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Electron Impact Promoted Fragmentation of Some 4-Quinolone Alkaloids and Related Compounds*

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The complete high resolution mass spectra and low resolution mass spectra of sixteen alkaloids and related compounds containing the 4-quinolone ring system fused to either a dihydropyran or a dihydrofuran ring system have been recorded, and rationalizations of their decomposition modes subsequent to electron impact have been suggested. Mass spectrometry provides a powerful tool for the recognition of these 4-quinolone bases, but differentiation between isomeric compounds having fused dihydropyran or dihydrofuran ring systems is more difficult; however, quantitative and in some cases also qualitative differences distinguish their respective mass spectra.

Mass spectrometry has been widely applied to structure elucidation problems in natural products chemistry,[1] being especially powerful in the field of alkaloid structure determination.[2] No systematic study of the mass spectral fragmentation of bases containing the 4-quinolone ring system, fused either to a dihydropyran or dihydrofuran ring, has appeared. However, some fragmentation processes have been described for a few alkaloids or derivatives bearing these skeletons.[3–6] To study the mass spectral reactions of these two types of quinolone bases the complete high resolution spectra of the sixteen compounds studied, *1–16*, were recorded and the data analyzed with the aid of the recently developed computer program, INTSUM.[7] Automated treatment of the large amount of information present in a series of high resolution spectra of complicated molecules has been shown [7,8] to be a valuable tool in reducing and summarizing the data in a form useful in the subsequent analysis. For the present series of compounds the INTSUM treatment proved less useful than expected. A preliminary examination of the spectra did, however, reveal the occurrence of a number of reactions that we would not have predicted *a priori*, and it was therefore decided to study the spectra more closely, using the traditional approach of organic mass spectrometrists, to elucidate the reactions upon electron impact of these compounds.

Nearly all reactions that give rise to abundant ions take place in the dihydropyran or dihydrofuran rings, which in itself reduces the number of possible fragmentations to consider; furthermore, many of the reactions that give rise to abundant ions are in fact rearrangement processes. A thorough examination of the course of these rearrangements would conceivably require extensive isotope- and substituent-labeling, which was, however, beyond the scope of this investigation. The present report describes the basic fragmentation processes occurring upon electron impact in the quinolone ethers examined, to show how mass spectrometry can differentiate within these two classes of alkaloid; it also provides further examples of how isomerization processes subsequent to electron impact may give rise to

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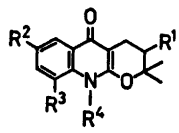


Khaplofoline (*1*): $R^1 = R^2 = R^3 = R^4 = H$.
N-Methylkhaplofoline (*2*): $R^1 = R^2 = R^3 = H$, $R^4 = CH_3$.
Ribalinine (*3*): $R^1 = OH$, $R^2 = R^3 = H$, $R^4 = CH_3$.
Ribalinidine (*4*): $R^1 = R^2 = OH$, $R^3 = H$, $R^4 = CH_3$.
Isobalfourodine (*5*): $R^1 = OH$, $R^2 = H$, $R^3 = OCH_3$, $R^4 = CH_3$.
7-*O*-Methylribalinidine (*6*): $R^1 = OH$, $R^2 = OCH_3$, $R^3 = H$, $R^4 = CH_3$.
3′-*O*-Acetyl-7-*O*-methylribalinidine (*7*): $R^1 = OCOCH_3$, $R^2 = OCH_3$, $R^3 = H$, $R^4 = CH_3$.

fragmentation modes that are ambiguous or even misleading when using mass spectrometry alone for structure elucidation. Ten of the compounds studied, *1*, *3*–*5*, *8*, *9*, *11*, *13*, *15*, and *16*, are natural bases whilst the others have not been found in nature.

4-Quinolone bases containing a fused dihydropyran ring system. All the alkaloids of this group exhibit abundant molecular ion peaks in their mass spectra. Loss of a hydroxyl radical from the molecular ion is common to all bases studied, except the C(3′) acetoxy derivative, *7*, and could well encompass the 4-quinolone oxygen atom, since the compounds lacking an oxygen function at C(3′), *1* and *2*, also show this fragmentation, and since a similar reaction was absent in the mass spectra of several natural products containing the 2,2-dimethylchroman ring system.[9]

Elimination of a methyl radical from their respective molecular ions gives rise to abundant ions for compounds *1* and *2*. The CH_3 group is presumably lost from the *gem*-dimethyl group by cleavage α to the ether oxygen atom. Methyl loss is considerably less pronounced for the C(3′) oxygenated compounds, *3*–*7*, possibly because scission of the C(2′)–C(3′) bond, which is in these compounds α to both oxygen atoms, becomes more favorable. The oxygenated compounds do, however, give rise to characteristic ions corresponding to the combined loss of H_2O and CH_3 (for *7*, of CH_3COOH and CH_3). Presumably, these ions arise by elimination of a methyl radical followed by dehydration of that species, but no metastable ion evidence was found to clarify this point. The 3′-acetoxy derivative, *7*, eliminates CH_3COOH prior to loss of CH_3·, to yield a species formally corresponding to the 2,2-dimethylchromene ring system; loss of CH_3· is characteristic of 2,2-dimethylchromenes.[9,10]

Expulsion of 29 a.m.u. from the molecular ion occurs for bases *1*–*6*. The high resolution data show that for *1* and *2*, the fragment eliminated is an ethyl radical, possibly C(3′), C(4′) plus an additional hydrogen atom, whereas for the oxygenated bases *3*–*6* the 29 a.m.u. fragment eliminated is CHO. This difference

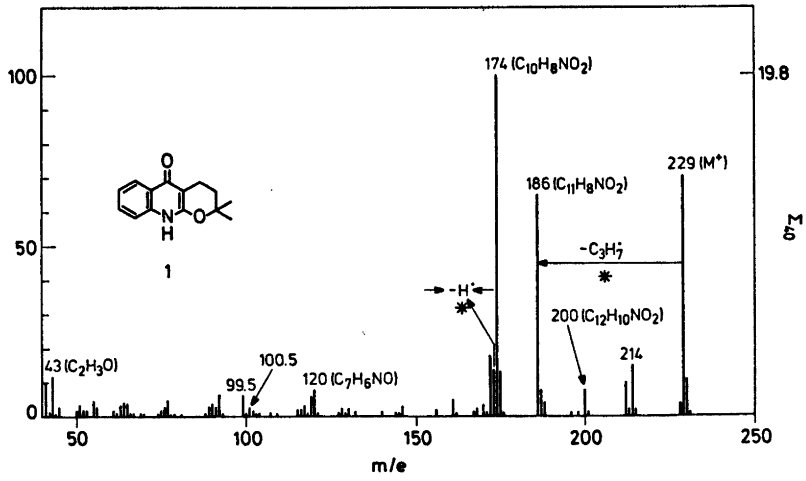
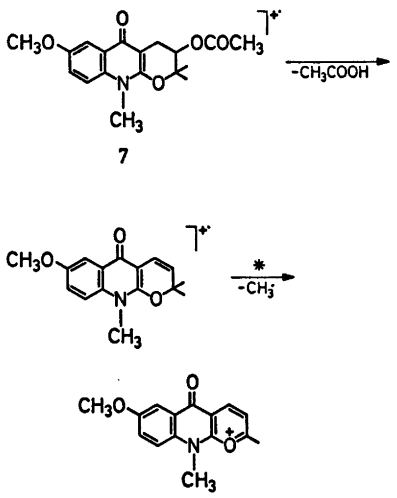


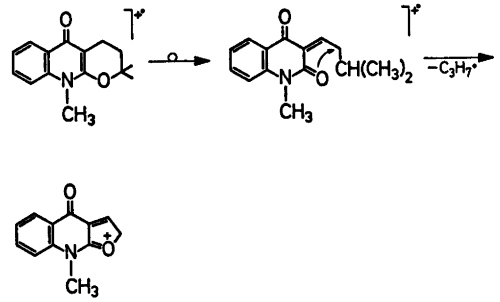
Fig. 1. Mass spectrum (70 eV) of khaplofoline (*1*).



Scheme 1.

in fragmentation is surprising since *N*-methyl-4-quinolone itself eliminates CHO,[11] and it was indeed overlooked in a previous study [6] of these compounds. The CHO fragment may incorporate the carbonyl group of the quinolone system, or it may be C(3′) with its attached oxygen function, less the hydroxyl hydrogen atom, since the mass spectrum of *6*-OD shows greater than 80 % retention of the isotopic label in the $[M-CHO]^+$ ion.

Loss of a C_3H_7 radical from the molecular ions of bases *1* and *2* gives rise to very abundant ions. This can be rationalized in terms of extrusion of the *gem*-dimethyl entity, as shown in Scheme 2; isomerization by ring contraction prior to $C_3H_7^{\cdot}$ elimination to an isopropyl-dihydrofuran structure (see below) is a viable mechanistic alternative. Convincing evidence that the analogous loss of a CH_3 fragment from chroman occurs by ring con-



Scheme 2.

traction has been presented by Djerassi and coworkers [12] and by Budzikiewicz and Lenz.[13] Also tetrahydropyrans have been shown to undergo ring contraction upon electron impact.[14] The spectra of compounds *3*–*6* show peaks corresponding to the loss of C_3H_7O rather than C_3H_7; 3-hydroxychroman analogously eliminates a CH_3O fragment.[13] This reaction may occur *via* transfer of the C-3′

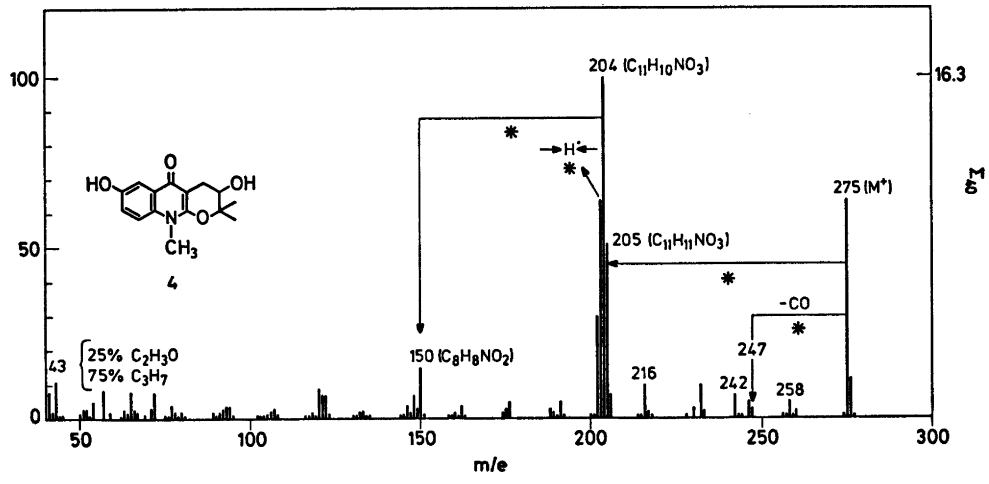
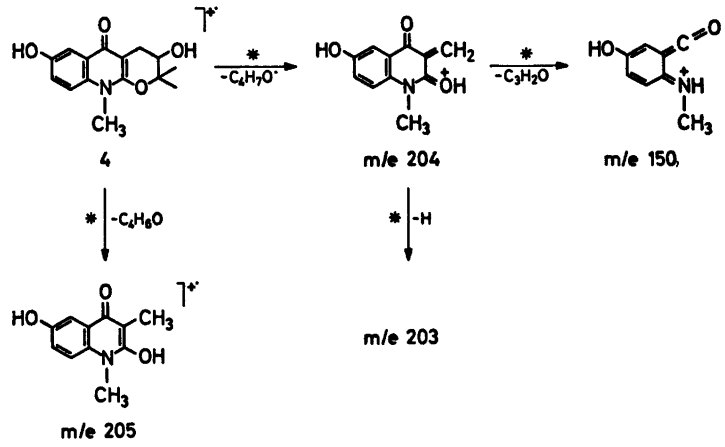


Fig. 2. Mass spectrum (70 eV) of ribalinidine (*4*).



Scheme 3.

hydroxyl to C-2′ as suggested for the latter compound,[13] or *via* ring contraction with formation of species similar to the dihydrofuran bases described below. Once again it should be noted that these reactions would not have been predicted from previous studies[9] of the related 2,2-dimethylchroman ring system.

Very intense peaks in the spectra of compounds *1* – *6* correspond to ions formed through elimination, after hydrogen migration, of fragments consisting of C(2′), C(3′), and their substituents (reactions of this type are sometimes classified as 'RDA + H' processes), and to ions formed herefrom by further loss of a hydrogen atom, as shown for compound *4* in Scheme 3 (see ions *m/e* 204 and 203). Analogous reactions have been observed for 2,2-dimethylchromanes[9] and other similar oxygen heterocycles.[15] The bases carrying a C(3′) hydroxyl group (*3* – *6*) in addition suffer extrusion of the C(2′) – C(3′) fragment after double hydrogen transfer (formation of *m/e* 205 in Scheme 3).

A characteristic ion present in all spectra corresponds in elemental composition to the molecular ion less the dihydropyran ring, plus one hydrogen atom (for *4*, *m/e* 150; see Scheme 3). Metastable ion evidence suggests that this ion is generated stepwise as shown, by loss of initially two, then four of the dihydropyran ring atoms, in what may be considered two successive RDA fragmentations.

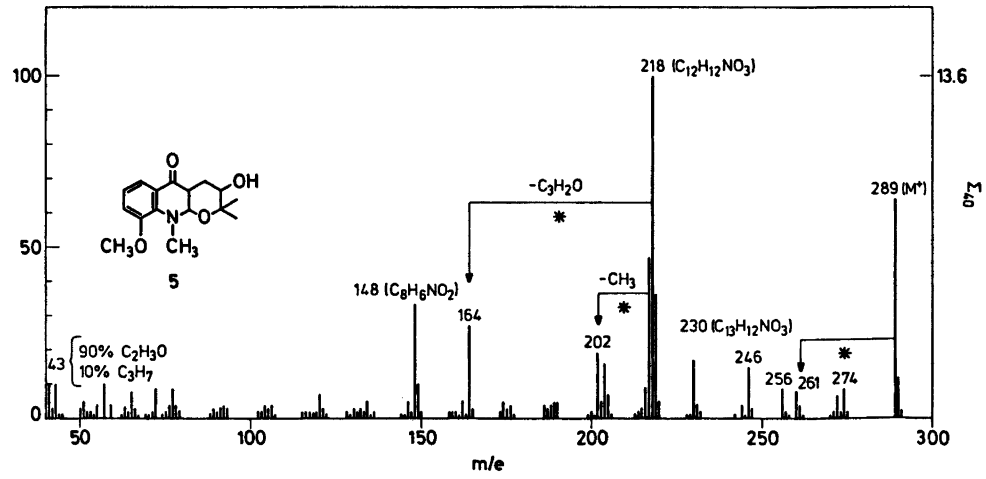
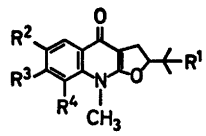
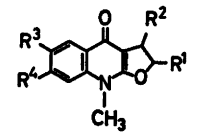


Fig. 3. Mass spectrum (70 eV) of isobalfourodine (*5*).



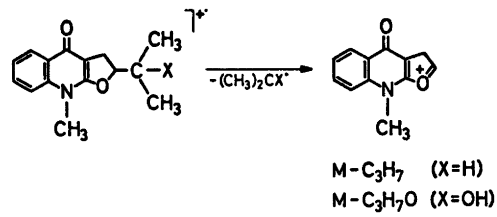
Lunacrine (*8*): $R^1=R^2=R^3=H$; $R^4=OCH_3$.
Lunine (*9*): $R^1=R^2=H$; R^3, $R^4=-OCH_2O-$.
6-Deoxyribaline (*10*): $R^1=OH$; $R^2=R^3=R^4=H$.
Ribaline (*11*): $R^1=R^3=OH$; $R^2=R^4=H$.
6-*O*-Methylribaline (*12*): $R^1=OH$; $R^2=OCH_3$; $R^3=R^4=H$.
Balfourodine (*13*): $R^1=OH$; $R^2=R^3=H$; $R^4=OCH_3$.

4-Quinolone alkaloids containing a fused dihydrofuran ring. The two alkaloids of this group which contain a 2′-isopropyl group, *8* and *9*, yield mass spectra that closely resemble those of the 2,2-dimethyldihydropyran analogs, *1* and *2* (*cf.* Figs. 1 and 4). Thus, bases *8* and *9* show reasonably intense peaks in their mass spectra corresponding to loss of OH, CH_3 and C_2H_5 radicals from the molecular ion, and very intense peaks for $[M-C_3H_7]^+$ and $[M-C_4H_4]^+$ ions, as do *1* and *2*. The occurrence of these reactions for both pairs of compounds, giving rise to spectra that are also quantitatively very similar, suggests isomerization to a common structure or mixture of structures. The facile methyl loss from the molecular ions of both pairs suggests 2,2-dimethyldihydropyran as the preferred structure; on the other hand, the presence of abundant $[M-C_3H_7]^+$ ions may conveniently be rationalized as α-cleavage from a 2-isopropyldihydrofuran structure.



Isodihydrokokusaginine (*14*): $R^1=R^2=H$; $R^3=R^4=OCH_3$.
Lemobiline (*15*): $R^1=(CH_3)_2$; $R^2=CH_3$; $R^3=R^4=H$.
Ifflaiamine (*16*): $R^1=CH_3$; $R^2=(CH_3)_2$; $R^3=R^4=H$.

Four of the dihydrofuran bases examined, *10*–*13*, contain a hydroxy substituted isopropyl group in the 2′-position. The fragmentation of these compounds is reminiscent of that of the two isopropyl compounds, *8* and *9*, except that the fragments lost are nearly all oxygen containing. Analogous to the loss



Scheme 4.

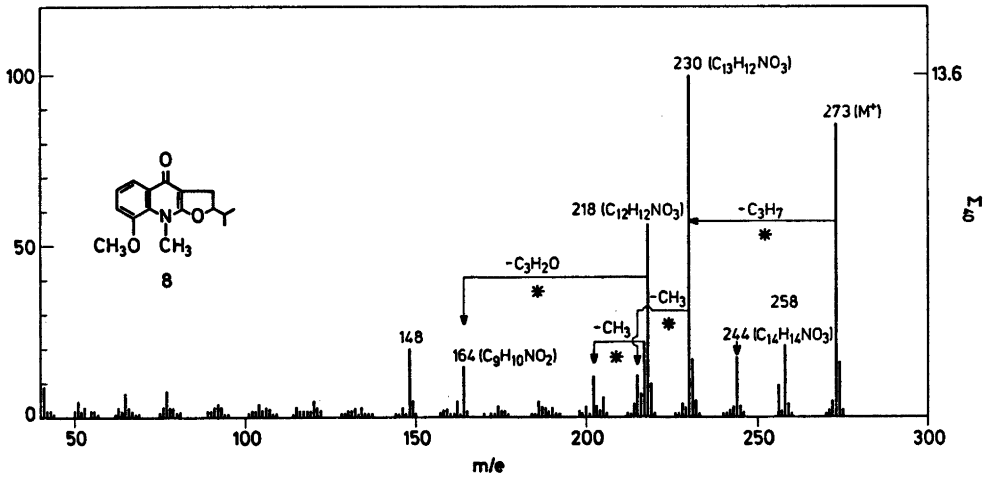


Fig. 4. Mass spectrum (70 eV) of lunacrine (*8*).

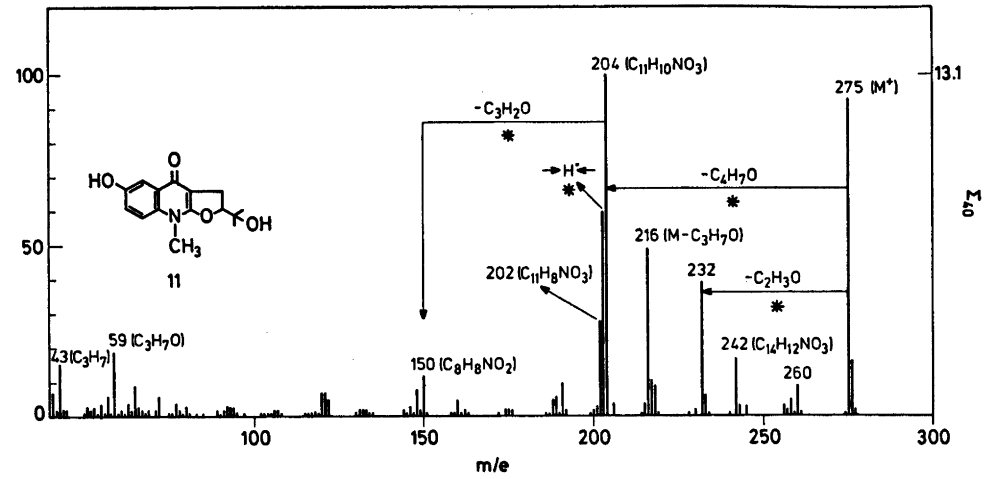


Fig. 5. Mass spectrum (70 eV) of ribaline (*11*).

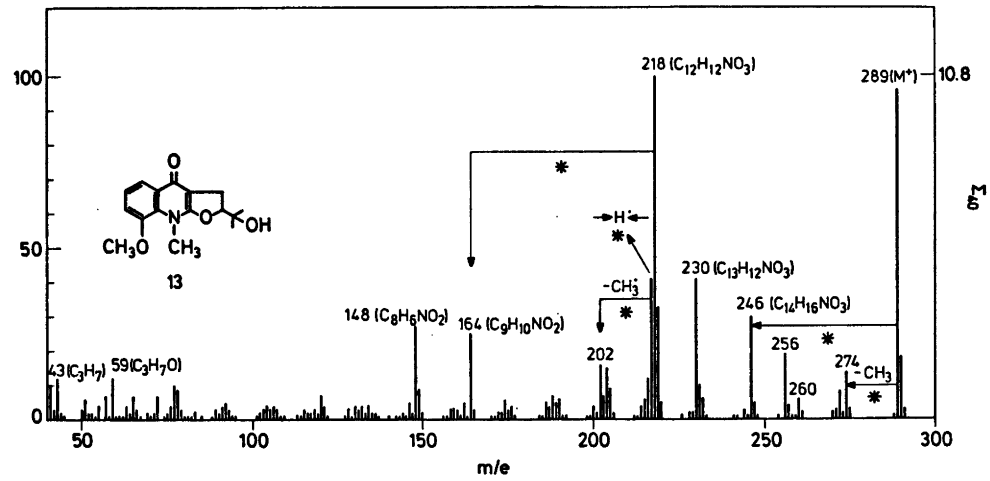


Fig. 6. Mass spectrum (70 eV) of balfourodine (*13*).

of C_3H_7 and C_4H_7 radicals from *8* and *9*, the spectra of *10*–*13* show intense peaks for $[M-C_3H_7O]^+$ and $[M-C_4H_7O]^+$ ions. The loss of $C_3H_7O^\cdot$ is visualized as cleavage α to both oxygen atoms in *10*–*13* (see Scheme 4). Similar elimination of $C_3H_7O^\cdot$ from 2-hydroxyisopropyl substituted di- and tetrahydrofurans has been observed previously.[16,17] The presence of $[M-C_3H_7O]^+$ peaks in the spectra of the 3′-hydroxydihydropyran bases *3*–*6* (see above) could be taken as evidence for the occurrence of a ring contraction process prior to fragmentation also in these compounds. It is, however, not very likely that complete isomerization to a common structure occurs prior to loss of $C_3H_7O^\cdot$ for the bases that have an oxygen function attached to the fused dihydrofuran (*10*–*13*) or dihydropyran ring (*3*–*6*), since the abundances of the corresponding ions differ considerably. The intensities of the $[M-C_3H_7O]^+$ peaks are on an average four times higher in the dihydrofuran spectra than in the dihydropyran spectra. Furthermore, only the dihydrofuran bases show appreciable

Table 1. Principal ions observed in the mass spectra of the 4-quinolone bases studied.[a]

N-Methylkhaplofoline (*2*)

M+ 243 (82), 242 (3), 228 (14), 226 (7), 214 (11), 200 (93), 188 (100), 187 (20), 186 (17), 175 (5), 134 (11), 132 (6), 130 (5), 107 (8), 105 (5), 104 (7), 77 (14), 51 (6), 41 (12).

Ribalinine (*3*)

M+ 259 (40), 242 (12), 230 (3), 226 (4), 216 (4), 200 (5), 189 (39), 188 (100), 187 (10), 186 (8), 160 (3), 134 (12), 104 (4), 77 (8), 72 (8), 57 (7), 43 (6), 41 (4).

7-*O*-Methylribalinidine (*6*)

M+ 289 (75), 274 (3), 272 (6), 261 (4), 260 (6), 256 (10), 246 (12), 244 (3), 230 (15), 219 (54), 218 (100), 217 (95), 216 (10), 205 (7), 204 (11), 203 (6), 202 (30), 164 (9), 148 (15), 136 (7), 120 (5), 77 (5), 72 (7), 59 (4), 57 (7), 43 (9), 41 (7).

3′-*O*-Acetyl-7-*O*-methylribalinidine (*7*)

M+ 331 (31), 272 (20), 271 (47), 256 (100), 254 (6), 242 (2), 230 (11), 219 (15), 218 (47), 217 (45), 216 (7), 202 (23), 164 (7), 148 (10), 136 (5), 128 (5), 120 (5), 92 (5), 77 (5), 72 (7), 65 (5), 57 (5), 43 (32), 41 (8).

Lunine (*9*)

M+ 287 (87), 272 (19), 270 (7), 258 (15), 244 (94), 232 (100), 231 (25), 230 (11), 219 (8), 178 (6), 176 (4), 148 (4), 147 (5), 91 (5), 90 (4), 65 (7), 41 (10).

6-Deoxyribaline (*10*)

M+ 259 (73), 244 (9), 242 (3), 230 (3), 226 (24), 216 (26), 201 (17), 200 (61), 189 (38), 188 (100), 187 (11), 186 (10), 175 (5), 173 (6), 144 (6), 134 (15), 132 (5), 106 (6), 77 (13), 72 (8), 59 (19), 57 (6), 51 (5), 43 (16), 41 (6).

6-*O*-Methylribaline (*12*)

M+ 289 (100), 274 (8), 272 (6), 260 (5), 256 (21), 246 (29), 230 (48), 219 (53), 218 (99), 217 (89), 216 (13), 204 (12), 202 (33), 188 (6), 164 (10), 148 (17), 136 (8), 120 (6), 92 (6), 77 (6), 72 (8), 65 (7), 59 (14), 57 (7), 43 (12), 41 (10).

Isodihydrokokusaginine (*14*)

M+ 261 (100), 246 (62), 232 (4), 230 (3), 218 (21), 216 (4), 200 (4), 190 (7), 188 (5), 178 (4), 150 (14), 122 (4), 82 (6), 69 (8), 53 (5).

Lemobiline (*15*)

M+ 243 (52), 228 (100), 226 (8), 214 (5), 200 (27), 187 (12), 183 (7), 134 (5), 77 (10), 51 (4), 41 (6).

Table 1. Continued.

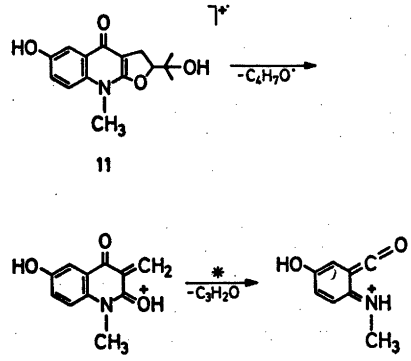
Ifflaiamine (*16*)

M+ 243 (31), 228 (100), 226 (5), 214 (12), 200 (5), 188 (5), 77 (7), 51 (3), 43 (3), 41 (3).

[a] This table is constructed of ion (intensity) pairs using relative intensity values (100 = base peak). Mass values below 3 % relative abundance have not been recorded. See also Figs. 1–6.

peaks corresponding to $[M-C_3H_7O]^+$ and $[M-C_3H_6O]^+$ ions.

A similar difference in abundance is not found for the $[M-C_4H_7O]^+$ ions, which are in both series the most abundant fragment ions, carrying between 15 and 30 % of the total ion current. This ion is formed by loss of C(2′) with its attached substituent, less one hydrogen atom for those bases carrying a fused dihydrofuran ring. This process presents an intriguing mechanistic problem, inasmuch as two skeletal bonds to the same carbon atom appear to be broken in the course of the reaction. It is not possible, in the absence of isotopic labeling data, to establish the origin of the migrating hydrogen atom, nor can the mechanism be established with certainty. One possibility would again be isomerization to a dihydropyran structure. It should be noted that the isomerization reaction taking the dihydrofuran bases *10–13* into their dihydropyran analogs, *3–6*, and *vice versa*, may be regarded as an intramolecular transetherification of a glycol mono-ether. The structure suggested (Scheme 5) for the $[M-C_4H_7O]^+$ ion, as well as the subsequent decomposition reactions of



Scheme 5.

this species, are the same as for the dihydropyran analog (Scheme 3).

In the high mass range the spectra of *10–13* show peaks corresponding to elimination of OH and CH_3 radicals from the molecular ion, as well as peaks corresponding in elemental composition to $[M-CH_3O]^+$ and $[M-C_2H_3O]^+$. The methyl fragment expelled probably originates in the C(2′) side chain, where it may be eliminated in an α-cleavage reaction. The $[M-CH_3O]^+$ is presumably formed by sequential loss of CH_3 and H_2O fragments, but no metastable ion evidence was found in support of this assumption. Loss of CH_3O has been observed in other systems incorporating a hydroxyisopropyl group attached to C-2 in a fused dihydrofuran ring.[16] Similarly, the $[M-C_2H_3O]^+$ ion is believed to arise through successive losses of CH_3 and CO neutrals, even though a rearrangement-decomposition reaction resulting in expulsion of an acetyl radical cannot be ruled out. This ion is diagnostically significant when attempting to distinguish between isomers in the present series, as it is nearly ten times more abundant for the dihydrofuran bases *10–13* than for their dihydropyran analogs *3–6*.

Three 4-quinolone bases lacking substitution or with only methyl substituents in the dihydrofuran ring, *14–16*, have been investigated in this study. All three compounds eliminate a methyl radical from their respective molecular ions, and the M − 15 species attain 62, 100 and 100 % relative intensity, respectively. In the case of *14* the eliminated methyl group could originate from the 6-methoxy group, in line with previous results [18] obtained from 6,7-dimethoxycoumarin. Subsequent loss of CO from the M − 15 species is observed and this is also in agreement with the behaviour of 6,7-dimethoxycoumarin on electron impact.[18] Compounds *15* and *16* both eliminate ethyl and propyl radicals from the molecular ion. The relative intensities of the M − 29 and M − 43 peaks in the two spectra show that extrusion of C(2′) plus a hydrogen atom is a favorable reaction for these compounds; for the remaining dihydrofuran bases extrusion of C(2′) with its attached substituents *less* a hydrogen atom is the observed reaction (see above).

CONCLUSION

The mass spectra of dihydropyran- and dihydrofuran-4-quinolone alkaloids can be of considerable value in the elucidation of the structure of these compounds. The presence of substituents in either the aromatic ring or in the dihydropyran or dihydrofuran rings is easily recognized, and the cleavage reactions of the cyclic ether portion of the molecule permit positional assignment of substituents to be made with confidence. Distinction between isomeric bases containing either a 2-isopropyl dihydrofuran ring or a 2,2-dimethyl dihydropyran ring system has, however, only been possible with certainty in the present series when the molecules possess an additional oxygen function (at C(3′) in the dihydropyran ring, or in the isopropyl group appended to C(2′) in the dihydrofuran ring. In this case the compounds containing a dihydrofuran ring are recognized by the presence in their mass spectra of abundant $[M-C_2H_3O]^+$ ions, which are nearly absent for the dihydropyran analogs, and by prominent $[M-C_3H_7O]^+$ ions, which are also of considerably reduced intensity in the dihydropyran spectra.

EXPERIMENTAL

Low resolution mass spectra were recorded by Mr R. G. Ross on an A.E.I. MS-9 mass spectrometer operating at 70 eV.

Samples were introduced into the ion source (temperature 180 °C) using the direct probe. Complete high resolution mass spectra were recorded by Ms A. Wegmann using a Varian MAT 711 mass spectrometer (ion source 200 °C). All high resolution measurements were accurate to ±4 ppm. Samples used in this investigation were of analytical purity, and except for the following compounds they are described in a previous publication.[19] The remaining bases were obtained from the following investigators: balfourodine (*13*) and isobalfourodine (*5*), Prof. H. Rapoport, Univ. of Calif., Berkeley, U.S.A.; lunacrine (*8*) and lunine (*9*), Dr. J. A. Lamberton, CSIRO, Melbourne, Australia; khaplofoline (*1*) and *N*-methylkhaplofoline (*2*), Prof. M. F. Grundon, The New University of Ulster, Coleraine, N. Ireland; ifflaiamine (*16*), Dr. W. C. Taylor, Univ. of Sydney, Australia; lemobiline (*15*), Dr. S. K. Talapatra, Univ. College of Science and Technology, Calcutta, India.

Preparation of isodihydrokokusaginine (*14*). 2,3-Dihydrokokusaginine (75 mg) and methyl iodide (1 ml) were heated in a sealed tube at

100 °C for 24 h. After evaporation to dryness anhydrous pyridine (1 ml) was added and the heating repeated at 80 °C for 12 h. The pyridine was removed *in vacuo* and the residue partitioned between chloroform (3 ml) and 5 % aqueous sodium sulfite solution (0.5 ml). The organic phase was dried ($MgSO_4$) and evaporated. The residue was crystallized from alcohol to constant m.p. 222–225 °C; yield 25 mg. M^+ found 261.1008; calc. for $C_{14}H_{15}NO_4$: 261.1001.

Preparation of 3'-O-deuterio-7-O-methylribalinidine. The parent base (3 mg) was dissolved in CH_3OD (1 ml) and the solvent removed *in vacuo*. This procedure was repeated twice and the mass spectrum immediately recorded. The product consisted of 65 % d_1 and 35 % d_0 species.

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REFERENCES

1. Budzikiewicz, H., Djerassi, C. and Williams, D. H. *Structure Elucidation of Natural Products by Mass Spectrometry*, Holden-Day, San Francisco 1964, Vol. 2.
2. Budzikiewicz, H., Djerassi, C. and Williams, D. H. *Structure Elucidation of Natural Products by Mass Spectrometry*, Holden-Day, San Francisco 1964, Vol. 1; Biemann, K. *Fortschr. Chem. Org. Naturst. 24* (1966) 1; Sastry, S. D. In Waller, G. R., Ed., *Biochemical Applications of Mass Spectrometry*, Wiley, New York 1972, p. 655; Hesse, M. *Prog. Mass Spectrom. 1* (1974) 1; Games, D. E. In Johnstone, R. A. W., Ed., *Specialist Periodical Reports, Mass Spectrometry*, The Chemical Society, London 1975, Vol. 3, p. 224.
3. Corral, R. A. and Orazi, O. O. *Tetrahedron 21* (1965) 909; see also Mitscher, L. A., Bathala, M. S. and Beal, J. L. *Chem. Commun.* (1971) 1040.
4. Talapatra, S. K., Maiti, B. C., Talapatra, B., and Das, B. C. *Tetrahedron Lett.* (1969) 4789.
5. Reisch, J., Szendrei, K., Pápay, V., Novák, I. and Minker, E. *Tetrahedron Lett.* (1970) 3365.
6. Rasches, Y. V., Faizutdinova, Z. S., and Yunusov, S. Y. *Khim. Prir. Soedin. 6* (1970) 107.
7. Smith, D. H., Buchanan, B. G., White, W. C., Feigenbaum, E. A., Lederberg, J. and Djerassi, C. *Tetrahedron 29* (1973) 3117.
8. Hammerum, S. and Djerassi, C. *Tetrahedron 31* (1975) 2391.
9. Duffield, A. M. *Org. Mass Spectrom. 2* (1969) 965, and references cited therein.
10. Barnes, C. S. and Occolowitz, J. L. *Aust. J. Chem. 17* (1964) 975; Willhalm, B., Thomas, A. F. and Gautschi, F. *Tetrahedron 20* (1964) 1185.
11. Clugston, D. M. and MacLean, D. B. *Can. J. Chem. 44* (1966) 781.
12. Trudell, J. R., Woodgate, S. D. S. and Djerassi, C. *Org. Mass Spectrom. 3* (1970) 753.
13. Budzikiewicz, H. and Lenz, U. *Org. Mass Spectrom. 10* (1975) 992.
14. Venugopalan, M. and Anderson, C. B. *Chem. Ind. London* (1964) 370; Venugopalan, M. and Anderson, C. B. *Ind. J. Chem. 3* (1965) 20; Cascon, S. C., Mors, W. B., Tursch, B. M., Aplin, R. T. and Durham, L. J. *J. Am. Chem. Soc. 87* (1965) 5237; Budzikiewicz, H., Djerassi, C. and Williams, D. H. *Mass Spectrometry of Organic Compounds*, Holden-Day, San Francisco 1967, pp. 254–257; Budzikiewicz, H. and Grotjahn, L. *Tetrahedron 28* (1972) 1881; Budzikiewicz, H. and Lenz, U. *Org. Mass Spectrom. 10* (1975) 987.
15. Drewes, S. E. *Prog. Mass Spectrom. 2* (1974) 1.
16. Rondest, J., Das, B. C., Ricroch, M.-N., Kan-Fan, C., Potier, P. and Polonsky, J. *Phytochemistry 7* (1968) 1019.
17. Ohloff, G., Schulte-Elte, K.-H. and Willhalm, B. *Helv. Chim. Acta 47* (1964) 602.
18. Shapiro, R. H. and Djerassi, C. *J. Org. Chem. 30* (1965) 955.
19. Corral, R. A., Orazi, O. O. and Benages, I. A. *Tetrahedron 29* (1973) 205.

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