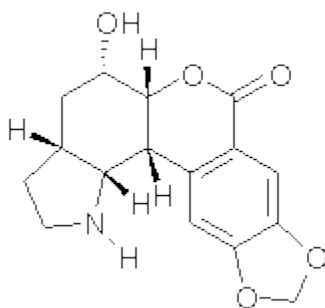


COMPUTED NMR SPECTRA PREDICTS THE STRUCTURE OF NOBILISITINE A

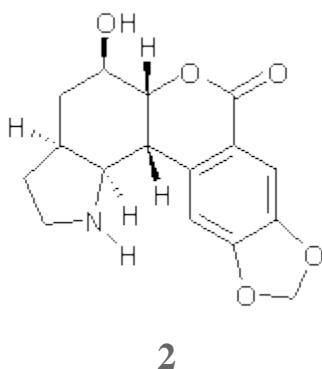
Nobilisitine A was isolated by Evidente and coworkers, who proposed the structure **1**.¹ Banwell and co-workers then synthesized the enantiomer of **1**, but its NMR did not correspond to that of reported for Nobilisitine A.; the largest differences are 4.7 ppm for the ¹³C NMR and 0.79 ppm for the ¹H NMR.²



1

Lodewyk and Tantillo³ examined seven diastereomers of **1**, all of which have a *cis* fusion between the saturated 5 and six-member rings (rings C and D). Low energy conformations were computed for each of these diastereomers at B3LYP/6-31+G(d,p). NMR shielding constants were then computed in solvent (using a continuum approach) at mPW1PW91/6-311+G(2d,p). A Boltzmann weighting of the shielding constants was then computed, and these shifts were then scaled as described by Jain, Bally and Rablen⁴.

The computed NMR shifts for **1** were compared with the experimental values, and the mean deviations for the ^{13}C and ^1H svalues is 1.2 and 0.13 ppm, respectively. (The largest outlier is 3.4 ppm for ^{13}C and 0.31 for ^1H shifts.) Comparison was then made between the computed shifts of the seven diastomers and the reported spectrum of Nobilisitine A, and the lowest mean deviations (1.4 ppm for ^{13}C and 0.21 ppm for ^1H) is for structure **2**. However, the agreement is not substantially better than for a couple of the other diastomers.



They next employed the DP4 analysis developed by Smith and Goodman⁵ for just such a situation – where you have an experimental spectrum and a number of potential diastereomeric structures. The DP4 analysis suggests that **2** is the correct structure with a probability of 99.8%.

Banwell has now synthesized the compound with structure **2** and its NMR matches that of the original natural product.⁶ Thus Nobilisitine A has the structure **2**.

Source: <http://comporgchem.com/blog/?p=1908>