Cycloheptatrienyl Oxyallyl. An Observable Oxyallyl?

B. Andes Hess, Jr.

Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37205

Oxyallyl (**1**) is thought to be a reactive intermediate in a wide range of organic[1] and biological[2] reactions that involve the rearrangement of allene oxides and cyclopropanones. For example, oxyallyl has been suggested as an intermediate in the rearrangements of allene oxide (**2**) to cyclopropanone (**3**)[3] and in the formation of
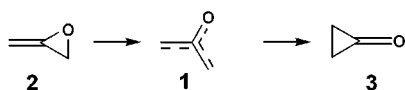
cyclopentenones formed from vinyl allene oxides (**4**) in the biosynthesis of prostaglandins.[4] Two important questions about
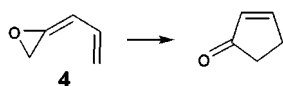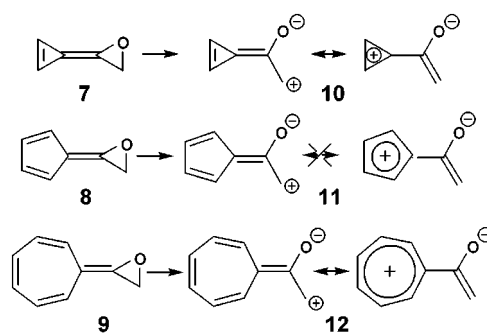

oxyallyl are whether it should be considered to have diradical (**5**) or zwitterionic (**6**) character and whether its incorporation into a
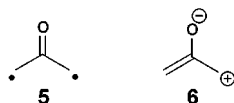

larger system might affect its characteristics. Both questions have implications with regard to the stability of oxyallyls, particularly in biological reactions where the oxyallyl is normally formed in solution and is also part of a larger system.[2] Borden et al.[5] have examined the effect of solvent on the ring opening of cyclopropanones to oxyallyl and concluded that oxyallyl is best described as a diradical rather than a zwitterion. With the exception of simple alkyl substitution,[5,6] the effect of substitution on oxyallyls that might favor its potential zwitterionic form has not been studied.

Examination of the calculated relative energies of appropriately substituted allene oxides, oxyallyls, and cyclopropanones would allow one to probe the electronic structure of oxyallyl. Recently Schepp et al.[7] have reported the synthesis and reactions of fluorenylideneallene oxide and were able not only to observe allene oxide in solution but also to measure the kinetics of its conversion to cyclopropanone. This suggested that one might take advantage of the cyclic delocalization present in the odd-membered conjugated cyclic carbocations to stabilize oxyallyl. Fusion of allene oxide to unsaturated three-, five-, and seven-membered rings would give structures **7**−**9** capable of ring opening to the substituted oxyallyls **10**−**12**.

If the oxyallyl is stabilized by polarization to the zwitterions **10** and **12**, this stabilization should be reflected in the energy of the oxyallyl, relative to the corresponding allene oxides (**7** and **9**) and cyclopropanones (**13** and **15**), due to the aromatic stabilization of the cyclopropenium and tropyllium ions. However, for **8** polariza-

tion should result in destabilization of oxyallyl **11** due to the antiaromatic nature of the cyclopentadienyl carbocation.
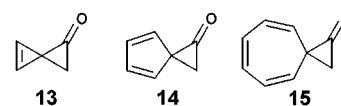
We have previously shown that the DFT method is reliable for the description of oxyallyls, since DFT results were essentially identical to the CASPT2/CASSCF results for the parent allene oxide system (**1**−**3**), despite the wave function of oxyallyl (**1**) having significant spin contamination ($S^2 = 0.805$).[3] Therefore, DFT calculations[8−10] were performed for the rearrangement pathways of the conversion of the allene oxides **7**−**9** to their respective cyclopropanones **13**−**15**. Transition structures linking the oxyallyls to the corresponding allene oxides and cyclopropanones were also located. Figure 1 depicts the DFT results for the three systems studied. For comparison, the previously published results[3] for the parent allene oxide system are also shown in Figure 1.[11]

It is immediately apparent from Figure 1 that fusion of the cyclopropenyl (**10**) and tropyllium (**12**) rings to oxyallyl has the dramatic effect of significantly stabilizing these intermediate oxyallyls. In both cases the oxyallyl is much lower in energy than its allene oxide (10.9 kcal/mol for **10** and 10.7 kcal/mol for **12**). This is in direct contrast to the parent system, where oxyallyl (**1**) is *higher* in energy than allene oxide (**2**) by 16.2 kcal/mol. Furthermore, in the case of the tropyllium oxyallyl, **12** is calculated to be of *lower* energy than both allene oxide **9** and cyclopropanone **15** by −10.7 and −5.3 kcal/mol, respectively. Hence, oxyallyl **12**, in the absence of nucleophiles, should be observable, since there is no driving force for it to rearrange to cyclopropanone **15**. Preparation of oxyallyl **12** might allow its spectroscopic identification and characterization.

The bond distances (see Figure 2) in oxyallyl **12** support significant delocalization of a positive charge into the seven-membered ring. They show less alternation than one would have expected for alternating double and single bonds in a cycloheptatriene and significantly less than in either **9** or **15**. While the long
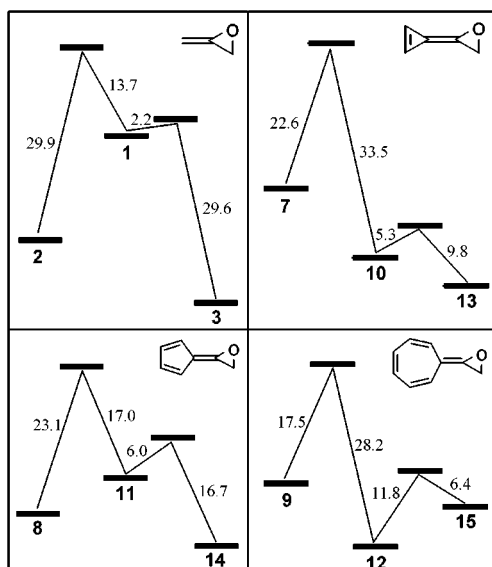
Figure 1. Relative energies with zero-point energy corrections (in kcal/mol) of the stationary points on the rearrangement pathways of allene oxide,[3] **7**, **8**, and **9**.
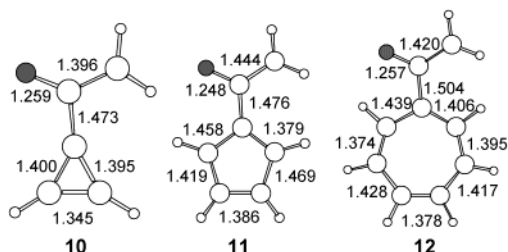

Figure 2. Bond distances (in Å) calculated for the three oxyallyls.

exo C−C bond (1.504 Å) in **12** might also be used as evidence of significant tropyllium ion character in **12**, it might also be ascribed to the steric repulsion between the oxygen atom and the nearby hydrogen of the seven-membered ring. Further support for the zwitterionic character of oxyallyls **10** and **12** is provided by their high calculated dipole moments (8.10 and 6.49 D, respectively) relative to those of the parent oxyallyl **1** (3.98 D).

From Figure 1 it is seen that even the fusion of the cyclopentadienyl ring to allene oxide (**8**) stabilizes oxyallyl **11**. However, this stabilization does not occur to the point that **11** is lower in energy than the allene oxide **8**. At first sight this is surprising, since presumably the anti-aromatic cyclopentadienyl ring should have the opposite effect, of destabilizing the oxyallyl intermediate relative to the parent system. It is possible that the stabilizing effect of the five-membered ring in this system is due to stabilization of the diradical via resonance:

In fact this might have been expected, since the bond dissociation energy of an allylic hydrogen in cyclopentadiene is 82 kcal/mol, which indicates that it is a reasonably stable free radical.[12] Examination of the bond distances in the five-membered ring of **11** (see Figure 2) also indicates that there is significant delocal-

ization of the radical into this ring. Its low calculated dipole moment (3.70 D) is also suggestive of diradical rather than zwitterionic character.

It is thus apparent that oxyallyls may potentially be stabilized by groups that stabilize free radicals as well as those that stabilize positive charges, though the latter appears to be the more effective. Hence, oxyallyl appears to be a versatile intermediate capable of "adapting itself to its environment". This may very well explain why, even though vinyl allene oxide (**4**) is predicted[4] (gas-phase calculations) to proceed through a concerted reaction to cyclopentenone, results of biological experiments are best explained by the zwitterionic pathway.[2] A combination of solvent effects and stabilization of the oxyallyl by the vinyl group are likely involved in favoring the zwitterionic pathway over the concerted pathway.

Finally, the DFT results suggest that the cyloheptatrienyl oxyallyl **12**, being the lowest minimum of those considered on its potential surface, might be observable in an appropriate environment.

Supporting Information Available: Cartesian coordinates, total and zero-point energies, and frequencies for structures **7**−**15** and transition structures linking these (see Figure 1) (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Kim, S. J.; Cha, J. K. *Tetrahedron Lett.* **1988**, *29*, 5613. (b) Malacria, M. Rournestant, M. L. *Tetrahedron Lett.* **1977**, *33,* 2813. (c) Bertrand, M.; Dulcere, J. P.; Gil, G.; Rournestatnt, M. L. *Tetrahedron Lett.* **1979**, 1845. (d) Doutheau, A.; Gore, J.; Diab, J. *Tetrahedron* **1985**, *41*, 329
(2) (a) Vick, B. A.; Zimmerman, D. C. *Biochem. Biophys. Res. Commun.* **1983**, *111*, 470. (b) Corey, E. J.; Matsuda, S. P. T.; Nagata, R.; Cleaver, M. B. *Tetrahedron Lett.* **1988**, *29*, 2555. (c) Hamberg, M.; Miersch, O.; Sembdner, G. *Lipids* **1988**, *23*, 521. (d) Brash, A. R.: Baertschi, S. W.; Ingram, C. D.; Harris, T. M. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 3382. (e) Song, W.-C.; Baertschi, S. W.; Boeglin, W. E.; Harris, T. M.; Brash, A. R. *J. Biol. Chem.* **1993**, *268*, 6293. (f) Koljak, R.; Boutaud, O.; Shieh, B.-H.; Samel, N.; Brash, A. R. *Science* **1997**, *277*, 1994.
(3) Hess, B. A., Jr.; Eckart, U.; Fabian, J. *J. Am. Chem. Soc.* **1998**, *120*, 12310.
(4) Hess, B. A., Jr.; Smentek, L.; Brash, A. R.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 5603.
(5) Lim, D.; Hrovat, D. A.; Borden, W. T.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1994**, *116*, 3494.
(6) Castillo, R.; Andrés, J.; Moliner, V.; Safont, V. S.; Oliva, M. *Int. J. Quantum Chem.* **1997**, *65*, 729.
(7) Clay, M. D.; Durber, J.; Schepp, N. P. *Org. Lett.* **2001**, *3*, 3833.
(8) The calculations were carried out with Gaussian 98W (Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; and Pople, J. A. *Gaussian 98W*; Gaussian, Inc.: Pittsburgh, PA, 1998) with the density functional method using Becke's three-parameter hybrid method (ref 7a) with the Lee−Yang−Parr correlation function (ref 7b) and the 6-31+G* basis set (ref 8). Zero-point energies were done with unscaled B3LYP/6-31+G* frequencies obtained analytically with G98W. Those structures which had an rhf wave function unstable toward UHF were computed with unrestricted DFT (B3LYP).
(9) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988***, 37*, 785
(10) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.
(11) Oxyallyl **10** was, surprisingly, found to have no spin contamination of its wave function ($S^2 = 0$). However, oxyallyls **11** and **12** have significant spin contamination ($S^2 = 1.03$ and 0.53, respectively), similar to that found for the parent oxyallyl **1**.
(12) (a) Furuyama, S.; Dolden, D. M.; Benson, S. W. *Int. J. Chem. Kinet.* **1971**, *3*, 237. (b) DeFrees, D. J.; McIver, R. T., Jr.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 3334.

JA0172823