rules out this reaction as a major pathway for malonic acid oxidation. Our scheme assumes that the first mole of HMA is oxidized to GA and that an additional mole of HMA is obtained in the Cr(V) step. Clearly some oxidation of GA has also occurred.

It is relevant to compare the Cr(VI) oxidation of malonic acid with other oxidizing agents. The formation of the radical $\cdot CH(COOH)_2$ has been suggested in oxidations by one-electron oxidizing agents[27] like V(V) and Mn(III) pyrophosphate. The postulation of this radical and the reported second-order dependence on V(V) and Mn(III) are in direct conflict. The involvement of the malonic acid radical has been demonstrated in the Ce(IV) oxidation by flow ESR techniques.[28,29] What makes the Ce(IV) oxidation so unique to be different from V(V), Mn(III), and Cr(VI) oxidations is not clear at this moment.

Acknowledgment. Financial support of this investigation from CSIR, New Delhi (Grant 1-933/81/EMR II), is gratefully acknowledged. We are grateful to Professor M. V. Bhatt, I.I.Sc. Bangalore, for his hospitality during the summer of 1981. Thanks are due to Professor M. P. Doyle, Trinity University, for critical comments and encouragement. We thank the reviewers for suggesting the enolization and isotope effect studies.

---

[27] Kemp, T. J.; Waters, W. A. *J. Chem. Soc.* **1964**, 339, 1192, 1489, 1610, 3101, 3193.

[28] Amjad, Z.; McAuley, A. *J. Chem. Soc., Dalton Trans.* **1977**, 304.

[29] Tischler, F.; Morrow, J. I. *Inorg. Chem.* **1983**, *22*, 2286.

Registry No. Malonic acid, 141-82-2; hydroxymalonic acid, 80-69-3; glyoxylic acid, 298-12-4; 2,4-dinitrophenylhydrazine, 119-26-6; glyoxylic acid 2,4-dinitrophenylhydrazone, 3158-42-7; oxalic acid, 144-62-7; formaldehyde, 50-00-0; ketomalonic, 473-90-5.

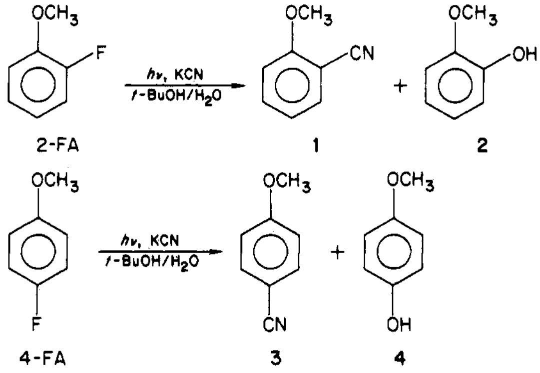
Communications

Anomalous Effects during Aromatic Nucleophilic Photosubstitutions of 2- and 4-Fluoroanisoles in Solvent Mixtures of Water and *tert*-Butyl Alcohol

Summary: The rate constant ratio for removal of fluorine by either cyano or hydroxy during aromatic nucleophilic photosubstitutions on 2- or 4-fluoroanisole displays a remarkable dependence upon the composition of the water/*tert*-butyl alcohol solvent and the distance between the methoxy group and the site of substitution in the solutes.

Sir: Our recently completed studies[1] indicated that the efficiency and selectivity of aromatic nucleophilic photosubstitutions (by water and cyanide) on 2- or 4-fluoroanisole (2- or 4-FA) are influenced in several different ways by addition of cyclodextrin, a torus-shaped polyalcohol, to an aqueous solvent. In order to separate some of these effects, we have examined the substitution reactions when *tert*-butyl alcohol replaces the cyclodextrin.

Nucleophilic strengths of cyanide and water in aqueous solvent mixtures usually fall between those measured in each of the neat solvent components[2] and are relatively insensitive to reactive substrates within the same class.[3,4] The Hughes–Ingold theory,[5] Swain–Scott equation,[6] and others which relate solvent bulk properties and rates of substitution reactions[6b,7] predict a monotonous decrease in the nucleophilicity of cyanide with respect to water (including hydroxide) as an aqueous solvent is enriched in a less polar cosolvent like an alcohol. We find that the selectivity of aromatic nucleophilic photosubstitutions on 2-FA or 4-FA in aqueous *tert*-butyl alcohol[8] is totally inconsistent with these relationships and varies in opposing ways with the FA isomer.



The mechanism of aromatic nucleophilic photosubstitution reactions of FA in aqueous *tert*-butyl alcohol has been reviewed recently[9] and Varma and co-workers[10] have

---

[1] (a) Liu, J. H.; Weiss, R. G. *Isr. J. Chem.*, in press. (b) Liu, J. H.; Weiss, R. G. *J. Photochem.*, in press.

[2] (a) Winstein, S.; Grunwald, E.; Jones, H. W. *J. Am. Chem. Soc.* **1951**, *73*, 2700. (b) Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7667.

[3] Ritchie, C. D. *Acc. Chem.* Res. **1972**, *5*, 348.

[4] (a) Wells, R. P. "Linear Free Energy Relationship"; Academic Press: London, 1968. (b) Shorter, J. "Correlation Analysis in Organic Chemistry: An Introduction to Linear Free-Energy Relationships"; Clarendon Press: Oxford, 1973.

[5] Ingold, C. K. "Structure and Mechanism in Organic Chemistry", 2nd ed.; Cornell University Press: Ithaca, New York, 1969.

[6] (a) Swain, C. G.; Scott, C. B. *J. Am. Chem. Soc.* **1953**, *75*, 141. (b) See: Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", 2nd ed.; Harper and Row: New York, 1981; pp 323ff and references cited therein.

[7] Pross, A. In "Advances in Physical Organic Chemistry"; Gold, V., Bethel, D., eds.; Academic Press: London, 1977; Vol. 14, p 69.

[8] (a) Traces of an oxidation product, 4-cyano-2-fluoroanisole, from 2-FA were detected. Small amounts of another unidentified photoproduct were obtained from 4-FA. No formation of anisole[8b] or *tert*-butoxyanisole was detected from either FA isomer. All products were identified by comparisons with authentic samples. They account for more than 85% of consumed FA. Product ratios were determined on the unadulterated reaction mixtures by HPLC and are corrected for differing UV detector responses. All experiments were conducted with 2×10^{-3} M FA and 0.1 M KCN in nitrogen-saturated solutions at room temperature. Irradiations at 254 nm for 2-FA and >260 nm for 4-FA were kept below 10% conversion for most runs and never reached 20%. A more detailed description of experimental procedures is included in ref 1. (b) Houser, J. J.; Siegman, J. R. *J. Org. Chem.* **1982**, *47*, 2773.

[9] Cornelisse, J.; Lodder, G.; Havinga, E. *Rev. Chem. Intermed.* **1979**, *2*, 231.

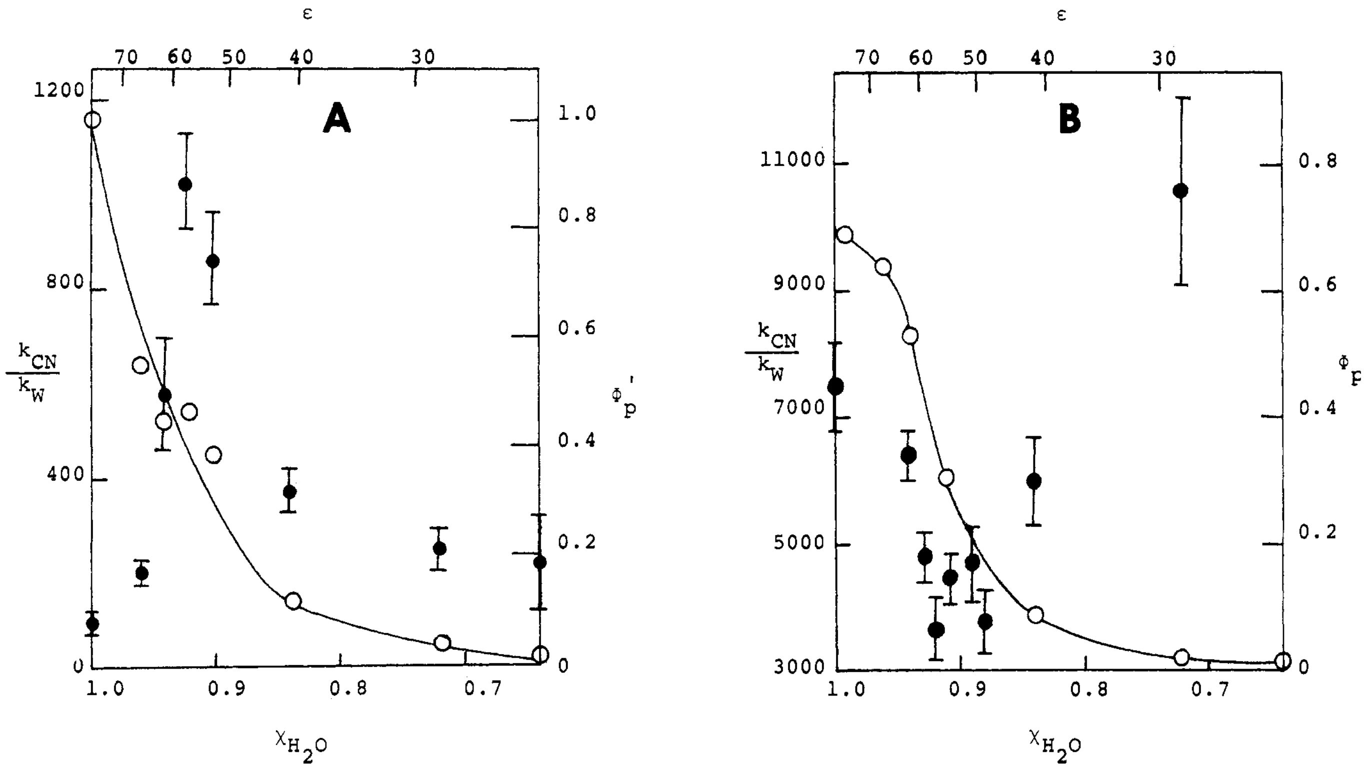
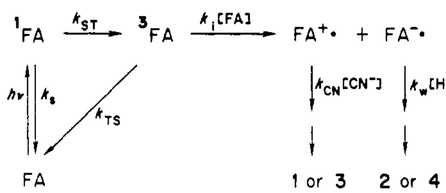


Figure 1. Plots of k_{CN}/k_W (0.1 M KCN) (●) and Φ_p' or Φ_p[12] (○) for 2-FA (A) and 4-FA (B) photosubstitutions in water/*tert*-butyl alcohol mixtures vs. the mole fraction of water and solvent dielectric constant. Curves through the Φ_p' and Φ_p points are drawn empirically.

Scheme I



confirmed that the reactive species is the cation radical. Its rate of disappearance corresponds to the rate of trapping by nucleophiles as shown in Scheme I. By analogy with the comportment of anisole[11a] and other aromatic molecules,[11b] k_{ST}, k_S, and k_{TS} should vary slightly as the mole fraction of *tert*-butyl alcohol in water increases. Large solvent-induced changes in Φ_p,[12] the quantum efficiency for total product formation, or Φ_p', the ratio of the quantum efficiencies in a water/*tert*-butyl alcohol mixture and in water (where both solvent systems contain 0.1 M KCN), can be attributed to k_i (N.B. To the ability of the polarity-sensitive k_i[FA] to compete with k_{TS}). From the scheme, the rate constant ratios of photocyanation to photohydroxylation, k_{CN}/k_w, equals ([1 or 3][H$_2$O])/([2 or 4][CN$^-$]) and can be calculated from data in Table I. The results, including the relationship between the mole fraction of water (χ_{H_2O}) and the dielectric constant (ε), are displayed in Figure 1.

Table I. Photosubstitution of 2 × 10^{-3} M FA in 0.1 M KCN *tert*-Butyl Alcohol/Water Solutions

t-BuOH/H$_2$O (v/v)	χ_{H_2O}	ε[a]	2-FA 2/1	4-FA 4/3
0/1	1.0	78.5	6.25	0.074
1/5	0.96	68.5	2.44	
1/3	0.94	62.5	0.73[b]	0.061
1/2.4	0.928	59.5		0.082
1/2.2	0.92	57	0.38	0.10
1/2	0.91	55.5		0.081
1/1.7	0.90	53	0.41	
1/1.5	0.89	51		0.071
1/1.4	0.88	49		0.091
1/1	0.84	41.5	0.75	0.043
2/1	0.72	28.0	0.74	0.016
3/1	0.64	22.0	0.64	

[a] References 9 and 19. [b] Cornelisse and co-workers[12] reported that the product mixture from irradiation of 2-FA in 1/3 (v/v) *tert*-butyl alcohol/water and 0.22 M KCN contains almost exclusively 1 (<5% of 2). We find from HPLC analyses of the unadulterated reaction mixture that a ca. 3/5 ratio of 2/1 is produced under their experimental conditions.

Although Φ_p[12] and Φ_p' decrease smoothly with increasing *tert*-butyl alcohol concentrations as expected of reactions dependent upon intermolecular electron transfer, k_{CN}/k_W exhibits bizarre excursions near $\chi_{H_2O} = 0.9$. For 2-FA, the ratio *increases* from 90 ± 15 at $\chi_{H_2O} = 1.0$ to 1020 ± 100 at $\chi_{H_2O} = 0.92$ and then decreases; for 4-FA, the ratio *decreases* from 7500 ± 700 to 3700 ± 500 over the same χ_{H_2O} range and then increases. Several other anomalous changes in rate constant ratios have been observed for a radical pair reaction,[13] for a hydrolysis,[14] and for competing nucleophilic attack by water and primary alcohols in water-rich mixtures of the two.[15] None is of the magnitude

---

[10] Lemmetyinen, L.; Varma, C. A. G. O. "Proceedings of the 10th IUPAC Symposium on Photochemistry"; Interlaken, Switzerland, July 1984, p 437.

[11] (a) Kohler, G.; Getoff, N. *J. Mol. Struct.* **1984**, *115*, 331. (b) Birks, J. B. "Photophysics of Aromatic Molecules", Wiley-Interscience: London, 1970. (c) Knibbe, H.; Rolling, K.; Schafer, F. P.; Weller, A. *J. Chem. Phys.* **1967**, *47*, 1184.

[12] den Heijer, J.; Shadid, O. B.; Cornelisse, J.; Havinga, E. *Tetrahedron* **1977**, *33*, 779. These authors have shown that Φ_p is completely independent of cyanide concentration. Their numbers are presented in Figure B.

[13] Nodelman, N.; Martin, J. C. *J. Am. Chem. Soc.* **1976**, *98*, 6579.

[14] Karzijn, W.; Engberts, J. B. F. N. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 513.

found here and none exhibits excursions whose direction depends upon the substrate isomer employed.[16]

Log $(k_{CN}/k_W)^7$ in aqueous KCN is 1.9 for 2-FA and 3.9 for 4-FA. The reported value for 4-FA is 3.8[9] and Ritchie[3] finds N^+ values near 3.9 for cyanation of a number of cations in water. Thus, it appears that 2-FA is the anomalous isomer. Hydrogen bonding by water to the methoxy group of 2-FA would place it very near the 2-carbon and allow photohydroxylation to occur preferentially. Similar complexation to 4-FA would leave a water molecule too distant and improperly oriented to displace a fluorine atom on the 4-carbon. The availability of cyanide as a charged nucleophilic may be compromised, as well, by varying solvent order.[17] Miscible water–alcohol mixtures are known to undergo intriguing changes in their thermodynamic and spectroscopic properties at $0.8 < \chi_{H_2O} < 1.0$.[18] Bulk solvent viscosity[13] and polarity (as exemplified by ϵ of aqueous *tert*-butyl alcohol solutions)[19] exhibit unexceptional changes. However, microscopic solvation (as measured by the partial molal heats of solution,[15b] transport numbers, and conductances of ions[20]) and microviscosity (as measured by internal pressure[13]) do exhibit extrema near $\chi_{H_2O} = 0.9$. *Therefore, any comprehensive explanation of our results must include the dynamic influence of solvent structure on both the substrates and the nucleophiles.*

Addition of small amounts of alcohol to water is known to increase total solvent order. Several qualitative and semiquantitative theories have been devised to express the microscopic alterations in intermolecular hydrogen bonding which must occur.[18,21,22] Application of these theories to our results will be discussed in a full report. Suffice it to say that alcohol molecules appear to induce formation of domains of highly structured water molecules which coexist with "free" (normal) water. When the total volume of the domains forces them to overlap (i.e., when $\chi_{t\text{-BuOH}} > 0.1$), solution order decreases.

Our results indicate that competitive aromatic nucleophilic photosubstitutions on 2-FA and 4-FA offer sensitive probes of both local solute–solvent interactions and the solvent structural changes which occur in the domain and free regions. Preliminary results with other water–alcohol mixtures demonstrate the generality of these phenomena. We intend to explore the extent of their importance upon other aromatic nucleophilic photosubstitutions.

Acknowledgment. Dr. Richard Boehm is thanked for his ideas concerning a possible microscopic model of aqueous *tert*-butyl alcohol solutions. The National Science Foundation is acknowledged for its support of this work (Grant No. CHE 83-01776).

Registry No. 1, 6609-56-9; 2, 90-05-1; 3, 874-90-8; 4, 150-76-5; 2-FA, 321-28-8; 4-FA, 459-60-9; KCN, 151-50-8.

Jerry H. Liu, Richard G. Weiss*
Department of Chemistry
Georgetown University
Washington, D.C. 20057

Received March 15, 1985

---

[15] (a) Blandamer, M. J. in ref 6, p 203. (b) Arnett, E. M. In "Physico-Chemical Processes in Mixed Aqueous Solvents", Franks, F., ed.; American-Elsevier: New York, 1967; p 105. (c) Engberts, J. B. F. N. In "Water. A Comprehensive Treatise"; Franks, F., ed.; Plenum Press: New York, 1979; Vol. 6, Chapter 4. (d) Aronovitch, H.; Pross, A. *Tetrahedron Lett.* **1977**, 2729. (e) Battistini, C.; Berti, G.; Crotti, P.; Ferretti, M.; Macchia, F. *Tetrahedron* **1977**, *33*, 1629. (f) Bunton, C. A.; Huang, S. K.; Paik, C. H. *Tetrahedron Lett.* **1976**, 1445.

[16] Engberts, J. B. F. N. *Pure Appl. Chem.* **1982**, *54*, 1797.

[17] Arnett, E. M.; McKelvey, D. R. *J. Am. Chem. Soc.* **1966**, *88*, 5031.

[18] (a) Franks, F.; Ives, D. J. G. *Q. Rev. Chem. Soc.* **1966**, *20*, 1. (b) Franks, F. in ref 15b, pp 50ff. (c) Vuks, M. F. *Mol. Fiz. Biofiz. Vod. Sist.* **1973**, *1*, 3; *Chem. Abstr.* **1974**, *81*, 30408d.

[19] Timmermans, J. "The Physico-Chemical Constants of Binary Systems in Concentrated Solutions"; Interscience: New York, 1960; Vol. 4.

[20] (a) Kay, R. L.; Broadwater, T. L. *J. Soln. Chem.* **1976**, *5*, 57. (b) Feakins, D.; O'Neill, R.; Waghorne, E. *Pure Appl. Chem.* **1982**, *54*, 2317. (c) Kay, R. L.; Evans, D. F.; Matesich, M. A. In "Solute-Solvent Interactions"; Coetzee, J. F., Ritchie, C. D., eds.; Marcell Dekker: New York, 1976; Vol. 2, Chapter 10. (d) Schneider, H. in ref 20c, Chapter 11.

[21] (a) Grunwald, E. *J. Am. Chem. Soc.* **1984**, *106*, 5414 and references cited therein. (b) Symons, M. C. R. *Acc. Chem. Res.* **1981**, *14*, 79. (c) Partington, J. R. "An Advanced Treatise on Physical Chemistry"; Longmans, Green and Co.: London, 1951; Vol. 2, p 2. (d) Partington, J. R., ref 21c, Vol. 5, p 390ff.

[22] Terms such as "hydrophobic hydration" and "hydrophobic interaction" have been used, also, to express the changes in the structure of the cybotactic region around a nonpolar solute.[16]

Intramolecular Catalysis of Oxygen Atom Transfer Reactions of α-Azo Hydroperoxides

Summary: α-Azo hydroperoxides containing phenolic groups were ~10^2 more reactive at epoxidations and S-oxidation than electronically similar analogues due to intramolecular acid catalysis of the ionic oxidations.

Sir: α-Azo hydroperoxides (α–hydroperoxy diazenes) have been shown to be important in free-radical chemistry.[2] Recently, we have shown[3] that α-azo hydroperoxides are of high reactivity in oxygen atom transfer reactions (reaction 1). Ionic oxidations by α-azo hydroperoxides occur

$$\underset{\alpha\text{-azo hydroperoxide}}{R_2C(OOH)N{=}NR} + {:}X \rightarrow \underset{\alpha\text{-azo hydroxide}}{R_2C(OH)N{=}NR} + X{=}O \qquad (1)$$

under mild conditions and (in aprotic medium) do not require general acid catalysis.[3] The mechanism of these oxygen atom transfer reactions is similar to that of peracids[4] and those of other heteroatom-containing hydroperoxides.[5] Interestingly, the ionic oxidations by α-azo hydroperoxides exhibit high selectivities[3] that are independent of the relative reactivities. Intramolecular proton-transfer (hydrogen-bonding) of the "hydroperoxy" proton to the azo function in the transition state has been proposed[3] to account for the reactivity of this system. Development of more reactive reagents requires the use of functional groups that catalyze the ionic oxidations but do not disrupt the internal hydrogen bond. We report the synthesis and characterization of α-azo hydroperoxides designed to exploit intramolecular acid catalysis of oxygen atom transfer reactions.

---

[1] Fellow of the Camille and Henry Dreyfus Foundation, 1981–1986.

[2] (a) Tezuka, T.; Narita, N.; *J. Am. Chem. Soc.* **1979**, *101*, 7413. (b) Tezuka, T.; Narita, N.; Ando, W.; Oae, S. *J. Am. Chem. Soc.* **1981**, *103*, 3045. (c) Tezuka, T.; Ichikawa, K.; Marusawa, H.; Narita, N. *Chem. Lett.* **1983**, 1013. (d) White-Dixon, D.; Barbush, M. *J. Org. Chem.*, in press. (e) Osei-Twum, E. Y.; McCallion, O.; Nazran, A. S.; Parricucci, R.; Risbood, P. A.; Warkentin, J. *J. Org. Chem.* **1984**, *49*, 336.

[3] (a) Baumstark, A. L.; Chrisope, D. R.; Landis, M. E. *J. Org. Chem.* **1981**, *46*, 4591. (b) Baumstark, A. L.; Pilcher, R. S. *J. Org. Chem.* **1982**, *47*, 1141. (c) Baumstark, A. L.; Chrisope, D. R. *Tetrahedron Lett.* **1981**, 4591. (d) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1983**, *48*, 65. (e) Baumstark, A. L.; Vasquez, P. C. *Tetrahedron Lett.* **1983**, 123.

[4] (a) Bach, R. D.; Willis, C. L.; Domagala, J. M. In "Applications of Molecular Orbital Theory in Organic Chemistry"; Csimada, I. G., Ed.; Elsevier: Amsterdam, 1977; pp 221–229. (b) Sharpless, K. B.; Verkoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63–74. (c) March, J. "Advanced Organic Chemistry", 2nd ed.; McGraw-Hill: New York, 1977; pp 750–751. (d) Swern, D. In "Organic Peroxides"; Wiley: New York, 1971; Vol. II, pp 450–75 and references therein.

[5] (a) Rebek, J.; McCready, R. *Tetrahedron Lett.* **1979**, 4337. (b) Heggs, R. P.; Ganem, B. *J. Am. Chem. Soc.* **1979**, *101*, 2485. (c) Rebek, J., Jr.; McCready, R. *J. Am. Chem. Soc.* **1980**, *102*, 5602. (d) Rebek, J., Jr.; McCready, R. *J. Chem. Soc., Chem. Commun.* **1980**, 705.

0022-3263/85/1950-3657$01.50/0