

Chapter 7

EXCITED-STATE PROTON TRANSFER OF 1-AZACARBAZOLE IN MIXED METHANOL AND METHANOL-OD SOLVENTS

7.1 Introduction

Isotope effects provide a valuable means for testing kinetic mechanisms and pictures of the transition state in chemical reactions involving proton transfer.¹⁻⁴ Within the Born-Oppenheimer approximation, the substitution of one isotope for another does not change the potential energy surface. Although the binding forces remain the same, the masses of the isotopic atoms do change. Kinetic isotope effects are especially significant for hydrogen because deuterium is twice as massive as hydrogen. Thus the reaction rate corresponding to atomic motion involving hydrogen may show a substantial decrease when deuterium replaces the hydrogen atom. The elucidation of the mechanism of excited-state proton-transfer in 1AC should therefore be aided by consideration of the observed isotope effects. After briefly summarizing and interpreting the magnitudes and temperature dependence of the kinetic isotope effects for 7AI and 1AC in a number of protic solvents, we consider the reaction of 1AC in the mixed solvent methanol/methanol-OD.

7.2 Magnitude of the Kinetic Isotope Effects for 7AI and 1AC

The magnitude of the isotope effects observed for the reactions involving 7AI and 1AC reveals information about the excited-state reactions. *Table 7.1* summarizes the kinetic isotope effects; in general, the kinetic isotope effects for 7AI and 1AC in alcohols are 3 and 5, respectively. We conclude that the magnitude of the kinetic isotope effects is due to reacting protons in 7AI and 1AC, for isotope effects on simple solvation dynamics account for a much smaller effect. For example, solvation dynamics of methanol-OD is only 10% slower than that of methanol as probed by coumarin 102 in time-resolved fluorescence experiments.⁵

7.3 Temperature Dependence of Kinetic Isotope Effects for 7AI and 1AC

Chapman, Boryschuk and Maroncelli revisited the temperature dependence of the kinetic isotope effect for 7AI and 1AC in several bulk alcohols and concluded that the isotope effect has little or no temperature dependence.^{6,7,8} The results of the temperature studies of 1AC in ethylene glycol and water are consistent with these earlier conclusions (as described in Chapters 5 and 6). The temperature independence of the kinetic isotopic effect is rather remarkable since the reaction rate depends strongly on temperature as summarized in *Table 5.11*. Sühnel and Schowen note in their review of the theoretical basis for isotope effects that neither transition-state theory nor the Marcus theory can explain such large, temperature-independent primary isotope effects.⁹ Instead, a quantum-statistical mechanical theory is required: temperature-dependent but isotope-

independent solvent fluctuations lead to a “critical state” that is followed by a temperature-independent but isotope-dependent tunneling reaction.⁹ This theory is conceptually very similar to the model being examined in this dissertation.

7.4 Kinetic Isotope Effect of 1AC in Mixed Methanol/Methanol-OD

Experiments utilizing solvents of mixed protiated and deuterated composition to probe reaction mechanisms are now common.¹⁰⁻²⁷ In one strategy called the “proton inventory experiment,” equilibrium or kinetic measurements are made as a function of solvent composition in an attempt to determine the number of active protons giving rise to the observed kinetic isotope effect.¹⁰⁻²⁷ Since the interpretation of the “proton inventory experiment” requires the exchange rates of the active hydrogen ligands with the solvent to be faster than their reaction rates,¹⁰⁻²⁷ it is not directly applicable to the excited-state reaction involving 1AC. (Recall from Chapter 6 that the kinetics of 1AC in water-methanol mixtures is consistent with rapid solvent exchange rather than rapid hydrogen ligand exchange.) Instead, a general strategy will be pursued in which the reaction rates are measured as a function of solvent composition (H/D), and then the predictions of kinetic models are compared to data to exclude unlikely mechanisms.

A recent study of the isotope effects for 7AI in mixed protiated and deuterated solvents provided evidence that this excited-state reaction involves the concerted motion of protons in a cyclic complex in alcohols such as methanol and ethanol.²⁷ Since the double proton-transfer reaction of 1AC is postulated to be like that of 7AI, 1AC was subjected to a similar solvent isotope-effect experiment to verify the reaction scheme. As

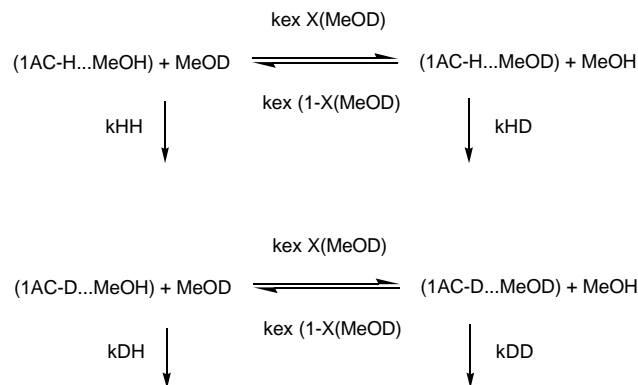
the isotope effect of 1AC is slightly larger than 7AI in alcohols [5 vs. 3], better experimental resolution for testing models is anticipated for this related proton-transfer molecule.¹⁸

The reactions of 1AC in methanol and methanol-OD mixtures were deemed the best systems for study. In these neat solvents, the normal time-resolved emission may be fit by clean, single lifetimes that allow accurate rate determinations. Experimental concerns limit the application of the solvent isotope-effect experiments in other solvents. For example, difficulties associated with the poor solubility and the possible contamination of observed rates by the normal deactivation rate k^N prevented the experiment in water and deuterium oxide. Likewise, multiple lifetimes required to fit the normal emission of 1AC in many alcohols and diols like 1-propanol and ethylene glycol complicate the extraction of rates. Thus this study of the 1AC reaction in methanol will be compared to the reported results of 7AI in methanol, ethanol, and water to examine the consistency of models proposed for both probes. Surprisingly, the results observed with 1AC appear to differ from those found with 7AI.

7.4.1 Determination of Reaction Rates

The first issue to address is the identification of the protons involved in the reaction.^{27,28} Two types of protons are involved, and each has a characteristic exchange rate. In the ground-state, the hydrogen or deuterium atoms bonded to the solute exchange (without reacting) negligibly slowly with the solvent compared to the time-scale of the reaction.²⁹ The hydrogen or deuterium atoms bonded to the solvent molecules in position

for reaction exchange rapidly as the solvent molecules exchange positions.³⁰ Thus a model of the ground-state systems prior to reaction may be divided into two independent populations (*Scheme 7.1*):



Scheme 7.1

Following excitation, the proton-transfer reactions proceed and depopulate these excited-state ensembles. Since the observed rates for 1AC in mixed methanol-water solvents are consistent with a rapid solvent exchange limit, the time-dependence of the populations in these kinetic schemes follow Equation 3.20 of Section 3.4:

$$1\text{AC-H}(t) = 1\text{AC-H}(0) [\exp\{-((1-X_D) k_{\text{HH}} + X_D k_{\text{HD}}) t\}] \quad (7.1)$$

$$1\text{AC-D}(t) = 1\text{AC-D}(0) [\exp\{-((1-X_D) k_{\text{DH}} + X_D k_{\text{DD}}) t\}] \quad (7.2)$$

The experiment measures the total population of 1AC in the excited state:

$$1\text{AC}(t) = 1\text{AC-H}(t) + 1\text{AC-D}(t) \quad (7.3)$$

$$1\text{AC}(t) = 1\text{AC}(0) \{(1-X_D) \exp[-k^{\text{H}} t] + X_D \exp[-k^{\text{D}} t]\}$$

where the initial populations of 1AC-H and 1AC-D are directly related to the composition of the mixed solvent.³¹ These expressions are identical to those derived by

Petrich and coworkers in their study of 7AI.²⁷ Reviewing the model leading to Equations 7.1, 7.2, and 7.3, we have only needed to specify the possible reacting species in the limit of rapid solvent exchange.

The time-resolved emission data required fitting by a biexponential function, as summarized *Table 7.2* and illustrated in *Figure 7.1*. Since this biexponential behavior is predicted by the model, and since the amplitudes in unconstrained fits are similar to the mole fractions describing the composition of the mixtures, the amplitudes were constrained to the experimental mole fractions to obtain best estimates for the rates $k^H = 1/\tau^H$ and $k^D = 1/\tau^D$ of Equation 7.3. These constrained fits are also recorded in *Table 7.2*. The individual rate constants k_{HH} , k_{HD} , k_{DH} , and k_{DD} are obtained from plots of the measured rates k^H and k^D as functions of the mixture composition X_D . Each plot displayed in *Figure 7.2* reveals a linear relationship whose intercepts and slopes are identified with the following rates:

$$k^H \text{ vs. } X_D: \quad k_{HH} + X_D (k_{HD} - k_{HH}) \quad (7.4)$$

$$k^D \text{ vs. } X_D: \quad k_{DH} + X_D (k_{DD} - k_{DH}) \quad (7.5)$$

From linear regressions to the data³² the following rates are calculated:

$$\begin{aligned} k_{HH} &= 1.97(3) \times 10^9 \text{ s}^{-1} \\ k_{HD} &= 0.55(5) \times 10^9 \text{ s}^{-1} \\ k_{DH} &= 1.18(1) \times 10^9 \text{ s}^{-1} \\ k_{DD} &= 0.38(2) \times 10^9 \text{ s}^{-1}. \end{aligned} \quad (7.6)$$

To confirm that the observed rates may be interpreted as reaction rates (*i.e.*, to confirm that the observed rates were not contaminated by the normal deactivation rate

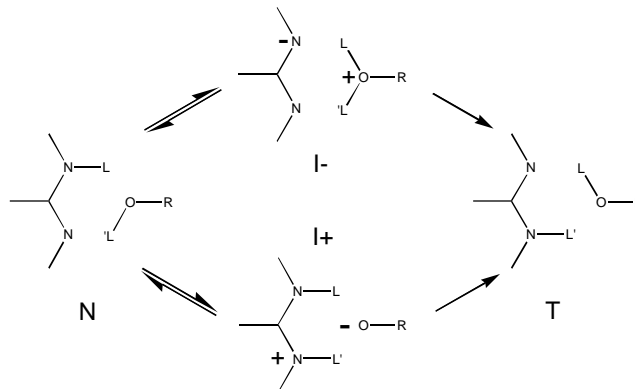
k^N), the mean proton-transfer rates were calculated using the irreversible proton-transfer scheme (Chapter 3) which predicts

$$k_{PT} = \frac{k_{rad}^N \mathbf{j}^T}{k_{rad}^T \mathbf{j}^N} k^T. \quad (7.7)$$

The ratio of radiative rates is nearly independent of solvent (7.4 for 1AC in methanol in particular), the ratios of quantum yields may be extracted from normalized steady-state emission spectra, and the tautomer deactivation rates are obtained from the rise times of the 1AC tautomer emission. The results demonstrate that the mean rates extracted from the normal and tautomer regions are within 10% agreement, which is less than the uncertainty inherent in the tautomer rise times.

7.4.2 Interpreting the Rates: Rule of the Geometric Mean

The rates for the four possible combinations of reacting species may provide insight into the pathway of the reaction. A kinetic model that tests the concerted nature of the two-proton switch leading to the formation of the excited-state tautomer has been studied.²⁰⁻²⁷ For each combination of hydrogen or deuterium atoms at the two sites L and L', the scheme appears as follows with emphasis on the postulated cyclic form (*Scheme 7.2*):



Scheme 7.2

Based on this scheme (Scheme 7.2), Petrich and coworkers²⁷ like Limbach and coworkers²⁰⁻²⁶ have derived the relationships necessary for the double-proton transfer to be a concerted process. Two conditions must be satisfied for a concerted reaction:²⁷ (1) If the reaction involves the stepwise transfer of the two protons, then an intermediate (I^- or I^+) will be formed during tautomerization. When the populations of the postulated short-lived intermediates (I^- and I^+) form the N and T species at equal rates ($k(I^- \rightarrow N) = k_{I^-N} = k_{I^-T}$ and $k(I^+ \rightarrow N) = k_{I^+N} = k_{I^+T}$), then the reaction occurs in one kinetic step (a concerted reaction). (2) All isotope effects associated with the solute and solvent must be equal. Only when these conditions are met will the measured rates k_{HH} , k_{HD} , k_{DH} , and k_{DD} satisfy the “rule of the geometric mean”:^{27,33} $k_{HD} = k_{DH} = (k_{HH} k_{DD})^{1/2}$.

Further explanation of the “rule of the geometric mean” is warranted here. In a concerted reaction, we expect that the isotope effects should be independent at each of the reactive sites. That is, if both protons are “in flight” in the transition state, one expects the isotope effects of the multiple sites in the single transition state to be independent.²⁷ When kinetic isotope effects fail to meet this expectation, the observation

is mechanistically significant.^{9,34} For the solvent-catalyzed, double-proton-transfer reaction of 1AC we must examine the independence of the isotope effects corresponding to the two protons exchanged in the reaction. Ratios of the four extracted rates may be formed to pursue this goal, where the rates are designated $k_{(L \text{ on } 1AC)(L' \text{ on methanol})}$. The isotope effect for L' is indeed independent of the hydrogen or deuterium atom L originally bonded to 1AC:

$$\frac{k_{HD}}{k_{HH}} = 0.28(3) \approx \frac{k_{DD}}{k_{DH}} = 0.32(2) \quad (7.8)$$

It is much less clear, however, that the isotope effect for L on 1AC is independent of methanol's L':

$$\frac{k_{DH}}{k_{HH}} = 0.60(1) \overset{?}{\longleftrightarrow} \frac{k_{DD}}{k_{HD}} = 0.69(7) \quad (7.9)$$

In these comparisons, the relative uncertainties of the ratios were estimated from the relative errors of the rates added in quadrature. In a generous interpretation we may conclude that the isotope effects are indeed independent at each reactive site.

The second condition that the rate constants should satisfy for a confident interpretation of a concerted reaction is that the solute and solvent isotope effects must be equal.²⁷ For site-independent isotope effects, this constraint leads to the equalities $k_{HD} = k_{DH} = (k_{HH} k_{DD})^{1/2}$ which indeed have the form of a geometric mean. The idea is that if the isotope effects are not identical, then the rate of transfer of one proton may differ from that of the other proton and thus the reaction may be more consistent with a stepwise transfer. In practice, the breakdown of this geometric mean is interpreted as evidence for either tunneling (in either a concerted or stepwise reaction) or a stepwise

reaction.^{22,27,34} The measured rates for 1AC in the methanol/methanol-OD mixtures clearly suggest that the primary isotope effects are different. The solute isotope effect is approximately

$$\frac{k_{HL'}}{k_{DL'}} \sim 1.6 \quad (7.10)$$

and the solvent isotope effect is approximately

$$\frac{k_{LH}}{k_{LD}} \sim 3.3. \quad (7.11)$$

These observations indicate that a concerted double proton transfer is not obviously the reaction mechanism.

One final comment about this analysis should be highlighted. If the observed reaction rates indeed may be decomposed into two terms – one for solvent effects and one for the actual proton transfer – then the ratios of observed rates are expected to be largely independent of the solvent effects terms. That is, the isotope effects reported in this section may be attributed directly to the intrinsic proton-transfer step.

7.4.3 Interpreting the Rates: Tunneling and Stepwise Double Proton Transfer

While the “rule of the geometric mean” is one criterion expected to be satisfied for a concerted reaction, its failure does not indicate that the reaction is not concerted.

Subsequently, two alternatives must be considered: tunneling may be involved in the transfer, or the reaction may involve a stepwise transfer of the two protons.

7.4.3.1 Tunneling

While tunneling may be a feature of proton or hydrogen transfer reactions even at room temperature,^{9,35-37} direct experimental detection of this quantum mechanical phenomenon in solution is often difficult. Indicators for tunneling include the breakdown of the rule of the geometric mean or other exponential relationships involving isotope effects, or the observation of nonlinear temperature dependence of isotope effects in Arrhenius plots.^{34,38-40} For example, a recent study of the ground-state intermolecular proton transfer (prototropic equilibria) of 7-hydroxyquinoline provides an illustration of affirmative experimental indicators for tunneling.⁴¹

In the case of 1AC, we have noted the breakdown of the rule of the geometric mean. And as noted earlier, the unusual temperature independence of the kinetic isotope effect does suggest proton tunneling. (The postulated reaction mechanism involves two steps: solvent fluctuations lead to a state from which tunneling occurs. Examining the temperature dependence of the (cumulative) observed rate constants on Arrhenius plots is not helpful since the rate constants corresponding to the elementary reaction involving the proton transfer have not been isolated.) Other observations of temperature-independent kinetic isotope effects have also been interpreted as reactions involving proton tunneling.⁴²⁻⁴⁵

The issue of proton tunneling has been considered by Limbach and coworkers in their careful examinations of double proton-transfer reactions in a number of well-defined, cyclically hydrogen-bonded systems.^{20-26,46} *Table 7.3* summarizes some of their work emphasizing the relationship between the experimental indicators for tunneling

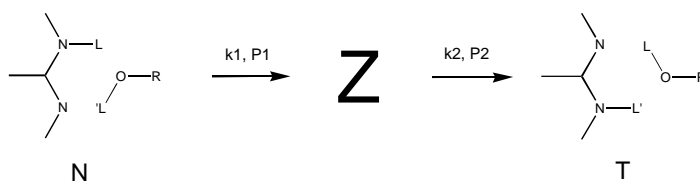
noted above and the mechanism of proton transfer deduced from each NMR study.

Their case studies of intermolecular proton transfer are good examples for comparison to the excited-state proton-transfer in systems involving 7AI and 1AC, and they highlight the difficulty in distinguishing a tunneling reaction from a stepwise transfer.

7.4.3.2 Stepwise Proton Transfer

To attribute the double-proton-transfer reaction of 1AC conclusively as a stepwise transfer, kinetic models must be examined for which the predictions are valid whether or not tunneling is present. For example, in a double-proton-transfer reaction in a *symmetric* complex, specific relationships among the observed rates have been derived that will indicate a stepwise reaction.^{21,22,27,47} These are valid for reactions over a barrier or for reactions proceeding through tunneling.²² Because of the symmetry of the reaction, the rate constants k_{HD} and k_{DH} are equal, and this is a necessary assumption of the derivations. The reaction of 1AC in alcohols is not symmetric, so the results of this particular example are not applicable to the 1AC reaction catalyzed by methanol. Further work with such kinetic models for consecutive stepwise proton transfers have not been fruitful.

Strong experimental evidence for stepwise double-proton transfer for 1AC in methanol is currently wanting. A consecutive, stepwise proton-transfer mechanism illustrated in *Scheme 7.3* suggests the presence of an intermediate before the tautomer species is finally formed.



Scheme 7.3

Biexponential decays have been reported for the excited-state proton transfer in 7AI dimers.^{55,57,58,66,67} These observations with subpicosecond time resolution have been interpreted to indicate the presence of an intermediate.⁵⁵⁻⁶⁴ (As discussed in Section 7.6, others have also offered different interpretations of the biexponential decays.) The time resolution of the time-correlated single-photon counting experiment used in the study of 1AC in mixed methanol solvents, however, is inadequate for revealing the possible presence of such an intermediate.

7.5 Discussion: Isotope Effects

The magnitude and temperature dependence of the kinetic isotope effects for 7AI and 1AC summarized in *Table 7.1* have already been discussed. Two final observations follow from this data. (1) The connection between the magnitude of primary isotope effects and the structure of the transition state has already entertained much discussion.^{39,48,49} Earlier work on proton dissociation reactions noted that the kinetic isotope effect is often *not* constant but depends on the relative activation energy in the transition state as determined by surrogate measures such as rate or equilibrium

constants.^{39,50-52} The estimated isotope effect for the ultrafast proton-transfer in 1AC:acetic acid complexes in methylcyclohexane is smaller (~2) than the observed KIE for the slower reaction in bulk alcohols (~5). If these differences are indeed real, then they provide evidence for the structure of the transition state, with the 1AC:acetic acid system having a more reactant-like transition state.

(2) Since the functional groups of 7AI and 1AC involved in the excited-state proton-transfer are the same, equal isotope effects for the two molecules in the same solvent might be expected. Interestingly, the isotope effects for 7AI and 1AC differ significantly in the alcohols. Although the source of this difference is currently unknown, future modeling of these isotope effects should provide additional insight into the nature of the excited-state reactions involving 7AI and 1AC.

The “proton inventory” experiments for 7AI in alcohols by Petrich and coworkers are consistent with a concerted reaction mechanism.²⁷ They concluded, however, that this reaction in water is qualitatively different than in bulk alcohols.²⁷ Note that the magnitude of the kinetic isotope effects reveals nothing obviously distinctive about the reaction of 7AI in water compared to 7AI in alcohols. In a similar comparison, the observed KIE for 1AC reactions in water and ethylene glycol are different than those for the bulk alcohols. Yet this thesis and other researchers⁵³ have argued that the 1AC reactions in water and ethylene glycol are not qualitatively different than those in bulk (primary) alcohols. This juxtaposition is a reminder that some caution is required in the interpretation of isotope effects.

7.6 Discussion: Stepwise or Concerted Reaction?

The observed rates of 1AC in the mixed solvent system methanol/methanol-OD, do not clearly support either a concerted or stepwise reaction mechanism. Since this experiment was completed, a number of papers have been published in support of either a stepwise or concerted reaction. The discussion has been intense.

Evidence for interpretation of a stepwise transfer has been reported by Hochstrasser and coworkers,⁵⁴ Zewail, Douhal and coworkers,⁵⁵⁻⁶¹ and Castleman and coworkers^{62-63,64} for the excited-state proton-transfer reaction in 7AI dimers in nonpolar solvents and in molecular beams. The photoelectron spectroscopy experiments of Lopez-Martens *et al.* are also taken as evidence for stepwise transfer.⁶⁵ On the other hand, Catalán, del Valle, and Kasha⁶⁹⁻⁷² and Takeuchi and Tahara^{66,67} argue that the double proton transfer reaction in 7AI dimers is a concerted reaction. Although these groups of researchers have already discussed the experimental evidence and its interpretations, a few observations are worthwhile to summarize here.

(1) Catalán, del Valle, and Kasha base their argument for a concerted reaction in gas-phase 7AI dimers on symmetry:⁶⁹

The lower state (S_{1a} , $2A_g$) in the C_{2h} geometry of the centro-symmetric planar H-bonded dimer is strictly electric-dipole forbidden for photon absorption from the ground state (S_0 , $1A_g$). The upper exciton split level is S_{1b} , B_u and is allowed as an electric-dipole photon absorption. The key observations on the reality of molecular exciton states were the definitive observation by Fuke *et al.* ...that, indeed, there is a two-photon allowed $1A_g \rightarrow 2A_g$ ($S_0 \rightarrow S_{1a}$) electronic excitation in 7-AI H-bonded dimer (supercooled molecular beam), followed at slightly higher energy by a one-photon-allowed $1A_g \rightarrow 1B_u$ ($S_0 \rightarrow S_{1b}$) electronic excitation.

...As a consequence, all wave functions must be centro-symmetric for the dimer, and the driving force for concerted PT likewise should be centro-

symmetric. This observation of a biphotonic absorption is the spectroscopic basis for a concerted biphotonic mechanism in the photo-excited 7-AI H-bonded dimer.

Douhal *et al.* have discussed the limitations of this argument and “emphatically contradict” their conclusions.⁵⁹ The lack of symmetry in the tautomerization reaction of 1AC in alcohols, diols, or water prevents the application of such an argument to the solvent-catalyzed reactions.

(2) An ultrafast biexponential decay in the fluorescence of reacting 7AI dimers in solution could indicate a stepwise reaction. Takeuchi and Tahara have observed such emission with subpicosecond resolution, but they have attributed the first quick lifetime (~200 fs) to internal conversion ($^1L_b \rightarrow ^1L_a$ transition) and the second 1.1 ps lifetime to the concerted proton transfer reaction.^{66,67} In a red-edge excitation experiment, the biexponential decays with blue excitation become single-exponential decays following excitation near the 0-0 transition. Takeuchi and Tahara explain that red-edge excitation selectively populates 1L_a state so that the ~200 fs lifetime in the biexponential decay vanishes.⁶⁷ In the fluorescence upconversion experiments of Fiebig *et al.*, red-edge excitation at 310 nm (*cf.* the 313 nm excitation in Takeuchi and Tahara’s experiment) also produces decays with one lifetime (~1 ps) that could be attributed to the reaction (the effective rate of formation of the tautomer).⁵⁸ However, Fiebig *et al.* declare the reaction to be stepwise based on transient absorption measurements following red-edge pump excitation (320 nm) which reveal biexponential character.⁵⁸ Fiebig *et al.* provide a summary of the interpretations of the observed rates. Near the 0-0 transition, the stepwise reaction $N \rightarrow I \rightarrow T^{\text{excited}}$ is observed with $k_1 \sim 200 \text{ fs}^{-1}$ and $k_2 \sim 1 \text{ ps}^{-1}$. The

relaxation of T^{excited} takes place within tens of picoseconds. The nanosecond background in the femtosecond-resolution experiments is due to the vibrationally-cold tautomer population decaying with lifetime 3.2 ns.⁵⁸

Excitation away from the red-edge of the absorption band may provide excess energy above the reaction barrier so that the normal forms the vibrationally-excited tautomer species directly ($N \rightarrow T^{\text{excited}}$).⁵⁸ Only when the internal energy is low, however, can one examine the processes of tunneling and concertedness.⁵⁸ And in the solution phase, the coupling of solvation dynamics to the symmetric and antisymmetric vibrational motion ($N-H\cdots N$) of the dimer must also be considered for the excited-state double-proton transfer reaction.⁵⁸ Thus the red-edge excitation is only selecting a special and appropriate subset of the dimers in solution for study, and the interpretation of the stepwise reaction depends on the experimental conditions.

(3) Two recent computer simulations of the excited-state reactions of 7AI dimers and 7AI:water complexes have indicated that a stepwise mechanism is most likely. Guallar *et al.* have used a semiclassical molecular dynamics simulation to show that in the isolated 7AI dimer the stepwise transfer is lower in energy than the route for the concerted transfer.⁶⁸ In this simulation, the intermediate is mostly covalent in character.⁶⁸ That is, the intermediate is not zwitterionic because an electron transfer accompanies the first proton-transfer. This work also indicates that the initial excitation is localized on one of the monomer sites.⁶⁸ In a different dynamics calculation, Fernandez-Ramos *et al.* learned that the tautomerization reaction of 7AI in aqueous solution likely requires the

participation of two water molecules.⁷³ Their best estimate is that the reaction is stepwise with one-proton tunneling occurring in the rate-determining first step.⁷³

7.7 Conclusion

Study of the excited-state proton-transfer reaction of 1AC in series of mixed methanol/methanol-OD solutions has afforded some insight into the mechanism of the reaction. The isotope effects at each of the reactive sites in 1AC appear to be independent of each other, although the magnitude of the isotope effects at each site are different. The KIE associated with the solute (1AC) is about 1.6, and the KIE associated with the solvent (MeOL, L = H or D) is about 3.3. Because the rates extracted from the experiment do not satisfy the “rule of the geometric mean,” the reaction does not obviously involve the concerted motion of both protons. This failure may indicate the presence of tunneling (in a concerted or a stepwise reaction) or of a stepwise reaction. The temperature dependence of the KIE does suggest that proton tunneling is present in the reaction. The data are unable to affirm, however, either a (tunneling) concerted or stepwise reaction mechanism. Several published studies do suggest that a stepwise reaction mechanism may be preferred to describe the excited-state tautomerization reaction of 7AI (and thus 1AC presumably as well).

Table 7.1: Summary of Isotope Effects for 7AI and 1AC

System	Solvent	KIE: Reaction Rate (Normal)	KIE: Tautomer Deactivation	Reference
7AI	Alcohols	2.9 ± 0.6	1.3 ± 0.1	1, 3
7AI	Ethylene Glycol	2 ± 0.1	1.4 ± 0.1	3, 7
7AI	Water	3.7, 3.4	2 ± 1	1, 2
7AI Dimers	Hexadecane	2.9		6
7AI Dimers	Nonpolar solvents	4.5 N, "direct" 1.4 T, "rise"		5 5
<hr/>				
1AC	Alcohols	4.9 ± 0.3	1.6 ± 0.2	4
1AC	Methanol	IE(solvent) = 3.4 IE(solute) = 1.6		7 7
1AC	Ethylene Glycol	3.0	1.4	7
1AC	Water	3.2	*	7
1AC:Acetic Acid Complexes	Methylcyclohexane	~ 2 *	1.6	7

* This is the best estimate for the isotope effect. The rates were not measured directly due to limited time resolution of the experiment.

- (1) Y. Chen, F. Gai, and J. W. Petrich, *J. Am. Chem. Soc.*, **115**, 10158 (1993).
- (2) C. F. Chapman and M. Maroncelli, *J. Phys. Chem.*, **96**, 8430 (1992).
- (3) R. S. Moog and M. Maroncelli, *J. Phys. Chem.*, **95**, 10359 (1991).
- (4) S. J. Boryschuk, M. S. Thesis, The Pennsylvania State University, 1993.
- (5) M. Chachisvilis, T. Fiebig, A. Douhal, and A. H. Zewail, *J. Phys. Chem. A*, **102**, 669. (1998).
- (6) P. Share, M. Periera, M. Sarisky, S. Repinec, and R. M. Hochstrasser, *J. Luminescence.*, **48/49**, 204 (1991).
- (7) Isotope effects estimated in this dissertation.

Table 7.2: Determination of Rate Constants for 1AC in Methanol / Methanol-OD Mixtures

X(MeOD)	Unconstrained Fits				Fixed				mean $1/\tau_1=k^H$ 10^9 s^{-1}	mean $1/\tau_2=k^D$ 10^9 s^{-1}
	a_1	a_2	τ_1 (ns)	τ_2 (ns)	A_1 $1-X_D$	A_2 X_D	τ_1 (ns)	τ_2 (ns)		
0.00	1.00		0.50				0.50		2.00	
0.00	1.00		0.50				0.50			
0.00	1.00		0.50				0.50			
0.13	0.97	0.03	0.58	1.35	0.88	0.13	0.55	0.94	1.81	1.07
0.25	0.88	0.12	0.67	1.14	0.75	0.25	0.63	0.99	1.58	0.993
0.25	0.85	0.15	0.66	1.14	0.75	0.25	0.63	1.02		
0.33	0.66	0.34	0.67	1.09	0.67	0.33	0.67	1.09	1.49	0.917
0.50	0.30	0.70	0.69	1.19	0.50	0.50	0.82	1.27	1.22	0.779
0.50	0.61	0.39	0.88	1.36	0.50	0.50	0.83	1.30		
0.67	0.20	0.80	0.77	1.52	0.33	0.67	0.95	1.58	1.05	0.633
0.75	0.16	0.84	0.90	1.69	0.25	0.75	1.06	1.73	0.932	0.573
0.75	0.29	0.71	1.13	1.78	0.25	0.75	1.08	1.76		
0.88	0.10	0.90	0.66	2.06	0.13	0.88	0.85	2.09	1.18	0.478
1.00		1.00		2.51				2.51		0.399
1.00		1.00		2.50				2.50		
1.00		1.00		2.51				2.51		
1.00		1.00		2.51				2.51		

Table 7.3: Double-Proton Transfer Studies by Limbach and Coworkers

System	Type of transfer	Rule of the Geometric Mean?	Arrhenius Plots	Concluded Mechanism	Reference
Bis (p-fluorophenyl)formaminide dimers	inter	Yes	observed linear; IE temperature dependent	concerted, or stepwise with compressed H-bonds	1
Acetic Acid + Methanol in THF, 1:1	inter	No	observed linear; IE temperature dependent	intermolecular tunneling	2
Acetic Acid + Methanol in THF, 2:1	inter	Yes	observed linear; IE temperature independent	intermolecular tunneling	2
Azophenine	intra	No	observed linear; IE temperature independent	stepwise transfer	3
Oxalamidines	intra	No	observed linear; IE temperature independent	stepwise transfer	4
Porphyrin	intra	No	observed linear, except at very low temperature; IE temperature dependent	stepwise transfer	5
Acetylporphyrin	intra	No	observed linear; IE temperature dependent	stepwise transfer	6
meso-Tetraphenylprophyrin	intra	No	observed nonlinear; IE temperature dependent	stepwise transfer	7

¹ L. Meschede and H.-H. Limbach, *J. Phys. Chem.*, **95**, 10267, 1991.

² D. Gerritzen and H.-H. Limbach, *J. Am. Chem. Soc.*, **106**, 869 (1984).

³ H. Rumpel and H.-H. Limbach, *J. Am. Chem. Soc.*, **111**, 5429 (1989).

⁴ G. Scherer and H.-H. Limbach, *J. Am. Chem. Soc.*, **116**, 1230 (1994).

⁵ J. Braun, M. Schlabach, B. Wehrle, M. Köcher, E. Vogel, and H.-H. Limbach, *J. Am. Chem. Soc.*, **116**, 6593 (1994).

⁶ M. Schlabach, H.-H. Limbach, E. Bunnenberg, A. Y. L. Shu, B.-R. Tolf, and C. Djerassi, *J. Am. Chem. Soc.*, **115**, 4554 (1993).

⁷ M. Schlabach, B. Wehrle, H. Rumpel, J. Braun, G. Scherer, and H.-H. Limbach, *Ber. Bunsenges. Phys. Chem.*, **96**, 821 (1992).

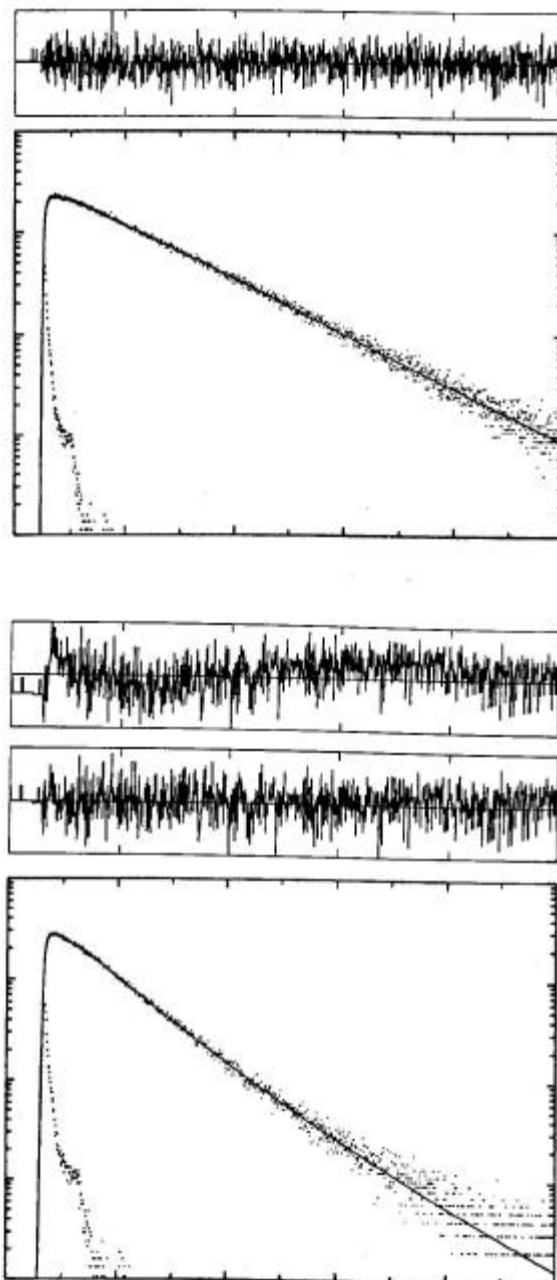


Figure 7.1: Time-Resolved Emission Spectra of PPO in Methanol and 1AC in Methanol/Methanol-OD Mixtures

Top Spectrum: PPO in dilute methanol solution decays with a single-exponential lifetime of 1.52 ns ($\chi^2 = 1.06$). This fluorescence standard provides a convenient means for confirming the time calibration and linearity of the photon-counting spectrometer.

Bottom Spectrum: 1AC in 75:25 MeOH:MeOD Mixture. One lifetime is inadequate for fitting the emission decay (upper panel of residuals: $\chi^2 = 1.48$), but the residuals in the lower panel indicate a good fit with two lifetimes ($\chi^2 = 1.08$).

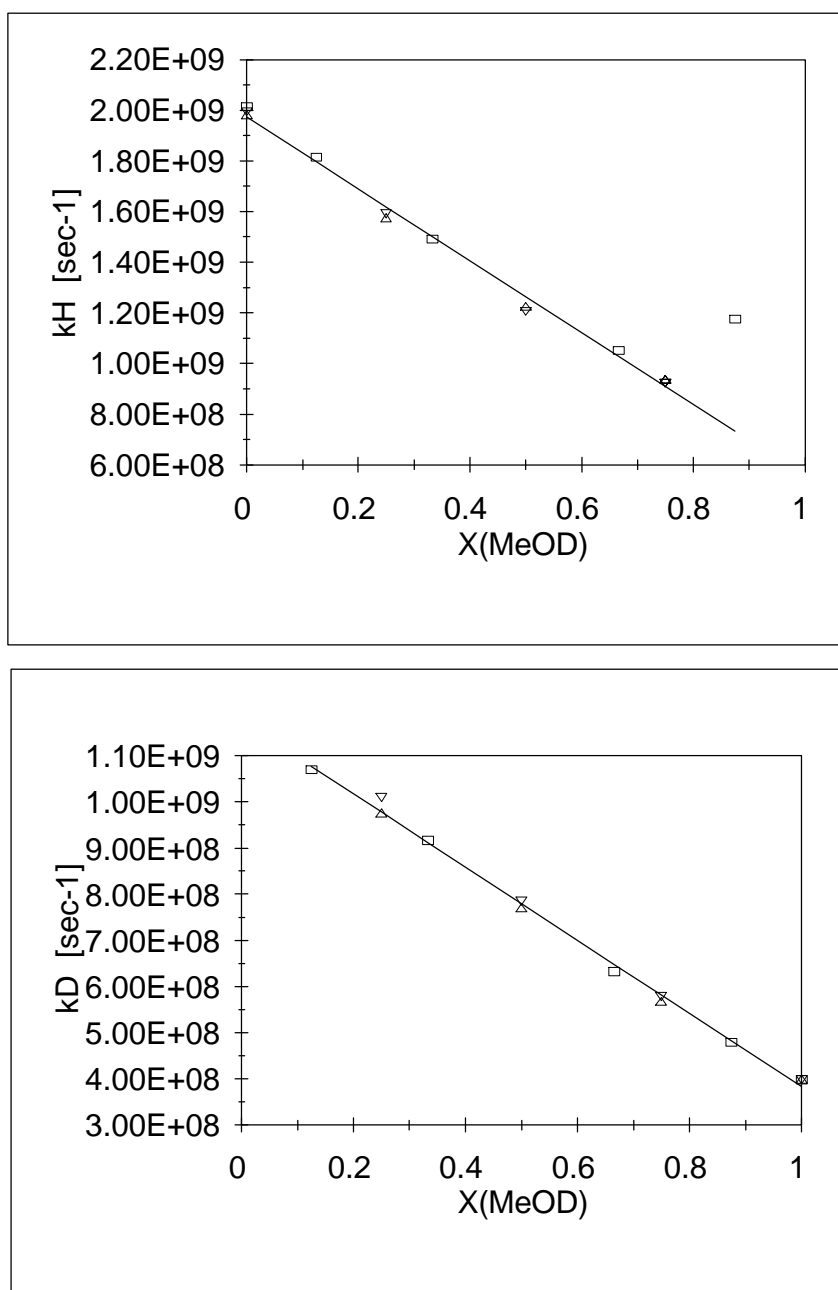


Figure 7.2: Reaction Rates of 1AC in Methanol/Methanol-OD Mixtures

These plots exhibit the linear dependence of the extracted rates with the solvent composition as predicted by the model discussed in Chapter 7. The different symbols represent independent measurements made for each solvent mixture, and the lines are least-squares fits to mean rates.

ENDNOTES

- ¹ For an introduction to isotope effects, see for example: T. H. Lowry and K. S. Richardson, *Mechanism and Theory in Organic Chemistry, Third Edition*, (New York, HarperCollinsPublishers, 1987). Section 2.9.
- ² L. Melander and W. H. Saunders, Jr., *Reaction Rates of Isotopic Molecules*. (New York, John Wiley & Sons, 1980).
- ³ C. J. Collins and N. S. Bowman, Eds., *Isotope Effects in Chemical Reactions*. ACS Monograph 167. (New York, Van Nostrand Reinhold, 1970).
- ⁴ A recent popular survey of the importance of isotope effects is: A. M. Rouhi, "The world of isotope effects." *C&EN*, 22 December 1997, 38-42.
- ⁵ H. Shirota, H. Pal, K. Tominaga, and K. Yoshihara, *J. Phys. Chem.*, **100**, 14575 (1996).
- ⁶ C. F. Chapman, Ph. D. Thesis, The Pennsylvania State University, 1993.
- ⁷ S. J. Boryschuk, M. S. Thesis, The Pennsylvania State University, 1993.
- ⁸ See pp. 2761-2762 of A. V. Smirnov, D. S. English, R. L. Rich, J. Lane, L. Teyton, A. W. Schwabacher, S. Luo, R. W. Thornburg, and J. W. Petrich, *J. Phys. Chem. B.*, **101**, 2758 (1997).
- ⁹ J. Sühnel and R. L. Schowen, "Theoretical basis for primary and secondary hydrogen isotope effects" in P. F. Cook, Ed., *Enzyme Mechanisms from Isotope Effects* (Boca Raton, FL, CRC Press, 1991).
- ¹⁰ J. Albery in *Proton Transfer Reactions*. [E. Caldin and V. Gold, Eds.] (London, Chapman and Hall, 1975). p. 263.
- ¹¹ J. G. Belasco, W. J. Albery, and J. R. Knowles, *Biochem.*, **25**, 2552, (1986).
- ¹² J. D. Hermes, C. A. Roeske, M. H. O'Leary, W. W. Cleland, *Biochem.*, **21**, 5106 (1982).
- ¹³ V. Gold, *Adv. Phys. Org. Chem.*, **7**, 259 (1969).
- ¹⁴ A. J. Kresge, *Pure Appl. Chem.*, **8**, 243 (1964).

- ¹⁵ A. J. Kresge, R. A. More O'Ferrall, and M. F. Powell in *Isotopes in Organic Chemistry, Volume 7: Secondary and Solvent Isotope Effects*. [E. Buncl and C. C. Lee, Eds.] (Amsterdam, Elsevier, 1987). p. 177.
- ¹⁶ K. S. Venkatasubban and R. L. Schowen, *Crit. Rev. Biochem.*, **17**, 1, (1984).
- ¹⁷ K. B. Schowen and R. L. Schowen, *Methods. Enzymol.*, **87**, 551 (1982).
- ¹⁸ K. B. J. Schowen, in *Transition State of Biochemical Processes*. [R. D. Gandour and R. L. Schowen, Eds.] (New York, Plenum, 1978). p.254.
- ¹⁹ R. L. Schowen in *Isotope Effects on Enzyme-Catalyzed Reactions*. [W. W. Cleland, M. H. O'Leary, and D. B. Northrop, Eds.] (Baltimore, University Park Press, 1977.) p. 64.
- ²⁰ L. Meschede and H.-H. Limbach, *J. Phys. Chem.*, **95**, 10267, 1991.
- ²¹ D. Gerritzen and H.-H. Limbach, *J. Am. Chem. Soc.*, **106**, 869 (1984).
- ²² H. Rumpel and H.-H. Limbach, *J. Am. Chem. Soc.*, **111**, 5429 (1989).
- ²³ G. Scherer and H.-H. Limbach, *J. Am. Chem. Soc.*, **116**, 1230 (1994).
- ²⁴ J. Braun, M. Schlabach, B. Wehrle, M. Köcher, E. Vogel, and H.-H. Limbach, *J. Am. Chem. Soc.*, **116**, 6593 (1994).
- ²⁵ M. Schlabach, H.-H. Limbach, E. Bunnenberg, A. Y. L. Shu, B.-R. Tolf, and C. Djerassi, *J. Am. Chem. Soc.*, **115**, 4554 (1993).
- ²⁶ M. Schlabach, B. Wehrle, H. Rumpel, J. Braun, G. Scherer, and H.-H. Limbach, *Ber. Bunsenges. Phys. Chem.*, **96**, 821 (1992).
- ²⁷ Y. Chen, F. Gai, and J. W. Petrich, *J. Am. Chem. Soc.*, **115**, 10158 (1993).
- ²⁸ M. Maroncelli, unpublished notes.
- ²⁹ (a) The dissociation rate of the N-H proton from 7AI is estimated to be on the order of milliseconds. M. Maroncelli, unpublished notes. (b) In the original analysis of the proton-inventory experiment for 7AI in Endnote 27, it was noted that the N₁-H proton of ground-state indole exchanges with the solvent on the order of seconds.
- ³⁰ (a) The expected exchange rate of two alcohol molecules is ~10-100 ps. M. Maroncelli, unpublished notes. (b) The 1AC experiments in mixed methanol-water also demonstrated that the observed rates are consistent with this rapid exchange limit.

- ³¹ This is equivalent to the assumption that the fractionation factor $\phi^R = 1$. For additional discussion, see Endnotes 18 and 27.
- ³² The one deviant point in the plot of k^H vs. X_D was excluded from the linear regression because the rate was significantly greater (~50%) than expected. The origin of this discrepancy remains unknown.
- ³³ J. Bigeleisen, *J. Chem. Phys.*, **23**, 2264 (1955).
- ³⁴ J. P. Klinman in *Enzyme Mechanism from Isotope Effects*. P. F. Cook, Ed. (Boca Raton, FL, CRC Press, Inc., 1991).
- ³⁵ Note the recent discussions in “Hydrogen Transfer: Experiment and Theory.” *Ber. Bunsenges. Phys. Chem.*, **102** (1998).
- ³⁶ A. Douhal, F. Lahmani, and A. H. Zewail, *Chem. Phys.*, **207**, 477 (1996).
- ³⁷ A. Douhal, *Science*, **276**, 221 (1997).
- ³⁸ R. P. Bell, *The Tunnel Effect in Chemistry*. (London, Chapman and Hall, 1980). Sections 3.7, 4.3.5, 5.5 and 7.2.
- ³⁹ R. A. More O’Farrell in *Proton Transfer Reactions*. [E. Caldin and V. Gold, Eds.] (London, Chapman and Hall, 1975). p. 201.
- ⁴⁰ H. Kwart, *Acc. Chem. Res.*, **15**, 401 (1982).
- ⁴¹ T.-G. Kim, S.-I. Lee, D.-J. Jang, and Y. Kim, *J. Phys. Chem.*, **99**, 12698 (1995).
- ⁴² J. Konijnenberg, A. H. Huizer, F. Th. Chaudron, C. A. G. O. Varma, B. Marciniak, and S. Paszyc, *J. Chem. Soc., Faraday Trans. 2.*, **83**, 1475 (1987).
- ⁴³ J. Konijnenberg, G. B. Ekelmans, A. H. Huizer, and C. A. G. O. Varma, *J. Chem. Soc., Faraday Trans. 2.*, **85**, 39 (1989).
- ⁴⁴ A. J. G. Strandjord and P. F. Barbara, *Chem. Phys. Lett.*, **98**, 21 (1983).
- ⁴⁵ A. J. G. Strandjord and P. F. Barbara, *J. Phys. Chem.*, **89**, 2355 (1985).
- ⁴⁶ H.-H. Limbach and J. Manz, *Ber. Bursenges. Phys. Chem.*, **102**, 289 (1998).

- ⁴⁷ H.-H. Limbach, J. Hennig, D. Gerritzen, and H. Rumpel, *Faraday Discuss. Chem. Soc.*, **74**, 229 (1982).
- ⁴⁸ F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).
- ⁴⁹ W. J. Albery, *J. Phys. Chem.*, **90**, 3774 (1986).
- ⁵⁰ See for example, M. M. Kreevoy and S. Oh, *J. Am. Chem. Soc.*, **95**, 4805 (1973).
- ⁵¹ A. J. Kresge, *J. Am. Chem. Soc.*, **102**, 7797 (1980).
- ⁵² A. J. Kresge, *Pure & Appl. Chem.*, **53**, 189 (1981).
- ⁵³ S. Mente and M. Maroncelli, *J. Phys. Chem. A*, **102**, 3860-3876 (1998).
- ⁵⁴ P. Share, M. Periera, M. Sarisky, S. Repinec, and R. M. Hochstrasser, *J. Lumin.*, **48/49**, 204 (1991).
- ⁵⁵ A. Douhal, S. K. Kim, and A. H. Zewail, *Nature*, **378**, 260 (1995).
- ⁵⁶ A. Douhal, V. Guallar, M. Moreno, and J. M. Lluch, *Chem. Phys. Lett.*, **256**, 370 (1996).
- ⁵⁷ M. Chachisvilis, T. Fiebig, A. Douhal, and A. H. Zewail, *J. Phys. Chem. A*, **102**, 669 (1998).
- ⁵⁸ T. Fiebig, M. Chachisvilis, M. Manger, A. H. Zewail, A. Douhal, I. Garcia-Ochoa, A. de La Hoz Ayuso, *J. Phys. Chem. A*, **103**, 7419-7431 (1999).
- ⁵⁹ Douhal, M. Moreno, and J. M. Lluch, *Chem. Phys. Lett.*, **324**, 75-80 (2000).
- ⁶⁰ Douhal, M. Moreno, and J. M. Lluch, *Chem. Phys. Lett.*, **324**, 81-87 (2000).
- ⁶¹ M. Moreno, A. Douhal, J. M. Lluch, O. Castano, and L. M. Frutos, *J. Phys. Chem. A*, **105**, 3887-3893 (2001).
- ⁶² M. Roubi, *C&EN*, **23 February 1998**, p. 17-18. [News of Castleman and coworkers establishment of a stepwise double-proton transfer in 7AI dimers using Coulomb explosion experiment.]
- ⁶³ D. E. Folmer, L. Poth, E. S. Wisniewski, and A. W. Castleman Jr., *Chem. Phys. Lett.*, **287**, 1-7 (1998).

- ⁶⁴ D. E. Folmer, E. S. Wisniewski, and A. W. Castleman Jr., *Chem. Phys. Lett.*, **318**, 637-643 (2000).
- ⁶⁵ R. Lopez-Martens, P. Long, D. Solgadi, B. Soep, J. Syage, and Ph. Millie, *Chem. Phys. Lett.*, **273**, 219-226 (1997).
- ⁶⁶ S. Takeuchi and T. Tahara, *J. Phys. Chem. A*, **102**, 7740-7753 (1998).
- ⁶⁷ S. Takeuchi and T. Tahara, *Chem. Phys. Lett.*, **347**, 108-114 (2001).
- ⁶⁸ V. Guallar, V. S. Batista, and W. H. Miller, *J. Chem. Phys.*, **110**, 9922-9936 (1999).
- ⁶⁹ J. Catalan, J. C. del Valle, and M. Kasha, *Proc. Natl. Acad. Sci. USA*, **96**, 8338-8343 (1999).
- ⁷⁰ J. Catalan, J. C. del Valle, and M. Kasha, *Chem. Phys. Lett.*, **318**, 629-636 (2000).
- ⁷¹ J. C. del Valle, M. Kasha, and J. Catalan, *Int. J. Quant. Chem.*, **77**, 118-127 (2000).
- ⁷² J. Catalan and M. Kasha, *J. Phys. Chem. A*, **104**, 10812-10820 (2000).
- ⁷³ A. Fernandez-Ramos, Z. Smedarchina, W. Siebrand, and M. Z. Zgierski, *J. Chem. Phys.*, **114**, 7518-7526 (2001).