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Vapor-Phase Photochemistry of Methyl- and Cyanopyridines: Deuterium Labeling Studies

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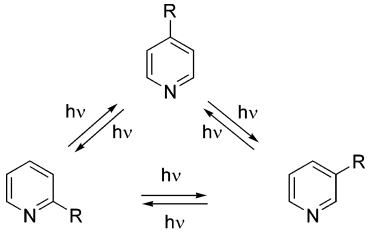


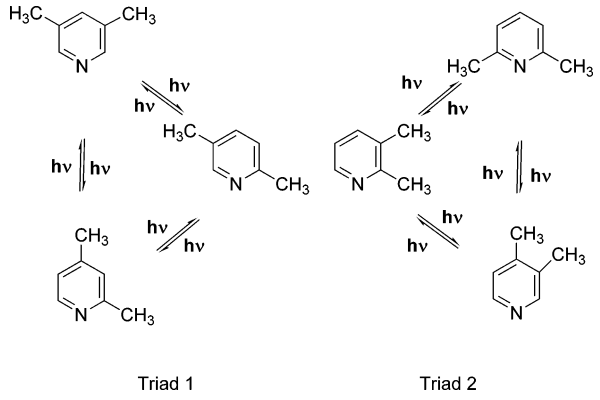
R = CH_3 or CN

The three isomeric methylpyridines and the three isomeric cyanopyridines each constitute a photochemical triad. Irradition of each methylpyridine or each cyanopyridine in the vapor phase at 254 nm results in the formation of the other two isomers as primary photoproducts. Dideuteration of the 2-substituted or 3-substituted methyl or cyanopyridines expanded each triad to a pentad. Due to symmetry, 2,6-dideuteration of 4-methyl-or 4-cyanopyridine did not expand the triad. Trideuteration of 4-methylpyridine removed this symmetry and resulted in a photochemical pentad. These results are consistent with a mechanism involving 2,6-photocylization, migration of nitrogen around the five sides of the cyclopentenyl ring, and rearomatization. This mechanism exactly predicts the observed distribution of deuterium in the photoproducts.

Introduction

Previous work in this laboratory[1] has shown that the six isomeric dimethylpyridines constitute two photochemical triads as shown in Scheme 1. Irradiation of any one member of each triad in the vapor phase at 254 nm resulted in the formation of the other two isomers of the triad. These observations were rationalized by suggesting that photochemical excitation at 254 nm results in 2,6-cyclization to yield an azaprefulvene diradical. Subsequently, one or two nitrogen migrations followed by rearomatization would allow nitrogen to insert between each pair of ring carbon atoms, resulting in the interconversion of the three members of each triad.[1] Similar mechanisms have been suggested to explain the phototransposition of both five-and six-membered heteroaromatic compounds,[2] and a similar mechanism was also proposed by Pincock et al. to explain the photoisomerization reactions of isomeric cyanotoluenes.[3]

SCHEME 1



Triad 1 Triad 2

These studies have now been extended to the photochemistry of monomethyl and monocyano substituted pyridines in the vapor phase. These results are described in this manuscript.

(1) Pavlik, J. W.; Kebede, N.; Thompson, M.; Day, A. C.; Barltrop, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 5666.

(2) See, for example: Pavlik, J. W.; Kurzweil, E. M. *J. Org. Chem.* **1991**, *56*, 6313; Pavlik, J. W.; Tongcharoensirikul, P.; Bird, N. P.; Day, A. C.; Barltrop, J. A. *J. Am. Chem. Soc.* **1994**, *116*, 2292; Pavlik, J. W.; Patten, A. D.; Bolin, D. R.; Bradford, K. C.; Clennan, E. L. *J. Org. Chem.* **1984**, *49*, 4523.

(3) MacLeod, P. J.; Pincock, A. L.; Pincock, J. A.; Thompson, K. A. *J. Am. Chem. Soc.* **1998**, *120*, 6443.

10.1021/jo070810u CCC: $37.00
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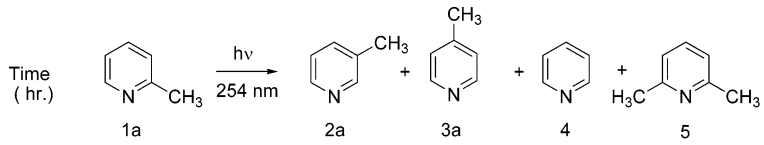
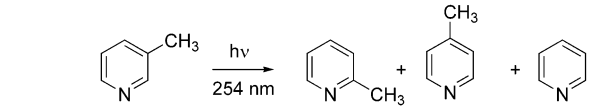
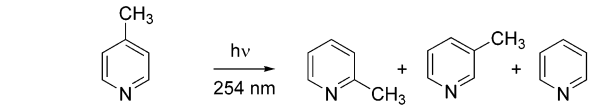
TABLE 1. Products from the Photolysis of Methylpyridines[a]



Time (hr.)	1a	2a	3a	4	5	Ratio 2a:3a
						(5.8)[b]
3	-5.0	3.4	0.6	trace	trace	5.7
6	-10.0	6.6	1.9	trace	trace	3.5
12	-20.0	13.2	4.4	trace	trace	3.0



	2a	1a	3a	4		1a:3a
						(1.8)[b]
3	-16.5	10.5	5.7	trace		1.8
6	-27.3	17.2	9.5	trace		1.8
12	-38.3	24.2	14.4	trace		1.7



	3a	1a	2a	4		2a:1a
						(1.5)[b]
3	-11.7	4.4	6.7	trace		1.5
6	-16.6	6.7	9.3	trace		1.4
12	-20.5	8.7	11.4	trace		1.3

[a] Numbers are percent of reactant consumed or the percent yields of products formed after irradiation for the time indicated. [b] Ratio at 0-irradiation time.

Results and Discussion

Each methylpyridine (**1a**−**3a**) or cyanopyridine (**1b**−**3b**) vapor, with a total pressure of 2.5−2.7 or 0.3−0.4 Torr, respectively, was irradiated at 254 nm in a 3.0 L quartz reaction flask for specific time periods. After each irradiation, the volatile materials were pumped out of the reaction flask, condensed, and dissolved in a standard volume of ether for quantitative GLC analysis. The recovered material accounted for 33−60 or 75−100% of the mass of the original methylpyridine (**1a**−**3a**) or cyanopyridine (**1b**−**3b**) reactant, respectively. Products were identified by GLC retention times, by GLC co-injections with authentic samples, by mass spectroscopy, and in the case of methylpyridines, by ^{13}C NMR spectroscopy. The ether solutions were then allowed to evaporate, and the residues were dissolved in $CDCl_3$ or acetone-d_6 and analyzed by NMR. Photolyses were also accompanied by formation of variable amounts of non-volatile polymeric material, which accumulated on the sides of the reaction flask and is partially responsible for the low mass balances, particularly in the case of the methylpyridines. ^1H NMR analysis of this material showed the presence of small quantities of the same photoproducts that were observed in the vapor phase and a large amount of aliphatic protons, suggesting that polymerization was accompanied by ring opening.

Methylpyridines. 2-, 3-, or 4-Methylpyridines (**1a**), (**2a**), or (**3a**) vapors were irradiated at 254 nm for 3, 6, or 12 h. GLC analysis after each irradiation time showed the continuous consumption of the reactants and the formation of increasing quantities of the other two isomeric methylpyridines and a trace quantity of pyridine (**4**). In addition, a trace quantity of 2,6-dimethylpyridine (**5**) was observed after irradiation of **1a**. The percent consumption of the reactants and the yields of the phototransposition products are shown in Table 1.

Table 1 shows that upon irradiation of 2-methylpyridine (**1a**) vapor, the yields[4] of 3-methylpyridine (**2a**) and 4-methylpyridine (**3a**) increased from 3.4 and 0.6%, respectively, after 3.0 h of irradiation to 13.2 and 4.4%, respectively, after 12.0 h. The ratio of the yields of **2a** and **3a** decreased in a linear manner from 5.7 after 3.0 h to 3.0 after 12.0 h of irradiation. This decreasing ratio suggests that once formed, **2a** undergoes phototransposition more rapidly than **3a**.

Upon irradiation of 3-methylpyridine (**2a**) vapor, analysis by GLC showed that the yield of 2-methylpyridine (**1a**) increased from 10.5% after 3.0 h of irradiation to 24.2% after 12.0 h of irradiation whereas the yield of 4-methylpyridine (**3a**) increased from 5.7 to 14.4% during the same irradiation period. The ratio of the yields of **1a:3a** remained essentially constant at 1.8 over the 12.0 h of irradiation. Analysis of the condensed product mixture by ^{13}C NMR spectroscopy confirmed the formation of **1a** and **3a**.

Irradiation of 4-methylpyridine (**3a**) vapor also resulted in the formation of the other two methylpyridine isomers **1a** and **2a**. In this case, the yield of 2-methylpyridine (**1a**) increased from 4.4% after 3.0 h of irradiation to 8.7% after 12.0 h whereas the yield of 3-methylpyridine (**2a**) increased from 6.7 to 11.4%

(4) All yields reported are absolute yields determined from the number of moles of products formed and the number of moles of reactant consumed.

TABLE 2. Products from the Photolysis of Cyanopyridines[a]

Time (min.)				Ratio
	1b	2b	3b	2b:3b (2.4)[b]
15	- 4.9	3.6	1.3	2.8
60	-22.7	18.4	4.3	4.3
75	-27.0	22.4	4.6	4.9
90	-35.3	29.4	5.9	5.0
	2b	1b	3b	1b:3b (0.8)[b]
60	- 3.0	1.5	1.6	0.9
120	-4.5	2.5	2.1	1.2
240	-8.9	5.1	3.8	1.3
360	-7.5	4.6	2.9	1.6
	3b	1b	2b	2b:1b (·13)[b]
23	- 26.6	2.1	24.5	11.7
45	-39.7	2.9	36.8	12.7
70	-47.0	3.5	43.5	12.4
90	-59.8	5.6	54.3	9.7

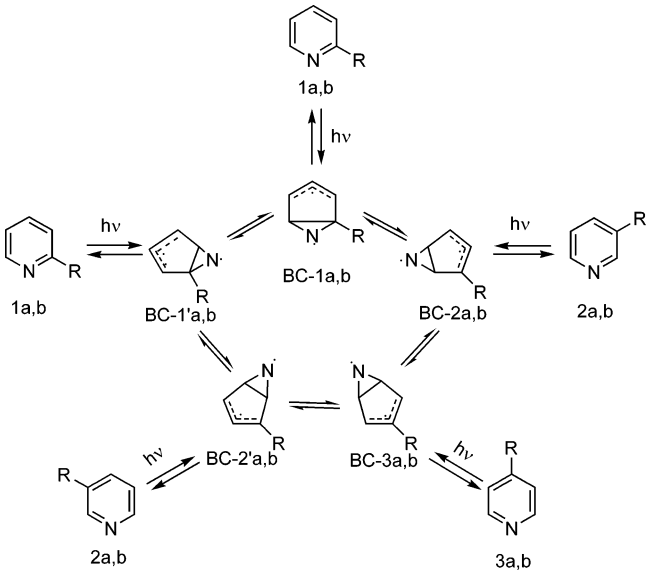
[a] Numbers are percent of reactant consumed or the percent yields of products formed after irradiation for the time indicated. [b] Ratio at 0-irradiation time.

during the same period of irradiation. The ratio of **2a:1a** decreased slowly from 1.5 after 3.0 h of irradiation to 1.3 after 12.0 h.

Cyanopyridines. 2-Cyanopyridine (**1b)** vapor (0.3−0.4 Torr) was irradiated at 254 nm for 5, 10, 15, 30, 60, 75, or 90 min. Although product formation was below the level of detectability at irradiation times shorter than 15 min, GLC analysis after 15−90 min of irradiation showed the consumption of various amounts of **1b** and the formation of 3-cyanopyridine (**2b)** and 4-cyanopyridine (**3b)**. The reactant consumption and product formation over this irradiation time are shown in Table 2. As shown, the yields of 3-cyanopyridine (**2b**) and 4-cyanopyridine (**3b**) increased from 3.6 and 1.3%, respectively, after 15 min of irradiation to 29.4 and 5.9%, respectively, after 90 min of irradiation. Over the range of 15−90 min of irradiation, the ratio of **2b:3b** increased linearly from 2.8 to 5.0. Since the ratio of **2b:3b** increased with irradiation time, it appears that, once formed, **3b** phototransposes to **2b** faster than **2b** is transposed. Subsequent experiments confirmed that **3b** is substantially more photoreactive than **2b**.

3-Cyanopyridine (**2b)** vapor was also irradiated at 254 nm. In this case, product formation could not be detected until after 60 min of irradiation, suggesting that **2b** is substantially less

SCHEME 2 [a]



[a] a = CH_3; b = CN.

reactive than **1b**. Table 2 shows the extent of reactant consumption and formation of **1b** and **3b** over the range of 60−360 min of irradiation. As shown, only 3.0% of **2b** was consumed after 60 min of irradiation whereas after 360 min of irradiation, only 7.5% of **2b** was consumed while the yields of **1b** and **3b** were 4.1 and 2.9%, respectively. During this irradiation time, the ratio of 2-cyanopyridine (**1b)** to 4-cyanopyridine (**3b)** formed increased linearly from 0.9 to 1.6.

4-Cyanopyridine (**3b**) vapor (0.3−0.4 Torr) was irradiated at 254 nm for 25, 45, 70, and 90 min. GLC analysis of the resulting product mixtures revealed that consumption of **3b** and the formation of 2-cyanopyridine (**1b**) and 3-cyanopyridine (**2b**). Table 2 shows the percent consumption of reactant **3b** and the percent of products **1b** and **2b** formed after each irradiation time. Thus, after 90 min of irradiation, approximately 60% of **3b** was consumed whereas the yields of **1b** and **2b** were approximately 6 and 54%, respectively. The table also shows that the ratio of **2b:1b** decreases from approximately 11.7 after 23 min of irradiation to 9.7 after 90 min.

Tables 1 and 2 also show the product ratios obtained by plotting the observed ratios as a function of irradiation time and extrapolating to zero irradiation time. In all cases, the values at zero irradiation time indicate that both products were formed at very short irradiation times and are therefore primary products.

The data in Tables 1 and 2 indicate that whereas 3-methylpyridine (**2a**) is the most reactive methylpyridine isomer, 3-cyanopyridine (**2b**) is the least reactive cyanopyridine isomer. Subsequent deuterium labeling experiments described later in this paper show that the major reaction of **2b** is to transpose to itself. The apparent low reactivity of **2b** is thus due to this "hidden" transposition not observed in the absence of labeling.

These results show that the three isomeric methylpyridines **1a**−**3a** and the three isomeric cyanopyridines **1b**−**3b** each constitute a photochemical triad. Irradiation of each methylpyridine **1a**−**3a** or each cyanopyridine **1b**−**3b** in the vapor phase at 254 nm results in the formation of the other two methyl or cyanopyridine isomers.

Inspection of the mechanism in Scheme 2 shows that 2,6-photocyclization of **1a**,**b** results in the formation of azapreful-

venes **BC-1a**,**b**. N-migration in the counterclockwise direction converts **BC-1a**,**b** to **BC-1′a**,**b**, which would rearomatize back to **1a**,**b**. This would be an energy wasting pathway. N-migration in the opposite direction, however, leads to **BC-2a**,**b**, the precursor of the 3-substituted pyridines **2a**,**b**. Thus, the 3-substituted pyridines **2a**,**b** can be formed from the 2-substituted isomers **1a**,**b** by either the one nitrogen migration pathway **1a**,**b** $\xrightarrow{h\nu}$ **BC-1a**,**b** → **BC-2a**,**b** → **2a**,**b** or the two nitrogen-migration pathway **1a**,**b** $\xrightarrow{h\nu}$ **BC-1a**,**b** → **BC-1′a**,**b** → **BC-2′a**,**b** → **2a**,**b**. Alternatively, conversion of **1a**,**b** to the 4-substituted pyridines **3a**,**b** cannot occur via a one nitrogen migration pathway but requires either two nitrogen migrations, **1a**,**b** $\xrightarrow{h\nu}$ **BC-1a**,**b** → **BC-2a**,**b** → **BC-3 a**,**b** → **3a**,**b** or the pathway **1a**,**b** $\xrightarrow{h\nu}$ **BC-1a**,**b** → **BC-1′a**,**b** → **BC-2′a**,**b** → **BC-3a**,**b** → **3a**,**b** involving three N-migrations. Since both **2a**,**b** and **3a**,**b** are primary photoproducts from **1a**,**b**, both one and at least two nitrogen migration pathways must be in operation.

Because of the stabilizing effects of the substituent at the end of the allyl system, **BC-2a**,**b**, is expected to be more stable than either **BC-1a**,**b** or **BC-3a**,**b**. The pathways **BC-2a**,**b** → **BC-1a**,**b** and **BC-2a**,**b** → **BC-3a**,**b** would therefore be expected to be slow compared to be rearomatization of **BC-2a**,**b** to 3-substituted pyridines **2a**,**b**. This presumably accounts for the greater yields of 3-stubstituted pyridines **2a**,**b** than either 2- or 4-substituted pyridines **1a**,**b** or **3a**,**b**. The difference in product distribution is particularly enhanced by cyano substitution. Thus, whereas photolysis of 4-methylpyridine (**3a)** resulted in 3-methlypyridine (**2a)** and 2-methylpyridine (**1a)** in a ratio of 1.3, 3-cyanopyridine (**2b)** and 2-cyanopyridine (**1b)** were formed in a ratio of 9.7 by photolysis of 4-cyanopyridine (**3b)**. The same selectivity for the formation of the 3-substituted pyridine was also observed upon photolysis of 2-substituted pyridines. Thus, whereas 2-methlypyridine (**1a)** transposed to 3-methlypyridine (**2a)** and 4-methylpyridine (**3a)** in a ratio of 3.0, irradiation of 2-cyanopyridine (**1b)** led to the formation of 3-cyanopyridine (**2b)** and 4-cyanopyridine (**3b)** in a ratio of 4.9. The greater regioselectivity exhibited by the cyanopyridines is presumably due to the greater stability of the cyano substituted azaprefuluene **BC-2b** than the methyl substituted intermediate **BC-2a**. This is consistent with AUMP2 calculations, which predict that allyl radicals are more stabilized by cyano substitution than by methyl substitution.[5]

Although it is assumed that both one and two nitrogen migration pathways operate from excited 3-substituted pyridines **2a**,**b**, inspection of Scheme 1 shows that the one nitrogen migration pathway **2a**,**b** $\xrightarrow{h\nu}$ **BC-2a**,**b** → **BC-1a**,**b** → **1a**,**b** and the two nitrogen migration pathway **2a**,**b** $\xrightarrow{h\nu}$ **BC-2a**,**b** → **BC-1a**,**b** → **BC-1′a**,**b** → **1a**,**b** both lead to 2-substituted pyridines **1a**,**b**. Thus, it is impossible to determine whether the observed 2-substituted pyridines **1a**,**b** were formed by the one or two nitrogen migration pathways. Furthermore, it is not possible to estimate the extent of involvement of the energy wasting pathway **2a**,**b** $\xrightarrow{h\nu}$ **BC-2a**,**b** → **BC-3a**,**b** → **BC-2′a**,**b** → **2a**,**b**.

Similar ambiguities exist in the photochemistry of 2-substituted pyridines **1a**,**b**. Thus, it is not possible to distinguish between 3-substituted pyridine **2a**,**b** formation via the one nitrogen migration pathway **1a**,**b** $\xrightarrow{h\nu}$ **BC-1a**,**b** → **BC-2a**,**b** → **2a**,**b** and the pathway involving two nitrogen migrations, **1a**,**b** $\xrightarrow{h\nu}$ **BC-1a**,**b** → **BC-1′a**,**b** → **BC-2′a**,**b** → **2a**,**b**. Furthermore, the pathway **1a**,**b** $\xrightarrow{h\nu}$ **BC-1a**,**b** → **BC-1′a**,**b** → **1a**,**b** leads back to the reactant and therefore would be an energy wasting hidden transposition.

(5) Lehd, M.; Jensen, F. *J. Org. Chem.* **1991**, *56*, 824.

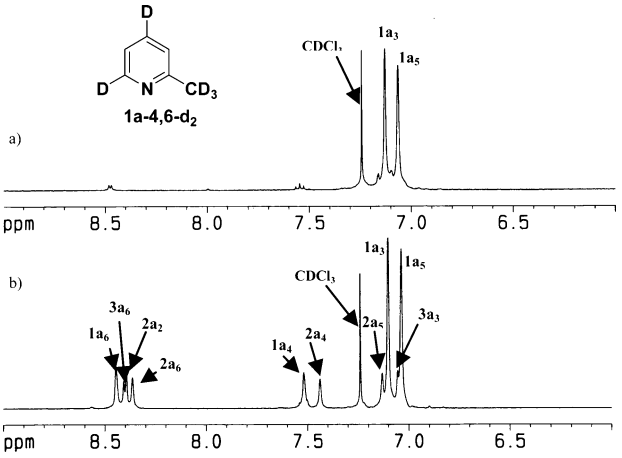


FIGURE 1. ^{1}H NMR spectrum from δ6.5 to 8.5 of 2-trideuteriomethylpyridine-4,6-d_2 (**1a-4,6-d_2**) in $CDCl_3$ (a) before irradiation and (b) after irradiation in the vapor phase at 254 nm.

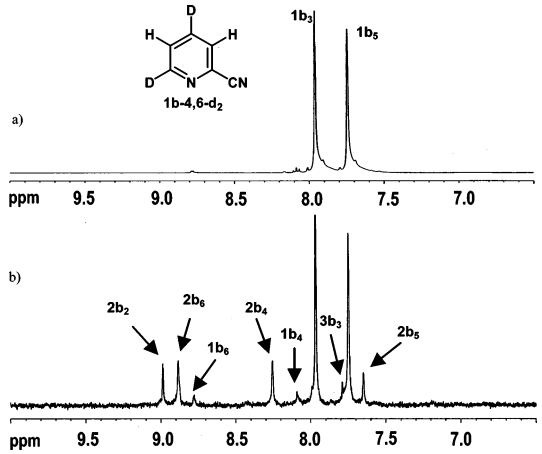
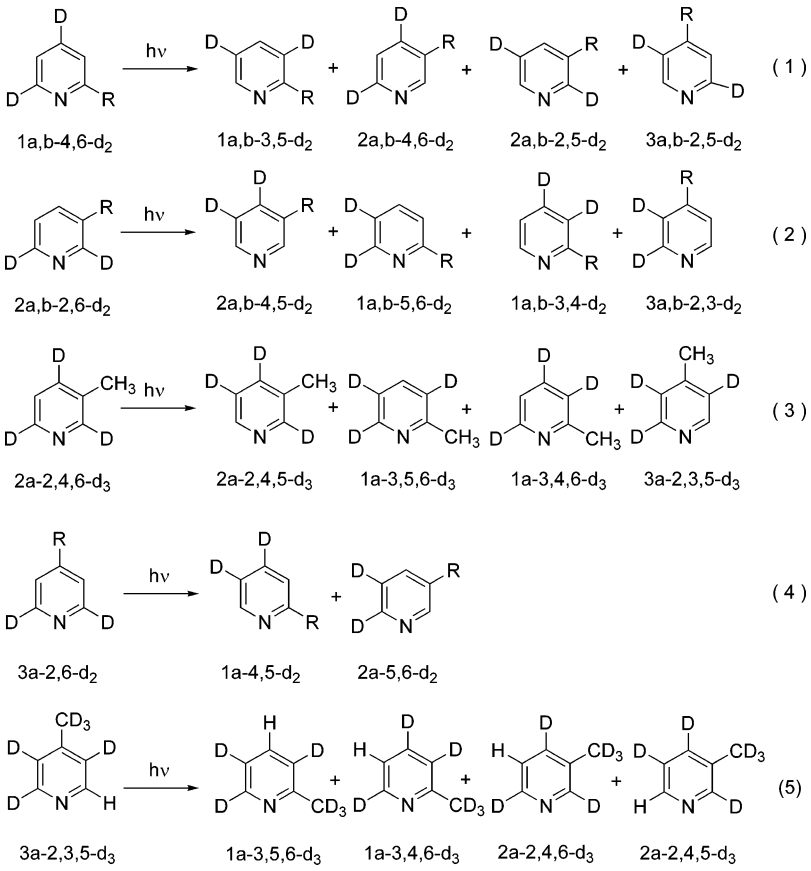


FIGURE 2. ^{1}H NMR spectrum from δ7.0 to 9.5 of 2-cyanopyridine-4,6-d_2 (**1b-4,6-d_2**) in acetone-d_6 (a) before irradiation and (b) after irradiation in the vapor phase at 254 nm.

Deuterium Labeling Studies. Figures 1 and 2 show the ^{1}H NMR spectrum of 2-trideuteriomethylpyridine-4,6-d_2 (**1a-4,6-d_2)** and 2-cyanopyridine-4,6-d_2 **(1b-4,6-d_2)** before and after 24 h of irradiation. After irradiation the spectrum in Figure 1b shows signals due to **1a-4,6-d_2** and eight new signals of essentially equal intensity due to the formation of photoproducts. Since each new trideuteriomethylpyridine photoproduct will bear two deuterium atoms and two protons bonded to ring positions, the formation of eight singlets means that four different trideuteriomethylpyridine isomers have been formed in this photoreaction. Furthermore, since all of the signals are singlets, none of the products can have hydrogen atoms on adjacent ring positions. These new singlets can be assigned by comparison with the known chemical shifts for the ring protons in 2-, 3-, and 4-methylpyridines. Thus, as shown in Figure 1b, the two singlets at δ7.52 and 8.44 were assigned to H4 and H6 of 2-trideuteriomethylpyridine-3, 5-d_2 (**1a-3,5-d_2**); the two singlets

TABLE 3. Deuterium Labeling Products[a]



[a] a, R = CH_3; b, R = CN.

at δ8.40 and 7.15 were assigned to H2 and H5 of 3-trideuteriomethylpyridine-4,6-d_2 (**2a-4,6-d$_2$**); the two singlets at δ7.45 and 8.36 were assigned to H4 and H6 of 3-trideuteriomethylpyridine-2,5-d_2 (**2a-2,5-d$_2$**), and the two singlets at δ7.05 and 8.41 were assigned to H3 and H6 of the 4-trideuteriomethylpyridine-2,5-d_2 (**3a-2,5-d$_2$**). The overall photoreaction is shown in Table 3(1). Dideuteration of the ring has thus expanded the triad to a pentad.

On the basis of the relative areas of the product signals in Figure 1b, it appears that the four products are formed in similar yields after 24 h of irradiation. **1a-4,6-d$_2$** was also irradiated for 12, 6, and 3 h. No evidence was observed indicating that the formation of **2a-4,6-d$_2$** and **3a-2,5-d$_2$**, the products of the two N-migration pathways, required an initial build-up and subsequent decrease in the concentration of **1a-3,5-d$_2$** and **2a-1,5-d$_2$**, the products of the one N-migration pathways. This would be expected if **2a-4,6-d$_2$** and **3a-2,5-d$_2$** were formed by two consecutive one N-migration photoreactions. This suggests that all four dideuterated compounds are primary photoproducts in this reaction.

The spectrum in Figure 2b shows that the photoreaction of 2-cyanopyridine- 4,6-d_2 (**1b-4,6-d$_2$**) is similar, but not identical, to the reaction of **1a-4,6-d$_2$**. In this case, after irradiation, the spectrum in Figure 2b shows the formation of four major singlets and three additional singlets of lower intensity. The major product signals at δ7.63, 8.65, 8.89, and 8.99 can be assigned to the protons at ring positions 5, 4, 2, and 6, respectively, of 3-cyanopyridine (**2**), indicating that the major products in this reaction are 3-cyanopyridine-2,5-d_2 (**2b-2,5-d$_2$**) and 3-cyanopyridine-4,6-d_2 (**2b-4,6-d$_2$**). In addition, small singlets at δ8.10 and 8.87 indicate that a minor product is 2-cyanopyridine-3,5-d_2 (**1b-3,5-d$_2$**). Finally, a small singlet is observed at δ7.79 due to the proton at ring position 3 of 4-cyanopyridine (**3b**). Since this signal is a singlet, the product must be 4-cyanopyridine-2,5-d_2 (**3b-2,5-d$_2$**). The reaction is also summarized in Table 3(1). Thus, although the products obtained from 2-cyanopyridine-4,6-d_2 (**1b-4,6-d$_2$**) are structurally analogous to those obtained from 2-trideuteriomethylpyridine-4,6-d_2 (**1a-4,6-d$_2$**), the different product distributions reflect the greater regiocontrol exhibited by the cyano group than by a methyl substituent.

Although in the case of undeuterated 2-methylpyridine **1a** and 2-cyanopyridine **1b** the two pathways leading to 3-substituted pyridines **2a** and **2b** via **BC-2a,b** and **BC-2′**a,b (Scheme 2) cannot be distinguished, 4,6-dideuteration of **1a** and **1b** has removed this ambiguity (Scheme 3). Formation of **2a,b-2,5-d$_2$** and **2a,b-4,6-d$_2$** thus confirms that the one N-migration pathway, **1a,b-4,6-d$_2$** $\xrightarrow{h\nu}$ **BC-1a,b-4,6-d$_2$** → **BC-2a,b-2,5-d$_2$** → **2a,b-2,5-d$_2$** and the two N-migration pathway **1a,b-4,6-d$_2$** $\xrightarrow{h\nu}$ **BC-1a,b-4,6-d$_2$** → **BC-1a,b-3,5-d$_2$** → **BC-2a,b-4,b-d$_2$** → **2a,b-4,6-d$_2$** (Scheme 3) are both in operation. Furthermore, the conversion of **1a,b-4,6-d$_2$** to **1a,b-3,5-d$_2$** confirms that phototransposition also occurs via the one N-migration pathway **1a,b-4,6-d$_2$** $\xrightarrow{h\nu}$ **BC-1a,b-4,6-d$_2$** → **BC-1a,b-3,5-d$_2$** → **1a,b-3,5-d$_2$** → which could not be observed in the absence of deuterium labeling.

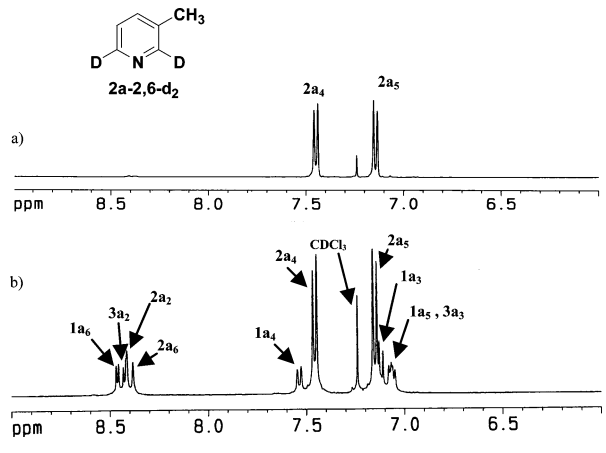
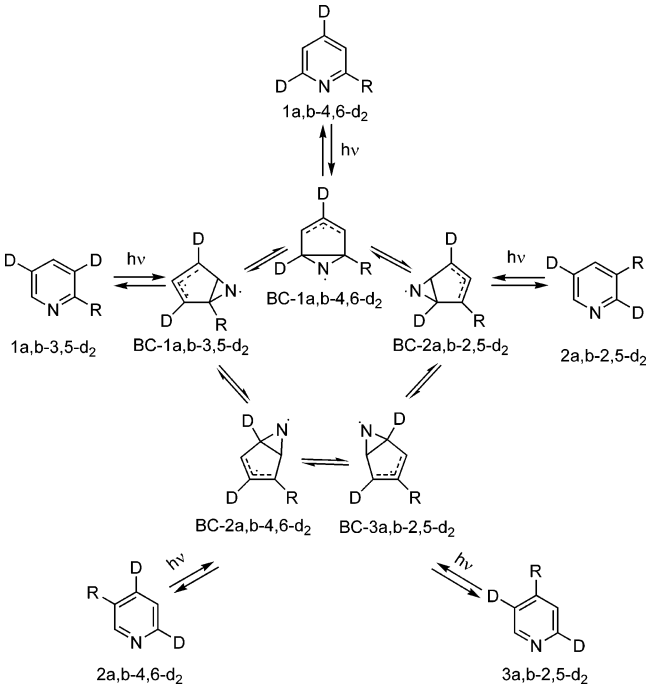


FIGURE 3. ^{1}H NMR spectrum from δ6.5 to 8.5 of 3-methylpyridine-2,6-d_2 (**2a-2,6-d$_2$**) in $CDCl_3$ (a) before irradiation and (b) after irradiation in the vapor phase at 254 nm.

SCHEME 3 [a]



[a] a = CD_3; b = CN.

Figures 3 and 4 show the ^{1}H NMR spectra of 3-methylpyridine-2,6-d_2 (**2a-2,6-d$_2$**) and 3-cyanopyridine-2,6-d_2 (**2b-2,6-d$_2$**) before and after 24 or 6 h of irradiation, respectively. Before irradiation, the spectra in Figures 3a and 4a show the H4 and H5 protons of **2a-2,6-d$_2$** or **2b-2,6-d$_2$** as pairs of doublets (J = 7.8 Hz) at δ7.58 and 7.18 or (J = 7.9 Hz) at δ8.09 and 7.48, respectively. In addition to signals due to **2a-2,6-d$_2$**, after irradiation, the two new doublets (J = 7.6 Hz) at δ7.12 and 7.54 in Figure 3b can be assigned to H3 and H4 of 2-methylpyridine-5,6-d_2 (**1a-5,6-d$_2$**). The doublet (J = 4.9 Hz) at δ8.45 can be assigned to H6 of 2-methylpyridine-3,4-d_2 (**1a-3,4-d$_2$**) but the additional doublet required for the H5 proton, known to absorb at δ7.07, is overlapping with the doublet at δ7.05 for H5 of 4-methylpyridine-2,3-d_2 (**3a-2,3-d$_2$**). The doublet due to H6 of the latter compound is observed at δ8.43 overlapping with the singlets at δ8.41 and 8.39 due to H2 and H6 of 3-methylpyridine-4,5-d_2 (**2a-4,5-d$_2$**). Thus, although some ambiguities exist because of the overlap of ^{1}H NMR signals, it appears that the reaction can be summarized as in Table 3(2).

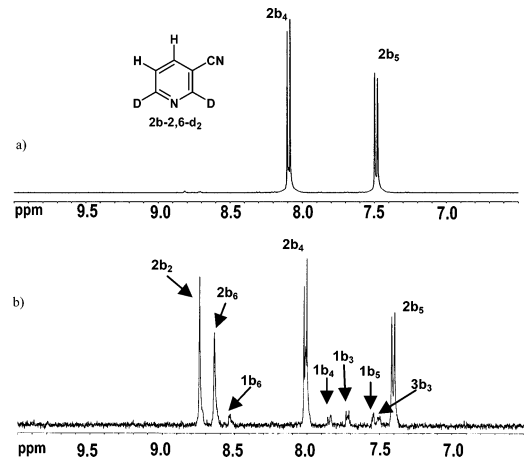


FIGURE 4. ^{1}H NMR spectrum from δ6.5 to 8.5 of 3-cyanopyridine-2,6-d_2 (**2b-2,6-d$_2$**) in acetone d_6 (a) before irradiation and (b) after irradiation in the vapor phase at 254 nm.

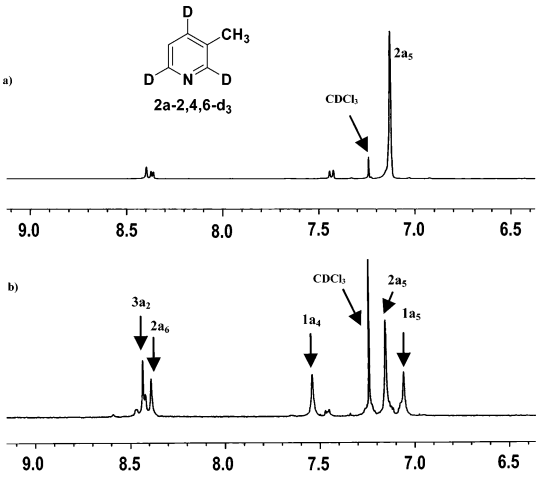
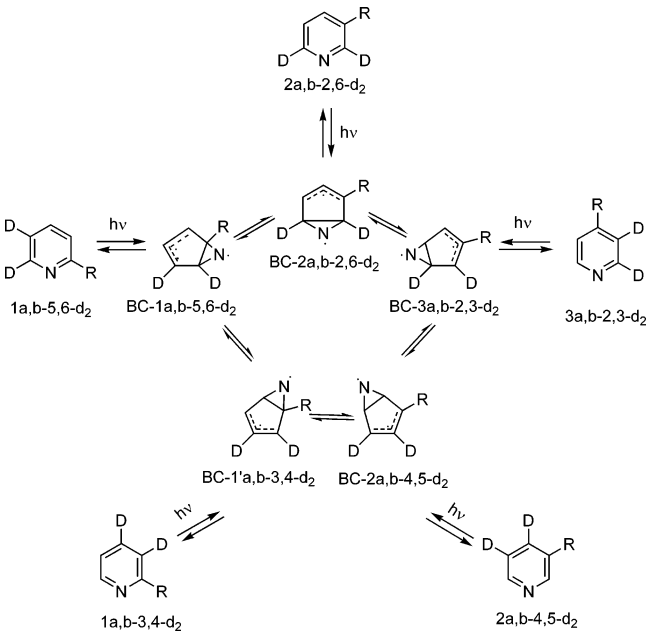


FIGURE 5. ^{1}H NMR spectrum from δ6.5 to 9.0 of 3-methlypyridine-2,4,6-d_3 (**2a-2,4,6-d$_3$**) in $CDCl_3$ (a) before irradiation and (b) after irradiation in the vapor phase at 254 nm.

To overcome the ambiguities due to the overlapping signals in the spectrum of the product mixture obtained from 3-methylpyridine-2,6-d_2 (**2a-2,6-d$_2$**) shown in Figure 3b, 3-methylpyridine-2,4,6-d_3(**2a-2,4,6-d$_3$**) was synthesized and its photochemistry was studied. Figure 5a shows the ^{1}H NMR spectrum in $CDCl_3$ before irradiation. The spectrum shows one intense singlet at δ7.1 due to the H5 ring proton and small signals due to residual protons at ring positions 2, 4, and 6. After 24 h of irradiation, the ^{1}H NMR spectrum of the condensed product (Figure 5b) shows the formation of four products as evidenced by the new singlets at δ7.58 due to the H4 proton of 2-methylpyridine-3,5,6-d_3 (**1a-3,5,6-d$_3$**), at δ7.10 due to the H5 proton of 2-methylpyridine-3,4,6-d_3 (**1a-3,4,6-d$_3$**), at δ8.43 due to the H6 proton of 3-methylpyridine-2,4,5-d_3(**2a-2,4,5-d$_3$**), and at δ8.46 due to the H2 proton of 4-methylpyridine-2,3,5-d_3 (**3a-2,3,5-d$_3$**). The reaction is summarized in Table 3(3). Unambiguous identification of these products also supports the conclusions shown in Table 3(2).

The ^{1}H NMR spectrum after irradiation of 3-cyanopyridine-2,6-d_2 (**2b-2,6-d$_2$**) in Figure 4b reveals the formation of three sets of signals. The major new signals are two singlets at δ8.63

SCHEME 4 [a]



[a] a = CH_3; b = CN.

and 8.74 where H2 and H6 of pyridine are known to absorb. Interestingly, these signals are due to the H2 and H6 protons of 3-cyanopyridine. This shows that the major product from irradiation of 3-cyanopyridine-2,6-d_2 (**2b-2,6-d_2**) is 3-cyanopyridine-4,5-d_2 (**2b-4,5-d_2**). Since this phototransposition would not be observed in the absence of the deuterium labels, this explains why undeuterated 3-cyanopyridine (**2b**) appears to be so photochemically unreactive.

In addition, a series of doublets of low intensity are also observed at δ7.55, 7.72, 7.74, and 8.53. On the basis of the chemical shifts and the multiplicities, these signals were assigned to protons at ring positions 3 and 4 and at ring positions 5 and 6 of 2-cyanopyridine indicating the formation of 2-cyanopyridine-3,4-d_2 (**1b-3,4-d_2**) and 2 cyanopyridine-5,6-d_2 (**1b-5,6-d_2**). Finally, the small signal at δ7.50 has the same chemical shift as H3 of 4-cyanopyridine. Since this signal is a doublet, this minor product is 4-cyanopyridine-2,3-d_2 (**3b-2,3-d_2**). These results are also summarized in Table 3(3).

Formation of **1a,b-5,6-d_2** and **1a,b-3,4-d_2** confirms that the phototransposition of 3-substituted pyridines to 2-substituted pyridines takes place by both the one N-migration pathway **2a,b-2,6-d_2** $\xrightarrow{h\nu}$ **BC-2a,b-2,6-d_2** → **BC-1a, b-5,6-d_2** → **1a,b-5,6-d_2** and the two N-migration pathway **2a,b-2,6-d_2** $\xrightarrow{h\nu}$ **BC-2a,b-2,6-d_2** → **BC-1a,b-5,6-d_2** → **BC-1a,b-3,4-d_2** → **1a,b-3,4-d_2** as shown in Scheme 4. In addition, the conversion of **2a,b-2,6-d_2** to **2a,b-4,5-d_2** also reveals that the two N-migration pathway **2-a,b-2,6-d_2** $\xrightarrow{h\nu}$ **BC-2a,b-2,6-d_2** → **BC-3a,b-2,3-d_2** → **BC-2a,b-4,5-d_2** → **2a,b-4,5-d_2**, which cannot be observed in the absence of deuterium labeling, occurs in these reactions. Indeed, because of the influence of the cyano group, this is the major reaction pathway for 3-cyanopyridine (**2b**).

The photochemistry of the 4-substituted pyridines was also investigated. The ^{1}H NMR spectra of 4-trideuteriomethylpyridine-2,6-d_2 (**3a-2,6-d_2**) and 4-cyanopyridine-2,6-d_2 (**3b-2,6-d_2**) are shown in Figures 6 and 7 before and after irradiation. Before irradiation, Figures 6a and 7a show the H3 and H5 protons of **3a-2,6-d_2** or **3b-2,6-d_2** as intense singlets at δ7.04 or 7.56

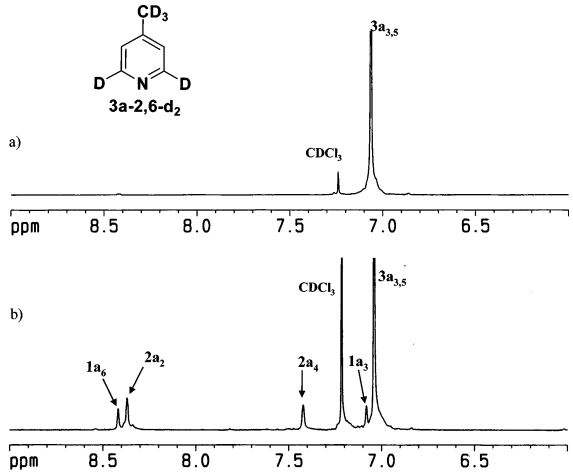


FIGURE 6. ^{1}H NMR spectrum from δ6.5 to 8.5 of 4-trideuteriomethylpyridine-2,6-d_2 (**3a-2,6-d_2**) in $CDCl_3$ (a) before irradiation and (b) after irradiation in the vapor phase at 254 nm.

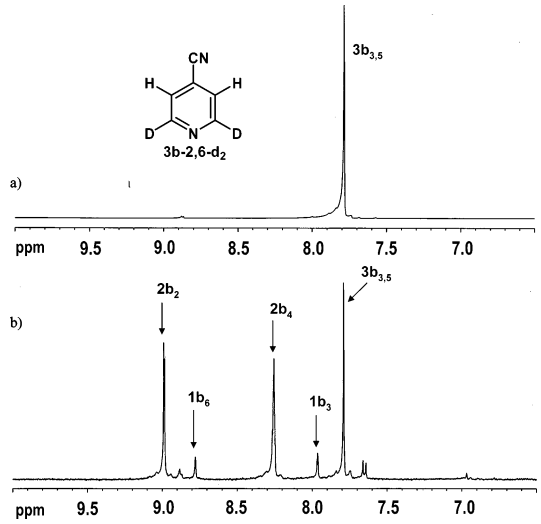


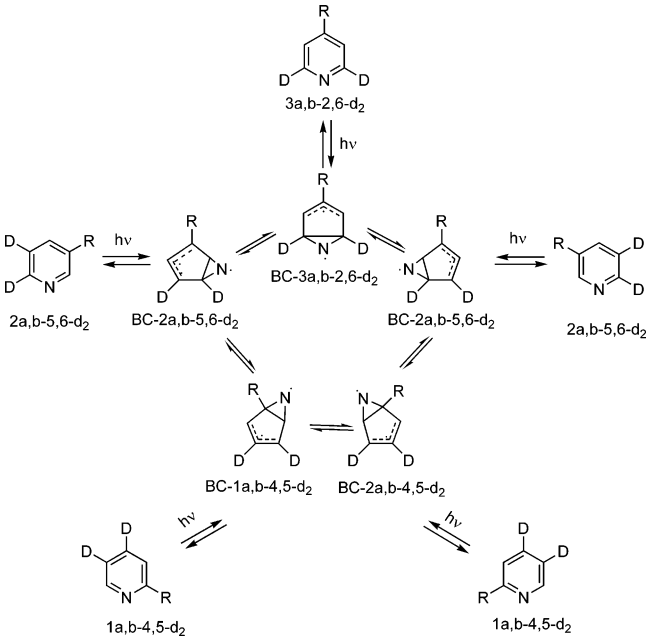
FIGURE 7. ^{1}H NMR spectrum from δ9.5 to 7.0 of 4-cyanopyridine-2,6-d_2 (**3b-2,6-d_2**) in acetone-d_6 (a) before irradiation and (b) after irradiation in the vapor phase at 254 nm.

respectively. After irradiation of **3a-4,6-d_2** or **3b-4,6-d_2**, the spectra in Figures 6b or 7b both show the appearance of four new singlets The new singlets in Figure 6b at δ7.09 and 8.41 were assigned to H3 and H6 of 2-trideuteriopyridine-4,5-d_2 (**1a-4,5-d_2**), whereas the new singlets at δ8.39 and 7.40 were assigned to H2 and H4 of 3-trideuteriomethylpyridine-5,6-d_2 (**2a-5,6-d_2**), as shown in Table 3(4). The relative areas of the new singlets indicate that the two products are formed in essentially equal yields.

The ^{1}H NMR spectrum of the analogous 4-cyanopyridine-2,6-d_2 (**3b-2,6-d_2**) before irradiation is shown in Figure 7a and also exhibits one intense singlet at δ7.56. In Figure 7b, the major singlets at δ9.00 and 8.27 were assigned to the H2 and H4 protons of 3-cyanopyridine-5,6-d_2 (**3b-5,6-d_2**) whereas the minor set of singlets at δ8.78 and 7.96 were assigned to the H6 and H3 protons of 2-cyanopyridine-4,5-d_2 (**2b-4,5-d_2**) as shown in Table 3(4). The relative areas of the new singlets indicates that the 3-cyano isomer **2b-5,6-d_2** is the major product formed in this reaction.

The observed products are those predicted by photocyclization followed by one or two N-migrations, as shown in Scheme 5.

SCHEME 5 [a]

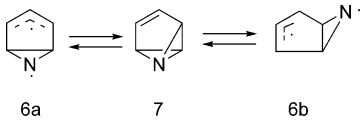


[a] a = CH_3; b = CN.

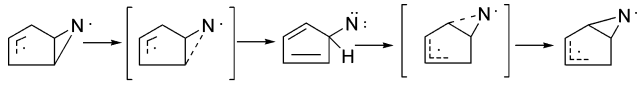
Because of the symmetry of the molecule, however, the dideuterated 4-substituted reactants remain photochemical triads instead of being expanded to pentads as in the case of the 2- and 3- substituted dideuterio isomers. This symmetry was removed by synthesizing and irradiating 4-trideuteropyridine-2,3,5-d_3, **3a-2,3,5-d_3**, which exhibited a singlet in the ^{1}H NMR spectrum at δ8.41 due to the C6 ring proton. After irradiation, ^{1}H NMR analysis revealed the appearance of new singlets at δ7.53 due to the C4 proton of 2-methylpyridine, at δ7.05 due to C5 proton of 2-methylpyridine, at δ7.14 due to the C5 proton of 3-methlypyridine, and at δ8.57 due to the C6 proton of 3-methylpyridine. The reaction is summarized in Table 3(5). These results confirm that when the symmetry of the molecule is removed, the triad is expanded to a pentad.

Mechanistic Discussion. Excitation of methyl- and cyanopyridines at 254 nm results in the formation of the $S_2(\pi,\pi^*)$ state with excess vibrational energy.[6] These vibrationally excited states have been considered to be the starting point for a nonradiative pathway termed Channel Three.[7−16] A variety of spectroscopic evidence[11−21] indicates that the onset for this

SCHEME 6



SCHEME 7



pathway in pyridine occurs at ~1600 cm^{-1} above the S_1 (n,π^*) origin[22] but occurs very rapidly from the higher energy S_2 (π,π^*) state. Previous calculations have indicated that the potential energy surfaces of the S_1 (n,π^*) and S_2 (π, π^*) states of pyridine have crossing points along the isomerization pathway leading to an azaprefulvene diradical.[14,23,24] On the basis of femto-second absorption studies and theoretical calculations, Zewail and Chachisvillis have shown that in solution phase the S_2 (π, π^*) state of pyridine can rapidly pass over a low-energy barrier and through a conical intersection to yield the azaprefulvene species, which has a lifetime of greater than 2 ns.[25]

The mechanism for the phototransposition of these pyridine isomers shown in Schemes 2−5 suggests that, during its lifetime, the azaprefulvene diradical undergoes N-migration around all five sides of the cyclopentenyl ring. This allows nitrogen to insert between each pair of carbons in the ring. This mechanism predicts the exact deuterium distribution observed in the photoproducts and does not predict the formation of any additional but unobserved products. A mechanism involving interconverting Dewar pyridine or azaprismane intermediates does not account for this selectivity.

Whether the photocyclization and nitrogen migration reactions take place by concerted or stepwise mechanisms is open to speculation. The interconversion of azaprefulvene diradicals **6a** and **6b** could involve the intermediacy of azabenzvalene **7** (Scheme 6). Such an intermediate was previously implicated in the phototransposition chemistry of N-methylpyridinium ions.[26] Although no compelling experimental evidence was observed that requires the inclusion or exclusion of such a species in the photoisomerization of these pyridine isomers, theoretical calculations by Cao, Zhang, and Payerimhoff suggest that an azabenzvalene originating from the S_1/S_0 decay subsequent to S_2/S_1 mixing is an intermediate of nitrogen migratory insertion on the singlet potential energy surface.[27]

Interestingly, the calculations carried out by these workers indicate that the interconversion of azaprefulvenes **6b** and **6c** on the triplet potential energy surface requires the intermediacy of azafulvene **8** as shown in Scheme 7. Their calculations suggest that transposition is very likely on the triplet potential energy surface because the energy barriers are very low.[27]

(6) The $S_0 \rightarrow S_2$ (π, π^*) $_{0-0}$ absorptions in the vapor phase are: 2-methylpyridine (266 nm), 3-methylpyridine (268 nm), 2-cyanopyridine (268 nm), 3-cyanopyridine (269 nm), and 4-cyanopyridine (277 nm).

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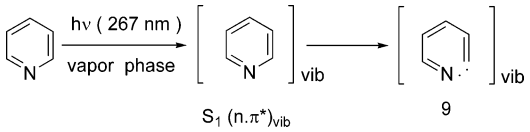
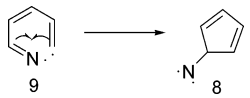
SCHEME 8



SCHEME 9



This theoretical suggestion is not supported by experimental results. Thus, the intersystem crossing yield reported by Roebke for 2-methylpyridine (**1a**) vapor is 0.21 for $S_0 \rightarrow S_1$ excitation at 280 nm but only 0.03 for $S_0 \rightarrow S_2$ excitation at 248 nm.[28] Irradiation at 280 nm thus leads to a greater yield of 2-methylpyridine triplets. The efficiency of photoisomerization of 2-methylpyridine (**1a**), however, exhibits the reverse wavelength dependence. Thus, upon $S_0 \rightarrow S_2$ excitation at 248 nm 2-methylpyridine (**1a**) transposed to 3- and 4-methylpyridine (**2a**) and (**3a**) with quantum yields of 3.4×10^{-4} and 3×10^{-5}, respectively, but was unreactive upon irradiaton in the n,π^* transition at 280 nm.[22] It should be noted, however, that since $(S_0, S_1)_{0,0}$ for 2-methylpyridine (**1a**) is 288 nm, irradiation at 280 nm is $\sim$600 cm^{-1} below the Channel Three threshold which may account for the lack of reaction.

Although the S_2 (π, π^*) state undergoes facile conversion to the azaprefulvene diradical, Zewail and colleagues have shown that the energy barrier is too high for formation of this species from the S_1 (n, π^*) molecule. Using ultrafast electron diffraction, these worker have shown that the primary product from the vibrationally excited S_1 (n, π^*) state of pyridine is a vibrationally excited ring-opened biradical **9** (Scheme 8) formed by cleavage of the C−N bond while a minor pathway leads to the formation of Dewar pyridine.[29]

No suggestions have been given for the role that such a ring-opened species might have in pyridine photochemistry. It is possible that the initially formed vibrationally excited biradical **9** could undergo rapid vibrational relaxation followed by recyclization to a ground state pyridine molecule. This ring opening-ring closure pathway would therefore be an energy wasting process. It is also possible that such a ring opened species could polymerize and be responsible for the significant amount of polymeric material observed on the walls of the reactor. It is also interesting to speculate that this ring opened biradical[9] could cyclize as shown in Scheme 9, leading to the azafulvene **8** predicted by Cao, Zheng, and Peyerimhoff.[27] This species could cyclize to the azaprefulvene intermediate implicated in the current studies.

In conclusion, the results of the deuterium labeling studies described here provide convincing evidence for the mechanism shown in Schemes 2−5 involving azaprefulvene diradical formation and nitrogen migration around the cyclopentenyl ring. The exact mechanistic details for the photocyclization and migration of nitrogen, however, are still open to speculation.

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Experimental Section

Instrumentation. ^{1}H and ^{13}C NMR spectra were recorded at 400 or 100 MHz on a FT-NMR system. GLC analyses were performed on an FID instrument equipped with either a 15 m × 3 μm methyl 50% phenylsilicon bonded phase capillary column (Column A) or with a 30 m × 0.53 μm Supelcowax-10 bonded phase capillary column (Column B). Mass spectra were recorded with a mass selective detector interfaced to an capillary gas chromatograph.

Materials. Cyanopyridines and methylpyridines were commercially available and were purified by distillation. Deuterated cyanopyridines and methylpyridines were prepared by procedures described elsewhere.[30]

Irradiation Procedure. The methylpyridine (0.140−0.200 g), deuteratedmethylpyridine (0.040−0.050 g), cyanopyridine (0.009−0.016 g), or deuteratedcyanopyridine (0.016−0.022 g) was placed in a Pyrex tube, attached to the vacuum line, and subjected to three freeze−thaw cycles. The remaining material was then allowed to vaporize into a 3 L quartz reaction flask that had been evacuated overnight. The resulting pressure in the reaction flask ranged from 2.5 to 2.7 Torr for methylpyridines, 3.0 to 4.0 Torr for deuteratedmethylpyridines, 0.3 to 0.4 Torr for cyanopyridines, and 0.4 Torr for deuterated cyanopyridines. The flask was irradiated in a Rayonet reactor equipped with 162 537 Å lamps for the indicated period of time.

Analysis Procedure. After irradiation by the above procedure, the 3 L reaction flask was attached to the vacuum line, and the volatile contents were recovered by pumping it out through a trap cooled in an acetone-dry ice bath. The contents of the trap were weighed and dissolved in a known volume of diethyl ether for GLC analysis. At 100 °C and a helium flow rate of 10.0 mL/min, the three cyanopyridines elute in Column A in the order 4-cyanopyridine (**3b**), 3-cyanopyridine (**2b**), and 2-cyanopyridine (**1b**) with retentions relative to 4-cyanopyridine (**3b**) of 1.0, 1.17, and 2.0, respectively. On column B using a temperature program [50 °C (2.0 min), 10 °C/min to 60 °C (3.0 min), 0.1 °C/min to 63 °C (30 min), 10 °C/minutes to 70 °C (5.0 min)], pyridine, the three methylpyridines, and 2,6-dimethylpyridine eluted in the order pyridine (**4**), 2-methylpyridine (**1a**), 2,6-dimethylpyridine (**5**), 3-methylpyridine (**2a**), and 4-methylpyridine (**3a**) with retentions relative to pyridine (**4**) of 1.0, 1.24, 1.40, 1.94, and 2.06, respectively. The product mixtures from the irradiation of methylpyridines were also analyzed by ^{13}C NMR. In $CDCl_3$, the three isomeric methylpyridines exhibited the following signals. 1a: δ 158.7 (*C*2), 149.5 (C6), 136.3 (C4), 123.6 (C3), and 121.1 (C5); 2a: δ 150.6 (*C*2), 147.3 (C6), 136.8 (C4), 133.5 (C3), and 123.5 (C5); 3a: δ 149.9 (*C*2,6), 147.4 (C4), and 125.0 (C3,5).

Quantitative GLC analysis of reactant consumption and product formation was accomplished using calibration curves constructed for all of the various compounds by plotting the detector response versus six standards of known concentrations. Correlation coefficients ranging from 0.976 to 1.000 were obtained. Quantitative results for reactant consumption and product formation after various irradiation times are given in Tables 1 and 2.

Supporting Information Available: Copies of the ^{1}H and ^{13}C NMR spectra of all deuterated methyl and cyanopyridines used in this study are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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