Absolute Stereochemistry of (+)-Abscisin II

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THE plant hormone abscisin II, also known as dormin, is the dextrorotatory[1] enantiomer of structure[2,3](Ia). We have deduced the absolute configuration around its one centre of asymmetry by comparing the $[M]_D$-values for the two diol esters (II), epimeric at C-4′, obtained by borohydride reduction of its methyl ester (Ib); applying Mills' rule[4] to assign absolute configurations at C-4′; and relating the geometry at C-1′ to that at C-4′.

The racemic epidioxide[3] (III) was hydrogenated in ethanol over Lindlar's catalyst, giving a diol acid, m.p. 158—159°, which was converted by ethereal diazomethane into its gummy methyl ester, R_f 0·30 (system A[*]), 0·51 (system B); λ_{max} (MeOH) 265·5 mμ, ϵ 20,900. From its method of preparation this was the *cis*-diol ester (IIa).

Racemic[3] abscisin II was methylated with ethereal diazomethane and the ester, in ether–methanol at −5°, was reduced with an excess of sodium borohydride to give a mixture from which

[*] R_f-values refer to thin-layer chromatography (t.l.c.) on Kieselgel-GF$_{254}$. System A was 1 : 1 (v/v) n-hexane–ethyl acetate; system B, 1 : 2 (v/v) cyclohexane–ethyl acetate; system C, 100 : 100 : 1 (v/v) chloroform–benzene–acetic acid, the plate being developed 8—10 times.

TABLE

Compound	λ_{max}, mμ	Cotton effect parameters				
		1st extremum $[M]$, Kilodeg. (λ, mμ)	2nd extremum $[M]$, Kilodeg. (λ, mμ)	for $[M] = 0$ mμ	Centre*, mμ	$[M]_D$, degrees
(+)-Abscisin II	260·5	+58 (289)	−190 (246)	269	266	+1100
cis-Diol ester	265·5	+12 (286)	− 12 (242)	263	262	+ 390
trans-Diol ester	267	+34 (287)	− 49 (243)	266	263	+ 990
(−)-Abscisin II	260·5	−65 (289)	+190 (246)	269	266	−1100
cis-Diol ester	265·5	−13 (286)	+ 12 (242)	263	262	− 340
trans-Diol ester	267	−32 (287)	+ 45 (243)	266	263	− 880

Bellingham-Stanley "Polarmatic 62" spectropolarimeter; concentration: 20—200 μg/ml; temperature: 20—22°; path-length: 5 mm.; solvent: methanol for the esters; acidified ethanol for the acids (*cf.* ref. 1.).

* Centre of Cotton effect on a linear *frequency* scale.

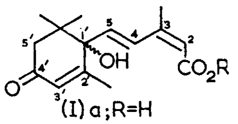
the gummy *cis*-diol ester (IIa), with R_f-values and ultraviolet and infrared spectra identical with those of the product described above; and the *trans*-diol ester (IIb), m.p. 114—115°, R_f 0·44 (system A), 0·67 (system B), λ_{max} (MeOH) 267 mμ (ϵ 22,200), were isolated by chromatography on a column of silica gel. The yields of the two diol esters were about equal at *ca.* 40%, and their infrared spectra in carbon disulphide differed. Satisfactory elemental analyses and spectroscopic data were obtained for the racemic compounds.

Since insufficient natural (+)-abscisin was available it was obtained, with difficulty, by resolution of the synthetic racemate. Fractional crystallisation of the brucine salt of (±)-abscisin II from aqueous methanol, and regeneration of the free acid, yielded samples of the (+)- and (−)-enantiomers of low optical purity (of many optically active bases and many solvents tried, only this one combination gave a crystalline salt). Further enrichment was achieved by repeated removal of the racemic compound from these samples, taking advantage of the low solubility of (±)-abscisin II, relative to that of its enantiomers, in ether, methylene chloride, and benzene. The residues in the final mother-liquors were sublimed in a vacuum, and recrystallisation of the sublimates from benzene yielded (+)- and (−)-abscisin II contaminated with the (largely racemic)2-*trans*-isomer of abscisin II.

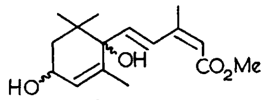
Synthetic (+)-abscisin II (1·2 mg.) was freed from its 2-*trans*-isomer by t.l.c. (system C). A small portion was used for polarimetry (Table 1), which indicated a high degree of optical purity; the rest was methylated for $\frac{1}{2}$ min. at 0° with ethereal CH_2N_2, and treated, in aqueous methanol at 0° for 40 min., with an excess of sodium borohydride. The resulting two diol esters, isolated with ether after acidification of the reaction mixture, were separated by t.l.c. (system A), using markers of the racemic diol esters (in pilot experiments the identity of the two products was also confirmed by mass spectrometry). The optical rotatory dispersion of each (Table) was then measured, the concentration being calculated from the absorbance of the solutions.

Synthetic (−)-abscisin II (1·5 mg.) was subjected to the same treatment to give a second pair of diols (Table).

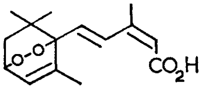
At the D-line, the *cis*-diol ester derived from (+)-abscisin II is more lævorotatory than the *trans*-diol ester [and conversely for the diol esters from (−)-abscisin II]. According to Mills' empirical rule[4] for allylic cyclohexenols, the absolute configurations at C-4′ of the dextrorotatory pair are as shown (IV and V), and the absolute stereochemistry of natural (+)-abscisin II follows (VI).



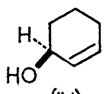
(I) a; R=H
b; R=Me



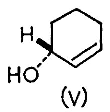
(II) a; *cis*-Diol
b; *trans*-Diol



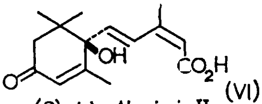
(III)



(IV)
(+)-*cis*-Diol ester



(V)
(+)-*trans*-Diol ester



(S)-(+)-Abscissin II (VI)

The amplitudes of the Cotton effects (attributable to the side-chain chromophore) exhibited in the 260 mμ region by the *cis*- and *trans*-diol esters differ by a factor of about 3. While this difference between 4′-epimers may contribute to the $\Delta[M]$ value at the remote D-line, it is hardly possible for the contribution to be great enough (it would have to exceed 540—600°) to invalidate our assignment based on the effect of the epimerisation on the rotational contribution of the cyclohexenol system. Mills' rule itself appears to have no exceptions. A far from exhaustive search of the literature has added 24 examples to Mills' list[4] of pairs of epimeric allylic cyclohexenols and their esters, in which the absolute stereochemistry had been determined by independent means and which obey the rule. Significantly, these examples include 6 pairs (*e.g.*, 7α- and 7β-hydroxy-11-oxo-8-ene steroids) in which the epimeric centre is close to a chromophore capable of showing a Cotton effect in the middle ultraviolet range, and which therefore present a closer analogy with our diol esters.

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[1] J. W. Cornforth, B. V. Milborrow, and G. Ryback, *Nature*, 1966, **210**, 627.
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[3] J. W. Cornforth, B. V. Milborrow, and G. Ryback, *Nature*, 1965, **206**, 715.
[4] J. A. Mills, *J. Chem. Soc.*, 1952, 4976.