Molecular and Crystal Structure of Prionostemmadione, a New Dioxofriedelane from *Prionostemma aspera*

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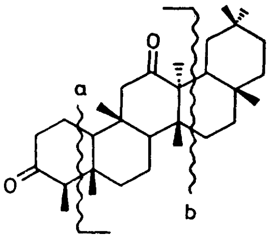
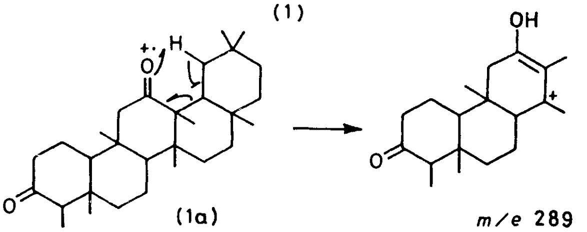
The root bark of *Prionostemma aspera* contains friedelin and a new C_{30} diketone, prionostemmadione, shown to be a friedelane derivative from spectroscopic data. One carbonyl group had the properties of a normal 3-oxo-group, and the other, which was not reduced by sodium borohydride, was located at C-12 on mass spectral evidence. The 3,12-dioxofriedelane structure was confirmed by *X*-ray crystallographic analysis, the crystals having an approximate chair–chair–chair–boat–boat conformation for rings A—E.

In continuation of our work [1] on the triterpenes in the closely related families Celastraceae and Hippocrateaceae we have isolated friedelin and a new diketone, prionostemmadione (1), from the root bark of *Prionostemma aspera* (Celastraceae). The dione, $C_{30}H_{48}O_2$ (M^+ 440), showed strong carbonyl absorption at 1 716 and 1 697 cm^{-1} attributable to two six-membered cycloketone groups but was otherwise saturated (i.r., n.m.r., negative tetranitromethane test). In view of the co-occurrence of friedelin it seemed likely that the dione belonged to the friedelane series, and this was supported by the n.m.r. spectrum which shows seven methyl singlets at high field [δ ($CDCl_3$–C_6D_6) 0.57, 0.74, 0.84, 0.95, 1.10, 1.17, and 1.27] and a methyl doublet at δ 0.86 (J 6.5 Hz) (not resolved in $CDCl_3$ alone). In the region δ 2.6—2.0 an AB system centred at 2.6 and 2.05 (J 12 Hz) was assigned to the axial and equatorial protons, respectively, of an isolated methylene group α to a carbonyl group, while signals from two/three other protons must also arise from $-CH_2-$ and $>CH-$ groups α to carbonyl since deuterium exchange under basic conditions afforded a tetradeuterio-derivative with a trace of pentadeuteriation (mass spectrum).



(1)



(1a) *m/e* 289

The two ketonic groups showed a marked difference in reactivity. Only one was reduced on treatment with sodium borohydride to give a keto-alcohol [M^+ 442; $\nu_{max.}$ 3 550 and 1 695 cm^{-1}; δ 3.75br (1 H, $W_{\frac{1}{2}}$ 7 Hz)] which formed an acetate, and could be dehydrated with phosphorus oxychloride to give an unsaturated ketone [M^+ 424; δ 5.05 (1 H, m) and 1.60 (3 H, s)]. This behaviour would be expected of the 3-keto-group in (1). In the n.m.r. spectra of these compounds the AB quartet arising from the isolated $-CH_2CO-$ system is still present. The other keto-group was reduced by hydrogenation over platinum to give a second, somewhat insoluble keto-alcohol (M^+ 442; $\nu_{max.}$ 3 560 and 1 703 cm^{-1}) as the main product. Its more soluble acetyl derivative (M^+ 484; $\nu_{max.}$ 1 719 and 1 682 cm^{-1}) showed n.m.r. signals at δ 4.9br (1 H, $W_{\frac{1}{2}}$ 7 Hz) and 2.0 (3 H, s).

The main fragmentations in the mass spectrum of the dione are also consistent with a friedelane skeleton [2] notably those at *a* and *b* [see (1)] which give intense ions at *m/e* 355 ($C_{25}H_{40}O$) and 289 ($C_{19}H_{29}O_2$), respectively. The latter indicates that both carbonyl groups are in rings A—C. Assuming that prionostemmadione is a 3-oxofriedelane the second carbonyl group must be located at C-6, -11, or -12, the 3,7-diketo-derivative being known.[3] Of these, C-12 is most likely as this accounts for the intense peak at *m/e* 289 by cleavage at the C–D ring juncture with hydrogen transfer [see (1a)]. The corresponding cleavage in 1,3- [4] and 3,7-dioxofriedelane [3] proceeds without hydrogen transfer to give a major ion at *m/e* 288.

To establish the existence of the friedelane skeleton in prionostemmadione attempts were made to convert it into friedelin by Wolff–Kishner reduction,[5] and by successive reduction (H_2–Pt and $NaBH_4$), dehydration, and hydrogenation. However the hydrocarbons obtained (M^+ 412) were different from friedelin [6] no doubt as a result of molecular rearrangements to which friedelane derivatives are prone.[7] In view of this prionostemmadione was submitted to *X*-ray crystallographic analysis (see Experimental section, and Tables 1—3) which established the 3,12-dioxofriedelane structure (1) and relative stereochemistry.

The conformation of friedelin-type terpenes has been discussed [8] following an *X*-ray crystallographic structure determination on a pachysandiol (friedelane-3β,16β-diol) derivative. Our present structure is of the same type, *i.e.* rings A—E are in the approximate form chair–chair–chair–boat–boat. The distortions from an ideal conformation of this type are considerable; they are apparent from Figure 2 and are quantitatively described by the torsion angles.

It follows that reduction of (1) with sodium borohydride gives the 12-oxo-3-ol while the isomer obtained by hydrogenation is the 3-oxo-12-ol.

EXPERIMENTAL

Isolation of the Triterpenes.—The powdered root bark (2 kg) of *Prionostemma aspera* was extracted with cold methanol. Concentration of the extract gave a precipitate which was chromatographed on a silica gel column in benzene to give friedelin (140 mg), m.p. 262—263°, ν_{CO} 1 690 cm^{-1}, identified by direct comparison (t.l.c., i.r., m.s.) with authentic material. Further elution with benzene–ethyl acetate (8 : 2) afforded prionostemmadione (800 mg), and minor amounts of two unidentified hydroxyprionostemmadiones.

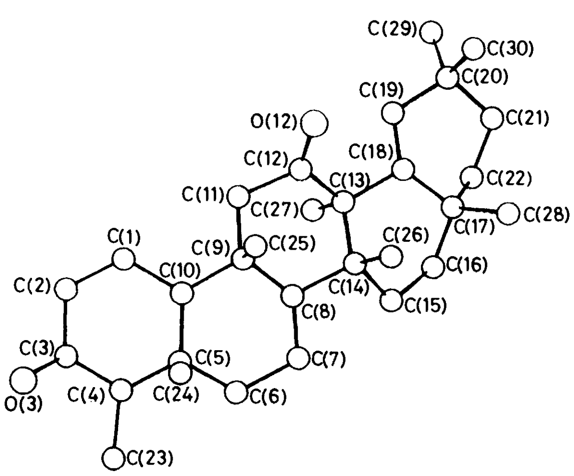
Prionostemmadione (1) had m.p. 282—284° (from chloroform–methanol) and 304° after sublimation (Found: C, 81.4; H, 10.6. $C_{30}H_{48}O_2$ requires C, 81.8; H, 10.9%), $[\alpha]_D^{25}$ −105° (*c* 1 $CHCl_3$); $\nu_{max.}$ (KBr) 1 716 and 1 697 cm^{-1}; δ (100 MHz; $CDCl_3$) 2.62 (1 H, d, *J* 12 Hz), 2.4—2.1 (3 H, m), 2.05 (1 H, d, *J* 12 Hz), 1.37 (3 H, s), 1.17 (3 H, s), 1.03 (3 H, s), 0.91 (3 H, s), 0.89 (6 H, s), 0.86 (3 H, s), and 0.70 (3 H, s) (see also Discussion section); *m/e* 440 (M^+, 100%), 425 (83), 422 (45), 407 (33), 397 (15), 355 (6), 289.216 8 (57) ($C_{19}H_{29}O_2$ requires 289.216 7), 262 (12), 247 (10), 235 (15), 233 (18), 219 (20), 217 (22), 205 (25), and 191 (47). After deuteriation (twice) according to ref. 9 it showed an M^+ cluster *m/e* (corrected relative intensity, %) 445 (*ca.* 1.0), 444 (24.2), 443 (57.2), 442 (14.2), 441 (*ca.* 2), and 440 (*ca.* 2).

12-*Oxofriedelan*-3-*ol*.—The dione (300 mg) was stirred in cold methanol–chloroform (2 : 1; 50 ml) with an excess of sodium borohydride for 2 h. Work-up in the usual way afforded the 12-*oxo*-3-*ol* (250 mg), m.p. 294—295° (from methanol–chloroform) (Found: C, 81.0; H, 10.9. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.3%), $\nu_{max.}$ (KBr) 3 550 and 1 695 cm^{-1}; δ (100 MHz; $CDCl_3$) 3.75br (1 H, $W_{\frac{1}{2}}$ 7 Hz, C*H*OH), 2.5 (1 H, d, *J* 11.5 Hz, H-11), 2.00 (1 H, d, *J* 11.5 Hz, H-11), 8.67, 8.84, 8.96, and 9.03—9.15 (15 H) (8 × Me); *m/e* 442 (M^+, 100%), 427 (70), 424 (30), 409 (10), 291 (50), 264 (11), 257 (16), 234 (22), 219 (40), and 191 (60). With acetic anhydride–pyridine it gave an *acetate*, m.p. 249—250° (from methylene chloride–hexane) (Found: M^+, 484.391 4. $C_{32}H_{50}O_3$ requires *M*, 484.391 6), *m/e* 484 (M^+, 100%), 469 (50), 466 (27), 456 (27), 451 (11), 381 (13), 333 (32), 306 (10), 279 (14), 273 (14), 234 (25), 219 (38), 217 (25), 205 (12), 203 (14), and 191 (50).

12-*Oxofriedel*-3-*ene*.—To the dione (200 mg) in pyridine (40 ml) was added phosphorus oxychloride (5 ml). The mixture was left overnight, heated under reflux for 20 min, poured onto ice, and extracted with chloroform. The crude product was passed down a silica gel column to give the 12-*oxo*-3-*ene* (130 mg), m.p. 218—220° (from chloroform–methanol) (Found: C, 84.9; H, 11.3. $C_{30}H_{48}O$ requires C, 85.2; H, 11.0%); $\nu_{max.}$ (KBr) 1 700 cm^{-1}; δ (60 MHz; $CDCl_3$) 4.95br (1 H, =CH); *m/e* 424 (M^+, 100%), 409 (57), 406 (37), 391 (21), 381 (20), 273 (40), 246 (12), 233 (14), 219 (44), and 191 (30).

3-*Oxofriedelan*-12-*ol*.—The dione (100 mg) in acetic acid was hydrogenated over platinum oxide at room temperature. Work-up by chromatography on silica gel in benzene gave the 3-*oxo*-12-*ol* (60 mg), m.p. 287—290° (Found: C, 81.5; H, 11.7. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.3%), $\nu_{max.}$ 3 560 and 1 703 cm^{-1}; δ (too insoluble); *m/e* 442 (M^+, 39%), 427 (31), 424 (16), 409 (12), 291 (21), 231 (13), 229 (22), 219 (100), 207 (30), 203 (25), and 191 (60). With acetic anhydride–pyridine it gave an *acetate*, m.p. 266—268° (from methylene dichloride–ethyl acetate) (Found: M^+, 484.391 4. $C_{32}H_{52}O_3$ requires *M*, 484.391 6), $\nu_{max.}$ ($CHCl_3$) 1 730 and 1 695 cm^{-1}; δ (60 MHz; $CDCl_3$) 4.90 (1 H, m, $W_{\frac{1}{2}}$ 7 Hz, C*H*OAc), and 2.00 (3 H, s, OAc); *m/e* 484 (M^+, 100%), 469 (52), 466 (31), 451 (14), 333 (17), 234 (12), 219 (20), and 191 (25).

Crystal Data.—$C_{30}H_{48}O_2$, $M = 440.7$. Orthorhombic, $a = 6.337(2)$, $b = 28.310(4)$, $c = 13.984(3)$ Å, $U = 2\,508.7$ Å^3, $D_c = 1.167$, $D_m = 1.15$ g cm^{-3}, $Z = 4$, $F(000) = 976$. Space group $P2_12_12_1$, Mo-K_α radiation (graphite monochromator), $\lambda = 0.710\,69$ Å, $\mu = 0.76$ cm^{-1}.



Perspective drawing of prionostemmadione

The cell parameters were initially found from oscillation and Weissenberg photographs and then refined by least squares from the setting angles of 23 reflections on a Hilger–Watt four-circle diffractometer. Reflections were scanned (ω—2θ mode) for θ ⩾ 25°. 2 574 Reflections were measurable in this range and 1 841 of these had a net count >3σ(*I*) and were used in the refinement. Lorentz and polarisation but not absorption corrections were made.

The structure was solved using MULTAN [10] in the 1977 version. Initial attempts, using the KS curve, to calculate *E* values were unsuccessful, but when the *E* values were estimated using the best straight line through the Debye curve a trial using 330 reflections with $E > 1.4$ and 4 000 relationships automatically revealed in the 'best' *E* map all the non-hydrogen atoms of the triterpene.

Refinement proceeded routinely by full-matrix least squares. After three cycles of anisotropic refinement a difference map revealed all the hydrogen atoms. Subsequently the hydrogen atoms were included in the refinement in their calculated positions which were kept fixed. Finally a weighting scheme of the form $W = 1.0/[A(0) . T(0) . X + A(1) . T(1) . X + A(2) . T(2) . X + A(3) . T(3) . X]$, where $A(0)$–$A(3)$ are the coefficients of a Chebyshev series in $T(1) . X$ with $X = F_o/F_{o(\max.)}$, was applied. The co-

TABLE 1

Fractional co-ordinates with standard deviations in parentheses

Atom	x/a	b/y	z/c
O(3)	0.834 4(6)	1.262 8(1)	0.463 7(3)
O(12)	1.263 8(6)	0.981 3(1)	0.524 6(2)
C(1)	0.967 8(8)	1.149 4(2)	0.527 7(3)
C(2)	0.811 6(9)	1.189 4(2)	0.546 4(3)
C(3)	0.796 2(7)	1.220 5(2)	0.460 7(3)
C(4)	0.737 8(8)	1.195 4(1)	0.368 7(3)
C(5)	0.911 5(7)	1.157 4(2)	0.346 5(3)
C(6)	0.843 8(9)	1.128 7(2)	0.258 7(3)
C(7)	0.970 6(8)	1.083 3(2)	0.243 0(3)
C(8)	0.957 1(7)	1.051 6(2)	0.331 3(3)
C(9)	1.052 2(6)	1.076 9(2)	0.420 3(3)
C(10)	0.918 2(7)	1.123 3(1)	0.435 0(3)
C(11)	1.020 1(8)	1.044 5(2)	0.508 2(3)
C(12)	1.106 0(7)	0.995 5(2)	0.486 1(3)
C(13)	0.989 7(7)	0.969 5(2)	0.407 4(3)
C(14)	1.026 9(7)	0.999 1(2)	0.314 8(3)
C(15)	0.893 3(9)	0.977 5(2)	0.232 0(3)
C(16)	0.849 9(9)	0.923 6(2)	0.240 9(4)
C(17)	1.005 6(8)	0.893 3(2)	0.298 7(3)
C(18)	1.079 8(7)	0.918 6(2)	0.394 0(3)
C(19)	1.034 1(8)	0.887 8(2)	0.483 3(3)
C(20)	0.115 2(9)	0.836 9(2)	0.477 1(4)
C(21)	1.036(1)	0.814 1(2)	0.383 4(4)
C(22)	0.894(1)	0.846 4(2)	0.324 2(4)
C(23)	0.697(1)	1.230 4(2)	0.287 8(4)
C(24)	1.120 8(9)	1.182 6(2)	0.326 4(4)
C(25)	1.291 3(7)	1.088 1(2)	0.415 6(4)
C(26)	1.262 0(8)	0.998 0(2)	0.284 3(3)
C(27)	0.751 8(8)	0.967 1(2)	0.436 0(3)
C(28)	1.196(1)	0.881 1(2)	0.233 7(4)
C(29)	1.030(1)	0.809 8(2)	0.562 6(4)
C(30)	1.359(1)	0.836 2(2)	0.480 9(5)

TABLE 2

Bond lengths (Å) with standard deviation in parentheses

C(1)–C(2)	1.525(7)	C(12)–C(13)	1.516(6)
C(1)–C(10)	1.526(6)	C(12)–O(12)	1.205(5)
C(2)–C(3)	1.491(6)	C(13)–C(14)	1.560(6)
C(3)–O(3)	1.220(5)	C(13)–C(18)	1.561(6)
C(3)–C(4)	1.516(6)	C(13)–C(27)	1.561(6)
C(4)–C(5)	1.571(7)	C(14)–C(15)	1.559(6)
C(4)–C(23)	1.527(6)	C(14)–C(26)	1.550(7)
C(5)–C(6)	1.533(6)	C(15)–C(16)	1.555(7)
C(5)–C(10)	1.570(6)	C(16)–C(17)	1.538(7)
C(5)–C(24)	1.532(7)	C(17)–C(18)	1.586(6)
C(6)–C(7)	1.531(7)	C(17)–C(22)	1.544(7)
C(7)–C(8)	1.529(6)	C(17)–C(28)	1.547(7)
C(8)–C(9)	1.556(6)	C(18)–C(19)	1.549(6)
C(8)–C(14)	1.569(6)	C(19)–C(20)	1.531(7)
C(9)–C(10)	1.577(6)	C(20)–C(21)	1.545(8)
C(9)–C(11)	1.546(6)	C(20)–C(29)	1.521(8)
C(9)–C(25)	1.550(6)	C(20)–C(30)	1.544(9)
C(11)–C(12)	1.521(6)	C(21)–C(22)	1.526(9)

efficients used were *A*(0) 79.6, *A*(1) 109.6, *A*(2) 33.4, *A*(3) 0.6. At convergence the maximum shift/standard deviation was 0.01 and the conventional *R* was 5.45%.

Table 1 gives the fractional co-ordinates of the non-hydrogen atoms. Tables 2 and 3 show the bond lengths and angles. The Figure is a perspective drawing of the molecule, with the crystallographic numbering.

Apart from MULTAN, crystallographic computations were done using the Oxford CRYSTALS [11] package, and the drawing was prepared from PLUTO.[12] Thermal parameters for non-hydrogen atoms, torsion angles, and a list of observed and calculated structure factors are available in Supplementary Publication No. SUP 22566 (45 pp.).*

TABLE 3

Bond angles (°) with standard deviations in parentheses

C(2)–C(1)–C(10)	111.8(4)	C(12)–C(13)–C(14)	105.5(3)
C(1)–C(2)–C(3)	110.1(4)	C(12)–C(13)–C(18)	111.0(4)
C(2)–C(3)–C(4)	114.8(4)	C(12)–C(13)–C(27)	107.7(4)
C(2)–C(3)–O(3)	122.6(5)	C(14)–C(13)–C(18)	110.0(3)
O(3)–C(3)–C(4)	122.5(4)	C(14)–C(13)–C(27)	112.4(4)
C(3)–C(4)–C(5)	108.6(4)	C(18)–C(13)–C(27)	110.1(4)
C(3)–C(4)–C(23)	111.5(4)	C(8)–C(14)–C(13)	110.2(3)
C(5)–C(4)–C(23)	114.7(4)	C(8)–C(14)–C(15)	109.1(4)
C(4)–C(5)–C(6)	109.0(4)	C(8)–C(14)–C(26)	109.3(4)
C(4)–C(5)–C(10)	106.5(4)	C(13)–C(14)–C(15)	108.9(4)
C(4)–C(5)–C(24)	108.9(4)	C(13)–C(14)–C(26)	111.3(4)
C(6)–C(5)–C(10)	108.2(3)	C(15)–C(14)–C(26)	108.0(4)
C(6)–C(5)–C(24)	110.0(4)	C(14)–C(15)–C(16)	114.9(4)
C(10)–C(5)–C(24)	114.1(4)	C(15)–C(16)–C(17)	118.5(4)
C(5)–C(6)–C(7)	114.3(4)	C(16)–C(17)–C(18)	112.3(4)
C(6)–C(7)–C(8)	110.3(4)	C(16)–C(17)–C(22)	108.0(4)
C(7)–C(8)–C(9)	110.8(4)	C(16)–C(17)–C(28)	108.3(4)
C(7)–C(8)–C(14)	115.0(4)	C(18)–C(17)–C(22)	109.2(4)
C(9)–C(8)–C(14)	116.3(4)	C(18)–C(17)–C(28)	111.3(4)
C(8)–C(9)–C(10)	106.1(3)	C(22)–C(17)–C(28)	107.5(4)
C(8)–C(9)–C(11)	108.2(3)	C(13)–C(18)–C(17)	114.2(4)
C(8)–C(9)–C(25)	116.1(4)	C(13)–C(18)–C(19)	110.8(4)
C(10)–C(9)–C(11)	108.6(3)	C(17)–C(18)–C(19)	111.6(4)
C(10)–C(9)–C(25)	111.2(4)	C(18)–C(19)–C(20)	114.9(4)
C(11)–C(9)–C(25)	106.5(4)	C(19)–C(20)–C(21)	109.4(5)
C(1)–C(10)–C(5)	112.1(3)	C(19)–C(20)–C(29)	108.2(4)
C(1)–C(10)–C(9)	113.9(4)	C(19)–C(20)–C(30)	110.3(5)
C(5)–C(10)–C(9)	115.1(4)	C(21)–C(20)–C(29)	109.9(4)
C(9)–C(11)–C(12)	109.4(4)	C(21)–C(20)–C(30)	110.4(6)
C(11)–C(12)–C(13)	114.6(4)	C(29)–C(20)–C(30)	108.7(6)
C(11)–C(12)–O(12)	120.8(4)	C(20)–C(21)–C(27)	113.7(4)
O(12)–C(12)–C(13)	124.4(4)	C(17)–C(22)–C(21)	111.7(5)

We thank the Leverhulme Trust for a European Visiting Fellowship to one of us (M. P.).

[8/2008 *Received, 20th November*, 1978]

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* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1978, Index issue.