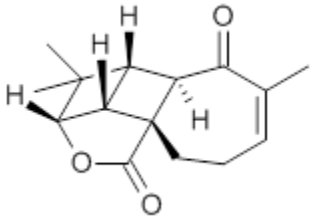
AQUATOLIDE – STRUCTURE REVISION BROUGHT ON BY COMPUTED NMR SPECTRA

The natural product aquatolide has the proposed structure **1**.[1] Before starting to investigate this rather unusual structure – the 2[ladderane] component is rare and likely to be a synthetic challenge – Shaw and Tantillo opted to reassure themselves that the structure is correct.[2] They computed the chemical shifts of this structure at mPW1PW91/6-311+G(2d,p)//B3LYP/6-31+G(d,p) including PCM to model chloroform. Surprisingly, the mean absolute deviation of the computed ^{13}C NMR shifts of**1** with the experimental values is 7.23 ppm, with the largest deviation of 24.3 ppm. The largest deviation between **1** and the experimental ^{1}H NMR shifts is 1.31 ppm. These large errors suggested that the structure is wrong. Surveying some 60 different possible alternative structures, largely based on other related compounds found in the same plant, they landed on **2**.

Here the mean absolute deviation of the computed ^{13}C chemical shifts is only 1.37 ppm, with a maximum deviation of only 4.3 ppm. Similar dramatic improvement is also seen with the proton chemical shifts. Excellent agreement is also seen in the computed ^{1}H-^{1}H coupling constants between those computed for **2** and the experimental spectrum. Crystallization of aquatolide and subsequent determination of the structure using x-ray diffraction confirms that the actual structure of aquatolide is **2**.



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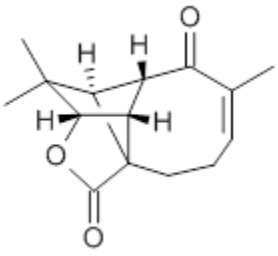

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