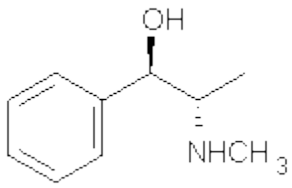
# CONFORMATIONS OF EPHEDRINE

The Alonso group has once again shown the power of the combination of molecular beam Fourier transform microwave spectroscopy (MB-FTMW) coupled with computations. They examined ephedrine, norephedrine and pseudoephedrine and determined the low energy conformations of each.[1] I discuss just the ephedrine case here, but similar results were obtained for the other two compounds.



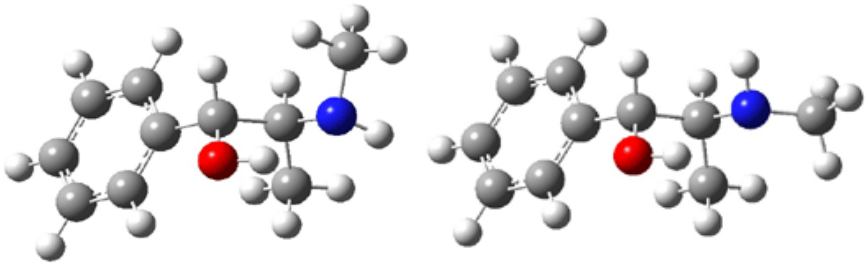

**1**

Ephedrine (**1**) has six potential conformations, differing by the rotation about the C-C bond and the orientation of the methyl group on the nitrogen. They optimized the 6 conformers at MP2/6-311+G(d,p) and corrected the energies for zero-point vibrational energies computed at B3LYP/6-311++G(d,p). The rotational constants and diagonal elements of the $^{14}$N quadrupole coupling tensor were computed and obtained by experiment. The comparison of these values (shown in Table 1) made possible the identification of three low energy conformers, labeled as **AGa**, **AGb**, and **GGa**. The structures are shown in Figure 1.

**Table 1.** Experimental and computed[a] spectroscopic constants for three conformers of ephedrine.[1]

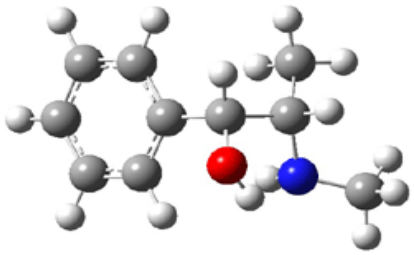
| | AGa | | AGb | | GGa | |
|---|---|---|---|---|---|---|
| | Expt | Comp | Expt | Comp | Expt | Comp |
| A/MHz | 1998.6382 | 2014 | 2115.8768 | 2112 | 1568.2454 | 1566 |
| B/MHz | 529.5495 | 533 | 503.7943 | 507 | 592.4485 | 597 |
| C/MHz | 500.1600 | 505 | 475.1734 | 480 | 572.4160 | 579 |
| $\chi_{aa}$/MHz | 2.535 | 2.63 | 2.559 | 2.70 | 2.448 | 2.51 |
| $\chi_{bb}$/MHz | -2.745 | -3.26 | -4.621 | -4.83 | -3.205 | -2.90 |
| $\chi_{cc}$/MHz | 0.210 | 0.63 | 2.062 | 2.14 | 0.7573 | 0.39 |

[a]Computed at MP2/6-311+G(d,p)



**AGa**
(0.0)

**AGb**
(1.35)



**GGa**

(0.73)

**Figure 1**. MP2/6-311+G(d,p) computed structures and relative energies (kcal $mol^{-1}$) of the three conformers of ephedrine.[1]

The agreement between the experimental and computed spectroscopic values is very good, less than 1.5% for the rotational constants. This excellent agreement makes possible the identification of these three conformers. The experimental population ratio of *N*(**AGa**):*N*(**GGa**):*N*(**AGb**) is 20:4:1, in nice agreement with the computed values. Of structural interest here is the intramolecular O-H···N hydrogen bond in each conformer. The authors also suggest a weak hydrogen bond-like interaction between the N-H and the benzene π-system.

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