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(−)-RUBRANINE FROM *ANIBA ROSAEODORA**

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Key Word Index—*Aniba rosaeodora*; Lauraceae; (−)-rubranine; citrylidene chalcone; pinocembrin; geranylation; pyrolysis; synthesis.

Abstract—*Aniba rosaeodora* wood was shown to contain (−)-rubranine. An optically inactive form of this citrylidene-chalcone was previously considered to be an artifact of extraction. The constitution of rubranine was confirmed by pyrolysis and syntheses, involving previously reported pyridine-catalysed condensation of pinocembrin and citral, whereby novel intermediates were prepared, and the acid-catalysed condensation of pinocembrin with geraniol followed by oxidation.

INTRODUCTION

At the outset of the present studies on Lauraceae species, the presence of an orange product in *Aniba rosaeodora* Ducke was reported [2]. Later named rubranine, its structural elucidation relied on spectral data, complemented by acid isomerization **1a** → **2a** [3], **3** and **4** [4], as well as syntheses involving pyridine-catalysed condensation of citral and either phloroacetophenone (followed by aldol condensation of the resulting product **1c** with benzaldehyde) [3, 5] or pinocembrin (**5a**) at 160°. At 100° the latter reaction gives **6** and **7** which at 180° yields rubranine (**1a**). Spectral evidence being incompatible with the existence of unchelated hydroxyl and carbonyl functions, structure **8** cannot represent either of the intermediates, invalidating structure **1b** for rubranine [6].

The distinction between **1a** and **1b** is impossible on spectral grounds [3, 6]. Even acid isomerization, on which the original structural proposal **1a** was based [3], lost weight as a decisive argument with the isolation of **4**. This was postulated to arise from **1a** by opening of both benzylic ether bonds, rotation of 180° about the Ar—C bond and ring closure [4]. The formation of compounds **2a** and **3** could, of course, be rationalized through an analogous sequence of events starting from **1b**.

With regard to acid isomerization, it may be relevant to mention that rubranine (**1a**), as well as racemic pinocembrin (**5a**) [8], were obtained from rosewood by a process [3] which involved extraction with boiling benzene and repeated washings of the solution with dilute HCl in order to separate anibine (**9a**) [2]. The rubranine was found to be optically inactive and this fact, as well as the absence of citral in the wood was explained postulating anibine-catalysed scavenging of citral by pinocembrin during extraction, Indeed, racemic rubranine was formed in excellent yield when the compounds were heated, presumably in benzene, to reflux temperature [3].

RESULTS AND DISCUSSION

Prior to examination of the possibility of artifact formation we wanted to confirm the structure of our (−)-rubranine. An analytical means of differentiating between the structures **1a** and **1b**, an alternative to acid isomerization, consists of pyrolysis. Lack of colour and the UV spectrum of the product indicated that the original chalcone chromophore had been isomerised to a flavanone type. In spite of its chromatographic behaviour (one TLC spot) and sharp mp. the product was a *ca* 1:1 mixture of two compounds, both showing a chelated hydroxyl (τ −2.23, −2.19). The derivatives were represented as the linear isomers **2a** and **2b**, rather than the angular ones, on account of a strongly positive Gibbs test [10]. Although this evidence is not completely reliable, due to the possibility of ring opening under the conditions (pH 9.2) of the test, the presence of both the linear and the angular isomers in this mixture is unlikely, in view of the sharpness of the PMR signal of the lone aromatic proton. Both derivatives, **2a** and **2b**, contain vinylic methyls (τ 8.1). No such groups, of course, could be generated from **1b** whose pyrolysis should yield a 5-hydroxyflavanone with an exocyclic vinyl group (**12**).

Confirmation of this reasoning was obtained upon hydrogenation of the pyrolytic product, Again a mixture of two compounds resulted. These, however, could be separated by chromatography on silica gel into a 5-hydroxyflavanone (**2c**) and a 2′,6′-dihydroxydihydrochalcone (**13**). As expected both contain one quaternary (τ 8.7, singlet) and two tertiary (τ 8.8 and 9.3, doublets) methyls. Hydrogenation of **12** would have led to a compound possessing one tertiary and two quaternary methyls.

As already pointed out, however, the safest means of structural confirmation is the synthesis of rubranine by condensation of citral with pinocembrin in pyridine.

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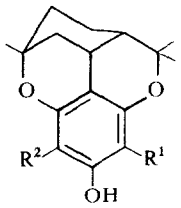
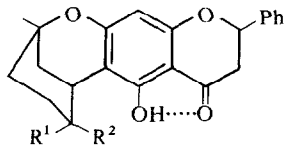
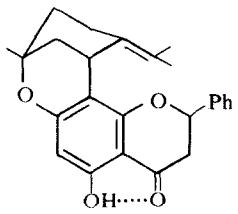


1a R^1 = COSt, R_2 = H
1b R^1 = H, R^2 = COSt
1c R^1 = COMe, R^2 = H
1d R^1 = H, R^2 = COMe



2a $R^1 = R^2 = CMe_2$
2b R^1 = H, $R^2 = CMeCH_2$
2c R^1 = H, $R^2 = CHMe_2$



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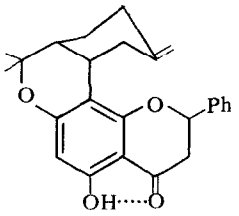

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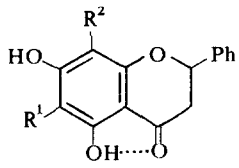
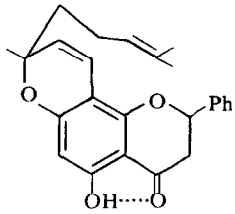


5a $R^1 = R^2$ = H
5b R^1 = H, R^2 = Ge
5c R^1 = Ge, R^2 = H



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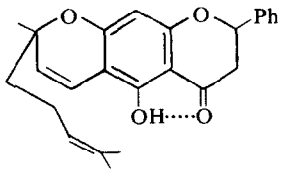

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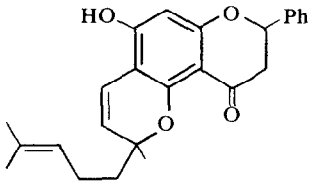

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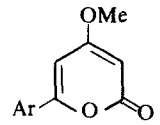
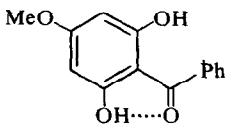


9a Ar = β-pyridyl
9b Ar = piperonyl

St = styryl, Ph = phenyl, Ge = geranyl

Indeed, this must lead to **1a** as the predominant citrylidene–chalcone [6], the precedence of Michael addition of the phenolate anion, formed from the hydroxyl of highest acidity, to the α,β-unsaturated aldehyde over C—C bond formation having been established [5]. Under conditions described for citral and phloroglucinol [11], a product resulted, which was fractionated by chromatography on silica gel into a 3:7 mixture of the flavanones **6** and **7** [6], a 10:13:77 mixture of the novel chalcones **14a**, **14b** and **15**, and a product which was indistinguishable from natural (−)-rubranine by TLC, mp, UV, IR, PMR and MS comparison. The relative proportion of the flavanones **6** and **7** was determined by measurement of the integrated intensities of the respective signals in the PMR spectrum of the mixture. The C-6 proton of **6** and the chromene protons of **7**, subject to the paramagnetic effect of the electron current in the vicinal chelate system, give rise to signals at lower field than the C-8 proton of 7 and the chromene protons of **6**. An analogous effect is responsible for the differences in chemical shifts of the signals due to the lone aromatic protons and the chromene protons in the chalcones. The former signals make the distinction between the rotamers **14a** and **14b** possible. Consideration of the intensities of the latter signals show that the major constituent of the chalcone mixture is the dichromene derivative **15**, a conclusion which was confirmed by MS.

Having satisfied ourselves with respect to the structure of (−)-rubranine, experiments were designed to show the feasibility of *in vivo* formation of the citrylidene system via condensation of geraniol and a phloroglucinol ring. In spite of the mildness of the chosen conditions, aqueous citric acid [12], phloroglucinol itself proved unsatisfactory as a model substrate. All 3 products, **16a**, **16b** and **17a**, obtained besides derivatives of geraniol [13], showed that the initial alkylating step had been followed by acid-catalysed cyclization. In order to produce the chromene intermediate of a citrylidene system, however, oxidative cyclization of the geranylphenol is required. The tendency for acid-catalysed cyclization can be diminished, using the less reactive phloroacetophenone as substrate. In this case, besides the two cyclized derivatives **16c** and **17b**, geranylphloroacetophenone (**18**) was obtained. This compound had



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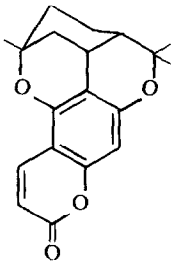

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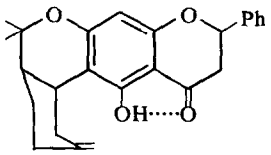

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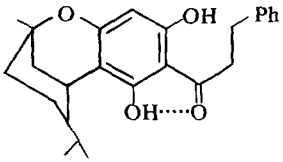

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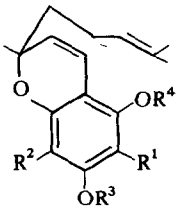
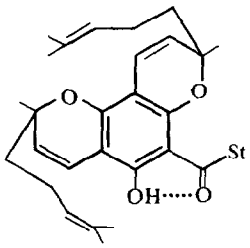


14a R^1 = COSt, R^2 = R^4 = H, R^3 = chelated H
14b R^1 = COSt, R^2 = R^3 = H, R^4 = chelated H
14c R^1 = COMe, R^2 = R^3 = R^4 = H
14d R^1 = R^3 = R^4 = H, R^2 = COMe



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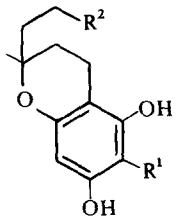
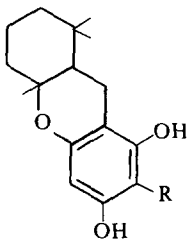
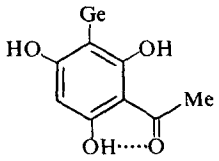


16a R^1 = H, R^2 = CH=CMe_2
16b R^1 = H, R^2 = CH_2COHMe_2
16c R^1 = COMe, R_2 = CH=CMe_2



17a R = H
17b R = COMe



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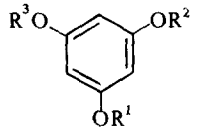

19a R^1 = COSt, R^2 = R^3 = H
19b R^1 = R^2 = COSt, R^3 = H
19c R^1 = R^2 = R^3 = COSt

already been prepared previously and oxidized with DDQ in refluxing benzene into the chromene **14c** [4]. At room temperature under reported conditions [14], we also succeeded in separating from the reaction product the isomeric chromene **14d** and a mixture of the citrylidene derivatives **1c** and **1d**. The components of the mixture were identified easily, having been obtained previously: **1c** (debenzylidenerubranine) by alkaline degradation of rubranine [3] or by heating of **14c** in pyridine [4], and **1d** by acid treatment of **14c** [4]. The surprising ease of production of these citrylidene derivatives, either during the oxidation reaction of geranylphloroacetophenone proper or during chromatographic separation of the products, favours the opinion that an analogous process may justify the biosynthesis of rubranine (**1a**) from pinocembrin (**5a**).

Pinocembrin (**5a**), for the final experiments, was prepared from cinnamoyl chloride and phloroglucinol according to a process [15] which does not describe the 3 side products **19a** **19b** [16] and **19c** we obtained in the reaction. Due to the slight solubility of pinocembrin in water, attempts at geranylation in aqueous citric acid failed. In a solution of TsOH in ethyl acetate, however, 8-geranylpinocembrin (**5b**) and 6-geranylpinocembrin (**5c**) were obtained in a 2:1 proportion. Oxidation of **5b** with DDQ in benzene at room temperature [14] gave the expected chromene **6**, a proven intermediate of rubranine synthesis [6]. Acid treatment of **6** was not optimized for obtaining rubranine. Under the rather vigorous conditions used, **3**, the major product of acid isomerization of rubranine [3,4] was produced directly.

In conflict with the statement that rubranine is an artifact [3] are the following observations: (1) (—)-rubranine can be isolated by washing *A. rosaeodora* wood for a few seconds at room temperature with hexene or benzene. (2) Citral does not accompany linalool and geraniol in *A. rosaeodora*. The same is true, however, for *A. duckei* Kosterm. [7], a species which, except for the replacement of pinocembrin by cotoin (**10**) [8] and the absence of rubranine, shows a very similar composition, including the presence of anibine [2]. Thus, by analogy with the reaction envisaged for the biosynthesis of deoxybruceol (**11**) [9], the formation of rubranine may also involve condensation of geranyl pyrophosphate, or even a linalool derivative, with a phloroglucinol system, in this case that of pinocembrin.

EXPERIMENTAL

Isolation of constituents. Ground branch wood of *A. rosaeodora* (2.6 kg) was percolated successively with C_6H_6 and EtOH. The C_6H_6 soln was evapd and the residue (48 g) was chromatographed on Si gel (400 g). Elution with C_6H_6 gave, in order, an oil, **1a** (4.5 g), **5a** [8] (8 g), with C_6H_6–$CHCl_3$ (2:1) gave **9b** [2] (0.3 g); and with C_6H_6–$CHCl_3$ (1:1) gave **9a** (0.6 g). The EtOH soln was evapd and 1/3 of the residue (50 g) was chromatographed on Si gel (400 g). Elution with C_6H_6–$CHCl_3$ (1:1) gave, in order, additional quantities of **5a** (0.2 g), **9b** (0.1 g) and **9a** (0.1 g).

(−)-Rubranine (**1a**) $[\alpha]_D^{25}$ −32.7 (7.63 mg/10 ml dioxane). MS (*m/e*). $M^{+\cdot}$ obs. 390.1845 (42%), $[C_{25}H_{26}O_4]^{+\cdot}$ req. 390.1831, obs. 375.1581 (4), $[M\text{-}Me]^+$ req. 375.1596, obs. 313.1454 (5), $[M\text{-}Ph]^+$ req. 313.1440; obs. 307.0993 (100), $[M\text{-}CH_2CH_2CH{=}CMe_2]^+$ req. 313.0970, obs. 203.0357 (31), $[M\text{-}CH_2CH_2CH{=}CMe_2{-}CH_2{=}CHPh]^+$ req. 203.0344. ORD (*c* 0.3416, $CHCl_3$, 25°, 420–250 nm) $[\phi]_{420}$ −570°, $[\phi]_{400}$ −570°, $[\phi]_{376}$ −2510°, $[\phi]_{348}$ 0°, $[\phi]_{315}$ −5760°, $[\phi]_{286}$ −3190°, $[\phi]_{260}$ −910°. Other data Refs [3, 6].

Pyrolysis of rubranine. **1a** 300 mg, 200–210°, 15 mm, 1 hr. The product was chromatographed on Si gel (2 g) and elution with petrol–C_6H_6 (1:4) gave a product, which, when washed with MeOH, gave colourless crystals (**2a** + **2b** (1:1) 92 mg) mp 124–126° (MeOH); (**2a** mp 135–137° [3]). λ_{max}^{MeOH} (nm): 229, 300, 349*sh* (ε 12900, 15000, 2350); no NaOAc shift; $\lambda_{max}^{MeOH+NaOH}$ (nm): 238, 251 *sh*, 299, 364 (ε 9500, 8300, 12100, 5450). ν_{max}^{KBr} (cm^{-1}): 3000 (*br*), 1629 (*br*), 1579, 1150, 1165, 760, 690. PMR ($CDCl_3$, 60 MHz, τ) **2a** [3]; **2b** −2.19 (*s*, OH-5), 2.57 (*s*, C_6H_5), 4.02 (*s*, H-8), 4.64 (*dd*, *J* = 11.5, 4 Hz, H-3), 5.36 (*m*, $=CH_2$), 6.5 (*m*, ArCH), 6.98 (*dd*, *J* = 17, 11.5 Hz, H-3), 7.3 (*dd*, *J* = 17, 4 Hz, H-3), 7.6–8.8 (*m*, 7 H), 8.13 (*bs*, Me), 8.66 (*s*, Me). MS (*m/e*) **2a** + **2b** $M^{+\cdot}$ obs. 390.1825 (31%), $[C_{25}H_{26}O_4]^{+\cdot}$ req. 390.1831, 375 (6, $[M\text{-}Me]^+$), 307 (100, $[M\text{-}C_6H_{11}]^+$), 203 (63, $[M\text{-}C_6H_{11}{-}CH_2CHPh]^+$).

Hydrogenation of pyrolytic product **2a** + **2b** 60 mg, Pd/C 120 mg, EtOH–$CHCl_3$ (1:1) 10 ml. The product was chromatographed on Si gel (2 g) and elution with C_6H_6 gave two fractions. The first gave **2c** (23 mg), colourless crystals, mp 59–60° (MeOH). λ_{max}^{MeOH} (nm): 217, 234 *sh*, 301, 248 *sh* (ε 21500, 12300, 16800, 4300). ν_{max}^{KBr} (cm^{-1}) 3400, 1630, 1575, 1160, 760, 700. Gibbs test positive. PMR ($CDCl_3$, 60 MHz, τ) −2.42 (*s*, CH-5), 2.56 (*s*, C_6H_5), 3.99 (*s*, H-8), 4.56 (*dd*, *J* = 11, 5 Hz, H-2), 6.98 (*dd*, *J* = 17, 11 Hz, H-3), 7.15 (*m*, ArH), 7.28 (*dd*, *J* = 17, 5 Hz, H-3), 7.8–8.9 (*m*, 8 H), 8.68 (*s*, Me), 8.78 (*d*, *J* = 5 Hz, Me), 9.26 (*d*, *J* = 5 Hz). MS (*m/e*) $M^{+\cdot}$ obs. 392.1979, $[C_{25}H_{28}O_4]^{+\cdot}$ req. 392.1988. The second fraction gave **13** (18 mg), colourless crystals, mp 80–82° (MeOH). λ_{max}^{MeOH} (nm): 212, 234 *sh*, 298, 351 *sh* (ε 19000, 12800, 14900, 4100). ν_{max}^{KBr} (cm^{-1}): 3350 (*br*), 1630–1580, 1158, 708. PMR ($CDCl_3$, 60 MHz, τ): −3.77 (*s*, OH-2'), 2.37 (*s*, C_6H_5), 3.76 (*s*, H-5'), 4.25 (*s*, OH-6'), 6.5–6.8 (*m*, $Ar(CH_2)_2CO$), 7.03 (*m*, ArCH), 7.8–8.9 (*m*, 8 H), 8.73 (*s*, Me), 8.80 (*d*, *J* = 5 Hz, Me), 9.28 (*d*, *J* = 5 Hz, Me). MS (*m/e*). $M^{+\cdot}$ obs. 394.2136 (30%), $[C_{25}H_{30}O_4]^{+\cdot}$ req. 394.2144, 309 (100, $[M\text{-}C_6H_{13}]^+$), 289 (18, $[M\text{-}(CH_2)_2Ph]^+$), 203 (5, $[M\text{-}C_6H_{13}{-}(CH_2)_2Ph]^+$).

Condensation of pinocembrin and citral **5a** 2 g, citral 4 ml, C_5H_5N 4 ml, 110–120°, 15 hr. Excess citral and C_5H_5N were evapd under vacuum and the residue chromatographed on Si gel (25 g). Elution with C_6H_6 gave, in order, **6** + **7** (3.7, 308 mg, data ref [6]), (±)-**1a** (51 mg) and a fraction which was rechromatographed twice on Si gel to give **14a** + **14b** + **15** (10:13:77, 18 mg). ν_{max}^{KBr} (cm^{-1}) 3400 (*br*), 1630, 1582, 1160, 770, 706. PMR ($CDCl_3$, 60 MHz, τ)· −4.30 (*s*, OH), 2.27–2.72 (*m*, C_6H_5), 1.88 (*d*, *J* = 16 Hz, PhCH=), 2.17 (*d*, *J* = 16 Hz, COCH=), 4.51 (*d*, *J* = 10 Hz, CCH=), 4.82 (*m*, CH=C), 7.5–8.6 (*m*); further signals of **14a** 3.98 (*s*, H-5'), 3.31 (*d*, *J* = 10 Hz, ArCH=), 8.43 (*s*, 2 × Me), 8.58 (*s*, Me); further signals of **14b** 4.03 (*s*, H-5'), 3.21 (*d*, *J* = 10 Hz, ArCH=), 8.43 (*s*, 2 Me), 8.58 (*s*, Me), further signals of **15** 3.21 and 3.31 (2*d*, *J* = 10 Hz, 2 × ArCH=), 8.37 (*s*, 2 × Me), 8.53 (*s*, Me). MS (*m/e*): **15** $M^{+\cdot}$ 524.2918 (20%), $[C_{35}H_{40}O_4]^{+\cdot}$ req. 524.2927, 509 (6, $[M\text{-}Me]^+$), 441 (100, $[M\text{-}C_6H_{11}]^+$), 337 (8, $[M\text{-}Me{-}C_6H_{11}{-}CH_2CHPh]^+$), **14a** + **14b** $M^{+\cdot}$ 390.1840 (1), $[C_{25}H_{26}O_4]^{+\cdot}$ req. 390.1831, 307 (7, $[M\text{-}C_6H_{11}]^+$), 203 (15, $[M\text{-}C_6H_{11}{-}CH_2CHPh]^+$).

Condensation of phloroglucinol and geraniol. Resp. 23 g and 14 ml, ascorbic acid 2 g, 5% aq. citric acid 400 ml, 80°, mixing, 11 hr. The oil, which pptd upon cooling to 0°, was separated and dissolved in Et_2O. The soln was washed with H_2O, dried and evaporated. The oily residue (30 g) was chromatographed on Si gel (500 g). Elution with a solvent gradient from C_6H_6–EtOAc (19:1) to (1:19) gave 11 fractions. Fraction 3 (11 g), upon filtration through Si gel (in C_6H_6–EtOAc 4:1), gave **16a** + **17a** which could not be separated on Si gel, Florisil, Sephadex LH-20 using a series of solvent systems. Fraction 9 (6 g), upon filtration through Si gel (C_6H_6–EtOAc, 1:1), gave **16b**, **16a** + **17a**, colourless oil. PMR (CCl_4, 60 MHz, τ) 3 (*br*, OH), 3.85 (*s*, ArH), 7.4 (*br*, $ArCH_2$), 8.9 (*m*); further signals of **16a** 4.8 (*m*, CH=), 8.3 (*s*, Me), 8.38 (*s*, Me), 8.68 (*s*, Me); further signals of **17a** 8.85 (*s*, Me), 9.09 (*s*, Me), 9.15 (*s*, Me). The acetate could not be resolved into components. PMR (CCl_4, 60 MHz, τ). 3.4 (*s*, ArH), 7.4 (*t*, *J* = 6 Hz, $ArCH_2$), 7.74 (*br s*, OCOMe), 7.7–8.8 (*m*); further signals of **16a** acetate 4.75 (*m*, CH=), 8.25 (*s*, Me), 8.34 (*s*, Me), 8.68 (*s*, Me), further signals of **17a** acetate 8.74 (*s*, Me), 8.85 (*s*, Me), 9.15 (*s*, Me). **16b**, colourless solid, mp 186–189°. ν_{max}^{KBr} (cm^{-1}): 3500, 3350, 3140, 1610, 1510, 1380 (d), 1195, 1150, 835, 830. PMR (DMSO, 60 MHz, τ) 3.98 (*d*, *J* = 2.5 Hz, ArH), 4.2 (*d*, *J* = 2.5 Hz, ArH), 7.45 (*t*, *J* = 7 Hz, $ArCH_2$), 8.3 (*t*, *J* = 7 Hz, $ArCH_2C\underline{H}_2$), 8.55 (*br s*, 6 H), 8.75 (*s*, Me), 8.88 (*s*, 2 × Me). MS (*m/e*): $M^{+\cdot}$ obs. 280.1684 (43%) $[C_{16}H_{24}O_4]^{+\cdot}$ req. 280.1675, 268 (8, $[M\text{-}Me]^+$), 179 (35, $[M\text{-}(CH_2)_3COHMe_2]^+$), 177 (48, $[179\text{-}2H]^+$), 139 (100, [tri-OH-tropylium]$^+$), 138 (43, retroDiels–Alder fragment). The acetate, oil. PMR (CCl_4, 60 MHz, τ): 3.4 (*d*, *J* = 2 Hz, ArH), 3.45 (*d*, *J* = 2 Hz, ArH), 7.45 (*t*, *J* = 6 Hz, $ArCH_2$), 7.74 (*s*, OCOMe), 7.78 (*s*, OCOMe), 8.22 (*t*, *J* = 6 Hz, $ArCH_2C\underline{H}_2$), 8.52 (*br s*, 6 H), 8.7 (*s*, Me), 8.82 (*s*, 2 Me).

Condensation of phloroacetophenone and geraniol. Resp. 50 g and 26 ml, ascorbic acid 4.3 g, 5% aq. citric acid 850 ml, 80°, mixing, 11 hr. Work-up as described for phloroglucinol gave 9 fractions. Fractions 2–4 (3.6 g), upon careful, prep-TLC on Si gel (C_6H_{14}–EtOAc 4:1), gave the slightly faster moving **16c** and the slightly slower moving **17b**. Fraction 6 (1.2 g) was crystallized from $CHCl_3$–hexane to **18** (0.84 g). Fraction 7 gave phloroglucinol (1.5 g). **16c**, ν_{max}^{KBr} (cm^{-1}). 3250, 1635, 1580, 1300, 1160, 1100. PMR (CCl_4, 60 MHz, τ)· −1.82 (*s*, OH), 2 (*s*, OH), 4.21 (*s*, ArH), 4.9 (*t*, CH=), 7.35 (*s*, COMe), 7.4 (*t*, $ArCH_2$), 8.1 (*t*, $ArCH_2C\underline{H}_2$), 7.8–8.8 (*m*, 4H), 8.35 (*s*, Me), 8.4 (*s*, Me), 8.7 (*s*, Me). MS (*m/e*): $M^{+\cdot}$ obs. 304.1688 (7%), $[C_{18}H_{24}O_4]^{+\cdot}$ req. 304.1675, 221 (9, $[M\text{-}C_6H_{11}]^+$), 219 (53, $[221\text{-}2H]^+$), 180 (67, retro-Diels–Alder fragment), 121 (37), 119 (98), 117 (100). **17b**, PMR (CCl_4, 60 MHz, τ): −3.6 (*s*, OH), 2.42 (*s*, OH), 4.32 (*s*, ArH), 7.38 (*s*, COMe), 7.3–8.8 (*m*, 9H), 8.78 (*s*, Me), 8.98 (*s*, Me), 9.1 (*s*, Me). MS (*m/e*). $M^{+\cdot}$ obs. 304.1670 (25%), $[C_{18}H_{24}O_4]^{+\cdot}$ req. 304.1675, 219 (25, $[M\text{-}C_6H_{11}\text{-}2H]^+$), 180 (100, retro-Diels–Alder fragment), 123 (25). **18**, pale yellow, mp 119–120° (**18** was obtained with commercial geraniol; according to ref. [4] geranylphloroacetophenone is a yellow oil and nerylphloroacetophenone is a colourless solid, mp 109–110°). ν_{max}^{KBr} (cm^{-1}): 3350, 1635, 1600, 1450, 1360, 1229, 880, 809. PMR [$(CD_3)_2CO$, 60 MHz, τ]: −3.83 (*s*, OH), 0.5 (*s*, OH), 1 (*s*, OH), 3.9 (*s*, ArH), 4.73 (*t*, *J* = 7.5 Hz, CH=), 4.84 (*t*, *J* = 7.5 Hz, CH=), 6.75 (*d*, *J* = 7.5 Hz, $ArCH_2$), 7.38 (*s*, COMe), 8 (*m*, 4H), 8.25 (*s*, Me), 8.4 (*br s*, 2 Me). MS (*m/e*): $M^{+\cdot}$ obs. 304.1666 (18%), $[C_{18}H_{24}O_4]^{+\cdot}$ req. 304.1675, 261 (8, $[M\text{-}COMe]^+$), 235 (33, $[M\text{-}C_5H_9]^+$), 219 (25, $[M\text{-}C_9H_{13}]^+$), 193 (25, $[261\text{-}C_5H_8]^+$), 181 (100, $[M\text{-}C_9H_{15}]^+$).

Oxidation of geranylphloroacetophenone **18** 600 mg, DDQ 454 mg, dry C_6H_6 100 ml, mixing, room temp., 4 hr. The mixture was filtered, evapd and the residue separated by prep-TLC on Si gel (C_6H_6–EtOAc, 4:1), in order of increasing R_fs into **18**, **14c** [4] (106 mg), **14d** (5 mg) and **1c** [3, 4] + **1d** [4] (40 mg). **14d** PMR (CCl_4, 60MHz, τ) −3.13 (*s*, OH), −2.55 (*s*, OH), 3.37 (*d*, *J* = 10 Hz, ArCH=), 4.23 (*s*, ArH), 4.62 (*d*, *J* = 10 Hz, CCH=), 7.43 (*s*, OCOMe), 8.33 (*s*, Me), 8.45 (*s*, Me), 8.66 (*s*, Me).

Synthesis of pinocembrin. As in ref. [15]. The crude reaction product was separated by chromatography on Si gel into **5a**

[8], **19a** [16], **19b** and **19c**. **19b**, mp 153–155° (C_6H_6), ν_{max}^{KBr} (cm^{-1}): 3400, 1710, 1600, 1580, 1270, 1235, 850, 830, 760, 695. PMR [$(CD_3)_2CO$, 60 MHz, τ]: 1.17 (*s*, OH), 2.2 (*d*, J = 16 Hz, CH=), 2.27 (*m*, 4 H), 2.6 (*m*, 6 H), 3.29 (*d*, J = 16 Hz, CH=), 3.39 (*s*, 3 H). **19c**, mp 147–148° (C_6H_6), ν_{max}^{KBr} (cm^{-1}): 1720, 1640, 1600, 1125, 870, 860, 760, 700. PMR [$(CD_3)_2CO$, 60 MHz, τ]: 2.23 (*d*, J = 16 Hz, CH=), 2.27 (*m*, 6 H), 2.6 (*m*, 9 H). 3.01 (*s*, 3 H), 3.3 (*d*, J = 16 Hz, CH=).

Condensation of pinocembrin and geraniol. A soln of **5a** (440 mg) and TsOH (24 mg) in EtOAc (24 ml) was maintained at 80° during dropwise addition of geranoil (1 hr) and for an additional 5 hr. After cooling to room temp., the soln was washed with aq. $NaHCO_3$, dried and evapd. The residue was chromatographed on Si gel and elution with C_6H_6 containing gradually increasing proportions of EtOAc gave **5b** (150 mg), **5c** (80 mg), **5a** (350 mg) and oils. **5b** and **5c** were purified by prep-TLC on Si gel (C_6H_6–EtOAc 4:1). **5b**, mp 110–111°, ν_{max}^{KBr} (cm^{-1}) 3150, 1639, 1600, 1282, 1176, 1081, 844, 769, 699. PMR ($CDCl_3$, 60 MHz, τ): −2 (*s*, OH), 2.57 (*s*, C_6H_5), 3.95 (*s*, H-6), 4.4–5.1 (*m*, 2 × CH=, H-2), 6.67 (*d*, J = 7 Hz, $ArCH_2$), 6.9–7.4 (*m*, 2H-3), 7.97 (*br s*, 2 × CH_2), 8.3 (*br s*, 2 × Me), 8.4 (*s*, Me). MS (*m/e*): $M^{+\cdot}$ obs. 392.1985 (16%), $[C_{25}H_{28}O_4]^{+\cdot}$ req. 392.1988, 307 (16%), 269 (100%), 219 (92%), 165 (50%), 123 (22%), 121 (22%). **5c**, mp 143–145° ($CHCl_3$–C_6H_{14}), ν_{max}^{KBr} (cm^{-1}): 3150 (*br*), 1639, 1587, 1299, 1176, 1156, 1087, 833, 766, 700. PMR ($CDCl_3$, 60 MHz, τ): −2.31 (*s*, OH), 2.6 (*s*, C_6H_5), 4.04 (*s*, H-8), 4.4–5.2 (*m*, 2 × CH=, H-2), 6.67 (*d*, J = 7 Hz, $ArCH_2$), 6.9–7.4 (*m*, 2 × H-3), 7.97 (*br s*, 2 × CH_2), 8.2 (*s*, Me), 8.34 (*s*, Me), 8.4 (*s*, Me). MS (*m/e*): $M^{+\cdot}$ obs. 392.1997 (18%), $[C_{25}H_{28}O_4]^{+\cdot}$ req. 392.1988, 307 (29), 269 (100), 219 (71), 165 (82), 123 (24), 121 (21).

Oxidation of 8-geranylpinocembrin. **5b** 25 mg, DDQ 14 mg, dry C_6H_6 4 ml, mixing, room temp., 8 hr. The mixture, treated as above, gave **5b** (8 mg) and **6** [6] (9 mg).

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