JCE Featured Molecules

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Molecular Models of Peroxides and Albendazoles

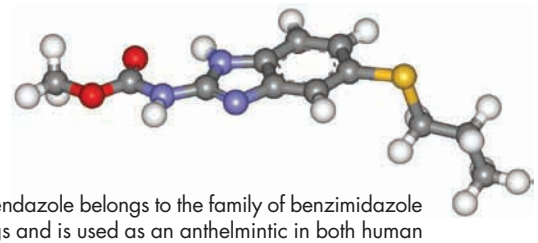
December Featured Molecules

This month our featured molecules come from two sources, the paper by Marina Canepa Kittredge, Kevin W. Kittredge, Melissa S. Sokol, Arlyne M. Sarquis, and Laura M. Sennet on the stability of benzoyl peroxide *(1)* and the paper by Graciela Mahler, Danilo Davyt, Sandra Gordon, Marcelo Incerti, Ivana Núñez, Horacio Pezaroglo, Laura Scarone, Gloria Serra, Mauricio Silvera, and Eduardo Manta on the synthesis of an albendazole metabolite *(2)*.

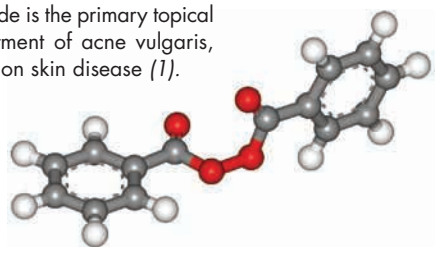
The benzoyl peroxide paper is targeted at non-majors courses, but the molecule and related peroxides contain a number of interesting structural features that could be explored in traditional introductory and in upper-level courses. The first feature is the O–O bond itself. In the three examples included in the collection the bond length computed at the B3LYP/6-311++G(d,p) level ranges from 133.8 pm for dimethyl peroxide to 144.9 pm for hydrogen peroxide. The experimental value for the latter is 147.5 pm and the Computational Chemistry Comparison and Benchmark DataBase (CCCBD) gives a wide range of computed O–O bond lengths in H_2O_2 for more than 20 model chemistries *(3)*.

The X–O–O–X′ dihedral angle in these peroxides also shows interesting properties that have been difficult to reproduce theoretically. In hydrogen peroxide the experimental value is 119.8°, while our calculation gives 121.5°. Again the CCCBD reports a wide variation in this angle, including methods that produce a value of 180°. On the other hand, our model of benzoyl peroxide has a dihedral angle of 86.6°, and dimethyl peroxide shows a dihedral angle of 180°. Weinhold and Landis discuss the angle in hydrogen peroxide in terms of a stabilization of the gauche form through an n–σ* interaction between oxygen lone pairs and empty C–O σ* orbitals *(4)*. Many levels of theory produce 180° dihedral angles for dimethyl peroxide and, as Tonmunphean, Parasuk, and Karpfen have pointed out, minima in the 120° range are not observed until coupled-cluster models are applied *(5)*. The accepted experimental structure with a 119±10° dihedral angle comes from an electron diffraction study *(6)*. These experimental and high-level theoretical calculations lead us to conclude that the model proposed by Weinhold and Landis applies to more complex peroxides as well as to H_2O_2.

In the case of albendazole and the oxygenated albendazoles, it is interesting to monitor the computed charges on the sulfur atoms with oxygenation. The charges on the sulfur atoms, computed at the B3LYP/6-311++G(d,p) level, are 0.066, 0.768 and 1.123 for 0, 1 and 2 oxygens on the sulfur atom respectively. Students could be asked to predict and explain the order of the charges, and to comment on how the charges inform the description of bonding about the sulfur atom. To what extent is the hypervalent species ionic? Does this influence how we should think of d-orbital participation in such molecules?



Albendazole belongs to the family of benzimidazole drugs and is used as an anthelmintic in both human and veterinary medicine *(2)*.



Benzoyl peroxide is the primary topical agent for treatment of acne vulgaris, the most common skin disease *(1)*.

Literature Cited

1. Kittredge, M. C.; Kittredge, K. W.; Sokol, M. S.; Sarquis, A. M.; Sennet, L. M. *J. Chem. Educ.* **2008,** *85*, 1655–1657.
2. Mahler, G.; Davyt, D.; Gordon, S.; Incerti, M.; Núñez, I.; Pezaroglo, H.; Scarone, L.; Serra, G.; Silvera, M.; Manta, E. *J. Chem. Educ.* **2008,** *85*, 1652–1654.
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4. Weinhold, F. ; Landis, C. R. *Valency and Bonding: A Natural Bond Orbital Donor–Acceptor Perspective;* Cambridge University Press: Cambridge, UK, 2003; pp 240-241
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6. Haas, B.; Oberhammer, H. *J. Am. Chem. Soc.* **1984,** *106,* 6146 .

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The molecules added to the collection this month are

from ref *1*: benzoyl peroxide; dimethyl peroxide; hydrogen peroxide

from ref *2*: albendazole; albendazole sulfoxide; albendazole sulfone