Highly Regioselective Anaerobic Photocyclization of 3-Styrylpyridines

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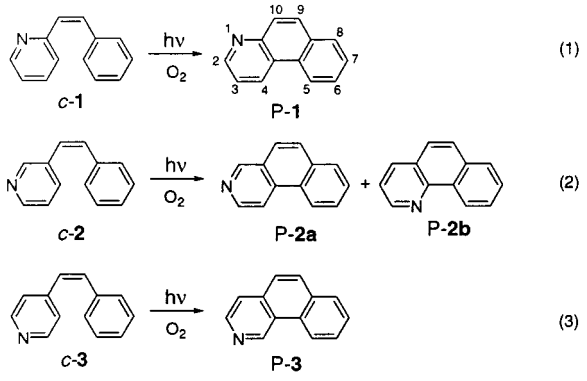
Received December 7, 2000. Revised Manuscript Received February 14, 2001

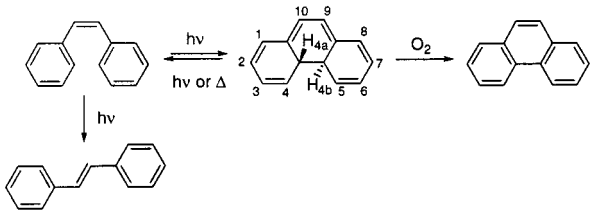
Abstract: The photochemical behavior of the cis isomers of the three isomeric styrylpyridines and two (aminostyryl)pyridines has been investigated under aerobic and anaerobic conditions. Both 3-styrylpyridine and its 3′-amino derivative undergo highly regioselective formation of 2-azaphenanthrene products under anaerobic conditions. In the presence of oxygen, mixtures of 4- and 2-azaphenanthrene products are obtained. The formation of 2-azaphenanthrenes in the absence of oxygen is attributed to conversion of the 4a,4b-dihydroazaphenanthrene primary photoproduct to a 1,4-dihydropyridine intermediate by means of a formal 1,7-hydrogen shift. This intermediate is moderately stable in the absence of oxygen and has been characterized by comparison of its ^{1}H NMR and electronic absorption spectra with calculated spectra. This intermediate is converted to the 2-azaphenanthrene in both the absence and presence of oxygen. The regioselectivity of photocyclization of 3-substituted stilbenes and related diarylethylenes is suggested to depend on the relative rate constants for ring opening and sigmatropic rearrangements of the dihydrophenanthrene intermediates as well as their rates of reaction with oxygen or other oxidants.

Introduction

Irradiation of *cis*-stilbene results in two competitive singlet state isomerization processes, cis,trans isomerization and photocyclization, to give *trans*-4a,4b-dihydrophenanthrene.[1,2] In the presence of oxidants such as molecular oxygen or iodine the dihydrophenanthrene is trapped to yield phenanthrene in good preparative yields (Scheme 1).[3] The cis isomers of the styrylpyridines **1**−**3** display qualitatively similar behavior.[4,5] Irradiation of either the trans or cis isomers of **1** and **3** yields the azaphenanthrenes P-**1** and P-**3**, whereas **2** yields a ca. 4:1 ratio of P-**2a** and P-**2b** (eq 1−3). Since most 3-substituted stilbenes yield a ca. 1:1 ratio of 4- and 2-substituted phenanthrenes, the regioselective formation of P-**2a** is viewed as something of an anomaly.[3]



Scheme 1



In the absence of oxygen the dihydrophenanthrene formed from *cis*-stilbene reverts to starting material either thermally or photochemically.[2] In the case of some substituted *cis*-stilbene derivatives, the dihydrophenanthrene intermediates are converted to stable products in competition with ring opening to regenerate the *cis*-stilbene in the absence of oxygen.[2] The occurrence of 1,*n*-hydrogen shifts to generate isomeric dihydrophenanthrenes which cannot revert to *cis*-stilbenes can occur in both the absence and presence of catalysts.[6−9] The formation of phenanthrenes in the absence of oxygen or other catalysts is less common, but has been observed upon photocyclization of ortho-substituted stilbenes to yield 4a-substituted dihydrophenanthrenes which can undergo exothermic elimination of a stable molecule such as methanol.[3,10] The preparative anaerobic irradiation of the styrylpyridines apparently has not been investigated.

In the course of our investigations of the effects of amine substituents upon the photochemical behavior of stilbenes,[11−14]

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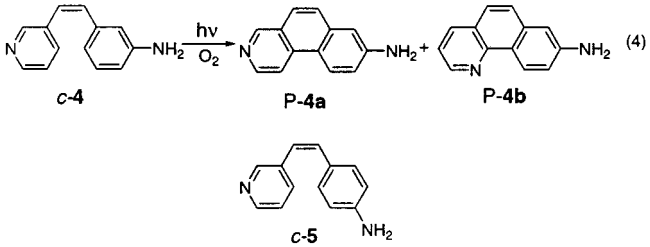
10.1021/ja0042027 CCC: $20.00
Published on Web 04/06/2001

Table 1. Spectroscopic Parameters for the Styrylpyridines[a]

	absorption max, nm	fluorescence max, nm	Φ_f	τ_s, ns
t-**1**	310[b]	365[c]	0.001[d]	0.001[d]
c-**1**	285[e]			
t-**2**	293[b]	358[c]	0.090[d]	0.24[d]
c-**2**	275[e]			
t-**3**	300[b]	356[c]	0.002[d]	0.003[d]
c-**3**	270[e]			
t-**4**[f]	301 (335)[g]	394	0.71	8.1
c-**4**	246 (285)[g]			
t-**5**[f]	336	390	0.021	0.31

[a] Data in hexane or cyclohexane solution. [b] Data from ref 16. [c] Data from ref 17. [d] Data from ref 19. [e] Data from ref 24. [f] Data from ref 11. [g] Position of shoulder in parentheses.

we observed that irradiation of *trans*- or *cis*-3-(3-aminostyryl)-pyridine (**4**) results in formation of a mixture of aminoazaphenanthrenes P-**4a** and P-**4b** in either the presence or absence of oxygen (eq 4), whereas the isomeric 3-(4-aminostyryl)-



pyridine (**5**) fails to undergo cyclization even in the presence of oxygen.[15] Furthermore, the regioselectivity of product formation from **4** was found to be much higher in the absence than in the presence of oxygen. Since *cis*-3-aminostilbene forms aminophenanthrenes only in the presence of oxygen,[14] it seemed likely that anaerobic photocyclization was characteristic of 3-styrylpyridines and not 3-aminostilbenes. We report here the results of an investigation of the effects of oxygen upon the photocyclization of isomeric styrylpyridines **1**−**3** and (aminostyryl)pyridines **4** and **5**. These results indicate that hydrogen migration in one of the regioisomeric azadihydrophenanthrenes formed from 3-styrylpyridines **2** and **4** competes effectively with ring opening in the absence of oxygen. Hydrogen migration leads to a 1,4-dihydropyridine intermediate that loses hydrogen to form azaphenanthrenes P-**2a** and P-**4a** even in the absence of oxygen. A possible mechanism for these unusual and highly regioselective transformations is discussed.

Results and Discussion

Electronic Spectra. The absorption and fluorescence spectra of the trans isomers of the styrylpyridines **1**−**3** and the aminostyrylpyridines **4** and **5** have previously been reported.[11,16−18] Absorption and fluorescence maxima in nonpolar solvents are summarized in Table 1 along with the fluorescence quantum yields (Φ_f)[11,18,19] and decay times (τ_s).[11,18,20] All of these molecules except for **4** have a single allowed long-wavelength absorption band attributed to a π,π^* transition

Table 2. Quantum Yields for Photoisomerization and Cyclization of the Styrylpyridines[a]

	oxidant	$\Phi_{t,c}$	$\Phi_{c,t}$	Φ_{cy}	ratio[b]
1	air	0.25	0.24	0.014	
2	oxygen				3.9:1[c]
	air	0.56	0.22	0.081	5.0:1[c]
	none				>25:1[c]
3	air	0.39	0.34	0.015	
4	oxygen		0.027	0.062	2.2:1
	air		0.033	0.067	2.7:1
	none	0.19	0.048	0.088	14:1
5	none	0.38			

[a] Quantum yield data for **1**−**3** in cyclohexane solution from ref 5. [b] Ratio of products P-**2a**/P-**2b** from **2** and products P-**4a**/P-**4b** from **4**. [c] Data in acetonitrile solution. This study.

similar to that of *trans*-stilbene.[11,19,21] The absorption spectrum of **4** consists of two overlapping bands, similar to that of 3-aminostilbene, for which lowered molecular symmetry is proposed to result in configuration interaction between several one-electron π,π^* transitions.[12,13] The values of Φ_f and τ_s for *t*-**2** and *t*-**5** are similar to those for *trans*-stilbene.[22,23] The much smaller values of Φ_f and τ_s for *t*-**1** and *t*-**3** have been attributed to perturbation of the π,π^* state by a nearly isoenergetic n,π^* state, resulting in greatly enhanced nonradiative decay.[18] The large values of Φ_f and τ_s for *t*-**4** are similar to those of 3-aminostilbene, which have been attributed to a large barrier for singlet state torsion.[12] The fluorescence decay of *t*-**4** is single exponential, even though it is expected to exist as an equilibrium mixture of four ground state rotamers. The decay times of the rotamers most likely are similar, as is the case for *trans*-3-aminostilbene.[12]

The absorption spectra of the cis isomers of **1**−**4** are blue shifted when compared to those of the trans isomers (Table 1) and have lower molar absorptivity.[5,24] These changes are typical of *cis*- vs *trans*-stilbenes and are attributed to the decreased planarity of the cis isomers.[21,25] The absorption maxima of both the cis and trans isomers of **4** and trans isomer of **5** display small red-shifts in polar solvents similar to those of other aminostilbenes.[12,13] The cis isomers of **1**−**4** are either nonfluorescent or very weakly fluorescent ($\Phi_f < 10^{-4}$) at room temperature in both polar and nonpolar solvents as is the case for other *cis*-stilbenes possessing nonconstrained central double bonds.[26] The absence of fluorescence is attributed to low barriers for singlet state cis,trans isomerization and cyclization (Scheme 1) and to low fluorescence rate constants.[26]

Cis,Trans Photoisomerization and Aerobic Photocyclization. Quantum yields for trans,cis and cis,trans photoisomerization (Φ_{tc} and Φ_{ct}) have been reported for the trans isomers of **1**−**5** and the cis isomers of **1**−**3**.[5,18,19] Literature data for nonpolar solvents are reported in Table 2 along with the values for *c*-**4** determined in the present study. Trans,cis photoisomerization is the only photochemical reaction observed for the trans isomers at low conversions. The short singlet lifetimes of the

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trans isomers of **1**−**3** and **5** are consistent with small barriers for singlet state double bond torsion to yield a perpendicular intermediate that decays to a mixture of trans and cis ground-state isomers. The lower values of Φ_{tc} for *t*-**1** and *t*-**3** vs *t*-**2**, like the lower values of Φ_f and τ_s (Table 1), are attributed to the occurrence of rapid singlet state nonradiative decay in competition with double bond torsion.[18−20] Photoisomerization of *t*-**5**, which has values of Φ_{tc} and τ_s similar to those for *trans*-stilbene or 4-aminostilbene, is also expected to occur via a singlet state mechanism.[1,12] In contrast, the relatively inefficient photoisomerization of *t*-**4** most likely occurs via a triplet state mechanism, as is the case for 3-aminostilbene.[12] The rate constant for intersystem crossing for *t*-**4** calculated from the isomerization quantum yield and singlet decay time ($k_{isc} = 2\Phi_{tc}/\tau_s$) is 2.6×10^7 s^{-1}, similar to the value for 3-aminostilbene (2.4×10^7 s^{-1}).[12]

The cis isomers *c*-**1**−*c*-**3** undergo both cis,trans isomerization and azaphenanthrene formation upon irradiation in oxygenated solution.[4,5] Irradiation of *c*-**1** or *c*-**3** results in the formation of a single cyclization product, 1-azaphenanthrene and 3-azaphenanthrene, respectively (eqs 1 and 3). Irradiation of *c*-**2** results in the formation of a 5.0:1 mixture of 2- and 4-azaphenanthrene (P-**2a** and P-**2b**, eq 2) at low conversions. This ratio decreases at higher conversions, plausibly accounting for the lower ratio reported by Bortolus et al.[4,5] A slightly higher ratio is observed for air vs oxygen-purged solutions (Table 2). Similarly, irradiation of *c*-**4** results in the formation of a 2.2:1 mixture of 2-amino-7-azaphenanthrene and 2-amino-5-azaphenanthrene (P-**4a** and P-**4b**, eq 4). The isomeric 4-aminoazaphenanthrenes were formed in <1% yield, based on NMR and GC analysis of the cyclization product mixtures. Irradiation of the trans isomers of **1**−**4** ultimately results in the formation of the same azaphenanthrene products as obtained from the cis isomers. In the case of *t*-**5** prolonged irradiation of oxygenated solutions results in only trace amounts of what are assumed to be photocyclization products. Highly inefficient photocyclization was previously observed for *cis*-4-aminostilbene.[14]

Quantum yields for cis,trans isomerization and azaphenanthrene formation from *c*-**1**−*c*-**4** are reported in Table 2. The values of Φ_{ct} for *c*-**1**−*c*-**3** are similar to that for *cis*-stilbene ($\Phi_{ct} = 0.35$).[1,5] The value of Φ_{ct} for *c*-**4** is distinctly smaller, as previously observed for *cis*-3-aminostilbene.[14] This difference may reflect the presence of a small torsional barrier for the *cis*-3-aminostilbenes that is not present for *cis*-stilbene, *cis*-4-aminostilbene, or *c*-**1**−*c*-**3**.[1,14] The quantum yield for cyclization *c*-**2** is larger than that of its isomers *c*-**1** and *c*-**3**.[5] An even more pronounced difference in cyclization efficiency is observed for *c*-**4** vs *c*-**5**, since the latter fails to form azaphenanthrenes in measurable quantum yield.

Anaerobic Photocyclization. Irradiation of the trans or cis isomers of **1**, **3**, and **5** in solutions that have been degassed by multiple freeze−pump−thaw cycles results in trans,cis isomerization but no detectable azaphenanthrene formation. In contrast, irradiation of the trans or cis isomers of **2** or **4** in degassed solutions results in the regioselective formation of the azaphenanthrenes P-**2a** and P-**4a**, respectively (eqs 2 and 4). Only traces (<6%) of their isomers P-**2b** and P-**4b** are detected by GC or NMR analysis. The optimum conversions of **2** to P-**2a** obtained upon complete conversion of **2** is ca. 40% both in analytical experiments with GC or NMR detection and by product isolation. Quantum yields for the conversion of *c*-**4** to *t*-**4** and the cyclization products P-**4a** and P-**4b** in deoxygenated solution and in the presence of air or oxygen are reported in Table 2. The cyclization quantum yield is observed to increase slightly with decreasing oxygen concentration while the regioselectivity increases dramatically. The value of Φ_{cy} is somewhat larger in benzene solution (0.11) and somewhat lower in methanol (0.069) compared to acetonitrile (0.088); however, the product ratio is similar in all three solvents.

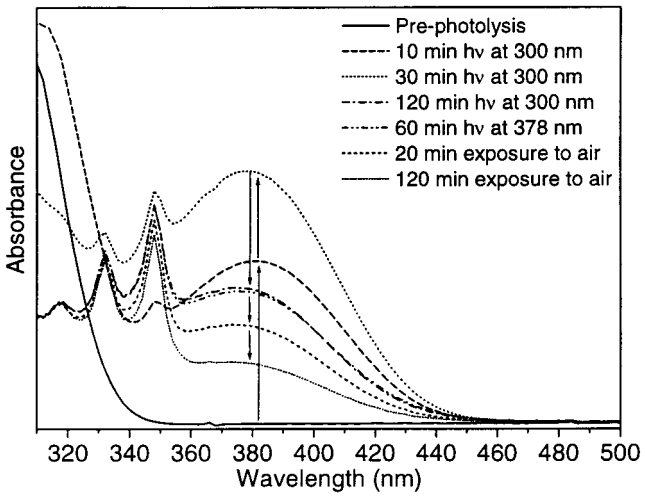


Figure 1. Photolysis of ***c*-2** in degassed acetonitrile.

To our knowledge, the reactions of **2** and **4** provide the first examples of the conversion of a stilbene derivative to a phenanthrene by formal loss of H_2 in the absence of an added oxidizing agent. To obtain information about the mechanism of anaerobic photocyclization of *c*-**2**, the progress of its irradiation in degassed solution was monitored by UV and NMR spectroscopy. The UV absorption spectra of a degassed solution of 1×10^{-3} M *c*-**2** in acetonitrile is shown in Figure 1. Irradiation at 300 nm results in growth of a new species with a broad, structureless absorption band at 378 nm as well as structured azaphenathene absorption at shorter wavelengths. After reaching its maximum intensity, this band slowly disappears upon continued 300 nm irradiation and somewhat more rapidly upon exposure of the degassed solution to air. The 378 absorption band is stable for hours at room-temperature either in the absence of light or upon 378 nm irradiation. This behavior stands in marked contrast to that of the 4a,4b-dihydrophenanthrene formed upon irradiation of *cis*-stilbene that undergoes rapid bleaching upon 400 nm irradiation and instantaneous bleaching upon exposure to oxygen.[2] Thus the 378 nm intermediate observed upon irradiation of *c*-**2** most likely is not a 4a,4b-dihydro-2-azaphenanthrene.

The ^{1}H NMR spectra of 10^{-3} M solutions of *c*-**2** in degassed methanol-d_4 after several incremental irradiation periods are shown in Figure 2. At long irradiation times the spectrum consists of an approximately equal mixture of 2-azaphenanthrene (P-**2a**)[27] and unidentified product(s) with complex signals in the 7−8 ppm region. At intermediate irradiation times, the formation and disappearance of a single set of signals is observed with the same growth and decay times as the 378 nm intermediate observed by UV spectroscopy (Figure 1). The structure of this intermediate is assigned as 2,4a-dihydro-2-azaphenanthrene (*i*-**2a**), based on comparison of the observed and simulated NMR spectra, as shown in Figure 3.[28] Salient features of the NMR spectrum of *i*-**2a** include a slightly broadened upfield signal for H_{4a} and the small coupling constant for H_{4a} and H_b. The latter feature is consistent with the calculated

(27) ^{1}H NMR spectral data for P-**2a** are provided as Supporting Information.

(28) Chemical shifts and coupling constants are provided as Supporting Information.

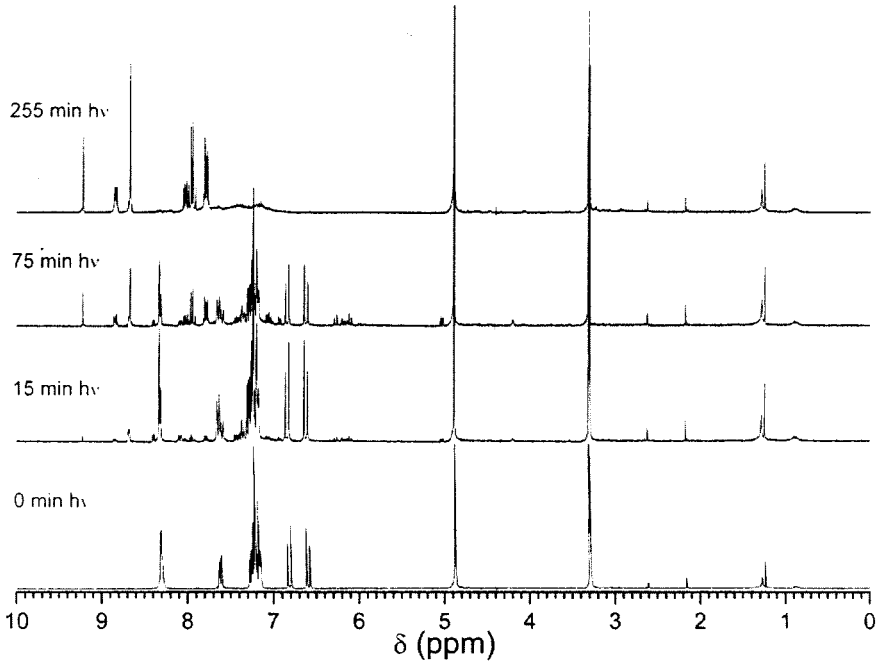


Figure 2. Photolysis of ***c*-2** in methanol-d_4.

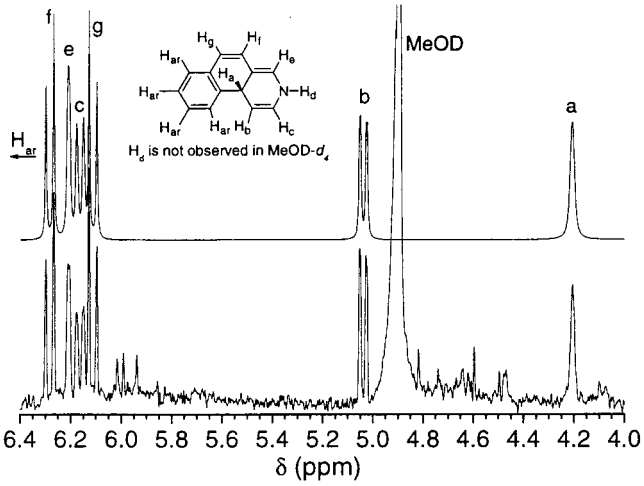


Figure 3. ^{1}H NMR (300 MHz) simulation (upper trace) of *i*-**2a** in methanol-d_4.

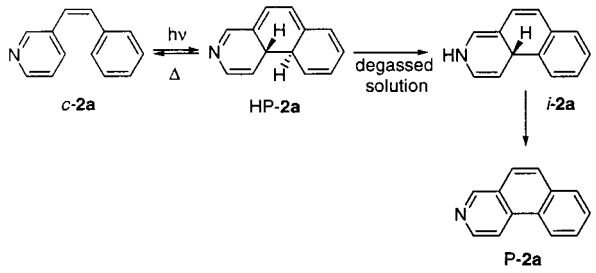
dihedral angle of 80−83° obtained from an AM1-geometry-optimized structure. Integration of the NMR signals assigned to *c*-**2**, *i*-**2a**, and P-**2a** at several irradiation times provides the concentrations of each species (see Supporting Information). The concentration of *i*-**2a** increases rapidly to a maximum value of ca. 15% and then decreases slowly, while the concentration of P-**2a** increases continuously to a maximum value of 40%, similar to the isolated yield.

Qualitatively similar results are obtained when the irradiation of *t*-**4** is monitored by UV or ^{1}H NMR in degassed methanol solution. Disappearance of *t*-**4** is accompanied by the formation of *c*-**4**, which in turn is converted to a mixture of azaphenthanthrene P-**4a** (eq 4) and unidentified product(s) with complex signals in the 6.8−7.5 ppm region.[29] In this case the UV spectrum of the presumed 2,4a-dihydro-2-azaphenanthrene intermediate is not clearly resolved from that of *t*-**4**.

Mechanism of Dihydropyridine Formation. Formation of the 1,4-dihydropyridine intermediate *i*-**2a** and its conversion to

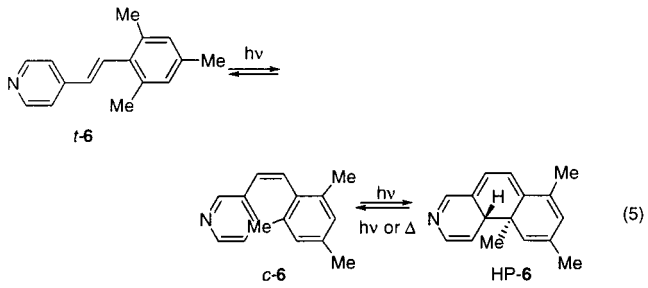
(29) ^{1}H NMR spectra for the sequential formation *c*-**4** and P-**4a** upon irradiation of *t*-**4** under nitrogen are provided as Supporting Information.

Scheme 2



the azaphenanthrene P-**2a** upon anaerobic irradiation of *c*-**2** is consistent with the mechanism outlined in Scheme 2. According to this mechanism, irradiation of the ground-state rotamer *c*-**2a** yields the 4a,4b-dihydroazaphenanthrene HP-**2a**, which undergoes a formal 1,7-hydrogen shift to yield intermediate *i*-**2a**. The first intermediate HP-**2a** is not detected by UV or NMR analysis of irradiated, degassed solutions and thus its conversion to *i*-**2a** must be more rapid than its formation. The formation of azaphenanthrene P-**2a** occurs upon irradiation of *t*-**2** at 170 K in methylcyclohexane−isopentane solution. Thus the activation energy for the conversion of HP-**2a** to *i*-**2a** must be small.

Evidence for the formation of HP-**2a** in the primary photoprocess leading to P-**2a** is provided by the behavior of 3-(2,4,6-trimethylstyryl)pyridine (**6**). Irradiation of *t*-**6** in degassed methylcyclohexane or acetonitrile solutions results in trans,cis isomerization and the formation of an intermediate with an absorption maximum at 470 nm assigned to the HP-**6** (eq 5).



(5)

Table 3. Calculated Ground State (S_0), Lowest Singlet State (S_1), Excitation ($\Delta E_{0,1}$) Energies, and Observed Absorption Maxima (λ_{max})

	S_0,[a] kcal/mol	S_1,[b] kcal/mol	$\Delta E_{0,1}$, kcal/mol (nm)	λ_{max}, nm
c-**2a**	79.4	174.8	95.4 (300)	270
HP-**2a**	92.5	161.4	68.9 (415)	470[c]
i-**2a**	69.1	154.8	85.7 (333)	378
P-**2a**	61.8	149.2	87.4 (327)	348
i-**2b**	75.7	149.8	74.1 (386)	

[a] Calculated using MOPAC/AM1. [b] Calculated using ZINDO. [c] Value for HP-**6**.

This intermediate does not undergo further reaction and reverts to *c*-**6** either thermally or upon long-wavelength irradiation. The 4b-methyl group in HP-**6** presumably prevents rearrangement to a dihydropyridine intermediate analogous to *i*-**2a**. Irradiation of 2,4,6-trimethylstilbene is reported to result in highly inefficient conversion to 1,3-dimethylphenanthrene, a process that requires the loss of methane.[3,30] The absorption maximum for HP-**6** is at substantially longer wavelength than that for the intermediate formed upon anaerobic irradiation of **2** (Figure 1), providing additional evidence that the latter species is not the primary photoproduct HP-**2a** (Scheme 2).

Rearrangements of 4a,4b-dihydrophenanthrene intermediates to more stable dihydrophenanthrene products have been observed to occur via both unimolecular and catalyzed mechanisms. Ho and co-workers[9,31,32] have observed the occurrence of 1,9-hydrogen shifts following anaerobic photocyclization of a number of stilbenes and related diarylethylenes. The primary dihydro intermediates formed upon photocyclization of aryl vinyl sulfides and 2-vinylbiphenyls are reported to undergo 1,4- and 1,5-hydrogen shifts, respectively.[33,34] Thus there is ample precedent for the occurrence of intramolecular 1,*n*-hydrogen shifts, including those which seemingly violate the selection rules for thermal suprafacial sigmatropic rearrangements.[35] Amine-catalyzed rearrangements of 4a,4b-dihydrophenanthrenes to 1,4-dihydrophenanthrenes are believed to occur via sequential 1,3-hydrogen transfer steps.[7,8,36] The formation of 9,10-dihydro-9,10-dicyanostilbene upon irradiation of α,α′-dicyanostilbene [6,37] requires two 1,3-hydrogen transfer steps and is proposed to occur via a radical chain mechanism.[3] We observe that the formation of *i*-**2a** upon irradiation of *c*-**2** is not influenced by the presence of added propylamine and conclude that it is formed by a unimolecular hydrogen shift. Whether the hydrogen shift is a concerted 1,7-process or occurs via two or more sequential shifts remains to be established.

The energetics of the sequential conversion of *c*-**2a** to HP-**2a** and *i*-**2a** (Scheme 2) has been explored by using semiempirical AM1 geometry optimized calculations to obtain the ground state energies and ZINDO calculations to obtain the vertical excited state energies for each of the ground state geometries (see Experimental Section). The gas-phase results are reported in Table 3 and shown in Figure 4. Also reported

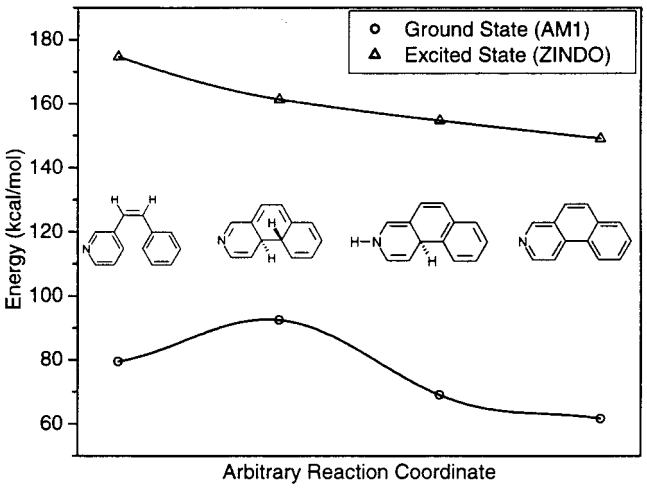


Figure 4. Calculated S_0 and S_1 energies for ***c*-2**, HP-**2a**, *i*-**2a**, and P-**2a**.

in Table 3 are the absorption maxima of these species, where available. The lines connecting the points in Figure 4 show their energetic relationship and do not imply the absence of barriers between ground or excited-state species. As expected, the initial cyclization process is exergonic in the excited state but endergonic in the ground state. The calculated S_0-S_1 energy gaps for *c*-**2a**, HP-**2a**, and *i*-**2a** are 95.4, 68.9, and 85.7 kcal/mol, in accord with the larger red-shift for the absorption maxima of HP-**6** vs *i*-**2a** (470 and 378 nm, respectively). Conversion of ground-state HP-**2a** to *i*-**2a** is calculated to be more exergonic than ring opening to *c*-**2a**. However, the activation energy for the latter process which is symmetry allowed may be lower, accounting in part for the low quantum yield for formation of P-**2a**.

Aromatization of the Dihydropyridine Intermediate. Aromatization of 4a,4b-dihydrophenanthrene in the presence of oxygen is known to be a free radical chain process that can be inhibited by additives such as 2,6-di-*tert*-butyl-4-methylphenol (BHT).[2,38] We find that irradiation of *t*-**2** in the presence of a 100-fold excess of BHT in degassed solution has no effect on the formation of P-**2a**. The formation of P-**2a** under anaerobic conditions is also insensitive to added propylamine, water, or traces of oxygen present in nitrogen-purged solutions. Conversion of *i*-**2a** to P-**2a** is calculated to be only ca. 7 kcal/mol exergonic (Table 3), plausibly accounting for the moderately long lifetime of *i*-**2a** at room temperature (Figures 1 and 3).

The spontaneous loss of hydrogen has not previously been observed for 4a,4b-dihydrophenanthrene intermediates.[3] However, irradiation of *N*-methyldiphenylamine in degassed solution results in the formation of the aromatized photocyclization product *N*-methylcarbazole.[39−43] Bowen and Eland[39] reported the formation of molecular hydrogen in this reaction; however, Förster et al.[42] disputed this report. Grellman et al.[43] proposed that the dihydro intermediate disproportionates to yield a mixture of carbazole and the unstable tetrahydrocarbazole. Disproportionation of *i*-**2a** to yield a mixture of P-**2a** and an unstable tetrahydrophenanthrene could account for both the formation of P-**2a** with a maximum yield of ca. 40% and the presence of

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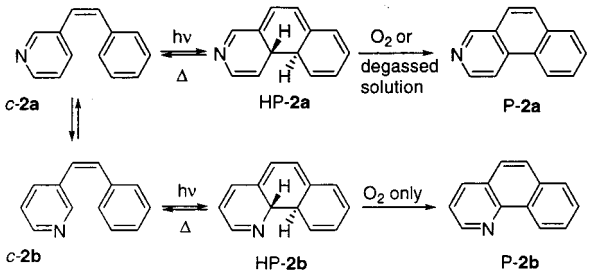
Scheme 3

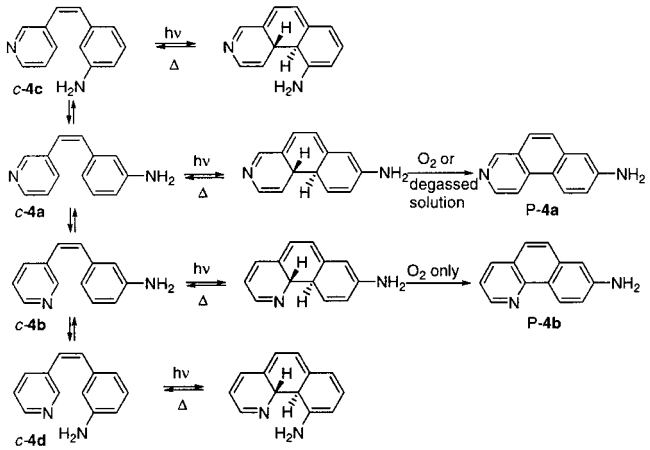


unassigned signals in the NMR spectrum of the irradiated solution (Figure 2). There have also been reports of the photochemical aromatization of 1,4-dihydropyridines.[44,45] However, *i*-**2a** is stable in the dark and irradiation at 378 nm does not accelerate its conversion to P-**2a** (Figure 1). Thus it seems unlikely that this conversion is a unimolecular thermal or photochemical process.

Photocyclization Regioselectivity. A simplified mechanism that accounts for the effect of oxygen upon the regioselectivity of photocyclization of *c*-**2** is shown in Scheme 3. The ground-state rotamers *c*-**2a** and *c*-**2b** are expected to have similar populations and absorption spectra and to undergo competing cyclization and isomerization reactions (Scheme 1). The regioselective formation of P-**2a** has been attributed to more favorable frontier orbital overlap in the transition state for cyclization of rotamer *c*-**2a** vs *c*-**2b**. Whereas there are numerous examples of rotamer specific photochemistry for *trans*- and *cis*-diarylethylenes,[46−49] most 3-substituted stilbenes give a nearly statistical mixture of 2- and 4-substituted phenanthrenes.[3] Thus the possibility that HP-**2a** and HP-**2b** are formed in similar yield, but that the former is aromatized more efficiently, should be considered.

In the absence of oxygen, HP-**2a** undergoes a thermal 1,7-hydrogen shift to form the 1,4-dihydropyridine intermediate *i*-**2a** in competition with ring opening to *c*-**2a** (Scheme 2), whereas HP-**2b** undergoes ring opening to *c*-**2b**. Evidently, an intramolecular hydrogen shift to form an unstable 1,2-dihydropyridine intermediate does not compete with ring opening in this case or in the case of the intermediates formed from the styrylpyridines **1** and **3**. The calculated energy of the 1,2-dihydropyridine that would be formed from HP-**2b** is 7 kcal/mol greater than that of *i*-**2a**, in accord with the greater stability of 1,4- vs 1,2-dihydropyridines.[50] Reaction of HP-**2b** with oxygen competes with ring opening under aerobic conditions, resulting in a decrease in cyclization regioselectivity. The observed 4.9:1 ratio of P-**2a**/P-**2b** in the presence of oxygen may reflect incomplete reaction of HP-**2b** with oxygen. Ring opening of dihydrophenanthrene-type intermediates is known to be more rapid than trapping by oxygen in some cases.[2,49] In fact a flash photolysis study of *c*-**1** and *c*-**2** by Bortolus et al.[5] suggests that the intermediates (presumably dihydroazaphenanthrenes) have short lifetimes in the absence of oxygen. Addition of iodine is often observed to increase the yields of 1,2-diarylethylene photocyclizations by intercepting the dihydrophenanthrene intermediates.[3] However, in the case of the styrylpyridines, cyclization yields are reported to decrease upon addition of iodine.[51]

Scheme 4



The photocyclization of the 3-(3-aminostyryl)pyridine **4** is regioselective in both the presence and absence of oxygen (Table 2). These results can be rationalized in terms of the simplified mechanism shown in Scheme 4. The four rotamers of *c*-**4** are anticipated to have similar ground-state populations and to undergo cyclization with comparable efficiency to yield four dihydroazaphenanthrene intermediates. In the presence of oxygen, rotamers *c*-**4a** and *c*-**4b** yield azaphenanthrenes P-**4a** and P-**4b** in a 2.2:1 ratio. However, rotamers *c*-**4c** and *c*-**4d** fail to yield azaphenanthrenes.

Steric acceleration of dihydrophenanthrene ring opening by bay-region substituents has been observed by Mallory and Mallory[30] for the photocyclization of 3,3′-dimethylstilbene, which forms 4,5-dimethylphenathrene only in the presence of high concentrations of iodine. The formation of both 2- and 4-aminophenanthrene in a 3:1 ratio is observed upon aerobic photocyclization of 3-aminostilbene.[14] However, the dihydrophenanthrene intermediates formed in this reaction are thermally stable in the absence of oxygen and can be detected by UV absorption. Thus the absence of products from rotamers *c*-**4c** and *c*-**4d** most likely results from the facile thermal ring opening of the dihydroazaphenanthrene intermediates, which is accelerated by the bay-region amino group.

The highly selective formation of aminoazaphenanthrene P-**4a** upon irradiation of **4** in the absence of oxygen is analogous to the formation of P-**2a** under similar conditions. Evidently the 4a,4b-dihydrophenanthrene intermediate from *c*-**4a** undergoes a 1,7-hydrogen shift to form a relatively stable dihydropyridine intermediate whereas the intermediate from *c*-**4b** fails to do so.

Unlike **4** which undergoes moderately efficient photocyclization, 3-(4-aminostyryl)pyridine **5** fails to form photocyclization products in either the presence or absence of oxygen. The behavior of **4** and **5** is analogous to that of *cis*-3- and 4-aminostilbene which have photocyclization quantum yields of 0.28 and 0.004, respectively.[52] We have attributed this difference to a lower barrier for the competing cis,trans photoisomerization process in the 4- vs 3-aminostilbene.[14] It is also possible that ring opening of the dihydrophenanthrene intermediate is more rapid than reaction with oxygen in the case of the 4-aminostilbenes. It is interesting to note that the aminostyrylpyridine **4** displays photocyclization behavior similar

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to that of the styrylpyridine **2** rather than that of 3-aminostilbene, whereas **5** displays behavior similar to that of 4-aminostilbene rather than the styrylpyridine **3**.

Concluding Remarks

Both 3-styrylpyridine (**2**) and its 3-aminostyryl derivative (**4**) undergo highly regioselective photocyclization under anaerobic conditions. The high regioselectivity is a consequence of a dark (nonphotochemical) 1,7-hydrogen shift that converts one of the two dihydroazaphenanthrene primary photoproducts into a 1,4-dihydropyridine, which is moderately stable under irradiation conditions but is converted to the 2-azaphenanthrene in both the absence and presence of oxygen. The other dihydroazaphenanthrene reverts to starting material rather than forming the less stable 1,2-dihydropyridine. In the presence of oxygen, the two regioisomeric dihydroazaphenanthrenes are oxidized to provide a mixture of 2- and 4-azaphenanthrenes. The 1,4-dihydropyridine intermediate has been characterized by simulation of NMR and absorption spectra; however, the mechanism of its anaerobic conversion to 2-azaphenanthrene remains to be fully elucidated. Similar behavior is observed for **4**, which selectively forms a single azaphenanthrene in the absence of oxygen and a mixture of two azaphenanthrenes in the presence of oxygen.

These results suggest that the regioselectivity of cyclization of 3-substituted stilbenes and related 1,2-diarylethylenes may be determined by the relative rates of ring opening and sigmatropic rearrangements of the dihydrophenanthrene-type intermediates as well as their rates of oxidation. These rates should be sensitive to the structure of the intermediate, solvent, temperature, and the concentration and reactivity of the oxidant. Further studies will be required to establish the kinetics of these processes.

Experimental Section

Materials. Styrylpyridines, *c*-**1**−*c*-**3**, were prepared by the standard Wittig procedure.[53] Corresponding pyridine carboxaldehydes (Aldrich) were reacted with triphenylphosphonium chloride (Aldrich) in a $CH_2Cl_2-H_2O$ dual phase system with tetrabutylammonium iodide (Aldrich) as a phase-transfer catalyst (10 mol %). The reaction mixture was stirred at room-temperature overnight under a N_2 atmosphere. After completion of the reaction, the CH_2Cl_2 layer was separated and washed with brine and deionized water several times. Purification was carried out by column chromatography (SiO_2/hexanes−EtOAc (80:20), 230−400 mesh SiO_2) to remove the trans isomer and triphenylphosphine oxide. Column chromatography was repeated to purify the cis isomers to ≥98% purity. All cis isomers were isolated as pale yellow oils with typical overall yields being 20%. The synthesis of *t*-**4** and *t*-**5** was carried out as described above with use of the corresponding pyridine carboxaldehyde and (nitrophenyl)triphenylphosphonium bromide.[15] The trans isomers were enriched by refluxing dilute benzene solutions with catalytic amounts of I_2 under nitrogen with exposure to visible light. Further purification of the nitro derivatives of styrylpyridines was carried out by recrystallization from methanol. Reduction of the nitro group to the amino group was carried out with $SnCl_2 \cdot 2H_2O$/EtOH (anhydrous) as the reducing agent.[15,54] Typical yields from the reduction were 80%. Purification of the corresponding *t*-**4** and *t*-**5** was carried out by recrystallization from HPLC grade MeOH (*t*-**4** mp 127.5−128.5 °C; *t*-**5** mp 181.5−182.5 °C).[15] All compounds were found to have greater than 98.5% purity as estimated by GC analysis. ^{1}H NMR and GCMS were used to establish the identity and purity of all compounds. All solvents used for spectroscopy and photolyses were either spectrophotometric or HPLC grade (Fisher) and were used as received.

Methods. ^{1}H NMR spectra were measured on a Varian Gemini 300 spectrometer. GLC analysis was performed on a Hewlett-Packard HP 5890 instrument equipped with a HP1 poly(dimethylsiloxane) capillary column. UV−vis spectra were measured on a Hewlett-Packard 8452A diode array spectrometer with a 1 cm path length quartz cell. Fluorescence spectra were measured on a SPEX Fluoromax spectrometer. Phenanthrene ($\Phi_f = 0.14$[55]) was used as a external standard for the measurement of fluorescence quantum yields of *t*-**4** and *t*-**5**. Fluorescence quantum yields were measured by comparing the integrated area under the fluorescence curve for the *trans*-aminostyrylpyridines and phenanthrene at equal absorbance at the same excitation wavelength. All fluorescence spectra are uncorrected and the estimated error for the fluorescence quantum yields is ±15%, although the quantum yields were corrected for the refractive index of the solvent. Fluorescence decays were measured on a Photon Technologies International LS-1 single photon counting apparatus with a gated hydrogen arc lamp using a scatter solution to profile the instrument response function. Nonlinear least-squares fitting of the decay curves were performed with the Levenburg-Marquardt algorithm as described by James et al.[56] as implemented by the Photon Technologies International Timemaster (version 1.2) software. Goodness of fit was determined by judging the χ^2 (<1.3 in all cases), the residuals, and the Durbin−Watson parameter (>1.6 in all cases). Measurements of quantum yields of photoisomerization for *t*-**4** and *t*-**5** were performed on optically dense degassed solutions ($\sim 10^{-3}$ M) with use of an excitation wavelength of 313 nm. The extent of photoisomerization (<5%) was quantified by GLC. Excitation at 313 nm was achieved with a 450 W medium-pressure mercury arc lamp filtered through an alkaline potassium dichromate solution. All quantum yield measurements and nitrogen-purged photolyses were performed on solutions that were purged with dry N_2 for 20−25 min. Photolyses were carried out on a Rayonet RPR-100 photochemical reactor fitted with 7-16, RPR-3000 Å bulbs (300 nm). Vacuum-degassed solutions were prepared in Pyrex cuvettes that were modified to permit a freeze−pump−thaw procedure (5 cycles; silicone oil diffusion pump, $<10^{-4}$ Torr) and were flame sealed. INDO/S-CIS-SCF (ZINDO) calculations (9 occupied and 9 unoccupied frontier orbitals) were performed on a Macintosh IIfx computer with the ZINDO Hamiltonian as implemented by Cache Release 3.5.[57,58] All molecular models used in the semiempirical calculations were based on SCF/AM1 optimized ground-state geometries by using the MOPAC (version 94.10) suite of programs as implemented under Cache Release 3.5.[58]

Acknowledgment. We thank Professor Frank Mallory for helpful suggestions and Xiaobing Zuo for measurements of some of the product ratios. Funding for this project was provided by NSF grant CHE-9734941.

Supporting Information Available: The NMR integration of the signals from the photolysis of ***c*-2**, ^{1}H NMR spectrum of P-**2a**, chemical shift and coupling constants for P-**2a** and *i*-**2a**, NMR integrals for the irradiation of *c*-**2** in methanol solution, and NMR spectra of *t*-**4** during irradiation (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA0042027

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