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# PANICEINS, UNUSUAL AROMATIC SESQUITERPENOIDS LINKED TO A QUINOL OR QUINONE SYSTEM FROM THE MARINE SPONGE *HALICHONDRIA PANICEA*

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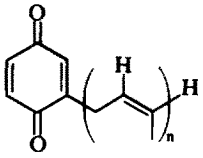
**Abstract**—Five new substances, panicein-A, -$B_1$, -$B_2$, -$B_3$ and C, containing an aromatic sesquiterpenoid moiety linked to a quinol or a quinone system, have been isolated from the sponge *Halichondria panicea*. The structures of these compounds were elucidated from their chemical and spectral properties.

The occurrence in marine sponges, *Ircinia sp.*, of the unsubstituted prenylated benzoquinones (1; n = 4, 6, 7, 8), a novel group of terpenoid quinones, and the corresponding quinols, present in much larger quantities, has been recently reported.[1] In pursuing our systematic search for metabolites from Porifera, we have now investigated the species *Halichondria panicea*, the ethanolic extracts of which were reported to have antibiotic activity against a number of microorganisms.[2] By a combination of column and TLC of solvent extracts of this species, collected in the Bay of Naples, we have now isolated five new related compounds designated panicein-A, -$B_1$, -$B_2$, -$B_3$ and -C in order of their polarities on silica gel. These substances proved to contain an aromatic sesquiterpenoid moiety linked to an unsubstituted benzoquinol or benzoquinone group, except for panicein-$B_2$, which is the chromenol (14), the cyclic isomer of the corresponding quinone panicein-$B_1$ (13), and probably an artifact of isolation.

Panicein-$B_3$ (2) has molecular formula $C_{21}H_{24}O_4$ deduced from accurate mass measurements ($m^+/e$ 340·16774; required: 340·17744). The UV (MeOH) spectrum has peaks at 276 and 346 nm ($\epsilon$ 12,600 and 3,400), supporting the presence of an aromatic *o*-hydroxycarbonyl structure,[3] and a shoulder at 294 nm ($\epsilon$ 5,100). The IR spectrum shows a CO band at 1640 $cm^{-1}$, the very low frequency of which indicated chelation with an OH group, confirmed by acetylation. Compound 2, in fact, forms a phenolic triacetate (3, $\nu_{max}$ 1760 $cm^{-1}$) $C_{27}H_{30}O_7$, in the IR spectrum of which the CO band at 1640 $cm^{-1}$ is replaced by an absorption at 1685 $cm^{-1}$.

Hence, all the O atoms in panicein-$B_3$ (2) are accounted for, three of them are present as phenolic groups, the other one forming a CO function which, from the NMR data must be an aldehyde (1H singlet at δ10·26). A singlet at δ12·01 (1H) exchangeable with $D_2O$ confirms the location of one phenolic group *ortho* to the aldehyde function.[4] Furthermore, the NMR spectrum of 2 shows four aromatic hydrogens (bm at δ6·59), two aromatic Me groups (δ2·45 and 2·27) and an Ar—$H_2C$—CH=$C(CH_3)$— grouping: the olefinic proton resonates as a broadened triplet at δ5·31 and its large coupling (J = 6Hz) to the methylene doublet which, from its chemical shift (δ3·28 ppm), must be also linked to an aromatic ring, was confirmed by double irradiation experiments; the vinyl Me group appears as a broad singlet at δ1·77, which is sharpened upon irradiation at the olefinic signal. A multiplet at δ2·62 (2H), assigned to a benzylic methylene group, coupled, as confirmed by decoupling experiments, to another methylene multiplet at δ2·09 (2H) which, from its chemical shift, must be linked to unsaturated carbon, and a broad signal centered at around δ5·7 exchangeable with $D_2O$ (2H, —OH), are the remaining signals in the NMR spectrum of 2.

From the foregoing spectroscopic data, panicein-$B_3$ would appear to contain two aromatic rings linked to each other by the aliphatic chain (4) and bearing the following substituents: 3 OH, 2 Me and a CHO function. A prominent ion at *m/e* 161 in the mass spectrum of 2, which is also given by the 2-polyprenyl benzoquinols[1] and attributed to the fragment a, suggests an 1,4-dihydroxybenzene structure for the ring linked to the vinyl methylene group of 4. This was confirmed by ozonolysis of the acetate (3), which, besides affording malonic and levulinic acids which definitely establish the nature of the aliphatic chain (4), yielded 2,5-diacetoxyphenylacetic acid (5), characterized as a methyl ester. From this it is possible to postulate the partial structure (6) for panicein-$B_3$. The base peak at *m/e* 163, attributable mainly to the expected benzylic fragmentation as depicted in 6, further supports this



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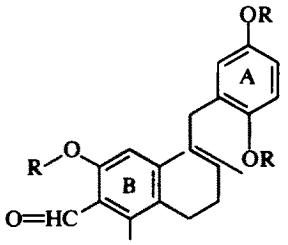
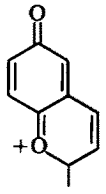
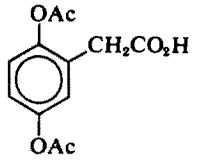


2: R = H
3: R = Ac—
—$CH_2$—CH=$C(CH_3)$—$CH_2$—$CH_2$—

4



a, *m/e* 161



5

conclusion. A peak at *m/e* 163 is also seen in the spectrum of the polyprenyl-1,4-benzoquinols and was ascribed[1] to the ion $C_6H_3(OH)_2CH_2CH$=$C(CH_3)^+$ and both spectra include peaks at *m/e* 161. However, the 163/161 intensity ratio is quite different in the two spectra.

The relative positions of the aromatic substituents in ring B of **6** were established by spin decoupling and NOE experiments. From the chemical shift (δ6·59) of the ring proton it must be *ortho* or *para* to the phenolic group which is *ortho* to the aldehyde function; this leads to six possible arrangements of the substituents on ring B in **6**, (**7–12**). In the spectrum of panicein-$B_3$ acetate (**3**), the aromatic proton on ring B is shifted from the other aromatic signals (3H b singlet at δ6·91; *cf* 2-polyprenylquinol acetates[1]) and resonates as a broad singlet at δ6·67. On irradiation at the aromatic Me signal resonating at higher field (δ2·31) the broad singlet at δ6·67 is distinctly sharpened; on the contrary, on irradiation at the downfield aromatic Me signal (δ2·51) the aromatic singlet at δ6·67 showed no change. From this it can be concluded that the aromatic Me at δ2·31 must be *ortho* to the ring proton. On saturation of the aromatic Me signal at δ2·51, the intensity of the aldehydic proton at δ10·25 was appreciably (14%) increased, thus establishing that the downfield Me group must be proximate to the aldehyde function.

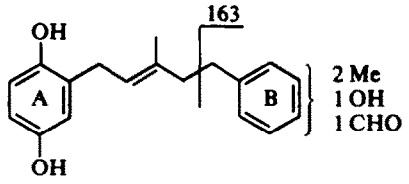
Out of the six possible structures(**7–12**), only **7** meets these conditions. Thus **2** should be the correct structure for panicein-$B_3$ apart from the stereochemistry of the double bond, for which we have no conclusive evidence.

Panicein-$B_1$ (**13**), $C_{21}H_{22}O_4$ ($m^+/e$ 338), is the quinone corresponding to panicein-$B_3$. The UV spectrum, besides bands at 274 and 346 nm characteristic of the aromatic *o*-hydroxyaldehyde moiety, exhibits an intense peak at 248 nm and very weak absorption at 440 nm, consistent with a *p*-benzoquinone chromophore as is the IR absorption at 1655 and 1595 $cm^{-1}$.

The NMR spectrum is almost identical to that of panicein -$B_3$, apart from slight differences in the aromatic region and the details are reported in the Experimental. The mass spectrum shows two main peaks at *m/e* 163 (benzylic cleavage, see **6**) and 161 (fragment **a**). Finally reduction of panicein-$B_1$ (**13**) with sulfur dioxide yielded a quinol, identical in all respects to panicein-$B_3$ (**2**).

Panicein-$B_2$, $C_{21}H_{22}O_4$ ($m^+/e$ 338) is the chromenol (**14**), the cyclic isomer of the quinone (**13**), and, from the fact that it exhibits no optical rotation, very probably artifact of isolation. The UV ($\lambda_{max}$ 273 and 340 nm; ε 8,100 and 2,800) and IR ($\nu_{max}$ 1635 and 1575 $cm^{-1}$) spectra are almost identical to those of panicein-$B_3$ (**2**). The NMR spectrum of panicein-$B_2$ (**14**) indicates the presence of a Me group on an ethereal carbon (δ1·38) and protons on a disubstituted double bond conjugated with aromatic ring (6·28, 5·51; 2H, J = 10Hz, AB pattern), consistent with a chromenol structure. The remainder of the spectrum, apart from the absence of signals due to the —$CH_2$—CH=$C(CH_3)$— grouping, is similar to that of **2** and the details are reported in the Experimental. The mass spectrum of **14** shows prominent peaks at *m/e* 163 and 161. These spectral data suggest structure **14** for panicein-$B_2$, confirmed by conversion of the quinone (**13**) into the chromenol (**14**) by treatment with pyridine.[5]

Panicein-A (**15**), $C_{22}H_{26}O_3$ ($m^+/e$ 338·18829; required: 338·18818) shows characteristic absorption maxima at 248, 282, 315 and 440 nm (ε 14·196; 2700; 220 and 15) and IR bands at 1660 and 1600

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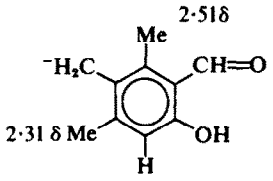


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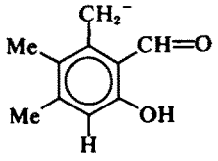


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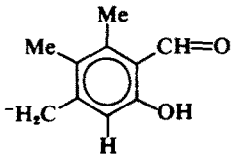


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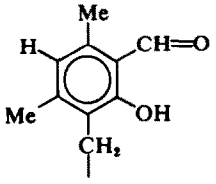


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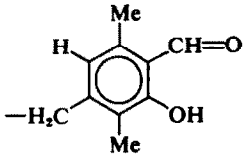


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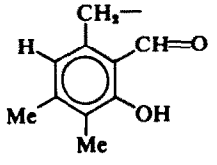


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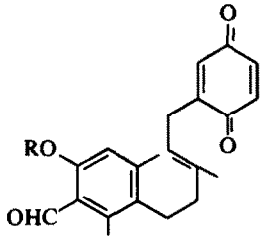
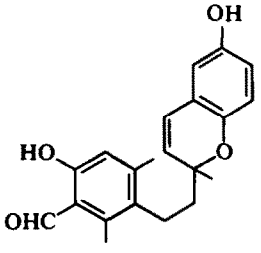



13: R = H
16: R = Me




14

cm$^{-1}$ due to a *p*-benzoquinone chromophore. The IR spectrum shows no OH absorption and the NMR spectrum lacks the signals for aldehydic and phenolic protons observed in **2**, **13**, and **14**; instead, it shows signals for a OMe group (δ3·70) and for an additional aromatic Me group. The remainder of the NMR spectrum is very similar to that of **2** and **13**, as is the mass spectrum. These results led us to believe that panicein-A has structure **15** which differs from that of above metabolites in having on ring B a Me group in place of the aldehyde function, and the OH group is methylated. This was confirmed by chemical correlations with panicein-$B_1$ (**13**). Treatment of (**13**) with methyl iodide and silver oxide in $CHCl_3$ afforded the monomethyl derivative (**16**; $m^+/e$ 352; δ OMe 3·85) which was converted by catalytic hydrogenation (Pd-C in acetic acid) into the quinol (**17**; $m^+/e$ 342) identical in all respects (MS, NMR and TLC, and GLC of their acetates) to the hydrogenation product of panicein-A.

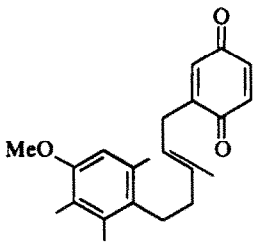
Panicein-C (**18**), $C_{21}H_{24}O_5$, m.p. 138–140° ($m^+/e$ 356·16261; required: 356·16236) shows the same NMR as that of panicein-$B_3$ (**2**), apart from the presence of only three aromatic protons instead of four, and their IR spectra are identical. Hence, the two compounds are very closely related and the additional O atom in panicein-C must be a phenolic OH group which was confirmed by formation of a tetra-acetate (νCO 1760, 1685 cm$^{-1}$). The extra OH group in (**18**) must be in ring B as the mass spectrum shows peaks at *m/e* 161 (fragment **a**) and 179 (corresponding to *m/e* 163 in 2 + 16 mass units). In agreement, the UV spectrum shows maxima at 291 and 380 nm (ε 15,300 and 2,100) corresponding to the bands at 276 and 346 nm in **2** bathochromically shifted. Finally, this was confirmed chemically by ozonolysis of panicein-C tetra-acetate,

which afforded, besides malonic and levulinic acids, 2,5-diacetoxyphenylacetic acid (**5**).

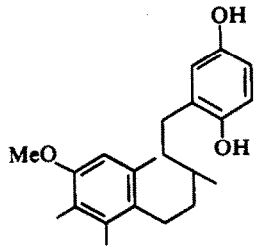
Our next concern was to establish the relative positions of the substituents (*i.e.* 2 Me, 2 OH and a CHO) in ring B. A green color with $FeCl_3$ and a borate shift in the UV spectrum of panicein-C, both suggest a catechol structure. From IR ($\nu_{max}$ 1635 $cm^{-1}$) and NMR (1H singlets at δ12·20 and 10·31, the former being exchangeable with $D_2O$) evidence, the aldehyde function must be located *ortho* to an OH group. Moreover, irradiation of the aromatic Me protons at δ2·47 increased the intensity (by *ca* 13%) of the signal from the aldehydic proton, thus establishing that one Me must be located *ortho* to the aldehyde function.

Consequently, two alternative structures (**18** and **19**) appear to be possible for panicein-C. However, the former, which has a carbon substitution pattern in ring B identical to those in the other paniceins, appears to be the more probable.

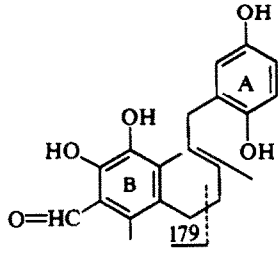
Inspection of the panicein structures suggests that these compounds might be derived biogenetically by a combination of a sesquiterpene and quinol residue and can be classified as "prenylphenols." Mixed biogenesis of this type is not unusual, for example farnesiferol-B (**20**) and its congeners,[6] and the mould metabolites grifolin (**21**)[7], tauranin (**22**)[8], siccanin (**23**)[9] and its congeners.[10] Paniceins are unique in that they contain in the sesquiterpenoid moiety an aromatic ring, which is reminiscent of the aromatic end groups of isorenieratene (**24**) and ren-



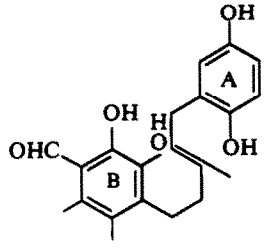

**15**



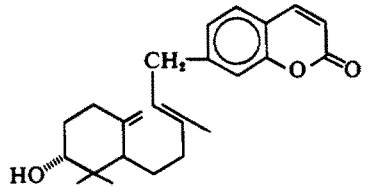

**17**




**18**




**19**

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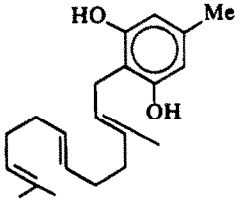


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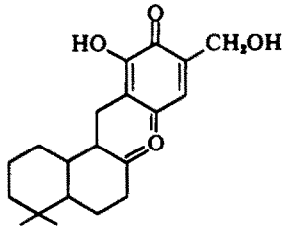


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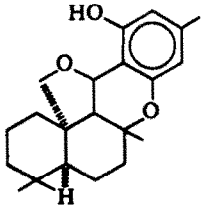
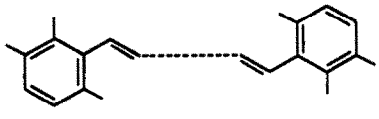
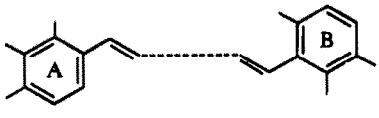



**23**



**24**




**25**

ieratene (25), arylcarotenoids[11] isolated from the marine sponge *Reniera japonica*[12] and from photosynthetic sulfur bacteria.[13] More recently phenolic carotenoids were isolated from a *Streptomyces sp.*[14] namely 3-hydroxyisorenieratene and 3,3¹-dihydroxyisorenieratene, with the OH groups in the same relative position as in the paniceins. It should be noted that the alternative structure (19) for panicein-C shows a carbon substitution pattern on ring B identical to that of ring A of renieratene (25). The biosynthetic derivation of these aromatic groups of terpenoid origin is a matter for conjecture, but it seems likely that they may arise by an electrophile-catalysed cyclization of the sesquiterpenoid part to an abscisane structure[15] which is typical of di- and triterpenoids, followed by a 1,2-Me migration and subsequent oxidation.

## EXPERIMENTAL

Instrumental techniques were given in a previous paper.[1] Columns chromatography was carried out on silica gel 0·05–0·2 mm (Merck), TLC and PLC were carried out on precoated silica gel plates (Merck).

*Extraction of* Halichondria panicea *and fractionation of paniceins.* Fresh material (27 g, dry after extraction), collected in the Bay of Naples, was extracted (× 3) with acetone at room temp for 3 days. The combined extracts (0·5 l.) were concentrated and the remaining aqueous soln was extracted with ether; the solvent was taken to dryness to give an oily residue (3·15 g) which was chromatographed on a silica gel (120 g) column (ϕ 3 cm). Elution with $C_6H_6$ (1·4 l.) allowed separation of the less polar components from paniceins which were eluted successively with $C_6H_6$-ether (95:5, 9:1, 8:2; 700 ml of each) mixtures. Fractions of 100 ml were collected and monitored by TLC. Fractions 1–6 yielded panicein-A (15), which was further purified by PLC in $C_6H_6$-ether, 95:5 ($R_f$ 0·6), 70 mg).

Fractions 9–10 gave panicein-$B_1$ (13) which was also further purified by PLC in $C_6H_6$-ether, 95:5 ($R_f$ 0·37, 25 mg). Fractions 11–14, upon concentration, furnished an oily residue (200 mg) which by PLC in $C_6H_6$-ether 85:15 gave further quantity of panicein-$B_1$ ($R_f$ 0·6, 20 mg) and the corresponding chromenol panicein-$B_2$ (14; $R_f$ 0·43, 45 mg). Finally, fractions 15–17 gave 200 mg of panicein-$B_3$ (2) homogeneous in TLC, and fractions 19–20 yielded 300 mg of panicein-C (28), which was crystallized from $CHCl_3$, m.p. 138–140°. The analytical figures and physical properties of these compounds are listed below.

*Panicein-A* (15) (*m⁺/e* 338·18829; $C_{22}H_{26}O_3$ requires: 338·18818): $\lambda_{max}$ (MeOH) 245, 282, 315 and 440 nm (ε 14,196; 2,700; 220 and 15); $\nu_{max}$ (liquid film) 1655 (C=O, quinone) 1595 (skeletal C=C, rings), 1460 and 1380 (Me), 1290 and 1115 (—OMe), 895, 830 and 750 (Ar H bendings) cm⁻¹; δ($CCl_4$) 6·62 (2 H, bs, ring protons), 6·39 (2 H, bs, ring protons), 5·14 (1 H, t, J = 6 Hz, olefinic proton), 3·70 (3 H, s, OMe), 3·07 (2 H, d, J = 6Hz, Q—C<u>H</u>₂—CH=C), 2·67 (2H, m, Ar—<u>C</u>H₂CH₂), 2·22, 2·15 and 2·04 (each 3 H, s, Ar—Me), 2·02 (2 H, m partially overlaid by singlet at δ 2·04, Ar $CH_2C\underline{H}_2C{=}C$) and 1·72 (3 H, bs, Me—C=C); *m/e* (%) 338 (<u>M</u>⁺, 7), 163 (100), 161 (5). (Found C, 77·7; H, 7·5; $C_{22}H_{26}O_3$ requires: C, 78·1; H, 7·7%).

*Panicein-$B_1$* (13) (*m⁺/e* 338·15171, $C_{21}H_{22}O_4$ requires: 338·15180) $\lambda_{max}$ (MeOH) 248, 274, 346 and 440 nm (ε 14,400, 11,500, 3,800 and 15); $\nu_{max}$ (liquid film) 2825 and 2710 (aldehyde CH), 2700 (b, OH chelated) 1655 (C=O, quinone), 1635 (C=O, aldehyde), 1595 (skeletal C=C rings), 1460 and 1380 ($CH_3$), 1340, 1300, 1280, 1220, 1200 and 895, 855 and 750 (Ar H bendings) cm⁻¹; δ ($CCl_4$) 11·8 (1 H, s exchangeable with $D_2O$, OH chelated), 10·25 (1 H, s, —CHO), 6·66 (2 H, s, ring protons), 6·55 and 6·43 (each 1 H, bs, ring protons), 5·17 (1 H, bt, J = 6Hz, olefinic proton), 3·10 (2 H, d, J = 6Hz, Q C<u>H</u>₂CH= C), 2·62 (2 H, m, partially overlaid by the singlet at 2·50, Ar<u>C</u>H₂CH₂), 2·50 (3 H, s, $ArCH_3$), 2·29 (3H, s, $ArCH_3$), 2·10 (2 H, m, $ArCH_2C\underline{H}_2C{=}C$), 1·75 (3 H, s, MeC=C); *m/e* 338 (M⁺, 10), 163 (100), 161 (70).

*Panicein-$B_2$* (14): (*m⁺/e* 338·15171; $C_{21}H_{22}O_4$ requires: 338·15180) $[\alpha]_D \pm 0°$; $\lambda_{max}$ (MeOH) 273 and 340 nm (ε 8, 100, 2,800); $\nu_{max}$ (liquid film) 3600–3200 (OH), 2825 and 2720 (CH aldehyde), 1635 (C=O), 1570 (skeletal C=C, rings) 1460 and 1380 ($CH_3$), 1200 (b, ether), 910, 855 and 750 (ArH bendings) cm⁻¹; δ($CCl_4$) 11·8 (1 H, s exchangeable with $D_2O$, OH chelated) 10·25 (1 H, s, C<u>H</u>O), 6·52 (3 H, m, Ar<u>H</u>), 6·40 (1 H, m, ArH), 6·28 (1 H, d, J = 10Hz, Ar<u>C</u>H=CH), 6·02 (1 H, b, exchangeable with $D_2O$, OH), 5·51 (1 H, d, J = 10 Hz, ArCH=C<u>H</u>), 2·60 (2 H, bm, Ar<u>C</u>H₂CH₂), 2·44 and 2·23 (each 3 H, s, Ar<u>C</u>H₃), 1·62 (2 H, bm, $ArCH_2C\underline{H}_2$) and 1·38 (3 H, s, t-Me); *m/e* 338 (M⁺, 8) 163 (20), 161 (100).

*Panicein-$B_3$* (2) (*m⁺/e* 340·16774; $C_{21}H_{24}O$ requires: 340·16744); $\lambda_{max}$ (MeOH) 276, 294 (shoulder) and 346 nm (ε 12,600, 5,100 and 3,400); $\nu_{max}$ ($CHCl_3$) 3600 (OH unbonded), 3400–3200 (broad, OH bonded), 2900–2600 (broad, OH chelated), 2825 and 2720 (CH aldehyde), 1640 (C=O), 1570 (skeletal C=C rings) cm⁻¹; *m/e* 340 (M⁺, 80) 163 (100) and 161 (60). (Found C, 73·7; H, 6·9, $C_{21}H_{24}O_4$ requires: C, 74·1; H, 7·1%).

*Panicein-C* (18) (*m⁺/e* 356·16261; $C_{21}H_{24}O_5$ requires: 356·16236: $\lambda_{max}$ (MeOH) 291 and 380 nm (ε 15,300 and 2,100); $\nu_{max}$ (liquid film) 3600–3100 (OH), 2900–2600 (OH chelated) 2825 and 2710 (CH aldehyde), 1630 (C=O), 1580 (skeletal C=C ring), 1450 and 1380 (Me), 760 cm⁻¹; δ ($CDCl_3$) 12·20 (1 H, s exchangeable with $D_2O$, OH chelated), 10·31 (1 H, s, CHO), 6·58 (3 H, bs, ArH), 5·85 (3 H, bm, exchangeable with $D_2O$, OH), 5·32 (1 H, bt, J = 6Hz, CH=C), 3·29 (2 H, d, J = 6Hz, $ArCH_2CH{=}$ C), 2·73 (2 H, m, Ar<u>C</u>H₂CH₂), 2·47 (3 H, s, ArMe), 2·26 (3 H, s, ArMe), 2·11 (2 H, m, $ArCH_2C\underline{H}_2C{=}C$), 1·82 (3 H, s, MeC=C); *m/e* 356 (M⁺, 25), 174 (100), 163 (5) 161 (15). (Found C, 70·3; H, 6·5. $C_{21}H_{24}O_5$ requires: C, 70·8; H, 6·8%).

*Acetylation of panicein-$B_3$* (2) *and —C* (18). Acetates were prepared by mixing the appropriate phenols (100 mg) with $Ac_2O$ (2 ml) and pyridine (3 drops) and refluxing for 20 min. Ice water (10 ml) was then added and the products extracted with ether and purified by silica gel chromatography in $C_6H_6$-ether, 9:1.

Panicein-$B_3$ triacetate (3): (*m⁺/e* 466·19928; $C_{27}H_{30}O_7$ requires: 466·19914); $\nu_{max}$ ($CHCl_3$) 1760 and 1785 cm⁻¹; δ ($CCl_4$) 6·92 (3 H, bs, ArH), 6·69 (1 H, s; ArH), 2·50 and 2·31 (each 3 H, s, $ArCH_3$), 2·24, 2·21 and 2·19 (singlets integrating together for 9 H, $CH_3CO$—), 1·78 (3 H, s, MeC=C).

Panicein-C tetraacetate: (*m⁺/e* 524·20445; $C_{29}H_{32}O_9$ requires: 524·20462) $\nu_{max}$ ($CHCl_3$) 1760 and 1685 cm⁻¹; δ ($CCl_4$) 6·90 (3 H, bs, arH), 2·48 (3 H, s, $ArCH_3$), 2·12, 2·09, 2·04 and 1·97 (each singlet integrating together for 15 H, ArMe and MeCO—), 1·75 (3 H, s, MeC=C).

*Ozonolysis of panicein-$B_3$* (2) *and —C* (18) *acetates.*

Each compound (panicein-$B_3$ and —C acetates) (80 mg) in EtOAc (15 ml) was ozonized (2% $O_3$) for 30 min at −15°. After evaporation of solvent *in vacuo*, the ozonides were decomposed with boiling water containing a few drops of $H_2O_2$. The mixture was extracted continuously with ether and the extract treated with $CH_2N_2$. After 2 min the solvent was removed and the ester mixtures were analysed by GLC (5% SE-30 and 10% DEGS at 100° and 175°, respectively) and found to contain methyl levulinate by comparison with authentic samples. The remaining parts were treated with $Ac_2O$-pyridine and the acetylation mixtures were subjected to PLC in $C_6H_6$-ether, 9:1 to give methyl 1,5-diacethoxyphenylacetate (**5**; $R_f = 0{\cdot}4$; 25 mg), identified by direct comparison (NMR, IR MS and TLC) with an authentic sample.

*Conversion of the quinone* (**13**) *into the quinol* (**2**). Sulfur dioxide was bubbled through a soln of **13** (15 mg) in MeOH–$H_2O$ (1:1, 5 ml) for 2 hr at room temp. Evaporation of solvent *in vacuo* and PLC in $C_6H_6$-ether, 8:2 afforded a quinol spectroscopically (MS, NMR, IR and UV) identical to **2**.

*Conversion of the quinone* (**13**) *into the chromenol* (**14**). A solution of 15mg of panicein-$B_1$ (**13**) in pyridine (5 ml) was heated under reflux for 20 min. Evaporation *in vacuo* and PLC on silica gel in $C_6H_6$-ether, 9:1 yielded a chromenol identical (MS, NMR, UV) to **14**.

*O-methyl derivative of panicein-$B_1$* (**16**). Compound **16** was prepared by stirring **13**, (100 mg), MeI (1 ml) and $Ag_2O$ (0·4 g) in $CHCl_3$ (5 ml) for 18 hr. After filtn and evapn of solvent, it was purified by PLC on silica gel in $C_6H_6$-ether, 95:5 ($R_f$ 0·6); $m^+/e$ 352; δ ($CCl_4 + CDCl_3$) 10·50 (1 H, s, CHO), 6·68 (2 H, bs, ring protons), 6·60 (1 H, bs, ring proton), 6·40 (1 H, bs, ring proton), 5·25 (1 H, bt, J = 6Hz, CH=C), 3·85 (3 H, s, OMe), 3·10 (2 H, d, J = 7Hz, $QCH_2CH$=C), 2·70 (2 H, bm, $ArC\underline{H}_2CH_2$), 2·47 and 2·23 (each 3 H, s, $ArCH_3$), 2·14 (2 H, bm, $ArCH_2C\underline{H}_2$), 1·75 (3 H, s, $CH_3$—C=C); $\nu_{max}$ ($CHCl_3$) 1685, 1655 and 1600 $cm^{-1}$. (Found C, 74·6; H, 6·7. $C_{22}H_{24}O_4$ requires C, 75·0; H, 6·9%).

*Hydrogenation of* **16**: *Formation of* **17**. Compound **16** (50 mg) was hydrogenated for 12 hr at room temp and 6 atm using Pd/C (5%, 50 mg) as catalyst and ACOH as solvent. Filtn, evapn and PLC ($C_6H_6$-ether, 9:1) yielded (**17**) (35 mg), $m^+/e$ 340; absence of CO bands in the IR; δ ($CDCl_3$) 6·56 (4 H, bs, ArH), 3·76 (3 H, s, $OCH_3$) 2·30, 2·21 and 2·12 (each 3 H, s, ArMe), 1·04 (3 H, d, J = 6Hz, sec-Me). (Found C, 77·1; H, 8·0. $C_{22}H_{28}O_3$ requires: C, 77·6; H, 8·3%).

The diacetate, $m^+/e$ 424, $\nu_{max}$ ($CHCl_3$). 1760 $cm^{-1}$; δ $MeCO_2$ ($CDCl_3$) 2·28, prepared with $Ac_2O$-pyridine as usual, gave a single peak in GLC (1% OV-1 at 275°, 2 mt glass column).

*Hydrogenation of panicein-A* (**15**): *Formation of* **17**. Hydrogenation of **15** (40 mg) was performed at room temp and pressure for 12 hr in ACOH using Pd/C (5%). Working up as above, it yielded a tetrahydroderivative identical (MS, NMR and TLC, and GLC of acetates) with **17**.

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