# Temperature-Dependent Regioselectivity of Nucleophilic Aromatic Photosubstitution. Evidence That Activation Energy Controls Reactivity

Gene G. Wubbels,* Ryo Tamura, and Emmett J. Gannon

Department of Chemistry, University of Nebraska at Kearney, Kearney, Nebraska 68849, United States

S *Supporting Information*

ABSTRACT: Irradiation (λ > 330 nm) of 2-chloro-4-nitroanisole (**1**) at 25 °C in aqueous NaOH forms three substitution photoproducts: 2-methoxy-5-nitrophenol (**2**), 2-chloro-4-nitrophenol (**3**), and 3-chloro-4-methoxyphenol (**4**), in chemical yields of 69.2%, 14.3%, and 16.5%. The activation energies for the elementary steps from the triplet state at 25 °C were determined to be 1.8, 2.4, and 2.7 kcal/mol, respectively. The chemical yields of each of the three products were determined for exhaustive irradiations at 0, 35, and 70 °C. The variation with temperature of the experimental yields is reproduced almost exactly by the yields calculated with the Arrhenius equation. This indicates that activation energy is the fundamental property related to regioselectivity in nucleophilic aromatic photosubstitution of the S_N2 Ar* type. The many methods proposed for predicting regioselectivity in reactions of this type have had limited success and have not been related to activation energy.
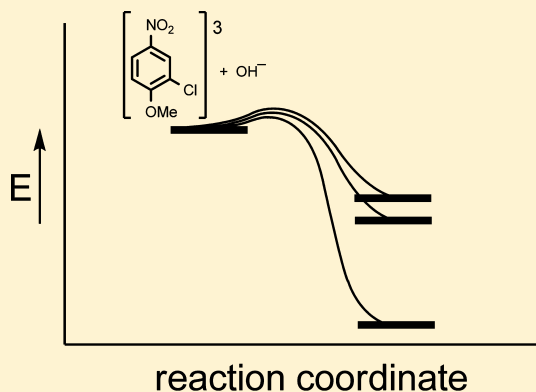
INTRODUCTION

The discovery in 1956[1] that nitrophenyl phosphates undergo photohydrolysis in alkaline aqueous solution and that the *meta* isomer reacts much more efficiently than the *para* isomer initiated extensive studies of nucleophilic aromatic photo-substitution reactions.[2,3] The odd regioselectivity of reactions of this type (S_N2 Ar*), denoted the "meta effect" in an early study,[4] has attracted extensive attention. The recognition in the 1930s that photoexcitation of molecules in solution rapidly generated thermally relaxed excited states led to the conclusion that reaction rates from such states would be governed by the Arrhenius equation.[5] Many studies have shown that the Arrhenius model applies to solution photoreactions,[6−9] but the many studies of nucleophilic photosubstitution regiose-lectivity are silent on the matter of activation energy. This seems a significant oversight. We know of no experimental study, other than our recent one,[10] showing that photochemical regioselectivity depends on relative activation energies or even that the primary criterion for a proxy method should be its representation of activation energy. Our report[10] concerned a reaction that gave two substitution photoproducts. The photolysis of a different compound that gives three substitution photoproducts in roughly comparable yields from a single excited state[11] presented the possibility of carrying out a more exacting test of whether activation energy is the fundamental property related to regioselectivity.

RESULTS

Photolysis of 2-chloro-4-nitroanisole (**1**) (2.2×10^{-4} M) with 313 nm light in 33% acetonitrile/water solution with 0.010 M NaOH gave the three products **2**, **3**, and **4**, shown in Scheme 1,

Scheme 1. Photoproducts of 2-Chloro-4-nitroanisole (1) in Aqueous NaOH Solution
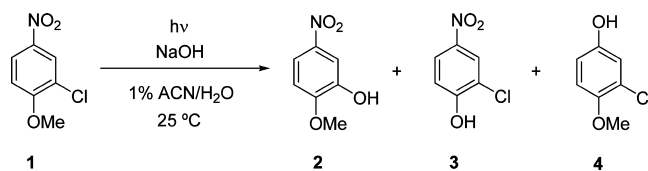
in approximate yields of 70%, 15%, and 15% by NMR and by UV−vis analysis.[11] We verified that with **1** at 1.05×10^{-4} M in argon-degassed 1% acetonitrile−water and 0.020 M NaOH at 25 °C with broad-band 350 nm light filtered through uranium glass (λ > 330 nm) the reaction gave the same products in roughly the same yields. For this investigation, however, we needed a method of product analysis that afforded reproducibility of about ±0.1% in the product yields.

The changes in the UV−vis spectrum upon irradiation of the reaction mixture at 0 °C are shown by the overlaid spectra in Figure 1. The sharp isosbestic points and the absence of
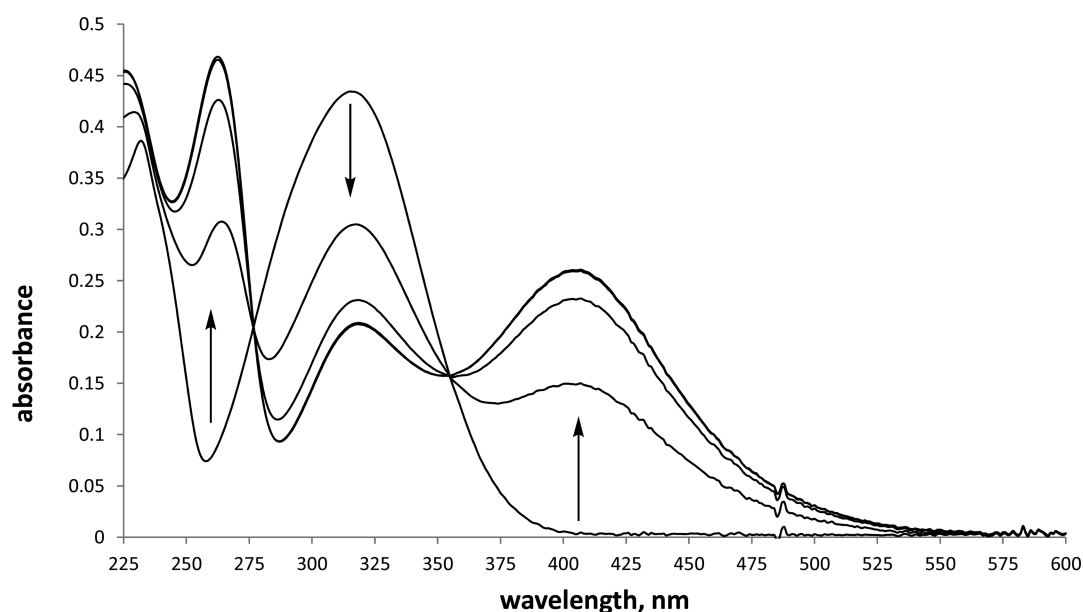
Figure 1. Electronic spectra for photolysis of 2-chloro-4-nitroanisole (5.0×10^{-5} M) in aqueous 0.0075 M NaOH after irradiation for 0, 48, 120, 300, and 1020 s at 0 °C.

appreciable spectral changes upon long irradiation after virtually complete reaction indicate that the reaction giving the three products is clean and quantitative. Maintaining the reaction mixture at 70 °C in the dark for the length of time for the photoreaction (15 min) caused no change in the UV−vis spectrum. This indicates that no thermal reaction occurs. The product maximum absorbances at 405, 318, and 263 nm represent the composite of absorption of the three photoproduct anions. We determined with authentic samples that the extinction coefficients of the three product anions at these three maxima are as shown in Table 1.

Table 1. Absorptivities of the anionic photoproducts at the detection wavelengths in 0.10 M aq. NaOH

product	ε 405 nm	ε 318 nm	ε 263 nm
2	3850	5175	12000
3	17400	1100	3960
4	0	2750	600

Since the photoreactions were carried to completion, the total absorbances at each wavelength at completion are given by eqs 1−3. If the reaction gives no side products, as appears to be the case, a conservation equation (eq 4) is warranted. With known extinction coefficients and experimental absorbances of products, eqs 1−3 represent a system of three equations and three unknowns that may be solved exactly. The exact solution results for the concentrations of **2**−**4** gave excellent

reproducibility and agreement with the total concentration (eq 4), but only for the reactions at 0 °C. To an increasing extent as the reaction temperature was increased, the absorbance at 263 nm was higher (ca. 1−2%) than expected and somewhat erratic. This caused the yields of all of the products to vary slightly from expected values, which was incompatible with our purpose. We suspect the cause was some unknown thermal reaction of product **4**.

$$A(405) = \varepsilon_{2(405)}[2] + \varepsilon_{3(405)}[3] + \varepsilon_{4(405)}[4] \quad (1)$$

$$A(318) = \varepsilon_{2(318)}[2] + \varepsilon_{3(318)}[3] + \varepsilon_{4(318)}[4] \quad (2)$$

$$A(263) = \varepsilon_{2(263)}[2] + \varepsilon_{3(263)}[3] + \varepsilon_{4(263)}[4] \quad (3)$$

$$[1] = [2] + [3] + [4] \quad (4)$$

Instability in the case of the unsubstituted 4-methoxyphenoxide ion, an analogue of **4**, was observed in a previous, related investigation.[10] We therefore carried out the yield determinations through use of eqs 1, 2, and 4, which also is a system of three equations and three unknowns. The concentration of **1** in eq 4 is given by the starting absorbance at 316 nm divided by the extinction coefficient of **1** at 316 nm (8600). Solving for the concentrations of **2**, **3**, and **4** gave working eqs 5−7, which were used with the experimental absorbance data to find the final product concentrations.

$$[2] = \frac{A_{318} - \varepsilon_{4(318)}\frac{A_{1(316)}}{\varepsilon_{1(316)}} + 0.094828 A_{405}}{2790.1} \quad (5)$$

$$[3] = \frac{A_{405} - \varepsilon_{2(405)}[2]}{\varepsilon_{3(405)}} \quad (6)$$

$$[4] = \frac{A_{1(316)}}{\varepsilon_{1(316)}} - [2] - \frac{A_{405} - \varepsilon_{2(405)}[2]}{\varepsilon_{3(405)}} \quad (7)$$

The product analyses given by this procedure for a set of triplicate reactions at the various temperatures are given in

Table 2. Very similar results were obtained for reactions conducted under slightly different conditions of solvent, NaOH

Table 2. Photoproduct Percent Yields at Various Temperatures[a]

temp (°C)	% **2**	% **3**	% **4**
0	71.3	13.7	14.9
25	69.2	14.3	16.5
35	68.5	14.5	17.0
70	65.9	15.2	18.9

[a]Photolysis ($\lambda > 330$ nm) of **1** (1.05×10^{-4} M) in 1% acetonitrile–water with 0.020 M NaOH.

concentration, irradiation setup, and spectrophotometer parameters. Temperature increases cause the yield of the major product, **2**, to decline, and the yields of the minor products to increase, **3** increasing about one-half as much as **4**.

The Arrhenius activation energies of each of the photo-substitution reactions can be obtained from results reported in our study of the element effect of halogens in nucleophilic photosubstitution.[11] Reactions in 33% acetonitrile–water occur from the triplet state of **1**, which is formed with a quantum yield of 0.90 and has a lifetime of 137 ns. The triplet was detected directly by nanosecond laser flash photolysis.[11] At approximately 25 °C in 33% acetonitrile/water, Stern–Volmer analysis gave a net reaction rate constant (Σk_r) of 2.0×10^8 M^{-1} s^{-1} for reaction of triplet **1** with hydroxide ion. This can be apportioned to the rate constants of the contributing reactions by the percent yields of each product and by accounting for the partitioning of intermediates. We assume that the photo-reaction parameters for 1% vs 33% acetonitrile in water are very similar. Studies of other nitrophenyl ether triplets[12] suggest that the change from 33% to 1% acetonitrile/water is likely to cause the triplet lifetime to be greater by about 10%. The effect of this solvent change on Σk_r is likely to be small and would slightly affect the absolute activation energies. The relative proportions of the three competing reaction channels, however, would be unaffected by changes in Σk_r.

The intermediate σ-complexes for displacement of chloride ion and nitrite ion are likely to partition entirely to product, with little or no reversion to ground state starting material, because of the expected nucleofugalities of the leaving groups. In the absence of complicating effects, nucleofugality is related to acidity of the conjugate acid of the leaving group.[13] For chloride displacement, chloride ion is vastly superior to hydroxide ion as a nucleofuge (conjugate acid pK_a's of −7 vs 16), and for nitrite displacement, nitrite ion is superior to hydroxide ion[14] (conjugate acid pK_a's of 3 and 16). That these partitionings should strongly favor expulsion of chloride ion and nitrite ion can be shown for the less favorable case of nitrite ion. The K_a difference corresponds to a free energy difference in the completely formed products (expulsion of NO_2^- vs OH^-) of about 18 kcal/mol at 25 °C. Application of the well-established principle[13] implies that an appreciable fraction of the product free energy difference is likely to differentiate the transition states.

The σ-complex for methoxy displacement, however, involves leaving groups whose conjugate acid acidities (methanol vs water) are exceedingly close.[15] The breakdown of this intermediate would be expected to make product and reactant in a ratio of about 1:1 because the methoxide and hydroxide nucleofuges are comparable. The actual rate constant for attack

at the methoxy-bearing carbon ($k_{methoxy}$), therefore, will be a factor of 2 greater than that inferred from the yield of **3**. That is, the product percent yields represent the nucleophilic attack rate constants in the proportion $k_{chloro}:k_{nitro}:0.5k_{methoxy}$. The total rate constant for loss of reactant (2.0×10^8 M^{-1} s^{-1}), obtained by Stern–Volmer kinetics, is equal to the sum of these parts. The nucleophilic attack rate constants at 25 °C, therefore, are $k_{chloro} = 1.4 \times 10^8$ M^{-1} s^{-1} for attack at the chloro-bearing carbon, $k_{methoxy} = 5.6 \times 10^7$ M^{-1} s^{-1} for attack at the methoxy-bearing carbon, and $k_{nitro} = 3.3 \times 10^7$ M^{-1} s^{-1} for attack at the nitro-bearing carbon. We assume that the pre-exponential factor, A, in the Arrhenius equation ($\ln k = -(E_a/RT) + \ln A$) corresponds to the fastest intermolecular reaction in the medium at 25 °C, which is approximated by the diffusion rate constant.[16] For reactants in water with no ionic attraction or repulsion, that rate constant is 3×10^9 M^{-1} s^{-1}.[17] On this basis we calculated the activation energies for the three elementary reactions involving nucleophilic attack. The values are 1.8, 2.4, and 2.7 kcal/mol, respectively. We then calculated the net rate constant for each displacement reaction at the other temperatures with the Arrhenius equation. The product yields so calculated are given in Table 3 along with the experimental

Table 3. Arrhenius Calculated and Experimental Product Percent Yields

temp (°C)	% **2**		% **3**		% **4**	
	calcd	exptl	calcd	exptl	calcd	exptl
0	71.4	71.3	13.6	13.7	14.9	14.9
35	68.4	68.5	14.6	14.5	17.1	17.0
70	65.8	65.9	15.3	15.2	18.9	18.9

product yields. The agreement of the Arrhenius product yields at various temperatures with those of experiment is excellent. This implies that the nucleophile attacks triplet **1** at three sites that have slightly different activation energies.

■ DISCUSSION

Competitive elementary reactions from a single electronic state are expected by Arrhenius theory to favor the reaction of higher activation energy at the expense of the reaction of lower activation energy as the temperature increases. Since the product percent yields in this case are similar, the system shows substantial variation of yields with modest temperature changes. That the experimental variation of yields with temperature is matched almost perfectly by the yields calculated on the basis of Arrhenius theory implies that activation energy is the fundamental property related to regioselectivity. We construe "fundamental property" to mean an experimentally measurable quantity. It is possible, as discussed below, that quantities of this kind of sufficient accuracy to predict regioselectivity might be obtained by computations based on quantum theory, but that is not feasible at this time.

The experimental results show the additional odd feature that the increases of yields of the minor products with temperature differ by a factor of 2.5. The yield of **3** increases by 1.5% (11% increment), while that of **4** increases by 4.0% (27% increment). This difference is attributable to partitionings in the pathways leading to **3** and **4**. Without partitioning, the similarity of the yields of **3** and **4** would imply that the processes leading to **3** and **4** have similar activation energies and should show similar variation with temperature. The variation of the yields with temperature, however, differs

substantially. This cannot be rationalized if transition states are the only complexes along the reaction coordinates. Partitioning requires an intermediate such as a σ-complex at which the partitioning can take place. This is strictly required only for the pathway leading to **3**, but since the element effect studies[11] show that a σ-complex also occurs for the halogen displacements, it is reasonable to conclude that all of the displacements in this system involve stepwise mechanisms and σ-complex intermediates. That the partitioning assumptions give activation energies that quantitatively predict product yields supports the mechanistic steps and the hypothesis that activation energy controls regioselectivity.

If it is true that energy of activation is the fundamental property governing regioselectivity, we should consider the nature and efficacy of the many alternative methods for predicting regioselectivity of S_N2 Ar* reactions. They include valence bond resonance structures of excited state reactants,[4] calculated charge density at ring positions of the reactant in excited singlet[18] or triplet[19] states, size of calculated frontier orbital coefficients of ring carbon atoms in the ground electronic state,[20−22] magnitude of the energy gap between the triplet σ-complex and the ground state singlet σ-complex,[19] and spin-polarized Fukui functions of density functional theory.[23] None of these models has referenced activation energy or has been related to activation energy.

The methods vary in their currency. The valence bond structures were qualified by the originator of them to be only a "simple qualitative rationale".[4b] Since the structures show only paired valence electrons and have no convention for antibonding electrons, they can represent excited states only approximately. In fact, S_N2 Ar* reactions typically occur from triplet states,[12,24,25] and valence bond structures provide no means of representing a triplet state. Despite these limitations, the structures are offered in a recent advanced textbook[26] to interpret regioselectivity of S_N2 Ar* reactions. The charge density methods[18,19] have been reported by their proposers to be unsatisfactory.[19] A recent theoretical study[23] concludes that the reactant charge descriptor could account only for the formation of the prereaction complex and not the reaction regioselectivity.

Prediction of regioselectivity in S_N2 Ar* reactions with frontier molecular orbital (FMO) theory[20] postulated that nucleophilic photosubstitution is favored at ring carbon atoms with a maximal ground state HOMO coefficient and a minimal ground state LUMO coefficient. This identifies the nuclear position of maximum ground state electron density in the frontier orbitals. The approach was extended to an electron transfer/geminate radical recombination mechanism ($S_N(ET)$ Ar*) of photosubstitution, first for intramolecular photo-substitutions (photo-Smiles rearrangements)[21] and then for intermolecular reactions.[22] These reactions were said to be LUMO-controlled, in contrast to the S_N2 Ar* type that were HOMO-controlled.[21,22] We[10,11] and others[23] have criticized this model. It rests on the assumption that the ground state frontier orbitals (HOMO and LUMO) persist in the reactive excited state, even if it is a triplet. No method of quantum chemical calculation verifies this assumption. Molecular orbitals of triplets and excited singlets are both calculated as one-electron orbitals (unrestricted). These have only accidental correspondence to the two-electron orbitals of the ground state. Application of the FMO model to nucleophilic attack on triplets also requires the implausible argument that intersystem

crossing to the singlet is so fast that the triplets react as if they were excited singlets.[20]

The postulate that reaction is favored at ring positions for which the energy gap between the triplet σ-complex and the ground state singlet σ-complex is small[19] also requires for triplet reactant states that intersystem crossing be implausibly fast at the step involving nucleophilic attack. That the element effect of halogens on nucleophilic photosubstitution rate constants of several nucleophiles showed no influence of large spin−orbit coupling effects[11] meant that the bond formation process must not involve intersystem crossing. The energy gap model, therefore, seemed inappropriate for predicting regioselectivity of S_N2 Ar* reactions of nitrophenyl ethers.

A recent theoretical study of the orientation rules for S_N2 Ar* reactions[23] put forward spin-polarized Fukui functions of density functional theory of the triplet prereactive π-complex as an index of reactivity with nucleophiles. The function represents the response of the electron density of an atom to perturbation of the total number of electrons in the system. For nucleophilic attack on a triplet, it was based on the coefficients of the α- and β-spin LUMO frontier orbitals of the prereaction π-complex. The method gave accurate qualitative predictions of regioselectivity between two reaction sites for most of the nitrophenyl ether photohydrolyses studied, but it gave conflicting predictions for triplet 2-chloro-4-nitroanisole and hydroxide ion. For this case, Fukui functions from a B3LYP/6-311g(d) calculation predicted the correct major product (displacement meta to the nitro group), while the Fukui functions derived from a B3LYP/6-311+g(d) calculation predicted incorrectly reaction at the position para to nitro.

The optimization computations[23] of these structures may be more problematic than they appear. The calculated transition state energies of the meta vs para transition states of triplet 2-chloro-4-nitroanisole with hydroxide ion by B3LYP/6-311+g(d) (that yielded an incorrect prediction of regioselectivity) showed lower energy for the favored meta transition state by 2.8 kcal. A calculation at a higher level of theory (MP2/6-31+g(d)), however, gave a lower energy transition state for the para reaction by 1.2 kcal. Reaction at the para site is a minor process. These discrepancies shake confidence that the computations give an accurate basis for the calculation of the Fukui functions. Neither the density functional computations nor the Møller−Plesset computation could optimize the structure of the triplet σ-complex intermediate. The failure to find a σ-complex energy minimum was interpreted by the authors[23] to mean that a stable σ-complex was not formed, and that the photodisplacement of chlorine by hydroxide ion in solution was concerted.

The conclusion of concertedness disagrees with experimental evidence.[11] There appear to be two errors. One is the failure to find a computation method that could optimize the structure of the triplet σ-complex, and the second is the use of a negative computed result for a gas phase ionic system to interpret an aqueous phase solution mechanism. That the triplet σ-complex is stable in solution may be inferred from the element effect of halogens.[11] The relative rates of the fast, elementary, nucleophilic attack steps of the halogen displacement reactions of triplet 2-halo-4-nitroanisoles with hydroxide ion were measured[11] and found to be 29:2.6:2.4:1 for F:Cl:Br:I, respectively. This shows the inverse halogen element effect. The normal halogen element effect, when the carbon−halogen bond breaks at the transition state, is about $1:10^5:10^6:10^7$ for F:Cl:Br:I.[27] The huge kinetic effect results from the large

differences of carbon—halogen bond strength; the bond enthalpies are about 115, 97, 80, and 65 kcal/mol, respectively. The inference that the inverse effect is incompatible with breaking the carbon—halogen bond at the transition state, as a concerted reaction requires, is one of the major advances in understanding mechanisms of thermal nucleophilic aromatic substitutions in solution.[28,29] The element effect work[11] extended this to photochemical substitutions of the S_N2 Ar* type. A stepwise reaction with a σ-complex intermediate allows for rate- or efficiency-determining formation of the σ-complex intermediate followed by kinetically invisible cleavage of the carbon—halogen bond.

It appears that the proxies for activation energy give generally unsatisfactory descriptions of regioselectivity for S_N2 Ar* reactions. The methods, except for the energy-gap model, share a weakness that was pointed out by Michael Dewar in the context of regioselectivity of thermal electrophilic aromatic substitution reactions.[30] In fact, the parallels in that case and the current one for nucleophilic photosubstitutions are striking. The flaw lies in "trying to relate the rates of chemical reactions to some calculated property of the reactants alone."[30] The reason for the popularity of proxy methods, according to Dewar, is that it is difficult to deduce the structures and energies of the competitive transition states. Three proxies of that time based on calculated properties are cited: "free valence" of valence bond theory and Hückel molecular orbital theory, "self-polarizability" that gives rise to calculated charge densities, and "the frontier orbital method", which Dewar thought had "even less to recommend it than the other approaches." Each of these except for the free valence notion is represented in the above list of proxies. That their efficacy is spotty should not be surprising. We do not know of a rapid method for accurately estimating relative transition state energies for nucleophilic photosubstitutions. We suggest it as a fit target for further research, as outlined below.

The energy relationships and reaction species for the current system are represented qualitatively in Scheme 2. Since we do

Scheme 2. Relation of Relative Activation Energies to Energy Changes of Forming σ-Complexes
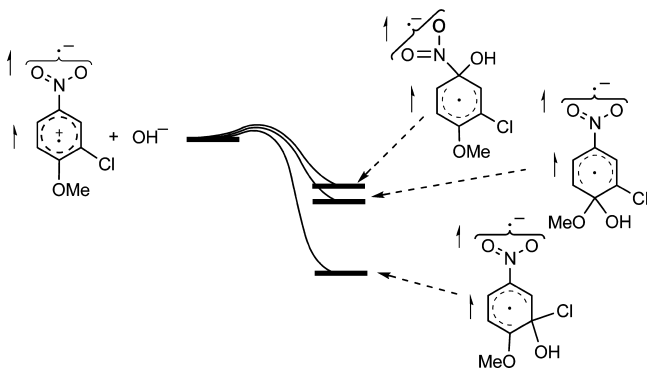
not know the energies of the triplet σ-complexes, the energy levels shown are approximations. The reaction species are valence bond structures adapted to represent triplet states. The predominant excited state of the reactant is triplet π,π^*, which entails excitation from a π molecular orbital chiefly on the ring to an antibonding π orbital chiefly on the nitro group. The electron in the antibonding orbital is shown, in the absence of any means of representing it in the valence bond convention, as an electron distributed in the area of the bracket. Parallel

electron spins are indicated by the arrows. Electron-paired bonding of hydroxide ion occurs in each transition state to the cation radical moiety of the cyclohexadienyl ring. Thus, electron-paired bond formation initiating each substitution reaction can occur at any of the three reaction sites as an adiabatic process that retains triplet multiplicity in the formed σ-complex.

That the bond formation process is adiabatic has been concluded in earlier work.[10,11] It can be rationalized simply. The triplet state of the reactant is actually the ground electronic state in the triplet manifold. There is no accessible state below it of the same multiplicity. The actual bond formation process in the activated complex that has an empirical rate constant of about 10^8 M^{-1} s^{-1} no doubt occurs for single molecules in a time frame of picoseconds. Any diabatic process of bond formation leading to an energetically accessible state would require intersystem crossing. It is exceedingly improbable that intersystem crossing could be coincident with the very fast bond formation process.

Assessment of regioselectivity of S_N2 Ar* reactions by rapid means might be sought first by making quantum chemical computations of the competing transition states. It is likely to be difficult, however, to find the energy increments of the transition states with sufficient accuracy for predicting regioselectivity by direct computation. An alternative approach, suggested by Scheme 2, would be to compute the triplet σ-complexes, which differ substantially in energy and are far easier to define structurally. It should be noted, however, that computations at high levels of theory could not optimize the triplet σ-complex for photosubstitution of chlorine in **1** by hydroxide ion.[23] If a successful computation method could be found for the σ-complexes, the relative energies of the transition states could be inferred through use of an energy correlation such as the Bell—Evans—Polanyi principle. Dewar has provided a detailed theoretical discussion of this method of estimating reactivity.[30] An approach of this kind has been used recently for thermal nucleophilic aromatic substitution regioselectivity.[31]

■ EXPERIMENTAL SECTION

Except as noted below, chemicals and solvents were commercial materials of high purity. Acetonitrile was chromatographic grade. The reactant, 2-chloro-4-nitroanisole, and each of the photoproducts were available from a previous study.[11] UV—vis spectra were obtained with a diode-array spectrophotometer with samples in quartz cuvettes.

Temperature-controlled photolyses were carried out with a Rayonet RPR-208 fitted with seven 350 nm broadband lamps in quartz septum-capped cuvettes suspended in water or water/ice in a uranium glass filter sleeve ($\lambda > 330$ nm) within a vacuum-jacketed quartz well. Reaction solutions were purged with argon through syringe needles for 10 min. UV—vis analyses were done directly in the irradiation cuvettes after exhaustive irradiation.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information
Spreadsheets for the calculation of the experimental product yields and the Arrhenius product yields. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: wubbelsg@unk.edu.

Notes
The authors declare no competing financial interest.

■ REFERENCES

(1) Havinga, E.; de Jongh, R. O.; Dorst, W. *Recl. Trav. Chim. Pays-Bas* **1956**, *75*, 378.

(2) Cornelisse, J.; Havinga, E. *Chem. Rev.* **1975**, *75*, 353.

(3) Fagnoni, M.; Albini, A. *Mol. Supramol. Photochem.* **2006**, *14*, 131.

(4) (a) Zimmerman, H. E.; Somasekhara, S. *J. Am. Chem. Soc.* **1963**, *85*, 922. (b) Zimmerman, H. E. *J. Am. Chem. Soc.* **1995**, *117*, 8988.

(5) Franck, J.; Rabinowitsch, E. *Trans. Faraday Soc.* **1934**, *30*, 120.

(6) Fischer, E. *J. Am. Chem. Soc.* **1960**, *82*, 3249.

(7) Encina, M. V.; Lissi, E. A.; Lemp, E.; Zanocco, A.; Scaiano, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 1856.

(8) Brozic, J. A.; Crosby, G. A. *Coord. Chem. Rev.* **2005**, *249*, 1310.

(9) Gonzales, C.; Pincock, J. *Photochem. Photobiol.* **2006**, *82*, 301.

(10) Wubbels, G. G.; Danial, H.; Policarpio, D. *J. Org. Chem.* **2010**, *75*, 7726.

(11) Wubbels, G. G.; Brown, T. R.; Babcock, T. A.; Johnson, K. M. *J. Org. Chem.* **2008**, *73*, 1925.

(12) van Zeil, P. H. M.; van Eijk, L. M. J.; Varma, C. A. G. O. *J. Photochem.* **1985**, *29*, 415.

(13) Stirling, C. J. M. *Acc. Chem. Res.* **1979**, *12*, 198.

(14) Broxton, T. J.; Muir, D. M.; Parker, A. J. *J. Org. Chem.* **1975**, *40*, 3230.

(15) Ballenger, P.; Long, F. A. *J. Am. Chem. Soc.* **1960**, *82*, 795.

(16) We have not determined the pre-exponential factor (A) by experiment and recognize that it is probably underestimated by the diffusion rate constant. The absolute values of the rate constants and activation energies may, therefore, be slightly inaccurate, but variation of the size of A does not change the calculated relative amounts of reaction in the three reaction channels.

(17) (a) Eigen, M. *Angew. Chem., Int. Ed.* **1964**, *3*, 1. (b) Weller, A. *Z. Physik. Chem.* **1958**, *17*, 224.

(18) Havinga, E.; Kronenberg, M. E. *Pure Appl. Chem.* **1968**, *16*, 137.

(19) van Reil, H. C. H. A.; Lodder, G.; Havinga, E. *J. Am. Chem. Soc.* **1981**, *103*, 7257.

(20) Epiotis, N. D.; Shaik, S. *J. Am. Chem. Soc.* **1978**, *100*, 29.

(21) Mutai, K.; Nakagaki, R.; Takeda, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2066.

(22) Cantos, A.; Marquet, J.; Moreno-Mañas, M.; González-Lafont, A.; Lluch, J. M.; Bertrán, J. *J. Org. Chem.* **1990**, *55*, 3303.

(23) Pintér, B.; De Proft, F.; Veszprémi, T.; Geerlings, P. *J. Org. Chem.* **2008**, *73*, 1243.

(24) Letsinger, R. L.; Steller, K. E. *Tetrahedron Lett.* **1969**, 1401.

(25) Bonhila, J. B. S.; Tedesco, A. C; Nogueira, L. C.; Diamantino, M. T. R. S.; Carreiro, J. C. *Tetrahedron* **1993**, *49*, 3053.

(26) Turro, N. J.; Ramamurthy, V.; Scaiano, J. C. *Modern Molecular Photochemistry of Organic Molecules*; University Science Books: Sausalito, CA, 2010; Chapter 12.

(27) Noyce, D. S.; Virgilio, J. A. *J. Org. Chem.* **1972**, *37*, 2643.

(28) Bunnett, J. F.; Garbish, E. W., Jr.; Pruitt, K. M. *J. Am. Chem. Soc.* **1957**, *79*, 385.

(29) Terrier, F. *Nucleophilic Aromatic Displacement: The Influence of the Nitro Group*; VCH Publishers: New York, 1991; Chapter 1.

(30) Dewar, M. J. S. *The Molecular Orbital Theory of Organic Chemistry*; McGraw-Hill: New York, 1969; Chapter 8.

(31) Liljenberg, M.; Brinck, T.; Herschend, B.; Rein, T.; Tomasi, S.; Svensson, M. *J. Org. Chem.* **2012**, *77*, 3262.