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The Photochemistry of the *N*-Oxide Function

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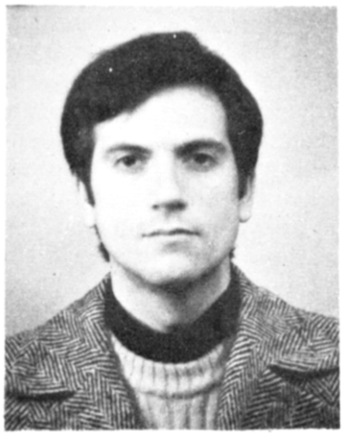

Angelo Albini was born in Milan in 1946 and studied chemistry in Pavia, presenting a thesis on the photochemistry of phenazine. After a year with the pharmaceutical company Lepetit he came back to the University of Pavia, where he then became associate professor of organic chemistry. He did postdoctoral work at the Max-Planck Institute for Radiation Chemistry, Mülheim (West Germany), and at the University of Western Ontario. Besides the photochemistry of heterocyclic *N*-oxides and in general of heterocycles, his research interests include electron-transfer photosensitized reactions, the mechanism of photofading of dyes, and the chemistry of metal complexes of nitrogen heterocycles.

Marco Alpegiani was born in Caminata in 1954 and studied chemistry in Pavia, presenting a thesis on the photochemistry of azanaphthalene *N*-oxides. He then took a position at the pharmaceutical company Carlo Erba-Famitalia, where he pursues his interest in heterocyclic chemistry, this time in the synthesis of antibiotics.

I. Introduction

Organic compounds containing the imino *N*-oxide function,[1] such as nitrones, azoxy derivatives, and heterocycle *N*-oxides generally exhibit photochemical reactivity, often with moderate quantum yield ($\Phi \geq 0.1$). Indeed, the photolability of these compounds that absorb solar light was already noticed at the beginning of the century.[3] Analogously, the photochemical reactivity of heterocycle *N*-oxides was first suspected when it was accidentally noticed in the instability of dilute solutions prepared for spectroscopic characterization.[4] Chemical yields are also high, at least in several cases, and this fostered the interest in these photochemical reactions since the beginning of the sixties, so that a review published in 1970 by Spence, Taylor, and Buchardt registered some 200 contributions.[5,6] Taking into account the work of the subsequent years, it can now be

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said that every relatively simple substrate containing the imino N-oxide function has been studied from the photochemical point of view.

The variety of photoprocesses which have been reported include several examples of synthetic value. Furthermore, photochemical reactions of N-oxides have also been proposed for diverse applications, such as photoinitiated polymerization or as a model for the biochemical oxygen transfer. On the other hand, an understanding of the mechanism of this photoreaction is less advanced. It would appear that this is due to (i) the products of the photochemical reaction are often labile under the conditions of the experiment or in the isolation procedures, so that care is required to distinguish the primary photoproducts from products arising from further transformation, and (ii) the imino N-oxides are mostly nonemitting species and undergo a very rapid photochemical reaction, so that only limited mechanistic information can be obtained from either photophysical studies or flash photolysis.

Besides the above mentioned systematic review, several other discussions concerning this area have been published, including a survey of the photochemistry of heterocyclic N-oxides by Kaneko,[7] a "critical review" by Streith,[8] a further survey by Buchardt about the preparative aspects of N-oxide photochemistry[9] and other contributions.[10]

The present review is intended to gather the new results up to 1980 (or, when possible, 1981) with particular emphasis on the conclusions about the primary photochemical process and the mechanistic interpretation. Whenever necessary, material already presented in the review by Spence, Taylor, and Buchardt is referred to simply as ref 5.

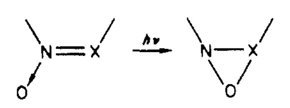
Sections II–VIII are concerned with the photorearrangement processes observed for the various classes of N-oxides, section IX with the deoxygenation processes, and section X with a general mechanistic discussion.

II. N-Oxides Other Than Heterocyclic Derivatives

This section will consider the photoreactivity of compounds in which the N-oxide function is not a part of an aromatic system, viz. of nitrones, azoxy derivatives, azine N-oxides, and N-oxides of saturated heterocycles.

A. Electrocyclic Rearrangement to Three-Membered Rings

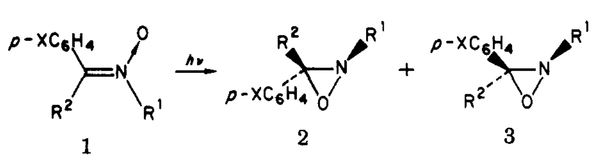
The irradiation of nitrones generally causes electrocyclic rearrangement. The same is true for alkylazoxy derivatives (eq 1) although not for their aromatic counterparts. The three-membered heterocycles thus formed are themselves photochemically reactive, but, as they absorb at shorter wavelength, it is generally possible to avoid a second photochemical reaction. Thus, the photochemical rearrangement of nitrones and azoxy derivatives represent a useful synthetic pathway to oxaziridines and oxadiaziridines. Indeed, in several cases only the photochemical synthesis is known. In recent years, the reaction has been extended to oxaziridines of virtually every structural type, such as oxaziridines bearing only alkyl substituents[11] as well as 2- or 3-aryl,[12,13] 3,3- or 2,3-diaryl-, and 2,3,3-triaryloxaziridines.[12,14-16] Starting from cyclic nitrones, oxaziridines condensed with five-,[17-20] six-,[21] and seven-membered[14] rings or spirooxaziridines[22,30] have been obtained.



(1)

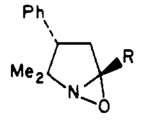
X = CH, N

SCHEME I



	a	b	c	d	e
X	H	NMe_2	NO_2	NO_2	OMe
R^1	Me	Me	Me	Et	Ph
R^2	H	H	H	H	Ph

The rearrangement is, at least in several cases, stereospecific. Thus, nitrones **1a** and **1b** (Scheme I) yield only the oxaziridines **2a** and **2b** by irradiation at −60 °C, while **1c** and **1d** yield a mixture of stereoisomers (**2c**,**d** amounting to 31%, **3c**,**d** to 69%), the lack of stereospecificity in this case being attributed to preliminary trans–cis isomerization of the nitrones.[13] Thus, it would appear that, with electron-withdrawing substituents, the geometrical isomerization becomes faster than cyclization. In fact, starting from a mixture of *trans*- and *cis*-(methoxyphenyl)nitrones (**1e** and the corresponding cis form) the oxaziridines **2** and **3** were obtained in the same stereoisomeric ratio as the starting material,[23] showing that in this case the cyclization is faster. Another example of stereospecificity is the exclusive formation of the *cis*-oxaziridino[2,3-*a*]pyrrolidines **4** by (formulas **4**–**6**) photorearrangement of the corresponding pyrroline N-oxides, while their trans isomers are obtained by peracid oxidation of the corresponding pyrrolines.[19,24]



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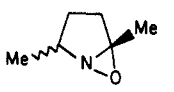

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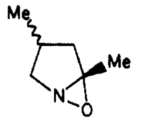


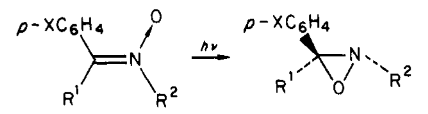
6

On the other hand, the oxaziridinopyrrolidines **5** and **6** are reported to be formed in stereoisomeric mixture by photorearrangement of the N-oxides, whereas the cis isomer of compound **6** is selectively formed by peracid oxidation of the pyrroline.[20] Any discussion about the stereoselectivity of the nitrone to oxaziridine rearrangement should take into account the possible intervening of the known[15] trans–cis isomerization of oxaziridines.

Apropos stereoselectivity, it is interesting to mention the surprisingly high optical yield (5–31%) observed in the photoarrangement of some nitrones in chiral solvents (mixtures of (+)- or (−)-2,2,2-trifluorophenylethanol and fluorotrichloromethane) at −78 °C.[12] At room temperature the selectivity is much lower (Scheme II).

As mentioned previously, aliphatic azoxy derivatives analogously rearrange to oxadiaziridines. Thus, the

SCHEME II



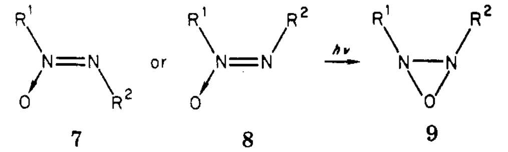
	X	R¹	R²	optical purity
a	H	Ph	*t*-Bu	31%
b	H	Ph	*i*-Pr	20%
c	NO_2	H	*t*-Bu	6%
d	NO_2	Me	*t*-Bu	3%

TABLE I. Conversion of Azoxy Compounds to Oxadiaziridines

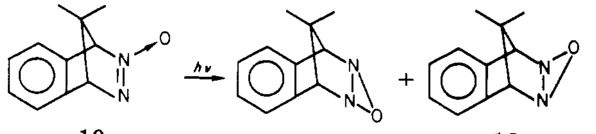
	starting material 7		yield of	
	R¹	R²	9, %	ref
a	*t*-Bu	*t*-Bu	75	25
b	*n*-Bu	*n*-Bu	*a*	25
c	Me	*t*-Bu	*a*	25
d	*i*-Pr	*i*-Pr	52	26
e	C_6H_{11}	Me	27	26
f	Me	C_6H_{11}	58	26

[a] Not reported.

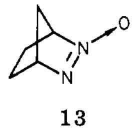
trans-azoxy **7a** yields the oxadiaziridine **9a**, thought to have trans configuration.[25] The isomeric azoxy **7d** and **8d** undergo, besides photochemical interconversion, cyclization to the *trans*-oxadiaziridine **9d**.[26] (See Table I.) Fused oxadiaziridines are also accessible, although less easily than fused oxadiaziridines. Thus, irradiation of the azoxy derivative **10** at −80 °C affords in high yield the isomeric oxadiaziridines **11** and **12** in the ratio 2.5 to 1, although at room temperature only chelotropic elimination is observed.[27] However, no oxadiaziridine was obtained from the model compound **13**.[25]



7 8 9 (2)



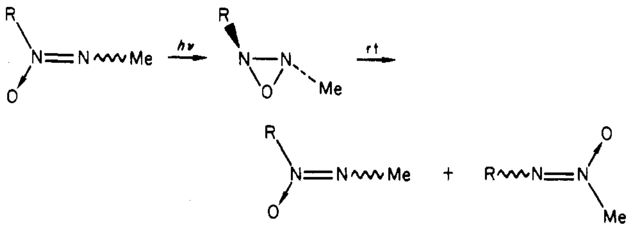
10 11 12 (3)



13

In several cases the photochemical cyclization is thermally or photochemically reversible.[28] The total process has been exploited for the preparation of different stereoisomers of the original nitrones or azoxy derivatives. Thus, the first authenticated *trans*-azoxy derivatives were obtained by this method.[26] Likewise, oxygen migration from one nitrogen atom to another nitrogen atom in aromatic azoxy derivatives has been observed and rationalized as occurring via reversible cyclization to an oxadiaziridine.[28] Correspondingly, photochemical racemization of the chiral oxaziridine **14** takes place through a photochemical equilibrium with the nitrone **15**.[29]

SCHEME III



R = C_6H_{11}

Z, 45%; *E*, 18% *Z*, 21%; *E*, 15%

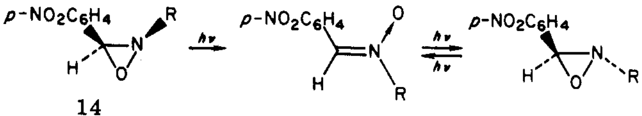
R = Ph

Z, 20%; *E*, 14% *Z*, 3%; *E*, 10%

TABLE II. Photolysis Products of Pyrrolidine *N*-Oxides

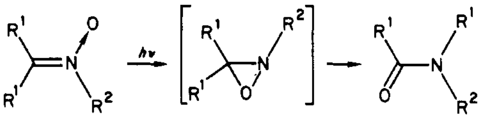
	pyrrolidine *N*-oxides		yield of products, %			
	X	R	17	18	19	ref
16a	CH_2	H	11			33a
b	CH_2	Me	28			33b
c	CH_2	CN		24-53		25
d	CO	Ph	31^a			17
			5^b	42	17	17
e	CO	Me		50		17
f	CO	*t*-Bu			46	17

[a] After irradiation for 5 h. [b] After irradiation for 18 h.



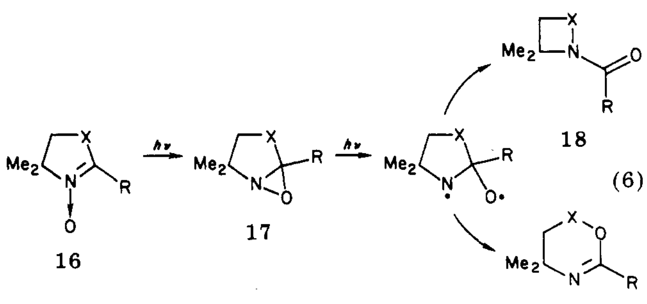
14 15 (4)

As previously mentioned, oxaziridines are both photo- and thermolabile, generally rearranging to amides.[30] This having been ascertained in a number of cases, the hypothesis that is usually made is that oxaziridines, although not isolated, are intermediates when amides are directly obtained from the irradiation of nitrones.



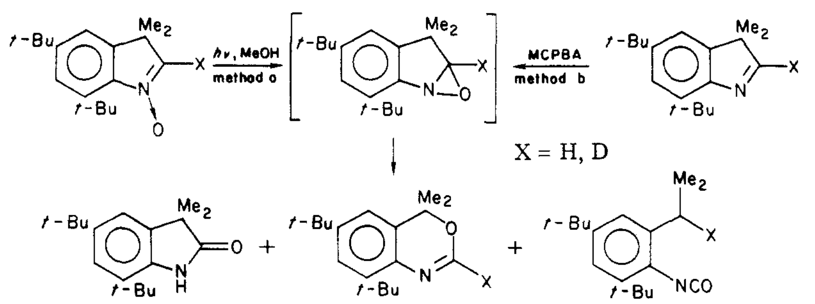
(5)

The rearrangement to amides may itself be preparatively useful. Thus, for example, if the carbon atom of the nitrone is part of a cycle, a ring-enlarged lactam is formed, via a hypothetical spirooxaziridine.[30-32] On the contrary, starting with cyclic nitrones, ring contraction is observed if the ring residue migrates. Thus, *N*-acylazetidines[33] and *N*-acyl-β-lactams[17] are obtained from pyrrolidine and pyrrolidine *N*-oxides (Table II), respectively. The ring size remains obviously un-



16 17 18 19 (6)

SCHEME IV



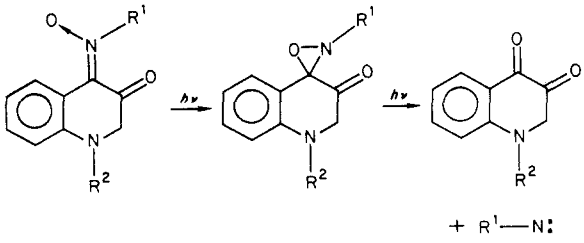
method a	11%	15-23%	48%
method b	47-48%	9-13%	32-40%

changed if the substituent rather than the ring residue migrates. Thus, *N*-formylpyrrolidones, which subsequently are hydrolyzed to 2-pyrrolidones, are formed from 2-formylpyrrolidine *N*-oxides.[34] From a dihydropyrazine *N*-oxide, hydrogen migration to form a pyrazine derivative has been reported.[35]

In several cases, amides are not the only products obtained, being accompanied by other photoproducts also formally deriving from oxaziridines. Thus, oxazinones, probably arising from oxaziridines via homolysis of the N-O bond and rearrangement, are formed together with β-lactams from pyrrolidinone *N*-oxides,[17] and are the exclusive products from 3*H*-3-oxoindole 1-oxides.[36] The same concurrence between ring enlargement and ring contraction has been observed in the case of benzodihydrodiazepinone *N*-oxides.[14] Still another process observed in 3*H*-indole *N*-oxides is ring opening to afford isocyanates (Scheme IV).[37-39] Although the oxaziridine has not been isolated, it has been shown that a similar product distribution is obtained by photolysis of the *N*-oxide and by peracid oxidation of the imine[38] (Note that the formation of the isocyanate involves 1,5 intramolecular hydrogen migration).

B. Oxygen Shift Accompanied by α-Fragmentation

In several nitrones, the shift of the oxygen atom from the nitrogen to the carbon is accompanied by breaking of the C-N bond, with formation of a carbonyl derivative and a nitrene. Since it is known that nitrenes can be generated by decomposition of oxaziridines, the process may be interpreted as another secondary process depending on previous cyclization to oxaziridine.[40] In one case the oxaziridine intermediate has actually been isolated.[22] Nitrenes generated in this way yield both azo compounds, usually considered as arising from the nitrene triplet state,[41] and products arising from electrophilic attack, which is characteristic of the nitrene singlet state.[41]



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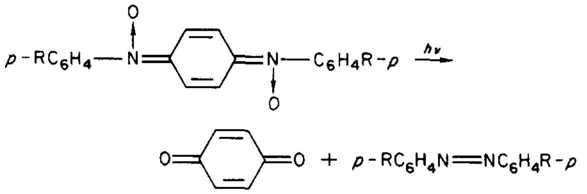

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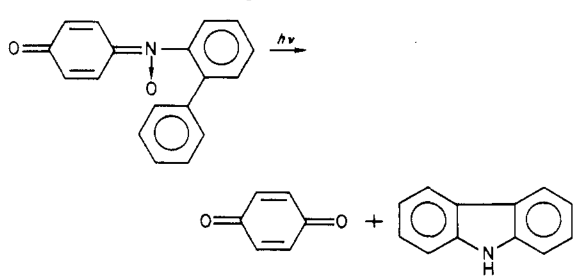
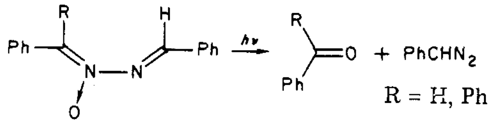


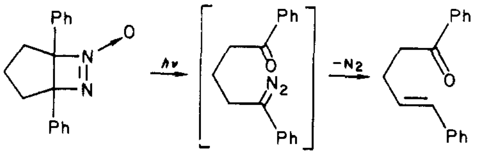
(9)

A mechanism involving the formation of an oxaziridine and its fragmentation to a diazo derivative has been analogously proposed to rationalize the photochemistry of the azine *N*-oxide **20**. The diazo compound decomposes to the corresponding carbene, which is trapped in high yield as the insertion product into benzene.[42] 3,6-Diphenyl-4,4,5,5-tetramethyl-3,4-dihydropyridazine 1-oxide reacts analogously.[42] The cyclic azoxy derivative **21** yields a diazo compound which has been detected spectroscopically and further reacts with loss of nitrogen followed by hydrogen shift.[42] The photochemical cleavage of aromatic azoxy compounds to yield diazonium salts, while formally analogous to the reaction mentioned above, differs in that its mechanism does not involve an oxaziridine[43] (see section IIC).



(10)

20



(11)

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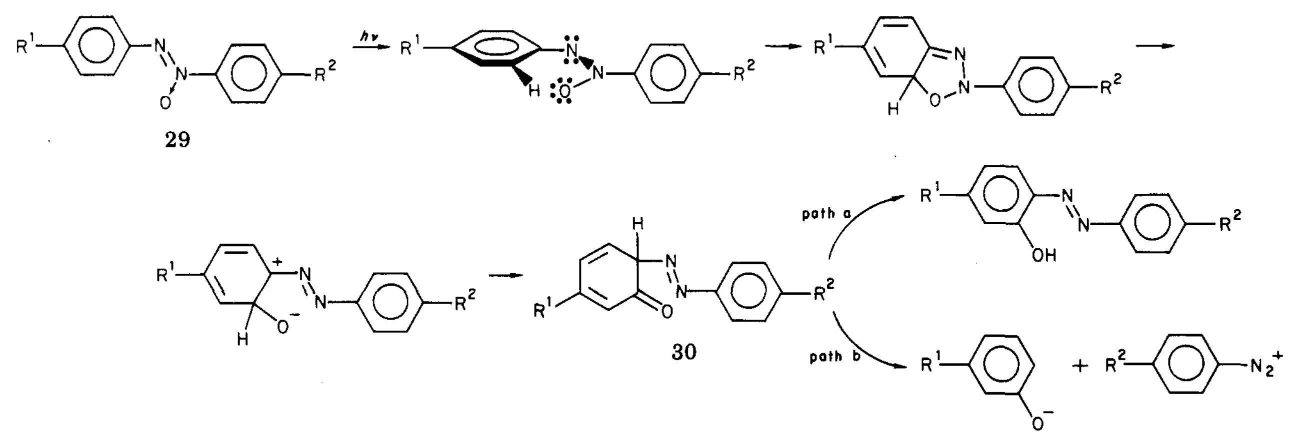
C. Azoxy to Hydroxyazo Rearrangement

The photochemical instability of aromatic azoxy derivatives is well known and has technological relevance

SCHEME V



29

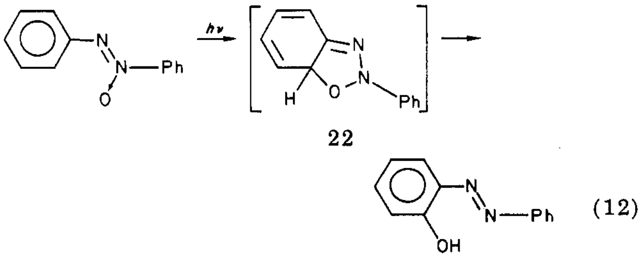
30

TABLE III. Relative Quantum Yield from the Azoxy Derivatives 29[50]

R^1	R^2	ϕ_{rel}
H	H	1
Me	H	0.75
H	Me	0.37
Me	Me	0.47
CF_3	H	0.27
H	CF_3	1.7
CF_3	CF_3	0.39
Me	CF_3	1.25

as the azoxy group might in some practical conditions be formed from azo dyes,[44a] thus impairing the excellent light stability of these dyes. The photolysis leads to hydroxy derivatives and thus has been termed the photo-Wallach rearrangement, although it differs from the authentic Wallach reaction both in the products obtained (*o*-hydroxy- rather than *p*-hydroxyazo derivatives), in the experimental conditions (the thermal Wallach rearrangement requires strongly acidic medium), and in the mechanism (intramolecular rearrangement in the photochemical reaction, rather than nucleophilic attack of water on a dication as is characteristic of the Wallach reaction).[5,44b] However, the mechanism of the photorearrangement might not be unequivocal. Indeed, Jaffé distinguishes two photoprocesses for azoxybenzene, one with a high quantum yield, requiring protonation or even biprotonation of the excited state, and a low quantum yield one occurring in neutral solutions.[45]

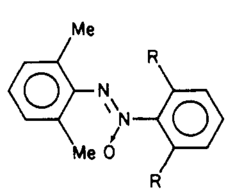
Already in 1954 it was noticed that the attack occurs on the ring "far" from the *N*-oxide function, and a five-membered cyclic intermediate (22) was accordingly proposed. Interestingly, the formation of a polarographically distinguishable intermediate was reported for the azoxybenzene rearrangement.[47] Although this intermediate was thought to be an oxadiaziridine, it may be the oxadiazolidine **22**.



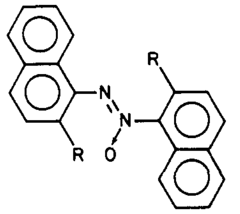
22

(12)

The rearrangement is rigorously specific, a free ortho position in the aromatic ring more distant from the *N*-oxide function being required to make the reaction possible. Thus, neither of the azoxybenzenes **23** or **24** undergo this rearrangement.[48] The azoxynaphthalene



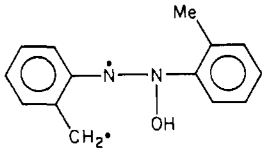
23, R = Me
24, R = H



25, R = H
26, R = Me

25 yields photochemically the expected 2-hydroxyazo derivative, while when position 2 is unavailable, as in compound **26**, no attack at the peri position, which would involve complete loss of aromaticity, is observed.[49]

The reaction does not proceed via hydrogen abstraction. If this were the case, a change in the reaction course would be expected when methyl groups or other groups with good hydrogen-donating properties (such as *i*-Pr, CH_2Ph, $CH(OMe)_2$) are present to form biradicals of structure **27**. In fact, the normal rearrangement to hydroxyazo derivatives is observed in each of the previously mentioned cases, the only exception being the formyl derivative **28**, which does undergo intramolecular hydrogen abstraction analogously to the structurally related *o*-nitrobenzaldehyde.[48]



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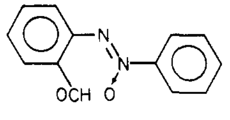
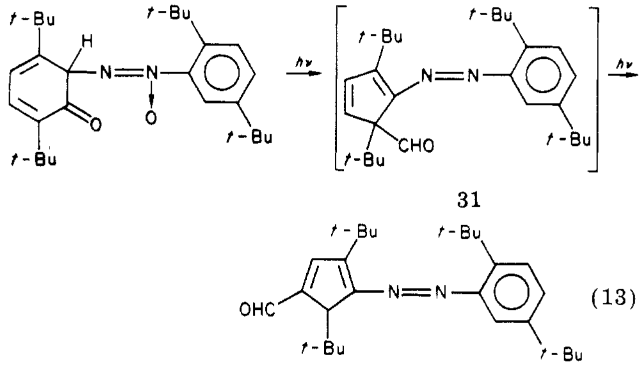


28

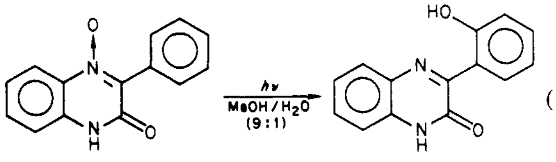
An accurate study of the substituent effect has allowed Bunce to formulate a detailed mechanistic scheme (Scheme V, Table III). The main points are (i) the reaction proceeds from the $n\pi^*$ singlet excited state, (ii) out-of-plane rotation is the first step, and (iii) electrophilic attack by the oxygen atom to the opposite aromatic ring ensues. The electrophilic character of the oxygen attack is shown by the effect of substituents such as CF_3 and Me, while groups like NR_2 and NO_2 inhibit the rearrangement as they change the character of the lowest excited state. This scheme accounts both for the rearrangement to hydroxyazo derivatives (path a) and for the fragmentation to phenolate and diazonium ions (path b).[43,50] Path a predominates in polar solvents, such as alcohols, which function as lone-pair donors, while path b is followed in "inert" solvents, e.g., benzene. In the latter case the diazonium ion can be trapped by adding naphthol.

Further work by Döpp[43a] supports the proposed mechanism, demonstrates its occurrence in solid state photolysis, and shows the intervening of a further process from the same intermediate **30**, viz. α-cleavage of the cyclohexadienone moiety and hydrogen shift to yield compound **31**, followed by a shift of the formyl group.[43b] Both steps are further photochemical reactions.



(13)

The azoxy-to-hydroxyazo rearrangement is undergone also by mixed aliphatic aromatic azoxy derivatives in concurrence with geometrical and positional isomerism.[51] Finally, it must be observed that a formally analogous rearrangement has been reported for the phenylnitrone **32**.[52] Furthermore, an analogy might be drawn also with the intramolecular oxygen transfer observed in 2-benzyl- and 2-(β-phenylethyl)pyridine N-oxides,[53] which should involve a six-membered cyclic intermediate if the analogy holds (see section IX).



32 20%

(14)

D. Other Photoprocesses

Geometrical isomerism around the double bond, when not occurring via an intermediate oxaziridine (see section IIA), is thought to involve the triplet rather than the singlet excited state (see section X). For the case of azoxybenzene, energetic data about this process have been calculated.[54a]

There are then a number of photochemical reactions in which the N-oxide function plays no special part, such as the electrocyclic rearrangement of azine mono-N-oxide,[42] the sigmatropic rearrangement of 4H-pyrazole N-oxides,[42] and the chelotropic elimination of N_2O from cyclic aliphatic azoxy derivatives.[27] The nitrone **33** is photochemically decomposed to benzophenone and methyl disulfide,[54b] a process that is formally analogous to the α-fragmentation discussed in section IIB, but, in fact, involves homolysis of the CH_2–S bond and further cleavage of the radical rather than direct photochemical reaction of the N-oxide function.

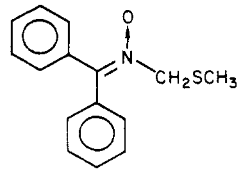


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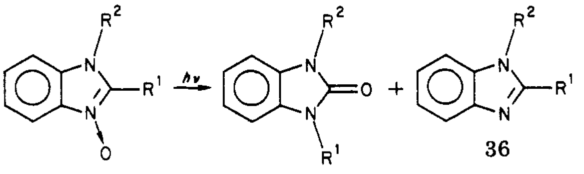
TABLE IV. Photolysis Products of Benzimidazole N-Oxides

starting material				yield of products, %				
	R^1	R^2	solvent	35	36	37	38	ref
34a	Et	n-Pr	MeOH	55				55
b	-$(CH_2)_5$-		MeOH	43	55			55, 56
c	Et	CH_2Ph	MeOH	71	1	1		55, 57
c	Et	CH_2Ph	dioxane		4	41	3	

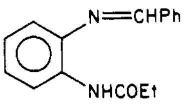
III. N-Oxides of Five-Membered Heterocycles

The photochemistry of the N-oxides of five-membered heterocycles shows, at least in part, an analogy to the photochemistry of nitrones. In no case was a fused oxaziridine isolated, but such a species might be an intermediate in the formation of lactams that are the main products. A typical example is offered by the photolysis of 3H-benzimidazole 1-oxides, which mainly yields benzimidazolones.[55-57] Similar photoprocesses are observed also in the monocyclic series, e.g., in the conversion of 1,2,4-triazole 4-oxides **39** into the corresponding 3-oxo derivatives.[58]



34 35 36

(15)



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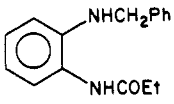

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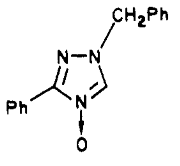
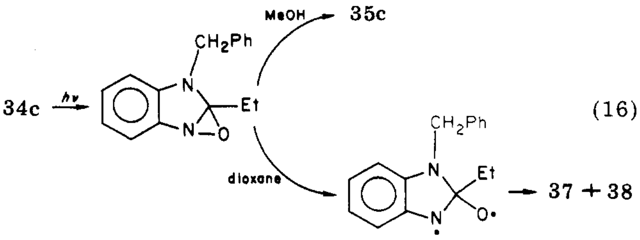


39

Besides the rearrangement to lactams, fragmentation is also observed. Thus, the benzimidazole N-oxide **34c**, while reacting in the normal way in methanol, yields mainly products **37** and **38** by irradiation in dioxane. The formation of the latter two compounds can be rationalized as involving homolysis of the intermediate oxaziridine followed by intra- or intermolecular hydrogen abstraction.[57] A related fragmentation was reported to occur on photolyzing some tetraarylimidazole N-oxides, with stereospecific formation of the Z,Z-diimines **40**.[59] In this case, however, the process was rationaized as a $\sigma^2 + \sigma^2 + \pi^2$ cycloreversion from the intermediate oxaziridine, taking place concertedly,



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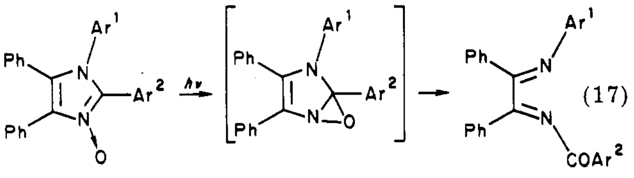


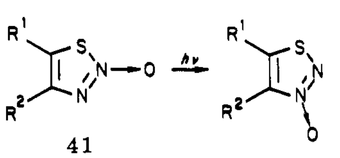
(17)

(68/75%)
40

Ar^1 = Ph, *p*-MeC_6H_4, *p*-$MeOC_6H_4$, *p*-ClC_6H_4, *p*-BrC_6H_4
Ar^2 = Ph, *o*-MeC_6H_4, *p*-$MeOC_6H_4$

rather than through a multistep process. An analogous process of ring cleavage is observed from 3-hydroxybenzimidazole 1-oxides, with formation of *o*-nitrosoanilines, which are in situ oxidized to the corresponding nitro derivatives.[60]

A second group of photoreactions from five-membered heterocycle *N*-oxides includes 1,2 oxygen migration, e.g., the formation of benzotriazole 2-oxides from the corresponding 1-oxides[61] or the rearrangement of the thiadiazole **41** to **42**, which is facilitated in the presence of Cu^{2+} salts.[62] In this case, too, the intermediacy of an oxaziridine has been proposed.

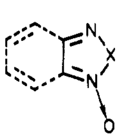


(18)

41

42

A third group of reactions is characteristic of furoxans and their chalcogen analogues (**43**).[63] These compounds undergo photochemical, as well as thermal, positional isomerism of the *N*-oxide function, accompanied in some cases by deoxygenation. The symmetric intermediate **44** has been hypothetized,[64] but these rearrangements probably involve reversible cleavage of the heterocyclic ring to form the corresponding ortho-substituted benzene derivatives **45**. Flash photolytic and matrix studies have shown the actual formation of the unstable derivatives **45** (X = S, Se).[64-67]



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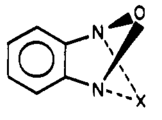

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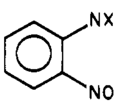


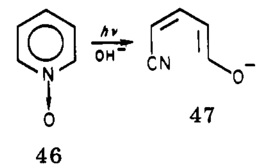
45

X = O, S, Se

IV. Azabenzene N-Oxides

A. Oxygen Shift and Fragmentation

Both in pyridine and diazine *N*-oxides one of the main photoprocesses is the shift of the oxygen to the carbon atom in the α-position, accompanied by cleavage of the N–Cα bond. A typical example is offered by pyridine *N*-oxide itself. Although several studies had led to the isolation of only minute amounts of characterizable products,[5] from which it was obviously difficult to reach mechanistic conclusions, it was recently shown that in basic aqueous solution the photolysis of **46** yields quantitatively the anion **47**.[68,69] Analogously, in the presence of secondary amines, added either before or after the photolysis of the solution, the conjugated nitriles **48** are obtained.[70] Previously, it had been shown that the irradiation of pyridine *N*-oxide in the presence of N^a,N^b-dimethyltryptamine affords analogously the nitrile **49**.[71]



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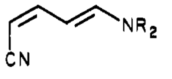
46 47



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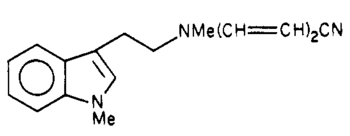

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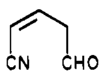

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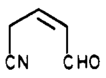
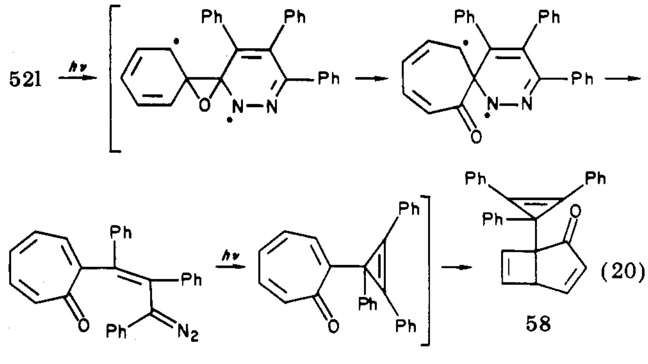


51

On the basis of these results, Buchardt suggested that, in the absence of bases, unsaturated nitriles such as **50** and **51** are formed and that the low yield of characterizable products obtained are due to the easy polymerization of these compounds.[68] Indeed, in the absence of bases intractable tars containing nitrile groups (as shown by IR absorption) are obtained predominantly. It is likely that the same main photochemical process is obtained also from several pyridine *N*-oxide derivatives, such as the alkyl derivatives, from which low yields of tractable products and high yield of tars also were obtained.[5]

Pyridazine *N*-oxides react analogously (Scheme VI). The oxygen atom migrates exclusively towards the carbon atom and not towards the nitrogen atom in position 2 so that diazo derivatives **53** are formed, as demonstrated spectroscopically.[72] The further evolution of compounds **53** follows different pathways. In general a further photochemical step leads to carbenes, which then cyclize to the furans **54** or to the cyclopropyl ketones **55**.[72-76] The latter compounds can be trapped in situ with amines to yield the pyrroles **57**.[73] However, if R^4 = Ph and in favorable conditions (flow absorbed intensity, low temperature) the diazo derivative has a chance to cyclize before undergoing photolytic decomposition, and the pyrazoles **56** are obtained.[72] Table V shows that chemical yields are low from alkylpyridazine *N*-oxides, but that they are high with pyridazine *N*-oxides carrying aryl substituents or substituents of strong electronic effect, such as OH or OMe. From the *N*-oxide **52i**, 3-cyanopropanal, thought to arise from a further rearrangement of the expected 2-aminofuran (**54i**) is obtained,[74] while from **52l** product **58** is obtained together with the expected furan **54l**. The mechanism



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58

SCHEME VI

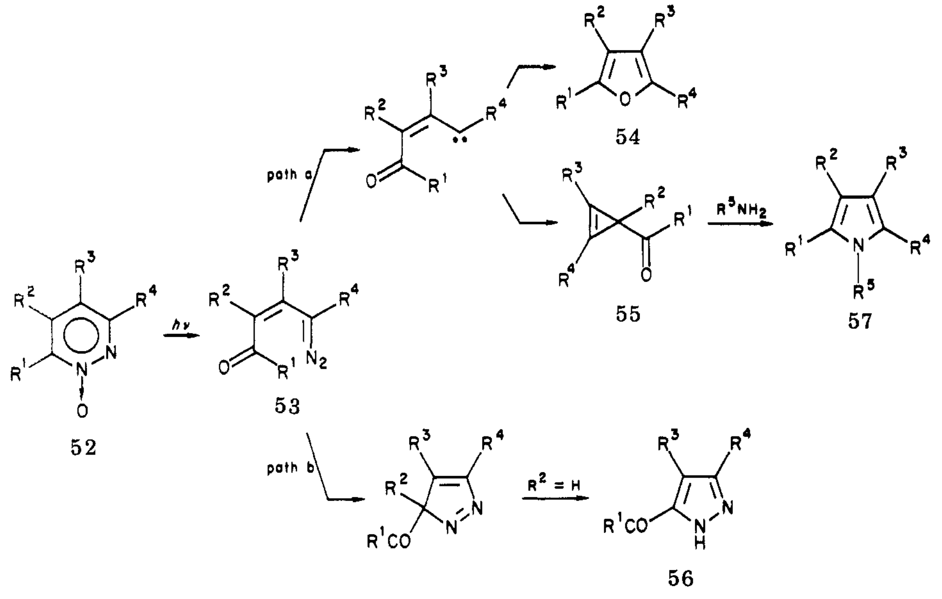


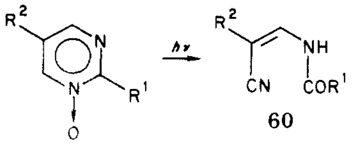
TABLE V. Photolysis Products of Pyridazine N-Oxides

	starting material				solvent	yield of products, %			ref
	R^1	R^2	R^3	R^4		54	55	56	
52a					CH_2Cl_2	5-10[a]	8-10		73, 74
b				Me	CH_2Cl_2	5-10[a]	8-10		74
c			Me		CH_2Cl_2	5-10[a]	8-10		74
d	Me				CH_2Cl_2	5-8	10		73, 74
e	Me			Me	CH_2Cl_2	5-8	10		73, 74
f				Ph	CH_2Cl_2	40-50			74[c]
g				OMe	CH_2Cl_2	40-50			74[c]
h				OH	CH_2Cl_2	50-55[b]			74[c]
i				NH_2	CH_2Cl_2				74[c,d]
j	Ph			Ph	Me_2CO	6		48	72
j					Me_2CO/C_6H_{12}	67		27	72[e]
j					EtOH	43			72[f]
k	Ph		Ph	Ph	Me_2CO	25[h]	9		75[g]
l	Ph	Ph	Ph	Ph	Me_2CO	30[h]			75, 76[g,i]

[a] Isolated as the adduct with N-phenylmaleimide. [b] As the tautomeric β,γ-butenolide. [c] Deoxygenation amounting to 20-30% is also observed. [d] Cyanopropanal is obtained in 3-4% yield. [e] By irradiation with a more powerful lamp. [f] By irradiating at −65 °C. [g] Deoxygenation amounting to 15% is also observed. [h] Total yield of the furan and its photooxygenation products, viz. *cis*- and *trans*-dibenzoylstilbenes. [i] Product 58 (see eq 26) is obtained in 25% yield.

proposed is a variation of the one discussed above, as it involves shift of the oxygen atom and of a ring residue before fragmentation to yield a diazo derivative.[75,76]

In the case of pyrimidine N-oxides (59), the photorearrangement takes place analogously with selective migration of the oxygen atom towards C_2 and not C_6 and formation of the 3-(acylamino)acrylonitriles 60[77-80] (Table VI). In several cases, 4-acylimidazoles are also obtained (see section IIIB). In that case, the oxygen atom migrates towards C_6.



59 60 (21)

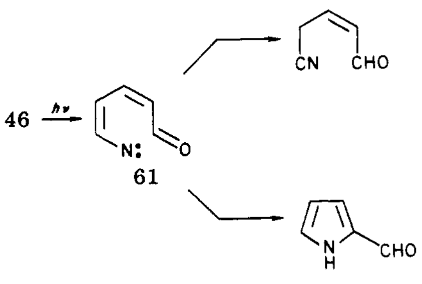
B. Formation of 2-Acylpyrroles and Analogues

This process could be classified as a variation of the ring cleavage discussed in section IVA if it is admitted that in both cases the nitrene 61 is the intermediate (see e.g., ref 79, 81). In the case of pyridine N-oxide it has

TABLE VI. Photolysis Products of Pyrimidine N-Oxides

	starting material		solvent	product 60, %	ref
	R^1	R^2			
59a			benzene	21	77, 78
b	Me		benzene	2.5	77[a]
c		Me	benzene	22	77, 78
d	NH_2		MeCN	64	77
e	OMe		MeCN	11	80[a]
f		OMe	MeCN	11	80[b]

[a] 4-Formylimidazoles are also obtained. [b] 4-(carboxymethyl)imidazole is obtained as the main product.



(22)

TABLE VII. Photolysis Products from Some 2-Substituted Pyridine *N*-Oxides[81]

starting material, R		yield of products, %[a] 63	64
62a	Me	19.5 (0.25)	8.5 (0.75)
b	Ph	3.5 (1)	
c	OMe	10 (10)	2 (3)

[a] Yields in the presence of Cu^{2+} salts. In parentheses the yields in the absence of the salt.

TABLE VIII. Formation of 4-Acylimidazoles (66) by Photolysis of Pyrimidine *N*-Oxides

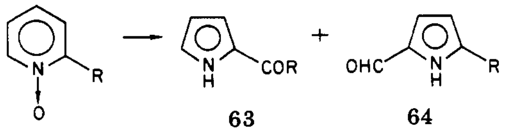
	starting material					
	R^1	R^2	R^3	solvent	yield, %	ref
65a		Me	Me	MeOH	28	83
b		Ph	Me	MeOH	17	83
c	Me	Me	Me	MeOH	15	84
c				benzene	53	84
d	Me	Cl	Me	benzene	56	84
e	Me	OMe	Me	MeOH	53	84

TABLE IX. Formation of 1,3-Oxazepines by Photolysis of Pyridine *N*-Oxides

	starting material					
	R^1	R^2	R^3	solvent	yield 68, %	ref
67a	Ph		Ph	benzene	*a*	85
b	Ph	Ph		benzene	84-87	85
c	Ph	Ph	Ph	benzene	80	85
d	CN			CH_2Cl_2	30	82
e	CN		Me	CH_2Cl_2	16	82

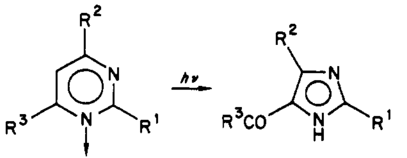
[a] Too unstable to allow isolation.

been noticed that the yield of 2-formylpyrrole is increased from 1–10% up to 40% in the presence of Cu^{2+} salts, and this has been taken as an evidence for the intermediacy of a nitrene.[81a] The effect of copper ions has been observed for several substituted pyridine *N*-oxides, with the exception of those carrying a methoxy group. Interestingly, in the 3-monosubstituted pyridine *N*-oxides, the oxygen migrates towards C_6 and not C_2, whereas in the 2-monosubstituted derivatives migration in both directions is observed.[81] See Table VII. This process is the main one in 2,6-dicyanopyridine *N*-oxide[82] and is observed as a minor pathway in several other pyridine *N*-oxides.



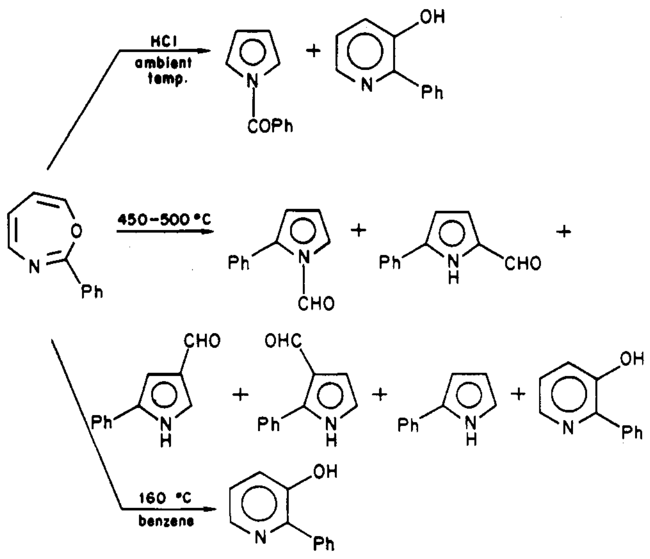
62 63 64 (23)

Several pyrimidine *N*-oxides undergo this type of rearrangement in good yield, with selective formation of 4-acyl- rather than 2-acylimidazoles.[83,84] See Table VIII.



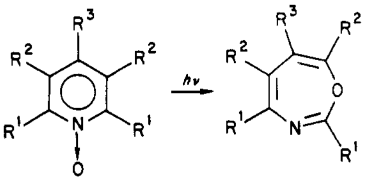
65 66 (24)

SCHEME VII

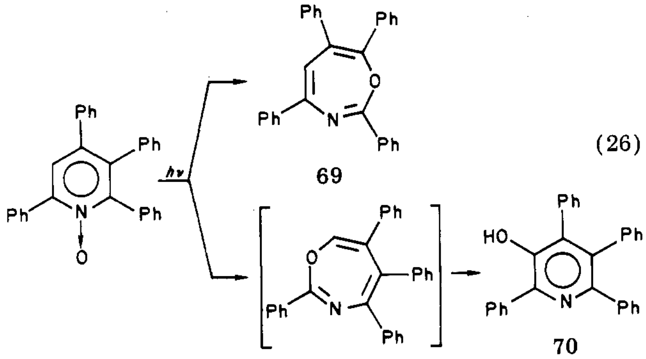


C. Ring Expansion

Ring expansion with formation of 1,3-oxazepine and analogues is observed only in a limited number of cases involving phenyl- or cyano-substituted azabenzene *N*-oxides.[82,85] Among phenyl-substituted pyridine *N*-oxides, **67a** gives only a low yield of **68a**, which was too unstable to allow purification, while **68b** and **68c** are obtained from the respective *N*-oxides in 80% yield (Table IX). From 2,3,4,6-tetraphenylpyridine *N*-oxide the oxazepine **69** and the hydroxypyridine **70** are obtained. The latter product could arise by rearrangement of the alternative oxazepine.[85]



67 68 (25)



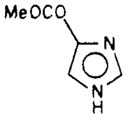
69 70 (26)

1,3-Oxazepines are generally unstable towards heat and acids. The decomposition of 2-phenyl-1,3-oxazepine (Scheme VII) has been studied in different conditions,[86-88] and determined to give, in different yields, 3-hydroxypyridine and the various benzoylpyrroles. As 3-hydroxypyridines, 1-acylpyrroles, and pyrroles, which could arise from the hydrolysis of the latter, are often obtained in low yield from the chromatography of the reaction mixture after photolysis of pyridine *N*-oxides,[5] it can be hypothesized that unstable oxazepines are formed, at least in low yield, also in those cases, and that they are decomposed during the workup. A related case is the formation of 3-phenyl-1,2,4-triazoles in 11–82% yields from the photolysis of some 6-phenyl-1,2,4-triazines 4-oxides, possibly through the intermediacy of oxatriazepines.[89] On the contrary, it does not appear likely that 2-acylpyrroles (see section IVB) are secondary products from 1,3-oxazepines. Indeed, 1,3-oxazepines are converted thermally into 2-acylpyrroles only under very drastic conditions[87] and they appear to be photochemically stable.[85]

D. Other Processes

Migration of the oxygen to the β-carbon atom is generally unimportant, an exception being the formation of the imidazole **71** as the main product (34% yield) from 5-methoxypyrimidine 1-oxide.[80]

Pyridones and analogue derivatives are often formed, particularly from pyrimidine *N*-oxides,[83-84] but in yield rarely exceeding 10%.[5] However, in the case of pyrazine-1,4-dioxide, a double rearrangement of this type takes place, yielding 2,5-dihydroxypyrazine (**72**).[90]



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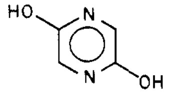
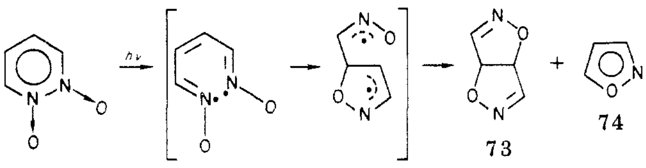


72

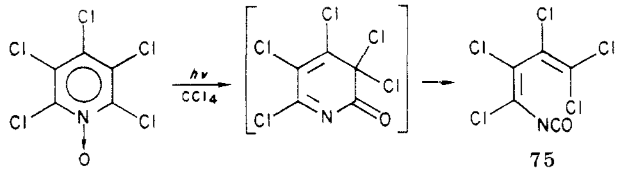
Pyridazine 1,2-dioxide undergoes a completely different photoprocess, with formation of 3,4-dihydroisoxazole-[4,5-*d*]isoxazole (**73**) and isoxazole (**74**, arising through a retrocyclization from the former). This process has been rationalized as involving initial homolysis of the N–N bond.[91-92]



73 74

(27)

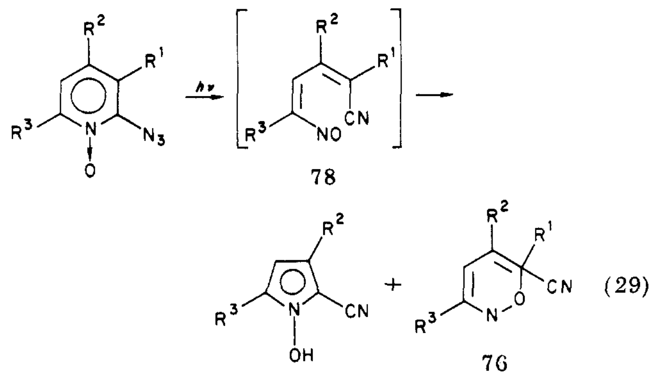
In the case of pentachloropyridine *N*-oxide, the normal migration of the oxygen atom to the position 2 is followed by cleavage of the C_2–C_3 bond, with formation of the isocyanate **75**.[93,94] The intermediacy of a 3*H*-2-pyridone has been postulated.



75

(28)

A different reaction is observed in the case of 2-azidopyridine *N*-oxides, which are photochemically transformed in good yield into 1,2-oxazines (**76**) or *N*-hydroxypyrroles (**77**), the latter products arising from further thermal reaction of the former.[95] This reaction, which has ample thermal analogy,[96-98] has to be considered a reaction of the nitrene formed from the primary photochemical act. This species is postulated to cleave to give the nitroso derivative **78**, which then undergoes electrocyclic rearrangement to **77**. Therefore, this reaction, as well as the photochemical decomposition of 4-azidopyridine *N*-oxide,[5] has to be considered a reaction of the azido function rather than of the *N*-oxide function.



78

77 (R^1 = H) 76

(29)

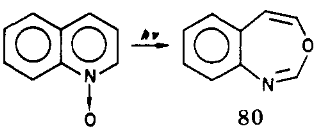
R^1, R^2, R^3 = H or Me

V. Azanaphthalene N-Oxides

The photochemical reactions of azanaphthalene *N*-oxides are generally better characterized than the reactions from azabenzene *N*-oxides, as the products are generally more stable—at least relatively—and chemical yields are higher. Furthermore, three general processes account for the large majority of observed reactions and the influence of the irradiation conditions has been more fully investigated.

A. Ring Enlargement

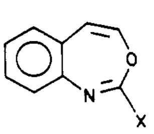
The most frequent photoprocess from azanaphthalene *N*-oxides in aprotic solvents is the ring enlargement to form benzoxazepines and their aza analogues. The photochemical method is surely the most practical synthesis available for this class of heterocycles. Care must be taken, however, due to the sensitivity to moisture of many of these compounds. Thus, e.g., the irradiation of quinoline *N*-oxide leads to a complex mixture unless it is carried out in rigorously anhydrous conditions. In that case and by avoiding chromatography, a 50% yield of pure 3,1-benzoxazepine is obtained by means of extraction and distillation. Product **80** can be stored indefinitely in the absence of moisture.[99]



79 80

(30)

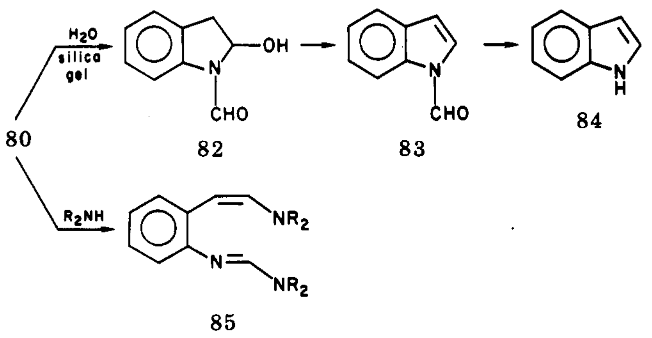
When substituents having a strong electronic effect or extending the conjugation are present in position 2, 3,1-benzoxazepines (**81**) are much more stable and chromatographic purification is possible. These products can be obtained from the corresponding



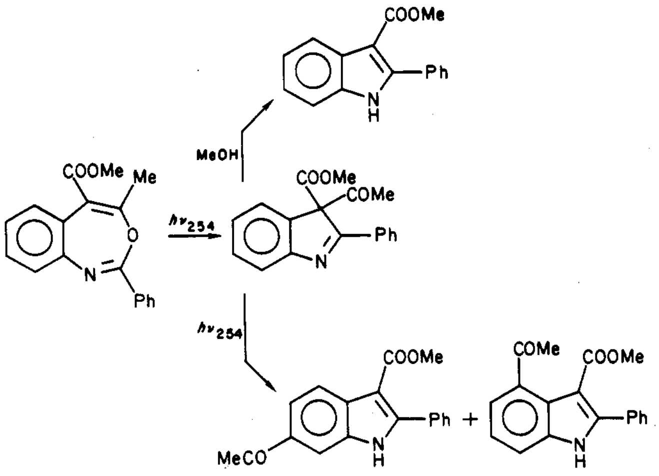
81

X = Ph,[5,100] CN,[5,100] MeO,[101] CF_3,[102] PhCH=CH[103]

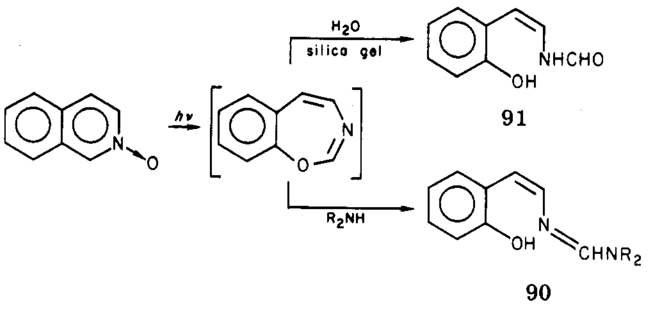
SCHEME VIII



SCHEME IX



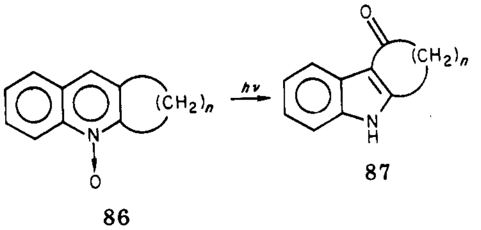
SCHEME X



quinoline *N*-oxides in yields from 70 to 90%, sometimes on irradiation in both protic and aprotic solvents.[5,100–103] 3-Phenylquinoline *N*-oxide also yields 80% of the corresponding benzoxazepine,[5] but usually the stabilizing effect is only observed when the substituents are in position 2.

In the absence of these stabilizing substituents, acid- and silica gel-catalyzed water addition is facile. Thus, chromatographic work up of the irradiation mixture from quinoline *N*-oxide yields 2-hydroxyindoline-1-carboxaldehyde (**82**) and lesser amounts of products **83** and **84**, which arise from further reaction of **82** (Scheme VIII). The same results are obtained by chromatography of purified **80**. Other nucleophilic additions are possible. Thus, with amines, ring cleavage to form **85** is observed.[99] 2-Cyano-3,1-benzoxazepine behaves differently, in that silica gel or, in general, Lewis acids cause rearrangement to 2-cyano-3-hydroxyquinoline.[5]

As for the photochemical behavior, it has been noticed that overirradiation causes a much lower yield of 3,1-benzoxazepine.[104] More precisely, it has been shown that a series of 3,1-benzoxazepines is stable towards Pyrex-filtered light, but rearranges on irradiation at 254 nm yielding 3-acylindoles (Scheme IX).[105] Further irradiation causes detachment (in protic media) or migration (in inert media, a photo-Fries rearrangement) of the acyl group.[106,107] The total process offers a valuable entry into some classes of substituted indoles. 3-Acylindoles are in other cases obtained without isolation of an intermediate oxazepine.[108] In the case of the quinoline *N*-oxides **86**, the yield of the 3-acylindoles **87** is 60–80% when $n = 3$, but it is only 10% when $n = 4$. In the latter case, a 1-acyl-2-hydroxyindoline analogue to **82** is the main product.[109] The mechanistic conclusions that have been drawn on this basis appear to be questionable, as it has been shown recently that 1-acylindoles (**88**) are photochemically converted into compounds **89**.[110]



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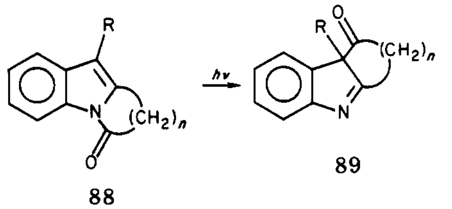
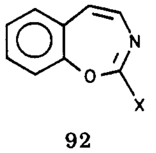


(32)

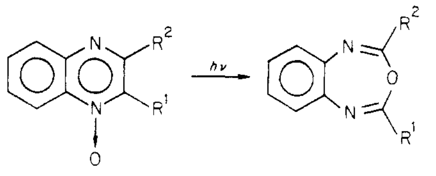
An analogous situation is found in the case of isoquinoline *N*-oxides, which are converted into 1,3-benzoxazepines (Scheme X). The parent compound has not been isolated, possibly because the diene part of this heterocycle makes it too susceptible to rapid polymerization. However, its formation has been deduced from the efficient trapping with amines to yield product **90**.[99] Chromatography of the irradiation mixture leads, in analogy to the case of quinoline *N*-oxide, to hydrated products, such as the phenols **91**, which, however, are themselves rather unstable, due to oxidation and polymerization processes, so that even the yield of secondary products is rather low.[99,111] In some cases, the action of acids on the irradiation products leads to indoles. Thus, 1-(alkoxycarbonyl)-4-hydroxyindoles can be prepared from 5-((alkoxycarbonyl)amino)isoquinoline 2-oxides by irradiation in aprotic solvents, followed by acid treatment.[112a] Substituents with strong electronic effects, when present in position 2, make 1,3-benzoxazepines much more stable, so that they are obtained from the corresponding isoquinoline *N*-oxides in yields of 55–90%.[5,101,102,112b]



92

X = Ph,[5] CN,[5] MeO,[101] CF_3[102]

Among diazanaphthalene *N*-oxides the reactivity is more differentiated, some of them, e.g., cinnoline and phthalazine *N*-oxides, not undergoing any ring enlargement. Quinoxaline *N*-oxide reacts in a different way, but its methyl derivatives **93** do yield 3,1,5-benzoxadiazepines, which are rather unstable.[113] Again, a cyano group in position 2 or a phenyl group in position 2 or 4 make these seven-membered heterocycles much more stable.[5] Finally, 4-phenylquinazoline 3-oxide has been found to yield the corresponding 1,3,5-benzoxadiazepine.[114]



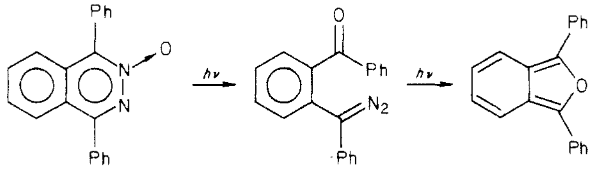
93

R^1, R^2 = H, Me

(33)

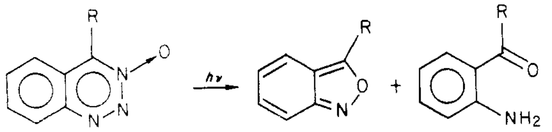
B. Ring Cleavage

Ring cleavage is less common among azanaphthalene than azabenzene *N*-oxides and the examples are mainly found among diaza- or polyazanaphthalene *N*-oxides. Two types of processes can be recognized, the first involving shift of the oxygen to the carbon atom in the α-position and cleavage of the N–C_α bond, analogously to what was seen for azabenzene *N*-oxides in section IVA. Thus, 1,4-diphenylphthalazine 2-oxide is directly converted into the diazo ketone **94** which then loses nitrogen to yield compound **95**.[72] The same mechanism is probably operative in the case of benzotriazine 3-oxides, from which the main products are anthranils (**96**, in 80–95% yield) together with the amino ketones **97** (ca. 5%).[115]



94 95

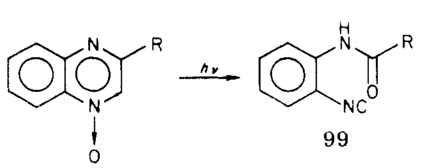
(34)



R = Me, Et 96 97

(35)

A different process of ring cleavage is found in the case of quinoxaline *N*-oxide. In this case, oxygen shift to the atom in the β position and cleavage of the C_α–C_β bond is observed. The reaction does not involve the intermediate formation of 3,1,5-benzoxadiazepine[113] and is the main process also from the methoxy derivative **98b**[113] and the carbamate **98c**,[116] although in the latter case a different mechanism has been invoked (Table X). The isonitriles **99** are rather unstable, so that secondary processes, such as water addition to yield the diamides **100** or intramolecular attack to yield the benzimidazoles **101** are usually observed. In addition to quinoxaline *N*-oxides, this type of cleavage is observed also from 3-methoxyquinoline *N*-oxide, which yields **102**,[101] a fact which seems to point to a particular influence of the methoxy group in position 3 (cf. ref 98b).

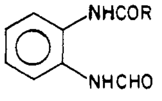


98 99

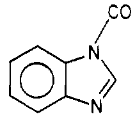
(36)

TABLE X. Formation of the Isonitriles 99 by Photolysis of Quinoxaline *N*-Oxides

starting material, R		solvent	yield, %	ref
98a		C_6H_{12}	65	113
b	OMe	C_6H_{12}	80	113
c	NHCOOMe	CH_2Cl_2	100	116



100



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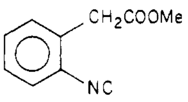
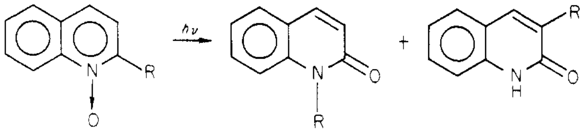


102

C. Rearrangement to Lactams

Rearrangement to lactams is the ubiquitous photoprocess from azanaphthalene *N*-oxides in protic media. Thus, with a few exceptions (see below), quinoline *N*-oxides are converted into carbostyrils with 70–100% yield in protic media, while a certain amount of these products is obtained also in aprotic media (ca. 10% from the parent compound, but the yields are greater from some of its derivatives, reaching 60% from 2-bromo- and 2-chloroquinoline *N*-oxides[5]). The group originally in position 2 migrates concurrently to the nitrogen atom and to the carbon atom in position 3. A study with the 2-deuterio derivative **103** (R = D) shows that, in water, migration to C_3 clearly predominates, while in aprotic media the two processes occur with almost equal probability.[117] With R = Me the two migrations are observed with similar yields,[5,108] while with R = Ph this kind of rearrangement has been observed only from 4-carboxy-2-phenylquinoline *N*-oxide, in which case the phenyl group migrates exclusively to C_3.[108] The chloro, bromo, and MeC_6H_4S groups migrate only to the 3-position,[5] while with R = COOMe the substituent is eliminated with formation of carbostyril,[5] a reaction which might involve migration of the substituent to the nitrogen atom followed by hydrolysis during the workup. 2-Methoxy-, 2-cyano-, 2-trifluoromethyl-, and 2-phenylquinoline *N*-oxides (with the exception seen above) do not rearrange to lactams, ring enlargement (see section VA) remaining the main process also in protic solvents.

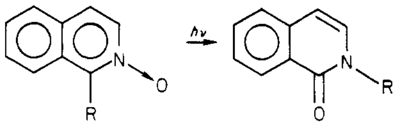


103

(37)

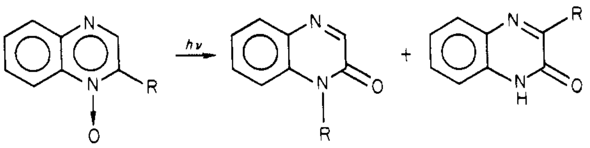
Overirradiation causes secondary photoprocesses from the carbostyrils, with formation of cyclobutane dimers, which usually crystallize out during the irradiation,[5] or ionic addition, e.g., of methanol,[118] or radical addition, e.g., of radicals formed from carboxylic acids.[119]

Isoquinoline *N*-oxides analogously give isocarbostyrils in medium-to-high yield in protic solvents.[5,100,111,112] From 1-alkyl-substituted isoquinoline *N*-oxides (with Me, $PhCH_2$, PhMeCH groups), *N*-alkyl-substituted isocarbostyrils are obtained.[111] 1-Methoxy-,[101] 1-phenyl-,[5] and 1-cyanoisoquinoline *N*-oxide[5] do not undergo this type of rearrangement.



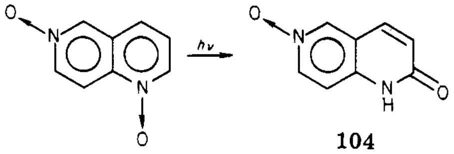
(38)

Among diazanaphthalene *N*-oxides, this process is documented from quinoxaline *N*-oxides, which behave analogously to quinoline *N*-oxides, with concurrent migration of alkyl substituents originally in position 2 to the nitrogen atom or to the carbon atom in position 3.[113] From some quinoxaline 1,4-dioxides it has been shown that the rearrangement takes place twice, yielding first quinoxalin-3-one 1-oxides and then quinoxaline-2,3-diones[120] (see, however, section VD for a different process). Notice that the irradiation of quinoxaline 1,4-dioxide in 0.5 N hydrochloric acid yields a chloroquinoxaline 1-oxide, with apparent substitution of a OH with a Cl group.[121]



(39)

In the case of 1,6-naphthyridine 1,6-dioxide only the oxygen atom in position 1 migrates, yielding the lactam **104**.[122]

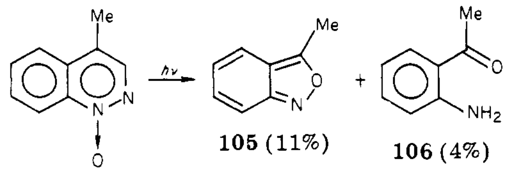


(40)

104

D. Other Photoprocesses

The photoprocesses considered in the previous sections account for the large majority of the reported reactions. Unless the formation of 3-acylindoles (see section VA) is considered to be an independent rather than a secondary process, only a few reactions remain to be considered, the main group being formed by elimination reactions from polyazanaphthalene *N*-oxides having vicinal nitrogen atoms. Thus, 4-methylcinnoline 1-oxide gives in low yield products **105** and **106**, with formal loss of HCN.[123] The former process is analogous to the nitrogen elimination from phthalazine and benzotriazine *N*-oxides (cf. eq 35). The isomeric 4-methylcinnoline 2-oxide yields products **107**, **108**, and **109** with formal loss of CO, NO, and N_2, respectively.[123] The formation of products **107** and **109** can be understood as involving the intermediacy of the 3*H*-benzopyrazole derivative **110**, thus making this reaction a variation of the process discussed in section IVB. Product **108** could result from the decomposition of a nitroso derivative and indeed there is evidence that a nitroso derivative is an intermediate in the analogous photochemical decomposition of the benzotriazine 3-oxide **111** which gives product **112**.[115]



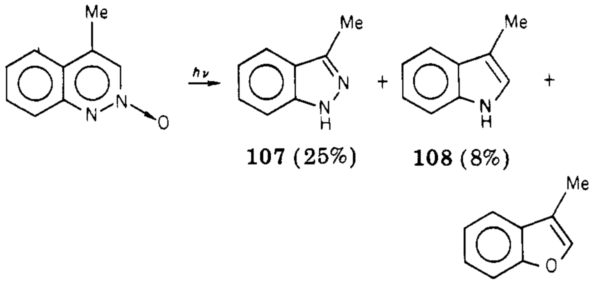
(41)

105 (11%) 106 (4%)

TABLE XI. Formation of Benzimidazolones 113 by Photolysis of Quinoxaline 1,4-Dioxides in Methanol

starting material			
R^1	R^2	yield	ref
Me	CH_2Ph	25	120
Ph	CH_2Ph	29	120
CH_2Ph	COPh	9	120
Ph	$COC_6H_4X^a$	40-62	124

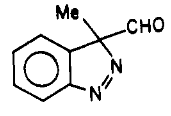
[a] X = *o*- or *p*-Me, OMe, NO_2, Br.



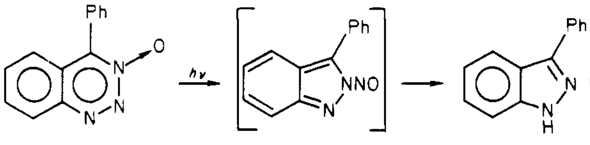
107 (25%) 108 (8%)

(42)

109 (1%)



110

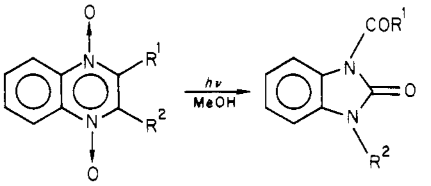


(43)

111 112

Finally, a characteristic reaction of quinoxaline 1,4-dioxides is the photorearrangement to *N*-acylbenzimidazolones **113**.[120,124,125] See Table XI. This process does not involve previous rearrangement of one of the *N*-oxide functions to give a quinoxalin-3-one 1-oxide, because these compounds, when formed, rearrange differently (see section VC). Though the mechanism remains unclear, this reaction appears interesting from the preparative point of view.

(41)



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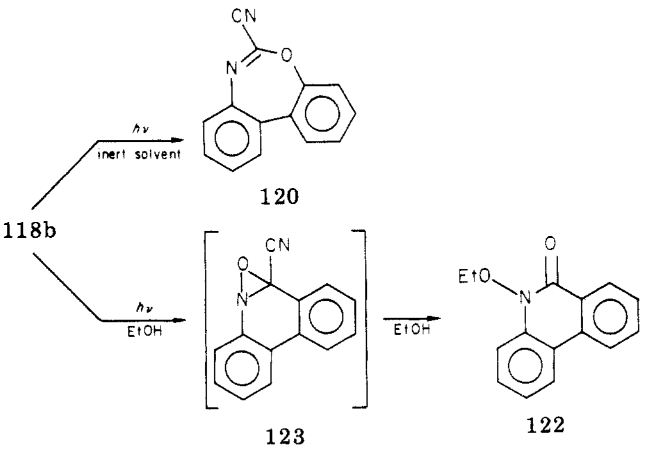
VI. Azaphenanthrene N-Oxides

The photochemical reactions reported for azaphenanthrene *N*-oxides are analogous to the two main

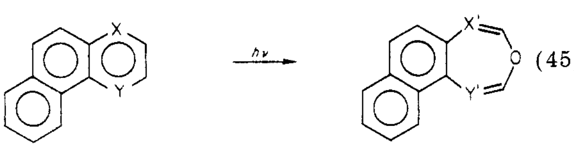
SCHEME XI



processes observed for azanaphthalene N-oxides (see section VA and VC).

A. Ring Enlargement

Both 1-azaphenanthrene and 4-azaphenanthrene N-oxides (**114** and **115**) undergo ring enlargement to the naphthoxazepines **116** and **117**, respectively, by irradiation in aprotic solvents.[126] These naphthoxazepines



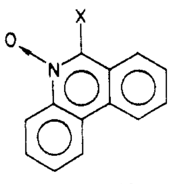
(45)

114, X = N→O; Y = CH
115, X = CH; Y = N→O

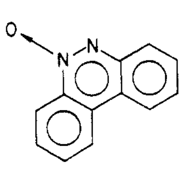
116, X' = N; Y' = CH
117, X' = CH; Y' = N

are more stable than 3,1-benzoxazepines, but they are analogously hydrolyzed on silica gel to give N-formylhydroxyindolines, the benzo analogues of compound **82**.

However, neither 9-azaphenanthrene N-oxide (or phenanthridine N-oxide, **118a**) nor benzo[c]cinnoline N-oxide (**119**) undergoes photochemical ring enlargement, the former rearranging only to the corresponding lactam also in aprotic solvents, the latter undergoing only photodeoxygenation.[5,126] 6-Alkylphenanthridine N-oxides behave like the parent compound, but 6-phenyl-[5] and 6-cyanophenanthridine N-oxides[127] do rearrange to the corresponding dibenzoxazepines **120**.



118a, X = H
b, X = CN
c, X = Me
d, X = CHMePh



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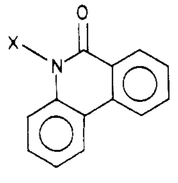


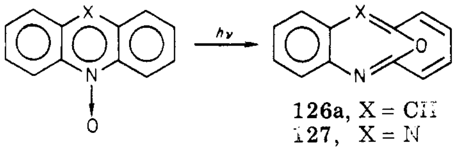
121

B. Rearrangement to Lactams

The rearrangement to the corresponding lactams takes place in high yield by irradiation of the N-oxides **114**, **115**, and **118** in protic media.[5,126] Alkyl or phenyl groups originally in the 6-position of phenanthridine N-oxides migrate to the nitrogen atom, yielding **121**. When an N-oxide carrying a chiral substituent has been studied, it was determined that the migrating center loses its configuration.[5] Although the N-cyano derivative **121b** is formed as a minor product in aprotic solvents, the photolysis of **118b** (Scheme XI) in ethanol does not yield the lactam but the N-ethoxy derivative **122**, which has been rationalized as arising from the solvolysis of the intermediate oxaziridine **123**.[127]

VII. Azaanthracene N-Oxides

There are no reports about the photochemistry of 1- and 2-azaanthracene N-oxides, which would be expected—at least at a naive guess—to behave similarly to quinoline and isoquinoline N-oxides, respectively. On the contrary, the photochemistry of acridine and phenazine N-oxide (**124** and **125**) has been explored extensively. Several types of photoprocesses have been recognized, which are generally different from those observed from azanaphthalene N-oxides. Thus, ring enlargement to form 1,3-oxazepines is observed only as a minor process from some acridine N-oxides[128,129a] and in trace amounts from phenazine N-oxide.[130] Phenazine N,N'-dioxide is reported to undergo this type of rearrangement, but the product identification is somewhat ambiguous.[129b] Notice that in the case of azaanthracene N-oxides, this type of rearrangement involves the loss of aromaticity of two benzene rings, which is only partially compensated for by the formation of the probably planar annulene system of compounds **126** and **127**. Nor is any process comparable to the quinoline N-oxide–carbostyril rearrangement observed.



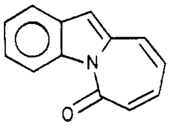
(46)

124a, X = CH
125, X = N

126a, X = CH
127, X = N

A. Ring Contraction and Ring Cleavage

The photochemical reaction which usually predominates in aprotic solvents is ring contraction to acylindoles (**128**–**130** from **124**[128,129a,131]) or acylbenzimidazoles (**131** from **125**[130]), respectively. A comparison with the photochemistry of other N-oxides shows that the formation of 2-acylindoles has ample analogy, in particular in the photochemistry of azabenzene N-oxides (section IVB), while the formation of 1-acylindoles from the irradiation of quinoline N-oxides is generally understood as a secondary process from the primary products, the benzoxazepines.



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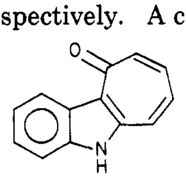

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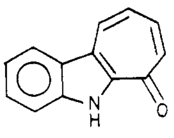

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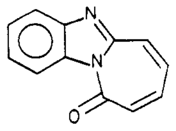

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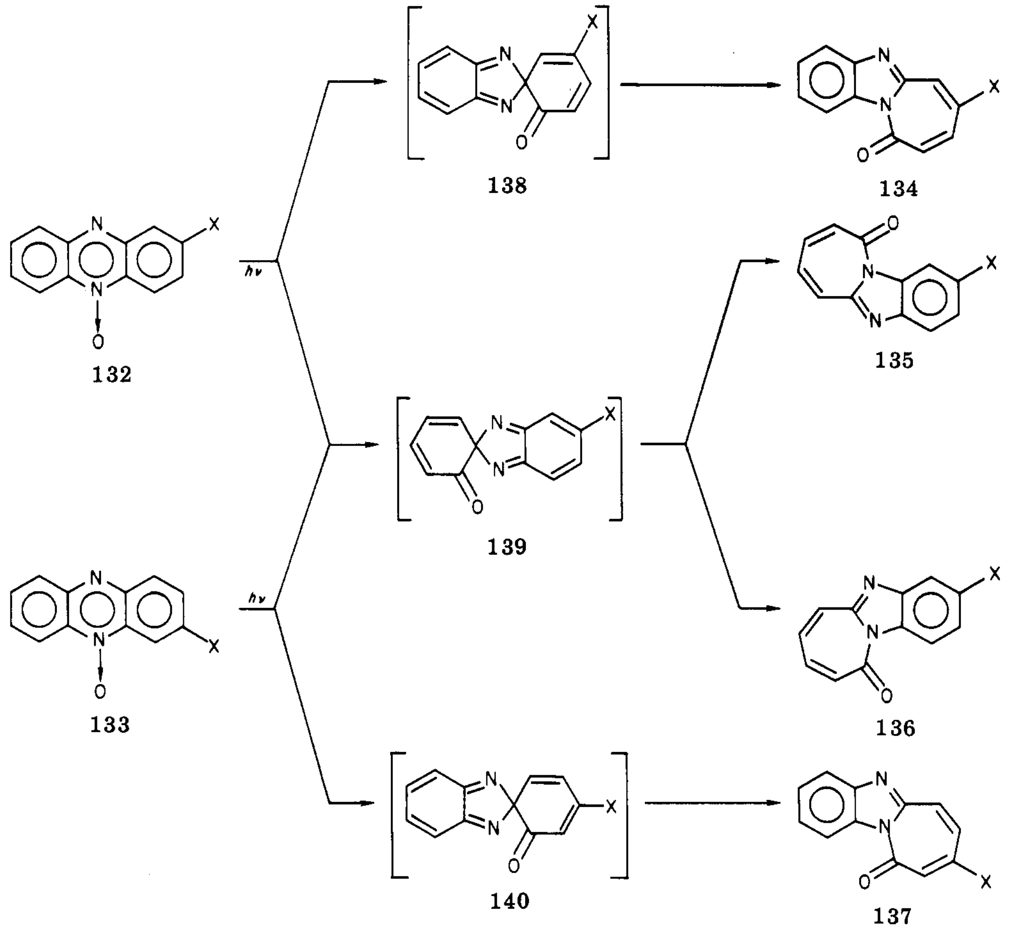
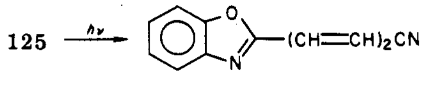
SCHEME XII



Whichever the mechanism might be in the present case, the intermediacy of the oxazepines **126** and **127** has to be excluded. On the contrary, the study of suitably substituted derivatives has shown that one of the carbocyclic rings is rotated out of the original molecular plane during the rearrangement. Thus, comparing the results from pairs of monosubstituted phenazine 5-oxides, it has been shown that from the 2-substituted *N*-oxide **132** the acylbenzimidazoles **134** to **136** are obtained, while from the isomeric *N*-oxide **133** the products are compounds **135** to **137**, the yields of products **135** and **136** being in the same ratio in both cases (Scheme XII).[132] This finding implies that the oxygen migration is accompanied by rotation of one ring, which at some stage becomes perpendicular to the original molecular plane. The configuration taken during the rearrangement is shown in the scheme by means of the spiro derivatives **138**–**140**, which need not however to be considered well-defined intermediates. The study of disubstituted acridine *N*-oxides had previously led to similar mechanistic conclusions.[128,129a]

A different process involving the cleavage of the heterocyclic ring has been reported in the case of phenazine *N*-oxide, viz. the rearrangement to the benzoxazole **141**.[130] The exact mechanism of this reaction

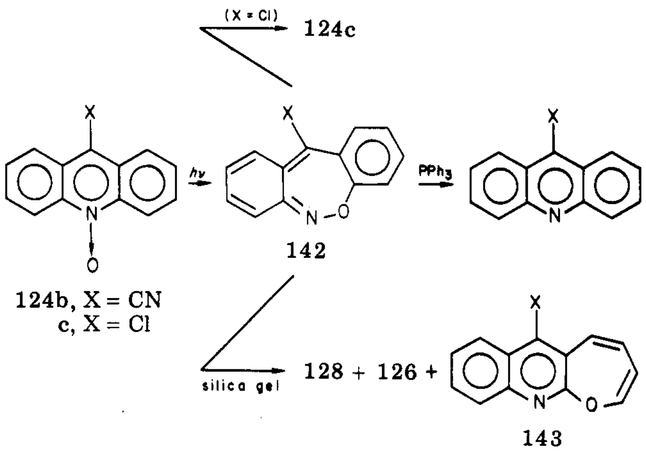


(47)

141

is not known, but it might be noticed that this is the only case, besides the quinoxaline *N*-oxide–isonitrile rearrangement, in which the heterocyclic ring is cleaved between the C_α and C_β atoms.

SCHEME XIII

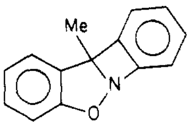


B. Ring Enlargement

While, as it has been discussed above, 1,3-oxazepines are only minor products from this class of *N*-oxides, a different ring enlargement process has been observed from several acridine *N*-oxides, this time leading to 1,2-oxazepines. These products are valence tautomers of the benzo[*b*]oxaziridines often invoked as intermediates in *N*-oxide photorearrangement (Scheme XIII). From 9-cyano- and 9-chloroacridine *N*-oxides, the corresponding dibenzo-1,2-oxazepines (**142**) have been obtained as stable products[133,134] while from 9-methylacridine *N*-oxide and from the parent compound it has been shown spectrophotometrically that similar derivatives are formed as intermediates.[134]

The chemical properties of these 1,2-oxazepines are relevant to the photochemistry of acridine *N*-oxides. Thus, in one case, thermal reversion to the original *N*-oxide has been observed to take place, reasonably via the tautomeric oxaziridine. Furthermore, these compounds are easily deoxygenated to the corresponding acridine, also via the oxaziridine, and, when chromatographed on silica gel, are rearranged to compounds such as **128**, **126**, and **143**, i.e., the same type of products that are obtained from the irradiation, and following chromatography, of all acridine *N*-oxides (see section VIIA and VIIC). This has led to the hypothesis that 1,2-oxazepines can be the general intermediates in the photochemistry of acridine *N*-oxides, further evolving by cleavage of the N–O bond to yield spiro derivatives which are analogues to compounds **138**–**140** and from them to products such as **128** and **130**, or by further oxygen migration via the tautomeric oxaziridine to yield, e.g., **126** and **143**.[131,133,134]

Another secondary process from the not isolated 1,2-oxazepines is the (probably photochemical) electrocyclic rearrangement to dibenzo[*c,f*]-2-oxa-1-azabicyclo[3.2.0]hepta-3,6-diene (**144**) observed in the case of some methylacridine *N*-oxides.[129a,181] To the reaction of the solvent with a 1,2-oxazepine has been ascribed also the formation of 11-alkoxy-5,11-dihydrodibenzo[*b,e*][1,4]oxazepines (**145**) by irradiation of acridine *N*-oxide in alcohols. The study of some disubstituted derivatives has shown that during the formation of compound **145** rotation of one carbocyclic ring had taken place.[129a]



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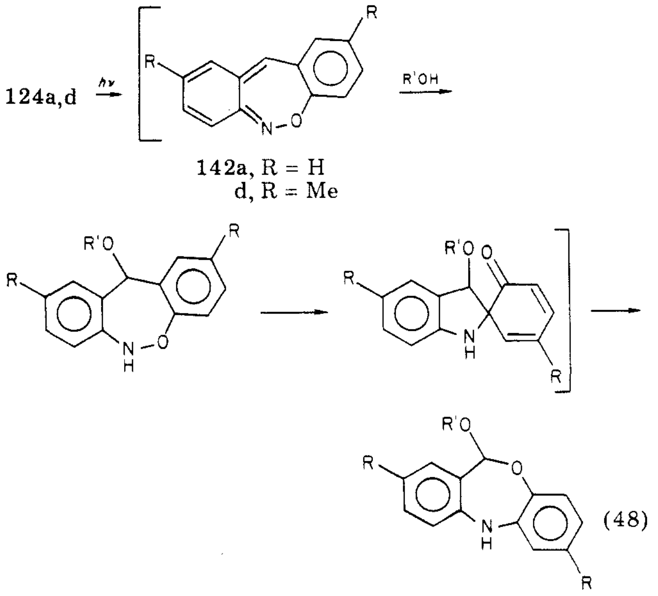
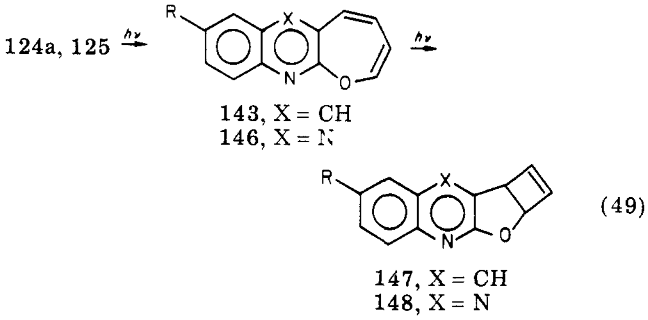


142a, R = H
d, R = Me

145

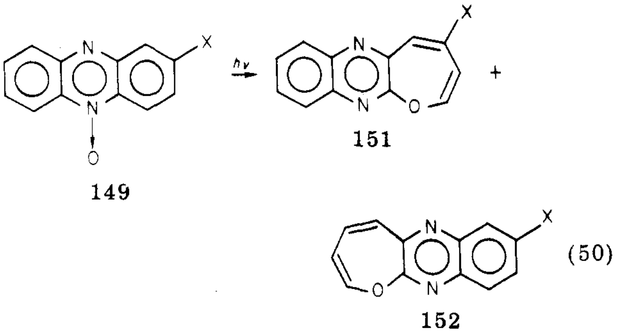
C. Oxygen Migration to the Neighboring Ring

An important process from both acridine and phenazine *N*-oxides is the oxygen migration to the neighboring ring to form oxepinoquinolines and oxepinoquinoxalines, respectively (**143** and **146**). If the irradiation of the *N*-oxide is carried out to complete consumption, these products are often not isolated as such, as they undergo an efficient secondary photochemical rearrangement to yield products **147** and **148**. Whether or not the rearrangement to **143** and **146** involves the intermediacy of an oxaziridine followed by 1,9-sigmatropic shift of the oxygen atom is speculative, but it has been shown that, contrary to the ring contraction process discussed in section VIIA, the molecular plane in this rearrangement is conserved and the oxygen atom migrates only to the two neighboring peri atoms.[128,129a] Thus, e.g., from the monosubstituted phenazine *N*-oxide **149**, the oxepinoquinoxalines **151** and **152** are obtained, while from the isomeric *N*-oxides **150**, the products are **153** and **154**.[132] Analogous conclusions have been reached for the mechanism of the analogous rearrangement from acridine *N*-oxides.[128,129a]



143, X = CH
146, X = N

147, X = CH
148, X = N



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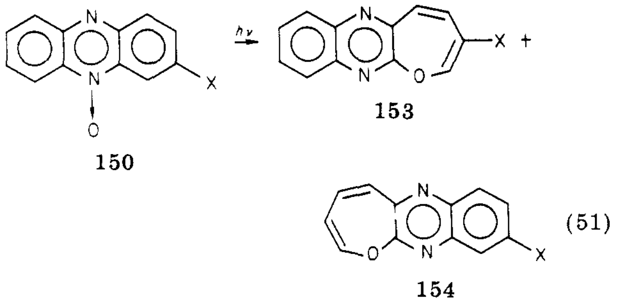
151

152



150

153

154

X = Cl, OMe

Similar to what was found in most of the previously discussed cases, the photochemical reactivity of azaanthracene *N*-oxides is strongly solvent dependent. In general, it can be said that ring contraction to acylindoles or benzimidazoles predominates in aprotic solvents, while rearrangement to oxepinoquinolines and, when observed, 1,3-oxazepines predominate in protic solvents, with the additional complication that different processes involving solvent addition are observed during the irradiation of some acridine *N*-oxides in alcohols (Table XII).

TABLE XII. Solvent Effect on the Photolysis of Azaanthracene *N*-Oxides

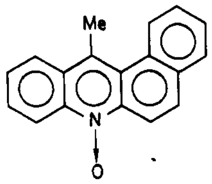
starting material	substituents	solvent	yield of products, %						ref
			126	**142**	**143**	**144**	**145**	**128-130**	
124a	none	benzene						57	129a
		MeCN-H_2O	12		30			3	129a
		MeOH					80		129a
124d	2,7-dimethyl	benzene	6-9		8-13			55-57	128
		MeOH	19		50		7	2	128
124	2,7,9-trimethyl	benzene	2		10	7		33	129a
		MeOH	15		56			2	129a
124b	9-cyano	benzene		59	3			9	133, 134
			127	**146**	**148**		**131**	**141**	
125	none	benzene	*a*	9	*a*		65	7	130
		MeOH		9	2		18	5	130[b]
125	2-chloro	MeCN			low		37		132
		MeCN-H_2O			42		low		132
125	3-chloro	MeCN			low		51		132
		MeCN-H_2O		6	25		low		132

[a] Traces. [b] Deoxygenation amounting to 25% is also observed.

VIII. Other Heterocyclic N-Oxides

A. Tetracyclic Aromatic *N*-Oxides

Some *N*-oxides with the skeleton of benz[*a*]anthracene and tetracene have been investigated from the photochemical point of view. As for benz[*a*]acridine *N*-oxide (**155**)[135] and benzo[*a*]phenazine 7-oxide (**156**),[136] the main process is, similar to that found for azanaphthalene *N*-oxides, ring enlargement to 1,3-oxazepines, accompanied by other rearrangements in lesser yield. The oxygen atom migrates toward the naphthalene rather than the benzene ring, a fact which might be related to the lesser loss of aromaticity. The product distribution from the irradiation of **156** in ethanol is shown in eq 52 (the yields in acetonitrile are not much different). Most of the compounds shown can be considered primary photoproducts as the annulene **157** is photochemically stable on irradiation with Pyrex-filtered light, although irradiation at 254 nm causes further reaction, with shift of the oxygen atom.[136]



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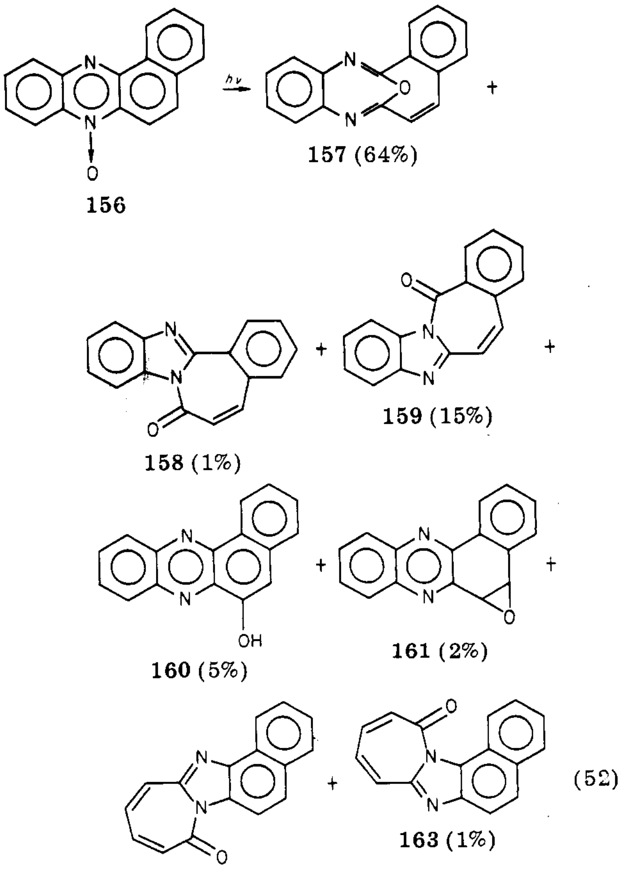
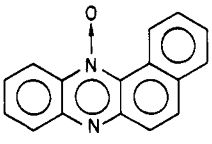


(52)

In the case of benzo[*a*]phenazine 12-oxide (**164**), however, migration toward the benzene ring to give the ring contraction products **162** and **163** (in 25 and 20% yield, respectively) takes place concurrently with migration toward the naphthalene ring, which gives the annulene **157** (30% yield).[135] Finally, benzo[*b*]phenazine *N*-oxide (**165**) has not been found to undergo photochemical rearrangement, the only consequence of irradiation being deoxygenation.[104]



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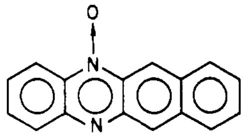

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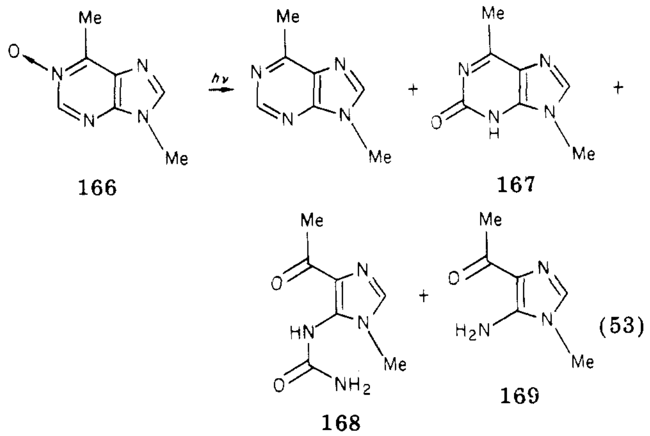
B. Purine *N*-Oxides

Previous studies show that deoxygenation usually is the main photochemical reaction of purine *N*-oxides. However, in some cases photorearrangement also has been observed.[5,137-139a] Thus, 6,9-dimethylpurine 1-oxide (**166**) undergoes oxygen migration in both the possible directions yielding the lactam **167** and the ring cleavage products **168** and **169**.[140] The same type of process has been reported for 6-methylpurine 1-oxide; in this case, however, as well as in the case of purine 1-oxide itself, the product distribution is strongly pH dependent.[140]

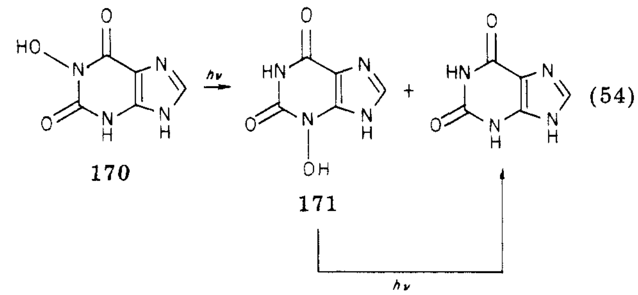
In general, an important problem when studying the photochemistry of purine *N*-oxides is to establish which tautomeric form absorbs the light and is in fact involved in the photoreaction. The problem is further complicated in the case of hydroxy- and aminopurine *N*-



166 167 168 169 (53)

oxides. In several cases, the reaction has to be ascribed to the N–OH rather than to the $N\rightarrow O$ function.

At any rate, some of these reactions have biological relevance, as in the case of the photorearrangement of the 1-hydroxyxanthine (**170**) to the carcinogenic 3-hydroxyxanthine (**171**),[141a] or preparative interest, as is shown in the synthesis of isoguanine nucleotides by photolysis of some adenine 1-oxides.[141]



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IX. *Photochemical Deoxygenation*

Deoxygenation is usually not the predominant process in the photochemistry of compounds containing the *N*-oxide function. However, this is a very common byprocess. Even if, in suitable conditions, photochemical deoxygenation can be made to become a quantitative process,[142,143] this can hardly be considered to have any synthetic advantage over the corresponding thermal methods, except in special cases, e.g., when it is desired to reduce the *N*-oxide group without affecting a nitro group also present in the molecule;[145] however, also in this case a selective thermal deoxygenation is possible.

Nevertheless, it is worthwhile to discuss in more detail this reaction, mainly under two aspects: (i) the relationship between deoxygenation and rearrangement with regard to the excited state implied and to the structural factors which favor one or the other pathway; and (ii) the mechanism of the oxygen transfer to the acceptor and the practical use of *N*-oxides for the oxidation of various substrates.

A. Deoxygenation vs. Rearrangement

Two interpretations have been given to the photochemical deoxygenation of *N*-oxides, namely (i) that analogously to the geometrical isomerization of nitrones it proceeds from the triplet state, while skeleton rearrangements proceed from the singlet state, or (ii) that both reactions are singlet and involve the same intermediate, an oxaziridine, which can both transfer an oxygen atom to the medium and rearrange further. Both hypotheses often have been presented, although direct experimental support (such as sensitization or quenching experiments in the first case or the ascertainment of the oxaziridine intermediacy and of its ability to transfer oxygen) is scarce, as it will be discussed in section X. Presently, the factors which affect the ratio of deoxygenation vs. rearrangement will be discussed.

TABLE XIII. Percent Yield of Photoreduction from Substituted Pyridine *N*-Oxides[81]

substituent	position of substituent		
	2	3	4
none	7		
Me	5		5
CN	23	25	5
OMe	0		0

TABLE XIV. Percent Yield of Photoreduction from Various Azabenzene *N*-Oxides

starting material	substituent	solvent	yield	ref
pyridazine *N*-oxide	none	CH_2Cl_2	20-25	74
	alkyl	CH_2Cl_2	25-35	73, 74
	phenyl	CH_2Cl_2	15-30	74-76
	alkoxy, hydroxy	CH_2Cl_2	20-30	74
pyrazine *N*-oxide	2,5-diphenyl	benzene	50	5
1,2,4-triazine 4-oxide	alkyl, phenyl	Et_2O	42-56	89

In some cases, an effect of the irradiation wavelength has been observed.[5,85] This might be related to a different intersystem-crossing yield from higher singlet to triplet states. The medium also plays a role with polar or protic solvents generally favoring deoxygenation. The yield in deoxygenation depends on the structure of the *N*-oxide. Although a comparison of studies carried out in different conditions can be misleading, it clearly appears that among heterocyclic *N*-oxides, electron-withdrawing substituents favor photoreduction. Thus, among pyridine *N*-oxides, a cyano group has a positive influence, a methoxy group a negative one (see Table XIII). Furthermore, 2,6-dicyanopyridine *N*-oxide reaches a 12% yield of photodeoxygenation in dichloromethane,[82] and yields of about 20% are observed when the carboxyl or carboxamide group are present.[144] From polyphenylpyridine *N*-oxides yields between 10 and 29% have been reported.[85] Aza substitution is also effective. Thus, while pyrimidine *N*-oxides, in which the second nitrogen atom has little electronic effect, do not differ appreciably from pyridine *N*-oxides, with at most some percent of deoxygenation,[5,77,80,84] pyridazine and pyrazine *N*-oxides are photodeoxygenated in much higher yields (Table XIV). These effects should be related to a change in the order of $n\pi^*$ and $\pi\pi^*$ excited states unless, in the light of the other hypothesis, they are related to a higher stability of the oxaziridine, which has thus more time to transfer oxygen to some substrate.

The idea that deoxygenation of heteroaromatic *N*-oxides is related to an $n\pi^*$ triplet state could find support in the lesser yield of this process from higher members of the series, in which the lowest triplet is probably $\pi\pi^*$. Thus, quinoline and isoquinoline *N*-oxides undergo practically no photoreduction, and the yields differ by only a few percent from those of their alkyl derivatives. However, the effect of substituents is also observed here, with yields of about 10% when

TABLE XV. Percent Yield of Photoreduction from Some Heterocyclic *N*-Oxides in the Presence of Acceptors

		solvent	
starting material	substituent	CH_2Cl_2 [a]	C_6H_6 [b]
quinoline *N*-oxide	none, alkyl		81-83
	2-phenyl	29	69
	3-phenyl		76
	4-chloro		85
	4-bromo		78
	2-cyano	88	
isoquinoline *N*-oxide	none		81
	1-cyano	78	
phenanthridine *N*-oxide	none	88	
	6-cyano	95	

[a] On irradiation in the presence of triphenylphosphine.[142] [b] On irradiation in the presence of boron trifluoride etherate.[143]

a phenyl and carboxyl group are present.[106] While a methoxy group in the heterocyclic ring has no effect,[101] photoreduction amounts to 40% from 6-methoxy-2-methylquinoline 1-oxide.[5] Two substituents may have a synergic effect, as is shown in the case of 4-methoxy-2-cyanoquinoline 1-oxide, which gives 80% of the corresponding quinoline.[5]

Among polyazanaphthalene *N*-oxides, the *N*-oxides of phthalazine,[72] quinolizine,[5] quinoxaline,[5,113] and benzotriazine[115] undergo little or no deoxygenation, while higher yields are obtained from cinnoline *N*-oxides, confirming the effect of two neighboring nitrogen atoms already noticed for pyridazine *N*-oxides. However, high yields (42% from 4-methylcinnoline 1-oxide and 58% from the corresponding 2-oxide[123]) are observed only in nitrogen-flushed methanol, the presence of oxygen lowering substantially the yields.

The same trend is observed in the *N*-oxides of azaphenanthrene and azaanthracene. Thus, deoxygenation is a minor process in phenanthridine *N*-oxides,[126] but it is the only photochemical process observed in benzo[c]cinnoline *N*-oxide,[5] and similarly deoxygenation of acridine *N*-oxides is almost negligible,[26,133] but phenazine *N*-oxide is deoxygenated with a 68% yield in nitrogen-flushed methanol[130] (but only 25% in oxygen-saturated methanol) and deoxygenation is the only photochemical process from nitrophenazine *N*-oxides.[146] Photodeoxygenation is the main process from purine *N*-oxides,[138-141,147-149] both in organic solvents, for molecules which are soluble enough to allow such a study (e.g., yields of 42–74% are reported from 7-methyl-1-hydroxyhypoxanthine[138]) and in water (at least when the neutral form or the cation are present, the yields at high pH being in general much lower). Triplet sensitizers enhance the yield.[138] Pteridine *N*-oxides behave similarly.[139a] Except for the purine *N*-oxides, the pH dependence of photodeoxygenation has been little investigated. Notice that in the case of 2-cyanoquinoline *N*-oxide, irradiation in acidified methanol leads to 6-methoxy-2-cyanoquinoline with simultaneous deoxygenation and solvent addition.[139b]

B. Chemistry of Oxygen Transfer from *N*-Oxides

Under suitable conditions, a high yield of the corresponding imine is obtained from the irradiation of *N*-oxides. The best acceptors are Lewis acids, such as boron trifluoride[143] and triphenylphosphine.[142] Amines, too, are effective in some cases.[146] As the same reagents are effective also for the thermal deoxygenation, the interest of the photochemical method is restricted to possible cases in which mild conditions are required.[145] See Table XV.

It is more interesting to consider the other side of the reaction, i.e., the use of *N*-oxides as photochemical oxidizers. Apart from the fact that the photochemical deoxygenation of heterocyclic *N*-oxides incorporated in polymeric chains has been found to be effective in initiating the cross-linking of acrylic polymers,[150] a large variety of substrates has been found to be liable to oxidation by means of *N*-oxides in photolytic conditions, including hydrocarbons, oxygenated derivatives, heterocyclic derivatives and other substrates.[71,156-164] See Table XVI.

The *N*-oxide is usually chosen among those more apt to photodeoxygenation, e.g., pyridazine *N*-oxides. However, when this point has been investigated, as it has been by using alkenes and aromatics as substrates, the product distribution has been found not to be much

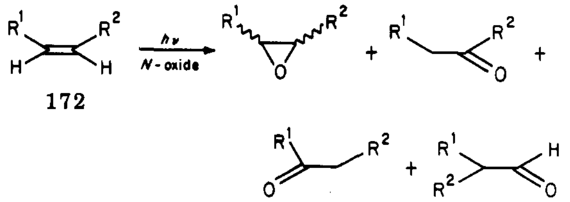

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TABLE XVI. Substrates Photooxidized by Heterocyclic *N*-Oxides

class	example	products[d]	*N*-oxide	solvent	ref
alkanes	cyclohexane	cyclohexanol	*a*	CH_2Cl_2	155
alkenes	*cis*-4-methylpent-2-ene	cis and trans epoxide	*b*	CH_2Cl_2	167
	trans-4-methylpent-2-ene	trans epoxide	*b*	CH_2Cl_2	167
	cyclohexene	epoxide and cyclohexanone	*a*, *b*	various	156-158
	styrene	epoxide and acetophenone	*b*	CH_2Cl_2	156
aromatics	benzene	phenol (30)	*a*	neat	155
	toluene	*p*-methylphenol (30)	*a*	neat	155, 167
	durene	tetramethylphenol (18), trimethylphenol (3)	*a*	CH_2Cl_2	159
	anisole	*p*-methoxyphenol	*a*	various	167
	naphthalene	1-naphthol	*b*	CH_2Cl_2	154, 167
	anthracene[e]	various phenols	*b*	various	161
alcohols	MeOH, EtOH	aldehydes	*b*	neat	
ethers	2-methyltetrahydrofuran	unknown	*c*	neat	163
epoxides	alkyl or phenyl epoxides	ketones (20-70)	*b*	CH_2Cl_2	164
sulfides	alkyl sulfides	alkyl sulfoxides	*b*	CH_2Cl_2	167
	phosphine sulfides	phosphine oxides	*a*	CH_2Cl_2	165
heterocycles	triptamine	epoxide	*b*	CH_2Cl_2	71, 166

[a] 3-Methylpyridazine 2-oxide. [b] Pyridine *N*-oxide. [c] 6-Cyanophenanthridine *N*-oxide. [d] Yields in parentheses. [e] Includes higher condensed hydrocarbons.

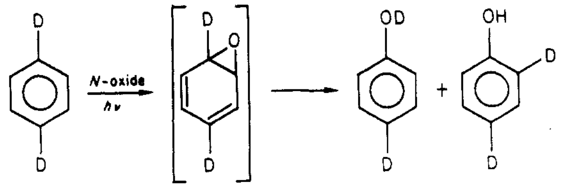
TABLE XVII. Percentage of Deuterium Retention by Photooxidation of the Benzene Derivatives 173

X	method[a] a	method[a] b	ref
Me	51, 59	54	165, 167
OMe	45, 49	60	165, 167
Cl	62, 64	54	165, 167
Br	49	40	167
$CONH_2$	28	30	167

[a] a, by photooxygenation with *N*-oxides. b, by microsomal oxidation.

influenced when the *N*-oxide is changed.[157,167] The action of *N*-oxides as photochemical oxidizers is remarkable both for its wide scope (notice, e.g., that simple alkenes are epoxidized, while thermally only electron-poor or strained alkynes[151,152] and isocyanates[153] react with *N*-oxides to give ylides) and for its specificity. In epoxides, oxygen is inserted in the C–O bond to give dioxetanes, which then cleave to ketones.[118]

From aromatics, benzene oxides are formed, which then rearrange to phenols (from naphthalene, 1-naphthol is obtained).[154] Due to this two-stage mechanism in the hydrogen atom originally linked to the attacked position in part shifts to the vicinal position, and thus starting from deuterated molecules the deuterium is found in part as exchangeable phenolic deuterium, in part linked to a vicinal carbon atom (N.I.H. shift[154,167]). See Table XVII. The interest lies in the fact that the same phenomenon is observed in microsomal oxidation, so that photochemical reaction with *N*-oxides can be considered one of the best models of biological oxidation. Thus, e.g., the percentage of deuterium retained in the phenols **174** prepared from the deuterated benzenes **173** by photooxidation or microsomal oxidation is remarkably similar.[165,167]



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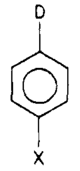

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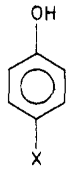

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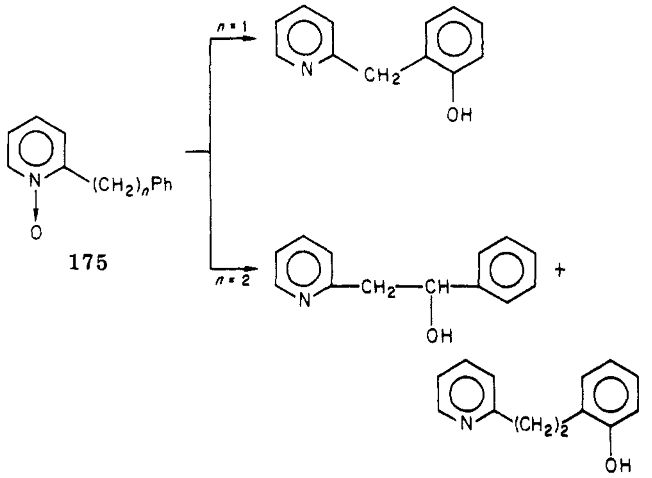
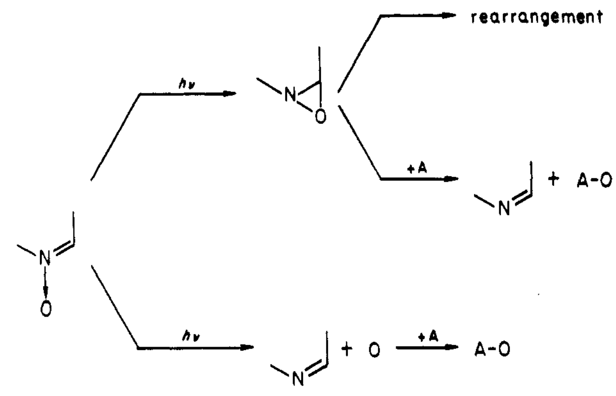
Oxygen transfer to the aromatic or benzylic position occurs also intramolecularly in suitably substituted *N*-oxides, e.g., from the pyridine *N*-oxides **175**.[53] See Scheme XIV. The yields are higher than in the intermolecular case, allowing the hypothesis that in this case oxygen is directly transferred via a five- or six-membered intermediate, analogously to what was found in the case of the azoxy to hydroxyazobenzene rearrangement (see section IID),[51] and that the same holds for the intramolecular oxygen transfer in the case of the nitrone **32** (see eq 14).[52] The photochemical reaction of compound **175** has a partial thermal analogy in thermal chemistry, as 2-methyl-, 2-ethyl- and 2-benzylpyridine *N*-oxides have been shown to eliminate OH· by flash vacuum pyrolysis yielding the corresponding 2-pyridinemethyl radicals.[168]

SCHEME XIV



SCHEME XV



For the general case the mechanism of the oxygen transfer has not been fully elucidated as yet. The ratio of deoxygenation vs. rearrangement has been found to depend on the acceptor concentration for several *N*-oxides in the case of the reaction with triphenylphosphine, 1.2 molar equivalents being sufficient to cause quantitative deoxygenation in the case of some phenanthridine *N*-oxides, but higher amounts being necessary in other cases.[142] This has been interpreted as an evidence for the involvement of an oxaziridine in the oxygen transfer (Scheme XV). This hypothesis has been considered also by other authors,[167] but it remains speculative to a certain extent, as the oxygen transfer from oxaziridines is not completely predictable, as some model compounds do transfer oxygen to some substrates, whereas from some other ones different reactions predominate (see section XD).

On the other side, the ratio of consumption of some pyridazine *N*-oxides and the amount of pyridazine formed have been found not to be affected by the presence of acceptors, although the yield of the oxidized products from the substrate does grow with the acceptor concentration. This has led to the opposite hypothesis that oxygen is liberated directly from the excited *N*-oxide (as atomic oxygen, "oxene") and then intercepted by the acceptor.[157] In another connection the liberation of oxygen as radical anion has been hypothesized.[150] The results obtained by photochemical oxidation with the *N*-oxides differ from those obtained with O (^3P) atoms, but evidence for the electrophilic character of the oxidizing species has been found.[160]

X. Mechanism of the Photoreaction

As has been shown in the previous sections, the *N*-oxide function exhibits a multifaceted photochemical reactivity. The primary photoprocess, understood as the one which leads to a ground-state product of reasonable stability, can be said to be clearly ascertained in the case of nitrones and azoxy derivatives. These compounds undergo electrocyclic ring closure to three-membered rings. These primary products have been isolated in a number of cases and the pathway of further reactions has been well characterized. On the contrary, heterocyclic *N*-oxides undergo various types of photoprocesses, several of which can be considered primary processes as no intermediates have been detected so far, although some other products are clearly recognized as arising from secondary processes. Thus, attempts to classify the entire *N*-oxide photochemistry under a common primary photoprocess cannot be said to be substantiated by the evidence available up to now. Considerable effort has been given by several groups to the elucidation of the mechanism, and the main points which have emerged will be discussed in the following sections.

A. Excited State Involved in the Photoreaction

It appears by now generally acknowledged that the rearrangement of the *N*-oxide group originates from the lowest singlet excited state. This conclusion is based upon some negative evidence, such as the failure to sensitize[100,169,170] or quench[171] the photorearrangement, as well as upon some positive evidence, viz., the demonstration that the primary photoprocess occurs at a much faster rate than the triplet decay[111,170] and that enhancement of the intersystem-crossing rate by inter- or intramolecular heavy atom effect lowers the rearrangement quantum yield.[169]

Although the above mentioned evidence is limited in number and scattered among different substrates and conditions, the recognition of the singlet character of the rearrangement appears convincing, as the *N*-oxide rearrangement, differently from the photodeoxygenation, is an ubiquitous process, generally observed under different experimental conditions, with little effect of dissolved oxygen.

The nature of the lowest excited state of heteroaromatic *N*-oxides has been discussed many times. Several groups have carried out calculations of the electronic absorption spectrum of pyridine *N*-oxide.[5,172-176] As it has been still recently confirmed, most semiempirical methods give a $n\pi^*(A_2)$ transition as the lowest in energy.[177] An easily distinguishable $n\pi^*$ band is generally not observed in *N*-oxides, but it could be submerged under a more intense $\pi\pi^*$ absorption band.[174] At any rate, even the lowest $\pi\pi^*$ state (B_2), which is predicted to be the lowest excited state by ab initio methods, has a strong charge transfer character from the oxygen atom to the aromatic nucleus.[178] This is reflected in the well-known blue shift undergone by the absorption spectrum in going from apolar to polar or protic solvents (see section XB).

N-oxides generally are only weakly emitting at room temperature in fluid solution. This fact, together with the high quantum yield of the photochemical reaction, makes the measurement of fluorescence spectra troublesome, at least with the lower members of the series. Azaanthracene *N*-oxides, however, fluoresce strongly, and emission was detected also from some methoxyazanaphthalene *N*-oxides.[169] The fluorescence is stronger in protic solvents, e.g., from phenazine *N*-oxide a fluorescence quantum yield of 0.17 in water and 0.012 in acetonitrile was measured.[179] A further increase is observed in acidic medium.[169] In the case of 6-cyanophenanthridine *N*-oxide, it was shown that fluorescence is also temperature dependent. In this case the emission, which is almost undetectable at room temperature, grows strongly at low temperature, while the contrary behavior is observed for the reaction quantum yield.[163]

An attempt to correlate the photochemical reactions observed with the characteristics of the singlet excited state has been made for a series of phenazine *N*-oxides, in which it has been shown that the *N*-oxides, which show a stronger solvatochromy of the absorption spectrum, and thus probably have singlet states of more pronounced charge-transfer character, rearrange mainly to products of type **131**, while those which show little solvatochromy rearrange mainly to products of type **146**.[180]

Positive evidence about the triplet state of *N*-oxides is also limited. Analogous to fluorescence, phosphorescence is generally very weak, and care is required to distinguish authentic phosphorescence from the *N*-oxide from the much stronger emission from the photoproducts. However, in the case of isoquinoline *N*-oxides the triplet state has been identified both by its emission[170] and T–T absorbance in flash photolysis[170,111] (τ 60 ms in EPA glass at 77 °C, 30 μs in methanol solution at room temperature[170]).

As for the chemistry of the triplet state, there is evidence for its involvement in the geometric isomerization of nitrones,[181,182] in the deoxygenation of nitrones (for which only high-energy sensitizers are effective, so that high lying triplet states rather than the lowest triplet are thought to be involved[16]), and in the deoxygenation of heteroaromatic *N*-oxides.[143,170,171,183,184] In several other cases deoxygenation from the triplet state has been suggested on the basis of the lower yield of deoxygenated products in oxygen saturated solvents (e.g., 33 vs. 47% from 2-cyanopyridine *N*-oxide,[171] 25 vs. 68% from phenazine *N*-oxide[130]), although this observation alone is obviously not conclusive. Furthermore, in the case of some quinoline *N*-oxides it has been shown that quenching by heavy atom containing anions enhance the intersystem crossing and lowers the rearrangement yield, once again showing that the triplet is not involved in the rearrangement.[169]

B. Influence of the Solvent

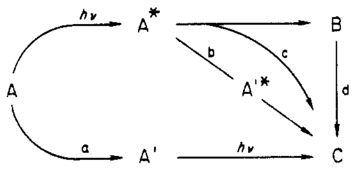
The problem of the excited state involved in the photoreaction is connected also with the influence of the solvent. Molecules containing the *N*-oxide function are strongly polar and easily form hydrogen bonds or complexes with protic species. As an example, complexes are formed with acids and water, which do not behave ideally, as has been shown by several spectroscopic investigations.[185,186] From the photochemical point of view the most interesting fact is the dramatic change in the product distribution generally observed

TABLE XVIII. Quantum Yield of the Photochemical Decomposition of Some *N*-Oxides

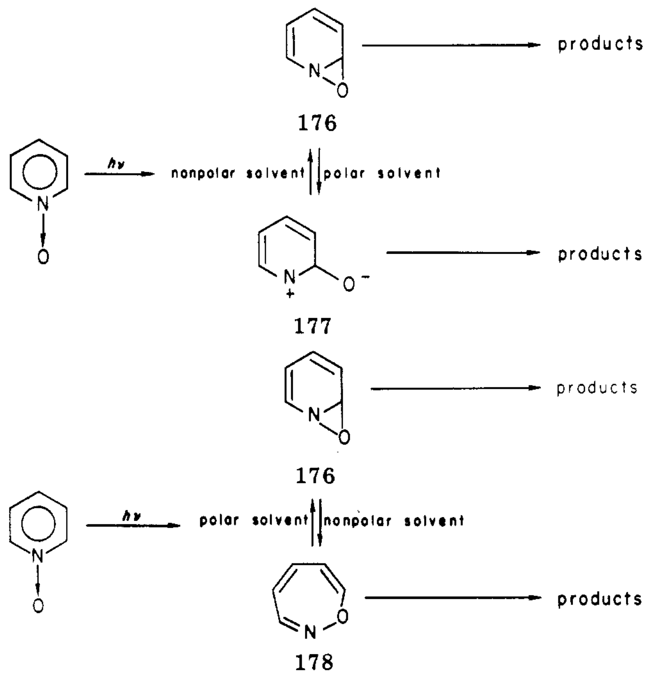
substrate[a]	ϕ_{dec}			ref
	C_6H_{12} or C_6H_6	EtOH or MeOH	H_2O	
α-(*n*-propyl)-*N*-cyclohexylnitrone	0.49	0.42		187
α-phenyl-*N*-methylnitrone	0.49	0.36		187
α,*N*-diphenylnitrone	0.52	0.36		187
pyridine *N*-oxide			0.10	104
quinoline *N*-oxide	0.30		0.20	104
2-phenylquinoline *N*-oxide	0.38	0.32		100
isoquinoline *N*-oxide	0.16	0.10	0.08	104, 100
quinoxaline *N*-oxide	0.39		0.18	104
2,3-dimethylquinoxaline *N*-oxide	0.31		0.32	104
1-azaphenanthrene *N*-oxide	0.33		0.16	126
4-azaphenanthrene *N*-oxide	0.22		0.03	126
phenathridine *N*-oxide	0.54		0.23	126
phenazine *N*-oxide	0.06		0.015	179

[a] Systematic names for the three nitrones: *N*-butylidenecyclohexanamine *N*-oxide, *N*-benzylidenemethanamine *N*-oxide, *N*-benzylidenebenzenamine *N*-oxide.

SCHEME XVI



SCHEME XVII



upon changing the solvent, particularly in going from aprotic to protic solvents, while the polarity of the medium usually has little effect as long as aprotic solvents are employed.

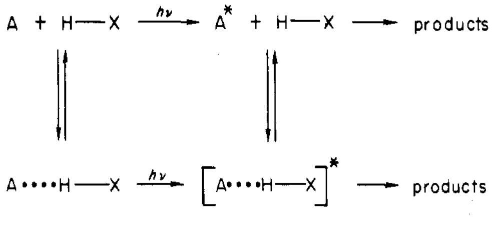
In principle, the interaction with the solvent which brings about the preference for the formation of product B (Scheme XVI) rather than product C can occur at different stages of the photoreaction starting from A: the solvent interacts (a) with the ground state of A, or (b) with the reactive excited state of A, or (c) at some stage during the conversion of A into the primary photoproduct, or (d) with the primary product itself, which is thus influenced in its further reaction.

As has been previously discussed, in several instances the primary photoproducts react with protic solvents, and thus the products that are actually isolated arise from some thermal reaction after the initial photochemical step, as is the case of indole from the photolysis of quinoline *N*-oxide. This case (case d) should be easily distinguishable by means of an accurate chemical analysis. At any rate, most mechanistic discussions of the photochemistry of *N*-oxides lend more importance to the last steps, i.e., it is felt that the "photophysical" part of the process (steps a and b) remains unaffected, while the solvent interacts at some later stage, either influencing the reactivity of an unstable intermediate or influencing the evolution of the chemical system before the attainment of a minimum of energy, the distinction between the two possibilities (cases c and d) being troublesome when the stability of the postulated intermediate is not known (see further discussion in section XC). Examples of this kind of reasoning are the rationalization of the effect of the solvent polarity as affecting the equilibrium between the oxaziridine **176** and the corresponding zwitterion (**177**)[5,117] or between oxaziridine and 1,2-oxazepine (**178**).[128] See Scheme XVII.

However, in a number of cases it has been recognized that the influence of protic solvent on the photochemical reaction is due to an interaction with the ground or excited state of the *N*-oxide, before chemical reaction. As for the extreme case of protonation in the ground state, it has been shown for a series of quinoline *N*-oxides that the protonated form is photochemically stable, while exhibiting strong fluorescence and phosphorescence.[169] Particularly interesting is the case of 4-methoxyquinoline *N*-oxide, which is considerably less basic in the excited ($pK_S = 0.8$) than in the ground state ($pK = -2.4$), and has been shown to undergo deprotonation before decay of the excited state, so that the plot of the reaction quantum yield vs. pH shows two drops in the correspondence of the two pK values. The fluorescence quantum yield changes in the contrary way.[169]

Formation of a hydrogen bond with the solvent is also of major importance. The strength of the hydrogen bond, like basicity, is lowered on excitation, and the existence of a hydrogen-bonding equilibrium in the fluorescent state has been demonstrated for the case of acridine *N*-oxide.[188] Formation of the hydrogen bond influences both the total photochemical quantum yield, which is generally higher in aprotic than in protic solvent for heterocyclic *N*-oxides, but changes little for

SCHEME XVIII



nitrones, and the yield of the different products (Table XVIII).

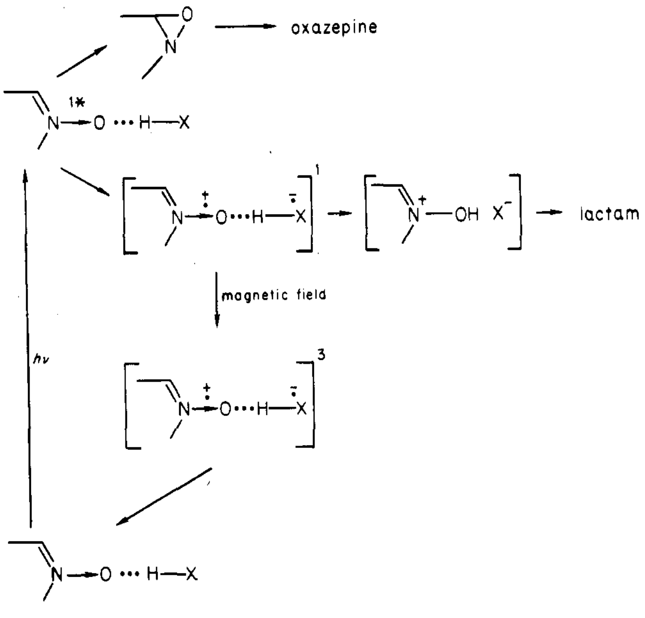
The quantum yield of isocarbostyril from isoquinoline *N*-oxide sharply increases on adding small amounts of methanol to a benzene solution,[100] and under these conditions a dramatic blue shift of the absorption band shows the formation of the hydrogen bond. In other cases, the hydrogen bond is less stable, and absorption spectrum and product distribution change less sharply. Thus, the quantum yield for the formation of the acylbenzimidazole **131** from phenazine *N*-oxide gradually drops on adding water to an acetonitrile solution, closely matching the variation of the absorption spectrum.[179]

These and analogous observations have led to the hypothesis that the hydrogen bond is retained in the excited state (Scheme XVIII) and influences the reaction of the latter towards different products. Hata has postulated that hydrogen-bonded *N*-oxides undergo charge transfer and that it is the excited protonated form that gives rise to the products found in protic solvents.[100] This rationalization disagrees with the reported photochemical stability of the cationic form of *N*-oxides;[169] however, the concept of the formation of a closely tight couple of radical ions is useful for the understanding of the magnetic field effect. Indeed, it has been found that an external magnetic field decreases the yield of isocarbostyril from isoquinoline *N*-oxide, but has no influence upon the yield of benzoxazepine from 2-cyanoquinoline *N*-oxide.[189,190] The first reaction is due to the hydrogen-bonded, charge-transfer singlet state, which undergoes an enhanced intersystem crossing to the (unreactive) triplet state in the presence of the magnetic field, while the latter process is thought to occur from the free *N*-oxide via the oxaziridine, and thus is not influenced by the magnetic field (Scheme XIX). When various alcohols were used, it has been shown that the value of the applied magnetic field which is effective in promoting the intersystem crossing is a function of the pK_a of the alcohol, thereby supporting the above rationalization.[191]

C. Mechanism of the Rearrangement

The exact understanding of the mechanism of the photorearrangement of *N*-oxides cannot be said to have been reached as yet. In the case of nitrones and aliphatic azoxy derivatives the situation has been clarified and the primary photoprocess has been recognized in the electrocyclic rearrangement to three-membered rings. The disrotatory pathway predicted by the Woodward–Hoffmann rules cannot be established from the stereochemistry of the products, as one of the extremes of the dipolar system is an oxygen atom. However, stereospecificity or stereoselectivity with reference to the substituent on the nitrogen atom have been observed in a number of cases (see section IIA) and a

SCHEME XIX

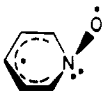


rationalization on an intuitive basis has been given[13] (on the other hand, among thermal cycloadditions of nitrones stereospecificity also has been observed[192,193]).

About the propensity of the rearrangement to occur from the excited rather than from the ground state, it has been calculated for a series of nitrones that there is an increase in the O–C_α π bond order in the singlet excited state and that the larger this change is, the larger is the reaction quantum yield.[187]

The situation is much more involved in the case of heterocyclic *N*-oxides, as in this case the products that are actually isolated have undergone a profound skeletal rearrangement, and this has prompted the search for intermediates, in order to decompose the reaction into a series of simple steps. Analogy with nitrones obviously suggests oxaziridines as intermediates.[194] Semiempirical MO calculations show a situation similar to that of nitrones. Thus, Kaneko has shown that the oxygen atom and the α-carbon atom have opposite sign in the ground state, but the same sign in the excited state. Furthermore, when the two α-carbon atoms are different (e.g., quinoline, isoquinoline, and phenanthridine *N*-oxides) migration occurs toward the carbon atom with the larger coefficient in the excited state.[196] In other cases, it has been shown that different semiempirical methods give contrasting predictions.[195] Kobayashi, while unsatisfied with the criterion of the atomic coefficients, finds that the calculation of the variation of the π bond order in the excited state correctly predicts the sense of the migration for the previously mentioned *N*-oxides as well as for 1,6-naphthyridine *N,N'*-dioxide and 1,6-phenanthroline *N,N'*-dioxide.[122]

Apart from the plausibility of an oxaziridine as intermediate, which will be discussed below, it is important to notice at this point that this approach postulates that excitation induces no change in the geometry of the molecule, which remains planar. This, however, is unlikely to be true. Indeed, the fact that from the singlet excited state both chemical reaction and internal conversion take place in high yield, while fluorescence and, as far as it is known, intersystem crossing to the triplet are very inefficient, suggests that a severe distortion occurs on excitation. This fits well with the nπ* or CT character of the singlet state, which causes an important loss of aromaticity, and thus probably loss of planarity, e.g., to reach a conformation similar to **179**.



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Indeed, when no charge transfer is possible, e.g., in the protonated form of *N*-oxides, fluorescence and intersystem crossing become major processes at the expense of the photochemical reaction.[169] It can be noticed that, at least judging from the case of 6-cyanophenanthridine *N*-oxide, the photochemical rearrangement requires a small activation energy.[163]

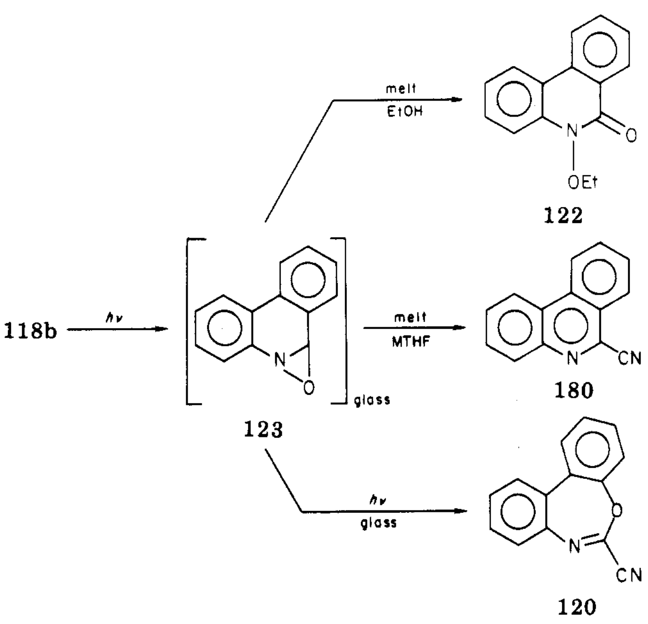
From the above observations about the geometry of the excited state, it follows that, a fortiori, no MO calculation of this kind can be taken as an indication of the effective pathway of the reaction (cf. ref 196). On the other side, a detailed calculation like that carried out for the oxaziridine–formamide conversion,[197] is still a difficult task for such complicated molecules as heterocyclic *N*-oxides.

D. The Search for the Intermediate

The hypothesis that an oxaziridine is primarily formed during the photorearrangement of *N*-oxides is attractive and simple, as it allows the understanding of the different processes as occurring through a common, photochemically "allowed" step (a step involving "two full arrows" in Kaneko's terminology, which is another way to express the generalized Woodward–Hoffmann rules[198]) followed by a series of different thermally allowed ("three full arrows") steps. There is little doubt that at some point during the rearrangement the oxygen atom is found between the nitrogen and the carbon atom, but it is still debatable whether there is a minimum of energy corresponding to the oxaziridine configuration, which is thus a real intermediate—at least in principle isolable—and has to be considered the primary photoproduct as the ground state is reached at this point, or the potential energy drops without encountering the ground-state surface or any minimum along the way until the end product configuration is reached. In the latter case, obviously, there is no intermediate, whichever intermediate configuration is taken during the rearrangement.

Among the evidence in favor of the oxaziridine intermediacy, there is the direct isolation in matrix of the oxaziridine **123** from the photolysis of 6-cyanophenanthridine *N*-oxide (**118b**) (Scheme XX). In this case, the UV spectrum obtained after irradiation of a glassy solution at 77 K and subtraction of the part due to the residual starting material is different from the spectrum of the known photolysis products obtained at room temperature. On melting the glass, product **122** is formed in ethanol and the deoxygenated product **180** in 2-methyltetrahydrofuran (MTHF).[163] Even at room temperature in ethanol solution, it is observed that a single laser flash does not yield **122**, more flashes being required.[199] Furthermore, irradiation of **123** in the glass yields product **120**, which is directly obtained by photolysis at room temperature. This kind of evidence clearly shows the presence of some intermediate along the reaction pathway. The attribution of the oxaziridine structure to this intermediate appears reasonable, although the spectroscopic characterization is limited to a differential UV spectrum. As for the reactions observed from this intermediate, they can be rationalized with the hypothesis of the oxaziridine, although the oxygen transfer to MTHF at −130 °C is unexpected. Other intermediates (zwitterions, biradicals) could be invoked equally well. At any rate this study, showing the instability even of those oxaziridines, such as **123**, which are "stabilized" by the cyano group (but no oxaziridines have been observed from 2-cyanoquinoline *N*-oxide and 1-cyanoisoquinoline *N*-oxide[200]), puts severe limits on the concept of an intermediate in the general case of the *N*-oxide photochemistry.

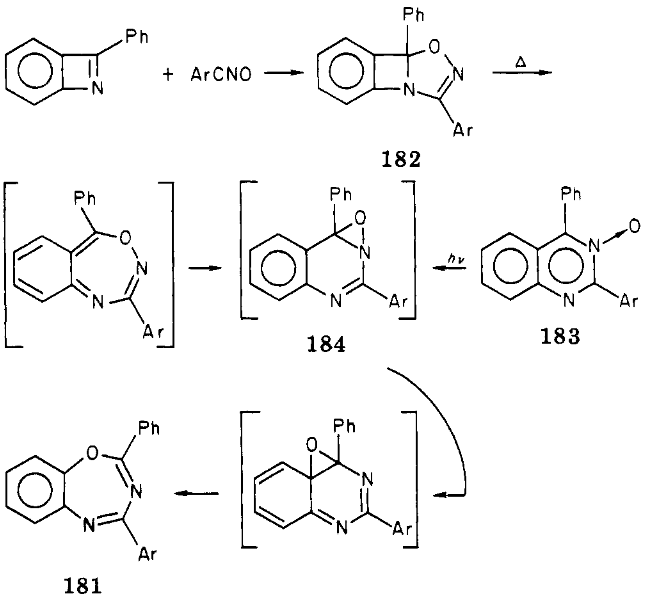
SCHEME XX



In several cases, however, indirect evidence for the intermediacy of an oxaziridine have been discussed. A first group of evidences is based on the comparison with thermal reactions occurring via oxaziridines. Thus, from some acridine *N*-oxides, 1,2-oxazepines are obtained.[131,134] These are valence tautomers of oxaziridines, and, in suitable conditions, thermally rearrange to the starting *N*-oxide, a process that can be rationalized as occurring via the oxaziridine (for the connection with the oxaziridine–nitrene rearrangement, see section IIA). However, the relevance of this observation for the establishing of the oxaziridine intermediacy in the *photochemical* rearrangement of the *N*-oxide has been questioned on the ground that the photochemical rearrangement occurs along a potential energy surface starting from the excited state, which in principle is not related to the surface connecting the ground state of the starting materials and the products, and thus the existence of a minimum at the oxaziridine configuration in the latter surface does not require an analogous minimum in the former one.[72]

The same kind of criticism can be applied to the observation that the benzoxadiazepine **181** (Scheme XXI) can be obtained both by thermal rearrangement of the azepinooxadiazole **182** and by photolysis of the phthalazine *N*-oxide **183**.[201] Although both reactions can be rationalized as occurring through a series of sigmatropic and electrocyclic reactions involving the

SCHEME XXI

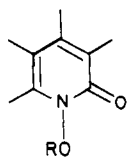


oxaziridine **184**, this is not unequivocal evidence of the formation of ground state **184** as the primary photoproduct from **183**.

A second body of evidence involves chemical trapping, e.g., with nucleophiles and oxygen acceptors. Oxaziridines are known to oxidize several species, such as Fe^{2+} and I^- ions.[202] In several cases the formation of an oxidizing species has been evidenced even when there is no other indication of the intermediacy of an oxaziridine (e.g., liberation of iodine during the photolysis of some quinoline *N*-oxides[100,203]).

Whether or not oxaziridines are involved in the photochemical oxygen transfer from *N*-oxides to various substrates is difficult to assess, due to the difficulty in establishing how much the invoked benzoxaziridines would differ from bona fide oxaziridines in their chemical properties.[204-207] Oxaziridines have been found to transfer oxygen to various substrates; in particular, sulfonyloxaziridines have been studied in this respect, and found to transfer oxygen to organic sulfur compounds[204,205] and alkenes.[207] However, with other substrates the reaction is not observed.[206] If the above mentioned reaction with methyltetrahydrofuran at −130 °C has to be attributed to the oxaziridine **123**, benzoxaziridines would be strong oxidizers indeed.

Reaction with alcohols[163] or amines[208] to form products such as **185** and **186** also has been invoked as evidence for the oxaziridine **176**, although such trapping could equally well involve an open zwitterionic species, such as **177**.[5] Here again, bona fide oxaziridines have been found to react with nucleophiles, e.g., amines, in different ways,[209,211] fragmentation rather than nucleophilic opening being observed in some cases. Thus, it appears that caution is needed in rationalizing a trapping reaction as an indication of the intermediacy of an oxaziridine rather than of some other species.



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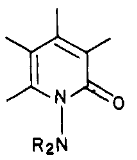

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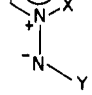
As has been shown, there is no single piece of evidence that can be considered as unambiguous and definitive proof of the intermediacy of an oxaziridine, although all the evidence taken together does lend some weight to this hypothesis. There is, however, also some evidence against it. Thus, in the case of some isoquinoline and phthalazine *N*-oxides it has been shown that the primary photoproduct (i.e., isocarbostyril or a diazo derivative, respectively) is formed within a few nanoseconds from the excitation, thereby excluding the existence of an intermediate of any stability at room temperature.[72,111] On the other side, no intermediate has been detected during the photolysis of pyridine *N*-oxide in matrix at 10 K.[69,212] Furthermore, the effect of the external magnetic field on some of the photorearrangements has been taken as evidence that at least some of the photoprocesses do not involve an oxaziridine[189] and the same conclusion has been reached from some of the photoprocesses from azaanthracene *N*-oxides, which appear difficult to rationalize via an oxaziridine intermediate.[180]

In view of the fact that flash photolysis and matrix experiments have given mainly negative evidence, other ways should perhaps be tried. Thus, in the case of the partially analogous rearrangement of pyridine *N*-imides to 1,2-diazepines, the study of the isotopic effect (D, ^{13}C) on the photolysis of compound **187** gave results interpreted as evidence in favor of the intermediacy of a three-membered ring.[213] No such experiment has been tried as yet in the field of *N*-oxides.



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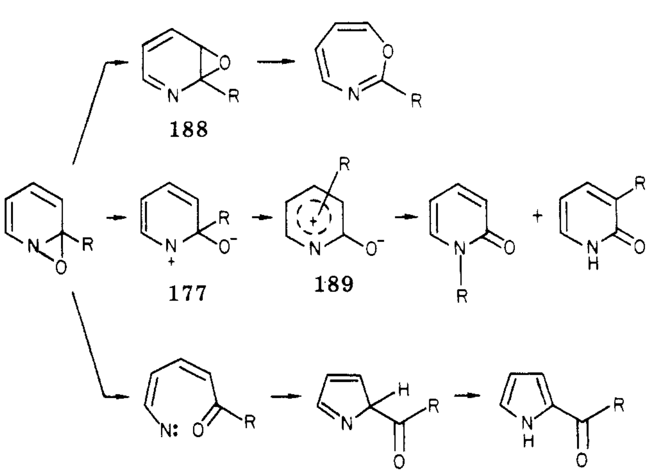
X = CH, CD, ^{13}CH
Y = COOR, COR, SO_2R

In conclusion, on the basis of what is presently known, it would appear that one cannot exclude that the excited state of the *N*-oxides is directly converted to the end products without the intermediacy of an oxaziridine, although this hypothesis might seem "daring".[84] Some light could come from the detailed calculation of the potential energy surface for the photochemical reaction of *N*-oxides, but no such data are available as yet. Furthermore, in some cases, e.g., the formation of isonitriles such as **99** from some quinoline and quinoxaline *N*-oxides, there is really no need to think that the oxaziridine configuration is ever attained during the rearrangement, as the oxygen could equally well directly migrate to the β-carbon atoms.[101,113]

Nor is there any direct evidence about other species involved during the further evolution of the reaction before the formation of the stable end products, whether arising from the oxaziridine or directly from the excited state. Thus, there is no identification of the epoxide **188**, i.e., the valence tautomer of the known oxazepines, or of zwitterionic intermediates **177**, or π-complexes **189**, or nitrenes (Scheme XXII). Indirect evidence is not unambiguous. Thus, the positive effect of electron-donating substituents upon the formation of lactams has been proposed as evidence for π-com-

SCHEME XXII

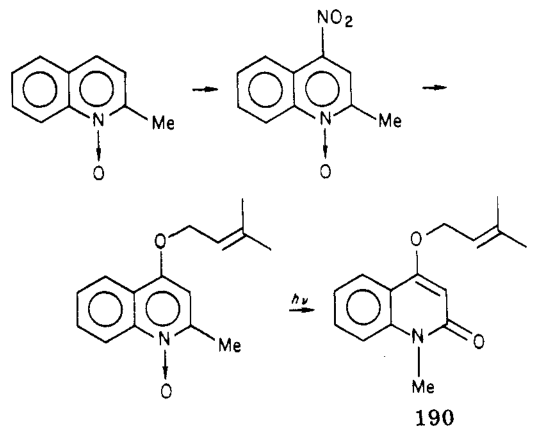


plexes, but, apart from the scarce documentation of this type of intermediate,[214] this substituent effect could equally well be referred to zwitterions or to a change in the charge-transfer character of the excited state (cf. ref 180). Also, the effect of metallic ions could be due to the stabilization of an intermediate nitrene,[81a] but again also to the complexation of a biradicaloid intermediate or to the modification of the excited state itself.

XI. Applicative Significance and Conclusions

The previous sections have shown the large variety of products that are formed by photolysis of compounds containing the *N*-oxide function and that the amount of knowledge is sufficient to make the result of the photolysis of a particular substrate often predictable.

Thus, the photorearrangement of *N*-oxides can be considered a valuable synthetic tool, particularly for the preparation of new heterocycles, e.g., oxaziridines and oxazepines. Oxazepines have received less attention than diazepines (which can be analogously prepared by photorearrangement) perhaps because the latter are closely related to compounds of recognized pharmaceutical significance.[215] However, the chemistry of oxazepines has still to be fully explored and may be more interesting than anticipated. Furthermore, ring contraction offers in some cases a useful entry into some classes of five-membered heterocycles. The synthesis of indole derivatives from cinchona alkaloids by photochemical ring contraction has been patented.[216] Even cleavage of the heterocyclic ring can have synthetic significance for the preparation of highly unsaturated compounds, e.g., pentadienenitrile derivatives from pyridine *N*-oxides.[68,70] Furthermore, advantage can be taken of the characteristic reactivity toward electrophilic as well as nucleophilic substitution of *N*-oxides, which can be conveniently exploited before the photochemical rearrangement, as is shown in the elegant synthesis of the alkaloid revenine (**190**).[118]



(57)

Nor, need the applicative significance be limited to synthetic achievements. Thus, e.g., the *N*-oxide group has been found to be effective in initiating the photocross-linking of polymeric materials. The process is quenched by naphthalene and sensitized by benzophenone, and is thought to be a radical process initiated by hydrogen abstraction on the part of the triplet state.[150,218] The method has been patented.[219] Homopolymers and copolymers prepared from 4-vinylpyridine *N*-oxide, 2-methyl-5-vinylpyridine *N*-oxide, 4-vinylquinoline *N*-oxide, and 9-vinylacridine *N*-oxide were studied in this respect, and the first three are rather effective. The pyridine *N*-oxide derivatives are the most active, although their absorption limited to the far UV makes these photoinitiators less interesting. Another patented application is the use of metal complexes of heterocyclic *N*-oxides for radiation-sensitive imaging material.[217]

Furthermore, the effectiveness of heterocyclic *N*-oxides as enzyme-mimicking photochemical oxidizers, together with the good absorbance in the near UV or even the visible of some of them, could make it worthwhile to devise some method for biological oxidation based on these compounds.

As has been discussed in section X, a satisfying picture of the rearrangement of heterocyclic *N*-oxides has not yet been reached. A partial cause of the dissatisfaction could lie in the psychological need of chemists to decompose the complicated process leading from the *N*-oxide to the end products into simple steps that might be exaggerated for an excited-state process. It might be that the excited state is so strongly deformed that the search for an intermediate is unreasonable. Still, it would be desirable to have a fuller picture of the excited state and of the stages of the rearrangement, whether these would have to be considered intermediates or not. From the foregoing it would appear that the exploration of the photochemistry of the *N*-oxide function not only has been replete with exciting results, but is still an interesting and challenging field of research.

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XII. References

(1) The present review only concerns the photochemistry of imino *N*-oxide derivatives, in which the nitrogen atom is sp^2 hybridized. Only sparse reports about photochemistry of amino *N*-oxides[2a,b] and nitrile oxides have appeared.[2c]

(2) (a) Buchardt, O. In "Houben-Weil, Methoden der Organischen Chemie", 4th ed.; Muller, E., Ed.; Thieme: Stuttgart, 1975; Vol. 4/5b, p 1282. (b) Stenberg, W. I.; Schiller, J. E. *J. Am. Chem. Soc.* **1975**, *97*, 424; *J. Org. Chem.* **1973**, *38*, 2566. (c) Rundel, W. in ref 2a, p 1316.

(3) Wacker, L. *Justus Liebigs Ann. Chem.* **1901**, *317*, 375.

(4) Landquist, J. K. *J. Chem. Soc.* **1953**, 2830.
(5) Spence, A. G.; Taylor, E. C.; Buchardt, O. *Chem. Rev.* **1970**, *70*, 231.
(6) See also: Buchardt, O. Ph.D. Thesis, University of Copenhagen, 1970.
(7) Kaneko, C. *J. Synth. Org. Chem., Jpn.* **1968**, *26*, 758.
(8) Bellamy, F.; Streith, J. *Heterocycles* **1976**, *4*, 1931.
(9) Buchardt, O. in ref 2a, p 1283.
(10) Lablanche-Combier, A. In "Photochemistry of Heterocyclic Compounds"; Buchardt, O., Ed.; Wiley: New York, 1976; p 123–207.
(11) Druelinger, M. L.; Shelton, R. W.; Lammert, S. R. *J. Heterocycl. Chem.* **1976**, *13*, 1001.
(12) Boyd, D. R.; Neill, D. C. *J. Chem. Soc., Chem. Commun.* **1977**, 51.
(13) (a) Splitter, J. S.; Su, T. M.; Ono, H.; Calvin, M. *J. Am. Chem. Soc.* **1971**, *93*, 4075. (b) Scheinbaum, M. L. *Tetrahedron Lett.* **1969**, 4221.
(14) Ning, R. Y.; Field, G. F.; Sternbach, L. H. *J. Heterocycl. Chem.* **1970**, *7*, 475.
(15) Ono, H.; Splitter, J. S.; Calvin, M. *Tetrahedron Lett.* **1973**, 4107.
(16) Splitter, J. S.; Calvin, M. *Tetrahedron Lett.* **1970**, 3995.
(17) Black, D. S. C.; Boscacci, A. B. *Aust. J. Chem.* **1970**, *30*, 1109.
(18) Black, D. S. C.; Blackmann, N. A.; Boscacci, A. B. *Tetrahedron Lett.* **1978**, 175.
(19) Black, D. S. C.; Watson, K. G. *Aust. J. Chem.* **1973**, *26*, 2505.
(20) Sliwa, W. *Bull. Acad. Pol. Sci., Ser. Chim.* **1976**, *50*, 667.
(21) Suginome, H.; Mizuguchi, T.; Masamune, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 987.
(22) Aurich, H. G.; Grigo, U. *Chem. Ber.* **1976**, *109*, 200.
(23) Calvin, M.; Ono, H. K., private communication in ref 9, p 1284.
(24) Bapat, J. B.; Black, D. S. C. *J. Chem. Soc., Chem. Commun.* **1967**, 73.
(25) Greene, F. D.; Hecht, S. S. *J. Org. Chem.* **1970**, *35*, 2482.
(26) Taylor, K. G.; Isaac, S. R.; Swigert, J. L. *J. Org. Chem.* **1976**, *41*, 1146.
(27) Dolbier, W. R.; Matsui, K.; Michl, J.; Horak, D. V. *J. Am. Chem. Soc.* **1977**, *99*, 3876.
(28) Bunce, N. J. *Can. J. Chem.* **1975**, *53*, 3477.
(29) Bjørgo, N. J.; Boyd, D. R.; Cambell, R. M.; Neill, D. C. *J. Chem. Soc., Chem. Commun.* **1976**, 162.
(30) For the photochemistry and thermochemistry of oxazirines, see, e.g.: Oliveros, E.; Rivière, M.; Lattes, A. *J. Heterocycl. Chem.* **1980**, *17*, 1205 and references cited therein.
(31) Eckroth, D. R.; Kinstle, T. H.; De la Cruz, D. O.; Sparacino, J. K. *J. Org. Chem.* **1971**, *36*, 3619.
(32) Oliveros, E.; Antoun, H.; Rivière, M.; Lattes, A. *J. Heterocycl. Chem.* **1976**, *13*, 623.
(33) (a) Bonnet, R.; Clark, V. M.; Todd, A. *J. Chem. Soc.* **1959**, 2102. (b) Kamisky, L. S.; Lamchen, M. *J. Chem. Soc. C* **1966**, 2295. (c) Cf.: Black, D. S. C.; Boscacci, A. B. *Aust. J. Chem.* **1973**, *26*, 2505; **1968**, *21*, 2507.
(34) Black, D. S. C.; Boscacci, A. B. *Aust. J. Chem.* **1977**, *30*, 1353; *J. Chem. Soc. Chem. Commun.* **1974**, 129.
(35) Tsuchiya, T.; Arai, H.; Hasebe, M.; Igeta, H. *Chem. Pharm. Bull.* **1974**, *22*, 2301.
(36) Eckroth, D. R.; Squire, R. H. *J. Chem. Soc., Chem. Commun.* **1969**, 312.
(37) Döpp, D.; Weiler, H. *Tetrahedron Lett.* **1974**, 2445.
(38) Döpp, D. *Chem. Ber.* **1976**, *109*, 3849.
(39) Döpp, D. *Tetrahedron Lett.* **1972**, 3215.
(40) Iddon, B.; Meth-Cohn, O.; Scriven, F. V.; Suschitzky, H.; Gallagher, P. T. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 900.
(41) Forrester, A. R.; Ogilivy, M. M.; Thomson, R. H. *J. Chem. Soc., Chem. Commun.* **1972**, 483.
(42) Williams, W. M.; Dolbier, W. R. *J. Am. Chem. Soc.* **1972**, *94*, 3955.
(43) (a) Döpp, D.; Muller, D. *Tetrahedron Lett.* **1978**, 3863. (b) Döpp, D.; Muller, D. *Proc.—IUPAC Symp. Photochem., 7th* **1975**, 118.
(44) (a) Gruen, N.; Shulte-Frohlinde, D. *J. Chem. Soc., Chem. Commun.* **1974**, 923. (b) Buncel, E. *Acc. Chem. Res.* **1975**, *8*, 132.
(45) Squire, R. H.; Jaffé, H. H. *J. Am. Chem. Soc.* **1973**, *95*, 8188.
(46) Badger, G. M.; Buttery, R. G. *J. Chem. Soc.* **1954**, 2243.
(47) Mauser, H.; Gauglitz, G.; Stier, F. *Justus Liebigs Ann. Chem.* **1970**, *739*, 84.
(48) Goon, D. J. W.; Murray, N. G.; Schoch, J. P.; Bunce, N. J. *Can. J. Chem.* **1973**, *51*, 3827.
(49) Bunce, N. J.; Goon, D. J. W.; Schoch, J. P. *J. Chem. Soc., Perkin Trans. 1* **1976**, 688.
(50) Bunce, N. J.; Schoch, J. P.; Zerner, M. C. *J. Am. Chem. Soc.* **1977**, *99*, 7986.
(51) Taylor, K. G.; Tilford, R. *J. Am. Chem. Soc.* **1972**, *94*, 250.
(52) Haddadin, M. J.; Hawi, A. A. *Heterocycles* **1980**, *14*, 457.
(53) (a) Serra-Errante, G.; Sammes, P. G. *J. Chem. Soc., Chem. Commun.* **1975**, 573. (b) Sammes, P. G.; Serra-Errante, G.; Tinker, A. C. *J. Chem. Soc., Perkin Trans. 1*, **1978**, 853.
(54) (a) Rhee, S. B.; Jaffé, H. *J. Am. Chem. Soc.* **1973**, *95*, 5518. (b) Evans, J. C.; Owen, E. D.; Wilson, D. A. *J. Chem. Soc., Perkin Trans. 1* **1974**, 557.
(55) Fielden, R.; Meth-Cohn, O.; Suschitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1973**, 702.
(56) Fielden, R.; Meth-Cohn, O.; Suscitzky, H. *J. Chem. Soc., Chem. Commun.* **1970**, 1658.
(57) Ogata, M.; Matsumotu, H.; Takahashi, S.; Kano, H. *Chem. Pharm. Bull.* **1970**, *18*, 964.
(58) Timpe, H. J.; Becker, H. G. O. *J. Prakt. Chem.* **1972**, *314*, 325.
(59) Woolhouse, A. D. *Aust. J. Chem.* **1972**, *32*, 2059.
(60) Haddadin, M. J.; Hawi, A. A.; Nazer, M. Z. *Tetrahedron Lett.* **1978**, 4581.
(61) Servé, M. P.; Feld, W. N.; Seybold, P. C.; Steppel, R. N. *J. Heterocycl. Chem.* **1975**, *12*, 844.
(62) Braun, H. P.; Zeller, K. P.; Meier, H. *Justus Liebigs Ann. Chem.* **1975**, 1257.
(63) Calzaferri, G.; Gleiter, R.; Knauer, K. H.; Martin, H. D.; Schmidt, E. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 86.
(64) Pedersen, C. L. *J. Chem. Soc., Chem. Commun.* **1974**, 704.
(65) Pedersen, C. L. *Acta Chem. Scand., Ser. B* **1976**, *B30*, 675.
(66) Pedersen, C. L. *Tetrahedron Lett.* **1979**, 745.
(67) Pedersen, C. L.; Lohse, C.; Poliakoff, M. *Acta Chem. Scand., Ser. B* **1978**, *B32*, 625.
(68) Finsen, L.; Becher, J.; Buchardt, O.; Koganty, R. R. *Acta Chem. Scand., Ser. B* **1980**, *B34*, 513.
(69) Buchardt, O.; Christensen, J. J.; Nielsen, P. E.; Koganty, R. R.; Finsen, L.; Lohse, C.; Becher, J. *Acta Chem. Scand., Ser. B* **1980**, *B34*, 31.
(70) Becher, J.; Finse, L.; Winchelmann, I.; Koganty, R. R.; Buchardt, O. *Tetrahedron* **1981**, *38*, 789.
(71) Nakagawa, M.; Kaneko, T.; Yamaguchi, H. *J. Chem. Soc., Chem. Commun.* **1972**, 603.
(72) Tomer, K. B.; Harrit, N.; Rosenthal, I.; Buchardt, O.; Kumler, P. L.; Creed, D. *J. Am. Chem. Soc.* **1973**, *95*, 7402.
(73) Tsuchiya, T.; Arai, H.; Igeta, H. *J. Chem. Soc., Chem. Commun.* **1972**, 550.
(74) Tsuchiya, T.; Arai, H.; Igeta, H. *Tetrahedron* **1973**, *29*, 2747.
(75) Tsuchiya, T.; Arai, H.; Tonami, T.; Igeta, H. *Chem. Pharm. Bull.* **1972**, *20*, 300.
(76) Tsuchiya, T.; Arai, H.; Igeta, H. *Tetrahedron Lett.* **1971**, 2579.
(77) Streith, J.; Leibovici, C.; Martz, P. *Bull. Soc. Chim. Fr.* **1971**, 4152.
(78) Streith, J.; Martz, P. *Tetrahedron Lett.* **1969**, 4899.
(79) Bellamy, F.; Streith, J.; Fritz, H. *Nouv. J. Chim.* **1979**, *3*, 115.
(80) Bellamy, F.; Martz, P.; Streith, J. *Tetrahedron Lett.* **1974**, 3189.
(81) (a) Bellamy, F.; Streith, J. *J. Chem. Res., Synop.* **1979**, *18*; *J. Chem. Res., Miniprint* **1979**, *101*. (b) Streith, J.; Singwalt, C. *Bull. Chim. Soc. Fr.* **1970**, 1157.
(82) Ishikawa, M.; Kaneko, C.; Yokoe, I.; Yamada, S. *Tetrahedron* **1969**, *25*, 295.
(83) Deelaman, R. A. F.; Van Der Plas, H. C. *Rec. Trav. Chim. Pays-Bas* **1973**, *92*, 317.
(84) Roeterdink, F.; Van Der Plas, H. C.; Koudijs, A. *Rec. Trav. Chim. Pays-Bas* **1975**, *94*, 16.
(85) Buchardt, O.; Pedersen, C. L.; Harrit, N. *J. Org. Chem.* **1972**, *37*, 3592.
(86) Mukai, T.; Sukawa, H. *Tetrahedron Lett.* **1973**, 1835.
(87) Tezuka, T.; Seshimoto, O.; Mukai, T. *Tetrahedron Lett.* **1975**, 1067.
(88) Tezuka, T.; Seshimoto, O.; Mukai, T. *J. Chem. Soc., Chem. Commun.* **1974**, 373.
(89) Neunhoeffer, H.; Böhnisch, V. *Justus Liebigs Ann. Chem.* **1976**, 153.
(90) Kawata, H.; Niizuma, S.; Kokubun, H. *J. Photochem.* **1980**, *13*, 261.
(91) Oshawa, A.; Arai, H.; Igeta, H.; Akimoto, T.; Tsuji, A.; Iitaka, Y. *Tetrahedron* **1978**, *35*, 1267.
(92) Arai, H.; Ohsawa, A.; Saiki, K.; Igeta, H.; Tsuji, A.; Akimoto, T.; Iitaka, Y. *J. Chem. Soc., Chem. Commun.* **1977**, 856.
(93) Ager, E.; Chivers, G. E.; Suschitzky, H. *J. Chem. Soc., Chem. Commun.* **1972**, 505.
(94) Ager, E.; Chivers, G. E.; Suschitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1125.
(95) Abramovitch, R. A.; Dupuy, C. *J. Chem. Soc., Chem. Commun.* **1981**, 36.
(96) Abramovitch, R. A.; Cue, B. W. *J. Am. Chem. Soc.* **1976**, *98*, 1478.
(97) Abramovitch, R. A.; Shinkai, I.; Cue, B. W.; Ragan, F. A.; Atwood, J. L. *J. Heterocycl. Chem.* **1976**, *13*, 415.
(98) Dirlam, J. D.; Cue, B. W.; Gombatz, K. J. *J. Org. Chem.* **1978**, *43*, 76.
(99) Albini, A.; Bettinetti, G. F.; Minoli, G. *Tetrahedron Lett.* **1979**, 3761.
(100) Hata, N.; Ono, I. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1794.
(101) Albini, A.; Fasani, E.; Maggi Dacrema, L. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2738.

(102) Kaneko, C.; Hayashi, S.; Kobayashi, Y. *Chem. Pharm. Bull.* **1974**, *22*, 2147.

(103) Ichiro, Y.; Masayuki, I.; Kaneko, C. *Iyo Kizai Kenkyusho Hokuko* (*Tokyo Ika Shika Daigaku*) **1972**, *6*, 18; *Chem. Abstr.* **1974**, *81*, 105233d.

(104) Unpublished results from the authors' laboratory.

(105) Kaneko, C.; Fujii, H.; Kawai, S.; Yamamoto, A.; Hashiba, K.; Kimata, T.; Hayashi, R.; Somei, M. *Chem. Pharm. Bull.* **1980**, *28*, 1157.

(106) Kitamura, R.; Fujii, H.; Kazuhiko, H.; Somei, M.; Kaneko, C. *Tetrahedron Lett.* **1977**, 2911.

(107) (a) Kaneko, C.; Kitamura, R. *Heterocycles*, **1977**, *6*, 111. (b) Kaneko, C.; Yamamoto, A.; Hashiba, M. *Chem. Pharm. Bull.* **1979**, *27*, 946.

(108) Kaneko, C.; Kitamura, R. *Heterocycles* **1977**, *6*, 117.

(109) Kaneko, C.; Yamada, S.; Ishikawa, M. *Chem. Pharm. Bull.* **1969**, *17*, 1290.

(110) Bau, Y.; Yoshida, K.; Goto, J.; Ohshi, T. *J. Am. Chem. Soc.* **1981**, *103*, 6990.

(111) Lohse, C. *J. Chem. Soc., Perkin Trans. 2* **1972**, 229.

(112) (a) Kaneko, C.; Okuda, W.; Karasawa, Y.; Somei, M. *Chem. Lett.* **1980**, 547. (b) Brommer, J. B. *Aust. J. Chem.* **1973**, *26*, 437.

(113) Albini, A.; Colombi, R.; Minoli, G. *J. Chem. Soc., Perkin Trans. 2* **1978**, 924.

(114) Field, G. F.; Sternbach, L. H. *J. Org. Chem.* **1968**, *33*, 4438.

(115) Horspool, W. M.; Kershaw, J. R.; Murray, A. W.; Stevenson, G. M. *J. Am. Chem. Soc.* **1973**, *95*, 2390.

(116) Burrel, R. A.; Cox, J. M.; Savins, E. G. *J. Chem. Soc. Perkin Trans. 1* **1973**, 2707.

(117) Buchardt, O.; Tomer, K. B.; Madsen, V. *Tetrahedron Lett.* **1971**, 1311.

(118) Kaneko, C.; Naito, T.; Hashiba, M.; Fujii, H.; Somei, M. *Chem. Pharm. Bull.* **1979**, *27*, 1813.

(119) Ide, A.; Mori, Y.; Matsumori, K.; Watanabe, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1959.

(120) Jarrar, A. A.; Fataftah, Z. A. *Tetrahedron* **1977**, *33*, 2127.

(121) Landquist, J. K. *J. Chem. Soc.* **1953**, *28*, 2830.

(122) Kobayashi, Y.; Kumadaki, I.; Sato, H. *Tetrahedron Lett.* **1970**, 2337.

(123) Horspool, W. M.; Kershaw, J. R.; Murray, A. W. *J. Chem. Soc., Chem. Commun.* **1973**, 345.

(124) Haddadin, M. J.; Agopian G.; Issidores, C. H. *J. Org. Chem.* **1971**, *36*, 514.

(125) Jarrar, A. A.; Halawi, S. S.; Haddadin, M. J. *Heterocycles* **1976**, *4*, 1077.

(126) Albini, A.; Bettinetti, G. F.; Minoli, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1159.

(127) Kaneko, C.; Hayashi, R.; Yamamori, M.; Tokumura, K.; Itoh, M. *Chem. Pharm. Bull.* **1978**, *26*, 2508.

(128) Yamada, S.; Ishikawa, M.; Kaneko, C. *Tetrahedron Lett.* **1972**, 971.

(129) (a) Yamada, S.; Ishikawa, M.; Kaneko, C. *Chem. Pharm. Bull.* **1975**, *23*, 2818. (b) Kawata, H.; Niizuma, S.; Kokubun, H. *J. Photochem.* **1978**, *9*, 463.

(130) Albini, A.; Bettinetti, G. F.; Pietra, S. *Tetrahedron Lett.* **1972**, 3657.

(131) Yamada, S.; Ishikawa, M.; Kaneko, C. *Tetrahedron Lett.* **1972**, 977.

(132) Albini, A.; Bettinetti, G. F.; Pietra, S. *Gazz. Chim. Ital.* **1975**, *105*, 15.

(133) Yamada, S.; Ishikawa, M.; Kaneko, C. *J. Chem. Soc., Chem. Commun.* **1972**, 1093.

(134) Yamada, S.; Kaneko, C. *Tetrahedron* **1979**, *35*, 1273.

(135) Kaneko, C.; Yamada, S.; Ishikawa, M. *Tetrahedron Lett.* **1970**, 2329.

(136) Albini, A.; Barinotti, A.; Bettinetti, G. F.; Pietra, S. *Gazz. Chim. Ital.* **1976**, *106*, 871.

(137) Parham, J. C.; Pullman, I.; Brown, G. B. *Tetrahedron* **1973**, *29*, 3329.

(138) Lam, F. L.; Parham, J. C. *J. Org. Chem.* **1973**, *38*, 2397.

(139) (a) Lam, F. L.; Lee, T. C. *J. Org. Chem.* **1978**, *43*, 167. (b) Kaneko, C.; Hasegawa, H.; Tanaka, S.; Sunayashiki, K.; Yamada, S. *Chem. Lett.* **1974**, 133.

(140) Lam, F. L.; Parham, J. C. *J. Am. Chem. Soc.* **1975**, *97*, 2839.

(141) (a) Lam, F. L.; Brown, G. B.; Parham, J. C. *J. Org. Chem.* **1974**, *39*, 1391. (b) Kazimierczuk, Z. *Acta Biochem. Pol.* **1973**, *20*, 395.

(142) Kaneko, C.; Yamamori, M.; Yamamoto, A.; Hayashi, R. *Tetrahedron Lett.* **1978**, 2799.

(143) Hata, N.; Ono, I.; Kawasaki, M. *Chem. Lett.* **1975**, 25.

(144) Caswell, L. R.; Lee, F. C.; Creagh, L. T. *J. Heterocycl. Chem.* **1972**, *9*, 551.

(145) Kaneko, C.; Yamamoto, A.; Gomi, M. *Heterocycles* **1979**, *12*, 227.

(146) (a) Minoli, G.; Albini, A.; Bettinetti, G. F.; Pietra, S. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1661. (b) Pietra, S.; Bettinetti, G. F.; Albini, A.; Fasani, E.; Oberti, R. *Ibid.* **1978**, 185.

(147) Brown, G. B.; Levin, G.; Murphy, S. *Biochemistry* **1964**, *3*, 880.

(148) Giner-Sorolla, A.; Gryte, C.; Cox, M.; Parham, J. C. *J. Org. Chem.* **1971**, *36*, 1288.

(149) Lee, T. C.; Lam, F. L.; Brown, G. B. *J. Org. Chem.* **1975**, *40*, 1547.

(150) Decot, J. C.; Lablanche-Combier, A.; Loucheux, C. *Photogr. Sci. Eng.* **1979**, *23*, 309.

(151) Acheson, R. M.; Selby, I. A. *J. Chem. Soc., Perkin Trans. 1* **1974**, *423* and references cited therein.

(152) Krebs, A.; Colberg, H.; Hoepfner, U.; Kimling, H.; Odenthal, H. *Heterocycles* **1979**, *12*, 1153.

(153) Hisano, T.; Matsuoka, T.; Tsutsumi, K.; Muraoka, K.; Ishikawa, M. *Chem. Pharm. Bull.* **1981**, *29*, 3706 and references cited therein.

(154) Jerina, D. M.; Witkop, B.; McIntosh, C. L.; Chapman, O. L. *J. Am. Chem. Soc.* **1974**, *96*, 5578.

(155) Igeta, H.; Tsuchiya, T.; Yamada, M.; Arai, H. *Chem. Pharm. Bull.* **1968**, *16*, 767.

(156) Tsuchiya, T.; Arai, H.; Igeta, H. *Tetrahedron Lett.* **1969**, 2747.

(157) Ogawa, Y.; Iwasaki, S.; Okuda, S. *Tetrahedron Lett.* **1981**, 2277.

(158) (a) Boberg, F.; Steigerwald, E. *Erdoel Kohle, Erdgas, Petrochem.* **1979**, *32*, 569; *Chem. Abstr.*, **1980**, *93*, 25555t. (b) *Ibid.* **1980**, *33*, 227; *Chem. Abstr.* **1980**, *93*, 204120u.

(159) Tsuchiya, T.; Arai, H.; Igeta, H. *Tetrahedron Lett.* **1970**, 2213.

(160) Ogawa, Y.; Iwasaki, S.; Okuda, S. *Tetrahedron Lett.* **1981**, 3637.

(161) Sergeev, B.; Gubergkitis, M.; Koblyakov, V. *Eesti NSV Tead. Akad. Toim., Keem.* **1979**, *28*, 270; *Chem. Abstr.*, **1980**, *92*, 93661d.

(162) Alkaitis, A.; Calvin, M. *J. Chem. Soc., Chem. Commun.* **1968**, 292.

(163) Tokumura, K.; Goto, H.; Kashibara, H.; Kaneko, C.; Itoh, M. *J. Am. Chem. Soc.* **1980**, *102*, 5643.

(164) Ito, Y.; Matsuura, T. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1871.

(165) Rowely, A. G.; Steedmann, J. R. F. *Chem. Ind.* **1981**, 365.

(166) Nakagawa, M.; Kaneko, T.; Yamaguchi, H.; Kawashima, T.; Hino, T. *Tetrahedron* **1974**, *30*, 2591.

(167) Akhtar, M. N.; Boyd, D. R.; Neill, J. D.; Jerina, D. M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1693.

(168) (a) Ohsawa, A.; Kawaguchi, T.; Igeta, H. *Chem. Pharm. Bull.* **1981**, *29*, 1481. (b) *Chem. Lett.* **1981**, 1737.

(169) (a) Aloisi, G. G.; Favaro, G. *J. Chem. Soc., Perkin Trans. 2* **1976**, 456. (b) Favaro, G. *Mol. Photochem.* **1970**, *2*, 323.

(170) Ono, I.; Hata, N. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3658.

(171) Bellamy, F.; Ruiz Barragan, L. G.; Streith, J. *J. Chem. Soc., Chem. Commun.* **1971**, 456.

(172) Leibovici, C.; Streith, J. *Tetrahedron Lett.* **1971**, 387.

(173) Kobinata, S.; Nagakura, A. *Theor. Chim. Acta* **1969**, *14*, 415.

(174) Seibold, K.; Wagniere, G.; Labhart, H. *Helv. Chim. Acta*, **1969**, *52*, 789.

(175) Evleth, E. M. *Theor. Chim. Acta* **1968**, *11*, 145.

(176) Yamakawa, M.; Kubota, T.; Akazawa, H. *Theor. Chim. Acta* **1969**, *15*, 244.

(177) Scholtz, M. *J. Prakt. Chem.* **1982**, *324*, 85.

(178) Ha, T. K. *Theor. Chim. Acta* **1977**, *43*, 337.

(179) Albini, A.; Bettinetti, G. F.; Pietra, S. *J. Chem. Soc., Perkin Trans. 2* **1974**, 342.

(180) Albini, A.; Barinotti, A.; Bettinetti, G. F.; Pietra, S. *J. Chem. Soc., Perkin Trans. 2* **1977**, 238.

(181) Shinzawa, K.; Tanaka, I. *J. Phys. Chem.* **1964**, *68*, 1205.

(182) Koyano, K.; Tanaka, I. *J. Phys. Chem.* **1965**, *69*, 2545.

(183) Hata, N. *Chem. Lett.* **1975**, 401.

(184) Kumler, P. L.; Buchardt, O. *J. Chem. Soc., Chem. Commun.* **1968**, 1321.

(185) Dega-Szafran, Z.; Szafran, M.; Rychiewzki, J. *J. Chem. Soc., Perkin Trans. 2* **1978**, 536.

(186) Dega-Szafran, Z.; Szafran, M.; Kreglewski, M. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1516.

(187) Koyano, K.; Suzuki, H.; Mori, Y.; Tanaka, I. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 3582.

(188) Kubota, T.; Mihyazaki, H. *Nippon Kagaku Zasshi* **1958**, *79*, 916.

(189) Hata, N. *Chem. Lett.* **1976**, 547.

(190) Hata, N. *Chem. Lett.* **1978**, 1359.

(191) Hata, N.; Ono, Y.; Nakagawa, F. *Chem. Lett.* **1979**, 603.

(192) Joucla, M.; Hamelin, J. *J. Chem. Res. Synop.* **1978**, 276.

(193) Joucla, M.; Grée, D.; Hamelin, J. *Tetrahedron*, **1973**, *29*, 2315.

(194) For a discussion of the oxaziridine intermediacy, see also: Nastasi, M.; Streith, J. In "Rearrangement in Ground and Excited States"; de Mayo, P., Ed.; Academic Press: New York, 1980, Vol. 3, p 445.

(195) Different predictions are obtained from HMO and PPP-SCF models in the case of some pyrimidine *N*-oxides, see ref 80.

(196) Kaneko, C.; Yamada, S.; Yokoe, I. *Tetrahedron Lett.* **1970**, 2333.

(197) Oliveros, E.; Riviere, M.; Malrieu, J. P.; Teichteil, C. *J. Am. Chem. Soc.* **1979**, *101*, 318.

(198) (a) Yamada, S.; Ishikawa, M.; Kaneko, C. *Chem. Pharm. Bull.* **1975**, *23*, 2818. (b) Kaneko, C. *Tetrahedron* **1972**, *28*, 4915.
(199) Tokumura, K.; Itoh, M.; Kaneko, C. *Tetrahedron Lett.* **1979**, 2027.
(200) Tokumura, K.; Goto, H.; Kashimira, H.; Itoh, M. *Kokagaku Toronkai Koen Yashishu* **1979**; *Chem. Abstr.* **1980**, *93*, 45588.
(201) Rees, C. W.; Somanathan, R.; Storr, R. C.; Woolhouse, A. D. *J. Chem. Soc., Chem. Commun.* **1975**, 740.
(202) Emmons, W. D. *Heterocycl. Compd.* **1964**, *19*, 624.
(203) Phenazine *N*,*N*-dioxide is deoxygenated in the presence of triphenylphosphine. The reaction is attributed to the oxadiazepine rather than to the oxaziridine (see ref 129b).
(204) Davis, F. A.; Jenkins, R.; Yocklovich, S. G. *Tetrahedron Lett.* **1978**, 5171.
(205) Davis, F. A.; Jenkins, R.; Rizvi, S. Q. A.; Panuto, T. W. *J. Chem. Soc., Chem. Commun.* **1979**, 600.
(206) Rastetter, W. H.; Frost, J. W. *Tetrahedron Lett.* **1969**, 3353.
(207) Davis, F. A.; Abdul-Malik, N. F.; Awad, S. V.; Harakal, M. E. *Tetrahedron Lett.* **1981**, 917.
(208) Kaneko, C.; Yokoe, I.; Ishikawa, M. *Tetrahedron Lett.* **1967**, 5237.
(209) Dinizo, S.; Watt, D. S. *J. Am. Chem. Soc.* **1975**, *97*, 6900.
(210) Hata, Y.; Watanabe, M. *J. Am. Chem. Soc.* **1979**, *101*, 6671.
(211) Rastetter, W. H.; Wagner, W. R.; Findeis, M. A. *J. Org. Chem.* **1982**, *47*, 419.
(212) Buchardt, O.; Christensen, J. J.; Lohse, C.; Turner, J. J.; Dunkin, I. R. *J. Chem. Soc., Chem. Commun.* **1977**, 837.
(213) (a) Kwart, H.; Benko, D. A.; Streith, J.; Harris, D. J.; Shuppiser, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 6501. (b) Kwart, H.; Benko, D. A.; Streith, J.; Shuppiser, J. L. *Ibid.* **1978**, *100*, 6502.
(214) Cf.: Arnold, D. R.; Wong, P. C. *J. Am. Chem. Soc.* **1977**, *99*, 3361.
(215) (a) Streith, J. *Pure Appl. Chem.* **1977**, *49*, 305. (b) Snieckus, V.; Streith, J. *Acc. Chem. Res.* **1981**, *14*, 348.
(216) Ishikawa, M.; Kaneko, C. Jpn Kokai **73**, 78 200; *Chem. Abstr.* **1974**, *80*, 82716b.
(217) Tsuboi, T.; Tamura, H.; Suzuki, Y.; Nagata, M. Jpn. Kokai 78 129 028; *Chem. Abstr.* **1979**, *90*, 199590f.
(218) Decout, J. L.; Lablanche-Combier, A.; Loucheux, C. *J. Polym. Sci., Polym. Chem. Ed.* **1980**, *18*, 2371; Ibid. **1980**, *18*, 2391.
(219) Anvar, Fr. Pat. **78**, 26 152, Sept 12, 1978.