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PHOTOCHEMICAL AND THERMAL REACTIONS OF SOME HETEROCYCLES CONTAINING C=N-O OR N=C-O GROUP

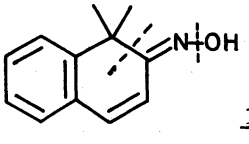
Toshio Mukai, Tsutomu Kumagai, and Osamu Seshimoto

Department of Chemistry, Faculty of Science, Tohoku University, Aramaki, Aoba, Sendai 980 Japan

Abstract - In connection with photochemistry of the non-constrained Ph-C=N-O system, those of several 2-isoxazoline derivatives containing cyclobutene, cyclobutane, cyclopropane and cyclohexane rings, have been investigated as the models of the rigid and constrained Ph-C=N-O system. In most cases, such 2-isoxazolines, upon irradiation, underwent the nitrogen-oxygen bond fission as the primary process, and produced a variety of products depending on the structures of the starting materials. For instance, the irradiation of 4-aryl-2-oxa-3-azabicyclo[3.2.0]hepta-3,6-dienes afforded 2-aryl-1,3-oxazepines, sometimes accompanied by pyrrole aldehydes, whereas 2-isoxazolines fused with small ring yielded β-aminoaldehydes, oxazolines, azirine aldehydes, and small fragments such as benzonitrile. The photochemical reaction mechanisms of several 2-isoxazolines have been studied using low-temperature technique. In addition, the pyrolytic reactions of 4-phenyl-2-oxa-3-azabicyclo[3.2.0]heptadiene and 1,3-oxazepines as well as their valence isomers have been examined to compare with their photochemical behavior. It was found that in pyrolysis of bicyclo[3.2.0]heptadiene derivatives containing the C=N-O or N=C-O group, the cyclobutene ring fission occurs prior to the nitrogen-oxygen or carbon-oxygen bond cleavage. Reaction mechanisms for the deep-seated rearrangements of the 1,3-oxazepines and of 2-oxa-3-azabicyclo[3.2.0]hepta-3,6-dienes to pyrrole aldehydes were discussed. The results indicate the major differences in the chemical behaviors of the photolytically and thermally excited states for those heterocycles.

INTRODUCTION AND HISTORICAL BACKGROUND OF OUR STUDIES

Several years after the de Mayo's first publication on photochemical Beckmann rearrangement (ref. 1), we started our studies on imine compounds photolysis which was little known compared to that of carbonyl compounds at that time. At first, we investigated the photoreaction of 1,1-dimethyl-2-naphthalenone oxime (1) (ref. 2) expecting to observe a photo-α-cleavage reaction mechanistically similar to the Type I cleavage reaction of carbonyl compounds. Contrary to our expectation, we noted good evidence for the formation of an oxaziridine intermediate which had been suggested (ref. 1) and subsequently proved (ref.3) by de Mayo as an intermediate in the photo-Beckmann rearrangement. Fortunately, the oxaziridines from (1) and styrylketone oxime (2) were relatively stable at room temperature. This enabled us to examine the photoreaction of (3) in detail, thus leading to the sequence outlined in Scheme 1. As the results, the complex photoreactions of oximes were clarified (ref. 4).



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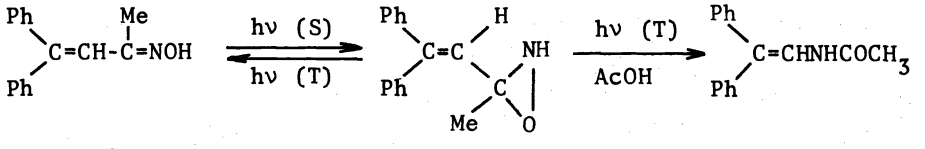
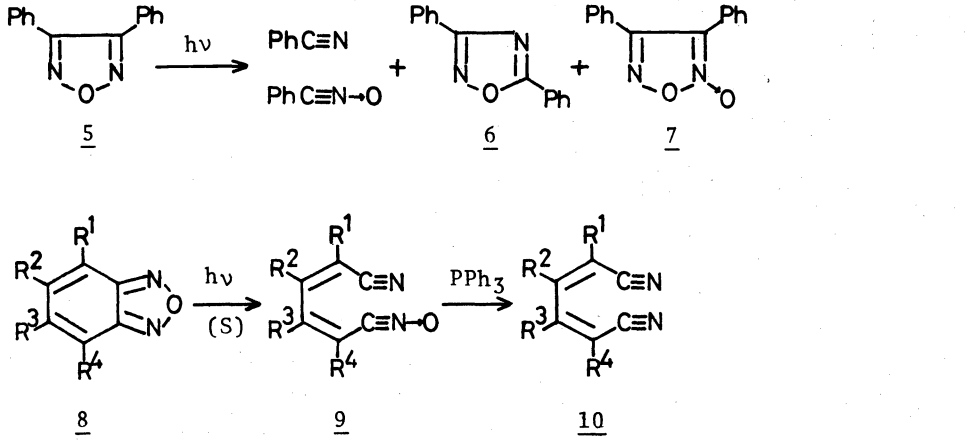


2 3 4

Scheme 1

Our effort was then extended to cover photochemistry of α-dioximes and furazan (5). Independently from Cantrell's study (ref. 6), we found a double cleavage-recombination reaction giving oxadiazole (6) and furazan oxide (7) (ref. 5). In addition, we pointed out the dual property of benzonitrile oxide formed during irradiation (ref. 7). Another intriguing example of the double cleavage reaction was the photoreaction of benzo- (8) and naphthofurazan wherein complicated products were formed presumably arising from highly reactive intermediate (9) (ref. 8). However, if an oxygen acceptor was present, 1,3-butadiene-1,4-dinitriles (10) were obtained in excellent yields (ref. 9). It was also suggested that the addition reactions of various substrates such as, unsaturated compounds, alcohols or amines, to (9) might provide a novel synthetic approach for nitrile derivatives having phenyl or vinyl group (ref. 10). The photochemistry of heterocycles (5) and (8) stimulate our interest in photochemical behavior of a constrained C=N-O system, and led us to examine photolysis of 2-isoxazoline fused with a cyclobutene ring. Before our study, we learned that certain 2-isoxazolines, upon irradiation, could undergo the nitrogen-oxygen bond fission (ref. 11). On the other hand, the Padwa's elegant study revealed that, for O-methyl ethers of acetophenone oxime, the syn-anti isomerization along with non-radiative decay provided the major route for deactivation of the excited state without any bond fission (ref. 12). Recently, several papers on the photoreaction of 3-phenyl-2-isoxazoline derivatives (ref. 13, 14, 15, 16, & 17) were published and clearly pointed out that various type of cleavage reactions, in addition to the nitrogen-oxygen bond fission, could occur depending on the substituents. Such a sharp contrast in photochemical behavior between open



5 6 7

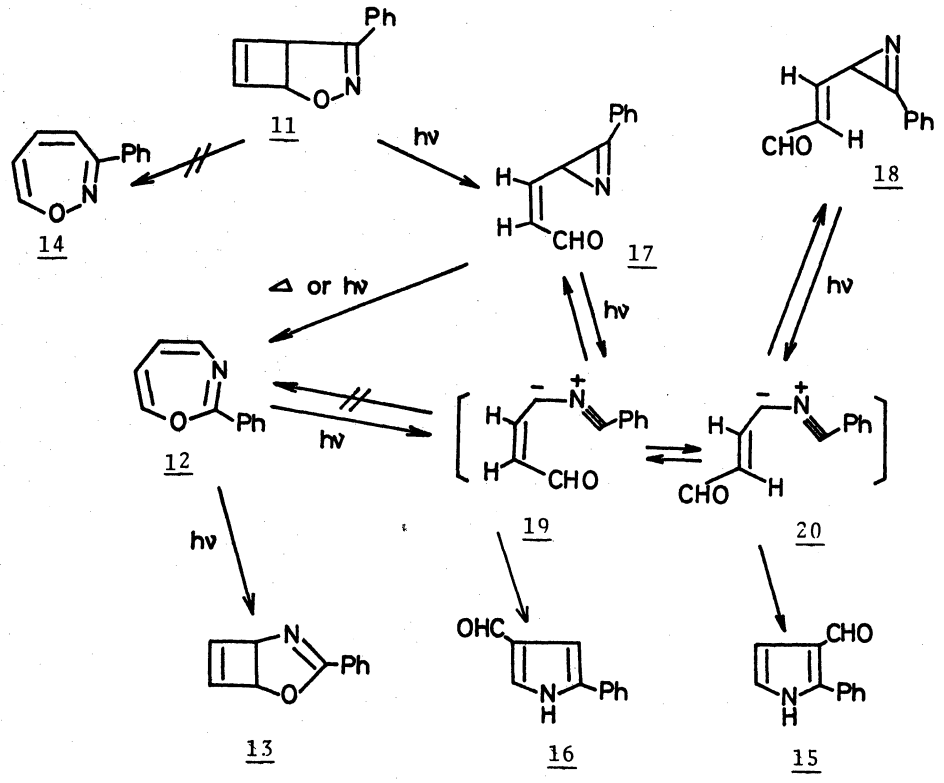
8 9 10

Scheme 2

and cyclic phenyl ketoxime systems reminds us of inherent difference in the behavior of simple and constrained imines (ref. 18). In addition, we have noticed that some 2-isoxazolines, upon heating, also underwent nitrogen-oxygen bond fission; the facility and extent of the decomposition and the subsequent reactions seemed somewhat different from those in the photolysis (ref. 19). A comparison of these two reactions is expected to afford informations about the electronically and vibrationally excited states. From these standpoints, we have studied the thermal reactions of 4-phenyl-2-oxa-3-azabicyclo[3.2.0]hepta-3,6-diene (11) and 2-phenyl-1,3-oxazepine (12) and its valence isomer (13).

PHOTOCHEMICAL REACTIONS OF 4-ARYL-2-OXA-3-AZABICYCLO[3.2.0]-HEPTA-3,6-DIENES

The theory of orbital symmetry control predicts that a cyclobutene should open the ring in the disrotatory fashion by photochemical process. However, such reactions induced by light are scarcely known in the bicyclo[3.2.0]hepta-3,6-diene system (ref. 20), probably due to lack of a suitable chromophore. In contrast, there are a number of examples of the thermally induced ring opening leading to the corresponding cycloheptatriene system, although, in general, it requires considerably higher temperatures. For instance, Streith et al. found that 2-isopropoxycarbonyl-2,3-diazabicyclo[3.2.0]heptadiene, on heating at 170°, yielded 1-isopropoxycarbonyl-1,2-diazepine in a quantitative yield (ref. 21). Thus, our attempted synthesis of 3-phenyl-1,2-oxazepine (14) (ref. 22) by photolysis of 4-phenyl-2-oxa-3-azabicyclo[3.2.0]heptadiene (11) was unsuccessful. Irradiation of a solution of (11) in n-hexane with light of 254nm initiates a clean reaction to give unexpected 2-phenyl-1,3-oxazepine (12) in 80% yield. Sensitization and quenching experiments indicate that the photoreaction proceeds via a singlet state without any noticeable solvent effect (ref. 14). However, on prolonged photolysis of (11) using light of >290 nm, the yields of (12) decrease and 3-phenyl-2-oxa-4-azabicyclo[3.2.0]hepta-diene (13) and two aldehydes (15) and (16) are obtained in 24 and 7% yields, respectively (ref. 23). Under the same conditions, irradiation of (12) gives (13) and (16) in 50 and 10% yields.



Scheme 3

In order to identify the precursor leading to (12), the change of the uv spectrum of (11) is monitored, as shown in Fig. 1. Curve a is the uv spectrum of (11) and curve b that after irradiation with light of 268 - 272nm for a short time where only 17% of (11) has been converted to intermediate (A) having max at 266nm, and curve c that after heating of b at 80°. It is apparent that curve c is a summation of curve a and d, the latter being due to (12). These changes show the exsistence of intermediate (A) which is thermally converted to (12). Fig. 2 shows the absorption spectrum of (11) and the emission spectra of (11), E-3-(3-phenylazirin-2-yl)acrolein (18) and intermediate (A). The remarkable resemblance between the fluorescence spectrum of (A) and that of (18) strongly suggests that (A) is the Z-isomer (17). It should be added that 2-phenyl-1,3-oxazepine (12) exhibits neither fluorescence nor phosphorescence at all.

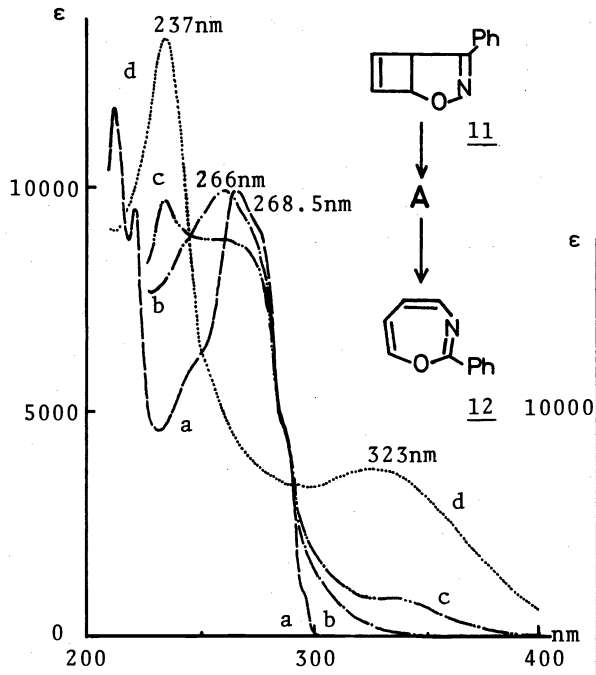


Fig. 1 Sequential changes in the uv spectrum of (11) after irradiation and followed by subsequent heating

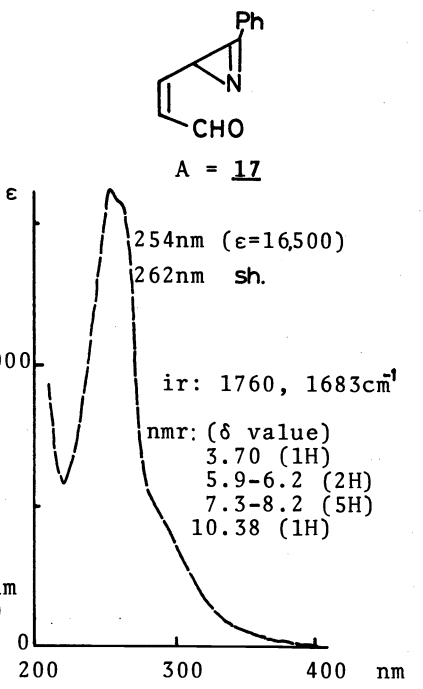


Fig. 1-a Spectral data of (17)

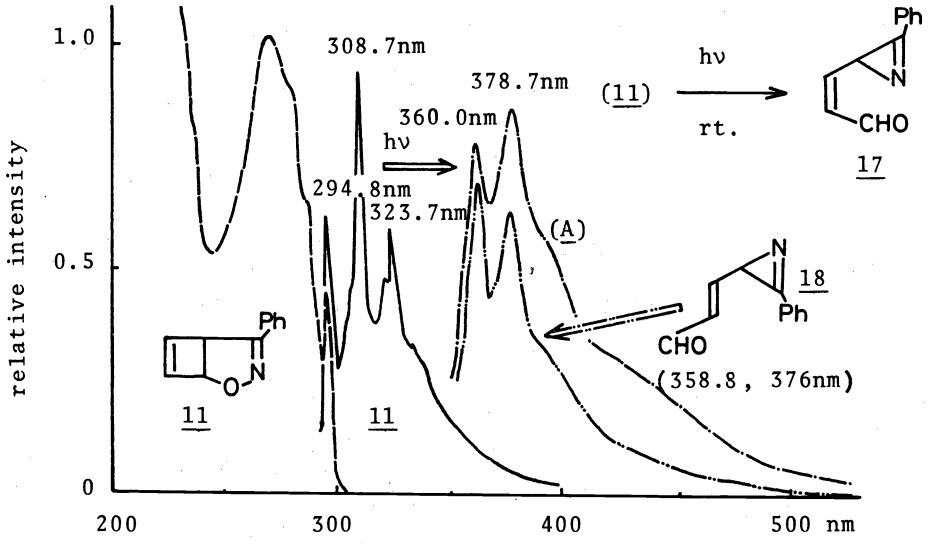


Fig. 2 Fluorescence spectra of (11), intermediate (A), and (18) which are measured in methylcylohexane at -196°.

Subsequently the intermediate (A) have been isolated as a labile oil in a 12% yield and been identified as Z-3-(3-phenylazirin-2-yl)acrolein (17) from its spectral data (see Fig. 1-a) and chemical evidence. Upon heating at 40-50° or irradiation with light of 300nm, (17) produces 2-phenyl-1,3-oxazepine (12) in excellent yields. Although another example of the thermal transformation

of Z-azirinylacrolein into 1,3-oxazepine was also discovered recently by Le Roux (ref. 24), we have observed in addition a temperature effect in the photochemical transformation of (11) to (12). The results are summarized in Table 1. While irradiation of (11) at -78° or -196° gives no 1,3-oxazepine (12), the yields of (12) increase as the temperature is raised. The evidence substantiates that a thermal process intervenes in the path from (11) to (17) and from (17) to (12).

TABLE 1. Temperature effect on the photoreaction of (11)[a]

Temperature (°C)	-196	-78	3	25	50	70
Yields of (12) (%)[b]	0	0	24.3	38.3	54.7	63.2
Yields of (17) (%)[c]	trace	10	7	2	----	----

a) 2.9 x 10^{-3}M in methylcyclohexane, 1 hr irradiation with 270-290nm.
b) yields determined by vpc.
c) by uv spectroscopy.

When a solution of (11) is irradiated with light of 255-280nm at -196°, the photolysate turns deep yellow and exhibits the uv maxima at 390 and 480nm (see Fig 3). Various structures such as 1,2-oxazepine (14), nitrile ylide (19) or (20), the nitrogen-oxygen bond cleaved species (21) can be suspected for this species. For comparison, the uv spectrum of (18) is measured under the same condition, and the spectrum having maximum at 390nm is obtained (see Fig. 3). This spectrum should be attributed to nitrile ylide (20) on the basis of Schmid's finding that photochemical equilibrium between azirines

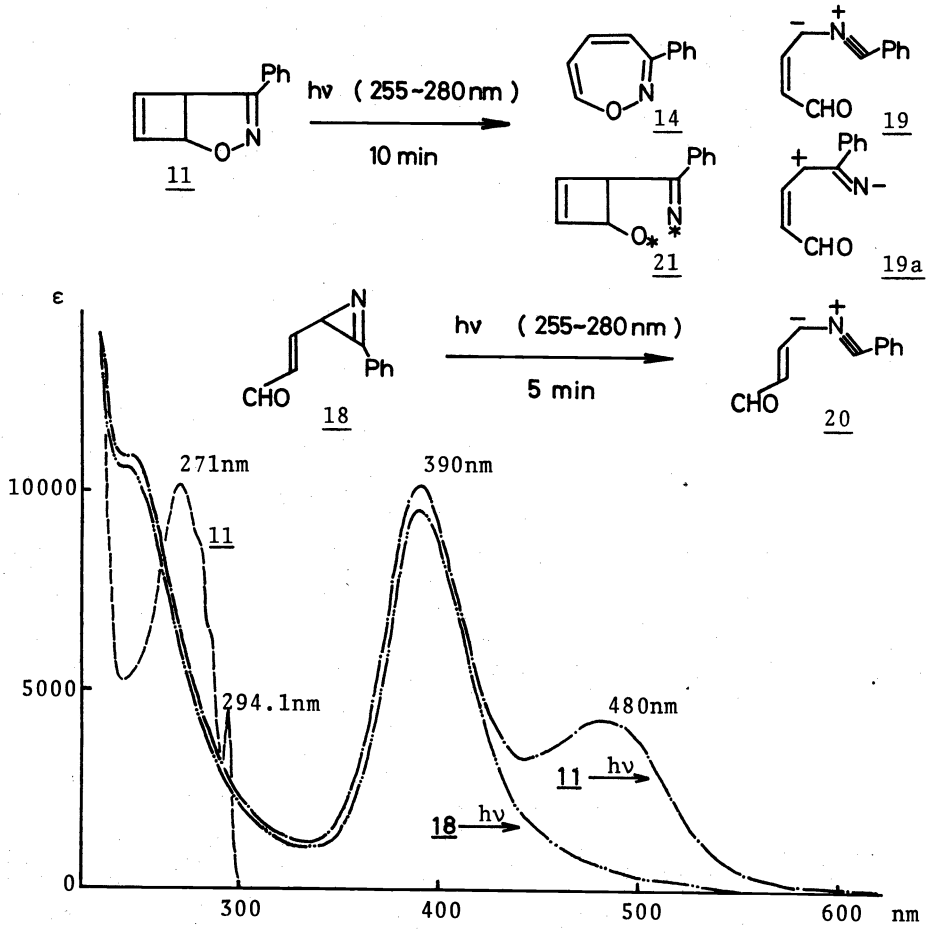
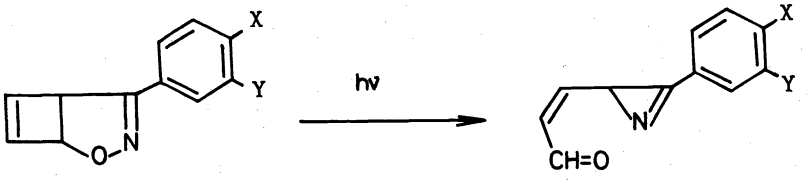


Fig. 3 Uv spectra of the irradiated samples of (11) and (18) at -196°

and nitrile ylides exists at low temperatures (ref. 25). Although it seems difficult how illustrate the maximum at 480nm, the ylide structure (19) or (20) could be assigned to the irradiated species of (11). The low temperature ir spectrum of the irradiated sample of (11) exhibits the absorption at 2230cm^{-1}, suggesting the presence of the nitrile ylide. However, there is no evidence to indicate that ylide (19) or (20) leads to 1,3-oxazepine (12). The reaction paths leading to pyrrole aldehydes (15) and (16) from (11) or (12) are still shrouded in ambiguity, but are suggested to occur by the pathway (17) or (18) → (19) or (20) → (15) and (16) in view of the Padwa's finding that E-azirinylacrolein (18), upon irradiation, converts to (15) via ylide (20) (ref. 26). It is further demonstrated by us that if the irradiation of (18) is carried out in benzene, not only 59% of (15) but also 17% of pyrrole 4-aldehyde (16) are formed. The formation of (16) is not quite straightforward, but can be accommodated by the pathway involving an internal crossed 1,3-dipolar addition in the nitrile ylide (19), as well as the photo-transformation of (12) to (19). The photochemical conversion of (15) to (16) is ruled out by the controlled experiment performed under the same condition (ref. 27). The plausible paths for the formation of (12), (15), and (16) starting from (11) are summarized in Scheme 3.

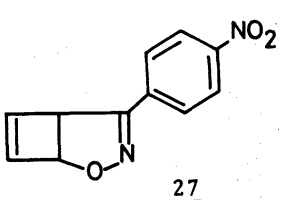
Subsequently the photochemistry of 4-aryl-2-oxa-3-azabicyclo[3.2.0]heptadienes carrying a substituent in the 4-aryl group is investigated. This corresponds to an investigation on the substituent effect on the Ph-C=N-O chromophore. The results are summarized in Table 2 together with the quantum yields. The quantum yields are determined by measuring uv spectra of the 1,3-oxazepines formed after heating the irradiated solution on our observation that such a thermal treatment converts the intermediate, 3-aryl-2H-azirinylacroleins to the 1,3-oxazepines quantitatively. Most of the compounds that can give the 1,3-oxazepines exhibit fluorescence, and their O-O bands are also listed in Table 2.

TABLE 2. Substituent effect on the photoreaction of 2,3-oxazabicyclo[3.2.0]heptadienes



	Substituent (aryl)		Ouantum yield		O-O Band of emission (nm) (singlet energies in kcal/mol)	
No.	X	Y	Cyclo-hexane	CH_3CN	Methylcyclo-hexane (MCH)	Ether-Isopen-tane-EtOH (EPA)
(11)	H	H	0.78	0.79	294.8 (97.0)	295.8 (96.7)
(22)	Me	H	0.77	0.76	298.7 (95.7)	300.1 (95.3)
(23)	Cl	H	0.61	0.72	301.8 (94.7)	303.6 (94.2)
(24)	OMe	Cl	0.12	0.13	313.5 (91.2)	315.5 (90.6)
(25)	H	NO_2	----	0.01	-----	-----
(26)	CN	H	0.69	0.69	310.0 (92.2)	316.7 (90.3)

non reacting compounds



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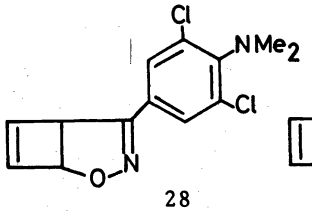

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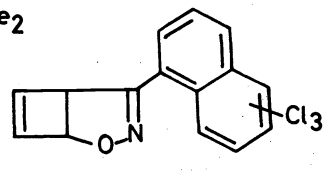

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There seems to be a general trend that an electron withdrawing group suppresses the photoreactions in the case of the substituted oximes (ref. 3). However such kind of electronic effect is not observed in this case. p-Cyano compound (26) undergoes efficient photoreaction, but (28) and (29) do not react under irradiation. While at present there is not enough data to predict the substituent effect in the reaction, there seems to be some relationship between the reactivity and the positions of the 0-0 bands of the fluorescence spectra (or absorption spectra). For example,trichloro-α-naphthyl derivative (29) which exhibits the 0-0 band at 347.2nm (Es=82.3 kcal/mol) does not react, while p-cyano derivative (26) having 0-0 band at 316.7nm (Es=90.3 kcal/mol, EPA) can react. It is speculated that those compounds which have their 0-0 bands in relatively shorter wavelength region (probably less 320nm) have a tendency to undergo photoreaction. No blue shift is observed in their emission spectra as a solvent changes from methylcyclohexane to EPA (ether-isopentane-ethanol). Thus the 0-0 bands might not be due to the n-π* or C-T excitation. Consequently photoreaction of these bicyclic heterocycles is considered to arise from the π-π* singlet state. It should be noted that there is no solvent effect in the photoreactions (see quantum yield in CH_3CN).

In order to learn more about the nature of the intermediates in the photoconversion of the 2,3-oxazabicyclo[3.2.0]heptadienes to the 1,3-oxazepines, we also have investigated the photoreaction of 3-phenyldihydrobenzocyclobutaisoxazole (30) (ref. 28), in which only Z-form azirine aldehyde can be formed. When irradiation of (30) in cyclohexane with light of 268-272nm is followed by uv spectroscopy, a set of isosbestic points is recorded (see Fig. 4); curve a is the uv spectrum of (30) and b that of o-(3-phenyl-2H-azirinyl)-benzaldehyde (31). Although the photoconversion of (30) to (31) is clean, the preparative scale photoreaction results in the complex products from which (31) is obtained in 26% yield. The photochemical and thermal reactions of (31) are not simple and require further investigations. Separate irradiation of either (30) or (31) at -196° affords ylide (32), and the spectra are shown in Fig. 5. Rate of the formation of (32) from (30) is slower than that from (31), and much slower than that of (19) from (11) (see Fig. 3)

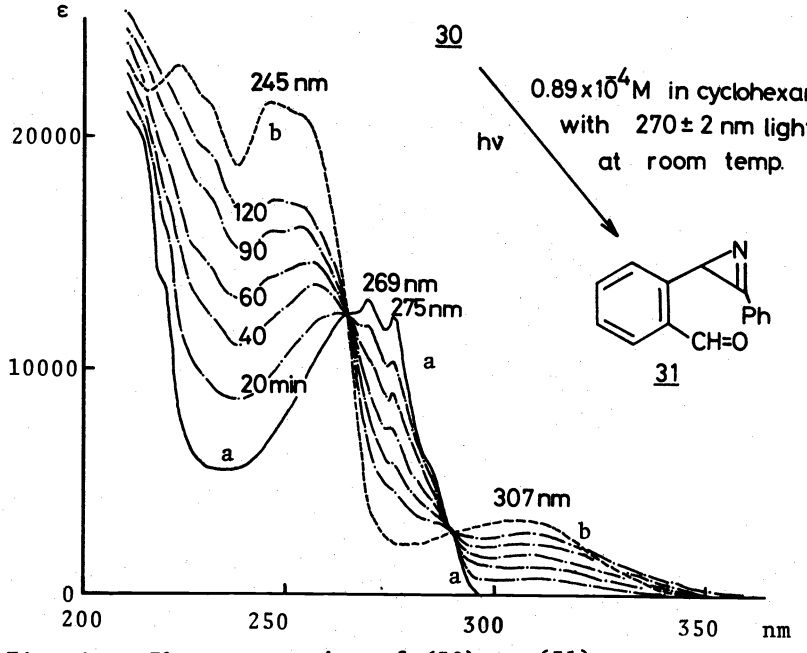
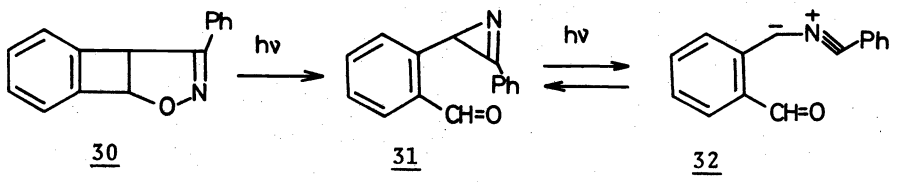


Fig. 4 Photoconversion of (30) to (31)



Scheme 4

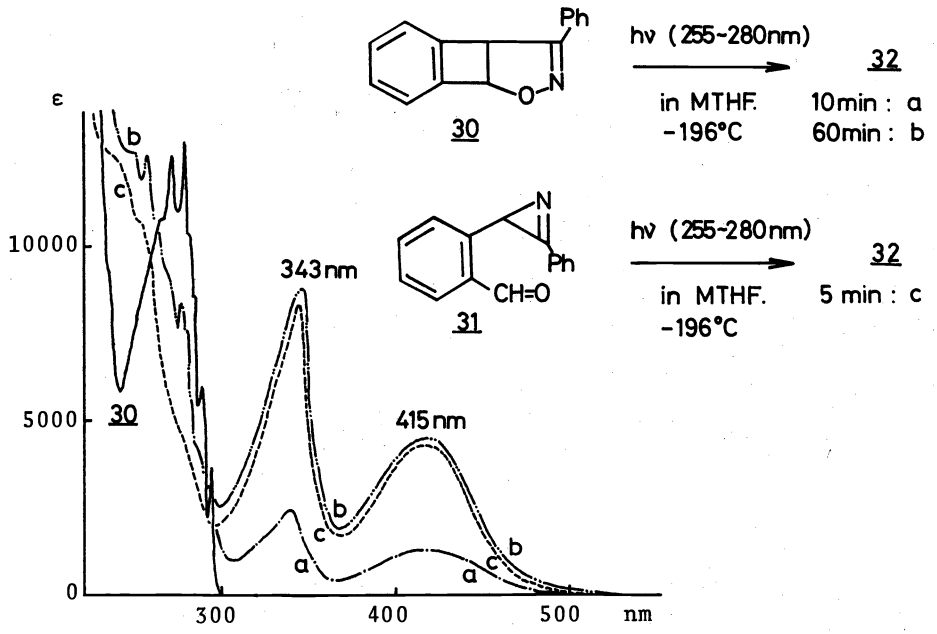
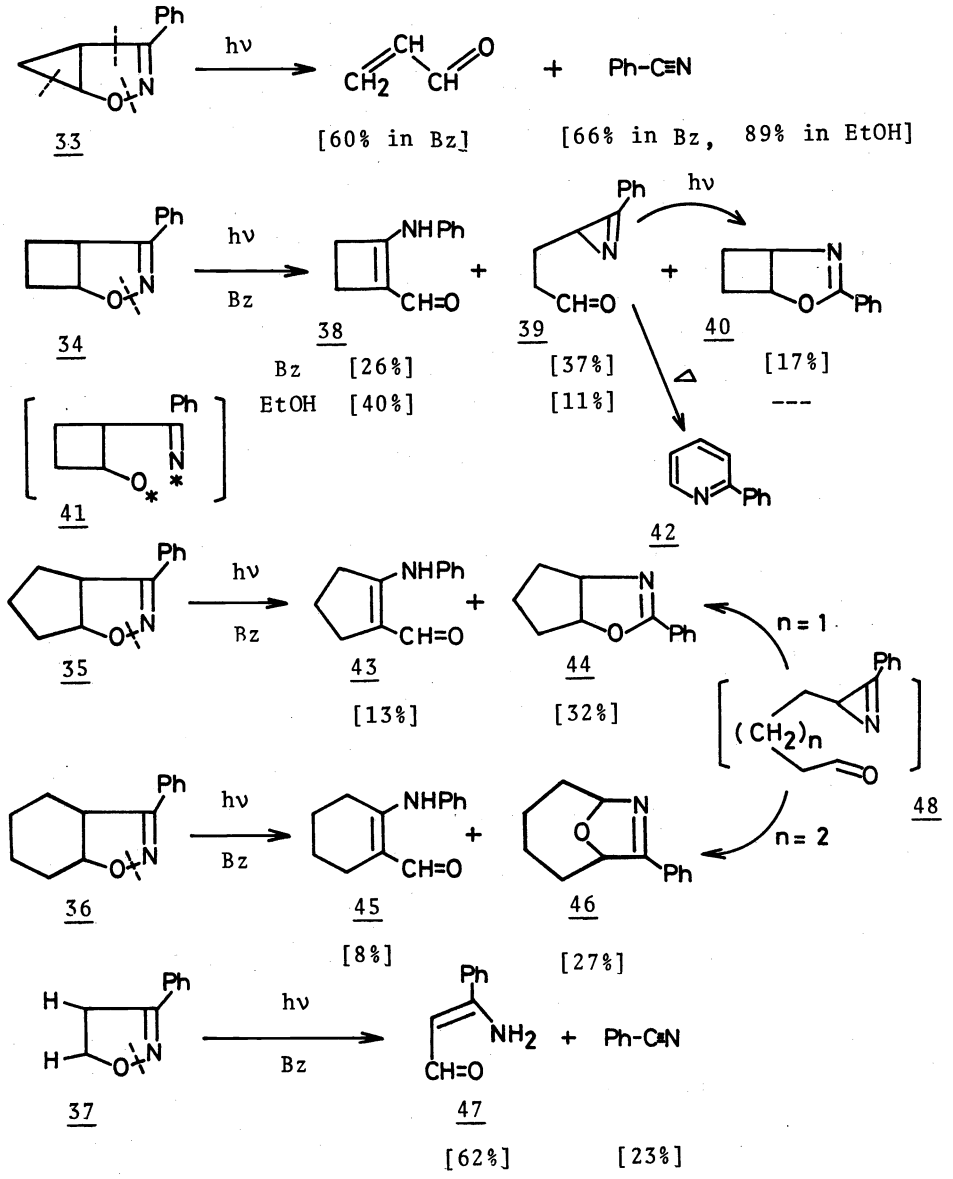


Fig. 5 Uv spectra of the irradiated samples of (30) and (31) at -196°

PHOTOREACTIONS OF 2-ISOXAZOLINES FUSED WITH CYCLOALKANE RINGS

Next attention is turned to the photochemical behavior of bicyclic 2-isoxazoline derivatives fused with a cyclopropane (33), cyclobutane (34), cyclopentane (35), and cyclohexane (36) rings at the C_4-C_5 positions of the heterocycle (ref. 29, 20, 30 & 31). Prior to our studies, Schmid (ref. 12 & 13) and Matsuura (ref. 15 & 16) have reported the photochemistry of 3-phenyl-isoxazolines where several modes of bond cleavage were found. The purposes of our study are firstly to compare the photoreaction of (11) with that of 4-phenyl-2-oxa-3-azabicyclo[3.2.0]hept-3-ene (34), and secondly to clarify the effects of the condensed ring, from which informations on the initial process of the photoreactions might be gained. For comparisons, the photoreaction of 3-phenyl-2-isoxazoline (37), the simplest heterocycles containing Ph-C=N-O chromophor, has also been investigated. Our results are shown in Scheme 5. On irradiation either in cyclohexane or ethanol, 4-phenyl-2-oxa-3-azabicyclo-[3.1.0]hex-3-ene (33) produces benzonitrile and acrolein in excellent yields. Photolysis of 4-phenyl-2-oxa-3-azabicyclo[3.2.0]hept-3-ene (34) results in the formation of variety of products such as phenylamino aldehyde (38) (ref. 32), 3-(3-phenylazirinyl)propanal (39), and 3-phenyl-2-oxa-4-azabicyclo-[3.2.0]hept-3-ene (40). Their yields are listed under the structures. The product distribution seems to depend on the nature of solvent used. In separate experiment, we confirm that irradiation of (39) yields (40), while heating of (39) forms 2-phenylpyridine (ref. 33). The photochemistry of (35) was already studied by Schmid et al. (ref. 30), but our result is a little different. By the same procedure, (36) produces 8-phenyl-9-oxa-7-azabicyclo-[4.2.1]non-7-ene (46) in addition to amino aldehyde (45). Benzonitrile is a common minor photoproduct obtained in photolysis of (34), (35) and (36). There are several points of particular interests in this series of photoreactions. The primary photochemical step of these isoxazolines seems to be the nitrogen-oxygen bond fission, but subsequent processes may depend on their structures. The fragmentation caused by the presence of the cyclopropane ring is particularly noteworthy but it is difficult to know whether the three bond cleavages in (33) occur in concerted manner or in a stepwise manner via diradical. The ring-strain affects rate of the photoreactions; generally the rate is faster, as the strain becomes larger. The recombination process of the intermediate radical, such as (41), competes with the other secondary process (see the quantum yields in Table 3). The corresponding azirine aldehydes can be isolated in the photolysis of (34), but not in those of (35) and (36). The reason is that, in azirine (39), the two-carbon bond is not long enough to undergo internal addition, whereas in the latter cases the longer linkage does not prevent it. Difference in the addition mode



Scheme 5

between (34), (35) and (36) is also noteworthy. Bicyclic 3-oxazoline (46) arises from the normal addition mode of azirines and carbonyl compounds (ref. 30, 34, & 35). On the other hand, the formations of (40) and (44) may be violating cases and are presumed to stem from restricted orientation of the azirine and the aldehyde groups. Photolysis of the simplest derivative (37) in cyclohexane leads mainly to the nitrogen-oxygen bond fission along with the double cleavage reaction producing β-aminoaldehyde (47) and benzonitrile in 62% and 23% yields. The result is compatible with that of 3,4-diphenyl-2-isoxazoline, but not with those of 3,5-diphenyl and 3,4,5-triphenyl derivatives(ref.12, 13, 15, & 16). The discrepancy may be attributed to factors such as substituent (or conjugate) effects, steric effects, and strain effects,etc (ref. 16). Thus, we may conclude that the key photochemical process is the nitrogen-oxygen bond cleavage in the constrained Ph-C=N-O system, which is in sharp contrast to the deactivation without bond fission in the non-constrained Ph-C=N-O system (ref. 17). While no emission spectra were observed in O-methyl ether of acetophenone oxime (ref. 17), all 2-isoxazolines discussed here exhibit fluorescence and their 0-0 bands are shown in Table 3. The quantum yields of the depletion of 2-isoxazolines are also listed in Table 3.

TABLE 3. Quantum yields and fluorescence spectroscopic data of (30), (33), (34), (35), (36) and (37)

Compd. No.	Quantum yield cyclohexane	0-0 band of fluorescence (nm) and (singlet energies, kcal/mol)	
		Methylcyclo-hexane (MCH)	Ether-Isopentane-EtOH (EPA)
(30)	0.82	293.6 (97.4)	294.9 (97.0)
(33)	0.71	-----	-----
(34)	0.72	294.1 (97.1)	295.2 (96.9)
(35)	0.075	295.6 (96.7)	296.8 (96.3)
(36)	0.11	294.1 (97.2)	295.1 (96.9)
(37)	0.61	292.5 (97.7)	293.8 (97.3)

Except for the strained compound (33), all listed compounds and (11) exhibit similar shapes in their fluorescence spectra having fine structures (see Fig. 2). Furthermore, their 0-0 bonds are located almost in the same position (see also Table 2). Such a similarity in the fluorescence spectra and lack of a blue shift in polar solvent suggests that the photoreaction of these 2-isoxazoline derivatives takes place from their (π-π^*) singlet states. However, the uv and esr profiles of the photolysate recorded at -196° show some difference between those of bicyclic 2-isoxazolines (11) and (30), which have the fused cyclobutene ring, and other derivatives (34) and (37). For instance, the esr spectra are observed for (11) and (30), but not for (34) and (37). Such indistinct signals shown in Fig. 6 are not useful to discriminate the species concerned. However at least it is suggested that they are not triplet diradicals, but probably escaped nitrogen-radicals resulting from hydrogen abstraction.

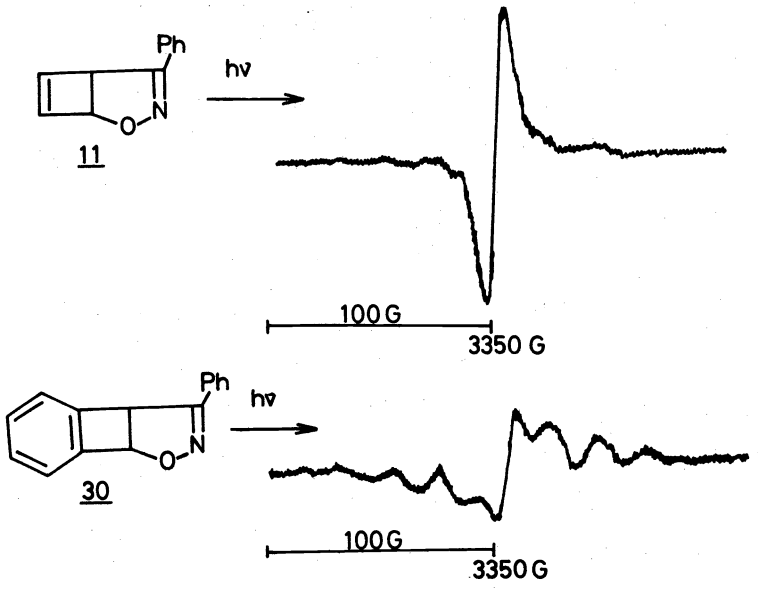


Fig. 6 Esr spectra of (11) and (30) in methylcyclohexane at -196°

The uv spectrum of a low temperature photolysate for (34) is shown in Fig. 7. In comparison to those of (19) and (32) (Fig. 3 and 5) the absorption maximum of the intermediate appears at a much shorter wavelength region at around 250 nm. Since the uv maximum of the ylide of 3-phenyl-2,2-dimethylazirine has been reported by Schmid et al to appear at 277nm (ref. 25) and also since 3-(azirinyl)propanal (39) exhibits a maximum at 242.5nm (Fig. 7), the intermediate species might be assigned either as the ylide (49) or 3-(azirinyl)propanal (39).

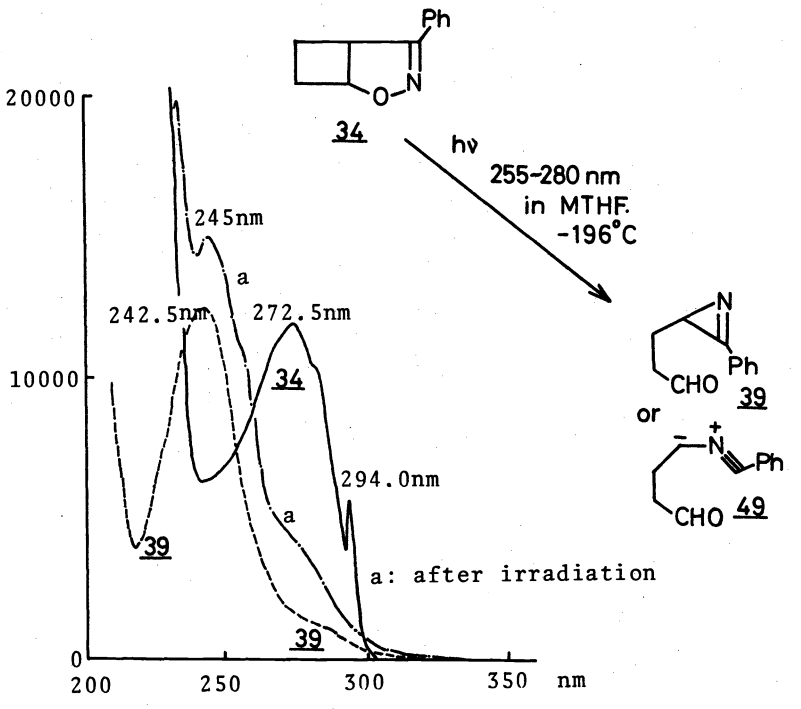
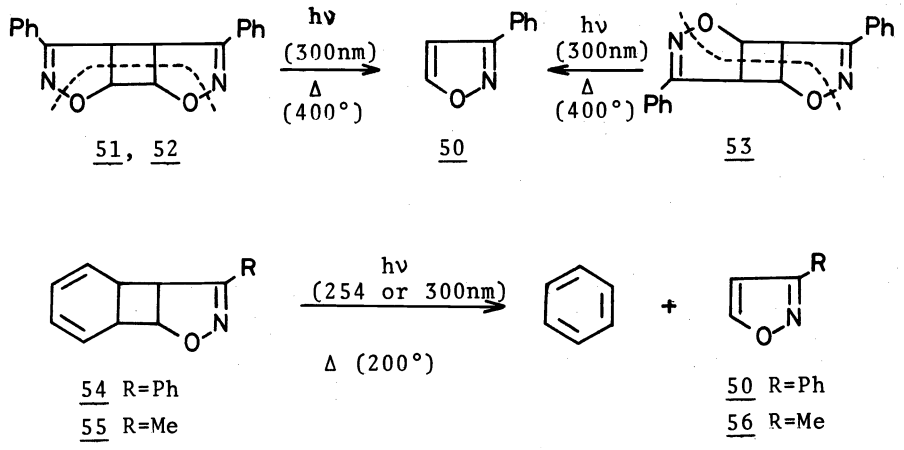


Fig. 7 Uv spectra of (34) and its irradiated sample at -196° and that of (39) at room temperature.

Summarizing the low temperature photolyzing experiments of (11), (30), (34), and (37), it should be noted that the electronic excitations of the former three compounds can lead to the corresponding azirine aldehydes (17), (31), and (39) at -196°, and that of (37) reverts to its ground state. Thus, it is concluded that the four membered ring of the intermediate species (21) has an important role in the subsequent secondary processes such as the ring opening affording azirine aldehydes or the recombination to the starting materials.

In connection with the photochemistry of 2-isoxazoline derivatives fused with a cyclobutane ring, such as (34), we have looked into photochemistry of the dimers of 3-phenyl-2-isoxazole (50) and their related compounds as our next problem. The addition reaction of (11) to benzonitrile oxide results in the formation of syn head-to-head (51), anti head-to-head (52), and anti head-to-tail isomers (53). A priori it is suspected that the double cleavage of the nitrogen-oxygen bond and the cyclobutane ring cleavage might repeat by a single photon process as shown in Scheme 6. However, the (2+2) type elimination occurs not only by irradiation but also in their thermal reactions. For instance, all of these dimers, upon irradiation with light of 300nm (Rayonet reactor) or heating at 400°, decompose to (50) in excellent yields. The structurally related 2-isoxazoline derivatives (54) and (55) undergo the similar type reactions by irradiation or heating. Since (54) and (55) contain both the R-C=N-O and the conjugated diene chromophors, irradiation with light of 300 or 254nm (Rayonet reactor) results in the (2+2) type elimination to give benzene and the corresponding 3-substituted 2-isoxazoles (50) and (56), both in good yields. Such photochemically induced monomerization is not so suprising and might be regarded as the same type of photodissocia-

tion of the dimers of cyclic α,β-unsaturated ketones, wherein the monomerization instead of α-cleavage reactions, occurs even by excitation of the carbonyl group.



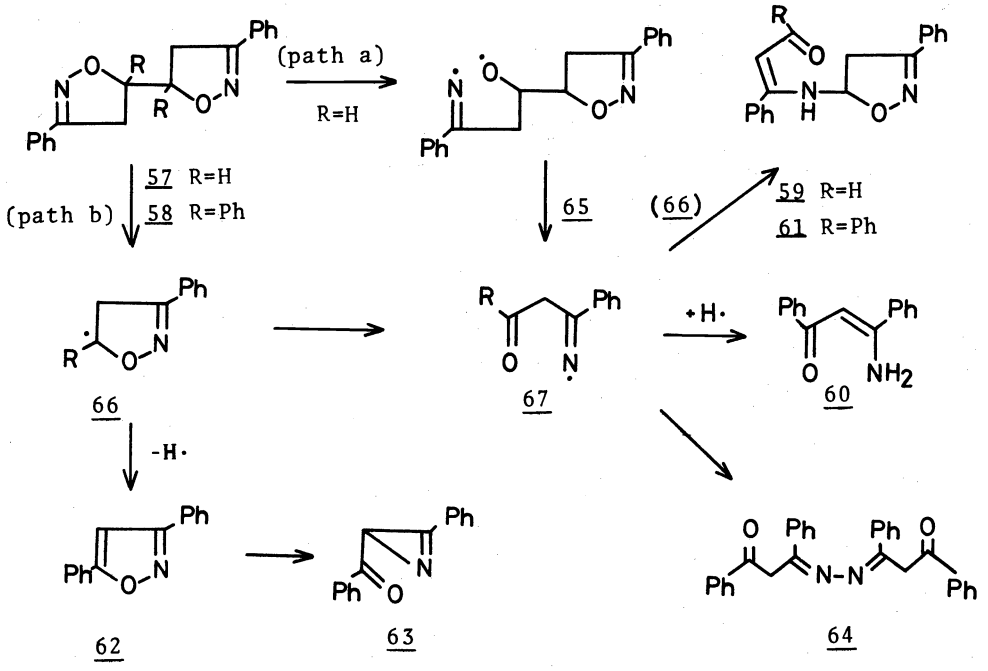
51, 52 50 53

54 R=Ph
55 R=Me

50 R=Ph
56 R=Me

Scheme 6

In connection with the photochemistry of the dimers, those of 5,5-bi(2-isoxazolinyl) type compounds such as (57) and (58) have been studied (ref. 36). When the uv spectra are monitored in photolysis of a dilute solution of (57) or (58), the isosbestic points are observed. In spite of the clean uv changes, the preparative scale photochemistry is relatively complex, and β-(2-isoxazolin-5-yl)aminoaldehyde (59) was obtained from the photolysate of (57). On the other hand, the irradiation of (58) produces β-aminochalcones (60), (61), 3,5-diphenylisoxazole (62), 2-benzoyl-3-phenyl-2H-azirine (63) and azine (64) in 23, 21, 6, 8, and 23% yields, respectively. The plausible reaction paths are illustrated in Scheme 7.



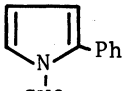
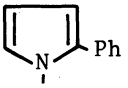
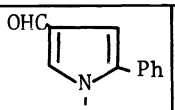
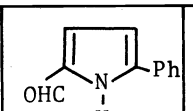
Scheme 7

The key intermediate is proposed as (67) which can be arrived at by either path a or b. Path a is initiated by the known nitrogen-oxygen bond scission followed by the carbon-carbon bond scission as indicated in (65) → (67). Path b involves the carbon-carbon bond scission as the initial step. Such reaction paths can easily be understood from the mechanistic view-point that the weakest bond must break in these photoreactions.

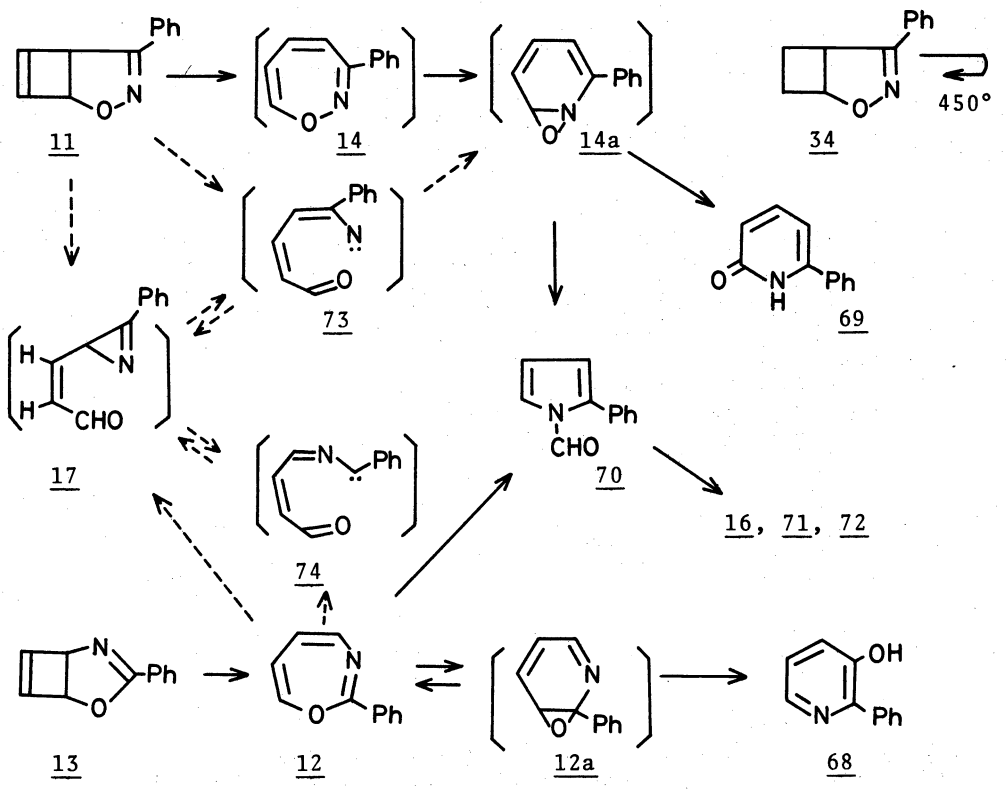
PYROLYSES OF 4-PHENYL-2-OXA-3-AZA- AND 3-PHENYL-2-OXA-4-AZA-BICYCLO[3.2.0]HEPTA-3,6-DIENES AND 1,3-OXAZEPINES

Among the photochemistries of 4-phenyl-2-oxa-3-aza- (11), and 3-phenyl-2-oxa-4-azabicyclo[3.2.0]heptadienes (13) and 2-phenyl-1,3-oxazepine (12), the most intriguing finding is that the nitrogen-oxygen bond fission precedes the cyclobutene ring opening in bicyclic isoxazoline system (11) (see Scheme 3). It is well known that the heterocycles containing C=N-O group, such as isoxazoles and isoxazolines, generally undergo the nitrogen-oxygen bond fission either by irradiation (ref. 37 & 38) or by heating (ref. 19 & 39). On the other hand, the thermally induced bond fission seems more difficult to occur in oxazoles and oxazolines (ref. 40 & 41), although a few examples are reported (ref. 40 & 42). In connection with these facts, it is of interest to learn difference in chemical behavior between photochemically and thermally excited (11), (12), and (13). Among them, 1,3-oxazepine (12), upon heating at 160° in benzene solution reacted cleanly to 2-phenyl-3-hydroxy-pyridine (68) in quantitative yields (ref. 23). Other compounds (11) and (13) are relatively stable under such conditions. Thus, high temperature decomposition is attempted not only with (11) and (13) but also with (12), (ref. 43 & 44). When a benzene solution of these compounds is passed through a column containing quartz helices preheated at 450°, several products are obtained as shown in Table 4.

TABLE 4. Product distribution form vapor phase pyrolysis at 450°

prod.% / reactant	 (70)	 (71)	 (16)	 (72)	other products
(11)	14	32	16	13	7 (69)
(12)	14	29	11	11	23 (68)
(13)	11	25	16	11	21 (68)
(70)	--	32	16	17	5 (15)

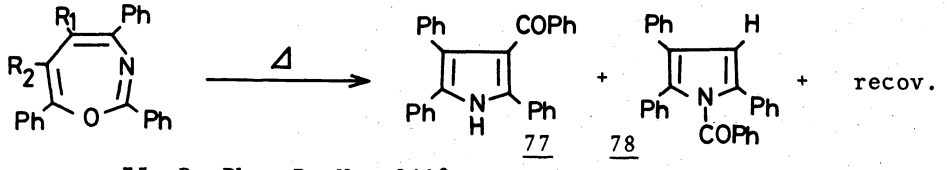
With the exception of the formation of 2-phenyl-3-hydroxy-pyridine (68) from (12) and (13), and of the formation of 6-phenyl-2-pyridone (69) from (11), all of these heterocycles suffer from a deep-seated rearrangement leading to pyrrole derivatives (16), (70), (71), and (72) (Table 4). It should be noted that there exists a similarity in the types and yields of the products among these pyrolyses. This apparently suggests the presence of a common intermediate. As it is known that N-acyl pyrroles, upon heating or irradiation, undergo a facile acyl migration (ref. 45), N-formyl-2-phenylpyrrole (70) is considered to be the primary product, which in turn, transforms into other pyrrole derivatives. This expectation has been supported by the results obtained in the pyrolysis of (70) under the same conditions, in which the product distribution and the yields are almost same as shown in Table 4. As shown in Scheme 8, the formation of both primary products (69) and (70) from (11) can be rationalized by the weakest nitrogen-oxygen bond fission in assumed intermediate (14a) followed by a hydrogen shift to (69) or a



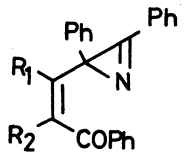
Scheme 8

carbon shift to (70). Resistance of 4-phenyl-2-oxa-3-azabicyclo[3.2.0]hept-3-ene (34), a dihydro compound of (11), to pyrolysis under the same conditions implies that in the pyrolysis of (11), the cyclobutene ring plays an important role in effecting the preferential opening of that ring. Thus, 1,2-oxazepine (14) is formed, probably as a transient, and then converted to (69) and (70) via (14a). However, at this stage, double cleavage pathway of (11) via Z-azirinyl-acrolein (17) and vinylnitrene (73) could not be ruled out for the formation of (14a) (ref. 24) (Scheme 8). If this were the case, the thermal conversion of (17) to 1,3-oxazepine (12) would occur as discussed above, and (12) should lead to 2-phenyl-3-hydroxypyridine (68) in addition to the pyrrole derivatives. Since we have not been able to find this readily isolable pyridine derivative (68), we conclude that 1,2-oxazepine (14) and its valence isomer (14a) are the most plausible intermediate for the formation of (69) and (70) in the pyrolysis of (11). The sharp contrast in the photochemical and thermal reactions of the bicyclo[3.2.0]hepta-3,6-diene system containing C=N-O group is noteworthy. In the pyrolyses of 1,3-oxazepine (12) and its valence isomer (13), the formation of 2-phenyl-3-hydroxypyridine (68) is readily accounted for as being derived from epoxynorcaradiene (12a). The reaction mode parallels that of pyrolysis of (11). Thus the cyclobutene ring opens to afford (12), which is in equilibrium with (12a) (Scheme 8). This understanding supports that both pyrolyses of (12) and (13) proceed completely parallel each other. However, the mechanistic interpretation for the formation of the assumed primary product, N-formyl pyrrole (70) is not straightforward. Sometimes ago we proposed that the reaction from (11) would be interrelated with that from (12) and (13) by using azirinylacrolein (17), iminocarbene (74), and vinyl nitrene (73) as the common links (ref. 44) (Scheme 8). The separate formation of 3-hydroxypyridine (68) and of pyridone (69) in these pyrolyses (see Scheme 8) may exclude the possibility that azirinylacrolein (17) and its related species (73) and (74) are the common intermediate. By using various substituted derivatives we wish to examine the rearrangement path from the 1,3-oxazepines to the N-formyl pyrroles in more detail. To our knowledge, the first paper dealing with the oxazepine-pyrrole rearrangement was Buchardt's one, in which the thermolysis of 2,4,5,7-tetraphenyl-1,3-oxazepine (75) affording pyrrole

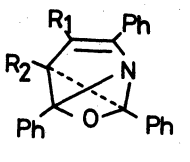
(77) was studied kinetically (ref. 46). We have chosen (75) and its isomer (76) as convenient model compounds for the mechanistic studies of the rearrangement. When the pyrolyses of (75) and (76) are carried out at 450° in vapor phase, N-benzoyl-2,3,5-triphenylpyrrole (78) and 3-benzoyl-2,4,5-triphenylpyrrole (77) are obtained almost in the same ratio (see Scheme 9). Furthermore an easy conversion of (78) to (77), namely, benzoyl migration, is also established under the same conditions.



75	R_1=Ph,	R_2=H	240°	93%	4%	trace
75	R_1=Ph,	R_2=H	450°	63%	25%	5%
76	R_1=H,	R_2=Ph	450°	55%	22%	6%



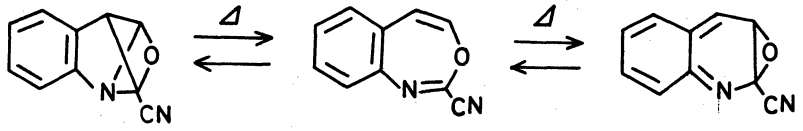
79



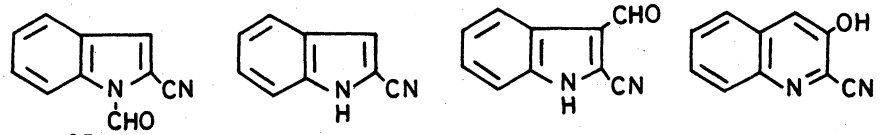
80

Scheme 9

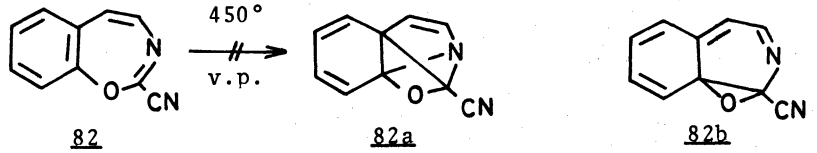
This rearrangement is probably not explained by the reaction path via azirinyl styrylketone (79) unless a benzoyl migration from the carbon to carbon atom on the pyrrole ring occurs. One of the attractive paths to explain the interchange between the substituents R_1 and R_2 is that proceeding via the cross-linked structure (80) followed by the bond cleavage at the O-C_1 and C_6-C_7 positions (or stepwise one formally corresponding to (80)). To verify the assumption of such a cross-linked structure, additional pyrolysis experiments have been carried out using benz-1,3-oxazepine derivatives (81) and (82)



81a 81 81b



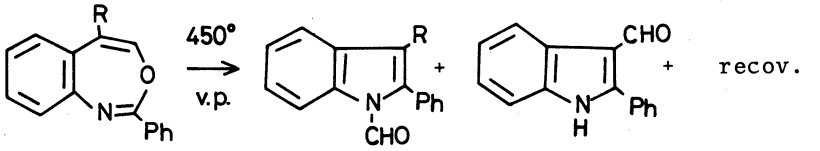
decomp temp. (recov.)	83	84	85	86
470°(25 %)	9.6%	30.6%	4.6%	2.0%(poor)
520°(5.3%)	13.1%	43.9%	4.7%	2.6%(poor)



82 82a 82b

Scheme 10

(Scheme 10) under the same conditions. Upon the pyrolysis (81) produces indole derivatives (83), (84), (85), and 2-cyano-3-hydroxyquinoline (86) along with a recovery of (81). Contrary to this, the isomeric compound (82), which is different from (81) only in the positions fused with the benzene, is completely recovered under the same conditions (Scheme 10). These observations might be accommodated in terms of the stability and the preferred cleavage of the cross-linked intermediate (81a) and (82a) and of the norcaradiene species (81b) and (82b). The poor yields of (86) may indicate that the quinonoid structure (81b) is less favored. On the other hand, stability of (82) may be attributed to the high energy level of structures (82a) and (82b), which must overcome the benzene ring aromaticity in addition to the high strain. Other examples are the pyrolyses of benzo-1,3-oxazepines (87) and (88), in which the expected indole derivatives (89), (90), and (91) are formed with a recovery of the starting materials (Scheme 11). It should be added that the replacement of the cyano group in (81) with a phenyl group gives no effect in the observed product pattern, indicating of easy accession of the cross-linked structures.



87 R=H
88 R=Me

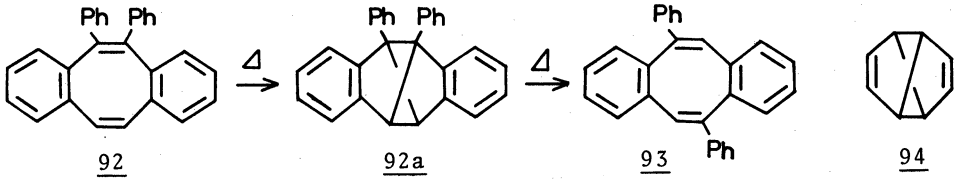
89 40%
90 34%

91 20%

87 35%
88 50%

Scheme 11

As summarised in Scheme 9 - 11, the pyrolytic conversion of benzene-fused 1,3-oxazepines to indoles requires higher temperatures than that of monocyclic 1,3-oxazepines leading to pyrrole derivatives, whereas polyphenyl derivatives such as (75) and (76) rearrange at lower temperatures. The pattern seems to be compatible with the reaction path involving the cross-linked structure, because the fused benzene ring raises the strain energy and the crowded phenyl groups tend to relieve the steric interference. In addition, it should be noted that dibenzo[a,e]cyclooctatetraene (92), upon heating, readily rearranged to its isomer (93) via cross-linked intermediate (92a) (ref. 48). This fact along with the isolation of tricycloctadiene (94). (ref. 49 & 50) could be invoked as an analogy to support the proposed cross-linked structures such as (80) and (81a).



92 92a 93 94

Scheme 12

However, it should be noted that the concerted ($\pi^2a + \pi^2a$) process is thermally forbidden; a corresponding stepwise pathway therefore must be assumed. We endeavor to clarify the reaction mechanism in future.

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