Phytochemistry, 1978, Vol 17, pp. 1383–1388 © Pergamon Press Ltd Printed in England 0031-9422/78/0801-1383$02 00/0

NEOFLAVONOIDS AND THE CINNAMYLPHENOL KUHLMANNISTYRENE FROM *MACHAERIUM KUHLMANNII* AND *M. NICTITANS**

W. DAVID OLLIS†, BRIAN T. REDMAN†, RICHARD J. ROBERTS†, IAN O. SUTHERLAND†, OTTO R. GOTTLIEB‡ and MAURO T. MAGALHÃES§

† Department of Chemistry, The University, Sheffield S3 7HF, England; ‡ Instituto de Química, Universidade de São Paulo, c.p. 20780, São Paulo; § Centro de Tecnologia Agrícola e Alimentar, EMBRAPA, Rio de Janeiro, Brasil

(*Received* 4 *October* 1977)

Key Word Index—*Machaerium kuhlmannii*; *M. nictitans*; Leguminosae–Lotoideae; cinnamylphenol; neoflavonoids; isoflavonoids; methyl dihydrocinnamate; phenols.

Abstract—The trunkwood of *Machaerium kuhlmannii* contains methyl palmitate, 3-*O*-acetyloleanolic acid and sitosterol; the benzene derivatives 2,3-dimethoxyphenol, 2,6-dimethoxyphenol, 2-hydroxy-3-methoxyphenol, 2,3-dimethoxybenzaldehyde and methyl 3-(2-hydroxy-4-methoxyphenyl)-propionate; the isoflavonoids formononetin and (6a*S*,11a*S*)-medicarpin; the neoflavonoids (*R*)-3,4-dimethoxydalbergione, (*R*)-3,4-dimethoxydalbergiquinol, kuhlmanniquinol [(*R*)-3-(4-hydroxyphenyl)-3-(5-hydroxy-2,3,4-trimethoxyphenyl)-propene], dalbergin, kuhlmannin (6-hydroxy-7,8-dimethoxy-4-phenylcoumarin) and kuhlmannene (6-hydroxy-7,8-dimethoxy-4-phenylchrom-3-ene), as well as the cinnamylphenol kuhlmannistyrene [*Z*-1-(5-hydroxy-2,3,4-trimethoxybenzyl)-2-(2-hydroxyphenyl)-ethylene]. Five of these compounds, in addition to (*R*)-4′-hydroxy-3,4-dimethoxydalbergione, were also isolated from a trunkwood extract of *M. nictitans*. Structural assignments were confirmed by chemical interconversion and by the synthesis of (±)-kuhlmanniquinol.

INTRODUCTION

In contrast to *Machaerium nictitans* (Vell.) Benth., *M. kuhlmannii* Hoehne was described only recently. The specific epithet honours the Brazilian botanist Dr. João Geraldo Kuhlmann (1883–1959). The considerable morphological kinship of both species [2] is reflected in the similarity of chemical composition. The benzene extracts of their trunkwood contain predominantly aromatic compounds which were separated by a combination of column and thick-layer chromatography on Si gel. *M. kuhlmannii* gave methyl palmitate, 3-*O*-acetyloleanolic acid [3] and fourteen aromatic compounds. These included six neoflavonoids, three of which were known compounds recognised by comparison with authentic samples, (*R*)-3,4-dimethoxydalbergione (**1a**) [4], (*R*)-3,4-dimethoxydalbergiquinol (**2a**) [4], and dalbergin (**3a**) [5]; the other three neoflavonoids, kuhlmanniquinol (**2b**), kuhlmannin (**3b**) and kuhlmannene (**4**), are new structures. The association of neoflavonoids with cinnamylphenols has previously been noted [6], and *M. kuhlmannii* contains a new cinnamylphenol, kuhlmannistyrene (**5a**). The isoflavonoids, formononetin [7] and (+)-medicarpin [(+)-demethylhomopterocarpin] [1], which have been found in other *Dalbergia* and *Machaerium* species, are also present in *M. kuhlmannii* and were readily identified by direct comparison with authentic samples. *M. kuhlmannii* contains, in addition, five simple benzene derivatives, 2,3-dimethoxyphenol, 2,6-dimethoxyphenol, 2-hydroxy-3-methoxyphenol, 2,3-dimethoxybenzaldehyde and methyl 3-(2-hydroxy-4-methoxyphenyl)-propionate; the latter has not previously been isolated as a natural product. From *M. nictitans*, again in addition to the isoflavonoids formononetin and (+)-medicarpin, five of the six neoflavonoids present in *M. kuhlmannii* were isolated, namely **1a**, **2a**, **2b**, **3b** and **4**, besides a new member (*R*)-4′-hydroxy-3,4-dimethoxydalbergione (**1b**).

The elucidation of the structure of the previously unknown natural products from *M. kuhlmannii* and *M. nictitans*, subject of preliminary communications [6, 8], is now discussed in detail.

RESULTS

(R)-4′-*Hydroxy*-3,4-*dimethoxydalbergione*, $C_{17}H_{16}O_5$

The red colour and the absorption spectra suggested a quinonoid structure, and comparison of the PMR and ORD data of the natural product and its monoacetate with the analogous data of (*S*)-4′-hydroxy-4-methoxydalbergione (**6**) from *D. nigra* Fr. Allem. [9] defined the structure as (*R*)-4′-hydroxy-3,4-dimethoxydalbergione (**1b**). This assignment was confirmed by synthesis of the compound through oxidative demethylation [10] of kuhlmanniquinol (**2b**), whose structure was established by unambiguous synthesis.

Kuhlmanniquinol, $C_{18}H_{20}O_5$

The UV spectrum is consistent with an oxygenated benzenoid chromophore, similar to that of latifolin (**2c**) [11]. The PMR spectrum of kuhlmanniquinol shows clearly that it is a 3,3-diarylpropene derivative from the

* Part 6 in the series 'The Neoflavonoid Group of Natural Products'. For Part 5 see ref. [1].

characteristic [9, 12] multiplet signals associated with the $CH—CH=CH_2$ grouping. This spectrum also shows an AA'BB' system, indicating that one of the benzene rings is oxygenated in the *para* position, and one further aromatic proton signal as a singlet, in addition to singlets assignable to three methoxy groups and two hydroxy groups. Acetylation of the compound caused a low field shift of the AA'BB' system, indicating that one of the hydroxy groups is located at position 4'. The similarity of the chemical shift of the single aromatic proton in kuhlmanniquinol (τ 3.62) with that of H-6 in **2a** (τ 3.60) suggests that both have the same oxygenation pattern. The shift to low field of this H-6 signal upon acetylation of kuhlmanniquinol (τ 3.44) suggests that the still unlocated hydroxy group may be situated at C-5 (**2b**), in analogy with the structure of latifolin (**2c**) and with all the other known neoflavonoids [13], which normally have hydroxy or oxo groups at this position. The absolute configuration of kuhlmanniquinol was established by $NaIO_4$ oxidation to (*R*)-3,4-dimethoxy-4'-hydroxydalbergione (**1b**). Unambiguous confirmation of constitution **2b** for kuhlmanniquinol was finally obtained by the synthesis of (±)-dihydrokuhlmanniquinol diethyl ether (**7**).

4-Ethoxybenzoic acid was condensed with pyrogallol in the presence of BF_3–Et_2O to give **8a**. The trimethyl ether (**8b**) of this benzophenone was selectively demethylated with $AlCl_3$ to give the dimethyl ether **8c** in good yield. Oxidation of **8c** with $K_2S_2O_8$ gave **8d**, which, by partial ethylation, gave the 5-ethyl ether **8e**. Methylation of **8e** gave **8f**, which reacted smoothly with ethyl magnesium bromide to give a mixture of *Z*- and *E*-1,1-diarylpropenes (**8g**). Hydrogenation gave a product (**7**) which has IR and PMR properties identical with those of diethyl dihydrokuhlmanniquinol.

Kuhlmannin, $C_{17}H_{14}O_5$

The spectroscopic properties are consistent with a 4-phenylcoumarin structure with one hydroxy and two methoxy substituents. The oxygenation pattern is not determined by the chemical shift of the single proton (τ 3.23) on the oxygenated benzene ring, but the physical properties of kuhlmannin, which resemble those reported [14] for synthetic 6-hydroxy-7,8-dimethoxy-4-phenylcoumarin (**3b**), and its co-occurrence with **1a**, **2a** and **3a**, suggest that kuhlmannin has structure **3b**. This hypothesis was found to be correct by the identity of kuhlmannin with synthetic 6-hydroxy-7,8-dimethoxy-4-phenylcoumarin, prepared by the reaction of ethyl benzoylacetate with 4-hydroxy-2,3-dimethoxyphenol.

Kuhlmannene, $C_{17}H_{16}O_4$

Kuhlmannene is optically inactive and its IR spectrum indicates the absence of carbonyl groups in its structure. The PMR spectrum shows singlets assigned to a phenyl group, a proton on an oxygenated benzene ring, one hydroxyl and two methoxyls, as well as multiplets of an AX_2 system associated with the structural unit CH_A–CH_{2X}. The chemical shifts of the protons in this AX_2 system indicate the olefinic nature of the methine group and the presence of an oxygen function adjacent to the methylene group. These data are compatible with a 4-phenylchrom-3-one structure and particularly with **4**, in view of the substitution patterns of the co-occurring metabolites **1a**, **2a** and **3b**.

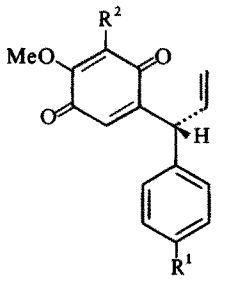
The relationship between this structural proposal for kuhlmannene (**4**) and (*R*)-3,4-dimethoxydalbergione (**1a**) suggested the possibility of interconversion. Treatment of **1a** with acids and bases was unsuccessful, but the cyclisation was achieved by allowing a chloroform solution to percolate through a column of dry neutral alumina. The product (**4**), formed in high yield, was identical in all respects with natural kuhlmannene. The transformation, **1a** → **4**, is mechanistically similar to the transformation of ubiquinone-10 (**9**) to ubichromene-10 (**10**) which has been carried out [15] using similar reaction conditions. The ease of the interconversion **1a** → **4** suggested the possibility that kuhlmannene (**4**) was an artifact of the isolation procedure which had employed chromatography on Si gel. This possibility was carefully checked and it was found that the transformation **1a** → **4** does not occur on Si gel. Kuhlmannene is thus a genuine natural product, a fact which is further supported by the isolation [4] of **1a**, but not of **4**, from *M. scleroxylon* Tul. The reverse process, **4** → **1a**, occurs with equal ease. The attempted oxidation of kuhlmannene (**4**) to kuhlmannin (**3b**), for example, resulted only in the formation of (±)-3,4-dimethoxydalbergione.

Kuhlmannistyrene $C_{18}H_{20}O_5$

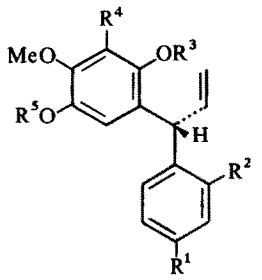
The UV spectrum is characteristic of a cinnamylphenol chromophore. The PMR spectrum shows multiplets assignable to the ABX_2, system of a $CH_A{=}CH_B{-}CH_{2X}$ grouping [cf. ref. 12] (J_{AB} = 11 Hz), consistent with a *Z*-cinnamylphenol structure for kuhlmannistyrene. The spectrum shows in addition a multiplet assignable to four hydrogen atoms on a single aromatic ring and singlets assignable to a single hydrogen atom (τ 3.52) on a more highly oxygenated benzene ring, three methoxy groups and two hydroxy groups. The MS of kuhlmannistyrene contains a prominent ion, *m/e* 107, to which the hydroxytropylium structure, C_7H_7O, may be assigned. One of the hydroxyls must thus be located on the disubstituted benzene ring, and the other hydroxyl, together with the three methoxyls, on the pentasubstituted benzene ring. The relative placement of these groups, as shown in **5a**, was established by the observation that dihydrokuhlmannistyrene is identical in all respects with the dihydro-derivative of petrostyrene (**11**) from *M. acutifolium* Vog. [1]. The double bond in kuhlmannistyrene (**5a**) was placed in conjugation with the least substituted aryl group, in analogy with the established position of the double bond in all other reported cinnamylphenols [6].

Methyl 3-(2-*hydroxy*-4-*methoxyphenyl*)-*propionate*, $C_{11}H_{14}O_4$

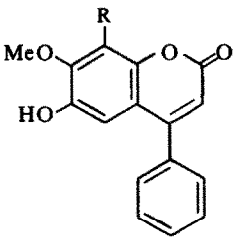
Identified as the methyl ester of a 3-arylpropionic acid by spectroscopic data, which also indicate that the aromatic ring is 1,2,4-trisubstituted with one methoxy and one hydroxy substituent. The possibility that the compound is a carboxylic acid was excluded by its failure to form a salt by reaction with $NaHCO_3$, and the hydroxyl was therefore considered to be located at position 2' on the aromatic ring to permit hydrogen bonding to the ester carbonyl group (ν_{max} 3250, 1700 cm^{-1}). The only structure consistent with these data is that of methyl 3-(2-hydroxy-4-methoxyphenyl)-propionate (**12**). The structure was confirmed by the reaction of 7-methoxy-3,4-dihydrocoumarin (**13**) with methanolic HCl which gave a synthetic sample of the ester, identical in all respects with the natural product.



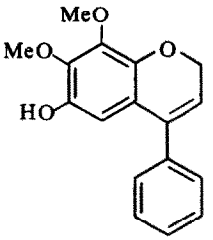
1a R^1 = H, R^2 = OMe
1b R^1 = OH, R^2 = OMe
1c R^1 = R^2 = H
1d R^1 = OAc, R^2 = OMe



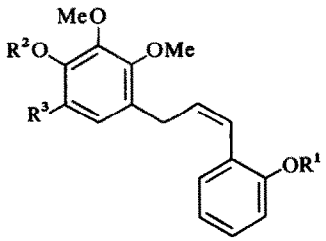
2a R^1 = R^2 = R^3 = R^5 = H, R^4 = OMe
2b R^1 = OH, R^2 = R^5 = H, R^3 = Me, R^4 = OMe
2c R^1 = R^4 = R^5 = H, R^2 = OH, R^3 = Me
2d R^1 = OAc, R^2 = H, R^3 = Me, R^4 = OMe, R^5 = Ac
2e R^1 = OEt, R^2 = H, R^3 = Me, R^4 = OMe, R^5 = Et



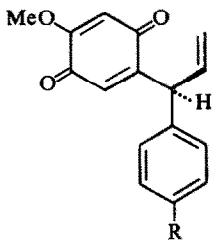
3a R = H
3b R = OMe



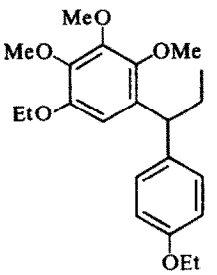
4



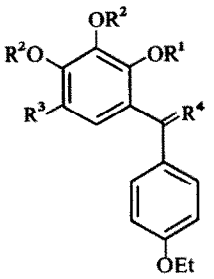
5a R^1 = H, R^2 = Me, R^3 = OH
5b R^1 = R^2 = R^3 = H
5c R^1 = Me, R^2 = R^3 = H



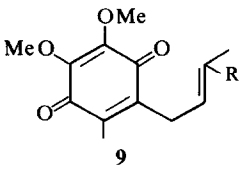
6 R = OH



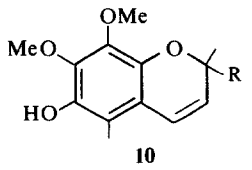
7



8a R^1 = R^2 = R^3 = H, R^4 = O
8b R^1 = R^2 = Me, R^3 = H, R^4 = O
8c R^1 = R^3 = H, R^2 = Me, R^4 = O
8d R^1 = H, R^2 = Me, R^3 = OH, R^4 = O
8e R^1 = H, R^2 = Me, R^3 = OEt, R^4 = O
8f R^1 = R^2 = Me, R^3 = OEt, R^4 = O
8g R^1 = R^2 = Me, R^3 = OEt, R^4 = CHMe

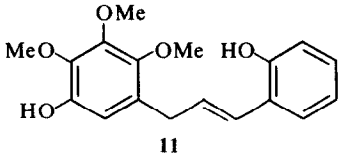


9

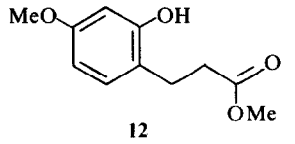


10

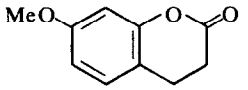
R = $CH_2(CH_2CH{=}CMeCH_2)_nH$



11



12



13

DISCUSSION

The co-occurrence of the neoflavonoids **2a**, **1a**, **4** and **3b** with the cinnamylphenol **5a** is of interest since both types of compounds are formally derivable by alkylation of the same phenol with a cinnamyl pyrophosphate or its equivalent [16]. Although *E*-cinnamylphenols have been more frequently isolated than *Z*-cinnamylphenols [6], two other examples of the latter have been recognised, mucronulastyrene (**5b**) and villostyrene (**5c**), isolated from *M. mucronulatum* Mart. ex Benth. and *M. villosum* Vog. [17]. In both cases the cinnamyl unit is oxygenated at position 2', as in kuhlmannistyrene (**5a**).

EXPERIMENTAL

Unless otherwise stated spectra were measured in EtOH (UV), $CHCl_3$ (IR), $CDCl_3$ (60 MHz PMR) and MeOH (ORD). All evapns of volatile material were performed under diminished pressure.

Isolation of the constituents of M. kuhlmannii. A specimen was collected near Carangola, MG, Brasil, and identified by Apparício Pereira Duarte. Ground trunkwood (13.2 kg) was continuously extracted with hot C_6H_6 and yielded an extract (58 g). A portion (56.8 g) was chromatographed on Si gel, eluting successively with C_6H_6 (K_1), C_6H_6–$CHCl_3$ mixtures (K_2–K_7), $CHCl_3$ (K_8), and MeOH–$CHCl_3$ (1:19) (K_9). K_1 (10.9 g) yielded *O*-acetyloleanolic acid (400 mg) on fractional crystallisation from MeOH. The remainder of this fraction was of a fatty nature. K_2 (0.8 g) was separated by TLC (Si gel, $CHCl_3$) and fractional crystallisation to give **12** (24 mg). K_3 (12.6 g) was rechromatographed on Si gel. Elution with C_6H_6 gave an oil which was distilled to give methyl palmitate (65 mg). Fractions eluted with $CHCl_3$–C_6H_6 (1:9) gave a mixture (7.4 g) which was further purified by TLC (Si gel, $CHCl_3$) to give **1a** (650 mg), **2a** (450 mg) and **4** (420 mg). K_4 (4.6 g) gave **3b** (400 mg) on fractional crystallisation from MeOH. The remainder of this fraction was separated by TLC (Si gel, $CHCl_3$) and fractional crystallisation to give 2,3-dimethoxybenzaldehyde (50 mg) and (+)-medicarpin (28 mg). K_5 (1.7 g) was rechromatographed (Si gel, $CHCl_3$). The first fractions gave a mixture (60 mg) of **3a** and **3b** which was partially separated by TLC (Si gel, $CHCl_3$). Later fractions gave **5a** (42 mg). K_6 (1.8 g) gave **3b** (240 mg) on fractional crystallisation from MeOH. The remainder of this fraction was separated by TLC (Si gel, $CHCl_3$) to give 2,6-dimethoxyphenol (70 mg) and an oil which was distilled to yield 2,3-dimethoxyphenol (95 mg). K_7 (1.8 g) was rechromatographed (Si gel, C_6H_6–$CHCl_3$, 1:1) to give a fraction which was distilled to yield 2-hydroxy-3-methoxyphenol (35 mg). K_8 (10.8 g) yielded formononetin (25 mg) on fractional crystallisation from MeOH. The residue was chromatographed (Si gel, $CHCl_3$) to give a fraction (1.4 g) which was further separated by TLC (Si gel, $CHCl_3$) to give **2b** (480 mg) and formononetin (35 mg). K_9 (11.8 g) was rechromatographed (Si gel, $CHCl_3$) to give a fraction (0.7 g) which was separated by TLC (Si gel, $CHCl_3$) to give **2b** (110 mg).

Isolation of the constituents of M. nictitans. A specimen was collected near Viçosa, MG, Brasil, and identified by Apparício Pereira Duarte. Ground trunkwood (12.5 kg) was continuously extracted with hot C_6H_6 and yielded an extract (69 g). This was chromatographed on Si gel (1.2 kg) giving various fractions with the indicated solvents: C_6H_6 (N_1), C_6H_6–$CHCl_3$ mixtures (1:1, N_2 and N_3) (1:3, N_4), $CHCl_3$ (N_5 and N_6), and MeOH (N_7). N_1 (19.6 g) was of a fatty nature. N_2 (11.1 g) was separated by TLC and yielded **1a** (200 mg) and **2a** (50 mg). N_3 (9.6 g) similarly yielded **4** (50 mg) and (+)-medicarpin (100 mg). N_4 (0.9 g) similarly yielded **3b** (45 mg). N_5 (9.2 g) similarly yielded **1b** (100 mg) and **2b** (100 mg). N_6 (1.9 g) yielded formononetin (20 mg) on concentration of a $CHCl_3$ soln. N_7 (15.0 g) was resinous material. Ground bark (7.2 kg) was continuously extracted with hot C_6H_6 and yielded an extract (58 g) which was chromatographed on Si gel (1200 g). Elution with C_6H_6, C_6H_6–$CHCl_3$ mixtures, and $CHCl_3$ yielded several fractions containing fatty materials. One of the C_6H_6 fractions was fractionated by TLC and yielded sitosterol (250 mg).

Identifications. *O*-Acetyloleanolic acid, mp 256–258°, and sitosterol, mp 138–140°, identical with authentic samples isolated from *Machaerium incorruptibile* [3]. Formononetin (7-hydroxy-4'-methoxyisoflavone), mp 257–259°, and (+)-medicarpin, [(+)-3-hydroxy-9-methoxypterocarpan], mp 133–134°, identical with an authentic sample isolated from *Dalbergia variabilis* [18]. **3a**, mp 209–210°, and **1a**, mp 41–42°, identical with authentic samples isolated from *Machaerium scleroxylon* [4]. 2,3-Dimethoxybenzaldehyde, mp 52–54° (lit. [19] mp 54°); 2,3-dimethoxyphenol, bp 80–82°/0.5 mm (lit [20] bp 124°/17 mm); 2,6-dimethoxyphenol, mp 55–56° (lit. [21] mp 55°); 2-hydroxy-3-methoxyphenol, mp 40° (lit. [22] mp 39–41°), identical with authentic samples obtained by synthesis. Methyl palmitate, oil, mp 0° (lit. [23] mp 29.5°). MW (MS) 270. Identical (IR and PMR spectra) with an authentic sample

(R)-4'-*Hydroxy*-3,4-*dimethoxydalbergione* (**1b**). Red oil $[\alpha]_D^{25}$ + 68° (*c* 0.98, $CHCl_3$). [Found: M (HRMS), 300.1010. $C_{17}H_{16}O_5$

requires: M, 300.0998]. λ_{max}^{MeOH} (nm): 230, 264 (ε 15800, 10500). ν_{max} (cm^{-1}): 3500, 3250, 1650, 1595. PMR (τ): 2.98, 3.23 (A_2B_2 system, J_{AB} = 8 Hz, H-2', H-6' and H-3', H-5'), 3.64 (*d*, *J* = 1 Hz, H-6), 3.7–4.2 (*m*, ArH), 4.6–5.3 (*m*, CH=CH_2), 6.00, 6.07 (2 *s*, 2 OMe). ORD (*c* 0.086): $[\phi]_{625}$ 0, $[\phi]_{476}$ +2380, $[\phi]_{443}$ 0, $[\phi]_{385}$ −12900, $[\phi]_{340}$ 0. *Acetate* (**1d**), yellow oil. [Found: M (MS), 342. $C_{19}H_{18}O_6$ requires: M, 342]. ν_{max} (cm^{-1}): 1750, 1650, 1595. PMR (τ): 2.78, 2.92 (A_2B_2 system, J_{AB} = 8 Hz, H-2', H-6' and H-3', H-5'), 3.60 (*d*, *J* = 1 Hz, H-6), 3.7–4.2 (*m*, ArH), 4.6–5.3 (*m*, CH=CH_2), 5.98, 6.03 (2 *s*, 2 OMe), 7.72 (*s*, OAc).

(R)-3,4-*Dimethoxydalbergiquinol* (**2a**). Oil. [Found: M (MS), 286. $C_{17}H_{18}O_4$ requires: M, 286]. ν_{max} (cm^{-1}): 3495, 1595. PMR (τ): 2.89 (*s*, C_6H_5), 3.60 (*s*, H-6), 3.5–4.1 (*m*, CH=), 4.68 (*br. s*, 2 OH), 4.7–5.3 (*m*, CH—CH=CH_2), 6.21 (*s*, 2 OMe). *Oxidation.* **2a** (50 mg) in Et_2O (20 ml) was aerated (4 hr) in contact with 0.1 N K_2CO_3 aq. (20 ml). Evapn of the Et_2O soln gave **1a** (50 mg), red oil, $[\alpha]_D^{20}$ + 60° (*c*, 1.0, $CHCl_3$), identical (IR, ORD) with the natural cmpd from *M. scleroxylon* [4], *M. kuhlmannii* and *M. nictitans*.

Kuhlmanniquinol (**2b**). Yellow oil, bp 130–140° (bath temp., 1 mm), $[\alpha]_D^{20}$ + 15° (*c* 1.07, $CHCl_3$). [Found: C, 68.21; H, 6.64. $C_{18}H_{20}O_5$ requires: C, 68.34; H, 6.34%]. λ_{max} (nm): 227 infl., 283 (ε 27000, 6000). ν_{max} (cm^{-1}): 3500, 3300 *br.*, 1630, 1600. PMR (τ): 2.97, 3.29 (A_2B_2 system, J_{AB} = 8.5 Hz, H-2', H-6' and H-3', H-5'), 3.62 (*s*, H-6), 3.5–4.1 (*m*, CH=, 2 OH), 4.8–5.3 (*m*, CH—CH=CH_2), 6.08, 6.10, 6.41 (3 *s*, OMe). *Oxidation.* **2b** (11 mg) in Et_2O (0.5 ml) was added to $NaIO_4$ (20 mg) in 60% aq. HOAc (0.5 ml). After 1 min the mixture was extracted with CH_2Cl_2. The CH_2Cl_2 soln was washed with aq. $NaHCO_3$, dried and evapd. TLC of the residue gave **1b** (7 mg), red oil, ORD (*c* 0.18): $[\phi]_{625}$ 0, $[\phi]_{476}$ +2380, $[\phi]_{443}$ 0, $[\phi]_{385}$ −12900, $[\phi]_{340}$ 0, identical (IR, ORD) with the natural compd from *M. nictitans*. *Diacetate* (**2d**), oil. [Found: M (MS), 400. $C_{22}H_{24}O_7$ requires: M, 400]. ν_{max} (cm^{-1}): 1750, 1630, 1600. PMR (τ): 2.88, 2.99 (A_2B_2 system, J_{AB} = 8.5 Hz, H-2', H-6' and H-3', H-5'), 3.44 (*s*, H-6), 3.5–4.2 (*m*, CH=), 4.7–5.3 (*m*, CH—CH=CH_2), 6.12, 6.16, 6.38 (*s*, 3 OMe), 7.75, 7.76 (*s*, 2 OAc). *Diethyl ether.* **2b** (130 mg), EtI (500 mg), K_2CO_3 (500 mg), Me_2CO (10 ml), reflux (16 hr), filtration, and TLC purification (Si gel, $CHCl_3$) gave **2e** (140 mg, 92%), pale yellow oil. [Found: C, 70.93; H, 7.68. $C_{22}H_{28}O_5$ requires: C, 70.94; H, 7.58%]. ν_{max} (cm^{-1}): 1630, 1600. PMR (τ): 2.93, 3.18 (A_2B_2 system, J_{AB} = 9 Hz, H-2', H-6' and H-3', H-5'), 3.58 (H-6), 3.5–4.0 (*m*, CH=), 4.7–5.3 (*m*, CH—CH=CH_2), 6.10 (*s*, 2 OMe), 6.40 (*s*, OMe), 6.02 (*q*), 6.19 (*q*), 8.63 (*t*) (2 A_2X_3 systems, J_{AX} = 7 Hz). *Dihydro-diethyl ether.* **2e** (50 mg) in EtOH (10 mg), 10% Pd/C (100 mg), H_2 (room temp., 1 atm, 14 hr) gave (*R*)-1-(5-ethoxy-2,3,4-trimethoxyphenyl)-1-(4-ethoxyphenyl)-propane (50 mg), oil. [Found: M (HRMS), 374.2089. $C_{22}H_{30}O_5$ requires: M, 374.2093]. ν_{max} (cm^{-1}): 1600. PMR (τ): 2.86, 3.21 (A_2B_2 system, J_{AB} = 8.8 Hz, H-2', H-6' and H-3', H-5'), 3.48 (H-6), 6.11 (*s*, 2 OMe), 6.37 (*s*, OMe), 5.93 (*t*), 8.05 (quintet), 9.12 (*t*) (AB_2X_3 system, J_{AB} = 7 Hz, J_{BX} = 7 Hz, CH_A—CH_{2B}—CH_{3X}), 6.01 (*q*), 6.17 (*q*), 8.60 (*t*), 8.62 (*t*) (2 A_2X_3 systems, *J* = 7 Hz, 2 OEt).

Kuhlmannin (**3b**). Fawn needles, mp 211° (MeOH). [Found: C, 68.61; H, 4.64. $C_{17}H_{14}O_5$ requires: C, 68.45; H, 4.73%]. λ_{max} (nm): 214, 300 (ε 25000, 6500). ν_{max} (cm^{-1}): 3500, 1710, 1555, 1395. PMR (τ): 2.51 (*s*, C_6H_5), 3.23 (*s*, H-5), 3.70 (*s*, H-3), 4.27 (*s*, OH), 5.89, 5.92 (2 *s*, 2 OMe).

Kuhlmannene (**4**). Needles, mp 139–141° (MeOH). [Found: C, 71.89; H, 5.41. $C_{17}H_{16}O_4$ requires: C, 71.82; H, 5.67%]. λ_{max} (nm): 221, 330 (ε 22000, 2400). ν_{max} (cm^{-1}): 3500, 1585. PMR (τ): 2.71 (*s*, C_6H_5), 3.65 (*s*, H-5), 4.26 (*t*, H-3), 5.23 (*d*, 2 H-2) (A_2X system, J_{AX} = 4 Hz), 4.6 (*br. s*, OH), 6.07, 6.09 (2 *s*, 2 OMe). *Ring opening.* 8N chromic acid (1 ml) was added to **4** (20 mg) in $CHCl_3$ (10 ml). TLC of the reaction mixture gave (±)-3,4-dimethoxydalbergione (20 mg), identical (IR and PMR) with **1a**. *Synthesis.* **1a** (20 mg) in $CHCl_3$ (10 ml) was poured over dry, neutral Al_2O_3 (2 g). Elution with $CHCl_3$ gave **4** (20 mg), identical (IR, PMR, mp) with the natural compd.

Methyl 3-(*2-hydroxy-4-methoxyphenyl*)-*propionate* (**12**). Cream needles, mp 88–89° (MeOH). [Found: C, 62.93; H, 6.97. $C_{11}H_{14}O_4$ requires: C, 62.85; H, 6.71%]. λ_{max} (nm): 211, 222 infl., 281 (ε 9000, 6600, 2200). ν_{max} (cm^{-1}): 3250 *br.*, 1700, 1600. PMR (τ): 2.81 (*br.*, OH), 3.06, 3.58, 3.61 (ABX system, J_{AB} = 3 Hz, J_{BX} = 9 Hz, H-3, H-5, H-6), 6.29, 6.34 (2 *s*, 2 OMe), 7.1–7.5 (*m*, 2 CH_2). *Synthesis.* HCl was passed through **13** (4 g) in MeOH (200 ml) (1 hr). Evapn gave a residue which cryst. from MeOH to give **12** (4 g, 91%), identical (IR, PMR, mp) with the natural compd.

Kuhlmannistyrene (**5a**). Pale yellow oil. [Found: M (HRMS), 316.1311. $C_{18}H_{20}O_5$ requires: M, 316.1312]. λ_{max} (nm): 253, 290 (ε 24000, 10700). ν_{max} (cm^{-1}): 3500, 3300 *br.*, 1600. PMR (τ): 2.6–3.2 (*m*, H-3', H-4', H-5', H-6'), 3.52 (*s*, H-6), 3.52 (*dt*), 4.06 (dt), 6.65 (*dd*) (ABX$_2$ system, J_{AB} = 11 Hz, J_{BX} = 7 Hz, J_{AX} = 1.5 Hz, CH_A=CH_B—CH_{2X}), 4.9 (*br. s*, 2 OH), 6.09 (*s*, 2 OMe), 6.28 (*s*, OMe). *Hydrogenation*, **5a** (20 mg), EtOH (10 ml), 10% Pd/C (100 mg), H_2 (room temp., 1 atm, 14 hr) gave 1-(5-hydroxy-2,3,4-trimethoxyphenyl)-3-(2-hydroxyphenyl)-propane (20 mg), oil. [Found: M (HRMS), 318.1461. $C_{18}H_{22}O_5$ requires: M, 318.1467], identical (IR, PMR) with dihydropetrostyrene [1].

Synthesis of (±)-1-(*5-ethoxy-2,3,4-trimethoxyphenyl*)-1-(*4-ethoxyphenyl*)-*propane* (**9**). 4-Ethoxybenzoic acid (20 g) [24], pyrogallol (15 g) and BF_3–Et_2O (200 ml) were heated (100°, 2 hr) and poured into 2N HCl (1 l.). Extraction with $CHCl_3$, evapn and cryst. of the residue from $CHCl_3$–petrol. (bp 60–80°) gave 4'-ethoxy-2,3,4-trihydroxybenzophenone (**10a**) (24 g, 73%), fawn needles, mp 104–105°. [Found: M (MS), 274. $C_{15}H_{14}O_5$ requires: M, 274]. ν_{max} (cm^{-1}): 3500, 3000 *br.*, 1625, 1600. PMR (τ): −2.5 (*br. s*, OH), 2.34, 3.06 (A_2B_2 system, J_{AB} = 9 Hz, H-2', H-6' and H-3', H-5'), 2.83, 3.53 (AB system, J_{AB} = 9 Hz, H-5, H-6), 3.9 (*br. s*, 2 OH), 5.91 (*q*), 8.57 (*t*) (A_2X_3 system, J_{AX} = 7 Hz, OEt). **10a** (23 g), Me_2SO_4 (25 ml), K_2CO_3 (25 g), Me_2CO (250 ml), reflux (16 hr), filtration, evapn and cryst. of the residue from petrol. (bp 60–80°) gave 4'-ethoxy-2,3,4-trimethoxybenzophenone (**10b**) (24 g, 91%), stout needles, mp 88–90°. [Found: C, 68.32, H, 6.48. $C_{18}H_{20}O_5$ requires: C, 68.34; H, 6.34%]. ν_{max} (cm^{-1}): 1650, 1600. PMR (τ): 2.22, 3.12 (A_2B_2 system, J_{AB} = 8.5 Hz, H-2', H-6' and H-3', H-5'), 2.93, 3.31 (AB system, J_{AB} = 8.5 Hz, H-5, H-6), 6.10 (*s*, 2 OMe), 6.24 (*s*, OMe), 5.92 (*q*), 8.57 (*t*) (A_2X_3 system, J_{AX} = 6.8 Hz, OEt). **10b** (22.5 g) and $AlCl_3$ (10 g) in $PhNO_2$ (25 ml) were heated (100°, 1 hr) and 2N HCl added. Removal of $PhNO_2$ by steam distillation, extraction with Et_2O, evapn and cryst. from MeOH gave 4'-ethoxy-2-hydroxy-3,4-dimethoxybenzophenone (**10c**) (15 g, 70%), pale yellow needles, mp 113–114°. [Found: C, 67.71; H, 6.33. $C_{17}H_{18}O_5$ requires: C, 67.54; H, 6.00%]. ν_{max}(cm^{-1}): 3000 *br.*, 1615, 1600. PMR (τ): −2.39 (*s*, OH), 2.37, 3.07 (A_2B_2 system, J_{AB} = 9 Hz, H-2', H-6' and H-3', H-5'), 2.63, 3.56 (AB system, J_{AB} = 9 Hz, H-5, H-6), 6.08 (*s*, 2 OMe), 5.87 (*q*), 8.55 (*t*) A_2X_3 system, J_{AX} = 6.9 Hz, OEt). **10c** (14.1 g), oxidised with $K_2S_2O_8$ (12 g) as in ref. [25], gave 4'-ethoxy-2,5-dihydroxy-3,4-dimethoxybenzophenone (**10d**) (3.5 g, 24%), pale yellow needles, mp 140–142° (C_6H_6). [Found: 63.96; H, 5.86. $C_{17}H_{18}O_6$ requires: C, 64.14; H, 5.70%]. ν_{max} (cm^{-1}): 3500, 2900 *br.*, 1615, 1600. PMR (τ): −2.10 (*s*, OH), 2.36, 3.08 (A_2B_2 system, J_{AB} = 8.5 Hz, H-2', H-6' and H-3', H-5'), 3.05 (*s*, H-6), 4.5 (*br. s*, OH), 5.89, 6.04 (2 *s*, 2 OMe), 5.91 (*q*), 8.56 (*t*), (A_2X_3 system, J_{AX} = 6.9 Hz, OEt). **10d** (2.8 g), EtI (1.2 g), K_2CO_3 (3 g) in Me_2CO (50 ml), reflux (16 hr), filtration, evapn and purification of the residue by TLC (Si gel, $CHCl_3$). The faster running product gave 5,4'-diethoxy-2-hydroxy-3,4-dimethoxybenzophenone (**10a**) (2.4 g, 79%), pale yellow needles, mp 60–61.5° [petrol (bp 40–60°).] [Found: C, 66.16; H, 6.40. $C_{19}H_{22}O_4$ requires: C, 65.88. H, 6.41%]. ν_{max} (cm^{-1}): 3000 *br.*, 1615, 1600. PMR (τ): −2.07 (*s*, OH), 2.35, 3.07 (A_2B_2 system, J_{AB} = 8.8 Hz, H-2', H-6' and H-3', H-5'), 3.12 (*s*, H-6), 5.97, 6.05 (2 *s*, 2 OMe), 5.90, 6.10 (2 *q*), 8.54, 8.63 (2 *t*) (2 A_2X_3 systems, J_{AX} = 7 Hz, 2 OEt). **10e** (1.8 g), MeI (1.5 g), K_2CO_3 (2.0 g) in Me_2CO (20 ml), reflux (16 hr), filtration and evapn gave 5,4'-diethoxy-2,3,4-trimethoxybenzophenone (**10f**) (1.1 g, 59%), oil. [Found: C, 66.61; H, 6.87. $C_{20}H_{24}O_6$ requires: C, 66.65; H, 6.71%]. ν_{max} (cm^{-1}): 1650, 1600. PMR (τ): 2.21, 3.10 (A_2B_2 system, J_{AB} = 9 Hz, H-2', H-6' and H-3', H-5'), 3.38 (*s*, H-6), 6.05 (*s*, 2 OMe), 6.31 (*s*, OMe), 5.90, 5.97 (2 *q*), 8.57 (*t*) (2 A_2X_3 systems, J_{AX} = 7 Hz, 2 OEt). EtI (2.5 ml) in anh. Et_2O (10 ml) was added to Mg turnings (500 mg) and I_2 (2 crystals).

After 1 hr stirring, **10f** (700 mg) in Et_2O (10 ml) was added and stirring continued (16 hr). H_2O (20 ml) and 2N H_2SO_4 (30 ml) were added. Et_2O extraction and evapn gave a *Z*/*E* mixture of 1-(5-ethoxy-2,3,4-trimethoxyphenyl)-1-(4-ethoxyphenyl)-propene (**10g**) (0.65 g, 90%), pale yellow oil. Without purification, **10g** (50 mg) in EtOH (10 ml) was hydrogenated (room temp., 1 atm., 20 hr) over 10% Pd/C (100 mg). Filtration and evapn gave **9** (50 mg), oil, identical) IR, PMR) with the dihydrodiethyl ether of kuhlmanniquinol.

REFERENCES

1. Ollis, W. D., Redman, B. T., Sutherland, I. O. and Gottlieb, O. R. (1978) *Phytochemistry* **17**, 1379.
2. Hoehne, F. C. (1941) *Flora Brasilica* Vol. XXV, fasc. III, pp. 69, 73. Secretaria da Agricultura, Indústria e Comércio de São Paulo, Brasil.
3. Alves, H. M., Arndt, V. H., Ollis, W. D., Eyton, W. B., Gottlieb, O. R. and Magalhães, M. T. (1966) *Phytochemistry* **5**, 1327.
4. Eyton, W. B., Ollis, W. D., Fineberg, M., Gottlieb, O. R., Guimarães, I. S. de S. and Magalhães, M. T. (1965) *Tetrahedron* **21**, 2697.
5. Ahluwalia, V. K. and Seshadri, T. R. (1957) *J. Chem. Soc.* 970.
6. Gregson, M., Kurosawa, K., Ollis, W. D., Redman, B. T., Roberts, R. J., Sutherland, I. O., Oliveira, A. B. de, Eyton, W. B., Gottlieb, O. R. and Dietrichs, H. H. (1968) *Chem. Commun.* 1390.
7. Matos, F. J. de A., Gottlieb, O. R. and Andrade, C. H. S. (1975) *Phytochemistry* **14**, 825.
8. Ollis, W. D., Redman, B. T., Roberts, R. J., Sutherland, I. O. and Gottlieb, O. R. (1968) *Chem. Commun.* 1392.
9. Eyton, W. B., Ollis, W. D., Sutherland, I. O., Gottlieb, O. R., Magalhães, M. T. and Jackman, L. M. (1965) *Tetrahedron* **21**, 2683.
10. Adler, E. and Magnusson, R. (1959) *Acta Chem. Scand.* **13**, 505.
11. Donnelly, D. M. X., Nangle, B. J., Prendergast, J. P. and O'Sullivan, A. M. (1968) *Phytochemistry* **7**, 647.
12. Barnes, M. F., Ollis, W. D., Sutherland, I. O., Gottlieb, O. R. and Magalhães, M. T. (1965) *Tetrahedron* **21**, 2707.
13. Donnelly, D. M. X. (1975) *The Flavonoids* (Harborne, J. B., Mabry, T. J. and Mabry, H. eds) p. 801. Chapman & Hall, London.
14. Ahluwalia, V. K., Rustogi, C. L. and Seshadri, T. R. (1959) *Proc. Indian Acad. Sci.* **49A**, 104.
15. Links, J. (1960) *Biochim. Biophys. Acta* **38**, 193; Isler, O., Langemann, A., Mayer, H., Ruegg, R. and Schadel, P. (1965) *Bull. Nat. Inst. Sci. India* **28**, 132.
16. Ollis, W. D. and Gottlieb, O. R. (1968) *Chem. Commun.* 1396.
17. Kurosawa, K., Ollis, W. D., Sutherland, I. O., Gottlieb, O. R. and Oliveira, A. B. de (1978) *Phytochemistry* **17**, 1389.
18. Kurosawa, K., Ollis, W. D., Sutherland, I. O. and Gottlieb, O.R. (1978) *Phytochemistry* **17**, MS 1417.
19. Pauly, H., Schubel, K. and Lockemann, K. (1911) *Ann. Chem.* **383**, 288.
20. Herzig, J. and Pollak, J. (1903) *Chem. Ber.* **36**, 661.
21. Graebe, G. and Hess, H. (1905) *Ann. Chem.* **340**, 232.
22. Baker, W., Montgomery, L. V. and Smith, H. A. (1932) *J. Chem. Soc.* 1281.
23. Fear, C. M. and Menzie, R. C. (1926) *J. Chem. Soc.* 938.
24. Cohen, J. B. and Dudley, H. W. (1910) *J. Chem. Soc.* 1732.
25. Baker, W. and Brown, N. C. (1948) *J. Chem. Soc.* 2303.