precursors **1** and **6** reported here prove the lack of a common intermediate in these two reaction manifolds. This is most consistent with the lack of rhodium migration to an alkyne carbon in the alkyne insertion reactions of **1**.

**Acknowledgment**. This investigation was supported by Grant GM-38854 awarded by the DHHS. We also thank Rohm & Haas and Glaxo for fellowship support.[1]

**Supplementary Material Available:** Summary of the syntheses of **6a/c** and **7b**, representative experimental procedures for $Rh_2(OAc)_4$-catalyzed reactions, characterization of all new compounds (**1a**, **6a**, **6c**, **7b**, (*E*)- and (*Z*)-**8a**, **9a**, **10a**, and **11c**), and descriptions of relevant control experiments (5 pages). Ordering information is given on any current masthead page.

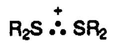
# Radical Cation–Arene π-Molecular Complexes. Thioether Radical Cations in Aromatic Solvents[†]

D. W. Werst

*Chemistry Division, Argonne National Laboratory*
*Argonne, Illinois 60439*

*Received February 4, 1991*

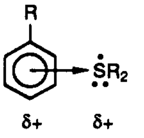
Thioether radical cations are known to be stabilized by coordination of the unpaired p electron of the oxidized sulfur atom to free p-electron pairs. Complex radical cations coupled by a three-electron $(\sigma)^2(\sigma^*)^1$ S–S bond are usually the only radical-cation species observed in liquid-phase studies of the oxidation of alkyl sulfides.[1-3] The dimer radical cations are more stable

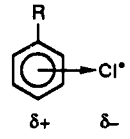


$$R_2\overset{+}{S} \therefore SR_2$$

than the monomer radical cations, which in aqueous solutions undergo fast deprotonation reactions.[1,4] Monomer thioether radical cations have previously only been observed in rigid matrices by EPR.[5-10]

Here we show that thioether radical cations are stabilized by electron donation from aromatic solvents, and we have observed their EPR spectra in the liquid phase by time-resolved fluorescence-detected magnetic resonance (FDMR) spectroscopy. The thioether radical cation EPR parameters are strongly solvent dependent and are a sensitive probe of the solvent to radical cation (electron) charge transfer. This is the first example of saturated radical cations that form compiexes with π-electron donors. Perhaps the closest analogue is the complexation of chlorine atoms with benzene, which was noted for the first time in the classical studies of the photochlorination of alkanes.[11-15]





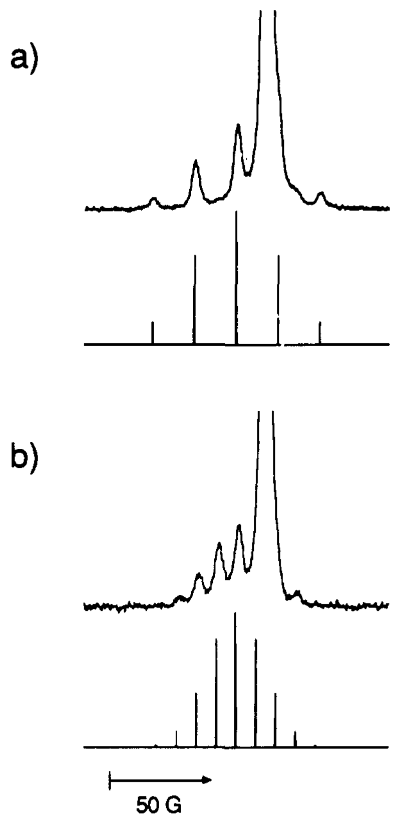


**Figure 1**. FDMR spectra observed in toluene/thietane mixtures: (a) 3 × $10^{-3}$ M thietane, $T = 205$ K; (b) $10^{-2}$ M thietane, $T = 290$ K. The anthracene-$d_{10}$ scintillator concentration was $10^{-3}$ M. The microwave pulse was applied from $t = 0$ to $t = 150$ ns. The multiplet spectrum ($a = 20.8$ G, 4 H) in part a is assigned to thietane radical cations which are formed via electron transfer to toluene radical cations formed by electron radiolysis. The multiplet spectrum ($a = 9.8$ G, 8 H) in part b is assigned to thietane dimer radical cations formed by reaction of thietane radical cations with neutral thietane molecules.

**Table I**. EPR Parameters for Thioether Radical Cations

| radical cation | matrix or solvent | *T*, K | *a*, G | $g^{a,b}$ | ref |
|---|---|---|---|---|---|
| $(CH_3)_2S^{\cdot+}$ | toluene | 205 | 13.1 (6 H) | 2.010 | *e* |
| | $CF_3CCl_3$ | 81 | 20.4 (6 H) | 2.013 | 7 |
| | $CF_2ClCFCl_2$ | 81 | 20.4 (6 H) | 2.017 | 8 |
| | $CFCl_3$ | 130 | 21 (6 H) | 2.014 | 9 |
| $(CH_2)_3S^{\cdot+}$ | toluene | 205 | 20.8 (4 H) | 2.013 | *e* |
| | $CFCl_3$ | 90 | 31.1 (4 H) | 2.019 | 7 |
| | $CFCl_3$ | ca. 120 | 31 (4 H) | 2.016 | 9 |
| $(CH_2)_4S^{\cdot+}$ | toluene | 205 | 21.2 (4 H) | 2.011 | *e* |
| | $CF_2ClCFCl_2$ | 81 | 28.4 (4 H)[c] | | 8 |
| | $CFCl_3$ | 77 | 30 (4 H)[d] | 2.014 | 9 |

[a] The *g* factors in toluene are relative to that of the anthracene radical anion ($g = 2.0027$) (Segal, B. G.; Kaplan, M.; Fraenkel, G. K. *J. Chem. Phys.* **1965**, *12*, 4191). [b] The *g* factors in Freons are averages of $g_x$, $g_y$, and $g_z$. [c] Average of 37.8 (2 H) and 18.9 (2 H). [d] Average of 40 (2 H) and 20 (2 H). [e] This work.

Figure 1 shows FDMR spectra obtained in toluene solvent containing thietane (trimethylene sulfide). In the pulse radiolysis/FDMR method, fluorescence from the recombination reaction between spin-correlated pairs of radical cations and aromatic scintillator radical anions, eq 1, is modulated at resonant magnetic field by a microwave pulse.[16] The plot of the magnetic field

---

[†] Work performed under the auspices of the Office of Basic Sciences, Division of Chemical Science, US-DOE, under Contract No. W-31-109-ENG-38.

(1) Gilbert, B. C.; Hodgeman, D. K. C.; Norman, R. O. C. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1748.

(2) Gara, W. B.; Giles, J. R. M.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1444.

(3) Asmus, K.-D. *Acc. Chem. Res.* **1979**, *12*, 436.

(4) Boniface, M.; Mockel, H.; Bahnemann, D.; Asmus, K.-D. *J. Chem. Soc., Perkin Trans. 2* **1975**, 675.

(5) Wang, J. T.; Williams, F. *J. Chem. Soc., Chem. Commun.* **1981**, 1184.

(6) Wang, J. T.; Williams, F. *J. Chem. Soc., Chem. Commun.* **1983**, 980.

(7) Qin, X.-Z.; Meng, Q.-C.; Williams, F. *J. Am. Chem. Soc.* **1987**, *109*, 6778.

(8) Williams, F.; Qin, X.-Z. *Radiat. Phys. Chem.* **1988**, *32*, 299.

(9) Rao, D. N. R.; Symons, M. C. R.; Wren, B. W. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1681.

(10) Bonazzola, L.; Michaut, J. P.; Roncin, J. *J. Chem. Phys.* **1985**, *83*, 2727.

(11) Russell, G. A. *J. Am. Chem. Soc.* **1957**, *79*, 2977.

(12) Russell, G. A. *J. Am. Chem. Soc.* **1958**, *80*, 4897.

(13) Russell, G. A. *J. Am. Chem. Soc.* **1958**, *80*, 4997.

(14) Raner, K. D.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1989**, *111*, 3652.

(15) Ingold, K. U.; Lusztyk, J.; Raner, K. D. *Acc. Chem. Res.* **1990**, *23*, 219.

$$R_2S^{\bullet +} + A^{\bullet -} \rightarrow R_2S + {}^1A^* \tag{1a}$$

$$^1A^* \rightarrow A + h\nu \tag{1b}$$

dependence (constant microwave frequency) of the observed fluorescence intensity yields the superimposed EPR spectra of the positive and negative ions.[17] The FDMR experiment has been described in detail elsewhere.[18,19]

The spectrum in Figure 1a consists of an intense feature due to the unresolved EPR lines of the anthracene radical anion and the five-line EPR spectrum of the thietane radical cation. At higher thietane concentrations and higher temperature, the monomer sulfide radical cation spectrum disappears and is replaced by the nine-line EPR spectrum (outer lines not visible) of the thietane dimer radical cation (Figure 1b). In similar experiments carried out in alkane solvents (e.g., *n*-hexane), monomer sulfide radical cations were not detected; only dimer radical cations were detected.[20]

The greater stability (with respect to dimer formation and/or deprotonation) of monomer thioether radical cations in aromatic solvents versus alkane solvents can be accounted for by complex formation in the former case. The charge-transfer interaction with the aromatic solvent can be inferred from the EPR parameters, which are significantly shifted from the values measured in Freon matrices. Table I lists the hyperfine coupling constants for the radical cations of thietane, tetrahydrothiophene, and dimethyl sulfide measured by FDMR in toluene and by EPR in Freon matrices. In every case the hyperfine coupling constant is $\sim$30% smaller in toluene. This is not a temperature effect or a matrix effect. Transfer of spin from sulfur to toluene accounts for the smaller coupling to the $\beta$-protons on the sulfide and should lead to a concomitant reduction in the $g$ factor, which is also observed.

When *m*-xylene is the solvent, the monomer radical cation coupling constants are between 10 and 15% smaller than in toluene and the $g$ factors also undergo a further reduction. This indicates an even greater degree of charge transfer in *m*-xylene and correlates with the relative gas phase ionization potentials of toluene (8.8 eV) and *m*-xylene (8.5 eV). The EPR parameters of dimer sulfide radical cations are not nearly as solvent dependent, which indicates that the solvent interaction is broken when the unpaired electron is coordinated instead to the free p-electron pair of another sulfur atom. Furthermore, the liquid-phase EPR parameters of the dimer radical cations are in good agreement with those measured in Freon matrices,[7] which shows the absence of any matrix effect.

Binding of chlorine atoms by benzene and substituted benzenes changes their reactivity. The arene–chlorine atom complex is a much more selective reagent (shows a greater preference for abstracting tertiary versus primary H atoms) than free chlorine atoms.[11-15] Likewise our results indicate that complexation of thioether radical cations in aromatic solvents decreases their reactivity. Solvent effects are very important factors in determining the reactivity of a wide variety of reactive radical intermediates and can be used to great advantage for achieving greater chemical selectivity.

In summary, we have made the first liquid-phase observation of thioether monomer radical cations by using time-resolved FDMR spectroscopy. The detection of the thioether radical cations was possible because of the formation of a unique radical cation–arene $\pi$-molecular complex in aromatic solvents involving the interaction of the predominantly 3p SOMO of the thioether radical cations with the arene $\pi$-systems and also because of the time-resolved capability of FDMR. FDMR detects radical ions on the $10^{-8}$–$10^{-6}$ s time scale and thus does not determine their long-term ($>10^{-6}$ s) stability. The thioether radical cation–arene complexes should possess charge-transfer bands in the visible or near-UV by analogy with the arene–chlorine atom complexes [21-23] and thus could be studied by optical methods as well.

**Acknowledgment.** I acknowledge helpful discussions with Drs. A. D. Trifunac and X.-Z. Qin.

---

(16) The FDMR experiment is carried out in the cavity of a pulsed X-band EPR spectrometer.

(17) Only radical ions that were present during the microwave pulse are detected.

(18) Smith, J. P.; Trifunac, A. D. *J. Phys. Chem.* **1981**, *85*, 1645.

(19) Werst, D. W.; Bakker, M. G.; Trifunac, A. D. *J. Am. Chem. Soc.* **1990**, *112*, 40.

(20) Werst, D. W., unpublished results.

(21) Raner, K. D.; Lusztyk, J.; Ingold, K. U. *J. Phys. Chem.* **1989**, *93*, 564.

(22) Buhler, R. E.; Ebert, M. *Nature (London)* **1967**, *214*, 1220.

(23) Buhler, R. E. *Helv. Chim. Acta* **1968**, *51*, 1558.

---

## Temperature of Polypeptide Inverse Temperature Transition Depends on Mean Residue Hydrophobicity

Dan W. Urry,* Chi-Hao Luan, Timothy M. Parker,
D. Channe Gowda, Kari U. Prasad, Michael C. Reid, and
Ahmad Safavy

*Laboratory of Molecular Biophysics*
*The University of Alabama at Birmingham*
*P.O. Box 300, University Station*
*Birmingham, Alabama 35294*

*Received January 17, 1991*

For the many hydrophobicity scales for amino acid residues in protein and polypeptides,[1-11] there is reasonable agreement for a sequence in which Phe (F) > Ile (I) $\simeq$ Leu (L) > Val (V) > Ala (A) > Gly (G). When these residues are substituted at position 4 within (Val$^1$-Pro$^2$-Gly$^3$-Val$^4$-Gly$^5$)$_n$, abbreviated poly(VPGVG), to give a structure written poly[$f_X$(VPGXG),$f_V$(VPGVG)] where $f_V$ is the mole fraction of pentamers with valyl residues at position 4 and $f_X$ is the mole fraction of pentamers with a guest residue, X, at position 4 with $f_X + f_V = 1$, the temperature of a reversible aggregational transition in water (actually a phase transition described as a coacervation) is here demonstrated to be inversely dependent on the mean hydrophobicity, and in addition, the heat of the transition is found to be directly proportional to the mean residue hydrophobicity in studies where the temperature and heat of the transition were determined by differential scanning calorimetry (DSC). With the use of transition temperature to determine relative hydrophobicity having been established in this molecular system, data for Trp (W), Tyr (Y), and Met (M) complete the values for residues comprising the apolar half of the natural amino acids in this first hydrophobicity scale based on a physical property so integral to the process of protein folding and assembly. Importantly, the transition temperature, in this relatively simple polypeptide (pro-

---

* Author to whom correspondence should be addressed.

(1) Prior to the present report, relative hydrophobicities were derived from relevant but indirect approaches. For example, the Nozaki and Tanford scale was based on relative solubilities of amino acids in organic solvents;[2] the Bull and Breese scale utilized surface tension of amino acid solutions;[3] Hopp and Woods used the correlation of hydrophilicity with antigenic determinants;[4] a number of scales derive from the distribution of residues buried within or on the surface of globular proteins;[5-10] and more recently and more closely related to the present report, the physically relevant partial molar heat capacities of peptide moieties and amino acid side chain equivalents have been used but with limitations due to low solubility of the side chains of the Ala, Val, Leu, and Ile amino acids and due to the assumed additivity of polar and apolar components.[11]

(2) Nozaki, Y.; Tanford, C. *J. Biol. Chem.* **1971**, *246*, 2211.

(3) Bull, H. B.; Breese, K. *Arch. Biochem. Biophys.* **1974**, *161*, 665.

(4) Hopp, T. P.; Woods, K. R. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 3824.

(5) Janin, J. *Nature* **1979**, *277*, 491.

(6) Manavalan, P.; Ponnaswamy, P. K. *Nature* **1978**, *275*, 673.

(7) Chothia, C. *J. Mol. Biol.* **1976**, *105*, 1.

(8) Levitt, M. *J. Mol. Biol.* **1976**, *104*, 59.

(9) Wertz, D. H.; Scheraga, H. A. *Macromolecules* **1978**, *11*, 9–15.

(10) Cornette, J. L.; Cease, K. B.; Margalit, H.; Spouge, J. L.; Berzofsky, J. A.; DeLisi, C. *J. Mol. Biol.* **1987**, *195*, 659–685.

(11) Makhatadze, G. I.; Privalov, P. L. *J. Mol. Biol.* **1990**, *213*, 375.

0002-7863/91/1513-4346$02.50/0