Phytochemistry, Vol. 20, No. 5, pp. 1089–1092, 1981.
Printed in Great Britain.

0031-9422/81/051089-04 $02.00/0
Pergamon Press Ltd.

LATINONE, A PHENANTHRENE-1,4-QUINONE FROM *DALBERGIA LATIFOLIA**

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(*Received* 1 *September* 1980)

Key Word Index—*Dalbergia latifolia*; Leguminosae; latinone; quinone; phenanthrene-1,4-quinone.

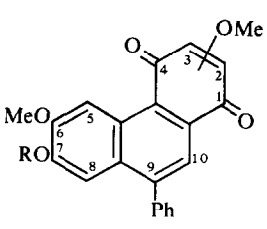
Abstract—Latinone, a substituted phenanthrene-1,4-quinone was isolated from *Dalbergia latifolia*. The structure was assigned from spectroscopic measurements and a synthesis was carried out using a Diels–Alder reaction to form the ring structure.

INTRODUCTION

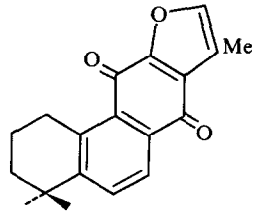
Dalbergia latifolia Roxb. (Leguminosae–Papilionoideae) is of common occurrence in India and is the source of Indian Rosewood. On the basis of phylogenetic classification, this species is placed in the specific series *Dalbergia pantropicales* [1]. In a previous series of papers on the heartwood extractives of *D. latifolia* [2–5], three neoflavanoids (*R*)-4-methoxydalbergione, (*R*)-latifolin, dalbergin and the flavonoid liquiritigenin were reported as present in addition to an unidentified quinone named dalatinone ($C_{23}H_{18}O_5$) [4].

RESULTS AND DISCUSSION

In the present study on the heartwood extract of *D. latifolia*, a red crystalline quinone, $C_{22}H_{16}O_5$, for which the name latinone is proposed, was obtained as a minor component. The spectral data of this quinone resembled the reported data for the unidentified 'dalatinone'. However, latinone has a different molecular formula. The spectroscopic measurements on latinone were carried out on its monoacetate. The UV spectrum is indicative of a quinonoid system, and the IR spectrum shows three absorptions in the carbonyl region (1770 cm^{-1} (acetate) and 1667, 1645 cm^{-1} (quinone)). Apart from two methoxy and one acetoxy groups, the ^1H NMR spectrum has signals for nine protons, five of which are assigned to an unsubstituted phenyl ring (δ 7.5–7.7). The polycyclic structure (**1**, R = H) is proposed for latinone. The unsubstituted phenyl signal is overlapped by a signal due to the 8-H which resembles the 5-H in 4-phenylcoumarins. The singlet δ 6.21 is ascribed to the proton on the quinone ring by comparison with the 4-methoxydalbergiones. The exact position (at 2 or 3) of this proton and the methoxyl group cannot be assigned unequivocally. The lack of a signal similar to the 6-H proton of the dalbergiones indicated either a condensed or disubstituted quinone. A singlet in the downfield aromatic region (δ 8.12) was attributed to C-10 proton and that at the even lower value of δ 9.38 is ascribed to H-5.



1 R = H; Me; Ac



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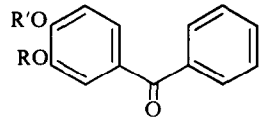
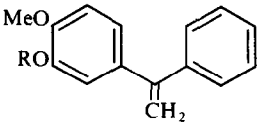


3 R = R' = Me
5 R = R' = H
6 R = H; R' = Me

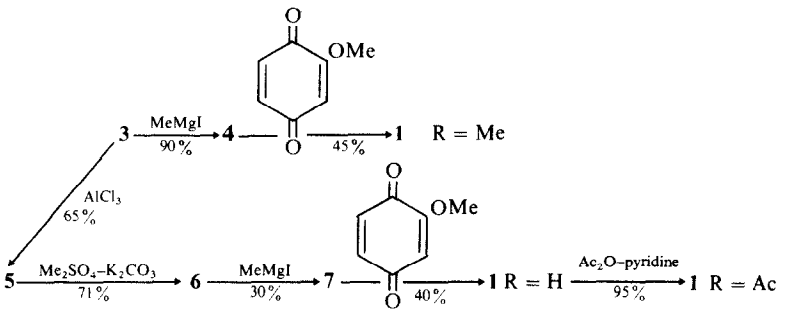


4 R = Me
7 R = H

The phenomenon of marked shielding due to the proximity of a carbonyl was observed previously in the spectra of *iso*-tanshinone 1 [6], 5,6-benzoflavone [7] and 2-methylphenanthrene-1,4-dione [8]. Further evidence for the proposed structure **1** can be gleaned from the ^1H NMR spectrum of latinone leucotriacetate. The signal for the H-2 (or H-3) in the leucotriacetate is moved downfield and the proton at C-10 moves upfield as the deshielding influence of the quinone carbonyl is removed. However, H-5 is still deshielded by the acetoxyl group and is moved upfield by δ 0.48. The base peak of the mass spectrum of 7-*O*-acetyllatinone is *m/z* 360 and is due to loss of acetate; the subsequent degradation is characteristic of a quinone.

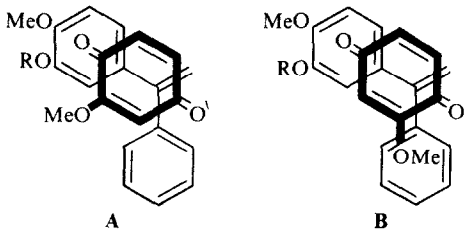
A synthesis of the quinone (**1**, R = H) and its monomethyl ether (**1**, R = Me) was undertaken and a Diels–Alder reaction was used to form the ring structure (Scheme 1). The problem of the orientation in the Diels–Alder adduct due to the unsymmetrical benzoquinone was similar to that encountered in the synthesis of *iso*-tanshinone 11 (**2**). In the report [9] on the tanshinone synthesis, the effect of substituents in the condensation was examined from two points of view (a) the radical stability in an assumed biradical intermediate and (b) the steric factor in the transition state. For latinone (**1**, R = H) and its monomethyl ether (**1**, R = Me) the transition state **A** would be energetically

* Part 13 in a series on *Dalbergia* wood constituents. For Part 12 see Donnelly, D. M. X., O'Reilly, J., and Whalley, W. B. (1975) *Phytochemistry* **14**, 2287.



Scheme 1.

more favoured than **B** in which the bulky OMe and Ph groups overlap.

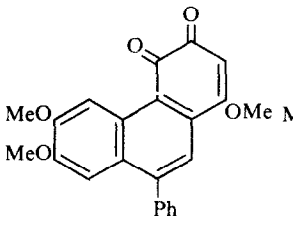


Treatment of the benzophenone **3** with methyl magnesium iodide gives the diphenylethylene (**4**). The vinyl protons appear in the ^{1}H NMR spectrum as a broad signal δ 5.40. Diels–Alder reaction of the diphenylethylene (**4**) with 2-methoxy-1,4-benzoquinone in acetic acid gives 9-phenyl-2(or 3)-6,7-dimethoxyphenanthrene-1,4-quinone (**1**, R = Me) a red crystalline compound which is characterized spectroscopically. In the ^{1}H NMR spectrum three methoxyl signals are displaced at δ 3.86, 3.97 and 4.13. The proton at position 2 (or 3) occurs as a singlet at δ 6.13, while the protons at positions 5, 8 and 10 occur as singlets at δ 7.25, 9.20 and 8.01 respectively. The IR spectrum showed the quinone character with stretching bands at 1667, 1635 and 1620 cm^{-1}, while elemental analysis suggested the empirical formula $C_{23}H_{18}O_5$.

Latinone was synthesized by a similar route. 3,4-Dimethoxybenzophenone (**3**) was demethylated with aluminium chloride to give 3,4-dihydroxybenzophenone (**5**) which was then selectively methylated at the 4-hydroxyl to yield the benzophenone (**6**). The position of methylation in the benzophenone (**6**) was confirmed by the UV spectrum: λ_{max} occurs at 315 (3.32), 280 (3.38), 237 (3.63) nm (log ε). Addition of sodium methoxide caused a bathochromic shift to occur, but with little change in the intensity of the absorption maxima [370 (3.01, 294 sh (3.28) 251 (3.76) nm (log ε)]. However, in the case of 4-hydroxy-3-methoxybenzophenone the same large bathochromic shift occurs in the UV spectrum on addition of sodium methoxide, but is accompanied by a significant hyperchromic shift.

3-Hydroxy-4-methoxybenzophenone (**6**) was then treated with methyl magnesium iodide and afforded the 1,1-diphenylethylene (**7**) which on reaction with 2-methoxy-1,4-benzoquinone in acetic acid yielded latinone as red crystals. The synthetic latinone was identical with the natural product (mp, mmp, IR). The insolubility of latinone precluded its further spectroscopic analysis. However, acetylation of the synthetic latinone gave an acetate which was identical spectroscopically, mp and mmp with the natural latinone acetate.

To locate the position of the methoxy group on the quinone ring, 7-*O*-methyllatinone was hydrolysed and the 2 (or 3)-hydroxyquinone obtained was reduced and immediately treated with boric acid. The free hydroxyl in the borate complex was methylated. The complex was then hydrolysed and the product oxidied to afford a mixture of *o*-quinone (**8**) and *p*-quinone (**9**, R = Me). Several attempts to obtain the *o*-quinone as a minor product of methylation of the hydrolysate without the addition of boric acid were unsuccessful. In the *o*-quinone (**8**) the change in the environment of the C-10 proton is evident in its ^{1}H NMR spectrum with the signal upfield at δ 7.83. From a comparison of the ^{1}H NMR spectra of the *o*-quinone (**8**) and the *p*-quinone (**9**, R = Me), the methoxyl group in the natural latinone can be assigned to position 3.



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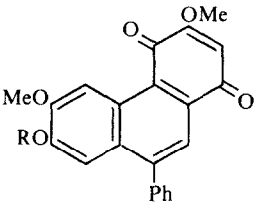

9 R = H; Me:Ac

Recently, a 1,4-phenanthraquinone with a 2-methoxyl substituent was reported. 7-Hydroxy-2,8-dimethoxy-1,4-phenanthraquinone (cypripedin) is the sensitizing quinone present in *Cypripedium calceolus* (Lady Slipper) [10]. The structure assignment for cypripedin is based on X-ray analysis.

Latinone (**9**, R = H) is composed of a quinone–C_6 unit condensed with a C_6–C_2–C_6 unit. By analogy with the proposed biosynthetic pathways of neoflavanoids this C_6–C_2–C_6 unit could arise by cinnamylation of a C-6 aromatic [11], but subsequent loss of one carbon must occur, possibly at the condensation step with the quinone.

EXPERIMENTAL

Separations by column chromatograph were carried out using Merck Si gel. Merck Kieselgel 60 F_{254} and $PF_{254+366}$ were used for TLC and prep. TLC respectively. The TLC plates were examined with UV illumination, and by spraying with 10% aq. H_2SO_4.

Extraction of Dalbergia latifolia *heartwood.* A sample of *Dalbergia latifolia* heartwood shavings (2.2 kg) which had previously been extracted with C_6H_6, was extracted continuously with Me_2CO for 4 days. Evapn of the Me_2CO gave a dark red oil (156 g). A portion (80 g) of this oil was chromatographed on a Si gel column (3 kg) using $CHCl_3$ as eluant. The factions (I–IV) were subdivided using TLC and column chromatography. The MeOH soln of fraction IV deposited a red crystalline solid, latinone (24 mg), mp 283–285°. ν_{max}^{KBr} cm^{-1}: 1670, 1540, 1620, 1485, 1228, 1098.

7-O-*Acetyllatinone* (**9**, R = Ac). The red material (10 mg) was dissolved in Ac_2O (2 ml) and pyridine (2 ml) and left for 18 hr at room temp. The soln was diluted with 10% HCl and extracted with Et_2O. The ethereal soln was washed with saturated $NaHCO_3$ soln, water, and dried. Evapn of the solvent and crystallization from MeOH gave 7-*O*-acetyllatinone as orange needles (7 mg), mp 245–246°. ν_{max}^{KBr} 1770, 1667, 1645, 1620, 1467, 1093 cm^{-1}. λ_{max}^{MeOH} nm (log ε): 206 (4.14), 240 (4.43), 288 (3.97), 310 sh (3.70), 400 (3.18) nm, δ ($CDCl_3$): 2.34 (3H, *s*, OCOMe), 3.99 (3H, *s*, −OMe), 4.09 (3H, *s*, −OMe), 6.21 (1H, *s*, 2-H), 8.12 (1H, *s*, 10-H), 9.38 (1H, *s*, 5-H), 7.5–7.7 (6H, *m*, unsubstituted phenyl group and 8-H). Found: C, 71.08; H, 4.34. $C_{24}H_{18}O_6$ requires: C, 71.6; H, 4.47%.

Latinone leucotriacetate. A soln of 7-*O*-acetyllatinone (10 mg) in $CHCl_3$ (25 ml) was shaken vigorously with an aq. soln of sodium dithionate (25 ml, 10%) until the orange colour had disappeared. The $CHCl_3$ fraction was immediately poured into a mixture of Ac_2O (5 ml) and pyridine (1 ml) and the $CHCl_3$ evapd. Ice, acidified with HCl, was added to the reaction mixture after 18 hr and the aq. mixture extracted with Et_2O. The Et_2O soln was washed with satd $NaHCO_3$ soln and water, dried and evapd to give an oil. Purification by prep. TLC (Et_2O–CCl_4, 1:1), yielded latinone leucotriacetate (**7**) (6 mg) as an amorphous solid. δ ($CDCl_3$): 2.33, 2.47, 2.56 (9H, *s*, 3x-OCOMe), 4.0, 4.07 (6H, *s*, 2x-OMe), 7.28–7.66 (8H, *m*, 2-H, 8-H, 10-H and unsubstituted phenyl group), 8.9 (1H, *s*, 5-H).

Synthesis of latinone and 7-O-*methyllatinone.* 3,4-*Dihydroxybenzophenone* (**5**). To a soln of 3,4-dimethoxybenzophenone (3 g) in dry C_6H_6 (40 ml) was added $AlCl_3$ (25 g) in small portions. The mixture was refluxed for 6 hr and then treated with ice–HCl. The aq. layer was washed with EtOAc. The organic layer was washed with NaOH (10%). The alkaline extract was then neutralized (HCl), extracted with EtOAc and dried. Evapn of the solvent yielded 3,4-dihydroxybenzophenone (1.7 g), which crystallized from MeOH as needles, mp 148–149° (lit. [12] 147–148°).

3-*Hydroxy*-4-*methoxybenzophenone* (**6**). To a soln of 3,4-dihydroxybenzophenone (1.6 g) in Me_2CO (20 ml) was added K_2CO_3 (1.2 g) and Me_2SO_4 (0.73 ml). The reaction mixture was refluxed for 90 min, then filtered and the solvent evapd to yield an oil. The oil was dissolved in Et_2O, washed with water and dried. Evapn of the solvent yielded 3-hydroxy-4-methoxybenzophenone (1.2 g) which crystallized in rhombs from EtOAc, mp 132.5–133° (lit. [13] 132–133°). λ_{max}^{MeOH} nm (log ε): 315 (3.32), 280 (3.38), 237 (3.63). $\lambda_{max}^{MeOH+NaOMe}$ nm (log ε): 370 (3.01) 294 sh (3.28), 251 (3.76). δ $CDCl_3$): 4.00 (3H, *s*, −OMe), 5.88 (1H, *s* (br), exchanged D_2O, OH), 6.98 (1H, *d*, *J* = 8 Hz, H-5), 7.83 (1H, *dd*, *J* = 8, 1.3 Hz, H-6), 7.31–7.66 (6H, *m*, H-2, phenyl).

1-*Phenyl*-1-(3-*hydroxy*-4-*methoxyphenyl*)*ethylene* (**7**). To a mixture of Mg (0.36 g) and dry Et_2O (1 ml) was added a soln of MeI (0.93 ml) in dry Et_2O (4 ml) during 15 min. The mixture was then stirred for 30 min. A soln of 3-hydroxy-4-methoxybenzophenone (1 g) in dry Et_2O (50 ml) was added over 30 min. The reaction mixture was stirred at room temp. for 16 hr, then treated at 0° with ice–HCl and stirred for 3 hr. The mixture was then extracted with Et_2O. The organic layer was washed with water, dried and the solvent evapd to yield an oil which was purified by prep. TLC ($CHCl_3$) to afford 1-phenyl-1-(3-hydroxy-4-methoxyphenyl)ethylene (210 mg) as an oil. λ_{max}^{MeOH} nm (log ε): 280 (3.01), 257 sh (3.20), 288 sh (3.58). δ ($CDCl_3$): 3.85 (3H, *s*, −OMe), 5.40 (2H, *s* (br), $=CH_2$, 5.78 (1H, *s* (br), exchanges D_2O, OH), 6.82–7.04 (3H, *m*, H-2, H-5, H-6), 7.36 (5H, *s*, phenyl). Found: C, 79.42; H, 6.11. $C_{15}H_{14}O_2$ requires: C, 79.64; H, 6.2%.

Latinone (**9**, R = H). 1-Phenyl-1-(3-hydroxy-4-methoxyphenyl)ethylene (150 mg) and 2-methoxy-1,4-benzoquinone (150 mg) in HOAc (1.5 ml) were maintained at 25° for 18 hr. Water (20 ml) was added and the mixture was extracted with $CHCl_3$. The organic layer was washed with aq. $NaHCO_3$, water and dried. The solvent was evapd and the residue crystallized from EtOH to yield latinone (40 mg) as a red amorphous solid, mp 284–285°. ν_{max}^{KBr} cm^{-1}: 3370, 1668, 1640, 1620, 1481, 1228, 1098. This compound is identical with the natural product.

1-*Phenyl*-1-(3,4-*dimethoxyphenyl*)*ethylene* (**4**). To a mixture of Mg (0.95 g) and dry Et_2O (5 ml) was added a soln of MeI (3.2 ml) in dry Et_2O over 15 min. The reaction mixture was stirred for 20 min. A soln of 3,4-dimethoxybenzophenone (3 g) in dry Et_2O (75 ml) was added slowly over 30 min. The reaction mixture was stirred at 20° for 16 hr, then treated with H_2SO_4 (10%) at 0° and extracted with Et_2O. The organic layer was washed with NaOH (10%), water and dried. Evapn of the solvent afforded 1-phenyl-1-(3,4-dimethoxyphenyl)ethylene (2.7 g) which crystallized as plates from MeOH, mp 93° (lit. [14] 93°).

7-O-*Methyllatinone* (**9**, R = Me). A mixture of 1-phenyl-1-(3,4-dimethoxyphenyl)ethylene (700 mg) and 2-methoxyl-1,4-benzoquinone (700 mg) in glacial HOAc (10 ml) was retained at 20° for 18 hr. Water (30 ml) was added, and the aq. layer extracted with $CHCl_3$. The organic layer was washed with aq. NaOH (10%), H_2O and dried. The solvent was evapd to afford 7-*O*-methyllatinone (120 mg) which crystallized as red needles from EtOH, mp 280–281°. ν_{max}^{KBr} cm^{-1}: 1667, 1635, 1620, 1482, 1229, 1092. δ ($CDCl_3$): 3.86 (3H, *s*, −OMe), 3.97 (3H, *s*, −OMe), 4.13 (3H, *s*, −OMe), 6.13 (1H, *s*, H-2), 7.25 (1H, *s*, H-5), 7.53 (5H, *s*, aromatic H), 8.01 (1H, *s*, H-10), 9.20 (1H, *s*, H-5). Found: C, 73.84; H, 5.12. $C_{23}H_{18}O_5$ requires: C, 73.80; H, 4.81%.

Preparation of o-*quinone* (**8**). A mixture of 7-*O*-methyllatinone (**9**, R = Me) (200 mg) and H_2SO_4 (40%, 2 ml) was refluxed for 7 min. The reaction mixture was cooled, diluted (20 ml H_2O) and extracted with $CHCl_3$. The extract was washed with H_2O, dried and evapd. Purification of the red solid by prep. TLC ($CHCl_3$) afforded 3-hydroxy-6,7-dimethoxy-9-phenylphenanthrene-1,4-quinone (95 mg), mp 218–219°. δ ($CDCl_3$): 4.16, 3.87 (6H, *s*, 2 × OMe) 6.35 (1H, *s*, 2-H), 7.30 (1H, *s*, 8-H) 7.58 (5H, *m*, Ph), 8.11 (1H, *s*, 10-H), 9.19 (1H, *s*, 5-H). The 3-hydroxyquinone (800 mg) was dissolved in Et_2O and treated with a satd soln of sodium dithionite in an atmosphere of N_2. The ethereal layer was dried, evapd and boric acid (0.4 g) in MeOH (7 ml) was added immediately to the residual oil. The reaction mixture was treated with aq. KOH (10%, 0.2 ml) and CH_2N_2 in Et_2O. An additional aliquot of CH_2N_2 was added after 24 hr and the reaction was kept at room temp. for 48 hr, then aq. HCl (10%, 1.5 ml) was added. Dilution of the reaction mixture and extraction with $CHCl_3$ gave an extract that on evapn yielded a red oil. Purification by prep. TLC ($CHCl_3$) afforded 7-*O*-methyllatinone (**9**, R = Me) (495 mg) and the *o*-quinone (**8**) (25 mg), mp 275–276°. ν_{max}^{KBr} cm^{-1}: 1668, 1648. δ ($CDCl_3$): 3.83, 4.04, 4.11 (9H, *s*, 3 × OMe) 5.95 (1H, *s*, 2-H) 7.17 (1H, *s*, 8-H), 7.55 (5H, *m*, Ph), 7.83 (1H, *s*, 10-H), 9.14 (1H, *s*, 5-H). Found: C, 73.4; H, 4.8. $C_{23}H_{18}O_5$ requires: C, 73.8; H, 4.8%.

Acknowledgements—We thank Professor R. Thomson for his helpful comments and the Minister for Education, Republic of

Ireland for a postdoctoral fellowship (M.J.M.) and a maintenance grant (M.O'S.).

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