NEW DIMERIC PRODUCTS FROM THE THERMAL AND PHOTOCHEMICAL DECOMPOSITION OF 2-AZIDOPHENAZINE§

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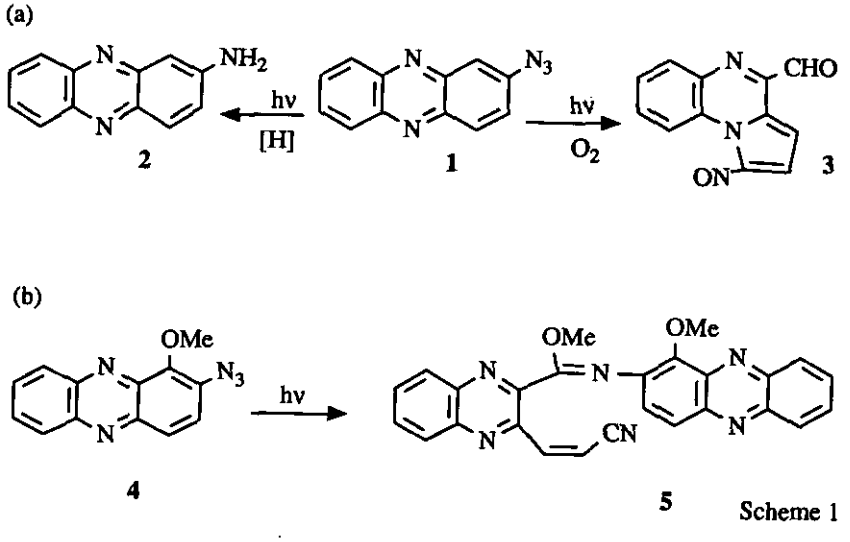
Abstract - Re-examination of the thermal and photochemical decomposition of 2-azidophenazine reveals new pathways. Thus, besides reduction to the amine, the triplet nitrene yields the azo derivative and phenazino[1',2':5,6]pyridazino[4,3-a]phenazine while the singlet nitrene rearranges to the dehydroazepine and adds a further molecule of azide to yield an open-chain imine. The factors leading to the predominance of "dimeric" products from this type of heterocyclic azides are discussed.

Extensive studies by Suschitzky[1] and by other authors[2-6] showed that triplet arylnitrenes are considerably stabilized with respect to their aliphatic counterpart and abstract hydrogen much less efficiently ("lazy triplets").[1] This description is even more appropriate for the triplet nitrenes of electron-poor heterocycles. In a study of the thermal and photochemical decomposition of 2-azidophenazine (**1**) we observed that hydrogen abstraction by the nitrene to yield 2-aminophenazine (**2**) required a good hydrogen donor as the solvent and/or a high temperature.[7] An unexpected finding, however, was that photodecomposition of **1** in non hydrogen-donating solvents gave mainly 1-nitrosopyrrolo[1,2-a]quinoxaline-4-carboxyaldehyde (**3**) by reaction with oxygen dissolved in the solvent while under degassed conditions no tractable product was obtained (Scheme 1a). In later studies we found that with some substituted 2-azidophenazines an unprecedented nitrene-azide addition took place, e.g. the 1-methoxy

§ Dedicated to professor Edward C. Taylor on occasion of his 70th birthday.

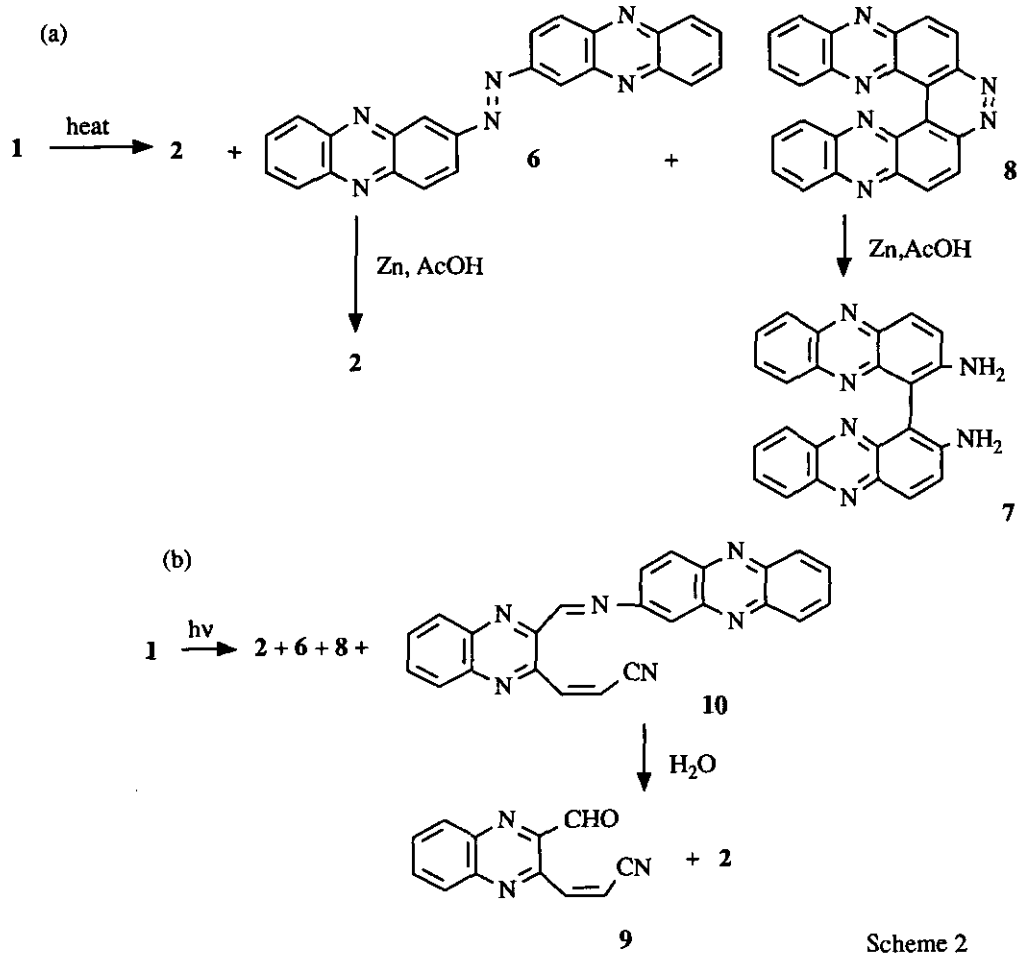


Scheme 1

derivative (4) gave compound (5) as one of the main products (Scheme 1b).[8,9] This led us to reconsider the decomposition of the parent compound (1) under deoxygenated conditions. As it appears from the following, this work did in fact reveal new significant features.

RESULTS

Thermal decomposition. Thermolysis of 10^{-3}M solutions of 2-azidophenazine (1) in various solvents was carried out in sealed vials at 140°C for 3 h after vacuum degassing. Under these condition decomposition of 1 occurred to a various extent and in every case the main product was, as expected, the amine (2) (Table 1, Scheme 2). However, in non hydrogen donating media a substantial amount of a highly insoluble brown material was also formed. Solubilization and chromatography of small portions of this material was possible and showed that it contained a mixture of two yellow crystalline solids. The more abundant one had formula $C_{24}H_{14}N_6$ (twice the nitrene) as shown by analysis and mass spectrum, was a 2-substituted phenazine as shown by the nmr spectrum, and was cleanly reduced to the amine (2) by treatment with zinc in acetic acid. Thus, it was the previously unreported trans-2-azophenazine (6). The latter one had formula $C_{24}H_{12}N_6$, showed a prominent $(M-N_2)^+$ peak in the mass spectra and was a 1,2-disubstituted phenazine (nmr). Reduction with Zn/AcOH gave a red solid of formula $C_{24}H_{16}N_6$. Since its



Scheme 2

Table 1. Products from the thermolysis of azide (1) for 3 h at 140°C

Solvent	% Converted	Yield % of the products		
	(1)	(2)	(6)	(8)
Tetraline	94	98	traces	-
Decaline	92	76	traces	-
n-Hexane	62	59	traces	traces
Cyclohexane	62	47	traces	traces
Acetonitrile	58	49	3	2
Benzene	38	33	25	6
Carbon tetrachloride	46	17	16	4

nmr spectrum showed only the signals of a 1-substituted 2-aminophenazine, this compound was the diamine (7), and the yellow solid from which it was obtained was the new heterocycle (8). When partially degassed benzene solutions of 1 were used, some percents of product (3) were also formed.

Photochemical Reactions. Irradiation of 10^{-3}M solutions of azide (1) in various solvents for 15 min after deoxygenation by flushing with purified argon caused in every case the complete decomposition of the substrate. Chromatographic separation as above gave the amine (2), the azo compound (6), the heterocycle (8) as well as small amounts of the previously recognized quinoxalinecarboxyaldehyde (9). However, two-dimensional tlc showed the last compound was not present in the photolysed solution, but was formed after prolonged stay in the absorbed state. Likewise, spectroscopic examination of the fresh photolisate showed none of that product, while if the solution was left in contact with silica gel for some hours the appropriate spectroscopic signals became apparent (diagnostic was the aldehyde absorption at δ 10.25 in nmr and 1720 cm^{-1} in ir). Quantitative analysis was possible by hplc. This showed that the silica gel treatment generated compound (9) and increased the amount of amine (2). Thus, one of the products from the photolysis of 1 underwent silica gel induced hydrolysis to yield the aldehyde (9) and part of the amine (2), the process yielding roughly equivalent amounts of the two products. An obvious canditate for this intermediate was the imine (10). Indeed, examination of the fresh photolysate showed that a product containing the -CH=CH-CN moiety was already present (ir absorption at 2219 cm^{-1}, doublet at 5.95 δ, J=11 Hz, in nmr; remember that product (9) was not present at this stage).

DISCUSSION

This work confirms that intermediate (11), a typical heterocyclic nitrene, is a poor hydrogen abstractor. Except than with good hydrogen donors like tetraline, formation of the amine (2) is thermally activated (see the photolises in cyclohexane). The thermal decomposition of the azide in probably catalyzed by radicals formed in the reaction, and is faster in better hydrogen donating solvents.

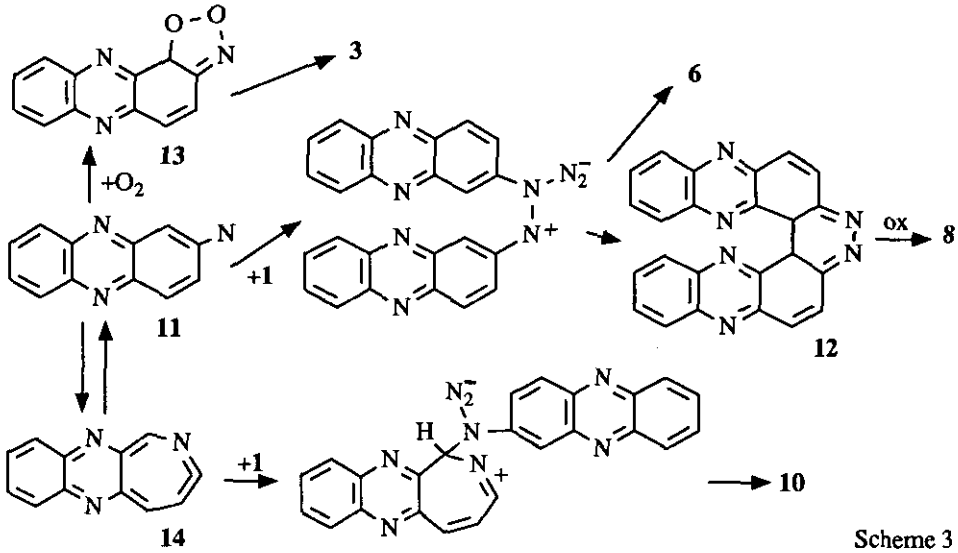
Furthermore the characteristic oxygen addition to yield product (3) takes place also under thermal conditions, though in low yield.

The most striking result is that all the other products are dimeric. One of these is the azo derivative (6). This is the expected product from "lazy" triplets,[1] and reasonably arises from the addition of the triplet nitrene to the ground state azide. Previous

Table 2. Products from the photolysis of azide (1) for 15 min[a]

Solvent	Assay	Yield % of the products			
		(2)	(6)	(8)	(9)
Tetraline	b	85	traces	-	-
Decaline	b	18	d	5	-
	c	27	12	5	traces
n-Hexane	b	7	d	11	-
	c	25	32	12	8
Cyclohexane	b	9	d	10	-
	c	15	23	11	6
Cyclohexane (80°C)	b	17	d	9	-
	c	19	15	10	5
Benzene	b	8	d	12	-
	c	22	11	14	7
Acetonitrile	b	15	d	19	-
	c	19	19	19	5

a. At room temperature unless otherwise stated. Conversion of azide (1) is in every case 98%. b. Hplc assay of the photolyzed solution. c. Hplc assay of the photolyzed solution left 18 h over silica gel. d. Not determined under these conditions.



Scheme 3

evidence for azo compounds from condensed heterocycles is scarce, but such products may have been overlooked due to their insolubility.

The other dimeric products are less usual. The heterocycle (**8**) is obtained both by thermolysis and by photolysis and even in the latter case it is not formed by a secondary photocyclization of the azo derivative (**6**), which is stable under these conditions (there is a literature precedent for the azobenzene → benzo[c]cinnoline photocyclization, but only in concentrated sulfuric acid).[10] Apparently the nitrene-azide adduct has another path available besides formation of the azo compound (**6**), viz cyclization to the dihydro derivative (**12**) which rearomatizes to the observed product.

The processes discussed up to now are those occurring under thermolytic condition. If it is reasonably assumed that such stables nitrenes thermally equilibrate before reacting, all these reactions can be attributed to the lower lying state, viz to the triplet.

Together with the previous finding of the reaction with oxygen suggested to occur via intermediate (**13**), these results show that extensive spin delocalization on the aromatic ring, while limiting the "normal" reactivity (hydrogen abstraction), opens new reactive paths involving in fact an attack to the ring, such as those leading to adducts (**12**) and (**13**).

Under photochemical conditions a further process is observed besides the previous ones. This leads again to a dimeric product but in this case the aromatic ring is cleaved. Analogy with previous cases[8,9,11-13] suggests that this reaction involves the dehydroazepine (**14**). Thus at room temperature (or below: the product distribution by irradiation at -20°C is the same that at +20°C) the singlet cyclizes to the dehydroazepine and this reacts at the very electrophile carbon atom in position 1 even with a weak nucleophile such as the ground state azide. This reaction is strictly analogous to that observed with the methoxyazide (**4**), although in that case it occurs with a higher yield, since the substituent favours the rearrangement to the dehydroazepine. As it may be expected the imine (**1c**) is more sensitive to hydrolysis than the iminoether (**5**) obtained from **4**, and it does not survive chromatography. However, unambigous proof of its formation was reached, as shown above.

It is important to reiterate that when oxygen is present, irradiation of azide (**1**) in non hydrogen-donating solvents mainly leads to product (**3**).[7] Thus in the presence of oxygen, the fast reaction from the triplet predominates over the slow reaction of the first-formed singlet nitrene with the weakly nucleophilic azide. On the other hand, in

the absence of fast triplet paths, the singlet reaction becomes significant. This suggests that singlet and triplet nitrene are in equilibrium. This is the same situation we found with all the azides of this type we studied,[8,9] viz with these strongly delocalized nitrenes change in spin multiplicity introduces no barrier and the reaction proceeds from either state according to which reaction is favoured by conditions. Apart from mechanistic intricacies, once again we found that the reaction of this type of azides is a useful and versatile tool for the synthesis of new heterocycles.

EXPERIMENTAL

2-Azidophenazine (**1**) was prepared and purified as previously described.[7] The spectra were taken with the following instruments. Ir: Perkin Elmer 287; nmr: Bruker 300 MHz; mass: Finnigan MAT; uv: Kontron Uvikon 941. Elemental analyses were performed by means of a Carlo Erba microanalyzer.

Preparative irradiation. A solution of the azide (**1**) (150 mg, 0.67 mmol) in 150 ml of acetonitrile (previously dehydrated by in situ azeotopic distillation was flushed with purified argon for 25 min and then irradiated for 20 min in a water-cooled immersion well apparatus by means of a Phylips HPK 125 W medium pressure lamp through Pyrex while lively stirring. A brown precipitate was formed and adhered to the walls of the vessel. The precipitate and the residue from the evaporation of the photolyzed solution were dissolved in $CHCl_3$ (70 ml) and chromatographed on a silica gel (Merck 60 HR) column prepared in benzene, and eluted with $CHCl_3$–AcOEt 8:2 to 1:1 mixtures to yield unreacted (**1**) (4 mg), the aldehyde (**9**) (9 mg, 6%), two fractions containing products (**6**) (18 mg, 14%) and (**8**) (25 mg, 20%) each one somewhat contaminated by the other product, as well as 2-aminophenazine (**2**) (28 mg, 21%).

trans-2-Azophenazine (**6**). Pure samples were obtained by repeated recrystallyzation from large amounts of $CHCl_3$. Orange crystals, mp > 250°C. *Anal. Calcd for* $C_{24}H_{14}N_6$: C, 74.60; H, 3.65; N, 21.75. Found: C, 74.40, H, 3.41; N, 21.89. Nmr ($CDCl_3$) δ 7.93 (m, 2H, H-7 and H-8), 8.33 (m, 2H, H-6 and H-9), 8.39 (d, J=9.5, 1H, H-4), 8.61 (dd, J=2, 9.5, 1H, H-3), 8.99 (d, J=2, 1H, H-1). Ir (Nujol) 3040, 1515, 1360 cm^{-1}. Mass (Chemical ionization) 386 (base peak), 196 (18%) *m/z*. Uv ($CHCl_3$), 398 *nm* (ϵ 5.09×10^4), 338 (6.27×10^4).

Phenazino[1',2':5,6]pyridazino[4,3-a]phenazine (**8**). Pure samples were obtained by repeated semicrystallization from $CHCl_3$ and final recrystallization from AcOH (10 mg from 35 ml). Yellow crystals, mp > 250°C. Anal. Calcd for $C_{24}H_{12}N_6$: C, 74.99; H, 3.15; N, 21.87. *Found:* C, 74.71; H, 3.04; N, 21.52. Nmr ($CDCl_3$) δ 7.74 (d, J=8, 1H, H-2), 7.81

(m, 1H, H-3), 8.00 (m, 1H, H-4), 8.41 (d, J=8, 1H, H-5), 8.53 (d, J=9, 1H, H-8), 8.88 (d, J=9, 1H, H-7). Ir (Nujol) 3040, 1535, 1340 cm^{-1}. Mass (Chemical ionization) 384 (94%), 356 (base peak), 178 (22%) m/z. Uv ($CHCl_3$) 389 nm (ϵ $1.26x10^4$), 303 ($3.12x10^4$).

Thermal reactions. 2 ml of $1x10^{-3}$M solutions of the azide (**1**) in the appropriate solvent were pipetted in Pyrex tubes and degassed by five degas-freeze-thaw cycles. The tubes were sealed and heated in a thermostated bath at 140°C for 3 h. The solution was evaporated, the residue dissolved in $CHCl_3$ and analized by hplc (Supelcosil™ LC-Si column, 25 cm x 4.6 mm, eluting with benzene-AcOEt 1:1 mixture, analyzing at 360 nm, internal standard 1-ethoxy-2-aminophenazine).

Photochemical reactions. 2 ml of $1x10^{-3}$M solutions of the azide (**1**) in the appropriate solvent were pipetted in 1 cm spetrophotometric couvettes, deaerated by flushing with purified argon for 20 min and then irradiated for 15 min by means of a focalized Osram HBO 150W high pressure mercury arc through a Pyrex ir absorbing filter while maintaining the argon stream. The solution was evaporated and the residue taken up in 5 ml of $CHCl_3$. Part of the solution was directly analyzed as above (see Table 2, b). To 2 ml of this solution 100 mg of silica gel were added. After 24 h the solution was filtered, and the silica gel washed repeatedly with AcOEt-$CHCl_3$ 1:1 mixture. The combined organic phase was evaporated and the residue was dissolved in $CHCl_3$ and analyzed as above (see Table 2,c).

Reduction of compound **6**. Compound (**6**) (6 mg, 0.015 mmol) was dissolved in 50 ml of AcOH by sonnication at 60°C, and then 50 mg (0.75 mmol) of zinc dust were added and the mixture was left overnight. The red solution obtained was evaporated under reduced pressure and the residue taken up with 20 ml of EtOH + 5 ml of conc. NH_4OH. The solution was evaporated and the residue was extracted with $CHCl_3$ (50 ml) to yield 5.5 mg (90%) of the amine (**2**) .

Reduction of compound **8**. Compound (**8**) (40 mg, 0.1 mmol) was dissolved in 200 ml of hot AcOH containing 10 ml of H_2O. The solution was cooled to 20°C and 400 mg (6 mmol) of zinc dust were added (40 mg portion every 2 h). The mixture was evaporated under reduced pressure, and the residue was treated with 10 ml of H_2O-10 ml of conc. NH_4OH and evaporated again. The residue was grinded and extracted with 7x50 ml of hot AcOEt. The organic phase was evaporated, the residue was dissolved in 100 ml of $CHCl_3$, and chromatographed on a silica gel column (7 g) eluting with benzene-AcOEt 8:2 to 1:1 mixtures to yield 2-amino-1-[1'-(2'-aminophenazinyl)]phenazine (**7**, 9.5 mg, 23%) brick-red crystals, mp > 250°C (from EtOH) (8 mg from 100 ml). Anal. Calcd for $C_{24}H_{16}N_6$:

C, 74.21; H, 4.15; N, 21.64. Found: C: 74.8; H, 4.11; N, 21.63. Nmr (DMSO) δ 5.72 (s, exch, 2H) 7.63 (s, 2H, H-3 and H-4), 7.72 (dd, J=8,1, 1H, H-8), 7.64 (m, 1H), 8.09 (m, 1H) (H-7 and H-8), 7.72 (dd, J=8, 1, 1H, H-9). Ir (nujol) 3470, 3300, 3197, 1628, 1597 cm^{-1}. Mass (Chemical ionization) 388, 372 (base peak), 356 (20%) m/z. Uv ($CHCl_3$) 440 nm (ϵ $1.12x10^4$), 361 ($1.32x10^4$). Compare 2-aminophenazine:ir 3393, 3319, 3200, 1642, 1597 cm^{-1}; uv 436 nm (ϵ $8.53x10^3$), 361 ($6.87x10^3$).

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