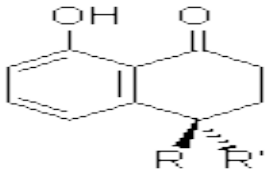
REGIOLONE AND ISOSCLERONE: ENANTIOMERS RESOLVED

It is striking to me that the absolute configuration of relatively simple compounds remains problematic even today. The structure of two naturally-occurring phytotoxic enantiomers **1**, called regiolone and isosclerone, are finally definitively defined using a computational approach.



(*R*)-1: R = OH, R' = H

(*S*)-1: R = H, R' = OH

Isosclerone is the dextrorotatory isomer, while regiolone is the levorotatory isomer. The question though is which one is *R* and which one is *S*? Evidente and co-workers arbitrarily decided to compute the spectral properties of the *S* isomer.[1] They located four low energy conformers at B3LYP/6-31G* and B3LYP/TZVP. (These conformers are not shown here as the authors did not deposit the coordinates. *Reviewers and editors – please insist that this computational data be mandatory for publication!*) The conformer relative energies, listed in Table 1, are dependent on the method, however, the two lowest

energy structures will dominate the population and both will be present to a significant extent, regardless of which energy set is used. The optical rotation $[\alpha]_D$ was computed at B3LYP/6-31G*//B3LYP/TZVP, and these too are listed in Table 1. The Boltzmann-weighted $[\alpha]_D$ is 21.8. Even though the lowest energy conformer contributes a negative rotation, the much larger positive rotation due to the second-lowest energy conformer, along with the two other conformers, will dominate to dictate the OR value. This suggests that the enantiomers are (*S*)(+)-**1** and (*R*)(-)-**1**. Computed ECD spectra confirm this assignment; the computed ECD of the (*S*) isomer is a near mirror image of the experimental ECD of the (-)-**1** compound. Therefore, regiolone is (*R*)(-)-**1** and isosclerone is (*S*)(+)-**1.**

Table 1. Relative free energies (kcal mol^{-1}) and $[\alpha]_D$ of the conformers of (*S*)-**1**.[a]

conformer	Δ*G*, 6-31G*	Δ*G*, TZVP	$[\alpha]_D$[b]
A	0.43	0.0	-17.50
B	0.0	0.32	67.92
C	1.21	1.03	95.72
D	1.84	1.48	17.72

[a]All computations performed with B3LYP. [b]At B3LYP/6-31G*//B3LYP/TZVP.

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