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(−)-5-METHYLMELLEIN AND CATECHOL DERIVATIVES FROM FOUR *SEMECARPUS* SPECIES*

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Key Word Index—*Semecarpus gardneri*; *S. obscura*; *S. subepeltata*; *S. walkeri*; Anacardiaceae; fruits; wood; 3-alk(en)yl catechols; (−)-5-methylmellein; taxonomic markers.

Abstract—Four *Semecarpus* species endemic to Sri Lanka, *S. gardneri*, *S. obscura*, *S. subpeltata* and *S. walkeri*, were investigated. The fruits of these species are rich in 3-alk(en)yl-catechols and the timber extractives of three species contained (−)-5-methylmellein.

INTRODUCTION

The medicinal uses of *Semecarpus* species are many and varied [1–3]. Nuts of *Semecarpus anacardium* Linn. are used [3] in India as a local irritant to procure abortion. Some extracts of *S. anacardium* have been found to exhibit antileukaemic activity [1] but this anticancer activity was lost on storage. These claims prompted us to investigate the endemic *Semecarpus* species. Seventeen species are reported [4] and we have studied 4 of these, namely *S. gardneri* Thw., *S. obscura* Thw., *S. subpeltata* Thw. and *S. walkeri* Hook. f. The study of 3 *Semecarpus* species growing in India has been undertaken by various groups [5–10]. Pillay and Siddiqui [6] isolated an oil called bhilawanol from *S. anacardium*. Later studies [7, 8] on methylated bhilawanol showed this to be a mixture of closely related compounds of which 1,2-dimethoxy-3-(pentadec-8′-enyl)benzene and 1,2-dimethoxy-3-(pentadec-7′,10′-dienyl)benzene were the major components. *S. heterophylla* Bl. and *S. travancoricus* Bed. also yielded catechol derivatives [9, 10].

RESULTS AND DISCUSSION

The fruits of the 3 *Semecarpus* species studied, namely *S. obscura*, *S. subpeltata*, and *S. walkeri*, all had the same phenolic oil as the major component (7.40, 6.46 and 5.80%, respectively) in their methanol extracts. Although the oil appeared homogeneous by TLC, HPLC studies revealed that there were at least 15 components, 3 of which were major. GLC examination of both the phenolic oil and its silylated derivatives confirmed this. The phenolic oil showed a bathochromic shift of 10 nm with H_3BO_3/NaOAc in its UV spectrum which was indicative of the presence of an *ortho*-dihydroxy pattern. The ^{1}H NMR spectrum of the oil showed signals at τ 9.1 and τ 8.7 indicating the presence of methyl and methylene groups. The presence of allylic and vinylic protons were shown by the signals at τ 7.4 and 8.0 for the former and at τ 4.65 for the latter. The signals for the aromatic protons appeared at τ 3.3. The most intense ion in the MS of the phenolic oil was at *m/e* 123 and the structure of this fragment ion in keeping with the above data would be **1**. The phenolic oil is therefore a mixture of alk(en)yl catechols. Methylation with diazomethane and dimethyl sulphate both gave mainly a monomethyl derivative, indicating that one of the hydroxyl groups is hindered by the presence of a side chain. This was shown by the bathochromic shift in the UV spectrum of the methyl ether when a few drops of NaOH were added. Also, the signal for the −OMe group at τ 6.13 in the ^{1}H NMR spectrum of the methyl ether integrated for only 3 protons. The MS studies identified 5 components of the alk(en)yl catechol mixture with M^+ *m/e* at 374, 348, 346, 320 and 318, the first 3 being the major components. The structures of 5 of the 15 compounds of the alk(en)yl catechols are given below in **2**.

The vesicatory characteristics of the oil and the difficulty in collecting fruits during periods other than May–June precluded further study of their components.

Semecarpus species studied elsewhere also gave a

*Part 38 in the series "Chemical Investigation of Ceylonese Plants". For Part 37 see Gunatilaka, A. A. L., Nanayakkara, N. P. D. and Sultanbawa, M. U. S. (1979) *Tetrahedron Letters* 1979, 1727.

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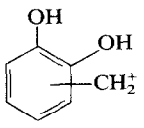

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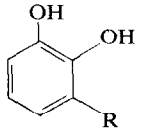


2

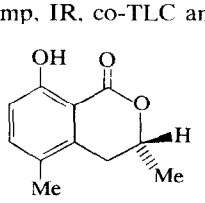
R = $C_{15}H_{29}$ (M^+ = 318)
R = $C_{15}H_{31}$ (M^+ = 320)
R = $C_{17}H_{33}$ (M^+ = 346)
R = $C_{17}H_{35}$ (M^+ = 348)
R = $C_{19}H_{37}$ (M^+ = 374)

mixture of these types of catechol derivatives. Table 1 gives the details of the plants and the components. Examination of this table shows that the phenolic oil isolated from the Sri Lanka *Semecarpus* species is much more complex than the oils, hitherto isolated and that a longer alkenyl side chain (**2**, R = $C_{19}H_{37}$) is also present with the usual C_{15} and C_{17} side chains. These vesicant phenolic oils are thus good chemotaxonomic markers for the *Semecarpus* species, and their presence could well explain the delayed contact dermatitis produced when the bruised plant is touched.

Table 1. Catechol derivatives isolated from *Semecarpus* species

Semecarpus species	Catechol derivatives isolated
S. anacardium	**2**, R = $C_{15}H_{29}$ [7]
	2, R = $C_{15}H_{27}$ [8]
S. heterophylla	**2**, R = $C_{15}H_{29}$ [9]
S. travancoricus	**2**, R = $C_{17}H_{31}$ [10]

Petrol extractives of the timber of *S. subpeltata*, *S. walkeri* and *S. gardneri* on column chromatography gave the same dihydroisocoumarin in yields of 0.003%, 0.0003%, 0.0007%, respectively. High resolution MS data gave $C_{11}H_{12}O_3$ as the molecular formula of the compound. The UV, IR and ^{1}H NMR data were in agreement with structure **3** for the dihydroisocomarin. This dihydroisocoumarin, 5-methyl-8-hydroxy-3,4-dihydro-3-methylisocoumarin was first isolated by Ballio *et al.* [11] during the purification of fusicoccin A, the main phytotoxic metabolite of the fungus *Fusicoccum amygdali*. The 5-methylmellein isolated by these authors was laevorotatory and they established the configuration of the chiral carbon as *R*. A direct comparison of the compound isolated in this study with (−)-5-methylmellein showed that they were identical (mmp, IR, co-TLC and rotation).



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In a recent report, Gottlieb [12] and his co-workers report the isolation of 5-methylmellein from several wood samples infested by fungi. These plant samples belong to different families such as Anacardiaceae, Guttiferae, Lauraceae, Leguminosae, Proteaceae and Sterculiaceae. 5-Methylmellein has not been isolated during any of our earlier investigations of several plant families even though the plant parts and extracts were stored under conditions similar to those used for storing the extracts of *Semecarpus* species in this study. Besides, one *Semecarpus* species, namely *S. gardneri*, was processed within a week of collection. It is therefore likely that (−)-5-methylmellein is a plant metabolite at least in this instance.

EXPERIMENTAL

Bark, timber and fruits of the *Semecarpus* species were obtained as follows: *S. obscura*—Uda Peradeniya, Sri Lanka; *S. subpeltata*, *S. walkeri* and *S. gardneri*—Kanneliya (south Sri Lanka). The bark and timber were separated, dried and powdered in a mill. Sequential extractions of the powdered bark and timber were carried out using hot petrol, hot C_6H_6 and hot MeOH as solvents. The fruits were immediately subjected to extraction with cold MeOH since the time taken to dry the fruits results in fungal attack. The solvents were removed under red. pres. Column chromatographic separations were carried out on Si gel (30–70 mesh). Si gel was used for analytical and preparative TLC seperations. ^{1}H NMR were recorded at 60 MHz.

Isolation of phenolic oil. Fruits of *S. obscura* (1.14 kg) gave 24.5 g of cold MeOH soluble and 31 g hot MeOH soluble fractions. The major fraction in both the extracts were the same as shown by TLC and co-TLC. The hot MeOH extract was separated by column chromatography to give a product homogeneous by TLC, yield 7.4%. The major product was distilled, most of it distilling between 240 and 250° at 3 mm Hg. The distillate, colourless at first, became dark when exposed to air. UV $\lambda_{max}^{(95\%\ EtOH)}$ nm: 208 and 278 $\lambda_{max}^{(95\%\ EtOH+NaOH)}$: 220 and 397. On addition of H_3BO_3–NaOAc there was a bathochromic shift of the 278 nm band to 288 nm. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 750, 950, 1200, 1270, 1460, 1590, 2820 and 3300. ^{1}H NMR ($CDCl_3$), 100 MHz): τ 3.3 (aromatic), 4.65 (vinylic), 7.4 and 7.0 (allylic), 8.7 (methylene) and 9.1 (methyl). MS (high resolution) showed the presence of at least 5 components with M^+ *m/e* at 374, 348, 346, 320, 318, 189, 163, 149, 136, 123 (100%).

Hydrogenation of phenolic oil. Oil (200 mg) in EtOH was hydrogenated using Adam's catalyst for 2 days. The product on work-up gave a brown solid, mp 48–53°. This was shown to be a mixture by TLC.

Methylation of phenolic oil. Oil (300 mg) was dissolved in Me_2CO (30 ml) and heated under reflux with Me sulphate (2 ml) in the presence of dry K_2CO_3 (2 g) for 4 hr. The cooled reaction mixture was filtered to remove K_2CO_3 and solvent was evaporated. The brown liquid (257 mg) was purified by PLC to give a pure Me derivative (45 mg). UV $\lambda_{max}^{(EtOH)}$ nm: 275, $\lambda_{max}^{EtOH+NaOH}$ 290. ^{1}H NMR ($CDCl_3$, 60 MHz): τ 3.27 (3H, *s*), 4.63 (2H, *t*), 6.13 (3H, *s*), 7.37–7.93 (allylic protons, *m*), 8.2–9.0 (CH_2 and Me). CH_2N_2 methylation of the phenolic oil also gave a mixture of products from which the above monomethylated product was isolated by PLC. The MeOH extracts of the fruits of *S. subpeltata* and *S. walkeri* also had the phenolic oil as the major product.

Isolation of sitosterol. Bark of *S. obscura* (6.2 kg) gave only 2.4 g of C_6H_6 extract which on column chromatographic separation gave 22 mg sitosterol, mp 137° (from MeOH) (lit. [13] 136–137°), $[\alpha]_D$ −36.5° (lit. [13] $[\alpha]_D$ −36°) which was found to be identical with an authentic sample. The C_6H_6 extract of *S. obscura* also gave another viscous oil (60 mg). UV λ_{max}^{EtOH} nm: 230 and 277. IR ν_{max} cm^{-1}: 740, 1070, 1120, 1270, 1380, 1450, 1720, 2900 and 3400. ^{1}H NMR ($CDCl_3$,

100 MHz): τ 2.38 (4H, *d*), 5.69 (2H, *t*), 7.84 (3H, *s*), 8.74 (CH_2), 9.1–9.16 (Me). MS *m/e* M^+ 280, 279 (22%), 167 (15), 150 (15), 149 (100), 113 (22), 71 (43), 69 (24), 57 (76), 58 (33). Sitosterol was not isolated from the bark extractives of the other *Semecarpus* species. However sitosterol was isolated from the timber extractives of *S. obscura*, *S. walkeri* and *S. gardneri*.

Isolation of (−)-5-*methylmellein*. Timber of *S. subpeltata* (4 kg) gave 5 g of petrol soluble fraction. This on separation by chromatography on Si gel and elution with $CHCl_3$–C_6H_6 (1:9) gave a white solid which was crystallized using petrol to give 5-methylmellein (120 mg, 0.003%), mp 124–6° (lit. [11] 126–127°), $[\alpha]_D$ −75° (lit., [11], $[\alpha]_D$ −105°). UV λ_{max}^{EtOH} nm (log ε): 214 (4.34), 248 (3.83) and 323 (3.63). On addition of an EtOH soln of $AlCl_3$ a shift of 14 nm of the band at 323 (3.63) nm to 337 (3.49) nm was observed. IR ν_{max}^{KBr} cm^{-1}: 670, 740, 800, 840, 900, 960, 990, 1050, 1120, 1170, 1210, 1320, 1380, 1480, 1600, 1660 and 2700–3200. ^1H NMR ($CDCl_3$, 100 MHz): τ −0.98 (1H, *s*), 2.72 (1H, *d*, J = 8.4 Hz, aromatic), 3.2 (1H, *d*, J = 8.4 Hz), 5.3 (1H, *m*), 7.24 (2H, *octet*), 7.8 (3H, *s*), 8.46 (3H, *d*, J = 6.4 Hz). M^+ 192, *m/e* 192 (100%), 174 (75), 163 (67), 148 (77), 120 (75) and 91 (67). Molecular formula (high resolution mass) $C_{11}H_{12}O_3$. It was identical with an authentic sample of (−)-5-methylmellein. (−)-5-Methylmellein was also isolated from the petrol extractives of timbers from *S. walkeri* and *S. gardneri*.

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REFERENCES

1. Gothoskar, S. V. and Ranadive, K. J. (1971) *Indian J. Exp. Biol.* **9**, 372; (1972) *Chem. Abstr.* **76**, I, 21234p.
2. Gothoskar, S. V., Chitnis, M. P., Adwankar, M. K. and Ranadive, K. J., (1971) *Indian J. Exp. Biol.* **9**, 399.
3. Chandrasena, J. P. (1935) *The Chemistry and Pharmacology of Ceylon and Indian Medicinal Plants*, pp. 97–100. H. & C. Press, Colombo.
4. Bandaranayake, W. M. and Sultanbawa, M. U. S. (1969) *List of Endemic Plants of Ceylon*. Department of Chemistry, University of Ceylon, Peradeniya.
5. Loev, B. (1960) *Nature* **186**, 389, 435.
6. Pillay, P. P. and Siddiqui, S. (1931) *J. Indian Chem. Soc.* **3**, 517.
7. Govindachari, T. R., Joshi, B. S., Kamat, V. N. and Voswanathan, N. (1971) *Indian J. Chem.* **9**, 1044.
8. Rao, N. S. P., Row, L. R. and Brown, R. T. (1973) *Phytochemistry* **12**, 671.
9. Backer, H. J. and Haack, N. H. (1938) *Rec. Trav. Chim.* **57**, 225; (1938). *Chem. Abstr.* **32**, 4965[2].
10. Puntambekar, S. V. and Beri, R. M. (1954) *Proc. Indian Acad. Sci.* **39**, 137; (1954) *Chem. Abstr.* **48**, 10858C.
11. Ballio, A., Barcellona, S. and Santurbano, B. (1966) *Tetrahedron Letters* 3723.
12. Gottlieb, O. R. *et. al.* (1978) *Phytochemistry* **17**, 511.
13. (1965) *Dictionary of Organic Compounds*, Vol. 5, p. 2902. Eyre & Spottiswood, London.