CHAPTER I

SYNTHESIS OF (±) TRANS NUCIFERAL
Nuciferal, a monocyclic aromatic sesquiterpene aldehyde was isolated, along with nuciferol, in dextro form, from the wood oil derived from the wood of *Torreya nucifera* sieb. et Zucc. (67).

Its carbon skeleton was proved by oxidation and reduction experiments. The spectral data supports the presence of \( \alpha - \beta \)-unsaturated aldehyde system contained in an \( \alpha \)-curcumene skeleton. The Wolf-Kishner reduction of nuciferal (I) afforded a hydrocarbon (A), which was identical with natural aromatic \( \alpha \)-curcumene as checked by infrared spectrometry and gas chromatography (58).
The configuration at the side chain double bond was deduced from the NMR spectral data (58). The natural nuciferol was assigned a cis-isomer configuration and alcohol obtained from nuciferal by lithium aluminium hydride reduction, a trans-isomer configuration:

![Structural formulas](image)

- Natural nuciferal (trans)
- Natural nuciferol (cis)
- Alcohol reduced from nuciferal (trans)

The configuration of the asymmetric centre was established by the ozonization of nuciferol which yielded S-(+)-α-methylglutaric acid and this was identical with an authentic sample (58).
The present investigations report a synthesis of (+) nuciferal with the trans geometry at the conjugated ethylenic bond in the side chain. The flow sheet given below illustrates the sequence of reactions:

1. \((\text{III})\) to \((\text{IV})\)
2. \((\text{IV})\) to \((\text{V})\)
3. \((\text{V})\) to \((\text{VI})\)
4. \((\text{VI})\) to \((\text{VII})\)
5. \((\text{VII})\) to \((\text{VIII})\)
6. \((\text{VIII})\) to \((\text{I})\)

\(+\) α-methyl glutaric acid
The starting material 4-(p-tolyl)-n-valeric acid (IV) (59,60) was converted via its acid chloride to 4-(p-tolyl)-N-methyl-n-valeranilide by treatment with N-methylaniline in pyridine solution in 86.5 per cent yield. The latter (V) when reduced with lithium aluminium hydride following the conditions laid down by Nigam and Weedon (61) furnished 4-(p-tolyl)-n-valeraldehyde (VI) in 44.4 per cent yield. The aldehyde (VI) was characterised through its IR characteristic absorption bands at 2720 (aldehydic C-H) and 1720 (C=O) cm⁻¹ (77) and by the formation of yellow 2,4-dinitrophenyl-hydrazone (62).

The aldehyde (VI) was submitted to the modified Wittig reaction (44) with ethyl-diethylphosphonopropionate in presence of sodium hydride, using diethylene glycol dimethyl ether as solvent, when 2-methyl-6-(p-tolyl)-trans-2-heptencarboxylate (VII) was obtained in 72.8 per cent yield. It has been reported (47) that Wittig reaction with an electron acceptor group at the ylid carbon of the phosphorylde molecule tend to be stereospecific, yielding only trans isomer, which has been explained on the basis of electronic density distribution and less steric interaction of substituents in the transition state. The formation of trans product (VII) is further supported by the work of Wadsworth et al (48), who reported that only trans olefins were formed by the action of phosphonate carbanion in
IR Spectra of (±)Trans Nuciferal & (±)Trans Nuciferol
modified Wittig reaction with aldehydes.

The unsaturated ester (VII) was reduced with lithium aluminium hydride when 2-methyl-6-(p-tolyl)-trans-2-hepten-1-ol (II) was obtained in 80 per cent yield. Its characteristic absorption peaks in IR and UV spectra are comparable with the natural occurring nuiferol. The IR spectrum showed characteristic peaks at 3350, 1518 and 818 cm$^{-1}$. (Lit. (58) 3340, 1518 and 819 cm$^{-1}$). The UV spectrum showed peaks at 255, 265 and 275 mp (log$\varepsilon$ 2.11, 2.60, 2.75) (Lit. (58) 252.5, 259, 264.5, 273 and 276 mp) (log$\varepsilon$ 2.57, 2.58, 2.75, 2.79 and 2.75).

The allylic carbinol (II) was smoothly oxidised with active manganese dioxide (63,64) to 2-methyl-6-(p-tolyl)-trans-2-hepten-1-al. The identity of the synthetic product (I) with the natural compound was established through comparison with IR and UV spectra. The IR spectrum showed peaks at 2720, 1690, 1650, 1520 and 818 cm$^{-1}$. (Lit. (58) 2720, 1690, 1645, 1518, and 818 cm$^{-1}$). The UV spectrum showed peaks at 222, 229, 265 and 275 mp (log$\varepsilon$ 4.17, 4.14, 2.93 and 2.90) (Lit. (58) 222.5, 229, 264.5, 266.5, 273 and 279.5 mp) (log$\varepsilon$ 4.19, 4.17, 2.97, 2.94, 2.96 and 2.50).

The 2,4-dinitrophenylhydrazone of (I) was prepared by the sulphuric acid method and crystallised from ethanol m.p. 124$^\circ$. (Lit. (58) records m.p. 139$^\circ$, due to dextroform).