A STUDY OF N-NITROSAMINE PHOTOADDITION

by

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ABSTRACT

The photoaddition of N-nitrosamines to simple olefins gave normal photolysis products, namely syn- and anti-oximes of α-aminoalkanones. The photoaddition of N-nitroso-piperidine to 1-hexene at low temperature with light >290 nm gave, in addition to a high yield of syn- and anti-1-piperidino-2-hexanone oximes, the dimer of 1-piperidino-2-nitrosohexane and 1-piperidino-2-(N-nitrosohydroxylamino)-hexane. The photolysis of the dimer in the presence of an excess of N-nitrosopiperidine also gave an N-nitrosohydroxyl-amine derivative. In order to study the stereochemistry of the photoaddition of N-nitrosamines to simple olefins, trans- and cis-2-butenes were chosen as model compounds. The photo-addition to these olefins was carried out either in an excess of N-nitrosopiperidine or in a large excess of olefin. The products were syn- and anti-2-piperidino-3-butanone oximes, the dimer derived from erythro- and threo-2-piperidino-3-nitrosobutanes, and erythro- and threo-2-piperidino-3-(N-nitrosohydroxylamino)-butanes. The isomer ratio of erythro to threo of the last mentioned compound was 4:1 for trans-2-butene and 4:6 for cis-2-butene. From these ratios, it was concluded that the photoaddition is non-stereospecific.

The photoaddition of N-nitrosopiperidine to simple acetylenic compounds, such as phenylacetylene and diphenylacetylene, gave mainly α-diketo monoximes, such as phenylglyoxal ketoxime (65%) and benzil monoxime (61%). In the photoaddition to phenylacetylene in the presence of an excess of N-nitrosopiperidine, however, secondary reaction products such as 2,2-dimethylacetophenone, 2-methoxy-2-piperidinoacetophenone were also obtained in addition to the formation of phenylglyoxal ketoxime. On the other hand, if phenylacetylene was present in excess, two high melting compounds were isolated.

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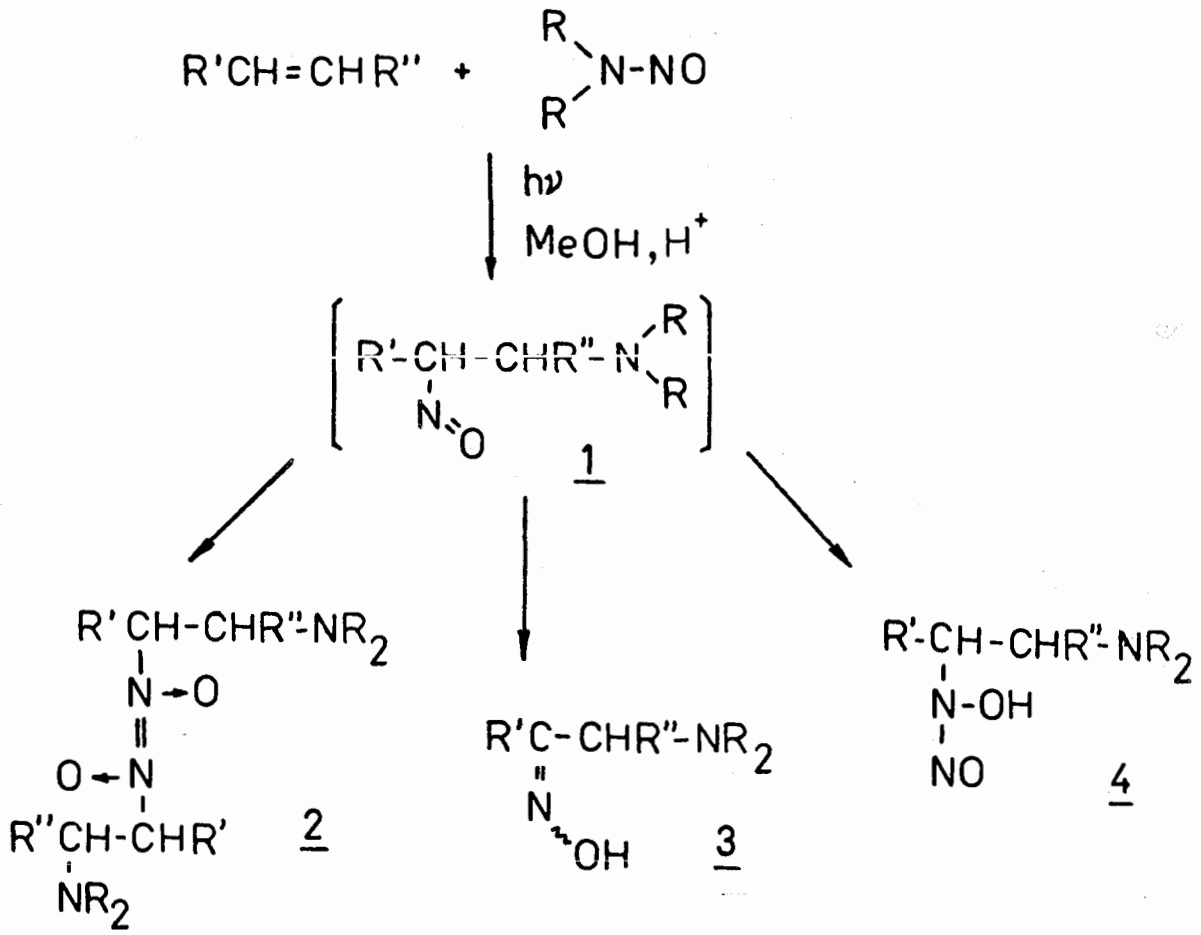
Introduction

Previous work (1,2) from this laboratory has established that the photoaddition of N-nitrosamine to a simple olefin in acidic methanol solution yields a β-aminoxime as the major product (3). The progress of the photoaddition was conveniently followed by recording the decrease in the u.v. absorption of the N-nitrosamine group at 340-350 nm, which remained unchanged unless the solution was irradiated. It was also observed that a new peak at about 290 nm emerged while the 340-350 nm peak decreased. On furthur irradiation of the solution, the new peak at 290 nm gradually disappeared (4).

Based on this information it was concluded that the primary photoadduct was a β-dialkylaminonitrosoalkane (1) which underwent dimerization to a C-nitroso dimer (2) and tautomerization to a β-dialkylaminoketoxime (3). The new peak at 290 nm was assigned to the C-nitroso dimer (2) which was isolated in some cases. The reaction pattern is summarized in Scheme I.

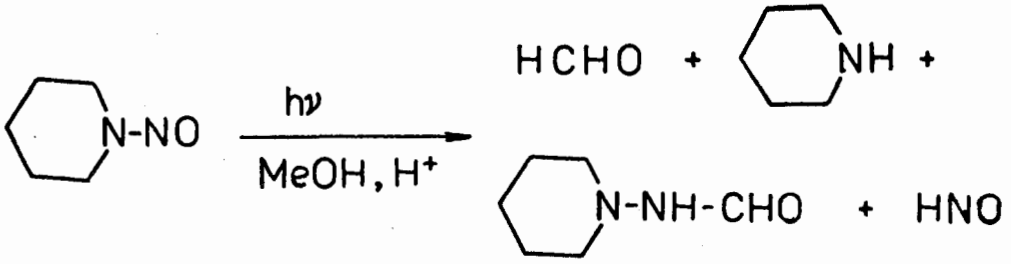
In the absence of an olefin, N-nitrosopiperidine in an acidic methanol solution photolytically decomposed to formaldehyde, piperidine, N-piperidinoformamide and HNO, although the last compound was not isolated (Scheme II) (6). In both photoadditions, the presence of an acid was

Scheme I



a requirement since no photoreaction occured in neutral solution.

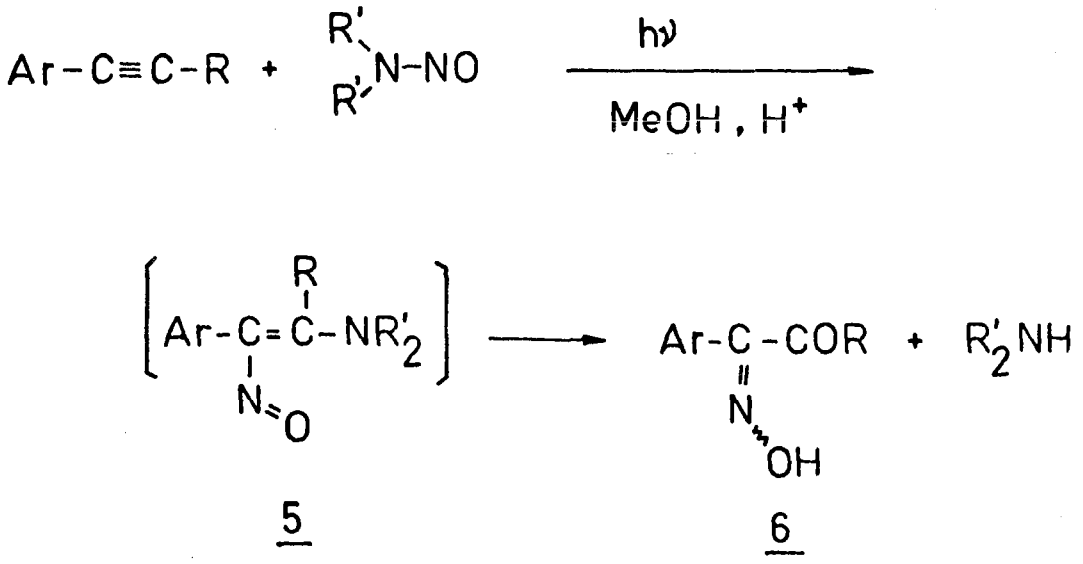
Scheme II



In order to determine the reaction mechanism, the stereospecificity of this photoaddition was investigated.

Since tautomerization of the C-nitroso compound 1 results in a loss of its stereochemistry, it was necessary to find a secondary reaction of 1 in which its configuration could be preserved. This led us to the discovery of the formation of an N-nitrosohydroxylamine derivative 4 under certain conditions. The photoaddition of N-nitrosopiperidine to acetylenic compounds was also studied and the reaction pattern could be interpreted as shown in Scheme III.

Scheme III



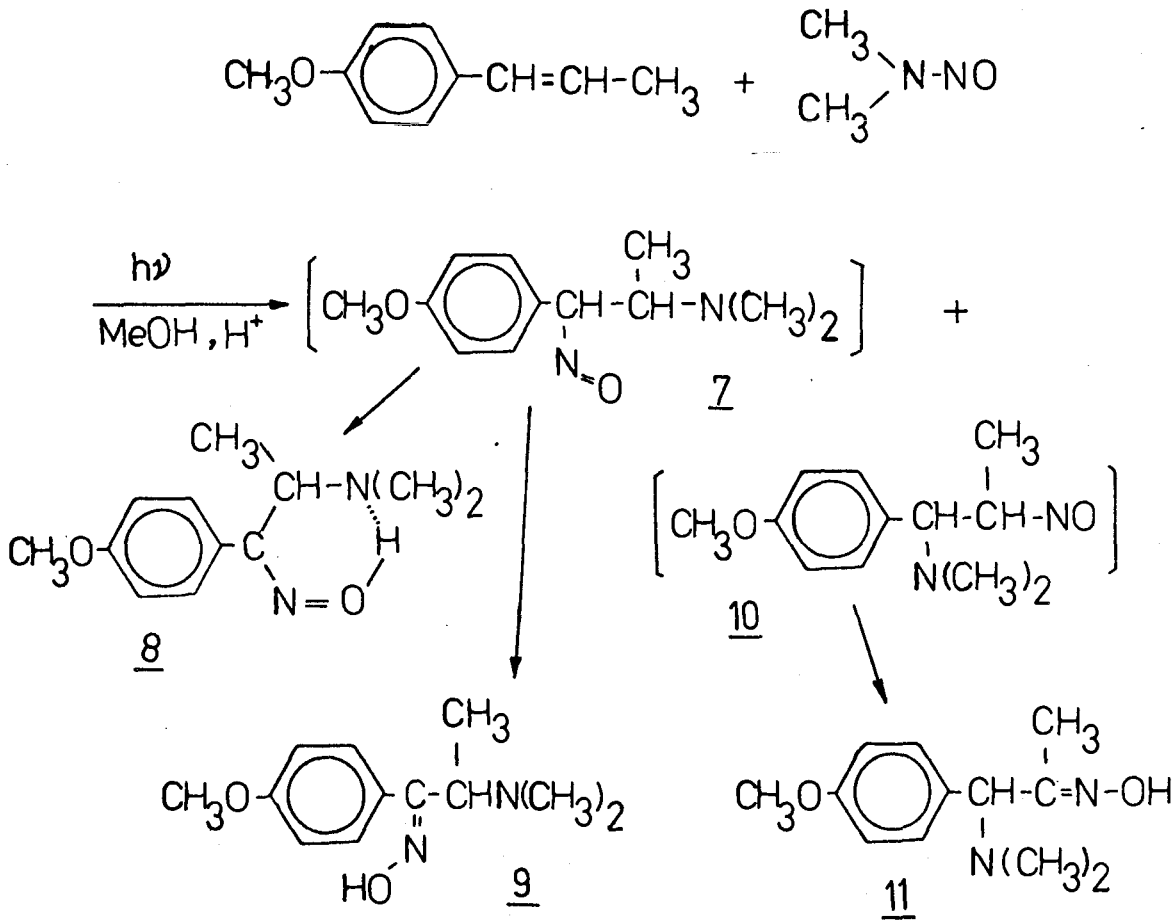
5 6

RESULTS

I. Addition of N-Nitrosodimethylamine to Anethole

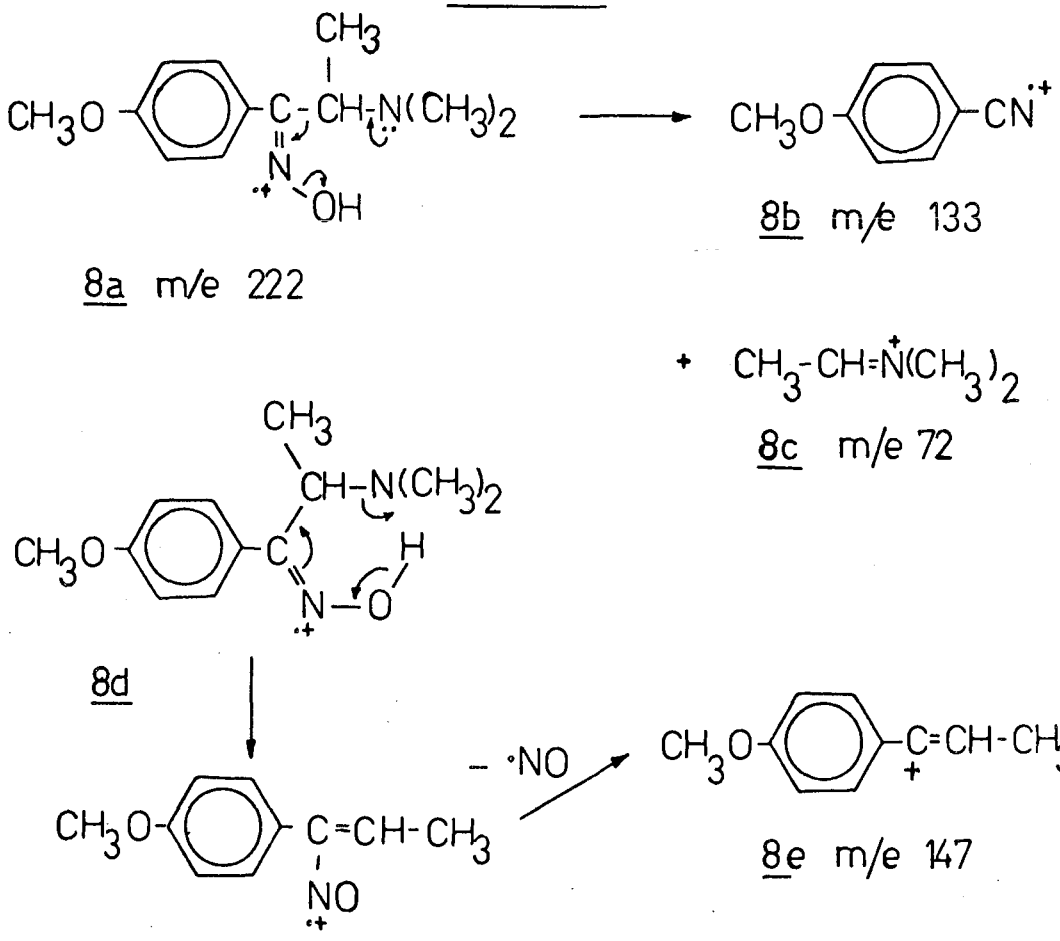
The photoaddition of N-nitrosodimethylamine to anethole proceeded smoothly in the usual fashion to give syn-1-(p-methoxyphenyl)-2-(N,N-dimethylamino)-1-propanone oxime (8, 68%), anti-1-(p-methoxyphenyl)-2-(N,N-dimethylamino)-1-propanone oxime (9, 11%) and a trace of 1-(p-methoxyphenyl)-1-(N,N-dimethylamino)-2-propanone oxime (11) as shown in Scheme IV.

Scheme IV



The elemental analysis as well as the mass spectrum of oxime 8 confirmed the molecular formula ($C_{12}H_{18}N_2O_2$). The i.r. absorptions at 1605, 1512, 926 and 854 cm^{-1} were in agreement with the assigned structure of 8 (7). The n.m.r. spectrum exhibited all the features expected for the structure 8; among them was the doublet (J=7Hz) assignable to the methyl group which was coupled to the quartet of the methine proton (τ 6.45). The mass spectrum of 8 showed major mass peaks that could be rationalized by the fragmentation pattern as shown in Scheme V.

Scheme V



The structure of oxime 9 was confirmed by the spectral data. The n.m.r. spectrum exhibited a quartet at τ6.63 assignable to the methine proton. Since this methine proton appeared at a higher field than that of oxime 8 (τ6.45), oxime 9 should possess the anti-configuration in agreement with the well known long range anisotropic effect of the amino group (8). Further support was gained by comparing the mass spectra of oximes 8 and 9 which were very similar except for the relative intensities, e.g., mass peaks at m/e 205 (20% for 8 and 100% for 9) and 149 (71% for 8 and 8% for 9). These differences might arise from an effect of the intramolecular hydrogen bonding in oxime 8 which is not possible in 9.

Oxime 11 was obtained in only a small amount and showed mass peaks at m/e 222 (M^+) and 205 (M^+-OH). The nmr spectrum contained a singlet at τ8.62 in agreement with the methyl ketoxime.

II. Addition of N-nitrosopiperidine to 1-hexene

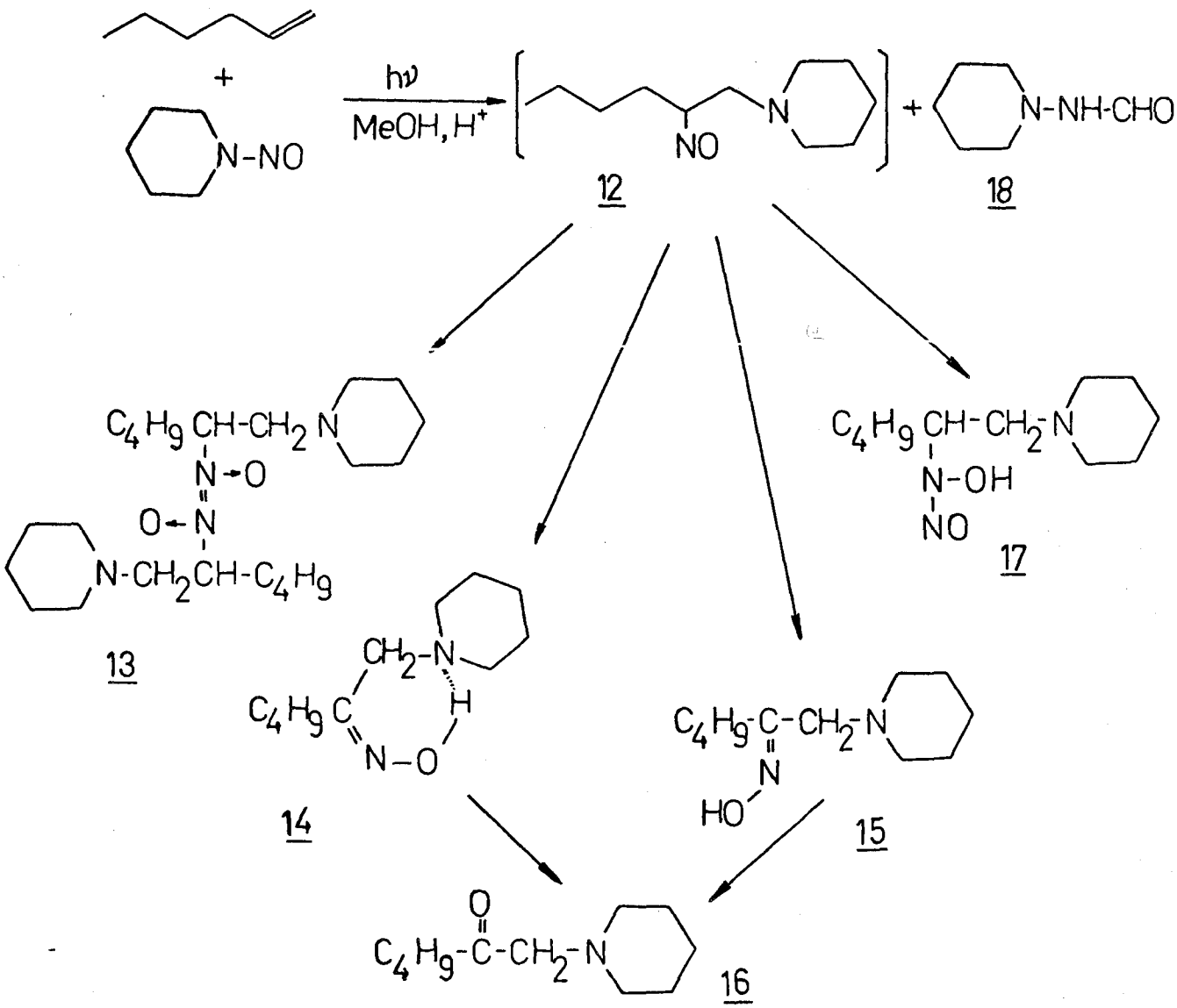
The photoaddition of N-nitrosopiperidine to 1-hexene was carried out under various conditions in order to investigate the secondary product derived from the C-nitroso compound 1. The results are summarized in Table Ia. The progress of this photoaddition was monitored by u.v. spectroscopy. The following information can be elicited from Table Ia.

Table Ia. The Photoaddition of N-Nitrosopiperidine to 1-Hexene

Run	N-nitroso-piperidine (mmoles)	1-hexene (mmoles)	Acidity (N)	Volume (ml)	Irradiation period	% Yield 13	14	15	16	17	18	Notes
1[r]	84	128	0.30	350	3 h 10 min	8	15	34	*	2		a,f,i,o.
2[r]	84	127	0.30	350	2 h 30 min	18	14	36	7			a,f,i,p.
3[r]	84	135	0.24	350	2 h 30 min	14	17	36	*			a,f,j,p.
4[r]	84	132	0.43	200	2 h 30 min	28	5	21	*			a,h,i,p.
5[u]	84	132	0.43	200	2 h 30 min		15	42	*	24		a,h,k,p.
6[u]	93	37	0.44	200	3 h 30 min		*	7	2	47	5	b,h,l,p.

* trace.
a. Hanovia lamp (450 W); b. Hanovia lamp (200 W); c. Rayonet lamp (350 nm); d. Rayonet lamp (310 nm); e. Mercury Par 38 projector bulb (100 W); f. Concentrated hydrochloric acid; g. Dry hydrogen chloride in anhydrous methanol; h. p-Toluenesulfonic acid; i. Uranium glass filter; j. Soft glass filter; k. Corex filter; l. Pyrex filter; m. Nickel sulfate filter solution; n. 2,7-Dimethyl-3,6-diazacycloheptane-1,6-diene perchlorate filter solution; o. Ice bath; p. Ice-salt bath; q. Dry ice-methanol bath; r. The dimer peak at 292 nm increased to maximum; u. Continuous irradiation to the dimer peak at 292 nm decreased to nil.

Scheme VI



The photoaddition of N-nitrosopiperidine in the presence of an excess of 1-hexene gave an excellent yield of a mixture of syn- and anti-1-piperidino-2-hexanone oximes (14 and 15, ratio = 3:7). A similar photoaddition using a combination of a Uranium glass filter and a medium pressure Hanovia lamp usually gave, in addition to a

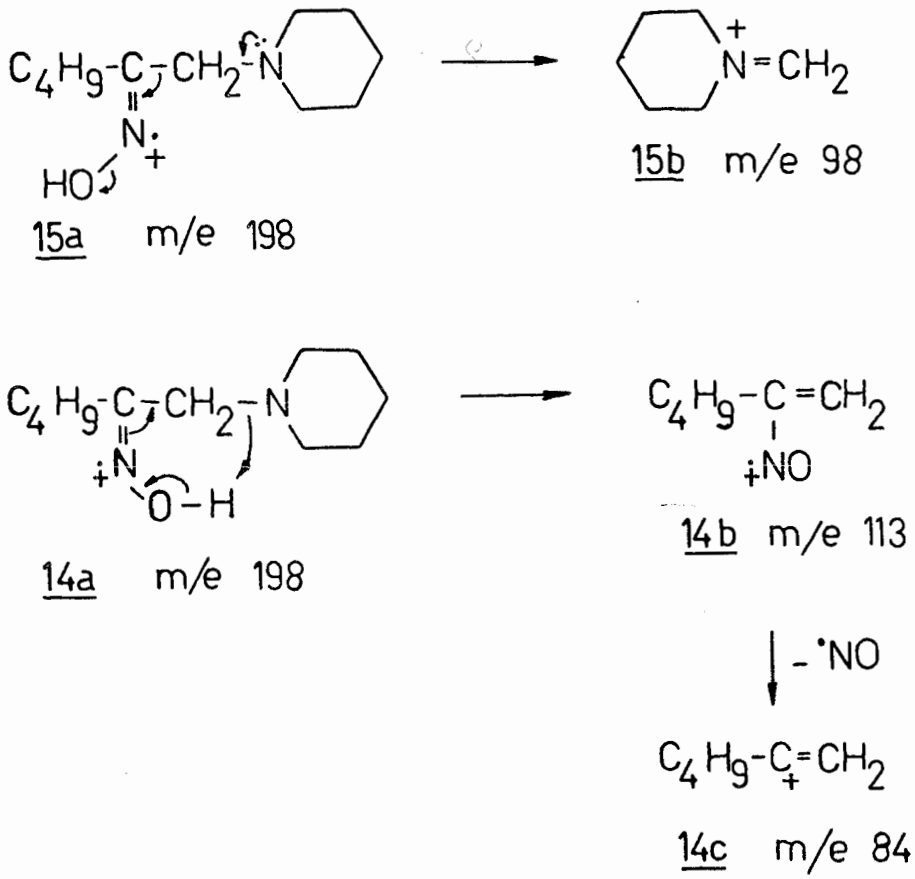
good yield of oximes 14 and 15, less than 10% of the trans-dimer of 1-piperidino-2-nitrosohexane (13). When the photolysis was terminated at the maximum intensity of the 292 nm peak, 28% of the dimer could be isolated. If the irradiation through a Corex filter was contiuned until the absorption at 292 nm disappeared, 1-piperidino-2-(N-nitrosohydroxylamino)-hexane (17) and oximes 14 and 15 were obtained. The yield of this N-nitrosohydroxyl-amine derivative 17 rose to 47% at the expense of oximes when the photoaddition was run using an excess of N-nitrosopiperidine in a pyrex apparatus.

The structure of oximes 14 and 15, dimer 13 and N-nitrosohydroxylamine derivative 17 were assigned based on spectral and analytical data. The trans-configuration of dimer 13 was indicated by a strong i.r. absorption at 1185 cm^{-1} (9). The n.m.r. spectrum of the dimer 13 showed an ABX pattern consisting of a double doublet at τ7.15 (J=10 and 13 Hz), a multiplet at τ4.28, and a broad signal at τ7.55 which was obscured by α-methylene protons of the piperidine ring. The molecular formula was further confirmed by elemental analysis and by its mass spectrum which showed the highest mass peak at m/e 198 as the mass corresponding to the C-nitroso monomer.

Anti-oxime 15 showed i.r. absorptions at 935, 1650 and 3220 cm^{-1} corresponding to N-O, C=N and O-H stretching

absorptions respectively (7, 10). The molecular formula was confirmed by elemental analysis and the molecular peak (m/e 198) in the mass spectrum. The parent peak (m/e 181, M^+-OH) and other prominent mass peaks could be interpreted as shown in Scheme VII.

Scheme VII



Syn-oxime 14 exhibited very similar i.r. and mass spectral patterns to those of anti-oxime 15. However, syn-oxime 14 showed very intense mass peaks at m/e 60

(100%), 73 (50%) and 84 (77%), but their origin is not clear. The methylene group in each of these two oximes resonated as a singlet at τ6.77 for 14 and τ7.03 for 15; the former was assigned as syn-oxime and the latter as anti-oxime (8). The assignment was further substantiated by t.l.c. mobility in which syn-oxime 14 moved faster than anti-oxime 15 (11), and by the color test with cupric sulfate solution in which only anti-oxime 15 gave a green coloration (12).

On oxime formation of ketone 16, a mixture of syn-oxime 14 and anti-oxime 15 was obtained, thus proving the identity of ketone 16. N-piperidinoformamide 18 was obtained upon prolonged photolysis and was identified by direct comparison of the i.r. and n.m.r. spectra with those of an authentic sample* (13).

The molecular formula of the N-nitrosohydroxylamine derivative 17 ($C_{11}H_{23}N_3O_2$) was confirmed by elemental analysis and its mass spectrum (M^+, 229). The i.r. absorption at 1045 cm^{-1} is characteristic of the N-O stretch in the N-nitrosohydroxylamino group (7). The n.m.r. spectrum contained an ABX pattern (similar to dimer 13) with a double doublet at τ6.93 (J=9 and 13 Hz) and a multiplet at τ5.55. The fragmentation pattern of the mass spectrum of 17 is shown in Scheme VIII.

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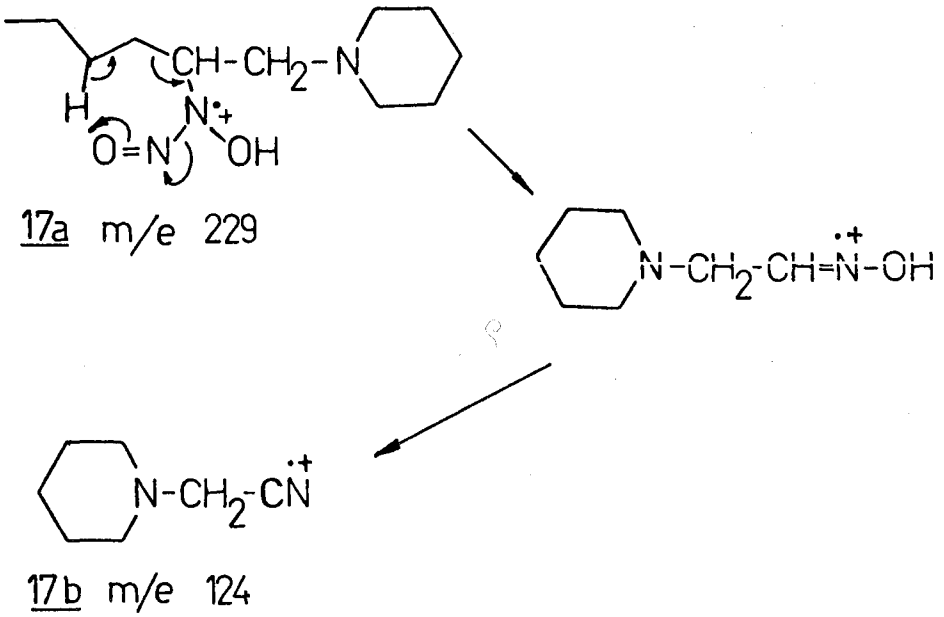
* The author thanks Mr. Lau for providing these spectra.

Scheme VIII



In the acidic solution (see Table Ib), the trans-dimer 13 was slowly converted to syn- and anti-oximes 14 and 15. When the dimer 13 was irradiated with a 280-320 nm light source in an acidic solution, either alone or in the presence of N-nitrosopiperidine, the absorption at 292 nm due to the dimer disappeared rapidly. In these reactions, syn- and anti-oximes 14 and 15 (ratio 1:1) were the only products obtained. The irradiation of an acidic solution of the dimer 13 and N-nitrosopiperidine in a pyrex apparatus, gave, in addition to oximes, N-nitrosohydroxylamine derivative 17 as the major product.

Table Ib. The photolysis of the nitroso dimer of 1-piperidino-2-nitrosohexane

Run	dimer 13 (mmoles)	N-nitroso-piperidine (mmoles)	acidicity (N)	volume (mls)	irradition peroid	% yield 14	15	16	17	18	notes**
1	0.45			43	1'20"	32	32				e,l,o.
2	0.95	1.0	0.012	100	27'	35	35				d,f,m,o.
3	1.30	4.1	0.052	100	1'10"	40	40		7		b,f,m,o.
4	2.90	17.5	0.240	120	10'	5	20	*	69	8	c,f,p.

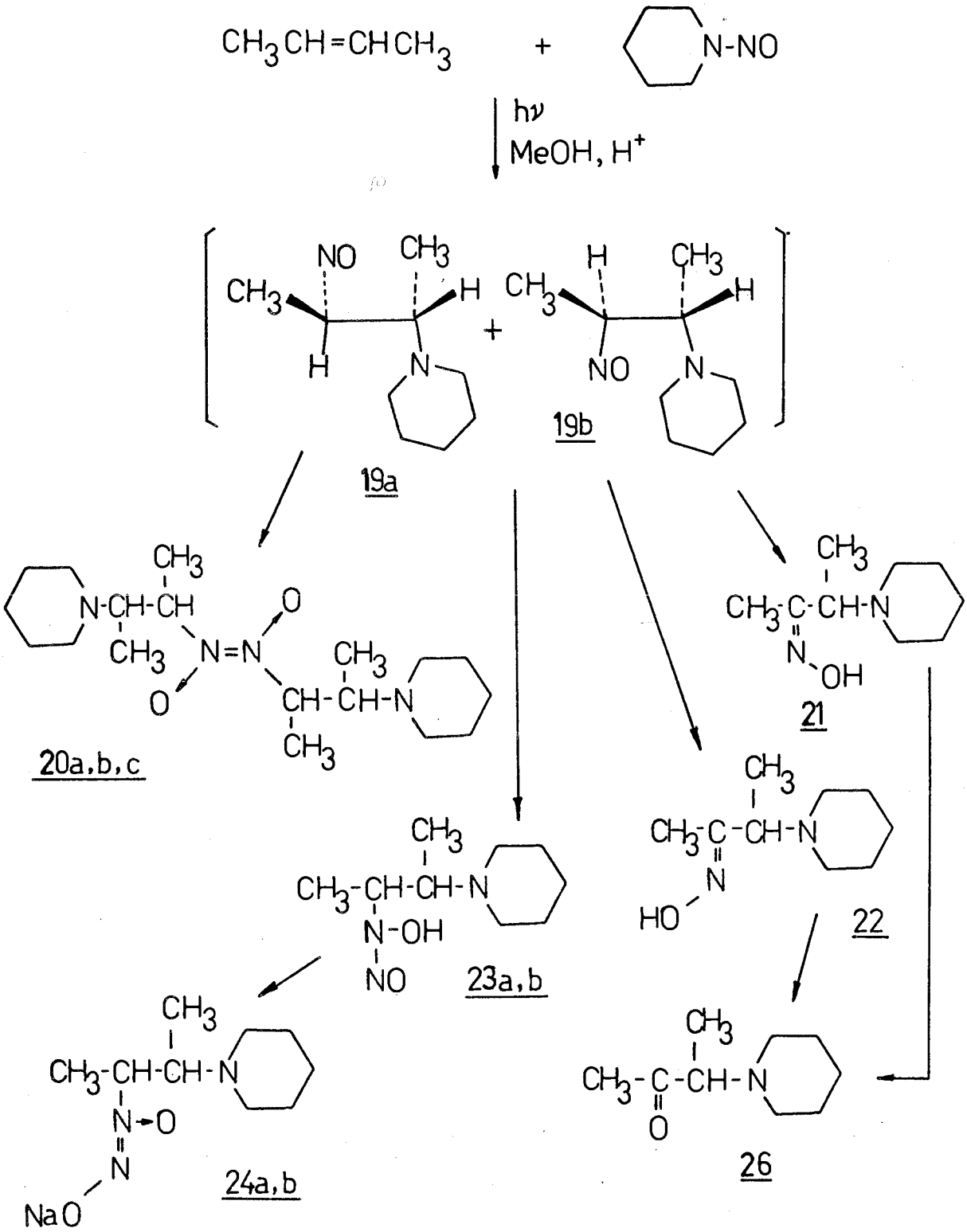
* trace.

** same as in Table Ia.

III. Addition of N-nitrosopiperidine to 2-butene

The photoaddition of N-nitrosopiperidine to 2-butene followed a pattern similar to that of its addition to 1-hexene and the results are summarized in Tables II and III. The primary photoadduct, which was not isolated, was again the C-nitroso compound 19, but in this case two stereoisomers, erythro-(19a) and threo-2-nitroso-3-piperidinobutane (19b), can be formed. The final products isolated under various conditions were two of the three possible trans-dimers of 19 (20a-20b), syn-2-piperidino-3-butanone oxime (21), anti-2-piperidino-3-butanone oxime (22), erythro-2-piperidino-3-(N-nitrosohydroxylamino)-butane (23a) and threo-2-piperidino-3-(N-nitrosohydroxylamino)-butane (23b). Oximes 21 and 22 are the regular photoadducts obtained by tautomerization of 19 in which the original stereochemistry is destroyed. The stereochemistry of the addition was, however, retained in 20 and 23. All the possible trans-dimers, erythro-erythro dimer 20a, erythro-threo dimer 20b and threo-threo dimer, were observed in the n.m.r. spectrum of the mixture. The reaction is summarized in the Scheme IX.

Scheme IX


CH3CH=CHCH3
+
N-NO
hν
MeOH, H+
NO
CH3
H
CH3
H
N
19a
19b
20a,b,c
21
22
23a,b
24a,b
26
NaO

The total yield of dimer 20 could be increased to 18% when the photolysis was carried out with a Uranium glass filter at low temperature in the presence of a large excess of trans-2-butene. Two isomers with melting points 156.5-158.5° (20a) and 104.5-106.5° (20b) were isolated in small amounts. In some experiments, a mixture of dimers was obtained, but they could not be separated by ordinary methods. The overall yield of the N-nitroso-hydroxylamine derivative 23 was increased from 3% (ratio of 23a:23b = 4:1) to 13% (ratio of 23a:23b = 6:4) when the filter was changed from Uranium glass to Corex. Due to the polar nature of the functional group and the acidic proton of the N-nitrosohydroxylamino group, erythro- and threo- isomers 23a and 23b were relatively more soluble in water than in organic solvents, and they formed a sodium salt with sodium carbonate.

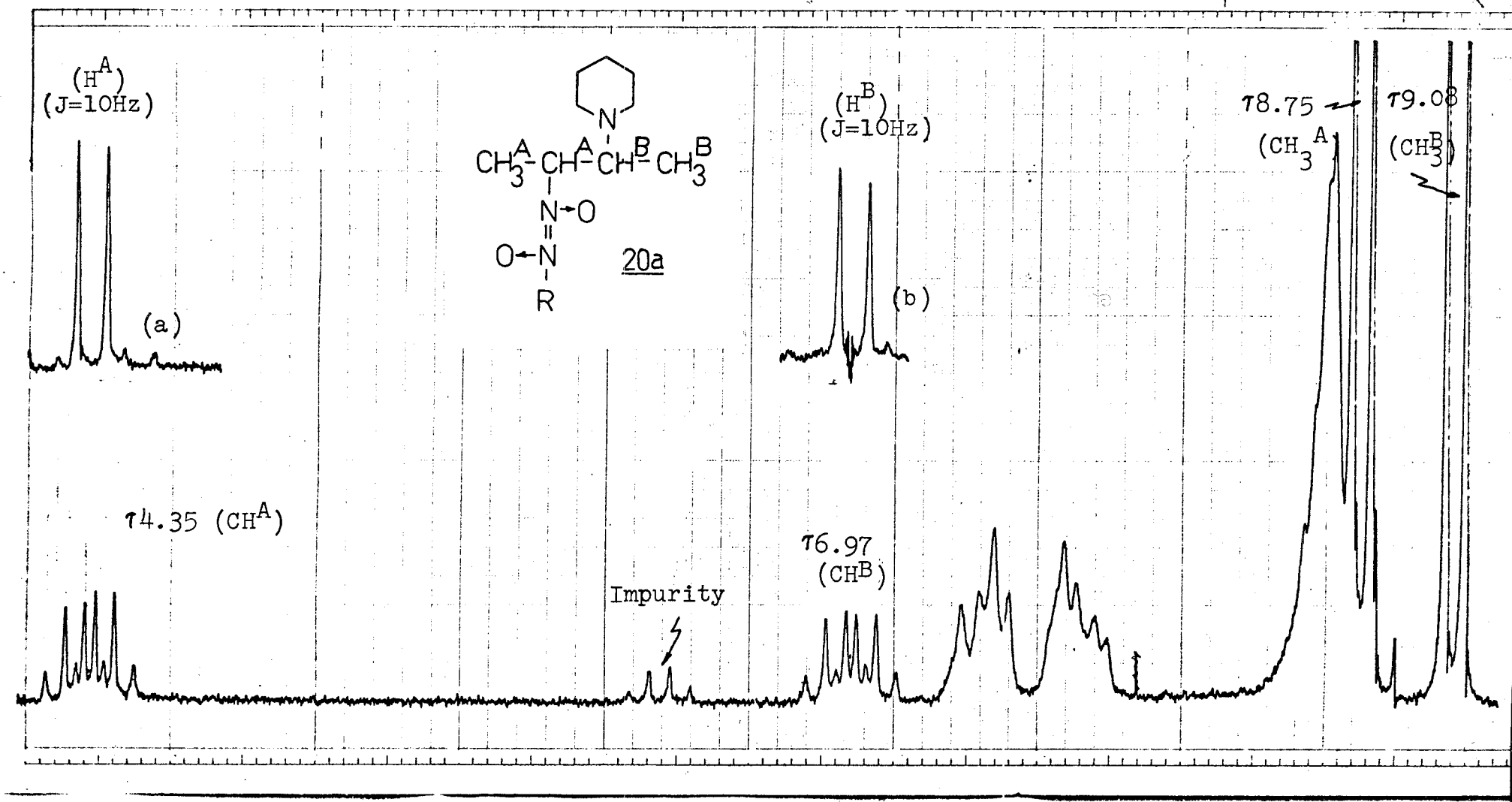
The trans configuration of dimers 20a and 20b was indicated by the strong i.r. absorption at 1190 cm^{-1}. The highest mass peak observed in these dimers was m/e 198 which is equivalent to the molecular weight of the monomer. The nmr spectra showed double quartets at τ6.95 and 4.35 (J=6.5 and 10 Hz) for dimer 20a and τ7.16 and 4.57 (J=6.5 and 10 Hz) for dimer 20b. These signals were assigned to the two methine protons in the respective dimer. The 100 Mc n.m.r. spectra of dimers 20a

and 20b are shown in Figures I and II. In the case of dimer 20a, irradiation of the methyl doublets at τ9.07 and 8.74 collapsed the signals at τ6.95 and 4.35 to an AB quartet (J=10Hz). Dimer 20b indicated four sets of methyl doublets at τ9.16, 9.07, 8.76 and 8.56 in its nmr. spectrum and was assigned the erythro-threo combination. Whether dimer 20a has an erythro-erythro or threo-threo combination cannot yet be concluded. Many attempts to reduce the dimers to the corresponding 2,3-diamino derivatives were not successful and unfortunately prevented further investigation of the stereochemistry.

The elemental analysis and the molecular ion peak of oximes 21 and 22 confirmed the molecular formula $C_9H_{18}N_2O$. Both oximes showed the expected i.r. absorptions at 3160, 1649 and 945 cm^{-1} for 22 and 3160, 1650 and 935 cm^{-1} for 21. The nmr. signal of the methine quartet of 21 appeared at a lower field (τ6.67) than that of 22 (τ7.12). Assignments of the syn-configuration to 21 and the anti-configuration to 22 were ascertained by this information (8) and by the color test with cupric sulfate solution in which a green color was observed only with the anti-oxime 22 (12).

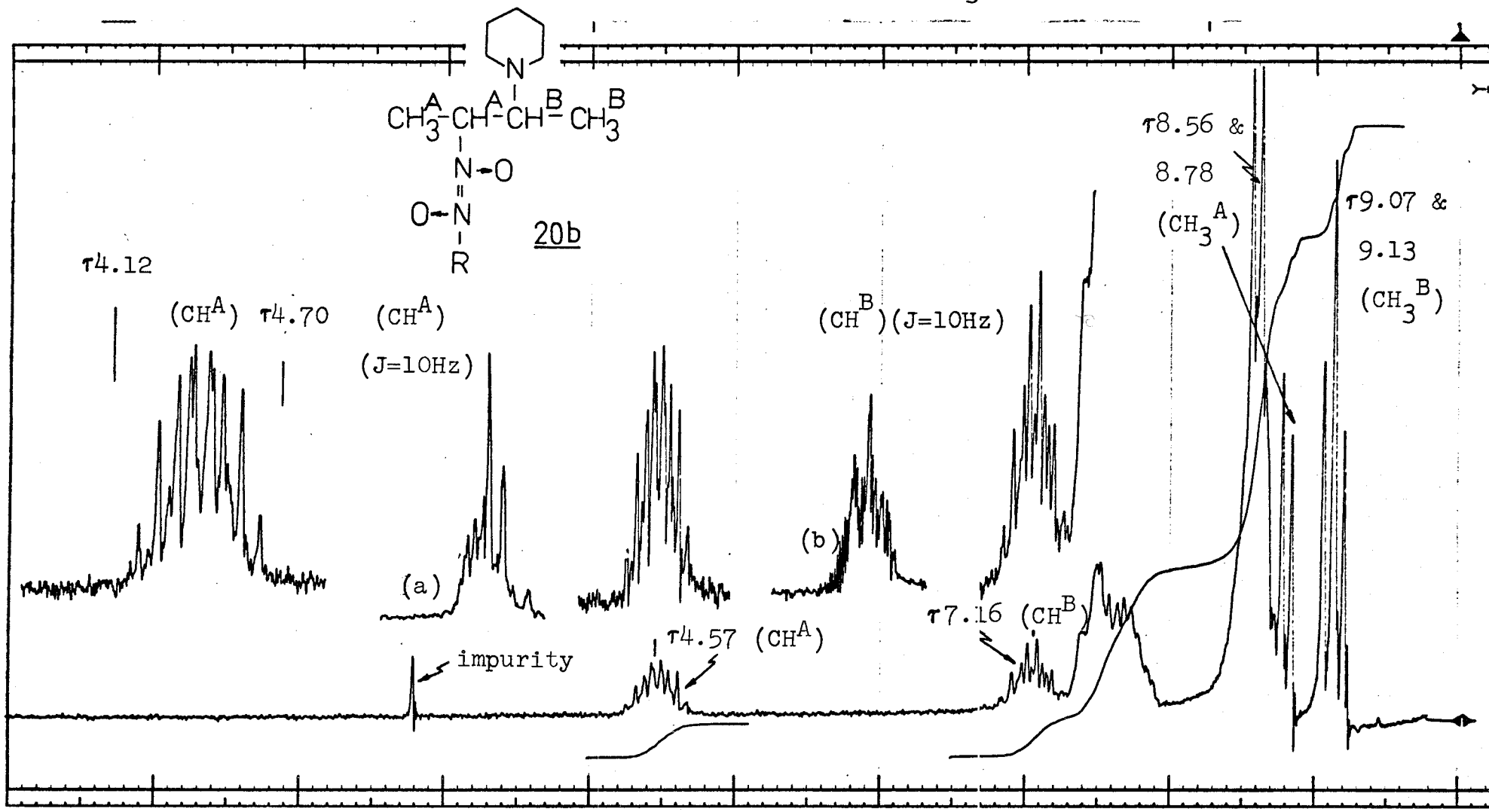
The mass spectral patterns of 21 and 22 were very similar, differing only in intensity. The mass peak

Figure I. The 100 Mc. n.m.r. spectrum of 20a in $CDCl_3$ with 500 Hz sweep width.



(a): irradiation at τ8.75 (CH_3^A); (b): irradiation at τ9.08 (CH_3^B).

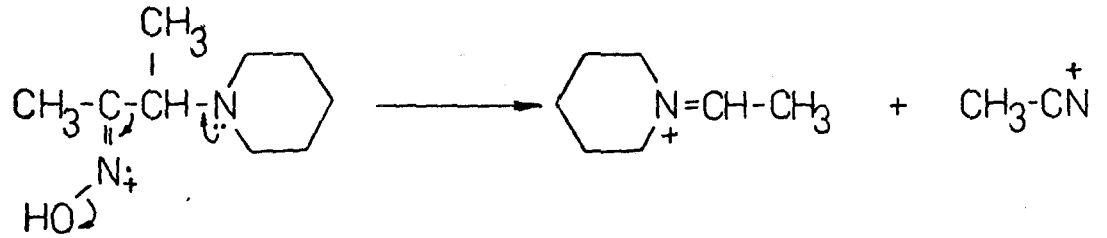
Figure II. The 100 Mc. n.m.r. spectrum of 20b in $CDCl_3$ with 1000 Hz sweep width.



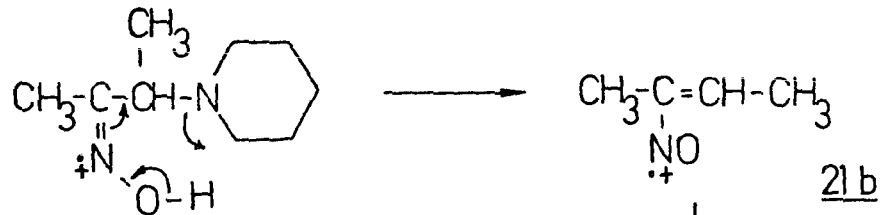
(a): irradiation at τ8.60; (b): irradiation at τ8.84.

corresponding to M^+-OH (m/e 153) was 66% for 22 and only 13% for 21, thus suggesting departure of the OH group in the anti-configuration. The major mass peaks in 21 and 22 could be explained by the fragmentation pattern depicted in Scheme X.

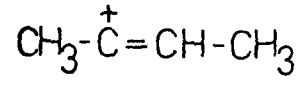
Scheme X



22a m/e 170 — 22b m/e 112 (100%) + 22c m/e 41 (30%)



21a m/e 170 — 21b — −·NO



21c m/e 55

The structure of ketone 26 was confirmed by the i.r. absorption at 1700 cm^{-1} and the nmr signal at

τ6.32. The compound was, however, not isolated from the mixture in a pure state.

The elemental analyses of 23a and 23b gave a molecular formula $C_9H_{19}N_3O_2$. The mass spectra of 23a and 23b showed the weak molecular ion peak at m/e 201 (see Fig. III). The fragmentation pattern of the compound could be rationalized as shown in Scheme XI.

Scheme XI

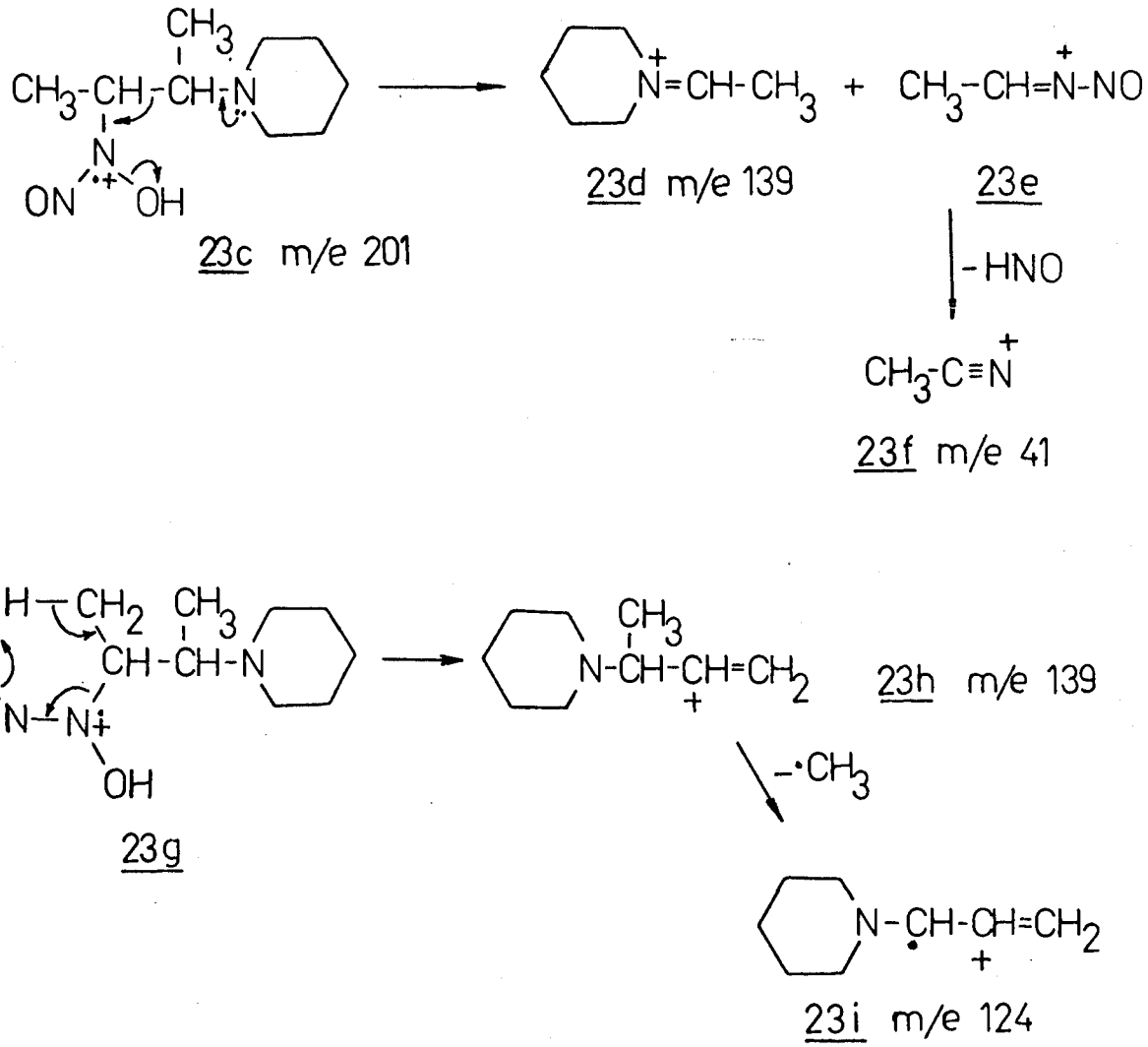


Fig. IV. The i.r. Spectra Dilution Studies of Compound 23b

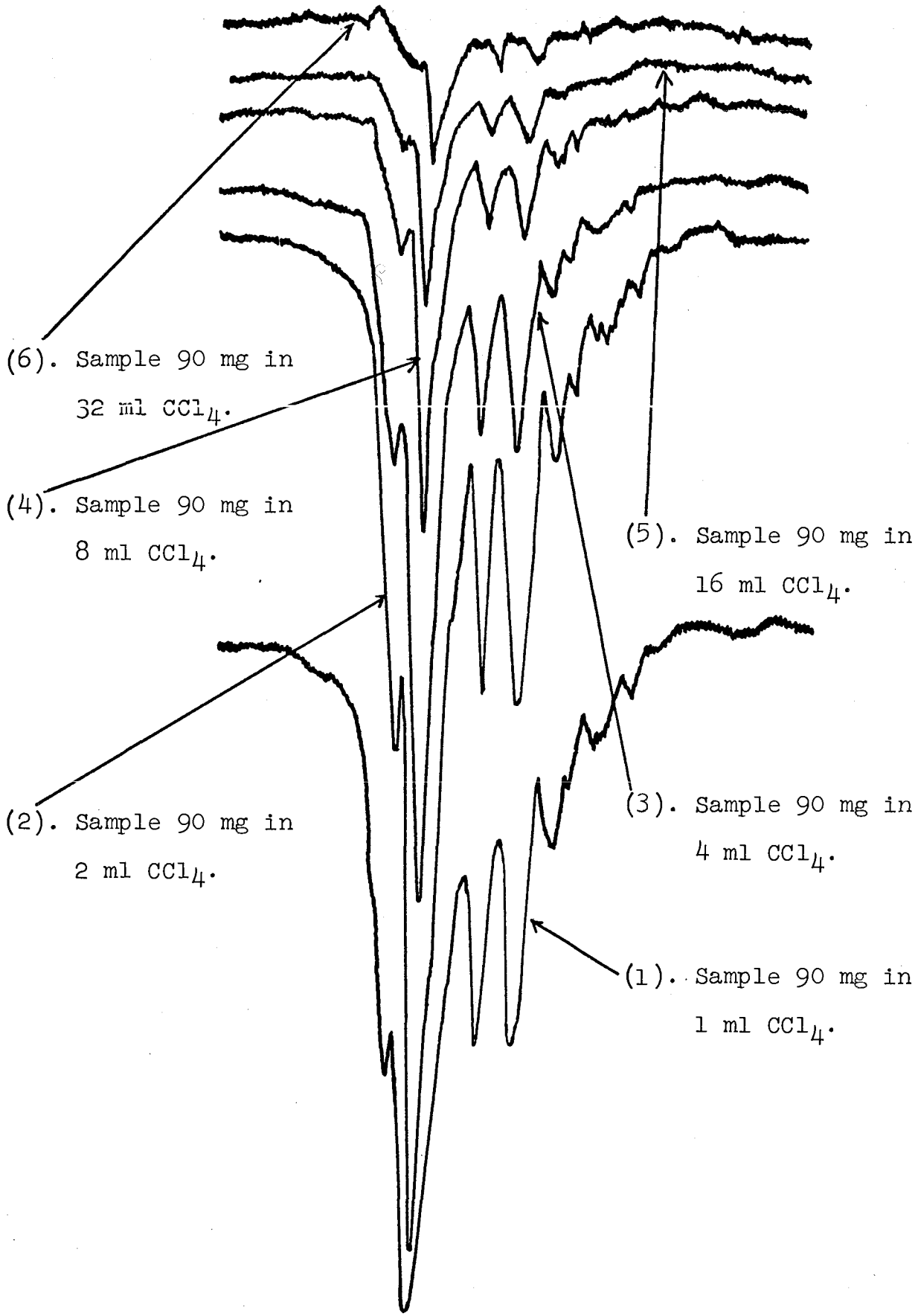


Fig. V. The i.r. Spectra Dilution Studies of Compound 23a

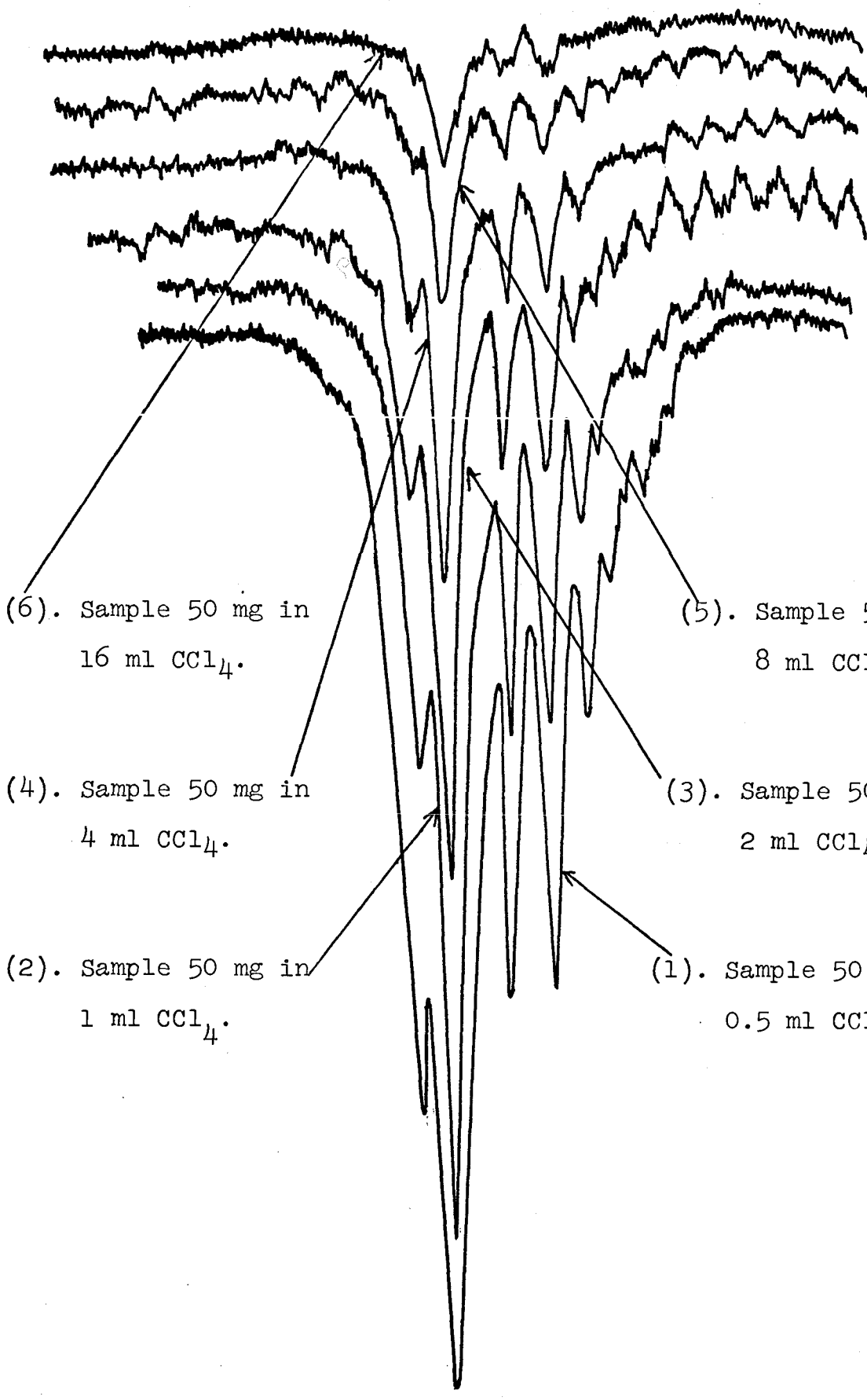
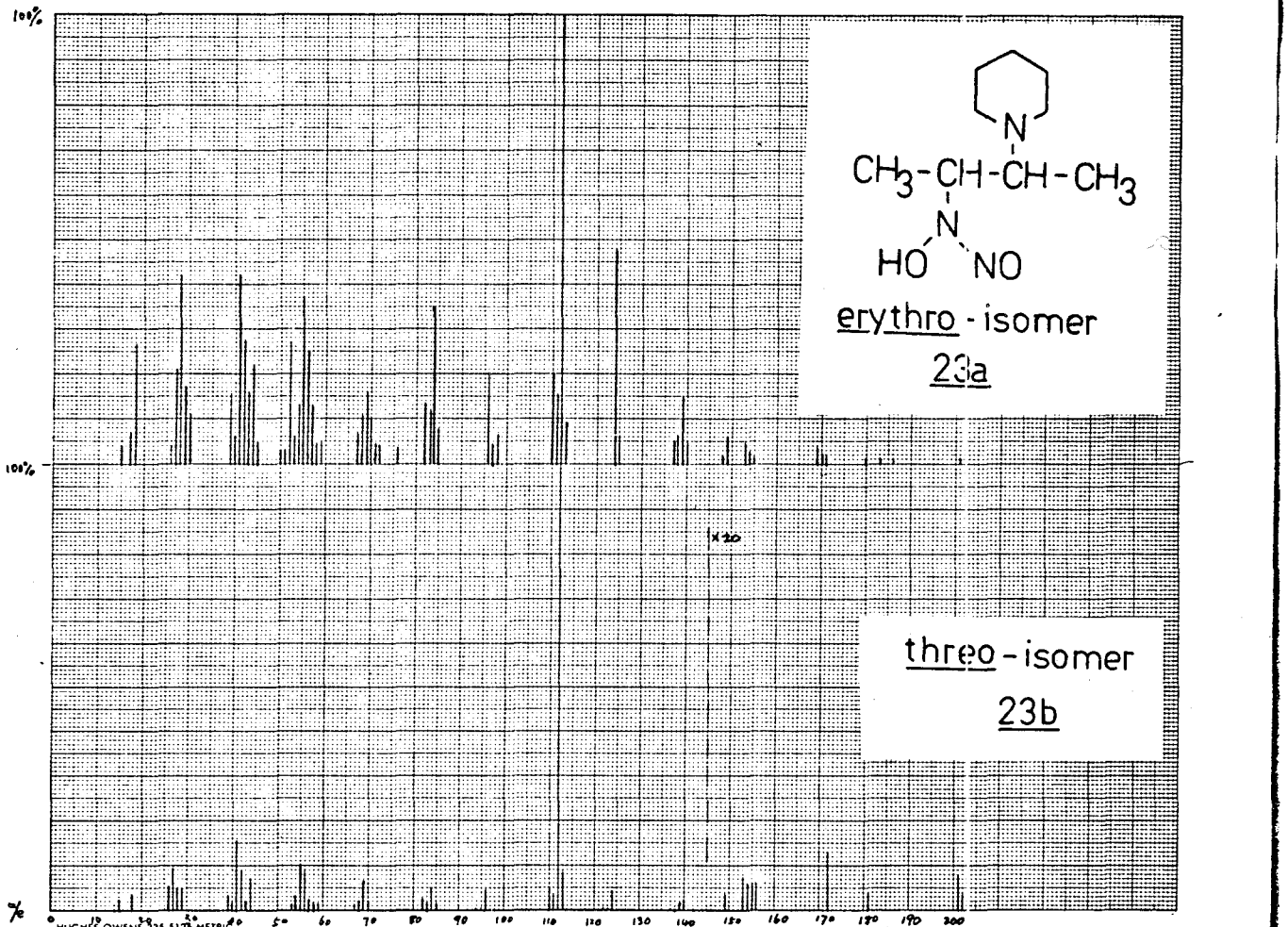


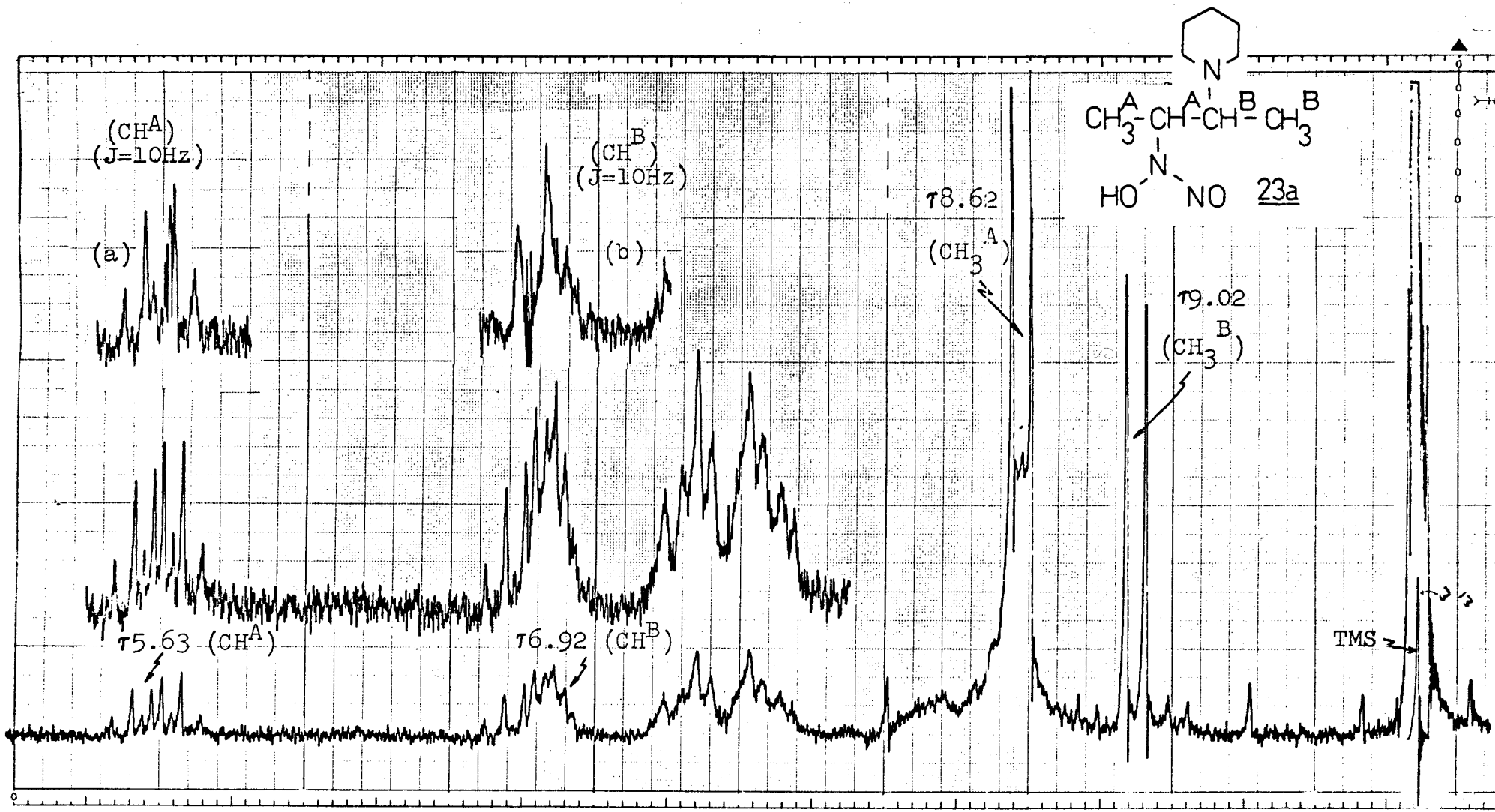
Fig. III. The mass spectra of N-nitrosohydroxylamine derivatives (23a and 23b)



The i.r. spectra of 23a and 23b showed strong absorptions at 1065 and 1055 cm^{-1} respectively, which were assigned to the N-nitrosohydroxylamino group. The study of the i.r. spectra by dilution technique in the region 2000-4000 cm^{-1} (Fig. IV and V) demonstrated that the relative intensity of OH stretching absorptions (3200-2800 cm^{-1}) remained about the same over a 32 fold dilution of 23a and 23b in CCl_4. The O-H stretching of both compounds occured in the 3200-2800 cm^{-1} region and was superimposed with C-H stretching absorption. The information indicated that both compounds possessed a certain degree of intramolecular hydrogen bonding, but was insufficient to allow assignment of the structures of 23a and 23b. The nmr spectra exhibited two double quartets of methine protons at τ7.02 and 5.72 (J=10Hz) for 23a and at τ6.92 and 5.62 (J=10Hz) for 23b (Fig. VI and VII). The coupling constant of 10 Hz for the methine protons was determined by decoupling experiments as shown in Fig. VI and VII. This indicated that both 23a and 23b preferentially assumed the configurations in which two methine protons are in the trans relation as shown.

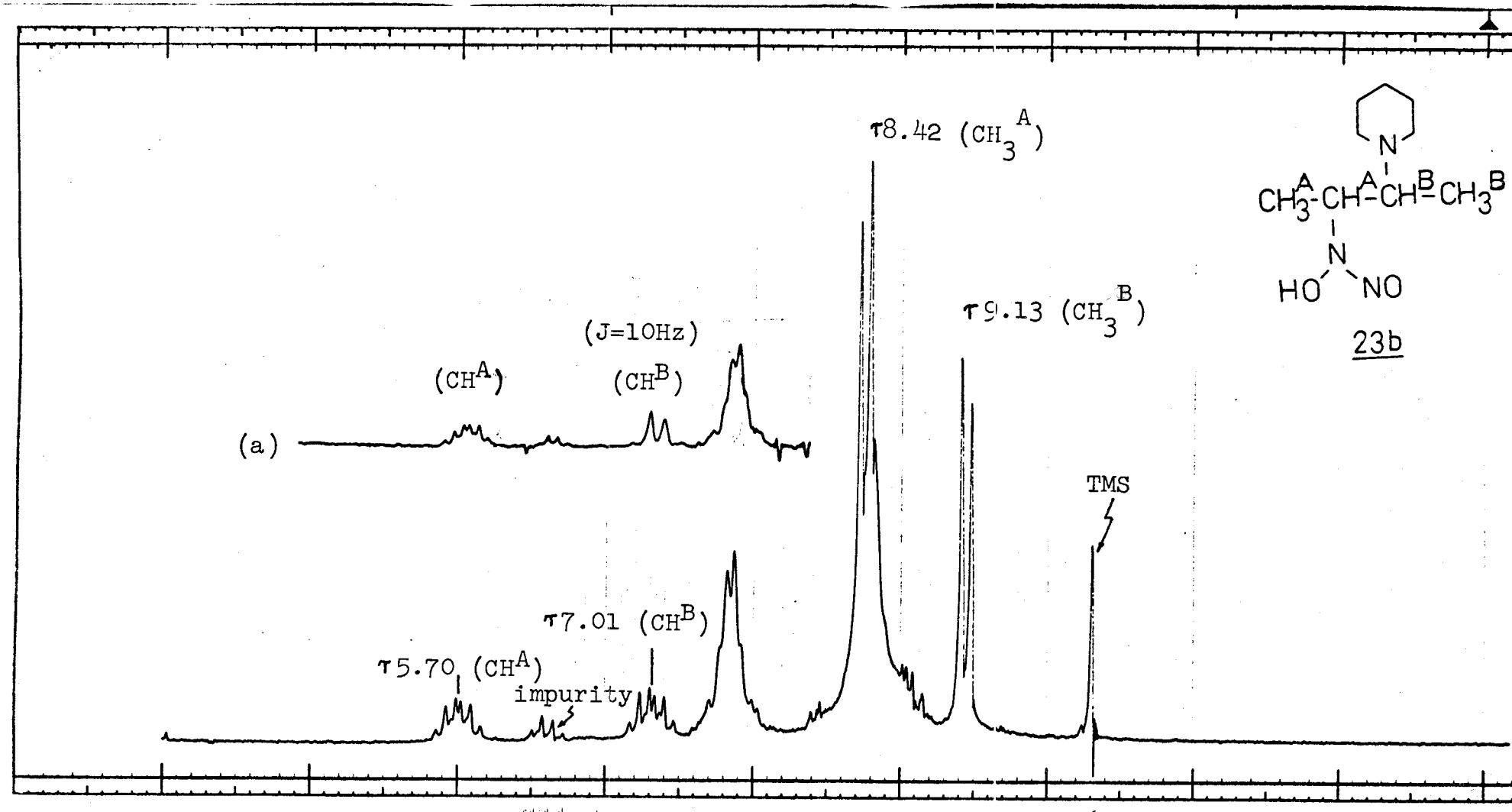
That 23a and 23b had the erythro- and threo- structures and that they had the conformers as indicated in Scheme XII was further shown by the following observations. First, the chemical shift in $CDCl_3$ solution of the hydroxyl group in 23b appeared at

Figure VI. The 100 Mc. n.m.r. spectrum of erythro-isomer 23a in $CDCl_3$ with 500 Hz sweep width.



(a): Irradiation at τ8.62; (b) irradiation at τ9.02.

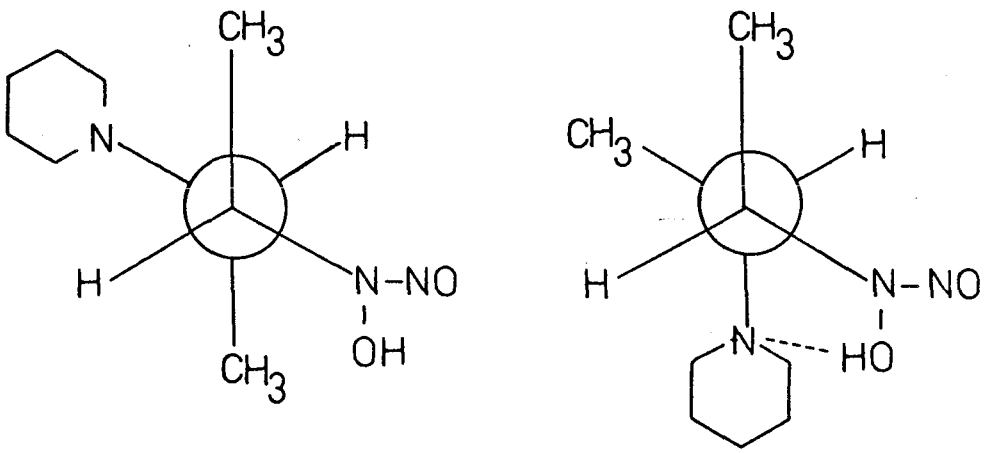
Figure VII. The 100 Mc. n.m.r. spectrum of threo-isomer 23b in $CDCl_3$ with 1000 Hz sweep width.



(a): irradiation at τ9.13.

lower field (τ 0.40-1.40) than that in 23a (τ 0.20-2.00) over a comparable concentration range. Secondly, while 23a instantaneously gave a positive color reaction with 2% cupric sulfate solution, 23b did not. Thirdly, 23a formed a sodium salt in dilute sodium carbonate solution, while in contrast, 23b formed the sodium salt to the extent of about 50% under the same conditions. This

Scheme XII



23a (erythro) 23b (threo)

information indicated that the hydroxyl proton of 23b is more tightly bound (probably by intramolecular hydrogen bonding to the nitrogen atom of the piperidine ring) than that of 23a. From a conformational point of view, the preferred conformations indicated in Scheme XII

are the most stable from steric considerations. It follows that this conformational stability facilitates the intramolecular hydrogen bonding to a greater extent in 23b than in 23a. Reduction of 23a and 23b by LAH was extensively attempted but without apparent success. Although reduction to the amine appeared to take place, attempts to isolate the product by acylation of the amine gave no identifiable products.

The photoaddition of N-nitrosopiperidine to cis-2-butene was carried out under conditions similar to those used in the case of trans-2-butene (Table IV). In this photoaddition, the products obtained were the same as in the photoaddition to trans-2-butene. However, the product ratio was not the same. From the complex nmr spectrum, a mixture of dimer 20 was shown to contain all three possible combinations of 19a and 19b. When the photoaddition was carried out through a Uranium glass filter in the presence of an excess of N-nitroso-piperidine, 23a and 23b were obtained in the ratio of 4:6. This ratio did not change significantly (35:65) when a Corex filter was used, but the total yield increased to 18%.

IV. Addition of N-Nitrosopiperidine to Acetylenic Compounds

When the photoaddition of N-nitrosopiperidine to

Table II. The photoaddition to trans-2-butene in the presence of N-nitrosopiperidine

Run	N-nitroso-piperidine (mmoles)	trans-2-butene (mmoles)	acidicity (N)	volume (mls)	irradiation peroid	% yield								notes**
						20a	20b	21	22	23a	23b	26	18	
1[r]	85	268	0.43	200	2'50"	3	1	56	2					a,h,i,o.
2[u]	168	60	0.90	220	23'15"			50	22	2.4	0.6	*		c,g,q.
3[u]	136	53	0.25	210	3'40"				34**	6	1	*		a,g,j,q.
4[u]	260	107	1.30	200	2'20"				70**	8	5	*		a,h,k,q.
5[r]	85	268	0.43	200	2'35"	11	5	32	1	0.7	*	*		a,h,i,q.
6[r]	86	268	0.43	200	2'25"	14	4	66	*	3	*	*		a,h,i,q.
7[u]	180	60	1.00	180	6'			75	*		4**	*		b,h,i,q.
8[u]	172	60	1.00	200	4'30"				75**	4	1			b,g,i,p.

* trace. ** same as in Table Ia.

** mixture of isomers.

Table III. The photoaddition to cis-2-butene in the presence of N-nitrosopiperidine

Run	N-nitroso-piperidine (mmoles)	cis-2-butene (mmoles)	acidicity (N)	volume (mls)	irradiation peroid	% yield							notes**
						20a	20b	21	22	23a	23b	26	18	
1[r]	86	160	0.43	200	3'		11*	47	*	2*		*		a,h,i,q.
2[u]	223	68	1.00	225	19'			65	5	3.5	4.5	*	17	a,g,i,q.
3[u]	269	100	1.40	200	2'30"			65*		6.3	11.7	*	*	a,k,h,q.

* trace. ** same as in Table Ia.

* mixture of isomers.

phenylacetylene was carried out and worked up in the usual manner, a complex mixture of products was obtained. From this mixture, phenylglyoxal ketoxime (32, 27%), 2,2-dimethoxyacetophenone (31, 22%) and 2-methoxy-2-piperidinoacetophenone oxime (30, 24%) were isolated as the major components and phenylglyoxal dioxime (33) and 2-(N-nitrosohydroxylamino)-2-phenylacetaldehyde (34) in small yields (Table IV). These products were obtained in only minor quantities when an excess of phenylacetylene was used and the reaction mixture worked up in the usual way. In this case, the new products turned out to be high melting solids (28 and 29) together with small yields of benzoic acid plus the products observed above. However, it was found that the ketoxime 32 could be obtained in good yield even in the presence of excess phenylacetylene if the photolysate was neutralized immediately after the irradiation and the reaction mixture worked up under neutral conditions. Assuming that the photoaddition takes place in a similar manner to the C-nitroso compound (27) as the primary adduct, the reaction pattern can be summarized as in Scheme XIII, and will be discussed later.

The structure of 32 was confirmed by its spectral data and by the preparation of its bis-phenylhydrozone derivative. The i.r. spectrum in chloroform solution exhibited a strong carbonyl absorption at 1700 cm^{-1}.

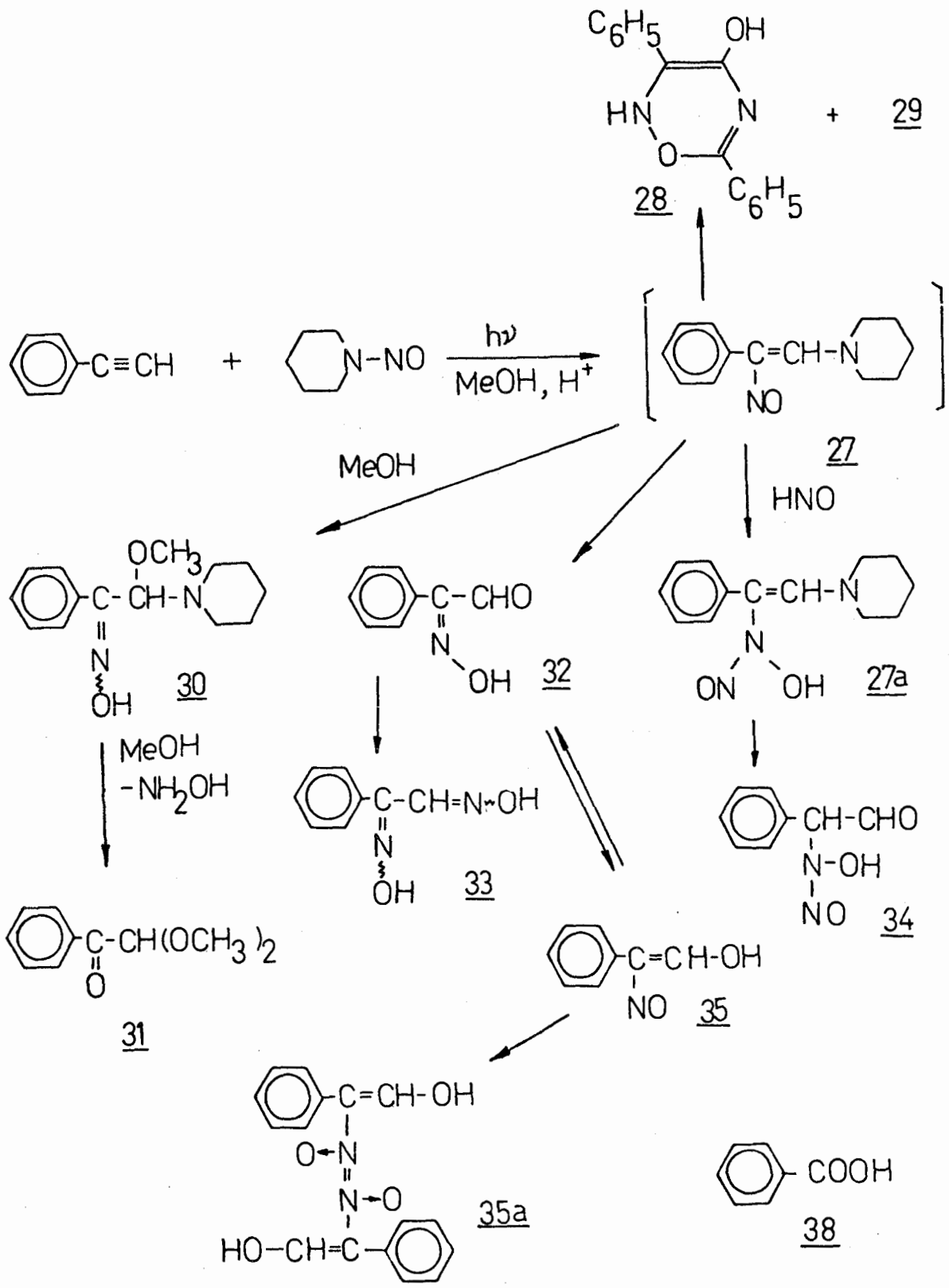
Table IV. The photoaddition to phenylacetylene in the presence of N-nitrosopiperidine

Run	N-nitroso-piperidine (mmoles)	phenyl-acetylene (mmoles)	acidicity (N)	volume (mls)	irradiation peroid	% yield								notes**
						30	31	32	33	34	38	28	29	
1	52	74	0.31	200	5'30"	5	8		1		3	(3.74g)	(0.9g)	a,h,i,m.
2	70	35	0.36	200	1'30"	24	22	27	9	*	*	*	*	a,f,o,n.
3[x]	69	82	0.24	300	5'			65						a,f,i,q.

* trace. ** same as in Table Ia.

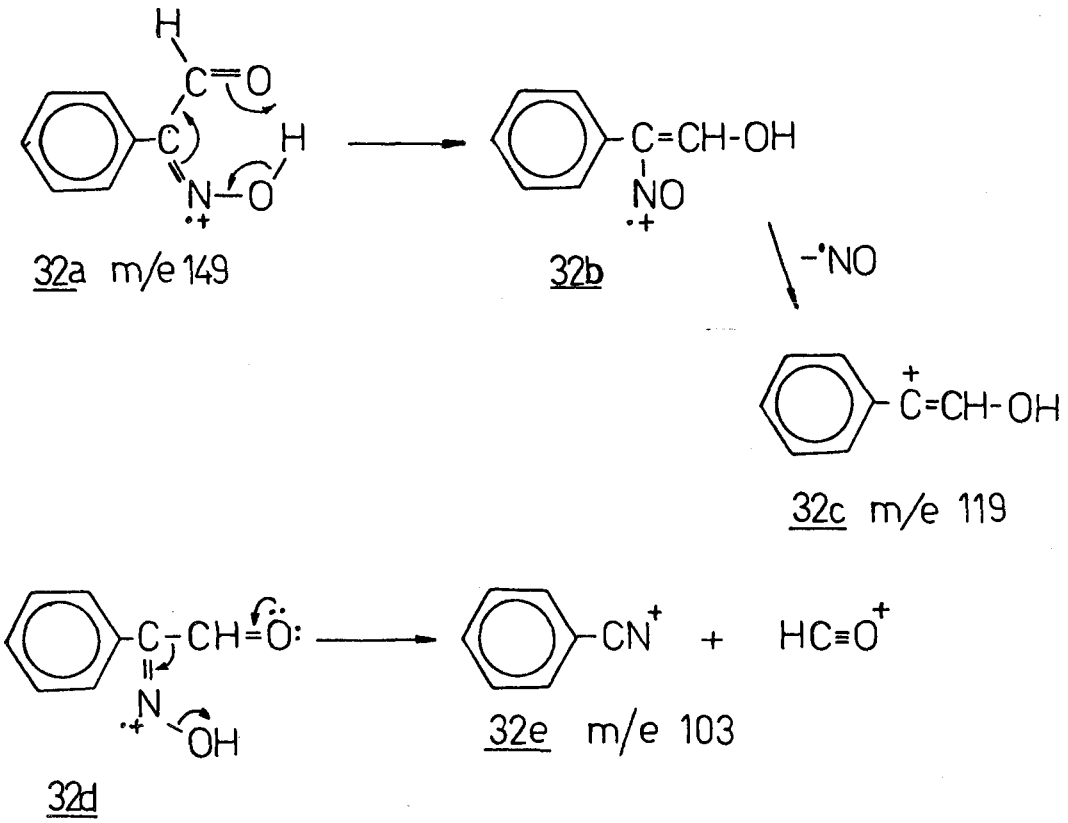
x: basified with solid sodium carbonate immediately when the photolysis was terminated.

Scheme XIII


C6H5
OH
HN
N
O
C6H5
28
+ 29
C≡CH
+
N-NO
hν
MeOH, H+
C=CH-N
NO
27
MeOH
HNO
OCH3
C-CH-N
N
OH
30
C-CHO
N
OH
32
C=CH-N
N
ON
OH
27a
MeOH
-NH2OH
C-CH=N-OH
N
OH
33
CH-CHO
N-OH
NO
34
C-CH(OCH3)2
O
31
C=CH-OH
NO
35
C=CH-OH
O-N
N-O
HO-CH=C
35a
COOH
38

The n.m.r. spectrum showed two signals at τ 2.53 and 0.20 with the ratio of 5:1. The molecular formula ($C_8H_7NO_2$) was confirmed by elemental analysis and by high resolution mass spectrometry which gave a mass of 149.0520 (calcd. 149.0478). The fragmentation pattern* of the other major mass peaks (m/e 149, 119 and 103) in the mass spectrum could be rationalized as shown in Scheme XIV.

Scheme XIV



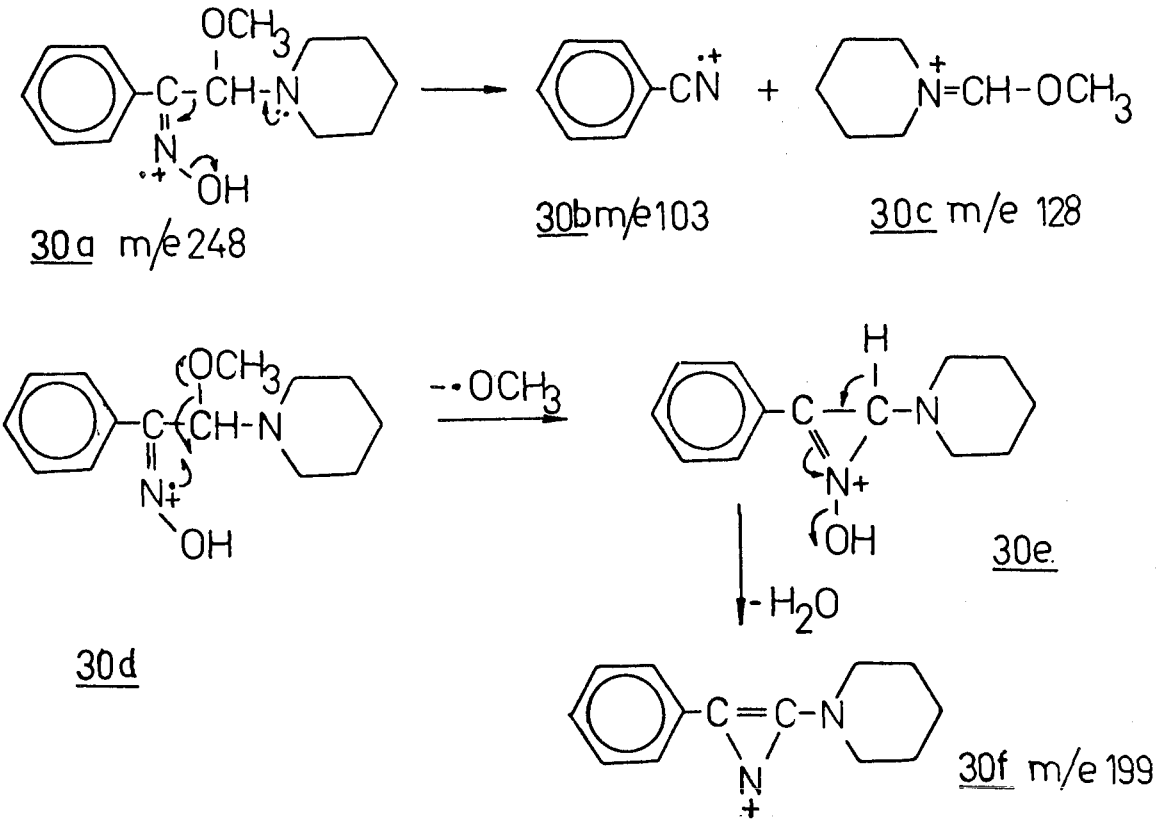
* The mass spectrum of the alternative oxime (phenylglyoxal aldoxime) showed main mass peaks at m/e 149 (44%), 105 (100%) and 77 (65%) but no peak at m/e 119 was observed.

A chloroform solution of the ketoxime 32 slowly gave crystals which were shown to be the dimer of 1-nitroso-2-hydroxylstyrene (35a). This solid dissolved in chloroform to give the same i.r. and nmr. spectra as shown by 32. In nujol mull, however, this solid showed no i.r. band at 1700 cm^{-1} but a strong absorption at 1210 cm^{-1} and a medium one at 1590 cm^{-1}, indicating the trans-dimer structure as shown in 35a. Sublimation of the solid gave 32 as a crystalline solid (m.p. 48-50°) and the mass spectrum showed the same pattern as that of 32, except for some variation in intensity (peak at m/e 119: 98% for 35a and 53% for 32).

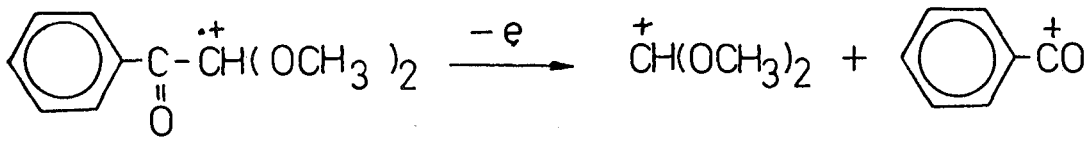
Oxime 30 showed a strong mass peak at m/e 231 which was confirmed by high resolution mass spectrometry to be the M^+-OH peak. The signal at τ6.17 for methoxy protons and the singlet at τ2.58 for the methine proton and broad multiplets at τ7.43 and 8.56 for the piperidine ring were in agreement with the structure assigned. The major mass peaks could be rationalized as shown in Scheme XV.

The spectral data of 2,2-dimethoxyacetophenone 31 agreed well with the reported figures (14,15). The i.r. absorptions at 1695, 1122 and 1070 cm^{-1} and the n.m.r. singlet at τ6.55 equivalent to six methoxy protons and a singlet at τ4.85 equivalent to one methine proton were highly indicative of the proposed structure. In

Scheme XV

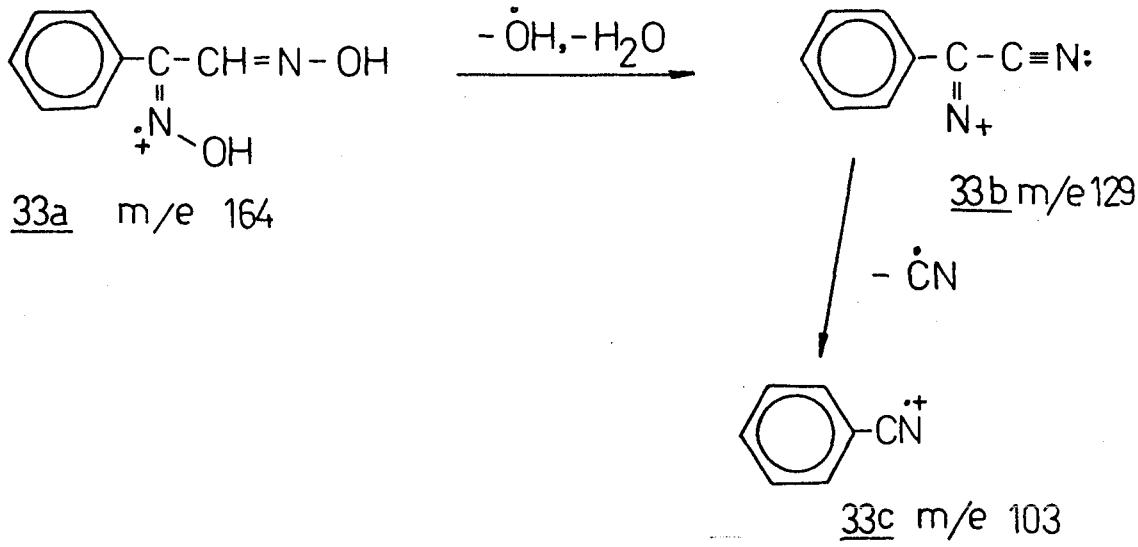


addition, the mass spectrum showed the characteristic mass peak at m/e 75 (100%) which could arise from the fragmentation as shown below.

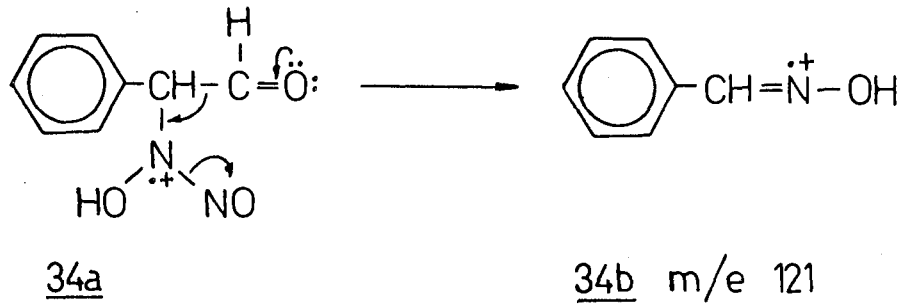


31a m/e 180 31b m/e 75 31c m/e 105

Dioxime 33 is a known compound and gave a melting point in agreement with the reported value (16). The mass spectrum showed an M^+ peak at 164 with 100% intensity and the other major mass peaks could be interpreted as 33a, 33b and 33c.

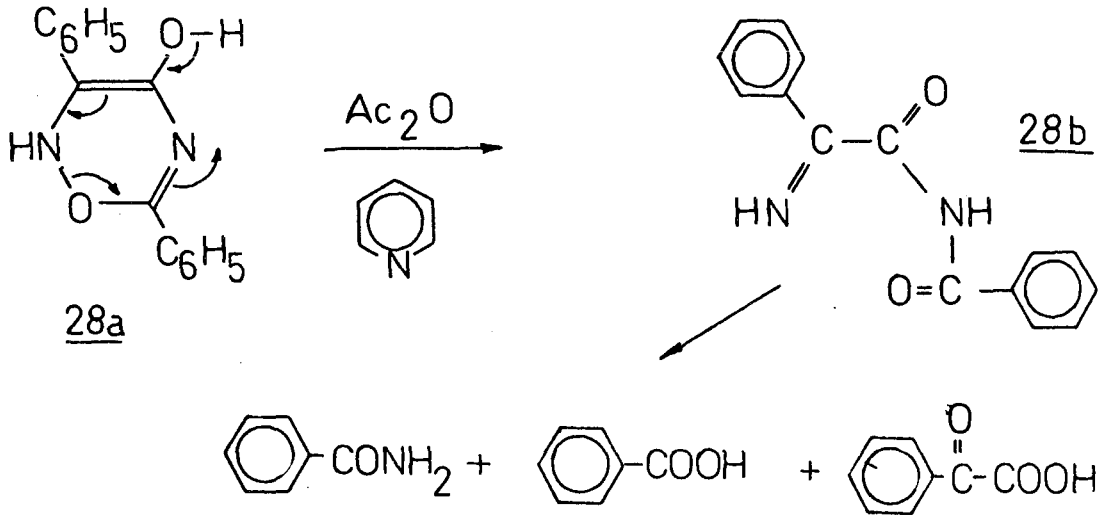


The N-nitrosohydroxylamine derivative 34 gave a strong mass peak at 121 which was shown by high reolution mass spectrometry to be m/e 121.0492, equivalent to C_7H_7NO and possibly arising from 34b.



Due to its poor solubility, the high melting product was difficult to purify and apparently decomposed on attempted recrystallization from a mixture of AcOH-Ac_2O. Based on the elemental analysis and the intense mass peak at m/e 149 (100%) the structure 28 was tentatively proposed. The mass peak of 149 indicated that the fragment of ketoxime 32 formed the integral part of 28. On attempted acetylation in a pyridine-acetic anhydride mixture, 28 gave benzoic acid and benzamide due, apparently, to decompositon. This decomposition can be visualized as shown in the following scheme. The spectral data exhibited by 29 does not allow definite proposal of its structure.

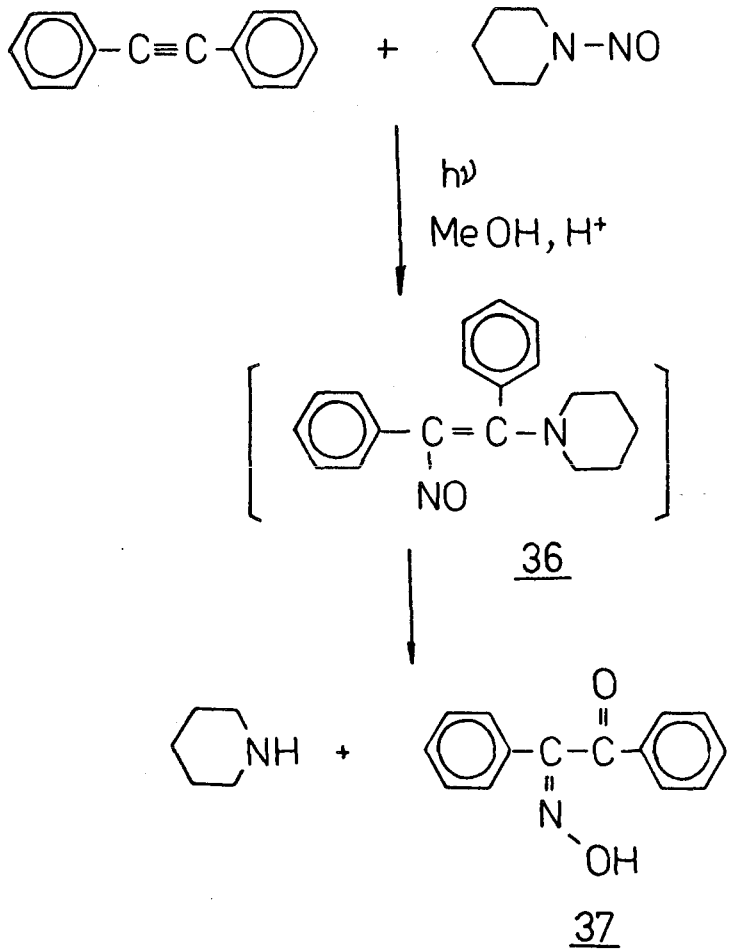
Scheme XVI



The photoaddition of N-nitrosopiperidine to diphenylacetylene gave, in good yield, benzil monoxime (37) which could be attributed to the hydrolysis

product of the primary adduct (36). The identity of this compound was confirmed by a mixed melting point with an authentic sample (17). The strong mass peaks at 105 and 103 can be assigned to fragments C_6H_5-CO^+ and $C_6H_5CN^+$.

Scheme XVII

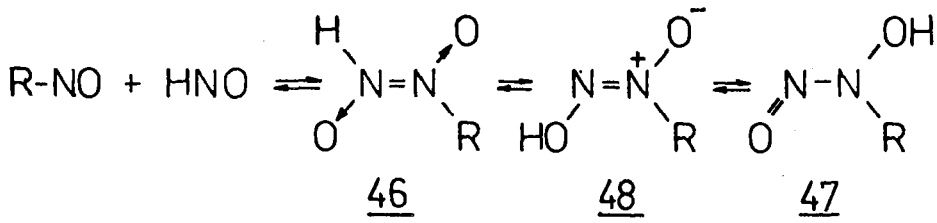


DISCUSSION

I. Addition of N-nitrosamines to simple olefins

A discussion on the structures of the oximes, the trans-dimer of the C-nitroso compounds and the N-nitrosohydroxylamines has been presented in the previous section. The experimental results and structural elucidations confirm that the primary photoadduct is a C-nitroso compound, as has been previously proposed (18). The blue to yellow photolysate obtained, particularly under low temperature photolysis conditions, provide visual confirmation of the presence of a C-nitroso compound in the solution.

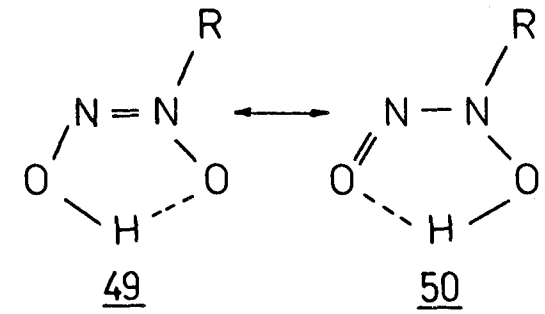
Tautomerization of C-nitroso compounds (19,20) to the syn- and anti-oximes (such as 8, 9, 14, 15, 21 and 22) and dimerization (19,20) to the trans-dimers (13 and 20) have been amply discussed in the publications emanating from this laboratory (21,4). The formation of an N-nitrosohydroxylamine from a C-nitroso compound requires addition of a molecule of HNO. Since HNO is the basic member of nitroso compounds, the first step of the reaction can be regarded, in a first approximation, as the formation of an azodioxy linkage (46) similar to that occuring in dimerization. Migration of the proton from the nitrogen atom to the oxygen atom and reorganization



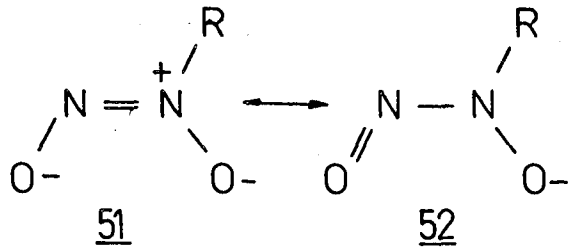
46 48 47

of the electron distribution can be visualized readily in various ways to give 48. N-Nitrosopiperidine has been shown to eliminate HNO when photolyzed in the presence of an acid which obviously supplies HNO required in the reaction (6). This view is confirmed in that 23 and 17 are formed when an excess of N-nitrosopiperidine was photolysed in the presence of dimers 20 and 13. From the data available, it is not known whether 23 and 17 have the structure 47 or 48. It is also possible to write the N-nitrosohydroxylamino group as a resonance hybrid of 49 and 50 (22). The similar resonance structures of anion 51 and 52 allow us to rationalize the acidity observed in 23a and 23b. The acidity of this proton is probably nearly the same or higher than carbonic acid ($K_1=4.30 \times 10^{-7}$) since the salt is formed in a sodium carbonate solution.

The discussion presented above explicitly assumes that the C-nitroso monomer, and not the dimer, is



49 50



51 52

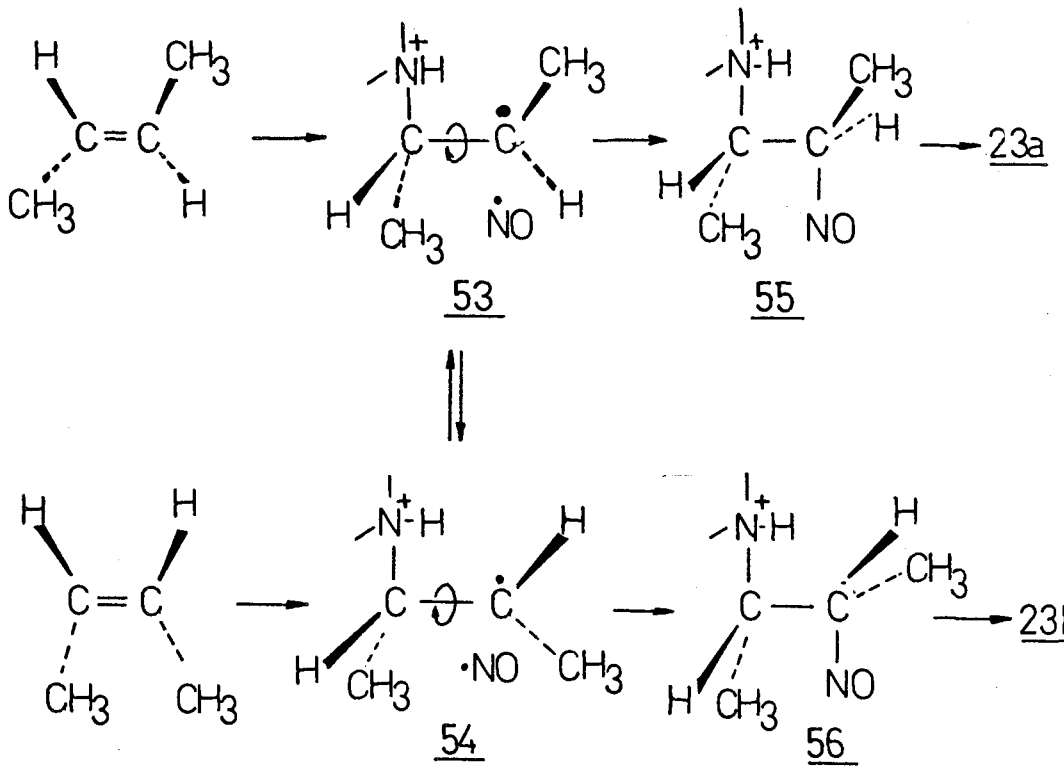
undergoing the secondary reactions. Since formation of 23 and 17 was realized only when the dimer peak at 292 nm was also irradiated in the presence of an excess of N-nitrosopiperidine, and since photocatalyzed dissociation of a dimeric C-nitroso compound to monomer is well known (23), it may reasonably be concluded that the C-nitroso monomer is the reactive species. The possibility that the formation of azodioxy compound 47 (or the general dimerization process) is a photocatalyzed process can be ruled out nor proved at this point. However it has been recognized that a C-nitroso compound rapidly and spontaneously sets up an equilibrium with the corresponding dimer in which the concentration of the dimer is more favored. Thus the pattern of the photo-addition of N-nitrosopiperidine to a simple olefin can

be defined as shown in Schemes VI and IX.

While the photoaddition of N-nitrosopiperidine to 1-hexene gives only one stereoisomer, the photoaddition to 2-butenes gave erythro (19a) or threo (19b) mixtures of the two isomers depending on the reaction mechanism. Since the stereochemical consequence of an addition often sheds more light on the addition mechanism, a considerable amount of experimentation has been carried out to define the stereochemistry of the addition. It is clear that the photoaddition to either cis- or trans-2-butene gives a mixture of the two stereoisomers. This was confirmed by the isolation of N-nitrosohydroxylamine derivatives 23a and 23b, whereas the analyses of the dimers 20 have not been successful due to the complexity of the n.m.r. spectra and to instability during the isolation process. The photoaddition is, therefore, non-stereospecific.

Although direct proof of the stereochemistry of 23a and 23b by i.r. dilution technique or by n.m.r. coupling constant has not been fruitful, the assignment of erythro to 23a and threo to 23b have been confirmed by the evidence presented. It follows that the photoaddition of N-nitrosopiperidine to trans-2-butene gives more erythro 23a, while that to cis-2-butene gives only slightly more threo-23b when a Uranium glass filter is used. A stepwise

trans-addition of nitrosamine to olefin (18) has been proposed. The results confirm this view and the mechanism of the addition can be explained by Scheme IX, assuming a free radical addition mechanism. The collapse of the radical pair 53 or 54 must be slow so that rotation around the C-C bond occurs to give 55 as well as 56. The extent of the rotation of the C-C bond is



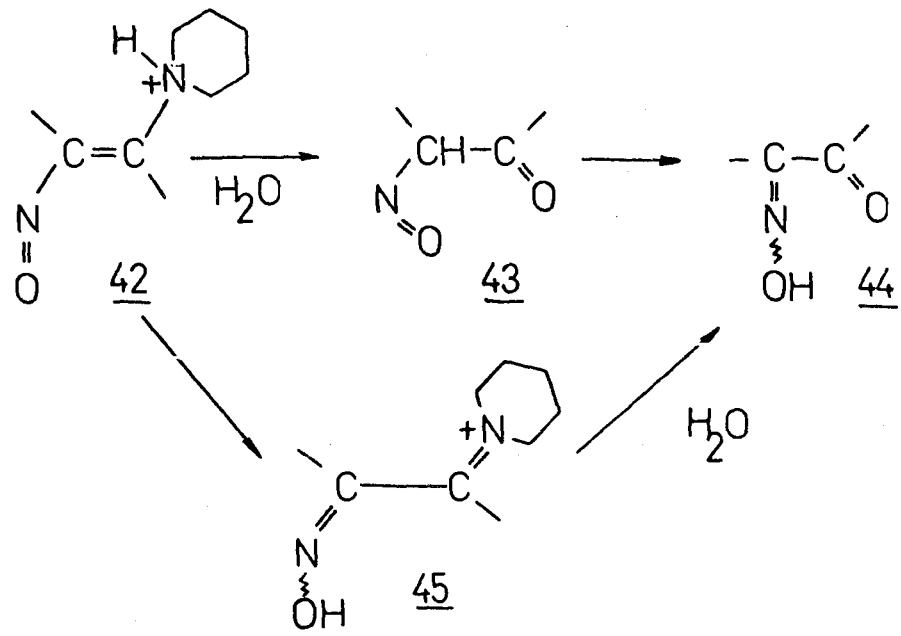
determined by steric factors and by the lifetime of 53 and 54; obviously cis- methyl groups exert a stronger interaction to cause more randomization giving a ratio

of 4:6 for 23a:23b. In comparison, the photoaddition of N-nitrosopiperidine to trans-2-butene results in a substantial retention of the configuration giving a ratio of 4:1 for 23a:23b when the solution was irradiated through a Uranium glass filter. When irradiated through a Corex filter, N-nitrosopiperidine possesses more excitation energy and 53 (as well as 54) has more vibrational energy to dissipate resulting in more loss of stereochemical purity. The observed ratio of 23a: 23b = 6:4 in the photoaddition to trans-2-butene under this condition is in good agreement with this argument.

It has been assumed that the photoaddition occurs by free radical mechanism. This assumption is deduced on the basis of the observation that neither ionic nor cyclic addition mechanisms are operative (18). For free radical addition, examples are known in which the degree of retention of the stereoisomerism is dependent on temperature; for example, the addition of DBr to cis-2-butene is stereospecific yielding pure isomer at -78° (24). In contrast, an erythro-threo ratio of 1:1 has been reported when the reaction is run at room temperature (25,26). It is expected that the photoaddition of a N-nitrosopiperidine to an olefin will be more stereospecific if the photolysis is carried out at a lower temperature. Such reactions should be tested in future.

II. Addition of N-Nitrosopiperidine to Simple Acetylenic Compounds

In contrast to the well investigated addition reaction to olefins, the addition reaction to acetylenes has been relatively neglected. Some typical addition reactions of methanol to acetylenic compounds has been reported in which methanol was added to photoexcited diphenylacetylene to give 1,2-diphenylvinylmethyl ether (27). In the present case, the photoaddition follows the same pattern as that to a simple olefin giving β-nitrosoenamines 27 and 36 as the primary photoadducts. This type of nitroso compound has not been reported previously and its behaviour is, a priori, not known. It is conceivable, however, that β-nitrosoenamine 42 can undergo hydrolysis followed by tautomerization to give an α-diketone monoxime (42 → 43 → 44). Alternatively, proton shift from the ammonium center to the nitroso group may take place, followed by the hydrolysis of the iminium linkage to give the oxime (42 → 45 → 44). Such reaction sequences are confirmed by the isolation of 32 and 37 as the major products which also proves the regiospecificity in the photoaddition. In the presence of an acid, the nitrosamine apparently undergoes a complex thermal reaction as shown by the isolation of various products 30-35. All these compounds can be

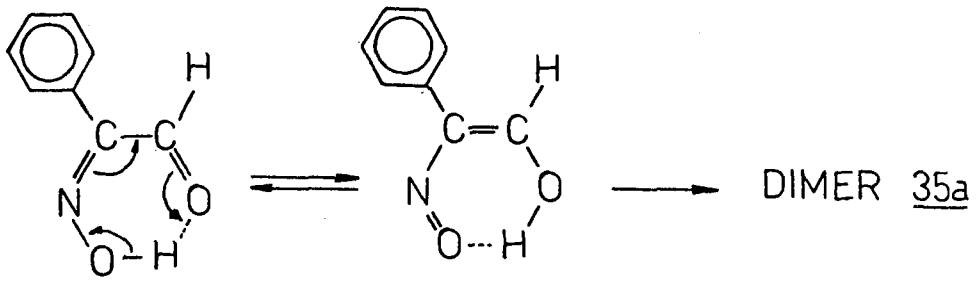


rationalized as being formed by an acid catalysed acetal formation, transoximation and addition reactions of β-nitrosoenamine 27.

The β-nitrosoenamine 27 apparently reacts extensively with phenylacetylene in the presence of an acid to give high melting products 28 and 29; the acid catalysis appears to be a necessary requirement for the formation since these compounds are not formed when the photolysate containing phenylacetylene is worked up in a neutral solution. Due to their limited solubility, purification of these products has not been successful, thus preventing structural elucidation. We have also shown that ketoxime 32 reacts with phenylacetylene in the presence of an acid

to give a high melting product. This reaction is being further studied.

The tautomeric structures can be written for the ketoxime, namely, the ketoxime-aldehyde structure 32 and the nitroso-enol structure 35. Since the transformation between these two compounds requires very little reorientation of atomic positions, it may be suggested that the ketoxime exists as a reasonable hybrid between 32 and 35. This resonance concept is supported by the observation of an i.r. absorption in solution at 1700 cm^{-1} which is a significantly lower frequency than the aldehyde absorption of phenylglyoxal (1730 cm^{-1}) (7,28). From a solution of 32 however, only dimer 35a crystallized indicating that this form is favored in the solid state. In solution, the dimer 35a apparently rapidly reverts to monomer 32 as can be seen from both the n.m.r. and the solution i.r. spectra. Also, on heating to 100-120°, dimer 35a gave an oily monomer which crystallized on cooling (32). This type of isomerism apparently has



32 35

been observed in p-dimethylaminophenylglyoxal aldoxime (29,30) in which the keto absorption is missing and in which the absorption at 1610 cm^{-1} shows with medium intensity in the solid state*. We also have observed that phenylglyoxal aldoxime exhibits 1655 (s) and 1675 cm^{-1} (sh) absorptions in $CHCl_3$ and 1235 (s) and 1675 cm^{-1}(s) in nujol; these data do not unambigiously show the presence of the reversible tautomerization-dimerization sequence as proposed above.

Phenylglyoxal derivatives 30, 31 and 33 are apparently derived from hydrolysis of the primary photoadduct 27. It is noteworthy that compound 30 contains the oximino group as well as the piperidine ring, while compound 31 contains the keto group and two methoxy groups. This suggests that the formation of these compounds is stepwise, and not random. Since the oximino group is generally not readily hydrolysed under the isolation conditions used, it is suspected that deoximation of 30 is assisted by participation of the neighboring piperidine ring which is then displaced by a methoxy group on addition of methanol followed by hydrolysis. A palusible mechanism is suggested below.

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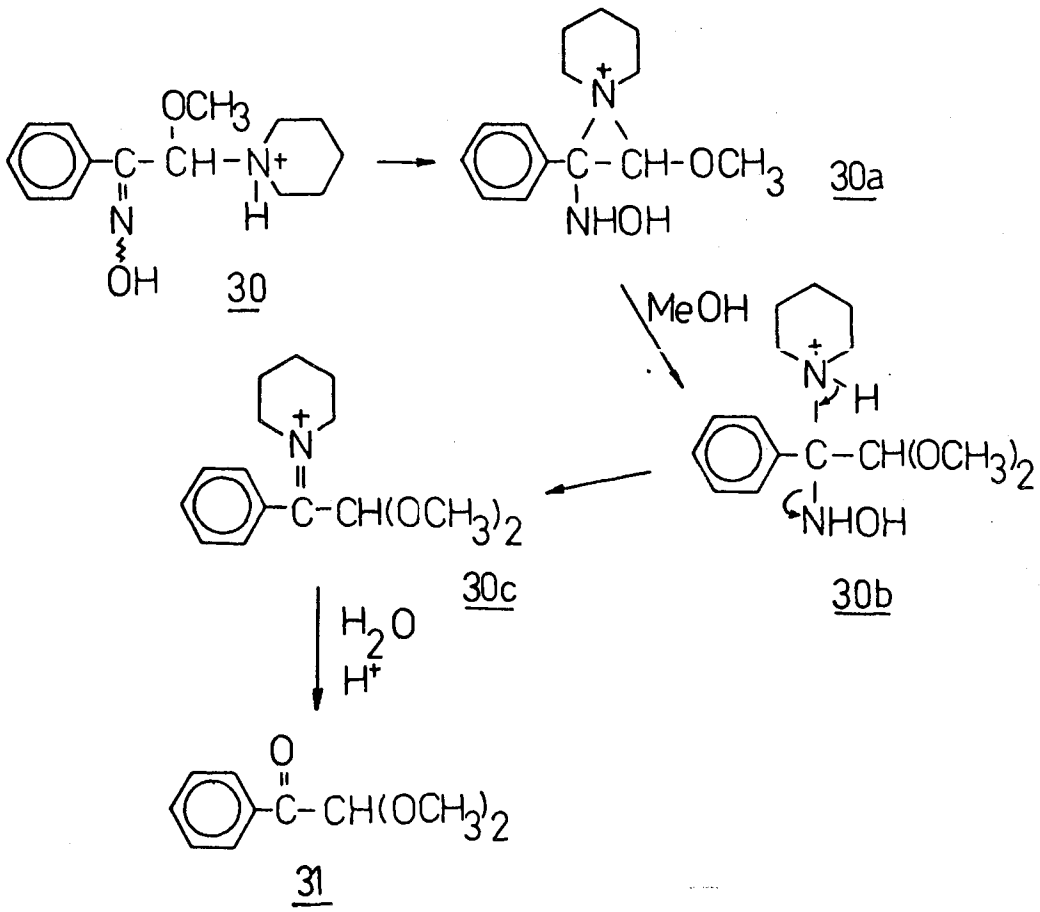
* Norman and his coworkers assigned this peak to the carbonyl stretching absorption. Because of the medium intensity, it is more reasonable to assign this band to the conjugated olefinic band.

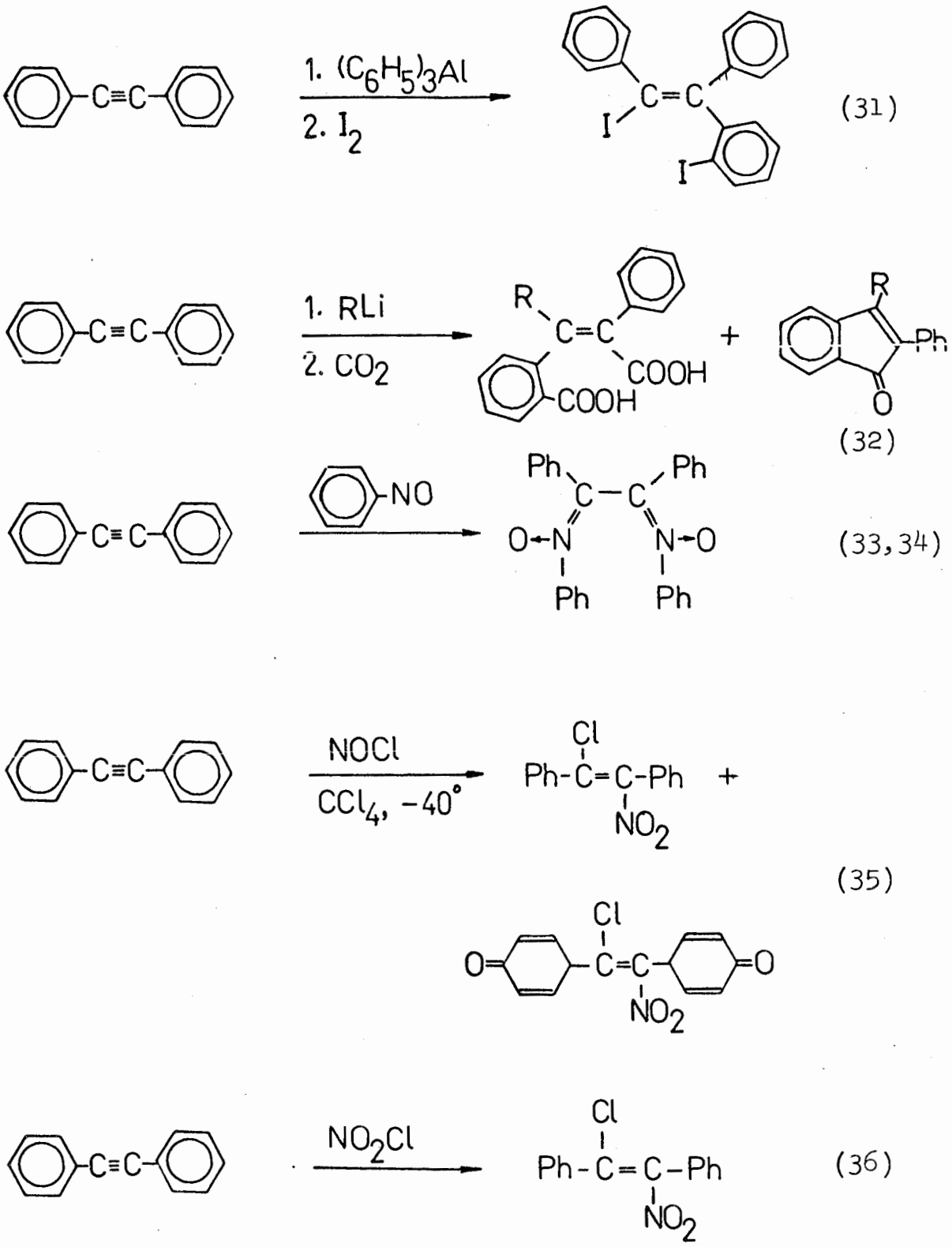


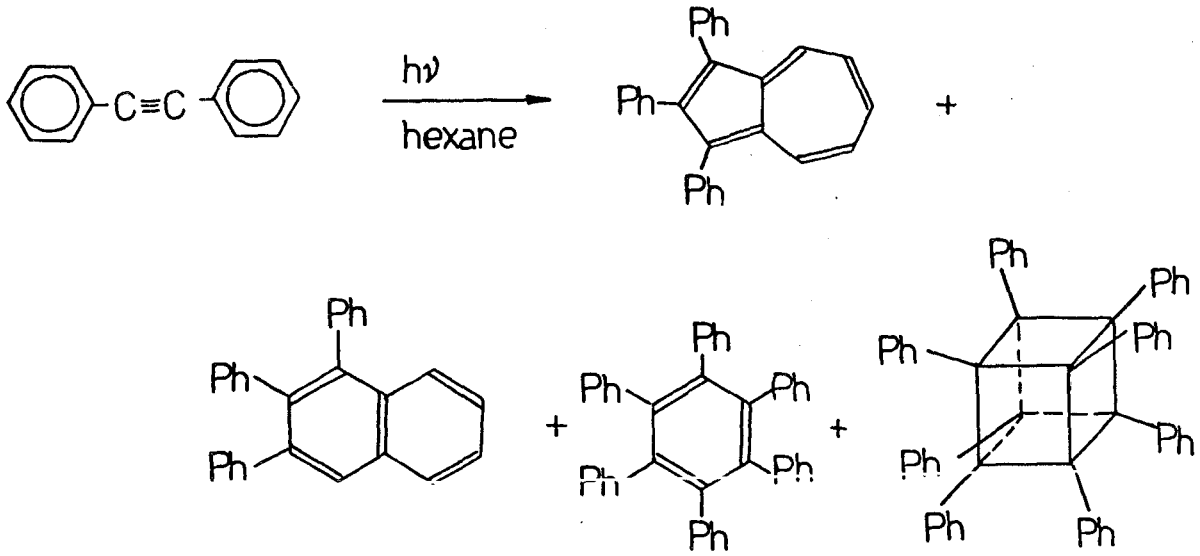
Dioxime 33 is probably formed from 32 by trans-oximation in which phenylglyoxal should also be fromed but was not isolated.

The formation of the N-nitrosohydroxylamine derivative 34 is analogous to that of 17 and 23 obtained in the previous photoaddition. The sequence of these reactions has been summarized previously. The formation of benzoic acid in one experiment requires cleavage and oxidation steps during the secondary reaction. At present, there is no ready explanation for this formation.

It is interesting to note that benzil monoxime 37 is the sole product obtained in good yield in spite of the fact that the photolysate had been isolated from an acidic medium. It is probable that the hydrolysis and tautomerization of the primary photoadduct 36 is very rapid and therefore the lifetime of 36 is not long enough to undergo side reactions. In conclusion, a preparation of α-diketo monoxime can be realized by the photoaddition of a nitrosamine to an acetylenic compound.

Scheme XVIII





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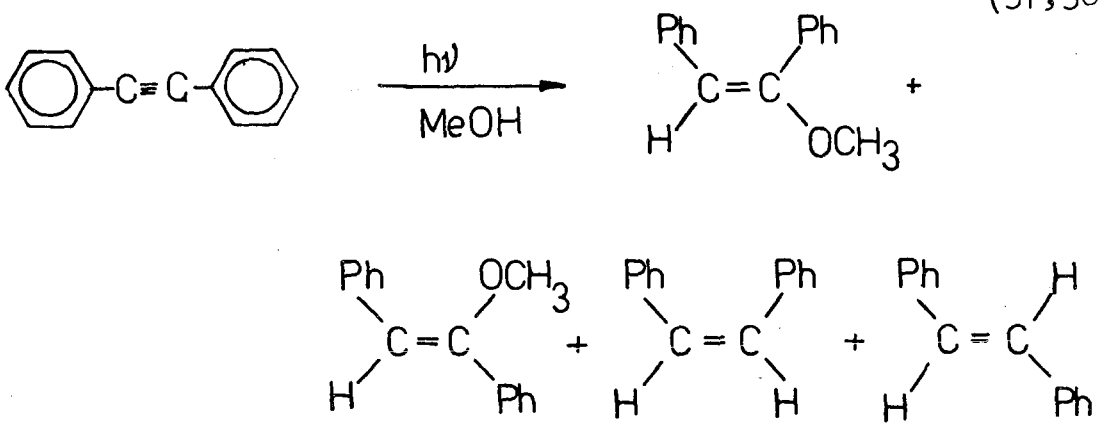
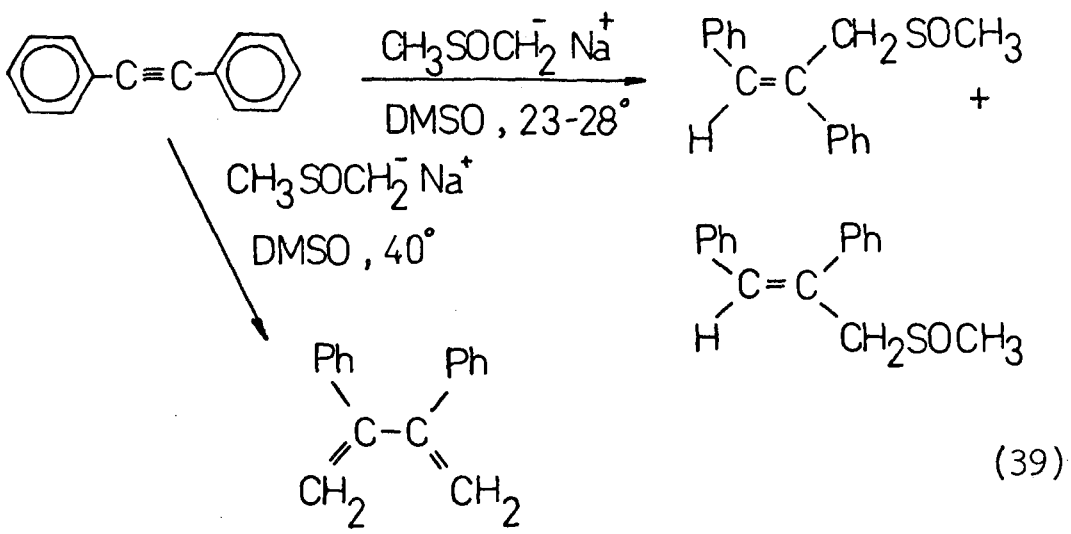
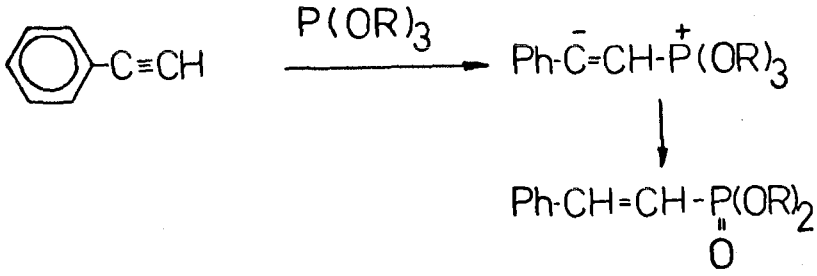


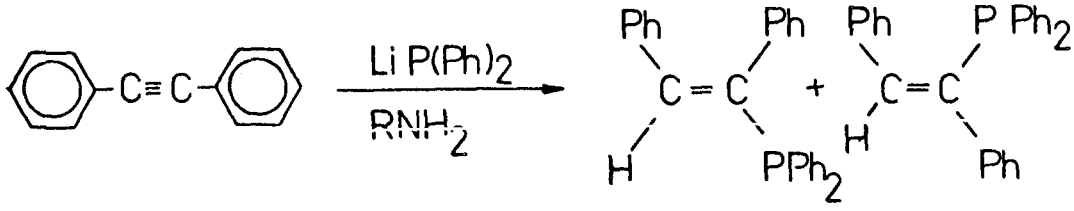
(27)



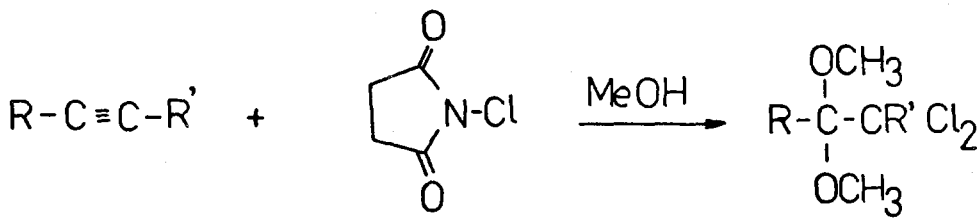
(39)



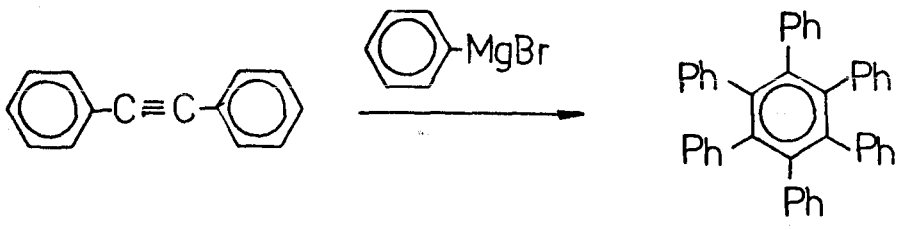
(40)



(41)



(42)



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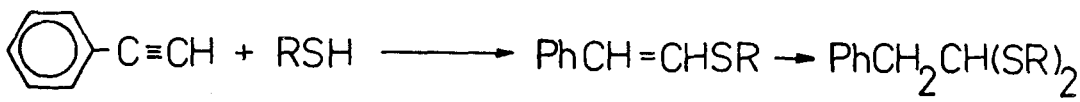

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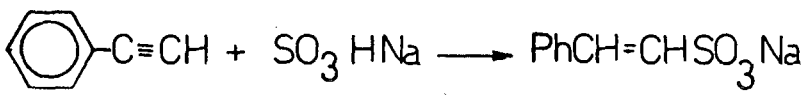

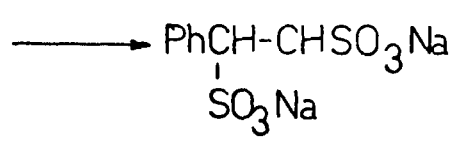

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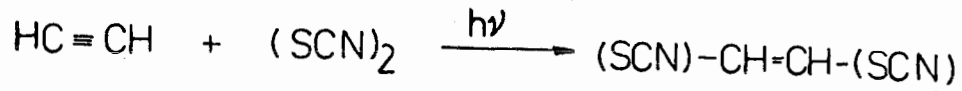
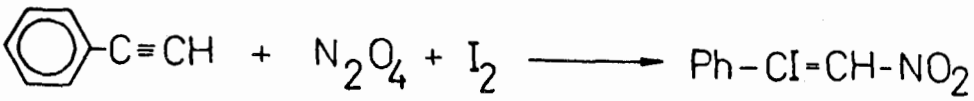


(47)



(48)

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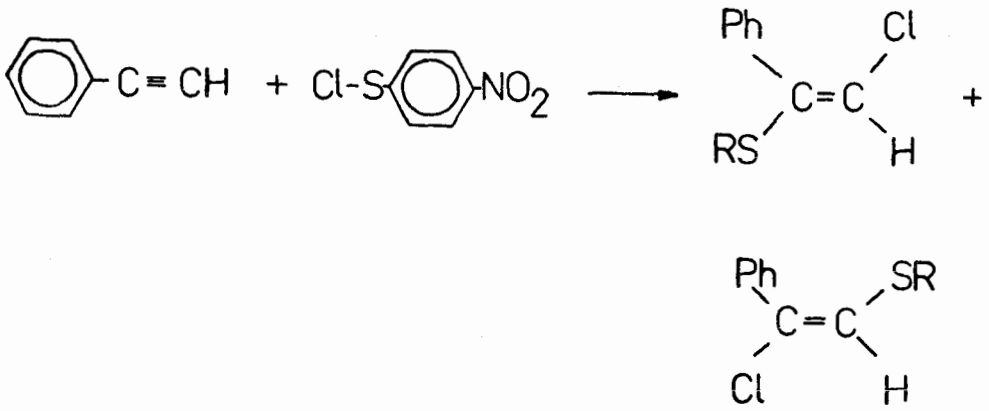

(51,52)

Experimental

I. General Conditions

Unless specified otherwise, the following experimental conditions prevailed.

(1) Infrared (i.r.) spectra were measured on a Unicam SP-200 or a Perkin Elmer 457 spectrophotometer in a liquid film or a nujol mull using NaCl windows. Only significant peaks are quoted from these spectra.

(2) Ultraviolet (u.v.) spectra were measured on a Unicam SP-800 instrument using a 10 mm cell and methanol as solvent.

(3) Nuclear magnetic resonance (n.m.r.) spectra were measured with a Varian A56/60 spectrometer in deuterochloroform. The chemical shifts are reported in τ values, the splitting patterns as s (singlet), b (broad), bs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (double doublet) and dq (double quartet) and the number of protons in the corresponding signals by H.

(4) Mass spectra were taken at 80 eV with a heated inlet using a Hitachi-Perkin-Elmer RMU-6D mass spectrometer. The significant peaks are reported and expressed ad m/e (relative intensity).

(5) Melting points were determined on a Gallenkamp heating block.

(6) Analytical thin-layer chromatography was performed on glass plates coated with silica gel using various solvent mixtures and developed by iodine vapor.

(7) Column chromatography using the conventional "wet column" technique was carried out on Mallinckrodt silicic acid (100 mesh) or Brockmann neutral alumina, activity 1 (80-200 mesh).

(8) The microanalyses were done by Dr. A. Bernhardt, Mikroanalytisches Laboratorium, West Germany.

II. The Chemicals

The following materials were used in the photolyses: Anethole from Eastman Organic Chemical was distilled at 128-129°/15 mm; 1-Hexene was obtained from Aldrich Chemical (H1260-9); trans- and cis-2-butenes from Matheson of Canada Ltd (Lecture Bottle); Phenylacetylene was distilled at 141.8-142.5°/750 mm; Diphenylacetylene was obtained from Aldrich Chemical (D20,480); N-nitroso-dimethylamine and N-nitrosopiperidine from Eastman Organic Chemical; Petroleum ether (30-60°) used in recrystallization was obtained from Allied Chemical.

III. Photolysis Apparatus

(1) Apparatus Type I:

The photolysis apparatus type I consists of a large cylindrical vessel fitted with a side arm in whcih a condenser is placed. A cold finger is inserted into the photolyzate (figure as shown in our previous publication)*. Nitrogen gas may be bubbled into the photolyzate through the gas inlet tube. A magnetic bar is used to stir the solution while the photolysis is proceeding. The lamp is inserted into the central sleeve of the cold finger. A filter solution, if required, is circulated through the cold finger. A glass filter can be inserted into the sleeve between the cold finger and the lamp.

(2) Apparatus Type II:

The apparatus type II consists of a flat, hamburger-shaped vessel fitted with a condenser and a gas inlet tube as shown in our earlier publication*. The whole vessel is immersed in running tap water for cooling purposes. The set-up is used only in conjunction with a Par 38 (100-W) spot lamp.

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* J.N.S. Tam's Ph.D. dissertation.

(3) Lamps used in the photolyses:

(i) Rayonet photochemical reactor lamp (cat. No. R.P.R.-3500A or 3100A).

(ii) Hanovia mercury lamp (200-W, cat. No. 654A-36 or 450-W, cat. No. 678A-36).

(iii) Mercury Par 38 projector bulb (100-W, H44-4GS).

(4) Fliters used in the photolyses:

(i) Nickel sulfate folution (276 g/l, as shown in figure VIII).

(ii) Uranium glass filter (the energy cut-off at ca.320 nm).

(iii) Corex glass filter (the energy cut-off at ca. 250 nm).

(iv) Soft glass filter (the energy cut-off at ca. 300 nm).

(v) Filter solution of 2,7-dimethyl-3,6-diaza-cycloheptan-1,6-diene perchlorate in water (1 mg/10 ml, figure VIII).

IV. General Procedure of Photolysis

A solution of nitrosamine (1 mole equiv.), olefin (0.4-1.2 mole equiv.) and acid (1 mole equiv.) in methanol (ca. 200 ml) was placed in a pyrex photolysis

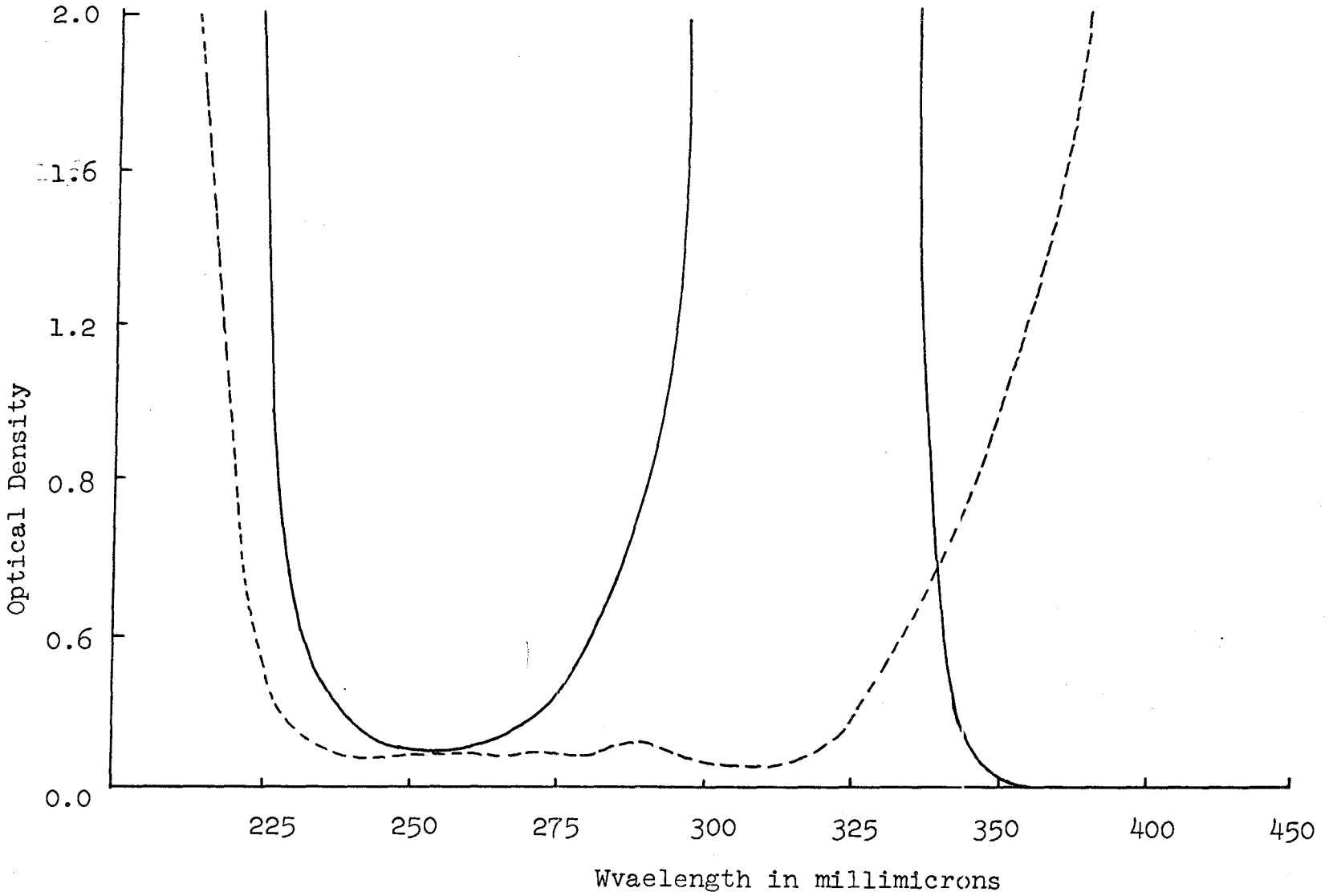

Figure VIII. Nickel Sulfate Filter Solution (-----) (276 g/l) and 2,7-Dimethyl-2,4-diazocyclohepta-1,6-diene perchlorate salt Filter solution (——) (0.1 g/l).

apparatus. The apparatus was externally cooled by placing it in an ice bath, an ice-salt bath or dry ice-methanol bath. The solution was agitated with a magnetic stirrer, and nitrogen, purified by passage through Fieser solution, was slowly bubbled through. Each photolysis solution showed a single u.v. absorption at 340-350 nm. Upon irradiation, the absorption decreased regularly to ca. 50-85% completion and was followed by periodically withdrawing an aliquot of the photolysate. The withdrawn sample was suitably diluted for the u.v. measurement in the region of 200-450 nm. Unless otherwise stated, the photolysis was continued until the characteristic N-nitrosamine absorption showed no further change.

To isolate the product from the photolysate, the solvent was removed under vacuum in a rotary evaporator at a bath temperature lower than 40°. In some cases, the protonated photoadducts crystallized immediately and were purified by recrystallization. In other cases, the residue was treated with water and the excess N-nitrosamines or olefins, if any, were removed by ether extraction. After rendering the aqueous phase basic with a saturated solution of sodium carbonate, the free base was extracted with methylene chloride. The aqueous solution was evaporated to dryness. The products were obtained by extraction of this residue with methylene chloride or 2-propanol. The crude photoadducts were

purified by chromatography or recrystallization. Generally, a small sample was further recrystallized from a suitable solvent followed by sublimation to afford a pure sample for analysis.

V. Addition of N-Nitrosodimethylamine to Anethole

A solution of N-nitrosodimethylamine (1.24 g, 17 mmoles), anethole (3.05 g, 21 mmoles) and concentrated hydrochloric acid (1.5 ml, 18 mmoles) in methanol (350 ml) was irradiated in an ice bath with a Rayonet lamp (350 nm) for 5 hours and 40 minutes. The photolysate was evaporated to dryness. Water (50 ml) was added and the aqueous solution was extracted with ether (3 x 25 ml). The combined ethereal solution was dried ($MgSO_4$) and evaporated to give the recovered anethole (0.63 g). The aqueous solution was adjusted with a saturated solution of sodium carbonate to pH 10, and extracted with methylene chloride (3 x 25 ml). The combined methylene chloride solution was evaporated to give a solid (2.97 g) which was taken up in benzene and chromatographed on a neutral alumina to give the following compounds in the order in which they were eluted:

(i) A solid (2.55 g, 68%) which was recrystallized from a benzene-cyclohexane mixture and was sublimed at 85°/0.1 mm to give syn-1-(p-methoxyphenyl)-2-N,N-dimethylaminopropan-1-one oxime (8): m.p. 93-94.5°; i.r. 1605,

1520, 1030, 954, 926 and 855 cm^{-1}; n.m.r. τ8.58 (d, J=7Hz, 3H), 7.63 (s, 6H), 6.45 (q, J=7Hz, 1H), 6.22 (s, 3H) and 2.83 (ABq, J=44 and 9Hz, 4H); m/e (%) 222 (M^+, 25), 205 (20), 189 (9), 176 (6), 163 (6), 147 (71), 133 (71), 115 (16), 103 (40), 90 (36), 78 (27) and 72 (100);

Anal. Calcd. for $C_{12}H_{18}N_2O_2$: C 64.84; H 8.16; N 12.60;
Found: C 65.06; H 8.27; N 12.46.

(ii) A solid (0.42 g, 11%) which was recrystallized from a benzene-cyclohexane mixture and sublimed at 90°/0.1 mm to give anti-1-(p-methoxyphenyl)-2-N,N-dimethylaminopropan-1-one oxime (9): m.p. 112.5-114°; i.r. 3300, 1620, 1525, 1260, 1182, 1038, 942 and 830 cm^{-1}; n.m.r. τ 8.82 (d, J=7Hz, 3H), 7.76 (s, 6H), 6.63 (q, J=7Hz, 1H), 6.23 (s, 3H) and 2.85 (AB q, J=35 and 9 H , 4H); m/e(%) 222(M^+,4), 205(100), 189(14), 179(14), 176 (24), 163(11), 147(8), 133(72), 118(10), 103(27), 90(30), 78(14) and 72(50).

The ratio of syn-oxime 8 and anti-oxime 9 was estimated from n.m.r. spectrum of the crude product to be 13:2.

(iii) an oil (trace) which was distilled at 85°/0.1 mm to give a colorless oil which was tentatively assigned as 1-(p-methoxyphenyl)-1-N,N-dimethylaminopropan-2-one oxime (11): i.r. 2940, 2870, 2830, 2780, 1675, 1600, 1510, 1455, 1260, 1235, 1170, 1100, 1030,

930 and 845 cm^{-1}; n.m.r. τ 8.62(s), 7.72(s), 6.30(s) and 2.85(AB q); m/e(%) 222(M^+, <1), 205(3), 176(2), 151(60), 148(100), 121(5), 107(5), 92(8), 77(15) and 72(10).

VI. Addition of N-Nitrosopiperidine to 1-Hexene

(i) A solution of N-nitrosopiperidine (9.45 g, 84 mmoles), 1-hexene (10.69 g, 128 mmoles) and concentrated hydrochloric acid (9 ml, 108 mmoles) in methanol (350 ml) was irradiated in an ice bath with a Hanovia lamp (450-W) through a Uranium flass filter for 190 minutes. The u.v. absorption at 348 nm decreased while a new absorption at 292 nm increased to a maximum after 3 hours of continuous irradiation. The solution was adjusted with a saturated solution of sodium carbonate to pH 7. The neutral solution was evaporated (ca. 20°) to ca. 30 ml. On standing, a solid (4.19 g) separated. The solid was filtered and was extracted with ether (3 x 25 ml). The combined ethereal solution was evaporated to give crystals (1.08 g, 8%) which was recrystallized from petroleum ether to give the dimer of 1-piperidino-2-nitrosohexane (13): m.p. 90-91°; i.r. 2810, 2770, 1380, 1240, 1185,1060 and 996 cm^{-1}; n.m.r. τ 9.04(t, J=5Hz, 3H), 8.55(broad, 12H), 7.55 (broad, 5H), 7.15(dd, J=10 and 13Hz, 1H) and 4.28(m, 1H); m/e(%) M^+ was absent, 198($\frac{1}{2}M^+$,2), 181(31), 164(5), 124 (5), 98(100) and 84(28);

Anal. Calcd. for $C_{22}H_{44}N_4O_2$: C 66.62; H 11.18; N 14.13;
Found: C 66.61; H 11.28; N 13.96.

The filtrate was evaporated to dryness and was taken up in water (100 ml). The aqueous solution was adjusted with saturated sodium carbonate solution to pH 10 and was extracted with methylene chloride (3 x 25 ml). The combined methylene chloride solution was dried ($MgSO_4$) and was evaporated to give an oil (11.22 g), a part of which (2.60 g) was chromatographed on a silicic acid column. With pure chloroform, three compounds were eluted in the following order:

(a) N-nitrosopiperidine (0.35 g).

(b) An oil (0.49 g, 15%) which was distilled at 85°/0.1 mm to give a colorless oil, syn-1-piperidino-2-hexanone oxime (14): i.r. 3240, 2930, 2870, 1645, 1120, 985 and 950 cm^{-1}; n.m.r. τ 9.10(t, J=5Hz, 3H), 8.50(broad, 12H), 7.60(broad, 4H), 6.77(s, 2H) and 2.15(bs, 1H, D_2O exchangeable); m/e(%) 198(M^+,6), 181(41), 127(12), 113 (14), 98(49), 84(77), 73(50) and 60(100).

This compound did not give a color reaction with a 2% solution of cupric sulfate.

(c) 1-piperidino-2-hexanone (16, trace): This compound was converted to a mixture of syn- and anti-oximes estimated from the n.m.r. spectrum to be in a ratio of 1:1 (53).

With 5% ethanol in chloroform, anti-1-piperidino-2-hexanone oxime (15, 1.10 g, 34%) was eluted and was

distilled at 85°/0.1 mm to give a colorless oil: i.r. 3220, 2930, 2860, 1650, 1455, 1010, 990 and 935 cm^{-1}; n.m.r. τ9.08(t, J=5Hz, 3H), 8.51(b, 12H), 7.60 (b,4H) 7.03(s,2H) and 2.25(bs,1H, D_2O exchangeable); m/e(%) (15 eV) 198(M^+,59), 181(100), 164(44), 156(21), 136(22), 124(18), 113(48), 98(79), 84(48), 73(18) and 60(35); Anal. Calcd. for $C_{11}H_{22}N_2O$: C 66.62; H 11.18; N 14.13;

Found: C 66.94; H 11.17; N 14.11.

This compound gave a green color on dissolving in a 2% solution of cupric sulfate.

With 10% ethanol in chloroform, a crude 1-piperidino-2-(N-nitrosohydroxylamino)-hexane (17, 0.39 g) was eluted: n.m.r. τ9.13(t, J=5Hz), 8.54(b), 7.55(b), 7.06(dd, J=8 and 10Hz), 5.67(m) and 2.01(s, D_2O exchangeable)(cf. below).

(ii) A solution of N-nitrosopiperidine (9.54 g, 84 mmoles), 1-hexene (10.67 g, 127 mmoles) and concentrated hydrochloric acid (9 ml, 108 mmoles) in methanol (350 ml) was irradiated in an ice-salt bath with a Hanovia lamp (450-W) through a Uranium glass filter for 2 hours and 30 minutes. During the photolysis, the u.v. absorption at 292 nm increased by ca. 2.5 times in intensity. On working up in the usual manner, the dimer 13 (2.61 g, 18%) was isolated. The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (1.43 g), oxime 14 (2.00 g, 14%), ketone 16 (1.01 g, 7%)

and oxime 15 (4.99 g, 36%).

(iii) A solution of N-nitrosopiperidine (9.57 g, 84 mmoles), 1-hexene (11.31 g, 135 mmoles) and concentrated hydrochloric acid (7 ml, 84 mmoles) in methanol (350 ml) was irradiated in an ice-salt bath with a Hanovia lamp (450-W) through a soft glass filter for 2 hours and 30 minutes. On working up in the usual manner, the dimer 13 (2.35 g, 14%) was isolated. The residue was evaporated and the aqueous solution was extracted to give an acidic and a basic fraction. The acidic fraction gave N-nitroso-piperidine (0.13 g) and the basic fraction was chromatographed on a silicic acid column to give oxime 14 (2.37 g, 17%), ketone (16, trace) and oxime 15 (6 g, 36%).

(iv) A solution of N-nitrosopiperidine (9.57 g, 84 mmoles), 1-hexene (11.10 g, 132 mmoles) and p-toluene-sulfonic acid (16.14 g, 85 mmoles) in methanol (200 ml) was irradiated in an ice-salt bath with a Hanovia lamp (450-W) through a Uranium glass filter for 2 hours and 30 minutes. The photolysate was evaporated to dryness and 2-propanol (30 ml) was added to give a solid (12.55 g). This solid was purified by recrystallization from ethanol to give a p-toluenesulfonate of the dimer 13: m.p. 105.5-107°; i.r. 2720, 1228, 1190, 1125, 1035, 1010, 820 and

685 cm^{-1}; n.m.r. (D_2O) τ9.14(t, J=5Hz, 3H), 8.35(b, 12H), 7.67(b, 3H), 6.92(b,5H), 6.12(dd, J=10 and 14 Hz, 1H), 3.42(d, J=8Hz, 1H) and 2.52(AB q, J=26 and 8Hz, 4H). This solid was made basic to give dimer 13 (3.40 g, 28%).

The filtrate was worked up in the usual manner to give N-nitrosopiperidine (2.40 g), oxime 14 (0.61 g, 5%) and oxime 15 (2.44 g, 21%).

(v) A solution of N-nitrosopiperidine (9.61 g, 84 mmoles), 1-hexene (11.10 g, 132 mmoles) and p-toluenesulfonic acid (16.14 g, 85 mmoles) in methanol (200 ml) was irradiated in an ice-salt bath with a Hanovia lamp (450-W) through a Corex glass filter for 2 hours and 30 minutes. The photolysate was evaporated to dryness, and acetone (30 ml) was added. The precipitated solid (4.98 g) was filtered. The solid was adjusted to pH 10 and was extracted with methylene chloride (3 x 25 ml). The solid (2.48 g, 24%) obtained from the combined methylene chloride layer was recrystallized from ethanol to give the sodium salt of 1-piperidino-2-(N-nitrosohydroxylamino)-hexane 17: m.p. 249-250.5°; i.r. 3400, 1650, 1242, 1180, 978 and 943 cm^{-1}; n.m.r. τ9.15 (t, J=5Hz, 3H), 8.55 (b, 12H), 7.56(b, 5H), 7.06(m, 1H) and 5.76(b, 1H, D_2O exchangeable;

Anal. Calcd. for $C_{11}H_{22}N_3O_2Na$: C 52.52; H 8.75; N 16.71; Na 9.15; Found: C 52.52; H 8.74; N 16.65;

Na 9.01.

An aqueous solution of this sodium salt was neutralized with dilute hydrochloric acid to pH 7 and was evaporated to dryness. The residue was extracted with methylene chloride (3 x 25 ml). The oil obtained from the combined methylene chloride solution was chromatographed on a silicic acid column and was sublimed at 85°/0.1 mm to give a solid 1-piperidino-2-(N-nitroso-hydroxyl)-hexane (17): m.p. 64.5-65.5°; i.r. ($CHCl_3$) 2950, 2870, 2810, 1450, 1065, 1045 and 655 cm^{-1}; n.m.r. τ 9.13(t, J=5Hz, 3H), 8.62(b, 12H), 7.54(b,5H), 6.93 (dd, J=9 and 13Hz), 5.55 (m, 1H) and -0.60 (s,1H,D_2O exchangeable); m/e(%) 229(M^+, 0.5), 212(0.5), 181(1), 168(5), 155(6), 138(8), 124(29), 105(6), 98(100) and 84(9);

Anal. Calcd. for $C_{11}H_{23}N_3O_2$: C 57.61; H 10.11; N 18.32;
Found: C 57.53; H 9.95; N 18.21.

The acetone filtrate was evaporated to dryness and was worked up in the usual manner to give oxime 14 (2.36 g, 15%), ketone 16 (trace), oxime 15 (6.70 g, 42%), unknown (A, 0.12 g) and unknown (B, trace). Unknown A was re-chromatographed on a silicic acid column, followed by preparative t.l.c. and was distilled at 75°/0.1 mm to give a colorless oil: i.r. 1660, 1540, 1450, 1360, 1260, 1140, 1085, 980 and 860 cm^{-1}; n.m.r. τ 9.12 (t, J=5Hz, 3H), 8.45 (b, 10H), 7.80 (b, 3H), 7.12 (b, 3H),

6.74 (b, 1H) and 3.14 (t, J=5.5Hz, 1H); m/e(%) 168 (4), 153 (4), 151 (4), 139 (11), 126 (34), 111(11), 99(11) and 84 (100). The unknown B was distilled at 80°/0.1 mm to give an oil: i.r. 3400, 2900, 2840, 2750, 1660, 1300, 1150, 1040, 1000, 860 and 780 cm^{-1}; n.m.r. τ 9.12 (t, J=4.5Hz), 8.60 (b), 7.65 (b), 7.20 (m), 6.42 (b) and 2.20 (b, D_2O exchangeable).

(vi) Photolysis of dimer 13:

(a) A solution of the p-toluenesulfonate of the dimer 13 (0.74 g, 0.95 mmole), N-nitrosopiperidine (0.12 g, 1 mmole) and concentrated hydrochloric acid (0.1 ml, 1.2 mmoles) in methanol (100 ml) was irradiated in an ice bath with a Rayonet lamp (310 nm) through a nickel sulfate filter solution for 27 hours. The unreacted dimer 13 salt (0.12 g) was filtered. The filtrate was worked up in the usual manner to give the acidic and the basic fractions. The acidic fraction gave N-nitrosopiperidine (0.10 g, 87% recovered). The basic fraction gave a mixture of oximes 14 and 15 (0.24 g, 71%) in a ratio of 1:1 as shown by the n.m.r. spectrum of the crude product.

(b) A solution of the p-toluenesulfonate of the dimer 13 (0.35 g, 0.45 mmole) in methanol (43 ml) was irradiated with a Hanovia lamp (100-W) for 1 hour and

20 minutes. The solution was worked up in the usual manner to give a mixture of oxime 14 and oxime 15 (0.12 g, 64%) in the ratio of 1:1 (estimated from the n.m.r. spectrum of the crude product).

(c) A solution of the p-toluenesulfonate of dimer 13 (0.96 g, 1.3 mmoles), N-nitrosopiperidine (0.47 g, 4.1 mmoles) and concentrated hydrochloric acid (0.45 g, 5.2 mmoles) in methanol (100 ml) was irradiated in an ice bath with a Hanovia lamp (200-W) through a nickel sulfate filter solution for 1 hour and 10 minutes. On working up in the usual manner, it gave N-nitrosopiperidine (0.19 g) and a basic fraction (0.38 g) which gave oximes 14 and 15. The aqueous solution was neutralized to pH 7 with dilute hydrochloric acid and was evaporated to dryness. The residue was extracted with methylene chloride (3 x 25 ml) and the combined methylene chloride fractions were evaporated to give a solid (40 mg) which was recrystallized from petroleum ether to give N-nitroso-hydroxylamine derivative 17. This was confirmed by n.m.r. spectroscopy.

(d) A solution of dimer 13 (1.95 g, 2.9 mmoles), N-nitrosopiperidine (2.00g, 17.5 mmoles) and concentrated hydrochlroic acid (2.4 ml, 28.8 mmoles) in methanol (120 ml) was irradiated in an ice-salt bath with a Rayonet lamp (350 nm) for 10 hours. The photolysate was

evaporated to dryness and acetone (30 ml) was added. The precipitated piperidine hydrochloride (0.58 g) was filtered. The filtrate was evaporated to dryness. On working up in the usual manner, it gave an acidic fraction which gave N-nitrosopiperidine (30 mg). The basic fraction was chromatographed on a silicic acid column to give unknown (X), N-formamido-piperidine (18, 0.15 g), oxime 14 (50 mg, 5%), ketone 16 (20 mg, 2%), oxime 15 (190 mg, 20%) and N-nitrosohydroxylamine derivative 17 (0.28 g). The unknown X showed i.r. absorptions at 2930, 2850, 2810, 1650, 1575, 1440, 1355, 1110, 1070, 965 and 900 cm^{-1}; n.m.r. signals at τ 8.44 (b, 10H), 7.00 (b, 5H) and 3.69 (AB q, J=11.5 and 15.5 Hz, 2H) and decomposed on attempted distillation at 90°/0.1 mm. The mass spectrum of unknown X showed intense mass peaks m/e(%), 268 (2), 211 (6), 196 (9), 154 (13), 141 (10), 139 (9), 126 (11), 112 (14), 99 (42) and 83 (100). From the residue fraction, compound 18 (0.13 g) and N-nitrosohydroxylamine derivative 17 (0.63 g) were obtained. The overall yield of compound 18 was 0.28 g (8%) and that of the nitrosohydroxylamine derivative 17 was 0.91 g (69%).

(vii) A solution of N-nitrosopiperidine (10.57 g, 93 mmoles), 1-hexene (3.09 g, 37 mmoles) and p-toluenesulfonic acid (17.67 g, 93 mmoles) in methanol (210 ml) was irradiated in an ice-salt bath with a Hanovia lamp (200-W) through a pyrex filter for 3 hours and 30 minutes. On

working up in the the usual manner, N-nitrosopiperidine (1.38 g) was obtained from the acidic fraction. The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (0.94 g), unknown X (0.90 g), compound 18 (0.49 g), ketone 16 (0.12 g, 2%), a mixture of oximes 14 and 15 (0.49 g, 7%) and the N-nitrosohydroxylamine derivative 17 (1.38 g). The residue fraction was worked up in the usual manner to give piperidine p-toluenesulfonate (4.37 g), compound 18 (trace) and the N-nitrosohydroxylamine derivative 17 (2.21 g). The overall yield of the N-nitrosohydroxylamine derivative 17 was 3.59 g (47%); compound 18, 0.50 g (5%).

VII. Addition of N-Nitrosopiperidine to Trans-2-butene

(i) A solution of N-nitrosopiperidine (9.67 g, 85 mmoles), a large excess of trans-2-butene (15 g, 268 mmoles) and p-toluenesulfonic acid (16.15 g, 85 mmoles) in methanol (200 ml) was irradiated in an ice bath with a Hanovia lamp (450-W) through a Unranium filter for 2 hours and 50 minutes. The N-nitroso peak at 348 nm in the u.v. spectrum decreased steadily while the new absorption at 292 nm increased to a maximum after 2 hours and 30 min. irradiation. The photolysate was evaporated to dryness and acetone (30 ml) was added to the residue. The precipitated solid (14.38 g) was filtered, then adjusted in aqueous solution to pH 10. The basic solution was

extracted with methylene chloride to give crystals (6.30 g) which were recrystallized twice from petroleum ether to give anti-2-piperidinobutan-3-one oxime (21): m.p. 87-88°; i.r. 3160, 1649, 1128, 1108, 1092, 1074, 980, 945, 922, 910 and 780 cm^{-1}; n.m.r. τ 8.95 (d, J= 6.5Hz, 3H), 8.66 (b, 6H), 8.27 (s, 3H), 7.73 (b, 4H), 7.12 (q, J=6.5Hz, 1H) and 0.45 (bs, 1H, D_2O exchangeable): m/e(%) 170 (M^+, 6), 153 (66), 137 (16), 112 (100), 96 (10), 84 (59), 69 (9), 55 (18) and 41 (30);

Anal. Calcd. for $C_9H_{18}N_2O$: C 63.49; H 10.66; N 16.45;
Found: C 63.42; H 10.71; N 16.40.

This compound gave a green color on dissolution in 2% cupric sulfate solution. The aqueous solution was evaporated to dryness and was extracted with 2-propanol (3 x 25 ml). The combined 2-propanol solution was evaporated to give sodium p-toluenesulfonate (2.16 g).

The acetone filtrate was reduced to ca. 10 ml. The second precipitate (2.38 g) was filtered and was adjusted in aqueous solution to pH 10 to give a solid (0.40 g) which was recrystallized from petroleum ether to give the nitroso dimer of 2-nitroso-3-piperidinobutane (20a): m.p. 156.5-158.5°; i.r. 1380, 1220, 1190, 1170, 1110 and 1060 cm^{-1}; n.m.r. τ 9.07 (d, J=7Hz, 3H), 8.74 (d, J=7Hz, 3H), 8.63 (b, 6H), 7.56 (b, 4H), 6.95 (dq, J=7 and 10Hz, 1H) and 4.35 (dq, J=6.6 and 10Hz, 1H); m/e(%) M^+ was absent, 137 (7), 122 (18), 112 (43), 96 (100), 84 (44) and 82 (57);

Anal. Calcd. for $C_{18}H_{36}N_4O_2$: C 63.49; H 10.66; N 16.45;
Found: C 63.71; H 10.56; N 16.28.

The aqueous solution was extracted with methylene chloride and the combined methylene chloride extracts were evaporated to give oxime 21 (0.83 g).

The acetone filtrate was then evaporated to dryness and the residue was worked up in the usual manner to give an acidic and a basic fraction by extraction. The acidic fraction gave N-nitrosopiperidine (0.49 g). The basic fraction (2.30 g) was treated with ether to give a solid (0.12 g) which was recrystallized from petroleum ether twice to give the dimer of 2-nitroso-3-piperidino-butane (20b): m.p. 104.5-106.5°; i.r. 2790, 2760, 1370, 1223, 1190, 1108, 1060, 1032, 855 and 760 cm^{-1}; n.m.r. τ 9.12 and 9.07 (d, J=6.5Hz, combined intensity 3H), 8.76 and 8.56 (d, J=6.5Hz, combined intensity 3H), 8.60 (b, 6H), 7.57 (b) and 7.16 (dq, J=6.5 and 10Hz, combined intensity 5H) and 4.57 (dq, J=6.5 and 10Hz, 1H); m/e (%) 170 (0.5), 153 (1), 140 (4), 124 (2), 112 (100), 96 (26), 84 (5) and 82 (12). Silica gel t.l.c. of this compound using 5% ethanol in chloroform as eluent showed one spot. Two dimensional t.l.c. showed four spots. The ether filtrate was evaporated to give a solid (1.98g) which was chromatographed on a silicic acid column. With pure chloroform, N-nitrosopiperidine (40 mg) was eluted first, followed by the dimer 20b (40 mg). With

5% ethanol in chloroform, a solid (0.22 g, 2%) was obtained and was recrystallized from petroleum ether and sublimed at 75°/0.1mm to give syn-2-piperidino-3-butanone oxime (22): m.p. 68.5-69.5°; i.r. 3160, 3050, 1650, 1332, 1217, 1125, 1110, 1070, 992, 935 and 788 cm^{-1}; n.m.r. τ 8.80 (d, J=6.5Hz, 3H), 8.53 (broad, 6H), 8.20 (s, 3H), 7.57 (broad, 4H) and 6.67 (q, J=6.5Hz, 1H); m/e (%) 170 (M^+, 4), 153 (13), 112 (100), 96 (49), 84 (26), 69 (18), 55 (24) and 41 (70). With 10% ethanol in chloroform, oxime 21 (0.52 g) was eluted. The first fraction of oxime 21 contained what appeared to be 2-piperidino-3-butanone (26, trace) as indicated by the n.m.r. signal at τ 6.32 and i.r. absorption at 1700 cm^{-1}.

The aqueous solution was evaporated to dryness, and the residue was extracted with 2-propanol. The 2-propanol solution was evaporated to give sodium p-toluenesulfonate.

The overall yield of dimer 20a was 0.44 g (3%), dimer 20b 0.19 g (1%), oxime 21 7.65 g (56%) and oxime 22 0.22 g (2%).

(ii) A solution of N-nitrosopiperidine (19.13 g, 168 mmoles), trans-2-butene (3.5 g, 60 mmoles) and anhydrous hydrogen chloride (200 mmoles) in methanol (220 ml) was irradiated in a dry ice-methanol bath with a Rayonet lamp (350 nm) for 23 hours and 15 minutes. The dimer peak at 292 nm increased to a maximum after 9 hours irradiation

and then decreased slowly to nil. The photolysate was evaporated and worked up in the usual manner to give an acidic, a basic and a residue fraction. The acidic fraction gave N-nitrosopiperidine (5.40 g). The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (0.87 g), syn-oxime 22 (2.32 g, 22%) and anti-oxime 21 (5.27 g, 50%). The first fraction of oxime 21 contained a trace of ketone 26 as indicated by the n.m.r. signal at τ6.32 and the i.r. absorption at 1700 cm^{-1}.

The residue fraction was chromatographed on a silicic acid column. With 1% ethanol in chloroform, compound 18 (trace) was eluted. With 2% ethanol in chloroform, two compounds were eluted in the following order:

(a) An oil which was sublimed at 110°/0.1 mm to give crystalline threo-2-piperidino-3-(N-nitrosohydroxylamino)-butane (23b): m.p. 54.5-55.5°; i.r. 1310, 1180, 1090, 1065, 1040, 940 and 700 cm^{-1}; n.m.r. τ 9.17 (d, J=6.5Hz, 3H), 8.52 (b, 6H), 8.47 (d, J=6.5Hz, 3H), 7.54 (b, 4H), 7.02 (dq, J=6.5 and 10Hz, 1H), 5.72 (dq, J= 6.5 and 10 Hz, 1H) and -0.15 (s, 1H, D_2O exchangeable); m/e(%) 201 (M^+, 0.4), 172 (0.6), 140 (2), 124 (4), 112 (100), 96 (4) and 84 (5). The decoupling experiments at 100 Mc are shown in Figure VII.

Anal. Calcd. for $C_9H_{19}N_3O_2$: C 53.71; H 9.52; N 20.88;
Found: C 53.91; H 9.30; N 21.02.

The threo-isomer 23b did not give a color reaction with 2% cupric sulfate solution. A dilution study of the i.r. spectrum of 23b is shown in Figure IV. The chemical shift of the hydroxyl group varied from τ 0.40 to -1.40 with a ten fold concentration change of 23b in $CDCl_3$. An aqueous solution of the threo-isomer 23b (0.1 g) was adjusted with a saturated solution of sodium carbonate to pH 10. The solution was evaporated to dryness and the residue was extracted with methylene chloride. The combined methylene chloride extracts were evaporated to give recovered threo-isomer 23b (41 mg). The residue was extracted again with hot 2-propanol to give a solid (51 mg) which was recrystallized from ethanol to give the sodium salt of threo-2-piperidino-3-(n-nitrosohydroxylamino)-butane (24b): m.p. 287-291°; i.r. 2820, 1430, 1260, 1200, 1110, 1045, 965 and 730 cm^{-1}; n.m.r. (D_2O) τ 9.07 (d, J=6.5Hz, 3H), 8.60 (d, J=6.5Hz) and 8.54 (b, combined intensity 9H), 7.47 (b, 4H), 7.07 (m, 1H) and 5.58 (m, 1H).

(b) An oil which was sublimed at 95°/0.1 mm to give crystalline erythro-2-piperidino-3-(N-nitrosohydroxylamino)-butane (23a): m.p. 34-35.5°; i.r. 3450, 1650, 1390, 1270, 1175, 1105, 1055, 1040, 955 and 710 cm^{-1}; n.m.r. (see Figure VI): τ 9.02 (d, J=6.5Hz, 3H), 8.62 (d, J=6.5Hz, 3H), 8.59 (b, 6H), 7.58 (b, 4H), 6.92 (dq, J=6.5 and 10Hz, 1H), 5.62 (dq, J=6.5 and 10Hz, 1H) and 0.20 (bs, 1H, D_2O exchangeable); m/e(%) 201 (M^+, 2), 169 (3), 153 (5), 149 (6), 139 (14), 124 (48), 112 (100), 96 (20)

and 84 (34);

Anal. Calcd. for $C_9H_{19}N_3O_2$: C 53.71; H 9.52; N 20.88;
Found: C 53.58; H 9.64; N 20.74.

The erythro-isomer 23a gave a green color on dissolving in 2% cupric sulfate solution. The dilution study of the i.r. spectrum is shown in Figure V. The chemical shift of the hydroxyl group proton varied from τ0.20 to 2.00 with a ten fold concentration change. An aqueous solution of the isomer 23a (63 mg) was adjusted with a saturated solution of sodium carbonate to pH 10. The solution was evaporated and the residue was extracted to give a solid (61 mg) which was recrystallized from ethanol once to give the sodium salt of erythro-2-piperidino-3-(N-nitrosohydroxylamino)-butane (24a): m.p. 243-246°; i.r. 1265, 1190, 965 and 730 cm^{-1}; n.m.r. (D_2O) τ8.91 (d, J=6.5Hz, 3H), 8.70 (d, J=6.5Hz, 3H), 8.56 (b, 6H), 7.41 (b, 4H), 6.88 (m, 1H) and 5.5 (m, 1H). The crude solid was essentially the pure sodium salt 24a.

The overall yield of these two isomers was 0.36 g (3%) and the ratio of threo-isomer to erythro-isomer was 23:77.

(iii) A solution of N-nitrosopiperidine (15.56 g, 136 mmoles), trans-2-butene (3 g, 53 mmoles) and dry hydrogen chloride (53 mmoles) in methanol (210 ml) was irradiated

in a dry ice-methanol bath with a Hanovia lamp (450-W) through a soft glass filter for 3 hours and 40 minutes. The u.v. spectra of the solution during the photolysis showed patterns similar to those in (ii). The photolysate was worked up in the usual manner to give an acidic, a basic and a residue fraction. The acidic fraction gave N-nitrosopiperidine (1.04 g). The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (0.48 g), unknown X (0.50 g), an oil (0.68 g) and a mixture of oximes 22 and 21 (3.08 g, 34%). The presence of ketone 26 in a fraction of 21 was indicated by the n.m.r. (τ 6.32) and i.r. (1700 cm^{-1}) spectra. The oil was distilled at 90°/0.1 mm to give 2-(N-piperidino-imino)-3-butanone (25): i.r. 2920, 2805, 1680, 1580, 1445, 1355, 1290, 1100, 1075 and 1020 cm^{-1}; n.m.r. τ 8.40 (b, 6H), 8.04 (s, 3H), 7.70 (s, 3H) and 6.92 (b, 4H); m/e (%) 168 (M^+, 5), 149 (4), 125 (5), 104 (4), 98 (4) and 84 (100).

The residue fraction was chromatographed on a silicic acid column to give compound 18 (61 mg), threo-isomer 23b (0.1 g, 1%) and erythro-isomer 23a (0.52 g, 6%). The ratio of threo-isomer to erythro-isomer was 1:6.

(iv) A solution of N-nitrosopiperidine (30.44 g, 260 mmoles), trans-2-butene (6 g, 107 mmoles) and p-toluene-sulfonic acid (49.77 g, 260 mmoles) in methanol (200 ml)

was irradiated in a dry ice-methanol bath with a Hanovia lamp (450-W) through a Corex filter for 2 hours and 20 minutes. The u.v. spectra of the solution during the photolysis showed a pattern similar to (ii). The photolysate was worked up in the usual manner to give an acidic, a basic and a residue fraction. The acidic fraction gave N-nitrosopiperidine (6.65 g). The basic fraction contained N-nitrosopiperidine (10.75 g) and a mixture of oximes 22 and 21 (13.25 g, 70%) as estimated from the n.m.r. spectrum. The residue fraction was chromatographed on a silicic acid column to give threo- isomer 23b (1.20 g, 5%) and erythro- isomer 23a (1.64 g, 8%). The ratio of threo to erythro isomers was 5:8.

(v) A solution of N-nitrosopiperidine (9.71 g, 85 mmoles), trans-2-butene (15 g, 268 mmoles) and p-toluenesulfonic acid (16.17 g, 85 mmoles) in methanol (200 ml) was irradiated in a dry ice-methanol bath with a Hanovia lamp (450-W) through a Uranium glass filter for 2 hours and 35 minutes. The photolysate was evaporated and acetone (30 ml) was added to the residue to give a precipitate (6.48 g). On working up in the usual manner, the precipitate gave dimer 20a (1.30 g, 11%), anti-oxime 21 (1.59 g) and sodium p-toluenesulfonate. The acetone filtrate was evaporated to dryness. The residue in an aqueous solution was separated into an

acidic, a basic and a residue fraction. The acidic fraction gave N-nitrosopiperidine (1.2 g). The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (0.46 g), syn-oxime 22 (0.17 g, 1%), anti-oxime 21 (2.28 g) and dimer 21b (0.59 g, 5%). The presence of ketone 26 in a fraction of 21 was indicated by the n.m.r. (τ 6.32) and i.r. (1700 cm^{-1}) spectra.

The overall yield of anti-oxime 21 was 3.87 g (32%).

The aqueous solution was evaporated and the residue was extracted with methylene chloride. The combined methylene chloride solution was evaporated to give a solid (0.12 g) which was recrystallized from ether to give the sodium salt 24a. The salt contained a trace of 24b as indicated by the n.m.r. signal at τ 9.07 (d, J=6.5Hz).

(vi) A solution of N-nitrosopiperidine (9.78 g, 86 mmoles), trans-2-butene (15 g, 268 mmoles) and p-toluenesulfonic acid (16.32 g, 86 mmoles) in methanol (200 ml) was irradiated in a dry ice-methanol bath with a Hanovia lamp (450-W) through a Uranium glass filter for 2 hours and 25 minutes. The dimer peak at 292 nm reached a maximum after 2 hours and 20 minutes irradiation. The photolysate was evaporated and the residue was separated into an acidic, a basic and a residue fraction. The acidic fraction gave N-nitroso-

piperidine (2.37 g). The basic fraction was recrystallized from petroleum ether to give dimer 20a (1.29 g, 14%). The mother liquor was evaporated and was chromatographed on a silicic acid column to give N-nitrosopiperidine (1.19 g), dimer 20b (0.36 g, 4%), syn-oxime 22 (trace) and anti-oxime 21 (6.08 g, 66%). The presence of ketone 26 was indicated by the n.m.r. (τ6.32) and i.r. (1700 cm^{-1}) spectra.

The aqueous solution was neutralized to pH 7 with dilute hydrochloric acid and was evaporated. The residue was extracted with methylene chloride. The combined methylene chloride extracts were evaporated to give a crude mixture of N-nitrosohydroxylamine derivatives 23a and 23b (0.56 g) as shown by the i.r. absorptions at 1055, 1040 and 955 cm^{-1}.

(vii) A solution of N-nitrosopiperidine (20.44 g, 180 mmoles), trans-2-butene (3.5 g, 60 mmoles) and p-toluenesulfonic acid (34.45 g, 180 mmoles) in methanol (180 ml) was irradiated in a dry ice-methanol bath with a Hanovia lamp (200-W) through a Uranium filter for 6 hours. The dimer peak at 292 nm reached a maximum after 2 hours and 30 minutes irradiation and the decreased slowly to nil. The photolysate was evaporated and the residue was separated to an acidic, a basic and a residue fraction. The acidic fraction gave N-nitrosopiperidine (5.28 g).

The basic fraction contained syn-oxime 22 (trace) and anti-oxime 21 (7.91 g, 75%).

The aqueous solution was evaporated and the residue was extracted with methylene chloride to afford a crude mixture of N-nitrosohydroxylamine derivatives 23a and 23b (0.49 g, 4%) as shown by comparison of the i.r. and n.m.r. spectra.

(viii) A solution of N-nitrosopiperidine (19.42 g, 172 mmoles), trans-2-butene (3.5 g, 60 mmoles) and dry hydrogen chloride (200 mmoles) in methanol (200 ml) was irradiated in an ice-salt bath with a Hanovia lamp (200-W) through a Uranium glass filter for 14 hours and 30 minutes. The photolysate was evaporated and an aqueous solution of the residue was separated into an acidic, a basic and a residue fraction. The acidic fraction gave N-nitroso-piperidine (3.72 g). The basic fraction was recrystallized from 2-propanol to give piperidine hydrochloride (0.54 g). The mother liquor was evaporated and was chromatographed on a silicic acid column to give a mixture of oximes 21 and 22 (8.76 g, 75%). The presence of ketone 26 in a fraction of 21 was indicated by the i.r. (1700 cm^{-1}) and n.m.r. (τ 6.32) spectra.

The residue fraction gave an oil which was chromatographed on a silicic acid column to give threo-isomer 23b (0.15 g) and erthyro-isomer 23a (0.52 g). The ratio of these two isomers 23b and 23a was 1 : 3.5.

VIII. Addition of N-Nitrosopiperidine to cis-2-Butene

(i) A solution of N-nitrosopiperidine (9.74 g, 86 mmoles), cis-2-butene (9.0 g, 160 mmoles) and p-toluenesulfonic acid (16.25 g, 86 mmoles) in methanol (150 ml) was irradiated in a dry ice-methanol bath with a Hanovia lamp (450-W) through a Uranium glass filter for 3 hours. The dimer peak at 292 nm reached a maximum after 2 hours and 45 minutes irradiation. The photolysate was evaporated and 2-propanol (25 ml) was added to the residue to give a mixture of dimers 20a and 20 b (1.25 g) and anti-oxime 21 (1.49 g). The 2-propanol filtrate was evaporated and the residue was worked up in the usual manner to give an acidic, a basic and a residue fraction. The basic fraction contained dimer 20b (20 mg), N-nitroso-piperidine (2.16 g) and anti-oxime 21 (4.55 g) which was contaminated with a trace of syn-isomer 22. The residue fraction contained a mixture of threo- and erythro-isomers 23b and 23a (0.24 g, 2%).

The overall yield of dimers was 1.27 g (11%), oximes 5.33 g (47%).

(ii) A solution of N-nitrosopiperidine (25.44 g, 223 mmoles), cis-2-butene (3.8 g, 68 mmoles) and dry hydrogen chloride (215 mmoles) in methanol (225 ml) was irradiated in a dry ice-methanol bath with a Hanovia lamp (450-W)

through a Uranium glass filter for 19 hours. The dimer peak at 292 nm reached a maximum after 3 hours and 30 minutes irradiation and then decreased slowly to nil. The photolysate was evaporated and an aqueous solution of the residue was extracted in the usual manner to give an acidic, a basic and a residue fraction. The acidic fraction gave N-nitrosopiperidine (1.21 g). The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (1 g), compound 18 (1.47 g), syn-oxime 22 (0.56 g, 5%) and anti-oxime 21 (7.52 g, 65%). The presence of ketone 26 in the first fraction of 21 was indicated by the n.m.r. (τ 6.32) and i.r. (1700 cm^{-1}) spectra. The residue fraction was chromatographed on a silicic acid column to give compound 18 (2.21 g), threo-isomer 23b (0.52 g) and erythro-isomer 23a.

The combined yield of N-nitrosohydroxylamine derivatives 23a and 23b was 0.97 g (8%). The ratio of these isomers 23b and 23a was 54:46.

(iii) A solution of N-nitrosopiperidine (30.61 g, 269 mmoles), cis-2-butene (5.6 g, 100 mmoles) and p-toluene-sulfonic acid (53.27 g, 280 mmoles) in methanol (180 ml) was irradiated in a dry ice-methanol bath with a Hanovia lamp through a Corex filter for 2 hours and 30 minutes. The photolysate was evaporated, and an aqueous solution

of the residue was worked up in the usual manner to give an acidic, a basic and a residue fraction. The acidic fraction gave N-nitrosopiperidine (3.50 g). The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (4.2 g), unknown X (1 g), syn-oxime 22 (trace) and anti-oxime 21 (11.10 g, 65%). The presence of ketone 26 in the first fraction of 21 was indicated by the n.m.r. (τ6.32) and i.r. (1700 cm^{-1}) spectra. The residue fraction was chromatographed on a silicic acid column to give compound 18 (0.27 g), threo-isomer 23b (2.41 g) and erythro-isomer 23a (1.26 g).

The combined yield of N-nitrosohydroxylamine derivatives 23b and 23a was 3.67 g (18%). The ratio of threo to erythro was 65:35.

IX. Addition of N-nitrosopiperidine to Phenylacetylene

(i) A solution of N-nitrosopiperidine (5.91 g, 52 mmoles), phenylacetylene (7.55 g, 74 mmoles) and concentrated hydrochloric acid (5.2 ml, 62 mmoles) in methanol (200 ml) was irradiated in a dry ice-methanol bath with a Hanovia (450-W) lamp through a Uranium glass filter for 5 hours and 30 minutes. While the N-nitroso peak at 348 nm decreased, a new peak at 275 nm gradually appeared and strongly tailed to overlap with the N-nitroso peak. The

photolysate was evaporated and the residue was taken up in 2-propanol (25 ml) from which, on standing, a solid (3.69 g) was obtained. The solid was recrystallized from 2-propanol to give piperidine hydrochloride as the first crop. The filtrate was evaporated to dryness and was diluted with water (50 ml) to give a solid (Y, 4.64 g): m.p. 213-217°; i.r. 1290, 1265, 1190, 1090, 1075, 760 and 700 cm^{-1}; n.m.r. (CF_3COOH) τ 2.50 (b). Solid Y was insoluble in most organic solvents but dissolved in acetic anhydride and acetic acid with decomposition.

Solid Y was washed with 2-propanol to give a residue (3.74 g) which was recrystallized three times from a mixture of benzene and trifluoroacetic acid to give crystals of 28: m.p. 233.5-234.5°; i.r. 3150, 1180, 1090, 1075, 760 and 700 cm^{-1}; n.m.r. (CF_3COOH) τ 2.39 (m, 10H) and 2.07 (m, 2H); m/e (%) 359 (0.5), 330 (1), 278 (31), 261 (2), 207 (1), 205 (1), 187 (2), 167 (45), 149 (100), 132 (3), 121 (4), 113 (9), 104 (8), 95 (5), 83 (11) and 76 (15);

anal. Calcd. for $C_{15}H_{12}N_2O_2$: C 71.42; H 4.97; N 11.10;
Found: C 70.92; H 5.03; N 10.92.

The 2-propanol wash solution was evaporated to give a solid (0.90 g) which was recrystallized three times from a mixture of benzene and trifluoroacetic acid to give crystals (29): m.p. 226-228°; i.r. 3260, 3150, 3070, 1260, 1240, 1162, 1100, 1048, 1025, 1002, 970, 845, 765

and 700 cm^{-1}; n.m.r. (CF_3COOH) τ 2.45 (b); m/e(%) 348 (4), 339 (3), 322 (2), 279 (22), 268 (30), 248 (14), 233 (10), 220 (10), 164 (7), 160 (8), 147 (6), 144 (9), 131 (8), 122 (46), 119 (15), 116 (17), 103 (73), 89 (23) and 77 (100);

Anal. Calcd. for $C_{22}H_{20}N_4O_5$: C 62.85; H 4.79; N 13.33;
Found: C 62.90; H 4.67; N 13.03.

The aqueous filtrate was worked up in the usual manner to give an acidic, a basic and a residue fraction. The acidic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (0.60 g), an oil (0.63 g, 8%), benzoic acid (0.14 g, 3%) and a solid (72 mg, 1%). The oil was purified by preparative t.l.c. and was distilled at 90°/0.1 mm to give 2,2-dimethyoxyacetophenone (31)*;i.r. 2940, 2840, 1695, 1600, 1285, 1194, 1122, 1070, 978, 865, 760 and 700 cm^{-1}; n.m.r. τ 6.55 (s, 6H), 4.85 (s, 1H), 2.58 (m, 3H) and 1.93 (m, 2H); m/e(%) 180 (M^+, 0.5), 149 (2), 121 (6), 105 (14), 91 (3), 77 (20) and 75 (100). The solid was recrystallizes from ether to give phenylglyoxal dioxime (33): m.p. 162.5-165° (lit. 168°, 16); i.r. 3260, 3030, 1600, 1295, 1110, 1000, 960, 935, 765 and 700 cm^{-1}; n.m.r. (DMSO-d_6) τ 2.67 (m, 5H), 2.16, 1.78 and 1.64 (combined intensity

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* A ketoacetal is characterized by an i.r. absorption at 1710 cm^{-1} due to a ketone carbonyl stretch, and a strong doublet at 1070-1110 cm^{-1} due to an acetal ether. The mass spectrum shows a peak at m/e 75 (15).

1H, not exchanged by D_2O over an extended period) and -1.67 (s, 1H, D_2O exchangeable); m/e (%) 164 (M^+, 100), 147 (38), 129 (9), 119 (20), 103 (36), 90 (30), 83 (14) and 77 (65).

The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (0.12 g) and an oil (0.61 g, 5%) which was distilled at 85°/0.1 mm to give 1-methoxy-1-piperidinoacetophenone (30): i.r. 3320, 3070, 3020, 2940, 2860, 1600, 1450, 1225, 1105, 1035, 975, 940, 760 and 710 cm^{-1}; n.m.r. τ 8.55 (b, 6H), 7.43 (b, 4H), 6.17 (s, 3H), 4.41 (s, 1H, D_2O exchangeable) and 2.58 (b, 6H); m/e (%) 248 (M^+, 3), 231.1457 (Calcd. for $C_{14}H_{19}N_2O$: 231.1497, 25), 217 (92), 199 (88), 171 (2), 144 (58), 128 (77), 111 (41), 103 (51), 98 (43), 83 (89) and 77 (86).

The residue (0.39 g) contained at least two very polar compounds (as shown by t.l.c.) and was not investigated.

The solid Y (1.5 g) was stirred overnight in a mixture of acetic anhydride (10 ml) and pyridine (10 ml) in an ice bath. The solution was poured into water (100 ml) and was extracted with ether (3 x 25 ml). The ethereal solution was washed first with a dilute solution of sodium bicarbonate, then with water. It was dried ($MgSO_4$) and finally evaporated to give an oil. The oil was chromatographed on a silicic acid column to give benzoic acid (0.19 g), an unknown Z, an oily mixture

(0.10 g) and benzamide (0.68 g). The unknown Z was recrystallized from a mixture of benzene and petroleum ether to give crystals (20 mg): m.p. 129-131.5°; i.r. 3260, 1710, 1680, 1670, 1590, 1340, 1300, 1240, 1210, 1060, 960, 900 and 710 cm^{-1}; m/e (%) 253 (5), 225 (21), 210 (32), 148 (32), 105 (100) and 77 (58). The oily mixture could not be purified by further chromatography.

(ii) A solution of N-nitrosopiperidine (8.07 g, 70 mmoles), phenylacetylene (3.50 g, 35 mmoles) and concentrated hydrochloric acid (6 ml, 72 mmoles) in methanol (200 ml) was irradiated in an ice bath with a Hanovia lamp (450-W) through the filter solution (v) for 2 hours. The u.v. absorption at 348 nm decreased slowly after 1 hour and 30 minutes irradiation. On continuous irradiation, new absorptions at 350 and 329 nm increased rapidly. The photolysate was worked up in the usual manner to give a precipitate, an acidic, a basic and a residue fraction. The precipitate gave piperidine hydrochloride (2.78 g) on recrystallization from 2-propanol. The acidic fraction (2.81 g) was chromatographed on a silicic acid column to give N-nitrosopiperidine (0.39 g), compound 30 (1.40 g, 22%), phenylglyoxal ketoxime (33, 0.93 g, 18%) (see below) and dioxime 31 (0.54 g, 9%). The basic fraction was chromatographed on a silicic acid column to give N-

nitrosopiperidine (20 mg), compound 18 (0.69 g), unknown L (0.12 g, 1%), unknown oil H (0.31 g), a solid (33 mg) and oxime 32 (2g, 24%). The unknown oil L was rechromatrographed om a silicic acid column and was distilled at 90°/0.1 mm. T.l.c. of this purified L showed a single spot only. This oil was tentatively assigned to 1-piperidinophenylglyoxal dioxime (39): i.r. 3400, 3280, 2950, 2860, 1575, 1380, 1335, 960, 780 and 700 cm^{-1}; n.m.r. τ 8.42 (b, 6H), 6.94 (b, 4H), 2.61 (bs, 6H) and 1.30 (s, 1H); m/e (%) 246 (M^+-1, 1), 230 (43), 226 (7), 215 (10), 188 (8), 146 (24), 130 (8), 127 (4), 118 (6), 112 (8), 110 (9), 105 (20), 90 (7), 84 (100) and 77 (20). The n.m.r. signal at τ 1.30 was exchanged by D_2O slowly (no other signal could be exchanged on further treatment with D_2O). The unknown oil H could not be purified by chromatography and was distilled at 90°/0.1 mm: i.r. 3320, 1610, 1390, 1365, 1330, 1280, 1210, 1070, 760 and 695 cm^{-1}; n.m.r. τ 8.74 (s), 8.03 (b), 7.67 (s), 7.00 (b), 6.18 (b), 2.53 (m) and 1.98 (m); m/e (%) 246 (5), 228 (7), 215 (34), 212 (100), 199 (24), 183 (11), 171 (60), 130 (13), 122 (43), 115 (20), 110 (13), 105 (71), 84 (17) and 77 (82). The solid was recrystallized from ethanol to give an unknown (t.l.c., single spot): m.p. 157-160°; i.r. 3140, 3040, 1600, 1010, 1000, 765 and 700 cm^{-1}; m/e (%) 228 (M^+, 72), 211 (100),

128 (40), 103 (65), 98 (40), 84 (74) and 77 (36).

The residue fraction was chromatographed on a silicic acid column to give compound 18 (0.2 g) and a solid (30 mg) which was recrystallized from ethanol to give crystals: m.p. 126-128°; i.r. 3305, 1650, 1570, 1335, 1322, 1170, 1030, 902, 800, 710 and 695 cm^{-1}; m/e (%) 180 (M^+, 0.5), 149 (2), 137 (3), 121.0492 (Calcd. for C_7H_7NO: 121.0527, 42), 119 (6), 105 (83), 103 (100), 91 (5) and 77 (83). This compound was assigned to 2-(N-nitrosohydroxylamino)-2-phenylacetaldehyde (34).

(iii) A solution of N-nitrosopiperidine (7.87 g, 69 mmoles), phenylacetylene (8.37 g, 82 mmoles) and concentrated hydrochloric acid (6 ml, 72 mmoles) in methanol (300 ml) was irradiated in a dry ice-methanol bath with a Hanovia lamp (450-W) through a Uranium glass filter for 5 hours. While the absorption at 348 nm decreased gradually, new peaks at 305, 280 and 276 nm increased. The photolysate was rendered basic with solid sodium carbonate (8 g) immediately on termination of the irradiation. The precipitate was filtered off and the filtrate was evaporated to dryness. An aqueous solution of the residue was worked up in the usual manner to give a basic and a residue fraction. The basic fraction was chromatographed on a silicic acid column to give N-nitrosopiperidine (2.58 g), a yellow liquid (49 mg), an oily major product (3.93 g) and an unknown solid mixture

(0.91 g). The yellow liquid (i.r. 2930, 2850, 1650, 1440, 1390, 1250, 1210, 1115, 1020 and 720 cm^{-1}; n.m.r. τ 8.38 (b, 6H), 6.6 (b, 4H), 2.54 (b, 5H) and 2.05 (s, 1H)) was not changed when it was treated with sodium carbonate solution. The structure was tentatively assigned to 1-phenyl-1-nitroso-2-piperidinoethylene (40). The major oil was distilled at 95°/0.1 mm to give crystalline phenylglyoxal ketoxime (32): m.p. 48.5-50°; i.r. ($CHCl_3$) 3240, 3060, 3030, 2840, 1700, 1590, 1440, 1370, 1280, 1050, 990, 960 and 685 cm^{-1}; n.m.r. τ 2.53 (s, 5H) and 0.20 (s, 1H); m/e.(%) 149.0520 (calcd. for $C_8H_7N_2O$: 149.0478, 20), 119 (53), 103 (45), 91 (24) and 77 (100);

Anal. Calcd. for $C_8H_7N_2O$: C 64.42; H 4.73;N 9.39;

Found: C 63.29; H 4.77;N 9.05.

The bis-phenylhydrazone (41) was prepared by refluxing a mixture of ketoxime 32, phenylhydrazine hydrochloride and concentrated hydrochloric acid in ethanol solution and was recrystallized once from dilute ethanol solution, and twice from a mixture of benzene and petroleum ether to give a crystalline solid: m.p. 147-149° (lit. 152°, 17); i.r. 3300, 3180, 1590, 1540, 1490, 1370, 1265, 1245, 1160, 1070, 1010, 950, 750 and 685 cm^{-1}; m/e (%) 314 (M^+, 100), 222 (75), 209 (36), 195 (12), 116 (12), 104 (24), 83 (80) and 77 (50). The ketoxime 32 was treated with phenylacetylene in an acidic methanol

solution to give a high melting product (m.p. 210-220°).

The neat oil resulting from chromatography, gave a crystalline product on standing overnight. The crystals partially dissolved on heating in chloroform, leaving a solid nitroso dimer of 1-nitroso-2-hydroxy-styrene (35a) which was filtered off: m.p. 113-115°; i.r. 3230, 3060, 1590, 1310, 1280, 1210, 1130, 1055, 990, 960 and 700 cm^{-1}; n.m.r. (DMSO-d_6) τ2.53 (s, 5H), and 0.20 (s, 1H); m/e (%) 149 ($\frac{1}{2}M^+$, 46), 119 (98), 103 (37), 91 (15) and 77 (100);

Anal. Calcd. for $C_{16}H_{14}N_2O_4$: C 64.42; H 4.73; N 9.39;
Found: C 64.07; H 4.92; N 9.12.

The dimer 35a was dissolved in chloroform on heating and the chloroform solution was evaporated to give 32 wa shown by the i.r. absorption at 1700 cm^{-1} and the n.m.r. signal at τ0.20. The dimer 35a was sublimed at 110°/0.1 mm to give an oil 32 which was crystallized to give a solid (m.p. 48-50°) which was characterised by i.r. and n.m.r. spectra.

The unknown solid mixture was rechromatographed on a silicic acid column and crysatllized from a mixture of benzene-petroleum ether to give a solid: m.p. 68-72°; i.r. ($CHCl_3$) 3160, 3060, 2990, 2940, 2860, 1700, 1665, 1445, 1375 and 690 cm^{-1}; m/e (%) 198 (95), 122 (10), 105 (34), 98 (18), 91 (16), 84 (10), 78 (100) and 77 (70).

The residue fraction was chromatographed on a silicic

acid column to give 32 (0.60 g), an unknown (N, 95 mg) and an unknown (M, 80 mg). The unknown N was recrystallized from ethanol to give a solid: m.p. 200-204°; i.r. 3060, 1560, 1170, 1160, 1030, 970, 800, 760, 705 and 690 cm^{-1}; m/e (%) 286 (M^+, 2), 246 (5), 228 (6), 215 (26), 211 (8), 198 (9), 194 (22), 149 (7), 126 (6), 119 (25), 110 (15), 103 (100), 84 (28) and 77 (65).

The unknown M was recrystallized from ethanol to give a solid: m.p. 210-214°; i.r. ($CHCl_3$) 3200, 2060, 1660, 1600, 1440, 1355, 1100, 1015, 900 and 685 cm^{-1}; m/e (%) 279 (100), 263 (50), 247 (25), 232 (26), 221 (10), 204 (9), 171 (12), 144 (14), 116 (20), 103 (60), 89 (22) and 77 (85).

The overall yield of ketoxime 33 was 4.53 g (65%).

X. Addition of N-nitrosopiperidine to Diphenylacetylene

A solution of N-nitrosopiperidine (7.72 g, 68 mmoles), diphenylacetylene (4.66 g, 26 mmoles) and concentrated hydrochloric acid (5.8 ml, 69 mmoles) in methanol (200 ml) was irradiated in an ice bath with a Hanovia lamp (450-W) through the filter solution (v) for 2 hours. The photolysate was evaporated to dryness. Water (50 ml) was added and the aqueous solution was extracted with ether (3 x 25 ml). The ethereal solution was evaporated to give an oil (4.37 g) which contained

N-nitrosopiperidine (0.22 g) and a solid (4.15 g, 61%). The solid was recrystallized from benzene to give benzil monoxime (37): m.p. 136-138°; (lit. 137°, 54); i.r. 3340, 3060, 1640, 1600, 1375, 1310, 1215, 1010, 930, 875 and 695 cm^{-1}; m/e (%) 225 (M^+, 7), 122 (18), 105 (100), 103 (56) and 77 (56).

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