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TRACER STUDIES IN CLEAVAGE OF ALLYL-1-C¹⁴-
TRIMETHYLAMMONIUM CHLORIDE, ALLYL CHLORIDE-1-C¹⁴,
ALLYL ALCOHOL-1-C¹⁴ AND p-TOLYL ALLYL-1-C¹⁴ SULFIDE
WITH METALS

A THESIS

Presented to
the Faculty of the Graduate Division
by
Suresh Chandra

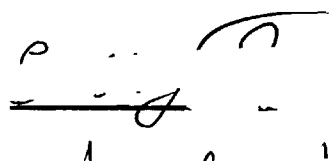
In Partial Fulfillment
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Doctor of Philosophy in the
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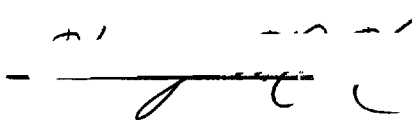
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March, 1961

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Approved:





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Feb. 13, 1961

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SUMMARY

Allyltrimethylammonium chloride, allyl chloride, allyl alcohol and *p*-tolyl allyl sulfide (all labeled in the allyl group with carbon-14 predominatingly at carbon-1) have been synthesized starting with radioactive sodium cyanide.

Reductive cleavages of radioactive and non-radioactive allyl compounds have been studied most extensively with sodium and lithium. Zinc dust in acetic acid was also used to cleave allyl chloride and allyltrimethylammonium chloride. Most of the reactions with alkali metals were carried out in liquid ammonia with or without the addition of ammonium chloride. The effect of addition of ammonium sulfate and of methanol was also studied in the reaction of allyltrimethylammonium chloride with sodium in liquid ammonia. Once 2-propanol was used as a solvent in reaction of allyltrimethylammonium chloride with sodium.

The gases evolved in the reactions were analyzed for propylene and methane by an infrared absorption technique. In a few reactions (only of non-radioactive allyltrimethylammonium chloride and allyl chloride) the products were analyzed for olefins by gas chromatography. Allyl chloride was found to react with sodium in liquid ammonia without ammonium chloride to give diallyl as major olefin with propylene and a few per cent of products which, on the basis largely of their

retention times, are judged to be isomers of bialllyl. Addition of ammonium chloride to the liquid ammonia solution greatly increased the yield of propylene relative to bialllyl and gave no detectable amount of isomers of bialllyl. Bialllyl and its isomers were also produced in cleavage of allyltrimethylammonium chloride though in poorer yields than in cleavage of allyl chloride. These results suggest that bialllyl is produced by reaction of allyl carbanion with allyl compounds by mechanism S_N2 and that ammonium chloride greatly reduces the amount of bialllyl by rapid protonation of allyl carbanion to give propylene. However these results do not rule out the possibility of concurrent or prior formation of allyl radical as an intermediate, and there is some possibility that part of the bialllyl is formed through dimerization of allyl radicals since ammonium chloride did not entirely eliminate the formation of bialllyl.

Ozonization of the propylene, formed from cleavages of allyl-1- C^{14} compounds, gave formaldehyde with 3.3 to 13.5 per cent greater radioactivity than in the concomitant acetaldehyde. These results are strikingly independent of the structure of the organic compound, the nature of the metal, the nature of the solvent or the reaction temperature (-72° to 50°). The addition of ammonium chloride lowers the radioactivity in formaldehyde by 2.0 to 9.8 per cent. A similar effect is observed on addition of methanol or upon using 2-propanol as solvent. It is likely that allyl-1- C^{14} -tri-

methyllumonium chloride and *p*-tolyl allyl-1-C¹⁴ sulfide are rearranged to the corresponding propenyl-1-C¹⁴ compounds to some extent by bases such as allyl carbanion or amide ion and that the rearranged reactants upon reductive cleavage give propylene-1-C¹⁴ (but no propylene-3-C¹⁴). No such rearrangement of the reactants seems likely in presence of ammonium chloride or other acid.

A tentative conclusion of this study is that a kinetically free allyl carbanion is produced as an intermediate during reductive cleavage of allyl compounds and that protonation of this carbanion gives propylene. In runs in which ammonium chloride, methanol, 2-propanol and acetic acid were present, the ratio of activity of formaldehyde methone derivative to that of acetaldehyde methone derivative (obtained from ozonization of propylene) was 1.056 ± 0.016 . The most likely explanation for this ratio is that an isotope effect (k_{12}/k_{14}) of this order of magnitude exists in the protonation of allyl carbanion.

CHAPTER I

INTRODUCTION

Reductive cleavage of allyl compounds with metals.--Ingold¹ has reviewed the topic of reduction by dissolving metals. It seems clear that such reductions generally occur not with "nascent" (or atomic) hydrogen but with electrons and protons supplied from different sources. It has been shown by Kraus and others^{2,3} that alkali metals dissolve in liquid ammonia with dissociation into electrons and metal ions^a. The

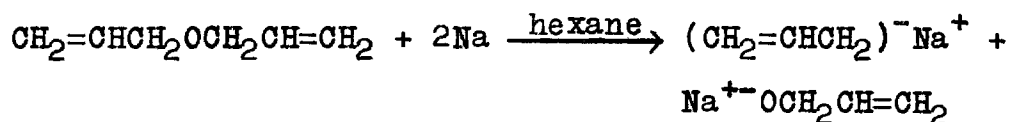
^aAccording to a recent review by Symons³ there are two general theories for metal solutions. These are known as the "expanded-metal" theory and the cavity theory. The former presents a solution containing solvated positive ions, with the valence electrons of the metal moving in "expanded orbitals" around these solvated ions. This theory is not new, but has recently been given prominence by Becker, Lindquist and Alder who explain the formation of electron-pairs by postulating an "expanded-metal" dimer in which two solvated cations are weakly bound together by two electrons of opposed spins. The cavity theory, favored by Kraus, presents a solution containing solvated metal ions and solvated electrons. The solution is thought to resemble that of any strong electrolyte except that, in place of negative ions in cavities or oriented solvent molecules, there are electrons in similar cavities.

¹C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., (1953) pp. 700-704.

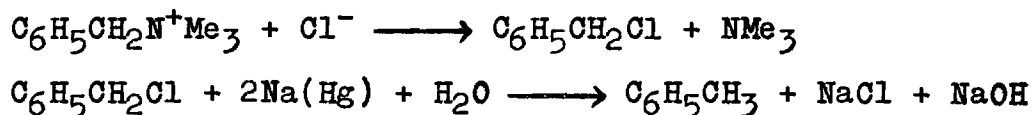
²(a) C. A. Kraus, J. Am. Chem. Soc., **30**, 653 (1908);
(b) S. Freed and N. Sugarman, J. Chem. Phys., **11**, 354 (1943).

³M. C. R. Symons, Quart. Rev. (London), **13**, 99 (1959).

question of whether protons enter the reducible system before, during, or after transfer of electrons from the metal can not be generally answered. In some cases, at least, protons need not be involved at all in order for reduction to occur. An example is the cleavage of diallyl ether by sodium in hexane⁴:



For reductive cleavage of quaternary ammonium halide Emde⁵ has suggested that the ammonium salt dissociates into alkyl halide and tertiary amine and subsequently the alkyl halide is reduced by sodium and water to hydrocarbon. Thus for benzyltrimethylammonium chloride Emde's scheme is:



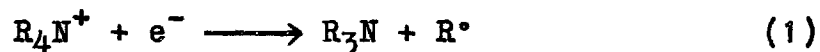
Arguments against this mechanism have been presented by Grovenstein and coworkers⁶. Two reasonable mechanisms have been suggested for the reductive cleavage reactions, the

⁴R. L. Letsinger and J. G. Traynham, J. Am. Chem. Soc., 70, 3342 (1948).

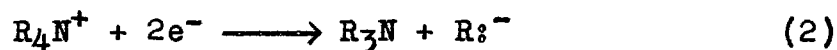
⁵(a)H. Emde, Arch. Pharm., 247, 314 (1909); (b) H. Emde and H. Kull, ibid., 272, 469 (1934).

⁶E. Grovenstein, Jr., E. P. Blanchard, Jr., D. A. Gordon and R. W. Stevenson, J. Am. Chem. Soc., 81, 4842 (1959).

carbanion and free radical mechanisms⁷. The electron transfer to a quaternary ammonium cation may consist of one-electron or two-electron addition in the cleavage step:



or



The radicals produced from 1 may be reduced readily to carbanions:



The final products then result from proton transfer from the solvent, S-H:



These mechanisms leave unanswered the complex questions as to whether the two-electron addition of equation 2 occurs as two successive one-electron additions or one two-electron addition and whether the cleavages shown in equations 1 and 2 occur during or after the indicated electron additions.

This general scheme of reductive cleavage has been discussed by Birch⁸ especially for the cleavage of ethers and alcohols. The influence of structure upon reaction rate (as generally judged by competitive reactions) was, in the

⁷E. Grovenstein, Jr. and R. W. Stevenson, *ibid.*, 81, 4850 (1959).

⁸A. J. Birch, *Quart. Rev. (London)*, 4, 69 (1950).

cases studied by Birch, such as to suggest that cleavage occurred by two-electron addition. Hazlehurst, Holliday and Pass⁹ have more recently suggested that the cleavage of tetra-n-alkylammonium halides was by one-electron addition. Their chief evidence was the formation of traces of ethane from methylammonium halides, though the production of dimeric products is not an argument in favor of radical-intermediates because sufficiently reactive anions can attack the starting material, but its absence is somewhat better evidence against the formation of radicals.

The principal evidence that proton transfer (equation 4) occurs after rather than simultaneously with the formation of carbanions (equations 2 and 3) is that cleavages⁷ of tetraalkylammonium halides with sodium gave similar ratios of products in liquid ammonia and dioxane though dioxane is a poorer proton donor than liquid ammonia.

It was concluded by Grovenstein and coworkers⁷ that methyl and the higher primary alkyl groups probably cleave from nitrogen as carbanions while secondary and tertiary alkyl groups predominantly cleave as free radicals. While the relative rates of cleavage are primarily due to stabilizing or destabilizing effect of α -alkyl groups upon incipient carbanions or radicals in the transition state for cleavage, secondary and especially tertiary alkyl groups are assisted by steric acceleration.

⁹D. A. Hazlehurst, A. K. Holliday and G. Pass, J. Chem. Soc., 4653 (1956).

Krug and Tocker¹⁰ studied the reductive cleavage of n-alkyl sulfides, allyl sulfide, allyl mercapton and thiophene in liquid ammonia in presence of ammonium ions. The metals most often used were lithium and sodium. Beryllium was also used in cleavage of allyl sulfide, but no reduction occurred. It was observed that a metal with a high-cell potential favors a greater reduction of the organic compound than a metal of lower potential (e.g. in reduction of allyl sulfide lithium gave 88 per cent of allyl mercapton and 12 per cent of hydrogen sulfide, while under the same conditions sodium gave 38 per cent of allyl mercapton and 2 per cent of hydrogen sulfide). The authors suggested the formation of carbonions as possible intermediates during their cleavage studies.

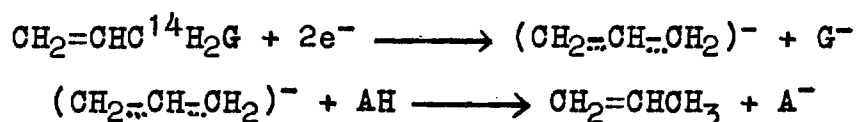
Alteration of the connecting atom can also change the ease of fission. From the order of acidities $\text{SH} > \text{OH} > \text{NH}$ (dependent in part on decreasing nuclear charge) it appears that the fission of sulfur compounds should be easier, and that of nitrogen compounds more difficult, than that of the corresponding oxygen compounds. Unlike saturated ethers, dialkyl sulfides are reduced readily with sodium in ammonia¹¹. Very few amines undergo fission except under drastic conditions¹².

¹⁰R. C. Krug and S. Tocker, J. Org. Chem., 20, 1 (1955).

¹¹F. E. Williams and E. Gebauer-Fuelnegg, J. Am. Chem. Soc., 53, 352 (1931).

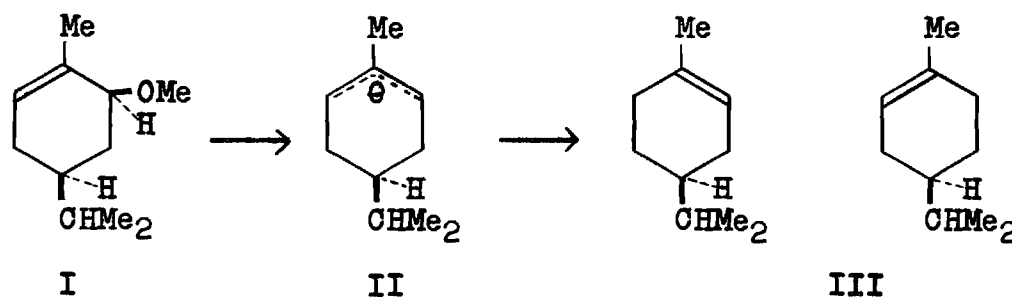
¹²E. Stoelzel, Ber., 74, 982 (1941).

In the present work an attempt is made to study cleavage of allyl compounds by metals by labeling one end of the allyl group with carbon-14. Such a study allows one to decide whether the suspected allyl carbanion formed is kinetically free.



If a kinetically free allyl carbanion is formed, then (neglecting any intramolecular isotope effect) the propylene produced should consist of a 50/50 mixture of $\text{C}^{14}\text{H}_2=\text{CHCH}_3$ and $\text{CH}_2=\text{CHC}^{14}\text{H}_3$. On the other hand, if proton donation occurs simultaneously with bond cleavage, then the product expected would be $\text{C}^{14}\text{H}_2=\text{CHCH}_3$ and/or $\text{CH}_2=\text{CHC}^{14}\text{H}_3$ but would not be an equimolar mixture of these two materials unless the two rate constants for the formation of the two materials just happened to be the same for all of the compounds studied under all of the conditions employed. The optically active methyl ether of carvotanacetol (I) has been found to give racemic *p*-menth-1-ene (III) upon reductive cleavage in ethylamine with lithium; the reaction has accordingly been interpreted to proceed by way of a symmetrical intermediate, presumably a mesomeric allylic carbanion¹³ (II).

¹³A. S. Hallsworth, H. B. Henbest and T. I. Wrigley, Chem. & Ind. (London), 522 (1956).



Reactions of some allyl-1-C¹⁴ compounds.--Recently some reactions of allyl-C¹⁴ have been reported by Nystrom and coworkers¹⁴. The normal bimolecular nucleophilic displacement, S_N2, has been observed in the reactions: conversion of allyl chloride-1-C¹⁴ to allyl-1-C¹⁴ ethyl ether, transformation of allyl chloride-1-C¹⁴ to diethyl allyl-1-C¹⁴-malonate, and the reduction of allyl chloride-1-C¹⁴ to propene-3-C¹⁴ by lithium aluminum hydride. The unimolecular substitution, S_N1, has been observed in the reactions: solvolysis of allyl chloride-1-C¹⁴ in 99.5 per cent formic acid, and the formation and subsequent hydrolysis of allyl-1-C¹⁴ and allyl-3-C¹⁴ magnesium chloride to propene-C¹⁴. Results not explainable on the basis of one of the more common mechanisms are: the solvolysis of allyl chloride-1-C¹⁴ to allyl alcohol-C¹⁴ by silver hydroxide and water, and the deamination of allylamine-1-C¹⁴ by nitrous acid in water and acetic acid.

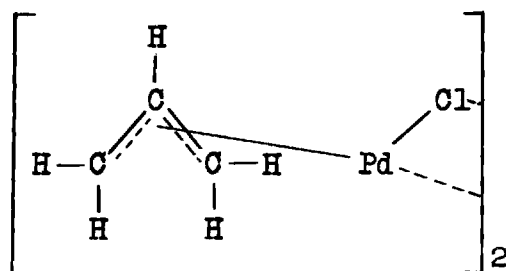
Structures of some allylic metallic compounds.--Recently some n. m. r. spectra studies have been carried out to elucidate

¹⁴C. R. A. Berger, J. C. Leak, C. C. Neto and R. F. Nystrom, p. 48-O, Abstracts of 137th Meeting of American Chemical Society in Cleveland, Ohio, April, 1960.

the structure of allyl metallic halides. Nordlander and Roberts¹⁵ concluded, on the basis of an n. m. r. spectrum which showed only two types of protons in a ratio of 4:1, that the two possible covalent forms of allylmagnesium bromide are in rapid dynamic equilibrium and the life-time of each form is long enough to permit rotation around its 1,2-carbon-carbon bond.



Dehm and Chien¹⁶ have shown from the n. m. r. spectral studies of allylpalladium chloride that there are three types of protons in the ratio of 1:2:2. The structure below is suggested:

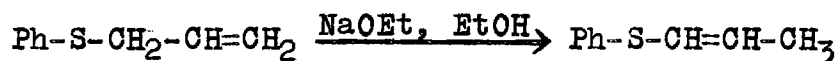


The infrared spectrum is also said to support this structure. The dotted lines are electron deficient bonds. The structure $\text{CH}_2=\text{CH}-\text{CH}_2-\text{M}$ with allyl group σ -bonded to metal should have 4 types of protons.

¹⁵J. E. Nordlander and J. D. Roberts, J. Am. Chem. Soc., 81, 1769 (1959).

¹⁶H. C. Dehm and J. C. W. Chien, ibid., 82, 4429 (1960).

Rearrangement of some allylic compounds by bases.---Alkyl and aryl allyl sulfides are rearranged to the corresponding propenyl sulfides under basic conditions¹⁷.



The rearrangements of allyl ethers to propenyl ethers have been studied by Prosser¹⁸. The bases used were potassium t-butoxide and sodium methoxide.

Shatenshtein et al¹⁹ studied first-order H-D exchange rate constants (sec^{-1}) for ethylenic hydrocarbon in deuterated ammonia in presence of 0.05 N KNH_2 . For propylene the rate constant was $(1-6) \times 10^{-4}$ at 25° . The rate constants for pentene-1 were 4.0×10^{-5} at 25° and 2.1×10^{-4} at 50° . The rate constants were found to fall with progress of the exchange and this drop was taken as an indication of the different reactivities of the various hydrogen atoms of the molecules. With propylene the values of $10^{-4} k$ were (number of hydrogen atoms exchanged in parentheses): after 15 minutes 6 (2.8); 30 minutes 5 (3.8); 1 hour 4 (4.8); 2 hours 2 (5.0); 5 hours 1 (5.1); 24 hours — (5.2); 640 hours — (6.0).

¹⁷(a) D. S. Tarbell and M. A. McCall, ibid., 74, 48 (1952); (b) D. S. Tarbell and W. E. Lovett, ibid., 78, 2259 (1956).

¹⁸T. J. Prosser, paper submitted for publication in J. Am. Chem. Soc.

¹⁹A. I. Shatenshtein, L. N. Vasil'eva, N. M. Dykhno and E. A. Izrailevich, Doklady Akad. Nauk S.S.S.R., 85, 381 (1952); Chem. Abs., 46, 9954d (1952).

Isotope effects.--Since 1948, the effect of isotopes on reaction rates has received increasing attention. Studies upon isotope effects²⁰ in organic chemistry have been undertaken to ascertain the limitations that are to be placed upon the quantitative interpretation of tracer experiments and in order to aid in the elucidation of organic reaction mechanisms. In the latter regard, isotope effects contribute to recognition of the rate-controlling step in a series of chemical reactions and provide information concerning the extent of bond-making and bond-breaking in the transition state of the rate-controlling step.

In a reaction involving only the breaking of a carbon-carbon bond it can be calculated on the basis of the Eyring semi-empirical equation²¹ and some simplifying assumptions that the single $C^{12}-C^{13}$ bond should react a little more slowly than $C^{12}-C^{12}$, and $C^{12}-C^{14}$ should react still more slowly. There should be slight concentration of carbon-13 and carbon-14 in the last residue of a reacting mass.

Outstanding among theoretical treatments of the isotope effect on reaction rates have been those of Bigeleisen²², who calculated the ratio of rates of reactions of isotopically-labeled compounds to be:

²⁰(a) G. A. Ropp, Nucleonics, 10, No. 10, 22 (1952);
(b) K. B. Wiberg, Chem. Revs., 55, 713 (1955).

²¹H. Eyring, J. Chem. Phys., 3, 107 (1935).

²²J. Bigeleisen, J. Chem. Phys., 17, 675 (1949).

$$\ln \frac{k_1}{k_2} \cdot \frac{s_2}{s_1} \cdot \frac{s_1^*}{s_2^*} = \ln \frac{K_1}{K_2} + \frac{1}{2} \ln \frac{\mu_2}{\mu_1} + \underbrace{\sum_1^{3n-6} G(u_1) \Delta u_1}_I - \underbrace{\sum_1^{3n'-6} G(u_1^*) \Delta u_1^*}_{I^*} \quad (1)$$

μ is the effective mass of the activated complex. s 's are symmetry numbers, K 's are transmission coefficients and n 's are number of atoms in molecules. $G(u)$ is the function, $1/2 - 1/u + 1/(e^u - 1)$, where u is hcw/kT and $\Delta u_1 = hc/k [w_1(1) - w_1(2)]$; w is vibrational frequency. h is Planck constant, c is velocity of light, k is boltzmann constant and T is absolute temperature. Starred terms refer to the activated complex. Equation (1) can be reduced to

$$k_1/k_2 = (\mu_2/\mu_1)^{1/2} \times (1 + I - I^*) \quad (2)$$

by making the assumptions that symmetry numbers and transmission coefficients remain the same in both reactions and that Δu is small.

According to Bigeleisen's equation, there are two factors to cause isotope effect, (1) a reduced mass effect, and (2) a zero point energy effect which expresses the effect of mass change on the equilibrium between the reactant molecules and the activated complexes. Lighter isotopic molecules will have a greater reaction rate constant than the heavy molecules. This results from reduced mass factor, $(\mu_2/\mu_1)^{1/2}$, which is always unity or larger, and the fact that the

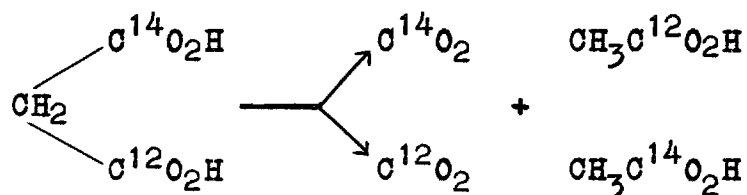
reacting molecule is in general more "tightly bound" than the activated complex, i.e. I is greater than I^* in equation 1 or 2. If the activated complex is sufficiently "tightly bound" so that I^* is greater than the sum of I and $1/2 \ln (\mu_2/\mu_1)$, the rate constant for the heavy molecule reaction will be greater than that of the light molecule, if the "tunnel" effect is neglected.

The largest ratio in the rates occurs when the isotopic atoms are essentially free in the activated complex. Here I^* is equal to zero. The individual terms I and I^* are always positive. If the isotopic atoms are free atoms in the initial state, then the rate constant for the heavy atom may be greater than that for the light atom. Here I is zero. The condition for the rate constant for the heavy atom reaction to be greater than the light atom reaction is, neglecting the "tunnel" effect, $I^* > 1/2 \ln (\mu_2/\mu_1)$. The latter condition is easily fulfilled for the isotopes of hydrogen. For isotopes of elements of higher atomic number than hydrogen the inequality $I^* > 1/2 \ln (\mu_2/\mu_1)$ may not be fulfilled and the rate constant for the light atom reaction will be greater than the one for the heavy atom.

In general accurate a priori calculation of isotope effects is still not possible since knowledge of the structure of the transition state and of the vibrational energy levels of reactants and transition state is required²³.

²³M. L. Bender and D. F. Hoeg, J. Am. Chem. Soc., **79**, 5649 (1957).

Bigeleisen²⁴ has pointed out that some simplification results in study of intramolecular isotope effects in the reactions of unsymmetrically labeled symmetrical compounds, such as the decarboxylation of malonic acid-1-C¹⁴, in that the reactant is the same molecule for reaction:



occurring at both the labeled and unlabeled position and, therefore, the term involving the effect of isotopic substitution upon the vibrational frequency of the ground state of the reactant cancels. Furthermore, intramolecular isotope effects are not complicated by such factors as rates of diffusion and rates of mixing reactants.

Until now, all the isotope effects of carbon that have been reported in the literature are normal, i.e., the ratio k_{12}/k_{13} or k_{12}/k_{14} is more than unity. These reactions have involved breaking of carbon-carbon bonds in the rate-controlling step. There are a few reports of "reverse" isotope effects but these have not been confirmed by subsequent work. Roe and Albenesius²⁵ observed a reverse isotope effect when acetone-1-C¹⁴ was treated with alkaline hypiodite. These authors accounted for this in terms of the greater stability

²⁴J. Bigeleisen, J. Phys. Chem., **56**, 823 (1952).

²⁵A. Roe and E. I. Albenesius, J. Am. Chem. Soc., **74**, 2402 (1952).

of the carbanion formed by proton loss from the C^{14} -methyl group. Ropp *et al.*²⁶ repeated the experiments with acetone-1- C^{14} , but they did not observe any measurable isotope effect. Stevens and Crowder²⁷ reported a reverse isotope effect of 7 per cent in the condensation of *o*-benzoylbenzoic acid carboxyl- C^{14} to anthraquinone. But Ropp²⁸ repeated the experiments and observed a normal isotope effect of 3.5 per cent in agreement with theoretical predictions. Roe, Cavin and Hellmann²⁹ observed a reverse isotope effect in the Schmidt reaction with acetone-1- C^{14} in which $C^{14}H_3$ migrates more readily than $C^{12}H_3$. But Ropp *et al.*²⁶ observed a small normal effect in this case. Roe, McPeters and Mathis²⁹ observed reverse isotope effects in the pinacol-pinacolone type rearrangements. It was observed that $C^{14}H_3$ migrated in preference to the $C^{12}H_3$. The results were explained by the authors that carbon-14 holds its electrons pair more firmly than carbon-12.

It seems clear from several studies that the greatest isotope effects are to be expected at low temperatures. In

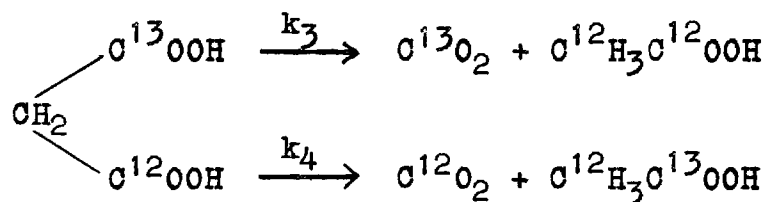
²⁶G. A. Ropp, W. A. Bonner, M. T. Clark and V. F. Raaen, *ibid.*, 76, 1710 (1954).

²⁷W. H. Stevens and D. A. Crowder, *Can. J. Chem.*, 32, 792 (1954).

²⁸G. A. Ropp, *J. Chem. Phys.*, 23, 2196 (1955).

²⁹(a) A. Roe, W. P. Cavin and M. Hellmann, p. 65-0, Abstracts of 124th. Meeting of American Chemical Society in Chicago, Sept., 1953; (b) A. Roe, A. L. McPeters and W. C. Mathis, *ibid.*, p. 66-0.

the dehydration of formic- C^{14} acid with sulfuric acid, Ropp et al.³⁰ found normal isotope effects of 11.11 ± 0.52 per cent at 0° and 8.59 ± 0.58 per cent at 24.75° . Fry and Calvin³¹ studied the carbon-13 and carbon-14 isotope effects in the decarboxylation of oxalic acid with sulfuric acid simultaneously at two different temperatures. The results showed that isotope effects were greater at lower temperatures. Lindsay, Bourns and Thode³² had observed carbon-13 intramolecular isotope effects in the thermal decarboxylation of malonic acid to be independent of the temperature. The values of k_4/k_3 were 1.020 and 1.021 at $138^\circ \pm 0.5$ and $199^\circ \pm 0.5$ respectively.



These results were in agreement with theoretical predictions by the Bigeleisen model for intramolecular effects. However these results were not confirmed by Yankwich and Belford³³

³⁰G. A. Ropp, A. J. Weinberger and O. K. Neville, J. Am. Chem. Soc., **73**, 5573 (1951).

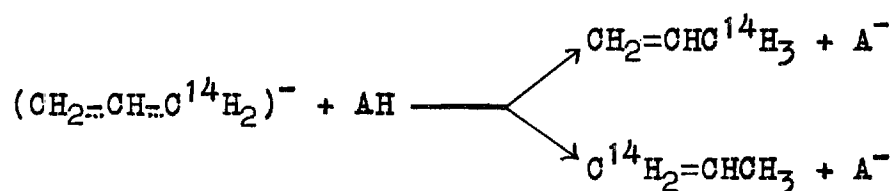
³¹A. Fry and M. Calvin, J. Phys. Chem., **56**, 897 (1952).

³²J. G. Lindsay, A. N. Bourns and H. G. Thode, Can. J. Chem., **29**, 192 (1951).

³³P. E. Yankwich and R. L. Belford, J. Am. Chem. Soc., **76**, 3067 (1954).

who found the intramolecular effect in decarboxylation of malonic acid to be temperature dependent. The values of k_4/k_3 range from 1.0455 ± 0.0008 at 86° to 1.0317 ± 0.0006 at 138° .

The present work was partly carried out in order to study a reaction in which bond-making at the labeled center was the dominant process. A possible example of such a process would appear to be afforded by reductive cleavage of allyl-1- C^{14} compounds with metals, provided that kinetically free carbanions are formed during such reactions:



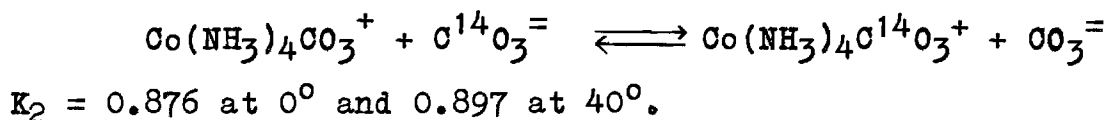
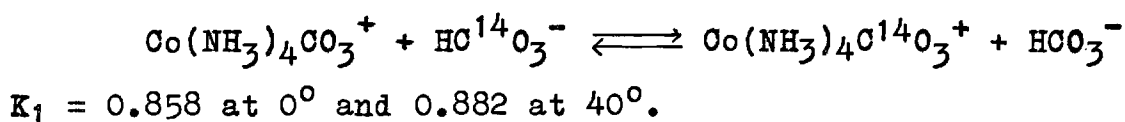
The equilibrium constants of a considerable number of isotopic exchange reactions have been predicted by the methods of statistical thermodynamics³⁴. Stranks and Harris³⁵ have investigated the carbon-14 exchange equilibrium in aqueous solution between carbonatotetrammine cobaltic complex ion and free carbonate ion. The equilibrium constant of the reaction, defined as:

³⁴(a) H. C. Urey, J. Chem. Soc., 562 (1947); (b) A. P. Tudge and H. G. Thode, Can. J. Research, B28, 567 (1950).

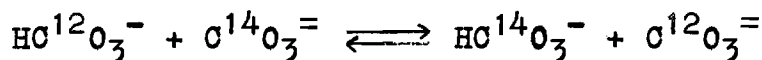
³⁵D. R. Stranks and G. M. Harris, J. Phys. Chem., 56, 906 (1952).

$$K = \frac{[\text{Co}(\text{NH}_3)_4\text{C}^{14}\text{O}_3^+]}{[\text{Co}(\text{NH}_3)_4\text{CO}_3^+]} \frac{[\text{HCO}_3^- + \text{CO}_3^-]}{[\text{HC}^{14}\text{O}_3^- + \text{C}^{14}\text{O}_3^-]}$$

was determined experimentally to be 0.875 ± 0.002 at 0° and 0.900 ± 0.004 at 30° . The values agreed satisfactorily with the values of K_1 and K_2 calculated by methods of statistical thermodynamics for the equilibria:



Stranks and Harris³⁶ have also predicted isotopic enrichment effects in some isotopic exchange equilibria involving carbon-14. The partition function ratios Q_{14}/Q_{12} are given for eighteen simple organic compounds. The equilibrium constant of any probable exchange reaction between a pair of these compounds is readily predicted by the division of the required pair of partition function ratios. Reactions involving species of great chemical similarity and which undergo rapid exchange show small enrichment effects. For example, from the partition function ratio for CO_3^- , 1.424, and for HCO_3^- , 1.451, one calculates $K = 1.451/1.424 = 1.019$ at 293.16° K for the reaction



³⁶D. R. Stranks and G. M. Harris, J. Am. Chem. Soc., **75**, 2015 (1953).

It would be good to mention some of the more recent books concerned with tracer studies and isotope effects. The book, "Isotopic Carbon," written by Calvin, Heidelberger, Reid, Tolbert and Yankwich³⁷ contains an excellent discussion of the analysis of radioactive and stable isotopes of carbon, sample preparations, syntheses of carbon-labeled compounds, criteria of purity and degradation procedures.

Burr³⁸ in his book, "Tracer Applications for the Study of Organic Reactions," has tried to provide a reasonably comprehensive survey of tracer applications in organic chemistry. Enough background information about reaction mechanisms has been given to enable the reader to judge the advantages and disadvantages of this type of work. A chapter on general considerations for the use of isotopic tracer methods is given.

The recent book, "Organic Syntheses with Isotopes," by Murray and Williams³⁹ is in two parts. The first part consists of the syntheses of organic compounds with carbon isotopes. The second part consists of organic compounds

³⁷M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert and P. E. Yankwich, "Isotopic Carbon," John Wiley & Sons, New York, 1949.

³⁸J. G. Burr, Jr., "Tracer Applications for the Study of Organic Reactions," Interscience Publishers, Inc., New York, 1957.

³⁹A. Murray, III and D. L. Williams, "Organic Syntheses With Isotopes," Part I and Part II, Interscience Publishers, Inc., New York, 1958.

with isotopes of halogens, hydrogen, nitrogen, oxygen, phosphorus and sulfur.

Melander⁴⁰ has made a brief presentation of the main principles of kinetic isotope effects in his book, "Isotope Effects on Reaction Rates." Though the book deals primarily with hydrogen isotope effects, carbon isotope effects in single reaction steps have also been discussed. Isotopic effects of oxygen and sulfur have also been mentioned.

⁴⁰L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press Company, New York, 1960.

CHAPTER II

REAGENTS AND SOLVENTS USED, WITH METHODS OF PURIFICATION

Acetic acid.--Commercial grade acetic acid was purified according to the method of Bradfield and Orton⁴¹. Two liters of acetic acid was refluxed for two hours with 40 g. of chromium trioxide and was distilled through a vacuum jacketed 90 x 2.2 cm. column packed with glass helices (1/8 inch I.D.). The product had b. p. 116-117° at 738 mm.

Ammonium chloride.--Baker reagent grade was used without further purification.

Ammonium sulfate.--Baker reagent grade was used without further purification.

Acetone.--Commercial grade acetone was purified according to the method of Conant and Kirner⁴². One liter of acetone was refluxed for 24 hours with 120 g. of calcium oxide and 40 g. of potassium permanganate and was distilled through an electrically heated 36 x 2.0 cm. column packed with glass helices (1/16 inch I.D.). The product had b. p. 56.5° at 738 mm.

⁴¹A. E. Bradfield and K. J. Orton, J. Chem. Soc., 960 (1924).

⁴²J. B. Conant and W. R. Kirner, J. Am. Chem. Soc., 46, 232 (1924).

Acetyl chloride.--Merck reagent grade was used without further purification.

Acrylic acid.--Eastman white label grade was used without further purification.

Acrylonitrile.--Eastman white label grade was used without further purification.

Allyl alcohol.--Matheson, Coleman, and Bell grade was dried over potassium carbonate and then distilled through a short Vigreux column at b. p. 95.0-96.5° at 739 mm.

Allyl bromide.--Eastman white label grade was dried over magnesium sulfate and then distilled through a Claisen flask at b. p. 69.5-70.0° at 741 mm.

Allyl chloride.--Eastman white label grade was dried over magnesium sulfate and distilled through a Claisen flask at b. p. 44.5-45.0° at 738 mm.

γ-Amino propanol.--Eastman white label grade was used without further purification.

Ammonia.--Matheson Company, Inc. anhydrous ammonia (99.9 per cent min. purity) was used without further purification.

Anion exchange resin.--Dow Chemical Company Dowex 2-X8, 100-200 mesh, medium porosity in chloride form was used.

Anisole.--Eastman white label grade was dried over magnesium sulfate and distilled at b. p. 153-154° at 741 mm.

Benzene.--Commercial grade benzene was purified according to the method of Fieser⁴³.

Benzoyl chloride.--Eastman white label grade was used without further purification.

p-Bromoaniline.--Eastman Kodak white label grade was used without further purification. Its m. p. was 64-65°.

β -Bromopropionic acid.--Eastman Kodak white label grade was crystallized with carbon tetrachloride. Its m. p. was 62.5°.

n-Butyl bromide.--Eastman white label grade was distilled through a Claisen flask at b. p. 99.5-100.0° at 742 mm.

Carbon dioxide.--Matheson Company, Inc. bone dry grade (99.8 per cent min. purity) was used without further purification.

Carbon disulfide.--Commercial grade carbon disulfide was purified according to the method of Fieser⁴⁴.

Carbon tetrachloride.--Commercial grade carbon tetrachloride was purified according to the method of Fieser⁴⁵.

⁴³L. F. Fieser, "Experiments in Organic Chemistry," Third Edition, D. C. Heath and Company, Boston, 1955, p. 282.

⁴⁴Ibid., p. 282.

⁴⁵Ibid., p. 283.

Chloroform.--Mallinckrodt U.S.P. grade was distilled at b. p. 60-61° at 737 mm.

Cyclohexane.--Matheson, Coleman, and Bell cyclohexane was used without further purification.

Di-n-butyl ether.--Eastman Kodak practical grade was dried over magnesium sulfate and distilled through a Claisen flask at 141-42° at 740 mm.

Diethylene glycol monoethyl ether (carbitol).--Eastman Kodak practical grade was distilled through a Claisen flask at b. p. 191-194° at 738 mm.

Diethyl ether.--Merck anhydrous reagent ether was stored over sodium wire in brown-glass screw-cap bottles.

5,5-Dimethyl-1,3-cyclohexanedione (methone).--Eastman white label grade was used without further purification.

Ethanol 95 per cent.--U. S. Industrial Chemical Co. commercial grade was used without further purification.

Ethanol.--U. S. Industrial Chemical Co. commercial absolute ethanol was purified according to the method of Fieser⁴⁶.

Ethylamine.--Matheson Company, Inc. anhydrous ethylamine (98.5 per cent min. purity) was condensed in the reaction tube in which it was to be used.

⁴⁶Ibid., p. 285.

Ethylene chlorohydrin.--Eastman white label grade was dried over magnesium sulfate, and distilled at b. p. 127-128° at 741 mm.

Formalin.--Baker's analyzed reagent grade 37 per cent formaldehyde solution was used without further purification.

Formic acid.--Eastman white label grade 98 per cent was used.

Hydracrylonitrile.--Eastman white label grade was distilled at b. p. 93° at 6 mm.

Hydrobromic acid.--Merck reagent grade 48 per cent solution was used.

Lead dioxide.--Baker reagent grade was used.

Lithium.--Lithium Corporation metal ribbon was used.

Lithium aluminum hydride.--Metal Hydrides Inc. lithium aluminum hydride of 95 per cent purity was used.

Methane.--Matheson Company, Inc. C. P. grade was used without further purification.

Methanol.--Commercial grade was purified according to the method of Fieser⁴⁷.

Methylamine.--Matheson Company, Inc. anhydrous methylamine (98.0 per cent min. purity) was condensed in the reaction tube in which it was to be used.

⁴⁷Ibid., p. 289.

Methyl iodide.--Eastman white label grade was used without further purification.

N-Methyl-N-nitroso-p-toluenesulfonamide.--Aldrich Chemical Co., Inc. grade was used without further purification.

α -Naphthyl isocyanate.--Eastman white label grade was used without further purification.

Oxygen.--Southern Oxygen Co. commercial grade was dried by passing through concentrated sulfuric acid.

Phosphoric acid.--Merck phosphoric acid 85 per cent was used.

Potassium cyanide.--Baker reagent grade was crystallized from water and dried at 100° at reduced pressure.

Potassium dichromate.--Baker reagent grade was used without further purification.

Potassium iodate.--Merck reagent grade was used without further purification.

2-Propanol.--Commercial 2-propanol was refluxed for two days over barium oxide and distilled at b. p. 82-82.5° at 738 mm.

Propylene.--Matheson Company, Inc. C. P. grade (99.0 per cent min. purity) was used without further purification.

Radioactive sodium cyanide-C¹⁴.--Tracerlab Inc. sodium cyanide-C¹⁴, one millicurie, specific activity 0.98 mc/mmole was used.

Sodium.--Baker purified grade was used.

Stannous chloride ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$).--Baker reagent grade was used without further purification.

Sulfuric acid fuming.--Baker reagent grade fuming sulfuric acid (20-23 per cent in sulfur trioxide) was used.

Tetrahydrofuran.--One and a half liter of Matheson grade tetrahydrofuran was kept over potassium hydroxide pellets overnight. It was refluxed with 10 g. of lithium aluminum hydride and then distilled from the same pot under nitrogen atmosphere at b. p. 65° at 738 mm.

p-Thiocresol.--Matheson, Coleman, and Bell p-thiocresol was used without further purification. Its m. p. was $43-44^\circ$.

Thionyl chloride.--Eastman white label grade was purified according to the method of Cottle⁴⁸. It was freshly distilled whenever used.

Tri-n-butylamine.--Eastman white label grade was kept over potassium carbonate for two days and then distilled without using a column at b. p. $208.0-209.5^\circ$ at 740 mm.

Trimethylamine.--Eastman white label grade, 25 per cent solution in methanol, was used without further purification.

⁴⁸D. L. Cottle, J. Am. Chem. Soc., 68, 1380 (1946).

Trimethylamine (anhydrous).--Eastman white label grade was used without further purification.

Zinc.--Baker reagent grade powdered zinc was used without further purification.

CHAPTER III

SYNTHESES OF RADIOACTIVE COMPOUNDS

Hydracrylonitrile-1-C¹⁴.--This preparation was carried out according to the method of Schmidt and Schmidt⁴⁹. A mixture of 10.27 g. (0.127 mole) of freshly distilled ethylene chlorohydrin and 50 ml. of absolute ethanol was heated to boiling under reflux. A solution of 8.79 g. (0.135 mole) of freshly crystallized potassium cyanide was made in 13.4 ml. of water. The radioactive sodium cyanide-1-C¹⁴ (1.0 mc, sp. activity 0.98 mc/mole) was dissolved in 1 ml. of the potassium cyanide solution and then was added to the ethylene chlorohydrin solution to which 1 ml. of the non-radioactive cyanide solution had already been added. The tube containing radioactive cyanide was rinsed repeatedly with the remainder of the potassium cyanide solution and these washings were added to the boiling solution of ethylene chlorohydrin. The contents were cooled after refluxing for 20 hours, diluted with 50 ml. of acetone, and then filtered. The inorganic material was washed with 40 ml. of acetone. All the washings were mixed with the filtrate. The inorganic material was stirred with a solution of 0.53 g. of non-radioactive hydracrylonitrile

⁴⁹H. Schmidt and K. Schmidt, Helv. Chim. Acta, 35, 1879 (1952).

in 10 ml. of acetone and was allowed to stand for two days before filtration. This filtrate was mixed with first filtrate. The solvent was removed by distilling through the short helices-packed column until the pot temperature reached 50° at 70 mm. The residue was transferred to a 50-ml. flask and was distilled through an electrically heated 25 x 0.8 cm. Vigreux column. A fraction (5.78 g.) of b. p. $80-81^{\circ}$ at 3 mm. was collected. To remove the remaining active product from the distilling apparatus, 5.0 g. of non-radioactive hydracrylonitrile was added to the 50-ml. flask and distilled to give 4.57 g. of b. p. $79.0-81^{\circ}$ at 3 mm.

β -Bromopropionic acid-1-C¹⁴.--In a 100-ml. flask, were boiled 74.5 g. (0.442 mole) of 48 per cent hydrobromic acid and 10.35 g. (0.146 mole) of hydracrylonitrile-1-C¹⁴ for two hours under reflux. The hydrobromic acid was then distilled until the temperature of the residue reached 128° at atmospheric pressure. The residue on cooling solidified. The solid was dissolved in 60 ml. of carbon tetrachloride, and insoluble ammonium bromide was filtered off and washed with 20 ml. more of the solvent. A brown aqueous layer which separated from the carbon tetrachloride filtrates, was extracted with 3.5 ml. of the solvent. This extract was mixed with the other filtrates and the mixture was heated to distill 48 ml. of carbon tetrachloride. On cooling, 14.16 g. of β -bromopropionic acid separated. To remove the remaining active product from the mother liquor, 4.9 g. of non-radio-

active β -bromopropionic acid was added. The mixture was heated and cooled. The acid which crystallized, was filtered off. This process was repeated. After two such dilutions, the product amounted to 21.73 g. It was sublimated twice to give 19.3 g. of crystals of m. p. 60-60.5°. After two more recrystallizations from carbon tetrachloride, the m. p. was 62.2-63.2°, and the product weighed 16.48 g. and its sp. act. was 3.605 $\mu\text{c}/\text{mmole}$. The mother liquor from the last crystallizations, was mixed with 2.96 g. of non-radioactive acid to recover 2.97 g. of diluted product m. p. 62.1-62.9° and sp. act. 1.504 $\mu\text{c}/\text{mmole}$. The radiochemical yield at this stage was 41.9 per cent based on the starting radioactive sodium cyanide.

p-Bromoanilide of β -bromopropionic acid-1-C¹⁴.--A mixture of 0.16 g. of β -bromopropionic acid-1-C¹⁴ and 0.9 ml. of thionyl chloride was refluxed for 30 minutes on a steam bath. A solution of 0.6 g. of p-bromoaniline in 16 ml. of benzene was added. The reaction mixture was refluxed for one hour, cooled, and then mixed with 3.5 ml. of water. After shaking, the benzene layer was separated and was washed with 3.5 ml. of 5 per cent hydrochloric acid, then with 3.5 ml. of 5 per cent sodium hydroxide solution, and finally with 4.0 ml. of water. The benzene was removed by evaporation on a steam bath. The residue on cooling, solidified. It was boiled with decolorizing charcoal in 6 ml. of 95 per cent ethanol. The hot solution was filtered and mixed with 5 ml. of water. The

solution was boiled until 3-4 ml. of solvent evaporated. On cooling, white crystals of the p-bromoanilide separated. These were recrystallized twice from carbon tetrachloride until a constant m. p. 136-136.5° was reached. The product was dried in vacuum. Its sp. act. was 3.460 μ c/mmole. This agreed fairly well with the sp. act. of the acid (3.605 μ c/mmole).

Methyl β -bromopropionate-1-C¹⁴.--In a 200-ml. long-necked distilling flask, fitted with a dropping funnel, a good condenser, and a receiver surrounded with ice, was placed a solution of 12.6 g. (0.225 mole) of potassium hydroxide in 21 ml. of water, 21 ml. of diethyl ether, and 73.5 ml. of freshly distilled diethylene glycol monoethyl ether. The mixture was heated at 68-70°. As the ether started distilling, a solution of 45.15 g. (0.211 mole) of N-Methyl-N-nitroso-p-toluenesulfonamide in 294 ml. of diethyl ether was added over 50 minutes. During the distillation, the flask was occasionally shaken. The rate of addition of the sulfonamide solution was about equal to the rate of distillation. When the addition was complete, two more 20 ml. portions of ether were added and the distillation was continued until the distilling ether was colorless. The solution of diazomethane which collected in the receiver was added slowly to a solution of 19.45 g. (0.127 mole) of β -bromopropionic acid-1-C¹⁴ in 60 ml. of anhydrous ether cooled in an ice-bath until a yellow color stayed. The solution was allowed to stand for three hours at

0°. The ether was removed through the electrically heated column packed with glass helices. The residue was dried over concentrated sulfuric acid for 48 hours in a desiccator. No effort was made to purify the ester further.

3-Bromopropanol-1- C^{14} .--The procedure followed was according to Nystrom⁵⁰. In a 1-l. Morton flask, fitted with a high-speed stirrer, a dropping funnel, a condenser and arrangement for a nitrogen atmosphere, were placed 4.82 g. (0.127 mole) of pulverized lithium aluminum hydride and 100 ml. of dry diethyl ether. To this solution was added with constant stirring a solution of 16.95 g. (0.127 mole) of anhydrous aluminum chloride in 120 ml. of ether. A solution of 0.127 mole of methyl β -bromopropionate-1- C^{14} in 100 ml. of ether was added to the mixed hydride reagent which was cooled at -78° with stirring. Thirty minutes after the last addition of ester, a solution containing 26 ml. of methanol and 20 ml. of ether was added to destroy the excess of hydride. After allowing the mixture to warm to room temperature, 100 ml. of water and then 127 ml. of 6 N sulfuric acid were added. Two clear layers were formed on leaving the mixture overnight. After separating the ether layer, the aqueous layer was continuously extracted with ether for 72 hours. The ether extracts were dried over Drierite. The ether was removed by distilling through the column packed with glass helices. The

⁵⁰R. F. Nystrom, J. Am. Chem. Soc., 81, 610 (1959).

residue was distilled through the small Vigreux column and the product (9.9 g.) was collected at 60° at 5.5 mm. To recover the remaining active product in the distilling apparatus, non-radioactive 3-bromopropanol (6.9 g.) was distilled twice. All the distillates after mixing, weighed 24.2 g. No attempt was made to calculate the radiochemical yield until allyl alcohol-1- C^{14} was prepared.

3-Hydroxy-3- C^{14} -propyltrimethylammonium bromide.--In a 1-l. flask fitted with a calcium chloride tube, was placed 110 ml. of 25 per cent solution of trimethylamine in methanol. The solution was cooled to -78° before 26.2 g. (0.1885 mole) of 3-bromopropanol-1- C^{14} was added slowly to it. The reaction mixture was kept at -78° for 5 hours, then after replacing the calcium chloride tube with a glass stopper, it was left in a refrigerator overnight. The mixture was kept at room temperature for one hour before refluxing for three hours. After cooling, 500 ml. of dry diethyl ether was added. A crystalline salt separated. The contents were left again in the refrigerator overnight. The salt was filtered off and was washed with dry ether. It was dried at $40-45^{\circ}$ for 24 hours in vacuum. The yield was 35.7 g. or 95.7 per cent based on 3-bromopropanol-1- C^{14} .

Allyl alcohol-1- C^{14} .--Silver oxide, formed by mixing a solution of 50.7 g. (0.298 mole) of silver nitrate in 150 ml. of water with a solution of 14.9 g. (0.373 mole) of sodium

hydroxide in 150 ml. of water, was washed with distilled water until it was free from alkali. The aqueous solution of 35.7 g. (0.180 mole) of 3-hydroxy-3- C^{14} -propyltrimethylammonium bromide in 110 ml. of water was added to the silver oxide. The contents were shaken vigorously on an electric shaker for one hour. The solid was filtered off. The filtrate was checked and found to be free of bromide ions. The solid was washed with water until the washings were free from hydroxide ions. The filtrate and washings were mixed together and were concentrated at reduced pressure on a steam bath until the pot temperature was 45° . The residue was transferred to a 100-ml. flask which was attached to a distilling head, a condenser, a receiver cooled in an ice bath, and a trap cooled in dry-ice acetone mixture. The residue was pyrolyzed by heating the flask in an oil bath at reduced pressure (175 mm.) in the beginning but later at atmospheric pressure. The temperature of the bath was slowly raised up to 185° . Thirty milliliter of water was added as chaser to get the remaining alcohol from the distilling apparatus. The distillate was neutralized with 26 ml. of 6 N sulfuric acid and was continuously extracted with ether for three days. The ether layer was dried over potassium carbonate. The ether was distilled through the column packed with glass helices until the pot temperature was 53° . The residue was distilled through the small Vigreux column. The earlier fraction, b. p. $35-85^{\circ}$, was kept separate. The later fraction, b. p. $85-98^{\circ}$, was

8.39 g. The aqueous layer was mixed with 6.0 ml. of non-radioactive allyl alcohol and was continuously extracted with ether for three days. After removing ether, the residue was mixed with the earlier fraction b. p. 35-85°. On distilling this mixture in the same pot and column used before, a fraction, b. p. 87-97°, was collected. To the pot, was added 4.5 ml. more of non-radioactive allyl alcohol and distilled. The diluted distillate was 9.68 g. Both the diluted and undiluted fractions were mixed and redistilled at b. p. 91-97° through the short Vigreux column. To purify further, this product was redistilled at b. p. 95-96.5° through the same column. It was further diluted with 9.16 g. more of non-radioactive allyl alcohol. After dilutions, the total weight of allyl alcohol-1-C¹⁴ was 24.2 g. The sp. act. was 0.545 μ c/mmole. The radiochemical yield at this stage was 22.8 per cent based on radioactive sodium cyanide.

Allyl-1-C¹⁴ N-(α -naphthyl)carbamate.--This preparation was carried out according to the procedure of Leak⁵¹. A mixture of 0.235 g. (4.0 mmoles) of allyl alcohol-1-C¹⁴ and 0.73 g. (4.3 mmoles) of α -naphthyl isocyanate was heated on a steam bath for fifteen minutes and then was left at room temperature overnight. The resulting solid was purified by boiling with decolorizing charcoal in cyclohexane. It was recrystal-

⁵¹J. C. Leak, Unpublished Ph.D. Thesis, University of Illinois, 1954, p. 73.

lized thrice from cyclohexane until its m. p. was constant at 109.5-110.5°. Its sp. act. was 0.554 $\mu\text{c}/\text{mmole}$.

Allyl-1- C^{14} -trimethylammonium chloride.--In this preparation, allyl chloride-1- C^{14} , which was an intermediate product, was prepared according to the method of Young and coworkers⁵². In a 300-ml. three-necked flat-bottomed flask, fitted with a thermometer, a dropping funnel, and a magnetic stirrer, were placed 23.9 g. (0.129 mole) of tri-n-butylamine, 7.50 g. (0.129 mole) of allyl alcohol-1- C^{14} (5.25 g. of radioactive allyl alcohol of sp. act. 0.545 $\mu\text{c}/\text{mmole}$ and 2.25 g. of non-radioactive allyl alcohol), and 24 ml. of di-n-butyl ether. Two receivers were attached to the flask in series. The first receiver (nearest the reaction flask) was cooled in an ice-salt bath and the second was cooled in a Dry Ice-acetone bath. The mixture in the flask was stirred and cooled in an ice-salt bath. Thionyl chloride (15.4 g., 0.129) was added dropwise. The cooling bath was then removed and the reactants were stirred for one hour at room temperature. The low-boiling point components were distilled at 150-160 mm. with slow heating of the flask until the temperature of the vapors distilling was 81°. The distillates, without warming them, were added to a solution of 17.1 g. (0.29 mole) of anhydrous trimethylamine in 110 ml. of acetone in 500-ml. flask cooled to -78°. The reaction mixture was kept in the

⁵²S. H. Sharman, F. F. Caserio, R. F. Nystrom, J. C. Leak, and W. G. Young, J. Am. Chem. Soc., **80**, 5965 (1958).

dry ice-acetone bath for 6 hours. Afterwards, it was kept in the refrigerator for 24 hours. A white crystalline salt separated. It was kept at room temperature for 2 hours, then 300 ml. of diethyl ether was added. The contents were shaken and allowed to stand for 2 more hours. The salt was filtered off and washed with ether. It was dried at 71° for 2 days in vacuum. Its yield was 15.1 g. or 86.5 per cent based on allyl alcohol- 1-C^{14} . The sp. act. was $0.365 \mu\text{c}/\text{mmole}$. The salt contained 1.23 per cent of allyl- 3-C^{14} -trimethylammonium chloride according to analysis by ozonization.

Anal. Calcd. for $\text{C}_6\text{H}_{14}\text{NCl}$: Cl, 26.20. Found: Cl, 26.36. (The percentage chlorine was determined by Volhard titration).

Picrate of allyl- 1-C^{14} -trimethylammonium chloride.--A solution of 0.215 g. of allyl- 1-C^{14} -trimethylammonium chloride in 1.5 ml. of alcohol was mixed with 3 ml. of a saturated solution of picric acid in alcohol. The reaction mixture was refluxed on a steam bath for 30 minutes and then was left overnight at room temperature. The picrate which separated was filtered off. It was recrystallized from ethanol until a constant m. p. of $218\text{--}219^{\circ}$ was reached. Its sp. act. was $0.374 \mu\text{c}/\text{mmole}$.

Allyl chloride- 1-C^{14} .--The apparatus and part of the procedure was the same as described in the preparation of allyl- 1-C^{14} -trimethylammonium chloride. The reactants used were 55.5 g.

(0.300 mole) of tri-n-butylamine, 17.4 g. (0.300 mole) of allyl alcohol-1-C¹⁴ (14.895 g. of radioactive allyl alcohol of sp. act. 0.545 μ c/mmole and 2.505 g. of non-radioactive allyl alcohol), 45 ml. of di-n-butyl ether and 35.7 g. (0.300 mole) of thionyl chloride. After addition of thionyl chloride, the cooling bath was removed and the reactants were stirred for one hour at room temperature. The low-boiling point components were distilled at 153-162 mm. and at room temperature for 20 minutes. Then, the flask was heated keeping the same pressure until the temperature of the vapors distilling reached 80°. The liquids collected in the receivers were mixed and shaken with 5 ml. of 5 per cent ice-cold sodium carbonate solution. The lighter layer was washed with ice-cold water. The liquid collected in the trap had to be shaken several times with 10 per cent ice-cold sodium carbonate solution until the aqueous layer stayed basic. The lighter layer was washed with ice-cold water. Both upper layers were mixed and dried over Drierite. The liquid was redistilled through a small Claisen flask at 153 mm. until the bath temperature was 78° and the temperature of the vapors distilling was 45°. During this preparation, the product was diluted with 4.0 ml. of non-radioactive allyl chloride. The yield was 21.6 g. or 77.5 per cent based on the amount of allyl alcohol used. The product contained 1.06 per cent of allyl chloride-3-C¹⁴ according to an analysis by ozononization.

p-Tolyl allyl-1-C¹⁴ sulfide as prepared in ethanol.--In a 300-ml. three-necked flat-bottomed flask containing a magnetic stirring bar and fitted with a reflux condenser was placed 125 ml. of absolute ethanol. Sodium (4.6 g., 0.20 g. atom) was added in small pieces. After the sodium had reacted, 25.62 g. (0.210 mole) of p-thiocresol was added. The flask was cooled in an ice-salt bath. The contents were stirred and 14.5 g. (0.190 mole) of allyl chloride-1-C¹⁴ was added dropwise. The reaction was fast as indicated by the quick appearance of sodium chloride. The reaction mixture was stirred for two hours at ice-salt temperature, then was left unstirred overnight at room temperature. Next day it was stirred for two hours more at room temperature. On adding water to the mixture, an oily layer separated. The oil was removed and washed with water. It was dried over Drierite and distilled through the short Vigreux column at b. p. 101-103° at 8 mm. The yield was 24.8 g. or 79.6 per cent based on allyl chloride-1-C¹⁴. No dilution was made in this preparation. The product contained 33.4 per cent of p-tolyl allyl-3-C¹⁴ sulfide according to an analysis by ozonization.

p-Tolyl allyl-1-C¹⁴ sulfide as prepared in acetone.--In a 300-ml. three-necked flat-bottomed flask containing a magnetic stirring bar, fitted with a reflux condenser and a dropping funnel, and blanketed with dry nitrogen, was placed 80 ml. of absolute ethanol. Sodium (1.77 g., 0.077 g. atom)

was added with stirring. After the sodium had reacted, 9.55 g. (0.0770 mole) of p-thiocresol was added. The ethanol was evaporated at room temperature by using a filter pump and then a vacuum pump until the residue was dry. One hundred and twenty milliliters of acetone was added to the sodium p-thiocresolate which was found to be soluble in it only at 15-20°, but insoluble below this temperature. A solution of 4.20 g. (0.0550 mole) of allyl chloride-1-C¹⁴ in 10 ml. of acetone was added dropwise to the solution at 20°. The reaction was fast as indicated by the appearance of sodium chloride. The reaction mixture was stirred at 20° for an hour and then was left unstirred at room temperature overnight. Next day it was stirred for two hours more at room temperature. On adding 130 ml. of water to the mixture, an oily layer separated. The aqueous layer was separated and extracted twice with 100 ml. portions of ether. The oily layer and the ether extracts were combined. The mixture was washed with 4 per cent sodium hydroxide and then with water. It was dried over Drierite. The ether and acetone were removed by distilling through the electrically heated column packed with glass helices until the pot temperature was 100°. The residue was transferred to a 50-ml. flask and was distilled through the short Vigreux column at b. p. 99-100.5° at 7.5 mm. The yield was 8.3 g. or 92.0 per cent based on allyl chloride-1-C¹⁴. The sp. act. was 0.414 μ c/mmole. The product contained 3.82 per cent of p-tolyl allyl-3-C¹⁴ sulfide according to an analysis by ozonization.

CHAPTER IV

SYNTHESES WITH NON-RADIOACTIVE REACTANTS

Hydracrylonitrile by Method I.--This preparation was carried out according to the method of Kendall and McKenzie⁵³. The yield of hydracrylonitrile was 53.0 g. or 60 per cent from 1.24 mole of ethylene chlorohydrin and 1.24 mole of sodium cyanide. The reported yield is 79-80 per cent.

Hydracrylonitrile by Method II.--The preparation was carried out according to the method of Schmidt and Schmidt⁴⁹. The yield was 65.6 per cent from 0.128 mole ethylene chlorohydrin and 0.128 mole of potassium cyanide. The reported yield is 83 per cent. This was the procedure which was later followed for synthesizing hydracrylonitrile-1-C¹⁴.

3-Aminopropanol by Method I.--In a 2-l. round-bottomed flask fitted with a reflux condenser were placed 21.3 g. (0.300 mole) of hydracrylonitrile and 600 ml. of absolute alcohol. The mixture was heated to boiling and 75 g. (3.26 g. atoms) of sodium was added in small pieces. Heating was discontinued since the heat of the reaction was enough to keep the solution boiling. When all the sodium had reacted, the contents were

⁵³E. C. Kendall and B. McKenzie, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1941, Coll. Vol. 1, p. 256.

cooled and mixed with 750 ml. of water and then with 300 ml. of concentrated hydrochloric acid. The mixture was evaporated to dryness by heating on a steam bath at reduced pressure (180 mm.). The dry residue was mixed with a syrupy solution of sodium hydroxide which was prepared by dissolving 120 g. of sodium hydroxide pellets in 120 ml. of water. The contents were shaken vigorously and then were distilled through a Claisen flask at b. p. 48-54° at 2-4 mm. The product was kept over potassium hydroxide pellets for two days and then was redistilled through a small Claisen flask at b. p. 110-195° at atmospheric pressure. The yield was 5.1 g. The liquid in trap was basic. It was neutralized with hydrochloric acid and the resultant solution was evaporated to a syrupy liquid. This liquid was mixed with 50 per cent sodium hydroxide solution and distilled through a small Claisen flask. A fraction (5 g.), b. p. 41° at 20 mm. was obtained. It was kept over potassium hydroxide pellets for two days and then was redistilled through the Claisen flask at b. p. 129-135° and at atmospheric pressure. As the product was impure and the yield poor, other methods were tried.

3-Aminopropanol by Method II.--In a 2-l. three-necked flask, fitted with a dropping funnel, a mercury sealed stirrer and a reflux condenser were placed 38.0 g. (1.00 mole) of pulverized lithium aluminum hydride and 1 l. of dry tetrahydrofuran. The solution was stirred and cooled by keeping the flask in an ice bath. A solution of 51.0 g. (0.72 mole) of

hydracrylonitrile in 80 ml. of tetrahydrofuran was added dropwise to the hydride solution. After addition of hydracrylonitrile, the reaction mixture was stirred for one hour at 0° , the cooling bath was removed, and the flask was heated at reflux for three hours. To destroy the excess of hydride, 44 g. of ethyl acetate, 28 ml. of water, 14 ml. of 20 per cent sodium hydroxide, and 98 ml. of water were added in succession to the mixture cooled to 0° . The inorganic material was separated as a white solid. It was filtered off and washed with tetrahydrofuran. The filtrate and washings were mixed together and were distilled through the electrically heated column packed with glass helices until the pot temperature was 80° . The residue was transferred to a 50-ml. flask and was distilled through the short Vigreux column at $78-80^{\circ}$ at 9 mm. The yield was 12 g. or 22.4 per cent based on hydracrylonitrile. An effort was made to recover the amine from the inorganic material by heating it slowly until the temperature was 150° and at 7 mm. It was found that the distillates contained 0.1 mole of basic material.

Hydracrylonitrile benzoate.---To a solution of 28.4 g. (0.40 mole) of hydracrylonitrile in 142 g. of freshly distilled pyridine, cooled to 0° , was added 62.0 g. (0.44 mole) of benzoyl chloride in small increments. The reactants were left overnight at room temperature with a drying tube attached to the flask. The reaction mixture was poured onto ice suspended in 155 ml. of concentrated hydrochloric acid. The

ester was extracted with 350 ml. of diethyl ether. The extracts were washed with 10 per cent sulfuric acid, then with 10 per cent sodium carbonate solution and finally with water. The extracts were dried over Drierite. The ether was removed by distilling through the electrically heated column packed with glass helices until the top temperature was 100° . The residue was distilled through a Claisen flask at b. p. $153.5-156^{\circ}$ at 6 mm. The yield was 61 g. or 87.2 per cent based on hydracrylonitrile.

3-Aminopropanol by Method III.---In a 1-l. Morton flask, fitted with a high-speed stirrer, a dropping funnel, a condenser and arrangement for a nitrogen atmosphere, were placed 28.0 g. (0.736 mole) of pulverized lithium aluminum hydride and 300 ml. of dry tetrahydrofuran. The mixture was stirred and cooled in an ice bath. Hydracrylonitrile benzoate (59.0 g., 0.337 mole) was added dropwise to the hydride solution. After addition of the ester, the reaction mixture was stirred for 45 minutes at 0° and then, after removing the cooling bath, it was refluxed for one hour. To destroy the excess of hydride, 14 ml. of water, 10 ml. of 20 per cent sodium hydroxide and 45 ml. of water were added in succession with a vigorous stirring to the mixture cooled to 0° . The inorganic material, which separated as a white solid, was filtered off and washed with tetrahydrofuran. The filtrate and washings were mixed and dried over sodium carbonate. The tetrahydrofuran was removed by distillation through the

electrically heated column packed with glass helices until the pot temperature was 102° . The residue was neutralized with concentrated hydrochloric acid and then mixed with 25 ml. of diethyl ether to extract benzyl alcohol. Two layers were formed on shaking and allowing the mixture to stand for some time. The layers were separated and the ether layer was washed with water. The washings and the aqueous layer were mixed. The mixture was evaporated to a viscous mass by heating on a steam bath at 120-150 mm. The viscous residue was mixed and shaken with a solution of 15 g. of sodium hydroxide in 15 ml. of water. The mixture was distilled through a Claisen flask at b. p. $50-75^{\circ}$ at 10 mm. The distillate was redistilled through the short Vigreux column. The b. p. and pressure could not be recorded accurately because of some leakage of air into the column. The yield was 4.5 g. or 17.8 per cent based on hydracrylonitrile benzoate.

Anal. Calcd. for C_3H_9NO : neut. equiv., 75; Found: neut. equiv., 81.2. (The neutral equivalent weight was determined through titration using a standard solution of hydrochloric acid and methyl red as indicator).

3-Aminopropanol by Method IV.---In a 2-l. Morton flask, fitted with a high-speed stirrer, a dropping funnel, a condenser, and arrangement for a nitrogen atmosphere, were placed 22.8 g. (0.600 mole) of pulverized lithium aluminum hydride and 700 ml. of dry tetrahydrofuran. To this solution was added with

constant stirring a solution of 80.0 g. (0.600 mole) of anhydrous aluminum chloride in 500 ml. of tetrahydrofuran. A solution of 28.4 g. (0.400 mole) of hydracrylonitrile in 71.5 ml. of tetrahydrofuran was added dropwise to the mixed hydride reagent at room temperature with stirring. After addition of the nitrile solution, the reaction mixture was stirred for one hour at room temperature and then was heated at reflux for 25 minutes. The mixture was cooled to 0° and to destroy the excess hydride, 20 ml. of water, 50 g. of sodium hydroxide in 80 ml. of water, and 20 ml. of water were added in succession with a vigorous stirring. The inorganic material which separated as a white solid was filtered off and washed with tetrahydrofuran. The distillate obtained on heating the inorganic material up to 150° at 7 mm. was mixed with the filtrate and washings. The mixture was distilled through the electrically heated column packed with glass helices until the pot temperature was 85° at atmospheric pressure. The residue was distilled through the short Vigreux column at b. p. 92-93° at 15 mm. The yield was 12.5 g. or 41.7 per cent based on hydracrylonitrile.

3-Hydroxypropyldimethylamine.--This amine was prepared from 3-aminopropanol by an adaptation of the procedure of Icke and coworkers for the methylation of β -phenylethylamine⁵⁴. In a

⁵⁴R. N. Icke and B. B. Wisegarver with G. A. Alles, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1955, Coll. Vol. 3, p. 723.

2-l. round-bottomed flask fitted with a reflux condenser was placed 370 g. (7.88 moles) of 98 per cent formic acid. The flask was cooled in tap water and 118 g. (1.58 g. mole) of 3-aminopropanol was added slowly. After all the amine had been added, 360 ml. (4.74 moles) of 37 per cent formaldehyde solution was added together with a small boiling stone. The flask was placed in an oil bath which had been heated to 90-100°. A vigorous evolution of carbon dioxide took place. The flask had to be removed from the oil bath until the gas evolution notably subsided; then it was returned to the bath and heated at 95-100° for 8 hours. After the solution had been cooled, 525 ml. of 6 N hydrochloric acid was added and the solution was evaporated to dryness under reduced pressure (water pump) by heating on a steam bath. The residue was mixed and shaken with 394 ml. of 18 N sodium hydroxide solution. The amine was extracted with four 120-ml. portions of benzene. The benzene extracts were kept over 100 g. of anhydrous potassium carbonate overnight. The solvent was removed by distilling through the electrically heated column packed with glass helices at 200 mm. The residue was distilled through a Claisen flask at b. p. 109-111° at 157-160 mm. This fraction was redistilled through the electrically heated column packed with glass helices at b. p. 109° at 163 mm. The yield was 109 g. or 67.0 per cent based on 3-aminopropanol.

3-Hydroxypropyltrimethylammonium iodide.---In a 500-ml. flask were placed 15.45 g. (0.150 mole) of 3-hydroxypropyldimethyl-

amine and 40 ml. of acetone. After the solution had been cooled in an ice-salt bath, 12.5 ml. (0.201 mole) of methyl iodide was added dropwise with shaking. The reactants were kept in the ice-salt bath for five hours. A white crystalline solid separated. The flask was kept in the refrigerator for 24 hours and then was left at room temperature for the same time. The white solid was filtered off and washed with ether. It was dried in at 50-60° in vacuum for eight hours. The yield was 33.4 g. or 91.0 per cent based on 3-hydroxypropyldimethylamine.

Anal. Calcd. for $C_6H_{16}NOI$: I, 51.80; Found: I, 51.30. (The percentage iodine was determined by Volhard titration).

Allyl alcohol by Method I.--Through a 108 x 3.2 cm. column packed with anion exchange resin in chloride form was passed a normal solution of sodium hydroxide until no more chloride ions were found in the eluate. The column was then washed with distilled water. A solution of 49.0 g. (0.200 mole) of 3-hydroxypropyltrimethylammonium iodide in 250 ml. of water was passed through the column. The column was washed with 2 l. of distilled water. The eluate and washings were evaporated to 125 ml. at 234 mm. The residue was transferred to a 200-ml. flask. Two traps were attached to the flask in series. The first trap (nearest the flask) was cooled in an ice bath and the second was cooled in a dry ice-acetone bath. The residue was heated on a steam bath at 50 mm. The vapors distilled at 38°. The distillates in the two traps were

mixed and were neutralized with hydrochloric acid. The resultant liquid was distilled through the electrically heated column packed with glass helices. An azeotrope (8.0 g.) was collected at b. p. 88° at 738 mm. The yield of allyl alcohol was 50.0 per cent based on the fact that the azeotrope contains 72.5 per cent of allyl alcohol and 27.5 per cent of water.

n-Butyl acrylate.--In a 1-l. round-bottomed flask, fitted with a reflux condenser and a drying tube, was placed 110 ml. of fuming sulfuric acid. The flask was cooled in an ice bath and 222 g. (3.0 moles) of n-butanol was added in small amounts with occasional shaking. After addition of the alcohol, 106.5 g. (1.5 mole) of hydracrylonitrile was added. The cooling bath was removed and the reactants were heated slowly and finally heated at reflux for two hours. The mixture was poured into 500 g. of crushed ice. The ester was extracted with 1 l. of diethyl ether. The ethereal extracts were washed with water and then with 10 per cent sodium bicarbonate solution. The extracts after drying over magnesium sulfate were distilled through the electrically heated column packed with glass helices until the pot temperature was 145° . The residue was distilled through the same column at $81-87^{\circ}$ at 106-111 mm. The yield was 87 g. or 45.3 per cent based on hydracrylonitrile.

Allyl alcohol by Method II.--In a 2-l. Morton flask, fitted with a high-speed stirrer, a dropping funnel, a condenser and

arrangement for a nitrogen atmosphere, were placed 18.5 g. (0.487 mole) of pulverized lithium aluminum hydride and 300 ml. of dry diethyl ether. A solution of 83.2 g. (0.65 mole) of n-butyl acrylate in 350 ml. of ether was added dropwise to the hydride reagent which was cooled at -78° with stirring. After addition of the ester, the reactants were stirred for 30 minutes at the same temperature. Later the dry ice-acetone bath was replaced with an ice bath. The excess of hydride was decomposed by adding 35 ml. (0.568 mole) of methyl formate and 63 ml. (1.18 mole) of concentrated sulfuric acid in 600 ml. of water. Two clear layers were formed. After separation from the ether layer, the aqueous layer was shaken vigorously with 400 ml. of ether. The combined ether extracts were washed with 30 ml. of 10 per cent solution of sodium bicarbonate and then with water. The extracts were dried over magnesium sulfate. The ether was removed by distilling through the vacuum-jacketed column packed with glass helices until the pot temperature was 60° . The residue was distilled through the electrically heated column packed with glass helices. No product boiling at constant b. p. could be obtained. The infrared spectrum of a fraction (9.0 ml.) at $90-108^{\circ}$ at 735 mm. indicated it to be a mixture of n-butanol and n-butyl acrylate.

Allyl alcohol by Method III.--This preparation was carried out according to the method of Benedict and Russell⁵⁵. The

⁵⁵G. E. Benedict and R. R. Russell, J. Am. Chem. Soc., 73, 5444 (1951).

product was distilled through the short Vigreux column at b. p. 93-97° and at local atmospheric pressure. It was quite impure as was revealed by its infrared spectrum. The yield of impure allyl alcohol was 2.43 g. or 9.8 per cent from 0.43 mole of acrylic acid and 0.526 mole of lithium aluminum hydride. The reported yield is 68.3 per cent.

β -Bromopropionic acid.--This preparation was carried out according to the method of Kendall and McKenzie⁵⁶. The yield of β -bromopropionic acid was 14.6 g. or 67.8 per cent from 10.0 g. (0.141 mole) of hydracrylonitrile and 72 g. (0.426 mole) of 48 per cent hydrobromic acid. The reported yield is 82-83 per cent. This procedure was followed for synthesizing β -bromopropionic acid-1-C¹⁴.

Methyl β -bromopropionate.--In a 500-ml. round-bottomed flask, fitted with a reflux condenser and a dry tube, were placed 30.6 g. (0.200 mole) of β -bromopropionic acid, 108 ml. (2.68 moles) of methanol and 3.0 ml. of concentrated sulfuric acid. The reactants were heated at reflux on a steam bath for two hours. The mixture was cooled to room temperature and 10 g. (0.119 mole) of sodium bicarbonate was added with shaking to neutralize the sulfuric acid. The bicarbonate was filtered off after two days and washed with ether. The filtrate and washings were mixed. The ether and methanol were removed by

⁵⁶E. C. Kendall and B. McKenzie, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1941, Coll. Vol. 1, p. 131.

distilling through the electrically heated column packed with glass helices until the pot temperature was 70°. The residue was transferred to a 50-ml. flask and was distilled through the short Vigreux column at b. p. 75-78° at 25-26 mm. The yield was 24.47 g. or 73.5 per cent of the theoretical amount.

3-Bromopropanol.--The procedure followed was that of Nystrom⁵⁰. The yield of 3-bromopropanol was 10.7 g. or 77.0 per cent from 16.7 g. (0.100 mole) of methyl β -bromopropionate and 0.100 mole of lithium aluminum hydride-aluminum chloride reagent. The reported yield was 90 per cent of the theoretical amount. This procedure was followed for synthesizing 3-bromopropanol-1-C¹⁴.

3-Hydroxypropyltrimethylammonium bromide.--The procedure was the same as described in the synthesis of 3-hydroxy-3-C¹⁴-propyltrimethylammonium bromide. The yield of the salt was 9.06 g. or 96.2 per cent from 6.62 g. (0.0476 mole) of 3-bromopropanol and 24 ml. of 25 per cent solution of trimethylamine in methanol.

Allyl alcohol by Method IV.--The procedure was similar to that described in the synthesis of allyl alcohol-1-C¹⁴. The yield of allyl alcohol was 7.4 g. or 76.2 per cent from 33.2 g. (0.1675 mole) of 3-hydroxypropyltrimethylammonium bromide.

Allyl n-butyl ether.--In a 500-ml. Morton flask, fitted with a high-speed stirrer, a dropping funnel, a condenser and

arrangement for a nitrogen atmosphere, were placed 300 ml. of tetrahydrofuran and 34.2 ml. (0.504 mole) of allyl alcohol. The solution was stirred and 19.5 g. (0.500 mole) of potassium was added in small amounts. After the potassium had reacted, the contents were cooled to room temperature and 53.0 ml. (0.495 mole) of butyl bromide was added dropwise. The reactants were then heated at reflux for six hours. The contents were cooled and the inorganic material was filtered off and washed with tetrahydrofuran. The filtrate and the washings were mixed together. The tetrahydrofuran was removed by distilling through the electrically heated column packed with glass helices until the pot temperature was 100° . The residue (45.0 ml.) was transferred to a 100-ml. flask and was distilled through the same column at b. p. $105-118^{\circ}$ at 740 mm. The yield was 16.9 g. or 29.6 per cent based on allyl alcohol. The reported⁵⁷ b. p. is $114-118^{\circ}$.

Diallyl ether by Method I.--In a 500-ml. Morton flask with similar attachments as used in the previous preparation, were placed 225 ml. of tetrahydrofuran and 34.2 g. (0.600 mole) of potassium. The mixture was stirred slowly and 34.2 ml. (0.500 mole) of allyl alcohol was added dropwise. The contents were heated to boiling and then stirred vigorously. After the potassium had reacted, 84.7 g. (0.700 mole) of allyl bromide was added slowly. The reaction mixture was

⁵⁷P. Kurtz, Ann., 572, 23 (1951). Chem. Abs., 45, 9463e (1951).

heated at reflux and stirred for 12 hours. The inorganic material was filtered off and washed with tetrahydrofuran. The filtrate and washings were mixed. The tetrahydrofuran was removed by distilling through the electrically heated column packed with glass helices until the pot temperature was 93° . The residue was mixed with 50 ml. of anisole. The mixture was distilled through the same column at b. p. $90-95^{\circ}$ at 737 mm. The yield was 35.0 ml. or 57.5 per cent based on allyl alcohol. Its infrared spectrum resembled fairly closely that of the commercial purified product.

Diallyl ether by Method II.---In a 1-l. Morton flask, with similar attachments as used in the preparation of allyl butyl ether, was placed 300 ml. of freshly distilled diethylene glycol monoethyl ether. Potassium (58.5 g., 1.500 mole) was added in small pieces. After the potassium had reacted, 34.2 ml. (0.500 mole) of allyl alcohol was added and then 132 ml. (1.525 mole) of allyl bromide was added dropwise. The reactants were heated at reflux with stirring for one hour and then left overnight. The inorganic material was filtered off and washed with 180 ml. of the solvent. The filtrate and washings were mixed and distilled through the electrically heated column packed with glass helices at b. p. $91-95^{\circ}$ at 741 mm. The product (44.5 ml.) contained allyl alcohol as impurity. It was shaken with 50 per cent calcium chloride solution and then kept over anhydrous calcium chloride. As it still contained allyl alcohol, another procedure was

carried out. The impure ether (21.0 ml.) was dissolved in 45 ml. of pyridine. The solution was cooled in an ice bath and was mixed with 17 ml. (0.147 mole) of benzoyl chloride. Next day the contents were distilled through the electrically heated column packed with glass helices until the temperature of the vapors distilling was 114° . The distillate was neutralized with 50 per cent hydrochloric acid. Two layers were formed. The lighter layer was removed and dried over calcium chloride. It was distilled through the short Vigreux column at b. p. $90-94^{\circ}$ at 739 mm. The product was free from allyl alcohol as judged by its infrared spectrum. The yield was 7.5 ml. or 12.3 per cent based on allyl alcohol.

3-Acetoxypropyldimethylamine.--In a 500-ml. flask, fitted with a reflux condenser and a drying tube, was placed 41.2 g. (0.400 mole) of 3-hydroxypropyldimethylamine. The flask was kept in an ice bath. Acetyl chloride (78.5 g., 1.00 mole) was added slowly through the condenser. After addition of the chloride, the flask was left in the ice bath for an hour more. The reactants were heated at reflux for two hours. The excess of acetyl chloride was removed by suction with a filter pump at room temperature. The crystalline residue was treated with 100 ml. of 8 N sodium hydroxide solution. The amine was extracted with 600 ml. of ether. The ether extracts were dried over potassium carbonate. The ether was removed by distilling through the electrically heated column packed with glass helices. The residue was distilled through the

same column at b. p. 110-113° at 135 mm. The yield was 48.0 g. or 82.7 per cent based on 3-hydroxypropyldimethylamine.

Allyldimethylamine by Method I.---Through a 60.0 x 2.2 cm. Vycor tube which was inserted vertically in a 12-inch FD303A Hoskins electric furnace, packed for 38 cm. of its length with glass helices (1/16 inch I.D.), heated at 510-520°, and attached to a water condenser and a receiver cooled in an ice bath, was passed a slow stream of nitrogen (20 bubbles per minute). A trap cooled in a Dry Ice-acetone bath and attached to the receiver was also used. 3-Acetoxypropyldimethylamine (36.0 g., 0.248 mole) was added dropwise from the top of the tube over forty minutes. The liquids which collected in the receiver and trap were extracted with dibutyl ether. The extracts were distilled through the electrically heated column packed with glass helices; a fraction (4.0 ml.) at b. p. 55-64° at atmospheric pressure was collected. The liquid was reacted with methyl iodide according to the procedure of preparing 3-hydroxypropyltrimethylammonium iodide. The yield of allyltrimethylammonium iodide was 4.0 g. or 7.1 per cent based on 3-acetoxypropyldimethylamine. The m. p. of its picrate was 219-220°.

Anal. Calcd. for C₆H₁₄NI: I, 56.0; Found: I, 55.7.
(The percentage iodine was determined by Volhard titration).

Allyldimethylamine by Method II.---The apparatus was the same as used in the previous preparation. This time the tube was

heated at 550° and 18.0 g. (0.124 mole) of 3-acetoxypropyldimethylamine was added dropwise over a period of two hours. The liquids collected in the receiver and trap were dissolved in 400 ml. of ether. The ether extracts were shaken with 50 ml. of 10 per cent potassium carbonate solution. The ether layer was separated and dried over magnesium sulfate. The ether was removed by distilling through the electrically heated column packed with glass helices until the temperature of the vapors distilling reached 45° . The residue (5.0 ml.) was distilled through a Claisen flask at b. p. $55-60^{\circ}$ at atmospheric pressure. A few drops of a product were obtained but this did not give the quaternary salt after reaction with methyl iodide under usual conditions.

Allyldimethylamine by Method III.---The apparatus was the same as used in the previous preparation. The tube was packed for 38 cm. of its length with a mixture of 75 per cent glass helices (1/16 inch I.D.) and 25 per cent barium oxide. The column was heated at $500-520^{\circ}$ and 22.5 g., (0.155 mole) of 3-acetoxypropyldimethylamine was added dropwise over twenty five minutes. No allyldimethylamine could be isolated under these reaction conditions.

Acrylonitrile.---This preparation was carried out according to the method of Sekino⁵⁸. In a 200-ml. flask fitted with a

⁵⁸M. Sekino, Repts. Research Lab., Asahi Glass Co., 1, 208 (1951); Chem. Abs., 50, 2420c (1956).

condenser and a drying tube were placed 71 g., (1.00 mole) of hydracrylonitrile and 5 g. of anhydrous sodium carbonate. The mixture was heated at reflux for one and a half hour. The contents were distilled through a Claisen flask at b. p. 75-103°. On allowing the distillate to stand for sometime, two layers were formed. The upper layer was separated and dried over sodium carbonate. The liquid was redistilled through the Claisen flask at b. p. 74-78° at atmospheric pressure. The yield was 27.5 g. or 51.9 per cent based on hydracrylonitrile.

Allylamine by Method I.--In a 1-l. Morton flask with similar attachments as used in the preparation of allyl butyl ether, were placed 10.5 g. (0.276 mole) of pulverized lithium aluminum hydride and 500 ml. of diethyl ether. The mixture was heated at reflux for one hour and then cooled in an ice bath. A solution of 26.5 g. (0.500 mole) of acrylonitrile in 100 ml. of ether was added dropwise with stirring. After addition of the nitrile, the reactants were stirred vigorously for one hour more at 0°. To destroy the excess of hydride, 10 ml. of water, 15 ml. of 20 per cent sodium hydroxide, and 35 ml. of water were added in succession. The inorganic material which separated as a white solid was filtered off and washed with ether. The white solid was mixed with water and the mixture was steam distilled until most of the basic material was obtained in the distillate. The ethereal filtrate and washings were mixed with the distillate. The

mixture was cooled in an ice bath and mixed with 125 ml. of 4 N hydrochloric acid. The mixture was evaporated to dryness on a steam bath. The residue was mixed with 20 g. of sodium hydroxide in 40 ml. of water while the reactants were cooled in an ice bath. The mixture was shaken with 100 ml. of toluene to extract the amine. The toluene extracts were dried over sodium carbonate and distilled through the electrically heated column packed with glass helices. A fraction (10 ml.), b. p. 55-107° was obtained. The alkaline aqueous layer was also distilled through the same column, a fraction (1.5 ml.) at b. p. 48-50° was collected. Both the fractions were mixed and redistilled through the short Vigreux column at b. p. 48-70° at 739 mm. The product (2.0 ml.) was quite impure as was revealed by its infrared spectrum.

Allylamine by Method II.--In a 1-l. Morton flask with similar attachments as used in the preparation of allyl butyl ether, were placed 19.0 g. (0.500 mole) of lithium aluminum hydride and 400 ml. of diethyl ether. To this solution, was added a solution of 66.7 g. (0.500 mole) of anhydrous aluminum chloride in 450 ml. of ether. Acrylonitrile (26.5 g., 0.500 mole) was added to the mixed hydride reagent which was cooled to 0° with stirring. After addition of the nitrile, the reactants were stirred for twenty five minutes at room temperature. To decompose the excess hydride 46 ml. of water, 42 g. of sodium hydroxide in 65 ml. of water, and 16 ml. of water were added in succession to the mixture cooled to 0°. The inorganic

material was separated as a white solid. The ether and the basic material were removed by distilling through a Claisen flask. It was found that the distillate contained only 0.08 mole of basic material. The inorganic material was mixed with water and steam distilled. The aqueous distillate contained 0.03 mole of basic material. The ethereal distillate was neutralized with 16 ml. of concentrated hydrochloric acid and the resultant liquid was evaporated to a viscous liquid. The residue was mixed with 20 g. of potassium hydroxide pellets. The oily layer separated, was removed and distilled through the short Vigreux column at b. p. 40-93° at 738 mm. No product boiling at constant b. p. could be obtained.

Allylamine by Method III.--This preparation was carried out in the same manner and with the same quantities of the reactants as in the previous experiment except that tetrahydrofuran was used instead of ether as a solvent. It was found that the tetrahydrofuran extracts contained only 0.05 mole of basic material. Since the yield was so poor, no effort was made to go further in this preparation.

Allyltrimethylammonium chloride.--The procedure was the same as described in the synthesis of allyl-1-C¹⁴-trimethylammonium chloride. The yield of the salt was 24.5 g. or 90.5 per cent from 11.6 g. (0.200 mole) of allyl alcohol.

p-Tolyl allyl sulfide as prepared in ethanol.--The procedure was the same as described in the synthesis of p-tolyl

allyl-1- C^{14} sulfide in ethanol. The yield of the sulfide (b. p. 118-119° at 16 mm.) was 21.2 g. or 85.5 per cent from 11.55 g. (0.151 mole) of allyl chloride, 3.8 g. (0.165 g. atom) of sodium and 19.6 g. (0.158 mole) of *p*-thiocresol.

p-Tolyl allyl sulfide as prepared in acetone.--The procedure was the same as described in the synthesis of *p*-tolyl allyl-1- C^{14} sulfide in acetone. The yield of the sulfide (b. p. 95-97° at 6.5 mm.) was 9.5 g. or 94.2 per cent from 4.7 g. (0.0615 mole) of allyl chloride, 1.98 g. (0.0862 g. atom) of sodium and 10.7 g. (0.0862 mole) of *p*-thiocresol.

3-Hydroxypropyltrimethylammonium chloride.--In a 500-ml. three-necked flask fitted with a sintered glass bubbler, a drying tube, and a dropping funnel, were placed 350 ml. of acetone. The flask was kept in a dry ice-acetone bath and 51.5 g. (0.500 mole) of 3-hydroxypropyldimethylamine was added dropwise as 24.0 g. (0.475 mole) of methyl chloride was passed through the sintered tube. The reactants were left at -78° for one hour, then at 0° for three hours, and finally at room temperature for two days. A white crystalline solid separated. It was filtered off and washed with acetone. It was dried at 60-70° in vacuum for two days. The yield was 59.0 g. or 81.0 per cent based on methyl chloride.

3-Chloropropyltrimethylammonium chloride.--This preparation was carried out according to the procedure of Gordon⁵⁹. The yield of the salt was 45.1 g. or 85.6 per cent from 47.1 g. (0.307 mole) of 3-hydroxypropyltrimethylammonium chloride and 51.5 ml. (0.708 mole) of thionyl chloride.

Anal. Calcd. for $C_6H_{15}NCl_2$: Cl, 20.65; Found: Cl, 20.80. (The percentage ionic chlorine was determined by Volhard titration).

Biallyl.--This preparation was carried out according to the method of Turk and Chanan⁶⁰. The yield of biallyl (b. p. 58-59.5° at 738 mm.) was 26.6 g. or 54.1 per cent from 91.8 g. (1.200 mole) of allyl chloride and 16.4 g. (0.675 g. atom). The reported yield is 55-65 per cent.

⁵⁹D. A. Gordon, Unpublished Ph.D. Thesis, Georgia Institute of Technology, 1953, p. 78.

⁶⁰A. Turk and H. Chanan, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1955, Coll. Vol. 3, p. 121.

CHAPTER V

CLEAVAGES OF ALLYL COMPOUNDS WITH METALS

Description of apparatus.--The apparatus used for carrying out these reactions was similar to that described by Stevenson⁶¹ except for a slight modification of the reaction vessel. This was a flat-bottomed tube 3.8 cm. in diameter by 25.0 cm. tall with a small diameter tube leading to the bottom but leaving enough space for a short magnetic stirring bar to work. Near the top of the reaction vessel were attached two $\frac{1}{8}$ 19/38 outer joints. Between these two joints, was a small opening fitted with a small rubber cap to introduce liquids with a hypodermic syringe. The joints were fitted to small retorts that were of such designs that by rotation their contents dropped into the reaction vessel.

Reactions with alkali metals in liquid ammonia at its boiling point.--The compounds used were allyltrimethylammonium chloride, allyl alcohol, allyl chloride and p-tolyl allyl sulfide. Sodium and lithium were the metals used. The reactions were carried out both in presence and absence of other added reagents. In many cases, the additional reagent was ammonium chloride but in a few cases methanol and ammonium sulfate

⁶¹R. W. Stevenson, Unpublished Ph.D. Thesis, Georgia Institute of Technology, 1958, p. 69.

were used. The general procedure for conducting a reaction in liquid ammonia at its boiling point was as follows. If the reaction was carried out in presence of ammonium chloride or ammonium sulfate, then these salts were weighed in a retort and poured into the reaction vessel before attaching the retort containing dried allyltrimethylammonium chloride. In the other retort, was placed the alkali metal freshly cut into two or more pieces and weighed just before starting the reaction. After fitting the retorts to the reaction vessel, gaseous ammonia was swept through the system until all air had been transferred to the gas collection chamber. The gas collection chamber was then refilled with fresh brine. The reaction vessel was kept in a Dry Ice-acetone bath to condense ammonia. After 50 ± 10 ml. of liquid ammonia had been collected, the cooling bath was removed. As the system warmed to its boiling point, qualitative observations concerning the solubility of reagents were made. It was found that ammonium chloride and allyltrimethylammonium chloride were soluble but ammonium sulfate did not dissolve appreciably in ammonia. Allyltrimethylammonium chloride was added before warming the system. The liquid reactants were introduced with a hypodermic syringe a little before the ammonia started boiling. The ammonia stream was reduced during warming so that a constant slow stream of ammonia bubbled through the liquid ammonia, and stirred the reaction contents in order to prevent bumping when the boiling point was reached. It was observed that

stirring with a short magnetic stirring bar (glass enclosed) served the same purpose without the need for bubbling ammonia through the solution. When the ammonia solution reached its boiling point, alkali metal was added by tipping the second retort. Metal was always used in excess of the theoretical amount. In presence of ammonium chloride or methanol, a blue color never appeared throughout the reaction solution. In other reactions including the one carried out in presence of ammonium sulfate, a permanent blue color remained after 10 to 45 minutes after addition of metal. Additional color changes were observed during reactions of *p*-tolyl allyl sulfide with lithium (not with sodium) and only once during reaction of allyltrimethylammonium chloride with sodium. After addition of metal, the color of the liquid ammonia solution turned yellow, then orange, and finally blue. Such color changes are indicative of the presence of free radicals or carbanions; the color of the allyl carbanion in solution is unknown. The hydrocarbon gases generated were swept into the collection chamber by gaseous ammonia. The liquid ammonia solution was allowed to evaporate slowly with continued stirring either by a slow stream of ammonia or the short magnetic bar. Evaporation of the last 5 to 10 ml. of liquid ammonia was accelerated by cautious warming of the reaction vessel with a beaker of cold water. After all the liquid ammonia had evaporated, the system was swept rather rapidly for a few minutes with gaseous ammonia.

The gaseous products were transferred quantitatively to an Orsat gas apparatus and were bubbled through a saturated brine solution which was one molar in hydrochloric acid until constant volume was attained. The volume of gas evolved in the reaction was then measured. Propylene and methane (the latter only from allyltrimethylammonium chloride) were analysed by infrared absorption by the procedure described by Stevenson⁶². The yields are given in Table 1. In one reaction of allyltrimethylammonium chloride with sodium under similar conditions, analysis of the gases was carried out by a gas chromatographic technique. The presence of diallyl and presumably two of its isomers was observed in this run; the yields of the products are given in Table 5.

The reactions of radioactive compounds with alkali metals in liquid ammonia at its boiling point were carried out in the same manner. The yields of the products in these reactions are given in Table 6.

Reactions with sodium in liquid ammonia at -72° .--The compounds reacted were allyltrimethylammonium chloride and allyl chloride. The metal used in these reactions, was sodium and the added reagent was ammonium chloride. In these reactions, the apparatus and part of the procedure was the same as described in reactions in liquid ammonia at its boiling point. A short magnetic stirring bar was always used as the reactants

⁶²Stevenson, op. cit., p. 42.

could not be stirred by bubbling in a slow stream of ammonia at -72° . A Dry Ice-ethanol bath was used to maintain the low temperature. From previous experiments, it was observed that ammonium chloride was fairly soluble in ammonia at -72° . Sometimes a little of it remained undissolved probably because of not having good stirring. Allyltrimethylammonium chloride was soluble at -72° . Ammonium chloride and allyltrimethylammonium chloride were added before keeping the reaction vessel in the Dry Ice-ethanol bath in order to give them more time to go into solution. Moreover stirring was better when the quantity of ammonia condensed was small. After 50 ± 10 ml. of liquid ammonia had collected, the supply of ammonia was cut off. A screwcock was used between the ammonia regulator and the apparatus to prevent the leakage of air into the system. When allyl chloride was reacted, it was introduced at this stage with a hypodermic syringe with constant stirring. In absence of ammonium chloride, allyl chloride was added after addition of sodium. In one reaction the order was reversed (see Table 5). When mercury rose to its maximum height in tube d^{61} , the temperature of the contents was taken to be -72° and sodium was added by tipping the retort. In presence of ammonium chloride, the reactions were fast and the mercury level in tube d^{61} used to drop completely in 5 to 10 minutes. The Dry Ice-ethanol bath was removed after all sodium had reacted. In presence of ammonium chloride a blue color observed only near the surface of the alkali metal. In absence of ammonium

chloride, a permanent blue color, dispersed through out the solution, appeared 10 to 30 minutes after addition of sodium. The reactants were stirred for three hours before removing the cooling bath. The gases evolved were collected, washed, and analyzed in the way as described in reactions in liquid ammonia at its boiling point. The yields are given in Table 2. The yields in reactions in which gases were analyzed by the gas chromatographic technique are given in Table 5.

The reactions of radioactive compounds in liquid ammonia at -72° were carried out in the same manner as described above. The yields of the products in these reactions are given in Table 6.

Reactions with sodium in alcohols.--Allyltrimethylammonium chloride was the only compound reacted. The alcohols used as solvents were 2-propanol and methanol. No ammonium chloride or sulfate were used. In these reactions, the apparatus was the same as described earlier. In the reaction vessel were placed 50 ± 15 ml. of 2-propanol or methanol. After fitting the retorts containing dry allyltrimethylammonium chloride and sodium to the reaction vessel, gaseous ammonia was swept through the system until all air had been transferred to the gas collection chamber. The reaction vessel was cooled in a big beaker containing tap water which was changed occasionally. The gas collection chamber was refilled with fresh saturated brine solution. The quaternary salt was added while sweeping

the air out of the system. It was observed that the salt was soluble in both of the alcohols. Sodium was added by tipping the second retort. The reaction in methanol was so fast that all sodium had reacted in a few minutes. The reactions in 2-propanol were quite slow and the sodium had not reacted completely even in 7 to 8 hours. The gases generated were swept into the collection chamber by gaseous ammonia. These were washed and analyzed in the same manner as described in reactions in liquid ammonia at its boiling point. The yields of the products are given in Table 3.

The yields of products in reaction of allyl- 1-C^{14} -trimethylammonium chloride with sodium in 2-propanol are given in Table 6.

Reactions with zinc dust in acetic acid.--Allyltrimethylammonium chloride and allyl chloride were the compounds reacted. The apparatus used was the same as described in the beginning. A short magnetic bar was used to stir the reactants. Carbon dioxide was used to sweep out the gases generated in these reactions. The gases were collected over a 10 per cent solution of sodium hydroxide. The same solution was used in the Orsat gas apparatus to wash the gases. Zinc dust, after activating with 0.5 N hydrochloric acid, was placed in the reaction vessel and was mixed with 50 ± 10 ml. of glacial acetic acid. The retorts, one of them containing allyltrimethylammonium chloride, were fitted to the reaction vessel.

When allyl chloride was reacted, both retorts were empty. Gaseous carbon dioxide was swept through the system until all air had been transferred to the gas-collection chamber. The hydrogen generated due to reaction between zinc dust and acetic acid was not significant. The gas collection chamber was refilled with fresh alkali solution. Allyltrimethylammonium chloride or allyl chloride were added to the reaction solution with fast stirring. As the reactions were not fast at room temperature, the reactants were heated in a hot water bath at 50-60°. The reactions were still slow though slightly faster than before. A solution of sodium iodide in 5 ml. of water was added to the reactants. It was observed that the aqueous sodium iodide did not make much change in reaction rate. The reactants were stirred from 6 to 24 hours. From analysis of the products, it was found that yields were better with greater reaction times and with better stirring. The analysis of the gases was carried out as usual by infrared absorption. The yields of propylene in these reactions are given in Table 4.

The yield of propylene in reaction of allyl chloride- C^{14} with zinc dust in acetic acid is given in Table 6.

Reactions of p-tolyl allyl sulfide with lithium in ethylamine at its boiling point.--The apparatus and part of the procedure are the same as described in reactions in liquid ammonia at its boiling point. No ammonium salts or alcohol were used in these reactions. A short Teflon enclosed magnetic stirrer was

used. The retorts, one containing lithium (25.7 mmoles) and the second empty, were fitted to the reaction vessel. Gaseous ethylamine was swept through the system until all air had been transferred to the gas-collection chamber. The gas-collection chamber was refilled with fresh saturated brine. A Dry Ice-acetone bath was placed about the reaction vessel. After 50 ± 10 ml. of liquid ethylamine had been collected, the Dry Ice-acetone bath was replaced with an ice bath. p-Tolyl allyl sulfide (6.1 mmoles) was added to the liquid ethylamine. Afterwards lithium was added. The reactants were stirred. The reaction did not proceed appreciably for four hours at 0° and therefore was allowed to warm to the boiling point of ethylamine. After half of the amine had evaporated, the reaction vessel was again kept in ice to condense more of the amine. The solution turned light yellow and then light blue. When the volume of the solution had increased to 50 ± 10 ml. the supply of ethylamine was turned off. The ice bath was removed and the solution was allowed to evaporate again. The blue color disappeared and 40 ml. of gas was collected. After no more gas collected, ethylamine was again condensed to increase the volume of the solution to 50 ± 10 ml. The reactants were stirred overnight at 0° . Next day the ice bath was removed. After all the liquid ethylamine had evaporated, the reaction vessel was kept in a hot water bath at 50° , and the system was swept rapidly with gaseous ethylamine for a few minutes. Some non-volatile liquid was left in the reaction vessel.

The Teflon enclosed stirrer turned from white to black during the reaction. The gases collected were washed and analyzed as usual by infrared absorption. The volume of gases was 51.7 ml. at S. T. P. The yield of propylene was 10.2 per cent based on p-tolyl allyl sulfide.

An effort was made to improve the yields in this reaction by using a glass-enclosed magnetic stirring bar, adding more lithium, and reversing the order of addition of lithium and the sulfide. In one run, the yield of propylene was 16.6 per cent from 6.1 mmoles of the sulfide and 61 mg. atoms of lithium. In another run, only traces of propylene were obtained. In a final run the infrared spectrum of the product showed a strong absorption band at 3.42 microns, medium absorption bands at 6.82, 7.20, and 7.27 microns, and weak absorption bands at 10.97 and 13.38 microns. This indicated the presence of a saturated hydrocarbon.

Reactions of p-tolyl allyl sulfide with lithium in methylamine at its boiling point.--The apparatus and procedure were the same as described in reactions of p-tolyl allyl sulfide in ethylamine. Only traces of propylene were obtained from 6.1 mmoles of p-tolyl allyl sulfide and 50 mg. atoms of lithium. The infrared spectrum showed a strong absorption band at 3.42 microns, medium absorption bands at 6.80, 7.18, and 7.26 microns, and weak absorption bands at 8.76, 10.95 and 13.35 microns. These bands indicate the presence of some saturated hydrocarbon.

CHAPTER VI

ANALYSES OF PRODUCTS

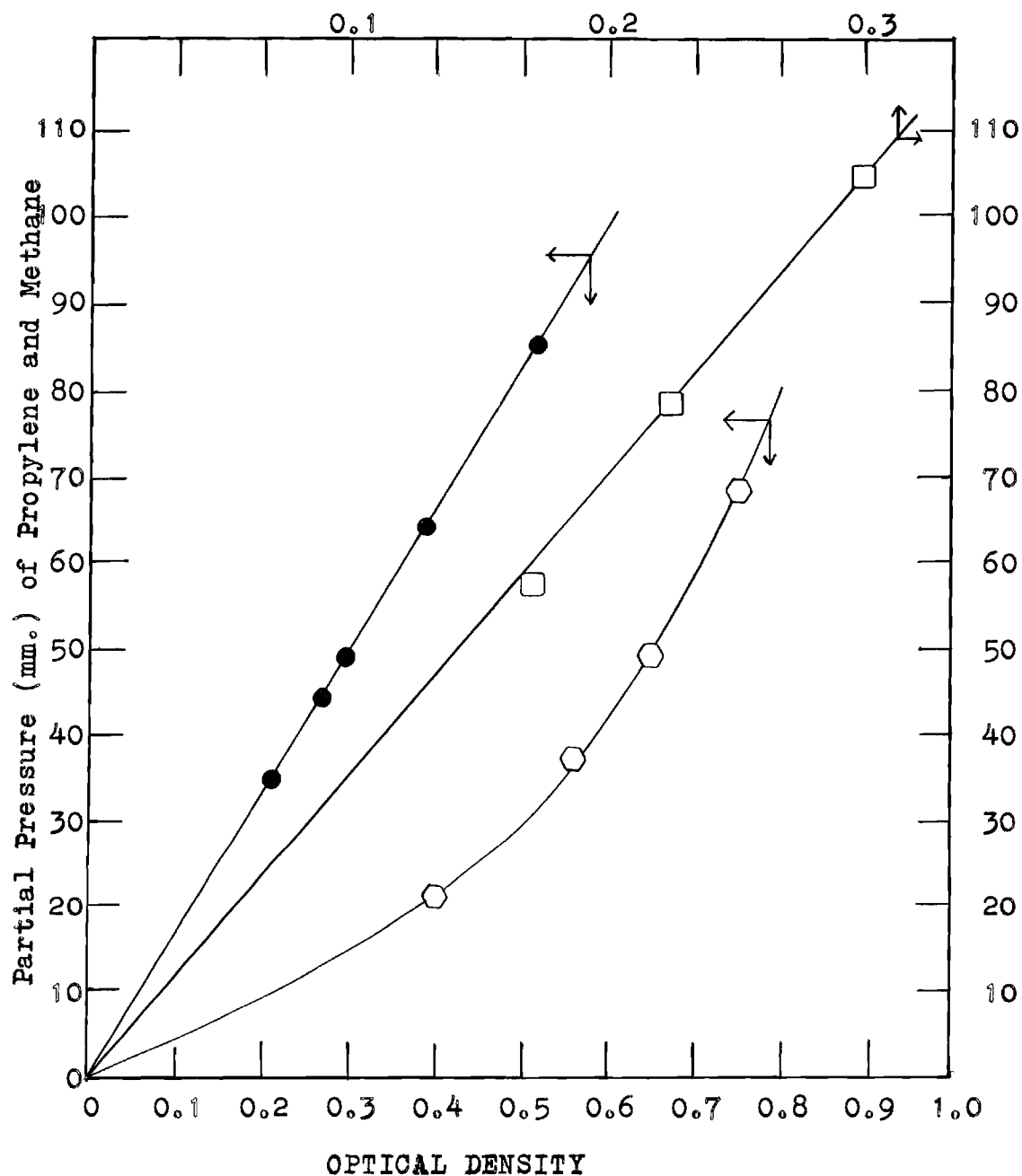
Analytical techniques.--The estimation of relative yields of propylene and methane in a mixture diluted with hydrogen and nitrogen was carried out by means of an infrared absorption technique. The infrared spectrum of the products from reactions of allyl chloride with sodium in absence of ammonium chloride strongly indicated the presence of bialllyl. The yields of propylene, bialllyl and some probable isomers of bialllyl were determined by gas chromatography. To determine the extent of rearrangement during syntheses of carbon-14 labeled compounds and the relative distribution of carbon-14 in positions 1 and 3 of propylene from reactions of radioactive compounds, an ozonolysis technique was employed.

Infrared analytical technique.--The procedure carried out was the same as described by Stevenson⁶². A Perkin-Elmer Model 21 spectrophotometer equipped with a removal ten-centimeter open-path gas cell with rock salt windows was used to measure absorption of infrared light by the samples. Calibration curves were prepared from optical density measurements made on known samples of methane and propylene. The samples at different partial pressures were made on the gas handling appa-

ratus designed by Blanchard⁶³. The method used to determine the optical density at the desired wavelengths was a "cell in-cell out" method. The spectrophotometer was zeroed and set at 100 per cent transmission with the cell out at 5.98 microns. Direct reading optical density paper was used. For samples of propylene, the cell was placed in the path of the sample beam, and the samples slowly scanned from 5.95 microns to 6.00 microns, the optical densities of the maxima (vicinity of 5.98 microns) were recorded. The samples of methane were scanned from 7.60 microns to 7.70 microns and optical densities of the maxima (vicinity of 7.67 microns) were recorded. A calibration curve for propylene at 7.67 microns was also made. Absorption of methane at 5.98 microns was found to be practically nil. Each sample was scanned twice. If two values did not agree, the sample was scanned again. The optical density of the cell with nitrogen was also determined at the requisite wavelengths. The calibration curves (Figure 1) were prepared after subtracting optical density of the cell with nitrogen from values of optical densities of the samples determined in the manner mentioned above.

The gases generated in the reactions were dried over Drierite before analysing them. The apparatus depicted in Figure 2 was used for this purpose. It consisted of two gas transferring vessels a and b and a drying tube c. A sample

⁶³E. P. Blanchard, Unpublished M.S. Thesis, Georgia Institute of Technology, 1954, p. 44.



- Propylene, 5.98 microns, 26°.
- Propylene, 7.67 microns, 28°.
- Methane, 7.67 microns, 24° (Absorption of methane at 5.98 microns was practically nil).

Figure 1. Partial Pressure of Propylene and Methane Vs. O. D.

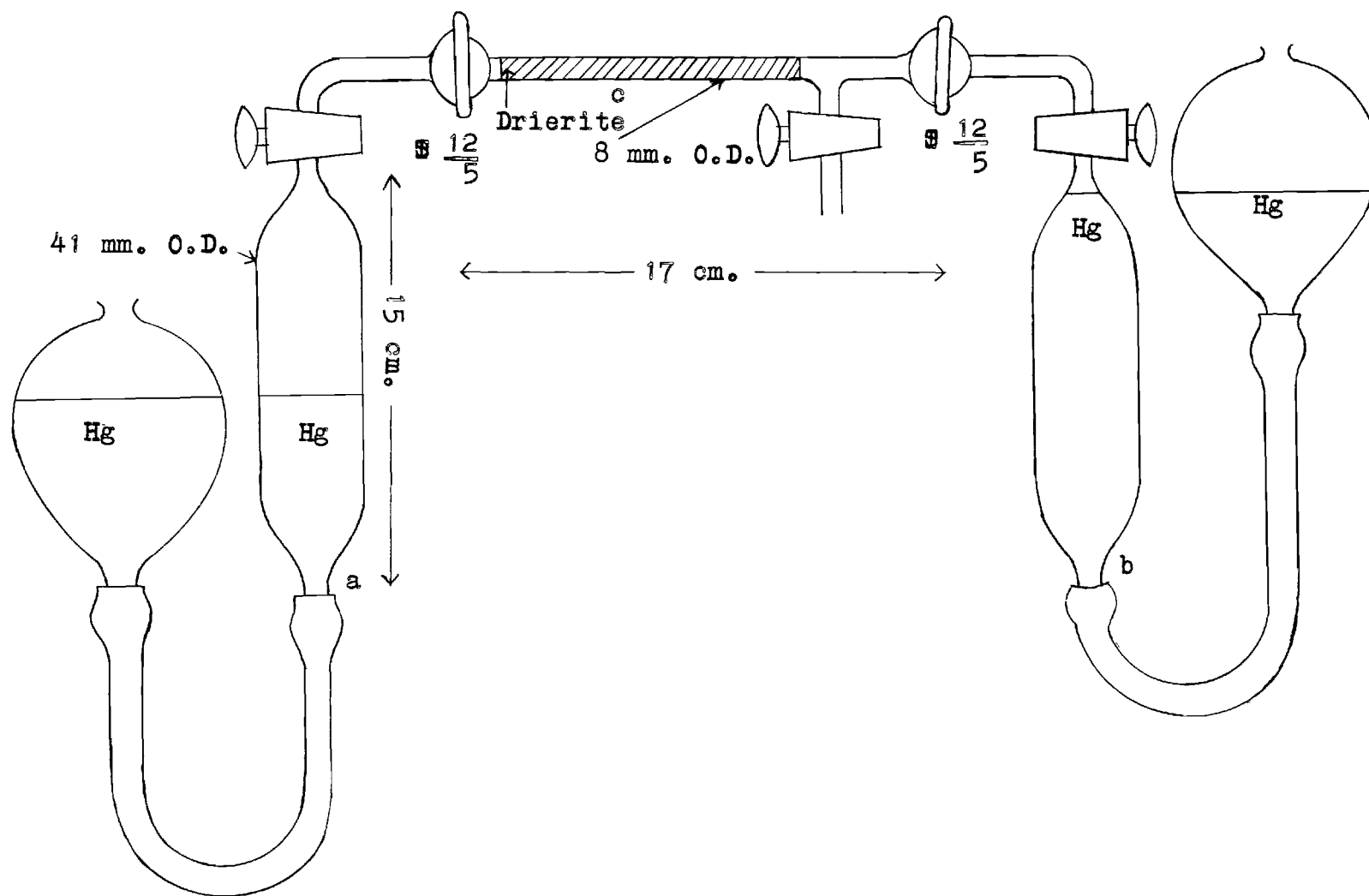


Figure 2. Apparatus for Drying Gases.

of gas to be analysed was transferred from the Orsat gas apparatus to one of the gas transferring vessels. This vessel was attached to the dry tube. The other end of the tube was attached to the second gas transferring vessel in which level of mercury was raised to the level of stopcock. The air in the dry tube was evacuated by a vacuum pump. The gas sample was dried by transferring it 10 to 12 times from one vessel to another. After drying the sample, the gas transferring vessel containing dried sample of the gas was attached by means of a ball and socket joint to one of the four stopcocks of the gas handling apparatus. The infrared cell was attached to one end of the apparatus and the other end was attached to a mercury manometer. One stopcock was connected to a vacuum pump and the other stopcock was connected to a nitrogen cylinder. The cell stopcock and the stopcock attached to the gas transferring vessel, were opened. The system was successively evacuated and filled at atmospheric pressure two or three times with nitrogen and finally it was evacuated and filled with the gas to be analysed at a reduced pressure. This pressure as read on the mercury manometer was recorded. The cell stopcock was closed, and the system outside the cell was again successively evacuated and filled with nitrogen some two times^b. Finally the system outside the cell was at or near atmospheric

^bThe system should always be successively evacuated and filled with nitrogen at least two times since the vacuum pump used reduced the pressure to only 2.5 mm. In the present work occasionally this evacuation and refilling may have been done only once and therefore some error was introduced in such cases.

pressure. The cell stopcock was opened slightly to admit nitrogen to the cell; the nitrogen cylinder valve was opened slightly to admit more nitrogen until the entire system, including the cell, was near atmospheric pressure, after which the cell stopcock was closed. The cylinder valve was closed and this pressure (near atmospheric) was recorded. The temperature was recorded. Sometimes the gas sample in the cell was too concentrated and therefore was diluted by a technique which has been described⁶⁴. The calculations were carried out as described by Stevenson⁶⁵.

Gas chromatographic technique.---The instrument used was a Perkin-Elmer Vapor Fractometer Model 154-C equipped with a Precision Gas Sampling system. The Precision Gas Sampling system was a device to introduce a reproducible volume of gaseous sample into the Vapor Fractometer system for each run. It had interchangeable sample volume tubes. In the present work, a 1/4 c.c. sample volume tube was used. A Perkin-Elmer column E[©] was fitted to the instrument. The carrier gas was helium and its pressure at the cylinder was set at 30 p.s.i. The pressure of helium at the instrument was set at 15 p.s.i.

⁶⁴Stevenson, op. cit., p. 44.

⁶⁵Stevenson, op. cit., p. 48.

[©]It is constructed of 1/4 inch O. D. stainless tubing two meters in length. The separating agent or fixed phase in column E is dimethylsulfolane (2,4-dimethyltetrahydrothiophene-1,1-dioxide) which is mixed with a supporting agent, a new form of diatomaceous earth that has been ground into fine granules.

The temperature of the column was kept at $33-33.5^{\circ}$. The flow rate of helium was 70-80 c.c. per minute. The detector was set at 8 volts. It took about 3 to 4 hours for the instrument to reach equilibrium.

Calibration curves for propylene and biallyl (Figure 3) were made by plotting peak heights against partial pressures of known samples. It was found that curves drawn on the basis of areas under peaks as deduced by paperweight method or product of height and width of peak at half height were less satisfactory in that not as many points fell on a straight line. Dimbat and coworkers⁶⁶ had shown that peak height was virtually insensitive to flow rate but sensitive to fluctuations of column operating temperature. The reverse was true of peak areas. In the present work, the temperature of the column was more constant than the flow rate. For calibrations, the Recorder Range (sensitivity scale) was set at 1 for biallyl and at 8 for propylene.

The samples at different partial pressures were made on the gas handling apparatus designed by Blanchard⁶³. The dilution of gases was carried out with helium instead of nitrogen. The gas transferring vessel as described in infrared absorption technique, was attached to one of the four stopcocks of the gas handling apparatus. A screwcock was used to stop the flow of mercury from the bulb to the tube

⁶⁶M. Dimbat, P. E. Porter, and F. H. Stross, Anal. Chem., 28, 290 (1956).

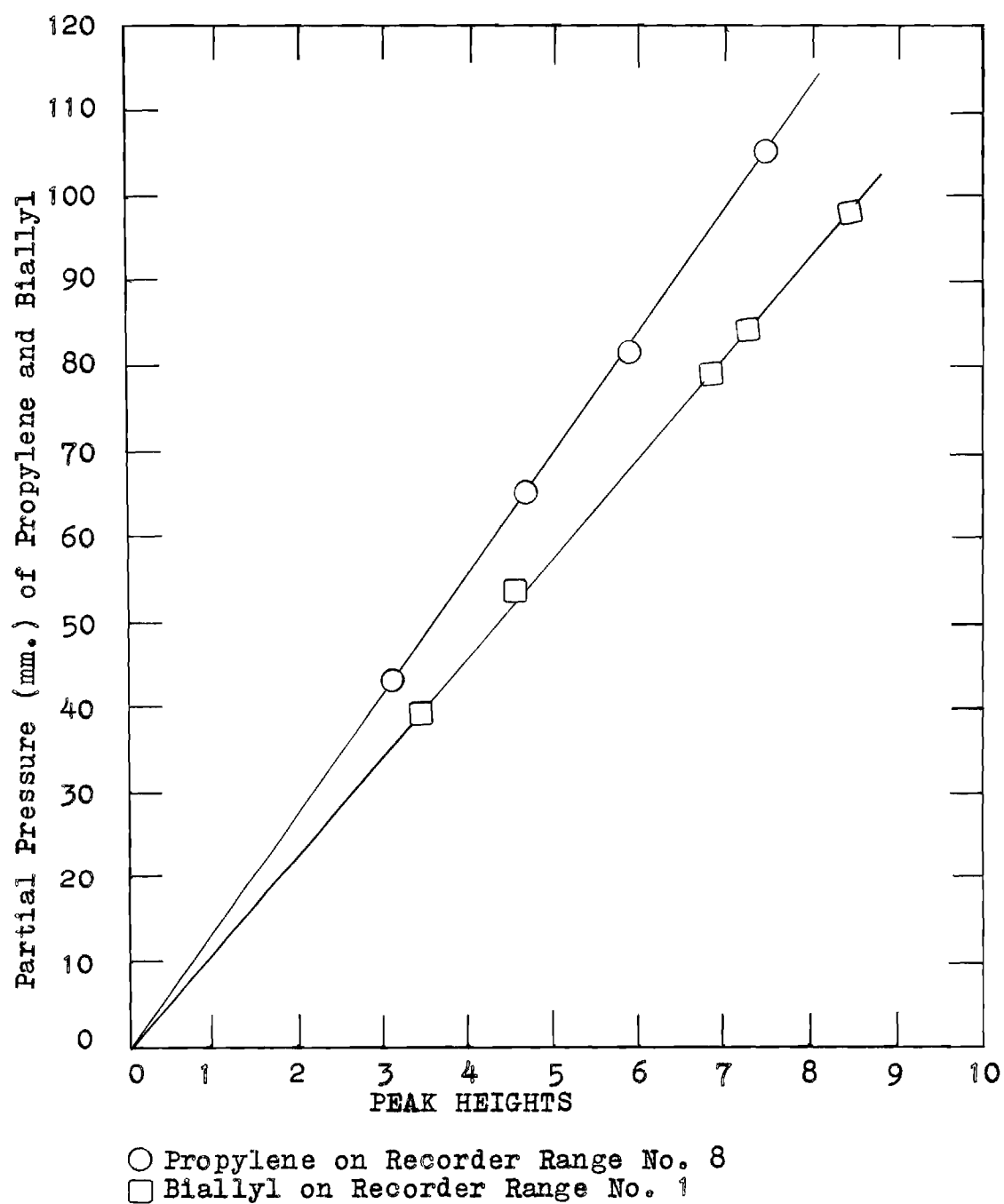


Figure 3. Partial Pressure of Propylene and Biallyl vs. Peak Height.

while the latter was evacuated. The mercury manometer, vacuum pump and helium cylinder were attached to the gas handling apparatus. A propylene cylinder or a tube containing 0.5 to 1 ml. of biiallyl was attached to the fourth stopcock. The end where infrared cell was attached, was closed with a 18/7 ball joint. The stopcock of the gas transferring vessel and the stopcock of the gas handling apparatus to which it was attached were opened. The system was then successively evacuated and filled at atmospheric pressure two or three times with helium and finally it was evacuated and filled with the sample gas at reduced pressure. The pressure was recorded. The stopcock of the gas transferring vessel was closed, and the system outside the vessel was again successively evacuated and filled with helium some two times^d. Finally the system outside the vessel was at or near atmospheric pressure. The vessel stopcock was opened slightly to admit helium to the vessel; the helium cylinder valve was opened slightly to admit more helium until the entire system, including the vessel, was near atmospheric pressure. The vessel stopcock was then closed. Each sample at a particular pressure was made separately. The gas transferring vessel containing the sample of gas was attached to the Precision Gas Sampling system. The Vapor Fractometer had already reached equilibrium and the recorder switch was turned

^dThe system should always be successively evacuated and filled with helium at least two times since the vacuum pump used reduced the pressure to only 2.5 mm. In the present work occasionally this evacuation and refilling may have been done only once and therefore some error was introduced in such cases.

on. A knob attached to the Precision Gas Sampling system, was turned to position 1, and the system was successively evacuated and filled with the sample gas one or two times, and finally the system was filled with the sample gas at atmospheric pressure. The sample was introduced to the Vapor Fractometer by turning the knob to position 2. The peaks for propylene appeared in 1.0 minute after introducing the samples. The peaks for biallyl appeared in 11.8 to 12.4 minutes. The peaks for biallyl isomer I appeared in 8.9 to 9.3 minutes and for biallyl isomer II in 10.1 to 10.7 minutes. Allyl chloride appeared in 28.1 to 28.6 minutes.

As biallyl (b. p. 59.5°) was one of the products obtained in the reactions, a special procedure was used to sweep the products from the apparatus. After a reaction was over and all ammonia had evaporated, as described in the chapter on reactions, the reaction vessel was heated in a hot water bath at $70-74^{\circ}$ and gaseous ammonia was swept through the system until the volume of the gases in the chamber was constant. This volume of gases was increased to 350-375 ml. (the maximum volume which the gas collection chamber could hold easily) by passing nitrogen slowly into the system and then sweeping it out with ammonia. A portion of the gases, usually 90-98 ml., was transferred to the Orsat gas apparatus and washed until its volume was constant. Its volume, temperature, and pressure were immediately recorded. The gas was then passed through a straight 0.8 x 17 cm. tube packed with

Drierite before collecting it in the gas transferring vessel. A correction was made for the air of the drying tube being introduced into the gas. A portion of the gas was then introduced in the Vapor Fractometer. During analysis of gases obtained from the reactions, the Recorder Range (sensitivity scale) was set at 128 for nitrogen, 32 to 8 for propylene and 1 for biallyl and its isomers. Another portion of the gases was drawn from the collection chamber. It was washed, dried, and analyzed as before. All the observations for the second portion were recorded. The remaining gases in the collection chamber were diluted with nitrogen by the procedure given previously and analyzed on the Vapor Fractometer. This process was repeated until the concentration of biallyl dropped in proportion to the dilution. A sample calculation for the percentage propylene, biallyl and isomers is given in Appendix A. The yields for biallyl isomer I and biallyl isomer II were calculated by using the calibration curve for biallyl.

The reactions in which yields of products were determined by the gas chromatographic technique are given in Table 5.

Ozonolysis.--The procedure used was similar to that of Leak⁶⁷. A simple laboratory ozonizer was used to generate ozone. It was found that 5.6 mmole of ozone was formed per hour when oxygen was passed at a rate of 120 bubbles per minute. For ozonizing compounds other than propylene, one 19 x 4.1 cm.

⁶⁷J. C. Leak, op. cit., p. 74.

ozonization tube with $\frac{3}{4}$ 45/50 joints and a bubbler made from a tube 8 mm. O. D. and having seven holes (each 2 mm. in diameter) was used and a solution of the compound to be ozonized in 50 ml. of chloroform was added. For propylene, two similar ozonization tubes joined in series were used. In the first tube (nearest the ozonizer), was placed 50 ml. of chloroform and in the second one 20 ml. The gases containing propylene were passed slowly into the first tube of chloroform which was cooled to -60 to -70° . A bubbler containing a solution of potassium iodide and sodium dihydrogen phosphate was attached in series to the second ozonization tube. During ozonization oxygen was bubbled into the system until the potassium iodide solution turned dark brown. In order to isolate the methone derivatives of the aldehydes, the chloroform solutions were combined and added to a 250-ml. Erlenmeyer flask containing 1.5 g. of powdered zinc and a magnetic stirring bar. To the rapidly stirred suspension was added an equal volume of water and 1.5 ml. of glacial acetic acid. The mixture was stirred for half an hour and the remaining solid was filtered off. The filtrate was mixed with a fresh solution of 1.5 to 2.0 g. of 5,5-dimethyl-1,3-cyclohexanedione "methone," in 25 ml. of 95 per cent ethanol. The resulting solution was allowed to stand overnight. Approximately 50 ml. of water was added to the solution and the chloroform was boiled off on a steam bath. On cooling, the mixture of methone derivatives was separated. It was filtered off and

dried in vacuum at room temperature. When commercial propylene was ozonized, the yield of the mixture of methone derivatives was 1.55 g. or 54.2 per cent from 4.75 mmoles of propylene and 20.0 mmoles of methone. From the mixtures of methone derivatives obtained after ozonization of *p*-tolyl allyl sulfide and allyltrimethylammonium chloride, the formaldehyde methone derivative was separated by dissolving the mixtures in boiling 95 per cent ethanol. Upon cooling, needles of formaldehyde methone derivative were separated. These were filtered off and recrystallized repeatedly until the m. p. was constant at 191.5° .

The components of methone mixture obtained from ozonization of radioactive propylene or allyl chloride⁶⁸, were separated as formaldehyde methone derivative and anhydride of acetaldehyde methone derivative by the procedure of Vorländer⁶⁸ with some modifications. The vacuum dried methone derivatives mixture was mixed with 7-10 ml. of glacial acetic acid. The contents were heated on a steam bath for 6 hours and then left at room temperature overnight. Next day the contents were mixed with water. A solid, which separated was filtered off and washed with water. It was dried and dissolved in 15 ml. of chloroform. The chloroform solution was extracted

⁶⁸D. Vorländer with C. Ihle and H. Volkholz, Z. anal. Chem., 77, 321 (1929).

^eOn ozonolysis of allyl chloride, acetaldehyde was obtained instead of chloroacetaldehyde doubtlessly because of reduction of the latter to the former by zinc dust in aqueous acetic acid.

with four 20 ml. portions of 4 per cent sodium hydride solution. The chloroform layer was washed with water and evaporated to dryness on a steam bath. The residue was the impure anhydride of acetaldehyde methone derivative. It was recrystallized repeatedly from 95 per cent ethanol until the m. p. was constant at $178-178.5^{\circ}$. The combined alkaline extracts were neutralized with 2 N hydrochloric acid. Formaldehyde methone derivative separated. It was filtered off, washed with water, and recrystallized repeatedly from 95 per cent ethanol until a constant m. p. at 191.5° was reached.

Technique of radioactive assays.--The apparatus depicted in Figure 4 was used for assaying all carbon-14 compounds. This apparatus was adapted from the design of Ropp⁶⁹. The combustion reagents used were prepared according to the procedure of Van Slyke and coworkers⁷⁰. The solid reagent was prepared by grinding two parts by weight of potassium iodate and one part of potassium dichromate. The liquid reagent was prepared by adding 33 ml. of phosphoric acid to 67 ml. of fuming sulfuric acid. The mixture of acids was mixed with 1 g. of potassium iodate and heated to $160-190^{\circ}$ till the iodate was dissolved. The U-tube g was filled with stannous chloride ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$) crystals. The straight tube h was

⁶⁹G. A. Ropp, personal communication to Dr. E. Grovenstein, Jr., see also O. K. Neville, J. Am. Chem. Soc., 70, 3501 (1948).

⁷⁰D. D. Van Slyke, J. Plazin, and J. R. Weisiger, J. Biol. Chem., 191, 299 (1951).

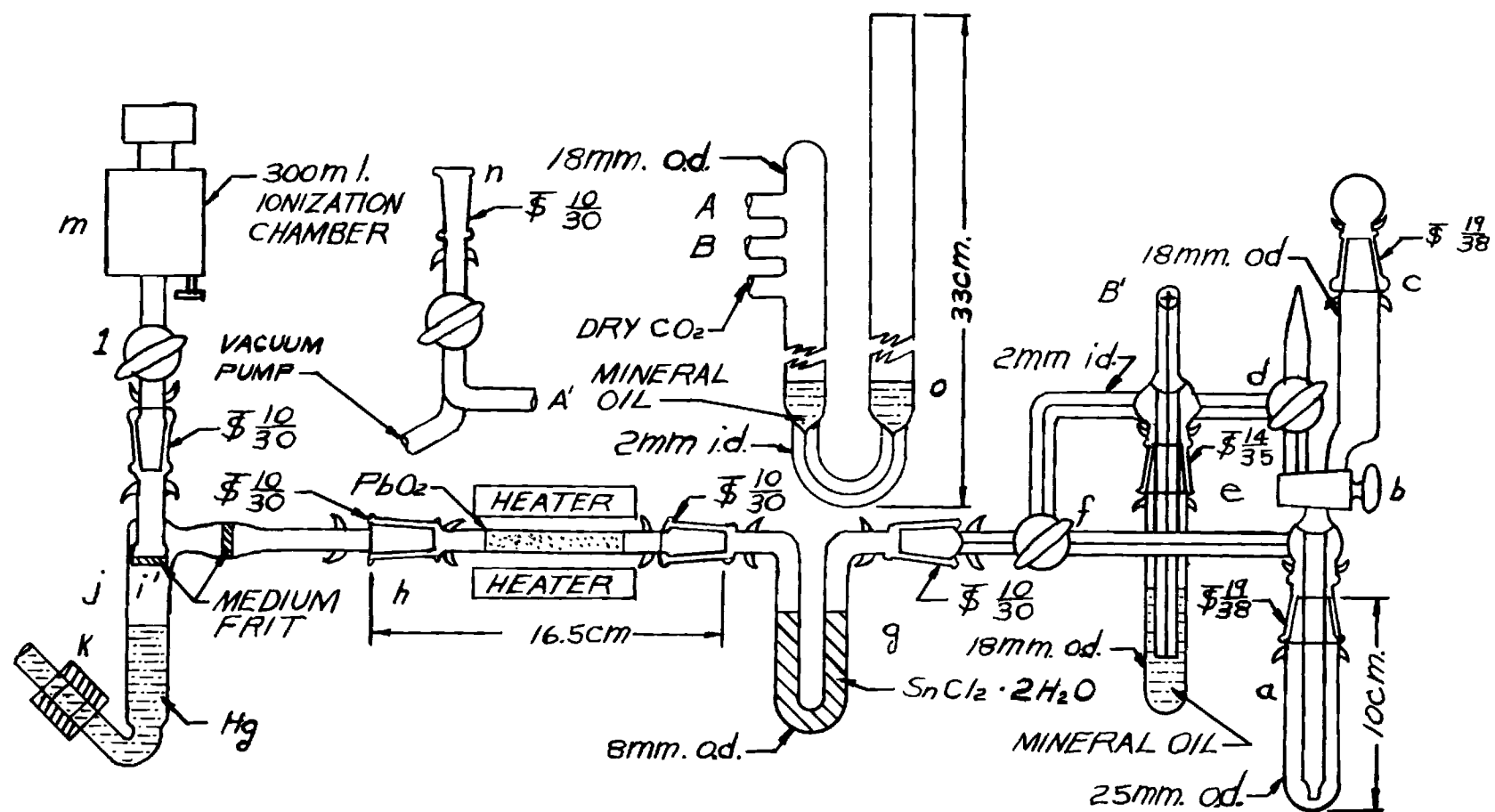


Figure 4. Wet Combustion Apparatus for Assaying Carbon-14 Compounds

packed with lead dioxide and was maintained at 180° with an electrical heater. The compound for radioactive assay was weighed accurately in a platinum boat on a microbalance. The usual amount of compound taken was 7 to 15 mg. The boat containing weighed amount of compound was placed in the combustion tube a. The compound was covered with approximately one gram of the solid combustion reagent. The combustion tube was fitted to the apparatus with springs. The care was taken that the boat was directly below the inner tube. Outlets B and A were connected with B' and A' respectively by means of rubber tubes. In the beginning, the ionization chamber m (Applied Physics Corporation, Serial 3095) was fitted to the joint n, and the three-way stopcock was turned in a position to evacuate it. A regular stream of carbon dioxide was passed through the U-shaped oil bubbler o. The stopcocks d, b and f were turned in positions so that carbon dioxide swept all air out of the system. This sweeping was conducted for 20 to 25 minutes. The ionization chamber was evacuated and filled with carbon dioxide. This process was repeated three times and finally the evacuated chamber was transferred and fitted to the tube j in which the height of mercury was pre-adjusted. In tube c was placed 7 ± 1 ml. of the liquid combustion reagent. Stopcock d was closed and stopcock l was opened. Mercury in j rose and touched frit i'. The liquid reagent was added dropwise. After all the liquid reagent had been added, the combustion tube was heated with

a small flame and the mixture was boiled carefully for a minute. Carbon dioxide was again swept through the system at such a rate that it took 15 to 20 minutes to fill the ionization chamber with gases. Finally stopcock f was turned to equalize pressure in the chamber. The ionization chamber was removed after closing stopcock l.

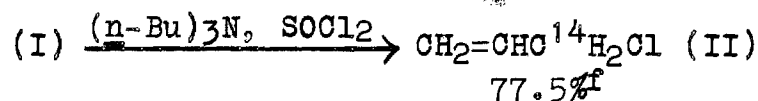
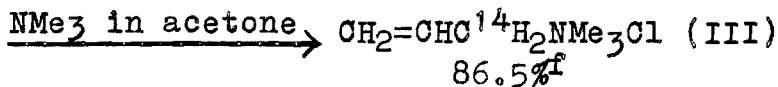
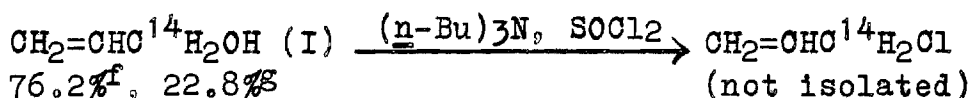
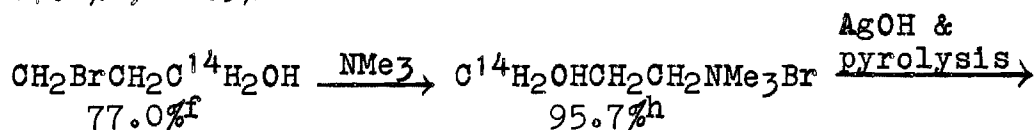
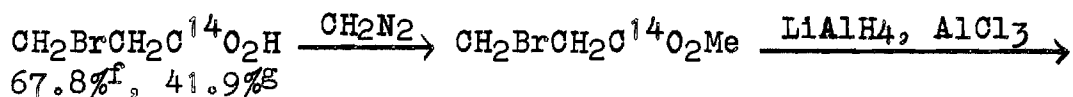
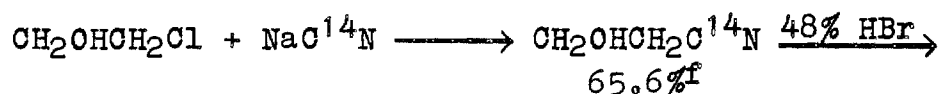
For allyl-1- C^{14} -trimethylammonium chloride which was very hygroscopic, a 2.2 x 0.9 cm. tube with a ground glass-stopper was used instead of a platinum boat. For liquids, sealoff bulbs were used. The sealed bulbs containing weighed amount of liquid compounds were broken in the combustion tube with the aid of a glass-enclosed magnet.

Radioactivities were determined by use of a Vibrating-reed electrometer (Applied Physics Corporation, Model 31). Specific activities of compounds were calculated in micro-curie per mmole. The specific activities of compounds through the stage of allyl alcohol-1- C^{14} were determined by the Steady Deflection Method. The specific activities of subsequent compounds and of methone derivatives were determined by the Rate of Drift Method. A sample calculation of specific activity for a radioactive compound is given in Appendix B.

CHAPTER VII

DISCUSSION

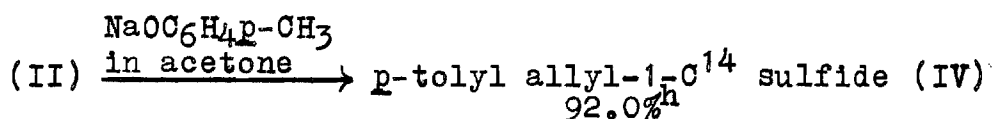
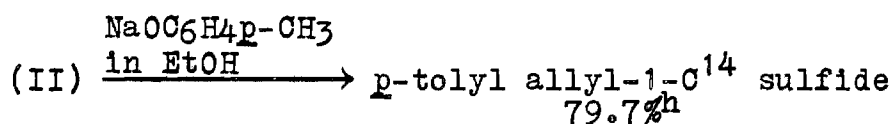
In this work cleavages of allyl-1-C¹⁴-trimethylammonium chloride (III), allyl chloride-1-C¹⁴ (II), allyl alcohol-1-C¹⁴ (I), and p-tolyl allyl-1-C¹⁴ sulfide (IV) with metals were studied. These compounds were synthesized according to the outline:



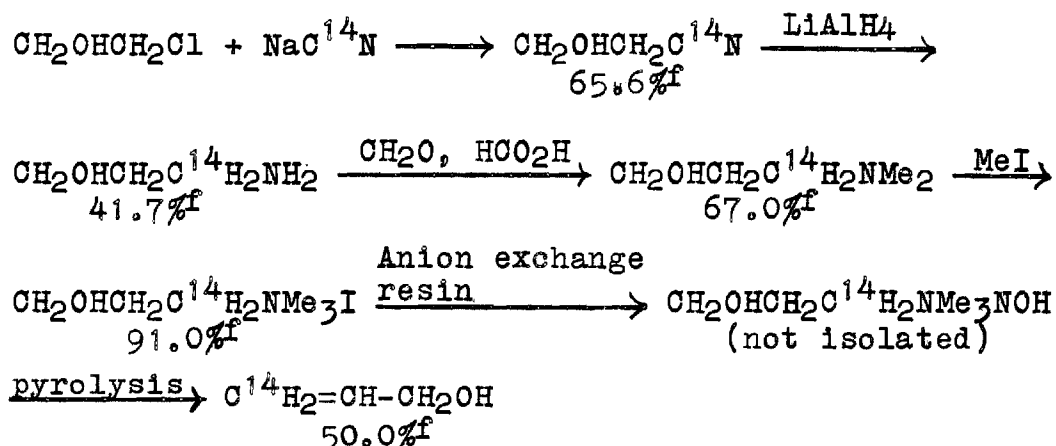
^fYields with non-radioactive compounds.

^gOverall radiochemical yields based on radioactive sodium cyanide.

^hYields with radioactive compounds.



In work with carbon-14 a preliminary preparation was carried out with non-radioactive materials in order to become familiar with the procedure and eliminate any step which may have caused loss of radioactive material. Originally it was planned to synthesize allyl-3-C¹⁴ compounds by synthesizing allyl alcohol-3-C¹⁴ through the scheme:



The yields at various steps in this scheme were satisfactory except the reduction of hydracrylonitrile to 3-aminopropanol which went in poor yield (41.7 per cent). The overall yield of allyl alcohol in the above scheme was 8.36 per cent based on sodium cyanide. This yield might be improved by carrying out the reduction of the nitrile with hydrogen at 10 atmos-

pheres pressure in liquid ammonia in presence of nickel catalyst. The reported yield of the amine under these conditions is 92 per cent⁷¹. The yield of allyl alcohol from 3-hydroxypropyltrimethylammonium iodide may be increased to 76.2 per cent by reacting the salt with silver hydroxide as carried out in the preparation of allyl alcohol-1-C¹⁴ from 3-hydroxy-3-C¹⁴-propyltrimethylammonium bromide.

As no standard was used to compare the radioactivities measured in the present work, it may be of some value to compare the radiochemical and chemical yields through the step leading to allyl alcohol. The non-radioactive and radioactive allyl alcohols were synthesized by following the same procedure except at one step in which esterification of β -bromopropionic acid was carried out differently. In the radioactive synthesis the esterification was carried out with diazomethane. In the non-radioactive synthesis the ester was obtained in 73.5 per cent yield by reacting the acid with methanol in presence of concentrated sulfuric acid. The yield of non-radioactive allyl alcohol was 18.5 per cent based on potassium cyanide. The radiochemical yield through the step leading to allyl alcohol-1-C¹⁴ was 22.8 per cent based on radioactive sodium cyanide.

Originally it was decided to study cleavage of diallyl ether but because of the difficulties which have been experi-

⁷¹F. Hoffmann-La Roche & Co., A.-G. Swiss Patent No. 244,837, Chem. Abs., 43, 6652g (1949).

enced in its preparation and because the presence of two allyl groups in diallyl ether complicates interpretations of the results, p-tolyl allyl sulfide was prepared instead.

Radioactive allyltrimethylammonium chloride, allyl chloride and p-tolyl allyl sulfide were ozonolysed to determine the extent of rearrangement of carbon-14 from position 1 to position 3 in the allyl group. No ozonolysis of radioactive allyl alcohol was carried out because this is a precursor of the other three compounds. The results of ozonolysis are interesting. The radioactive allyl chloride and allyltrimethylammonium chloride contained 1.06 per cent of allyl chloride-3-C¹⁴ and 1.23 per cent of allyl-3-C¹⁴-trimethylammonium chloride respectively. When radioactive p-tolyl allyl sulfide was prepared in ethanol, the percentage of p-tolyl allyl-3-C¹⁴ sulfide formed was 33.4, but when prepared in acetone its percentage was only 3.82. The results can be explained on the basis of the greater ionizing power of ethanol than acetone. Solvents of high ionizing power favor mechanism S_N¹ (or possibly mechanism S_N²¹).

It is interesting to note also that even though allyltrimethylammonium chloride and p-tolyl allyl sulfide were both prepared in acetone, rearrangement was more extensive in the sulfide than in the ammonium salt. This may be explained by differences in reaction temperature and nucleophilicity of attacking reagents. Lower temperatures are expected to favor more selective reactions than higher tem-

peratures. Stronger nucleophilic reagents would probably react less selectively than weaker nucleophilic. *p*-Thiocresolate ion has been found to be far more nucleophilic than trimethylamine. Bunnett and Davis⁷² have estimated the rate constants ($l. \text{ mole}^{-1} \text{ min.}^{-1}$) for thiophenoxide ion and piperidine with 2,4-dinitrochlorobenzene in 60 per cent aqueous dioxane at 25° to be 1300 and 4.48 respectively. Therefore the reaction of allyl chloride-1-¹⁴C with *p*-thiocresolate ion at 20° would be expected to be less selective than with trimethylamine at -78°.

The radioactive compounds at various steps (β -bromopropionic acid, allyl alcohol and allyltrimethylammonium chloride) were checked for radiochemical impurities by making suitable derivatives of these compounds and comparing the specific activities of the compounds with their corresponding derivatives. The derivatives of allyl alcohol and allyltrimethylammonium chloride were richer in sp. activities (microcurie per millimole) by 1.6 and 2.5 per cent respectively than their parent compounds.

Some interpretations and generalizations can be made concerning the yields of products in the reductive cleavages studied in this work. In liquid ammonia the yields of propylene were better in cleavages of allyltrimethylammonium chloride and *p*-tolyl allyl sulfide than in cleavages of allyl

⁷²J. F. Bunnett and G. T. Davis, J. Am. Chem. Soc., **76**, 3011 (1954).

alcohol and allyl chloride (Tables 1, 5 and 6). When these reactions were conducted in presence of ammonium chloride, the yields of propylene were poorer due to reaction of ammonium ions with electrons from the metals to give ammonia and hydrogen. The presence of methanol also reduced the yields of propylene though not to such an extent as ammonium ions. This result may be due to a lower concentration of methanol than of ammonium ions. In reactions of allyltrimethylammonium chloride with sodium in presence of ammonium sulfate (Run 3, Table 1; Run 4, Table 6) the difference in yields of propylene was large. This lack of reproducibility may be due to experimental error or to not having a good arrangement for stirring the reactants. As ammonium sulfate is only slightly soluble in ammonia, its effective mole may be altered by differences in the efficiency of stirring. The nature of the metal (Li or Na) used in these reactions did not have any systematic effect on yields, though Krug and Tocker¹⁰ found a greater reduction of organic sulfur compounds with lithium than sodium in liquid ammonia.

The yields of propylene in reactions of allyl alcohol with alkali metals in absence of any added reagent were in the range of 46.5 to 50.6 per cent (Run 6 and 7, Table 1; Run 11, Table 6). These values seem to agree with Chablay's observations that only half of the allyl alcohol is reduced by sodium in liquid ammonia, unless ethanol is present⁷³.

⁷³E. Chablay, Ann. Chim., 8, 145 (1917).

Table 1. Products from Reactions with Alkali Metals in Liquid Ammonia at Its B. P.

Run No.	Compounds	Compound mmoles	Metal mg. atoms	Added Reag.	Added Reag. mmoles	Yield ^a Propylene %	Yield ^a Methane %
1.	AllylNMe ₃ Cl	5.95	Na (24.8)	None	None	75.9	0.24
2.	AllylNMe ₃ Cl	5.32	Li (24.3)	None	None	82.5	None
3.	AllylNMe ₃ Cl	6.72	Na (15.4)	(NH ₄) ₂ SO ₄	3.71	86.2	0.23
4.	AllylNMe ₃ Cl	5.76	Li (25.7)	NH ₄ Cl	36.1	57.7	None
5.	AllylNMe ₃ Cl	6.56	Na (18.7)	MeOH	18.95	70.4	0.13
6.	CH ₂ =CHCH ₂ OH	10.00	Li (16.4)	None	None	48.0	
7.	CH ₂ =CHCH ₂ OH	10.00	Na (23.5)	None	None	46.5	
8.	CH ₂ =CHCH ₂ Cl	7.05	Na (14.1)	(NH ₄) ₂ SO ₄	Traces	22.8	
9.	p-Tolyl allyl sulfide	5.80	Na (15.2)	None	None	62.2	
10.	p-Tolyl allyl sulfide	6.10	Li (14.3)	None	None	64.7	

^aYields are based on allyl compounds.

Table 2. Products from Reactions with Sodium in Liquid Ammonia at -72° .

Run No.	Compounds	Compound mmoles	Sodium mg. atoms	Added Reag.	Added Reag. mmoles	Yield ^a Propylene %	Yield ^a Methane %
1.	AllylNMe ₃ Cl	5.91	20.9	NH ₄ Cl	33.1	44.3	None
2.	CH ₂ =CHCH ₂ Cl ^b	10.0	30.0	NH ₄ Cl	30.0	52.8	
3.	CH ₂ =CHCH ₂ Cl	8.0	20.0	NH ₄ Cl	40.0	23.9	
4.	CH ₂ =CHCH ₂ Cl ^c	10.0	15.2	None	None	19.5 ^d	

^aYields are based on starting allyl compounds.

^bThe gases analyzed contained a small amount of allyl chloride.

^cAllyl chloride was added after addition of sodium.

^dIn this particular reaction yield of propylene is not very significant as the gases analyzed contained considerable portion of diallyl.

Table 3. Products from Reactions with Sodium in Alcohols^a.

Run No.	Compounds	Compound mmoles	Sodium mg. atoms	Alcohol	Yield ^b Propylene %	Yield ^b Methane %
1.	AllylNMe ₃ Cl ^c	5.17	22.6	2-propanol	28.5	0.06
2.	AllylNMe ₃ Cl	4.65	44.6	Methanol	10.5	0.36

^aNo additional added reagents were used in these reactions.

^bYields are based on allyltrimethylammonium chloride.

^cThe reaction was run for 8 hours.

Table 4. Products from Reactions with Zinc Dust in Acetic Acid.

Run No.	Compounds	Compound mmoles	Zinc mg. atoms	Added Reag.	Added Reag. mmoles	Yield ^a Propylene %	Yield ^a Methane %
1.	AllylNMe ₃ Cl	5.76	20.6	None	None	2.3	Not Calcd.
2.	CH ₂ =CHCH ₂ Cl ^b	8.0	21.4	NaI ^d	8.0	70.5	
3.	CH ₂ =CHCH ₂ Cl ^c	8.0	21.4	NaI ^d	8.0	35.9	

^aYields based on starting allyl compounds.

^bThe reaction was run for 24 hours at 35° most of the time and then the reaction vessel was kept for 3 to 4 hours in hot water bath at 50°.

^cThe reaction was run for 6 hours at 50-60°.

^dUsed in 5 ml. of water.

Table 5. Reactions in Which Products Were Analyzed by Gas Chromatography.

Run No.	Reactions ^a	Added Reag. mmoles	Yield ^b Propylene %	Yield ^b Biallyl %	Yield ^b Biallyl Isomer I %	Yield ^b Biallyl Isomer II %
1.	CH ₂ =CHCH ₂ Cl ^c (10.0) + Na (15.0) in liquid ammonia at -72°	None	16.4	27.2	10.5	2.54
2.	CH ₂ =CHCH ₂ Cl (10.0) + Na (15.0) in liquid ammonia at -72°.	None	11.0	57.2	8.88	2.38
3.	CH ₂ =CHCH ₂ Cl (10.0) + Na (15.0) in liquid ammonia at -72° ^d .	NH ₄ Cl (30.0)	31.0	6.12	None	None
4.	AllylNMe ₃ Cl (7.08) + Na (21.3) in liquid ammonia at its b. p.	None	86.0	3.92	2.32	0.25
5.	AllylNMe ₃ Cl (6.38) + Na (19.6) in liquid ammonia at -72°.	None	72.4	9.46	2.01	0.57

^aFigures in parentheses indicate mmoles or mg. atoms of the substances reacted.

^bYields are based on starting allyl compounds.

^cAllyl chloride was added after addition of sodium. In other reactions sodium was always added after addition of allyl compounds.

^dThe gases analyzed contained a small amount of allyl chloride.

Table 6. Reactions of Allyl-1-C¹⁴ Compounds

Run No.	Reactions ^a	Added Reag. mmoles	Yield ^b C ₃ H ₆ %	Yield ^b CH ₄ %	Sp. Act. ^{c,d}		Sp. Act. ^{c,d}	
					Formaldehyde Methone Der.		Acetaldehyde Methone Der.	
1.	AllylNMe ₃ Cl ^h (5.61) + Na (14.2) in liquid ammonia at its b. p.	None	69.7	0.15	1882 ± <1 (6) 1828 ± 10 (6)		1708 ± 1 (4) 1752 ± <1 (4)	
2.	AllylNMe ₃ Cl ^h (5.09) + Na (18.9) in liquid ammonia at its b. p. (22.3)	MeOH	58.2	0.21	1895 ± 20 (6) 1851 ± 1 (6)		1769 ± 6 (3) ^g 1857 ± 6 (4)	
3.	AllylNMe ₃ Cl ^h (5.16) + Na (45.0) in 2-propanol at 28°.	None	Not det.	Not det.	1776 ± 2 (6) 1795 ± 6 (7)		1706 ± 5 (3) 1654 ± 5 (4)	
4.	AllylNMe ₃ Cl ^h (5.46) + Na (15.2) in liquid ammonia at its b. p. (2.9)	(NH ₄) ₂ SO ₄	40.1	0.20	1866 ± 5 (6) 1881 ± 7 (6) 1857 ± 10 (7)		1738 ± 19 (4) 1748 ± 13 (4)	
5.	AllylNMe ₃ Cl ^h (4.43) + Li (25.7) in liquid ammonia at its b. p.	None	64.2	0.35	1896 ± 4 (4) 1909 ± 6 (5) 1903 ± 15 (6) 1825 ± 15 (6) ^e 1819 ± 14 (6) ^e		1696 ± 4 (3) 1640 ± 3 (4) 1691 ± 13 (5) 1634 ± 3 (5) ^e 1649 ± 6 (5) ^e	
6.	AllylNMe ₃ Cl ^h (6.49) + Li (19.3) in liquid ammonia at -78°.	NH ₄ Cl	44.2	0.03	1770 ± 6 (5) 1838 ± 9 (6)		1707 ± 12 (3) 1714 ± 10 (4)	
7.	AllylNMe ₃ Cl ^h (6.65) + Li (25.7) in liquid ammonia at its b. p. (32.7)	NH ₄ Cl	Not det.	Not det.	1800 ± 5 (6) 1807 ± 6 (6)		1730 ± 14 (4) 1747 ± 3 (4)	

Table 6. Reactions of Allyl-1-C¹⁴ Compounds (Continued)

Run No.	Reactions ^a	Added Reag. mmoles	Yield ^b		Sp. Act. ^{c,d}		Sp. Act. ^{c,d}	
			C ₃ H ₆ %	CH ₄ %	Formaldehyde Methone Der.		Acetaldehyde Methone Der.	
8.	AllylNMe ₃ Cl ^h (7.16) + Na (23.0) in liquid ammonia at -72°.	NH ₄ Cl (32.9)	45.2	None	1855 ± 6 (6) 1858 ± 7 (6)		1788 ± 13 (4) 1769 ± 5 (4)	
9.	CH ₂ =CHCH ₂ Cl ⁱ (8.00) + Zn (21.4) in acetic acid at 35-50°.	NaI ^f (8.0)	53.7 ¹		2015 ± 8 (6) ^e 2040 ± 3 (6) ^e		1880 ± 8 (4) ^e 1893 ± 8 (4) ^e	
10.	CH ₂ =CHCH ₂ Cl ⁱ (8.00) + Na (23.0) in liquid ammonia at -72°.	NH ₄ Cl (24.0)	54.2 ¹		2035 ± 13 (6) ^e 2064 ± 10 (6) ^e		1916 ± 14 (4) ^e 1888 ± 15 (4) ^e	
11.	CH ₂ =CHCH ₂ OH ^j (10.00) + Li (18.6) in liquid ammonia at its b. p.	None	50.6		1737 ± 15 (6) ^e 1715 ± 17 (6) ^e		1583 ± 6 (4) ^e 1593 ± 2 (4) ^e	
12.	CH ₂ CHCH ₂ OH ^j (15.0) + Li (30.0) in liquid ammonia at its b. p.	NH ₄ Cl (40.0)	27.9		1698 ± 8 (6) ^e 1689 ± 4 (6) ^e		1585 ± 4 (4) ^e 1589 ± 3 (4) ^e	
13.	p-Tolyl allyl sulfide ^k (6.1) + Na (15.2) in liquid ammonia at its b. p.	None	63.6		2176 ± 17 (6) ^e 2124 ± 14 (6) ^e		1938 ± 34 (4) ^e 1923 ± 11 (4) ^e	
14.	p-Tolyl allyl sulfide ^k (7.32) + Li (22.9) in liquid ammonia at its b. p.	NH ₄ Cl (36.1)	49.2		2082 ± 6 (6) ^e 2070 ± 7 (6) ^e		1979 ± 7 (4) ^e 1972 ± 1 (4) ^e	

Table 6. Reactions of Allyl- i -C¹⁴ Compounds (Continued)

Run No.	Reactions ^a	Added Reag. mmoles	Yield ^b C ₃ H ₆ %	Yield ^b CH ₄ %	Sp. Act. ^{c,d}		Sp. Act. ^{c,d}	
					Formaldehyde Methone Der.		Acetaldehyde Methone Der.	
15.	p-Tolyl allyl sulfide ^k (6.1) + Li (14.3) in liquid ammonia at its b. p.	None	41.6		2213 ± 9 (6) ^e 2166 ± 9 (6) ^e 2181 ± 5 (7) ^e 2186 ± 7 (7) ^e 2172 ± 13 (7) ^e		1722 ± 17 (4) ^e 1721 ± 1 (4) ^e	
16.	p-Tolyl allyl sulfide ^k (7.3) + Li (15.7) in liquid ammonia at its b. p.	None	57.1		2112 ± 1 (6) ^e 2121 ± 2 (7) ^e 2131 ± 1 (7) ^e		1943 ± 5 (4) ^e 1920 ± 6 (4) ^e	

^aFigures in parentheses indicate mmoles or mg. atoms of the substances reacted.

^bYields are based on starting allyl compounds.

^cSpecific activities are given in microcurie per millimole of compound and multiplied by 10⁴, and were determined by Rate of Drift Method except where specified. The ± values after the sp. act. give the average deviations in measurement of radioactivities upon the particular sample.

^dFigures in parentheses by specific activities indicate number of crystallizations of methone derivatives before their radioactive assays were carried out.

^eSecond Ionization Chamber (Applied Physics Corporation, Serial 3095) was used.

^fUsed in 5 ml. of water.

^gThe sp. act. was determined by Steady Deflection Method.

Table 6. Reactions of Allyl-1-C¹⁴ Compounds (Continued)

^hThe sp. act. was 0.3650 $\mu\text{c}/\text{mmole}$. The salt contained 1.23 per cent of allyl-3-C¹⁴-trimethylammonium chloride.

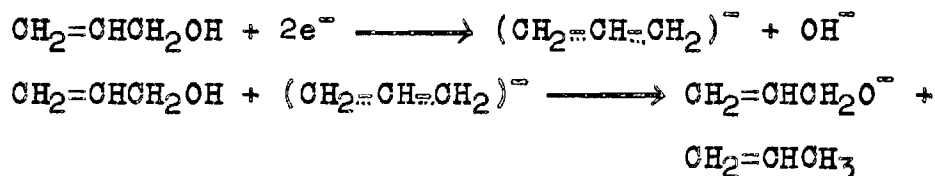
ⁱThe sp. act. of allyl chloride was assumed to be the same as that of p-tolyl allyl sulfide which was 0.4140 $\mu\text{c}/\text{mmole}$, as the latter was prepared from the former without any dilution. The sum of sp. act. of formaldehyde methone derivative and anhydride of acetaldehyde methone derivative obtained after ozonolysis of the chloride was 0.3964 $\mu\text{c}/\text{mmole}$. The chloride contained 1.06 per cent of allyl chloride-3-C¹⁴.

^jThe sp. act. was 0.3340 $\mu\text{c}/\text{mmole}$. The alcohol was not ozonolysed.

^kThe sp. act. was 0.4140 $\mu\text{c}/\text{mmole}$. The sulfide contained 3.82 per cent of p-tolyl allyl-3-C¹⁴ sulfide.

^lThe gases analyzed contained a small amount of allyl chloride which was removed by passing the gases back and forth through a U-tube cooled at -55° to -60° before passing them for ozonolysis.

The reductive cleavage of the remainder of the allyl alcohol is evidently prohibited by formation of the corresponding sodium alkoxide:



Ethanol liberates allyl alcohol by the process:



This explanation is partly the same as given by Birch⁸.

Allyltrimethylammonium chloride with zinc dust in acetic acid gave a much lower yield of propylene than allyl chloride under similar conditions (Table 4). This may be accounted for on the basis of the known more ready displacement of Cl^- than of NMe_3 by nucleophilic reagents.



Also after two-electron addition to a molecule of allyl chloride, the like charges on chlorine and the allyl group may facilitate cleavage of the C-Cl bond.

In all the reactions at -72° (Table 2; Runs 6 and 8, Table 6) either "zero" or only traces of methane were observed. These may be attributed to the low temperature. "Zero" per cent yields of methane were also found at -33°

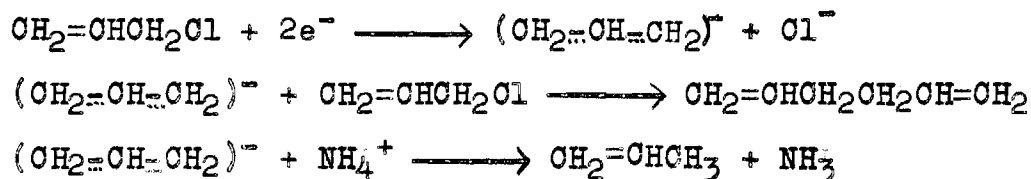
(Runs 2 and 4, Table 1), but it is notable that in both these runs lithium rather than sodium was used as the metal. However in Run 5, Table 6 lithium gave an expected yield of methane. This lack of reproducibility may be due to experimental error in infrared measurements. For this the calibration curves should have been checked occasionally.

The infrared spectrum of the products obtained from reactions of allyl chloride with sodium in absence of ammonium chloride strongly indicated the presence of bialllyl. In a few reactions of non-radioactive allyl chloride and allyltrimethylammonium chloride with sodium the yields of propylene, bialllyl and some probably isomers of bialllyl were determined by gas chromatography (Table 5)¹

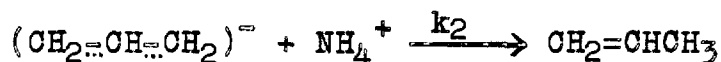
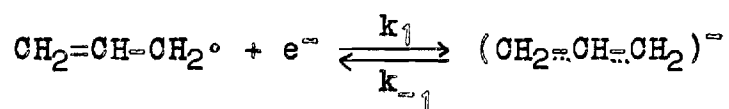
Allyl chloride reacted with sodium in liquid ammonia in absence of ammonium chloride gave bialllyl as major olefin along with propylene and a few per cent of products which, on the basis largely of their retention times, are judged to be isomers of bialllyl. Saturation of the liquid ammonia solution with ammonium chloride greatly increased the yield of propylene relative to bialllyl and gave no detectable amount of isomers of bialllyl. These results suggest that bialllyl is

¹In a private communication, Mr. L. C. Rogers reported 2.20 per cent of propane and 6.10 per cent of propylene, but no bialllyl and its isomers in reductive cleavage of allyl alcohol in liquid ammonia at -33° with lithium. Under similar conditions but with sodium, p-tolyl allyl sulfide gave 0.73 per cent of propane, 82.0 per cent of propylene, 2.4 per cent of bialllyl, 0.57 per cent of bialllyl isomer I and 0.05 per cent of bialllyl isomer II. The gases from these runs were analyzed by gas chromatography in the usual manner reported in this thesis.

produced by reaction of allyl carbanion with allyl chloride and that ammonium chloride greatly reduces the amount of bialllyl by rapid protonation of allyl carbanion to give propylene:



That bialllyl is probably produced by reaction of allyl carbanions with allyl chloride rather than by dimerization of allyl radicals is indicated by the very high ratio of propylene to bialllyl in the reactions of allyltrimethylammonium chloride with sodium. If bialllyl results from reaction of allyl carbanion with allyl chloride or allyltrimethylammonium ion, then allyl chloride would be expected to be a more reactive source of allyl group than the allyltrimethylammonium ion because of the greater reactivity of allyl chloride over allyltrimethylammonium ion toward common nucleophilic reagents. However this is not a rigorous mechanistic argument because allyl chloride may and probably does react with sodium faster than does allyltrimethylammonium ion and, therefore, could give a higher concentration of allyl radicals which would lead to a higher yield of bialllyl from allyl chloride than from allyltrimethylammonium ion. Ammonium ions should not directly lower the concentration of allyl radical but could do so indirectly:



It is difficult to explain the effect of ammonium ions except on the basis of formation of allyl carbanions or at least that steps k_1 and k_2 are concerted.

Since ammonium chloride greatly reduced but did not entirely eliminate the formation of bialllyl, there is possibility that the cleavage of allyl compounds takes place both by one-electron and two-electrons addition with the result that both allyl radicals and allyl carbanions are intermediates:

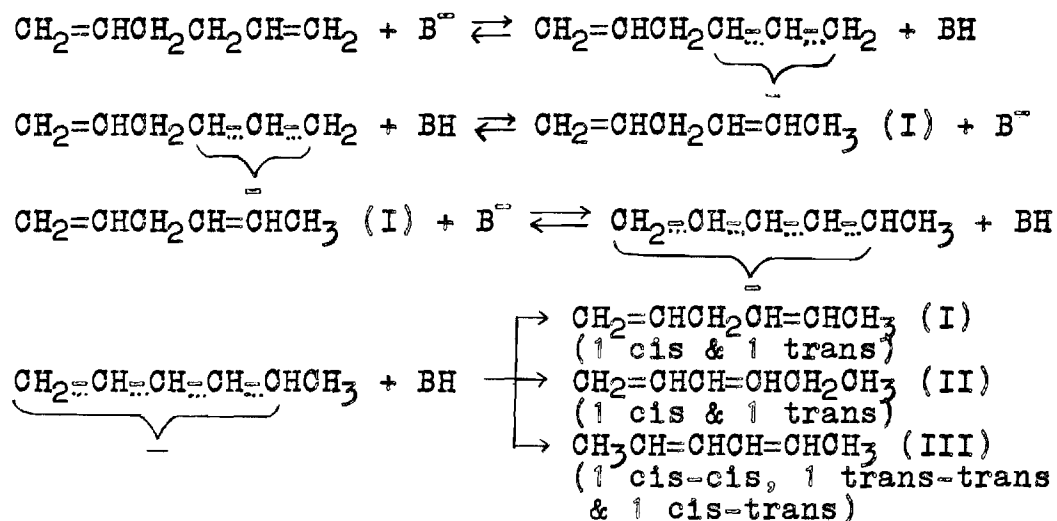


Ammonium ions could cut down the yield of bialllyl resulting from allyl carbanions but might not do so to the portion being formed through allyl radicals.

The results of this study give strong support for allyl carbanions as an intermediate in reductive cleavages of allyl compounds, however these results can not rule out the possibility of concurrent or prior formation of allyl radicals as an intermediate. To clear up this point further work is required.

Bialllyl isomers evidently result from isomerization of bialllyl by strong bases (B^-) such as amide ions or allyl carbanions and this interpretation is strengthened by the

absence of these isomers in the run with ammonium chloride which should readily destroy these strong bases (Run 3, Table 5). A possible mechanism is as follows:



The isomers called (II) and (III) should be more stable than (I), and (III) more than (II) on the basis of the extent of conjugation. Only two isomers of bialllyl were detectable in appreciable concentration on the basis of gas chromatographic separation (Table 5).

The order of addition of allyl chloride and sodium made a significant difference in the relative proportion of bialllyl and propylene (Runs 1 and 2, Table 5). When allyl chloride was added first (Run 2), the yield of bialllyl was increased while that of propylene was decreased. This is understandable since when sodium is added first (Run 1) the concentration of sodium throughout the solution is large and therefore the rate of formation of allyl carbanions is is greater and the concentration of allyl chloride is rapidly

reduced. Since bialllyl formation, in the present interpretation, depends upon the reaction of allyl chloride with allyl carbanion, less bialllyl is formed when the concentration of allyl chloride is low. However when sodium is added after addition of allyl chloride, carbanions are produced only near the surface of sodium at a rate which may depend on the rate of solution of the sodium. Greater yields of bialllyl isomers in Run 1 than 2 are explained on a similar basis namely, that higher concentration of allyl carbanions or amide ions in Run 1 causes more extensive isomerization of bialllyl.

The temperature also appears to make some difference in relative proportion of bialllyl and propylene. When allyltrimethylammonium chloride was cleaved with sodium at -72° , the ratio of bialllyl to propylene was larger than in the similar reaction carried out at -33° . This indicates that by lowering reaction temperature, the rate of formation of propylene is lowered to a greater extent than that of bialllyl.

No butene-1 was observed in cleavage of allyltrimethylammonium chloride according to analysis of the products by gas chromatography^j. Butene-1 would be formed if allyl carbanion reacts with a methyl group of allyltrimethylammonium ion by mechanism S_N2 .

The relative distribution of carbon-14 in positions 1 and 3 of propylene obtained from reactions of allyl-1- C^{14} -

^jThe retention time for butene-1 was 1.8 min. at 15 p.s.i. of pressure of helium at a rate of 85 c.c. per min. The same column E, as used in other cases, was used.

-trimethylammonium chloride, allyl chloride-1-C¹⁴, allyl alcohol-1-C¹⁴ and *p*-tolyl allyl-1-C¹⁴ sulfide with metals was determined by ozonization. The methone derivatives of the resultant formaldehyde and acetaldehyde were assayed for radioactivity and the data are collected in Table 6. The average of these values for each reaction together with average deviations are given in Table 7. The results indicate that the formaldehyde had 3.3 to 13.5 per cent greater radioactivity than the acetaldehyde produced from ozonization of propylene. The results of Run 15 are not considered reliable since on repetition a more normal distribution of carbon-14 was observed (Run 16). These results appear to be strikingly independent of the structure of the organic compound, the nature of the metal (only Na and Li studied extensively), and the reaction temperature.

The reason for studying a variety of allylic compounds, in which the allyl group was attached to different groups was to see whether the distribution of radioactivity in the product was dependent on the nature of the group cleaved. It was thought conceivable, for example, that electron addition to *p*-tolyl allyl sulfide or allyl chloride might occur rapidly and reversibly followed by slow proton addition in the cleavage step to give C¹⁴H₂=CHCH₃ and/or CH₂=CHC¹⁴H₃ but not a 50/50 mixture of these substances since the intermediate anion could hold the added electrons in an unfilled 3d orbit of sulfur or chlorine. The results obtained, however, show

Table 7. Isotope Effects in Reactions of Allyl-1- C^{14} Compounds

Run No.	Reactions	Average Sp. Act. Formaldehyde Methone ^a Der.	Average Sp. Act. Acetaldehyde Methone ^a Der.	Apparent Isotope Effect ^a , k_{12}/k_{14}
1.	AllylNMe ₃ Cl + Na in NH ₃ at -33°.	0.1855 ± 0.0027	0.1730 ± 0.0022	1.072 ± 0.029
2.	AllylNMe ₃ Cl + Na in NH ₃ at -33°, MeOH added.	0.1873 ± 0.0022	0.1813 ± 0.0044	1.033 ± 0.037
3.	AllylNMe ₃ Cl + Na in 2-propanol at 28°.	0.1785 ± 0.0009	0.1680 ± 0.0026	1.062 ± 0.022
4.	AllylNMe ₃ Cl + Na in NH ₃ at -33°, (NH ₄) ₂ SO ₄ added.	0.1868 ± 0.0009	0.1743 ± 0.0016	1.072 ± 0.015
5.	AllylNMe ₃ Cl + Li in NH ₃ at -33°.	0.1903 ± 0.0009 0.1822 ± 0.0008	0.1676 ± 0.0024 0.1642 ± 0.0008	1.135 ± 0.022 1.110 ± 0.010 ^b
6.	AllylNMe ₃ Cl + Li in NH ₃ at -78°, NH ₄ Cl added.	0.1804 ± 0.0034	0.1711 ± 0.0011	1.054 ± 0.027
7.	AllylNMe ₃ Cl + Li in NH ₃ at -33°, NH ₄ Cl added.	0.1804 ± 0.0006	0.1739 ± 0.0009	1.037 ± 0.008

Table 7. Isotope Effects in Reactions of Allyl-1-C¹⁴ Compounds (Continued).

Run No.	Reactions	Average Sp. Act.		Apparent Isotope Effect ^a , k_{12}/k_{14}
		Formaldehyde Methone ^a Der.	Acetaldehyde Methone ^a Der.	
8.	AllylNMe ₃ Cl + Na in NH ₃ at -72°, NH ₄ Cl added.	0.1857 ± 0.0007	0.1779 ± 0.0010	1.044 ± 0.010
9.	CH ₂ =CHCH ₂ Cl + Zn in acetic acid at 35-50°.	0.2028 ± 0.0013	0.1887 ± 0.0008	1.075 ± 0.011 ^b
10.	CH ₂ =CHCH ₂ Cl + Na in NH ₃ at -72°, NH ₄ Cl added.	0.2050 ± 0.0015	0.1902 ± 0.0014	1.078 ± 0.016 ^b
11.	CH ₂ =CHCH ₂ OH + Li in NH ₃ at -33°.	0.1726 ± 0.0016	0.1588 ± 0.0005	1.087 ± 0.014 ^b
12.	CH ₂ =CHCH ₂ OH + Li in NH ₃ at -33°, NH ₄ Cl added.	0.1694 ± 0.0006	0.1587 ± 0.0003	1.067 ± 0.006 ^b
13.	p-Tolyl allyl sulfide + Na in NH ₃ at -33°.	0.2150 ± 0.0026	0.1931 ± 0.0034	1.113 ± 0.033 ^b
14.	p-Tolyl allyl sulfide + Li in ammonia at -33°, NH ₄ Cl added.	0.2076 ± 0.0007	0.1976 ± 0.0004	1.051 ± 0.006 ^b

Table 7. Isotope Effects in Reactions of Allyl-1-C¹⁴ Compounds (Continued).

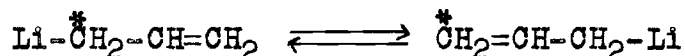
Run No.	Reactions	Average Sp. Act. Formaldehyde Methone ^a Der.	Average Sp. Act. Acetaldehyde Methone ^a Der.	Apparent Isotope Effect ^a , k_{12}/k_{14}
15.	p-Tolyl allyl sulfide + Li in NH ₃ at -33°.	0.2184 ± 0.0013	0.1721 ± 0.0019	1.269 ± 0.021 ^b
16.	p-Tolyl allyl sulfide + Li in NH ₃ at -33°.	0.2121 ± 0.0006	0.1932 ± 0.0012	1.098 ± 0.010 ^b

^aThe number following the symbol ± is the average deviation.

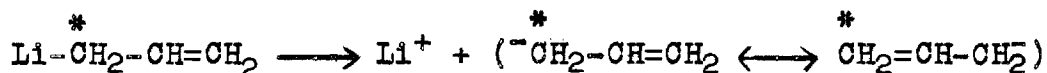
^bSecond Ionization Chamber was used.

that the distribution of carbon-14 in the resultant propylene are independent of the nature of the group cleaved.

The results also indicate that the reductive cleavage is independent of the metal used. Lithium might be expected to form a more covalent allyl compound than sodium. Even so, however, allyllithium would be expected to be in a state of rapid dynamic equilibrium as found for allylmagnesium bromide¹⁵.



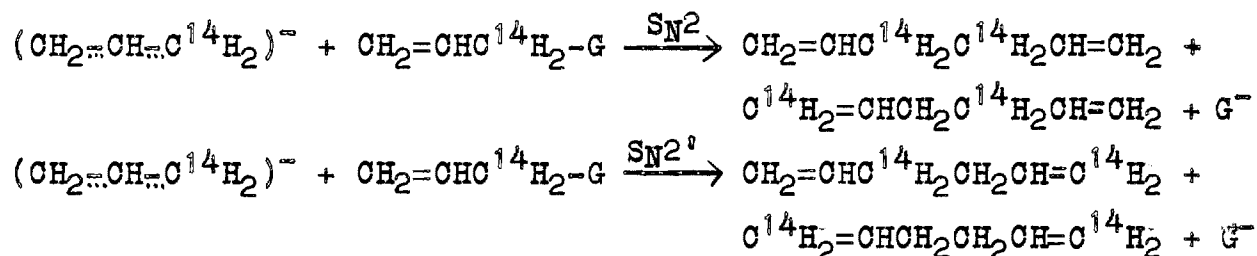
Such an isomerisation would bring about equilibration of carbon-14 between carbons 1 and 3 of the allyl system and, in the present study, would be indistinguishable from an equilibration brought about by ionization to give the symmetrical allyl carbanion:



A close examination of the summarized results in Table 7 indicates that addition of ammonium chloride lowers the apparent isotope effect by 2.0 to 9.8 per cent. The same effect is observed when allyltrimethylammonium chloride is reacted in liquid ammonia containing methanol or in 2-propanol as solvent. The presence of ammonium sulfate does not appear to make much difference apparently because it is only slightly soluble in liquid ammonia.

The analysis of products by gas chromatography from reactions of allyltrimethylammonium chloride and allyl chlo-

ride has revealed that bialllyl and its isomers are also formed along with propylene. The yield of bialllyl is reduced considerably in presence of ammonium chloride. It is possible that the presence of bialllyl and its isomers in the propylene which was ozonized may be the reason for some enrichment of radioactivity in formaldehyde methone derivative relative to acetaldehyde methone derivative. Bialllyl can be formed through two reaction mechanisms, S_N2 and S_N2' :

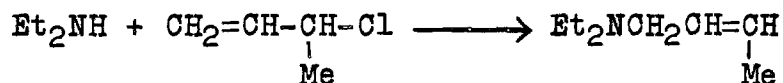


If bialllyl is formed through mechanism S_N2' then after ozonolysis three fourth of its radioactivity would be in the formaldehyde^k. If it is formed through mechanism S_N2 then only one fourth of its radioactivity would be in the formaldehyde. However there is less possibility of bialllyl being formed through mechanism S_N2' since this mechanism is generally observed to occur to an appreciable extent only when bimolecular substitution at the α position of the allyl derivative (but not at its γ position) is retarded by steric hindrance. Thus Young, Webb and Goering⁷⁴ have shown that while the

^kThese and subsequent estimates of the distribution of carbon-14 in the products for various mechanisms ignore any isotope effects.

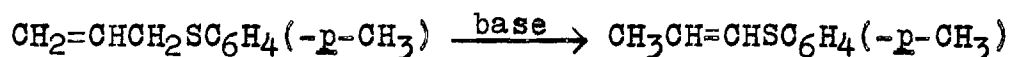
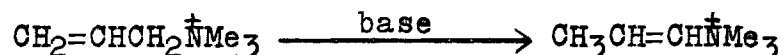
⁷⁴W. G. Young, I. D. Webb and H. L. Goering, J. Am. Chem. Soc., 73, 1076 (1951).

reaction of diethylamine with α -methylallyl chloride in benzene yields at least 82 per cent of crotyldiethylamine, the corresponding reaction of crotyl chloride gives 85 per cent yield of the same amine.

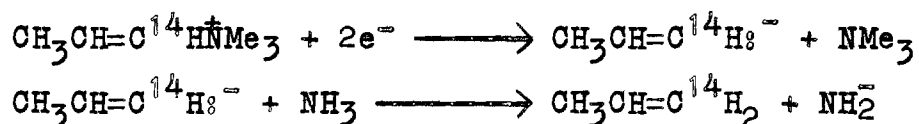


If biallyl is formed through dimerization of allyl radicals then half of its radioactivity would be in the formaldehyde, and therefore such biallyl could not account for the non-random distribution of carbon-14 in the product.

A discussion of the possibilities of rearrangements of reactants and products under the conditions of reductive cleavage is pertinent to an explanation for the location of carbon-14 in the product. Amide ions or allyl carbanions produced in such reactions may rearrange the products and reactants. A few rearrangements of this kind have been reported. The rearrangements of allyl ethers to propenyl ethers have been studied by Prosser¹⁸. Tarbell et al. studied the rearrangements of alkyl and aryl allyl sulfides under basic conditions¹⁷. Shatenshtein et al. studied the mobility of hydrogen in some ethylenic hydrocarbons in deuterated ammonia in presence of potassium amide¹⁹. Allyltrimethylammonium ion and *p*-tolyl allyl sulfide may be rearranged to propenyltrimethylammonium ion and *p*-tolyl propenyl sulfide:



By analogy with the ease of cleavage of the phenyl group from nitrogen⁷⁵, a propenyl group of the rearranged products might be expected to be cleaved by alkali metals almost as easily as the allyl group. If cleavage of the rearranged reactants takes place, then it would increase the radioactivity in the formaldehyde:



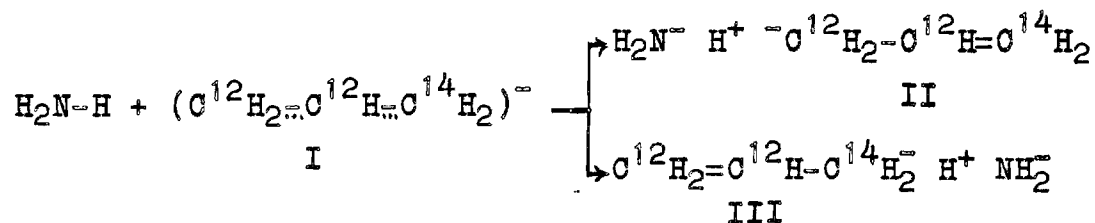
The above process seems like a reasonable explanation for that portion of excess radioactivity in the formaldehyde from propylene which is eliminated by addition of ammonium chloride, but cannot account for the 5.6 per cent excess radioactivity in the formaldehyde from runs in presence of ammonium chloride.

There is a possibility that some of the propylene might have been rearranged after its formation. A calculation was made on the basis of the results of Shatenshtein et al.¹⁹ to determine the extent of rearrangement in propylene which was evolved in the reactions studied in this work. As the rate constant for H-D exchange for propylene was given only at one temperature, the activation energy for hydrogen

⁷⁵P. Groenewoud and R. Robinson, J. Chem. Soc., 1692 (1934).

No reasonable explanation has yet been offered for the greater radioactivity of formaldehyde than that of acetaldehyde from the ozonization of propylene from reductive cleavages in presence of ammonium chloride or other acid. In runs in which ammonium chloride, methanol, 2-propanol and acetic acid were present, the ratio of activity of formaldehyde methone derivative to that of acetaldehyde methone derivative was 1.056 ± 0.016^m . The most likely explanation for this ratio is that an isotope effect (k_{12}/k_{14}) of this order of magnitude exists in the protonation of allyl carbanion. It is difficult to calculate the magnitude of the expected isotope effect on the basis of Bigeleisen's equation. For some attempted calculations see Appendix C. A qualitative interpretation of the isotope effect is as follows.

Protonation of allyl carbanion (I) at the terminal positions gives transition states which are approximately represented by structures II and III.



Consider the double bond $\text{C}^{12}=\text{C}^{14}$ in structure II, this bond is expected to be more stable than the double bond $\text{C}^{12}=\text{C}^{12}$

^mThe apparent isotope effects (k_{12}/k_{14}) with \pm average deviations of the reactions (Runs 2, 3, 6, 7, 8, 9, 10, 12, and 14) have been averaged.

in structure III because bonds with heavier isotopes have lower frequencies than those with lighter isotopes. Similarly the $C^{12}-C^{14}$ single bond of structure III should be more stable than the $C^{12}-C^{12}$ single bond of structure II. However the effect due to the double bond may reasonably be expected to outweigh the effect due to the single bond with the result that transition state II should be slightly more stable than transition state III. Hence somewhat more propylene-3- C^{14} should be formed than propylene-1- C^{14} as was indeed found to be the case.

The results of carbon-14 distribution in propylene appear to be independent of the temperature (-72° to 50°), though it is difficult to say this with certainty due to deviations in the present results. Lindsay, Bourns and Thode³² had observed carbon-13 intramolecular isotope effect in the thermal decarboxylation of malonic acid to be independent of the temperature in agreement with theoretical predictions by Bigeleisen model for intramolecular effects. However these results were not confirmed by Yankwich and Belford who found the intramolecular effect in decarboxylation of malonic acid to be temperature dependent.

The following conclusion can be drawn from the present study. During reductive cleavage of allyl compounds an important intermediate formed is allyl carbanion which upon protonation gives propylene. The presence of allyl radicals as intermediates in such cleavage reactions is not entirely

excluded by the available data. Addition of electrons and protons to allyl compounds to give propylene does not occur simultaneously since $C^{14}H_2=CHCH_3$ and $CH_2=CHC^{14}H_3$ are obtained in almost equal proportion from allyl-1- C^{14} compounds. In runs in liquid ammonia any divergence from a random distribution of carbon-14 in the terminal positions of propylene is likely due to the presence of an isotope effect in protonation of allyl carbanions and to the formation of $C^{14}H_2=CHCH_3$ from cleavage of propenyl-1- C^{14} compounds which are formed by rearrangement of allyl-1- C^{14} compounds by strong bases. In runs in which ammonium chloride, methanol, 2-propanol and acetic acid were present, the ratio of activity of formaldehyde methone derivative to that of acetaldehyde methone derivative was 1.056 ± 0.016^m . The most likely explanation for this ratio is that an isotope effect of this order of magnitude exists in the protonation of allyl carbanion since in such reactions there is little possibility of rearrangement of reactants.

CHAPTER VIII

RECOMMENDATIONS FOR FUTURE WORK

In order to strengthen the interpretations and make the results of this study more conclusive further studies would be useful.

Reductive cleavage of an allyl-1-C¹⁴ compound should be carried out twice or more in liquid ammonia at -33° without any added reagent and a check should be made for the deviations in the results of carbon-14 distribution between carbon-1 and carbon-3 of propylene formed. The gases obtained from the reactions should be passed through a U-tube cooled at a suitable temperature to remove diallyl and its isomers before passing them through the ozonizer for ozonolysis of propylene. It would also be interesting to study a reaction of the same compound under similar conditions but at -72°. All the reactions studied at -72° in the present work, were carried out with ammonium chloride. This will lead to a more definite conclusion if the isotope effect in these reactions is temperature dependent or not.

The cleavage products of allyltrimethylammonium chloride, allyl alcohol and *p*-tolyl allyl sulfide with alkali metals in liquid ammonia in presence of ammonium chloride should be examined carefully with the aid of gas chromato-

graphy. It is anticipated that little if any bialllyl will be produced under these conditions. If the presence of ammonium ions does not reduce the yield of bialllyl to a low value, then evidently part of the bialllyl results from dimerization of bialllyl radicals

The isomerization of bialllyl by sodium amide in liquid ammonia should be studied and the unknown substances called "bialllyl isomers I and II" should be more definitely characterized.

The distribution of carbon-¹⁴ in bialllyl and its isomers from the reactions of allyl chloride-¹-C¹⁴ and allyl-¹-C¹⁴-trimethylammonium chloride with sodium should be examined. This can be done by ozonization of the bialllyl and its isomers. If bialllyl results from coupling of allyl radicals, then the formaldehyde from the ozonization will have one half of the molar activity of the starting compound; while if it results from direct S_N2 displacement of allyl carbanion on allyl compound, the formaldehyde will have one forth of the molar activity of the starting compound; and if it results from S_N2' displacement, the formaldehyde will have three fourths of the molar activity of the starting compound. (These estimates ignore isotope effects).

The position of carbon-¹⁴ in the acetaldehyde obtained from ozonization of propylene should be established by conversion of the acetaldehyde to iodoform and radioactive assay of the latter. In the present work it has been tacitly

assumed that the carbon-14 is in the methyl group of the acetaldehyde.

In order to be more definite whether the 5.6 ± 1.6 per cent higher radioactivity in the formaldehyde than in the acetaldehyde from ozonization of propylene is due to an isotope effect in the protonation step or to other causes, some of the reactions of allyl-1-C¹⁴ compounds should be repeated on allyl-3-C¹⁴ compounds. If the slightly unsymmetrical distribution of carbon-14 at the carbon-1 and carbon-3 positions in the product propylene is due to an isotope effect in the protonation step, it will make no difference in the final result whether the carbon-14 is at carbon-1 or carbon-3 in the starting allyl compound. This work can also be carried out by cleavage of allyl compounds which are 50/50 mixtures of allyl-1-C¹⁴ and allyl-3-C¹⁴ compounds. The syntheses of such mixtures may be easier than of allyl-3-C¹⁴ compounds.

An attempt should be made to isomerize allyl-1-C¹⁴-trimethylammonium chloride by sodamide in liquid ammonia to propenyl-1-C¹⁴-trimethylammonium chloride and reductive cleavage of the latter, if formed, should be attempted.

APPENDICES

APPENDIX A

A SAMPLE CALCULATION FOR THE PERCENTAGE OF PROPYLENE,
BIALLYL AND ITS ISOMERS

The data and calculations are of the reaction of allyl-trimethylammonium chloride with sodium in liquid ammonia at -72° (Run 5, Table 5).

Amount of the salt reacted: 0.865 g. (6.38 mmole).

The gases obtained in the above reaction were diluted with nitrogen, washed, and analyzed by gas chromatographic technique as described in Chapter VI. The observations recorded are given below.

Volume of Gases Analyzed	Propylene	Heights of Peaks ⁿ		
		Biallyl	Biallyl Isomer I	Biallyl Isomer II
After first dilution				
97.4 ml.	5.45 (32)	0.97 (1)	0.22 (1)	0.10 (1)
98.3 ml.	5.70 (32)	1.60 (1)	0.35 (1)	0.10 (1)
After second dilution				
97.1 ml.	1.55 (32)	0.67 (1)	0.15 (1)	0.04 (1)
95.3 ml.	5.00 (8)	0.50 (1)	0.11 (1)	0.02 (1)
After third dilution				
368.0 ml.	2.72 (8)	0.29 (1)	0.06 (1)	0.01 (1)

Temperature: 29°

Atmospheric pressure: 735 mm.

Water vapor pressure over saturated brine at 29° : 22.8 mm.

ⁿFigures in parentheses indicate the number of the Recorder Range setting.

Calculations for propylene---

Partial pressure for propylene corresponding to peak height (5.45) at Recorder Range 32:

$$75.5 \times 4 \text{ mm.}^{\circ} \text{ or } 302.0 \text{ mm.}$$

Volume of the dry gases (97.4 ml.) at S. T. P.:

$$\frac{97.4 \times 273 \times (735.0 - 22.8)}{760 \times 302} \text{ ml.}$$

Volume of propylene at S. T. P. in the gases (97.4 ml.):

$$\frac{302.0}{735} \times \frac{97.4 \times 273 \times 712.2}{760 \times 302} \text{ ml.}$$

or $\frac{302 \times 97.4}{1} \times \frac{273 \times 712.2}{735 \times 760 \times 302} \text{ ml.}$

or $302.0 \times 97.4 \times (0.1155 \times 10^{-2})^{\text{P}} \text{ ml.}$

or 34.0 ml.

Volume of propylene at S. T. P. in the gases (98.3 ml.):

$$4 \times 79.0 \times 98.3 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 35.9 ml.

Volume of propylene at S. T. P. in the gases (97.1 ml.):

$$4 \times 21.5 \times 97.1 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 9.7 ml.

Volume of propylene at S. T. P. in the gases (95.3 ml.):

$$1 \times 69.0 \times 95.3 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 7.6 ml.

Volume of propylene at S. T. P. in the gases (368.0 ml.):

$$1 \times 38.0 \times 368.0 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 16.2 ml.

^oThe calibration curves for propylene were made at Recorder Range 8.

^P0.1155 x 10⁻² is the fraction common in subsequent calculations.

Total volume of propylene at S. T. P. evolved in the reaction:

103.4 ml. or 4.62 mmoles

Yield of propylene in the reaction:

$4.62/6.38 \times 100$

or 72.4 per cent

Calculations for biallyl.--

Volume of biallyl at S. T. P. in the gases (97.4 ml.):

$1 \times 11.0 \times 97.4 \times 0.1155 \times 10^{-2}$ ml.

or 1.24 ml.

Volume of biallyl at S. T. P. in the gases (98.3 ml.):

$1 \times 19.0 \times 98.3 \times 0.1155 \times 10^{-2}$ ml.

or 2.16 ml.

Volume of biallyl at S. T. P. in the gases (97.1 ml.):

$1 \times 8.5 \times 97.1 \times 0.1155 \times 10^{-2}$ ml.

or 0.95 ml.

Volume of biallyl at S. T. P. in the gases (95.3 ml.):

$1 \times 6.4 \times 95.3 \times 0.1155 \times 10^{-2}$ ml.

or 0.70 ml.

Volume of biallyl at S. T. P. in the gases (368.0 ml.):

$1 \times 4.0 \times 368.0 \times 0.1155 \times 10^{-2}$ ml.

or 1.72 ml.

Total volume of biallyl at S. T. P. evolved in the reaction:

6.77 ml. or 0.302 mmole

Yield of biallyl in the reaction:

$(0.302/6.38) \times 2 \times 100$

or 9.46 per cent

Calculations^q for biallyl isomer I.--

Volume of biallyl isomer I at S. T. P. in the gases
(97.4 ml.):

$$1 \times 2.5 \times 97.4 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.282 ml.

Volume of biallyl isomer I at S. T. P. in the gases
(98.3 ml.):

$$1 \times 4.15 \times 98.3 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.472 ml.

Volume of biallyl isomer I at S. T. P. in the gases
(97.1 ml.):

$$1 \times 1.91 \times 97.1 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.215 ml.

Volume of biallyl isomer I at S. T. P. in the gases
(95.3 ml.):

$$1 \times 1.23 \times 95.3 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.136 ml.

Volume of biallyl isomer I at S. T. P. in the gases
(368.0 ml.):

$$1 \times 0.775 \times 368.0 \times 0.11555 \times 10^{-2} \text{ ml.}$$

or 0.329 ml.

Total volume of biallyl isomer I at S. T. P. evolved in the
reaction:

$$1.434 \text{ ml. or } 0.064 \text{ mmole}$$

^qThe partial pressures for biallyl isomer I and biallyl isomer II were calculated by using the calibration curve for biallyl.

Yield of biallyl isomer I in the reaction:

$$(0.064/6.38) \times 2 \times 100$$

or 2.01 per cent

Calculations^q for biallyl isomer II.--

Volume of biallyl isomer II at S. T. P. in the gases
(97.4 ml.):

$$1 \times 1.14 \times 97.4 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.129 ml.

Volume of biallyl isomer II at S. T. P. in the gases
(98.3 ml.):

$$1 \times 1.19 \times 98.3 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.135 ml.

Volume of biallyl isomer II at S. T. P. in the gases
(97.1 ml.):

$$1 \times 0.51 \times 97.1 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.056 ml.

Volume of biallyl isomer II at S. T. P. in the gases
(95.3 ml.):

$$1 \times 0.27 \times 95.3 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.030 ml.

Volume of biallyl isomer II at S. T. P. in the gases
(368.0 ml.):

$$1 \times 0.13 \times 368.0 \times 0.1155 \times 10^{-2} \text{ ml.}$$

or 0.055 ml.

Total volume of biallyl isomer II at S. T. P. evolved in the
reaction:

$$0.405 \text{ ml. or } 0.0181 \text{ mmole}$$

Yield of biallyl isomer II in the reaction:

$$(0.0181/6.38) \times 2 \times 100$$

or 0.57 per cent

APPENDIX B

DETERMINATION OF SPECIFIC ACTIVITIES

To measure the ionization chamber current two methods were used.

Steady deflection method.--The ionization chamber was set on the head of the vibrating-reed electrometer. The amplifier was set at a suitable amplification. The turret switch was turned from ground to position 4 to connect the system with the high-resistance-leak resistor (10^{12} ohms). The electrometer system was allowed to come to its equilibrium voltage. This voltage was recorded, and the background voltage was subtracted from it.

Rate of drift method.--The ionization chamber was set on the head of the vibrating-reed electrometer. The amplifier was set at suitable amplifications (usually 1 or 3 volt scale). The turret switch was turned from ground to open position. The interval of time was recorded as the pointer in the Brown Recorder moved from 8 to 88. The process was repeated 3 or 4 times for the same sample in the ionization chamber, and an average value (time in seconds) was calculated. As the rate of charge is inversely proportional to the current, a conversion factor was used to convert time into current. To obtain the value of the conversion factor, readings were taken by both the methods on the same sample in the ionization chamber.

Calculation of specific activity.--On the same sample of carbon dioxide collected in the ionization chamber after combustion of allyl-1-C¹⁴-trimethylammonium chloride, the following observations were made:

Voltage (by steady deflection method):

0.1685 volt

Average time on 1 volt scale (by rate of drift method):

62.25 seconds

Conversion factor:

$0.1685 \times 62.25 = 10.5$

Specific activities of radioactive compounds were calculated in microcurie per mmole by the approximate formula:⁷⁶

Sp. act. in $\mu\text{c}/\text{mmole}$:

$$\frac{\text{potential difference in volts} \times \text{molecular wt. of sample}}{\text{resistance}^r \text{ in ohms} \times 1.3 \times 10^{-16} \times 3.7 \times 10^4 \times \text{wt. sample in mg.}}$$

A typical determination of specific activity, showing numerical data, follows. The data were taken from combustion of the formaldehyde methone derivative (Run No. 15, Table 6).

Weight of the formaldehyde methone derivative:

11.94 mg.

Average time on 1 volt scale:

240.9 seconds

⁷⁶G. A. Ropp, personal communication to Dr. E. Grovenstein, Jr.

^r₁₀¹² ohms when the turret switch is in position 4.

Calculated voltage:

$$\frac{10.5}{240.9} = 0.04359 \text{ volt}$$

Calculated voltage after subtracting background voltage:

$$0.04359 - 0.00098 = 0.04261 \text{ volt}$$

Molar weight of the formaldehyde methone derivative:

$$292$$

Specific activity of the formaldehyde methone derivative:

$$\frac{0.04261 \times 292}{10^{12} \times 1.3 \times 10^{-16} \times 3.7 \times 10^4 \times 11.94} = 0.2166 \mu\text{c/mmole}$$

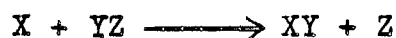
APPENDIX C

DETERMINATION OF REDUCED MASS FACTORS

The following expression⁷⁷ was used for calculating the reduced mass factor, $(\mu_2/\mu_1)^{\frac{1}{2}}$:

$$\left[\frac{1/m_Y(1) + 1/m_Z(1) + p\{1/m_Y(1) + 1/m_X(1)\} + 2p^{1/2} 1/m_Y(1)}{1/m_Y(2) + 1/m_Z(2) + p\{1/m_Y(2) + 1/m_X(2)\} + 2p^{1/2} 1/m_Y(2)} \right]^{\frac{1}{2}}$$

The expression applies to the linear transition state of a three-center reaction:



The value of p is 1, if the transition state is symmetrical.

For a reductive cleavage which takes place according to the process:



The value of the reduced mass factor is 1.00108, when $p = 1$, $m_Y(1) = m_Y(2) = 1$, $m_Z(1) = m_Z(2) = 16$, $m_X(1) = 14$ and $m_X(2) = 16$

⁷⁷L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press Company, New York, 1960, p. 39.

The situation defined by $p = \infty$ corresponds to the simple combination of X and Y, for which the simple expression for the reduced mass factor, $(\mu_2/\mu_1)^{1/2}$, is written as:

$$\left[\frac{1/m_{X(1)} + 1/m_Y}{1/m_{X(2)} + 1/m_Y} \right]^{\frac{1}{2}}$$

The value of the reduced mass factor is 1.00419, when

$m_{X(1)} = 14$, $m_{X(2)} = 16$ and $m_Y = 1$.

If one assumes that the particles involved in the bond formation are CH_2^+ and NH_3 , then $p = \infty$, $m_{X(1)} = 14$, $m_{X(2)} = 16$, $m_Y = 17$, and the reduced mass factor is 1.0362. However, no good justification can be given for this assumption.

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*The full form of abbreviations used in this section may be found in Chemical Abstracts (1956).

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