

STRUCTURE OF CONICASTEROL F

Here is an interesting twist on using computations in conjunction with experimental NMR to solve for molecular structure. I have blogged a number of times on comparing computed chemical shifts with experimental values to identify structure, and also on using the comparison of computed and experimental coupling constants to accomplish this purpose.

Butts and Bifulco were interested in the structure of conicasterol F **1** and opted to make two sets of comparison.¹ The first uses the traditional approach of comparing the computed and experimental ¹³C chemical shifts. The second comparison uses the distances between protons, coming from the optimized structure and the rotating-frame nuclear Overhauser effect (ROE).

Standard analysis of the NMR spectra of **1** allowed for the determination of all of the stereochemistry except for the epoxy ring at C₈ and C₁₄. The possible options are shown as **1a** and **1b**. The optimized geometries (MPW1PW91/6-31G) of these two diastereomers are shown in Figure 1.

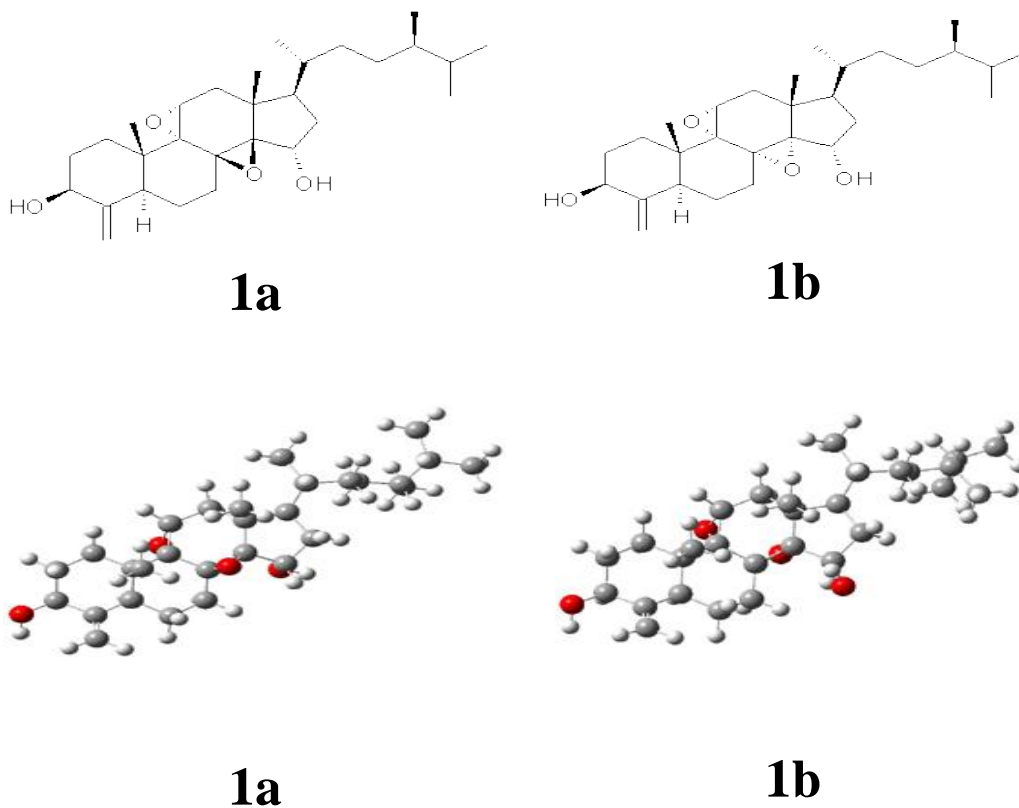


Figure 1. Optimized geometries of **1a** and **1b**.

Comparison of 15 distances between protons determined by the ROE experiment and by computation led to a mean absolute error of 7.8% for **1a** and 3.0% for **1b**, suggesting that the latter is the correct structure. Similar comparison was then made between the experimental chemical shifts of 12 of the carbon atoms with the computed values of the two isomers. The mean absolute error in the chemical shifts of **1a** is 3.7ppm, but only 0.8 ppm for **1b**. Both methods give the same conclusion: conicasterol F has structure **1b**.

Source: <http://comporgchem.com/blog/?p=2215>