Absolute Configurations of some Tartaric Acid Derivatives Determined by a Key–Lock Complexation Method

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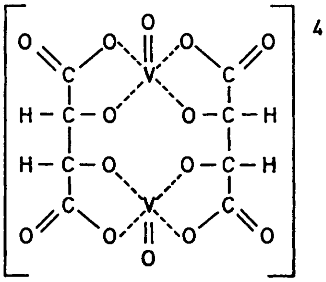
Summary Absolute configurations of the enantiomers of *threo*-2-methyltartaric acid and 2,3-dimethyltartaric acid have been determined from stereoselective differences observed in the extent of binding at a chiral vanadyl(IV) site; the method can also rapidly distinguish between *erythro* and *threo* isomers and is applicable to other substituted tartaric acids.

Although many instances are known where enantiomeric ligands ("keys") bind to different extents with a chiral centre ("lock"),[1] such differences have apparently not been used to assign previously unknown absolute configurations based on an analysis of the steric requirements for binding. We report such an assignment herein. The method described permits a rapid determination of the absolute configuration of any optically active alkyl- or aryl-substituted *threo*-tartaric acid having a water-soluble salt. The same technique also permits the assignment of *erythro* or *threo* configurations to tartaric acid derivatives.

In aqueous solution above pH 7, vanadyl(IV) co-ordinates with tartaric acid to give 2:2 binuclear complexes (**1**).[2] The observed isomer stability ordering, DL>DD=LL,† is consistent with the steric requirements on the ligands in these complexes.[3] The ligand bridges in the DL complex are significantly better staggered than are those in the DD and LL isomers.



(1)

Upon addition of L(+)-tartrate to a solution of the DD complex, a rapid ligand displacement occurs accompanied by a change from the 4-band visible absorption spectrum characteristic of the DD isomer to the 3-band spectrum of the DL [(a) in the Figure]. An analogous ligand displacement giving a more stable "DL" isomer is expected when any

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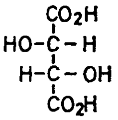
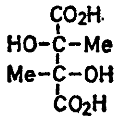
† These isomer designations gave the absolute configurations (relative to glyceraldehyde)[4] of the two ligands in a complex. *E.g.*, "DD" designates the isomer containing two D(−)-tartrate (**2**) bridges. All signs of optical rotation are for aqueous solutions of the free acids at 589 nm.

alkyl- or aryl-substituted L-tartrate is allowed to react with the DD vanadyl(IV) unsubstituted-tartrate complex. On the other hand, significant ligand displacement from this complex by a substituted D-tartrate is not predicted owing to the expected increase in strain when a substituted ligand is forced into the unfavourable conformation required by a "DD" isomer.



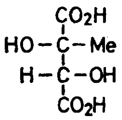
$$\begin{array}{c} \mathrm{CO_2H} \\ \mathrm{HO-C-H} \\ \mathrm{H-C-OH} \\ \mathrm{CO_2H} \end{array}$$

(2)



$$\begin{array}{c} \mathrm{CO_2H} \\ \mathrm{HO-C-Me} \\ \mathrm{Me-C-OH} \\ \mathrm{CO_2H} \end{array}$$

(3)



$$\begin{array}{c} \mathrm{CO_2H} \\ \mathrm{HO-C-Me} \\ \mathrm{H-C-OH} \\ \mathrm{CO_2H} \end{array}$$

(4)

For the evaluation of these predicted ligand displacements as a tool for determining absolute configuration, the "key" compounds (±)-2,3-dimethyltartaric acid and *threo*-2-methyltartaric acid were synthesized,[5,6] resolved,[7] and converted into their sodium salts. An equimolar mixture of the sodium salts of (+)-2,3-dimethyltartaric acid and of DD vanadyl(IV) tartrate[2] was found to exhibit a 4-band solution spectrum which differed little from that of the pure DD tartrate complex [compare (a) and (b) in the Figure] and which did not resemble solution spectra observed for either the pure bis-(+)-2,3-dimethyltartrate complex or for a mixture of this compound and the DD tartrate complex. On the other hand, in a rapidly established equilibrium, a similar mixture employing the sodium salt of (−)-2,3-dimethyltartaric acid exhibited a solution spectrum (Figure) markedly different from that of either the pure DD vanadyl(IV) tartrate or the bis-(−)-2,3-dimethyltartrate complex and essentially identical to that which we have observed for the (−)-2,3-dimethyltartrate–D(−)-tartrate mixed-ligand complex. These experiments show that there is little displacement of D(−)-tartrate (**2**) from the DD complex by (+)-2,3-dimethyltartrate but extensive displacement by (−)-2,3-dimethyltartrate. These results permit the unambiguous assignment of a D configuration to (+)-2,3-dimethyltartaric acid (**3**). Very similar results obtained in an analogous experiment with *threo*-2-methyltartaric acid allow us to assign a D absolute configuration to the (+) isomer of the derivative (**4**) also.

In separate experiments, we also find that neither *meso*-2,3-dimethyltartrate[5] nor (±)-*erythro*-2-methyltartrate[6] will displace tartrate ligands from the DD vanadyl(IV) complex in agreement with experimental evidence and ligand conformation considerations which show vanadyl(IV) *meso*-tartrate-containing complexes to be unstable.[3] Thus, this key–lock complexation method is also applicable to rapid *erythro*–*threo* assignments for tartrate derivatives.

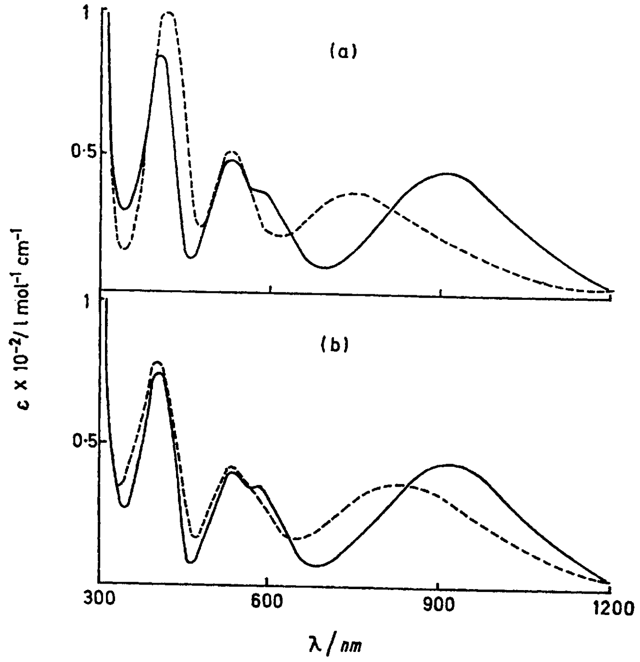


FIGURE. (a) Absorption spectrum of 0·01 M DD vanadyl(IV) tartrate complex in the presence of 0·01 M D(−)-tartrate (———) and of 0·01 M L(+)-tartrate (– – –). (b) Absorption spectrum of 0·01 M DD vanadyl(IV) tartrate complex in the presence of 0·01 M (+)-2,3-dimethyltartrate (———) and of 0·01 M (−)-2,3-dimethyltartrate (– – –).

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