STEREOCHEMICAL DEPENDENCE OF ISOTOPE EFFECTS IN THE ENE REACTION OF N-PHENYL-1,2,4-TRIAZOLINE-3,5-DIONE WITH ISOMERS OF BUTENE-d₃

Michael Orfanopoulos¹, Christopher S. Foote^{2*}, and Ioulia Smonou¹ Department of Chemistry and Biochemistry University of California, Los Angeles California 90024

Abstract. The magnitude of the primary isotope effect of the title reaction depends on the relative stereochemistry of the competing groups, being large when the groups are *cis* and small when they are on opposite sides of the double bond. An intermediate such as a diaziridinium imide is required to rationalize the results.

Although several groups have studied the ene reaction of N-Phenyl-1,2,4-triazolinedione (PTAD)³ and shown its synthetic utility,⁴ only one detailed mechanistic study has been reported.⁵ The key question regarding the ene reaction of PTAD with olefins is whether the reaction proceeds via an intermediate. The elegant study by Greene⁵ using Stephenson's isotope effect test⁶ provides evidence for an intermediate such as 1 in the reaction of (Z)- and (E)-2,3-bis-(trideuteriomethyl)-2-butene. As in the reaction with singlet oxygen,⁶ a significant isotope effect was found with *cis*-related methyl and deuteromethyl groups, but only a small isotope effect with *trans*- groups. The intermediate, if it has the geometry shown below, should be able to discriminate between hydrogen and deuterium only when they are on the same side of the double bond. Hydrogen and deuterium would not compete in this intermediate if they are on opposite sides of the double bond since the intermediate can reach only the atoms on one side.



We now report a study of the reaction of PTAD with *cis*- and *trans*-butene-d₃ (2, 3) and 2-methyl-1-propened₃ (4).⁷ These olefins react quantitatively with PTAD in dichloromethane at -5°. The isotope effects were measured by ¹H NMR integration of the product mixtures (Bruker WP-200 and AM 500 spectrometers) with an accuracy of $\pm 2\%$. *Trans*-butene-d₃ (3) and 2-methyl-1-propene-d₃ (4) show a small but significant isotope effect $(k_H/k_D = 1.29 \text{ and } 1.25$, respectively). However, *cis*-butene-d₃ (2) gives a large effect $(k_H/k_D = 5.36)$. An identical isotope effect was measured at -40°.



The isotope effect for the *cis*- compound is much larger than that with (E)-2,3-bis-(trideuteriomethyl)-2butene (3.8),⁵ and is one of the largest ever observed for an ene reaction. The effect in the *trans*- and *gem*compounds, while much smaller, is significant, and is also much larger than the corresponding effect observed with (Z)-2,3-bis-(trideuteriomethyl)-2-butene (1.1).⁵

These results provide strong evidence for an intermediate with structural requirements similar to the aziridinium imide proposed by Greene⁵ or the perepoxide intermediate suggested by Stephenson⁶ for the singlet oxygen reaction. An analogous aziridinium imide adduct of adamantylideneadamantane is stable at low temperatures and has recently been characterized by Nelsen.⁹ Intermediates in ene or ene-like reactions have been clearly shown in a few cases by observation of intramolecular (product) isotope effects that greatly exceed intermolecular (kinetic) effects;¹⁰ in other cases, such intermediates are probably absent.^{10,11}

In a concerted reaction mechanism, one would expect similar isotope effects for 2, 3, and 4. A dipolar or diradical intermediate would give a β secondary isotope effect which is difficult to predict, since it would be a composite of effects on the C-O bonding and ion or radical positions. If an aziridinium imide or a loose complex with similar configurational structure is formed *irreversibly*, then an isotope effect should be found when H and D are in the *cis*- configuration (i. e., in 2) and thus both accessible to the intermediate and able to compete, but should be absent with *trans*- (3) or geminal (4) olefins, where the isotopes are on opposite sides of the double bond. The observed results are consistent with such an intermediate in that a large isotope is indeed observed with the *cis* olefin.

However, the substantial *trans* isotope effect observed for *trans*-2 (1.29) and isobutylene (4) (1.25) requires a further hypothesis. This large an effect could be the result either of partial reversion of the intermediate complex to starting materials or isomerization of an intermediate or loose complex by opening to a zwitterion or diradical or some other mechanism. It is hard to visualize a mechanism leading to this large an isotope effect for the competition of *trans*- hydrogens which does not allow for interconversion of intermediates. If one or both of these processes operate to a significant extent, an isotope effect would be expected even for methyl groups on opposite sides of the double bond.



It is also interesting that although the *trans*- isotope effects for the tetramethylethylenes with $PTAD^5$ are very small, they are not zero, and an interconversion process is required for these olefins as well. The magnitude of the isotope effect should be dependent on the relative contributions of the direct reaction and the interconversion. If the intermediate reverts to starting material, this process should be more efficient with the butenes than with the more electron-rich olefins, where the bonding should be stronger. A larger *trans* isotope effect would therefore be expected from the butenes than the tetramethylethylenes, as observed.

The fact that the isotope effect at -40° is the same as at -5° within experimental error implies a negligible activation enthalpy for the isotope effect. According to Kwart, this combination of a large isotope effect and small temperature dependence is characteristic of a nonlinear transition state, consistent with the model suggested above.¹² However, this view has been challenged by McLennan and Gill¹³ on the basis of theoretical calculations.

Very similar results are found with these olefins and singlet oxygen, and will be reported elsewhere.⁸

REFERENCES

- 1. Present address: Department of Chemistry, P. O. Box 1470, University of Crete, 71110 Iraklion, Crete, Greece.
- 2. Supported by NSF Grant No. CHE-83-11804. C. S. F. thanks the Alexander von Humboltstiftung for a Senior Scientist Award, and the Hahn-Meitner Institute, Berlin, for hospitality.
- 3. (a) W.H. Pirkle, J.C. Strickler, J. Chem. Soc., Chem Comm., 760 (1967).
 - (b) S. Ohashi, K. Leong, K. Matyjaszewski, G.B. Bulter J. Org. Chem. 45, 3467 (1980).
 - (c) A. Gopalan, R. Moerck, P. Magnus J. Chem. Soc., Chem. Comm. 548 (1979).
 - (d) T. R. Hoye, K. J. Bottorff, A.J. Caruso, J.F. Dellaria J. Org. Chem. 45, 4287 (1980).
- 4. (a) R. C. Cookson, S. S. H. Gilani, I.D.R. Stevens J. Chem. Soc. 1905 (1967).
 - (b) D. H. R. Barton, T. Shiori, D.A. Widdowson *ibid.*, 1971, (1968).
 - (c) E. J. Corey, B. B. Snider Tetrahedron Letters, 3091 (1973).
 - (d) B. B. Snider, R. J. Corcoran, R. Breslow J. Am. Chem. Soc., 97, 6580 (1975).
 - (e) S. C. Eyley, D.H. Williams J. Chem. Soc., Perkin I, 731 (1976).
- 5. C. C. Cheng, C.A. Seymour, M. A. Petti, F. D. Greene, J.F. Blount J. Org. Chem. Soc. 49, 2910 (1984).
- 6. S. B. Grdina, M. Orfanopoulos, L. M. Stephenson J. Am. Chem. Soc. 101, 3111 (1979).
- 7. Preparation and characterization of these olefins will be described in detail in another place.⁸
- 8. M. Orfanopoulos and C. S. Foote, in preparation.
- 9. S. F. Nelsen and D. L. Kapp, J. Am. Chem. Soc. 107, 5548 (1985).
- W. Starflinger, G. Kresze and K. Huss, J. Org. Chem. 51, 37 (1986) and references therein; P. Beak and K. R. Berger, J. Am. Chem. Soc. 102, 3848, (1980).
- 11. L. M. Stephenson and M. Orfanopoulos, J. Org. Chem. 46, 2200 (1981)
- 12. H. Kwart Acc. Chem. Res. 15, 401 (1982) and references therein.
- 13. D. J. McLennan and P. M. W. Gill J. Am. Chem. Soc. 107, 2971, (1985).
- (Received in USA 19 August 1986)