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RING ENLARGEMENT IN THE PHOTOLYSIS OF PHENYL AZIDE[1]

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Abstract—The photolysis of phenyl azide in diethylamine leads to ring enlargement with the formation of 2-diethylamino-3H-azepine (I–3H). Photolysis in trimethylamine containing aniline leads to the corresponding 2-anilino derivative (II–3H), whereas photolysis in liquid ammonia leads to the 2-amino derivative (III–3H). Photolysis in diethyl ether saturated with hydrogen sulfide affords a low yield of 1,2-dihydro-2-thienoketo-3H-azepine (V–3H), which can be prepared more conveniently by treatment of II or III with hydrogen sulfide. Hydrolysis of III affords 1,2-dihydro-2-keto-3H-azepine (IV–3H). Vogel's assignment to this molecule of the 3H structure has been confirmed by NMR examination of the tetradeuterio derivative.

SEVERAL years ago in 1949, the photochemical decomposition of phenyl azide was selected as a promising source of monovalent nitrogen for comparison with the emergent organic chemistry of divalent carbon. How unfortunate a choice this was is eloquently attested by the elegant and productive investigations *inter alia* of J. W. ApSimon, D. H. R. Barton, K. Hafner, W. Lwowski, P. A. S. Smith and G. Smolinsky.[3] Instead of insertions into the carbon-hydrogen bond or additions to olefins and benzene, Wolff's "dibenzamil" rearrangement, albeit in a previously unknown photochemical modification, was encountered and, perforce, elucidated.

Initial efforts to trap a monovalent nitrogen intermediate centered on the photolysis of phenyl azide in benzene. By analogy with the photolysis of diazomethane in benzene, which produces toluene and tropilidene, this reaction was expected to lead to diphenylamine and N-phenylazepine (or a transformation product thereof). In fact, the bulk of the product was intractable, although small amounts of azobenzene (4%) were isolated. The use of cyclohexene, a more reactive trap for carbenes, was no more satisfactory. In acetic acid, the irradiation led to *p*-acetoxyando-acetoxyacetanilide in yields of 11 and 1% of theory, respectively.[4] Although these products

[1] The bulk of this work is taken from a dissertation submitted in 1953 in partial fulfillment of the requirements for the Degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University: R. A. Odum, *A New Rearrangement of Phenyl Azide, Dissertation Abstracts* **20**, 3958 (1960).

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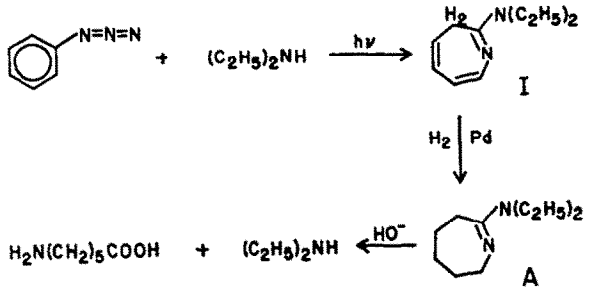
[3] For references, see the excellent review by R. A. Abramovitch and B. A. Davis, *Chem. Rev.* **64**, 149 (1964).

[4] Recently L. Horner, A. Christman and A. Gross, *Chem. Ber.* **96**, 399 (1963), report similar results in the photolysis of phenyl azide in acetic acid, but were unable to isolate azobenzene from the photolysis in benzene.

can be envisaged to arise by way of the elusive phenyl nitrene,[5] there are other plausible modes of formation.

As a consequence of the hypothesis that the electron-deficient phenyl nitrene should react as an electrophile, phenyl azide, in dilute solution, was photolyzed in the stronger nucleophile, diethylamine. Distillation afforded an unknown product, I, $C_{10}H_{16}N_2$, in 34% of theory. Here, we will concentrate on the arrangement of hydrogen atoms in the molecule and will do no more than summarize the observations which led to the establishment of its gross structure,[1] in view of the publication by Huisgen[6–9] of the structure of the related "dibenzamil". This molecule had been discovered originally by Wolff as the product of the pyrolysis of phenyl azide in aniline.[10]

Chart 1



The new substance (I) is basic and forms a crystalline picrate. Catalytic hydrogenation leads to a basic, tetrahydro derivative, alkaline hydrolysis of which affords ε-aminocaproic acid and diethylamine. The tetrahydro derivative is, therefore, the amidine, 2-diethylamino-4,5,6,7-tetrahydro-3H-azepine (Chart 1, A). Its UV spectrum (λ_{max} 224 mμ, log ε 4·00) closely resembles that of acetamidine (λ_{max} 224 mμ, log ε 3·60).[11] The absence of NH absorption in the IR spectrum and the presence of an intense absorption of 1600 cm^{-1} (compared to 1621 cm^{-1} reported for N,N,N¹-trimethyl- benzamidine[12]) are in accord with the structural assignment.

The UV absorption spectrum of I (λ_{max} 297; log ε 3·90) is at wavelengths much longer than that of saturated amidines. One is, therefore, justified in assigning the two additional elements of unsaturation in I to a pair of double bonds. In theory, there are seven arrangements of three double bonds, I–1H through I–7H (Chart 2). Of these, neither I–1H nor I–2H could give the tetrahydro amidine (A) on catalytic hydrogenation without concomitant rearrangement of hydrogen and neither is a

[5] Uncomfortable with the sight and sound of "phenylimidogen", we stick with the colloquial "nitrene."

[6] R. Huisgen, *Congress Handbook:* XIVth *International Congress of Pure and Applied Chemistry* p. 109. Zurich (1955).

[7] R. Huisgen, D. Vossius and M. Appl, *Angew. Chem.* **67**, 756 (1955).

[8] R. Huisgen, D. Vossius and M. Appl, *Chem. Ber.* **91**, 1 (1958).

[9] M. Appl and R. Huisgen, *Chem. Ber.* **92**, 2961 (1959).

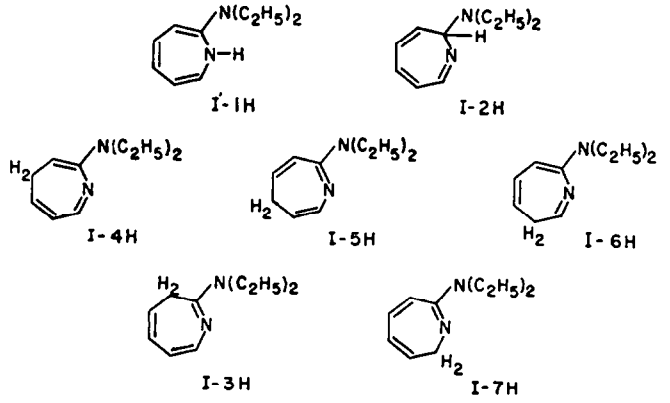
[10] L. Wolff, *Liebigs Ann.* **394**, 59 (1912).

[11] J. C. Gage, *J. Chem. Soc.* 221 (1949).

[12] G. Fabian and M. Legrand, *Bull. Soc. Chim. Fr.* 1462 (1956).

probable structure. Although I–1H is a substituted azepine inviting hopeful attention,[6] the absence of N–H absorption in the IR is decisive.[13]

Chart 2



The NMR spectrum of I provides a sounder basis for deciding among these structures.[14] The pair of N-ethyl groups appears unequivocally as a triplet (9·08, 8·96, 8·84) of relative area 6 and a quartet (6·91, 6·79, 6·68, 6·56) of relative area 4. The uncomplicated nature of this system requires that the chemical shift of the two methylene groups be identical, a condition which can be fulfilled either by chance or by a sufficiently rapid rotation about the bond between nitrogen and the ring. Of primary significance is the appearance of a doublet (7·52, 7·41) of relative area 2 corresponding to a pair of equivalent hydrogen atoms split by coupling with a single, chemically shifted hydrogen atom. The position of these two hydrogen atoms leaves no doubt of their identification as a methylene group. Arrangements I–1H and I-2H are irreconcilably inconsistent with this feature of the NMR spectrum.

The splitting of this methylene group into a doublet also permits the exclusion of structures I–4H, I–5H and I–6H. These structures all demand that the methylene group be split at least into a triplet or a quartet. This doublet persists in the spectra of the other members of the series, to be discussed later, and is taken as unequivocal evidence against tautomers of the 4H, 5H and 6H type.

The remaining four hydrogen atoms are of the olefinic type and, through good fortune, are sufficiently different from each other in chemical shift to appear as separate systems, each of 1 area unit. Three are split at least into quartets and one appears as a doublet (3·04, 2·92). Both structures I–4H and I–6H would have shown *one doublet* and *one triplet* in the olefinic region, while I–5H would have given rise to *two doublets*. The appearance of *no triplet* and only *one doublet* is inconsistent with each of these three structures and serves as strong additional basis for their exclusion.

[13] In our original assignment of structure[1] it was assumed that (1) the amidine system must be intact, and that the double bonds would be (2) conjugated with each other and (3) with the amidine in the 7H sense. When NMR became available the arguments could be strengthened and ultimately structure 1-3H was made the more reasonable.

[14] The NMR spectra were determined recently (April, 1960) by M. R. Willcott, III, of Yale University, to whom we express our thanks. The measurements were made with a Varian Associates High Resolution Spectrometer at 60 megacycles, all in CCl_4, with the exception of 2-anilino-3H-azepine which was dissolved in $CDCl_3$. The spectra are referred to tetramethylsilane as an internal standard and are expressed on the τ scale in ppm [G. V. D. Tiers, *J. Phys. Chem.* **62**, 1151 (1958)].

Structures I-3H and I-7H both contain the system, $—C_\epsilon H=C_\delta H—C_\gamma H=C_\beta H—C_\alpha H_2—$, and should give rise to *one doublet* ($—C_\epsilon H$) and *no triplet* in the olefinic region and to a simple doublet of relative area 2 in the region of allylic hydrogen atoms.

A more detailed assignment of peaks to the individual hydrogen atoms in the system can be assayed on the assumption that the differences in chemical shifts are sufficiently larger than coupling constants to permit a simplified, admittedly approximate, analysis. The doublet at 2·92 and 3·04 must arise from $C_\epsilon H$, split by the single adjacent hydrogen atom, $C_\delta H$, whence the observed separation of 7·80 c/s may be equated with $J_{\delta\epsilon}$.

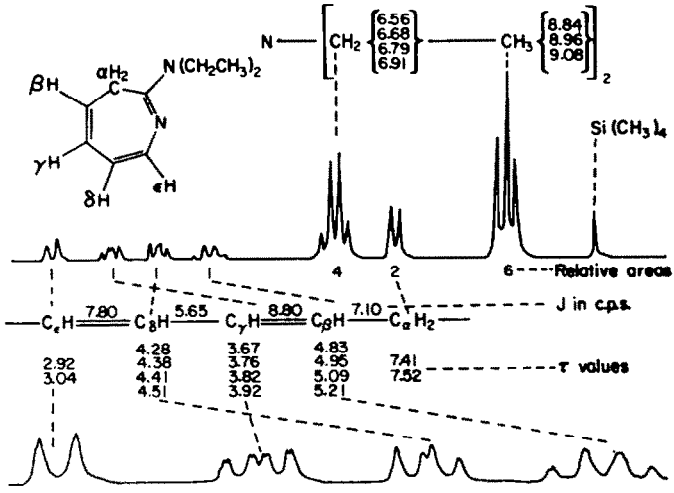


FIG. 1. The NMR spectrum of I in carbon tetrachloride solution. The lower curve is an expanded trace of the four hydrogen atoms.

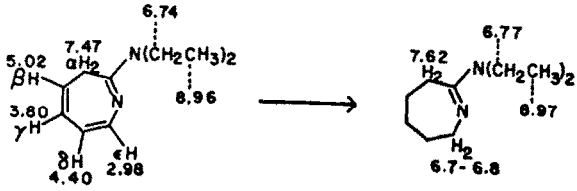
This same separation is seen again in the once removed pair of doublets (4·28, 4·38, 4·41, 4·51) which may then be assigned to $C_\delta H$. The second coupling constant extractable from this pair of doublets is 5·65 c/s and must correspond to $J_{\gamma\delta}$. This same coupling constant appears in the adjacent pair of doublets (3·67, 3·76, 3·82, 3·92), which shows in addition a second separation 8·80 c/s assignable to $J_{\beta\gamma}$ (a minor spacing corresponds to $J_{\gamma\epsilon} = 0·85$ c/s). Accordingly, this pair of doublets is attributable to $C_\gamma H$.

Finally, the system of four peaks at 4·83, 4·95, 5·09 and 5·21 can be interpreted as the superposition of two triplets (fortuitously appearing like a quartet) arising from coupling with $C_\alpha H_2$($J_{\alpha\beta} = 7·10$ c/s) and $C_\gamma H$. From the previously deduced value of $J_{\beta\gamma}$(8·80 c/s) the total separation within the grouping is calculated to be 23·0 c/s whereas the measured value is 22·2 c/s. This system may thus be assigned to $C_\beta H$.

This $C_\beta H$ vinyl hydrogen could be split into a triple by the adjacent methylene group and, by coupling with the adjacent $C_\gamma H$ vinyl hydrogen, could appear as a triplet, a quartet, a quintet or more complicated configurations depending on the ratio of the two coupling constants and the chemical shifts. Since the two groups of four peaks centered at 3·80 and 4·40 have components of roughly equal area and thus appear to arise from the superposition of two doublets, the group of peaks centered at 5·02 is the most appropriate for association with $C_\beta H$. In this group the two side

peaks (4·83 and 5·21) are clearly of much smaller area than the central peaks (4·95 and 5·04). The complete assignment is also consistent with the general observation that the coupling constants between hydrogen atoms on the same double bond are larger than the coupling constant between adjacent hydrogen atoms on different double bonds.

Distinction between structures I–3H and I–7H depends on arguments based on chemical shifts, which follow those developed by Vogel and Erb[15] in their establishment of the structure of 1,2-dihydro-2-keto-3H-azepine (*vide infra*). Were I–7H the correct structure, $C_\varepsilon H$ would be α to the amidine carbon atom while $C_\delta H$ would be β. In α, β-unsaturated aldehydes, ketones, acids and nitriles the β-hydrogen is always shifted to lower field than is the α-hydrogen atom. Assuming not unreasonably the electronic similarity of the amidine function, one concludes that structure I–7H would find $C_\delta H$ at lower field than $C_\varepsilon H$, contrary to fact. In double bonds attached to atoms with unshared electrons, the α-hydrogen appears at lower field: α-hydrogen (1·50) and β-hydrogen (3·02) in pyridine;[16] α-hydrogen (3·78) and β-hydrogen (5·46) in dihydropyran;[16] α-(2·60) and β-(3·70) hydrogen in furan;[16] α(3·59) and β(5·06) hydrogen in N-phenyl-1,2-dihydropyridine.[17] By analogy, the $C_\varepsilon H$ would be shifted further down-field if the structure were I–3H. This argument likewise points to structure I–3H as the more consistent of the two.



A further argument is based on the fact that the two methylene groups adjacent to the C=N group of the amidine in the tetrahydro derivative lie at 7·62 and 6·7–6·8 ppm. By analogy with caprolactam (*vide infra*) in which the C-methylene group lies at 7·69 while the N-methylene group lies at 6·88, it can be assumed with some confidence that the methylene group at higher field (7·62) in tetrahydro-I–3H is bonded to carbon and not to nitrogen. Since the methylene group in I (7·47) has already suffered some down-field shift by the effect of the adjacent olefinic linkage, and is considerably up-field from the N-methylene group in tetrahydro-I–3H (6·7–6·8), it must be a C-methylene group as it is in structure I–3H.

Irradiation of phenyl azide with aniline in trimethylamine as solvent leads to the same compound, "dibenzamil" (II), obtained by Wolff[10] from the thermal decomposition of phenyl azide in aniline. The gross structure of this substance was established[1] by methods sufficiently comparable to those published subsequently by Huisgen *et al.*[6–8] that the reader is simply referred to the experimental section of this paper for details.

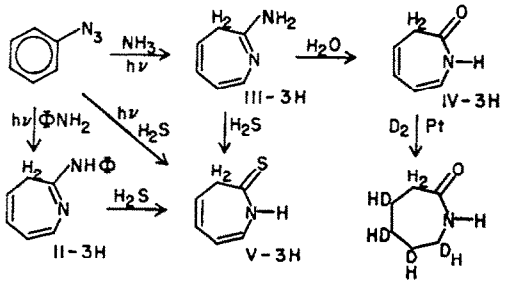
Without analyzing the NMR spectrum of II in detail, one should emphasize that the presence of a methylene doublet at 7·23 and 7·37 admits only II–3H and II–7H

[15] E. Vogel and R. Erb, *Angew. Chem.* (Inter. Ed.) **1**, 53 (1962).
[16] L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy In Organic Chemistry.* Pergamon Press, London (1959).
[17] M. Saunders and E. H. Gold, *J. Org. Chem.* **27**, 1439 (1962).

as reasonable possibilities for the refined structure.[18] Despite the fact that the presence of one hydrogen atom in the amidine system allows two choices for the disposition of the carbon-nitrogen double bond—either endo or exocyclic—the NMR spectrum of the olefinic hydrogen atom is surprisingly similar to that of I: a doublet of infirm assignment (without removing the overlapping N–H absorption) at 3·30 and 3·39, a group of two doublets (3·70, 3·76, 3·83, 3·91), a second group of two doublets (4·18, 4·28, 4·36, 4·46) and a quartet (4·66, 4·80, 4·92, 5·03). The similarity in spectrum implies that I and II have identical ring systems.

Irradiation of phenyl azide in liquid ammonia gives the simple amino analogue (III). Its gross structure is established by catalytic hydrogenation to 2-iminohexamethyleneimine previously prepared by Oxley and Short.[19] The presence in III of a doublet at 7·33 and 7·43 indicates that the methylene group is adjacent to a *single* hydrogen atom. Thus III–3H and III–7H are again the only consistent structures.

The pattern of the NMR spectrum of the olefinic hydrogens in III is quite similar to that in I and II: a doublet at 3·10 and 3·25; a pair of doublets at 3·75, 3·80, 3·86 and 3·95; another pair at 4·13, 4·20, 4·25 and 4·39; and quartet (observable after washing out -NH with deuterium oxide) at 4·49, 4·61, 4·73 and 4·86. It is concluded that I, II and III are closely related and have in common the structure of a 2-substituted-3H-azepine.



It is interesting that an attempt to improve the yield of product by adding potassium amide evoked a rapid, non-photolytic reduction leading to aniline. Thus, there is a limit to the strength of the nucleophile tolerated by phenyl azide. To this limitation on the scope of the photorearrangement should be added the one exemplified by

[18] Husigen originally formulated Wolff's phenyl azide-aniline product ("dibenzamil") as the theoretically interesting, 8-electron vinylog of pyrrole, 2-anilinotropazol (2-anilino-1H-azepine).[a] Later, amidine structures were considered and finally embraced[b] in place of the IH-azepine formulation. However, basis for the reassignment was tenuous. (a) From a Zerewitinoff determination in anisole in which 1·02–1·14 molar equivs of methane were evolved, it was concluded that "dibenzamil" had only one N—H bond. If such a conclusion were to be credible, it had to be assumed that the IH-azepine tautomer would have evolved 2 molar equivs of methane. Since this assumption was not justified by analogy or by theoretical argument, the conclusion itself carried little force. (b) In the IR spectrum of "dibenzamil", there is a band at 1582 cm^{-1}. With inadequate analogy, this band was not only assumed to be an amidine (C=N stretching vibration), but also was taken to demonstrate simultaneously the presence of a *conjugated* amidine. (c) An oily product of the reaction of phenyl azide with N-methylaniline showed no N—H stretching frequency in accord with the amidine formulation. Although it formed a picrate, this product was surprisingly unstable to light and was not further characterized even as a member of the "dibenzamil" family.

[19] P. Oxley and W. F. Short, *J. Chem. Soc.* 1514 (1948).

the failure of the photolysis in acetic acid to produce isolable products of rearrangement.

Merely boiling with water serves to hydrolyze III to 1,2-dihydro-2-keto-3H-azepine (IV) which is identified by catalytic hydrogenation to caprolactam. Compound IV has the same m.p., UV spectrum and composition as a substance obtained by Vogel and Erb[15] in the Curtius rearrangement of *cis*-2-vinylcyclopropane-1-carboxazide to which structure IV–3H was assigned by the IR and UV data as well by the NMR spectrum (adjacency of the CH_2-group to the carbonyl group). In more detail the argument of Vogel and Erb[20] runs in the following way. The presence of a doublet of relative area 2 in the NMR at 7·20 and 7·07 excludes all structures but IV–3H and IV–7H. From the fact that in caprolactam the carbonyl–CH_2 is at 7·69 and the amido-CH_2 is at 6·88,[21] and from the reasonable anticipation that the adjacency of a double bond would shift the position to lower fields, the value of 7·20, 7·07 can only be accommodated by placing the methylene group in IV adjacent to the carbonyl group. This structure is confirmed by the isolation of malonic acid from the ozonolysis of IV.[20]

Consistently, the carbonyl frequency is at 1672 cm^{-1} and may be compared with the range of 1623–1632 cm^{-1} given by Crombie[22] for the four stereoisomeric N-butyl amides of deca-2,4-dienoic acids and the value 1669 cm^{-1} given for caprolactam.[23] It is a little more difficult to draw a conclusion from the UV absorption spectrum. The extinction coefficient (λ_{max} 256; ε 4600) is lower than that reported by Crombie for the series of deca-2,4-dienoic acid amides (λ_{max} 258–259; ε 17,500–29,500) but is comparable to that of cycloheptadiene (λ_{max} 248; ε 3700).

Independent confirmation of the structure IV-3H is obtained by catalytic deuteration of IV. This reaction affords a tetradeuterio derivative of caprolactam in which the only CH_2 group must be identical with that originally present in IV, since all the other methylene groups are of the CHD type. The peak at 6·76 in tetradeuterio-IV corresponds in chemical shift to the amido CH_2 group of caprolactam and has a relative area of 1. It therefore represents one of the CHD groups and not the CH_2 group. The doublet at 7·47 and 7·58 corresponding to the carbonyl CH_2 of caprolactam split by an adjacent CHD group has a relative area of 2 and is therefore the original CH_2 group of IV. The three remaining hydrogen atoms of the CHD type at 8·28 had a relative area of 3. The intact CH_2 group in 4,5,6,7-tetradeuteriocaprolactam is therefore adjacent to the carbonyl group at position 3 and must have been adjacent to the carbonyl group in IV. This evidence gives strong support to the structure, 1,2-dihydro-2-keto-3H-azepine (IV–3H), for IV.

The corresponding thio analogue V, C_6H_2NS, can be made in low yield by irradiation of phenyl azide in anhydrous ether saturated with hydrogen sulfide. Compound

[20] Graciously communicated privately by Professor E. Vogel and R. Erb and now in print: E. Vogel, R. Erb, G. Lenz and A. A. Bothner-By, *Liebigs Ann.* **682**, 1 (1965).

[21] The assignments in caprolactam are given by G. V. D. Tiers, Characteristic NMR "Shielding Values", Minnesota Mining and Manufacturing Co., 28 March 1958, and are confirmed by analogy with the position of the CH_2 group in propionamide (7·77) and the N—CH_2 group in N-β-phenethylacetamide (6·52), both reported in NMR Spectra Catalog, Varian Associates, Palo Alto, California, 1962.

[22] L. Crombie, *J. Chem. Soc.* 1007 (1955).

[23] R. Mecke, Jr. and R. Mecke, Sr., *Chem. Ber.* **89**, 343 (1956).

V can also be prepared by the reaction of 2-amino(III)- or, more conveniently, 2-anilino-3H-azepine (II) with hydrogen sulfide in refluxing ethanol. The IR spectrum of V shows absorption at 3340 cm^{-1} indicative of the presence of an N—H bond and no absorption at 2480 cm^{-1} which would have indicated the presence of an S—H bond.

In assigning structures to II and III a prototropic ambiguity remains concerning the equilibrium point of attachment of the one and two protons, respectively, contained in the amidine group. This question cannot arise in connection with I and its structure may be considered established with the least ambiguity. Although the same problem arises in theory in IV and V, evidence from the IR points strongly to structures in which nitrogen bears the proton as it does in acyclic amides and thio amides.

It may be pertinent to this problem to point out that the NMR spectra of I, II and III are remarkably similar, but for the phenyl hydrogen atoms in II which mask one of the olefinic hydrogen atoms of the azepine ring and the N-hydrogen atoms of III which mask part of the olefinic region unless washed out with deuterium oxide. In molecules I, II and III, the methylene doublet at C_3 appears at 7·40 and 7·52, 7·23 and 7·37, and 7·33 and 7·43, respectively. In all these molecules, the olefinic hydrogen presumed to be at C_4 appears as a quartet, less well resolved than the other systems and easily interpretable as the imprecise superposition of two triplets: I: 4·83, 4·95, 5·09, 5·21; II: 4·66, 4·79, 4·92, 5·05; III: 4·49, 4·61, 4·76, 4·87. The C_5 hydrogen appears as a pair of doublets: I: 3·67, 3·76, 3·82, 3·92; II: 3·59, 3·68, 3·73, 3·83; III: 3·58, 3·68, 3·73, 3·82. The C_6 hydrogen likewise appears as a pair of doublets I: 4·28, 4·38, 4·41, 4·51: II: 4·12, 4·19, 4·25, 4·33; III: 4·02, 4·12, 4·15, 4·25. The C_7 hydrogen appears as a doublet in I and III and cannot be identified with certainty in II: I: 2·92, 3·04, III: 3·03, 3·17.

By contrast the system of olefinic hydrogens in IV and V, which both contain an N—H structure, are compressed within the range 3·63–4·66 and 3·60–4·61, respectively. These bits of evidence are interpreted to indicate identical ring structures for I, II and III and, thus, no hydrogen on the nitrogen atom of the azepine ring.

In respect of the mechanism of the photolyses of phenyl azide reported here, the same hypothetical scheme proposed by Huisgen and Appl[24,25] to accommodate the thermal "dibenzamil" rearrangement seems satisfactory. In this mechanism the hypothetical phenyl nitrene closes to the azacyclopropene,[26] 7-azabicyclo[4.1.0]hepta-2,4,6-triene, which then reacts with aniline to form the observed seven-membered ring. Impressed by the fact that the intermediate azacyclopropene did not appear to be involved in the thermolysis of phenyl azides in solvents other than amines, and that as good a nucleophilic reagent as thiophenol failed to trap the hypothetical intermediate, Smolinsky[27] suggested that the azacyclopropene might only be formed in concert with the addition of the amine. In at least one of the photolyses reported here another nucleophile, hydrogen sulfide, has reacted to give the ring-enlarged product.

Since previous photolyses of phenyl azides have not led to products of a type suggesting an intermediate azacyclopropene,[4] a fundamental difference between

[24] R. Huisgen and M. Appl, *Chem. Ber.* **91**, 12 (1958).
[25] M. Appl and R. Huisgen, *Chem. Ber.* **92**, 2961 (1959).
[26] G. Smolinsky, *J. Org. Chem.* **27**, 3557 (1962).
[27] G. Smolinsky, *J. Org. Chem.* **26**, 4108 (1961).

thermolysis and photolysis was indicated.[3] On the evidence of the present work one may credibly hypothesize phenyl nitrene[28] and the azacyclopropene in both types of decomposition.

EXPERIMENTAL[29]

Phenyl azide

The procedure given in "Organic Synthesis" [30] was followed with a modification which served to remove phenol and increase the stability of phenyl azide to storage. The modification, exemplified at five times the scale of the reference, involves repeated extraction of the combined ethereal extracts of the steam distillate with 2N NaOH until no phenol can be detected by a $FeCl_3$ test on the acidified extract. Concentration and vacuum distillation afforded 57 g (31%) of a light yellow, mobile oil: b.p. 53–54°/13 mm; $n_D^{25.5}$ 1·5591.

Photochemical reaction of phenyl azide in benzene

A refluxing solution of 2·5 g phenyl azide in 200 cc benzene was irradiated[29] for 4 hr by which time N_2 evolution had ceased. The benzene solution was concentrated to 50 cc by distillation and then steam-distilled from aqueous acid. Upon separation and concentration the benzene phase yielded an oily orange solid. Crystallization from aqueous EtOH gave 0·07 g (5%) orange needles, m.p. 61·0–62·5°. Further recrystallization yielded light orange needles, m.p. 67·0–67·5°; m.p. 67·5–68·0° in admixture with azobenzene.

Photochemical reaction of phenyl azide in acetic acid

A solution of 4 g phenyl azide in 350 cc glacial acetic acid was irradiated[29] for 24 hr in a flask connected to a gas burette. Within a few min gas evolution began and finally ceased after 500 cc had been collected. The acetic acid was removed from the clear, reddish orange solution by distillation at 50° under red. press. The residual, dark brown oil was partially dissolved in boiling n-heptane–benzene (1:1) leaving a dark brown, tarry residue which was separated. A mixture of large, brown needles and fine, white needles crystallized fron the filterate on cooling, These were separated by taking advantage of the large difference in their sedimentation rates in the solvent.

The large, brown needles, 0·8 g (12%), m.p. 149·0–151·0°, were recrystallized from MeOH to give colorless needles, m.p. 154·0–155·5°, or from aqueous EtOH as large plates, m.p. 154·5–155·5°; m.p. 154·0–155·5° in admixture with authentic *p*-acetoxyacetanilide.

The fine, white needles, 0·6 g (9%), m.p. 122·0–123·0°, were recrystallized from 95% EtOH to give material, m.p. 124·5–125·0°; m.p. 124·0–124·5° in admixture with authentic *o*-acetoxyacetanilide.

In a control experiment, an identical solution of phenyl azide in acetic acid was kept in the dark for 48 hr without change.

Photochemical reaction of phenyl azide in diethylamine

A clear, pale yellow solution of 15 g phenyl azide in 3 l. diethylamine was irradiated[29] at 15°. Gas evolution started within a few min and continued through most of the 16-hr reaction period. Most of the diethylamine was recovered from the dark brown solution by distillation on a steam bath until the residual volume was 100–200 cc.

The irradiation was repeated two more times in recovered diethylamine made up to 3 l. with fresh material as required. The combined residues were finally concentrated to approximately 200 cc by distillation on a steam bath. The remainder of the solvent was removed on a water bath at 50° under red. press. The residue was distilled *in vacuo* under N_2 through a 10″-Vigreux column and yielded 30·5 g (34%) 2-diethylamino-3H-azepine (I) as a pale yellow liquid, b.p. 81·0–83·5° mm, $n_D^{25.5}$ 1·5500. (Found: C, 73·3; H, 9·6; N, 17·4. $C_{10}H_{16}N_2$ requires: C, 73·1; H, 9·8; N, 17·0%.)

[28] See also J. H. Hall, J. W. Hill and H. Tsai, *Tetrahedron Letters* 2211 (1965).

[29] All irradiations were carried out in Pyrex flasks with a model "L" Hanovia Mercury Vapor lamp and a plate glass filter transmitting UV light between 325–366 mμ. M.ps are corrected. Microanalyses are by Schwarzkopf Microanalytical Laboratories, 56-19 37th Ave., Woodside 77, New York.

[30] *Organic Synthesis* Col. Vol. III, p. 710. J. Wiley, New York (1955).

Further purification of I was effected through its picrate. A solution of 0·192 g I in 4 cc absolute EtOH saturated with picric acid yielded 0·297 g of the yellow picrate of I, m.p. 98·0–99·5°. A second crop obtained by concentration of the filtrate weighed 0·070 g: m.p. 97·0–98·5°. The combined fractions (80%) gave yellow plates, m.p. 99·0–100·0°, on recrystallization from 95% EtOH. (Found: C, 48·9; H, 5·2; N, 18·1. $C_{16}H_{19}N_5O_7$ requires: C, 48·9; H, 4·9; N, 17·8%.)

The regeneration of I from its picrate was effected by shaking 2·3 g of the picrate with 4 cc sat LiOH aq and 10 cc ether. Separation and repeated extraction of the ether phase with LiOH alternated with water, finally produced an almost colorless ether phase. The ether solution was dried over pellets of KOH, decanted, and concentrated to an oil by distillation through a small Vigreux column. Evaporative distillation of the residue at 2 mm with a pot temp of 65–80° afforded 0·806 g (85% based on picrate) of pure I, a colorless mobile liquid: $n_D^{25.5}$ 1·5513, d^{21} 0·9632. (Found: C, 73·4; H, 9·6; N, 17·0. $C_{10}H_{16}N_2$ requires: C, 73·1; H, 9·8; N, 17·0%.)

Hydrogenation of 2-*diethylamino*-3H-*azepine* (I)

A solution of 3·15 g I in 15 cc 95% EtOH was hydrogenated using 0·7 g 5% Pd–$BaCO_3$. The total absorption of H_2 was 101% of the theoretical quantity calculated for 2 molar equivs. The filtered solution was concentrated by distillation through a Vigreux column. Distillation *in vacuo* afforded two fractions with the same refractive index: b.p. 58–63°/1 mm. The combined fractions of 2-diethylamino-4,5,6,7-tetrahydro-3H-azepine (Chart I, A) weighed 1·95 g (60%): $n_D^{25.5}$ 1·4892; d^{21} 0·9145. (Found: C, 71·8; H, 11·7; N, 16·5. $C_{10}H_{20}N_2$ requires: C, 71·4; H, 12·0; N, 16·7%.)

In the NMR spectrum of this molecule, it appeared from quite satisfactory determinations of relative areas that three methylene groups were located between 6·7 and 6·9. To be sure of presence of the third methylene group the two methylene groups from the diethylamino group were contracted to a singlet (at 6·78) by decoupling the methyl groups at 8·95. The third methylene then appeared clearly as a broad multiplet centered about 6·75.

A solution of 0·122 g 2-diethylamino-4,5,6,7-tetrahydro-3H-azepine and 3·4 cc absolute EtOH saturated with picric acid afforded 0·111 g (39%) of bright yellow needles of the picrate of tetrahydro I, m.p. 108·0–109·0°. The m.p. was raised to 109·0–109·5° by recrystallization from 95% EtOH. (Found: C, 48·9; H, 6·3; N, 17·6. $C_{16}H_{23}N_5O_7$ requires: C, 48·4; H, 5·8; N, 17·6%.)

Hydrolysis of 2-*diethylamino*-4,5,6,7-*tetrahydro*-3H-*azepine* (*Chart* I, A)

A stream of N_2 was passed successively through a refluxing solution of 3 g $Ba(OH)_2 8H_2O$ and 0·253 g tetrahydro-I in 5 cc water, a drying tube filled with KOH and a 2% ethanolic solution of picryl chloride. After 2 hr no more N,N-diethylpicramide precipitated and the hydrolysis was stopped.

The yield of N,N-diethylpicramide was 0·091 g (21%), m.p. 165·0–166·5°. Recrystallization from acetic acid raised the m.p. to 166·5–167·0°; m.p. 166·5–167·5° in admixture with authentic N,N-diethylpicramide.

The clear aqueous solution was diluted to 500 cc with water, saturated with carbon dioxide, refluxed, and filtered to remove $BaCO_3$, which was washed with hot water. The combined filtrate and washings were concentrated by distillation. When the volume was very small, the remainder of the water was evaporated under N_2 on a steam bath. The solid residue was extracted with hot MeOH. Evaporation of the solvent from the MeOH extract under N_2 afforded 0·186 g of a slightly brown material. Crystallization from MeOH yielded 0·159 g (80%) of a slightly brown solid m.p. 199·0–200·5°. Recrystallization from MeOH produced colorless crystals, m.p. 203·0–203·5° (dec); m.p. 203·5–204·0° in admixture with ε-aminocaproic acid (reported m.p. 202–203°).[21]

Photolysis of phenyl azide in a solution of aniline in trimethylamine

A solution of 1·19 g phenyl azide and 0·93 g aniline in 100 cc trimethylamine was irradiated for 8 hr during which time the reaction gradually became dark yellow and deposited a dark, solid. Evaporation of the trimethylamine left an oil which partially dissolved in 35 cc 2N HCl. The aqueous extract was extracted with two 50-cc portions of ether, treated with 50 cc 2N NaOH and then extracted with two 25-cc portions of benzene.

After concentration to roughly 25 cc, the benzene solution was chromatographed on a column of Alcoa F-20 alumina: dark brown material was strongly absorbed while yellow material was eluted

[21] S. Gabriel and T. A. Maass, *Ber. Dtsch. Chem. Ges.* **32**, 1259 (1899).

with benzene; further elution with ether removed 0·075 g of a yellow solid of m.p. 118–144°. Crystallization from 95% EtOH afforded 0·036 g (2%) of II, m.p. 149–151·5°; recrystallization gave material, m.p. 151·0–152·5° alone and 151·5–153·0° in admixture with an authentic sample of m.p. 152·0–153·0°, prepared according to Wolff[10] in much the same manner as that described by Huisgen, Vossius and Appl.[8]

Hydrogenation of 5·40 g of the amidine in 15 cc 95% EtOH over 0·3 g of a Pd catalyst (5% on $BaCO_3$) resulted in the uptake of 95·5% of 2 equiv H_2. Filtration, concentration and sublimation yielded 4·95 g (90%) 2-phenyliminohexamethylenimine, m.p. 103·5–105·0° alone and m.p. 103·5–105·5° in admixture with an authentic sample of m.p. 105° prepared according to Oxley and Short.[19] Solution of 0·58 g of this amidine in 4 cc of an ethanolic solution of picric acid saturated at room temp afforded 0·30 g (85%) of the picrate, m.p. 151·5–152·0°. Two recrystallizations from 95% EtOH yielded pure 2-phenyliminohexamethyleniminium picrate; m.p. 161·0–162·0° alone and m.p. 160·5–162·0° in admixture with an authentic sample[19] of m.p. 161–162°. (Found: C, 76·9; H, 8·8; N, 15·0. Calc. for $C_{12}H_{16}N_2$: C, 76·6; H, 8·6; N, 14·9%.)

Hydrolysis of 2-phenyliminohexamethylenimine was effected by heating a 0·604-g sample in 5 cc 20% H_2SO_4 in a sealed tube at 195–200° for 5 hr. The solution was made basic by adding an excess $Ba(OH)_2$aq, concentrated to ca. 20 cc, saturated with NaCl and extracted with ether. After being dried over KOH and concentrated by distillation, the ether extract gave an oil which when dissolved in 3 cc 2% ethanolic picryl chloride, deposited 0·080 g (8%) of orange precipitate, m.p. 180·8–181·2°. Recrystallization from glacial acetic acid gave picranilide, m.p. 181·0–181·5° alone and in admixture with an authentic sample.

The $Ba(OH)_2$ solution was diluted to 200 cc, saturated with CO_2, filtered, concentrated to 10 cc by distillation and then taken to dryness on a steam bath by a stream of N_2. The solid was extracted with 1·5 cc boiling MeOH. Addition of 4 cc ether to the cooled methanolic solution gave 0·100 g (24%) of tan solid, m.p. 192–197°. Recrystallization from MeoH gave colorless ϵ-aminocaproic acid, m.p. 203° (dec) alone and in admixture with authentic material.

Photolysis of phenyl azide in liquid ammonia

A solution of 5·00 cc (5·45 g) phenyl in 1 l. of liquid ammonia was irradiated for 7 hr in a vacuum-jacketed Pyrex flask fitted with a Dry-Ice condenser. The residue from evaportaion of the ammonia was extracted with 25 cc boiling benzene. Concentration of the dark brown solution to 4 cc afforded 1·35 g brown crystals; m.p. 85–90·5°. Sublimation at 80–90°. and 0·2–0·3 mm yielded 1·22 g (25%) of colorless 2-amino-3H-azepine, (III), m.p. 90·0–91·0°. (Found: C, 66·4; H, 7·2; N, 25·7. $C_6H_8N_2$ requires: C, 66·6; H, 7·5; N, 25·9%.)

The mixing of 1·7 cc saturated absolute ethanolic picric acid and a solution of 0·50 g III in absolute EtOH afforded 0·135 g (87%) of the crystalline picrate of III, m.p. 195·5–197·0° (m.p. 200·0–201·0° (dec) after recrystallization from 95% EtOH). (Found: C, 42·9; H, 3·5; N, 20·7. $C_{12}H_{11}N_5O_7$ requires: C, 42·7; H, 3·3; N, 20·8%.)

Hydrogenation of 0·131 g III was effected in 10 cc ether with 0·02 g Pd catalyst (5% on $BaCO_3$). The ethereal solution was filtered, concentrated and treated with 3 cc of a saturated benzene solution of picric acid. The precipitated picrate (0·295 g; 75%; m.p. 193·5–195·5°) was recrystallized from 95% EtOH ; m.p. 195·5–196·5°; reported[19] m.p. 195·5–196·5°. (Found: C, 42·4; H, 4·4; N, 21·0. Calc. for $C_{12}H_{15}N_5O_7$: C, 42·2; H, 4·4; N, 20·5%.)

An attempt to improve the yield of III by using potassium amide led to reduction. When 2·38 g phenyl azide was added to 2·19 g potassium amide in 200 cc liquid ammonia, a vigorous reaction took place. After 1 hr 4 cc MeOH was added, ammonia was allowed to evaporate and the residue was shaken with a mixture of 50 cc ether and 100 cc water. After separation, the aqueous phase was extracted with 50 cc ether which was united with the first extract. Concentration and evaporative distillation at 50° and 2–3 mm afforded 0·92 g (50%) aniline which was converted by the Schotten-Baumann procedure to acetanilide, m.p. 114–115·0° alone and in admixture with an authentic sample.

Hydrolysis of 2-amino-3H-azepine to 1,2-dihydro-2-keto-3H-azepine (IV)

After being refluxed in 2 cc water for 5 hr, 0·108 g III no longer evolved ammonia. The chilled solution was acidified with 5 drops 2N HCl and extracted 5 times with 1 cc each of $CHCl_3$. Concentration of the dried (anhydrous $MgSo_4$) extract afforded an oil which was distilled in a sublimator at 50–70° and 0·3–0·5 mm to give 0·096 g (88%) of colorless, crystalline material, m.p. 47·0–49·0°. One

recrystallization from cyclohexane and a second sublimation afforded colorless plates of IV, m.p. 47·5–48·5°. (Found: C, 66·3; H, 6·3; N, 12·7. Calc. for C_6H_7NO: C, 66·0; H, 6·5; N, 12·8%); reported[20] m.p. 48–50°.

Hydrogenation of 0·108 g IV in 5 cc 95% EtOH with a Pd catalyst (5% on $BaCO_3$) resulted in the absorption of 96% of 2·0 theoretical equivs H_2. Filtration, evaporation of solvent under N_2 and sublimation of the residue at 70–100° and 0·1–0·3 mm afforded 0·108 g (96%) of caprolactam (2-ketohexamethyleneimine); m.p. 66·5–69·0°. Although recrystallization from cyclohexane failed to raise the m.p., recrystallization from benzene gave material of m.p. 67·5–69·5° (m.p. 68·0–69·5° in admixture with a sample of authentic material of m.p. 67·9–69·4°).

Hydrogenation of 0·216 g IV in 15 cc 95% EtOH with deuterium and a Pd catalyst (5% on $BaCO_3$) resulted in the absorption of 2·0 theoretical equivs of deuterium. Filtration, evaporation of solvent under N_2 and sublimation of the residue at 100° and 0·5 mm afforded 0·220 g (95%) of 4,5,6,7-tetradeuteriocaprolactam; m.p. 68·5–70·0°. This material was used for the NMR studies without further purification.

1,2-*Dihydro-2-thienoketo*-3H-*azepine* (V)

(a) *Photolysis of phenyl azide in anhydrous ether saturated with hydrogen sulfide.* While H_2S was being bubbled through slowly and continuously, a solution of 1·09 g phenyl azide in 200 cc anhydrous ether was irradiated[29] for 8 hr. The dark yellow solution was then concentrated to 50 cc by distillation, filtered and chromatographed on Alcoa F-20 alumina. After anhydrous ether would elute no more material, moist ether eluted a reddish brown band. The resulting solid material was sublimed at 90–100° at 0·3–0·5 mm and yielded 0·065 g of light yellow powder, m.p. 101·5–105·5°. Recrystallization from benzene gave 0·054 g (5%) of 1,2-dihydro-2-thienoketo-3H-azepine (V) in the form of light yellow plates; m.p. 106·0–107·5°. (Found: C, 57·8; H, 5·4; N, 11·2; S, 25·8. C_6H_7NS requires: C, 57·6; H, 5·6; N, 11·2; S, 25·6%.)

An attempt to improve the yield by carrying the reaction in triethylamine led to reductions. When H_2S was bubbled into 30 cc trimethylamine containing 0·45 g phenyl azide, one equiv N_2 was evolved and collected in an azotometer. The viscous red oil which precipitated during the reaction was removed by decantation and recrystallized from benzene to afford S; melting at 111·5°, resolidifying and finally melting at 117·5–118·5°.

The solution of trimethylamine was treated with 1 cc acetic anhydride, concentrated by distillation first at atm. press. and finally *in vacuo*. Crystallization from water afforded 0·35 g (69%) acetanilide; m.p. 111·0–112·0°. One recrystallization from 95% EtOH afforded colorless material; m.p. 114·0–115·0° alone and m.p. 114·0–115·0° in admixture with authentic acetanilide of m.p. 114·5–115·5°.

(b) *Reaction of* 2-*anilino*-3H-*azepine* (II) *with hydrogen sulfide.* Hydrogen sulfide was bubbled through the refluxing solution of 10·0 g II in 35 cc absolute EtOH for 45 hr. The solution was decanted and concentrated to an oil which was triturated with ether. The ethereal solution was extracted with 2N HCl. When this acidic extract was made alkaline with 2N NaOH, a precipitate (0·15 g, m.p. 143–150°) was obtained. The ethereal solution was concentrated to a solid which was sublimed at 105° and 0·3–0·5 mm to afford 0·22 g (33%) of light yellow needles, m.p. 100·5–103·0°. Recrystallization from benzene gave pure V, m.p. 107–108° alone and in admixture with the sample above.

(c) *Reaction of* 2-*amino*-3H-*azepine* (III) *with hydrogen sulfide.* With H_2S bubbling through continuously, a solution of 1·22 g III in 10 cc absolute EtOH through which H_2S was passed continuously, was refluxed for 3 hr. On being cooled, the solution deposited 0·336 g of yellow plates, m.p. 106·5–108·0°. Concentration of the ethanolic filtrate gave a brown solid, which was sublimed at 80–100° and 1–2 mm to afford an additional 0·961 g of material; m.p. 99·5–106·5°. Recrystallization from benzene and resublimation afforded 0·789 g V, m.p. 106·0–107·5° alone and 107·0–107·5° in admixture with the sample obtained from III. The total yield of 1·125 g corresponds to 80% of theory.

Rearrangement of 2-*diethylamino*-3H-*azepine* (I) *with* p-*nitrobenzoyl chloride*

After being refluxed for 15 min, a hot solution of 0·500 g I and 0·600 g *p*-nitrobenzoyl chloride in 5 cc anhydrous pyridine was poured onto 50 g ice. The resulting yellow oil solidified (0·835 g; m.p. 56–63°) and was recrystallized from 95% EtOH [0·475 g (50%); m.p. 73·5–74·5°]. After one additional crystallization, the m.p. was raised to 74·5–75·5°.

Authentic *o*-(*p*-nitrobenzamido)-diethylaniline was prepared by boiling 1·0 g *o*-diethylaminoaniline and 1·2 g *p*-nitrobenzoyl chloride in 5 cc anhydrous pyridine under reflux for 15 min. The red oil which separated when the solution was poured into 50 cc water solidified (1·00 g, 52%; m.p. 69·0–74·0°) and was recrystallized from 95% EtOH as pale yellow needles; m.p. 75·0–75·5° and 75·0–75·5° in admixture with the sample above. (Found: C, 65·3; H, 6·1; N, 13·7. Calc. for $C_{17}H_{19}N_3O_3$: C, 65·2 H, 6·1; N, 13·4%.)

Rearrangement of 2-anilino-3H-azepine (II)

After being boiled under reflux for 5 min, a mixture of 1·0 g II and 1·84 g acetic anhydride was diluted with 5 cc water, cooled and extracted with 10 cc ether. The ether layer was washed with 2N HCl and with water, and then concentrated to a solid: 0·25 g (22%); m.p. 119·5–121·0° after recrystallization from 95% EtOH. A second crystallization from EtOH raised the m.p. to 121·5–122·0°. This material did not depress the m.p. of authentic *o*-acetamidodiphenylamine, m.p. 121·5–122·0°.