Protonated Cyclopropanes. II. The Solvolysis of Cyclopropane in Tritiated Sulfuric Acid[1,2]

C. C. Lee and L. Gruber[3]

Contribution from the Department of Chemistry and Chemical Engineering, University of Saskatchewan, Saskatoon, Saskatchewan, Canada.

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Abstract: Passage of cyclopropane at room temperature for 3 hr through 9.2 *M* or 13.8 *M* H_2SO_4-*t* resulted in the formation of 1-propanol and 1-propyl hydrogen sulfate. The 1-propanol recovered with the aid of inactive carrier, before or after the hydrogen sulfate was hydrolyzed, showed the presence of tritium in all three carbon positions, the smallest amount being located at C-2. In the 13.8 *M* acid, the heating of the reaction mixture at 50 ± 2° for 30 hr to effect the ester hydrolysis also led to the formation of some 2-propanol. After heating 1-propanol-1-*t* at 50 ± 2° for 30 hr, the recovered 1-propanol also showed some rearrangement of the *t* label to C-2 and C-3. From the experiments which did not involve any complication arising from subsequent reactions of the 1-propanol, the average *t* distribution in the 1-propanol derived from solvolysis of cyclopropane in H_2SO_4-*t* was about 37, 26, and 37%, respectively, at C-1, C-2, and C-3. The mechanistic pathways involving protonated cyclopropane intermediates and the possible influence of isotope effects on the observed isotopic distributions are discussed.

Since the demonstration in 1965 that protonated cyclopropane intermediates are likely responsible for the isotope position rearrangements observed in the 1-propanol obtained from the deamination of isotopically labeled 1-propylamine,[4] there has been an increase in interest in protonated cyclopropanes. Recently, a number of workers have invoked such intermediates in explaining various experimental observations.[5] In considering the problem of 1,3 elimination, Nickon and Werstiuk[6] have listed a large number of references on the formation of three-membered rings by net 1,3 eliminations under a variety of circumstances; protonated cyclopropane intermediates probably may be involved in at least some of these reactions. It appears that these intermediates may be preferably represented as equilibrating edge-protonated cyclopropanes rather than a face-protonated entity.[2,5] The first suggestion of an equilibration of unsubstituted edge-protonated cyclopropanes was made in 1964 by Baird and Aboderin[7] to explain the results from their study on the solvolytic ring opening of cyclopropane in deuterated sulfuric acid. These workers noted that the reaction in 8.4 *M* D_2SO_4 resulted in the formation of 1-propanol and 1-propyl hydrogen sulfate, and after the hydrolysis of the latter, the combined sample of 1-propanol had 0.38, 0.17, and 0.46 D atoms, respectively, at the C-1, C-2, and C-3 positions. More recently, however, Deno[5d,8] has reported that 1-propyl hydrogen sulfate resulting from passage of cyclopropane through D_2SO_4 of various concentrations showed an equal distribution of deuterium atom at each of the three carbon positions. As an attempt to resolve this discrepancy between the observations of Deno and Baird, a study was undertaken on the solvolysis of cyclopropane in tritiated sulfuric acid.

Results and Discussion

Experiments were carried out by passing cyclopropane through 40 ml of 9.2 *M* or 13.8 *M* H_2SO_4-*t* at room temperature for 3 hr. The 1-propanol was then recovered, with the aid of added inactive carrier, either before or after the reaction mixture was heated at 50 ± 2° for 30 hr to hydrolyze the 1-propyl hydrogen sulfate.[7] It was found that in the more concentrated 13.8 *M* acid, the heating of the reaction mixture also resulted in the formation of some 2-propanol. These alcohols were degraded (see Experimental Section) and the distributions of *t* activity ascertained. The results are summarized in Tables I and II.

From Tables I and II, it may be noted that the overall *t* distributions in the 1-propanol from all of the experiments showed lesser *t* contents at C-2 than at C-1 or C-3. Since an unequal rather than an equal *t* distribution was found over the three carbon positions and the smallest amount of label was located at C-2, these results might be regarded as in better agreement with the observations of Baird. Deno,[8b] however, has indicated that the precision of the early data of his group may be about ±5%, and 33 ± 5% of the label on each carbon position would be in fairly good agreement with the present results. As originally suggested by Baird and Aboderin,[7] the observed *t* distributions could be attributed to product formation from equilibrating edge-protonated cyclopropanes, possibly *via* methyl-bridged ions, a lesser amount of

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[1] Supported by a grant from the National Research Council of Canada.

[2] For the first paper in this series, see C. C. Lee and J. E. Kruger, *Tetrahedron*, **23**, 2539 (1967).

[3] Visiting scientist, on leave from the Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest, Hungary.

[4] (a) C. C. Lee, J. E. Kruger, and E. W. C. Wong, *J. Am. Chem. Soc.*, **87**, 3985 (1965); C. C. Lee and J. E. Kruger, *ibid.*, **87**, 3987 (1965); (b) G. J. Karabatsos, C. E. Orzech, Jr., and S. Meyerson, *ibid.*, **87**, 4394 (1965).

[5] (a) C. C. Lee and J. E. Kruger, *Can. J. Chem.*, 44, 2343 (1966); (b) B. M. Benjamin, B. W. Ponder, and C. J. Collins, *J. Am. Chem. Soc.*, **88**, 1558 (1966); (c) H. Hart and R. H. Schlosberg, *ibid.*, **88**, 5030 (1966); (d) N. C. Deno and D. N. Lincoln, *ibid.*, **88**, 5357 (1966); (e) G. J. Karabatsos, N. Hsi, and S. Meyerson, *ibid.*, **88**, 5649 (1966); G. J. Karabatsos, R. A. Mount, D. O. Richter, and S. Meyerson, *ibid.*, **88**, 5651 (1966); (f) A. J. Jurewicz and L. Friedman, *ibid.*, **89**, 149 (1967); (g) G. A. Olah, J. M. Bollinger, C. A. Cupas, and J. Lukas, *ibid.*, **89**, 2692 (1967); (h) G. J. Karabatsos and J. L. Fry, *Tetrahedron Letters*, 3735 (1967).

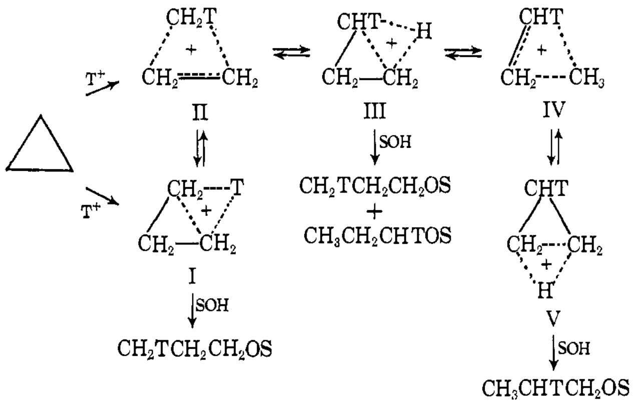
[6] A. Nickon and N. H. Werstiuk, *J. Am. Chem. Soc.*, **89**, 3915, 3917 (1967).

[7] R. L. Baird and A. A. Aboderin, *ibid.*, **86**, 252 (1964).

[8] (a) N. C. Deno, lecture given at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 12–16, 1966. (b) Private communications from Professor Deno.

tritium being incorporated into C-2 since that would require more extensive equilibration (Scheme I).

Scheme I



It is of interest to note that heating of the reaction mixture to hydrolyze the 1-propyl hydrogen sulfate caused no significant changes in the results from the experiments in 9.2 *M* acid (Table I), while such a treatment appeared to give rise to some differences in the over-all *t* distributions in the 1-propanol obtained from reactions in 13.8 *M* acid (Table II). The yields of 1-propanol, as estimated from isotope dilution calculations, indicated no consistent differences between experiments with and without the hydrolysis of the 1-propyl hydrogen sulfate. Probably, any additional 1-propanol liberated during the heating of the acidic reaction mixture might be more or less counterbalanced by the loss of 1-propanol through decomposition.

Table I. Activity Distribution in the 1-Propanol Derived from Solvolysis of Cyclopropane in 9.2 *M* H_2SO_4-*t*

Expt	Yield of 1-C_3H_7-OH, mg[b]	Specific activity,[a] cpm/mmol 1-C_3H_7OH[c]	CH_3CH_2-COOH[d]	CH_3-COOH[d]	*t* distribution, % C-1	C-2	C-3
1[e]	157	9980	6340	3560	36.5	27.8	35.7
2[e]	85	5510	3480	2050	36.8	26.0	37.2
3[f]	142	9140	5700	3330	37.6	25.9	36.5
4[f]	156	9960	6260	3790	37.1	24.8	38.1

[a] Measured by a liquid scintillation counter. [b] Estimated by isotope dilution calculations. [c] Assayed as the 3,5-dinitrobenzoate and corrected for quenching by this derivative; the α-naphthylurethan previously employed in this assay[2] is not suitable since the hydroxyl group of 1-C_3H_7OH would contain tritium. [d] Assayed as the *p*-bromophenacyl esters. [e] The reaction mixture was not heated to hydrolyze the 1-$C_3H_7HSO_4$. [f] The reaction mixture was heated at 50 ± 2° for 30 hr to hydrolyze any 1-$C_3H_7HSO_4$ before the carrier was added and the product isolated.

Table II. Activity Distribution in the 1-Propanol and 2-Propanol Derived from Solvolysis of Cyclopropane in 13.8 *M* H_2SO_4-*t*

	Yield of	Specific activity,[a] cpm/mmol					*t* distribution, %				
	1-C_3H_7OH,		CH_3CH_2-				In 1-C_3H_7OH			In 2-C_3H_7OH	
Expt	mg[b]	1-C_3H_7OH[c]	COOH[d]	CH_3COOH[d]	2-C_3H_7OH[c]	CH_3COCH_3[g]	C-1	C-2	C-3	C-1,3	C-2
5[e,h]	228	49,200	30,600	17,800	...	...	37.8	26.0	36.2	...	...
6[e]	112	24,600	15,700	8,930	...	...	36.2	27.5	36.3	...	...
7[f,h]	196	42,700	25,200	14,100	1,280,000	1,110,000	41.0	26.0	33.0	86.7	13.3
8[f]	131	33,000	19,800	11,100	701,000	590,000	40.0	26.3	33.7	84.1	15.9

[a-f] As in Table I. [g] Assayed as the oxime. [h] From a single experiment, with one-half of the reaction mixture worked up without heating and the other half heated at 50 ± 2° for 30 hr prior to product isolation.

In the more concentrated 13.8 *M* acid, heating of the reaction mixture at 50 ± 2° for 30 hr resulted in the conversion of some of the 1-propanol to 2-propanol. The extraordinarily high specific activities observed in the 2-propanol (Table II) arose obviously from incorporation of tritium from the H_2SO_4-*t* through exchange reactions. Deno[8b] has noted that between 2-propyl hydrogen sulfate and concentrated D_2SO_4, H–D exchange takes place rapidly at C-1 and C-3 and more slowly at C-2. Because of the complication arising from exchange, no mechanistic interpretations could be made on the limited data on *t* distribution at C-1,3 and C-2 of the 2-propanol (Table II).

Baird and Aboderin[7] have reported that there is no exchange between 1-propanol-1,1-d_2 and 8.4 *M* D_2SO_4 at 50°. This has essentially been confirmed. There is no appreciable H–T exchange for the hydrogens of the propyl group of 1-propanol with 9.2 *M* H_2SO_4-*t* at room temperature or 50°, or with 13.8 *M* H_2SO_4-*t* at room temperature. On the other hand, when ordinary 1-propanol was heated in 13.8 *M* H_2SO_4-*t* at 50 ± 2° for 30 hr, about a 30% recovery of a mixture of 1-propanol and 2-propanol was obtained, and of this mixture, roughly one-third was 1-propanol. The observed specific activity per mmole of the recovered 1-propanol, assayed as the 3,5-dinitrobenzoate, was about 5–10% of the specific activity per milligram ion of proton in the H_2SO_4-*t*. This observation suggested the probability that there was some H–T exchange. However, because exchange between 2-propanol and H_2SO_4-*t* was much more rapid (*vide supra*), the specific activity of the 2-propanol, also assayed as the 3,5-dinitrobenzoate, was some 70–80 times that of the 1-propanol. Thus any cross-contamination between these isomeric alcohols through slight overlaps between peaks during the vpc separation would render the observed activity of the 1-propanol quite unreliable.

The effect of the subsequent heating of the reaction mixture in the experiments with 13.8 *M* acid was investigated using 1-propanol-1-*t* (CH_3CH_2CHO + $LiAlH_4$-*t*). When this labeled alcohol was heated at 50 ± 2° for 30 hr in ordinary 13.8 *M* H_2SO_4, the specific activity of the 3,5-dinitrobenzoate of the recovered 2-propanol was only about one-tenth of that of the recovered 1-propanol, thus minimizing any difficulties arising from possible contamination of the 1-propanol by 2-propanol. The low activity of the 2-propanol also further confirmed the loss of some of its *t* activity through exchange with the H_2SO_4. The 1-propanol fractions from two of these experiments were diluted

Table III. Activity Distribution in the Recovered 1-Propanol after Heating 1-Propanol-1-*t* in 13.8 *M* H_2SO_4 at 50 ± 2° for 30 hr

Run	Specific activity,[a] cpm/mmol: Original 1-C_3H_7OH[b]	Recovered 1-C_3H_7OH[b] cor[c]	Recovered 1-C_3H_7OH[b] diltd[d]	CH_3CH_2COOH[e]	CH_3COOH[e]	*t* distribution, %: C-1	C-2	C-3	Activity ratio of 1-C_3H_7OH[f]
1	859,000	988,000	161,000	8,320	4270	94.8	2.5	2.7	1.15
2	859,000	1,000,000	175,000	12,000	5580	93.1	3.7	3.2	1.17
3	859,000	1,020,000[g]	...	...	...	...	...	...	1.19

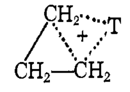
[a] Measured by a liquid scintillation counter. [b] Assayed as the 3,5-dinitrobenzoate. [c] Corrected for dilution with inactive carrier. [d] After dilution with inactive carrier. [e] Derived from the recovered 1-C_3H_7OH after dilution with carrier; assayed as the *p*-bromophenacyl esters. [f] (The corrected specific activity of the recovered 1-C_3H_7OH)/(the specific activity of the original 1-C_3H_7OH). [g] No carrier was added in this run.

with carrier and degraded to give the *t* distributions. The results are summarized in Table III.

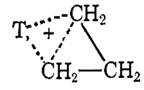
From Table III, it is seen that of the recovered 1-propanol, most of the *t* label remained unrearranged at C-1. Of that portion of the reaction which led to isotopic rearrangements, the label was approximately equally distributed at C-2 and C-3. This behavior of 1-propanol upon being heated at about 50° in 13.8 *M* H_2SO_4 are quite similar to those observed in the deamination of 1-propylamine.[2,4a] The major reaction pathway likely involved the classical 1-propyl cation which could either undergo 1,2-hydride shift to give 2-propanol or react without rearrangement to give unrearranged 1-propanol. Under the present experimental conditions, some 8–10% of the recovered 1-propanol could be derived from processes involving equilibrating protonated cyclopropane intermediates which rendered the three carbon positions of the propyl group equivalent or approaching equivalence. These reactions of 1-propanol upon being heated in 13.8 *M* H_2SO_4 (as well as the possibility of a small extent of H–T exchange between the propyl group and H_2SO_4) likely were responsible for the small differences in the over-all *t* distributions observed in the solvolysis of cyclopropane in 13.8 *M* H_2SO_4-*t*, with and without the subsequent heating of the reaction mixtures (*cf.* expt 5 and 6 with expt 7 and 8, Table II).

Of considerable interest is the finding, recorded in the last column of Table III, that the corrected specific activity of the recovered 1-propanol was some 15–19% greater than the specific activity of the 1-propanol originally used in the experiment. Exchange reactions between the labeled alcohol and the H_2SO_4 medium would be expected to cause a decrease, rather than the observed increase, in the specific activity of the recovered alcohol. The present results thus indicated an apparent enrichment of the *t* label in the recovered 1-propanol. Since only about 30% of a mixture of 1-propanol and 2-propanol was recovered, some 70% of the 1-propanol employed in each experiment was lost by decomposition, probably largely through elimination processes. If there is an isotope effect such that H is lost more readily than T, then the residual alcohol would have a higher *t* content, thus providing for a possible explanation of the observed results. Pertinent to this point is the recent finding of Nickon and Werstiuk[6] that a primary H–D isotope effect of about 2.1 was observed in the 1,3 elimination of *exo*-norbornyl-6-*endo*-*d* tosylate to give nortricyclene at "low base" concentrations which involved an ionic mechanism. An isotope effect involving H and T would, of course, be of greater magnitude than that for H and D. Considering the present studies with 1-propanol-1-*t*, a simple E1 process involving only the classical 1-propyl-1-*t* cation would not require the removal of the *t* label. If indeed a H–T isotope effect were largely responsible for the higher specific activity of the recovered 1-propanol, the observation could be regarded as lending further support to the involvement of protonated cyclopropanes. Movement or shifting of the *t* label of the original 1-propanol, such as in equilibrating protonated cyclopropanes intermediates, would have to be invoked before the elimination of H or T.

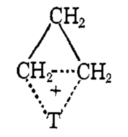
From the present experiments that did not involve complications arising from subsequent reactions of the 1-propanol (expt 1–6, Tables I and II), the average *t* distribution in the 1-propanol was about 37, 26, and 37%, respectively, at the C-1, C-2, and C-3 positions, while Baird and Aboderin[7] have noted that the analogous *d* distribution was 38, 17, and 46%. The difference between these two sets of results, if significant, might also be interpreted in terms of isotope effects. Scheme I shows all the isotopically different protonated cyclopropane intermediates involved in the present reaction. If protonation proceeds initially to give II as the first intermediate,[9] there could be an isotope effect in the subsequent T shift to I and the H shift to III. If a D label were involved, the H–D isotope effect would be smaller than the H–T isotope effect. Consequently, with T labeling, the contribution to product formation from I would be less and from III and V would be more than the analogous processed involving the D label. The over-all effect would fit qualitatively the difference between the present results and those of Baird and Aboderin.[7] It is also possible that edge-protonated cyclopropane I might be formed directly without proceeding through II as the first intermediate. Along with the H shifts shown in Scheme I, T shifts could also occur to give rise to the isotopically equivalent Ia–c, all of which would lead to a product with the label at C-3. The difference in isotope effect from the



Ia



Ib



Ic

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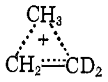
[9] Karabatsos and coworkers[4b] have suggested the initial formation of



as one possible explanation for the production of an equal amount of $C_2H_4DCHDOH$ from the deamination of either 1-propyl-1,1-d_2-amine or 1-propyl-2,2-d_2-amine.

use of D or T as label would result in a relatively smaller contribution of Ia–c in the case of T labeling. The net effect would again qualitatively account for the difference between the present results and those obtained from protonation in D_2SO_4.[10]

Experimental Section

Solvolyses and Degradations. Each reaction was carried out by passing Matheson 99% cyclopropane, purified as described by Baird and Aboderin,[7] through a sintered-glass bubbler in a gas washing bottle containing 40 ml of 9.2 *M* (20 ml of 98% H_2SO_4 and 20 ml of H_2O-*t*) or 13.8 *M* (30 ml of 98% H_2SO_4 and 10 ml of H_2O-*t*) tritiated sulfuric acid. The bubbling was allowed to continue at room temperature for 3 hr at a rate of about 30 ml of cyclopropane/min.[7] In some of the experiments, the resulting solution was heated at 50 ± 2° for 30 hr to hydrolyze any 1-propyl hydrogen sulfate,[7] while in other cases, this hydrolytic treatment was omitted. The reaction mixture was cooled and neutralized by 25% NaOH solution. Inactive 1-propanol (3.0 ml) was then added as carrier, and the resulting aqueous solution was distilled, about 5–10 ml of of distillate being collected. To the distillate 200 ml of ether was introduced, and the water present was removed by drying over anhydrous $MgSO_4$. After concentration of the ether solution, the 1-propanol was recovered by preparative vpc using a column packed with 20% Carbowax 20M on Chromosorb P.[2] The 1-propanol was degraded by oxidation to propionic acid and then to acetic acid.[2] All samples were converted to the appropriate solid derivatives, purified, and counted to give the *t* distribution as described previously.[2]

In the cases in which some 2-propanol was also formed, this alcohol, without any carrier, was separated from the 1-propanol by preparative vpc through the same Carbowax column. It was then diluted with inactive 2-propanol before being oxidized in acid dichromate to acetone.[11]

Yields of 1-Propanol from Isotope Dilution. The isotope dilution calculations were based on the following considerations. Assuming the incorporation of one proton per molecule of cyclopropane, let x = mmoles of active 1-propanol formed, then (cpm/mg ion of H^+ of the H_2SO_4-*t*)x = (x + mmoles of carrier)(cpm/mmol of the recovered 1-C_3H_7OH). Knowing the specific activities of the H_2SO_4-*t* and the recovered 1-propanol, x can be calculated.

Studies with 1-Propanol-1-*t*. Four milliliters of 1-propanol-1-*t* in 40 ml of 13.8 *M* H_2SO_4 was heated at 50 ± 2° for 30 hr. The resulting mixture was worked up as in the solvolysis of cyclopropane to give about 0.25 g of recovered 1-propanol and about 0.70 g of 2-propanol. After dilution with some carrier, the 1-propanol was degraded the usual way to give the *t* distribution.

Acknowledgment. The valuable comments of Dr. R. L. Baird and Professors N. D. Deno and C. J. Collins in regard to the present work were highly appreciated.

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(10) A referee has suggested that if I were the first formed species and if there is a kinetic isotope effect in the conversion of I to II (Scheme I), then this would favor more product formation from I than from III, and one would expect an even greater excess of T at C-3 than is found in studies with D labeling. If such an effect were of greater importance than the argument that product formation from Ia–c would be smaller in the case of studies with T labeling than with D labeling, then the present results would be more in accord with II as the first formed species,[9] with kinetic isotope effect favoring its conversion to III over its conversion to **I**.

(11) F. G. Mann and B. C. Saunderson, "Practical Organic Chemistry," 4th ed, Longmans, Green and Co. Ltd., London, 1960, p 333.

Protonated Cyclopropanes. III. The Reactions of Lucas Reagent with Cyclopropane and with 1-Propanol[1]

C. C. Lee, W. Kao-Ying Chwang, and Kwok-Ming Wan

Contribution from the Department of Chemistry and Chemical Engineering, University of Saskatchewan, Saskatoon, Saskatchewan, Canada.

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Abstract: Passage of cyclopropane through $ZnCl_2$ in 12 *M* HCl-*t* resulted in the formation of 1-chloropropane with no detectable 2-chloropropane. The *t* label was found in all three carbon positions of this product, the isotopic distribution being about 38, 19, and 43%, respectively, at C-1, C-2, and C-3. The reaction of 1-propanol-1-*t* with ordinary Lucas reagent gave chiefly 1-chloropropane with 4–6% 2-chloropropane. Degradation of this 1-chloropropane showed a total of about 1% isotope position rearrangements, the rearranged isotopic label being about equally distributed at C-2 and C-3. The roles played by equilibrating protonated cyclopropane intermediates in these two reactions and in others suggested by previous tracer work are discussed.

In the preceding paper,[2] the results of Baird and Aboderin,[3] obtained from their study on the solvolysis of cyclopropane in D_2SO_4, have essentially been confirmed by a reinvestigation using H_2SO_4-*t*. In order to explore another possibility of protonation of cyclopropane followed by ring opening product formation, the reaction of cyclopropane with Lucas reagent containing HCl-*t* has been studied. In addition, the reaction of 1-propanol-1-*t*[2] with ordinary Lucas reagent was investigated to ascertain whether protonated cyclopropane intermediates would play any role in this conversion of 1-propanol to 1-chloropropane.

Results and Discussion

Cyclopropane was passed through tritiated Lucas reagent, made up of equimolar quantities of 12 *M* HCl-*t* and $ZnCl_2$, for 24 hr at room temperature. The chloropropane formed was swept out by the excess cyclopropane and collected in cold traps containing inactive 1-chloropropane as carrier. Isotope dilution calculations showed that the yields of 1-chloropropane were of the order of 5 g. The magnitude of such yields was confirmed by inactive experiments without the use of any carrier; such inactive experiments also

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(1) Supported by a grant from the National Research Council of Canada.

(2) C. C. Lee and L. Gruber, *J. Am. Chem. Soc.*, **90**, 3775 (1968).

(3) R. L. Baird and A. A. Aboderin, *ibid.*, **86**, 252 (1964).