1962

Synthesis and isomerization of cyclopropanols

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SYNTHESIS AND ISOMERIZATION OF CYCLOPROPANOLS

by

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A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

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Signature was redacted for privacy.

Dean of Graduate College

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Of Science and Technology
Ames, Iowa

1962

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INTRODUCTION

Cyclopropanol was for long thought to be incapable of existence as all attempts to prepare it had resulted in the formation of allyl alcohol. However, Cottle, et al.[1, 2] in 1942, was able to prepare crude cyclopropanol from epichlorohydrin and modified Grignard reagents. In 1961, DePuy, et al.[3] reported the first successful preparation of cyclopropanol in the pure state. The purification involved a gas phase chromatographic separation of the alcohol. There have been no reports in the literature of the successful synthesis of substituted cyclopropanols.

The present work is based on the observation that cyclopropanol undergoes a facile isomerization to propionaldehyde in carbon tetrachloride at 80°, whereas it is stable for days in such solvents as methylcyclohexane, water and acetonitrile.[4] In order to investigate this unusual phenomenon, it was necessary to develop a better and more economical method for the preparation of pure

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[1]Magrane, J. K. and Cottle, D. L., J. Am. Chem. Soc., 64, 484 (1942).

[2]Stahl, C. W. and Cottle, D. L., ibid., 65, 1782 (1943).

[3]DePuy, C. H., Mahoney, L. R. and Eilers, K. L., J. Org. Chem., 26, 3616 (1961).

[4]Mahoney, L. R., The Hydrolysis of Cyclopropyl Acetate. Unpublished Ph. D. Thesis, Ames, Iowa, Library, Iowa State University of Science and Technology, 1960, pp. 49-51.

cyclopropanol. The ability to synthesize substituted cyclopropanols would also be advantageous for the same type of isomerization studies.

The object of this work was to improve on the synthesis of pure cyclopropanol, to attempt to prepare and isolate substituted cyclopropanols in the pure state, to investigate the isomerization of cyclopropanol to propionaldehyde in some detail and to investigate the isomerization of substituted cyclopropanols in somewhat less detail.

HISTORICAL

Most of the early attempts to prepare unsubstituted cyclopropanol involved the reaction of 1,3-dihalo-2-propanols with an active metal. In 1871, Hubner and Muller[5] reacted 1,3-dichloro-2-propanol with sodium and obtained allyl alcohol as a product. This work was repeated by Tornoe[6] in 1891. Again allyl alcohol was the only product isolated. Allyl alcohol was also obtained by Aschan[7] in 1890 from the reaction of 1,3-dibromo-2-propanol with sodium. Epihalohydrins were shown to be intermediates in these reactions.

Kishner[8] attempted to prepare cyclopropanol by the diazotization of cyclopropylamine, however, allyl alcohol was the only product obtained from the reaction.

Magrane and Cottle[1] reported the first successful preparation of cyclopropanol in 1942. The crude alcohol was isolated as a product of the reaction between epichlorohydrin, magnesium bromide and ethylmagnesium bromide (Eq. 1). The alcohol could also be obtained from the reaction of magnesium bromide 1-bromo-3-chloro-2-propoxide (I) with ethylmagnesium bromide (Eq. 1). Other products of the reaction were ethane,

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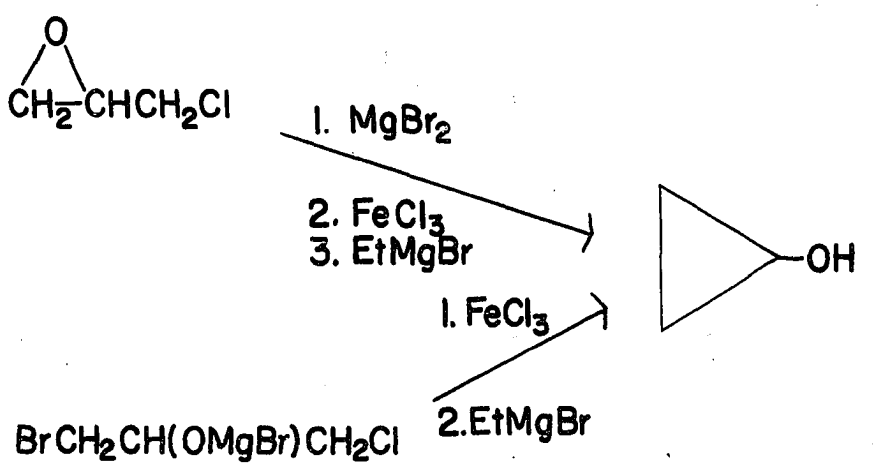
[5]Hubner, H. and Muller, K., Ann., 159, 168 (1871).

[6]Tornoe, H., Ber., 24, 2674 (1891).

[7]Aschan, O., ibid., 23, 1833 (1890).

[8]Kishner, N., Chem. Zentr., 76, 1704 (1905).

ethylene, hydrogen and unreacted 1,3-dihalo-2-propanol.



(Eq. 1)

I

In an extension of this work, Stahl and Cottle[2] observed that cyclopropanol was not formed in the above reactions if a very pure grade of magnesium was used. They observed that the addition of small amounts of ferric chloride to the reaction mixture led to shorter reaction times and cyclopropanol fractions of comparable size to those previously reported even if magnesium of high purity was used. Cyclopropanol isomerized to propionaldehyde during repeated distillations, and on standing for several days over potassium carbonate the aldol product, 2-methyl-2-penten-1-al, was formed.

Roberts and Chambers[9] repeated the synthesis of cyclopropanol by the procedure of Cottle, and they were able to obtain a purer product by a slight modification of the

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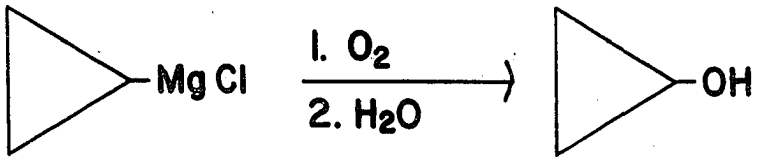
[9]Roberts, J. D. and Chambers, V. C., J. Am. Chem. Soc., 73, 3176 (1951).

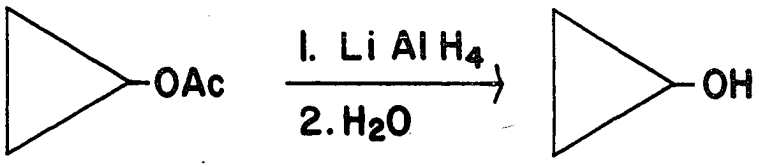
isolation procedure. Analytically pure cyclopropanol could not be obtained however, and, in agreement with Cottle's observations, the material isomerized rather easily to propionaldehyde. They also prepared cyclopropanol in very low yield (3%) by the air oxidation of cyclopropylmagnesium chloride (Eq. 2). The derivatives of the crude cyclopropanol



(Eq. 2)

formed by this method were identical to those prepared via the procedure of Cottle.

DePuy, et al.[3] reported the first successful preparation of cyclopropanol in the pure state in 1961. The method involved the reduction of cyclopropyl acetate with lithium aluminum hydride in ether (Eq. 3). The isolation of the pure

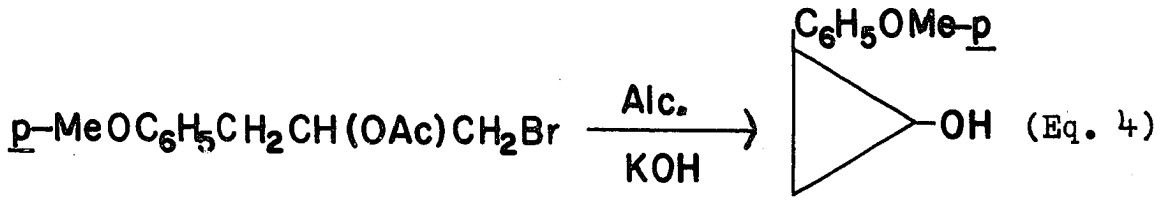


(Eq. 3)

alcohol was achieved by a gas phase chromatographic separation using a polyethylene oxide column at 80°. Cyclopropanol was shown to have a long retention time on this column, and it was easily separated to give a colorless, stable, water-soluble liquid. Its derivatives agreed in melting point with those

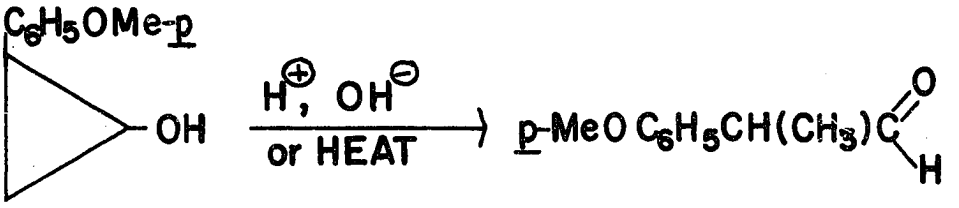
reported by Cottle and Roberts.

The first reported synthesis of a substituted cyclopropanol was by Tiffeneau and Daufresne[10] in 1907. 2-p-Methoxyphenylcyclopropanol was obtained from the reaction of alcoholic potassium hydroxide with 1-bromo-2-acetoxy-3-p-methoxyphenylpropane (Eq. 4).



(Eq. 4)

The alcohol isomerized to α-p-methoxyphenylpropionaldehyde (Eq. 5) during distillation, on heating with sulfuric acid, on heating with potassium carbonate and while standing at room temperature.



(Eq. 5)

In a later paper,[11] they reported that the alcohol was not 2-p-methoxyphenylcyclopropanol, but, in fact, was 2-methyl-2-p-methoxyphenylethenol which isomerized under the conditions described above to α-p-methoxyphenylpropionaldehyde

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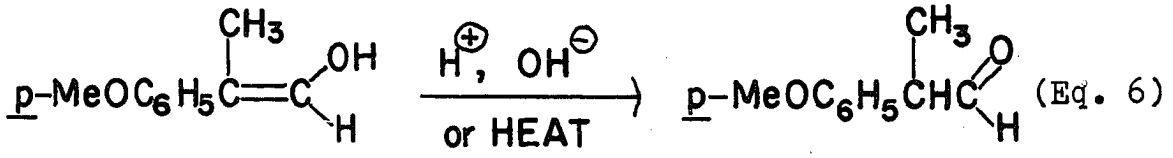
[10]Tiffeneau, M., and Daufresne, M., Compt. rend., 144, 924 (1907).

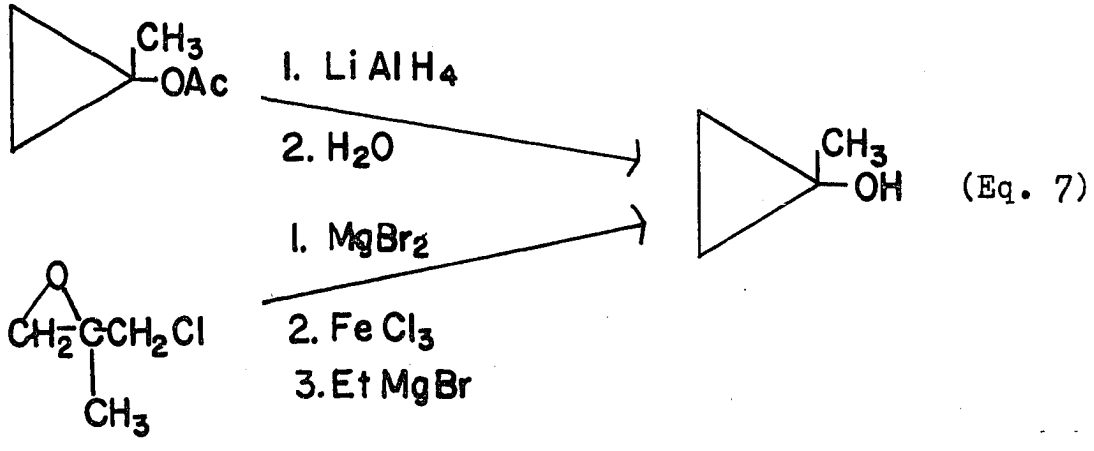
[11]Tiffeneau, M., and Daufresne, M., ibid., 145, 628 (1907).

(Eq. 6). The validity of either of the proposed structures is doubtful since cyclopropanols are known to isomerize[1, 2, 3, 9] in strong base and vinyl alcohols are known to be incapable of existence.



(Eq. 6)

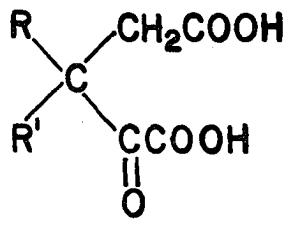
DePuy, et al.[3] have recently reported the preparation of 1-methylcyclopropanol and trans-2-phenylcyclopropanol. Lithium aluminum hydride reduction of 1-methylcyclopropyl acetate followed by gas phase chromatographic purification afforded 1-methylcyclopropanol (Eq. 7) in very poor yields. Reaction of 1-chloro-2-methyl-2,3-epoxypropane according to the procedure of Cottle[5, 6] followed by gas phase chromatographic purification afforded 1-methylcyclopropanol (Eq. 7) in 35% yield.



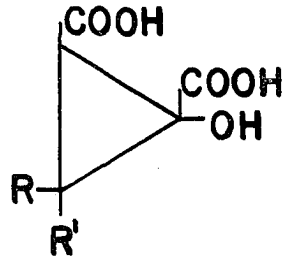
(Eq. 7)

Treatment of trans-2-phenylcyclopropyl acetate with lithium aluminum hydride or with methyllithium affords trans-2-phenylcyclopropanol in moderate yield. 1-Methylcyclopropanol and trans-2-phenylcyclopropanol isomerize[12] to methyl ethyl ketone and dihydrocinnamaldehyde, respectively.

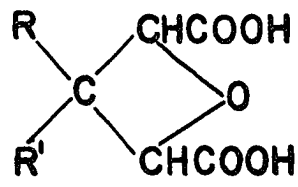
There have been a few reports in the literature regarding the isomerization of cyclopropanols to aldehydes or ketones, however, only one extensive study of this phenomenon has been reported. This was the early work of Thorpe, et al.[13,14,15] and Ingold[16,17] in 1921-1923. The structural assignments of the compounds were incorrect, however, and were not α-keto acid (II)-hydroxycyclopropane (III) isomers, but, in fact, were cis-trans isomers of the cyclic ether (IV).



II



III



IV

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[12]DePuy, C. H., Dappen, G. M. and Hausser, J. W., J. Am. Chem. Soc., 83, 3156 (1961).

[13]Lanfear, E. W. and Thorpe, J. F., J. Chem. Soc., 123, 1683 (1923).

[14]Des Lapanda, S. S. and Thorpe, J. F., ibid., 121, 1430 (1922).

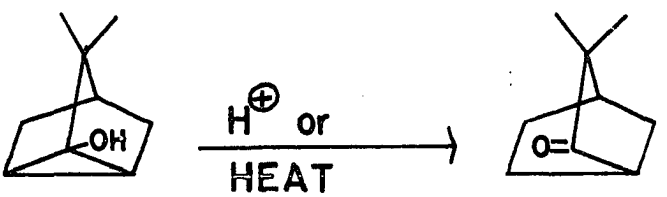
[15]Barnes, L., and Thorpe, J. F., ibid., 123, 1206 (1923).

[16]Ingold, C. K., ibid., 119, 305 (1921).

[17]Ingold, C. K., ibid., 121, 2676 (1922).

Recent infrared and nuclear magnetic resonance (NMR) studies on 1,2-dicarboxy-3,3-diethylcyclopropanol by Wiberg and Holmquist[18] have revealed this error.

Lipp and Padberg[19] in 1921 reported the isomerization of the tricyclic system (V) to the ketone (VI) by means of dilute sulfuric acid or heat (Eq. 8).



(Eq. 8)

V VI

Lipp, et al.[20] in 1932 reported the isomerization of cyclopropanone mono-ethyl ketal and cyclopropanone hydrate to ethyl propionate and propionic acid (Eq. 9), respectively, on treatment with dilute potassium hydroxide. Cyclopropanone mono-ethyl ketal was obtained from the reaction of diazomethane with ketene in the presence of alcohol and cyclopropanone hydrate was obtained in the absence of alcohol.

Mahoney[4] has recently observed that cyclopropanol isomerizes to propionaldehyde in carbon tetrachloride at 80°.

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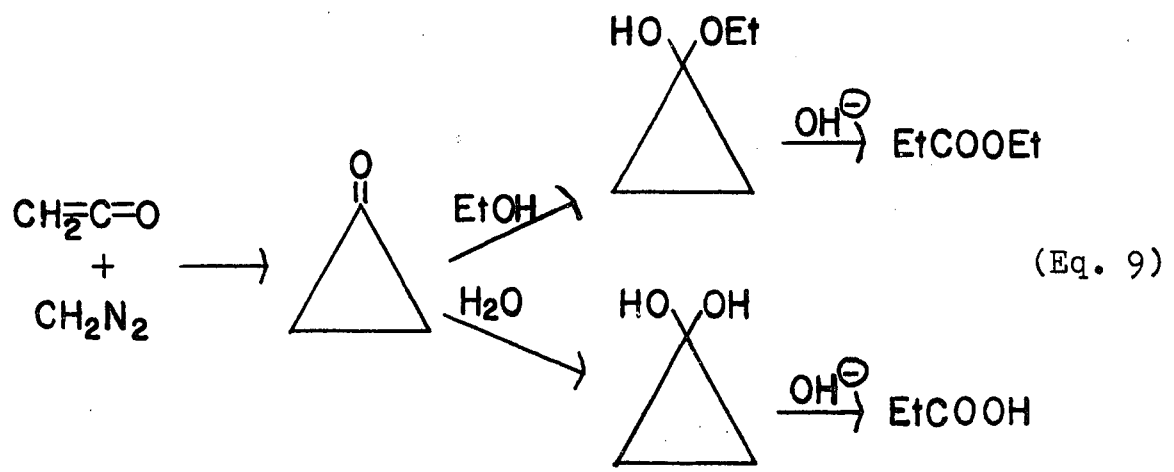
[18]Wiberg, K. B. and Holmquist, H. N., J. Org. Chem., 24, 578 (1959).

[19]Lipp, P. and Padberg, C., Ber., 54, 1316 (1921).

[20]Lipp, P., Buchkremer, J. and Seeles, H., Ann., 499, 8 (1932).



(Eq. 9)

The half-life of the reaction was estimated to be one hour. This is unusual since cyclopropanol was completely stable for days at 80° in water, methyl cyclohexane and acetonitrile.

DISCUSSION

Synthesis of cyclopropanols

Since it appeared that cyclopropyl acetate could be prepared economically by the methods reported in the literature, the route which looked most promising initially for the preparation of pure cyclopropanol was the lithium aluminum hydride reduction of cyclopropyl acetate, followed by a gas phase chromatographic separation.[3] In several experiments Mahoney[21] was not able to prepare cyclopropyl acetate by the method described by Simmons and Smith,[22] and several other attempts using the improved method of Shank and Shechter[23] also met with failure. The only other route to cyclopropyl acetate was the Baeyer-Villiger oxidation of methyl cyclopropyl ketone with peroxytrifluoroacetic acid.[24] This route gives low yields, is tedious and very expensive. The low yield of cyclopropyl acetate obtained in the Baeyer-Villiger oxidation may have been due to the fact that the

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[21]Mahoney, L. R., The Hydrolysis of Cyclopropyl Acetate. Unpublished Ph. D. Thesis, Ames, Iowa, Library, Iowa State University of Science and Technology, 1960, pp. 54-55.

[22]Simmons, H. E. and Smith, R. D., J. Am. Chem. Soc., 81, 4256 (1959).

[23]Shank, R. S. and Shechter, J. Org. Chem., 24, 1825 (1959).

[24]Emmons, W. D. and Lucas, G. B., J. Am. Chem. Soc., 77, 2287 (1955).

hydrogen peroxide which was used to prepare the peroxytrifluoroacetic acid had decomposed to some extent during standing. The lithium aluminum hydride reduction of cyclopropyl acetate gave cyclopropanol in low yields. Several experiments failed to improve the yield of cyclopropanol. All of the above results indicate that this route to cyclopropanol was not satisfactory for the quantities of cyclopropanol we desired. The observation[3] that cyclopropanol was stable and easily separated in the pure state by gas phase chromatographic workup has been of considerable importance in obtaining larger quantities of cyclopropanol by another method as well as in the isolation of pure substituted cyclopropanols.

Since all attempts to prepare sizable quantities of cyclopropyl acetate were either unsuccessful or not economically feasible, it became obvious that a better route to cyclopropanol had to be found. The fact that cyclopropanol was stable to gas phase chromatographic separation led us to believe that the early method of Cottle[1,2] for the synthesis of cyclopropanol might be satisfactory if the crude reaction mixture was separated by gas phase chromatography instead of distillation. Cottle was never able to isolate a pure product because the alcohol isomerized to some extent during distillation. The Cottle procedure was carried out and gas phase chromatographic separation yielded as much as fifteen grams of pure cyclopropanol from an initial one mole of

epichlorohydrin. In an attempt to improve the yield of cyclopropanol by this method, epibromohydrin was used in place of epichlorohydrin. However, lower yields of cyclopropanol were obtained. This method for the preparation of cyclopropanol was more economical, involved essentially the same reaction time and gave larger quantities of cyclopropanol than the previous method.

The mechanism of this reaction is not well understood. However, two logical mechanistic schemes can be proposed. The reaction involves treating epichlorohydrin with magnesium bromide followed by ethylmagnesium bromide, or the reaction of magnesium bromide 1-chloro-3-bromo propoxide with ethylmagnesium bromide. If a high purity of magnesium were used, the reaction did not give cyclopropanol unless small amounts of ferric chloride were added to the reaction mixture. Epichlorohydrin when reacted with magnesium bromide yields magnesium bromide 1-chloro-3-bromo propoxide. This explains why cyclopropanol is obtained from either epichlorohydrin or magnesium bromide 1-chloro-3-bromo propoxide. Ethane, ethylene and 1-chloro-3-bromo-2-propanol are the major by-products of the reaction. The mechanisms proposed by Kharasch, et al.[25] for the reaction of phenylmagnesium bromide with propylene oxide seem to be well suited to this reaction.

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[25]Kharasch, M. S., Biritz, L., Nudenberg, W., Bhattacharya, A. and Yang, N. C., J. Am. Chem. Soc., 83, 3229 (1961).

Phenylmagnesium bromide has been shown to react with ferric chloride to give an unstable organoiron intermediate which then decomposes to give biphenyl and a reduced iron salt.[26] Thus, it would be reasonable to assume that ethylmagnesium bromide would behave in the same manner as shown in Eqns. 10 and 11. Transition metal salts in the reduced form are known

$$2\ C_2H_5MgBr + FeCl_3 \longrightarrow (C_2H_5)_2FeCl + 2\ MgBrCl \quad \text{(Eq. 10)}$$

$$(C_2H_5)_2FeCl \longrightarrow C_4H_{10} + C_2H_4 + C_2H_6 + FeCl \quad \text{(Eq. 11)}$$

to be reactive intermediates which attack organic halides to give a radical (VII) and to regenerate the salt in its higher oxidation state (Eq. 12).

$$ClCH_2CH(OMgBr)CH_2Br \longrightarrow ClCH_2CH(OMgBr)CH_2^{\bullet} + FeClBr$$

VII (Eq. 12)

The reaction is thus a chain reaction with Eqns. 10 to 12 as the propogating steps. The method of subsequent formation of cyclopropanol from the radical (VII) thus generated is not clear, and two alternative routes seem to be the more logical. These are shown in Eqns. 13 - 16. Eqns. 13 and 14 involve further attack of the radical (VII) by a reactive iron intermediate to give a carbanion which now can close the cyclopropane ring by displacing the chloride ion. Eqns. 15 and 16 involve attack of the radical (VII) by the reactive

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[26] Champetier, G., Bull. soc. chim., 47, 1131 (1930).

$$ClCH_2CH(OMgBr)CH_2^{\bullet} + FeCl \longrightarrow ClCH_2CH(OMgBr)CH_2^{-} + FeCl_2^{+} \qquad \text{(Eq. 13)}$$

$$ClCH_2CH(OMgBr)CH_2^{-} \longrightarrow \text{(cyclopropane)} + OMgBr + Cl^{-} \qquad \text{(Eq. 14)}$$

$$ClCH_2CH(OMgBr)CH_2^{\bullet} + FeCl \longrightarrow {}^{\bullet}CH_2CH(OMgBr)CH_2^{\bullet} + FeCl_2 \qquad \text{(Eq. 15)}$$

$${}^{\bullet}CH_2CH(OMgBr)CH_2^{\bullet} \longrightarrow \text{(cyclopropane)}\text{-}OMgBr \qquad \text{(Eq. 16)}$$

iron intermediate at the 3-position, reduction taking place in rapid succession or in a concerted manner, to give cyclopropanol with the ring closure. The fact that epibromohydrin gives lower yields of cyclopropanol from this reaction was difficult to rationalize since by either Eqns. 13 and 14 or Eqns. 15 and 16 a higher yield of cyclopropanol would be predicted. Kharasch, et al.[27] have observed little difference in the amount of cyclopropane isolated from the reaction of phenylmagnesium bromide with 1,3-dibromopropane or 1-chloro-3-bromopropane in the presence of ferric chloride. Apparently a side reaction is favored over ring closure when the magnesium bromide 1,3-dibromo propoxide intermediate is involved.

An extensive mechanistic study of this reaction as a function of Grignard reagent, catalyst and epihalohydrin is

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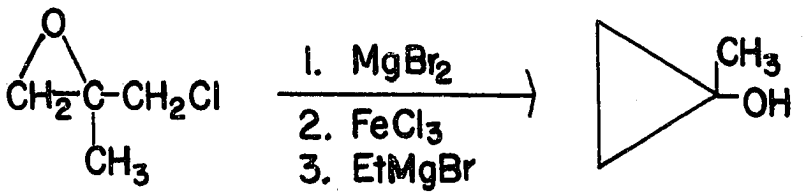
[27]Kharasch, M. S., Weiner, M., Nudenberg, W., Bhattacharya, A., Wang, T. and Yang, N. C., J. Am. Chem. Soc., 83, 3232 (1961).

now in progress.

It seemed reasonable to assume at this point that the Cottle procedure for the preparation of cyclopropanol might be applicable to the preparation of substituted cyclopropanols if substituted epichlorohydrins were used in place of epichlorohydrin. The one drawback to this idea was the fact that chloroepoxides other than epichlorohydrin are not commercially available. This was not critical, however, since chloro-olefins could be purchased or synthesized and epoxidized by standard methods.

The first attempt to prepare a substituted cyclopropanol by an extension of the Cottle procedure involved the use of 1-chloro-2-methyl-2,3-epoxypropane (VIII). This epoxide could be prepared in good yield from the reaction of either peroxytrifluoroacetic acid or perbenzoic acid with 3-chloro-2-methyl-1-propene. The method of choice for the epoxidation was perbenzoic acid since it could be prepared in better yield and was much easier with which to work. The only advantage in using peroxytrifluoroacetic acid was that shorter reaction times were required to effect the epoxidation of the olefin. 1-Chloro-2-methyl-2,3-epoxypropane (VIII) was then subjected to the Cottle procedure (Eq. 17). Gas phase chromatographic separation on a polyethylene oxide column at 80° afforded a 36% yield of pure 1-methylcyclopropanol. The yield of alcohol from this reaction compares favorably with



VIII (Eq. 17)

the yield of cyclopropanol obtained from epichlorohydrin. This would be expected if either of the two proposed mechanisms for the Cottle procedure are correct, since the introduction of the methyl group in the 2-position of the intermediate should have little, if any, effect on the ring closure by either mechanism. Positive identification of the alcohol was obtained from infrared data, nuclear magnetic resonance (NMR) data (Figure 4), analytical data, the fact that the alcohol had a retention time similar to cyclopropanol and the fact that the alcohol underwent a facile isomerization in carbon tetrachloride at 80° to give methyl ethyl ketone as the only product. Micro boiling point determinations on the pure alcohol revealed that it decomposed at its boiling point (103.5°) to methyl ethyl ketone. However, no decomposition was observed during the gas phase chromatographic separation.

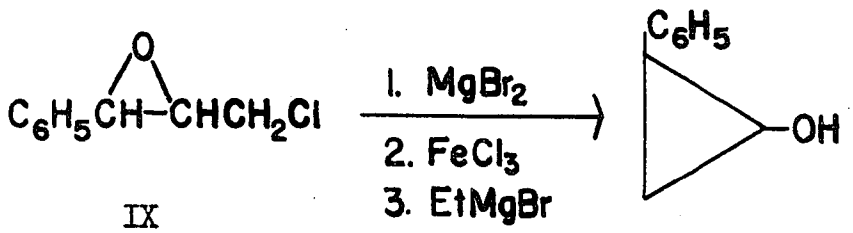
We next set out to prepare 2-methylcyclopropanol from 1-chloro-2,3-epoxybutane by the same procedure. This epoxide could also be prepared in good yield from the reaction of either peroxytrifluoroacetic acid or benzoic

acid with 1-chloro-2-butene. Higher yields were obtained using perbenzoic acid, and it again seemed to be the better method for carrying out the epoxidation. 1-Chloro-2,3-epoxybutane was then subjected to the Cottle procedure. Gas phase chromatographic separation on a polyethylene oxide column at 80° gave a crude sample of 2-methylcyclopropanol. Gas phase chromatographic separation of this crude sample on a hydroxylic column at 80° afforded a 23.5% yield of pure 2-methylcyclopropanol. The yield of alcohol from this reaction was somewhat less than the yield of cyclopropanol obtained from epichlorohydrin when the same molar quantities of starting materials were used. This would be expected if either of the two proposed mechanisms for the Cottle procedure are correct, since the introduction of the methyl group in the 3-position of the intermediate should sterically hinder to some extent the removal of the bromine atom by the reduced iron salt. Positive identification of the alcohol was obtained from infrared data, NMR data (Figure 7), analytical data, the fact that the retention time of the alcohol was similar to cyclopropanol and the fact that the alcohol underwent a facile isomerization in carbon tetrachloride at 80° to give an approximate mixture of 25% butyraldehyde and 75% <u>iso</u>-butyraldehyde. Micro boiling point determinations on the pure alcohol revealed that it decomposed at its boiling point (126.5°) to a mixture of the aldehydes. However, no

decomposition was observed during the gas phase chromatographic separation. The stereochemistry of the alcohol is not known, but it would seem reasonable to assume that a predominance of the trans-isomer was present. The NMR spectrum (Figure 7) of the alcohol appears to indicate the presence of a mixture of the isomers in a 3:1 ratio. There are two absorption peaks present at 180 c/s, 7.00τ, and 200 c/s, 6.67τ, which are highly split. The combined area of the two peaks amounts to one proton. The peaks are in the correct region for a proton on a carbon atom to which a hydroxyl group is attached in the cyclopropyl system (see NMR spectrum of cyclopropanol, Figure 1). Since the compound analyzes correctly, one of the peaks is apparently not an impurity. It would appear that one set of peaks corresponds to the trans-alcohol and the other set to the cis-alcohol. The isomerization of this 3:1 mixture of cis, trans-2-methylcyclopropanol gives an approximate 3:1 mixture of iso-butyraldehyde to butyraldehyde. This suggests the possibility of each isomer isomerizing to only one aldehyde. The NMR spectrum (Figure 8) of the isomerized alcohol clearly indicates the presence of two different aldehydes at 573 c/s, 0.45τ, and 581 c/s, 0.32τ, in an approximate 3:1 ratio. These clearly correspond to a mixture of 25% butyraldehyde (Figure 9), aldehyde proton absorption at 581 c/s, 0.32τ, and 75% iso-butyraldehyde (Figure 10), aldehyde proton absorption

at 573 c/s, 0.45τ.

In order to further test the generality of this reaction, we set out to prepare 2-phenylcyclopropanol, even though it had previously been prepared in good yield from the reaction of trans-2-phenylcyclopropyl acetate with either lithium aluminum hydride or methyllithium.[3] 1-Chloro-3-phenyl-2-propene was prepared[28] and epoxidized with perbenzoic acid to give 1-chloro-3-phenyl-2,3-epoxypropane (IX) in high yield. The epoxide (IX), thus obtained, was subjected to the Cottle procedure (Eq. 18). Fractional distillation afforded one



IX (Eq. 18)

gram of a compound which from its infrared and NMR spectrum appeared to be a mixture of 2-phenylcyclopropanol and its isomerization product. Various attempts to purify the alcohol were unsuccessful. The reaction led to a considerable amount of tar and polymer formation which accounts for the small amount of alcohol isolated. This reaction was not pursued any further at this point since it appeared that it would be impossible to improve on the reported method for the preparation of 2-phenylcyclopropanol.

We then turned our attention to 1-phenylcyclopropanol, a

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[28]Wichterle, O. and Cerny, J., Chem. Listy., 49, 1038, 1955.

compound which had not been previously reported. The desired olefin, 1-chloro-2-phenyl-2-propene, was not commercially available and its preparation involved a tedious synthetic scheme.[29] A one step synthesis of 1-bromo-2-phenyl-2-propene was available.[29] So, in an attempt to save time, we prepared the bromo compound even though epibromohydrin gave lower yields of cyclopropanol by the Cottle procedure. Attempted epoxidation of the bromo compound with perbenzoic acid was not clean cut. Two products were obtained in low yield while the bulk of the reaction mixture polymerized during distillation. The only course left at this point was to synthesize the chloro compound. The synthesis of the chloro compound went smoothly and the expected yield was realized. The chloro compound was more stable to heat and easier to work with than the corresponding bromo compound. Attempted epoxidation of the chloro compound with perbenzoic acid led to the same mixture of products which was isolated from the epoxidation of the bromo compound, but no polymerization took place during distillation. A reasonable separation of this mixture was obtained by fractional distillation, but the desired product, 1-chloro-2-phenyl-2,3-epoxypropane, was the minor component of the mixture. Monoperphthalic acid would probably have been better for this epoxidation since phthalic acid is insoluble in methylene chloride and would not react with the epoxide.

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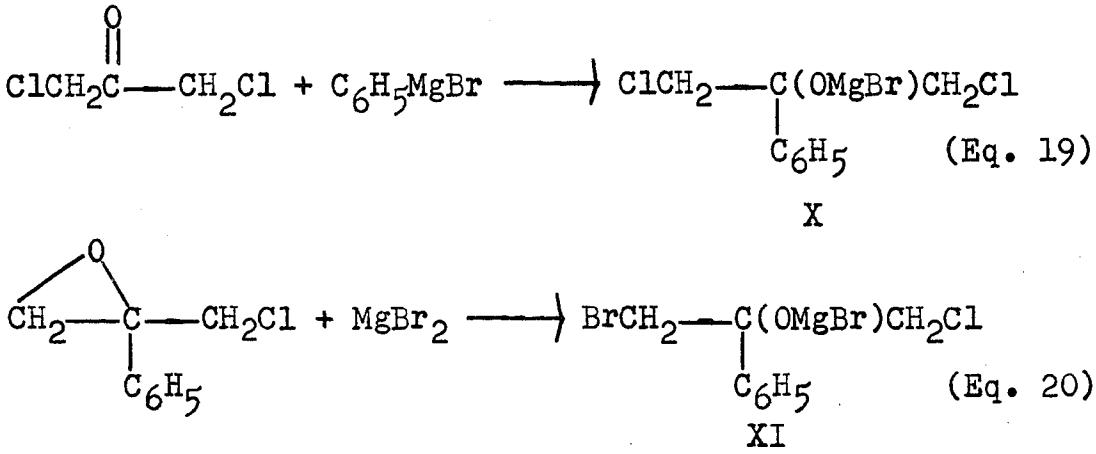
[29]Hatch, L. F. and Patton, T. L., J. Am. Chem. Soc., 76, 2705 (1954).

Benzoic acid can and apparently does react with the epoxide in this particular reaction. 1-Chloro-2-phenyl-2,3-epoxypropane was then subjected to the Cottle procedure. Fractional distillation afforded 3.1 grams of a compound which from its infrared and NMR spectrum appeared to be a mixture of 1-phenylcyclopropanol and its isomerization product. Attempts to purify the alcohol by gas phase chromatographic separation were unsuccessful. Attempted purification by elution chromatography on silica is now in progress. The purification of this alcohol is made difficult by the fact that its isomerization product, propiophenone, has approximately the same boiling point.

A more convenient route to the intermediate magnesium bromide 1,3-dihalo propoxide which is necessary for the preparation of 1-phenylcyclopropanol might be through the reaction of 1,3-dichloro-2-propanone with phenylmagnesium bromide. In this way only one step would be required, whereas several tedious steps are required to achieve this intermediate by the method previously described. The only difference would be that from 1,3-dichloro-2-propanone, magnesium bromide 1,3-dichloro-2-phenyl propoxide (X) would be formed as an intermediate (Eq. 19), whereas from 1-chloro-2-phenyl-2,3-epoxypropane, magnesium bromide 1-bromo-3-chloro-2-phenyl propoxide (XI) would be the intermediate formed (Eq. 20). This is essentially the same situation



(Eq. 19)

X

(Eq. 20)

XI

which arose when epibromohydrin was used in place of epichlorohydrin in the Cottle procedure. The fact that bromine atoms are more easily removed than chlorine atoms coupled with the fact that a bromine is not present in the intermediate from 1,3-dichloro-2-propanone might hinder the reaction considerably if the first step in the reaction is the removal of a bromine atom. This reaction should certainly be attempted, however, because if successful, it could be a more convenient route to other substituted cyclopropanols. The reaction should also provide information as to the mechanism of the Cottle procedure.

In summary, it can be said that the Cottle procedure for the preparation of cyclopropanol is apparently general, being best suited for the preparation of alkyl-substituted cyclopropanols. The preparation of alkyl-substituted cyclopropanols by this method is economically feasible from the standpoint of starting materials, but the preparations involve a considerable amount of time. The method would certainly

appear more attractive if other cycloroepoxides other than epichlorohydrin became commercially available.

It is hoped at least that this work will serve as a beginning toward more extensive research on improved methods for the synthesis of cyclopropanols.

It is interesting to compare the gas phase chromatography retention times of cyclopropanol, 1-methylcyclopropanol and 2-methylcyclopropanol on a polyethylene oxide column at 80°. Although 1-methylcyclopropanol is heavier than cyclopropanol, it has a smaller retention time. This is apparently due to the fact that the hydroxyl group of 1-methylcyclopropanol is tertiary and more sterically hindered. 2-Methylcyclopropanol is heavier than cyclopropanol and less sterically hindered than 1-methylcyclopropanol since it is a secondary alcohol. Thus it should and does have a larger retention time than either of the two.

Cyclopropanols are very hygroscopic and thus quite difficult to analyze. The only way in which satisfactory carbon, hydrogen analyses could be obtained was to collect the alcohols from the gas phase chromatograph in a collection tube which could be sealed off immediately. If any transfer of the alcohol was attempted before sealing the collection tube, the analyses were very erratic and varied by as much as 1-2% from the theoretical values.

Isomerization of cyclopropanols

Having access to sizable quantities of pure cyclopropanol made it possible to study its isomerization in more detail.

In order to study the isomerization, it was necessary to devise a method for following the progress of the reaction. After careful consideration, it became apparent that gas phase chromatography using a polyethylene oxide column would best serve our purposes for two reasons. First, cyclopropanol has a long retention time on this particular column, and, secondly, a micro-dipper attachment was available for the gas phase chromatograph which enabled us to introduce a constant sample size each injection. Utilizing this method by following the disappearance of the cyclopropanol peak, we were able to obtain quite reproducible results. The over-all error was expected to be $\pm$ 5%.

We first studied the effect of solvents on the isomerization of cyclopropanol to propionaldehyde. The results are given in Table 1. It can be seen that the isomerization was quite solvent dependent, occurring only in carbon tetrachloride and chloroform to any extent with an approximate half-life of 20-25 minutes. For the case of 0.1 M cyclopropanol in carbon tetrachloride the isomerization was much slower, the half-life being approximately 80 minutes.

During the initial stages of this study, the reaction vials were always sealed under an atmosphere of air. In an

Table 1. The effect of solvent on the isomerization of 0.5 M cyclopropanol to propionaldehyde at 80°

Solvent	Atmosphere[b]	Percent cyclopropanol remaining[a] 0 hr.	1/2 hr.	1 hr.	1-1/2 hr.	2 hr.	4 hr.	24 hr.	Esti. half-life
Carbon tetrachloride[c]	Air	100	31	18	--	6	--	--	20 min.
Carbon tetrachloride[d]	Air	100	--	--	46	--	--	--	80 min.
Chloroform	Air	100	43	25	--	20	--	--	25 min.
Methylene chloride	Air	100	100	102	--	100	86	--	--
1,2-Dichloroethane	Air	100	99	88	--	88	88	--	--
Cyclohexane	Air	100	--	97	--	--	--	--	--
Triethylamine	Air	100	98	93	--	92	--	88	--
Benzene	Air	100	--	--	--	100	--	--	--

[a]This was determined by measuring the area of the cyclopropanol peak on the GPC with a planimeter. An average of at least three or four trials is given.

[b]Refers to the atmosphere under which the vial was sealed before heating.

[c]The values of the areas given for 0.5 M cyclopropanol in carbon tetrachloride are typical of at least ten runs which were made.

[d]This solution is 0.1 M in cyclopropanol.

attempt to follow the course of the isomerization by NMR, the NMR tube, containing 1/2 ml. of 0.5 M cyclopropanol in carbon tetrachloride, was evacuated and heated at 80°. At various time intervals, the tube was withdrawn and an NMR spectrum was recorded. The isomerization was very slow in the NMR tube, oxygen apparently having an effect on the rate of isomerization. Further studies in which the vials were sealed under nitrogen and oxygen have confirmed this. The results are given in Table 2. The fact that oxygen was involved in the isomerization suggests the possibility of a reaction between it and some species, the nature of which is still obscure, to produce peroxyradicals.

The experiments in Tables 3 and 4 lend support to the idea of peroxyradicals being involved in the isomerization. The isomerization was very slow when small amounts of 2,6-di-tert-butyl-4-methyl phenol, an efficient trap for peroxyradicals, was added to the reaction vial before heating. The isomerization was much more rapid when small amounts of 2,4,6-tri-tert-butyl phenol, an inhibitor which is not particularly effective for peroxyradicals, was added to the reaction vial before heating. Peroxide and hydroperoxide initiators were very effective in enhancing the rate of the isomerization even under an atmosphere of nitrogen. Di-tert-butyl peroxide was not effective since the reaction temperature, 80°, was not high enough to effect its

Table 2. The effect of oxygen on the isomerization of 0.5 M cyclopropanol to propionaldehyde in carbon tetrachloride at 80°

Atmosphere[b]	Percent cyclopropanol remaining[a]					
	Blank	1/2 hr.	3/4 hr.	1 hr.	1-1/2 hr.	2 hr.
Air	100	42	24	16	10	--
Nitrogen	100	72	58	54	44	35
Oxygen	100	36	11	7	3	--

[a]This was determined by measuring the area of the cyclopropanol peak on the GPC with a planimeter. An average of at least three or four trials is given.

[b]Refers to the atmosphere under which the vial was sealed before heating.

dissociation into peroxyradicals to any extent. Initiators such as α,α'-azo-bis-isobutyronitrile and triphenylmethylazobenzene, which do not product peroxyradicals, are not effective initiators for the isomerization. In fact, they inhibit the isomerization to some extent.

Table 10 shows that no reaction occurs when cyclopropyl acetate or methyl ethyl ketone was treated under the same conditions in which cyclopropanol isomerized. The addition of benzoyl peroxide and propionaldehyde to the carbon tetrachloride solution did not effect any reaction of the acetate or ketone either. These results can be explained in one of two ways. First, the driving force may not be great enough

Table 3. The effect of free radical inhibitors on the isomerization of 0.5 M cyclopropanol to propionaldehyde in carbon tetrachloride at 80°

Inhibitor[b]	Atmosphere[c]	Percent cyclopropanol remaining[a]			
		Blank	1/2 hr.	1 hr.	2 hr.
--	Air	100	34	11	2
--	Oxygen	100	17	7	1
2,6-di-tert-butyl-4-methyl phenol	Oxygen	100	85	77	81
2,4,6-tri-tert-butyl phenol	Oxygen	100	88	85	12

[a]This was determined by measuring the area of the cyclopropanol peak on the GPC with a planimeter. An average of at least three or four trials is given.

[b]The amount of inhibitor added was approximately five milligrams.

[c]Refers to the atmosphere under which the vial was sealed before heating.

to open the cyclopropane ring when an electrophilic species attacks cyclopropyl acetate or methyl ethyl ketone. This is substantiated by the fact that cyclopropyl acetate and methyl ethyl ketone are completely stable at their respective boiling points, whereas cyclopropanol isomerizes to some extent when distilled at its boiling point or at lower temperatures under reduced pressure. Secondly, the results may indicate that the hydroxyl group of cyclopropanol is in some way involved in the isomerization.

Table 4. The effect of free radical initiators on the isomerization of 0.5 M cyclopropanol to propionaldehyde at 80°

Initiator[b]	Atmosphere[c]	Solvent	Percent cyclopropanol remaining[a]					
			Blank	1/2 hr.	1 hr.	2 hr.	4 hr.	6 hr.
--	Air	Carbon tetrachloride	100	34	11	2	--	--
--	Oxygen	"	100	17	7	1	--	--
--	Air	Benzene	100	--	--	--	102	--
--	Nitrogen	Carbon tetrachloride[d]	100	91	82	74	--	--
--	Nitrogen	"	100	70	71	--	--	--
α,α'-Azo-bis-isobutyronitrile	Air	"	100	80	79	70	--	--
"	Oxygen	"	100	46	--	46	--	--
"	Nitrogen	"	100	--	--	91	--	--
"	Air	Benzene	100	--	--	--	102	--
Benzoyl peroxide	Air	Carbon tetrachloride	100	44	11	0	--	--
" "	Nitrogen	"	100	82	26	4	--	--
" "	Nitrogen	" [d]	100	7	2	--	--	--
" "	Air	Benzene	100	--	--	--	--	97
Cumyl hydroperoxide	Nitrogen	Carbon tetrachloride	100	33	--	0	--	--
Di-tert-butyl peroxide	Nitrogen	"	100	--	--	75	--	--
Triphenylmethyl-azo-benzene	Nitrogen	"	100	--	--	93	--	--
"	Air	Benzene	100	--	--	--	98	--

[a]This was determined by measuring the area of the cyclopropanol peak on the GPC with a planimeter. An average of at least three or four trials is given.

[b]The amount of initiator added was approximately five milligrams.

[c]Refers to the atmosphere under which the vial was sealed before heating.

[d]In these runs, the solution was also 0.25 M in propionaldehyde.

Isomerization of cyclopropanol will not occur if carbon tetrachloride or chloroform and oxygen are not present. A 0.5 M solution of cyclopropanol prepared in carbon tetrachloride which had been heated in the presence of air for two hours at 80° did not show a significant enhancement of the isomerization rate when heated for two hours at 80° (Table 10). This suggests that a reaction between carbon tetrachloride and oxygen was not occurring to produce a species which was effecting the isomerization of cyclopropanol to propionaldehyde. The only possibility remaining was an initial reaction between oxygen, carbon tetrachloride and cyclopropanol or oxygen, carbon tetrachloride and propionaldehyde to produce initially a short-lived peroxyradical intermediate which reacts further to generate an electrophilic species. The role of propionaldehyde is not clear. It was shown previously that the half-life of 0.5 M cyclopropanol in carbon tetrachloride is considerably less than the half-life of 0.1 M cyclopropanol in carbon tetrachloride. This clearly indicates that the isomerization was faster when larger amounts of propionaldehyde were present. Further evidence for this is given in Table 4. The isomerization of cyclopropanol in carbon tetrachloride in the presence of benzoyl peroxide has an induction period, but when propionaldehyde was added there was no induction period. This supports the idea of a reaction occurring between oxygen, carbon tetrachloride and

propionaldehyde to generate an electrophilic species. Further evidence was provided by the fact that when propionaldehyde was added to a 0.5 M solution of cyclopropanol in carbon tetrachloride, and the solution was heated for two hours at 80° under an atmosphere of nitrogen, Table 4, the isomerization was very slow because oxygen was not present. The initiation of the isomerization could result from trace amounts of propionaldehyde which might be present in cyclopropanol as an impurity. If propionaldehyde is not, then cyclopropanol must be reacting with oxygen and carbon tetrachloride in a somewhat similar manner to generate an electrophilic species.

The presence of an electrophilic species was substantiated by the experiments in Table 5. When 0.00035 M of triethylamine, 0.0005 M diethylamine and 0.00062 M pyridine were added to vials of 0.5 M cyclopropanol in carbon tetrachloride, an inhibition of the isomerization rate was observed, but the reaction was not completely inhibited. This would suggest that the amines were competing with cyclopropanol for the electrophilic species. The addition of triethylamine was complex since it reacts with the carbon tetrachloride and makes the analysis difficult. It has been shown previously that a 0.5 M solution of cyclopropanol in benzene was stable for hours at 80°. If one drop of benzene saturated with hydrogen chloride was added before sealing the

Table 5. The effect of the addition of acids and bases on the isomerization of 0.1 M cyclopropanol to propionaldehyde at 80°

Additive	Atmosphere[b]	Solvent[c]	Percent cyclopropanol remaining[a]				
			Blank	1/2 hr.	1 hr.	1-1/2 hr.	2 hr.
---	Air	Carbon tetrachloride	100	--	--	46	--
Triethylamine[d]	Air	Carbon tetrachloride	100	--	--	90	--
Diethylamine[e]	Air	Carbon tetrachloride	100	--	--	69	--
Pyridine[f]	Air	Carbon tetrachloride	100	--	--	67	--
---	Air	Benzene[g]	100	100	99	--	99
Hydrogen chloride	Air	Benzene[g,h]	100	32	32	--	32

[a]This was determined by measuring the area of the cyclopropanol peak on the GPC with a planimeter. An average of at least three or four trials is given.

[b]Refers to the atmosphere under which the vial was sealed before heating.

[c]The solvent was degassed before use.

[d]The solution was 0.7 molar in triethylamine.

[e]The solution was 0.96 molar in diethylamine.

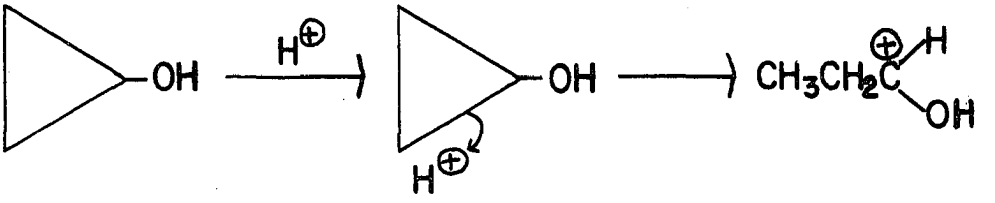
[f]The solution was 1.2 molar in pyridine.

[g]These solutions are 0.5 M in cyclopropanol.

[h]The hydrogen chloride was introduced by saturating benzene with the gas and adding one drop of this solution to the 0.5 M cyclopropanol solution of benzene.

reaction vial under nitrogen (Table 5), the alcohol isomerized until all of the hydrogen chloride was used up and then no further reaction took place. This clearly shows that benzene is not capable of reacting with oxygen and propionaldehyde or cyclopropanol to generate an electrophilic species.

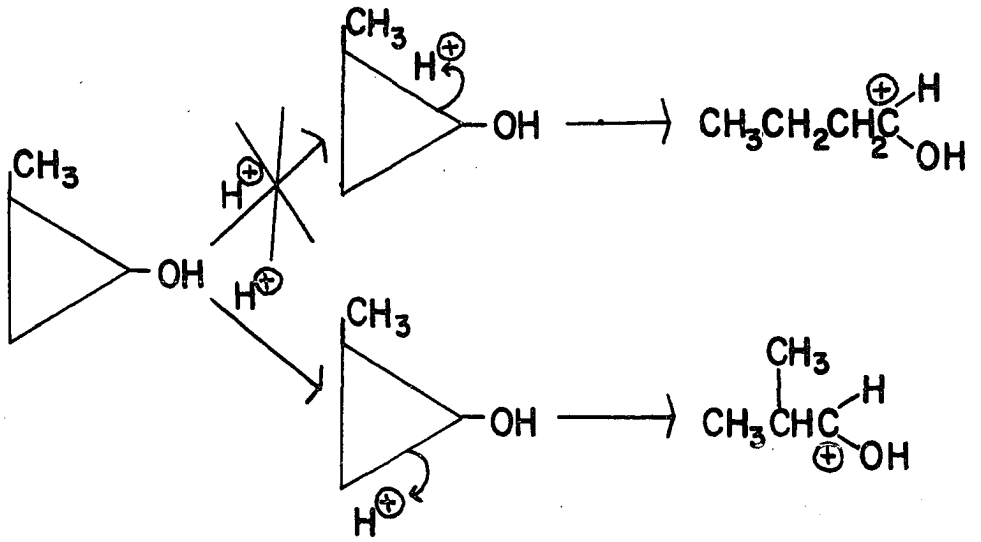
On the basis of the above results, it was possible to suggest a mechanism for the isomerization of cyclopropanol to propionaldehyde. The nature of the electrophilic species was not clear, but a reasonable assumption would be that it was a proton. The mechanism for the reaction was developed on the assumption that the electrophilic species was a proton, keeping in mind that this need not be correct since a species which transfers a proton could also be involved. The first step in the reaction would probably involve protonation of the cyclopropane ring followed by simultaneous ring opening, since protonation of the oxygen would not lead to propionaldehyde. This is shown in Eq. 21. The final step



(Eq. 21)

would involve formation of propionaldehyde with the liberation of a proton which can now attack another cyclopropanol molecule. The isomerization of 2-methylcyclopropanol in carbon tetrachloride at 80° to a mixture of 25% butyraldehyde

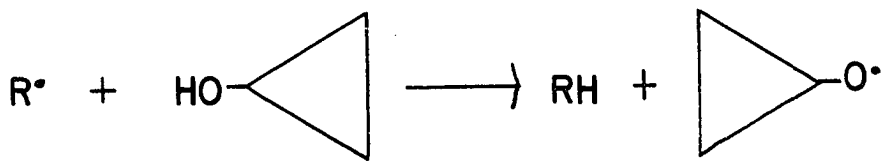
and 75% iso-butyraldehyde can be explained quite nicely by this mechanism. Protonation should occur more readily at a secondary carbon atom than at a tertiary carbon atom, since less steric hindrance would be involved. This would lead to iso-butyraldehyde as the major product as shown in Eq. 22.



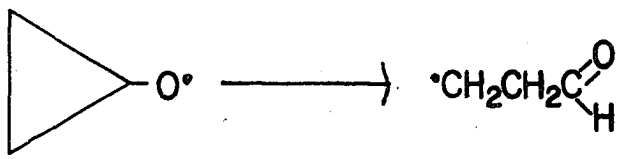
(Eq. 22)

It has previously been suggested that short-lived peroxyradicals were intermediates in the isomerization of cyclopropanol to propionaldehyde in carbon tetrachloride. This was substantiated by the fact that peroxyradical inhibitors effectively inhibit the isomerization and peroxide and hydroperoxide initiators initiate the isomerization in the absence of oxygen. This is shown in Tables 3 and 4. These results make it difficult to completely rule out a free radical mechanism[12] for the isomerization. A free radical mechanism would probably involve the attack of some radical species, probably a peroxyradical, on the hydroxyl hydrogen of cyclopropanol to produce an alkoxyl radical (Eq. 23) which

undergoes a simultaneous ring opening (Eq. 24). The radical,

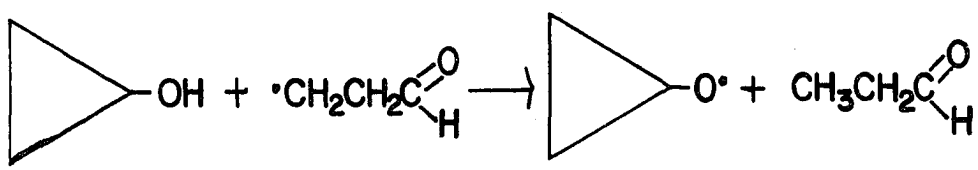


(Eq. 23)



(Eq. 24)

thus generated, can attack another cyclopropanol molecule (Eq. 25) to start a chain reaction. Radical attack on the



(Eq. 25)

cyclopropane ring seems unlikely for several reasons. First, cyclopropyl acetate and methyl ethyl ketone, as previously stated, were completely inert under the conditions of the isomerization. Secondly, radical abstractions from cyclopropane rings are known to be quite difficult.[30] Lastly, if hydrogen atom abstraction from the cyclopropane ring did occur, it would be easiest adjacent to the hydroxyl group. This is shown in Eq. 26. Such abstraction would be expected

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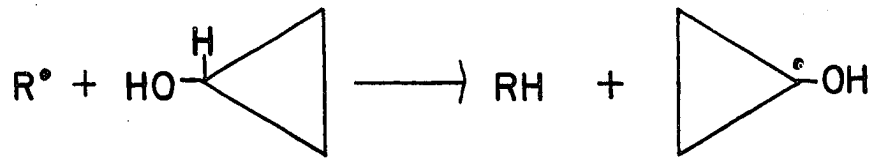
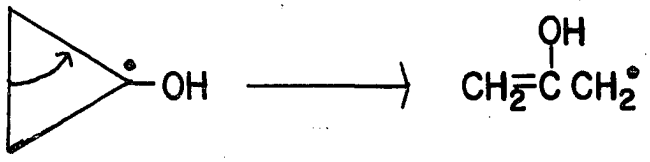
[30]McNesby, J. R. and Gordon, A. S., J. Am. Chem. Soc., 79, 825 (1957).



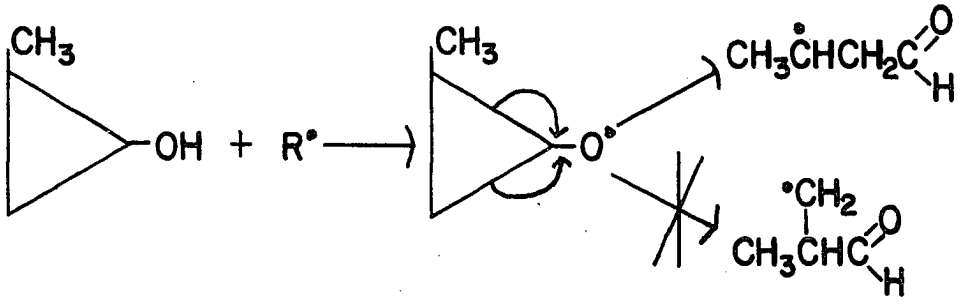
(Eq. 26)

to lead to acetone, rather than propionaldehyde, as a product (Eq. 27). Eqns. 23-25 do not appear likely for two reasons.



(Eq. 27)

First, cyclopropanol remains inert in benzene when peroxide initiators are added (Table 4) even though benzene is known to be a good solvent for radical reactions. Secondly, butyraldehyde might be expected as the predominate product of the isomerization of 2-methylcyclopropanol in carbon tetrachloride at 80° if the reaction proceeds by a radical mechanism, since a secondary radical would be more easily generated than a primary radical. This is shown in Eq. 28.



(Eq. 28)

It is remotely possible that the mechanism based on the generation of an electrophilic species and the free radical

mechanism are occurring simultaneously.

A study was undertaken to determine if 1-methylcyclopropanol isomerized in carbon tetrachloride at 80° in the same manner in which cyclopropanol did. The results are given in Tables 6-9. The progress of the isomerization of 1-methylcyclopropanol to methyl ethyl ketone was followed in the same manner as previously described for cyclopropanol.

Table 6 shows that the isomerization has the same solvent dependency which was observed for the isomerization of cyclopropanol. The half-life of the isomerization in carbon tetrachloride was approximately 15 minutes which was less than that observed for the isomerization of cyclopropanol. The results in Table 7 are quite striking as it appears that the removal of oxygen has little effect on the isomerization rate. This could be accounted for by the fact that the rate of isomerization of 1-methylcyclopropanol was somewhat more rapid than the isomerization of cyclopropanol. The driving force for ring opening should be enhanced by the methyl group in 1-methylcyclopropanol since electrophilic attack would lead to a tertiary carbonium ion which would be more stable than the secondary carbonium ion that is formed by electrophilic attack on cyclopropanol. This is shown in Eqns. 29 and 30. Table 8 shows that inhibitors which are effective for peroxyradicals inhibit the isomerization effectively, whereas other inhibitors are not as effective.

Table 6. The effect of solvent on the isomerization of 0.5 M 1-methylcyclopropanol to methyl ethyl ketone at 80°

Solvent	Atmosphere[b]	Percent 1-methylcyclopropanol remaining[a] Blank	1/2 hr.	1 hr.	2 hr.	10 hr.	Esti. half-life
Carbon tetrachloride	Air	100	26	10	--	--	15 min.
Cyclohexane	Air	100	--	--	98	97	--
Triethylamine	Air	100	--	--	96	96	--
Benzene	Air	100	--	95	98	95	--

[a]This was determined by measuring the area of the 1-methylcyclopropanol peak on the GPC with a planimeter. An average of three or four trials is given.

[b]Refers to the atmosphere under which the vial was sealed before heating.

Table 7. The effect of oxygen on the isomerization of 0.5 M 1-methylcyclopropanol to methyl ethyl ketone in carbon tetrachloride at 80°

Atmosphere[b]	Percent 1-methylcyclopropanol remaining[a] Blank	1/2 hr.	1 hr.
Air	100	--	17
Nitrogen	100	41	22

[a]This was determined by measuring the area of the 1-methylcyclopropanol peak on the GPC with a planimeter. An average of three or four trials is given.

[b]Refers to the atmosphere under which the vial was sealed before heating.

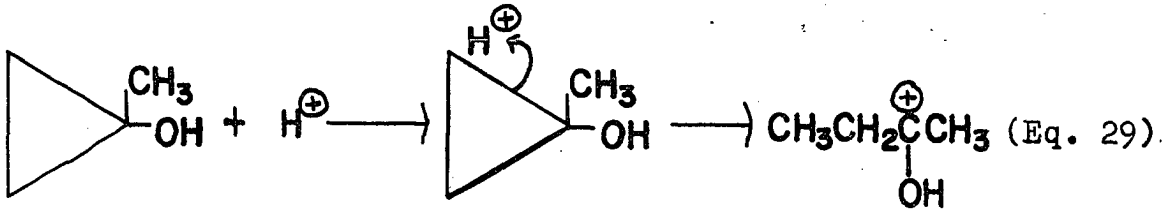
Table 8. The effect of free radical inhibitors on the isomerization of 0.5 M 1-methylcyclopropanol to methyl ethyl ketone in carbon tetrachloride at 80°

Inhibitor[b]	Atmosphere[c]	Percent 1-methylcyclopropanol remaining[a]				
		Blank	1/2 hr.	1 hr.	3 hr.	4 hr.
--	Air	100	26	10	--	--
2,4,6-tri-tert-butyl phenol	Air	100	--	21	--	0
2,6-di-tert-butyl-4-methyl phenol	Air	100	--	87	--	71
P-methylene-bis-2,6-di-tert-butyl phenol	Air	100	--	90	--	22

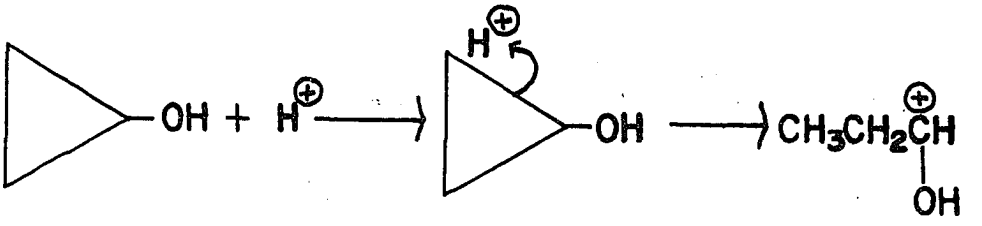
[a]This was determined by measuring the area of the 1-methylcyclopropanol peak on the GPC with a planimeter. An average of three or four trials is given.

[b]The amount of inhibitor added was approximately ten milligrams.

[c]Refers to the atmosphere under which the vial was sealed before heating.



(Eq. 29)



(Eq. 30)

The effect of initiators on the isomerization was difficult to observe since the isomerization could not be retarded by the removal of oxygen. This is shown in Table 9.

Table 9. The effect of free radical initiators on the isomerization of 0.5 M 1-methylcyclopropanol to methyl ethyl ketone in carbon tetrachloride at 80°

Initiator[b]	Atmosphere[c]	Percent 1-methylcyclopropanol remaining[a]		
		Blank	1/2 hr.	1 hr.
--	Air	100	--	17
--	Nitrogen	100	41	22
Benzoyl peroxide	Nitrogen	100	50	48
Cumyl hydroperoxide	Nitrogen	100	36	31

[a]This was determined by measuring the area of the 1-methylcyclopropanol peak on the GPC with a planimeter. An average of three or four trials is given.

[b]The amount of initiator added was approximately five milligrams.

[c]Refers to the atmosphere under which the vial was sealed before heating.

In general, it can be said that the isomerization of cyclopropanol to propionaldehyde was very similar to the isomerization of 1-methylcyclopropanol to methyl ethyl ketone in carbon tetrachloride. The observed difference in the effect of oxygen on the respective isomerizations could

be attributed to the enhanced reactivity of 1-methylcyclopropanol toward electrophilic species. The isomerization of both alcohols probably proceeds by the same mechanism, which appears to be the attack of an electrophilic species, probably a proton, on the cyclopropane ring with simultaneous ring opening.

A detailed investigation into the isomerization of cyclopropanol and substituted cyclopropanols is now in progress in an attempt to further elucidate the mechanism of the isomerization reaction.

EXPERIMENTAL

Boiling points

All boiling points are uncorrected and in degrees Centigrade.

Infrared spectra

All infrared spectra were recorded on a Perkin Elmer Model 21 infrared spectrophotometer.

Gas phase chromatography

All gas phase chromatography (GPC) analyses were performed on a Perkin-Elmer Vapor Fractometer Model 154C equipped with a Micro-Dipper attachment.

Cyclopropyl acetate

Cyclopropyl acetate was prepared by the procedure of Emmons and Lucas.[24] A solution of peroxytrifluoroacetic acid was prepared from 67.6 ml. (0.48 mole) of trifluoroacetic anhydride and 10.8 ml. (0.4 mole) of 90% hydrogen peroxide in 100 ml. of methylene chloride. This solution was added over a 30 minute period to a well stirred mixture of 142 grams (1.0 mole) of anhydrous disodium hydrogen phosphate and 16.8 grams (0.2 mole) of methyl cyclopropyl ketone in 200 ml. of methylene chloride. After addition was complete, the mixture was heated under reflux for one hour. The resulting solution was filtered to remove the mixed salts and washed with 100

ml. of methylene chloride. The combined filtrates were washed with 150 ml. of 10% sodium carbonate solution and dried over magnesium sulfate. Most of the solvent was removed by distillation and the residual liquid was dissolved in a mixture of 180 ml. of methanol and 20 ml. of acetic acid containing 37.4 grams of Girard's reagent P. The resulting solution was refluxed for 12 hours and poured into 60 ml. of ice water. The solution was partially neutralized with 25.2 grams of sodium bicarbonate in 100 ml. of water and was then extracted with six 50-ml. portions of methylene chloride. The extracts were washed with 50 ml. of 10% sodium bicarbonate, dried, and most of the solvent was removed by distillation at atmospheric pressure. The residual liquid was fractionated yielding 5.6 to 6.5 grams (28-33%) of cyclopropyl acetate, b.p. 109.5-111° (lit. b.p. 109-111°).[24]

Attempted preparation of cyclopropyl acetate by an alternative method

Another route to cyclopropyl acetate was the method described by Simmons and Smith,[22] who reported a 31% yield from the reaction of vinyl acetate with a zinc diiodomethane complex previously formed from a zinc-copper couple and methylene iodide. Mahoney[21] obtained very poor yields of cyclopropyl acetate by this method apparently due to the lack of reactivity of the zinc-copper couple. Recently Shank and Shechter[23] have reported the preparation of a

simple zinc-copper couple which will effect the reaction of methylene iodide with olefins to give cyclopropanes. The latter method of preparing the zinc-copper couple was used in the following experiments.

Thirty-two and eight-tenths grams (0.5 mole) of zinc powder (Mallinckrodt Analytical Reagent) was washed successively with four 25-ml. portions of 3% hydrochloric acid, four 30-ml. portions of conductivity water, two 50-ml. portions of 2% copper sulfate, four 30-ml. portions of conductivity water and five 25-ml. portions of absolute ether. The couple was finally transferred to a Buchner funnel, washed with additional anhydrous ether, covered tightly with a rubber dam, and suction-dried until it reached room temperature.

One hundred seven and two-tenths grams (0.4 mole) of methylene iodide and 0.3 grams (0.0012 mole) of iodine were added to a mixture of 32.8 grams (0.5 mole) of zinc-copper couple and 330 ml. of anhydrous ether in a three-necked flask equipped with a reflux condenser, stirrer and addition funnel. The iodine color disappeared immediately and the solution was stirred at reflux for 30 minutes. Heating was discontinued and 38.7 grams (0.45 mole) of vinyl acetate in 50 ml. of anhydrous ether was added dropwise over a period of 30 minutes. No exothermic reaction was observed. Heating was initiated again and the mixture was refluxed for 18 hours. The reaction mixture was cooled and filtered through a Super

Cel pad on a Buchner funnel. The residue was washed thoroughly with ether. The ether solution was extracted with three 50-ml. portions of 5% hydrochloric acid to remove dissolved zinc iodide, three 50-ml. portions of aqueous sodium bicarbonate and saturated aqueous sodium chloride. The aqueous washings were extracted with ether and the combined ether extracts were dried over magnesium sulfate. The solvent was removed by distilling through a packed column. Fractionation of the residual liquid failed to yield any cyclopropyl acetate.

The conditions of this reaction were varied in several experiments but only in one experiment could any cyclopropyl acetate be isolated. In this run there was isolated 1.5 grams (4%).

Cyclopropanol

From cyclopropyl acetate Cyclopropanol was prepared from cyclopropyl acetate by the procedure of DePuy, et al.[3] To a solution of 5.6 grams (0.056 mole) of cyclopropyl acetate in 30 ml. of anhydrous ether in a three-necked flask equipped with reflux condenser, stirrer and addition funnel, cooled to 0°, 145 ml. of 0.21 M lithium aluminum hydride in ether was added dropwise so as to maintain a constant refluxing of the ether. The addition was complete in 15 minutes. A slurry of sodium sulfate-water was then added in small amounts to destroy the excess lithium aluminum hydride. The

resulting solution was filtered to remove the basic salts and dried over sodium sulfate. Most of the solvent was removed by distillation through a twelve-inch packed column. The residual liquid was then analyzed by GPC on a 2 meter X 15 mm 30% Ucon LB550X on 60/80 mesh firebrick column at 80°. Samples of 1 ml. were injected into the instrument and 1.0 grams (31%) of cyclopropanol was collected, b.p. 101.0° (lit. b.p. 100.5-101°).[31] The infrared spectrum in carbon tetrachloride showed the non-bonded and bonded hydroxyl absorption at 2.78 μ and 3.03 μ, respectively. The absorption for the cyclopropane ring was also present at 9.90 μ. See nuclear magnetic resonance spectrum (NMR) Figure 1. This reaction was repeated several times but the yield of cyclopropanol could not be improved.

From epichlorohydrin Cyclopropanol was prepared from epichlorohydrin by the procedure of Magrane and Cottle[1] utilizing the modifications described by Stahl and Cottle[2] and Roberts.[9] Fifty-five grams (0.03 mole) of magnesium bromide in 200 ml. of anhydrous ether was prepared from 7.2 grams (0.3 mole) of magnesium and 48.0 grams (0.3 mole) of bromine in a three-necked flask equipped with reflux condenser, stirrer and addition funnel. Three-tenths gram (0.0012 mole) of ferric chloride hexahydrate was added and stirring

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[31]Mahoney, L. R., The Hydrolysis of Cyclopropyl Acetate. Unpublished Ph. D. Thesis, Ames, Iowa, Library, Iowa State University of Science and Technology, 1960, pp. 71-72.

was continued for 30 minutes. To this mixture was added over a period of 30 minutes 28.0 grams (0.3 mole) of epichlorohydrin dissolved in 30 ml. of anhydrous ether. Stirring was continued for one hour after which time approximately 0.9 mole of ethylmagnesium bromide, prepared from 21.6 grams (0.9 mole) of magnesium and 98.1 grams (0.9 mole) of ethyl bromide in 800 ml. of anhydrous ether over an atmosphere of nitrogen, was added over a period of two hours. Gas evolution was complete two hours after complete addition of the Grignard reagent, however, the reaction mixture was stirred overnight. The reaction mixture was hydrolyzed by pouring into an iced ammonium chloride solution, filtered, the ether layer separated and extracted with eight 100-ml. portions of water. The combined aqueous extracts were then extracted continuously with ether for two days. The ether solution was then dried over magnesium sulfate and most of the ether was removed by distillation through a twelve-inch packed column. The residual liquid was worked up by GPC as described previously. There was isolated 5.9 grams (34%) of cyclopropanol. Yields of pure cyclopropanol in the range 23-34% were obtained by this method. The higher yields were obtained from smaller sized runs.

From epibromohydrin Forty-eight grams (0.26 mole) of magnesium bromide in 200 ml. of anhydrous ether was prepared from 6.24 grams (0.26 mole) of magnesium and 41.6 grams

(0.26 mole) of bromine in a three-necked flask equipped with reflux condenser, stirrer and addition funnel. Three-tenths gram (0.0012 mole) of ferric chloride hexahydrate was added and stirring was continued for 30 minutes. To this mixture was added over a period of 30 minutes 35.5 grams (0.26 mole) of epibromohydrin dissolved in 30 ml. of anhydrous ether. Stirring was continued for one hour after which time approximately 0.8 mole of ethylmagnesium bromide, prepared from 19.2 grams (0.8 mole) of magnesium and 87.2 grams (0.8 mole) of ethyl bromide in 700 ml. of anhydrous ether over an atmosphere of nitrogen, was added over a period of two hours. Gas evolution was complete two hours after complete addition of the Grignard reagent, however, the reaction mixture was stirred overnight. The reaction mixture was worked up in the manner described for cyclopropanol. There was isolated 3.0 grams (20%) of cyclopropanol.

1-Chloro-2-methyl-2,3-epoxypropane

From peroxytrifluoroacetic acid 1-Chloro-2-methyl-2,3-epoxypropane was prepared from peroxytrifluoroacetic acid by the procedure of Emmons and Pagano.[32] Peroxytrifluoroacetic acid prepared from 60 ml. (0.425 mole) of trifluoroacetic anhydride and 10.8 ml. (0.4 mole) of 90% hydrogen peroxide in 100 ml. of methylene chloride was added over a period of

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[32]Emmons, W. D. and Pagano, A. S., J. Am. Chem. Soc., 77, 89 (1955).

30 minutes to a well stirred mixture of 18.1 grams (0.2 mole) of 3-chloro-2-methyl-1-propene and 142 grams (1.0 mole) of disodium hydrogen phosphate in 200 ml. of methylene chloride. The reaction mixture was stirred for an additional hour after which time it was filtered to remove the insoluble salts. The solvent was removed by distillation at room temperature. Distillation of the residual liquid at reduced pressure yielded 16 grams (68%) of 1-chloro-2-methyl-2,3-epoxypropane, b.p. 75-77°/200 mm (lit. b.p. 46°/50 mm).[33] The infrared spectrum showed characteristic epoxide absorption at 11.12 μ and 11.35 μ.

From perbenzoic acid Perbenzoic acid was prepared by the procedure of Braun.[34] Fifty-one grams (0.37 mole) of perbenzoic acid in 740 ml. of methylene chloride was placed in a three-necked flask equipped with stirrer and addition funnel. Thirty-two and six-tenths grams (0.36 mole) of 3-chloro-2-methyl-1-propene in 30 ml. of ether was then added over a period of 45 minutes to the perbenzoic acid. The reaction was maintained with stirring for 36 hours at room temperature after which time iodometric titration indicated only a slight excess of perbenzoic acid remaining. The reaction mixture was neutralized by shaking with a 10%

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[33]Union Carbide and Carbon Corp., Brit. Patent 735,974 (1956) [Chemical Abstracts, 50, 8730 (1956)].

[34]Braun, G., Organic Syntheses, Coll. Vol. 1, New York, John Wiley and Sons, 1941, pp. 431.

sodium hydroxide solution and the sodium hydroxide was removed by washing with water. Most of the methylene chloride was removed by distillation at room temperature. Distillation of the residual liquid at reduced pressure yielded 30.0 grams (78%) of 1-chloro-2-methyl-2,3-epoxypropane, b.p. 75°/200 mm.

1-Methylcyclopropanol

Thirty grams (0.16 mole) of magnesium bromide in 150 ml. of anhydrous ether was prepared from 3.84 grams (0.16 mole) of magnesium and 12.8 grams (0.16 mole) of bromine in a three-necked flask equipped with reflux condenser, stirrer and addition funnel. Three-tenths grams (0.0012 mole) of ferric chloride hexahydrate was added and stirring was continued for 30 minutes. To this mixture was added over a period of 30 minutes 16.0 grams (0.15 mole) of 1-chloro-2-methyl-2,3-epoxypropane dissolved in 30 ml. of anhydrous ether. Stirring was continued for one hour after which time approximately 0.48 mole of ethylmagnesium bromide, prepared from 11.5 grams (0.48 mole) of magnesium and 51.9 grams (0.48 mole) of ethyl bromide in 500 ml. of anhydrous ether over an atmosphere of nitrogen, was added over a period of 90 minutes. The reaction was very exothermic and a considerable amount of gas was given off. The reaction mixture was stirred overnight and then hydrolyzed by pouring into an iced ammonium chloride solution. The solution was filtered, the ether layer separated and extracted with eight 100-ml. portions of water.

The combined aqueous extracts were then extracted with twelve 50-ml. portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate and the ether was removed by distillation through a twelve-inch packed column. The residual liquid was analyzed by GPC on a 2 meter X 15 mm 30% Ucon LB550X on 60/80 mesh firebrick column at 80°. A fraction was collected which had a retention time 0.7 times that of cyclopropanol. This fraction amounted to 3.1 grams (36%) of 1-methylcyclopropanol, b.p. 103.5°. The infrared spectrum in carbon tetrachloride showed the non-bonded and bonded hydroxyl absorption at 2.78 μ and 3.00 μ, respectively. The absorption for the cyclopropane ring was also present at 9.95 μ. See NMR spectrum Figure 4.

Anal. Calcd. for C_4H_8O: C, 66.67; H, 11.10. Found: C, 66.54, 66.62; H, 11.30, 11.20.

1-Chloro-2,3-epoxybutane

From peroxytrifluoroacetic acid The procedure is the same as previously described for the epoxidation of 3-chloro-2-methyl-1-propene with peroxytrifluoroacetic acid. Starting with 18.1 grams (0.2 mole) of 1-chloro-2-butene, there was isolated 15.0 grams (71%) of 1-chloro-2,3-epoxybutane, b.p. 80-81°/200 mm (lit. b.p. 49°/50 mm).[35] The infrared spectrum showed characteristic epoxide absorption at 11.02 μ and

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[35]Phillips, B. and Starcher, P. S., Brit. Patent 784,620 (1958) [Chemical Abstracts, 52, 7347 (1958)].

11.62 μ.

From perbenzoic acid The procedure is the same as previously described for the epoxidation of 3-chloro-2-methyl-1-propene with perbenzoic acid. Starting with 28.0 grams (0.31 mole) of 1-chloro-2-butene, there was isolated 23.0 grams (70%) of 1-chloro-2,3-epoxybutane, b.p. 85-86°/210 mm.

2-Methylcyclopropanol

Twenty-seven and six-tenths grams (0.15 mole) of magnesium bromide in 200 ml. of anhydrous ether was prepared from 3.6 grams (0.15 mole) of magnesium and 24.0 grams (0.15 mole) of bromine in a three-necked flask equipped with reflux condenser, stirrer and addition funnel. Three-tenths grams (0.0012 mole) of ferric chloride hexahydrate was added and stirring was continued for 30 minutes. To this mixture was added over a period of 20 minutes 15.0 grams (0.14 mole) of 1-chloro-2,3-epoxybutane in 30 ml. of anhydrous ether. Stirring was continued for one hour after which time approximately 0.5 mole of ethylmagnesium bromide, prepared from 12.0 grams (0.5 mole) of magnesium and 54.5 grams (0.5 mole) of ethyl bromide in 50 ml. of anhydrous ether over an atmosphere of nitrogen, was added at such a rate that a gentle reflux was maintained. Gas evolution was complete in two hours, however, the reaction mixture was stirred overnight. The reaction mixture was worked up in the manner described for 1-methylcyclopropanol. The liquid remaining after removal

of most of the ether by distillation through a twelve-inch packed column was analyzed by GPC on a 2 meter X 15 mm 30% Ucon LB550X on 60/80 mesh firebrick column at 80°. A fraction was collected which had a retention time 1.3 times that of cyclopropanol. This fraction amounted to 2.2 grams of crude material. This material was again subjected to GPC analysis on a 1 meter X 6 mm 1:3 Hyprose on 60/80 mesh firebrick column at 80°. There was isolated 1.9 grams (23.5%) of 2-methylcyclopropanol, b.p. 126.0°. The infrared spectrum in carbon tetrachloride showed the non-bonded and bonded hydroxyl absorption at 2.77 μ and 3.02 μ, respectively. The absorption for the cyclopropane ring was also present at 9.95 μ. See NMR spectrum Figure 7.

Anal. Calcd. for C_4H_8O: C, 66.67; H, 11.10. Found: C, 66.65, 66.55; H, 11.30, 11.21.

1-Phenyl-3-chloropropene

1-Phenyl-3-chloropropene was prepared by the procedure of Wichterle and Cerny.[28] Seventy-eight grams (0.75 mole) of styrene, 375 ml. of concentrated hydrochloric acid and 75 grams of a 40% aqueous solution of formaldehyde were heated with vigorous stirring for eight hours in a one-necked flask equipped with reflux condenser. The reaction mixture was diluted with an equal volume of water and the oily layer was separated. The aqueous layer was extracted with two 50-ml. portions of ether. The combined ether extracts and oily layer

were washed with water, dried over calcium chloride, and distilled. There was isolated 32.0 grams (30%) of 1-phenyl-3-chloropropene, b.p. 117-119°/15 mm (lit. b.p. 114-115°/13 mm).[28]

1-Chloro-3-phenyl-2,3-epoxypropane

The procedure is the same as previously described for the epoxidation of 3-chloro-2-methyl-1-propene with perbenzoic acid. Starting with 21.5 grams (0.15 mole) of 1-phenyl-3-chloropropene, there was isolated 24.0 grams (95%) of 1-chloro-3-phenyl-2,3-epoxypropane, b.p. 127-129°/20 mm (lit. b.p. 125°/17 mm).[36] The infrared spectrum showed characteristic epoxide absorption at 10.65 μ and 11.4 μ.

Attempted preparation of 2-phenylcyclopropanol

Thirty-three grams (0.18 mole) of magnesium bromide in 200 ml. of anhydrous ether was prepared from 4.3 grams (0.18 mole) of magnesium and 28.8 grams (0.18 mole) of bromine in a three-necked flask equipped with reflux condenser, stirrer and addition funnel. Three-tenths grams (0.0012 mole) of ferric chloride hexahydrate was added and stirring was continued for 30 minutes. To this mixture was added over a period of 30 minutes 24.0 grams (0.14 mole) of 1-chloro-3-phenyl-2,3-epoxypropane in 30 ml. of anhydrous ether.

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[36]Fourneau, J. P. and Chantalou, S., Bull. soc. chim., 12, 845, 1945 (Original not available for examination; abstracted in Chemical Abstracts, 40, 6466 (1946)).

Stirring was continued for one hour after which time approximately 0.5 mole of ethylmagnesium bromide, prepared from 12.0 grams (0.5 mole) of magnesium and 54.5 grams (0.5 mole) of ethyl bromide in 500 ml. of anhydrous ether over an atmosphere of nitrogen, was added over a period of two hours. Gas evolution was complete in two hours, however, stirring was continued for several hours. The reaction mixture was worked up in the manner described for 1-methylcyclopropanol. The liquid remaining after removal of most of the ether was distilled at reduced pressure. There was isolated 1.0 grams of a yellow liquid, b.p. 75°/0.6 mm, which appeared to be a mixture of 2-phenylcyclopropanol (lit. b.p. 75°/0.2 mm)[3] and its isomerization product. The infrared spectrum in carbon tetrachloride showed the non-bonded and bonded hydroxyl absorption at 2.79 μ and 2.9 μ. The absorption for the cyclopropane ring was also present at 9.7 μ. Carbonyl absorption is present at 5.85 μ and 5.95 μ. Absorption due to the aldehydic hydrogen is present at 3.62 μ. The material did not crystallize on standing and further attempts to isolate the 2-phenylcyclopropanol were unsuccessful. There was a considerable amount of tar and polymer obtained from this reaction.

3-Bromo-2-phenyl-1-propene

The procedure of Hatch and Patton[29] was used for this preparation. Two hundred thirty-six grams (2 mole) of

2-phenyl-1-propene, 178.0 grams (1 mole) of N-bromosuccinimide, 450 ml. dry carbon tetrachloride and 6.0 grams of benzoyl peroxide were placed in a one-necked flask equipped with reflux condenser. This mixture was heated for 54 hours on a steam bath. The reaction mixture was filtered and the carbon tetrachloride was removed in vacuo at 40°. Distillation of the residual liquid at reduced pressure was not smooth and a product boiling over the range 90-110°/15 mm was obtained. Two redistillations resulted in a considerable amount of polymerization, however, 23.5 grams (12%) of 3-bromo-2-phenyl-1-propene, b.p. 108-110°/15 mm (lit. b.p. 90°/5 mm),[29] was obtained. The infrared spectrum had all the absorption peaks which were described for 3-bromo-2-phenyl-1-propene in the literature.[29]

Attempted preparation of 1-bromo-2-phenyl-2,3-epoxypropane

The procedure is the same as previously described for the epoxidation of 3-chloro-2-methyl-1-propene with perbenzoic acid. Starting with 23.5 grams (0.12 mole) of 3-bromo-2-phenyl-1-propene, only a small trace of the corresponding epoxide was obtained and it was contaminated with a carbonyl compound. Most of the reaction mixture had polymerized during distillation. The reaction was repeated using 17.5 grams (0.09 mole) of olefin, however, again only a small amount of material was obtained and it appeared to be the same mixture as obtained in the first experiment. Again a

considerable amount of polymerization had taken place during the distillation process.

3-Chloro-2-phenyl-1-propene

The procedure of Hatch and Patton[29] was used for this preparation. Eighty grams (0.7 mole) of selenium dioxide was added in small portions to a vigorously stirred mixture of 236 grams (2.0 mole) of 2-phenyl-1-propene, 158 grams (1.55 mole) of acetic anhydride and 108 grams (1.8 mole) of acetic acid. The mixture had an initial temperature of 30° which increased to 90° during the addition of selenium dioxide. After addition of the dioxide the temperature was maintained at 125° for four hours. The selenium metal was removed by filtration and distillation at reduced pressure removed the acetic acid and acetic anhydride. Further distillation yielded 136.5 grams of crude 3-acetoxy-2-phenyl-1-propene, b.p. 134-136°/20 mm (lit. b.p. 112-113°/5 mm).[29] A solution of 32.8 grams (0.82 mole) of sodium hydroxide in 300 ml. of water was added to 136.5 grams (0.77 mole) of crude 3-acetoxy-2-phenyl-1-propene and 0.1 grams of hydroquinone. The mixture was refluxed with vigorous stirring for seven hours. The aqueous layer was separated from the alcohol layer and extracted with three 100-ml. portions of ether. The ether extracts and the alcohol layer were combined and dried over anhydrous potassium carbonate. The solvent was removed by distillation at room temperature. Distillation

of the residual liquid at reduced pressure yielded 66.0 grams (63.5%) of 2-phenyl-2-propen-1-ol, b.p. 125.5-130°/20 mm (lit. b.p. 116-118°/11 mm).[29] The infrared spectrum had all the absorption peaks which were described for 2-phenyl-2-propen-1-ol in the literature.[29] Fifty-four grams of pyridine and 50 ml. of dry chloroform were placed in a 250-ml. Erlenmeyer flask and cooled to 0-10°, and 76 grams (0.64 mole) of thionyl chloride was added over a period of 10 minutes while the temperature was kept below 10°. This solution was then added over a period of two hours to a solution of 65.5 grams (0.49 mole) of 2-phenyl-2-propen-1-ol dissolved in 100 ml. of dry chloroform. The temperature was kept below 10° during the addition of the thionyl chloride. When all of the thionyl chloride had been added, the mixture was refluxed for one hour. The reaction mixture was distilled at reduced pressure to remove the chloroform and excess thionyl chloride. Further distillation at reduced pressure yielded 32.3 grams (43.5%) of 3-chloro-2-phenyl-1-propene, b.p. 106-108°/20 mm (lit. b.p. 87-88°/5 mm).[29] The infrared spectrum had all the absorption peaks which were described for 3-chloro-2-phenyl-1-propene in the literature.[29]

1-Chloro-2-phenyl-2,3-epoxypropane

The procedure is the same as previously described for the epoxidation of 3-chloro-2-methyl-1-propene with perbenzoic acid. Starting with 31.5 grams (0.21 mole) of 3-chloro-2-

phenyl-1-propene, there was isolated 11.0 grams (32%) of crude 1-chloro-2-phenyl-2,3-epoxypropane, b.p. 92-95°/1.5 mm. The crude material was used without further purification for the next experiment. The infrared spectrum showed characteristic epoxide absorption at 10.65 μ and 11.52 μ. There was also isolated 18.0 grams of a carbonyl compound which appeared to be the same as the carbonyl component obtained from the reaction of 3-bromo-2-phenyl-1-propene with perbenzoic acid. This compound boiled over the range 81-91°/1.5 mm.

1-Phenylcyclopropanol

Thirteen grams (0.07 mole) of magnesium bromide in 100 ml. of anhydrous ether was prepared from 1.68 grams (0.07 mole) of magnesium and 11.2 grams (0.07 mole) of bromine in a three-necked flask equipped with reflux condenser, stirrer and addition funnel. Three-tenths grams (0.0012 mole) of ferric chloride hexahydrate was added over a period of 30 minutes to 11.00 grams (0.065 mole) of 1-chloro-2-phenyl-2,3-epoxypropane in 30 ml. of anhydrous ether. Stirring was continued for one hour after which time approximately 0.21 mole of ethylmagnesium bromide, prepared from 5.04 grams (0.21 mole) of magnesium and 22.9 grams (0.21 mole) of ethyl bromide in 200 ml. of anhydrous ether over an atmosphere of nitrogen, was added over a period of 45 minutes. The reaction was very exothermic and a considerable amount of gas was given off. Gas evolution was complete in one hour, however, stirring was

continued overnight. The reaction mixture was worked up in the manner described for 1-methylcyclopropanol. The liquid remaining after removal of most of the ether was distilled at reduced pressure. There was isolated 3.0 grams of an almost colorless liquid, b.p. 59-68°/1.0 mm. Infrared and NMR data indicate that the liquid contains 1-phenylcyclopropanol contaminated with some impurity. Elution chromatography on silica is being used in an attempt to purify the 1-phenylcyclopropanol.

Isomerization of cyclopropanol to propionaldehyde in carbon tetrachloride

Fifty milligrams of cyclopropanol was dissolved in 400 µl. of carbon tetrachloride, containing 1% tetramethylsilane, in a 2 ml. glass vial. The vial was sealed and placed in a constant temperature bath at 80° for 12 hours. The solution was removed from the vial and an NMR spectrum was recorded. The NMR spectrum (Figure 2) was identical with that of an authentic sample of propionaldehyde (Figure 3) with the exception of a small amount of aldol product that had formed during the heating period.

Isomerization of 1-methylcyclopropanol to methyl ethyl ketone in carbon tetrachloride

Fifty milligrams of 1-methylcyclopropanol was dissolved in 400 µl. of carbon tetrachloride, containing 1%

tetramethylsilane, in a 2 ml. glass vial. The vial was sealed and placed in a constant temperature bath at 80° for 12 hours. The solution was removed from the vial and an NMR spectrum was recorded. The NMR spectrum (Figure 5) was identical with that of an authentic sample of methyl ethyl ketone (Figure 6).

Isomerization of 2-methylcyclopropanol to a mixture of butyraldehyde and iso-butyraldehyde in carbon tetrachloride

Fifty milligrams of 2-methylcyclopropanol was dissolved in 400 µl. of carbon tetrachloride, containing 1% tetramethylsilane, in a 2 ml. glass vial. The vial was sealed and placed in a constant temperature bath at 80° for 12 hours. The solution was removed from the vial and an NMR spectrum was recorded. The NMR spectrum (Figure 8) had peaks corresponding to a mixture of 25% butyraldehyde (Figure 9) and 75% iso-butyraldehyde (Figure 10).

Isomerization of cyclopropanol to propionaldehyde

Effect of solvents In a typical experiment 0.5 ml. samples of 0.5 M cyclopropanol in carbon tetrachloride were sealed in 2 ml. glass vials (initially the vials were treated according to the method described by Mahoney,[37]

[37]Mahoney, L. R., The Hydrolysis of Cyclopropyl Acetate. Unpublished Ph. D. Thesis, Ames, Iowa, Library, Iowa State University of Science and Technology, 1960, pp. 78.

however, control experiments (Table 10) indicated that this was not necessary) and placed in a constant temperature bath at 80°. Samples were withdrawn at various time intervals and cooled in a dry ice-acetone bath. The progress of the reaction was followed by the disappearance of the cyclopropanol peak on the GPC at 50° using a 1 meter X 6 mm 1:3 Ucon LB550X on 60/80 mesh firebrick column. A micro-dipper attachment for the GPC was used so that a sample of constant volume could be injected into the instrument. Fifty μl. was found to be a convenient sample size. The solvents used in this study were cyclohexane (spectral grade), benzene (Mallinckrodt reagent grade), 1,2-dichloroethane, methylene chloride, chloroform (Baker reagent grade), carbon tetrachloride (Mallinckrodt reagent grade was purified initially by the procedure of Gunther, et al.,[38] however, control experiments (Table 10) indicated that this was not necessary) and triethylamine.

Effect of oxygen Samples were prepared and analyzed in the manner described above with the exception that the vials were sealed under an atmosphere of oxygen or nitrogen instead of air. Carbon tetrachloride was the only solvent used in this study. Before use, the carbon tetrachloride was degassed by bubbling nitrogen through it for several minutes.

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[38]Gunther, P., van der Horst, H. D. and Cronheim, G., Z. Elektrochem., 34, 616 (1928).

Effect of additives Samples were prepared and analyzed in the manner described above with the exception that for the most part the vials were sealed under an atmosphere of nitrogen. The additive was added to the vial before it was sealed. The additives used in this study were free radical initiators, free radical inhibitors, acids and bases. Carbon tetrachloride and benzene were the only solvents used in this study. They were degassed in the manner described above before use.

Isomerization of 1-methylcyclopropanol to methyl ethyl ketone

1-Methylcyclopropanol was subjected to the same studies described for the isomerization of cyclopropanol to propionaldehyde. The progress of the reaction was also followed by the disappearance of the 1-methylcyclopropanol peak on the GPC as described above for the isomerization of cyclopropanol to propionaldehyde.

Cyclopropyl acetate in carbon tetrachloride heated to 80°

In a typical experiment 0.5 ml. samples of 0.5 M cyclopropyl acetate in carbon tetrachloride were sealed in 2 ml. glass vials and placed in a constant temperature bath at 80°. Samples were withdrawn at various time intervals and cooled in a dry-ice acetone bath. The progress of the reaction was followed by the disappearance of the cyclopropyl acetate peak on the GPC as described above for the isomerization of

cyclopropanol to propionaldehyde.

Methyl cyclopropyl ketone in carbon tetrachloride heated to 80°

Samples were prepared in the manner previously described for cyclopropyl acetate. The progress of the reaction was followed by the disappearance of the methyl cyclopropyl ketone peak on the GPC as described above for the isomerization of cyclopropanol to propionaldehyde.

Table 10. Miscellaneous reactions in carbon tetrachloride at 80°

Solution	Atmosphere[b]	Percent component remaining[a]					
		Blank	1/2 hr.	1 hr.	2 hr.	4 hr.	12 hr.
0.5 M Cyclopropanol[c]	Air	100	--	10	--	--	--
" " [d]	Air	100	--	9	--	--	--
" " [e]	Air	100	40	15	6	--	--
" " [f]	Air	100	38	16	5	--	--
" " [g]	Nitrogen	100	90	80	52	--	--
" " [h]	Nitrogen	100	92	82	73	--	--
0.5 M Cyclopropyl acetate	Air	100	--	97	98	96	--
0.5 M Methyl ethyl ketone	Air	100	--	100	100	100	--
0.5 M Cyclopropyl acetate[i]	Air	100	--	--	--	--	100
0.5 M Methyl ethyl ketone[i]	Air	100	--	--	--	--	96

[a]This was determined by measuring the area of the component peak on the GPC with a planimeter. An average of three or four trials is given.

[b]Refers to the atmosphere under which the vial was sealed before heating.

[c]The vial which was used for this reaction was cleaned according to the procedure of Mahoney.[37]

[d]The vial which was used for this reaction was not cleaned before use.

[e]The carbon tetrachloride was purified[38] before use.

[f]The carbon tetrachloride was not purified before use.

[g]The solution was made from carbon tetrachloride which had been heated at 80° for two hours in the presence of air.

[h]The carbon tetrachloride was not treated in any way before use.

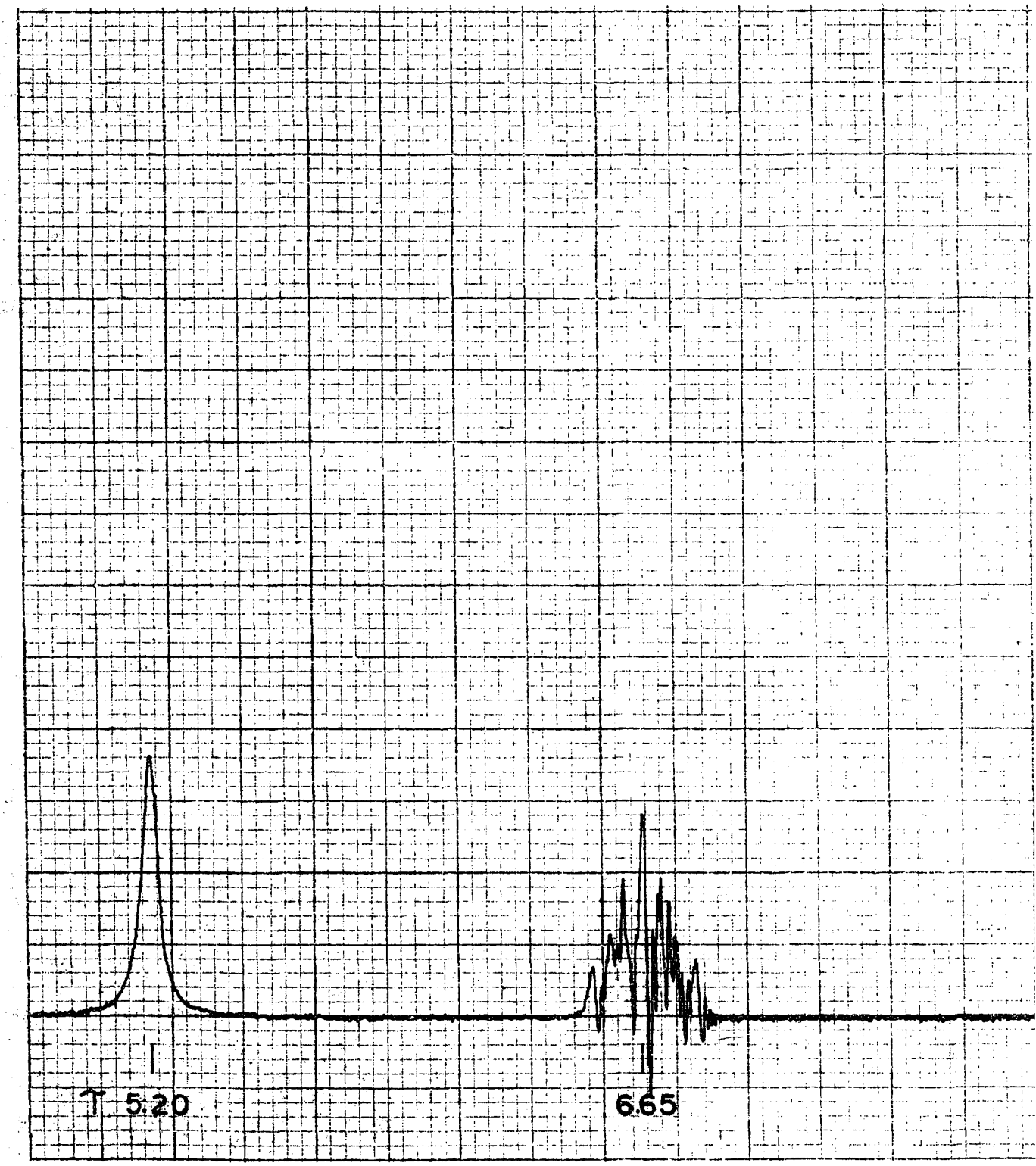
[i]The solution is also 0.25 M in propionaldehyde and contains five milligrams of benzoyl peroxide.

SPECTRA

The nuclear magnetic resonance spectra were recorded on a Varian Model HR-60 high-resolution n.m.r. spectrometer.

Chemical shifts were measured with respect to tetramethylsilane as an internal reference using side-bands applied by a calibrated audio oscillator.

Figure 1. NMR spectrum of cyclopropanol


T 5.20
6.65

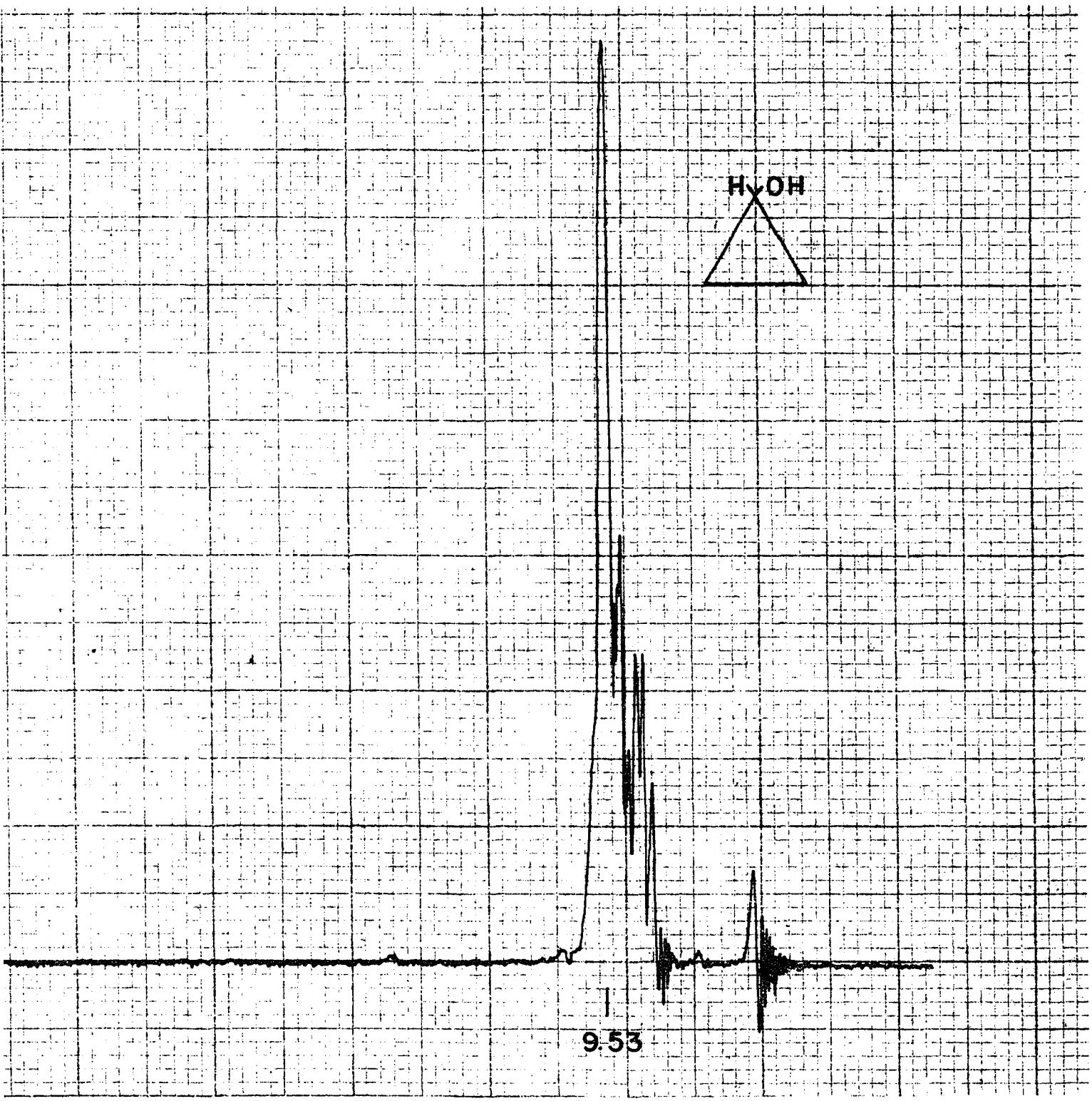
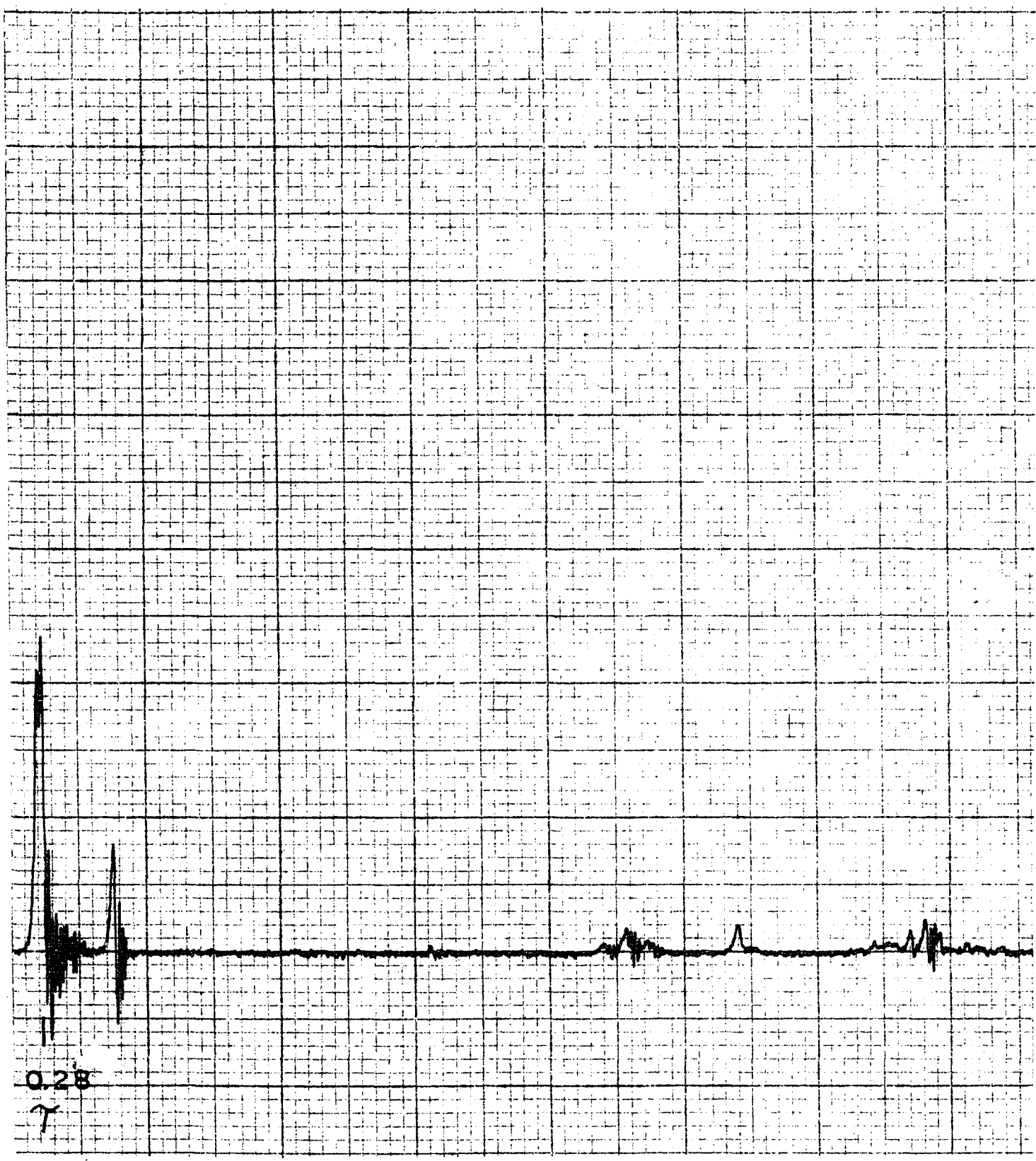

H
OH
9.53

Figure 2. NMR spectrum of the isomerization product from cyclopropanol


0.2 s
T

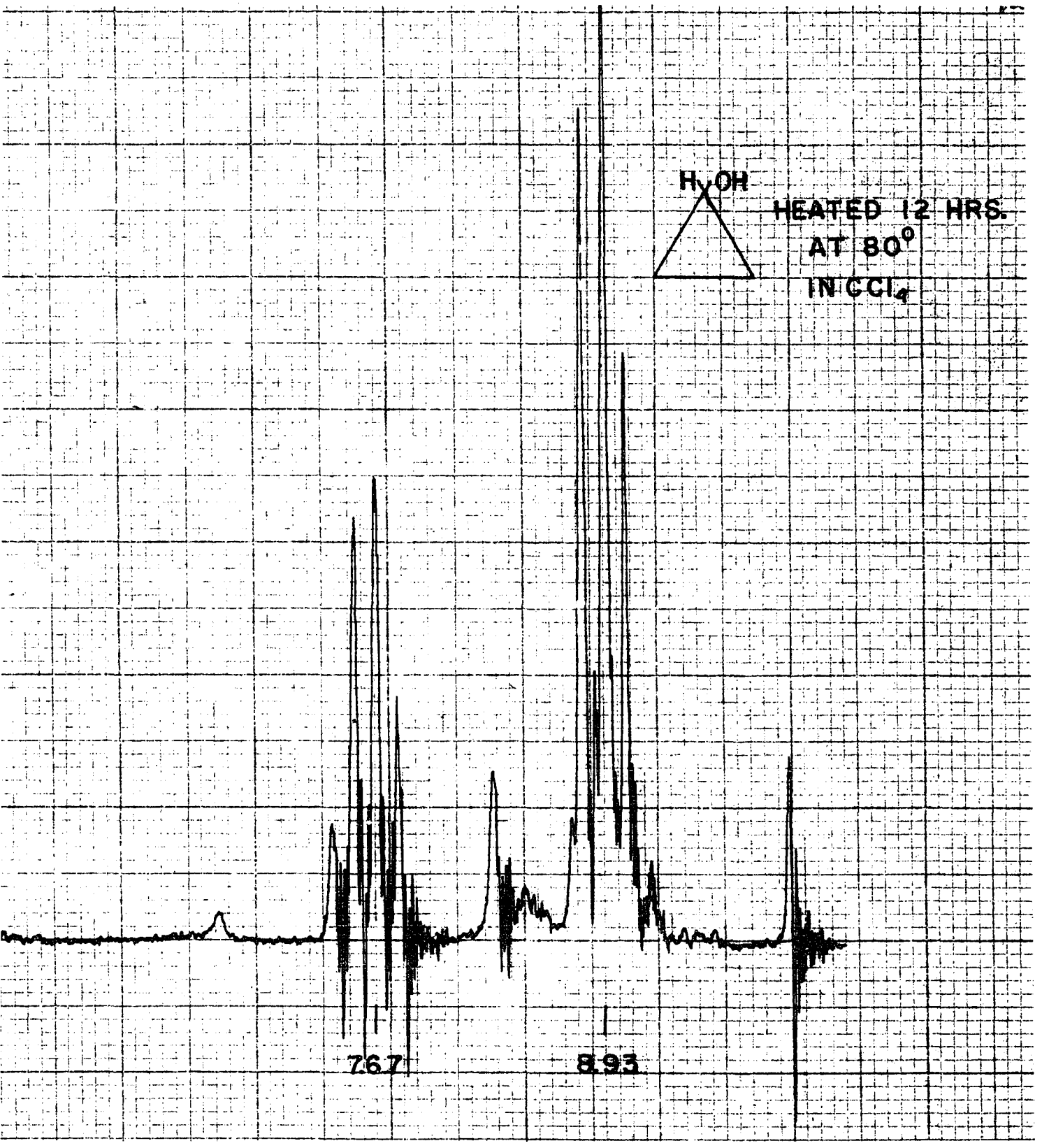
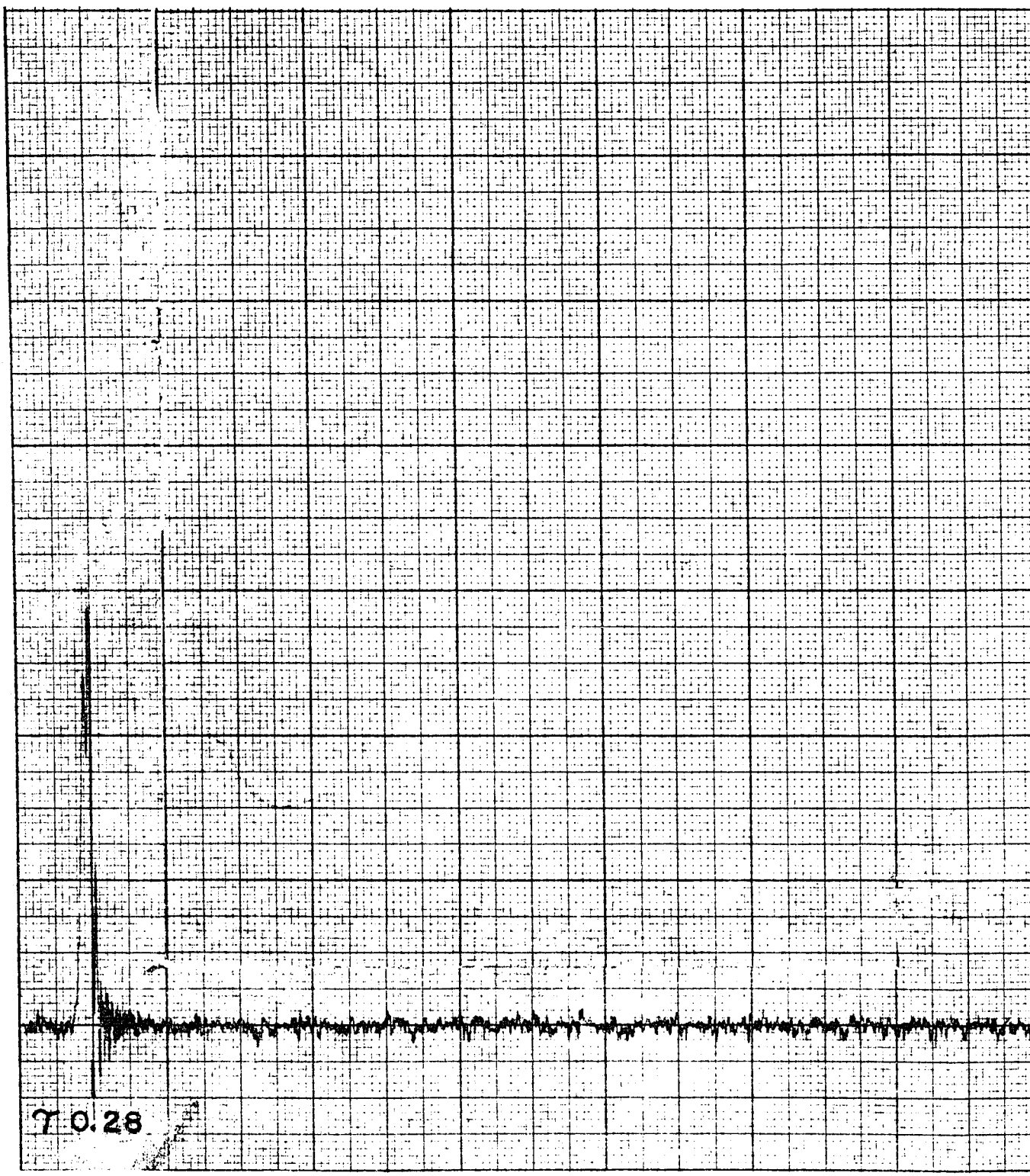

H
OH
HEATED 12 HRS.
AT 80°
IN CCl4
7.67
8.93

Figure 3. NMR spectrum of propionaldehyde


τ 0.28

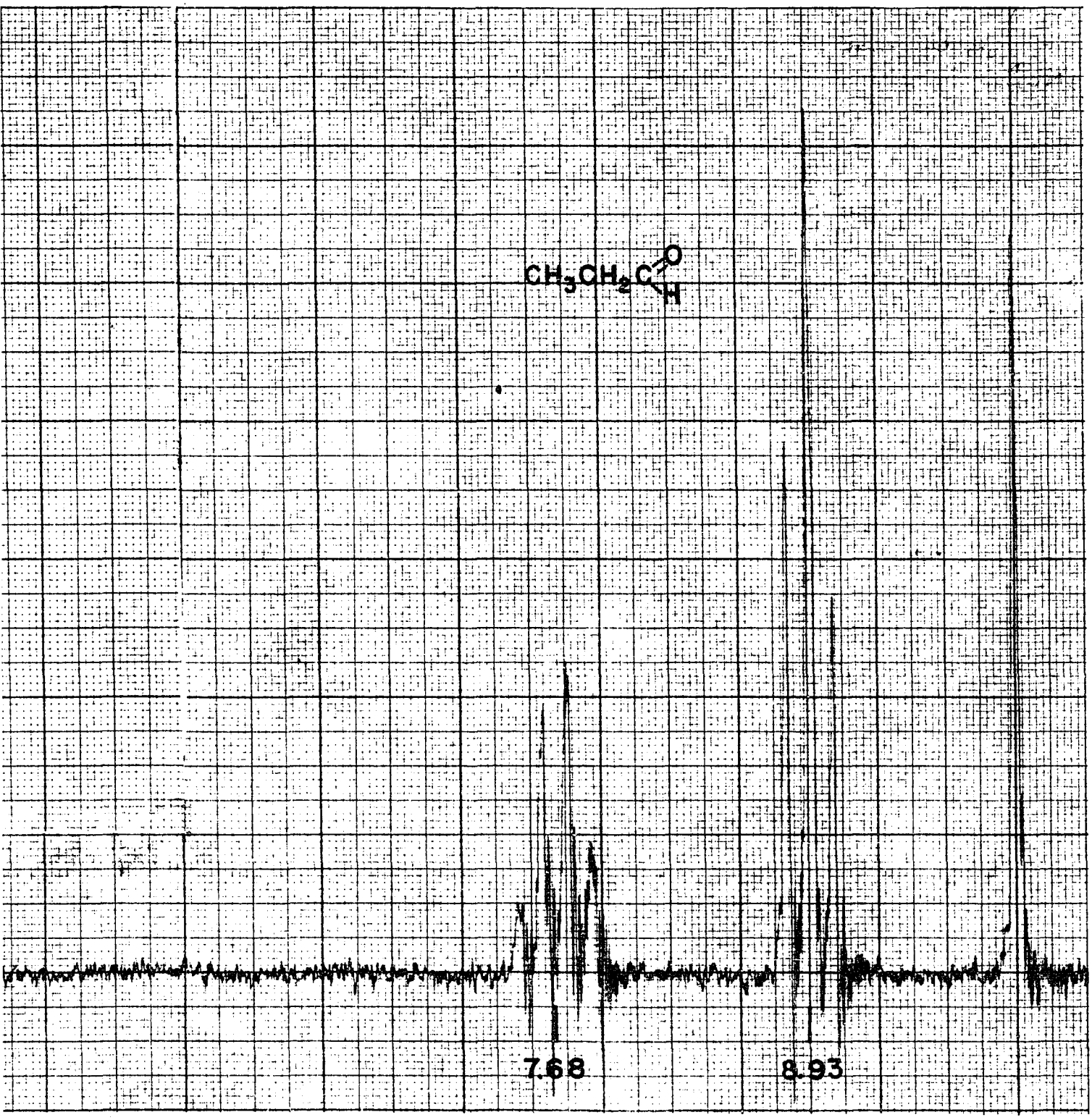
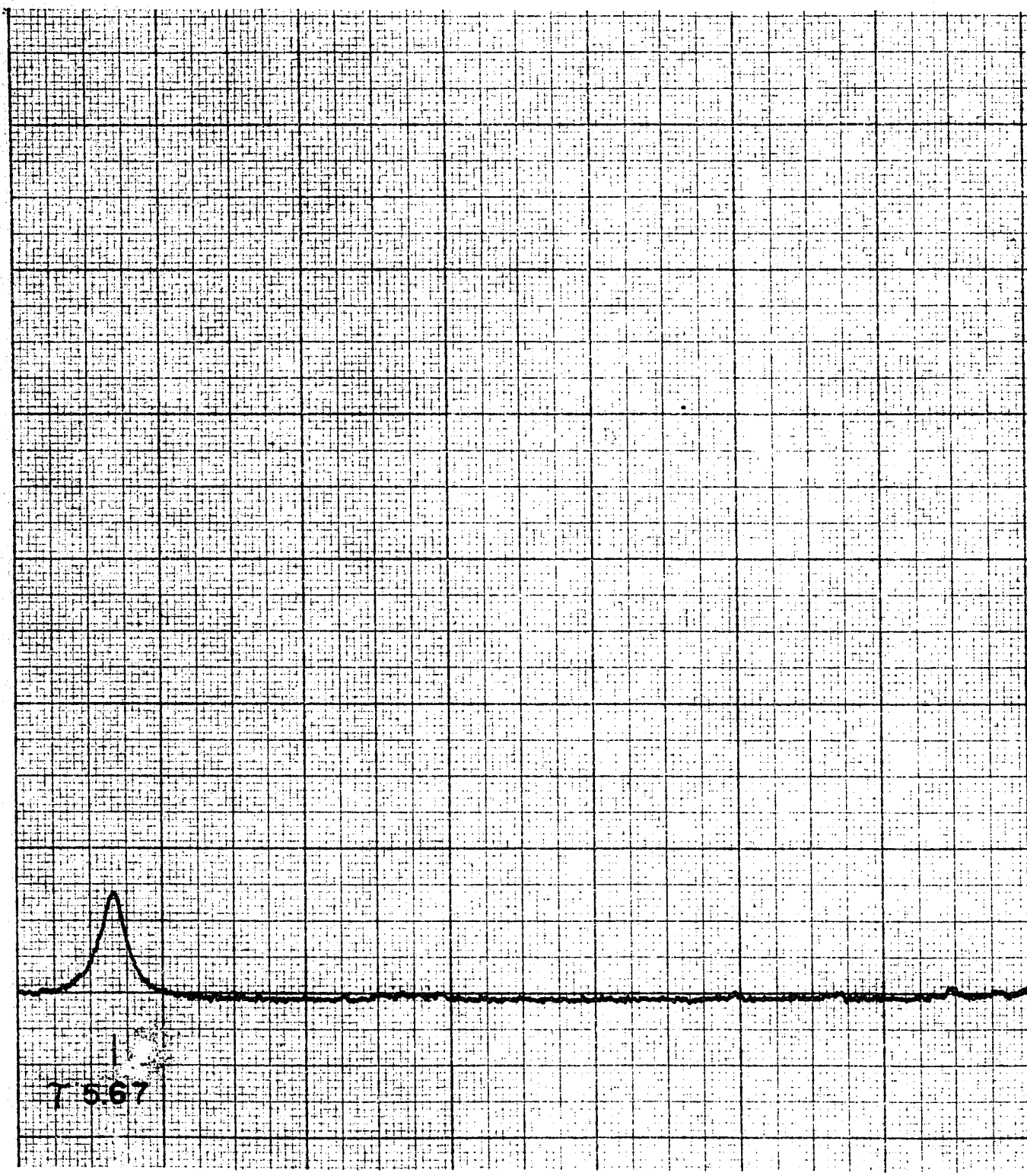

CH3CH2C
O
H
7.68
8.93

Figure 4. NMR spectrum of 1-methylcyclopropanol


T 5.67

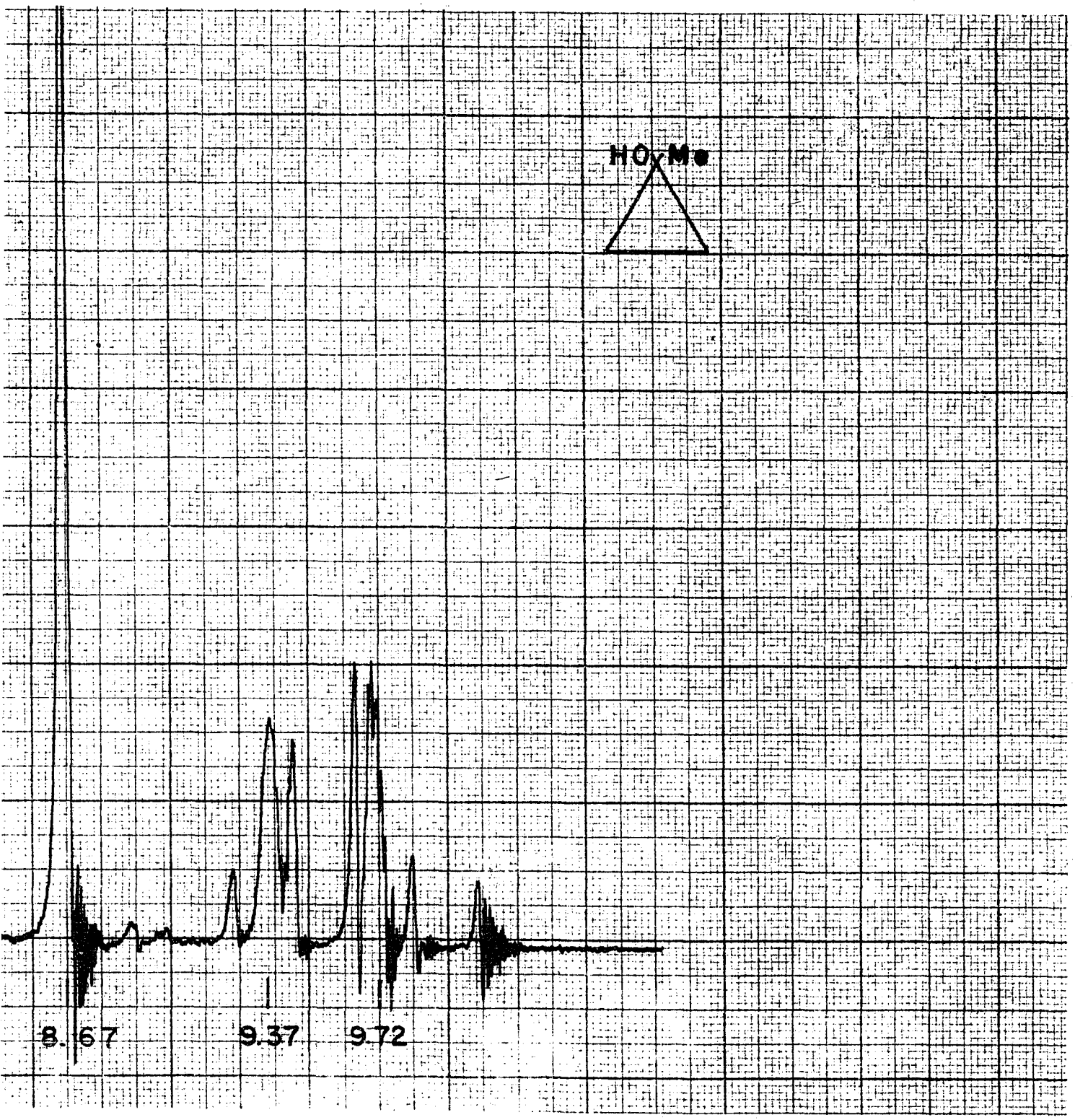
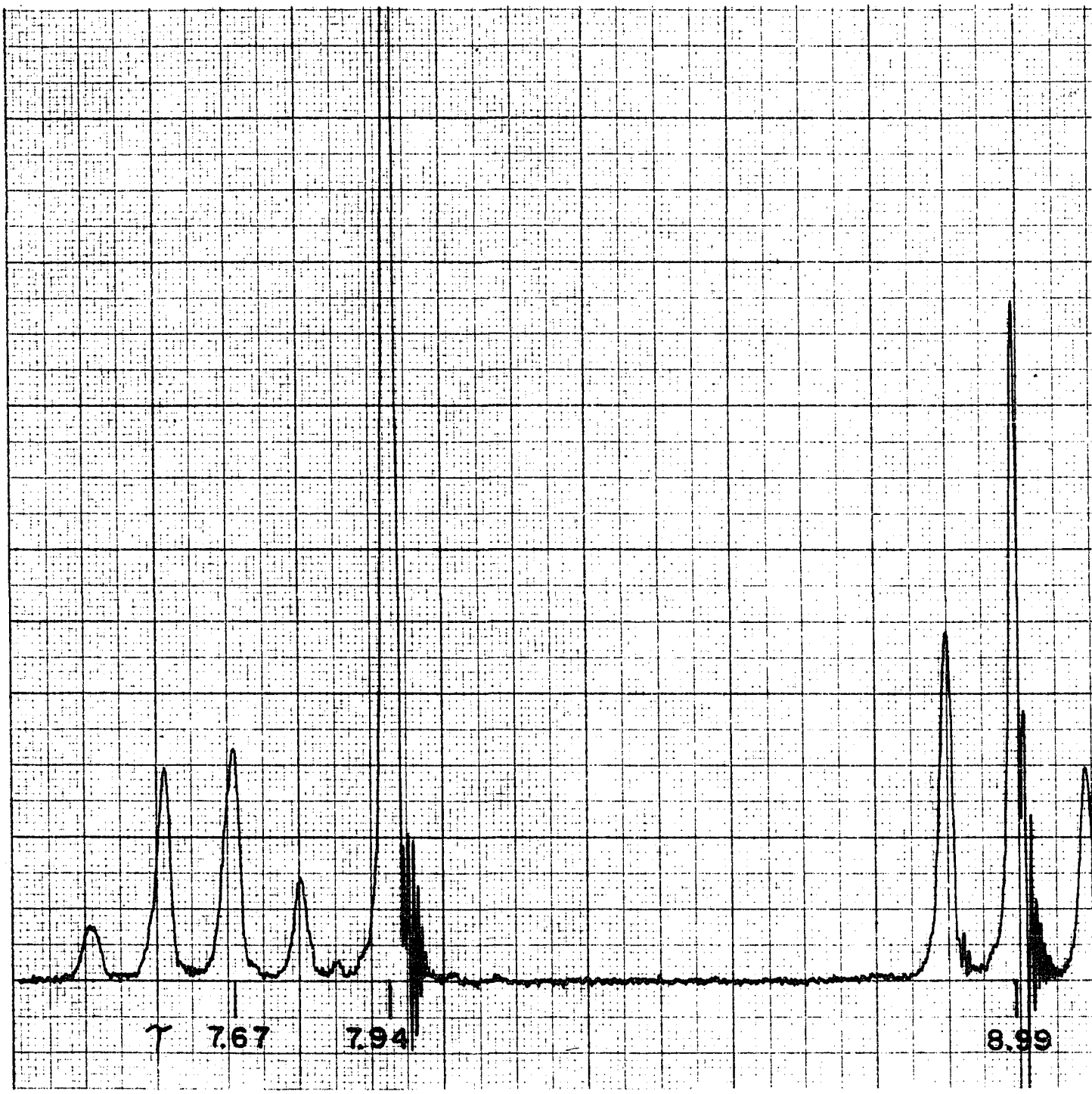

HO
Me
8.67
9.37
9.72

Figure 5. NMR spectrum of the isomerization product from 1-methylcyclopropanol


τ
7.67
7.94
8.99

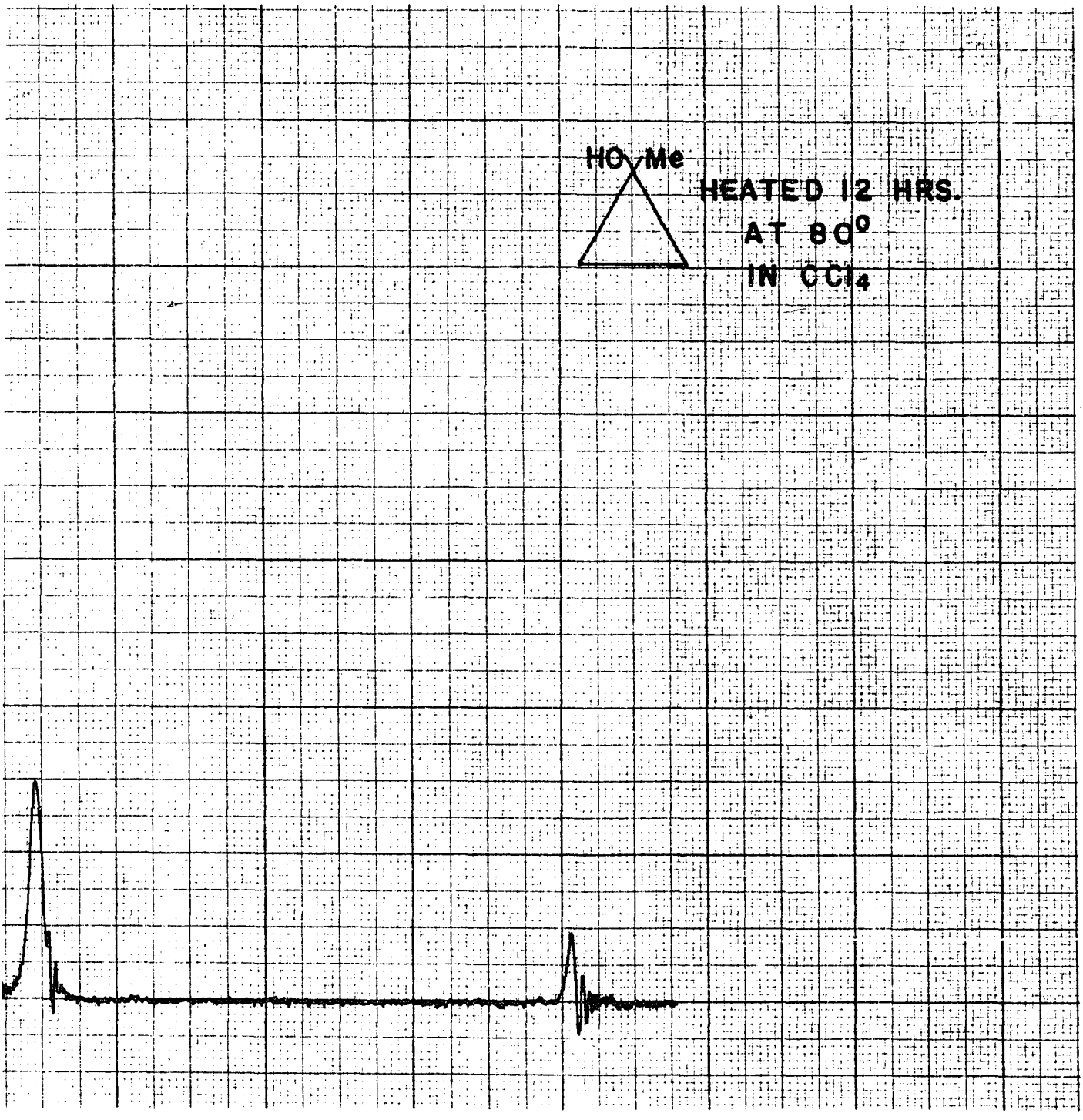
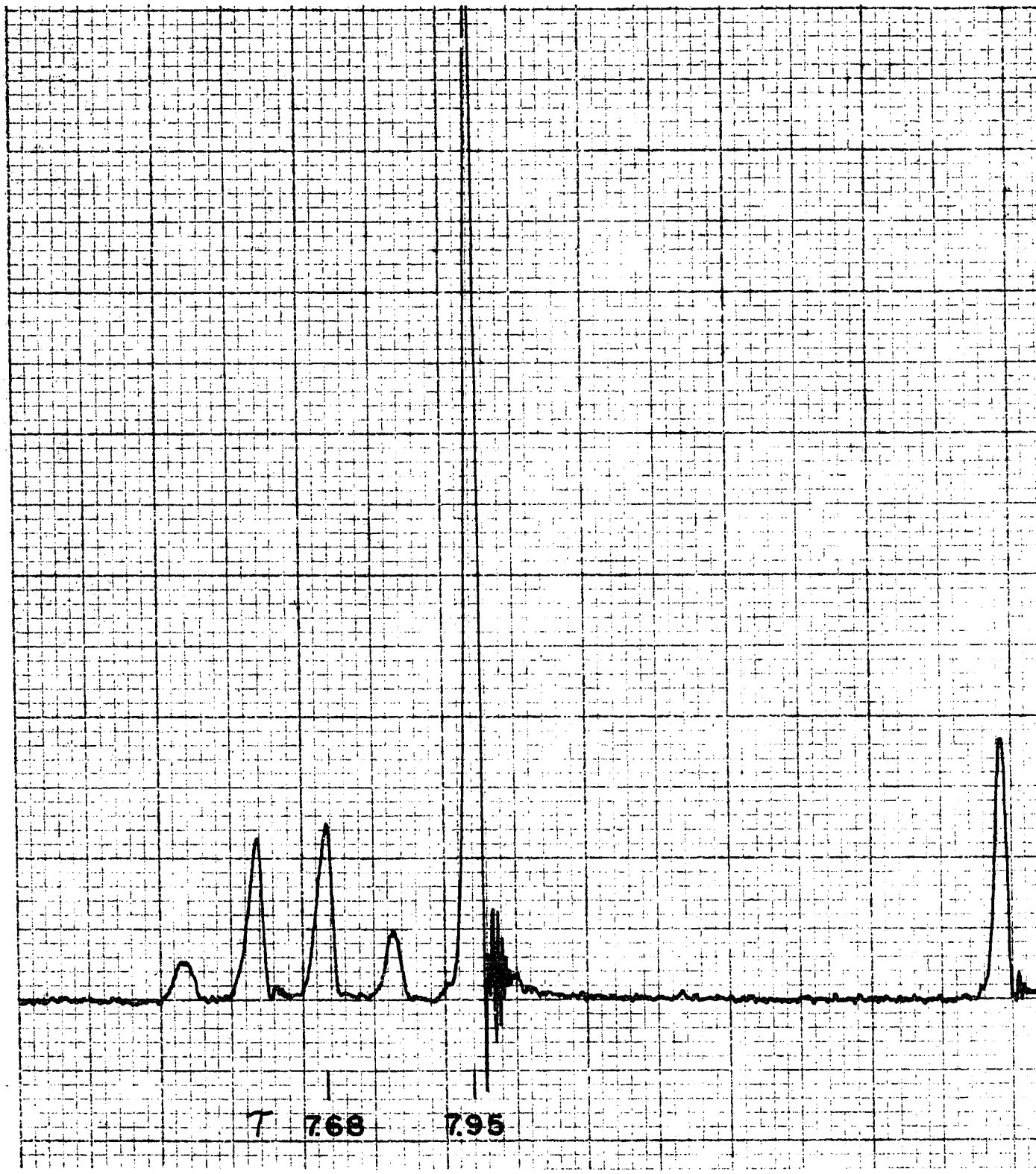

HO
Me
HEATED 12 HRS.
AT 80°
IN CCl4

Figure 6. NMR spectrum of methyl ethyl ketone


T
7.68
7.95

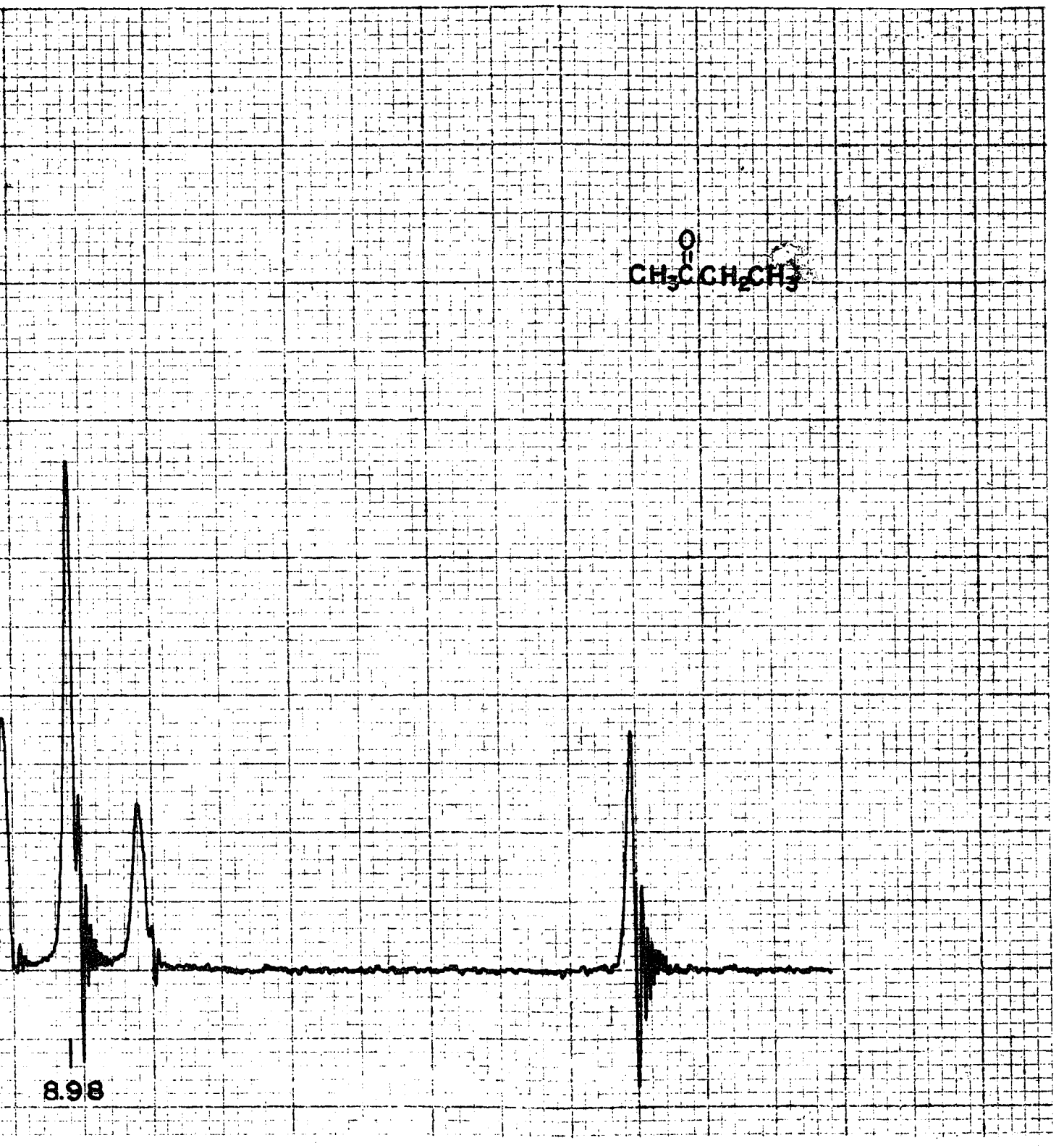
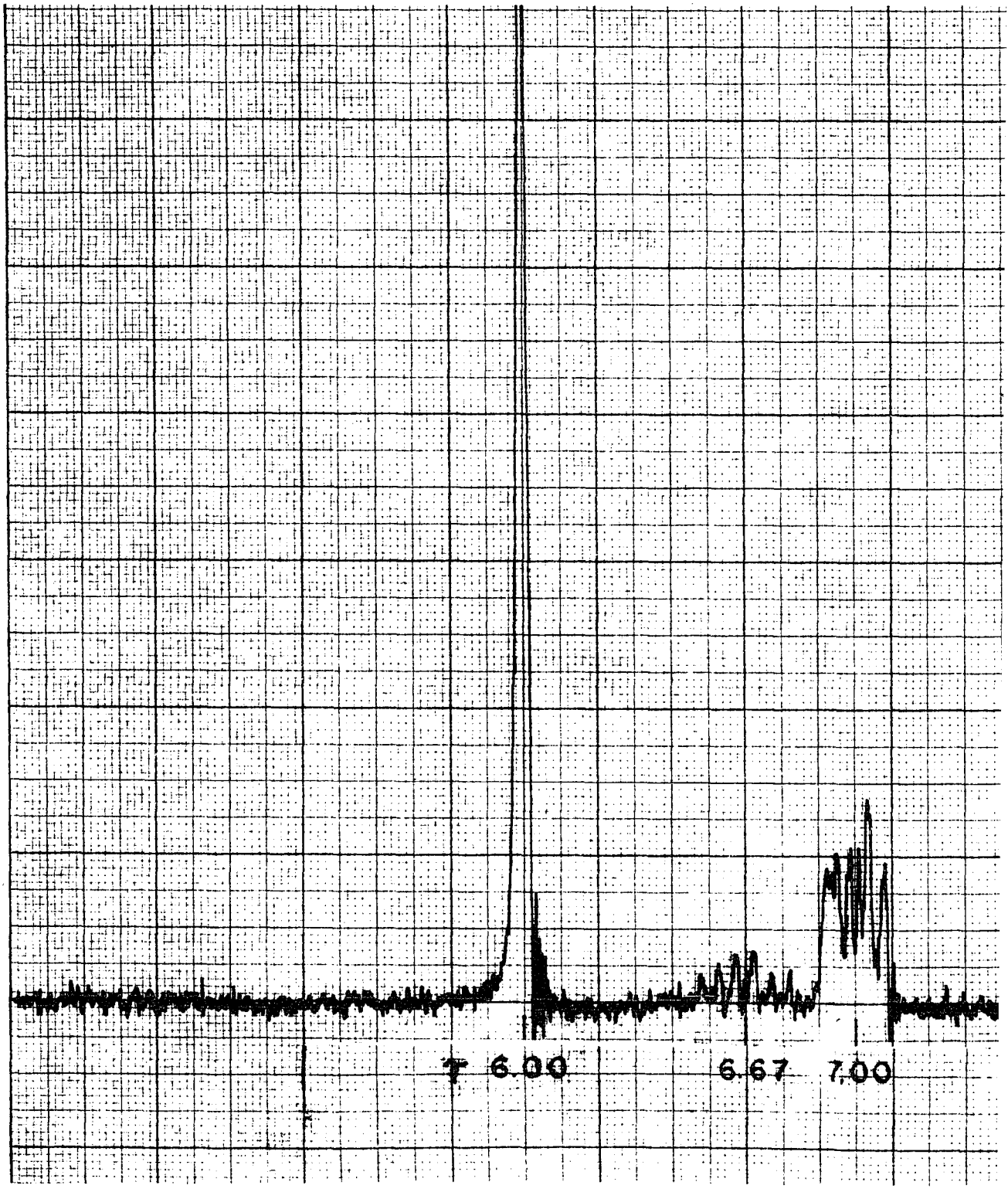

O
CH3CCH2CH3
8.98

Figure 7. NMR spectrum of 2-methylcyclopropanol


T 6.00
6.67
7.00

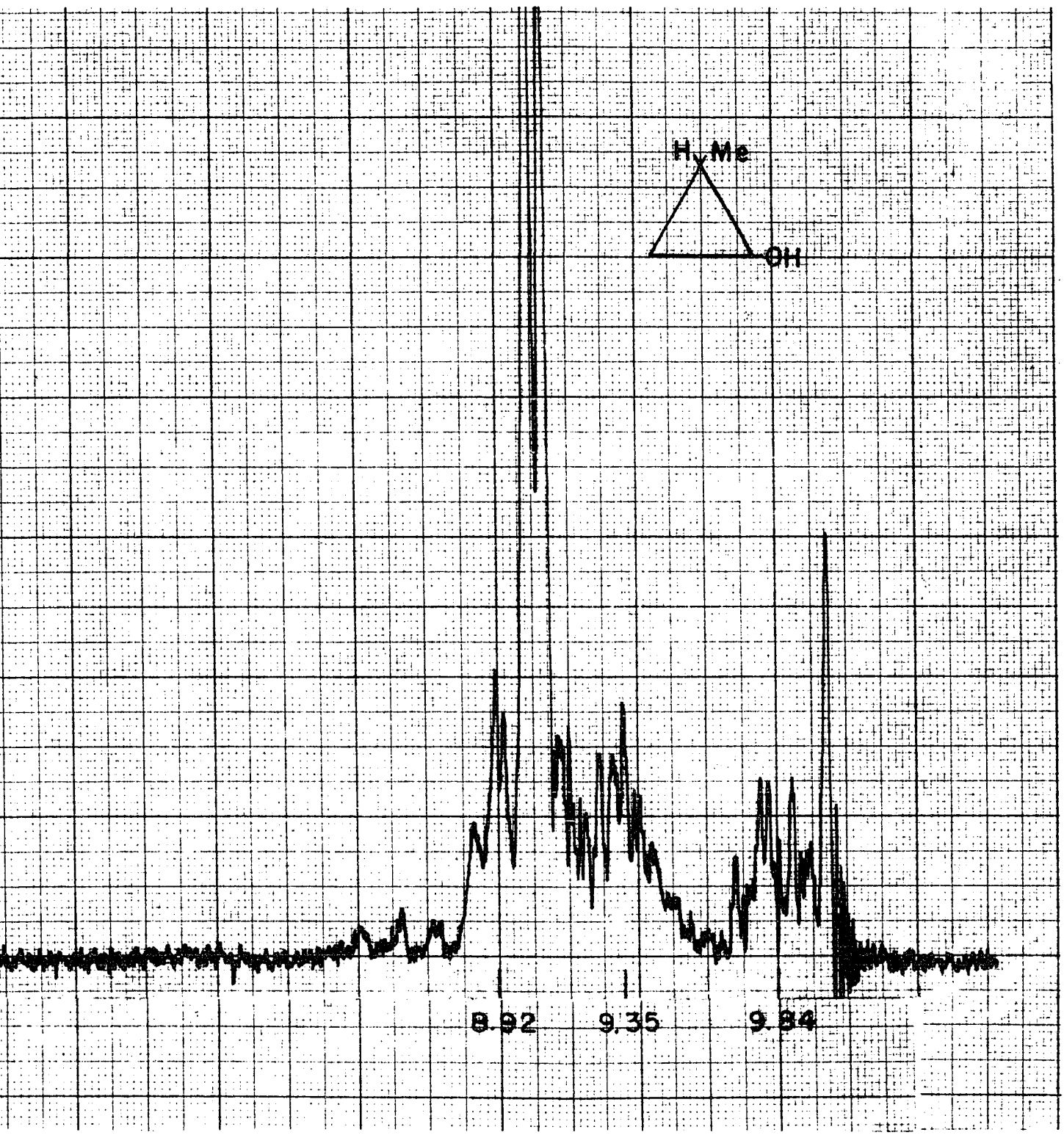
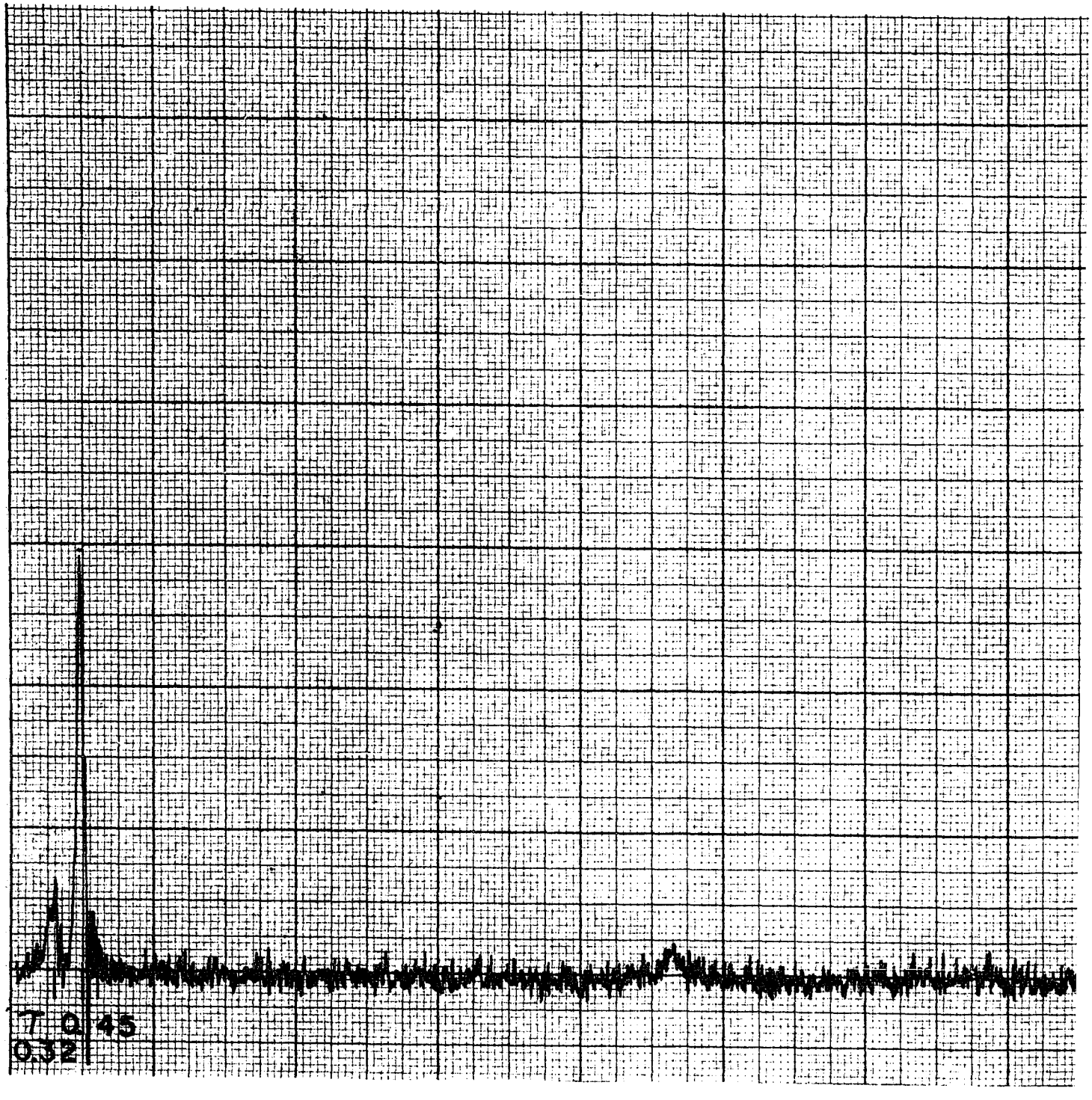

H
Me
OH
8.92
9.35
9.84

Figure 8. NMR spectrum of the isomerization product from 2-methylcyclopropanol


7 0 45
0.32

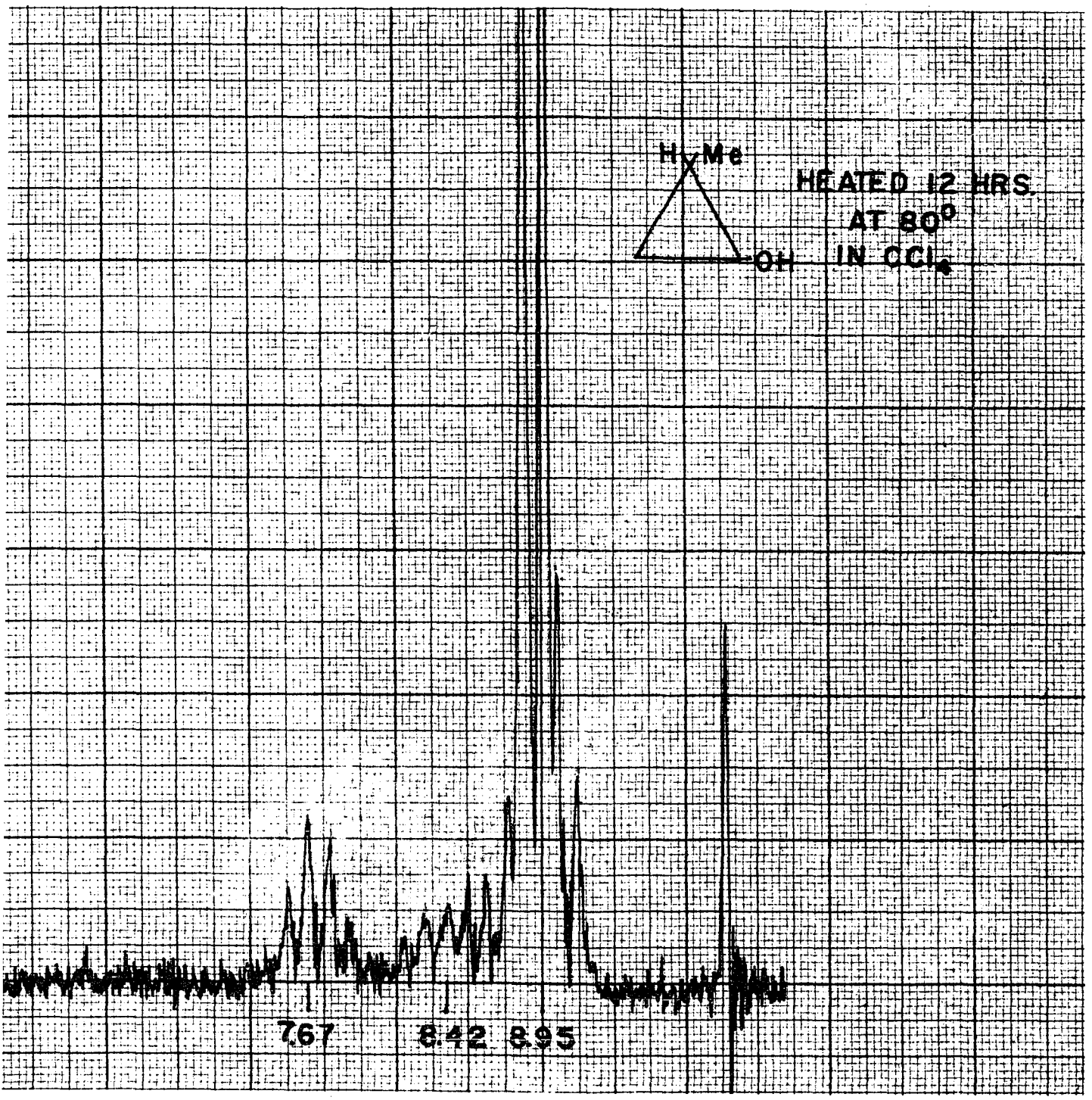
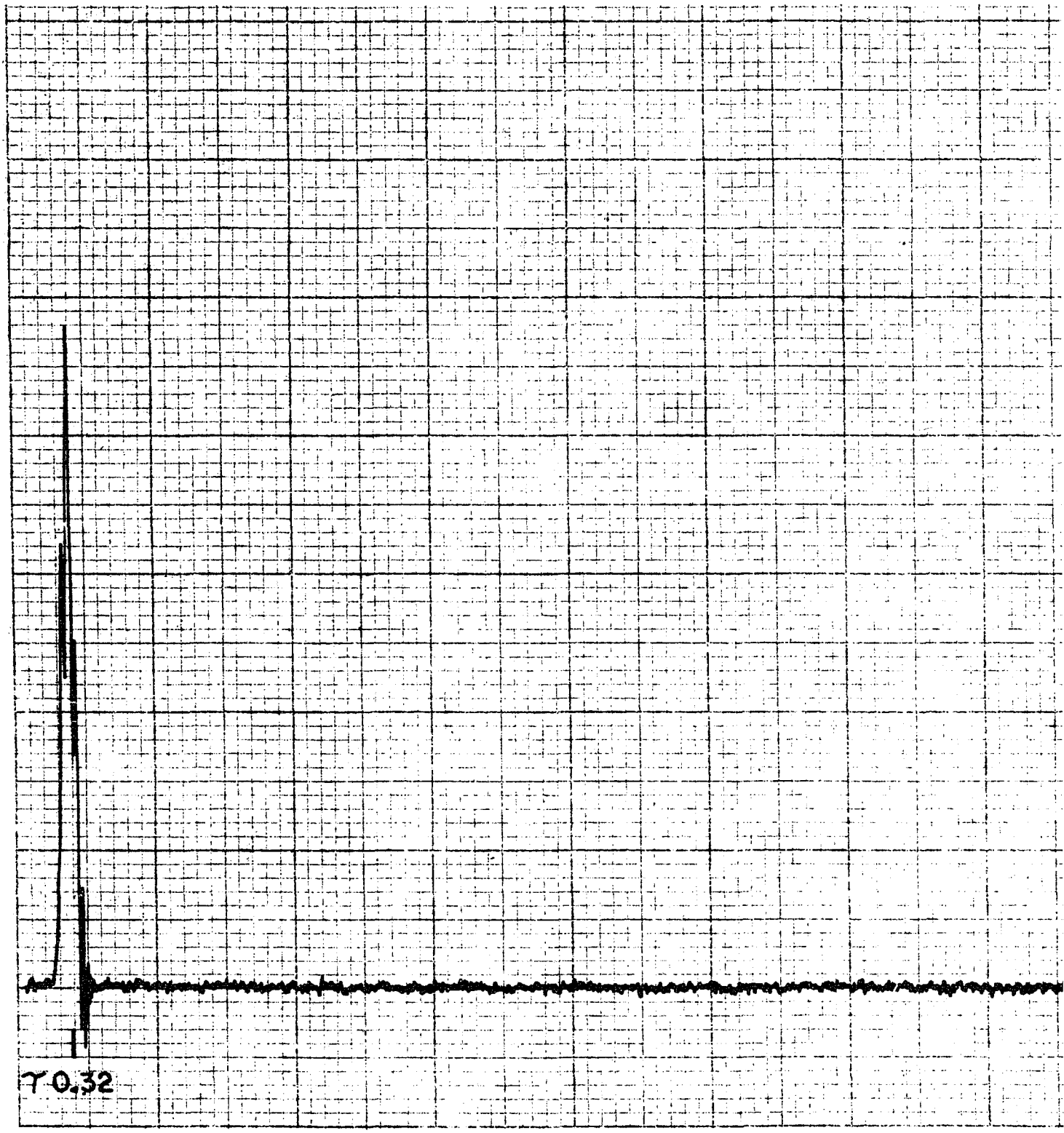

H
Me
OH
HEATED 12 HRS.
AT 80°
IN CCl4
7.67
8.42
8.95

Figure 9. NMR spectrum of butyraldehyde


T 0.32

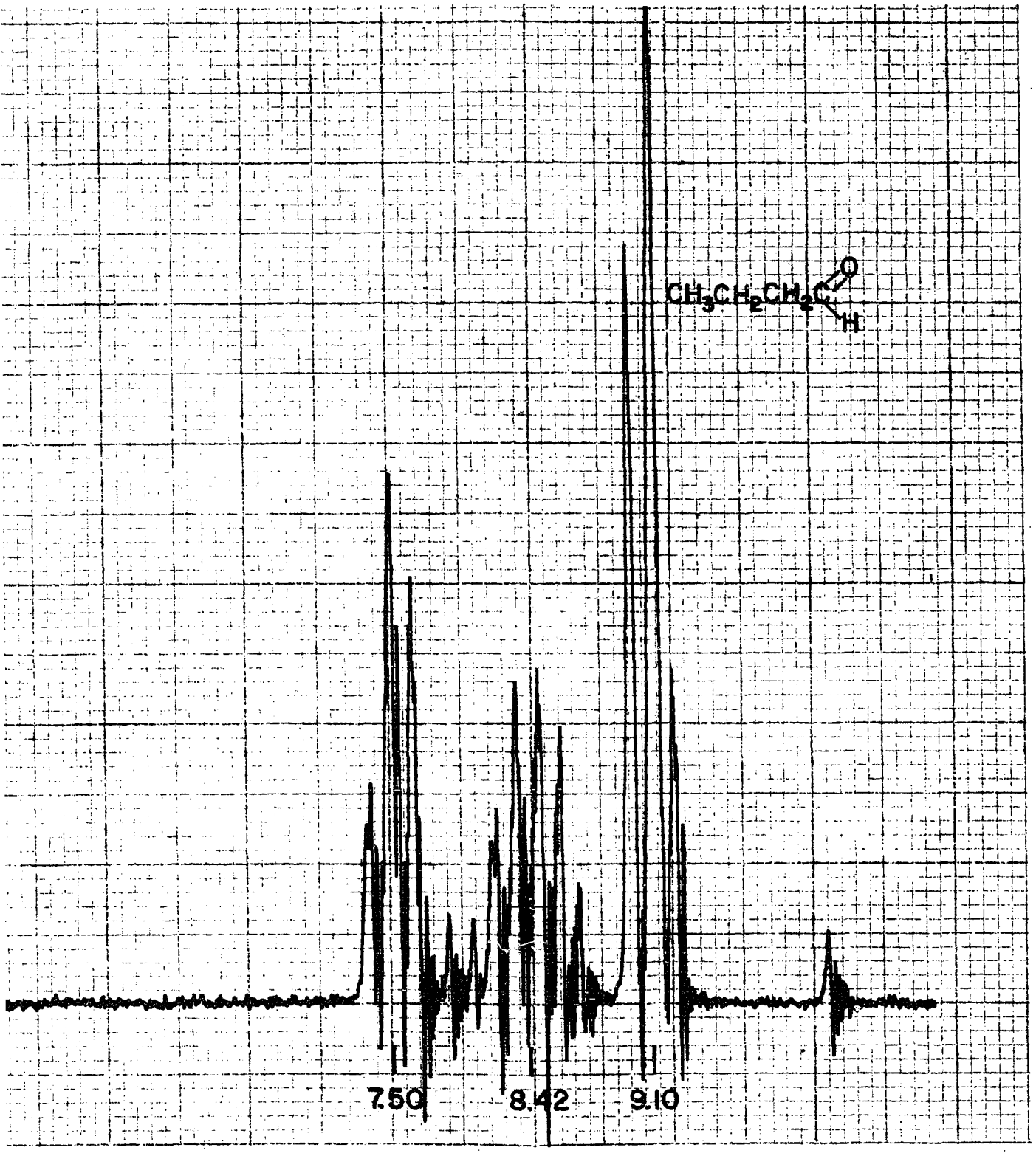
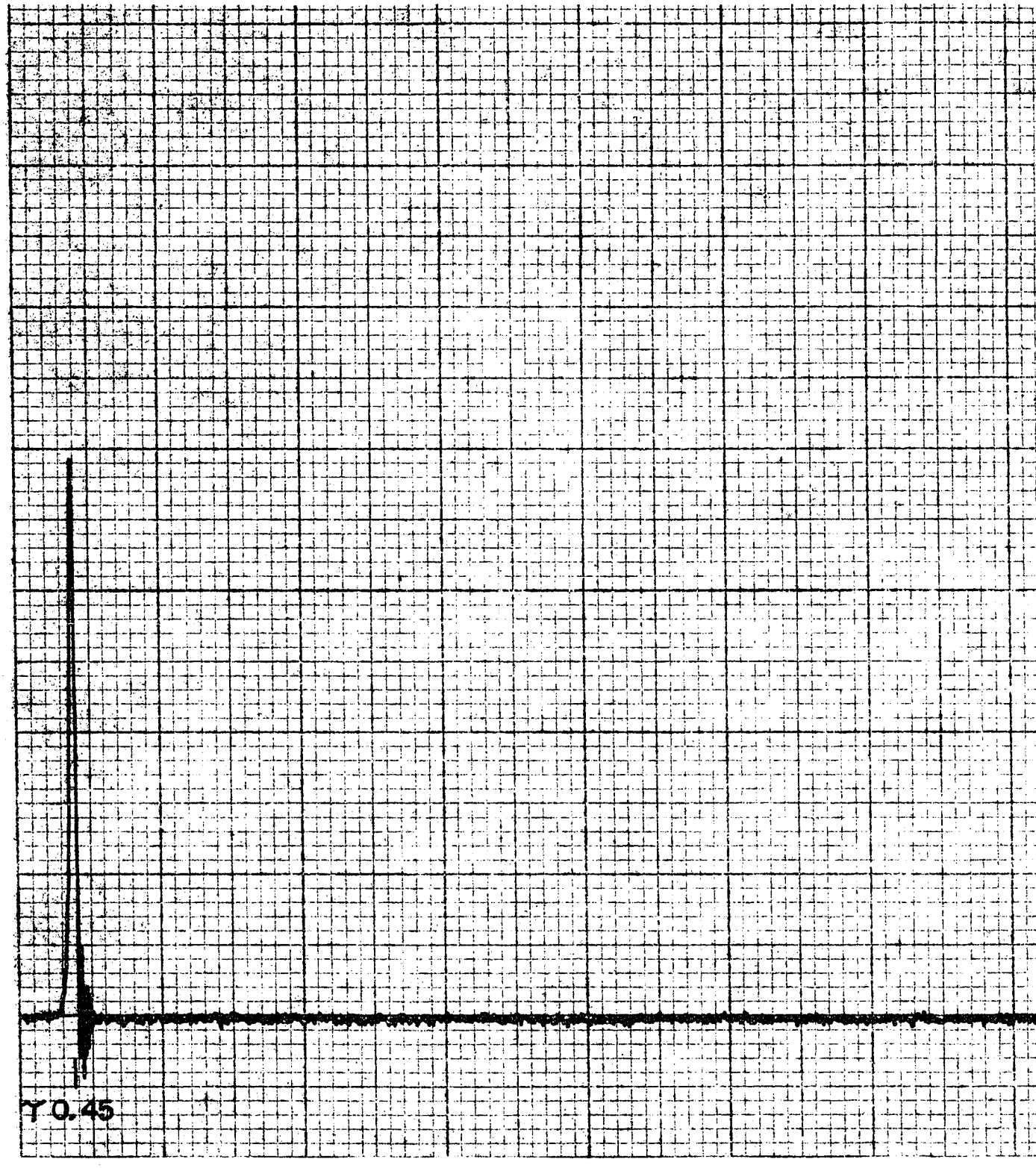
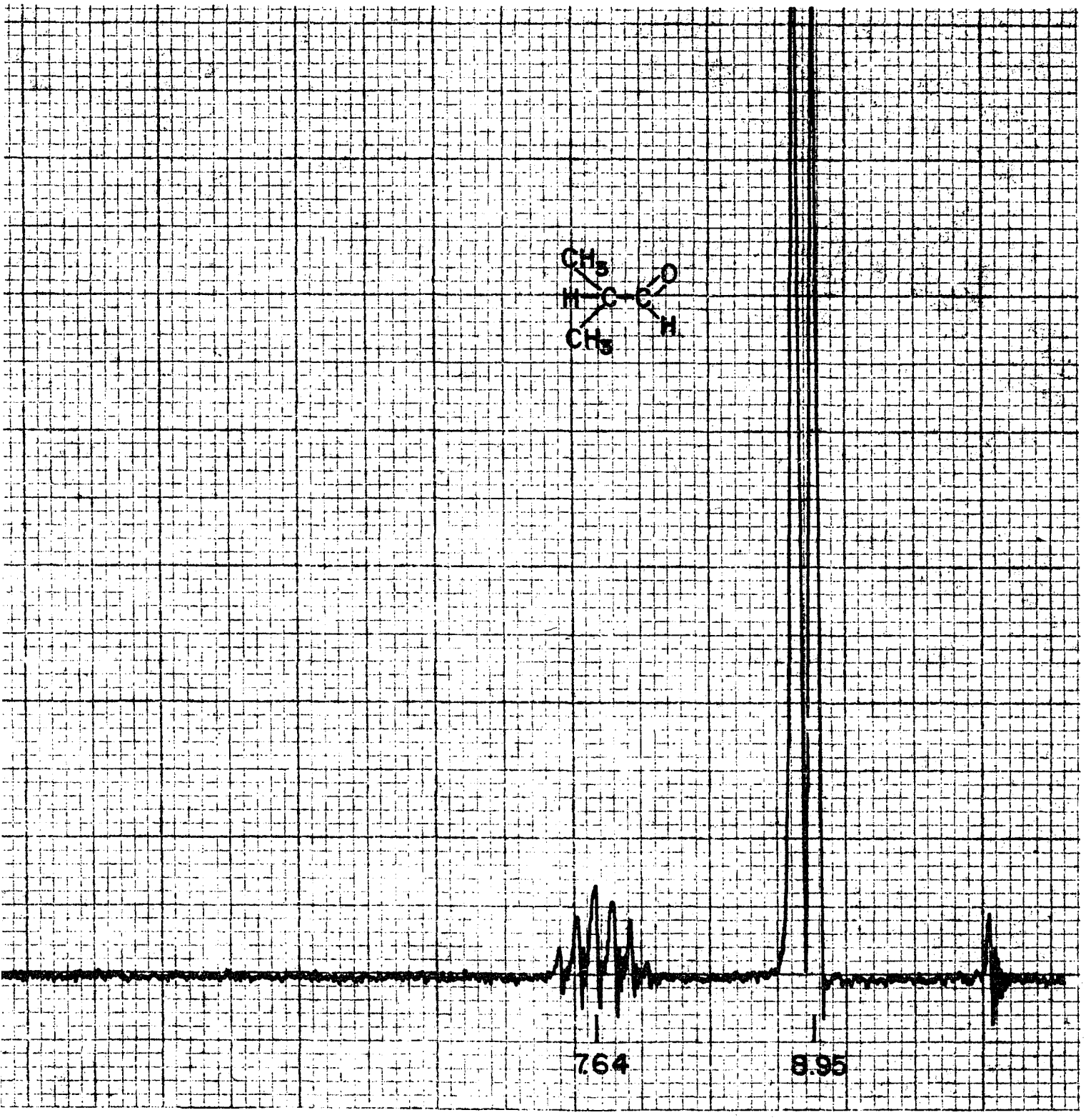

CH3CH2CH2C
O
H
7.50
8.42
9.10

Figure 10. NMR spectrum of iso-butyraldehyde


T 0.45


CH3
H
C
C
O
H
CH3
7.64
8.95

SUMMARY

By an extension of a method previously reported in the literature, pure cyclopropanol has been prepared economically and in sizable quantities for the first time. This method was extended to the preparation of pure 1-methylcyclopropanol and 2-methylcyclopropanol. Crude 1-phenylcyclopropanol and 2-phenylcyclopropanol could also be prepared by this method, but attempts to separate them from their isomerization products have thus far proved unsuccessful.

Nuclear magnetic resonance studies have shown that cyclopropanol and 1-methylcyclopropanol isomerize in carbon tetrachloride at 80° to give exclusively propionaldehyde and methyl ethyl ketone, respectively. Nuclear magnetic resonance studies have shown that 2-methylcyclopropanol isomerizes under the same conditions to give a mixture of 25% butyraldehyde and 75% iso-butyraldehyde.

A detailed investigation into the isomerization of cyclopropanol to propionaldehyde was undertaken. The isomerization was found to be quite solvent dependent, occurring only in carbon tetrachloride and chloroform to any extent. Most of the evidence obtained during this investigation indicate that the isomerization of cyclopropanol in carbon tetrachloride probably proceeds by the attack of an electrophilic species, probably a proton which was generated from the reaction of oxygen, carbon tetrachloride and

propionaldehyde or cyclopropanol, on the cyclopropane ring with simultaneous ring opening. An alternative mechanism involving free radical attack on the hydroxyl hydrogen of cyclopropanol followed by simultaneous ring opening seems unlikely.

The isomerization of 1-methylcyclopropanol to methyl ethyl ketone in carbon tetrachloride was investigated in some detail. In general, the isomerization was quite similar to the isomerization of cyclopropanol to propionaldehyde, the only observed difference being in the effect of oxygen. This difference could be attributed to the enhanced reactivity of 1-methylcyclopropanol toward electrophilic species.

ACKNOWLEDGMENTS

The author is deeply indebted to Dr. C. H. DePuy for his encouragement and guidance during the course of this investigation.

The author would also like to thank Dr. Jack W. Hausser for many helpful discussions and suggestions. Thanks are also extended to Dr. Roy W. King for the NMR spectra and for many helpful suggestions.

Finally, the author would like to thank his wife and parents for the encouragement and financial assistance which they have given and for the sacrifices which they have made so that all this could be possible.