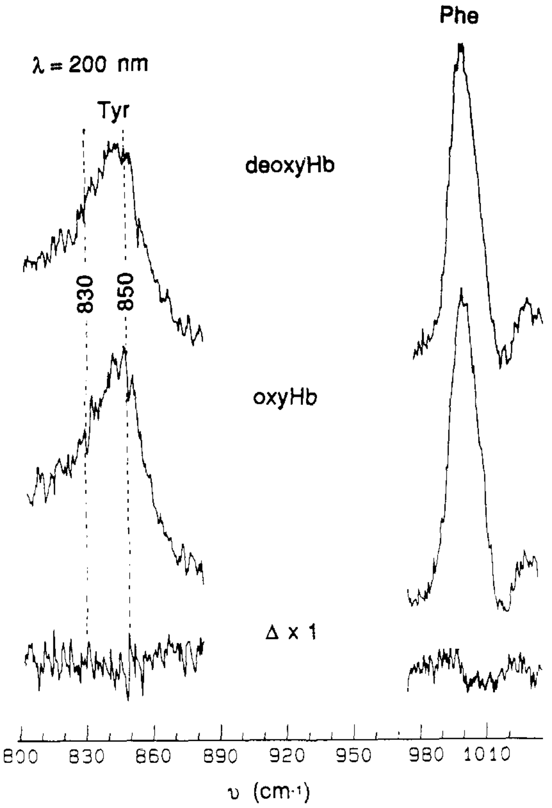

Figure 3. UVRR spectra of oxy- and deoxyHb as in Figure 1 but obtained with 200-nm excitation; a 3600 groove/mm grating was used in first order, and 100 scans were coadded. (Spectra reported in ref 8 and 9 were obtained with 20–40 scans.) The sharp 1000-cm^{-1} band is a Phe breathing mode, while the broad band at ~840 cm^{-1} contains 830/850 cm^{-1} Fermi doublet contributions from the six inequivalent Tyr residues. The difference spectrum is featureless at this signal/noise level.

Photoexcitation of HbCO molecules is followed by very rapid electronic relaxation, with a time constant of 0.35 ps.[8] Subsequent relaxaton to the final deoxyHb spectrum has been determined[2] to occur in at least three kinetically distinguishable steps, with time constants of ~100 ns, ~1 μs, and ~20 μs. This last step is coincident with the transition from fast to slow recombining forms of hemoglobin,[1] which has been assumed to involve the quaternary rearrangement of the Hb tetramer between the R and T states.[13] As shown in Figure 2, the rise time of the deoxyHbCO UVRR difference spectrum likewise coincides with this transition, and we therefore attribute the difference bands to changes in the Tyr and Trp environments which are associated with the quaternary change. Indeed, these spectra represent the first direct probe of this structural rearrangement, since the signals arise from aromatic residues rather than the heme group itself.

It is likely that the R–T difference UVRR signals are associated with aromatic residues at the critical $\alpha_1\beta_2$ subunit interface where most of the relative motion occurs in the quaternary switch.[14] In particular, the Trp β37 indole NH proton is H-bonded to the backbone carbonyl group of Asn-102 in the R state but to the carboxylate side chain of Asp α94 (a stronger interaction) in the T state.[4] The Tyr α42 OH group accepts an H-bond from the peptide NH of Asp 94 in both the R and T states, but in the T state it also forms a donor interaction with the side chain of Asp 99. We tentatively attribute the W_3 and ν_{8a}/ν_{8b} difference signals to these H-bond changes. The intermediate W_3 signal seen in the 10 μs transient spectrum suggests that the R–T transition occurs in a step-wise fashion, the intermediate step perhaps affecting the environment of Trp β37 but not Tyr α42.

These preliminary results are encouraging with respect to the development of UVRR spectroscopy as a probe of protein dynamics. By monitoring the environment of residues in various parts of the protein, one can probe for specific conformational changes along a reaction pathway, following rapid initiation of the reaction.

Acknowledgment. This work was supported by NIH Grant GM 25158.

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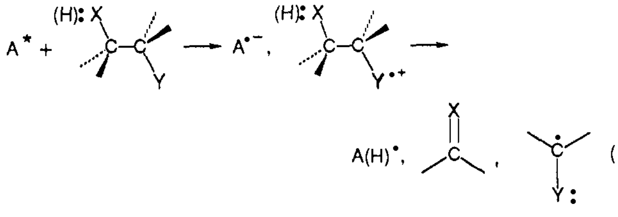
Photofragmentation via Single-Electron Transfer: Selective Labilization of C–C Bonds in Amino Alcohols with Several Bonds between Heteroatom Substituents

Xiaohong Ci and David G. Whitten*

Department of Chemistry, University of Rochester
Rochester, New York 14627

Received January 6, 1989

A number of recent studies have shown that oxidative photofragmentation of α,β-diheteroatom-substituted organics can occur as a consequence of single-electron transfer as outlined in eq 1, where X = N or O and Y = N, O, or S.[1-13] The photoredox process, although involving radical ion intermediates, shows close analogies to the "2-electron" Grob fragmentation.[14] Mechanistic studies with a variety of electron acceptors and aminoalcohols indicate that both acceptor anion-radical basicity and a drastically reduced C–C bond energy in the cation-radical contribute to the low (2.5–5 kcal/mol) activation energy[5,7] for fragmentation in the ion-radical pair. Since reaction of α,β-diheteroatom-substituted compounds is observed to proceed very cleanly via relatively low energy excitation, an interesting question is whether a correspondingly clean C–C bond fragmentation can occur in molecules in which two heteroatoms are separated by greater distances. Here we report results that indicate selective cleavage can occur for vinylogous aminoalcohols and related compounds via pathways that involve both net reduction and catalytic roles for the photoexcited acceptor.



(1)

Amines **1–3** were prepared by catalytic hydrogenation or chemical reduction of 4,4′-dimethylaminobenzoin. The reduction

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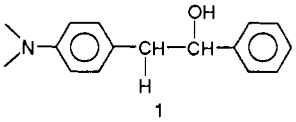
of 4,4'-dimethylaminobenzoin with tin in ethanolic HCl leads to the formation of both α- and β-*p*-dimethylaminodesoxybenzoin, which were separated and purified.[15] The reduction of α- and β-isomers by sodium borohydride gives rise to amines **1** and **2**, respectively. Amine **3** was obtained through catalytic hydrogenation of 4,4'-dimethylaminobenzoin in the presence of platinum oxide. Compound **4** was prepared by a sequence of reduction of 1,2-dibenzoylethylene with LiAlH$_4$,[16] reaction with chlorotrimethylsilane under nitrogen, and addition of morpholine under vigorously anhydrous conditions. As listed in Table I, all four amines quench the fluorescence of thioindigo (TI) in benzene solution at near diffusion-controlled rates. Irradiation of degassed benzene solutions of TI or β-lapachone and the amines also leads to reaction of both the acceptor and the donor in each case, although the net course of the reaction depends strongly upon the donor. The photoreactions were monitored by UV-vis and NMR; photoproducts were determined by HPLC, NMR, and GC/MS techniques. Structural assignments were confirmed by direct comparison with authentic samples. Product quantum yields are summarized in Table I.



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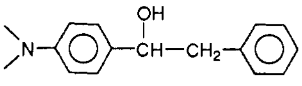

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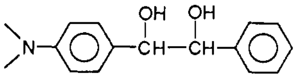

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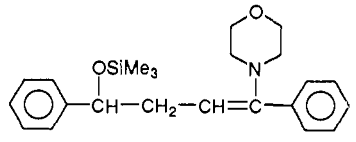
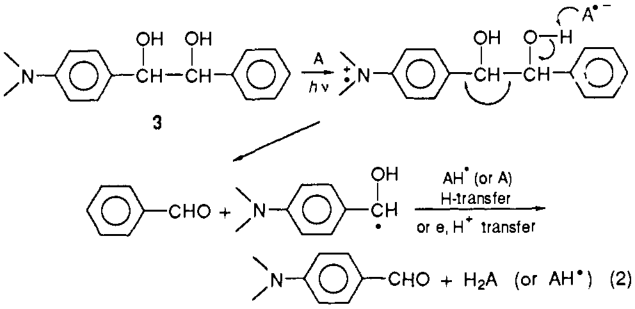
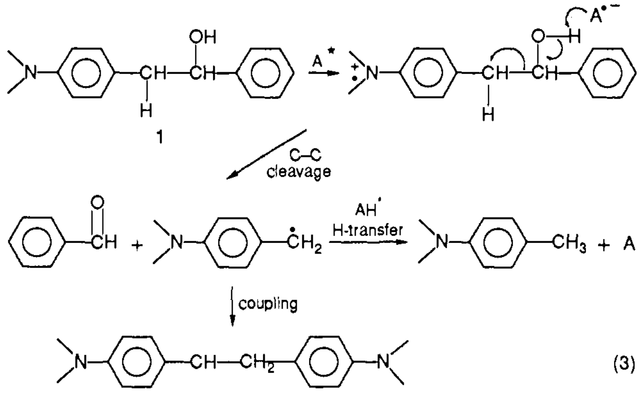


4

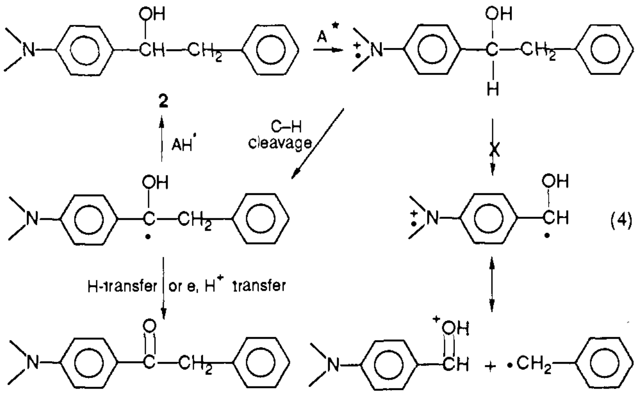
Amine diol **3** undergoes reaction with both β-lapachone and TI in degassed benzene or acetonitrile solutions to give clean oxidative photofragmentation concurrent with one- or two-electron reduction of the acceptor analogous to the reactions of 1,2-aminoalcohols observed previously.[3,4,17] For TI the total yield of aldehydes and two-electron reduced acceptor are in a roughly 2:1 ratio, consistent with reaction according to the mechanism and stoichiometry of eq 2; the quantum yields for products with β-lapachone, a one-electron acceptor, are in accord with concurrent net 2-electron oxidation of **3** and reduction to AH•.[17] Aminoalcohol **1** also undergoes photofragmentation when reacted with photoexcited TI or β-lapachone in degassed benzene or acetonitrile (Table I). The major products from **1** are benzaldehyde and *p*-dimethylaminotoluene in an approximately 1:1 ratio; although some net reduction of the acceptor is observed in each case, the yields are much lower than those for fragmentation. Accordingly, the predominant reaction of **1** is a fragmentation that leads ultimately to both oxidized and reduced donor products while the light absorbing acceptor functions mainly as a photocatalyst.[18-21] Although the net reaction observed with **1** is different from that of **3** or the aminoalcohols investigated previously,[3-6,17] the process likely occurs by an analogous mechanism (eq 3). In contrast to **1** and **3**, aminoalcohol **2**, isomeric with **1**, gives no C–C fragmentation upon irradiation with TI or β-lapachone, even though it strongly quenches TI fluorescence and promotes reduction of both acceptors. Although other, as yet unidentified, minor products are produced, none of the anticipated cleavage products are detected and the major product identified is the corresponding aminoketone. Yields of aminoketone and reduced acceptor are roughly comparable and suggest that the major path for the photoredox reactions of **2** with the two acceptors is an electron–proton–electron (or electron–hydrogen atom) transfer sequence as outlined in eq 4.



(2)

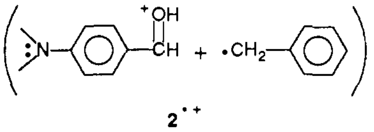


(3)



(4)

The striking differences in reactivity of aminoalcohols **1**–**3** with the same photoexcited electron acceptors underlines both the versatility and structural sensitivity of the oxidative photofragmentation reaction. Thus, while all three aminoalcohols undergo facile single-electron transfer oxidation with the acceptors used, only **1** and **3** have available paths analogous to the Grob fragmentation and accordingly no cleavage of **2** is observed, even though formation of moderately stable cleavage products from $\mathbf{2}^{\bullet+}$ is possible. Although similar mechanisms for fragmentation of **1** and **3** are suggested, the products formed are quite different with net donor–acceptor redox predominating for **3** but not for **1**. As noted above, this can be attributed to different fates for



$\mathbf{2}^{\bullet+}$

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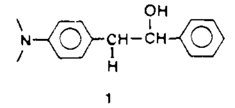
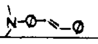
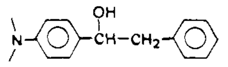
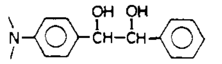
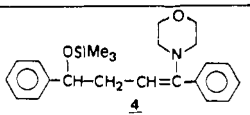
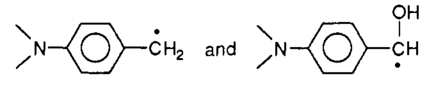
Table I

Donor	Acceptor	Solvent	Products (quantum yield)[a]				K_q ($M^{-1}s^{-1}$)[b]
 1			ØCHO	>NØCH$_3$		H_2A or ·HA	
	Tl	benzene	4.85×10^{-3}	3.73×10^{-3}		1.4×10^{-4}	1.3×10^{10}
	Tl	CH_3CN	7.73×10^{-4}	9.96×10^{-5}	6.72×10^{-4}	1.1×10^{-4}	
	β-Lap	benzene	0.764	0.669	0.095	0.283	
 2			>NØC(=O)-CH$_2$Ø			H_2A or ·HA	
	Tl	benzene	5.88×10^{-4}			5.28×10^{-4}	4.2×10^{9}
	Tl	CH_3CN	1.12×10^{-4}	+ other products		4.59×10^{-4}	
	β-Lap	benzene	0.029			0.027	
 3			ØCHO	>NØCHO			
	Tl	benzene	1.2×10^{-3}	0.7×10^{-3}		1.2×10^{-3}	5.3×10^{9}
	Tl	CH_3CN	6.2×10^{-4}	4.8×10^{-4}		4.7×10^{-4}	
	β-Lap	benzene	0.25	0.22		0.35	
 4			ØCHO				
	Tl	benzene	0.063			2.0×10^{-4}	2.7×10^{9}
	Tl	CH_3CN	0.021			7.7×10^{-5}	

[a] Samples were vacuum degassed through several freeze-pump-thaw cycles. Quantitative measurement of products formed from donors were obtained from HPLC analysis. The reduction products from the electron acceptors were determined by monitoring the absorbance change during irradiation. Incident light intensities were measured by Ferrioxatate actinometry. [b] Quenching experiments were performed in benzene solvent with Tl as electron acceptor, and samples were degassed by bubbling with argon for 30 min through a serum cap prior to each measurement.

the two radicals formed in the acceptor amine-radical mediated cleavage from **1** and **3**, **5**, and **6**, respectively. While **6** should



5 6

be an excellent electron or H-atom donor, readily oxidized to the corresponding aldehyde, **5** should undergo preferential reduction or dimerization. Although the dimer of **5** has not been detected, the presence of substantial amounts of reduced acceptor suggests that some non-redox routes for consumption of **5** are operative.

To further test the possibility that vinylogous diheteroatom-substituted molecules can undergo oxidative photofragmentation as a general process, amino silyl ether **4** was studied under irradiation in solution with Tl (the corresponding alcohol has not proved isolable). Although **4** is stable and unreactive in the dark, irradiation of Tl in solutions containing **4** in degassed acetonitrile or benzene leads to rapid and relatively efficient formation of benzaldehyde as the major product. Here again, quenching of the excited acceptor most likely involves single-electron transfer from the "donor" enamine center, in this case followed by fragmentation to give the neutral allylic radical $CH_2{=}\dot{C}HC(Ph)\text{-}N(CH_2)_2OCH_2CH_2$, benzaldehyde, and silylcation.[22] The relatively low yields of reduced Tl for reaction of **4** compared to fragmentation indicate a largely "catalytic" role of the light-absorbing acceptor in this case. Recent results[2-4] demonstrating parallel reactivity for aminoalcohols, 1,2-diamines, and aminothiols suggest that many additional examples of electron-transfer-induced photofragmentation may be possible for other diheteroatom-substituted organics.

Acknowledgment. We are grateful to the U.S. Department of Energy (Grant DE-FG02-86ER13504) for support of this research.

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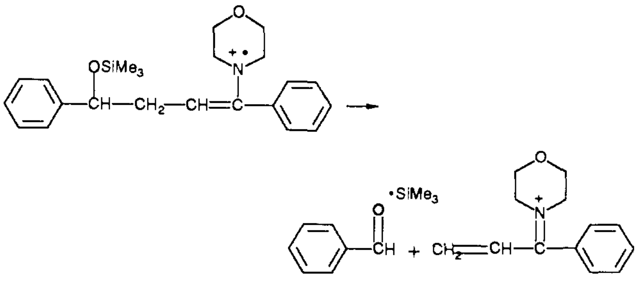
(22) An alternative possibility is that cleavage to generate a silyl radical occurs:



We thank a referee for pointing this out.

Long-Range Electron Transfer in a Cytochrome c Derivative Containing a Covalently Attached Cobalt-Cage Complex

David W. Conrad and Robert A. Scott*[1]

School of Chemical Sciences, University of Illinois, 1209 W. California Street
Urbana, Illinois 61801

Received September 2, 1988

Much emphasis has been placed recently on understanding the factors that control the rates of long-range (>10 Å) electron transfer in biological systems.[2,3] We have chosen to focus specifically on the relationship between the rate of intramolecular electron transfer and the distance between redox sites. This may be accomplished through the use of covalently modified proteins in which intramolecular rates of electron transfer between two fixed metal sites, separated by a known distance, can be measured. These protein derivatives can be prepared through modification of specific sites on structurally characterized redox proteins with inorganic probes. Using horse heart cytochrome *c* as a molecular

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(1) Present address: Department of Chemistry, University of Georgia, Athens, GA 30602.

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