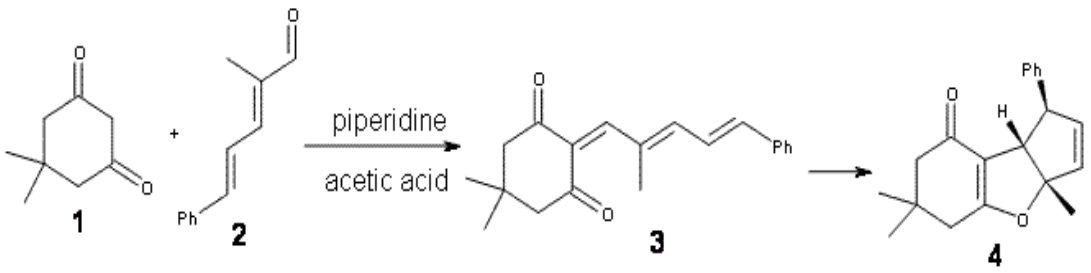
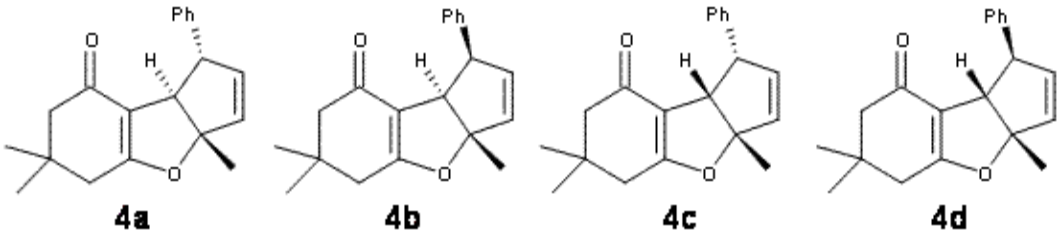
CYCLOPENTA [B] BENZOFURAN – STEREOCHEMISTRY AND MECHANISM OF FORMATION

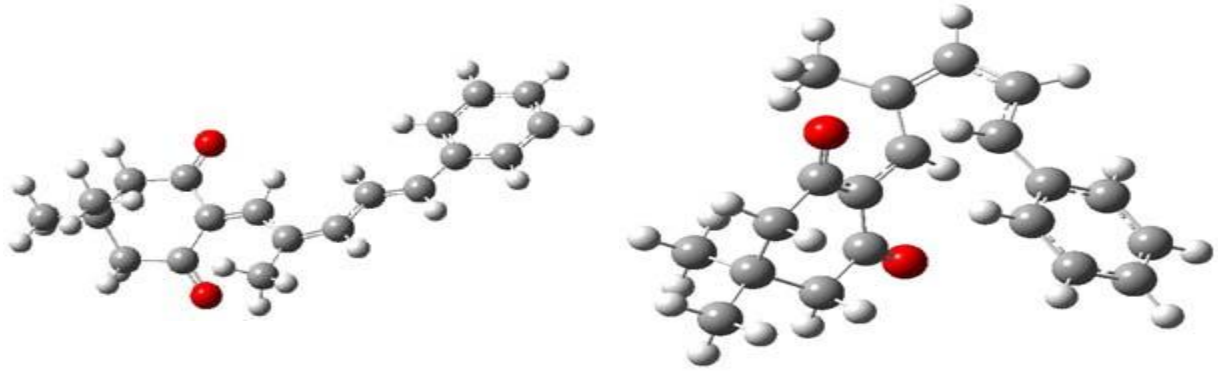
Here is a nice example of an interesting synthesis, mechanistic explication using computation (with a bit of an unanswered question), and corroboration of the stereochemistry of the product using computed NMR shifts. Gil and Mischne[1] reacted dimedone **1** with dienal **2** under Knoevenagel conditions to give, presumably, **3**. But **3** is not recovered, rather the tricycle **4** is observed.



There are four stereoisomers that can be made (**4a-d**). Computed ^{13}C chemical shifts at OPBE/pcS-1 (this is a basis set suggested for computing chemical shifts[2]) for these four isomers were then compared with the experimental values. The smallest root mean squared error is found for **4d**. Better still, is that these authors utilized the DP4 method of Goodman[3], which finds that **4d** agrees with the experiment with 100% probability!



Lastly, the mechanism for the conversion of **3** to **4** was examined at M06/6-31+G**. The optimized geometries of the starting material, transition state, and product are shown in Figure 1. The free energy barrier is a modest 14.5 kcal mol^{-1}. The TS indicates a conrotatory $4\pi e^-$ electrocyclization. The formation of the C-O bond lags far behind in the TS. They could not identify a second transition state. It would probably be worth examining whether the product of this $4\pi e^-$ electrocyclization could be located, perhaps with an IRC starting from the transition state. Does this TS really connect**3** to **4**?



3 **TS**

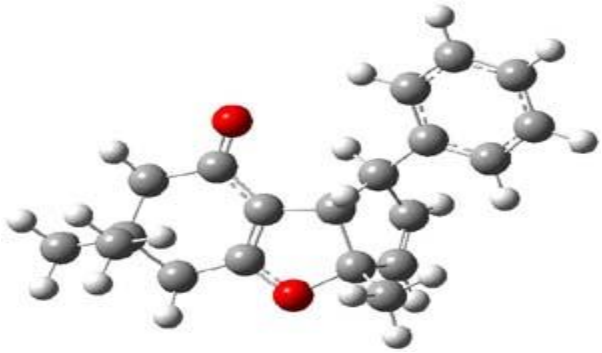


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Figure 1. M06/6-31+G** optimized geometries of **3** and **4** and the transition state connecting them.

Source: http://comporgchem.com/blog/?p=1618