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Photochemical Smiles Rearrangement and Meisenheimer Complex Formation Catalyzed by Hydroxide Ion via Electron Hole Transfer Catalysis

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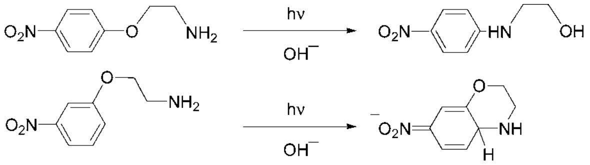
ABSTRACT



Photochemical para-to-nitro Smiles rearrangement and para-to-nitro Meisenheimer complex formation occurs for nitrophenoxyethylamines with high concentrations of hydroxide ion in aqueous solution. Both photoreactions show first-order dependence on hydroxide ion concentration, but the mechanism involving hydroxide ion does not involve acid–base catalysis. The reactions take place from the triplet excited states of the nitrophenyl ethers. Analysis of quantum yields and kinetics is consistent with an electron hole transfer catalysis mechanism.

Nucleophilic aromatic photosubstitution reactions have been studied extensively, revealing a complex array of mechanisms.[1] Certain aspects of these reactions such as the “meta effect”,[2] acid−base chemistry,[3] involvement of geminate radical intermediates,[4] and application in photoremovable blocking groups[5] have been clarified mechanistically by study of the intramolecular versions of the reactions known as Smiles photorearrangements.[6] A mechanistic dichotomy has emerged from these studies[7] that systems having unfavorable energetics for excited-state electron transfer from side-chain nucleophile to the triplet nitrophenoxy moiety undergo photosubstitution meta-to-nitro, whereas those favorable to electron transfer undergo reaction para-to-nitro. We were surprised, therefore, to find that two molecules in the former category could be made to react para-to-nitro at high solution concentrations of hydroxide ion.

We have reported that **1** undergoes photoconversion to a dihydrobenzene derivative, **2,** resulting from intramolecular meta-to-nitro attack when irradiated at low NaOH concentrations in water.[8] The compound also undergoes base-catalyzed thermal Smiles rearrangement,[9] but no appreciable photochemical Smiles rearrangement at low base concentration.[8] We now report that photolysis of **1** (0.010 M) in D_2O

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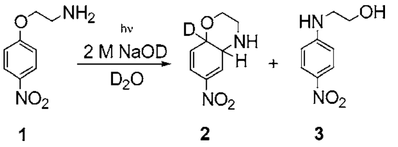
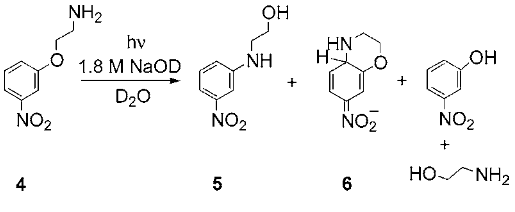
containing 2.0 M NaOD in a Pyrex NMR tube at 0 °C with broadband light centered at 300 nm gave the previously reported dihydrobenzene derivative **2** and Smiles rearrangement product **3** as the only products in yields of 24% and 76%. The Smiles product was identified by enhancement of its NMR spectrum with an authentic sample. The pseudo-first-order rate constant for thermal Smiles rearrangement of **1** in 2.0 M NaOD/D_2O at 0 °C is $2.5 \times 10^{-7}\ \mathrm{s}^{-1}$. Thus, thermal rearrangement accounts for less than 1% of the observed Smiles product, and its production is almost entirely photochemical.



We have reported also[10] on the clean, base-catalyzed Smiles photorearrangement of **4**. We were surprised to find that photolysis of **4** (1.0×10^{-4} M) in 2.0 M NaOH/H_2O gave rise to a strong, stable UV absorption at 368 nm ($\epsilon > 9000$) that could not be attributed to the Smiles photoproduct (λ_{max} 405 nm, ϵ 1110; ϵ_{Smiles} at 368 nm is 1160). Photolysis of **4** (0.012 M) in 1.8 M NaOD/D_2O in a Pyrex NMR tube at room temperature with broadband 300 nm light for 50 min caused 68% loss of starting material. The products were analyzed by NMR. They consisted of Smiles photorearrangement product **5** (73%), 3-nitrophenol and ethanolamine (12% each), and a previously unreported nitronate anion **6** (15%). Smiles product, **5**, and the photohydrolysis[11] products, 3-nitrophenol and ethanolamine, were identified by enhancement of their NMR spectra with authentic samples. Compound **6** was characterized by its NMR spectrum (shifts relative to terephthalate anion at δ 7.86 in D_2O): δ 6.95, 1H, d of d ($J = 9.6$ and 2.0 cps); δ 6.61, 1H, d ($J = 2.0$ cps); δ 6.47, 1H, d ($J = 9.6$ cps); δ 4.08, 2H, t ($J = 5.2$ cps); δ 3.75, 2H, t ($J = 5.2$ cps) (other hydrogens not found). The required proton couplings were shown by COSY. The % yields of these products were determined for photolyses at several NaOD concentrations between 0.10 and 2.50 M. This showed a steady increase in the percent yields of **6** and the photohydrolysis products at the expense of **5** with increasing hydroxide ion concentration.



These new photochemical reactions were both shown occur from the triplet states by sensitizing them with the triplet sensitizer 3-methoxyacetophenone. The sensitized quantum yields were higher than the direct ones.

We also determined the dependence of the quantum yields for appearance of **3** from **1**, and of **6** from **4**, on the hydroxide ion concentration. Figure 1 shows the former data, and Figure 2 shows the latter. The data for Figure 1 were obtained by irradiating **1** in NMR tubes at 0.0050 M in NaOD/D_2O at 0 °C to approximately 20% conversion with 300 nm light and monitoring the reactions quantitatively by the NMR signals of the products integrated against an internal standard (terephthalate anion). The actinometer was azoxybenzene in ethanol.[12] The data for Figure 2 were obtained by exhaustively irradiating **4** in cuvettes at 1.0×10^{-4} M in NaOH/H_2O with 300 nm light and monitoring the reaction progress by the growth of absorption at 368 nm. In this case, three products are produced in varying yields at different hydroxide ion concentrations that all contribute to the product absorbance. Product yields were determined by NMR analysis as described above, and the relative contributions to the final absorbance at 368 nm were calculated based on their concentrations and extinction coefficients. (The extinction

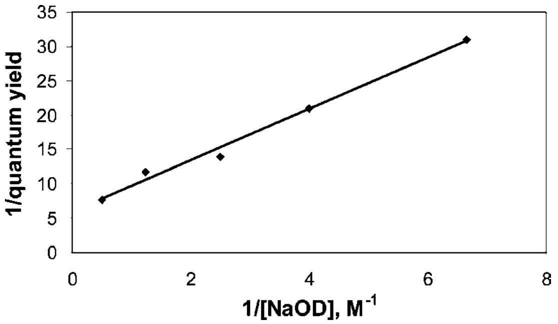


Figure 1. Reciprocal quantum yields of **3** at reciprocal NaOD concentrations in D_2O solutions.

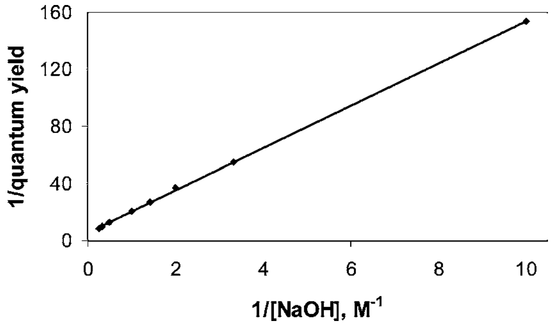


Figure 2. Reciprocal quantum yields of **6** at reciprocal NaOH concentrations in H_2O solutions.

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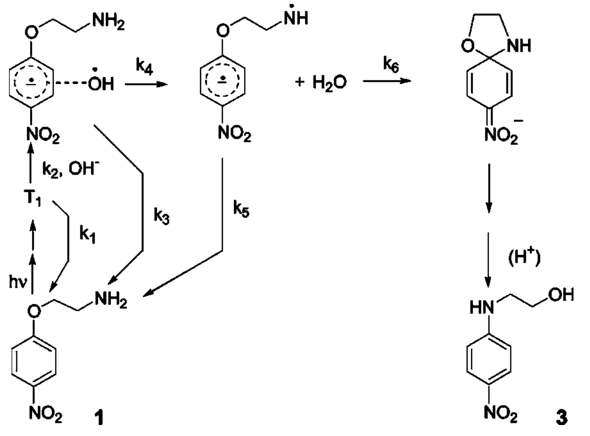
coefficient of **6** was calculated to be 49 000 at its λ_{max} of 368 nm.) Since the ratio of **5** to **6** to 3-nitrophenol is constant throughout the reaction, the quantum yields of **6** were calculated at different hydroxide ion concentrations based on the known efficiency of the Smiles photorearrangement.[10a] Both of the plots show linear, first-order dependence of the product on the concentration of hydroxide ion. Since hydroxide ion does not appear in the stoichiometry, it is clearly a catalyst of each of these photochemical reactions.[10b]

The equation of the best fit line in Figure 1 is $y = 3.72x + 5.97$. The reciprocal of the intercept, the limiting quantum yield of the Smiles product, is 0.17. The equation of the best fit line in Figure 2 is $y = 14.8x + 5.73$. The reciprocal of the intercept, the limiting quantum yield of the Meisenheimer complex, is also 0.17.

These results are remarkable from several perspectives. Photoproduct **6**, a nitrocyclohexadienyl anion with only a single stabilizing electron-withdrawing group, has no precedent in the vast literature on stable Meisenheimer complexes.[13] Its occurrence here can be rationalized by the lack of any anionic leaving group of adequate stability, and the unique photochemical route to its creation. Thermal routes to comparable complexes have been unsuccessful[14] no doubt because any workable approach to such a complex on a ground-state surface also represents a reversion route from the complex. The photochemical approach deposits the complex from an excited-state surface that does not provide an accessible reversion route.

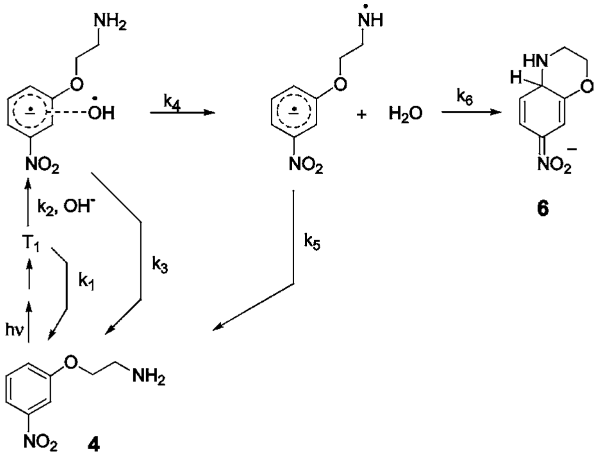
Because the chemical changes are simple, mechanistic possibilities are few. Encounter of the nitrophenyl ether triplet, a predominant π,π^* state, with the internal nitrogen nucleophile has already been established as proceeding via meta-to-nitro bond formation, the products of which are evident in these reactions. These reactions are not sources of para-to-nitro bond formation. The rate constant for this attack in the case of **4** is about 4 × 10^8 s^{-1}.[15] Encounter of the triplet with hydroxide ion at a ring position also proceeds by meta-to-nitro attack, which gives photohydrolysis only in the case of **4**. The second-order rate constant for this attack on the prototypical 3-nitroanisole in water is also about 4 × 10^8 M^{-1} s^{-1}.[16] No proton transfer from the triplet to hydroxide ion is feasible. The only other precedented primary process fast enough to compete with the above would be an electron transfer interaction. Formation of an exciplex from triplet 3,5-dinitroanisole and hydroxide ion has been proposed, the formation rate constant being at least 3 × 10^9 M^{-1} s^{-1}.[17] Evidence also exists for exciplexes formed from triplet 9,10-anthraquinone-2-sulfonate and oxidizable inorganic ions in water, the case of hydroxide ion having a formation rate constant of 3 × 10^8 M^{-1} s^{-1}.[18] These reports indicate the only possibility competitive with the known fast reactions.

Scheme 1. Proposed Mechanism for Hydroxide-Catalyzed Photoformation of Para Meisenheimer Complex



From this starting point, we propose the mechanism for forming **3** from **1** in Scheme 1 and for forming **6** from **4** in Scheme 2. The steps are formation of an exciplex (k_2), hydrogen atom abstraction from an NH bond by the hydroxyl radical within the exciplex (k_4), radical coupling at a para-to-nitro position dictated by the odd electron distribution of the aromatic radical (k_6), and (for **1**) opening of the sigma complex.[19] Precedent for an intramolecular reaction of a photochemically generated hydroxyl radical exists in a recently reported photohydroxylation system.[20] Hydroxyl

Scheme 2. Proposed Mechanism for *p*-Hydroxide-Catalyzed Smiles Photorearrangement



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(19) More complete schemes would show that k_1 (triplet decay) goes not only back to starting material but also to other photoproducts. Since amide ions have negligible leaving group ability, the σ-complex in Scheme 1 can go only to **3** in alkaline media.

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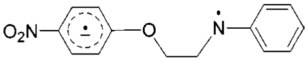
radicals are known to react with aliphatic amines at close to the diffusion-limited rate.[21]

The quantum yield expression for both mechanisms is shown in eq 1. Equation 2 is the reciprocal expression that corresponds to the linear graphs of Figures 1 and 2. The slopes and intercepts given above yield the results that the k_1/k_2 ratios are 0.69 for **1**, and 2.6 for **4**. The reciprocal of the intercepts (0.17 in both cases) represents the product of

$$\Phi = \Phi_{\mathrm{T}}\left(\frac{k_2[\mathrm{OH}^-]}{k_1 + k_2[\mathrm{OH}^-]}\right)\left(\frac{k_4}{k_3 + k_4}\right)\left(\frac{k_6}{k_5 + k_6}\right) \qquad (1)$$

$$\frac{1}{\Phi} = \frac{1}{\Phi_{\mathrm{T}}}\left(1 + \frac{k_1}{k_2[\mathrm{OH}^-]}\right)\left(1 + \frac{k_3}{k_4}\right)\left(1 + \frac{k_5}{k_6}\right) \qquad (2)$$

the quantum yield to the triplet, the partitioning of the exciplex ($k_4/(k_3 + k_4)$), and the partitioning of the diradical ($k_6/(k_5 + k_6)$). That our result is reasonable can be seen by comparing it to the partitioning ratio (0.17) that was found for cyclization vs decay of the comparable diradical, **7**, in another study of a para-to-nitro Smiles photorearrangement.[22] Since the quantum yield to the triplet is close to 0.7 for nitrophenyl ethers, the total partitioning of the exciplex and the diradicals toward the products for our systems is 0.17/0.7 = 0.24. This indicates that about a quarter of the exciplex makes it to product. It seems likely that the diradical cyclization fraction ($k_6/(k_5 + k_6)$) for **1** and **2** would be similar to that of **7**, which implies that the efficiency of hydrogen abstraction (k_4) is high. That these cyclization fractions are all close is strong evidence for the mechanism.



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That the k_1/k_2 ratios are also reasonable can be ascertained by realizing that both triplets are being removed by intramolecular nucleophilic attack at roughly 4 × 10^8 s^{-1}. Thus, k_1/k_2 ratios on the order of unity are seen, corresponding to a rate of attack by hydroxide ion of about the same order of magnitude as the decay by other processes. This rationalizes why we see the reported chemistry only at relatively high hydroxide ion concentrations.

We have reported several examples of electron hole transfer catalysis, those cases involving nitrobenzenes with chloride ions and isopropyl alcohol,[4,23] 9,10-anthraquinone with ammonia and *tert*-butyl alcohol,[24] and 4-nitrobenzaldehyde with water.[25] The latter was the only intramolecular case previously recognized. The current cases are particularly clear examples of what may be a widespread phenomenon in natural systems.

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Supporting Information Available: ^{1}H NMR and COSY spectra of products from **4** and data for Figures 1 and 2. This material is available free of charge via the Internet at http://pubs.acs.org.

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