Photolysis of Ortho-Substituted Aryl Azides in Diethylamine. Formation and Autoxidation of 2-Diethylamino-1*H*-azepine Intermediates[1]

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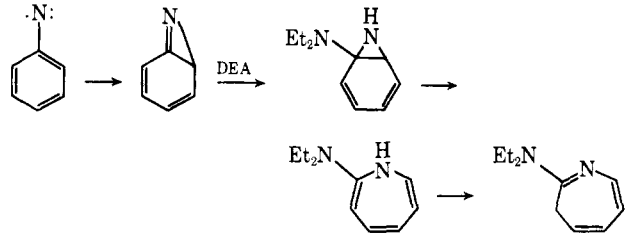
Abstract: Photolysis of ten ortho-substituted aryl azides in diethylamine (DEA) has been shown to lead mainly to oxygen-sensitive metastable intermediates, rather than directly to the 2-diethylamino-3*H*-azepines which are commonly obtained from such photolyses. The oxidation products of the intermediates have been identified as 3-alkyl-2-diethylaminopyridines, 5-acyl-3-alkyl-2-diethylaminopyridines, and 6-alkyl-7-diethylamino-2*H*-azepin-2-ones. When oxygenation is carried out in the presence of cupric ion 6-alkyl-7-diethylamino-4*H*-azepin-4-ones are also formed in some cases. Nmr spectral data indicate that the oxygen-sensitive intermediates are 3-alkyl-2-diethylamino-1*H*-azepines and this structural assignment permits mechanistic interpretation of the oxidation process. Phenyl azide and *p*-tolyl azide, which lack ortho substituents, give no evidence that analogous 1*H*-azepines have appreciable lifetimes under the conditions of the photolysis, although they may exist as short-lived intermediates. An azide bearing an *o*-mesityl substituent, 2-azido-2′,4,4′-6′-tetramethylbiphenyl, behaves in an anomalous fashion giving a 4*H*-azepine, 7-diethylamino-3-methyl-6-(2,4,6-trimethylphenyl)-4*H*-azepine, as the primary product. Six of the seven azides studied which bear only a single ortho substituent are found to undergo ring expansion only in the direction of migration of the unsubstituted ortho carbon atoms.

Phenyl azide undergoes a ring expanison when it is decomposed thermally[2] or photolytically[3] in primary or secondary amines to give 2-alkylamino-3*H*-azepines. The process is quite efficient with yields of up to 70% of 2-diethylamino-3*H*-azepine being formed when phenyl azide is photolyzed to about 50% completion in diethylamine (DEA).[4] The mechanism of the ring expansion has been proposed to involve formation and subsequent intramolecular cyclization of phenylnitrene followed by reaction with the amine.[2,5] It has been suggested that the 2-alkylamino-1*H*-azepine tautomer is probably an intermediate in the process.[5] The ring expansion reaction has come to be used as a



mechanistic tool indicating the involvement of phenyl nitrene as an intermediate.[6] This paper describes the photolysis of several 2-substituted aryl azides in DEA. The results establish the existence of a metastable intermediate. The reactivity of the intermediate toward oxygen and its probable structure are discussed.

(1) Partial support from a NIH Biomedical Support Subgrant is gratefully acknowledged.

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

(3) W. von E. Doering and R. A. Odum, *Tetrahedron*, **22**, 81 (1966).

(4) R. J. Sundberg, M. Brenner, S. R. Suter, and B. P. Das, *Tetrahedron Lett.*, 2715 (1970).

(5) G. Maier, *Angew. Chem. Int. Ed. Engl.*, **6**, 402 (1967).

(6) (a) V. Snieckus and G. Kan, *Chem. Commun.*, 172 (1970); (b) C. Wintner, *Tetrahedron Lett.*, 2275 (1970); (c) R. J. Sundberg, B. P. Das, and R. H. Smith, Jr., *J. Amer. Chem. Soc.*, **91**, 658 (1969); (d) J. I. G. Cadogan and M. J. Todd, *J. Chem. Soc. C*, 2808 (1969); (e) J. S. Splitter and M. Calvin, *Tetrahedron Lett.*, 1445 (1968); (f) R.A. Odum and M. Brenner, *J. Amer. Chem. Soc.*, **88**, 2074 (1966); (g) E. Meyer and G. W. Griffin, *Angew. Chem.*, **79**, 648 (1967); (h) M. A. Berwick, *J. Amer. Chem. Soc.*, **93**, 5780 (1971).

Results

Photolysis of azides **1b–1g** in DEA followed by evaporation of the reaction mixture using a rotary evaporator and chromatography on silicic acid gave mixtures of compounds **3b–3g**, **4b–4g**, and **5b–5g**, which could be resolved by preparative glpc. Spectral data, particularly the distinctive nmr spectra of the azepines **4b–4g** and pyridines **5b–5g**, summarized in Table I, permitted structural assignment. The 2-diethylamino-3-methylpyridine, **5b**, formed by photolysis of **1b** was further identified by comparison with an authentic sample prepared by alkylation[7] of 2-amino-3-methylpyridine. The yields of pyridines **5b–5g** obtained by this procedure were variable but were typically in the range 2–6% based on starting azide. The structures of the pyridines revealed that the 4-carbon atom of the starting azide is extruded in the formation of the pyridines. Thus the azides **1d** and **1g**, which have 4-methyl substituents, are converted to the same pyridines as **1b** and **1f**, respectively, in which the 4 position is unsubstituted. On the other hand, methyl groups at C-2 (**1b–1g**), C-3 (**1c**), C-5 (**1e**), and C-6 (**1f**, **1g**) are retained in the isolated pyridines.

It was established that the 3*H*-azepines **4** are not precursors of the 2-diethylaminopyridines **5** by photolyzing *o*-ethylphenyl azide, **1i**, in the presence of 2-diethylamino-3-methyl-3*H*-azepine, **4b**. Under these conditions, 2-diethylamino-3-ethylpyridine was formed but 2-diethylamino-3-methylpyridine was not, as determined by glpc analysis. This experiment also indicated that formation of the pyridine involved atmospheric oxidation of a precursor of the 3*H*-azepine. Immediately after the photolysis, glpc analysis of the reaction solution indicated approximately equal amounts of **4b** and **4i**, small amounts of **5i** and no **5b**. After brief exposure to the atmosphere the relative amount of **4i** decreased significantly while **5i** increased.

(7) A. R. Lepley, A. G. Guimanini, A. B. Guimanini, and W. A. Khan, *J. Org. Chem.*, **31**, 2051 (1966).

Table I. Nmr Spectral Data[a,b]

	R_2	R_3	R_4	R_5	R_6	H_3'[c]
			2-Diethylamino-3*H*-azepines			
4b	*0.68* (7)	5.18 (7, 8)	6.25 (6, 9)	5.58 (6, 8)	7.06 (8)	4.18
4c	*0.71* (7)	*1.90*	6.02 (6)	5.48 (6, 8)	6.93 (8)	3.85
4d	*0.75* (7)	4.95 (8)	*1.87*	5.45 (8)	6.92 (8)	~3.8
4e	*0.72* (7)	5.17 (9, 9)	6.10 (9)	*1.92*	6.91	4.00
4f	*0.68* (7)	5.16 (9, 9)	6.30 (9, 6)	5.63 (6)	*2.08*	4.20
4g	*0.70* (7)	4.88 (8)		5.42		~3.6
4h	2.60	4.90 (7)	*1.90*	5.63 (8)	7.01 (8)	2.60
4i		5.28 (9, 9)	6.36 (9, 7)	5.64 (6, 8)	7.11 (6)	4.00
4j		5.10 (9, 9)	6.30 (9, 6)	5.56 (6, 8)	7.05 (8)	~3.8[f]
4ka	*0.72* (7)	5.04 (8, 7)	6.19 (6, 9)	5.54 (6)		~4.0
4kb		4.98 (8, 7)	6.16 (6, 8)	5.46 (6)	*2.06*	~4.0
			2-Diethylaminopyridines			
5b	*2.30*	7.50 (7, 2)		6.90 (7, 5)	8.31 (5, 2)	
5c	*2.25*	*2.25*		6.75 (5)	8.11 (5)	
5d[d]						
5e	*2.26*	7.29 (2)		*2.26*	8.06 (2)	
5f	*2.20*	7.25 (7)		6.62 (7)	*2.42*	
5g[e]						
5i		7.53 (7, 2)		6.93 (7, 5)	8.29 (5, 2)	
5j		7.53 (2, 8)		6.95 (8, 5)	8.21 (5, 2)	
5l		*f*		6.75 (7, 5)	8.11 (5, 2)	
			2-Diethylamino-5-acylpyridines			
6b	*2.35*	7.80 (2)	9.87		8.50 (2)	
6c	*2.19*	*2.57*	9.99		8.39	
6d	*2.32*	7.90 (2)	*2.52*		8.70 (2)	
6f[g]	*2.30*	7.70	10.20		*2.70*	
6g	*2.24*	7.62	*2.48*		*2.62*	
6i		7.85 (2)	9.81		8.46 (2)	
6j		8.02 (2)	9.95		8.59 (2)	
6l		7.75 (2)	9.82		8.53 (2)	
			7-Diethylamino-2*H*-azepin-2-ones			
7a	6.70	6.70	6.70	6.70		
7b	2.19	6.52	6.52	6.52		
7c[h]	*1.60*	*1.60*	6.50 (12)	6.01 (12)		
7d	*2.00* (?)	6.42	*2.18* (?)	6.42		
7e	*2.10* (?)	6.20 (6)	6.45 (6)	*2.15* (?)		
7h	6.60	6.60	*2.05*	6.41		
7i		6.49	6.49	6.49		
7j		6.47	6·47	6.47		
7l[h]		6.17 (6)	5·92 (10, 6)	6.57 (10)		
			7-Diethylamino-4*H*-azepin-4-ones			
8i		6.83 (3)		5.80 (8, 3)	7.51 (8)	
8j		6.48 (2)		5.47 (8, 2)	7.25 (8)	

[a] In $CDCl_3$ unless otherwise noted. [b] Position numbering is that used in Scheme I. Methyl signals are shown as italic numbers. Coupling constants in hertz are given in parentheses. [c] Signal of the ring C-3 proton(s). [d] Same as **5b**. [e] Same as **5f**. [f] Obscured by other signals [g] Compound not isolated in pure form. Values quoted are from mixtures containing the compound. [h] In benzene-d_6.

There was no decrease in the relative amount of **4b** and no **5b** was formed. Since authentic **4i** can be exposed to the atmosphere for extended periods without formation of **5i**, it follows that the glpc peak at the retention time characteristic of **4i** which is present immediately after photolysis must actually be due to a substance which is converted to **4i** under the conditions of the glpc analysis and also by the standard product isolation procedure.

The conclusion that the photolyzed solutions, in general, contained mainly a readily oxidized precursor of **4**, rather than **4** itself, was verified by passing air or oxygen through solutions resulting from photolysis of **1b**, **1c**, **1i**, and **1j**. Before exposure to oxygen glpc analysis showed large peaks at the retention time corresponding to **4b**, **4c**, **4i** and **4j**, respectively. From 80 to 95% reduction in these peaks followed exposure of such solutions to oxygen and formation of the appropriate pyridine **5** was noted.

Table II. Yields of Oxidation Product[a]

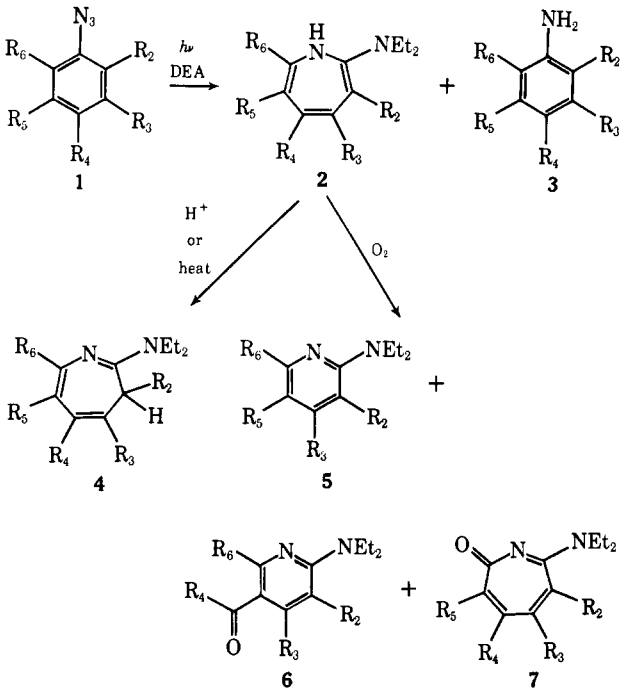
Starting azide	Yields (%)				
	3	**5**	**6**	**7**	**8**
1b	13	20	6	31	*b*
(Cu II added)	10	4	5	22	*b*
1c	12	13	6	36	*b*
1d	35	2	4	11	*b*
1e	15	3	*b*	20	*b*
1f	23	8	7[c]	*b*	*b*
1g	29	3	8	*b*	*b*
1i	12	14	2	18	*b*
(Cu II added)	13	4	2	2	4
1j	11	8	4	8	*b*
(Cu II added)	11	2	3	10	13
11[d]	5	4	1[c]	17	*b*

[a] Based on starting azide. [b] Not isolated or identified, yield less than 2%. [c] Identified by spectral data but complete purification not effected. [d] Carbazole (23%) and 3-phenyl-2-diethylamino-3*H*-azepine (17%) also isolated.

The product mixtures from such oxidations were complex. In addition to the 2-diethylaminopyridines (**5**), 5-acyl-2-diethylaminopyridines (**6**) and 7-diethylamino-2*H*-azepin-2-ones (**7**) were generally present. Table II summarizes yield data for these oxidation products as determined by isolation after column chromatography.

Spectral data permitted assignment of structures to **6i** and **7i** and the spectral data obtained for the various other analogs support these assignments. The molecular formula of **6i** was verified by elemental analysis and mass spectrometry. The presence of an aldehyde group was indicated by a sharp 1-proton singlet at δ 9.87 and by a strong carbonyl band at 1685 cm^{-1}. A meta relationship for the two aromatic hydrogens at δ 7.85 and 8.47 followed from their mutual coupling of about 2 Hz. The peak positions and multiplicities of the aromatic signals in the aldehydes **6b**, **6c**, **6f**, **6j**, and **6l** are mutually consistent with the structural assignments defined by Scheme I.

Scheme I

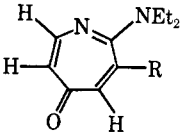


	R_2	R_3	R_4	R_5	R_6
a	H	H	H	H	H
b	CH_3	H	H	H	H
c	CH_3	CH_3	H	H	H
d	CH_3	H	CH_3	H	H
e	CH_3	H	H	CH_3	H
f	CH_3	H	H	H	CH_3
g	CH_3	H	CH_3	H	CH_3
h	H	H	CH_3	H	H
i	C_2H_5	H	H	H	H
j	*i*-C_3H_7	H	H	H	H
k	*i*-C_3H_7	H	H	H	CH_3
l	C_6H_5	H	H	H	H

The 4-methyl azides **1d** and **1g** gave methyl ketones **6d** and **6g**, respectively. The nmr spectrum of **6d** showed two methyl signals and two aromatic signals, the latter signals being coupled with a coupling constant of 2 Hz. Ketone **6g** showed a single unsplit aromatic proton at a chemical shift consistent with the proton being located on C-4.

The molecular formula of compound **7i** was established by mass spectrometry and elemental analysis. The infrared showed strong bands at 1630, 1575, and 1540 cm^{-1}. The latter two are characteristic of the amidine group in 3*H*-azepines while the former band suggested the presence of a highly conjugated carbonyl. The *C*-ethyl and *N*-ethyl groups were evident in the nmr. The only other signal in $CDCl_3$ was a 3-proton singlet at δ 6.49, indicating that no pyridine ring was present. This signal appeared as two multiplets in benzene, making it clear that the singlet in $CDCl_3$ is the result of an accidental chemical shift coincidence, rather than three chemically equivalent protons. Although not completely definitive, the nmr suggests the 2*H*-azepin-2-one (**7**) formulation in preference to any of the other possible isomeric azepinones since all other isomers would be expected to have one downfield vinyl proton due to the proton adjacent to nitrogen at the 7-(2-) position. The nmr spectra of **7c**, **7e**, and **7l** reported in Table I confirm the structural assignment. The two vinyl protons of **7c** show a mutual coupling of 12 Hz in agreement with these protons being located on adjacent doubly bound carbon atoms. The two vinyl protons in **7e** are coupled with a coupling constant of 6 Hz indicating that the protons are located on adjacent singly bound carbon atoms. The three vinyl protons of **7l** are sufficiently resolved that couplings are readily identified and establish that the three protons are on adjacent carbon atoms.

Cupric halides have been shown to have a catalytic effect on enamine oxidations.[8,9] Photolyzed solutions of **1b**, **1i**, and **1j** were oxygenated in the presence of small amounts of cupric ion to determine if this would effect the yield or structure of the oxidation products. The amounts of compounds **5b**, **5i**, and **5j** found were reduced and in the case of **1i** and **1j** new oxidation products, **8i** and **8j**, respectively, were isolated. Com-



8i, R = C_2H_5
8j, R = *i*-C_3H_7

pound **8i** showed strong bands at 1505, 1580, and 1630 cm^{-1} in the infrared. The three vinyl protons of **8i** appeared as a doublet, J = 8 Hz, a doublet J = 3 Hz and a doublet of doublets J = 8,3 Hz. Assuming that an amidine linkage is present in this compound, the nmr leads to the assignment of the 7-diethylamino-6-alkyl-4*H*-azepin-4-one structures, **8i** and **8j**.

Attempts to isolate the oxidizable intermediate failed. Removal of the DEA led to mixtures containing primarily the stable 3*H*-azepines **4**. However, when the photolyzed solutions were concentrated by evaporation under a stream of nitrogen, the vinyl proton region could be examined by nmr without interference from the remaining DEA. Figure 1 shows the spectra obtained in the region δ 5–6 for **1e**, **1g**, and **1j**. The significance of these spectra for assignment of structures to the oxidizable intermediate is considered in the discussion section. Addition of small amounts of acetic acid dissolved in DEA to these samples resulted

(8) V. Van Rheenen, *Chem. Commun.*, 314 (1969).
(9) S. K. Malhotra, J. J. Hostynek, and A. F. Lundin, *J. Amer. Chem. Soc.*, **90**, 6565 (1968); J. K. Kochi and E. A. Singleton, *Tetrahedron*, **24**, 4649 (1968).

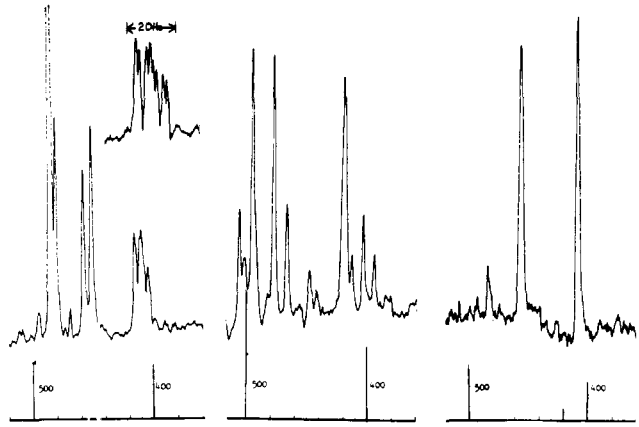


Figure 1. 100-MHz nmr spectra of photolyzed solutions of **1j** (left), **1e** (center), and **1g** (right) from 360 to 520 Hz downfield from the methyl triplet of DEA.

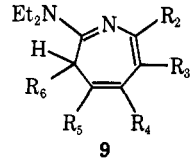
in the development of signals characteristic of the corresponding 3*H*-azepines **4**. Attempts to obtain similar spectra using **1b** and **1c** gave spectra dominated by the 3*H*-azepines **4b** and **4c**, respectively.

The formation of oxidized products was avoided by refluxing the photolyzed reaction mixtures with methanol prior to exposure to oxygen. The isolated yields of 3*H*-azepines found from several of the azides under these conditions are recorded in Table III. In the case

Table III. Product Yields after Methanol Reflux

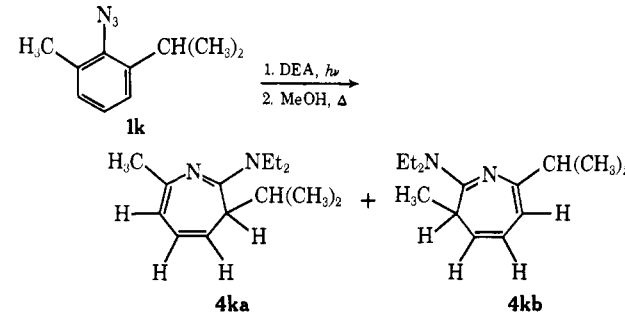
Azide	3	4
1b	~10	67
1d	30	28
1e	18	46
1g	34	33
1i	~10	56
1j	~10	65
1k	16	45

of **1b**, **1e**, **1i**, and **1j** only a single azepine was detected. None of the isomeric azepines represented by the general structure **9** was detected.



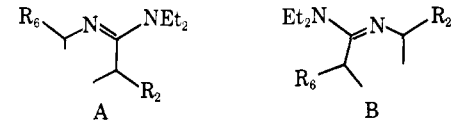
9

This high structural specificity has been noted previously in our laboratory and by Odum for **1b**.[6c,10] Similarly, thermal[11] or photochemical[6c] deoxygenation of *o*-nitrotoluene in the presence of DEA gives only **4b**. The 2,6-disubstituted azides **1g** and **1k** gave yields of 3*H*-azepines not greatly reduced from those observed for **1b**, **1e**, **1i**, and **1j**. The azepine mixture from **1k** consisted of nearly equal amounts of the two possible isomers **4ka** and **4kb** as determined by glpc and nmr



1k **4ka** **4kb**

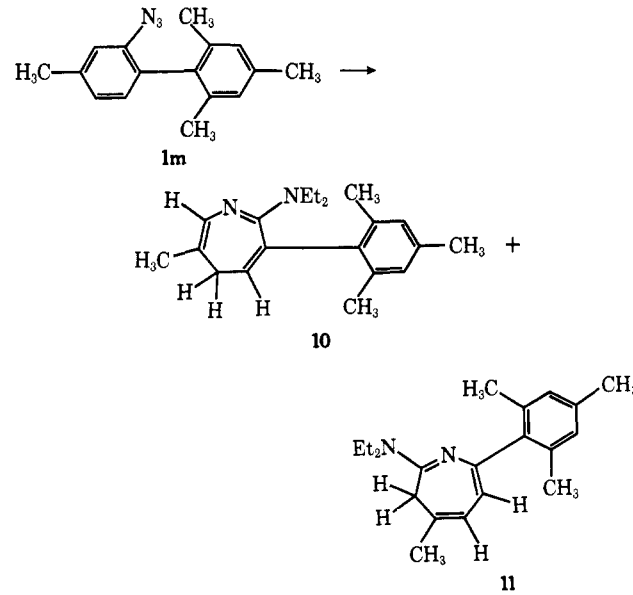
data. All of the oxidation products which were characterized from the various azides also contain only the structural unit A, to the exclusion of structural unit B.



A B

Photolyzed solutions of phenyl azide and *p*-tolyl azide gave no evidence for an oxidizable intermediate at the end of photolysis. The peak present in the glpc trace immediately after photolysis was not diminished by exposure to oxygen. The vinyl proton regions of the nmr spectra of a concentrated solution of the photolyzed reaction mixture showed only peaks attributable to the 3*H*-azepines **4a** and **4h**, respectively. Photolysis of *p*-tolyl azide in DEA in an atmosphere of oxygen followed by the chromatographic work-up used for isolation of the various oxidation products gave no detectable pyridine derivatives but an 8% yield of the azepinone **7h** was obtained. The azepine **4h** was isolated after chromatography and distillation in 16% yield. Photolysis of phenyl azide in DEA under an oxygen atmosphere gave no detectable amounts of pyridines but the azepinone **7a** was isolated in 2% yield. The azepine **4a** was isolated in 22% yield. The photolysis of *o*-ethylphenyl azide under similar conditions gave the pyridine **5i** in 5% yield and **4i** in 1 ± 0.5% yield by glpc analysis.

2-Mesityl-5-methylphenyl azide (**1m**) also showed no evidence of an oxidizable intermediate. The product



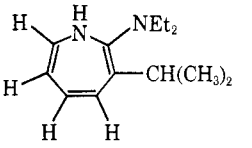
1m **10** **11**

(10) R. A. Odum, private communication.
(11) J. I. G. Cadogan and R. K. Mackie, *J. Chem. Soc.*, 2819 (1969).

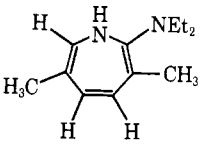
in this case, however, was, mainly the 4*H*-azepine **10** along with small amounts of **11**. Compound **10** showed a signal at δ 5.70 as a triplet, J = 7 Hz, and a signal at δ 6.59 Hz with partially resolved allylic coupling to a methyl group. Trace amounts of a phenyl analog of **10**, 7-diethylamino-6-phenyl-4*H*-azepine, were encountered in previous work with *o*-biphenyl azide.[4] The 3*H*-azepine **11** showed the two hydrogens at C-3 as a broad singlet at δ 2.76 and the vinyl protons as a doublet at δ 5.52 (J = 6 Hz) and a doublet (J = 6 Hz) with incompletely resolved allylic coupling at δ 6.08. The azepine **11** is the first exception to the previously noted tendency for ring expansion involving migration of the less substituted ortho carbon. The 4*H*-azepine **10** underwent thermal rearrangement to 3-amino-2-diethylamino-2′,4′,4,6′-tetramethylbiphenyl on heating under nitrogen at 160° or under the conditions of preparative glpc.

Discussion

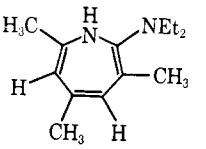
The data reported in the Results section indicate that when aryl azides bearing *o*-alkyl substituents are photolyzed in DEA, 3-alkyl-2-diethylamino-3*H*-azepines are not the major initial reaction products. Instead, the azepines are formed *via* intermediates which have the property of being rapidly destroyed by oxygen. The products of such oxidations contain most or all of the carbon skeleton found in the 2-diethylamino-3*H*-azepines and all contain the diethylamino group. This fact, along with the relatively facile conversion of the intermediates to the 3*H*-azepines suggests that the intermediate might be a tautomeric azepine system. The proposed reaction mechanism[2,5] would immediately suggest the 1*H* tautomer. Of the other possible tautomers, the 6-alkyl-7-diethylamino-4*H*-azepines and 6-alkyl-7-diethylamino-2*H*-azepines which are amidines seem quite unlikely to possess the easy oxidizability shown by the intermediate. The 3-alkyl-2-diethylamino 2*H* tautomer is a conjugated cyclic imine but the electron-releasing diethylamino group is isolated from the conjugated system. The 3-alkyl-2-diethylamino-4*H*-azepine and 6-alkyl-7-diethylamino-3*H*-azepines are cyclic enamines and dienamines, respectively. Both enamines[12] and dienamines[9] have been found to be susceptible to oxidation in the atmosphere. However, the above two tautomers fail to provide a ready mechanistic explanation for the structure of the oxidation products since they would be expected to undergo oxidation at C-3 and C-5, respectively. Identification of the unstable azepine intermediates as 3-alkyl-2-diethylamino-1*H*-azepines is strongly supported by the nmr data shown in Figure 1. These are spectra of concentrated DEA solutions of the photolyzed reaction mixture prior to exposure to oxygen. In addition to aromatic signals these spectra show signals 360–520 Hz downfield from the DEA triplet ($\delta \approx$ 4.6–6.2), *i.e.*, in the vinyl proton region. These signals are attributed to the azepine precursor. The evidence for this identification is the fact that these signals disappear and are replaced by the signals of the 3*H*-azepine when small amounts of acetic acid in DEA are added to the nmr samples. These spectra are consistent with identification of the azepine precursor as the 1*H* tautomer. The first spectrum is that of a solution derived from **1j**. The doublet at 454 Hz is assigned to the C-7 proton. It is coupled with the multiplet at 411 Hz with a coupling constant of 7 Hz. The multiplet at 411 Hz reveals additional couplings of 5 and 1.3 Hz. This signal is attributed to the 6-proton, with the additional couplings being those to the C-5 and C-4 protons, respectively. The C-5 and C-4 protons overlap giving rise to the multiplet at 484 Hz. The center spectrum is derived from **1e** and is assigned to 3,6-dimethyl-2-diethylamino-1*H*-azepine. The singlet at 420 Hz is assigned to the C-7 proton and the AB pattern to the C-4 and C-5 protons. The triplet at 408 Hz and the signal at 505 Hz are portions of the spectrum of the 3*H*-tautomer **4e**. Finally, the spectrum on the right is assigned to 2-diethylamino-3,5,7-trimethyl-1*H*-azepine, the higher field signal being assigned to the C-6 proton the relative chemical shifts of the various signals are in agreement with previous studies of 1*H*-azepines in which it has been noted



2j



2e



2g

that the protons β to the nitrogen appear at highest field with α-protons intermediate and γ-protons at lower field.[13,14]

Identification of the azepine precursors as 2-diethylamino-1*H*-azepines provides a rational mechanistic basis for the formation of each of the types of oxidation products. This heterocyclic system, being a diaminopolyene, should be very susceptible to oxidation, and following mechanisms believed to operate in similar systems,[9] could lead to hydroperoxides **12** and **13**. Decomposition of **13** by loss of water can account for formation of the 2*H*-azepin-2-ones (**7**). The 2-diethylamino-3-alkylpyridines (**5**) and 5-acyl-3-alkyl-2-diethylaminopyridine (**6**) can arise by competing modes of decomposition of **14**, a valence isomer of **12**. Analogy for the oxidations involving carbon extrusion and ring contraction can be cited from the case of cycloheptatrienyl hydroperoxide which decomposes to benzene and benzaldehyde.[15] The effect of added cupric ion, although not investigated in detail, may be to catalyze decomposition of **12**, relative to the valence isomerism which leads ultimately to **5** and **6**.

Electronegative substituents at positions 1 or 3 stabilize the 1*H*-azepine ring and have permitted extensive investigation of the synthesis and reactions of such compounds,[14,16] most notably by Paquette. In

(12) R. A. Jerussi, *J. Org. Chem.*, **34**, 3648 (1969).

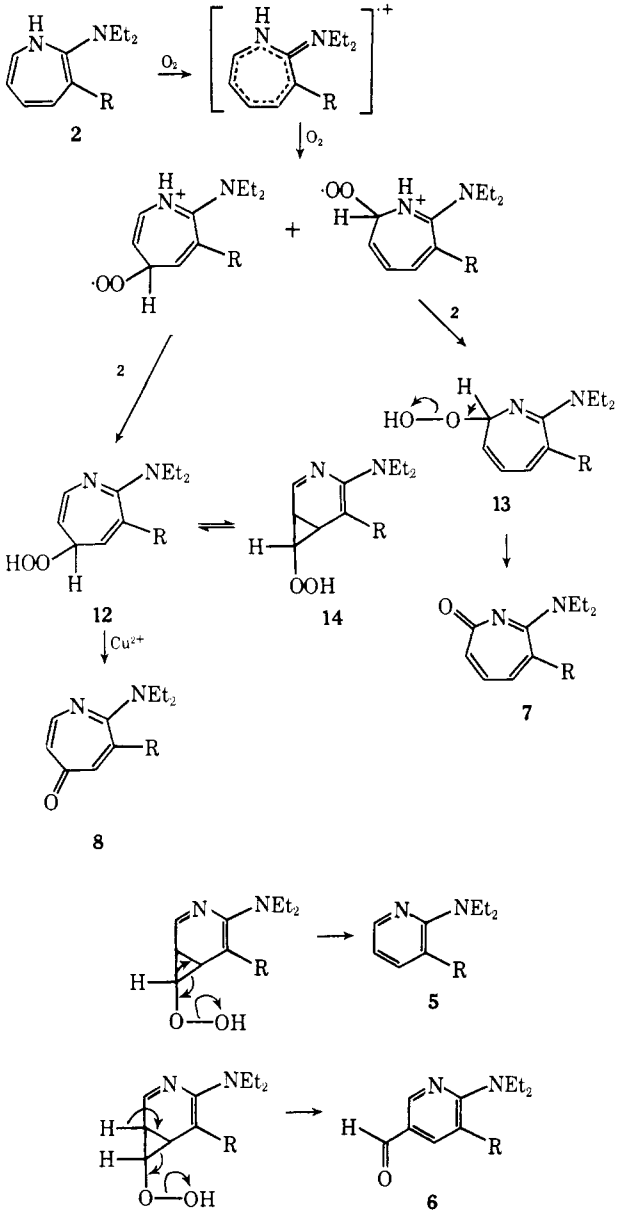
(13) R. J. Cotter and W. F. Beach, *ibid.*, **29**, 751 (1964).

(14) L. A. Paquette, D. E. Kuhla, J. H. Barrett, and R. J. Haluska, *ibid.*, **34**, 2866 (1969).

(15) M. E. Volpin, D. N. Kursanov, and V. G. Dulova, *Tetrahedron*, **8**, 33 (1960).

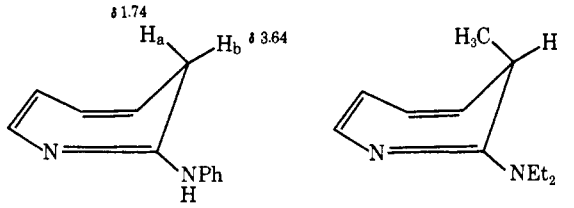
(16) L. A. Paquette, J. H. Barrett, and D. E. Kuhla, *J. Amer. Chem. Soc.*, **91**, 3616 (1969); L. A. Paquette, D. E. Kuhla, and J. H. Barrett,

contrast, the parent compound[17] and simple methyl derivatives[14,18] have limited stability. 1-Phenylazepine has been reported[19] but its chemistry remains to be studied. The limited stability of the 2-diethylamino-1*H*-azepine intermediates is not unexpected. It remains to be seen if techniques for isolation of the pure compounds can be developed.



The 2*H*-azepin-2-one and 4*H*-azepin-4-one (azatropone) systems also have been inaccessible. Excluding hydrogenated derivatives, very few monocyclic derivatives of these systems have been reported. 2,7-Dimethyl-4*H*-azepin-4-one was prepared in 1962[20] but no subsequent reports of its properties have appeared. Maniscalco[21] has described some 7-ethoxy-4*H*-azepin-4-ones and some 4-ethoxy-2*H*-azepin-2-ones. Several 2*H*-azepine-2,5-diones have also been prepared.[22]

As pointed out in the results section, the formation of 1*H*-azepine intermediates with lifetimes sufficiently long that they are present at the conclusion of the photolysis is restricted to aryl azides bearing at least one ortho substituent. Only 2-diethylamino-3*H*-azepines are present immediately after photolysis of phenyl azide or *p*-tolyl azide. *o*-Biphenyl azide appears to represent an intermediate case. Some 2-diethylamino-3-phenyl-3*H*-azepine (~15–20%) is isolated after oxidation indicating that only about half of the total azepine is present in the oxidizable 1*H* form. The conversion of 2-diethylamino-1*H*-azepines to the stable 3*H*-tautomer is apparently strongly retarded by a 3-alkyl substituent. We believe that the nmr spectra of the 3*H*-azepines **4** provide a clue to the nature of this substituent effect. In each of the 3-methyl-3*H*-azepines studied, the 3-methyl resonances appear at abnormally high field, 0.70 ± 0.05 ppm. The 3-H signals, shown in Table I as H_3', are at very low field for methinyl protons (δ 3.6–4.2). Temperature dependent nmr studies of 2-anilino-3*H*-azepine have shown that one of the 3-protons, H_a, is highly shielded while the other is strongly deshielded.[23] It follows from our nmr data that the dominant conformation of the 2-diethylamino-



3*H*-azepines is that with the methyl group in the "inside" position where it is strongly shielded by the C_6–C_7 double bond. The reason that this conformation is preferred is presumably the $A^{1,2}$ strain[24] which is present in the eclipsed "outside" position.[25] The stereoelectronically preferred route for protonation would presumably be from an axially-like direction, introducing the proton in the "inside" conformation. The $A^{1,2}$ strain which develops as this process occurs is believed to be the cause of the retardation of 3-protonation by the 3-alkyl substituent.

The divergent behavior observed with the highly hindered azide **1m** may be the result of a steric effect associated with the mesityl substituent. It is not surprising that the 3*H*-azepine is not formed in this case, since the mesityl group introduces severe steric interactions in either conformation of this tautomer. The observed 4*H*-tautomer **10** may be preferred to the 1*H* tautomer because the dihedral angle between the

J. Org. Chem., **34**, 2879 (1969); L. A. Paquette and D. E. Kuhla, *ibid.*, **34**, 2885 (1969); L. A. Paquette, D. E. Kuhla, J. H. Barrett, and L. M. Leichter, *ibid.*, **34**, 2888 (1969); H. Prinzbach, R. Fuchs, and R. Kitzing, *Angew. Chem. Int. Ed. Engl.*, **7**, 67 (1968); H. Prinzbach, D. Stusche, and R. Kitzing, *ibid.*, **9**, 377 (1970); A. L. Johnson and H. E. Simmons, *J. Amer. Chem. Soc.*, **89**, 3191 (1967); R. F. Childs and A. W. Johnson, *J. Chem. Soc. C*, 1950 (1966); M. Anderson and A. W. Johnson, *ibid.*, 2411 (1965); J. Ashby, L. A. Cort, J. A. Elvidge, and U. Eisner, *ibid.*, *C*, 2311 (1968).

(17) K. Hafner, *Angew. Chem. Int. Ed. Engl.*, **3**, 165 (1964).

(18) K. Hafner and J. Mondt, *ibid.*, **5**, 839 (1966).

(19) R. J. Sundberg and R. H. Smith, Jr., *Tetrahedron Lett.*, 267 (1971).

(20) E. Bullock, B. Gregory, and A. W. Johnson, *J. Amer. Chem. Soc.*, **84**, 2260 (1962).

(21) I. A. Maniscalco, Ph.D. Thesis, Fordham University, 1971.

(22) D. Misti, H. W. Moore, and K. Folkers, *Tetrahedron*, **22**, 1201 (1966); *cf.* R. W. Rickards and R. M. Smith, *Tetrahedron Lett.*, 2361 (1966); G. R. Bedford, G. Jones, and B. R. Webster, *ibid.*, 2367 (1966).

(23) A. Mannschreck, G. Rissman, F. Vögtle, and D. Wild, *Chem. Ber.*, **100**, 335 (1967).

(24) F. Johnson, *Chem. Rev.*, **68**, 375 (1968).

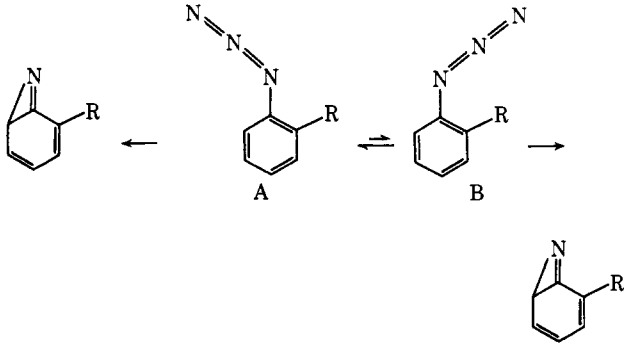
(25) Heyd and Cupas have very recently discussed the role of $A^{1,2}$ strain in determining conformational equilibria in certain cycloheptatrienes; W. E. Heyd and C. A. Cupas, *J. Amer. Chem. Soc.*, **93**, 6056 (1971).

mesityl and diethylamino groups is about 30° in the former whereas it is 0° in the latter.

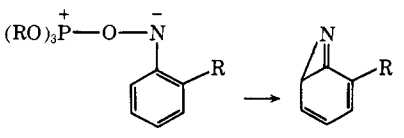
Although our data clearly indicate that 1*H*-azepines are intermediates in the formation of nearly all of the 2-diethylamino-3*H*-azepine formed from *o*-alkyl azides, the situation is less clear in the case of azides without ortho substituents. The isolation of azepinones from photolyses of *p*-tolyl azide and phenyl azide in an oxygen atmosphere indicates that at least part of the reaction passes through a 1*H*-azepine intermediate. The isolation of some 3*H*-azepine **4h** and **4a** under these conditions demands either that some 3*H*-azepine is formed without intervention of a 1*H*-azepine intermediate or that tautomerization of the 1*H* to the 3*H* form is competitive with oxidation.

The present work provides additional data on the matter of the directional specificity of the ring expansions. In addition to the previously reported cases of **1b**[6c] and **11**,[4] the azides **1c**, **1d**, **1i**, and **1j** are all found to undergo ring expansion with apparently exclusive migration of an unsubstituted ortho carbon atom in preference to a substituted one. However, ring expansion occurs with **1f**, **1g**, and **1k**, in which both ortho carbon atoms are substituted. In the case of **1k** where the substituents are nonidentical, methyl *vs.* isopropyl, there is about an equal amount of migration of each carbon atom. Minor amounts of migration of a substituted carbon occur in the case of **1m** in DEA and in 1:10 DEA–THF this mode of migration is dominant. The recent work of Berwick[6h] indicates that both modes of ring expansion occur with 2-acyl substituents.

Recent work with alkyl azides has indicated that ground state conformational equilibria can determine migratory aptitude.[26] Conformation A is presumably



dominant in an aryl azide bearing a single ortho substituent. A requirement for preferential bonding in the direction of departure of the nitrogen would be required to explain the observed directional specificity on a conformational basis. A rationale for such a requirement is lacking at this point and it appears that, at least in the case of **1m**, the directional specificity is solvent sensitive. Furthermore, since deoxygenations show similar specificity,[6c,11] the thermal, but highly exothermic, cleavage of C would have to be subject to



similar conformational control. At the present time, we are unable to satisfactorily illuminate this matter and further work on the problem is continuing.

Experimental Section[27]

Aryl Azides. All the azides were prepared from the corresponding amine. In most cases, method A of Smith and Brown[28] was used. The exceptions were for **1j**, **1k**, and **1m** which were prepared according to Smolinsky's modification[29] of method B of Smith and Brown. Analytical data for the new azides are recorded elsewhere.[27] The anilines used were commercially available or were prepared by reduction of available nitro compounds with the following exceptions. 2-Isopropylaniline and 2-isopropyl-6-methylaniline were obtained from the Ethyl Corporation. 2-Amino-2′,4,4′,6′-tetramethylbiphenyl was prepared by arylation of mesitylene with 2-nitro-4-methylphenyldiazonium ion according to a procedure of Elks, *et al.*,[30] followed by catalytic reduction. 2-Nitro-2′,4,4′,6′-tetramethybiphenyl had mp 77.5–78.5°; 2-amino-2′,4,4′,6′-tetramethylbiphenyl had mp 103–104°.[27]

Photolysis Conditions. Diethylamine (DEA) was usually redistilled from sodium hydroxide and stored over sodium hydroxide pellets. Use of DEA from freshly opened bottles of reagent grade from Fischer Scientific Company or Matheson, Coleman and Bell gave apparently identical results. Solutions of the azide in the concentration range 0.5–2 g/100 ml of DEA were prepared and purged with nitrogen for at least 0.5 hr prior to photolysis. Photolysis was carried out under a nitrogen atmosphere using a water-cooled immersion well containing a 450-W Hanovia mercury lamp. The photolyses were carried to essentially complete reaction of the azide, approximately 1 hr per g of azide in the usual apparatus. The resulting solutions were worked up by the following procedures.

A. Standard Procedure. The solution was transferred to a rotary evaporator and concentrated. It was usually stored overnight and then chromatographed on silicic acid. Elution with benzene and benzene–ether mixtures gave mixtures containing **3**, **4** and **5**. The individual components were isolated by preparative glpc using a 5 ft 5% SE 30 column at 110° or a 6 ft 10% Carbowax 20M column at 175–190°. Yields of the 3*H*-azepines were determined for **4c** (41%), **4g** (5%), and **4i** (31%). Yields of pyridine were determined for **5d** (7%) and **5i** (6%) and were in a similar range for **5b**, **5c**, and **5f**.

B. With Heating in Methanol. The photolyzed solution was transferred by syringe or under a nitrogen atmosphere to a dropping funnel which was attached to a reaction flask containing a volume of refluxing methanol equal to the volume of the photolyzed solution. The entire system was preflushed with nitrogen. The DEA solution was added to the refluxing methanol over a period of 1 hr and the solution was refluxed 1 more hr. The reaction solution was cooled, concentrated, and distilled. The yields of 3*H*-azepines obtained by distillation are shown in Table III. No pyridines were detected in the 3*H*-azepine samples obtained in this way. The anilines **3** were present in amounts which varied with substituent groups as noted in Table III.

C. With Oxidation by Oxygen. The photolyzed solution was transferred, under nitrogen, to a dropping funnel attached to a reaction flask containing 100 ml of DEA. An inlet for oxygen gas was placed below the DEA. Nitrogen, and oxygen flows were established in such a fashion as to maintain the photolyzed solution under a nitrogen atmosphere until it dropped into the flask. The photolyzed solution was added to the flask over a period of 1 hr and a stream of oxygen was maintained through the solution for an additional hour. The solution was then kept at room temperature overnight and the DEA removed by evaporation under aspirator vacuum. The residue was dissolved in benzene and chromatographed on Florisil (~50 g/g of azide). The solvent sequence used was 1:50 ether–benzene; 1:1 ether–benzene; 1:4 chloroform–ether, and 1:4:15 methanol–chloroform–ether. The first fractions

(26) R. A. Abramovitch and E. P. Kyba, *J. Amer. Chem. Soc.*, **93**, 1537 (1971); R. M. Moriarty and P. Serridge, *ibid.*, **93**, 1534 (1971); R. M. Moriarty and R. C. Reardon, *Tetrahedron*, **26**, 1379 (1970).

(27) Analytical data for new compounds will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Reprint Department, ACS Publications, 1155 Sixteenth St., N.W., Washington, D. C. 20036 by referring to author, title of article, volume, and page number. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

(28) P. A. Smith and B. B. Brown, *J. Amer. Chem. Soc.*, **73**, 2435 (1951).

(29) G. Smolinsky, *ibid.*, **82**, 4717 (1960).

(30) J. Elks, J. W. Haworth, and D. H. Hey, *J. Chem. Soc.*, 1284 (1940).

Table IV. Melting Points[a]

Compound	Mp (°C)
1m	40–42
7a	80–81
7b	84–85
7d	110–112
7e	115–116
7h	77–78
7i	61–62
7j	80–81
7l	116–118

[a] All other new compounds were liquids.

Table V. Ultraviolet Absorption Data[a]

Compd	λ_{max} (log ϵ)
6b	227 infl (3.71), 297 (3.78), 340 (4.31)
6c	235 (3.79), 295 infl (3.72), 340 (4.25)
6g	225 infl (3.88), 332 (4.30)
6i	225 infl (3.59), 292 (3.72), 340 (4.27)
7a	249 (4.21), 270 infl (4.08)
7b	260 (4.19)
7h	249 (4.21), 275 infl (4.04)
7i	261 (4.18)
7l	268 (4.10)
8i	240 infl (4.03), 287 (3.76), 372 (4.12)
8j	240 infl (3.98), 285 (3.62), 376 (4.10)

[a] In 95% ethanol.

gave the aniline **3**, often contaminated with **5**. Compounds **5** and **6** were eluted next, in that order, although separation was often incomplete. Yield data in Table II were obtained from the weights of the evaporated fractions. In the case of mixtures, estimation of the composition was possible by integration of nmr spectra. The azepinones **7** were eluted by the methanol–chloroform–ether solvent mixture.

D. Oxidation in the Presence of Cupric Ion. The procedure was identical with the prior oxidation procedure except that 50 mg of cupric chloride per g of azide was added to the DEA in the oxidation flask. The same work-up and chromatographic sequence was used. The azepinones **8** were eluted by ether–chloroform.

Analytical Samples. Analytical samples of the 3*H*-azepines **4** and the diethylaminopyridines **5** were prepared by preparative glpc using either a 6 ft 10% Carbowax 20M column at 175–190° or a 5 ft Apiezon–KOH column at 220°. The 5-acyl-2-diethylaminopyridines **6** were usually contaminated by the corresponding **5** after Florisil chromatography. These components were separated by preparative tlc on aluminum oxide plates using 1:50 ether–benzene for elution and then distilled (bulb-to-bulb). The 2*H*-azepin-2-ones **7** were purified by preparative tlc on aluminum oxide plates using 1:20:20:60 methanol–ether–chloroform–benzene for development followed by recrystallization from hexane or ether–hexane. The 4*H*-azepin-4-ones **8** were purified on aluminum oxide preparative tlc plates using 1:20:20:60 methanol–ether–chloroform–benzene for development and then distilled (bulb-to-bulb). Analytical data for the new compounds are recorded in the microfilm edition.[27] Melting points of solid compounds are reported in Table IV. Ultraviolet absorption data for representative compounds are shown in Table V.

Photolyses in an Oxygen Atmosphere. Experiments involving **1a, 1h,** and **1i** were carried out. The photolysis was effected in reaction vessels equipped with a gas inlet. A slow stream of oxygen was bubbled through the reaction solution throughout the course of the photolysis. Glpc analysis of the crude product from **1a** indicated that **4a** (18%) was the only significant volatile product. Glpc analysis of the crude product from **1i** showed **5i** (5%) and **4i** (1%). The reaction mixtures from **4a** and **4h** were processed by the chromatographic sequence described in C above. The azepine **4a** was isolated (22% yield after distillation) and a small amount (~2%) of the azepin-7-one **7a** was obtained from the polar fractions. From **1h** there was obtained a small amount of *p*-toluidine, **4h** (16%) and **7h** (8%).

Nmr Spectra of 1*H*-Azepines. Solutions of the azides (90–110 mg) in DEA (4 ml) were placed in quartz test tubes sealed with a septum and purged for at least 0.5 hr with N_2 and then irradiated for 3 hr using a Merry-Go-Round apparatus and a 450-W Hanovia mercury lamp. The resulting solutions were concentrated to about 0.5 ml by passing N_2 rapidly over the solution using hypodermic needles as the gas inlet and outlet. The spectra shown in Figure 1 were recorded using such samples and a Varian HA 100 instrument.

Photolysis of 1m. A. In Diethylamine. A solution of **1m** (0.251 g, 100 mmol) in DEA (20 ml) in a Pyrex test tube was purged with nitrogen and then irradiated for 6 hr. Glpc comparison of the solution before and after exposure to oxygen gave no indication of an oxygen-sensitive intermediate. After removal of the DEA, the residue was chromatographed on silica gel. Benzene eluted a small amount of unreacted azide and 33 mg (16%) of 2-amino-2′,4,4′,6′-tetramethylbiphenyl. Benzene–ether eluted **10** (125 mg), 47%). The analytical sample was obtained by rechromatography. A minor component (~10%) isolated by chromatography was identified as **11** by spectral comparison with another sample isolated by photolysis in 9:1 THF–DEA (part B). The analytical sample of **10** was prepared by rechromatography on silica gel giving 7-diethylamino-3-methyl-6-(2,4,6-trimethylphenyl)-4*H*-azepine;[27] nmr peaks (CCl_4) at δ 6.80 (broad s, 2 H), 6.59 (s, 1 H), 5.70 (t, 1 H, J = 7.5 Hz), 3.11 (q, 4 H, J = 6.5 Hz), 1.8–2.3 (m, 14 H), 0.76 (t, 6 H, J = 6.5 Hz); λ_{max} 315 (log ϵ 3.30) in 95% ethanol; picrate, mp 179–179.5°.

B. In 9:1 Tetrahydrofuran–Diethylamine. A photolysis was carried out as described in A using 9:1 THF–DEA as solvent. Analysis by glpc immediately after photolysis indicated the minor product (**11**) from the DEA photolysis was the only significant volatile product and this was confirmed by nmr examination of the crude product. Chromatography on silica gel gave 2-amino-2′,4,4′,6′-tetramethylbiphenyl (22 mg, 19%) and **11** (104 mg, 39%). An analytical sample of **11** was prepared by rechromatography on silica gel giving 2-diethylamino-4-methyl-7-(2,4,6-trimethylphenyl)-3*H*-azepine;[27] nmr peaks (CCl_4) at δ 6.79 (s, 2 H), 6.08 (d, 1 H, J = 6.0 Hz), 5.52 (d, 1 H, J = 6.0 Hz), 3.40 (q, 4 H, J = 6.5 Hz), 2.76 (broad s, 2 H), 2.25 (s, 3 H), 2.20 (s, 6 H), 1.95 (s, 3 H), 1.10 (t, 6 H, J = 6.5 Hz); λ_{max} 293 (log ϵ 3.87) in 95% ethanol.

Pyrolysis of 10. A neat sample of **10** (90 mg) was heated at 175° under nitrogen for 5 min. The residue was chromatographed on silica gel. Elution with benzene–ether gave 3-amino-2-diethylamino-2′,4′,4,6′-tetramethylbiphenyl (41 mg, 46%). The analytical sample[27] was obtained by rechromatography on silica gel; nmr peaks (CCl_4) at δ 6.88 (d, 1 H, J = 7.5 Hz), 6.82 (broad s, 2 H), 6.15 (d, 1 H, J = 7.5 Hz), 4.12 (broad s, 2 H), 2.60 (m, 4 H), 2.30 (s, 3 H), 2.19 (s, 3 H), 1.99 (s, 6 H), 0.98 (t, 6 H, J = 7.0 Hz)