Reactivity of Singlet and Triplet Arylnitrenes: Temperature-Dependent Photodecomposition of 1-(2-Azidophenyl)-3,5-dimethylpyrazole

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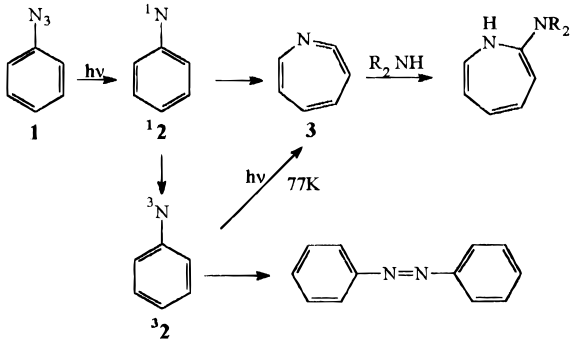
Abstract: At >200 K photolysis of 1-(2-azidophenyl)-3,5-dimethylpyrazole (**5**) gives 1,3-dimethylpyrazolobenzotriazole (**6**, by electrophilic cyclization of singlet nitrene ^{1}**4**) or, in the presence of diethylamine, aminoazepine **8** (by addition of the nucleophile and rearrangement). At lower temperatures, the yield of these products decreases and the azo derivative **9** (from the dimerization of triplet nitrene ^{3}**4**) as well as products from intramolecular radical cyclization (again via ^{3}**4**) is obtained, to become the only products at <100 K. Differential thermodynamic parameters for the reactions of ^{1}**4** and ^{3}**4** are determined by analysis of the temperature dependence of products distribution ($\Delta\Delta H^{\ddagger} = -10$ kJ mol^{-1} and $\Delta\Delta S^{\ddagger} = 34$ J mol^{-1} K^{-1} in ethanol). Addition of the amine may require previous ring enlargement to give the dehydroazepine **12**; there is no indication that this is an intermediate of any stability, however, and if formed, this is in equilibrium with ^{1}**4**. Triplet nitrene ^{3}**4** is characterized in matrix by UV spectroscopy, and its photoreactions (to give mainly intramolecular hydrogen abstraction) are separately studied.

There is now current agreement that the photolysis of phenyl azide (**1**) in solution generates singlet nitrene (^{1}**2**) and this partitions between intersystem crossing to the triplet ^{3}**2** and ring enlargement to the dehydroazepine **3** (Scheme 1).[1−5] Irradiation of a solution of **1** at room temperature gives some azobenzene, in a yield depending on the initial phenyl azide concentration, and untractable "tars" arising via a polymerization process thought to be initiated by a reaction of **3**. The latter intermediate can be trapped by nucleophiles, typically amines, to give isolable azepines in a moderate yield. However, lowering the temperature slows down the reaction with amines and below 160 K the main product formed is azobenzene, arising from triplet nitrene. A brief irradiation in a glassy matrix at 77 K yields predominantly ^{3}**2**, recognized by its UV and EPR spectra, but continuous photolysis leads to **3**.[4,6] IR detection has been particularly valuable, and after some initial conflict it is now clear that ^{3}**2** is the main product also in Ar matrix[4,5,7,8] and **3** has been revealed at room temperature in solution.[2c]

While the mechanism shown in Scheme 1 can be regarded as fully satisfactory and the pertinent kinetic parameters have been estimated,[4] it may be disappointing that the data obtained are based on a reaction of the dehydroazepine and not on a direct reaction of singlet nitrene, which is the primary photoproduct and the temperature-dependent branching point. On other hand, no direct reaction of singlet phenylnitrene has been reported, except for nucleophilic addition by amines to give a hydrazine in the case of 4-nitro and 4-cyanophenyl azide.[9]

Scheme 1



We reasoned that a further improvement of the model could be obtained by resorting to *intramolecular* trapping, and particularly studying the (nitrenophenyl)dimethylpyrazole **4**. This species was originally proposed by Suschitzky and colleagues as a probe for testing the nucleophilic/radical character of phenylnitrene through addition to the pyrazole nitrogen and hydrogen abstraction from the methyl group, respectively (Scheme 2).[10] We found that, with some modifications, this model is satisfactory. Noteworthy, photolysis of azide **5** yields the heteropentalene **6** (see below), the product from intramolecular trapping of singlet nitrene, in a good yield at room temperature.[11,12] This is an advantage with respect to parent **1** and its simple derivatives and gives confidence that a temperature-dependence study may offer new mechanistic

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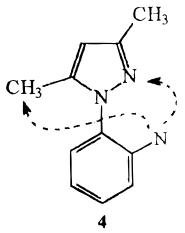
Scheme 2



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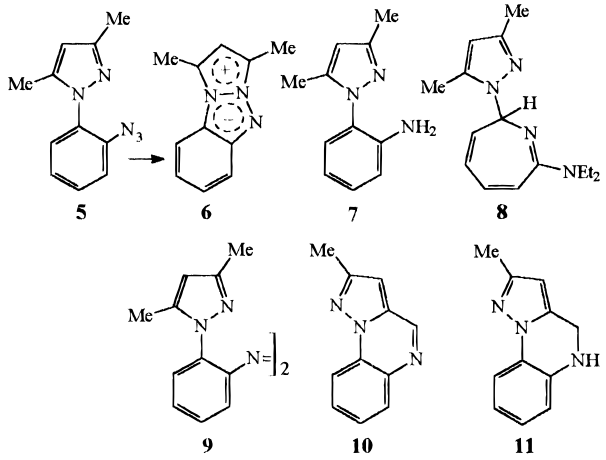
Scheme 3



5 **6** **7** **8** **9** **10** **11**

Table 1. Products from the Preparative Irradiation of Azide **5** (Isolated Yields from Column Chromatography)

solvent (additive)	products (% yield)
EtOH[a]	**6** (66), **7** (9)
MeCN[a]	**6** (58)
C_6H_{12}[a]	**6** (53), **7** (1)
C_6H_{12}, Et_2NH 0.06 M	**6** (7), **7** (tr),[b] **8** (51)

[a] See ref 17. [b] tr = trace.

insight, since a satisfactory material balance is expected under all conditions. We found that this is indeed the case, as reported in the following.

Results

Room Temperature Photolysis. Irradiation of azide **5** at room temperature gave the heteropentalene **6** in good yield along with a minor amount of the amine **7** in a variety of solvents (see Scheme 3; the scheme gathers the products formed under various conditions, see below). Typical results from preparative irradiation and chromatographic separation are reported in Table 1. As it appears from the table, the reaction is little affected by the medium. In the presence of amines, the yield of **6** was decreased and the aminoazepine **8** was obtained as a major product.

Temperature-Dependent Photolysis. Experiments in EtOH. A set of small-scale experiments was carried out at different temperatures. 2-Methylpentane (MP) and ethanol were chosen as suitable solvents for this study. The product distribution was determined by standardized HPLC measurements. Compound **6** is sensitive to irradiation in the presence of oxygen,[13] and thus the experiments were routinely carried out in degassed solutions. The amount of azide decomposed did not significantly change on decreasing the temperature, but the yield of the products was deeply affected. Thus, in EtOH the azo derivative **9**, not significantly formed at room temperature, was detected below 230 K, was found in equal amounts to **6** at 140 K, and became the main product at lower temperatures when **6** was present only in trace amounts (Table 2, Figure 1). Apart from a small amount of the amine **7**, further products formed at low temperature were 2-methylpyrazolo[1,2-*a*]quinoxaline (**10**) and its dihydro derivative **11** (see Experimental Section for the characterization). In the presence of 0.1 M diethylamine (DEA) the azepine **8** was formed competitively with heteropentalene **6** at 150 K, but not at lower temperatures, where the azo compound **9** remained the main product, with qualitatively the same product distribution as in neat EtOH.

Experiments in MP. The behavior in MP was roughly similar, but more complex. In this case, the yield of product **6** decreased in the 220−150 K range, more abruptly than in the EtOH case (Table 3, Figure 2), in a temperature range where compound **9** was still unimportant. The formation of further peaks was chromatographically revealed in this range, and

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Table 2. Products from the Variable Temperature Irradiation of Azide **5** in Ethanol (HPLC Monitoring)[a]

	in neat solvent				with 0.1 M DEA				
T/K	**6**	**7**	**9**	**10** + **11**	**6**	**7**	**8**	**9**	**10** + **11**
297	72	tr[c]			36	4	22	*b*	2
270	85	tr			48	4	23	*b*	
230	82	tr	1	*b*	64	3	23	*b*	
180	60	tr	6	*b*	65	3	18	5	
140	27	tr	27	*b*	29	5	4	15	
100	2	4	42	13	5	7		27	6

[a] 8 min irradiations; conversion is ca. 90%. See Figure 1 for data at more temperatures. [b] Low amount, difficult to quantify due to peak superimposition in the HPLC trace. [c] tr = trace.

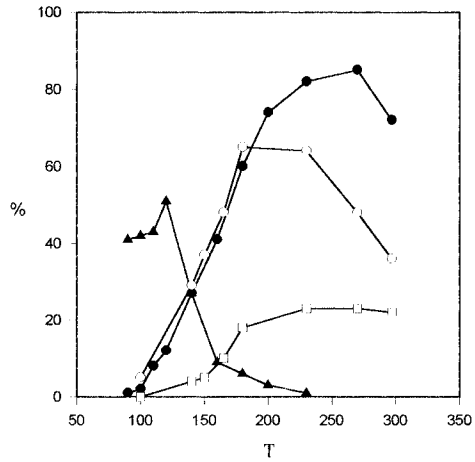

Figure 1. Temperature dependence of the photoproducts yield by irradiation of azide **5** in EtOH, (●) product **6**, (▲) product **9**, as well as in EtOH containing 0.1 M DEA, (○) product **6**, (□) product **8**.

Table 3. Products from the Variable Temperature Irradiation of Azide **5** in MP[a]

	in neat solvent				with 0.1 M DEA				
T/K	**6**	**7**	**9**	**10** + **11**	**6**	**7**	**8**	**9**	**10** + **11**
295	56	tr[f]		8	11	3	46		tr
295[b]	54	tr							
240	59	2	5	3	11	*c*	42		
200	33	2	4		11	*c*	39		
160	9[d]	tr	3	*c*	7	*c*	19		
90		4	15	11					
77		5	13	19		7		14	10
77[b]		tr		21[e]					

[a] 8 min irradiations; conversion is ca. 90%. See Figure 2 for data at more temperatures. [b] In oxygen-equilibrated solution. [c] Low amount, difficult to quantify due to peak superimposition in the HPLC trace. [d] Further products ($M^+ + 1$, 371) revealed by HPLC; see text. [e] 3,5-Dimethyl-1-(2′-nitrosophenyl)pyrazole and the corresponding nitro derivative also present. [f] tr = trace.

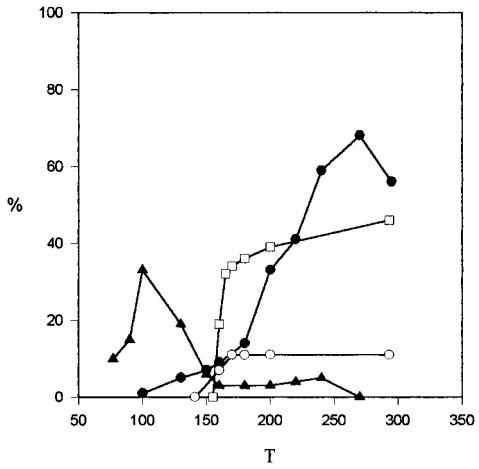

Figure 2. Temperature dependence of the photoproducts yield by irradiation of azide **5** in MP, (●) product **6**, (▲) product **9**, as well as in MP containing 0.1 M DEA, (○) product **6**, (□) product **8**.

although we were unable to isolate them, HPLC/MS analysis demonstrated that the molecular weight was *m/e* 370 (twice that of the nitrene **4**). In turn, the yield of these products decreased by further lowering the temperature, and below 130 K the main product was, as in the EtOH case, the azo derivative **9** along with compounds **7**, **10**, and **11**. Notice finally that below 100 K the last two derivatives increased at the expense of **9**.

In the presence of 0.1 M DEA the azepine **8** was formed competitively with **6**, and indeed in a higher proportion than in EtOH. Lowering the temperature at 220 K and below decreased the yields of both **6** and **8**, but this change could be explored only down to 160 K, since then the amine separated out. Irradiation at 77 K (apparently involving an inhomogeneous glass) formed no azepine and gave products **7**, **9**, **10**, and **11** in yields similar to those obtained in a neat MP glass.

The effect of oxygen was tested in a few cases. At room temperature the effect was small, while a 77 K in MP 1-(2-nitrosophenyl)- and 1-(2-nitrophenyl)-3,5-dimethylpyrazole were formed (see Table 3).

Irradiation in a Glassy Matrix. Irradiation at 90 K in glassy EtOH by using a 254 nm light source led to the formation of a colored intermediate (Figure 3a). After a few minutes of irradiation, virtually complete consumption of the azide was obtained (compare initial and final spectra in Figure 3b). The spectrum did not change for hours at 90 K. Heating up to 105 K caused some change in the spectrum (see Figure3c), and at a higher temperature the spectrum bleached upon melting the glass. A similar spectrum was obtained in MP at 77 K (Figure 4). At ca. 90 K the MP glass became less rigid and the intermediate accumulated to a lesser degree. On the other hand, when degassing was omitted, a different spectrum was observed (see Figure 5).

Secondary Photolysis. Prolonged irradiation at 254 nm led to disappearance of the above spectrum. More expediently, a clean bleaching of that spectrum could be obtained by irradiation into the visible band. Taking advantage of this property, solutions of **5** were first irradiated at 254 nm until a complete conversion of the azide was reached and then at $\lambda > 455$ nm until the visible absorption was bleached. Chemical analysis after this double irradiation showed that compounds **10** and **11** were the main products in MP as well as in EtOH, where, however, a sizeable amount of heteropentalene **6** was also obtained (Table 4). The product distribution was little affected by the temperature (in the range 110−90 K) in EtOH and somewhat more in MP (in the range 100−77 K). The presence of DEA did not greatly change the result, in particular did not gave the azepine **8**, except in a 2% yield in MP.

Discussion

The availability of intramolecular reaction paths for (singlet and triplet) nitrene **4** results in a better chemical yield than that from parent **2**. Analysis of product distribution and of the temperature effect on it, as well as spectroscopic evidence, allow a detailed discussion of the mechanism.

Identification of the Intermediate in a Glassy Matrix and Chemistry of Triplet Nitrene. It is convenient to start the discussion from the experiments in glassy matrix. The spectra shown in Figures 3 and 4 are closely related to those previously reported for triplet phenylnitrene,[4,6] and accordingly the present species is identified as nitrene ^{3}**4**. The spectrum of the nitrene has a minimum in the 250−280 nm region, where the azide has a maximum (see Figure 3b). Due to the efficient photodecomposition of the latter, irradiation for a few minutes at 254 nm leads to its full consumption with negligible further reaction of the primarily formed triplet nitrene (vide infra). Therefore, the spectrum in Figure 3a does not require deduction for unreacted azide and can be regarded as that of the nitrene, free also from other contaminants (see the chemical evidence below). It shows several well-resolved bands. In particular, the lowest energy absorption is further shifted to the red with respect to parent ^{3}**2** (λ_{oo} 560 nm in the present case, ca. 500 experimental,[4] 540 nm calculated[14] in the latter one). The entire spectrum is similar but more intense in the present case, λ_{max} 510 nm (log ϵ 3.3), 339 (3.6), 315 (3.8), 305 (3.9), 231 (4.3) in EtOH, 542 (3.3), 345 (3.72), 307 (4), 236 (4.5) in MP. Actually, the spectrum of ^{3}**4** is nearly identical to that of triplet (2,6-dimethylphenyl)nitrene.[4] Thus, the pyrazole ring, expected to be noncoplanar with the phenyl ring due to steric hindrance,[15a] exerts only a moderate effect and the electronic structure of the present considered nitrene is quite similar to that of parent ^{3}**2**. The spectrum undergoes a modest solvent effect, with a slight red shift in MP with respect to EtOH (compare Figures 3a and 4).

The persistence of the spectrum in the glass and its bleaching upon melting are consistent with what previously observed with parent ^{3}**2**. Heating of the EtOH glass from 90 to 105 K (i.e., below the melting point) induces some modification of both the visible band and of the groups of bands in the 290−400 nm region (see Figure 3c). This is reasonably due either to a temperature-dependent complexation with the nucleophilic solvent (see below) or to a conformational equilibrium.

The chemistry occurring upon melting the glass (the glassy solution softens at ca. 95 K for MP and 120 K for EtOH) is fully compatible with ^{3}**4** being the only species present under these conditions, since all products arise from triplet nitrene, with no significant amount of those arising from singlet nitrene or the deydroazepine **12** (see below). The main reactions are dimerization to yield an azo compound (**9**) as well as intramolecular hydrogen abstraction, here monitored by the formation of products **10** and **11**, the latter arising from oxidation of the former one, and to a minor degree by intermolecular hydrogen abstraction to give the amine **7**. Previous experiments had shown that these products are formed upon triplet-sensitised photodecomposition of azide **5**.[11,12] At 90−100 K in EtOH hydrogen abstraction is largely the minor process, in accordance with the poor radical character of triplet arylnitrenes previously documented for the present nitrene[12] as well as for the general case,[1] although the ratio (**10** + **11**)/**9** is larger in the experiments in MP.

Temperature Dependence of the Reaction. Singlet−Triplet Nitrene Competition. In a fluid solvent, triplet nitrene obviously does not accumulate upon steady state irradiation.

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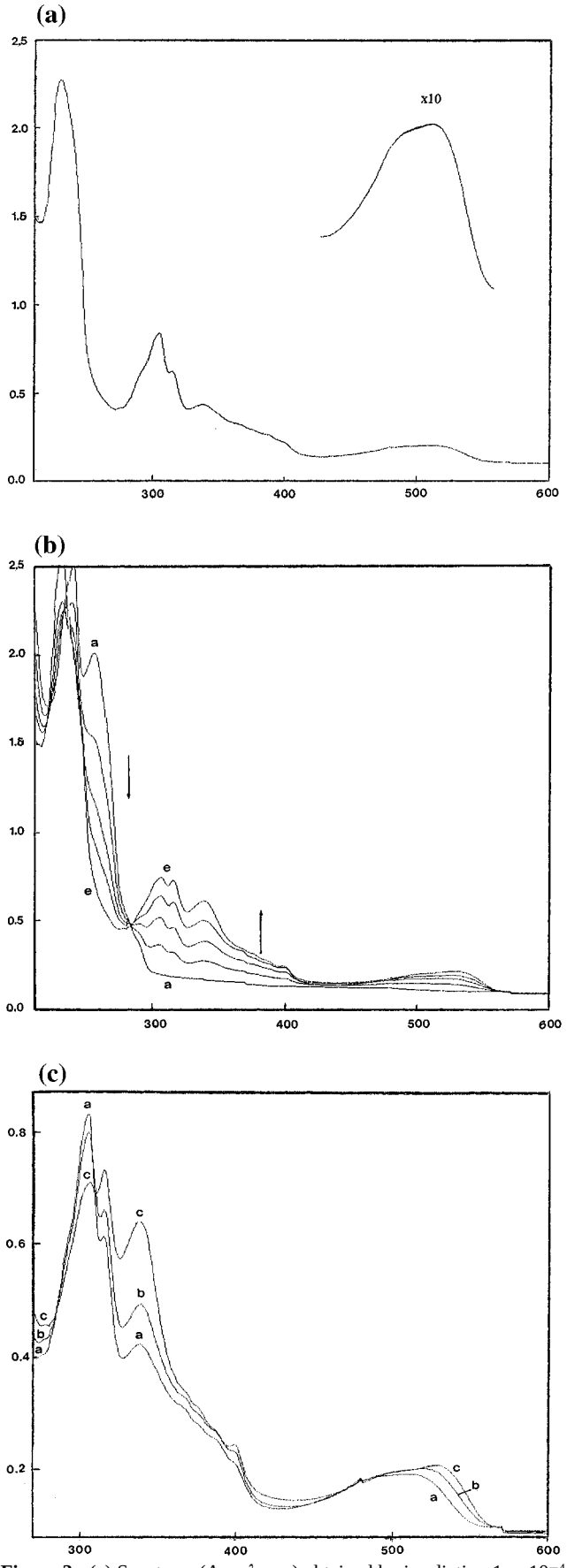


Figure 3. (a) Spectrum (A vs λ, nm) obtained by irradiating 1×10^{-4} M azide **5** in EtOH at 90 K for 8 min. (b) Evolution of the absorption spectrum by irradiation of 1×10^{-4} M azide **5** in EtOH at 100 K. Spectra were registered at 2 min intervals (a, initial spectrum, e spectrum after 8 min). (c) Spectrum obtained by irradiating 1×10^{-4} M azide **5** in EtOH at 90 K for 8 min (a) and spectra observed by heating the solution at 95 (curve b) and 105 K (curve c).

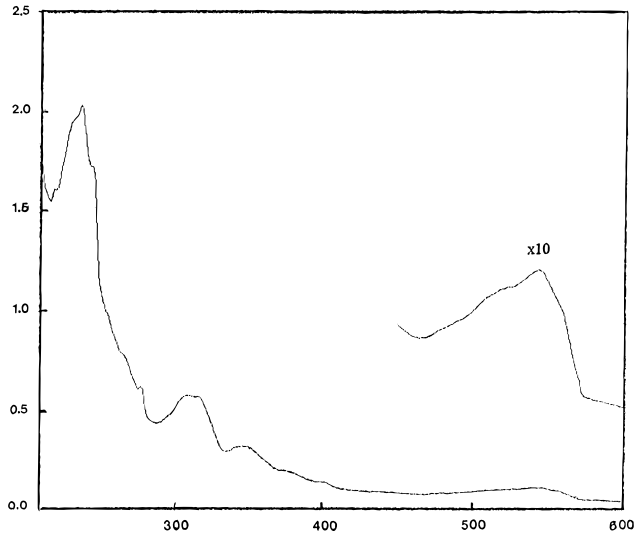


Figure 4. Spectrum (A vs λ, nm) obtained by irradiating 6.15×10^{-5} M azide **5** in MP at 77 K for 8 min.

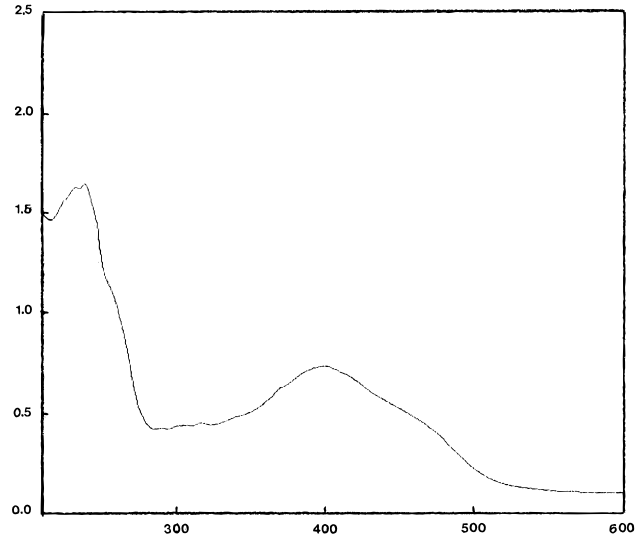


Figure 5. Spectrum (A vs λ, nm) obtained by irradiating an air equilibrated 1×10^{-4} M azide **5** in EtOH at 100 K for 8 min.

Table 4. Products from Double Irradiation Experiments[a]

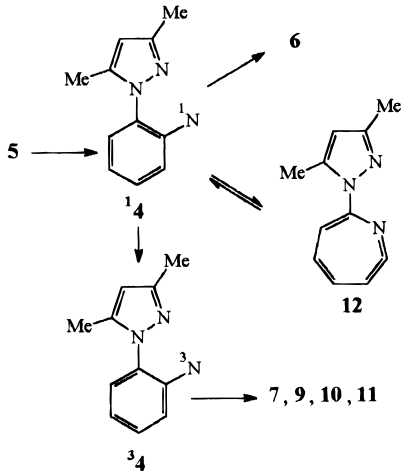
solvent	T/K	**6**	**7**	**8**	**9**	**10 + 11**
EtOH	110	22	3		tr[b]	41
	100	20	5		tr	48
	90	12	6			54
EtOH/0.1 M DEA	100	17	2	tr	tr	20
MP	100	6	10		20	15
	90	tr	5		19	20
	77		2		tr	64
MP/0.1 M DEA	77	2	7	2	2	58

[a] Glassy solutions of azide **5** were first irradiated for 8 min at 254 nm and then for 10 min at $\lambda > 455$ nm. [b] tr = trace.

However, the intermediacy of triplet nitrene is recognized from product distribution[15b] and is significant when a solution of the azide **5** is irradiated at a sufficiently low temperature. Indeed, enhancing the temperature induces a regular decrease of the

(15) (a) Crystallographic analysis on azide **5** shows that the pyrazole is tilted out of the phenyl ring plane; two independent molecules in the cell, torsion angles 65.77 and 83.30°, respectively (B. Bovio, Pavia, personal communication). Molecular model calculation reproduce a similar result both from the azide and the nitrene. (b) The glassy solution softens at a relatively low temperature (95 K for MP and 120 K for EtOH). This makes the observed product distribution significant for the *irradiation temperature*, since the intermediates are directly converted to the final products in the experiments at these temperatures or immediately upon softening of the glass for the few experiments below them.

Scheme 4



triplet-derived products (**7**, **9**−**11**, see Tables 2 and 3, Figures 1 and 2) over the whole range explored. In EtOH, this is accompanied by a regular increase of the singlet nitrene derived product, heterocycle **6**, and the overall yield of identified products remains high and close to constant throughout the range considered, from the glass to room temperature. In MP, on the other hand, the yield of **6** increases more slowly with temperature, and in the 150−230 K range some (two main) further products are formed. These have a molecular weight corresponding to a nitrene dimer. There is previous literature evidence for photoproducts with molecular weights twice that of the nitrene. These are the ring-cleaved products (unsatured iminonitriles) obtained from the photolysis of quinoxalyl[16a] and phenazinyl azides.[16b] These have been rationalized as arising from nitrene−azide addition. Analogy suggests that products of structure **13** should be the products formed under this condition (see the mass spectra in the Experimental Section).

Amine Trapping and Temperature Effect on It. In the presence of DEA the aminoazepine **8** is formed, and the combined yields of **6** + **8** are close to the yield of **6** alone in the absence of DEA (see Figure 1). The temperature dependence of the yield of azepine **8** follows a pattern similar to that seen above for **6**. At a very low temperature (<150 K in EtOH) addition of the amine has little influence on the yield of triplet nitrene derived products; in MP the examination cannot be extended below 160 K due to phase separation. At relatively high temperatures the azepine **8** is formed and is obtained in a larger amount in MP than in EtOH. The yield of the azepine in EtOH decreases more rapidly with decreasing temperature than that of heteropentalene **6**, but the effect is relatively small: the ratio **8**/**6** decreases from 0.6 to 0.14 from 297 to 140 K. The trend is qualitatively similar in the MP/DEA experiments above 160 K, except that, as mentioned above, the **8**/**6** ratio is here much higher (decreasing from 4.2 to 2.7 in the 295−160 K range) and that examination at a lower temperature is precluded by nonmiscibility (see Figure 2).

Mechanistic Scheme. The previous evidence is rationalized through the mechanism depicted in Scheme 4. This is an adapted version of Scheme 1, with the difference that intramolecular trapping of singlet nitrene is also taken into account. As with related phenyl azides, photodecomposition proceeds from singlet excited azide (sensitised experiments give largely different results)[11,12] and its quantum yield does not change with temperature. There is no doubt that singlet nitrene ^{1}**4** is the first-formed intermediate. This had been previously also supported by the demonstration that the same type of chemistry is observed by generating the nitrene both from the azide and from other precursors, as reported both for the present azide (**5**)[17] and for parent **1**.[5] ^{1}**4** is a branching point in the process and has available two irreversible reactions: intramolecular electrophilic cyclization to give **6** and intersystem crossing to give ^{3}**4**. The former process predominates at a high temperature, the latter one below ca. 140 K. A reversible rearrangement between ^{1}**4** and dehydroazepine is also indicated, justifying the fact that, in the presence of DEA, azepine **8** is formed and at all temperatures explored the sum **6** + **8** remains close to the yield of **6** alone in the absence of DEA.

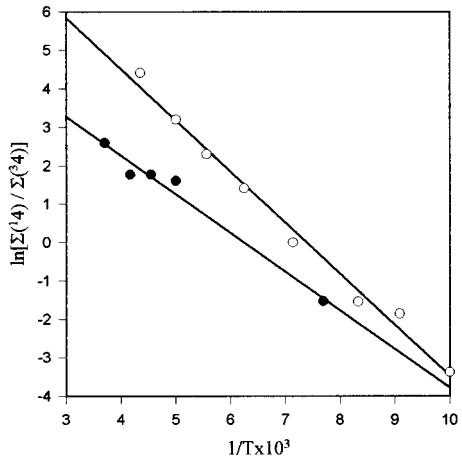


Figure 6. Arrhenius plot for the ratio of the singlet nitrene derived product **6** vs the triplet derived products **7**, **9**, **10**, and **11**, (○) in EtOH, (●) in MP.

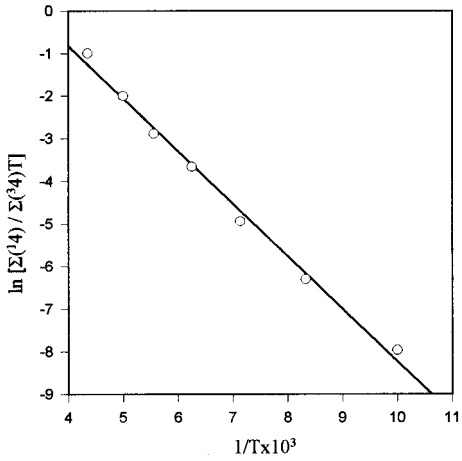


Figure 7. Eyring plot for the ratio of the singlet nitrene derived product **6** vs the triplet derived products **7**, **9**, **10**, and **11** in EtOH.

Differential Thermodynamic Parameters. At least in ethanol, a reasonable material balance is obtained over all the temperature domain explored, 297−90 K. Furthermore, viscosity changes do not affect the result, since unimolecular processes are compared. Thus, differential thermodynamic parameters for the reactions of ^{1}**4** can be obtained. Arrhenius analysis applied to the ratio of the singlet nitrene derived product **6** vs the summation of the triplet-derived products (**7** + **9** + **10** + **11**) gives a linear plot (Figure 6). This yields $\Delta E_a = -10.5 \pm 2$ kJ mol^{-1} for the above competing process. Similarly, Eyring analysis gives $\Delta\Delta H^{\ddagger} = -10 \pm 2$ kJ mol^{-1} and $\Delta\Delta S^{\ddagger} = 34 \pm 3$ J mol^{-1} K^{-1} (Figure 7). Assuming that intersystem crossing has negligible activation enthalpy, the observed quantity (10 kJ mol^{-1}) is directly the activation enthalpy of intramolecular

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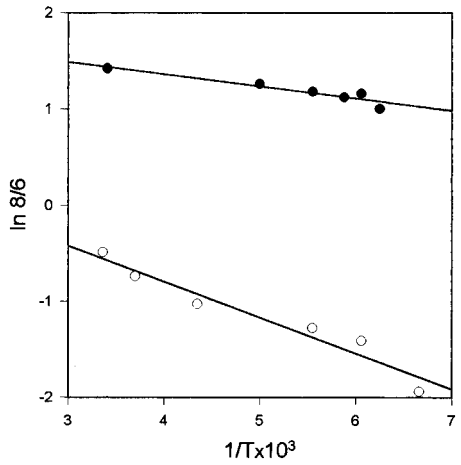

Figure 8. Arrhenius plot for the ratio of the azepine **8** vs the singlet nitrene derived product **6**, (○) in EtOH), (●) in MP.

ring closure to give **6**. As expected, this is small. It compares with the previously estimated activation energy for the singlet phenylnitrene−dehydroazepine rearrangement, 12 ± 4 kJ mol^{-1} (also evaluated as a differential parameter in comparison with intersystem crossing to the triplet), but it refers in this case to a chemical reaction directly from singlet nitrene. This enables determination of the differential entropy, which is favorable to the singlet cyclization. Analysis of the data in MP is less straightforward, since the material balance of isolated products is low in the intermediate temperature range. A rough estimate can be obtained by using the high- and low-temperature points (Figure 6). The slope is somewhat smaller than that in EtOH, with $\Delta E_a \approx -8$ kJ mol^{-1}.

As seen above, the aminoazepine vs heteropentalene ratio depends on the solvent but changes little with the temperature. Figure 8 shows that the two processes encounter very similar barriers, $\Delta E_a = -3$ kJ mol^{-1} in EtOH and -1 kJ mol^{-1} in MP. Thus, intermolecular reaction with a nucleophile encounters a barrier only slightly higher than intramolecular cyclization onto a nucleophilic center.

Detailed Mechanism. The mechanism can now be discussed in more detail, taking also in account the difference between the two solvents explored. Ethanol, as the EPA mixture and methyltetrahydrofuran used in previous studies,[4,5] offers some stabilization to the electrophilic nitrene, whereas this is not possible with MP. As seen above, in EtOH there is a smooth transition in the 140−200 K range between triplet and singlet nitrene chemistry, and a uniformly good material balance is maintained near the turning interval as well as in all the ranges studied. Adding the good nucleophile DEA simply involves partial substitution of the azepine **8** for the singlet nitrene product **6**.

Thus, intersystem crossing from ^{1}**4** to the strongly stabilized triplet state ^{3}**4** (the energy difference between parent singlet and triplet **2** has been recently estimated as ca. 70 kJ mol^{-1};[14,18a,b] previous estimates have given a much lower value, 17 kJ mol^{-1})[18c,d] involves probably negligible activation enthalpy, but it is kinetically disfavored, with a 34 J mol^{-1} K^{-1} difference in the entropic term. There is previous evidence that ISC from ^{1}**2** to ^{3}**2** is relatively slow (10^6−10^7 s^{-1}) due to the large energy gap, spatial differentiation of the singly occupied MOs, and poor contribution from spin−orbit coupling.[1c] The small entropic barrier we measure for **4** is reasonably explained on this basis

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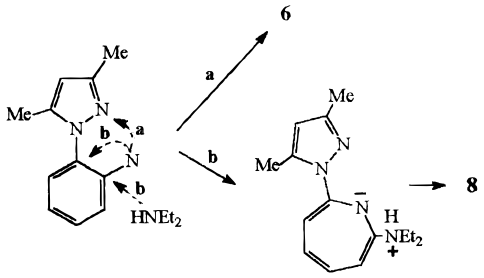
Scheme 5



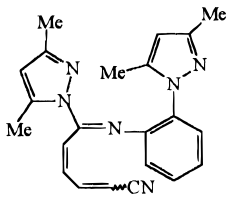
and in view of the similar structure is expected to be very similar to that of parent **2**.

In the present case, two intramolecular processes are compared, cyclization to **6** and ISC to ^{3}**4**. Previous studies had compared ISC with amine addition, supposed to occur with negligible E_a after rate-determining cyclization (again an intramolecular electrophilic attack) to a dehydroazepine[1,4,5] (in our case **12**). The equivalence of the combined **6** + **8** yield to that of **6** alone in the absence of the amine shows that if **12** is an intermediate, it is in equilibrium with ^{1}**4**. The thermodynamic parameters for reactions attributed to the two species are very similar. If cyclization of ^{1}**4** to **12** is the rate-determining step for amine addition, then such a process has $E_a = 3$ kJ mol^{-1}, which is a really low value.

Alternatively, it may be held that the dehydroazepine is not formed as a kinetic distinct intermediate and amine addition occurs concertedly with ring enlargement (see Scheme 5), although there is no precedent for such a mechanism. Notice also that the molecular vibration involved in the conversion of ^{1}**4** to both **6** and **12** (or directly to **8**) is the same, in plane bending of the C−N bond (Scheme 5).

The activation energy measured[4] for amine addition to ^{1}**2** is only slightly larger than that for ^{1}**4**, thus the same mechanism should hold also for the parent phenylnitrene, and also in that case the dehydroazepine is formed reversibly, if at all. Such intermediates are well characterized in a matrix at a low temperature, where they are formed by secondary photoreaction of the primarily formed triplet nitrene. Furthermore, they have been detected at room temperature by flash photolysis with IR detection.[2c] However, the present data suggest that such transients are not necessarily an intermediate on the path to the azepine, or at any rate that no significant minimum is associated to the dehydroazepine configuration in fluid solution.

When generated in MP, singlet nitrene enjoys no solvent stabilization. Such a stabilization is small, however, and no major change intervenes in the mechanism. In particular, the activation energy for cyclization to **6** does not increase (indeed, from the limited data available, its difference from that of ISC to ^{3}**4** rather decreases). However, *intermolecular* reactions are here more important (see below), showing that the advantage for intramolecular attack observed in EtOH is in part due to a weak bond with the slightly nucleophilic solvent which maintains the nitrene in the correct configuration for cyclization but does not compete for nucleophilic addition. In accordance with this, **6** is quantitatively formed at relatively high temperatures (above ca. 220 K). However, the above evidence suggests that below that point even a weak nucleophile such as azide **5** adds (giving **13**). In the presence of DEA the ratio **8**/**6** is much higher than that in EtOH, and trapping continues also below 220 K, where the intramolecular reaction is too slow, until the point is reached where, as in EtOH, ISC to ^{3}**4** takes over. Again Figure 6 shows that ΔE_a for formation of **6** and **8** is minimal, and thus there is no evidence for **12** being a kinetically distinguished intermediate in this temperature range. As for the chemistry of ^{3}**4**, this is little affected by the solvent, in accordance with



13

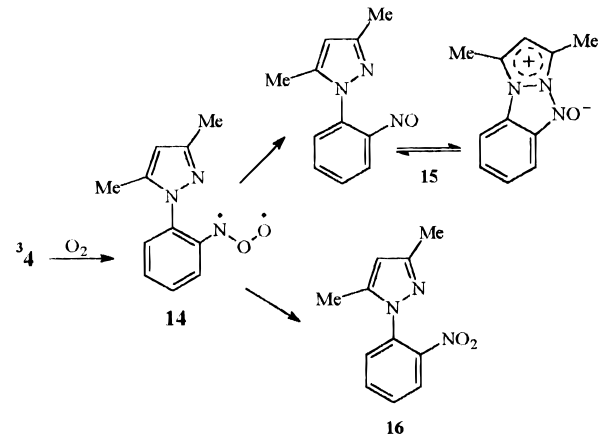
the well-known poor radical character of arylnitrene triplet. Thus hydrogen absorption from the solvent is ineffective over all the temperature ranges where the triplet is the key intermediate.

Reactions of Triplet Nitrene with Oxygen. As pointed out above, triplet nitrene ^{3}**4** is virtually the only product obtained by irradiation of the azide **5** in a glassy matrix. Noteworthy, when degassing is omitted the transient spectrum observed is completely different (compare Figure 5 with Figures 3 and 4). This is reasonably attributed to oxygen addition to the nitrene to yield a diradical or an oxygen-centered radical (see, e.g., formula **14**, see Scheme 6). Similar intermediates have been previously suggested for explaining the formation of nitro, nitroso, and azoxy derivatives from the decomposition of some aromatic and heterocyclic azides in the presence of oxygen.[2c,19,20] Indeed, irradiation in oxygen-equilibrated MP gave some nitroso derivative (**15**) with a minor amount of nitro compound **16**, along with products **10** and **11**, while only **6** is formed at room temperature (see Table 2). This shows that singlet nitrene is unaffected by oxygen, while the triplet adds to it, and the nitroso derivative is formed under this condition in place of the azo compound. On the other hand, a complete temperature-dependence study in the presence of oxygen was discouraged by the previously observed sensitivity of compound **6** to radicals and various oxidative conditions,[13] which would have made it difficult to obtain clear-cut conclusions.

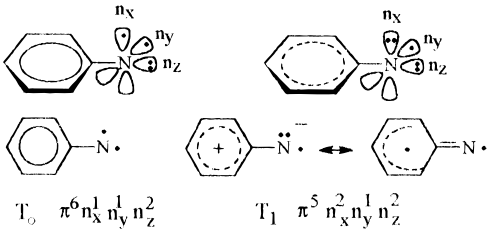
Photochemistry of the Triplet Nitrene. As mentioned above, the spectrum of ^{3}**4** (see Figures 3 and 4) is rather close to that of parent ^{3}**2**, and the electronic structures of the two species are similar, since the noncoplanar pyrazole ring has only a marginal effect. In particular, we observe a low-intensity, long-wavelength band above 500 nm. A similar (somewhat blue shifted) band of ^{3}**2** has been observed by Leyva et al. and attributed to an nπ* or πn transition.[4] Detailed calculations by Kim et al. showed that the T_1 state results from the promotion of an electron from the highest lying π orbital to the n_x orbital (see Scheme 7), with a predicted adiabatic energy of 18 600 cm^{-1} (539 nm).[14] This state is considerably puckered.

Visible irradiation of triplet nitrene in MP at 77 K caused conversion of the main part of the nitrene to products **10** and **11**, rather than to the azo compound obtained by thermal dimerization of the nitrene (see Table 4). However, at a higher temperature (90 or 100 K) more of the azo and, in the latter case, also some of the cyclization product **6** were obtained. As for the EtOH glass, irradiation of ^{3}**4** in the 90−110 K range gave none of the azo compound and a ca. 1 to 2 proportion of compounds **6** and **10** + **11**. Electronic excitation as shown in Scheme 7 is expected to increase the radical character of the nitrene which would now be more similar to an iminyl radical. In the noncomplexing MP intramolecular radical hydrogen abstraction to give **10** and **11** is the exclusive process at 77 K, while at a higher temperature, where the glass is less rigid, nitrene dimerization to give **9** and, to a small extent, electrocyclic cyclization to **6** are also observed. In EtOH, some interaction with the solvent occurs; the reaction is not very temperature-dependent and, although intramolecular radical attack remains predominant, 12−22% cyclization to **6** occurs. On the other hand, very little (≤2%) azepine **8** is obtained by irradiation in the glass in the presence of DEA in both solvents, although the yield of **10** + **11** decreases. In contrast, some azepine has been obtained from triplet phenyl azide.[4,7] Thus, photoconversion of ^{3}**4** to **12** is unimportant, or at least is slower than the other reactions of ^{3}**4*** under the present conditions. Obviously, intramolecular radical attack (to give **10** and **11**) is possible only with the present nitrene, not with ^{3}**2**, but this reaction at least shows that ring enlargement occurs with a relatively low rate from the excited nitrene triplet and that the iminyl radical character of this species is revealed when a suitable model is chosen.

Scheme 6



Scheme 7



Conclusion. The discussion above has shown that the structure of the nitrene **4** is similar to that of parent **2**. Therefore the conclusion presented here should be significant for phenylnitrene and its simple derivatives. With respect to what was previously known in the literature, this work documents directly the competition between an electrophilic reaction of singlet nitrene and intersystem crossing and shows that the former has a differential activation enthalpy 10 kJ mol^{-1} lower than the latter one, but is favored from the entropic point of view. It is further recognized that a dehydroazepine is either not a kinetically distinguished isomer or is in equilibrium with singlet nitrene. It has been previously suggested that the lack of *intermolecular* electrophilic reactions of singlet phenylnitrene (as compared, for example, with the carbene) is due to the fast (10−100 ps at room temperature) ring enlargement.[1c] It is now shown that intramolecular electrophilic reaction is fast when there is a convenient nucleophilic group, and on the other hand, amine addition seems not to necessarily require previous rearrangement (and indeed it appears difficult to prove participation of a dehydroazepine in a fluid solution, since the involved reactions are too fast). It may be that azepines arise via attack to the C atom α to the nitrene function by a nucleophile. Thus the difference between singlet nitrene and carbene may be due to an intrinsic difference of the rates of reaction with various nucleophiles, which are significant with the latter species only with polar nucleophiles. As for triplet nitrene, this is strongly

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stabilized with respect to the carbene and shows a poor radical reactivity, even in the intramolecular case.

A further part of this study takes advantage of the fact that triplet nitrene is obtained in a clean way in a glassy solution. This allows the study of the secondary photochemistry of this species and reveals that its excited state behaves as an electrophilic radical.

Experimental Section

General. ^{1}H NMR spectra were run on a Brucker 300 instrument, IR spectra on a Perkin-Elmer Paragon 1000 spectrophotometer, UV−visible spectra on a Kontron Uvikon 941 spectrophotometer, and mass spectra on a Finnigan LCQ instrument. Methylpentane and 95% ethanol were spectroscopic grade solvents and used without further purification. Column chromatography was performed with silica gel Merk HR 60. Compounds **5**, **6**, **7**, **9**, and **10** were prepared as previously reported.[17]

2-(3,5-Dimethylpyrazolyl)-7-(diethylamino)-2*H*-azepine (8). Anhydrous cyclohexane (300 mL) in an immersion well irradiation apparatus was refluxed and cooled under argon. Azide **5** (300 mg, 4.66×10^{-3} M) and diethylamine (1.9 mL , 6×10^{-2} M) were added and after a further 15 min of Ar flushing the solution was irradiated by means of a 15 W low-pressure mercury arc while maintaining an Ar stream. After 30 min the solvent was evaporated under reduced pressure and the residue chromatographed on a silica gel column eluting with a 7:3 cyclohexane−ethyl acetate mixture to give 135 mg (51%) yield of the title compound, mp 55−56 °C (*n*-hexane); IR (Nujol) 1560, 1508 cm^{-1}; UV (MeCN) λ 301 nm (log ϵ 3.89), 268 (sh, 3.75); ^{1}H NMR δ 0.87 (t, 6H, J = 7 Hz), 2.15 (s, 3H), 2.25 (s, 3H), 2.87 (m, 2H), 3.20 (m, 2H), 4.02 (dd, 1H, J = 6.5, 1 Hz, H-2), 5.87 (s, 1H), 5.88 (ddt, 1H, J = 7.5, 5.5, 1 Hz, H-5), 6.27 (dd, 1H, J = 9, 6.5 Hz, H-3), 6.46 (ddt, 1H, J = 9, 5.5, 1 Hz, H-4), 7.25 (dt, 1H, J = 7.5, 1 Hz, H-6).

2-Methyl-4,5-dihydropyrazolo[5,4-*a*]quinoxaline (11). A solution of compound **10** (37 mg, 0.2 mmol) in 10 mL of ethanol containing 1 mg of Pd/C was hydrogenated at room temperature and pressure until 1 equiv of hydrogen was adsorbed. The mixture was separated on a silica gel column eluting with a benzene−ethyl acetate 9:1 mixture under argon to afford the title compound (15 mg) as well as some amine **7** and unreacted **10**. **11**: oil which solidifies on treating with *n*-hexane, mp 69−70 °C; IR (Nujol) 3235 cm^{-1}; UV (MeCN) λ 317 (log ϵ 3.68), 267 (3.66); ^{1}H NMR δ 2.35 (s, 3H), 3.9 (s, 1H, NH), 4.5 (s, 2H), 5.92 (s, 1H), 6.7 (dd, 1H, J = 1.5, 7 Hz, H-6), 6.85 (dt, 1H, J = 1.5, 7 Hz, H-8), 6.98 (dt, 1H, J = 1.5, 7 Hz, H-7), 7.27 (s, 1H, H-3), 7.76 (dd, 1H, J = 1.5, 7 Hz, H-9).

Variable Temperature Irradiation. A 1×10^{-4} M solution of azide **5** in EtOH (2 mL) in a 1 cm optical path spectrophotometric quartz cell with a quartz to glass graded seal was degassed by means of four freeze−degas−thaw cycles and sealed. This was inserted into an Oxford DN 1704 liquid nitrogen cryostat fitted with a calibrated ITC4 temperature controller and placed in a UV−vis Kontron Uvikon 941 spectrophotometer. The cell was irradiated from the bottom by means of a bifilar low-pressury mercury arc inserted below the cell (Helios Italquartz 15 W). Irradiation was discontinued when taking the spectra. 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 solution was allowed to reach room temperature (within 30 min). 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 Supelcosil LC-ABZ column (and a Supelguard LC-ABZ precolumn). The eluant was a MeCN−water 1:1 mixture and the flux was 0.5 mL/min. The analyzing wavelength was 290 nm, and the spectra of every peak were routinely measured in the range 200−400 nm. All of the main peaks corresponded to compounds isolated form preparative irradiations, and the analysis was based on a comparison with authentic samples of the photoproducts prepared as above (**5**, t_R 14.8 min; **6**, t_R 11.7 min; **7**, t_R 10.4 min; **8**, t_R 18.4 min; **9**, t_R 23.4 min; **10**, t_R 12.8 min; **11**, t_R 12.3 min). The results are shown in Table 2 and Figure 1.

It is important to note that in this instrumental setting not all the contents of the cell was illuminated. Therefore, analysis at the end of the irradiation time showed the presence of some residual azide (ca. 10%) even if the UV spectrum of the irradiated sample showed complete consumption of this compound.

The experiments in MP were analogously carried out using 6.15×10^{-5} M solutions (Table 3, Figure 2).

The softening and melting temperatures of the solutions were determined in parallel cryoscopic experiments. In this way it was checked that the glass softens at ca. 95 K for the MP frozen solution and at ca. 120 K for the EtOH frozen solution.

Double Irradiation Experiments. Samples irradiated as above were further irradiated by means of a focalized high-pressure mercury arc (Osram 150 W) through a cutoff filter (λ_{tr} > 455 nm). The beam reached the cell through a side opening perpendicular to the analyzing beam.

HPLC MS Measurements. HPLC examination of the photolysate in MP at a temperature in the range 230−150 K range showed the presence of some peaks different form those reported above. HPLC MS analysis for those peaks (t_R 7.4 min, t_R 8.6 min) showed an identical mass fragmentation pattern [chemical ionization, *m/z* 371 ($M^+ + 1$), 275, 198] which was consistent with the structure of isomeric unsatured imino nitriles **13** (loss of pyrazole, 96, and of the unsaturated chain, 78).

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