

## 2008 GRADUATE RESEARCH DESCRIPTION

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### MATRIX ESR STUDIES OF RADICALS AND RADICAL IONS:

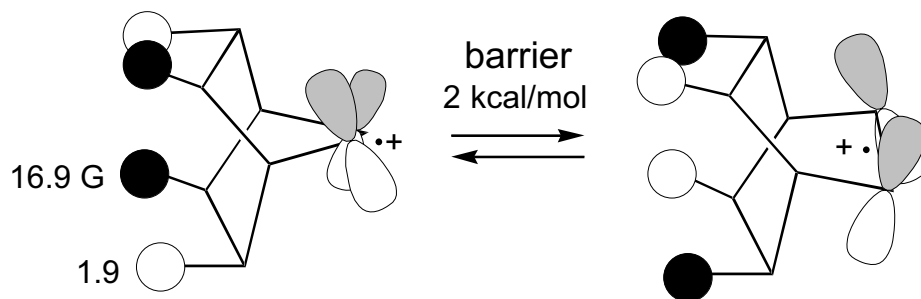
1. THE PSEUDO JAHN-TELLER EFFECT AND THE ROLE OF VIBRONIC COUPLING
2. APPLICATIONS TO AMINE OXIDATION AND DRUG ACTION IN THE BRAIN

Our interest is in the study of reactive chemical intermediates, especially free radicals and radical ions produced by the exposure of molecules to light and ionizing radiation. We use ESR (Electron Spin Resonance) spectroscopy to detect these radical intermediates because this spectroscopic method responds specifically to paramagnetic molecules with unpaired electrons, and therefore discriminates against the much larger concentration of diamagnetic molecules which is usually present in the sample. ESR spectroscopy can do much more, however, than just detect radicals. Usually, the ESR spectrum of a radical consists of a well-defined pattern resulting from nuclear hyperfine interaction with the unpaired electron, and the analysis of this hyperfine pattern provides direct information about the molecular and electronic structure of the radical. In practice, this ability to make the structural assignment from first principles is an important feature of the ESR method since it allows the discovery of new radicals, and our work on irradiated solids has led to the characterization of several novel paramagnetic species.

Over the last two decades, we have employed matrix ESR spectroscopy to reveal interesting and unusual rearrangements of organic radical cations (details are given in the publication list below). Both thermal and photochemical reactions have been studied by this method. As an example of a thermal rearrangement, the radiolytic oxidation of 1,5-hexadiene leads to the formation of the cyclohexane-1,4-diyl radical cation which then undergoes intramolecular hydrogen transfer to give the cyclohexene radical cation. Photoinduced changes can be equally remarkable. Thus, the cyclooctatetraene radical cation undergoes a symmetry-allowed 1,5 closure on photoexcitation to produce the resonance-stabilized bicyclo[3.3.0]octa-2,6-diene-4,8-diyl radical cation, the reaction being photochromic with a striking change in both the optical and ESR spectra. These examples illustrate how much can be learned by combining the technique of radiolytic oxidation in matrices with structure determination by ESR spectroscopy.

This approach to the elucidation of molecular rearrangements, which combines both structural and reactivity studies on intermediate species, can, in principle, be applied equally well to the study of reduction products (for examples, see Journal Articles 1, 3, and 4 listed below on the radical anions of perfluorocompounds). Such radical anions can clearly play an important role in the chemistry of electron-transfer reactions. In particular, the role of vibronic coupling between the ground and excited states of radical cations in bringing about geometric distortions (pseudo-Jahn-Teller effect) has been elucidated. For example, ionized bicyclo[2.2.2]oct-2-ene is an example of a twisted olefinic radical cation where the two enantiomeric forms undergo rapid interconversion (see diagram below) as a result of vibronic coupling via the torsional mode at the one-electron  $\pi$  bond (*Chem. Eur. J.*, 8, 1074-1081 (2002)).

The pseudo-Jahn-Teller effect is evidenced by the experimental detection of a double minimum along this  $a_2$  vibrational mode at the olefin bond. In each of the twisted enantiomers, the hyperfine coupling is largely restricted to the two diagonal exo-hydrogens (filled circles in figure shown below\*). Thus, as the twisting rate increases with temperature, the ESR spectrum changes from a 16.9 G triplet ( $2H_{\text{exo}}$ ) to a quintet ( $4H_{\text{exo}}$ ) with a 9.4 G average hfc. Theoretical calculations confirm the role of vibronic coupling. Moreover, these vibronic effects can be important in defining both the reaction coordinate and the bond-breaking steps for the unimolecular rearrangements of radical cations formed from strained molecules (Robert S. Pappas, *Ph.D. Thesis*, University of Tennessee, August 1995).



\*S. F. Nelsen, L. A. Reinhardt, H. Q. Tran, T. Clark, G.-F. Chen, R. S. Pappas, and F. Williams, Ionized Bicyclo[2.2.2]oct-2-ene: A Twisted Olefinic Radical Cation Showing Vibronic Coupling, *Chem. Eur. J.*, 8, 1074-1081 (2002).

Recently, we have also become interested in the mechanism whereby substituted cyclopropylamines, allylamines, and propargylamines function as efficient inactivators of oxidation enzymes such as monoamine oxidase and cytochrome P-450. Essentially, it has been proposed that the key step leading to enzyme inactivation by these substrates is the conversion of the initially-formed aminium radical cation (a nitrogen-centered radical) of the substrate to a carbon-centered radical which subsequently attacks the active site of the enzyme. This kind of rearrangement proceeds through distonic radical cation formation in which the spin (on carbon) and positive charge (on nitrogen) become separated. We have in fact observed this radical cation rearrangement for the parent cyclopropylamine and allylamine molecules by ESR studies. We have collaborated on this problem with a Surface Modification Group at the University of Leipzig in Germany; and kinetic studies reveal that the transformation of the allylamine radical cation occurs with a half-life of *ca.* 40 min at 77 K (Journal Article 2 listed below).

Remarkably, many of the drugs (tranylcypromine, selegiline, vigabatrin) that are used in the treatment of depression, Parkinson's disease, and epilepsy (*C&EN*, August 23, 1999, p. 8) through the regulation of amine oxidation in the brain contain a cyclopropyl or unsaturated group adjacent to the amine function. Accordingly, these drug molecules are ideally structured to undergo the same type of radical cation rearrangement. We therefore plan to study model compounds (*e.g.*, *N,N*-dimethylpropargylamine) related to these drugs with the aim of identifying the distonic radical cation intermediate responsible for enzyme (monoamine oxidases A and B) inactivation.

#### **Publications from 2000-2008**

1. M. Shiotani, A. Lund, S. Lunell, and F. Williams, "Structures of the Hexafluorocyclopropane, Octafluorocyclobutane, and Decafluorocyclopentane Radical Anions Probed by Experimental and Computational Studies of Anisotropic ESR Spectra," *J. Phys. Chem. A* **2007**, *111*, 321-338. Published on Web 12/22/2006.
2. W. Knolle, I. Janovský, S. Naumov, and F. Williams, "EPR Studies of Amine Radical Cations, Part 2: Thermal and Photoinduced Rearrangements of Propargyl and Allylamine Radical Cations in Low-Temperature Matrices," *J. Phys. Chem. A* **2006**, *110*, 13816-13826. Published on Web 12/07/2006.
3. M. Shiotani, P. Persson, S. Lunell, A. Lund, and F. Williams, "Structures of Tetrafluorocyclopropene, Hexafluorocyclobutene, Octafluorocyclopentene, and Related Perfluoroalkene Radical Anions Revealed by Electron Spin Resonance Spectroscopic and Computational Studies," *J. Phys. Chem. A* **2006**, *110*, 6307-6323. Published on Web 04/27/2006.
4. (with A. M. ElSohly, G. S. Tschumper, R. A. Crocombe, and J. T. Wang) "Computational and ESR Studies of Electron Attachment to Decafluorocyclopentane, Octafluorocyclobutane, and Hexafluorocyclopropane: Electron Affinities of the Molecules and the Structures of their Stable Negative Ions as Determined from the <sup>13</sup>C and <sup>19</sup>F Hyperfine Coupling Constants," *J. Am. Chem. Soc.* **2005**, *127*, 10573-10583. Published on Web 07/08/2005.
5. "Re-evaluation of the Propagation Rate Constant in the Radiation-Induced Cationic Polymerization of Isobutylene in Solution," *Macromolecules* **2005**, *38*, 206-209. Published on Web 12/08/2004.
6. (with I. Janovsky, W. Knolle, and S. Naumov) "EPR Studies of Amine Radical Cations, Part 1: Thermal and Photoinduced Rearrangements of n-Alkylamine Radical Cations to their Distonic Forms in Low-Temperature Freon Matrices," *Chem. Eur. J.*, *10*, 5524-5534 (2004). Published on Web 09/29/2004.
7. "Nanotech numbers," *Chem. & Eng. News*, *82*, Issue No. 9, p 5 (March 1, 2004).
8. "Vibronic Coupling in Ionized Organic Molecules: Structural Distortions and Chemical Reactions," *Radiat. Phys. Chem.*, *67*, 211-218 (2003).
9. (with I. A. Shkrob and K. Takeda) , "Electron Localization in Solid Acetonitrile," *J. Phys. Chem. A*, *106*, 9132-9144 (2002).
10. (with S. F. Nelsen, L. A. Reinhardt, H. Q. Tran, T. Clark, G.-F. Chen, and R. S. Pappas) "Ionized Bicyclo[2.2.2]oct-2-ene: A Twisted Olefinic Radical Cation Showing Vibronic Coupling," *Chem. Eur. J.*, **8**, 1074 (2002).
11. (with A. Marcinek, J. Rogowski, J. Gebicki, and G.-F. Chen) "Isomerization of Cubane Radical Cation," *J. Phys. Chem. A.*, *104*, 5265 (2000).
12. (with T. Bally, S. Bernhard, S. Matzinger, L. Truttman, Z. Zhu, J.-L. Roulin, A. Marcinek, J. Gebicki, G.-F. Chen, H. D. Roth, and T. Herbertz) "The Radical Cation of *anti*-Tricyclooctadiene and Its Rearrangement Products," *Chem. Eur. J.*, *6*, 849 (2000).
13. (with T. Bally, S. Bernhard, S. Matzinger, J.-L. Roulin, G. N. Sastry, L. Truttman, Z. Zhu, A. Marcinek, J. Adamus, R. Kaminski, J. Gebicki, G.-F. Chen, and M. Fülcher) "The Radical Cation of *syn*-Tricyclooctadiene and Its Rearrangement Products," *Chem. Eur. J.*, *6*, 858 (2000).

#### **Recent Ph.D. Theses**

1. Bin Jiang, *Part 1. A Matrix ESR Study of Radical Cations of Acyclic Ene-diyne Compounds*, December 1999.
2. Robert S. Pappas, *Vibronic Coupling Interactions in Organic Radical Cations: A Matrix ESR Study*, August 1995.
3. Sheng Dai, *Electron Spin Resonance Spectroscopic Studies of Radical Cation Reactions*, December 1990.