl-1-^{14}C) with $AlCl_3$ at 0° for 20 Min

Expt	Specific activity, cpm/mmol— CH_3COCH_3[a]	C_6H_5COOH	^{14}C content at C-2, %
1	1,595,000	23,000	1.4
2	1,071,000	16,900	1.6
3	175,000	3,880	2.2
4	347,000	10,500	3.0

[a] Assayed as the semicarbazone.

First of all, let us consider the results in Table II. The data indicate a small amount (1.4–3.0%) of isotope position rearrangement to the C-2 position of the 2-chloropropane (IV-Cl-^{14}C) obtained from the $AlCl_3$-induced partial isomerization of 1-^{14}C-1-chloropropane (I-Cl-1-^{14}C). On the other hand, Karabatsos, *et al.*,[6] reported that in the partial isomerization of 1-^{13}C-1-bromopropane (I-Br-1-^{13}C) with $AlBr_3$, the resulting 2-bromopropane has undergone essentially no isotope position rearrangement. In similar studies using deuterium-labeled I-Br-1-d_2 and I-Br-2-d_2, although the recovered I-Br-d_2 showed substantial amounts (15–20%) of isotopic scrambling, the IV-Br-d_2 obtained was found to be better than 97% isotope position unrearranged.[6] The apparent difference between the present results and those reported by Karabatsos, *et al.*, for the analogous bromopropane systems, however, may not be very significant, and it may reasonably be stated that only relatively small extents of isotope position rearrangements in the 2-halopropanes could have occurred in both of these two sets of experiments. Deno[10] has pointed out that in such partial isomerizations of labeled 1-halopropane to 2-halopropane, since some isotope position rearrangements have taken place in the 1-halopropane, during the course of the reaction, some of the 2-halopropane should have been derived from isotopically scrambled 1-halopropane. The small amount of ^{14}C at the C-2 position of the IV-Cl-^{14}C recorded in Table II could thus be accounted for as arising from isomerizations involving isotopically scrambled I-Cl-2-^{14}C.

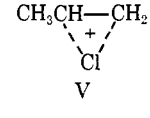
From Table I, it is seen that in all four experiments, there was rearrangement of the ^{14}C label from C-1 to both C-2 and C-3 in the recovered I-Cl-^{14}C, and that more of the rearranged activity was found at C-3 than C-2. These findings, at first glance, might be regarded as in support of a mechanism *via* equilibrating edge-protonated cyclopropanes (IIIa $\rightleftarrows$ IIIb), if Collins' treatment of the isotope scrambling data from 1-^{14}C-1-propyl systems can be applied.[4] However, reversible isomerizations between I-Cl and IV-Cl, as

$$CH_3CH_2C^*H_2Cl \rightleftarrows CH_3CHClC^*H_3 \rightleftarrows ClCH_2CH_2C^*H_3 \quad (1)$$

depicted in (1), could be another route which would cause the rearrangement of the ^{14}C label from C-1 to C-3. Thus a combination of (1) and equilibrating protonated cyclopropanes would also result in locating more of the rearranged label at C-3 than C-2. When 10.0 g of 2-chloropropane (IV-Cl) was treated with 1.0 g of anhydrous $AlCl_3$ at 0° for 10, 20, or 30 min, vpc analysis of the resulting material showed the presence of 1.5–2.0% I-Cl besides the IV-Cl, indicating the occurrence of some reversible isomerizations under the present reaction conditions. If the processes depicted in (1) could reach complete equilibration, then 50% rearrangement of the ^{14}C label from C-1 to C-3 would be observed in any residual I-Cl-^{14}C. In expt 3 and 4, the ^{14}C rearrangement to C-3 is about 22%, indicating that reversible isomerizations between I-Cl-^{14}C and IV-Cl-^{14}C is not complete under the present conditions. However, the fact that some reversible isomerization could have taken place would invalidate, for the present system, the suggestion that a greater amount of rearrangement from C-1 to C-3 than to C-2 may be regarded as evidence in support of edge protonation.

It may also be of interest to consider other scrambling data from 1-propyl systems labeled at C-1 with isotopic carbon. In the nitrous acid deamination of 1-^{14}C-1-propylamine,[3b,11] and in the trifluoroacetolysis of 1-^{14}C-1-propyl tosylate,[1b] the rearranged ^{14}C label in the products was about equally distributed between C-2 and C-3, suggesting that in these reactions equilibration between protonated cyclopropane intermediates has reached equilibrium before product formation and a differentiation between corner and edge protonation is not possible. The implication of reversible isomerizations in the present work, which possibly may also apply in the partial isomerization of I-Br-1-^{13}C,[6] would also render the data from these experiments unsuitable for a differentiation between corner and edge protonation. However, the small amounts of isotope position rearrangement, 0.68% to C-3 and 0.15% to C-2, observed in the formolysis of I-OTs-1-^{14}C,[5] would still fit Collins' criterion that when the equilibration of protonated cyclopropanes has not yet reached equilibrium before product formation, a greater amount of rearrangement of the label to C-3 than C-2 is evidence in support of equilibrating edge-protonated cyclopropanes.[12]

Of pertinence to the present discussion is the report of Frigerio and Shaw[13a] that reaction of ^{36}Cl-1-chloropropane (I-^{36}Cl) with ordinary $AlCl_3$ showed little or no halogen interchange. The actual results, however, did not rule out all halogen exchanges.[13b] For example, when I-^{36}Cl was treated with 2.19 mol % of ordinary $AlCl_3$, the distribution of the total ^{36}Cl activity in the resulting products was 34.9, 63.5, and 1.6%, respectively, in the 1-chloropropane, 2-chloropropane, and chloride ion. The data thus indicated that exchange between $AlCl_3$ and I-^{36}Cl was not complete and these workers[13b] have suggested that one of the possible mechanisms for the isomerization of I-Cl to IV-Cl may involve the formation of chloronium ion V. Since reversible 1,2-hydride shifts involving the 1-propyl and 2-propyl cations were found to be un-



V

(10) N. C. Deno, private communications.

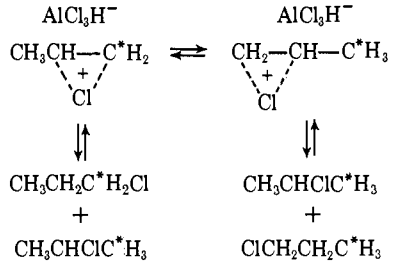
(11) C. C. Lee and K.-M. Wan, *J. Amer. Chem. Soc.*, **91**, 6416 (1969).

(12) Under the formolysis conditions, W. Chwang, in this laboratory, has found that there is no interconversion between 1-propyl and 2-propyl formates.

(13) (a) N. A. Frigerio and M. J. Shaw, Abstracts, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968, ORGN 6; (b) N. A. Frigerio, M. J. Shaw, and D. J. Rausch, Argonne National Laboratory Biological and Medical Research Division Annual Report, ANL-7535, 1968, pp 49–51; private communications from Dr. Frigerio.

important in the deamination of 1-propylamine,[2b] $AlCl_3$-induced reversible isomerizations that led to the rearrangement of I-Cl-1-^{14}C to I-Cl-3-^{14}C (eq 1) probably might have proceeded *via* chloronium ion $AlCl_3H^-$ anion ion pairs (Scheme I) rather than through the classical 1-propyl and 2-propyl cations. Since all halogen exchange between $AlCl_3$ and I-^{36}Cl has not been excluded, formation of the propyl cation $AlCl_4^-$ anion pair or complex has not been eliminated. In such a complex, the cationic moiety could behave as a

Scheme I



classical 1-propyl cation which would undergo irreversible 1,2-hydride shift to give the 2-propyl cation or isomerize to equilibrating protonated cyclopropanes, with the latter collapsing to give a 1-propyl product with rearrangement of the ^{14}C label from C-1 to both C-2 and C-3. Thus the presence of ^{14}C activity at the C-2 position of the recovered I-Cl-^{14}C as recorded in Table I indicated some involvement of equilibrating protonated cyclopropanes (corner or edge protonated) during the treatment of I-Cl-1-^{14}C with $AlCl_3$. Formally, it is possible to account for all the data in Table I by assuming only processes with classical ions, namely, a combination of reversible 1,2-hydride shifts between the 1-propyl and 2-propyl cations and 1,2-methide shifts in the 1-propyl cation. As pointed out above, reversible 1,2-hydride shifts were not observed in the deamination reaction and a 1,2-methide shift in the 1-propyl cation would have to proceed *via* corner-protonated cyclopropane, either as a transition state or an intermediate.

Experimental Section

Reaction of 1-^{14}C-1-Chloropropane (I-Cl-1-^{14}C) with $AlCl_3$. I-Cl-1-^{14}C (10.0 g, 127 mmol) was cooled to 0° in an ice bath and anhydrous $AlCl_3$ (1.0 g, 7.5 mmol) was added. The mixture was stirred for 20 min at 0° and then 100 ml of ice–water was introduced. The organic layer was separated, dried over $MgSO_4$, and analyzed for 1-chloropropane (I-Cl-^{14}C) and 2-chloropropane (IV-Cl-^{14}C) by vpc using a FFAP column.[7] The recovery of the mixture of chloropropanes was in the order of 60%. The aqueous layer from the above treatment was extracted with small portions of ether. The extract was dried and then combined with the main portion of the mixed chloropropanes for conversion to the alcohols.

Degradation Procedures. The mixture of I-Cl-^{14}C and IV-Cl-^{14}C was converted to the corresponding mixed alcohols through reaction of the Grignard reagent with oxygen.[8] The alcohols, I-OH-^{14}C and IV-OH-^{14}C, were separated by preparative vpc[3b] and then diluted with inactive carriers to give sufficient amounts of materials for degradation. The I-OH-^{14}C was degraded by conversions to propionic acid, to acetic acid, and to methylamine as previously described.[3b] In expt 1 and 2, an additional degradation was carried out in order to give a direct measure of the ^{14}C activity at C-2. Part of the active HOAc, as NaOAc, was dissolved in aqueous H_2SO_4 and inactive carrier was added to make up a total HOAc content of 5.0 g. The solution was saturated with NaCl and then continuously extracted with ether. The extract was dried and fractionated in the presence of a high-boiling hydrocarbon to assist the distillation of the HOAc. The recovered HOAc was stirred with 4.0 g of PCl_3 at room temperature for 15 min and then heated under reflux at about 40° for an additional 30 min. The acetyl chloride was recovered by fractionation, the material boiling below 55° being collected. Some benzene was then added and the final traces of acetyl chloride were distilled with the benzene. The resulting solution of acetyl chloride in benzene was diluted with 15 ml of benzene, cooled to about 10°, 5.0 g of anhydrous $AlCl_3$ was added and the mixture was stirred for 1 hr. The resulting material was poured into ice–water. The organic layer was separated, dried over $MgSO_4$, and the benzene was fractionated off to give the crude acetophenone (the overall crude yield was about 50%). Part of the acetophenone was converted to its semicarbazone, mp 198–199°, which was repeatedly crystallized to constant specific activity before being used for ^{14}C assay. The remaining crude acetophenone was oxidized to benzoic acid which was also repeatedly crystallized to constant specific activity.

The IV-OH-^{14}C was first oxidized to acetone. Typically, to a solution of 2.7 g (45 mmol) of IV-OH-^{14}C and 7.5 g of $K_2Cr_2O_7$ in 18 ml of water, 6 ml of concentrated H_2SO_4 was added dropwise. The mixture was refluxed for 10 min and then the acetone was recovered by fractionation, the yield being 2.0 g (77%). Part of the acetone was converted to its semicarbazone, mp 187–188°, which was recrystallized to constant specific activity for ^{14}C assay. The remaining acetone was treated with an excess of phenylmagnesium bromide in dry ether. The reaction mixture was refluxed for 10 min before being decomposed with dilute HCl. The ether layer was separated, dried, and the ether distilled off. The residual dimethylphenylcarbinol, without further purification, was oxidized with $K_2Cr_2O_7$ in 18 *N* H_2SO_4 to give benzoic acid which was also repeatedly crystallized to constant specific activity before being used for ^{14}C assay.