Section A:

Synthesis of 2,6-dimethyl-\(\Delta^7\)-octen-4-one:

This acyclic monoterpene ketone (XLVII) occurs in conjunction with its dehydro derivative, tagetone (A), limonene etc. in the flowers of *Tagets glandulifera*. It was isolated by Jones and Smith (120) in 1925 and constitution (XLVII) was suggested for the ketone on the basis of oxidation experiments (120).

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{CH} - \text{CH}_2 - \text{C} - \text{CH}_2 - \text{CH} - \text{CH} = \text{CH}_2 \\
& \quad \quad \quad \text{(XLVII)}
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{CH} - \text{CH}_2 - \text{C} - \text{CH} = \text{C} - \text{CH} = \text{CH}_2 \\
& \quad \quad \quad \text{(A)}
\end{align*}
\]

Treatment of the ketone (XLVII) with potassium permanganate in acetone solution, yielded in addition to formic acid, acetic acid and isovaleric acid (B), a ketonic acid (C) (\(\beta\)-isovaleryl-\(\alpha\)-methyl propionic acid).

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{CH} - \text{CH}_2 - \text{C} - \text{CH}_2 - \text{CH} - \text{CH} = \text{CH}_2 \\
& \quad \quad \quad \text{KMO}_{4} \\
\text{H}_3\text{C} & \quad \text{O} \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{CH} - \text{CH}_2 - \text{C} - \text{CH}_2 - \text{CH} - \text{COOH} \\
& \quad \quad \quad \text{(C)}
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{CH} - \text{CH}_2 - \text{COOH} \\
& \quad \quad \quad \text{H}_3\text{C} \quad \text{CH} - \text{CH}_2 - \text{COOH} \\
& \quad \quad \quad \text{HCOOH} \quad \text{CH}_3\text{COOH}
\end{align*}
\]
The structure of the ketonic acid (C) was established through synthesis (121).

Further chemical evidence in favour of formulation (XLVII) was sought through its conversion to 2:6-dimethyl-Δ^7-octan-4-one (E) via the carbinol (D), the structure of the former compound being well established through synthesis (122).

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \quad \text{CH}_3 \\
\text{H}_3\text{C} \quad \text{CH} - \text{CH}_2 - \text{C} - \text{CH}_2 - \text{CH} - \text{CH} = \text{CH}_2 \\
\text{H}_3\text{C} & \quad \text{OH} \downarrow \\
\text{H}_3\text{C} \quad \text{CH} - \text{CH}_2 - \text{CH} - \text{CH}_2 - \text{CH} - \text{CH}_2 - \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{O} \downarrow \\
\text{H}_3\text{C} \quad \text{CH} - \text{CH}_2 - \text{C} - \text{CH}_2 - \text{CH} - \text{CH}_2 - \text{CH}_3 \\
\end{align*}
\]

In the absence of any synthetic evidence, the present studies suggest an unambiguous synthesis of dl-2:6-dimethyl-Δ^7-octen-4-one which further corroborates the formulation (XLVII).

The following flowsheet represents the reactions involved in the synthesis:
Claisen rearrangement of allyl vinyl ether (45, 46) obtained by transetherification of an appropriate allylic alcohol with ethyl vinyl ether in presence of mercuric acetate (47) has been utilised as a key step in the present investigations.

Crotyl vinyl ether (XLIX) was obtained by mercuric acetate catalysed (47) vinyl transetherification of crotyl alcohol in 50.8 % yield. I.R. spectrum displayed typical vinyl ether absorption at 1639, 1613 and 1190 cm⁻¹. The crotyl vinyl ether (XLIX) when subjected to Claisen rearrangement (45, 46) under nitrogen in a sealed tube immersed in an oil bath at temperature 145-50 °C for 30 minutes generated 3-methyl-pent-4-en-1-al (L) in 88.8 % yield as a colourless oil. Compound (L) exhibited characteristic
I.R. absorption spectrum bands at 1720 cm\(^{-1}\) (-CHO) and 988, 910 cm\(^{-1}\) (-CH=CH\(_2\)). The aldehyde (L) was characterised through its 2:4-dinitrophenyl hydrazone which melted at 92°C (recrystallised from ethanol).

The aldehyde (L), on oxidation with silver oxide \((123)\) (prepared from silver nitrate) was converted to its corresponding acid, 3-methyl-pent-4-en-1-oic acid (LI) in 77.5% yield. Its I.R. absorption spectrum showed peaks at 910, 988 cm\(^{-1}\) (-CH = CH\(_2\)) and 1700 cm\(^{-1}\) (-COOH). The acid (LI) on treatment with thionyl chloride gave the corresponding acid chloride (LII) in 97.4% per cent yield. The compound (LII) on subjecting to Grignard reaction with cadmium di-isobutyl furnished the title compound (XLVII) in 42.9% per cent yield.

The synthetic ketone (XLVII) was characterised through its I.R. absorption spectrum which showed peaks at 910, 988 cm\(^{-1}\) (-CH = CH\(_2\)) and 1702 cm\(^{-1}\) (-C = O).

The synthetic ketone gave the semicarbazone derivative which melted at 92° after recrystallisation from ethanol. Lit. \((124)\) reports the melting point 92.5°.
Section B:

Synthesis of 1-acetyl-4-isopropenyl-1-cyclopentene:

A new ketone \( \text{C}_{10} \text{H}_{14} \), having kummel and anise-like odour from Spanish Eucalyptus Globulus was isolated by Schmidt who suggested the constitution (A), for the ketone (125).

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \\
\text{C} & \quad \text{CH}_3 \\
\text{C} & \quad \text{CH}_3 \\
\text{C} \quad \text{C} \\
\text{C} \quad \text{H}_3
\end{align*}
\]

(A)

The salient features of the structure (A) are the presence of acetyl group at carbon 1 and the isopropylidene function at position 4 in the cyclopentene skeleton. The position 1,4 of the substituents and the presence of the two ethylenic linkages were established by its hydrogenation over nickel to give 1-acetyl-4-isopropyl cyclopentane (B), which on oxidation with sodium hypobromite gave 4-isopropyl cyclopentane carboxylic acid (C) (125).
Conjugation of one double bond with the keto group was suggested not only by the molecular refractivity, but also by the formation of an oxide by treatment with alkaline hydrogen peroxide (125).

The chemical reduction of the naturally occurring ketone using sodium and moist ether, followed by oxidation of the resulting alcohol, afforded an unsaturated ketone, pinolone which has generally been considered to be a mixture of (D) and (E).
On this basis it was concluded that the natural ketone was either l-acetyl-4-isopropylidene-l-cyclopentene (A) or l-acetyl-4-isopropenyl-l-cyclopentene (LIII). Schmidt favoured the constitution (A) for the ketone because of its optical inactivity (125).

However, Woblinsky and Barker, who synthesised l-acetyl-4-isopropenyl-l-cyclopentene (126) found it to be identical with the natural ketone. They revised the formulation of the ketone proposed by Schmidt.

The evidence for the isopropenyl side chain in the natural ketone was provided by ozonolysis which afforded formaldehyde, isolated as 2:4-dinitrophenylhydrazone. Chromatography of this derivative demonstrated the absence of detectable amounts of acetone 2:4-dinitrophenylhydrazone. The structure (LIII) is further confirmed by infra-red, ultra-violet and nuclear magnetic resonance spectral studies of the ketone (126).

The first synthetic route towards its structure investigated by Woblinsky and Barker as outlined below, began with acid catalysed hydrolysis of limonene oxide (F), Cleavage of the resulting diol (G) with sodium meta periodate led to the keto aldehyde (H). It was anticipated that the cyclisation of the keto aldehyde (H) would lead to either
the unsaturated aldehyde (I) or the unsaturated ketone (LIII) while the seven membered ring ketone (J) might also be derived from (H), it was never seriously considered in view of the precedent for condensations giving five membered rings (126):
Recently Wohlinsky and coworkers (127) have reported that the cyclisation of the intermediate ketoaldehyde (H) in presence of piperidine and dilute acetic acid yields \( \alpha - \beta \)-unsaturated aldehyde (I). However, the cyclisation of the compound (I) in ether with base mainly gives 1-acetyl-4-isopropenyl-1-cyclopentene (LIII).

The present route makes use of an easily accessible starting material 6-methyl-hept-5-ene-2-one. The following chart depicts the sequence of the reactions employed as:
Ketalisation of 6-methyl-hept-5-en-2-one (XVIII) with ethylene glycol in refluxing benzene in the presence of catalytic amount of p-toluene-sulphonic acid (57) afforded the corresponding dioxolane derivative (LIV) in 98 per cent yield. Oxidation of the ketal (LIV) with selenium dioxide was carried out exactly according to the procedure described in literature (123) and the crude aldehyde obtained on purification by treatment with water solution of sodium sulphite heptahydrate and sodium bicarbonate (123) furnished a pure product (LV) in 35 per cent yield. The ketal aldehyde (LV) exhibited characteristic I.R. absorption bands at 1685 cm$^{-1}$ ($\alpha,\beta$-unsaturated
The compound (LV) was subjected to lithium aluminium hydride reduction to give ketal alcohol (LVI) in 73.5 per cent yield. It showed I.R. absorption peaks at 3460, 1050 cm\(^{-1}\) (-OH) and 1065 cm\(^{-1}\) (ketal). The allylic alcohol (LVI) when treated with ethyl vinyl ether under the catalytic influence of freshly crystallised mercuric acetate (45,46) afforded 2-methyl-6,6-ethylenedioxy-2-heptenyl vinyl ether (LVII) in good yield. It was characterised through its I.R. absorption spectra which showed peaks at 1639, 1613 and 1190 cm\(^{-1}\) (vinyl ether), 1065 cm\(^{-1}\) (ketal).

The vinyl ether (LVII) thus obtained, on pyrolysis (47) under nitrogen, in a sealed tube provided the ketal aldehyde (LVIII) in 80 per cent yield. It gave characteristic I.R. absorption peaks at 1720 cm\(^{-1}\) (-CH\(_2\)), 1065 (ketal) and 890 cm\(^{-1}\) (-CH\(_3\)).

The aldehyde (LVIII) gave its semicarbazone which melted at 136-37 after recrystallisation from ethanol. The ketal aldehyde (LVIII) was deketalised with dilute hydrochloric acid in acetone solution at room temperature and the keto aldehyde (LIX) thus obtained was characterised through its 2:4-dinitrophenyl hydrazone derivative, m.p. 145-46\(^{\circ}\), Lit. reports m.p. 146-47\(^{\circ}\) (126).

Cyclisation of the keto aldehyde (LIX) was conducted according to the conditions laid down by Wolinsky and Barker (126).
when 1-acetyl-4-isopropenyl-1-cyclopentene (LIII) was obtained.

The synthetic ketone was characterised through its I.R. absorption spectrum which showed characteristic peaks at 1660 cm\(^{-1}\) (\(\mathrm{C}=\mathrm{O}\)), 1618 cm\(^{-1}\) (conju.) and 890 cm\(^{-1}\) (\(\mathrm{R}_1 \mathrm{C} = \mathrm{CH}_2\)).

However, a very weak band at 2705 cm\(^{-1}\) was observed which indicated the presence of the aldehyde (I) may be in small amounts.

The synthetic ketone (LIII) gave 2:4-dinitrophenyl hydrazone derivative which melted at 181\(^\circ\) after crystallisation from ethanol. Conia and Faget (128) who recently prepared this compound report the melting point of its D.N.P. 179-180\(^\circ\).