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THE DITERPENES OF DACRYDIUM COLENSOI. PART V.[1]

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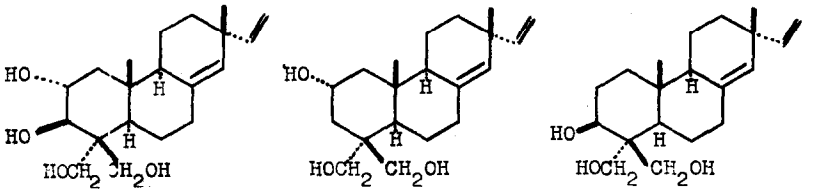
We wish to report the structures of a series of hydroxylated diterpenes possessing the novel geminal hydroxymethyl grouping. This is the first report of both geminal methyls being hydroxylated in a naturally occurring terpenoid compound.

The sublimed hexane insoluble material from the heartwood extract of Dacrydium colensoi was previously considered to be a tetrahydroxy diterpene, dacrydol.[2] It has been shown by t.l.c. to consist of three major compounds, D_1, D_2, and D_3 which were separated on florisil as the acetonides. D_1, D_2, and D_3 have been shown by degradative studies to have structures (1), (2), and (3) respectively.



(1) (2) (3)

D_1, $C_{20}H_{32}O_4$;* m.p. 210-214°, formed a monoacetonide, $C_{23}H_{36}O_4$, m.p. 163-165°, and (in low yield) a diacetonide, $C_{26}H_{40}O_4$, m.p. 109-112° thus accounting for all the oxygen atoms as hydroxyl groups.

D_2 acetonide, $C_{23}H_{36}O_3$, m.p. 125-130°, and D_3 acetonide, $C_{23}H_{36}O_3$, m.p. 148-150°, both showed hydroxyl absorption in the infrared showing that D_2, $C_{20}H_{32}O_3$, m.p. 224-227°, and D_3, $C_{20}H_{32}O_3$, m.p. 163-166° were triols.

The infrared spectra of D_1 and D_1 monoacetonide showed bands characteristic of a vinyl group (3080, 1634, 994, 910 cm.$^{-1}$) and a trisubstituted double bond (1660, 835 cm.$^{-1}$). D_2 and D_3 showed similar infrared spectral characteristics. Thus the compounds were tricarbocyclic and based on a perhydrophenanthrene skeleton since selenium dehydrogenation of the dacrydol complex gave pimanthrene. In the NMR spectrum of D_1 acetonide, the vinyl group appeared as an ABX system (H_A 5.10, H_B 5.10, H_X 4.20τ; J_{AB} 1.7, J_{BX} 17.9, J_{AX} 9.5 c/s) while the olefinic proton of the trisubstituted double bond appeared as a singlet (½ band width 3.8 c/s) at

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*Satisfactory analyses were obtained for all compounds reported.

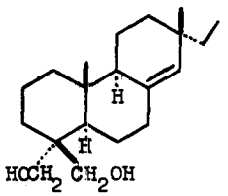
4.69τ, thus fixing the nuclear double bond in the 8-14 position. D_2 and D_3 showed similar spectral values.

The NMR spectra of D_1, D_2, D_3, and the acetonides showed only two (9.25, 8.96τ) of the usual four methyl groups associated with a pimarane type skeleton. Two methyl groups had been replaced by hydroxymethyl groups which appeared as two AB or collapsed AB systems in the 6.00-6.25τ region. The signal in the 8.95-9.00τ region could be assigned to the C-13 methyl group since it moved to 9.10τ on reduction of the vinyl group.[3] This required the hydroxymethyl groups to be attached to ring A. Oxidation of D_2 acetonide and D_3 acetonide gave the ketones oxo-D_2 acetonide, $C_{23}H_{34}O_3$, m.p. 100-103° (1703 $cm.^{-1}$) and oxo-D_3 acetonide, $C_{23}H_{34}O_3$, m.p. 146-148° (1700 $cm.^{-1}$) and showed that the third hydroxyl group in D_2 and D_3 was secondary and that acetonide formation involved the hydroxymethyl groups, either between the 4β and 10β or 4α and 4β positions, i.e. the ring A methyl at the 4α or the 10β position.

Since oxo-D_2 acetonide showed four activated hydrogens (NMR), the secondary hydroxyl group in D_2 must be at C-2. Sodium borohydride reduction of oxo-D_2 acetonide gave epi-D_2 acetonide, $C_{23}H_{36}O_3$, m.p. 118.5-121.5°, which showed a paramagnetic shift of the ring A methyl signal (0.23δ) as compared with D_2 acetonide due to an OH:Me diaxial interaction. As metal hydride reductions of 2-oxo-lanostane derivatives[4] and 2-oxo-oxidoditerpenes[5] give almost exclusively the 2β-alcohol, the ring A methyl group must be in the angular 10β position and the hydroxyl group in D_2 in the equatorial 2α orientation.

The ORD of oxo-D_2 acetonide (a^{310}_{262}+116) was in agreement with an A/B trans ring junction, although the large amplitude was not consistent with an all-chair conformation.

Wolff-Kishner reduction of dihydro-oxo-D_2 acetonide, $C_{23}H_{36}O_3$, m.p. 83-84°, and subsequent hydrolysis gave dihydro-2-deoxy D_2 (4), $C_{20}H_{34}O_2$, m.p. 124.5-126.5° which on mild acetylation gave a mixture of monoacetates, oxidised to a mixture of aldehydo-acetates (CHO at 0.15 and 0.61τ). Under mild alkaline conditions this mixture underwent a reverse aldol reaction[6] to give formaldehyde (characterised as the dimedone derivative) and the nor-aldehyde (5), $C_{19}H_{30}O$, (characterised as the oxime $C_{19}H_{31}NO$, m.p. 66-68°) in which the aldehyde proton appeared as a doublet (0.54τ, J 4 c/s). These reactions can only be accounted for by a geminal hydroxymethyl grouping.



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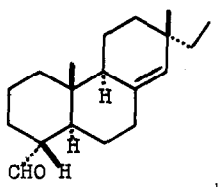

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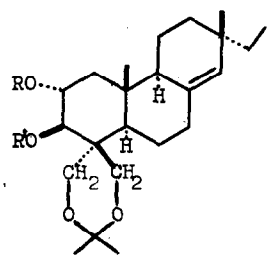

(6) R = Ac, R' = H

(7) R = H, R' = Ac

D_1 monoacetonide contained an α-glycol linkage which was cleaved with lead tetra-acetate. Dihydro-D_1 monoacetonide,

$C_{23}H_{38}O_4$, m.p. 163-165°, formed two monoacetates $C_{25}H_{38}O_5$, m.p. 119-120.5° and 126.5-128.5° formulated as the 2α-acetoxy-3β-hydroxy (6) and 3β-acetoxy-2α-hydroxy (7) derivatives respectively. This diequatorial orientation was confirmed by the trans diaxial coupling[7] of the proton attached to the carbon bearing the acetate group in the 3β-acetoxy derivative (7) (doublet, 5.42τ, J 9.9 c/s). Oxidation of the monoacetates gave the 2α-acetoxy-3-keto, $C_{25}H_{36}O_5$, b.p. 130°/0.002 mm. (C-2 βH, quartet at 4.68τ, J_{aa}+ J_{ae} 20 c/s) and 3β-acetoxy-2-keto, $C_{25}H_{36}O_5$, m.p. 166.5-167.5°, derivatives which on deacetoxylation with calcium in liquid ammonia[8] gave dihydro-oxo-D_3 acetonide and dihydro-oxo-D_2 acetonide. That the secondary hydroxyl group in D_3 was at C-3 and not the alternative C-1 position followed from a comparison of the NMR signals of D_3 derivatives with the corresponding 1, and 3 oxygenated derivatives in the oxidoditerpene series. The D_2 signals are also included (Table 1).

The equatorial orientation of the secondary hydroxyl group in D_3 followed from the large coupling of the carbinol proton (quartet at 5.65τ, J_{AX} + J_{BX} 15.5 c/s), in dihydroacetoxy-D_3 acetonide $C_{25}H_{40}O_4$, m.p. 123.5-125.5°. Since metal hydride reduction of oxo-D_3 acetonide gave D_3 acetonide as the only product this eliminated the alternative C-1 position for the secondary hydroxyl in D_3 as metal hydride reduction of 4,4-dimethyl-1-oxo-5α-steroids[9] and 1-oxo-oxidoditerpenes[3] gives predominantly the axial alcohol (73% and 85% respectively). In D_1 diacetonide the second acetonide linkage is between the 2α and 3β hydroxyl groups.

TABLE 1

	τ	Dihydro Derivative of	τ	Dihydro Derivative of	τ
D_3	9.25	3β-OH-Manoyl oxide	9.23	1β-OH-Manoyl oxide	9.14
D_3 acetonide	9.32	3α-OH-Manoyl oxide	9.21	1α-OH-Manoyl oxide	9.18
*Acetoxy-D_3 acetonide	9.32	3β-OAc-Manoyl oxide	9.19	1β-OAc-Manoyl oxide	9.04
Oxo-D_3 acetonide	9.08	3-Oxo-manoyl oxide	9.12	1-Oxo-manoyl oxide	8.83
		Sandaraco-pimaradien-3β,19-diol	9.27		
	τ	Compound	τ	Compound	τ
D_2	9.25	2α-OH-Manoyl oxide	9.16	2α,18-DiOH-Manoyl oxide	9.20
D_2 acetonide	9.25	2α-OH-Dihydro M.O.	9.15	2α,18-DiOH-Dihydro M.O.	9.19
Epi-D_2 acetonide	9.02	2β-OH-Manoyl oxide	8.96	2β,18-DiOH-Manoyl oxide	8.93
Oxo-D_2 acetonide	9.26	2-Oxo-manoyl oxide	9.20	2-Oxo-18-OH-Manoyl oxide	9.20

Chemical shifts of the C-10 methyl group in D-2, D-3, and reference oxidoditerpenes. Note that the 18 position in the oxidoditerpenes is equivalent to the 19 position in the pimarane type. *Dihydro derivative.

The basic skeleton of the dacrydol series was established by conversion of D_2 to the nor-aldehyde (5) which on Wolff-Kishner reduction gave the hydrocarbon $C_{19}H_{32}$, b.p. 110°/0.5 mm., identical in all respects (NMR, IR, t.l.c.) to the hydrocarbon obtained from the Wolff-Kishner reduction of 19-nor-sandaracopimaradien-3-one. This determined the stereochemistry of the remaining asymmetric centres, C-9 and C-13, since these centres remain unaffected in this reaction sequence.

Thus the structures of D_1, D_2, and D_3 are established as sandaracopimaradien-2α, 3β, 18,19-tetrol, sandaracopimaradien-2α, 18,19-triol, and sandaracopimaradien-3β,18,19-triol respectively.

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