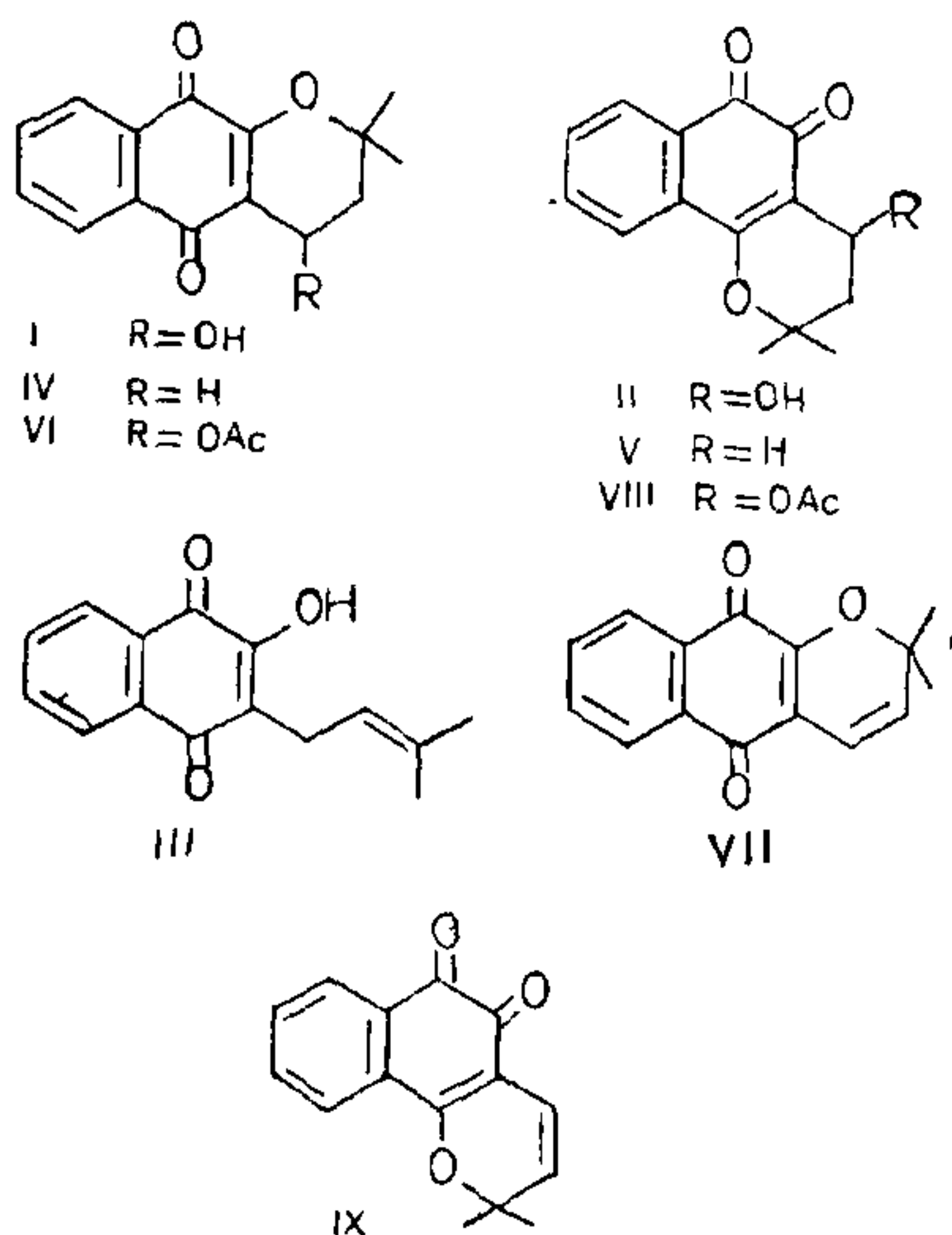


SYNTHESIS OF 4-HYDROXY- α -LAPACHONE AND ITS β -ISOMER

RECENTLY Duarte Weinberg *et al.*¹ reported the isolation of 4-hydroxy- α -lapachone (I) along with other compounds from the trunk wood of *Zeyhera tuberculosa* (Vell) Bur. The assigned structure was based on chemical and spectral studies. We have now carried out the synthesis of 4-hydroxy- α -lapachone (I) and its β -isomer *viz.*, 4'-hydroxy- β -lapachone (II) starting from lapachol (III). The synthesis involves the successful extension of the allylic acetoxylation first carried out by Barton *et al.*² during the course of synthesis of β -amyrin using N-bromosuccinimide and lead tetraacetate. Recently Talapatra *et al.*³ reported the failure of this reaction when carried out with dihydroxanthyletin.



Lapachol (III) was cyclised with HCl in glacial acetic acid and conc. H_2SO_4 ⁴ separately to give α -lapachone (IV) and β -lapachone (V) respectively. IV when refluxed with N-bromosuccinimide and lead tetraacetate in dry benzene furnished 4-acetoxy- α -lapachone (VI) in good yields. VI was then hydrolysed with dil. HCl to give 4-hydroxy- α -lapachone (I). The structure of the compound I was confirmed by converting it into dehydro- α -lapachone (VII) with *p*-toluene sulphonic acid and dry benzene. For comparison the authentic sample of the compound VII was prepared by the dehydrogenation of α -lapachone with DDQ⁶. Further the compound VII was also obtained by dehydrogenation of I with conc. HCl. I on acetylation gave compound VI. The compound I and its acetate (VI) agreed with the natural sample of I and its acetate (VI) respectively on TLC. The

IR, UV and NMR spectra of I and VI agreed with the reported values¹ of the natural sample of I and its acetate (VI).

β -lapachone (V) was similarly refluxed with N-bromosuccinimide and lead tetraacetate in dry benzene to give 4'-acetoxy- β -lapachone (VIII) as major product. VIII was hydrolysed with dil. HCl to give II. The structures of II and VIII were assigned on the basis of spectral and chemical studies.

II when dehydrated with *p*-toluenesulphonic acid in dry benzene gave VII, instead of expected dehydro- β -lapachone (IX). The latter is very prone to rearrange to the α -isomer (VII), especially if a trace of acid is present⁶.

Details of this work will be published elsewhere.

The authors wish to express their grateful thanks to Professor G. G. de Oliveira for the supply of natural sample of 4-hydroxy- α -lapachone and its acetate. One of the authors (R. B. G.) is grateful to the Centre of Advanced Studies in Chemistry, Department of Chemistry, University of Delhi, for the award of a fellowship.

Department of Chemistry,
University of Delhi,
Delhi 110 007, India,
January 20, 1977.

R. B. GUPTA,
R. N. KHANNA.

1. Duarte Weinberg, M. D. L., Gottlieb, O. R. and Oliveira, G. G., *Phytochemistry*, 1976, 15 (4), 570.
2. Barton, D. H. R., Lier, E. F. and McGhie, J. F., *J. Chem. Soc., C*, 1968, p. 1031.
3. Talapatra, B., Mukhopadhyay, S. K., Chaudhuri, M. K. and Talapatra, S. K., *Indian J. Chem.*, 1976, 14 (B), 129.
4. Gupta, S. R., Malik, K. K. and Seshadri, T. R., *Ibid.*, 1969, 7, 457.
5. Hooker, S. C., *J. Chem. Soc. (Trans.)*, 1892, 61, 611.
6. Burnette, A. R. and Thomson, R. H., *J. Chem. Soc., C*, 1967, p. 1261.

PHOTOOXIDATION OF PTEROSTILBENE FROM *PTEROCARPUS MARSUPIUM* ROXB.

Pterocarpus marsupium Lam. Leguminosae is a commercial timber available in the Telangana region of Andhra Pradesh (India), known to be resistant to termites and used in the treatment of diabetes¹. We now report the isolation of pterostilbene from *Pterocarpus marsupium* and the photooxidation of its derivatives.

The heartwood of this plant on extraction with petroleum ether (60-80°) gave 0.04% of a colourless compound (I) with m.p. 87°. Oxidation of its O-acetyl derivative (II) (m.p. 135°)² with potassium permanganate in acetone gave *p*-acetoxy benzoic acid (m.p. 185°)² and 3,5-dimethoxy benzoic acid (m.p. 184°)². Its m.p., its superimposable IR spectrum and

its undepressed m.p. with an authentic sample of pterostilbene confirmed it to be pterostilbene (I).

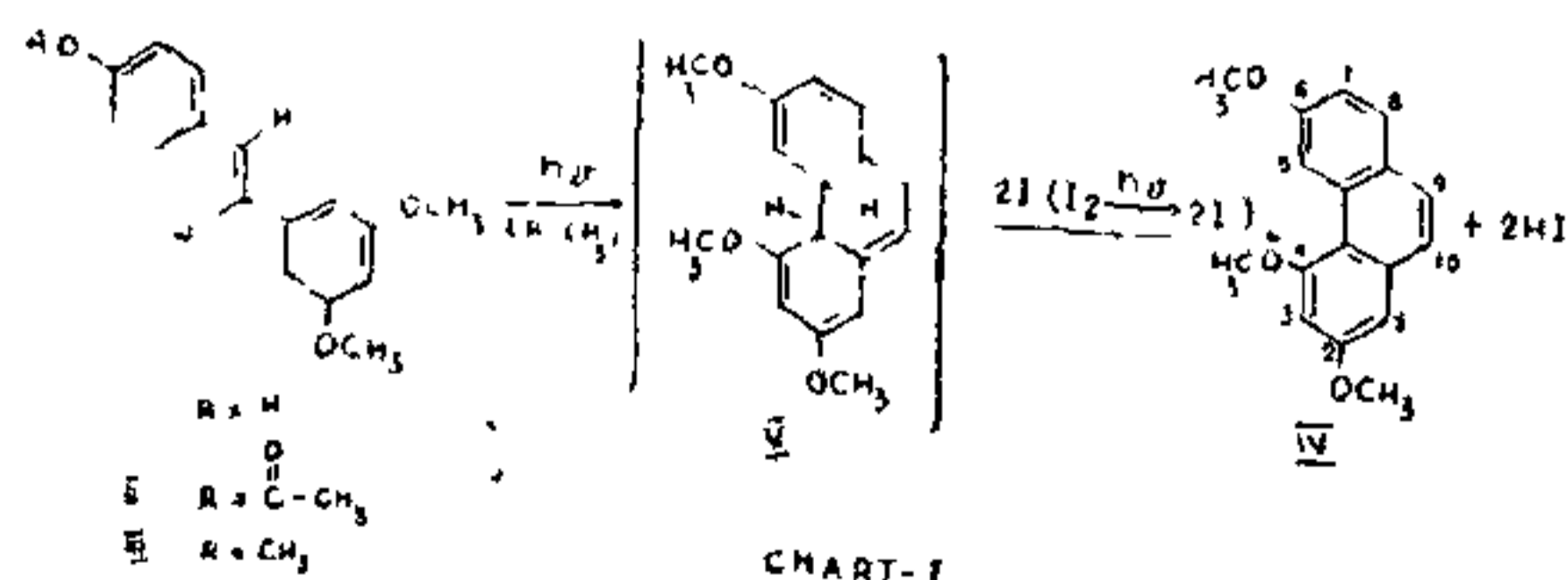
The I.R. spectrum of pterostilbene (I) and its O-acetate (II) in CHCl_3 showed an absorption around 965 cm^{-1} attributable to trans $-\text{CH}=\text{CH}-^3$. The U.V. spectrum of (II) in CH_3OH gave λ_{max} (log. ϵ , 226 nm (3.06); 242 nm (3.63) and 308 nm (3.98) similar to that of trans stilbene⁴. Thus (I) appears to be a trans stilbene.

Photolysis of O-methyl pterostilbene (III): O-Methyl pterostilbene (III) (m.p. 57°)² was dissolved in purified cyclohexane ($3.7 \times 10^{-3}\text{ M}$) containing 5 mole-% of resublimed iodine and irradiated using medium pressure mercury lamp for 36 hr. The use of iodine in the photooxidation of synthetic stilbenes is well known.⁵ At the end of the reaction period the solvent was removed under reduced pressure. The residue, on column chromatography using silica gel as adsorbant and benzene-petroleum ether ($60-80^\circ$) (9:1) as eluent gave two products. One of the two products was considered to be a polymerised material which was not further investigated. The other product obtained in 20% yield with m.p. 103° was characterised to be 2, 4, 6-trimethoxy phenanthrene (IV) on the basis of the following evidence.

The mass spectrum of (IV) shows M^+ at m/e 268 as a base peak and together with elemental analysis (C, 76.11%; H, 5.96%) the molecular formula was found to be $\text{C}_{17}\text{H}_{16}\text{O}_3$.

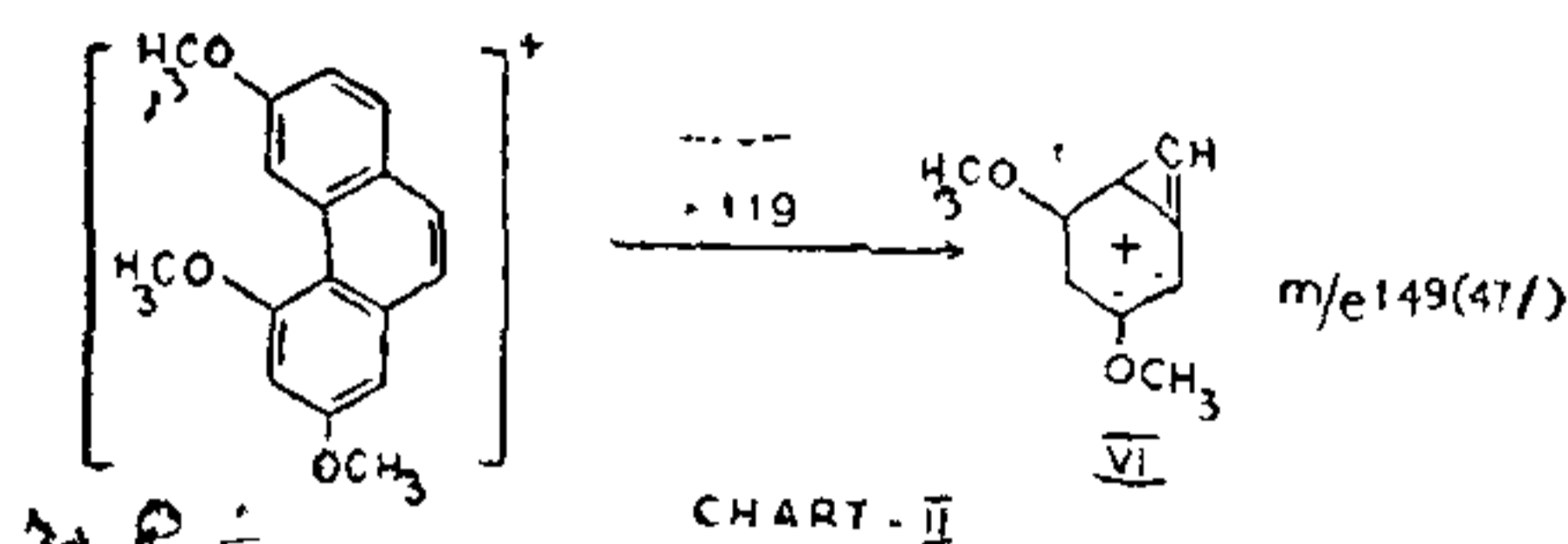
The I.R. (CHCl_3) of (IV), ν_{max} 1620, 1601, 1570 (aromatic), and 840 cm^{-1} , U.V. (CA_3OH) λ_{max} (log ϵ) 240 nm (3.14), 263 nm (3.84), 293 nm (3.01) and 326 nm (2.70) are characteristic of phenanthrene⁶, NMR (60 MHz) CDCl_3 , TMS, δ 3.80, 3.86 and 3.98 (s, 3H each, three- OCH_3), δ 6.60 (d, $J = 3\text{ Hz}$, 1H, $\text{C}_3\text{-H}$), δ 6.73 (d, $J = 3\text{ Hz}$, 1H, $\text{C}_1\text{-H}$), δ 8.92 (d, $J = 3\text{ Hz}$, 1H, $\text{C}_5\text{-H}$), and δ 7.10-7.70 (m, 4H, aromatic). It is reported⁷ that $\text{C}_4\text{-H}$ and $\text{C}_6\text{-H}$ in phenanthrene appear downfield. Hence the proton δ 8.92 is assigned to $\text{C}_5\text{-H}$ of the photo-product (IV).

Photooxidation of O-methyl pterostilbene (III) consists of first isomerisation⁵ to dihydrophenanthrene (V) which then undergoes oxidation in the presence of iodine to 2, 4, 6-trimethoxy phenanthrene (IV).



The mass spectral fragmentation pattern also confirms the phenanthrene structure for (IV). The loss of $-\text{CH}_3$ and $-\text{CO}$ units appears to be characteristic of methoxy substituted phenanthrenes. m/e 268

(100%) $\xrightarrow{-\text{CH}_3}$ 253 (10%) $\xrightarrow{-\text{CO}}$ 225 (23%) $\xrightarrow{-\text{CH}_3}$ 210
 (10%) $\xrightarrow{-\text{CH}_3}$ 195 (10%) $\xrightarrow{-\text{CO}}$ 167 (10%) $\xrightarrow{-\text{CO}}$ 139
 (20%). The prominent ion m/e 149 (47%) arising from the parent ion by the symmetrical cleavage by losing 119 units, may be represented by the structure (VI) (Chart II).



Photolysis of pterostilbene (I) under similar conditions described for (III) gave a mixture of four compounds as shown by tlc using benzene-petroleum ether ($60-80^\circ$) (9:1) as solvent system, and the characterisation of these compounds is under investigation. O-Acetylpterostilbene (II) was not photooxidised on irradiating it for longer duration (72 hr) and also passing oxygen. The failure of synthetic stilbenes carrying electron withdrawing groups like $-\text{NO}_2$ and $-\text{OCOCH}_3$ to undergo photooxidation was earlier noticed and this failure is attributed to inter-system crossing.⁵

The authors wish to thank Prof. T. Navaneeth Rao, Head of the Department of Chemistry for providing facilities. Our thanks are also due to Prof. F. E. King, University of Nottingham for authentic sample of pterostilbene and Prof. M. R. Suxena, Emeritus Professor, Department of Botany, Osmania University, for providing the plant material.

Department of Chemistry, JAMES MATHEW.
 Osmania University, A. V. SUBBA RAO.
 Hyderabad 500007 (A.P.), N. V. SUBBA RAO (Late).
 December 24, 1976.

1. Seshadri, T. R., "Polyphenols of pterocarpus and Dalbergia Wood (Review article)," *Phytochemistry*, 1972, 11, 881.
2. King, F. E., Cortell, C. B., Godson, D. H., Jurd, L. and King T. J., *J. Chem. Soc.*, 1953, p. 3693.
3. Kariyone, T., et al., *Pharmaceutical Soc., Japan*, 1959, 79, 219. Yamaguchi, K., *Spectral Data of Natural Products*, Elsevier Publ. Co., 1970, 1, 61.
4. Phillips, J. P., *Spectra-structure Correlation*. Pub. Academic Press (N.Y.), 1964, p. 63.
5. Mellory, F. B., Wood, C. S., Gordon, J. T., Lindquist, L. C. and Savitz, M. L., *J. Am. Chem. Soc.*, 1962, 84, 4361.
6. Newman, M. S. and Hussey, A. S., *Ibid.*, 1947, 69, 3025.
7. Jonathan, N., Gordon, S. and Dalley, B. P., *J. Chem. Phys.*, 1962, 36, 2443.