CHAPTER VI

SYNTHESSES OF THE ISOMERS OF (+) AR.-CURCUMENE
Ar. Curcumene, the monocyclic sesquiterpene hydrocarbon occurs in conjunction with its dihydro derivative, \( \alpha \)-curcumene as a major component in the oil of rhizomes of curcuma aromatica salisb (62,93,94).

On treatment with hydrogen chloride \( \alpha \)-curcumene(XXVI) afforded a liquid mono-chloride (A) which gave cadalene (B) on dehydrogenation with selenium (95). Oxidation with manganese dioxide and sulphuric acid (95) afforded terephthalic acid (C) and p-toluic acid (D), thus indicating the presence of benzene nucleus with long side chain containing the ethylenic linkage and attached in the p-position to the methyl group.
The position of the ethylenic linkage in α-curcumene skeleton was indicated by a careful study of the products obtained by ozonolysis of natural hydrocarbon. From the nature of oxidation products so formed, it was concluded (95) that α-curcumene is a mixture of (XXXVIa) and (XXXVIb) with (XXXVIa) predominating.

Several syntheses (96-99) have been reported for (+)-α-curcumene but in all these cases the final product was an inseparable mixture of (XXXVIa) and (XXXVIb). Simonsen et al (96) prepared the hydrocarbon by Grignard reaction of methyl magnesium iodide with methyl δ-p-tolyl-n-hexoate (E) resulting in the formation of both isomers (XXXVIa) and (XXXVIb).
The sequence of reactions employed for the other syntheses (97, 98) for α-curcumene isomer (XXXVIa) are given below:

\[
\begin{align*}
&\text{(Methyl heptene) -CH-0-0-CH-CH_3} \\
&\text{(-Toluene Sulphonate of Methyl heptenol)}
\end{align*}
\]

These syntheses for the isomers (XXXVIa) admit uncertainty in the position of the side chain double bond in a isopropenyl or isopropylidene form. In the synthetic (+)-curcumene it depends on the constitution of the methyl heptene employed which is probably mostly the isopropylidene derivative.

Howard and Rao (99) obtained (+)-curcumene and (+)-α-curcumene isomers (isopropylidene and isopropenyl) starting from 4-(p-tolyl)-n-pentyl bromide (XXVIII). The sequence of reactions employed is as under:
Farther, the absolute configuration of natural α-circumene has been established as shown (F) (99).

In the present investigations the unambiguous syntheses of the two isomers, isopropylidene (XXXVIa) and isopropenyl (XXXVIb) of (+) α-circumene separately and exclusive of one another have been achieved. The new approach utilizes the Wittig method (81) which results in the fixation of double bond even when it occupy energetically unfavourable position.
Synthesis of isopropylidene isomer (XXXVIa):

4-(p-Tolyl)-n-valeraldehyde (VI) prepared in the synthesis of (+) nuciferal (Chapter I, p. 20), was subjected to Wittig reaction (81) with isopropyltriphenylphosphonium iodide in dimethyl sulphoxide in presence of sodium hydride, when hydrocarbon (XXXVIa) was formed in 61 per cent yield. The synthetic hydrocarbon (XXXVIa) was characterised through IR spectrum which showed characteristic peaks at (77), 1660 (triply substit. double bond), 1445, 1385 (C-CH₃) and 815 (triply substit. double bond and aromatic bands superimposed).

\[\text{Synthesis of isopropenyl isomer (XXXVIIb):}\]

Alkylation of ethyl-acetoacetate with 3(p-tolyl)-n-butyl bromide (80) in the presence of potassium tert.butoxide gave 1-methyl-α-carboethoxy- (p-tolyl)-pentyl ketone (XXXVII) in 57.5 per cent yield. Hydrolysis of β-ketoester (XXXVII) with alcoholic potassium hydroxide and subsequent decarboxylation with copper powder furnished
1-methyl-$S$-(p-tolyl) pentyl ketone. This ketone (XXXVIII) was characterised through IR spectrum (77) and semicarbazone derivative (94). The Wittig reaction (81) with methyltriphenylphosphonium iodide on the ketone (XXXVIII) in presence of methyl sulphinyl carbanion under nitrogen atmosphere gave the hydrocarbon (XXXVIb) in 63 per cent yield. The hydrocarbon (XXXVIb) was characterised through IR spectrum (77) which showed characteristic peaks at 1660, 885 (terminal methylene), 1460, 1385 (C-CH₃), 817 and 725 (1:4 benzene substitution).