Photodecomposition of Some Para-Substituted 2-Pyrazolylphenyl Azides. Substituents Affect the Phenylnitrene S−T Gap More Than the Barrier to Ring Expansion

Angelo Albini, Gianfranco Bettinetti,* and Giovanna Minoli

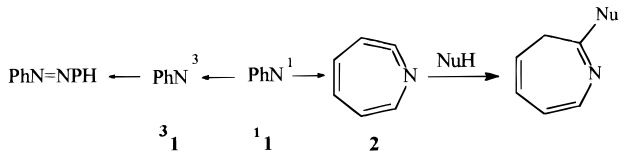
Contribution from the Dipartimento di Chimica Organica, Università di Pavia, Viale Taramelli 10, I-27100 Pavia, Italy

Received July 21, 1998

Abstract: A series of para-substituted (H, Me, Cl, F, CF_3, OMe, NMe_2) phenyl azides bearing a dimethylpyrazolyl group in position 2 allowing intramolecular trapping of singlet nitrene have been photolyzed at both 295 and 90 K in ethanol. For three significant models (H, CF_3, NMe_2), the reaction has been further studied in the presence of diethylamine (DEA) and of oxygen. With all substituents but NMe_2, singlet nitrene (trapped intramolecularly to give pyrazolobenzotriazoles) and didehydroazepine (trapped with DEA to give 5*H*-azepines and then rearranging to 3*H*-azepines) are in equilibrium. With the NMe_2 derivative, the nonelectrophilic singlet is not trapped, while DEA adds to the benzoazirine, the precursor of the didehydroazepine. Thus, electronic effects do not hinder the equilibrium between singlet nitrene and its cyclic isomers, while determining which of the above intermediates decays to a stable end product. The electron-donating group NMe_2 has a second important effect, causing a drastic enhancement of the triplet nitrene energy and reduction of the S−T gap, so that triplet nitrene is also in equilibrium with the singlet and the benzoazirine. As for triplet nitrenes, these have been characterized in matrix at 90 K, and the competition between dimerization (to give azo compounds, as typical of such stabilized species) and hydrogen abstraction from the solvent (involving a sizable barrier) has been studied. The energetic *p*-dimethylamino triplet undergoes hydrogen abstraction exclusively. When present, oxygen adds efficiently to all of the nitrenes, giving a nitroso oxide, likewise characterized in the matrix, which then converts to the nitroso and nitro derivatives in good yields. Photochemical excitation of the triplet in matrix leads to intramolecular hydrogen abstraction.

Phenylnitrenes are conveniently generated under mild conditions by photolysis of the corresponding azides[1] and are largely used both in industrial polymer chemistry for cross-linking (e.g., for photoresists) and in biochemistry for photoaffinity labeling.[2] The chemistry of these species is quite complex, and various groups have devoted much work to the unraveling of the mechanism. A limitation for mechanistic studies is that a poor yield of isolable products is obtained from photolysis of phenyl azides at room temperature, in contrast with the good yields generally obtained from the seemingly related phenylcarbenes.[3] This appears to be due to fast rearrangement of the primarily formed phenylnitrene (^{1}**1**) to dehydroazepine (**2**).[3e] In turn, **2** polymerizes (mainly giving "tars") under this condition.[4] In the presence of a nucleophile, adducts (azepines) have been obtained and characterized.[3] At low temperature, ^{1}**1** preferentially rearranges to the corresponding triplet ^{3}**1** and this dimerizes to azobenzene (Scheme 1).[3,5] Recent advances in the field include spectroscopic detection of ^{1}**1** by picosecond flash photolysis[6] and the determination of differential thermodynamic parameters for singlet and triplet phenylnitrene in suitable models where the singlet is trapped intramolecularly.[7]

Scheme 1



Substitution on the aromatic ring is expected to affect the reactivity of the nitrene, and choosing the right substituted derivative is important for optimal results in the above applications in particular by favoring intermolecular rections, as obtained, for example, with some poly(fluorophenyl azides).[8,9] However, it has not been clarified as yet which step(s) of the mechanism is (are) affected. Two main alternatives should be

* Corresponding author: (fax) 39-382-507323; (e-mail) albini@chifis.unipv.it.

(1) Iddon, B.; Meth-Cohn, O.; O.; Scriven, E. F. V.; Suschitzky, H.; Gallagher, P. T. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 900; *Angew. Chem.* **1979**, *91*, 965. Scriven, E. F. V., Ed. *Azides and Nitrenes: Reactivity and Utility*; Academic Press: Orlando, 1984. Lwowski, W., Ed. *Nitrenes*; Interscience: New York, 1970.

(2) Kotzyba-Hilbert, F.; Kapfer, I.; Goeldner, M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1296; *Angew. Chem.* **1995**, *107*, 1391.

(3) (a) Wentrup, C. *Reactive Molecules*; Wiley-Interscience: New York, 1984; Chapter 4. (b) Wentrup, C. *Adv. Heterocycl. Chem.* **1981**, *28*, 279. (c) Platz, M. S.; Leyva, E.; Haider, K. *Org. Photochem.* **1991**, *11*, 367. (d) Schuster, G. B.; Platz, M. S. *Adv. Photochem.* **1992**, *17*, 69. (e) Platz, M. S. *Acc. Chem. Res.* **1995**, *28*, 487 and references cited.

(4) Meijer, E. W.; Nijhuis, S.; Von Vroonhoven, F. C. B. M. *J. Am. Chem. Soc.* **1988**, *110*, 7209.

(5) Leyva, E.; Platz, M.; Persy, G.; Wirz, J. *J. Am. Chem. Soc.* **1986**, *108*, 3873.

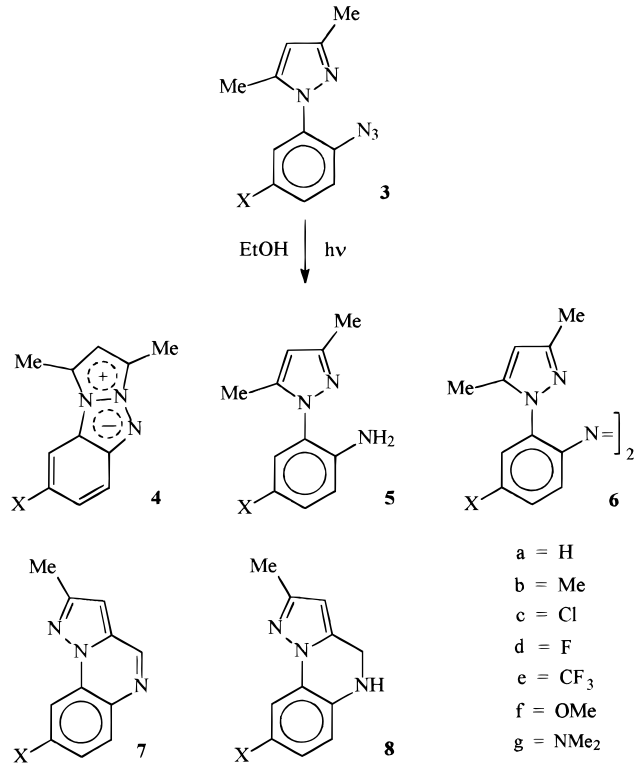
(6) Gritsan, N. P.; Yuzawa, T.; Platz, M. S. *J. Am. Chem. Soc.* **1997**, *119*, 5059. Singlet nitrene had been previously observed upon photolysing *p*-dimethylaminophenyl azide: Kobayashi, T.; Ohtani, H.; Suzuki, K.; Yamaoka, T. *J. Phys. Chem.* **1985**, *89*, 776.

(7) Albini, A.; Bettinetti, G.; Minoli, G. *J. Am. Chem. Soc.* **1997**, *119*, 7308.

(8) Karney, W. L.; Borden, W. T. *J. Am. Chem. Soc.* **1997**, *119*, 1378.

10.1021/ja982585r CCC: $18.00
Published on Web 03/19/1999

Scheme 2



confronted: (1) the substituent affects the barriers for the interconversion of singlet and triplet nitrene and rearranged isomers such as dehydroazepine **2** (see Scheme 1), and (2) the intrinsic reactivity of some of these intermediates is changed.

In the hope of providing some experimental evidence for clarifying the above issue, we made recourse to 1-(2-azidophenyl)-3,5-dimethylpyrazole (**3a**), which has been previously shown to be a useful model because singlet and triplet nitrene give well-characterized products through intramolecular trapping.[7,10] We present here a systematic study of derivatives substituted in position 5 of the phenyl ring (para to the azido functionality) at different temperatures and in the presence of suitable nucleophile and radical traps.

Results

Photochemistry of Azides 3 at Room Temperature. In a previous preparative study, we showed that the products from thermal and photochemical decomposition (in acetonitrile) of a range of substituted 1-(2-azidophenyl)-3,5-dimethylpyrazoles **3** were the heteropentalenes **4**, the amines **5**, the azo derivatives **6**, and the pyrazoloquinoxalines **7**, the last ones via oxidation of the corresponding 4,5-dihydro derivatives **8** (Scheme 2).[10c] The product distribution depended strongly on the structure and on the decomposition method used.

In the present work, we considered most of the above derivatives and also the fluoro derivative. Small-scale photolyses were carried out, and the products were determined by HPLC. The products obtained by irradiation in carefully deoxygenated ethanol at 295 K are shown in Table 1. The heteropentalenes **4** are the main products from the parent azide **3a** as well as from the 5-methyl (**3b**), chloro (**3c**), fluoro (**3d**), and trifluoromethyl (**3e**) derivatives. With **3b** and **3d** an about equimolecular amount of the corresponding amine was also formed, however. With the 5-methoxy (**3f**) and 5-(dimethylamino) (**3g**) azides no heteropentalene was formed, and the main products were the corresponding amines **5** and azo compounds **6**, with a minor amount of the pyrazoloquinoxalines **7** and **8**.

Table 1. Products from the Photodecomposition of Azides **3a**−**g** in Ethanol

			products[a]			
azide	subst	*T*, K	**4**	**5**	**6**	**7** + **8**[b]
3a	H	295	72	tr[c]		
		90[d]	1	4	41	10
3b	Me	295	32	24		3
		90		6	36	18
3c	Cl	295	64		7	
		90	tr	15	45	19
3d	F	295	27	28		1
		90	tr	15	64	7
3e	CF_3	295	66	1		2
		90	11	17	44	8
3f	OMe	295		3	1	3[e]
		90		10	31	4
3g	NMe_2	295		33	5	3
		90		29	5	19

[a] Percent yield on the converted azide (conversion 50−75%). [b] The total yield **7** + **8** is reported. Except for the case of azide **3g**, which gives only **7g**, the dihydro derivatives **8** predominate in low-temperature experiments. These are slowly oxidized to the corresponding **7** in solution (∼1 month); attempts to accelerate the reoxidation caused partial loss of the products. [c] Traces (<1%). [d] Irradiation in ethanol glass at 90 K followed by "fast heating" (see text). [e] The azo compound is obtained in good yield under different conditions, e.g., 62% by irradiation of a 4×10^{-3} M solution in MeCN.[10c]

In representative cases, the irradiation was carried out in the presence of 0.1 M diethylamine (DEA). Under such condition, the yield of heteropentalene **4a** from azide **3a** decreased from 72 to 36% and a 22% yield of the 3*H*-2-diethylamino-3-pyrazolylazepine **9a** was obtained (Table 2, Scheme 3). The structure of this adduct was suggested by NMR evidence and finally proved through single-crystal X-ray analysis, thus correcting a previous assignment as the isomeric 2-(diethylamino)-7-pyrazolyl derivative[7] (see Experimental Section).

With the trifluoromethyl azide **3e**, the yield of heteropentalene **4e** likewise decreased to less than half of the original value and two aminoazepines were formed. One of these was by far the main product immediately after irradiation. However, we did not succeed in isolating it in the pure state because it converted to the latter one (itself stable and easily crystallized) during attempted purification. This compound was quantitatively rearranged by stirring a benzene solution of the reaction products in the presence of silica gel. Mass spectroscopy and NMR analysis showed (see Experimental Section) that the original main product was the 5*H*-2-(diethylamino)-3-pyrazolylazepine **10e** and the rearranged product was the 3*H* tautomer **9e**, the structural analogue of **9a** (Scheme 3).

The dimethylamino azide **3g** also gave an adduct with DEA, with corresponding lowering of the yield of the other products, in particular of amine **5g**. This had a different structure, however, and spectroscopic evidence (see Experimental Section) showed that it was the triaminophenylpyrazole **11** (Scheme 3).

Matrix Spectroscopy. Azides **3a**−**g** were irradiated in glassy ethanol at 90 K by using a 254-nm light source. In all cases,

(9) (a) Poe, R.; Schnapp, K.; Young, M. J. T.; Grayzar, J.; Platz, M. S. *J. Am. Chem. Soc.* **1992**, *114*, 5054. (b) Schnapp, K. A.; Poe, R.; Leyva, E.; Soundararajan, N.; Platz, M. S. *Bioconjugate Chem.* **1993**, *4*, 172. (c) Schnapp, K. A.; Platz, M. S. *Bioconjugate Chem.* **1993**, *4*, 178. (d) Gritsan, N. P.; Zhai, H. B.; Yuzawa, T.; Karweik, D.; Brooke, J.; Platz, M. S. *J. Phys. Chem. A* **1997**, *101*, 2833. (e) 4-Cyano- and 4-nitrophenyl azides react with amines to give hydrazines, however: ref 9f, g. (f) Liang, J. M.; Schuster, G. B. *J. Am. Chem. Soc.* **1987**, *109*, 7804. (g) Odum, R. A.; Aaronson, A. M. *J. Am. Chem. Soc.* **1969**, *91*, 5680.

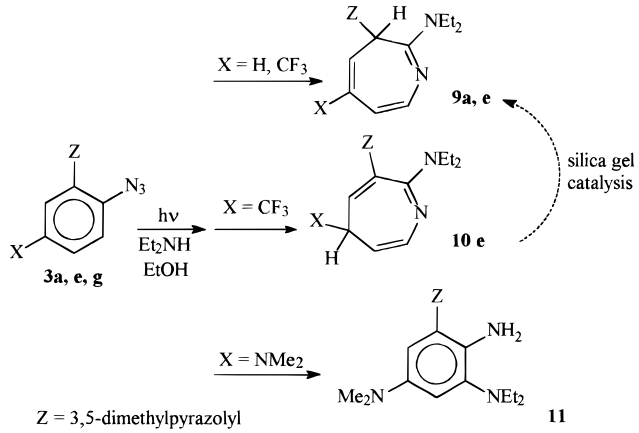
(10) (a) Lindley, J. M.; McRobbie, I. M.; Meth-Cohn, O.; Suscitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1980**, 982. (b) Albini, A.; Bettinetti, G.; Minoli, G. *J. Am. Chem. Soc.* **1991**, *113*, 6928. (c) Albini, A.; Bettinetti, G.; Minoli, G. *Heterocycles* **1995**, *40*, 597.

Table 2. Products from the Irradiation of Azides **3a**, **3e**, and **3g** under Various Conditions

				products[a]				
azide	subst	*T*, K	condition	**4**	**5**	**6**	**7** + **8**[b]	other
3a	H	295		72	tr[c]			
		160		37	1	9	<10	
		90	fast heating[d]	1	4	41	10	
		90	slow heating[d]		43	23	4	
		90	double irrad[d]	12	6	54		
		295	DEA 0.1 M	36	4	5	2	**9** (22)
		165	DEA 0.1 M	41	1	7		**9** (10)
		140	DEA 0.1 M	29	5	15		**9** (4)
		100	DEA 0.1 M[e]	5	7	27	6	
		90	O_2[e]		1		1	**12** (49), **13** (13)
3e	CF_3	295		66	1		2	
		165		36	3	9		
		90	fast heating[d]	11	17	44	8	
		90	slow heating[d]	6	72		15	
		90	double irrad[d]	10	9		77	
		295	DEA 0.1 M	30	1			**9** (21), **10** (3)
		165	DEA 0.1 M	23	1	12		**9** (5), **10** (tr)
		90	DEA 0.1 M[e]	6	12	39	6	**10** (5)
		90	O_2[e]	3	1			**12** (40), **13** (18)
3g	NMe_2	295			33	5	3	
		165			31	4	3	
		90	fast heating[d]		29	5	19	
		90	slow heating[d]		36	1	15	
		90	double irrad[d]		22		38	
		295	DEA 0.1 M		14		2	**11** (23)
		165	DEA 0.1 M		13		3	**11** (25)
		90	DEA 0.1 M[e]		17		10	**11** (9)
		90	DEA 0.1 M[f]		14		9	**11** (7)
		90	O_2[e]		20		13	**12** (10), **13** (14)

[a] Percent yield on the converted azide (conversion 50−75%). [b] See note *b*, Table 1. [c] Traces (<1%). [d] See text. [e] Fast heating, see text. [f] Slow heating, see text.

Scheme 3



virtually complete consumption of the azide was obtained after a few minutes of irradiation, and a colored intermediate was formed. The spectra observed by photolysis of azides **3a**−**e** were rather similar, with several well-separated bands extending out to 550−600 nm. As it appears from Figure 1 and Table 3, there were three main bands (or group of bands) well recognizable along the series in the range 300−550 nm. The bands were sensitive to substitution, as far as both the position and the intensity are concerned. The longest wavelength band was not detected with azide **3f**. On the other hand, **3g** gave rise to a characteristic spectrum, little comparable to the previous ones (see Figure 1). In all cases, the spectrum observed remained unchanged for hours at 90 K, underwent minor modifications by raising the temperature by 5−10 K, and faded upon melting of the glass.

Temperature-Dependent Photolysis. The above study at 295 K was complemented by product determination at low temperatures. The results obtained by photolysis in the matrix at 90 K are reported in Table 1. Under this condition, the azo compounds **6** were the main products from all of the azides tested, including the methoxy-substituted azide **3f**, but not from the dimethylamino derivative **3g** from which amine **5g** predominated.

The temperature effect was more extensively examined for azides **3a**, **3e**, and **3g**, for which it was also extended to experiments in the presence of DEA (see Table 2). The photolysis was carried out at 165 and at 90 K. In the latter case, two follow-up procedures were used after photolysis. The first one was the same used for the general case above; viz. the temperature was allowed to increase quickly and the glass melted in a few minutes. In the latter one, the temperature was maintained at 90 K for 90 min and then kept at 100 (2 h) and at 110 K (3 h). Spectra were taken at regular intervals; after this time the sample was heated to room temperature and analyzed. The main products obtained from azides **3a** and **3e** by quick melting of the glass were the azo derivatives (>40%), with none (from **3a**) or little (from **3e**) of the heteropentalene obtained at room temperature. The results were similar in the presence of DEA, with the azo as the main product and none or only a little of the azepine. Slow heating of the glass, on the other hand, mainly gave the amines **5a** and **5e**. Indeed, in the case of **1e**, the spectrum at 110 K after 3 h was virtually identical to that of the amine (Figure 2a) and in fact no azo was formed under this condition. Small amounts of the dihydropyrazoloquinoxalines **8a** and **8e** were also formed. The product distribution at 165 K was intermediate between the two previous conditions.

In the case of the dimethylamino azide **3g**, the yield of the main product in ethanol, amine **5g**, was only marginally affected by the temperature, but the yield of the pyrazoloquinoxaline **7g** increased considerably upon lowering the temperature; the low amount of azo compound formed at room temperature was maintained when the 90 K glass was rapidly melted, not upon slow heating. In the presence of DEA, amine addition to give **11** was maintained, although with a lower yield than at 295 or 165 K.

Double-Irradiation Experiments. The formation of a colored intermediate at 90 K suggested the possibility of a double-irradiation experiment. Thus, after the initial 254-nm photolysis was completed, the samples were submitted to visible (λ > 455 nm) light irradiation. This led to bleaching of the visible band and a change in the product distribution as determined after melting the glass (see Table 2). Under this condition, the main products from **3a** and **3e** were by far the dihydroquinoxalines **8**, accompanied by minor amounts of the heteropentalenes and

Table 3. Absorption Spectra of Substituted Triplet Phenylnitrenes **16** and of the Nitroso Oxides **22** in Ethanol Matrix

substrate	subst	main bands, λ, nm (log ϵ)[a]		
16a	H	510 (3.3)	339 (3.6)	315 (3.8)
16b	Me	498 (2.8)	339 (3.6)	315 (3.8)
16c	Cl	501 (2.9)	348 (3.6)	314 (4.1)
16d	F	491 (2.8)	341 (3.8)	313 (3.8)
16e	CF_3	574 (3.2)	354 (3.3)	315 (3.7)
16f	OMe		351 (3.7)	
16g	NMe_2	492 (3.6)	378 (3.8)	298 (3.8)
22a	H	406 (3.9)		
22e	CF_3	380 (3.9)		
22g	NMe_2	514 (3.5)		

[a] Log ϵ are approximate values. For comparison, triplet phenylnitrene in EPA at 77 K shows the following bands: ~500 (log $\epsilon \approx 2.5$), 400 (3), 320 (3), and 240 (4) nm.

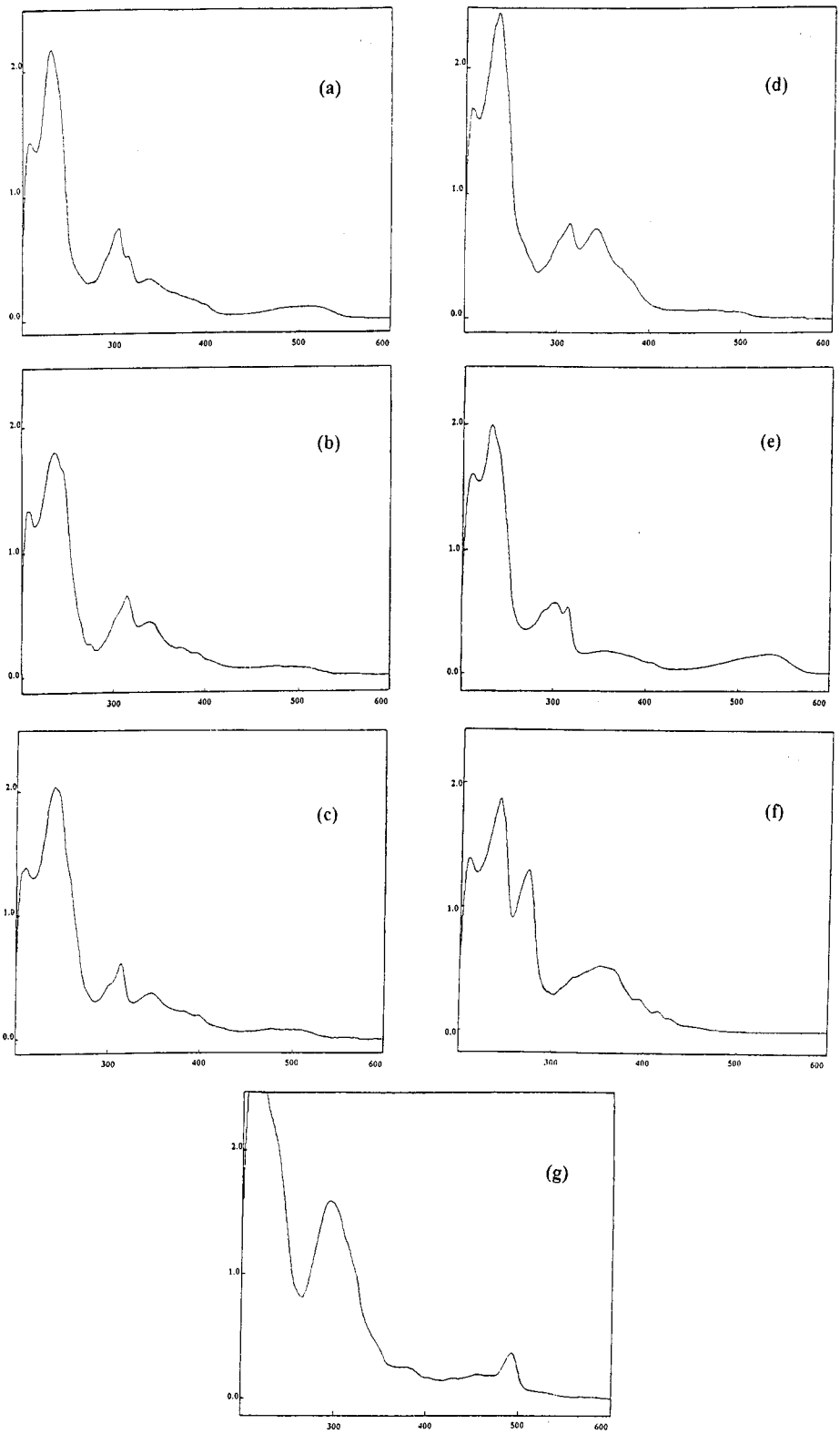


Figure 1. (a) Spectrum (A vs λ) obtained by irradiating (254 nm) 1×10^{-4} M azide **3a** in EtOH (after degassing) at 90 K for 8 min. (b−g) Same for azides **3b**−**3g**.

amines. As shown in Figure 2b for the case of the trifluoromethyl derivative, the cyclized compound **8e** was present before melting of the glass, and the spectrum observed after double irradiation was virtually identical to that of **8e**. With the dimethylamino derivative the quinoxaline **7g** was the main product, but the yield of the amine was decreased only slightly.

Matrix Photolysis in the Presence of Oxygen. Room-temperature photolysis was carried out only in deoxygenated solutions, since the efficient self-sensitized oxygenation of heteropentalenes **4**, the main products from most of these azides, would otherwise complicate the result due to the intervening of secondary photoreactions. Better suited for mechanistic studies was irradiation in an ethanol matrix using an oxygen-equilibrated solution. Under this condition, spectra different from those observed after degassing were obtained (see Figure 3, Table 3). Noteworthy, a portion of the same transient observed

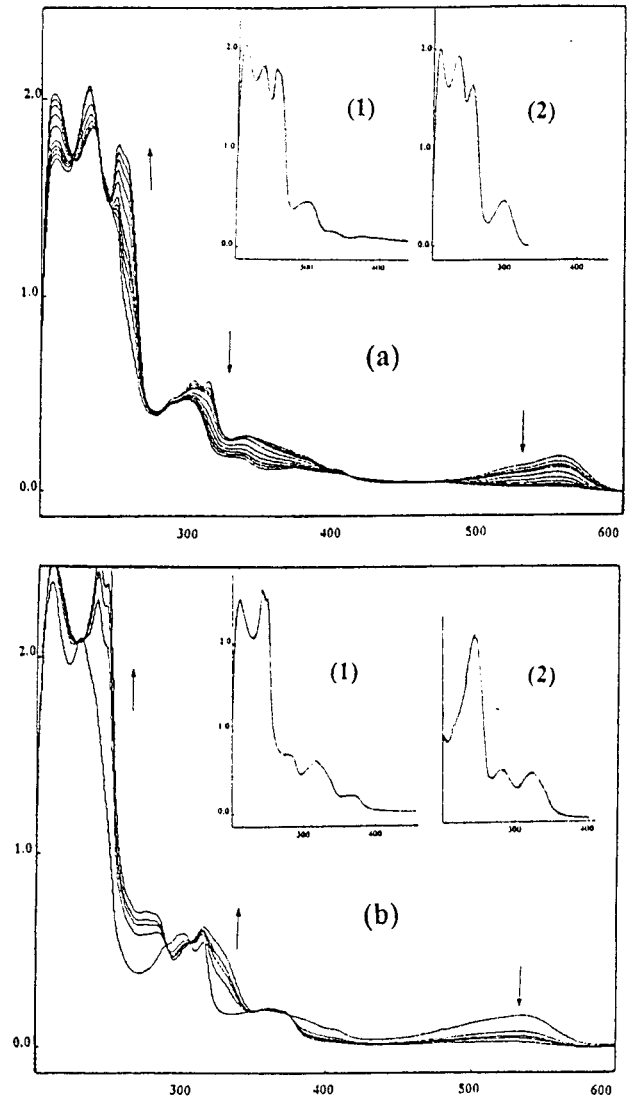


Figure 2. (a) Evolution of the spectrum (A vs λ) obtained by irradiating 1×10^{-4} M azide **3e** in EtOH (after degassing) at 90 K upon heating. The spectrum does not change for several hours at 90 K; bringing the temperature a 100 K causes only a slight red shift of the long-wavelength band. The spectra are taken at 30-min intervals at 100 K (the first four lines) and then every 30 min at 110 K. Insets: (1) Final spectrum; (2) spectrum of amine **5e** in ethanol. (b) Evolution of the spectrum (A vs λ) obtained by irradiating 1×10^{-4} M azide **3e** in EtOH (after degassing) at 90 K upon further irradiation at $\lambda > 455$ nm at 90 K. Initial spectrum, as observed after the 254-nm irradiation; following spectra, after 4, 8, 12, and 24 min of 455-nm irradiation. Insets: (1) Final spectrum after 24-min irradiation at 90 K; (2) spectrum of dihydroquinoxaline **7e** at room temperature; the band at ~370 nm in inset 1 is due to heteropentalene **4e** formed as a minor product under this condition (see Table 3).

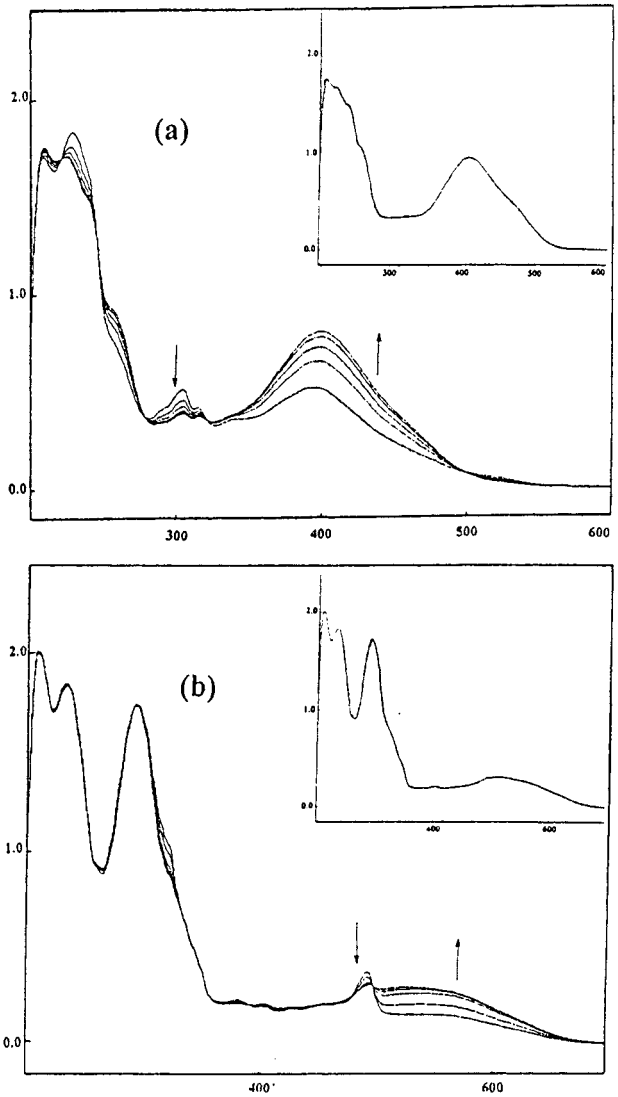
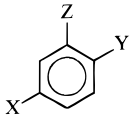


Figure 3. (a) Evolution of the spectrum (A vs λ) obtained by irradiating (254 nm) 1×10^{-4} M azide **3a** in EtOH (oxygen equilibrated) at 90 K for 8 min. The first spectrum is taken after complete consumption of the azide, and following spectra are taken after 7, 17, 32, and 47 min, respectively, at 90 K. The bands around 300 nm are due to residual triplet nitrene. Inset: the spectrum after further 40 min at 115 K. (b) Evolution of the spectrum (A vs λ) obtained by irradiating (254 nm) 1×10^{-4} M azide **3g** in EtOH (oxygen equilibrated) at 90 K for 8 min. The first spectrum is taken after complete consumption of the azide, and following spectra are taken at 20-min intervals at 90 K. The band at 492 nm is due to residual triplet nitrene. Inset: the spectrum after 80 min at 90 K.

in oxygen-free glass could be detected immediately after irradiation (see Figure 3) and was largely converted to the final spectrum in minutes.

The matrix spectra both at 90 and at 115 K in the presence of oxygen were stable for hours at these temperatures. Upon further heating, the transient decomposed and the main products from **3a** and **3e** were the nitroso derivatives **12a**, and **12e**



Z = 3,5-dimethylpyrazolyl

12 a, e, g Y = NO

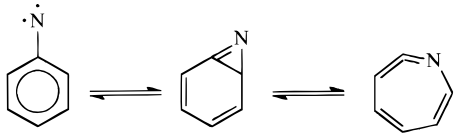
13 a, e, g Y = NO_2

accompanied by minor amounts of the corresponding nitro compounds **13a** and **13e** (see Table 2). The corresponding derivatives **12g** and **13g** were formed also in the case of **3g**; this occurred at the expense of quinoxaline **7g**, while the yield of the amine **5g** did not decrease.

Discussion

The present azides can be divided into two groups as far as their photochemical behavior at room temperature is concerned. Thus, the parent compound **3a**, the 5-methyl derivative **3b**, and all compounds containing an electron-withdrawing substituent in position 5 (chloro, **3c**; fluoro, **3d**; trifluoromethyl, **3e**) give the heteropentalenes **4** by direct irradiation; compounds **4** are by far the main product with **3a**, **3c**, and **3e** and are formed in

Scheme 4



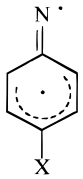
^{1}**1** **14** **2**

an amount equivalent to the amines **5** in the case of **3b** and **3d** (see Table 1). We previously showed[10c] that acetophenone-sensitized photolysis of the same azides gave the azo derivatives **6** as the main products (with a substantial amount of the amine **5e** and the pyrazoloquinoxaline **7e** from the trifluoromethyl derivative **3e**). The azides bearing an electron-donating substituent (methoxy or dimethylamino) form the second group. No heteropentalene is formed from these substrates, and the products are the corresponding azo and amino derivatives as well as the pyrazoloquinoxalines. In this case, the same products were obtained both from direct and from sensitized photolysis, although in different yields.

This confirms the idea that led Suschitzky[10a] to originally propose the present model. Thus, electrophilic singlet nitrene is intramolecularly trapped by the pyrazole nitrogen to yield the heteropentalene. Triplet nitrene, formed by sensitization, abstracts a hydrogen atom from the neighboring methyl group or from the solvent, yielding respectively the dihydropyrazoloquinoxaline or the amine, or alternatively dimerizes to the azo compound; the last one turns out to be the most efficient process.

In the present series, the nitrene reactivity is modulated by the para substituent. The selective intramolecular trapping of both singlet and triplet nitrene, in connection with the use of external nucleophilic (DEA) or radical (oxygen) traps, forms the basis of the present study.

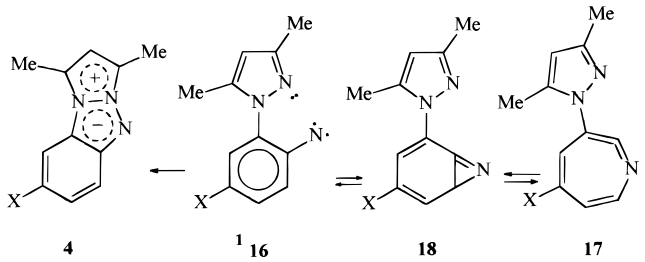
Singlet Nitrene, Benzoazirine, and Dehydroazepine. As mentioned above, the failure of trapping singlet phenylnitrene ^{1}**1** has been attributed to fast rearrangement to didehydroazepine **2**.[3e] The intermediacy of **2** has been demonstrated both spectroscopically[5,11,12] and by reaction with amines (the rate constants for the addition of DEA to para-substituted **2** is in the range 10^6-10^8 M^{-1} s^{-1} in heptane).[12] Recent computational evidence by Karney and Borden[13] supports the view[14] that the rearrangement is a two-step process via the benzoazirine **14** (Scheme 4) and shows that it proceeds from the lowest lying singlet state ($^1A_2$), in which the p$-\pi$ orbital is delocalized and the C$-$N bond has double bond character (compare **15**). The



15

first step (^{1}**1** $\rightarrow$ **14**) is rate determining ($\sim$25 kJ mol^{-1} barrier) and is followed by a symmetry-allowed six-electron electrocyclic ring opening.[13] Benzoazirine **14** is thus expected to be quite

Scheme 5



4 ^{1}**16** **18** **17**

short-lived and furthermore lacks the structural features that make **2** easily identified by spectroscopy. Thus it is not surprising that it has never been detected, although the analogue in the naphthalene series has.[15] Chemical trapping of **14** has been reported in a single case up to now, with the isolation of 2-ethylthioaniline in the presence of EtSH;[16] in the case of a 3-acetamido-4-trifluoroacetamidophenyl azide trapping of the benzoazirine has been obtained also with amines.[17] The above-mentioned calculations also show that **2** is only marginally stabilized with respect to the $^1A_2$ nitrene ($\sim$21 kJ mol^{-1}). Thus, all three species, ^{1}**1**, **14**, and **2**, are predicted to be in equilibrium at room temperature.

With the present pyrazolylphenyl azides **3**, the singlet is trapped to give **4**. Our previous study demonstrated that ^{1}**16a** and didehydroazepine **17a** (see Scheme 5) are in equilibrium. The difference between the activation energies for **4a** (intramolecular trapping of singlet nitrene) and for **9a** (DEA addition to the didehydroazepine, where the rate-determining step is thought to be cyclization to benzoazirine **18a**), is minimal (3 kJ mol^{-1}). Intuitively, it is not surprising that a similar (and low) barrier is encountered in these two rearrangements. In both cases, the reaction involves bending of the nitrene C$-$N bond to reach either cyclization onto the n_N pyrazole orbital or onto the phenyl π orbital (Scheme 5).

As for substituents, recent calculations showed that the electronic effect on the cyclization barrier is small (e.g., for both 2-fluoro and 4-fluorophenylnitrene).[8,18] On the contrary, steric hindrance is determining (in the same way for both fluorine and methyl).[8] Indeed, experiments show that pyridine trapping of unrearranged singlet nitrene is easier with 2,6-disubstituted phenyl azides[9] and that with 2-substituted phenyl azides cyclization always occur away from the substituent, as shown by the isolation of 3-(not 2-)substituted 3*H*-2-dialkylaminoazepines in the presence of secondary amines.[12]

We explored the electronic effect of substituents by comparing the photochemistry of the trifluoromethyl- and the dimethylamino-substituted azides **3e** and **3g**. The first one behaved similarly to **3a** and gave **4e** in neat ethanol and both **4e** and azepines **9e** and **10e** in the presence of DEA (with 0.1 M DEA the heteropentalene/aminoazepine(s) ratio is 1.6 from unsubstituted **3a** and 1.25 from **3e**). Thus, an electron-withdrawing substituent has little effect on the partitioning of singlet nitrene between cyclization onto the pyrazole and onto the phenyl ring (see Scheme 5).[9]

With a strong electron-donating substituent as in **3g**, on the other hand, cyclization to the heteropentalene is suppressed. Donation from the substituent generates a negative charge on

(11) (a) Schrock, A. K.; Schuster, G. B. *J. Am. Chem. Soc.* **1984**, *106*, 5228. (b) Marciniek, A.; Leyva, E.; Whitt, D.; Platz, M. S. *J. Am. Chem. Soc.* **1986**, *108*, 3783. (c) Chapman, O.; Le Roux, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 282. (d) Hayes, J. C.; Sheridan, R. S. *J. Am. Chem. Soc.* **1990**, *112*, 5879.

(12) Li, Y. Z.; Kirby, J. P.; George, M. W.; Poliakoff, M.; Schuster, G. B. *J. Am. Chem. Soc.* **1988**, *110*, 8092.

(13) Karney, W. L.; Borden, W. T. *J. Am. Chem. Soc.* **1997**, *119*, 3347.

(14) Huisgen, R.; Vossius, D.; Appl, M. *Chem. Ber.* **1958**, *91*, 1. Huisgen, R.; Appl, M. *Chem. Ber.* **1958**, *91*, 12.

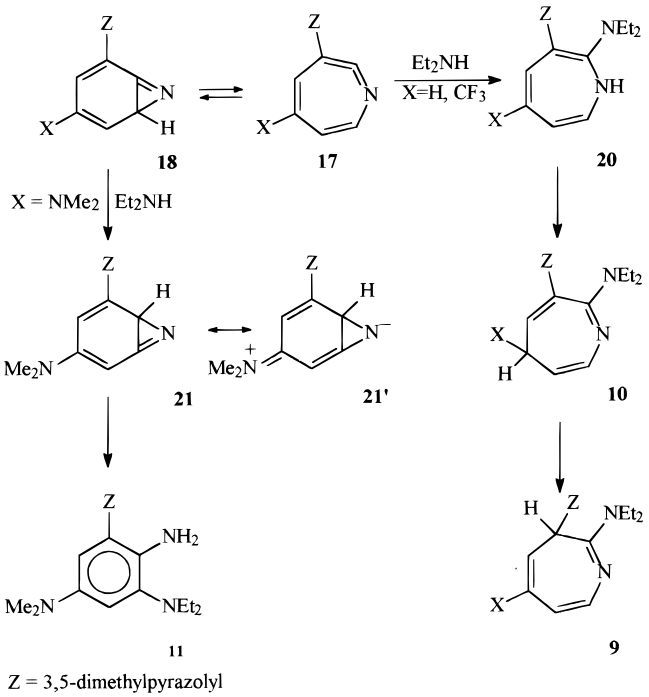
(15) Dunkin, I. R.; Thompson, P. C. P. *J. Chem. Soc., Chem. Commun.* **1980**, 499.

(16) Carrol, S. E.; Nay, B.; Scriven, E. F. V.; Suscitzky, H.; Thomas, D. R. *Tetrahedron Lett.* **1977**, 3175.

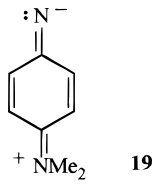
(17) Younger, C. G.; Bell, R. A. *J. Chem. Soc., Chem. Commun.* **1992**, 1359.

(18) Smith, B. A.; Cramer, C. J. *J. Am. Chem. Soc.* **1996**, *118*, 5490.

Scheme 6



the nitrene nitrogen (**19**), and this inhibits electrophilic attack onto the pyrazole nitrogen. This does not hold for cyclization



19

onto the phenyl ring, however, possibly because the decrease in the nitrene electrophilicity is compensated for by the zwitterionic character of the nitrene (see **19**). Indeed the isolated yield of DEA addition products, whatever their structure, remains the same (22−24% with 0.1 M DEA) with the three azides examined (**3a**, **3e**, **3g**).

The *mode* of nucleophile trapping of such intermediates deserves some comment. Previous studies by Schuster showed that para-substituted phenyl azides give a 3*H*-2-aminoazepine.[12] We obtained the corresponding azepines **9a** and **9e** from azides **3a** and **3e**, but in the latter case the main product after photolysis actually was isomeric **10e**, which then tautomerized to **9e** under mild acid catalysis. This is informative, because the primary product must be the 1*H* tautomer **20** (see Scheme 6), and this is expected to undergo symmetry-allowed 1,5-suprafacial shift to **10**, while a further (forbidden) rearragement to **9** does not occur concertedly but, for example, through acid catalysis. This has now been demonstrated in the case of **10e**, but presumably occurs also with other azepines. As for the regiochemistry of ring expansion, we confirm that, at least at room temperature, nitrenes cyclize at position 6 and not position 2 in 2-substituted phenyl azides independently from the electronic nature of the substituent.[13]

In the case of the dimethylamino azide **3g**, DEA gives the benzenetriamine **11**. This is the product expected from addition to a benzoazirine, actually not the one directly formed by nitrene cyclization (see **18**, Scheme 6) but the rearranged intermediate **21**. Thus, the initial nitrene rearrangement occurs as in the other cases toward position 6, but the cyclization is followed by a hydrogen shift rather than ring opening. Notice also that Schuster did not detect a didehydroazepine intermediate from *p*-(dimethylamino)phenyl azide.[12] A way to rationalize this result is to assume that the dimethylamino group stabilizes intermediate **21** through mesomeric structure **21′** and this provides the driving force favoring hydrogen shift (reasonably a base−DEA−catalyzed process, not a pericyclic reaction) over ring enlargement.

Nitrene Intersystem Crossing (ISC) and Temperature Dependence of Azide Photoreactions. Calculation and experiments show that triplet phenylnitrene is stabilized by ∼70 kJ mol^{-1} with respect to the singlet state but ISC is slow (10^6−10^7 s^{-1}).[3e] Thus, the triplet nitrene product (azobenzene) is obtained by photolysis of phenyl azide only at low temperature (<160 K). With the pyrazolyl azide **3a**, where there is no reason to expect that the S−T gap is different, the differential activation parameters for the singlet reaction and ISC were measured as $\Delta\Delta H^{\ddagger} = -10 \pm 2$ kJ mol^{-1} and $\Delta\Delta S^{\ddagger} = 34 \pm 3$ J mol^{-1} K^{-1}, showing that it is the entropic term that disfavors ISC.[7] Assuming that the latter process has negligible activation enthalpy, the observed quantity (10 kJ mol^{-1}) is directly the activation enthalpy of intramolecular ring closure of singlet nitrene ^{1}**16** to give **4** (see Scheme 5). As shown above, the barrier of the other singlet nitrene rearrangement, cyclization to **18** and hence to **17**, is only 3 kJ mol^{-1} larger, thus ∼13 kJ mol^{-1}.[7] This is somewhat lower than recent experimental and calculated data for the rearrangement of parent ^{1}**1** to **14** (25 kJ mol^{-1}).[13]

The substituents affect the ISC to various degrees. The Cl and CF_3 groups have little effect, and as with the parent compound, there are essentially no triplet products at room temperature and only triplet products at 90 K. With the methyl and fluoro derivatives, however, the proportion of triplet-derived products (mainly the amines **5**) is large already at 295 K (45 and 51%, respectively; the rest is the singlet derived heteropentalene) and increases to 100% at 90 K. Thus, ISC is more effective with these substrates.

The case of the dimethylamino-substituted azide **3g** has been studied in more detail. In this case, direct intramolecular trapping of singlet nitrene does not occur. However, the competition between nucleophile trapping of the benzoazirine **18g** and triplet-derived products (**5g**, **7g**) can be studied. Azide **3g** shows the smallest temperature effect, and nucleophile trapping (in the presence of 0.1 M DEA) accounts for 59% of the total isolated products (the rest being triplet-derived products) at 295 K and moderately decreases to 25% in the glass at 90 K. This is the lower limiting value for the benzoazirine, since bimolecular trapping by DEA is hindered in the glass. Thus, triplet ^{3}**16g** and azirine **18g** compete over the entire range explored, and the situation is really completely different from that of unsubstituted **3a**, where the triplet products increase from 0 to 100% in this interval. We see no explanation but to conclude that the singlet triplet *gap* is dramatically reduced in this case, so that singlet nitrene, benzoazirine, *and* triplet nitrene are *all* in equilibrium.

This implies that the electronic structure of the nitrene must be different in **16g**: as mentioned above, the lowest lying singlet state in phenylnitrene is the open shell $^1A_2$ where electron are placed in pure p orbitals. With the dimethylamino group donation from the ring to the nitrene nitrogen becomes important (see **19**) and this limits admixing of the N 2s orbital with the nitrene lone pair. This removes the factor explaining the greater

thermodynamic stability of nitrenes relative to carbenes[3e,19] and makes the structure of this nitrene more similar to that of phenylcarbene. In the latter species, the singlet−triplet gap is small (calculated 8−16 kJ mol^{-1})[19,20] and ISC is faster than bimolecular reactions of both states, so that the triplet functions as a reservoir for the faster reacting singlet.[3e,21] With nitrene **16g** the singlet is unreactive, but the triplet is a reservoir for the azirine (in the presence of DEA, **11** is formed at the expense of **5g**; see Table 3). A support for the enhancement of triplet energy comes from the observed chemistry: the main product from ^{3}**16g** (both at 295 and 90 K) is the amine from intermolecular hydrogen abstraction, rather than the azo compound typical of "lazy" triplets such as ^{3}**16a** and most phenylnitrenes (see further below).

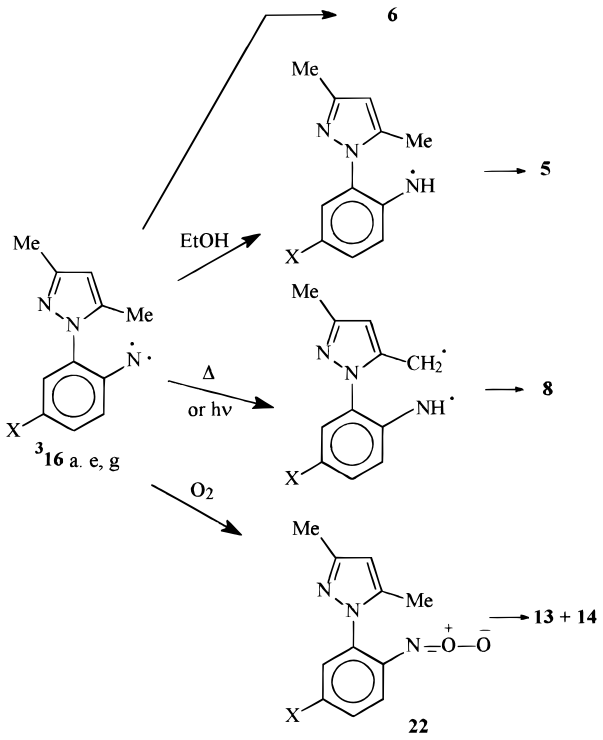
Spectrum of Nitrene Triplets. Irradiation in an ethanol glass at 90 K allows complete decomposition of the azides. With parent **3a** and with derivatives **3b**−**3e** the spectra maintain the same habitus and are closely comparable to those observed by Platz and Wirz for phenyl azide (Figure 1, Table 3).[5] These spectra are attributed to triplet nitrene, and the observed thermal and photochemistry of these transients (see below) is that expected from a triplet. The longest-wavelength band is a πn_x transition.[5,22] The systematic survey in Figure 1 shows that an electron-withdrawing para substituent has little effect on this band (see Figure 1a−d and Table 3, note a), while it affects the complex band system in the 300−400-nm region. With the trifluoromethyl derivative there is a marked red (and ipsochromic) shift of the low-energy band while the system at 300−400 nm is split into two groups of bands (Figure 1e).

With electron-donating substituents, the spectra observed are quite different. Apart from the introduction of strong bands at 270 nm (for the methoxy) and 300 nm (for the dimethylamino derivative) related to the substituted π system, also the long-wavelength part of the spectrum is also different. The structure of the triplet is thus different in these cases, even though some other transient may be present in the matrix and contribute to the observed spectrum.

Triplet Chemistry. Rapid heating allows nitrene migration as soon as the glass softens and under such condition by far the main process from ^{3}**16a** (90%) and from ^{3}**16e** (70%) is dimerization to azobenzene, since hydrogen abstraction from the solvent is too slow under this condition. On the other hand, if the temperature is slowly raised, the matrix softens gradually and hydrogen abstraction to give the anilines **5a** (61%, azo reduced to 33%) and **5e** (83%, no azo) predominates. The fact that it is sufficient to increase mobility through quick glass softening to make coupling to the azo compound dominant and that no intramolecular H abstraction from the pyrazole methyl groups occurs demonstrate the poor radical character of triplet phenylnitrenes ("lazy triplet" as dubbed by Suschitzky).[10a]

The CF_3 group marginally increases hydrogen abstraction, but this process is much more efficient with the dimethylamino-substituted nitrene ^{3}**16g**. In this case, the competition among the three paths, viz. H abstraction from the solvent, intramolecular H abstraction (to give **8g**), and coupling to the azo derivative, depends very little on conditions (the ratio is 55/36/9 at 90 K, with fast heating, 68/28/<4 with slow heating, and 89/11/0 at 295 K). This demonstrates that this nitrene resembles more a good hydrogen abstractor such as the phenylcarbene triplet than the stabilized phenylnitrene.

Scheme 7



Oxygen Trapping. All of the present nitrenes add oxygen. The matrix spectrum in the presence of oxygen is different from that under degassed conditions (as an example, see Figure 3 vs Figure 1), and the products obtained after melting are the nitroso and nitro derivatives. The transient reasonably is the nitroso oxide **22** (compare Figure 3b, where the residual absorption due to triplet nitrene is observed immediately after irradiation and gives way to the final spectrum in minutes, while oxygen penetrates in the matrix). This is an expected process from arylnitrenes, although it has been sparsely documented up to now.[23] Flash photolysis at room temperature has failed to reveal any transient similar to that reported in Figure 3b,[11a] but oxygen-transfer studies by Sawaki et al. are consistent with the expected chemistry of nitroso oxides.[24]

Matrix studies reveal this transient and show a consistent blue shift in the spectrum with electron-attracting substituents (see Table 3; λ_{max} **22g** > **22a** > **22e**). Notice that oxygen addition predominates (>90%) with "lazy" triplets (^{3}**16a** and ^{3}**16e**) while H abstraction from the solvent remains competitive from ^{3}**16g** (58−42%), once again demonstrating the high reactivity of this species (see Scheme 7).

Photochemistry of Nitrene Triplet. Selective excitation of the triplet nitrenes by irradiation in the visible increases the radical character and leads to intramolecular hydrogen abstrac-

(19) Kemnitz, C. R.; Karney, W. L.; Borden, W. T. *J. Am. Chem. Soc.* **1998**, *120*, 3499.

(20) Matzinger, S.; Bally, T.; Patterson, E. V.; McMahon, R. J. *J. Am. Chem. Soc.* **1996**, *118*, 1535. Wong, M. W.; Wentrup, C. *J. Org. Chem.* **1996**, *61*, 7030. Schreiner, P. R.; Karney, W. L.; Schleyer, P. v. R.; Borden, W. T.; Hamilton, T. P.; Schaefer, H. F. *J. Org. Chem.* **1996**, *61*, 7030.

(21) Moss, R. A.; Dolly, U. H. *J. Am. Chem. Soc.* **1971**, *93*, 954. Baer, T. A.; Gutsche, C. D. *J. Am. Chem. Soc.* **1971**, *93*, 5180. Savino, T. G.; Kanakarajan, K.; Platz, M. S. *J. Org. Chem.* **1986**, *51*, 1305.

(22) Kim, S. J.; Hamilton, T. P.; Schaefer, H. F. *J. Am. Chem. Soc.* **1992**, *114*, 5349.

(23) (a) Phenyl azide and some of its substituted derivatives have been shown to give 5−20% of the nitro derivative and 0−18% of the azoxy compound upon photolysis in oxygen-flushed solution at 30 °C;[23b] 4-nitrophenyl azide gives a better yield[23c] and an oxygen adduct is obtained in close to quantitative yield by photolysis of 2-phenazinyl azide.[23d] (b) Abramovitch, R. A.; Challand, S. R. *Chem. Commun.* **1972**, 964. (c) Liang, T. Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1987**, *109*, 7803. Bettinetti, G.; Fasani, E.; Minoli, G.; Pietra, S. *Gazz. Chim. Ital.* **1988**, *100*, 175.

(24) Sawaki, Y.; Kishikawa, S.; Iwamura, H. *J. Am. Chem. Soc.* **1987**, *109*, 584.

tion (since the viscosity of the matrix does not allow for intermolecular processes). The reaction is in accord with the $\pi \rightarrow$ n character of this state, which favors a radical reactivity, similarly to an iminyl radical (see **15**). This is apparent with ^{3}**16e**, where intramolecular hydrogen abstraction occurs quite cleanly (see Figure 2b and the high yield of **8e**). With ^{3}**16g**, intramolecular abstraction is the main process (64%), but—as in the thermal reactions—intermolecular abstraction remains important.

Substituent Effect. As pointed out by Platz,[3e] phenylnitrene is a poor reagent in organic chemistry, giving a low yield of characterized products, since ring enlargement to the didehydroazepine precludes the electrophilic *intermolecular* attack so characteristic of phenylcarbene. This postulate is satisfactory, and the study of the present pyrazolyl derivatives shows that *intramolecular* electrophilic attack occurs efficiently in suitable models and that singlet nitrene and the didehydroazepine are in equilibrium (via the benzoazirine). Some effort has been recently given to establish whether ring substitution may change the situation, making intermolecular electrophilic reaction from the singlet more competitive.[8,13,18] This expectation is not borne out by the present study, showing that the proportion of trappable cyclized intermediates (the didehydroazepine or the azirine) is only moderately affected by the substituent (at 295 K, 34% of the isolated products from the parent azide, 44% from the trifluoromethyl, and 59% from the dimethylamino derivative). This is in accord with calculations demonstrating that electronic factors exert a small effect on this rearrangement.[8] Thus, singlet trapping is effective only with ortho-disubstituted phenyl azides, not on simple derivatives (unless, as in the present case, the reaction is intramolecular) and only with unhindered n nucleophiles such as pyridine, not with π nucleophiles, which would be much more interesting from the synthetic point of view. The electron-donating NMe_2 group does not affect the rearrangement of the singlet; it only allows the trapping of the first intermediate, the benzoazirine.

Substituents have a more important effect on ISC. The rationalization of this effect is not straightforward, since groups as different as methyl and fluoro both enhance the proportion of triplet-derived products at room temperature. At least with the dimethylamino derivative **16g**, where the largest effect is observed, the reason appears to be a substantial enhancement of the phenylnitrene energy and a reduction of the singlet−triplet gap. This phenylnitrene is thus closer to phenylcarbene in the radical reactivity, but obviously not as far as electrophilic reactions from the singlet are concerned, since these are precluded by electron donation from the substituent. The higher energy of the triplet in this case is reflected in the efficient intermolecular hydrogen abstraction, as opposed to the usual dimerization of phenylnitrenes. Triplet reactions may also be exploited for applications. Reaction with oxygen is a limitation, but the triplets that are efficiently produced, such as ^{3}**16g**, are also the most reactive ones, and abstract hydrogen also in the presence of oxygen.

Thus, one may summarize that the introduction of substituents does not cause electrophilic reactions of singlet phenylnitrene to occur in a convenient way, while enhancement of the triplet radical reactivity can be accomplished. This is of little significance in synthesis, but may be important for applications such as photochemical labeling and polymer cross-linking.

Conclusion. High-energy species such as arylnitrenes have available a variety of accessible paths, not necessarily leading to characterized end products. The use of "internal trapping" models gives better yields allowing us to draw conclusions from product studies.[25] This has been applied here to the substituent effect. The main points are a negative result; viz. there is no influence on singlet nitrene cyclization to the benzoazirine and hence to the dehydroazepine, and a positive one; an electron-donating substituent enhances the energy of triplet nitrene and adds it to the pool of species in equilibrium.

Experimental Section

General Information. NMR spectra were run on a Brucker 300 instrument and are reported in $CDCl_3$ with TMS as the internal standard. IR spectra were on a Perkin-Elmer Paragon 1000 spectrophotometer, and mass spectra on a Finnigan LCQ instrument. 95% Ethanol was spectroscopic grade solvent. Column chromatography was performed with silica gel Merk HR 60. The azides **3a−c** and **3e−f** were prepared and purified as previously reported.[10a,c, 27]

Synthesis of 1-[(2-Azido-5-(fluorophenyl)]-3,5-dimethylpyrazole (3d). To a solution of acetylacetone (5 g, 50 mmol) in 150 mL of ethanol containing 2 drops of concentrated HCl, 3.42 g (20 mmol) of 2-nitro-5-fluorophenylhydrazine[28] was added and the mixture was refluxed for 30 min. After cooling, a yellow precipitate formed was discarded. Evaporation of the filtrate and recrystallization from cyclohexane gave 1-(2-nitro-5-fluorophenyl)-3,5-dimethylpyrazole (**13d**, 2.5 g, 53% yield), light orange prisms, mp 93−94 °C. Anal., found C, 56.0; H, 4.1; N, 17.6. Calcd for $C_{11}H_{10}FN_3O_2$: C, 56.17; H, 4.25; N, 17.87. Catalytic hydrogenation of this product according to the usual procedure gave the *amine* **5d** as colorless crystals (65% yield), mp 69−70 °C (petroleum ether). Anal., found C, 64.1; H, 5.9; N, 20.1. Calcd for $C_{11}H_{12}FN_3$: C, 64.39; H, 5.85; N, 20.49. IR (neat) 3442, 3320, 3207 cm^{-1}; ^{1}H NMR δ 2.2 (s, 3H), 2.3 (s, 3H), 3.9 (br, exch, 2H), 6.0 (s, 1H), 6.77 (dd, 1H, J = 5, 9 Hz), 6.87 (dd, 1H, J = 3, 9 Hz), 6.93 (ddd, 1H, J = 3, 8, 9 Hz). Diazotisation of this material in AcOH−HBF_4 and reaction with sodium azide gave **3d** as colorless needles, mp 57−58 °C (petroleum ether, 79% yield). Anal., found: C, 56.8; H, 4.5; N, 30.0. Calcd for $C_{11}H_{10}FN_5$: C, 57.14; H, 4.33; N, 30.30. IR (KBr) 2127 cm^{-1}; UV 286 nm (3.46), 239 (4.18); ^{1}H NMR δ 2.15 (s, 3H), 2.3 (s, 3H), 6.0 (s, 1H), 7.1 (dt, 1H, J = 2, 6 Hz), 7.18 (d, 1H, J = 2, 6 Hz), 7.25 (s, 1H).

Preparation of 1-[2-nitroso-5-(trifluoromethyl)phenyl]-3,5-dimethylpyrazole (12e). A solution of 1.0 g (3.9 mmol) of the corresponding amine in 10 mL of chloroform was added with 2.6 g of 3-chloroperoxybenzoic acid (52% assay, 7.8 mmol) in 10 mL of chloroform at room temperature, while stirring, in 15 min. The solution turned yellow and after 2 h was extracted with 3 × 10 mL saturated sodium carbonate. Evaporation of the organic solvent and chromatography of the residue gave 0.6 g (55%) of a slightly yellow solid which was recrystallized from ethanol, mp 122−23 °C. Anal., found: C, 53.6; H, 3.9; N, 15.6. Calcd for $C_{12}H_{10}F_3N_3O$: C, 53.53; H, 3.74; N, 15.61. ^{1}H NMR δ 2.1 (s, 2H), 2.38 (s, 3H), 6.15 (s, 1H), 6.35 (d, 1H, J = 8 Hz), 7.63 (dd, 1H, J = 2, 8 Hz), 8.18 (d, 1H, J = 2 Hz). It should be noted that in previous studies we showed that a nitroso derivative such as **12a** is better described as being in equilibrium with isomeric 1,3-dimethylpyrazolo[1,2-*a*]benzotriazole 5-oxide.[29]

Preparative Irradiation. Preparative irradiation and product separation were carried out as in previous communications.[7,10] The characterization of several of the photoproducts was previously reported. The main data about the new photoproducts are reported below.

1,3-Dimethylpyrazolo-8-fluoro[1,2-*a*]benzotriazole (4d): lemon yellow needles, mp 115−117 °C (cyclohexane). Anal., found: C, 64.8; H, 5.0; N, 21.0. Calcd for $C_{11}H_{10}FN_3$: C, 65.02; H, 4.92; N, 20.69. ^{1}H

(25) (a) Other groups functioning as internal traps are phenyl[25b,c] and methoxycarbonyl.[26] (b) Swenton, J. S.; Ikeler, T. J.; Williams, B. H. *J. Am. Chem. Soc.* **1970**, *92*, 3103. (c) Sundberg, R. J.; Heintzelman, R. W. *J. Org. Chem.* **1979**, *39*, 2546.

(26) Tomioka, H.; Ichikawa, N.; Kamatsu, K. *J. Am. Chem. Soc.* **1993**, *115*, 8621.

(27) Albini, A.; Bettinetti, G.; Minoli, G. *J. Org. Chem.* **1983**, *48*, 1080.

(28) Menzel, K. H.; Puetter, R. Belg. Pat. 643 802; *Chem. Abstr*. **1965**, *63*, 4440f.

(29) Albini, A.; Bettinetti, G.; Minoli, G. *J. Chem. Soc., Perkin Trans.1* **1983**, 581.

NMR δ 2.55 (s, 1H), 2.7 (s, 1H), 6.3 8s, 1H), 7.08 (td, 1H, $J = 2.5$, 9.5 Hz), 7.33 (dd, 1H, $J = 5$, 9 Hz), 7.37 (dd, 1H, $J = 2.5$, 8 Hz).

2,2′-Bis[1-(3,5-dimethylpyrazolyl)]-4,4′-difluoroazobenzene (6d): orange-yellow crystals, mp 184−185 °C. Anal., found: C, 64.7; H, 5.2; N, 20.5. Calcd for $C_{22}H_{20}F_2N_6$: C, 65.02; H, 4.92; N, 20.69. ^{1}H NMR δ 2.02 (s, 3H), 2.32 (s, 3H), 6.05 (s, 1H), 7.1 (ddd, 1H, $J = 2.5$, 7.5, 9 Hz), 7.3 (dd, 1H, $J = 2.5$, 9), 7.5 (dd, $J = 5.5$, 9 Hz).

8-Fluoro-3-methyl-8-pyrazolo[1,2-*a*]quinoxaline (8d): light yellow crystals, mp 132−133 °C (cyclohexane). Anal., found: C, 65.6; H, 4.1; N, 20.6. Calcd for $C_{11}H_8FN_3$: C, 65.67; H, 3.98; N, 20.89. ^{1}H NMR δ 2.6 (s, 3H), 6.65 (s, 1H), 7.25 (s, 1H), 7.27 (dt, 1H, $J = 2.5$, 9 Hz), 8.05 (dd, 1H, $J = 5.5$, 9 Hz), 8.1 (dd, 1H, $J = 2.5$, 9 Hz).

3*H*-2-(Diethylamino)-3-[1-(3,5-dimethylpyrazolyl)]azepine (9a): erroneously reported as *2H*-2-(3,5-dimethylpyrazolyl)-7-diethylaminoazepine in ref 7; ^{1}H NMR δ 0.85 (t, 6H), 2.12 (s, 3H), 2.25 (s, 3H), 2.78 (m, 2H), 3.15 (m, 2H), 4.02 (d, 1H, $J = 6$ Hz, H-3), 5.9 (s, 1H), 5.9 (dd, 1H, $J = 6$, 7.5 Hz, H-6), 6.2 (dd, 1H, $J = 6$, 9 Hz, H-5), 6.45 (dd, 1H, $J = 6$, 9 Hz, H-4), 7.23 (d, $J = 7.5$ Hz, H-7), attribution on the basis of double-irradiation experiments. NOE experiments: irradiation of the 4.02 d enhances both CH_2 m of the NEt_2 group and the azepine protons, in particular H-5 and H-7; irradiation of the 7.23 d enhances the 5.9 d and the 4.02 d, but not the CH_2 m of the NEt_2 group; irradiation of either the 2.78 or the 3.15 m enhances the 4.02 d; irradiation of the 2.25 s enhances the 4.02 d. The structure was finally demonstrated by means of a single-crystal determination (data deposited at the Cambridge Crystallographic Centre, no. 101778).

3*H*-2-(Diethyamino)-3-[1-(3,5-dimethylpyrazolyl)]-5-trifluoromethylazepine (9e): light yellow crystals, mp 75−78 °C (*n*-pentane). Anal., found: C, 59.2; H, 6.5; N, 17.0. Calcd for $C_{16}H_{21}F_3N_4$: C, 58.89; H, 6.44; N, 17.18. ^{1}H NMR δ 0.9 (t, 6H), 2.15 (s, 3H), 2.3 (s, 3H), 2.8 (m, 2H), 3.22 (m, 2 H), 3.95 (d, 1H, $J = 6.5$ Hz), 5.85 (s, 1H), 5.95 (d, 1H, $J = 8$ Hz), 6.7 (d, 1H, $J = 6.5$ Hz), 7.35 (d, 1H, $J = 8$ Hz). NOE experiments: irradiation of the 3.95 d enhances the CH_2 m at 3.22 as well as the azepine protons, similarly to the above isomer; ^{13}C NMR δ 10.7 (Me), 12.4 (Me), 13.4 (Me), 43.5 (CH_2), 51.3 (CH), 103.5 (CH), 106.4 (CH), 111.8 (CH), 123.7 (CF_3), 128.9 (C−CF_3), 140.3, 142.3 (CH), 143.0, 148.1.

5*H*-2-(Diethyamino)-3-[1-(3,5-dimethylpyrazolyl)]-5-trifluoromethylazepine (10): obtained in a chromatographic fraction admixed with some (20%) of the above isomer. ^{1}H NMR δ 0.9 (t, 6H), 2.92 (m, 1H), 3.2 (m, 4H), 5.05 (dd, 1H, $J = 5$, 7.5 Hz), 5.8 (s, 1H), 6.13 (d, 1H, $J = 7.5$ Hz), 6.87 (d, 1H, $J = 5$ Hz); ^{13}C NMR δ 12.4 (Me), 13.2 (Me), 13.5 (Me), 40.3 (CH−CF_3), 43.5 (CH_2), 104.6 (CH), 106.4 (CH), 125.0 (CF_3), 125.1 (CH), 128.9 (C−CF_3), 140.5, 140.3 (CH), 149.3, 158.5.

1-[2-Amino-3-(diethylamino)-5-(dimethylamino)phenyl]-3,5-dimethylpyrazole (11): yellow oil (purified by repeated chromatography). Anal., found: C, 67.3; H, 9.3; N, 23.0. Calcd for $C_{17}H_{27}N_5$: C, 67.73; H, 9.03; N, 23.24. Mass spectrum, M^+ 301 *m*/*e*; UV (EtOH) 330 nm (log ϵ 3.58), 238 (4.24); IR (neat) 3420, 3332 cm^{-1}; ^{1}H NMR δ 1.0 (t, 6H), 1.7 (m, 2H), 2.12 (s, 3H), 2.3 (s, 3H), 2.8 (s, 6H), 2.95 (q, 4H), 3.8 (br, exch, 2H), 5.95 (s, 1H), 6.4 (d, 1H, $J = 4$ Hz), 6.6 (d, 1H, $J = 4$ Hz); ^{13}C NMR δ 11.4 (Me), 12.6 (Me), 13.5 (Me), 42.0 (Me), 47.5 (CH_2), 105.1 (CH), 109.6 (CH), 110.6 (CH), 126.1, 133.4, 139.1, 140.6, 143.3, 148.9. A COLOC experiment on the δ 6.4 signal at 5 Hz shows a coupling with the carbon signal at 126.1—a doublet attributed at 1′-C; the signal at δ 133.4 is a triplet, showing that there is no vicinal hydrogen for this amino-substituted carbon atom. NOE experiments: irradiation of the δ 6.65 signal gives a 2.5 enhancement of the 2.8 singlet and of the 2.95 q; irradiation of the 2.95 q gives a 1% enhancement of the 6.6 d. This demonstrates that the 4′-C is flanked by dimethylamino and diethylamino groups.

Variable-Temperature Irradiation. A 1×10^{-4} M solution of one of the azides **3** in EtOH (2 mL) in a 1-cm optical path quartz cell with a quartz to glass graded seal was degassed by means of four freeze−degas−thaw cycles and sealed. A series of experiments were carried out by using oxygen-equilibrated solutions (see text). The cell was inserted into an Oxford DN 1704 liquid nitrogen cryostat fitted with a calibrated ITC4 temperature controller and placed in a UV−visible Kontron Uvikon 941 spectrophotometer. The cell was irradiated from the bottom by means of a bifilar low-pressure mercury arc inserted below the cell (Helios Italquartz 15 W). Irradiation was discontinued when the spectra were taken. In a typical experiment, the solution was equilibrated for 30 min at the desired temperature and then irradiated for 8 min. After this time, the temperature was either gradually raised (see text) or allowed to quickly reach room temperature (within 30 min in the latter case). The solution was washed down in a round-bottomed flask and evaporated in the dark, and the residue was redissolved in 1 mL of MeCN and analyzed by HPLC. A Jasco PU 980 instrument with UV-975 detector was used, with a 25 cm × 4.6 mm Merck Purospher RP-18 LiChroCART 250-4 column (and a Purospher RP-18 LiChroCART 4-4 precolumn). Various water−acetonitrile mixtures were used as the eluent.

Double-Irradiation Experiments. Samples irradiated at 254 nm as above were further irradiated by means of a focalized high-pressure mercury arc (Osram 150 W) through a cutoff filter (>455 nm). The beam reached the cell through a side opening perpendicular to the analyzing beam. The sample was then rapidly heated at room temperature and analyzed as above. Under this condition, dihydroquinoxalines **8** often were important products in the place of their rearomatized counterpart (compounds **7**) generally dominating upon photolysis at room temperature (except than for the dimethylamino derivative, which gave **7g** under any condition). **8a** was independently prepared and characterized. As for the other derivatives, these rearomatized spontaneously in ethanol solution at room temperature in ∼1 month.[7] In Tables 1 and 3, the total amount **7** + **8** is reported.

Acknowledgment. Partial support of this work by CNR, Rome, and MURST, Rome, is gratefully aknowledged.

JA982585R