A KINETIC STUDY OF N-NITROSAMINE PHOTODECOMPOSITION

by

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TO MY LATE PARENTS

ABSTRACT

The photodecomposition of nitrosamines has been studied both on a preparative scale and by flash photolysis. The catalytical effect of acid media for the photodecomposition is clearly demonstrated as previously observed. Kinetic evidence by flash photolysis shows that cyclohexene reacts with the transient precursor of N-nitrosopiperidine with a rate constant of $1 \times 10^{11} M^{-1} S^{-1}$ which greatly exceeds the diffusion controlled rate constant. The result is interpreted as the reaction from a ground state complex of N-nitrosopiperidine, olefin and proton which adds from its lowest excited singlet state.

The N-nitrosopiperidine transient observed by flash excitation of the $\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ transition band of the nitrosamine in methanol solution has been assigned to the piperidinium radical on the bases of its absorption spectrum, absence of oxygen quenching, mixed solvent study and quenching experiments of different triplet transients. The assignment is substantiated by the isolation of the Hofmann Löeffler rearrangement product, 4-(N-nitrosohydroxylamino)-dipentylamine, in the photodecomposition of N-nitrosodi-n-pentylamine. The aminium radical is believed to be derived from the lowest excited singlet state of the nitrosamine. No emission has been detected for N-nitroso-

piperidine and N-nitroso-N-methylaniline, but the triplet energy of the former is estimated to be about 59 kcal/mole by quenching the triplet of 2,2´-binaphthyl. Preparatively, the photodecomposition products obtained from the $\pi \rightarrow \pi^*$ excitation of the nitrosamine (2537A) is shown to be different from those from the $n \rightarrow \pi^*$ excitation. With 2537A light, elimination of HNO to the corresponding alkylimine constitutes the major product. In contrast, the major product documented in literature with $\lambda > 290$ nm excitation of the nitrosamine is the corresponding amidoxime. The wavelength dependence of product formation is ascribed to the difference in vibrational energy possessed by the aminium radical as a consequence of the difference in excitation energy. A mechanism is proposed to account for the formation of the photodecomposition products.

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CHAPTER 1

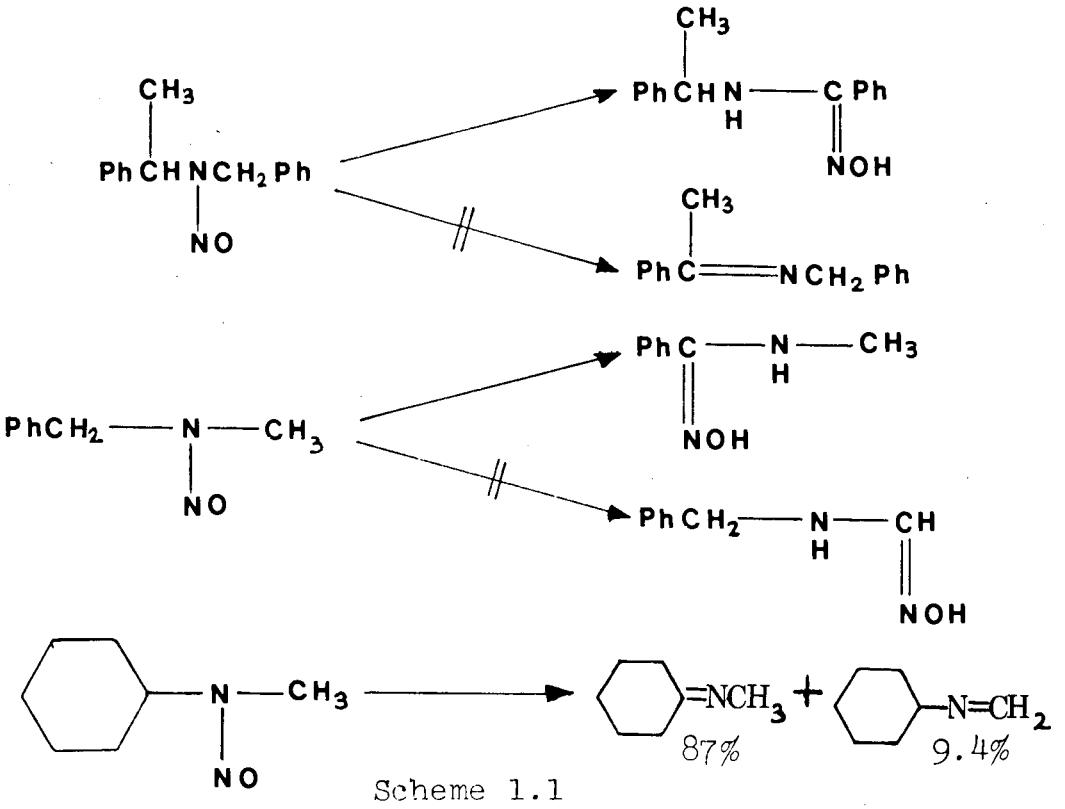
INTRODUCTION

The photochemical study of nitrosamines dates back to the early report in 1939 on gas-phase photolysis of N-nitrosodimethyl and N-nitrosodiethylamine in which the formation of dialkylamino-radical ($R_2N\bullet$) and nitric oxide as the primary photoproducts was proposed (1). It was also noted that the quantum yield of the gas-phase decomposition was low and that the vapour of nitrosamines did not exhibit any fluorescence. The photodecomposition of nitrosamines in condensed phase was only reported in recent years by Chow and Burgess independently (2,3). Both groups observed that nitrosamines were photolytically inert in a neutral medium with the possible exception of N-nitrosodibenzylamine (3). In the presence of a strong acid such as hydrochloric acid or trifluoroacetic acid, rapid photodecomposition took place. The term, photodecomposition, here signifies a light-induced chemical change of a nitrosamine and is irreversible in nature. Similarly, the term, photoaddition, signifies a light-induced chemical process involving the addition of a nitrosamine to a carbon-carbon double bond.

Since Chow and Burgess' observation (2,3), considerable information concerning the photochemistry of nitro-

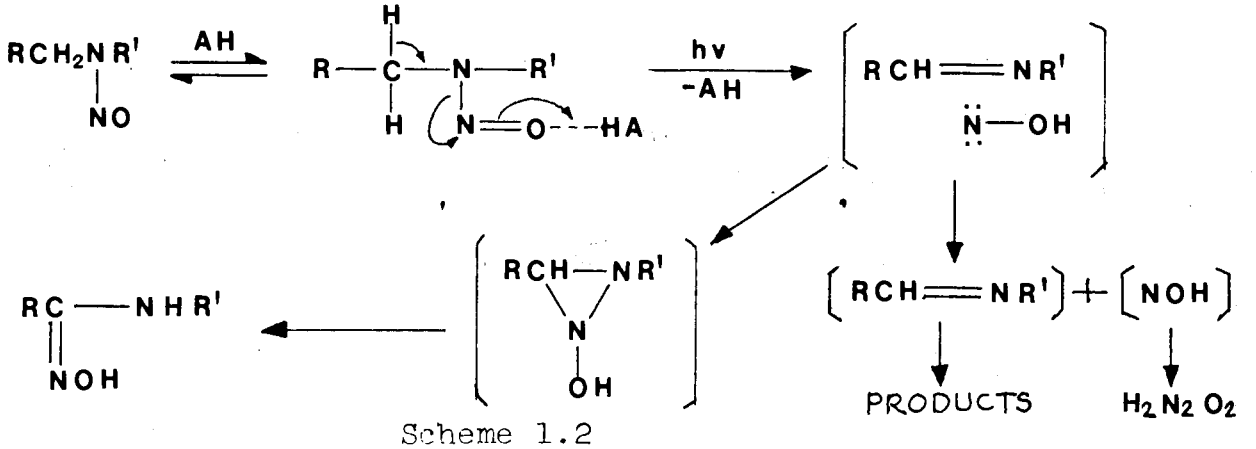
samines has been accumulated by work in this laboratory (4 - 10) and by other investigators (11 - 13). The photodecomposition has been shown to follow zero-order kinetics up to 75% completion (2,7). The products of the photolysis are amidoximes, the parent amines and secondary reaction products of alkylideneimines. From the detection of nitrous oxide, the decomposition product of hyponitrous acid (HNO dimer), Chow has suggested the elimination of nitroxyl to form the imine as the primary photochemical process (2,7). Reverse addition of the nitroxyl to the alkylideneimine followed by tautomerisation produces the amidoxime. A cage mechanism for the formation was proposed (2,14). Recent evidence by an isotope cross-over experiment (11,12) however showed that the elimination of HNO can involve protons on either side of the N-nitrosamine group and that a cage mechanism is not operating.

The stability of amidoxime to irradiation has also been demonstrated (11). Symmetrical nitrosamines with di-substituted carbon atoms at α-and α'-positions such as N-nitrosodicyclohexylamine gave the alkylideneimine as the major product (3). The facility of the elimination of an α proton is in the order of tertiary >secondary >primary (7). Unsymmetrical nitrosamines rearrange with selective orientation as outlined below (3,7) (Scheme 1.1).



Scheme 1.1

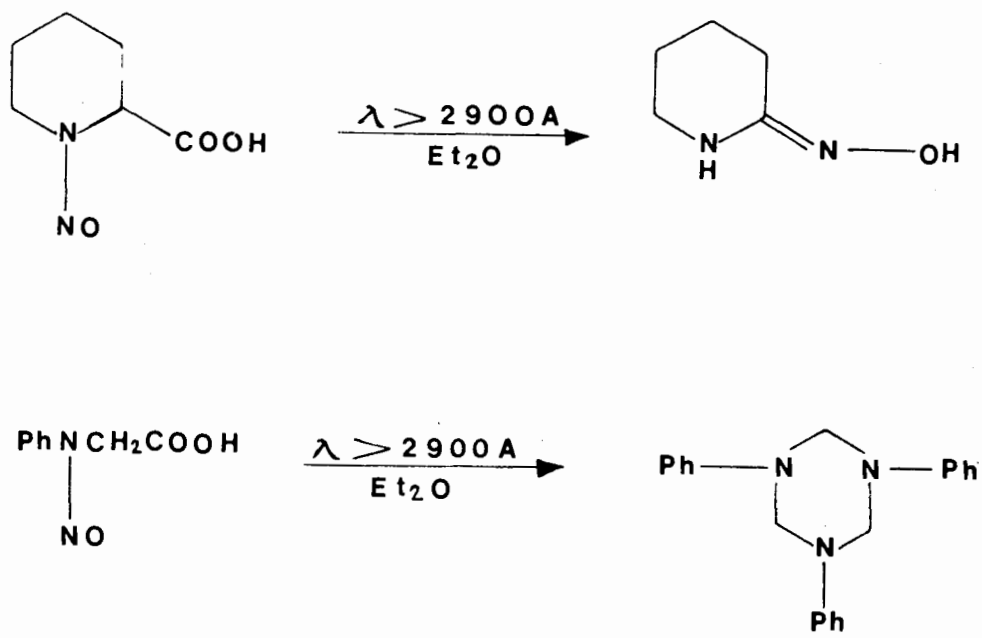
The selectivity suggests that elimination was subject to electronic and steric requirements. The species undergoing the photodecomposition has been suggested to be a hydrogen bonded nitrosamine-acid complex (2,3,7). The intermediate has not been identified but a mechanism has been proposed as follows though aziridine intermediate has not been isolated (Scheme 1.2).



Scheme 1.2

The spin state responsible for the photodecomposition has not been studied although the $n \rightarrow \pi^*$ excitation of a nitrosamine to give a triplet aminium radical ion has been suggested as the primary photoprocess (3). A free radical mechanism has been disfavoured inasmuch as the photolysis was not altered by the presence of oxygen (2). On the basis of certain similarity in the irradiation of N-nitrosamines and N-chloramines in the presence of olefins in acid media, Axenrod et al have recently proposed that the aminium radical may be the intermediate for the nitrosamine photolysis (11). The proposal, however, is apparently in contradiction to the observation that both N-nitrosodibutylamine (2,3,7) and N-nitroso-α-(o-tolyl)-dimethylamine (3) do not give the Hofmann Löeffler reaction products although both possess accessible δ-hydrogens.

The role played by the acid in the photodecomposition of nitrosamines is not well understood. Thus although N-nitrosopiperidine in the presence of one equivalent of acetic acid does not undergo significant change on prolonged photolysis, irradiation of N-nitrosoderivatives of α-amino acids alone in a neutral solvent leads to oxidative decarboxylation (Scheme 1.3) indicating the requirement of correct molecular geometry in the association of proton with the N-nitrosamine group is essential for the photodecomposition (2,9). The formation of parent amines has



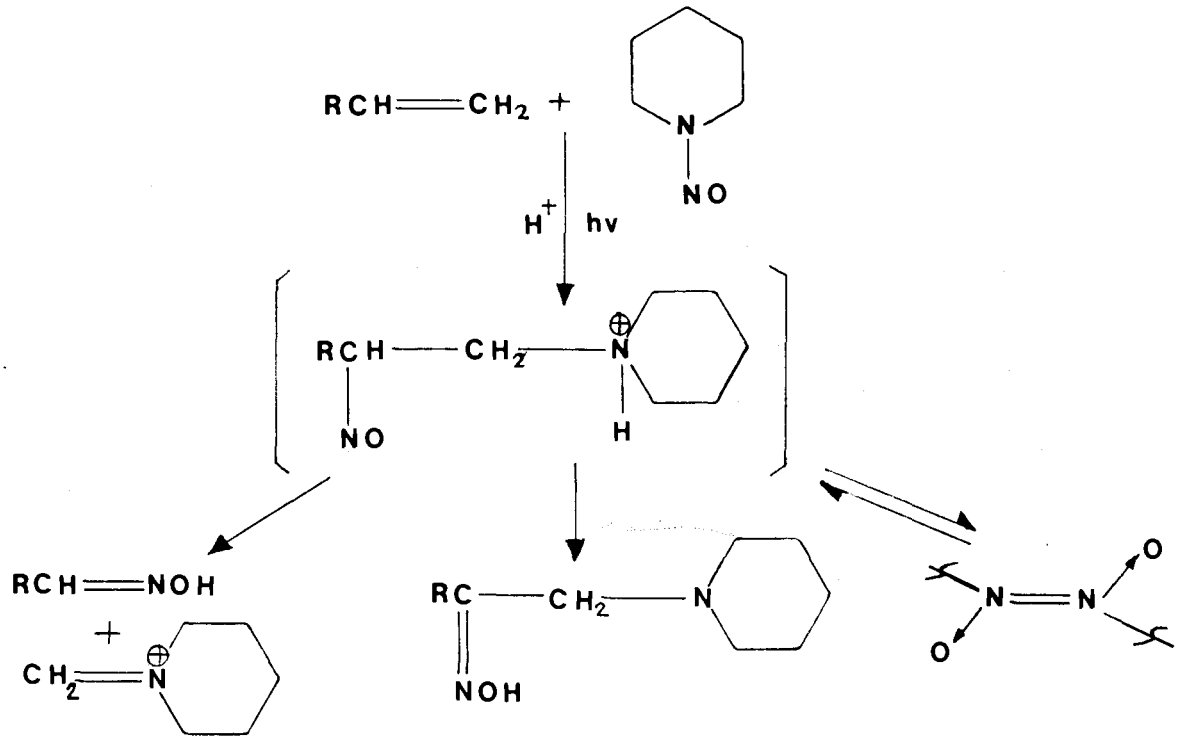
Scheme 1.3

been shown to be a light-induced process and cannot be the result of a thermal hydrolysis of nitrosamines (7).

The photoaddition of nitrosamines to olefins has been extensively studied in this laboratory (4-6, 8,10) and the reaction pattern can be summarised as shown in Scheme 1.4. In addition, the following conclusion has been enunciated.

(i) Both light energy and acid catalysis are required.

(ii) The nitrogen-nitrogen bond of the nitrosamine is broken at certain stages with the dialkylamino group going to the less substituted carbon atom.



Scheme 1.4

(iii) The photoaddition was insensitive to the presence of oxygen.

(iv) In general, photoaddition is favoured over photodecomposition. However, photoaddition to more hindered olefins, such as 3,3-dimethyl-1-butene is slow enough to be competed by photodecomposition. These observations have led to the inference that photoaddition and photodecomposition follow two independent pathways without sharing a common intermediate (8).

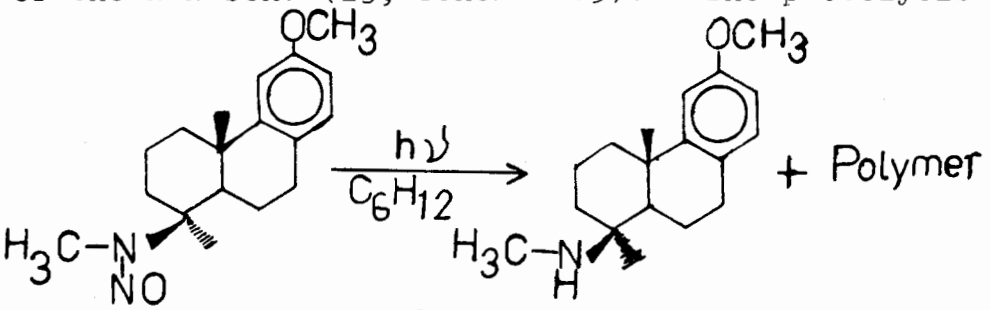
Simultaneous with the present study, the addition of nitrosamines to 1,3-dienes and aromatic hydrocarbons (15) as well as the sterochemistry of nitrosamine addition to olefins have been investigated (16, 17).

In sharp contrast to the nitrosamines, the related N-nitrosamides are thermally labile (18) and readily undergo photodecomposition under neutral conditions (19). The primary photochemical process involves the homolysis of the N-N bond giving amidyl radicals which can abstract hydrogen atoms intermolecularly from the solvent as well as intramolecularly from the δ-carbon of the alkyl chain (19,20). The functionalisation at the unactivated δ-carbon site of the alkyl chain can be achieved in 55% yield and compares favourably with nitrite photolysis as a potential synthetic tool. Where hydrogen transfer reactions are impossible, β-scissions involving C-C and C-H bonds of amidyl radicals take place giving rise to formylideneacetamide and alkylideneacetamides.

The cyclisation of N-chloramines to pyrrolidine derivatives has long been known as the Hofmann Löeffler rearrangement (21-23). The rearrangement can be initiated thermally or photolytically. Conclusive evidence for the participation of the aminium radical as chain carrier in the reaction has been established recently by Corey and by Ingold (23,24). The addition of dialkyl-N-chloramines to aliphatic 1,3-dienes, 1,2-dienes, terminal olefins and

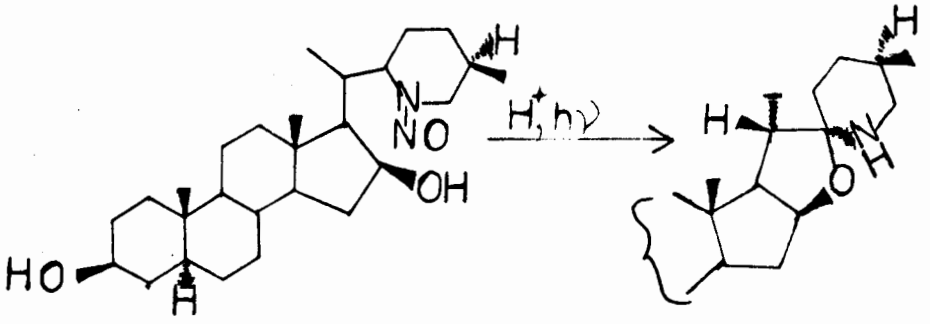
acetylenes in sulphuric acid-acetic acid medium has been extensively studied (25-27). The reaction can be initiated thermally or photolytically (25,26) or with a metal ion such as ferrous sulphate (25-27). The adduct is a β-chloramine and involves a free radical chain sequence in which the key propagation step has been proposed to be the addition of an aminium radical to the carbon-carbon double bond. The competing reactions in the photoaddition are ionic chlorination and the Hofmann Löeffler rearrangement.

The photolysis of a diterpene nitrosamine in neutral media gave only the parent amine through homolytic fission of the N-N bond (13, Scheme 1.5). The photolysis of



Scheme 1.5

steroid nitrosamines in the presence of acid (28) has been used to introduce new functional groups (Scheme 1.6)



Scheme 1.6

A preliminary study of the photolysis of N-nitramines has been reported (14,29). The products are the corresponding nitrosamine and small amount of imine. The reaction apparently has little synthetic interest. The thermolyses of both nitrosamines (30) and nitramines (acid catalysed rearrangement, 29, 31,32) have been reported and apparently yield products of insignificant synthetic utility.

Since all the previous photolyses of nitrosamines were investigated with light source longer than 2800A, the present study was carried out in an attempt to determine:

(i) if there is any difference in product distribution upon irradiation with 2537A light which corresponds to excitation of the $\pi \rightarrow \pi^*$ (see sec. 2.1) transition band of the nitrosamine as compared to that obtained by irradiation with light >2800A;

(ii) the excited state responsible for the photoaddition to olefins;

(iii) the excited state responsible for the photodecomposition;

(iv) the intermediate undergoing the photoreaction and the mechanism for the formation of photodecomposition products.

CHAPTER 2

RESULTS

2.1 General

The spectral properties of nitrosamines have been well described in literature (33). In the infrared spectrum, nitrosamines show a strong absorption at 1500 - 1430 cm^{-1} (34) attributable to N=O stretching. In the ultraviolet region, the longest wavelength absorption at 350 nm of nitrosamines has been identified as the $n \rightarrow \pi^*$ transition band (35-38) from its low transition energy, intensity, and blue shift of absorption spectrum in polar solvents (38). The more intense absorption at shorter wavelength (230-240 nm) is attributed to the $\pi \rightarrow \pi^*$ transition band (35,36,38) or an intramolecular charge-transfer band (37). Nuclear magnetic resonance studies have demonstrated the existence of restricted rotation about the N-N bond in nitrosamines which is an evidence for a marked conjugation between the nitroso group and the unshared pair of the amine nitrogen (Scheme 2.1) (39 - 42). The contention of inversion at

Scheme 2.1

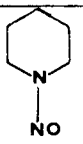
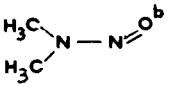
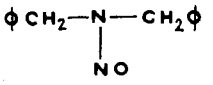
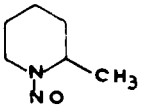
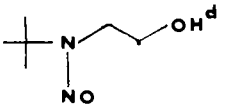
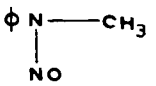
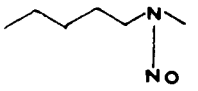
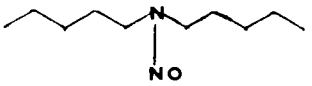
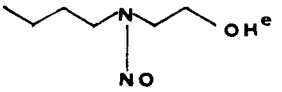
the amine nitrogen can be ruled out from the observation that the benzylic protons of 3 (Table 2-1) show only two singlets instead of an AB quartet expected from the non-equivalence of the methylene protons if nitrogen inversion is indeed the process. In fact both conformational isomers of N-nitroso-N-benzyl-2,6-dimethylaniline has recently been isolated by a two-fold preparative thin layer chromatography at 6° on silica gel with benzene eluent (43). The spectral data of the nitrosamines in the present study are summarised in Tables 2-1 - 2-3 and are in agreement with those reported in literature.

2.2 The Photodecomposition of Nitrosamines.

2.2.1 N-nitrosopiperidine (1)

(a) In methanol: Irradiation of 1 in methanol with a 2537A light source produced nitrogen dioxide (maxima at 312, 318, 328, 338, 350 and 363 nm) which disappeared on further irradiation (Fig. 2.1). This implies nitrogen dioxide is reacting chemically with the photolysate or it is being removed from the system by the continuous stream of nitrogen. Of these possibilities, the latter is preferred. The reaction mixture after the usual working up afforded piperidine hydrochloride (10, 42%), N-piperidinoformamide (11, 20%) and 2-piperidonoxime (12, 2.2%).

Table 2-1. NMR spectral data of nitrosamines (τ values)

Compound	Nitrosamine	trans[a] >NCH$_2$	cis[a]	trans[a] >NCH$_3$	cis[a]
1		5.87(m)	6.32(t)	-	-
2		-	-	6.27(s)	7.03(s)
3		4.9(s)	5.43(s)	-	-
4		∿5.5(m)	6.35(t)	8.55(d)[c]	8.95(d)[c]
5		-	6.32(m)	-	-
6		-	-	-	6.84(s)
7		5.85(t)	6.46(m,b)	6.25(s)	6.95(s)
8		5.92(t)	6.48	-	-
9		5.83(t)	6.02(t)	-	-

a. With respect to nitroso-oxygen; b. Taken in CCl_4;

c. >N-C-CH_3; d. t-Butyl, τ8.50(s); e. -CH_2-OH, τ6.32(m).

Table 2-2 Infrared spectral data of nitrosamines

Compound	$\nu_{N=O}$ cm^{-1}	Other individual characteristic absorption cm^{-1}
1	1435(s)	1295, 1030, 675
2	1410(m)	1320, 1285,1050, 680
3	1430(s)	3030, 1495, 694(s)
4	!430(s)	1305, 1060, 680
5	1430(s) 1428(m)[a]	3330(b,s), 1290, 1050(s) 3430, 3020(sh), 1390, 1368, 1025
6	1408	1605, 1505, 1480, 1300, 1040, 700, 695
7	1430(s)	1045(s), 660
8	1430(sh)	1310(w), 1080(s), 725
9	1425(m)	3400(b,s), 1305, 1050(s), 655

a. Taken in $CHCl_3$.

Table 2-3 Ultra-Violet spectral data of Nitrosamines

Compound	Solvent		$n \rightarrow \pi^*$ band		$\pi \rightarrow \pi^*$ band	
		HCl,M	λ_{max} nm	ε	λ_{max} nm	ε
1	methanol	0.02	349	88.5	235	8300
	water	-	338	86.7	235	~8000
2	methanol	-	345	98	230	~7500
3	methanol	-	360	63.5	238	7900
4	methanol	0.04	349	90	a	
5	water	0.01	345	~74	a	
6	methanol	-	~360 b	~200	270	7300
7	water	0.02	334	62	228	5240
8	methanol	0.02	308	90	234	7350
9	methanol	-	355	86.5	235	7000

a. The $\pi \rightarrow \pi^*$ band has not been determined. b. Shoulder only.

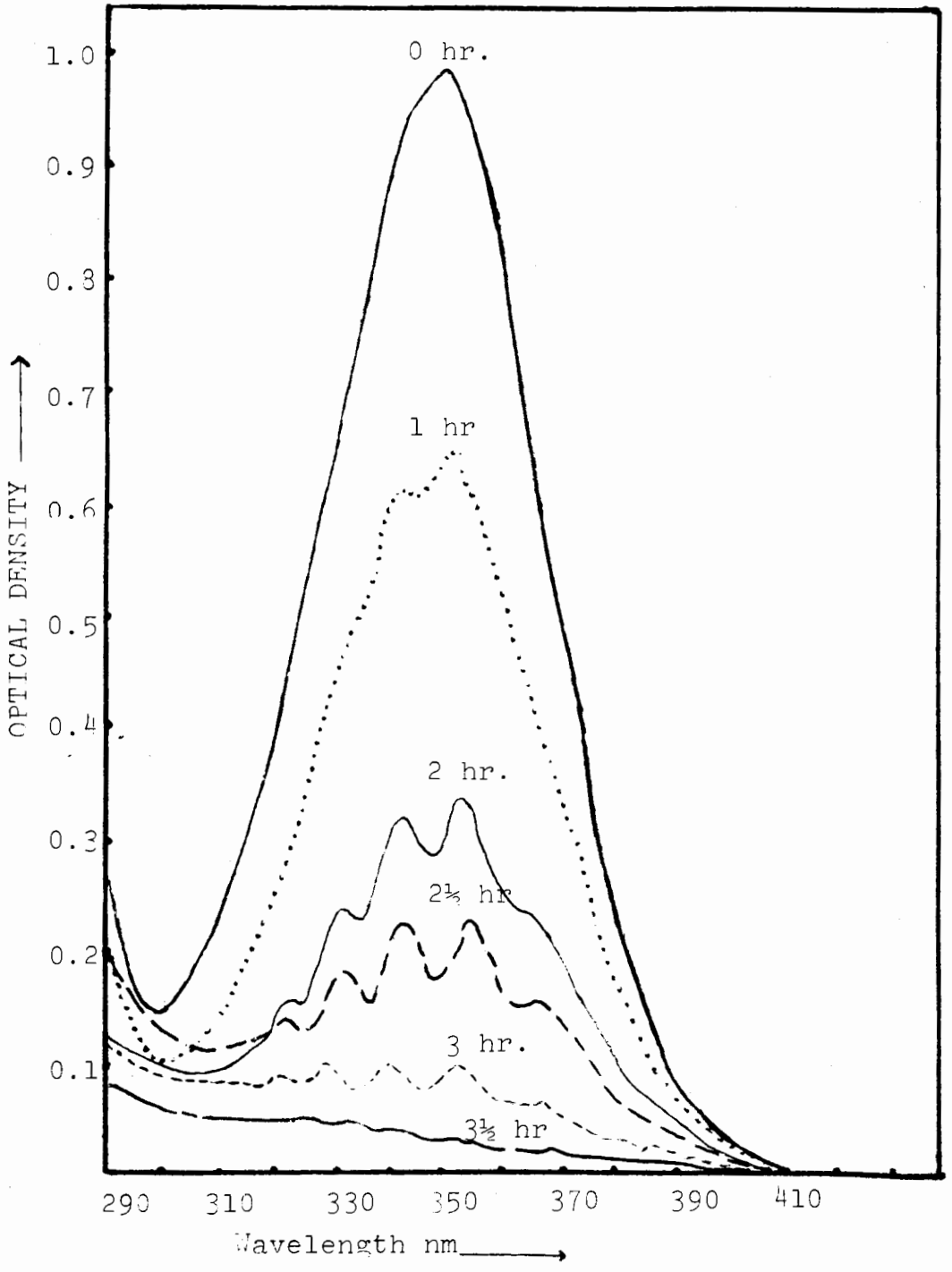
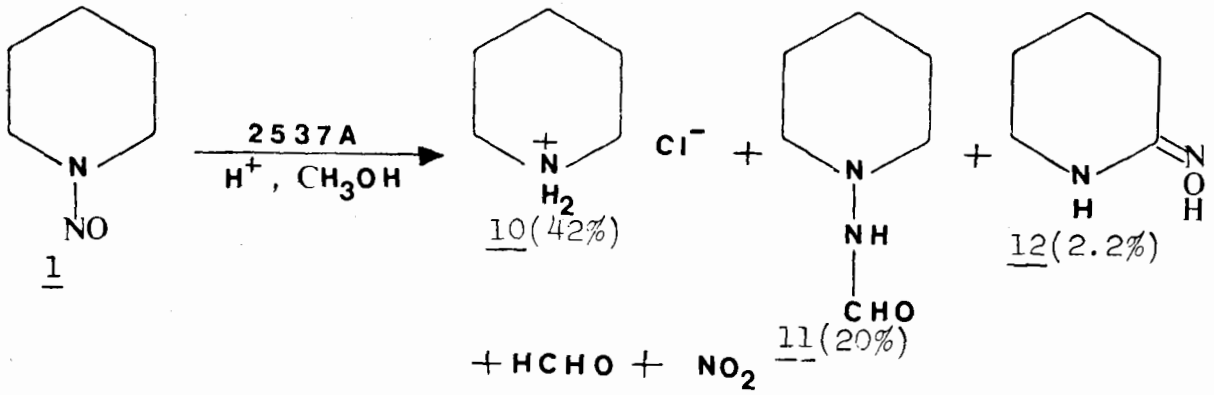


Fig. 2.1 The absorption curve of the diluted photolysate of 1 and HCl in methanol at various intervals.



1

10(42%)

11(20%)

12(2.2%)

All these compounds were characterised by their ir and nmr spectra, and the tlc mobilities by comparison with authentic samples. In addition, formaldehyde was isolated from the trapped solvent.* N-formylpiperidine (13) was detected by tlc in one fraction of the basic extract but was not isolated. Compound 11 gave the correct elemental analysis. Its nmr signals at τ1.67 and 2.15 showed an AB coupling pattern in which the former collapsed to a singlet and the latter disappeared after exchange with D_2O. The former was assigned to the formyl proton and the latter to NH. The structure of 11 was further confirmed by comparison of its spectral data and m.p. with an authentic sample prepared by the known method (44). The mass spectrum of 11 showed intense fragments at m/e 99, 83, and 55 (base peak). The latter two fragments were reminiscent of the fragmentation pattern

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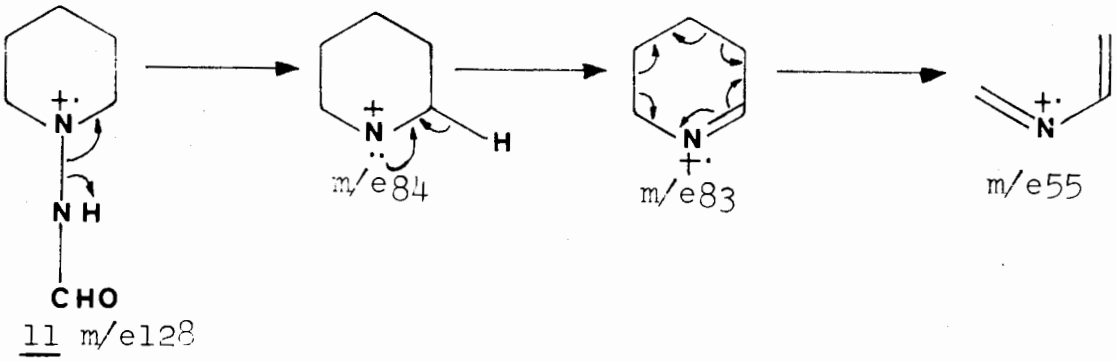
* All aldehydes were isolated as their 2,4-DNPH derivatives unless specified otherwise.

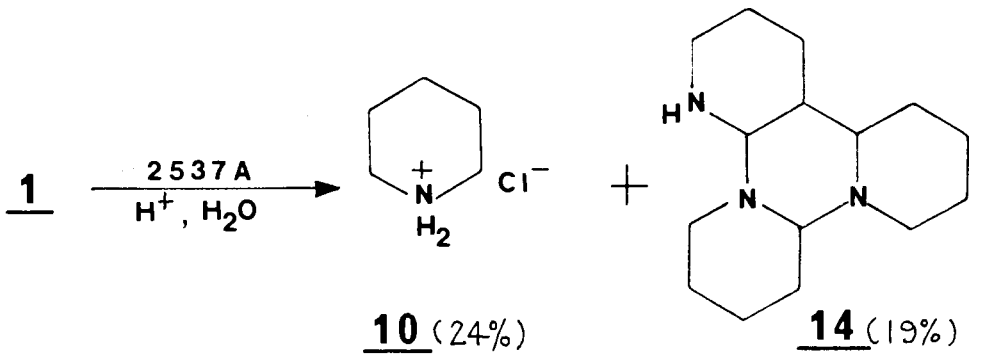
for piperidine (45) and could be rationalised as shown in Scheme 2.2.



Scheme 2.2

When 1 was irradiated in methanol with 2537A light in the absence of acid, no detectable change in the absorption spectrum was observed after 23 hours. Working up in the usual manner, only the starting nitrosamine (93%) was recovered. In this photolysis formaldehyde was not detected.

(b) In water: The photolysis of an aqueous solution of 1 at 2537A afforded the hydrochloride 10 (24%) and isotripiperidein (14, 19%) as the only isolable products.



When the solution was irradiated with $\lambda > 340$ nm (2,7-dimethyl-3-6-diazacyclohepta-1,6-diene perchlorate solution as filter), the products obtained were an unknown salt (15, 1.76g), amidoxime 12 (31%) and 2-piperidone (16, 0.74%). No piperidine hydrochloride (10) was formed in contrast to other cases. 2-piperidone was presumably derived from 12 by hydrolysis. Various attempts to crystallise 15 failed. The corresponding free base appeared to decompose during continuous extraction. The basic oil obtained from neutralisation of 15 yielded no isolable product on florisil chromatography. The sizeable quantity of 15 showed this was a major product of the photolysis. The broad nmr signals from τ6.33-8.77 of 15 and its complex ir absorption suggested this might be the hydrochloride of the trimer of Δ^1-piperidein, namely α-tripiperidein or isotripiperidein. The free base of both forms is known (46), with the latter being more stable.

(c) Quenching of the photodecomposition of 1 by naphthalene:

The distribution of products obtained from the photolysis of 1 under various conditions is compared with that reported in literature in Table 2-4.

Irradiation of 1(0.098M) at $\lambda>340$ nm in the presence of naphthalene (0.105M) as added quencher (the absorption of naphthalene above 330 nm was negligible) was found to take a course quite different from that described above. The nitrosamine absorption increased instead of decreasing as was usually observed in the absence of naphthalene. The broadened absorption showed no maximum below 400 nm after irradiation for 6 hrs; at the same time the photolysate turned brownish red.

From the reaction mixture, naphthalene (70% recovery), nitrosamine (2.5%), 10 (35.5%), 14 (4.6%) and an unknown compound(17, 31 mg) were isolated. Unknown 17 contained an aromatic ring system as indicated by its ir absorption at 3060, 1595, 1580, 1510 and 1425 cm^{-1} and nmr signals at τ3.4 - 1.7. The signals at τ7.0 and 8.27 (both broad) indicated the possible presence of a piperidine ring. This indicated that 1 was reacting with naphthalene although the identity of 17 has not been established due to insufficient sample. The rate of photolysis in the present case however was slower when compared to that of the control run (vide infra). Under similar operational procedure as the control run(without naphthalene), the presence of formaldehyde was

Table 2-4. Summary of product distribution of the photolysis of 1 under various conditions.

Run	Solvent	Light[a] Source (filter)	Irradiation Range nm	Product, Yield (%) 11	10	12	14	Other	Origin
1	H_2O	1 (1)	>340			31		15,1 16 (0.74)	This work
2	H_2O	2	>290			50	41		2
3	H_2O	3 (2)	254		24		19		This work
4	CH_3OH	1 (1)	>340		57	3.5		18,HCHO	This work
5	CH_3OH	3 (2)	254	20	42	2.2		HCHO,13[b]	This work
6	CH_3CH_2OH	4 (3)	>310	d	c			CH_3CHO	50

a. Lamp 1, Hanovia (200W); filter 1,2,7-dimethyl-3-6-diazacyclohepta-1,6-diene perchlorate solution; Lamp 2, Hanovia (140w); Lamp 3, 2537A low pressure mercury arc, filter 2, nickel sulphate solution; Lamp 4, RPR 3500A, filter 3, soft glass filter; b. Detected by tlc, not isolated; c. No percentage given; d. N-piperidinoacetamide indicated by nmr but no percentage given.

only isolated in a small amount indicating its formation was very inefficient.

When photolysis of 1 was rerun in the presence of a lower concentration of naphthalene (0.01M), the nitrosamine absorption decreased during the first hour then increased upon further irradiation and no maximum was then observed in the region above 320 nm indicating the nitrosamine must have decomposed. The survival of naphthalene was shown by its λ_{max} at 310 nm and its characteristic bands between 295-320 nm (O.D. below 290 nm >2). The slopes obtained from a plot of the decrease in optical density at 348 nm of the nitrosamine (Fig. 2.2) is smaller than that of the control run (without naphthalene, vide infra). It was therefore obvious that the photodecomposition of 1 was quenched by naphthalene.

A similar irradiation of 1 in methanol in the absence of naphthalene (irradiation at λ>340 nm) proceeded rapidly and completely in 3 hrs. No starting nitrosamine was recovered. The products were hydrochloride 10 (57%), amidoxime 12 (3.5%) and an unknown compound 18. Compound 18 showed nmr signals at τ8.46 (m,6H) and 6.86 (m,4H,2-CH_2NCOR) (47), and strong ir absorption at 1640 cm^{-1} (N-CO-N, six ring) (48). From these spectral data, 18 was tentatively assigned as N,N,N',N'-bis-pentamethylene

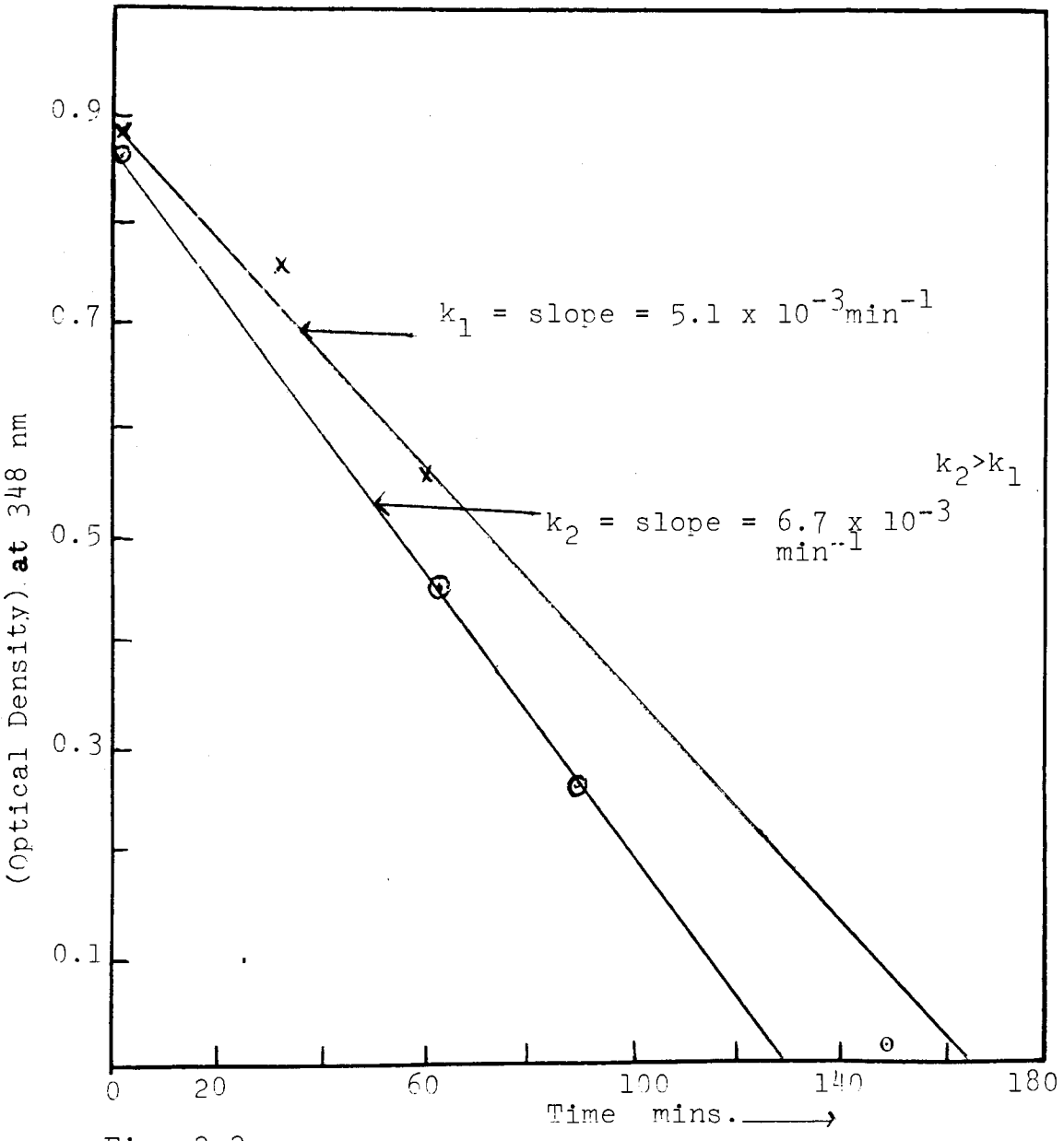


Fig. 2.2 Plot of decrease of optical density of I with time in the presence and absence of naphthalene.

× I (0.03 mole) + HCl + [0][0] (0.0036 mole) in methanol

⊙ I (0.03 mole) + HCl in methanol

urea. The mass spectrum of 18 showed the fragment at m/e 222. The fragment at m/e 196(3%) expected for the assumed molecular structure was also present. Both the neutral and the basic extract showed no nmr signals below τ3.0, indicating the absence of 11* In addition, formaldehyde was isolated from the trapped solvent.

(d). Naphthalene sensitization: An attempt was made to sensitize the photodecomposition of 1 with naphthalene by irradiating in the region 290-340 nm (nickel sulphate filter solution) where naphthalene absorbed most of the light energy (ca. 80%). The nitrosamine peak at 350 nm increased slowly (compare c above) instead of decreasing, and completely covered the region below 400 nm after 10 hours of irradiation. The reaction mixture yielded only naphthalene (83.5%), 1 (65%) and a small amount of hydrochloride 10 (1.7%)

In the absence of naphthalene, irradiation for 10 hrs. led to 20% decomposition as indicated by the decrease of the nitrosamine absorption at 350 nm.

Unless specified otherwise, the following reactions were run in the type II apparatus (sec. 6.4) with 2537A light source. The conditions for the photolysis of the

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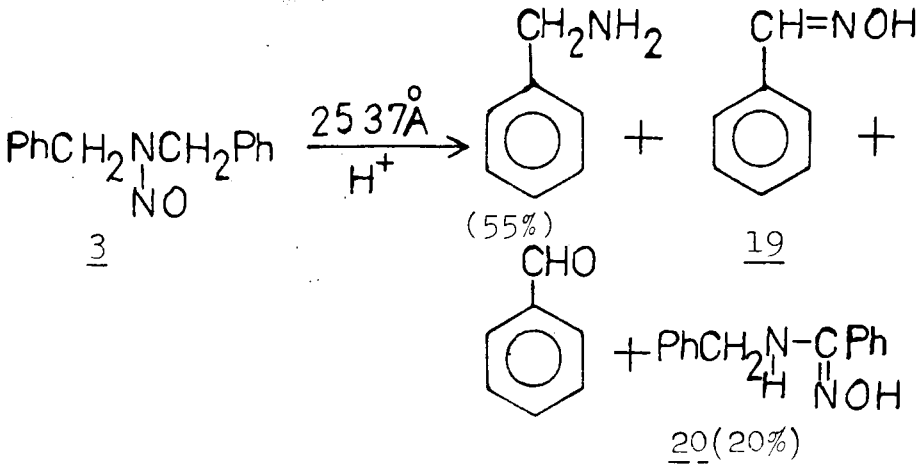
* A small amount of 11 had been obtained in the photoaddition of 1 to olefins under ice-salt temperature (pyrex filter) (49).

various nitrosamines are summarised in Table 2-5 (for structures of compounds, see Appendix I).

2.2.2 N-nitrosodibenzylamine (3)

Photolysis of 3 yielded benzylamine (55%), benzaldehyde, benzaldehyde oxime 19, 3 (5.6%), N-benzylbenzamidoxime (20, 20%) and a small amount of an unknown compound 21. Unknown 21 had nmr signals at τ8.73(s)



indicating the possible presence of CH_3C-OR (51) group; the signal at τ2.35-3.15(m,ca.10H) and its ir absorption at 1605, 1587, 1563 and 1494 cm^{-1} showed that the aromatic moiety was present.

2.2.3 2-Methyl-N-nitrosopiperidine (4).

The photolysis of 4 proceeded rapidly, and gave the same uv profile as that described for 1 (Fig. 2.1). The products obtained were formaldehyde, the parent amine (isolated as the hydrochloride), N-(2-methylpiperidino)-formamide (22) and an unknown compound 23. Unknown 23 showed similar ir and nmr absorption as 18, and was there-

Table 2-5. Summary of conditions for the Photodecomposition of Nitrosamines

Expt.	Nitrosamine (mole)	HCl (mole)	Solvent (ml)	Filter	Lamp Source	Irradiation time, mins.	Nitrosamine recovered %
1	1(0.024)	0.024	CH_3OH (240)	$NiSO_4$	1	215	
	1(0.053)	0.054	"	"	1	600	
2	1(0.044)	0.053	H_2O (240)	"	1	540	
3	1(0.043)	0.054	H_2O (240)	1[b]	2	540	
4	1(0.030)	0.054	CH_3OH (330)	1	2	180	
5	4(0.062)	0.097	CH_3OH (240)	$NiSO_4$	1	600	
6	3(0.024)	0.030	CH_3OH (240)	"	1	270	5.6
7	7(0.008)	0.048	H_2O (240)	"	1	150	
	7(0.021)	0.060	"	"	1	330	
8	8(0.037)	1.310[c]	$HOAc$(260)	Nonex	3	450	73.0
9	8(0.023)	0.060	CH_3OH (240)	$NiSO_4$	1	210	
10	5(0.018)	0.022	H_2O (240)	"	1	270	10.0
11	9(0.029)	0.060	CH_3OH (240)	"	1	420	

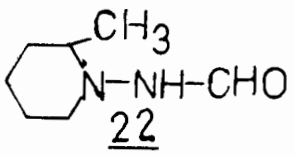
a. Lamp 1, NFUV-300 source (2537A low pressure mercury arc lamp; Lamp 2, Hanovia (200W) lamp; Lamp 3, Hanovia (450W); b. Filter Solution 1, 2,7-dimethyl-3,6-diazacyclohepta-1, 6-diene perchlorate; c. H_2SO_4(4M,70 ml).

fore tentatively assigned as 2,2'-dimethyl-N,N,N',N'-bispentamethylene urea. Vapour phase chromatographic analysis of the crude basic extract indicated the presence of at least five volatile components. Tlc analysis showed that formamide 22 was one of the major components of this mixture (> 10%).

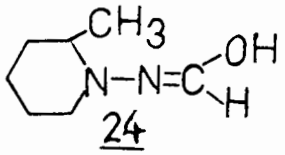
The formamide 22 was identified by direct comparison with an authentic sample prepared by the known method (44). Its ir spectrum shows two strong amide absorptions at 1694 and 1660 cm^{-1}. Its nmr spectrum shows that the formyl proton (τ1.77) is coupled to the NH (τ2.31) signal. Its mass spectrum shows intense peaks at m/e 113, 97 (base peak) and 69. These peaks are interpretable in terms of a fragmentation pattern similar to that shown in Scheme 2.2 for the analogous compound 11.

From the preparation of 22, a minor liquid product (24) was obtained. The mass spectrum of 24 shows fragments at m/e 113, 97, 69 and 41, that are also present in 22, and indicates the possible presence of a 2-methylpiperidino ring skelton. The fragment at m/e 142 (8%) suggests that 24 is possibly an isomer of 22. The signal at τ2.44 can be assigned to -CH=N- (52) although the integrated area of this absorption is apparently greater than one proton (ca. 2-3 H). The strong ir band of 24 at ca. 1600 cm^{-1} is indicative of the presence of the C=N- chromophore. On the bases of the above spectral

data, 24 is tentatively assigned as the enol isomer of 22.



22



24

2.2.4 N-nitroso-2-(t-butylamino)-ethanol (5).

Photolysis of 5 in water gave t-butylamine (v.p.c. and nmr analysis), starting nitrosamine (10%), parent amine (15%) and two unidentified compounds. Unknown 25 showed its highest fragment at m/e 89. This together with its nmr signal at τ 8.0(s) and 2.4(s), and ir absorption at 3160(b), 990, 970(s) and 950 cm^{-1} suggests that the compound could be N-t-butylhydroxylamine. The compound however did not give the correct m.p. expected for this structure (reported m.p. 64-5°) (53), and its identity remains unestablished.

2.2.5 N-nitroso-N-methylaniline (6).

Irradiation of 6 at 254 nm under neutral conditions (nickel sulphate solution as filter) produced no detectable change in u.v. absorption (<5%) after 10 hours. When the solution was irradiated with a Hanovia (450W) lamp in a quartz apparatus, the photolysate turned dark purple after 10 hours. At the same time a new absorption peak at ca. 250 nm appeared. The original λmax at 270 nm, however, was still prominent and appeared as a shoulder indicating the nitrosamine was still present. The photolysate, after

the working-up, yielded only the starting nitrosamine (77%) and a small amount of N-methylaniline. Formaldehyde was shown to be absent in the photolysate.

2.2.6 N-Nitroso-N-methyl-N-n-pentylamine(7)

The photolysis of 7 in water gave a complex misture. Since the basic extract was volatile and not enough sample had been obtained for characterisation, an attempted chromatographic separation failed. The presence of N-methyl-valerylamidoxime was indicated in the ir and nmr of one of the impure fractions. In addition, n-valeraldehyde and N-methyl-n-pentylamine hydrochloride were obtained.

2.2.7 N-nitroso-di-n-pentylamine(8)

Photolysis of 8 in glacial acetic acid containing sulphuric acid (4M) (21) was very sluggish. In this acid concentration, the nitrosamine peak shifted to 332 nm (ε38) and showed a colourless solution before irradiation.* The low extinction coefficient observed indicated that the nitrosamine existed predominantly as its conjugate acid in the ground state (3,35,40). The u.v. absorption of the mixture remained unchanged after 5½ hours irradiation. From the reaction mixture, the only products isolated were the starting nitrosamine (73%), a small amount of di-n-pentylamine hydrochloride, and acetone. The origin of the acetone is

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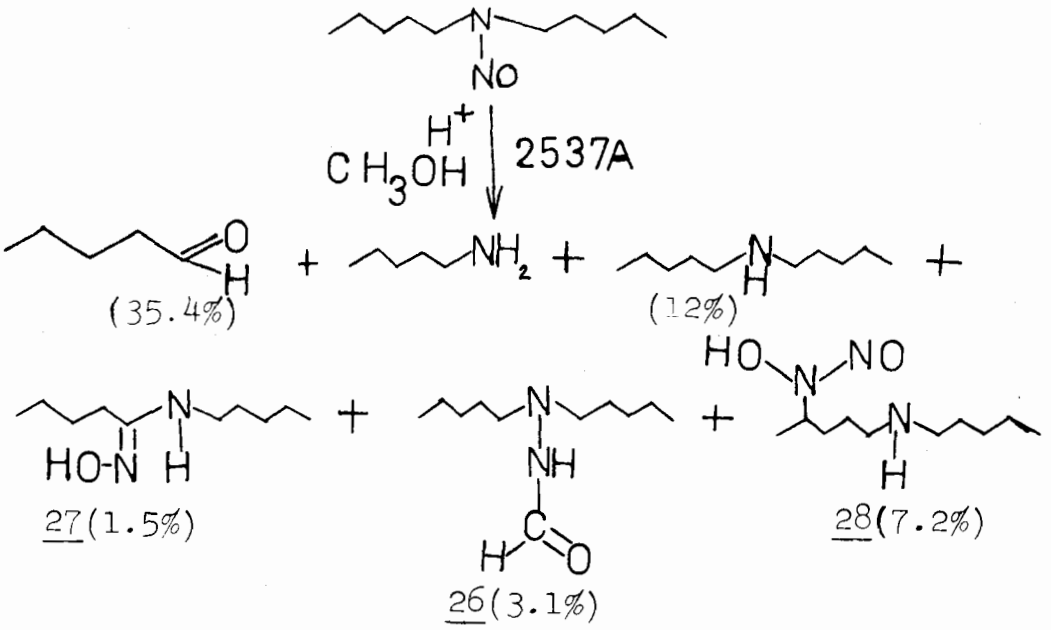
* A solution of 8 of similar concentration in methanol was light yellow.

not clear. The mass spectrum of its isolated 2,4-DNPH derivative showed fragments at m/e 238 (M^+,100%), 224 (14%), 252 (2.2%) and 266 (2.2%). The fragment at m/e 224 was possibly due to acetaldehyde present as a contaminant (54) in acetic acid. Fragments at m/e 252 and 266 suggested that n-butanal and n-pentanal were also formed in the photolysis. The crude basic extract (43 mg) showed no ir bands in the 900-1000 cm^{-1} (7,55) region indicating that no amidoxime were formed in the photolysis.

When the photolysis of 8 was performed in methanol in the presence of hydrochloric acid, the reaction proceeded rapidly. The isolated products were valeraldehyde (35.4%), parent amine (12%), N-di-n-pentylaminoformamide(26,3.1%) N-(n-penty)-pentanamidoxime (27, 1.5%) and 4-(N-nitrosohydroxylamino)-dipentylamine (28, 7.2%). In addition n-pentylamine hydrochloride and two unknown substances, 29 and 30, were isolated in small quantities (Scheme 2.3). The crude products represent 85% of the starting material.

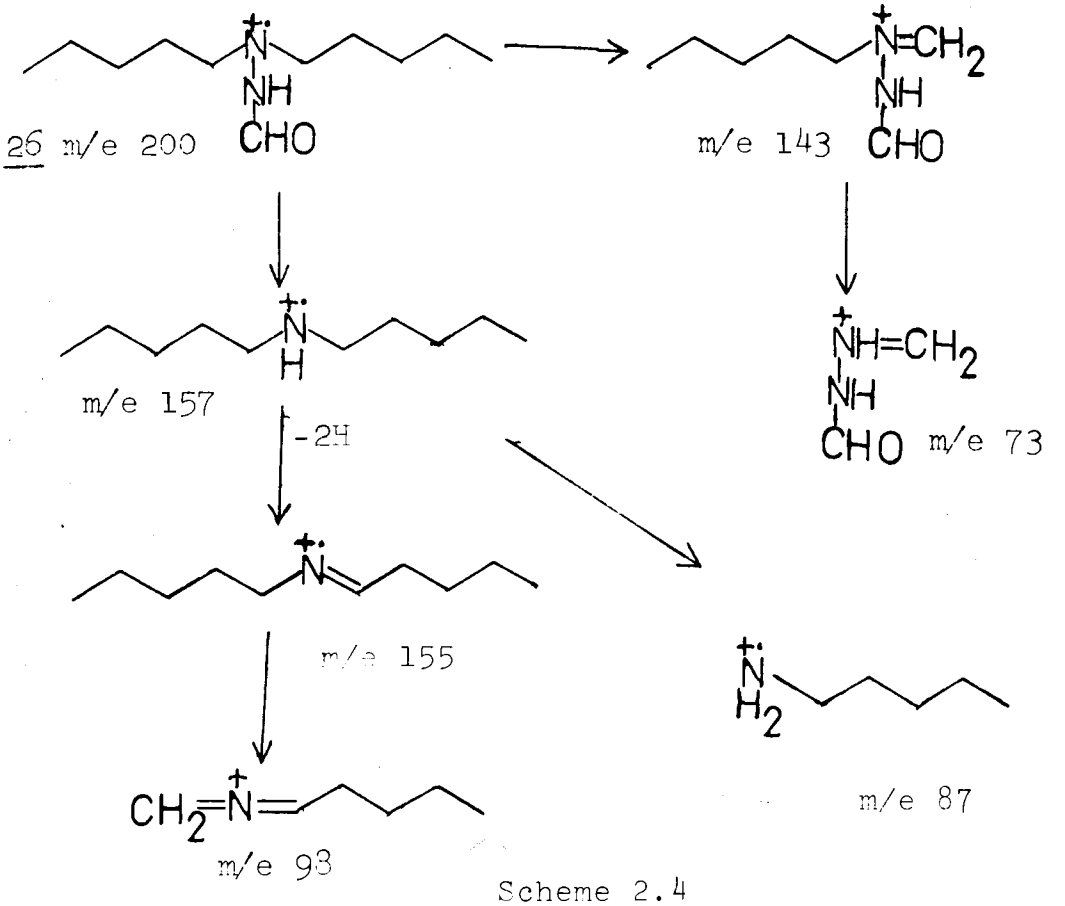
The formamide 26 shows ir and nmr absorptions similar to those of the analogous compounds 11 and 22. Its molecular formula was confirmed by exact mass measurement (M^+ calc. for $C_{10}H_{20}N_2O_2$, 200.1524; found 200.1526). Its mass spectrum shows strong peaks at m/e 171, 157, 143, 98 (base peak), 87 and 73 (base peak). These fragments can be



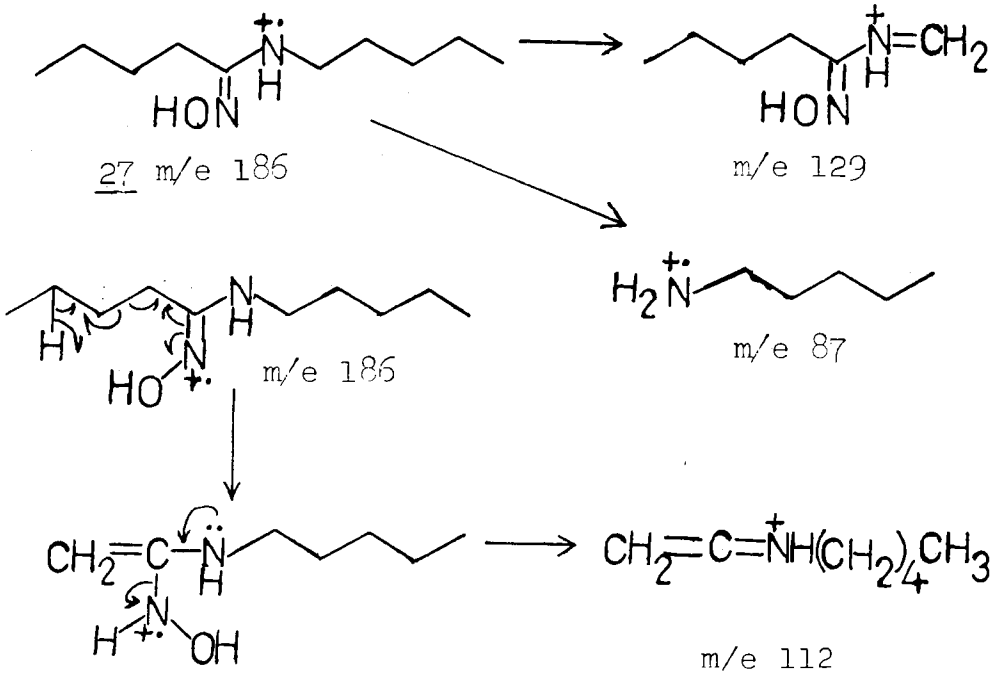
Scheme 2.3

interpreted as shown in Scheme 2.4 in terms of typical amine cleavage pattern (viz. α-cleavage and N-C cleavage) (56) although the assignment will have to be confirmed by exact mass measurement.

The amidoxime 27 showed typical ir peaks at 3410, 1640 and 900 cm^{-1}, and nmr signals similar to that reported for the analogous compound N-n-butylbutyramidoxime (7). Its molecular formula is confirmed by exact measurement (m/e calc. for $C_{10}H_{22}N_2O$: 186.1732; found 186.1738). Its mass spectrum shows strong fragments at m/e 129,112, 87 (base peak) and 30 (base peak), and can be interpreted as shown in Scheme 2.5.

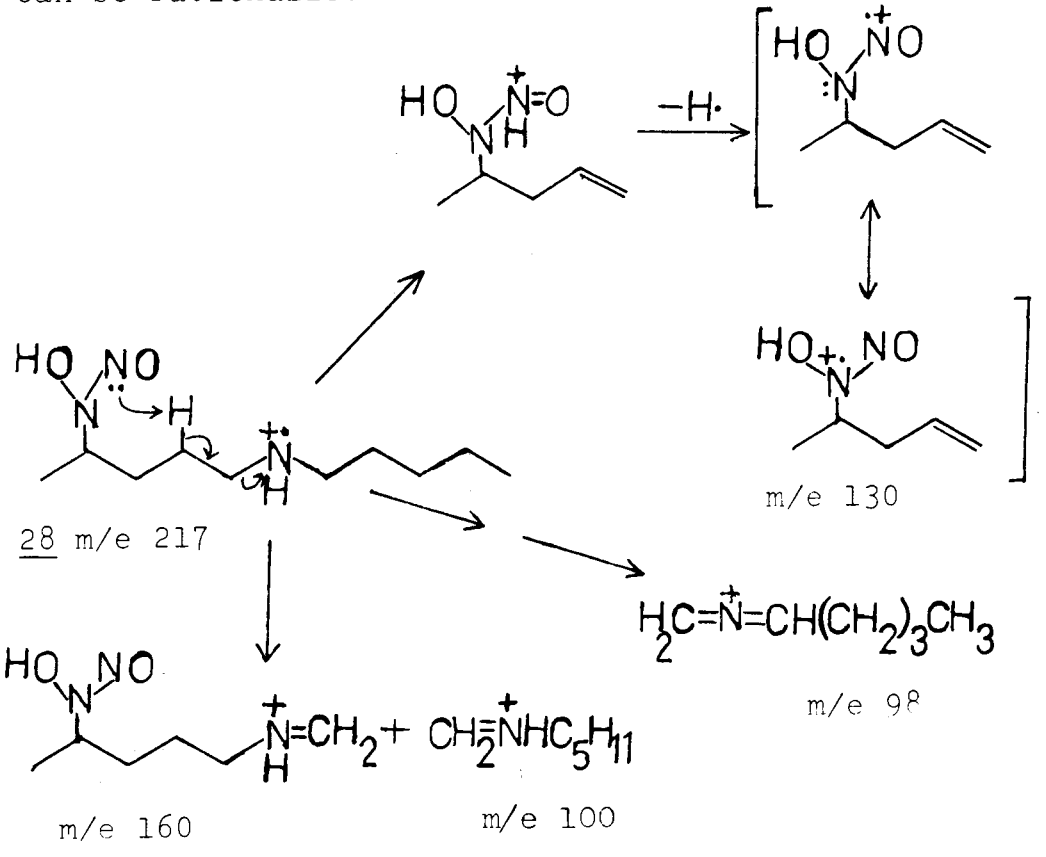


Scheme 2.4



Scheme 2.5

Compound 28 showed the methyl group as the doublet (J = 6.5 cps) at τ8.59 which collapsed to a singlet when the methine proton signal (m) at τ5.7 (Fig. 2.3) was irradiated. The chemical shift of the methine proton at τ5.7 is in agreement with those of N-nitrosohydroxylamino derivatives found in the previous work (17). Its structure was confirmed by exact mass measurement (m/e calc. for $C_{10}H_{23}N_3O_2$: 217.1790; found 217.1785). Its mass spectrum showed strong fragments at m/e 187, 160, 130 (base peak), 100 (base peak) and 98. The fragments at m/e 187 and 44 might be attributed to (M^+-NO) and $N_2O^{+\cdot}$. The other fragments can be rationalised as shown in Scheme 2.6.



Scheme 2.6

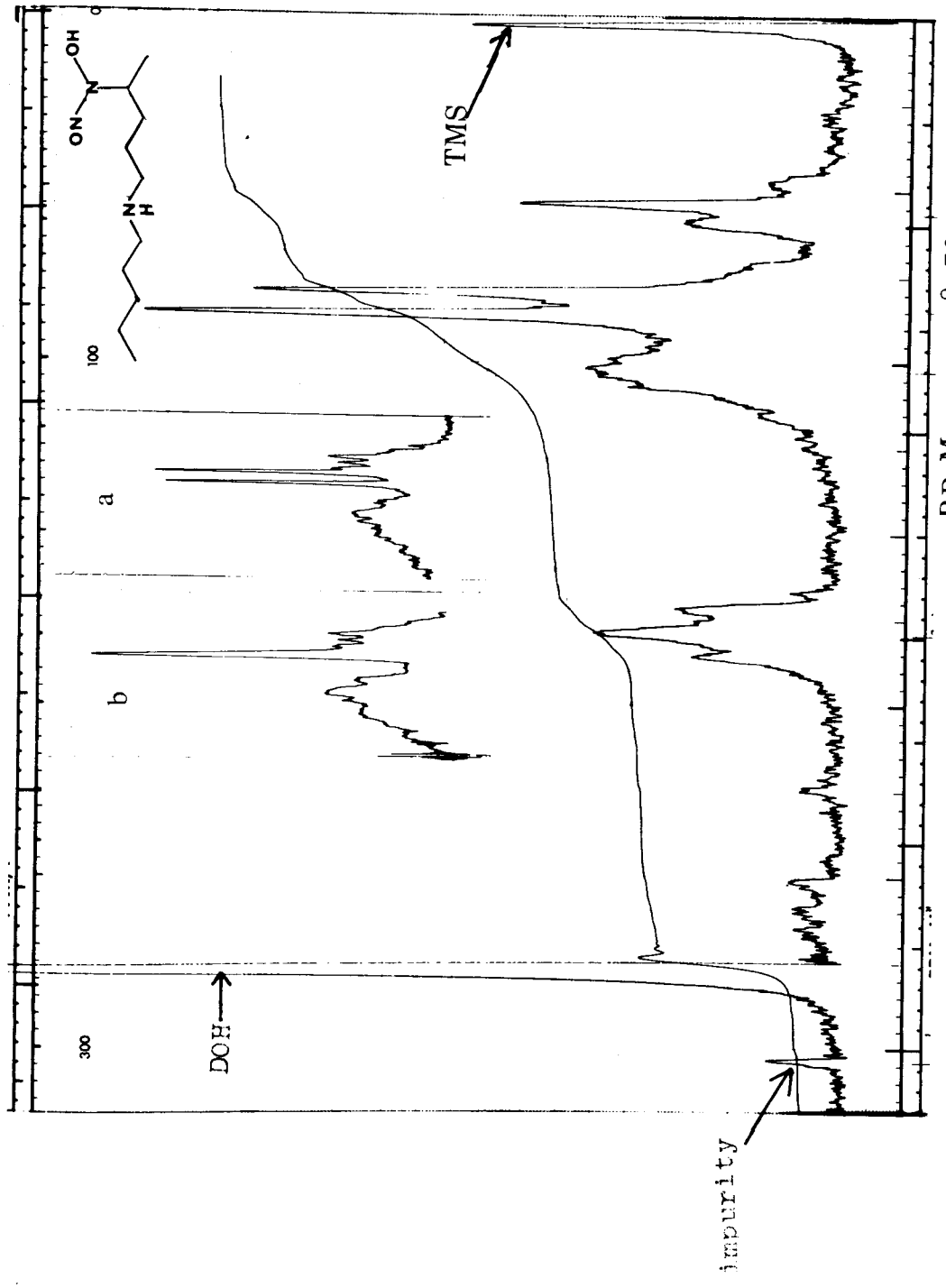
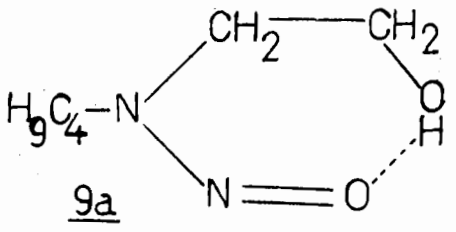


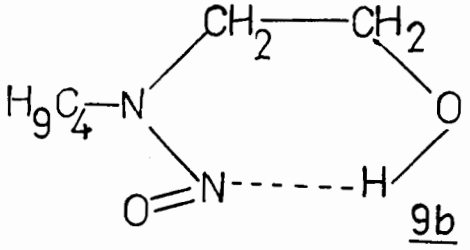
Fig. 2.3 The 60 Mc nmr spectrum of 4-(N-nitrosohydroxylamino)-dipentylamine (28). Insert a, the methyl doublet at τ8.59 before irradiation; insert b, after irradiation at τ5.7.

2.2.8 N-nitroso-2-(n-butylamino)-ethanol (9)

The nitrosamine (9) obtained by the nitrosation of N-n-butylethanolamine is a mixture of two rotamers which showed two overlapping spots in the tlc. These rotamers cannot be separated by vacuum distillation, column chromatography or preparative tlc. The spectroscopic data, however, are entirely consistent with its structure 9a and 9b (Table 2-1 - 2-3). This structural assignment is further substantiated by the preparation of its acetate derivative. The acetylated product shows only a single spot in tlc in contrast to the two overlapping spots



9a



9b

observed in 9. The other nitrosamines in the present study only show one spot in the tlc. The observation of two spots in 9 is possibly due to intramolecular hydrogen bonding in 9 resulting in a slow rotation in the N-NO bond as shown. Its intense fragments at m/e 115, 103, 84 (base peak), 73, 57, 42, 30 and 27 however follow the typical fragmentation mode characteristic of dialkylnitrosamines (57).

The photolysis of 9 proceeded normally. The absorption of the photolysate below 300 nm continued to decrease

after 5 hours despite the fact that the absorption above 300 nm remained constant. This indicated that secondary reactions (such as photolysis of products) might have taken place. The photolysate after irradiation for 7 hours showed negligible absorption above 200 nm; the absorption below 300 nm increased towards shorter wavelength without any maximum indicating that the nitrosamine had decomposed. The isolated products were n-butyraldehyde (12.6%), n-butylamine (isolated as its picrate, 1.3%), parent amine (18.5%) and an unknown product 31. The neutral and basic fractions were shown to be complex mixtures by tlc analysis and gave no separation on chromatography in a silicic acid column. Unknown 31 showed similar ir absorption as that described for 25. Its mass spectrum showed no peak beyond the fragment at m/e 89, and suggested that it was an isomer of 25. The results of photodecomposition of the above nitrosamines are summarized in Table 2.6.

Table 2-6. Nitrosamine photodecomposition with 2537A light source [a]

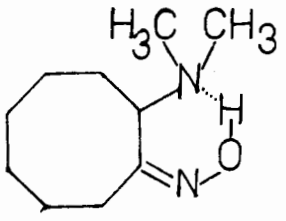
Run	Nitrosamine	Solvent	Products, yield (%)				
			Imine[b]	Amidoxime	Formamide	Parent amine	Others
1	1	CH_3OH	-	12 (2.2)	11 (20)	(42)	HCHO, 13[c]
2	1	H_2O	14(19)[d]	-	-	(24)	-
3	4	CH_3OH	-	-	22 (> 10)	+	HCHO, 23
4	3	CH_3OH	(55)[e]	20(20)	-	-	ϕCHO,19,21
5	5	H_2O	+[f]	-	-	(15)	5(10),25
6	7	H_2O	+	g	-	+	-
7	8	CH_3OH	(35.4)	27(1.5)	26(3.1)	(12)	28(7.2),29,30
8	9	CH_3OH	(12.6)	-	-	(18.5)	n-butylamine(1.3), 31

a. (i).Reaction condition: 2537A low pressure Hg arc lamp, nickel sulphate filter solution; (ii). Product yield based on starting nitrosamine; b. Yield of imine based on isolated 2,4-DNPH derivative of its hydrolyzed product; c. Detected by the tlc, not isolated; d. Isolated as isotripiperidein; 3. Based on benzylamine formed; f. Isolated as t-butylamine; g. Indicated by ir and nmr, not isolated; + not quantitatively determined.

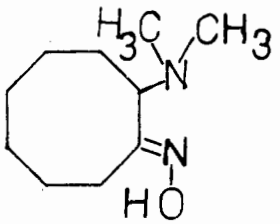
2.3 Addition of nitrosamines to olefins

2.3.1 Addition of 2 to cis-cyclooctene

Although the photoaddition to cyclooctene was conducted at different excitation wavelengths (350 nm, 254 nm, 260-350 nm respectively), the same u.v. absorption pattern was observed in all cases. The new absorption emerging at ∿293 nm was indicative of the formation of a C-nitroso dimer in the reaction (4). From the reaction mixture syn and anti-2-dimethylaminocyclooctanone oxime (32) were isolated in good yield,and that both isomers had been separated pure by column chromatography. The syn* isomer was eluted first from the column. Subsequent elution gave a mixture of the isomers and then the anti-isomer. The result shows that the photoaddition of 2 to cis-cyclooctene is independent of the excitation wavelength.



syn 32



anti 32

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* The syn- and anti- nomenclature described here was adapted from ref. 4.

2.3.2 Addition of 1 to limonene

The photoaddition of 1 to limonene was not successful and resulted in a complex mixture. The starting olefin was subsequently found not to give identical ir (58) and nmr (59) reported for pure limonene. It was therefore apparent that the limonene used was contaminated with impurities.

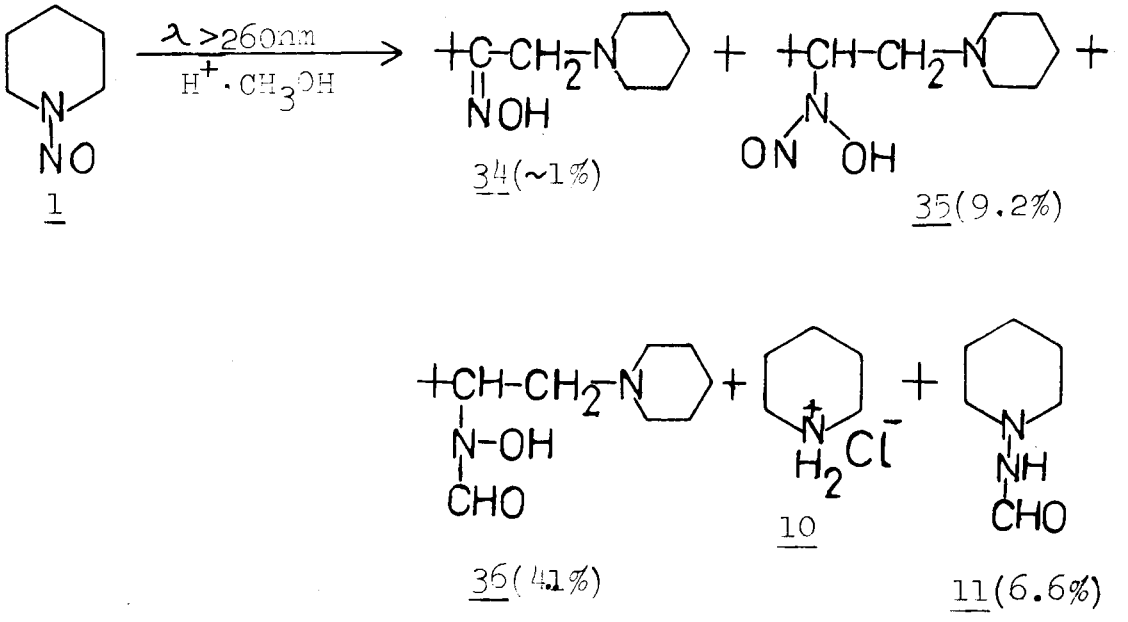
2.3.3 Addition of 1 to cyclohexene

The photoaddition of 1 to cyclohexene by the excitation of the $n \rightarrow \pi^*$ transition band of the nitrosamine ($\lambda > 290$ nm) has been described by Chow (5). The present photoaddition was rerun by irradiation at the $\pi \rightarrow \pi^*$ transition band of the nitrosamine. The crude basic extract showed a weak ir absorption at 1710 cm^{-1} which vanished after oximation. This band was possibly due to 2-piperidinocyclohexanone as had been observed in the same photolysis with light source >290 nm (5). The reaction mixture yielded the same 2-piperidinocyclohexanone oxime (33, 42%) as the only isolable product. The yield of 33 estimated from the crude basic fraction of the reaction mixture by nmr analysis was ca.60%.

2.3.4 Addition of 1 to 3,3-dimethyl-1-butene

The photoaddition of 1 to 3,3-dimethyl-1-butene ($\lambda > 260$ nm) yielded 1-piperidino-2-oximino-3,3-dimethylbutane (34 ~1%), 1-piperidino-2-(N-nitrosohydroxyl-

amino)-3,3-dimethyl-butane (35, 9.2%) and 1-piperidino-2-(N-formylhydroxylamino)-3,3-dimethyl-butane (36, 4.1%). These compounds have been described by Chen and were identified by comparisons of their ir, nmr and tlc mobility with those of authentic samples (6). In addition, small amounts of hydrochloride 10 and formamide 11 (6.6%) were obtained. These products could only be derived from the photodecomposition of the nitrosamine and served to indicate that for sterically hindered olefins (such as in the present case), photodecomposition might compete with photoaddition (8).



The results of photoaddition are summarized in Table 2-7.

Table 2-7. Photoaddition of nitrosamines to olefins

Nitrosamine	Olefin	Irradiation Range nm	Product, yield %	Ref.
2	cis-cyclooctene	350 [a]	32 (86%), syn:anti = 2:7[b]	This work
2	"	254	32 (75%), syn:anti = 2:6[b]	This work
2	"	>260 [c]	32 (77%)	This work
2	"	>290	32 (97%)	4
1	cyclohexene	254	33 (42%)	This work
1	"	>290	33 (75%)	5
1	3,3-dimethyl--1-butene	>260	34 (~1%), 35 (9.2%) 36 (4.1"), 11 (6.6%), 10[d]	This work
1	"	350	34[d], 35 (15%), 36 (2%), 10[d]	6

a. Light source, RPR 3500A lamp, pyrex filter; b. Estimated from nmr; c. Hanovia lamp (200W), quartz vessel (corex filter); d. Trace amount.

CHAPTER 3

FLASH PHOTOLYSIS OF NITROSAMINES - RESULTS AND DISCUSSION

3.1 Flash photolysis of N-nitrosopiperidine (1)

3.1.1 General features of the N-nitrosopiperidine transient

The results on the flash excitation of various nitrosamines in solution are summarised in Table 3-1.

Flash excitation of a methanol solution containing 1 (1×10^{-4}M) and HCl(0.01M) produced a transient which decayed by first order kinetics with a lifetime of 8±2 μsecs. A typical oscillographic trace is shown in Fig. 3.1 and the corresponding kinetic plot in Fig. 3.2. From Fig. 3.2, it is obvious that the transient decay does not follow second order kinetics. When an acidified aqueous solution of 1(0.62×10^{-4}M) was flashed, the same transient (sec. 3.1.5) was produced but with a longer lifetime (54±4 μs). Flash excitation of either solution over a total time-sweep of 1 msec produced no detectable long-lived transient. When either solution was flashed through a pyrex filter, no transient was detected. The transient was observalble but with much reduced intensity when the solution was excited through a nickel sulphate filter solution which has a transparent window between 330-230 nm (Fig. 6.2)

Table 3-1. Flash excitation of nitrosamines in solution

Sample Number	Nitrosamine conc. x 10^4M		HCl conc.M	Solvent	Monitoring wavelength nm	Transient Lifetime usecs
42,45	1	1.06	0.012	CH_3OH	300 - 425	8±2
48,49,51	1(air)[a]	1.06	0.012	CH_3OH	310 - 360	7±2
38	1	0.62	0.012	H_2O	270 - 425	54±4
44	1(air)[a]	0.62	0.012	H_2O	250 - 425	56±7
5,7,10	1	3.00	-	CH_3OH	325 - 675	b
43	1	0.62	-	H_2O	350 - 600	b
52	2	1.00	0.06	CH_3OH	310 - 425	9.5±1
74	2(air)[a]	1.00	0.06	CH_3OH	325 - 400	12±1
57	2	1.00	-	CH_3OH	325 - 550	b
40	6	0.54	0.06	CH_3OH	375 - 475	c
41	6	0.54	-	CH_3OH	375 - 525	47±6
26	3	1.01	0.06	CH_3OH	305 - 500	variable
27	3	1.01	-	CH_3OH	310 - 400	66±7[d]
89	3(air)[a]	0.50	-	CH_3OH	330 - 375	170±20

a. Solution undegassed; b. Control run, no transient observed. c. Transient lifetime variable > 50 μsec; d. Transient lifetime was concentration dependent.

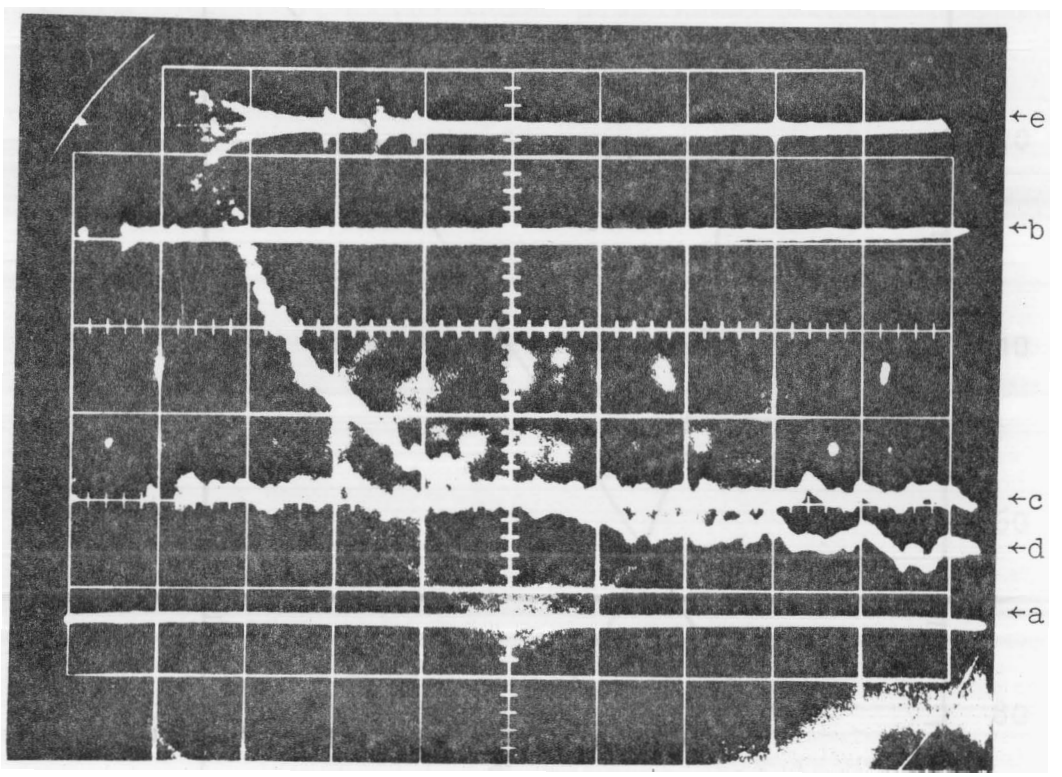


Fig. 3.1 Typical oscilloscope trace of transient observed on flashing methanol solutions of N-nitrosopiperidine (1); {1} = 1×10^{-4}M; {HCl} = 0.01M; monitoring wavelength, 330 nm; time base, 5 μsec/div.; photoflash energy, 90J; a,b - light "on" - light "off" voltage 0.5v/div.; c - baseline of the balanced beams 0.05v/div.; d - transient voltage 0.05v/div.; e - scattered light due to photoflash alone 0.05v/div.

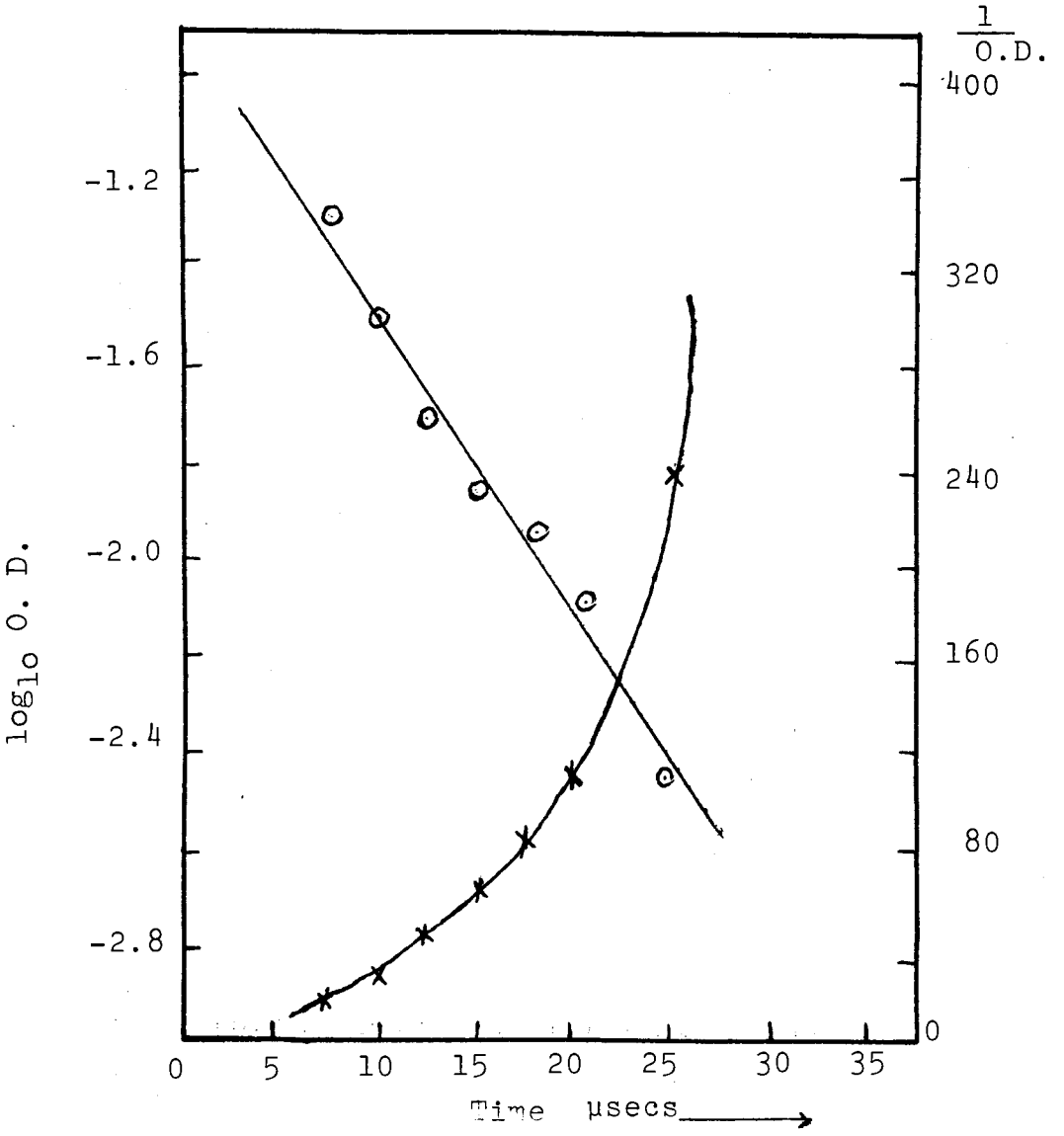


Fig. 3.2. Plot of $\log_{10}$O.D. vs. time (μs) {I} = 1×10^{-4}M; {HCl} = 0.01M; monitoring wavelength, 330 nm. Data obtained from Fig. 3.1; Inserted curve, $\frac{1}{O.D.}$ v.s. time (μs).

The observations prove that the excitation of the $\pi \rightarrow \pi^*$ transition band of the nitrosamine leads to the formation of the transient since 1 has negligible absorption above 300 nm under the concentration employed (ca. 10^{-4}M, see Fig. 3.7). The result also serves to indicate that light absorption of the nitrosamine is indispensable in order to generate the transient.

By determining the transient absorption at various wavelengths, the absorption spectrum of the transient was obtained by a point to point plot at each wavelength. Due to the rapid rate of photodecomposition of 1 upon flashing* (i.e. the concentration of 1 was changing continuously with successive number of flashes), it was not possible to obtain an accurate spectrum of the transient either in methanol or in aqueous solution. In methanol solution, the transient absorbed from 300 nm and decreased gradually to 425 nm with the transient lifetime remained constant throughout the

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* A crude estimation showed that a 1×10^{-4}M solution of 1 containing HCl in methanol can last about 30 flashes at 100J per flash. Therefore, each flash decomposes 1 by ca. 3% (average). The rate of decomposition with the successive number of flashes, however, is not linear, being more rapid in the first few flashes (ca. 10). The rate of decomposition of 1 in water is slower than that in methanol.

region scanned. Above 425 nm, the transient absorption was too weak to measure (see Table 3-2 and Fig. 3.3). The transient of 1 in water, either degassed or undegassed, gave the same absorption pattern. The absorption spectrum of the transient generated in aqueous solution (see Table 3-2 Fig. 3.4) shows an absorption pattern similar to that generated in methanol. Absorption increased from ca. 425 nm towards shorter wavelength with no clear maximum being detected in the region scanned. Because of ground state absorption, it was not possible to scan much below 300 nm with accuracy. Since the plot of the intensity of the nitrosamine absorption against the successive number of flashes was not lineraly related, it was not possible to introduce a correction factor. The fact that the transient is observed from the first flash of the solution shows clearly that it must come from the nitrosamine but not from a subsequent photoproduct.

When a methanolic or aqueous solution of 1 (5×10^{-3}M) in the presence of HCl (0.012M) was flash excited at the $n \rightarrow \pi^*$ transition band of 1 through potassium acid phthalate filter solution (or soft glass filter, see Table 6-1 and Fig. 6.2) a weaker transient than that observed by excitation at the $\pi \rightarrow \pi^*$ transition band (Table 3-3) was produced. The observed lifetime of the transient, however, was about the same as that produced by excitation of the $\pi \rightarrow \pi^*$ transition band of 1 (6.5 and 44.3 μsec as compared to 8 and 54

Table 3-2. Absorption spectrum of the transient of 1

Monitoring wavelength, nm	In methanol[a] Initial optical density	In water [b] Initial optical density
300	-	0.031
310	0.380	-
315	0.231	0.025
320	0.180	0.026
325	0.251	0.026, 0.021
330	0.214	0.021
340	-	0.023
350	-	0.022
360	-	0.024,0.014
375	0.126	0.020,0.009
385	-	0.011
400	0.110,0.178	0.006,0.009
425	0.096	-

a. {1} = 3.8×10^{-4}M, {HCl} = 0.012M, photoflash energy = 153J; b. Solution undegassed, {1} = 6.2×10^{-5}M, {HCl}= 0.012M, photoflash energy = 46J.

Conc. of 1 = 3.8×10^{-4}M; Conc. of HCl = 0.012M; Flash energy = 153J

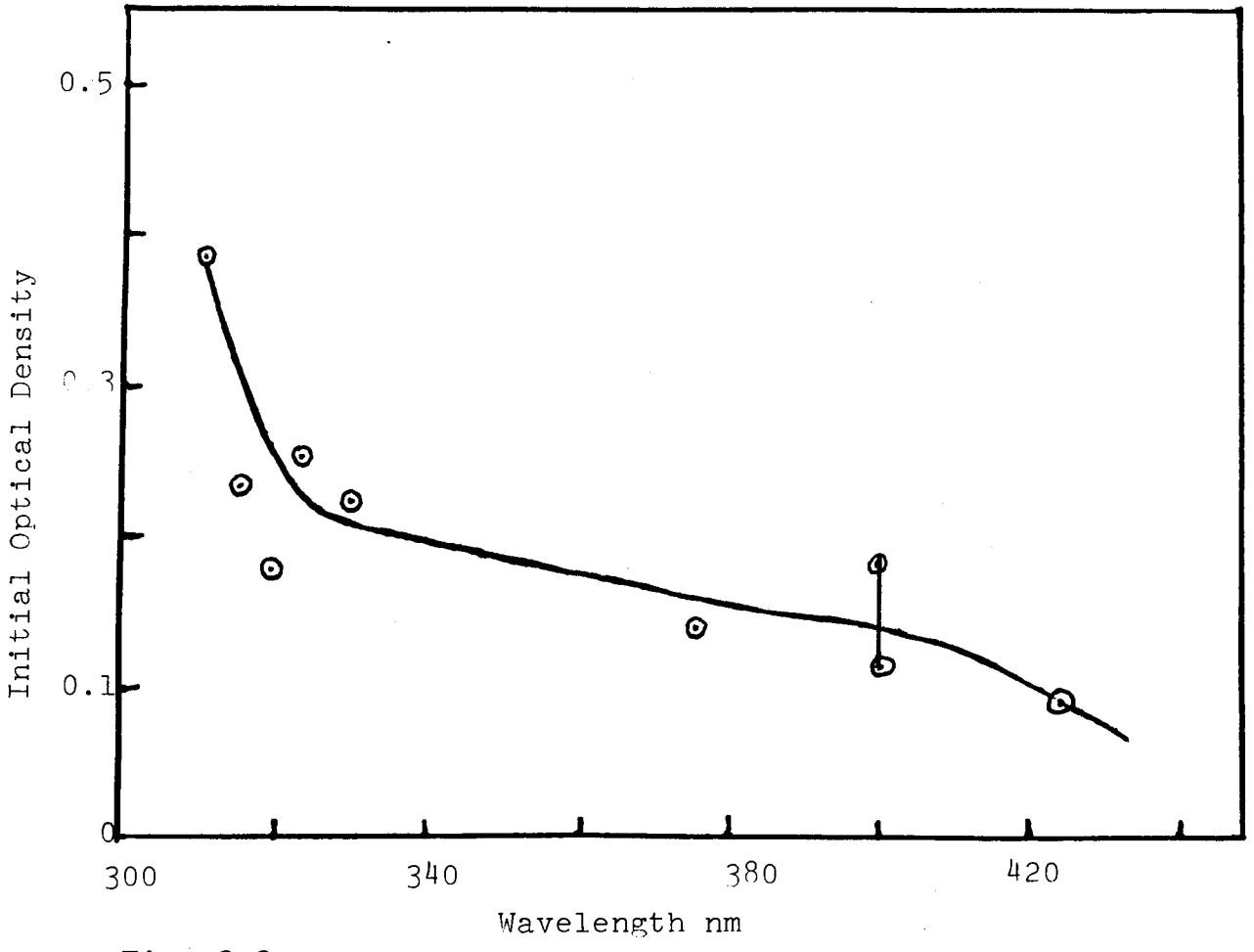
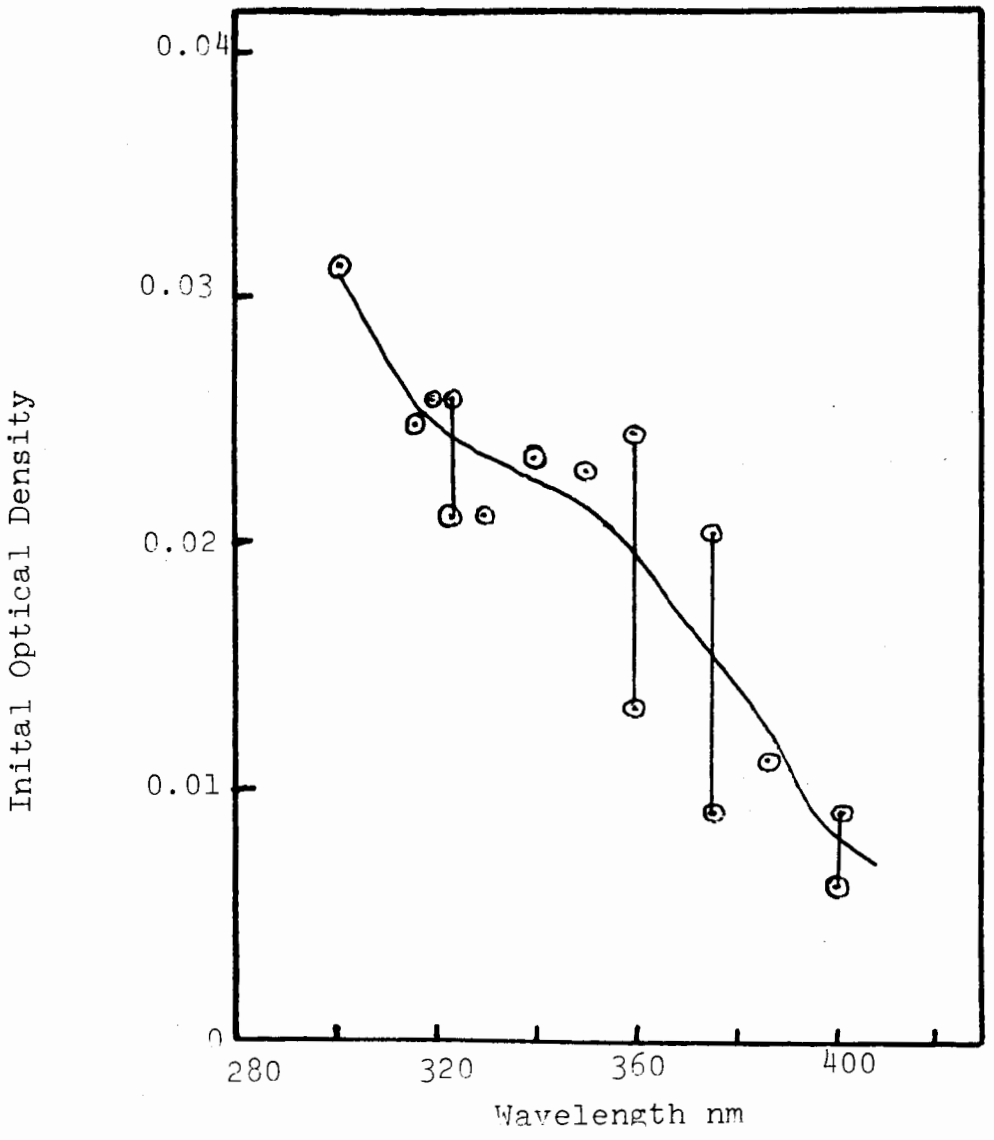


Fig. 3.3. Absorption spectrum of N-nitrosopiperidine transient in methanol



Fib. 3.4 Absorption spectrum of N-nitrosopiperidine (1) transient in water (undegassed solution)
{1} : 6.2 x 10^{-5}M; {HCl} : 0.012M; Photoflash energy : 46J.

Table 3-3. Comparison of the effect on the transient of 1 by flash excitation of its $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition band

Sample Number	Conc. of 1 M	HCl conc.M	Solvent	μsec	Monitoring wavelength nm	$(O.D.)_{10}$	$(O.D.)_o$
69[b]	5.2×10^{-3}	0.012	CH_3OH	5.4	400	0.011	0.058
42,67	1.1×10^{-4}	0.012	CH_3OH	8.2	400	0.020	0.061
90[c]	5.2×10^{-3}	0.012	CH_3OH	7.6	400	0.010	0.050
91[c]	5.3×10^{-3}	0.06	H_2O	44.3	400	-	0.017
38,44[d]	6.2×10^{-5}	0.012	H_2O	54	400	-	0.018

a. Flash energy = 120J ; b. Soft glass or potassium acid phthalate as filter; c. Solution undegassed, potassium acid phthalate as filter solution; d. Solution either degassed or undegassed.

μsec) within experimental error. In addition, the same result was obtained when the solution was flashed without degassing (rows 3 and 4) in agreement with the observation in sec. 3.1.2 (vide infra). Due to the high concentration of 1 employed here, it was possible only to obtain measurements above 375 nm. The weaker intensity of the transient may be derived from one of the several reasons stated below:

(i) The integrated area of the ground state absorption spectra of the solutions is not the same since both the concentration of the solutions and the extinction coefficient of the two absorption bands are different.

(ii) The intensity difference in the spectral output from the flash lamps since the energy output is known to be not uniform but has a parabolic distribution extending from 2000A to the visible region.

(iii) A lower quantum efficiency of the formation of the transient by the $n \rightarrow \pi^*$ excitation as compared to the $\pi \rightarrow \pi^*$ excitation.

The evidence available does not permit a differentiation between these factors. From the observation, it is concluded that the same transient of 1 is produced irrespective of excitation wavelength.

In the absence of an acid, flash photolysis of 1, either in methanol or in water, gave no observable transient. The ground state absorption spectrum of the neutral

solutions showed no decomposition after 15 flashes. The finding is in agreement with the observations reported earlier (2,3,7) that nitrosamines are photolytically inert in neutral media and has reaffirmed the requirement of an acid for a successful photoreaction.

3.1.2 Effect of oxygen on the transient of 1

When a solution of 1 (0.6-1.0x10^{-4}M) and HCl (0.012M) was flashed in methanol without degassing or in aqueous solution saturated with oxygen, the transient produced also decayed by first order kinetics with a lifetime of 7±2 and 56±7 μsecs respectively (Table 3-1). Typical traces of the transient observed in aqueous solution are shown in Fig. 3.5. In addition, the transient generated from the undegassed sample, either in methanol or in water, gives the same absorption pattern as that of the degassed solution. Comparison of the optical densities of the transient produced by flash excitation of degassed or undegassed samples in methanol leads to some uncertainty (Table 3-4), due to the very short lifetime of the transient (see Experimental). The general trend, however, indicates that there is no significant alteration in $(O.D.)_o$ in the presence of oxygen, implying that oxygen is not quenching the lifetime or the precursor of the transient. The slight discrepancy in $(O.D.)_{20}$ and $(O.D.)_{10}$ in the case of aqueous samples may be due to the energy conversion factor introduced

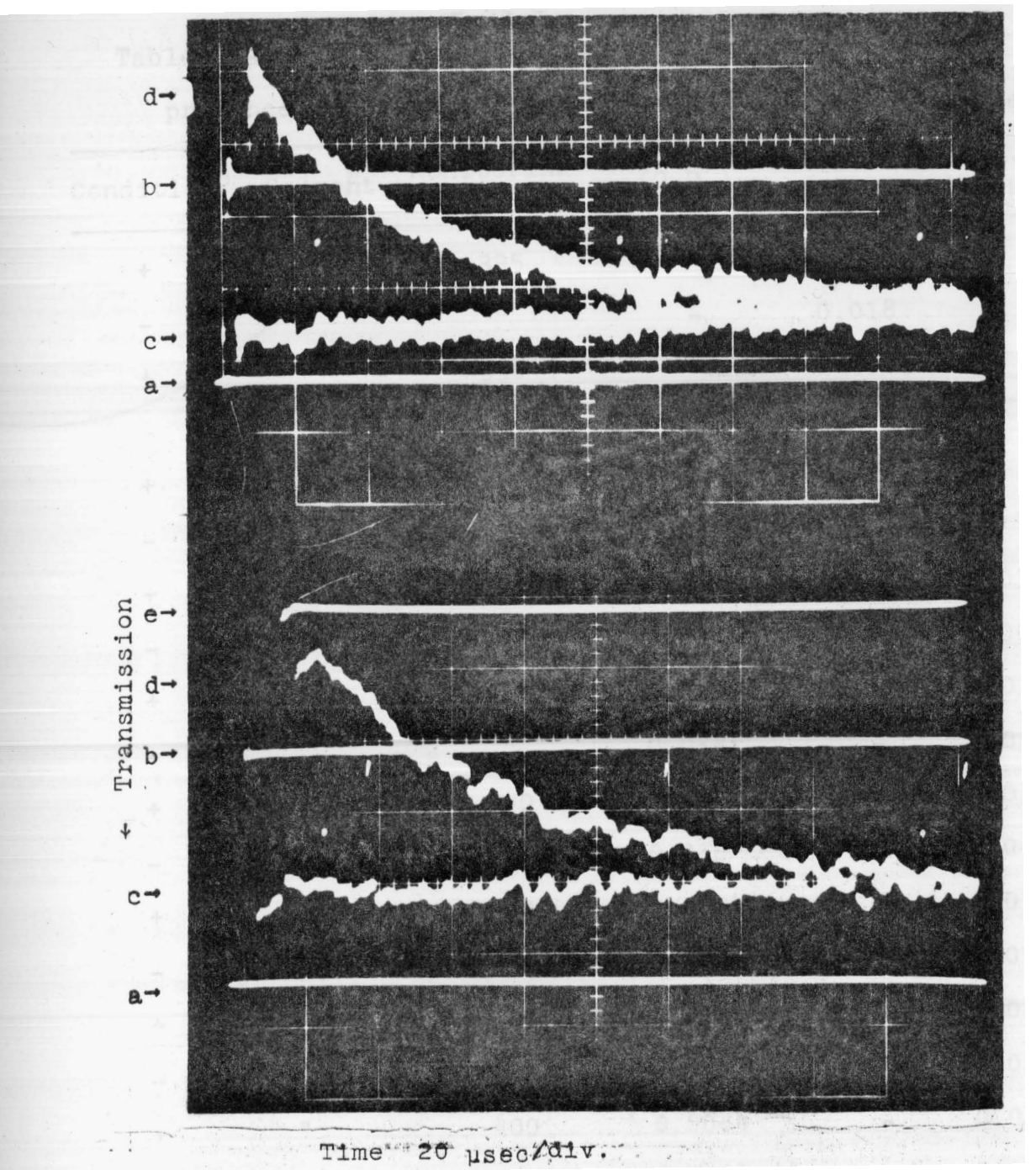


Fig. 3.5 The decay profile (oscillogram) of the transient (produced by photoflash (90J) of an aqueous solution containing N-nitrosopiperidine (1 x 10^{-4}M) and HCl (0.012M). Above: degassed solution monitored at 350 nm. Below: undegassed solution monitored at 325 nm. cf. Fig. 3.1.

Table 3-4 Comparison of O.D. of transient of 1 in the presence (undegassed) and absence (degassed) of oxygen[a]

Condition[b]	Solvent	Monitoring wavelength nm	$(O.D.)_{20}$	$(O.D.)_{10}$	$(O.D.)_{o}$
+	CH_3OH	325	-	>0.013	-
-	"	"	-	0.018	-
+	"	330	-	0.021	-
-	"	"	-	0.021	-
+	"	350	-	0.0243	-
-	"	"	-	0.0234	-
+	H_2O	315	0.027	-	0.038
-	"	"	~0.038	-	0.049
+	"	325	0.0274	-	0.038
-	"	"	0.0341	-	0.046
+	"	340	0.025	-	0.036
-	"	"	~0.036	-	0.045
+	"	350	0.0234	-	0.032
-	"	350	~0.031	-	0.043
+	"	375	0.015	-	0.023
-	"	"	0.018	-	0.028
+	"	400	0.0084	-	0.011
-	"	"	~0.0088	-	0.016

a. $\{1\}=1\times10^{-4}$M in CH_3OH or 0.62×10^{-4}M in H_2O, $\{HCl\}=0.012$M, all O.D. corrected w.r.t. 90J as flash energy; b. + = degassed solution, - = undegassed solution.

(46J in the case of undegassed sample as compared to 90J in the degassed sample).

Oxygen has long been known to be a triplet quencher and radical scavenger (60) for photoreactions in the vapour and solution phase. Recently it has been shown by flash technique that oxygen quenches the transient of N-nitroso-N-methylacetamide (61) and the triplet of orotic acid (62). In the former case the transient has been demonstrated to be derived from a triplet excited state by benzophenone sensitization. The solubility* of oxygen in water at 25° is 1.28×10^{-3}M (63) which places an upper limite on oxygen quenching at 10^6 sec^{-1} by assuming a k_Q** value of $1 \times 10^9 M^{-1} S^{-1}$. This rate seems to be low for triplet quenchin in aqueous solution# (62,64,65) and that the value is closer

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* Calculted by assuming Henry's Law, $P_B = KX_B$, using $K = 3.30 \times 10^7$ for the solubility of oxygen in water (63); here P_B= 1 atm., X_B=mole fraction of oxygen; ** Calculated from $k = k_Q\{Q\} = k_Q\{O_2\}$; the k_Q value is taken from the result of quenching of the naphthalene triplet by 1 (sec.3.1.3); # The quenching rate constant of fluorescein triplet by oxygen was 1.7×10^9 $M^{-1}S^{-1}$ (65), that of orotic acid triplet by 2,4-hexadien-1-ol was 2.9×10^9 $M^{-1}S^{-1}$ (64); ## The quenching rate constant for reactions of cycloalkyl radical with oxygen in solution was 3.9×10^6-4.3×10^7 $M^{-1}S^{-1}$ (66).

to those observed for quenching of reactive radicals by oxygen[##] (66). The absence of oxygen quenching shows that the transient of 1 can not be an excited triplet state of the nitrosamine in the presence of an acid since most triplets had a lifetime longer than 1 μsec. Since it is known that the transient is a chemically active species (see sec. 3.1.5) and that its precursor was reacting with cyclohexene (see sec. 3.1.6), the present observation shows that the genesis of the transient (i.e. the precursor of the transient) is possibly initiated from the lowest excited singlet state of the nitrosamine.

It has also been observed that while the xanthen-9-one (E_T74kcal/mole) triplet transient, generated by flash photolysis in an acidic solution, was quenched by 1 with nearly diffusion controlled rates (k_Q=1.4x10^9 $M^{-1}S^{-1}$)(67), 1 did not undergo a xanthenone sensitized photodecomposition (68). Further attempts to sensitize the photodecomposition of 1 with acetophenon (E_T74 kcal/mole) and benzophenone (E_T69kcal/mole) were also unsuccessful (68). This result further supports the correctness of the assignment that the photodecomposition of 1 is initiated by a reactive transient derived from the lowest excited singlet state of the

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The quenching rate constant for reactions of cycloalkyl radical with oxygen in solution was 3.9x10^6-4.3x10^7$M^{-1}S^{-1}$(66).

nitrosamine. The possibility that a short-lived triplet* initiates the photodecomposition can also be ruled out on the ground that it can account for the absence of quenching by oxygen, but cannot account for the failure to sensitize the photodecomposition by the above sensitizers.

3.1.3 Quenching of naphthalene triplet by 1

Flash excitation of naphthalene in hydrocarbon solvents had long been known to generate its triplet transient(69, 70,71) and was chosen as the sensitizer. Flash excitation of naphthalene ($2x10^{-2}M$) and HCl ($8.4x10^{-2}M$) in methanol alone gave rise to a strong transient which decayed by first order kinetics with a lifetime of 164 μsec. This strong transient is identified as the naphthalene triplet by its absorption spectrum (Fig. 3.6) which is in agreement with that reported (71). This naphthalene triplet observed showed considerable deviation from first order decay under high intensity of photoflash energy (ca.150J) due to triplet-triplet annihilation**. However, good first order

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* The triplet lifetime must be less than 1 μsec in order to account for the absence of oxygen quenching.

** A similar phenomenon has been reported for the quenching of naphthalene triplet by methyl orotate in aqueous solution (64).

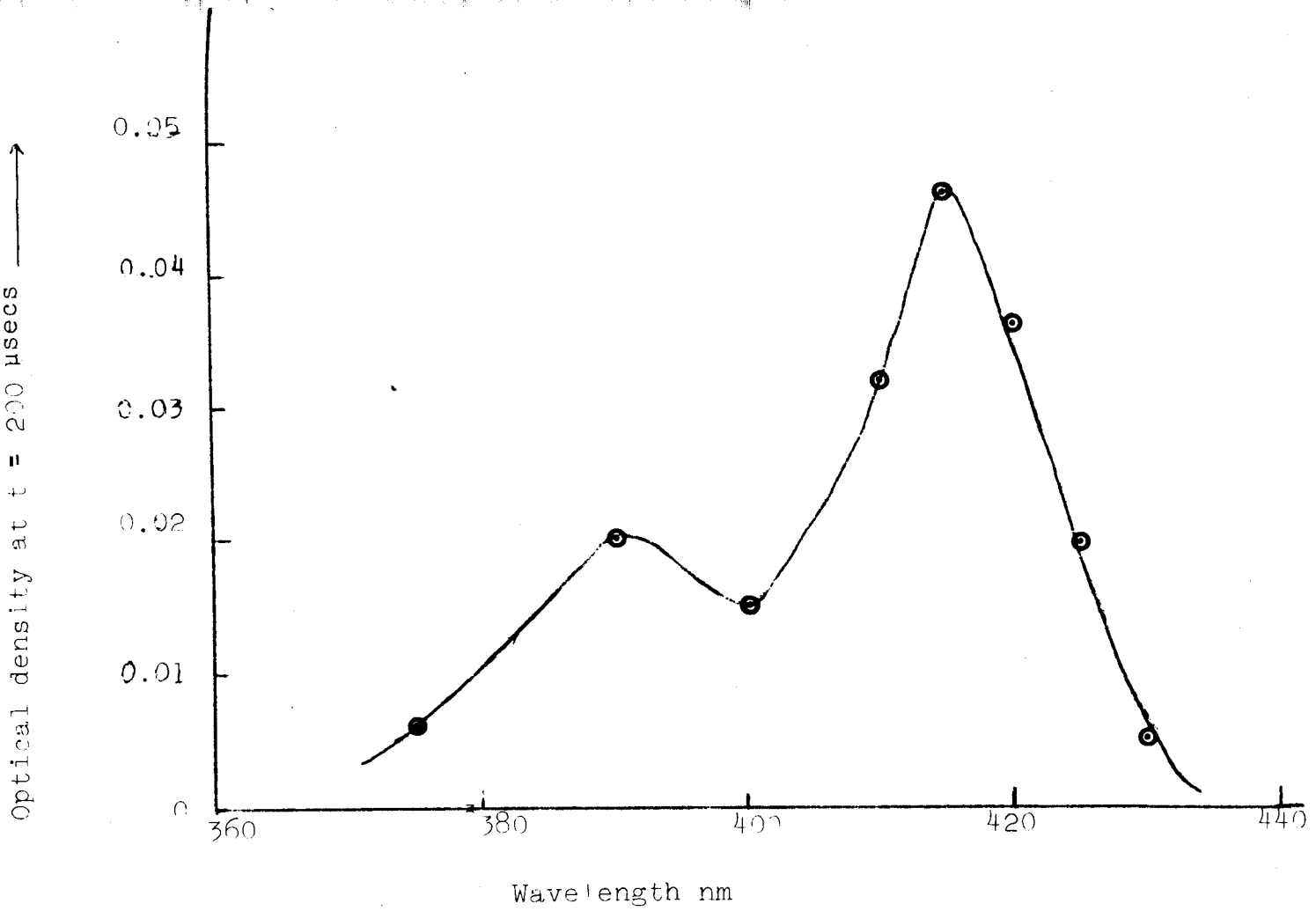

Fig 3.6. Absorption spectrum of naphthalene triplet in methanol (71)
{Naphthalene} : 2 x 10^{-2}M, {HCl} : 8.4 x 10^{-2}M.

kinetics was easily restored by using 0.02M N-nitroso-dimethylamine as the filter solution to reduce the flash intensity and hence the triplet concentration. With this filter solution, naphthalene was preferentially excited through the window at 300 nm region but nitrosamine 1 was not irradiated (Fig. 3.7). When 1 was added, the naphthalene triplet was quenched either in the presence or absence of acid. At high concentration of 1 ($>10^{-3}$M), the naphthalene transient lifetime was extremely short and lay beyond the time resolution of the instrument. At low concentration of the nitrosamine (1.26-9.8 x 10^{-5}M) a reduction in the lifetime (74.3-16.1 μsec) of the naphthalene triplet was observed. However, at this concentration, the transient of 1 even if it was produced would not have been detected since the strong absorption of the naphthalene triplet would mask it completely. These results are summarised in Table 3-5.

Table 3-5 Quenching of Naphthalene Triplet by 1*

Sample Number	Conc$_5$ of 1 x 10^5M	τ_{obs} of naphthalene triplet μsec	k_{obs} x 10^{-4} S^{-1}
15	0	164	0.61
17	1.26	74.3	1.35
34	2.38	20.1	4.98
14	3.80	23.9	4.19
21	6.94	19.7	5.07
16	9.80	16.1	6.21

*{Naphthalene}=2 x 10^{-2}M; {HCl}=8.4 x 10^{-2}M.

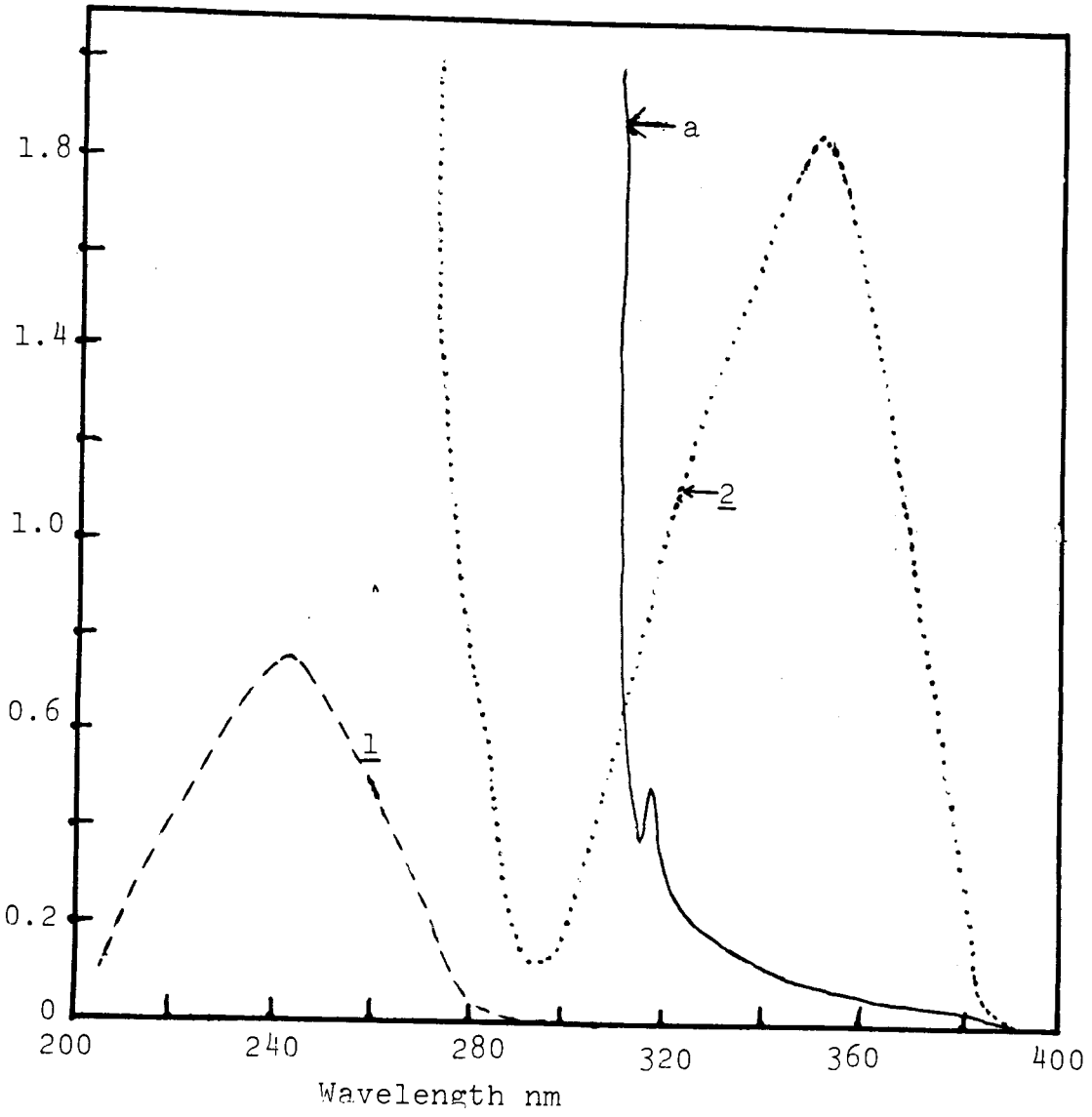

Fig. 3.7 Absorption spectra of a. N-nitrosopiperidine (0.98×10^{-4}M) and naphthalene (2×10^{-2}M); N-nitrosopiperidine (1) (1×10^{-4}M); N-nitrosodimethylamine (2) (0.02M) filter solution. Solvent: methanol, Optical path: 10 mm.

The primary photophysical processes can be represented as follows:

$$N^o \xrightarrow{h\nu} N^1$$

$$N^1 \xrightarrow{k_{isc}} N^3$$

$$N^3 \xrightarrow{k_p} N^o + h\nu'$$

$$N^3 \xrightarrow{k_{ic}} N^o + \text{heat}$$

$$Q + N^3 \xrightarrow{k_Q} N^o + Q^3$$

where N^o, N^1, N^3 represented naphthalene in its S^o, S^1 and T^1 state; k_{isc}, k_p, k_{ic}, k_Q represented the rate constants of intersystem crossing, phosphorescence, internal conversion from T^1 to S^o of naphthalene and the bimolecular quenching rate constant of the naphthalene triplet by 1.

From the above steps, the rate of decay of naphthalene triplet can be represented by the expression

$$\frac{-dN^3}{dt} = (k_p + k_{ic} + k_Q Q)N^3$$

$$= (k_o + k_Q Q)N^3$$

$$= k_{obs} N^3$$

where $k_o = k_p + k_{ic}$ = decay rate constant of naphthalene triplet in the absence of 1, and

k_{obs} = observed decay rate constant of naphthalene triplet in the presence of 1

$$k_{obs} = k_o + k_Q\{Q\} \quad \{5\}$$

According to eq. {5}, if the energy transfer is the only process, a plot of k_{obs} against the quencher concentration {Q}(Fig. 3.8) should give a straight line the slope of which is equivalent to k_Q. By the method of least squares (72), k_Q was found to be $5.14 \pm 1.6 \times 10^8$ $M^{-1}S^{-1}$.

The naphthalene triplet lifetime has been reported to be about 100 μsec ($k_O = 1.1 \times 10^4 S^{-1}$) in hexane (70). The observed value of 164 μsec appeared to be too long. Subsequent redetermination* by using a lower concentration of naphthalene (2×10^{-4}M) gave a lifetime of 101 μsec for the naphthalene triplet which agrees well with the reported value. The value of k_Q determined in this separate series (2 runs, each with lss than 10% deviation) is 1.4×10^9 $M^{-1}S^{-1}$. This value suggests that triplet energy transfer from naphthalene to 1 is almost a diffusion controlled process** since the experimental value of k_Q appears to be always less than the value calculated by the Debye equation for non-viscous solvents (64, 74). The result indicates that the triplet energy level of 1 is lower than that of

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* The flash duration of the flash apparatus was reduced to 1.1 μsec and the sensitivity of the instrument was much improved during these runs.

** k_{diff}, calculated by the modified Debye equation is 1.1×10^{10} $M^{-1}S^{-1}$ in methanol at 20° (73).

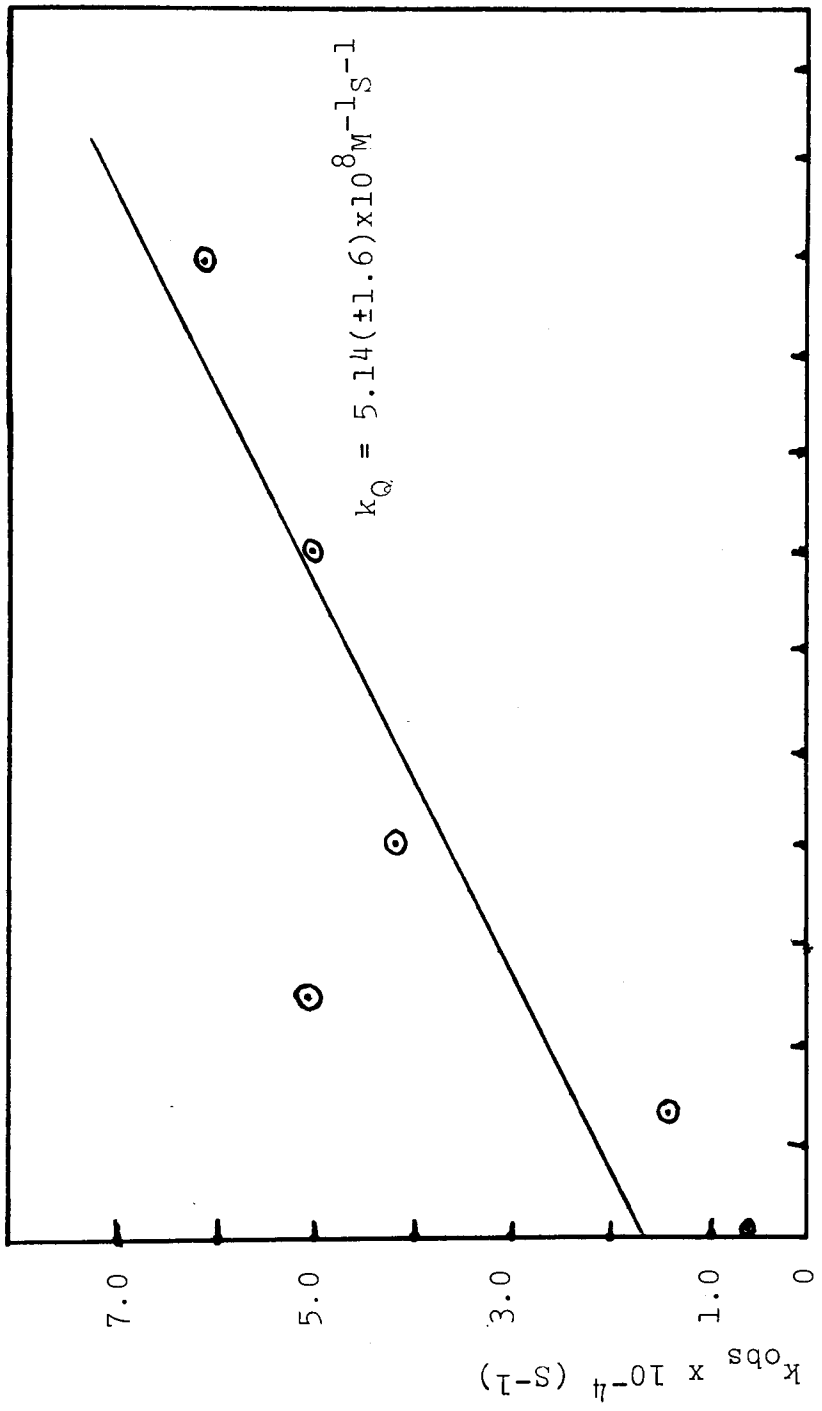

Fig. 3.8 Quenching of Naphthalene triplet by N-nitrosopiperidine in methanol, {Naphthalene}=2 x 10^{-2}M, {HCl}=8.4 x 10^{-2}M.

naphthalene (E_T = 61 kcal/mole). In the absence of an acid, k_Q was determined to be 6.3 x $10^8 M^{-1}S^{-1}$ and is virtually the same as that found in the presence of acid.

Since the quenching of the naphthalene triplet and the 2,2'-binaphthyl triplet (see sec. 3.1.4) by 1 shows that the triplet energy of 1 is lower than that of naphthalene, an attempt was made to sensitize the photodecomposition of 1 by naphthalene. The sample solution containing 1, naphthalene and HCl in methanol was flashed under identical conditions against a blank sample without naphthalene. The solution was flashed either without a filter (irradiation of both 1 and naphthalene) or with soft glass, or potassium acid phthalate solution filter (ca. 75% light energy absorbed by 1, see Table 6-1 and Fig. 6.2 for filters). At the concentration of 1 used (4 x 10^{-3}M), the naphthalene triplet was completely quenched and was not detectable. However, because of the weak intensity of the N-nitrosopiperidine transient produced, the result was not clear cut. Comparison of the initial optical density, $(O.D.)_o$, of the sensitized sample with that of a blank run in the absence of naphthalene was not possible due to the short lifetime of the transient (see Experimental). Comparison of the O.D. at 10 μsec after flash, however, indicated that there was a slight enhancement of the transient intensity by naphthalene (Table 3-6). The percentage

Table 3-6 Naphthalene sensitization of 1[a]

Sample Number	Naphthalene conc. x 10^2M	Monitoring wavelength nm	$(O.D.)_{10}$	Enhancement of transient intensity %
69	-	400	0.0126	15.9[b]
70	108	400	0.0146	
69	-	400	0.0088	10.2[c]
70	1.08	400	0.0097	
69	-	410	0.0082	17.1[c]
70	1.08	410	0.0096	
69	-	420	0.0067	70.0[c]
70	1.08	420	0.0114	
69	-	420	0.0064	34.4[d]
70	1.08	420	0.0086	
				30 (average)

a. {1}= 5.2 x 10^{-3}M; {HCl} = 0.012M, Solvent: methanol; photoflash energy = 120J;

b. Without filter; c. Soft glass filter; d. Potassium acid phthalate filer solution.

of the enhancement of transient intensity is calculated according to eq. {6}

$$\text{Transient enhancement} = \frac{(\text{O.D.})_{\text{with naph.}} - (\text{O.D.})_{\text{without naph.}}}{(\text{O.D.})_{\text{without naph.}}} \times 100\% \quad \{6\}$$

Based on the observed quenching rate constants of 1×10^9 for triplet energy transfer and $1 \times 10^{10} M^{-1}S^{-1}$ for singlet energy transfer (sec. 3.1.9), the quantum efficiency of singlet and triplet energy transfer (i.e. the fraction of sensitizer singlet or triplet that transfers energy to 1) can be determined from eq. {7} (75)

$$Q_{ET} = \frac{k_Q \{Q\}}{k_Q \{Q\} + k_0} \quad \{7\}$$

Where k_0 represents the composite decay rate constant of the naphthalene triplet and singlet states, and Q_{ET} the quantum efficiency of energy transfer from naphthalene triplet and singlet state of 1 respectively.

From eq. {7}

$$Q_{ET}^T = \frac{5 \times 10^{-3} \times 10^9}{5 \times 10^{-3} \times 10^9 + 10^4} = 1$$

$$Q_{ET}^S = \frac{5 \times 10^{-3} \times 10^{10}}{5 \times 10^{-3} \times 10^{10} + 10^7} = 0.8$$

where k_0 for the lowest triplet of naphthalene is taken as $1 \times 10^4\ S^{-1}$ (this work and ref. 70) and k_0 for the singlet

state of naphthalene $\sim 10^7$ S^{-1} (76). At the present nitrosamine concentration, both singlet and triplet energy transfer are very efficient. The observed average enhancement of the transient intensity (Table 3-6) is 30%, and does not permit a differentiation between triplet and singlet energy transfer although the latter is favoured since the lowest triplet state of 1 is chemically not active (sec. 3.1.2).

As a control run, a methanol solution containing 1 (5.2×10^{-3}M) and naphthalene (2×10^{-4}M) in the absence of acid was flashed without any filter. No transient was detected in this case. As before the naphthalene triplet would be completely quenched under the concentration of 1 employed, but the failure to observe the N-nitroso-piperidine transient renders further support that an acid is essential for the photodecomposition (sec. 3.1.1). In addition, the ground state absorption spectrum of the solution showed no detectable change after 20 flashes. From this fact it is obvious that although triplet energy transfer from naphthalene to 1 takes place efficiently, the lowest triplet state (T_1) of 1 is chemically unreactive in the absence of an acid. Since no phosphorescence is observed from 1 (sec. 3.1.9), energy dissipation of T_1 to the ground state (S_o) of the nitrosamine must follow a radiationless decay which is necessarily an efficient process.

3.1.4 Quenching of 2,2´-binaphthyl triplet by 1

Flash excitation of a methanol solution containing 2,2´binaphthyl (6.9×10^{-5}M) and HCl (8.4×10^{-2}M) through a pyrex filter (or without filter) gave a strong transient which decayed by first-order kinetics with the lifetime of 56.6 μsecs. The strong transient is assigned to the triplet of the aromatic hydrocarbon by analogy to naphthalene (70,71). It absorbs in the region 340-675 nm with several maxima. When a methanol solution containing 1 (1.24×10^{-5}M), HCl(8.4×10^{-2}M) and 2,2´-binaphthyl (4.2×10^{-5}M) was flashed either without a filter or with a pyrex filter, the same transient was observed but the lifetime was reduced to 37 μsec. At the concentration of 1 employed, ca.90% of the incident light energy was absorbed by 2,2´binaphthyl (Fig. 3.9) when the solution was flash excited without a filter. With a pyrex filter, only 2,2´-binaphthyl was irradiated. The observed reduction in lifetime shows that the binaphthyl triplet is quenched as in the case of naphthalene. The quenching rate constant, k_Q, calculated from eq. {5} was 7.5×10^7 $M^{-1}S^{-1}$ which was one order of magnitude lower than that of naphthalene quenching. The quenching is inefficient* implying that the triplet energy level of 1 is

* It has been observed in the quenching of biacetyl (E_T=56) phosphorescence in benzene solution at 20° that for quenchers with triplet levels higher than 55 kcal/mole, there is a general trend towards a lowering of k_q(2×10^3-$3\times10^7 M^{-1}S^{-1}$) with increasing E_T (78,79).

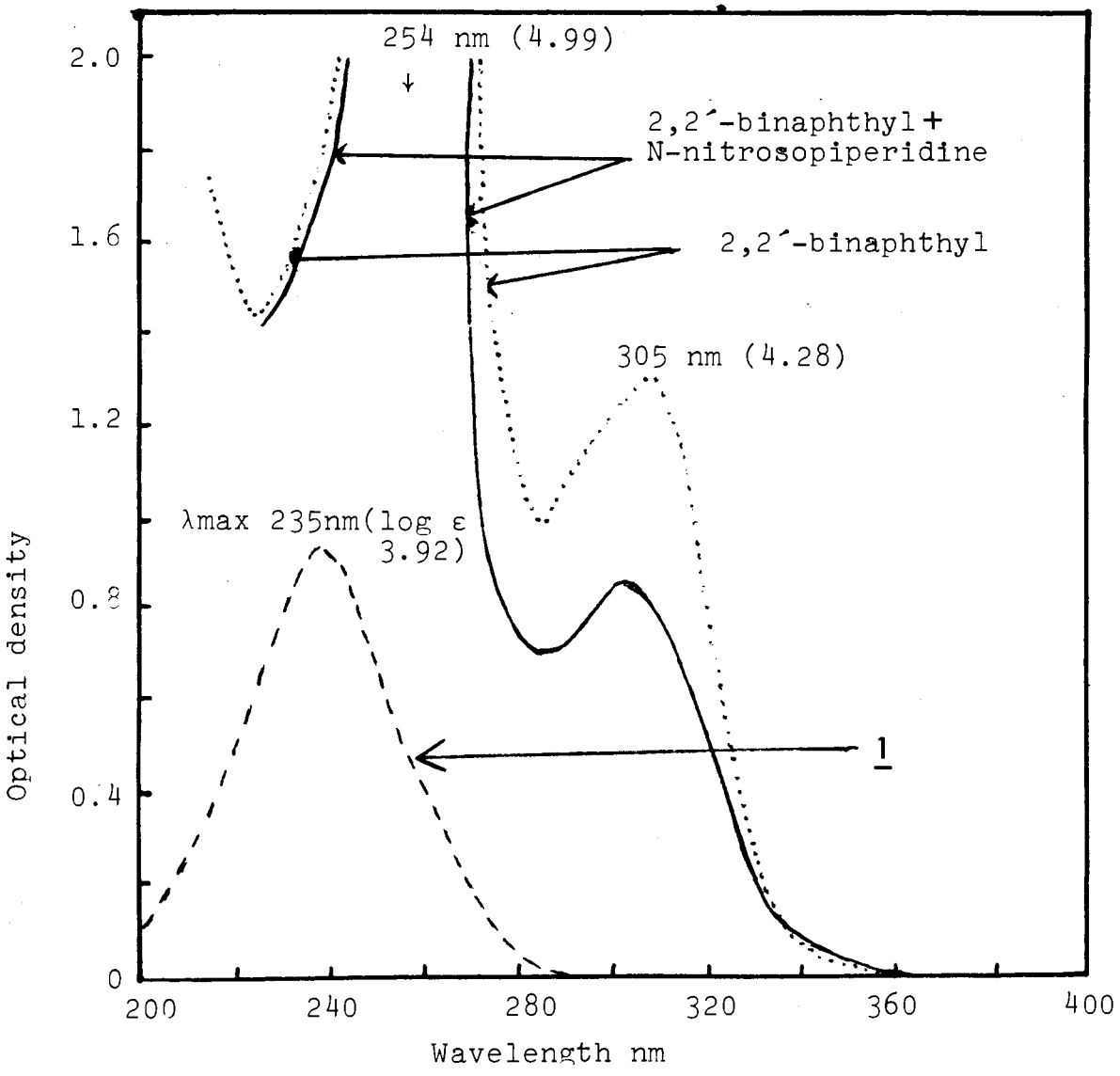

Fig. 3.9 Absorption spectra of N-nitrosopiperidine(1) (1.1×10^{-4}M); 1(1.2×10^{-4}M) and 2,2´-binaphthyl (4.2×10^{-5}M); 2,2´-binaphthyl (6.9×10^{-5}M); Solvent, Methanol; Optical path, 10mm.

higher than that of binaphthyl (E_T 56 kcal/mole) (77).

Sandros (78) has described the reversibility of triplet energy transfer when the triplet levels of donor-acceptor moleculars are within 3 kcal/mole of one another. The rate constant of back transfer, k_b, was related to that of the forward transfer (k_q) by eq. {8}

$$k_b = k_f \exp \frac{-\Delta E_T}{RT} \qquad \{8\}$$

where ΔE_T is the difference in triplet energy levels. Assuming ΔE_T is 3 kcal/mole

T is 298^0 (25^oC)

k_f is equal to the diffusion controlled rate, 1.1×10^{10} $M^{-1}S^{-1}$ (73)

$$k_b = 1.1 \times 10^{10} \exp. \frac{-3}{2 \times 10^{-3} \times 298}$$

$$= 7.1 \times 10^7 \ M^{-1}S^{-1}$$

The rate of reverse energy transfer k_b, is in good agreement with the rate constant of quenching k_Q, determined by the experiment. This gives the triplet energy level of 1 as ca. 59 kcal/mole which is lower than the triplet energy of naphthalene (E_T 61 kcal/mole) and is in agreement with the finding that the quenching of naphthalene triplet by 1 (sec. 3.1.3) is an efficient process.

An indication of the spin rate responsible for the formation of the transient of 1 was provided by the following observation. In the presence of 1 (1.24×10^{-4}M), a plot of

the lifetime of the binaphthyl triplet versus the number of successive flashes showed a general trend of increase in the lifetime of the binaphthyl triplet with increasing number of flashes indicating the decrease of the concentration of 1 by decomposition upon flashes. The ground state absorption spectrum of the flashed solution (taken in a 10 cm cell) after 57 flashes showed a decrease in optical density in the region of 340-400 nm which was too large to be accounted for by the slight decomposition of aromatic hydrocarbons upon flash excitation (80). The observation implies that 1 is consumed on flashing. Since E_T of binaphthyl is lower than that of 1, one would expect that the photodecomposition of 1 would be quenched if its lowest triplet (T_1) is responsible for the photodecomposition. The lowest excited singlet energy level of binaphthyl(E_{s_1}) estimated from its longest absorption band at 333 nm and the shortest emission band at 342 nm (81) is 85±1kcal/mole. The result from fluorescence quenching of naphthalene by 1 (sec. 3.1.9) shows that the E_{s_1} of 1 is lower than 85 kcal/mole. The possibility of singlet energy transfer from binaphthyl to 1 therefore exists; but in view of the concentration of 1 used (10^{-4}M), singlet energy transfer would be very minor. The decomposition of 1 was possibly due to the small percentage of light absorbed by 1 when the solution was flashed without filter resulting in its direct

excitation to the S_1 state from which chemical reaction took place. The transient of 1, however, would not be observable due to the strong overlapping absorption of the binaphthyl triplet and the abnormally long scattered light* (duration more than 50 μsec) presumably caused by the fluorescence of binaphthyl.

3.1.5 Mixed solvent study

It has been observed that the transient of 1 generated in methanol is identical to that in water (sec. 3.1.1) on the basis of the similarity of the absorption spectra in the two solvents. The difference in lifetime must therefore be due to methanol reacting chemically with the transient. As expected, flash excitations of aqueous solutions of 1 (6.2×10^{-5}M) in the presence of HCl (0.012M) and varying quantities of methanol give a transient which decayed by pseudo first-order kinetics with a lifetime intermediate between that in water and in pure methanol. The results are summarized in Table 3-7.

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* Similar scattered light not found in other systems had been observed in the region below 350 nm in the quenching of naphthalene triplet by 1.

Table 3-7. Quenching of transient of 1 by Methanol[a]

Sample Number	$\{CH_3OH\}M$	τ_{obs} μsecs	$k_{obs} \times 10^{-4}(S^{-1})$
38	0	54.0	1.85
53	2.48	43.6	2.29
80	6.19	26.6	3.76
58	12.40	14.0	7.14
42,67[b]	24.80	8.0	12.50

a. $\{1\} = 6.2 \times 10^{-5}$m, {HCl} = 0.012M, solvent, water;

b. $\{1\} = 1.1 \times 10^{-4}$M.

The plot of k_{obs} versus concentration of methanol is linear (Fig. 3.10) showing that methanol is indeed reacting with the transient. The results presented so far permit us to represent the photochemical process by the following sequences of reactions.

$$N \xrightarrow{h\nu} N^*$$

$$N^* \xrightarrow{k_o} No$$

$$N^* + M \xrightarrow{k_M} Product$$

where No and N* represent molecules of 1 in its ground and excited state respectively, k_o is the composite first order rate constant for the decay of N* in the absence of M (as outlined in eq. {5}). Since the concentration of methanol, {M}, was greater than N*, the experimental rate constant (k_{obs}) must be due to pseudo first-order

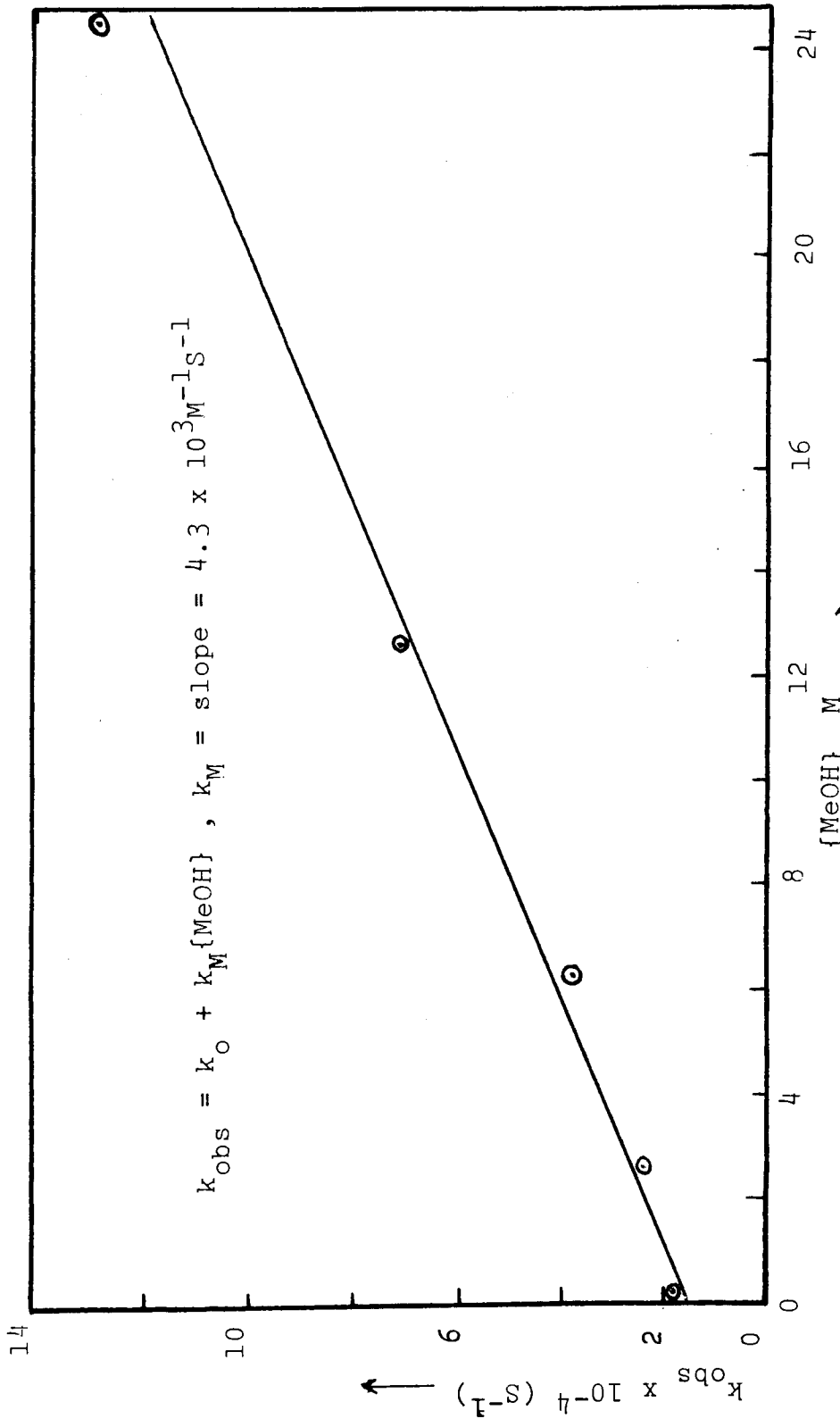

Fig. 3.10 Reaction of N-nitrosopiperidine transient with methanol

kinetics, and is related to k_o and k_M by eq. {9} by the same argument as for eq. {5}.

$$k_{obs} = k_o + k_M \times \{M\} \qquad \{9\}$$

The reaction rate constant k_M, determined from the slope of the straight line (Fig. 3.10) is 4.3×10^3 $M^{-1}S^{-1}$.

In the presence of HCl, comparison of initial optical densities $(O.D.)_o$ of the transient of 1 in aqueous methanol (Table 3-8) revealed a random fluctuation, within a factor of 1.35 over a ten-fold variation in the concentration of methanol (0-12.4M). The random variation of $(O.D.)_o$ shows clearly that the methanol is not reacting or reacting to a negligible extent with the precursor of the transient.

The magnitude of k_M determined (4.3×10^3 $M^{-1}S^{-1}$) in the presence of HCl suggests that the chemical process is radical abstraction of hydrogen from the solvent* The available data, together with complementary observations from this laboratory (67) leads to the assignment of the piperidinium radical 37 for the transient on the following grounds. The exchange of hydrogen for chlorine in an N-chloroamine has recently been shown to occur via an aminium radical intermediate (23, 24). The rate constant

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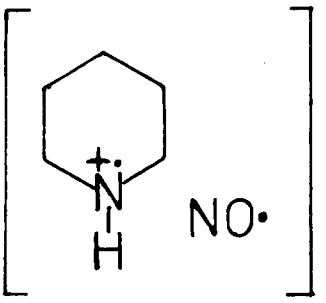
* The rate constant for hydrogen abstraction of benzophenone triplet from benzene is $9 \times 10^2 M^{-1}S^{-1}$ while that from benzhydrol was $2 \times 10^6 M^{-1}S^{-1}$ (82).

Table 3-8 Comparison of initial optical densities of transient of 1 in $CH_3OH - H_2O$ solution [a]

Methanol Conc. M	Monitoring Wavelength nm	$(O.D.)_o$
0	325	0.037
12.4	"	0.027
0	330	0.039
2.48	"	0.030
6.19	"	0.035
12.40	"	0.028
0	340	0.036
2.48	"	0.024
0	350	0.032
2.48	"	0.023
6.19	"	0.027
12.40	"	0.024
0	375	0.023
2.48	"	0.018
0	400	0.011
6.19	"	0.014
12.40	"	0.014

a. {1} = 0.62 x 10^{-4}M , {HCl} = 0.012M, Photoflash energy 90J.



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for propagation is estimated to be in the range 7 x 10^2 to 1 x 10^4 $M^{-1}S^{-1}$ (24). This value is in good agreement with the observed bimolecular rate constant for the reaction of the transient with methanol (4.3 x $10^3 M^{-1}S^{-1}$). Flash excitation of N-chloropiperidine (1 x 10^{-3}M) in aqueous solution (undegassed) containing H_2SO_4(0.01M) gives a transient which decays by first-order kinetics with a lifetime of 100±5 μsec (67). Flash excitation of 1 (2 x 10^{-4}M) under similar conditions gives a transient with a lifetime of 44.6 μsec. Both transients have the same absorption spectrum (see Figs. 3.11 and 3.12); this is similar to that determined for 1 in HCl (sec. 3.1.1). In addition, the bimolecular rate constant (k_M) of the N-chloropiperidine transient with methanol is 4.9 x $10^3 M^{-1}S^{-1}$ (67) in good agreement with that observed from 1 in HCl. The difference in the lifetime of the transient generated in aqueous solution from N-nitroso and N-chloropiperidine is attributable to the different partner (Cl. or NO.) present in the cage. This would imply that the rate constant for photodissociation is somewhat dependent on the radical

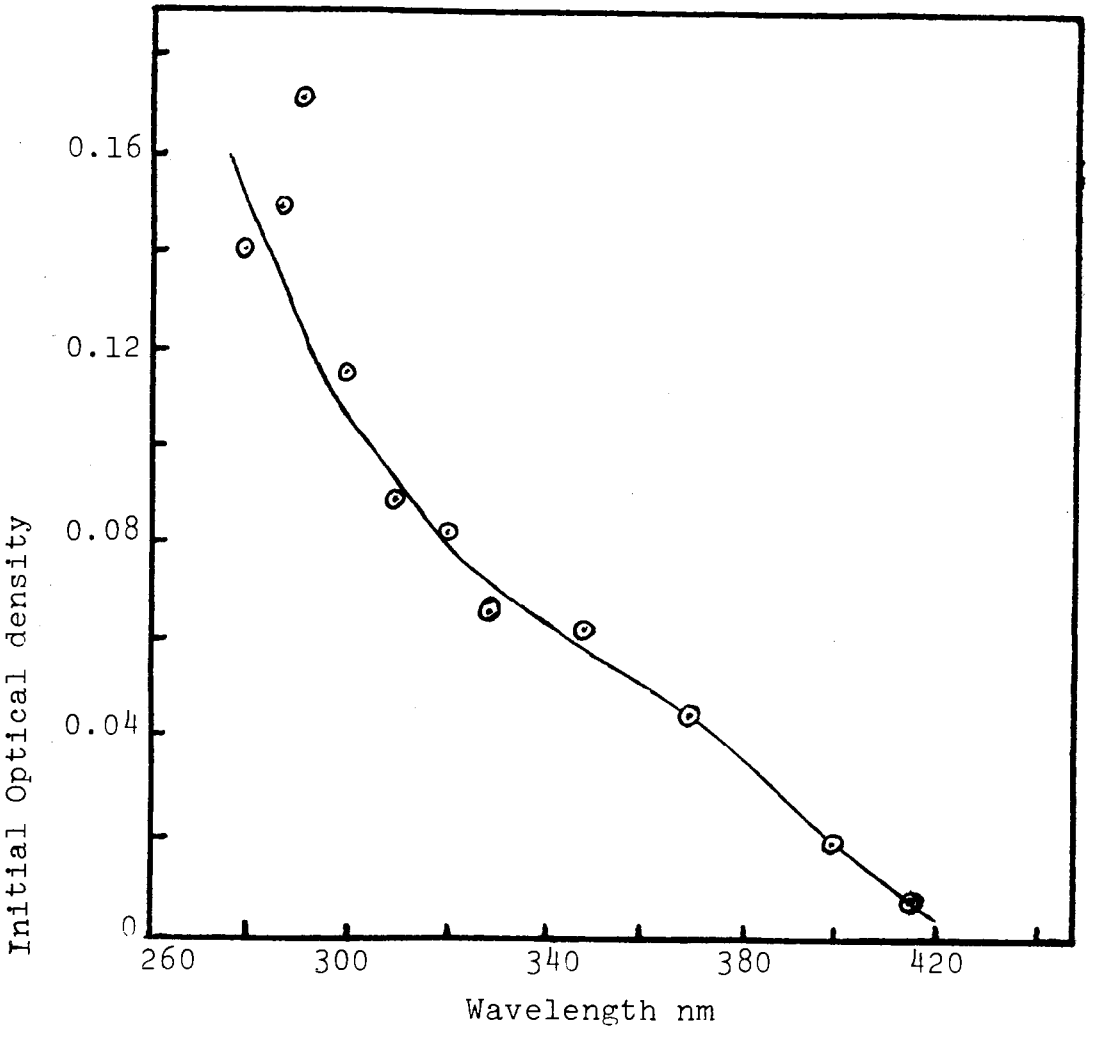

Fig. 3.11 Absorption spectrum of transient of 1 in water (undegassed). $\{1\} = 2 \times 10^{-4}$M; $\{H_2SO_4\}$ = 0.01M; Flash energy: 132J, Vycor filter; (Reproduced by kind permission of Dr. R.W. Yip et al) (67).

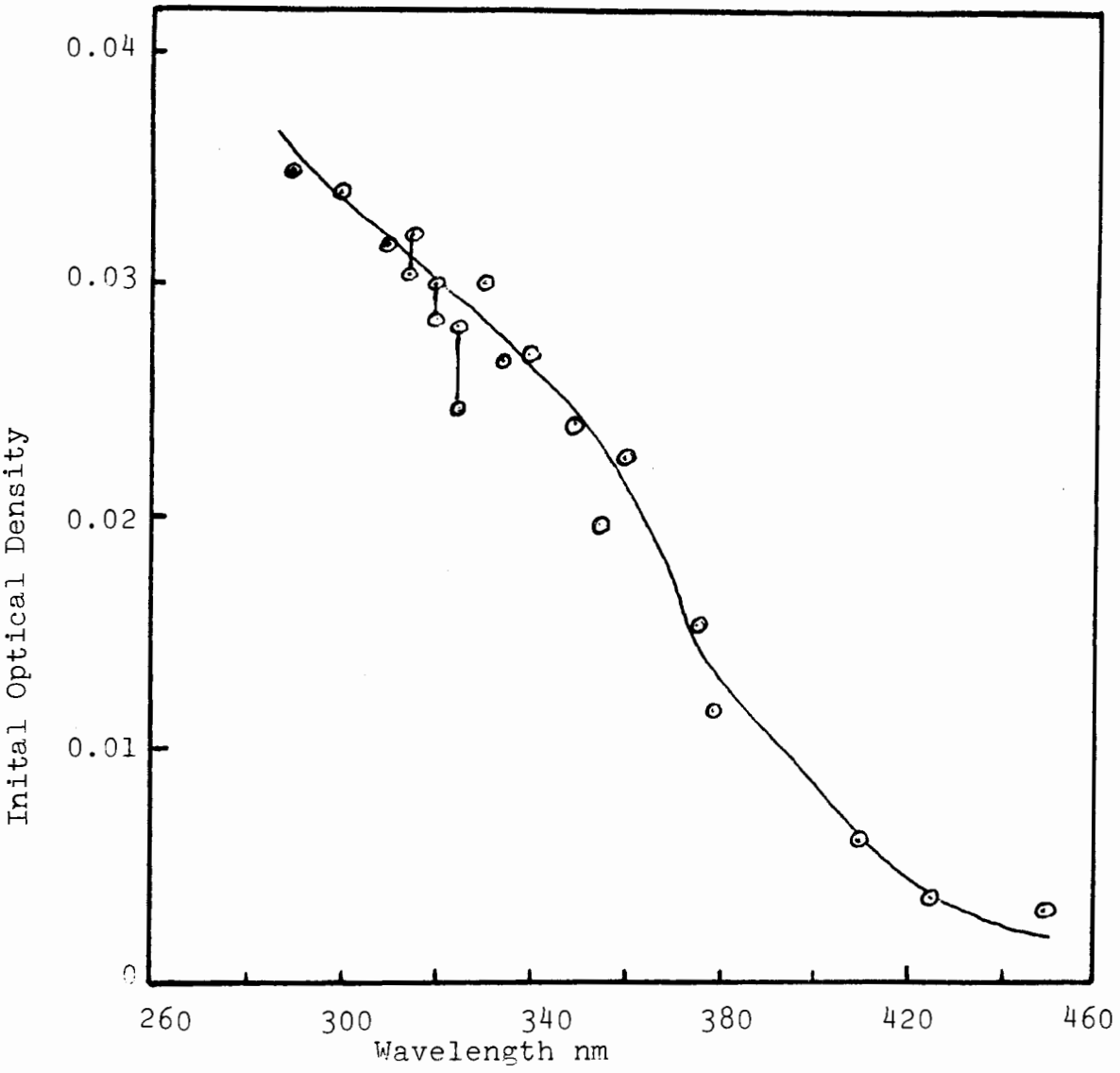

Fig. 3.12 Absorption spectrum of N-chloropiperidine transient in water (undegassed), $\{H_2SO_4\}$ = 0.01M; Flash energy: 67J, vycor filter; (Reproduced by kind permission of Dr. R.W. Yip et al) (67).

partner and on the tightness of the radical pair. The above observations lead to the conclusion that the observed reactive transients in both cases are identical, viz., the piperidinium radical. That the transient of 1 is not quenched by oxygen is possibly due to an inefficient reaction of the piperidinium radical with oxygen. Assuming a bimolecular rate constant of 10^6 $M^{-1}S^{-1}$ between the transient radical and oxygen* and the solubility of oxygen in water at ambient temperature as 1×10^{-3}M (63), this would place an upper limit of $10^3 S^{-1}$ for oxygen quenching of the transient. Since the decay rate constant of 1 in water is about 2×10^4 S^{-1}(ca. 50 μsec, sec. 3.1.1), the observed effect of oxygen would be negligible. In view of observations on the cycloalkyl radical** reaction with oxygen (66), it is possible that in water the rate constant for the reaction of the transient of 1 with oxygen is lower than 10^6 $M^{-1}S^{-1}$.

3.1.6 Reaction of the transient precursor with cyclohexene

The effect of added cyclohexene on the transient of 1 was investigated. Flash excitation of a methanol solution containing 1 (1.06×10^{-4}M), HCl (0.012M) and

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* See footnote * on Page 55.

** See footnote ## on Page 55.

cyclohexene (0.12M) gave no detectable transient. At intermediate concentrations of cyclohexene (10^{-3} - 10^{-2}M), the transient observed was weaker, and decayed with first-order kinetics; its lifetime remained fairly constant (8.2 μsec, average of 5 runs) within experimental error. The intensity of the transient, however, was proportionally reduced as the concentration of olefin increased. The observation demonstrates clearly that cyclohexene is reacting with the precursor of the transient but not the transient itself. The available data treated in a quantitative manner permits us to evaluate approximately the rate constant of photoaddition between cyclohexene and the transient percursor. The photoaddition scheme can be formulated as follows:

$$N^* \xrightarrow{k_x} \text{transient of } \underline{1} \qquad \text{(i)}$$

$$N^* + C \xrightarrow{k_r} \text{Adduct} \qquad \text{(ii)}$$

$$N^* \xrightarrow{k_1} \text{ground state} + h\nu + \text{other processes} \qquad \text{(iii)}$$

where N* and C represent N-nitrosopiperidine in its lowest singlet excited state and cyclohexene respectively. The competing reactions are the demotion of the transient k_x and all other deactivation processes of the singlet nitrosamine (k_1). If A_o/A represents the ratio of the yield of the transient in the absence of olefin to the

yield in the presence of olefin, then A_o/A is equal to ϕ_o/ϕ (relative quantum yield). From the above steps (i) - (iii), in the absence of olefin,

$$\phi_o = \frac{k_x}{k_x + k_1}$$

in the presence of olefin $\phi = \frac{k_x}{k_x + k_1 + k_r\{C\}}$

Combination of the two expressions gives eq. {10}

$$\frac{A_o}{A} = 1 + \frac{k_r}{k_x + k_1}\{C\} \qquad \{10\}$$

The conventional form of the Stern-Volmer equation (83) is written as eq. {11}

$$\frac{\Phi_o}{\phi_Q} = 1 + k_Q\tau\{Q\} \qquad \{11\}$$

where ϕ_o and ϕ_Q represent a measurable physical parameter (such as emission intensity) of the excited molecule D* in the absence and in the presence of a second molecule Q (such as a quencher) respectively; k_Q is the bimolecular quenching constant for deactivation of D* by Q; τ is the measured lifetime of D* in the absence of Q and can be represented by eq. {12} (83)

$$\tau = \frac{1}{\Sigma k_i} \qquad \{12\}$$

Here the rate constants (k_i) represent unimolecular or

pseudo-unimolecular processes which deactivate D*.

Comparison of eqs. (10) and (11) shows that eq. (10) is actually another form of the Stern-Volmer equation in which the following relationships hold:

$$\text{(a)} \qquad \frac{A_o}{A} = \frac{\phi_o}{\phi_Q}$$

$$\text{(b)} \qquad \frac{1}{k_x + k_1} = \tau$$

$$\text{(c)} \qquad k_r = k_Q$$

Here the quenching rate constant, k_Q, is being replaced by the reaction rate constant (k_r) of the olefin with the transient precursor.

The data for the Stern-Volmer plot are shown in Table 3-9. The Stern-Volmer plots shown in Figs. 3.13 and 3.14 yielded a straight line within the experimental error. The slopes obtained from the two plots are 70 and 87 M^{-1} respectively, giving the average of 78.5 ≈ 80 M^{-1}, i.e.,

$$\frac{k_r}{k_x + k_1} = 80M^{-1} \qquad \{13\}$$

Table 3-9 Quenching of transient of 1[a] by cyclohexene

Entry	cyclohexene conc. M	τ usec	A_0	A	$\frac{A_o}{A}$ [b]
1	0.00	9.0	0.064[c]	0.064	1.00
2	5.51×10^{-3}	8.6	0.064[c]	0.041	1.56
3	0	8.1	0.105	0.105	1.00
4	0.95×10^{-3}	7.9	0.105	0.098	1.08
5	5.51×10^{-3}	7.4	0.105	0.086	1.22
6	1.18×10^{-2}	6.9	0.105	0.059	1.78
7	0	7.3	0.0286	0.0286	1.00
8	0.95×10^{-3}	7.2	0.0286	0.0235	1.23
9	5.51×10^{-3}	6.5	0.0286	0.0227	1.26
10	1.18×10^{-2}	8.1	0.0286	0.0168	1.85
				(0.0148)[d]	(2.21)[d]
11	0	8.8	0.0216[e]	0.0216	1.00
12	5.51×10^{-3}	9.1	0.0216[e]	0.0147	1.52

a. $\{1\}=1.06\times10^{-4}$M, {HCl}=0.012M, Solvent: CH_3OH. b. Engry 1-6 $A_o=(O.D.)_o$ at 330nm in the absence of cyclohexene, $A=(O.D.)_o$ at 330nm with added cyclohexene; Entry 7-12; $A_o=(O.D.)_{10}$ at 330nm without cyclohexene, $A=(O.D.)_{10}$ at 330nm with cyclohexene; In all cases, the following conditions were observed by both A_o and A: (i) Average of at least 2 kinetic traces; (II) Flash energy= 120J; (iii) $6 \leq \tau \leq 10$ μsec; (iv) Difference in number of flashes <5; (v) $R \geq 0.995$; c. $(O.D.)_o$ at 400nm. d. Average of 4 kinetic traces; e. $(O.D.)_{10}$ at 400nm.

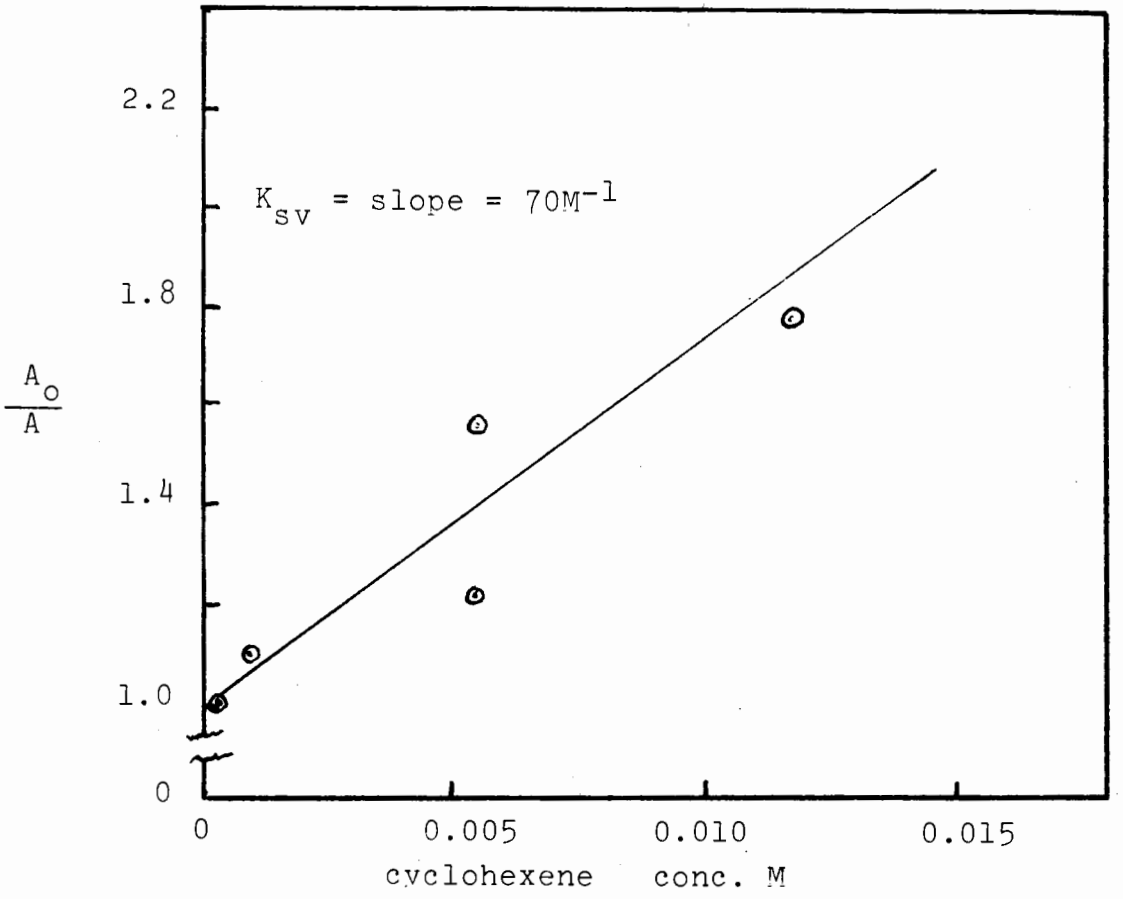

Fig. 3.13 Stern-Volmer plot of quenching of transient of 1 by cyclohexene, {1} = 1.06×10^{-4}M, {HCl} = 0.012M, Solvent: CH_3OH; $(\text{data for O.D.})_o$.

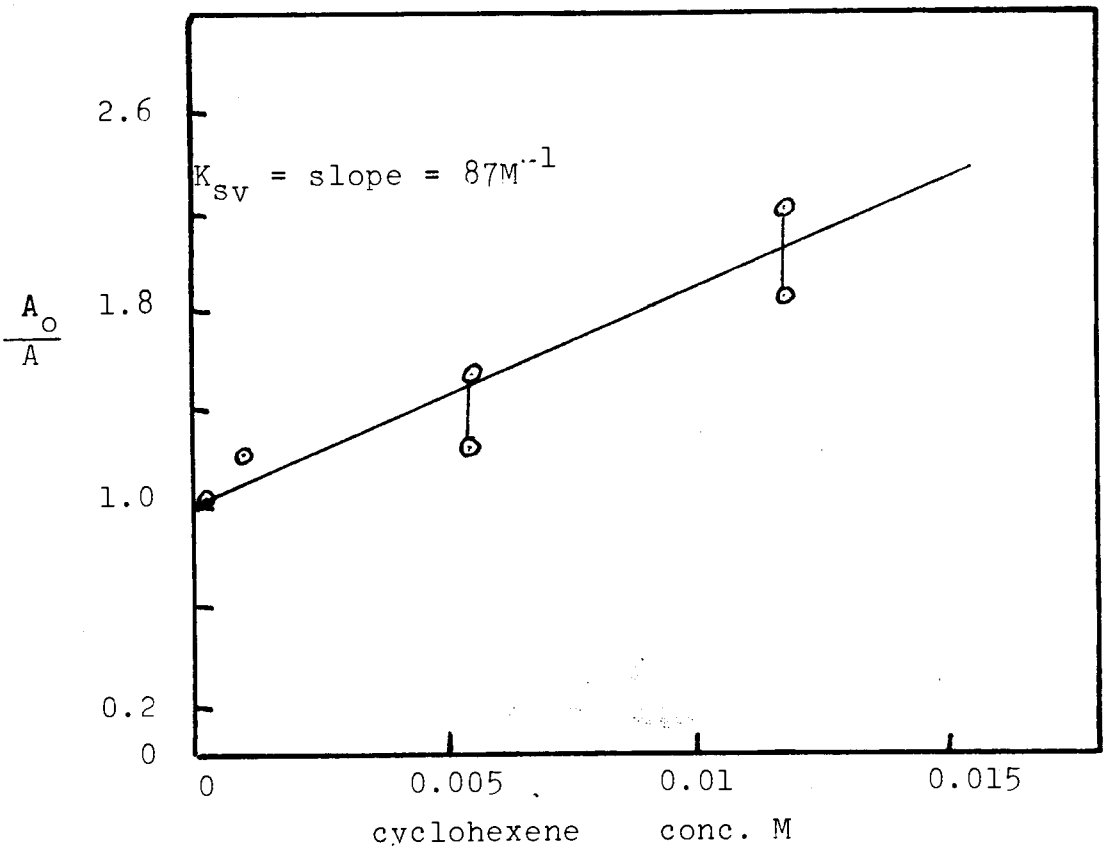

Fig. 3.14 Stern-Volmer plot of quenching of transient of 1 by cyclohexene, {1} = 1.06 x 10^{-4}M, {HCl} = 0.012M, Solvent: CH_3OH; (data for $(O.D.)_{10}$).

The natural lifetime of the lowest excited singlet state can be calculated from the longest absorption band of $\underline{1}$ ($n \rightarrow \pi$) by the approximate relationship of eq. {14} (84).

$$\tau_o = \frac{3.5 \times 10^8}{\bar{\nu}^2 \, \varepsilon \Delta\bar{\nu}_{\frac{1}{2}}} \text{ sec.} \qquad \{14\}$$

where $\bar{\nu}$ = mean frequency for the absorption band at 349 nm

$= 2.86 \times 10^4 \text{ cm}^{-1}$

$\varepsilon = 88.5$

$\Delta\bar{\nu}_{\frac{1}{2}}$ = half width of $n \rightarrow \pi^*$ transition band

$= 3.9 \times 10^3 \text{ cm}^{-1}$

from which τ_o is determined to be 1.24 μsec. The detectable limit of ϕ_F, the quantum yield of fluorescence is estimated to be 2×10^{-4}*. The actual lifetime τ of the lowest excited singlet state is related to τ_o and ϕ_F by eq. {15}(86)

$$\phi_F = \frac{\tau}{\tau_o} \qquad \{15\}$$

From these data and eq. {15}, $k_x + k_1$ is calculated to be larger than $2 \times 10^9 \text{ sec}^{-1}$. Substitution of this value into eq. {13} the reaction rate constant is calculated to be $>1 \times 10^{11} \text{ M}^{-1}\text{S}^{-1}$(lower limit)#. This value is one order of magnitude higher than the diffusion controlled rate constant in methanol which is calculted to be $1.1 \times 10^{10} \text{ M}^{-1}\text{S}^{-1}$ (73). Since the maximum rate constant for collisional process

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* Estimated from the fluorescence quantum yield of 0.01 and signal/noise ratio for the fluorescence of biacetyl in aqueous solution obtained with the instrument (85).

See note on P.220.

in solution is the diffusion-controlled rate, the present finding is interpreted as evidence for a ground state complex formation between 1, cyclohexene and proton, which reacted immediately upon photoexcitation with the nitrosamine in its lowest singlet excited state. Evidence for the presence of a ground state complex between nitrosamine and the π-electron cloud of carbon-carbon double bond has been demonstrated by nmr studies (39,87) which also suggest a finite orientation of the complex (87).

The rising time of the transient formation, which is a measure of the decay of the precursor, has recently been found to be ∿0.2 μsec from the oscillographic trace in which the light scatters were eliminated (67). This implies that the lifetime of the precursor must be <0.1 μsec assuming the decay of the excited species is exponential in nature (i.e., first order or pseudo first order decay). For the precursor with the decay rate of $\sim 10^7$ sec^{-1} to be reacting with 0.01M cyclohexene at a comparable rate as was observed (Table 3-9) would entail a bimolecular rate constant of $\geqslant 10^9 M^{-1} S^{-1}$ for the addition reaction. There is so precedent for addition of a radical species to a carbon-carbon double bond with such a high rate constant. Therefore, the aminium radical can not be the species which initiates the photoaddition. That this is is the case is demonstrated by

the failure of N-chlorodiethylamine and 1-butene to give the 1-amino-2-chloro compound under Ingold's conditions (24), using azobisisobutyronitrile as the initiator (88), in spite of the reported yield of the β-chloramine under Neale's conditions (25,26).

The assignment of the lowest excited singlet state to the transient precursor is in agreement with the observation that the fluorescence quantum yields of acetophenone, triphenylene, naphthalene, 1,2-benzanthracene, anthracene and 1,4-dimethylanthracene can be correlated linearly with the rate of photosensitization in the photoaddition of 1 to cyclohexene (15), an observation which serves to indicate that the photoaddition is related to the excited singlet state of 1.

3.1.7 Control runs

Flash excitation of a solution of HCl (0.012M) in methanol (degassed or undegassed) by monitoring in the region 300-700 nm gave no detectable transient. The result serves as a control to show that the observed transient of 1 is not due to solvent impurity but is generated from excitation of 1. Flash excitation of an undegassed solution containing HCl(0.06M) in water, however, gave an extremely weak, long-lived transient (total time sweep >1 msec) which gave no measurable transient when scanned on the same time scale with which the nitrosamine had been flashed. The very

weak transient was believed to originate from the presence of an impurity in the acid. An observation similar to this has been reported in the study of orotic acid by flash photolysis (64). Since all samples were run at an acid concentration much lower than 0.1M (Table 3-1), the presence of the weak, long-lived transient was insignificant and had no effect on the transient measurement.

3.1.8 Quantum yield measurements.

To ascertain the quenching effect of added naphthalene on the photodecomposition of 1, the quantum yield of the disappearance of the nitrosamine was determined with a 366 nm light source, using potassium ferric oxalate actinometry (89). Irradiation of the solution was carried out up to 10-15% decomposition of the nitrosamine. The data were treated in the same manner as previously described (61,90). The results are summarized in Table 3-10

Table 3-10 Effect of naphthalene on the quantum yield of disappearance of 1 [a]

1 x 10^3M	{Naphthalene} M	{HCl} M	ϕ
7.03	0	0.10	3.61[b]
4.36	5.65×10^{-4}	0.06	3.76
4.36	1.02×10^{-3}	0.06	4.08
4.36	1.12×10^{-2}	0.06	3.64

a. Solvent: Methanol; b. Ref. 91.

The data indicate that the quantum yield varies only slightly and randomly, and imply that there is no appreciable quenching on the photodecomposition of 1 by naphthalene at the concentration range of naphthalene employed.

A quantum yield of 0.75 for the formation of N-benzylbenzamidoxime in the photodecomposition of dibenzylnitrosamine in trifluoroacetic acid-benzene system has been reported (14). The data from Table 3-10 show that the quantum yield of disappearance of 1 is about 3.6. The quantum yield of disappearance of 1 reported by Colon (15) was 2.46, 2.74 (in the presence of cyclohexene) and 3.02 (in the presence of 1,3-dienes). These observations suggest that a short radical chain process is possibly involved in the photoreaction. The quantum yield determined here represents the sum of all product formation and does not reflect the quantum yield of amidoxime formation since the photolysis of 1 gives more than one product whereas amidoxime formation is the exclusive product in the photolysis of 3 (3,11).

3.1.9 Quenching of naphthalene fluorescence by 1

Emission of 1 and 6 have been studied in methanol solution under neutral and acidic conditions. Within the instrumental sensitivity, no emission from the nitrosamines other than that due to background signals was detected. The details of these experiments are summarized in Table 3-11.

Since 1 does not emit, and flash photolysis has shown that triplet energy transfer from naphthalene to 1 takes place efficiently (sec. 3.1.3), an attempt was made to quench the fluorescence of naphthalene by 1. The concentrations of both naphthalene and HCl were the same in all samples. The degassed samples containing 1 (0.523-4.22 x 10^{3}M), HCl (0.012M) and naphthalene (4.94 x 10^{-4}M) in methanol were run in the emission apparatus (Fig. 6.6) against a control sample (without 1) under identical operational conditions.

Table 3-11 Conditions for emission study of 1 and 6

Nitrosamine (conc.x10^{3}M)	O.D. at excitation wavelength, nm $(O.D.)_{350}$	$(O.D.)_{300}$	$(O.D.)_{270}$	$(O.D.)_{250}$
1 (2.65)[b]	0.24	0.065	-	>2
1 (2.64)[c]	0.24	0.060	-	>2
6 (1.42)[b]	0.41	-	>2	-
6 (1.42)[d]	0.40	-	>2	-

a. Solvent, CH_3OH; Temperature, 77°k. b. No acid.
c. With 0.012M HCl. d. With 0.097M HCl.

The concentrations of 1 chosen were those that, in methanol at room temperature, gave an optical density of 0.16 (1 cm path) at 300 nm (the excitation wavelength), in order to avoid an inner filter effect. The observed fluorescence spectrum of naphthalene in HCl-CH_3OH solution is the same

as that reported (92), extending from 300-375 nm. In the presence of 1, the naphthalene fluorescence intensity is much reduced indicating that the energy of the naphthalene singlet is transferred to 1. These experients are summarized in Table 3-12.

Table 3-12 Naphthalene fluorescence quenching by 1

conc. 1 x 10^3M	I_o	I_Q	$\frac{I_0}{I_Q}$ a
0	0.95	0.95	1.0
0.528	0.93	0.59	1.58
1.06	0.95	0.44	2.16
4.22	0.93	0.15	6.20

a. I_o = emission intensity of naphthalene fluorescence at 323 nm in the absence of 1, I_Q = emission intensity of naphthalene fluorescence at 323 nm in the presence of 1.

The Stern-Volmer expression (93) can be represented by eq. {16} since $\frac{\phi_o}{\phi_Q} = \frac{I_o}{I_Q}$

$$\frac{I_o}{I_Q} = 1 + k_Q \tau_s \{Q\} \qquad \{16\}$$

Here ϕ_o and ϕ_Q represent the quantum yield (as emission intensity) of donor fluorescence in the absence and in

the prescence of quencher respectively; k_Q is the rate constant for the quenching process; τ_s is the excited singlet lifetime of naphthalene in the absence of quencher (9.6×10^{-8} sec) (76); {Q} (i.e., 1) is the quencher concentration; I_o and I_Q are as defined in Table 3-12

The plot of I_o/I_Q against Q yielded a straight line (Fig. 3.15) from which k_Q is found to be 1.24×10^{10} $M^{-1}S^{-1}$. This value demonstrates that singlet energy transfer from naphthalene to 1 is virtually a diffusion controlled process and implies that the lowest excited singlet energy level (E_{s_1}) of 1 must be at least 5 kcal lower than that of naphthalene (E_{s_1}, 90 kcal/mole). It can thus be inferred that E_{s_1} of 1 is less than 85 kcal/mole.

3.1.10 Effect of biacetyl on the transient of 1

An attempt to quench the transient of 1 by biacetyl (E_T55 kcal/mole) was not successful. Flash excitation of a methanolic solution containing 1 (1×10^{-4}M), HCl (0.012M) and biacetyl (1×10^{-2}M) with monitoring in the region 330-400 nm gave a transient of the same lifetime as that observed in the transient of 1. The initial optical density of the transient however was lower than that of a control sample (no biacetyl) indicating that the precursor of the nitrosamine transient was quenched by biacetyl. However, flash excitation of a methanol solution containing only biacetyl (1×10^{-2}M) and HCl (0.012M) by monitoring in the

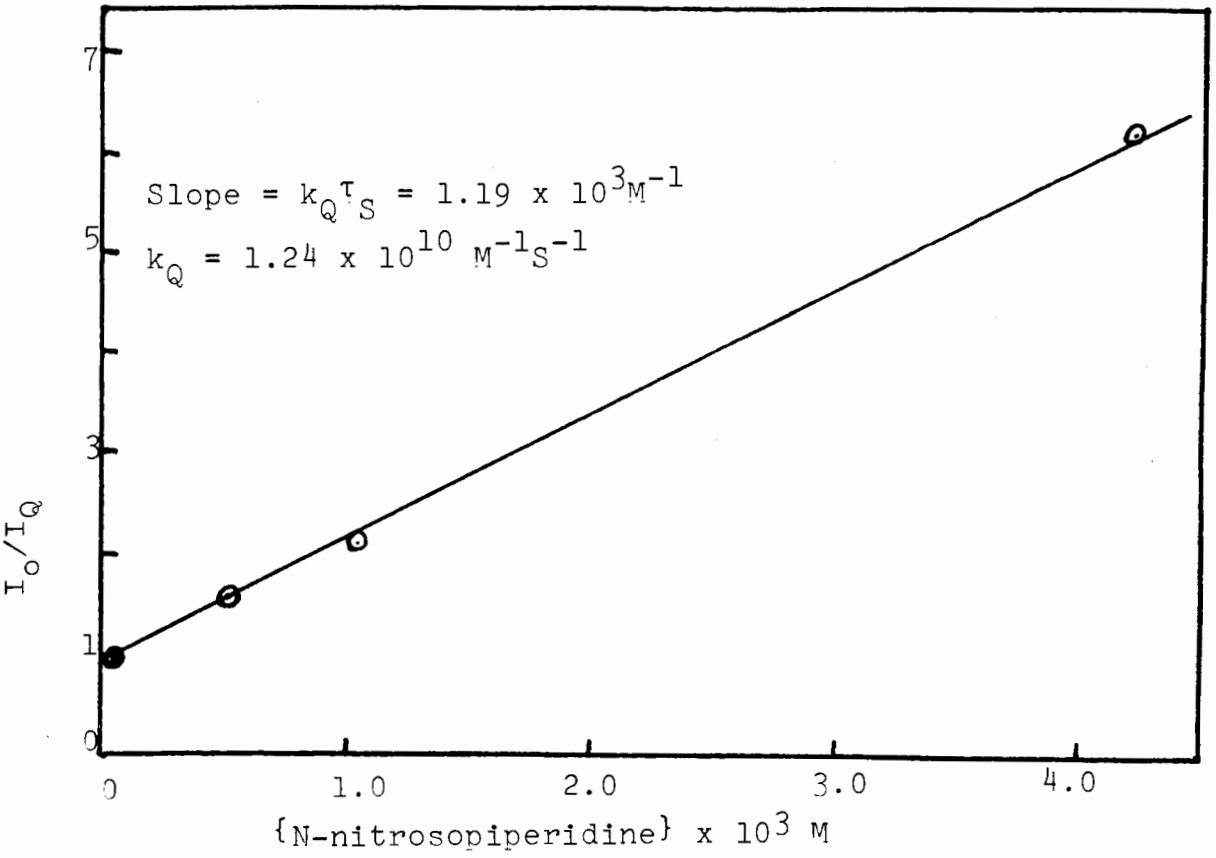


Fig. 3.15 Stern-Volmer plot of Naphthalene fluorescence quenching by N-nitrosopiperidine. {Naphthalene} = 4.9 x 10^{-4}M, {HCl} = 0.012M, Solvent = CH_3OH, Temp: RT, Excitation λ: 300 nm.

310-550 nm region gave neither the biacetyl triplet (which is known to absorb below 330 nm with a maximum at 317 nm and a lifetime of 300±100μsec in benzene) (70,71) nor any detectable transient. The ultraviolet absorption spectrum of the undegassed stock solution shows that the first $n \rightarrow \pi^*$ transition band of biacetyl at 415 nm, which is observable in a neutral solution, (sec. 6.8) is missing. In the presence of acid the usual biacetyl fluorescence also disappeared. It was therefore apparent that biacetyl had undergone a chemical change in the acidic condition although the nature of the species formed had not been investigated.

3.2 Flash photolysis of other nitrosamines

3.2.1 N-nitrosodimethylamine 2

Flash excitation of a methanol solution containing 2 (9.98×10^{-5}M) and HCl (0.06M) gave a transient which absorbed in the same region as the absorption of the transient 1. The transient of 2 decayed with first-order kinetics with a lifetime of 9.5±1 μsec. The transient was not observable when the solution was flashed through a pyrex filter. This is to be expected as at the concentration of 2 employed, there is virtually no absorption above 300 nm. Flash excitation of 2 under similar conditions but in the absence of acid gave no detectable transient.

When an undegassed methanol solution of 2 (1×10^{-4}M) in HCl (0.06M) was flashed, the same transient as described

above was obtained. In this case, the transient lifetime was 12±1 μsec. In addition no appreciable variation in the the intensity of the transient was observed. The result shows that oxygen has no effect on the transient of 2.

Flash excitation of a methanol solution containing 2 (1×10^{-4}M), HCl (0.06M) and cyclohexene (9.75×10^{-2}M) gave rise to no detectable transient showing that the nitrosamine transient was quenched by the olefin. When the cyclohexene concentration was 3.94×10^{-3}M, the transient was observable, with a mean lifetime of 9.5 μsec, but the intensity of the transient was reduced. Comparison of the optical densities of the transient in the presence and absence of olefin (Table 3-13) showed that there was a decrease in the optical density in the presence of added olefin. Thus, cyclohexene, like 1, is reacting with the precursor of the transient. Although the reaction rate constant of 2 (k_r) with cyclohexene has not been determined, the efficient quenching of the transient precursor by the olefin at a concentration of 3.94×10^{-3}M suggests k_r for 2 has the same order of magnitude as that for 1 and cyclohexene.

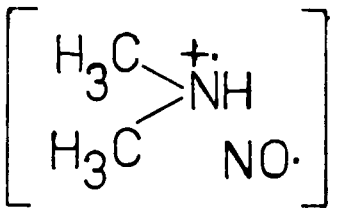
The above results show that the transient of 2 behaves chemically in an analogous manner to the transient of 1 and suggests, therefore, that this flash photolysis pattern may be a general characteristic of N-nitrosodialkylamines. In analogy to the transient of 1 which has

Table 3-13 Quenching of transient of 2 by cyclohexene[a]

Sample	Cyclohexene	Monitoring wavelength nm	τ μsec	(O.D.) 10	$(O.D.)_0$
52	-	330	11.9	0.034	0.074
74[b]	-	330	12.1	0.036	0.085
65	3.9	330	10.5	0.016	0.046
65	3.9	330	9.2	0.028	0.070
52	-	325	9.5	0.023	0.073
52	-	325	8.1	>0.017	0.084
74[b]	-	325	12.0	0.046	0.106
65	3.9	325	8.4	0.018	0.063
74[b]	-	350	10.8	0.029	0.077
65	3.9	350	9.3	0.020	0.061

a. {2} = 9.98 x 10^{-5}M, {HCl}= 0.06M, Solvent: CH_3OH, Flashing energy: 150J; b. Sample undegassed.

been assigned as the piperidinium radical, the transient of 2 is assigned as the corresponding dimethylaminium radical 38.



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3.2.2 N-nitroso-N-methylaniline (6)

Flash excitation of a methanol solution containing 6 (5.4×10^{-5}M) and HCl (0.06M) gave rise to a transient which decayed by first-order kinetics. The lifetime of the transient, however, varied over a wide range with the number of flashes. This observation indicates that the nitrosamine decomposes upon flashing (evidenced by the change in its ground state absorption spectrum with the number of flashes) and that the products give rise to secondary transients. The available data show that $\tau > 50$ μsecs, and that the transient absorbs in the region of 375-525 nm with a maximum at about 450 nm.

Under neutral conditions, flash excitation of a methanol solution containing 6 (5.4×10^{-5}M) also gave rise to a transient which decayed by first order kinetics with a constant lifetime of 47±6 μsecs. The solution decomposed at a rate slower than that containing acid. It was therefore possible to obtain a relatively reliable absorption spectrum of the transient. The available data (see Table 3-14 and Fig. 3.16) show that the transient absorbs in the region of 375-525 nm (too weak to measure) with a maximum around 420-430 nm and is different from that observed in the presence of acid, since the latter transient has no absorption below 375 nm. The transient species is not the N-methylanilino radical which has been reported to have an absorption maximum at 314 nm (94). Identification of this

Table 3-14. Absorption spectrum of the transient of 6 in methanol [a]

Flash Number	Monitoring wavelength nm	Initial Optical density	τ usec
9	400	0.115	39.8
10	400	0.107	39.4
11	400	0.069	41.0
39	425	0.107	44.5
42	425	0.111	45.5
43	425	0.092	58.9
51	440	0.076	49.2
52	440	0.063	65.8
27	450	0.076	46.0
28	450	0.082	44.6
44	450	0.067	53.4
48	450	0.059	55.6
49	460	0.049	52.6
50	460	0.050	43.0
37	475	0.048	36.3
16	500	0.038	31.0
21	500	0.041	39.4

a. $\{6\} = 5.4 \times 10^{-5}$ M, Flash energy = 90J.

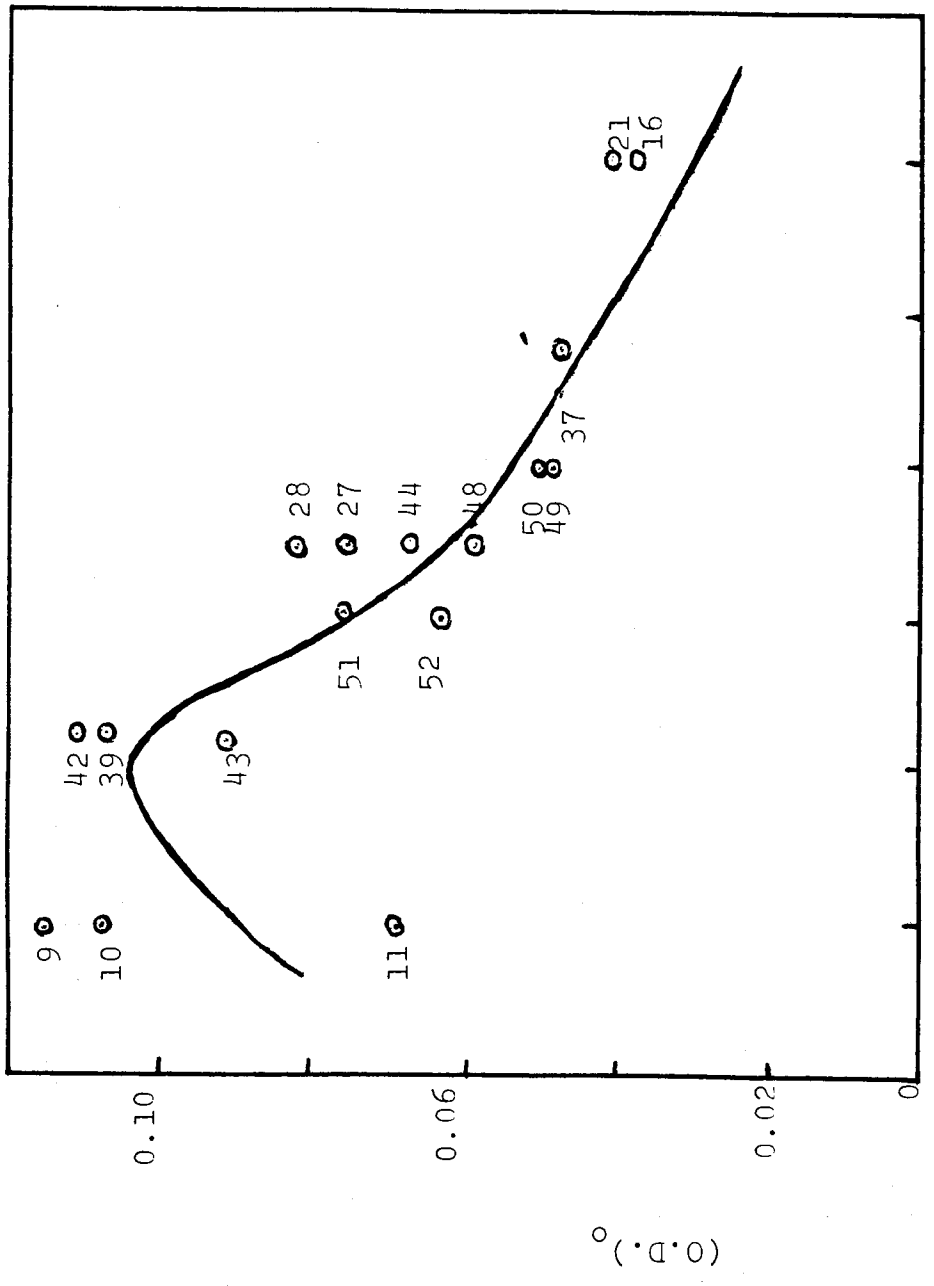


Fig. 3.16 Absorption spectrum of transient of 6
{6} : 5.4 x 10^{-5} M, Solvent: MeOH, numerals referred
to no. of flashes.

transient will require further investigation.

3.2.3 N-nitrosodibenzylamine(3)

Flash excitation of a methanol solution containing 3 (1.0×10^{-4}M) and HCl(0.06M) gave rise to a transient. Due to the rapid decomposition of the transient, the available data could only indicate that the transient absorption extending from about 500-315 nm increased towards shorter wavelength. The transient decayed with first-order kinetics but the lifetime increased as the number of flashes of the solution increased. This observation indicates that the nitrosamine decomposes during flash photolysis and that the photoproduct also gives rise to additional transients. The initial transient observed, taken from the first 10 flashes, has a lifetime of about 55 μsecs. It is premature to attempt an identification of the transient from these data, although the possibility that it is an aminium radical is reasonable since the chemical properties of 3 are very similar to those of 1.

Flash excitation of 3 (1.01×10^{-4}M) in methanol under neutral conditions gave rise to a transient which decayed by first-order kinetics with a constant lifetime of 67±7 μsecs. The transient absorbs from 300 nm (shortest wavelength detectable due to interference from ground state absorption), and the optical density decreases towards 425 nm (too weak to measure). Scanning on a longer time-base with a total time-sweep over 1 msec revealed no other detectable

transient. After many flashings the solution showed a new absorption peak at about 245 nm presumably due to the absorption of the photoproduct. The lifetime of this transient is dependent on the concentration of 3 since it decreases as the concentration of 3 is increased. This result is summarized in Table 3-15.

Table 3-15 Concentration dependency of the lifetime of the transient of 3 in neutral media[a]

Sample Number	Conc. x 10^4M	τ_{obs} (μsec)	k_{obs} x 10^{-3} S^{-1}
85	0.495	108	9.25
27	1.01	67±7	14.90
29	1.99	41±2	24.40

a. Solvent, methanol; photoflash energy, 90-150J.

The photochemical process can be approximated as follows:

$$N_o \xrightarrow{h\nu} N^*$$

$$N^* \xrightarrow{k_o} N_o$$

$$N^* + N_o \xrightarrow{k_r} \text{Product}$$

where N^* and N_o represent excited and ground state molecules of 3, respectively.

Since the concentration of N_o is much greater than that of N*, the observed rate constant is pseudo first order. The rate of decay of the transient is represented by eq. {17}.

$$\frac{-dN^*}{dt} = k_{obs}N^* \qquad \{17\}$$

with $k_{obs} = k_o + k_r N_o$ {18}

where k_{obs} is the observed pseudo first order rate constant for the decay of the transient N* and k_o is the composite first order rate constant for the decay of N* at infinite dilution of the nitrosamine. The plot of k_{obs} versus concentration of 3 (Fig. 3.17) according to eq. {18} is linear, from which the self-quenching rate constant (i.e. reaction rate constant with the starting material), k_r, is found to be $\sim 1 \times 10^8$ $M^{-1}S^{-1}$.

Flash excitation of an undegassed methanolic solution of 3 (4.95×10^{-5}M) in the absence of an acid gave a transient of similar absorption pattern, but weaker intensity. The transient decayed by first-order kinetics with an average lifetime of 171±20 μsecs. In view of its weaker intensity and longer lifetime in comparison to that from the corresponding degassed sample (Table 3-15, 108 μsecs), the transient is tentatively assigned as a new species different from that in the absence of oxygen.

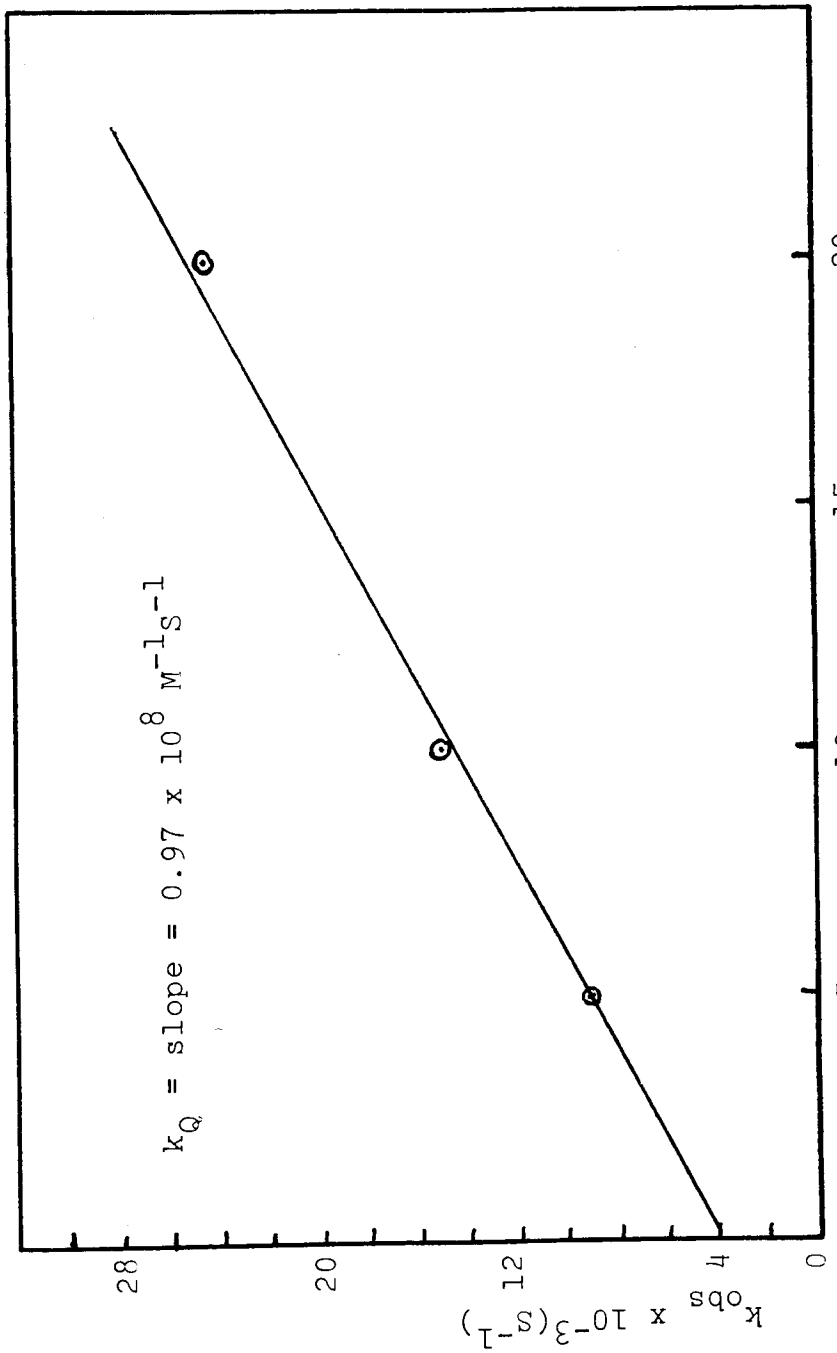
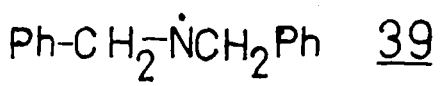


Fig. 3.17 Concentration quenching of transient of 3 by 3
Solvent: MeOH.

The photolysis of 3 in neutral media under nitrogen or oxygen atmosphere has been reported (3,11). The products under a nitrogen atmosphere are dibenzylamine and N-benzylidenebenzylamine. Under an oxygen atmosphere the same products, together with a salt, dibenzylammonium nitrate, are obtained. From the product distribution, it would appear that the same intermediate is formed either in the absence or presence of oxygen. Although oxygen undoubtedly would act as a secondary reactant, the formation of a new transient species in the photolysis of 3 under an oxygen atmosphere is difficult to reconcile with the preparative observation, and the validity of the oxygen effect on 3 may have to await further verification. The reaction of the transient of 3 with the starting material in neutral solution (Fig. 3.17), however, is consistent with the proposed radical abstraction mechanism (3,11). On this basis, the transient of 3 in methanol is assigned as the dibenzylamino radical 39.



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The fact that 3 can undergo photodecomposition in neutral medium is in sharp contrast to other dialkylnitrosamines (2,3,11). This unusual behaviour may be attributed to the presence of readily accessible benzylic protons for hydrogen abstraction. This supposition is

further substantiated by the observed high reaction rate constant ($k_r \sim 1 \times 10^8$ $M^{-1}S^{-1}$) which indicates that the abstraction process must be sufficiently exothermic. Similar observations have been made in the analogous self-quenching of N-nitroso-N-methylacetamide by the N-methylacetamidyl radical (61).

CHAPTER 4

DISCUSSION OF THE MECHANISM

The conclusions reached by flash photolysis of 1 are summarized as follows:

i. Acid is required for generating the nitrosamine transient.

ii. The same transient is produced by exciting either the $n \rightarrow \pi^*$ or the $\pi \rightarrow \pi^*$ transition band of 1 but the transient has weaker intensity in the former case.

iii. The spin state responsible for the photoaddition is assigned to the lowest excited singlet state of 1 and is envisaged to involve an excited complex derived from the photoexcitation of a ground state nitrosamine-olefin-proton complex.

iv. The transient undergoing photodecomposition has been assigned to the piperidinium radical.

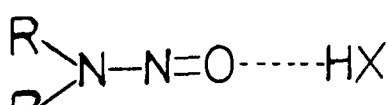
v. The piperidinium radical is formed from the lowest excited singlet state of 1.

vi. The lowest excited triplet of 1 is chemically unreactive.

The following discussion deals with the results from preparative photolysis and is also based on the conclusions derived from flash photolysis.

4.1 The role of acid and the photoprocess

The catalytic effect of acid upon the photoreaction has been demonstrated conclusively from previous work (2,3) and from the present investigation (sec. 2.2.1, 2.2.5 , 3.1.1 and 3.2.1). Thus 1 and 2, the model nitrosamines chosen for the investigation, do not undergo photodecomposition and do not give rise to a transient on flash excitation in the absence of acid. Layne et al (35, 95) have concluded from their basicity study of 2 in cyclohexane-trichloroacetic acid and in aqueous sulphuric acid that in the presence of one mole equivalent of acid, the predominant species is an associated complex of nitrosamine and acid such as 40. From the ultraviolet spectral shift between the free base and the hydrogen associated



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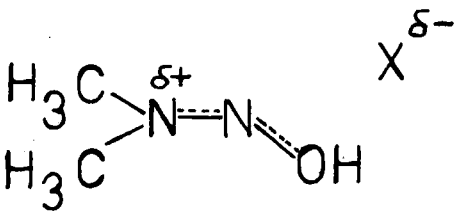
species in aqueous solution, an energy difference of 5.8 kcal/mole had been estimated for nitrosamine 2 (95). This value is reasonable for a hydrogen-bonding reaction, but not for a protonation reaction. The site of the association has been suggested to be the nitroso-oxygen and is supported by the formation of an O-methyl ether upon reaction of

nitrosamines with trimethyloxonium-hexachloroantimonate (96). From this is is inferred that the ground state species responsible for the photoexcitation is the hydrogen associated complex 40. The alternative explanation of excitation of a small percentage of the free nitrosamine followed by protonation of the excited state would entail a bimolecular (or termolecular in the case of added olefin) process and can not exceed the diffusion controlled rate even if the collisionals occurred with unit efficiency ($k_{diff} \sim 1.1 \times 10^{10}$ $M^{-1}S^{-1}$ in methanol at 20°). The observation that photoaddition takes place from an excited complex with a rate constant exceeding k_{diff} is another support that photodecomposition is derived from complex 40 but not from a neutral species.

Nuclear magnetic resonance study of 2 in strong acid and low temperature (3,40) and u.v. study (95) have led to the assignment of structure 41 for the conjugate acid of 2. It has been suggested that in 9M H_2SO_4, N-nitroso-dibutylamine exists entirely as the conjugate acid (3)



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since the solution shows no absorption above 300 nm and fails to undergo any amidoxime formation upon prolonged irradiation. In the present study, photolysis of 8 (sec. 2.2.7) in 4M sulphuric acid was very sluggish and yielded only a small amount of the parent amine together with 73% of recovered 8 after 7½ hours of irradiation. The solution prior to irradiation showed u.v. absorption at 332 (ε 38) nm as compared to the u.v. maximum at 348 (ε 90) nm in methanol with the same concentration of 8, indicating that the nitroso chromophore is absent and that the nitrosamine may exist largely in its conjugate acid form (ca.70%)*. From these observations, it seems clear that the conjugate acid of the nitrosamine can not undergo photodecomposition, and that the species undergoing photoexcitation must be the hydrogen-bonded complex 40.

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* Calculted by assuming Layne et al's data (95) for N-nitrosodiisopropylamine in water with 3.78 M H_2SO_4. Taking $K_1=K_2=0.7$, where K_1 and K_2 represent the equilibrium constants of the following processes respectively

$$R_2NNO\ldots(H_2O)_x \rightleftarrows R_2NNO\ldots(H_2O)_x H_2SO_4 \qquad K_1$$

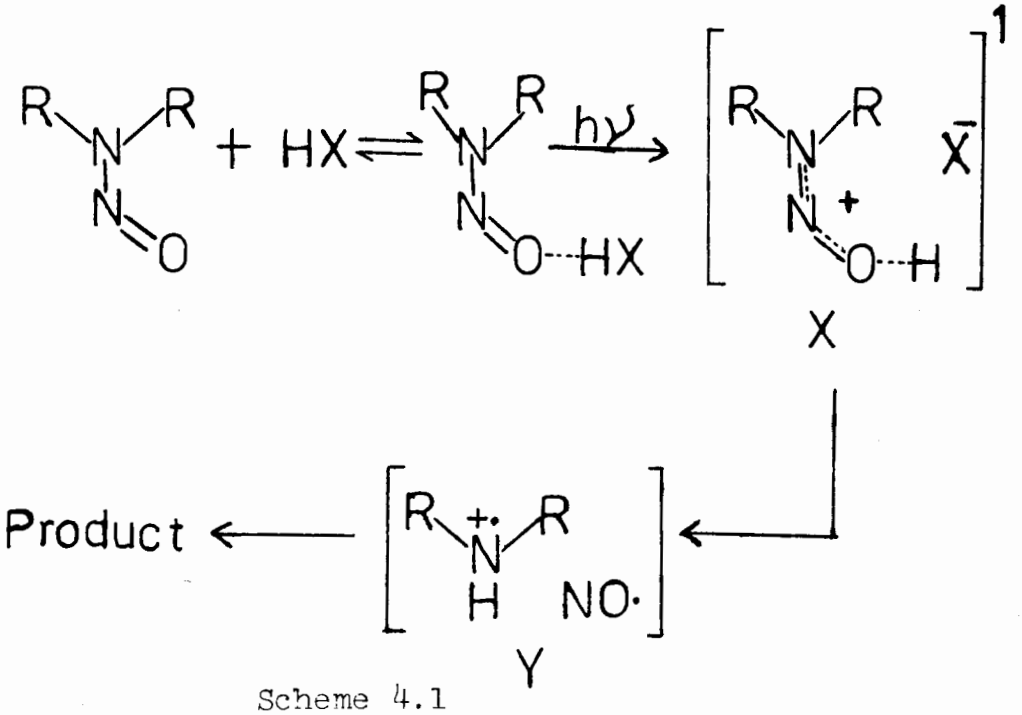
I II

$$II \qquad \rightleftarrows R_2NNOH^+\ldots(H_2O)_x \qquad K_2$$

by definition, $K_1 = \frac{C_{II}}{C_1(H_2SO_4)}$; $K_2 = \frac{C_{III}}{C_{II}(H_2SO_4)}$

..continued next page

From the flash photolysis it is established that the aminium radical is generated as the reactive species. Assuming ground state geometry is retained in the excited state, the mechanism leading to the aminium radical can be formulated as shown in Scheme 4.1. The decay of the lowest singlet excited state X to the aminium radical Y has been proved (sec. 3.1.2, 3.1.5, 3.1.6) and will be discussed later.



Scheme 4.1

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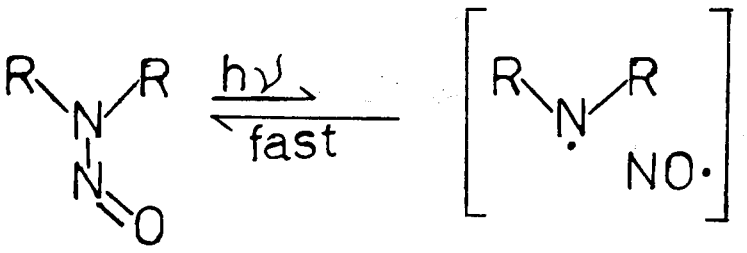
* continued ....,

From which $C_{111} = 9C_1$; $C = 13C_1$; where $C = C_1 + C_{11} + C_{111}$ and represents the total concentration of the nitrosamine. The calculated value for the concentration in the conjugate acid form, i.e. C_{111}, from the above data is 70%.

It is suggested that the inertness of nitrosamines in neutral solutions towards photolysis may be due to a rapid recombination of the radical pair generated upon excitation (if the cleavage of the N-N bond is indeed the primary photoprocess) within the solvent cage to yield the starting nitrosamine (Scheme 4.2). An allied phenomenon has been shown in the photolysis of alkyl nitrites (97). The low quantum yield observed in the gas photolysis of 2 also supports this proposition (1).

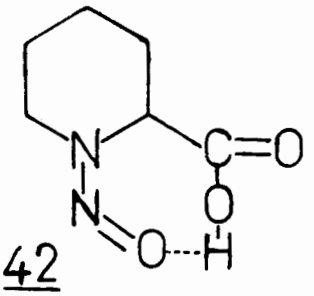


Scheme 4.2

It may be further suggested that an aminium radical is energetically more reactive than the corresponding neutral nitrogen radical. That this may be the case is indicated by the much slower photodecomposition of 3 in neutral media than that in acid media (11).

On the basis of this assumption, it is not surprising that N-nitrosopipecolinic acid (42) undergoes rapid oxidative decarboxylation to yield the corresponding 2-piperidonoxime in the absence of an acid whereas N-nitrosonipecotinic acid (43) under the same condition (9)

does not. Presumably the carboxyl group in the former is locked in the position to facilitate the intramolecular proton transfer to give an intermediate such as that shown in 42 which can undergo concerted elimination of HNO.



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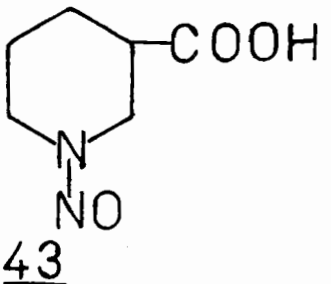

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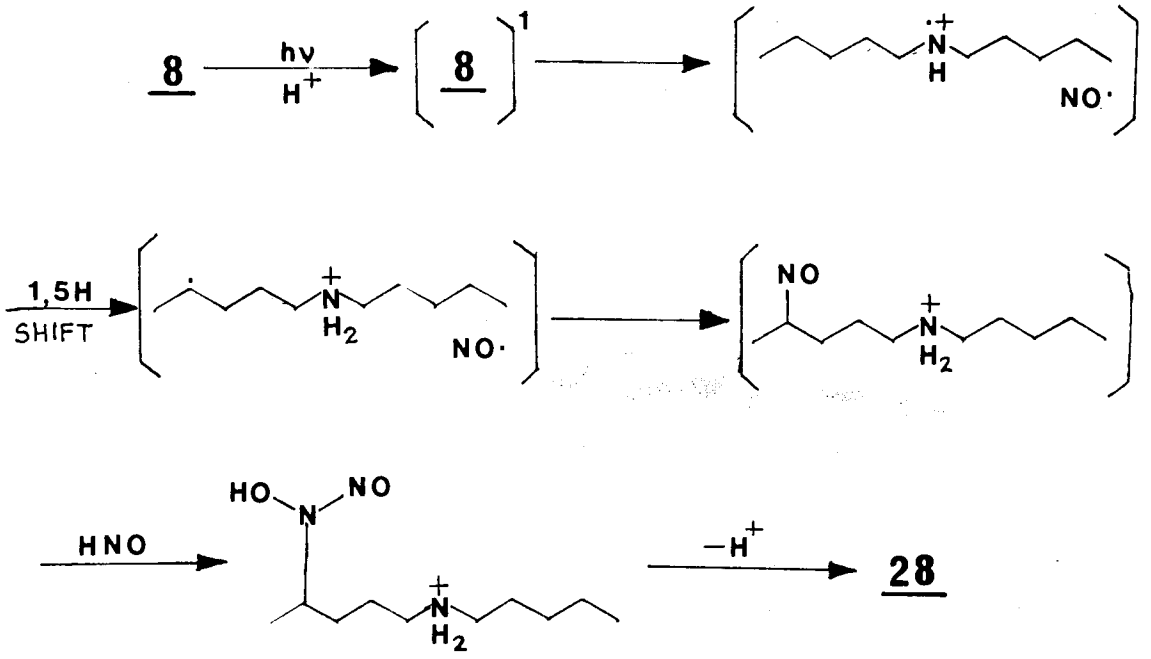
4.2 The mechanism of the photodecomposition

The major competing reactions in the photolysis of nitrosamines are photoelimination to the alkylideneimine, and photoreduction to the N-dialkylaminoformamide and parent amine. These processes are all observed in the photodecomposition of 8 (Scheme 2.3), the products of which reflect the general reaction pattern in the photodecomposition of nitrosamines (see Tables 2-6 and 4-1) and its competitive nature. That aminium radical is the reactive intermediate in the photodecomposition of nitrosamines (sec. 3.1.5) is substantiated by the isolation of 4-(N-nitrosohydroxylamino)-dipentylamine (28, 7.2%) in the photolysis of 8 (sec. 2.2.7). The formation of this δ-nitroso compound indicates that the intramolecular hydrogen abstraction characteristic of the Hofmann-Löeffler-Freytag reaction (22-24) occurs possibly from the aminium

radical intermediate. Since the formation of N-nitrosohydroxylamine derivatives have been demonstrated to involve the addition of HNO to the C-nitroso monomer (6), the formation of 28 can be formulated as shown in Scheme 4.3.

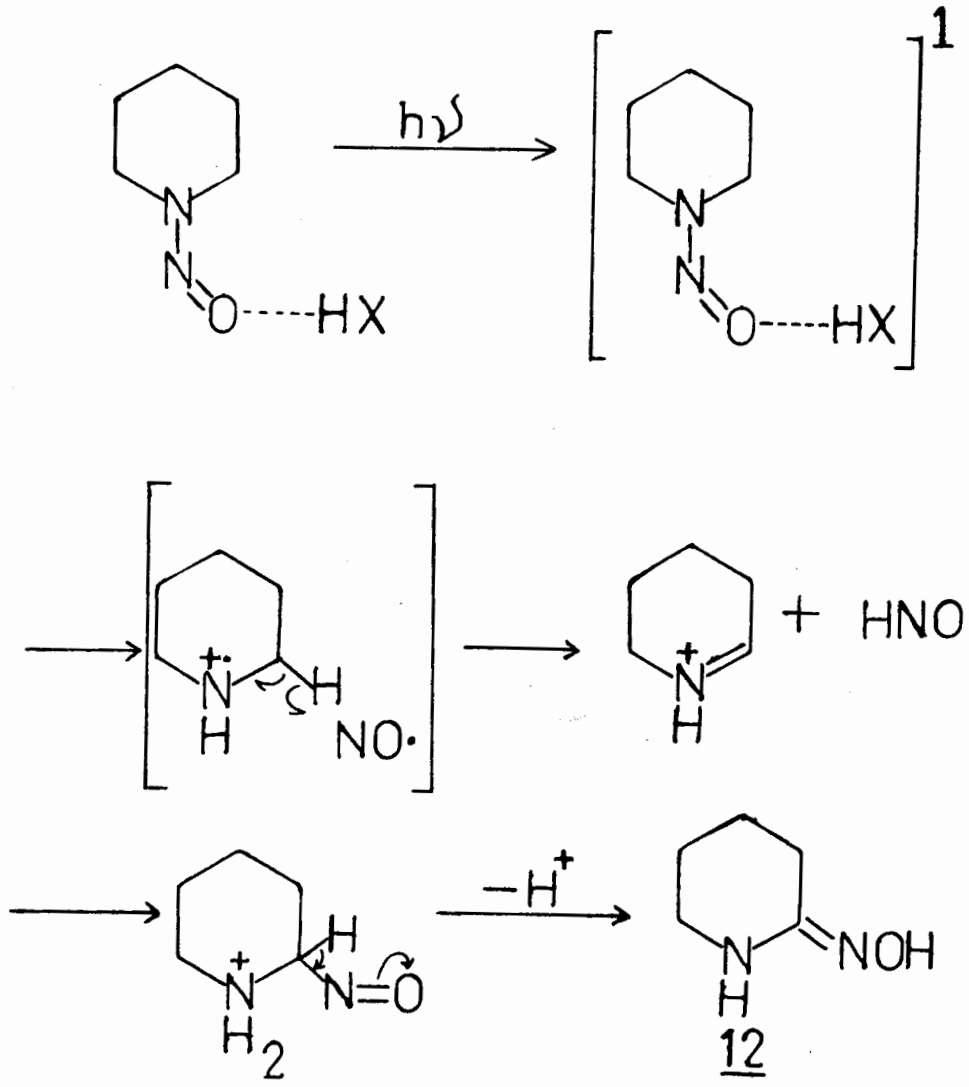


Scheme 4.3

In the photolysis of 7 and 9, the related N-nitrosohydroxylamine derivative may be formed in a small yield but this point has not been carefully investigated. In these cases, the derivative may not have been extracted out of the aqueous mother liquor since experience (e.g. 28 and ref. 6) has shown that this type of compound is very polar (the r_f of 28 is zero in 50% $CH_3OH/CHCl_3$ eluent), and can only be isolated by extracting the solid residue

of the basic mother liquor. Whether this kind of product is formed from 7 or 9, therefore, must await furter investigation. The failure to detect similar derivatives from the photodecomposition of N-nitrosodibutylamine (3,7) which also possesses a δ-carbon atom can possibly be ascribed to the poor reactivity of the primary hydrogen (23). Evidence for this has been obtained by Corey (23) from the cyclization of N-chloro-N-n-amyl-N-n-butylamine which yielded only 1-n-buty-2-methylpyrrolidine but no 1-n-amylpyrrolidine. That the Hofmann-Löeffler Rearrangement product, 28 , is not formed predominantly as has been observed in the analogous N-chloroamine photolysis (22) to pyrrolidine derivatives is possibly due to the competing facile elimination of HNO to give the imine or reduction to give the parent amine.

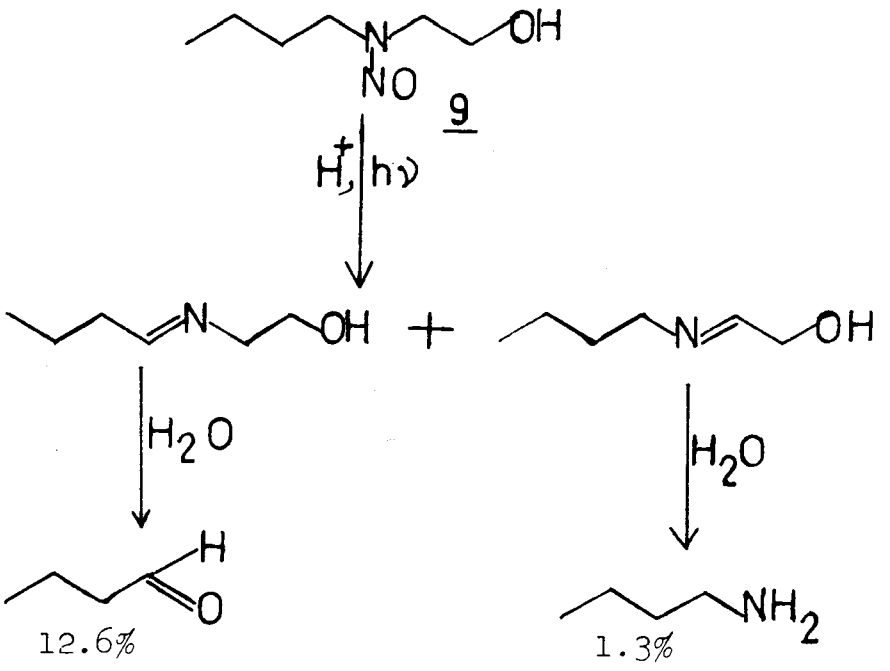
The formation of alkylideneimine as a primary photodecomposition product involving elimination of HNO from the nitrosamine has been demonstrated (2,7) by the isolation of isotripiperidein (14) (entry 1 of Table 4-1) and supported by the cross-over experiment between $(PhCH_2)_2N^{15}NO$ and $(PhCD_2)_2NNO$(12). The reverse intermolecular addition of HNO to the alkylimine can account for the formation of the amidoxime (such as 12, Scheme 4.4). In the present study, the alkylimines are isolated as their hydrolysis products, i.e., the aldehydes and the amines (run 4-8 of Table 2-6), and the trimer 14. The formation



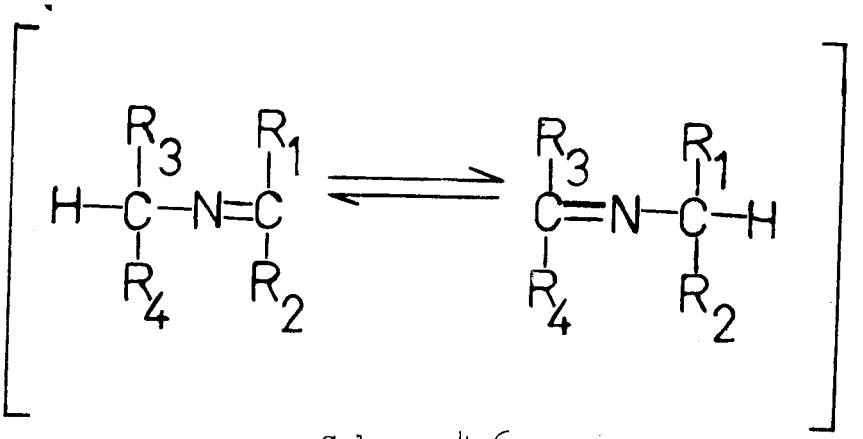
Scheme 4.4

of n-butyraldehyde and n-butylamine from the photolysis of 9 (run 8 of Table 2-6) shows that elimination of hydrogen from either α-carbon is possible (Scheme 4.5). The elimination appears to be selective, the dominant factor is possibly electronic rather than steric in nature judging from the structure of 9. Similar observations have been made for the photolysis of N-methyl-cyclohexyl-

nitrosamine with λ> 290 nm light (entry 8 (a) of Table 4-1). It has been shown by deuterium isotopic labelling studies (14) that an alkylideneimine does not tautomerise to the imine structure (Scheme 4.6).



Scheme 4.5



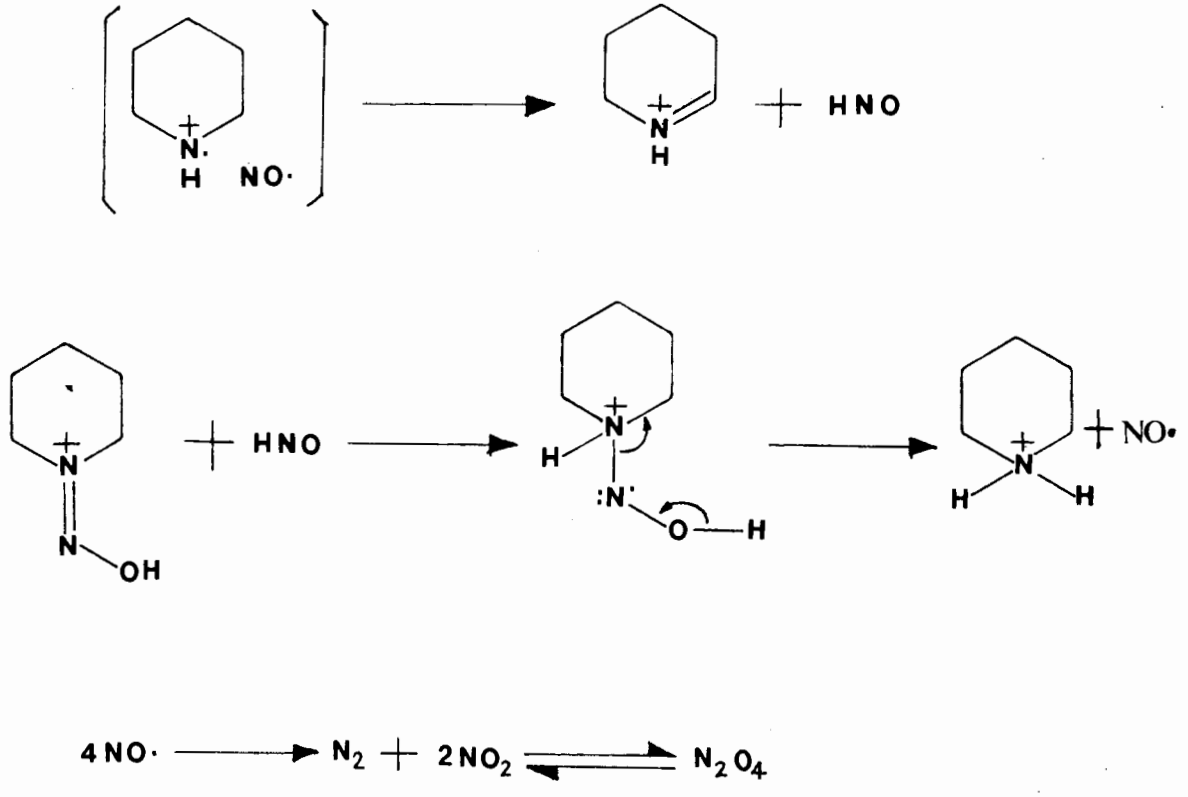
Scheme 4.6

Table 4-1. Photodecomposition of nitrosamines in acid media by irradiation at $\lambda \geq 290$ nm

ENTRY	NITROSAMINE	SOLVENT	ACID	MAJOR PRODUCTS (%)	REFERENCE
1	1	H_2O	HCl	12 (50), 14 (41)	2,7
2(a)	Dibutylnitrosamine	1:1 CH_3OH-H_2O	HCl	N-n-butylbutyramidoxime (66), di-n-butylamine (17), butyraldehyde (very minor).	7
(b)	"	Heptane	CF_3COOH	Amidoxime (40)	3
3(a)	3	Benzene	"	20 (90), dibenzylamine (~5)	3
(b)	3	1:4 H_2O-CH_3OH	HCl	20 (83)	11
4	α-(O-tolyl)-dimethylnitrosamine	Benzene	CF_3COOH	N-methyl-o-methylbenzamidoxime	3
5	N-methylbenzylnitrosamine	"	"	N-methyl-benzamidoxime	3
6	Dicyclohexylnitrosamine	"	"	Cyclohexylidenecyclohexylamine (96)	3
7	"	1:4 H_2O-CH_3OH	HCl	Imine (76), dicyclohexylamine (8)	7
8(a)	N-methylcyclohexylnitrosamine	"	"	Methylamine (87), cyclohexylamine (9.4)	7
(b)*	"	CH_3OH	"	N-methylcyclohexylamine	9 1
9	3-azabicyclo-(3,2,2)-nonanenitrosamine	1:2 H_2O.CH_3OH	"	2-oximino-3-azabicyclo-(3,2,2)-nonane (~25), polymer	7
10	2-ethylpiperidinenitrosamine	9:1 CH_3OH-H_2O	"	Possibly 1,2-dehydro-2-ethylpiperidine, 6-ethylpiperidonoxime (very minor)	7
11	4	CH_3OH	"	1,2-dehydro-2-methylpiperdine	6 8
12	N-nitrosopyrrolidine	H_2O	"	2-pyrrolidonoxime (~37)	7
13	6	9:1 CH_3OH-H_2O	"	6 (>75), p-nitroso-N-methyl aniline (very minor)	7
14	N-nitrosojervine	aq CH_3OH	"	Parent amine only	7
15	N-nitroso-trans-decahydro-quinoline	"	"	"	7
16	N-nitroso-N-butylbenzylamine	1:1 H_2O-CH_3OH	"	N-t-butylbenzylamidoxime (28)	11

* Irradiation by 2537A light in a quartz vessel with nickel sulphate as filter solution.

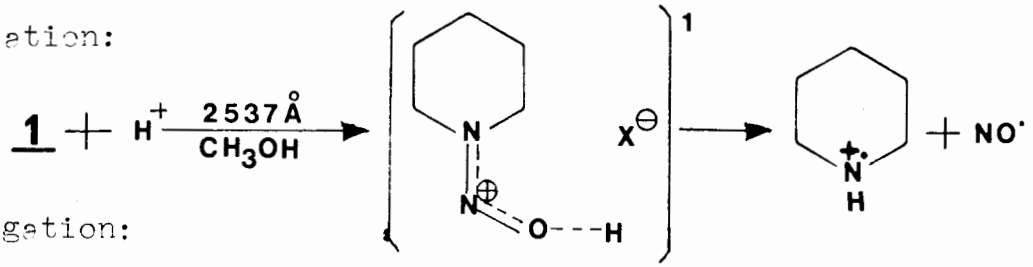
That the formation of the parent amine is a light induced process (and is not due to hydrolysis of the nitrosamine) has been shown by the control dark reaction in this study and more rigorously by Chow (7). Its formation is possibly the result of hydrogen abstraction from the solvent in alcoholic solutions (vide infra). For aqueous solution (run 2,5 and 6 of Table 2-6), a plausible interpretation is formulated in Scheme 4.7 for the formation of piperidine and is consistent with the true first order decay of the transient in water as has been observed by flash photolysis.



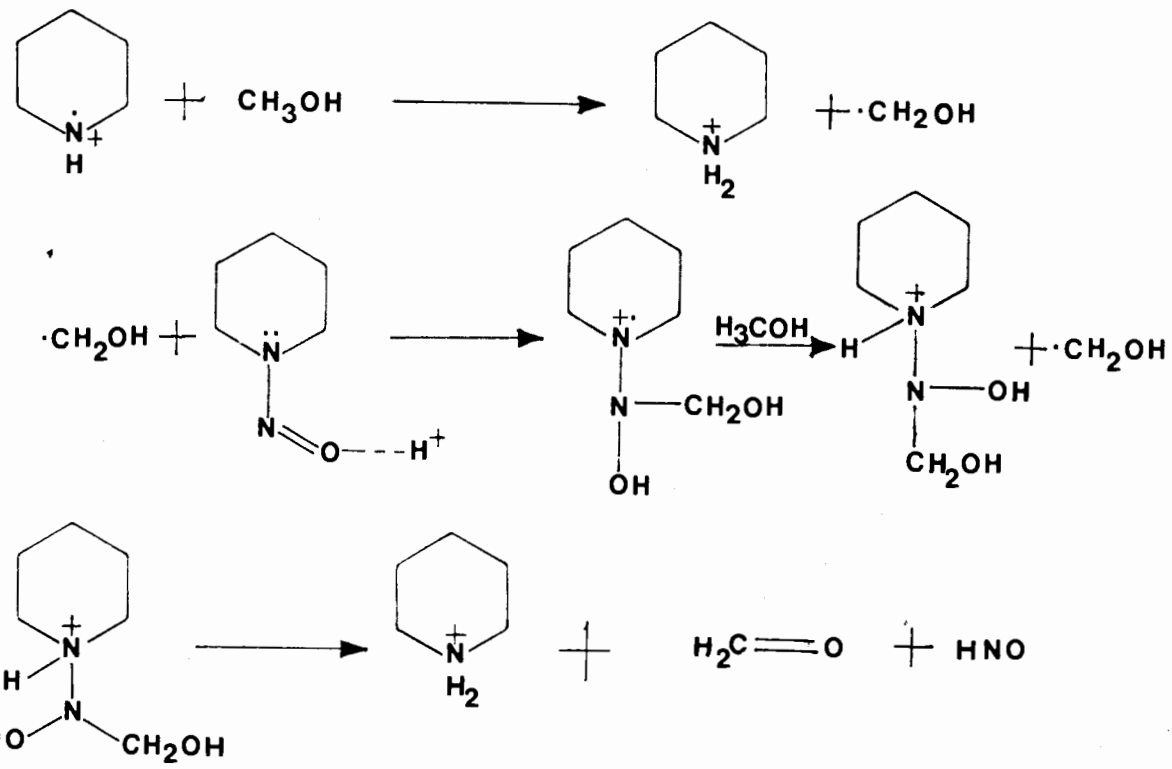
Scheme 4.7

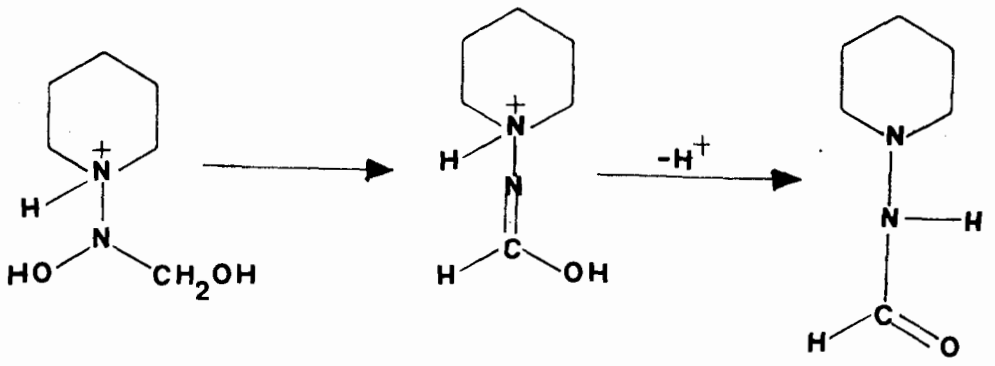
The structure of N-dialkylaminoformamide (11, 22, 26) suggests that its formation must involve the addition of methanol to the nitrosamine and a redox process. The reduction to parent amine is probably the same process in which methanol is oxidized to formaldehyde. The whole process can be proposed as the photoreduction of the nitrosamine (Scheme 4.8) and is very similar to the photoreduction of carbonyl compounds (98). This mechanism can also account for the formation of the parent amine and

Initiation:



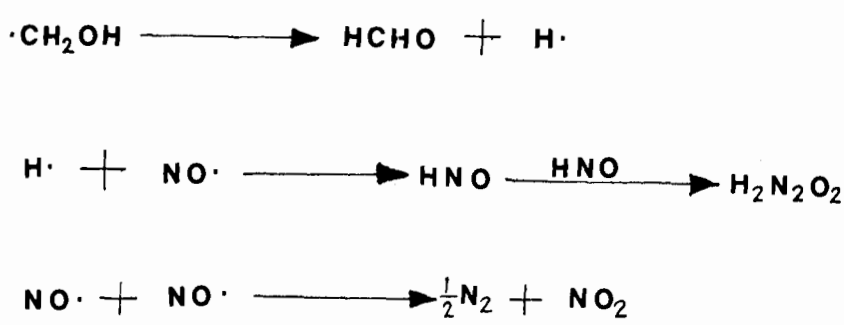
Propagation:





11

Termination:



Scheme 4.8

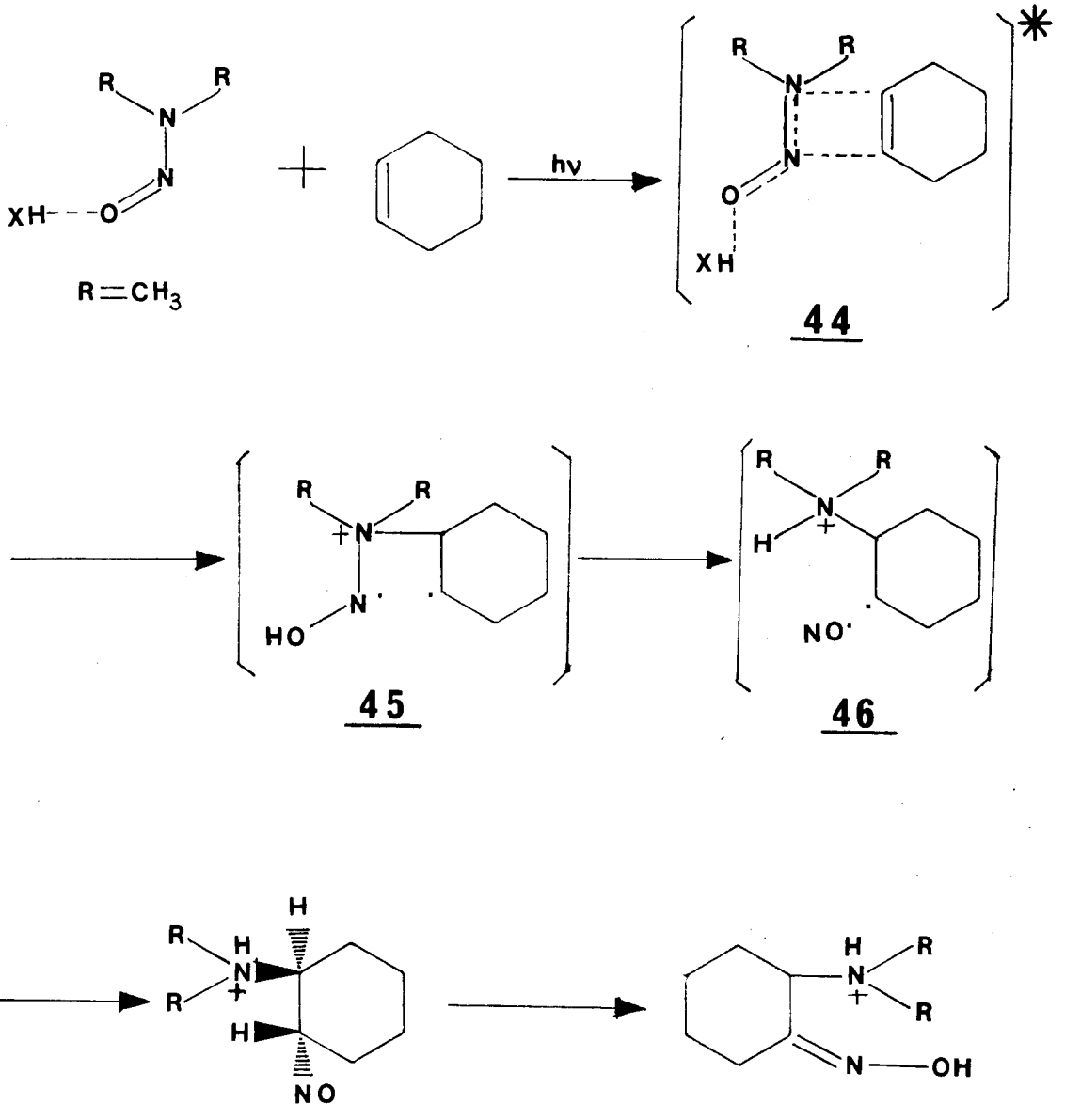
is consistent with the observed pseudo first order kinetics of the aminium radical transient. The u.v. evidence of the formation of nitrogen dioxide towards the end of photolysis of 1 in methanol with 2537A light source (sec. 2.2.1) is support of this mechanism. Since Strausz and Gunning (99) have shown that the mercury photo-sensitized decomposition products of nitric oxide are N_2, N_2O and higher oxides of nitrogen, presence of N_2O_4 in the photolysate is not unexpected.

Since the parent amine is formed in almost all cases in methanol (run 1, 3, 7 and 8 of Table 2-6), it may be

inferred that hydrogen abstraction from the solvent is an efficient process. That the above mechanism is operating is substantiated by the photolysis of 1 in methanol or ethanol with light source >310 nm (run 4 and 6 of Table 2-4) in which formaldehyde and acetaldehyde are isolated respectively via a ketyl radical as shown in Scheme 4.8. On the other hand, the yield of formamides 11 and 22 are only moderate (20% and >10% respectively) and is perhaps not significant in the photodecomposition of aliphatic nitrosamines (3.1% for 26).

4.3 The mechanism of the photoaddition

The presence of a ground state complex between a nitrosamine and the π-electron cloud of a carbon-carbon double bond has been demonstrated in the case of 4-t-butyl-1-nitrosopiperidine and benzene (87). The results of flash photolysis suggest that both photoaddition and photodecomposition of nitrosamines are initiated from the lowest excited singlet state. The observed high reaction rate constant $k_r > 1 \times 10^{11} M^{-1} S^{-1}$ (sec. 3.1.6) between the singlet nitrosamine of 1 and cyclohexene is clear evidence that the species undergoing excitation is a nitrosamine/monoacid/cyclohexene complex since the rate is faster than the diffusioned controlled process, and explains why no photodecomposition products are formed in the presence of an olefin. At either the $n \rightarrow \pi^*$ or $\pi \rightarrow \pi^*$ transition band,



Scheme 4.9

photoaddition of 1 or 2 to simple olefins take place to give the same adducts (Table 2-7). The result implies that addition must take place via a common intermediate. The absence of skeletal arrangement in the isolated products of photoaddition of 1 to 3,3-dimethyl-1-butene argues against the possibility of an open carbonium ion as an intermediate and suggests that an ionic mechanism is not operating (100). The photoaddition of 2 to cyclohexene gives 2-dimethylaminocyclohexanone oxime and the dimer of trans-1-nitroso-2-dimethylaminocyclohexane, whose stereochemistry has been established to be trans-orientation (16). The mode of addition is trans-diaxial and suggests that the photoaddition takes place by a stepwise and probably free radical process as shown in Scheme 4.9. The ground state complex is envisaged to involve loose association between the π-electron cloud of the olefinic double bond and the N-NO moiety. Spectroscopic evidence (39-41) and theoretical calculations (101) show that electronic density is delocalised over the $\ddot{N}$-$\ddot{N}$=O moiety in the ground state nitrosamine ($\ddot{N}$-$\ddot{N}$=O$\overrightarrow{}$ $\overleftarrow{}\dot{N}$=$\ddot{N}$-O$^-$) and the N-N bond has about 49% partial double bond character (101). Rapid dissociation of the excited complex 44 may give an intermediate diradical such as 45 which further dissociates to give the radical pair 46. Collpase of the radical pair gives the photodecomposition

products. The addition of 1 to either cis- or trans-2-butene gives a mixture of erythro- and threo-2-piperidino-3-(N-nitrosohydroxylamino)-butane (17) confirming that the photoaddition is a stepwise process.

4.4 The wavelength dependence of the photodecomposition

From its u.v. spectrum, irradiation of the nitrosamine at >290 nm corresponds mainly to excitation of its $n\rightarrow\pi^*$ transition and part of the $\pi\rightarrow\pi^*$ transition band since the tail of the latter extends to ca. 310 nm.

Comparison of the product distribution pattern for the photodecomposition of 1 under various wavelengths of excitation (Table 2-4) reveals that a $\pi\rightarrow\pi^*$ excitation of 1 in water (run 3) gave the hydrochloride 10 and the trimer 14 but no amidoxime 12 while a $n\rightarrow\pi^*$ excitation (run 1) gave 12 and the trimer salt 15 but no 10. In methanol, the formamide 11 obtained in the $\pi\rightarrow\pi^*$ excitation (run 5) is not observed when 1 is irradiated at the $n\rightarrow\pi^*$ transition band (run 4)*. The observation shows that the photodecomposition products are wavelength dependent. This wavelength dependence is further illustrated in the photolysis of other nitrosamines (Tables 2-6 and 4-1). The prominent features observed are:

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* A small amount of 11 may have escaped detection; see run 6 of Table 2-4 and footnote on 2.2.1(C).

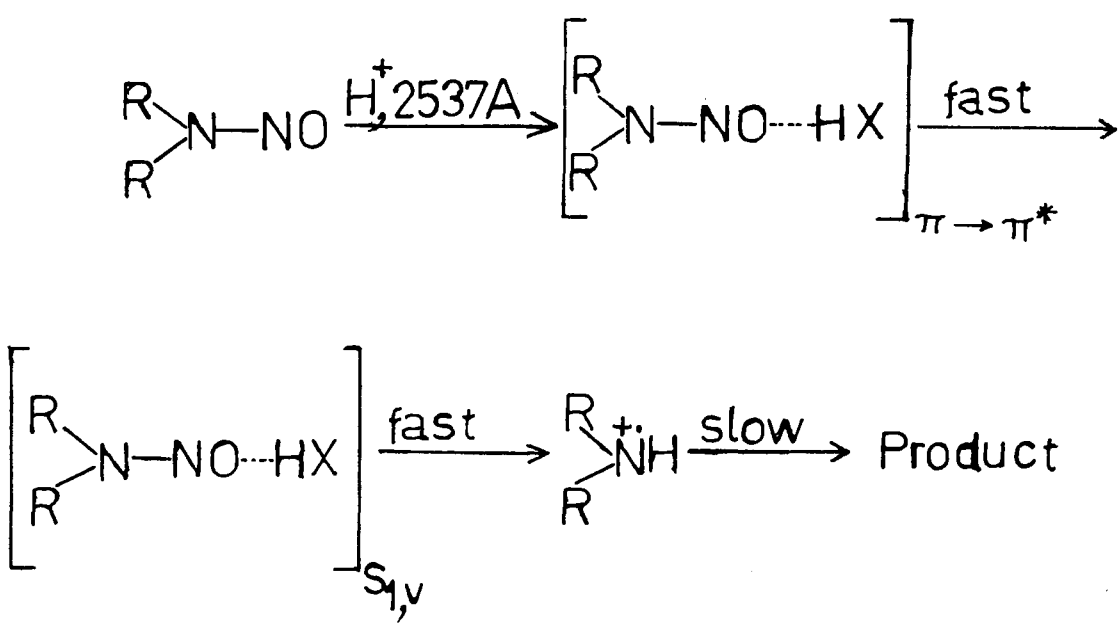
(i) On the basis of the mechanism proposed (Scheme 4.4), it is apparent that elimination of HNO to form the corresponding alkylimine is an efficient process with either λ>290 nm (entries 1-8(a), 9-12 and 16 of Table 4-1) or λ=254 nm (run 2, 4-8 of Table 2-6). In the latter case, the alkylimine appears to be the major product whereas in the former case, amidoxime is formed predominantly (entries 1-5, 9, 12 and 16 of Table 4-1). That this difference is not due to the effect of the solvent is also evident from the observation that for nitrosamine under comparable conditions (contrast entry 2(a) of Table 4-1 and run 7 of Table 2-6; entry 3(b) of Table 4-1 and run 4 of Table 2-6); amidoxime is still formed predominantly in aqueous alcohol solvents with λ>290 nm (see also entries 9 and 16 of Table 4-1) whereas in methanol solutions with λ=254 nm, amidoxime formation is negligible. This observation signified that the difference in excitation wavelength leads to a difference in the subsequent reverse addition of HNO to the alkylimine.

(ii) Irradiation of N-methylcyclohexylnitrosamine in 1:4 H_2O-CH_3OH with λ>290 nm light gives methylamine and cyclohexylamine (entry 8 (a) of Table 4-1) whereas irradiation with 2537A light in methanol gives only the parent amine (entry 8 (b) of Table 4-1).

(iii). With light >290 nm, formamide type products such as 11 are not formed in alcoholic solvents (entries 2 (a), 3 (b), 8 (a), 9-11, 15-16 of Table 4-1) although an oxidation of the solvent to give the corresponding aldehyde has been observed (run 4 and 6 or Table 2-4). The formamides 11, 22 and 26 are formed with 2537A light (run 1,3 and 7 of Table 2-6) and appear to be unique with this excitation wavelength.

The difference in product distribution from the above comparison, however, is not completely clear; and as can be seen from Tables 2-4, 2-6 and 4-1, apart from formamide type products, the end products from either wavelength of excitation are the imine (or its hydrolysed products), amidoximes and parent amine. Since excitation of either the $n\rightarrow\pi^*$ or $\pi\rightarrow\pi^*$ transition band of 1 gives rise to the same piperidinium radical transient (sec. 3.1.1) which reacts differently in water and in methanol solvent, the wavelength dependence of product formation is possibly due to the difference in vibrational energy possessed by the aminium radical as a consequence of the difference in excitation energy. Thus excitation of the $n\rightarrow\pi^*$ transition of the nitrosamine may promote the nitrosamine to its lowest excited singlet state (presumably the $n\rightarrow_{\pi}^*$ excited signlet or S_1) whereas excitation of the $\pi\rightarrow\pi^*$ transition of the nitrosamine would first promote the nitrosamine to a higher singlet state (presumably the

$\pi \rightarrow \pi^*$ state or S_2) which then rapidly cascades down to the lowest excited singlet state possessing excess vibrational energy (i.e. the $S_{1,v}$ state, where v stands for some vibrational level of S_1). The aminium radical generated from this $\pi \rightarrow \pi^*$ excitation would be expected to possess more vibrational energy, be more reactive, and therefore undergo other chemical processes not observed in the $n \rightarrow \pi^*$ irradiation. To compete with the rapid thermal relaxation process, the cross-over from the $S_{1,v}$ state to the aminium radical is expected to be a very fast process (Scheme 4.10). Since relatively few authentic examples of wavelength dependent reactions (102-104) in solution involving only one species are known, the photolysis of nitrosamines appears to be a rare example of a



Scheme 4.10

reaction in which the same intermediate undergoes different reactions depending on the vibrational energy of the intermediate.

4.5 Naphthalene quenching of the photodecomposition of 1

Attempted quenching of the photodecomposition of 1 by naphthalene does not lead to a clean cut result (sec. 2.2.1 c). With high concentrations of naphthalene (0.1M), the photodecomposition of 1 is slower than in the absence of naphthalene and no amidoxime is isolated. However, the broadening and increase in intensity of the nitrosamine absorption at 350 nm as well as the formation of the semipure unknown 17 indicates that naphthalene is reacting with 1. A singlet quenching of 1 by naphthalene should be very inefficient since the lowest excited singlet energy of 1 has been estimated to be lower than that of naphthalene by more than 5 kcal/mole (sec. 3.1.9). It is apparent that naphthalene reacts with 1 to give the red colouration during photolysis which acted as an internal filter contributing the sluggishness of the photoreaction. The red coloured product may be derived from an adduct between naphthalene and the singlet excited nitrosamine which may further decomposes to products such as unknown 17.

When the same reaction was run with a lower concentration of naphthalene (0.01M), the rate of the photodecomposition is slower than that of the control run

(Fig. 2.2). The u.v. absorption at the end of the photolysis shows that the nitrosamine has decomposed and that at least a part of the naphthalene survived indicating that reaction between 1 and naphthalene (with 9-fold excess of 1) must be very inefficient. This is not surprising since Colon (15) has demonstrated that addition of 1 or 2 to aromatic hydrocarbons such as pyrene, azulene and phenanthrene is very sluggish and affords only small yields of basic products. The low yield has been attributed to the poor reactivity of the aromatic compound in addition reactions. The result is perhaps related to the absence of significant variation in the quantum yield measurement (sec. 3.1.8) in the presence of added naphthalene ($1x10^{-2}M$).

Attempted sensitization of the photodecomposition of 1 with naphthalene (sec. 2.2.1 d) was equally unsuccessful. From the nitrosamine decomposition (20%) in the control run and the recovery of 1 (65%) in the sensitized case, and on the assumption of a 10% operational loss of 1, the slight sensitization observed (ca.5%) is however hardly convincing enough to draw a conclusion.

CHAPTER 5

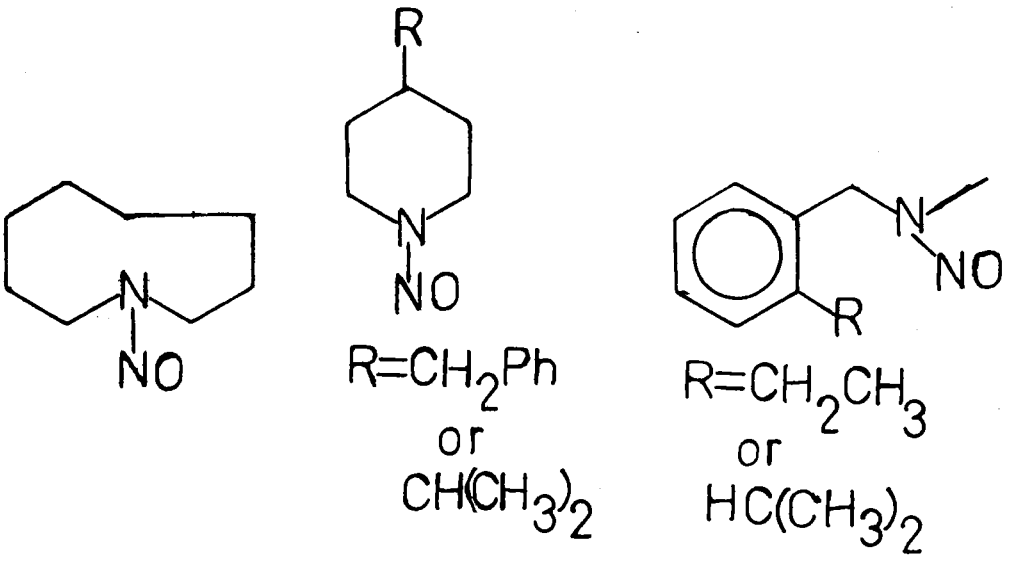
RESEARCH PROPOSAL

5.1 Solvent effect

In order to test the efficiency of intermolecular hydrogen abstraction, the nitrosamine photodecomposition can be carried out in hydrogen-donating solvents such as ethanol, isopropanol, tetrahydrofuran and toluene with simple alicyclic nitrosamines such as N-nitrosopyrrolidine and N-nitrosopiperidine. If a good yield of amide type products is obtained, the photolysis with 2537A light may provide a new route to this class of compounds.

5.2 Intramolecular hydrogen transfer

Since the present study has demonstrated the existence of intramolecular nitroso-hydrogen transfer in the photolysis of N-nitrosodipentylamine, it may be worthwhile to run the photolysis with nitrosamines possessing easily abstractable δ-hydrogens (Scheme 5.1) to see whether cyclised pyrrolidine derivatives can be obtained. In order to avoid hydrogen abstraction from the solvent, the reaction can be run in inert solvents such as water (with HCl) or benzene (with trifluoroacetic acid). Alternatively, the reaction can be run in the presence of t-nitrosobutane (which is known to give nitroxyl and isobutylene upon photolysis) (105) to see if the yield of any δ-N-nitrosohydroxylamine derivative formed can be increased.



Scheme 5.1

5.3 Quenching of the photoreduction

In the present study, it was observed that the initial rate of photodecomposition of 1 was slower at a conconcentration of 0.01M of added naphthalene although prolonged irradiation caused the nitrosamine absorption to increase again. A quantum yield determination of the photodecomposition of 1 (to 10-15% completion) in the presence of naphthalene (10^{-3}-5×10^{-2}M) can give the Stern-Volmer plot according to eq. { 11 } (sec. 3.1.6). The expression for the slope of the plot is

$$\text{slope} = k_Q \tau_N$$

By assuming a diffusion controlled rate for k_Q, the lifetime,

τ_N, of the excited nitrosamine can be evaluated. From the order of magnitude of τ_N, the nature of the excited species (S_1 or T_1) responsible for the photodecomposition can be inferred. Alternatively, the quenching study can be reinvestigated with appropriate triplet quenchers whose triplet energy is close to that of 1 (such as 1-acetonaphthone, E_T 56 kcal/mole, and 2-acetonaphthone, E_T 59 kcal/mole), but care may have to be exercised to check that the ketones have not enolised in the presence of acid and do not react with the nitrosamine chemically.

5.4 The effect of acid concentration on the photodecomposition

To get a better understanding of the role played by the acid medium in the photoreaction, a quantum yield study of the nitrosamine photodecomposition with various acid concentrations may be helpful. The observed variation of the quantum yield of disappearance of the nitrosamine with acid concentration when correlated with the corresponding change in the ground state absorption of the nitrosamine solution may provide information concerning the basicity of the excited nitrosamine relative to the ground state and a better insight of the species undergoing excitation. This kind of study finds an example in the photochemistry of nitrobenzene (106).

5.5 Low temperature photolysis

The photodecomposition of nitrosamines apparently involves more than one competitive pathway and a short radical chain with the aminium radical as the intermediate. A study of the photodecomposition at low temperature such as dry-ice-methanol may suppress some of the competing side reactions and provide a clearer picture of the primary photochemical process. For instance, at low temperature, bimolecular process involving hydrogen abstraction would be expected to be less efficient and intramolecular process may become predominant. With a nitrosamine possessing abstractable δ-hydrogen, the products resulting from an intramolecular hydrogen-nitroso exchange may be formed in a higher yield.

CHAPTER 6

EXPERIMENTAL

Part 1: Preparative photolysis

6.1 General Procedure

Ultraviolet (u.v.) spectra were measured either with a Unicam SP 800 or a Cary 14 Ultraviolet spectrophotometer, infrared (ir) spectra either with a Unicam SP 200 or with a Perkin-Elmer model 457 grating infrared spectrophotometer; only the significant peaks were quoted from these spectra. The symbols, s, v.s., m, w, sh, b, designate strong, very strong, medium, weak, shoulder and broad respectively. Unless otherwise stated, the i.r. spectra were recorded in Nujol mulls, and nuclear magnetic resonance (nmr) spectra were determined with a varian A 56/60 spectrometer in deuterochloroform with tetramethysilane as an internal standard. The symbols, s, d, t, q, J, b, m, stand for singlet, doublet, triplet, quartet, coupling constant in c.p.s., broad and multiplet respectively. Mass spectra were taken with a Hitachi-Perkin-Elmer RMU-6E instrument at 80 e.v. with a heated inlet. The significant peaks recorded were expressed as m/e (relative intensity, %).

Gas chromatography (vpc) analyses were carried out with a Varian Model 1200 gas chromatograph fitted with a flame ionisation detector, using 8' x 1/8" columns.

Analytical thin layer chromatography (tlc) were performed on glass plates coated with aluminium oxide or silica gel (0.3-0.4 mm thickness) using various mixture solvents and developed by iodine vapour. Preparative thin layer chromatography were performed on silica gel plates (20 x 20 cm^2, 0.4mm thickness) and the chromatogram was identified with a u.v. detector. Column chromatography using the conventional "wet column" technique were carried out with Brockmann alumina (neutral or basic, activity 1, 80-200 mesh) and florisil (100-200 mesh) supplied by Fisher Scientific Co., or with Mallinckrodt silicic acid (100 mesh).

Melting points were determined on a Gallenkamp heating block or a Fisher-Johns hot-stage apparatus and were uncorrected.

Microanalyses were performed by Dr. A. Bernhardt West Germany.

The crude yield of the reaction product was estimated on the base of one mole of starting nitrosamine to yield one mole of product. Isolated yield

from column chromatography was based on the starting nitrosamine and represented a lower limit of the yield of that specific product.

6.2 Chemicals

Unless specified otherwise, all solvents and reactants used were of reagent grade and were used without further purification. Petroleum ether (Allied Chemical) had b.r. 65-110°. Hydrochloric acid (C.P. grade, S.G. 1.19, 37%), sulphuric acid (S.G. 1.84, 96%) and acetic acid (glacial U.S.P.) were supplied by Allied Chemical Inc. 2-(t-Butylamino)-ethanol and N-n-butyl-ethanolmine were from Aldrich Chemical Co. Inc. Nitrogen dioxide was supplied in cylinder by Matheson Company. Naphthalene (Allied Chemical) was recrystallized once from methanol before use, m.p. 79-80°. Chloroform used from column chromatography was either of reagent grade, supplied by the McArthur Chemical Co. Ltd., or purified before use according to the procedure described by Fieser (107).

6.3 Nitrosation Procedure.

Some N-nitrosamines were prepared from the corresponding amines by Curtin's method (108), and were

purified by vacuum distillation. Alternately, the commercially available nitrosamine were vacuum distilled before use. A typical procedure for the preparation of N-nitroso-dipentylamine (8) was described below.

To a stirred solution of dipentylamine (35g, 0.22 mole) and hydrochloric acid (23 ml, 0.27 mole) in water (25 ml) was added a solution of sodium nitrite (17 g, 0.25 mole) in water (50 ml) over a period of 20 minutes, after which the mixture was stirred at room temperature for 4 hours. The reaction mixture was then extracted with methylene chloride, the yellow bottom layer was washed with water (50 ml) and dried over anhydrous magnesium sulphate. Removal of solvent gave a yellow liquid which was distilled under vacuum to give N-nitrosodipentylamine (8), b.p. 134°/ 10 mm Hg, (reported b.p. 136°/14 mm) (108).

Other nitrosamines prepared in a similar manner were N-nitrosopiperidine (1), b.p. 106-108° (12 mm); N-nitroso-2-(t-butyl-amino)-ethanol (5), b.p. 133-136° (12mm); this was purified by recrystallization from petroleum ether-benzene-chloroform to give pale greenish yellow needless, m.p. 60-61.5°; N-nitroso-N-methylaniline (6), b.p. 137-138° (40mm); N-nitroso-N-methyl-N-n-pentylamine (7), b.p. 90-91° (10mm);

N-nitroso-N-n-butyl-ethanolamine (9), b.p. 143-144° (3 mm).

Usually the yield of the crude product before distillation was almost quantitative unless the nitrosamine (such 1, 5, and 9) was water soluble, in which case, the reaction mixture was basified with sodium carbonate to pH about 9 before extraction. The distilled product was 75-80% of the crude product. All nitrosamines obtained were identified by their spectroscopic data that were summarized in Tables 2-1 - 2-3.

6.3.1 Preparation of N-methyl-N-nitroso-n-pentylamine (7)

(a). A solution of valeryl chloride (25g, 0.21 mole) in anhydrous ether (ca. 200 ml) was treated with methylamine until the solution showed pH ~10. The white solid precipitated during the addition was filtered and washed with ether (2 x 30 ml). The ether solution was worked up in the usual manner to give N-methyl-valeryl amide (26g, 100%); ir(neat) 3280(s), 3090(m), 1640(s), 1550(s) cm^{-1}; nmr τ 2.42 (bd, D_2O exchangeable), 7.2 (d, J = 5 cps, 3H), 7.79 (t, 2H, -$\underline{CH_2}$-CONH-), 8.47 (m,4H), 9.05 (m,3H); ms $\frac{m}{e}$ (%) 116(M+1, 2.3), 115(M^+,1.2), 114(M-1, 1.2),

100(3.5), 73(100), 58(77), 57(31), 29(22).

(b). A suspension of the prepared crude amide (25g) and LAH (12g, 3 fold excess) in anhydrous ether (100 ml) was refluxed for 10 hrs. Sosium hydroxide solution (15%, 50 ml) was added to the reaction mixture followed by water (20 ml) and ether (50 ml). The precipitated white solid was filtered and the liquid phase dried over anhydrous magnesium sulphate. The ether solution was worked up in the usual manner to give N-methyl-n-pentylamine (11.9 g, 53%): b.p. 117-118°(760 mm); ir(neat) 3300,2800,1145, 1120 and 725 cm^{-1}; nmr τ7.6 (s, 3H, N-CH_3), 7.46(2H), 8.7 (m,6H), 9.1 (m, 4H, CH_3C and HN, 1H D_2O exchangeable); ms $\frac{m}{e}$ (%) 101(M^+, 7.3), 44(100).

(c). The amine prepared was nitrosated and distilled by the standard procedure outlined above.

6.3.2 Preparation of N-nitroso-N-n-butyl ethanolamine (9)

This was prepared from N-n-butyl-ethanolamine by the standard method. The crude product was distilled in vacuum to give a yellow liquid: b.p.123-124°(0.5mm) (decomposed at 155° under 14 mm Hg); it had spectral properties as shown in Tables 2-1 - 2-3. The compound,

however, displayed two overlapping spots in tlc with low r_f values (3%CH_3OH in $CHCl_3$ eluent, silica gel plate). Redistillation of this yellow liquid at 128°/4 mm did not change its spectral and tlc patern. Separation by preparative tlc only afforded fractions identical in ir and nmr with the distilled compound.

A solution of acetyl chloride (2ml) in ether (40 ml) was added dropwise to a cooled solution of 9 (ca.0.90 g) and pyridine (2 ml) in ether (ca.100ml). A white precipitate was formed instantaneously. The white solid was hygroscopic and showed ir absorption at 3360 and 2500 (diffused), 2080, 1700(m). 1595(m), 1515, 750, and 680(vs) cm^{-1}. The solid was worked up in the usual manner to afford a yellow liquid which was chromatographed on a silicic acid column. Elution with chloroform affored the yellow liquid of the acetate of N-nitroso-N-n-butyl-ethanolamine (563 mg, ca. 80%, one spot of tlc); ir(neat) 3460, 1735 (vs), 1430 (sh), 1230 (s), 1040 (C-O); nmr τ5.72-6.35 (complex m, 6H), 8.0 (s, 3H, $-COCH_3$), 8.7 (m,4H), 9.06 (m,3H); ms $\frac{m}{e}$ (%) 189 (1.1), 188 (M^+, 2.3), 158 (5.7), 145 (8.0), 116 (11), 115 (11), 87 (24), 86 (13), 84 (40), 74 (9), 57 (23), 56 (18), 55 (30),

44 (13), 43 (100), 42 (29), 41 (17).

Further elution with chloroform yielded a yellow liquid (308 mg) which was identical in ir, nmr, and tlc mobility with the starting nitrosamine 9; m.s. $\frac{m}{e}$ (%) 147 (1.7), 146 (M^+, 1.7), 115 (15.8), 103 (21), 84 (100), 73 (21), 57 (68), 45 (26), 44 (32), 43 (47), 42 (79), 30 (58), 27 (21).

6.4 General procedure of photolysis

Two types of photolysis apparatus were used which differed only slightly in their configuration and light transparency.

Type 1: For irradiation of the $n \rightarrow \pi^*$ transition band (λ_{max} ca. 350 nm) (35,36) of the nitrosamine, the nitrosamine (ca. 0.02-0.05 mole), concentrated hydrochloric acid (ca. 1.2-2 equivalent) and solvent (ca. 300 ml) were placed in a pyrex photolysis vessel as previously described (16,61). In the inner sleeve of the cold finger a Hanovian medium-pressure mercury lamp (200W, NO. 645A-36; 450W, NO.679A-36 or a RPR-3500A uv lamp) was placed. Tap water or a cold filter solution was circulated through the cold finger depending on the requirement. The filtered solution was cooled externally and pumped through the system

with a peristatic pump. In some cases, glass filters were used. The reaction mixture was purged with a slow stream of nitrogen, purified by passage through Fieser's solution (110), for 15 minutes before irradiation. At suitable time intervals an aliquot of the photolysate was pipetted out and properly diluted (usually 1/10th dilution) for spectroscopic measurement in the 250-400 nm region. Unless specified otherwise, the photolysis was continued until the nitrosamine absorption at 350 nm was no longer observable.

As a control experiment, the 0 hr sample was kept in a dark ice box ($>0^{\circ}$) and its optical density was checked again at the end of the reaction. This optical density and shape of the curve were shown to be the same as that of the 0-hr sample.

For working up of the photolysate, the major part of the solvent was removed under vacuum with a rotary evaporator at temperatures lower than 60°. In some cases, the solvent was trapped by cooling the receiver with a bath of dry ice methanol. The collected solvent was then treated with Brady's reagent to detect any volatile carbonyl compound that might be present. After the removal of solvent,

in some cases the hydrochlorides of the photolysate crystallized out immediately and were recrystallized from a suitable solvent. In other cases the residue was treated with cold water. Extraction of the aqueous solution with ether afforded the neutral fraction. On basification of the aqueous phase the basic products was freed and was extracted with methylene chloride. These crude basic products were either distilled, chromatographed of recrystallized in order to effect purifications.

Type 11: For irradiation in the $\pi \rightarrow \pi^*$ region of the N-nitrosamine (λ_{max} ca. 230-240 nm), a Nester Faust Model NFUV-300 low pressure mercury resonance lamp (90% of the light output energy at 2537A) was used. The pyrex vessel was fitted with a quartz cold finger whose configuration was shown in Fig. 6.1. A saturated nickelous sulphate solution was circulated through the cold finger to cut off the incipient light above 340 nm. The photolysis procedure and the isolation of products were otherwise similar to that described above. The filter solutions used were summarized in Table 6-1 and Fig.6.2.

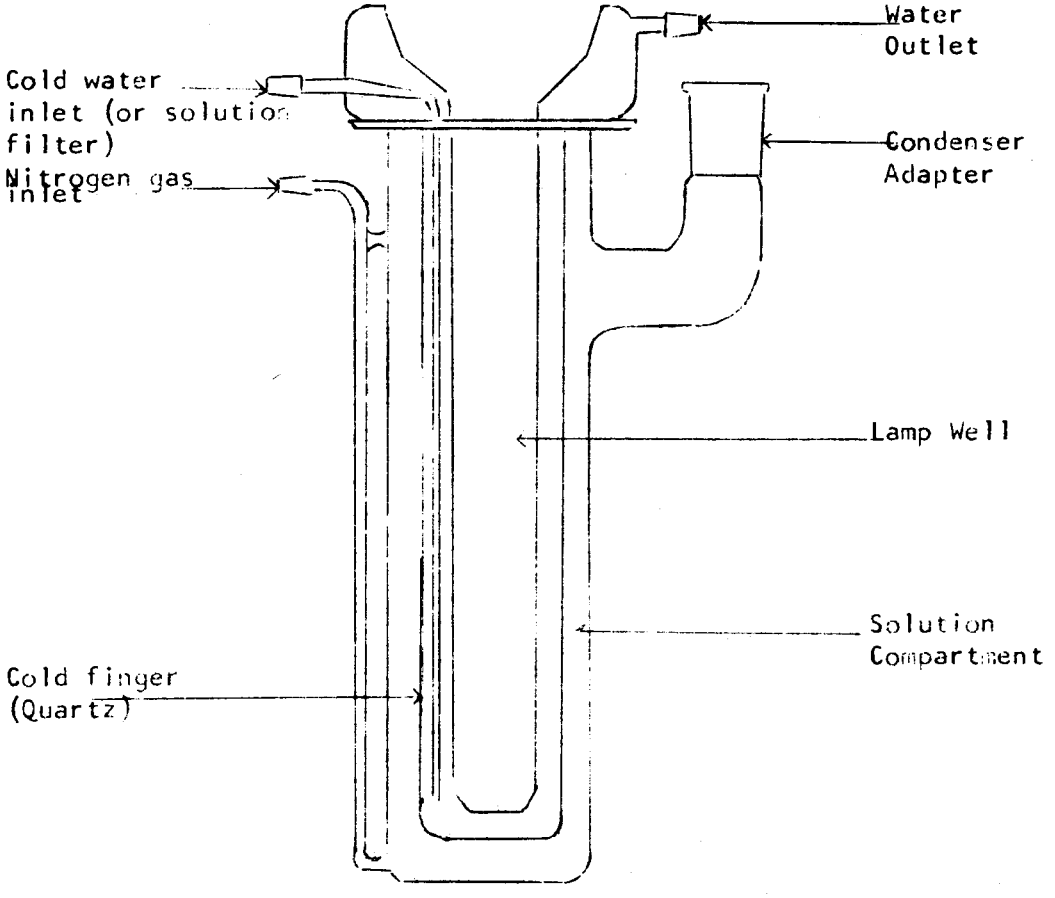


Fig. C.1 Type II Apparatus

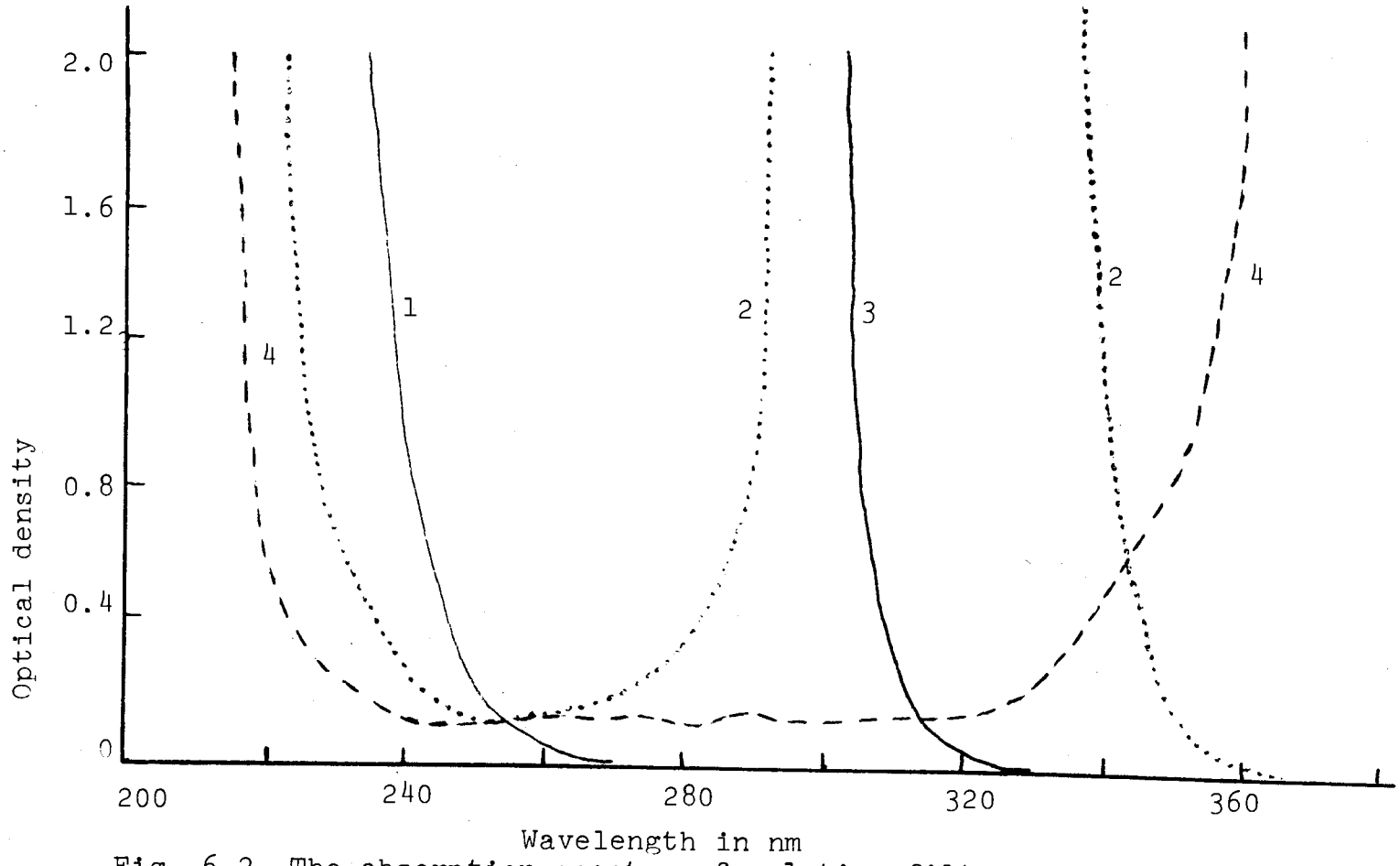


Fig. 6.2 The absorption spectra of solution filters used. Filter 1, Acetic acid (neat); filter 2, 2,7-dimethyl-3,6-diaza-cyclohepta-1,6-diene perchlorate solution (0.1g/l in water); filter 3, potassium acid phthalate (5g/l in water); filter 4, nickel sulphate (60g/100 ml in water).

Table 6-1

Absorption Characteristics of Filters Used

Filter	Special characteristics
Pyrex	cut off below 280 nm
Corex	cut off below 260 nm
CS 7-60	300-400 nm (transparent), 360 nm (65% transmission)
Nonex	cut off below 340 nm
Soft glass	cut off below 310 nm

6.5 Addition of nitrosamines to olefins

6.5.1. Addition of N-nitrosopiperidine (1) to limonene

Limonene was vacuum distilled before use. The middle fraction was used: b.p. 66-67° (12 mm): ir(neat) 3050 (sh), 2700, 1770, 1725, 1640, 1587, 1510 (m), 910, 885 (vs), 810 (s), 795 cm^{-1}; nmr (CCl_4) τ3.1 (IH?), 4.7 (IH), 5.38 (s, 2H), 7.35 (m, IH?), 7.75 (s), 8.06 (m), 8.34 (d), 8.77 (d?), 9.05 (m).

Limonene (9.65 g, 0.071 mole), 1 (5.16 g, 0.045 mole), and HCl (3.7 ml, 0.045 mole) in 90% methanol-water mixture (300 ml) was photolysed in a pyrex flask

(type 1) with a Royonet RPR 3500 A lamp for 6½ hrs. After the usual work-up, the neutral extract (2.76 g, 53%) was shown by its ir to be mainly the starting nitrosamine. The basic extract (4.24 g) was shown to be a complex mixture by tlc. Attempted crystallization of this basic fraction gave a solid (130 mg) showing ir absorption at 3300 (b) 2150, 2435, 2535, 1595 cm^{-1} and nmr signals at τ8.25 (6H), 6.9 (4H), 1.3 (2H, D_2O exchangeable). These spectra were shown to be identical with an authentic sample of piperidine hydrochloride (10). Small scale chromatography of the mother liquor of the basic extract (1.0 g) gave an impure fraction (F17-18, 120 mg, 8% CH_3OH in $CHCl_3$ as eluent). This fraction was an oily solid (one major spot in tlc): m.p. 155-162°; ir 3350 (m), 1630 (w), 1110 (s), 940 (s) cm^{-1}; nmr τ3.6 (s,b,), 7.57 (s,b,), 7.85 (s), 8.0 (m), 8.57 (s.b), and 8.92 (m); these signals were in ratio of ca. 1:4:2:1:6:6. No other isolable product was obtained from this chromatography.

It was subsequently found that dl-limonene did not show any ir absorption at 1725, 1587, 810 cm^{-1} and nmr signals at τ3.1, 7.35, 7.75 and 9.05 (56,57) while d-limonene had no ir absorption at 1725, 1510, and 810 cm^{-1} (58). In addition, the nmr of the

limonene used did not give the correct integration expected for its structure. It was therefore apparent that the olefin used was contaminated with other impurities.

6.5.2 Addition of 1 to cyclohexene

Cyclohexene was distilled at atmospheric pressure prior to use: b.p. 81.8°.

A solution of 1 (3.17 g, 0.028 mole), redistilled cyclohexene (2.72 g, 0.033 mole) and HCl (3.5 ml, 0.04 mole) in methanol (240 ml) were photolysed with the 2537 Å mercury arc lamp in Type 11 apparatus. Irradiation was stopped after 1 hr. 35 min. when the 350 nm peak of the nitrosamine disappeared.

The usual work-up procedure gave the neutral fraction (350 mg) which was identified by ir, nmr and tlc as the starting nitrosamine. The basic extract (2.49 g) was a yellow oil: ir(neat) 3300 (b) 1710 (m), 1660 (w), 1625, 900-1000 (complex) cm^{-1}. This oil was treated with petroleum ether and cooled to give a crop of rhombic crystals (473 mg, m.p. 115-117°); tlc (4% MeOH/$CHCl_3$, Al_2O_3 plate) showed one spot with tailing. Recrystallization of this solid from petroleum ether yielded colourless crystals of 2-piperidino-cyclohexanone oxime (33) (281 mg): m.p.

120-121° (lit. m.p. 118-120°) (5); ir 3350, 2820 (sh), 2780 (sh), 1680 (w), 880-980 (complex) and 775 cm^{-1} (5).

A second crop of 33 (300 mg) was obtained from the mother liquor. Attempted v.p.c. analysis (column 20% XF-1150 on Aeropak 30) of the mother liquor of the basic extract led to an extensive decomposition in the column as shown by the complex pattern of the chromatogram. Injection of the pure adduct 33 into the same column gave no less than six peaks.

The basic mother liquor (1.1g) was chromatographed on a silicic acid column. The fractions 4-12 (ca. 70mg) ccntained mainly one component and decomposed on sublimation at 70°. The fractions 14-20 (550 mg) upon crystallization from petroleum ether yielded 33 (232 mg); mp. 108-112°. Chromatography of this mother liquor gave another crop of adduct (40 mg). No other pure product was obtained.

In the separate photolysis with 1 (3.07 g, 0.0274 mole) the crude mixture after removal of solvent to about 10 ml, was treated with acetone (20 ml) to give a pale yellow oily solid (2.31 g). Recrystallization of this solid from 2-propanol yielded a crystalline solid; ir 3180, 3100 (w), 2600, 2520, 2420 (sh), 1660 (w), 1490 (w), 900-1000 (complex) and 740 (s)

cm^{-1}. This spectrum was superimposable with that of an authentic spectrum of the hydrochloride of 2-piperidinocyclohexanone oxime (33).

The mother liquor of the reaction mixture on standing turned to dark brown. Addition of water to this mother liquor, basification, extraction and evaporation gave a black viscous oil. Trituration of this oil with petroleum ether and separation by decanting afforded a brown solution and a tarry substance (845 mg). This substance was recrystallized from carbon tetrachloride to give two crops of 33 (184 mg). Further treatment of the mother liquor yielded no isolable product other than impure 33 as indicated by its tlc mobility.

The brown solution from above upon removal of solvent gave a yellow oil (785 mg) which showed in the ir an absorption at 1710 cm^{-1}. This oil was then refluxed with hydroxylamine hydrochloride (1g) and solium acetate (1.99 g) in an ethanolic aqueous solution and was worked up in the usual manner to give a brown oil (486 mg). This oil showed no 1710 cm^{-1} absorption and contained oxime 33 and other minor products as indicated by tlc. Chromatography of this oil yielded 1 (43 mg) and 33 (41 mg) as

identified by their ir spectra. The isolated yield of 33 was 42%. The yield of 33 estimated from the crude basic fractions by nmr analysis was ca. 60%.

6.5.3 Addition of 2 to cis-cycloocetene

This photoaddition had been reported earlier by Chow et al (irradiation at $\lambda > 290$ nm) (4). The following irradiations were carried out under slightly different conditions.

(a) Redistilled cis-cyclooctene (b.p. 55°/36mm, 8.93 g, 0.081 mole), 2 (4.877g, 0.066 mole) and concentrated hydrochloric acid (8.5 ml, 0.102 mole) in methanol (350 ml) were photolysed in a pyrex vessel (Type I apparatus) with the Rayonet RPR 3500A lamp for 12½ hours.

The basic extract was a yellow oil (10.4g, 86%) nmr τ0.1 (b. D_2O exchangeable, 1H), 6.75 and 7.3 (b,t, 1H), 7.78 (d, J=2cps, 6H) and 8.53 (b, m, 12H). These spectral data were consistant with that reported for 2-dimethylamino-cyclooctanone oxime (32) (4). Recrystallization of this oil from petroleum ether (25 ml) gave a white crystalline solid (7.05 g, m.p. 79-81°, lit. 84-85°) (4); tlc ($CHCl_3$ eluent) showed one major spot overlapping with a trace spot: ir 3200, 3090 (sh), 2240 (w), ~1820 (b), 1640 (w),

1505 (sh), 960 (vs), 920 (vs), 745 (s), 700 (vs) cm^{-1}; nmr (CCl_4) τ0.1 (1H, D_2O exchangeable), 7.26 (t, J=6.5 cps, 1H),7.8 (s, 6H), 8.47 (bs, 12H). These spectra were identical with those of anti-oxime 32 (4).

Chromatography of one third of the mother liqour of the basic extract (1.11g) on a silicic acid column gave a crude fraction of syn- and anti- 32, and pure anti-isomer 32. The crude sample of syn- 32 was rechrmoatographed on silicic acid to yield pure syn- 32 (291 mg, one spot in tlc). Sublimation gave colourless crystals of syn-32: m.p. 67-69° (lit. 71-73°) (4); ir 3200, 2700, ~1860 (b) ~1650 (w), 1510 (sh), 960 (vs), 925 (vs), 745 (s) cm^{-1}; nmr (CCl_4) τ0.0 (1H, D_2O exchangeable), 6.37 (t, J=7 cps, 1H), 7.83 (s, 6H), 8.5 (bs, 12H) (4).

(b) Cis-cycloocetene (4.42g, 0.040 mole), 2 (2.566g, 0.035 mole) and concentrated hydrochloric acid (4.5 ml, 0.054 mole) in methanol (ca. 240 ml) were photolyzed with the low pressure mercury resonance lamp in Type 11 apparatus for 3 hrs. 15 min. The nitrosamine peak at 344 nm decreased rapidly upon irradiation and a new peak appeared at ~ 293 nm after 30 min. irradiation indicating the formation

of a C-nitroso dimer (4, 111). Both peaks continued to decrease upon subsequent irradiation and were completely gone towards the end of photolysis.

The light yellow photoyzate was wotked up in the usual manner to give a greenish-yellow basic oil (4.793 g,75%); ir(neat) 3300, 3150, 1650 (w), 920(s), 960 (s), 1000 and 1030 (s) cm^{-1}.

The ir, nmr and tlc mobility identified this oil as a mixture of syn and anti-isomer of 32. Recrystallization of this oil from petroleum ether yielded anti-32 (1.63 g). Chromatography of one third of the mother liquor (1.05 g) on a silicic acid column yielded syn-32 (262 mg, 12%) and anti-32 contaminated with syn-32. The anti: syn-32 ratio estimated from the nmr spectrum of the basic fraction was 7:2.

(c) When a same mixture of starting material was photolyzed with Hanovia lamp (200W) through a corex filter for 1 hr 35 min., a white solid (2.88g) was obtained on evaporation of solvent to 20 ml. The solid showed nmr (D_2O) signals at τ6.06 (poorly resolved q, 1H), 7.12 (s, 6H), ~7.6 (m, 4H), 8.42 (unresolved s, 8H). Recrystallization of this solid from 2 propanol gave a white crystalline solid (2.23 g,

m.p. 198-201°, lit. 204-205°) (4); ir 3270 (sh), 2580, 2520, 2490, 1635 (w), 990 (vs), 932(vs) cm^{-1}. These spectra were identical with those of an authentic sample of the hydrochloride of 2-dimethylamino-cyclooctanone oxime (32) (4).

The mother liquor of the crude reaction mixture was then worked up in the usual manner to afford a basic extract (2.82 g). This was identified by its ir and nmr as a mixture of syn- and anti-32 contaminated by trace of impurity which showed a small nmr signal at τ 7.73 (s). Attempted chromatograph of this solid (1g) on an alumina column (basic, activity 1) gave no separation and yielded fractions of syn- and anti-32 mixture as the only isolable product. The combined yield of 32 was 77%.

6.5.4. Addition of 1 to 3,3-dimethyl-1-butene

A solution of 1 (2.93 g, 0.026 mole), 3,3-dimethyl-1-butene (2.74 g, 0.033 mole) and hydrochloric acid (3.2 ml, 0.038 mole) in methanol (250 ml) was photolyzed through a corex filter with a quartz cold finger using Hanovia (200W) lamp for 1 hr 30 min. A series of new peaks appeared between 320-360 nm (same as in Fig. 2.1) after 30 min; these peaks disappeared

upon subsequent irradiation.

The colourless photolysate was worked up in the usual manner to furnish the neutral and basic extract. The neutral fraction (15 mg) was discarded. The basic fraction (1.34 g) was chromatographed on silicic acid to afford the following fractions:

(a) F3-4 (80 mg, $CHCl_3$ eluent) was a mixture and was sublimed to give an oily solid (50 mg). This oil was identified as a 1:1 mixture of N-piperidinoformamide (11) (vide infra) and 1-piperidino-3,3-dimethyl-2-butanone oxime (34) by tlc, ir and nmr comparison (6).

(b) F5-12 (85 mg, 0-1% CH_3OH in $CHCl_3$ eluent); ir 3180, 3100, 2710 (w), 1730 (s), 1645 (s), 657 cm^{-1}; nmr τ1.67 (d, J=10 cps, collapsed to singlet in the presence of D_2O, 1H), 2.15 (bd, J=10 cps, D_2O exchangeable, 1H), 7.27 (t, 4H), 8.4 (m, 6H). After one recrystallization from petroleum ether and one sublimation 54°/0.2 mm), it gave colourless N-piperidinoformamide (11): m.p. 75-76° (lit. m.p. 77-78°) (44); ms m/e (%) 128 (M^+, 3.0), 99 (46), 83 (81) 55 (100), 41 (35).

Anal. Calc. for $C_6H_{12}N_2O$: C, 56.23; H, 9.44; N, 21.86.

Found: C, 56.40; H, 9,43; N, 22.02.

The ir and nmr spectra of this compound were superimposable with those of the sample prepared by a known method.

In addition 1-piperidino-2-(N-nitroso-hydroxylamino)-3,3-dimethyl-butane (35) and 1-piperidino-2-(N-formylhy-droxylamino)-3,3-dimethyl-butane (36) (6) were isolated. The overall estimated yield were 11 (217 mg, 6.6%), 35 (272 mg, 9.2%) and 36 (240 mg, 4.1%).

Preparation of 11

A solution of formic acid (25 ml) and redistilled N-aminopiperidine (5.2 g, 0.05 mole, b.p. 91-3°/30 mm) (44) was refluxed for 20 hrs. The formic acid and water was removed by distillation under atmospheric pressure; further distillation under vacuum afforded two fractions at 103-105°/14 mm (lit. b.p. 111-114°/1mm) (44) and a residue.

A part of the first fraction (1.08g) was next chromatographed on a silicic acid column to yield 11 (80 mg) and a colourless liquid 13 (283 mg, one spot in tlc); ir(neat) 3500, 1670 (vs), 1398, 1120, 1030, 650 cm^{-1};nmr τ2.06 (s, 1H), 6.64 (m, 4H), 7.07 (s, D_2O exchangeable, impurity), 8.37 (m, 6H);

ms (80 ev) m/e (%) 114 (M+1, 10), 113 (M^+, 100), 112 (M-1, 42), 98(42), 84 (45), 56 (56); ms (15 ev) m/e (%) 114 (8.7), 113 (M^+, 100) and 98 (2.5). The ir spectrum of 13 was identical to that of authentic N-formylpiperidine except for a small peak at 1720 cm^{-1} that was observable in the authentic smaple.

The second fraction (4.39g) was distilled as a colourless liquid which solidified on cooling. It was recrystallized from petroleum ether to give colourless crystals of 11: m.p. 76-78° (lit. m.p. 77-78°) (44).

The residue from the distillation (0.86g) was shown by tlc analysis to be pure 11. The preparative yield of 11 was 6.3g (90%).

6.6 photodecomposition of nitrosamines

6.6.1 Photolysis of N-nitrosopiperidine (1)

(a) In methanol: A solution of 1 (2.75 g, 0.024 mole), concentrated hydrochloric acid (2 ml, 0.024 mole in methanol (240 ml) was irradiated with the low pressure mercury resonance lamp in Type 11 apparatus (Fig 6.1) for 3 hrs. 35 min. The nitrosamine absorption at 347 nm decreased rapidly initially and was replaced by a series of new peaks

between 320-360 nm with fine structure (see Fig. 2.1) after 2 hrs; these peaks continued to decrease upon subsequent irradiation and disappeared completely after 3 hrs. 35 min. These new series of absorptions was subsequently shown to be identical with that of the u.v. absorption of nitrogen dioxide in methanol.

The reaction mixture was worked up in the usual manner. The ether extract gave an oil (50 mg) which proved to be 11* by comparison of its tlc mobility and nmr spectrum with that of an authentic sample except for an extra small signal at τ8.75.

The basic extract, a brown oil (955 mg) was chromatographed on silic acid. Elution with chloroform gave 11 (F5-10, 281 mg), identified by its ir, nmr and tlc with that of an authentic sample. Further elution

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* The formamides 11, 22 and 26 had been observed in the neutral extract. It is believed that these compounds are very weak bases and that under the acid concentration employed (pH ~2), the free base may not be completely protonated. In the latter two cases, the presence of sodium bicarbonate in the aqueous solution may act as a buffer.

gave no other pure product; the recovery of material from column was 70%**.

The aqueous basic residue (pH ~10) was continuously extracted with ether for 50 hrs; removal of solvent gave an oil (275 mg) which was shown to contain by its nmr, about 70% of 11 and was not further investigated.

In another reaction, 1 (6g, 0.053 mole), HCl (4.5 ml, 0.054 mole) and methanol (240 ml) were photolysed for 10 hrs. The photolysate was distilled in a rotary evaporator in which the distillate was trapped with a liquid nitrogen bath. The remaining reaction mixture was treated with 2-propanol (ca. 20 ml) and cooled to give three successive crops of piperidine hydrochloride (10) (2.69 g, 42%) which was identified by its ir and nmr. The mother liquor of the reaction mixture was next worked up in the usual manner. The ether extract (68 mg) was proved by its nmr to be 11. Chromatography of the basic

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** The low recovery of reaction products from column chromatography had been observed quite often (last eluent was usually pure methanol).

extract (785 mg) on a silicic acid column yielded 11 (80 mg) as the only isolable product.

The basic aqueous solution was continuously extracted with ether for 7 days, removal of solvent gave a brown oil (523 mg). The aqueous mother liquor was next evaporated to dryness in vacuum; the solid residue was extracted with methylene chloride (3 x 40 ml): removal of solvent gave a dark oil (285 mg). This dark oil was combined with the oil obtained form the continuous extract and chromatographed on silic acid. Elution with chloroform gave a fraction (195 mg) which had identical ir, nmr and tlc (2% $CH_3OH/CHCl_3$, alumina plate) mobility with authentic 11. The presence of trace of N-formylpiperidine (13) in this fraction was indicated by tlc mobility by comparison with authentic 13 (same r_f value and same light yellow spot). Further elution yielded F16-17(63 mg, 10% CH_3OH in $CHCl_3$ eluent), an oily crystalline solid; ir 3380 (s), 3050 2740, 2510, 1650 (s), 990, 960, 910 (s), 640 cm^{-1}; nmr τ3.5 (2H, D_2O exchangeable). 6.83 (poorly resolved t, 2H), 7.76 (unresolved t, 2H), 8.27 (m, 4H) (7). These spectral data established that F16-17 (1.1%) was 2-piperidonoxime 12. The last fraction (112 mg),

eluted from methanol, was shown by tlc to contain ca. 50% of 12. The overall estimated yield of 12 was 2.2%.

The trapped distillate was treated with 2, 4-dinitrophenylhydrazine solution* (10 ml) to give yellow needle crystals of the 2,4-DNPH of formaldehyde (190 mg): m.p. 158-160° (lit. m.p. 167°) (113); ir 3315, 3095, 1615 (s), 1585, 1510, 1445 cm^{-1}. The spectrum was superimposable with that of an authentic sample.

When the reaction was repeated with a solution of 1 (2.57 g, 0.023 mole) in methanol (240 ml) in the absence of HCl, irradiation with 2537A light source in a quartz vessel (Type 11 apparatus) for 23 hrs. produced no detectable change in the u.v. spectrum of the photolysate ($<2\%$). The solvent, methanol, was trapped in the usual manner. The residue, a greenish yellow liquid (2.38 g, 92.5%), was identified by its ir and nmr as the starting nitrosamine 1.

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* Solution prepared according to (112), 4g of 2,4-DNPH reagent per 100 ml methanol or ethanol solution.

The trapped distillate was treated with Brady's reagent; from the concentrated solution no 2, 4-DNPH derivative was obtained, only a minor amount (<10 mg) of the starting 2,4-DNPH reagent was recovered.

(b) In water: A solution of 1 (5.03 g, 0.044 mole), hydrochloric acid (4.4 ml, 0.053 mole) in water (240 ml) was photolysed in type II apparatus (Fig. 6.1) for 9 hrs. The photolysate, after removal of solvent was treated with 2-propanol (ca. 20 ml). The resulting solution was cooled to give a crystalline solid of hydrochloride 10 (1.28 g, 24%).

The mother liquor of the reaction mixture on working up in the usual way gave a crude basic extract, an oil (1.59g), which showed no nmr signal below τ6.0. Chromatography of this basic fraction (1.06 g) on florisil and elution with 1-2% $CH_3OH/CHCl_3$ yielded a semi-solid (F3-6, 460 mg). This solid was identified as isotripiperidein (14) (19%) by its superimposable ir with an authentic sample (7) except for the 1650 cm^{-1} band (of medium intensity) which could be ascribed to C=N stretching. The nmr of this semi-solid is superimposable with that of authentic isotripiperidein showing signals at τ6.28 (bd, 1H), 6.88 (bd, 2H), 7.39 (m, 3H), 8.42 (19 or 20H).

Attempted purification of this solid by sublimation at 70° (0.3 mm) led to decomposition as indicated by the tlc pattern (showing more than four extra spots) and the ir spectrum of the sublimate which showed an extra peaks at 1500 cm^{-1} and the absence of strong absorption at 1190, 900 and 790 cm^{-1} as compared to that before sublimation.

The basic aqueous solution was further extracted with methylene chloride continuously to give an oil (114 mg). Recrystallization of this oil from petroleum ether afforded only small amount of 14 (ca. 10 mg): m.p. 92-93° (lit. m.p. 95-96°) (7); Amidoxime 12 was neither isolated nor detected.

In a separate reaction, a solution of 1 (4.86 g, 0.043 mole), hydrochloric acid (4.5 ml, 0.054 mole) and water (ca. 240 ml) in a pyrex vessel (Type 1 apparatus) was photolysed with Hanovia (200W) lamp for 9 hrs. using 2,7-dimethyl-3,6-diazacyclohepta-1, 6-diene perchlorate as the filter solution (see Table 6-1 and Fig. 6.2). The reaction mixture was stripped off solvent. To the residue, acetone (ca. 30 ml) was added and the solution cooled overnight to give a light yellow crystalline solid 15 (1.76 g): m.p. 93-96°; it 3250, 3200 (w), 2630, 2510, 2420, 2160, 2120 (s), 1600 (m), 800-1200 (very complex) cm^{-1}; nmr (D_2O) τ8.27 (bm) 6.33-7.15 (bm). Various attempts

to recrystallize the salt failed. An aqueous solution of the salt was basified with sodium carbonate to pH~10 and was continuously extracted with chloroform for 2 days. Removal of chloroform gave an oil (959mg). Chromatography of this oil on florisil yielded no isolable pure fraction. The compound appeared to have decomposed during the continuous extraction process. Only 37% of the crude free base was recovered from the column. It was possibly a mistake here in using chloroform as the extractant and that a carbene reaction might have taken place leading to the decomposition.

The absence of nmr signal below τ6.0 in 15 and its complex ir pattern suggested that it might be the hydrochloride of isotripiperidein.

The mother liquor of the reaction mixture was then worked up in the usual manner. The neutral extract (174 mg) was shown to be the starting nitrosamine.

The basic extract, an oil (1.81 g), was recrystallized from carbon tetrachloride to give an oily solid (1.319 g) identified as slightly impure amidoxime 12 by its ir and nmr and was not further investigated. Chromatography of the mother liquor

after removal of 12 on a silicic acid column yielded 2-piperidone (16) (F4-5, 30 mg. 0.74%); ir(neat) 3260(s), 1650 (vs), 1500 (m) cm^{-1}; nmr τ8.7 (impurity), 8.18 (4H), 7.62 (2H), 6.67 (2H) and 3.22 (1H, diffused and D_2O exchangeable). These spectra were found to be identical with those of the authentic 16. Further elution from 10% $CH_3OH/CHCl_3$ afforded 12 (F6-9, 139mg). The total yield of amidoxime 12 was31%.

(c) Quenching of the photodecomposition of 1 by napthalene

(i) A solution of 1 (3.58 g, 0.033 mole, 0.098 M), naphthalene (4.23 g, 0.034 mole, 0.105M), hydrochloric acid (4.5 ml, 0.054 mole, 0.17M) in methanol (320 ml) was photolyzed in a pyrex vessel (Type 1 apparatus) with Hanovia (200W) lamp using 2,7-dimethyl-3,6-diaza-cyclohepta-1,6-diene perchlorate as the filter solution (irradiation at $\lambda > 350$ nm, Fig 6.2). Upon irradiation, the solution turned yellow after 30 min. The nitrosamine peak at 350 nm increased instead of decreasing as was normally observed. Absorption at 350 nm continued to rise and gradually broadened on further irradiation with no peak below 400 nm being observed after 6 hrs when the photolysis was stopped; the reaction mixture became a brownish red solution.

The solvent of the reaction mixture was trapped in the usual manner, The residue, a brownish red solid, was triturated with water (50 ml); the precipitated greyish solid was filtered off. This solid (3.036g, m.p. 74-77°, 70% recovery) was identified as naphthalene. The aqueous mother liquor was then stripped off water, triturated with acetone and cooled to give the hydrochloride 10 (1.35 g, 35.5%): m.p. ca. 225° (decomp).

The mother liquor was taken up in water (30 ml) and was extracted in the usual manner to give a neutral (447 mg) and a basic extract (666 mg). The neutral extract, a brown oil, was chromatographed on florisil (1:25 ratio). Elution with chloroform gave a major fraction (240 mg) which was rechromatographed on a silicic acid column (1:50 ratio). Elution with chloroform yielded 1 (90 mg, 2.5%) and an unknown compound 17 (31 mg). Unknown 17 showed ir absorption at 3060, 2860, 2800, 2750 (w), 1595 (m), 1580 (sh), 1510, 1425, 1100 and 770 cm^{-1}, nmr signals at τ8.75 (s), 7.0 and 8.27 (both bs), 6.07 (s), 3.4-1.7 (m). Both ir and nmr of 17 indicated the presence of an aromic ring and possibly the piperidino group. Its identity however had not been

established due to insufficient sample.

The basic extract, an oil (666 mg), was chromatographed on florisil. Elution from chloroform yielded an unknown fraction (19 mg); ir(neat) 3070, 1630 and 1600 (m), 1510, 1100, 790 cm^{-1}; nmr τ8.75 (s), 8.3 (bs), 7.0 (b), 6.0 (s), 3.0-2.0 (m). These spectral data suggested that this unknown fraction might be the same compound as 17. Further elution from 1-2% methanol in chloroform afforded trimer 14 (120 mg, 4.6%).

The trapped methanol distillate was treated with Brady's reagent to give a small crop of solid (ca. 30 mg) which was identified as the 2,4-DNPH of formaldehyde by its tlc mobility (benzene eluent) and superimposable ir with an authentic specimen.

(ii) In another reaction, a solution of 1 (3.55 g, 0.031 mole, 0.0945 M), hydrochloric acid (4.5 ml, 0.054 mole, 0.164 M) and naphthalene (0.46 g, 0.0036 mole, 0.0108 M) in methanol (330ml) was photolysed in the same manner as described in (i). The nitrosamine absorption at 350 nm decreased during the first hour, then increased on further irradiation in the similar manner as was observed in (i). The absorption of the solution stopped to increase after

6 hrs. of irradiation. The brown photolysate was not worked at, but discarded. A plot of the decrease in the optical density of 1 at 350 nm with time for the present run and control experiment (without naphthalene, see (iii) below) was shown in Fig. 2.2.

(iii) As a control run, a solution of 1 (3.56 g, 0.03 mole), hydrochloric acid (4.5 ml, 0.054 mole) in methanol (330 ml) was photolysed for 3 hrs. under the same condition as (i) above. The nitrosamine peak at 350 nm decreased rapidly on irradiation and completely disappeared at the end of the third hour.

The distillate of the colourless photolysate was trapped in the usual manner. This distillate was treated with Brady's reagent (15 ml) to afford yellow needles (166 mg) which was identified as the 2,4-DNPH of formaldehyde by its ir and nmr spectra.

The residue of the reaction mixture was triturated with acetone and was cooled to yield a crop of crystalline hydrochloride 10 (1.89 g). The mother liquor was then worked up in the usual manner. The neutral extract (269 mg) showed ir(neat) absorption at 3340, 1700 (m) and 1050 cm^{-1} but no nmr signal below τ5.0 indicating the absence of formamide 11; this fraction was not investigated.

The basic extract, a semi-solid (1.66 g) was obtained by continuous extraction at pH 9. Attempted crystallization of this basic fraction from 2-propanol yielded another crop of 10 (275 mg). The overall yield of 10 was 57% (2.16 g). The residue (945 mg) after the removal of 10 showed ir peaks at 3260 (b), 1644 (m) and 750 (s) cm^{-1} but no nmr signal below τ 3.0 This fraction was chromatographed on a florisil column (1:40 ratio). Elution from chloroform afforded 18 (80 mg): ir(neat) 3400 (b), 1750 (w, impurity), 1640 (s), 1250 (s) cm^{-1}; nmr τ8.46 (m, 6H), 6.9(m, 4H) and a small signal at τ8.77 (s) possibly due to impurity: m/e (%) 222 (8.5), 196 (2.8), 113 (8.5), 112 (6.7), 99 (13.5), 84 (100), 83 (35), 56 (35), 55 (56), 42 (75), 41 (68). These spectral data suggested 18 to be N,N,N',N'-bispentamethyleneurea. Subsequent elution with 10 - 25% ethanol in chloroform afforded amidoxime 12 (125 mg, 3.5%).

(d) Sensitization of the photodecomposition of 1 by naphthalene

(i) A solution of 1 (2.95 g, 0.026 mole, 0.019M), naphthalene (18.26 g, 0.14 mole, 0.10 M) and hydrochloric acid (20 ml, 0.024 mole, 0.17 M) in methanol (1400 ml) was photolyzed in a pyrex vessel with a

Rayonet 310 nm lamp using nickel sulphate as filter solution (see Fig. 6.2). Under this condition, the irradiation was provided in the region 290-340 nm where naphthalene absorbed most of the light (ca. 80%). The photolysis proceeded very slowly. The 350 nm peak increased in the same manner as described in sec.(c)(i) with no maximum being observed after 10 hrs. of irradiation.

After removal of solvent, water (50 ml) was added to the residue. The white precipitate was filtered off, and was identified as naphthalene (15.27 g, 83.5%). The aqueous mother liquor was worked up in the usual manner. The ether extract, a brown liquid (1.66 g) was identified as 1. Methylene chloride of the basic extract was distilled off and collected (ca 130ml). Attempted v.p.c. analysis of the distillate failed to detect any component other than that of the solvent. Any volatile component present would be less than 100 mg since by assuming a molecular weight of 100, 1 μl $\sim 10^{-8}$ mole, which was the detection limit by v.p.c. The distillate was then treated with anhydrous hydrogen chloride; removal of solvent gave the hydrochloride 10 (6 mg).

The basic residue (354 mg) was shown by its ir and nmr to be mainly the unreacted nitrosamine except

for a singlet at τ2.55, which could be due to NH_2 of 10. Recrystallization of this basic fraction yielded only 10 (28 mg). The total yield of 10 was 1.7% (53 mg). Attempted chromatography of the basic residue gave only 1 (80 mg; overall yield 1.91 g, 65%) with no other isoble product.

(ii). As a control reaction, a solution of 1 (2.86 g, 0.025 mole, 0.018 M) and hydrochloric acid (20 ml, 0.024 mole, 0.17M) in methanol (1400 ml) was photolysed under the same condition as described above for 10 hrs. The 350 nm peak decreased by 20% after 10 hrs. of irradiation. The reaction was not investigated.

6.6.2 Photolysis of 2-methyl-N-nitrosopiperidine (4)

A solution of 4 (7.95 g, 0.062 mole) and hydrochloric acid (8.0 ml, 0.097 mole) in methanol (240 ml) was photolysed in Type II apparatus with the low pressure mercury arc lamp for 10 hrs. A series of new peaks with fine structure was observed in the 320-350 nm region at the fourth hour analogous to the described in 6.6.1 (a) (Fig 2.1). These peaks disappeared upon subsequent irradiation. The photolysate was distilled and methanol was trapped with a liquid nitrogen bath. The distillate was treated

with Brady's reagent and cooled to give yellow needles of formaldehyde-2,4-DNPH.

The residue of the reaction mixture was worked up in the usual manner. The neutral extract (22 mg) was dascarded. Methylene chloride of the basic extract was distilled off and collected. The basic residue, a brown liquid (5.29 g). on treatment with petroleum ether (ca. 20 ml) precipated a colourless crystalline solid (51 mg): m.p. 196-199° (lit. m.p. 207) (114); ir 3190, 2570, 2530, 2480, 2410, 2160, 2070, 1880, 1610, 1590 (s) cm^{-1}; nmr τ1.05 (2H), 6.43-7.35 (m, 3H, $\overset{+}{N}CH_2$ and CH), 8.16 (m, 6H), 8.45 (d, J=6 cps, 3H). These spectra were shown to be superimposable with that of the hydrochloride of 2—methylpiperidine. The methylene chloride collected on treatment with dry HCl yielded a small amount of the parent amine hydrochloride.

Attempted chromatography of the remaining basic extract (5.0 g) on a silic acid column (75 g) did not acheive a separation; the recovery was however only 38% (1.88 g). Fraction 1-10 (565 mg, 4 spots on tlc) of the previous chromatography was rechromatographed on a silicic acid column. Elution with chloroform yielded two impure fractions: Fractions 2-3 (108 mg)

and Fractions 4-9 (305 mg). The latter fraction showed ir absorption, tlc mobility corresponding to N-2-methylpiperidinoformamide (22) (vide infra). The former fraction showed ir(CCl_4) peaks at 2860, 2820, 2100 (w), 1680 (m), 1635 (s), 1200-1100 (complex) cm^{-1}. Rechromatography of this fraction (65 mg) on silicic acid gave an unknown compound 23 (48 mg, one spot in the tlc); ir(neat) 3400 (diffused), 2100 (w), 1680 (m), 1635, 1555 cm^{-1}; nmr τ6.1 (1H), 6.82 (b, 2H), 8.42 (m, 6H), 8.86 (d, J=6 cps, 3H) and 3.65 (impurity). The nmr signals suggested 23 might be 2,2'-dimethyl-N,N,N',N'-bispentamethyleneurea.

In a separate reaction, a solution of 4 (7.91 g, 0.062 mole) and HCl (8.0 ml, 0.097 mole) in methanol (240 ml) was photolysed under similar conditions for 10 hrs. The reaction mixture was neutralized (ca pH 7) with sodium bicarbonate solution before evaporation of the solvent. The residue was then taken up in water in the usual manner. Ether of the neutral extract was removed by distillation. The residue showed ir (CCl_4) peaks at 3340 (b), 1675 (vs), 1414 cm^{-1}, and nmr signals at τ9.0 (d), and 1.8 (s). These spectral data suggested the presence of formamide 22. This residue was sublimed (100-110°/ 0.1 mm) to give an oil (141 mg, one spot on tlc); nmr τ 1.85 (d, collapsed to singlet in the presence of D_2O),

ca. 2.28 (b.d, D_2O exchangeable), 5.1 (d, impurity), 7.0, 7.5, 8.4 (m)., 8.96 (d, J=6 cps); ms m/e (%) 143 (M+1, 6.1), 142 (M^+, 4.3), 141 (3.7), 127 (27), 113(45), 97 (100), 69 (52), 55 (70), 45 (67), 42 (63), 41 (82), 29 (44), 27 (61). These data agreed with those of authentic N-2-methylpiperidinoformamide (22) (vide infra).

Vapour phase chromatographic analysis (5% SE 30 on Chr. W, oven temperature 100°) of the basic extract gave five minor peaks and a major very polar component (possibly 22). Attempted bulb to bulb distillation (3 stages) gave no separation; this basic fraction was not further characterized.

A mixture of 4 (14 g) and lithium aluminum hydride (10 g, 1.2 equiv.) in ether was stirred over night. On working up in the usual manner, a crude amine was obtained in 15% yield (1.8 g). This crude product of 2-methyl-N-aminopiperidine (1.8 g) was disolved in excess formic acid (91%, 20 ml) with constant stirring and external cooling by an ice bath during the addition(44). The homogeneous solution was refluxed for 2 hrs. The reaction mixture was distilled to remove the forerun. Further distillation gave one major fraction (oily soild, 890 mg, b.p. 114-115°/12 mm) and a residue (380 mg). The oily

solid was chromatographed on a silicic acid column. Elution from chloroform gave an oil (single spot in tlc). Sublimation of this sample yielded an oil which soon solidified to a colourless solid of formamide 22: m.p. 72-73°; ir 3200(m), 3080, 2725 (w), 2670 (w), 1694 (vs), 1660 (vs), 740, and 650 cm^{-1}; nmr τ8.92 (d, J=6 cps, $HC\underline{CH_3}$), 8.38 (m, 6H), 7.5 (m, 2H), 6.91 (bd, $\underline{H}CCH_3$), 2.31(bd, J=11 cps, D_2O exchangeable, NH), 1.77 (d, J=11 cps, collapsed to singlet in D_2O HCO-). Its mass spectra was the same as that isolated from the reaction mixture described above.

Anal. Calcd. for $C_7H_{14}N_2O$: C,59.2; H, 9.85; N, 19.72.

Found: C, 59.03; H, 9.71; N, 19.65.

The last fraction (235 mg) eluted from methanol was liquid of 24: ir(neat) 3280, 3160, 2860, 2720, ca. 1600 (vs), 770 (s) cm^{-1}; nmr τ8.64 (d, J=6 cps, 3H), 8.26 (m, 6H), 6.47-6.99 (m, 3H, $\underline{NCH_2}$and $\underline{NCH}CH_3$), 2.44 (s, ~3H), 1.51 (s, 1H); ms m/e (%) 142 (8.0), 141 (3.2), 140 (4.0), 139 (4.0), 113 (13.5), 99 (28), 98 (29), 97 (28), 84 (100), 69 (17.0), 56 (57), 43 (47), 42 (53), 41 (35). This fraction was not further characterissed.

6.6.3 Photolysis of N-nitrosodibenzyl--amine (3)

A solution of 3 (5.45g, 0.024 mole) and hydro-

chloric acid (2.5 ml, 0.030 mole) in methanol (240 ml) was photolysed in Type 11 apparatus for 4⅓ hrs. The reaction proceeded very rapidly upon irradiation, the nitrosamine peak at 360 nm decreased from an optical density of 1.42 to 0.75 in the first hour; to 0.58 at 1⅓ hr and appeared as a shoulder with no distinct maximum. The decrease in optical density was rather slow on subsequent irradiation, and the uv profile remained constant after 4 hrs. of irradiation. The colourless solution turned to yellowish green at the end of the photolysis.

The methanol was distilled and trapped in a liquid nitrogen bath. The trapped distillate was treated with Brady's reagent (ca. 75 ml). The small amount of precipitated crystalline solid (~20 mg, m.p. 228-233°; lit m.p. 237°) (113) was identified as the 2,4-DNPH of benzaldehyde* by its superimposable ir spectrum with an authentic sample. The residue

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* Isolation procedure was not vigorous as total volume of solution was ca. 250 ml; absence of formaldehyde could not be drawn conclusively.

of the reaction mixture, a yellow oily liquid, was crystallized from isopropanol to give colourless plates of benzylamine hydrochloride (1.69 g) which was identified by its superimposable ir spectrum with an authentic sample: m.p. 249-254° (subl.); nmr(D_2O) τ2.72 (s, 5H), 6.03 (s, 2H)#.

The mother liquor was worked up in the usual manner. The neutral extract, a yellow liquid with almond odour (1.49 g), was shown by its tlc, ir(neat) absorption at 2820, 2740, 1705 (vs)cm^{-1} and nmr signal at τ0.2 (s, ca. 1H, -CHO) to contain benzaldehyde as major product. Chromatography of this liquid on a silicic acid column yielded three major fractions. Elution with chloroform gave a yellow liquid (1.012 g) which was shown to be a mixture of benzaldehyde (910 mg) and nitrosamine 3 (304 mg) by its ir and nmr spectra. Further elution with chloroform afforded benzaldhyde oxime 19 (211 mg); ir(neat)3320(b,s), 3070, 2740 (sh), 1695 (m), 1635,

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The compound was not dibenzylamine hydrochloride (lit. m.p. 256°) (114) which had different ir patterm and nmr chemical shifts.

1600, 1580, 1495 (m), 955 (vs) cm^{-1}; nmr τ0.75(bs, D_2O exchangeable, 1H), 1.9 (s, 1H), 2.48 (m, 2H), 2.77 (m, 3H). These spectra were identical with that of an authentic sample. Elution with 1% methanol in chloroform afforded amidoxime 20 (46 mg) (vide infra).

The basic extract (1.41 g) on standing deposited yellow crystalline solid of N-benzylbenzamidoxime 20 (642 mg); ir 3422 (m), 3035 (w), 1645 (s), 1608-1580 (w), 1485, 890 (vs) cm^{-1}; nmr τ 2.66 (s, 5H), 2.82 (s, 5H), 5.8 (s, 2H), ca. 4.2 (b, D_2O exchangeable) (11). Recrystallization from benzene, it showed no change in its ir spectrum; m.p. 108-111° (lit. m.p. 114°) (3). The mother liquor (694 mg) after removal of 20 was chromatographed on a silicic acid column to give two major fractions and an unidentified compound 21. Elution with chloroform gave 21 (24 mg, an oil, single spot in tlc); ir(neat) 3360, 3067 (m), 3034 (m), 1955(w), 1705 (m) 1645, 1587, 1605, 1563, 1494, 1070(m), 1028 (m), 756, 730, 696 (s) cm^{-1}; nmr τ 1.84 (b), 2.35-3.16(m) and 8.73 (s, CH_3C-O) in ratio 10:3, ca. 6.3 (b, D_2O exchangeable). Subsequent elution with chloroform gave 20 (328 mg); further elution with 4-8% methanol in chloroform

gave benzylamine (79 mg). The overall yield of amidoxime 20 was 20% (1.02 g out of 5.15 g nitrosamine consumed). The overall yield of benzylamine was 55% (1.34 g).

6.6.4 Photolysis of N-nitoroso-N-methylaniline (6) in neutral media

A solution of 6 (1.83 g, 0.035 mole) in methanol was photolyzed in Type 11 apparatus for 10 hrs. The solution truned dark slowly upon irradiation but the nitrosamine absosrption at 270 nm (using 1/1000th dilution) remained unchanged after 10 hrs.

In a separate reaction, a solution of 6 (1.12 g 0.008 mole) in methanol (250 ml) was photolysed in a pyrex flask (Type 1) fitted with a quartz cold finger using the Hanovia (450 W) lamp for 10 hrs. Upon irradiation, the shoulder of the nitrosamine absorption at ca. 360 nm increased slowly while the solution started to change from colourless to purple black. Dilution by a factor of 250 indicated the nitrosamine peak at 270 nm had shifted to shorter wavelength with a maximum at ca. 250 nm (concentration dependent). The shoulder at 270 nm was still prominant indicating the nitrosamine was still present.

The methanol of the photolysate was trapped in the usual manner and was treated with Brady's reagent to give no derivatives even under vigorous conditions. The residue (983 mg) was chromatographed on a silicic acid column. Elution with chloroform gave 6 (a brown liquid, 859 mg, 77% recovery). Further elution with chloroform afforded a fraction (69 mg) which was identified by its ir and nmr as N-methylaniline slightly contaminated by 6 as also indicated by tlc. Subsequent elution yielded no other product.

6.6.5 Photolysis of N-methyl-N-nitroso-n-pentylamine (7)

A solution of 7 (1.09 g, 0.008 mole) and hydrochloric acid (4 ml, 0.048 mole) in water (240 ml) was photolysed in Type 11 apparatus for 2½ hrs. The reaction mixture was worked up in the usual manner. The neutral extract (8 mg) was discarded. The basic extract, an oil (474 mg), was combined with the oil (169 mg) obtained by continuous extraction with methylene chloride. Attempted chromatography of this combined fraction (590 mg) on a silicic acid column yielded fractions which evaporated easily and could

not be identified. The presence of N-methyl-valerylamidoxime was indicated in one of the impure fraction (26 mg, eluted from 2% CH_3OH in $CHCl_3$). This fraction showed ir ($CHCl_3$) peaks at 3420, 3220 (b), 1655 (s), 890 cm^{-1}, and nmr signals at τ 3.0 (D_2O exchangeable), 7.15 (s, H_3CN-CO-), 7.7 (m, H_2CCONR_2), 8.66 (m) and 9.1 (m).

In another reaction, a mixture of 7 (2.73 g, 0.021 mole) and Hydrochloric acid (5 ml, 0.06 mole) in water (240 ml) was photolyzed for 5⅓ hrs. The nitrosamine was not completely soluble in water and a part of it floated on the top of the aqueous phase. As the reaction proceeded, the suspension gradually disappeared.

The solvent was trapped in the usual manner and was extracted under acid condition (ca. pH 1) with ether 3 x 30 ml). This ether extract was diluted with methanol and was treated with Brady's reagent. The solution was concentrated and cooled to give a crop of yellow needle crystals (160 mg): m.p. 103-105° (lit. m.p. 107) (113). Its ir spectrum was superimposable with that of an authentic sample of 2,4-DNPH of n-valeraldehyde; ms m/e (%) 267 (18), 266 (M^+, 74), 206 (100), 140 (47); nmr τ 2.5 (t, J=5 cps, 1H), 7.6 (m, 2H), 8.5 (m, 4H), 9.01 (m, 3H), -1.0 (bd, J=10 cps, D_2O exchangeable), 1.0-2.5 (m, ABX pattern,

aromatic ring proton).

The reisdue of the reaction mixture was worked up in the usual manner. The neutral extract (21 mg) was discarded. The methylene chloride recovered from the basic extract gave small amount of N-methyl-n-pentylamine hydrochloride (ca. 20 mg) on treatment with dry hydrogen chloride. The residue of the basic extract, an oil (872 mg), was shown to be a complex mixture (tlc indicated no less than 6 spots); ir(neat) 3400-3200 (diffused), 2460, 2100, 1710 (m), 1660, 1540 (w) cm^{-1}; nmr τ9.15, 8.72 (m), 8.1 (d), 7.9 (s), ca. 7.46 (m), 4.72 (D_2O exchangeable). Chromatography of this basic extract led to no isoble product as the fractions appeared to be volatile.

The basic aqueous solution was continuously extracted with dichloromethane for 12 hrs. Removal of solvent gave an oil (387 mg) which had not been investigated.

6.6.6. Photolysis of N-nitroso-di-n-pentylamine (8)

(a) A solution of 8 (6.92 g, 0.037 mole, 0.11M) and concentrated sulphuric acid (70 ml, 1.31 mole, 4M) in glacial acetic acid (ca. 260 ml) was photolyzed

through a Nonex filter in a pyrex vessel (Type 1 apparatus) using the Hanovia (450 W) lamp for 7⅛hrs. A calcium chloride drying tube was placed on the top of the condenser. Under the present acid concentration used, the nitrosamine peak shifted to 332 nm* (ε38). The reaction mixture showed no change in u.v. absorption after irradiation for 7⅛ hrs. Dilution by a factor of 250 of the photolysate showed no new absorption between 300-240 nm.

The photolysate was poured into a beaker containing water (200 ml) and ice (300 g), and extracted with ether (3 x 100 ml) at pH o. The ether layer was washed with sodium chloride solution and dried. The aqueous solution was next basified to pH 10 and extracted with methylene chloride (3 x 150 ml), washed and dried.

The neutral extract was distilled. The distillate was diluted with ethanol and treated with Brady's reagent to give yellow needles of 2,4-DNPH of acetone (44 mg, m.p. 115-118°); ms m/e (%) 238 (M^+ 100),

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* cf. λ_{max} 348 nm (ε90) in methanol with 0.025 M HCl under 6.6.6 (b).

224 (14), 252 (2.2), 266 (2.2). The residue (5.07 g, 73%) was shown by its tlc, ir and nmr to be the starting nitrosamine. Attempted crystallization of this residue afforded only small amount of di-n-pentyalamine hydrochloride (ca. 20 mg).

The methylene chloride extract was distilled. The distillate was treated with Brady's reagent to yield another crop of 2,4-DN PH of acetone (43 mg). The basic residue was an oily solid (43 mg, 5 spots in tlc), ir($CHCl_3$) 3300 (b), 1700 (m), 1660 (m), 1250, 1090, 1014 and 810 cm^{-1}. This residue was not further investigated.

(b) A solution of 8 (4.36 g, 0.023 mole) and hydrochloric acid (5ml, 0.06 mole) in methanol (240 ml) was photolyzed with the low pressure mercury resonance lamp in Type 11 apparatus for 3½ hrs. The solution exhibited the maximum at 348 nm (ε90) which decreased rapidly upon irradiation. Dilution by a factor of 250 times of the photolysate after 3 hrs. 30 min. showed no peak below 400 nm indicating that the nitrosamine had decomposed.

The light yellow photolysate was neutralised with sodium carbanate to pH 7 and the solvent was removed. The trapped distillate (100 ml from a

total volume of 250 ml) was treated with Brady's reagent (20 ml). Concentration and cooling of the solution yielded yellow needles of 2,4-DNPH of n-valeraldehyde (471 mg).

The residue of the reaction mixture was worked up in the usual manner to afford the neutral and basic extract. The ether of the neutral extract was removed by distillation and treated with Brady's reagent to afford the 2,4-DNPH of n-valeraldehyde (153 mg). From the combined 2,4-DNPH mother liquors, a further crop of valeraldehyde-2,4-DNPH (258 mg) was obtained. The overall yield of n-valeraldehyde was 35%.

The residue of the neutral extract (590 mg) was crystallised from acetone to give di-n-pentylamine hydrochloride (42 mg). The mother liquor (380 mg) was chromatographed on a silicic acid column. Elution with chloroform gave Fractions 1-3 (150 mg), a mixture of 26 and one other major component. Further elution with chloroform yielded a semi-solid (107 mg); ir($CHCl_3$)* 3290, 3150 1680 (vs), 1080, 1050, 1024, 1005 cm^{-1}; nmr τ9.17 (very poorly resolved t, 6H), 8.7

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* cf. ir($CHCl_3$) of 11 3310, 3200, 3000, 1685(vs), 1118, 1108, 1040 and 1008 cm^{-1}.

(m, 12H), 7.4 (t, ~4H), 1.85 (m, collapsed to singlet in D_2O HNCOH). This fraction was sublimed twice at 90° (0.2 mm) to give a colourless oil of N-di-n-pentylaminoformamide (26); ms m/e (%) 201 (3.3), 200 (M^+, 7.2), 199 (2.2), 171 (10.0), 157 (11), 143 (94), 115 (56), 113 (28), 98 (99), 87 (41), 73 (100), 45 (51), 43 (100), 41 (81), 29 (73); (M^+) Calc. for $C_{10}H_{20}N_2O_2$, 200.1524; Found 200.1526. Further elution with 5% methanol in chloroform gave di-n-pentylamine hydrochloride (42 mg).

The basic extract was distilled and the distillate was treated with dry hydrogen chloride to give a solid (190 mg). Repeated crystallization of this solid from acetone afforded the hydrochlorides of dipentylamine (8 mg) and n-pentylamine (16 mg).

The residue of the basic extract(an oil, 1.32 g) was chromatographed on a silicic acid column to yield five fractions described in the order of elution.

(i) Unknown 29 (Fl, 10 mg, one spot in tlc, chloroform eluent); ir ($CHCl_3$) 3030 (w), 2720 (w), 1720 and 1675 (s), 1634 (w), 1400 (sh), 1260 (m) and 810 cm^{-1}.

(ii) Fractions 2-12 (132 mg, $CHCl_3$ eluent) was a mixture and was separated by preparative thin

layer chromatography to give 26 (36 mg). The overall yield of 26 was 3.1% (144 mg).

(iii) Fractions 16-18 (161 mg, 2% CH_3OH in $CHCl_3$ as eluent) was crystalized from petroleum ether to give colourless needles of the unknown 30 (ca. 10 mg): m.p. 99-100°; ir 3350, 3180, 1655, and 1625(s), 1140 cm^{-1}; ms m/e at 170. The ir spectrum suggested this to be a primary amide.

The mother liquor after removal of 30 was sublimed twice (70°/0.3 mm) to give a colourless oil of N-n-pentyl-valerylamidoxime (27) (64 mg, 1.5%): ir ($CHCl_3$) 3410, 3220 (b), ~1760 (sh, impurity), 1640 (vs), 900 (s), 942, 690 cm^{-1}; nmr τ 9.08 (poorly resolved t, 6H), 8.6 (m, 10H), 7.82 (m, 2H), 6.9 (poorly resolved t, 2H), 4.87 (diffused, D_2O exchangeable); ms m/e (%) 187 (M+1, 19), 186(M^+, 22) 171 (8.3), 157 (15), 129 (22), 112 (42), 87 (97), 44(33), 43 (62), 30 (100), 29 (45): m/e calc. for $C_{10}H_{22}N_2O$: 186.1732; found 186.1738.

(iv) Elution with 5-6% methanol in chloroform afforded dipentylamine hydrochloride (232 mg).

(v) Further elution with 10-20% methanol in chloroform yielded di-n-pentylamine (180 mg). The combined isolated yield of parent amine was 12%.

The basic aqueous mother was evaporated to dryness under vacuum. The solid residue was extracted with methylene chloride from which an oily solid (395 mg) was obtained. Recrystallization of this oil from chloroform afforded a colourless solid of 4-(N-nitrosohydroxylamino)-dipenthylamine (28) (183 mg, 7.2%): m.p. $>200^{\circ}$(dec.); ir ca. 2680 and 2480 (b), 1600 (diffused), 1395, 1230,1200, 1145, 930 (m), 900 cm^{-1}; nmr (D_2O) τ 4.94 (s, impurity), 5.7 (m, weak, $H_3CC\underline{H}$), 7.01 (t, J=4 cps, 4H), 8.0-8.83 (m, 12 or 13H) with a submerged signal at 8.59 (d, J=6.5 cps), 9.05 (poorly resolved t, 3H) (Fig. 2.3). After one recrystallisation from acetone-ethanol, it gave colourless 28 with unchanged ir spectrum: m.p. 188-190°; ms m/e (%) 217 (M^+, 3.4, Calc. for $C_{10}H_{23}N_3O_2$: 217.1790; Found: 217.1785), 218 (1.1), 2.6 (1.1),187 (6.8), 160 (22), 130 (100), 113 (15), 100 (100), 98 (39), 84 (34), 70 (43), 56 (19), 44 (71), 43 (64), 41 (45), 30 (59). The difference in m.p. was apparently due to slight contamination by inorganic salt in the sample before recrystallisation.

When the signal* at τ5.7 was irradiated, the doublet at τ8.6 collapsed to a singlet indicating the presence of H_3C-CH moiety (Fig. 2.3). Another sample sublimed from the mother liquor at 100°/0.3 mm showed identical mass spectrum described above.

6.6.7 Photolysis of N-nitroso-2-(t-butylamino)-ethanol (5)

A solution of 5 (2.69 g, 0.1018 mole) and hydrochloric acid (1.8 ml, 022 mole) in water (240 ml) was photolysed in Type 11 apparatus for 4 hrs 30 min.

The photolysate was worked up in the usual manner. The neutral extract (an oil, 317 mg) on standing deposited an unidentified crystalline solid 25 (40 mg); m.p.164°(dec., started to turn brown above 130°); ir 3160 (b), 2720, 1420, 990, 970 (s), 950 cm^{-1}; nmr (pyridine) τ8.0(s); (acetone) τ2.4(s); ms m/e (%) 89(5.8) 88(92), 71(21), 70(53), 58(30), 57(5.8), 44(62), 43(100), 41(19), 30(26), 28(81), and 27(39). The

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* The author wished to thank Dr. K.R. Kopecky, the Department of chemistry, the University of Alberta, Edmonton, for providing the decoupling experiment with a Varian HA-100 spectrometer, and for the MS-9 mass spectrum of 26, 27 and 28.

residue (261 mg) after removal of 25 was chromatographed on a silicic acid column to yield the starting nitrosamine (204 mg, chloroform eluent) and 25 (41 mg, 2-5% CH_3OH in $CHCl_3$ eluent).

The basic extract was distilled and the distillate was analyzed by v.p.c. (10% XF-1150 on Aeropak 30, 5' x 1/8") from which t-butylamine (retention time 1'14",110°) was identified by a mixed injection with an authentic sample. No other peaks were observed. The residue of the basic extract (373 mg) was chromatographed on silicic acid to afford the following fractions.

(i) An impure fraction (68 mg, fractions 1-3, chloroform eluent) which showed ir peaks at 3320 (b,s), 3060 (w), 2760 (w), 1670(vs), 1530 (m), 760 cm^{-1}. Separation by preparative tlc gave 5 (17 mg) and a fraction (13 mg) which showed similar ir as that described above.

(ii) Fraction 4 (49 mg, chloroform eluent) was identified as 5 by its superimposable ir spectrum. The total recovery of 5 was 10% (270 mg).

(iii) An unknown compound (Fractions 9-10, 40 mg, chloroform eluent), ir(neat), 3360 (b,s.), 1640 (s), 970 - 1100 (b,s); nmr τ1.7 (b,d), 4.74 (b,m), 6.45 (b,m), 8.67 (s). An attempted separation

of this fraction by preparative tlc was not successful.

The basic aqueous mother liquor continuously was extracted with methylene chloride for 48 hrs. Removal of solvent gave crystalline 2-t-butylaminoethanol (282 mg, 15%).

6.6.8 Photolysis of N-nitroso-N-n-butylethanolamine (9)

A sloution of 9 (4.22 g, 0.029 mole) and hydrochloric acid (5 ml, 0.06 mole) in methanol was photolysed in Type 11 apparatus for 7 hrs. The u.v. spectrum of the solution above 300 nm was constant after irradiation for 5 hrs. With 250 time dilution, however, the solution showed that absorption below 300 nm continued to decrease. The light yellow photolysate was neutralized with sodium carbonate to pH 6-7 and the solvent was removed. A portion (100 ml) of the trapped distillate (250 ml) was treated with Brady's reagent to yield 2,4-DNPH of n-butyraldehyde (366 mg): mp 119-121° (lit. m.p. 123°) (113). The overall yield of 2,4-DNPH of n-butyraldehyde was 12.6% (915 mg).

The residue of the photolysate was extracted successively at pH 1 (with ether), 9, and 13 (with

methylene chloride) and worked up in the usual manner to afford the neutral extract and two basic extracts.

Crystallization of the extract at pH 1 (101 mg) from chloroform afforded a crystalline solid, unknown 31 (10 mg): m.p. 166-170° (sinters above 140°): ir 3130 (diffused), 2720 942 970 952 677 and 655 cm^{-1}; nmr (D_2O) τ7.2, 8.3 and 9.3 (all diffused and weak signals), 2.25 sharp s); ms m/e (%) 89 (M^+, 5.8), 88 (58), 71 (16), 70 (42), 52 (47), 44(53), 43 (74), 40 (58), 30 (26), 28 (100), 27 (90), 18 (69). Chromatography of the residue after removal of 31 gave no isolable product.

The first basic extract was an oil (527 mg) which gave no separation upon chromatography on a silicic acid column. The solvent of the second basic extract (pH 13) was trapped in a dry ice-methanol bath. The oily residue (584 mg, 18.5%) showed ir(neat) absorption at 3300 (b,s), 1650 (w), 1120, 1060 (s), 735 (m)*. Its ir and tlc mobility indicated the oily liquid

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* cf. Authentic parent amine of 9; ir(neat) 3280 (b), ca. 1600 (diffused), 1405 (w), 1120, 1060 (s), 730 (w) cm^{-1}.

to be mainly N-n-butylethanolamine. A half of the trapped solvent (140 ml) was treated with picric acid (606 mg) in methanol. The third crop (55 mg), following two crops of picric acid was yellow needles and was found to possess the identical ir spectrum with an authentic sample of the picrate of n-butylamine: m.p. 144-145°, (lit. m.p. 151°) (114). The total yield of n-butylamine was 1.3%.

PART 11. Flash Photolysis

6.7 General Procedure

Unless specified otherwise, the following conditions prevail in all the experiments.

1. The flash solutions were degassed by the conventional freeze-pump-thaw technique repeated four times; the degassing vessel was shown in Fig. 6.3. When carefully degassed and properly sealed off, the air pressure inside the sample solution was less than 0.001 mm of mercury. Apiezon N grease was used on all stopcocks

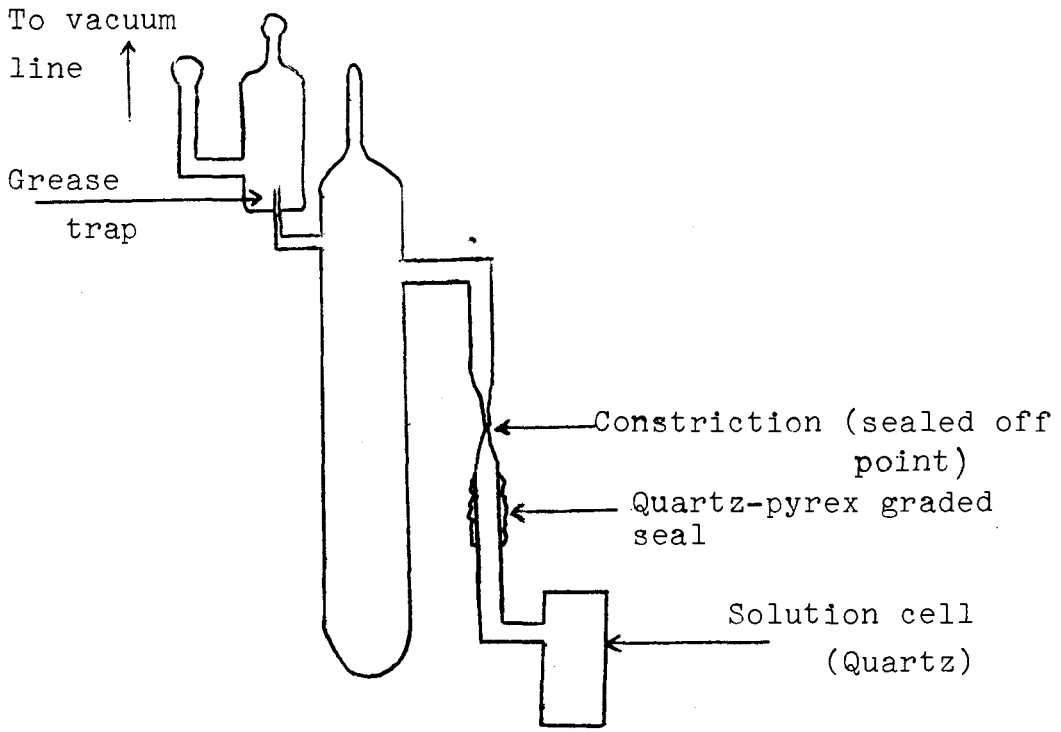


Fig. 6.3 Degassing Reservoir

and ground joints. The degassing reservoir had a grease trap which prevented grease from getting into the reservoir.

2. The quartz solution cell was 10 cm long, 22 mm in outer diameter, and had a capacity of about 35 ml. For degassing it was connected to a pyrex vessel by means of a graded seal (Fig. 6.3).

3. The absorption characteristics of the various filters and filter solutions were as shown in Table 6-1 and Fig. 6.2.

4. The solution was irradiated at all wavelengths above 200 nm unless specified otherwise. At the concentration (10^{-4}M) of the nitrosamine employed, irradiation was mainly in the $\pi \rightarrow \pi^*$ transition band since light absorption by the $n \rightarrow \pi^*$ transition band of the nitrosamine was negligible $\varepsilon_{230}/\varepsilon_{350}$ ca. 50-100, see Table 2-3).

5. To prepare the solution for degassing, a stock solution (ca. 10^{-2}M) was prepared by dissolving a certain weighed amount of the nitrosamine in methanol or water to form a 50 or 100 ml solution; an aliquot of the solution was then pipetted out and diluted with solvent to the desired concentration. The concentration of the prepared solution was checked by u.v. spectrum and in no case was the observed deviation being greater than 5%. Other solutions were prepared in a similar manner.

6. The concentration of the nitrosamine was monitored before and between flashes by u.v. absorption measurements using a Bausch and Lomb (single beam double grating spectrophotometer. The spectrum of the solution after flashing was usually recorded with a Cary 14 double beam u.v. spectrophotometer (using 1 cm cell) and served as a check for any abnormality due to default in degassing.

6.8 Materials

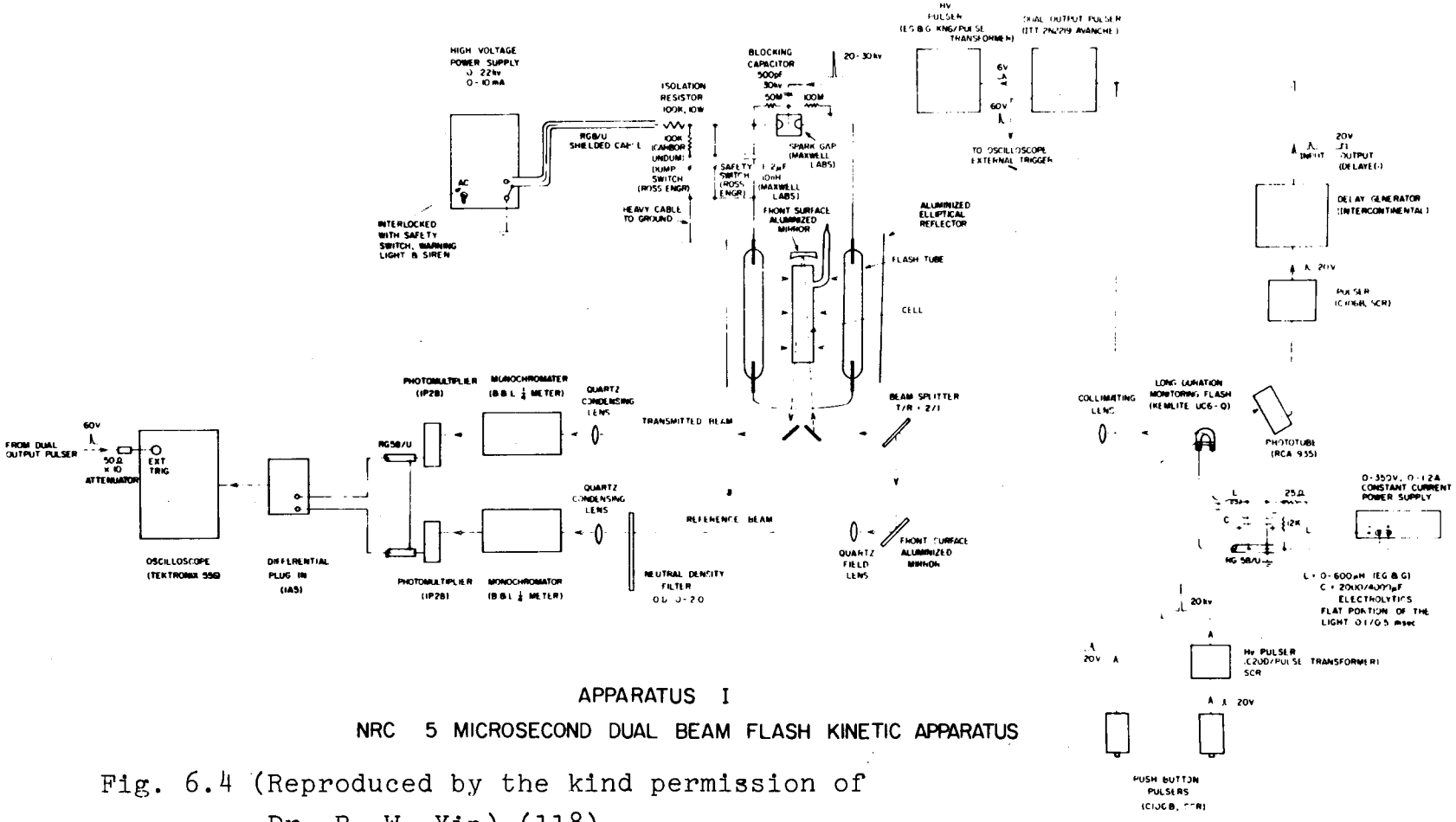
Reagent grade N-nitrosopiperidine and N-nitrosodimethylamine were vacuum distilled before use. N-nitroso-N-methylaniline was distilled with a spinning band apparatus (Nester Faust Inc.). N-nitrosodibenzylamine was recrystallized once from n-hexane. Concentrated hydrochloric acid (C.P. grade) was used without further purification. Naphthalene (Koch-Light Laboratories) was zone-refined and was used without further purification. 2,2'-Binaphthyl was sublimed once (190-200^{o}/0.1 mm) and recrystallized three times from spectrograde chloroform before use: m.p. 187-8^{o} (lit. 187-8^{o}) (115). Cyclohexene was either prepared by dehydration of cyclohexanol with 85% phosphoric acid or the reagent grade olefin purified by refluxing with maleic anhydride overnight. Both material from above were purified by distillation and filtered through Woelm neutral alumina immediately before use. Biacetyl was purified by distillation, the middle cut

fraction was used: b.p. 89° (lit. b.p. 89-90°) (115). All solvents were of spectrograde. Fluorescence grade methanol was used for emission study. Water was doubly-distilled.

All starting materials except N-nitrosodibenzylamine and 2,2´-binaphtyl were analyzed for purity by v.p.c. (5% SE30 on chr. W, 6' x 1/8") and in no case was the impurity greater than 0.5% detected. Both nitrosamine 3 and 2,2´-binaphthyl gave one spot on the tlc analysis and satisfactory u.v. spectrum. The u.v. data of 3 was as shown in Table 2-3. 2,2´-Binaphthyl had λ_{max} (CH_3OH) (log ε), 305 nm (4.28); 254 nm (4.99) (lit. λ_{max} (EtoH) (log ε), 305 nm (4.2) and 255 nm (5.0)) (116). Biacetyl had λ_{max} (CH_3OH) (ε), 415 nm (5.9); 288 nm (27.2) (lit. λ_{max}(EtoH) (ε) 285.5 nm (25.4) and 416 nm (8.37)) (117).

6.9 The Flash Apparatus

The 5 μsec flash apparatus with dual beam was as described earlier by Yip (118), a schematic diagram of which is reproduced in Fig. 6.4. The monitoring source was a 150 joule xenon arc lamp. Two monochromators which selected the analyzing wavelength were used in conjunction with an 1P 28 Type 6 stage photomultiplier, the output of which was displayed on an oscilloscope and photographed by a Polaroid Camera. The flash energy was usually in the



APPARATUS I

NRC 5 MICROSECOND DUAL BEAM FLASH KINETIC APPARATUS

Fig. 6.4 (Reproduced by the kind permission of Dr. R. W. Yip) (118)

range of 100-200 joules which gave a light output, as detected in the reaction vessel, of $\sim 10^{16} - 10^{18}$ quanta per flash.

In the latter phase of this work, modifications of the instrument improved the flash duration to ca. 1.1 μsecs (1/3 of the peak value) (64), resulting in better accuracy in analyzing the data.

6.10 Treatment of Data

The transient decay recorded in the photographic trace was analyzed in a manner similar to that described by Porter (119). Sufficiently long sweep times were used to allow unambiguous definition of the baseline from the transient trace alone. The observed transient trace was measured from the baseline. In general, data were taken to at least 2 half-lives of the transient. For each sample, at least 6 traces were taken and the results averaged. A sketch of such a trace was shown in Fig. 6.5. The sequence of the operations was normally as follows:

1. The scan was triggered with both beam light off;
2. The scan was triggered with the reflected beam light on only;
3. The scan was triggered with the baseline slightly shifted up and the sensitivity increased 10 x or 20 x;

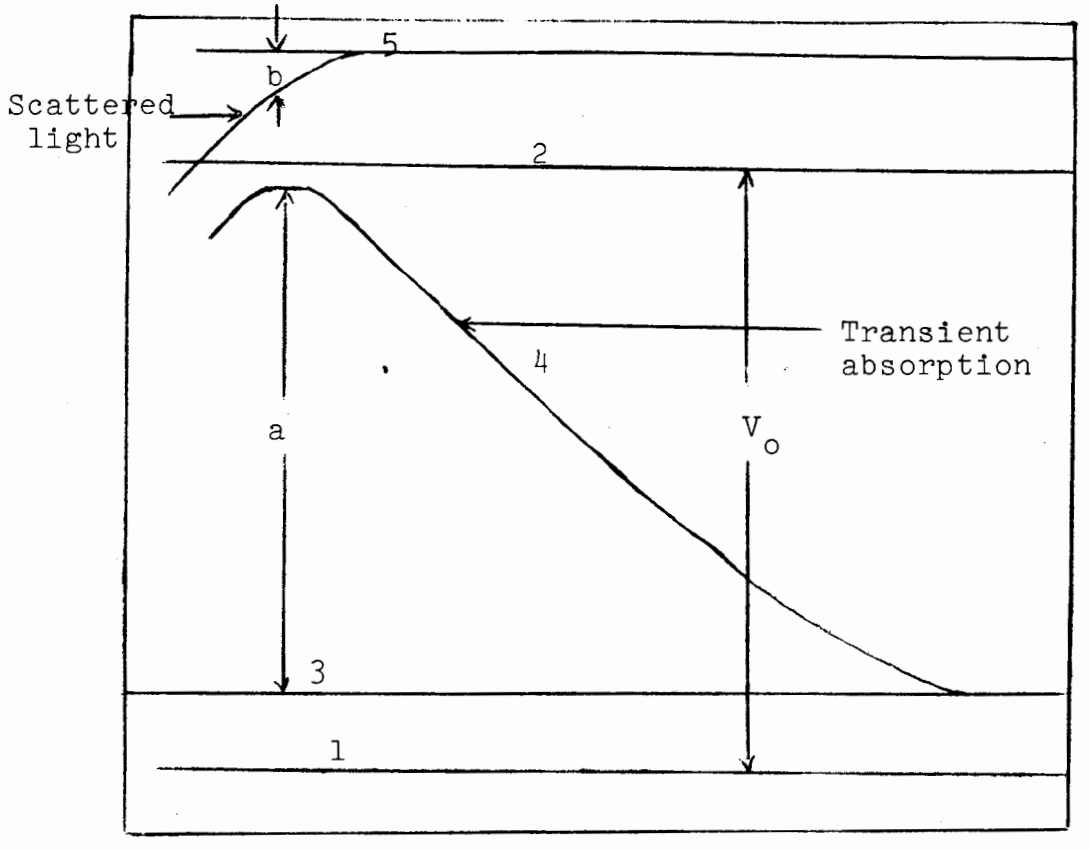


Fig. 6.5 Record of Oscillograph Trace

4. The photolysis flash was triggered and the absorption by the transient was recorded.
5. The scattered light from the photolysis flash was recorded with the monitoring light off.

These steps were designated as 1,2,3,4 and 5 in Fig. 6.5.

The oscilloscope response was proportional to the light intensity with

I_o = k ("light on" deflection - "light-off" deflection

= kv_o.

I = k ("transient" deflection - "light-off" deflection) = kv = k(a + b ± c)

where v_o = light output before flash

v = light output after flash

k = a constant

a = absorption due to transient

b = correction due to scattered light

c = base-line correction, in the ideal case shown, c = o.

From Lambert and Beer's laws,

Optical density (O.D.) of transient absorption = $\log \frac{I_o}{I}$

$$= \log \frac{kv_o}{kv} = \log \frac{v_o}{v}$$

For first-order kinetics, (62),

$$2.303 \log (O.D.) = -k_{obs} t + \text{Constant} \qquad \{1\}$$

A plot of log (O.D.) vs. time should give a straight line for a first-order decay according to eq. {1}. Similarly, a plot of 1/O.D. vs time should be linear for a simple second order reaction.

The symbols $(O.D.)_o$, $(O.D.)_{10}$, k_{obs} and τ designate the optical density at zero time (i.e. initial optical density), optical density at 10 μsec, the observed first-order decay rate constant and the lifetime of the transient species. According to eq. {1} and

$$k_{obs} = 2.303X \text{ slope of the plot} \quad \{2\}$$

by setting t=o, (O.D.) = $(O.D.)_o$, t = τ, O.D. = $\frac{(O.D.)_o}{e}$ (by definition). The lifetime of the transient τ, is related to k_{obs} by eq. {3} for first-order kinetics.

$$\tau = \frac{1}{k_{obs}} \quad \{3\}$$

From eqs. {2} and {3}, τ can be determined from the first-order kinetic plotting according to eq. {4}.

$$\tau = \frac{1}{2.303 \text{ slope of plot}} \quad \{4\}$$

$(O.D.)_o$ can be obtained by extrapolation of the first-order kinetic plot (see Fig. 3.2) to zero time. The antilog of the intercept gave $(O.D.)_o$. The value so obtained is a measure of the statistical distribution of the whole set of points. As can be seen from eq. {4}, the slope of the plot is dependent on the lifetime of the transient species; for very short-lived transients (of the order of 10 μsec.), a slight variation in τ can cause an appreciable error in the slope of the plot and hence in the value of $(O.D.)_o$. In this case, $(O.D.)_{10}$ is more accurate since this is a parameter directly measurable by experiment and is independent of τ.

In the second phase of this work, analysis of data

was facilitated by the use of a computer program*. Data taken from the Polaroid photographs were processed using an IBM 360/50 computer from which best value rate were obtained. The decay kinetics were plotted on an X-Y recorder linked to the output of the computer. The linear plot was equivalent to the plotting by the least square method (72). The program included the parameter, R, which was the correlation of linearity. A plot with $R \geqslant 0.990$ was generally acceptable within experimental error.

6.11 Quantum Yield Measurements

The quantum yield was determined with a split-beam irradiation apparatus described earlier by Tam (61), it will therefore not be elaborated here. The light source was a PEK #202 200W high pressure mercury arc. Isolation of the 366 nm mercury resonance line was achieved with a Corning glass filter CS 7-60 (#5840).

6.12 Emission Study

Emission study was carried out in a spectrofluorometer as shown in Fig. 6.6. The light source was a high pressure 150W Hanovia Xenon compact arc with a Farrand

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* The author wishes to thank Dr. A.G. Szabo of Radiation Biology, National Research Council, Ottawa, for permission to use his program.

grating monochromator for excitation. The apparatus employed a right-angle arrangement. A Jarrell-Ash 82-410 monochromator with an EMI 6256A photomultiplier tube which could supply a maximum of 1500 volts was used as the detecting system. To measure the complete emission spectra, the emission monochromator was electrically operated and its driving motor was coupled with the photomultiplier output and an XY (HP 7101B) recorder. For low temperature emission of nitrosamines, the cyclindrical quartz specimen tube (o.d. ca. 8 mm) was fitted into a Dewar flash containing liquid nitrogen. The lower part of the Dewar flash was an unsilvered quartz vacuum flask. For fluorescence quenching studies, the cylindrical tube

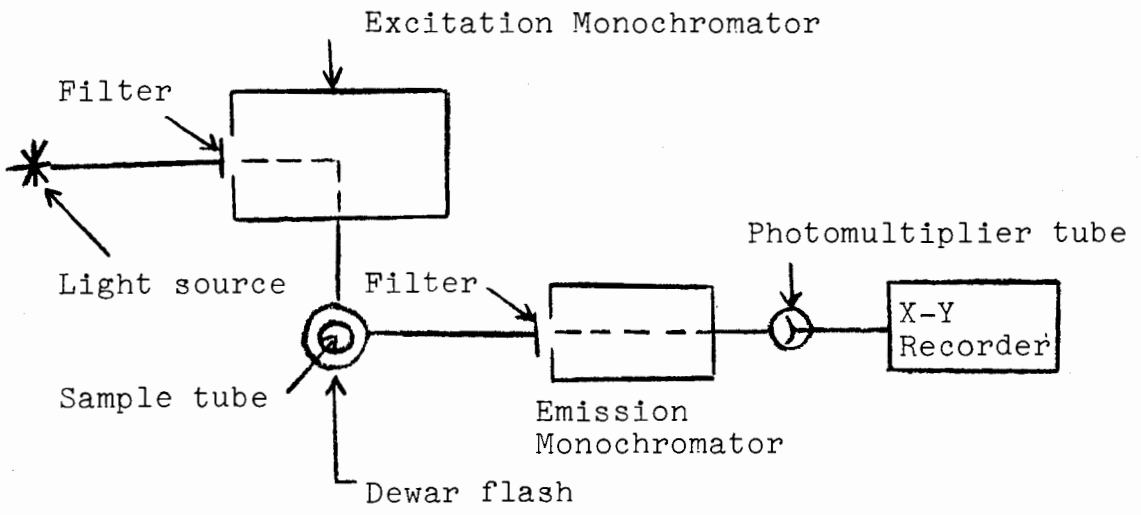


Fig. 6.6 Emission Apparatus

was replaced by quartz rectangular cells (optical path 10 mm) fitted into a cuvet housing which was linked directly to the emission monochromator. The sample was run at ambient temperature.

REFERENCES

1. C.H. Bamford, J. Chem. Soc., 12 (1939).
2. Y.L. Chow, Tetrahedron Letters, 2333 (1964).
3. E.M. Burgess and J.M. Lavanish, Tetrahedron Letters, 1221 (1964).
4. Y.L. Chow, C. Colon and S.C. Chen, J. Org. Chem., 32, 2109 (1967).
5. Y.L. Chow, Can. J. Chem., 43, 2711 (1965).
6. Y.L. Chow, S.C. Chen and D.W.L. Chang, Can. J. Chem., 48, 157 (1970).
7. Y.L. Chow , Can. J. Chem., 45, 53 (1967).
8. Y.L. Chow and C.J. Colon, Can. J. Chem., 45, 2559 (1967).
9. Y.L. Chow, Tetrahedron Letters, 2473 (1965).
10. Y.L. Chow, J. Am. Chem. Soc., 87, 4642 (1965).
11. T. Axenrod and G.W.A. Milne, Tetrahedron, 24, 5775 (1968).
12. T. Axenrod and G.W.A. Milne, Tetrahedron Letters, 4443 (1967).
13 W.B. Watkins and R.N. Seelye, Can. J. Chem., 47, 497 (1969).
14. J.M. Lavanish, Ph. D. Thesis, Yale University (1966).
15. C.J. Colon, Ph. D. Thesis, Simon Fraser University (1970).

16. S.C. Chen, Ph. D. Thesis, Simon Fraser University (1970)..

17. D.W.L. Chang, M. Sc. Thesis, Simon Fraser University (1970)..

18. E. H. White and C.A. Aufdermarsh, J. Am. Chem. Soc., 83, 1174, 1179 (1961).

19. Y.L. Chow and A.C.H. Lee, Chem. and Ind., 827 (1967); Y.L. Chow, N.S. Tam and A.C.H. Lee, Can. J. Chem., 47, 2441 (1969).

20. O.E. Edwards and R.S. Rosich, Can. J. Chem., 45, 1287 (1965); L.P. Kuhn, G.G. Kleinspehn and A.C. Duckworth, J. Am. Chem. Soc., 89, 3858 (1967).

21. R.S. Neale and M.R. Walsh, J. Am. Chem. Soc., 87, 1255 (1965).

22. M.E. Wolff, Chem. Rev., 63, 55 (1966).

23. E.J. Corey and W.R. Hertler, J. Am. Chem. Soc., 82, 1657 (1960).

24. J. Spanswick and K.U. Ingold, Can. J. Chem., 48 546 (1970); ibid., 48, 554 (1970).

25. R.S. Neale and R.L. Hinman, J. Am. Chem. Soc., 85, 2666 (1963); R.S. Neale, Tetrahedron Letters, 483 (1966).

26. R.S. Neale, J. Org. Chem., 32, 3263 (1967); R.S. Neale and N.L. Marcus, J. Org. Chem., 32, 3273 (1967).

27. F. Minisci, R. Galli and M. Cecere, Tetrahedron Letters, 3163 (1966).

28. G. Adam and K. Schrieber, Tetrahedron Letters, 3591 (1966).

29. D.V. Banthorpe and J.A. Thomas, J. Chem. Soc., 7158 (1965).

30. W. Rickatson and T.S. Stevens, J. Chem. Soc., 3960 (1963).

31. W.N. White, J.R. Klink, D. Lazdins, C. Hathaway, J.T. Golden and H.S. White, J. Am. Chem. Soc., 83, 2024 (1961); W.N. White and J.T. Golden, J. Org. Chem., 35, 2759 (1970).

32. J.T. Barnes and W.J. Hickinbottom, J. Chem. Soc., 2616 (1961).

33. P.A.S. Smith, "The Chemistry of Open-Chain Nitrogen Compounds", Vol. 2, W.A. Benjamin, Inc., N.Y. 1966, P. 455.

34. K. Nakanishi, "Infrared Absorption Spectroscopy", Holden-Day, Inc., San Francisco and Nankodo Co. Ltd., Tokyo 1966, P. 50.

35. W.S. Layne, H.H. Jaffe and H. Zimmer, J. Am. Chem. Soc., 85, 435 (1963).

36. M. Kasha, Discuss. Far. Soc., 9, 14 (1950).

37. M. Tanaka, J. Tanaka and S. Nagakura, Bull. Chem. Soc., Japan, 39, 766 (1966).

38. J. Mason and J. Banus, J. Chem. Soc., 3904 (1957); J.W. Sidman, Chem. Rev., 58, 689 (1958).

39. G.J. Karabatsos and R.A. Taller, J. Am. Chem. Soc., 86, 4373 (1964).

40. S.J. Kuhn and J.S. McIntyre, Can. J. Chem. 44, 105 (1966).

41. C.E. Looney, W.D. Philips and E.L. Reilly, J. Am. Chem. Soc., 79, 6136 (1957); Y.L. Chow, Angew. Chem., 79, 51 (1967).

42. T. Axenrod and P.S. Pregosin, Chem. Commun., 702 (1968).

43. A. Mannschreck, H. Münsch and A. Mattheus, Angew Chem. (Intern. Ed.), 5, 728 (1966).

44. P.A.S. Smith and N.W. Kalenda, J. Org. Chem., 23, 1599 (1958).

45. H. Budzikiewicz, C. Djerassi and C.H. Williams, Mass Spectrometry of Organic Compounds, Holden-Day Inc., 1967, P. 313.

46. C. Schöpf and K. Otto, Ber. 89, 335 (1956).

47. S.K. Freeman, "Interpretive Spectroscopy", Reinhold Publishing Corporation, N.Y., 1965, P.216.

48. I. Fleming and D.H. Williams, "Spectroscopic Methods in Organic Chemistry", McGraw-Hill Book Co., 1966, P. 64.

49. Ref. 17; H.H. Quon, private communication.

50. Ref. 15, P. 139.

51. Ref. 48, P. 126.

52. G. Slomp and J.G. Lindberg, Analyt. Chem., 39, 60 (1967).

53. W.D. Emmons, J. Am. Chem. Soc., 79. 5739 (1957).

54. L.F. Fieser, "Experiments in Organic Chemistry", D.C. Heath and Company, 1955, P. 281.

55. J. J. Norman, Can. J. Chem., 40, 2023 (1962).

56. Ref. 45, P. 297 and ref. 48 Ch. 5.

57. Ref. 45, P. 329; J. Collin, Bull Soc. Roy. Sci. Liegè, 23, 201 (1954); G. Schroll, R.G. Cooks, P. Klemmensen and S.O. Lawesson, Ark. Chem., 28, 413 (1968).

58. "Infrared Spectral Data", American Petroleum Institute Research Project 44, Spectrum No. 462 and 563.

59. J.R.Dyer,"Applications of Absorption Spectroscopy of Organic Compounds", Prentice Hall, Inc., N.Y., 1965, P. 49, 87.

60. Ref. 73, P. 599; G. Porter and M. W. Windsor, Discussions Faraday Soc., 17, 178 (1954); J.P. Simons, Quart. Rev., 13, 3(1959); D.W. Setser, D.W. Placzek, R.J. Cvetanovic and B.S. Rabinovitch, Can. J. Chem., 40, 2179 (1962).

61. J.N.S. Tam, Ph. D. Thesis, Simon Fraser University (1970).

62. M.A. Herbert, J.W. Hunt and H.E. Johns, Biochem. and Biophys. Res. Commun., 33, 643 (1968).

63. The K value was taken from F. Daniels and R.A. Alberty, "Physical Chemistry", John Wiley and Sons, Inc. (2nd Ed.), 1961, P. 154.

64. R. W. Yip, W.D. Riddell and A.G. Szabo, Can. J. Chem., 48, 987 (1970).

65. V. Kasche and Lars Lindquist, J. Phys. Chem., 68, 817 (1964).

66. B. Smaller, J.R. Remko and E.C. Avery, J. Chem. Phys., 48, 5174 (1968).

67. Y.L. Chow, A. Cessna and R.W. Yip, unpublished observation.

68. C.J. Colon, private communication.

69. G. Porter, Science, 160, 1299 (1968).

70. G. Porter and F. Wilkinson, Proc. Roy. Soc., 264A, 1 (1961).

71. G. Porter and M.W. Windsor, Proc. Roy. Soc., 245A, 238 (1958).

72. F. Daniels, J.H. Mathews, J.W. Williams, P. Bender and R.A. Alberty, "Experimental Physical Chemistry", McGraw-Hill, 1956, P. 339.

73. J.G. Calvert and J.N. Pitts, Jr., "Photochemistry", John Wiley and Sons, Inc., 1967, P. 627.

74. J. Heicklen and N. Cohen in "Advances in Photochemistry", Vol. 5, Interscience Publishers, 1968, P. 55.

75. L. M. Stephenson and G.S. Hammond in "Organic Photochemistry", Vol. 2 (I.U.P.A.C.), 1967, P. 127.

76. I.B. Berlman, "Handbook of fluorescence spectra of aromatic molecules", Academic Press, N.Y., 1965, P. 104.

77. W.G. Herkstroeter and G.S. Hammond, J. Am. Chem. Soc., 88, 4769 (1966).

78. K. Sandros, Acta Chem. Scand., 18, 2355 (1964).

79. K. Sandros and H.L.J. Backstrom, Acta. Chem. Scand., 16, 958 (1962).

80. M.Z. Hoffman and G. Porter, Proc. Roy. Soc., 268A, 46 (1962).

81. B.L. Van Durren, Anal. Chem., 32, 1436 (1960).

82. (a). J.A. Bell and H. Linschitz, J. Am. Chem. Soc., 85, 528 (1963); (b). W.M. Moore, G.S. Hammond and R.P. Foss, J. Am. Chem. Soc., 83, 2789 (1961).

83. N.J. Turro, "Molecular Photochemistry", W.A. Benjamin Inc., 1965, N.Y., P. 54, P. 93.

84. H.H. Jaffè and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy", John Wiley and Sons, Inc., 1962, P. 541.

85. R.W. Yip, private communication.

86. Ref. 83, Ch. 4; C.A. Parker, "Photoluminescence of Solutions", Elsevier, Amsterdam, 1968, P. 72.

87. Y.L. Chow and M.M. Feser, Chem. Commun., 239 (1967).

88. R. Perry, private communication.

89. C.G. Hatchard and C.A. Parker, Proc. Roy. Soc., 235A, 518 (1956).

90. Ref. 73, P. 786.

91. J.N.S. Tam, private communication.

92. C.A. Parker and C.G. Hatchard, The Analyst, 87, 664 (1962); ref. 84, P. 544.

93. J.T. Dubois and R.L. Van Hemert, J. Chem. Phys., 40, 923 (1964).

94. L. Land and G. Porter, Trans. Far. Soc., 59, 2027 (1963).

95. W.S. Layne, H.H. Jaffè and H. Zimmer, J. Am. Chem. Soc., 85, 1816 (1963).

96. A. Schmidpeter, Tetrahedron Letters, 1421 (1963).

97. M. Akhtar and M.M. Pechet, J. Am. Chem. Soc., 86, 265 (1964).

98. J.N. Pitts, Jr., R.L. Letsinger, R.P. Taylor, J.M. Patterson, G. Reckterwald and R.B. Martin, J. Am. Chem. Soc., 81, 1068 (1959); K.R. Kopecky, G.S. Hammond, P.A. Leermakers, J. Am. Chem. Soc., 84, 1015 (1962); ref. 82 (b).

99. Ref. 74, P. 175.

100. J. Meinwald, Y.C. Meinwald and T.N. Baker, III, J. Am. Chem. Soc., 86, 4074 (1964).

101. J. Tanka, Nippon Kagaku Zasshi, 78, 1647 (1957).

102. E.F. Ullman, E. Babad and M. Sung, J. Am. Chem. Soc., 91, 5792 (1969); N. Baumann, M. Sung and E.F. Ullman, ibid., 90, 4157, 4158 (1968); E.F. Ullman and B. Singh, ibid., 88, 1844 (1966); 89, 6911 (1967).

103. N.C. Yang, M. Nussim, M.J. Jorgensen and S. Murov., Tetrahedron Letters, 3657 (1964).

104. R.C. Helgeson and D.J. Cram, J. Am. Chem. Soc., 88. 509 (1966).

105. K.D. Anderson, C.J. Crumpter and D.L. Hammick, J. Chem. Soc., 1679 (1935); Ref. 73, P. 476; J.W. Kraus and J.G. Calvert, J. Am. Chem. Soc., 79, 5921 (1957).

106. R. Hurley and A.C. Testa, J. Am. Chem. Soc., 89 6917 (1967).

107. Ref. 54, P. 283.

108. R.L. Schriner, R.C. Fuson and D.Y. Curtin, "The Systematic Identification of Organic Compounds", John-Wiley and Sons Inc., 1965, P. 262.

109. "H. Druckney, R. Preussmann, S. Ivankovic and D. Schmaehl, Z Krebsforsch., 69, 103-201(1967)" cited in C.A. 67, 32277v (1967).

110. Ref. 54, P. 299.

111. B.G. Gowenlock and W. Luttke, Quart. Rev. (London), 12, 321 (1958).

112. H.T. Openshaw, "A Laboratory Manual of Qualitative Organic Analysis", Cambridge University press, 1959, P. 46.

113. Ref. 112, P. 49.

114. Tables for identification of Organic Compounds, 1964, P. 213-4, 219.

115. Handbook of Chemistry and Physics, The Chemical Rubber Co., 48th ed., 1967, P.C-207, C-221.

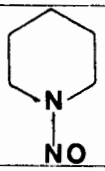
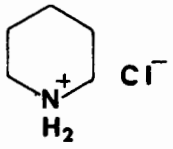
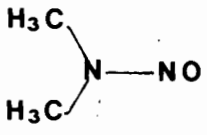
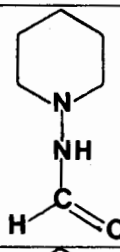
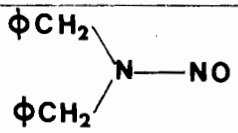
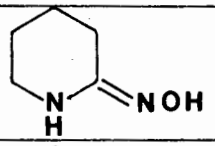
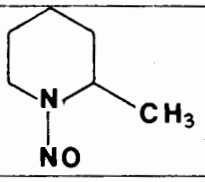
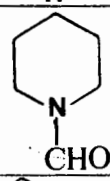
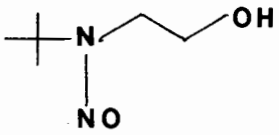
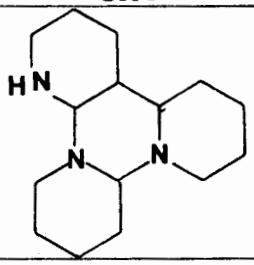
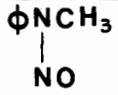
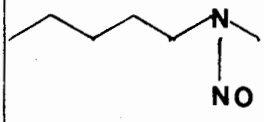
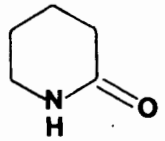
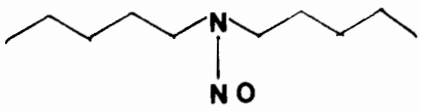
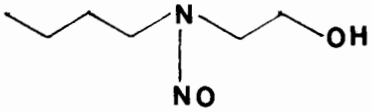
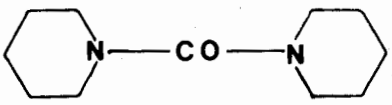
116. V.L. Frampton, J.D. Edwards, Jr., and H.R. Henze, J. Am. Chem. Soc., 70, 2284 (1948).

117. Photosentiser and Quencher Kit, J.T. Baker Chem. Co. Ltd., N.J. (1967).

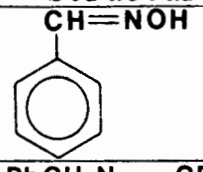
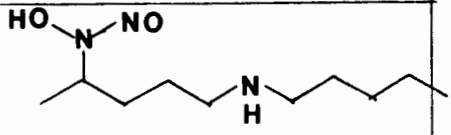
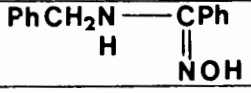
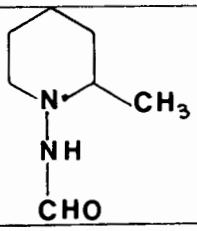
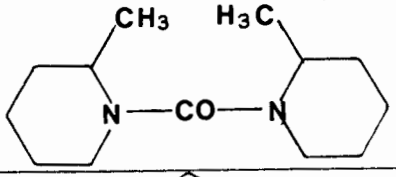
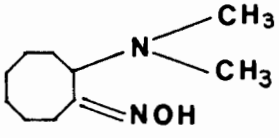
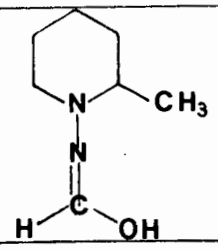
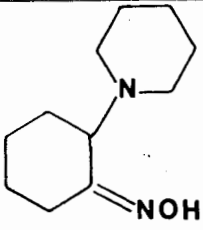
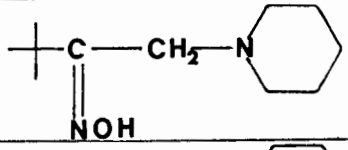
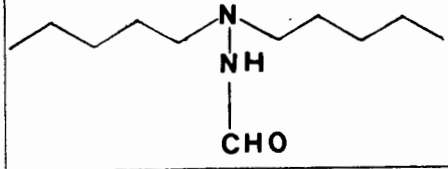
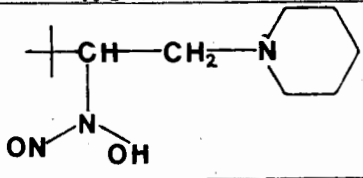
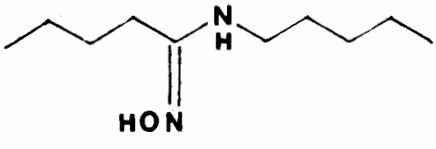
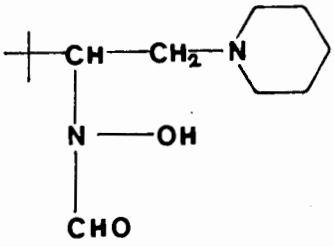
118. R.W. Yip, Rev. Sci. Instruments, 40, 1035 (1969).

119. G. Porter in "Techniques in Organic Chemistry", Vol. 8 (Part 2), Interscience, N.Y., 1963, P. 1055.

Appendix 1
List of structures for compounds

Compound	Structure	Compound	Structure
1		10	
2		11	
3		12	
4		13	
5		14	
6		15 [a]	-
7		16	
8		17 [b]	-
9		18 [c]	

a. Trimer salt, not confirmed; b. Unknown; c. not confirmed.

Compound	Structure	Compound	Structure
19		28	
20		29 [b]	–
21 [b]	–	30 [b]	–
22		31 [b]	–
23 [c]		32	
24 [c]		33	
25 [b]	–	34	
26		35	
27		36	

Appendix 11

An estimation of the error in the k_r value determined is as follows:

Let $A'_o = A_o \pm \Delta A_o$

$$A' = A \pm \Delta A$$

Where ΔA_o and ΔA represent the uncertainty (i.e. deviation) in A_o and A respectively.

Assuming $\Delta A_o = 0.5A_o$

$$\Delta A = 0.5A$$

then $$\frac{A'_o}{A'} = \frac{A_o \pm \Delta A_o}{A \pm \Delta A}$$

If P_1 stands for the maximum uncertainty in A_o/A, then

$$\frac{A_o}{A} \times P_1 = \frac{A_o + \Delta A_o}{A - \Delta A} = \frac{A_o + 0.5A_o}{A - 0.5A}$$

$$= 3\frac{A_o}{A}$$

i.e. $P_1 = 3$

The expression $\frac{A_o - \Delta A_o}{A + \Delta A}$ gives the same uncertainty in $\frac{A_o}{A}$.

The uncertainty in the slope of the plot (P_2) estimated from Figs. 3.13 and 3.14 is <1.25 (i.e. about 25% deviation).

Assuming a 50% deviation in the estimation of ϕ_F, then the uncertainty in $\phi_F(P_3)$ is given by $P_3 = 1.5$.

The factors P_1, P_2, and P_3 apparently determine the uncertainty in k_r. Since these factors are independent of each other, they are multiplicative in nature. Consequently, the uncertainty in $k_r(P)$ can be represented by

$$P = P_1 \times P_2 \times P_3$$

$$= 3 \times 1.25 \times 1.5$$

$$= 5.6$$

The numerical value determined for k_r is given by

$$k_r = 3.2 \times 10^{11}\ M^{-1}S^{-1}$$

Allowing for the uncertainty factor, P.

$$k_r' = \frac{k_r}{P} = \frac{3.2 \times 10^{11}}{5.6}$$

$$= 5.7 \times 10^{10}\ M^{-1}S^{-1} \text{ (lower limit)}$$

The value of k_r obtained in this case, i.e. k'_r, is still considerably greater than the diffusion controlled rate constant.