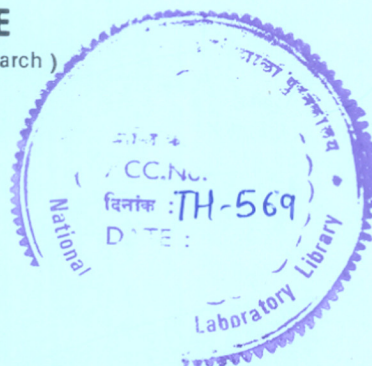


BORATE ESTERS PROMOTED EPOXIDATION

COMPUTERISED

A THESIS
SUBMITTED TO THE
UNIVERSITY OF POONA
FOR THE DEGREE OF
MASTER OF SCIENCE
(Partly by Papers & Partly by Research)
IN
CHEMISTRY



BY
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MARCH 1989

* * DEDICATED

TO THE MEMORY OF


MY MOTHER * *

COMPUTERISED

CERTIFICATE

CERTIFIED that the work incorporated in the thesis entitled, " BORATE ESTERS PROMOTED EPOXIDATION", submitted by Shri SHRIPAD DAGADOPANT DESHPANDE was carried out by the candidate under my supervision. Such material as has been obtained from other sources, has been duly acknowledged in the thesis.

Pune-411008.


(S.C. Sethi)
Supervisor

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CHAPTER-I
INTRODUCTION

INTRODUCTION

Epoxides are very useful and commercially valuable compounds. The facile nature of the oxirane ring and the ability of oxygen atom in this ring system to donate electrons to active hydrogen atoms in compounds such as organic acids, alcohols, water and ammonia giving rise to corresponding derivatives has led to many commercial applications. Ethylene oxide condensates with fatty alcohols, alkylphenols and polyols eg. sorbitol are widely used as household detergent and industrial surfactants. Epoxidized soyabean oil and linseed oil are used as plasticizers for the PVC and vinyl chloride + vinyl acetate copolymers as well as various epoxy resins. Use of various epoxides as important intermediates in variety of chemical reaction sequences is well established. For example, oxirane ring opening has been utilized in the synthesis of the following compounds, (1) dendrobatid toxin 215D¹, (2) pederamide², (3) α -tocopherol³, (4) prostaglandins⁴, etc.

Oxiranes undergo ring opening when reacted with nucleophilic reagents due to ring strain and basic nature of the oxygen atom⁵. The nucleophilic opening of epoxides provides a convenient route for forming C-C [or C-X where X = N, O, S, Se and Te] σ bonds. In general, it is possible to anticipate the stereochemistry and regio-chemistry of the ring opening.

The opening of oxirane ring system predominantly involves nucleophilic attack at the less substituted carbon and is termed as normal opening. On the other hand, under special circumstances the ring opening involves attack at the more substituted carbon atom and is termed as abnormal opening. Extensive reviews⁶⁻¹¹ have appeared with detailed discussions regarding synthesis, importance and synthetic applications of epoxides.

Synthesis of Epoxides

Epoxides can be synthesized from a variety of compounds such as olefins, halohydrins and ketones¹² using various reagents such as peracids, base or diazomethane respectively. Microbial systems furnish epoxides in high enantioselectivity due to enzymes, such as epoxidation of 1-octene by *Pseudomonas oleovorans*¹³ and of 1-hexadecene by *Corynebacterium equi* IFO 3730¹⁴.

However, due to the easy availability of olefins as starting materials and the simplicity and high yields of epoxides, epoxidation using either peracids or N-bromo-succinimide/N-bromo-acetamide followed by treatment with strong base are the methods of choice in the laboratory.

1] Epoxidation using peracids

Number of peracids are routinely used to convert olefins into epoxides. The reaction is known as Prilezhaev

reaction¹⁵. The olefin undergoing the reaction can have alkyl, aryl, hydroxyl, ester groups as substituents. The epoxidation is believed to proceed by an electrophilic attack^{16,17} and is presented in Scheme-1. The peracid usually attacks the olefin from the less hindered side to produce the less hindered epoxide as the major product. As the epoxide ring opens very easily in acidic medium, giving monoester of 1-2 diols, usually *m*-chloroperbenzoic acid or perbenzoic acid in aprotic solvents like chloroform or methylene chloride or monopero-phthalic acid in ether or peracetic acid in ethyl acetate^{18,19} are commonly preferred systems. Epoxidations carried out in the presence of an excess of the corresponding carboxylic acid frequently yield the hydroxy ester obtained from originally formed epoxide. For example, olefin III when treated with a mixture of peroxytrifluoroacetic acid and trifluoroacetic acid in methylene chloride yielded a mixture of esters IV and V²⁰ [Scheme-2].

According to the mechanism suggested in Scheme-1, two conclusions can be derived.

- (i) Substituents which enhance the electron density of the double bond increase the rate of reaction.
- (ii) Peracids in which oxygen atom in O-H linkage becomes more positive due to electron withdrawing effect of R are more reactive, thus trifluoroperacetic acid is more reactive than peracetic acid.

2] Epoxidation of olefins via halohydrin formation

Olefins when treated with N-bromosuccinimide or N-bromoacetamide in aqueous solutions yield halohydrins which after further reaction with alkali yield epoxides [Scheme-3].

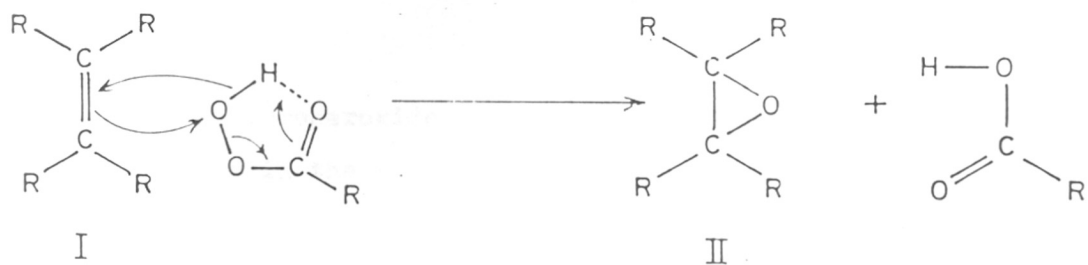
The reaction is supposed to proceed by an electrophilic attack on olefin (VI) by protonated bromoamide (VII) and finally resulting on the trans addition of bromide and hydroxyl groups yielding the halohydrin (VIII). The bromide gets attached from the less hindered side, in the initial step. The bromohydrin (VIII) when treated with strong base loses proton from the hydroxyl group and attacks the carbon atom bearing the bromine to yield epoxide (IX). This method enables to obtain more hindered epoxide in contrast to the epoxide obtained using peracids. Car-3-ene (X) when treated with peracid yields 3 α , 4 α epoxide²¹ (XI). Alternately treatment with NBS followed by a base yields 3 β , 4 β epoxide (XII)²² [Scheme-4].

Autoxidation as epoxidation method

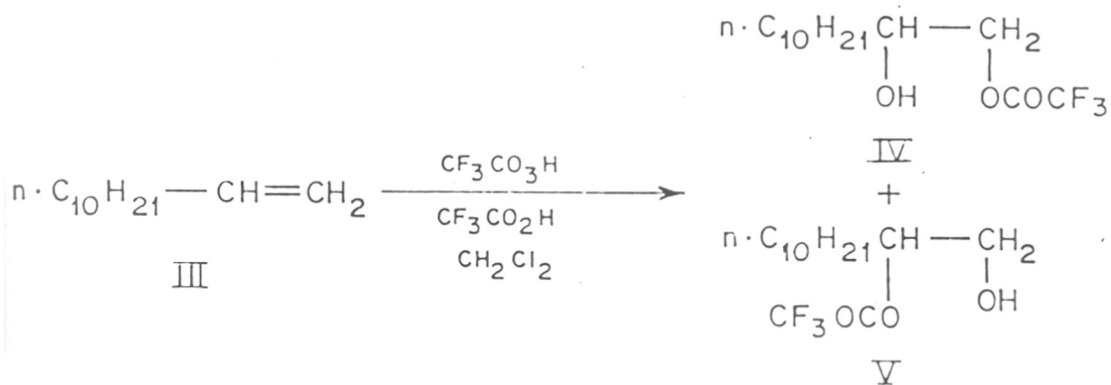
Autoxidation of alkenes is one of the most common reaction which proceeds continuously even at room temperature. Autoxidation usually yields a complex mixture of products along with considerable amount of polymerized product.

SCHEME - 1.

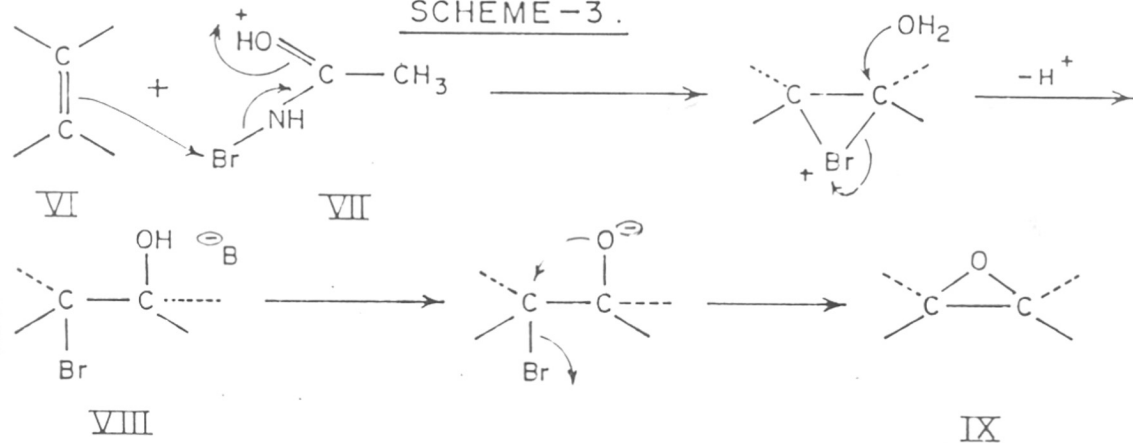
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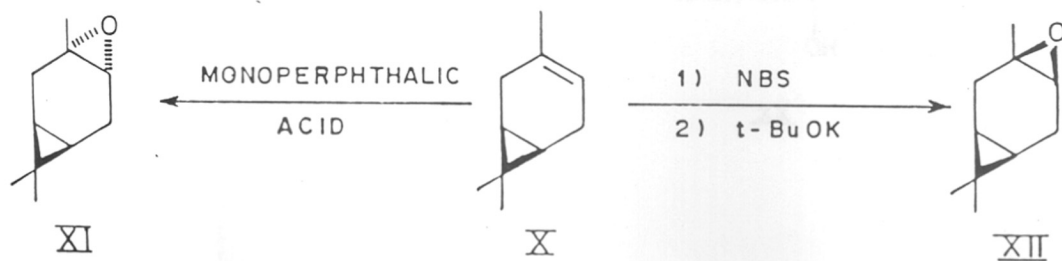
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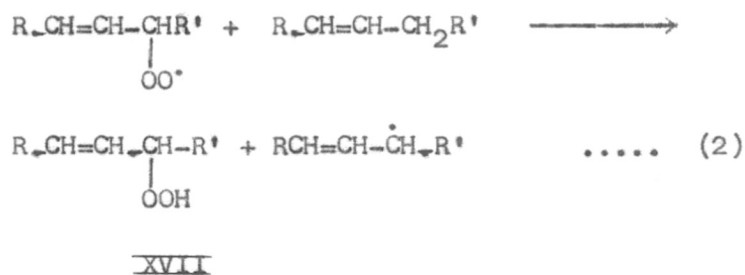
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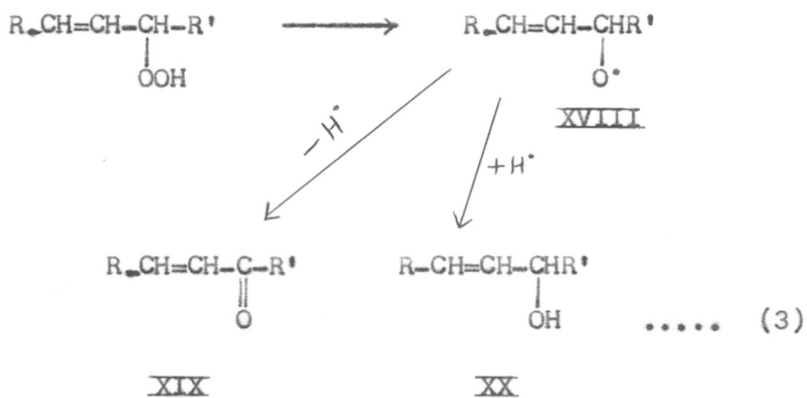
SCHEME - 4.



Usually hydroperoxides are the predominant products as suggested in the following equations.



Allylic alcohols and ketones are also formed.



- 1] Allylic hydrogen abstraction which leads to the formation of hydroperoxides, allylic alcohols and ketones.
- 2] Carbon-carbon double bond rupture which may lead either to epoxidation or polymerization [Eq.6].

The competition between abstraction and addition is greatly influenced by, (i) the accessibility of a coplanar geometry permitting allylic delocalization of the hydrocarbon radical formed by the hydrogen abstraction and (ii) the stability of the radical formed by the addition of oxygen to the double bond²⁶. Due to these two competitive reactions unconjugated olefins preferentially yield allylic hydrogen abstraction products as compared to epoxidation products.

Borate esters assisted epoxidation

There are only a few references on using boric acid or its esters to promote the formation of epoxides. Thus, Kamzolkin²⁷ et.al. initially reported that addition of boric acid increased the proportion of olefin α -oxides in the reaction product. Bashkirov²⁸ et.al. used monobutyl borate to improve the yields of epoxides in the air oxidation of olefins prepared by dehydration of C₁₄₋₁₈ alcohols. Kobayashi²⁹ reported about 73% selectivity in epoxide formation from 1,5,9-cyclododecatriene though in low conversions [about 16% only]. Dimitrov³⁰ et.al. reported that the addition of borate esters yielded increased

amount of epoxides in the liquid phase oxidation of unsaturated compounds and also reduced the polymerization of the starting olefin.

Very few references are available regarding oxidation of terpene olefins in the presence of borate esters. In a kinetic study on the oxidation of α -pinene and p-menth-3-ene in the presence of boron, Angelov³¹ et.al. reported the formation of alcohols and epoxides. However, there was no mention regarding the product composition or conversions of the starting olefins to other products. Sethi and others²⁶ reported epoxidation of arylcycloalkenes during the autoxidation of these olefins in the presence of cobalt-naphthenate. However, under these conditions car-3-ene yielded no epoxide and in case of α -pinene it was one of the minor products³².

Present work

The present study on the borate esters promoted epoxidation of a few easily available olefins was undertaken with the following objectives :

- 1] To study the reaction in details.
- 2] To develop suitable experimental conditions for best possible conversion of the olefins into their epoxides by this simple method.
- 3] To study the effects of steric hinderance on the product composition and

- 4] To apply the method for preparing epoxides from the constituents of Indian turpentine oil such as α -pinene car-3-ene, β -pinene and camphene [which is obtained by α -pinene isomerization]. These epoxides can be valuable intermediate compounds for the stereoselective synthesis of related alcohols etc.^{21,22}

As it was intended to develop a simple and convenient method for epoxidation of olefins it was decided to carry out the reactions at atmospheric pressure and without using any solvents.

The reactions were carried out using a modified special reactor originally designed by Vodnar³³ [Fig.1]. The reactor consists of a tank of suitable capacity with a sintered glass plate near its bottom. Towards the upper part of the tank is a spiral tube having a recirculatory tube fitted with a capillary tip at the lower end. A reflux condenser and a sampling device complete the assembly. The substrate is taken in the tank which is maintained at the desired temperature [by means of oil bath] and dry oxygen is passed in it through a sintered plate. The pressure of the incoming gas pushes the liquid from the tank into the spiral tube creating a gas liquid interface. The liquid reaching at the top of the spiral comes back to the tank by gravity through the central capillary. The reaction takes place at the liquid gas interface in the spiral tube. The large contact area provided in the spiral

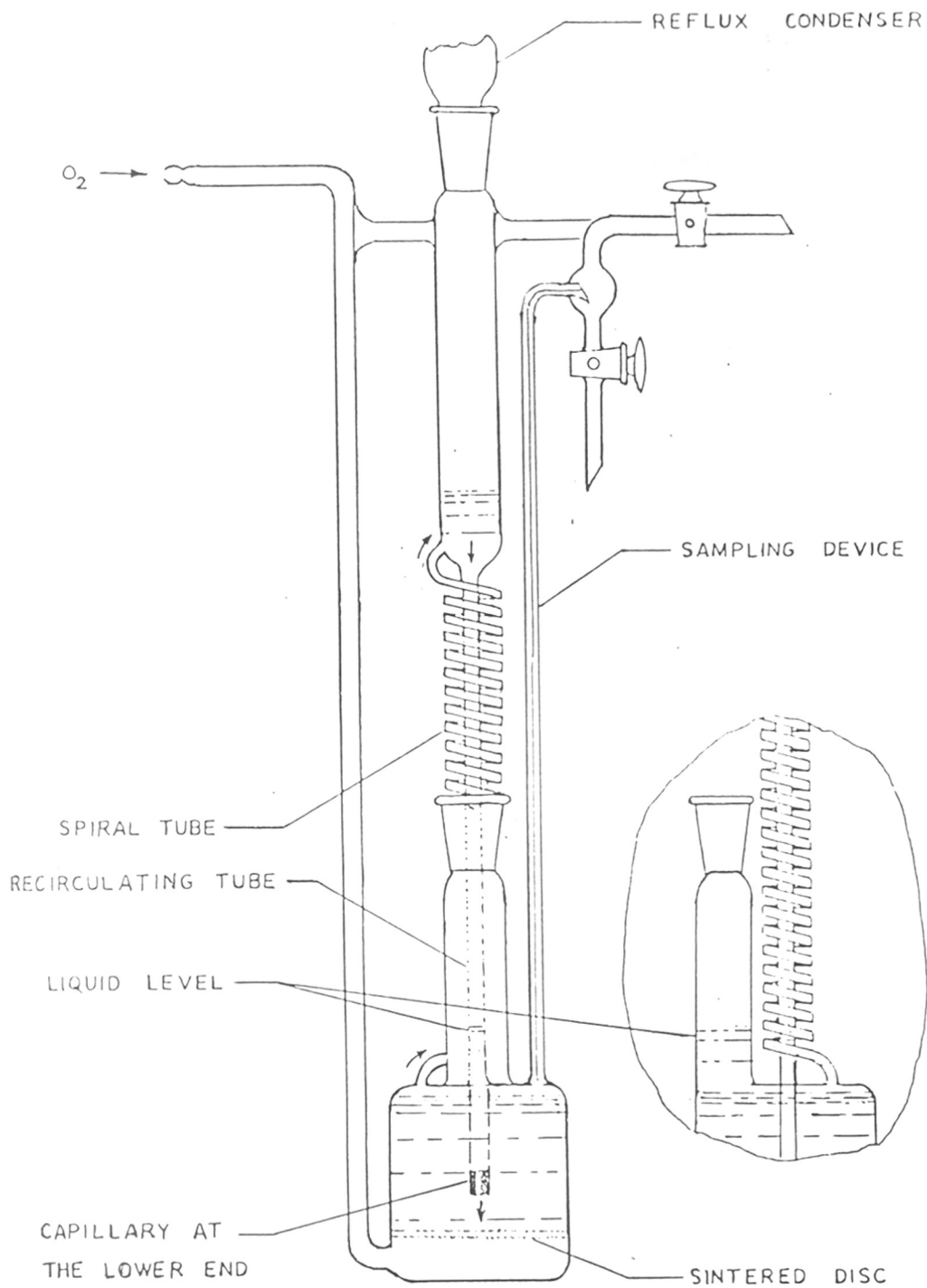


FIG. 1. REACTOR FOR EPOXIDATION

tube and continuous circulation of liquid greatly enhances the rate of the reaction.

As the nature of the double bond was expected to play a major role in deciding the final product composition, epoxidation of α -pinene and car-3-ene, which possess endocyclic trisubstituted double bonds are discussed together in the next chapter, along with cyclohexene, the simplest cyclic compound with endocyclic double bond, as a model compound. Two other terpene olefins viz. β -pinene and camphene containing exocyclic double bond are discussed separately in the subsequent chapter.

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CHAPTER-II
EPOXIDATION OF
CYCLOHEXENE, α -PINENE AND CAR-3-ENE

CHAPTER - 2

The results of the epoxidation reactions of cyclohexene (1), α -pinene (8) and car-3-ene (18) are incorporated in this chapter.

All these olefins have a common feature i.e. endocyclic double bond in a six carbon ring. However, there is a differing degree of steric hinderance for the approach of the reagents to the double bond and other reactive sites such as allylic position. It was expected that this difference will have a dominant role in deciding the course of the reaction and the product composition.

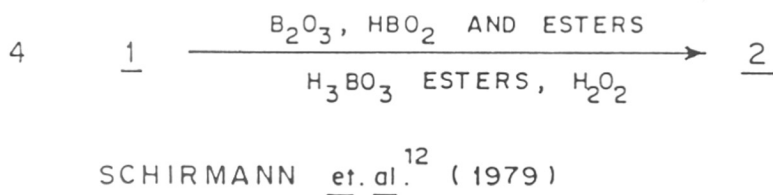
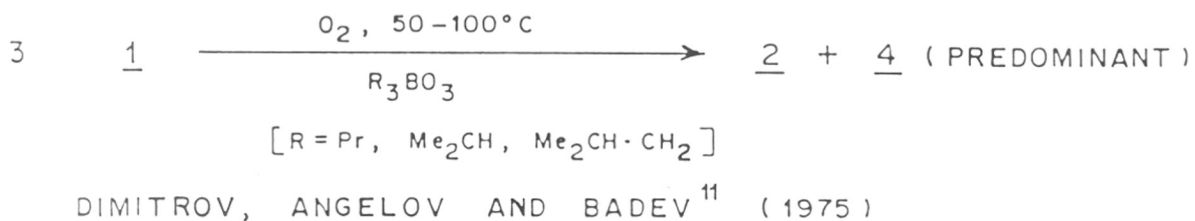
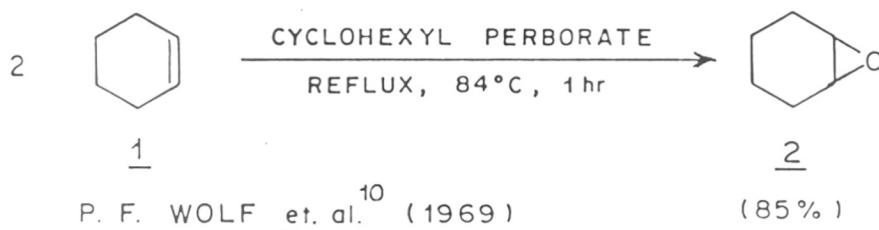
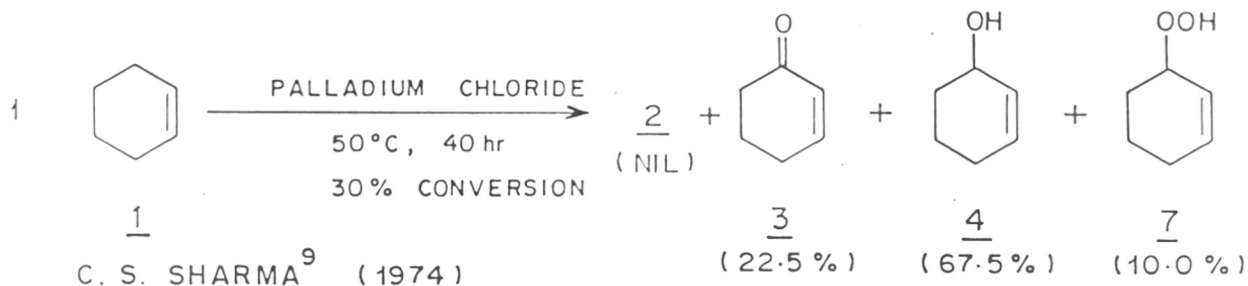
Section A

Epoxidation of cyclohexene (1)

Earlier work [Chart 2.1]

Apart from two standard methods of epoxidation using 1) per acids, and 2) hydrobromination followed by treatment with base, several workers have reported¹⁻⁴ formation of cyclohexene epoxide during their investigation of the kinetics and mechanism of the oxidation of cyclohexene. A number of catalysts have been employed for the oxidation of cyclohexene to get desired products. Conversion of cyclohexene to 2-cyclohexen-1-ol and 2-cyclohexen-1-one via the intermediate 2-cyclohexen-1-yl-hydroperoxide has been effected

EARLIER WORK ON EPOXIDATION OF CYCLOHEXENE



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with molecular oxygen using Iron phthalocyanine⁵, Manganese dioxide⁶, Platinum and Rhodium salts⁷ and Cobalt stearate⁸, though in poor yields. Formation of a number of undesired products have also been reported, which makes the separation of the desired compounds difficult.

In earlier work reported from this laboratory, Sharma⁹ et.al. obtained cyclohexenol and cyclohexenone as two major products using palladium chloride as catalyst. Wolf¹⁰ et.al. reported formation of epoxycyclohexane in 85% yield using cyclohexyl perborate. There are two other reports on the epoxidation of cyclohexene using boron^{11,12} compounds, but details regarding product composition and conversions were lacking. By using tertiary butyl hydroperoxide in the presence of various Molybdenum complexes Yamazaki et.al.¹³ obtained epoxy cyclohexane in 50-80% selectivity. Camps¹⁴ et.al. have obtained epoxy cyclohexane in above 95% selectivity by using mixture of m-chloroperbenzoic acid and potassium fluoride. These results along with few other¹⁵⁻¹⁶ catalytic epoxidations of cyclohexene are summarized in chart 2.1. From the above results, it is clear that epoxide was obtained in good yields only when peracids or esters were used as catalysts.

Present work

For initial work on the epoxidation of olefins using borate esters and molecular oxygen, cyclohexene was chosen,

as a model compound as it happens to be a simplest six carbon cyclic olefin with endocyclic double bond.

The increasing formation of epoxides along with other products with rise in temperature in the case of cyclohexene provided useful clues for the epoxidation of α -pinene and car-3-ene at various temperatures. The effect of change in the concentration and type of borate esters were studied in details in the case of α -pinene and car-3-ene.

Results

A] Epoxidation of cyclohexene [Fig.2.1, Table 2.1]

Cyclohexene (1) was placed in the Vodnar reactor [Fig.1, Chapter-1] along with isopropyl borate and dry oxygen gas was bubbled through the reaction mixture at desired temperature maintained by heating the reactor in an oil bath. The reaction was monitored by GLC by withdrawing aliquots after fixed time intervals. The reaction product after usual work up displayed GLC analysis as shown in Fig.2.1. The total reaction product displayed four peaks. After careful fractional distillation component I was obtained in pure form.

Component I [R.T. 1.17] : This was found to be unreacted cyclohexene from it's boiling point and spectral data. The other components were isolated by column chromatography using neutral alumina¹⁷.

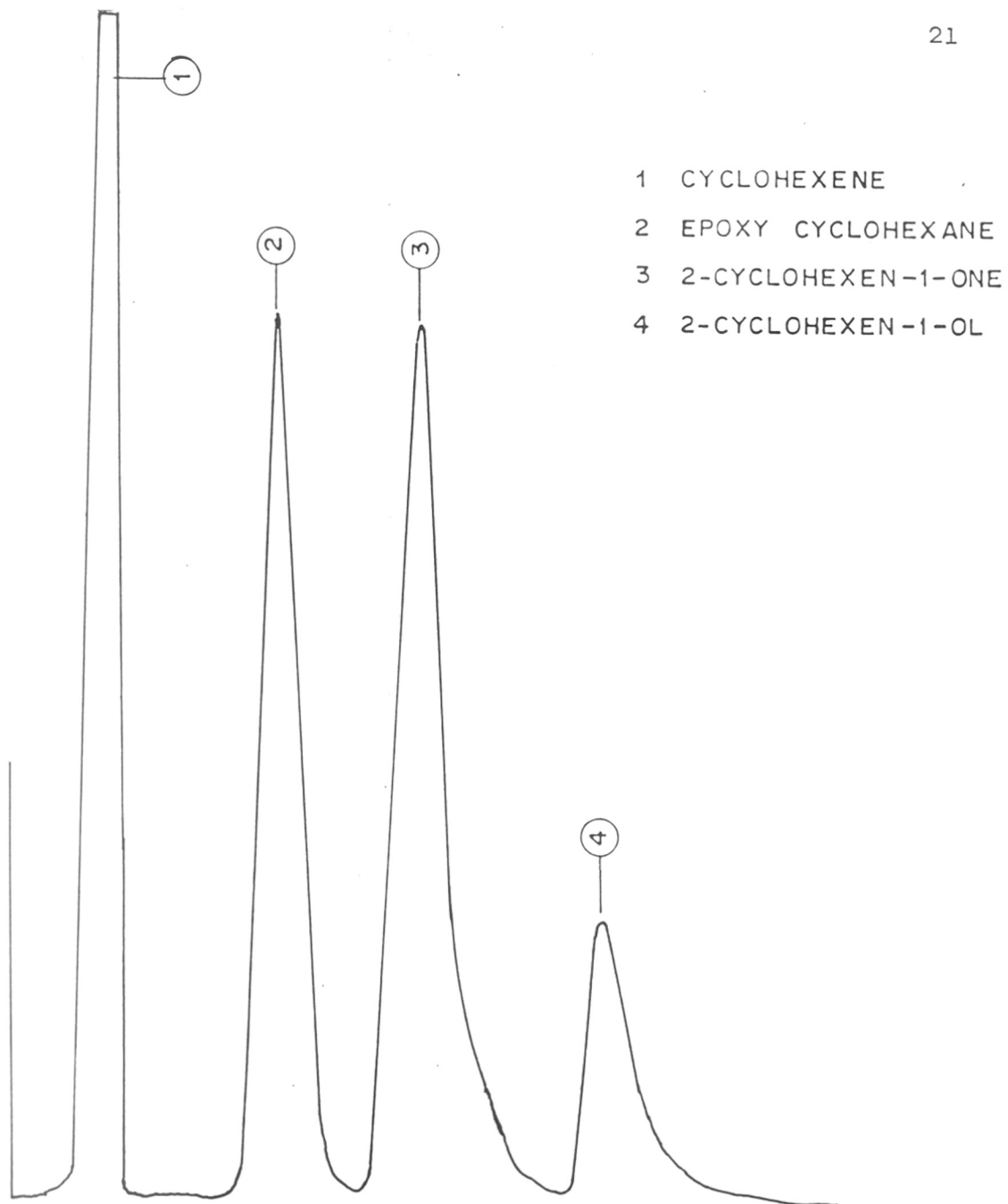


FIG. 2-1. : GLC OF REACTION MIXTURE FROM
CYCLOHEXENE EPOXIDATION



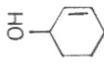
Component II [R.T. 2.92] : The IR spectrum of the compound displayed characteristic epoxide absorption signals at 1260, 900 and 840 cm^{-1} . A two proton multiplet at 2.93 δ for oxirane protons in PMR spectrum and m/e signal at 98 in mass spectrum, in addition to ^{above} was good enough to identify it as epoxy cyclohexane (2). This was confirmed by comparing it's spectral data with authentic sample prepared by known method¹⁸ and mixed GLC.

Component III [R.T. 3.54] : The pure compound isolated from column was distilled [bp. 167-68 $^{\circ}$ C]. It's IR spectrum showed a strong absorption at 1690 cm^{-1} characteristic of ketone function in conjugation with double bond. This was confirmed by a multiplet at 7.0 δ and a broad signal at 5.8 δ for one proton each in PMR spectrum. The GC mass analysis displayed m/e signal at 96. This data indicated that the compound under investigation was cyclohexenone (3). This was confirmed by comparing the data with those reported for cyclohexenone.

Component IV [R.T. 4.30] : The reaction mixture obtained from the reaction carried out at 50 $^{\circ}$ C, showed very poor conversion of cyclohexene (\sim 5.6%), however it was a mixture of only two components apart from cyclohexene [distilled out fractionally]. The first one was already isolated and characterized as epoxycyclohexane (2). The other component was isolated in pure form, after careful

TABLE 2.1

Cyclohexene Epoxidation^a

Expt. No.	Temp. °C	Time in hrs	Conversion %	Reaction products ^b (%)			Unidenti- fied products (%)
				 Epoxy Cyclohexane	 Cyclohexenone	 Cyclohexenol	
1	50 ± 2	54.5	5.6	42.30	-	57.47	-
2	70 ± 2	24	55.3	34.0	45.6	15.3	5.6

a - Neat, Catalyst - Isopropyl borate 10%

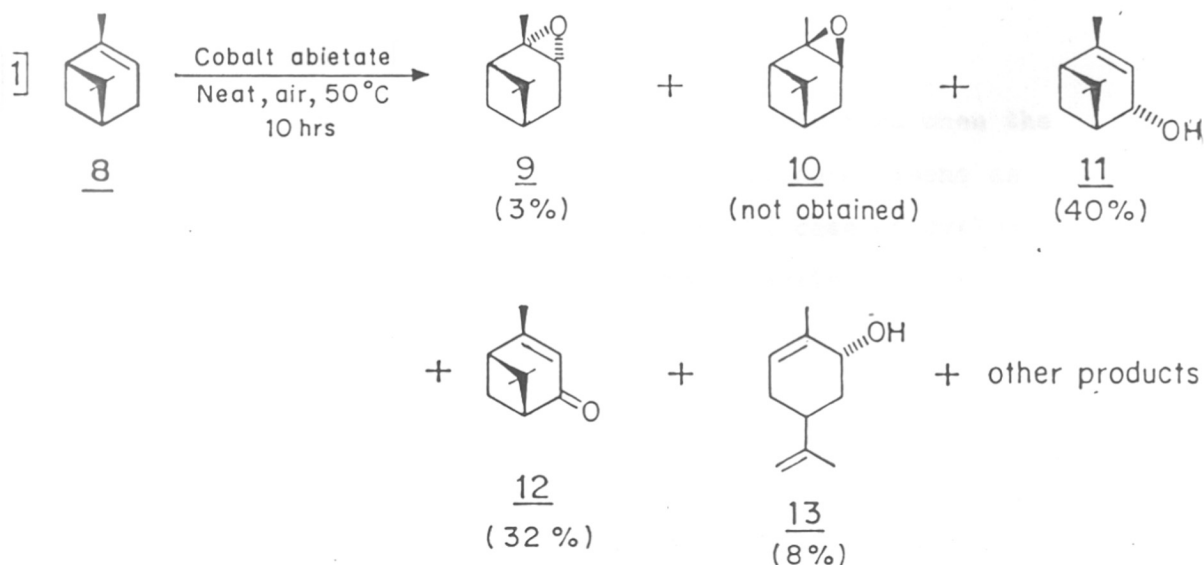
b - based on GLC, excluding starting olefin.

fractional distillation, by removing cyclohexene and epoxy-cyclohexane as low boiling components. The IR spectrum of the higher boiling fraction (corresponding to component IV) displayed strong signal at 3350 cm^{-1} indicative of hydroxyl function. The PMR spectrum had a one proton singlet at $3.75\ \delta$ which disappeared after exchanging with D_2O , confirming -OH function. The signals at $4.1\ \delta$ and $5.7\ \delta$ for one and two protons respectively were indicative of carbinol proton and olefinic protons. The m/e signal at 98 and (m-18) signal at m/e 80 in the mass spectrum indicated that the compound could be cyclohexenol (4). The oxidation of this compound to cyclohexenone (3) using Jones reagent confirmed the structural assignment.

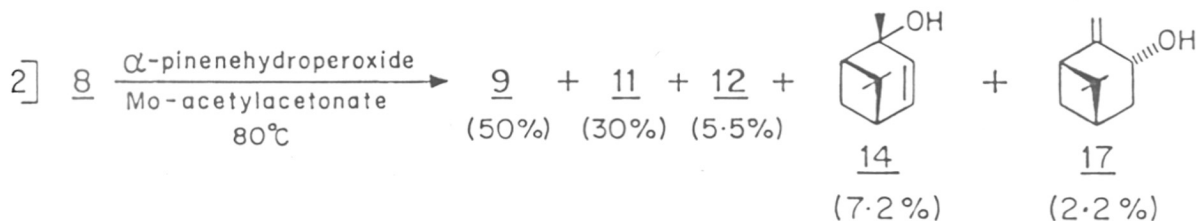
B] Epoxidation of α -pinene : Previous work [Chart 2.2]

The earlier work carried out by various workers using different catalysts to epoxidise α -pinene (8) is summarised¹⁹⁻²¹ in chart 2.2. The yields varied from as low as 3% reported by Tsankova¹⁹ using cobalt abietate to about 50% obtained by Romanikhin²⁰ using α -pinenehydroperoxide and molybdenum acetylacetonate. It may be noted that the hydroperoxide catalyst react almost in similar fashion as peracids. Angelov²¹ et.al. have reported formation of α -pinene epoxide along with other products such as trans-verbenol and verbenone, however neither the actual composition of the reaction product nor the conversion has been mentioned.

EARLIER WORK ON EPOXIDATION OF α -PINENE AND CAR-3-ENE



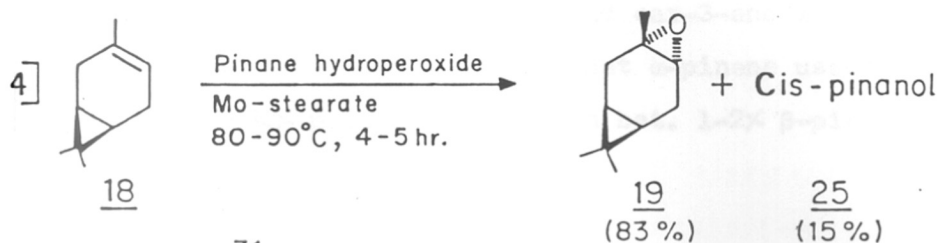
Tsankova et.al.¹⁹ (1972)



A.M. Romanikhin²⁰ (1977)



Angelov, Dimitrov et.al.²¹ (1975)



Sukh Dev.³¹ (1982)

Present work : [Fig. 2.2A, Table 2.2]

Practically no conversion was observed when the epoxidation reaction was carried out using α -pinene as substrate at 50° and 75°C unlike in the case of cyclohexene. Hence, the subsequent reactions were carried out at 100° and 140°C using isopropyl borate as catalyst. It was considered worthwhile to study the course of the reaction and product composition using a comparatively less bulky borate ester such as n-propyl borate. The results of these experiments are tabulated in table no.2.2. A representative GLC chart showing product composition is depicted in Fig.2.2A.

Component 1 [R.T. 1.75] : The reaction product was distilled fractionally, the first fraction was characterized as unreacted α -pinene corresponding to peak no.1 [R.T.1.75] from its spectral data and mixed GLC.

The second fraction consisted of mostly oxidation products along with trace amounts of α -pinene. Chromatographic separation over neutral alumina furnished component 8 [R.T.6.13] in pure form and component 7 [R.T. 4.60] about 85% pure. The component 4 corresponding to peak no.4 was not isolated in sufficiently pure form for characterization.

Component 2 and 3 [R.T. 2.13 and 2.53] : These were characterized as β -pinene and car-3-ene respectively from mixed GLC analysis and the fact that α -pinene used for the reaction was \sim 93% pure and contained bet. 1-2% β -pinene and 5-6% car-3-ene.

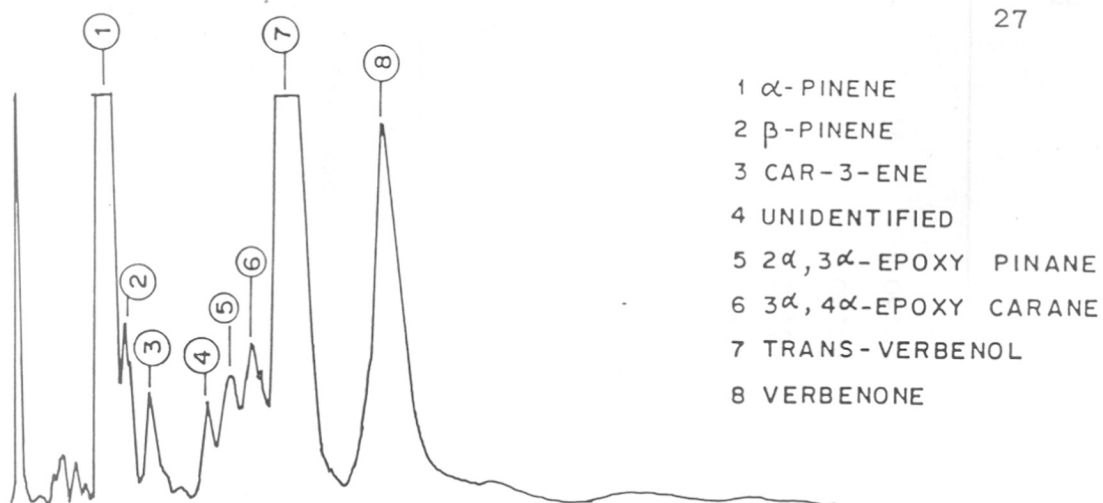


FIG. 2.2 A. GLC OF REACTION MIXTURE FROM
 EPOXIDATION OF α -PINENE

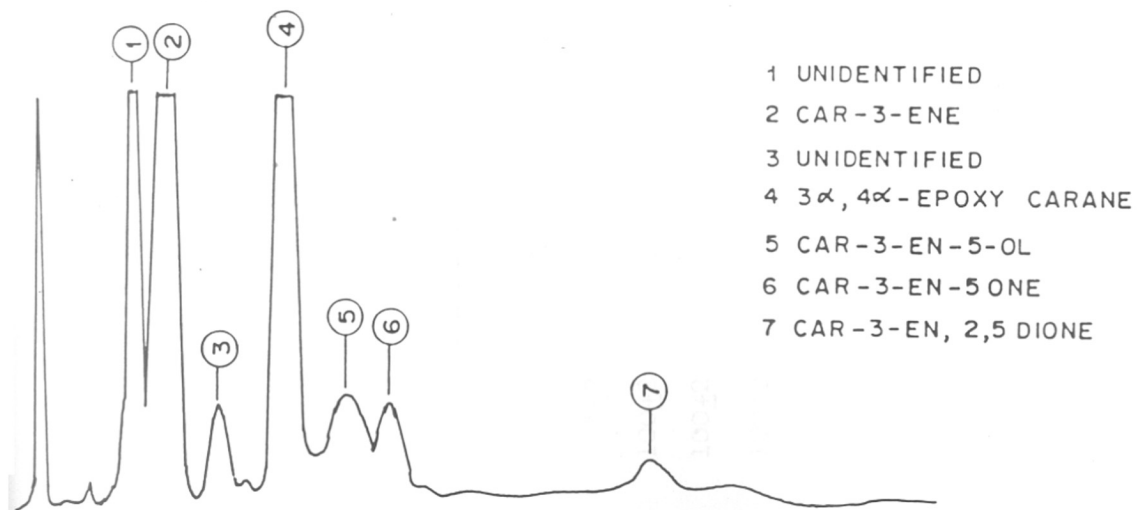

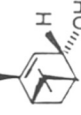



FIG. 2.2 B. GLC OF REACTION MIXTURE FROM
 EPOXIDATION OF CAR-3-ENE.

TABLE 2.2

 α -Pinene Epoxidation^a

Expt. No.	Temp. °C	Catalyst ^b and its concn.	% Conversion	Reaction products ^c (%)			Unidentified products (%) and number of components (in bracket)
				 2 α , 3 α -Epoxy pinane	 Trans-Verbenol	 Verbenone	
1	50±2	A, 30%	Nil	-	-	-	-
2	75±2	A, 30%	Nil	-	-	-	-
3	100±2	A, 30%	48.6	1.78	57.60	30.5	10.1 [5]
4	100±2	A, 10%	40	4.8	54.90	31.7	8.5 [5]
5	100±2	B, 30%	45.4	6.4	32.85	55.70	5.0 [3]
6	140±2	B, 30%	45.15	4.6	25.8	55.30	14.3 [9]
7	140±2	B, 10%	55.9	8.2	28.30	48.50	15.0 [4]
8	140±2	A, 10%	53.5	7.6	33.0	49.50	9.9 [4]

a - Neat, 44 hrs.

b - Catalyst A - Isopropyl borate

B - n-propyl borate

c - based on GLC, excluding starting olefin.

Component 5 [R.T. 3.74] : This compound was obtained in pet. ether fraction of chromatography in about 72% purity along with some α -pinene. The IR spectrum of this compound displayed absorptions at 1200, 1060, 940 and 830 cm^{-1} . There was no absorption in the C=O region or corresponding to free OH, indicating presence of epoxide ring system. This was confirmed by a broad signal at $3.0\ \delta$ for one proton in the PMR spectrum which also displayed two singlets at 0.9δ and $1.2\ \delta$ for 3 and 6 protons respectively and mass spectrum of this compound showed m/e signal at 152 for M^+ ion. This data indicated that the compound under consideration could be 2α , 3α -epoxypinane (9). The stereochemistry of the epoxide ring was assigned on the basis of the position of oxirane proton which appears at $2.8\ \delta$ and methyls at 0.74δ , 1.13δ and $1.2\ \delta$ in the case of β -epoxide (10) reported by Arbuzov²² et.al. The structure assignment was confirmed by preparing an authentic sample of 2α , 3α -epoxypinane using peracid method.

Component 6 [R.T. 4.08] : This was characterized as 3α , 4α -epoxycarane by mixed GLC with the authentic sample prepared and considering the results obtained in car-3-ene epoxidation experiments discussed later.

Component 7 [R.T. 4.60] : The IR spectrum of this compound displayed a strong absorption at 3350 cm^{-1} indicating hydroxyl group. Its PMR spectrum showed one proton multiplet at $5.17\ \delta$ characteristic of olefinic proton, another multiplet

at 4.03 δ for one proton indicating presence of $\text{CH}_2\text{-OH}$ grouping. There were signals at 0.85 δ and 1.3 δ as singlets integrating three protons each and another multiplet at 1.7 δ for three protons indicating vinyl methyl group. Its mass spectra indicated M^+ signal at m/e 152. All this data and comparison with authentic sample conclusively established this compound to be trans-verbenol (11).

Component 8 [R.T. 6.13] : The material corresponding to this component was isolated from column chromatography and was purified by distillation [bp. 101-103 $^\circ\text{C}/5$ mm]. Its IR spectrum indicated absence of hydroxyl group and strong absorptions at 1700 and 1680 cm^{-1} characteristic of ketone function in conjugation with double bond. This was confirmed by downward shift of vinylic methyl group and vinyl proton in the PMR spectrum which appeared at 1.93 δ and 5.59 δ respectively. [In the case of trans-verbenol these appear at 1.7 δ and 5.17 δ respectively]. The PMR spectrum also displayed two methyl singlets at 0.93 δ and 1.43 δ . The mass spectrum of this compound had M^+ ion at m/e 150. Based on this spectral data the compound was assigned the structure (12) representing verbenone. This was further confirmed by comparing the data with that of the authentic sample prepared.

C] Epoxidation of car-3-ene (18)

Previous work [Chart 2.2]

Sukh Dev²³ et.al. reported formation of epoxy carane

in very good yields but again using pinanehydroperoxide as catalyst. Many other workers²⁴⁻²⁷ have carried out carene autoxidation using various catalysts and obtained various products in different conversions, but none of them obtained epoxide.

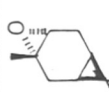
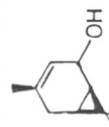
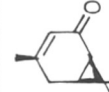
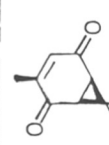
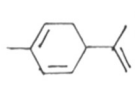
Present work [Fig.2.2B, Table 2.3]

Car-3-ene (18) (neat) was placed in the glass reactor [described earlier] along with borate ester. Epoxidation was carried out at 100°C, with constant oxygen flow of 2-3 lt/hr. The reaction was monitored by GLC by withdrawing aliquots after fixed time interval. The reaction product after workup displayed GLC analysis as shown in Fig.2.2B. The total reaction product displayed seven peaks. After careful fractional distillation lower boilings [bp.60-70°C/30-35 mm] were collected together as first fraction. Second fraction [bp. 50-80°C/1.5 mm] contained mostly oxygenated products, whose components were isolated by column chromatography using neutral alumina.

The lower boiling fraction contained component 1 [R.T. 2.02] and component 2 [R.T. 2.47] with traces of component 3 [R.T. 3.37]. The various attempts to separate these two components by either distillation or column chromatography were unsuccessful. The elemental analysis of this mixture showed that it was a hydrocarbon mixture

TABLE 2.3

Car-3-ene Epoxidation^a

Expt. No.	Time in hrs.	Catalyst ^b and its conc. ⁿ	Con- version %	Reaction products ^c (%)				Unidentified product (%)	
				 3α,4α-Epoxy Carane	 Car-3-en-5-ol	 Car-3-en-5-one	 Car-3-en-2,5-dione		 (probable)
1	24	A, 30%	51.2	52.43	9.9	5.86	4.7	17.95	9.1
2 ^d	45	A, 10%	60	51.16	6.12	9.40	3.8	18.64	10.8
3	24	B, 30%	60	44.61	10.68	12.80	2.0	16.11	13.8

a - Neat, temp. 100±2°C, 8 g. scale

b - Catalyst A - Isopropyl borate

B - n-propyl borate

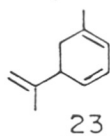
c - based on GLC, excluding starting olefin

d - 40 g scale reaction.

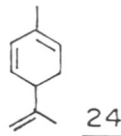
Note - Reaction at 140±2°C showed lot of polymerization.

[C = 89.4%, H = 10.6%]. The component 2 was characterized as unreacted car-3-ene using mixed GLC technique and the fact that GC-Mass analysis showed M^+ signal at m/e 136 and other major signals at m/e 93, 91, 79, 77, 41, 39 and 27 which were comparable with the reported mass spectral data²⁸ for car-3-ene.

Component 1 [R.T. 2.02] : The GC-Mass analysis indicated M^+ at m/e 134 and a major peak at m/e 91 which may be due to tropolium ion formation after loosing isopropylene fragment. The PMR spectrum of the mixture containing component 1 and 2 displayed a complex multiplet between 5.47-5.97 δ characteristic of protons in the conjugated olefinic system. When this mixture was loaded on neutral alumina column for separation, a new compound was formed whose PMR spectrum displayed again complex multiplet between 7-7.4 δ and a singlet at 2.31 δ , (these signals can be attributed to aromatic protons and aromatic methyl group), apart from original signals due to olefinic protons of conjugated system, with reduced integration. These facts indicated that the original compound might have aromatized on the column. A similar observation was reported by Lipnicka²⁹ et.al. All these observations indicated that the compound under consideration could be



or



However, as this compound was not isolated in pure form, this structure could not be conclusively established.

Component 2 [R.T. 2.47] : This was characterized as unreacted car-3-ene as mentioned earlier.

Component 3 [R.T. 3.37] : As this component was formed in minor amounts and could not be separated in sufficiently pure form its structure assignment was not possible.

Component 4 [R.T. 4.34] : The pure compound isolated from column was distilled [bp. 92-93°C at 23 mm]. IR spectrum of the compound displayed characteristic epoxide bands at 1200, 840 and 790 cm^{-1} . A one proton broad signal at 2.6 δ appeared for oxirane proton in PMR spectrum. The three methyls signals were at 0.7 δ , 1.0 δ and 1.16 δ as three sharp singlets. In the Mass spectrum of this compound M^+ was seen at m/e 152 and ($m-15$) signal at m/e 137. All the above spectral data was good enough to indicate that the compound under investigation was 3 α , 4 α -epoxy carane (19). This was confirmed by comparing its spectral data with authentic sample prepared by peracid method.

Compound 5 [R.T. 5.35] : By using flash chromatography, the compound obtained with R.T. 5.35 was found to be \sim 91% pure by GLC. The IR spectrum of this compound showed a broad signal at 3420 characteristic of -OH group and a olefinic absorption at 1670 cm^{-1} . In the PMR spectrum of the compound three methyls appeared at 1.2 δ , 1.28 δ and 1.7 δ as singlet, singlet and multiplet respectively, the carbinol proton was present at 3.46 δ as doublet and olefinic proton appeared as multiplet, at 5.66 δ . The Mass

spectrum of this compound showed M^+ at m/e 152. From this spectral data the compound was identified as car-3-en-5ol (20). Jones oxidation of this compound afforded a ketone, which was characterized as car-3-en-5one. This confirmed that the compound isolated must be car-3-en-5ol.

Component 6 [R.T. 6.01] : This component was obtained in pure form by flash chromatography using neutral alumina. The IR spectrum of the compound showed characteristic α,β unsaturated ketone at 1670 cm^{-1} . The PMR spectrum showed that the three methyl were appeared at $1.12\ \delta$, $1.31\ \delta$ and $1.95\ \delta$ as three singlets. The olefinic protons appeared at $5.8\ \delta$ as multiplet, the methylene protons at $2.42\ \delta$ as multiplet and cyclopropyl protons were at $1.5\ \delta$ as multiplet. GC-Mass of this compound showed M^+ peak at m/e 150. With this spectral data, the compound was identified as car-3-en-5one (21). This was confirmed by comparing the data with the reported one for car-3-en-5one.

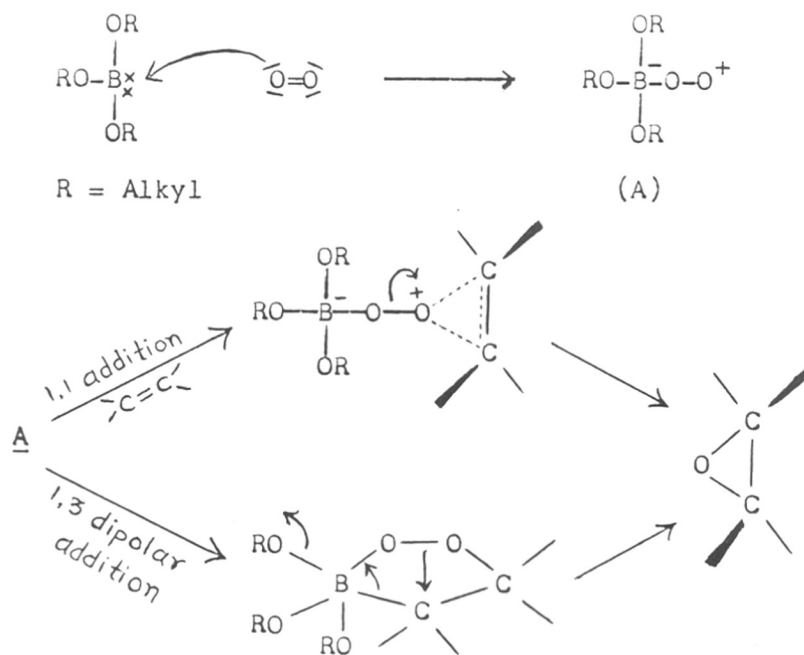
Component 7 [R.T. 10.3] : This component was obtained in solid form by chromatography. The GLC of this compound was $\sim 85\%$ pure along with $\sim 15\%$ impurity as component 6. The IR spectrum of this component showed characteristic α,β unsaturated ketone frequency at 1645 cm^{-1} and its PMR showed singlet at $1.25\ \delta$ for corresponding to six protons of gem-dimethyls. The methyl on the double bond was seen at $1.9\ \delta$. The olefinic proton appeared as singlet at $6.45\ \delta$. GC-Mass of this compound showed M^+ peak at m/e 164. This data indicated that the compound obtained was car-3-en-2,5-dione (22). This was confirmed by comparing this data with the reported sample of car-3-en-2,5-dione.

Discussion

The results presented earlier clearly indicate that there are two competitive reaction pathways which yield different products. The first one is more common and usual path of allylic oxidation, discussed in the first chapter. The second one is the epoxide formation, facilitated by borate esters. Scheme-1 illustrates the formation of epoxide as proposed by Kobayashi³⁰.

He proposed that electron attraction by boron might arise by overlap of the occupied 2p-orbitals of oxygen atom with the vacant 2p-orbitals of boron atom. The resultant boron peroxide (A) epoxidizes the carbon carbon double bond via the electrophilic 1,1 addition as suggested by Bartlett³¹ or 1,3 dipolar addition as suggested by Kwart³² et.al.

Scheme-1



The product composition obtained in the case of each substrate depends on which of these pathways is the favoured one. As can be seen this preference depends on various parameters such as, i) the reactivity of olefin, ii) temperature of the reaction, iii) steric hinderance to the approaching reagents and iv) the bulk of approaching reagent. The factors i) and ii) are interrelated in a way that the reaction proceeds at lower temperatures in the case of more reactive olefins.

[1] Reactivity of the olefins : From the results obtained it is very clear that the reactivity order of the three olefins is as follows :



The following observations support the above mentioned order.

[a] Optimum reaction temperature : In the case of cyclohexene even at 70°C, there was about 55% conversion, while there was practically no reaction in the case of α -pinene. In the case of car-3-ene and α -pinene the optimum reaction temperatures were 100°C and 140°C respectively.

[b] Duration of the reaction : In the case of cyclohexene during 24 hrs there was 55.3% conversion [at 70°C] in the case of car-3-ene 51.2% [but at 100°C] and in the case of α -pinene only 40.0% [at 100°C]. These reactions

were compared from table no.2.1, 2.2 and 2.3. It may be pointed out that in the case of α -pinene the reaction was continued for 44 hrs, when the sample after 24 hrs of the reaction was analysed by GLC, the conversion was still lower i.e. 27.5%.

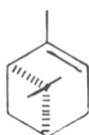
[2] Effect of temperature : As it was decided to carry out the reactions without using any pressure, there was obvious limitation regarding the maximum temperature that could be employed that is the boiling temperature of the particular olefin. Again it was observed that when refluxing temperature conditions were employed, there was considerable loss of starting olefin by way of evaporation due to constant stream of oxygen bubbled through the reaction mixture. Therefore the maximum temperature employed was about 10°C lower than the refluxing temperature. The results tabulated in all the three tables 2.1-2.3 conclusively indicate that there is considerable increase in the conversion of starting olefin with the rise in temperature. In the case of cyclohexene, particularly, there was almost tenfold increase in the conversion in about 55% less time. The other significant observation in the case of cyclohexene was that at lower temperature selectivity towards the epoxide formation was about 25% higher, even though the overall conversion was poor.

In the case of car-3-ene the optimum temperature seemed to be 100°C, as against 140°C in the case of α -pinene, when the reaction of car-3-ene was conducted at 140°C there was lot of polymerization and even the removal of reaction product from the reactor was very difficult. One interesting feature in the product formation can be mentioned, in the case of α -pinene at lower temperature the amount of allylic alcohol is more when isopropyl borate was used as catalyst, while at higher temperature the amount of corresponding ketone is more, this may be due to further oxidation of the alcohol at higher temperature.

[3] Steric hinderance to approaching reagent : Cyclohexene, car-3-ene and α -pinene all have one common structural feature, i.e. a cyclohexene ring system. However, in the case of cyclohexene endocyclic double bond is disubstituted and in other two cases it is trisubstituted with one methyl group attached to vinyl carbon atom. The other structural difference is the presence of additional cyclopropane ring in car-3-ene and a cyclobutane ring in α -pinene. Both α -pinene and car-3-ene exist in two isomeric forms each 8, 8a and 18, 18a respectively.



8

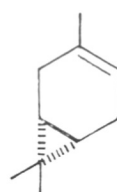
(+) α -Pinene

8a

(-) α -Pinene

18

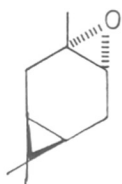
(+)-Car-3-ene



18a

(-)-Car-3-ene

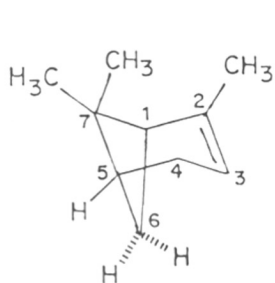
In this study the α -pinene and car-3-ene used belong to structure 8 and 18 respectively, as naturally occurring constituents of Indian turpentine oil. It is evident from these structures that in both these cases the double bond is flanked by the gemdimethyl group on the β -face, albeit to a different degree, and hence almost block the approach of the reagent towards the double bond from the β -face. This is the reason why only one epoxide was obtained in both the cases. The epoxides 19 and 9 could be obtained by the attack of the reagent on the double bond from α -face in both the cases. Other two isomers 26 and 10 were absent, which could have been obtained by the attack of the reagent on the double bond from hindered β -face. The same reasoning explains the formation of only one isomer of allylic alcohol formed during the reaction.

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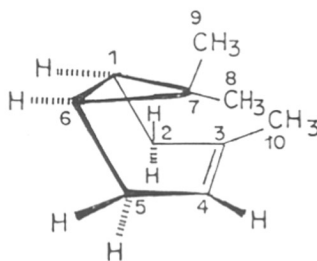
Another aspect of epoxide formation is that in the transition state the methyl group and the hydrogen atom on the double bond are pushed towards the β -face by the attacking

boron peroxide which comes from the α -face. α -Pinene with its comparatively crowded β -face offers more resistance to this process as compared to car-3-ene, thereby increasing the energy barrier as compared to car-3-ene where the β -face is less crowded. This may be the reason for the overall less reactivity of α -pinene as compared to car-3-ene, observed in this study.

[4] The bulk of approaching reagent : Although in the case of both α -pinene and car-3-ene β -face is blocked for the approach of the reagent, the α -face is also not totally open for the approach of the reagent in the case of α -pinene.



α -pinene



car-3-ene

From the above structures it is obvious that the hydrogen atom on C-6 carbon atom in α -pinene partly blocks the approach of the reagent from the α -face while in the case of car-3-ene there is no such hinderance. This structural

feature in the case of α -pinene implies that bulk of the attacking molecule might also hinder its approach towards the double bond. Thus a less bulky reagent could be expected to react faster. The comparison of the results of Experiment 1 and 3 in table 2.2 indicates that the rate of the formation of epoxide increases 4.5 times when isopropyl borate is replaced by n-propyl borate in the case of α -pinene, while the amount of epoxide formed in the case of car-3-ene remained more or less the same with these two reagents [Expt. 1 and 3 in table 2.3].

EXPERIMENTAL

1. General Remarks

All mps. and bps. are uncorrected.

IR : The Infrared spectra of solid samples were recorded in nujol and those of liquid samples as neat, employing PYE-UNICAM SP3 - 300 IR spectrophotometer. A few spectra were recorded in carbon tetrachloride solution.

PMR : The proton magnetic resonance spectra were recorded on a Varian T-60 and Jeol 60 spectrometer, using carbon tetrachloride as solvent. 80 MHz spectra were recorded on Varian FT-80A model using deuterated chloroform as solvent. Tetramethylsilane was used as an internal standard in all cases. All the chemical shifts are expressed in parts per million (δ), relative to TMS as zero. The following abbreviations have been used while presenting the data, s = singlet, d = doublet, t = triplet, m = multiplet and br = broad.

MS : Mass spectra were recorded on a Finnigan-Mat-1020B spectrometer model using an ionisation potential of 70 eV and a direct inlet system.

GC-MS : GC-MS was recorded on the same Finnigan-Mat 1020B spectrometer model using following column.

SE-54, 3% Loading, capillary column 15 M x 0.285 mm.

Helium gas was used as carrier at a rate of three ml. per minute.

Optical rotations $[\alpha]_D$: These were measured on JASCO DIP-181 Polarimeter model using sodium lamp. $[\lambda_{\max}$ 589 nm] as the source at 25°C employing methyl alcohol as solvent in a 5 cm. cell. Optical rotation measurements have been restricted to compounds of very high purity.

Flash Chromatography : Flash chromatography was carried out on EYELA Flash. chromatography model using Alumina Gr.II (TLC grade)¹⁷ and silica gel flash chromatographic grade.

GLC : Analytical gas liquid chromatography of the reaction products were carried out on a Hewlet-Packard model 5790A, using following column -

Column : OV-101 Steel column

6 ft long and 1/8 inch diameter.

5% wt. loading of liquid methyl silicon-phase.

Integrator used 3390A model of Hewlet-Packard. Nitrogen gas was used as a carrier gas normally at a rate 40 ml per minute and flame ionisation detector (FID) was used. The percentage composition of the reaction products have been obtained on the basis of GLC peak areas.

Silica gel and Aluminium oxide basic or neutral used for column chromatography were graded according to Brockman's scale¹⁷.

The solvents such as diethyl ether (henceforth termed as ether), pet. ether (60-80°C range unless otherwise stated),

benzene, ethyl acetate, methanol, etc. were purified by standard procedures³³ before using either in column chromatography or in the reactions. The solvent extracts either in the isolation of products or in the preparation of authentic samples, were dried over anhydrous sodium sulphate.

2. Starting Materials

All the five olefins used in the present study α -pinene, cyclohexene, car-3-ene, β -pinene and camphene were available in our laboratory. The olefins employed were freshly distilled over sodium before use. They displayed 95% + purity by GLC and satisfactory spectral data except camphene which contained about 12% tricyclene (GLC).

Catalyst preparation : Both the catalysts, i.e. Iso-propyl and n-propyl borate were synthesized by known method of preparation of borate esters³⁴.

Procedure : In a 1 lt. 3 necked RB flask placed in heating mantle and equipped with a thermowell, dropping funnel, 30 cms column filled with glass beads and connected to Dean and Stark apparatus with 40 cms long reflux condenser, was placed 62 g (1 M) of boric acid, 270 g (4.5 M) Isopropyl or n-propyl alcohol, 340 g (4.35 M) benzene and a few chips of porous plate. The reaction mixture was refluxed. Water-benzene azeotropic mixture was collected and allowed to separate in

two layers in the Dean and Stark apparatus and the top benzene layer was recycled, till the desired amount of water was collected from the reaction. When all the boric acid got dissolved, the reaction mixture was refluxed further for one hour to ensure complete esterification. [Time required for complete esterification for isopropyl and n-propyl alcohol were 12 and 4 hrs respectively]. Excess alcohol and solvent benzene were removed by distillation to afford almost quantitative yields of borate esters. Crude esters were distilled to obtain pure borate esters. Their spectral data compared favourably with the data reported³⁵.

In the further discussions isopropyl borate will be referred as catalyst A and n-propyl borate as catalyst B.

3. General procedure of epoxidation

The olefin and a catalyst were taken in a specially prepared Vodnar reactor³⁶ [Fig.1, Chapter 1] which was kept in an electrically heated oil bath. Reflux condenser was attached to it and the condenser outlet was connected to a trap immersed in ice-bath. Dry oxygen gas [after passing through concentrated sulphuric acid and potassium hydroxide pellets traps.] was bubbled through the liquid. Gas flow was measured by means of a specially prepared and calibrated flow meter. Initially, gas flow was 1 litre per hour, after two hrs it was increased to 2-3 litres per hour. Reaction was monitored by TLC and GLC and was terminated after desired time.

General workup procedure

The reaction products or the aliquots taken out after definite time interval were first tested for the presence of peroxides using potassium iodide and acetic acid method. The test showed the presence of peroxides everytime. The sample was refluxed for two hrs with 10% sodium bicarbonate solution to destroy peroxides and extracted with ether thoroughly; the absence of peroxides was confirmed in the combined organic phase which was washed with distilled water. Dried over anhydrous sodium sulphate and the solvent was stripped off to yield a crude reaction product.

Section A

[A] Epoxidation of cyclohexene (neat)

The alkene (1) [33 g, 0.402 M] and isopropyl borate [7.5 g, 0.04 M] were taken in a specially prepared reactor as described in the general epoxidation procedure. The epoxidation was carried out at $70^{\circ}\text{C} \pm 2^{\circ}$. Reaction was stopped after 24 hours. Aliquots were taken out after 8, 16 and 24 hours of reaction time. They all showed three peaks apart from a peak due to unreacted (1).

Reaction product [35 g] was worked up as mentioned earlier to get 30 g product. Unreacted olefin was distilled out [16.6 g] as first fraction on water bath. Then second

fraction was distilled out as oxidation products [8.5 g] on oil bath, leaving a residue (3.8 g), Loss = 1 g. Oxidation product displayed the following percentage composition on GLC [OV-101 at 80°C] Peak 1 [t_R - 2.92, 34%], Peak 2 [t_R - 3.54, 45.6%], Peak 3 [t_R - 4.3, 15.3%].

Some of this oxidation product [1.5 g] was used for separation by column chromatography over basic alumina gr.III¹⁷ (45 g).

CHROMATOGRAM - 1

Material loaded	... 1.5 g	Basic alumina - 45 g
Column length	... 60 cms	Column dia. - 1.5 cms

Fractions	Eluent	Quantity	Remarks (based on GLC)
1	pet.ether	1 x 80 ml	<u>pure 2.</u> (0.172 g)
2-8	pet.ether	7 x 50 ml	Mixture of 2,3
9-10	pet.ether:Benzene (9:1)	2 x 50 ml	Mixture of 2,3
11	(3:1)	1 x 50 ml	Mixture of 2,3
12	(1:1)	1 x 50 ml	Mixture of 2,3
13	(1:1)	1 x 50 ml	<u>Major 3</u> (87%) [0.15 g]
14	Benzene	1 x 100 ml	Mixture of 3,4
15	Methanol	1 x 200 ml	Mixture of 3,4

Fr.1 was identified as epoxy cyclohexane 2 from its spectral data and confirmed by direct comparison [GLC, IR, NMR] with an authentic sample. The relative retention time $t_R = 2.92$ of this compound showed it to be peak 1 from the total oxidation products.

Compound (2) : Epoxy cyclohexane [$C_6H_{10}O$]

bp. $129-30^\circ C$ [Lit.¹⁸ $131.5^\circ C$]

IR : Characteristic epoxide bands at 1260, 900 and 840 cm^{-1} .

PMR¹⁸ (CCl_4) : 1.33 [m, 4H]
 1.8 [m, 4H]
 2.93 [m, 2H] oxirane protons.

GC-Mass M^+ 98.

Fr.13 found to be 87% pure by GLC with $t_R = 3.54$. i.e. Peak 2 from total oxidation product. Its spectral data was quite comparable with 2-cyclohexen-1-one, reported in the Lit.³⁷

Compound (3) : 2-Cyclohexen-1 one [C_6H_8O].

bp. $167-68^\circ C$ [Lit.³⁷ $169-71^\circ C$]

IR³⁷ (neat) : 1690, 1475, 1460, 1390, 1255,
 1240, 1220, 1130, 1110 and 760 cm^{-1}

PMR [$CDCl_3$] : 0.9 - 2.3 [m, 6H] Methylene protons
 5.8 [b, 1H] $CO-CH=CH-$
 7.0 [m, 1H] $CO-CH=CH-CH_2$

GC-Mass³⁸ - M^+ at 96.

From another experiment of cyclohexene at lower temperature [50°C] and lower conversion [$\sim 5\%$], after usual workup and distillation of unreacted 1 and epoxide as first fraction, compound with $t_R = 4.3$ was obtained in pure form. This was identified as 2-cyclohexen-1-ol by comparison of its spectral data with reported values in the Lit.³⁹

Compound (4) : 2-Cyclohexen-1-ol [$\text{C}_6\text{H}_{10}\text{O}$]

bp. $62-4^{\circ}/12$ mm [Lit.⁹ $63-5/10$ mm]

IR³⁹ (neat) : 3350, 3080, 2985, 2900, 1460, 1450, 1400, 1340, 1170, 1140, 1080, 980, 940, 920, 820 and 730 cm^{-1} .

PMR [CDCl_3] : 1.5-2.1 [m, 6H] Methylene protons.
 3.75 [s, 1H] OH exchanged with D_2O
 4.1 [br. 1H] CH-OH
 5.7 [m, 2H] $-\text{CH}=\text{CH}-$

Mass⁴⁰ M^+ at 98, $m/e = 80$.

Jone's oxidation of Cyclohexenol

0.2 g Cyclohexenol and 20 ml ether was stirred in 50 ml RB flask. To this stirring solution was then added Jone's reagent (5 ml) dropwise. Stirred at 25°C for 3 hrs. Reaction mixture was ether extracted (3 x 150 ml) and washed with 5% NaHCO_3 solution (2 x 50 ml) and finally with distilled

water (3 x 150 ml). Dried over Na_2SO_4 . Removal of ether by distillation afforded (0.13 g) product. This compound showed identical spectral data with those reported for cyclohexenone.

[II] Preparation of Authentic sample [Chart 2.3]

Preparation of Epoxy cyclohexane (2)

Epoxide (2) was prepared by the method of Guss and Rosenthal¹⁸.

Cyclohexene [10.25 g, 0.125 M], N-bromo succinimide (NBS) [23.5 g, 95% pure] and water (40 ml) were stirred vigorously at room temperature until solid NBS disappeared [1 hr]. To this was added sodium hydroxide (7.5 g) in water [25 ml] and stirred for 30 minutes at 50-55°C. Cooled and extracted with ether [3 x 100 ml]. Ether extract was washed with distilled water [3 x 100 ml] till neutral, dried over anhydrous Na_2SO_4 and removal of ether gave the epoxide 2 [9.2 g, 90% yield] bp : 129-30°C.

IR Spectrum - epoxy 840 cm^{-1} .

PMR Spectrum - 2.93 [s, 2H], oxirane protons.

Above spectral data was quite comparable with the reported values for Epoxy cyclohexane in the literature¹⁸.

Section B

[I] Epoxidation of α -pinene (8)

Epoxidation of α -pinene at lower temperatures

Initially, epoxidation of α -pinene (neat) was carried

out at 50° and 75°C in a glass reactor as described earlier, using borate esters as catalyst. Even after a period of ~60 hrs GLC obtained shows that there was no appreciable conversion of α -pinene. In order to overcome this difficulty, reactions were carried out at 100°C.

A mixture of α -pinene (8) [7 g, 0.051 M] and catalyst A [1 g, 0.005M] was subjected to epoxidation in the reactor as described earlier. The reaction was carried out at 100 \pm 2°C. After 44 hours reaction was stopped. GLC of aliquots after 12, 24, 34 and 44 hrs was carried out on OV-101 column [120°C temperature]. All aliquots showed five peaks and a peak due to unreacted (8). Reaction product after 44 hrs was worked out as usual yielded 6 g product. Out of this 5.5 g material was subjected for distillation.

Fr. 1 : bp. 70-105°C (oil)/50 mm pr. = 2.2 g (unreacted-8).
bath

Fr. 2 : bp. 80-150°C (oil)/2 mm pr. = 2.3 g (oxidation
bath product)

Residue : - = 1.0 g -

The above distillation data showed that unreacted (8) was 40% i.e. conversion was 60%.

Some part of fr.2 (1.5 g) was subjected to separation by column chromatography over neutral alumina.

CHROMATOGRAM-2

Material loaded - 1.5 g Neutral alumina - 50 g
 Column length - 60 cms Column dia. - 1.5 cms

Fr.No.	Eluent	Quantity (ml)	Remarks based on GLC
1-2	pet.ether	2 x 50 ml	Mix.of 8, 9, 12 (0.1 g)
3-7	pet.ether	5 x 100 ml	Mix.of 9, 12 (0.240 g)
8	Benzene	1 x 100 ml	<u>Pure 12</u> (0.327 g)
9	Benzene	1 x 100 ml	Mix.of 12,11 (0.290 g)
10	Benzene	1 x 100 ml	<u>Major 11</u> (~84%)(0.214 g)
11-12	Ether	2 x 100 ml	Mix.of 11+12 and other components (0.31 g)

Fr.8 from above chromatogram was found to be pure by glc [$t_R=6.2$]. This compound was identified as verbenone (12) from it's spectral data. This was then confirmed by direct comparison [GLC, IR, NMR] with the authentic sample.

Compound (12) : Verbenone [$C_{10}H_{14}O$]

bp. : 95°C oil bath/2 mm [Lit.⁴¹ 110-5°C/16 mm]

$[\alpha]_D^{25} = -14.82^\circ$ as 10% soln.in methanol.

IR : 2920, 1700, 1680, 1620, 1460, 1390, 1370, 1320, 1240, 1200, 1070, 1020, 950, 860, 820 and 760 cm^{-1} .

PMR⁴¹ (CCl₄) : 0.93 and 1.43 [2s, 6H] -C-(CH₃)₂
 1.93 [d, 3H] -C=C-CH₃
 5.59 [q, 1H] -C=CH

Mass : M⁺ at m/e = 150.

Fr.10, from chromatogram-2 was found to be 84% pure by glc [t_R=4.6]. This compound was identified as trans-verbenol (12). This was confirmed by comparison of it's spectral data (IR, NMR and GLC) with that of authentic sample prepared⁴¹.

Compound (11) : Trans-Verbenol [C₁₀H₁₆O]

bp. : 105^o/2 mm

IR⁴¹ (neat) : 3350, 2900, 1660, 1600, 1490, 1470,
 1450, 1380, 1365, 1340, 1240, 1130,
 1100, 1020, 1000 and 750 cm⁻¹.

PMR⁴¹ (CCl₄) : 0.85 and 1.3 [2s, 6H] -C $\begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix}$
 1.7 [m, 3H] -C=C-CH₃
 4.03 [m, 1H] CH-OH
 5.17 [m, 1H] -C=CH

GC-Mass : M⁺ at 152, 92 (base peak).

From another experiment of α -pinene (8) with catalyst B [where formation of epoxide (9) was more as compared to reaction with catalyst A] after usual work up and removal of unreacted (8) by distillation, the remaining

material was subjected to column chromatographic separation by using basic alumina grade III¹⁷.

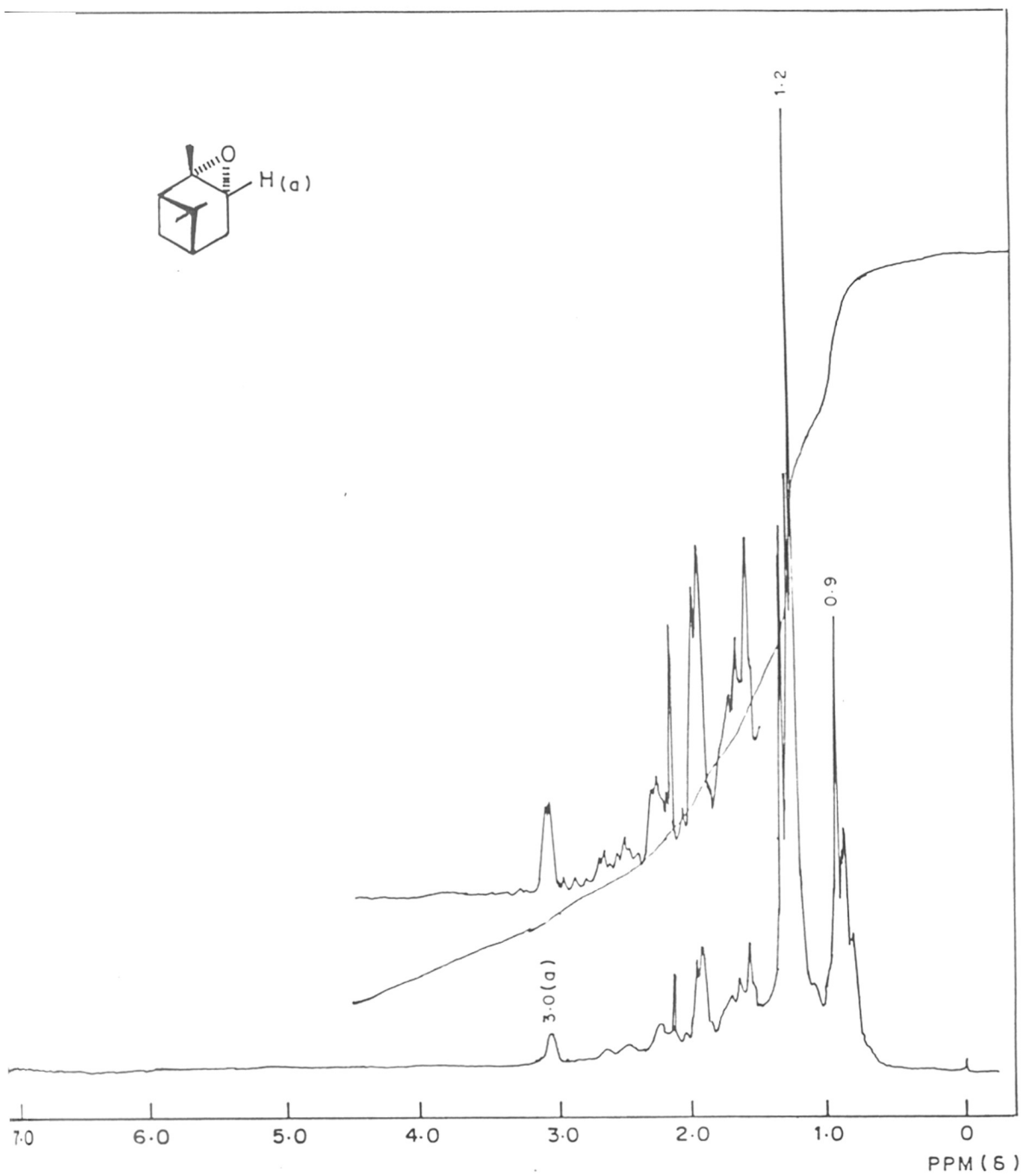
CHROMATOGRAM - 3

Material loaded - 1.12 g Basic alumina - 35 g
 Column length - 60 cms Column dia. - 1.5 cms

Fr.No.	Eluent	Quantity	Remarks based on GLC
1-3	pet.ether	3 x 75 ml	Mix.of 8, 9 [0.118 g]
4	pet.ether	1 x 75 ml	<u>Major 9</u> (~72%) [0.075 g]
5-6	pet.ether	2 x 75 ml	Mix.of 9, 12 [0.120 g]
7-10	pet.ether:ether 9:1	4 x 75 ml	Mix.of 12, 11 [0.265 g]
11	8:2	1 x 75 ml	<u>Pure 12</u> [0.125 g]
12	7:3	1 x 75 ml	Mix.of 12, 11 [0.098 g]
13	Methanol	1 x 200 ml	Mix.of 12, 11 [0.260 g]

Fr.4 from above chromatogram was found to contain a compound (9) to the extent of 72% by GLC [$t_R=3.75$]. It's spectral data indicated it to be a 2 α , 3 α -Epoxy-pinane (9). It was confirmed by direct comparison [IR, NMR and GLC] with that of authentic sample prepared⁴².

Compound (9) : 2 α , 3 α -Epoxy-pinane [C₁₀H₁₆O]

FIG. 2.3. PMR SPECTRUM OF 2 α ,3 α -EPOXY PINANE (9)

IR : 2900, 1440, 1380, 1360, 1290, 1200, 1130,
(neat) 1060, 1030, 1000, 940, 830, 760, 730 cm^{-1} .

PMR (CDCl_3) : 0.9 [s, 3H]
(Fig.2.3) 1.2 [s, 6H]
3.0 [br. 1H] oxirane proton.

GC-Mass : M^+ at $m/e = 152$.

The Fr.11, from chromatogram-3 was found to be pure by GLC. This was identified as Verbenone 12 and was confirmed as described earlier.

[II] Preparation of authentic samples [Chart 2.3]

[a] Preparation of the 2 α , 3 α -Epoxy-pinane (9)⁴²

α -Pinene (8) [10.8 g] in ether [25 ml] was added slowly to a stirred ethereal solution of monopero-phthalic acid⁴² [200 ml 9%] at 0°C and then kept at 5-6°C till all the starting olefin was consumed [60 hrs, as monitored by TLC and GLC]. Then the solution was transferred to a separatory funnel and washed with 10% Na_2CO_3 solution [3 x 100 ml] till all the acid was completely removed, washed with water [2 x 100 ml] and finally dried over anhydrous Na_2SO_4 . Evaporation of ether gave a liquid which was distilled to give desired compound [8.2 g, bp. 91-93°C/27 mm (lit.⁴² : 90°C/21 mm)]. It's PMR spectrum matched favourably with that of reported⁴³ for 2 α , 3 α -Epoxy-pinane (9).

[b] Preparation of trans-verbenol (11)

Trans-verbenol was prepared by the method reported by G.H. Whitham⁴⁴.

To the stirred solution of α -pinene (8) [27 g] in 500 ml dry benzene was added slowly Lead tetracetate [84 g, freshly prepared by method given in Fieser and Fieser⁴⁵] at about 65°C. Stirred further for 30 minutes at 60-65°C cooled and filtered. To the filtrate was added 500 ml water. Lead dioxide (PbO₂) precipitate which was filtered out. Solvent removal from benzene layer followed by distillation afford Cis-2-acetoxypin-3-ene (15) [21.2 g, 55%, bp. 96-97°C/9 mm].

5 g of (15) was taken to which 25 ml glacial acetic acid was added. Kept aside for 30 min. After addition of 100 ml of water the material was ether extracted [2 x 100 ml]. Ether extract was washed with aq. Na₂CO₃. Dried over Na₂SO₄. Evaporation of ether followed by distillation gave trans-verbenyl acetate (16) [4.25 g] [IR showed two diagnostic bands at 970 and 773 cm⁻¹].

3.5 g (16) was taken in RB flask. To this was then added 25 ml methanol and 1.5 g NaOH in 2 ml water, refluxed for 2 hrs. Cooled and ether extracted [2 x 100 ml]. The material washed with distilled water till pH neutral, dried over Na₂SO₄, removal of ether gave compound 11 [3 g]. This compound was

found to be pure by GLC. It's spectral data compared quite favourably with the reported⁴⁰ for trans-verbenol (11).

[c] Preparation of verbenone (12)

Verbenone was prepared by the Jone's oxidation of trans-verbenol (12).

A mixture of 1.5 g trans-verbenol (11) in 25 ml ether and 8 ml Jone's reagent [freshly prepared] was stirred at 25° for 4 hrs [till the reddish brown colour persists]. The product was ether extracted [2 x 100 ml] and washed with 5% NaHCO₃ [2 x 50 ml] and water [2 x 50 ml]. Ether extract dried over Na₂SO₄. Removal of solvent followed by distillation (bp. 85-90°/1 mm) gave 1.1 g verbenone 12. This compound was found to be pure by GLC. It's spectral data was quite comparable with those reported in the Lit.⁴¹ for verbenone 12.

Section C

[I] Epoxidation of car-3-ene (18)

A mixture of car-3-ene (18) [5.65 g, 0.041 M] and catalyst A [2.65 g, 0.014 M] was subjected to epoxidation in the reactor as described earlier. The reaction was carried out at 100 ± 2°C. After 24 hours reaction was stopped. GLC of aliquots after 12, 18 and 24 hrs was carried out on OV-101 column [120°C temperature]. All aliquots showed eight peaks apart from a peak due to unreacted (18). Reaction product after 24 hrs after usual work up yielded 3.8 g product.

From this 3.5 g material was taken for distillation.

Fr.1 : bp. 65°-90°C/30-35 mm. 1.68 g unreacted (18)

Fr.2 : bp. 40-90°C/2 mm. 1.3 g Oxidation product.

Residue : - 0.52 g

This distillation data showed that recovery of unreacted (18) was 48%, hence the conversion was about 52%. The residue obtained was 15%.

A part of second fraction (Fr.2) was subjected for column chromatography using neutral alumina gr.II¹⁷.

CHROMATOGRAM - 4

Material loaded - 1 g Neutral alumina - 30 g

Column length - 60 cms Column dia. - 1.5 cms

Fr.No.	Eluent	Quantity	Remarks based on GLC
1-2	pet.ether	2 x 50 ml	Unreacted 18 [0.041 g]
3-4	pet.ether	2 x 50 ml	Mixture 18+19 [0.11 g]
5-8	pet.ether	4 x 50 ml	<u>Pure-19</u> [0.218 g]
9	Benzene	1 x 50 ml	-
10-11	Benzene	2 x 50 ml	Mix.of 20+21+22 [0.307 g]
12	ether	1 x 200 ml	Mix.of 20+21+22 [0.322 g]

Fr.5-8 from above chromatogram found to be pure from GLC [$t_R=4.34$]. The compound was identified as 3 α , 4 α -Epoxy

carane (19) from its spectral data. This was confirmed by direct comparison [GLC, IR, NMR] with an authentic sample.

Compound (19) : 3 α , 4 α -Epoxy carane [C₁₀H₁₆O]

bp. 80-82°C/20 mm [Lit.⁴⁶ 81^o/21 mm]

$[\alpha]_D^{25} = +10.17^\circ$ as 10% solution in methanol.

IR (neat) : 2900, 1420, 1370, 1200, 1120, 1050,
980, 940, 840, 790, 750 and 720 cm⁻¹

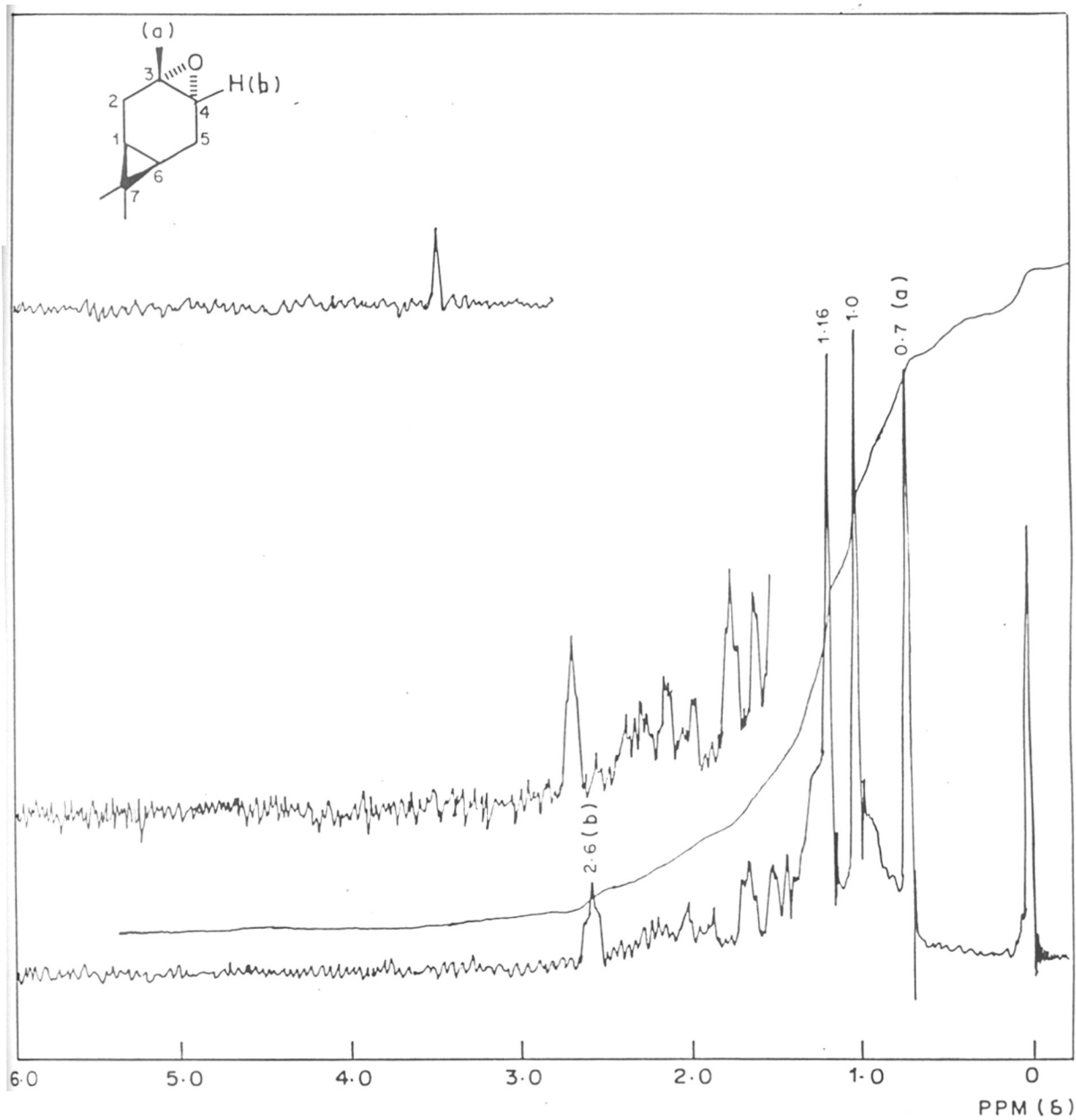
PMR⁴⁶ (CCl₄) : 0.7 [s, 3H] -O-C-CH₃
1.0 [s, 3H] }
1.16 [s, 3H] } -C < CH₃
2.6 [bs 1H] oxirane proton.

Mass : M⁺ at m/e = 152.

152 [3%], 137 [45%], 123 [22%], 119 [30%],
109 [100%], 95 [27%], 91 [24%], 81 [32%],
67 [30%].

Fr.10-12 from above chromatogram was further subjected for separation by using Flash Chromatography.

The material to be separated was adsorbed on TLC grade alumina using solvent to make a good slurry and then evaporating the solvent. The specially prepared column [20 cms long, 2 cm dia] was packed with TLC grade alumina [25 g] and from the top solvent was introduced under little pressure for even packing of the column, then alumina impregnated with

FIG. 2.4. PMR SPECTRUM OF 3 α ,4 α -EPOXY CARANE (19)

mixture [0.63 g] to be separated was loaded and fractions were collected as usual. The speciality of this technique is that solvent used for elution is introduced at the top of the column under pressure and fractions of small volume can be collected automatically at predetermined rate [from 1 to 10 ml] in a test tube stand.

CHROMATOGRAM - 5

Fr.Nos.	Eluent	Quantity	Remarks based on GLC
1-20	pet.ether	20 x 5 ml	Mix.of 19-22 [0.080 g]
21-40	pet.ether:benzene 1:1	20 x 5 ml	Mix.of 20-22 [0.120 g]
41-55	Benzene	15 x 5 ml	Mix.of 20-22 [0.036 g]
56-80	Benzene	25 x 5 ml	<u>Pure-20</u> [0.1050 g]
81-100	Benzene	20 x 5 ml	Mix.of 21+22 [0.1080 g]
101-120	Ether	20 x 5 ml	Mix.of 21+22 [0.18 g]

Fr.56-80, from above chromatogram was found to be pure from GLC [$t_R=5.35$]. The compound was identified as car-3-en-5-ol [20] by it's mode of formation and spectral data. This was confirmed by Jones oxidation of this alcohol to yield ketone (car-3-en-5one).

Compound (20) : Car-3-en-5-ol [$C_{10}H_{16}O$]

IR (neat) : 3420, 2980, 1670, 1460, 1380, 1370,
1130, 1020, 840, 820, 750 and 680 cm^{-1} .

PMR (CCl₄) :

1.06 [s, 2H]	cyclopropyl
1.2 [s, 3H]	$\left\{ \begin{array}{l} \\ \\ \end{array} \right. -C-(\underline{CH_3})_2$
1.28 [s, 3H]	
1.7 [m, 3H]	$-C=C-\underline{CH_3}$
2.25 [m, 2H]	$\underline{CH_2}-C=C$
3.46 [d, 1H]	$\underline{CH}-OH$
5.66 [d, 1H]	$-C=\underline{CH}$

Mass : M^+ at $m/e = 152$.

Jones oxidation of Car-3-en-5-ol

To the stirred mixture of (0.07 g) car-3-en-5-ol and 15 ml ether, was added 4 ml of Jones reagent dropwise. Reaction mixture was stirred for 2 hrs at 25°C. Then it was extracted with (2 x 50 ml) ether. Ether layer was washed with 5% NaHCO₃ (2 x 50 ml) and finally with distilled water (2 x 50 ml) and dried over sodium sulphate. Removal of ether by distillation gave a compound (0.05 g) which showed similar spectral data as reported for car-3-en-5-one.

Combined fr.81-120 was found to be a mixture of two components 21 and 22. Some solid material separated out on keeping this mixture overnight at room temperature, which was filtered out under suction. From GLC analysis it was observed that the solids were rich in compound 22 (~85%) with balance impurity due to compound 21 (~15%).

The compound 22 was characterized as car-3-en-2,5-dione from its spectral data and comparing it with the reported^{47,48} earlier.

Compound (22) : Car-3-en-2,5-dione [$C_{10}H_{12}O_2$]

mp. : $92^{\circ}C$ [Lit.²⁶ mp : $94-95^{\circ}C$]

IR : α, β -unsaturated ketone - 1645 cm^{-1}

-C=C- - 1608 cm^{-1}

PMR ($CDCl_3$) : 1.25 [s, 6H] -C $\begin{cases} \text{CH}_3 \\ \text{CH}_3 \end{cases}$
 1.9 [d, 3H] -C=C- $\underline{\text{CH}_3}$
 2.25 [s, 2H] cyclopropyl H.
 6.45 [s, 1H] -C= $\underline{\text{CH}}$

Mass : M^+ at $m/e = 164$.

The liquid portion i.e. filtrate was found about 85% pure as compound 21 [$t_R=6.01$] by GLC. From its spectral data this compound was identified as car-3-en-5-one (21). Its spectral data compared favourably with one reported earlier²⁷.

Compound (21) : Car-3-en-5-one [$C_{10}H_{14}O$]

bp. : $58^{\circ}C/0.5\text{ mm}$.

IR : α, β -unsaturated ketone - 1670 cm^{-1}

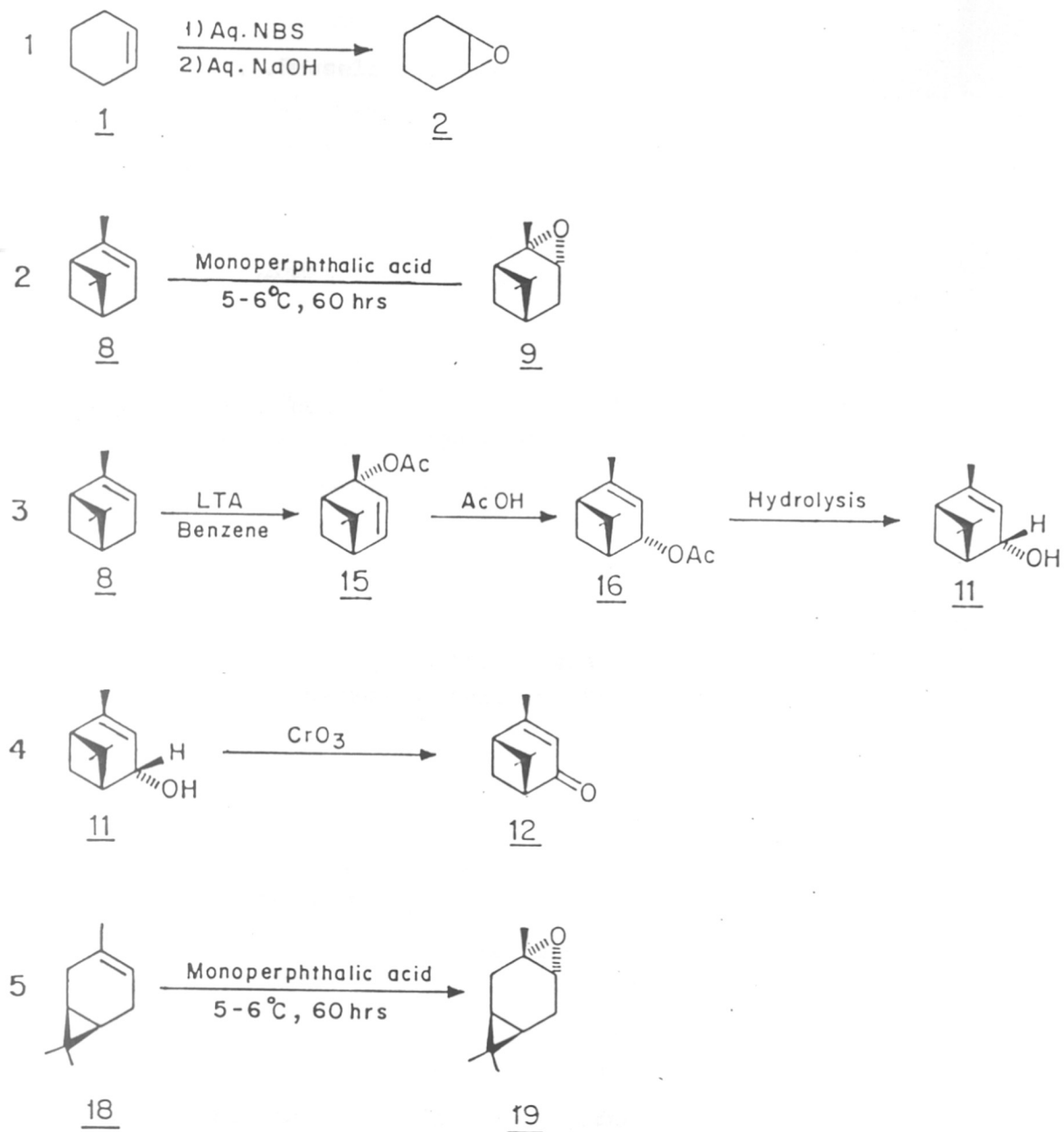
PMR ($CDCl_3$) : 1.12 [s, 3H] $\left\{ \begin{array}{l} \text{-C-(CH}_3\text{)}_2 \\ \text{1.31 [s, 3H] } \end{array} \right\}$
 1.5 [m, 2H]
 1.95 [m, 3H] -C=C- $\underline{\text{CH}_3}$
 2.42 [m, 2H]
 5.8 [m, 1H] -C= $\underline{\text{CH}}$

Mass : M^+ at $m/e = 150$.

[II] Preparation of authentic sample [Chart 2.3]

Preparation of 3 α , 4 α -Epoxy-carane (19)

Car-3-ene (18) [4 g] in 25 ml ether was added slowly to an ethereal solution of monopero-phthalic acid⁴² [115 ml, 6%] at 0°C with continuous stirring and then kept at 5-6°C till all the starting olefin (18) was consumed [\sim 60 hrs, as monitored by TLC and GLC]. Then the solution was transferred to a separatory funnel and washed with 10% Na₂CO₃ solution [3 x 100 ml] till all the acid was completely removed, then washed with water [2 x 50 ml] and finally dried over anhydrous Na₂SO₄. Evaporation of ether gave a liquid which was distilled to give pale yellow liquid [3.6 g, bp. 60-62°C/2 mm]. This was found to be pure by GLC and TLC. It's spectral data was quite identical with that of reported⁴⁶ for 3 α , 4 α -epoxy-carane (19).

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CHAPTER - III
EPOXIDATION OF β -PINENE AND CAMPHENE

CHAPTER - 3

In the previous chapter the epoxidation of olefins with endocyclic double bond using borate esters has been described. This chapter deals with a different set of olefins having exocyclic double bond. This study was expected to yield valuable information regarding the effect of the nature of the double bond on the course of the reaction.

The olefins selected for this study are β -pinene (27) and camphene (32). Both are bicyclic monoterpenes with vastly different bicyclic skeletons. Also there are no previous references in either case regarding epoxidation using borate esters.

Section A

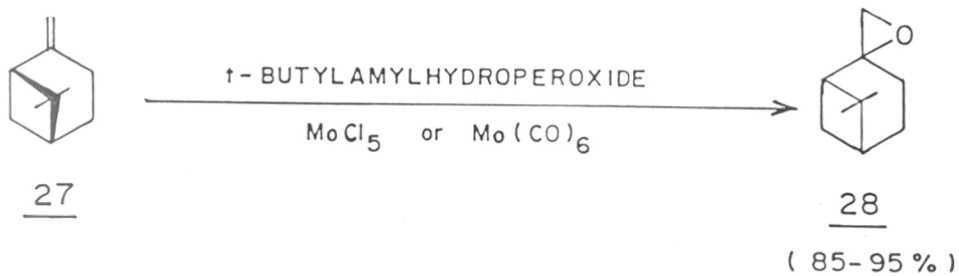
Epoxidation of β -pinene (27)

Previous work : [Chart 3.1]

In the past, Yur'ev¹ et.al. carried out epoxidation of β -pinene using t-butyl amyhydroperoxide in the presence of various molybdenum complexes. They obtained β -pinene epoxide (28) in 85-95% yield. Other workers^{2,3} using different catalysts have carried out autoxidation of β -pinene. But none of these workers have obtained epoxide in their study.

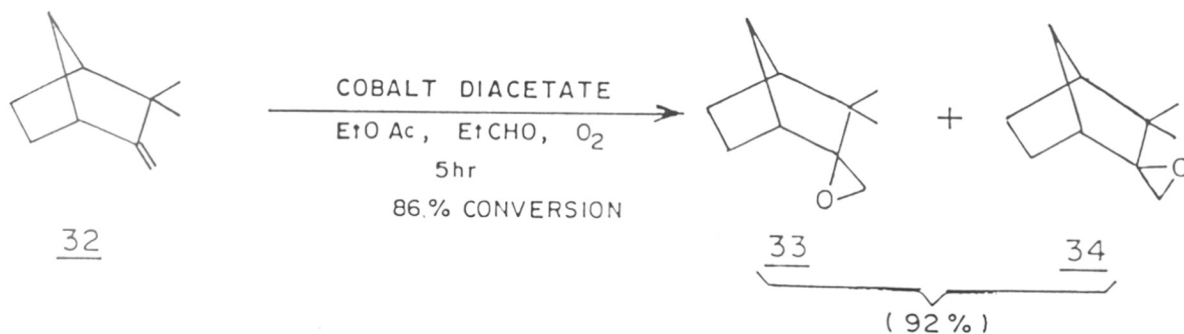
EARLIER WORK ON
EPOXIDATION OF β -PINENE AND CAMPHENE

1



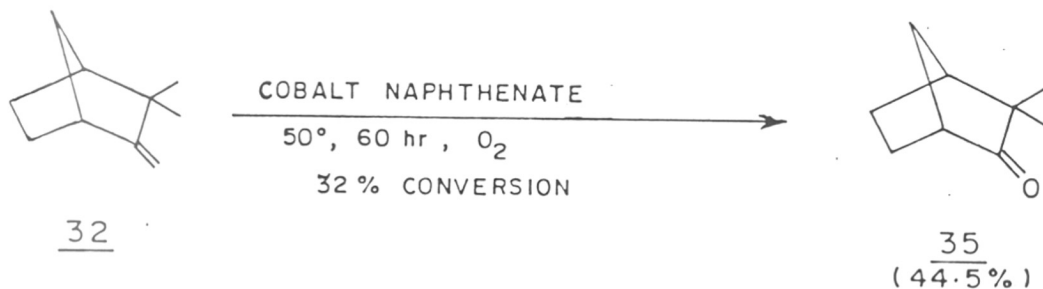
Yurev, Isaeva et al.¹ (1974)

2

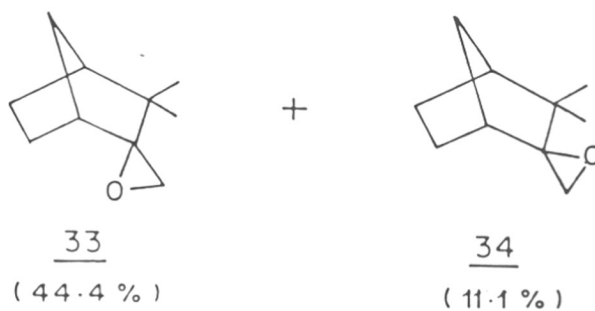


Mulder et al.¹¹ (1984)

3



A. D. Natu¹² (1983)



Present Work [Table 3.1]

In the specially prepared glass reactor, β -pinene [99% pure] was placed along with isopropyl or n-propyl borate ester. The epoxidation was carried out at $100 \pm 2^\circ\text{C}$ using constant flow of oxygen at 2 lt/hr. The reaction was monitored by withdrawing samples after fixed time intervals and analysing on GLC [OV-101 column, 120°C temp.]. The reaction product after 24 hrs reaction time after usual workup displayed the GLC as shown in Fig.3.1. There were five components in the total reaction mixture. These were separated by fractional distillation followed by column chromatography using neutral alumina⁴.

Component 1 [R.T. 2.31] : By careful fractional distillation of the reaction product, this compound was obtained as the lower boiling fraction [80-90°C/40-50 mm]. From its boiling point and mixed GLC, this compound was easily identified as unreacted β -pinene (27). This was then confirmed by its PMR spectra in which gem dimethyls were at 0.76 δ and 1.26 δ as singlets integrating for three protons each. There was a broad signal at 4.73 δ integrating for two protons, characteristic of olefinic protons.

Component 2 [R.T. 4.59] : This component obtained by column chromatography was further purified by distillation [bp : 104-5°C/27 mm]. This compound in its IR spectrum showed a broad absorption signal at 3420 cm^{-1} which is characteristic

- 1 β -PINENE
- 2 TRANS-PINOCARVEOL
- 3 β -PINENE EPOXIDE
- 4 NOPINONE
- 5 MYRTENOL

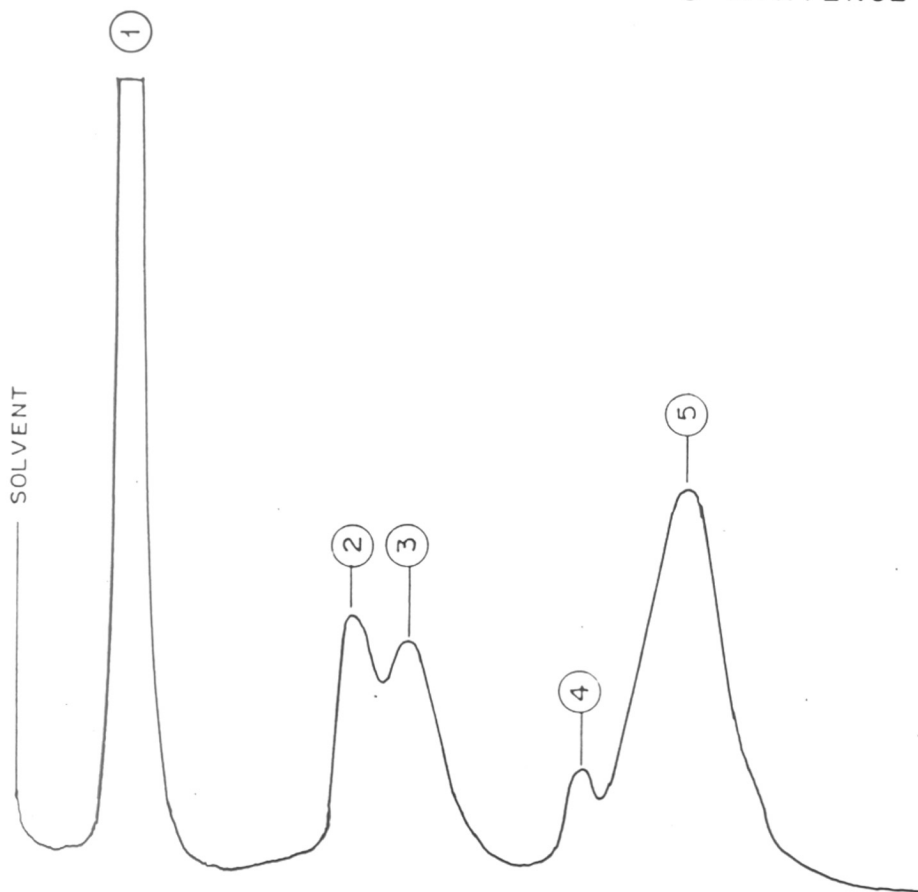


FIG. 3.1. GLC OF REACTION MIXTURE FROM
 β -PINENE EPOXIDATION

of OH group. The absorptions at 1380 and 1360 cm^{-1} were indicative of gem dimethyl group. This was confirmed by two methyl singlets at 0.67 δ and 1.3 δ in the PMR spectrum, the multiplet at 4.38 δ for one proton showed methine proton α to OH. Absorption at 1650 cm^{-1} in IR indicated C=C presence which was confirmed by two signals appearing at 4.78 δ and 4.95 δ integrating for one proton each for vinylic protons. The mass spectrum of this compound showed M^+ peak at m/e 152. From this spectral data the compound under investigation was identified as trans-pinocarveol 17. This was confirmed by comparing its spectral data with the authentic sample prepared⁵.

Component 3 [R.T. 4.87] : This component was obtained in 90% purity by chromatographic separation. The IR spectrum of this compound showed characteristic epoxide absorption bands at 1260 cm^{-1} , 940 cm^{-1} and 860 cm^{-1} . The two sharp signals at 1380 and 1370 cm^{-1} showed the presence of gem dimethyl group. This was confirmed by its PMR spectrum, showing two sharp singlets at 0.9 δ and 1.25 δ integrating for three protons each. The multiplet at 2.65 δ whose integration equivalent to two protons was indicative of oxirane protons. The complex multiplet was seen in the region 1.5-2.2 δ integrating for eight protons. In the mass spectrum of this compound M^+ ion was seen at m/e 152. All above data was good enough to identify this compound as β -pinene epoxide (28). This was confirmed by direct comparison of its spectral data with the authentic sample prepared by known method⁶.

TABLE 3.1

 β -Pinene Epoxidation^a

Expt. No.	Time in hrs.	Catalyst ^b and its conc ⁿ . (%)	% Conversion	Reaction products ^c (%)				Unidenti- fied products (%)	
				β -pinene epoxide	Trans-pino- carveol	Myrtenol	Nopinone		Allylic dimers
1	24	A, 30	39.1	7.7	21.74	51.63	3.6	8.3	7.0
2	24	B, 30	45.4	19.28	16.76	53.60	3.80	3.1	3.4
3 ^d	44	B, 30	56.6	23.10	11.47	54.15	3.00	3.8	4.45

a - Neat, 100 \pm 2°C, 8 g scale

b - Catalyst A = Isopropyl borate

B = n-propyl borate

c - Based on GLC, excluding starting olefin

d - 40 g/batch scale

Component 4 [R.T. 5.69] : This component obtained from column chromatography was found to be pure by GLC. This compound corresponded to component 4 from GLC of the total reaction mixture. The IR spectrum of this compound showed very strong absorption band at 1700 cm^{-1} characteristic of saturated ketone function, gem dimethyl frequencies were observed at 1380 and 1360 cm^{-1} . This was confirmed in PMR spectrum of this compound by two methyl singlets at $0.91\ \delta$ and $1.33\ \delta$. From above spectral data, the compound was identified as nopinone (30), which was confirmed by comparison of its spectral data with the data reported earlier⁷.

Component 5 [R.T. 6.38] : The major compound isolated by column chromatography was carefully distilled [bp : $70-80^{\circ}\text{C}$ (bath)/1 mm]. The IR spectrum of this compound showed broad absorption band at 3470 cm^{-1} characteristic of OH group. The absorption at 1675 cm^{-1} was due to the presence of C=C linkage. Characteristic gem dimethyls were at 1388 and 1368 cm^{-1} . This data was supported by its PMR, showing two methyl singlets at $0.93\ \delta$ and $1.4\ \delta$, and the broad signal at $5.5\ \delta$ for one proton due to olefinic linkage. The multiplet centered at $4.0\ \delta$ was indicative of methylene protons on carbon carrying OH group. The signal at $2.3\ \delta$ for one proton which exchanged with D_2O was due to hydroxylic proton. The mass spectrum of this compound furnished M^+ ion peak at $m/e\ 152$. Based on this spectral data the compound was identified as myrtenol (29). This was confirmed by comparing its spectral data with the reported one^{8,9}.

Component 6 : Allylic dimer of β -pinene (31)

This component was obtained as first component by using column chromatography. The IR spectrum of this compound was free of any oxygen function showed it to be hydrocarbon. This compound showed elemental analysis as C = 88.2%, H = 11.7%. The PMR spectrum indicated presence of olefinic protons. In the mass spectrum of this compound M^+ ion appeared at m/e 270 and base peak at m/e 135 indicating dimeric linkage. From above spectral data and high retention time observed on GLC, the compound was characterized as allylic dimer of β -pinene (31). It was then confirmed by comparison of this spectral data with the reported¹⁰ one.

Section B

Epoxidation of camphene (32)

Previous work [Chart 3.1]

There are very few reports on the epoxidation of camphene (32). The reported work is summarized in the chart 3.1^{11,12}. As can be seen from the chart, Mulder¹¹ et.al. have obtained camphene epoxide in very good yield using cobalt diacetate and oxygen at relatively low reaction period. Earlier, from our Laboratory Natu¹² obtained camphene epoxide and camphenilone about 55.5% and 44.5% in the conversion of 32%, using cobalt naphthenate and oxygen. Few other workers^{13,14} have carried out autoxidation of camphene using different

catalysts. They reported the formation of camphenilone as the only major product. No reports have been found on the camphene epoxidation using borate esters. It is particularly interesting in this terpene hydrocarbon that the only allylic hydrogen available is a bridgehead hydrogen. So it was felt that epoxide formation which is the competing reaction would be highly favoured. Epoxidation of such hydrocarbons might, therefore, provide a useful synthetic method for obtaining epoxides.

Present work [Table 3.2]

A] Epoxidation of camphene at lower temperature

The glass reactor was charged with camphene and borate ester. The epoxidation was carried out at $100 \pm 2^\circ\text{C}$ using controlled oil bath. The reaction was monitored by withdrawing aliquots after fixed time intervals and analysed on GLC. The reaction product after 60 hrs showed that the percentage conversion was only about 3.5%. So at 100°C the reactivity of camphene seemed to be sluggish. In order to overcome this difficulty it was decided to carry out reaction at still higher temperature (125°C).

B] Epoxidation of camphene at higher temperature

In the same modified Vodnar glass reactor camphene and borate ester were placed together. This mixture was subjected for epoxidation using dry oxygen gas at a flow rate of 2-3 lt/hr and temperature of $125 \pm 2^\circ\text{C}$. The reaction was

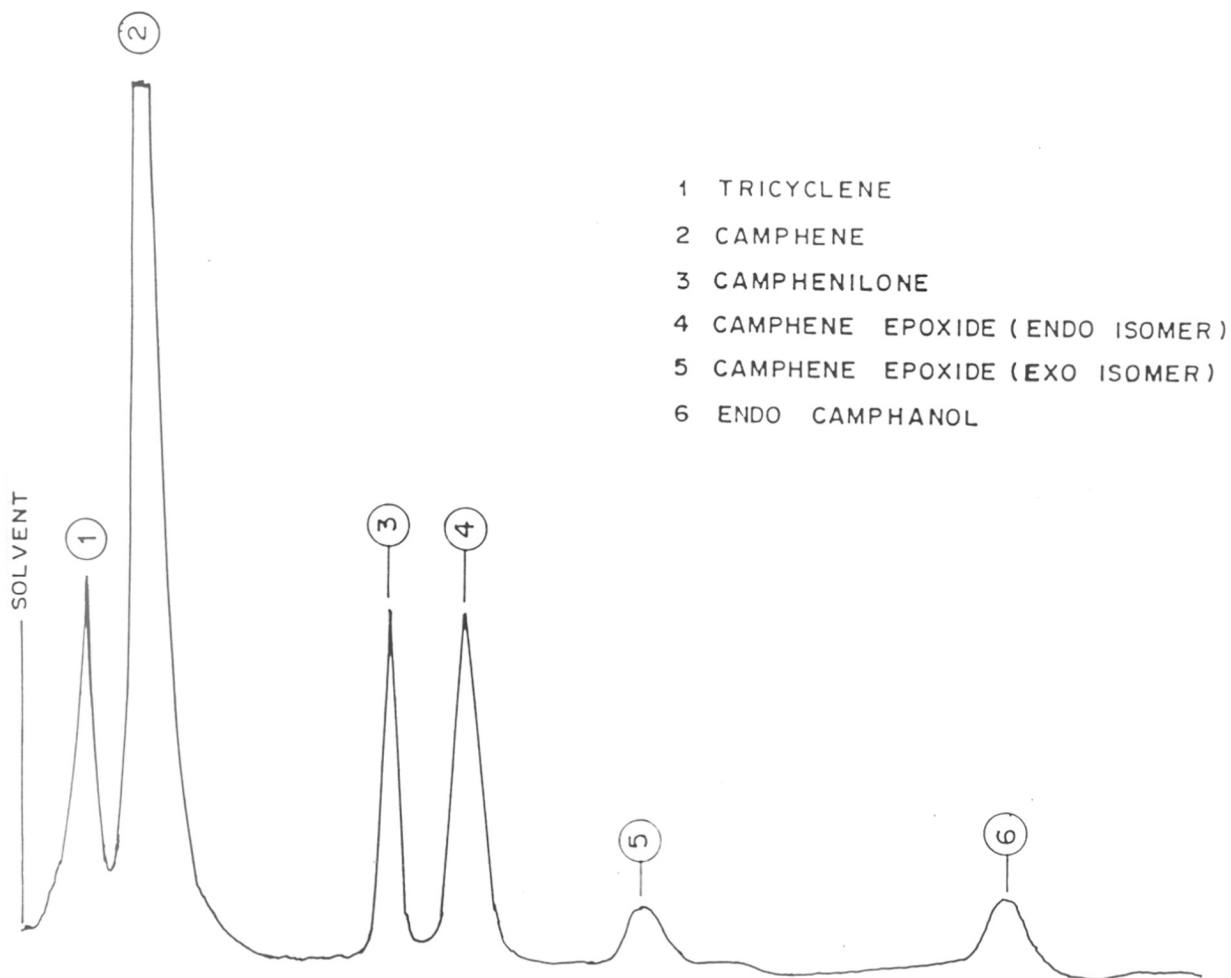


FIG. 3.2. GLC OF REACTION MIXTURE FROM
CAMPHENE EPOXIDATION

monitored by GLC analysis of the samples withdrawn after fixed time intervals. The reaction was stopped after 60 hrs and on usual workup displayed the GLC as shown in Fig. 3.2. It clearly indicated that there were six components present in the total reaction mixture. After careful fractional distillation the first fraction was collected as a lower boiling fraction [bp : 90-100°C/50-55 mm] and it was found to contain the first two components of the reaction mixture. The other components were separated by column chromatography.

Component 1 [R.T. 1.95] : This component was obtained along with component 2 by fractional distillation. This component was identified as tricyclene by mixed GLC with authentic sample of tricyclene.

Component 2 [R.T. 2.17] : This component was obtained as a lower boiling fraction, by the fractional distillation of total reaction product. It solidified on keeping at R.T. This compound was confirmed as camphene (32) from its spectral data and by mixed GLC technique.

Component 3 [R.T. 3.64] : This component obtained from column chromatography was found to be pure by GLC. This solid component showed its melting point as 40-41°C. The IR spectrum of this compound showed a strong absorption band at 1730 cm⁻¹ which is a characteristic of saturated ketone function. The gem dimethyl group appeared at 1370 and 1350 cm⁻¹. This was confirmed by its PMR spectrum which showed two sharp singlets

TABLE 3.2

Camphene Epoxidation^a

Expt. No.	Temp. °C	Catalyst ^c and its Conc. ⁿ (%)	% Conversion	Reaction products ^d (%)				Unidenti- fied products (%)
				Camphene epoxide (endo)	Camphene epoxide (exo)	Campheni- lone	Endo- camphanol	
1 ^b	100±2	A, 30	3.5	96.7	Negligible	3.05	-	-
2	125±2	A, 30	61.45	41.38	10.80	30.62	10.26	6.9
3	125±2	B, 30	64.6	35.56	14.52	36.52	6.88	6.48

a - Neat, 60 hrs

b - 44 hrs reaction

c - Catalyst A = Isopropyl borate

B = n-propyl borate

d - Based on GLC, excluding starting olefin.

at 1.025 δ and 1.05 δ integrating for three protons each. There was complex multiplet in the region 1.4 δ -2.5 δ integrating for eight protons. The mass spectrum of this compound showed M^+ ion peak at m/e 138. From this spectral data the compound could be easily identified as camphenilone (35). This was confirmed by direct comparison with the authentic sample prepared by reported method^{15,16}.

Component 4 [R.T. 4.18] and 5 [R.T. 5.53] : These components 4 and 5 were obtained from the column chromatography as a mixture. By GLC analysis it was found that they were in the ratio of 8:2 respectively. The component mixture obtained as solids showed the melting point 85-87°C. In the PMR spectrum of this mixture the two methyls appeared as sharp singlets at 0.86 and 0.88 δ integrating for three protons each. Both the oxirane protons appeared as two sharp singlets at 2.6 δ and 2.7 δ indicating that it may be a mixture of exo and endo epoxides. The mass spectrum of this component showed M^+ ion at m/e 152. With this spectral data the compound under consideration was identified as camphene epoxide (33), (34) [Endo and Exo mixture]. This was further confirmed by comparing its spectral data with the authentic sample of camphene epoxide prepared by per acid method¹⁷. [It may be pointed out here that epoxide obtained by known per acid method also yields a mixture of endo and exo epoxides]. This was further confirmed by reduction of epoxides using lithium in ethylene diamine,

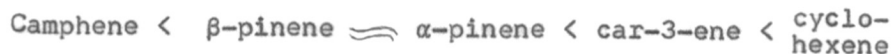
which yielded a mixture of corresponding endo and exo alcohols, where endo alcohol was predominant.

Component 6 [R.T. 8.29] : This component was obtained in about 80% purity [with epoxide mixture as remaining impurity] by column chromatography as the last component. The IR spectrum of this compound showed a broad absorption band at 3400 cm^{-1} , which is a characteristic of -OH group. The gem dimethyl group appeared at 1370 and 1358 cm^{-1} . The PMR spectrum of this compound showed a broad signal at $2.43\ \delta$ integrating for one proton which exchanged with D_2O indicative of hydroxyl proton. The doublet at $3.43\ \delta$ integrating for two protons was for methylene protons on carbon carrying hydroxyl group. The two methyl groups were at $0.93\ \delta$ and $1.0\ \delta$ as singlets counting for three protons each. In the mass spectrum of this compound, one M^+ ion was observed at $m/e\ 154$ the other M^+ at $m/e\ 152$ was due to epoxide impurity. This spectral data was good enough to identify the compound as Endo camphanol (36). This was confirmed by comparison of its spectral data with the reported one¹⁸.

Discussion

The results of the epoxidation experiments of β -pinene and camphene indicate that the reaction proceeds as in α -pinene and car-3-ene. In the case of β -pinene, allylic oxidation products are obtained along with the corresponding epoxides. However, the course of reaction in camphene is totally different, due to the presence of only one allylic hydrogen atom and that too at the bridgehead position. As the formation of a radical at the bridgehead, in a rigid system like camphene, is extremely difficult, the products arising out of allylic oxidation reaction were not obtained.

1] Reactivity of olefin :- From the tables 3.1 and 3.2, it is clear that β -pinene is more reactive than camphene. When isopropyl borate was used as a catalyst, at 100°C/24 hrs, the conversion figures for β -pinene and camphene were 39.1% and 2.5% respectively. Incidentally, it can be pointed out that considering the conversion after fixed time intervals β -pinene is almost as reactive as α -pinene. The overall order of reactivity for these olefins can be indicated as follows :



2] Effect of temperature :- Better conversion of olefin was observed at higher temperatures in both the cases. However,

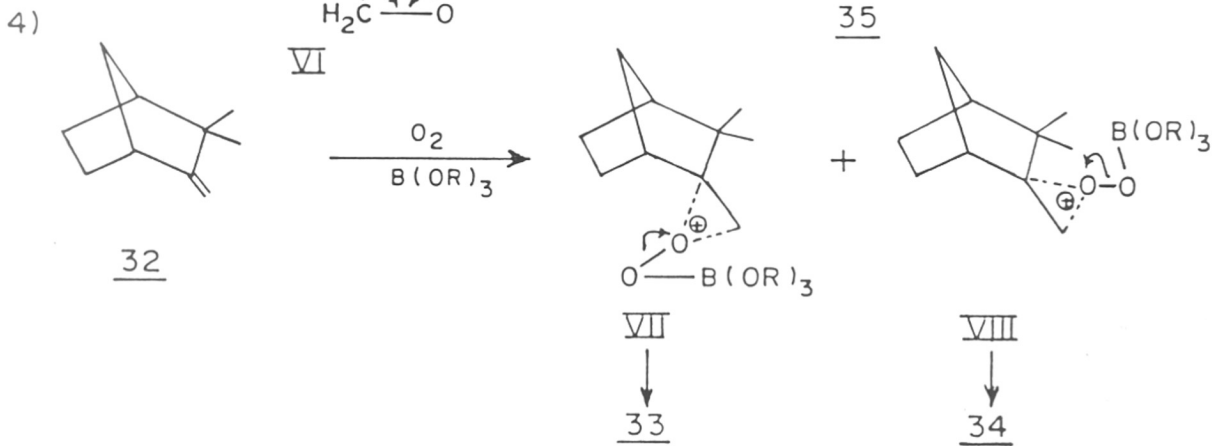
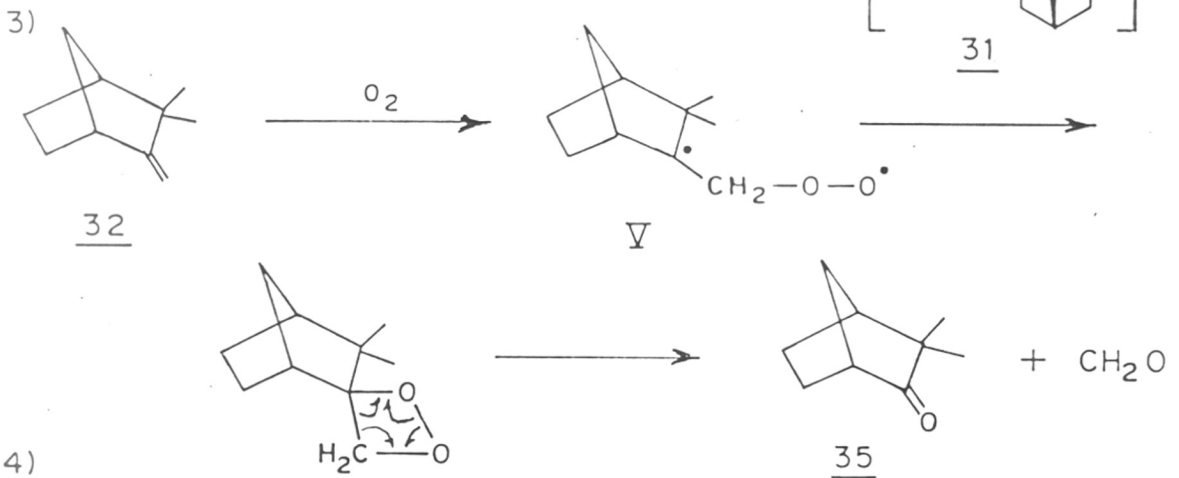
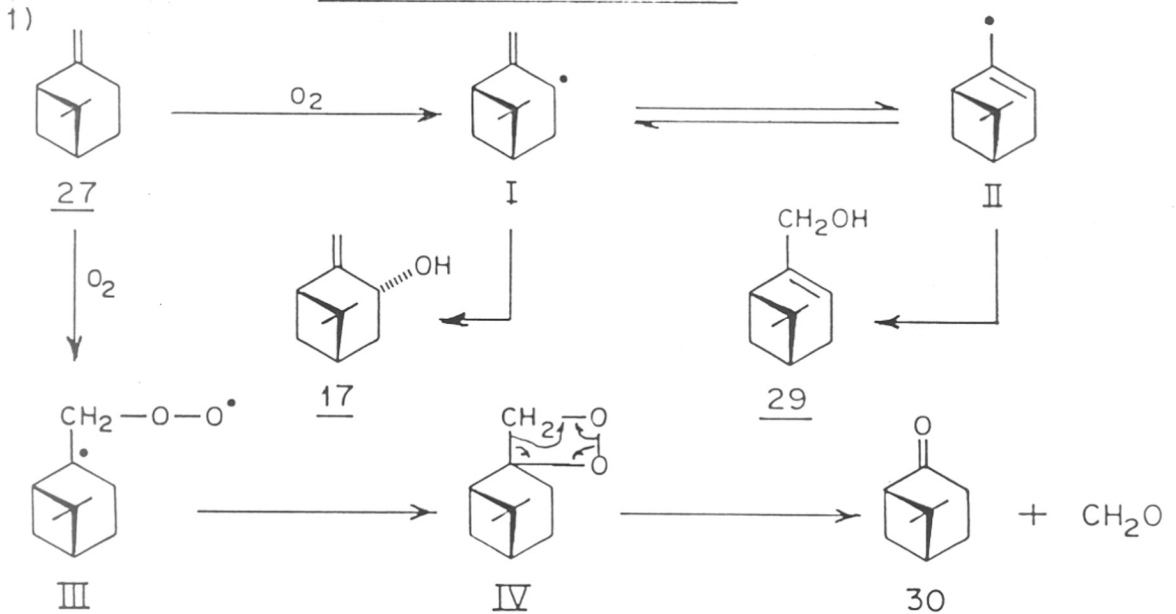
in the case of β -pinene more of polymerized product was obtained. β -Pinene has a peculiar tendency towards polymerization and even around 30°C , the rate of polymerization of β -pinene is considerably higher as compared to α -pinene. When β -pinene was subjected to the reaction at 125°C , it gave a lot of polymerized product (as in the epoxidation reaction of car-3-ene at 140°C). A comparison between the two pinenes is also interesting. At 100°C , both gave about 40% conversion but in the case of α -pinene polymerized product was about 18% of the total reaction product while in the case of β -pinene it was about 28%.

3] Mode of formation of the products [Chart 3.2] :-

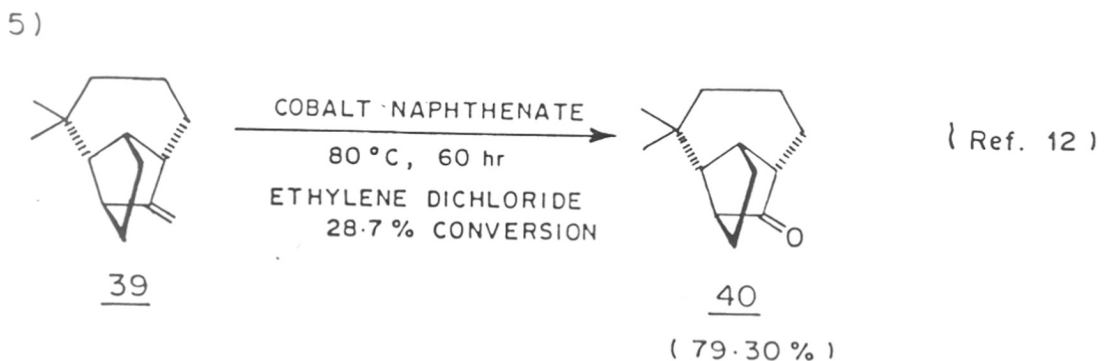
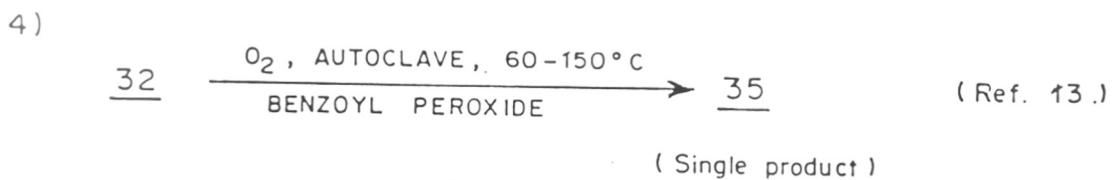
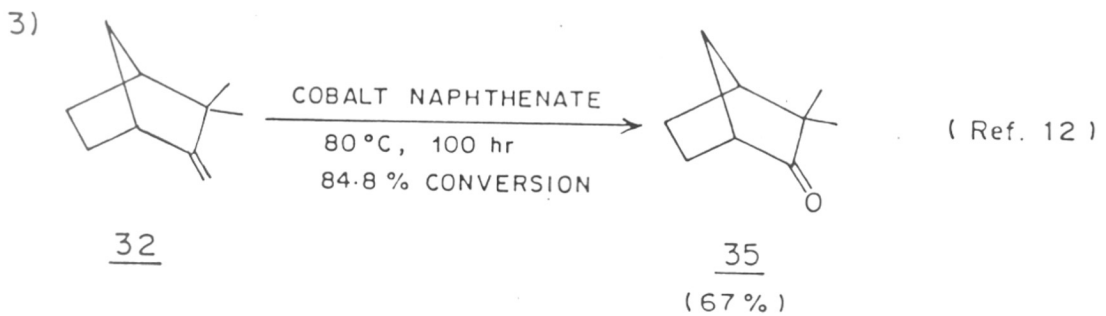
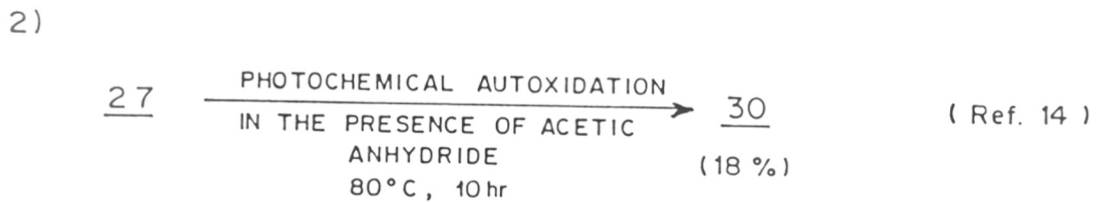
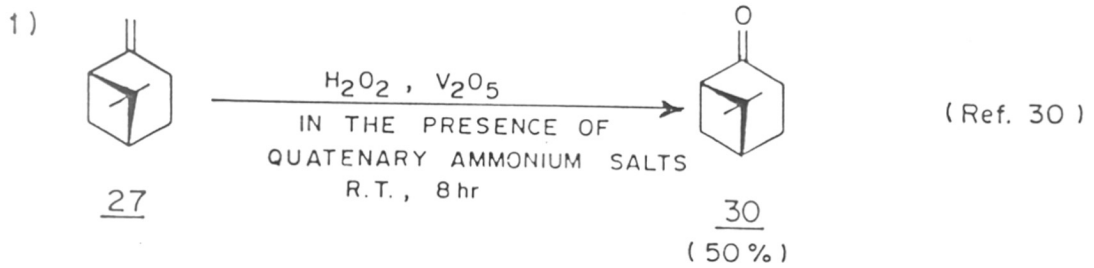
The likely mode of formation of various products is indicated in chart 3.2. In the case of β -pinene (27), the allylic radical generated due to the abstraction of hydrogen can exist in two forms (I) and (II), due to rapid interconversion caused by the migration of the double bond. These radicals are expected to furnish trans-pinocarveol (17) and myrtenol (29) respectively, in a similar manner as the formation of trans-verbenaol in the case of α -pinene discussed in previous chapter. As the attack of oxygen to form peroxy radical preferably takes place from the less hindered side, trans alcohols only, are obtained in both the cases.

4] Formation of Noraketones [Chart 3.3] :- In the autoxidation reactions catalyzed by various reagents, formation of noraketone is a typical reaction of terpenes having exocyclic

CHART - 3.2.
MODE OF FORMATION



REPORTED FORMATION OF NORKETONES



double bonds, viz. camphene^{12,13}, β -pinene¹⁴, longifolene¹², etc.

Oxygen can either attack the double bond [Chart 3.2] and form a diradical (III), which subsequently yields norketone or alternately it can abstract allylic hydrogen to yield stable allylic radicals which lead to the formation of allylic alcohols or ketones. In the case of endocyclic olefins, the first mode is less favourable, probably due to the steric hinderance to the intermediate dioxetane ring system and hence second mode becomes the more preferred one leading to allylic oxidation products.

On the contrary, in the terpenes with exocyclic double bonds, the dioxetane intermediate is far more favourable due to less steric hinderance, and its formation becomes a competing reaction to allylic oxidation.

Thus if we compare the epoxidation of β -pinene with camphene [Chart 3.2], it becomes obvious that in the case of β -pinene there is a possibility of attack of oxygen at the two sites i) allylic position and ii) double bond leading to the formation of trans-pinocarveol and myrtenol in the first case and nopinone in the other. Camphene has a peculiar structure. As mentioned earlier, it does not have easily abstractable allylic hydrogen. The only allylic hydrogen available is at the bridgehead. Although bridgehead radicals are not impossible to form, they are formed very rarely¹⁹, presumably due to the strains involved²⁰.

This is the reason that in the case of camphene, no allylic product is obtained and the norketone is formed in appreciable amounts (~30%). While in the case of β -pinene, the corresponding norketone e.g. nopinone is only a minor product (~3-4%) whereas myrtenol and trans-pinocarveol are the major products.

Stereochemistry of the camphene epoxide

An interesting feature of the camphene epoxidation is the stereochemistry of the epoxide. The reaction results in the formation of the mixture of endo- and exo-epoxides in which endo-epoxide is predominant. Moreover, at low temperatures the amount of exo-epoxide formed is negligible.

The boron peroxide can attack the camphene double bond either from the endo face or the exo face yielding intermediates (VII) and (VIII) respectively. In (VIII) O-O-B(OR)₃ is sterically more hindered due to the gem-dimethyls and the methylene bridge as compared to (VII) and hence (VIII) which ultimately yields exo epoxide becomes less preferred intermediate and consequently the epoxide mixture obtained is rich in endo isomer (33). Similar results have been reported recently by Sethi et.al.²¹ in their autoxidation reactions of camphene.

Formation of allylic dimers

The allylic radicals (I) and (II) generated from β -pinene can dimerize before undergoing further reaction

and yield isomeric dimers. Similar allylic dimers have been reported earlier²².

Influence of the size of the approaching reagent

In β -pinene (as in the case of α -pinene) the amount of epoxide formed increases if less bulky borate ester, e.g. n-propyl borate, is used. There is almost a threefold increase in the epoxide formed when n-propyl borate was used instead of isopropyl borate [Table 3.1].

In the case of camphene, if we compare the model with those of pinenes, it can be observed that both the endo as well as exo faces are far less hindered. This reflects in vastly increased epoxide yields in the case of camphene, where about 50% of the reaction product is made-up of isomeric epoxides (33 and 34), as compared to about 20% epoxide in the case of β -pinene and only about 7% in the case of α -pinene. The higher amount of epoxide formed in β -pinene, when compared to α -pinene may be due to less steric hinderence at the site of the reaction i.e. at the double bond.

Regioselectivity

From the results of β -pinene epoxidation experiments, it appears that oxygen preferably abstracts the allylic hydrogen leading to allylic oxidation products, than attack the double bond, leading to the norketone formation. In the case of β -pinene this preference is about 18 fold [ratio of allylic products to norketone]. Only when there is no allylic hydrogen available, as in the case of camphene, formation of norketone occurs to an appreciable extent.

EXPERIMENTALSection A[I] Epoxidation of β -pinene (27)

In the modified Vodnar glass reactor, β -pinene [5.65 g, 0.0415 M] and isopropyl borate [2.35 g, 0.0125 M] were mixed. The mixture was epoxidized at $100 \pm 2^\circ\text{C}$, with constant flow of 2-3 lts/hr of dry oxygen. Reaction was stopped after 24 hrs. GLC of aliquots after 8, 12, 18 and 24 hrs was carried out on OV-101 column at 120°C temperature. Reaction product after 24 hrs period was first tested for the presence of peroxides, using KI and acetic acid method. The test showed the presence of peroxides. The sample was refluxed for two hrs with 10% NaHCO_3 solution to destroy peroxides and extracted with ether thoroughly; the absence of peroxides was confirmed in the organic phase which was washed subsequently with distilled water. Dried over anhydrous Na_2SO_4 and the solvent was stripped off to yield a crude reaction product. The reaction product displayed the GLC as shown in Fig. 3.1.

Part of the reaction product [3.1 g] was taken out for distillation. The first fraction (1.6926 g) was distilled out as lower boiling fraction [bp : $90-95^\circ\text{C}/50\text{ mm}$] and the second fraction (0.8517 g) was distilled out as higher boiling fraction containing mostly oxygenated products [bp : $80-100^\circ\text{C}/$

4 mm] leaving behind a residue (0.55 g). The first fraction was readily identified as β -pinene by mixed GLC. The above distillation data showed that unreacted β -pinene was about 54.6%. It showed that the conversion was 45.4%. All the other components from second fraction were separated by column chromatography using basic alumina⁴.

CHROMATOGRAM - 1

Material loaded ... 0.63 g Basic alumina - 25 g
 Column length ... 50 cms Column diameter - 1.5 cms

Fractions	Eluent	Quantity	Remarks based on GLC
1-3	pet.ether	3 x 25 ml	Mixture of 27, 28
4	pet.ether	1 x 25 ml	<u>Compd.28 major</u> (0.05 g)
5-6	pet.ether	2 x 25 ml	Mixture of 28,29 and 17
7-8	pet.ether:Benzene (3:1)	2 x 25 ml	Mixture of 28,29 and 17
9-14	(1:1)	6 x 25 ml	Mixture of 29 and 17.
15-16	Benzene	2 x 25 ml	<u>Compd.29 major</u> (0.12 g)
17-20	Ether	4 x 50 ml	Mixture of 29 and 17

Fr. 4 from chromatogram-1 was found to be 90% pure by GLC [R.T. 4.87]. This compound was identified as β -pinene epoxide (28) from its spectral properties. This was confirmed

by direct comparison [GLC, PMR] with an authentic sample prepared by known method⁶.

Compound (28) : β -pinene epoxide [$C_{10}H_{16}O$]

bp : 98-100°C/27 mm

IR²³ (neat) : 2950, 1420, 1380, 1370, 1260, 1055,
960, 940, 860, 830, 770 and 710 cm^{-1} .

PMR²⁴ ($CDCl_3$) : 0.9 and 1.25 [2s, 3H each] $-C-(\underline{CH_3})_2$
(Fig.3.3) 1.5 to 2.2 [m, 8H] methylene protons
2.65 [m, 2H] oxirane protons

GC : Mass : M^+ at $m/e = 152$.

Fr. 15 + 16 from chromatogram - 1 was found to be 87% pure by GLC [R.T. 6.38]. From its spectral properties this compound was readily identified as Myrtenol (29). This was then confirmed by direct comparison [IR, PMR] with the reported^{8,9} spectral data for Myrtenol.

Compound (29) : Myrtenol [$C_{10}H_{16}O$]

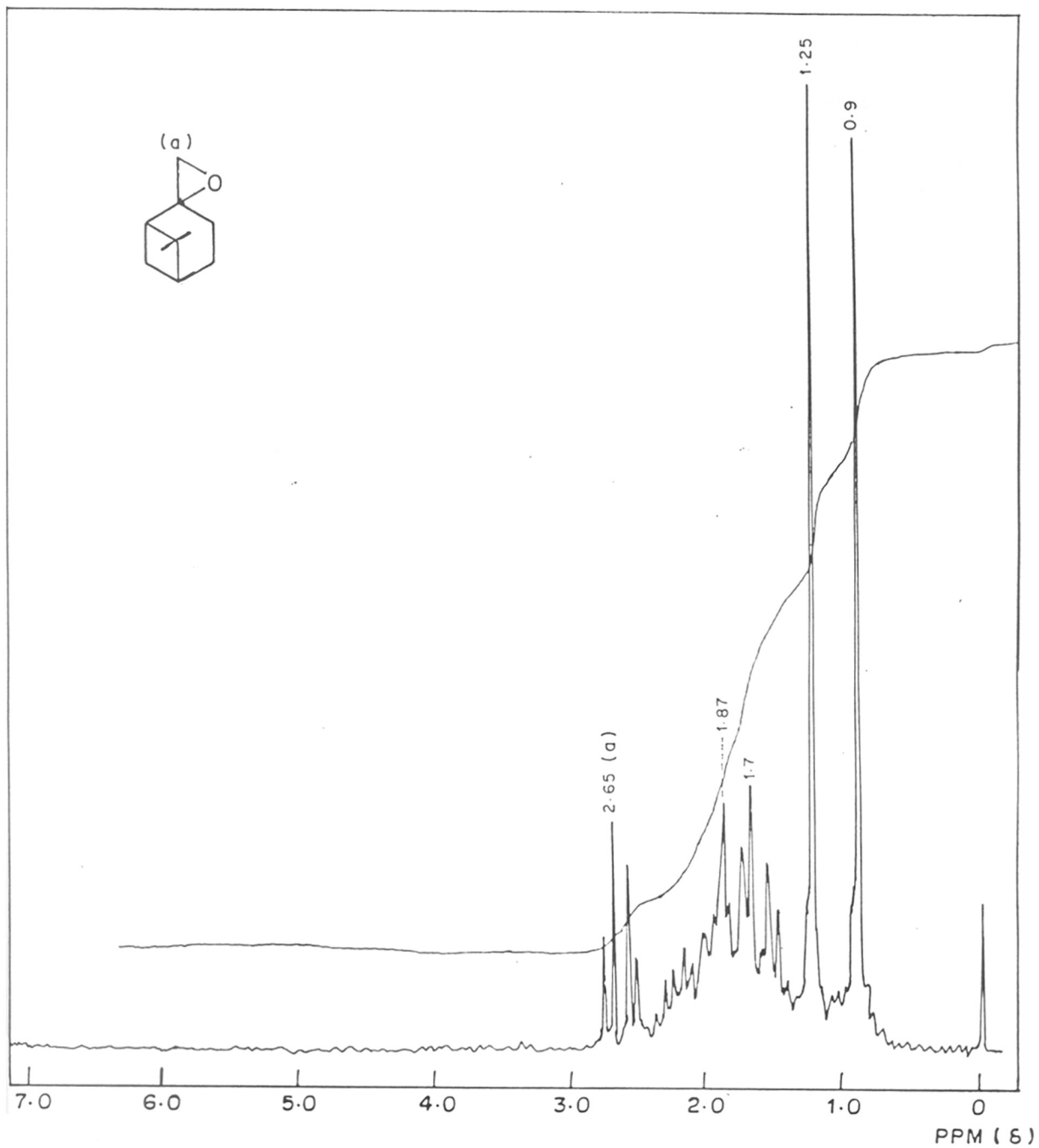
bp : 70-80°C oil bath/1 mm

IR⁹ (neat) : 3470, 2930, 1675, 1452, 1388, 1368,
1265, 1060-40 (br), 900 and 820 cm^{-1} .

PMR⁸ (CCl_4) : 0.93 and 1.4 [2s, 3H each] $-C-(\underline{CH_3})_2$
2.3 [s, 1H] hydroxylic proton exchanged
with D_2O .

4.0 [m, 2H] methylene protons on carbon
carrying hydroxyl group.

5.5 [br, 1H] olefinic proton.

FIG. 3-3. PMR SPECTRUM OF β -PINENE EPOXIDE (28)

Fr.9-14 from chromatogram - 1 was found to be a mixture of two components and was further subjected to separation by using flash-chromatography. The component obtained first in this chromatography was found to be pure by GLC [R.T. 4.59]. This compound was easily identified as Trans-pinocarveol (17) from its spectral properties. This was confirmed by direct comparison [IR, PMR, GLC] with the authentic sample prepared⁵.

Compound (17) : Trans-pinocarveol [$C_{10}H_{16}O$]

bp : 108-10°C/35 mm

IR²⁵ (neat) : 3420 (br), 3000, 2940, 1700, 1650, 1470, 1450, 1380, 1360, 1145, 1020 and 1000 cm^{-1} .

PMR⁸ ($CDCl_3$) : 0.67 and 1.3 [2s, 3 H each] $-C-(\underline{CH_3})_2$
 (Fig.3.4) 4.38 [m, 1H] methine proton α to OH.
 4.78 [s, 1H] }
 4.95 [s, 1H] } Vinylic protons.

Mass : M^+ at $m/e = 152$.

From another experiment of β -pinene epoxidation, the reaction mixture after usual work up was distilled out to remove unreacted olefin. A part (0.4 g) of the remaining reaction mixture was subjected to separation using flash chromatography.

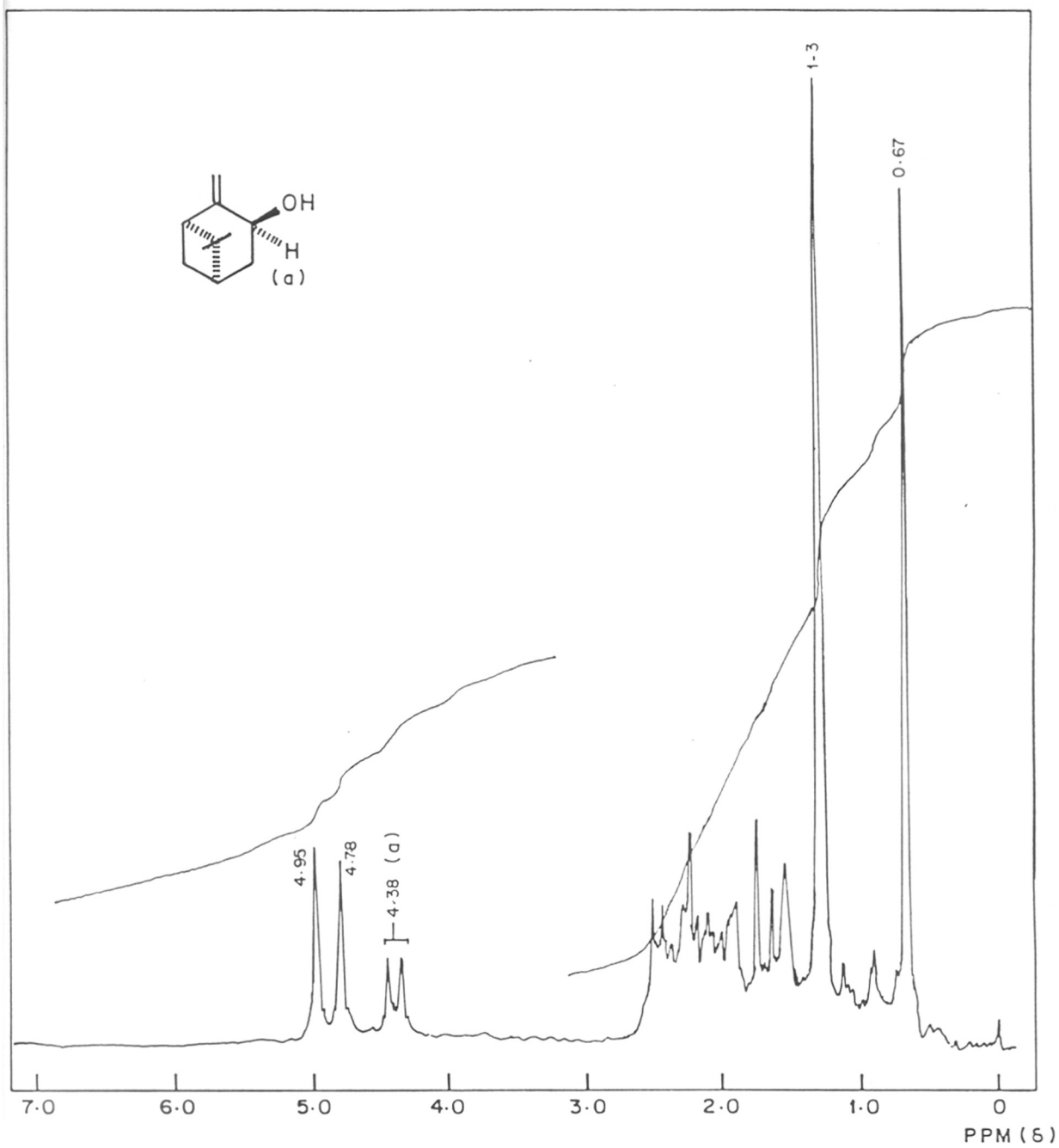


FIG. 3.4. PMR SPECTRUM OF TRANS-PINOCARVEOL (17)

CHROMATOGRAM - 2

Material loaded ... 0.4 g Neutral alumina .. 15 g

Fraction	Eluent	Quantity	Remarks based on GLC
1-5	pet,ether	5 x 5 ml	-
6-20	pet.ether	15 x 5 ml	<u>Compd.31 major</u> (0.07 g)
21-40	pet.ether	20 x 5 ml	<u>Compd.30 major</u> (0.075 g)
41-80	Methanol	40 x 5 ml	Mix.of 28,29,17,30.

Fr. 6-20 from chromatogram - 2 was found to be about 90% pure by GLC. This compound was identified as allylic dimer (31) of β -pinene.

Compound (31) : Allylic dimer of β -pinene [$C_{20}H_{30}$]

Analysis : C = 88.9% and H = 11.1% (theoretical)

C = 88.2%, H = 11.7% (observed)

IR (neat) : 2925, 1640, 1610, 1450, 1380, 1365, 978, 890 and 790 cm^{-1} .

PMR (CCl_4): 0.8 and 1.35 [two sharp signals]

1.46, 1.63 and 2.4 [three sharp signals]

4.06 and 6.7 [two multiplets]

Mass : m/e 270 (M^+), 195 (13%), 181 (15%), 166 (10%), 151 (22%), 135 (100%), 123 (48%), 107 (25%), 93 (28%).

From the above spectral data and the high retention time observed on GLC the compound was characterized as allylic dimer of β -pinene and represented as 31, as one of the possible combinations.

Fr. 21-40 from chromatogram - 2 was found to be pure by GLC. From the spectral properties this compound was easily identified as Nopinone (30). This was confirmed by direct comparison of spectral data [IR, PMR] with the reported for Nopinone.

Compound (30) : Nopinone [$C_9H_{14}O$]

bp : 212-15°C

IR (neat) : 2980, 1700, 1630, 1420, 1380, 1360,
1270, 1080, 960, 820 and 750 cm^{-1} .

PMR⁷ (CCl_4) : 0.91 and 1.33 [2s, 3H each] -C-(CH₃)₂
2.0 to 2.5 [m, 8H]

GC : Mass : M^+ at $m/e = 138$.

[II] Preparation of authentic samples [Chart 3.4]

(1) Preparation of β -pinene epoxide⁶ (28)

In a 100 ml 2 neck RB flask was added 20 ml methanol, 0.8 g potassium bicarbonate, 4 g olefin 27 and 3 g benzonitrile. Contents of the flask were stirred magnetically and then 5 ml 30% H_2O_2 was added dropwise. The reaction mixture was stirred at room temperature for 24 hrs and for additional 5 hrs at

45-50°C. The reaction mixture was cooled and transferred into separatory funnel. Excess per acid was destroyed with (2 x 50 ml) 10% sodium sulphite solution. Then 100 ml saturated solution of sodium bicarbonate was added. Aqueous layer was separated and extracted with 2 x 100 ml ether. The combined organic layer was washed with distilled water (2 x 100 ml) and dried over Na_2SO_4 . Removal of solvent, followed by distillation (60-65°C at 3-4 mm), yielded 3.2 g epoxide. Spectral data was found quite comparable with the reported²⁴ one.

(2) Preparation of trans-pinocarveol⁵ (17)

Freshly prepared lead tetraacetate (14.5 g) was added (10 min) to a stirred suspension of CaCO_3 (1 g) in dry benzene (80 ml) containing β -pinene (9 g). The reaction mixture was stirred at about 60°C (30 min), cooled and the precipitated material was filtered off. The benzene solution was washed with aqueous bicarbonate and water till neutral. Solvent was distilled from dried benzene extract, and the residue (6.4 g) was hydrolyzed (10% alcoholic KOH, 100 ml, at 90-95°C, 3 hrs). Usual workup and careful fractionation of the resulting alcohol yielded trans pinocarveol 17 as the major component. The spectral data of the trans-pinocarveol was in agreement with the reported^{8,25}.

Section B[I] Epoxidation of camphene (32)

In the same glass reactor camphene (32) [6.1 g, 0.0448 M] and isopropyl borate [2.5 g, 0.0132 M] was mixed together. Epoxidation was carried out at $125 \pm 2^\circ\text{C}$. Reaction was monitored by withdrawing aliquots after definite time interval i.e. after 12, 24, 34, 44, 52 and 60 hrs. GLC of aliquots were carried out using OV-101 column at 120°C . Reaction was stopped after 60 hrs. Reaction product, after usual work up, showed the GLC pattern as shown in Fig. 3.2.

4.5 g Reaction product was taken for distillation, 1.8 g of lower boiling fraction [bp : $70-80^\circ\text{C}$ (oil)/35-40 mm] was obtained. From its spectral properties and mixed GLC this fraction was easily identified as mixture of unreacted camphene and tricyclene. The other components of the reaction mixture were separated by column chromatography. Based on above distillation data, the conversion was about 60%.

CHROMATOGRAM - 3

Material loaded	...	2.5 g	Basic alumina	...	100 g
Column length	...	120 cms	Column diameter	..	2.5 cms

Fraction	Eluent	Quantity	Remarks based on GLC
1-2	pet.ether	2 x 25 ml	Compound 32 and tricyclene
3	pet.ether	1 x 25 ml	Mixture of 32,33,34 and 35

continue,

contd...

<u>Fraction</u>	<u>Eluent</u>	<u>Quantity</u>	<u>Remarks based on GLC</u>
4	pet.ether	1 x 25 ml	<u>Mixture of 33 and 34</u> (0.31 g) (TLC single spot)
5-6	pet.ether	2 x 50 ml	Mixture of 33,34,35 and 36.
7-10	pet.ether	4 x 50 ml	Mixture of 33,34,35 and 36.
11-16	pet.ether	6 x 50 ml	Mixture of 33,34,35 and 36.
17	ether	1 x 200 ml	Mixture of 33,34,35 and 36.

Fr. 4 from chromatogram - 3 was found to be a mixture of two compounds in the ratio of 8:2 by GLC. This mixture was identified as endo and exo isomers of camphene epoxide from its spectral properties. This identity was then confirmed by direct comparison [PMR, GLC] with the authentic sample prepared by known method^{17,26}.

Compound (33) and (34) : Camphene epoxide mixture
[C₁₀H₁₆O]

mp : 85-87°C [Lit.²⁷ 86-88°C]

PMR¹⁷ (CDCl₃) : 0.8 and 0.88 [2s, 3H] -C-(CH₃)₂
(Fig. 3.5) 0.92-2.0 [m, 8H]

2.6 [s] }
2.7 [s] } 2H oxirane protons.

Mass : M⁺ at m/e = 152.

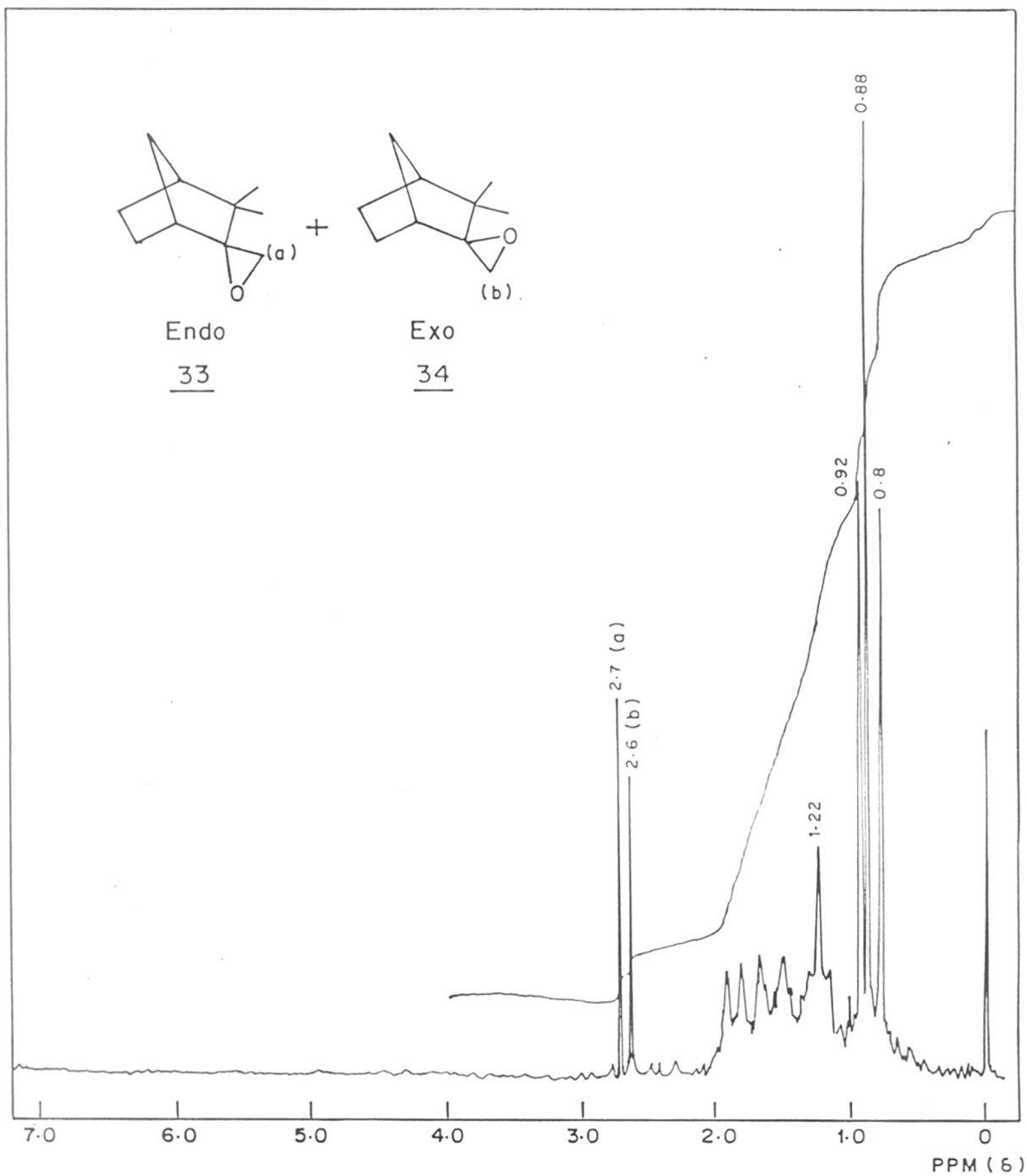


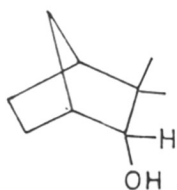
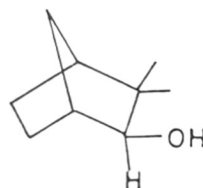
FIG.3-5. PMR SPECTRUM OF CAMPHENE EPOXIDES (33,34)

In order to ascertain the stereochemistry of this epoxide obtained during epoxidation, it was reduced with lithium in ethylenediamine.

Reduction of camphene epoxide (obtained from epoxidation) by lithium in ethylenediamine²⁸.

To a three-necked flask having a magnetic bar and nitrogen inlet was added camphene epoxide (0.2 g) and anhydrous ethylene diamine (10 ml). To this lithium (0.15 g) was added at room temperature under vigorous stirring. The temperature was maintained at 50°C for 1 hr. Reduction was continued till a blue purple colour persisted. The reaction mixture was cooled and water (10 ml) was added to destroy the excess reagent. Then it was extracted with tetrahydrofuran (3 x 100 ml) and dried over Na₂SO₄. THF was removed by distillation. Total material obtained was purified by chromatography over silica gel. It was eluted first with pet. ether (~125 ml) and then with ether (~100 ml). Material collected from ether was pure alcohol from its IR spectrum.

This alcohol from its PMR²⁹ spectrum was found to contain about 80-82% of endo-2,3,3-trimethyl-2-norbornanol 37 and about 18% of the exo-isomer 38.

3738

by direct comparison [IR, PMR, GLC] with authentic sample of camphenilone prepared by known method^{15,16}.

Compound (35) : Camphenilone [$C_9H_{14}O$]

mp : 40-41°C

IR (neat) : 1730-1735 cm^{-1} C=O

PMR ($CDCl_3$): 1.025 and 1.05 [2s, 3H each] -C-(CH_3)₂

Mass : M^+ at m/e = 138.

Fr.17 from chromatogram - 3 was further subjected to separation by column chromatography.

CHROMATOGRAM - 5

Material loaded ... 0.8 g Neutral alumina ... 40 g
Column length ... 50 cms Column diameter ... 1.5 cms

Fractions	Eluent	Quantity	Remarks based on GLC
1-5	pet.ether	5 x 25 ml	Mixture of 33,34,35 and 36
6-8	pet.ether:benzene (8:2)	3 x 25 ml	Mixture of 33,34,35 and 36
9-10	(6:4)	2 x 25 ml	Mixture of 33,34,35 and 36
11-13	Benzene	3 x 30 ml	Mixture of 33,34,35, and 36
14	Methanol	1 x 100 ml	<u>Major 36</u> (0.135 g)
15	Ether	1 x 100 ml	Mixture of 36 and 35.

Fr. 14 from chromatogram - 5 was found to be 80% pure by GLC. This compound was identified as endo-camphanol (36) from its spectral properties. This was confirmed by comparing its spectral properties with that of reported¹⁸ for endo-camphanol.

Compound (36) : Endo-camphanol [$C_{10}H_{18}O$]

mp : 78-79°C (Reported 81°C)

IR¹⁸ (neat) : 3400, 2930, 1460, 1370, 1358, 1030,
1020 and 980 cm^{-1} .

PMR¹⁸ (CCl_4): 0.93 and 1.0 [2s, 3H each] C-(CH₃)₂
2.43 [br. signal, 1H], exchanged with D_2O
-OH.

3.43 [d, 2H] methylene protons on carbon
carrying hydroxyl group.

Mass : M^+ at $m/e = 154$.

[II] Preparation of authentic samples [Chart 3.4]

1] Preparation of camphene epoxide by using
perbenzoic acid

(a) Preparation of perbenzoic acid²⁶

Sodium metal (3 g) was added in portions to methanol (100 ml) in a dry conical flask (500 ml) equipped with a reflux condenser and mechanical stirring. When all the sodium was dissolved, resulting solution was cooled in ice-salt

mixture and benzoyl peroxide (25 g) in chloroform (50 ml) was added with stirring. Some more (50 ml) chloroform was added and the flask was kept in an ice-salt mixture (5-10 minutes) when it became milky. It was transferred to a separating funnel and extracted with ice-cold water (300 ml) to remove sodium perbenzoate. The aqueous layer was extracted twice with portions of (100 ml) cold CHCl_3 to remove methyl benzoate. Then, to the aqueous layer 1 N H_2SO_4 [125 ml] was added till the solution was clearly acidic and extracted with cold chloroform [3 x 100 ml]. Chloroform layer containing perbenzoic acid was separated, dried over anhydrous Na_2SO_4 and was estimated²⁶ for per acid content using standard sodium thiosulfate.

(b) Epoxidation of camphene using perbenzoic acid¹⁷

To the chloroform solution of perbenzoic acid [\sim 300 ml, 4.8 g] was added 3 gms camphene³² in 25 ml chloroform and kept at \sim 6-7°C for about 60 hrs. [Monitored by TLC and GLC]. The reaction was continued till all the olefin was consumed. The reaction mixture was transferred to a separating funnel. Washed with (2 x 100 ml) of 10% Na_2CO_3 solution to remove excess per acid present. Finally washed with distilled water (2 x 100 ml). Dried over Na_2SO_4 . Removal of solvent under reduced pressure followed by distillation yielded 2.4 g epoxide. GLC showed 2 peaks in the ratio of 60:40. From the PMR spectrum it appeared to be 60:40 mixture of exo and endo

camphene epoxides. These PMR values were in agreement with those reported in the literature¹⁷.

2] Preparation of camphenilone (35) from camphene (32)

(a) Camphene to ω -nitrocamphene¹⁵

To an ice-cooled and stirred mixture of pet. ether solution of Camphene (8.2 g, 0.06 mole, 20 ml) and aqueous NaNO_2 (66 g, 0.95 mole, 40 ml), AcOH-water (100:1, 41 ml) was added in drops over a period of one day. The organic layer was separated and the aqueous layer was extracted with pet. ether several times ($\sim 4 \times 25$ ml). The combined extracts (~ 125 ml) were dried and solvent was evaporated. The viscous residue was triturated with methanol (5 ml), left overnight at 5°C and the crystals collected to give ω -nitrocamphene (3.3 g) mp 64°C [Lit.¹⁵ mp. $64-66^\circ\text{C}$].

(b) ω -Nitrocamphene to camphenilone (35)¹⁶

ω -Nitrocamphene (3.1 g) and alcoholic base (8.5 g KOH in 12 ml ethanol and 85 ml water), was refluxed for 20 hrs. The mixture was then subjected to steam distillation to remove camphenilone [1.95 g], mp $37-38^\circ\text{C}$ [Lit.¹⁶ mp $38-38.5^\circ\text{C}$].

PREPARATION OF AUTHENTIC SAMPLES:

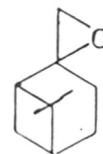
1



27

BENZONITRILE

Alk. H₂O₂



28

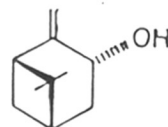
2



27

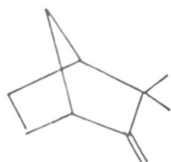
1) LTA

2) HYDROLYSIS



17

3



32

PERBENZOIC ACID

0-5°, 60 hr



33

ENDO-EPOXIDE

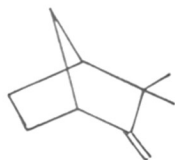
+



34

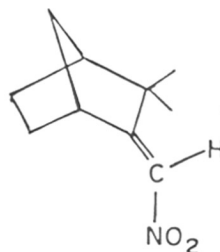
EXO-EPOXIDE

4

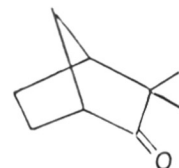


32

NaNO₂ - AcOH



KOH
STEAM DIST.



35

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SUMMARY

SUMMARY

Based on the work presented in this thesis, the results can be summarized as follows :

- [1] Borate esters can be considered as good catalyst for epoxidation as they are more stable and safe compared to hydroperoxides. These can be prepared more easily and in near quantitative yields.
- [2] Generally the epoxide formation increases with rise in reaction temperature till it reaches an optimum level, characteristic for a particular olefin.
- [3] There are two competing reactions, i.e. the addition of boron peroxides to the double bond yielding epoxides and the abstraction of allylic hydrogen leading to further products, viz. allylic alcohols and ketones.
- [4] In the case of olefins where double bond is less hindered, such as cyclohexene and car-3-ene more epoxide is obtained whereas in the case of α -pinene where double bond is considerably more hindered, epoxide formation becomes a less favoured pathway.
- [5] At higher temperatures the amount of allylic ketone formed is more as compared to allylic alcohol, indicating the possibility of further oxidation of allylic alcohol to ketone.

- [6] In the case of α -pinene where double bond is considerably hindered the bulk of the attacking borate ester also governs the reaction pathway to a great extent.
- [7] In the case of terpenes with exocyclic double bond such as β -pinene and camphene, oxygen attacks the double bond probably forming dioxetane type intermediates, these intermediates finally lead to norketones. However, it seems that this is a less preferred pathway and wherever there is an allylic hydrogen present, its abstraction becomes a preferred pathway leading to allylic oxidation products.
- [8] It is interesting to note that the epoxidation of camphene yields camphene epoxide [50% of the reaction product, with 60% conversion] having the endo- and exo-isomers in the ratio of 80:20. Whereas, the reported epoxidation of camphene with peracids gives the epoxides in the ratio of 40:60 respectively. Hence, the present method can be considered as a preparative route for obtaining the endo-epoxide.

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NCL, Pune-411008.
9th March, 1989

S.D. Deshpande
(S.D. Deshpande)