Direct Observation of C–C Bond Fragmentation in α-Amino Alcohol Radical Cations

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The kinetics of heterolytic fragmentation of the 1,2 C–C bond in the radical cations of *erythro-* and *threo-* 2-(*N*-phenylamino)-1,2-diphenylethanol (*e*-1 and *t*-1, respectively) have been directly determined by using laser flash photolysis. The 298 K rates and activation parameters are as follows (CH$_3$CN solution): $k_{BF}(e\text{-}1^{\bullet+}) = 4.3$ (1) $\times 10^5$ s^{-1}, $\Delta H^{\ddagger}_{BF}(e\text{-}1^{\bullet+}) = 7.6$ (1) kcal, $\Delta S^{\ddagger}_{BF}(e\text{-}1^{\bullet+}) = -9$ (4) em; $k_{BF}(t\text{-}1^{\bullet+}) = 2.6$ (1) $\times 10^5$ s^{-1}, $\Delta H^{\ddagger}_{BF}(t\text{-}1^{\bullet+}) = 4.8$ (1) kcal, $\Delta S^{\ddagger}_{BF}(t\text{-}1^{\bullet+}) = -19$ (4) eu. Fragmentation of *e*-1$^{\bullet+}$ is catalyzed by a series of substituted pyridines. A linear Brønsted correlation (log k_{base} vs pK_a, $\beta = 0.62$) indicates that under base-catalyzed conditions endothermic H$^+$ transfer from *e*-1$^{\bullet+}$ to base is the rate-determining step for C–C bond fragmentation.

Introduction

There has been considerable recent interest in the kinetics of rearrangement and fragmentation in radical ions.[1-8] This interest has stemmed in part from the fact that radical ion reactions provide "clocks" that allow the determination of back electron transfer (ET) rates in radical ion pairs formed by photoinduced electron transfer (PET).[9-35]

In a recent series of investigations, Whitten and co-workers used photosensitizers to generate radical cations of α-amino alcohols (α-AA$^{\bullet+}$) by PET.[36-40] This work demonstrated that C–C bond fragmentation in α-AA$^{\bullet+}$ competes effectively with back ET. Product and quantum yield studies indicate a reaction sequence that is initiated by heterolytic C–C bond fragmentation of α-AA$^{\bullet+}$ producing an α-amino radical (α-A$^{\bullet}$), a carbonyl compound, and H$^+$ (eq 1).[36-40] Their steady-state experiments also suggest that (1) the rates of C–C fragmentation (k_{BF}) in α-AA$^{\bullet+}$ range from 10^5 to 10^7 s^{-1}, (2) the sensitizer radical anions act as bases, accelerating C–C bond fragmentation in α-AA$^{\bullet+}$ by deprotonating the hydroxy group, and (3) *erythro*-α-AA$^{\bullet+}$ fragments faster than the corresponding *threo* diastereomer.

$$\text{α-AA}^{\bullet+} \longrightarrow \text{α-A}^{\bullet} + \overset{\text{O}}{\underset{}{\text{C}}} + \text{H}^+ \qquad (1)$$
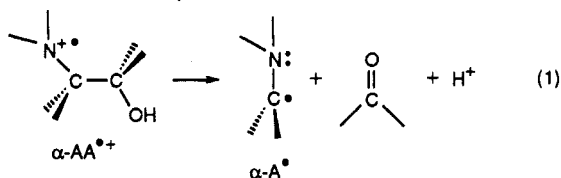
As part of a program which seeks to develop reactive electron donor ligands that can be used as "clocks" to investigate the electronic structure and dynamics of charge-transfer excited states in metal complexes,[41,42] we have directly determined the rate of C–C bond fragmentation in radical cations of the diastereomeric pair of α-AAs, *e*-1 and *t*-1. The present report demonstrates that at 298 K *e*-1$^{\bullet+}$ and *t*-1$^{\bullet+}$ fragment with $k_{BF} \approx$ (2-4) $\times 10^5$ s^{-1}, in good agreement with the k_{BF} range predicted by the prior studies. Examination of k_{BF} for *e*-1$^{\bullet+}$ in the presence of a series of substituted pyridine bases clearly demonstrates that under these conditions deprotonation of the hydroxy group by base is the rate determining step for C–C bond fragmentation.

Experimental Section

Details concerning the synthesis and characterization of *e*-1 and *t*-1 are available as supplementary material. *t*-1-OD was prepared by dissolving *t*-1 in a mixture of CDCl$_3$ and D$_2$O (5:1
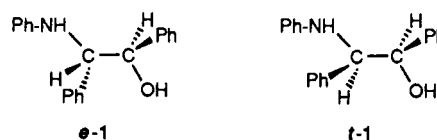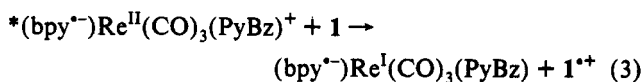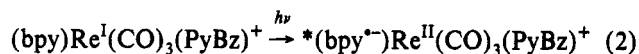

v:v) and swirling the mixture for 30 min. The metal complex photosensitizer [*fac*-(bpy)Re^I(CO)$_3$(PyBz)][PF$_6$] (bpy is 2,2'-bipyridine and PyBz is 4-benzylpyridine, acronym = **Re**) was prepared and purified as previously described.[43]

The laser flash photolysis apparatus has been previously described.[44] All experiments were carried out using the third harmonic of a Q-switched Nd:YAG laser for excitation (355 nm, 6 ns fwhm, 2 mJ/pulse). Solutions were contained in a recirculating flow cell that accommodates 100-mL volume. Degassing was effected by purging the solutions with Ar for 1 h. Temperature-dependent rates were measured by using a water-jacketed flow cell that was cooled using a recirculating refrigerated bath (glycol/water). Kinetic analysis was carried out using the KINFIT program on a PC compatible computer.[45]

Results and Discussion

Radical cations *e*-1$^{\bullet+}$ and *t*-1$^{\bullet+}$ were generated by laser flash photolysis of *e*-1 and *t*-1 in the presence of metal complex sensitizer **Re**. Pulsed 355-nm excitation of a degassed CH$_3$CN solution containing **Re** ($c = 2 \times 10^{-5}$ M, OD$_{355}$ = 0.2) and **1** ($c = 10$ mM) produces the metal-to-ligand charge-transfer excited state of the sensitizer (eq 2) which is subsequently quenched by rapid ET from **1** producing reduced metal complex and radical cation **1**$^{\bullet+}$ (eq 3).[46]

$$\text{(bpy)Re}^I\text{(CO)}_3\text{(PyBz)}^+ \xrightarrow{h\nu} \text{*(bpy}^{\bullet-}\text{)Re}^{II}\text{(CO)}_3\text{(PyBz)}^+ \quad (2)$$

$$\text{*(bpy}^{\bullet-}\text{)Re}^{II}\text{(CO)}_3\text{(PyBz)}^+ + \mathbf{1} \rightarrow$$
$$\text{(bpy}^{\bullet-}\text{)Re}^I\text{(CO)}_3\text{(PyBz)} + \mathbf{1}^{\bullet+} \quad (3)$$

A series of transient absorption spectra of a mixture of *e*-1 and **Re** at 1–6-μs delay after laser excitation are shown in Figure 1. At 1-μs delay the spectrum is characterized by weak absorption throughout the near-UV and visible. This transient absorption spectrum is assigned to a mixture of the reduced metal complex sensitizer, (bpy$^{\bullet-}$)Re^I(CO)$_3$(PyBz), and the radical cation, *e*-1$^{\bullet+}$. The spectrum evolves during the 1 → 6 μs time scale to produce a new spectrum having a strong absorption band in the near-UV ($\lambda_{max} \approx 360$ nm) and decreased absorption in the mid-visible
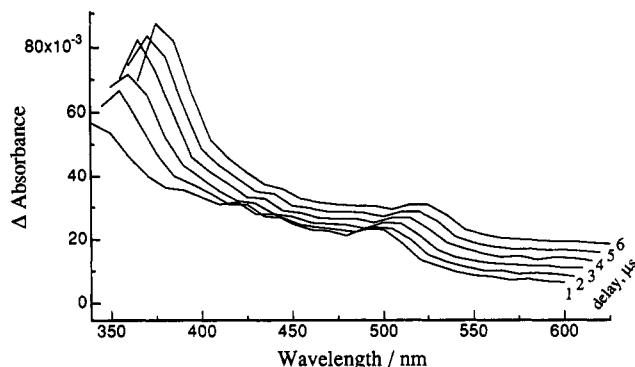
Figure 1. Transient absorption spectra of Re and e-1 in degassed CH_3-CN; [Re] = 2 × 10⁻⁵ M (OD_{355} ≈ 0.2), [e-1] = 10 mM. Third harmonic Q-switched Nd:YAG laser excitation (355 nm, 6 ns fwhm, 2 mJ/pulse). Spectra obtained at the following delay times following laser pulse: 1, 2, 3, 4, 5, and 6 µs. Note that plots are shifted successively 5 nm to longer wavelength to facilitate display.
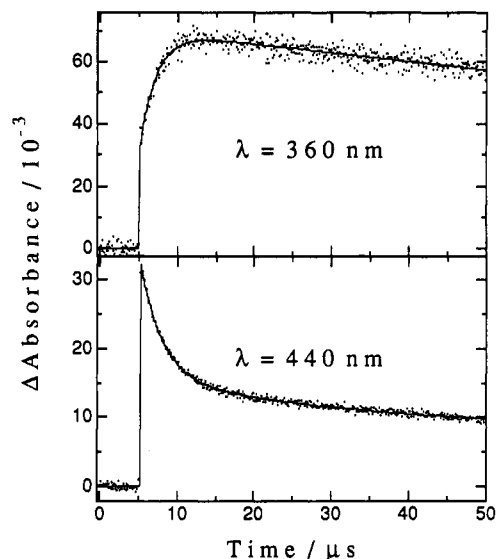

Figure 2. Transient absorption kinetics for same sample and conditions as used in Figure 1: upper trace, λ = 360 nm; lower trace, λ = 440 nm.

(400–480 nm). Figure 2 illustrates the temporal profile of the transient absorption signals at 360 and 440 nm. At both wavelengths a fast process occurs within 10 µs of excitation that leads to production of species that are comparatively stable on the 50-µs time scale. The solid lines in Figure 2 were calculated using a two-exponential expression; in both cases the fast rise (or decay) component is fitted using a rate constant of 4.3 × 10⁵ s⁻¹.[47]

The changes observed within 10 µs of excitation are attributed to bond fragmentation in e-1•⁺

$$e\text{-}1^{\bullet+} \xrightarrow{k_{BF}} Ph\text{–}NH\text{–}\overset{\bullet}{C}H\text{–}Ph + Ph\text{–}CHO + H^+ \qquad (4)$$
$$\mathbf{2}$$
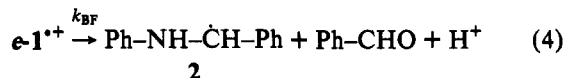
Aniline radical cation e-1•⁺ should absorb in the blue region of the visible spectrum;[48] the decrease in absorption observed between 400 and 480 nm (Figure 2) is consistent with destruction of this chromophore by C–C bond fragmentation. Radical 2 is an amine-substituted benzyl radical and should absorb in the near-UV; on this basis the strong absorption that grows in at 360 nm (Figure 2) is attributed to 2.[49]

Based on the above analysis, the 360-nm rise component and the 440-nm fast decay component are assigned to bond fragmentation, $k_{BF}(e\text{-}1^{\bullet+})$ = 4.3 (1) × 10⁵ s⁻¹. Laser flash photolysis of t-1 with sensitizer Re gives rise to dynamic near-UV and visible spectroscopic features that are essentially identical to those observed for e-1. By fitting the fast decay component observed at 440 nm for this diastereomer, $k_{BF}(t\text{-}1^{\bullet+})$ = 2.6 (1) × 10⁵ s⁻¹,
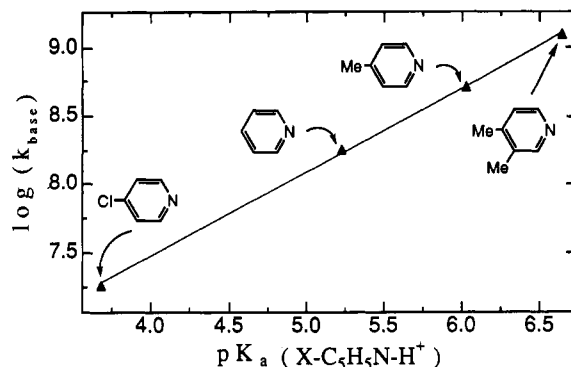

Figure 3. Brønsted plot (log k_{base} vs pK_a) for fragmentation of e-1 in CH_3CN solution.

which is slightly, but reproducibly, smaller than k_{BF} for e-1•⁺. The activation parameters for C–C bond fragmentation in e-1•⁺ and t-1•⁺, determined from the temperature dependence of the fast decay component at 440 nm over the range from –15 to 35 °C, are $\Delta H^\ddagger_{BF}(e\text{-}1^{\bullet+})$ = 7.6 (1) kcal, $\Delta S^\ddagger_{BF}(e\text{-}1^{\bullet+})$ = –9 (4) eu, $\Delta H^\ddagger_{BF}(t\text{-}1^{\bullet+})$ = 4.8 (1) kcal, and $\Delta S^\ddagger_{BF}(t\text{-}1^{\bullet+})$ = –19 (4) eu.

The decay rate of e-1•⁺ was determined as a function of the concentration of a series of substituted pyridine bases in CH_3CN solution. Bond fragmentation in e-1•⁺ is accelerated substantially by even moderately low concentrations of pyridine bases. The decay rate of e-1•⁺ (k_{obs}) was analyzed by the equation k_{obs} = k_{BF} + k_{base}[base], which assumes that the base-catalyzed pathway operates in parallel with unimolecular fragmentation. Plots of k_{obs} vs [base] were linear for each of the four substituted pyridines, and values of k_{base} were determined from the slope of the plots. Figure 3 illustrates a plot of log (k_{base}) vs the pK_a of the conjugate acid of the substituted pyridine bases (Brønsted correlation); an excellent linear correlation is observed with a slope of 0.62 (Brønsted β).[50]

Previous studies of photosensitized oxidation of α-AAs indicate that in solution bond fragmentation occurs via C–C bond heterolysis as shown in eq 1.[36–40] The strong near-UV absorption attributed to radical 2 that appears concurrent with C–C bond fragmentation of 1•⁺ supports this mechanistic view.

The relatively rapid rate and low $\Delta H^\ddagger_{BF}$ for fragmentation of e-1•⁺ indicates that single electron oxidation of these isomeric α-AAs significantly decreases the strength of the 1,2 C–C σ bond. While the present experiments do not allow determination of the free energy for bond heterolysis in 1•⁺ ($\Delta G^{1^{\bullet+}}_{BF}$), because $\Delta G^{1^{\bullet+}}_{BF}$ must be ≤ $\Delta G^\ddagger_{BF}$, the 298 K rates indicate that an upper limit for $\Delta G^{1^{\bullet+}}_{BF}$ is +10 kcal/mol. Literature information is unavailable to allow estimation of the C–C bond energy in 1. However, using the bond energy of 2-aminoethanol (80 ± 2 kcal) as a guide[51–53] and estimating that 1,2-diphenyl substitution decreases the C–C bond strength by approximately 15–25 kcal suggests that the 1,2 C–C σ bond energy in 1 is 55–65 kcal/mol. This estimate indicates that single electron oxidation of 1 weakens the C–C bond by ≥40–50 kcal.

The relatively large negative $\Delta S^\ddagger_{BF}$ values for e-1•⁺ and t-1•⁺ are substantially more negative than values typically observed for solution- and gas-phase bond homolysis reactions.[54] However, the $\Delta S^\ddagger_{BF}$ values are comparable to those typically observed for heterolytic fragmentation of neutral and charged substrates in solution.[2,55] The negative $\Delta S^\ddagger_{BF}$ values for e-1•⁺ and t-1•⁺ suggest that as the reaction proceeds there is substantial positive charge localization (possibly at the hydroxy oxygen) leading to organization of polar solvent molecules.

Previous work indicated that for 1,2-diphenyl-substituted α-AAs *erythro* isomers fragment 2–4 times more efficiently at 298 K compared to the corresponding *threo* diastereomers.[36,37,40] Consistent with the previous work, the present study reveals that at 298 K e-1•⁺ fragments approximately 2 times more slowly

than t-$1^{\bullet+}$. In addition, the two diastereomers display a significantly different temperature dependence of k_{BF} as reflected by lower $\Delta H^{\ddagger}{}_{BF}$ and more negative $\Delta S^{\ddagger}{}_{BF}$ for t-$1^{\bullet+}$ compared to e-$1^{\bullet+}$. Note that the results indicate an "isokinetic relationship"[50] between the activation parameters for the two diastereomers: the lower $\Delta H^{\ddagger}{}_{BF}$ for t-$1^{\bullet+}$ compared to that for e-$1^{\bullet+}$ is partially compensated by a more negative $\Delta S^{\ddagger}{}_{BF}$.

The increased reactivity of the *threo* diastereomer was previously attributed to the requirement that in the transition state for fragmentation the hydroxy and amino groups must be *anti* with respect to the N–C–C–O dihedral angle. It was argued that the reactive *anti* conformation is less stable in the *threo* diastereomer due to an unfavorable steric interaction between the vicinal phenyl substituents; this interaction raises the energy of the transition state relative to the energetically preferred conformation of the radical cation.[37,40] An alternative explanation for the increased reactivity of *erythro* is that the radical cation reactant is more stable in the *threo* diastereomer. In support of this argument, preliminary *ab initio* calculations (HF/STO-3G level) on the radical cation of 2-aminoethanol indicate that in the gas phase the conformation in which the hydroxy and amino groups are *syn* is by far the most energetically stable conformation. Note that in the *syn* conformer steric interactions between the vicinal phenyl groups in the *erythro* isomer would *destabilize* this conformation, potentially raising the energy of the reactant and decreasing the activation energy for fragmentation. At the present time we can only conclude that the difference in the kinetics of fragmentation of e-$1^{\bullet+}$ and t-$1^{\bullet+}$ is due to differences in stability of conformations of either reactant or transition states. A detailed analysis in terms of enthalpies and entropies of different conformers will require kinetic studies of a wider range of substituted α-AA systems.

The kinetic experiments with added base provide unequivocal evidence that bond fragmentation in e-$1^{\bullet+}$ is base catalyzed. The strong dependence of k_{base} on the base strength of the substituted pyridine, the slope of the Brønsted correlation, and the deuterium isotope effect on the pyridine-catalyzed reaction (k^H_{base}/k^D_{base} = 2.0) indicate that in the presence of base the rate-determining step for fragmentation is moderately endothermic H$^+$ transfer from e-$1^{\bullet+}$ to the base. Since H$^+$ transfer is rate-determining in the base-catalyzed reaction, bond fragmentation in the conjugate base of e-$1^{\bullet+}$ must be very rapid ($k_{BF} \geq 10^9$ s^{-1}). This is apparent because fragmentation must be more rapid than back H$^+$ transfer from the pyridinium ion to the conjugate base of $1^{\bullet+}$ and back H$^+$ transfer must be exceedingly rapid because it is moderately exothermic.

Supplementary Material Available: Details concerning the synthesis and characterization of e-$1^{\bullet+}$ and t-$1^{\bullet+}$ (2 pages). Ordering information is given on any current masthead page.

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