[Chem. Pharm. Bull.
16(8)1533—1542(1968)]

UDC 547.831.03 : 543.51

Studies on the N-Oxides of π-Deficient N-Heteroaromatics. XIII.[1)] Mass Spectra of Azanaphthalene N-Oxides and Their Photochemical Reaction Products[2,3)]

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(Received October 31, 1967)

The mass spectra of a series of quinoline 1-oxides have been determined in conjunction with those of the related compounds, such as quinolines and benz[*d*]-1,3-oxazepines derived photochemically from these N-oxides. For example, the major decomposition processes of 2-cyanoquinoline 1-oxide (**1**) are loss of O and loss of CO. Existence of the latter process requires prior formation of a C-O bond and virtually demands isomerization to the corresponding oxaziridine ion (**c**). This species would then undergo rearrangement to the corresponding benzoxazepine ion (**d**) before the fragmentation takes place. This supposition seems to be testified by comparison of the spectra of **1** and the corresponding oxazepine (**3**). The results obtained provide a striking example of parallel behavior of **1** and its related N-oxides in photolysis and electron impact. It is also shown that on electron impact the molecular ions of benz[*d*]-1,3-oxazepine derivatives eliminate carbon monoxide as a neutral molecule and the resultant ions behave as indole derivatives.

The mass spectrum of 1-cyanoisoquinoline 2-oxide (**18**), on the contrary, contains M-O and M-$(CN)_2$ ions, and the occurence of M-CO ion is very weak. The presence of M-$(CN)_2$ ion can be regarded as a criterion for the intermediary of the corresponding oxazepine ion, since this ion is a base peak in the spectrum of the corresponding photo-product, benz[*f*]-1,3-oxazepine-2-carbonitrile (**20**).

Exceptions from these rules can be explained in terms of the presence of specific structural features, and general decomposition sequences of benz[*d*]- and benz[*f*]-1,3-oxazepines have also been clarified.

A series of photo-products obtained by the irradiation of quinoline 1-oxides having a cyano or phenyl group in their α-position has been proved to be the corresponding benz[*d*]-1,3-oxazepines[5,6)] (I) and a strong evidence for the intermediary formation of the corresponding oxaziridines (II) in these photochemical isomerizations has been provided by a recent experiment, in which a series of aliphatic amines was successfully used as trapping agents for these short-lived oxaziridine intermediates.[7)] A similar photochemical isomerization of 1-cyanoisoquinoline 2-oxides to benz [*f*]-1,3-oxazepine-2-carbonitriles[8,9)] (III) may also proceed *via* the corresponding oxaziridines (IV) as transient intermediates.

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1) Part XII: C. Kaneko and I. Yokoe, *Tetrahedron Letters*, **1967**, 5355.
2) Presented at the 24th Annual Meeting of the Pharmaceutical Society of Japan, Kyoto, April 9, 1967, Abstracts of papers, p. 379.
3) Preliminary communications of a part of the present work appeared in *Chem. Pharm. Bull.* (Tokyo), **15**, 1079 (1967) as our cooperative work with three laboratories (Professors A. Tatematsu, E. Hayashi, and H. Nakata).
4) Location: *a*) *Yayoi-cho, Chiba*; *b*) *Kanda, Surugadai, Chiyoda-ku, Tokyo.*
5) O. Buchardt, *Tetrahedron Letters*, **1966**, 6221.
6) C. Kaneko, Sa. Yamada, I. Yokoe, and M. Ishikawa, *Tetrahedron Letters*, **1967**, 1873.
7) C. Kaneko, I. Yokoe, and M. Ishikawa, *Tetrahedron Letters*, **1967**, 5237
8) C. Kaneko, Sa. Yamada, and I. Yokoe, *Rept. Res. Inst. Med. Engi., Tokyo Medico-Dental Univ.*, **1967**, 1, and references cited therein.
9) O. Buchardt, C. Lohse, A.M. Duffield, and C. Djerassi, *Tetrahedron Letters*, **1967**, 2741.

Chart 1

A common formation of the oxaziridines (II and IV) as the unstable intermediates has also been suggested in the photochemical reaction of quinoline 1–oxide, isoquinoline 2–oxide, and their alkyl–substituted derivatives.[10,11]

The formation of these oxaziridines as the unstable intermediates in all of these reactions is most conveniently described in terms of the n, π^* excited state of the N–oxides. If this assumption is correct, then there is a possibility that the related rearrangement of the N–oxides occurs on the electron impact–induced ionization as well, because the lowest energy ionization presumably involves removal of an electron from the nonbonding orbital of oxygen atom and therefore the resulting species (V) is like an n,π^* excited state (VI), except that there is no electron in the π^* orbital.

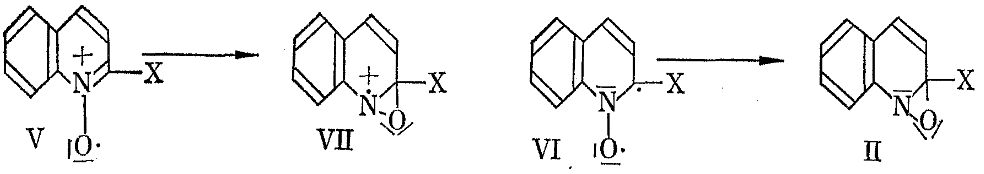

Chart 2

To help clarify these assumptions, we examined the mass spectra of a series of quinolines, isoquinolines, their N–oxides, and their photochemical reaction products (*i.e.*, I and III).[12]

The results obtained clearly indicate that in some of quinoline and isoquinoline N–oxides (2–cyanoquinoline 1–oxide, 1–cyanoisoquinoline 2–oxide, *etc.*), a decomposition *via* the corresponding oxaziridine ions (such as VII) actually does exist, while in the N–oxides having a methyl or a phenyl group at the position *ortho* to the N–oxide function (2–position in quinoline ring and 1– and 3–positions in isoquinoline ring), an entirely different process from those of photochemistry takes place as the major process.

For the sake of convenience, the mass spectra of quinoline 1–oxides and their related compounds will be discussed before those of isoquinoline derivatives.

1. Mass Spectra of Quinoline 1-Oxides and Their Related Compounds

2-Cyanoquinoline 1-Oxide and Its Related Compounds

The 70 eV spectrum of 2–cyanoquinoline 1–oxide (**1**) shows the relative intensities listed in Table I. The decomposition scheme shown can account for the major ionic products (throughout this paper, the fragmentation patterns illustrated have arrows accompanied by an asterisk to represent transitions confirmed by the existence of a metastable peak, and hypothetical transitions are shown with simple arrows).

Clearly, the major primary decomposition processes are loss of CO (path *a*) and O (path *b*). The fact that at 20 eV, the M–16 ion is virtually the only fragment ion observed suggests

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[10] *a*) C. Kaneko and Sa. Yamada, *Rept. Res. Inst. Dental Materials, Tokyo Medico-Dental Univ.*, **1966**, 804; *b*) M. Ishikawa, Sa. Yamada, H. Hotta, and C. Kaneko, *Chem. Pharm. Bull.* (Tokyo), **14**, 1102 (1966); *c*) M. Ishikawa, Sa. Yamada, and C. Kaneko, *Chem. Pharm. Bull.* (Tokyo), **13**, 747 (1965).

[11] *a*) O. Buchardt, and C. Lohse, *Tetrahedron Letters*, **1966**, 4355; *b*) O. Buchardt, J. Becher, and C. Lohse, *Acta Chem. Scand.*, **20**, 2467 (1966).

[12] It seems worthy to note that the formation of simple deoxygenation products was observed without exception, though in minor amounts, in the photolysis of these aromatic amine N–oxides.[10b]

Table I. Relative Intensities of the Significant Peaks in the Spectra of 2-Cyanoquinoline 1-Oxide and Its Related Compounds

Mass	2-Cyanoquinoleine 1-oxide (**1**)	2-Cyanoquinoline (**2**)	2-Cyanobenz[*d*]-1,3-oxazepine (**3**)
170	8	—	40
154	100	100	—
142	16[a]	—	100
127	36[a]	32	—
115	10	—	70
102	22	18	—
101	18	14	—
100	16	10	—
89	10.4	—	68
87	10	8	10
76	36	28	6
75	32	24	4
63	28	14	68

a) The compositions of ions at *m/e* 142 and 127 were confirmed as $C_9H_6N_2$ and C_9H_5N, respectively, by accurate mass measurement.

$$\begin{tikzcd}
 & 142 \arrow[r, "-HCN", "*"'] & 115 \arrow[r, "-CN", "*"'] & 89 \arrow[r, "-C_2H_2"] & 63 & \text{path } a \\
170 \arrow[ur, "-CO", "*"'] \arrow[dr, "-O"', "*"] & & & & & \\
 & 154 \arrow[r, "-HCN", "*"'] & 127\ \textit{etc.} & & & \text{path } b
\end{tikzcd}$$

that its formation can be initiated by the lowest energy ionization of the N-oxide and hence the species thus produced should be represented as **a**, which then eliminates an oxygen atom to afford the 2-cyanoquinoline ion (**b**). This behavior is characteristic for most of aromatic amine N-oxides[13] having no alkyl substituent at *ortho*-position to the N-O function.[14,15]

If the whole fragmentation process of **1** is initiated by the primary loss of oxygen atom (path *b*), most of the fragments observed in the spectrum of this N-oxide should be similar to those of the corresponding parent base (**2**). In this connection, the spectrum of **2** was taken under the same condition (Table I and Fig. 1). Comparison of the spectra of **1** and **2** revealed that in the N-oxide an entirely different decomposition process (path *a*), which requires prior formation of a C-O bond, exists and this virtually demands isomerization to the oxaziridine species (**c**). This oxaziridine ion (**c**) would then undergo rearrangement to the corresponding oxazepine ion (**d**) before fragmentation takes place.

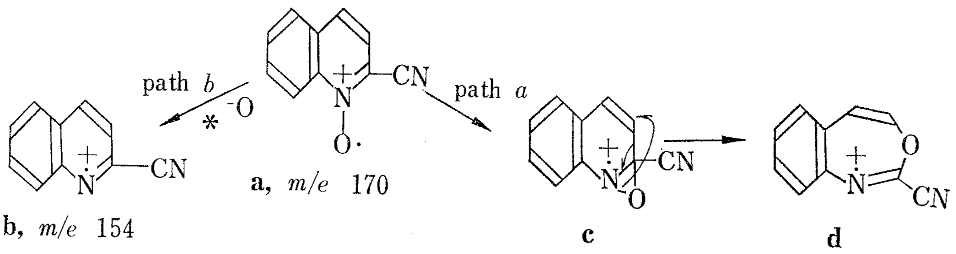

Chart 3

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[13] T.A. Bryce and J.R. Maxwell, *Chem. Commun.*, **1965**, 206.
[14] R. Grigg and B.G. Odell, *J. Chem. Soc.* (B), **1966**, 218.
[15] A. Tatematsu, H. Yoshizumi, E. Hayashi, and H. Nakata, *Tetrahedron Letters*, **1967**, 2985.

In the mass spectrometry, the oxaziridine ion formation from nitroaryl cation[16] and the insertion of the methylene or oxygen atom[17] into the adjacent ring position in some benzenoid compounds to form a seven-membered ring has now been quite settled and these facts may support the above rearrangement processes by analogy. The mass spectrum of benz[*d*]-1,3-oxazepine-2-carbonitrile (**3**) derived photochemically from **1** was then measured and the results obtained confirmed the correctness of the above deduction. As shown in Table I and Fig. 1, the whole fragments of its spectrum are almost identical with those belonging to path *a* of **1**. The most reasonable pathway of the decomposition of **d** may be formulated as in the following scheme.

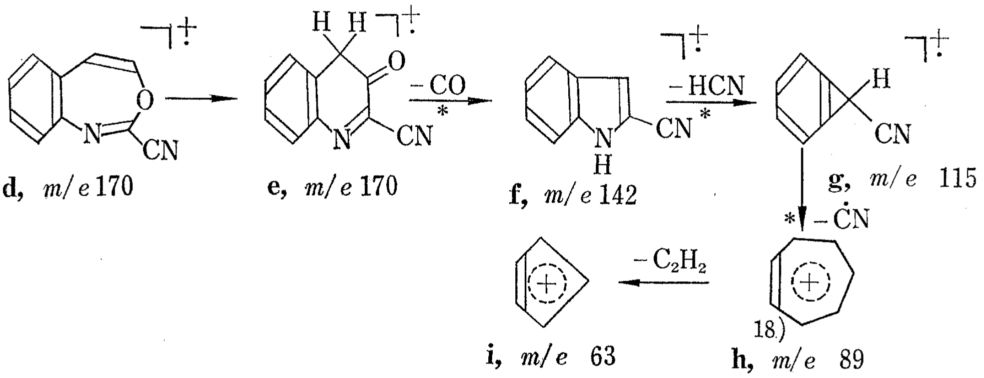

Chart 4

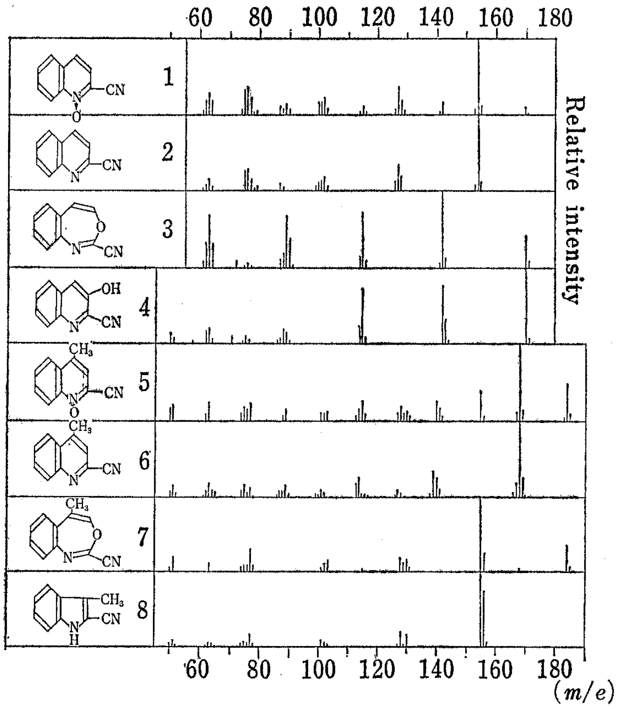

Fig. 1. Mass Spectra of 2-Cyanoquinoline 1-Oxide and Related Compounds

The elemental compositions of each fragment ion (**d**—**i**) were confirmed by accurate mass measurement. As the mass spectrum of 3-hydroxyquinoline-2-carbonitrile (**4**), obtained from **3** by the action of trifluoroacetic acid,[20] is almost identical with that of **3**, we may suggest the intermediary formation of ion, **e**. The mass spectra of 4-methyl derivatives (**5**—**7**) were then examined and the results are summarized in Fig. 1. Here again, it is evident that a part of the molecular ion of 4-methyl-2-cyanoquinoline 1-oxide (**5**) undergoes rearrangement to the corresponding benz[*d*]-1,3-oxazepine ion (**j**) before fragmentation takes place. The most intense fargment ion (*m*/*e* 155, M-CO-H) of **7** may then

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16) *a*) O.L. Chapman, D.C. Heckert, J.W. Reasoner, and S.P. Thackaberry, *J. Am. Chem. Soc.*, **88**, 5550 (1966); *b*) J.H. Beynon, R.A. Saunders, and A.E. Williams, *Z. Naturforsch.*, **20a**, 180 (1965); *c*) M.M. Bursey and F.W. McLafferty, *J. Am. Chem. Soc.*, **88**, 529 (1966).

17) F.W. McLafferty, M.M. Bursey, and S.M. Kimball, *J. Am. Chem. Soc.*, **88**, 5022 (1966), and references cited therein.

18) Dehydrotropylium cation, **h**, has been proposed[19] for the fragment at *m*/*e* 89 in the spectra of benzofuran and its 2-acylated derivatives.

19) B. Willhalm, A.F. Thomas, and F. Gautschi, *Tetrahedron*, **20**, 1185 (1964).

20) *a*) C. Kaneko, Sa. Yamada, and M. Ishikawa, *Tetrahedron Letters*, **1966**, 2145; *b*) C. Kaneko and Sa. Yamada, *Chem. Pharm. Bull.* (Tokyo), **15**. 663 (1967).

be the 2-cyanoquinolinium cation (**l**) which may be derived by the loss of hydrogen atom from M-CO ion (**k**). The presence of the metastable peak at mass 154 supports the above deduction.

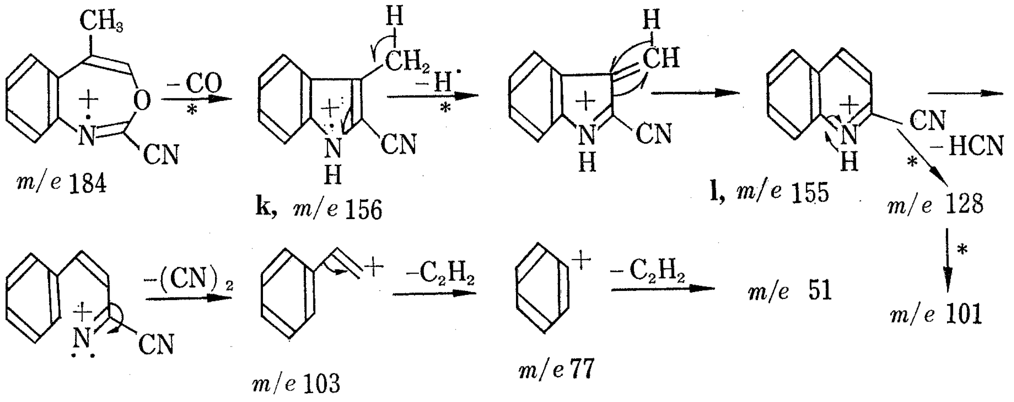

Chart 5

The presence of a metastable peak at *m/e* 105.7 indicates that the peak at *m/e* 128 is formed from **l** by loss of HCN. The peak at *m/e* 130 may probably arise from ***k*** by loss of CN radical. As a support to the mechanism shown in the above scheme, it was found that below *m/e* 156 the spectrum of **7** was very similar to that of skatole-2-carbonitrile (**8**). It is also worthy to note that the compound (**8**) was obtained from **7** by 2537 Å irradiation in an appropirate solvent.[21]

Quinoline 1-Oxide and Its Related Compounds

The results described in the previous section provide another striking example of parallel behavior of an organic molecule in photolysis and electron impact.[16a,22] To investigate other such examples the mass spectra of quinoline 1-oxide (**9**), its 4-methyl derivative (**11**), and some of their photo-products were examined (Fig. 2).

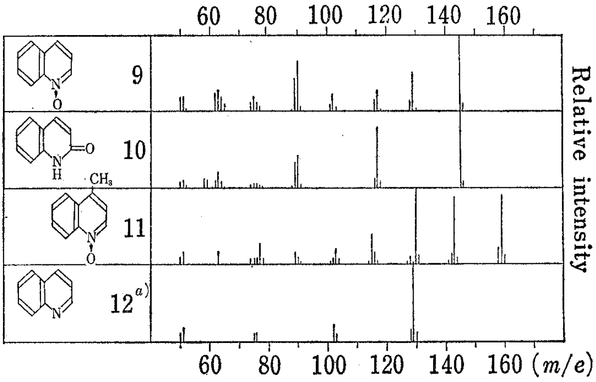

Fig. 2. Mass Spectra of Quinoline 1-Oxide and Related Compounds

a) This spectrum was reproduced from the data obtained from Ref. 25.

It is evident from comparison of the mass spectra of **9**, carbostyril (**10**), and quinoline[25] (**12**) that appreciable amount of the M^+ ion of **9** undergoes rearragement to the corresponding oxaziridine ion (**m**) since the fragments at *m/e* 117 (M-CO) and other fragments at *m/e* 90, 89, 63, *etc.*, are not observed in the mass spectrum of **12**, and appear in the spectrum of **9** as the significant peaks. As the spectrum

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21) C. Kaneko and Sa. Yamada, *Chem. Pharm. Bull.* (Tokyo), **14**, 555 (1966).

22) Isomerization of 2-cyanoquinoline 1-oxide (**1**) to benz[*d*]-1,3-oxazepine-2-carbonitrile (**3**) by UV irradiation contains two steps, namely, formation of the corresponding oxaziridine (II, X=CN) and its subsequent rearrangement to **3**, as already mentioned. At present we assume that the second step proceeds thermally.[23] If this is the case, the process such as **c**→**d** upon electron impact gives an example of parallel behavior in thermolysis and electron impact.[24]

23) C. Kaneko, Sa. Yamada, and I. Yokoe, *Tetrahedron Letters*, **1966**, 4701.

24) D.C. DeJongh, R.Y. Van Fossen, and C.F. Bourgeois, *Tetrahedron Letters*, **1967**, 271, and the reference cited therein.

25) A. Cornu and R. Massort, "Compilation of Mass Spectral Data," Heyden & Son, 1966.

of **10**, which is obtained from **9** by photolysis in a protic solvent, contains essentially the same fragments (*m/e* 117, 90, 89, 63 *etc.*), the following decomposition scheme (solid arrow) could be postulated.

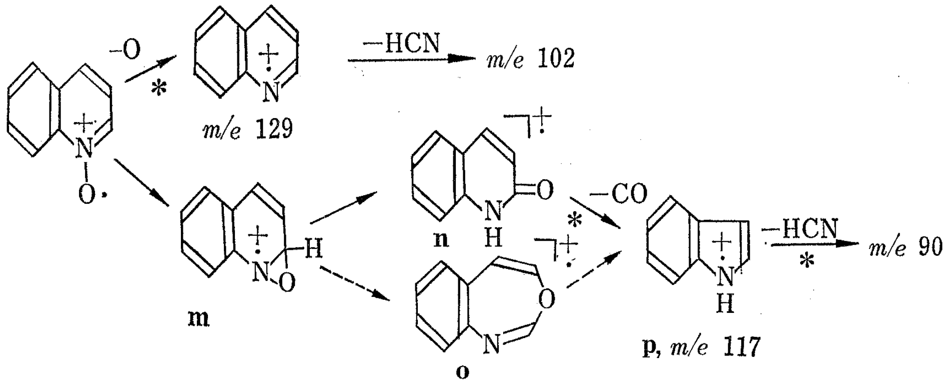

Chart 6

Since all of quinoline 1-oxides having no substituent in their 2-position so far examined fail to give the stable oxazepines[26] and this prevents the direct mass comparison, the pathway (dotted line) via the corresponding oxazepine ion (**o**) could not be excluded and, therefore, should remain as a possible alternative. The definite choice between these two alternative processes responsible in the production of M–CO ion (**p**) must await a labeling experiment.

The spectrum of 4-methylquinoline 1-oxide (**11**) also demonstrates the existence of M–CO ion (**q**) which then loses hydrogen atom to yield the stable quinolinium ion (**r**). The fate of this ion is well known[28] and all of the fragment ions derived from this ion are actually found in the spectrum of **11**.

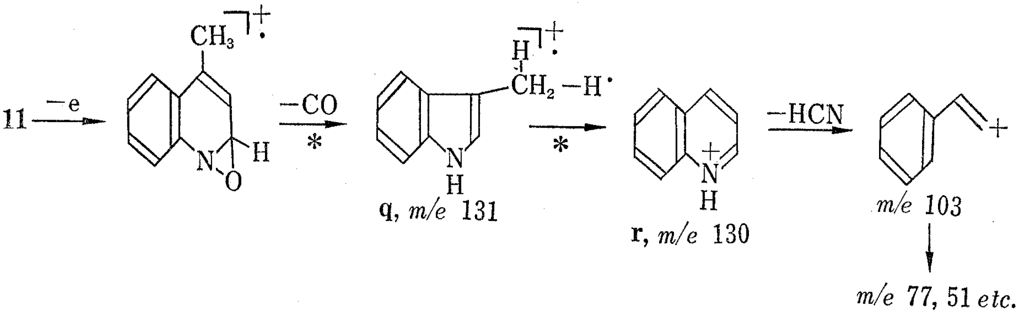

Chart 7

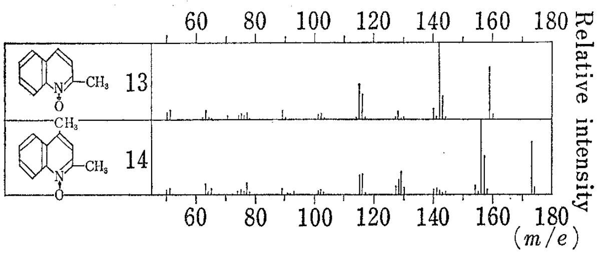

Fig. 3. Mass Spectra of 2-Methyl- and 2,4-Dimethyl-quinoline 1-Oxides

2-Methyl- and 2,4-Dimethyl-quinoline 1-Oxides

The N-oxides so far examined have a strong M–16 ion, without exception, together with an appreciable amount of M–CO ion. By comparison with the spectra of the related compounds (such as the corresponding benz[*d*]-1,3-oxazepines), it can be concluded that the

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26) Streith, *et al.* isolated N-formyl-2-hydroxy-2,3-dihydroindole (VIII) as a major product from the irradiated benzene solution of quinoline 1-oxide.[27] Since the corresponding N-acetyl derivative was obtained from 2-methylbenz[*d*]-1,3-oxazepine (I, X=CH_3),[23] it was evident that the direct photo-product of quinoline 1-oxide in an aprotic solvent is benz[*d*]-1,3-oxazepine (I, X=H).

27) J. Streith, H.K. Darrah, and M. Weil, *Tetrahedron Letters*, **1966**, 5555.

28) H. Budzikiewicz, C. Djerassi, and D.H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, 1964, p. 252.

presence of M–CO ions in the spectra of these 1–oxides can be regarded as a criterion for the intermediary of the corresponding oxaziridine ions, and hence, in most cases, the corresponding oxazepine ions. However, in the mass spectra of quinoline 1–oxides having 2–methyl group (**13** and **14**), the most abundant ions are M–17 ions (Fig. 3).

The formation and further decomposition of these ions may be represented by the following formulae:

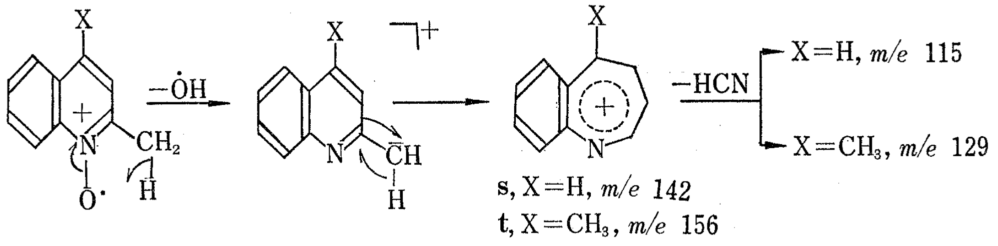

Chart 8

As discussed already, 4–methylquinoline 1–oxide (**11**) does not show M–17 ion and hence, the *ortho*–effect of the methyl group in **13** and **14** should be responsible for the formation of these benzazatropylium ions (**s** and **t**). These observations are in good agreement with the results obtained by Grigg and Odell.[14] By the predominance of this process, the expected M–CO ion (or M–29 ion) from the rearrangement process forming oxaziridine and oxazepine ions becomes almost negligible in the spectra of **13** and **14**.

2-Phenylquinoline 1-Oxide and Its Related Compounds

The mass spectrum of 2–phenylquinoline 1–oxide (**15**) has two abnormal features compared to those of the previously described N–oxides. These are (i) the M–1 ion is quite intense and, (ii) though the loss of CO is evident, no similarity exists between the mass spectra of **15** and the corresponding photo–product (**17**).

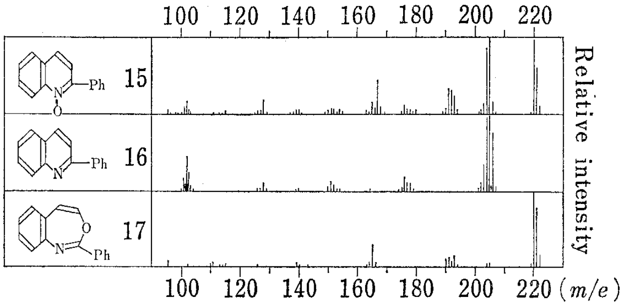

Fig. 4. Mas Spectra of 2–Phenylquinoline 1–Oxide and Related Compounds

These abnormalities can partly be explained by postulating a cyclic structure (**u**) for M–1 fragment ion. Similar cyclic intermediates have been proposed to explain the mass spectra of 2–phenyltropone and its related compounds.[29] The abnormality of **17** from other oxazepines mentioned is again evident, since the base peak of its spectrum is M–1 ion and the M–CO ion is very weak (14%). A more thorough experiment seems to be needed to understand the apparent complex processes operating in these three compounds (**15**—**17**).

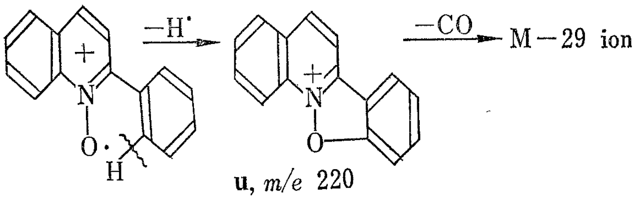

Chart 9

2. Mass Spectra of Isoquinoline 2-Oxides and Their Related Compounds

1-Cyanoisoquinoline 2-Oxide and Its Related Compounds

In Fig. 5 are shown the mass spectra of 1–cyanoisoquinoline 2–oxide (**18**), its 3–methyl derivative (**21**), and their related compounds (**19, 20, 22,** and **23**).

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[29] J.M. Wilson, M. Ohashi, H. Budzikiewicz, C. Djerassi, S. Ito, and T. Nozoe, *Tetrahedron*, **19**, 2247 (1963).

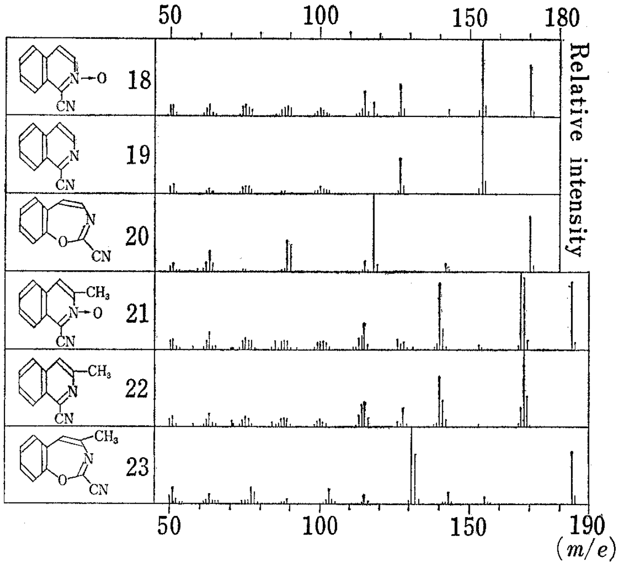

Fig. 5. Mass Spectra of 1-Cyanoisoquinoline 2-Oxide and Related Compounds

Benz[*f*]-1,3-oxazepine-2-carbonitriles (**20** and **23**) exhibit striking difference in their behavior from that of benz[*d*]-1,3-oxazepine-2-carbonitriles. Loss of $(CN)_2$ becomes more predominant than loss of CO which was observed in the spectra of **3** and **7**. Thus, **20** exhibits M-52 peak[30] (*m/e* 118) as the base peak in its spectrum and, in the spectrum of **23**, the base peak appears at *m/e* 131 (M-53). The presence of the metastable peak at mass 130 indicates that this ion is derived by the loss of hydrogen atom from the corresponding M-52 ion. The following decomposition scheme seems to be the most reasonable.

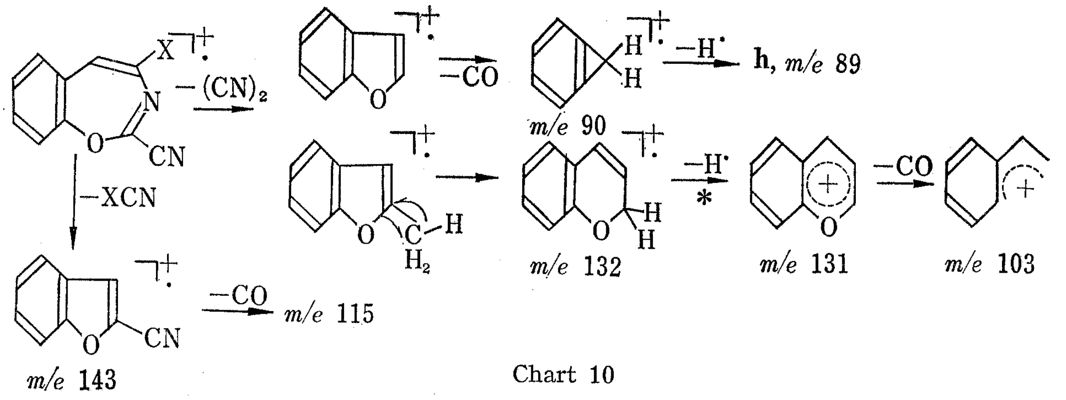

Chart 10

The mass spectra of benzofuran and its 2-substituted derivatives are well known,[19] and all of the expected fragment ions appear in the spectra of **20** and **23**. The loss of X-CN from the molecular ions of **20** and **23** yields an ion of mass 143, which then expels carbon monoxide to yield a fragment of mass 115.[31]

The mass spectrum of **18** exhibits ions at *m/e* 118, 115, 90, 89, *etc.*, of low abundance together with all the fragments coinciding with those of the corresponding 1-cyanoisoquinoline (**19**). Since the former ions are all observed in the spectrum of **20**, it can be concluded that some of the molecular ion of **18** undergoes rearrangement to the corresponding benz[*f*]-1,3-oxazepine ion before fragmentation takes place. However, in **21**, the lack of ion at *m/e* 131 may suggest that none of the fragmentation of this N-oxide proceeds via the corresponding oxazepine ion. The abnormality of this N-oxide is probably due to the *ortho*-effect of the methyl group neighboring the N-O function.

Isoquinoline 2-Oxide and Its Related Compounds

The mass spectra of isoquinoline 2-oxide (**24**), isocarbostyril (**25**), and isoquinoline (**26**) are shown in Fig. 6. The mass spectrum of **25** which is obtained from **24** by ultraviolet (UV)

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30) The elemental composition of M-52 ion was demonstrated as C_8H_6O by accurate mass measurement.

31) The mass spectra of **20** and **23** have been reported by Buchardt, *et al.*[9] and their assignment are in good accord with ours. The structure given to *m/e* 90 in Ref. 9 was incorrect and should be given to *m/e* 89.

irradiation in protic solvents (*i.e.*, methanol, water, *etc.*) is very interesting, since the most abundant fragment ion is at *m/e* 118 (M–HCN) and this fact contrasts strongly with the ease of formation of M–CO ion from carbostyril (**10**). The direct attachment of the carbonyl carbon to benzene ring in **25** may hinder the fission of this bond which is the key step to produce the M–CO ion.[32]

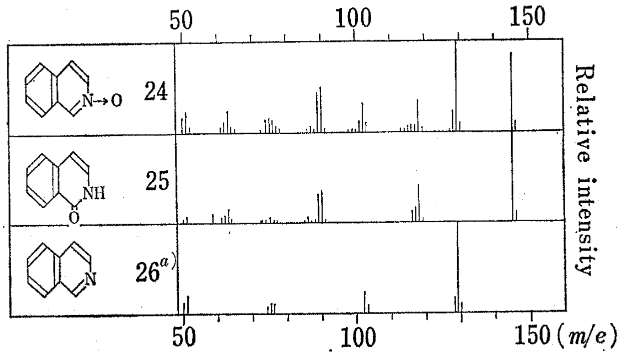

Fig. 6. Mass Spectra of Isoquinoline 2–Oxide and Related Compounds

a) This spectrum was reproduced from the data obtained from Ref. 25.

The formation of indole ion from the molecular ion of **25** is evident though minor in amount, since the spectrum of **25** contains a peak at *m/e* 117 and the metastable peak at mass 99.2 due to transition of $117^+ \rightarrow 90^+ + 27$. It is not possible to establish in detail the process by which hydrogen cyanide can be eliminated, but M–HCN ion seems to be represented as **w**, since at lower mass numbers the spectrum of **25** is very similar to that of benzofuran. Thus the suggested process would be as follows:

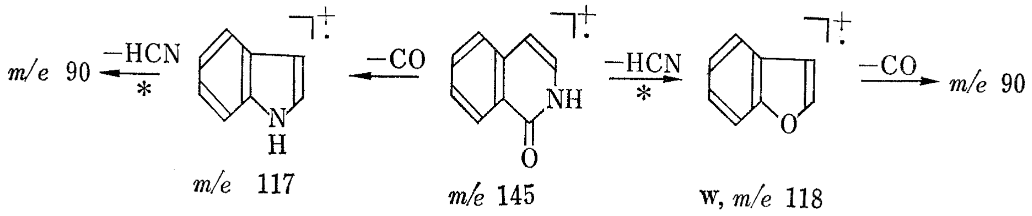

Chart 11

It should be reminded that the species represented was in this and the subsequent schemes may also be an isobenzofuran ion.

The mass spectrum of isoquinoline 2–oxide (**24**) contains all the peaks observed in that of isoquinoline (**26**), together with other significant peaks at *m/e* 118, 117, 90, 89, *etc.*, and all these peaks are observed in the spectrum of **25** as the sole significant peaks. Therefore, the following major decomposition scheme for **24** could be postulated.

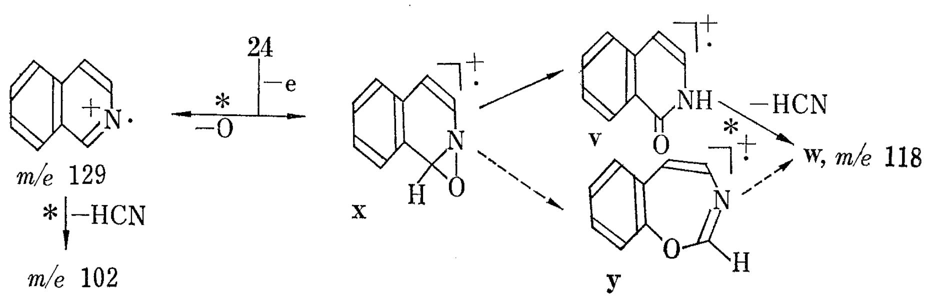

Chart 12

The alternative course from **x** to **w** via the corresponding oxazepine ion (**y**), may also be considered as a possible one as in the case of **m** to **p**. These results therefore indicate that a parallelism between electron impact and photolysis again exists in isoquinoline 2–oxide itself.

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[32] These results suggest that the similarity (especially the common existence of M–CO ion with comparable abundance) in the mass spectra of 1– and 2–naphthols[25] may be due to randomizing isomerization of the molecular ions *via* the corresponding benzoxepine or epoxynaphthalene ions. This type of randomizing isomerization of aryl alkyl ethers was proposed recently by McLafferty, *et al.*[17]

Experimental

Compounds——The compounds used in the present work were prepared by previously reported methods.[6,7,8,10,20,21,23]

Mass Spectral Measurements——The spectra were measured by a Hitachi Double-focussing Mass Spectrometer Model RMU-6E, using an all-glass inlet system. Heating temperature of the sample was about 120° for the oxazepines and about 200° for the N-oxides. The accurate mass measurements were made by a peak-matching method. The ionizing energy was kept at 70 eV unless otherwise noted.

Acknowledgement Three of the authors (C.K., Sa. Y., and I.Y.) are greatly indebted to Professor Masayuki Ishikawa of Tokyo Medico-Dental University for his encouragement during this study. The measurement of high-resolution mass spectrum of **3** was kindly performed by Dr. T. Aoyama of Japan Electron Optics Laboratory Co., Ltd., by using a JMS-01S double-focussing mass spectrometer. One of the authors (C.K.) deeply acknowledges to Fuji Photo-Film Co., Ltd. for the grant by which a part of the expenses was defrayed.