# Tetranortriterpenoids and Related Substances. Part 19.[1] Revised Structures of Atalantolide and Atalantin, Limonoids from the Root Bark of *Atalantia monophylla* Correa (Rutaceae)

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Atalantolide and atalantin, two tetranortriterpenoids from the root bark of *Atalantia monophylla* Correa (Rutaceae), have been assigned the revised structures (5) and (13), respectively, on chemical and spectroscopic evidence. The diketone (9) obtained on oxidation of atalantolide undergoes ready enolisation.

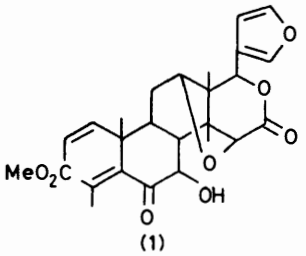
THE structures (1) and (2) proposed recently [2,3] for atalantolide and atalantin, two tetranortriterpenoids from the root bark of *Atalantia monophylla* Correa (Rutaceae), have several biogenetically unusual features.[4,5] In particular they lack the 14,15-epoxy-system which is common to limonoids from the Rutaceae. The principal factor which led the previous workers to assign structures (1) and (2) was the failure of atalantolide and atalantin to react with chromium(II) chloride, a reagent which reduces the typical ring D epoxy-lactone (3) to the deoxy-derivative (4). We now present spectroscopic evidence which supports the presence of a ring D epoxy-lactone in these compounds, and leads to the revised structures (5) and (13), respectively, for atalantolide and atalantin.†

Atalantolide (5), $C_{27}H_{32}O_8$, has resonances for five *C*-methyl groups in the $^1H$ n.m.r. spectrum (Table 1), three tertiary and two attached to a tetrasubstituted double bond. This, together with the presence of an αβ-unsaturated methyl ester, suggested a ring-A-cleaved tetranortriterpenoid skeleton similar to that of methyl obacunoate (6).[7] The $^1H$ n.m.r. spectrum also shows characteristic signals for a β-substituted furan, H-17, H-15, and a secondary hydroxy-group [δ 4.83 (H-7) and 4.24 (OH) (both d, *J* 2.9 Hz)] forming part of an α-ketol. The unsaturated nature of the ketonic function [$\nu_{max.}$ ($CCl_4$) 1 667 $cm^{-1}$; $\lambda_{max.}$ 256 nm (ε 6 300)] required it to be at C-6. These data readily led to the biogenetically reasonable structure (5) for atalantolide. Convincing support was provided by the $^{13}C$ n.m.r. spectrum (Table 2). The proton resonating at δ 3.39 (m, H-9), previously thought to be an epoxide proton,[3] is associated with a carbon doublet at δ 44.3 and hence cannot be attached to a carbon atom bearing oxygen. The $^{13}C$ chemical shifts for C-14 and -15 of the typical ring D epoxy-lactone system of limonoids are well documented; [6,8,9] *e.g.* limonin (7) δ 67.4 (s, C-14) and 53.9 (d, C-15). The presence of this system in atalantolide followed from the resonances at δ 67.4 (s, C-14) and 51.3 (d, C-15). In addition the mass spectrum of atalantolide has a peak at *m/e* 361 resulting from the characteristic cleavage of the ring D epoxy-lactone.[10] The β-configuration of the C-7 hydroxy-function was assigned on the basis of the low-field chemical shift of H-15 (Table 1) and the shifts of this signal to high field on formation of the acetate (8) (0.43 p.p.m.) and the

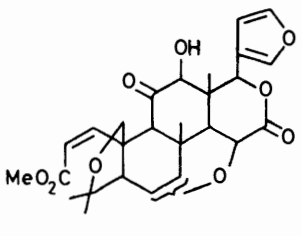
† During our work Dreyer and his colleagues published definitive evidence [6] for the revised structure (13) for atalantin. They also suggested structure (5) for atalantolide although they did not isolate it from the extract. In addition they obtained an interesting novel compound, cycloepiatalantin (14).

[1] Part 18, K. K. Purushothaman, S. Chandrasekharan, J. D. Connolly, and D. S. Rycroft, preceding paper.
[2] M. R. Thaker and B. K. Sabata, *Indian J. Chem.*, 1969, **7**, 870.
[3] J. D. Shringarpure and B. K. Sabata, *Indian J. Chem.*, 1975, **13**, 24.
[4] D. L. Dreyer, *Fortschr. Chem. org. Naturstoffe*, 1968, **26**, 190.
[5] J. D. Connolly, K. H. Overton, and J. Polonsky, *Progr. Phytochem.*, 1970, **2**, 385.
[6] D. L. Dreyer, R. D. Bennett, and S. C. Basa, *Tetrahedron*, 1976, **32**, 2367.
[7] D. H. R. Barton, S. K. Pradhan, S. Sternhell, and J. F. Templeton, *J. Chem. Soc.*, 1961, 255.
[8] D. A. H. Taylor, *J.C.S. Perkin I*, 1974, 437.
[9] D. A. H. Taylor, *J. Chem. Research*, 1977, (*S*)2; (*M*)0114.
[10] M. A. Baldwin, A. G. Loudon, A. Maccoll, and C. W. L. Bevan, *J. Chem. Soc.* (*C*), 1967, 1026.

diketone (9) (0.52 p.p.m) [*cf.* rutaevin (10);[11] corresponding shifts 0.33 and 0.54 p.p.m.]. This assignment is supported by the observation that irradiation at the



(1)



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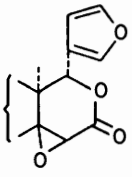
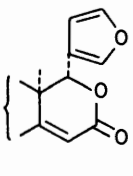
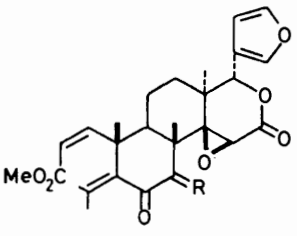


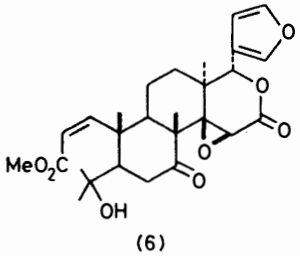
(3)



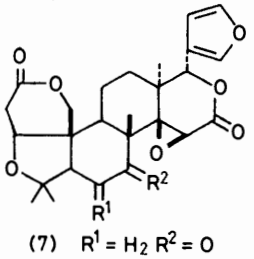
(4)



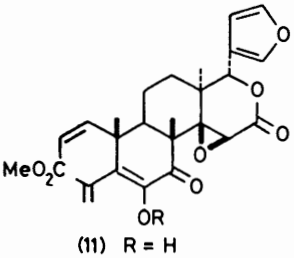
(5) R = H, β-OH
(8) R = H, β-OAc
(9) R = O



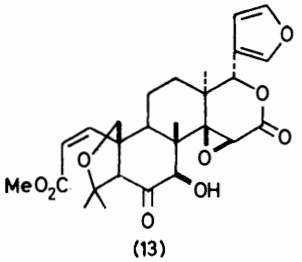
(6)



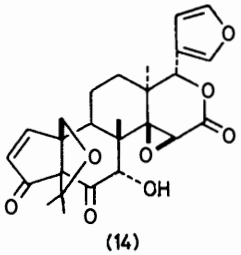
(7) $R^1$ = H, $R^2$ = O
(10) $R^1$ = O, $R^2$ = H,β-OH



(11) R = H
(12) R = Ac



(13)



(14)

frequency of H-9 produced a 15% nuclear Overhauser enhancement in the H-7 signal.

[11] D. L. Dreyer, *J. Org. Chem.*, 1967, **32**, 3442.

Further evidence for the structure (5) for atalantolide was obtained by examination of the products of Jones oxidation. The reported product,[3] the yellow crystalline diketone (9), was difficult to purify. Analytical t.l.c. and the $^1$H n.m.r. spectrum revealed the presence of a second component. The u.v. spectrum [$\lambda_{max.}$ 284 nm (ε 6 000); $\lambda_{max.}$ ($OH^-$) 352 nm (ε 6 300); $\lambda_{max.}$ ($H^+$) 284 nm] suggested that this was the corresponding enol form. Treatment of (9) with base followed by acidification and preparative t.l.c. afforded the non-crystalline enol, whose spectroscopic properties indicated the structure (11). The significant resonances in the $^1$H n.m.r. spectrum (Table 1) included those for three tertiary methyl groups (δ 1.10, 1.12, and 1.48), a vinylic methyl (δ 1.90), an exocyclic methylene (δ 4.91 and 5.16), and an enolic hydroxy-group (δ 6.10; exchangeable with $D_2O$). Irradiation at the vinylic methyl frequency resulted in sharpening of the exocyclic methylene signals. These results show that enolisation of (9) involved removal of a proton from one of the methyl groups attached to C-4. Acetylation of (11) afforded the enol acetate (12) [$\lambda_{max.}$ 246 nm (ε 6 200); $^1$H n.m.r. parameters in Table 1].

Atalantin (13), $C_{27}H_{32}O_9$, the second limonoid from the extract, has spectroscopic properties similar to those of atalantolide (Table 1). Immediately recognisable are the β-substituted furan, H-17, H-15, αβ-unsaturated methyl ester, H-9, and α-ketol [$\nu_{max.}$ ($CCl_4$) 1 710 $cm^{-1}$; δ 4.77 (s, after $D_2O$ exchange, H-7)] signals. The appearance of four tertiary methyl $^1$H n.m.r. signals and an AB quartet [δ 3.79 and 4.17 (*J* 9.5 Hz, $H_2$-19)] suggested a carbon skeleton related to that of limonin (7) [12] with an ether bridge from C-19 to C-4. Biogenetically this can arise by hydroxylation of C-19 in atalantolide followed by Michael addition of the hydroxy-group to the enone system. This arrangement is further supported by a one-proton singlet at δ 3.11, attributable to H-5. Decoupling experiments demonstrated a long-range coupling (1 Hz) between H-5 and H-7, which requires a boat conformation for ring B. Consideration of the chemical shift of H-15 in atalantin and its derivatives and comparison with data for atalantolide (5) and rutaevin (10) [11] led to the assignment of the β-configuration to the C-7 hydroxy-group. As with atalantolide (5) this assignment is corroborated by observation of nuclear Overhauser effects between H-7 and H-9 (*ca.* 15% enhancement either way), even though the geometry of a ring B boat conformation is not such as to maximise these effects. The above information, together with the previous chemical results,[2] can be satisfactorily accommodated in the structure (13) for atalantin. The $^{13}$C n.m.r. spectrum of atalantin (see Table 2) is in accord with this assignment. As in the case of atalantolide the signals at δ 68.5 (s, C-14) and 52.9 (d, C-15) confirm the presence of the ring D-epoxylactone system.

[12] D. Arigoni, D. H. R. Barton, E. J. Corey, O. Jeger, and collaborators, *Experientia*, 1960, **16**, 41.

TABLE 1

$^1$H N.m.r. spectra * of atalantin, atalantolide, and derivatives

| | Atalantolide (5) | Acetate (8) | Dione (9) | Enol (11) | Enol acetate (12) | Atalantin (13) |
|---|---|---|---|---|---|---|
| *C*-Me | 0.68 ($H_3$-30) | 0.82 | 1.04 | 1.10 | 1.07 | 0.89 ($H_3$-30) |
| | 1.36 ($H_3$-18) | 1.30 | 1.08 | 1.12 | 1.17 | 1.24 ($H_3$-18) |
| | 1.41 | 1.41 | 1.63 | 1.48 | 1.48 | 1.30 |
| | 1.81 | 1.78 | 1.96 | 1.90 | 1.82 | 1.36 |
| | 2.04 | 2.00 | 2.16 | | | |
| $H_2$-19 | | | | | | 3.79 (d, *J* 9.5) |
| | | | | | | 4.17 (d, *J* 9.5) |
| H-9 | 3.39 (m) | 3.40 (m) | 3.46 (m) | 3.34 (m) | 3.32 (m) | 3.34 (m) |
| H-5 | | | | | | 3.11br |
| $CO_2$Me | 3.57 | 3.61 | 3.52 | 3.63 | 3.64 | 3.69 |
| OH | 4.24 (d, *J* 2.9) | | | | | 3.84br |
| H-15 | 4.24 | 3.81 | 3.72 | 4.01 | 3.87 | 4.44 |
| H-7 | 4.83 (d, *J* 2.9) | 6.00 | | | | 4.77br |
| H-17 | 5.51 | 5.48 | 5.44 | 5.42 | 5.42 | 5.53 |
| H-2 | 5.75 (d, *J* 12.4) | 5.70 (d, *J* 12) | 5.69 (d, *J* 12) | 5.85 (2 H, s) | 5.86 (2 H, s) † | 5.90 (d, *J* 12) |
| H-1 | 6.37 (d, *J* 12.4) | 6.30 (d, *J* 12) | 6.38 (d, *J* 12) | | | 6.62 (d, *J* 12) |
| H-22 | 6.39 (dd, *J* 1.0 and 1.8) | 6.36 (m) | 6.38 (m) | 6.37 (m) | 6.37 (m) | 6.36 (m) |
| H-21 and -23 | 7.40 (m) | 7.39 (m) | 7.40 (m) | 7.41 (m) | 7.39 (m) | 7.41 (m) |
| OAc | | 2.26 | | | 2.16 | |
| >C=$CH_2$ | | | | 4.91br | 4.76br | |
| | | | | 5.16br | 5.08br | |

* Obtained at 100.2 MHz from solutions in $CDCl_3$ at room temperature (*ca.* 25 °C); shifts are given as positive downfield from internal $Me_4Si$. Parameters are derived from first-order analyses (*J* in Hz). † Very weak lines of an AB quartet were visible, $J_{AB}$ 13 Hz.

TABLE 2

$^{13}$C N.m.r. spectra * of atalantolide and atalantin

| Carbon no. | Atalantolide (5) | Atalantin (13) |
|---|---|---|
| 1 | 158.4 | 163.3 |
| 2 | 118.0 | 120.1 |
| 3 | 166.3 | 165.9 |
| 4 | 152.8 | 84.4 |
| 5 | 135.8 | 64.5 |
| 6 | 201.1 | 209.1 |
| 7 | 79.8 | 80.0 |
| 8 | 45.0 † | 43.9 |
| 9 | 44.3 | 40.2 |
| 10 | 45.2 † | 52.7 |
| 11 | 20.3 | 20.4 |
| 12 | 32.4 | 30.6 |
| 13 | 37.9 | 38.1 |
| 14 | 67.4 | 68.5 |
| 15 | 51.3 | 52.9 |
| 16 | 167.7 | 167.7 |
| 17 | 78.3 | 78.1 |
| 19 | | 75.0 |
| 20 | 120.5 | 120.5 |
| 21 | 141.0 | 141.1 |
| 22 | 110.1 | 110.0 |
| 23 | 142.9 | 143.0 |
| *C*-Me | 29.1 | 31.1 |
| | 25.6, 24.4 | 25.0 |
| 18 | 20.0 | 19.7 |
| 30 | 13.0 | 12.5 |
| $CO_2$*Me* | 51.4 | 51.9 |

* Pulse FT spectra with 1.25 Hz per data point were obtained at 25.2 MHz from solutions in $CDCl_3$ at room temperature (*ca.* 25 °C). Shifts are given as positive downfield (p.p.m.) from internal $Me_4Si$. Assignments are based on chemical shift rules, multiplicities in off-resonance-decoupled spectra, correlation with $^1$H chemical shifts using two off-resonance-decoupled spectra, and comparison with published data for similar compounds.[6,8,9,13] The assignments of C-21 and -23 agree with ref. 13 but not with refs. 6 and 9; we have confirmed our assignment by means of [$^{13}$C-{$^1$H}] double resonance correlation for compounds where H-21 and -23 are chemically shifted. Multiplicities in the off-resonance-decoupled spectrum of atalantin require that the assignments of C-10 and $CO_2$*Me* and of C-11 and -18 are reversed as compared with ref. 6. † These assignments may be interchanged.

Atalantolide and atalantin fit well into the general structural pattern of limonoids found in the Rutaceae although the 19, 4-ether system of atalantin is a novel feature.

## EXPERIMENTAL

For general experimental details see ref. 1. The isolation and characterisation of atalantolide and atalantin are described in refs. 2 and 3.

*Oxidation of Atalantolide.*—Jones reagent (10 drops) was added slowly to a stirred solution of atalantolide (50 mg) in acetone (5 ml) at 0 °C. The solution was left at 0 °C for 5 min, diluted with water, and extracted with chloroform. The crude product was crystallised from chloroform–light petroleum and then methanol to give the dione (9) (20 mg) as yellow crystals, m.p. 180—181° (lit.,[3] 170—172°). Analytical t.l.c. of the dione and the mother liquors indicated the presence of a less polar compound, which was isolated by preparative t.l.c. to yield the non-crystalline *enol* (11) (24 mg), $\nu_{max.}$ ($CCl_4$) 3 455, 1 683, 1 731, and 1 754 cm$^{-1}$ (Found: *m/e*, 482.194 11. $C_{27}H_{30}O_8$ requires *M*, 482.194 04). Exposure of the dione (9) to mild aqueous alkali followed by acidification and preparative t.l.c. afforded mainly the enol (11).

*The Enol Acetate* (12).—The enol (11) (30 mg) was acetylated with acetic anhydride–pyridine at room temperature overnight. Preparative t.l.c. of the crude product gave the non-crystalline *enol acetate* (12) (15 mg), $\nu_{max.}$ ($CCl_4$) 1 707, 1 730, and 1 762 cm$^{-1}$ (Found: *m/e*, 524.204 67. $C_{29}H_{32}O_9$ requires *M*, 524.204 6).

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[13] I. Kubo, S. P. Tanis, Y-W. Lee, I. Miura, K. Nakanishi, and A. Chapya, *Heterocycles*, 1976, **5**, 485.