

**672.** *The Nature of a Cyclitol isolated from Macrozamia Riedlei.*

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Crude macrozamin from *Macrozamia Riedlei* contains sequoyitol, a mesoinositol mono-methyl ether. Consideration of the periodate oxidation favours the view that sequoyitol is the 2-methyl ether rather than the 5-methyl ether.

For a recent structural study the toxic nitrogenous compound macrozamin was isolated from the Western Australian plant *Macrozamia Riedlei* (Lythgoe and Riggs, this vol., p. 2716). The crude product had a low optical rotation, and this was traced to the presence of an impurity which could be removed by extraction with methanol, in which macrozamin is insoluble. From the cooled methanolic extract a substance separated as colourless leaflets, m. p. 237—238° (Found: C, 43.6; H, 7.6; OMe, 15.4. Calc. for  $C_6H_{11}O_5 \cdot OCH_3$ : C, 43.3; H, 7.3; OMe, 16.0%). It was nitrogen-free, optically inactive, had no reducing properties, and did not give Molisch's reaction. Its aqueous solutions were neutral, and it was not affected by treatment with hot dilute acid or alkali, or by reagents for carbonyl compounds. Acetic anhydride and pyridine converted it into a penta-acetate, which formed long needles, m. p. 200—201.5°, from ethyl acetate—light petroleum (Found: C, 50.3; H, 5.4. Calc. for  $C_{17}H_{24}O_{11}$ : C, 50.5; H, 6.0%).

These properties agree with those of sequoyitol, a monomethyl ether of mesoinositol, isolated from Californian redwood, *Sequoia sempervirens*, by Sherrard and Kurth (*J. Amer. Chem. Soc.*, 1929, **51**, 3139). These authors recorded for sequoyitol m. p. 234—235° and for its penta-acetate m. p. 198°; demethylation of sequoyitol by hot hydriodic acid yielded mesoinositol. Similar treatment of the substance from *M. Riedlei* also gave mesoinositol, m.p. 222—224° (hexa-acetate m. p. 216°), so that the identity of this substance with sequoyitol seems certain.

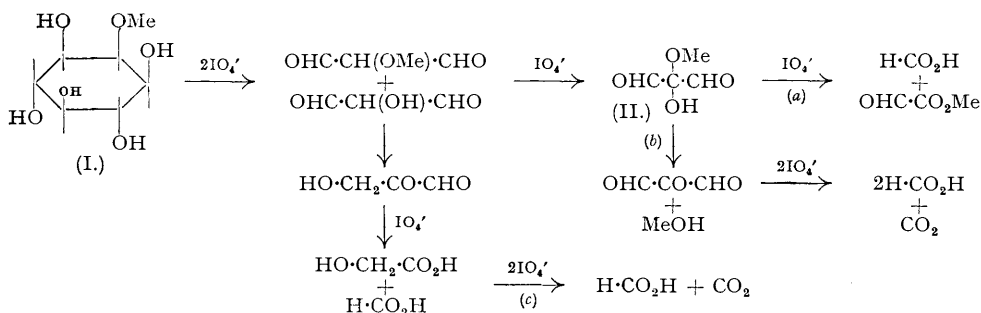
Some years after the first isolation of sequoyitol, mesoinositol was shown by Posternak (*Helv. Chim. Acta*, 1942, **25**, 746) and by Dangschat and Fischer (*Naturwiss.*, 1942, **30**, 146) to have the configuration  $\frac{1235}{46}$ , and sequoyitol, which is almost certainly a meso-compound must therefore be the 2- or 5-methyl ether. Some light is thrown on the orientation of the methoxyl group by the course of the oxidation of sequoyitol with sodium metaperiodate, shown in the following table.

Time (hours) .....	5.8	23.8	30.2	47.0	62.0
Periodate consumed (mols.) .....	5.46	5.81	6.02	6.29	6.92
Strong acid * liberated (equivs. per mol.) .....	3.17	3.77	3.83	3.79	3.49

\* Determined by using methyl-red as indicator.

The above results may be compared with those obtained by Fleury, Poirot, and Fievet (*Compt. rend.*, 1945, **220**, 664) on the periodate oxidation of the parent compound *mesoinositol*. Both compounds consume periodate and liberate strong acid rapidly at first, then the periodate consumption becomes slower, and the titre of strong acid remains constant; at the end of the reaction the amount of periodate which has been used is greater, and the amount of strong acid liberated is less, than would be expected if only simple  $\alpha$ -glycol fission took place. Fleury and his co-workers (*loc. cit.*) isolated, from the oxidation products of *mesoinositol*, both formic acid and glycollic acid; the latter acid reacted slowly and incompletely with periodate, without change in the acid titre. The overall reaction was therefore assumed to occur by an initial fission of *mesoinositol* into two molecules of tartrondialdehyde, which rearranged rapidly to hydroxypyruvaldehyde; this was cleaved in its turn to glycollic and formic acid.

It is difficult to explain the course of the oxidation of sequoyitol if the latter is formulated as *mesoinositol* 5-methyl ether, since if, as is usual, *cis*- $\alpha$ -glycol groups react faster than *trans*-systems, and if the intermediate methoxymalondialdehyde undergoes hydroxylation and fission (Huebner, Ames, and Bubl, *J. Amer. Chem. Soc.*, 1946, **68**, 1621), then not less than 4 equivalents of strong acid should be formed per mole of sequoyitol oxidised. If, however, sequoyitol is the 2-methyl ether of *mesoinositol* (I), it contains only *trans*- $\alpha$ -glycol systems, and the course of the oxidation can be explained by the following reactions, in the first of which the molecule is split into tartrondialdehyde and methoxymalondialdehyde:



Reaction (c) is slow and incomplete, requiring *ca.* 1.3 moles of periodate (Fleury, Poirot, and Fievet, *loc. cit.*). Reactions (a) and (b) represent alternative paths for the oxidation of the intermediate compound (II); probably both occur simultaneously, leading to the observed uptake of *ca.* 6 moles of periodate and the liberation of <4 g.-equivalents of strong acid per mole of sequoyitol. The increase in periodate uptake, and the decrease in strong acid liberated after 47 hours from the start of the experiment, are probably due to the slow oxidation of formic acid noted by Huebner and his co-workers (*loc. cit.*).

These results therefore favour the structure (I) for sequoyitol.