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THE STRUCTURE OF DISPERMOQUINONE

A TRITERPENOID QUINONE METHIDE FROM *MAYTENUS DISPERMUS*

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Abstract—Structure 1 for dispermoquinone, a triterpenoid quinone methide isolated from *Maytenus dispermus* is proposed on the basis of chemical and spectroscopic evidence.

Previous investigations have shown that the quinonoid triterpene pristimerin (3) is the major coloured constituent of the yellow outer root bark of the tree *Maytenus dispermus*.[1] We report here the isolation of two further triterpenes, the yellow pigment dispermoquinone (1) and the known compound β-amyra-11:13(18)dien-3-one (6), which does not appear to have been isolated previously from natural sources. The yellow triterpene dispermoquinone appears to be new, and the sequel presents its structural elucidation in detail.

The molecular formula $C_{30}H_{40}O_5$, was assigned to dispermoquinone (1) on the basis of elemental analysis and mass spectrometry. The quinonoid nature of the pigment was indicated by the reversible reduction and oxidation of its aqueous-alcoholic solution with dithionite and air. The compound gave a brown insoluble ferric salt, a purple sodium salt, and formed a green complex when shaken with aqueous copper acetate. These properties, together with the infrared spectrum of dispermoquinone, which had bands at 3400 (H-bonded OH), 1670 (quinonoid CO), and 1620 cm^{-1} (H-bonded quinonoid CO), suggested the presence of a hydroxy-*p*-benzoquinone system[4]). However, the UV spectrum of dispermoquinone: λ_{max}^{EtOH} 318 (ε 19,100), 328 (ε 18,200), and 414 nm (ε 2,300), was consistent with a quinone methide unit.[5]

The UV spectrum, measured in neutral and alkaline solutions; and the IR spectrum, in the quinonoid CO absorption region, of dispermoquinone and maytenoquinone[6] were very similar which was indicative of the presence of the same chromophore in these two pigments.

The molecular formula ($C_{30}H_{40}O_5$, eleven double-bond equivalents) and the PMR spectrum, led to consideration of a pentacyclic skeleton for dispermoquinone. The striking similarity in the upfield region of the PMR spectrum of dispermoquinone to that of pristimerin[7-9] immediately indicated the same type of pentacyclic skeleton for these two compounds, and the structure (1) was proposed for dispermoquinone. Four singlets at τ 8·73 (6H), 8·81 (3H), 8·91 (3H), and 9·21 (3H) indicated five tertiary Me groups. A 3-proton singlet at τ 7·91 was assigned to the Me group on C-4, for rings A and B are almost co-planar and the Me group attached to ring A would appear at a value nearer to that of an aromatic Me. One 3-proton singlet at τ 6·37 was attributed to the ester Me group on C-20, an assignment further supported by a band at 1·725 cm^{-1} in the IR spectrum, and the loss of 59 mass units from the molecular ion to give a prominent peak at *m/e* 421 (m* 369·25) in the mass spectrum of dispermoquinone.[10] A one-proton singlet at τ 7·09 was attributed to a tertiary proton α to a CO group. In the low-field region, three protons appeared, a one-proton broad signal at τ 3·08 (exchangeable with D_2O), assigned to the enolic OH proton on C-3, and two one-proton doublets centred at τ 3·62 and 3·65 (J = 1·5 Hz) attributed to the protons on the quinone methide system, attached to C-1 and C-6. The integration of the signals in the methylene and methine region (τ 8·10–8·60) indicated the presence of 15 protons. In all, signals for 40 protons were found.

In order to check the implied dispermoquinone-pristimerin relationship, the following experiments were performed. The reduction of dispermoquinone by LAH in THF gave an orange product, which was shown by TLC to be a mixture of two main compounds. The component with smaller R_f, which was not isolated pure, appeared to be a colourless hydroxycatechol, giving a green coloration with ferric chloride and having an absorption maximum at 287 nm. in the UV and IR bands at 3,530 (free OH), 3,410 and 3,300 cm^{-1} (bonded OH). The major component, which was red showed an UV spectrum similar to that of pristimerin:[1] λ_{max}^{EtOH} 223 (infl ε 8,620). When air was passed through the mixture in benzene, the colour of the solution changed from light orange to deep red,

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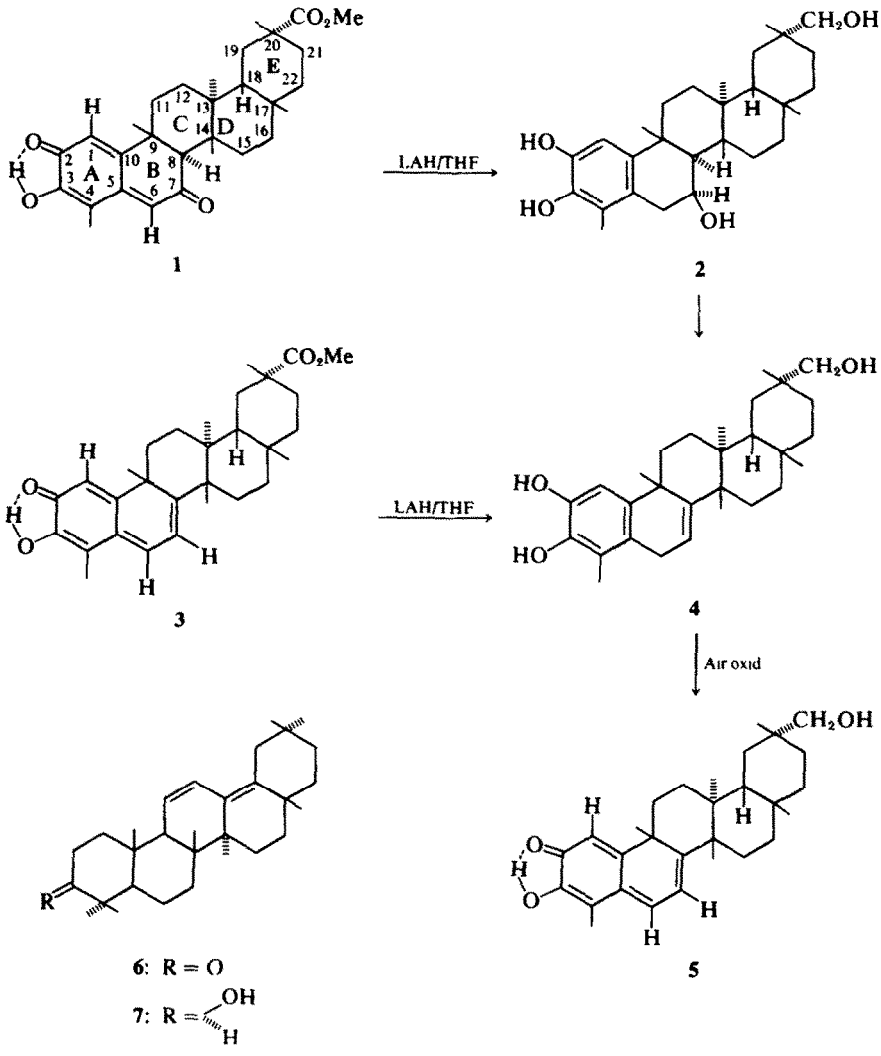

1 2 3 4 5

and after 2 days, only the red component was present in the solution. The IR spectrum of the air oxidation product, showed bands at: 3·370 (OH), 1,636, 1,580 (H-bonded quinonoid CO), 1·544 and 1·512 cm^{-1}, which were very similar to that of pristimerin. The PMR spectrum proved most informative. In the up-field region five 3-proton singlets appeared at τ 8·60, 8·67, 8·82, 9·00 and 9·24 indicating five tertiary Me groups. A 3-proton singlet at τ 7·80 was attributed to the Me group attached to the ring A on C-4 (τ 7·80 in pristimerin[7-8]). The AB type two-proton quartet at τ 6·58 and 6·84 ($J = 10$ Hz) was assigned to a hindered primary OH group, and this indicated that the methoxy CO group in dispermoquinone was attached to a quaternary C atom. In the low-field region three protons appeared in an ABX type system: a one-proton doublet centred at τ 3·64 ($J = 8$ Hz), a one-proton doublet centred at τ 3·48 ($J = 1·2$ Hz), and a one-proton quartet centred at τ 2·94 ($J = 1·2$ and 8 Hz). These data led to the assignment of the structure **5** for the air oxidation product, and **4** for the corresponding hydroxycatechol. The compound **5** was shown to be identical, by direct comparison with an authentic sample, with the quinonoid compound obtained by air oxidation of the hydroxycatechol produced by LAH reduction of pristimerin.[8] The fact that the compounds **4** and **5** were the main components of the dispermoquinone reduction products, indicated that the tetrol (**2**) was dehydrated to **4**, by the presence of base, during its formation.

This reaction sequence did not rigorously establish the stereochemistry at C-8. However, the ready dehydration of **2** to **4** supported an α-axial configuration for the C-8 proton. This assignment was confirmed by the rotatory dispersion curve of dispermoquinone. Maytenoquinone and dis-

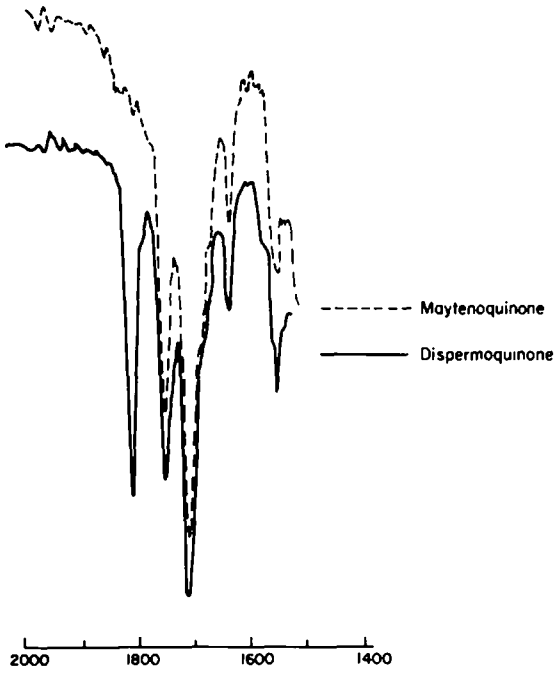

Fig 1.

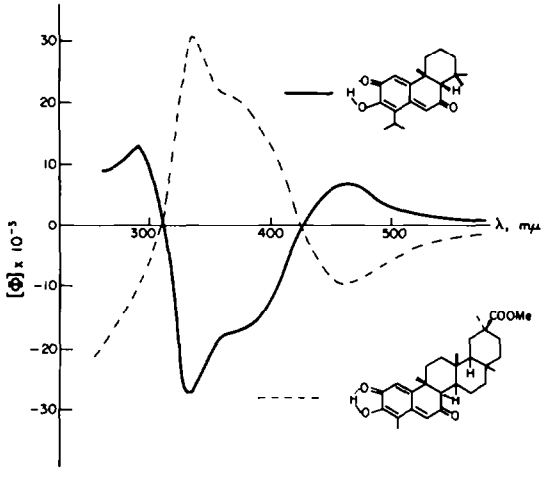

Fig 2.

permoquinone were found to be optical antipodes by comparison of their dispersion curves (Fig 2), which are mirror images. This indicated a β-axial configuration to the C-9 Me group and an α-axial configuration to the C-8 proton in dispermoquinone, on the basis of maytenoquinone stereochemistry C-5 α H (axial) and C-10 β CH_3 (axial).[6]

The co-ocurrence of β-amyra-11:13(18)dien-3-One with pristimerin and dispermoquinone in the *Maytenus dispermus* root bark, supports the thesis that these two pigments are triterpenes in an advanced state of oxidation, derived by logical biogenetic transformations from a β-amyrin type precursor.

EXPERIMENTAL

M.ps were determined on a Kofler block and are uncorrected. UV and visible spectra were measured on EtOH solns with a Unicam S.P. 700 spectrophotometer; IR spectra were determined with a Unicam S.P. 200. PMR spectra were measured in $CDCl_3$ solns on a Perkin-Elmer R.S. 10 instrument at 60 MHz. or a Varian H.A. 100 at 100 MHz. with TMS as internal reference, chemical shifts have been recorded in τ values. Mass spectra were determined with an A.E.I. MS-902 instrument. Rotatory dispersion curves were measured in dioxane solns on a Bendix Polarmatic 62 instrument.

β-Amyra-11:13(18)*dien*-3-*one* (**6**). The fraction A (0·10 g) obtained from the chromatography of the light petroleum extract of the outer root bark of the tree *Maytenus dispermus*,[6] was purified by recrystallization from light petroleum ether to yield large colourless needles of **6**: m.p. 239–241°; $\alpha = -56$ ($CHCl_3$); UV λ_{max}^{EtOH} 237 (ϵ 16,500), 242 (ϵ 23,310), 250 (ϵ 26,510), and 260 nm. (ϵ (16,750); IR ν_{max}^{KBr} 3,050, 1,700, 1,620, 1,468, 1,386, 1,364, 980 and 780 cm^{-1}; PMR, 3·62 (1H, q, $J = 4$ and 12 Hz), 4·53 (1 H, q, $J = 2$ and 12 Hz); 8·96, 9·03, 9·24 and 9·29 (24H, eight t-Me). Mass spectrum, *m/e* 422 parent ion, 417, 283, 269, 255, 243, 241, 229, 215 and 203. Lit.[3] m.p. 341–242; $[\alpha]_D - 54$; λ_{max} 242, 250 and 260 nm (ϵ 26,900; 30,400 and 19,600 respectively).

β-Amyra-11:13(18)*dien*-3 *β-Ol* (**7**). A soln of **6** (83 mg) in dry ether (10 ml) was added dropwise to an ice-cold Soln of LAH (100 mg). The mixture was stirred in an atmosphere of N_2 for 6 hr and then left at room temp for 4 hr more. The excess of LAH was destroyed by dropwise addition of EtOAc followed by MeOH. After dilution with water the mixture was extracted with ether. Evaporation of the dried ($MgSO_4$) ether extract furnished a colourless crystalline solid (74 mg). Recrystallization from MeOH **7** as long colourless needles: m.p. 225–228°; $[\alpha]_D - 72$ ($CHCl_3$) λ_{max} 238 (ϵ 16,890), 241 (ϵ 24,680), 250 (ϵ 28,050) and 260 nm (ϵ 17,790); ν_{max}^{KBr} 3,050; 1,620, 1,460, 1,380, 1,360, 989, 979, 948 and 770 cm^{-1}, τ 3·65 (1H, q, $J = 4$ and 12 Hz), 4·55 (1H, q, $J = 2$ and 12 Hz), 6·55 (1H, C-3αH); τ 8·94 (s, 3H), 9·02 (s, 9H), 9·09 (s, 3H), 9·23 (s, 6H) and 9·29 (s, 3H) (eight t-Me) Lit.[2] m.p. 228–229; $[\alpha]_D - 72$. A direct comparison by mixed m.p. with a sample applied by Professor D. H. R. Barton Confirmed the identity of the alcohol.

Dispermoquinone (**1**). The fraction F[6] (0·20 g) was rechromatographed on a silica gel column (30 g) packed in benzene. Elution with benzene gave a crystalline fraction (0·18 g) which was recrystallized from MeOH to yield large yellow needles of *dispermoquinone* (**1**, 0·16 g) m.p. 255–257°; $[\alpha] - 263°$ ($CHCl_3$); λ_{max} 318 (ϵ 19,100), 328 (ϵ 18,200) and 414 nm (ϵ 2,300); ν_{max}^{KBr} 3,400, 1,720, 1,660, 1,619, 1,543, 1,085, 995 and 880 cm^{-1}; mass spectrum *m/e* 480 (parent ion), 465, 452, 448, 421, 420, 405, 337, 311, 309, 297 and 286. (Found: C, 74·8; H, 8·2; M, 480·288. $C_{30}H_{40}O_5$ requires: C, 75·0; H, 8·3; M, 480·295%).

Conversion of dispermoquinone to pristimerin derivative (**5**). To a cooled soln of dispermoquinone (150 mg) in

THF (40 ml, distilled from LAH), LAH (20 mg) was added slowly and the mixture was refluxed with constant stirring in an atmosphere of N_2 for 6 hr, and then left at room temp for 12 hr more. The colour of the soln changed from yellow to colourless. The excess of hydride was destroyed by dropwise addition of EtOAc followed by MeOH. After dilution with water (100 ml) and acidification with dil HCl the mixture was extracted with ether. The ethereal extract was washed and dried. The colour of the soln changed to orange. Removal of the solvent gave a residue which was mainly a mixture of **4**, UV 287 nm; IR, 3,530 (free OH), 3,410 and 3,300 cm^{-1} (bonded OH) and the air oxidation product (**5**). The mixture (120 mg) was dissolved in benzene (50 ml) and a current of air was passed through the soln for 2 days. The colour of the soln changed from orange to deep red. Removal of the solvent gave a red solid which was dissolved in benzene (20 ml) and placed on a neutral alumina column (50 g) packed in benzene. Elution with benzene gave a deep red crystalline compound (23 mg), which on crystallisation from light petroleum-methylene chloride gave red plates of **5**; m.p. 208–210; UV 223 (infl. ϵ 8,770), 256 (ϵ 5,900) and 425 nm (ϵ 8,620); IR ν_{max}^{KBr} 3,360, 1,640, 1,580, 1,543, 1,513, 1,080, 1,010, 864 and 732 cm^{-1}. Lit.[8] m.p. 211–213; UV λ_{max} 425 nm (ϵ 5,470), inflection at 258 and 284 mμ (ϵ 5,880 and 2,260).

The identity of **5** with the compound obtained by air oxidation of the hydroxycatechol produced by LAH reduction of pristimerin[8] was confirmed by comparison of IR, UV and visible spectra, m.p. mixed m.p. and TLC behaviour.

REFERENCES

[1]P. K. Grant and A. W. Johnson, *J. Chem. Soc.* 4079, 4669 (1957); P. K. Grant, A. W. Johnson, P. F. Juby and T. J. King, *Ibid.* 549 (1960)

[2]L. Ruzicka, G. Müller and H. Schellenberg, *Helv. Chim. Acta* **22**, 767 (1939); L. Ruzicka and O. Jeger, *Ibid.* **24**, 1236 (1941)

[3]D. H. R. Barton, A. J. Head and P. J. May, *J. Chem. Soc.* 935 (1957)

[4]B. W. Bycroft and J. C. Roberts, *J. Org. Chem.* **28**, 1429 (1963); H. Nakata, K. Sasaki, I. Morimoto and Y. Hirata, *Tetrahedron* **20**, 2319 (1964); S. Natori, H. Nishikawa and H. Ogawa, *Chem. and Pharm. Bull. Japan* **12**, 237 (1964)

[5]S. Morris Kupchan, A. Karim and C. Marks, *J. Org. Chem.* **34**, 3912 (1969)

[6]*Tetrahedron*

[7]R. Harada, H. Kakisawa, S. Kobayashi, M. Musya, K. Nakanishi and Y. Takahashi, *Tetrahedron Letters* 603 (1962)

[8]A. W. Johnson, P. F. Juby, T. J. King and S. W. Tam, *J. Chem. Soc.* 2884 (1963)

[9]K. Nakanishi, Y. Takahashi and H. Budzikiewicz, *J. Org. Chem.* **30**, 1729 (1965)

[10]H. Budzikiewicz, J. M. Wilson and C. Djerassi, *J. Am. Chem. Soc.* **85**, 3688 (1963)