"SOME 1,2,3-TRISUBSTITUTED CYCLOPENTANES"

A THESIS
SUBMITTED TO THE
FACULTY OF PURE AND APPLIED
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FULFILLMENT OF THE REQUIREMENTS
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PREFACE

Dr. Lemieux and coworkers have determined the coupling constants for protons on neighboring carbon atoms in six membered ring compounds. This led them to attempt to determine, if possible, the coupling constants between hydrogens in other orientations such as exist in five-membered ring compounds.

As a first step in this work it was decided to make 1,2,3-cyclopentanetriols since these would be the ultimate reference compounds in the configurational assignments. Also it was desirable to prepare some 1,2,3-trisubstituted cyclopentanes of known configuration with the signal for 2-hydrogen on the ring carbon sufficiently well separated in the spectrum to allow determination of its fine structure. Dimethoxy cyclopentane acetates in which the substituted hydrogens exist in a trans-trans and cis-trans relationship were considered worth trying for this work.

ACKNOWLEDGMENT

The author would like to express his deep appreciation and sincere gratitude to Dr. R. U. Lemieux for his guidance and constructive criticism throughout the course of this investigation.

The author also would like to acknowledge the financial assistance received from a grant from the National Research Council, Ottawa, to Dr. R. U. Lemieux.

This acknowledgment would be incomplete without mentioning the efforts of other faculty members, especially Dr. L. Westland, Miss Busk, and friends in creating a pleasant, cordial and enthusiastic environment and making his stay a profitable one.

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Abstract

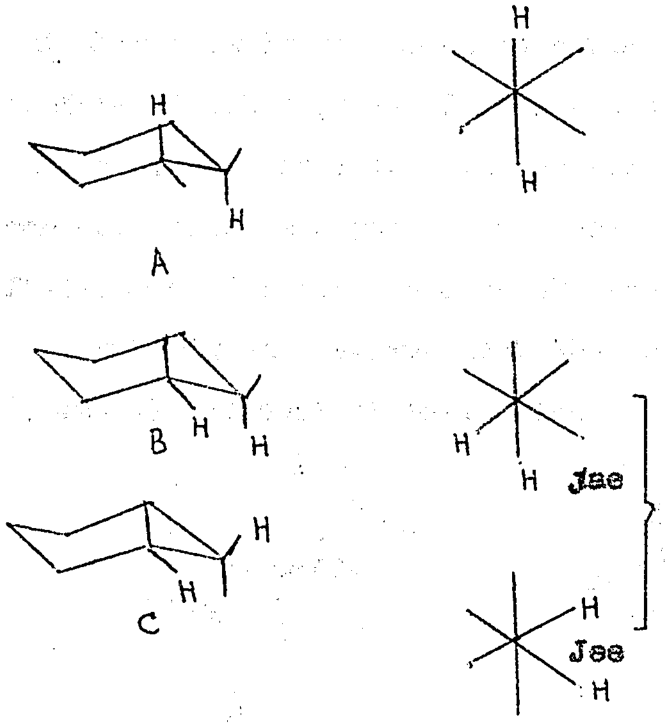
This thesis is concerned with the preparation of five membered ring compounds. Some 1,2,3-trisubstituted cyclopentanes were prepared in order to get information related to conformational analysis in the reactions of centres in five membered ring compounds.

3-Acetoxycyclopentene and 3-methoxycyclopentene were used as starting materials for the preparation of these compounds. Treatment of 3-acetoxycyclopentene and 3-methoxycyclopentene with perbenzoic acid gave the corresponding *trans*-oxides. The structure of these oxides were determined by chemical means. 1,2,3-Cyclopentanetriols obtained by way of wet and dry Prevost reactions of 3-acetoxycyclopentene and from the hydrolysis of *trans*-oxide of 3-acetoxycyclopentene were separated by partition chromatography using Celite to hold the static aqueous phase and n-butanol equilibrated with five percent boric acid solution as solvent system. Structures of 1α,2α,3β and 1α,2β,3α cyclopentanetriols were proved by chemical means and some solid derivatives of these compounds were prepared. The proton resonance spectra of 1α,3α-dimethoxy-2β-acetoxycyclopentane and 1α-p-nitrobenzoate-2β-bromo-3α-acetoxycyclopentane were taken. The reactions of above mentioned substances and other related five membered ring compounds are reported in the thesis.

INTRODUCTION

I. Conformations of cyclopentene and derivatives

Kullnig, Lemieux, Schneider, Bernstein and Moir (1,2) have determined the proton magnetic resonance spectra of a variety of six-membered ring compounds. As a result of this work, they were able to conclude that the magnetic moments of the nuclei of two hydrogens situated on neighboring carbons in a six-membered ring are about three times more strongly coupled when both the hydrogens are in axial orientations than when one or both the hydrogens are in equatorial orientations.

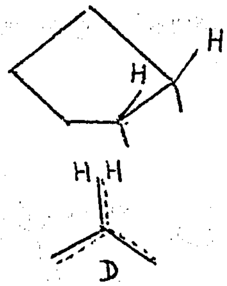


Staggered structure
Jaa 7-9 c.p.s.

Skew or Gauche structure

2 - 3 c.p.s.

It was now of interest to determine, if possible, the coupling constants between hydrogens in other orientations such as exist in five-membered ring compounds.



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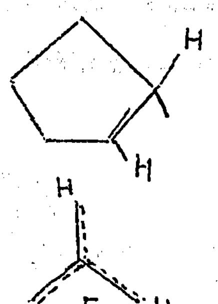
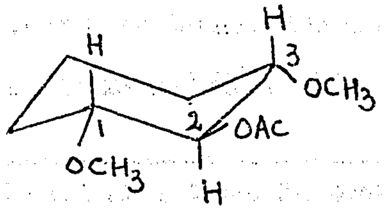


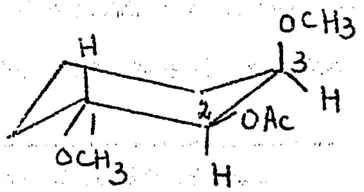
E

In order to obtain this information it was necessary to prepare cyclopentane derivatives of known configuration with the signal for at least one of the hydrogens on the ring carbon sufficiently well separated in the spectrum to allow determination of its fine structure. Also, the cyclopentane derivative should have the ring, if possible, suitably substituted so as to render the molecule highly conformationally pure. It was anticipated that in the course of such an investigation new information related to conformational analysis in the reactions of centres in five-membered rings would be obtained.

Kullnig and Lemieux used the following compounds (I and II) in part of their work.

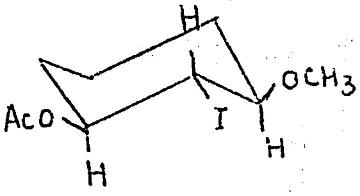


I



II

Thus, in each case, the signal for the 2-hydrogen was well separated from the signal for the other hydrogens and had the structures expected on the basis of the above mentioned coupling constants. Kavadias and Lemieux (3) have had similar experience with the following compounds (III-V).



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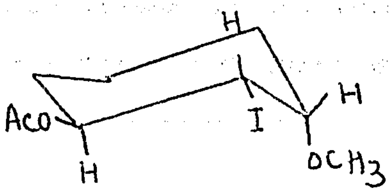

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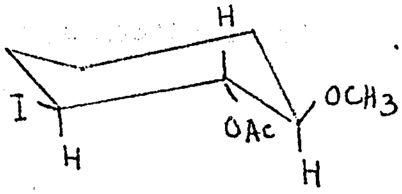
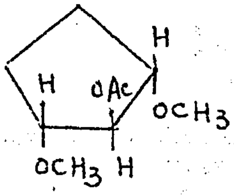
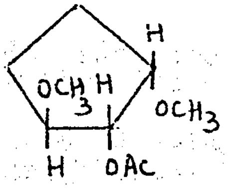


V

The line of research followed was, therefore, to prepare the compounds (VI and VII) and to establish their structure and configurations by unequivocal chemical means and to examine their NMR* spectra.



VI



VII

Karplus (4) has presented quantum mechanical calculations which assign coupling constants for neighboring hydrogens as the dihedral angle defined by these hydrogens varies from 0-180°. His treatment is based on the

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* abbreviated from Nuclear Magnetic Resonance.

assumption that the carbon hybrid orbitals are tetrahedral (sp^3), and the carbon-carbon bond is 1.543 Å and that the electron-orbital and electron-dipole interactions do not contribute significantly to the magnitude of the coupling constant. Jardetzky (5) has presented the results of Karplus's calculations in the form of the plot shown in Fig. 1. This information which was not available at

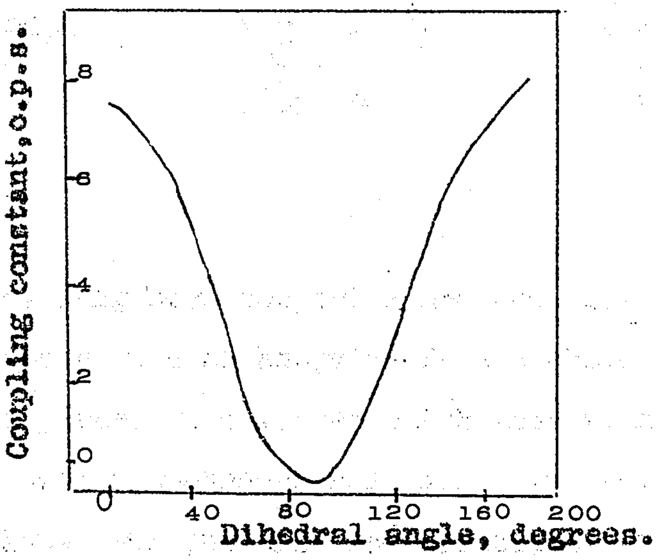
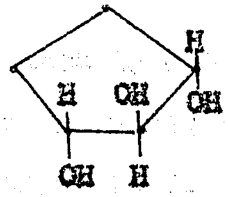


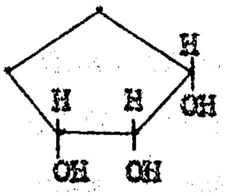
Figure 1. - Theoretical curve relating the coupling constant for neighboring hydrogens and the dihedral angle which they define.

the beginning of this work, should make possible a more ready interpretation of the spectra of the trisubstituted cyclopentanes than was hitherto possible, and perhaps allow conclusions as to their actual conformations.

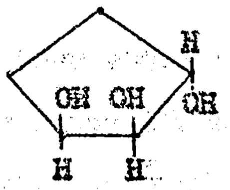
As a first step in this work it was decided to make 1,2,3-cyclopentanetriols since these would be the ultimate reference compounds in the configurational assignments. Four isomers are theoretically possible, VIII, IX, X and the enantiomer of X.



VIII



IX

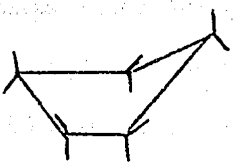


X

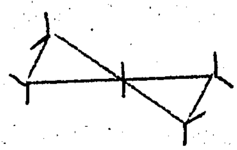
It has long been suspected and now well established that the atoms in a carbocyclic five membered ring do not lie in one plane. The forces which tend to make a carbon atom to retain tetrahedral bond angle are well accommodated both by planar and puckered conformations. Non-bonded interactions are mainly responsible for the fact that these rings are not planar.

Aston, Schumann, Fink and Doty (6) have measured the entropy of gaseous cyclopentane and found that it possesses a non-planar structure. This effect is attributed to hydrogen-hydrogen interactions of the type which hinder the internal rotation found in ethane.

It has been calculated (7,8) that the potential energy for the planar conformation is about four kcal./mole greater than that of the two types of non-planar structures (F and G) which are possible without undue distortion of the carbon valence angles. In the puckered conformations either



F



G

one atom is out of the plane of the other four atoms as in F or two atoms are out of the plane of the other three atoms as in G. These forms as well as a multitude of intermediate types differ little in energy and, therefore, it is not possible to describe cyclopentane itself by a single structure. In direct contrast to these conclusions Le-Fevre and Le-Fevre (9) have shown recently by polarizability measurements that while stucture F does not fit their data structure G does. They conclude that structure G best approaches an equally staggered form of cyclopentane which cannot be readily represented on paper. It is difficult to envisage any factors which would stabilize the form G over form F by appreciable amounts (i.e., 2 kcal./mole).

The substitution of a hydrogen in cyclopentane by a bulkier group should render form F most stable since it allows the greatest degree of staggering with the neighboring hydrogens.

II. Wet and dry Prevost reactions

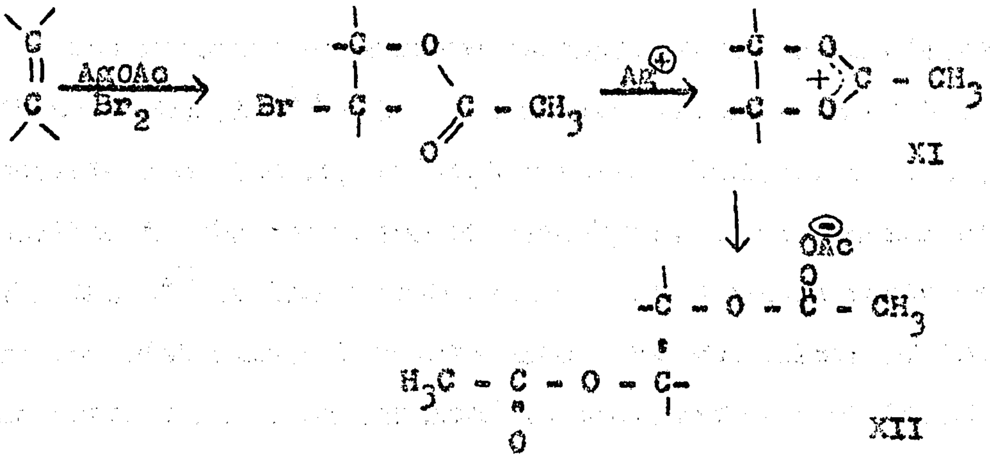
Many years ago, the reaction of silver salts and iodine (10) either in ether or benzene was shown by Simonini (11) to give an active complex intermediate $(RCOO)_2AgI$ which could be isolated. Birkenback (12) later established that reaction of equimolecular amounts of silver acetate and iodine in ether at -80° yielded a filtrate which added IOAc to cyclohexene to give the acetate of trans-2-iodo-1-cyclohexanol. Finally, in a well known series of experiments, Prevost (13,14) showed that in benzene solution the complex reacted with olefins in the presence of a molar excess of the silver salt of the carboxylic acid to give the diester of a *trans*-glycol.

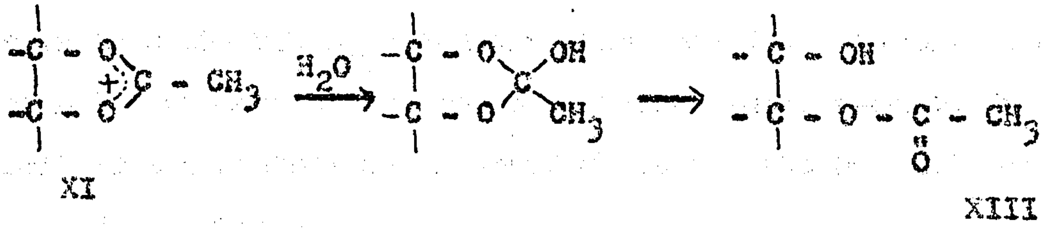
$$2\ C_6H_5CO_2Ag + I_2 \longrightarrow AgI + (C_6H_5CO_2)_2AgI$$

$$(C_6H_5CO_2)_2AgI + R\text{-}CH{=}CH_2 \longrightarrow C_6H_5CO_2Ag + R\text{-}CH(OCOC_6H_5)\text{-}CH_2I$$

$$\longrightarrow AgI + R\text{-}CH(OCOC_6H_5) - CH_2OCOC_6H_5$$

It has been shown recently that the reaction of an olefin with silver acetate and bromine in the presence of some water will give a product with a *cis*-configuration (16-20). The same reaction carried out in a dry solvent gives a product with the addends in *trans*-relationship. The wet Prevost reaction has been postulated to involve a cyclic acetoxonium ion intermediate (XI) which may add water and then be cleaved to the *cis*-hydroxyacetate (XIII) formed in analogy with the work of Winstein on the neighboring group displacement of a bromide by an acetoxy group (21,22). The same acetoxonium ion intermediate (XI) is involved in the dry Prevost reaction. Ring-opening by acetate ion will give the trans-diacetate (XII).





Wiberg and Saegabarth (15) have established this scheme by labeling the carbonyl group of the acetoxybromide with O^{18}. In the cyclic acetoxonium ion intermediate, the two oxygens will become equivalent and each will have one-half of the original O^{18}. If the intermediate reacts with water giving the hydroxyacetate, the product will have the label distributed equally between the original oxygens and no O^{18} will be lost in the hydrolysis to the diol.

If the intermediate reacts with acetate ion to give the diacetate, one of the carbon-oxygen bonds will be broken. Thus, the diacetate will have the same O^{18} content as the bromoacetate, but the diol formed by hydrolysis will have only one half of the original O^{18}, and the other half will be lost in the acetate ion.

The reaction of erythro-1-benzoxy-2-bromo-1,2-diphenylethane-carbonyl O^{18} (15) with silver benzoate under the conditions of the dry Prevost reaction followed by hydrolysis resulted in the formation of meso-hydrobenzoin having one half the O^{18} of the bromobenzoate. The bromobenzoate when treated with silver benzoate under the conditions of the wet Prevost reaction resulted in the formation of threo-2-benzoxy-1,2-diphenylethanol. The hydroxybenzoate on hydrolysis gave the D,L-hydrobenzoin which was found to have the same O^{18} content as the bromobenzoate. These results fit well in the mechanisms proposed above for the wet and dry Prevost reactions.

The nature of the product between the silver salt and halogen is dependent upon five factors as pointed out by Kleinberg, (a) the nature of the silver salt (b) the ratio of the silver salt to halogen (c) temperature of the reaction (d) the presence or absence of other reactive materials (e) the effect of the solvent. Reaction between one equivalent of silver salt of a carboxylic acid and one mole of halogen produces an active intermediate of the formula $R-\overset{O}{\overset{\|}{C}}-OX$ in which the halogen apparently has positive character and adds rapidly to olefins. The reaction fits definite patterns only when the ratio of equivalents of silver salt and halogen is 1:2 or 1:1.

EXPERIMENTAL

Melting points were determined on a Microscope Heating Stage Model 350 and are uncorrected.

The nuclear magnetic resonance spectra were measured using a high resolution Varian spectrometer operating at 60 Mc/s. The chemical shifts were established by interpolation using the side-band technique.

The cyclopentene was prepared from commercial cyclopentanone (23). The cyclopentadiene was prepared by thermal decomposition of dicyclopentadiene (24). All other reagents and solvents were commercial grade except where noted.

The microanalyses were performed by Miss E. Busk of this laboratory.

Cis-1,2-diacetoxycyclopentane

(a) Finely pulverized iodine, 25.4 g. (0.1 mole), was added over a period of one hour to a vigorously stirred suspension of 39 g. (0.234 mole) of silver acetate in 150 ml. of glacial acetic acid containing 6.8 g. (0.1 mole) of cyclopentene and 3 ml. (0.166 mole) of distilled water. After this time, 50 ml. of glacial acetic acid was added and the mixture was stirred for 40 hours at room temperature. The silver iodide precipitate was gathered on a Gooch crucible and washed four times with 20 ml. amounts of benzene. The filtrate was evaporated *in vacuo* at 65-70° to about 15 ml. volume. The acetic acid was neutralized with saturated sodium bicarbonate solution and the solution was extracted continuously with ether for 32 hours. Evaporation of the ether left a light brown oil which was distilled at 78.5-80° (0.05 mm.) to give 11.2 g. (77.7% as a monoacetate) of a colourless oily substance n_D^{30} 1.4542, (lit. b.p. 104-105/20 mm., n_D^{17} 1.4576 (23)) saponification equivalent 128.5. The saponification equivalent expected for cis-2-acetoxycyclopentanol is 144.

The infrared spectrum of the distilled product showed the presence of both hydroxyl and acetoxy groups and the NMR spectrum is recorded in Fig. 2. Acylation of 1.42 g. (9.8 m mole) of cis-2-acetoxycyclopentanol with a two-fold excess of p-nitrobenzoyl chloride in 30 ml. of dry pyridium gave 2.31 g. (78.5%) of light yellow crystals. Three recrystallizations from ethyl acetate gave a product melting at 91-92°. The melting point of p-nitrobenzoate of cis-2-acetoxycyclopentanol is reported (23) to be 93-94°. The product had saponification equivalent of 150.6 while the calculated value is 151.5. The infrared spectrum of 2% solution of the product in carbon tetrachloride showed the absence of hydroxyl group.

The proton magnetic resonance spectrum of the compound is reproduced as Fig. 3.

The cis-2-acetoxycyclopentanol was acetylated using sodium acetate and acetic anhydride and the product was isolated in the usual manner. The diacetate distilled at 81° (2 mm.), n_D^{26} 1.4425. The compound is reported to boil

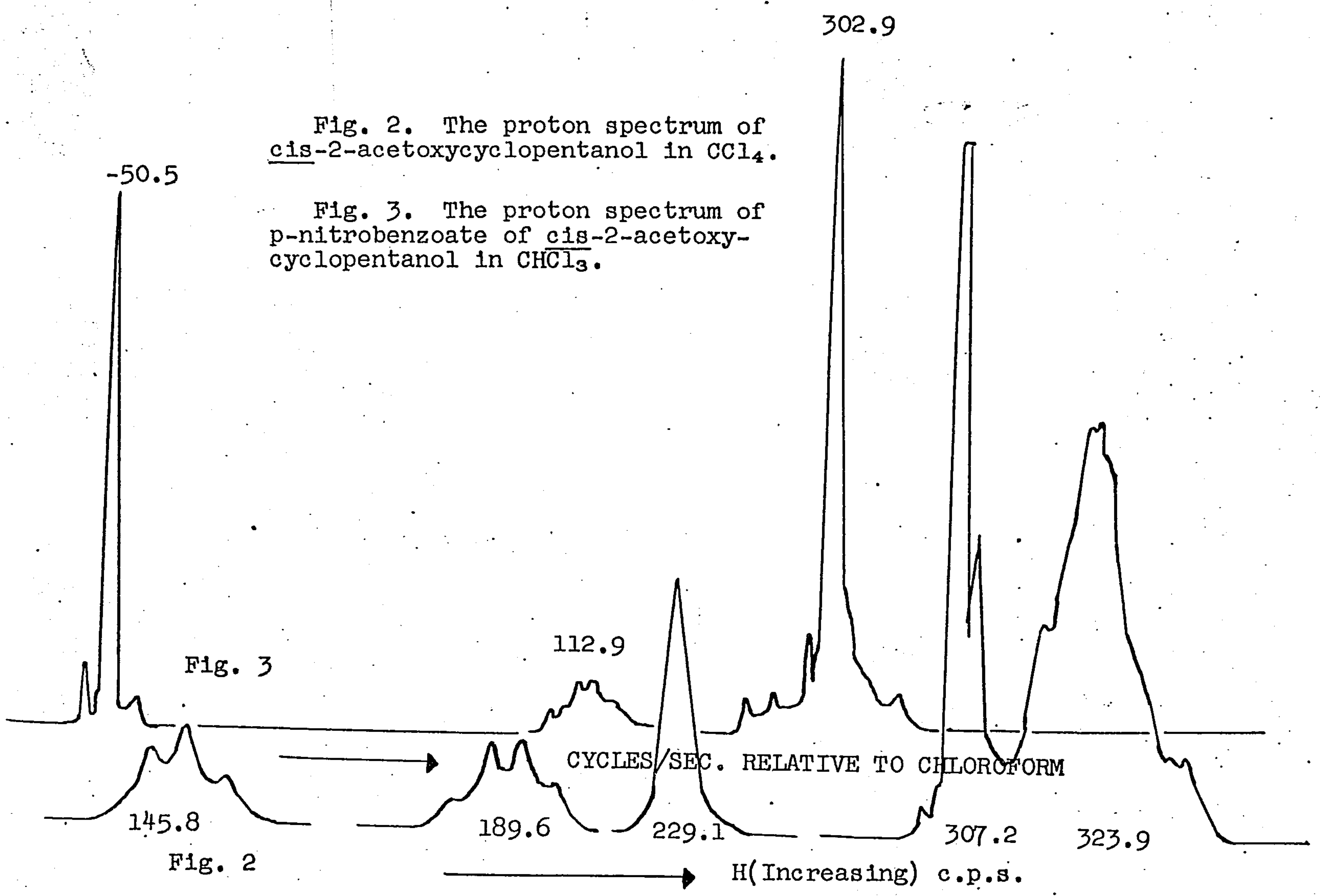


Fig. 2. The proton spectrum of <u>cis</u>-2-acetoxycyclopentanol in CCl_4.

Fig. 3. The proton spectrum of p-nitrobenzoate of <u>cis</u>-2-acetoxycyclopentanol in $CHCl_3$.

at 80° (2 mm.) (25). The saponification equivalent was 92.5 (calc. 93). Deacetylation afforded cis-1,2-cyclopentanediol which showed an R_f value of 0.79 using Whatmann No. 1 filter paper and the n-butanol saturated with water system. The diol consumed 0.99 mole of sodium periodate at 0° within 2 minutes as required for this compound. The purity of this diacetate was examined by vapor-phase chromatographic analysis. Only one peak having retention time of 7 min. 21 sec. was obtained using a 6 ft. long column C (silicon oil) at 171° with a 58 ml./min. flow of helium gas.

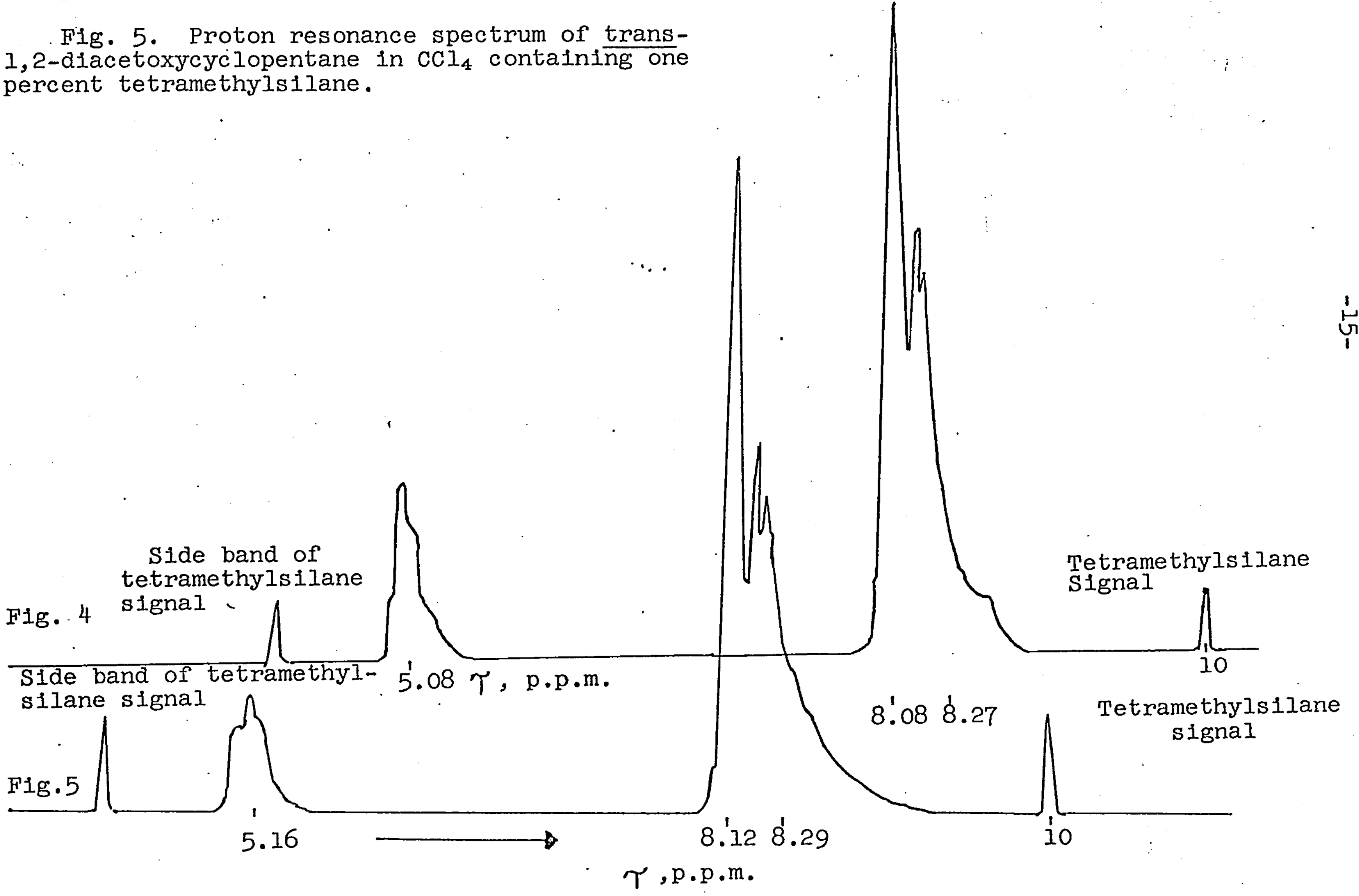
Anal. Calcd. for $C_9H_{14}O_4$: C, 58.06; H, 7.80.

Found: C, 58.04; H, 7.62.

(b) A solution of cyclopentene, 7 g., in 200 ml. of ethanol was cooled to -55° with acetone and dry ice and a solution of 13.3 g. of potassium permanganate in 265 ml. of water was added at once. After 2 minutes, the mixture was decolorized with 20% sulfuric acid and solid sodium bisulfite. After evaporating to about a 100 ml. volume, the solution was extracted continuously with ether. The ether extract was dried over anhydrous sodium sulphate, evaporated to a residue which was distilled, b.p. 88-92°/2 mm., to give 4.0 g. (40%) of cis-1,2-cyclopentanediol. Acetylation with acetic anhydride and sodium acetate gave the sample of cis-1,2-diacetoxycyclopentane with NMR spectrum shown in Fig. 4. The infrared spectrum of this

Fig. 4. Proton resonance spectrum of *cis*-1,2-diacetoxycyclopentane in CCl_4 containing one percent tetramethylsilane.

Fig. 5. Proton resonance spectrum of *trans*-1,2-diacetoxycyclopentane in CCl_4 containing one percent tetramethylsilane.



compound was identical to that for the preparation by way of the wet Prevost reaction described above.

Trans-1,2-diacetoxycyclopentane

(a) A 30.5 g. (0.12 mole) amount of finely pulverized iodine was added over a period of an hour to a suspension of 8 g. (0.118 mole) of cyclopentene in 200 ml. of dry glacial acetic acid containing 52.5 g. (0.314 mole) of silver acetate. The dry glacial acetic acid was prepared by refluxing 240 ml. of the commercial sample (99.8%) with 5 ml. of acetic anhydride for six hours. After all the iodine was added, 40 ml. of the dry acetic acid was added and the mixture was stirred for another 70 hours. The contents were filtered, and silver iodide was washed five times with 20 ml. amounts of benzene. The filtrate was evaporated in vacuo at 60-65° to about a 15 ml. volume and the acetic acid was neutralized with saturated sodium bicarbonate solution. The solution was extracted four times using 75 ml. amounts of ether. Evaporation of the extract gave a reddish brown viscous mass. Distillation at 0.05 mm. gave a product, n_D^{30} 1.4468, the infrared spectrum of which showed a weak absorption band at 3450 cm^{-1} for hydroxyl. Consequently, the product was acetylated using sodium acetate and acetic anhydride in the usual manner. The hydroxyl-free product (infrared) possessed a saponification equivalent of 92 (calc. 93). The diol obtained by deacetylation of the diacetate consumed 0.97 mole of sodium periodate at 0° within 33 minutes and had an R_f value of 0.78 using Whatmann No. 1 filter paper and n-butanol saturated water as the solvent system. As seen above, under the same conditions the R_f value for the cis isomer is 0.79.

Anal. Calcd., for $C_9H_{14}O_4$: C, 58.06; H, 7.80.

Found: C, 57.91; H, 7.80.

An attempt to establish the purity of the diacetate by gas phase chromatography failed since the one peak obtained had a retention time of 7 min. 2 sec. almost the same as that (7 min. 12 sec.) noted above for the cis-isomer. However, the infrared spectra of both cis- and trans-1,2-diacetoxycyclopentanes preparations taken as liquid film, were distinctly different. A comparison of their NMR spectra (Figs. 4 and 5) clearly indicates that the compounds were essentially pure.

(b) A mixture of 30% aq. H_2O_2 (13 g.) and 105 g. of formic acid was added to 6.6 g. of cyclopentene. Much heat was generated. The temperature was allowed to fall and maintained at 40° for 4 hours. The product, 6 g., b.p. 93° (2 mm.), was isolated in the usual manner (23). Acetylation in the usual manner afforded the trans-1,2-diacetoxycyclopentane with the NMR spectrum shown in Fig. 5. The compound had the same infrared spectrum as that of the preparation described above by way of the dry Prevost reaction.

Trans-2-bromocyclopentanol

A 27 g. (0.152 mole) amount of N-bromosuccinimide was added to 10.5 g. (0.154 mole) of cyclopentene in 180 ml. of distilled water contained in a 250 ml. three necked flask equipped with a stirrer. The stirring was continued until N-bromosuccinimide dissolved. The temperature rose to 39° during this operation. After 17 min. the flask was cooled in ice water mixture and the bromohydrin of cyclopentane was extracted with ether. The ether was removed and the flask was heated in vacuo at 50-55° for half an hour. After storing in a refrigerator overnight, the precipitated succinimide was removed by filtration and the filtrate, a light brown oil, was distilled at 58-58.5° (0.05 mm.), $n_D^{30.5}$ 1.5102. The distillate, 20.9 g. (82.25%) of light yellow oil, possessed the physical properties of trans-2-bromocyclopentanol, b.p. 92°/12 mm., n_D^{20} 1.5162 (23).

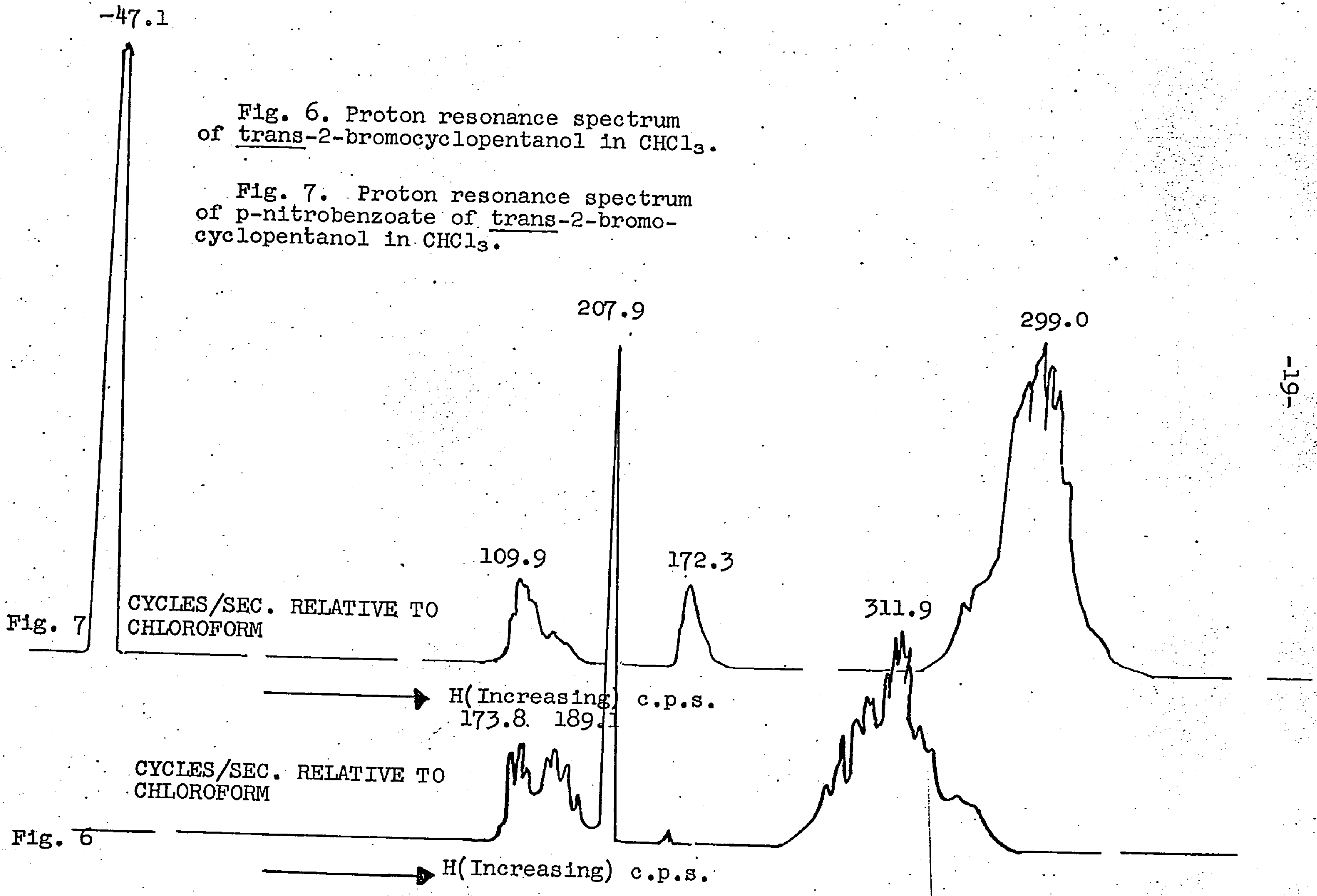
The proton magnetic resonance spectrum of the substance in chloroform solution is recorded in Fig. 6.

The p-nitrobenzoate of trans-2-bromocyclopentanol was prepared in the usual manner, 80% yield. The melting point of the product when recrystallized thrice from ethyl acetate was 97-97.5°, lit. m.p. 98° (23). The saponification equivalent was 162.3 (calc. 157).

The proton magnetic resonance spectrum of the substance in chloroform solution is reproduced in Fig. 7.

Fig. 6. Proton resonance spectrum of trans-2-bromocyclopentanol in $CHCl_3$.

Fig. 7. Proton resonance spectrum of p-nitrobenzoate of trans-2-bromocyclopentanol in $CHCl_3$.



Cyclopentene Oxide

Cyclopentene, 4 g. (0.059 mole), was treated with 10.97 g. (0.079 mole) of perbenzoic acid in 300 ml. of ether and the container was placed in a refrigerator at 4° for 68 hours. The oxide, isolated in the usual manner (26) was fractionally distilled, b.p. 95-98°, 2.5 g. (50.6%), n_D^{35} 1.4330, b.p. 98-100°, 1.05 g. (21.2%), n_D^{32} 1.4338.

The infrared spectra of both the fractions were nearly the same except that in the second fraction two weak bands at 3480 cm^{-1} and 1716 cm^{-1}.

2-Methoxycyclopentanol

Fraction I (b.p. 95-98°) was heated with 2 g. (0.087 equivalent) of sodium dissolved in 20 ml. of anhydrous methanol and the mixture was heated at 90° for 60 hours. The colourless oily product distilled at 70-71° (25 mm.), n_D^{30} 1.4497.

Trans-2-acetoxycyclopentyl Benzoate

6.8 g. (0.1 mole) amount of cyclopentene was added to 16.7 g. (0.1 mole) of silver acetate suspended in 75 ml. of dry benzene. To the vigorously stirred suspension, 25.4 g. (0.1 mole) of finely pulverized iodine was added over a period of one hour. During this addition, the temperature of the reaction mixture rose to the boiling point. The stirring was continued for two hours after which the mass was filtered. The precipitate was washed three times with benzene and the free iodine present in the combined filtrates was removed by shaking it with sodium thiosulphate solution. The benzene layer was evaporated and the liquid residue which displayed a tendency to decompose was converted to trans-2-acetoxycyclopentanyl benzoate by reaction with silver benzoate. The product, after recrystallization from ethyl acetate, melted at 113-115°.

3-Chlorocyclopentene

This compound was prepared as described in "Organic Synthesis" (24). An excess of hydrogen chloride promotes polymerization and should be avoided. It is advisable to stop the addition at about 10% less than the theoretical quantity. 3-Chlorocyclopentene polymerizes at room temperature and should therefore be used immediately.

3-Acetoxycyclopentene

Potassium carbonate, 35 g. (0.253 mole), was added with stirring to 70 ml. of glacial acetic acid containing 30 ml. of acetic anhydride. 3-Chlorocyclopentene, 51.3 g. (0.5 mole), was dissolved in 260 ml. of petroleum ether (30-60°) and to this mixture the slurry of potassium acetate in acetic acid was added with stirring and cooling at 0°. The petroleum ether phase gave a negative test for chloride. Water, 200 ml., was added and the aqueous layer was extracted four times with 30 ml. amounts of petroleum ether (30-60°).

The petroleum ether layers were combined, dried over anhydrous sodium sulphate, and the solvent was removed. The residue was distilled at 76-77° (51-52 mm.) to give 57.2 g. (90.8%) of product, n_D^{25} 1.4475, saponification equivalent 128.7 (calc. 126).

Calcd. for $C_7H_{10}O_2$: C, 66.66; H, 7.93.

Found: C, 64.90; H, 8.02.

An attempt to distill the product at atmospheric pressure caused elimination of acetic acid.

The following procedure was used to determine the amount of oxidant consumed in the periodate-permanganate oxidation of 3-acetoxycyclopentene (27). Two solutions were prepared.

Solution I, 0.126 g. (1 mM) of 3-acetoxycyclopentene and 0.138 g. (1 mM) of potassium carbonate were mixed with distilled water in a volumetric flask and the solution was diluted to 100 ml. Solution II, 1.712 g. (8 mM) of sodium periodate and 0.2054 g. (0.13 mM) of potassium permanganate were dissolved in distilled water separately, mixed and diluted to 100 ml. in a volumetric flask.

Solution II, 10 ml., was mixed with 10 ml. of 0.1 M potassium carbonate solution and the strength of the solution was determined iodometrically using the arsenite procedure described below. The difference between the titer in this titration and that in the runs in the following experiment was taken as equivalent to the oxidant consumed.

Fifty ml. aliquot of solutions I and II were mixed at zero time. After the time intervals indicated, 10 ml.

portions were added to 10 ml. volumes of 0.1 N arsenous oxide solution. Sodium bicarbonate, 0.5 g., a few crystals of potassium iodide, and 50 ml. of distilled water were also added. After 10 mins., the excess arsenous oxide was determined by titration with 0.1 N iodine solution using a starch solution as indicator.

After 1, 20, 40, 80, 160 and 1440 minute reaction times, the amounts of oxidant consumed in equivalents per mole of 3-acetoxycyclopentene were 1.8, 5.1, 6.4, 6.8, 8.02, 9.03, respectively.

Reaction of 3-acetoxycyclopentene with iodine, silver acetate and wet acetic acid at room temperature: - To a solution of 3.15 g. (0.025 mole) of the olefin in 100 ml. of glacial acetic acid containing 3 ml. (0.166 mole) of distilled water, silver acetate, 11 g. (0.065 mole) was added. Finely pulverized iodine, 6.35 g. (0.025 mole) was added over a period of one hour with vigorous stirring. The mixture was stirred at room temperature for 24 hours, and filtered. The yellow precipitate of silver iodide was washed four times with 30 ml. amounts of glacial acetic acid. The filtrate was evaporated at 50-55° in vacuo to a nearly 15 ml. volume. The residue was neutralized with saturated sodium bicarbonate solution and was continuously extracted with ether for 24 hours. Solvent removal left a thick yellow oily mass which was distilled at 116-118° (0.01 mm.) to give 4.01 g. (79.4%) of a colourless pleasant smelling oil, n_D^{25} 1.4832.

Saponification equivalent, 107; calc. for diacetoxycyclopentanol, 101.

To 0.5182 g. of the above mentioned product in 3 ml. of methanol, cooled in crushed ice, was added at 0° 3 ml. of methanol saturated with ammonia. The mixture was allowed to stand at room temperature for 36 hours. After this time the solvent was removed on water pump and the material was examined by paper chromatography using Whatmann no. 1 filter paper and n-butanol saturated with water as solvent system. The periodate-permanganate spray reagent (28) detected two zones, R_f = 0.15 (faint) and 0.46.

The distilled product, 6.0 g. (0.0297 mole), obtained from a second wet Prevost reaction of 3-acetoxycyclopentene was saponified with 5.0 g. (0.125 mole) of sodium hydroxide in 50 ml. of distilled water and 25 ml. of ethanol by heating for 3 hours on a steam bath. After neutralization, the solution was evaporated to dryness <u>in vacuo</u> and triturated with methanol. The extract was decolorized with charcoal, the methanol removed and the residue was dissolved in water for removal of sodium ion using a styrene-type sulphonic acid resin. The water was evaporated <u>in vacuo</u> to leave 3.29 g. (91.4%) of sirupy residue.

The mixture containing 3.29 g. of the material, 30 ml. of acetic anhydride and 3 g. of powdered fused sodium acetate was heated on the steam bath, with occasional shaking, for three hours. At the end of this time the warm soludion was poured, with vigorous stirring, into 120 ml. of ice water. The mixture was allowed to stand, with occasional stirring, until excess of acetic anhydride had been hydrolysed. The mixture was extracted with ether and the solvent was removed on steam bath. The light yellow product was distilled, b.p. 127-129 (3 mm.) to give 5.33 g. (80.8%) of an oily substance, n_D^{25} 1.4475. The saponification equivalent was 81.4. The calculated value for it for triacetoxycyclopentane is 81.3.

Calcd. for $C_{11}H_{16}O_6$: C, 54.09; H, 6.56.

Found: C, 53.66; H, 6.56.

Vapor phase chromatographic analysis of the product using 6 ft. long Apiezon-Celite column at 226° with flow rate of Helium gas as 32 ml./min. indicated two components in the ratio of 81.4 to 18.6%.

After standing for nearly a year, the above described triacetoxycyclopentane preparation partially crystallized. The crystalline component was recrystallized from alcohol and after a second crystallization the substance melted at 39-40°. The purity of this triacetate was confirmed by vapor-phase chromatographic analysis since only one peak was observed using column C (silicon oil) at 176° and a 60 ml./min. flow of Helium gas. The saponification equivalent was 81.5. The calculated value is 81.3.

Calc. for $C_{11}H_{16}O_6$: C, 54.09; H, 6.56.

Found: C, 54.15; H, 6.44.

The R_f value of the triol obtained by deacetylation using n-butanol-water system and Whatman no. 1 paper was 0.47.

A gram of the crystalline triacetate was deacetylated and distilled at 200-202° (air-bath temperature) and 2 mm. pressure to yield 0.25 g (52%) of the triol as a sirup which did not crystallize. Oxidation of 0.0130 g. (0.0011 mole) in 100 ml. of 0.004 M sodium metaperiodate showed a rapid (within about 5 minutes) uptake of one mole of periodate per mole of triol. This fast stage was followed by a slow uptake of a second mole of periodate over the next six hours. At this point, ethylene glycol was added to an aliquot of the mixture and titration with standard sodium hydroxide to phenolphthalein indicator showed the liberation of 1.0 mole of acid per mole of triol oxidized.

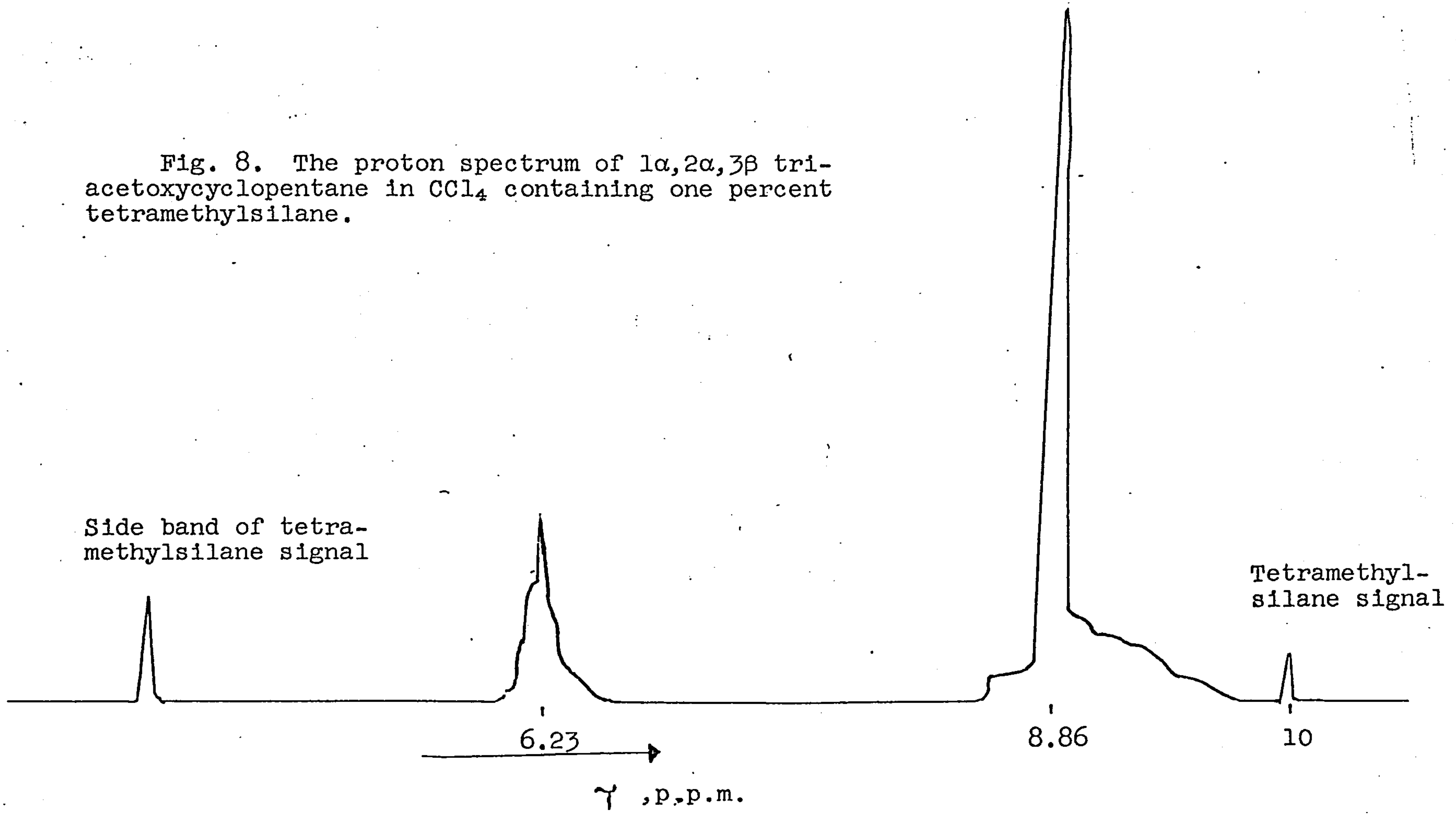
p-Nitrobenzoate (s) of the triol (s) of cyclopentane as obtained above

The procedure used for the preparation of p-nitrobenzoate(s) of triol(s) (obtained by a separate experiment) of cyclopentane is the same as described previously, 80.5% yield. The substance was recrystallized from ethyl acetate and after the third crystallization product melting at 135-136.5° was obtained. The saponification equivalent of the p-nitrobenzoate of triol was 193.5 while the calculated value should be 188.3. The R_f value of the triol using n-butanol-water system and Whatman no. I filter paper was 0.45.

The proton magnetic resonance spectrum of the crystalline triacetate is recorded in Fig. 8.

The mother liquors from the crystalline triacetate were examined by vapor phase chromatography. A 4 ft. long Apiezon M. column at 162° was used with 10 ml./14.9 sec. flow of Argon gas. The presence of four components was detected one of which had the same retention time as that

Fig. 8. The proton spectrum of 1α,2α,3β triacetoxycyclopentane in CCl_4 containing one percent tetramethylsilane.



for the crystalline triacetate. This chromatogram is recorded in Fig. 9 as a characterization of the products from the wet Prevost reaction. The mixture, 0.3 ml., was deacetylated using 4 ml. of dry methanol and 0.2 ml. of normal potassium methoxide in the usual manner and the product was examined by paper chromatography. Whatman no. 1 filter paper was dipped in 5% boric acid solution and dried. The chromatograms of this boric-acid impregnated paper were developed using n-butanol saturated with 5% boric acid solution in water. Three spots were obtained on spraying with the periodate-permanganate solution with R_f values of 0.77, 0.60, 0.45. In view of this success, this solvent system was applied for preparative partition chromatography using Celite to hold the static phase (29). Acid washed Celite, 40 g., was packed in 2.2 cm. (diam.) column in the form of a slurry and the chromatogram was performed as described by Lemieux, Pelletier and Bishop (29). Fractions, 6 ml., of the eluate were collected in an automatic fraction collector. The residues, after evaporation of individual fractions, were examined by the above described paper chromatographic procedure to establish that the fractions of the eluate corresponding to tubes 1 to 4, 7 to 13 and 16 to 28 contained the three different substances. The tubes for each zone were combined, evaporated and freed of boric acid by treatment with methanol and distillation of the methyl borate. The yields were: tubes 1 to 4, 0.01749 g.;

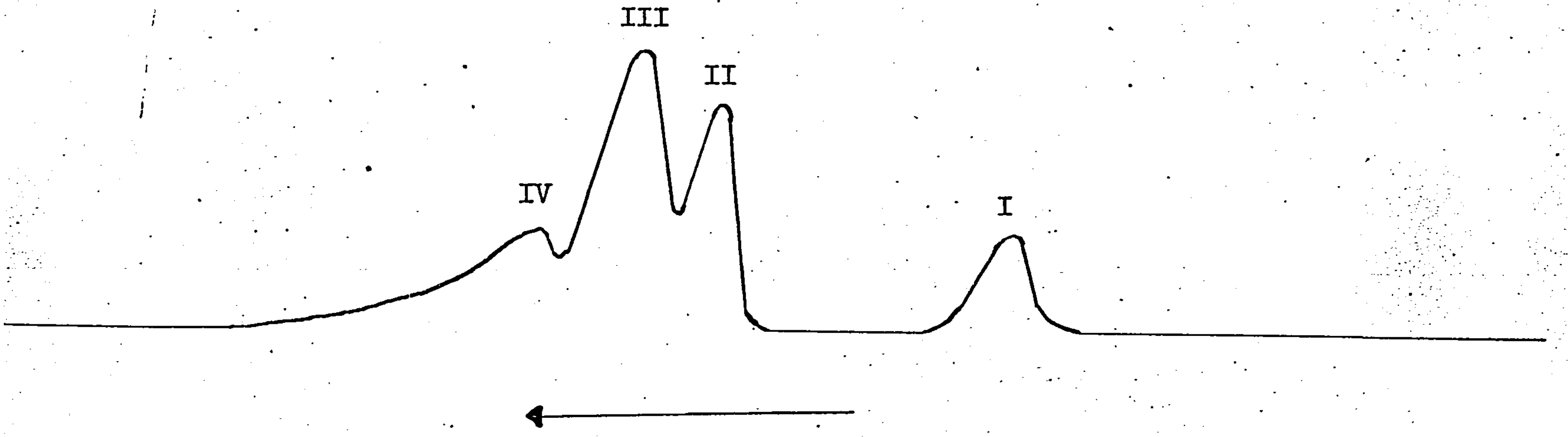


Fig. 9: The vapor phase chromatogram from the mother liquor obtained from the crystallization of the main component (III) in the mixture formed on acetylating the product of the wet Prevost reaction of 3-acetoxycyclopentene. The chromatogram was performed using an Apiezon M on Celite 435 column at 162° and an Argon flow rate of 10 ml./14.9 sec. The retention times were as follows: I, 8 min; II 11.8 min; III, 12.7 min; IV, 14 min.

tubes 7 to 13, 0.06358 g.; tubes 16 to 28, 0.04992 g. The R_f value of the substance present in the tubes 7 to 13 was found to be the same as that of the triol obtained from the crystalline triacetate, m.p. 39-40°. The triols present in the tubes 1 to 4 and 16 to 28 were acetylated using acetic anhydride and sodium acetate and the products were isolated in the usual manner.

Reaction of 3-acetoxycyclopentene with iodine and silver benzoate in dry xylene

Finely pulverized iodine, 2.54 g. (0.01 mole), was added to a mixture of 1.26 g. (0.01 mole) of 3-acetoxycyclopentene, 5.6 g. (0.0244 mole) of silver benzoate and 100 ml. of dry xylene. The mixture was refluxed for 16 hours. After this time, the precipitate was gathered by filtration and was washed twice with 40 ml. amounts of hot xylene. The combined filtrates were washed first with saturated bicarbonate solution and then with water. The organic layer was dried over anhydrous sodium sulphate. Removal of the solvent at 60-65° gave 1.687 g. (45.8%) of crude product n_D^{25} 1.5669.

Reaction of 3-acetoxycyclopentene with iodine, silver acetate and dry acetic acid at room temperature

The method employed was exactly similar to that already mentioned for the reaction in wet acetic acid at room temperature. The dry acetic acid was prepared by refluxing the supplied glacial acetic acid with acetic anhydride and the same quantities of reagents were used. The product was worked up in the same way as described for the wet Prevost reaction except that, after the neutralization with saturated sodium bicarbonate solution, the mass was extracted four times with 40 ml. amounts of ether. Evaporation of the ether gave an oily mass which when distilled gave 4.2 g. (68.8%) of a light-yellow liquid, b.p. 105-107° (0.01 mm.), $n_D^{25.5}$ 1.4808. The saponification equivalent of the distilled product was 102 whereas the calculated value for triacetoxycyclopentane is 81.3. Paper chromatography using Whatman no. 1 filter paper and n-butanol saturated with water system of the product after deacetylation gave two spots when developed with the periodate-permanganate spray with R_f values of 0.15 (faint) and 0.42.

In a second preparation, the product distilled at 134-136° (7.2 mm.), to give a very light brown oily substance, n_D^{25} 1.4598. The saponification equivalent was 82.8.

Chromatography of the mixture of triols obtained (deacetylation) using boric-acid impregnated paper and the butanol-water system showed the presence of two triols when sprayed with periodate-permanganate solution. The R_f values were 0.44 and 0.60. Thus, the substance with R_f = 0.77 formed by way of the wet Prevost reaction was not present in this product.

The two isomeric triols were separated by partition chromatography on Celite using the boric acid-butanol-water system described above. The mixture, 0.12 g., was thus separated into two fractions, 0.80 g. with R_f = 0.60 and 0.022 g. with R_f = 0.44.

Estimation of perbenzoic acid and its reaction with 3-acetoxycyclopentene

A solution of perbenzoic acid in ether was prepared from benzoyl peroxide using the standard procedure (30) and its concentration was established by iodometric titration. 3-Acetoxycyclopentene, 13.86 g. (0.11 mole), was added to 25.1 g. (0.182 mole) of perbenzoic acid contained in 500 ml. of ether and the solution was placed in the refrigerator at 5°. The rate of epoxidation was followed by titration. After reaction was complete the mixture was stirred for 16 hrs. with 29 g. of freshly prepared calcium hydroxide. The solids were removed by filtration and the filtrate was freed of perbenzoic acid by treatment with sodium iodide. After shaking with 30 ml. of saturated sodium bicarbonate solution, the ethereal layer was dried over anhydrous sodium sulphate. The ether was removed and the residue distilled between 83-114° at 55 mm. to yield 15 g. (96%) of a product, n_D^{24} 1.4460-1.4520.

The mixture (92-114°), 13 g., was fractionated using the Todd fractionating column, at 12.4 mm. to yield two fractions, 7.5 g. of material, b.p. 88-89° and $n_D^{26.5}$ 1.4498 and 0.5 g. of material, b.p. 93-94.5° and n_D^{26} 1.4504.

The residue weighed 4.5 g. The fraction boiling at 88-89° was analyzed.

Anal. Calc. for $C_7H_{10}O_3$: C, 59.15; H, 7.04.
Found: C, 59.34; H, 7.20.

The infrared spectra of both the fractions were nearly the same and the band at 847 cm^{-1} can be attributed to the oxide ring. Vapor phase chromatography at 97° using a glycerol-Celite column indicated only one component.

The mixture of triols, 1 g., obtained on treatment of the 3-acetoxycyclopentene oxide, b.p. 88-89 with sodium hydroxide were separated by partition chromatography using Celite to hold the static aqueous phase containing 5 per-cent boric acid and saturated with n-butanol. Elution with the n-butanol phase gave two fractions, 0.018 g., with R_f = 0.60 and 0.073 g. with R_f = 0.44 when chromatographed using boric-acid impregnated paper as described above. The triacetate obtained from the fraction with R_f = 0.60 had the same retention time on vapor-phase chromatography as did the crystalline triacetate obtained by way of the wet Prevost reaction of 3-acetoxycyclopentene.

Bromohydrins of 3-acetoxycyclopentene: - (31-34)

N-Bromosuccinimide (17.8 g., 0.1 mole), 3-acetoxy-cyclopentene (12.6 g., 0.1 mole) and 50 ml. of distilled water were mixed at 24°. The temperature of the stirred solution rose to 40° and a thick mass was formed. Stirring was continued for 24 hours. The product was isolated by extraction with ether. The residue obtained by solvent removal was placed overnight at 5°, and the precipitated succinimide was removed by filtration. The thick light brown oily filtrate was distilled, b.p. 125-132° (13 mm.), to give 15.01 g. (67.3%) of the product n_D^{25} 1.5060 - 1.5065. Most of the material distilled at 130-131° as a light-yellow, thick oil.

The p-nitrobenzoate(s) was prepared in the usual manner. Three crystallizations from ethyl acetate gave a 17% yield of material, m.p. 74-75.5°.

Anal. Calcd. for $C_{14}H_{14}O_6NBr$: C, 45.1; H, 3.76; N, 3.76.

Found: C, 46.1; H, 3.95; N, 3.29.

A second fraction was obtained as a colourless crystalline substance melting at 150-170°, which was not characterized.

<u>3-Methoxycyclopentene</u>: - (35)

3-Chlorocyclopentene, 102.5 g. (1 mole), was treated with 40.4 ml. (1 mole) of dry methanol containing 84 g. (1 mole) of sodium bicarbonate and 300 ml. of ether. After standing overnight with occasional shaking, the ethereal layer was separated and the precipitate was washed with ether. The ether was carefully removed by distillation and the product; 53 g., (55% yield) boiling at 105-106°, n_D^{27} 1.4366, was collected. Periodate permanganate oxidation of the compound showed the consumption of 8 milliequivalents of oxidant per mole as 3-methoxycyclopentene. This consumption corresponds to that expected for the formation of 2-methoxy glutaric acid.

Wet Prevost reaction of 3-methoxycyclopentene:-

Finely pulverized iodine, 16.51 g. (0.065 mole) was added to a mixture of 6.37 g. (0.065 mole) of 3-methoxycyclopentene, 28.0 g. (0.167 mole) of silver acetate and 350 ml. of glacial acetic acid containing 4 ml. of distilled water. The mixture was stirred for 49 hours. After this time, the silver iodide precipitate was gathered on Gooch crucible and was washed four times with 25 ml. amounts of benzene. The filtrate was evaporated in vacuo at 50-60° to about a 15 ml. volume. The acetic acid was neutralized with saturated sodium bicarbonate solution and the product was continuously extracted with ether for 40 hours. The ether was removed on water pump and the yellow coloured oily substance when distilled gave 8.5 g. (75%), n_D^{25} 1.4606, of the product, having saponification equivalent as 159.7 while the theoretical value calculated from the formula should be 174. The liquid obtained after titration was evaporated to dryness on water pump at nearly 60°. Some dry methanol was added to it and the filtrate was tested for R_f values of diols. Two spots were obtained with R_f values as 0.31 and 0.65 when the Whatman no. 1 filter paper was used and sprayed with ammoniacal silver nitrate solution. The paper was heated at 110° in an oven for nearly 5 minutes. N-butanol saturated with water was used as a solvent system for paper chromatography.

The infrared spectrum of the distilled product taken as a liquid film showed major bands at 3442 cm^{-1}, 2920 cm^{-1}, 1740 cm^{-1}, 1370 cm^{-1}, 1245 cm^{-1}, 1120-1100 cm^{-1} and 1060 cm^{-1}, thus indicating the presence of both hydroxyl and acetoxy groups.

Bromohydrins of 3-methoxycyclopentene:- N-bromosuccinimide 9.4 g. (0.0528 mole), 3-methoxycyclopentene 5.1 g. (0.052 mole) and 30 ml. of distilled water were mixed at 23° in a 100 ml. three necked flask equipped with a "truebore" stirrer and a thermometer. Stirring was continued until N-bromosuccinimide dissolved (12 minutes) and a heavy light milky layer separated during which time temperature rose to 50°. The two phases system was allowed to cool to room temperature and the bromohydrins were extracted five times with ether using 50 ml. of it each time. The ether was removed on water pump and the residue was placed overnight at 5°, and the precipitated succinimide was removed by filtration under water pump. The brown coloured filtrate was distilled, b.p. 89-94° (3 mm.), n_D^{20} 1.5092 - 1.5098, to give 8.6 g. (84.8%) of light yellow coloured oily substance.

The infrared spectrum of the distilled product taken as a liquid film showed the presence of hydroxy group.

Anal. Calcd. for $C_6H_{11}O_2Br$: C, 36.92; H, 5.64; Br, 41.00.

Found: C, 36.71; H, 5.64; Br, 40.82.

Preparation of 3-methoxy 1,2-cyclopentanediol by treating 3-methoxycyclopentene with alkaline permanganate

5.75 g. (0.0587 mole) of olefin in 300 ml. of 66% aqueous ethanol containing 3 drops of 1N NaOH was cooled to -60° (dry ice and acetone mixture) in a Dewar flask and a solution of 18.6 g. of potassium permanganate in 300 ml. of distilled water was added to it at once with stirring. The colour of the mixture became dark brown due to the formation of manganese dioxide. After 2 minutes an acidified solution of 75 g. of sodium bisulphite in 175 ml. of water was added. The resulting clear solution was freed from ethanol and some water on water pump at 30° and was then continuously extracted with ether for 36 hours. The ether was distilled off and the solvent was removed which came until 101°. The weight of the substance left was 1.92 g. The R_f value of the diol using n-butanol saturated with water as solvent system and Whatman no. 1 filter paper was 0.69. The paper was sprayed with periodate-permanganate solution.

Epoxidation of 3-methoxycyclopentene with perbenzoic acid;-

8.37 g. (0.085 mole) of 3-methoxycyclopentene was treated with 20.41 g. (0.148 mole) of perbenzoic acid contained in 400 ml. of ether and the container was placed at 5°. The rate of epoxidation was followed by titration. At the end of this reaction the mixture was stirred for 18 hours with 35 g.

of freshly prepared calcium hydroxide (calcium hydroxide was prepared from calcium chloride and sodium hydroxide and the precipitate was washed with distilled water till it was free from chloride test, then with alcohol and acetone and dried), but still it contained 0.15 g. of perbenzoic acid. The precipitated calcium salts of acids were washed several times with ether. Saturated sodium iodide solution was added to the above filtrate and the iodine liberated was removed by shaking it with saturated sodium thiosulphate solution. The ethereal solution was washed with 30 ml. of distilled water and dried over anhydrous sodium sulphate. The ether was distilled off using a small column while the remaining substance was distilled, b.p. 138-144°, n_D^{26} 1.4403, to give 9.2 g. (94.4%) of the epoxide(s).

This distilled product was further fractionated on Todd's fractionation column using spiral type column. The first fraction which came between 45-46° at 12 mm. was collected and weighed 6.1 g., n_D^{25} 1.4410.

Anal. Calcd for $C_6H_{10}O_2$: C, 63.16; H, 8.77.

Found: C, 63.90; H, 8.65.

The infrared spectrum of the product was in accordance with that expected for 3-methoxy 1,2 epoxide of cyclopentane and the band at 846 cm^{-1} may be attributed to the presence of oxirane ring.

The other fraction came up to 81° at 12 mm. but mainly in between 80-81°, $n_D^{25.5}$ 1.4735 and weighed 1.7 g. The infrared spectrum of the product showed bands at 3336 cm^{-1}, 1710 cm^{-1} and 1275 cm^{-1} in addition to the bands already present in the first fraction.

The gas phase chromatographic analysis of the first fraction using 6 feet long column C (silicon oil) at 98° when the flow rate of helium gas was 60 ml/minute showed the presence of only one component.

Lithium aluminum hydride reduction of epoxide of 3-methoxycyclopentene (45-46° at 12 mm.).

1.75 g. (0.015 mole) of the epoxide in dry ether was added to 0.4 g. (0.0105 mole) of lithium aluminum hydride contained in dry ether at such a rate that the reaction mixture boiled gently. The total volume of dry ether used was 35 ml. The reaction mixture was refluxed for 36 hours. After this time the excess of lithium aluminum hydride was decomposed by adding carefully moist ether and a few drops of ethyl acetate. To the reaction mixture was then added excess of ice-cold dilute hydrochloric acid to decompose the complex aluminum compounds and to dissolve the precipitated aluminum hydroxide. The solution was continuously extracted with ether for 24 hours. The ethereal layer was dried over anhydrous sodium sulphate and the solvent was removed. Some substance distilled up to 150° (oil bath temperature) and weighed 0.25 g. (14.3%). The remaining substance when distilled in a two bulbed tube gave 1.3 g. (74.3%) of the reduced product, n_D^{25} 1.4503.

The infrared spectrum of reduced produce (n_D^{25} 1.4503) taken as a liquid film showed strong bands at 3430 cm^{-1}, 2935 cm^{-1} and 1110-1095 cm^{-1}.

The gas phase chromatographic analysis of the first fraction which came up to 150° using 12 feet long glycerol-Celite brick column at 145° when the flow rate of helium gas was 40 ml./minute, showed the presence of two components in the ratio of 88% to 12% while the second fraction (n_D^{25} 1.4503) using the above mentioned column and conditions showed the presence of only one peak. When the later fraction was mixed with 2-methoxycyclopentanol, obtained by treating cyclopentane epoxide with sodium methoxide, and was run under the same conditions only one peak was obtained showing that these might be identical compounds.

The infrared spectrum of 2-methoxycyclopentanol obtained by lithium aluminum hydride reduction of 3-methoxy-1,2 epoxide of cyclopentane using Beckmann recording spectrophotometer and lead sulphide cell and having concentration of 0.0096 molar in carbon tetrachloride gave only one band at 3628.8 cm^{-1}.

<u>Treatment of 2-methoxycyclopentanol with HI</u>: - 1.2 g. 0.0105 mole) of 2-methoxycyclopentanol were placed in a tube with 4 ml. of cold hydriodic acid and the tube was

sealed off. The contents were now cautiously mixed and the tube was placed in a water bath held at 58° for 20 minutes and was then rapidly cooled with crushed ice containing sodium chloride. The tube was opened (some pressure had developed) and was washed with water. The contents were neutralized with saturated sodium bicarbonate solution. Some water and methyl iodide were removed at the water pump and the remaining product was continuously extracted with ether for 48 hours. The ethereal layer was dried over anhydrous sodium sulphate and was removed in vacuo. The remaining product was distilled at 100-105° (air bath) (2.5 mm.) to give 0.45 g. (42.1%) of material which solidified when placed in the refrigerator. The purity of the diol was confirmed by sodium periodate oxidation at 0° when it consumed 0.97 mole of periodate after 19 minutes. The vapor-phase chromatographic analysis of the product using column C (silicon oil) at 154° when flow rate of helium gas was 58 ml./min. gave only one peak. The R_f value of the diol using Whatmann no. 1 filter paper and n-butanol saturated with water as solvent system was 0.78.

p-Nitrobenzoate of cyclopentane diol:- The procedure used for the preparation of p-nitrobenzoate of cyclopentanediol was the same as described earlier. The yield of the product was 85% and after two recrystallizations from ethyl acetate the substance melted at 139.5-141°. The mixed melting point with the authentic sample remained unchanged and the infrared spectra of both the samples in chloroform solution were identical.

Reaction of 3-methoxy 1,2 epoxide of cyclopentane with sodium methoxide: - 1.2 g. (0.0105 mole) of the epoxide were treated with 0.6 g. of clean sodium dissolved in 10 ml. of dry methanol and the brown colored mixture was refluxed for 65 hours at 100°. After this time the mixture was allowed to cool and was neutralized with dilute sulphuric acid. This solvent system was continuously extracted with ether for 26 hours. The ethereal layer was dried over anhydrous sodium sulphate and the solvent was removed in vacuo. The remaining substance when distilled in a two bulbed tube, 105-112° (21 mm.), gave 0.8 g. (52.3%) of dimethoxycyclopentanol(s), $n_D^{29} = 1.4120$.

The infrared spectrum of the product taken as a liquid film showed strong bands at 3400 cm^{-1}, 2900 cm^{-1} and 1095 cm^{-1}.

Acetylation of dimethoxycyclopentanol(s): - 0.7 g. (0.0048 mole) of dimethoxycyclopentanol(s) was acetylated using acetic anhydride and sodium acetate and the product was worked up as usual. Distillation of the product at 95-100° (air bath) (1.8 mm.) gave 0.68 g. (75.5%) of the dimethoxy cyclopentane acetate(s), n_D^{27} 1.4465.

The saponification equivalent of the product was 184 while the calculated value from the formula should be 188.

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.44; H, 8.51.

Found: C, 57.37; H, 8.21.

The gas phase chromatographic analysis of the distilled product using column C (silicon oil) at 154° with the flow rate of helium gas as 52 ml./minute showed the presence of two components in the ratio of 72% to 28%.

<u>Separation of the acetates on silicic acid column</u>: - The silicic acid used for this experiment was dried at 120° for 15 hours after which it was placed in a desiccator. A slurry of it was made in chloroform and was then packed in the column by placing a small piece of glass wool at the bottom. Some pressure was applied from the top so that it was nicely packed in the column. 0.55 g. of the substance was separated on 25.1 cm. long column with 1.5 cm. as internal diameter.

The substance was dissolved in the least amount of chloroform and was then applied at the top of the column with a pipette. Some pressure was applied from the top. It was eluted with chloroform after it had dispersed in the column. A small amount of the substance came with the solvent front and the eluate was collected in 20 ml. fractions. Only 20 mg. of the substance came when the column was eluted with 180 ml. of chloroform. The fraction that came in between 200 - 260 ml. weighed 0.35 g. (63.6%). The gas phase chromatographic analysis of the product showed the presence of one component with the presence of a small amount of another component. When the mixture and this component were run under the same conditions, the retention time of the latter coincided with that component present in the major amount (72%) of the mixture.

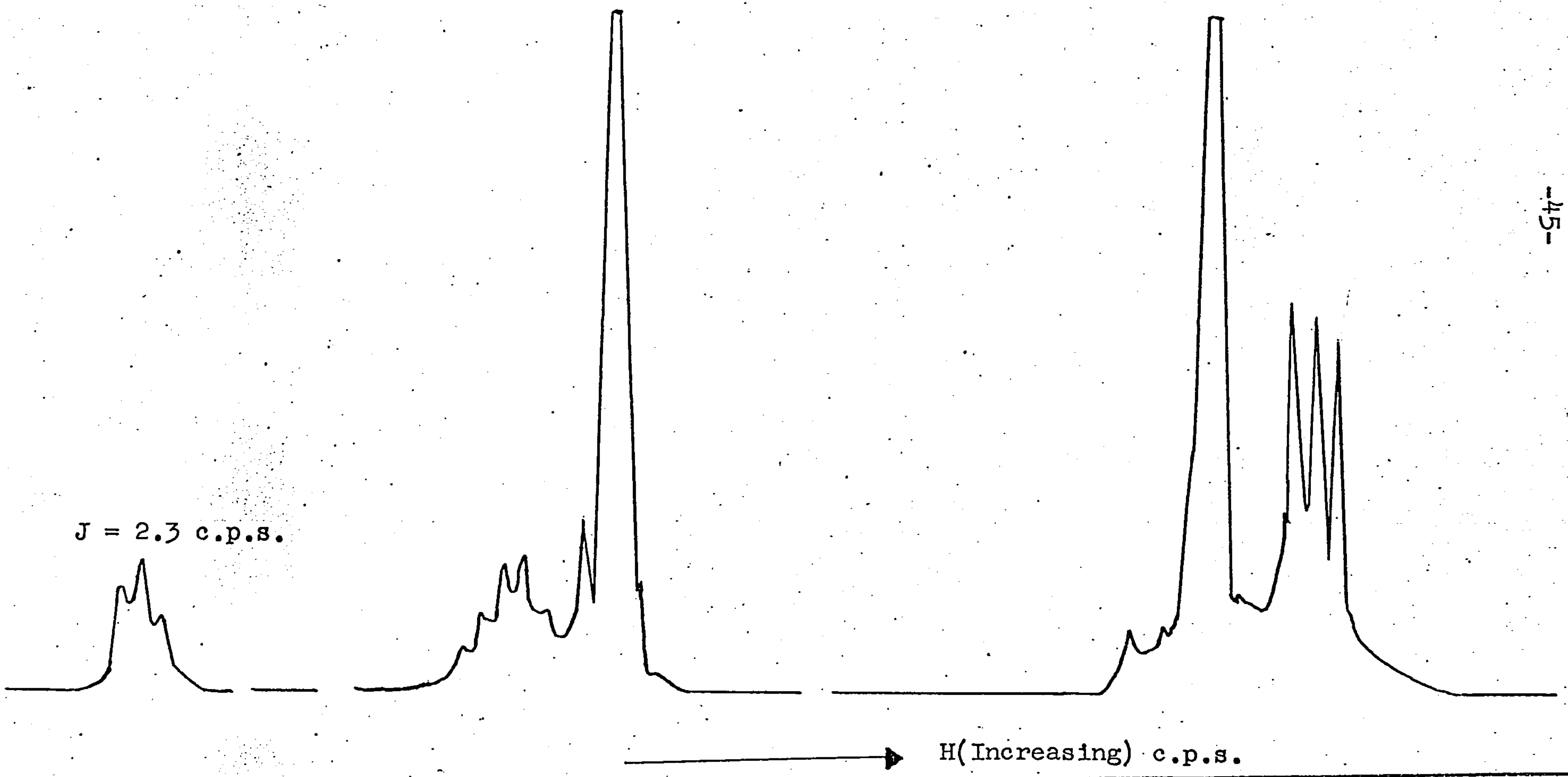
The component weighing 0.35 g. was distilled at 96-98° (1.8 mm.), n_D^{25} 1.4472.

The proton magnetic resonance spectrum of the distilled product is shown as Fig. 10 (80 mg. of the substance dissolved in 0.5 ml. of carbon tetrachloride containing 1% tetramethylsilane gave signals which can be assigned to the different kinds of hydrogens present in the molecule simply through the inspection of their intensities, positions and structure of the bands.)

Reaction of 3-methoxy 1,2-epoxide of cyclopentane with sodium hydroxide: - 0.25 g. (0.0022 mole) of the epoxide in dioxane was treated with 0.12 g. of sodium hydroxide dissolved in 8 ml. of distilled water and the contents were refluxed for 70 hours. After this time the excess of base was neutralized with dilute sulphuric acid and the solution was continuously extracted with ether for 48 hours. The ether was removed in vacuo and the remaining substance when distilled gave 0.202 g. (69.7%) of the product.

Reaction of triols obtained by way of dry Prevost reaction of 3-acetoxycyclopentene with acetone: - 1.18 g. of triols were treated with 25 ml. of dry acetone in presence of 3 g. of anhydrous copper sulfate and the contents were shook for 24 hours. The contents were filtered and the precipitate was washed thrice with 20 ml. amount of dry acetone. The

Fig. 10. The proton spectrum of 1α,3α-dimethoxy-2β-acetoxycyclopentane in CCl_4 containing one percent tetramethylsilane.



solvent from the filtrate was removed on water pump. Sixty-five ml. of distilled water were added to it and the mixture was continuously extracted with ether for 24 hours. The ether extract contained an oil which when distilled, 100-102° (air bath)(0.5 mm.), in a two bulbed tube gave 1.22 g. (7%) of isopropylidine derivative. The substance moved as a single component on gas-phase chromatographic analysis and possessed an infrared spectrum in general agreement with that expected for a monoisopropylidine derivative of 1,2,3-trihydroxy cyclopentane. There was, however, a weak carbonyl absorption band which showed the compound to be impure. No further work was done with this compound(s).

The aqueous layer was evaporated to near dryness and the residue 0.236 g. (20%) was subjected to preparative partition chromatography using n-butanol-water as the solvent system and Celite to hold the static aqueous phase. The fractions which contained triol were located by paper chromatography, combined and evaporated to a sirupy residue which was dehydrated by azeotropic distillation with benzene. This triol was acetylated by the procedure described earlier.

Lithium aluminum hydride reduction of epoxide of 3-acetoxycyclopentene: The same procedure was used in this case as described under the lithium aluminum hydride reduction of 3-methoxy 1,2 epoxide of cyclopentane.

Separation of triols obtained by way of dry Prevost reaction of 3-acetoxycyclopentene: - These were separated by partition chromatography using Celite to hold the aqueous phase and n-butanol-acetic acid-water as solvent system. The results are described in the discussion section.

DISCUSSION

A systematic survey of the conformations of compounds which possess a flexible, five-membered ring and their derivatives by NMR studies was planned. It seemed possible that in certain cases specific conformations could be proposed on the basis of quantitative information obtained regarding the coupling of neighboring protons.

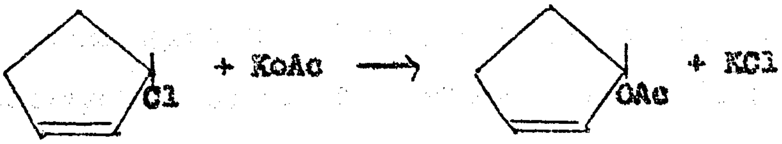
It was decided to approach this problem by synthesizing 1,2,3-trisubstituted cyclopentanes wherein the chemical shift for the 2-hydrogen could be considerably different to those of the other hydrogens in the molecule. Thus, its position in the field and its fine structure for a given conformation could be anticipated with a high degree of certainty.

As a first step it was decided to prepare as starting materials, 3-methoxycyclopentene and 3-acetoxycyclopentene. Dr. Vaughn (35) has reported a substance which may be 3-methoxycyclopentene.

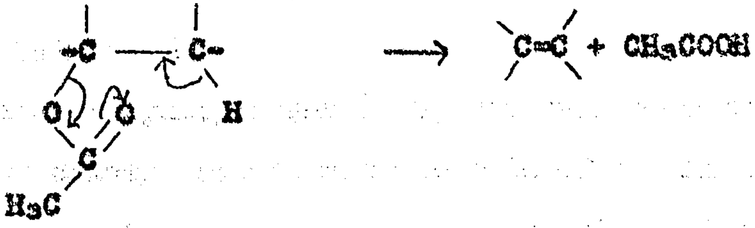
Pyrolysis of bicyclopentadiene gave cyclopentadiene (24). Cyclopentadiene polymerizes spontaneously by a Diels-Alder addition to dicyclopentadiene which depolymerizes at its boiling point (165°) to the monomer. The mechanism of this reaction has been recently discussed by Woodward (36,37).

Cyclopentadiene was converted to the 3-chlorocyclopentene, a previously well characterized compound, by the addition of dry hydrogen chloride gas to the freshly distilled cyclopentadiene at the dry ice-acetone mixture temperature according to the procedure reported in Organic Synthesis (24).

3-Acetoxycyclopentene was prepared by treating 3-chlorocyclopentene with potassium acetate in acetic acid at 0°. The mixture was diluted with water and extracted with ether. The residue after evaporation of the ether was distilled at reduced pressure. An attempt to distill the product at atmospheric pressure caused nearly quantitative decomposition to acetic acid and cyclopentadiene. This ready decomposition could be interpreted as indicating that the product was in fact an allylic acetate of the type presented by 3-acetoxycyclopentene. Elimination reaction giving acetic acid is explained by the type of mechanism proposed by Hurd and Blunck in 1938 (38, 39).



XIV



Doering and Vaughn (35) had similar difficulties in the preparation of 3-hydroxycyclopentene. It is mentioned in the thesis presented by Vaughn that the carbinol is very sensitive to acid and underwent extensive dehydration on distillation. The practice of washing the glassware, which had been cleaned in an acid bath, with ammonia water followed by careful rinsing eliminated this problem. It was recommended that 3-substituted cyclopentenes be distilled over a pinch of anhydrous potassium carbonate.

The distilled product in the preparation of 3-acetoxycyclopentene boiled at 76-77° at 52 mm, n_D^{25} 1.4475, and gave a saponification equivalent of 128, gave only one zone on vapor phase chromatography and consumed 2 moles of periodate per 126 g. on periodate-permanganate oxidation (27). Although the carbon analysis was not extremely good (no doubt due to the difficulties inherent in the analysis of a volatile compound), the NMR (Fig. 11) and the IR spectra for the compound agree in all respects with those expected for 3-acetoxycyclopentene. The latter compound is calculated to possess a molecular weight of 126. These data, therefore, leave no doubt as to the identity of the compound obtained.

3-Acetoxycyclopentene (XIV) was treated with two equivalents of silver acetate and one mole of iodine in the presence of wet acetic acid. The product which was isolated

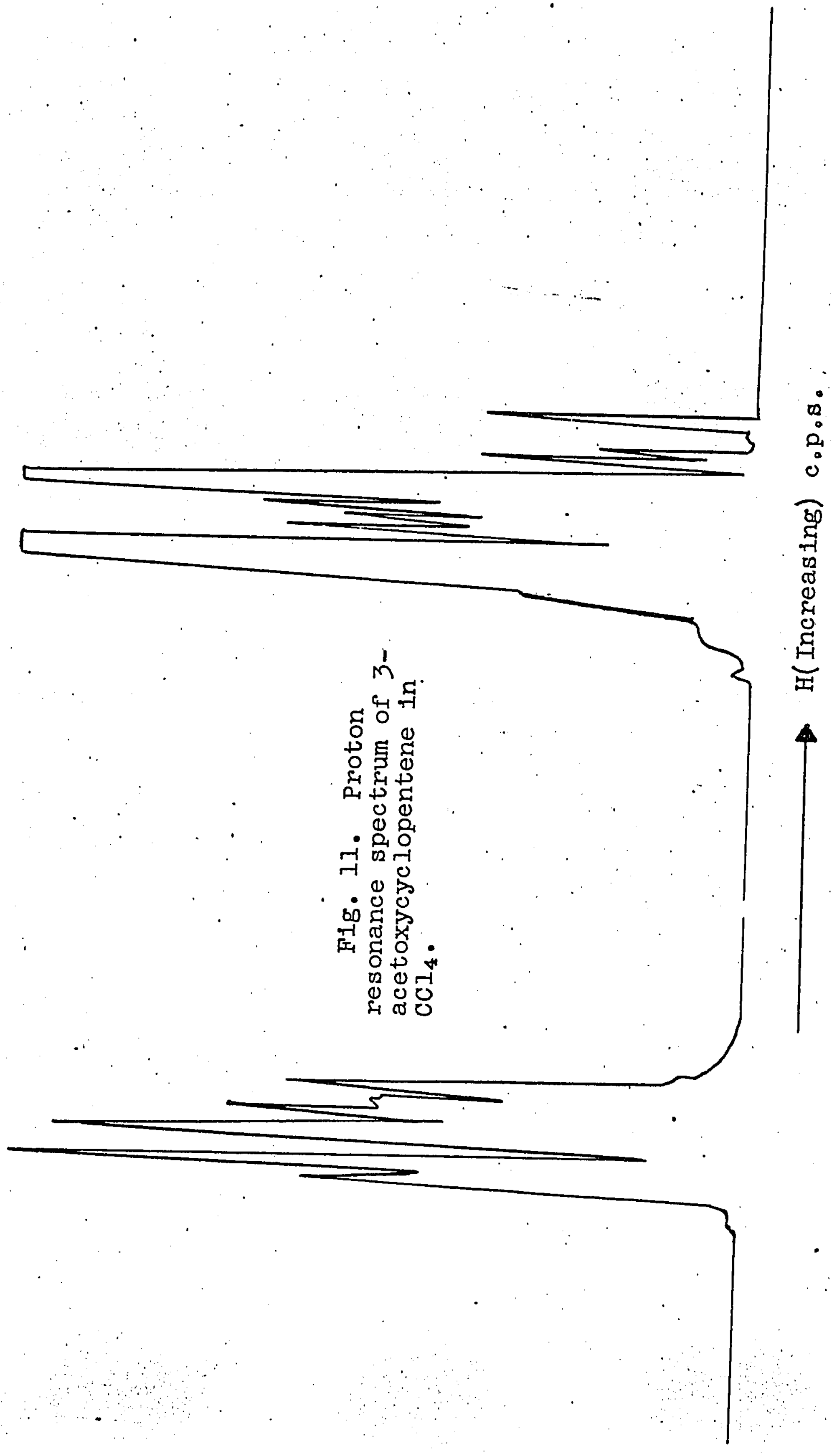


Fig. 11. Proton resonance spectrum of 3-acetoxycyclopentene in CCl_4.

possessed a saponification equivalent of 108 and its infrared spectrum showed that it contained both the acetoxy and hydroxyl groups. Paper chromatography of the deacetylated product showed only one spot when different solvent systems were used and the paper was sprayed with periodate-permanganate. The R_f value in butanol-water system was 0.45, a value close to that of a cyclohexane triol in the n-butanol-acetic acid-water solvent system. Thus it seemed likely that the compound(s) was a trihydroxycyclopentane. Acetylation of the trihydroxy compound(s) gave the corresponding triacetate(s). On standing for some time the mixture of triacetates deposited crystals which were purified by recrystallization from alcohol. The pure compound melted at 39-40° and gave the saponification equivalent and carbon and hydrogen contents expected for a 1,2,3-triacetoxycyclopentane. The NMR spectrum for the compound is shown in figure 8.

The mother liquor left after separating the crystalline triacetate was subjected to vapor-phase chromatographic analysis using an apiezon grease column. This analysis showed the presence of four components (figure 9). The zone (III) with retention time of 12 minutes 18 seconds corresponded to that for the major product which crystallised. There can be only three diastereoisomeric 1,2,3-trihydroxycyclopentanes.

It has long been recognized that cis-diols form complexes with boric acid (40). Therefore, chromatography on boric acid impregnated paper was examined using cyclopentane and cyclohexane diols. The results are presented in Table 1.

It is seen that although chromatography on paper using n-butanol saturated with water as developing phase effected no separation, the use of boric acid-impregnated paper effected a separation of cis and trans-cyclopentanediols.

The mother liquor remained after removing the crystalline triacetate of cyclopentane was deacetylated and the product was chromatographed using the boric acid-impregnated paper technique. In this way, the substance was found to contain three components which gave a positive reaction with periodate-permanganate reagent with R_f values of 0.44, 0.60 and 0.70. In the absence of the boric acid only a single spot with R_f value of 0.45 was obtained. This observation provided the key to the solution of the present problem.

The solvent system used for the above mentioned paper chromatography, n-butanol equilibrated with 5 percent aqueous boric acid solution, was used to separate the triols by partition chromatography using Celite to hold the static aqueous phase (29). This procedure effected the separation of the three isomers of the 1,2,3-trihydroxycyclopentanes. The fractions obtained in this way were acetylated and the acetates were examined by vapor-phase chromatography. The results of the partition chromatograms are summarized in Table II.

Table I

Chromatography on Boric Acid-Impregnated Paper

Substance	Whatmann no. 1 filter paper (a)	Boric acid-impregnated Whatmann no. 1 filter paper (b)
Cis-1,2 cyclopentanediol	0.79	0.81
Trans-1,2-cyclopentanediol	0.78	0.71
Cis-1,2-cyclohexanediol	0.80	0.80
Trans-1,2-cyclohexanediol	0.79	0.78

(a) The solvent system was n-butanol saturated with water.

(b) The solvent system was n-butanol equilibrated with 5 percent aqueous boric acid solution.

Table II

Chromatographic Characterization of the Products Formed in the Wet Prevost Reaction of 3-Acetoxycyclopentene

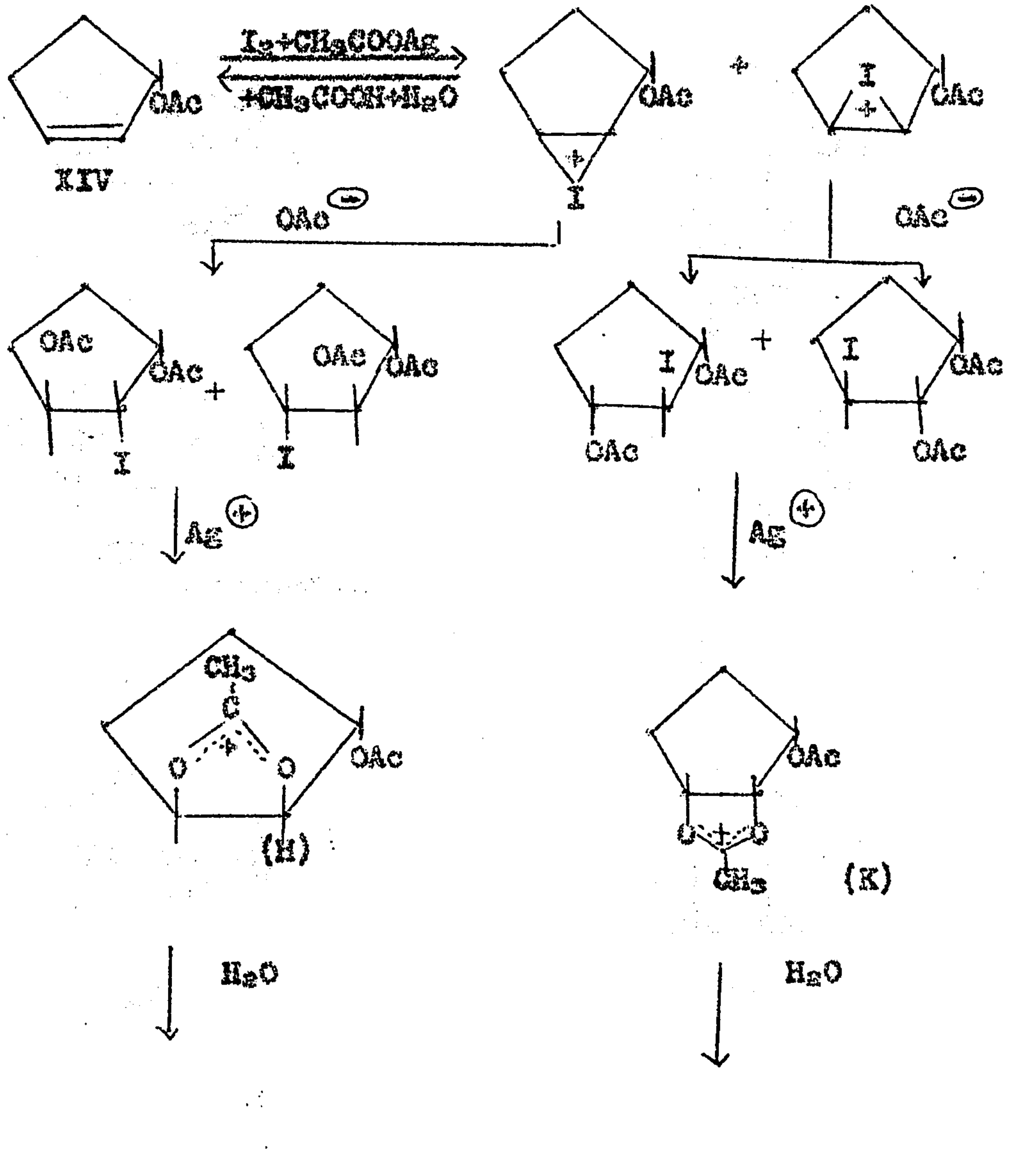
Column (a)	Paper (a)	Vapor Phase (b)
Tube No.	R_f	R_T
1-4	0.77	8 minutes
7-13 (c)	0.60	12 minutes, 18 seconds
16-28	0.45	11 minutes, 22 seconds

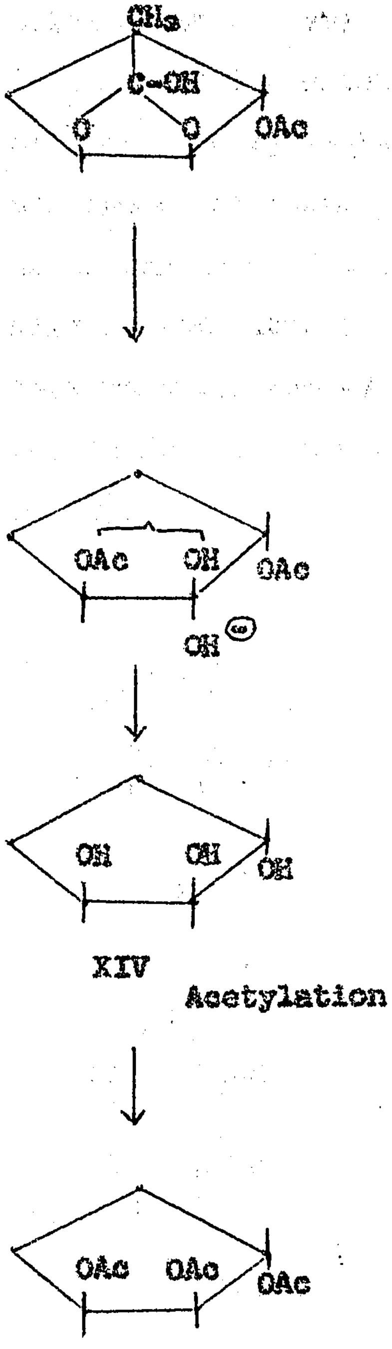
(a) Product as triol using boric acid impregnated paper.

(b) Product as triacetate using (a)

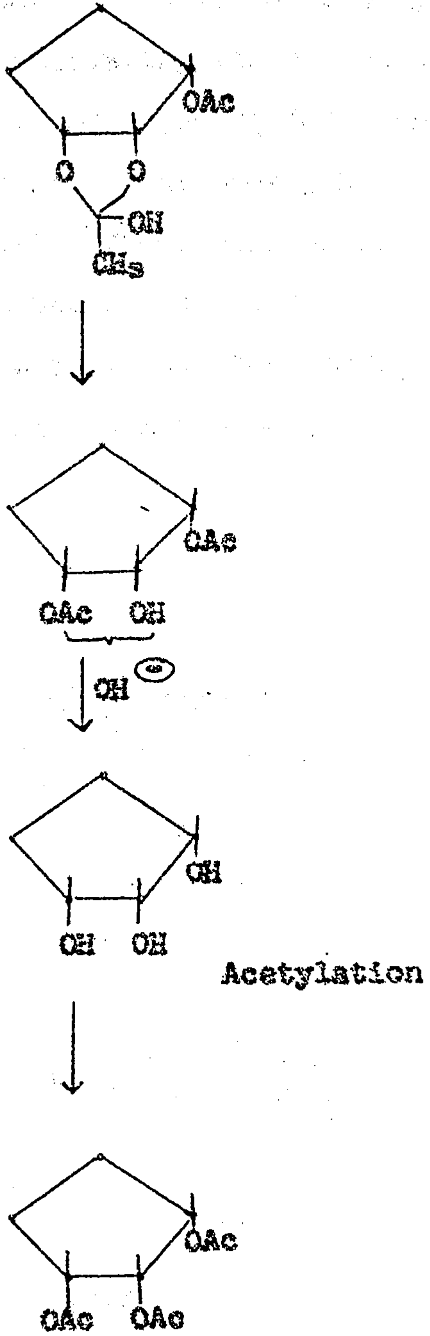
(c) The crystalline triacetate under these conditions showed a retention time of 12' 16" and gave a triol with R_f = 0.60.

Thus, it became apparent that the three theoretically possible 1,2,3-cyclopentanetriols were formed in the wet Prevost reaction. In the light of the mechanism for the wet Prevost reaction (15), the sequence of reactions could be expected to yield only compounds XV and XVI. The reason for the formation of the third isomer is still obscure.



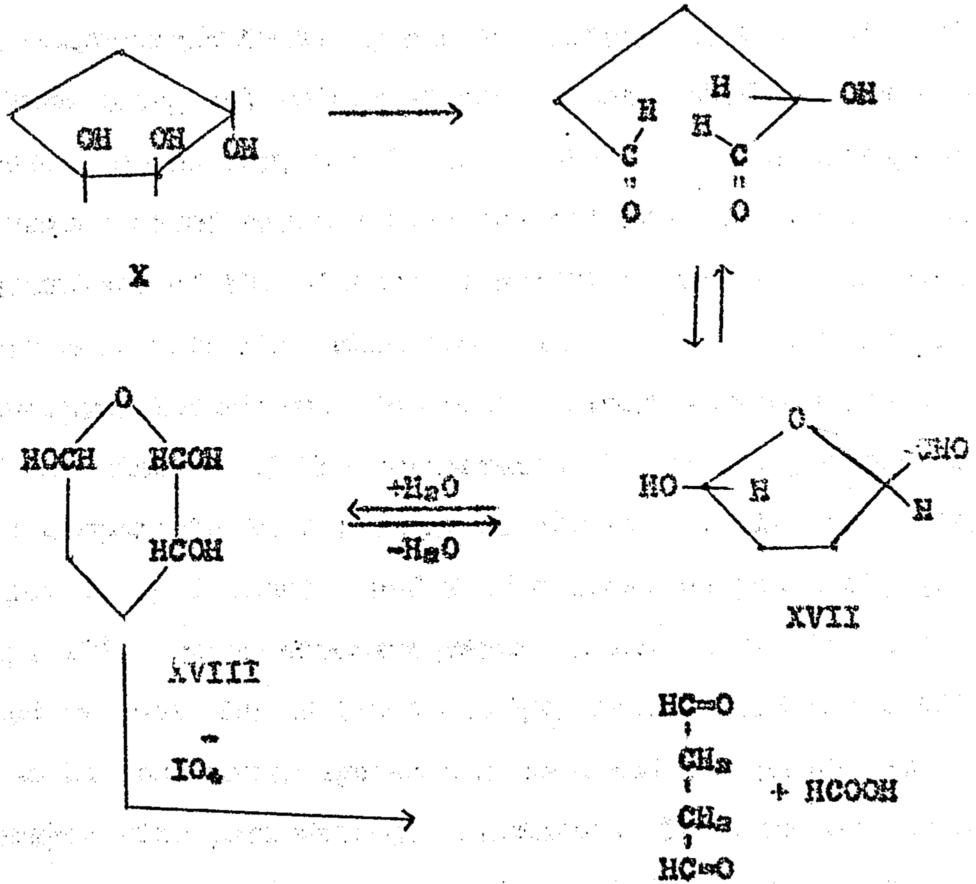

CH₃
C-OH
O
O
OAc
OAc
OH
OAc
OH⊖
OH
OH
OH
XIV
Acetylation
OAc
OAc
OAc

XV


OAc
O
O
OH
CH₃
OAc
OAc
OH
OH⊖
OH
OH
OH
Acetylation
OAc
OAc
OAc

XVI

The triacetate (XV) was deacetylated to a cyclopentanetriol which resisted crystallization. It consumed rapidly (3 minutes) 1.3 moles of periodate indicating the presence of at least one 1,2,-cis-diol grouping. On standing for nearly six hours the total periodate consumption was nearly 2 moles per mole of triol with formation of one mole of formic acid as indicated by titration with base. The course of this reaction can be rationalized as follows. The configuration for compound X is that established later on (see p. 70).



The hydrated structure XVIII would be expected to undergo rapid oxidation by periodate in the manner shown. However, the lactol structure (XVII) would resist periodate action. The slow second stage of the periodate oxidation clearly indicates that XVII was rapidly formed and is substantially more stable than XVIII.

Treatment of 3-acetoxycyclopentene with two equivalents of silver acetate and one mole of iodine in dry acetic acid gave a product, the infrared spectrum of which showed a weak hydroxyl band in the 3500 cm^{-1} region. The product which contained the hydroxyl group was separated from the triacetoxycyclopentanes by chromatography on a silicic acid column using chloroform as the eluent. The hydroxylated product moved very slowly while the 1,2,3-triacetoxycyclopentanes moved rapidly down the column. The saponification equivalent of the mixture of acetates was 82.8, in close agreement with the calculated value of 81.3 for the triacetoxycyclopentane. Gas phase chromatographic analysis of the mixture of the triacetates showed the presence of two components in the ratio of 72% to 28% with retention times of 25.1 minutes and 22.8 minutes respectively (see Fig. 12). Paper chromatographic analysis of the deacetylated product showed two spots (R_f values 0.15 and 0.42) when butanol-water system was used and the paper was sprayed with periodate-permanganate. The fast moving zone gave such a faint reaction with periodate-permanganate

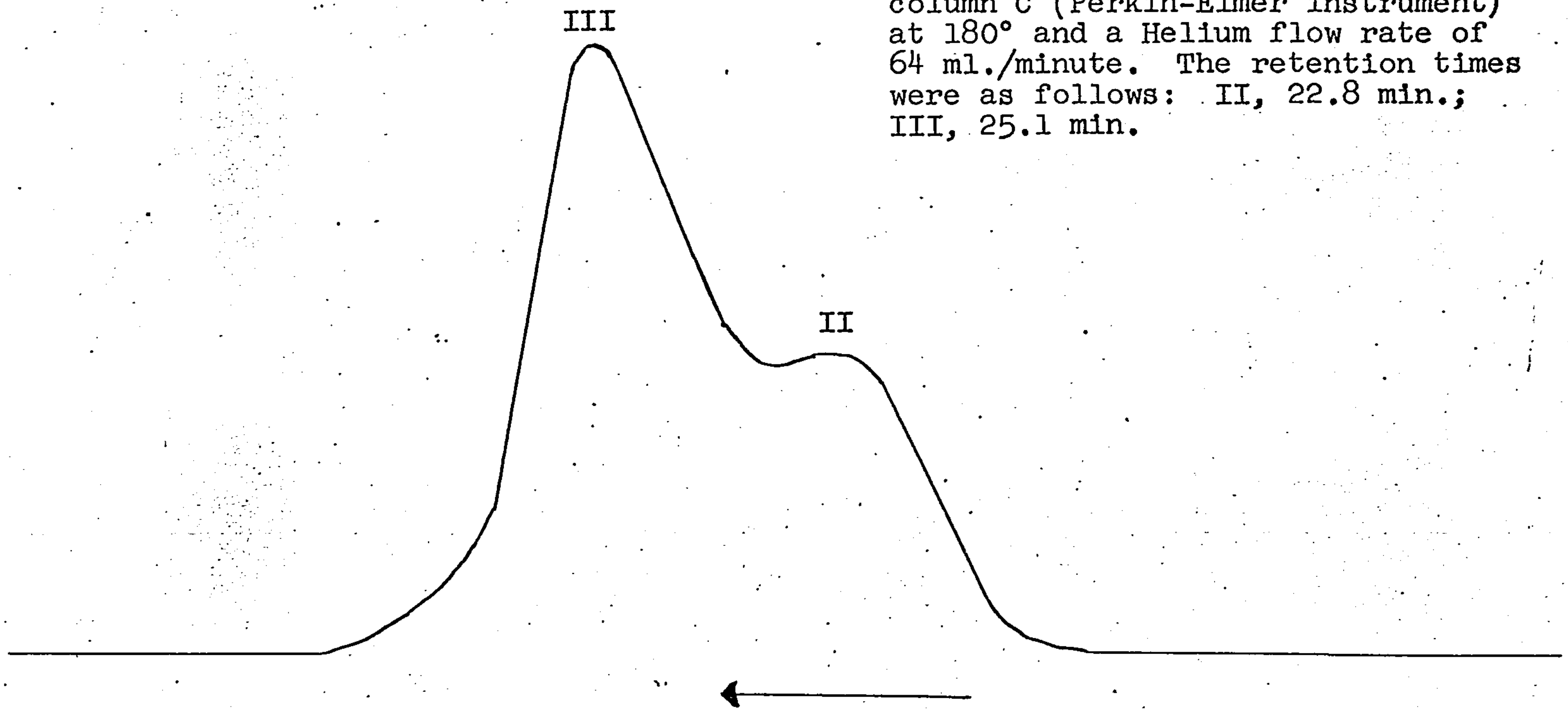


Fig. 12. The vapor phase chromatogram of mixture of triacetates obtained from 3-acetoxycyclopentene by treating it with two equivalents of silver acetate and one mole of iodine in dry acetic acid. The chromatogram was performed using column C (Perkin-Elmer instrument) at 180° and a Helium flow rate of 64 ml./minute. The retention times were as follows: II, 22.8 min.; III, 25.1 min.

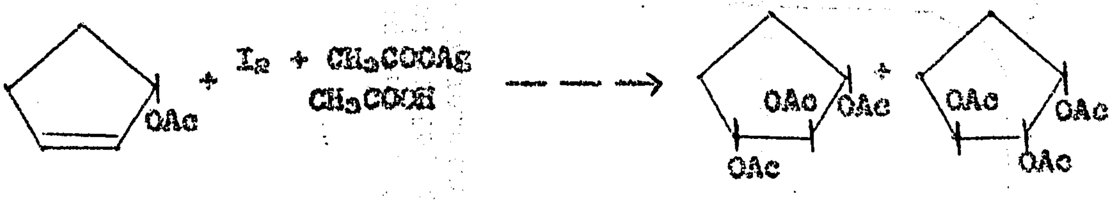
reagent that it seemed unlikely that it represented one of the compounds identified in the vapor-phase chromatogram of the acetylated mixture. Therefore, a search for a more suitable solvent system was made. It proved possible to separate the mixture into three components using the following solvent systems.

butanol-acetic acid-water (4:1:5 by volume)
0.31 0.53 and 0.89 (faint)
methyl-ethyl-ketone-xylene-water (1:1:1 by volume)
0.54 0.69 and 0.84 (faint)

Since the paper chromatographic analysis using n-butanol-acetic acid-water system showed a separation of the triols, this solvent system was used for separation by partition chromatography using Celite to hold the aqueous phase (29). Fractions of the eluate were collected and after combining the appropriate fractions as detected by paper chromatography, the solvent was removed and the residue was dried *in vacuo*. The fractions were oxidized with sodium periodate at room temperature for 24 hours and this was followed by a distillation using the lyophilization procedure described by Lemieux and Barette (41) to test for formic acid. Except for the fast moving spot fraction, nearly one mole of volatile acid was formed as expected for the oxidation of a 1,2,3-cyclopentanetriol using an excess of periodate. Therefore, it was apparent that the two slower moving substances were indeed isomeric 1,2,3-cyclopentanetriols. The p-nitrobenzoates of these two fractions, R_f 0.53 and R_f 0.31, were found to melt at 135-136.5° and 200-204°, respectively.

In a separate experiment, the triols obtained by way of the dry Prevost reaction were treated with excess of dry acetone in the presence of anhydrous copper sulphate and, after dilution with water the isopropylidene derivative was isolated by continuous extraction with ether. The ether extract contained an oil which was distilled. The substance moved as a single compound on vapor phase chromatography and possessed an infrared spectrum in general agreement with expected for a monoisopropylidine derivative of a 1,2,3-trihydroxycyclopentane. There was, however, a weak carbonyl absorption band which showed the compound to be impure. No further work was done with this fraction.

The aqueous layer from the above extraction was evaporated to near dryness and the residue was subjected to preparative partition chromatography using n-butanol-water as the solvent system and Celite to hold the static aqueous phase. The fractions which contained triol were located by paper chromatography and combined to yield a syrup which was dehydrated by azeotropic distillation with benzene. On periodate oxidation, the substance consumed 1.17 and 1.94 moles of the oxidant per mole, assuming that the material was 1,2,3-cyclopentanetriol, after 2 and 161 mins., respectively, at 0°. One equivalent of volatile acid was liberated after oxidation for 24 hours. Therefore, the substance can be assumed to be 1,2,3-cyclopentanetriol. The material was acetylated and the product was distilled. Analysis (saponofication equivalent, carbon and hydrogen) gave values in agreement with those expected for a triacetoxycyclopentane. The NMR spectrum of this substance is reproduced in Fig. 13. The triacetate was analyzed by gas-phase chromatography. Only one peak was obtained with a retention time of 22.8 minutes. This retention time was the same as that for the minor component (28%, zone II of Fig. 12) of the mixture obtained in the dry Prevost reaction. There was no indication of the major component and it could therefore be concluded that the reaction with acetone had effected a separation. Also, presumably, the triol which resisted reaction with acetone possessed no 1,2,cis-diol group. Consequently, the indication was that the all trans 1α,2β,3α-triacetoxycyclopentane was the minor component in the dry Prevost reaction.



XIV XIX XX

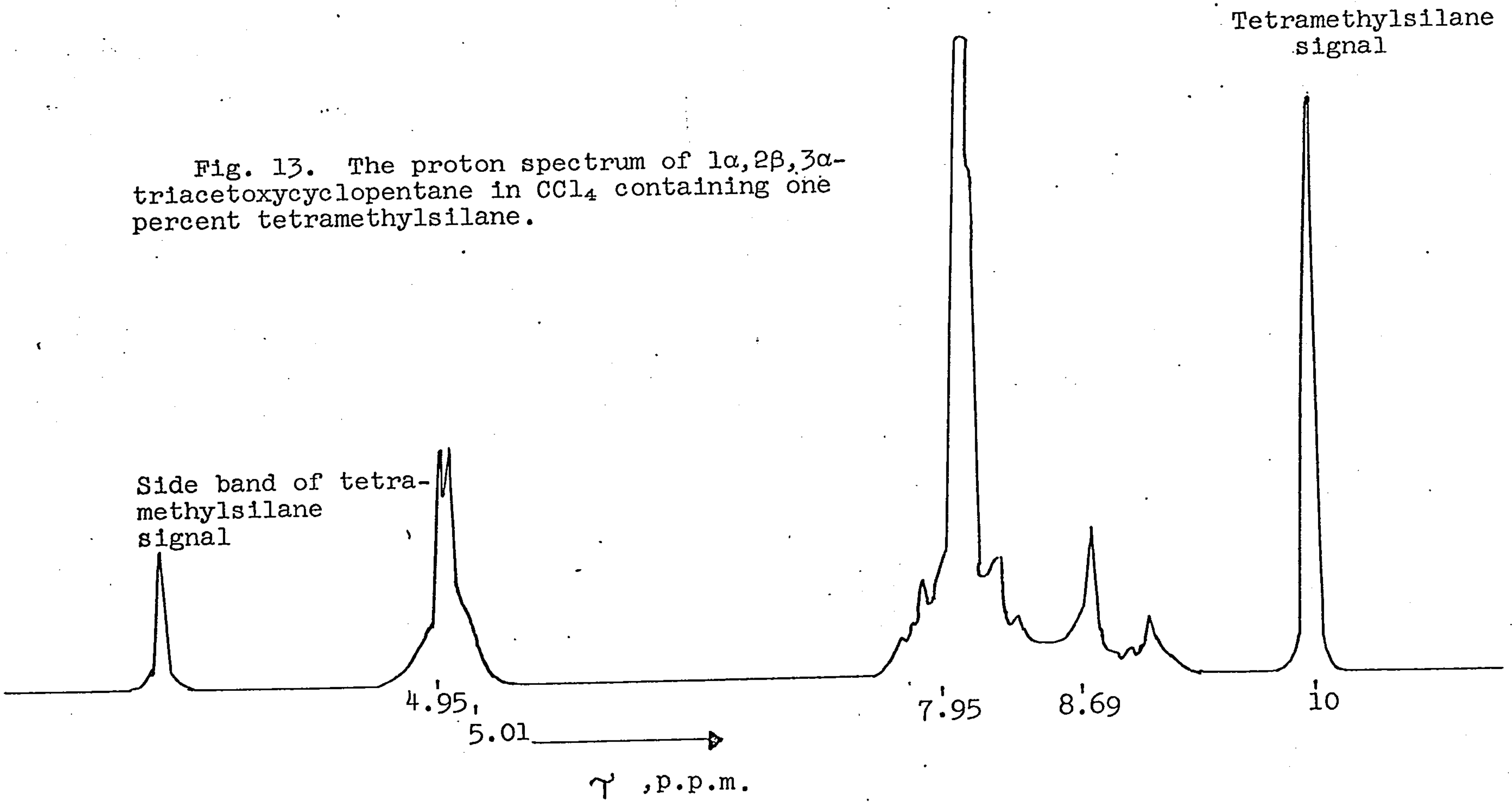
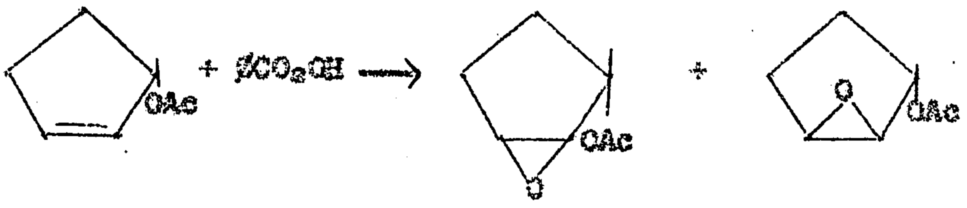


Fig. 13. The proton spectrum of 1α,2β,3α-triacetoxycyclopentane in CCl_4 containing one percent tetramethylsilane.

The product obtained by the dry Prevost reaction of 3-acetoxycyclopentene was deacetylated and the corresponding triols were examined by chromatography using boric acid impregnated paper. Two spots having R_f values as 0.44 and 0.60 were seen when the paper was sprayed with periodate-permanganate solution. Then two isomeric 1,2,3-trihydroxycyclopentanes were separated by partition chromatography as described in the case of triols obtained from the wet Prevost reaction of 3-acetoxycyclopentene. The results of the partition chromatograms are summarized in Table III.

A study was made of the epoxidation of 3-acetoxycyclopentene. The epoxidation with perbenzoic acid could be expected to yield both the *cis* and *trans* oxides (XXI, XXII). In fact, a vapor-phase chromatographic analysis of the product suggested the presence of only one component both when glycerol and silicon oil columns were used.



XIV XXI XXII

The compound, b.p. 88-89° (12.5 mm.) $n_D^{26.5}$ 1.4498, possessed the expected carbon and hydrogen contents. A comparison of its infrared spectrum with that of 3-acetoxy-

Table III

Chromatographic Characterization of the Products Formed in the Dry Prevost Reaction of 3-Acetoxycyclopentene

Tube No. (a)	R_f (b)
1-15	0.60 (c)
19-27	0.44

(a) Celite partition column chromatography

(b) Paper chromatography

(c) This material was acetylated and the product showed a retention time of 12'15" under conditions where the crystalline triacetate showed a retention time of 12'16".

cyclopentene suggests that a band at 897 cm^{-1} is characteristic of oxide ring.(42).

The configuration of the oxide was established by reduction with lithium aluminum hydride. The product of the reduction was shown to contain at least two cyclopentanediols by vapor-phase chromatography using a glycerol column. The reduced product was chromatographed using boric acid-impregnated paper. *Cis* and *trans* 1,2 cyclopentanediols were also run along with the reduced product of the epoxide. The latter product had the same R$_f$ value as that of *trans*-1,2-cyclopentanediol. Therefore, *trans*-oxide was formed when 3-acetoxycyclopentene was treated with perbenzoic acid. This result is in agreement with a prediction based on the results obtained by Henbest and Wilson (43) on the epoxidation of 3-acetoxycyclohexene with perbenzoic acid. Only the *trans*-oxide was formed.

The product of the oxidation of 3-acetoxycyclopentene with perbenzoic acid was converted to a material on alkaline hydrolysis which produced a spot on paper chromatography (n-butanol-water system) in the region characteristic of cyclopentane triols. The product was converted to the corresponding triacetate(s), the vapor-phase chromatographic analysis of which showed the presence of two components in the ratio of 82% to 18% when silicon oil column was used (see Figure 14). The retention times for these components were slightly different from those of the corresponding

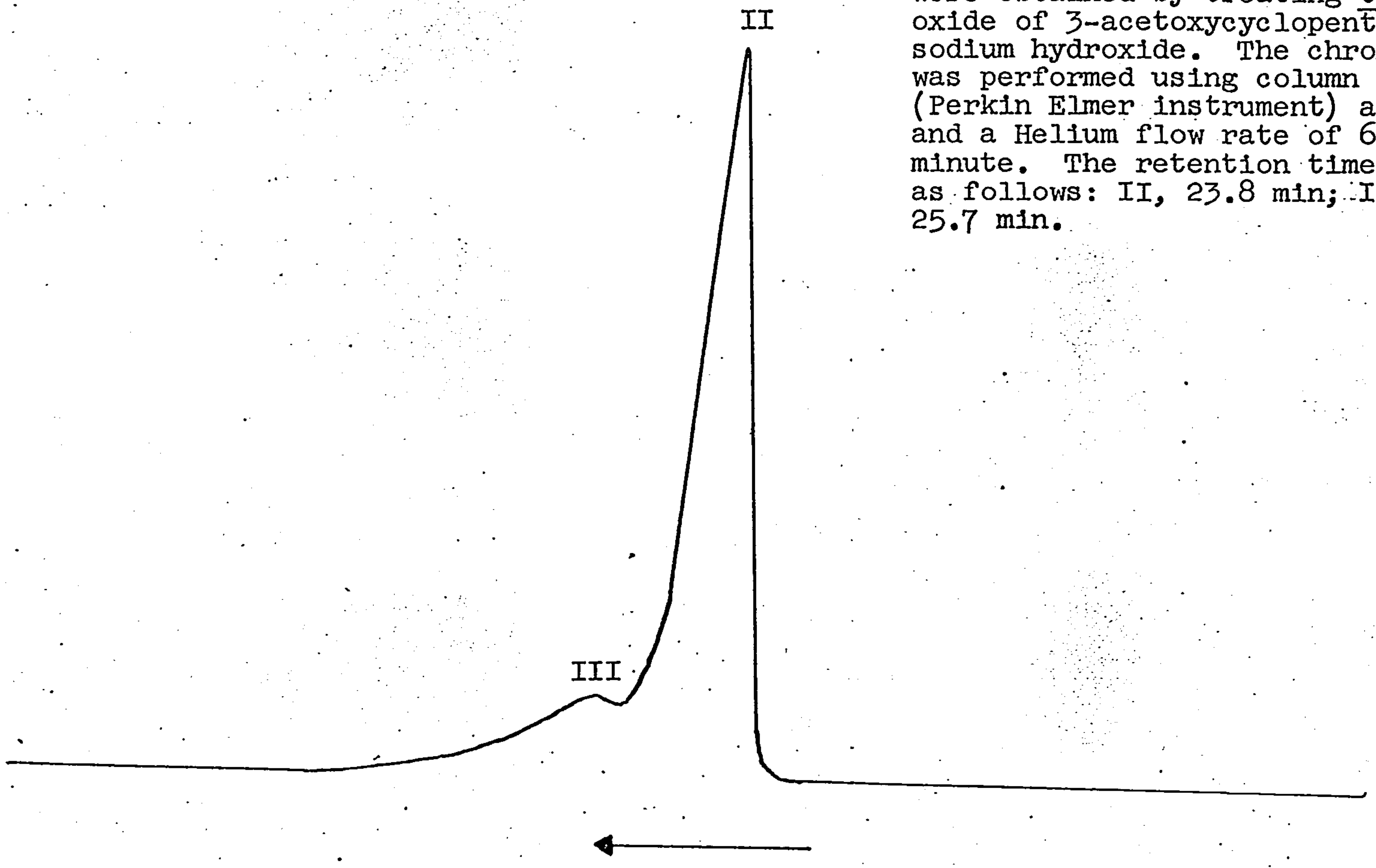


Fig. 14. The vapor phase chromatogram of mixture of triacetates obtained from triols which were obtained by treating *trans*-oxide of 3-acetoxycyclopentene with sodium hydroxide. The chromatogram was performed using column C (Perkin Elmer instrument) at 176° and a Helium flow rate of 60 ml./minute. The retention times were as follows: II, 23.8 min; III, 25.7 min.

triacetates obtained in the case of dry Prevost reaction of 3-acetoxycyclopentene when these were run under the same conditions. (See Table IV). The triols obtained by treatment of epoxide with sodium hydroxide were separated by partition chromatography under the conditions used for triols obtained from wet Prevost reaction of 3-acetoxycyclopentene. The triacetate prepared from the triol obtained as the minor component on the hydrolysis of the epoxide (XXII) had the same retention time as that of crystalline triacetate obtained in wet Prevost reaction of 3-acetoxycyclopentene.

The opening of an oxide ring by alkaline hydrolysis requires inversion of the reacting center. Therefore, the hydrolysis of a 3-acetoxycyclopentene oxide must lead to a mixture of the 1α,2α,3β- and 1α,2β,3α-cyclopentanetriols. A comparison of the chromatographic properties of the product of the hydrolysis (Table IV) with the corresponding substances obtained from 3-acetoxycyclopentene by way of the dry Prevost reaction (Table III) clearly indicates that the same cyclopentanetriols were obtained in each series of experiments. This is not surprising in view of the mechanism of the dry Prevost reaction (see p. 8). However, it is to be noted that evidence has accumulated that 1,2-acetoxonium ions may undergo a ring-opening reaction to yield a 1,2-*cis*-diacetate even in dry, non-acidic media (44).

Table IV

Chromatographic Characterization of the Products Formed by Alkaline Hydrolysis of Epoxide of 3-Acetoxycyclopentene

Tube No. (a)	R_f (b)
1-16	0.60 (c)
19-26	0.44

(a) Celite partition column chromatography

(b) Paper chromatography

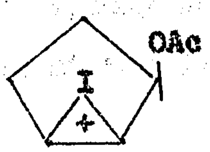
(c) This material was acetylated and the product showed a retention time of 12'15" under conditions where the crystalline triacetate showed a retention time of 12'16".

A comparison of the results described in Tables III and IV with those given in Table II allows the conclusion that the compound with $R_f = 0.77$ which formed in the wet Prevost reaction is the all- cis- 1α,2α,3α-cyclopentanetriol. There remains the problem of the identification of the two triols (1α,2α,3β and 1α,2β,3α) described in Tables III and IV. The wet Prevost reaction is designed to yield a 1,2-cis-glycol grouping. Lemieux and Cipera (45) have shown the acetoxonium ion to be highly effective scavenger for water molecules. It is therefore inconceivable that the major product of the wet Prevost reaction, namely the compound which yielded the crystalline triacetate (XV) of the triol with $R_f = 60$ (boric acid-impregnated paper), does not contain a cis-1,2-diol grouping. Therefore, it can be concluded that the crystalline acetate possesses the 1α,2α,3β configuration.

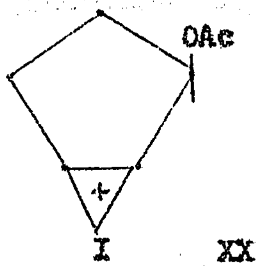
Table V summarizes the approximate yields, as indicated by vapor phase chromatography, of isomers formed in the wet and dry Prevost reactions of 3-acetoxycyclopentene and in the hydrolysis of the trans-3-acetoxycyclopentene oxide. It is of interest to attempt a conformational analysis of these stereochemical results.

First of all, it is evident that the formation of the 1α,2α,3β-isomer in about 81% yield in the wet Prevost reaction requires that the cis-iodonium ion XXIII reacts more rapidly with acetate than does the trans-iodonium ion XXIV.

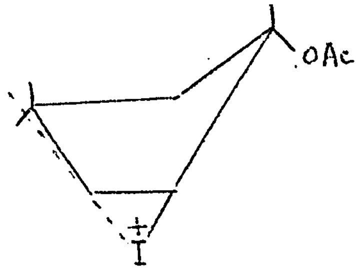
This conclusion is based on the assumption that the iodonium ions are formed reversibly and rapidly as compared to the second stage of the reaction. Kavadias (46) has reported evidence in support of this contention. Thus, it is apparent that, as found by Kavadias for analogous derivatives of cyclohexane, the *cis*-iodonium ion(XXIII) reacts by way of the transition state (XXV).



XXIII

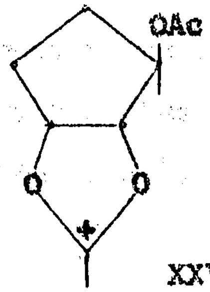


XXIV



XXV

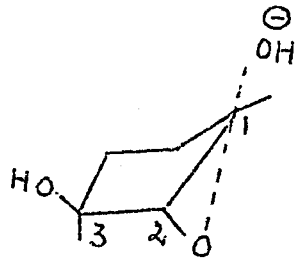
The 1α,2α,3β-configuration of the main product of the wet Prevost reaction can only be achieved by way of the *trans*-acetoxonium ion XXVI.



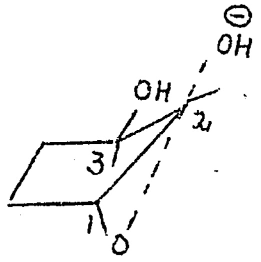
XXVI

In view of the high concentration of the trans-acetoxonium which must have prevailed in view of the result of the wet Prevost reaction, it is apparent that this is a favorable route for reaction.

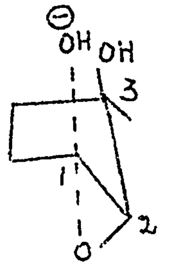
The composition of the product obtained in the hydrolysis of trans-3-acetoxycyclopentene oxide (see Table V) indicates that the 1-position was attacked about four times more rapidly than the 2-position preferentially taken place at the 1-position in (a).



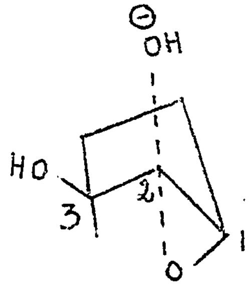
(a)



(b)



(c)



(d)

Out of the different transition states for the opening of the trans-epoxide with sodium hydroxide (four conformations can exist for this oxide), form (a) seems to be more

Table V

Yields of Isomeric 1,2,3-Cyclopentanetriols or Acetyl Derivatives

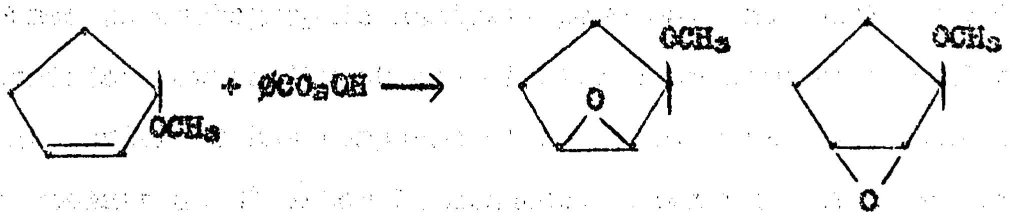
Reaction		Yield	
	1α,2α,3β	1α,2β,3α	1α,2α,3α
Wet Prevost	81%	12%	8%
Dry Prevost	72%	28%	
Hydrolysis of Oxide	18%	82%	

suitable than forms (b), (c), or (d), since this will give α,β,α triol by diaxial opening of the oxide. Also, there will not be much interaction between the incoming group and the group already present in the ring. The transition state will be colinear.

The hydrolyzate obtained by the alkaline hydrolysis of 3-acetoxy 1,2 epoxide of cyclopentane was converted to the tri-p-nitrobenzoyl ester derivative which was chromatographed on silicic acid-Celite with Rhodamine 6G as internal indicator (47-49) to yield two crystalline compounds, m.p. 88-91 and 200-203. Both the compounds on saponification gave alcohols with R_f values identical to the product obtained on hydrolysis of the 3-acetoxycyclopentene oxide. The higher melting ester was identical (mixed m.p. and infrared) as the tri-p-nitrobenzoate of a triol obtained by way of the dry Prevost reaction (see page 61). Although there was not sufficient material to properly analyze the above compounds, they were definitely observed to move at different rates on the column and cannot be identical. In view of the fact that the triols derived from these p-nitrobenzoates were prepared by the opening of the oxide ring, there must be present a 1,2-<u>trans</u> glycol grouping in both the triols. Since both the p-nitrobenzoates showed no hydroxyl band in the infrared, both the compounds must be tri-p-nitrobenzoates. The tri-p-nitrobenzoate obtained from the triol prepared from the crystalline triacetate melted at 135-136.5° and hence the triol which gave a tri-p-nitrobenzoate melting at 200-203° must have a β α configuration. The solid derivative, m.p. 88-91°, obtained from the triol present in the minor amount of epoxide hydrolyzate may be a mixture of high and low melting derivatives.

It was felt that 3-methoxycyclopentene (XXVII) could serve as a starting material for the preparation of a variety of 1,2-disubstituted 3-methoxycyclopentanes. The only mention of 3-methoxycyclopentene found in the literature was that in the Ph.D. Dissertation by Vaughn (38) and involved the reaction of 3-chlorocyclopentene with methanol in the presence of sodium bicarbonate. The procedure was found to proceed in 55% yield.

The epoxidation of 3-methoxycyclopentene with perbenzoic acid could be expected to yield both the cis and trans oxides (XXVIII, XXIX).



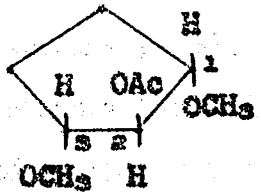
XXVII XXVIII XXIX

In fact, a vapor-phase chromatographic analysis suggested the presence of only one compound in the product. That this was in fact the case was proved by the lithium aluminum hydride reduction of the product of the epoxidation when it gave only two methoxycyclopentanols as indicated by vapor-phase chromatography. These alcohols were present in the ratio of 88% to 12%. The major component was found to have the same infrared spectrum and to show the same retention time on vapor-phase chromatography as an authentic sample of 1,2-trans-methoxycyclopentanol. The authentic sample was obtained by methanolysis of cyclopentene oxide. The infrared spectrum of 2-methoxycyclopentanol obtained by lithium aluminum hydride reduction of 3-methoxycyclopentene oxide using Beckmann Recording Spectrophotometer and lead sulphide cell and having concentration of 0.0096 molar in CCl_4 gave only one band at 3628.8 cm^{-1}. Since the hydroxyl group was not bonded and hence it was trans to the methoxy group in the 2-methoxycyclopentanol.

Treatment of 2-methoxycyclopentanol with hydriodic acid gave a product which when tested for purity by gas phase chromatographic analysis gave only one peak. Sodium periodate oxidation of the distilled product also confirmed the purity of the compound since it consumed 0.97 mole of periodate at 0° after 19 minutes. When this diol was converted into p-nitrobenzoate it gave a solid derivative which when crystallized twice from ethyl acetate melted at 139.5-141°. The mixed melting point with the authentic sample, m.p. 141-142°, remained unchanged and the infrared spectra of both the samples in chloroform solution were the same.

In view of the above results it could be concluded that at least the main product of the perbenzoic acid oxidation of 3-methoxycyclopentene is the trans oxide. This result is thus similar to that obtained by Kavadias (46) in the perbenzoic acid oxidation of 3-methoxycyclohexene. The trans-3-methoxycyclopentene oxide was obtained in 94.4% yield.

Treatment of the trans-oxide of 3-methoxycyclopentene with sodium methoxide gave the corresponding dimethoxycyclopentanols, which on acetylation gave the corresponding acetates. The vapor-phase chromatographic analysis of the acetates showed that they are present in the ratio of 72% and 28% respectively. The separation of the two acetates was achieved by silicic acid column using chloroform as an eluent. The NMR spectrum of the major component (Fig. 10) in carbon tetrachloride containing 1% tetramethyl silane as an internal standard gave a triplet for the hydrogen atom attached to the acetate group.



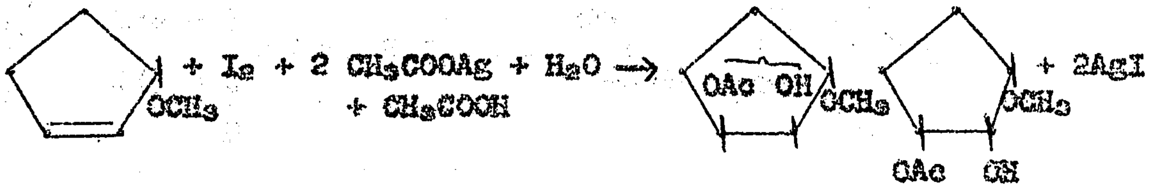
VI

The spacing of the triplet suggests that the average found coupling constant for the H_2 with H_1 and H_3 protons is 2.3

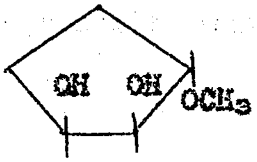
c.p.s. This coupling constant is remarkably small considering the fact that the substance may have the 1α,2β,3α-configuration and, if so, could be expected to possess the conformation (VI) wherein all the large substituents are equatorially oriented.

3-Methoxycyclopentene oxide when treated with sodium hydroxide gave a mixture of methoxycyclopentane diols, the vapor-phase chromatographic analysis of which showed the presence of two components.

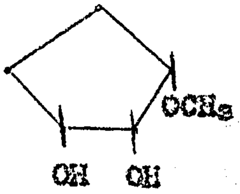
Treatment of 3-methoxycyclopentene with two equivalents of silver acetate and one mole of iodine in wet acetic acid gave the corresponding trisubstituted cyclopentane compounds containing the methoxy, acetoxy and hydroxyl groups as shown by the infrared spectrum. When saponified the product apparently gave two methoxycyclopentane diols (XXX, XXXI) in the ratio of 89% to 11% as determined by vapor-phase chromatography. The purity of the diols obtained in the wet Prevost reaction of 3-methoxycyclopentene was confirmed by sodium periodate oxidation when it consumed 0.98 mole of periodate within 11 minutes at 0°. The infrared spectrum of the diols using Beckmann Recording Spectrophotometer and lead sulphide cell and having concentration of 0.009 molar in CCl_4 gave bands at 3636 cm^{-1}, 3576 cm^{-1} and a little shoulder at 3490 cm^{-1}. On the basis of the above described experience with the reaction of 3-acetoxycyclopentene under the conditions of the wet Prevost reaction, it seems likely that the configurations are these shown.



XXVII

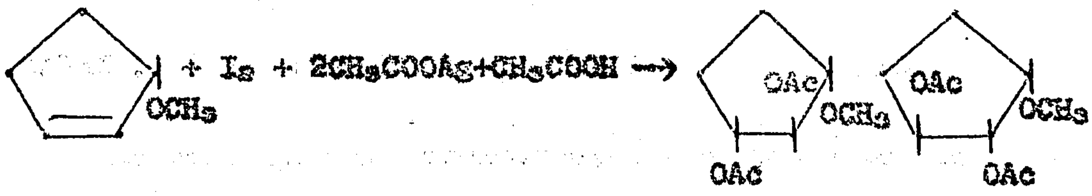


XXX



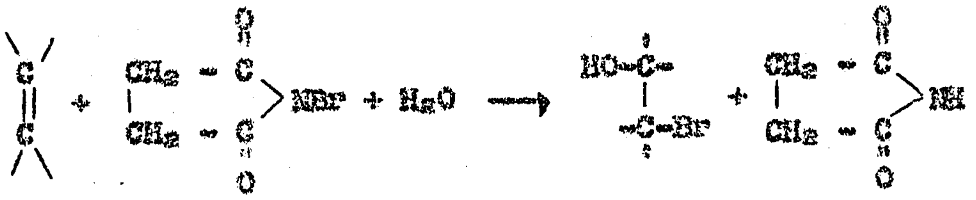
XXXI

When 3-methoxycyclopentene was treated with two equivalents of silver acetate and one mole of iodine in dry acetic acid, it gave two isomers of methoxycyclopentane diacetates in the ratio of 57% to 43% as determined by vapor phase chromatography.

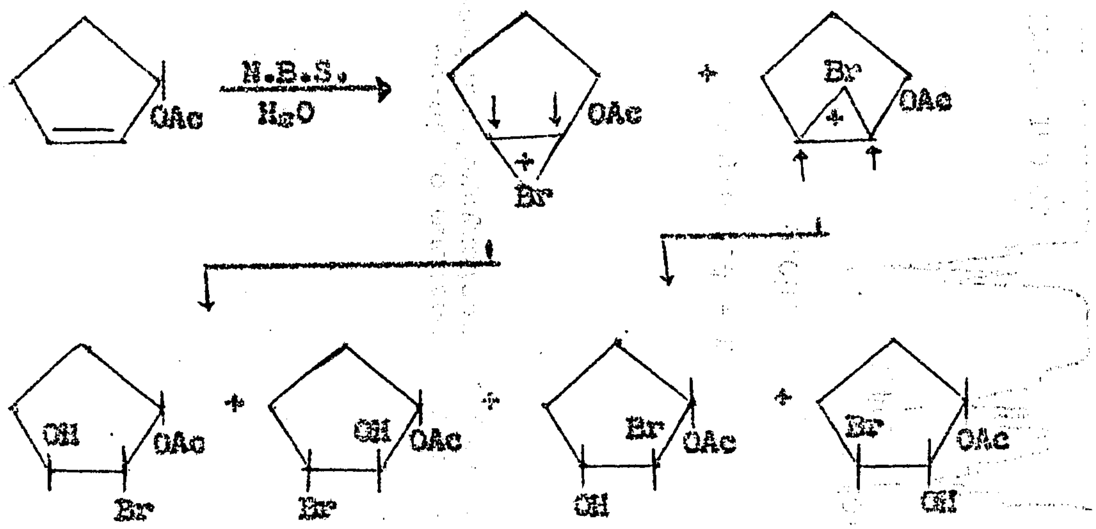


XXVII XXXII XXXIII

Treatment of an olefin with N-bromosuccinimide in water gives bromohydrin (31-36). It is believed that first of all bromonium ion is formed which is then opened by water.



It is expected that four isomers will be formed when 3-acetoxycyclopentene is treated with N-bromosuccinimide in the presence of water.



XXXVII XXXVI XXXIV XXXV

The corresponding bromohydrins were converted into p-nitrobenzoates and the separation of these solid derivatives was tried by adsorption chromatography on Celite-silicic acid column containing some Rhodamine 6G to follow the location of bands. A product melting at 75-76.5° (17%) gave an NMR spectrum as shown in Figure 15. The nice triplet for the hydrogen attached to bromine suggested that it had the structure as given below.

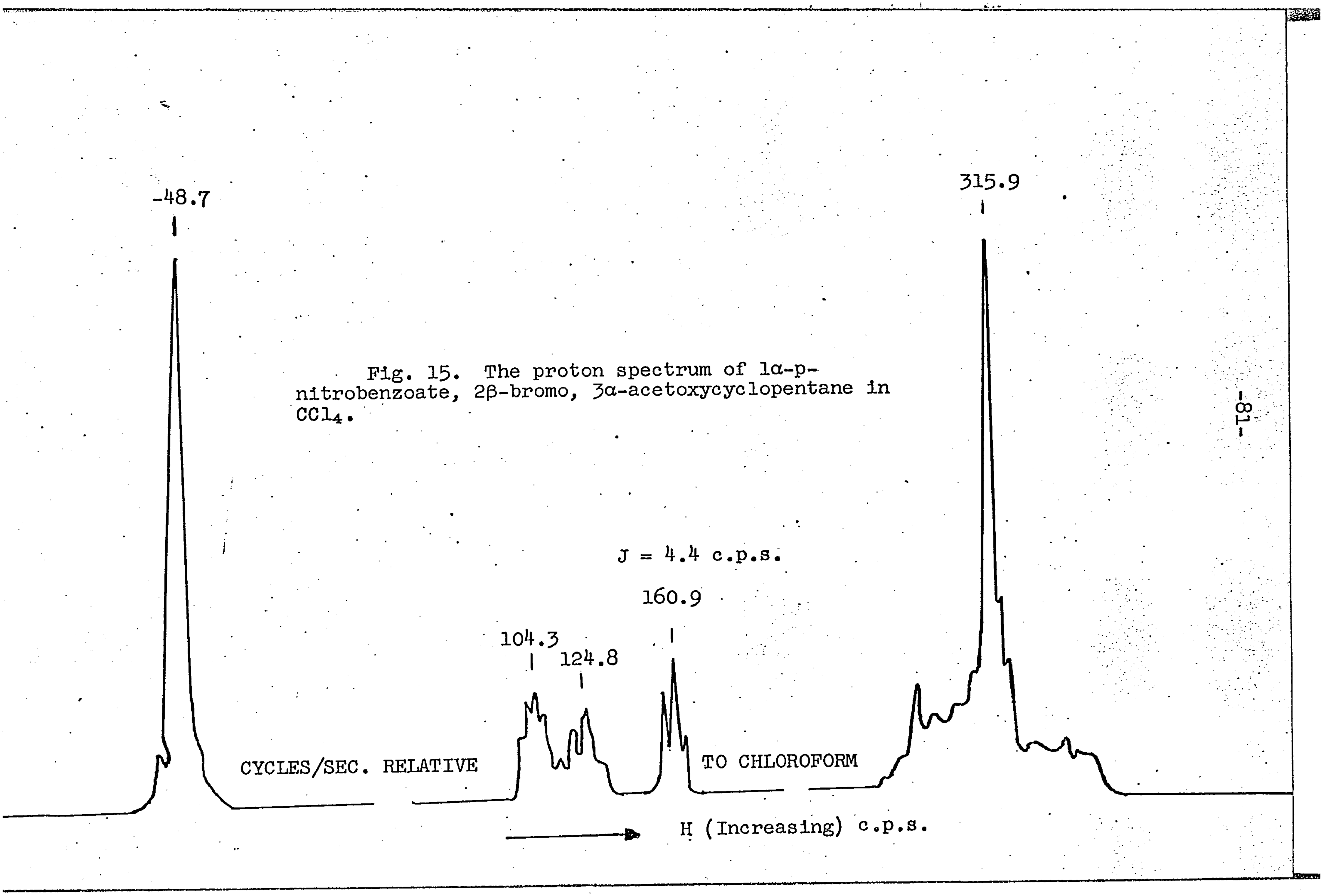
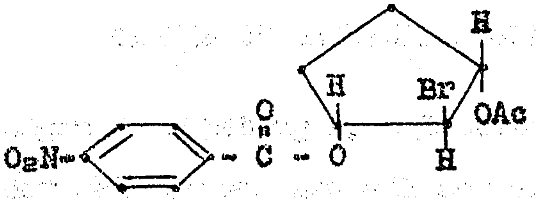


Fig. 15. The proton spectrum of 1α-p-nitrobenzoate, 2β-bromo, 3α-acetoxycyclopentane in CCl_4.



XXXVIII

The compound (XXXVIII) was found to be extremely resistant to solvolysis in acetic acid containing silver acetate. This reactivity could best be rationalized by assuming that the compound possesses the 1α,2β,3α-configuration with bromine atom at the 2-position. Thus, the solvolysis would be hindered through the presence of two highly electronegative neighboring substituents and the participation of one of the acyl groups could be hindered by the presence of the other. The NMR spectrum is in agreement with this contention that the compound has the bromine atom at the 2-position.

CLAIMS OF ORIGINAL RESEARCH

Compounds starting from 3-acetoxycyclopentene and 3-methoxycyclopentene are all new and hence are not reported in the literature.

1. The configuration of the epoxide obtained from 3-acetoxycyclopentene by treating it with perbenzoic acid.

2. The configuration of the epoxide obtained from 3-methoxycyclopentene by treating it with perbenzoic acid.

3. Quantitative determination of the products of the alkaline hydrolysis of *trans*-oxide of 3-acetoxycyclopentene in order to establish the extent of the observed preference of this compound to react at carbon atom -1.

4. New method of separation of diols and triols (cyclopentane and cyclohexane series) by paper chromatography using boric acid impregnated paper and by partition chromatography using Celite to hold the static aqueous phase and n-butanol equilibrated with 5-percent boric acid solution as solvent system.

5. (a) Formation of products other than depicted by mechanism of wet Prevost reaction of 3-acetoxycyclopentene.

(b) Quantitative determination of products formed in the wet and dry Prevost reaction of 3-acetoxycyclopentene.

6. Proof of structures of 1α,2α,3β and 1α,2β,3α cyclopentanetriols and preparation of some solid derivatives of these compounds.

7. Quantitative estimation of methoxycyclopentanols obtained by treating <u>trans</u>-oxide of 3-methoxycyclopentene with lithium aluminum hydride in order to establish the extent of the observed preference of this compound to react at carbon atom -1.

8. Quantitative determination of products formed in the wet and dry Prevost reaction of 3-methoxycyclopentene.

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