A Correction to the Molecular Structure of Enantiomeric Gossypol

Sir:

In the November 1999 issue of the *Journal of the American Oil Chemists' Society*, we reported the structure of an enantiomeric crystalline form of gossypol (1). The crystal form was produced from a solution of gossypol acetic acid and acetone and was described as being an inclusion complex between gossypol and acetic acid in a 1:3 ratio. Subsequent work now indicates that our initial interpretation of the diffraction data was incorrect and that this structure is actually an inclusion complex between gossypol and acetone. The same number and configuration of nonhydrogen atoms in acetic acid and acetone, the known tendency of gossypol to complex with acetic acid, and the low R-factor obtained during the first study led to the incorrect determination. The error was uncovered by additional experiments on an enantiomeric form of gossypol crystallized from a solution containing (−)-gossypol, (±)-lactic acid, and acetone. The unit cell dimensions of this structure were the same as the unit cell dimensions of the first structure, which strongly suggested that the crystal forms were identical. Because acetone was present in both crystallization solutions, this suggested that the complex was gossypol-acetone (1:3).

The crystal form in question is unstable outside the crystallization solution, which was found to be due to the diffusion of the guest molecules from large open channels within the structure (1). This instability was exploited to confirm the identity of the guest molecules. A large single crystal was selected, briefly washed with 90:10 (vol/vol) hexane/acetone to remove surface contaminants, and blotted dry with tissue paper. The crystal was then allowed to stand in hexane for 1 h. Analysis of the hexane solution by gas chromatography (split injector, FFAP capillary column, flame-ionization detector) indicated the presence of acetone and not acetic acid.

In hindsight, some evidence existed that the initial determination was in error. Carbon-oxygen bond distances for the acetic acid hydroxyl groups were longer than expected and similar to sp^2-sp^3 carbon-carbon bond lengths. Also, no hydrogen bonding was observed between the guest molecules. These points were mentioned in the report (1), but were taken to be indications of disorder within the structure.

Although the guest molecules were incorrectly identified in the initial report (1), the crystal form is chiral and can be used to resolve the gossypol enantiomers from a racemic solution. We routinely make gram quantities of (+)- and (−)-gossypol *via* this crystal form (Dowd, M.K., unpublished data).

Updated crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 166194. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, United Kingdom (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk), or the data can be obtained from the authors. We regret any inconvenience caused by the error.

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REFERENCES

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