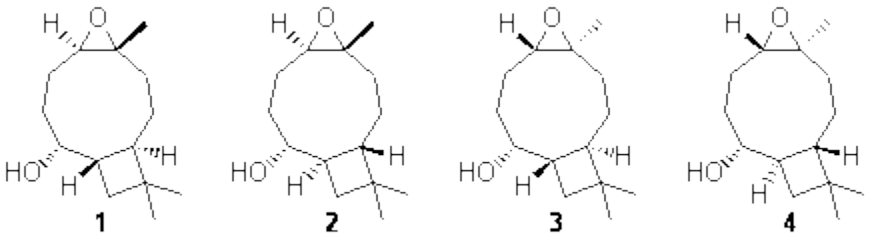
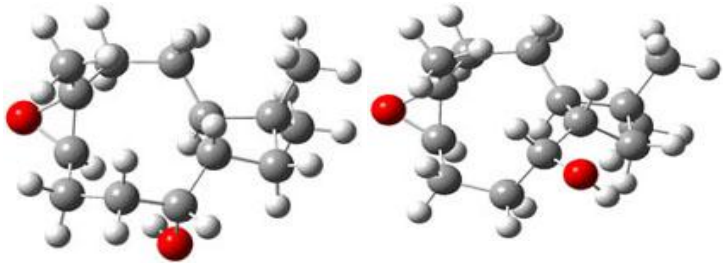
PREDICTING THE STRUCTURE OF ARTARBOROL

Here's one more nice application of computationally-derived NMR chemical shifts towards solving a structure. Fattarusso and co-workers[1] identified a component of wormwood called artarborol. COSY and ROESY experiments allowed for deducing four possible diasereomeric structures of artarborol,**1-4**.



They then took two computational approaches towards resolving the structure. First, they performed an MM search for low energy conformers of **1-4**. These conformers were then screened for those having a dihedral angle of around 90° for the C-8 and C-9 protons, due to a low couple constant for between these protons. Only conformers of **1** and **3** satisfied this criterion. An intense couple of the H-1 and H-5 protons indicated a trans annular arrangement, and only conformers of **1** satisfy this criterion.

The second computational approach was to optimize some of the low energy conformers of **1** and **3**at mPW1PW91/6-31G(d,p) and compute their ^{13}C chemical shifts. The five low energy conformers, two of **1** and three of **3**, are shown in Figure 1. The resulting chemical shifts were averaged according to a Boltzmann distribution. These computed chemical shifts were then fit against the experimental values. The correlation factor for the computed shifts for **1** (r^2=0.9997) was much better than that of **3** (r^2=0.9713). The average deviation of the chemical shifts (after being corrected using the fitting procedure from the above correlation) was only 0.8ppm for **1** but 2ppm for **3**. They therefore conclude that the structure of artarborol is **1**.

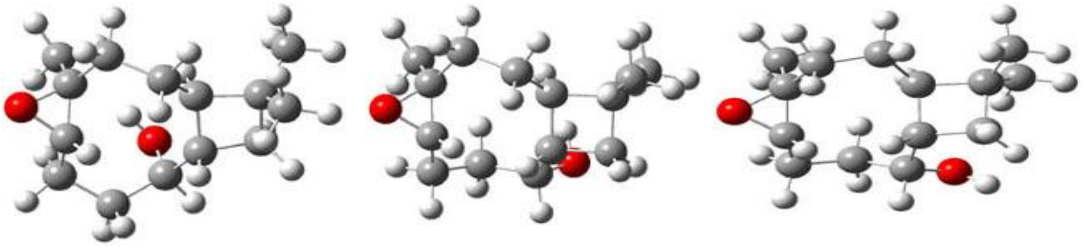


1a

xyz

1b

xyz



3a
xyz

3b
xyz

3c
xyz

Figure 1. mPW1PW91 optimized conformations of possible artarborol diasteromers.[1]

Source: http://comporgchem.com/blog/?p=26