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SYNTHESIS OF QUINONES, POLYCYCLIC COMPOUNDS AND SOME TRANSFORMATIONS OF CARBOHYDRATES

A THESIS
SUBMITTED TO THE
UNIVERSITY OF POONA
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN CHEMISTRY

BY
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PUNE - 411008 (INDIA)
1984

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Dedicated to

my parents and brothers

Certified that the work incorporated in the thesis "Synthesis of quinones, polycyclic compounds and some transformations of carbohydrates", submitted by Shri P.L. Joshi was carried out under my supervision. I have Such materials as ~~has~~ been obtained from other sources are ~~were~~ duly acknowledged in the thesis.

A. S. Rao

(Dr.A. Somasekar Rao)
Supervisor

A C K N O W L E D G E M E N T

I take this opportunity to express my sincere gratitude to Dr. A. Somasekar Rao, Scientist, National Chemical Laboratory, Poona, for suggesting the problems tackled herein and offering me invaluable guidance and encouragement throughout the course of this work.

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(P.L. Joshi)

Poona-411008

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CONTENTS

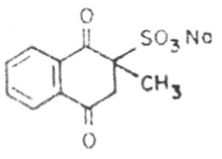
GENERAL REMARKS

1. All melting points and boiling points are uncorrected.
2. All liquid samples whose b.p. are reported were checked for purity on GLC.
3. All extracts were finally dried over anhydrous Na_2SO_4.
4. Pet.ether refer to the fraction boiling between 60-80°.
5. Alumina refers to neutral alumina made in this laboratory.
6. IR Spectra were recorded as liquid film or nujol mull on Perkin-Elmer Infrared Spectrometer-model 137B or 599B; ν_{max} values are given in cm^{-1}.
7. NMR spectra were recorded on a Varian T-60 or WH-90 FT spectrometers, using TMS as internal standard (chemical shift in ppm).
8. Mass spectra were recorded on CEC-21-110B spectrometer.
9. Optical rotations were taken on JASCO-DIP 181 polarimeter.
10. Microanalysis were carried out in the microanalytical section of this laboratory.
11. TLC was performed on silica gel, made in this laboratory. R_f values refers to TLC using the solvent system mentioned in the bracket.
12. The numbers assigned to the charts and figures in each chapter of this thesis refer only to that particular chapter.

CHAPTER – 1

SYNTHESIS OF

6-ACETYL-1,4-DIMETHOXY-2-METHYLNAPHTHALENE



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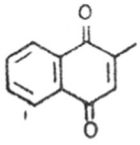

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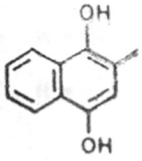

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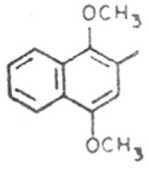

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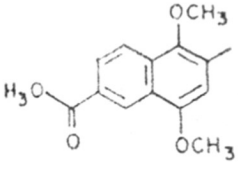

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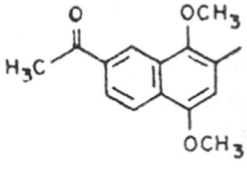

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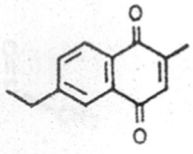

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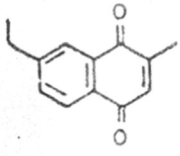

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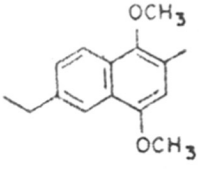

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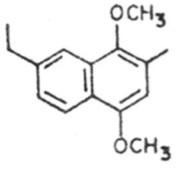

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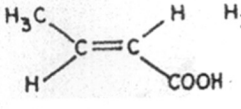

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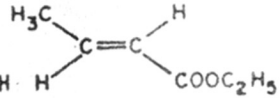

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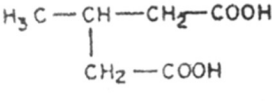

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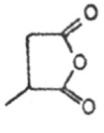

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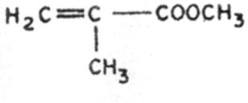

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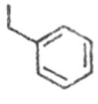

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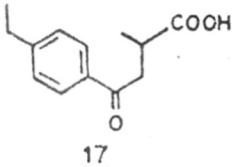

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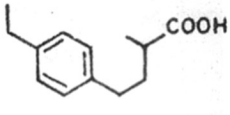

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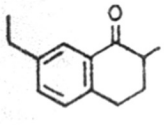

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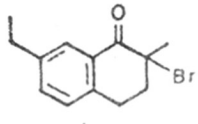

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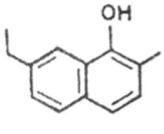

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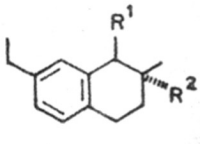
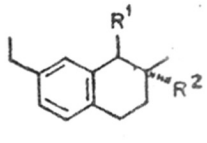


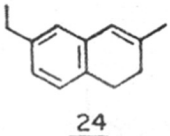
22a R^1 = β-OH, α-H; R^2 = H

22b R^1 = α-OH, β-H; R^2 = H



23a R^1 = β-OAc, α-H, R^2 = H

23b R^1 = α-OAc, β-H, R^2 = H



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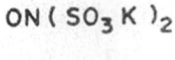

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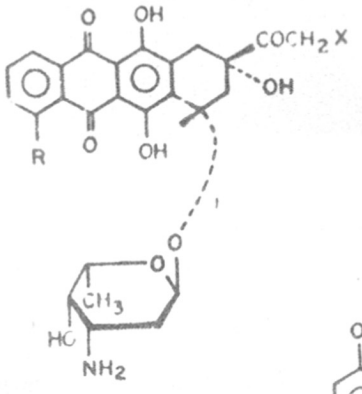
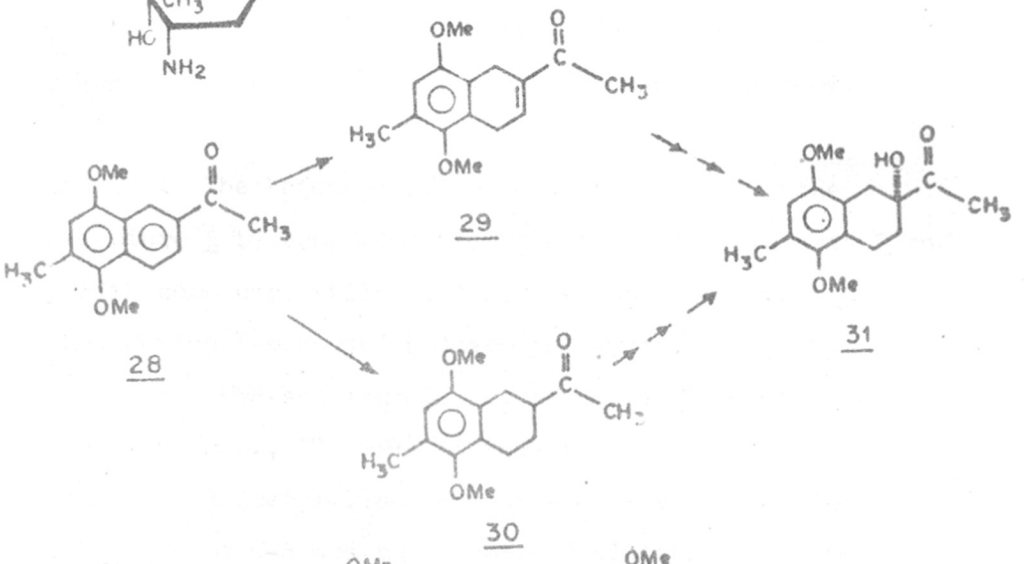


26 R = OCH_3 , X = H

27 R = —OCH_3 , X = OH



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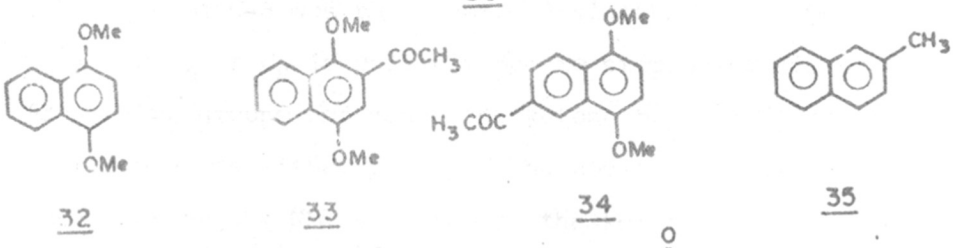

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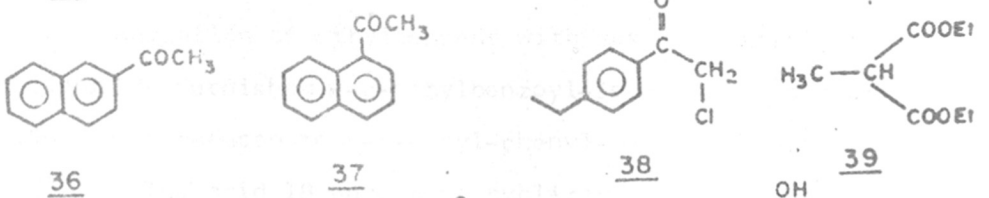

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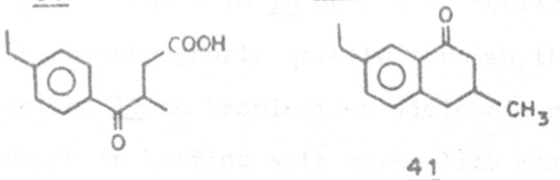

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S U M M A R Y

Acetylation of the arene (4) with acetic anhydride in the presence of anhydrous aluminium chloride furnished a mono acetylation product m.p.105°C, the structure elucidation of which forms the subject matter of this chapter. The ketone m.p.105° has been assigned the structure 5 by comparing its transformation products 7 and 9 with compounds which must have structures 8 and 10 considering the route employed for synthesising them.

From NMR spectrum of ketone m.p.105° and the non-identity (m.p., IR, NMR) of this ketone with an authentic sample of 3-acetyl-1,4-dimethoxy-2-methyl naphthalene, acylation at C-3 was ruled out. Acylation at the peri-position C_5 or C_8 is unlikely due to steric interference from $-OCH_3$ groups and hence the ketone m.p.105°C may be represented as either 5 or 6. The above conclusion was supported by the NMR spectrum of the ketone.

Acylation of ethylbenzene with methyl succinic anhydride furnished β-p-ethylbenzoyl-isobutyric acid (17) which was reduced to γ-p-ethyl-phenyl-α-methyl butyric acid (18). The acid 18 underwent cyclization in the presence of polyphosphoric acid to furnish the ketone (19). The ketone 19 on bromination yielded a monobromo compound (20) which on heating with morpholine was converted to naphthol (21). The naphthol (21) on oxidation with Fremy's salt furnished the quinone (8). The quinone 8 was reduced

and methylated to yield the compound (10).

When the Huang- Minlon reduction of ketone m.p.105° was carried out at 210° for 6 hrs without taking special precautions to exclude air, a naphthoquinone was obtained. The quinone is not identical with authentic 8 since its m.p. was depressed on admixture with authentic sample of 8 and also the NMR spectra of the quinones were found to be different. In view of this observation and conclusion arrived earlier that ketone m.p.105° must have structure 5 or 6, it is evident that the quinone obtained after Huang-Minlon reduction is 7 and consequently ketone m.p.105° has the structure 5.

Huang-Minlon reduction of ketone m.p.105° at 200° for 30 mins. under nitrogen atmosphere furnished a product whose NMR spectrum agreed with the structure 9. Comparison of NMR spectra of 9 with authentic 10 clearly showed that they are not identical. Further more oxidation of compound 9 with ceric ammonium nitrate furnished the quinone 7. Considering all these observations the ketone m.p.105°C is assigned the structure 5.

INTRODUCTION

Cancer is still one of the scourges of man, but encouraging results with various types of treatment offer hope for continuing advances in the fight against this disease. The most frequently used treatments at present are surgery, radiation (including radioactive isotopes) and chemotherapy, with future possibilities for immunotherapy.

Although most of current neoplastic drugs were discovered emperically considerable insight has been gained into the mechanisms by which many of these compounds affect cell growth and this was allowed a more rational therapeutic application of these agents. The insight has also led to the development of new drugs designed to kill the cancer cell either directly or by depleting its essential growth elements. In addition to the discovery of new experimental compounds chemotherapy research has been directed towards alteration in dosimetry and employment of various drug combinations to enhance tumerocidal effects and decrease toxicity. Decrease in tumor mass and metastatic involvement may be ob ained with chemotherapy alone. Moreover it has proved to be a valuable adjunct to surgical and irradiation procedures. Today several neoplastic diseases can be associated with a normal life expectancy after drug treatment, alone or in combination with other type of therapy.

Among the various compounds which are promising as antitumor agents, natural products, either of plant or microbial origin are showing much more specificity in their anticancer properties. Many of them possess structures and clinical properties which suggest that they may act by selective alkylation of growth regulatory macromolecules.

The utility of certain anthracycline antibiotics as antineoplastic agents is now widely accepted. Both daunomycin (26) and adriamycin (27) produced by streptomyces peucetius (Family: streptomycetaceae) and a mutant strains respectively have shown pronounced anticancer activity in some types of human cancer[1,2]. Daunomycin (26) and adriamycin (27) are main representatives of the anthracycline group of antibiotics which also includes nogalamycin, cinerubin, rhodomycins and rubomycins. Daunomycin has achieved a significant place in the treatment of acute lymphocyclic and myelogenous leukemias. Adriamycin is also an active antileukemic drug but is of much greater interest because of its activity against a broad spectrum of solid tumors.

Taking into consideration the earlier literature reports compound (31) can act as a key intermediate in the synthesis of adriamycin analogues. Considering the possibility of obtaining (31) starting from a naphthalene precursor an acylation on 1,4-dimethoxy-2-methylnaphthalene was studied.

Literature[2] shows that when 1,4-dimethoxy naphthalene was acylated using C_4-C_{12} acid chlorides in presence of aluminium chloride in carbondisulphide as a solvent to furnish 6-acetyl-1,4-dimethoxynaphthalene in 19-33% yield and 2-acyl-1-hydroxy-4-methoxynaphthalene in 21-44% yields. By this analogy it was felt that the acetylation of 1,4-dimethoxy-2-methyl-naphthalene would produce single 6-acetyl-1,4-dimethoxy-2-methylnaphthalene since 2 position is blocked by methyl group.

Available literature suggests that metal ammonia reduction of (28) may furnish compounds (29) or (30) which are potential intermediates for the preparation of (31) which can be further converted into (26) or (27).

Methyl group at 2 position may be expected to serve as a convenient handle to introduce the A and B rings in (26) and (27).

Though we were successful in an initial objective to synthesise (5), we have not carried out further work to transform (5) to adriamycin analogues since Dr.A.V.Rama Rao and his group started work in this area in our laboratory and we decided to avoid duplication of studies.

PRESENT WORK

It is reported in the literature[3] that acetylation of 1,4-dimethoxynaphthalene furnished a mixture of 2-acetyl-1, 4-dimethoxy naphthalene and 6-acetyl-1,4-dimethoxy-naphthalene in varying ratios depending on experimental conditions. Another literature reference[4] states that 2-alkylnaphthalenes react predominantly in the amphi (6) position during Friedel-Craft reaction e.g. 2-methyl-naphthalene. Acetylation at C-3 would be difficult due to steric interference of methyl at C-2 and $-OCH_3$ at C-4. Attack at C-5 and C-8 would be unlikely due to steric interference of methoxy groups. Hence attack at amphi(C-6) position is anticipated. Considering these facts and keeping in mind the synthetic target as 6-acetyl-1,4-dimethoxy-2-methylnaphthalene (5), Friedel-Craft acetylation reaction on 1,4-dimethoxy-2-methylnaphthalene was studied.

2-Methyl-1,4-naphthoquinone (2) was obtained by treating the bisulphite adduct (1) with saturated aqueous sodium carbonate. The naphthoquinone (2) was reduced with stannous chloride to obtain the hydroquinone (3) which was subsequently methylated using dimethyl sulphate to get 1,4-dimethoxy-2-methylnaphthalene (4).

Friedel-Craft's acetylation of 4 with acetic anhydride and anhydrous aluminium chloride in carbon-

disulphide as a solvent, furnished a monoacetylation product, m.p.105°. Its IR spectrum shows bands at 1670 cm^{-1} and 1625 cm^{-1} indicating the presence of conjugated carbonyl group. The NMR spectrum in carbontetrachloride exhibits signals at 2.45 (3H, s, Ar-$C\underline{H}_3$), 2.67 (3H, s, -$COC\underline{H}_3$), 3.85 (3H, s, -$OC\underline{H}_3$), 4.02 (3H, s, -OCH_3), 6.60 (1H, s, C_3-$\underline{H}$), 8.03 (1H, s, C_8-H), 8.03 (1H, d, J = 2 Hz, C_7-H), 8.73 (1H, d, J = 2 Hz, C_5-H).

Microanalytical data fits well with the molecular formula $C_{15}H_{16}O_3$, confirming that the product obtained is a monoacylation product.

The acetylation product exhibitted a one proton singlet at 6.6 in the NMR spectrum showing the presence of hydrogen at C-3 thereby ruling out the possibility of acylation at C-3. Further support was provided by the nonidentity (m.p., IR, NMR) of this ketone m.p.105°C with a sample which must be 3-acetyl-1,4-dimethoxy-2-methyl-naphthalene considering the method employed for its preparation. Treatment of 1,4-dimethoxy-3-formyl-2-methylnaphthalene with methyl magnesium iodide furnished the alcohol 1-[1,4-dimethoxy-2-methyl-2-naphthyl]-ethanol which on oxidation yielded the ketone, 3-acetyl-1,4-dimethoxy-2-methylnaphthalene m.p.68°. Evidently during acylation of 4 the acetyl group has been introduced in the ring not carrying -OCH_3 groups. Acetylation at the

periposition is unlikely due to steric interference from $-OCH_3$ groups and hence the ketone m.p.105° may be represented by either structure 5 or 6. This was supported by the NMR spectrum of ketone which exhibited a one proton doublet (J= 2 Hz) at 8.73. Reported[5] NMR data of 1-acetyl naphthalene (37) and 2-acetylnaphthalene (36) is as follows

1-Acetylnaphthalene (37)		2-Acetylnaphthalene (36)	
H-2	7.794	H-1	8.296
H-3	7.340	H-3	7.921
H-4	7.838	H-4	7.75
H-5	7.727	H-5	7.749
H-6	7.413	H-6	7.478
H-7	7.491	H-7	7.434
H-8	8.760	H-8	7.825

The above data shows that in case of 1-acetyl-naphthalene only C-8(peri) proton goes quite downfield If the acylation in our reaction has taken place at 5 or 8 position then there should not be any downfield signal since there is no proton at C-1 (peri to 8) or C-4 (peri to 5) which are blocked by $-OCH_3$ groups. So possibility of acylation at C-5 and C-8 was ruled out.

If we consider the data for 2-acetyl naphthalene it shows a signal at 8.296 for C-1 proton. If the acylation has taken place at C-6 or C-7, in each case there is a

proton av ailable at C-5 and C-8 respectively, which can show a marked downfield signal. Such a downfield signal is observed (8.73) in NMR of ketone m.p.105. So the acylation might have taken place at C-6 or C-7. To establish whether 5 or 6 is the structure of ketone m.p.105° we unambiguously synthesised the reference compounds (8) and (10).

Methyl succinic acid was prepared from methylmetha acrylate via (1) Michael addition of CN employing NaCN and (2) hydrolysis of the Michael adduct with barium hydroxide in 66% yield. Methyl succinic acid was reacted with acetyl chloride to furnish methyl succinic anhydride (14). Acylation of ethyl benzene (16) with methyl succinic anhydride in presence of anhydrous aluminium chloride in nitrobenzene furnished the keto acid 17. The NMR spectrum of 17 exhibited a A-B type quartet for the aromatic H. It shows signals at 7.06 (2H, d, J = 8 Hz, aromatic H) and 7.7 (2H, d, J = 8 Hz, aromatic H), which indicates that acylation has taken place para to ethyl group. Huang-Minlon reduction of keto acid 17 produced the acid 18 in 85% yield. The acid 18 was cyclized in presence of polyphosphoric acid to furnish the ketone 19. Bromination of the ketone 19 in chloroform yielded the monobromo compound (20) which exhibited a 3H singlet at 1.95. On heating with morpholine, bromo ketone 20 was transformed to the naphthol 21. Fremy's salt was prepared according to

literature method[6], was used for the oxidation of naphthol to naphthoquinone (8). Quinone 8 was reduced using sodium hydrosulphite and subsequently methylated using dimethyl sulphate to yield compound (10).

Since compounds (8) and (10) play a key role as reference compounds in this investigation, it is necessary to establish their structures unambiguously.

The acylation product obtained from ethylbenzene is a crystalline solid m.p.107°. It has been observed[7] that acylation reactions using methyl succinic anhydride furnish α-methyl propionic acid derivatives as a major product rather than derivatives of β-methyl propionic acid. So the structure 17 is more likely for the keto acid, obtained after acylation. Cocker et al.[8] have carried out the condensation of methyl succinic anhydride with ethyl benzene to yield a keto acid, m.p.107°C. Its identity was also established by an unambiguous synthesis. ω-Chloro-4-ethylacetophenone (38) (Auwers, Ber., 1906, 39, 3759) with ethyl methylmalonate (39) gave an ester which on hydrolysis and heating above its melting point yielded β-p-ethyl benzoyl isobutyric acid, m.p. 107°C, undepressed by a sample prepared by the acylation of ethyl benzene. This proves that the keto acid obtained after acylation of ethyl benzene has the structure 17.

Consequently the tetralone prepared from 18 through the route described above must be 19 wherein the methyl

group is located on the carbon adjacent to C=O group. The three proton singlet for the methyl group at 1.95 in the NMR of bromo compound 20 derived from 19 further supports this conclusion.

Sodium borohydride reduction of 19 furnished a mixture of alcohols 22a and 22b which on acetylation furnished a mixture of acetates 23a and 23b. The NMR spectrum of the mixture of acetates showed signals at 2.03 and 2.1 due to $-OCOCH_3$ and 5.93 (J = 3 Hz) and 5.68 (J = 6 Hz) due to CH-OAc, comparable[9] with the NMR spectra of acetate of cis-2-methyl-1-tetralol and acetate of trans-2-methyl-1-tetralol*. Acetate of cis-2-methyl-1-tetralol shows signals at 1.95 for $O-COCH_3$ and 5.92 for -CH-OAc. Acetate of trans-2-methyl-1-tetralol shows signals at 2.08 for $O-COCH_3$ and 5.75 for $-CH-OCOCH_3$-

Dehydration of mixtureof alcohols 22a and 22b furnished the hydrocarbon (24) whose NMR spectrum displayed the presence of CH_3 on a double bond (3H doublet at 1.88) and only one proton signal at 6.2**.

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*The NMR of alcohols and acetates (22) and (23) further supports the structure (17) of keto acid m.p.107. If the keto acid has the structure (40) it would have been given alcohol (42) and corresponding acetate (43). In the NMR of (42) and (43), signals for CH-OH or CH-OAc would have been more complex due to the presence of two adjacent hydrogens.

**The NMR of olefin obtained from keto acid m.p.107° further supports the structure of keto acid. If the keto acid has the structure (40) it would have furnished the olefin (44) which would not have shown a signal for $-CH_3$ on a double bond. In the NMR of the olefin obtained from the keto acid m.p.107° shows a signal for $-CH_3$ on C=C, so the olefin must have obtained from keto acid which has the structure17.

Thus it can be concluded that the structures of compounds (8) and (10) have been unambiguously established. The spectral data for compounds (8) and (10) are as follows.

I) Compound (8): m.p. = 73°C.

IR (nujol): 1660, 1610, 1585, 1450, 1350, 1250, 900, 845.

NMR ($CDCl_3$): 1.31 (3H, t, J = 7 Hz, $C\underline{H}_3-CH_2$) 2.2 (3H, d, J = 2 Hz, $C_2-C\underline{H}_3$), 2.80 (2H, q, J = 7 Hz, $CH_3-C\underline{H}_2$), 6.8 (1H, q, J = 2 Hz, $C_3-\underline{H}$), 7.53 (1H, dd, J = 2 and 8 Hz, $C_6-\underline{H}$) 7.91 (1H, d, J = 2 Hz, C_8-H), 7.96 (1H, d, J = 8 Hz, $C_5-\underline{H}$).

II) Compound (10): Liquid R_f = 0.78. (pet.ether-acetone 9:1)

IR (liq.film): 3000, 1740, 1615, 1460, 1360, 1225, 934, 830, 755.

NMR (CCl_4): 1.33 (3H, t, J = 7 Hz, $C\underline{H}_3-CH_2$) 2.37 (3H, s, $Ar-C\underline{H}_3$), 2.78 (2H, q, J = 7 Hz, $CH_3-C\underline{H}_2$), 3.78 (3H, s, $-OCH_3$), 3.85 (3H, s, $-OC\underline{H}_3$), 6.33 (1H, s, C_3-H), 7.10 (1H, dd, J = 8 and 2 Hz, C_6-H), 7.67 (1H, d, J = 2 Hz, $C_8-\underline{H}$), 7.93 (1H, d, J = 8 Hz, C_5-H).

When the Huang-Minlon reduction of ketone m.p.105° was carried out at 210° for 6 hrs. without taking special precautions to exclude air, a naphthoquinone, m.p.49° was obtained. It shows IR bands as given below.

IR: 1667, 1631, 1610, 1439, 1299, 1171, 1036, 943, 858, 735, 692.

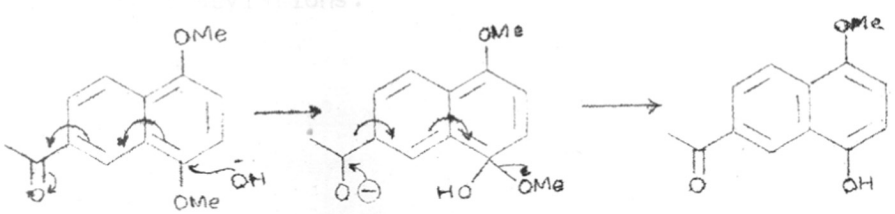
NMR ($CDCl_3$): 1.29 (3H, t, J = 7 Hz, $C\underline{H}_3-CH_2$) 2.18 (3H, d, J = 2 Hz, $C_2C\underline{H}_3$), 2.78 (2H, q, J = 7 Hz, $CH_3-C\underline{H}_2$), 6.8 (1H, q, J = 2 Hz, C_3-H), 7.53 (1H, dd, J = 2 and 8 Hx, C_7-H),

CHEMICAL LABORATORY
Acc. No. TH-450
Date

7.87 (1H, d, J = 2 Hz, C_5-H), 8.00 (1H, d, J = 8 Hz. C_8-H).

This quinone is not identical with quinone 8 since its m.p. was depressed on admixture with authentic sample of 8. The NMR spectra of quinone m.p. 49° and 8 were not identical, whereas signals due to C_5-H and C_8-H were clearly separated in the spectrum of quinone m.p.49°, the corresponding signals overlap in the spectrum of 8. The IR spectra are also not superimposible, In view of this observ ation and the conclusion arrived earlier that the ketone m.p.105° must have structure (5) or (6), it is evident that the quinone m.p.49° has the structure 7 and consequently ketone m.p.105° has the structure 5.

Huang-Minlon reduction of ketone m.p.105° at 200° for 30 min. under nitrogen atmosphere furnished a product which was subsequently methylated using dimethyl sulphate in presence of KOH. A product before methylation showed a signal for - OH in its IR spectrum since there is an acetyl group at C-6 position there is a prob ability of demethylation taking place in a strongly alkaline medium. The probable mechanism is shown below.



547.454+547.567(043)
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The product thus obtained after methylation was purified by column chromatography using silica gel to get a liquid (9), having R_f = 0.78 (pet.ether-acetone 4:1). IR (liq.film): 3000, 1600, 1450, 1350, 1265, 1225, 1190. NMR (CCl_4): 1.33 (3H, t, J = 7 Hz, $C\underline{H}_3$-CH_2), 2.38 (3H, s, Ar-$C\underline{H}_3$), 2.78 (2H, q, J = 7 Hz, CH_3-$C\underline{H}_2$), 3.78 (3H, s, -OCH_3), 3.88 (3H, s, -OCH_3), 6.37 (1H, d, J = 8 Hz, C_3-H), 7.17 (1H, dd, J = 8 and 2 Hz, C_7-H), 7.77 (1H, d, J = 8 Hz, C_8-H), 7.85 (1H, d, J = 2 Hz, C_5-H).

A careful observation of the aromatic region in the NMR spectrum of 9 (obtained from ketone m.p.105), and authentic (10), clearly showed that they were not identical. Further more, oxidation of 9 with ceric ammonium nitrate furnished naphthoquinone 7. On the basis of the observations described above, the ketone m.p.105° must have the structure 5.

It is thus concluded that acetylation of 4 involves substitution at C-6. Our results are in full agreement with the literature reports[4] that 2-alkylnaphthalenes react predominantly in the amphi (6) position during Friedel-Craft acylations.

EXPERIMENTAL

2-Methyl-1,4-naphthoquinone (2)

A mixture of bisulphite adduct 1 (2.76 g, 10 mmol) and saturated sodium carbonate solution (30 ml) was shaken for 15 minutes. The solid was filtered and then washed with water till free from alkali and dried to furnish (2). Yield = 1.62 g (94%). M.p. 104° (lit.[10] m.p. = 104-5°)

1,4-Dihydroxy-2- methylnaphthalene (3)

A solution of 2-methyl-1,4-naphthoquinone (2) (50 g) in hot ethanol was cooled rapidly to room temperature and the resulting solution was treated with stannous chloride (200 g) in conc. HCl (200 ml). The quinone dissolved at once giving a transient deep brown colour rapidly fading to light yellow and the solution became hot. Water (275 ml) was added and the reaction mixture was boiled to obtain a clear solution. The hot solution was filtered, the filtrate diluted with an equal volume of boiling water and set aside for crystallization. The product, which separated as colourless needles was washed with cold water and dried. Yield = 44 g (87%). M.p. 158° (lit.[11] m.p.158-60).

IR: 3500 (OH), 1450, 1335, 1255, 1160, 1040, 845, 750, 715.

1,4-Dimethoxy-2-methylnaphthalene (4)

1,4- Dihydroxy-2-methylnaphthalene (3) (36.8 g, 211 mmoles) was added to dimethyl sulphate (107 g, 850 mmol)

in a flask equipped with a reflux condenser, mercury sealed stirrer and a gas inlet tube. Under nitrogen atmosphere was added 10 ml portions of a solution of KOH [95.2 g (1.7 moles) in 200 ml water]. The mixture was then heated on water bath for 45 minutes and allowed to stand overnight. The reaction mixture was diluted with ice-water and extracted with ether. Ether extract was washed with water and dried (Na_2SO_4). After removing solvent an oily product was obtained which was distilled at 175-180°(bath temp.)/15 mm. The distilled product on cooling solidified. Recrystallization from pet.ether furnished (4) as a white crystalline solid. Yield = 28.6 g. (67%), m.p.48° (lit.[12] m.p.48-9°).

IR (liq. film) showed bands at: 3005, 1625, 1595, 1350, 1205, 1105, 1020, 970, 835, 755, 705.

NMR (CCl_4): 2.3 (3H, s, Ar-CH_3), 3.66 (3H, s, -OCH_3), 3.76 (3H, s, -OCH_3), 6.3 (1H, s, C-3 H), 7.66 (4H, m, aromatic H).

6-Acetyl-1,4-dimethoxy-2-methylnaphthalene (5)

Acetic anhydride (13 ml, 135 mmol) was added during 20 mins. with stirring to a mixture of dimethoxy compound (4) (4.0 g, 19.8 mmol), carbondisulphide (100 ml) and anhydrous $AlCl_3$ (12.0 g, 90 mmol) at 20°C. The reaction mixture was heated under reflux for 1 hr, the solvent ev aporated, residue cooled to 0°C, treated carefully with ice water and extracted with chloroform. The chloroform

layer was washed with water, dried (Na_2SO_4) and the solvent evaporated. The residue was dissolved in hot pet.ether and cooled. The solid which separated was filtered and recrystallized from pet.ether to furnish (5). Yield = 2.21 g (45.8%), m.p.105°.

IR (Nujol): 3000, 1675, 1650, 1600, 1600, 1475, 1345, 1260, 1000, 990, 940, 820, 715.

NMR (CCl_4): 2.45 (3H, s, Ar-CH_3), 2.67 (3H, s, -$COCH_3$), 3.85 (3H, s, -CCH_3), 4.02 (3H, s, -OCH_3), 6.60 (1H, s, C-3 H), 8.03 (1H, s, C-8 H), 8.03 (1H, d, J = 2 Hz, C_7H), 8.73 (1H, d, J = 2 Hz C-5 H). (Found: C, 73.5; H, 6.8. $C_{15}H_{16}O_3$ requires C, 73.8; H, 6.6%).

1,4-Dimethoxy-6-ethyl-2-methylnaphthalene (9)

A mixture of acetyl compound(5) (1.0 g, 4.1 mmole), hydrazine hydrate (85%, 2.5 ml), diethylene glycol (10 ml) and KOH (2.0 g) was heated under nitrogen at 190-200°C for 30 mins. It was cooled, diluted with water, acidified and extracted with chloroform. Chloroform layer was washed with water and dried (Na_2SO_4). Removal of solvent furnished a residue (0.96 g) which was stirred with dimethyl sulphate (2.32 g, 18.4 mmol), KOH (2.04 g, 36.4 mmol) and water (14 ml) for 1 hr. at room temperature and 1 hr. on steam bath. The resulting product was finally purified through chromatography on silica gel column. Column was successively eluted with (i) pet.ether

(ii) pet.ether-ethyl acetate (99:1). Fraction eluted with 99:1 pet.ether-ethyl acetate after removing solvent furnished (9). Yield = 0.78 g (82.7%). R_f = 0.78 (pet.ether-acetone 9:1).

IR (liq.film): 3000, 1600, 1450, 1350, 1265, 1225, 1190.

NMR (CCl_4): 1.33 (3H, t, J = 7 Hz, $C\underline{H}_3$-CH_2), 2.38 (3H, s, Ar-$C\underline{H}_3$), 2.78 (2H, q, J = 7 Hz, CH_3-$C\underline{H}_2$), 3.78 (3H, s, -$OC\underline{H}_3$), 3.88 (3H, s, -$OC\underline{H}_3$), 6.37 (1H, s, -C-3 $\underline{H}$), 7.17 (1H, dd, J = 8 and 2 Hz, C-7 $\underline{H}$) 7.77 (1H, d, J = 8 Hz, C-8 $\underline{H}$), 7.85 (1H, d, J = 2 Hz, C-5 $\underline{H}$).

(Found: C, 78.2; H, 8.1. $C_{15}H_{18}O_2$ requires C, 78.2; H, 7.9%).

6-Ethyl-2-methyl-1,4-naphthoquinone (7)

Method (a)

A mixture of acetyl compound 5 (1.0 g, 4.1 mmole), hydrazine hydrate (85%, 3 ml), diethylene glycol (20 ml) and KOH (3.0 g, 53.6 mmol) was heated at 125°C for 2 hrs and at 210°C for 6 hrs. without taking special precautions to exclude air.

The reaction mixture was cooled, diluted with water, acidified and extracted with chloroform. Chloroform layer was washed with water and dried (Na_2SO_4). The residue obtained after evaporation of solvent was chromatographed on a silica gel column, eluting only with pet.ether. The fraction eluted with pet.ether was (7). Yield = 0.092 g (9.3%), m.p.49°C, R_f = 0.49 (benzene-pet.ether 1:1).

IR (Nujol): 1667, 1631, 1610, 1460, 1439, 1376, 1351,

1299, 1193, 1062, 1012, 903, 858, 805, 735, 692.
NMR (CCl_4): 1.29 (3H, t, J = 7 Hz, $C\underline{H}_3$-CH_2), 2.18 (3H, d, J = 2 Hz, C_2-$C\underline{H}_3$), 2.78 (2H, q, J = 7 Hz, $C\underline{H}_2$-CH_3), 6.80 (1H, q, J = 2 Hz, C_3-H), 7.53 (1H, dd, J = 2 and 8 Hz, $C_7\underline{H}$), 7.87 (1H, d, J = 2 Hz, C_5-H), 8.0 (1H, d, J = 8 Hz, C_8-H).

Method b

A mixture of compound (9) (0.078 g, 0.34 mmole) in acetonitrile (5 ml) and ceric ammonium nitrate (1.5 g) in water (5 ml) was stirred at room temp. for 10 min. to afford (7) (0.053 g, 68%), identical (m.p., mixed m.p. IR and NMR) with a sample prepared according to method a.

Methylsuccinic acid (13)

A mixture of methylmetha acrylate (15) (50 g, 505 mmole), rectified spirit (230 ml) and powdered sodium cyanide (27 g, 551 mmole) was refluxed for 5 hrs. To it was added barium hydroxide solution (75 g, in 145 ml hot water). The reaction mixture was concentrated to a volume of about 200 ml and refluxed over steam bath for 16 hrs. Then the solution was concentrated till it formed a paste and to it was added conc. nitric acid (1.4 d, 85 ml). The reaction mixture was warmed on steam bath for 30 min.in a fume cupboard, and evaporated to dryness. The residual mass extracted with ether (6 x 100 ml) and finally with boiling benzene (2 x 150 ml). Combined extracts were dried over sodium sulphate and concentrated upto 90 ml. After cooling

in the refrigerator, it was filtered. The solid obtained was dried to yield (13). Yield = 42 g (66%), m.p. = 111-112°C. The identity of (13) was established by direct comparison (m.p., mixed m.p., IR) with the compound prepared according literature method.[13]

Methyl succinic anhydride (14)

A stirred mixture of acetyl chloride (15 ml), methyl succinic acid (13) (5 g, 37.8 mmole) was heated carefully on steam bath till the reaction subsided. Then the reaction mixture was refluxed for 2 hrs and was concentrated under vacuum. The residue obtained was distilled under reduced pressure to furnish (14). Yield = 3.595 g (83.3%), b.p.80-84°/4.5 mm (lit.[14] b.p.118-120°/7 mm)

β-p-Ethylbenzoyl-isobutyric acid (17)

A mixture of methylsuccinic anhydride (14) (3.42 g, 30 mmole) and ethylbenzene (16) (3.5 g, 33 mmole) in nitrobenzene (25 ml) was cooled to -10°C. To it was added anhydrous aluminium chloride (13.22 g, 99 mmole) in about 10 lots, during 1.25 hrs, maintaining the reaction temperature between -3 to +3°C. The reaction mixture was stirred for 3 hrs at 0-5°C, kept overnight at room tempe ature and poured over a mixture of crushed ice and conc HCl (20 ml). After keeping for 1 hr. at 0°C the reaction mixture was steam distilled till no nitrobenzene was distilling . The residual aqueous solution was cooled

to 5-10°C to get a solid. The solid was filtered, washed with water and dried to furnish (17). Yield = 4.3 g (65%) M.p. 108-9° (lit.[3] m.p. = 108)

IR (Nujol): 1700, 1660, 1600, 1445, 1430, 1325, 1250, 1185, 1070, 1000.

NMR (CCl_4): 1.23 (3H, t, J = 7 Hz, $-CH_2-\underline{CH_3}$), 1.25 (3H, d, J = 7 Hz, $CH-\underline{CH_3}$), 2.63 (2H, q, J = 7 Hz, $\underline{CH_2}-CH_3$), 1.5 to 2 (3H, m, $-CH_2-\underline{CH}$), 7.06 (2H, d, J = 8 Hz, aromatic), 7.7 (2H, d, J = 8 Hz, aromatic), 11.0 (1H, s, $-COO\underline{H}$).

γ-p-Ethylphenyl-α-methylbutyric acid (18)

KOH (12 g, 21.4 mmole) was carefully dissolved in diethylene glycol (80 ml) by heating with low flame. After the exothermic reaction subsided, reaction mixture was cooled to 60-70°C and keto acid 17 (13.2 g, 60 mmole) was added. After shaking for 2 min. hydrazine hydrate (12 ml, 85%) was added and the reaction mixture was refluxed for 2 hrs. Then it was slowly distilled till inner temperature rose upto 195-6° (about 13 ml distillate was collected). The reaction mixture was refluxed for 5 hrs, cooled, poured over crushed ice and acidified till pH 2 with conc. HCl. After extracting it with chloroform, the chloroform layer was washed with water (4 x 100 ml), dried (Na_2SO_4) and chloroform recovered to get a liquid. It was distilled under reduced pressure to get (18). Yield = 10.5 g (85%), b.p.135-140°/1.5 mm. (lit.[8] b.p.193-4°/5 mm).

IR(Liq.film): 3000, 1700, 1610, 1515, 1410, 1115, 1052, 820. NMR (CCl_4): 1.18 (3H, t, J = 7 Hz, $-CH_2-CH_3$), 1.18 (3H, d, J = 7 Hz, $-CH_2-CH_3$), 2.51 (2H, q, J = 7 Hz, $-CH_2-CH_3$), 1.5 to 1.67 (5H, m, $-CH_2-CH_2-CH$), 6.83 (4H, s, aromatic), 11 (1H, s, - COOH).

7-Ethyl-2-methyl-3,4-dihydro-1(2H)-naphthalenone (19)

A mixture of acid (18) (6.5 g, 31.55 mmole) and polyphosphoric acid prepared from P_2O_5 (40 g) and ortho-phosphoric acid (32 ml) was heated on a steam bath with occasional stirring for 1 hr, cooled to room temperature and diluted with ice water. The reaction product was extracted with chloroform. Chloroform extract was washed with sodium carbonate solution (2 x 50 ml) and finally with water(2 x 100 ml), dried (Na_2SO_4). Solvent removed to get a liquid which was distilled under vacuum to furnish (19). Yield = 3.47 g (58.4%), b.p. 100-101°/3 mm (lit.[8] b.p. 166-67°/20 mm).

IR (liq.film): 1675 (C=O), 1610, 1495, 1446, 1160, 1020, 908. NMR (CCl_4): 1.15 (3H, d, J = 7 Hz, CH_3-CH), 1.17 (3H, t, J = 7 Hz, CH_3-CH_2), 2.52 (2H, q, J = 7 Hz, CH_3-CH_2), 6.78 (1 H, d, J = 8 Hz, C_5-H), 7.00 (1H, dd, J = 8 and 2 Hz, C_6-H), 7.52 (1H, d, J = 2 Hz, C_8- H).

2-Bromo-7-ethyl-2-methyl-3,4-dihydro- 1(2H)-naphthalenone (20)

A solution of bromine (1.5 g) in chloroform (2 ml) was added dropwise to (19) (1.34 g, 7.1 mmole) dissolved in chloroform (10 ml). The reaction mixture was stirred at

room temperature for 4 hrs and the chloroform was removed under suction to furnish (20). Yield = 1.85 g (97%) as an oil.

IR (liq. film): 1680 (C=O), 1605, 1490, 1430, 1420, 1365, 1350, 1290, 1264, 1160, 1090, 1055, 1025, 995, 908, 868, 835, 765.

NMR (CCl_4): 1.23 (3H, t, J = 7 Hz, $-CH_2-\underline{CH_3}$), 1.95 (3H, d, J = 7 Hz, $-CH-\underline{CH_3}$), 2.5 (4H, m-$\underline{CH_2}-\underline{CH_2}$) 2.95 (2H, m, $-\underline{CH_2}-CH_3$), 6.86 to 8 (3H, m, aromatic).

Br

7-Ethyl-2-methyl-1-naphthol (21)

A mixture of bromo ketone (20) (1.8 g, 6.7 mmole) and morpholine (2 ml) was heated on a steam bath for 5 min. It was cooled, diluted with ether and filtered. The filtrate was washed with aqueous sulphuric acid (10%, 20 ml), water and dried (Na_2SO_4). The solvent was evaporated and the residue was recrystallized from benzene-pet.ether (3:7) to furnish (21). Yield = 0.62 g (49%), m.p.86°C.

IR (Nujol): 3490 (-OH), 1445, 1370, 1275, 1190, 885, 830.

NMR (CCl_4): 1.45 (3H, t, J = 7 Hz, $-CH_2-CH_2-\underline{CH_3}$), 2.51 (3H, s, Ar-$\underline{CH_3}$), 2.9 (2H, q, J = 7 Hz, $-\underline{CH_2}-CH_3$), 5.03 (1H, broad singlet, -O$\underline{H}$, exchanges with D_2O) 7.1 to 7.8 (5H, m, aromatic $\underline{H}$).

(Found: C, 83.7; H, 7.6. $C_{13}H_{14}O$ requires C, 83.8; H, 7.6%).

Fremy's salt (25)

Fremy's salt was prepared according to literature method[6].

7-Ethyl-2-methyl-1,4-naphthoquinone (8)

KH_2PO_4 solution (0.17 M, 20 ml) was added to a solution of Fremy's salt (1.3 g) in water (70 ml). This solution was added gradually to naphthol (21) (0.37 g, 1.93 mmol) dissolved in methanol (20 ml). The reaction mixture was stirred at 25°C for 10 mins. and at 0°C for 30 mins. The separated solid was filtered and washed with water. The solid on recrystallization from pet.ether furnished (8). Yield = 0.28 g (70.4%), m.p.73°C.

IR (Nujol): 1660, 1610, 1585, 1450, 1350, 1315, 1290, 1250, 1130, 900, 845.

NMR ($CDCl_3$): 1.31 (3H, t, J = 7 Hz, $C\underline{H}_3-CH_2$), 2.2 (3H, d, J = 2 Hz, $C_2-C\underline{H}_3$), 2.80 (2H, q, J = 7 Hz, $CH_3-C\underline{H}_2$), 6.8 (1H, q, J = 2 Hz, C_3-H), 7.93 (1H, dd, J = 2 and 8 Hz, C_6-H), 7.91 (1H, d, J = 2 Hz, C_8-H), 7.96 (1H, d, J = 8 Hz, C_5-H).

7-Ethyl-1,4-dimethoxy-2- methylnaphthalene (10)

A solution of (8) (0.62 g, 3.1 mmol) in ethyl acetate (25 ml) was shaken vigorously with a solution of sodium hydrosulphite (4 g) in water (30 ml) till the brown colour which developed initially, virtually disappeared. The ethyl acetate layer was separated, washed with water, dried and the solvent evaporated to furnish a dark mass (IR shows strong -OH) which was used as such for the next step. To the dark mass obtained, dimethyl sulphate (12 ml) was added

under nitrogen atmosphere. Subsequently a solution of KOH (1.5 g) in water (5 ml) was added gradually with stirring and the reaction mixture was heated on steam bath for 1 hr. The methylation product was purified through chromatography on silica gel column to furnish (10).
Yield = 0.60 g (84%) R_f = 0.78 (pet.ether-acetone 9:1).
IR (liq. film): 3000, 1740, 1615, 1460, 1400, 1360, 1265, 1225, 1100, 934, 892, 830, 755.
NMR (CCl_4): 1.33 (3H, t, J = 7 Hz, $C\underline{H}_3$-CH_2), 2.37 (3H, s, Ar-$C\underline{H}_3$), 2.78 (2H, q, J = 7 Hz, CH_3-$C\underline{H}_2$) 3.78 (3H, s, -OCH_3), 3.85 (3H, s, -OCH_3), 6.33 (1H, s, C_3-H), 7.10 (1H, dd, J = 8 and 2 Hz, C_6-$\underline{H}$), 7.67 (1H, d, J = 2 Hz, C_8-H), 7.93 (1H, d, J = 8 Hz, C_5H).
(Found: C, 78.0; H, 7.8. $C_{15}H_{18}O_2$ requires C, 78.2; H, 7.9%).

cis-7-Ethyl-2-methyl-1,2,3,4-tetrahydro-1-naphthalenyl acetate (23a) and trans-7-ethyl-2-methyl-1,2,3,4-tetrahydro-1-naphthalenyl acetate (23b):

Ketone (19) (0.5 g, 2.66 mmole) was reduced with sodiumborohydride (0.4 g, 10 mmole) in ethanol (10 ml) at room temperature for 5 hrs. The reduction product after one crystallization gave solid product (0.45 g) (89%) which showed m.p.72°C and was found to be a mixture of (22a) and (22b).
IR (Nujol): 3400 (-OH), 1490, 1445, 1365, 1175, 1125, 1080, 1035, 950, 900, 884, 870, 835, 820, 810, 780.

NMR(CCl_4): 1.0 (3H, d, J = 7 Hz, $CH-C\underline{H}_3$), 1.23 (3H, t, J = 7 Hz, $-CH_2-C\underline{H}_3$), 1.7 (3H, m, $C\underline{H}-CH_3$ and $-C\underline{H}_2-CH_2-Ar$), 2.1 (1H, broad, $-O\underline{H}$ exchanges with D_2O), 2.6 (4H, m, $CH_2-C\underline{H}_2$ and $Ar-C\underline{H}_2-CH_3$), 4.03 (0.7H, doublet, J = 6 Hz, $-C\underline{H}-OH$), 4.33 (0.3 H, d, J = 3 Hz, $-C\underline{H}-OH$), 7.0 (3H, aromatic $\underline{H}$).

Acylation of a mixture (0.5 g) of 22a and 22b with pyridine and acetic anhydride furnished a mixture of acetates 23a and 23b. Yield = 0.5 g (91%), R_f = 0.69 (4:1 pet.ether-acetone).

IR (Nujol): 1732 (C=O), 1500, 1442, 1430, 1380, 1225, 1148, 1010, 875.

NMR (CCl_4): 1.01 (3H, d, J = 7 Hz, $-CH-C\underline{H}_3$), 1.23 (3H, t, J = 7 Hz, $-CH_2-CH_3$), 2.03 (singlet, minor $-OCOC\underline{H}_3$), 2.1 (singlet, major $-OCOC\underline{H}_3$), 2.6 (2H, q, J = 7 Hz, overlaps with $Ar-C\underline{H}_2-CH_2$), 5.68 (0.7 H, d, J = 6 Hz, $C\underline{H}-OAc$), 5.93 (0.3H, d, J = 3 Hz, $-C\underline{H}-OAc$), 7.0 (3H, s, aromatic $\underline{H}$).

7-Ethyl-2-methyl-3,4- dihydronaphthalene (24)

A mixture of 22a and 22b (0.32 g, 1.68 mmol) and iodine (10 mg) was heated on steam bath for 3 hrs. The product (24) was isolated by distillation under reduced pressure, yield = 0.23 g (79.4%), b.p. (bath) 110°/3 mm. R_f = 0.83 (benzene-pet.ether 2:8).

IR (liq. film): 1650, 1600, 1560, 1500, 1480, 1450, 1440, 1360, 1320, 1260, 1220, 1145, 1060, 970, 954, 935, 890, 838, 818, 765.

NMR (CCl_4): 1.2 (3H, t, J = 7 Hz, $C\underline{H}_2-CH_3$), 1.88 (3H, s, $HC=C(\underline{CH}_3)$), 2.63 (2H, q, J = 7 Hz, overlaps with $Ar-C\underline{H}_2-C\underline{H}_2$), 6.15 (1H, s, $C\underline{H}=C$), 6.7 to 7.6 (3H, m, Ar-H(.

Found: C, 90.41; H, 9.51. $C_{13}H_{16}$ requires C, 90.70; H, 9.30%.

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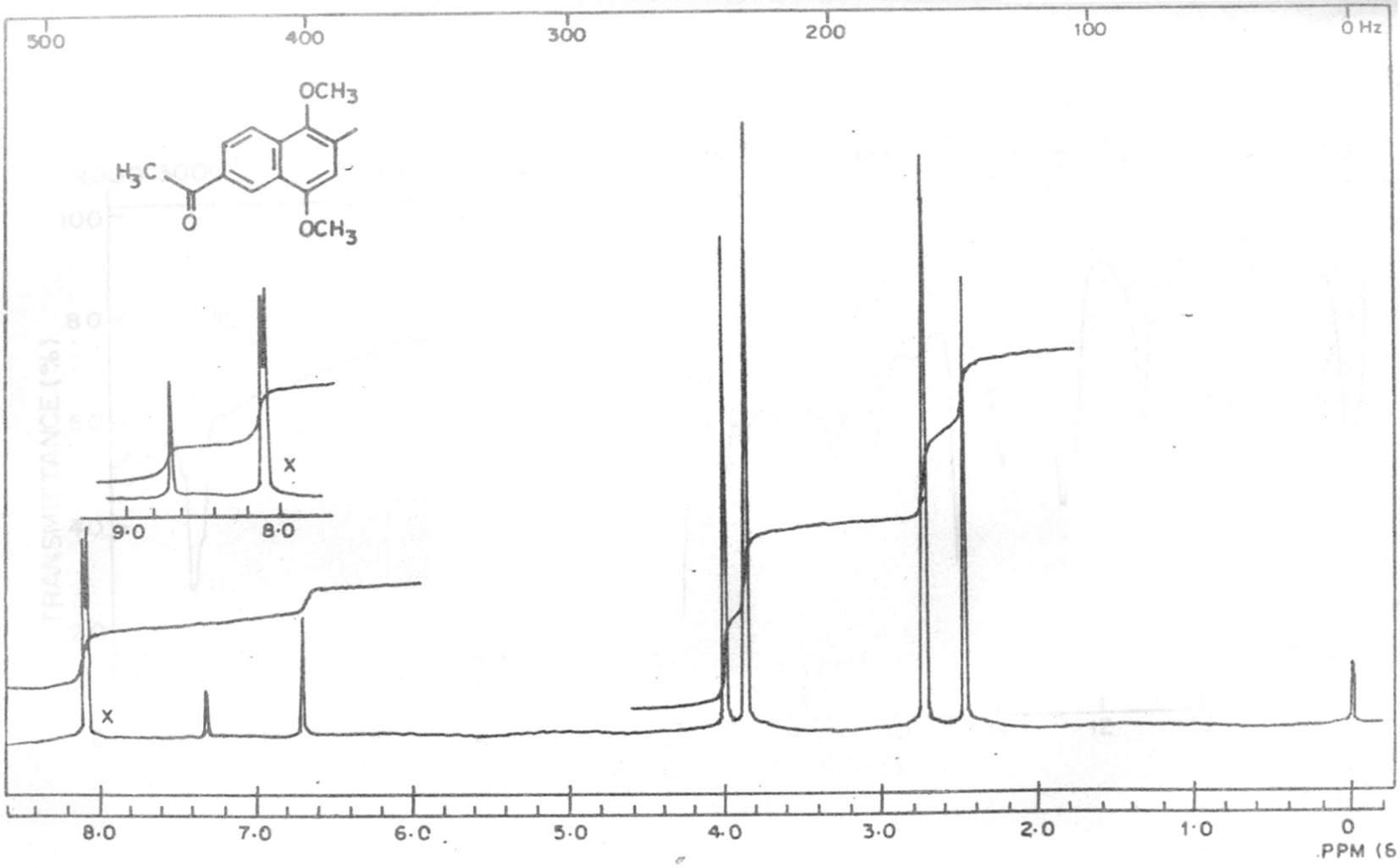
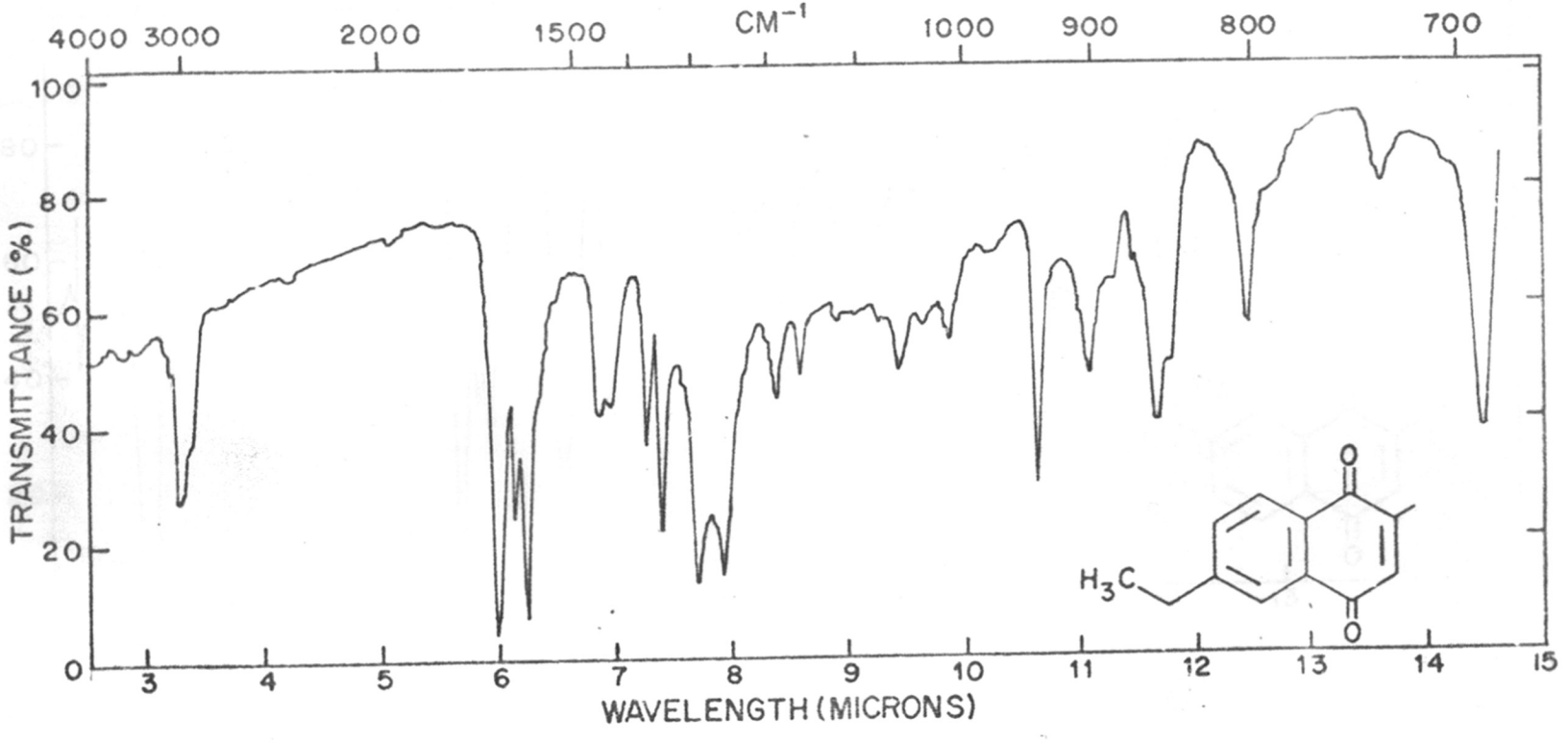
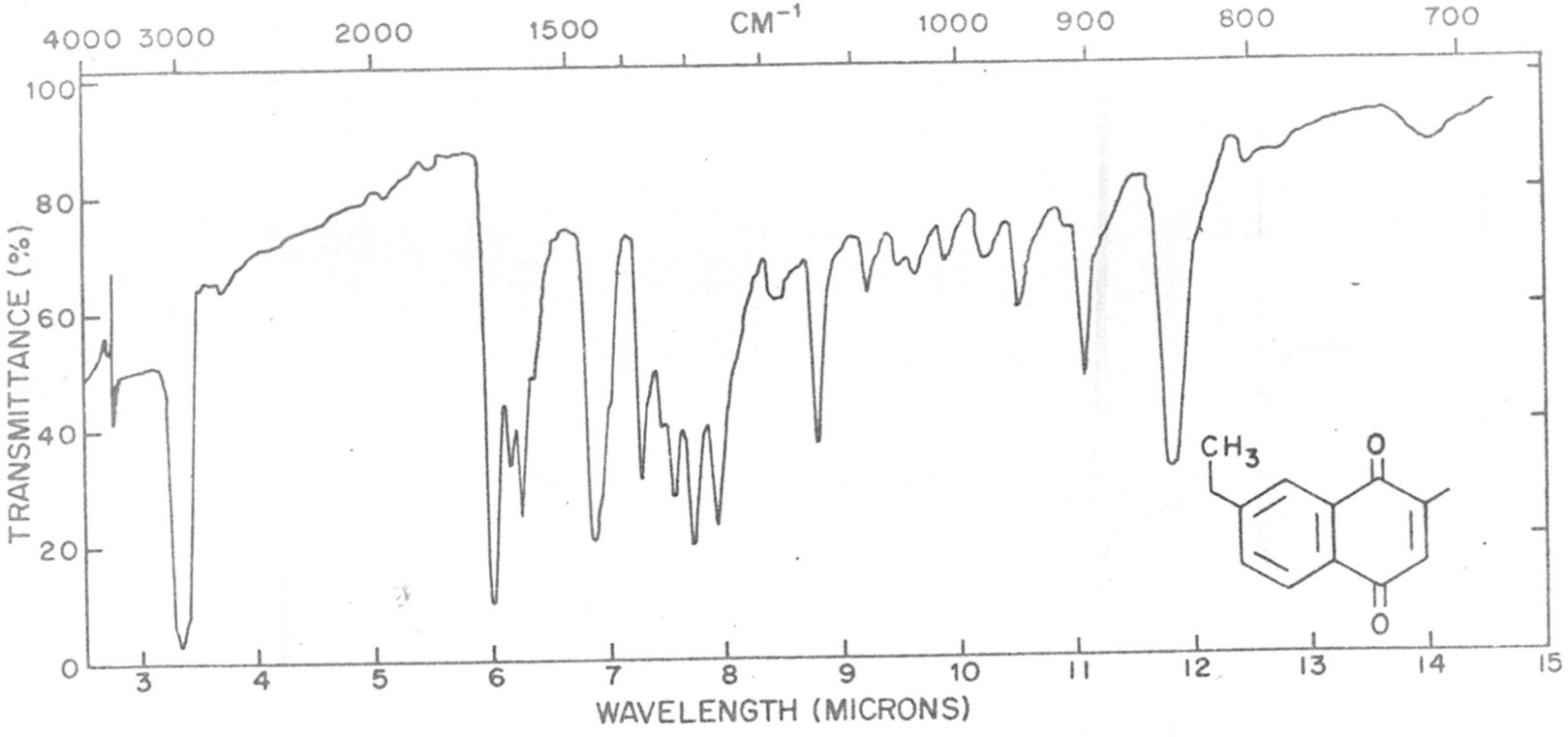


NMR OF 6-ACETYL-1,4-DIMETOXY-2-METHYLNAPHTHALENE



IR OF 6-ETHYL-2-METHYL-1,4-NAPHTHOQUINONE.



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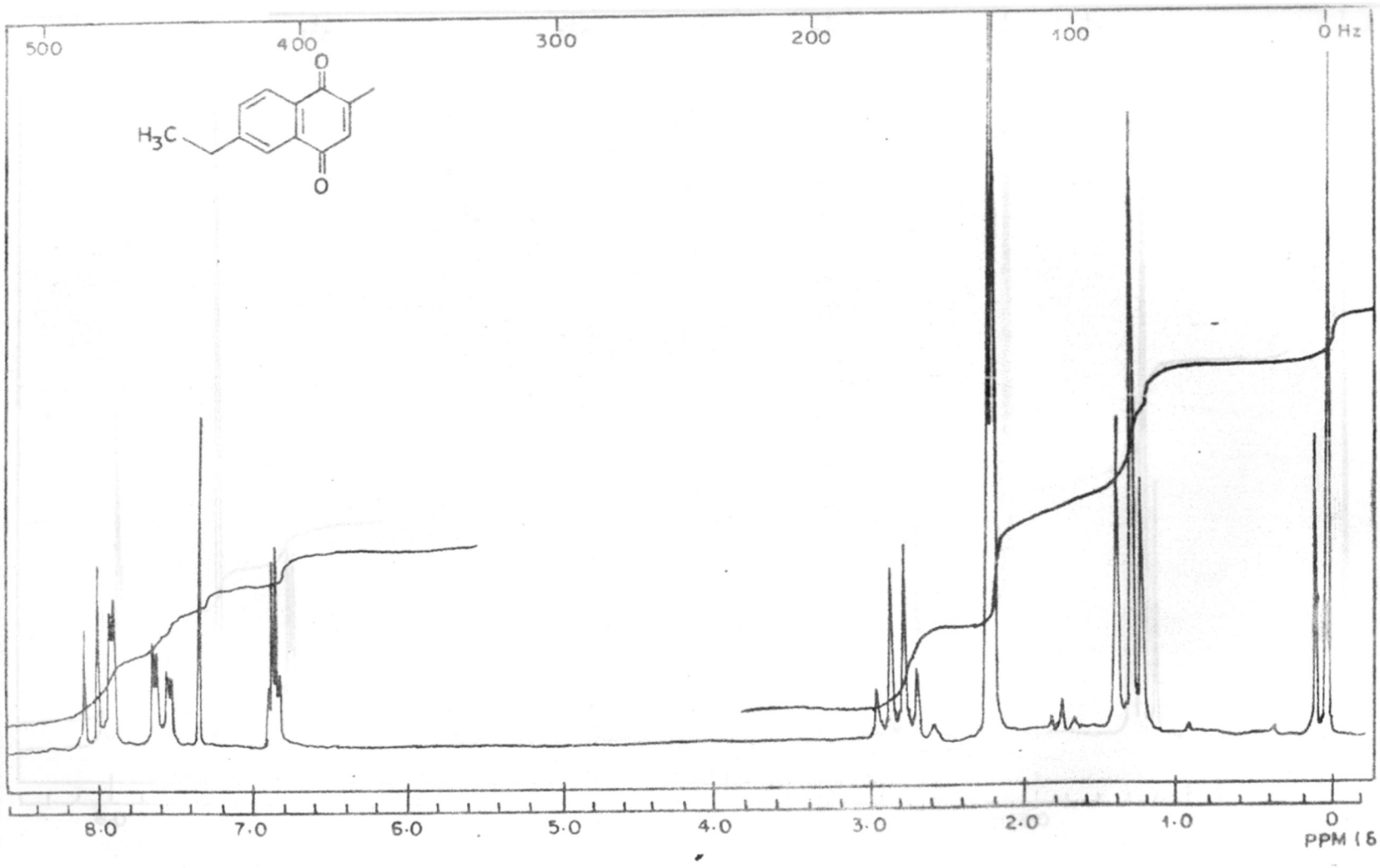

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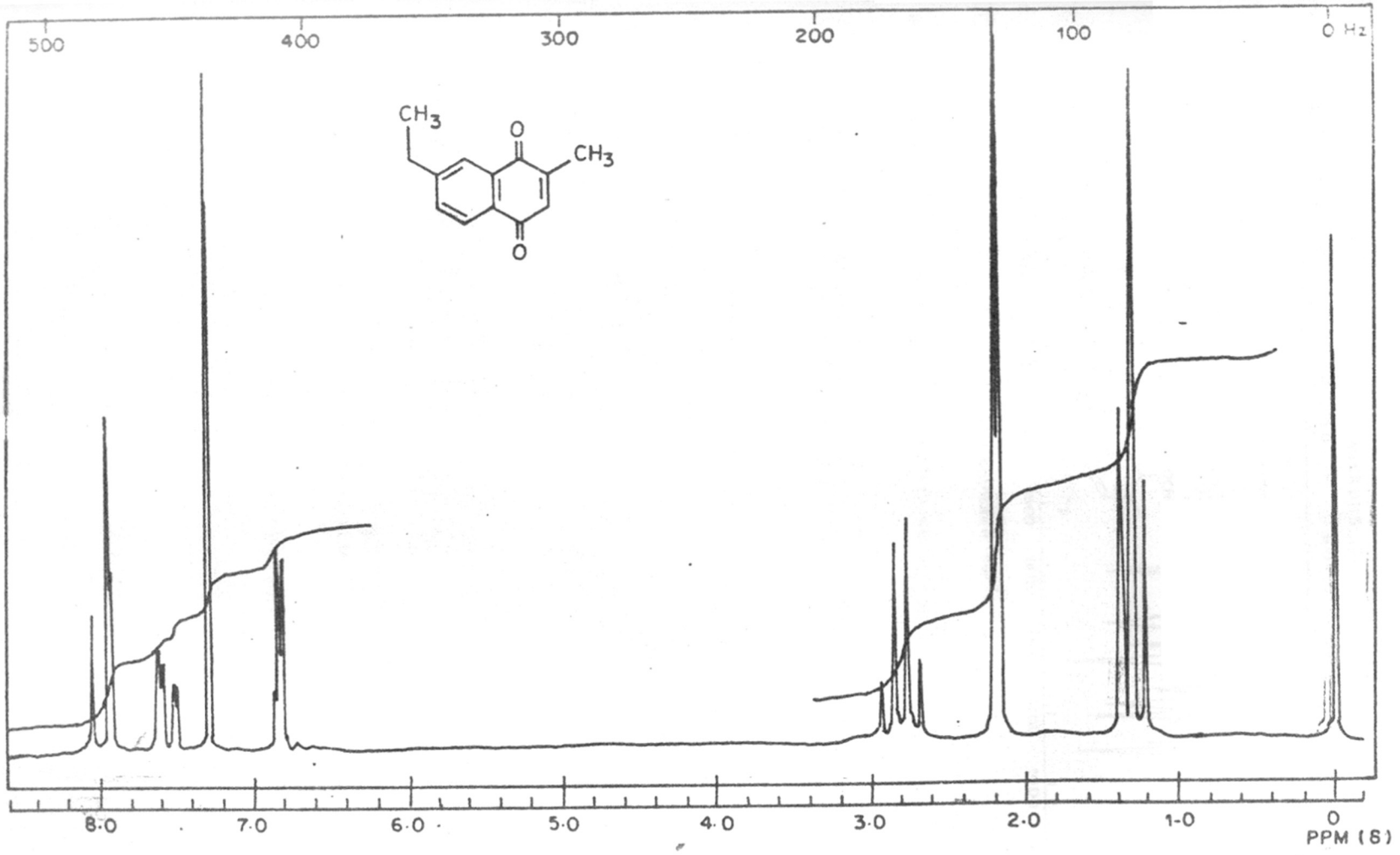

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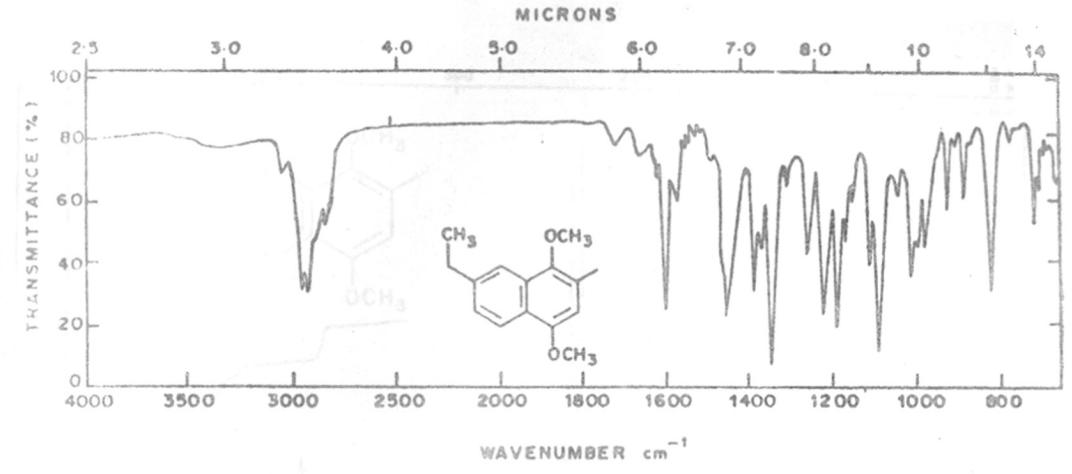

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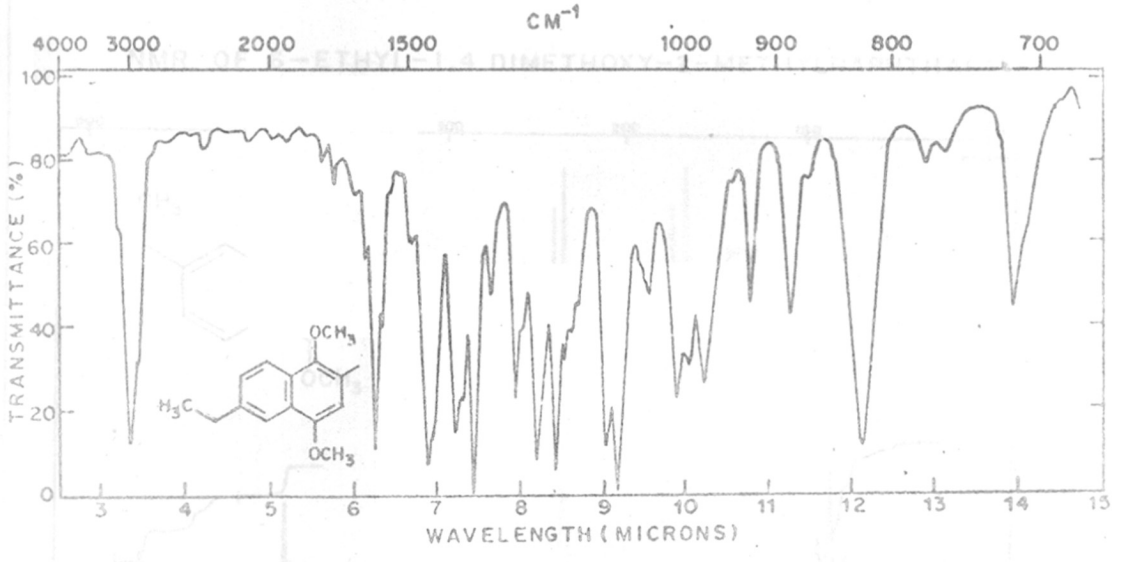

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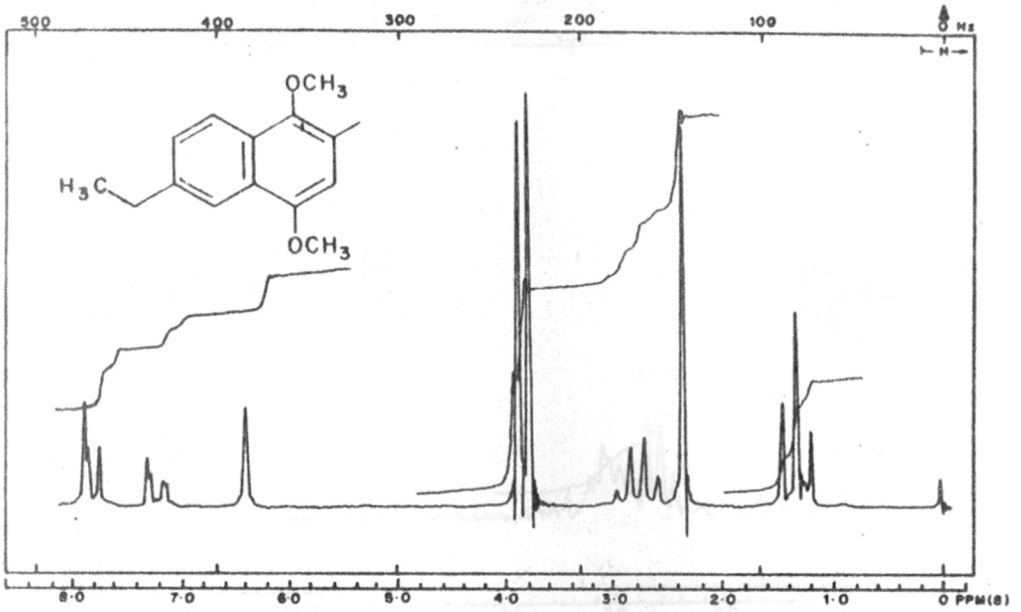

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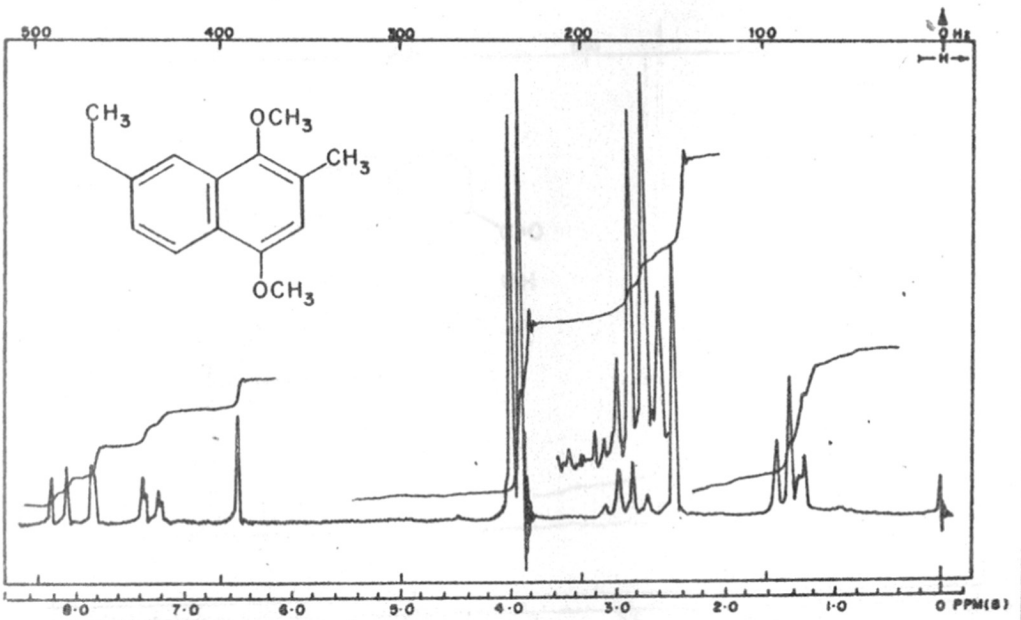

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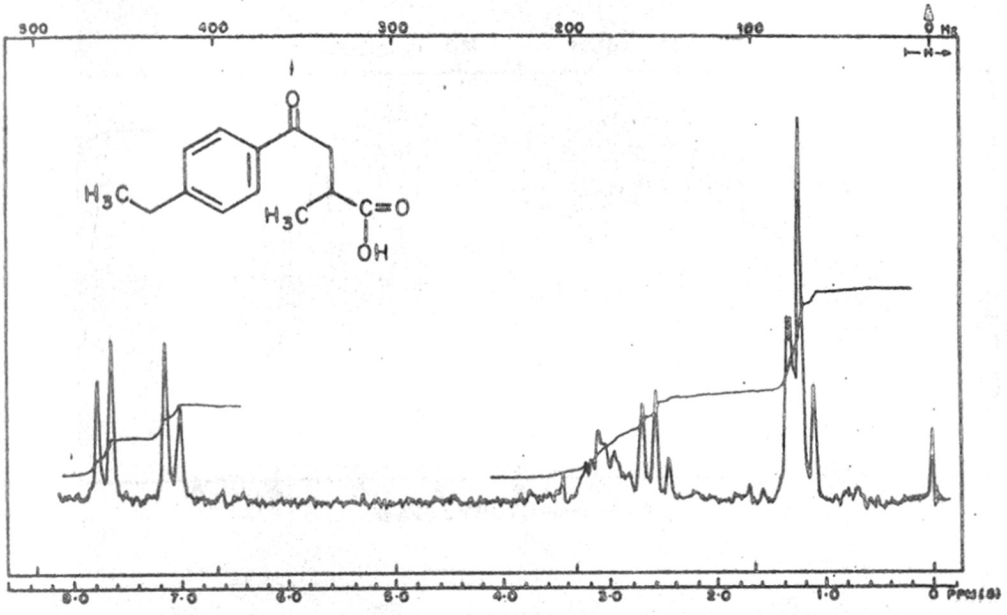
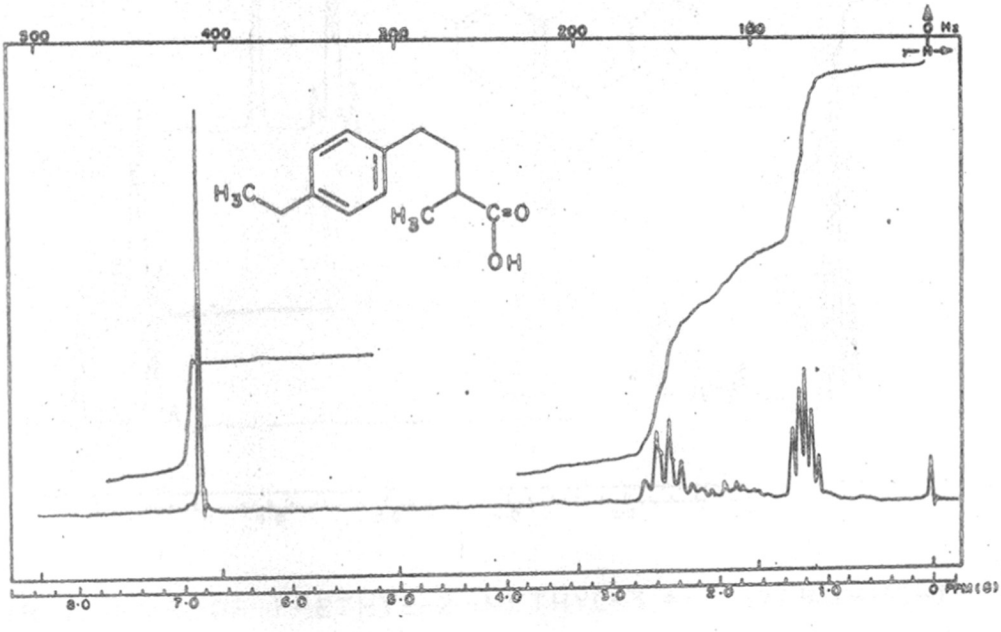
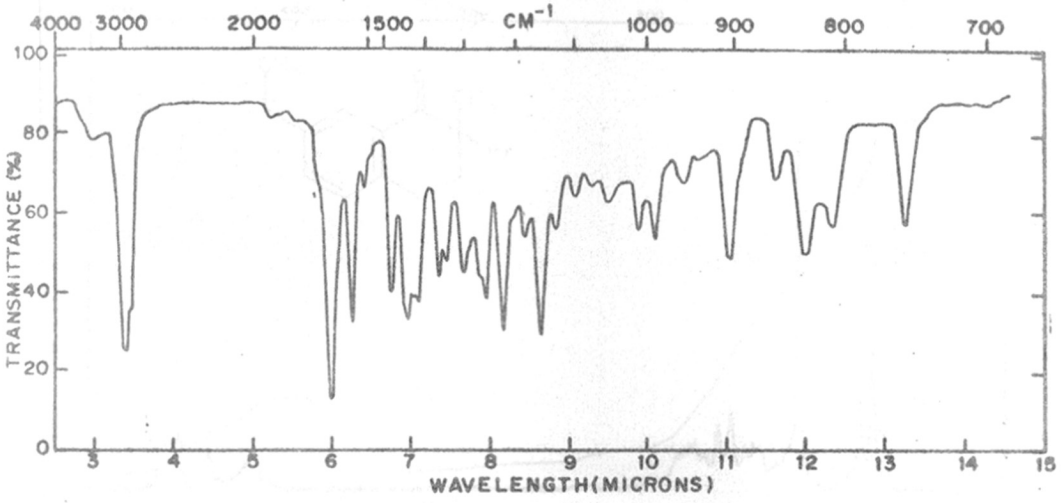
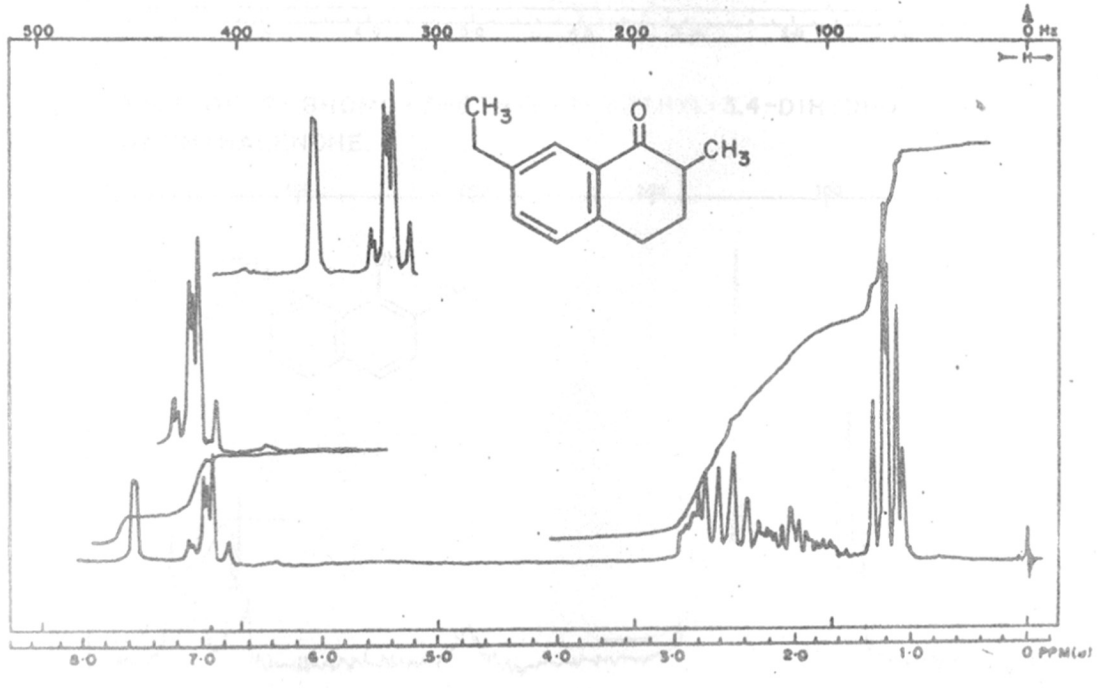


NMR OF β-p-ETHYLBENZOYL ISOBUTYRIC ACID.

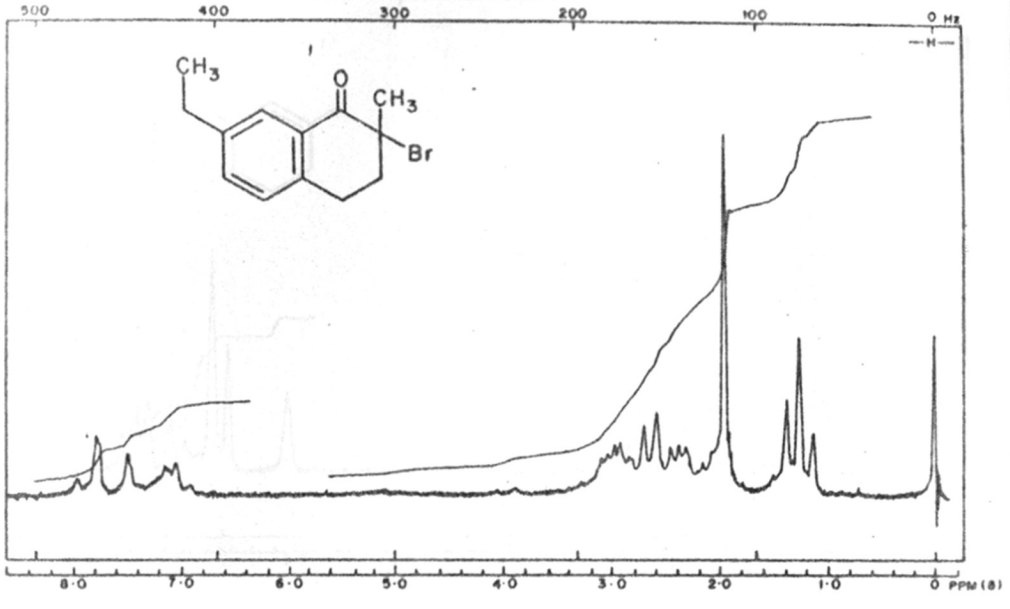


NMR OF ϑ-p-ETHYLPHENYL-α-METHYL BUTYRIC ACID.





IR & NMR OF 7-ETHYL-2-METHYL-3,4-DIHYDRO-1(2H)-NAPHTHALENONE.



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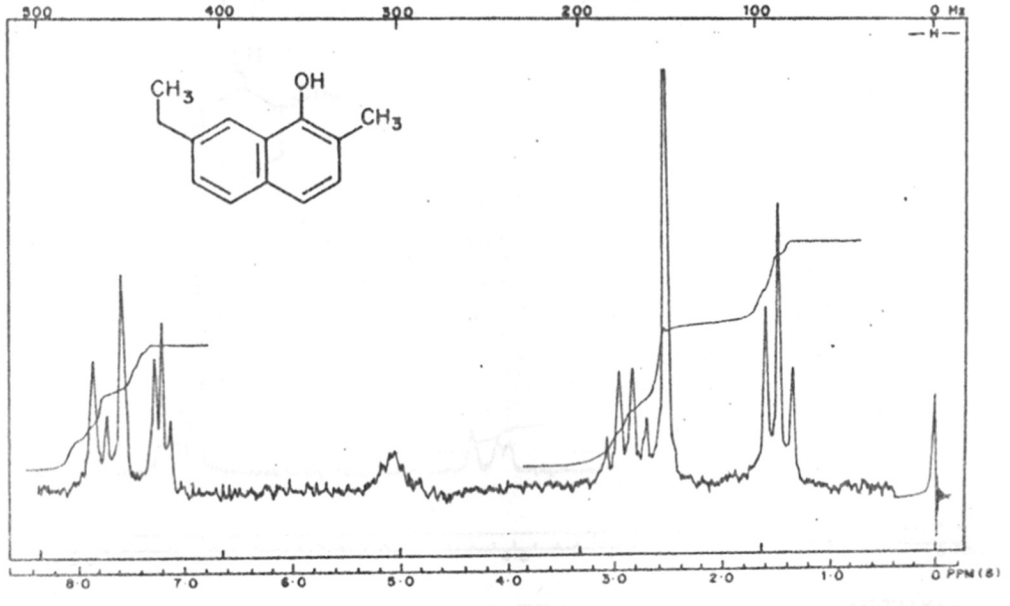
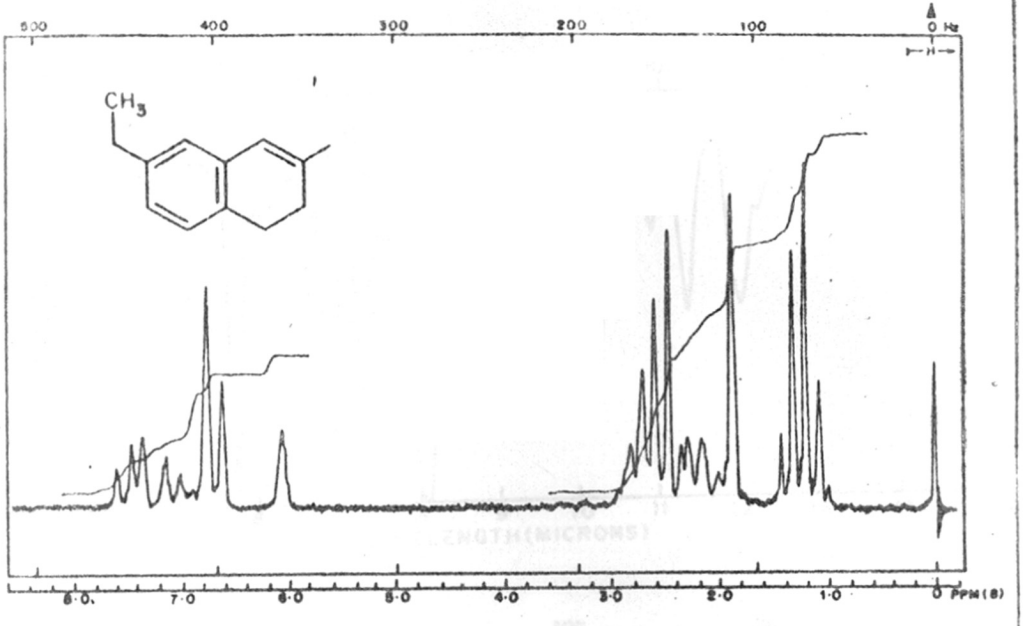
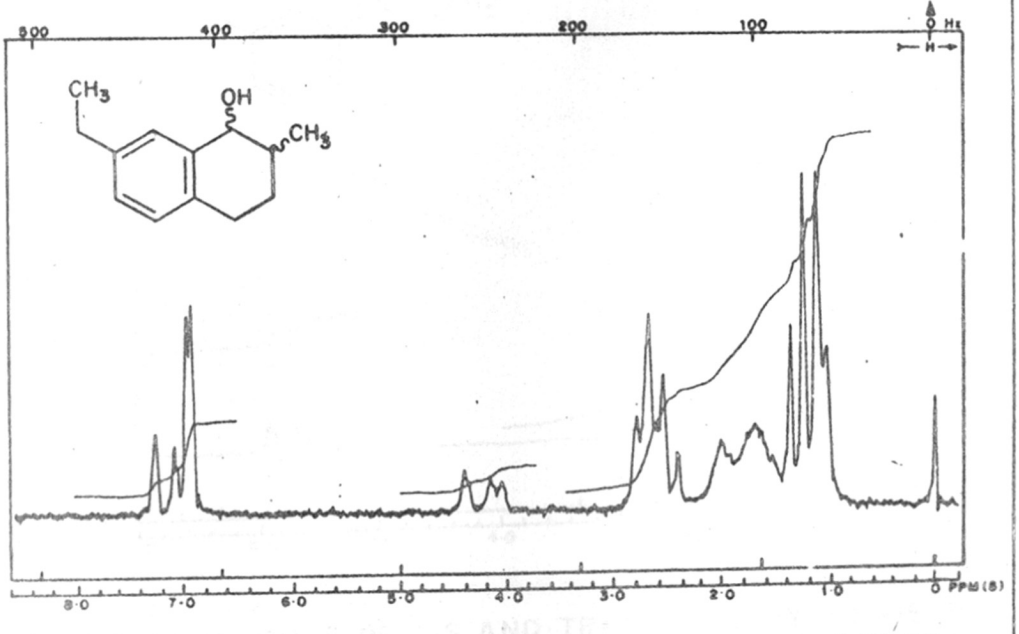


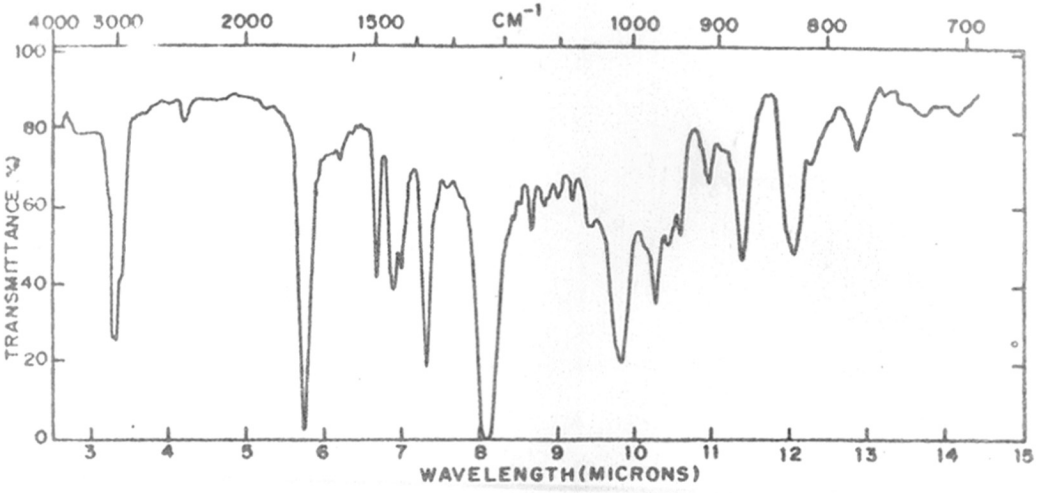
NMR OF 7-ETHYL-2-METHYL-1-NAPHTHOL.

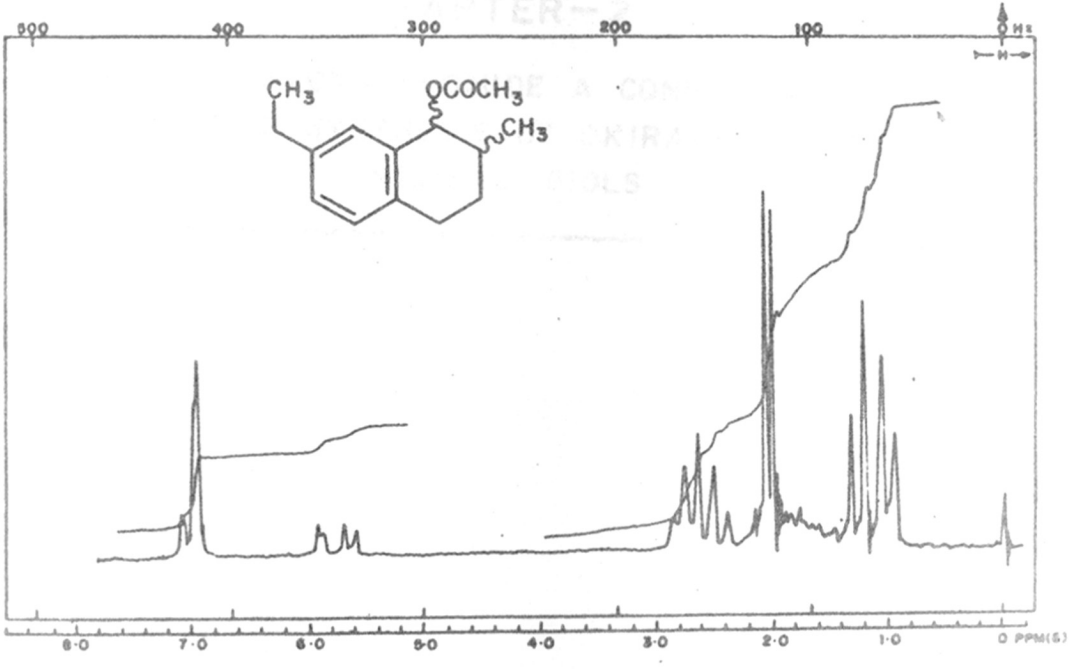


NMR OF 7-ETHYL-2-METHYL-3,4-DIHYDRONAPHTHALENE.



NMR OF MIXTURE OF CIS AND TRANS-7-ETHYL-2-METHYL-1,2,3,4-TETRAHYDRO-1-NAPHTHOL.

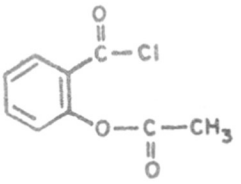




IR & NMR OF MIXTURE OF CIS AND TRANS-7-ETHYL-2-METHYL-1,2,3,4-TETRAHYDRO-1-NAPHTHALENYL ACETATE.

CHAPTER-2

2-ACETOXYBENZOYL BROMIDE A CONVENIENT REAGENT FOR THE SYNTHESIS OF OXIRANES FROM VICINAL DIOLS



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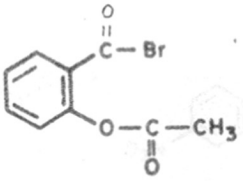

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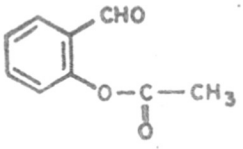

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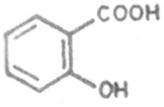

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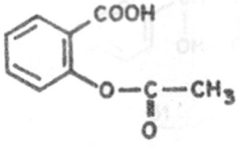

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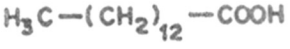

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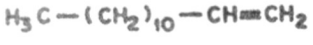

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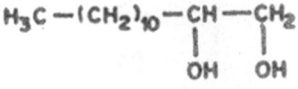

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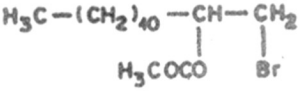

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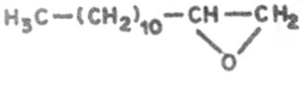

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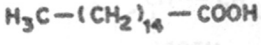

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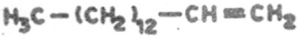

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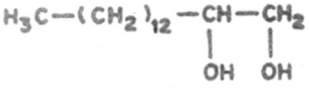

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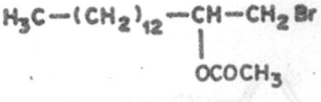

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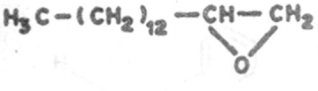

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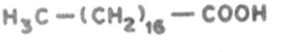

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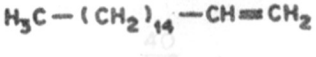

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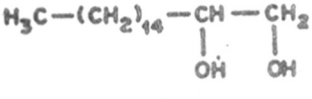

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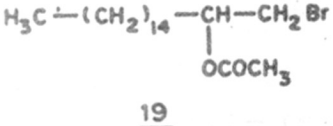

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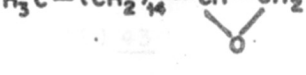

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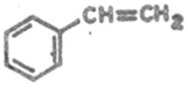

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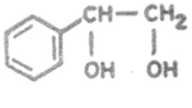

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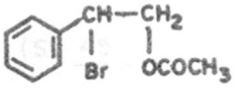

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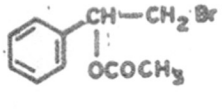

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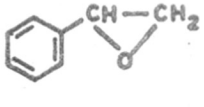

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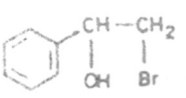

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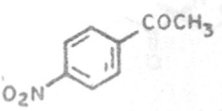

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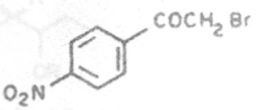

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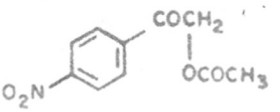

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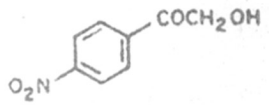

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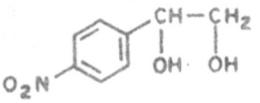

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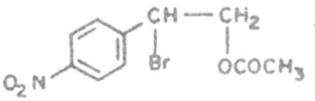

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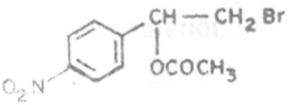

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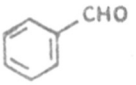

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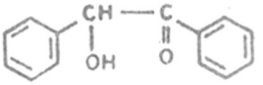

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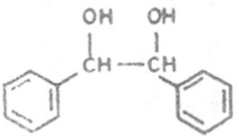

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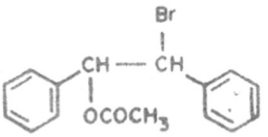

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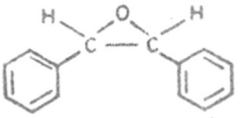

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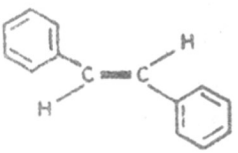

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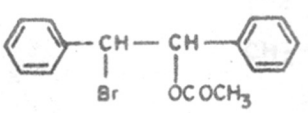

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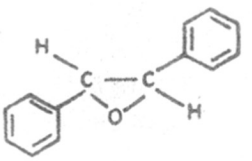

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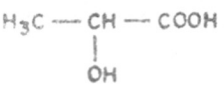

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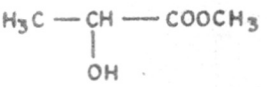

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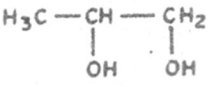

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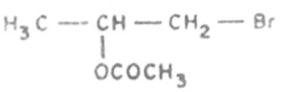

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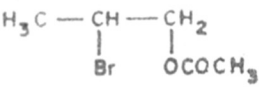

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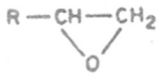

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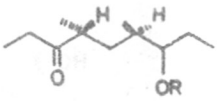
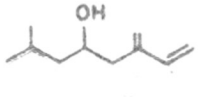
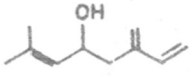


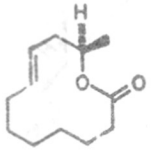
R = H (4R, 6R, 7R)
SERRICORNIN
48



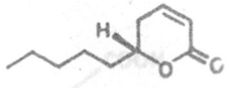
IPSENOL
49



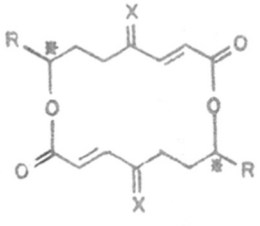
IPSDIENOL
50



R (-) RECIFEIOLIDE
51

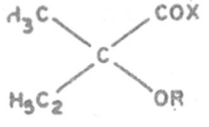


MASSOILACTONE
52



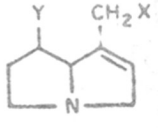
VERMICULIN
53

R = CH_3COCH_2
X = O



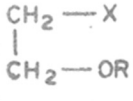
54

a) R = H, X = OH
b) R = Ac, X = OH
c) R = Ac, X = Cl
d) R = Ac, X = OMe



55

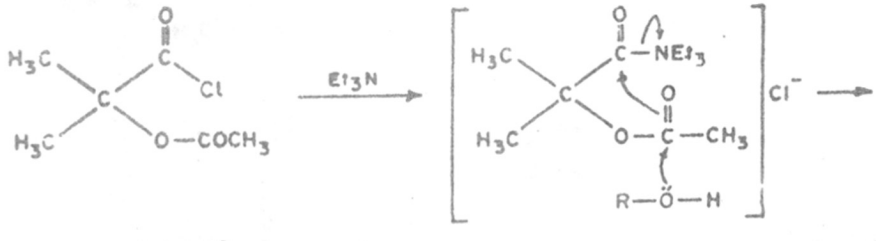
a) X = Y = OH
b) X = Cl, Y = OAc
c) X = Cl, Y = OH



56

a) R = H, X = OH
b R = Ac, X = Cl

SCHEME – 1



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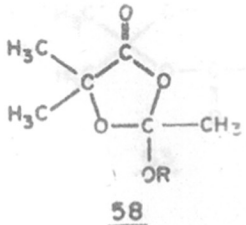

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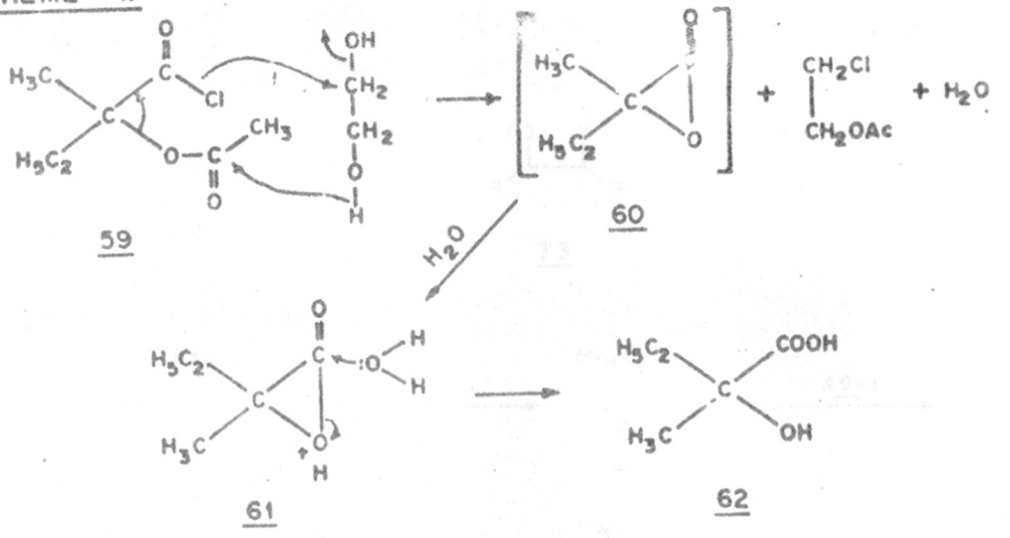
SCHEME – II



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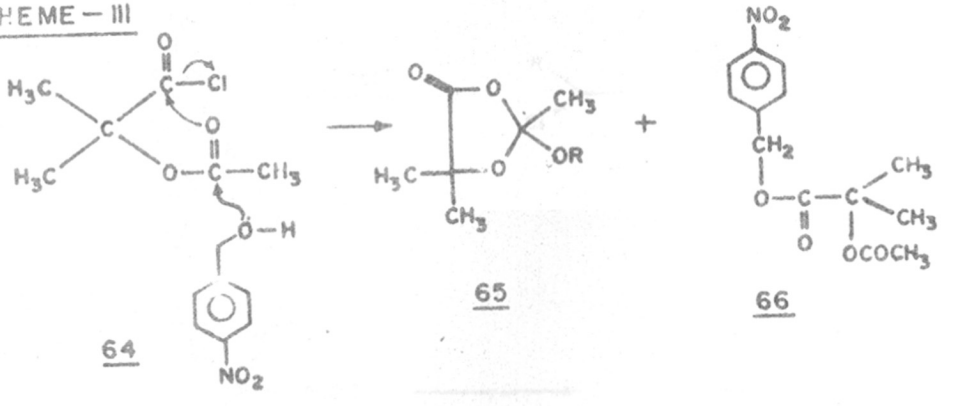

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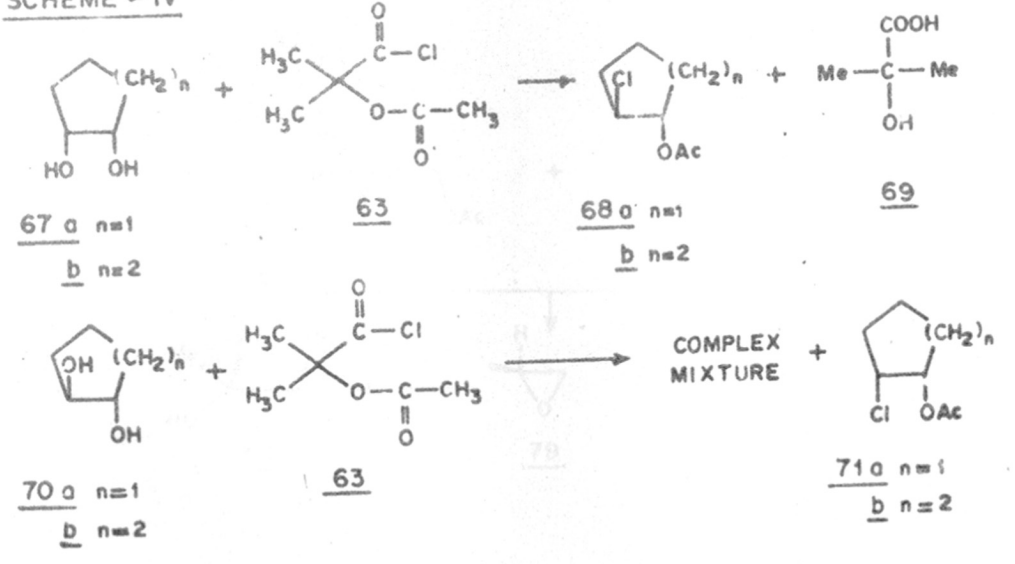

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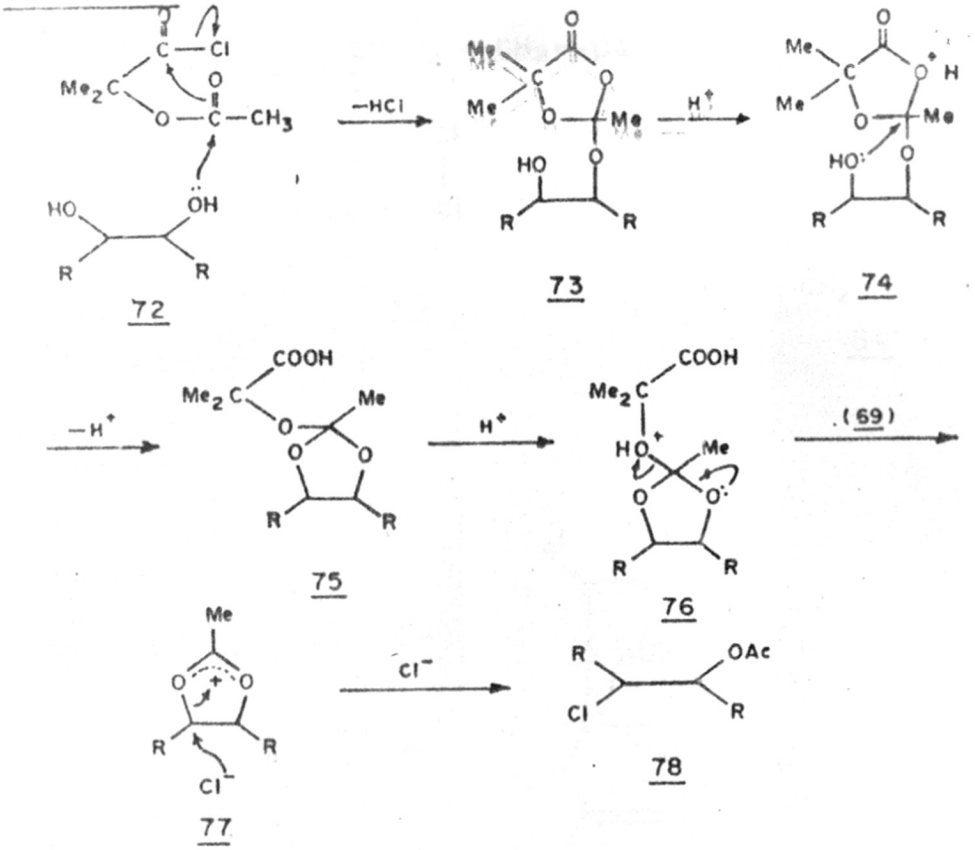
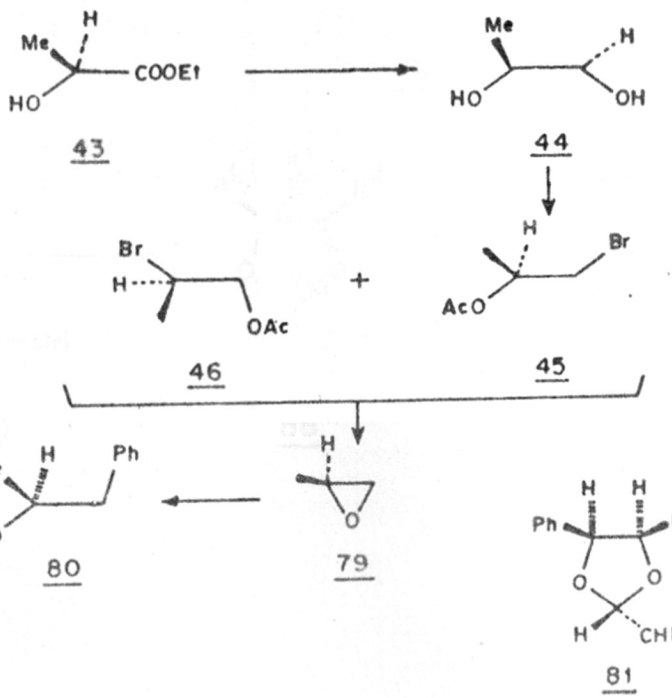


72 73 74 75 76 77 78

SCHEME – VI



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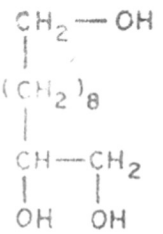

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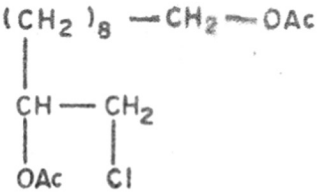

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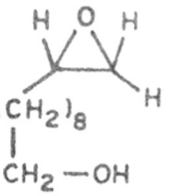

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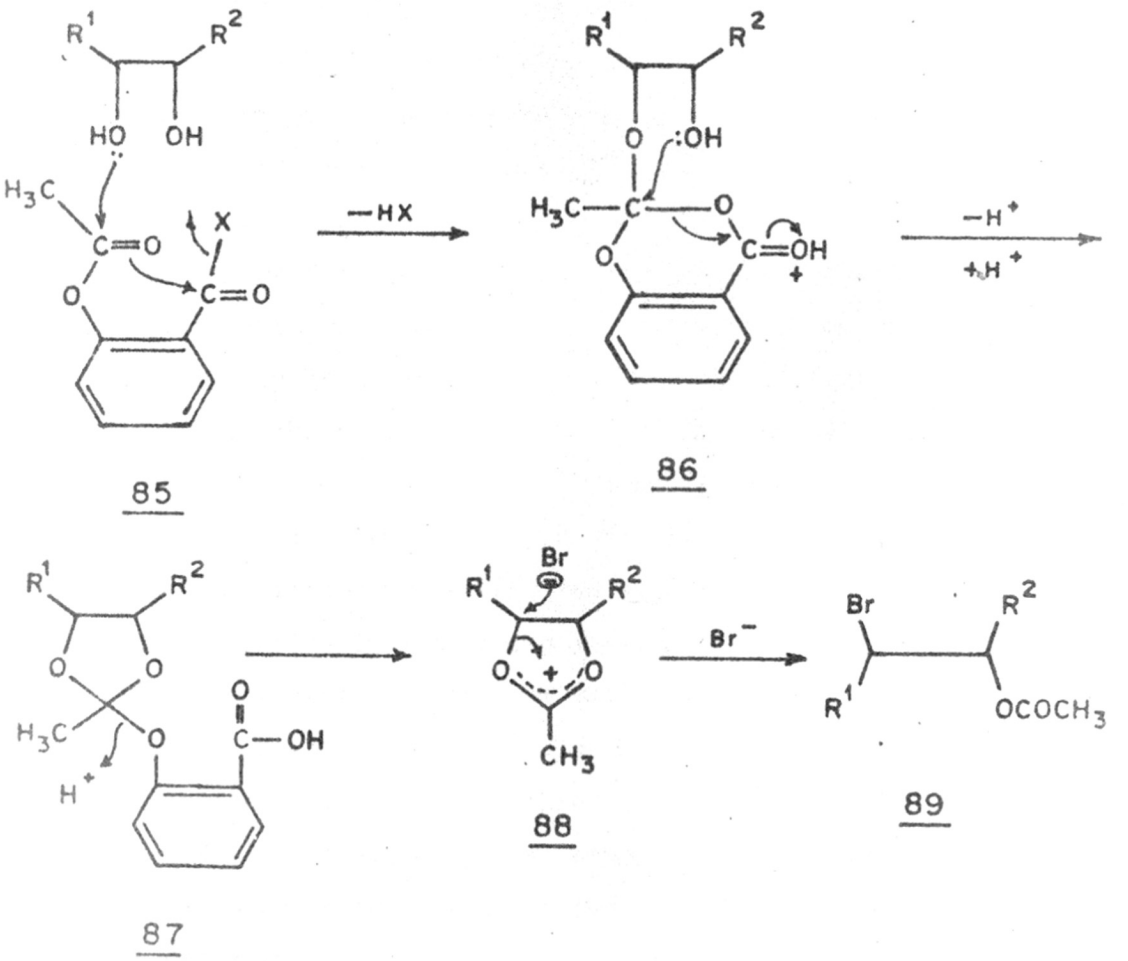
SCHEME — VII



SUMMARY

2-Acetoxybenzoyl bromide (2) is successfully used for the conversion of 1,2-diols to corresponding bromoacetates which in turn on treatment with sodium methoxide in methanol furnish oxiranes in excellent overall yields.

Action of 2-acetoxybenzoyl bromide (2) on diols (8), (13) and (18) in acetic acid at 90°C, furnish bromoacetates (9), (14) and (19) respectively. When treated with sodium methoxide in methanol bromoacetates (9), (14) and (19) furnish corresponding oxiranes (10), (15) and (20) in excellent yields.

Action of reagent (2) on 1-phenyl-1,2-ethane diol (22) in acetic acid at 90°C furnishes a 1:1 mixture of primary and secondary bromides (23) and (24) respectively. Similar was the observation when 1-(p-nitrophenyl)-1,2-ethane diol when treated with reagent (2) in acetic acid furnishes a 1:1 mixture of (32) and (33). When 1:1 mixture of bromoacetates (23) and (24) was reacted with sodium methoxide in methanol gives (dl) styrene oxide (25). It is of interest to note that meso 1,2-diphenylethane-1,2-diol (36) on reaction with the reagent (2) in acetic acid furnishes a 15:1 mixture of threo and erythro isomers of 1-acetoxy-2-bromo-1,2-diphenyl ethane. When the mixture of isomeric bromoacetates was treated with sodium methoxide in methanol furnished cis stilbene oxide as a major product.

Optically active (+)-(S)-propane-1,2-diol after reacting with the reagent (2) furnishes the bromoacetate (45) as a major product having high optical purity. This shows that the reagent (2) is useful for the preparation of optically active terminal oxiranes from the optically terminal diols.

In all the cases except diols (22) and (31), the reaction is regiospecific furnishing predominantly the primary bromides. Corresponding secondary bromides are obtained in minor quantities (ratio of primary bromides: secondary bromides is 90-97:10-3).

INTRODUCTION

Oxiranes of type (47)- Terminal oxiranes, undergo facile cleavage of the strained three membered ring, regioselectively. When R=alkyl, in basic or mildly acidic medium, due to steric interference the nucleophile attacks on the less substituted i.e. terminal carbon atom. When R = phenyl or substituted phenyl, in basic or mildly acidic medium the nucleophile attacks on the more substituted carbon atom. Hence they have been used widely as intermediates in synthetic organic chemistry. Some of the compounds thus synthesised are (i) oxprenolol- an important β-adrenergic blocking agent[1] (ii) The pheromones serricornin[2] (48), ipsenol[3] (49), ipsdienol[4] (50) and the stereoisomers of sex pheromone of pine sawflies[5] (iii) the pheromone of black tailed deer[6] (iv) methyl nonactinates[7] (v) (24R)-24,25-dihydroxyvitamin D_3[8] (vi) (R)-recifeiolide[9] (51) (vii) Massoilactone[10,11] and (viii) vermiculin[12] (53). Since many of the products prepared from terminal oxiranes exhibit interesting biological activity and contain one or more asymmetric centres, it is essential to obtain the products optically pure. This is turn requires that the terminal oxiranes, employed as intermediates should also be optically pure. Racemic terminal oxiranes can be prepared conveniently via per-acid epoxidations of terminal alkenes. However, the

reagents available at present are not satisfactory for the direct transformation of unfunctionalized prochiral alkenes to terminal oxiranes having high optical purity[13]. Optically active terminal 1,2-diols can be prepared readily from -hydroxy acids or -amino acids[2,14,15] e.g. S-(-)-phenyl-alanine, S-(-)-methyl lactate etc. Hence the preferred method for the synthesis of optically active terminal oxiranes employs the corresponding terminal 1,2-diols as starting material.

It is reported in literature[16] that -acetoxy -methylbutyryl chloride (54c) react abnormally with 1,4-diol (55a) to give the unexpected products (55b) and (55c) in yields of 54 and 20% respectively. To study the reaction still further a simple diol, ethylene glycol (56a) was used. Equimolar amounts of acid chloride (54c) and ethylene glycol (56a) reacted rapidly at room temp. to give -hydroxy- -methyl butyric acid (54a) (90%) and 2-chloro ethyl acetate (82%). As no other products were detected in significant amounts, it is likely that this surprising reaction is nearly quantitative.

In seeking a clue to the mechanism of the above reaction, a study was made of the reaction of -acetoxy- -methyl butyryl chloride (54c) with some mono alcohols. With an excess of methanol and of triethylamine the expected methyl -acetoxy- -methyl butyrate (54d) was not obtained, instead the only product M was a neutral oil which

was obtained in 90% yield. Using ethanol in place of methanol a similar compound E was obtained. A compound of this type was not isolated when alcohol is omitted. With triethylamine in acetone, (54b) was the only product. The interesting compounds M and E are formulated as 5-ethyl-2-methoxy-2,5-dimethyl-1,3-dioxolan-4-one [(58), R=CH_3] and its 2-ethoxy-homologue (58, R=C_2H_5) respectively. From the hydrolysis studies of compounds M and E under different conditions and the IR spectra, the mechanism can be suggested as shown in Scheme I.

In the intermediate (57) first formed, the strongly electrophilic carbon atom attached to the quaternary nitrogen reacts with the carbonyl oxygen atom of the acetyl group, which is sterically in a favourable position, simultaneous electrophilic attack by the carbonyl atom of the acetyl group on an alcohol molecule leads to the cyclic compound [(58), R = CH_3 or C_2H_5].

The mechanism for the reaction of ethylene glycol (56a) with -acetoxy- -methylbutyryl chloride (54c) was suggested by Mattocks[16] which is summarized in Scheme II.

On the basis of these considerations it was suggested that the nucleophilic attack upon -acetoxy acid chlorides bearing bulky substituents on the -positions occurred primarily at the acetoxy carbonyl group rather than at the acyl chloride function.

The above observations were confirmed and extended by Moffatt[17], by examining the reactions of 2-acetoxy-isobutyryl chloride (63) with p-nitrobenzyl alcohol (64) under different conditions. The mechanism is as given in Scheme III.

It has been reported[17] that the reaction of (63) with pure cis-cyclopentane- 1,2-diol (67a) gave almost exclusively (95%) a product that was identical with trans-2-chloro-cyclopentyl acetate (68a) but different from the corresponding cis isomer (71a).

On the other hand the reaction of 98.8% pure trans-cyclopentane- 1,2-diol with (63) was studied in several solvents and in each case gave at least ten products by VPC examination following removal of acidic byproducts. Where ether was used as a solvent the formation of only 1.6% of the trans chloroacetate (68a) and none of its cis isomer (71a) was observed.

Similar observations were noted when cis-cyclohexane-1 2-diol (67b) and trans-cyclohexane- 1,2-diol (70b) reacted with 63.

From the above results it is clear that contrary to the conclusions of Mattocks[16], the formation of chloroacetates is characteristic of only cis diols and proceeds with inversion of configuration at one of the centres. The products arising from trans diols appear to be mainly simple esters and dioxolanones and contain only minor amounts

of chloroacetates. On the basis of these results Moffatt[17] proposed a mechanism for the formation of chloroacetates involving the intermediate formation of acetoxonium as given in Scheme V.

The mechanism involves initial formation of the hydroxy dioxolanone (73) followed by acid-catalyzed rearrangements involving the cis hydroxyl group to give the carboxyl substituted ortho ester (75). In its protonated form (76) is opened by chloride ion to the trans chloroacetate (78).

Mattocks[18] has shown that the reaction of (54c) with propane-1,2-diol gave almost exclusively 3-chloropropyl acetate with replacement of only primary hydroxyl group by halide Moffatt[17] reported the reaction of dl-1-phenyl ethane- 1,2-diol with (63) gave a single product which was isolated in 75% yield and shown by VPC and NMR to be identical with 2-chloro-2-phenyl ethanol.

Golding et al.[14] have studied the reaction of several vicinal diols with 6M-hydrogen bromide in acetic acid to afford vicinal acetoxybromides in excellent yields. Its mechanism involves monoacylation of the diol, cyclization to a 1,3-dioxolan-2-ylium ion and capture of this intermediate by bromide ion. This has been established by kinetic studies, determination of substrate, stereospecificity and observation of intermediate 1,3-dioxolan -2-ylium ions by NMR spectroscopy. Golding[14] et al. also

studied the reaction of 6M-hydrogen bromide in acetic acid with cis as well as trans-cyclohexane-1,2-diols (67b and 70b) at 37°C. trans diol is getting converted into trans-1,2-diacetoxycyclohexane. cis-Cyclohexane-1,2-diol (67b) when treated with 6M-hydrogen bromide in acetic acid gave trans-1-acetoxy-2-bromocyclohexane. The exclusive trans-stereochemistry of this product was shown by its reaction with potassium hydroxide in methanol to give a high yield of 1,2-epoxy cyclohexane but no trace of cyclohexanone.

The reaction between propane- 1,2-diol and 6M hydrogen bromide in acetic acid is regioselective giving 94% of 2-acetoxy-1-bromopropane. In this case the reaction is also stereospecific, treatment of the mixture of acetoxybromides [i.e. (S)-2-acetoxy-1-bromopropane (45) and R-1-acetoxy-2-bromopropane (46) obtained from (+)-(S)-propane-1,2-diol] with potassium pentylate gave (+)-S-propylene oxide having optical rotations in a variety of solvents comparable with the best literature values[19]. Further more, the (-)-S-1-phenylpropan-2-ol obtained from treating this epoxide with phenyl lithium has optical rotations in several solvents which are numerically nearly identical with those measured for the (R)- and (S)-isomers prepared by a classical resolution of (RS)-1-phenylpropan-1,2-ol[20] (80). The whole sequence of reactions is summarized in Scheme VI.

When meso-1,2-diphenylethane- 1,2-diol was exposed to 6M hydrogen bromide in acetic acid, the reaction mixture solidified after 2 mins. and gave 30% of the dioxolan (81) and polymeric products, but no acetoxy bromide (NMR analysis). Compound (81) arises via pinacol type rearrangement at the expense of formation of acetoxybromide and has been reported[21] as a product from treating meso-1,2-diphenyl-ethane- 1,2-diol with sulphuric acid or phosphorous pentoxide.

Optically active propylene oxide has been prepared in one step from propane-1,2-diol using the reagents triphenyl phosphine/diethyl azodicarboxylate; however, the enantiomeric excess is only 67%[22]. 1,2-Diols have been transformed in two steps to acetates of chlorohydrin by Newman[23]. Golding et al.[14] have transformed terminal 1,2-diols to bromoacetates in one step by reacting with 6M-hydrogenbromide-acetic acid; the bromoacetates are then transformed to oxiranes on treatment with a base. This route has been utilized by several investigators for the preparation of optically active oxiranes. However, due to the high acidity of the reaction medium this method is not suitable in the case of diols which can furnish readily carbonium ion intermediates, e.g. bromoacetate from meso-1,2-diphenylethane-1,2-diol could not be obtained by Golding's method.

K.A. Watanabe et al.[24] found that the relatively inexpensive and commercially available 2-acetoxybenzoyl chloride (1) is as effective as -acetoxy isobutyryl chloride for the generation of 2,2'-anhydropyrimidene nucleosides from ribonucleosides.

In our present work we have studied the reaction of 2-acetoxybenzoyl bromide (2) on several vicinal 1,2-dils and subsequent conversion of resulting bromo acetates into oxiranes, thus providing a convenient route for the preparation of oxiranes from 1.2-diols in excellent vields.

PRESENT WORK

We have observed that the acid chloride (1) reacts with the triol (82) to furnish in 75% yield the chloroacetate (83) which when treated with methanolic sodium methoxide gives oxirane (84) in only 47% yield. Since the yields in the above two steps are not very high, we decided to examine the action of 2-acetoxybenzoyl bromide (2) on various vicinal 1,2-diols. Since it may be anticipated that 2-acetoxybenzoyl bromide (2) would be more reactive than the corresponding acid chloride, and as bromine is a better leaving group than chlorine better yields were anticipated in both the steps.

It has been reported[25] that aldehydes can be converted into corresponding acid bromides (R-CHO-RCOBr) by reacting with N-bromosuccinimide. This reaction has now been applied for the preparation of hitherto unknown 2-acetoxybenzoyl bromide (2). In all experiments on 1,2-diols the freshly distilled reagent (2) was used.

From earlier studies[17], it is evident that reaction of 2-acetoxyisobutyryl chloride (63) with 1,2-diol system is solvent dependent, solvents like acetonitrile, DMF and acetic acid have been used. Reaction in acetic acid medium has been shown to furnish a single product in high yield. Hence in our study we have used acetic acid as a solvent.

The present study deals with the reaction of 2-acetoxybenzoyl bromide (2) on following diols (8), (13), (18), (22), (31), (36) and (44). In all the cases except 1-phenyl-1,2-ethanediol (22) the reaction is regiospecific furnishing predominantly primary bromides; corresponding secondary bromides are formed only in minor quantities (ratio of primary bromides:secondary bromides = 90-97:10-3). Separation of these mixtures of primary and secondary alkyl bromides is not necessary since the same oxiranes are obtained upon treatment of primary or secondary bromides with sodium methoxide in methanol[23].

Synthesis of oxiranes (10), (15) and (20)

The alkenes (7), (12) and (17) were prepared through oxidative decarboxylation of the corresponding acids (6), (11) and (16), using lead tetraacetate and catalytic amount of cupric acetate and pyridine. The diols (8), (13) and (18) were synthesised through hydroxylation of corresponding alkenes with t-butyl hydroperoxide and catalytic quantities of osmium tetroxide[26].

Freshly distilled 2-acetoxybenzoyl bromide (2) is reacted with tridecane-1,2-diol (8) in acetic acid at 90°C for 2 hrs. Reaction mixture after work up furnished a liquid which after chromatography on grade II alumina gave pure bromoacetate (9) in 85% yield. It was characterised by elemental analysis, IR and NMR spectral data. IR spectrum shows band at 1750 cm^{-1}. Characteristic

of acetate. NMR shows signals at 0.88 (m, 3H, $-C\underline{H}_3$), 1.30 [m, 20H, $-(CH_2)_{10}-$], 2.03 (s, 3H, $-OCOC\underline{H}_3$), 3.40 (d, 2H, J = 5 Hz, $-C\underline{H}_2-Br$), 4.83 (t, 1H, J = 5 Hz, $C\underline{H}$-OAc).

Similarly 2-acetoxybenzoyl bromide (2) is treated with diols (13) and (18) in acetic acid at 90°C for 2 hrs. to furnish corresponding bromoacetates (14) and (19); which were characterised by elemental analysis, IR and NMR.

When pure bromoacetate (9) was treated with excess of 1M NaOMe in MeOH at room temperature for 1.5 hrs. it furnished in 80% yield, the epoxide (10). The epoxide (10) was characterisèd by elemental analysis, IR and NMR. IR spectrum shows bands at (cm^{-1}), 1471, 1408, 1252, 917 and 833. NMR shows signals at 0.83 (m, 3H, $-C\underline{H}_3$), 1.33 [m, 20H, $-(C\underline{H}_2)_{10}-$], 2.25 (m, 1H, $-C\underline{H}-O-$), 2.60 (m, 2H, $-C\underline{H}_2-O-$). Signals at 2.25 and 2.60 are the characteristic signals of terminal oxiranes.

Similarly oxiranes (15) and (20)were obtained in 89% and 87% yields respectively from the corresponding bromo-acetates (14) and (19). They were characterised by elemental analysis, IR, and NMR spectral data.

The identity of epoxides (10), (15) and (20) was established by direct comparison (b.p., IR and NMR) with the respective authentic oxirane prepared by by reacting corresponding alkene with meta-chloroperbenzoic acid.

These observations indicate that the acid bromide (2) can be successfully used for the conversion of 1,2-diols to corresponding bromoacetates which in turn give oxiranes in excellent overall yields. Based on existing literature (as discussed in the introduction), the mechanism for the conversion of 1,2-diols to bromoacetates is suggested according to Scheme VII.

This mechanism involves the formation of hydroxy dioxane (86) which undergoes acid-catalysed rearrangement involving the cis hydroxyl group to give the carboxyl substituted ortho ester (87). (87) on protonation can callapse to the acetoxonium ion (88) which is opened by bromide ion to the bromoacetate (89).

Action of 2-acetoxybenzoyl bromide (2) on (dl) 1-phenylethane-1,2-diol (22) and subsequent conversion to styrene oxide (25)

1-Phenylethane-1,2-diol is prepared according to the literature method[27] in 59% yields.

2-Acetoxybenzoyl bromide (2) reacts with 1-phenylethane-1,2-diol (22) in acetic acid at 90°C for 2 hrs to furnish a mixture of bromoacetates (23) and (24) which we could not separate by column chromatography over grade II alumina and the two component mixture itself was characterised by analytical data. Elemental analysis shows the molecular formula as $C_{10}H_{11}BrO_2$. IR spectrum shows bands at 1754 (C=O) and 1235 cm^{-1} a characteristic of

acetate. NMR spectrum shows that it is a mixture of bromoacetates (23) and (24) in approximately 1:1 proportion. NMR shows following signals 1.9 (1.5H, s, CH_2-OAc), 4.38 (1H, m, -CH_2-OAc), 5.23 (0.5H, m, -CH-Br) corresponding to the bromoacetate (23). It also shows signals at 2.0 (1.5 H, s, CH-OCOCH$_3$), 3.7 (1H, d, J = 6 Hz, -CH_2Br) and 5.8 (0.5H, t, J = 6, CH-OAc) assignable to the bromoacetate (24). For aromatic protons both gave an overlaping singlet at 7.1.

The comparison of the above NMR spectrum with (i) NMR of unambiguously synthesised authentic sample of (24) and (ii) the NMR data given by Golding et al.[14] is in agreement with the conclusion that it is a mixture of bromoacetates (23) and (24) in approximately 1:1 ratio.

To study the effect of p-nitro substituent on the proportions of bromoacetates formed during the reaction of diol with 2-acetoxybenzoyl bromide, the reaction of acid bromide (2) with 1-(p-nitrophenyl)-1,2-ethane-diol was carried out.

p-Nitroacetophenone (27) was brominated to get -bromo compound[28] (28) which was treated with sodium acetate in acetic acid at reflux temperature to get (29)[29]. The keto acetoxy compound was hydrolysed using alkali to get (30) and without isolating it, it was reduced with sodium borohydride to furnish pure 1-(p-nitrophenyl)-1,2-ethanediol (31).

Diol (31) was treated with 2-acetoxybenzoyl bromide (2) in acetic acid at 90°C for 2 hrs. After usual work up it gave a liquid which on chromatographic (grade II alumina) purification furnished a two component mixture of (32) and (33) in 86% yield. IR shows a band at 1740 (ester C=O), NMR suggests that it is a 1:1 mixture of 1-bromo-1-(p-nitrophenyl)-2-acetoxyethane (32) and 1-acetoxy-1-(p-nitrophenyl)-2-bromoethane (33).

Haubenstock et al.[30] attempted the synthesis of bromoacetates (23) and (24) by independent routes. Both approaches led to the mixtures of (23) and (24) after distillation. The mixtures had identical IR spectra and each was reduced with lithium aluminium hydride in tetrahydrofuran to an alcohol mixture containing roughly equal amounts of 1-phenylethanol and 2-phenylethanol. It was subsequently shown that each bromoacetate isomer rearranged to a mixture of both isomers on distillation (at 105-8°/2 mm). For example when crude bromoacetate (24) was not distilled but was reduced directly with lithium aluminium hydride only 1-phenylethanol was formed.

The addition of acetyl hypobromite to styrene followed by hydride reduction of the crude undistilled product yielded 1-phenyl ethanol as the only carbinol. When the bromoacetate was distilled prior to the hydride reduction approximately equal amounts of 1-phenylethanol and 2-phenylethanol were formed. The fact that on hydride reduction

of the distilled bromoacetate both phenylethanols were formed and that reduction of crude (not distilled) bromoacetate consistenly gave only 1-phenylethanol preclurdes the possibility of a common intermediate such as the epoxide involved in the reduction of both styrene bromoacetate isomers.

Haubenstock[30] has shown that bromoacetates (23) and (24) are in equilibrium at around 105°C. This may suggest that due to such thermal equilibration we are getting a 1:1 mixture of primary bromide and secondary bromide during the present study.

The mixture of bromoacetates (23) and (24) after treating with sodium methoxide in methanol furnishes (dl) styrene oxide. The product obtained (yield = 90%) was vacuum distilled and characterised by IR and NMR. The identity of the sample was confirmed by direct comparison (b.p., IR, NMR) with an authentic sample of styrene oxide).

Since Golding et al.[14] could not get 1-bromo-2-acetoxy-1,2-diphenylethane (isomer 37 or 40) when meso-1,2-diphenyl ethane-1,2-diol (36) was treated with 6M hydrogen bromide in acetic acid, there was considerable interest in carrying out the reaction of meso diol (36) with 2-acetoxybenzoyl bromide in acetic acid.

Meso 1,2-diphenylethane-1,2-diol (36) was prepared by sodium borohydride reduction of benzoin (35) following the same method used by J. Dale[31]. The meso diol (36) was

purified by crystallization and then treated with 2-acetoxy-benzoyl bromide (2) in acetic acid at 90°C) for 2 hrs. After usual work up it afforded a thick liquid which was purified by column chromatography to get a glassy liquid in 65% yield. It was characterised by microanalysis, IR and NMR. Microanalysis fits with the molecular formula $C_{16}H_{15}BrO_2$. IR shows a band at 1754 (C=O) characteristic of acetate. NMR shows signals at 2.06 (s, 3H, $-OCOCH_3$), 5.03 (d, 1H, J = 9, -CH-Br), 6.10 (d, 1H, J = 9, CH-OAc), 7.0 (s, 5H, aromatic) 7.07 (s, 5H, aromatic).

To know whether the obtained product is threo or erythro bromo acetate, we have prepared authentic erythro 1-acetoxy-2-bromo-1,2-diphenyl ethane (40) by unambiguous method. Benzoin (35) was reduced by Zn-Hg amalgum and HCl to get trans stilbene[32] (39). trans-Stilbenzene was converted to erythro-2-bromo-1,2-diphenylethanol by treating it with N-bromosuccinimide in DMSO-H_2O mixture[33]. This bromohydrin obtained was converted to bromoacetate with pyridine and acetic anhydride. The bromoacetate thus obtained was recrystallized (EtOH). IR shows bands at 1755. NMR shows signals at 1.80 (s, 3H, $-OCOCH_3$), 4.80 (d, 1H, J = 7, CH-Br), 5.8 (d, 1H, J = 7 Hz, -CHOAc), 6.83 (s, 10H, aromatic).

Comparing the NMR spectra of (37) and authentic erythro isomer (40) we can conclude that the product obtained after treating 2-acetoxybenzoyl bromide with

meso 1,2-diphenyl ethane-1,2-diol (36) is a 15:1 mixture of threo and erythro isomers. The above conclusion was confirmed by taking NMR spectrum of 1:1 mixture of (37) and (40)*.

The bromoacetate obtained (37) was treated with sodium methoxide in methanol to get cis-stilbene oxide (38) as a major product and a very minor quantity of trans-stilbene oxide (41). When treated with sodium methoxide in methanol, erythro bromoacetate (40) furnished authentic trans-stilbenene oxide (41).

The NMR of (38) shows signals at 4.03 (s, 2H, -CH-O-CH-) and 6.83 (s, 10H, aromatic) which are quite different from the NMR signals of (41) which shows signals at 3.57 (2H, s, -CH-CH), 7.0 (10H, s, aromatic). By taking the NMR spectrum of 1:1 and mixture of (38) and (41) it was confirmed that both compounds are different**. NMR data obtained for compounds (38) and (41) is in agreement with the literature[34] values of cis and trans stilbene oxides.

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*The NMR spectrum of (1:1) mixture of erythro (40) and threo (37) bromoacetates gave as expected separate signals for erythro and threo isomers. This observation rules out the possibility that the difference in the chemical shift v alues obtained for the NMR signals for erythro and threo bromoacetates may be due to experimental errors.

**The NMR spectrum of (1:1) mixture of epoxides (38) and (41) gave as expected separate signals for cis and trans isomers. This observation rules out the possibility that the difference in chemical shift v alues obtained for the NMR signals for cis and trans epoxides may be due to experimental errors.

As the optically active oxiranes are synthetically and biologically important compounds (as discussed in the introduction) we were quite interested in using the reagent 2-acetoxybenzoyl bromide (2) for the synthesis of bromoacetate (45) from (+)-(S)-propane-1,2-diol (44).

Fluka make lactic acid [(+)-(S)-lactic acid] was esterified using diazomethane to get (-)-(S)-methyl lactate, It was reduced according to the literature[14] method and vacuum distilled to get pure (+)-(S)-propane-1, 2-diol (44) in 77% yield. It shows

$(\alpha)_D^{27}$ = + 20.05 (c, 0.7 in H_2O)

[lit.[14] $(\alpha)_D^{25}$ = + 20.7 (c, 7.5 in H_2O)]

Distilled (+)-(S)-propane-1,2-diol (44) was treated with 2-acetoxybenzoyl bromide (2) in acetic acid at 90°C for 2 hrs. Usual work up furnished a liquid which was vacuum distilled. NMR gives signals at 1.34 (d, 3H), 3.43 (d, 2H) and 5.02 (m, 1H) due to 2-acetoxy-1-bromo propane (45) (92% by integration) and 1.7 (d, 3H) and 4.18 (d, 3H) due to 1-acetoxy-2-bromopropane (46) (8% by integration).

$(\ )_D^{25}$ = -12.65 (c, 8, $CHCl_3$) [lit.[14] $(\ )_D^{25}$ = -13.55 (c, 5.8 in $CHCl_3$)]

Specific rotation shows that the bromoacetate (45) prepared during this reaction has enantiomeric excess 93% and thiswas confirmed by preparing from it propylene oxide

(47) and determining the enantiomeric excess of the resulting propylene oxide.

The present investigation shows that the reaction between (+)-(S)-propane-1,2-diol (44) and 2-acetoxybenzoyl bromide (2) in acetic acid is

(i) regioselective giving 92% of 2-acetoxy-1-bromo propane and

(ii) resulting bromoacetate is of high optical purity.

EXPERIMENTAL

2-Acetoxybenzaldehyde (3)

A mixture of salicyaldehyde (30 g, 246 mmols), pyridine (25 ml), pyridine (25 ml) and aceticanhydride (40 ml) was kept overnight. It was poured over ice and after keeping for 1 hr it was extracted with ether. Ether extract was washed with water (3 x 100 ml), copper sulphate (10%, 2 x 100 ml) and finally with saturated brine. It was dried over anhydrous Na_2SO_4. After solvent removal a liquid was obtained which was distilled in vacuum. Yield = 29.5 g, (73%) b.p.140-50°C(bath)/1 mm (lit.[35] B.p.142°/18 mm).

2-Acetoxybenzoyl brommide (2)

A mixture of 2- acetoxybenzaldehyde (3, 12.5 g, 76 mmol), N-bromosuccinimide (14.00 g, 78 mmol), benzoyl peroxide (0.2 g) and carbon tetrachloride (120 ml) was heated under reflux with continuous stirring under N_2 for 1 hr, during heating reaction mixture was irradiation with 250 W tungsten lamp. The reaction mixture was cooled, the solid was filtered off and the filtrate was concentrated. The residue was distilled under vacuum to furnish 2. Yield: 11 g (59%); 160-70° (bath temp.)/ 0.3 mm ^{1}H-NMR ($CDCl_3$): 2.20 (s, 3H, $-OCOCH_3$); 7.17 ppm (m, 4H, aromatic).

2-Acetoxybenzoyl bromide obtained as above was digested with sodium carbonate solution (20%, 20 ml) at 60-70° for 15 min. and cooled. Resulting mixture was extracted with ethyl acetate to remove neutral part. Sodium carbonate extract was acidified and the solid was filtered off. The solid thus obtained is shown to be 4:1 mixture of 2-hydroxybenzoic acid (4) and 2-acetoxybenzoic acid (5) by ^{1}H-NMR study; yield = 0.50 g (89%).

2-Acetoxybenzoyl bromide (2, 89% purity) obtained as described above was used as such for the investigations described below. Found: C, 44.47; H, 2.90. $C_9H_7BrO_3$ requires C, 44.89; H, 3.13%.

1-Tridecene (7)

To a stirred mixture of myristic acid (6, 13.60 g, 60 mmol), cupric acetate (1 g, 5.5 mmol), pyridine (2 ml, 25 mmol) and benzene (150 ml), lead tetraacetate (50 g, 113 mmol) was added. Reaction mixture was stirred under reflux for 8 hrs. Excess of lead tetraacetate was destroyed by the addition of ethylene glycol (15 ml) and the benzene layer was separated. Organic layer was washed with sodium carbonate solution (5%, 120 ml), water and dried (Na_2SO_4). The benzene was removed and the residue was distilled under vacuum to furnish 7. Yield: 5.2 g (48%) b.p.125.6°(bath temp.)/10 mm. (Lit.[36] 104°/11 mm)
IR (liq. film): 1750, 1650(C=C), 990, 908, 722.
NMR (CCl_4): 0.86 (3H, m, CH_3), 1.32 [18 H, m, $-(CH_2)_9-$], 2.04 (2H, m, $CH_2-CH=CH_2$), 4.83 (m, 2H, $-CH=CH_2$), 5.33 to 5.80 (m, 1H, $-CH=CH_2$).

1,2-Tridecanediol (8)

A mixture of tert-butyl alcohol (20 ml), aqueous triton B (40%, 1.7 ml) and olefin 7 (2 g, 11 mmol) was cooled to 0° and to this cooled solution 90% tert-butyl hydroperoxide (2 ml, 18 mmol) was added followed by 1.2 ml of 0.5 OsO_4 in tert-butylalcohol (0.1 mmol). The resulting solution was stirred for 2 hr at 0°C and then stored in a refrigerator overnight. Aqueous $NaHSO_3$ (5%, 50 ml) was added to the reaction mixture and the resulting mixture was allowed to warm to room temperature, while stirring. This mixture was concentrated on a rotary evaporator to remove most of the tert-butyl alcohol and water and the resulting residue was extracted with ether. The organic extract was washed with saturated brine, dried (Na_2SO_4), concentrated and residue was distilled under vacuum to furnish 8; yield 1.81 g (76 %); b.p.154-155°(bath temp.)/1 mm. M.p. = 49.50°C. R_f = 0.4 (1:1 pet.ether - acetone).

IR (Nujol): 3450 (OH), 1470.

NMR (CCl_4): 0.83 (3H, m, $-CH_3$); 1.23 [20 H, m, $-(CH_2)_{10}-$] 3.27 [m, 3H, $-CH(OH)-CH_2OH$, exchanges with D_2O).

(Found: C, 72.29; H, 12.88. $C_{13}H_{28}O_2$ requires C, 72.16; H, 13.05).

1-Bromo-2-acetoxy-tridecane (9)

A mixture of 8 (1.0 g, 4.6 mmol), freshly distilled 2-acetoxybenzoyl bromide (1.73 g, 71 mmol) and acetic acid

(5 ml) was stirred at 90°C for 2 hrs. Acetic acid was removed under reduced pressure, the residue was treated with sodium carbonate solution (5%, 50 ml) and extracted with ether. Organic extract was washed with water, dried and concentrated. The residue was purified through column chromatography over grade II alumina. Fraction eluted with petroleum ether/ethyl acetate (99:1) furnished analytically pure bromo aceateYield: 1.26 g (85%)

Rf = 0.59 (4:1 pet.ether-acetone.

IR (liq. film) 1750 (C=O), 1475, 1375, 1240, 1050.

NMR (CCl_4): 0.88 (m, 3H, $-C\underline{H}_3$), 1.30 [m, 20H, $-(CH_2)_{10}-$] 2.03 (s, 3H, $-OCOC\underline{H}_3$), 3.40 (d, 2H, J = 5, $C\underline{H}_2-Br$), 4.83 (t, 1H, J=5, $C\underline{H}-OAc$). (Found: C, 56.07; H, 9.03; Br, 21.02. $C_{15}H_{29}BrO_2$ requires C, 56.20; H, 9.21; Br, wl.2%).

1:2 Epoxytridecane (10)

A mixture of bromoacetate (9) (0.35 g, 1.09 mmol) and 1 M methanolic sodium methoxide (3 ml) was kept at room temp. for 1.5 hr. Reaction mixture was diluted with water (15 ml) and extracted with ether (50 ml). Organic extract was washed with water, dried (Na_2SO_4) and concentrated. The residue was distilled under vacuum to furnish 10, yield: 0.173 g (80%); b.p. 130-35 (bath temp.)/ 10 mm (lit.[37] 138-39°/15 mm).

IR (liq.film): cm^{-1}: 1471, 1408, 1252, 917, 833

NMR (CCl_4): 0.83 (m, 3H, $-C\underline{H}_3$), 1.33 [m, 20H, $-(CH_2)_{10}-$], 2.25 (m, 1H, ), 2.60 (m, 2H )

The identity of the epoxide was established by comparison (b.p., IR, NMR) with an authentic sample prepared by following method.

A mixture of 1-tridecene (7) (0.96 g, 5.27 mmol), metachloroperbenzoic acid (1.6 g, 7.9 mmol) and 25 ml chloroform was kept at room temp. for 72 hrs. and filtered (to remove m-chlorobenzoic acid). The filtrate was washed successively with sodium bisulfite solution, sodium-bicarbonate solution, water and finally with saturated brine. Dried (Na_2SO_4). The residue obtained after removing chloroform was distilled at 130-35 (bath temp.)/10 mm. (lit.[37] 138-39°/15 mm) to get (10), yield = 0.95 g (91%).

2-Pentadecene (12)

By using the same method for oxidative decarboxylation (preparation of 1-trdecene), palmitic acid (15.36 g, 60 m mole) was transformed into 2-pentadecene (12). Yield: 6.32 g (51%), b.p.135-40 (bath.temp.)/10 mm. (lit.[36] 135.2°/11 mm.).

IR (liq.film): 1652 cm^{-1} (C=C).

NMR (CCl_4):).88 (m, 3H, $-C\underline{H}_3$), 1.29 (m, 22H, $-(CH_2)_n$), 2.00 (m, 2H, $C\underline{H}_2-CH=CH_2$), 4.88 (m, 2H, $-CH=C\underline{H}_2$), 5.41-5.9 (m, 1H, $-C\underline{H}=CH_2$).

1,2- Pentadecanediol (13)

2-Pentadecene (12) (2.31 g, 11 mmole) was converted into 1,2-pentadecanediol by following the same method used in the preparation of diol (8). The product obtained

was distilled under vacuum to furnish 13; yield 2.02 g (75%) b.p.158-60°(bath temp.)/1 mm, m.p. = 53-4°C R_f = 0.38 (1:1 pet.ether-acetone).

IR (Nujol): 3440 (OH).

NMR (CCl_4): 0.91 (m, 3H, $-CH_3$), 1.28 [m, 24H, $-(CH_2)_{12}-$] 3.40 - 4.1 [m, 5H, $-CH(OH)-CH_2OH$]. (Found: C, 73.50; H, 13.09. $C_{15}H_{32}O_2$ requires C, 73.71; H, 13.2%).

1-Bromo-2-acetoxy-pentadecane (14)

A mixture of 13 (0.71 g, 29 mmol), freshly distilled 2-acetoxy benzoyl bromide (1.06 g, 43.5 mmol) and acetic acid (5 ml) was stirred at 90°C for 2 hrs. Acetic acid was removed under vacuum, the residue was treated with sodium carbonate solution (5%, 50 ml) and extracted with ether. Organic extract was washed with water, dried and concentrated. The residue was purified through column chromatography over grade II alumina. Fraction eluted with pet.ether/ethyl acetate (99:1) furnished analytically pure bromo acetate (13). Yield = 0.88 g (86.4%). R_f = 0.58 (4:1 pet.ether-acetone).

IR (liq.film): 17.54 (C=O).

NMR (CCl_4): 0.90 (m, 3H, $-CH_3$); 1.31 (m, 24H, $-(CH_2)_{12}$; 2.04 (s, 3H, $-OCOCH_3$); 3.36 (d, 2H, J = 5 Hz CH_2Br); 4.86 (t, 1H, J = 5 Hz CH-OAc).

(Found: C, 58.15; H, 9.26; Br, 22.77. $C_{17}H_{33}BrO_2$ requires C, 58.45; H, 9.45; Br, 22.9).

1:2 Epoxypetadecane (15)

A mixture of bromoacetates (14) (0.42 g, 1.2 mmol) and methanolic sodium methoxide (4 ml) was kept at room temp. for 1.5 hrs. Reaction mixture was diluted with water (15 ml) and extracted with ether (50 ml). Organic extract was washed with water, dried (Na_2SO_4) and concentrated. The residue was distilled under vacuum to furnish 15, yield = 0.24 g (88%) b.p.140-145°/0.5 mm (lit.[38] 115-119°/0.2 mm).

IR (liq. film): 1460, 1408, 1252, 917, 833. NMR 0.86 (m, 3H, $-CH_3$); 1.40 [m, 24H, $-(CH_2)_{12}-$] 2.30 (m, 1H $CH-O-$), 2.62 (m, 2H, $-CH_2-O-$). The identity of the epoxide was confirmed by direct comparison (b.p., IR, NMR) with authentic sample prepared by reacting 1-pentadecene with meta-chloroperbenzoic acid.

1-Heptadecene (17)

1-Heptadecene (17) was prepared by oxidative decarboxylation of stearic acid (16) by repeating the method used in the preparation of olefins (7) and (12). The product obtained from stearic acid (17.04 g, 60 mmol) was distilled under vacuum. Yield: 7.05 g (49.4%), b.p.150-55°(bath temp.)/10 mm (lit.[36] 157°/11 mm).

IR (liq.film): 1653 (C=C).

NMR (CCl_4): 0.91 (m, 3H, $-CH_3$), 1.30 [m, 26H, $-(CH_2)_{13}-$]; 1.95 (m, 2H, $-CH_2-CH=CH_2$); 4.96 (m, 2H, $-CH=CH_2$) 5.40-6.00 (m, 1H, $-CH-CH_2$).

1,2-Hentadecanediol (18)

By following the same method for hydroxylation used in preparation of diols (8) and (13), 1-heptadecene (17) was converted into 1,2- heptadecane diol (18). The product obtained by reacting 1-heptadecene (2.61 g, 11 mmol) was distilled under reduced pressure.

Yield = 2.2 g (76% yield), b.p.160-5°/1 mm.

M.p. = 64-5°C. R_f = 0.38 (1:1 petroleum ether-acetone).

IR (Nujol): 3435 (OH).

NMR (CCl_4): 0.94 (m, 3H, $-CH_3$); 1.30 [m, 28H, $-(CH_2)_{14}-$] 3.42 - 4.00 [m, 5H, $-CH(OH)-CH_2-OH$]. (Found: C, 75.09; H, 13.13. $C_{17}H_{36}O_2$ requires C, 74.94; H, 13.32).

1-Bromo-2-acetoxy-heptadecane (19)

A mixture of 18 (1.8 g, 6.6 mmol), freshly distilled 2-acetoxy-benzoyl bromide (2.41 g, 9.9 mmol) and acetic acid (8 ml) was stirred at 90°C for 2 hrs. Acetic acid was removed under vacuum, the residue was treated with sodium carbonate solution (5%, 50 ml) and extracted with ether. Organic extract was washed with water, dried and concentrated. The residue was purified through column chromatography over grade II alumina. Fraction eluted with pet.ether/ethyl acetate (99:1) furnished analytically pure bromoacetate (19),

Yield = 2.1 g (85%), R_f = 0.56 (4:1 pet.ether-acetone).

IR (liq. film): 1752 (C=O).

NMR (CCl_4): 0.92 (m, 3H, $-CH_3$); 1.30 ⌈m, 28H, $(CH_2)_{14}$-⌋; 2.06 (s, 3H, $OCOCH_3$); 3.43 (d, 2H, J = 5 Hz, $-CH_2-Br$); 4.93 (t, 1H, J = 5 Hz, CHOAc). (Found: C, 60.22; H, 9.65. $C_{19}H_{37}BrO_2$ requires C, 60.48, H, 9.81%)

1:2 Epoxy-heptadecane (20).

A mixture of bromoacetate (19) (0.47 g, 1.24 mmol) and in methanolic sodium methoxide (4 ml) was kept at room temp. for 1.5 hrs. Reaction mixtures was diluted with water (15 ml) and extracted with ether (50 ml). Organic extract was washed with water, dried (Na_2SO_4) and concentrated. The residue was distilled under vacuum to furnish 20; yield = 0.28 g, (87.3%), b.p.145°/0.5 - (lit.[28] 136-141°/0.3 mm).

IR (liq. film): 1460, 1408, 1258, 917, 833 .

NMR (CCl_4): 0.85 (m, 3H, $-CH_3$), 1.41⌈m, 28H, $-(CH_2)_{14}$-⌋, 2.28 (m, 1H, -CH-O-), 2.63 (m, 2H, $-CH_2-O$),

The identity of the epoxide was established by direct comparison (b.p., IR, NMR) with an authentic sample, prepared in quantitative yields by reacting m-chloroperbenzoic acid with 1-heptadecene (17).

Styrene-1,2-diol (22)

A mixture of tert-butyl-alcohol (50 ml), aqueous triton B (40%, 7.4 ml) and (21) (5 g, 48 mmol) was cooled to 0°C and to this cooled solution 90% tert-butyl hydroperoxide (8.7 ml, 78.5 mmol) was added, followed by 5.2 ml of 5% OsO_4 (0.4 mmol). Keeping the temperature between 0- 3°C. The resulting solution was stirred for

2 hrs at 0°C and then stored in refrigerator overnight. Aqueous $NaHSO_3$ (5%, 100 ml) was added to the reaction mixture and the resulting mixture was allowed to warm to room temperature while stirring. This mixture was was concentrated on a rotary evaporator to remove most of the tert-butyl alcohol and water and the resulting residue was extracted with ether. The organic extract was washed with saturated brine, dried (Na_2SO_4), concentrated and residue was crystallized from benzene + pet.ether (2:8) to furnish 22. Yield = 3.9 g (58.8%). Mp. = 65-66°C (lit.[27] m.p. 66°C), R_f = 0.35 (1:1 pet.ether-acetone).

IR (Nujol): 3500 cm^{-1} (OH), 1613, 1493, 1449, 1379.

NMR ($CHCl_3$): 3.66 (4H, m, $-C\underline{H}_2OH$, two $O\underline{H}$), 4.59 (1H, t, J = 4 Hz, $-C\underline{H}-CH_2OH$).

Reaction of 2-acetoxybenzoyl bromide with styrene-1,2-diol (22)

A mixture of 22 (2.08 g, 15 mmol), freshly distilled 2-acetoxybenzoyl bromide (5.5 g, 22.6 mmol) in acetic acid (15 ml) was stirred at 90°C for 2 hrs. Acetic acid was removed under reduced pressure, the residue was treated with sodium carbonate solution (5%, 100 ml) and extracted with ether. Organic extract was washed with water, dried and concentrated. The residue was purified through column chromatography over grade II alumina. Fraction eluted with petroleum ether/ethyl acetate (98.2) furnished

bromo acetate. Yield = 3.23 g (88%). R_f = 0.54 (4:1) pet. ether-acetone).

IR (liq. film): 1754, 1493, 1449, 1370, 1235, 1064, 1031, 935.

NMR (CCl_4): 1.9 (15 H, s, CH_2-OAc), 2.0 (1.5H, s, CH-O-$COCH_3$), 3.47 (1H, d, J = 6 Hz, -CH_2Br) 4.38 (1H, m, -CH_2-OAc), 5.23 (0.5 H, m, -CH-Br) 5.8 (0.5 H, t, J = 6, CH-OAc), 7.1 (5H, s, aromatic H), (Found: C, 49.47; H, 4.71; Br, 32.64. $C_{10}H_{11}BrO_2$ requires C, 49.38; H, 4.53; Br, 32.90).

Styrene oxide (25)

A mixture of bromoacetate (0.71 g, 2.93 mmol) and methanolic sodium methoxide (3 ml, 1 M) was kept at room temp. for 1.5 hr. Reaction mixture was diluted with water (20 ml) and extracted with ether organic extract was washed with water, dried (Na_2SO_4) and and concentrated. The residue was distilled under vacuum to furnish 25, yield = 0.298 g (84.8%) b.p.120-128°/25 mm. (lit.[16] 83-84/17 mm). NMR (CCl_4): 2.77 (1H, m, H trans to benzylic H), 3.12 (1H, m, H cis to benzolic H), 3.83 (1H, m, benzylic H), 7.28 (5H, s, aromatic H).

Authentic 2-bromo-1 acetoxy-1-phenyl ethane (24)

To a stirred suspension of styrene (2.6 g, 25 mmol), water (12 ml) and N-bromosuccinimide (5 g, 28 mmol) was added dimethyl sulphoxide (3 ml) and the resulting reaction

mixture was shaken vigorously for 15-20 minutes. Reaction mixture was extracted with ether and organic layer was washed with water, dried (Na_2SO_4) to get 26, yield = 4.08 g, 81.2%.

IR: 3550, 1500, 1450, 1220, 1190, 1062, 1030, 988, 920,

NMR (CCl_4): 2.7 (1H, s, -OH, exchanges with D_2O), 3.35 (2H, m, CH_2-Br), 4.61 (1H, dd, J = 6 Hz, -CH-OH), 7.03 (5H, s, Aromatic H). Mixture of bromohydrin (26) (4.0 g, 19.9 mmol) pyridine (5 ml), acetic anhydride (10 ml), kept overnight. After usual work up furnished 24.

Yield = 4.1 g (84.8%).

IR: 1750 (C=O), 1365, 1240.

NMR: 2.0 (3H, s, CH-O-$COCH_3$), 3.47 (2H, d, J = 6 Hz, -CH_2Br), 5.8 (1H, t, J = 6 Hz, CH-OAc), 7.1 (5H, s, aromatic H).

Separation of 1-acetoxy-2-bromo-1-phenylethane (24) from the mixture of 1-acetoxy-2-bromo-1-phenyl ethane (24) and 2-acetoxy-1- bromo-1-phenylethane (23)

A mixture of bromoacetates (23) and (24) (0.291 g, 1.19 mmol) was dissolved in dioxane (5 ml) and to it was added calcium carbonate (0.14 g), and water (5 ml). The reaction mixture was heated at 70°C for 45 minutes, cooled, diluted with water (150 ml) and extracted with ether. Ether layer was washed with water, dried (Na_2SO_4) and concentrated. Residue was chromatographed using grade II alumina. Column was successively eluted with (i)pet.ether

(ii) pet.ether-ethyl acetate (98:2). Fraction eluted with pet.ether-ethyl acetate (18:2), after removing solvent furnished pure 24. Yield = 0.128 g. R_f = 0.54 (4:1 pet.ether-acetone).

IR: 1750, 1365, 1240,.

NMR (CCl_4): 2.0 (3H, s -CH-OCOC$\underline{H}_3$), 3.47 (2H, d, J = 6 Hz, -C$\underline{H}_2$Br), 5.8 (1H, t, J = 6 Hz; -C$\underline{H}$-OAc), 7.1 (5H, s, aromatic H). All data was identical with that of authentic (24).

x-Acetoxy-4-nitro-acetophenone (29)

A mixture of p-nitro-acetophenone (27) (4.95 g, 30 mmol), anhydrous aluminium chloride (0.1 g, 0.75 mmol) in 75 ml of dry ether was cooled to 5°C. To this cold mixture was slowly introduced bromine (2.3 ml, 43 mmol). Keeping the reaction temp. 0-5°C. Stirred for 10 minutes and solvent was removed under suction. To the residue obtained was added sodium acetate (8 g, 97 mmol) and acetic acid (50 ml) and the reaction mixture was refluxed for 2.5 hr. Cooled and poured in water. It was extracted with chlorofmrm, organic layer was washed with water, dried (Na_2SO_4) and concentrated to get a residue which after crystallization from ethanol furnished 29. Yield = 3.6 g, (53.8%). M.p.121-2°C (lit.[29] m.p. = 121-2°C).

IR: 1750, 1700, 1600, 1530, 1450, 1370.

1-(-Nitrophenyl)-1,2-ethanediol (31)

A solution of sodium hydroxide (1.03 g, 26 mmol), sodium borohydride (3 g, 80 mmol) in 70 ml methanol was slowly added to the suspension of -acetoxy-4-nitro-aceto-phenone (2.6 g, 11.6 mmol) in 50 ml methanol. Keeping the temp. below 15°C. The solution became dark pink red and was kept stirred at room temperature overnight. The reaction mixture was refluxed for 10 min and methanol removed 20 ml water was added to it and the reaction mixture was saturated with sodium chloride. It was extracted with ether, dried (Na_2SO_4) and concentrated. Residue obtained was crystallized from ethanol to furnish 31. Yield = 1.41 g (66.19%). M.p. = 80-81°C (lit.[29] m.p. = 81-82°C). IR: 3510, 1590, 1500, 1432, 1325, 1325, 11.82, 1190.

Reaction of 2-acetoxybenzoyl bromide with 1-(p-nitrophenyl)-ethane-1,2-diol

A mixture of 1-(p-nitrophenyl) ethane-1,2-diol (31) (0.63 g, 34.5), 2-acetoxybenzoyl bromide (1.26 g, 51.7 mmol) in acetic acid (15 ml) was heated at 90°C for 2 hrs. Acetic acid was removed under reduced pressure, the residue was treated with sodium carbonate solution (5%, 100 ml) and extracted with ether. Organic extract was washed with water, dried and concentrated. The residue was purified through column chromatography over grade II alumina. Column [illegible] was eluted successively with (i) pet.ether (ii) pet.ethr-ethyl

acetate (98:2) (iii)pet.ether-ethyl acetate (96:4) (iv) Pet.ether-ethyl acetate (94:6). Fraction eluted with pet.ether-ethyl acetate (94:6), after solvent removal furnished bromoacetate. Yield 0.836 g (84.5%), R_f = 0.42 (4:1 pet.ether-acetone).

IR: 1740, 1654, 1600, 1570, 1516, 1475, 1440, 1345, 1270, 1230, 1150, 1110, 1025, 878, 855,

NMR: 1.9 (3H, s, $-OCOCH_3$) and 2.0 (3H, s, $-OCOCH_3$) in a ratio of 1:1 by integration.

Meso 1,2-diphenylethane- 1,2-diol (36)

Benzoin (35) was prepared according to literature method.[39]

A solution of sodium borohydride (1.5 g, 39 mmol) and sodium hydroxide (0.22 g, 5.5 mmol) in 50 ml of methanol was added slowly. To a stirred suspension of benzoin (35) (5.3 g, 25 mmol) in 50 ml methanol, keeping the temp. around 8-10°C. Stirring was continued at this temp. for 1 hr more and then reaction mixture was refluxed for 10 minutes. Reaction mixture was completely evaporated to dryness and then treated with dilute sulphuric acid (10%, 50 ml). After shaking for 5 mins. it was extracted with chloroform. Organic layer was washed with saturated brine and dried (Na_2SO_4). Chloroform was recovered and the solid obtained was crystallized from 60 ml benzene to get crystalline 36; yield = 3.58 g (67%), M.p. = 136-7°C (lit.[39] m.p. = 136-7°C).

IR: 3490, 1450, 1380, 1282, 1030, 1020, 915, 818, 755, 700.

Reaction of 2-acetoxybenzoyl bromide with meso 1,2-diphenyl-ethane-1,2-diol (36)

A mixture of 36 (2.14 g, 10 mmol) and freshly distilled 2-acetoxybenzoyl bromide (3.65 g, 15 mmol) in acetic acid (15 ml) and stirred at 90°C for 2 hrs. Acetic acid was removed under reduced pressure, the residue was treated with sodium carbonate solution (5%, 100 ml) and extracted with ether. Organic extract was washed with water, dried (Na_2SO_4) and concentrated. The residue was purified through column chromatography using grade II alumina. The column was successively eluted with (i) pet.ether (ii) 99:1, pet.ether-ethyl acetate (iii) 98.2 pet.ether-ethylacetate. The fraction eluted with 98.2 pet.ether-ethyl acetate, on solvent removal gave bromo acetate (37) Yield = 2.074 g (65%). R_f = 0.47 (4.1 pet.ether-acetone). (liq.film)
IR: 1754, 1667, 1626, 1600, 1493, 1449, 1370, 1325, 1266. NMR: (CCl_4): 2.06 (3H, s, CH-OAc), 5.03 (1H, d, J = 9 Hz, CH-Br), 6.10 (1H, d, J = 9 Hz, CH-OAc), 7.0(5H, s, aromatic), 7.07 (5H, s, aromatic). (Found: C, 60.00; H, 4.81; Br, 24.92. $C_{16}H_{15}BrO_2$ requires C, 60.19; H, 4.70; Br, 25.06).

cis-Stilbene oxide (38)

A mixture of bromoacetate (37) (0.45 g, 1.4 mmol) and 1 M methanolic sodium methoxide (5 ml) was kept at room

temp. for 1.5 hr. Reaction mixture was diluted with water (20 ml) and extracted with ether (50 ml). Organic extract was washed with water, dried (Na_2SO_4) and concentrated. The residue was distilled to get 38, Yield = 0.24 g (86.3%) b.p.130-4° (bath temp)/3 mm. (lit.[49] b.p.126-34° at 4 mm).
IR (liq. film): 1667, 1626, 1600, 1497, 1460, 1408, 1282, 1064, 943, 803.
NMR (CCl_4): 4.03 (s, 2H, -CH-CH), 6.83 (s, 10H, aromatic)

trans-Stilbene (39)

Trans-Stilbenzene (39) was synthesised by reduction of benzoin (35) using literature method.[32]

Erythro 1-acetoxy-2-bromo-1,2-diphenylethane (40)

A mixture of trans stilbene (39) (1 g, 5.5 mmole), dimethyl sulphoxide (40 ml), water (1 ml) was cooled to 10°C and to it was added N-bromo succinimide (2 g, 11 mmole) slowly, maintaining the temp. at 10-15°C. Reaction mixture was kept stirred at this temperature for 15 mins. to get a clear solution, poured in water and extracted with ether. Ether removed and resulting residue was crystallized from pet.ether to get bromohydrin. yield = 1.12 g (72.7%). M.p.83-4 (lit.[33] m.p.83.5-85°).
IR: 3350 (OH).

The bromohydrin was acylated using acetic anhydride (10 ml) and pyridine (5 ml). After usual workup obtained a solid, which after crystallization from acetone-pet.ether

(1:9) furnished (40). Yield = 0.98 g (85.2%) M.P.100- 1°.
R_f = 0.47 (4:1 pet.ether-acetone).
IR: 1755 (C=O).
NMR (CCL_4): 1.80 (3H, s, CH-OcO$\underline{CH}_3$), 4.8 (1H, d, J = 7 Hz, $\underline{CH}$-Br), 5.8 (1H, d, J = 7 Hz, $\underline{CH}$-OAc), 6.83 (10H, s, aromatic). (Found: C, 60.04; H, 4.54; Br, 24.86.
$C_{16}H_{15}BrO_2$ requires C, 60.19; H, 4.70; Br. 25.06%).

Authentic trans- stilbenzene oxide (41)

A mixture of erythro-2-bromo-1-acetoxy-1,2-diphenyl-ethane (0.59, 1.55 mmole) and M methanolic sodium methoxide (4 ml) was kept at room temp. for 1.5 hr. Poured in water (20 ml) and extracted with ether. Ether extract was washed with water, dried (Na_2SO_4). After ether removal furnished a solid which was crystallized from ethanol to furnish (41). Yield = 0.28 g (92.5%). R_f = 0.68 (4:1 pet.ether-acetone), m.p.67-8°C (lit.[43] m.p.69-70°C).
IR (Nujol): 1613, 1493, 1449, 1370, 1351, 1242, 1176, 1093, 1031, 794, 746.
NMR (CCl_4): 3.57 (2H, s, -$\underline{CH}$ - $\underline{CH}$-), 7.0 (10H, s, aromatic).

L(+)-(s)-methyl lactate (43)

L(+)-(s)-lactic acid (Fluka make) $(\alpha)_D^{27}$ = -13.25 (c, 1.54 in H_2O [lit.[14] $(\alpha)_D^{27}$ = - 14.6 (neat)] (5 g, 55 mmole) was esterified using diazomethane to furnish -(-)-(s)-methyl lactate . Yield = 5.03 g (87%).

IR: 3510 (OH), 1745 (C=O)

$(\alpha)_D^{27}$ = - 12.9 (c, 1.72 in $CHCl_3$) [lit.[14] $(\alpha)_D^{26}$ = -13.9 neat]

(+)-(s-)Propane-1,2-diol (44)

To a stirred suspension of lithium aluminium hydride (3 gms, 79 mmole) in dry ether (75 ml) was added an ether solution of -(-)-(s)-methyl lactate (43) (4.9751 g, 47.8 mmole) slowly, maintaining the temperature at 0-3°C. After the addition was over, the reaction mixture was stirred for 3 hrs. at room temperature and kept overnight. It was refluxed for 3 hrs and cooled to 0°C. The excess lithium aluminium hydride was carefully decomposed by introducing wet ether (10 ml) followed by water (10 ml). Stirring was continued at 0°C for 2 hrs. By this time reaction mixture turned completely white. Ether was decanted and the solid was washed with dichloromethane (total 200 ml). Combined extracts were dried (Na_2SO_4) and evaporated to get a liquid which on distillation furnished 44. Yield = 2.792 g (76.8%), b.p.120-22° (bath temp.)/25 mm. (lit.[14] 93°/18 mm) $(\alpha)_D^{25}$ = + 20.05 (c, 0.7 in H_2O) [lit.[14] $(\alpha)_D^{20}$ = + 20.7 (c, 7.5 in H_2O)].

IR: 3500 (OH)

Acetoxy-bromopropanes

A mixture of (+)-(s)-propane-1,2-diol (1 g, 13 mmol) and 2-acetoxybenzoyl bromide (4.74 g, 19.5 mmole) in acetic acid (10 ml) was heated at 90°C for 2 hrs. Acetic acid

was removed under reduced pressure, the residue was treated with sodium carbonate solution (5%, 50 ml) and extracted with ether. Organic extract was washed with water, dried (Na_2SO_4) and concentrated. The residue was purified through column chromatography over grade II alumina. Column was successively eluted with (i) pet.ether (ii) pet.ether-ethyl acetate (99:1). Fraction eluted with pet.ether-ethyl acetate (99:1), after removing solvent furnished bromoacetates. Yield = 2.08 g (87.3%), b.p.105-10 (bath)/40 mm (lit.[14] b.p.57°/11 mm).

IR (liq. film): 1752 (C=O).

NMR (CCl_4): 1.34 (2.76 H, d, -O-COC$\underline{H}_3$), 3.43 (1.84 H, d, C$\underline{H}_2$-Br), 5.02 (0.92 H, m, -CH-OAc) due to 2-acetoxy-1-bromopropane (92% by integration) and 1.7 (0.24 H, d, -C$\underline{H}_3$), 4.18 (0.24 H, m, -C$\underline{H}_2$-OAc and C$\underline{H}$-Br) due to 1-acetoxy-2-bromopropane (8% by integration).

$(\alpha)_D^{27}$ = -12.65 (c, 5.5 in $CHCl_3$) [lit.[14] $(\alpha)_D^{2}$ = - 13.55 (c, 5.8 in $CHCl_3$). Enantiomeric excess is 93%

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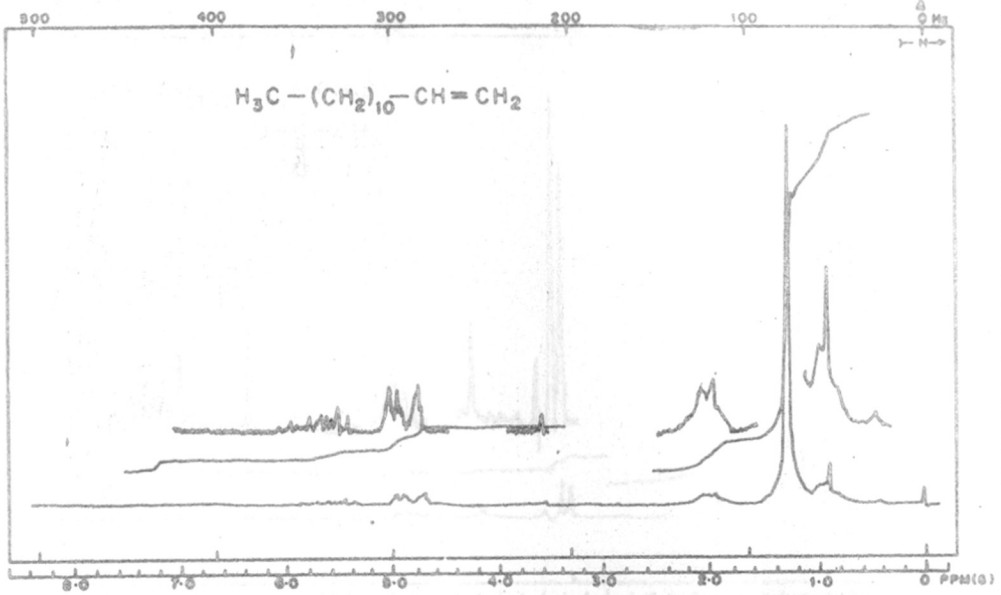
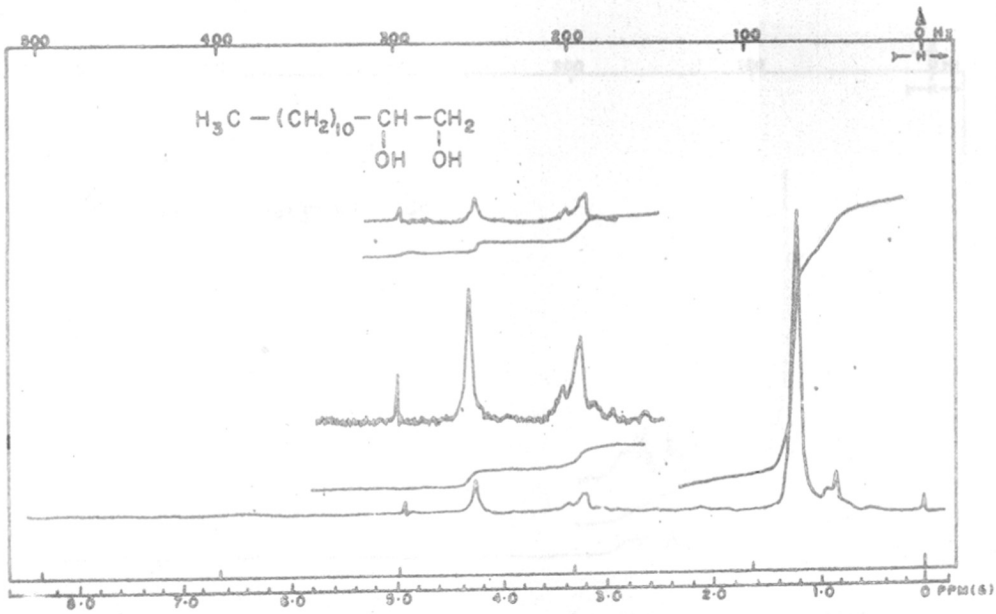
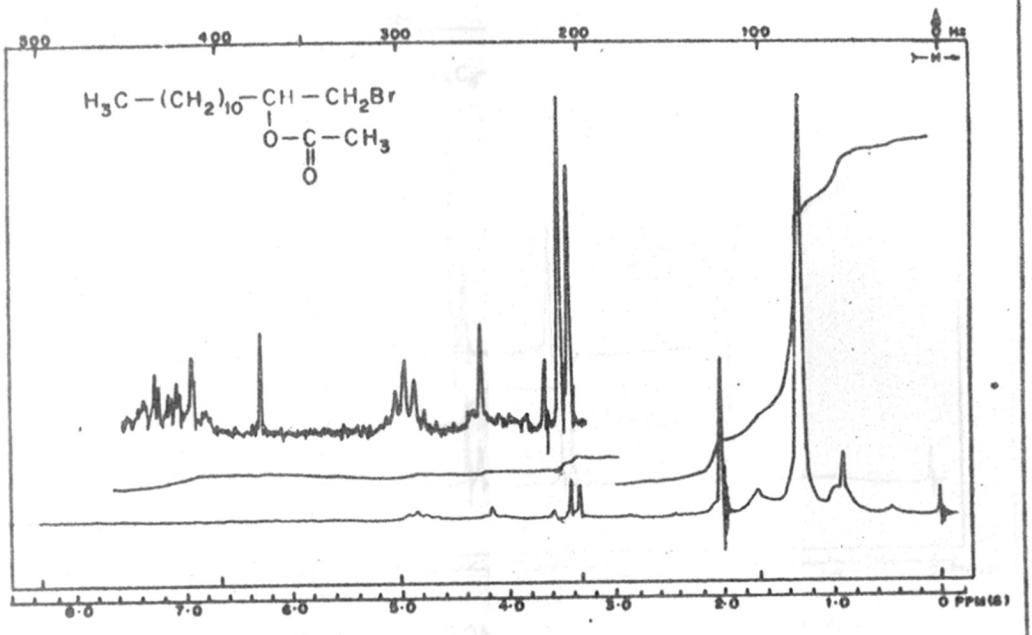


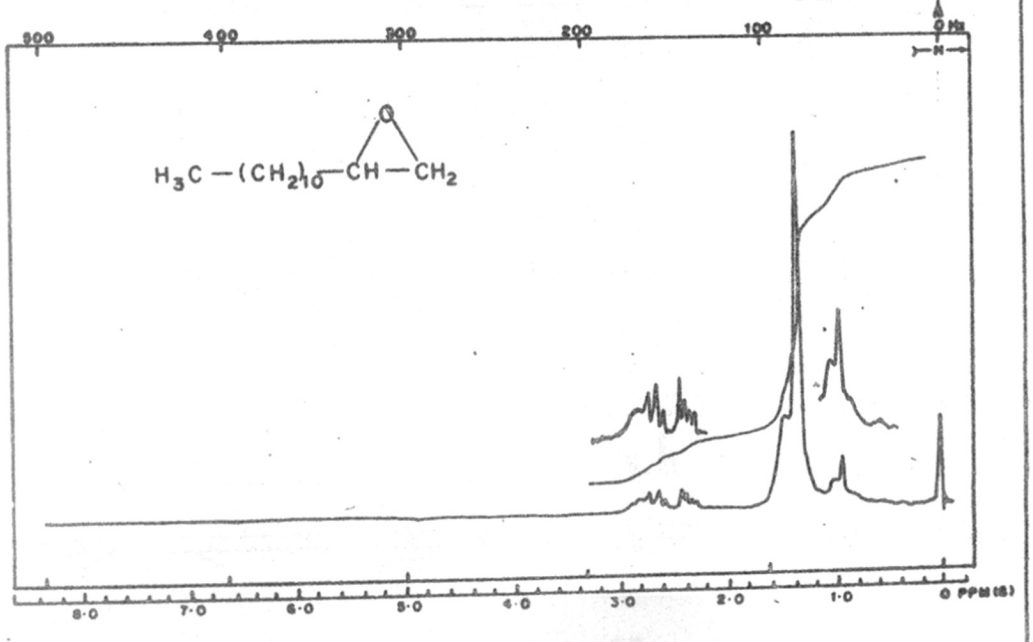
NMR OF 1- TRIDECENE.



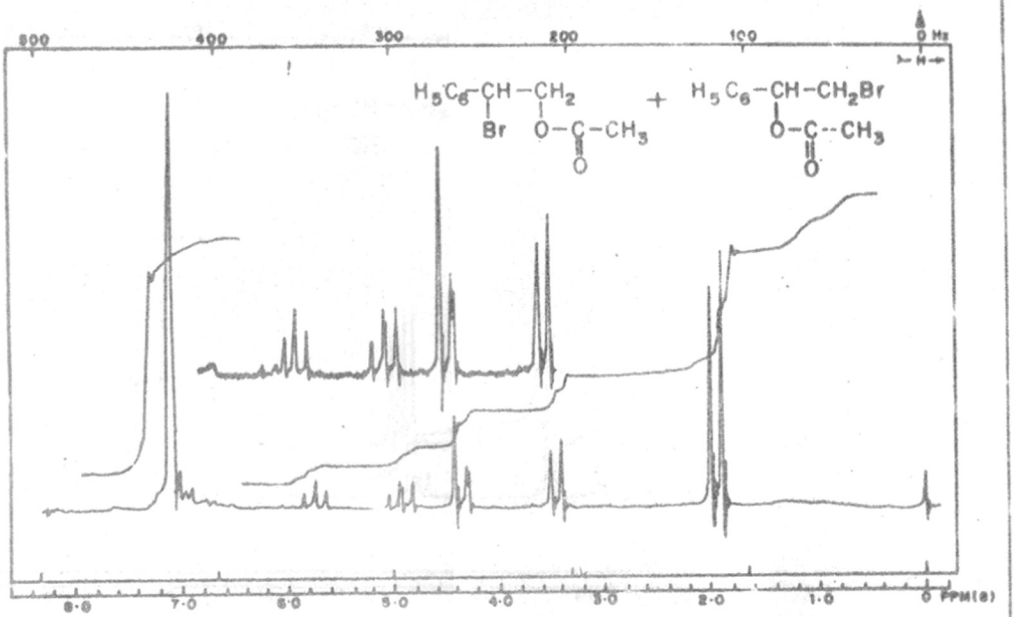
NMR OF 1,2-TRIDECANEDIOL.



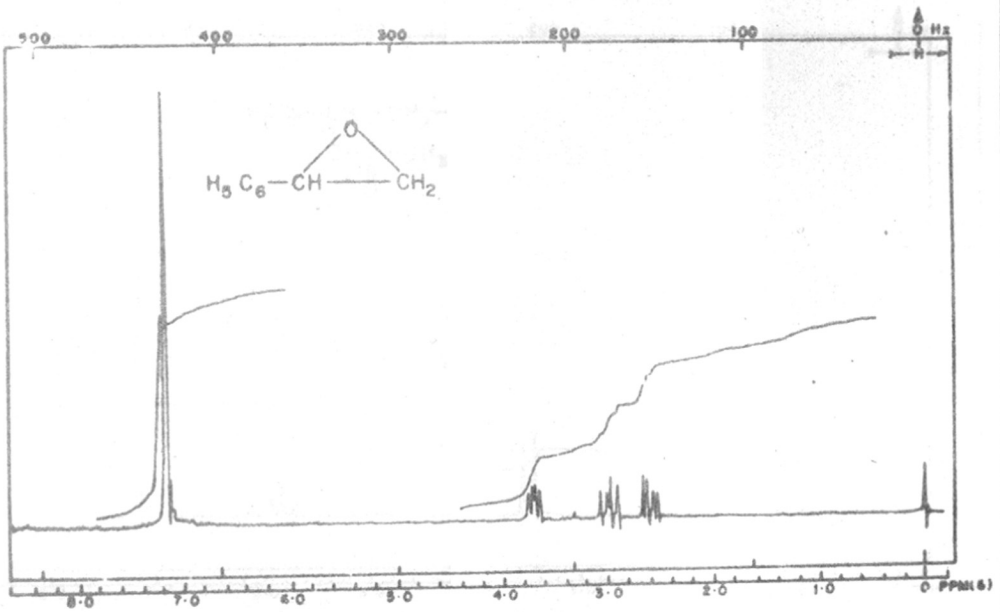
NMR OF 1-BROMO-2 ACETOXYTRIDECANE.



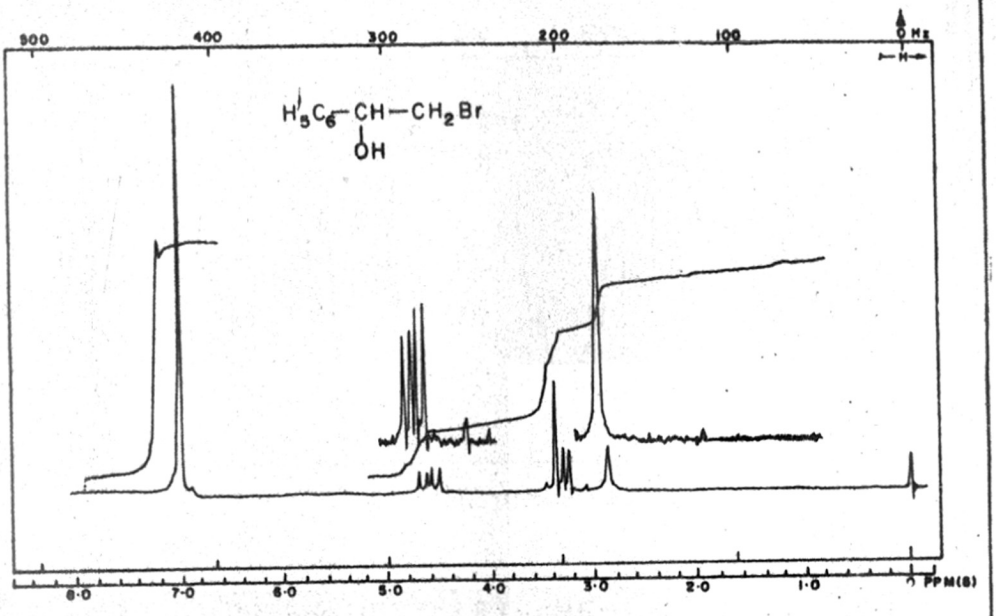
NMR OF 1:2 EPOXYTRIDECANE.



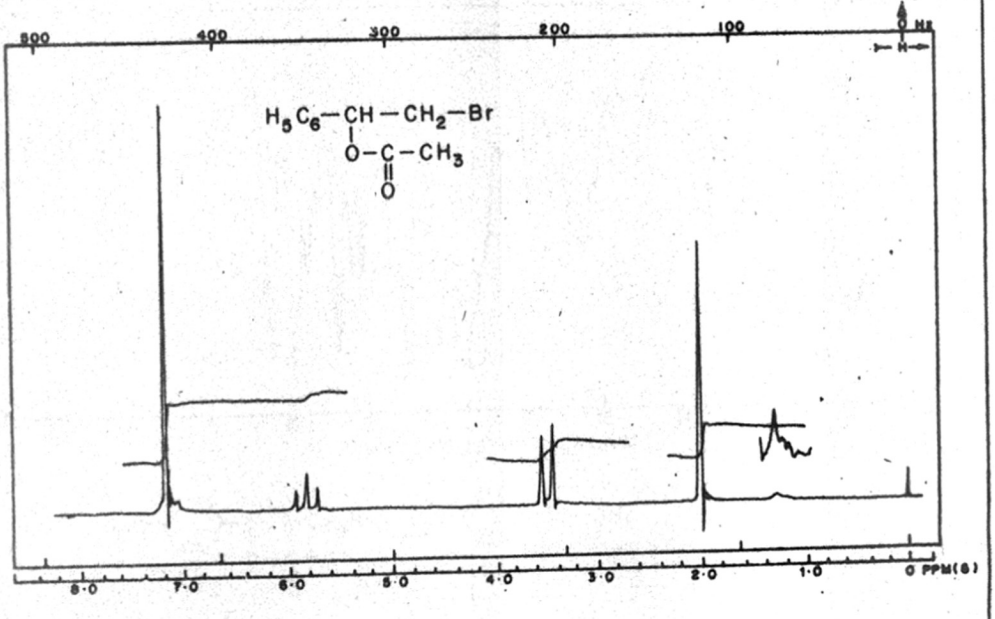
NMR OF MIXTURE OF 1-BROMO-2-ACETOXY-1-PHENYLETHANE AND 1-ACETOXY-2-BROMO-1-PHENYLETHANE.



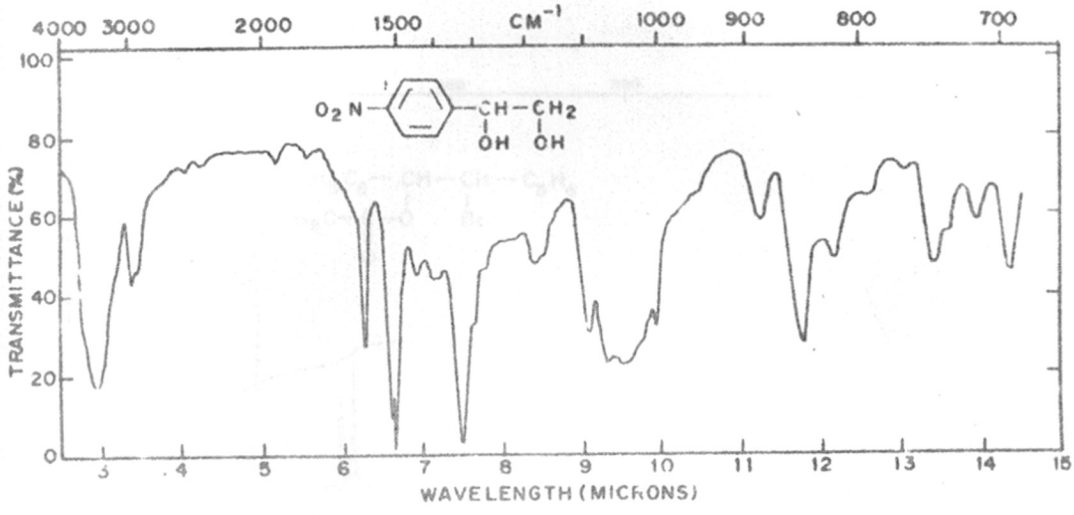
NMR OF STYRENE OXIDE.



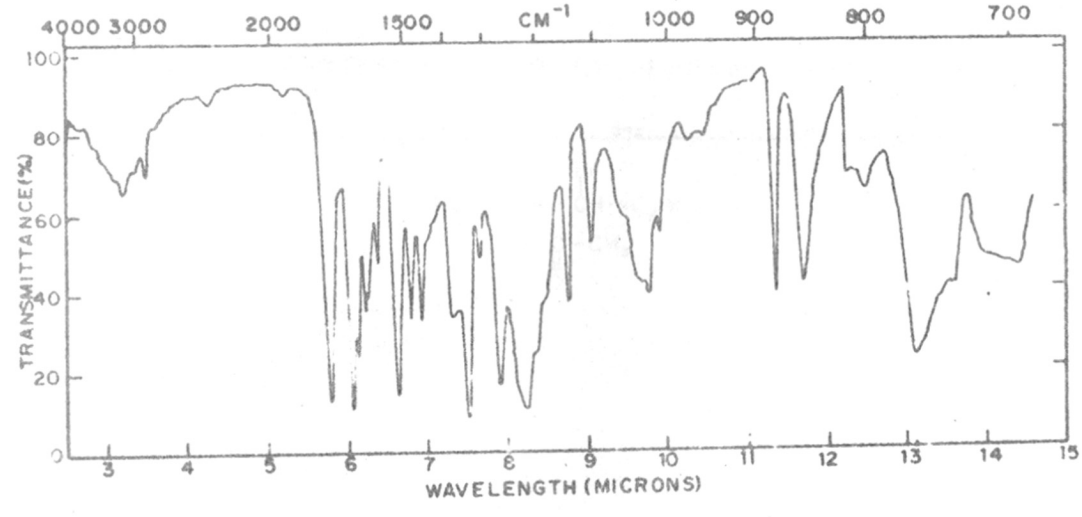
NMR OF 2-BROMO-1-HYDROXY-1-PHENYLETHANE.

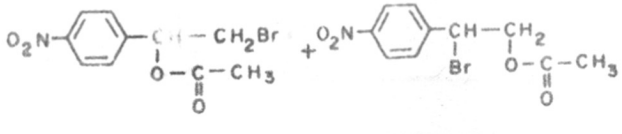


NMR OF 2-BROMO-1-ACETOXY-1-PHENYLETHANE.

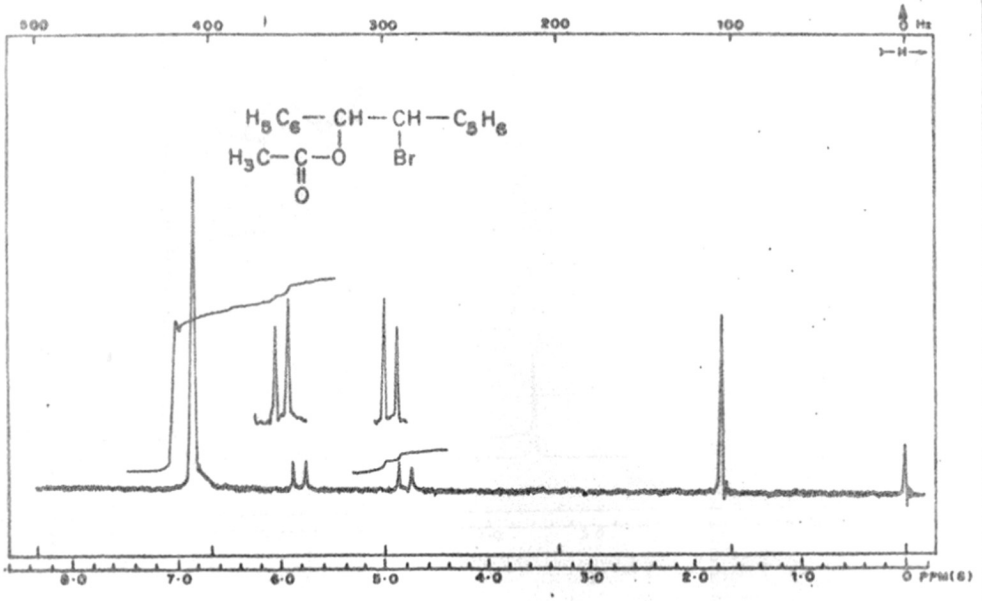


IR OF 1-(p-NITROPHENYL) ETHANE-1,2 DIOL.

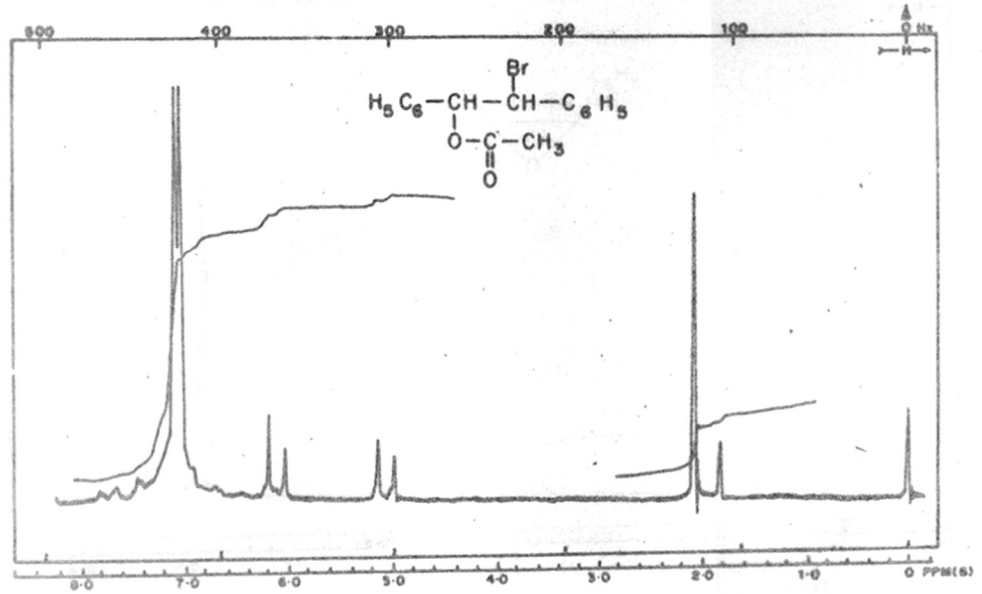




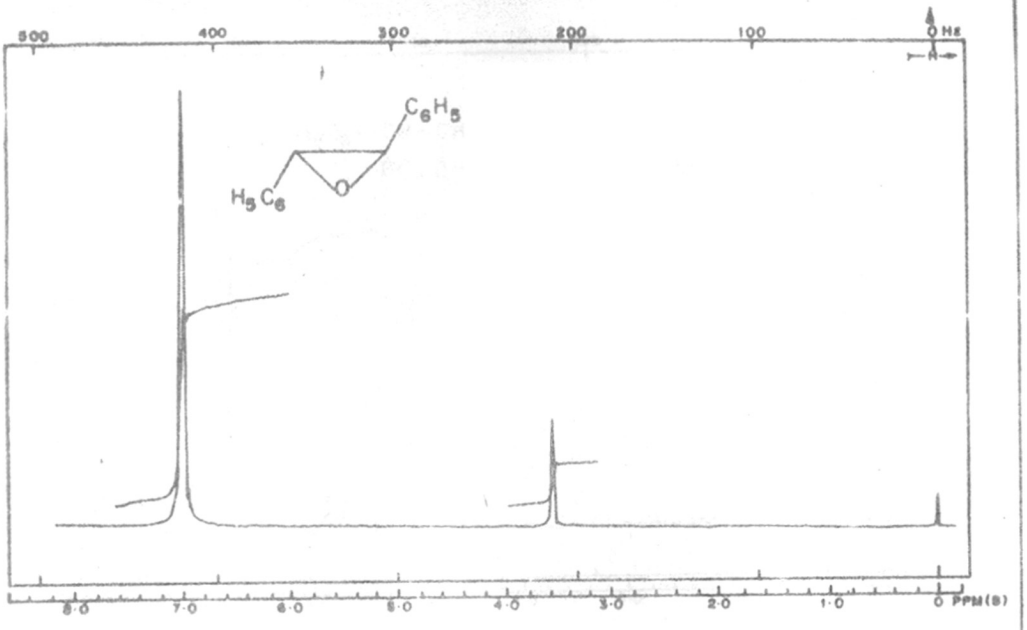
IR OF MIXTURE OF 1-BROMO-1-(p-NITROPHENYL)-2-ACETOXY--ETHANE( ) & 1-ACETOXY-1-(p-NITROPHENYL)-2-BROMOETHANE.



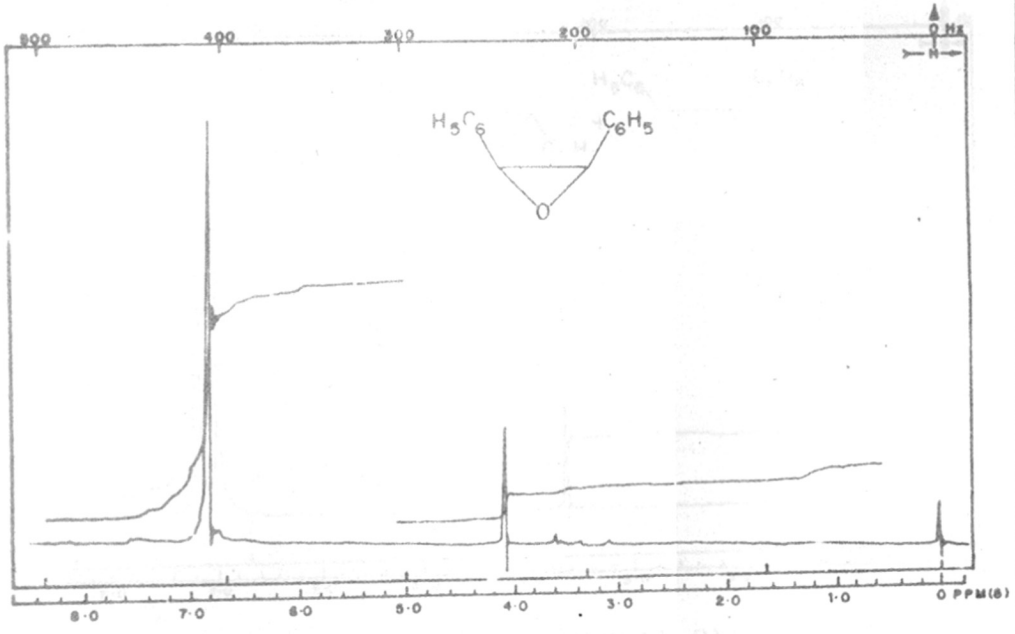
NMR OF ERYTHRO 1-BROMO-1,2 DIPHENYL-2-ACETOXYETHANE.



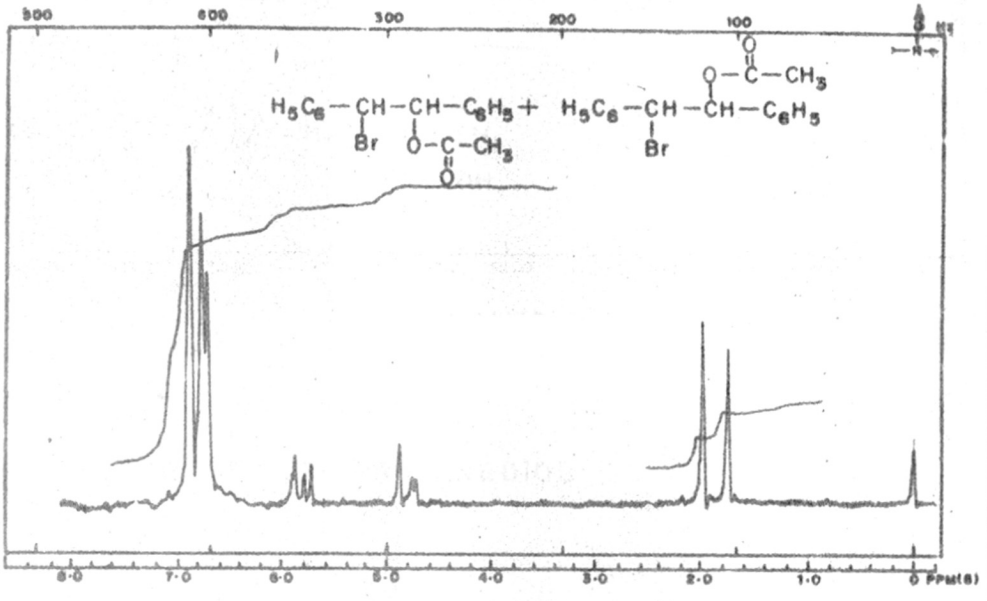
NMR OF THREO 1-BROMO-1,2 DIPHENYL-2-ACETOXYETHANE.



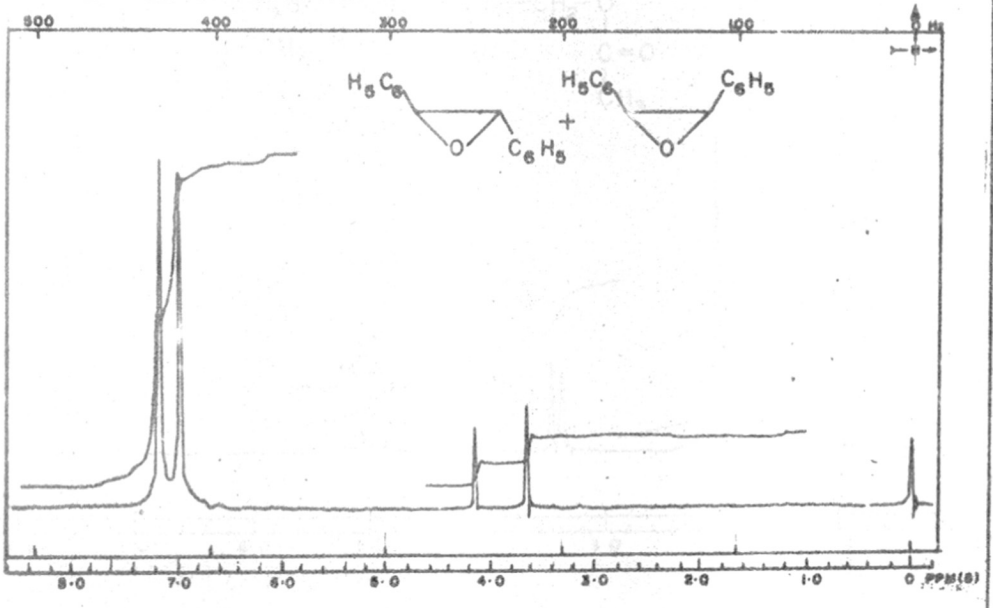
NMR OF TRANS-STILBENE OXIDE.



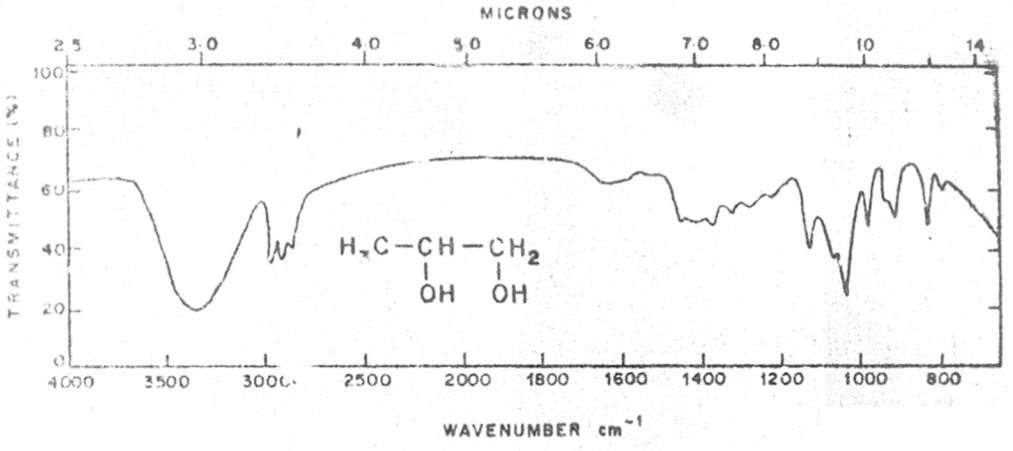
NMR OF CIS-STILBENE OXIDE.



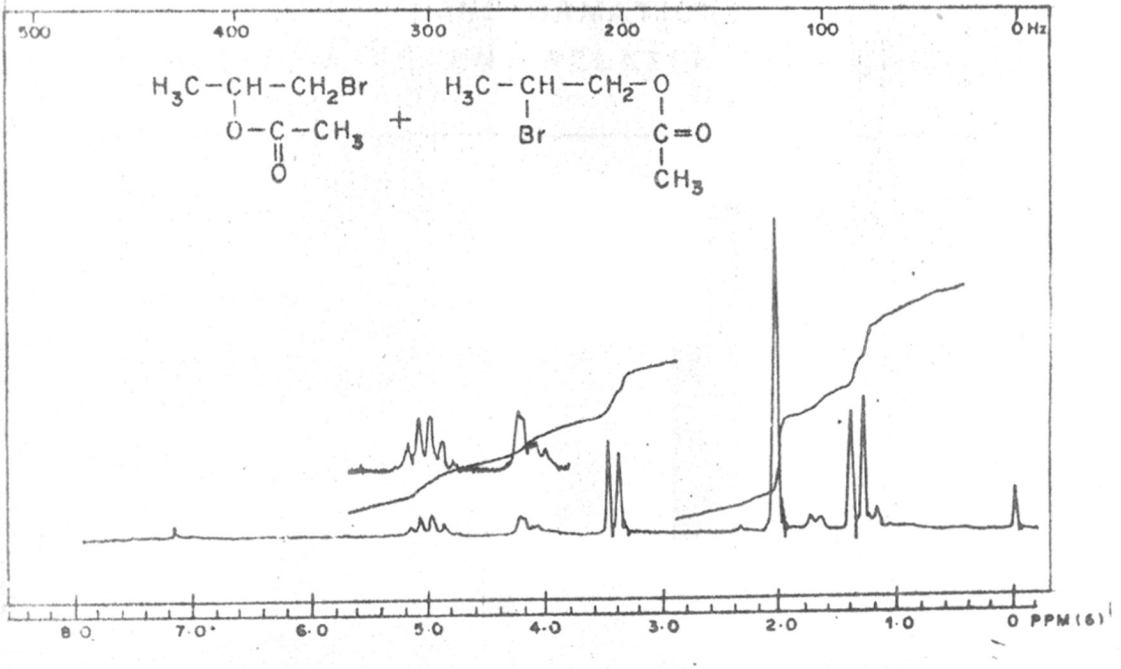
NMR OF MIXTURE OF ERYTHRO 1-BROMO-1,2-DIPHENYL-2-ACETOXYETHANE ( ). AND THREO 1-BROMO-1,2-DIPHENYL-2-ACETOXYETHANE.



NMR OF MIXTURE OF TRANS-STILBENE OXIDE ( ). AND CIS-STILBENE OXIDE.



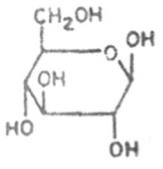
IR OF 1,2-PROPANEDIOL



NMR OF MIXTURE OF 1-BROMO-2-ACETOXYPROPANE( )AND 1-ACETOXY-2-BROMOPROPANE.

CHAPTER–3

SOME TRANSFORMATIONS OF CARBOHYDRATES AND RELATED COMPOUNDS



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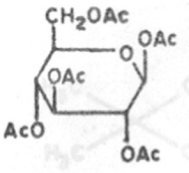

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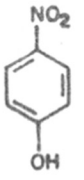

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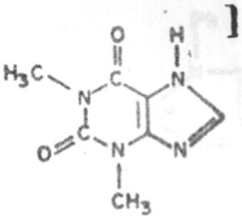

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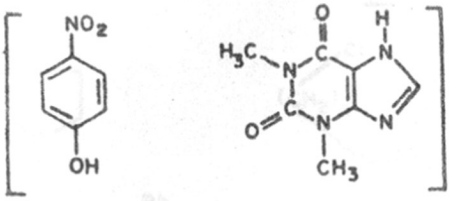
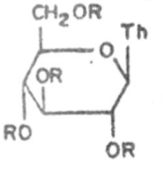


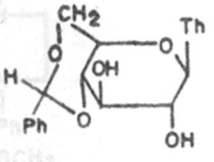
Complex (1:1)

5



6a : R = OAc

6b R = OH



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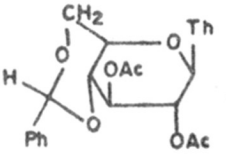

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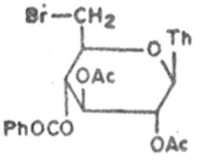

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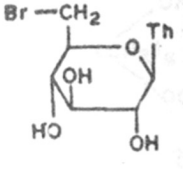
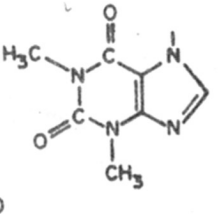
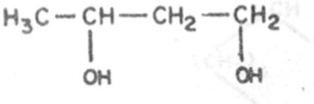


10 Where Th =





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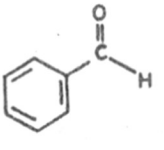

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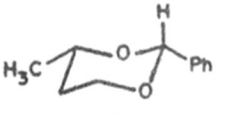

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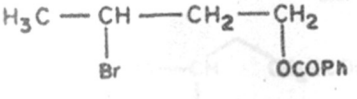

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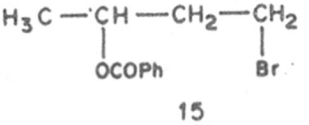

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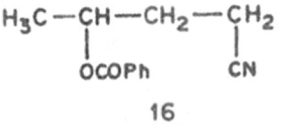

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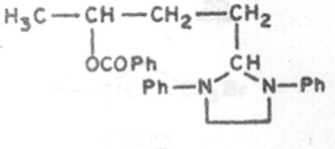

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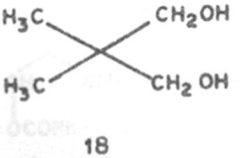

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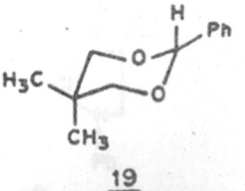

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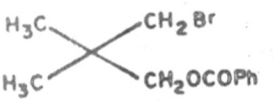

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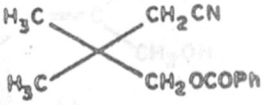

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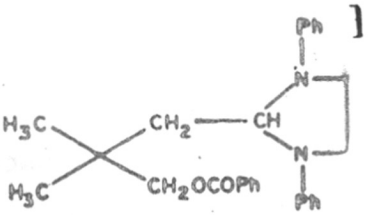

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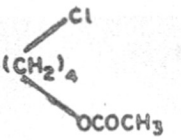

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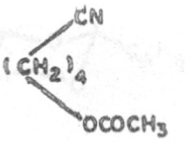

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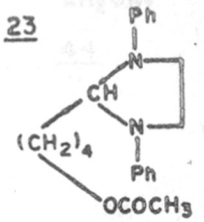

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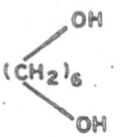

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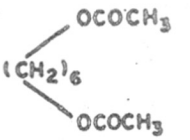

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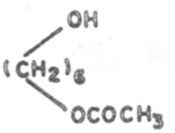

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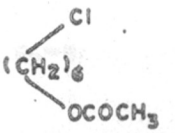

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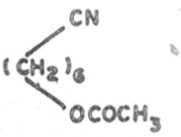

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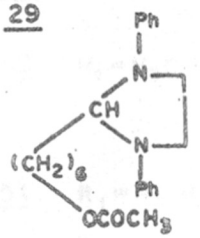

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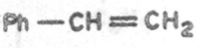

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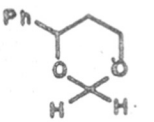

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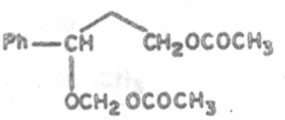

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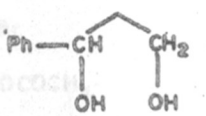

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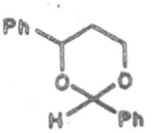

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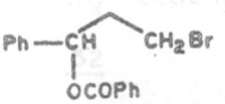

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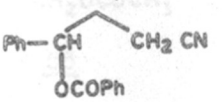

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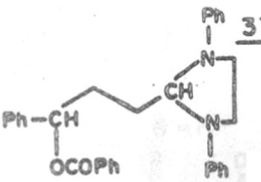

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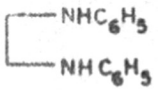

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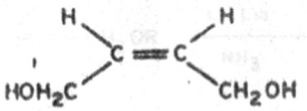

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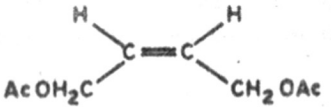

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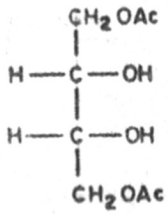

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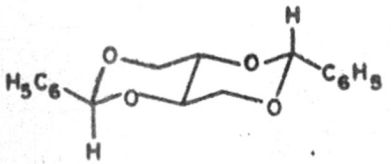

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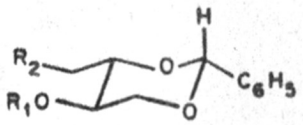


46, $R_1 = H_5C_6-\overset{O}{\overset{\|}{C}}-$, $R_2 = Br$

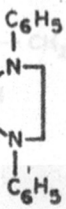
47, $R_1 = H$, $R_2 = Br$

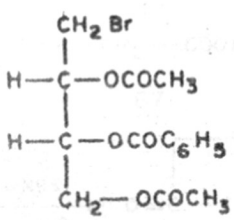
48, $R_1 = H_3C-\overset{O}{\overset{\|}{C}}-$, $R_2 = Br$

49, $R_1 = H_3C-\overset{O}{\overset{\|}{C}}-$, $R_2 = CN$

50, $R_1 = H_3C-\overset{O}{\overset{\|}{C}}-$, $R_2 =$

51 $R_1 = H$, $R_2 =$





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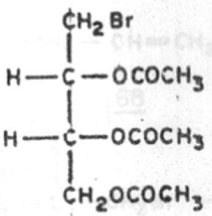

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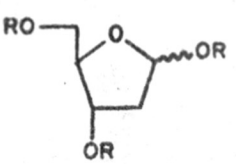
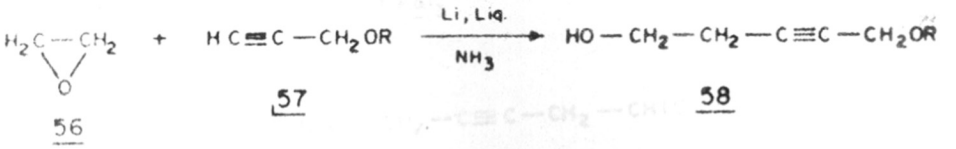


54 R = H

55 R = $-\overset{O}{\overset{\|}{C}}-CH_3$

SCHEME — A



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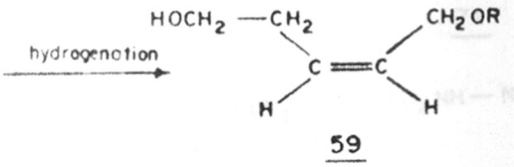

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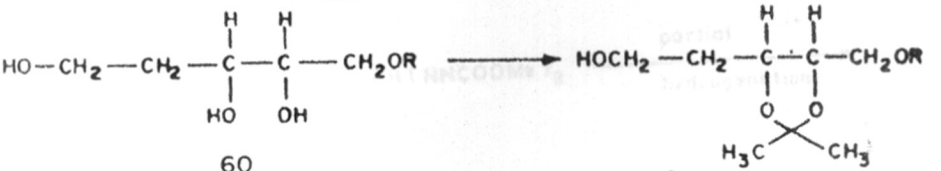
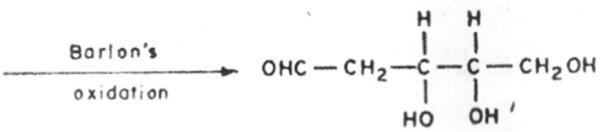


60 61

R = Tetrahydropyranyl



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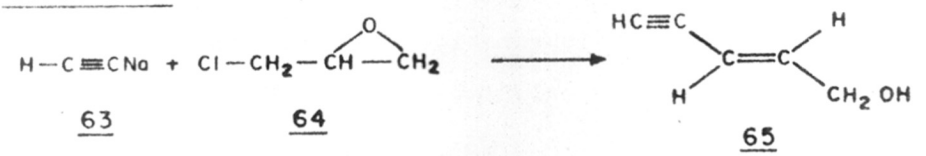
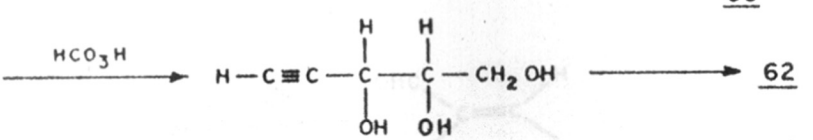
SCHEME — B



63 64 65



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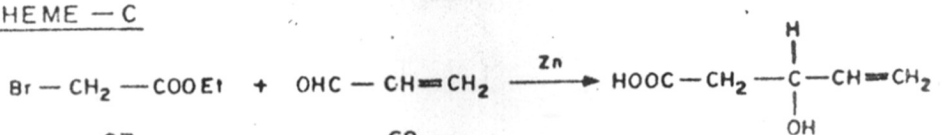
SCHEME — C



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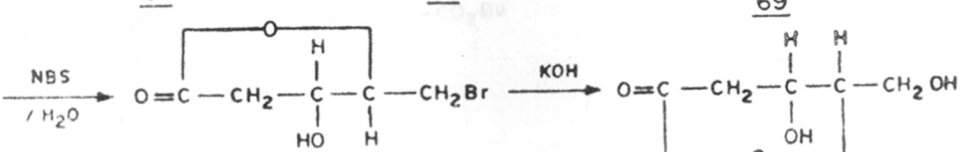

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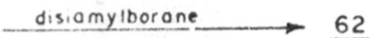

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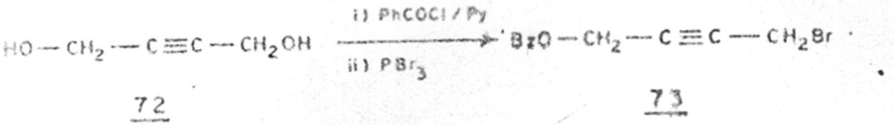
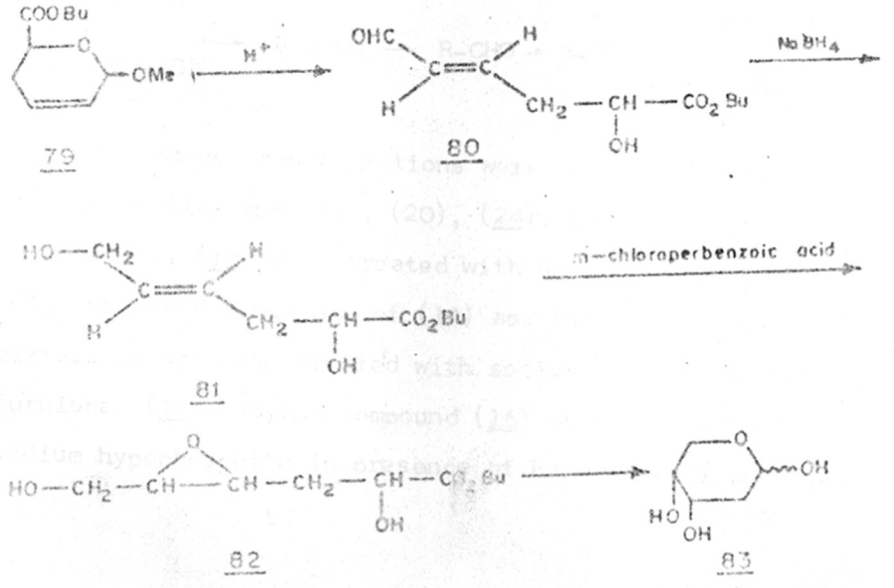
SCHEME — D



SCHEME — E

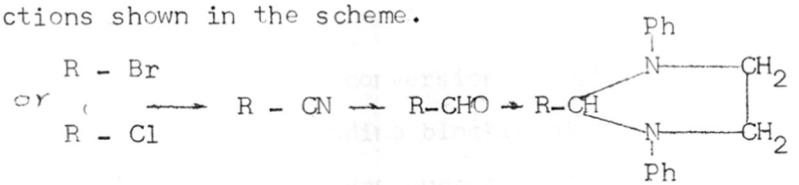


SUMMARY

A synthesis of 7,β-D-glucopyranosyltheophylline (6b) was carried out keeping in mind its higher solubility in water than a well known antiasthmatic and diuretic drug theophylline penta-acetate (2) on condensation with theophylline in the presence of p-nitrophenol and p-toluene sulphonic acidyielded (6a). The nucleoside 6a on treatment with methanolic ammonia furnished (6b)

(6b) when treated with benzaldehyde in the presence of zinc chloride furnished (7). Acetal 7 on acylation with pyridine and acetic anhydride yielded (8). Action of N-bromosuccinimide on (8) furnished (9). Bromo compound(9) when treated with methanolic ammonia yielded nuceloside(10).

A convenient route for preparing aldehydes from alkyl halides was studied employing the sequence of reactions shown in the scheme.



The above transformations were carried out on mixture of (14) and (15), (20), (24), (30) and (38).

Acetal (13) when treated with N- bromosuccinimide in CCl_4 furnished a mixture of (14) and (15). When the mixture as such was treated with sodium cyanide in DMSO it furnished (16). Cyano compound (16) when reduced with sodium hypophosphite in presence of Raney nickel and 1,2-

dianilino ethane furnished (17).

Repeating all reactions as above on bromo compound (20) furnished cyano compound (21) and finally a blocked aldehyde (22).

Similarly chloroacetate (24) on treatment with sodium cyanide in DMSO gives cyano compound (25) which on reduction (as in the case of 16) furnishes (26).

Following similar sequence of reactions on chloro acetate (30), cyano compound (31) and compound 32 were isolated.

Diol (36) was reacted with benzaldehyde in presence of p-toluene sulphonic acid to get acetal (37). Acetal (37) when reacted with N- bromosuccinimide in CCl_4 furnished a bromo compound (38) which on treatment with sodium cyanide in DMSO afforded cyano compound 39. Reduction of 39 with sodium hypophosphite in presence of Raney nickel and 1,2-dianilino ethane produced (40).

Thus the route for conversion of alkyl chloridesor bromides to the corresponding blocked aldehydes was standardized and then it was successfully applied to synthesise hydroxy compound (51), which is a key intermediate in the synthesis of 2-deoxy ribose[1], as follows.

Action of N-bromosuccinimide on 1,3:2,4-di-O-benzylidene erythritol (45) furnished bromo compound (46) which on treatment with alcoholic KOH gave the hydroxy compound(47).

Hydroxy compound (47) was acetylated using acetic anhydride in presence of pyridine to get acetate (48). When treated with sodium cyanide in DMSO 948) afforded a cyano compound (49) which on reduction with sodium hypophosphite in presence of Raney nickel and 1,2-dianilino-ethane furnished compound (50). Alkaline hydrolysis of (50) with methanolic NaOH gave hydroxy compound (51) which is a key intermediate in the synthesis of 2-deoxy-ribose.

When bromo compound (46) was treated with acylating mixture of acetic anhydride, acetic acid and conc.H_2SO_4 yielded a bromo benzoate 52. The hydroxy compound (47) was treated with acylating mixtureto furnish the bromo-triacetate.(53)

INTRODUCTION

The synthesis of theophylline nucleosides is of current interest[2,3,4,5], since many purine nucleosides show interesting biological activities. A commercial route for the manufacture of theophylline starting from 1,3-dimethyl urea has been developed in our laboratory and the author (P.L. Joshi) of this thesis has taken part in the development of the process which is now being utilized by some industries. Hence it is of interest in synthesising nucleosides using theophylline and readily available sugars e.g. α -D-Glucose.

Because of the low solubility of theophylline in water it has to be suitably modified to be used as a drug. Since 7- β -D-glucopyranosyl theophylline (6b) has a higher solubility in water, a plan for developmental work for synthesis of (6b) and for antiviral activity testing at National Virological Research Institute has been chalked out. Due to this programme there was a scope for studying the transformations of nucleoside (6b), which has been carried out in our laboratory.

The thermal fusion method for the synthesis of nucleosides is very widely employed. Normally a catalyst is used during fusion reaction. Hashizume[4] used bis (p- nitrophenyl) hydrogen phosphate and its methyl derivative as a catalyst during the fusion of penta-

acetate (2) and (4). Literature[6] describes a method for synthesis of (6b) using thermal fusion of (2) and (4) under vacuum in presence of p-toluene sulphonic acid as a catalyst. A nucleoside synthesis is reported[7] according to which the reactants are heated in the presence of stannic chloride as a catalyst. A fusion reaction of acylated sugars with some purine derivatives and phenols is also reported[8]. Another method for the synthesis of nucleoside (6b) is reported which involves condensation of acylated glycosyl bromide with bis (theophylline-7 yl) mercury[5]. A convenient method in which a 1:1 complex of theophylline and p-nitrophenol was reacted with (2) in the presence of p- toluene sulphonic acid as a catalyst is described[9].

Since halo sugars can be readily converted to deoxy sugars or cyano sugars or amino sugars, they are an important class oc compounds in carbohydrates. Hence we became interested in the synthesis of bromonucleoside (10).

The deoxy sugars, long known as components of natural product are an important class of carbohydrates. Many deoxy sugars confer unique biological properti s on the natural products of which they are a part. The terminal deoxy and 2- deoxy sugars occurring as components of cardiac glycosides and as antigenic determinants in bacterial polysaccharides have received special attention from the biological stand point. Several unusual sugars have been isolated from other natural products in recent

years[10]. Since 2-deoxy-pentoses are carbohydrate components of the deoxy- nucleic acids, they possess a particular biological importance[11]. One of the members of this class has been extensively investigated since (i) it occurs naturally as the carbohydrate component of DNA and (ii) nucleosides derived from it show antiviral and antineoplastic activity. Some of the available approaches in literature for the synthesis of 2-deoxy-DL-ribose are presented here. 1. M. Nakagawa et al.[12] prepared 2-deoxy-DL-erythropentose (62) starting from ethylene oxide and propargyl alcohol (Scheme A). The reaction of lithium acetylide of propargyl alcohol derivative (57) in refluxing liquid ammonia with ethylene oxide (56) gave C_5-acetylenic compound (58). A half reduction of (58) by means of Lindlar catalyst afforded C_5-cis-ethylenic compound (59). Compound 59 was treated with potassium permanganate to cause cis-hydroxylation of the cis-ethylenic bond to furnish triol (60), which on reaction with acetone and anhydrous cupric sulphate yielded (61). The Barton's oxidation of crude (61) followed by acid hydrolysis of the protective groups resulted in 62. In another route (Scheme B), 62 was prepared by the hydroboration of DL-erythro-4-pentyn-1,2-3-triol (66) followed by hydrogen-peroxide oxidation. Reaction between epichlorohydrin (64) and sodium acetylide (63) furnished trans-2-pentene-4-yn-1-ol (65) which on trans-hydroxylation by means of performic

acid yielded DL-erythro-4-pentyn-1,2,3-triol (66). Triol(66) was treated with excess of bis (1,2-dimethylpropyl)borane and the reaction product was oxidised with hydrogen peroxide under careful addition of 1N sodium hydroxide solution to furnish 62.

2. This method of preparation of 2-deoxy-DL-ribose (62) involved[13], Reformatsky reaction of ethyl bromoacetate (67) with acrolein (68), followed by alkaline hydrolysis furnished DL-hydroxy acid (69), which on treatment with N-bromosuccinimide in water followed by chromatographic purification on silica gel yielded bromo-lactone 70. Lactone 70 with aqueous 1N potassium hydroxide at room temperature followed by standing at pH 1 for 24 hr. afforded 2-deoxy-erythro-penteno-γ-lactone (71). Lactone (71) was reduced by the use of bis (1,2-dimethyl-propyl) borane (disiamyl borane) to furnish 62. Reaction sequence is shown in Scheme C.

3. This method involved[14] the conversion of but-2-yne-1,4-diol (72) into 2-deoxy-DL-ribose (62) (Scheme D). Mono-benzoylation of diol (72) and treatment of the resulting half- ester with phosphorous tribromide furnished 1-benzoyloxy -4-bromobut-2yne (73). The bromo compound (73) with ethyl sodiomalonate gave the expected ethyl 5-benzoyloxy-pent-3-yne-1:1-dicarboxylate (74). Treatment of hydrazine on (74) yielded dihydrazide (75). Compound (75) was subjected to double curtius degradation with nitrous acid, followed

by treatment of the resulting diazide with methanol produced the acetylenic diurethane (76), which on partial catalytic hydrogenation gave the corresponding cis-ethylenic diurethane (77). cis-Hydroxylation of (77) using potassium permanganate or osmium tetroxide hydrogen peroxide yielded (78). Acid hydrolysis of (78) furnished (62).

4. M. Chmielewski[15] reported a synthesis of 2-deoxy-DL-ribose (83) starting from butyl 2-methoxy-5,6-dihydro-2H-pyran-6-carboxylate (79) (Scheme E). Compound (79) with mineral acid furnished butyl E-2,3,4-tri-deoxy aldehydo-DL-hex-2-enuronate (80) which was easily reduced to diol (81). Diol (81) was epoxidised with m-chloroperbenzoic acid to give a mixture of stereoisomeric epoxides (82). Opening of the epoxide ring of (82) with aqueous acetic acid followed by Ruff-degradation of the calcium salt of resulting 3-deoxy hexonic acid gave (83).

PRESENT WORK

A synthesis of 7-(6'-bromo-6'-deoxy-β-D-glucopyranosyl) theophylline (10) is presented, starting from 7,β-D-glucopyranosyltheophylline (6b).

The condensation reaction of 1,2,3,4,6-penta-O-acetyl β-D-glucopyranose (2) with theophylline was studied under various conditions. As reported in the literature there are various types of catalysts which can be used for the condensation reactions of (2) and (4). The most suitable and easily available catalyst p-toluene sulphonic acid was employed in the fusion reactions.

Penta acetate (2) was easily prepared in good yields by acetylation of α-D-glucose, using acetic anhydride in presence of sodium acetate at reflux temperature. It was recrystallized from ethanol and used in further reactions. To standardize the conditions for the condensation reaction, following four different approaches were employed

(1) Equimolar quantities of penta acetate (2) and theophylline (4) were heated together at 160°(bath). To it was added p-toluene sulphonic acid and heating was continued for 1 hr. more After workup reaction mixture furnished (6a) in 20% yield.

(2) Equimolar quantities of pentaacetate (2) and (4) were heated at 140°C, p-toluene sulphonic acid was added and the reaction mixture was heated at 140-150°C for 1 hr, under

40 mm vacuum. After usual workup about 77% of the theophylline was recovered back. The yield of (6a) obtained was only 25% after correcting for the recovery of theophylline.

(3) According to literature[9], theophylline (4) and p-nitrophenol (3) form a 1:1 complex. By the same method a complex (5) was prepared.

Equimolar quantities of pentaacetate (2) and complex (5) were fused together in presence of p-toluenesulphonic acid at 150° and heated further for 3 hrs. After usual workup (6a) was obtained in 50% yield.

(4) A mixture of (3) (3 equivalents), (4) (1 equivalent) and p-toluene sulphonic acid (0.055 equivalent) was fused at 132°C and to it was added pentaacetate (2)(1 equivalent). Reaction mixture was heated at 130-35°C for 1.5 hrs. After usual workup it furnished (6a) in 70% yield.

7- (2',3',4',6', tetra-O-acetyl-β-D-glucopyranosyl) theophylline (6a) when treated with a saturated methanolic solution of ammonia furnished (6b) in good yields.

Tetraacetate (6a) was recrystallized from water to get a crystalline product having half molecule of water of crystallization. This fact was proved by its NMR spectrum as well as microanalysis. In its NMR spectrum it shows a signal for hydrogen of water of crystallization at 1.66 (s, exchanges with D_2O). The microanalysis values fits well with the molecular formula $(C_{21}H_{26}N_4O_{11}) \frac{1}{2} H_2O$.

Nucleoside (6b) when treated with benzaldehyde in presence of zinc chloride furnished the benzylidene acetal (7) in 68% yield. The acetal (7) was acetylated using acetic anhydride in the presence of pyridine to get 7-(4',6'-O-benzylidene, 2',3'-di-O-acetyl-β-D-glucopyranosyl) theophylline (8).

Diacetyl compound (8) when treated with N-bromo-succinimide in CCl_4 in the presence of the acid scavenger barium carbonate furnished a crystalline product whose structure was assigned as 7-(6'-bromo,4'-obenzoyl, 2',3'-diacetyl-6'-deoxy-β-D-glucopyranosyl) theophylline (9). Bromo ester (9) when treated with a saturated solution of ammonia in methanol furnished the bromo nucleoside (10). Compound (10) has been sent for testing of antiviral activity at National Virological research institute.

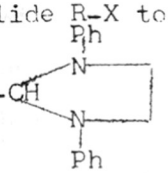
In order to get 7,β-D-glucopyranosyl-8-bromo-theophylline, bromination of (6b) was attempted at different temperature conditions. At room temp. bromination did not take place whether reaction was performed by taking aqueous solution of pH 4. When bromination of (6b) was attempted at 60° in the presence of glacial acetic acid, the starting material was recovered quantitatively. When the bromination reaction was carried out at 100°C a complex mixture was obtained and was not examined.

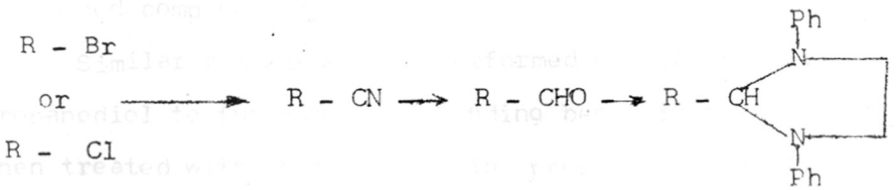
8-Bromotheophylline was obtained by brominating theophylline in acetic acid at 80°C. 8-Bromotheophylline

does not form a molecular complex with p-nitrophenol. A mixture of pentaacetate (2), p-nitrophenol (3) and 8-bromotheophylline was heated at 130°C for 1 hr., however, it was not possible to isolated the required condensation product from the reaction mixture.

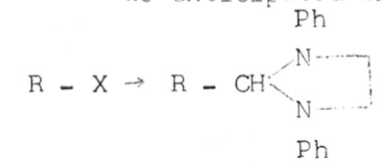
The transformation R = X (X = Cl or Br) R-CN has been known for long time and reaction is known to proceed smoothly particularly when DMSO is used as a solvent. Though several methods are available for the conversion RCN-R-CHO, considering the sensitivity of aldehyde group we were interested in a route in which the sensitive aldehyde group is blocked as soon as it has been formed.

Reduction of cyano group to aldehyde with sodium hypophosphite and Raney nickel under comparatively mild condition is reported by Backebery[16]. Recently it has been reported that aldehydes readily react with 1,2-dianilinoethane to furnish corresponding imidazolidine derivatives. So above literature observations suggested that it may be possible to convert an alkyl halide R-X to the corresponding suitably blocked aldehyde R-CH group employing the following sequence of reactions





We anticipated that such a transformation



will be of value for synthsis of 2-deoxy ribose. Hence it was decided to carry out initially above transformations on readily available R - X and establish the optimum conditions. The report dealing with such transformations carried out during the present study is given below.

The above transformations were carried out on following halides (i) mixture of (14) and (15) (ii)(20) (iii) (24) (iv) (30) and (v) (38).

1,3-Butane diol (11) when reacted with benzaldehyde (12) in presence of catalytic amount of sulphuric acid yielded the corresponding benzylidene acetal (13). Action of N- bromosuccinimide on acetal (13) gave a mixture of bromobenzoates (14) and (15) in 1:3 ratio. The ratio of bromob enzoates was calculated from the NMR spectrum of the mixture. The mixture as such was treated with sodium cyanide in dimethylsulphoxide to furnish the cyano compound (16) which was reduced with sodium hypophosphite in the presence of Raney nickel and 1,2-dianilino ethane, furnished compound (17).

Similar reactions were performed on 2,2-dimethyl-1,3 propanediol to furnish corresponding benzylidene acetal (19) when treated with benzaldehyde in presence of catalytic

amount of sulphuric acid. Acetal (19) reacted with N-bromosuccinimide to furnish the bromobenzoate (20) which when treated with sodium cyanide in DMSO yielded the cyano compound (21). Reduction of the cyano compound(21) with sodium hypophosphite in the presence of Raney nickel and 1,2-dianilino ethane furnished the compound (22).

When tetrahydrofuran (23) was refluxed with acetyl chloride in the presence of zinc chloride as a catalyst it furnished the chloroacetate (24) in good yields. Cyanation of chloroacetate (24) produced a cyano compound (25) which was reduced (as in the earlier cases) to furnish compound (26).

1,6-Hexanediol (27) was acetylated using anhydride in presence of pyridine to yield the diacetate (28). The diacetate (28) was hydrolysed under mild basic conditions to furnished hydroxy acetate (29) in about 24% yield. The hydroxy acetate (29) was refluxed with thionyl chloride in the presence of catalytic amount of dimethyl formamide to get the corresponding chloroacetate (30). Cyanation of chloroacetate (30) yielded a cyano compound (31) which was reduced in usual manner to get compound (32).

Styrene was converted into 4-phenyl-1,3-dioxane (34) according to literature method[17]. It was converted into diacetate (35) following the literature method[18]. The alkaline hydrolysis of (35) with methanolic KOH furnished

a diol (36). Diol (36) after reacting with benzaldehyde in presence of p-toluenesulphonic acid furnished acetal (37) which on treatment with N-bromosuccinimide resulted in bromobenzoate (38). The bromobenzoate after cyanation furnished the cyano compound (39) which was reduced (as in the earlier cases) to furnish (40).

A new synthesis of (±)2-deoxy ribose has been carried out starting from the dibenzylidene derivative (45) 1,3:2,4-Di-O-benzylidene-erythritol (45) ir prepared according to the literature method[19].

Literature reports[20] that 1,3:2,4-di-O-benzylidene erythritol must have the bicyclic structure (45) which is related to transdecalin and has two equatorial phenyl groups, a thermodynamically stable structure. Further it is optically inactive since it has a centre of symmetry. The product of partial hydrolysis is a (dl)-mixture.

According to the literature method[1] the bromo compound (46) was prepared by the action of N-bromosuccinimide on the compound (45) in CCl_4 at 76°C in 55% yield; however, the yield when corrected for recovered starting material, was 75%.

The bromobenzoate (46) was hydrolysed with methanolic KOH to furnish (dl) (47) in 77% yield*.

*The hydroxy compound (47) is a potential intermediate for optical resolution which may be achieved by esterifying the dl alcohol (47) with an optically active acid. However, this optical resolution has not yet been attempted by us. If one of the enantiomers of (47) can be obtained optically pure, application of sequence of reactions given below will furnish optically active 2-deoxy ribose.

The hydroxy compound obtained was characterised by spectral and analytical data. IR spectrum shows strong -OH band at 3420 cm^{-1}. The hydroxy compound analysed for $C_{11}H_{13}BrO_3$.

The bromohydroxy compound (47) was acetylated using acetic anhydride in the presence of pyridine to furnish the acetate (48). IR spectrum of (48) shows bands at 1730 and 1240 cm^{-1} (acetate). NMR spectrum in $CDCl_3$ shows following bands at 2.11 (3H, s, $-OCOCH_3$), 3.59 (3H, m, $-CH_2Br$ and axial H of $-OCH_2-$), 4.03 (1H, m, -CH-O), 4.42 (1H, dd, J = 5 and 10 Hz, equatorial H of $O-CH_2-$), 4.93 (1H, dt, J = 5 and 10 Hz, -CH-OAc), 5.58 (1H, s, $\phi - CH<^{O}_{O}$ 7.36 - 7.62 (5H, m, aromatic).

Following the earlier reports[21], the primary bromide (±) 48 is reacted with sodium cyanide in dimethyl sulphoxide to furnish a product which shows several spots on TLC. IR spectrum of the product indicated that appreciable amount of cyano compound is not present (no prominant peak at 2240 cm^{-1}). Hence the product was not investigated. The cyanation of acetate 48 was carried out using potassium cyanide in dimethyl sulphoxide to furnish (±) (49) in 12% yield. The structure for compound (49) was assigned as 4-O-acetyl-3,5-O-benzylidene-2-deoxy-DL-erythropentono-nitrile (49) based on the following data. It shows IR bands at 2240 (C≡N), 1740 and 1245 cm^{-1} (acetate). It shows NMR signals at 2.1 (3H, s, $-OCOCH_3$), 2.78 (2H, d,

J = 6 Hz, $C\underline{H}_2$- CN), 3.73 (1H, t, J = 10 Hz, axial H of $-OCH_2$), 4.12 (1H, m, $-OC\underline{H}-CH_2-CN$), 4.48 (1H, dd, J = 5 and 10 Hz, equatorial H of $-OCH_2$), 4.98 (1H, dt, J = 5 and 10 Hz, -CH-OAc) 5.50 (1H, s, $\emptyset-C\underline{H}<^{O}_{O}$), 7.10 to 7.55 (5H, m, aromatic). Microanalysis agrees with the molecular formula $C_{14}H_{15}NO_4$.

The next aim is to convert cyano group in (49) to aldehyde group, during this conversion it is desirable to retain the benzylidene as well as acetate blocking groups. The reductive hydrolysis reaction of (49) with sodium hypophosphite and Raney nickel in aqueous acetic acid-pyridine in the presence of 1,2-dianilino ethane[22] furnished (±) (50). Under these conditions the blocking groups e.g. benzylidene and acetate originally present in (49) were left intact and aldehyde group is blocked to give 1,3-diphenyl imidazolidine (50) in 70% yield. Compound (50) analysed for $C_{28}H_{30}N_2O_4$. IR spectrum shows bands at 1742 cm^{-1} (C=O). There was no band at 2240 cm^{-1}. region indicating the absence of C=N moiety in (50). NMR shows signals at 1.93 (3H, s, $-OCOCH_3$), 1.73-2.4 (2H, m, $\frac{3}{4}CH-C\underline{H}_2-CH$), 3.40 - 3.71 (5H, m, $-N-C\underline{H}_2-C\underline{H}_2-N$) and axial H of - OCH_2-) 3.87 (1H, dt, J = 2 and 8 Hz, $-O-C\underline{H}-CH_2$), 4.29 (1H, dd, J = 5 and 10 Hz, equatorial H of $-OCH_2$-), 4.69 (1H, dt, J = 5 and 10 Hz, -CH-OAc), 5.42 (1H, s, $\emptyset-C\underline{H}(O-)-O-$), 5.48 (1H, dd, J = 2 and 8 Hz - $CH<^{N}_{N}$ 6.6 - 7.6

(15H, m, aromatic).

Literature reports that 1,3-diphenylimidazolidine derivatives are stable to alkali. Hence saponification of (50) with sodium hydroxide in aqueous methanol yields hydroxy compound ± (51) in 93% yield. IR spectrum of compound (51) shows a band at 3600 cm^{-1} (OH). NMR spectrum exhibits signals at

2.24 (2H, m, -CH-C<u>H</u>$_2$-CH), 5.46 (1H, s, Ø-  , 5.67

(1H, m, -<u>H</u>C  7.00 - 7.90 (15H, m, aromatic).

The identity of compound was established by direct comparison (m.p., IR, NMR) with an authentic sample prepared according to literature method 1. The transformation of hydroxy compound dl (51) to (dl) 2-deoxy ribose* is already reported in the literature[1,23].

The deblocking of the benzylidene group in compounds (46) and (47) was effected on treatment with an acylating mixture of acetic anhydride (17.5 ml) acetic acid (7.5 ml) and sulphuric acid (0.5 ml). Bromo benzoate (46) gave 2,4-di-O- acetyl-3-O-benzoyl-1-bromo-1-deoxy-erythritol (52) in 58% yield . The structure was confirmed by the following analytical data.

The IR spectrum it shows bands at 1750 (C=O) and at 1240 (acetate). NMR spectrum shows following signals:

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* When the investigation on the synthesis of 2-deoxy ribose reported in this thesis was in progress Dr.K.S. bhat[2] working in our laboratory showed that bromobenzoate (46) can be transformed in good yields to 2-deoxy ribose via hydroxy compound (51).

2.1 (6H, s, two -OCOC$\underline{H}_3$), 3.6 (2H, m, -C$\underline{H}_2$-Br) 4.3 (2H, m, - C$\underline{H}_2$-OAc), 5.3 (2H, m, -C$\underline{H}$-OAc and -C$\underline{H}$-OBz), 7.4 (3H, m, aromatic), 7.9 (2H, m, aromatic H ortho to C=O). Micro-analysis fits with the molecular formula $C_{15}H_{17}BrO_6$.

When hydroxy compound (47) was treated with acylating mixture it furnished a triacetate (53) which was characterised by following analytical data. IR of triacetate (53) shows strong bands at 1750 cm^{-1} and 1240 cm^{-1} (acetate). NMR spectrum shows signals at 2.09 (3H, s, - OOOCH_3), 2.12 (3H, s, -O OOCH_3), 2.14 (3H, s, -OOOCH_3), 3.58 (2H, m, -C$\underline{H}_2$-Br), 4.29 (2H, m, C$\underline{H}_2$-OAc), 5.29 (2H, m, two C$\underline{H}$-OAc).

1,2,3,4,6-Penta-O-acetyl- -D-glucopyranose (2)

A suspension of 20 g (244 mmole) of anhydrous sodium acetate in 280 ml of acetic anhydride in a one lit. round bottom flask was heated over a flame upto its boiling point in an efficient fume hood. About 2 g. of anhydrous α-D-glucose from a 40 g (222 mmole) supply was added and the flask without shaking was heated carefully at the point nearest, the sugar lying at the bottom. Initiation of the reaction was indicated by continued boiling after removal of the flame. The flask was kept on a cork-ring and the flame was extinguished. The remainder of the sugar (38 g) was then added in small portions at a rate which maintains the boiling temperature of the reaction mixture. The flask was shaken occasionally to prevent an accumulation of solid sugar at the bottom of the flask (if the reaction stopped it was started again by heating, before much more sugar was added to the flask). After the addition of all the sugar and after the reaction has subsided, the solution was brought to a full boil. It was then cooled and poured with stirring on 1 kg of crushed ice. After standing 3 hrs with occasional stirring the crystalline material was fallen out which was filtered, washed with cold water and dried.

Recrystallization from ethanol furnished 2. Yield = 65 g (75.0%) m.p.131-2°C. (lit.[24] m.p. = 132°C).

Complex of p-nitrophenol and theophylline (1:1) (5)

p-Nitrophenol (4.8 g, 17.1 mmole) was dissolved in hot chloroform (300 ml) and filtered hot. To the hot solution was added powdered theophylline (5.4 g, 15 mmole) slowly with shaking. After all addition was over, it was boiled on water bath for 5-10 mins. and kept for cooling. After cooling upto room temperature solid was obtained. It was filtered, washed with chloroform and dried. Yield = 9 g (94%) m.p. = 149-150°(lit.[9] m.p. = 148-50°).

7-β-D-glucopyranosyltheophylline 6b, Method

Method (a)

A finely powdered mixture of glucose-pentaacetate 2 (3.9 g, 0.01 m) and theophylline 1.8 g (4) (0.01 mole) was heated to 160°C in a test tube. PTS acid (100 mg) was added and heating continued for 1 hr. The dark coloured masscooled and dissolved in hot chloroform (50 ml). Chloroform solution was concentrated upto 7 ml and directly loaded on a Grade II alumina column. Elution was started with benzene. Polarity was increased using chloroform. Fraction eluted with 20% chloroform in benzene furnished crude product 1.54 g. The crude product was recrystallized from methanol to get 7 (2',3',4',6'-tetra-o-acetyl-glucopyranosyl) theophylline 6a yield = 1 g (20%),

m.p. 164°C.

Tetra-acetate 6a was deacylated using a saturated solution of ammonia in methanol (40 ml) to yield 6b.
Yield = 0.66 g, m.p. 266-7° (lit.[7] m.p. = 265.7°).

Method b

A mixture of glucose-pentaacetate 2 (3.9 g, 0.01 mole) theophylline (1.8 g, .01 mole) and p-toluene sulphonic acid (800 mg) was heated in a round bottom flask to 140°C. The partly molten mass was stirred with a glass rod. The flask was attached to a water aspirator vacuum (40 mm). Heating was continued at 140-150° under vacuum for 1 hr. The dark mass was dissolved in hot chloroform and unreacted theophylline was recovered (1.4 g). Filtrate was concentrated to 2 ml and loaded on a alumina (Grade II) column. Fraction eluted with 20% chloroform in benzene furnished 6a. Yield = 289 mg (25% considering the recovery of theophylline). It was subsequently deacylated using saturated solution of ammonia in methanol to yield 300 mg of 6b.

Method c

To a fused mixture of 2 (3.9 g, 10 mmoles) and 5 (3.2 g, 10 mmoles) was added p-toluenesulphonic acid (0.15 g) and it was heated at 150°C for 3 hrs.

with stirring. After cooling it was dissolved in chloroform (200 ml). Chloroform solution was washed thoroughly with 1 M NaOH (1.2 lits) and finally twice with water. After drying over Na_2SO_4, chloroform was recovered to get a thick syrup which was dissolved in methanol (30 ml). A saturated solution of ammonia in methanol (100 ml) was added and reaction mixture kept in refrigerator overnight. Methanol was removed under reduced pressure to get a thick syrup. After treating with cold ethanol it was transformed in to a crystalline solid. It was filtered and dried. Yield = 258 (50.2%). M.p.264-6°C (lit.[9] m.p. 265-7°C).

Method d

A mixture of p-nitrophenol (37.8 g, 272 mmole), theophylline (16.2 g, 90 mmole), and p-toluene sulphonic acid (1 g, 5 mmole) was heated upto 132°C and 2 (35.1 g, 90 mmole) was added. The reaction mixture was stirred at 130-35°C for 1.5 hrs. It was cooled and to it was added chloroform (175 ml). The chloroform solution was washed many times with 1 M NaOH solution (about 3 lit. NaOH) till free from p-nitrophenol. After final washing with water (200 ml) it was dried (Na_2SO_4). Solvent recovered to furnish 6a. Yield = 32.5 g (70%), m.p. = 164-5°C. IR: 1755, 1720, 1665, 1612, 1595, 1545, 1520, 1500, 1455, 1430, 1380, 1370, 1225, 975, 920, 760, 600.

A sample was crystallized from water and NMR of it was recorded in $CDCl_3$. It shows 0.5 mole of water of crystallization.

NMR ($CDCl_3$): 1.66 (1H, s, exchanges with D_2O, -OH), 1.91 (3H, s, $-OCOCH_3$), 2.03 (3H, s, $-OCOCH_3$), 2.08 (6H, s, two $-OCOCH_3$), 3.42 (s, 3H), 3.59 (3H, s), 4.0 (1H, m, broad), 4.2 (2H, m narrow), 5.22 (1H, t, J = 8 Hz), 5.63 (1H, m). Found: C, 48.83; H, 5.12; N, 10.56. $C_{21}H_{26}N_4O_{11}$). $\frac{1}{2}$ H_2O requires C, 48.55; H, 5.2; N, 10.79%.

6a (32.1 g, 63 mmole) was dissolved in methanol (100 ml) and to it was added a saturated solution of ammonia in methanol (600 ml) and kept in refrigerator overnight. Methanol was removed under vacuum and the residue was treated with cold acetone-water to furnish 6b. Yield = 20.6 g (66.9% based on theophylline, m.p.266-7°C (lit.[9] m.p. = 265-7°C).

Compound obtained was identical with those obtained by methods a,b and c.

IR (Nujol): 3420, 1690, 1550, 1540, 1450, 1370, 1342, 1270, 1220, 1100, 960, 860, 780, 746, $(\alpha)_D^{27}$ = -2.89 (c, 1.0 in H_2O) [$(\alpha)_D^{21}$ - 3° (c, 1.0 in H_2O)][9].

7-(4',6'-o-Benzylidene-β-D-glucopyranosyl)theophylline 7

A mixture of crushed anhydrous zinc chloride (10 g) and freshly distilled benzaldehyde (50 ml) was stirred at room temperature for 4 hrs to obtain a thick paste. To it was added 5 g of powdered 6b (5 g, 14.6 mmole) and kept

stirred at room temperature for 72 hrs. The homogenous mixture was shaken vigorously with water (50 ml) and pet.ether (50 ml) which resulted in precipitation of the product. Filtration, followed by washing with water, pet.ether and acetone furnished the acetal 7. Yield = 4.3 g (68.5%), m.p. = 271.2 (lit.[3] m.p. = 272-3°C). IR (Nujol): 3585 (OH), 2995, 1700, 1675, 1550, 1495, 1430, 1310, 1185, 1135, 1070, 975, 918, 835, 748, 695. $(\alpha)_D^{27}$ = -58.68 (c, 1.3 in pyridine) [lit.[3] $(\alpha)_D^{20}$ = -59 (c, 1.4 pyridine)_7.

7-(4',6'-O-Benzylidene, 2',3'-diacetyl-β-D-glucopyranosyl) theophylline 8

A mixture of 7 (1.2 g, 2.7 mmol), pyridine (10 ml) and acetic anhydride (5 ml) was kept in refrigerator for 48 hrs. It was filtered, solid washed with water and dried. Solid was recrystallized from 2-methoxyethanol-methanol mixture to furnish 8. Yield = 1.025 g (71.5%), M.p. = 267°C (lit.[3] m.p. = 267-9°). IR (Nujol): 300, 1750, 1735, 1715, 1675, 1630, 1540, 1445, 1335, 1260, 1215, 1145, 1030, 905, 848, 786, 766, 750, 702. $(\alpha)_D^{27}$ = -75.66 (c, 1 in $CHCl_3$) [lit.[3] $(\alpha)_D^{20}$ = - 76 (c, 1 in $CHCl_3$)_7.

7-(6'-Bromo,4'-O-benzoyl, 2',3'-diacetyl-6'-deoxy- -D-glucopyranosyl)theophylline 9

A mixture of acetal 8 (0.5149 g, m mmole), barium carbonate (0.4 g, 2.0 mmole) and N- bromosuccinimide

(0.21 g, 1.18 mmole) was gently refluxed in 100 ml of CCl_4 for 4 hrs. It was hot filtered and filtrate was evaporated to dryness to get a sticky solid (0.8 g). Sticky solid was extracted with ether (4 x 50 ml). Combined ether extract was washed with water (2 x 25 ml) and dried (Na_2SO_4). After removing solvent, a solid was obtained which on recrystallization from acetone-pet.ether furnished 9. Yield = 0.475 g (80%), m.p. = 238-9°C.

IR : (Nujol): 1755, 1725, 1700, 1675, 1600, 1550, 1450, 1370, 1280, 1140, 1085, 1060, 1040, 1020, 970, 960, 885, 785, 760, 750.

NMR ($CDCl_3$): 1.2 (3H, s), 1.93 (3H, s), 3.44 (3H, s), 3.62 (3H, s), 3.54 (7H, m), 4.17 (1H, m), 5.64 (3H, mostly t, J = 10 Hz), 6.31 (1H, m), 7.37 - 7.67 (3H, m), 7.87-8.0 (3H, m).

$(\alpha)_D^{27}$ = - 33.25 (c, 2.4 in $CHCl_3$).

Found: C, 48.81; H, 4.51; N, 9.26; Br, 13.77.

$C_{24}H_{25}BrN_4O_9$ requires C, 48.56; H, 4.21; N, 9.44; Br, 13.49.

7-(6'-Bromo-6'-deoxy-β-D-glucopyranosyl)theophylline 10:

9 (0.6 g, 1.01 mmole) was mixed with a saturated solution of ammonia in methanol (100 ml) and kept at 0°C for 48 hrs. Methanol was removed under reduced pressure to get a glassy mass which when treated with cold acetone furnished a solid. Solid was recrystallized from acetone-water mixture (8:2) to get 10. Yield = 0.336 g. (82%). M.p. = 126-7° (decomposition).

IR: 3450 (broad), (OH), 1740, 1700, 1660, 1600, 1500, 1450, 1390, 1370, 1310, 1290, 1225, 1180, 1090, 920, 825, 755, 695, 660, 645.

Found: C, 38.32; H, 4.11; N, 13.71; Br. 19.61.

$C_{13}H_{17}BrN_4O_6$ requires C, 38.52; H, 4.2; N, 13.83; Br, 19.75%.

2-Phenyl-4-methyl-1,3-dioxane (13)

A mixture of 1,3-butanediol 11 (15 g, 167 mmole), benzaldehyde 12 (21.3 g, 200 mmole) and sulphuric acid (0.2 ml, 3.7 mmole) in benzene (150 ml) was distilled azeotropically in about 1.5 hr. to give 3 ml of water. The reaction mixture was cooled and poured in sodium carbonate solution (10%, 200 ml). Organic layer was washed with water and dried (Na_2SO_4). Solvent was removed to get a crude 13. It was distilled at 96°C/2 mm (lit.[25] b.p.75°/0.15 tor). Yield = 26.16 g, 88%.

IR (liq. film): 2970, 2850, 1450, 1400, 1380, 1360, 1310, 1250, 1220, 1170, 1110, 1060, 1030, 1000, 970, 910, 950, 820, 750, 700, 665

NMR: 1.27 (3H, d, J = 6 Hz, CH_3-CH), 1.7 (2H, m, CH_2-CH)- 3.83 (3H, m, $-OCH_2$ and O-CH), 5.3 (1H, s, Ph-CH-O) 7.23 (5H, m, aromatic).
(CCl_4)

Reaction of N-bromosuccinimide on 13

A mixture of acetal 13 (5.34 g, 30 mmole), N-bromo-succinimide (6.4 g, 36 mmole), barium carbonate (2.0 g,

10 mmole), benzoylperoxide (0.3 g, 0.24 mmole) and CCl_4 (150 ml) was refluxed with stirring for 2 hrs under nitrogen atmosphere. When bath temperature reached 74°C, the reaction started suddenly and colour changed to dark red. After 2 hrs the reaction mixture became colourless. It was hot filtered and solid obtained was washed with hot CCl_4. Combined filtrate was washed with water, dried (Na_2SO_4) and solvent evaporated to get a liquid. It was distilled at 134-5°/3 mm (lit.[26] b.p. 124-25/2 mm) to furnish mixture of 14 and 15 in a ratio of 1:3.

IR (liq. film): 2970, 1720, 1600, 1590, 1495, 1450, 1380, 1360, 1320, 1280, 1220, 1180, 1110, 1070, 1030, 1000, 940, 870, 850, 715.

NMR (CCl_4): 1.38 (2.25 H, d, J = 6 $-CH_3$), 1.75 (0.75 H, d, J = 6, $-CH_3$), 2.0 to 2.45 (2H, m, $-CH_2-$); 3.43 (1.5H, q, J = 6 and 8 Hz, $-CH_2Br$), 4.1 to 4.55 (0.75H, m, $-CH_2-OBz$ and $CH-Br$), 5.0 to 5.55 (0.75 H, m, CH-OBz), 7.1 to 8.1 (5H, m, aromatic H).

Reaction of bromo compound (mixture of 14 and 15) with sodium cyanide

To a hot (70°C), stirred mixture of sodium cyanide (1 g, 20 mmole) and dimethyl sulphoxide (10 ml) was added the freshly distilled mixture of bromobenzoates 14 and 15 (2.6 g, 10 mmol) in lots (5 minutes). Heating was continued at 95-100°C for 5 hrs. It was cooled, poured in water and extracted with chloroform. Organic layer was washed

thoroughly with waterand finally with saturated brine, dried (Na_2SO_4) and chloroform recovered to get a liquid crude 16 which was purified by column chromatography using grade II alumina. Column was successively eluted with (i) pet.ether, (ii) Pet.ether-ethylacetate 99:1 (iii)pet. ether-ethylacetate 98:2 (iv) pet.ether-ethyl-acetate 96:4. The fraction eluted with pet.ether-ethyl acetate 96:4, after removing solvent furnished pure 16. Yield = 1.3765 g. (68.5%). Rf = 0.48 (pet.ether-acetone 4:1).

IR (liq. film): 2980, 2920, 2240, (C=N), 1720 (strong), 1600, 1590, 1495, 1450, 1430, 1380, 1360, 1320, 1280, 1180, 1115, 1070, 1030, 1000, 860, 715, 690, 675.

MS: m/z 203 (M^+).

NMR: 1.4 (3H, d, CH-CH_3), 2.2 (4H, m, CH_2-CH_2CN), 5.13 (CCl_4) (1H, m, CH-OBz), 7.4 (3H, m aromatic H), 7.96 (2H, m, aromatic H ortho to C=O).

Found: C, 70.64; H, 6.67; N, 6.85. $C_{12}H_{13}NO_2$ requires C, 70.91; H, 6.45; N, 6.89%

1,2-Dianilino ethane (41) was prepared according to a literature method.[22]

1-Methyl-3-(1,3-diphenyl-2-imidazolidyl)propyl benzoate 17

To a stirred mixture of cyano compound 16 (1.015 g, 5 mmole), 1,2-dianilinoethane (2.0 g, 9.4 mmole), Raney nickel (12 g, 204 mmole), pyridine (34 ml) and water (17 ml) was added glacial acetic acid (17 ml)followed by sodium hypophosphite (7 g, 79.5 mmole). The reaction mixture

became warm and it was stirred for 16 hrs at room temp. It was filtered and the catalyst was washed thoroughly with chloroform (300 ml). Chloroform layer was washed successively with water (5 x 200 ml). Copper sulphate solution 10%, 5 x 100 ml) and finally with saturated brine, dried (Na_2SO_4). After solvent removal a thick liquid was obtained which was purified through column chromatography using grade II alumina. Column was successively eluted with (i) pet.ether (ii) pet.ether-ethyl acetate 99:1 (iii) pet.ether-ethyl acetate 98:2. Fraction eluted with pet.ether-ethyl acetate 99:1, after removing solvent furnished 17. Yield = 1.431 g (71.55%). R_f = 0.4 (pet.ether-acetone (4:1).

IR (Nujol): 1710 (strong), 1600, 1500, 1460, 1380, 1355, 1320, 1280, 1250, 1230, 1160, 1130, 1080, 1030, 1022, 940, 930, 875, 810, 750, 720, 720, 695.

NMR: 1.2 (3H, d, J = 6 Hz, CH_3-CH-), 1.6 (2H, m, CH_2-CH_2-CH-); 2.1 (2H, m, CH_2-CH_2-CH-), 3.6 (4H, m, -N-CH_2-CH_2-N-); 4.9 (1H, m, -CH-O); 5.3 (1H, m, -CH(N)(N)) 6.3 to 7.8 (15H, m, aromatic). (CCl_4)

Found: C, 78.13; H, 7.36; N, 7.24; $C_{26}H_{28}N_2O_2$ requires C, 77.97; H, 7.05; N, 7.00%).

2-Phenyl-5,5-dimethyl-1,3-dioxane 19

A mixture of 2,2-dimethyl-1,3-propanediol (18) (15 g, 144 mmole benzaldehyde 12 (15.28 g, 1.44 mmole) and sulphuric acid (0.2 ml, 3.7 mmole) in benzene (150 ml) was

distilled azeotropically in about 1.5 hrs. to give 3 ml of water. The reaction mixture was cooled and poured in sodium carbonate solution (10%, 200 ml). Organic layer was washed with water, dried (Na_2SO_4). Solvent was removed and the residue was distilled under vacuum to furnish 19. Yield = 24.78 g (89.5%). B.p.105-110°/5 mm. (lit.[25] b.p.82°/0.2 mm).

IR (liq. film): 2950, 2840, 1500, 1470, 1455, 1390, 1360, 1310, 1230, 1215, 1100, 1020, 990, 975, 910, 870, 750, 700, 680, 640.

NMR (CCl_4): 0.7 (3H, s, $-CH_3$ axial), 1.2 (3H, s, $-C\underline{H}_3$ equitorial), 3.5 (4H, m, two-$C\underline{H}_2$), 5.1 (1H, s, Ph-C<u>H</u>-O), 7.2 (5H, m, aromatic).

3-Bromo-2,2-dimethylpropyl benzoate 20

A mixture of acetal 19 (5.76 g, 30 mmole), N-bromo-succinimide (6.0 g, 33.7 mmole) barium carbonate (2 g, 10 mmole), benzoyl peroxide (0.3 g, 0.24 mmole) and CCl_4 (150 ml) was refluxed with stirring for 2 hrs. under nitrogen atmosphere. The reaction mixture decolurized after 2 hrs refluxing. It was hot filtered and solid obtained was washed with hot CCl_4. Combined filtrate was washed with water and dried (Na_2SO_4). After solvent removal a liquid was obtained which was purified by column chromatography using grade II alumina. Column was successively eluted with (i) pet.ether (ii) pet.ether-ethyl acetate 99:1.

Fraction eluted with pet.ether-ethyl acetate 99:1, after solvent removal furnished 20. Yield = 7.50l (92.3%).

R_f = 0.72 (pet.ether-acetone 4:1).

IR (liq.film): 2960, 1725, 1600, 1590, 1470, 1450, 1430, 1400, 1375, 1315, 1270, 1180, 1115, 1070, 1030, 970, 935, 910, 790, 760, 710.

NMR: 1.2 (6H, s, two $-CH_3$), 7.3 (3H, m, aromatic H), 7.9 (2H, m, aromatic ortho to C=O).

MS: m/z 271 (M^+).

Found: C, 52.85; H, 5.33; Br, 29.2. $C_{12}H_{15}BrO$ requires C, 58.14; H, 5.54; Br, 29.52%.

3-Cyano-2,2-dimethyl propyl benzoate 21

To a hot (70°C), stirred mixture of sodium cyanide (2.0 g, 40 mmole) and dimethyl sulphoxide (10 ml) and dimethyl sulphoxide (10 ml) was added bromobenzoate 20 (5.44 g, 20 mmole) in lots. The reaction mixture was heated for 8 hrs. at 100-110°C (bath), cooled and poured in water. It was extracted with chloroform, chloroform layer was washed thoroughly with water and finally with saturated brine. Dried over Na_2SO_4. Chloroform was removed to get a liquid, which was purified through column chromatography using grade II alumina. Column was eluted successively with (i) pet.ether (ii) pet.ether-ethyl acetate99:1 (iii) pet.ether-ethyl acetate 98:2 (iv) Pet.ether-ethyl acetate 97:3. Fraction eluted with pet.ether-ethyl acetate 97:3 after removing solvent

furnished 21. Yield = 3.019 g (69.31%). R_f = 0.50 (pet. ether-acetone 4:1).

IR (liq.film): 2960, 2240 (-CN), 1790 (strong), 1600, 1450, 1430, 1370, 1270 (strong), 1180, 1110, 1070, 1030, 975, 710.

NMR (CCl_4): 1.2 (6H, s, two -CH- CH_3), 2.4 (2H, s, $-CH_2$-CH 4.1 (2H, s, $-CH_2$-OBz), 7.4 (3H, m, aromatic H), 7.9 (2H, m, aromatic H ortho to C=O).

MS: m/z 217 (M^+).

(Found: C, 71.99; H, 7.05; N, 6.52. $C_{13}H_{15}NO_2$ requires C, 71.86; H, 6.96; N, 6.45%).

2,2-Dimethyl-3-(1,3-diphenyl-2-imidazolodyl)propyl benzoate 22

To a stirred mixture of cyano compound 21 (1.085 g, 5 mmole), 1.2-dianilinoethane (2.0 g, 9.4 mmole), Raney nickel (12 g, 204 mmole), pyridine (34 ml) and water (17 ml) was added glacial acetic acid (17 ml) followed by sodium hypophosphite (7 g, 79.5 mmole). It was kept stirred for 16 hrs at room temp. and filtered. The catalyst was thoroughly washed with chloroform (300 ml), chloroform layer was washed successively with water (3 x 200 ml), copper sulphate solution (10%, 5 x 100 ml), finally with saturated brine and dried (Na_2SO_4). After solvent removal a thick liquid was obtained which was purified through column chromatography using grade II alumina. Column was successively eluted with (i) pet.ether (ii) pet.ether-

ethyl acetate (99:1) (iii) Pet.ether-ethyl acetate (99:2). Fraction eluted with 99.1 pet.ether-ethyl acetate, after removal of solvent furnished 22. Yield = 1.487 g 73.61%.

R_f = 0.42 (pet.ether-acetone (4:1).

IR (liq. film): 2950, 1720, 1600, 1500, 1470, 1450, 1430, 1370, 1320, 1275, 1230, 1180, 1160, 1120, 1070, 1030, 992, 870, 750, 715, 695.

NMR (CCl_4): 1.0 (3H, s, $-CH_3$), 1.13 (3H, s, $-CH_3$), 1.2 (2H, m, $-CH_2-CH$), 3.36 (4H, m, two $-N-CH_2$), 4.06 (2H, s,s, $-OCH_2$), 5.33 (1H, t, $-N-CH-N-$) 6.3 to 7.8 (15H, m, aromatic).

Found: C, 77.81; H, 7.05; N, 6.42; $C_{27}H_{30}N_2O_2$ requires C, 78.23; H, 7.30; N, 6.76.

4-Chlorobutyl acetate 24

A mixture of tetrahydrofuran (50 g, 694 mmol), acetyl chloride (65 g, 828 mmol) and zinc chloride (10 mg) was refluxed for 1.5 hrs. and the reaction mixture was directly distilled under vacuum to furnish 24.

Yield = 79 g (76%), b.p.110-12°/40 (lit.[27] b.p.98°/32 mm).

IR (liq. film): 2910, 1735, 1460, 1360, 1240, 1150, 1040, 970, 895, 730, 675.

NMR (CCl_4) : 1.8 (4H, $-CH_2-CH_2-CH_2OAc$)

2.0 (3H, s, $O-COCH_3$)

3.83 (2H, m, $-CH_2-Cl$)

4.0 (2H, m, $-CH_2-OAc$)

4-Cyanobutyl acetate 25

To a stirred suspension of sodium cyanide (2.0 g, 40 mmole) in dimethyl sulphoxide (10 ml) at 70°C was added the chloroacetate 24 (3.0 g, 19.9 mmole) in one lot. It was kept stirred at 75-80°C for 2.5 hrs during which a white solid had separated out. It was cooled and poured in water, extracted with chloroform. Organic layer was washed with water (3 x 100 ml) and finally with saturated brine dried (Na_2SO_4). Chloroform was removed to get a liquid which was distilled under reduced pressure to furnish 25. Yield = 2.51 g (89%) b.p. = 140.5°(bath)/20mm

IR (liq. film): 2950, 2240 (C≡N), 1740 (strong), 1460, 1430, 1390, 1370, 1240, 1050, 950, 900.

NMR (CCl_4): 1.7 (4H, m, $-CH_2-CH_2$), 2 (3H, s, $-OOOCH_3$), 2.3 (2H, t, J = 6 Hz, $-CH_2-CN$), 4 (2H, J = 6 Hz $-CH_2$ -OAc).

MS: m/z 141 (M^+).

Found: C, 59.27; H, 8.04; N, 9.92. $C_7H_{11}NO_2$ requires C, 59.55; H, 7.85; N, 9.92%.

4-(1,3-Diphenyl-2-imidazolidyl)butyl acetate 26

To a stirred mixture of cyano compound 25 (1.06 g, 7.5 mmol), 1.2-dianilinoethane (2.97 g, 14 mmol), Raney nickel (15 g, 256 mmol), pyridine (50 ml) and water (25 ml) was added glacial acetic acid (25 ml) followed by sodium hypophosphite (10 g, 113.6 mmol). It was stirred at room temp. for 16 hrs. and filtered. Catalyst was washed

thoroughly with chloroform (300 ml). Chloroform extract was washed successiv ely with water (3 x 200 ml), copper sulphate (5 x 100 ml) and finally with saturated brine and dried. After solvent removal a thick liquid was obtained which was purified through column chromatography using grade II alumina. The column was successively eluted with (i) pet.ether (ii) pet.ether-ethyl acetate 99:1 (iii)pet. ether-ethyl acetate 98:2. Fraction eluted with pet.ether-ethyl acetate 99:1, after solvent removal furnished 26. Yield = 1.79 g. 70.68%. R_f = 0.42 (pet.ether-acetone 4:1). IR (liq.film): 2930, 2840, 1735, 1600, 1500, 1475, 1430, 1380, 1320, 1245, 1155, 1070, 1030, 990, 865, 745, 690. NMR (CCl4): 1.4 (6H, m, $-C\underline{H}_2-C\underline{H}_2-$), 1.9 (3H, s, $-O-COC\underline{H}_3$), 3.6 (4H, m, $N-C\underline{H}_2-C\underline{H}_2-N$), 3.8 (2H, t, J = 6 Hz, $-C\underline{H}_2-O-$), 5.3 (1H, m, $-N-\underset{\underline{H}}{C}-$), 6.4 to 7.3 (10 H, m, aromatic).

Found: C, 74.31; H, 7.62; N, 9.28. $C_{21}H_{26}N_2O_2$ requires C, 74.52; H, 7.74; N, 9.46%

1,6-Diacetoxyhexane 28

To a mixture of 1,6-hexanediol (40 g, 339 mmol) and pyridine (65 ml) was added acetic anhydride (100 ml) in lots with cooling. When exothermic reaction subsided reaction was kept at room temperature overnight. It was poured over crushed ice and extracted with ether. Ether layer was washed with water (2 x 200 ml) copper sulphate (10%, 2 x 200 ml), finally with saturated brine and dried.

Ether was removed to get a liquid which was distilled to furnish 28. Yield = 63.7 g (93%). B.p.90-95°/5 mm. (lit.[25] b.p. 103-5°C/6 mm.

IR (liq. film): 2940, 2930, 1740, 1470, 1440, 1390, 1370, 1240, 1040, 980.

NMR (CCl4): 1.6 (8H, m, $-\underline{CH_2}-\underline{CH_2}-\underline{CH_2}-\underline{CH_2}$)

2.0 (3H, s, $-O-\ COC\underline{H_3}$)

4.0 (4H, t, J_1 = 6; J_2 = 6; two $C\underline{H_2}-OCOCH_3$).

1-Hydroxyhexyl acetate 29

A mixture of diacetate 28 (24.0 g, 118.8 mmole), sodium carbonate (6.3 g, 59.4 mmole), ethanol (100 ml) and water (75 ml) was kept stirred at room temperature for 2.5 hrs. Concentrated under vacuum at room temp. upto a volume of 50 ml and then saturated with sodium chloride. It was extracted with ether and dried (Na_2SO_4). After removing ether a liquid was obtained which was chromatographed using grade II alumina. Column was eluted successively with (i) pet.ether (ii) pet.ether-ethyl acetate 98:2 (iii) pet. ether-ethyl acetate 96:4 (iv) pet.ether-ethyl acetate 94.5 (v) pet.ether-ethyl acetate (92:8). (vi) pet.ether-ethyl acetate 90:10. Fraction eluted with pet.ether-ethyl acetate 90:10 after removing solvent furnished 29 Yield = 4.031 g, 21.1%. VPC of the crude product shows 24% of mono hydroxy acetate 29. R_f 0.33 (pet.ether-acetone 7:3).

IR (liq. film) 3500 (OH, strong), 1750 (strong), 1475, 1400, 1370, 1250 (strong), 1050 (strong).

NMR : 1.5 (8H, m, $-C\underline{H}_2-C\underline{H}_2-C\underline{H}_2-C\underline{H}_2$)

2 (3H, s, $-O-COC\underline{H}_3$)

3.4 (3H, m, $-C\underline{H}_2-OH$ and $O\underline{H}$)

3.9 (2H, t, J = 6 Hz, $-C\underline{H}_2-OCOCH_3$)

MS: m/z 160 (M^+)

Found: C, 59.75; H, 10.12; $C_8H_{16}O_3$ requires C, 59.98; H, 10.07%.

1-Chlorobexyl acetate 30

Mono hydroxy acetate 29 (3.6 g, 22.5 mmol) was cooled to 0°C and to it was added thionyl chloride (25 ml) dropwise with stirring and maintaining the temp. between 0-5°C. Dimethyl fermamide (2 ml) was added to it and the reaction mixture was refluxed for 2 hrs. Excess thionyl chloride was distilled off under reduced pressure and residue was poured slowly in water. It was extracted with ether, organic layer was washed with water, bicarbonate (10%, 50 ml), finally with saturated brine and dried (Na_2SO_4). After ether removal a liquid was obtained which was distilled under vacuum to furnish 30. Yield = 3.4 g, (83.7%) b.p.100-5°C/5 mm (b.p.[29] 88-90°/3.4 mm).

IR (liq. film): 2920, 2850, 1735 (strong), 1460, 1360, 1240 (strong), 1150, 970, 900, 730, 675, 650.

NMR (CCl_4) : 1.6 (8H, N), $-\underline{CH_2}-\underline{CH_2}-\underline{CH_2}-\underline{CH_2}$)

2 (3H, s, $-OCOCH_3$)

3.5 (2H, t, J = 6 Hz $-\underline{CH_2}-Cl$

4 (2H, t, J = 6 Hz $-CH_2-OAc$)

1-Cyano hexyl acetate 31

To a hot suspension of sodium cyanide (2.37 g, 48.4 mmole) in dimethyl sulphoxide (25 ml), chloroacetate 30 (4.32 g, 24.2 mmol) was added in one lot. Reaction mixture was stirred at 80-85°C for 2 hrs cooled and poured in water. It was extracted with chloroform, organic layer was washed successively with water, finally with saturated brine and dried (Na_2SO_4). After solvent removal a dark liquid was obtained which was vacuum distilled to furnish 31. Yield = 2.8 g (68.5%), b.p.120-25°/0.3 mm.

IR (liq.film): 2930, 2860, 2240, 1735, 1460, 1430, 1390, 1365, 1240 (strong), 1050, 1035, 970, 755.

NMR (CCl_4) : 1.6 (8H, m, $-\underline{CH_2}-\underline{CH_2}-\underline{CH_2}-\underline{CH_2}-\underline{CH_2}-$)

2 (3H, s, $-OCO\underline{CH_3}$)

2.3 (2H, t, J = 6 Hz, $-\underline{CH_2}-CN$)

4 (2H, t, J = 6 Hz, $-\underline{CH_2}-O-$)

MS: m/z 169 (M^+)

Found: C, 63.69; H, 8.95; N, 8.24. $C_9H_{15}NO_2$ requires C, 63.88; H, 8.94; N, 8.28.

1-(1-3-Diphenyl-2-imidazolidyl) hexyl acetate 32

To a stirred mixture of cyano compound 31 (1.27 g, 7.5 mmole), 1,2-dianilinoethane (2.97 g, 14 mmole), Raney

nickel (16 g, 276 mmole), pyridine (60 ml) and water (17 ml) was added glacial acetic acid (25 ml) followed by sodium hypophosphite (10 g, 113.6 mmole). It was stirred for 16 hrs at room temp. It was filtered and the catalyst was washed thoroughly with chloroform (300 ml). Chloroform layer was washed successively with water (3 x 200 ml), copper sulphate solution (10%, 5 x 100 ml), dried (Na_2SO_4). After solvent removal a thick liquid was obtained which was purified through column chromatography using grade II alumina. The column was successively eluted with (i) pet.ether (ii) pet.ether-ethyl acetate 99% (iii) p.et.ether-ethyl acetate 98:2 (iv) pet.ether-ethyl acetate 97:3. The fraction eluted with pet.ether-ethyl acetate 98:2, after solvent removal furnished 32. Yield = 1.872 g, 69.98%. Yield. R_f = 0.44 (pet.ether-acetone 4:1).

IR (Nujol): 2920, 2840, 1705, 1600, 1500, 1460, 1380, 1355, 1280, 1250, 1230, 1160, 1130, 1080, 1070, 1060, 1030, 1020, 940, 930m 875, 810, 750, 718, 695.

NMR (CCl4): 1.16 (10H, m, - $(CH_2)_5$, 1.9 (3H, d, J = 3 Hz, might be $-OCOCH_3$), 3.5 (4H, m, N-CH_2-CH_2) 3.9 (2H, m, -CH_2-OAc), 5.33 (1H, m, CH- N), 6.26 to 7.33 (10H, m, aromatic)

Found: C, 75.01; H, 7.95; N, 7.31. $C_{23}H_{30}N_2O_2$ requires C, 75.37; H, 8.25; N, 7.64%.

4-Phenyl-1,3-dioxane 34

A mixture of styrene 33 (63 g, 605.7 mmole), formalin (1.35 g, 1.500 mmole) and conc. sulphur acid (5 ml, 91.8 mmole) was refluxed for 7.5 hrs and then cooled. Benzene (100 ml) was added and shaken well. Benzene layer was removed and water layer was extracted with benzene (2 x 75 ml). Combined benzene extract was washed with water and finally with saturated brine dried (Na_2SO_4). After removing benzene a liquid was obtained which on fractional vacuum distillation furnished 34.

Fraction 1: From 80°C to 96°C at 2 mm, 16.32 g.

Fraction 2: From 96°C to 103°C at 2 mm.

(lit. b.p.[17] 96-103°/2 mm).

Fraction 2 was the required product.

Yield = 72.10 g (72.58%).

IR (liq. film): 2965, 2845, 1450, 1400, 1375, 1360, 1305, 1260, 1225, 1170, 1110, 1060, 1035, 1000, 975, 910, 855, 815, 750, 700, 670.

NMR (CCl_4) : 1.8 (2H, m, O-CH-$\underline{CH_2}$)

3.7 (2H, m, CH_2-CH_2-O)

4.6 (2H, m, $\underline{CH_2}$ O O)

5.0 (1H, dd, J = 6 Hz, $\underline{CH}$-O)

7.2 (5H, s, aromatic)

1,5-Diacetoxy-3-phenyl-2-oxapentane 35

A mixture of acetal 34 (41 g, 250 mmole), acetic anhydride (60 ml, 600 mmole), conc. HCl (3 ml) was heated in an oil bath with stirring at 85-87°C (bath temp.) for 6 hrs. It was cooled and poured in 200 ml of water, neutralized using aqueous NaOH and finally made alkaline to pH 8-8.5. (total quantity of alkali solution required is 175 ml of 15% solution). It was extracted with ether and ether layer was washed with water (2 x 100 ml) and dried (Na_2SO_4). After removing ether a liquid was obtained which was distilled under reduced pressure to furnish (35). Yield = 62.3 g (93.68%). B.p.152-5°/2 mm (lit.[13] b.p.137°/0.8 mm).

IR (liq.film): 2950, 1740, 1490, 1450, 1365, 1240, 1160, 1120, 1090, 1040, 1010, 945, 830, 760, 700, 600.

NMR (CCl$_4$) : 1.96 (8H, m, - CH-CH_2-CH_2- and two -O-$COCH_3$)
4.1 (2H, m, CH_2-O)
4.6 (1H, m, -CH-Ø)
5.1 (2H, m, CH_2<O, O)
7.2 (5H, m, aromatic)

1-Phenyl-1,3-propane diol

A solution of potassium hydroxide (11.26 g, 20 mmole) in methanol (50 ml) was added to a solution of diacetate 35 (18.0 g, 67.66 mmole) and shaken well. Reaction mixture was stirred at room temperature for 1 hr and then heated

on water bath upto boiling. Methanol was distilled out under reduced pressure, water (20 ml) was added to it and the resultant solution was saturated with sodium chloride and extracted with chloroform. Chloroform layer was washed with saturated brine and dried (Na_2SO_4). After removing chloroform a thick liquid was obtained which was distilled under reduced pressure to furnish 36.

Yield = 9.0 g, (89%), B .p. 165°/10 mm (lit.[30] 126°/2 mm).

IR : 3300 (very broad, OH), 1650 (broad), 1600, 1490, 1450, 1420 (broad), 1330 (broad), 1200, 1170, 1050, 1030, 985, 920, 890, 860, 840, 820, 750, 700.

NMR ($CDCl_3$): 1.9 (2H, m, $-CH-C\underline{H}_2-CH_2$)

3.2 (1H, broad, $-O\underline{H}$)

3.7 (2H, t, J = 6 Hz, $-C\underline{H}_2-OH$)

4.8 (3H, t, J = 6 Hz, $-CH-\phi$)

7.2 (5H, s, aromatic H)

2,4-Diphenyl-1,3-dioxane 37

A mixture of diol 36 (3.6 g, 23.68 mmole), benzaldehyde (2.51g, 23.6 mmole), p-toluene sulphonic acid (0.1 g) and benzene (100 ml) was distilled azeotropically in about 4 hrs. It was cooled and poured in saturated sodium bicarbonate solution. Benzene layer was washed with water and dried (Na_2SO_4). After removing benzene under reduced pressure, a liquid was obtained. A vacuum distillation was attempted but only benzaldehyde was obtained as distillate and the residue was polymerized. Due to this

the crude product as such a was analysed.

Yield = 5.054 g (88.91%).

IR: 2975, 2955, 1600, 1585, 1495, 1450, 1425, 1400, 1365, 1310, 1270, 1240, 1200, 1180, 1120, 1100, 1070, 1020, 1095, 910, 880, 850, 825, 745, 700, 650, 600.

NMR : 1.9 (2H, m, HC-C<u>H</u>$_2$-CH$_2$)

4.2 (2H, m, -C<u>H</u>$_2$-O-)

4.8 (1H, m, -C<u>H</u>-O)

5.5 (1H, s, Ø-CH<O>O), 7.3 (10H, m, aromatic H)

The compound <u>37</u> seemed to be quite pure so was used directly for subsequent steps without purification.

<u>Reaction of N-bromosuccinimide on 37</u>

A mixture of benzylidene acetal <u>37</u> (5.3 g, 22.1 mmole) N-bromo succinimide (4.92 g, 27.6 mmole), barium carbonate (2 g, 10 mmole) and benzoyl peroxide (0.3 g, 1.24 mmole) in CCl_4 (100 ml) was refluxed under stream of nitrogen for 1.25 hrs, during which it has completely decolurized. It was hot filtered and the solid obtained was washed with hot CCl_4. CCl_4 layer was washed with water (2 x 100 ml) and once with saturated brine dried (Na_2SO_4). Benzene was recovered to get a thick liquid (<u>38</u>). Purification through column chromatography using grade II alumina was attempted but from t.l.c. it showed formation of some other products after chromatography. The product was analysed as such

Yield = 6.12 g (86.80%).

IR (liq.film): 1720, 1600, 1580, 1490, 1450, 1380, 1350, 1310, 1270, 1200, 1175, 1110, 1070, 1025, 1000, 760, 710,

NMR (CCl_4) : 2.66 (2H, m, $C\underline{H}_2$-CH)

4.43 (2H, t, J = 6 Hz, $C\underline{H}_2$-Br)

5.13 (1H, t, J = 8 Hz, C<u>H</u>-OBz)

7.06 to 8.13 (10H, m, Aromatic H)

Reaction of sodium cyanide on NBS reaction product

To a stirred suspension of sodium cyanide (0.645 g, 13.16 mmole) in dimethyl sulphoxide (10 ml) was added a solution of bromo compound (2.1 g, 6.6 mmole) in dimethyl sulphoxide (5 ml) at 50°C. Stirring continued at 60-67 (bath temp.) for 2 hrs. It was cooled, poured in water, ext with chloroform. Chloroform layer was washed with water (3 x 100 ml) and finally with saturated brine and dried (Na_2SO_4). After recovering chloroform a thick liquid (<u>39</u>) was obtained. A purification through column chromatography was attempted using grade II alumina, but t.l.c. indicated a formation of some new products after chromatography. Due to this the compound was analysed as such.

Yield = 1.142 (65.46%).

IR (liq.film): 2230 (C=N), 1715(ester), 1600, 1580, 1490, 1450, 1310, 1270, 1200, 1175, 1110, 1070, 1020, 825, 750, 710, 695, 650.

NMR: (CCl_4) 1.9 to 2.5 (4H, m, $C\underline{H}_2$-$C\underline{H}_2$CN)

4.26 (1H, t, J = 6 Hz, CH-O)

6.86 to 7.96 (10H, m, Aromatic H)

Sodium hypophosphite reduction of the product obtained after sodium cyanide reaction. To a stirred mixture of cyano compound (1 g, 3.77 mmole); 1,2-dianilino-ethane (1.49 g, 7.028 mmole); Raney nickel (7.8 g, 133 mmole), pyridine (25 ml) and water (12.5 ml) was added glacial acetic acid (12.5 ml) followed by sodium hypophosphite (5 g, 56.8 mmole). It was kept stirred at room temperature for 16 hrs. Filtered and the catalyst was thoroughly washed with chloroform (300 ml). Chloroform layer was washed successively with water (3 x 300 ml), copper sulphate (10%, 3 x 300 ml) and with saturated brine, dried (Na_2SO_4). Solvent recovered to get a thick liquid which was purified through column chromatography using grade II alumina. Column was successively eluted with (i) pet.ether (ii) pet.ether-ethyl acetate 99:1 (iii) pet. ether-ethyl acetate 98:2. The fraction eluted with pet. ether-ethyl acetate 98:2, after removing solvent furnished a single spot product (40).

Yield = 1.1363 g (65.17). R_f = 0.45 (pet.ether-acetone 4:1).

IR (liq.film): 2950, 1740 (ester), 1670, 1600, 1580, 1500, 1450, 1390, 1330, 1270, 1230, 1180, 1160, 1110, 1080, 1030, 990, 940, 760, 710, 695, 650.

NMR: 1.16 (2H, m, $-CH_2$)
2.16 (2H, m, $-CH_2$)
3.26 (4H, s, two $N-CH_2$)
4.9 (1H, m, -CH-OCOPh)
5.2 (1H, m $-CH<^{N}_{N}$)
6.26 to 7.9 (20H, m, aromatic)

1,4-Di-O-acetyl-cis-but-2-ene-1,4-diol (43)

A mixture of cis-but-2-ene-1,4-diol (42) (100 g, 1.14 mole), pyridine (180 g, 2.28 moles) and acetic anhydride (350 g, 3.42 mole) was kept overnight. After usual workup it furnished (43). Yield 1.75 g,(89.7%), b.p.105°/0.8 mm (lit. 203°).

NMR: 2.0 (6H, s, $-OCOCH_3$), 4.6 (4H, d, J = 6 Hz, $-CH_2-OAc$), 5.6 (2H, t, J = 6 Hz, vinylic H).

1,4-Di-O-acetyl-erythritol (44)

To a stirred and ice-cooled mixture of diacetate (43) (5.14 g, 30 mmole), acetone (80 ml) and water (2 ml); $KMnO_4$ (4.74 g, 30 mmole) was added portion by portion maintaining the temperature of reaction mixture at 0-5°C. After complete addition of $KMnO_4$, reaction mixture was warmed to room temperature and stirred for 2 hrs. Residue was filtered off, washed with acetone (25 ml x 2). Combined filtrate was evaporated and the residue was recrystallized using acetone + pet.ether (5:1). Filtration of the solid furnished diol (44) Yield 3.82 g (61.8%). M.p.93-4° (lit.[32] m.p.93-4°).

1,3:2,4-Di-O-benzylidene-erythritol (45) was prepared according to literature method m.p.201-202°(lit.[19] 201-202).

3-O-Benzoyl-2,4-O-benzylidene-1-bromo-1-deoxy-DL-erythritol (46)

A mixture of dibenzylidend derivative (45) (8.94 g, 30 mmol), N-bromosuccinimide (5.34 g, 30 mmol), barium carbonate (1.5 g, 7.6 mmol), benzoyl peroxide (0.3 g, 1.2 mmol) and CCl_4 (250 ml) was heated under reflux with efficient stirring for 1 hr and filtered hot. The cake was washed with hot CCl_4 (100 ml). The filtrates were combined and the solvent removed on steam bath. The residue was extracted with ether (80 ml x 3) to furnish (i) ether extract and (ii) ether insoluble residue. Ether extract after evaporation of solvent furnished (46). Yield = 6.20 g (55%). A sample recrystallized from 5:2 mixture of benzene and pet.ether (60-80°) showed m.p.128-130°. (lit.[1] m.p. = 128-30°). The insoluble residue (ii) on recrystallization from 9:1 mixture of benzene and pet.ether furnished recovered starting material (45). The yield of (46) when corrected for recovered starting material is 75%. R_f = 0.72 (pet.ether-acetone 3:1).

IR (Nujol): 1735 (OBz)

NMR ($CDCl_3$): 3.58 (2H, d, J = 6 Hz, $-C\underline{H}_2-Br$) 3.76 (1H, t, J = 10 Hz, axial H of $-OCH_2-$), 4.18 (m, 1H, $-OC\underline{H}-C\underline{H}_2-Br$), 4.53 (1H, dd, J = 5 and 10 Hz, equitorial H-$OC\underline{H}_2-$), 5.14 (1H, dt, J = 5 and 10 H_z -CH-OBz), 5.61 (1H, s, Ø - 
7.4-8.0 (10H, m, aromatic).

2,4-O-Benzylidene-1-bromo-1-deoxy-DL-erythritol (47)

A mixture of bromo compound (46) (2 g, 5.3 mmole), methanolic solution of KOH (5 ml, 10%) and water (10 ml) was refluxed on water bath for 3 hrs. Methanol was removed under reduced pressure and residue was extracted with chloroform. Chloroform layer was washed with saturated brine and dried (Na_2SO_4); chloroform was removed to furnish a thick liquid, which was purified by passing through a column using grade II alumina. The column was eluted successively with (i)pet.ether (ii) 95:5 mixture of pet.ether and ethyl acetate (iii) 95:10 mixture of pet.ether-ethyl acetate. The fraction eluted with 90:10 mixture of pet.ether and ethyl acetate, on solvent removal furnished (±)(47). Yield = 1.12 g (77%). R_f = 0.35 (pet. ether-acetone 1:1).

IR (liq.film): 3420 (broad, -OH), 2860, 1700, 1495, 1450, 1400, 1375, 1295, 1140, 1080, 990, 940, 920, 875, 750, 700, 660, 650.

Found: C, 48.41; H, 4.52. $C_{11}H_{13}BrO_3$ requires C, 48.35; H, 4.76.

3-O-Acetyl-2,4-O-benzylidene-1-bromo-1-deoxy-DL-erythritol(48)

A mixture of hydroxy compound (47) (1.0 g, 3.66 mmole), pyridine (3 ml) and acetic anhydride (5 ml) was kept overnight. It was poured over crushed ice and extracted with ether. Ether layer was washed with water (2 x 50 ml),

aqueous copper sulphate solution (1 x 50 ml, 10%) and finally with saturated brine. After drying (Na_2SO_4) ether was evaporated to get a solid, which was chromatographed on a column of alumina (Grade II). The column was eluted successively with (i) pet.ether (ii) 99:1 mixture of pet.ether and ethyl acetate (iii) 98:2 mixture of pet. ether and ethyl acetate. The fraction eluted with 98:2 mixture of pet.ether and ethyl acetate on solvent removal furnished (±) (48). Yield = 1.01 g (87.8%). R_f = 0.52 (pet.ether-acetone 3:1) m.p. = 86-87°C.

IR(Nujol): 2920, 1730 (ester), 1460, 1440, 1410, 1370, 1320, 1305, 1240, 1150, 1100, 1050, 1010, 970, 920, 880, 865, 765, 705, 650.

NMR ($CDCl_3$): 2.11 (3H, s, $-OCOCH_3$), 3.59 (3H, m, $-CH_2-Br$ and axial H of OCH_2), 4.03 (1H, m, $-CH-O$), 4.42 (1H, dd, J = 5 and 10 Hz, equotorial H of $-OCH_2-$), 4.93 (1H, dt, J = 5 and 10 Hz, $-CH-OAc$), 5.58 (1H, s, $\phi - CH<^{O}_{O}$), 7.36-7.62 (5H, m, aromatic).

Found: C, 49.31; H, 4.62; Br, 25.16. $C_{13}H_{15}BrO_4$ requires C, 49.52; H, 4.76; Br, 25.4 %.

4-O-Acetyl-3,5-O-benzylidene-2-deoxy-DL-erythropentanonitrile (49)

A stirred mixture of potassium cyanide (1.3 g, 20 mmole) and DMSO (10 ml) was heated to 80°C. Bromide (48) (3.15 g, 10 mmole) was added to this mixture gradually at such a rate that the reaction temperature did not exceed 100°C.

After completing addition of (48), reaction mixture was stirred at 108-110°C for 20 min, cooled to room temperature, diluted with water (100 ml) and extracted with chloroform (50 ml x 3). The $CHCl_3$ extract was washed with water, dried (Na_2SO_4) and the solvent evaporated. The residue was chromatographed on a column of grade II alumina. The column was eluted successively with (i) pet.ether (ii) 99:1 mixture of pet.ether and ethyl acetate (iii) 97:3 mixture of pet.ether and ethyl acetate (iv) 95:5 mixture of pet.ether and ethyl acetate. The fraction eluted with 95:5 mixture of pet.ether-ethyl acetate on solvent removal furnished (±) (49)
yield = 0.31 g (12%). M.p. = 85-86°C, R_f = 0.32 (pet.ether-acetone, 8:2).

IR (Nujol): 2840, 2240 (C≡N), 1740, 1730, 1630, 1560, 1490, 1470, 1460, 1380, 1340, 1310, 1245 (strong), 1220, 1045, 980, 900, 880, 760, 650, 640.

NMR ($CDCl_3$): 2.1 (3H, s, $-OCOCH_3$), 2.78 (2H, d, J = 6 Hz, $-CH_2-CN$), 3.73 (1H, t, J = 10 Hz, axial H of $-OCH_2$) 4.12 (1H, m, $-OCH-CH_2-CN$), 4.48 (1H, dd, J = 5 and 10 Hz, equitorial H of $-OCH_2$), 4.98 (1H, dt, J = 5 and 10 Hz, -CH-OBz), 5.50 (1H, s, Ø -  7.10 to 7.55 (5H, m, aromatic).

Found: C, 64.21; H, 5.68; N, 5.01. $C_{14}H_{15}NO_4$ requires C, 64.37; H, 5.75; N, 5.36.

(±) 3,O-Acetyl-2,4-O-benzylidene-1-deoxy-1-(1,3-diphenyl-2-imidazolidyl)-erythritol (50)

A mixture of pyridine (10 ml), cyano compound (49) (0.18 g, 0.69 mmole), 1,2-dianilino ethane (41) (0.267 g, 1.26 mmole), Raney nickel (3 g, 50 mmole) and water (5 ml) was stirred for 10 minutes. To this stirred mixture was added acetic acid (5 ml) followed by sodium hypophosphite (2.0 g, 23 mmole). The reaction mixture was kept stirred for 16 hrs at room temperature and filtered. The precipitate was washed with $CHCl_3$ (50 ml). $CHCl_3$(50 ml) was added to the filtrate. Combined chloroform extract was washed with water (3 x 100 ml), aqueous copper sulphate solution (10%, 3 x 100 ml), finally with saturated brine and dried (Na_2SO_4). The residue obtained after removal of solvent was chromatographed on a column of alumina (grade II). The column was eluted successively with (i) pet.ether (ii) mixture of pet.ether-ethyl acetate (97:3) (iii) mixture of pet.ether-ethyl acetate (95:5). The fraction eluted with 95:5 mixture of pet.ether and ethyl acetate, after solvent removal and crystallization from 1:1 mixture of benzene and pet.ether furnished (±) (50). Yield = 0.220 g (69.6%). M.p. = 152°C. R_f = 0.45 (pet.ether-acetone 4:1). IR (Nujol): 2840, 1742, 1600, 1500, 1480, 1450, 1390, 1330, 1235, 1210, 1130, 1090, 1045, 975, 900, 750, 690. NMR ($CDCl_3$): 1.93 (3H, s, -OOOC$\underline{H}_3$), 1.73-2.40 (2H, m, -CH-C$\underline{H}_2$-CH), 3.40-3.71 (5H, m, -N-C$\underline{H}_2$-C$\underline{H}_2$-N and

axial H of -O-CH$_2$-), 3.87 (1H, dt, J = 2 and 8 Hz, -OCH-CH$_2$) 4.29 (1H, dd, J = 5 and 10 Hz, equitorial H of -OCH$_2$), 4.69 (1H, dt, J = 5 and 10 Hz, -CH-OAc), 5.42 (1H, s, Ø-CH-O) 5.48 (1H, dd, J = 2 and8 Hz, C-H-N), 6.6 - 7.6 (15H, m, aromatic H).

(Found: C, 51.28; H, 6.41; N, 5.94. $C_{28}H_{30}N_2O_4$ requires C, 51.53; H, 6.55; N, 6.11%).

(±)-2,4-O-Benzylidene-1-deoxy-1-(1,3-diphenyl-2-imidazolidyl)-erythritol (51)

A mixture of sodium hydroxide (0.5 g, 12.5 mmol), water (10 ml), methanol (20 ml) and acetate (50) (0.7 g, 1.54 mmol) was heated under reflux for 8 hr, cooled, diluted with water and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water and dried (Na_2SO_4). The residue obtained after removal of solvent was recrystallized from benzene-pet.ether mixture (8:2) to furnish (±) (51). Yield = 0.596 g (93%) m.p.130-132°, R_f = 0.30 (pet.ether-acetone 3:1).

IR: 3600 (OH).

NMR ($CDCl_3$): 2.24 (2H, m, -CH-CH$_2$-CH-), 5.46 (1H, s, Ø-CH<O,O>), 5.67 (1H, m, -CH<N,N>), 7.00 - 7.90 (15H, m, aromatic).

(Found: C, 74.95; H, 7.01; N, 6.79. $C_{26}H_{28}N_2O_3$ requires C, 74.97; H, 6.78; N, 6.73%).

2,4-di-O-Acetyl-3-O-benzoyl-1-bromo-1-deoxy-erythritol (52)

An acylating mixture was prepared by adding conc. H_2SO_4 (0.5 ml) to an ice-cooled mixture of acetic anhydride (17.5 ml) and acetic acid (7.5 ml) with stirring.

Acylating mixture (25 ml) was added to bromobenzoate (46) (1.0 g, 2.6 mmole) and the resulting solution was kept overnight. It was poured over crushed ice and then extracted with chloroform. Chloroform layer was washed with water (2 x 100 ml), saturated brine and dried (Na_2SO_4). Chloroform was removed to get a liquid which was purified by preparative TLC to furnish (52). Yield = 0.575 g (58.1%). R_f = 0.46 (pet.ether-acetone, 4:1).

IR (liq. film): 1750 (broad), 1605, 1590, 1500, 1455, 1370, 1280, 1240, 1180, 1110, 1100, 1050, 1030, 930, 760, 715, 700, 605.

NMR (CCl_4): 2.1 (6H, s, two -O-$COCH_3$), 3.6 (2H, m, -CH_2-Br), 4.3 (2H, m, -CH_2-OAc), 5.3 (2H, m, -CH-OAc and -CH-OBz), 7.4 (3H, m, aromatic), 7.9 (2H, m, aromatic H ortho to C=O).

Found: C, 48.13; H, 4.71; Br, 21.21. $C_{15}H_{17}BrO_6$ requires C, 48.26; H, 4.56; Br, 21.45%.

2,3,4-tri-O-Acetyl-1-bromo-1-deoxy-erythritol (53)

An acylating mixture was prepared, using same quantities as used in preparation of 52).

Acylation mixture (25 ml) was added to hydroxy compound (47) (1.2 g, 4.4 mmole) and the reaction mixture

was stirred overnight. It was poured over crushed ice and extracted with ether. Ether extract was washed with water (2 x 100 ml), saturated brine and dried (Na_2SO_4). After removal of solvent a liquid was obtained which was purified by passing through a column using grade II alumina. Column was eluted successively with (i) pet.ether (ii) mixture of pet.ether-ethyl acetate 99:1 (iii) mixture of pet.ether-ethyl acetate 98:2. The fraction eluted with a mixture of pet.ether-ethyl acetate 98:2, after solvent removal furnished (53). Yield = 0.864 g (63.2%). R_f = 0.46 (pet.ether-acetone 3:1).

IR (liq. film): 1750 (broad), 1440, 1375, 1320, 1240, 122[illegible] 1125, 1090, 1060, 1045, 1010, 970, 920, 760, 700, 600.

NMR ($CDCl_3$): 2.09 (3H, s, $-OCOCH_3$), 2.12, (3H, s, $-OCOCH_3$), 2.14 (3H, s, $-OCOCH_3$), 3.58 (2H, m, $-CH_2-Br$), 4.29 (2H, m, $-CH_2-OAc$), 5.29 (2H, m, two $CH-OAc$).

Found: C, 38.51;H, 4.91; Br, 25.41. $C_{10}H_{15}BrO_6$ requires C, 38.59; H, 4.82; Br, 25.72%).

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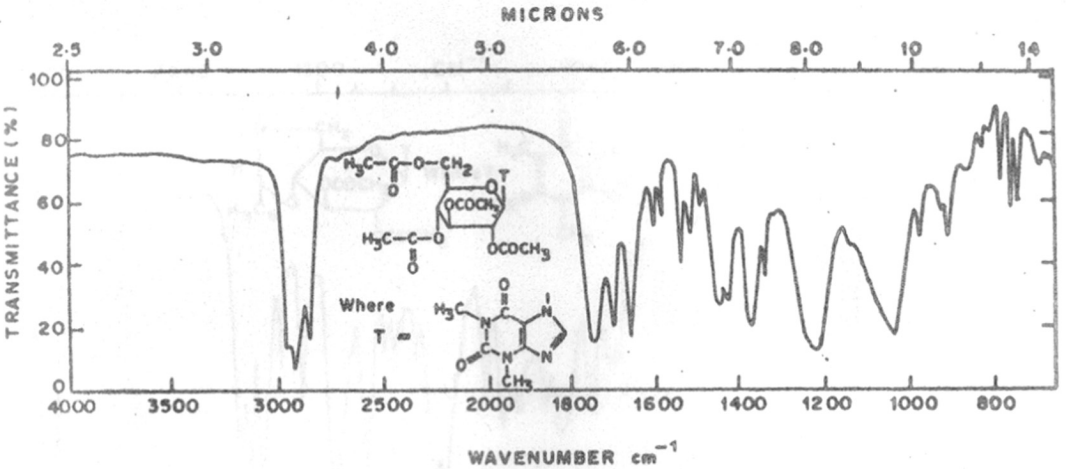
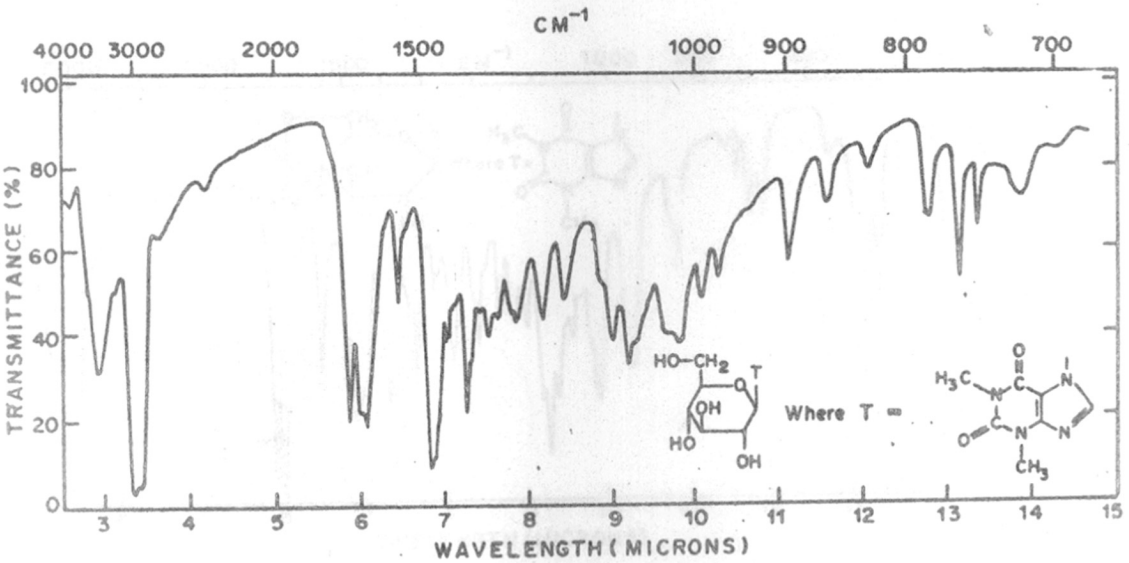


IR OF 7-(2',3',4',6'-TETRA-O-ACETYL-β-D-GLUCOPYRANOSYL) THEOPHYLLINE



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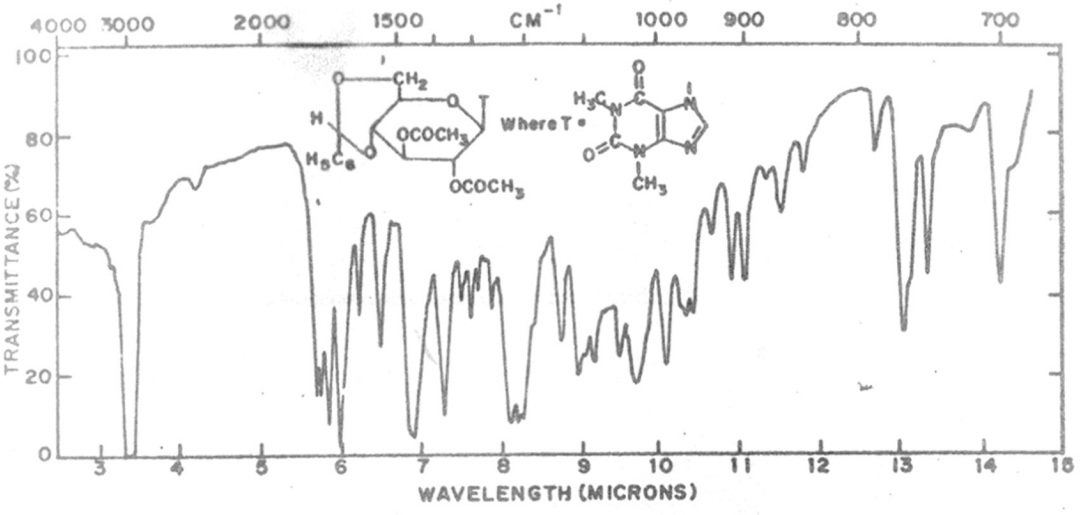

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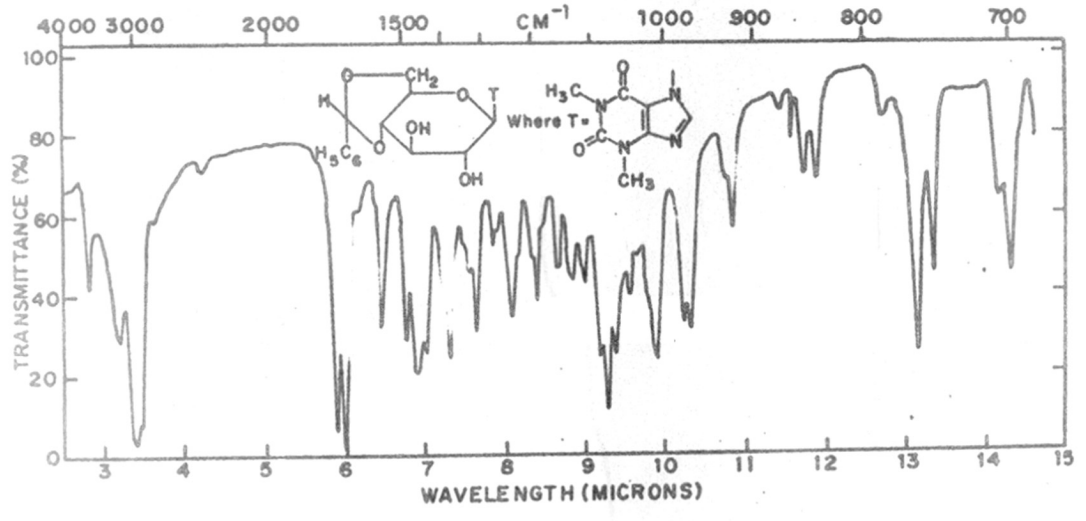

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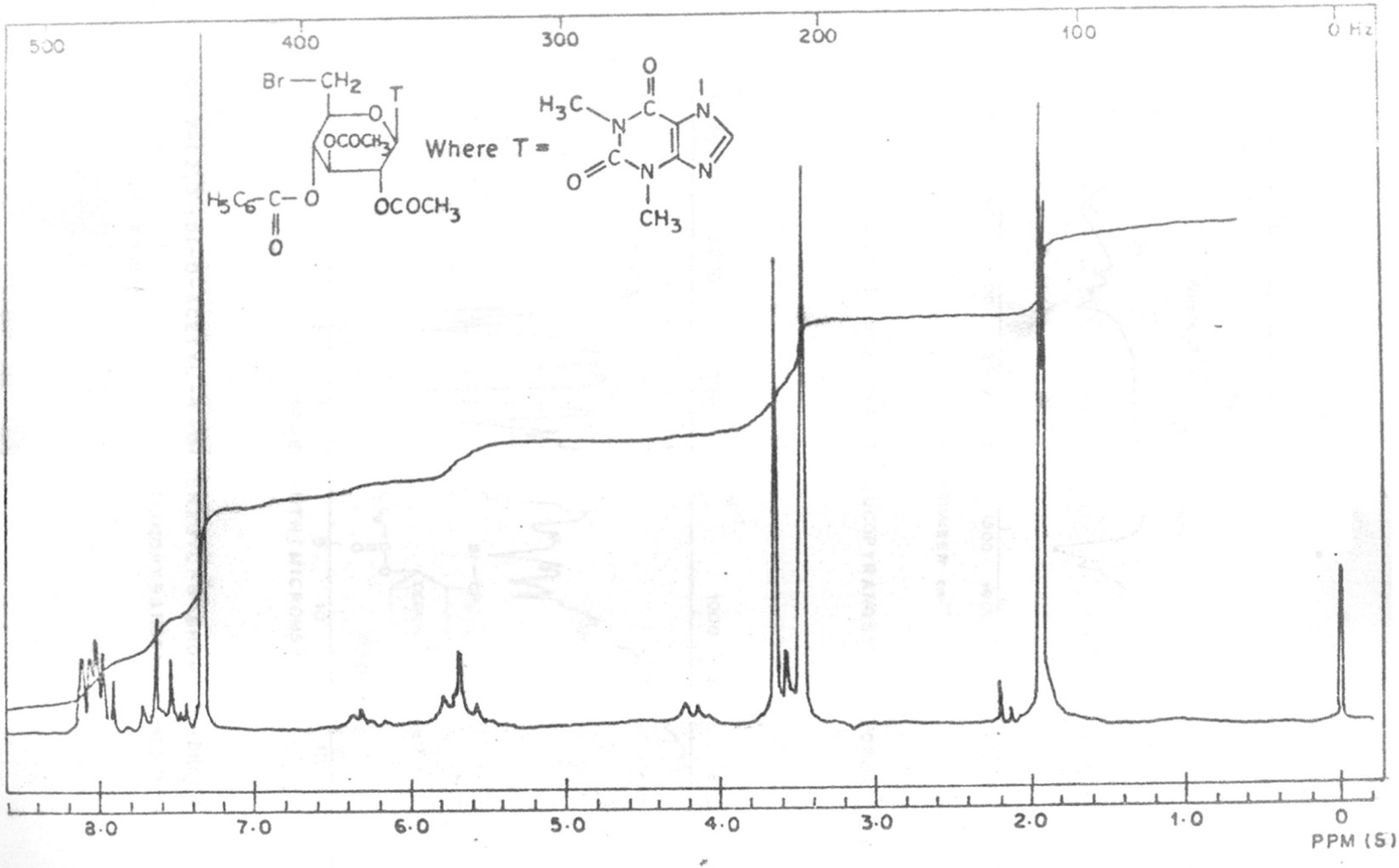
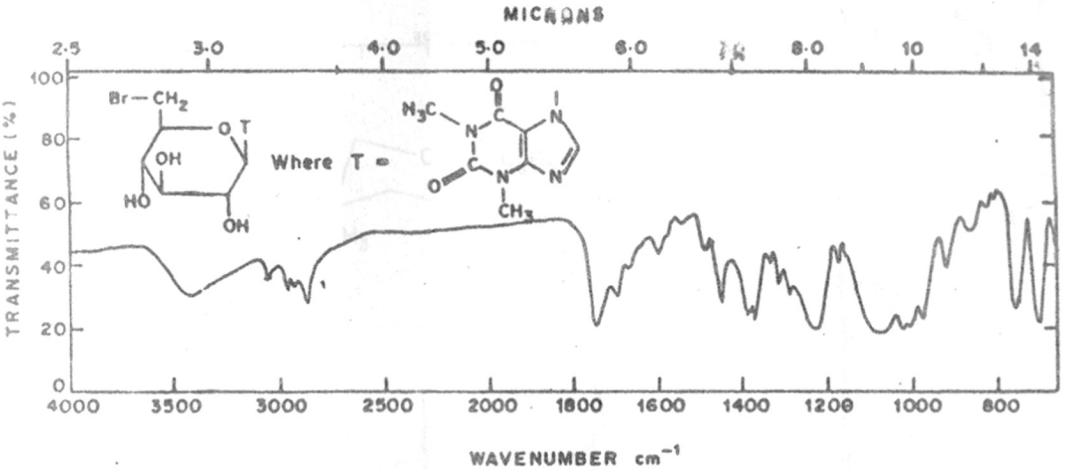


NMR OF 7-(2',3'-DI-O-ACETYL-4'-O-BENZOYL-6'-BROMO-6'-DEOXY-β-D-GLUCOPYRANOSYL) THEOPHYLLINE



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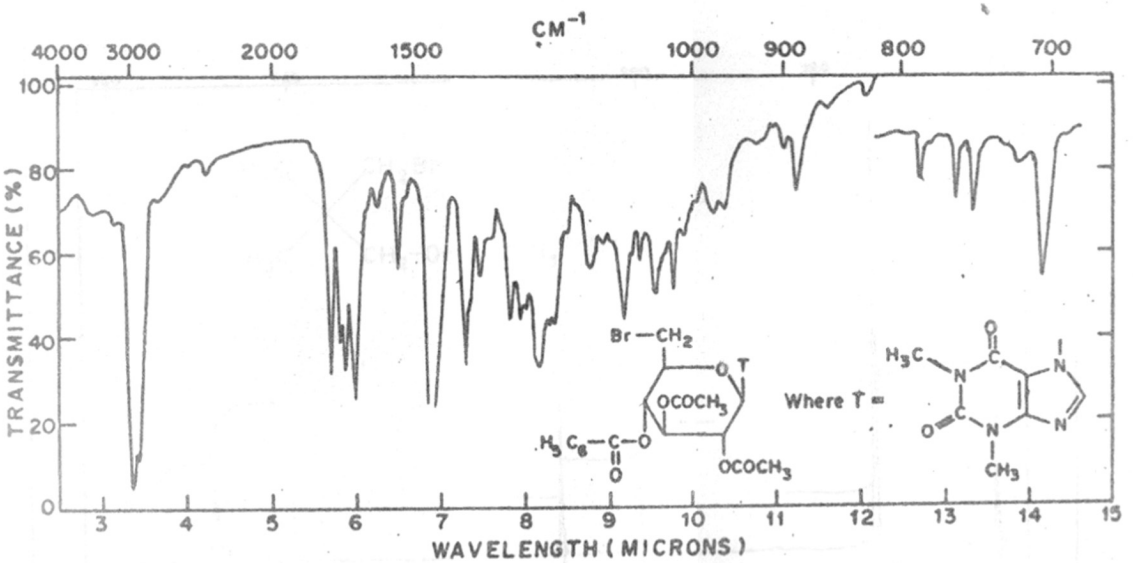

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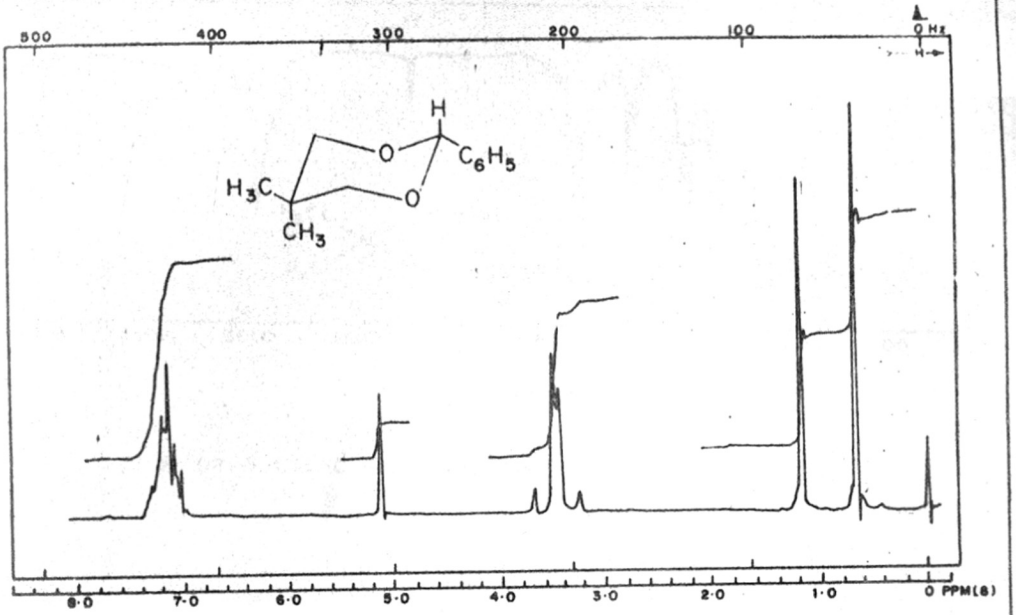
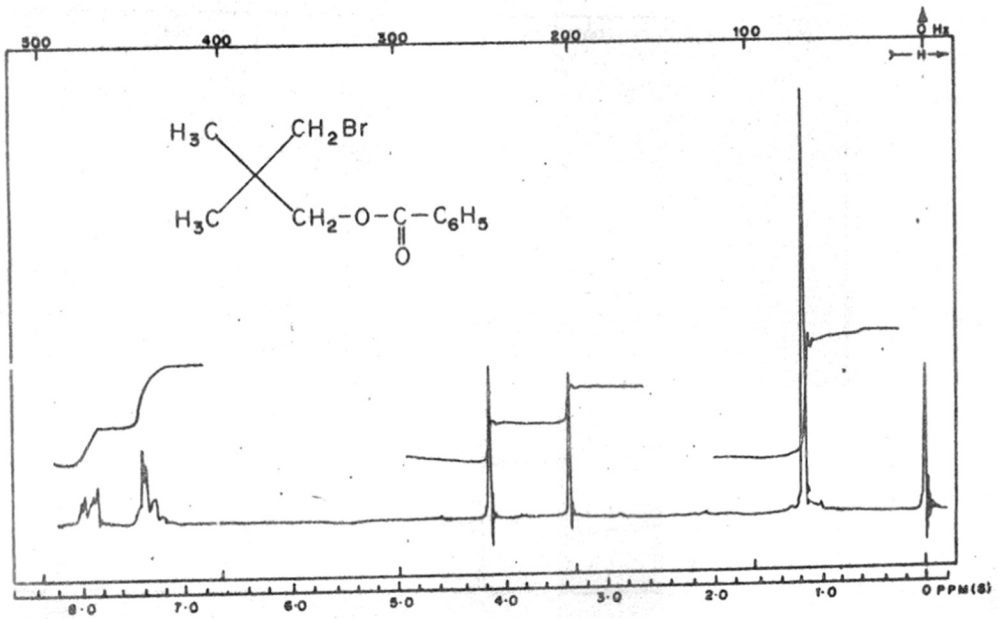
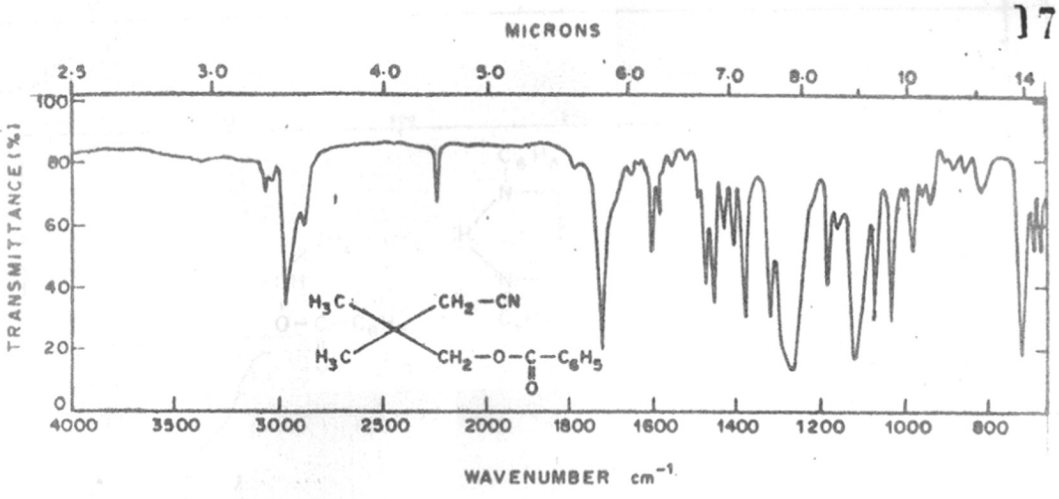
-GLUCOPYRANOSYL) THEOPHYLLINE



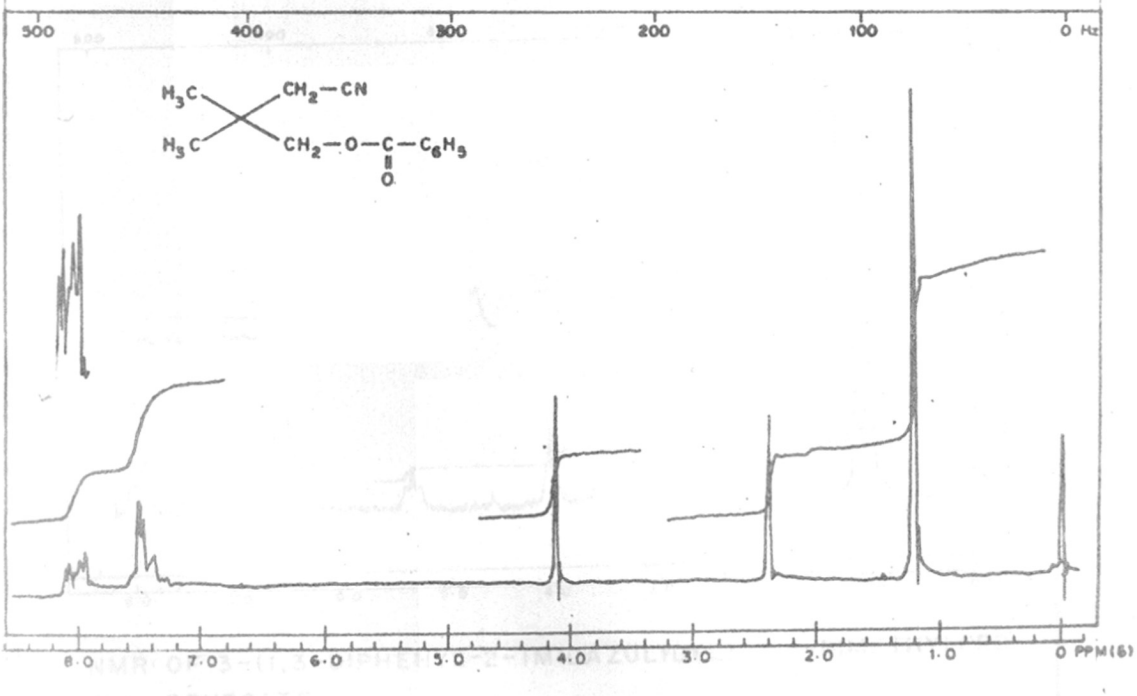
NMR OF 2-PHENYL-5,5-DIMETHYL-1,3-DIOXANE.



NMR OF 3-BROMO-2,2-DIMETHYLPROPYL BENZOATE.



IR OF 3-CYANO-2,2-DIMETHYLPROPYL BENZOATE



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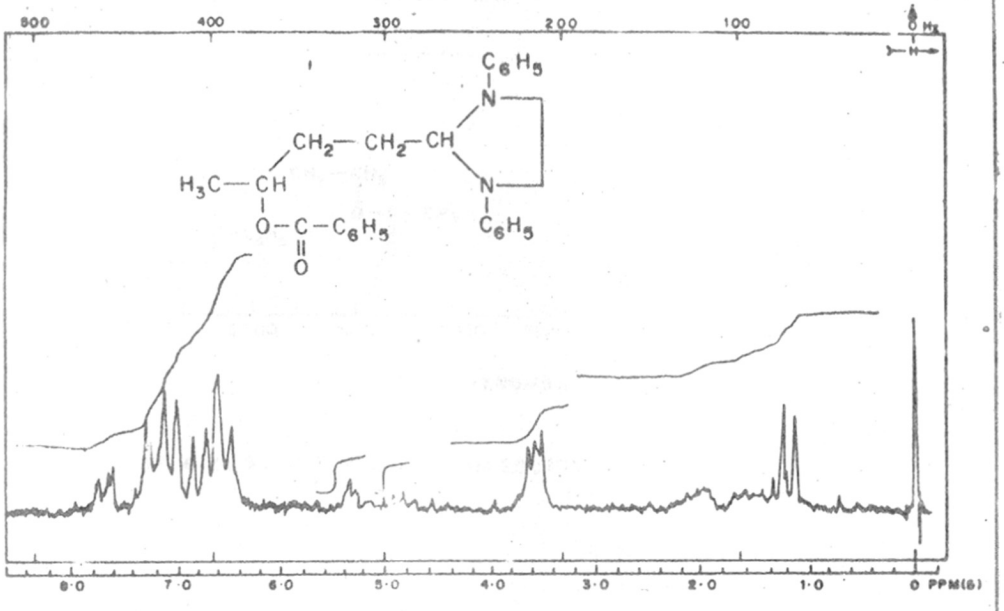
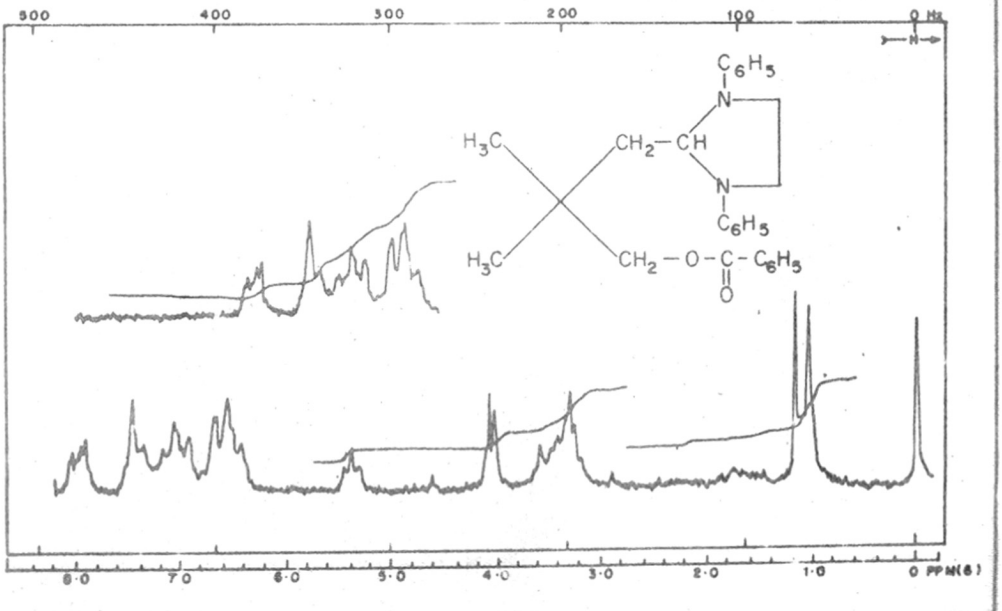
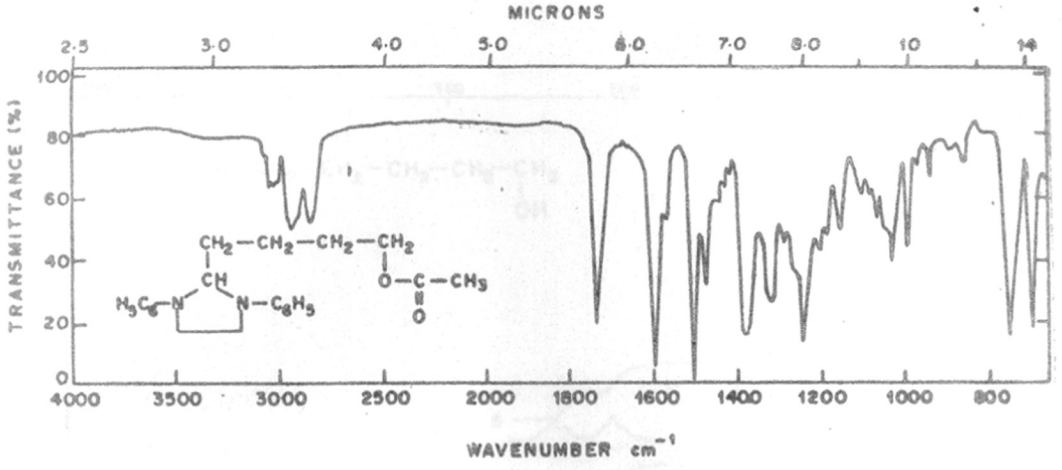


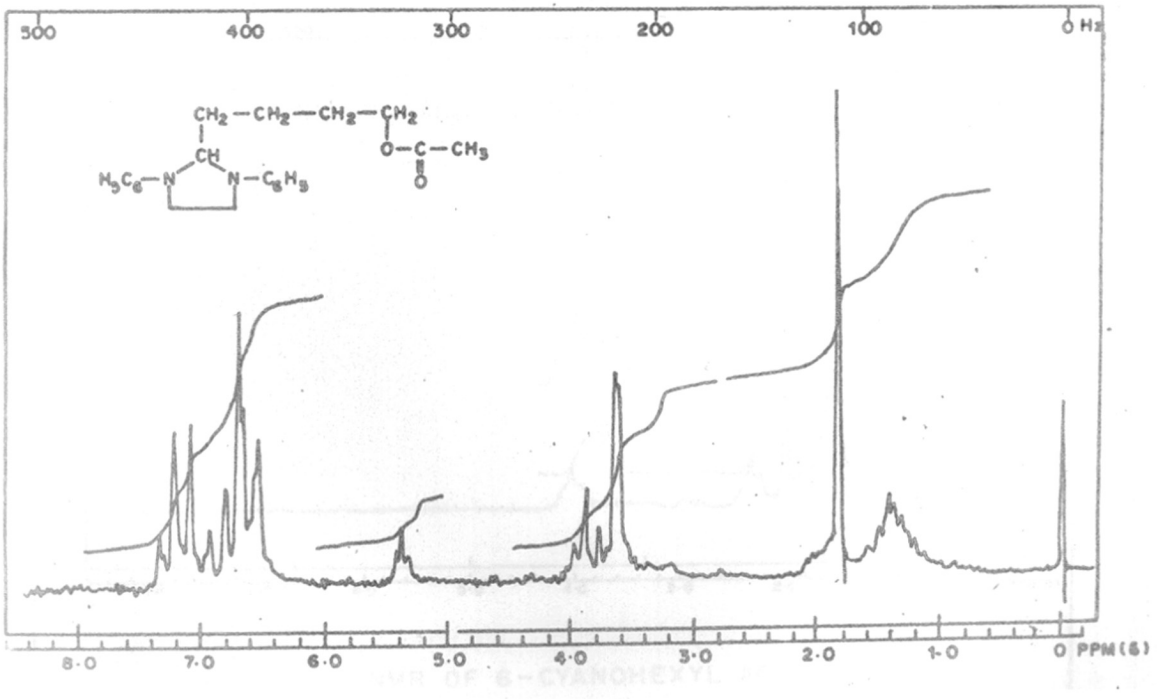
NMR OF 1-METHYL-3-(1,3-DIPHENYL-2-IMIDAZOLIDYL) PROPYL BENZOATE.



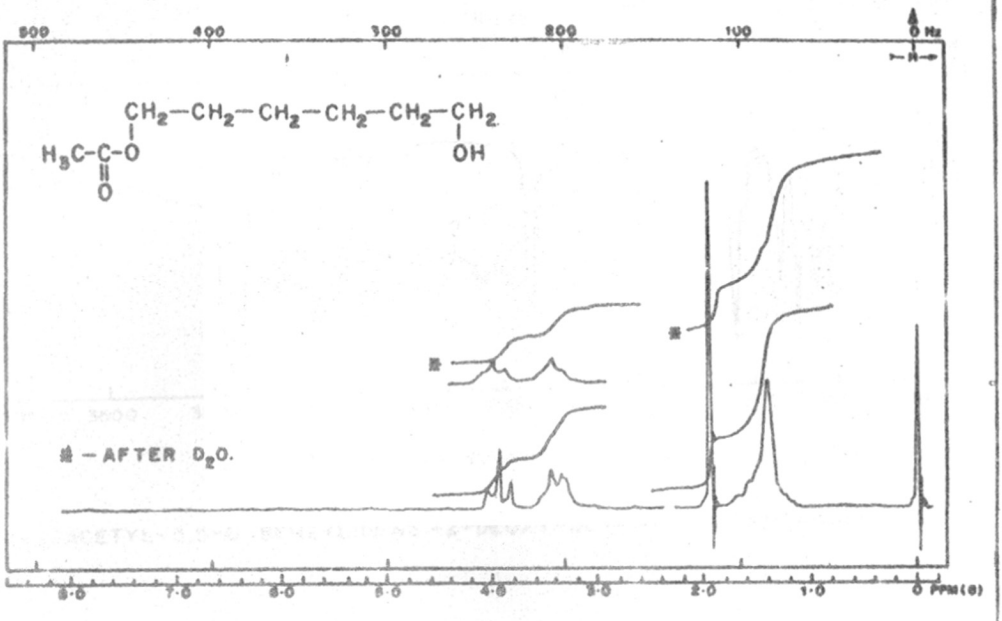
NMR OF 3-(1,3-DIPHENYL-2-IMIDAZOLIDYL)-2,2-DIMETHYLPROPYL BENZOATE.



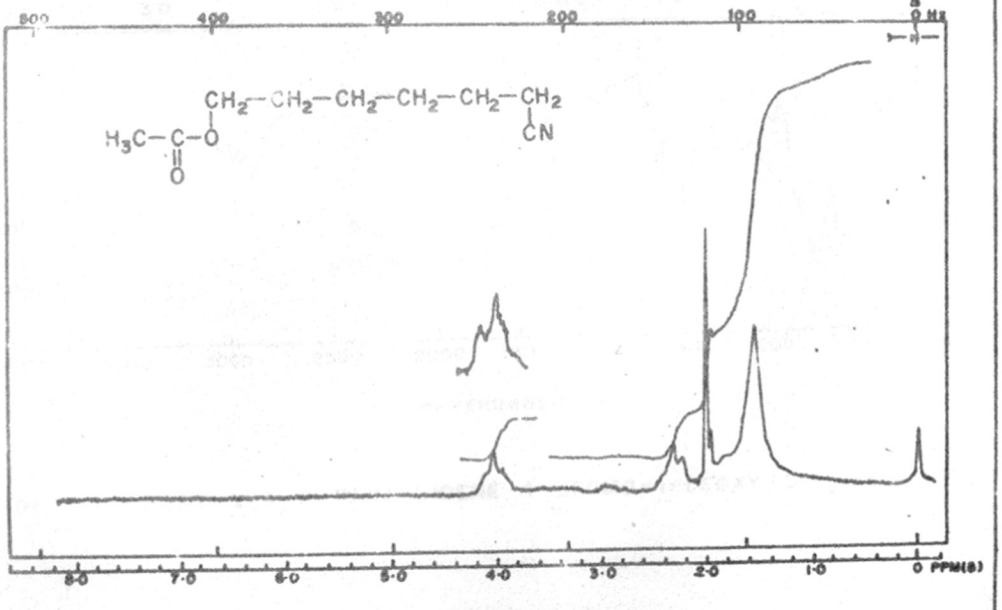
IR OF 4-(1,3-DIPHENYL-2-IMIDAZOLIDYL) BUTYL ACETATE



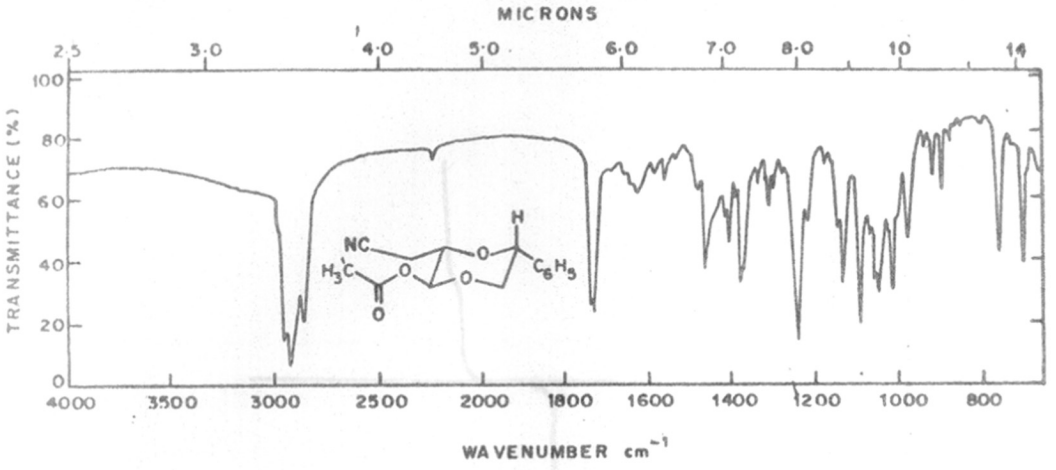
NMR OF 4-(1,3-DIPHENYL-2-IMIDAZOLIDYL) BUTYL ACETATE



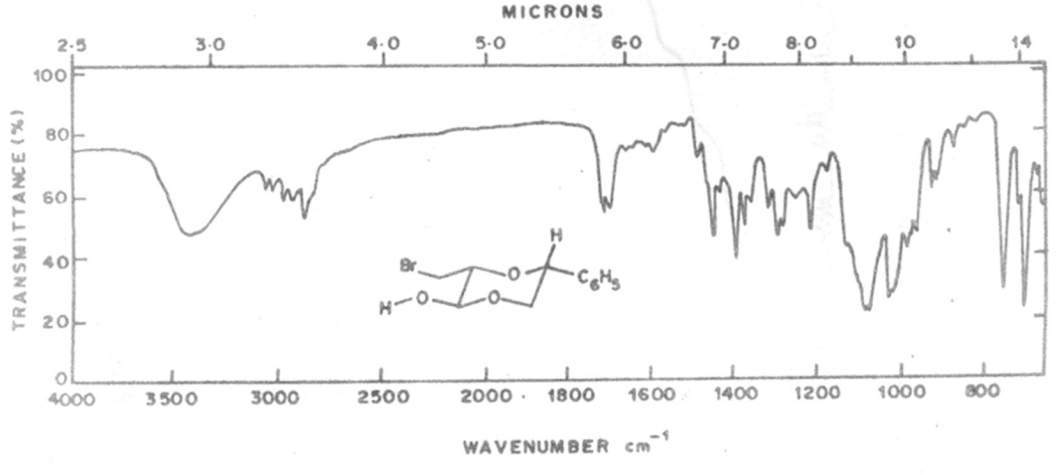
NMR OF 6-HYDROXYHEXYL ACETATE.



NMR OF 6-CYANOHEXYL ACETATE.



IR OF 4-O-ACETYL-3,5-O-BENZYLIDENE-2-DEOXY-DL-ERYTHROPENTANONITRILE



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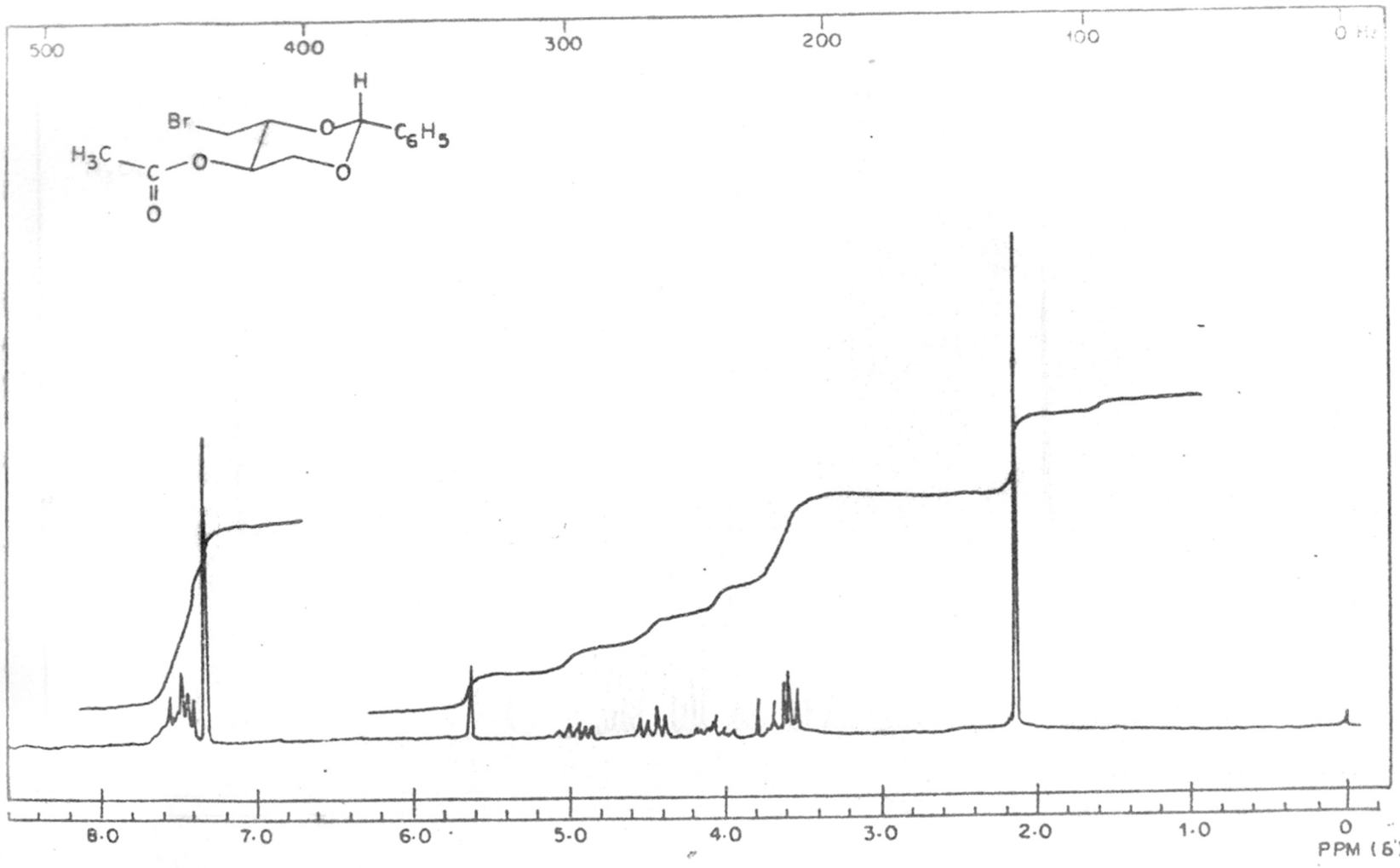
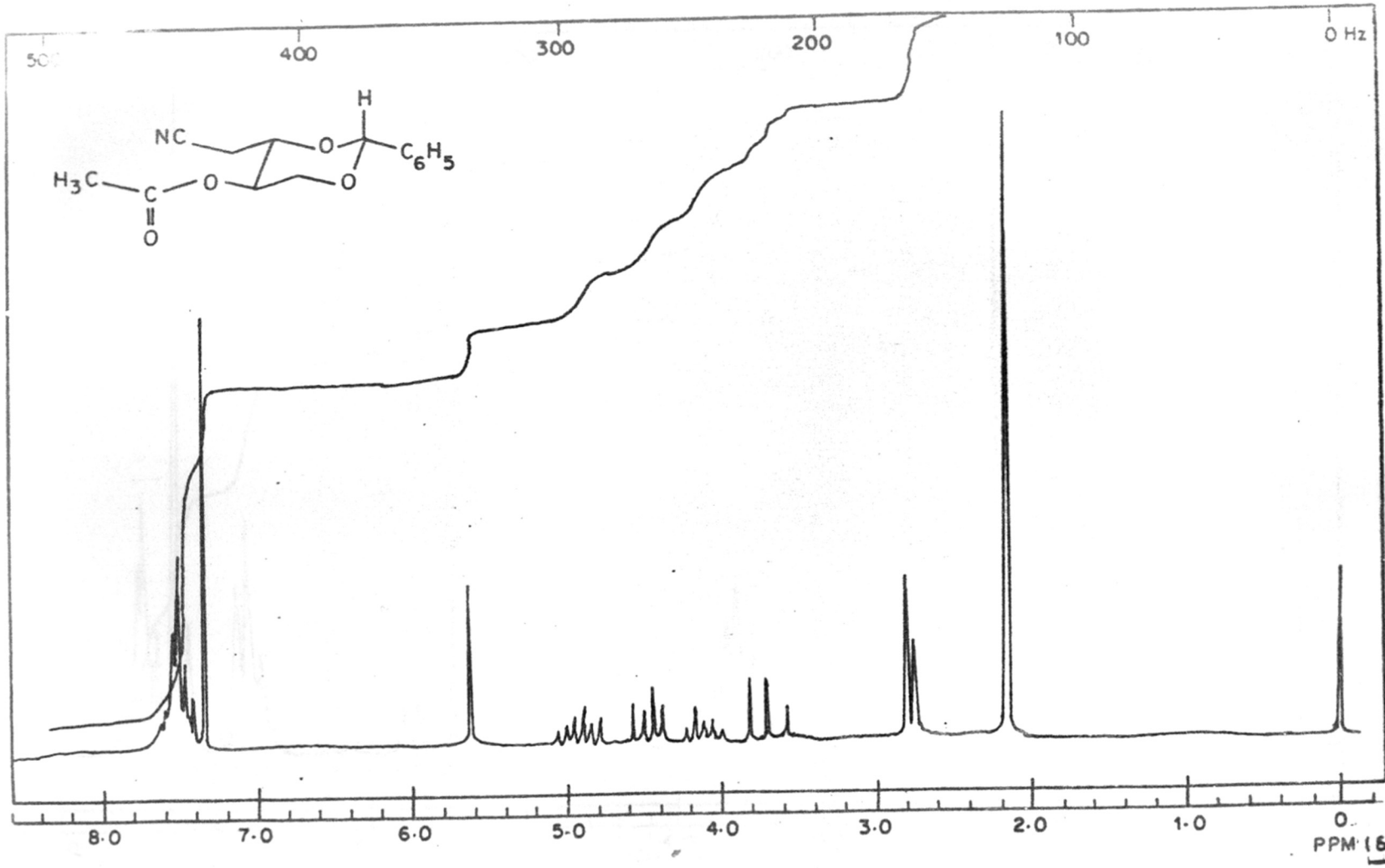


NMR OF 3-O-ACETYL-2,4-O-BENZYLIDENE-1-BROMO-1-DEOXY-DL-ERYTHRITOL



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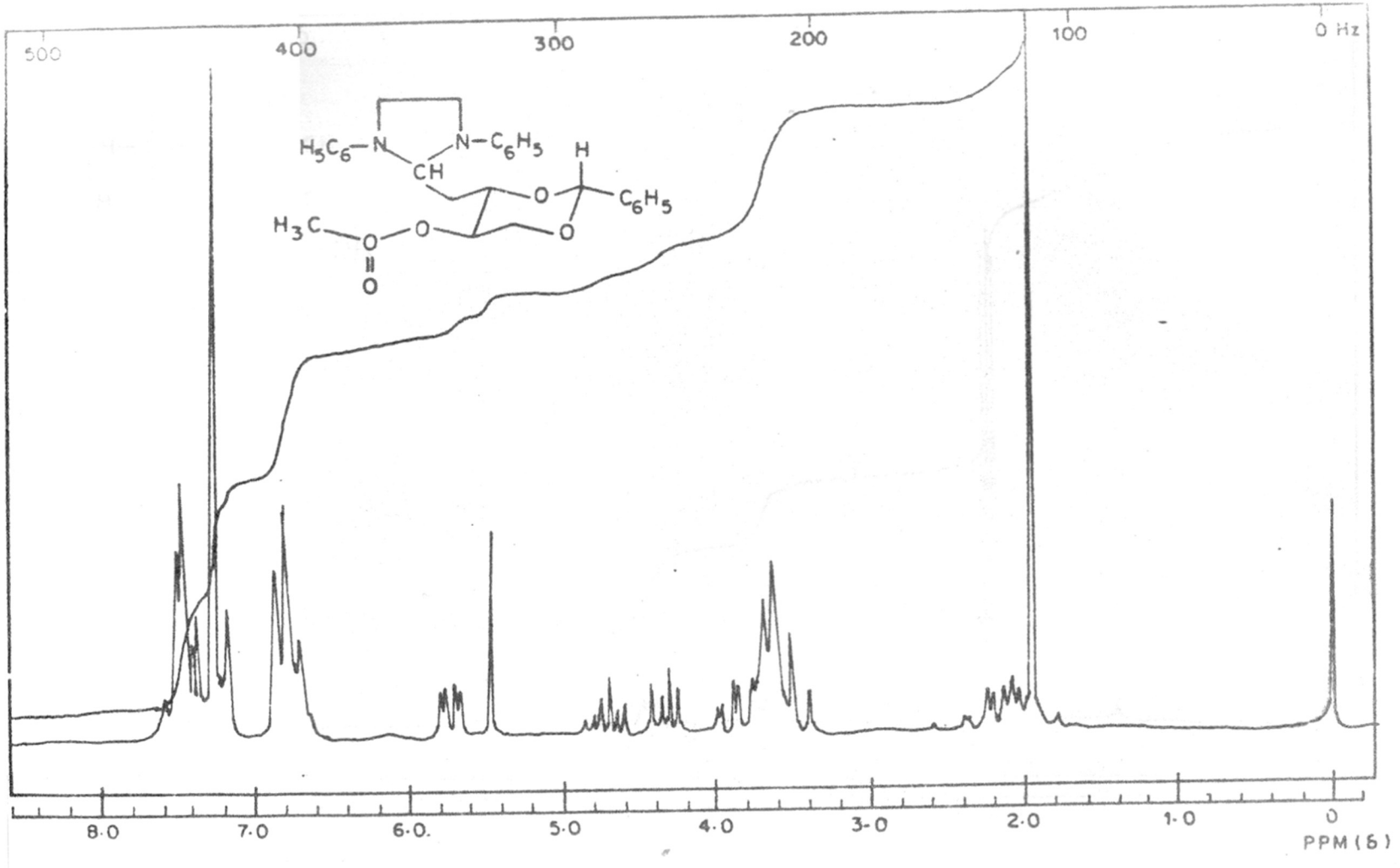
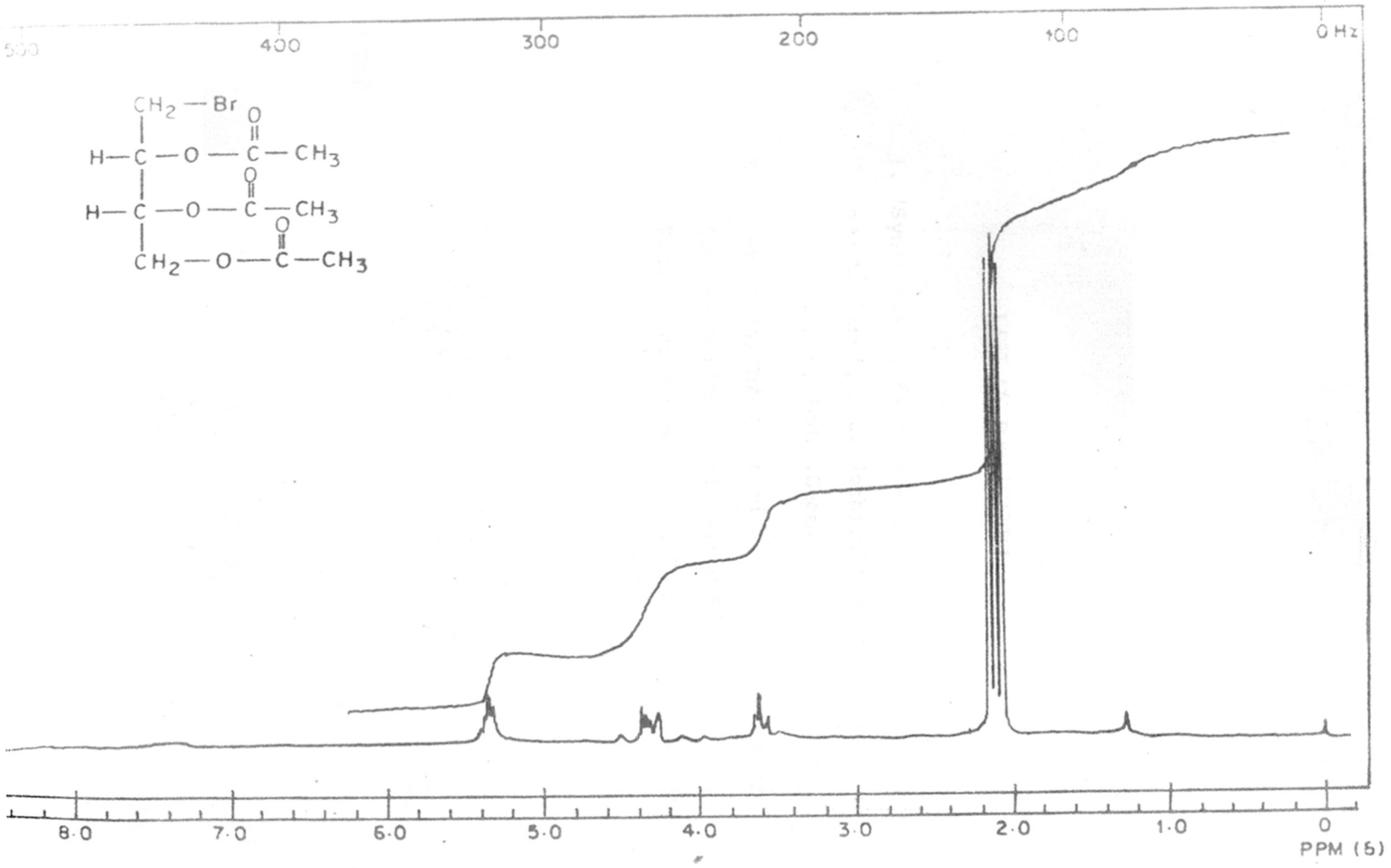


NMR OF (±)-3-O-ACETYL-2,4-O-BENZYLIDENE-1-DEOXY-1-(1,3-DIPHENYL-2-IMIDAZOLIDYL) ERYTHRITOL



NMR OF 2,3,4-TRI-O-ACETYL-1-BROMO-1-DEOXY-ERYTHRITOL

LIST OF PUBLICATIONS

1. 'Synthesis of 6-acetyl-1,4-dimethoxy-2-methyl-naphthalene', P.L. Joshi, Vijay V. Dhekne and A.S. Rao, Ind.J.Chem. 22B (I), 23, 1983.

2. '2-Acetoxybenzoyl bromide, a convenient reagent for the synthesis of oxiranes', K.S. Bhat, P.L. Joshi and A.S. Rao, Syn thesis, 142 (1984).