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CALLITRISIC ACID: A NEW DITERPENOID

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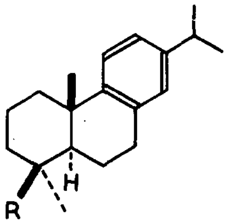
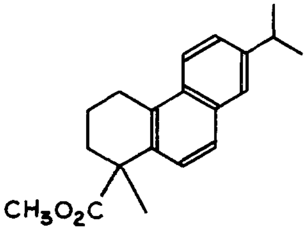
The resins of several Callitris species (Cupressaceae)(Australian sandarac resin), previously studied by Henry (1) and more briefly by Baker and Smith (2), have been examined and found to contain a new diterpenoid acid (Ia), named callitrisic acid (3). It can be isolated in yields of up to 10% from the light petroleum-soluble acids by a process involving partial reduction of the accompanying pimaric-type acids followed by lactonisation of their dihydro-derivatives with trifluoroacetic acid and isolation of the unchanged callitrisic acid by chromatography.

While this manuscript was in preparation, Carman and Deeth (4) reported the isolation of the same acid (under the name 4-epidehydroabietic acid) from Callitris columellaris resin, and arrived at the same structure by a chemical correlation with dehydroabietic acid. The properties of methyl 4-epidehydroabietate (4) were virtually identical with those of methyl callitrisate (below), and the identity of the two compounds was confirmed by IR and $[\alpha]_D$ comparisons and a mixed m.p. determination. The author thanks Dr. Deeth for making these comparisons, and for providing a copy of his paper prior to publication.

Callitrisic acid, $C_{20}H_{28}O_2$, has not been obtained in an absolutely pure, crystalline state (c.f. ref. 4), but the methyl ester (Ib) is crystalline, m.p. 30.5-31°, $[\alpha]_D^{22}$ +136° (c 1.0, EtOH), λ_{max}^{EtOH} 276, 268, 262(sh) mμ (log ε 2.87, 2.83, 2.66), and analyses as $C_{21}H_{30}O_2$, MW 314 (mass spectrum). Spectroscopic data indicate the presence of a 1,2,4-trisubstituted aromatic ring (δ 6.92 (1H), 7.12 (2H; AB quartet, J 7.8 c/s);[*] ν 823, 890 (CS_2), 1495, 1606 (CCl_4) cm^{-1}). The mass spectra of methyl callitrisate and methyl dehydroabietate (5) are very similar, and these esters, when dehydrogenated under a variety of conditions, afford identical series of products, including retene, in nearly identical amounts (analysed by GLC (6)). Partial dehydrogenation with selenium affords what are probably (from their chromatographic behaviour, UV and IR spectra) the enantiomeric naphthalenic esters (II) (λ_{max}^{EtOH} 323, 315.5, 309, 289(sh), 269.5, 232.5mμ (log ε 2.8, 2.6, 2.8, 3.6, 3.7, 4.9), λ_{min} 249mμ (log ε 3.4); ν 1107, 1179, 1189, 1251, 1723 (ester), 815, 888, 1493, 1602 (aromatic system) cm^{-1}) (not completely pure).



(Ia) R = CO_2H
(Ib) R = CO_2CH_3
(Ic) R = CH_2OH



(II)

These data indicate callitrisic acid to have the structure (Ia) (<u>without</u> stereochemical implications), and unambiguously locate the carboxyl group at C-4. Callitrisic acid was shown not to be identical with either dehydroabietic acid (7) or 5β-dehydroabietic acid (8) by direct comparisons (IR and ORD of the acids, mixed m.p., IR, and GLC of the methyl esters). It must therefore be either (Ia) or the 5β-isomer of (Ia). Three sets of evidence show it to have the A/B-trans (5α) stereochemistry of (Ia).

The chemical shifts of the C-4 and C-10 methyl groups in methyl callitrisate agree well with those reported (8,9) for suitable A/B-trans 4β-methoxycarbonyl model compounds, but not for those with A/B-cis (or 4α) configurations.

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* All NMR data reported in this paper refer to 60 Mc/s spectra on solutions in $CDCl_3$, with TMS internal standard.

TABLE I

Configuration	Compound	δ_{C-4}	δ_{C-10}
	Methyl callitrisate	1.27	1.03
A/B-*trans*, 4β-CO_2Me	Methyl deoxypodocarpate (10)	1.27	1.03
A/B-*trans*, 4β-CO_2Me	Methyl *O*-methylpodocarpate	1.27	1.03
A/B-*cis*, 4β-CO_2Me	Methyl 5β-deoxypodocarpate (11)	1.09	1.22

The IR spectrum of methyl callitrisate shows eight bands common to esters of A/B-*trans* diterpenoid acids having an axial (β) 4-carboxyl group (12, 13). Several of these bands, including the strongest at *ca*.1151cm^{-1}, are absent from the spectrum of the A/B-*cis* compound, methyl 5β-deoxypodocarpate. The spectra of callitrisic acid and the liquid alcohol callitrisol (Ic) also correlate well with those of A/B-*trans* 4β-acids and alcohols (13).

The ORD curves of callitrisic acid and four reference types of aromatic diterpenoid acids (with *cis*- and *trans*-A/B ring junctions and with carboxyl groups in 4α- and 4β-configurations) were measured. The curves down to 233mμ were all essentially plain, with negligibly weak aromatic Cotton effects around 260-275mμ. The following values are given for the reference acids in the "normal" 10β-series.

TABLE II

Type	Configuration		Compound	$[\phi]_{233}$
(a)	A/B-*trans*, 5α-H;	4α-CO_2H	Dehydroabietic acid	+7460
(b)	A/B-*trans*, 5α-H;	4β-CO_2H	Deoxypodocarpic acid	+8560
(c)	A/B-*cis*, 5β-H;	4α-CO_2H	5β-Dehydroabietic acid	-6700
(d)	A/B-*cis*, 5β-H;	4β-CO_2H	5β-Deoxypodocarpic acid	-530

The curve for callitrisic acid, $[\phi]_{233}$ +12950 (methyl callitrisate, $[\phi]_{233}$ +15000), may be compared with these values. It is clearly only comparable with types (a), (b), or the *enantiomer* of type (c); type (d) is a whole order of magnitude smaller. Direct comparisons (above) have eliminated types (a) and (c) from consideration, so callitrisic acid must, by exclusion, and in conformity with the other data, be of type (b). It is therefore the 4-epimer of dehydroabietic acid. Further, the ORD data define its absolute configuration as depicted in (Ia).

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