PHOTOCHEMISTRY OF OXIMES

by

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TO

SUZANNE and NATALIE

ABSTRACT

Cycloalkanone oximes and acyclic oximes yield Beckmann-type products upon irradiation in methanol. Unsymmetrically α-substituted cyclohexanone oximes give mixtures of both possible lactam isomers. The photolysis of oximes epimeric at the α-carbon gives lactams in which the α-centre has retained its configuration. The results are interpreted in terms of a concerted breakdown of an oxazirane intermediate.

Oxaziranes have been prepared and shown to be thermally and photochemically unstable. The formation of Beckmann-type products arise by a photodecomposition pathway. Thermal decomposition of the oxaziranes is relatively slow and results in ketal formation. Formation of the oxazirane is rate determining. During the irradiation, oxaziranes are present in very low, steady-state concentrations.

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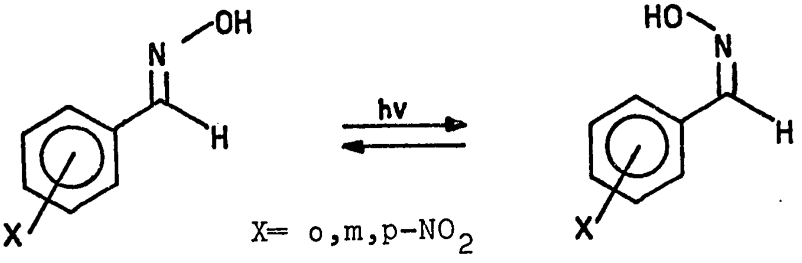
INTRODUCTION

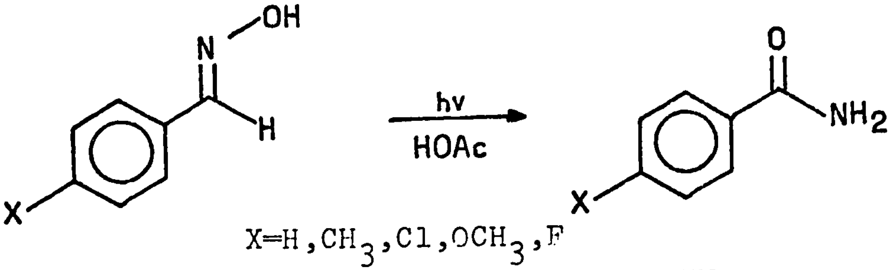
Much evidence has been accumulated concerning the sensitivity of oximes to ultra-violet light. The syn-anti isomerization of oximes, particularly of the benzaldoximes I and II, was noted as early as 1903 (1a-d).



X= o,m,p-NO_2

I II

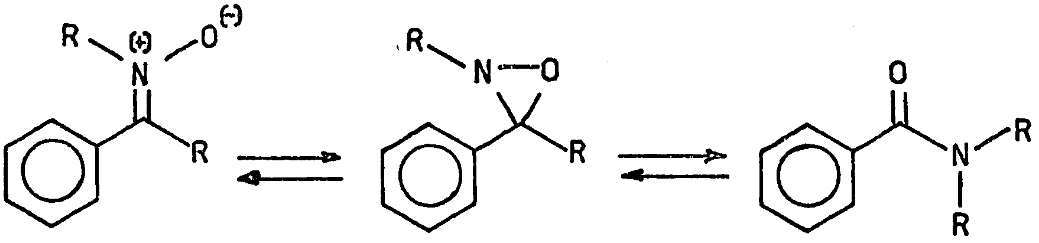
The first evidence that a rearrangement process had occurred was obtained by de Mayo and co-workers (2a,b), who found that various benzaldoximes (III) gave the corresponding benzamides (IV) upon irradiation in acetic acid.



X=H,CH_3,Cl,OCH_3,F

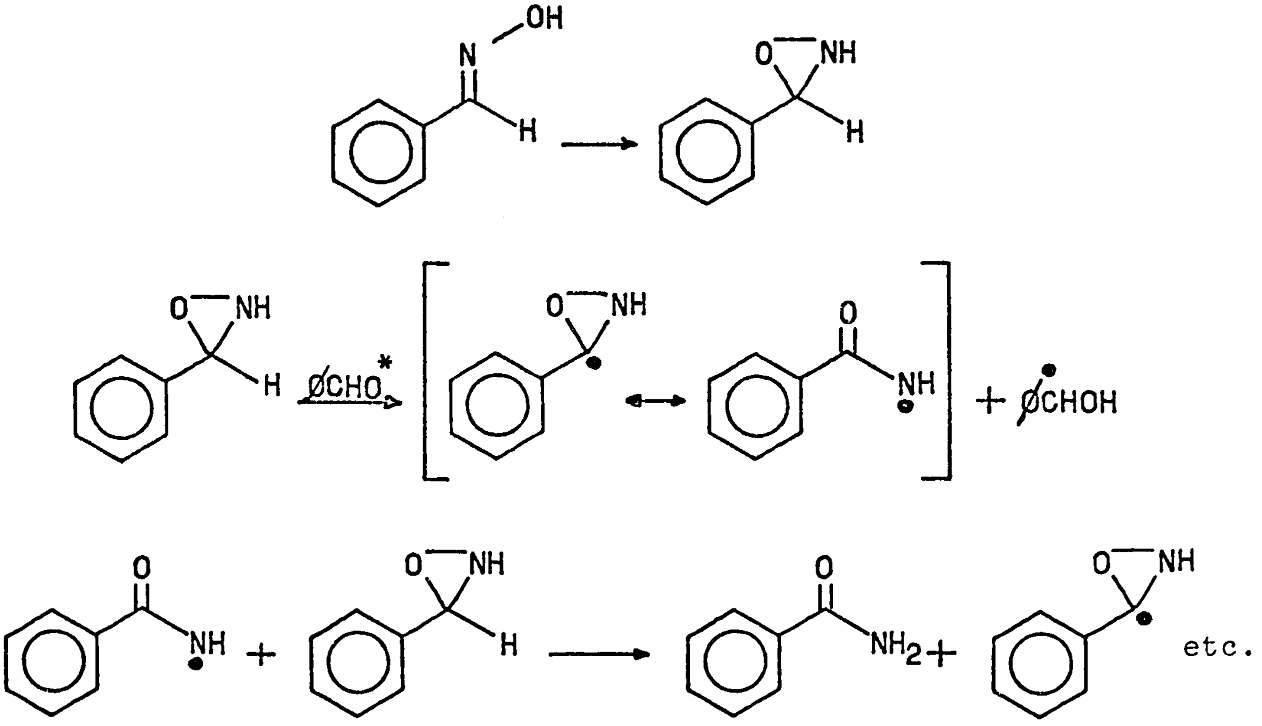
III IV

At that time the photolysis of nitrones (V), which are closely related to oximes, was well understood (3a-i) and known to result in the formation of amides via the oxaziranes (VI). In several cases (3e-h) the oxaziranes were isolated from the photolysis mixtures and shown to undergo further photolytic and/or thermal rearrangement to the amides and thermal conversion to the nitrones.

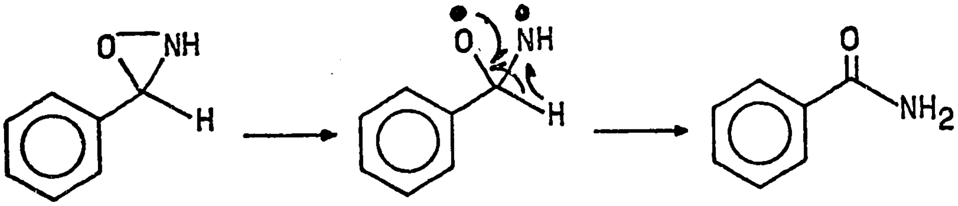


V VI

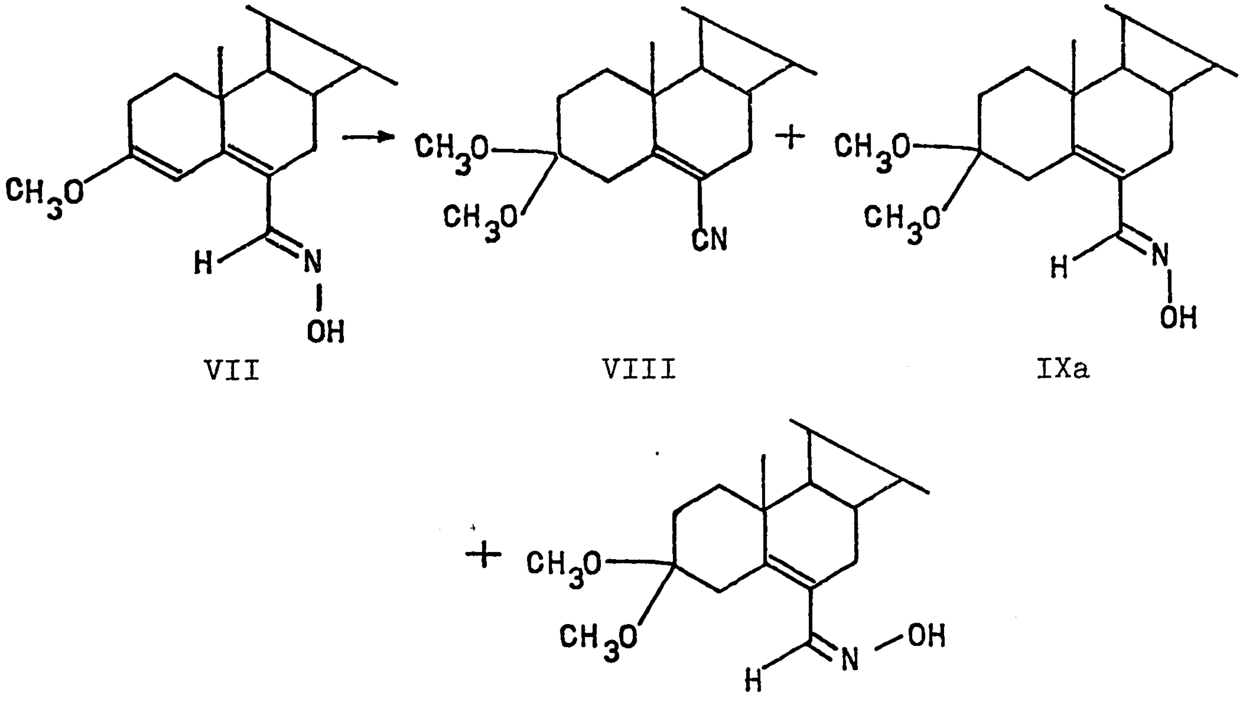
The mechanism proposed by de Mayo (2b) for the photolysis of benzaldoxime incorporated this feature of an oxazirane intermediate. A free radical mechanism for the conversion of oxazirane to amide was proposed with traces of aldehyde acting as initiator.



An alternative mechanism was proposed by Kan (4) for the direct conversion of oxazirane into amide.



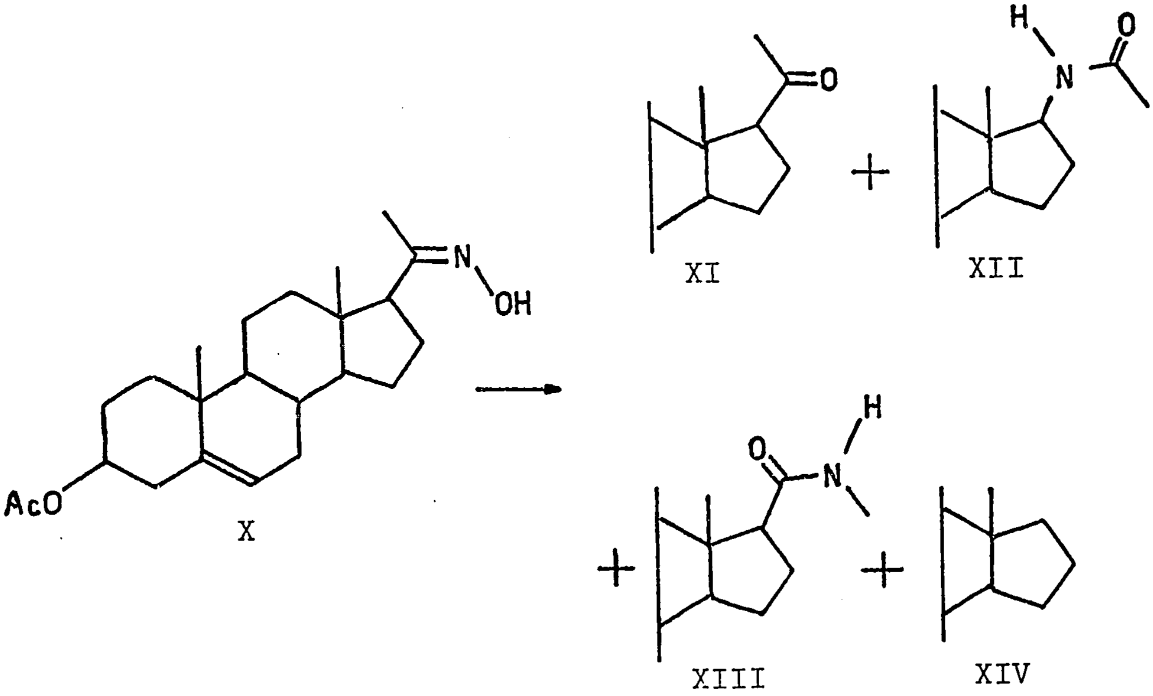
Recently many oximes, other than aromatic aldoximes, have been found to be photosensitive. Thus, Just and Pace-Asciak (5) found that the oxime of 17β-acetoxy-6-formyl-3-methoxyandrosta-3,5-diene (VII) gave nitrile (VIII) as well as the syn-anti isomers (IXa,b) on irradiation in methanol.



VII VIII IXa

IXb

Taylor (6) had found that irradiation of 3β-acetoxy-pregnenolone oxime (X) in methanol gave several products, the parent ketone (XI), Beckmann-type rearrangement products (XII and XIII) and an α-cleavage product (XIV).



X

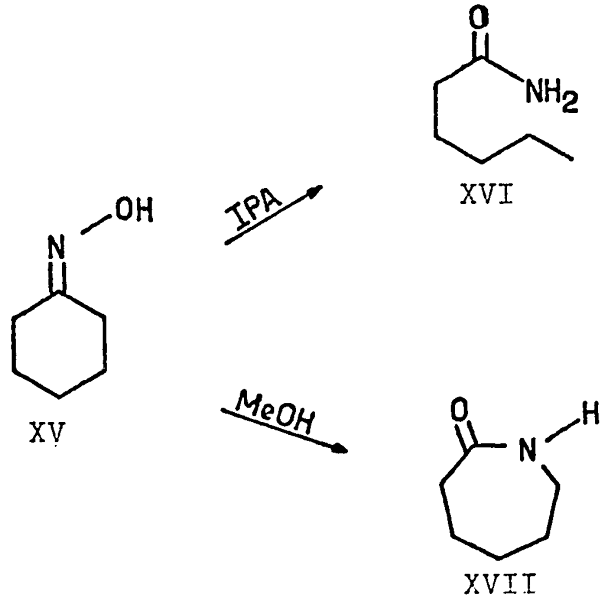
XI

XII

XIII

XIV

The photoreactions of saturated cyclic ketoximes were studied by Douek (6). The photolysis behavior of cyclohexanone oxime (XV) was found to be similar to that of pregnenolone oxime



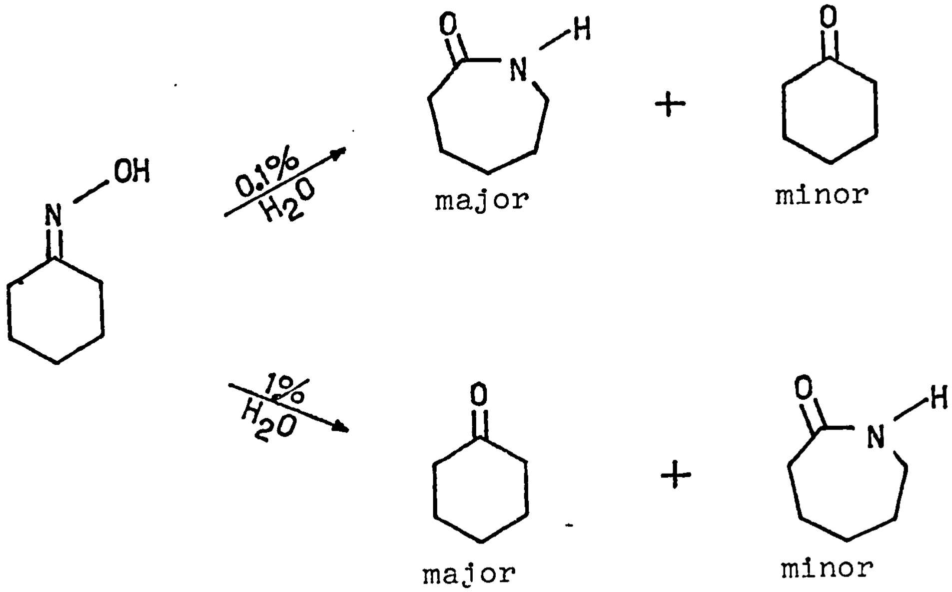
XV

XVI

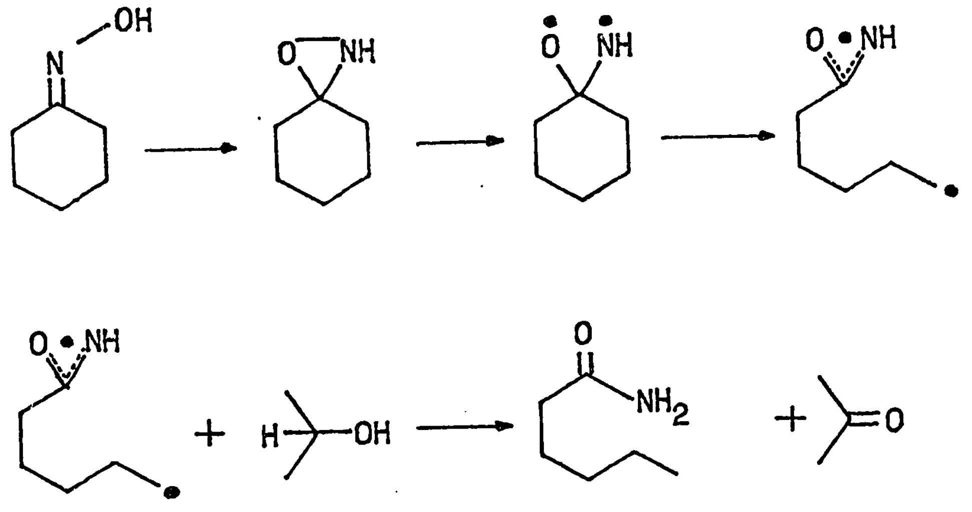
XVII

and gave a product distribution that was solvent dependent, caproamide (XVI) being formed in iso-propanol and caprolactam (XVII), the Beckmann-type product, being favored in methanol. Other saturated oximes, 3,3,5,5-tetramethylcyclohexanone oxime, caprostanone oxime, and 17β-acetoxy-4,4-dimethylandrost-5-ene-3-one oxime behaved similarly.

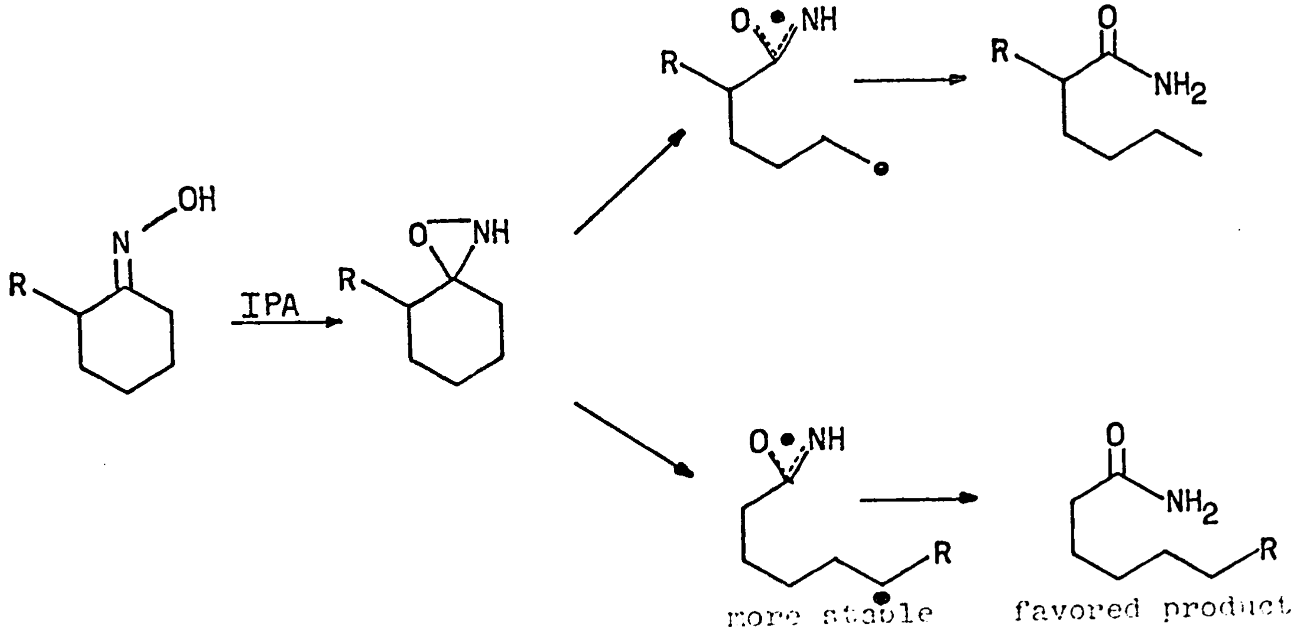
Ng (7b,7d) reported a remarkable concentration effect for the photolysis of cyclohexanone oxime. Irradiation of an 0.1% solution of oxime in water gave caprolactam as the major product and a small amount of cyclohexanone. Irradiation of a 1% solution of oxime in water gave cyclohexanone as the major product and a small amount of caprolactam !



The photoreaction of the saturated cyclic ketoximes in iso-propanol has been further studied by Just and Ng (7d). Although the intermediacy of an oxazirane could not be proven, the products of the reaction were rationalized on the basis of this intermediate. Their mechanism is given on the next page.

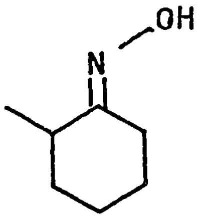
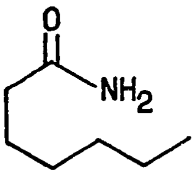
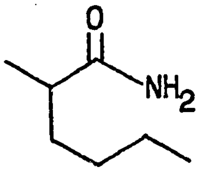
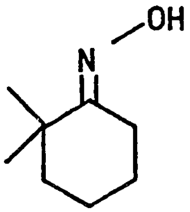
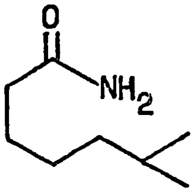
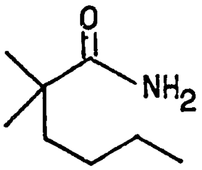
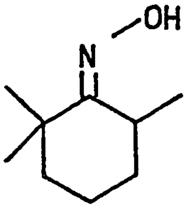
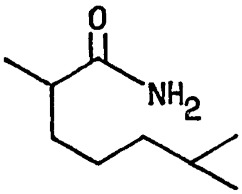
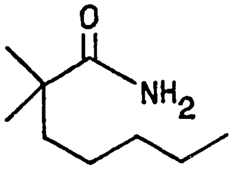


In support of this mechanism, it was pointed out that the reaction was quenched by oxygen (a characteristic of a relatively long lived biradical (8)) and that acetone, formed by hydrogen abstraction from the solvent, was isolated from the photolysis mixture. Furthermore, in unsymmetrically substituted cyclohexanone oximes, preference for cleavage of the bond leading to formation of the more stable free radical was observed.



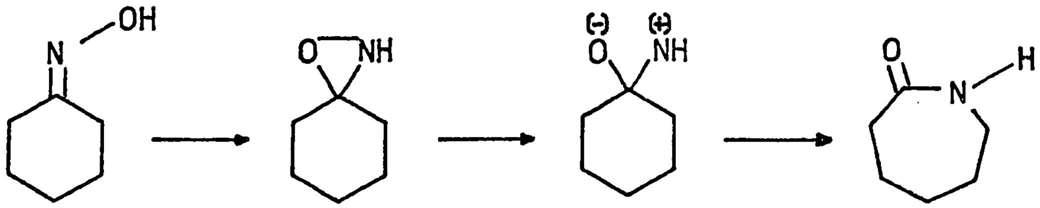
The ratios of the resulting amide isomers were found to vary between 7:1 and 12:1 (Table 1).

TABLE 1

Starting Oxime	Amide Isomers		Ratio
			7:1
			10:1
			12:1

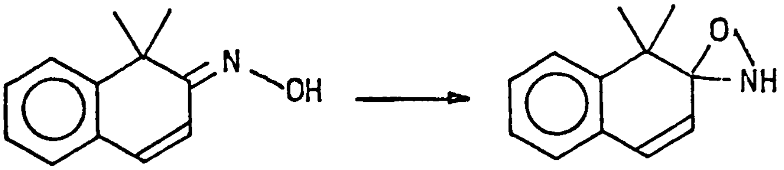
It soon became apparent that no biradical intermediate similar to that resulting in amide formation was involved in the photoreaction in methanol. Douek (6) found that while the amide forming reaction was completely quenched by oxygen, the lactam forming reaction was only partially quenched. The photolysis of unsymmetrically substituted cyclohexanone oximes in methanol gave mixtures of equal amounts of both possible lactam isomers (7c) instead of the expected ratios of between 7:1 and 12:1. Furthermore, a large ring ketoxime, cyclopentadecanone oxime, photolyzed normally giving a good yield of lactam. Had the ring opened during the photolysis, it would have been expected to close again to the lactam only to a limited extent (9).

A singlet mechanism was proposed for these conversions of oximes into lactams via the oxaziranes (7c).



No proof of the intermediacy of an oxazirane was obtained and no further evidence for the concerted mechanism shown was offered.

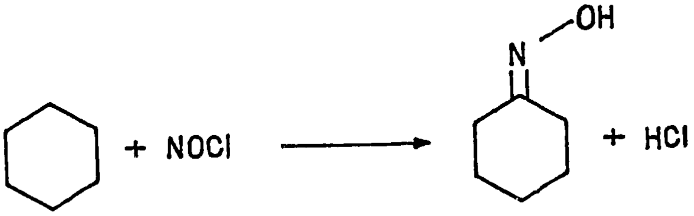
The photolysis of several other oximes have now been roported (7a-g) and the intermediacy of oxaziranes has been proposed in almost all cases. Supporting evidence has, to



XVIII

date, only been provided by Oine and Mukai (7e) for the particular case of an α,β-unsaturated ketoxime (XVIII). The mechanism of decomposition of the saturated cyclic ketoximes had not, at the writing of this thesis, been determined.

Much of the current interest in the photoreactions of oximes stems from the transformation of cyclohexanone oxime (XV) into caprolactam (XVII) under photolytic conditions. Currently prepared from cyclohexanone oxime by the Beckmann rearrangement, caprolactam is an industrially important chemical since it can be polymerized into Nylon-6 and spun into fibre. A photochemical route to cyclohexanone oxime already exists (10) and is used by several firms.



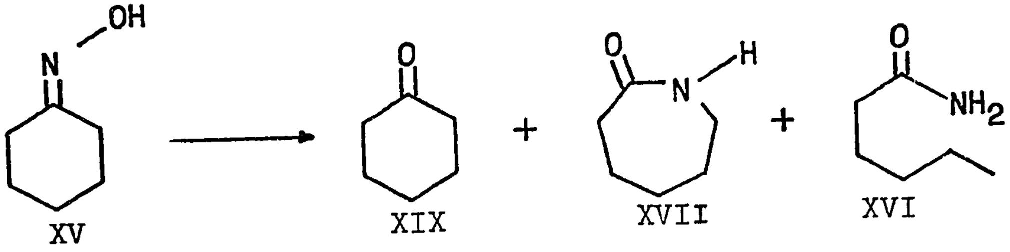
This process, in combination with the previously described photoreaction of cyclohexanone oxime, could provide a new, all photochemical route to caprolactam.

With the economic interest of the reaction as impetus, the photochemistry of oximes was studied with a view to determining the generality of the reaction and its mechanism.

CHAPTER I. THE PHOTOLYSIS OF VARIOUS CYCLOHEXANONE OXIMES

A. The Photolysis Yields

Taylor, Douek and Just (6) have reported that irradiation of cyclohexanone oxime (XV) in methanol gave caprolactam (XVII) and small amounts of caproamide (XVI) and cyclohexanone (XIX).



The photolysis of various α-substituted cyclohexanone oximes in methanol have been shown to behave analogously giving lactams as the major products (7b,c).

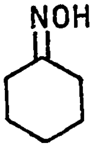
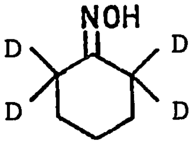
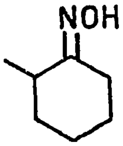
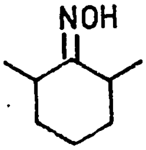
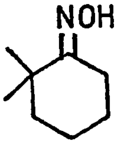
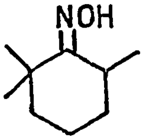
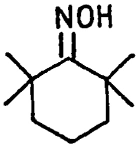
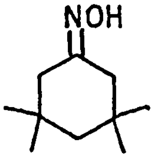
Unfortunately, no comparison could be drawn among the rates and yields of the various photolyses since they were carried out on varying amounts of oxime and under varying conditions. To allow such comparisons to be drawn, all these photolyses were repeated under constant conditions.(1) The data obtained for these and several other substituted cyclohexanone oximes are summarized in Table 2. Gas-liquid chromatograms (g.l.c.) of the resulting photolysis mixtures are appended at the end of the chapter (figs. 1-8).

---

(1) The constant conditions used for the photolyses are described in the experimental section.

TABLE 2

The photolysis yields of various cyclohexanone oximes (1)

Starting Oxime	% Yield % ketone	 % oxime	 % amide	 % lactam
	5	27	4	37
	5	27	7	35
	6	25	4(2)	38(2)
 (3)	4	15	3	43
	7	30	3(2)	36(2)
	6	23	1(2)	42(2)
	13	11	6	44
	9	23	4	41

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(2) These are combined yields of both possible isomers. The various possibilities for the amides are shown in Table 1 and the lactam isomers in Table 3.

(3) This oxime was a mixture of the cis and trans forms (90% cis).

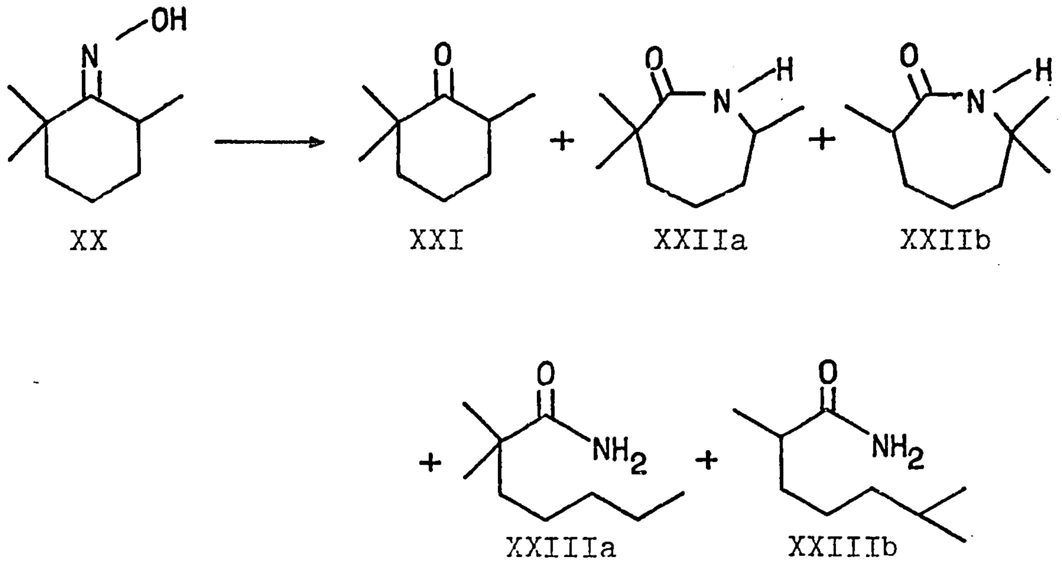
B. The Recovery of the Photoproducts

The recovery of the photoproducts in Table 2 is not quantitative but varies between 70% and 80%. Similar recoveries will be noted throughout this thesis. Losses are expected to arise from two principle sources. The photoproducts resulting from the photolysis of 10 mmolar solutions of oximes are too dilute for direct measurement of their concentration. The data of Table 2 is determined after a 10 fold concentration of the irradiated solutions. Some loss probably occurs through "stripping out" of volatile components during distillation of solvent. Upon photolysis of 1% solutions of oxime, where concentration is not required, the recoveries increase to 90 - 95% (11).

Another source of loss is due to the photosensitivity of the ketone product (12). Following the ketone concentration during the photolysis of a 1% solution of oxime shows the ketone to increase rapidly to a steady state concentration. At this point, ketone is apparently being destroyed as rapidly as it is formed. The "% ketone" listed in Table 2 represents only the steady state concentration whereas the actual ketone yield must be considerably higher. Ng (13) has reported that under the photolysis conditions, 68mg of a typical ketone, cyclododecanone, was recovered when 100mg in 100ml of methanol was photolyzed.

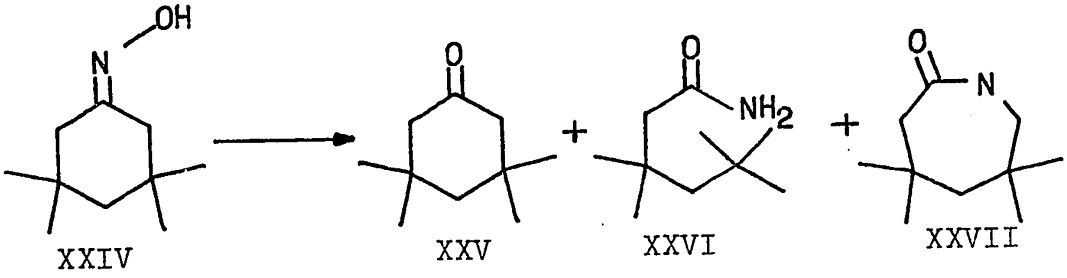
C. The Photolysis of 2,2,6-trimethylcyclohexanone Oxime (XX)

Included in Table 2 is the previously unreported photolysis of 2,2,6-trimethylcyclohexanone oxime (XX) in methanol. Separation of the products by preparative thin-layer chromatography (t.l.c.) gave 2,2,6-trimethylcyclohexanone (XXI), unreacted oxime (XX), a mixture of lactams (XXIIa and XXIIb), and a mixture of amides (XXIIIa and XXIIIb). Proof of structure of these products is included in the experimental section.



D. The Photolysis of 3,3,5,5-tetramethylcyclohexanone Oxime (XXIV)

The photolysis of 3,3,5,5-tetramethylcyclohexanone oxime (XXIV) had been previously described by Douek (14) to give 3,3,5,5-tetramethylcyclohexanone (XXV), 3,3,5,5-tetramethylcaproamide (XXVI), and 3,3,5,5-tetramethylcaprolactam (XXVII).



He also reported that more amide (XXVI) than lactam (XXVII) was formed during the photolysis of XXIV in methanol (15). Since this was the first instance in which the photoreaction deviated from the normal pathway, the photolysis of this oxime was reinvestigated.

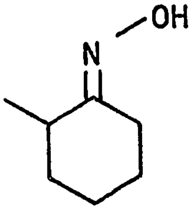
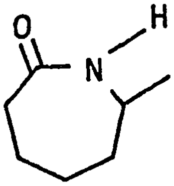
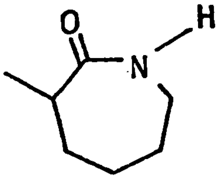
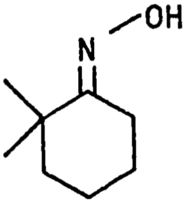
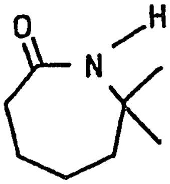
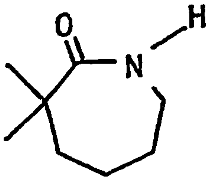
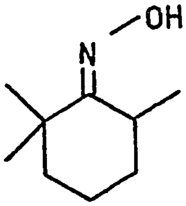
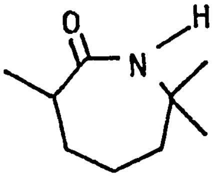
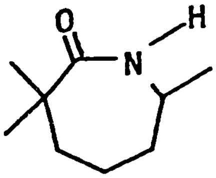
Photolysis of 3,3,5,5-tetramethylcyclohexanone oxime (XXIV) and separation of the products by t.l.c. gave unreacted oxime (XXIV) and 3,3,5,5-tetramethylcaprolactam (XXVII). No amide (XXVI) was detected on t.l.c. Separation of the products by g.l.c. (fig. 8) showed mainly lactam (XXVII) and only traces of material corresponding in retention time to the amide (XXVI). The finding of Douek that more amide than lactam was formed during the photoreaction in methanol could not be repeated.

E. The Ratios of Lactam Products from Unsymmetrically Substituted Cyclohexanone Oximes

It has already been reported that irradiation of unsymmetrically substituted cyclohexanone oximes gave mixtures of both possible lactam isomers (7c). These mixtures could not be separated on t.l.c. and gave a single peak in the gas chromatograph on a non-polar (5% DC710) column, however, a polar column (Carbowax 20M) resolved the mixtures into two components. In the case of the lactam isomers from the photolysis of 2-methylcyclohexanone oxime, the first component was eluted from the column with the same retention time as 6-methylcaprolactam (XXVIII). The elution order is easily explained since a strongly polar liquid phase such as Carbowax is known to interact strongly with compounds capable of hydrogen bonding (16). In the case of the mixture of 6-methylcaprolactam (XXVIII) and 2-methylcaprolactam (XXIX), the isomer which was first eluted was that in which the N-H group is most hindered by neighboring groups preventing interaction with the liquid phase. The other mixtures behaved similarly, the peak assignments in Table 3 being based on this argument.

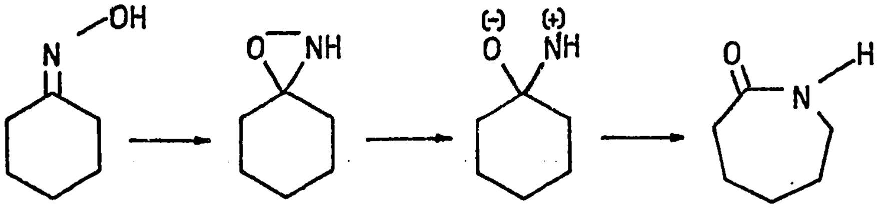
TABLE 3

Ratio of lactam isomers from the photolysis of unsymmetrically substituted cyclohexanone oximes

Oxime	Lactam Isomers		Ratio
	 XXVIII	 XXIX	50/50 ± 0.5
			50/50
			44/56

E. Discussion of Results

Douek (14) had completed his study of the photoreactions of cyclohexanone oxime at the time this work was undertaken and had advanced a mechanism to account for the photolysis results in methanol.



His scheme envisaged lactam formation to arise from a polar intermediate. That lactam was a major photoproduct in methanol but not in iso-propanol was believed due to a requirement of the intermediate for stabilization by a solvent of high dielectric constant. In support of this hypothesis it was shown that lactam formation occurred best in water. Two points show this simple model to be inadequate. A necessary conclusion of the above argument is that photolysis in t-butanol would give little lactam because of the low dielectric constant of the medium. Ng (17) found that photolysis in t-butanol gave a good lactam yield. Neither does this scheme explain why the lactam forming reaction was partially quenched by oxygen.

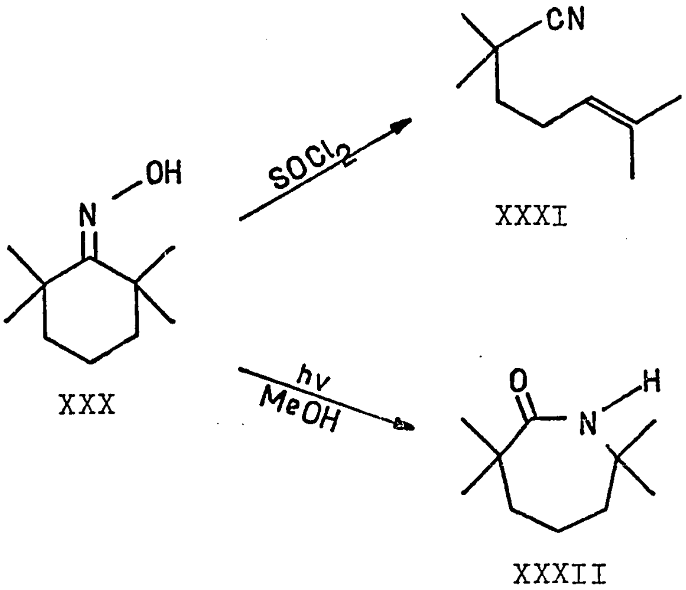
The oxygen quenching results indicate that triplet is somehow involved in the photoreaction in methanol. A reasonable hypothesis might be that there exists more than one pathway to lactam of which one (or more) triplet pathways are affected by oxygen. It had been expected that support for this idea might be forthcoming from the photolysis of 3,3,5,5-tetramethylcyclohexanone oxime. A low lactam yield was expected since ring closure of a triplet would be opposed by the resulting 1,3 diaxial interactions. Contrary to Douek's finding, the photolysis proceeded normally.

No evidence for the existence of a triplet or radical pathway was found in the photolysis of the unsymmetrically substituted cyclohexanone oximes. Were these pathways involved, lactam ratios similar to the amide ratios (Table 1 - 7:1 to 12:1) could be expected. As Table 3 shows, no preference was observed for migration of the more substituted carbon atom, the lactam ratios being approximately 1:1 in all cases. The question of radical intermediates will be further pursued in the next two chapters.

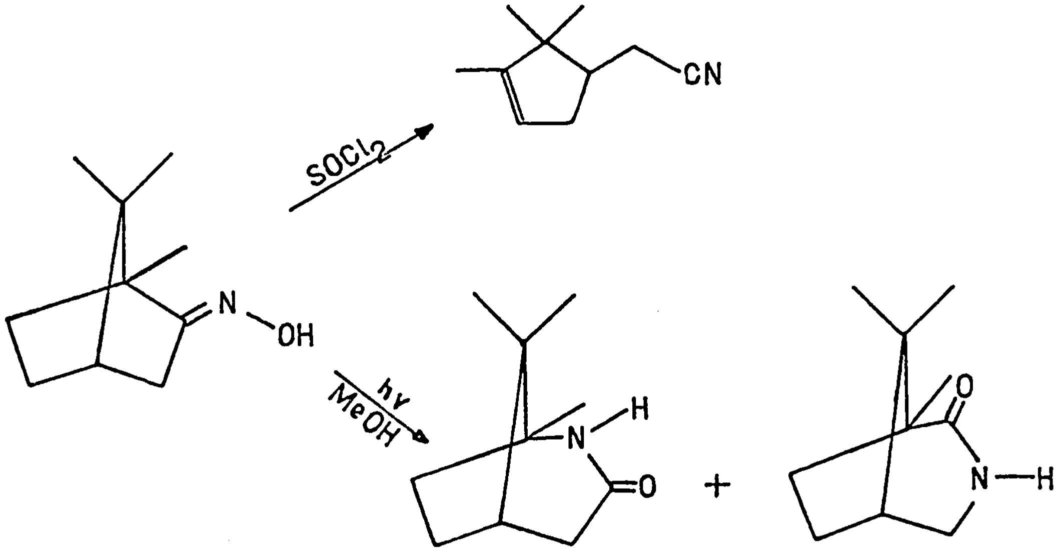
The lack of an isotope effect was observed for the photolysis of 2,2,6,6-tetradeuterocyclohexanone oxime. When the deuterated and undeuterated oximes, identical in molar concentration, were photolyzed, the rates of disappearance of both oximes were identical. The absence of the expected second order effect can only mean that the migration of the α-carbon occurs after the rate determining step of the reaction. This evidence strongly suggests slow formation of an intermediate (oxazirane) which rapidly rearranges to photoproducts.

Finally, the lactam yield appeared to be relatively constant as the degree of α-substitution increased (Table 2). Under these conditions, the lactam yield of the classical

Beckmann reaction drops drastically (18). Typically, 2,2,6,6-tetramethylcyclohexanone oxime (XXX) gives no lactam under typical Beckmann conditions. Nitrile (XXXI) which results from a second order process is the only product. The photoreaction gives 2,2,6,6-tetramethylcaprolactam (XXXII) in good yield.



Similarly, camphor oxime gives no lactam under typical Beckmann



conditions (18) while photolysis in methanol gives both lactams (19).

Furthermore, as is pointed out in Table 3, the photoreaction of unsymmetrically substituted oximes gives both possible lactam isomers in approximately equal amounts while the classical Beckmann reaction gives one predominant isomer. These results suggest that the photolytic process might possess considerable synthetic utility as an extension of the usefulness of the Beckmann rearrangement.

Fig. 1

Gas-liquid chromatogram of the photolysis products of cyclohexanone oxime

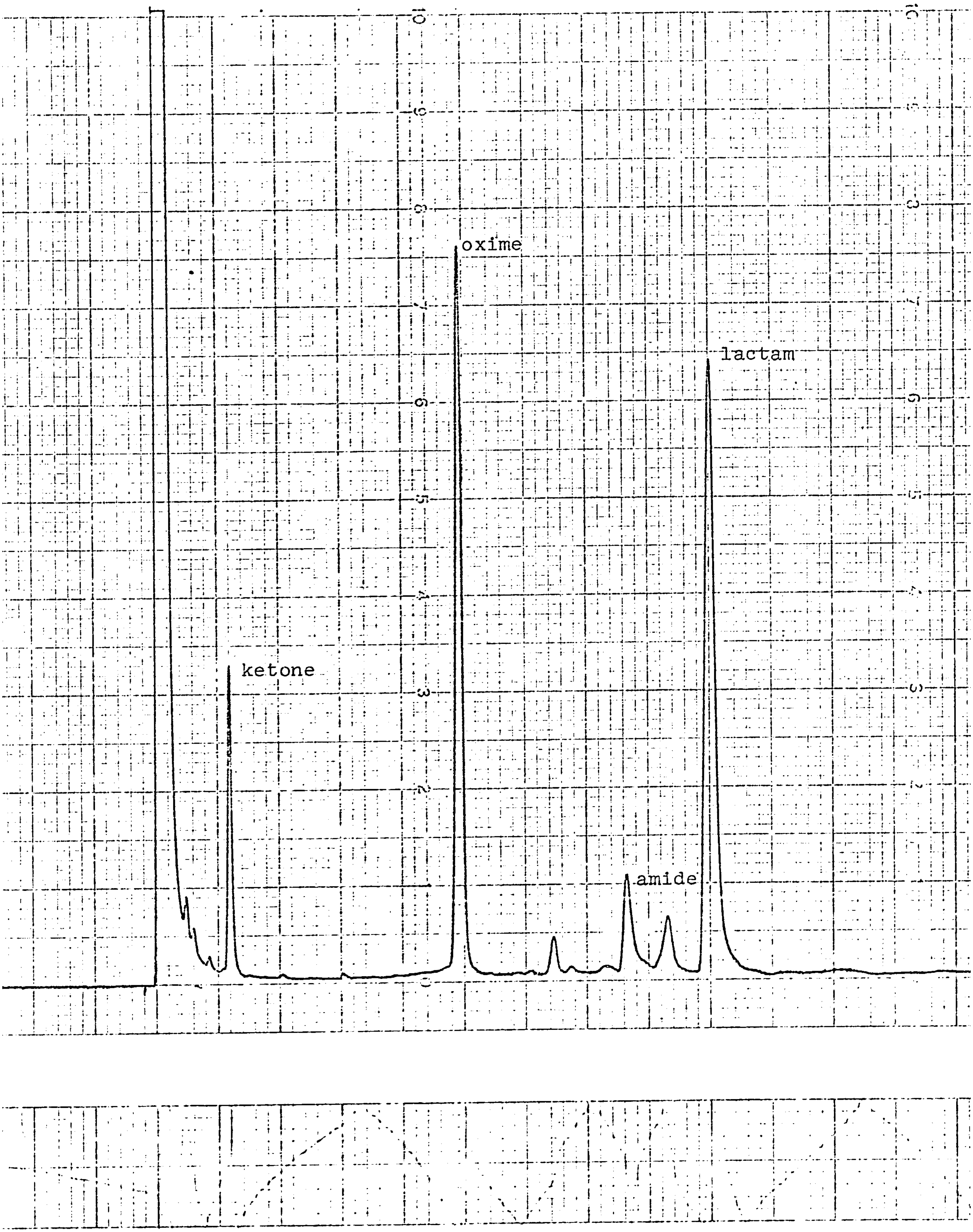

ketone
oxime
lactam
amide
10
9
8
7
6
5
4
3
2
0

Fig. 2

Gas-liquid chromatogram of the photolysis products of 2,2,6,6-tetradeuterocyclohexanone oxime

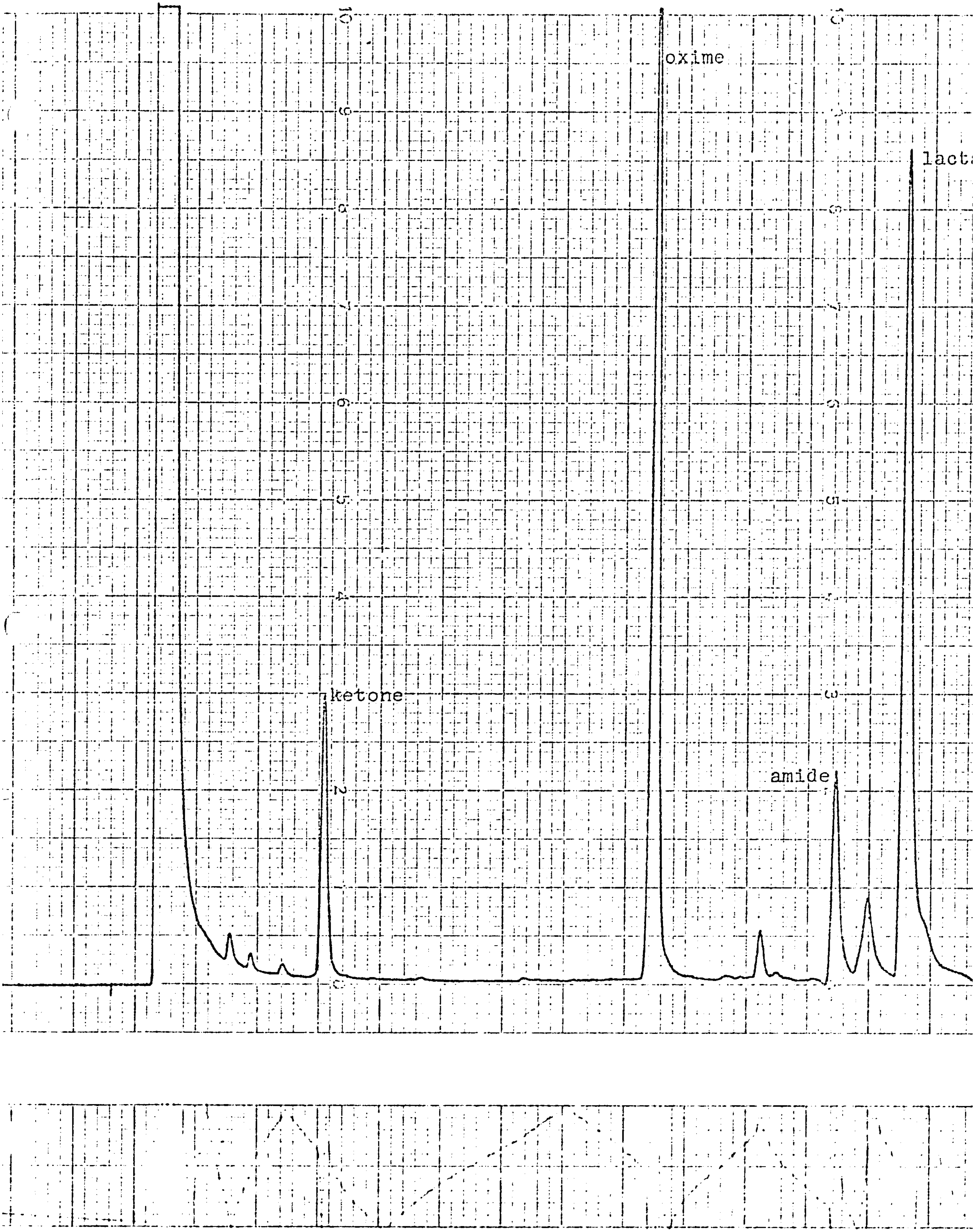

10
9
8
7
6
5
4
3
2
0
ketone
oxime
amide
lact

Fig. 3

Gas-liquid chromatogram of the photolysis products of 2-methylcyclohexanone oxime

11

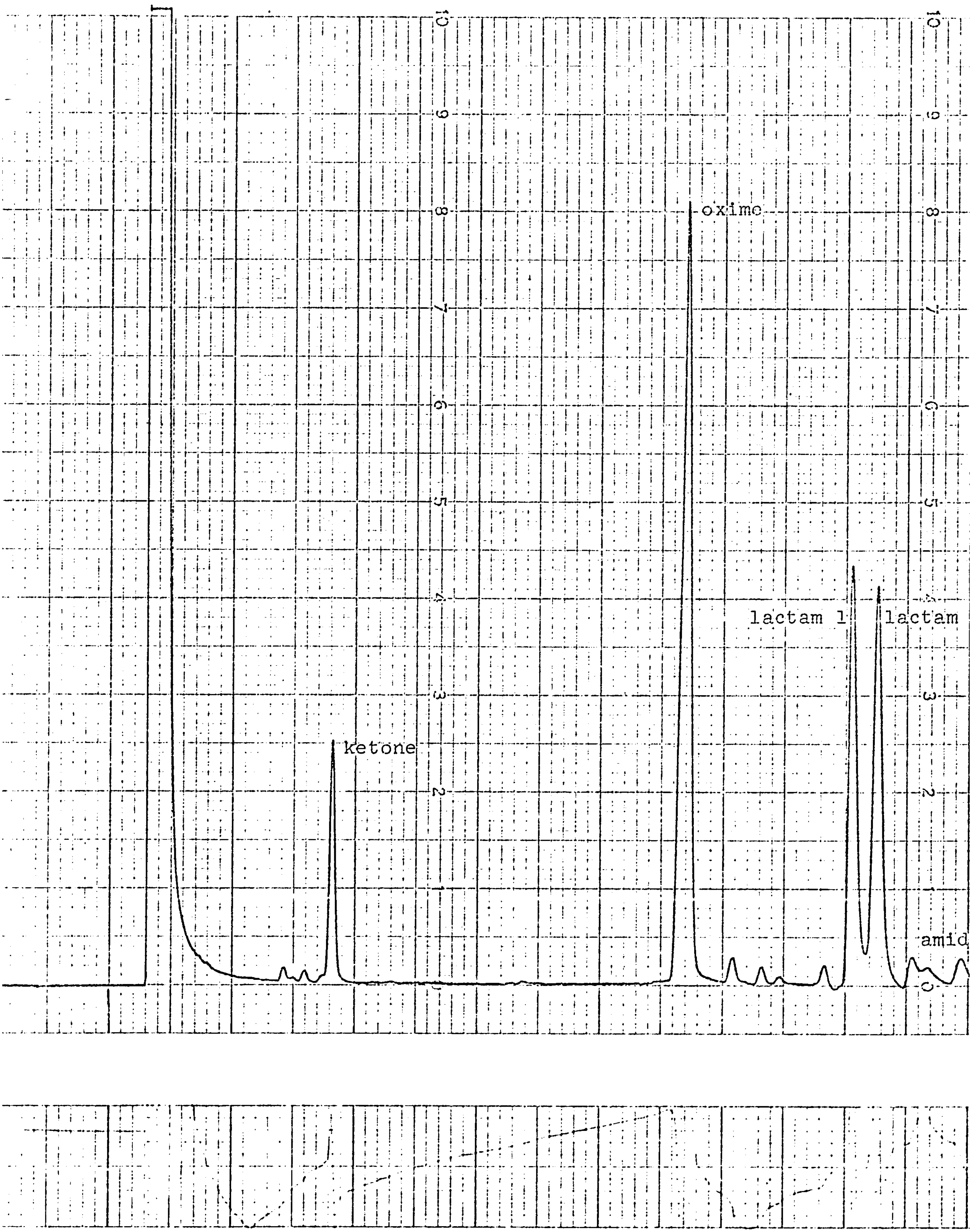


Fig. 4

Gas-liquid chromatogram of the photolysis products of 2,6-dimethylcyclohexanone oxime

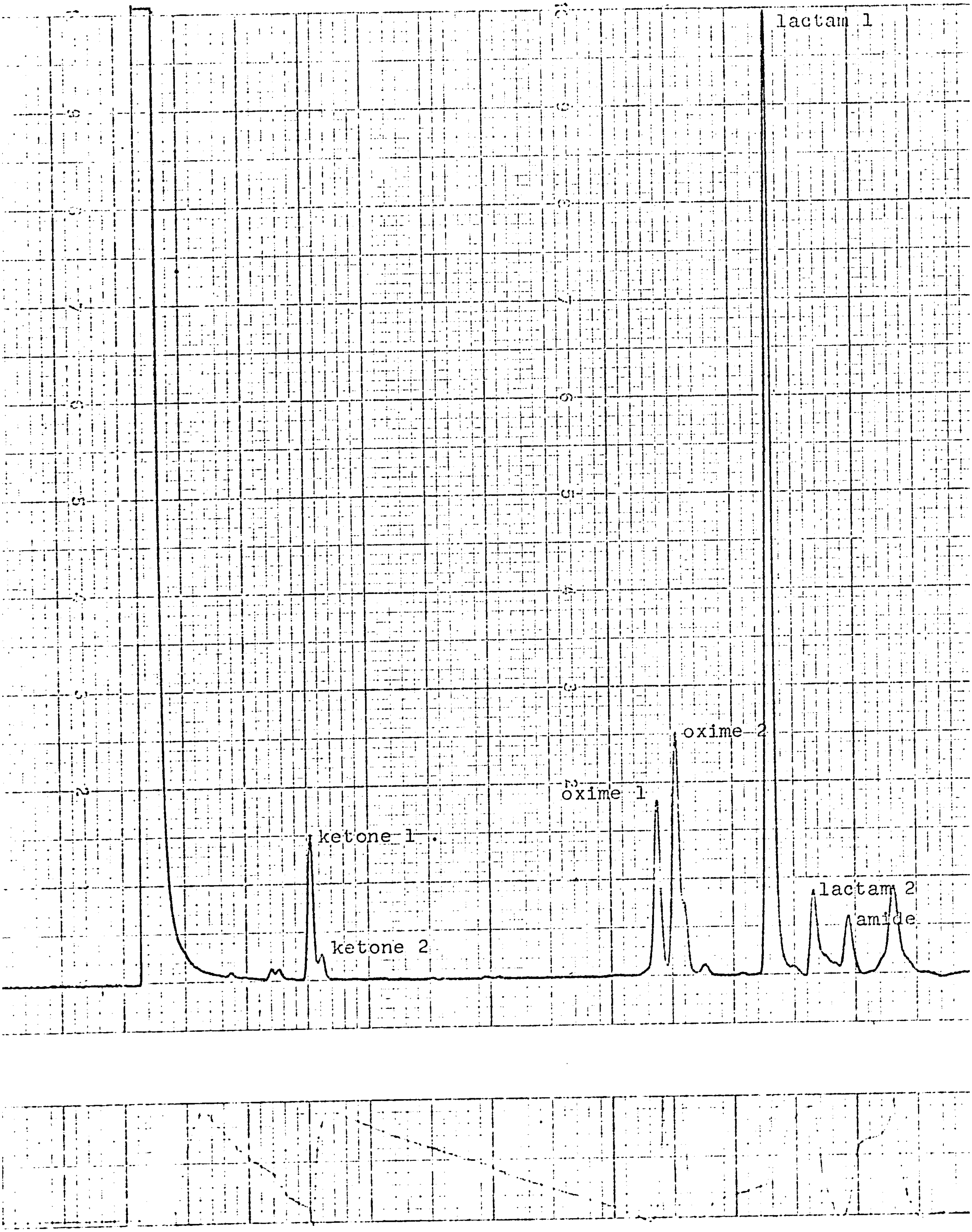

lactam 1
oxime 2
oxime 1
ketone 1
ketone 2
lactam 2
amide

Fig. 5

Gas-liquid chromatogram of the photolysis products of 2,2-dimethylcyclohexanone oxime


10
9
8
7
6
5
4
3
2
ketone
oxime
lactam 1
lactam 2
amides
1,2

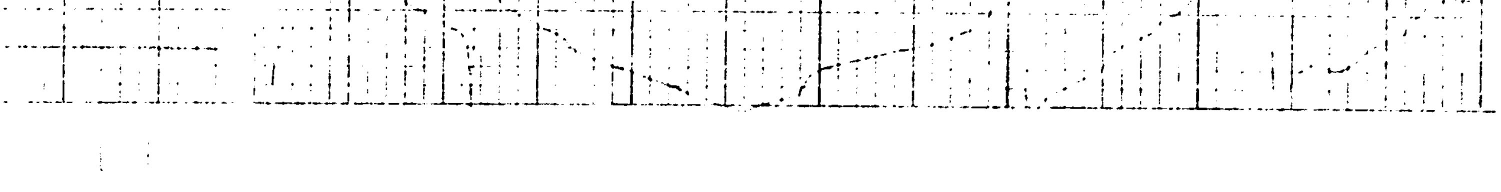
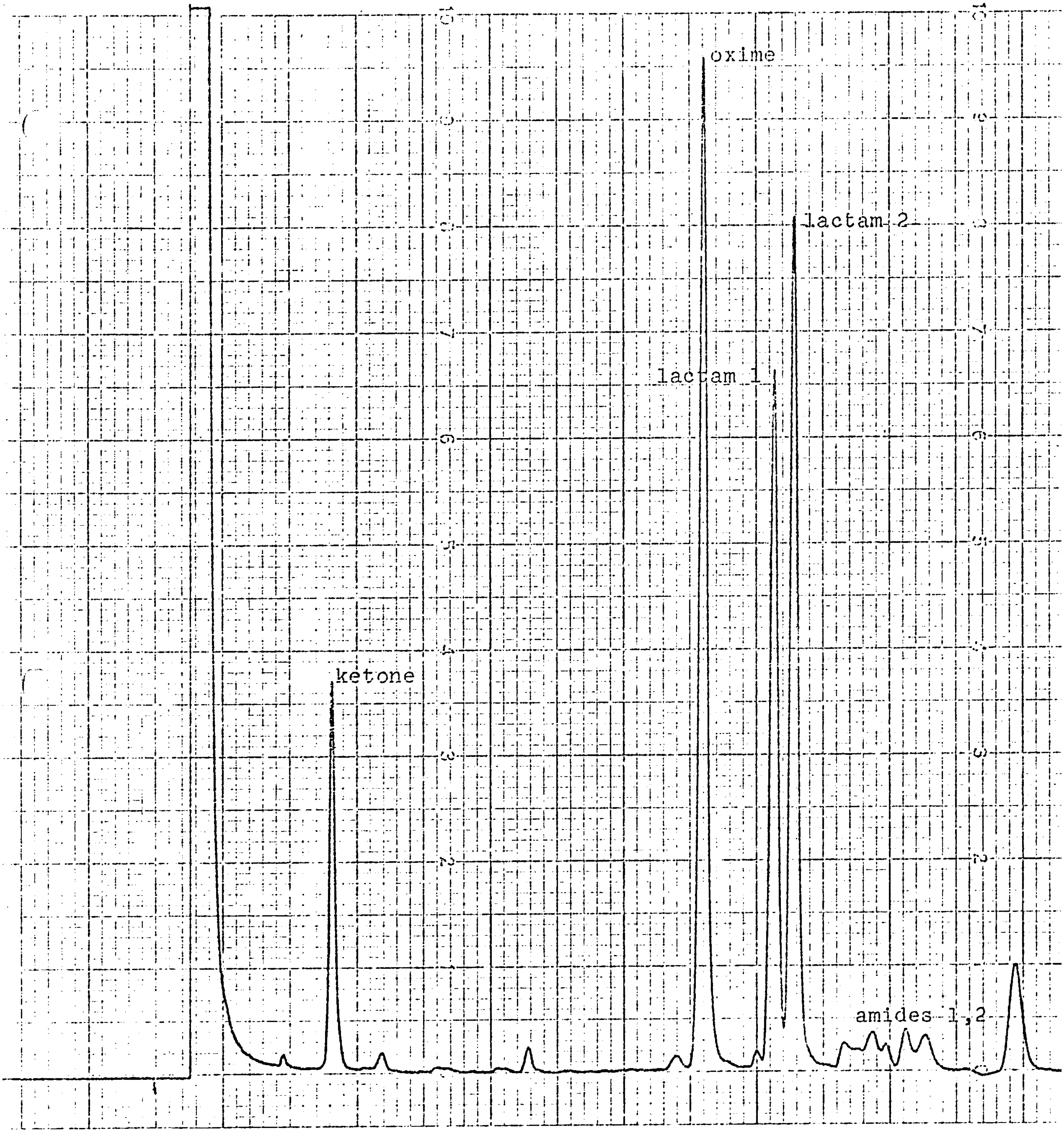


Fig. 6

Gas-liquid chromatogram of the photolysis products of 2,2,6-trimethylcyclohexanone oxime


10
9
8
7
6
5
4
3
2
oxime
lactam 2
lactam 1
ketone
amides 1,2

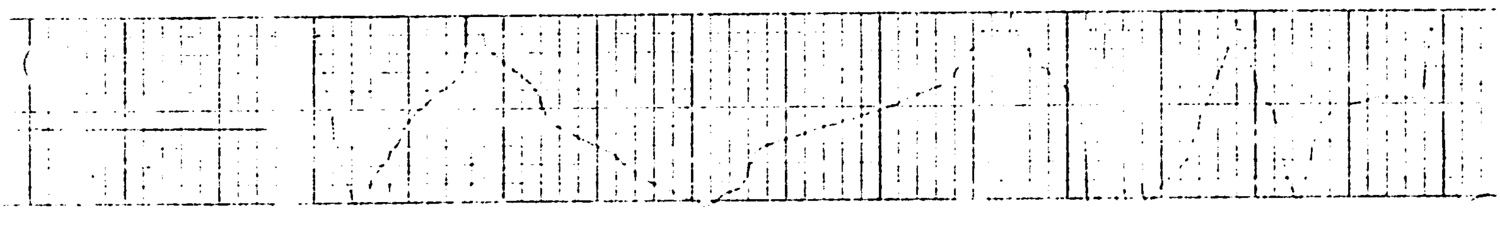


Fig. 7

Gas-liquid chromatogram of the photolysis products of 2,2,6,6-tetramethylcyclohexanone oxime


10
9
8
7
6
5
4
3
2
0
lactam
ketone
oxime
amide

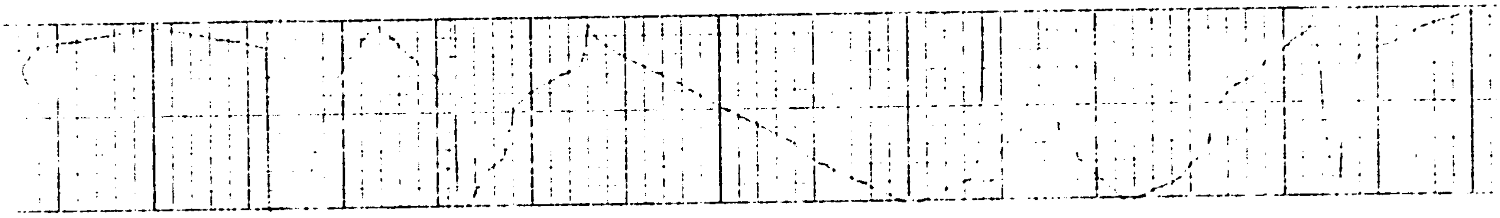
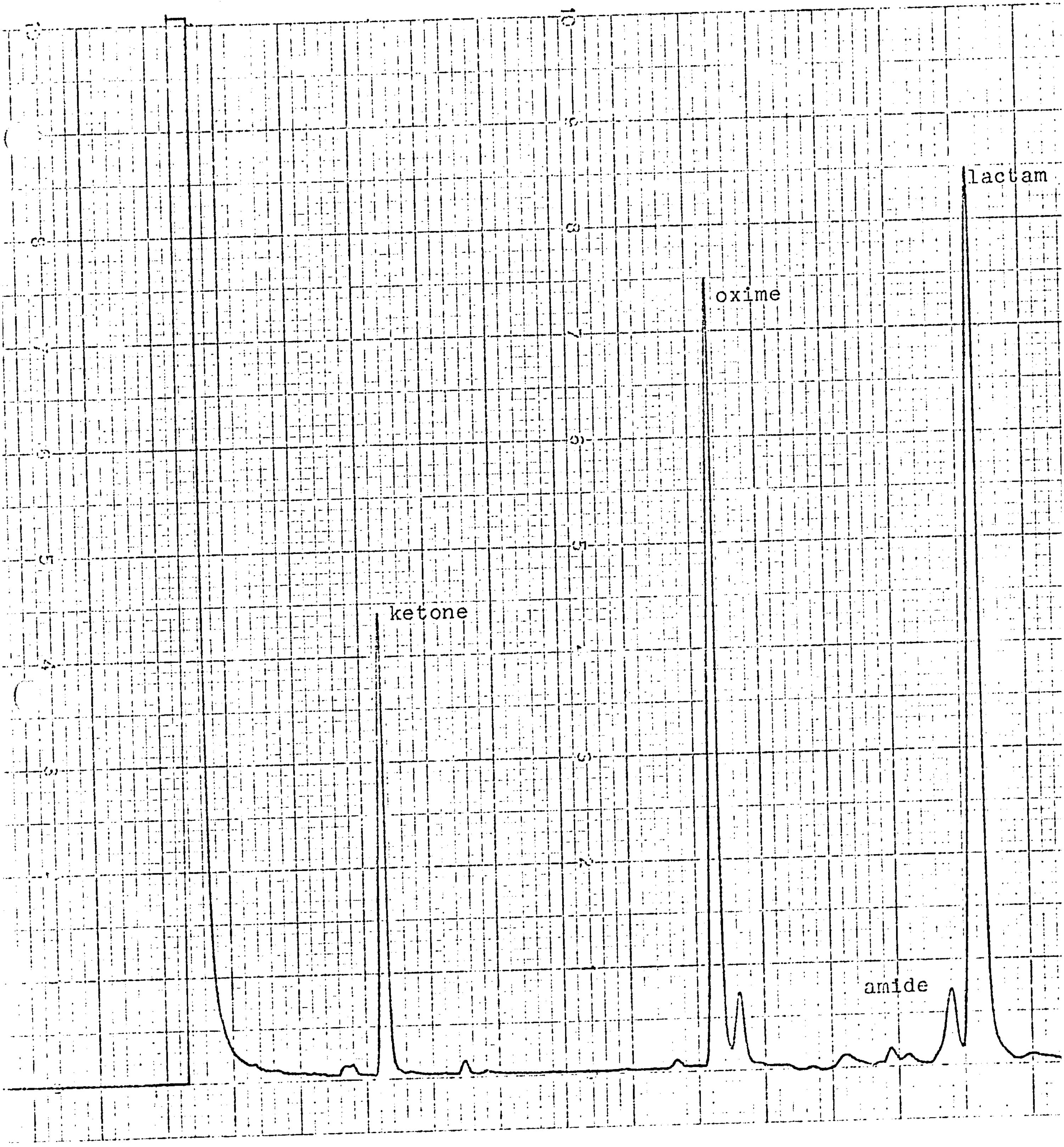
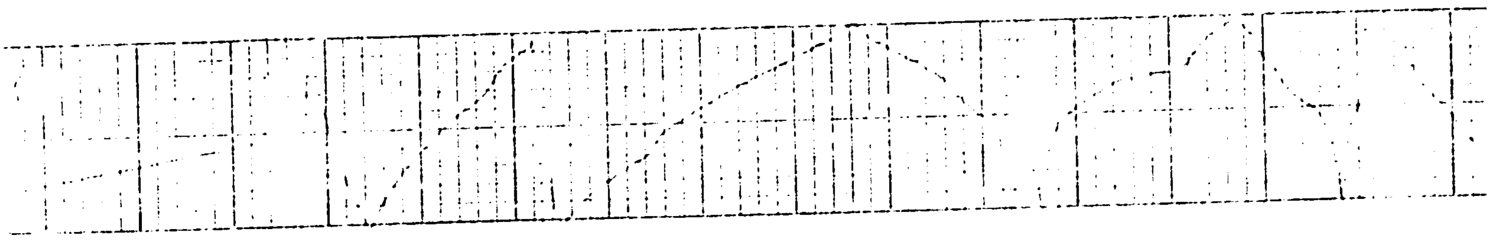


Fig. 8

Gas-liquid chromatogram of the photolysis products of 3,3,5,5-tetramethylcyclohexanone oxime



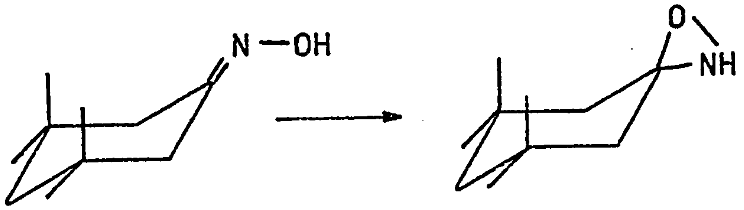
10
9
8
7
6
5
4
3
2
1
lactam
oxime
ketone
amide



CHAPTER II. THE PHOTOLYSIS OF CYCLIC KETOXIMES OF VARIOUS RING SIZES

A. The Photolysis Yields

It has been shown that 3,3,5,5-tetramethylcyclohexanone oxime photolyzes normally (Table 2). Some change in photolysis behavior might have been expected in this case since oxazirane formation involves a change in hybridization from sp^2 to sp^3 which is opposed by the resulting 1,3 diaxial methyl interactions (20).



Although little effect upon the photoreaction was observed in this case, the possible influence of strain was pursued further by investigation of the photolysis of the saturated cyclic ketoximes of ring size four to fifteen members. In particular, photolysis of the medium ring ketoximes of nine and ten members should prove most interesting since ring strain increases to a maximum (21) in these cases. An important consideration in this work was that the usefulness of the Beckmann reaction is seriously curtailed in the medium rings where poor lactam yields have been associated with ring strain (22).

The data obtained for the photolysis of the various rings in methanol is summarized in Table 4. The photolyses were carried out under the same constant conditions described for Table 2. Gas-liquid chromatograms of the photolysis mixtures are given at the end of the chapter.

TABLE 4

The effect of ring size on the photoreaction (1)

Starting Ketoxime	% Yield(4)			
	% ketone	% oxime	% amide	% lactam
cyclobutanone oxime	2	65	4	4
cyclopentanone oxime	2	55	7	13
cyclohexanone oxime	5	29	4	37
cycloheptanone oxime	10	16	10	32
cyclooctanone oxime	11	6	15	38
cyclononanone oxime	12	4	13	42
cyclodecanone oxime	17	8	13	34
cycloundecanone oxime	13	11	9	40
cyclododecanone oxime	9	16	6	42
cyclopentadecanone oxime	10	42	6	44

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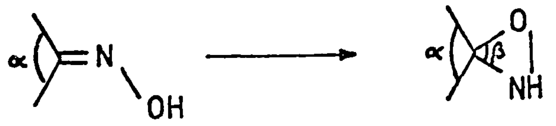
(4) As usual, the recovery varied between 70% and 80%. See Section B, Chapter 1.

B. Discussion of Results

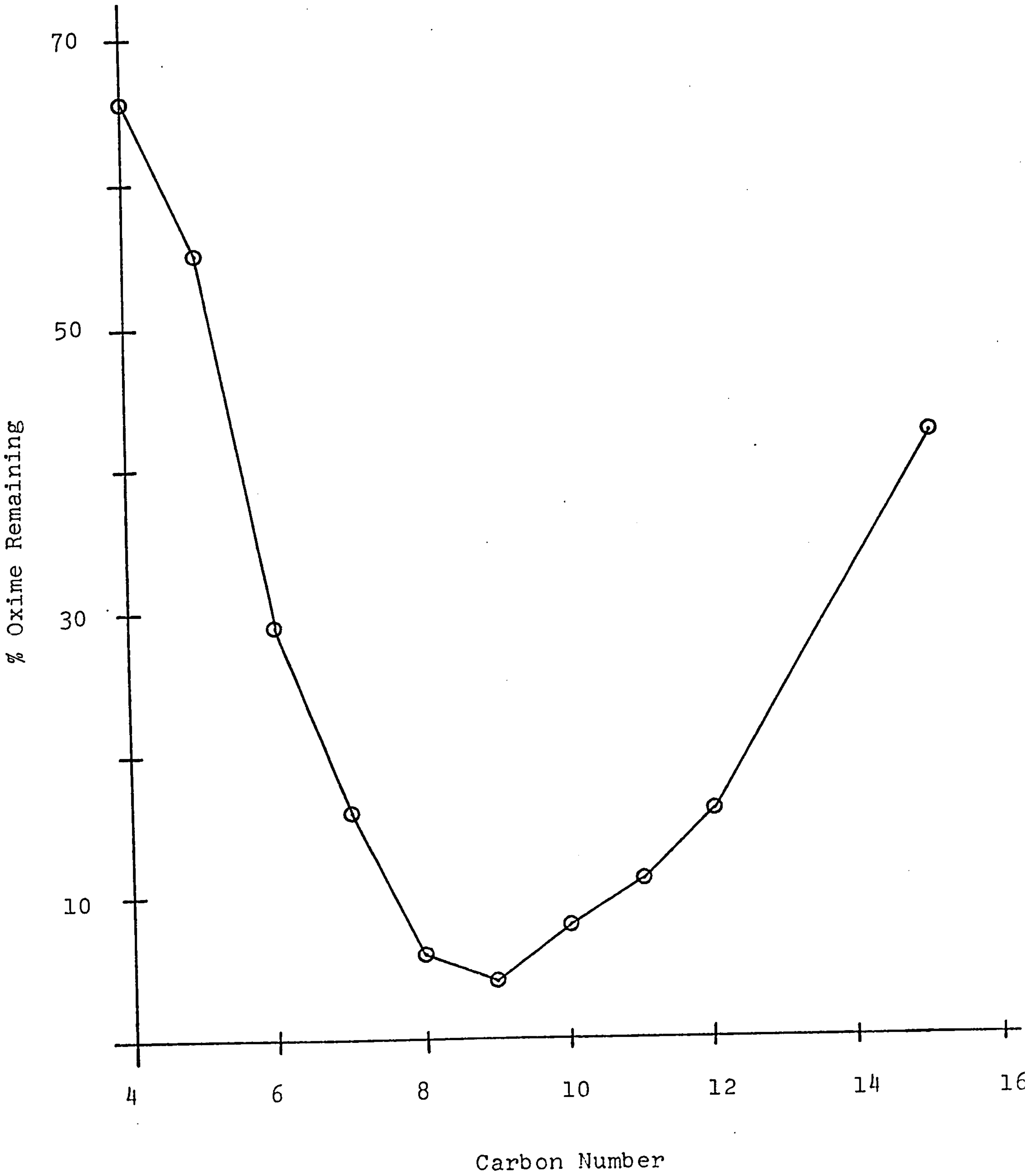
Some of the data of Table 4 has been plotted on graphs 1 and 2. Graph 1 is a plot of the amount of oxime remaining as a function of ring size. The rate of decomposition of oxime, measured by the amount remaining after photolysis, is seen to be strongly ring size dependent. The effect cannot be due to ring strain, however, since cyclobutanone oxime, the most strained ketoxime (23), reacts slowest. A possible explanation for the photolysis behavior can be given in terms of the intermediacy of an oxazirane.

Formation of an oxazirane results in a change in hybridization of the exocyclic bonds from sp^2 to sp^3. The small ring ketoximes seek to relieve bond angle strain by favoring an sp^3 configuration over sp^2 while the medium ring ketoximes relieve hydrogen-hydrogen interactions by favoring an sp^2 configuration over sp^3 (24). Oxime disappearance occurs at a rate opposite to this effect increasing to a maximum in the medium rings. The effect can be explained by reference to the variation of the oxazirane angle β with ring size.



Graph 1

Amount of oxime remaining
as a function of ring size

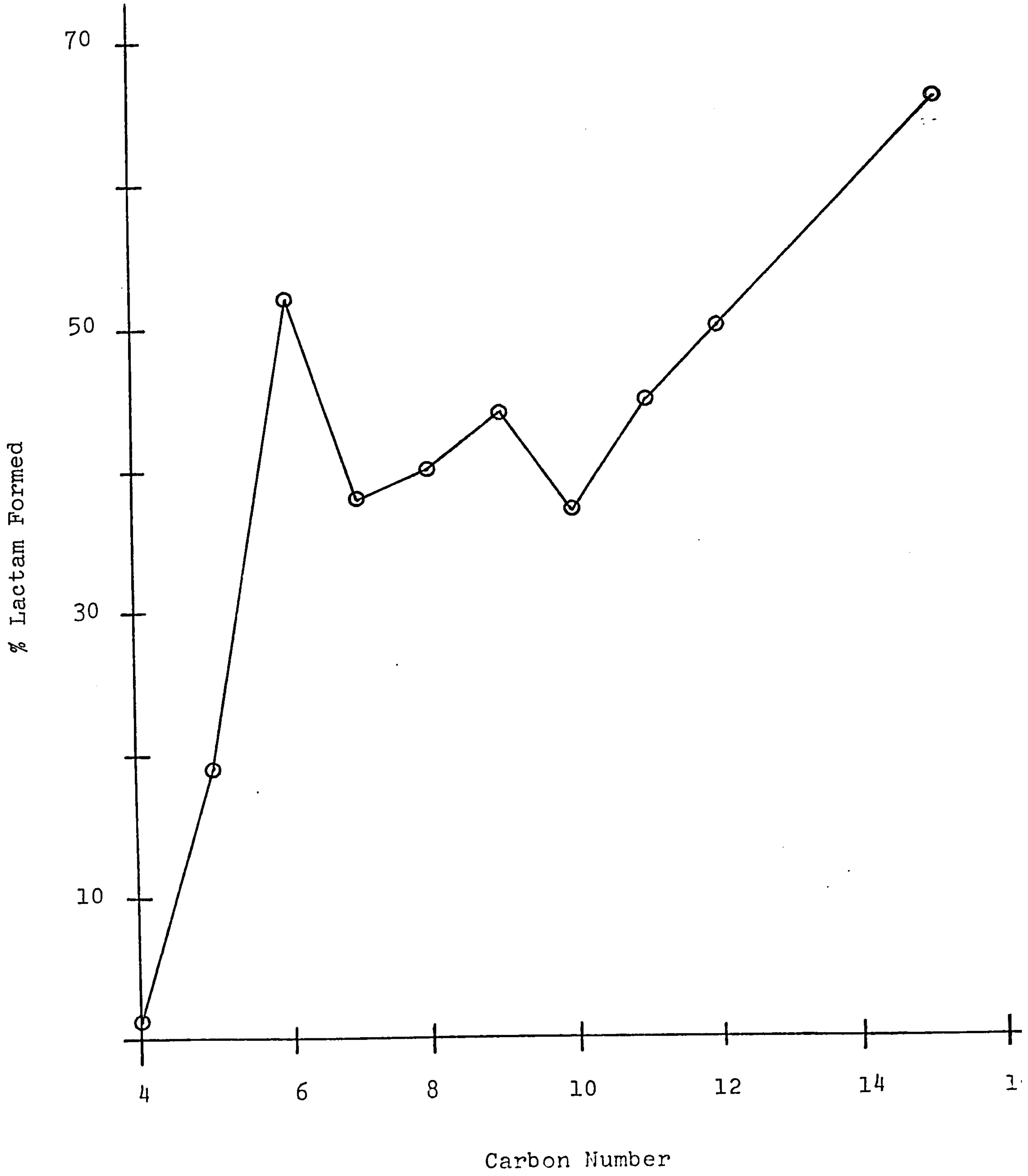

70
50
30
10
% Oxime Remaining
4
6
8
10
12
14
16
Carbon Number

As the ring angle α increases with ring size, the oxazirane angle β decreases resulting in a shortening of the N-O bond length (25). In view of the weakness of the N-O bond estimated at about 35 Kcal/mole (26) and the strain of the three membered oxazirane ring, changes in bond length are expected to be dramatic. In the small rings, the oxazirane angle β is sufficiently large that the N-O bond is so long as to almost prevent bond formation resulting in a very slow photolysis rate. As the angle α increases, the photolysis rate increases going to a maximum at the nine membered ring. The rate of photolysis then parallels the shortening of the N-O bond which is of shortest length and probably most easily formed in the nine membered ring. Beyond the nine membered ring, the angle α decreases again to the normal tetrahedral angle resulting in a lengthening of the N-O bond and a decreasing photolysis rate. By the time the large rings are reached, the rings are unstrained and cyclopentadecanone oxime photolyzes at the same rate as cyclohexanone oxime. The success of this interpretation provides powerful evidence for the intermediacy of oxaziranes during the photolysis of oximes.

Of particular interest is the efficiency of the lactam forming reaction. When the lactam yields are extrapolated to complete decomposition of the oxime (necessary since different amounts of oxime are reacted in each case) and plotted versus carbon number, the curve of Graph 2 results. Beyond the seven membered ring, the lactams possess the internal strain of the medium rings. Accordingly, the lactam yields from medium ring

Graph 2

Lactam yield as a function of ring size

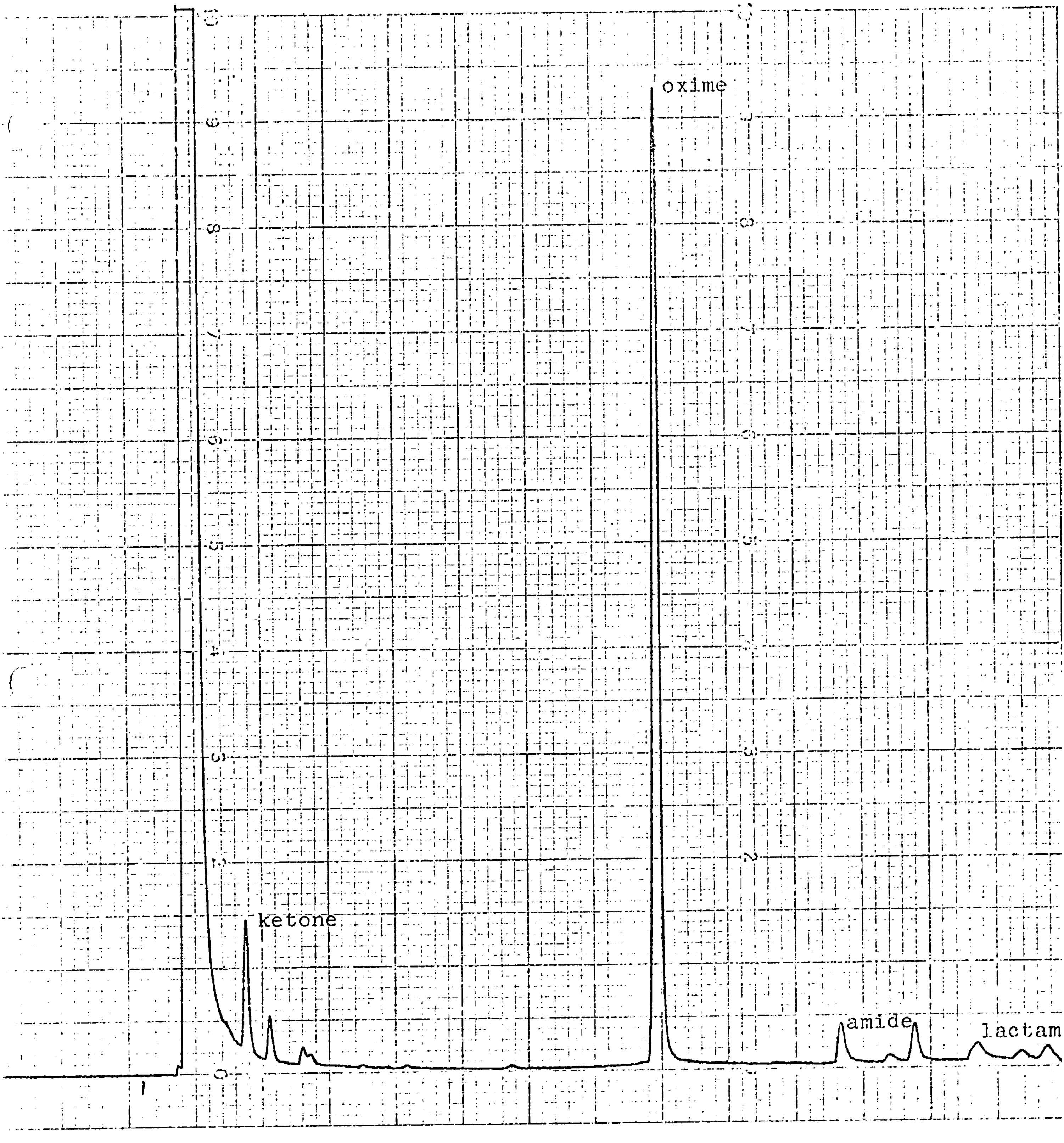

70
50
30
10
% Lactam Formed
4
6
8
10
12
14
1
Carbon Number

ketoximes were expected to drop considerably. In fact, they remained relatively constant. Again this result rules against a biradical recombination mechanism since it would be expected that such a recombination, opposed by ring strain, would result in a drastic drop in lactam yield in the photolysis of the eight- and nine membered ring oximes. These results again point to the possible synthetic use to which the photoreaction can be put since, unlike the Beckmann reaction, it seems to be relatively unaffected by ring strain.

The question of radical intermediates being responsible for the lactam forming reaction will be answered in the next chapter where the stereochemical course of the reaction will be elucidated.

Fig. 9

Gas-liquid chromatogram of the photolysis products
of cyclobutanone oxime



10
9
8
7
6
5
4
3
2
0
ketone
oxime
amide
lactam

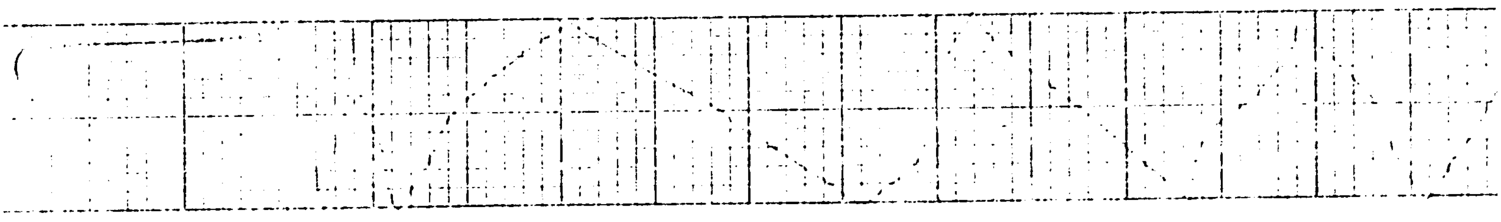


Fig. 10

Gas-liquid chromatogram of the photolysis products of cyclopentanone oxime

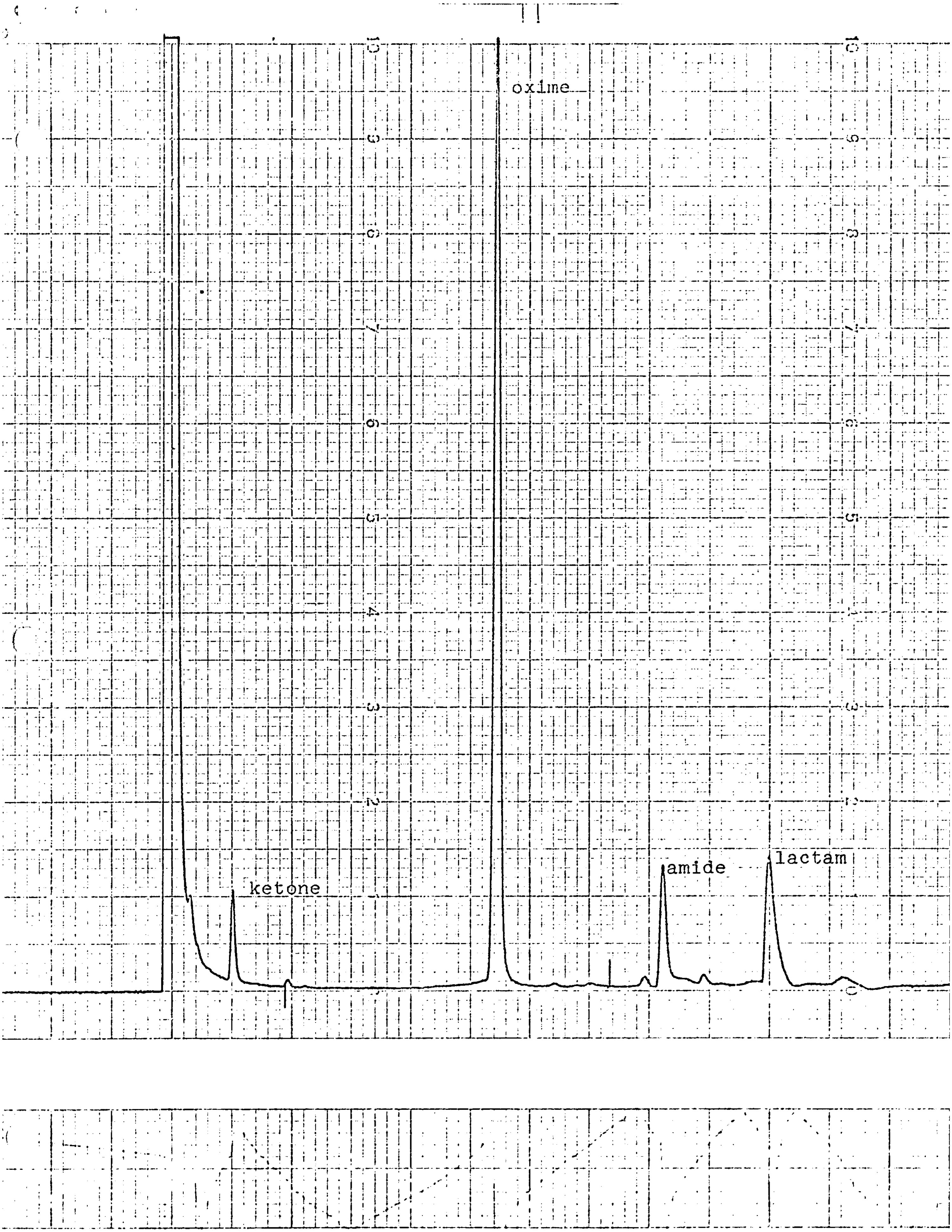

oxime
ketone
amide
lactam
10
9
8
7
6
5
4
3
2
0

Fig. 11

Gas-liquid chromatogram of the photolysis products of cycloheptanone oxime


ketone
oxime
lactam
amide

Fig. 12

Gas-liquid chromatogram of the photolysis products of cyclooctanone oxime


ketone
lactam
amide
oxime
10
9
8
7
6
5
4
3
2
1
0

Fig. 13

Gas-liquid chromatogram of the photolysis products of cyclononanone oxime

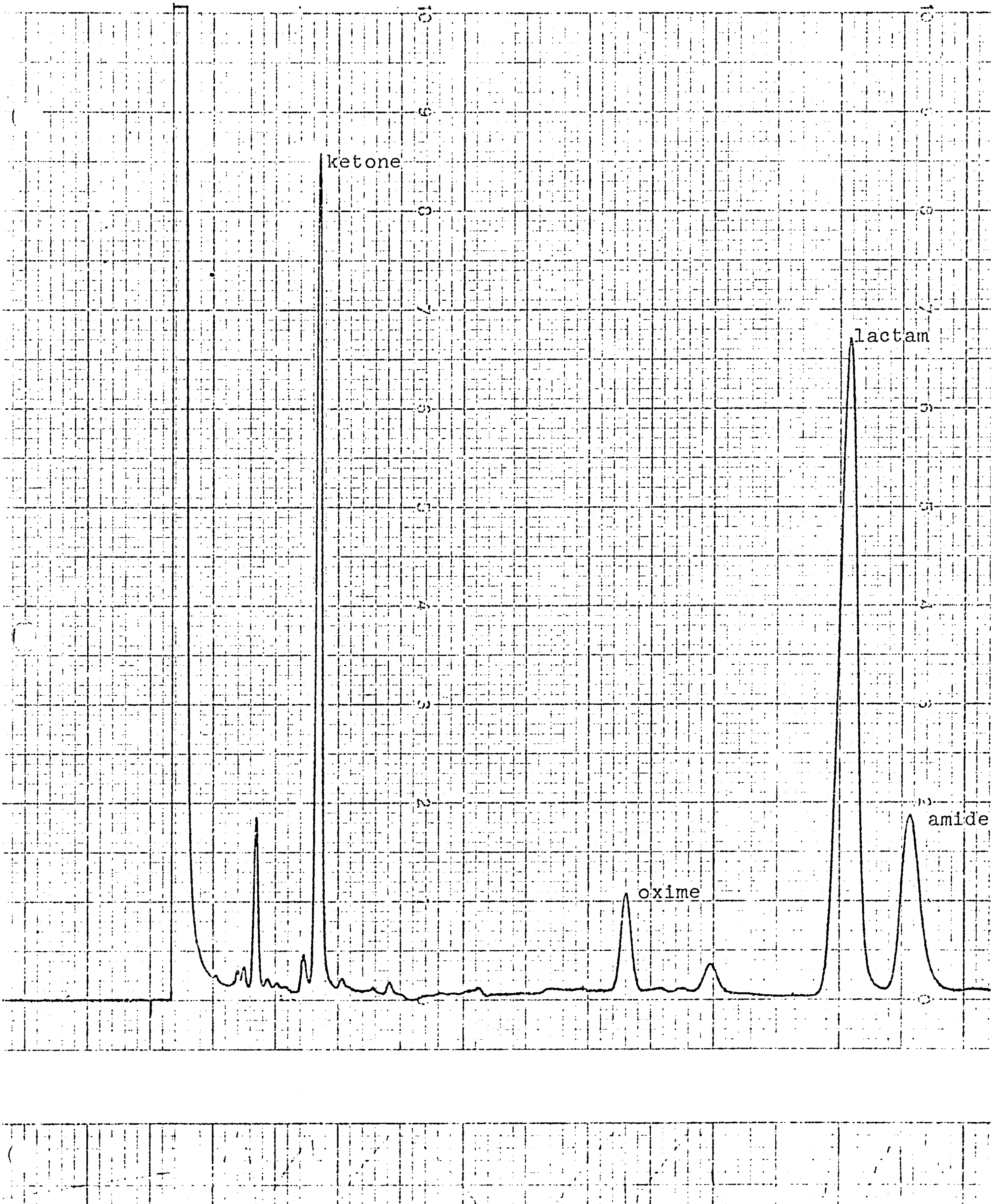
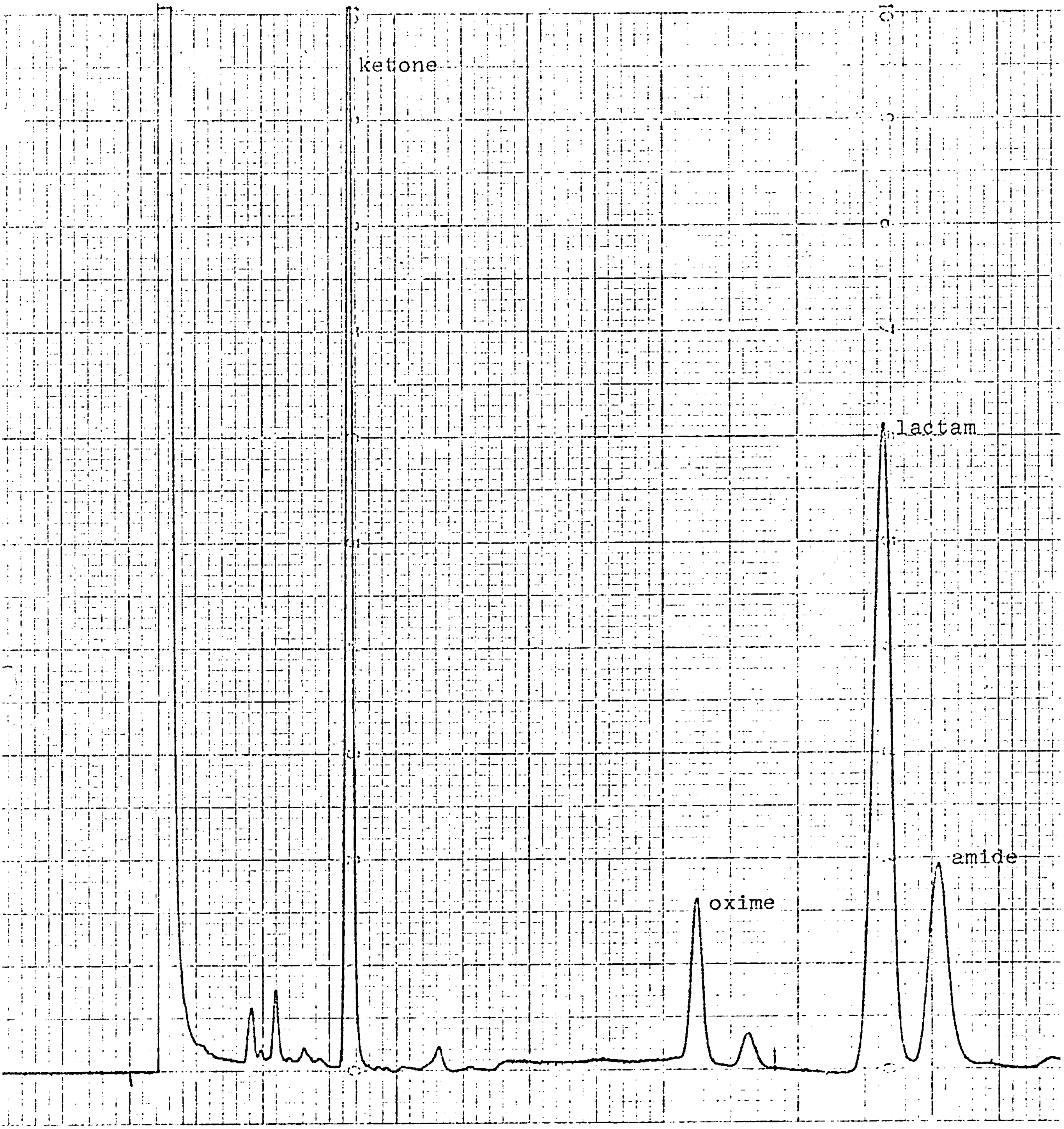

ketone
lactam
amide
oxime
10
9
8
7
6
5
4
3
2
0

Fig. 14

Gas-liquid chromatogram of the photolysis products of cyclodecanone oxime


ketone
lactam
amide
oxime

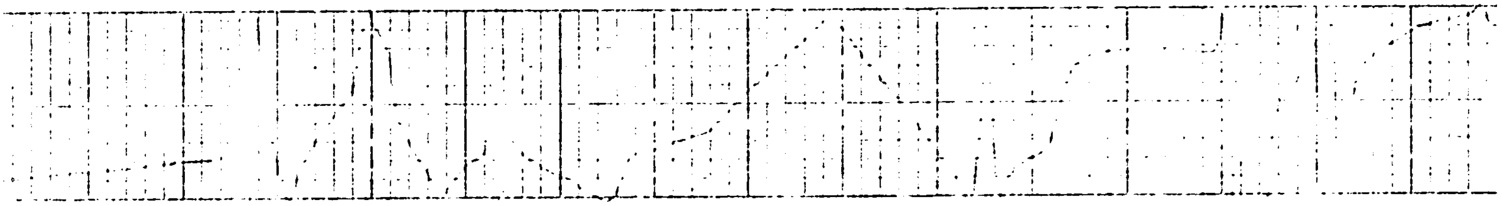


Fig. 15

Gas-liquid chromatogram of the photolysis products of cycloundecanone oxime

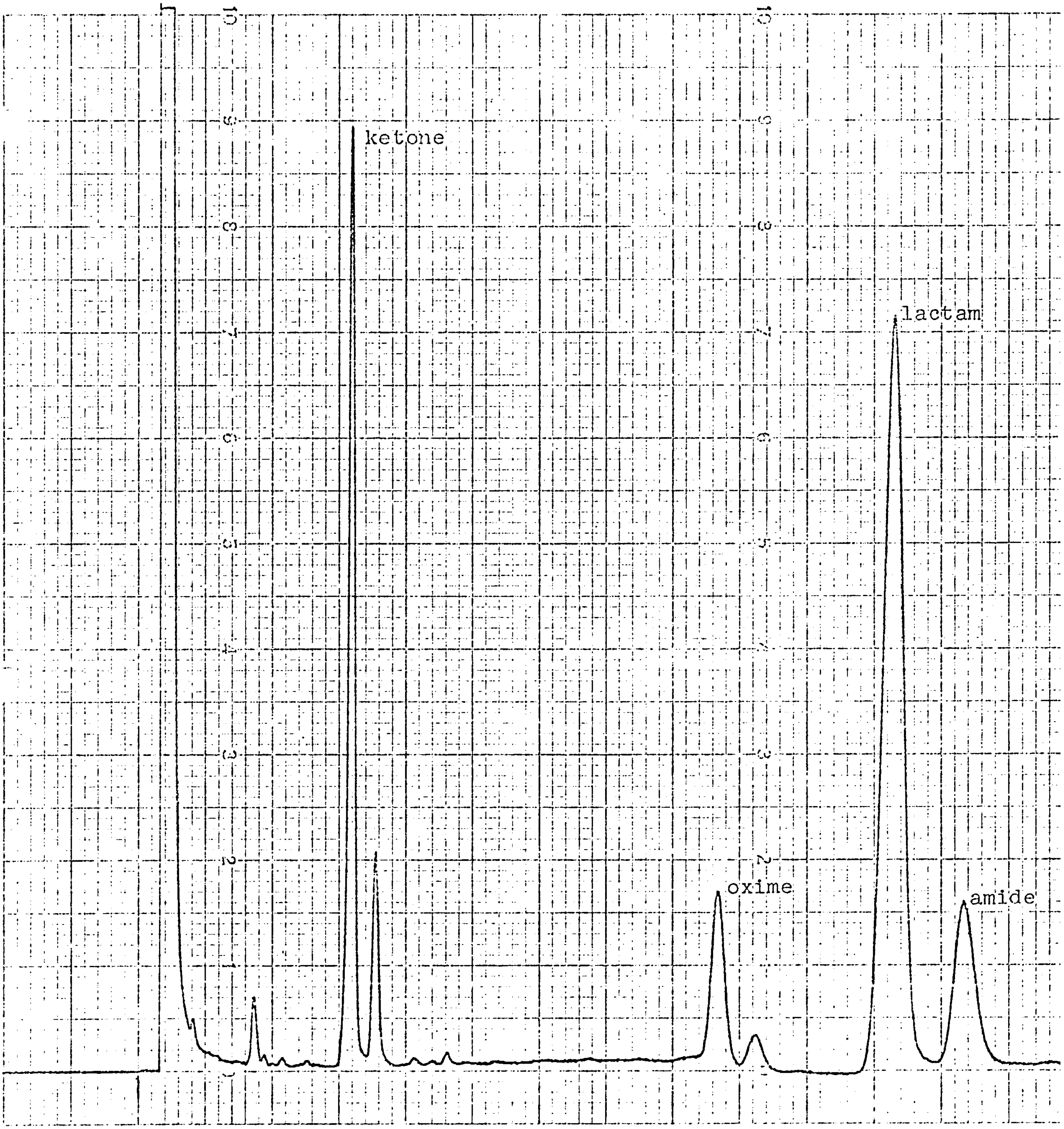

ketone
lactam
oxime
amide
10
9
8
7
6
5
4
3
2

Fig. 16

Gas-liquid chromatogram of the photolysis products of cyclododecanone oxime

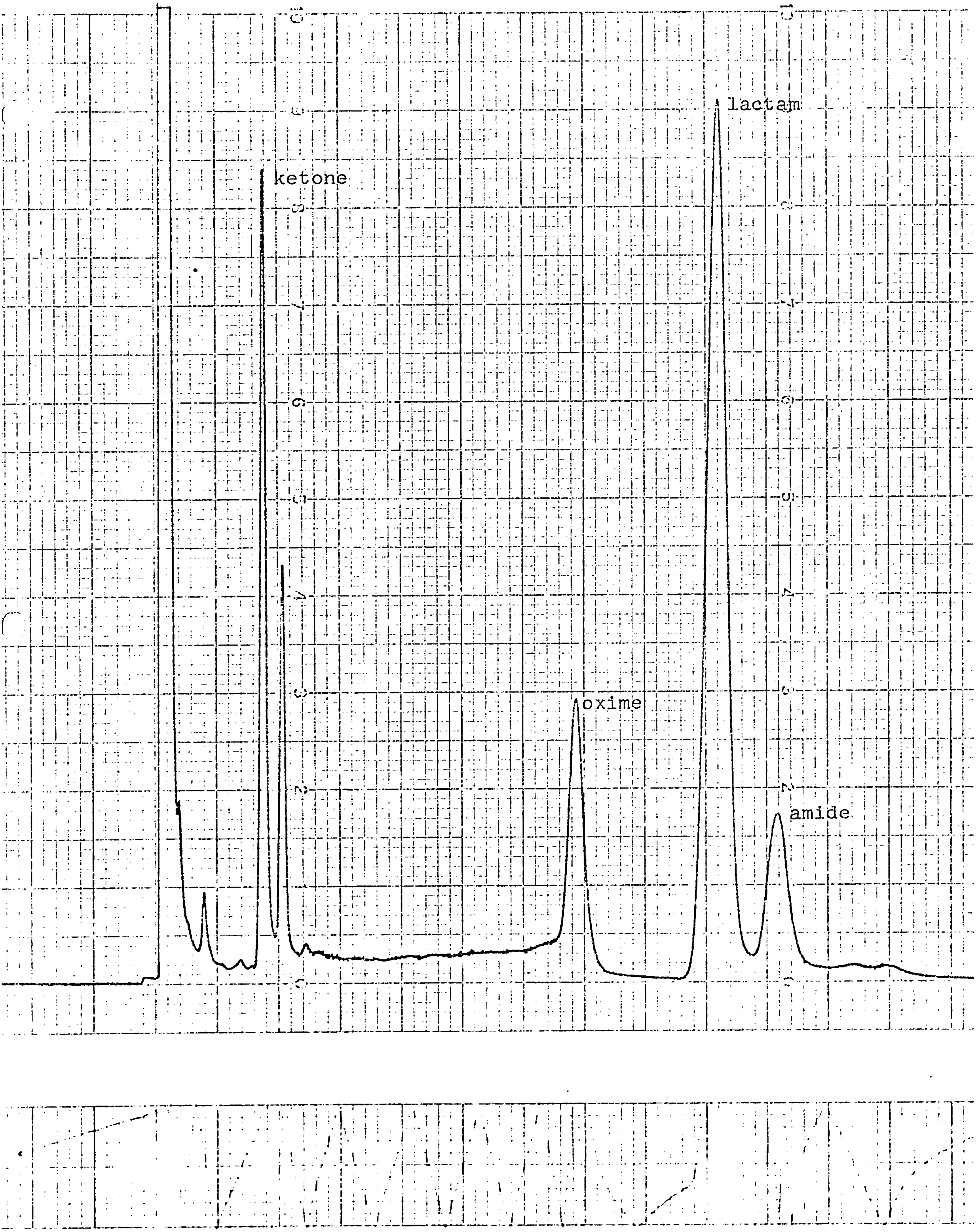
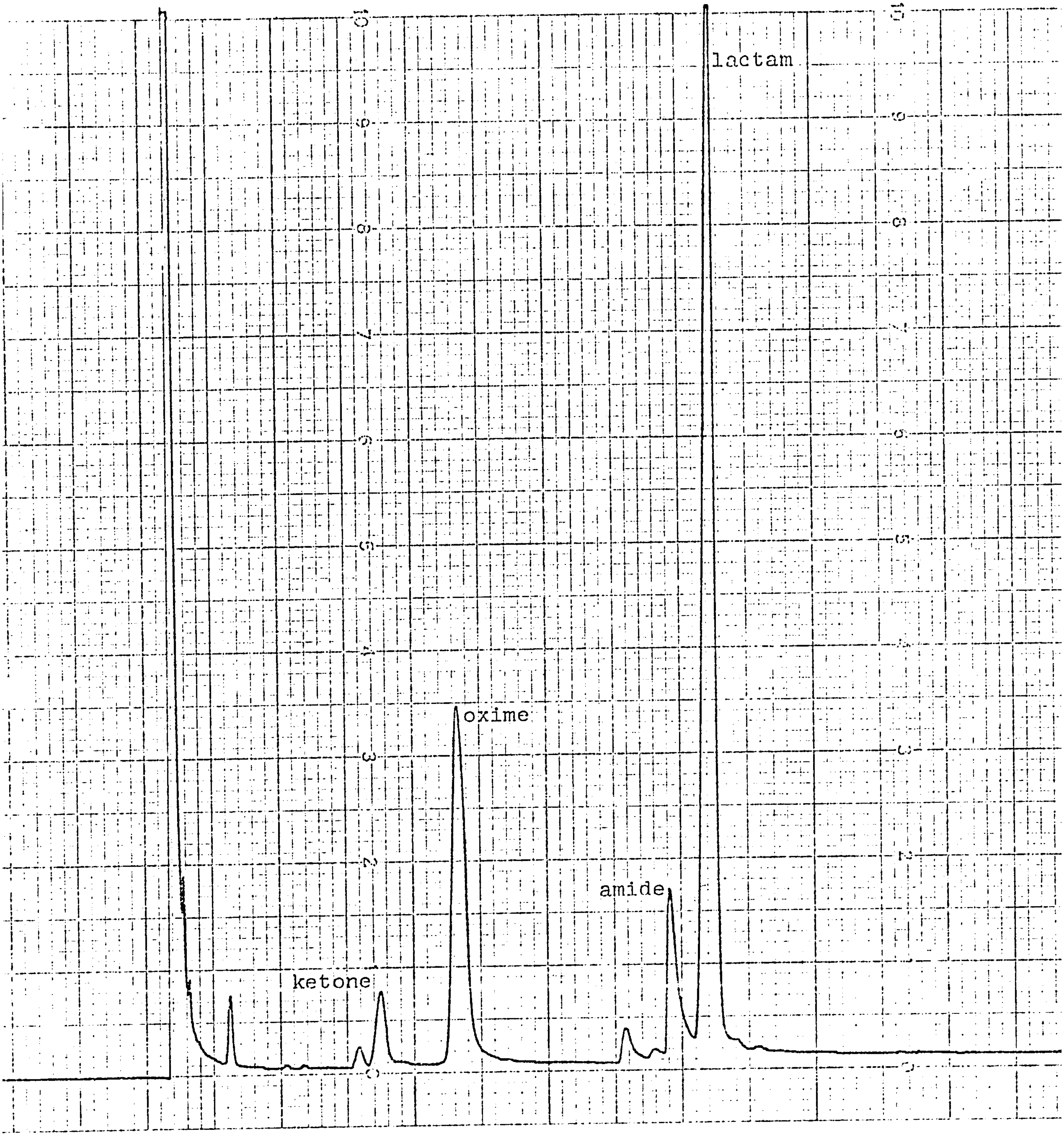
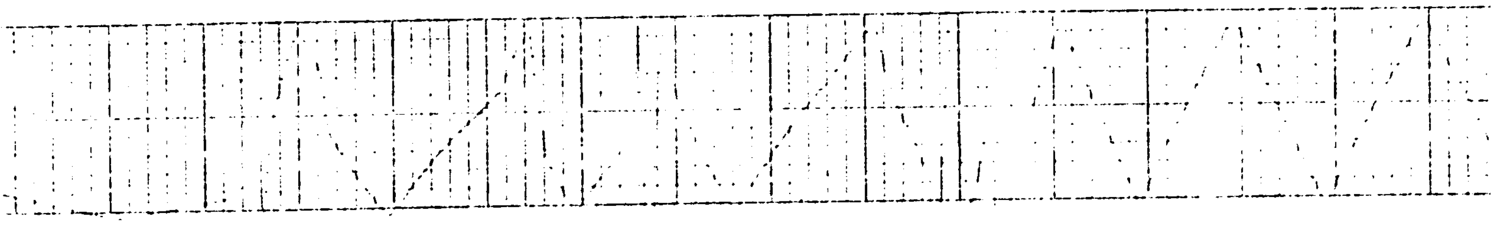

ketone
lactam
oxime
amide
10
9
8
7
6
5
4
3
2
0

Fig. 17

Gas-liquid chromatogram of the photolysis products of cyclopentadecanone oxime

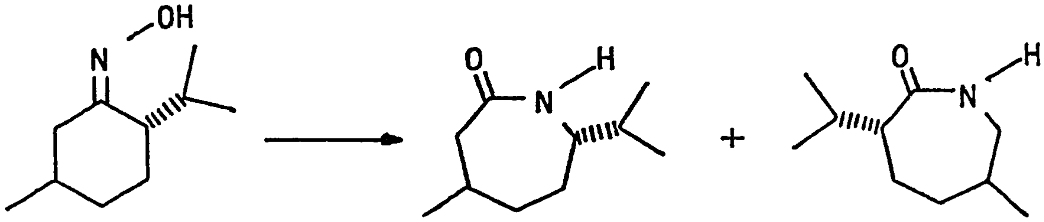

lactam
oxime
amide
ketone
10
9
8
7
6
5
4
3
2
0
10
9
8
7
6
5
4
3
2
0



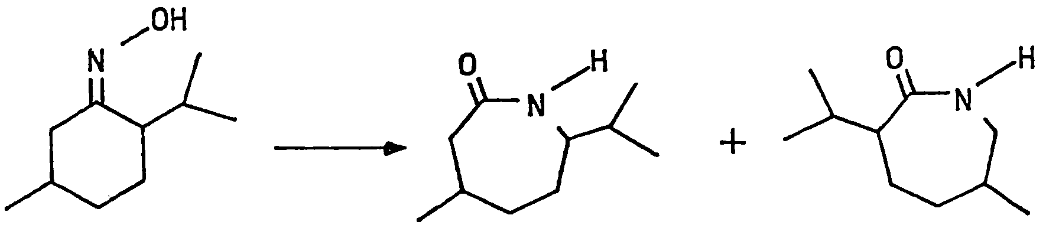
CHAPTER III. THE PHOTOLYSIS OF OXIMES EPIMERIC AT THE α-CARBON

A. The Photolysis Yields

All the data collected at this point ruled against the intermediacy of free radicals in the lactam forming reaction. A final attempt to demonstrate their intermediacy was carried out by the study of the photolysis of oximes epimeric at the α-carbon. If free radical intermediates were involved in the photoreaction, one ought to observe the formation of lactams in which the migrating α-center had undergone epimerization (27). In particular, the photolysis of either menthone oxime (XXXIII) or isomenthone oxime (XXXIV) could each be expected to result in the formation of four isomeric lactams (XXXV, XXXVI, XXXVII, XXXVIII).



XXXIII XXXV XXXVI



XXXIV XXXVII XXXVIII

The Beckmann rearrangement is known to occur with retention of configuration of the migrating α-carbon (28).

Thus, only lactams XXXV and XXXVI result from a Beckmann rearrangement on menthone oxime. Similarly, only lactams XXXVII and XXXVIII are obtained from isomenthone oxime.

Photolysis of menthone oxime only gave lactams XXXV and XXXVI which were identical with the lactams formed by a Beckmann rearrangement on menthone oxime. No lactams corresponding to epimerization of the α-center (XXXVII or XXXVIII) were detected among the photoproducts. Similarly, photolysis and a Beckmann reaction on isomenthone oxime gave the same lactam isomers (XXXVII and XXXVIII). No epimeric lactams (XXXV or XXXVI) were detected among the photoproducts of isomenthone oxime. The photolysis yields are tabulated in Table 5. Gas-liquid chromatograms of the photolysis mixtures are given at the end of the chapter.

TABLE 5

The photolysis of oximes epimeric at the α-center(1)

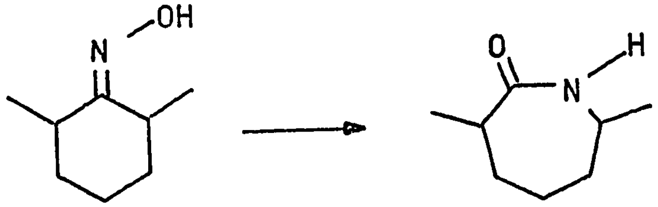
Starting Oxime	% Yield(4)				
	%ketone	%oxime	%amide	%lactam (Beckmann)	%lactam (epimeric)
menthone oxime	7	29	3(2)	45(2)	0
isomenthone oxime	6	16	3(2)	53(2)	0
cis-2,6-dimethyl-cyclohexanone oxime	6	14	3	44	<1
trans-2,6-dimethyl-cyclohexanone oxime	5	47	1	26	<1

Also of mechanistic significance was the observed epimerization of the starting oximes. Thus a small amount of menthone oxime (2.6%) was detected among the photoproducts of isomenthone oxime. Only a trace of isomenthone oxime (0.7%) was detected among the photoproducts of menthone oxime. The significance of these results will be discussed later.

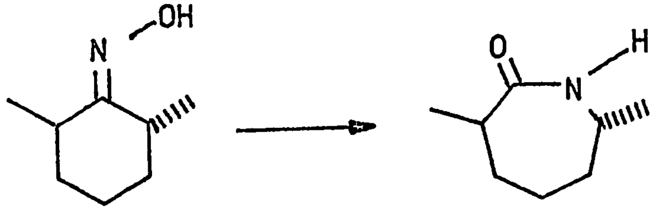
Separation of the four isomeric lactams derived from menthone oxime and isomenthone oxime was extremely difficult and could only be accomplished by g.l.c. on a non-polar column. The "tailing" which resulted made impossible the detection of small amounts of epimeric lactams which must have been present in view of the observed slight degree of epimerization of the starting oximes. Accordingly, a second pair of α-epimeric oximes were chosen, the photoproducts of which were more amenable to a g.l.c. separation.

In a manner analogous to menthone oxime, the epimeric <u>cis</u>-2,6-dimethylcyclohexanone oxime (XXXIX) and <u>trans</u>-2,6-dimethylcyclohexanone oxime (XL) could give rise to two epimeric lactams (XLI and XLII).

Experimentally, photolysis and a Beckmann rearrangement on <u>cis</u>-2,6-dimethylcyclohexanone oxime (XXXIX) gave the same lactam (XLI). Only a trace of the epimeric lactam (XLII) was detected among the photoproducts. Similarly, photolysis and a Beckmann reaction on <u>trans</u>-2,6-dimethylcyclohexanone oxime (XL) gave one lactam (XLII). A trace of the epimeric lactam (XLI) was detected among the photoproducts. The results are tabulated in Table 5. Gas-liquid chromatograms of the



XXXIX XLI



XL XLII

photolysis mixtures are appended at the end of the chapter.

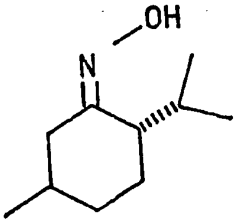
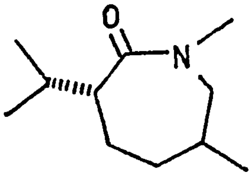
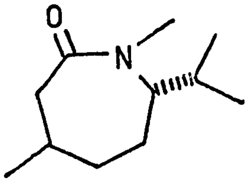
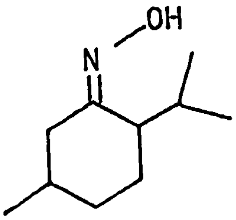
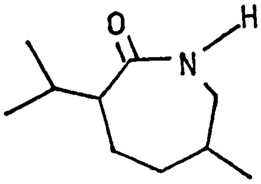
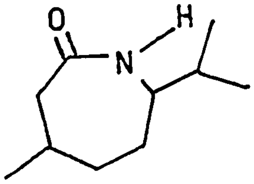
As before, a slight degree of epimerization of the starting oxime was observed. Thus, some trans-2,6-dimethylcyclohexanone oxime (XL) (0.8%) was detected among the photoproducts of cis-2,6-dimethylcyclohexanone oxime (XXXIX). No cis-2,6-dimethylcyclohexanone oxime (XXXIX) was detected, however, among the photoproducts of trans-2,6-dimethylcyclohexanone oxime (XL).

B. The Lactam Ratios

As usual, photolysis of the unsymmetrically substituted oximes, menthone oxime (XXXIII) and isomenthone oxime (XXXIV), gave rise to mixtures of two isomeric lactams. Separation of the mixture was possible only in the gas chromatograph using a specific liquid phase (OV-210). In the case of the lactam mixture resulting from the photolysis of menthone oxime (XXXIII), the second component was eluted from the column with the same retention time as trans-6-isopropyl-3-methylcaprolactam (XXXV). Similarly, the second component of the lactam mixture resulting from isomenthone oxime (XXXIV) was eluted from the column with the same retention time as cis-6-isopropyl-3-methylcaprolactam (XXXVII). The ratios of the lactam isomers are given in Table 6.

TABLE 6

Lactam ratios from the photolysis of menthone oxime and isomenthone oxime

Oxime	Lactam Isomers		Ratio(5)
			57/44 ± 1
			32/68

ratio from menthone oxime (XXXIII) (see above), the ratio of the isomeric lactams from isomenthone oxime (XXXIV) seemed

---

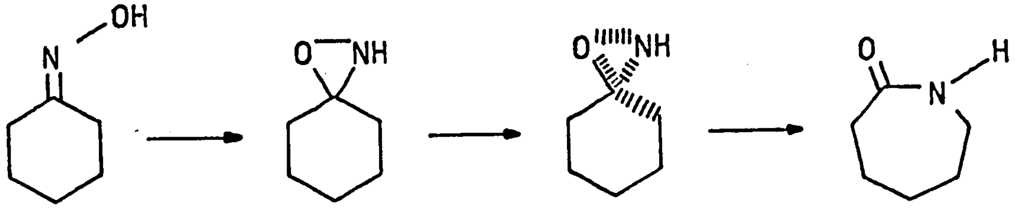
(5) The tailing of the lactam isomers prevented a measurement of the peak areas and the peak heights were used to determine the ratios.

relatively high. One other case in which the lactam ratio was not near 1:1 has been found. Taylor (6) reported that photolysis of the anti-isomer of 3β-acetoxypregnenolone oxime (X) gave a ratio of 39:61 of the Beckmann-type products (XIII and XII respectively). Photolysis of the syn-isomer of X gave a 1:1 ratio of these products.

It should be emphasized, however, that although most unsymmetrically substituted oximes investigated in this thesis gave approximately a 1:1 ratio of the two Beckmann-type products, there exists no reason for expecting such a ratio in all cases.

C. Discussion

The data of Table 5 demonstrates that the photo-rearrangement, like the Beckmann rearrangement, proceeds in a stereospecific fashion. The observed retention of configuration of the migrating α-carbon can only mean that the α-center never becomes kinetically free of the migration terminus and clearly rules out any free radical intermediates. Bond breaking and bond forming reactions must either be concerted or very fast occurring at rates greater than that



of oxygen quenching (Chapter 1) or bond rotation. A concerted mechanism for the photoreaction is given on the previous page.

An interesting development was the observed epimerization of isomenthone oxime and cis-2,6-dimethylcyclohexanone oxime upon irradiation in methanol. It will be hypothesized later that epimerization occurs from the triplet state of the oxazirane. If this hypothesis is correct, the observed epimerization clearly establishes the existence of an equilibrium between oxime and oxazirane as shown on the previous page.

A considerable amount of data has been rationalized on the basis of an oxazirane as the reactive intermediate. The intermediacy of such a species has, to date, been justified only on the basis of the similarity of the oxime photochemistry to that of the nitrones. In chapter 5 it will be shown that oxaziranes are the intermediates responsible for the formation of photoproducts and some aspects of their chemistry will be studied. But first, it will be shown that what has been said about the photochemistry of the cyclic ketoximes can be carried over to the acyclic case.

Fig. 18

Gas-liquid chromatogram of the photolysis products of menthone oxime


10
9
8
7
6
5
4
3
2
1
0
ketone
oxime
lactam
amide

Fig. 19

Gas-liquid chromatogram of the photolysis products of isomenthone oxime

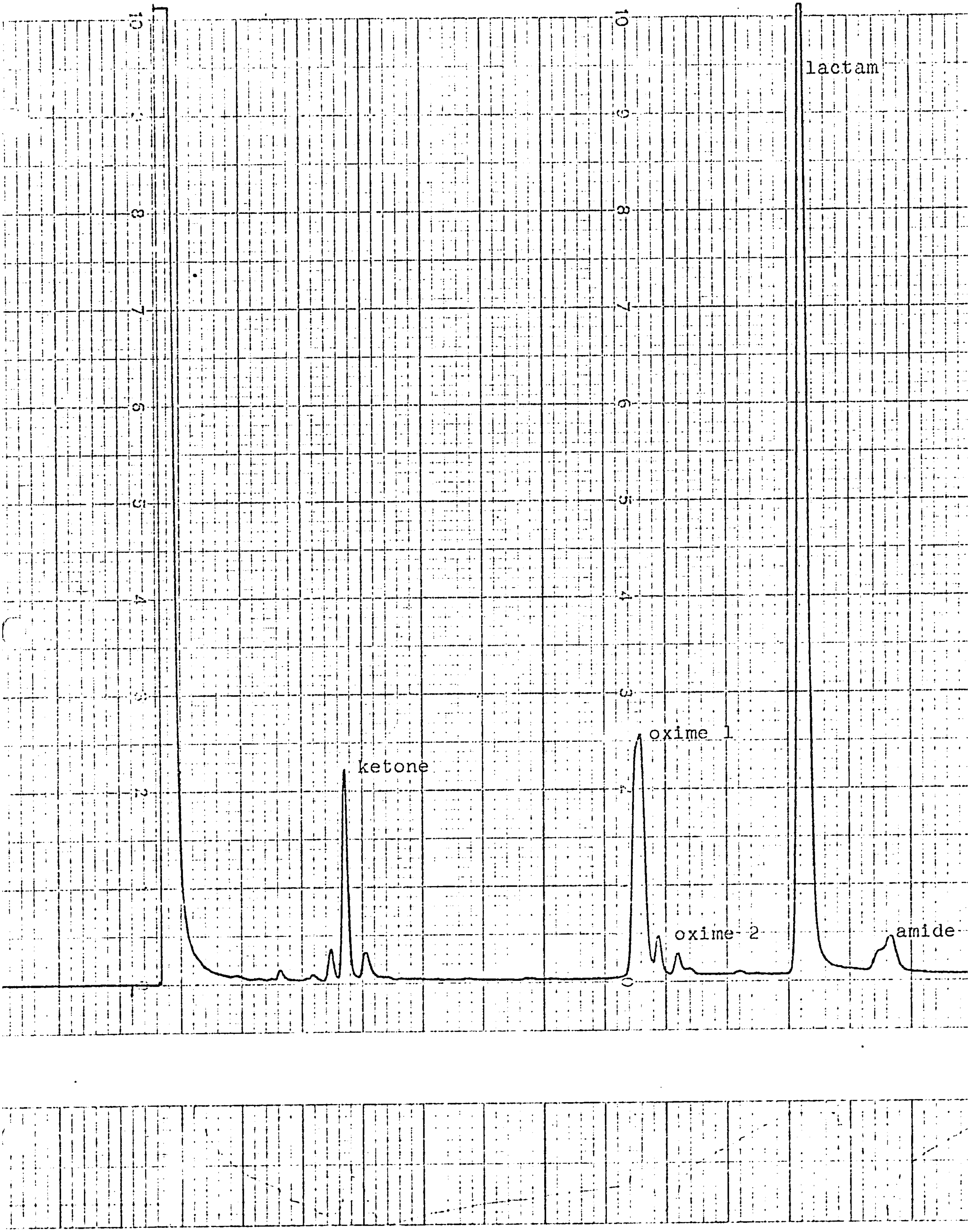

10
9
8
7
6
5
4
3
2
0
lactam
oxime 1
ketone
oxime 2
amide

Fig. 20

Gas-liquid chromatogram of the lactam isomers of menthone oxime on OV-210

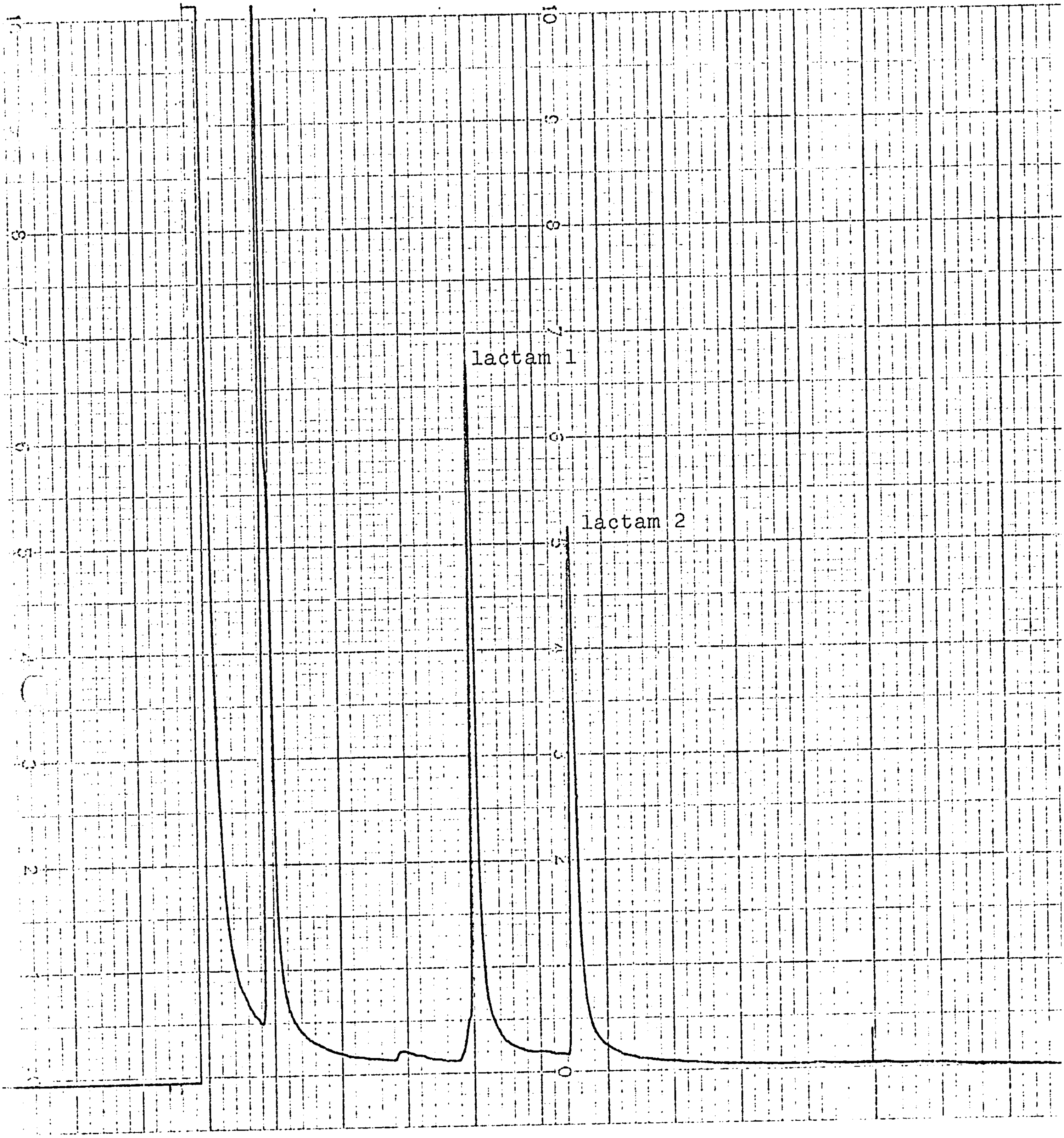
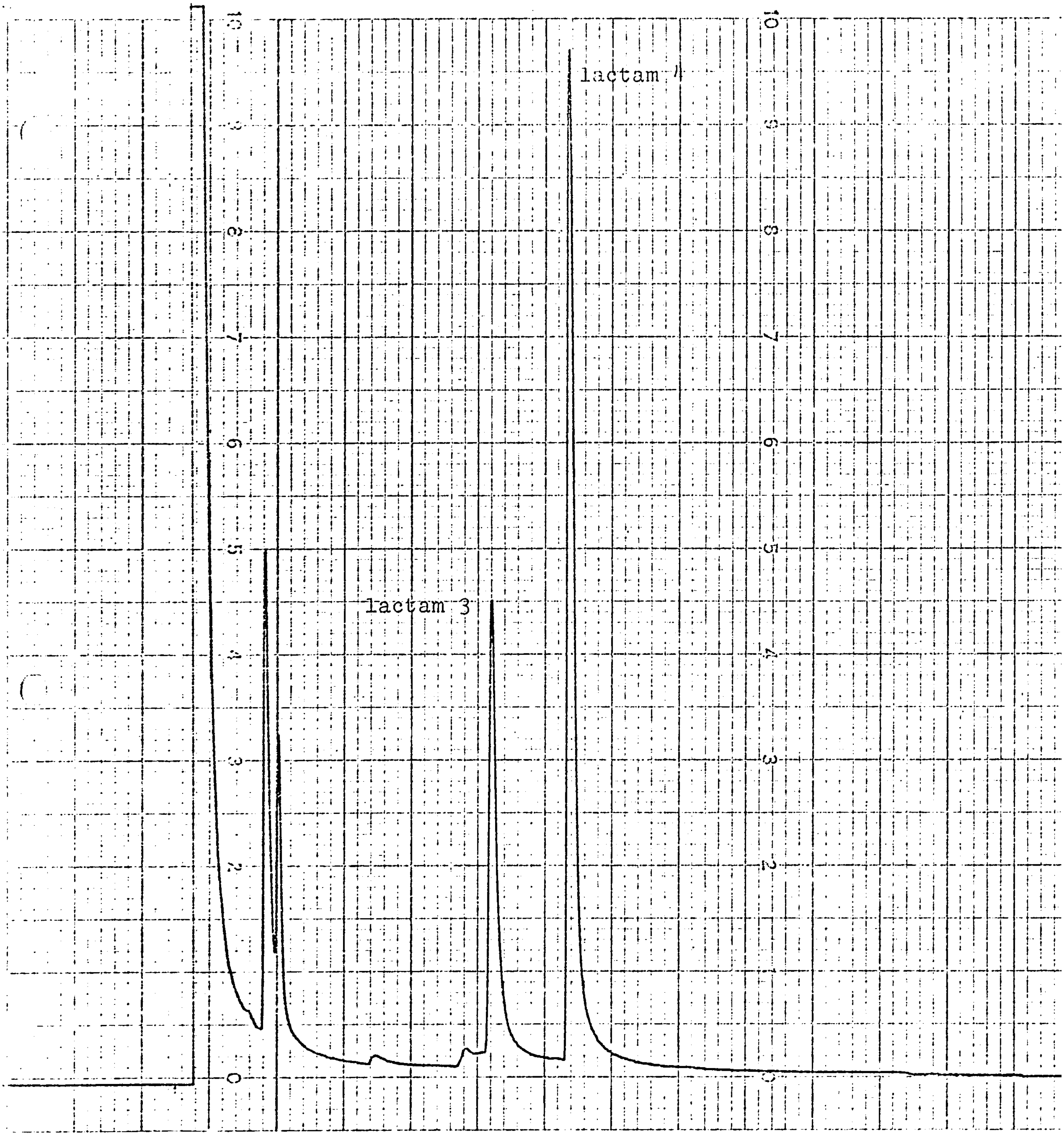

10
9
8
7
6
5
4
3
2
0
lactam 1
lactam 2

Fig. 21

Gas-liquid chromatogram of the lactam isomers of isomenthone oxime on OV-210



10
9
8
7
6
5
4
3
2
0
lactam 4
lactam 3
10
9
8
7
6
5
4
3
2
0

Fig. 22

Gas-liquid chromatogram of the photolysis products of cis-2,6-dimethylcyclohexanone oxime

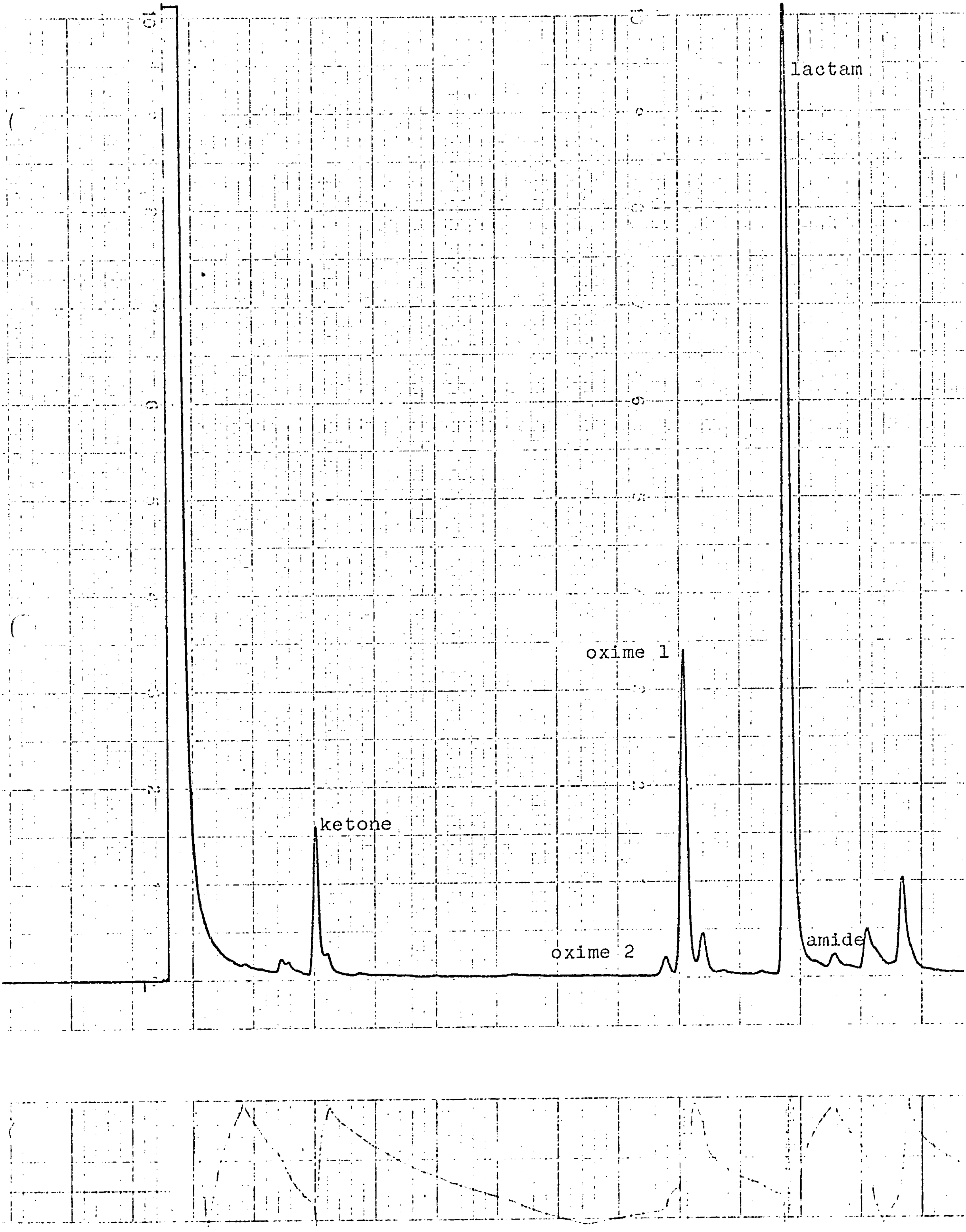
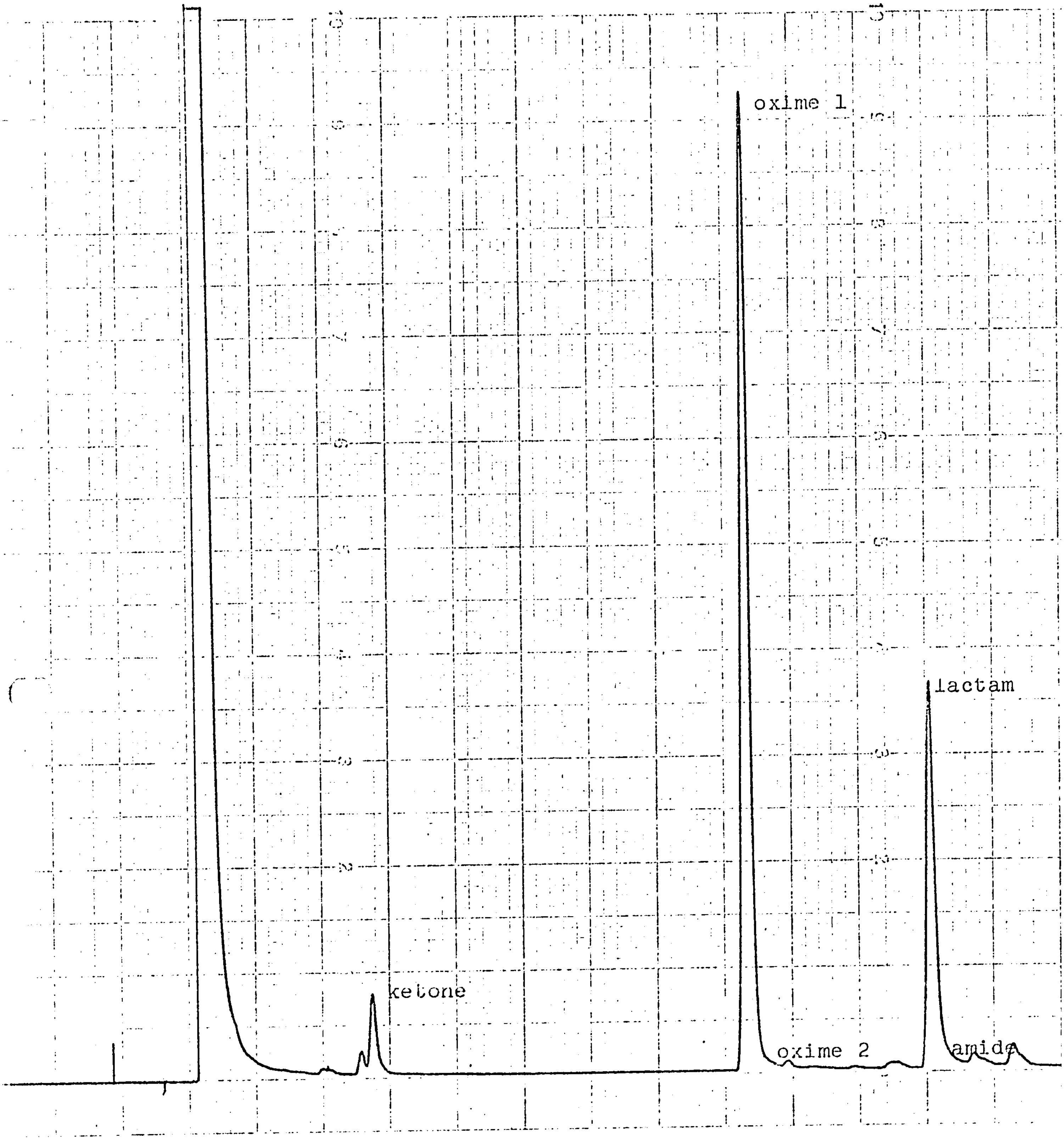
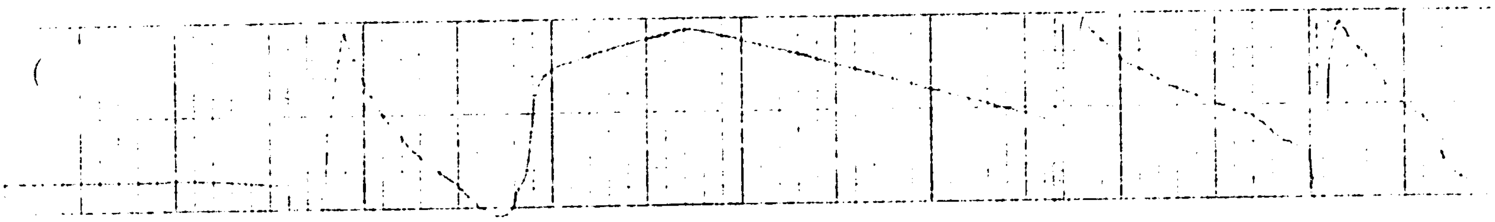

10
lactam
oxime 1
ketone
oxime 2
amide

Fig. 23

Gas-liquid chromatogram of the photolysis products of trans-2,6-dimethylcyclohexanone oxime

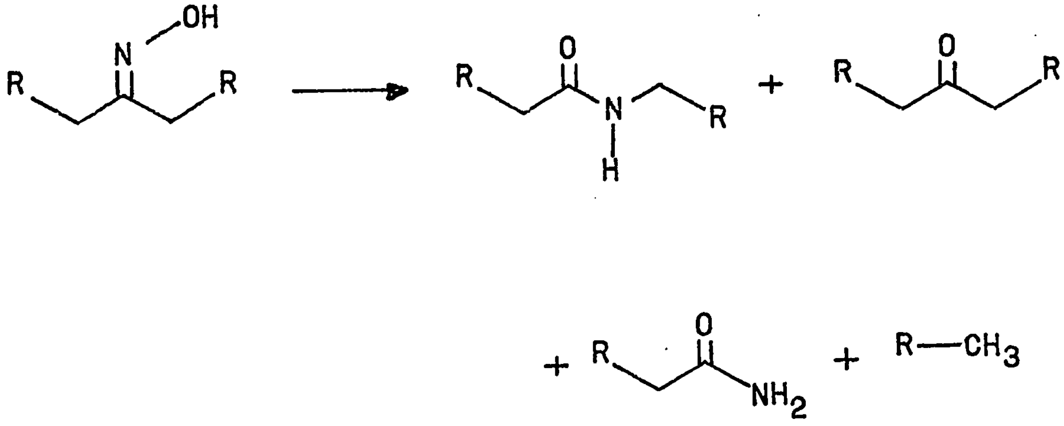

oxime 1
lactam
ketone
oxime 2
amide



CHAPTER IV. THE PHOTOLYSIS OF ACYCLIC KETOXIMES

A. The Photolysis Yields

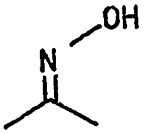
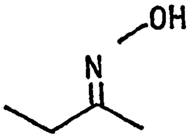
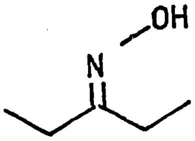
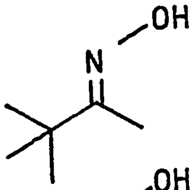
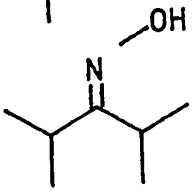
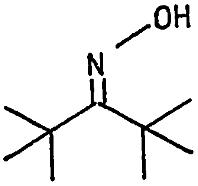
The photolysis behavior of the cyclic ketoximes being reasonably well understood, it was of interest to see if the photoreaction could be generalized to include the acyclic ketoximes. In analogy with the results of the photolysis of cyclohexanone oxime, the photolysis of a typical acyclic ketoxime should give an N-alkyl secondary amide as the major product accompanied by small amounts of ketone, amide and an alkane.



The results of the photolysis of a number of acyclic ketoximes are given in Table 7. Temperature programmed gas-liquid chromatograms of the photolysis mixtures are given at the end of the chapter.

TABLE 7

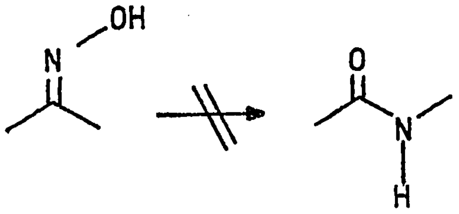
The photolysis yields of various acyclic oximes(1)

Starting Oxime	% Yield			
	% ketone	% oxime	% product of α-cleavage	% Beckmann-product
	N.D.	44	11	2
	N.D.	41	10	12
	<1	31	10	21
	<1	54	2	10
	4	28	4	34
	5	28	5	24

N.D. - not determined

B. The Methyl Ketoxime Effect

It will be noted from Table 7 that compared to the cyclic ketoximes, the photolysis of the acyclic ketoximes does not give good yields of the Beckmann-type products. This is particularly true of the methyl ketoximes for which acetone oxime (XLIII) represents the extreme case. The expected product, N-methylacetamide (XLIV), was formed in very poor yield.


XLIII XLIV

It was observed, however, that the photolysis of progressively α-substituted oximes gave increasingly better yields of the Beckmann-type product.

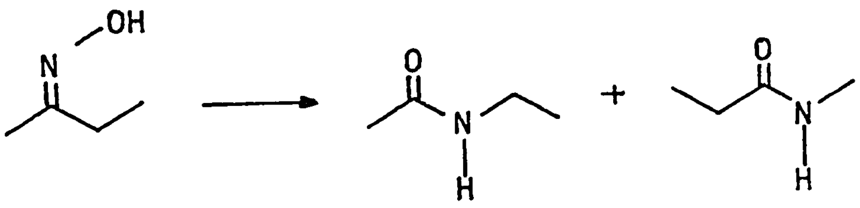
It was also noted that photolysis of methyl ketoximes gave large amounts of amides compared to the yield of the Beckmann-type product. Similar results were noted in the photolysis of a steroidal methyl ketoxime. Taylor (6) reported that photolysis of the syn- and anti-oximes of 3β-acetoxypregnenolone (X) gave a high yield of the α-cleavage product (XIV). The ratio of the α-cleavage product yield to that for both Beckmann-type products was found to be approximately 1:1.

The data of Table 7 shows that the ratio of the α-cleavage product yield to that of the Beckmann-type product depends on the degree of α-substitution and varies in a regular manner, from 5:1 for acetone oxime to 1:7 for 2,4-dimethyl-3-pentanone oxime. The ratio obtained from the photolysis of cyclohexanone oxime in methanol is about 1:9.

The cause of the anomalous results from the photolysis of acetone oxime and the other methyl ketoximes is as yet unknown. It was observed, however, that compared to cyclohexanone oxime, the ultra-violet absorption spectrum of acetone oxime was shifted about 10nm to shorter wavelength. The low photolysis yields might be a result of this wavelength shift.

C. The Ratios of Beckmann-type Products from Unsymmetrically Substituted Oximes

Photolysis of unsymmetrically substituted acyclic oximes gave mixtures of both possible Beckmann-type products, as expected. The resulting secondary amide isomers separated well in the gas chromatograph on a Carbowax 20M column, the first component eluted being that with the more hindered N-H group (see Section E, Chapter 1). Thus, for the photoproducts of 2-butanone oxime (XLV), N-ethylacetamide (XLVI) was eluted

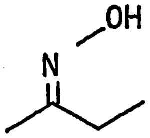
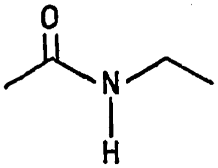
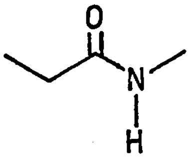
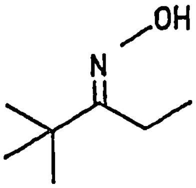
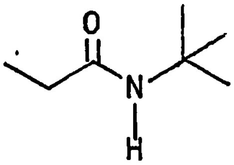
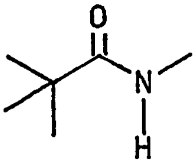


XLV XLVI XLVII

from the column before N-methylpropionamide (XLVII). The ratios were determined in the usual way and recorded in Table 8.

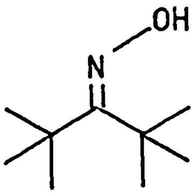
TABLE 8

Ratios of secondary amide isomers from the photolysis of unsymmetrically substituted acyclic oximes

Oxime	Amide Isomers		Ratio
			72/28 ± 0.5
			55/45

Again it was observed that the methyl ketoxime (XLV) gave a ratio of Beckmann-type products different from 1:1. These results must be qualified since the recoveries are low and the yield of the Beckmann-type product was very poor.

D. The Preparation of Highly Hindered Ketoximes

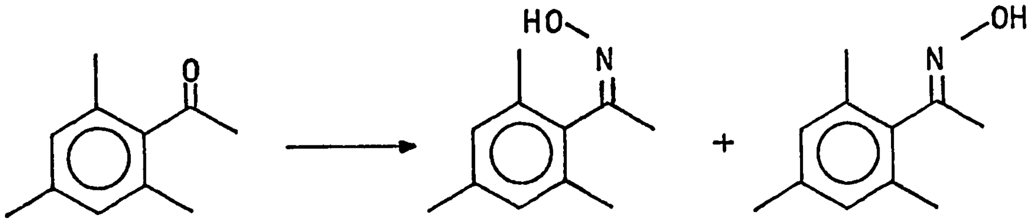


XLVIII

Included in Table 7 is the previously unreported 2,2,4,4-tetramethyl-3-pentanone oxime (XLVII).

Preparation of the oxime of 2,2,4,4-tetramethyl-3-pentanone is inordinately difficult due to steric hindrance from the t-butyl groups. The method which finally proved successful consisted in heating the ketone to reflux with a large excess of a concentrated solution of hydroxylamine acetate in methanol for one to two weeks. Thus XLVIII was obtained as a crystalline compound in 22% yield.

Treatment of 2,4,6-trimethylacetophenone (XLIX) under the same conditions resulted in complete conversion to oxime. Oximation of this highly hindered ketone was previously reported by Pearson and Keaton (29), the reaction time under their conditions being six months! Under the above conditions, however, the product was an oil which was shown by g.l.c. to contain two components. The product was probably a mixture of the syn- (La) and anti (Lb) oximes.



XLIX La Lb

E. Discussion

As was pointed out, the photolysis of the methyl ketoximes did not go well resulting in very poor yields of the Beckmann-type products. Progressively better yields were obtained, however, as the degree of α-substitution increased. The conclusion that the photoreaction might provide a possible extension to the usefulness of the Beckmann rearrangement applies equally well to the photolysis of the acyclic ketoximes. Even the highly strained and fully α-substituted di-t-butylketoxime (XLVIII) gave a reasonable yield of the Beckmann-type product although it is quite certain that normal Beckmann conditions would not give the amide.

As observed for the cyclic ketoximes, unsymmetrically substituted acyclic ketoximes gave mixtures of both possible Beckmann-type products. The ratio of the two products for two acyclic oximes are given in Table 8. The lactam ratios observed were similar to those obtained from the cyclic ketoximes.

Finally, it has been shown that oximes of highly sterically hindered ketones can be easily prepared and in the case of at least one unsymmetrically substituted, hindered ketone, a mixture of both the syn- and anti oximes appears to have been formed.

Fig. 24

Gas-liquid chromatogram of the photolysis products of acetone oxime

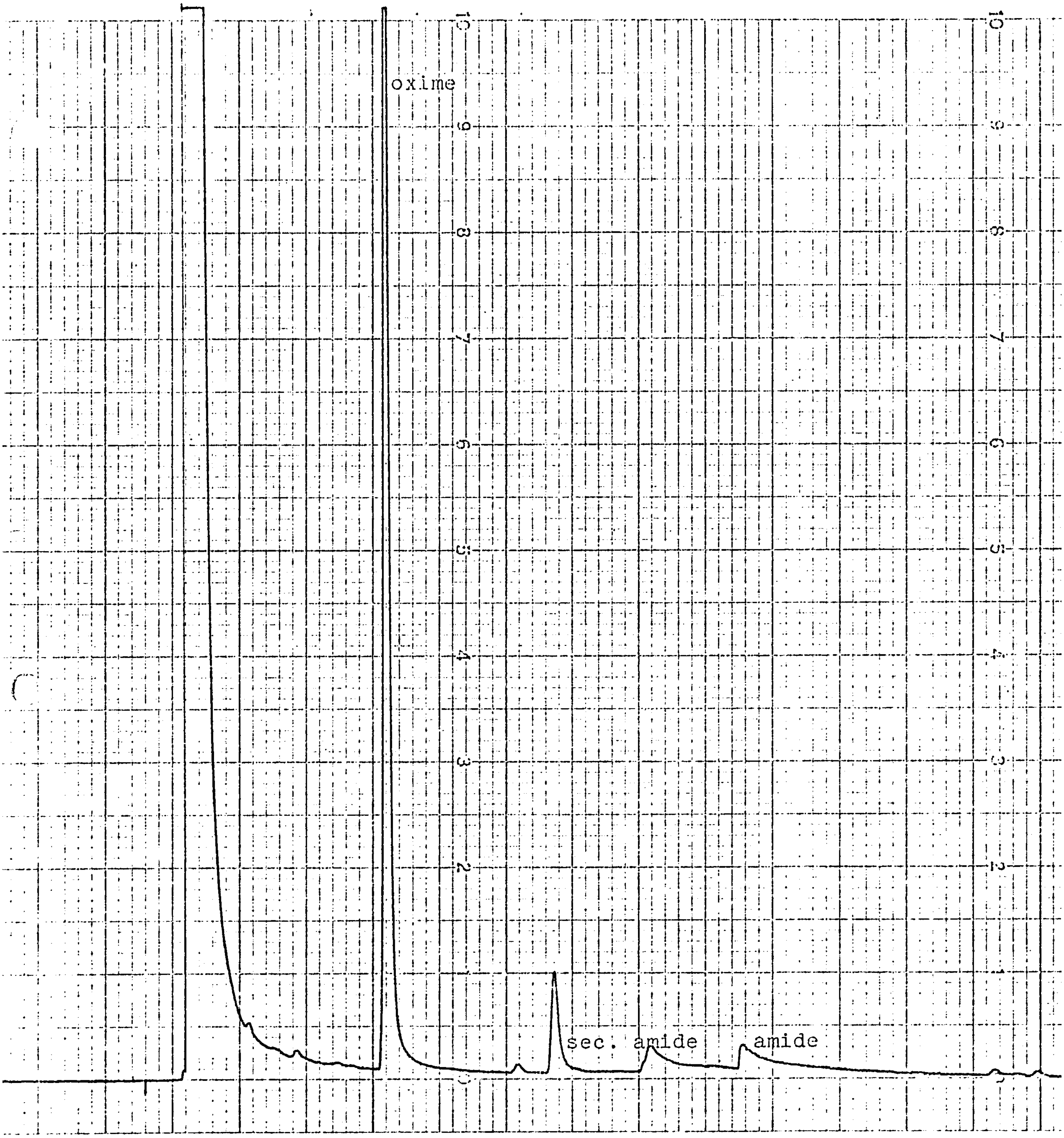

oxime
sec. amide
amide
10
9
8
7
6
5
4
3
2
1
0

Fig. 25

Gas-liquid chromatogram of the photolysis products of 2-butanone oxime

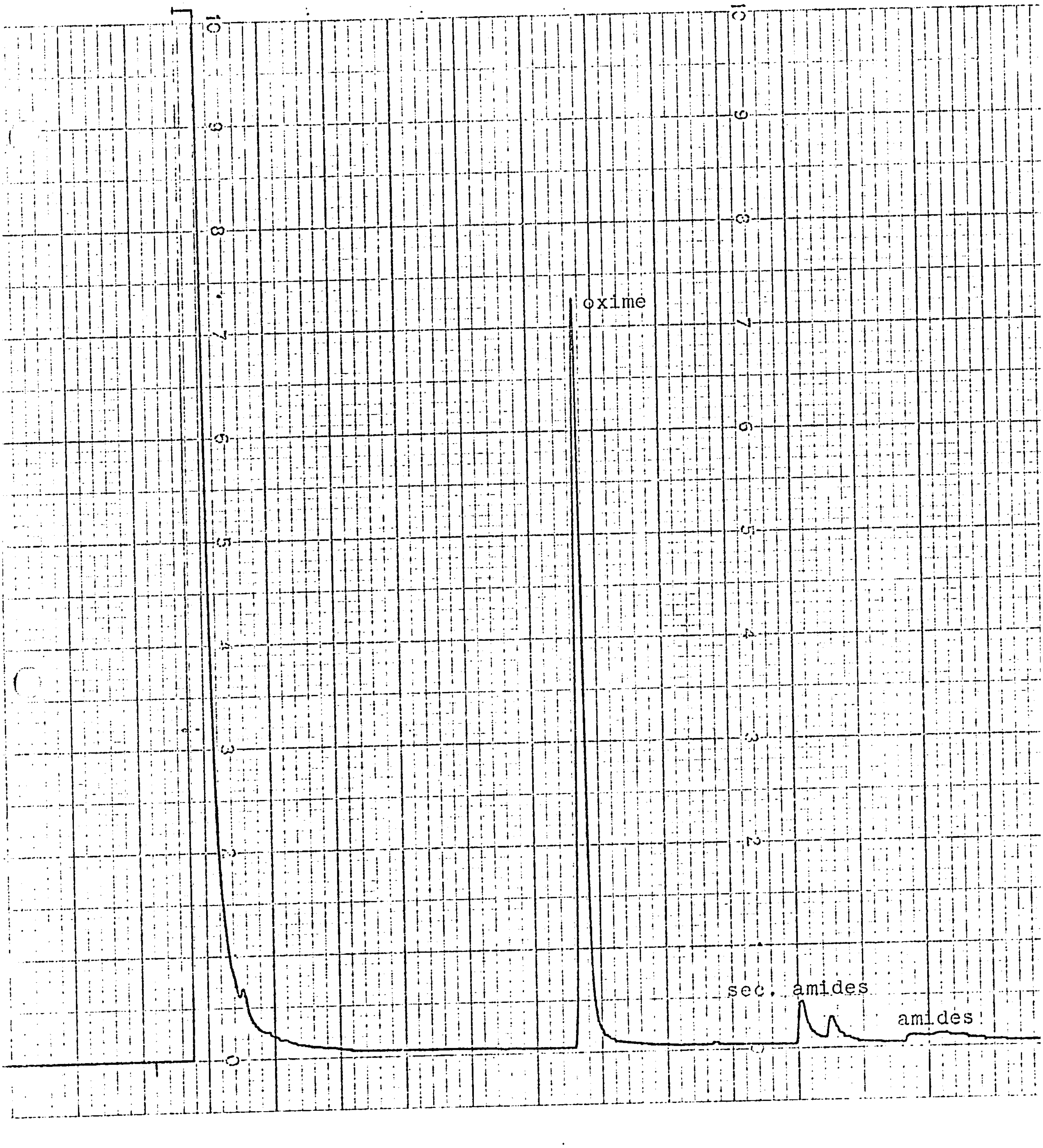

10
9
8
7
6
5
4
3
2
0
oxime
sec. amides
amides

Fig. 26

Gas-liquid chromatogram of the photolysis products of 3-pentanone oxime

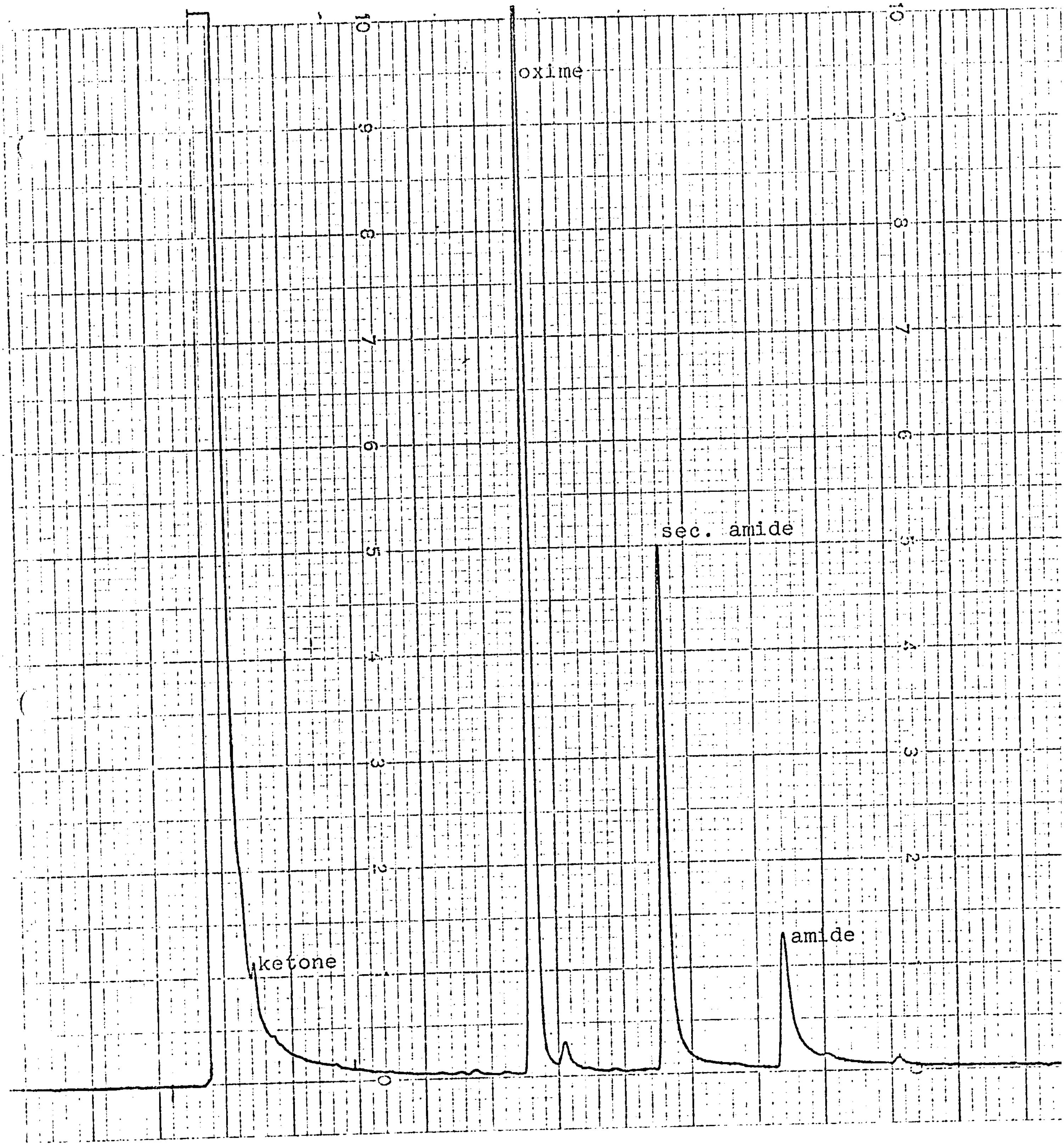

oxime
sec. amide
amide
ketone
10
9
8
7
6
5
4
3
2
0

Fig. 27

Gas-liquid chromatogram of the photolysis products of 3,3-dimethyl-2-butanone oxime

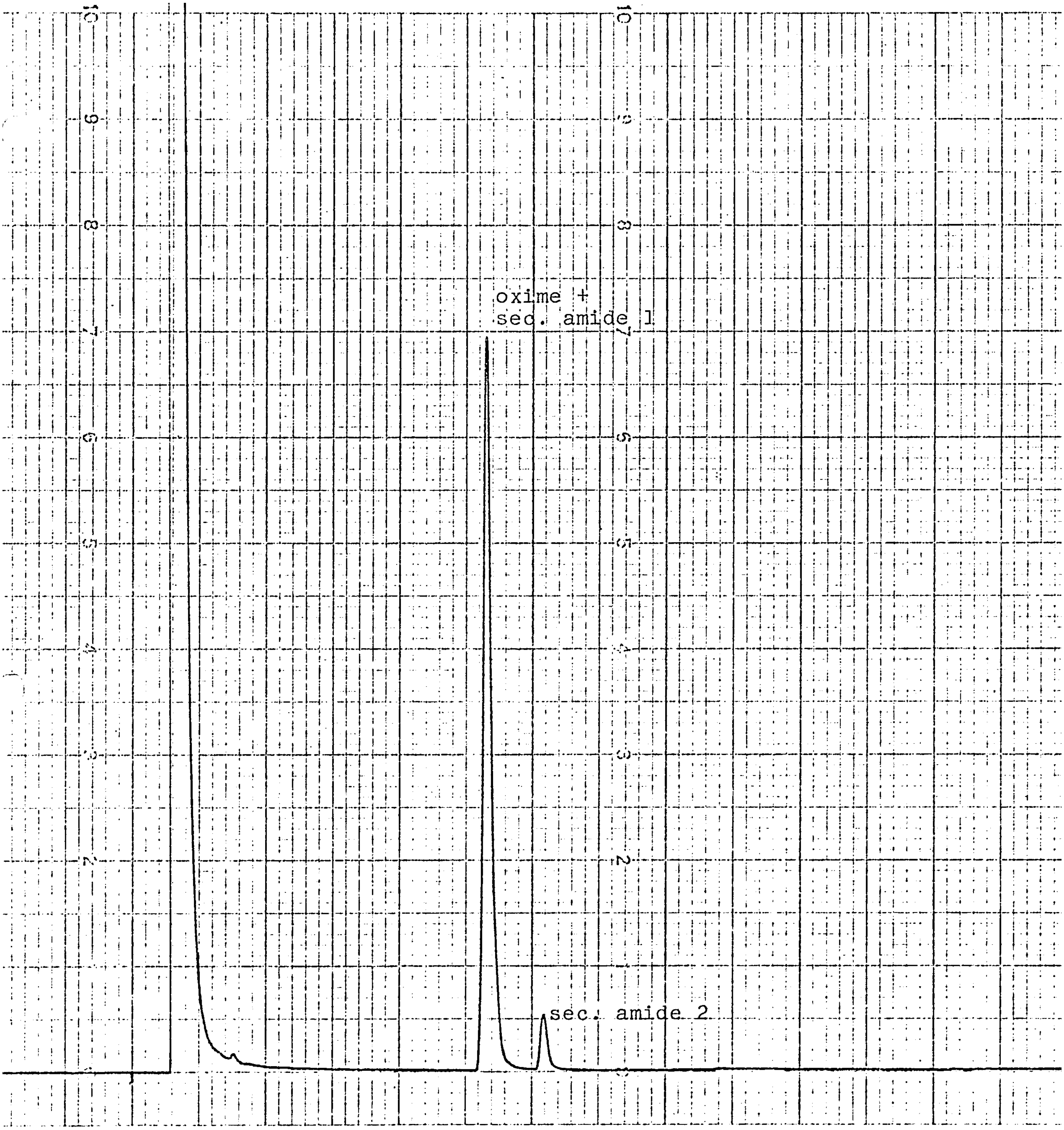

10
9
8
7
6
5
4
3
2
10
9
8
7
6
5
4
3
2
oxime +
sec. amide 1
sec. amide 2

Fig. 28

Gas-liquid chromatogram of the photolysis products
of 2,4-dimethyl-3-pentanone oxime

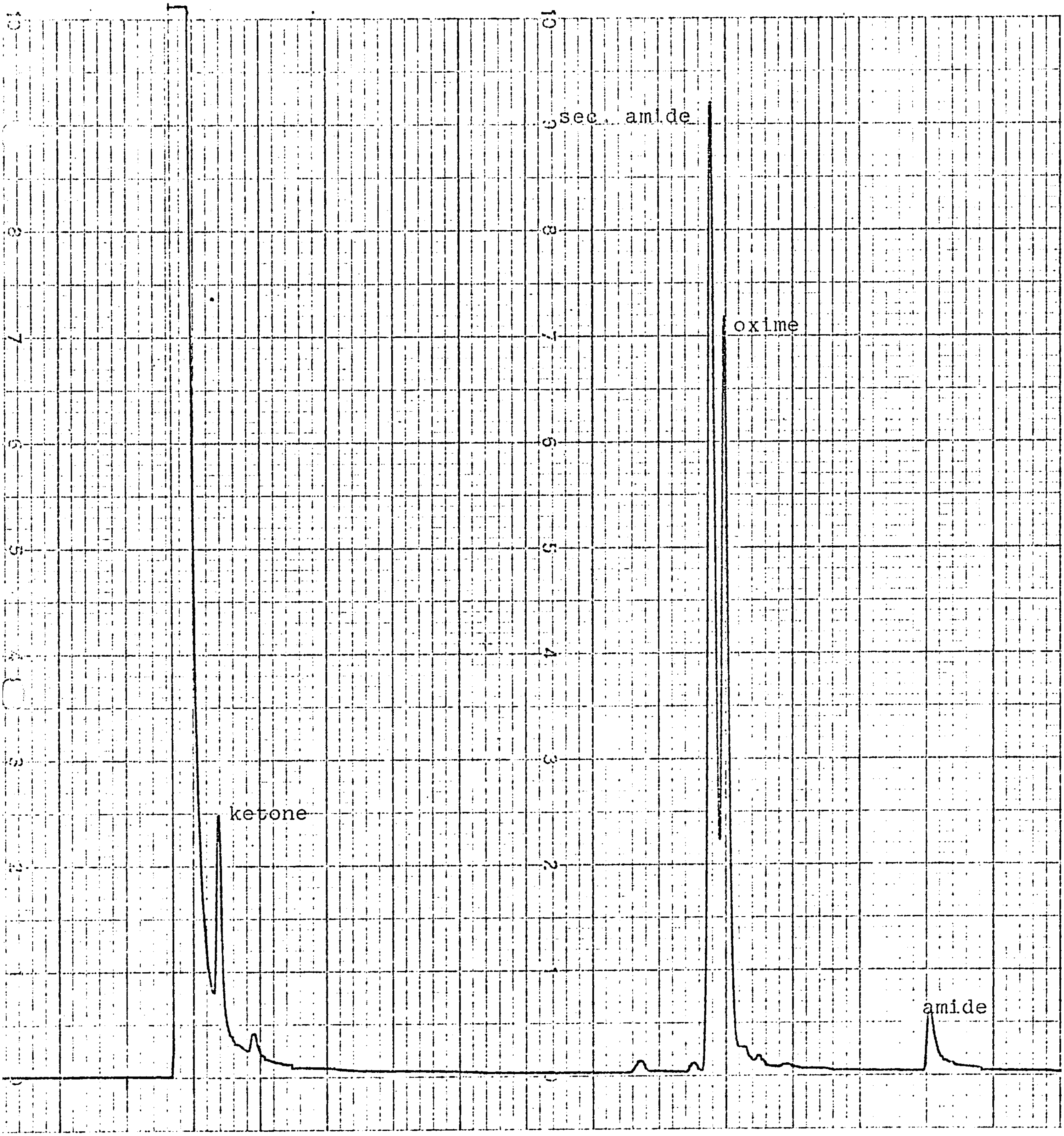

10
9
sec. amide
8
oxime
7
6
5
4
3
ketone
2
1
amide
0

Fig. 29

Gas-liquid chromatogram of the photolysis products of 2,2,4,4-tetramethyl-3-pentanone oxime

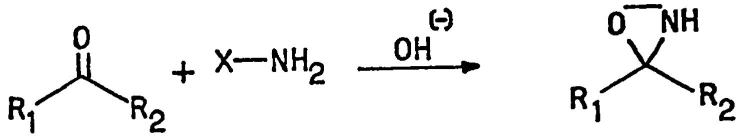
ketone
sec. amide
oxime
amide
10
9
8
7
6
5
4
3
2
1
0

CHAPTER V. OXAZIRANES AS INTERMEDIATES IN THE PHOTOREACTION

A. Introduction

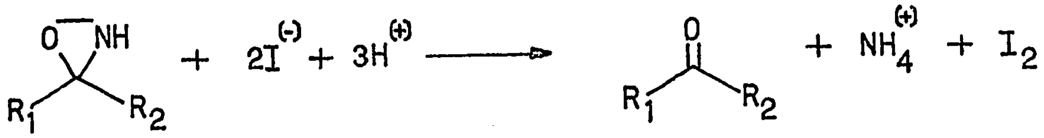
At the writing of this thesis, the photolysis of various oximes had been undertaken by several investigators. The photolysis behavior has, in almost all cases (2a,2b,7b-h) been rationalized on the basis of oxaziranes as intermediates. In order to carry this study further, it seemed appropriate to prepare oxaziranes in order that their behavior under the photolysis conditions could be investigated.

Oxaziranes have been known for some time, those substituted on nitrogen being particularly stable and easily isolable in a pure state. Only recently, has it become possible to prepare N-unsubstituted oxaziranes, the most general method being that of Schmitz and co-workers (30).

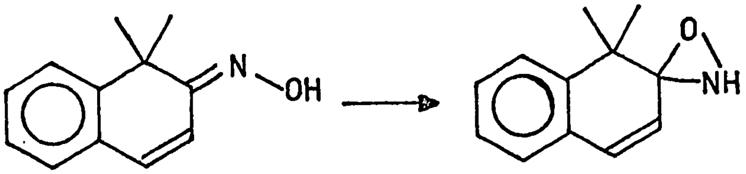


$X=OSO_3H,Cl$

N-unsubstituted oxaziranes are highly unstable. That prepared from cyclohexanone is reported to explode upon concentration of dilute solutions (31). Accordingly, such compounds are prepared and handled as dilute solutions. Storage life of these materials, even in the cold, is generally of the order of hours. Oxaziranes are generally detected and assayed by virtue of their powerful oxidizing properties. In acidic solutions of potassium iodide, oxazirane decomposition results in instantaneous and quantitative conversion of iodide ion to iodine which can be measured by the usual methods.



In view of this instability, the claim by Oine and Mukai (7e) that they had prepared a relatively stable oxazirane by the photolysis of 1,1-dimethyl-2-napthalenone oxime (XVIII) was somewhat surprising.

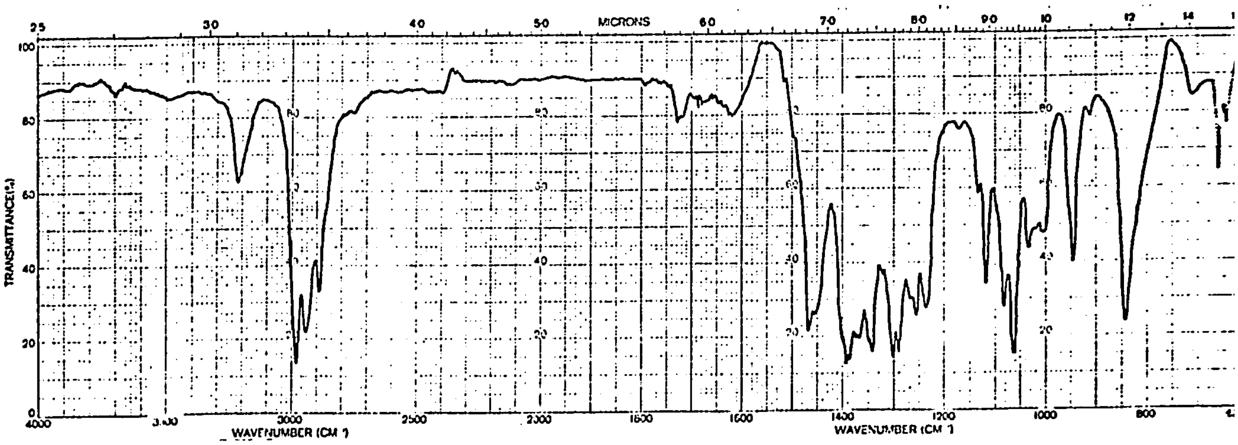


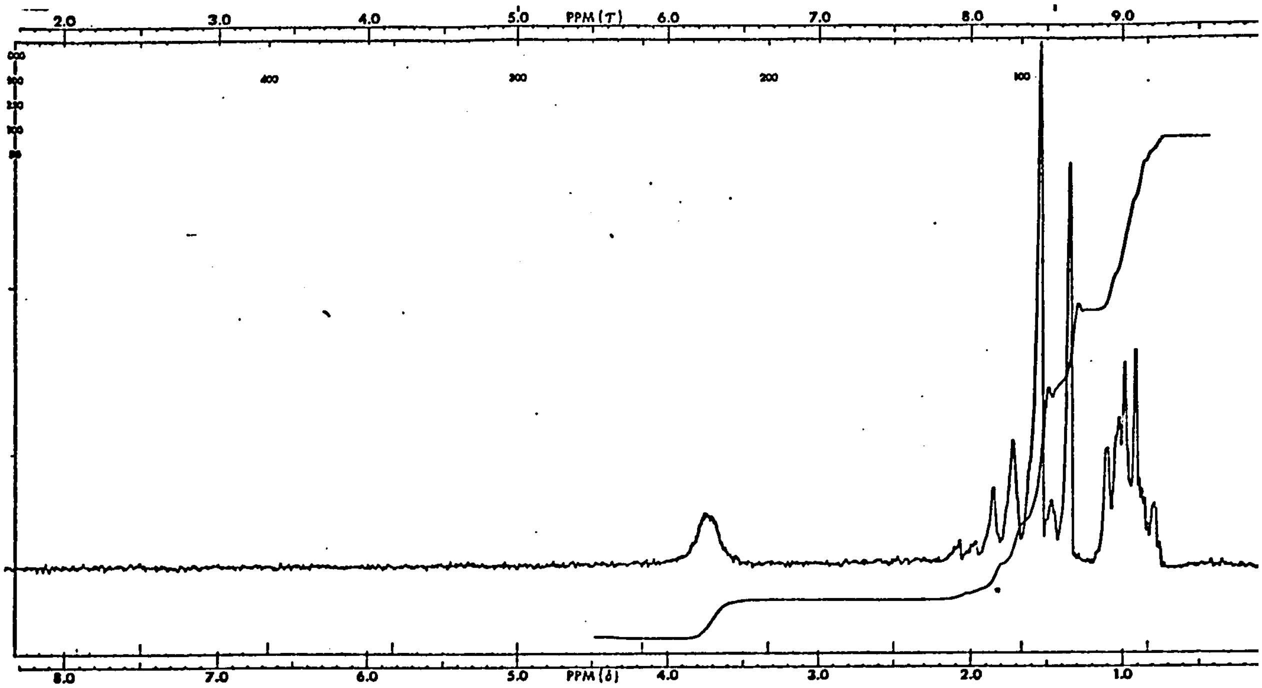
XVIII

They also claimed to have obtained direct proof for the existence of an oxazirane intermediate during the photolysis of cyclohexanone oxime. Fox and Rosenberg (7g) have made a similar claim. These results prompted us to study the oxaziranes and their behavior under the photolysis conditions. Accordingly, oxaziranes corresponding to methylethylketone

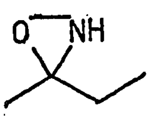
Fig. 30

The infra-red and n.m.r. spectra of
3-methyl-3-ethyloxaziridine (LI)

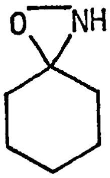

MICRONS
2.5
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
12
14
TRANSMITTANCE(%)
100
80
60
40
20
0
4000
3000
2500
2000
1800
1600
1400
1200
1000
800
WAVENUMBER (CM⁻¹)


PPM (τ)
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
400
300
200
100
PPM (δ)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

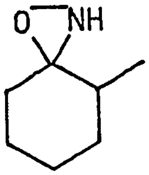
(LI), cyclohexanone (LII), and 2-methylcyclohexanone (LIII) were prepared.



LI



LII



LIII

B. Preparation of the Oxaziranes

a. 3-Methyl-3-ethyloxaziridine (LI)

The title compound was prepared by a variation of the method of Schmitz (30b) and obtained in a pure state by fractional distillation. The colorless liquid obtained appeared to be stable at -78° but began to decompose exothermically and violently upon standing a short time at room temperature. The infra-red and n.m.r. spectra of the compound are given in figure 30. The oxazirane was much more stable in a dilute carbon tetrachloride solution, its decomposition being monitored by the change in its infra-red spectrum. After 6 hours, the N-H absorption of the oxazirane had disappeared and the spectrum showed a strong absorption in the carbonyl region typical of methylethylketone.

The n.m.r. spectrum of the compound is very complicated. The only easily discernable feature is the broad N-H absorption at 3.8 p.p.m. Since the infra-red spectrum shows no free N-H absorptions, the molecule is probably associated through hydrogen bonds or has dimerized.

The ultra-violet absorption spectrum in methanol solution showed only end band absorption similar to that of the oxime.

Solutions of the oxazirane were strongly oxidizing. Addition of the oxazirane to acidic solutions of potassium iodide instantaneously liberated iodine as reported. A vigorous reaction occurred on treatment of the oxazirane with water. The products of this unreported reaction were found to be methylethylketone, ammonia, and an unidentified, odorless gas , most probably oxygen.

b. 3,3-Pentamethylene oxaziridine (LII)

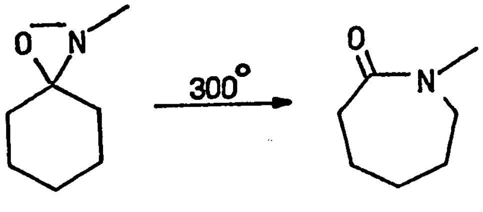
This material was prepared by a variation of the method of Schmitz (30b). Its reported instability (31) prevented isolation of the compound in a pure state. In dilute solutions the oxazirane could only be kept a few days in the cold (-20°). Solutions of the oxazirane were strongly oxidizing as reported, instantaneously liberating iodine when added to acidic solutions of potassium iodide. The compound similarly reacted with water giving cyclohexanone, ammonia, and oxygen.

c. 3,3-[α-Methylpentamethylene]-oxaziridine (LIII)

This unreported oxazirane was prepared in a manner similar to that for 3,3-pentamethyleneoxaziridine (LII). Solutions of the oxaziridine showed the usual oxidizing properties. This material was similarly thermally unstable and could only be stored a short time even in the cold (-20°).

C. Products of the Thermal and Photochemical Decompositions of the Oxaziranes

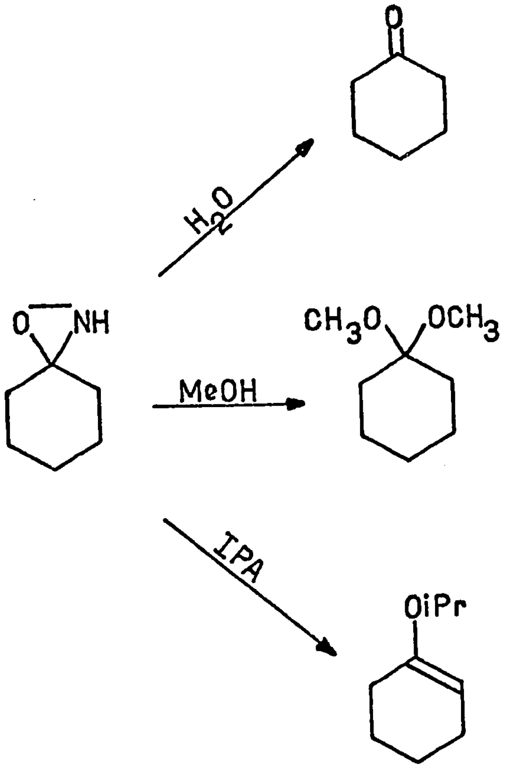
Although several investigators postulated oxaziranes as the intermediates in the photolysis of oximes (7b-h), no indication has, to date, been given as to whether the thermally unstable oxazirane underwent a thermal or photochemical reaction to give the final product. In view of the finding of Schmitz (30c) that exposure of the N-methyl oxazirane (LIV) to high temperatures (300°) converted the oxazirane into N-methylcaprolactam (LV), an attempt was made to determine whether oxaziranes decomposed photochemically and/or thermally under the conditions of the photolysis. This was accomplished by determining the products and the relative rates of these two, possibly competing, reactions.



LIV LV

a. Products of the thermal decompositions of the oxaziranes

The thermal decomposition of the oxaziranes of methylethylketone (LI) and cyclohexanone (LII) in water has already been described (section B) as leading to ketone, ammonia and oxygen. Decomposition of the oxazirane of cyclohexanone in methanol gave 1,1-dimethoxycyclohexane (LVI). The analogous reaction in iso-propanol gave predominately 1-isopropoxycyclohexene (LVII), presumably via loss of iso-propanol from the iso-propyl ketal (32), and a minor (15%) amount of caproamide. Decomposition in refluxing benzene gave cyclohexanone.

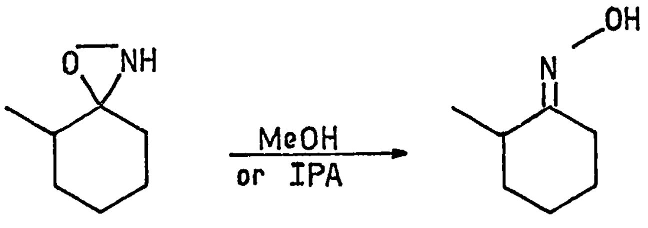


LVI

LVII

The products of the analogous reactions on the oxazirane of methylethylketone (LI) in alcoholic solvents could not be determined due to their volatility and subsequent loss on work-up. Decomposition in carbon tetrachloride gave methylethylketone as reported in section B.

The oxazirane of 2-methylcyclohexanone (LIII) behaved completely differently undergoing complete rearrangement to the oxime.



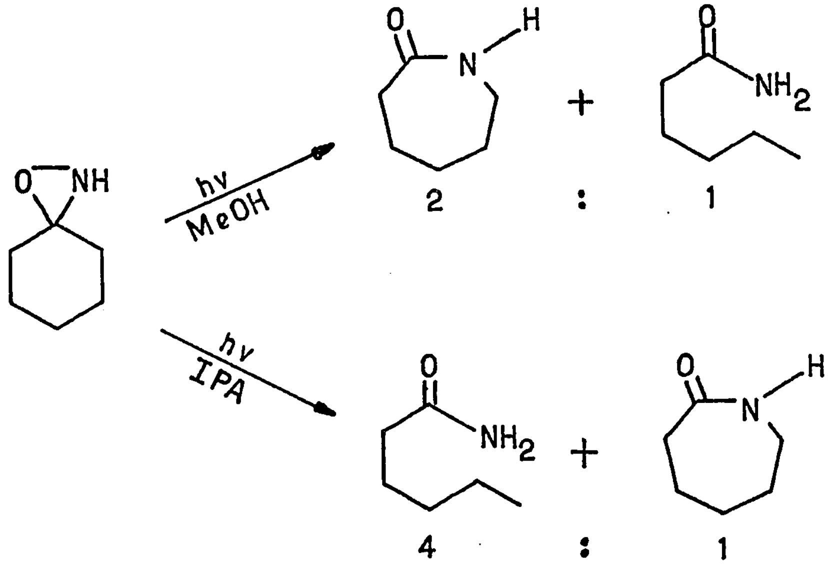
LIII

b. Products of the photochemical decompositions

The products of the photolytic decompositions of the oxaziranes were similarly determined. No products corresponding to N-substituted amides were detected among the photoproducts of the oxazirane of methylethylketone (LI). In view of the poor results (chapter 4) of the photolysis of the oxime, these results are not surprising.

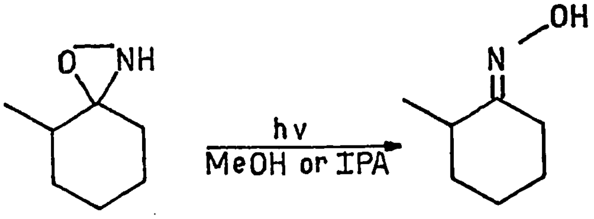
Photolysis of the oxazirane of cyclohexanone (LII) in methanol gave caprolactam and caproamide in a ratio of 2:1. Measurement of the lactam yield was complicated by some thermal decomposition of the oxazirane upon standing a short time in solution prior to irradiation. Correction of the lactam yield for only the photolytically decomposed oxazirane gave a yield of 59%.

Photolysis of the oxazirane in iso-propanol gave caproamide and caprolactam in a ratio of 4:1. Some thermal decomposition of the oxazirane similarly occurred on standing in iso-propanol solution for a short time prior to irradiation. Lack of an authentic sample of iso-propoxycyclohexene prevented correction of the amide yield for only the photolytically decomposed oxazirane. It must have been very good, however, since the uncorrected amide yield was 42%.



Gas-liquid chromatograms of the photolysis and thermolysis mixtures (figures 31-34) are appended at the end of the chapter. It should be noted that cyclohexanone is shown on the chromatograms. It has been shown that the oxazirane of cyclohexanone is highly unstable and decomposes in non-protic solvents to give cyclohexanone. Thus it is not a photoproduct and has not been mentioned. Its presence, however, points out the unstable nature of the oxazirane which was freshly prepared just prior to irradiation.

When the oxazirane of 2-methylcyclohexanone (LIII) was irradiated in either methanol or iso-propanol solution, 2-methylcyclohexanone oxime was the only product. It is not known whether this conversion occurred thermally or photochemically (see above).



LIII

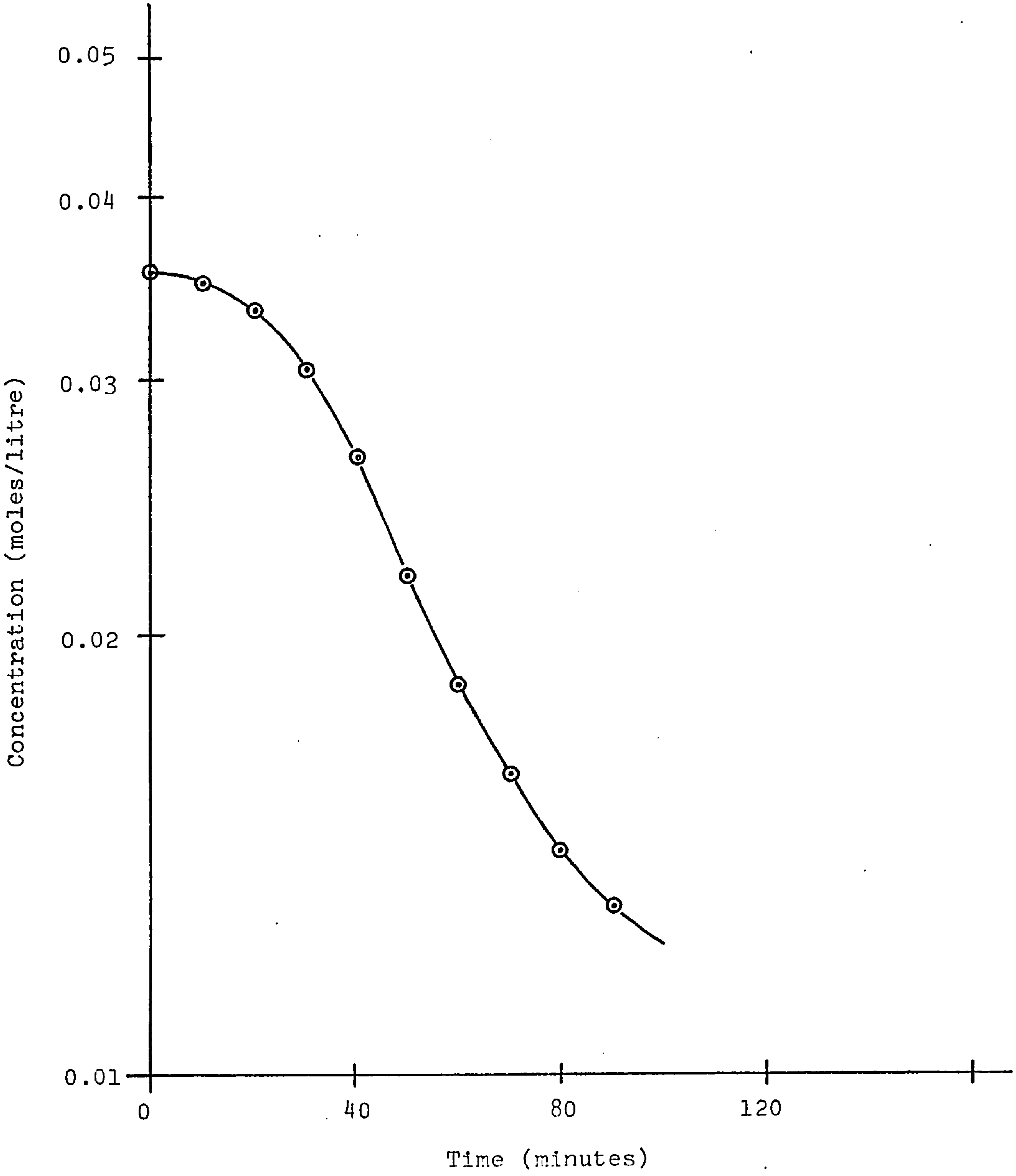
D. Reaction Rates of the Thermal and Photochemical Decompositions of the Oxaziranes

The results obtained to this point show that although oxaziranes are thermally unstable, the photoproducts of cyclohexanone oxime must be generated by a photochemical decomposition of the oxazirane intermediate. The same conclusion can be drawn from the determination of the rates of the thermal and photochemical decomposition reactions.

The oxaziranes of methylethylketone (LI) and cyclohexanone (LII) were prepared as dilute solutions and allowed to decompose thermally in various alcoholic solvents. The concentration of remaining oxazirane was determined at various time intervals by iodometry and plotted semi-logarithmically. A typical plot of a thermal decomposition, that of the oxazirane of cyclohexanone in methanol, is given on graph 3. In all the

Graph 3

Oxazirane concentration versus time
for the thermal decomposition
of 3,3-pentamethyleneoxaziridine in methanol


0.05
0.04
0.03
0.02
0.01
Concentration (moles/litre)
0
40
80
120
Time (minutes)

thermal cases, the curves obtained were not straight lines as expected for first order decomposition but instead assumed an "S" shape. It has already been shown that thermal decomposition results in ammonia production. The non-linear nature of the curve might be due to ammonia catalyzing the decomposition. Since a rate constant could not be determined from the data, the half-lives of decomposition (the time required for the oxazirane concentration to decay to one-half the initial concentration) were used to characterize the oxazirane's stability. The half-life data is tabulated in Table 9.

In a similar manner, the stability of the oxaziranes under photolytic conditions was studied. A typical plot, that of the photochemical decomposition of the oxazirane of cyclohexanone in methanol is shown in graph 4. The half-lives of photochemical decomposition are similarly tabulated in Table 9.

The data clearly shows that under the photolysis conditions in methanol, the oxazirane of cyclohexanone undergoes a photochemical decomposition ($t_{1/2}$=8min.) in preference to a thermal decomposition ($t_{1/2}$=63min.). Furthermore, if oxaziranes are the intermediates in the photolysis of cyclohexanone oxime ($t_{1/2}$=65min.), the oxazirane can only be present in low concentration.

A different conclusion has been reached by Oine and Mukai (7e) who reported that irradiated solutions of cyclohexanone oxime in methanol exhibited oxidizing properties converting acidic solutions of iodide ion to iodine. This reaction being characteristic of the oxaziranes, the authors

TABLE 9

Half-lives of decomposition of the oxaziranes

Thermal			Photochemical(6)		
Solvent	Oxazirane		Solvent	Oxazirane	
	MEK*	CHO*		MEK*	CHO*
Water	6	3	Water		1
Methanol	40	63	Methanol	8	10
Ethanol	61	253	Ethanol		
iso-Propanol	370	320	iso-Propanol		
t-Butanol	810	900	t-Butanol		51

Temperature effect on the half-life of 3,3-pentamethyleneoxaziridine in water

Temperature (C)	Half-life (min.)
0	20
25	2

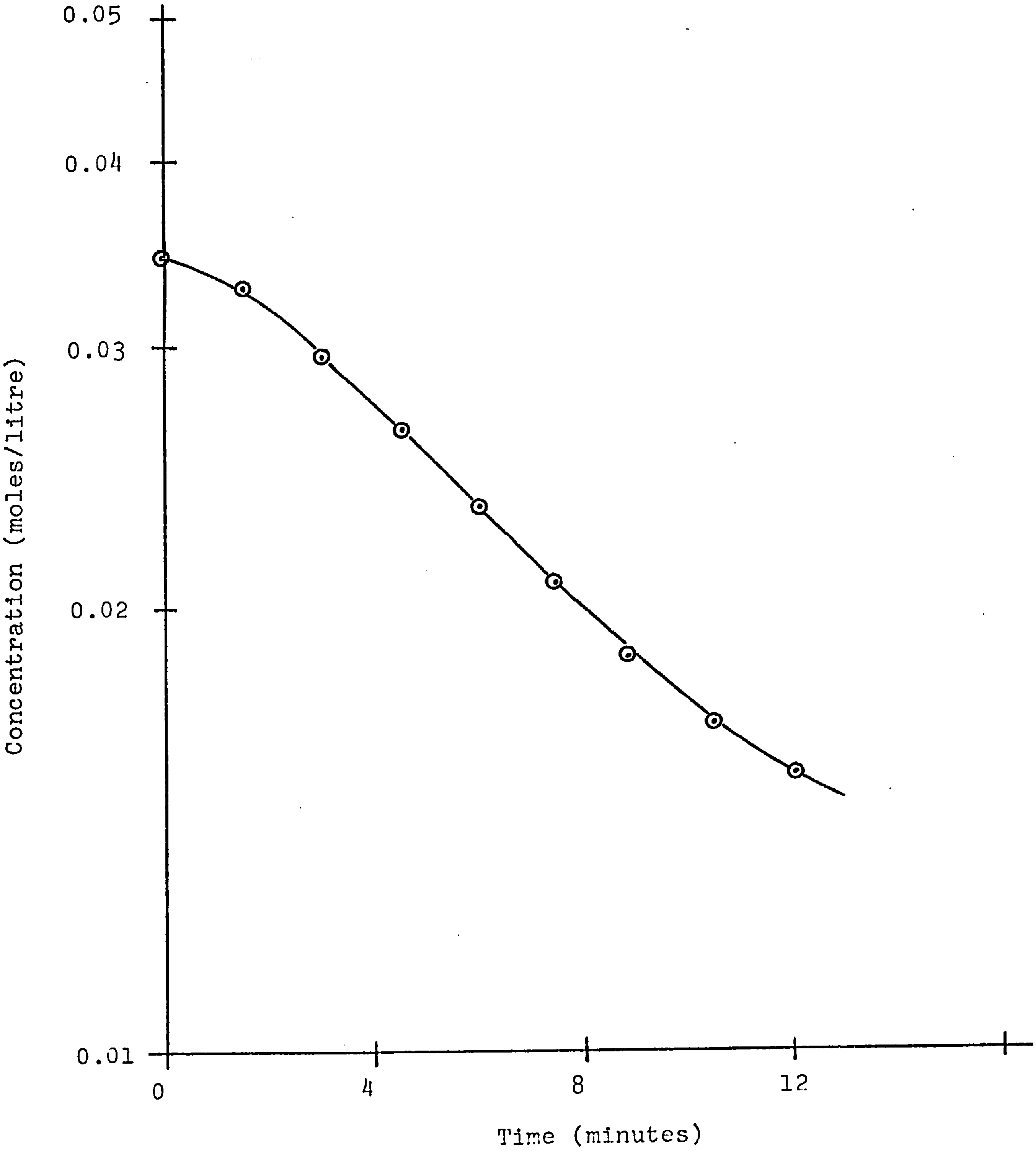
*MEK-methylethylketone
*CHO-cyclohexanone

---

(6) By comparison $t_{1/2}$ for cyclohexanone oxime in methanol is about 65 minutes.

Graph 4

Oxazirane concentration versus time
for the photochemical decomposition
of 3,3-pentamethyleneoxaziridine in methanol



0.05
0.04
0.03
0.02
0.01
Concentration (moles/litre)
0
4
8
12
Time (minutes)

suggested that oxaziranes were the intermediates in the photolysis of cyclohexanone oxime and that the "oxazirane" concentration was greater than 10% of starting oxime!

E. An Attempt to Trap the Oxazirane Intermediate

Oine and Mukai's work was repeated under various conditions. The results are summarized in Table 10.

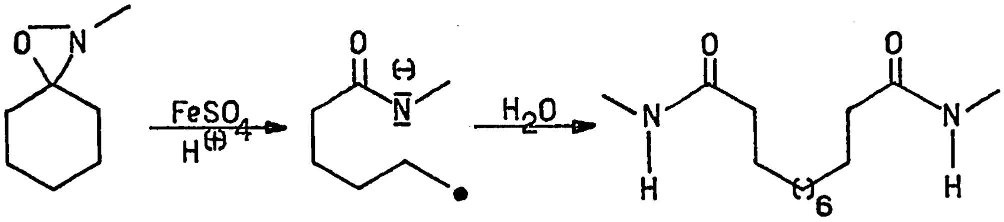
Table 10

Oxazirane concentration during the photolysis of cyclohexanone oxime

Conditions	Temperature	"% Oxazirane"
methanol, under oxygen	45	30
methanol, under nitrogen	45	5
methanol, under nitrogen	7	7
t-butanol, under nitrogen	45	5

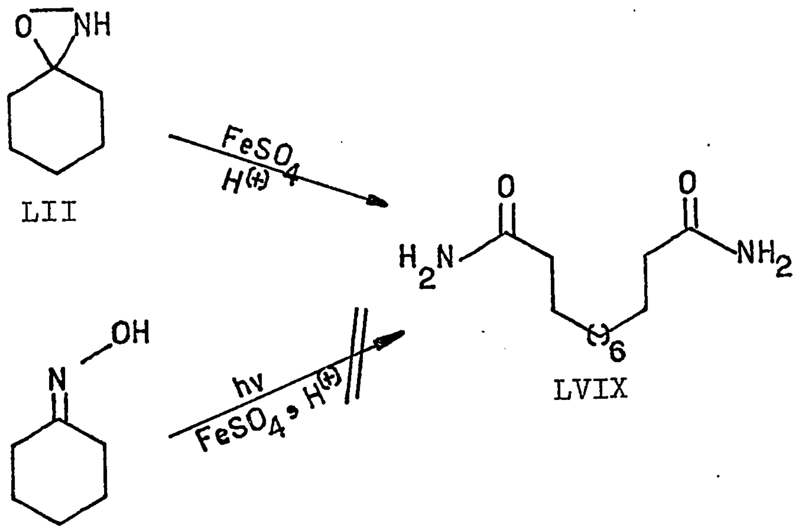
The "oxazirane" concentration was found to be strongly oxygen dependent and relatively unaffected by changes in solvent or temperature. The data of Table 9 shows oxazirane stability to be strongly dependent on these parameters. An attempt to prove the oxidizing properties to be due to oxaziranes was carried out by trapping the "oxazirane" by reaction with acidic ferrous sulphate.

Emmons (33) has shown the reaction with ferrous ion to be general for oxaziranes giving a radical ion. Schmitz (30c) has shown the N-methyl oxazirane of cyclohexanone (LIV) to react to give N,N-dimethyldodecanediamide (LVIII) under these conditions.



LIV LVIII

If the oxazirane of cyclohexanone were to behave analogously, it should be possible to trap the photochemically formed oxazirane. When the oxazirane (LII) was treated with ferrous sulphate, dodecanediamide (LVIX) was indeed formed in good yield. However, photolysis of cyclohexanone oxime in the presence of ferrous ion gave little, if any, diamide.


LII

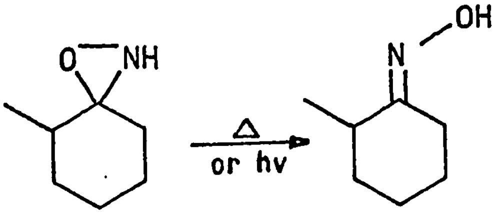
LVIX

F. Discussion

It has been pointed out that during the course of this investigation, several authors have postulated oxaziranes as the intermediates in the photolysis of oximes. Although compelling evidence to support this claim is now available for the aromatic oximes (2b,7e), no such evidence has been given for the case of the saturated cyclic oximes, the subject of this thesis. Furthermore, no evidence has been presented to determine whether the thermally unstable oxazirane underwent a photochemical or dark reaction to give the observed photoproducts of oximes.

In support of the hypothesis that oxaziranes are the intermediates in the photoreaction, it has been shown that oxaziranes, prepared by known methods, do give the same photoproducts as those resulting from the photolysis of the parent oximes. Thus, photolysis of both the oxazirane of cyclohexanone and cyclohexanone oxime in methanol give caprolactam as the major product while photolysis in iso-propanol gives caproamide mainly. Furthermore, it has been shown the observed photoproducts result from a photochemical, rather than a dark reaction since thermal decomposition of the oxazirane of cyclohexanone in alcoholic solvents gave only ketals instead of α-cleavage or Beckmann-type products. Since photolysis of oximes gives no detectable ketals, the photochemical pathway must be the predominant mode of decomposition of the oxazirane intermediate.

It had been hoped that photolysis of the oxazirane of 2-methylcyclohexanone would provide further evidence for these ideas since the ratio of the lactam isomers in methanol and the amide ratio in iso-propanol could be compared to the ratios of the products obtained from photolysis of 2-methylcyclohexanone oxime in these solvents. Instead, the oxazirane behaved completely differently undergoing complete rearrangement to 2-methylcyclohexanone oxime under both thermal and photochemical conditions.

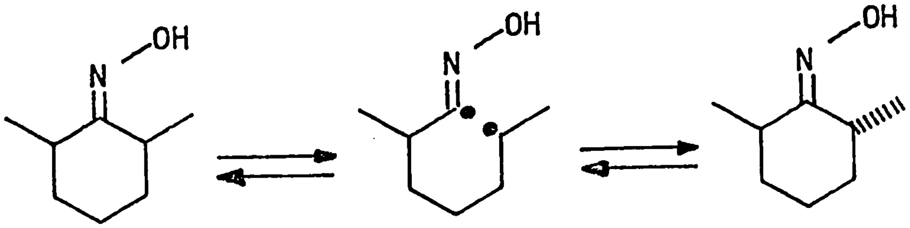


It was observed that photolysis of the oxazirane of cyclohexanone in methanol resulted in a ratio of lactam to amide (2:1) different from the ratio obtained by photolysis of cyclohexanone oxime (9:1). Similarly, photolysis of the oxazirane in iso-propanol resulted in a ratio (1:4) of lactam to amide different from that obtained from photolysis of the oxime (1:50). Considering the experimental difficulties, however, which prevented the two photolyses from being carried out under comparable conditions, these results can hardly be construed as disproving the intermediacy of the oxazirane. Alternatively, these results might indicate that ground state oxazirane is only in part involved in the photoreaction and that singlet oxazirane is derived from another excited species (nitrone).

According to the data of Table 9, the oxazirane of cyclohexanone will undergo a photochemical rearrangement in preference to a thermal decomposition in methanol. The data shows the half-lives of decomposition in water, however, to be much closer in magnitude. Ng (7b,d) reported that photolysis of cyclohexanone oxime at an 0.1% concentration in water gave lactam but on raising the concentration to 1%, cyclohexanone was formed. The data of Table 9 indicate that at a 1% concentration, the thermal mode of decomposition may predominate. The products formed by photolysis of a 1% aqueous solution of cyclohexanone oxime - ketone, ammonia, and oxygen - are exactly those formed by thermal decomposition of the oxazirane. The successful interpretation of these results in terms of an oxazirane provides strong evidence for the hypothesis of oxaziranes as the intermediates in the photoreaction of oximes.

It had been hoped that further confirmation of this hypothesis might be forthcoming through trapping of the oxazirane with ferrous sulphate. The trapping reaction was not successful. Since the reaction of the N-methyl oxazirane of cyclohexanone with ferrous sulphate is slow (30c), however, the negative result might be due to the oxazirane undergoing thermal decomposition in water to cyclohexanone (which is quite fast - Table 9).

Another possible reaction of the oxazirane is rearrangement to the parent oxime. The observed epimerization of oximes epimeric at the α-carbon was interpreted on the basis of an equilibrium between oxime and oxazirane. The results obtained with the oxazirane of 2-methylcyclohexanone which completely rearranges to oxime under both thermal and photochemical conditions is a remarkable vindication of this hypothesis. Although this explanation is entirely consistent with all the results obtained to date, other modes of epimerization i.e. a direct pathway from oxime, cannot be discounted.

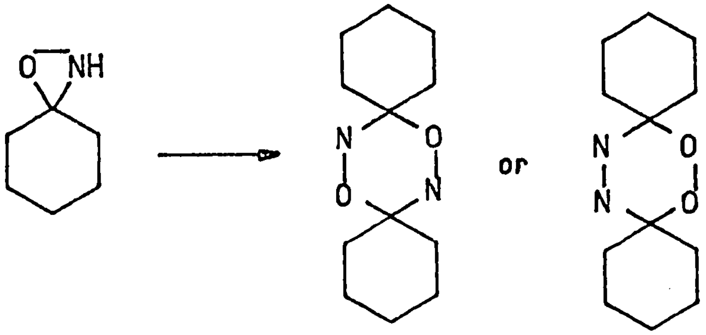


The results obtained to this point strongly suggest oxaziranes to be the intermediates in the photoreaction. During the photoreaction, however, they can only be present in low, steady-state concentrations. Two principle pieces of evidence clearly show that oxaziranes are not present in 10% concentrations (7e).

It has been shown that thermal decomposition of the oxazirane of cyclohexanone in methanol gives ketal LVI quantitatively. If a 10% yield of oxazirane were present in the irradiated solutions, a 10% yield of the ketal should have been observed in the photoproducts of cyclohexanone oxime. No ketal has ever been detected in this case.

Furthermore, the data of Table 9 clearly shows that compared to the photolysis of cyclohexanone oxime, the rate of photolysis of the oxazirane is very rapid, the ratio of half-lives being 1:10. Clearly oxazirane is photochemically destroyed much faster than it is formed and can only be present in small quantities.

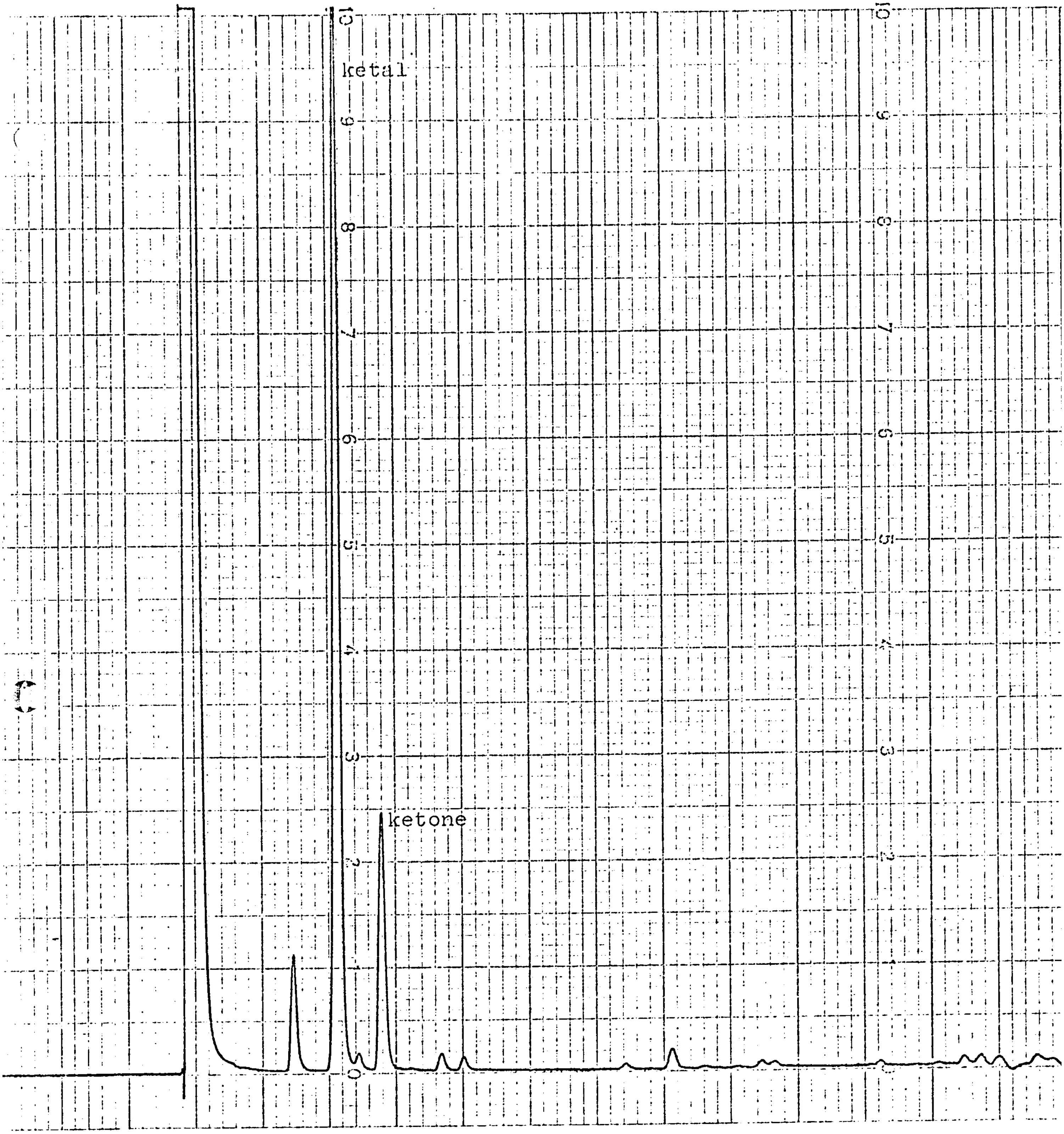
A reasonable possibility for the oxidizing species is a dimeric form of the oxazirane.



Precedent for the existence of these forms has been given by Schmitz (34).

Fig. 31

Gas-liquid chromatogram of the thermolysis products of 3,3-pentamethyleneoxaziridine in methanol


10
9
8
7
6
5
4
3
2
0
ketal
ketone

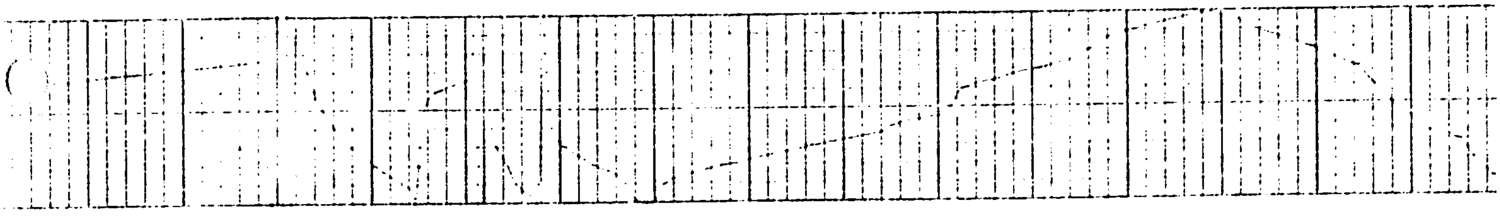
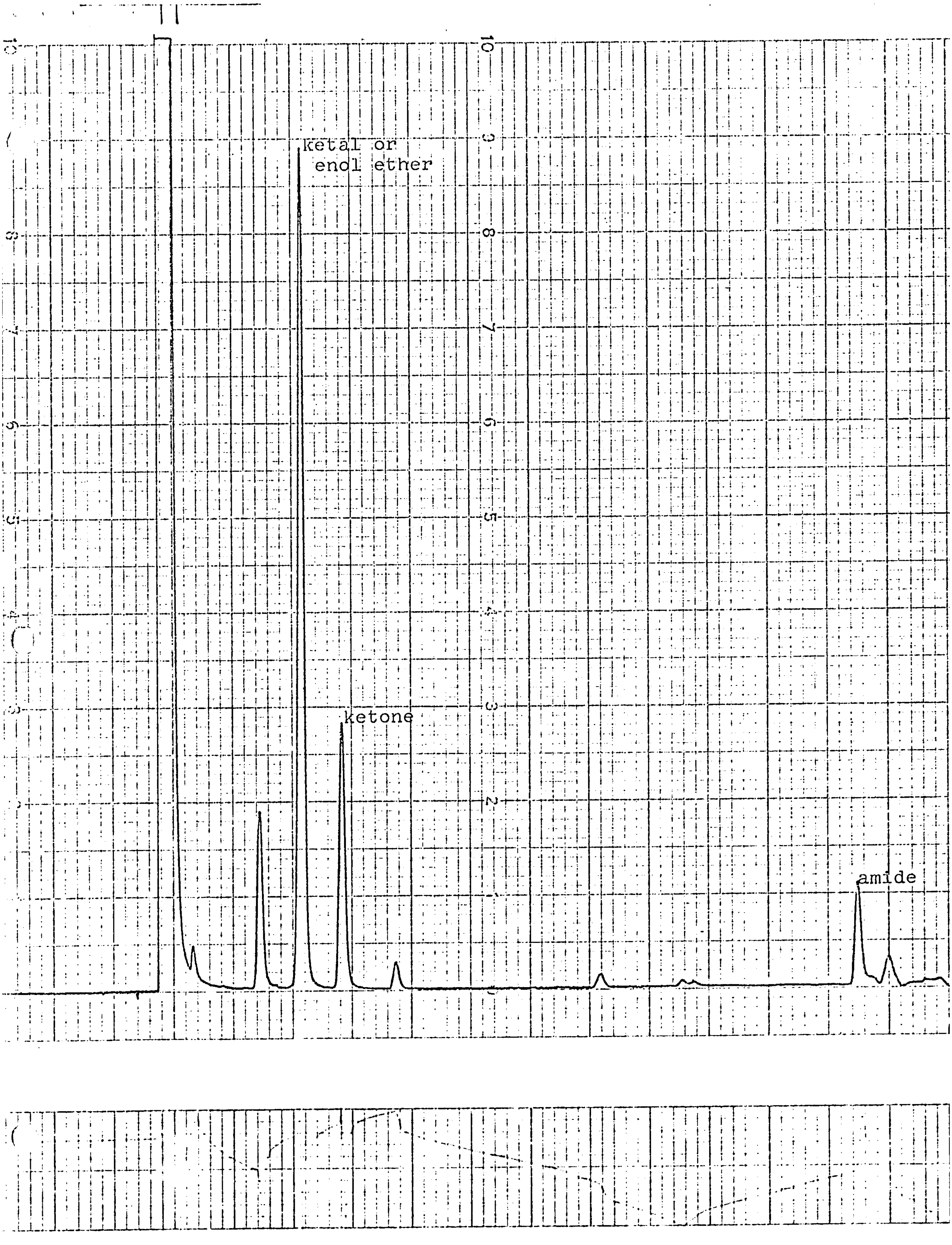


Fig. 32

Gas-liquid chromatogram of the thermolysis products of 3,3-pentamethyleneoxaziridine in iso-propanol


10
9
8
7
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4
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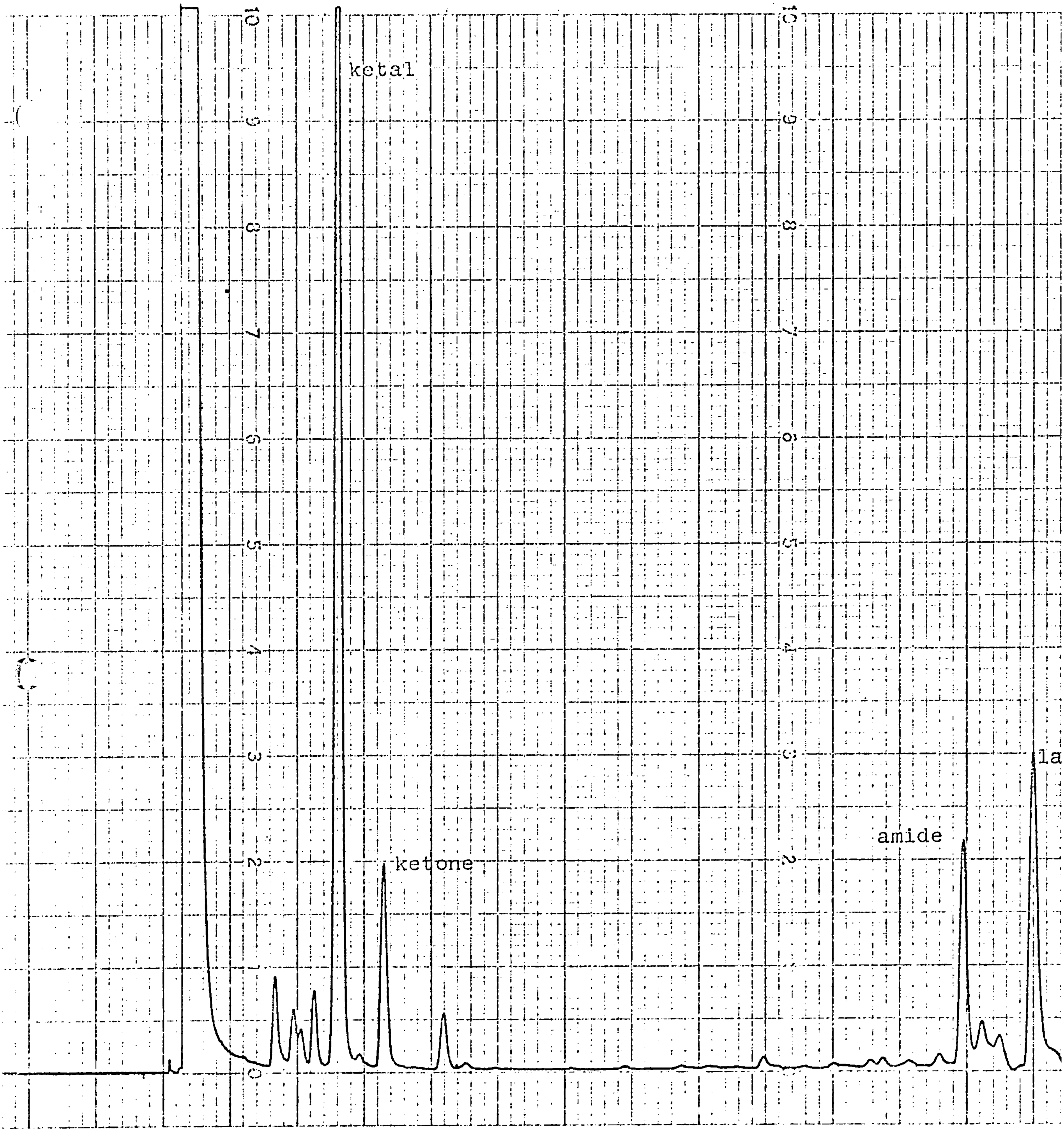
ketal or
enol ether
ketone
amide

Fig. 33

Gas-liquid chromatogram of the photolysis products of 3,3-pentamethyleneoxaziridine in methanol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ketal
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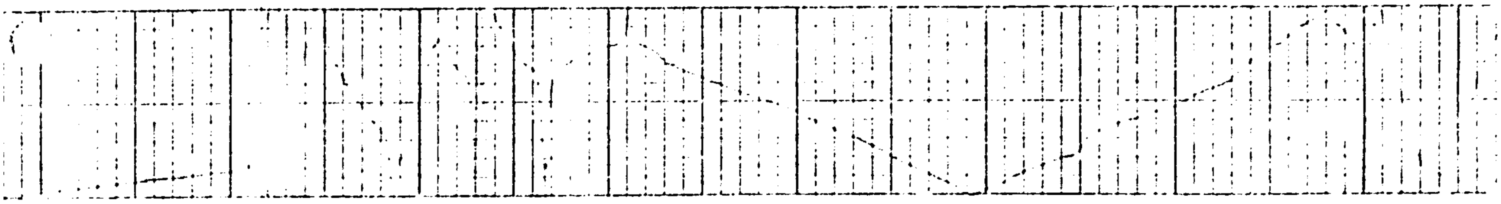
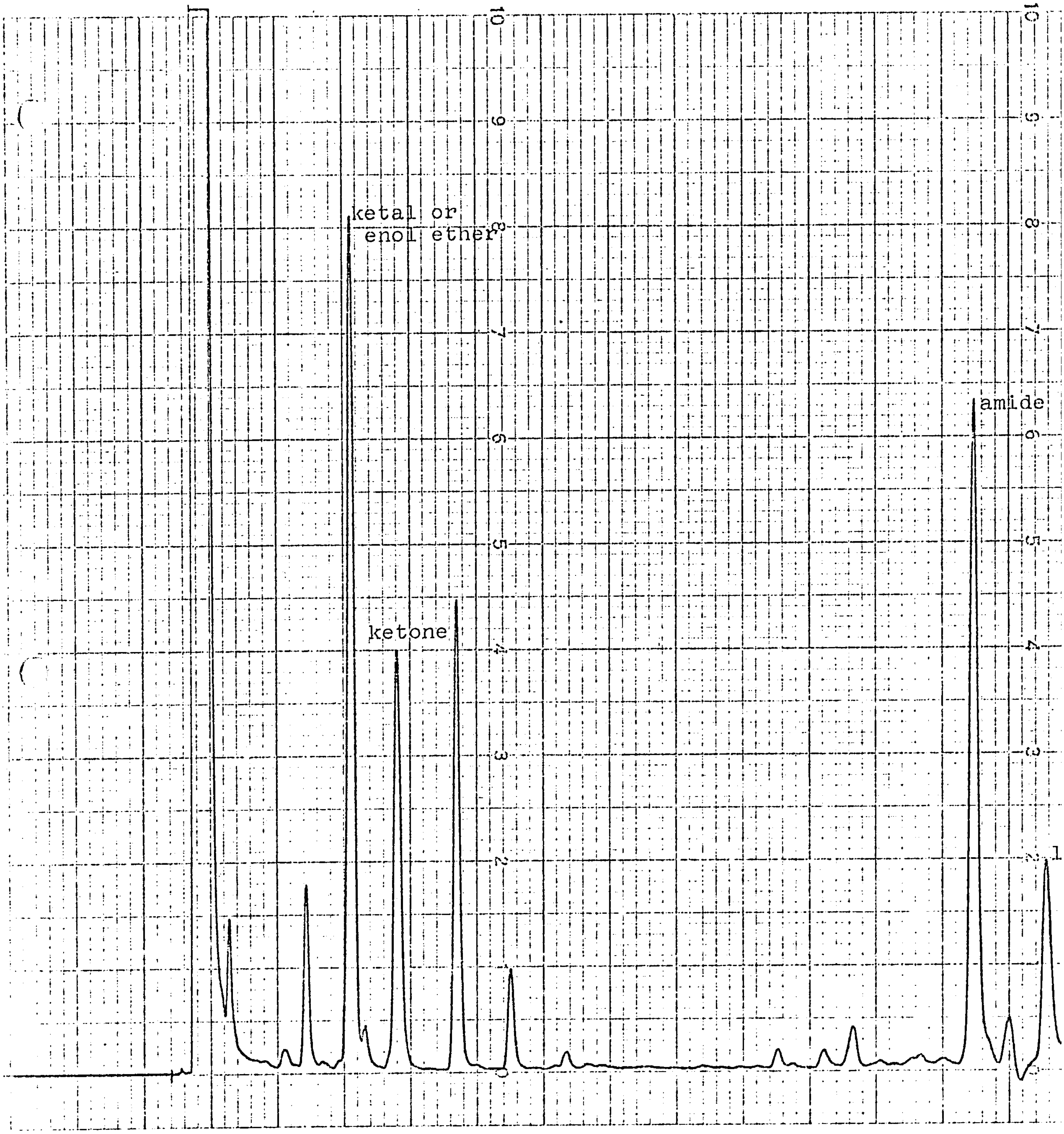


Fig. 34

Gas-liquid chromatogram of the photolysis products of 3,3-pentamethyleneoxaziridine in iso-propanol


ketal or
enol ether
ketone
amide
10
9
8
7
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4
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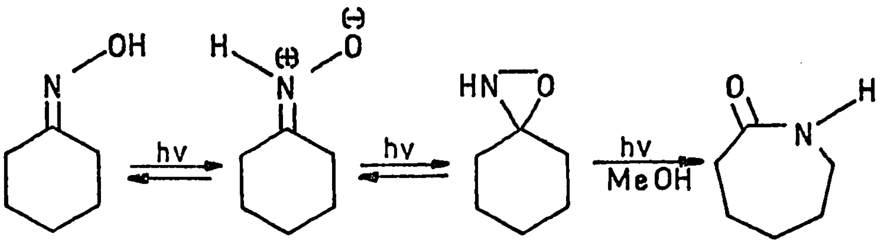
2
1
0

CHAPTER VI. THE MECHANISM OF THE PHOTO- AND THERMAL REACTIONS OF THE OXAZIRANES

Considerable evidence has now been advanced in this thesis for the intermediacy of oxaziranes during the photolysis of oximes. The photochemistry of nitrones (chapter 1) which has been well studied, bears direct analogy to the photochemistry of the oximes. All the observed photolyses of the cyclic oximes, both substituted and unsubstituted, and the rates of these photolyses are well explained by this hypothesis. Oxaziranes have been prepared by known methods and shown, in the case of cyclohexanone oxazirane, to give the same photoproducts as photolysis of the oxime. Finally, the anomalous concentration effect, noted for the photolysis of cyclohexanone oxime in water, is well explained by this hypothesis. These results leave little doubt as to the intermediacy of oxaziranes in the photoreaction. In direct analogy with the photolysis of nitrones, the following mechanism for oxazirane formation can be written:



It will be the object of this chapter to deduce the mechanism of the conversion of oxazirane into the various photo- and thermal products. The data of Table 9 (chapter 5) will be of considerable aid in this venture. The enormous effect of solvent (specifically solvent dielectric constant) on the half-lives of decomposition for both the thermal and photochemical decompositions of the oxaziranes clearly shows the transition state to be dipolar in both cases. Enough evidence is now available to write reasonable mechanisms for most of the thermal and photochemical pathways. Only a few minor points require clarification; the effect of temperature on the photoreaction and the thermal intermediate responsible for ketal formation.

A. The Effect of Temperature on the Photoreaction

The results obtained to date show that under the photolysis conditions in methanol, the preferred mode of decomposition of the oxazirane intermediate is photochemical. It should be possible, however, to cause the thermal decomposition to increase in importance by raising the temperature of the reaction. The data obtained when the photoreaction was carried out at different temperatures is tabulated in Table 11.

The data reveal two interesting points: 1) the amount of oxime remaining is temperature dependent and 2) increasing the temperature results in a dramatic lowering of the lactam yield and a corresponding increase in the ketone yield. The variation of oxime remaining with temperature is not unexpected if an oxime-oxazirane equilibrium exists; however, the formation of ketone, rather than ketal, was

TABLE 11

The photolysis yields of cyclohexanone oxime in methanol at varying temperatures

Temperature	%ketone	%oxime	%amide	%lactam
10	4	38	2	33
20	5	28	3	39
30	5	27	3	39
40	4	27	4	33
50	9	24	4	16
60	10	39	5	19
65	11	43	5	13

unexpected.

The ketone product cannot be a thermal product of ground state oxazirane. This follows since it has been shown that the oxazirane of cyclohexanone undergoes thermal decomposition to ketal exclusively. Furthermore, some ketone is formed even during photolysis at low (10°) temperatures even though, as has been shown, oxaziranes are much more stable at low temperatures. Ketone must then be generated from an excited state. The lifetime of a vibrationally excited ground state (10^{-9}sec. - 10^{-12}sec. (35)) is far too short to be important as an intermediate (36). The two remaining possibilities are the first excited singlet and triplet states, the much longer lived triplet (35) being the prime possibility. Photochemical decomposition of N-substituted oxaziranes to give ketones is a rather general reaction often used to generate nitrenes (37). Evidence that the ketone forming reaction occurs via the triplet state has been given by Splitter and Calvin (37b) who found the formation of products derived from nitrenes to be quenched by the presence of oxygen.

If this interpretation is correct, the strong quenching of the lactam forming reaction with increasing temperature and the observed quenching in methanol in the presence of oxygen must mean that an appreciable amount of excited oxazirane exists in the triplet state. This point will be pursued later.

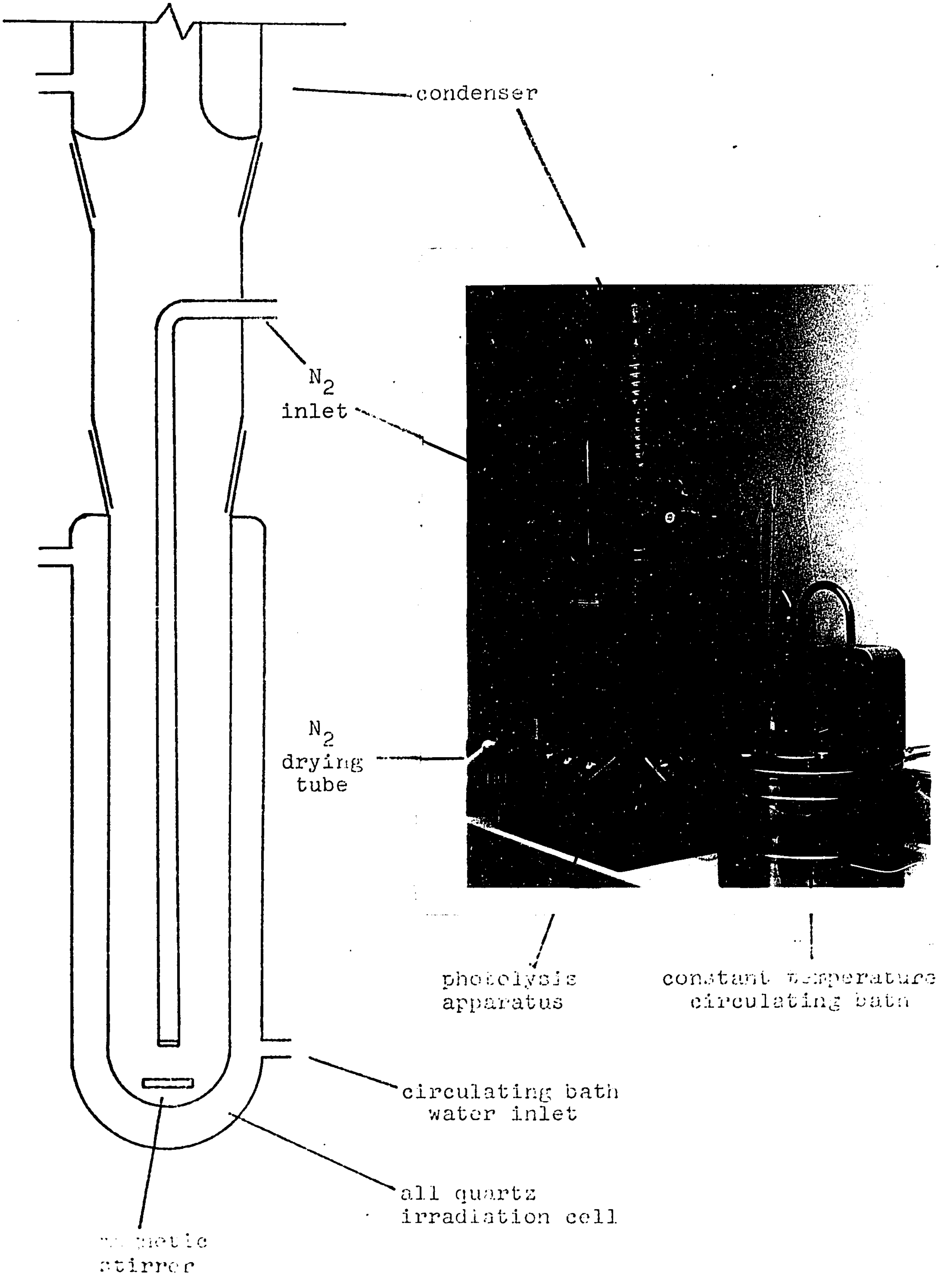
Since photochemical reactions in solutions are generally insensitive to small changes in temperature, apparatus for carrying out such reactions at varying temperatures has not been described in the literature. An appropriate arrangement for this purpose is shown in figure 35 where a photograph of the apparatus and a diagram of the irradiation cell are given.

B. The Intermediate Responsible for Ketal Formation

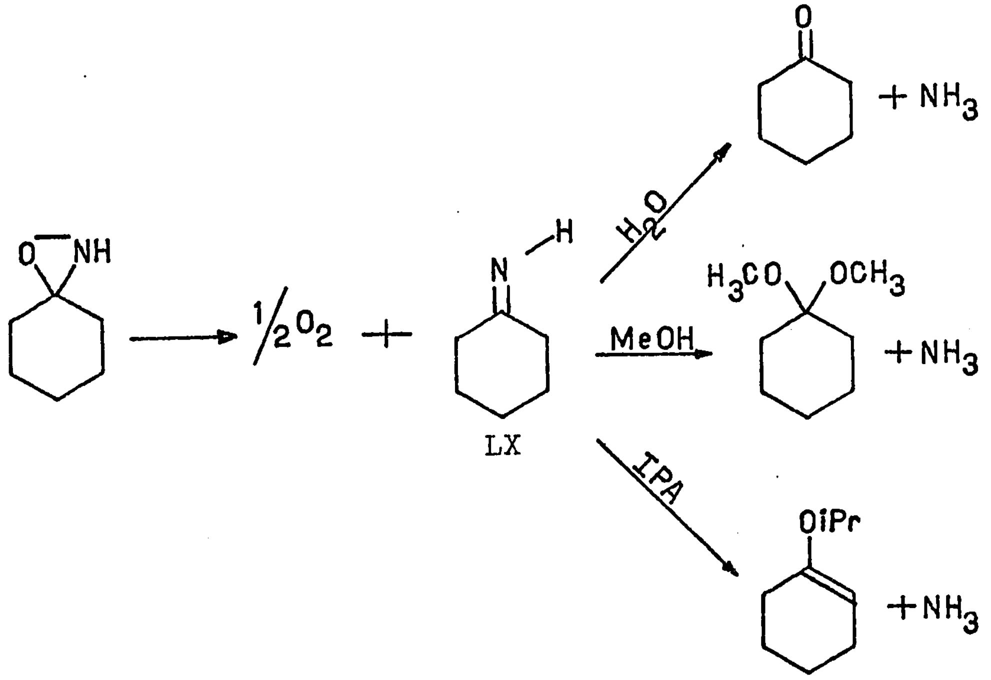
It was previously shown that thermolysis of an oxazirane in water gave ketone, ammonia and oxygen. The analogous reaction in methanol gave ketal presumably accompanied by ammonia and oxygen which were formed too slowly to

Fig. 35

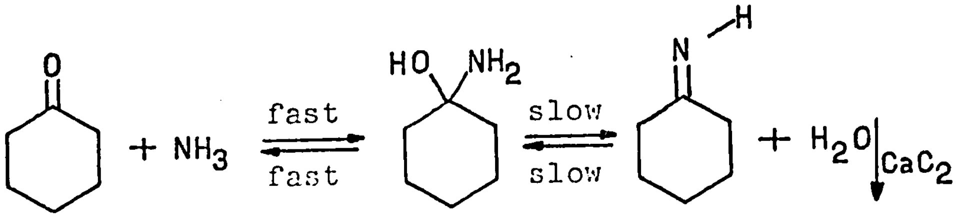
Diagram of apparatus used for photolyses at varying temperatures


condenser
N_2 inlet
N_2 drying tube
photolysis apparatus
constant temperature circulating bath
circulating bath water inlet
all quartz irradiation cell
magnetic stirrer

be detected. Decomposition in iso-propanol gave the isopropyl enol ether. The products formed are those expected from intermediate formation of an imine.

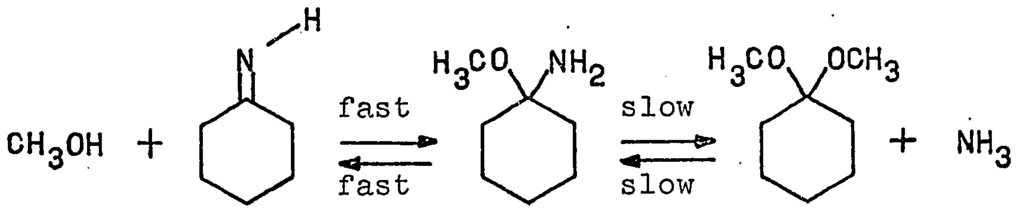


This hypothesis is difficult to test since the imine of cyclohexanone (LX) is difficult to prepare and highly unstable (38). A plausible synthesis involves the treatment of cyclohexanone in methanol solution with ammonia in the presence of an excess of calcium carbide. In analogy with the



known condensation of amines (39) with carbonyl compounds the above scheme was envisaged.

It was expected that treatment of the methanol solution with calcium carbide might displace the equilibrium to the right by continuous removal of water. In view of the acid catalyzed nature of the slow steps, it was expected that imine formation would be very slow under these conditions. On distillation of the bulk of the methanol, the imine was expected to behave similarly giving ketal.

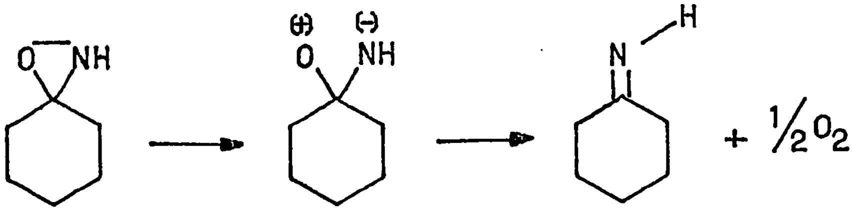


Again the equilibrium would be expected to be shifted to the right by distillation which removes ammonia as fast as it is formed.

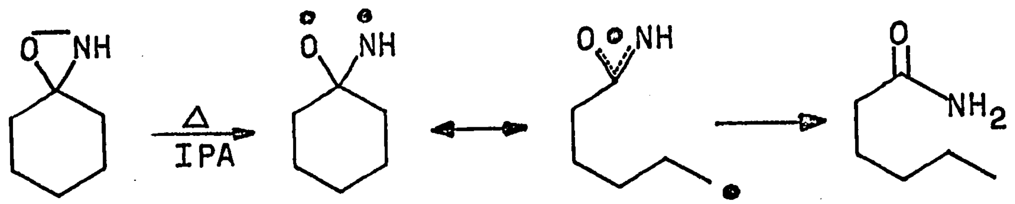
In fact, when the experiment was carried out, a small amount (5-10%) of a product having the same gas chromatographic retention time as 1,1-dimethoxycyclohexane (LVI) was obtained. This result is interesting not only because it strongly supports the hypothesis of an imine as precursor to ketal in the methanol case but also because it represents the first reported base catalyzed ketalization.

C. The Mechanism of the Thermal Decomposition of Ground State Oxazirane

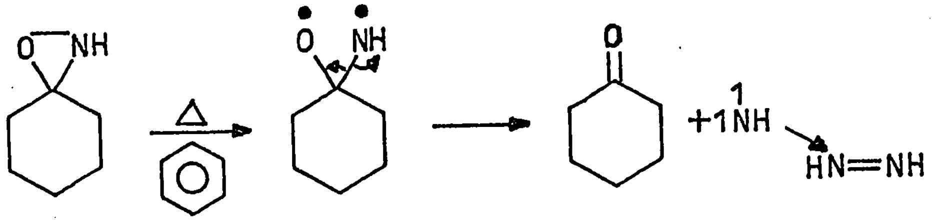
It has been shown that decomposition of oxaziranes to imines satisfactorily accounts for the thermal formation of ketone and ketals. It remains only to deduce the mechanism of conversion of oxazirane to imine. The data of Table 9 clearly shows the thermal reaction to be acutely sensitive to solvent dielectric strength, the half-life of decomposition varying some 300 fold over the range from water to t-butanol. The following mechanism for imine formation appears to account for it satisfactorily:



It might have been anticipated, however, that as the dielectric constant of the medium decreased, the imine-forming reaction, requiring charge separation, would become less important. One expected pathway for thermal decomposition would involve homolytic cleavage of the weak N-O bond to give a biradical. The observed formation of some caproamide by the thermal decomposition of the oxazirane of cyclohexanone in iso-propanol probably arises via this mechanism.

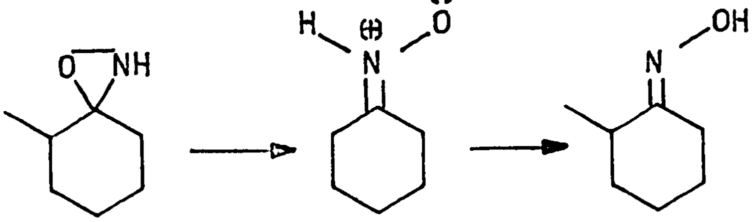


In non-protic solvents such as benzene, apparently the diradical pathway is the major decomposition route, the observed product being cyclohexanone postulated to arise in the following manner:



Considerable support for this hypothesis has been given by Schmitz (34) who reported that thermal decomposition of the oxazirane of cyclohexanone in non-protic solvents in the presence of diazobenzene resulted in the formation of cyclohexanone and hydrazobenzene.

The thermal production of oxime from the oxazirane of 2-methylcyclohexanone is envisaged to be the reverse of the photochemical conversion of oxime to oxazirane:



D. The Mechanism of the Photochemical Decompositions

a. The relative energies of the singlet and triplet states of the oxazirane

A considerable amount of evidence has been presented which strongly suggests that photolytic excitation of oxaziranes can result in the formation of either a singlet or triplet state. Thus, it has been shown that photolysis in iso-propanol produces an excited oxazirane which is quenched by oxygen, which is capable of hydrogen abstraction, and which decomposes to give products from unsymmetrically substituted oximes in a manner so as to generate the more stable radical (7b). These results are typical of triplet species. In contrast, the excited oxazirane in methanol is only partially quenched by oxygen, is partially quenched by heating during irradiation, does not exhibit radical characteristics, and gives an approximately statistical distribution of products from the unsymmetrically substituted oximes (7c).

The results of the photolysis in methanol have, in the past, been interpreted in terms of the singlet species only (7b,7c,11). It will now be shown that the triplet is important in methanol and that the efficiency of intersystem crossing is solvent dependent.

The data obtained by Ng (7b) and Douek (14) for the photolysis yields in the presence of oxygen have been collected and rearranged in Table 12.

Since the singlet is unaffected by oxygen while the triplet is completely quenched, the degree of quenching is a direct measure of the efficiency of intersystem crossing.

TABLE 12

Quenching efficiency of the photoproduct(7) yield from cyclohexanone oxime as a function of solvent

Solvent	Total Photoproduct Yield		% Quenching
	under nitrogen atmosphere	under oxygen atmosphere	
Water	43	46	0
Methanol	51	23	55
iso-Propanol	53	11	80

The data shows that, in methanol, the probability of an excited singlet rearranging to product or undergoing intersystem crossing is approximately equal. Accordingly, about one-half of the photo-excited molecules of oxazirane will make their way to the triplet state. In iso-propanol, most of the excited oxazirane will cross to triplet and thence to amide. If, as in methanol, the triplet cannot abstract hydrogen from solvent, bimolecular quenching will occur accompanied by intersystem crossing to the ground state (40). Excited singlets which do not rearrange to products can then recycle through the triplet state and become available for reexcitation.

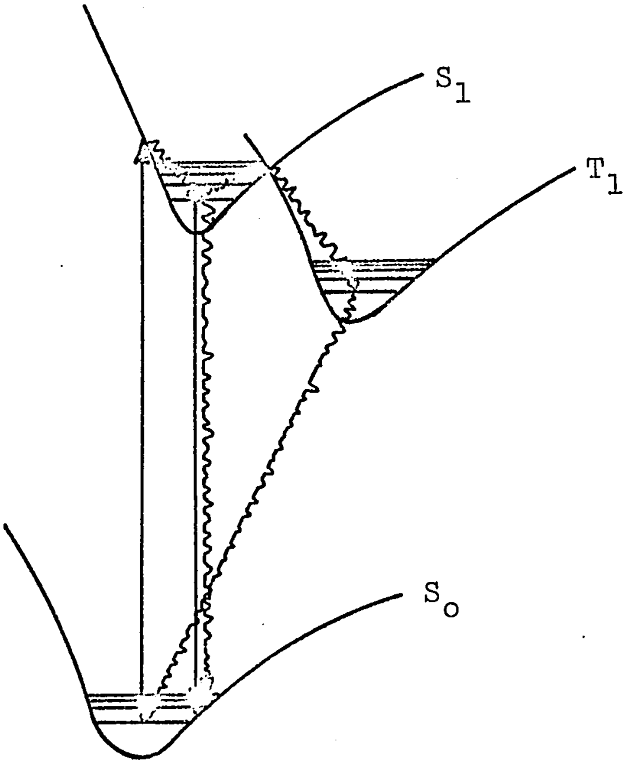
---

(7) Sum of the amide and lactam yields.

Further evidence of this behavior can be deduced from the data of Table 9. Comparison of the half-life of oxazirane in water with the known photon output of the photolysis chamber indicates that for every photon entering the system approximately one molecule of lactam is formed. Since the process is highly efficient, little light can be lost by recycling through the triplet. In methanol, the half-life of the oxazirane drops to one-half that in water corresponding to passage through the triplet. In t-butanol, the data suggests that about 50 cycles are required before all the oxazirane is rearranged. It will be shown later that evidence of this recycling behavior can be found in the photolysis of α-epimeric oximes in t-butanol.

A pictorial representation of the above hypothesis is given on the following page where the ground state of the oxazirane S_o, the first excited singlet S_1 and the first excited triplet T_1 are represented schematically. The solid lines represent radiative transitions while the wavy lines represent radiationless transitions by which the excited states can undergo decay.

Some conclusions regarding the energies and lifetimes of the excited states can be drawn from the above evidence. It has been shown that in the absence of appreciable spin-orbital coupling, the curves for the S_1 and T_1 states intersect near the j=o level of the excited singlet state (41). This follows since the vibrational level near the crossover point must be appreciably thermally populated for efficient

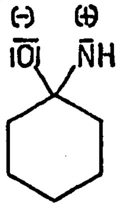


intersystem crossing to occur. It has similarly been shown that the efficiency of intersystem crossing is directly related to the difference in energy of the two states (42). Efficient crossing must mean that the energies of the singlet and triplet levels are close together. The results strongly suggest that the energy levels of the singlet and triplet states vary with solvent with the energy separation becoming smaller as the dielectric constant of the medium decreases.

b. The nature of the electronically excited state

Since the oxazirane possesses no π bond, the electronic transition involves either a $\sigma-\sigma^*$ or $n-\sigma^*$ transition. Usually, transitions of this type are of relatively high energy and therefore seldom encountered in photochemistry. The inherent weakness of the N-O bond and its inclusion into a cyclopropyl ring are responsible for weakening the bond and making these transitions facile in this case. Which of the transitions is involved in the present case is not yet known. It could be determined by measuring the shift of the wavelength of maximum absorption (λ_{max}) with solvent, transitions involving n electrons being known to undergo "blue shifts" with increasingly polar solvents (43). The instability of the oxazirane prevented such measurements. Several points indicate that the n electrons are involved in the present case. Transitions involving n electrons are generally of lower energy than those involving bonding electrons and much more frequently encountered. Furthermore, a strong solvent effect upon the photochemical half-life of the oxazirane has been noted. Finally, the solvent effect seems to indicate that some charge separation has occurred in the transition state. This dipole is much more easily visualized for transitions involving n electrons than those involving bonding electrons. It will be assumed, therefore, that n electrons are involved in the photoreaction.

Two valence bond structures can be written for the singlet transition state resulting from the $n-\sigma^*$ transition. Previous studies (7b,7c,14) have considered the singlet to be best represented by <u>1</u>. It now appears, however, that in some



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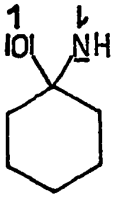

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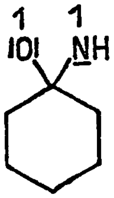
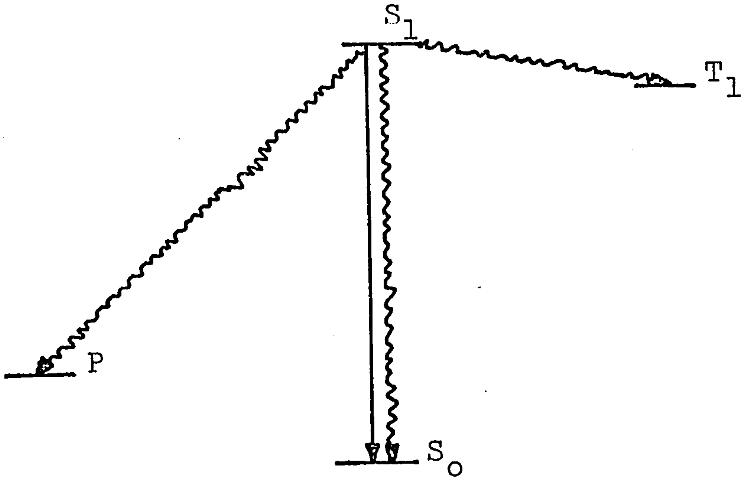
of its reactions, a better representation of the transition state is afforded by 2. In this thesis, it will be assumed that the structure of the singlet lies somewhere between these two extremes. The triplet is represented by 3 only.



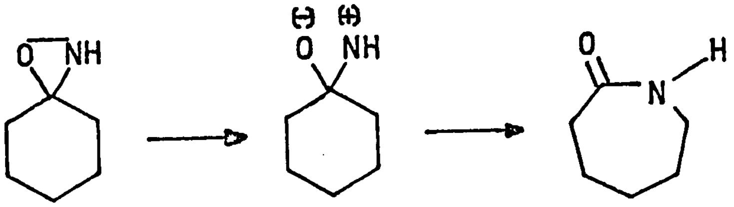
3

c. The mechanism of the singlet reactions

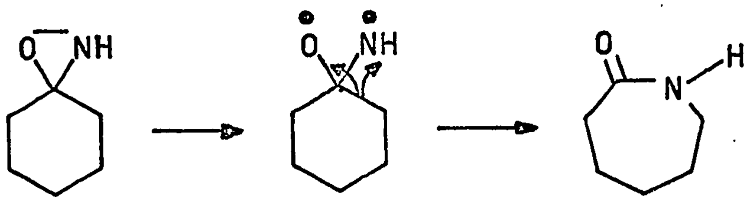
The singlet has been shown to have a lifetime of between 10^{-9} and 10^{-5} seconds (35) during which time it is envisaged to undergo the processes shown schematically on the following page. Thus the excited singlet can undergo fluorescence to S_o, non-radiative decay to S_o, conversion to products P or intersystem crossing to T_1.



In view of the short lifetime of the singlet, the lactam forming reaction must be very rapid. The reaction has been shown to be unaffected by oxygen and to proceed with retention of configuration about the migrating carbon. An ion-type mechanism has been previously proposed (7b,7c,14).



It is conceivable, however, that the reaction proceeds via a radical-type process. This process is expected to be unaffected by oxygen and to occur with retention of



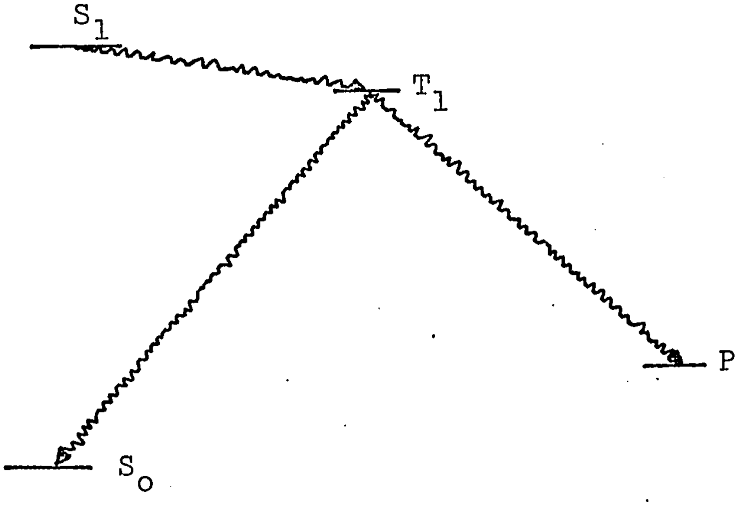
stereochemistry because of the singlet's very short lifetime. The very rapid lactam forming reaction does not produce radicals sufficiently long lived to epimerize or suffer diffusion controlled oxygen quenching (44).

Excited singlets which do not undergo conversion to products P or transitions to S_o will undergo intersystem crossing to T_1. The efficiency of this radiationless transition appears to be strongly dependent on the dielectric constant of the medium.

d. The mechanism of the triplet reactions

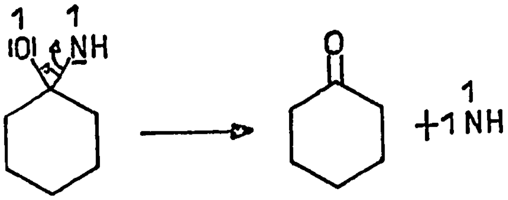
The lifetime of the triplet state in condensed phases has been shown to vary between 10^{-5} and 10^{-3} seconds (35). The triplet is envisaged to undergo the processes shown schematically on the figure on the following page. Thus the triplet T_1 formed by intersystem crossing from S_1 can undergo quenching to S_o or conversion to products P.

The radiationless transition from T_1 to S_o is known to occur by diffusion controlled bimolecular quenching (40). This mode of deactivation is important in solvents in which the hydrogen abstraction reaction is unfavorable.



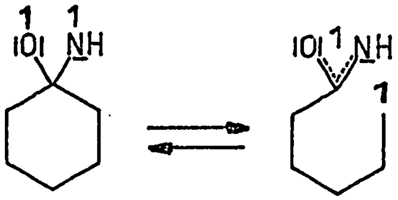
Each molecule of triplet which is not converted to amide undergoes quenching to the ground state from which the oxazirane is available for another excitation.

Apparently, the triplet can be thermally quenched (see section B) to give ketone. The mechanism offered is the following:



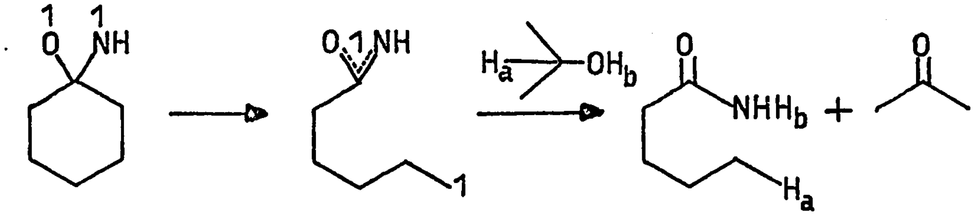
This reaction is important at elevated temperatures but somewhat less important at room temperature.

A process of major importance is the establishment of an equilibrium between the initially formed triplet 3 and the ring-opened form 4.



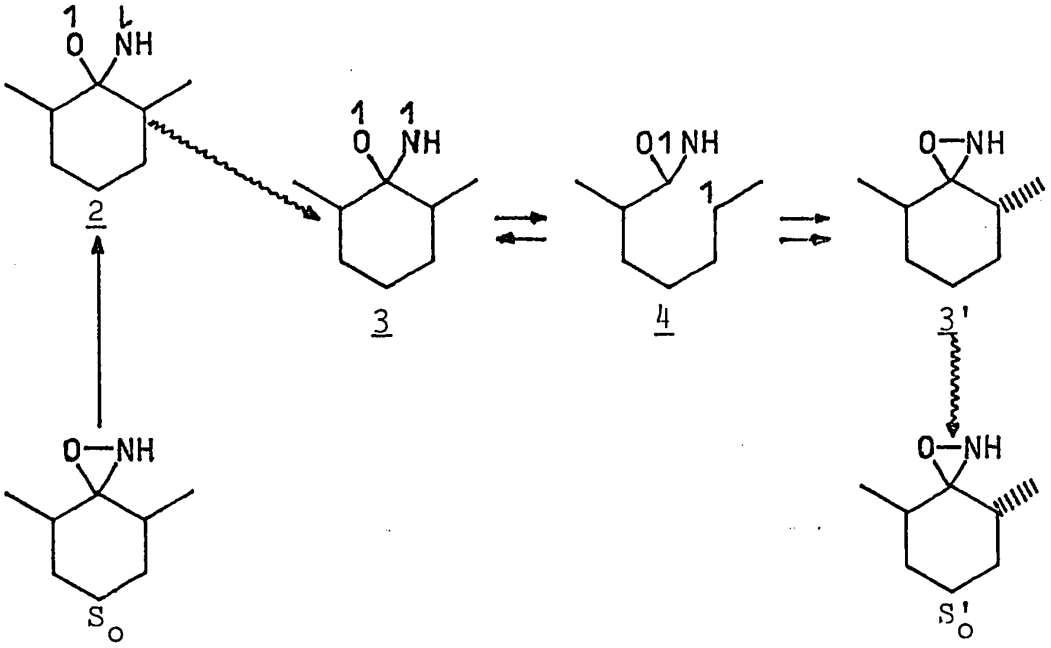
3 4

The conversion of 3 into 4 was proposed by Ng (7b) to account for the formation of amide. The mechanism proposed is given below.



Evidence for the existence of an equilibrium between 3 and 4 has been found in the observation of the epimerization of oximes epimeric at the α-carbon. This feature of the triplet state is best explained by reference to the figure on the following page.

It has been pointed out that the triplet is relatively long lived. The lifetime of 4 should be sufficient to permit a radical at the α-carbon to undergo epimerization. Since oxime and oxazirane are in equilibrium, any epimerization



occurring in the triplet state will rapidly become evident in epimerization of the starting oxime. This process is illustrated on the figure for the case of the oxazirane of <u>cis</u>-2,6-dimethylcyclohexanone (S_o). Further evidence for this hypothesis is forthcoming from the photolysis of α-epimeric oximes in t-butanol.

e. The photolysis of α-epimeric oximes in t-butanol.

Photolysis of oximes in t-butanol is hypothesized to result in recycling of the oxazirane many times through the triplet state before lactam is formed. If this hypothesis is correct, two conclusions concerning the photolysis, in t-butanol, of oximes epimeric at the α-carbon can be drawn:

1) photolysis of unsymmetrically substituted cyclohexanone oximes should give the same lactam ratio as photolysis in methanol.

Fig. 36

Gas-liquid chromatogram of the photolysis products of isomenthone oxime in t-butanol

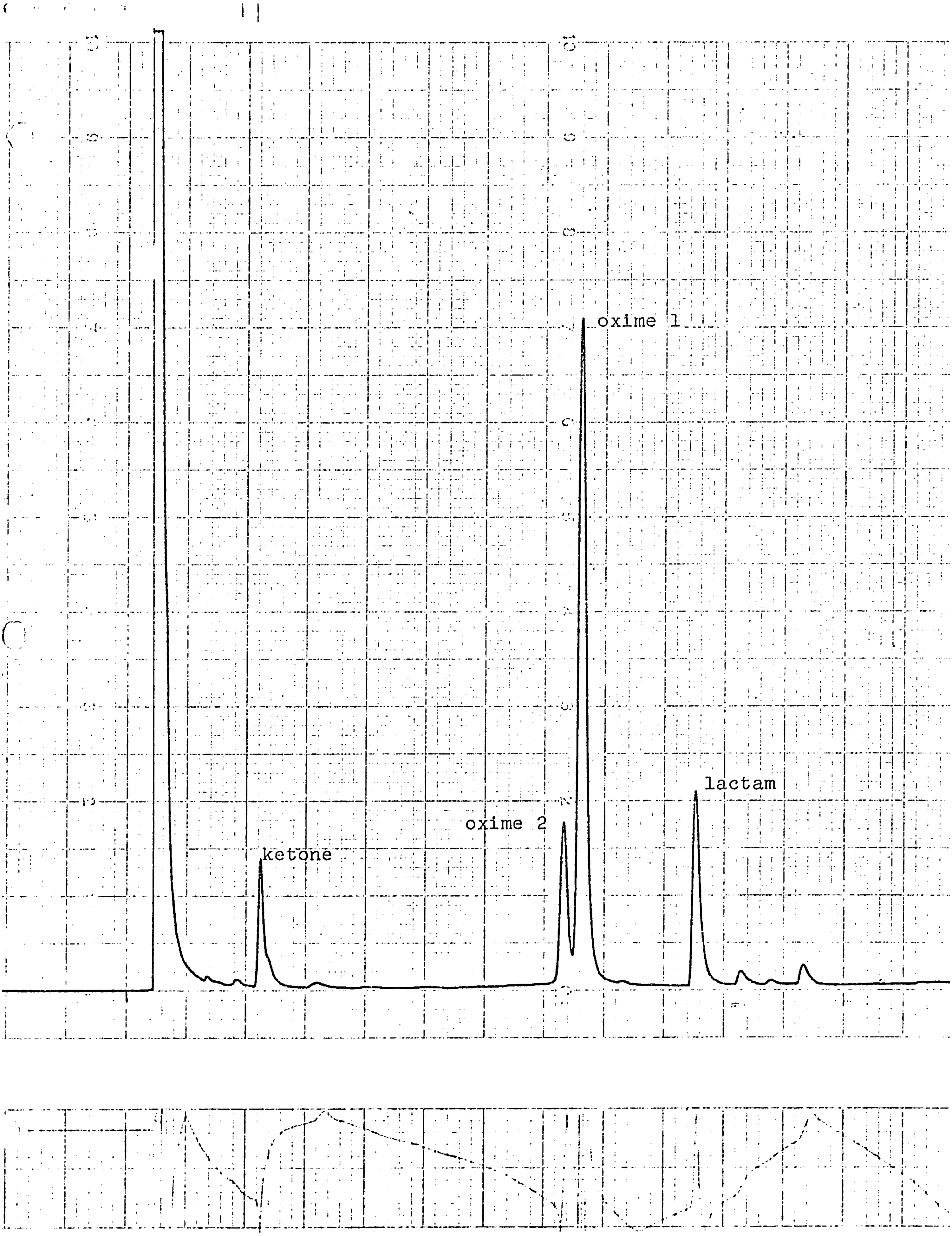
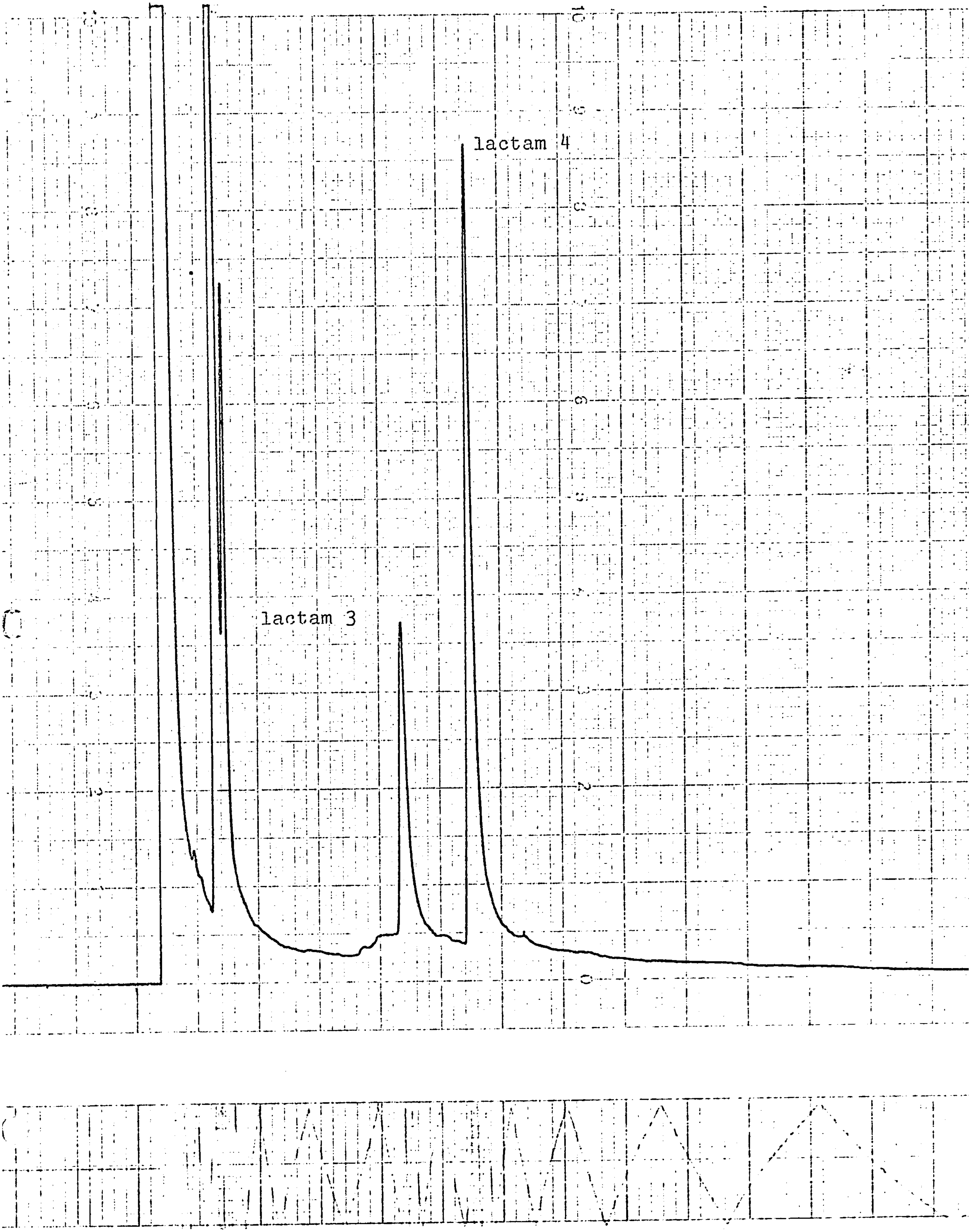

oxime 1
lactam
oxime 2
ketone

Fig. 37

Gas-liquid chromatogram of the photolysis products of cis-2,6-dimethylcyclohexanone oxime in t-butanol


lactam 4
lactam 3
10
9
8
6
2
0

2) compared to the photolysis in methanol, a greater degree of epimerization of oxime should be found corresponding to far more recycling through the triplet.

A preliminary test of conclusion (1) was undertaken to show that lactam is still being generated from the singlet in t-butanol. Comparison of the gas-liquid chromatogram of the lactams from isomenthone oxime in t-butanol (figure 36) with that obtained in methanol (figure 23) shows the lactam ratios to be almost identical in the two solvents. Conclusion (1) is thus verified.

It was shown (section A - chapter III) that photolysis of <u>cis</u>-2,6-dimethylcyclohexanone oxime in methanol gave 2.5% of <u>trans</u>-2,6-dimethylcyclohexanone oxime, i.e. 6% of remaining oxime, among the photoproducts. Photolysis in t-butanol, (figure 37) under the same conditions increased the yield of the epimeric oxime to 10% i.e. 21% of total oxime remaining. Since the rate of oxime photolysis in t-butanol is only one-half that in methanol, the amount of epimerization of oxime in t-butanol is calculated to be about 8 times that in methanol. Conclusion (2) is thus verified.

These results will be summarized in the discussion section.

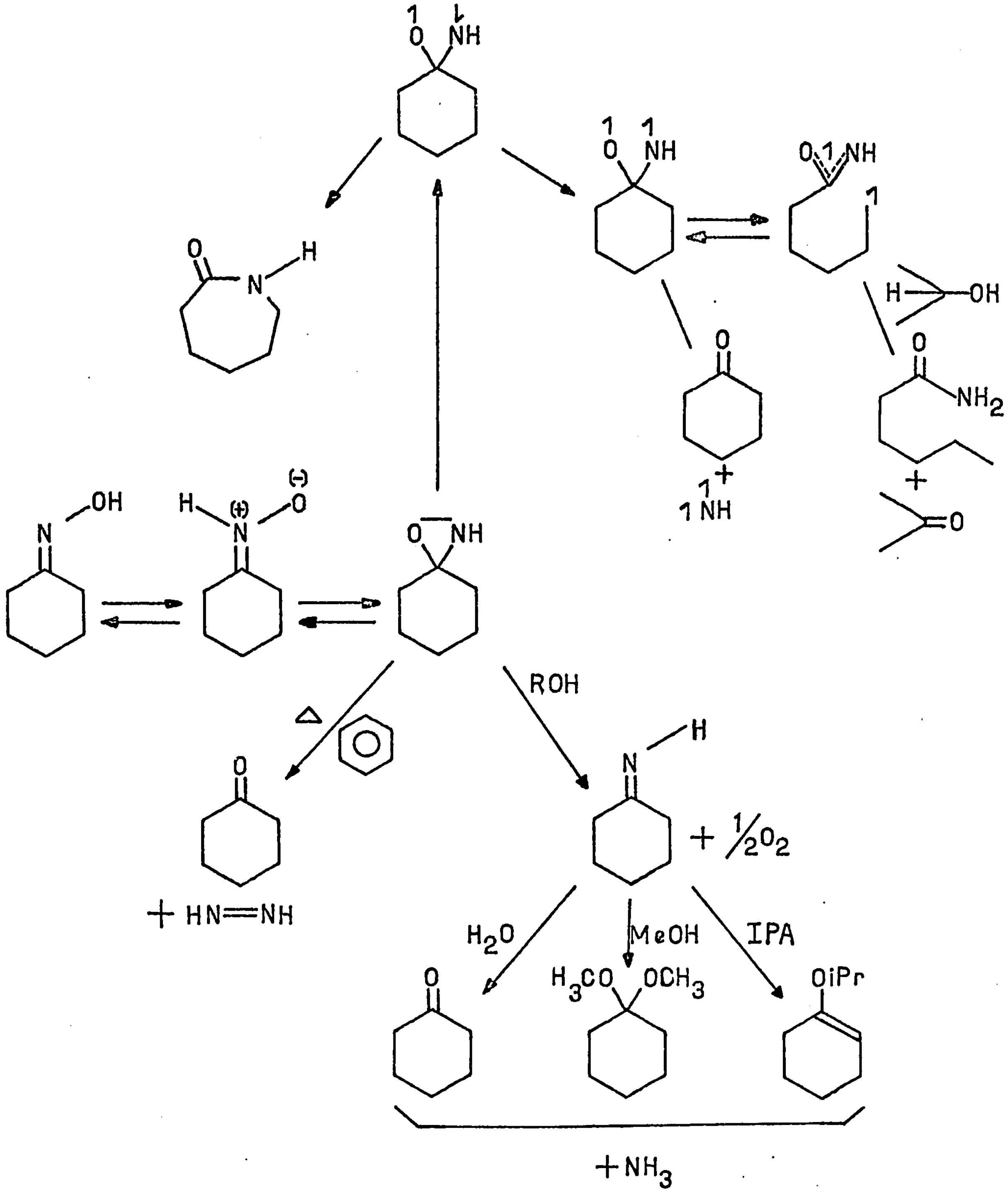
E. Discussion and Summary

All the observed reactions of the oximes and oxaziranes are shown on figure 38.

A great deal of data regarding photolysis of oximes has been explained on the basis of the intermediacy of oxazi-

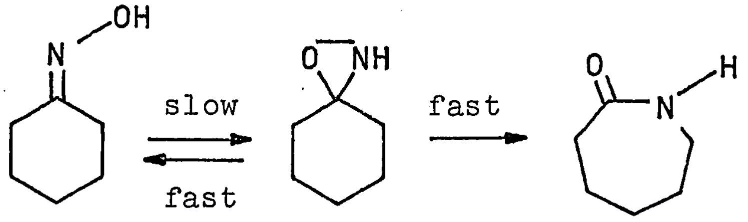
Fig. 38

The reactions of the oximes and oxaziranes



O NH
O NH
O NH
O
N
H
H OH
O
NH2
O
NH
+
O
N OH
H N O
O NH
ROH
N H
+ 1/2 O2
O
+ HN=NH
H2O
MeOH
IPA
O
H3CO OCH3
OiPr
+ NH3

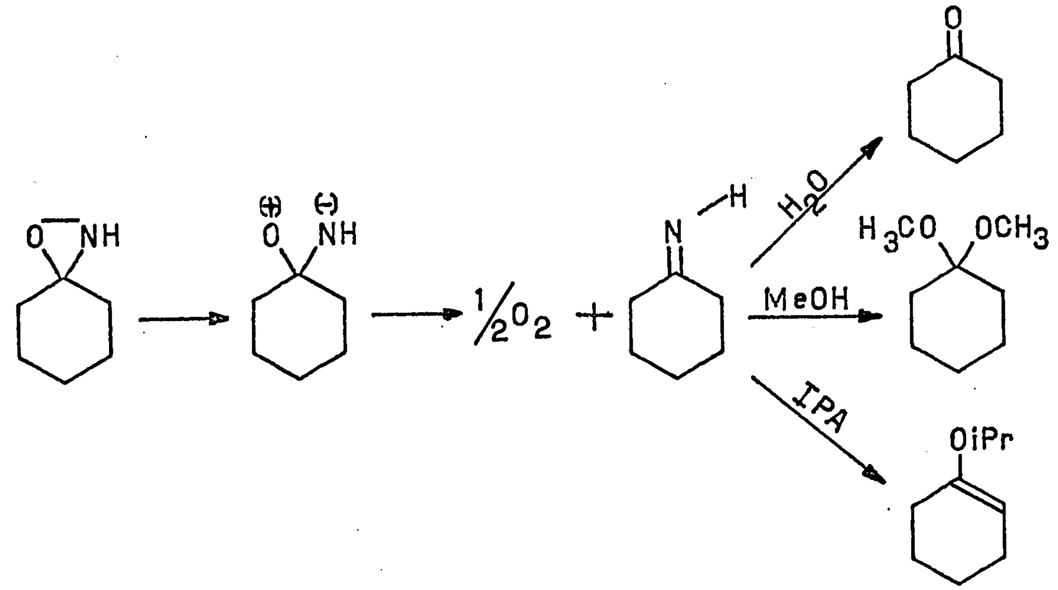
ranes. The data accumulated for the rates of the photo- and thermal decompositions of the oxazirane show that the photorearrangement of oxaziranes is very rapid and that the oxime to oxazirane conversion is rate determining.



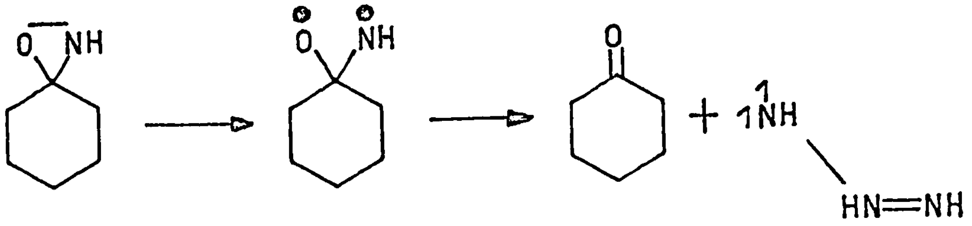
The behavior of the oxazirane of 2-methylcyclohexanone and the observed oxime photo-epimerization show the rearrangement of oxazirane to oxime to be rapid. During the photolysis, oxazirane is present only in low, steady-state concentrations.

The rate data of Table 9 and the observed photo- and thermal product distributions show the oxazirane to decompose photochemically rather than thermally under the photolysis conditions in alcoholic solvents. The thermal reaction can, however, be made to predominate in water.

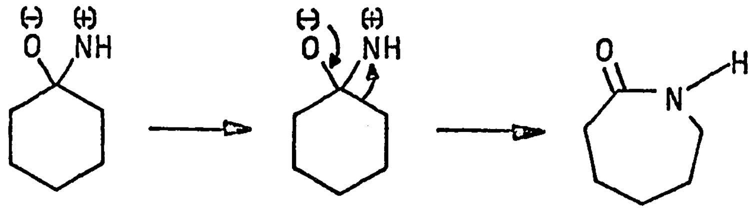
The thermal products of oxazirane decomposition in water and alcoholic solvents have been shown to result from imines. This result represents the first reported alcoholysis of an imine. A test of this mechanism provided the first reported base catalyzed ketalization.



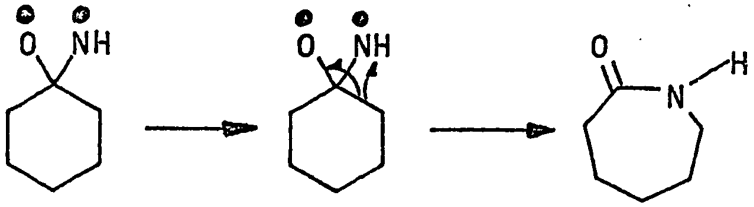
Decomposition of the oxazirane of cyclohexanone in non-protic solvents gives cyclohexanone possibly accompanied by diimide.



Lactam formation is envisaged to result from a singlet whose structure can be written as a hybrid of 1 and 2. Pathways to lactam from both contributing forms can be written.



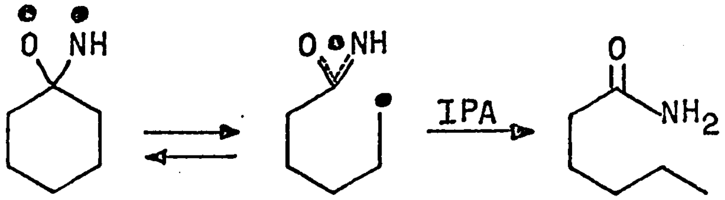
1



2

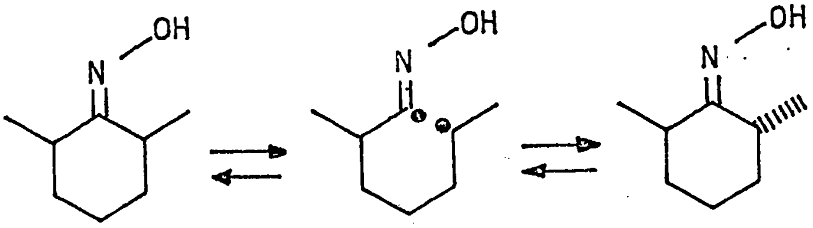
It has been proposed that with decreasing dielectric constant, the efficiency of intersystem crossing to triplet increases. Preliminary results of the photolysis of α-epimeric oximes in t-butanol support this hypothesis.

The oxazirane triplet is envisaged to be in equilibrium with the ring opened form (4).



3 4

Epimerization of the oximes is envisaged to arise in this manner although other processes, i.e. a direct pathway from the oxime, cannot yet be ruled out.



Ketone formation is envisaged to arise either thermally from the triplet or by hydrolysis of oxazirane by traces of water.

EXPERIMENTAL

The melting points were determined either in open capillaries on a Gallenkamp melting point apparatus or on a Kofler hot stage and are uncorrected. The elemental analyses were carried out by Beller Mikroanalytisches Laboratorium, 34 Gottingen, Theaterstrasse 23, Germany. The infra-red spectra were recorded on a Perkin-Elmer 337 grating spectrometer as dilute carbon tetrachloride solutions. The nuclear magnetic resonance (n.m.r.) spectra were recorded on a Varian A-60 spectrometer operating at 60 megacycles (tetramethylsilane = 0 p.p.m.). Merck silica gel HF was used for thin-layer chromatography (t.l.c.). Woelm alumina was used for column chromatography. The photolysis yields were determined, in all cases, by gas-liquid chromatography (g.l.c.) on a Hewlett-Packard 5751 B instrument equipped with dual flame ionization detectors and a disc integrator. The yields were determined, in all cases, by comparison of the peak area with that of a standard solution of an authentic sample. Except where noted, the chromatograms were carried out using 6 ft. x 1/8 in. stainless steel columns packed with 10% Carbowax 20M on High Performance Chromosorb W (100/120 mesh). All photolyses were carried out in quartz cells in a Rayonet Photochemical Reactor, model 1061, available from the Southern New England Ultra-violet Company, Middletown, Connecticut. The energy output of the reactor was 32 watts of which about 90% was emitted at the 253.7 nm mercury line. All photolyses were carried out in either spectroquality methanol, spectroquality iso-propanol or special high purity t-butanol, all available from Matheson, Coleman and Bell Company.

Standard Procedure for the Photolysis of Oximes

A solution of the oxime (10^{-3} mole) in methanol (100 ml) was placed in a quartz cell and nitrogen was bubbled through the solution for 20 minutes. The nitrogen atmosphere was maintained by a mercury seal. All solutions were photolyzed for 2 hours, then concentrated, by distillation of solvent, to 10 ml for g.l.c. analysis or 1 ml for separation of the photoproducts by t.l.c.

CHAPTER 1

a) The Preparation of Authentic Samples

Most of the ketones of table 2 were commercially available and were purified by distillation to the literature boiling point. 2,2,6,6-Tetradeuterocyclohexanone was prepared by the method of Best (45). The n.m.r. spectrum of the ketone showed the deuterium content to be 96 ± 2% by comparison with an undeuterated sample. Commercially available 2,6-dimethylcyclohexanone(10) was found to be a mixture of 90% cis- and 10% trans-2,6-dimethylcyclohexanone by g.l.c. 2,2-Dimethylcyclohexanone was prepared by the method of Johnson and Posvic (46), and purified by distillation, b.p. 127-8/ 200 mm (lit. (46) b.p. 168-174°). 2,2,6,6-Tetramethylcyclohexanone (47) was a gift of K. Dahl of this laboratory.

The oximes of Table 2 were prepared, except where noted by the method of Shriner, Curtin and Fuson (48) using hydroxylamine hydrochloride and sodium hydroxide. The melting points of the oximes obtained after extraction and recrystallization (hexane) are listed in Table 13.

TABLE 13

The melting points of the oximes of Table 2

Oxime	m.p. (°C)	Literature m.p. (°C)	Reference
cyclohexanone oxime	90-90.5	90	49
2,2,6,6-tetradeutero-cyclohexanone oxime	91-91.5	-	-
2-methyl-cyclohexanone oxime	46-46.5	43	49
2,6-dimethyl-cyclohexanone oxime(3)	57-59	79(cis) 119(trans)	50
2,2-dimethyl-cyclohexanone oxime	93.5-94	92.5-93	46
2,2,6-trimethyl-cyclohexanone oxime	106-107	106	51
2,2,6,6-tetramethyl-cyclohexanone oxime	151.5	148-149	52
3,3,5,5-tetramethyl-cyclohexanone oxime	146-147	144-145	53

2,2,6,6-Tetramethylcyclohexanone oxime (47) was a gift of K. Dahl. 2,2,6,6-Tetradeuterocyclohexanone oxime was prepared by treating the ketone with a slight excess of hydroxylamine hydrochloride and sodium acetate in methanol solution. After stirring several hours at room temperature, the oxime was extracted and recrystallized (pentane). The deuterium content was estimated by n.m.r. to be 96 ± 2% by comparison with an undeuterated sample.

Authentic samples of the amides resulting from the photolyses of unsymmetrically substituted cyclohexanone oximes were provided by L.S. Ng of this laboratory. Samples of 3,3,5,5-tetramethylcaproamide and 2,2,6,6-tetramethylcaproamide were not available. Their retention temperatures in the gas chromatograph were determined by photolyzing 3,3,5,5-tetramethylcyclohexanone oxime and 2,2,6,6-tetramethylcyclohexanone oxime in methanol and iso-propanol and comparing the g.l.c. traces of the photolysis mixtures.

TABLE 14

The melting points of the lactams of Table 2

Lactam	m.p. (°C)	Literature m.p. (°C)	Reference
2,2,6,6-tetradeutero-caprolactam	68-68.5	-	
6-methyl-caprolactam	92-93	90-91	54
2,6-dimethyl-caprolactam	72.5-73.5	-	
2,2,6,6-tetramethyl-caprolactam	114-115	-	
3,3,5,5-tetramethyl-caprolactam	148-148.5	147	55

The lactams described in Table 2 were prepared by the methods described below. The melting points are listed in Table 14.

2,2,6,6-Tetradeuterocaprolactam (7c) and 3,3,5,5-tetramethylcaprolactam were prepared by treating the oximes with p-toluenesulphonylchloride and pyridine, and treating the reaction mixture with water. The lactams were purified by recrystallization (hexane) and sublimation.

2-Aza-3-methylcycloheptanone (6-methylcaprolactam) was prepared by treating 2-methylcyclohexanone oxime (2 g) with polyphosphoric acid (10 ml) at 120° for 30 minutes. Extraction, recrystallization (hexane) and sublimation gave the pure lactam (1.2 g) in 60% yield.

2-Aza-3,6-dimethylcycloheptanone (2,6-dimethylcaprolactam) was prepared by treating 2,6-dimethylcyclohexanone oxime$^{(3)}$ with thionyl chloride and then water (7c). Extraction gave a 64% yield of crude product which was purified by recrystallization (hexane). The lactam was later shown to be pure <u>cis</u>-2,6-dimethylcaprolactam.

All attempts to prepare 2,2,6,6-tetramethylcaprolactam by a Beckmann rearrangement were without success. In every case, the crude product obtained after extraction showed no carbonyl band in the infra-red spectrum but always a strong nitrile band. The lactam was obtained in 60% yield by photolysis of 2,2,6,6-tetramethylcyclohexanone oxime in methanol (7c).

Prior to their use as authentic samples, all these compounds - oximes, ketones, amides, and lactams - were shown to be more than 99% pure by g.l.c.

b) The Photolysis of 2,2,6-Trimethylcyclohexanone Oxime(XX)

Photolysis of 2,2,6-trimethylcyclohexanone oxime in methanol and separation of the products by preparative t.l.c. using a chloroform-ether-methanol (8:2:0.5) eluant gave unreacted oxime (XX), $R_f = 0.63$; a mixture of lactams (XXIIa, XXIIb), $R_f = 0.55$; and a mixture of amides (XXIIIa, XXIIIb), $R_f = 0.34$. That the band at $R_f = 0.55$ was a mixture was shown by the n.m.r. spectrum which showed six signals in the methyl region assigned as: two methyl singlets at 1.28 p.p.m. and 1.13 p.p.m. and two methyl doublets centered at 1.29 p.p.m. (J = 8 c.p.s.) and 1.07 p.p.m. (J = 9 c.p.s.). Comparison of these values with the methyl singlets of 2,2,6,6-tetramethylcaprolactam ($\delta = 1.30$ p.p.m. and $\delta = 1.17$ p.p.m.) and the methyl doublets of 2,6-dimethylcaprolactam ($\delta = 1.21$ p.p.m. and $\delta = 1.02$ p.p.m., J = 7 c.p.s. each) clearly shows two compounds to be present in the mixture; 2,2,6-trimethylcaprolactam and 2,6,6-trimethylcaprolactam. That the band at $R_f = 0.34$ was a mixture was shown by the gas-liquid chromatogram which gave two peaks having the same retention times as 2,2-dimethylheptanamide and 2,6-dimethylheptanamide.

c) The Photolysis of 3,3,5,5-Tetramethylcyclohexanone Oxime (XXIV)

Photolysis of 3,3,5,5-tetramethylcyclohexanone oxime in methanol and separation of the products by preparative t.l.c.

using a chloroform-ether-methanol eluant (8:2:0.5) gave unreacted oxime, $R_f = 0.69$ and 3,3,5,5-tetramethylcaprolactam, $R_f = 0.47$. The isolated lactam was found to be identical in all respects with an authentic sample. Comparison of the gas-liquid chromatograms of the photolysis products of the oxime in methanol and iso-propanol showed that little amide was formed in methanol.

CHAPTER 2

a) The Preparation of Authentic Samples

TABLE 15

The melting points of the oximes of table 4

Oxime	m.p. (b.p.) (°C)	Literature m.p. (°C)	Reference
cyclobutanone oxime	84.5-86	84-85	56
cyclopentanone oxime	59-60	56	49
cycloheptanone oxime	(230)	(150-152/ 20mm)	57
cyclooctanone oxime	41-42	36-37	57
cyclononanone oxime	86-86.5	79	57
cyclodecanone oxime	84-85	80	57
cycloundecanone oxime	85.5-87	80-81	57
cyclododecanone oxime	137-138	132	57
cyclopentadecanone oxime	79.5-80	76-77	57

The ketones of Table 4 were commercially available and were purified by distillation or sublimation to literature boiling point or melting point.

The oximes of Table 4 were prepared by treating the parent ketones with an excess of hydroxylamine hydrochloride and sodium acetate in methanol solution. After refluxing for two hours, the oximes were formed in quantitative yield. The melting points of the oximes obtained after extraction, recrystallization and sublimation are listed in Table 15.

The amides of Table 4 were prepared by refluxing a benzene solution of the parent acid with a slight excess of thionyl chloride followed by cautious addition of concentrated aqueous ammonia solution. The melting points of the amides obtained after extraction and recrystallization (hexane) are listed in Table 16.

TABLE 16

The melting points of the amides of table 4

Amide	m.p. (°C)	Literature m.p. (°C)	Reference
heptanamide	98-99	96	58
octanamide	106-107	110	59
decanamide	102-102.5	108	60
dodecanamide	105-105.5	110	61
pentadecanamide	105-106	102.5	62

The lactams of Table 4 which were not commercially available were prepared by a Beckmann rearrangement. To a solution of the oxime (100 mg) in chloroform (10 ml) was added pyridine (0.5 ml) and 1.05 equivalents of p-toluenesulphonylchloride. The air above the solution was displaced by nitrogen and the solution left standing overnight at room temperature. Acetic acid (2 ml) was then added and the solution heated to reflux for 3 hours under nitrogen. Water (2 ml) was then added and the mixture maintained at reflux a further 3 hours. The melting points of the lactams obtained after extraction, purification by preparative t.l.c., recrystallization (pentane) and sublimation are listed in Table 17.

TABLE 17

The melting points of the lactams of table 4

Lactam	m.p. (°C)	Literature m.p. (°C)	Reference
2-azacyclononanone	75.5-76.5	72-73	57
2-azacyclodecanone	141.5-143	138-139	57
2-azacycloundecanone	165-165.5	162	57
2-azacyclododecanone	155.5-156.5	154-154.5	57
2-azacyclotridecanone	152-153	153-153.5	57
2-azacyclohexadecanone	135	133.5	57

Prior to their use as standards, all the authentic samples described above - ketones, oximes, amides, and lactams - were shown to be more than 99% pure by g.l.c.

b) The Photolysis of the Various Ring Size Ketoximes

The photolysis of the various cyclic ketoximes of ring size 4 to 15 behaved analogously with that of cyclohexanone oxime giving the corresponding lactams and traces of amides and ketones. All the photo-products listed in Table 4 and present in greater than 5% yield were obtained pure by preparative t.l.c. In all cases, they were shown to be

TABLE 18

The R_f values of the photoproducts of table 4

Starting oxime	R_f value			
	ketone	oxime	amide	lactam
cyclobutanone oxime	-	0.50	0.32	-
cyclopentanone oxime	0.60	0.48	0.33	0.32
cyclohexanone oxime	0.60	0.49	0.33	0.37
cycloheptanone oxime	0.59	0.52	0.36	0.38
cyclooctanone oxime	0.60	0.54	0.32	0.39
cyclononanone oxime	0.60	0.54	-	0.38
cyclodecanone oxime	0.64	0.59	0.33	0.40
cycloundecanone oxime	0.64	0.59	-	0.42
cyclododecanone oxime	0.63	0.62	0.33	0.45
cyclopentadecanone oxime	0.63	0.62	0.31	0.51

identical in infra-red spectrum, R_f (t.l.c.), and retention time (g.l.c.) with authentic samples. The R_f values of all these compounds, for the eluant system chloroform-ether-methanol (8:2:0.5), are recorded in Table 18.

c) The Photolysis Yields

The yields of the photoproducts listed in Table 4 were determined by quantitative g.l.c. Authentic samples of some of the photoproducts were not available. Peaks on the gas-liquid chromatograms corresponding to cyclodecanone, cycloundecanone, nonanamide, and undecanamide, for which authentic samples were not available, were identified by taking advantage of the elution behavior of members of a homologous series in g.l.c. It is known that during temperature programmed gas chromatography, the temperature at which the members of a homologous series are eluted varies linearly with the carbon number (63). A plot of the observed retention temperatures of the authentic samples versus the carbon number is given on graph 5. The data is tabulated in Table 19. The retention temperatures of unavailable compounds were determined by interpolation and peaks corresponding to these compounds were thus identified.

Samples of 2-azacyclodecanone, 2-azacycloundecanone, and 2-azacyclododecanone were not available in sufficient quantities to prepare standard solutions. The yields of these products were determined by taking advantage of another homologous series relationship. It is known that the relative molar flame response of members of a homologous series varies linearly

TABLE 19

The retention temperatures of the photoproducts of table 4

Starting oxime	Retention temperature (°C)[8]			
	ketone	oxime	amide	lactam
cyclobutanone oxime	-	-	98	-
cyclopentanone oxime	-	76	101	126
cyclohexanone oxime	66	87	111	134
cycloheptanone oxime	78	-	-	144
cyclooctanone oxime	-	115	133	152
cyclononanone oxime	103	-	-	-
cyclodecanone oxime	-	140	156	-
cycloundecanone oxime	-	-	-	-
cyclododecanone oxime	139	162	177	186
cyclopentadecanone oxime	170	191	204	-

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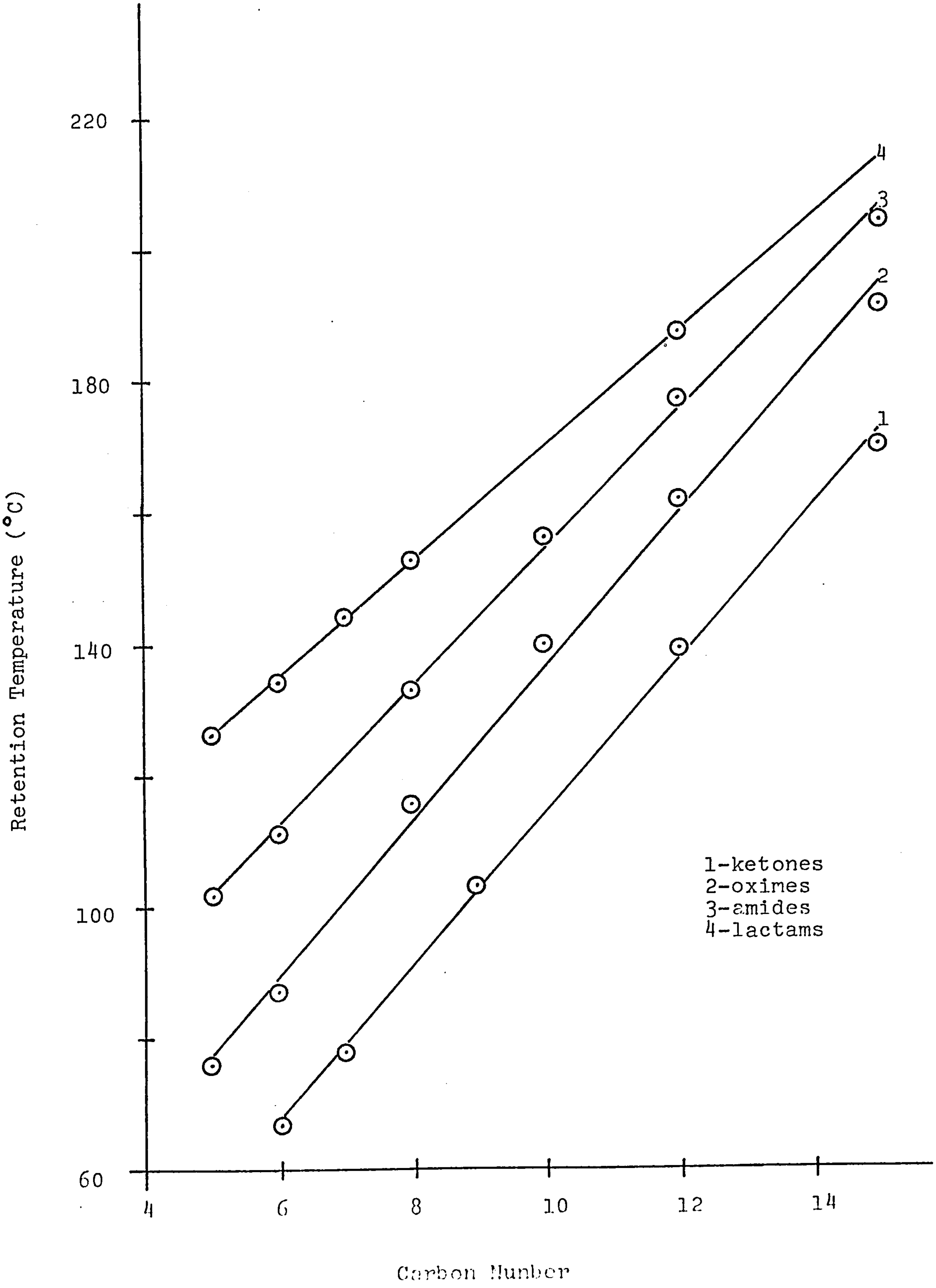
(8) Determined on a 6ft. stainless steel column (1/8in. O.D.) packed with 3% OV-25 on High Performance Chromosorb W. Gas flow was 25 ml/min. while the program ran from 60° to 200° at 4°/min.

GRAPH 5

The variation of the gas chromatographic
retention time with carbon number
for the products of Table 4



220
180
140
100
60
4
6
8
10
12
14
Retention Temperature (°C)
Carbon Number
1
2
3
4
1-ketones
2-oximes
3-amides
4-lactams

with the carbon number (64). A plot of the observed flame response versus carbon number of the authentic samples is given on graph 6. The relative molar responses are tabulated in Table 20.

TABLE 20

The relative molar flame response of the photoproducts of table 4

Starting oxime	Relative molar response[9]			
	ketone	oxime	amide	lactam
cyclobutanone oxime	-	-	-	-
cyclopentanone oxime	0.85	0.87	-	-
cyclohexanone oxime	1.00	1.11	-	0.86
cycloheptanone oxime	1.30	-	-	0.97
cyclooctanone oxime	-	1.54	1.09	1.25
cyclononanone oxime	1.75	-	-	-
cyclodecanone oxime	-	1.77	1.46	-
cycloundecanone oxime	-	-	-	-
cyclododecanone oxime	2.25	2.02	1.81	1.92
cyclopentadecanone oxime	2.55	-	-	-

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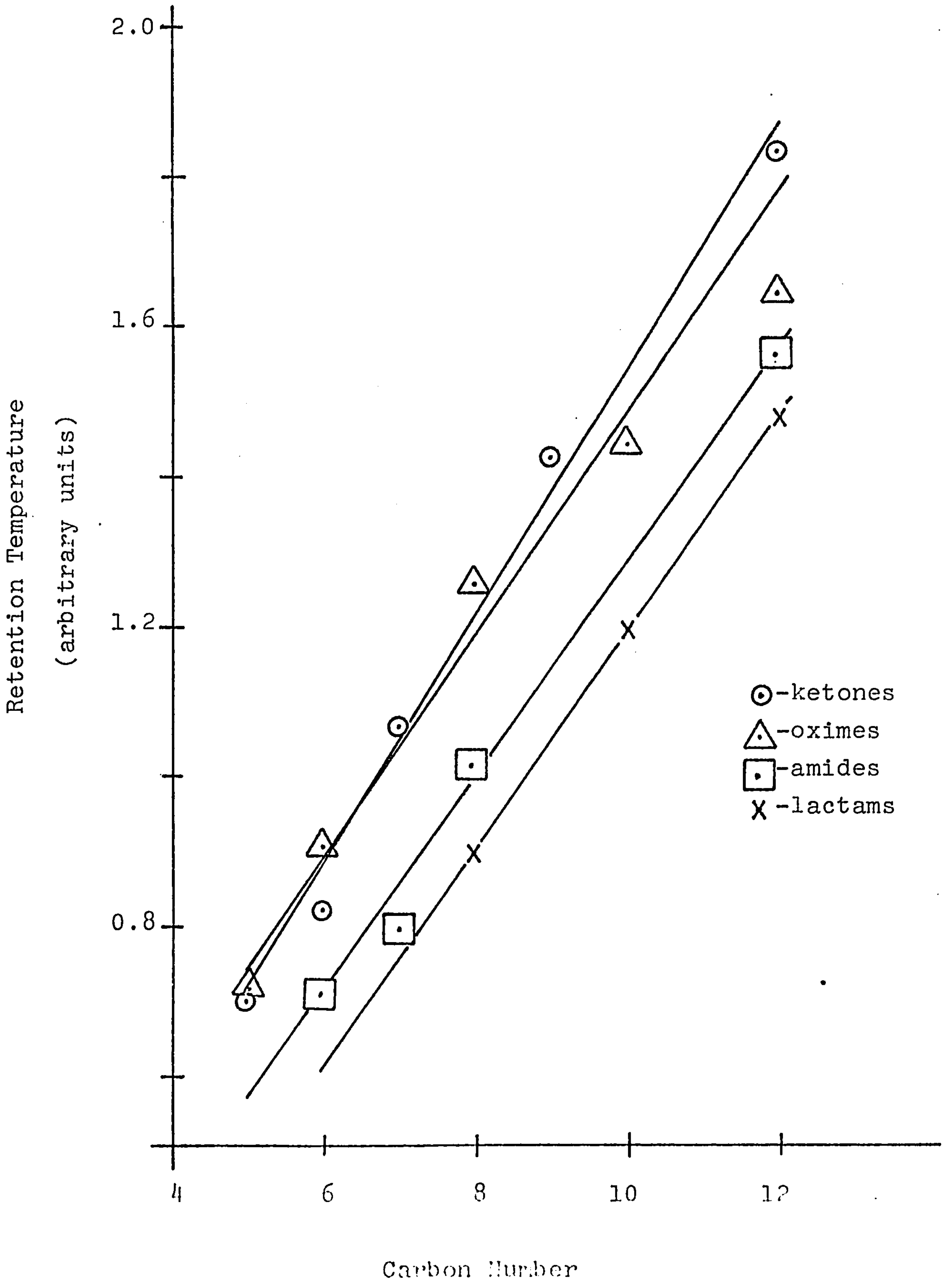
(9)Relative molar response of cyclohexanone taken as 1.00

GRAPH 6

The variation of the molar flame response versus carbon number for the photoproducts of Table 4


2.0
1.6
1.2
0.8
Retention Temperature
(arbitrary units)
⊙-ketones
△-oximes
⊡-amides
X-lactams
4
6
8
10
12
Carbon Number

The molar flame response of the unavailable samples were determined from the graph by interpolation.

CHAPTER 3

a) The Preparation of Authentic Samples

Menthone was prepared following the method of Brown and Garg (65) which had to be somewhat modified. d,l-Menthol was treated with sodium dichromate and dilute sulphuric acid for 2 hours. Extraction of the ketone and g.l.c. analysis showed the crude product to contain 25% unreacted menthol. The crude product was then retreated with sodium dichromate and dilute sulphuric acid. Extraction gave a crude product in 98% overall yield which was shown by g.l.c. to contain only menthone and a small amount (2%) of isomenthone.

Isomenthone was prepared by the method of Nigain and Levi (66) from a commercially available mixture of menthone and isomenthone[10]. The final product, obtained in 43% overall yield, was shown by g.l.c. to contain isomenthone and a small amount (1%) of menthone.

Menthone oxime and isomenthone oxime were prepared by treatment of the ketones in methanol solution with an excess of hydroxylamine hydrochloride which had been exactly neutralized with sodium bicarbonate. The solutions were stirred several hours at room temperature then warmed to complete the oximation reaction. Extraction gave quantitative yields of

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[10] Aldrich Chemical Company

the crude oximes which were purified by recrystallization (hexane).

cis-2,6-Dimethylcyclohexanone oxime was prepared by treating commercially available[10] 2,6-dimethylcyclohexanone (90% cis) with hydroxylamine hydrochloride and sodium acetate in methanol solution. Extraction and several recrystallizations (hexane) gave the pure cis isomer.

trans-2,6-Dimethylcyclohexanone oxime was obtained by treating commercially available 2,6-dimethylcyclohexanone with 2 equivalents of hydroxylamine hydrochloride and 3 equivalents of potassium hydroxide in methanol solution. After refluxing overnight, the oxime was extracted and shown by g.l.c. to be a mixture (68% trans - 32% cis). Several recrystallizations from methanol gave the pure trans isomer.

The melting points of the oximes of Table 5 are tabulated in Table 21.

The required amides were gifts of Miss L.S. Ng of this laboratory.

trans-3-Methyl-6-isopropylcaprolactam was prepared by treating an ice cold ether solution of menthone oxime (1 g) with phosphorus pentachloride (1.2 g). The resulting solution was allowed to warm to room temperature, stirred a further 3 hours, then poured over crushed ice. Extraction by ether gave 0.57 g (57%) of crude lactam which was purified by column chromatography on silica gel (ethyl acetate eluant) followed by recrystallization (hexane).

TABLE 21

The melting points of the oximes of table 5

Oxime	m.p. (°C)	Literature m.p. (°C)	Reference
menthone oxime	83.5-84	81-82	67
isomenthone oxime	101.5-102.5	99-100	68
cis-2,6-dimethyl-cyclohexanone oxime	77-78	80-81	69
trans-2,6-dimethyl-cyclohexanone oxime	120.5-121	118	69

cis-3-Methyl-6-isopropylcaprolactam was prepared analogously from isomenthone oxime (1 g). Extraction gave 0.62 g (62%) of crude lactam which was purified by column chromatography and recrystallization (hexane).

trans-2,6-Dimethylcaprolactam was prepared by treating _trans_-2,6-dimethylcyclohexanone oxime (1 g) with thionyl chloride (1 ml) in methylene chloride solution at 0°. After stirring for 30 minutes, the solvent and volatile products were distilled off under reduced pressure and water was added. The mixture was heated to reflux for 10 minutes, then allowed to cool and extracted with ether. The product (0.86 g, 86%) was shown to be a mixture of cis- and trans lactams by g.l.c. Chromatography on alumina (activity 1) enriched the composition of the mixture to 15% cis and 85% trans (g.l.c.). The pure trans lactam was finally obtained by fractional sublimation (40°/1 mm) of the enriched mixture.

cis-2,6-Dimethylcaprolactam was prepared in an analogous manner from cis-2,6-dimethylcyclohexanone oxime. The crude product obtained in 64% yield was purified by recrystallization (hexane).

The melting points of the lactams are tabulated in Table 22.

TABLE 22

The melting points of the lactams of table 5

Lactam	m.p. (°C)	Literature m.p. (°C)	Reference
trans-3-methyl-6-isopropylcaprolactam	116.5-117.5	114-115	70
cis-3-methyl-6-isopropylcaprolactam	93-93.5	94-95	71
trans-2,6-dimethylcaprolactam	77-78	-	-
cis-2,6-dimethyl caprolactam	71-72	-	-

Conditions for the separation of the epimeric oximes and lactams have already been described. Prior to use as authentic samples, the epimeric purity of all these compounds were checked by g.l.c. and shown to be greater than 99.9%.

b) The Photolysis of Menthone Oxime and Isomenthone Oxime

Photolysis of menthone oxime and separation of the products by preparative t.l.c. using a chloroform-ether-methanol eluant (8:2:0.5) gave unreacted oxime, $R_f = 0.57$ and a mixture of lactams, $R_f = 0.49$. The mixture at $R_f = 0.49$ gave a single peak in the gas chromatograph on a polar column (10% Carbowax 20M) but separated into two peaks on a 5% OV-210 column. These peaks had the same retention times as the two lactam isomers resulting from a Beckmann rearrangement on menthone oxime and were different from the retention times of the two lactam isomers resulting from a Beckmann rearrangement on isomenthone oxime.

Photolysis of isomenthone oxime similarly gave unreacted oxime, $R_f = 0.53$ and a mixture of lactams, $R_f = 0.49$ on work-up by preparative t.l.c. The mixture at $R_f = 0.49$ similarly gave two peaks in the gas chromatograph on a 5% OV-210 column which had the same retention times as the two lactam isomers resulting from a Beckmann rearrangement on isomenthone oxime. The retention times were different from those of the lactam isomers formed from menthone oxime.

Photolysis of <u>cis</u>-2,6-dimethylcyclohexanone oxime gave unreacted oxime, $R_f = 0.52$ and <u>cis</u>-2,6-dimethylcaprolactam, $R_f = 0.48$ on work-up by preparative t.l.c. using the chloroform-ether-methanol eluant (8:2:0.5). Only a trace of <u>trans</u>-2,6-dimethylcaprolactam was detected by g.l.c. among the photoproducts

Photolysis of <u>trans</u>-2,6-dimethylcyclohexanone oxime gave unreacted oxime, $R_f = 0.59$ and <u>trans</u>-2,6-dimethylcaprolactam, $R_f = 0.45$ by preparative t.l.c. Only a trace of the epimeric lactam was detected by g.l.c. among the photoproducts.

CHAPTER 4

a) The Preparation of Authentic Samples

With the exception of 2,2,4,4-tetramethyl-3-pentanone, (di-t-butyl ketone) all the ketones of Table 7 were commercially available. 2,2,4,4-tetramethyl-3-pentanone was prepared by treating ethyl pivalate with t-butyllithium at -78° as suggested by Dubois (72). Extraction and distillation gave the pure ketone, b.p. 61-62°/30 mm, in 71% yield. The literature b.p. is 70°/43 mm (73). The ketone showed a strong carbonyl absorption in the infra-red spectrum at 1685 cm^{-1}. The required ethyl pivalate was prepared by treating commercially available[10] pivaloyl chloride with ethanol. Extraction and distillation gave the pure ester, b.p. 50-51°/64 mm in quantitative yield.

The oximes of Table 7 were prepared by the method of Shriner, Curtin and Fuson (48). The melting points of the oximes obtained after extraction and recrystallization or sublimation are listed in Table 23.

2,2,4,4-Tetramethyl-3-pentanone oxime was prepared by heating the ketone to reflux with a concentrated solution of hydroxylammonium acetate (0.64 g/ml) in methanol for 2 weeks. The oxime was isolated as a crystalline compound in 22% yield and purified by sublimation and recrystallization. The infra-red spectrum showed an absorption (O-H) at 3600 cm^{-1}. The n.m.r. spectrum showed signals at δ = 1.25 p.p.m. (9H), 1.40 p.p.m. (9H) and 9.50 p.p.m. (1H - D_2O exchangeable).

TABLE 23

The melting points of the oximes of table 7

Oxime	m.p. (b.p.) (°C)	Literature m.p. (°C)	Reference
acetone oxime	62.5-64	59	49
2-butanone oxime	(82-83/ 42mm)	(152)	74
3-pentanone oxime	(71-72/ 12mm)	(165)	75
2,4-dimethyl-3-pentanone oxime	34.5	34	49
2,2-dimethyl-3-butanone oxime	78.5-79.5	78.5-79.5	76
2,2-dimethyl-3-pentanone oxime	85-86.5	79-80	77
2,2,4,4-tetramethyl-3-pentanone oxime	159-161	-	-

Analysis:

Calculated for $C_9H_{19}NO$	C, 68.74	H, 12.18	N, 8.91
Found	C, 69.08	H, 12.08	N, 8.90

Most of the required α-cleavage products (primary amides) were commercially available.

Most of the Beckmann-type products (secondary amides) were prepared by heating the appropriate acid chloride with the appropriate amine. The melting points (boiling points) of the compounds obtained after extraction and recrystallization (distillation) are tabulated in Table 24.

TABLE 24

The melting points of the secondary amides of table 7

Secondary Amide	m.p. (b.p.) (°C)	Literature m.p. (°C)	Reference
N-methylpropionamide	(92.5/8mm)	(146/90mm)	78
N-ethylacetamide	(91.5/8mm)	(98.5/14mm)	79
N-ethylpropionamide	(76-77/1mm)	(111/18mm)	80
N-isopropyl-2-methylpropionamide	106	102	81
N-t-butylacetamide	99.5-101	98	82
N-metyylpivalamide	92-93	91	83
N-t-butylpivalamide	120-121	-	-

N-Isopropyl-2-methylpropionamide was prepared by heating 2,4-dimethyl-3-pentanone oxime with thionyl chloride in ether solution. The solvent and volatile products were removed under reduced pressure, and water was added. Extraction and several recrystallizations (hexane) gave the pure amide.

Prior to their use as authentic samples, the purity of the oximes and secondary amides described above was shown by g.l.c. to be greater than 99%.

b) The Photolysis of the Acyclic Ketoximes

Photolysis of the oximes of Table 7 gave Beckmann-type products. These photo-products and the unreacted oximes were isolated in a pure state from the photolysis mixtures by preparative t.l.c. In all cases, they were shown to be identical to authentic samples. The R_f values of these compounds for the solvent system chloroform-ether-methanol (8:2:0.5) are listed in Table 25.

CHAPTER 5

a) The Preparation of the Oxaziranes

3-Methyl-3-ethyloxaziridine was prepared by dissolving 14.2 g (0.2 mole) of methylethylketone in a mixture of 350 ml of methylene chloride and 100 ml of 2N sodium hydroxide. The mixture was cooled to -10° by means of an ice-salt bath. Ice-cold solutions of 100 ml of 2N sodium hydroxide and of 200 ml of 1M hydroxylamine-O-sulphonic acid were simultaneously and rapidly added to the vigorously stirred

TABLE 25

The R_f values of the oximes and secondary amides of table 7

Starting oxime	R_f value	
	oxime	Secondary amide
acetone oxime	0.55	-
2-butanone oxime	0.61	0.36*
3-pentanone oxime	0.63	0.40
2,4-dimethyl-3-pentanone oxime	0.65	0.50
2,2-dimethyl-3-butanone oxime	0.68	0.43*
2,2-dimethyl-3-pentanone oxime	0.70	-
2,2,4,4-tetramethyl-3-pentanone oxime	0.72	0.56

*Both isomers appeared at the same R_f value

mixture. After stirring for 20 minutes, the organic layer was removed, washed successively with 2 x 50 ml of ice-cold water and an ice-cold solution of 0.35M hydroxylamine-O-sulphonic acid, and dried with anhydrous magnesium sulphate. The organic layer was concentrated under reduced pressure to 50 ml, the resulting solution being used as a stock solution of the oxazirane in subsequent experiments. The concentration of the solution was 0.4M as determined by iodometry, representing an overall yield of 10%.

Fractional distillation of the solution (25°/0.6 mm) gave the pure oxazirane after two distillations. The resulting liquid is a powerful lachrymator and very unstable. The compound could only be maintained at -78°. On warming to room temperature it underwent an exothermic decomposition. The infra-red, n.m.r. and ultra-violet spectra of the oxazirane have been described.

3,3-Pentamethyleneoxaziridine was similarly prepared except that ether was used as the organic solvent. The resulting stock solution was 0.8M (iodometric) representing an overall yield of 20%. The oxazirane could not be further purified.

3,3-[α-Methylpentamethylene]-oxaziridine was similarly prepared using ether as solvent. The stock solution was 0.4M representing an overall yield of 10%. The oxazirane could not be further purified.

Commercially available[11] hydroxylamine-O-sulphonic acid typically gave analyses indicating a purity of 50 - 60% (iodometric) and was unsuitable for the above preparations. Purification procedures described by Fieser (84) and Brown (85) resulted in samples of unreproducible purity. The pure salt was obtained using a method described by Matsuguma and Audrieth (86).

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[11] Eastman Chemical Company

b) Products of the Thermal Decompositions of the Oxaziranes

i) Thermal decomposition in water

Treatment of 3-methyl-3-ethyloxaziridine with water at 30° resulted in vigorous evolution of an odorless gas. Extraction of the water layer with methylene chloride gave a compound shown by its n.m.r. spectrum to be methylethylketone. Treatment of the ketone with 2,4-dinitrophenylhydrazine gave the hydrazone, m.p. 116°, lit. (49) m.p. 117°. The water layer was basic to litmus paper. Neutralization with p-toluenesulphonic acid and evaporation of the water gave a salt whose infra-red spectrum (KBr) was identical with that of an authentic sample of ammonium p-toluenesulphonate.

Treatment of 3,3-pentamethyleneoxaziridine under the same conditions gave cyclohexanone isolated as the 2,4-dinitrophenylhydrazone m.p. 161.5 - 163°, lit. (49) m.p. 162°. The water layer was basic and upon treatment with p-toluenesulphonic acid gave a salt identical to ammonium p-toluenesulphonate.

ii) Thermal decomposition in alcoholic solvents

The oxaziranes were thermally decomposed in alcoholic solvents by heating a solution of the oxazirane in either methanol or iso-propanol to reflux for 2 hours. The resulting solutions were concentrated by distillation to 10 ml for g.l.c. analysis or 1 ml for separation of the products by t.l.c.

Thermal decomposition of 3,3-pentamethyleneoxaziridine in methanol resulted in quantitative formation of

1,1-dimethoxycyclohexane. The ketal was identical with an authentic sample, b.p. 80°/45 mm, lit. (88) b.p. 80°/44 mm which was prepared in 75% yield by the method of Lorette and Howard (87).

Decomposition of the oxazirane in iso-propanol and injection of the resulting solution into the gas chromatograph gave two products different from cyclohexanone. In view of the known instability of the di-iso-propyl ketals (87) the two products are probably 1,1-di-iso-propylcyclohexane and 1-iso-propoxycyclohexene. Their identity was confirmed by treating cyclohexanone with p-toluenesulphonic acid in iso-propanol and injecting the resulting solution into the gas chromatograph. Under these "ketalization" conditions, two products different from cyclohexanone were formed. Their retention times were identical to those of the ketals resulting from the thermal decomposition of the oxazirane.

Decomposition of 3,3-[α-methylpentamethylene]-oxaziridine in either methanol or iso-propanol gave only 2-methylcyclohexanone oxime which was identical in all respects with an authentic sample.

c) Photochemical Decompositions of the Oxaziranes

Photolysis of 3,3-pentamethyleneoxaziridine in methanol gave caprolactam as the major product and some caproamide. The photoproducts were separated by preparative t.l.c. and shown to be identical to authentic samples.

Photolysis of the oxazirane in iso-propanol gave caproamide as the major product and some caprolactam.

Photolysis of 3,3-[α-methylpentamethylene]-oxaziridine in either methanol or iso-propanol gave only 2-methylcyclohexanone oxime which was identical with an authentic sample.

d) Reaction Rates of the Thermal and Photo Decompositions of the Oxaziranes

The reaction rates were determined by measuring the concentration of unreacted oxazirane at various time intervals. The following procedure was used in all cases:

A solution of the oxazirane (100 ml) was made up in the concentration range of 0.02 molar to 0.03 molar. At various time intervals, 10 ml aliquots were added to a vigorously stirred solution of 1 g of potassium iodide in 20 ml of 2N sulphuric acid. The liberated iodine was titrated with N/10 sodium thiosulphate (1 ml = .05 milliequivalents of oxazirane) to the starch end-point. Except where specified, the decompositions were carried out at a temperature of 45°, the operating temperature of the photolysis reactor.

e) An Attempt to Trap the Oxazirane Intermediate

An authentic sample of dodecanediamide was prepared by treating dodecanedioc acid (89) in methylene chloride solution with thionyl chloride followed by cautious addition of ammonia.

The resulting amide (1 g) was chromatographed on activity I alumina (30 g), the eluant being changed in a stepwise manner from ethyl acetate to methanol. The pure amide was eluted from the column when the gradient reached 16%

methanol in ethyl acetate.

3,3-Pentamethyleneoxaziridine (about 1 g) was added to a vigorously stirred solution of ferrous sulphate (3.4 g) in 2N sulphuric acid (6 ml). After stirring 2 hours, the mixture was neutralized with 2N sodium hydroxide and the mixture taken to dryness on a steam bath. Dry ethanol (300 ml) was then added, the mixture heated to reflux 3 hours and the hot solution was filtered. The filtrate was taken to dryness and the residue chromatographed on activity I alumina. Dodecanediamide (0.6 g) eluted from the column when the gradient reached 16% methanol in ethyl acetate. The isolated amide was identical in all respects with the authentic sample.

Photolysis of cyclohexanone oxime (1.13 g) for 60 hours in a solution of ferrous sulphate (3.4 g) and 2N sulphuric acid (6 ml) in 500 ml of water gave a product which was isolated in a manner identical with that described above. The major product was shown by g.l.c. and n.m.r. to be caprolactam. Chromatography of the product on activity I alumina (30 g) gave an oil (2.5% by weight of oxime) when the gradient reached 16% methanol in ethyl acetate. Little, if any, of the diamide was present in the photolysis mixture.

CHAPTER 6

a) Imines as the Intermediates in the Ketal Forming Reaction

A mixture of calcium carbide (1.4 g) and cyclohexanone (1 g) in methanol (50 ml) was treated with gaseous ammonia for 15 minutes. After stirring overnight, the mixture was filtered then heated to reflux for 30 minutes. A sample of the solution was injected into the gas chromatograph. A peak, identical in retention time to that of 1,1-dimethoxycyclohexane, was eluted.

REFERENCES

1.a. G. Ciamician and P. Silber, Ber., 36, 4266 (1903).

b. R. Stoermer, Ber., 44, 637 (1911).

c. O.L. Brady and F.P. Dunn, J. Chem. Soc., 103, 1619 (1913).

d. O.L. Brady and G.P. McHugh, J. Chem. Soc., 125, 547 (1924).

2.a. H. Amin and P. de Mayo, Tetrahedron Letters, 1585 (1963).

b. H. Izawa, P. de Mayo and T. Tabata, Canad. J. Chem., 47, 51 (1969).

3.a. L. Chardonnes and P. Hendrick, Helv. Chim. Acta, 32, 656 (1949).

b. J. Laudgest, J. Chem. Soc., 2830 (1953).

c. M.J. Kamlet and L.A. Kaplan, J. Org. Chem., 22, 576 (1957).

d. F. Kröhnke, Ann., 604, 203 (1957).

e. J.S. Splitter and M. Calvin , J. Org. Chem., 23, 651 (1958).

f. R. Bonnett, V.M. Clark and A. Todd, J. Chem. Soc., 2102 (1959).

g. J. Hamer and A. Macaluso, Chem. Rev., 64, 473 (1964).

h. J.S. Splitter and M. Calvin, J. Org. Chem., 30, 3427 (1965).

i. L. Kaminsky and M. Lamchen, Chem. Commun., 130 (1965).

4. R.O. Kan, Organic Photochemistry, McGraw-Hill Book Co., New York and London, p. 149 (1966).

5. G. Just and C. Pace-Asciak, Tetrahedron Letters, 1069 (1966).

6. R. Taylor, M. Douek and G. Just, Tetrahedron Letters, 4143 (1966).

7.a. T. Sato and H. Obase, Tetrahedron Letters, 1633 (1967).
   b. L.S. Ng, Ph.D. Thesis, McGill University, Montreal, Canada, p. 110 (1968).
   c. M. Cunningham, M.Sc. Thesis, McGill University, Montreal, Canada, p. 17 (1969).
   d. G. Just and L.S. Ng, Canad. J. Chem., <u>46</u>, 3381 (1968).
   e. T. Oine and T. Mukai, Tetrahedron Letters, 157 (1969).
   f. J.-P. Vermes and R. Beugelmans, Tetrahedron Letters, 2091 (1969).
   g. B.L. Fox and H. Rosenberg, Chem. Commun., 1115 (1969).

8.a. R.O. Kan, <u>Organic Photochemistry</u>, McGraw-Hill Book Co., New York and London, p. 79 (1966).
   b. L.S. Ng, Ph.D. Thesis, McGill University, Montreal, Canada, p. 16 (1968).
   c. D. Setser et al., Canad. J. Chem., <u>40</u>, 2179 (1962).
   d. H.S. Johnson and J. Heicklen, J. Am. Chem. Soc., <u>86</u>, 4249, 4255 (1964).

9. J. Kenyon and D. Young, J. Chem. Soc., 264 (1941).

10.a. German Patent, 973, 677, August 6 (1955).
   b. British Patent, 788, 436, July 26 (1956).
   c. German Patent, 1, 079, 036, May 30 (1958).
   d. German Patent, 1, 001, 983, August 9 (1955).
   e. British Patent, 789, 732, August 8 (1956).
   f. French Patent, 1, 337, 512, August 21 (1962).

11. L.S. Ng, Ph.D. Thesis, McGill University, Montreal, Canada, p. 13 (1968).

12.a. J. Calvert and J. Pitts, Jr., <u>Photochemistry</u>, John Wiley and Sons, Inc., New York, London and Sydney, p. 377-427, 532-536 (1966).

b. R.O. Kan, Organic Photochemistry, McGraw-Hill Book Co., New York and London, p. 71-93 (1966).

c. N.J. Turro, Molecular Photochemistry, W.A. Benjamin, Inc., New York and Amsterdam, p. 154-156 (1965).

13. L.S. Ng, Ph.D. Thesis, McGill University, Montreal, Canada, p. 16 (1968).

14. M. Douek, Ph.D. Thesis, McGill University, Montreal, Canada, p. 50 (1966).

15. ibid, p. 55.

16. M.B. Evans and J.F. Smith, J. Chromatog., 36, 489 (1968).

17. L.S. Ng, Ph.D. Thesis, McGill University, Montreal, Canada, p. 90 (1968).

18. L. Donuruma and W. Heldt, "The Beckmann rearrangement," in Organic Reactions, ed. R. Adams, John Wiley and Sons, Inc., New York and London, Vol. 11, p. 1 (1960).

19. L.S. Ng, Ph.D. Thesis, McGill University, Montreal, Canada, p. 98 (1968).

20.a. O.H. Wheeler and J.Z. Zabicky, Canad. J. Chem., 36, 656 (1958).

b. E. Eliel, N. Allinger, S. Angyal and G. Morrison, Conformational Analysis, Interscience Publishers, New York, London and Sydney, p. 51-2 (1965).

21. E. Eliel, Stereochemistry of Carbon Compounds, McGraw-Hill Book Company, New York, San Francisco, Toronto, London, p. 189 (1962).

22.a. M. Vinnik and N. Zarakhani, Russ. Chem. Revs., **36**, 51 (1967).

b. C. McCarty in *The Chemistry of the Carbon-Nitrogen Double Bond*, ed. Saul Patai, Interscience Publishers, New York, p. 435 (1970).

c. P. Smith in *Molecular Rearrangements*, Part I, ed. Paul de Mayo, Interscience Publishers, New York, p. 483 (1963).

23. E. Eliel, *Stereochemistry of Carbon Compounds*, McGraw-Hill Book Company, New York, San Francisco, Toronto, London, p. 189 (1962).

24. ibid p. 266-7.

25. ibid, p. 197.

26. K.S. Pitzer, J. Am. Chem. Soc., **70**, 2140, (1948).

27. E. Eliel, *Stereochemistry of Carbon Compounds*, McGraw-Hill Book Company, New York, San Francisco, Toronto, London, p. 381 (1962).

28. J. Kenyon and D. Young, J. Chem. Soc., Part I, 263 (1941).

29. D. Pearson and O. Keaton, J. Org. Chem., **28**, 1557 (1963).

30.a. E. Schmitz, R. Ohme and D. Murawski, Angew. Chem., **73**, 708 (1961).

b. E. Schmitz, R. Ohme and S. Schramm, Chem. Ber., **97**, 2521 (1964).

c. E. Schmitz and D. Murawski, Chem. Ber., **98**, 2525 (1965).

31. M. Schutz, A. Rieche and D. Becker, Chem. Ber., **99**, 3233 (1966).

32. W.L. Howard and N.B. Lorette, J. Org. Chem. **25**, 525 (1960).

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

34.a. E. Schmitz and R. Ohme, Angew. Chem. Internat. Ed., 2, 157 (1963).

b. E. Schmitz and R. Ohme, Ber. 97, 2521 (1964).

35. R.O. Kan, Organic Photochemistry, McGraw-Hill Book Co., New York and London, p. 11 (1966).

36. N.J. Turro, Molecular Photochemistry, W.A. Benjamin, Inc., New York and Amsterdam, p. 19 (1965).

37.a. E. Meyer and G.W. Griffin, Angew. Chem., 79, 648 (1967).

b. J.S. Splitter and M. Calvin, Tetrahedron Letters, 1445 (1968).

c. H. Shindo and B. Umezawa, Chem. Pharm. Bull. (Tokyo), 10, 492 (1962).

38. C. David Gutsche, The Chemistry of Carbonyl Compounds, Prentice-Hall, Inc., Englewood Cliffs, N.J. p. 52 (1967).

39. W.P. Jencks, Catalysis in Chemistry and Enzymology, McGraw-Hill Book Company, New York, p. 490-2 (1969).

40. N.J. Turro, Molecular Photochemistry, W.A. Benjamin, Inc., New York and Amsterdam, p. 81 (1969).

41. ibid, p. 66.

42. ibid, p. 28-29.

43. J.R. Dyer, Applications of Absorption Spectroscopy of Organic Compounds, Prentice-Hall, Inc., Englewood Cliffs, N.J., p. 8 (1965).

44. N.J. Turro, Molecular Photochemistry, W.A. Benjamin, Inc., New York and Amsterdam, p. 93-96 (1969).

45. P. Best, J. Lettler and W. Waters, J. Chem. Soc., Part I, 822 (1962).

46. W. Johnson and S. Posvic, J. Am. Chem. Soc., 69, 1361 (1949).

47. K. Dahl, Ph.D. Thesis, McGill University, Montreal, Canada, (1966).

48. R. Shriner, R. Fuson and D. Curtin, The Systematic Identification of Organic Compounds, 5th Edition, John Wiley and Sons, Inc., New York, London and Sydney, p. 290 (1964).

49. ibid, p. 362.

50. I. Heilbron, ed., Dictionary of Organic Compounds, Eyre and Spottiswood Publishers, London, Vol. 2, p. 1163 (1965).

51. ibid, Vol. 5, p. 3166.

52. Beilstein, III, 7, 163.

53 ibid

54. ibid, I, 2, 242.

55. M. Douek, Ph.D. Thesis, McGill University, Montreal, Canada, p. 54 (1966).

56. I. Heilbron, ed. , Dictionary of Organic Compounds, Eyre and Spottiswood Publishers, London, Vol. 2,p. 772 (1965).

57. L. Ruzicka et al, Helv. Chim. Acta, 32, 544 (1949).

58. R. Shriner, R. Fuson and D. Curtin, The Systematic Identification of Organic Compounds, 5th Edition, John Wiley and Sons, Inc., New York, London and Sydney, p. 309 (1964).

59. I. Heilbron, ed., Dictionary of Organic Compounds, Eyre and Spottiswood Publishers, London, Vol. 4, p. 2561 (1949).

60. R. Shriner, R. Fuson and D. Curtin, The Systematic Identification of Organic Compounds, 5th Edition, John Wiley and Sons, Inc., New York, London and Sydney, p. 312 (1964).

61. I. Heilbron, ed., Dictionary of Organic Compounds, Eyre and Spottiswood Publishers, London, Vol. 3, p. 1319 (1965).

62. ibid, Vol. 4, p. 2619.

63. W. Harris and H. Habgood, Programmed Temperature Gas Chromatography, John Wiley and Sons, Inc., New York, etc., p. 142 (1966).

64. L. Ettre and A. Zlatkis, The Practice of Gas Chromatography, Interscience Publishers, New York, p. 397 (1967).

65. N.C. Brown and C.P. Garg, J. Am. Chem. Soc., 83, 2952 (1961).

66. I.C. Nigain and L. Levi, Anal. Chem., 35, 1087 (1963).

67. Beilstein, II, 7, 42.

68. ibid, 43.

69. ibid, III, 7, 92.

70. ibid, II, 21, 222.

71. ibid, 223.

72. E. Dubois et al., Bull. Soc. Chim., 2024 (1964).

73. I. Heilbron, ed., Dictionary of Organic Compounds, Eyre and Spottiswood Publishers, London, Vol. 5, p. 3025 (1949).

74. ibid, Vol. 1, p. 505.

75. ibid, Vol. 4, p. 2632.

76. ibid, Vol. 5, p. 3155.

77. ibid, Vol 2, p. 1205.

78. Beilstein, III, 4, 126.

79. ibid, 208.

80. ibid, 210.

81. ibid, I, 4, 154.

82. ibid, III, 4, 324.

83. ibid, 59.

84. L. Fieser and M. Fieser, Reagents for Organic Synthesis, John Wiley and Sons, Inc., New York, p. 481 (1967).

85. M. Rathke, N. Inoue, K. Varma and H.C. Brown, J. Am. Chem. Soc., 88, 2870 (1966).

86. H.J. Matsuguma and L.F. Audrieth, Inorganic Synthesis, 5, 122 (1970).

87. N.B. Lorette and W.L. Howard, J. Org. Chem., 25, 521 (1960).

88. British Patent, 876, 335; Chem. Abstracts, 56, 4622f.

CONTRIBUTIONS TO KNOWLEDGE

1. The formation of Beckmann-type products has been shown to be a rather general photoreaction of cyclic and acyclic ketoximes.
2. The photolysis of unsymmetrically α-substituted cyclohexanone oximes has been shown to result in the formation of both possible lactam isomers in approximately 1:1 ratio.
3. The photolysis of several highly α-substituted and ring strained oximes has been shown to result in the formation of Beckmann-type products in good yield.
4. The photolysis of oximes epimeric at the α-center has been shown to yield lactams in which the α-center has maintained its configuration.
5. On the basis of these results, the photo-Beckmann reaction has been proposed to extend the usefulness of the classical Beckmann rearrangement. Unlike the classical reaction, the photoreaction is relatively unaffected by α-substitution and strain and does not suffer the occasional breakdown of retention of configuration observed in the classical reaction. Furthermore, both lactam isomers can be isolated from the reaction of unsymmetrically α-substituted oximes whereas only one isomer is obtained by the classical Beckmann rearrangement. Conditions for the separation of the lactam isomers have been described. The yields of the lactams from cyclic ketoximes have been shown to be relatively insensitive to ring size in contrast to the classical Beckmann reaction.

6. A comprehensive mechanism for the photoreaction of oximes in alcoholic solvents has been offered. Oxaziranes have been suggested as the reactive intermediate and considerable supporting evidence has been presented.
7. It has been shown that oxazirane formation is rate determining; the subsequent reactions of the oxazirane are very rapid.
8. Contrary to previous opinion, the oxazirane has been demonstrated to be present in very low, steady-state concentrations during oxime photolysis. It has been shown that the observed oxidizing power of irradiated solutions of cyclohexanone oxime is not due to oxaziranes.
9. Oxaziranes have been prepared and shown capable of undergoing both thermal and photochemical decompositions. It has been demonstrated that under the photolysis conditions the oxazirane undergoes photodecomposition exclusively.
10. It has been shown that photolysis of the oxazirane of cyclohexanone gives the same products as photolysis of cyclohexanone oxime. It has been shown that the oxazirane of 2-methylcyclohexanone rearranges thermally to 2-methylcyclohexanone oxime when dissolved in protic solvents.
11. Thermal decomposition of the oxazirane of cyclohexanone has been shown to result in ketal formation. Ketal formation has been shown to be derived from an imine. The rate of thermal decomposition has been shown to be strongly dependent on the dielectric constant of the medium.
12. The anomolous effect of oxygen on the photoreaction in

methanol has been suggested to be due to quenching of the oxazirane triplet. Evidence that the efficiency of intersystem crossing to this triplet is solvent dependent has been presented.

13. The photolysis of oximes epimeric at the α-center has been shown to result in slow epimerization of the oxime. Evidence that the epimerization results from a triplet has been presented.
14. A temperature effect on the photoreaction has been observed.
15. A base catalyzed ketalization preceding via an imine has been described.
16. A method for the preparation of oximes of highly hindered ketones has been described.