Coumarins V

Mass Spectra of Columbianetin and Its Esters

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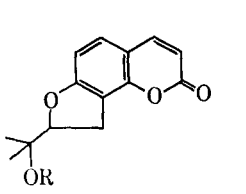
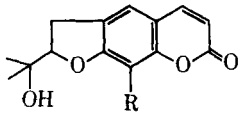
The mass spectra of columbianetin and its acetate, angelate, tiglate, and 3-bromoangelate have been determined. Columbianetin shows M →188 → 187 (base peak 187) as the principal fragmentation pathway whereas the esters show M→ 228 → 213 (base peak 213) as the major fragmentation route. Probable mechanisms for fragmentation are suggested.

In connection with our interest in physiologically active naturally occurring coumarins (1) a number of new representatives of this class have been isolated and structurally characterized. Among these were two dihydrofurocoumarins, columbianin and columbianadin, which were reported by Willette and Soine (2) as the D-glucoside (I) and angelate (II), respectively, of the parent alcohol, columbianetin (III). Since then, the structure of columbianin has been revised (3) to that of a β-D-gentiobioside of columbianetin (IV). During the research leading to the revised structure, employment of mass spectrometry for a molecular weight determination also led to an examination of the mass spectral characteristics of III and certain of its esters. The present report concerns itself with the spectra of III, its acetate (V), angelate (II), tiglate (VI), and 3-bromoangelate (VII).



R

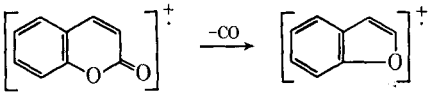
I—D-Glucosyl
II—Angeloyl
III—H
IV—β-D-Gentiobiosyl
V—Acetyl
VI—Tigloyl
VII—3-Bromoangeloyl



VIII—H
IX—OH

Mass spectrometry has been employed by others on similar coumarins both for structural elucidation and for determination of fragmentation patterns. Abdel-Hay *et al.* (4), for example, carried out mass spectral studies on linear dihydrofurocoumarins including marmesin (VIII) which is the linear isomer of III and, similarly, Schneider *et al.* (5) examined rutaretin (IX). The mass spectra of VIII, IX, and III have common features except that, in IX, the peaks are displaced to 16 higher *m/e* units because it possesses an extra phenolic group. Virtually all of the important peaks found in the case of III are to be found in the spectra of VIII and IX. It may be pointed out that, in the case of IX, the fragmentation mechanisms have been supported by accurate mass measurements. Seshadri *et al.* (6) reported the mass spectral characteristics of selinidin, the angelate of lomatin (7), which is a closely related coumarin of the dihydroseselin type. Here, again, the spectrum bore similarities to the isomeric II.

Barnes and Occolowitz (8) studied the mass spectra of a number of oxygen-containing heterocyclic compounds occurring in nature and Budzikiewicz *et al.* (9) reviewed the work done on this aspect up to 1964. According to the latter authors, and agreeing with the present study, CO is a highly stable neutral particle and, therefore, fragments arising due to its loss are characteristic features of all coumarins. For example, coumarin itself shows a stepwise loss of two molecules of CO and umbelliferone (7-hydroxycoumarin) loses 3 molecules of CO in a similar manner. Barnes and Occolowitz (8) suggest that the molecular ion of coumarin (X) loses the first molecule of CO by way of the lactone carbonyl and that the resulting ion has the structure of the molecular ion of benzofuran (XI) as indicated by a close similarity



m/e 146 X — *m/e* 118 XI

of the spectra of these two compounds. The validity of the benzofuran structure, however, has been challenged by Pirkle (10). Nevertheless, structures written for certain ions are often simply a convenient means of representing fragmentation pathways and are not intended to imply an actual ion structure. In this sense, the present paper employs the benzofuran system as resulting from loss of CO from the coumarinic

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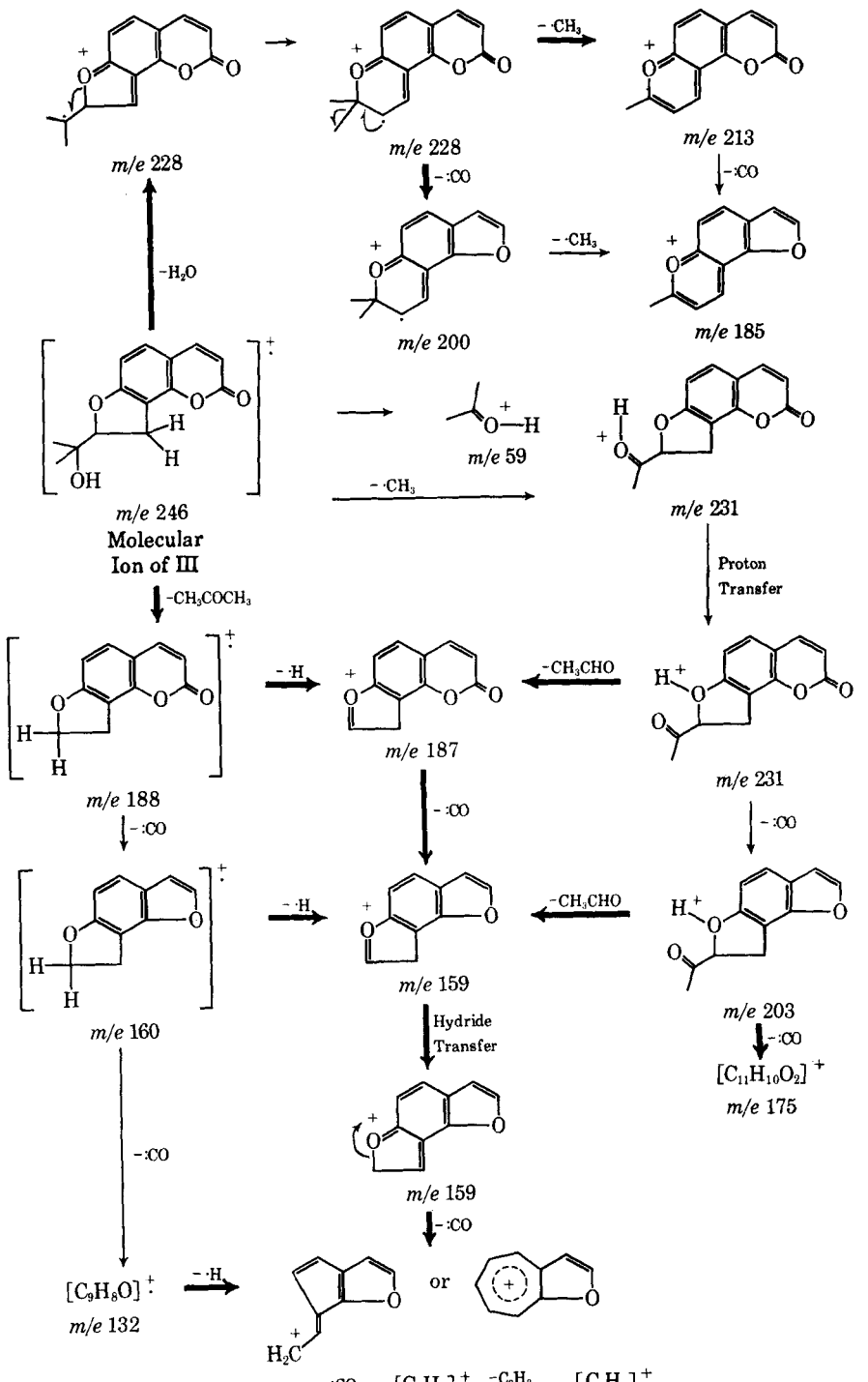

m/e 228
m/e 228
m/e 213
m/e 200
m/e 185
m/e 59
m/e 246
Molecular
Ion of III
m/e 231
Proton
Transfer
m/e 188
m/e 187
m/e 231
m/e 160
m/e 159
m/e 203
[C11H10O2]+
m/e 175
Hydride
Transfer
m/e 159
[C9H8O]+
m/e 132
or
m/e 131
[C8H7]+
m/e 103
[C6H5]+
m/e 77

Scheme I

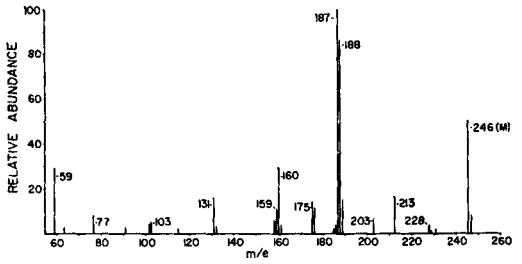
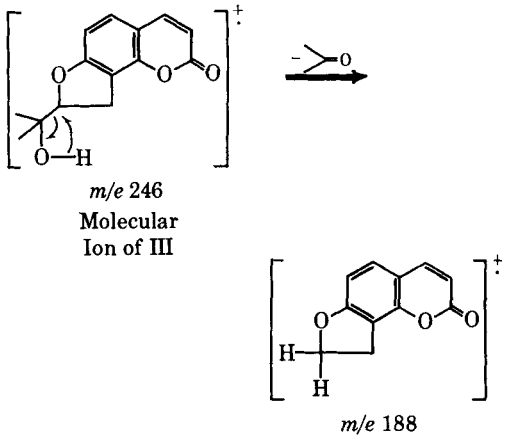


Fig. 1—Mass spectrum of III. Peaks of abundance ratio less than 3% have been omitted in all spectra unless a reference has been made to them in the text. Numbers in all figures correspond to those cited in the text.

lactone carbonyl. In many cases, the proposed fragmentation pathways are supported by the appearance of metastable ions, these being indicated in the several schemes by heavily lined arrows.

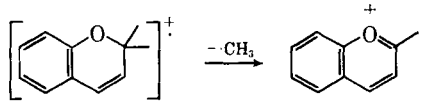
The mass spectrum of III (see Fig. 1) shows a molecular ion which fragments by different routes as shown in Scheme I. The principal pathway of fragmentation involves loss of acetone from the side chain of the molecular ion giving rise to a rearranged ion of *m/e* 188 which has the probable structure shown in Scheme I. This ion then loses an H atom to give rise to a highly stabilized ion of *m/e* 187 which forms the base peak in the spectrum. The *m/e* 188 and 187 ions each lose two molecules of CO in a stepwise manner to generate the ions of *m/e* 160 and 132 in the first case and ions of *m/e* 159 and 131 in the latter case. The ion of *m/e* 159 can also arise from the ion of *m/e* 160 by loss of H atom as indicated by the corresponding metastable ion peak. In a similar fashion the ion of *m/e* 131 can also arise from the ion of *m/e* 132. The ion of *m/e* 131 could be a highly stabilized allylic carbonium ion or could be a rearranged furotropylium ion as proposed in the case of osthol and dihydroosthol (8). This ion then shows loss of another molecule of CO to generate an ion of *m/e* 103 which fragments by losing a molecule of C_2H_2 to give an ion of *m/e* 77. Aromatic systems are known to lose C_2H_2 as a neutral fragment (11). The mechanism of fragmentation M → 188 can be rationalized as shown in Scheme II.

The peak at *m/e* 228 is due to an ion arising through loss of H_2O from the molecular ion. A mechanism similar to that suggested in the case of VIII (4) can be proposed for its formation. This ion then loses a methyl radical, giving rise to an ion of *m/e* 213 which probably has a stabilized benzopyrilium structure. The appearance of this type of ion is the most prominent feature in the mass spectra of the esters of III, selinidin (6),



Scheme II

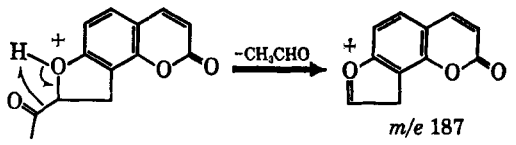
seselin (8), braylin (8), 2,2-dimethylchromene (8), and substituted 2,2-dimethylchromenes (8). The molecular ion of 2,2-dimethylchromene (XII), for example, shows a loss of methyl radical with the resulting ion (XIII) being assigned the structure of a stabilized benzopyrilium ion (8). This ion forms the base peak and there are no other peaks of comparable intensity in its entire spectrum. The ion of *m/e* 213 shows a loss of CO giving rise to an ion of *m/e* 185. The pathway M → 228 → 213 → 185 is very prominent in



the spectra of the esters of III. The alternate pathway for the formation of the ion of *m/e* 185 is probably 228 → 200 → 185 as shown in Scheme I.

The M-15 peak at *m/e* 231 is apparently due to the loss of methyl radical from the molecular ion. This ion, in turn, can lose a molecule of CO to generate an ion of *m/e* 203 which can further lose another molecule of CO to give rise to an ion of *m/e* 175. The ion of *m/e* 231 can also lose CH_3CHO by rearrangement and thus give rise to the ion of *m/e* 187 which represents an alternate pathway for the formation of the latter ion. Similarly, the ion of *m/e* 203 can give rise to an ion of *m/e* 159. Both of these pathways are substantiated by the appearance of metastable ions in the present study as well as in the case of IX (5). However, the metastable peak at *m/e* 151.1 can represent either the transformation 231 → 187 or 203 → 175 or both. A possible rearrangement mechanism leading to formation

of the ion of *m/e* 187 from the ion of *m/e* 231 is shown in Scheme III.



Scheme III

A peak at *m/e* 59 is due to the protonated form of acetone arising from the side chain of III. The appearance of this ion is a characteristic feature of coumarins containing the 2-hydroxyisopropyl grouping [*e.g.*, marmin (12)]. This ion forms the base peak in the spectrum of *tert*-butyl alcohol (13).

The probable fragmentation pathway for V (see Fig. 2) is shown in Scheme IV. The molecular ion loses acetic acid giving rise to a peak at *m/e* 228 which further loses a methyl radical providing an ion of *m/e* 213 which forms the base peak. This fragmentation is quite similar to that of the parent compound and, as mentioned before, is the principal pathway. The ion of *m/e* 213 loses a molecule of CO giving an ion of *m/e* 185. An alternate pathway, 228 → 200 → 185, could also operate in this case as shown in Scheme I. The molecular ion also shows loss of ketene which generates the molecular ion of III by rearrangement. Hence, it is expected that all the ions found in the spectrum of III should also be found in this case. An additional pathway is available for formation of the ion of *m/e* 187, *i.e.*, M → 229 → 187 as shown in Scheme IV. The transformation 229 → 187 is substantiated by a metastable peak at *m/e* 152.8 in the case of the D-glucoside of III (14). The ion of *m/e* 229 is produced from the molecular ion by loss of an acetate radical. This ion can lose an H atom to give the ion of *m/e* 228. Finally, the peak at *m/e* 231 is quite intense in the case of V as compared to III. The reasons for this difference are not entirely clear.

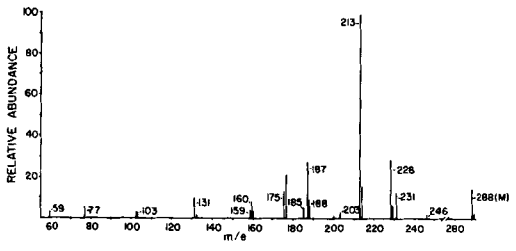
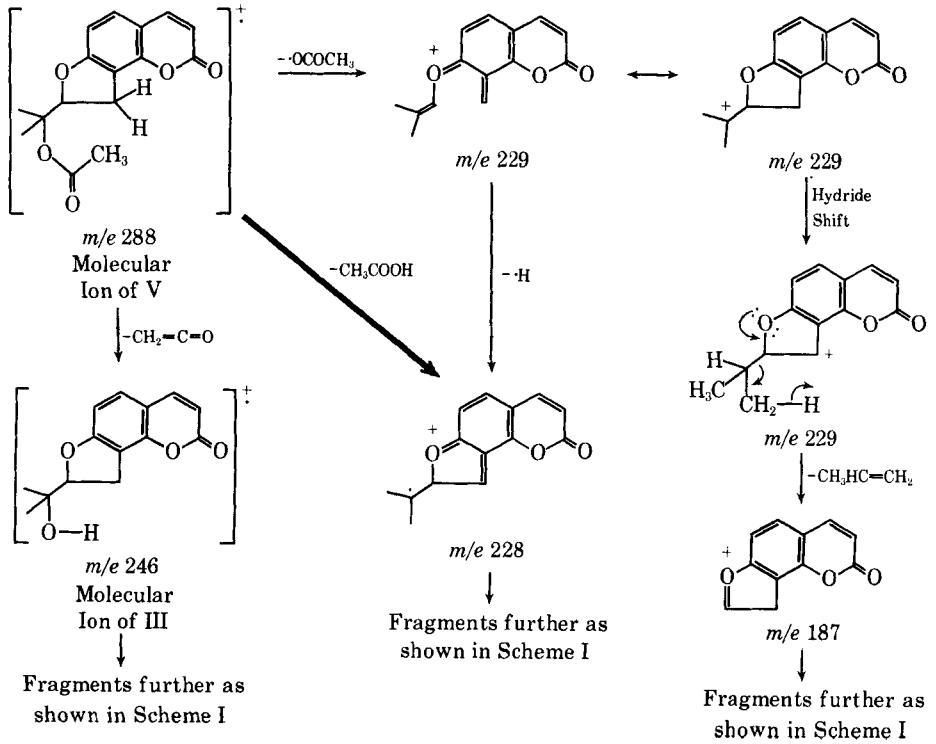


Fig. 2—Mass spectrum of V.

The major fragmentation pathways for II (see Fig. 3) are represented in Scheme V and are similar to those of selinidin (5), the dihydroseselin-type coumarin isomeric with II. As in the case of the acetate ester, the principal pathway for fragmen-



VI Scheme

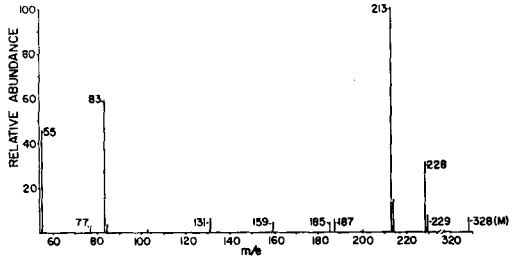


Fig. 3—Mass spectrum of II.

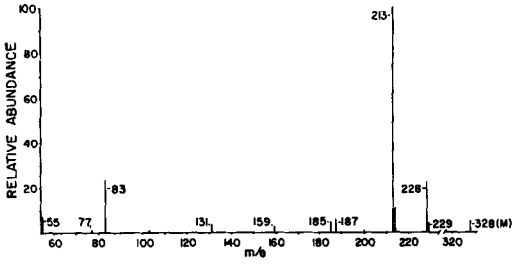
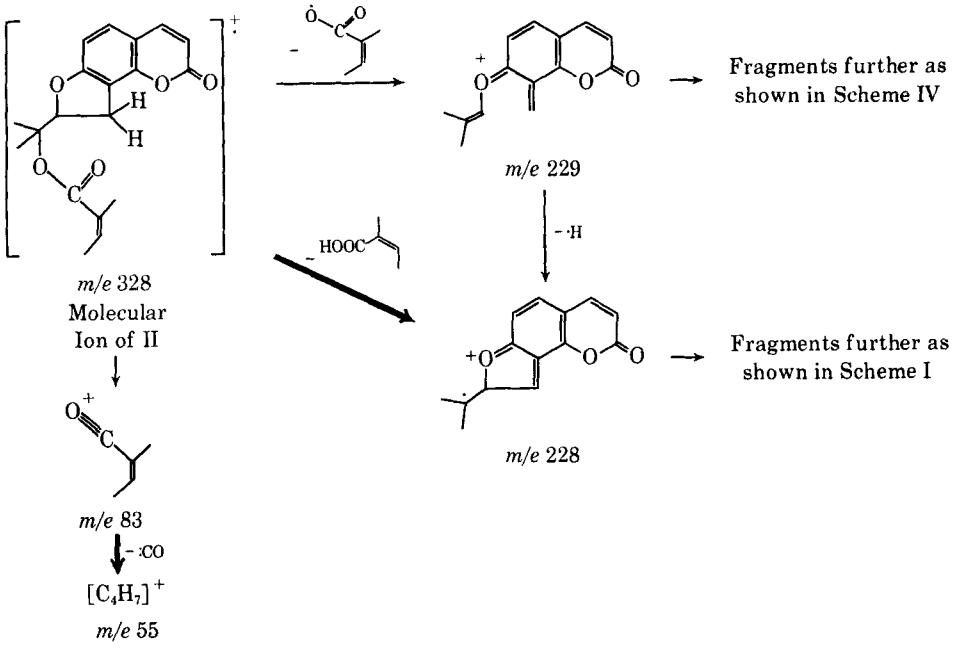


Fig. 4—Mass spectrum of VI.



Scheme V

tation is M → 228 → 213 → 185. Another important pathway is the generation of an ion of *m/e* 83 arising by α-cleavage from the acid part of the ester which further loses a molecule of CO to give an ion of *m/e* 55. This latter transformation is substantiated by the corresponding metastable ion peak. The peak at *m/e* 188 is quite inconspicuous and, therefore, the ion of *m/e* 187 can only arise from the ion of *m/e* 229.[1] Furthermore, a rational rearrangement mechanism cannot be written for the generation of the molecular ion of III which then fragments further to generate the ion of *m/e* 188 as in the case of V. Peaks at *m/e* 160 and 132, due to the ions arising from the ion of *m/e* 188, are also inconspicuous.

The spectrum of VI (see Fig. 4), the geometric isomer of II, shows all the peaks present in the spectrum of II. However, there are substantial differences in the abundance ratios in certain cases, namely the peaks that can be ascribed to the acid portion of the ester. Presumably, the fragmentation pathways as represented for II in Scheme V are valid for VI.

The principal fragmentation pathways for VII are shown in Scheme VI (see Fig. 5). They are quite similar to those for II and show twin peaks of molecular ions at *m/e* 406 and 408. These ions fragment in the same manner as does the corresponding ion for II. The ions which do not involve the acid part of the ester appear at the

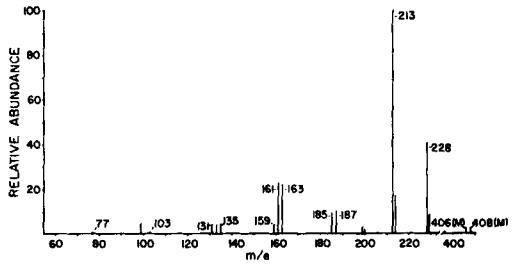
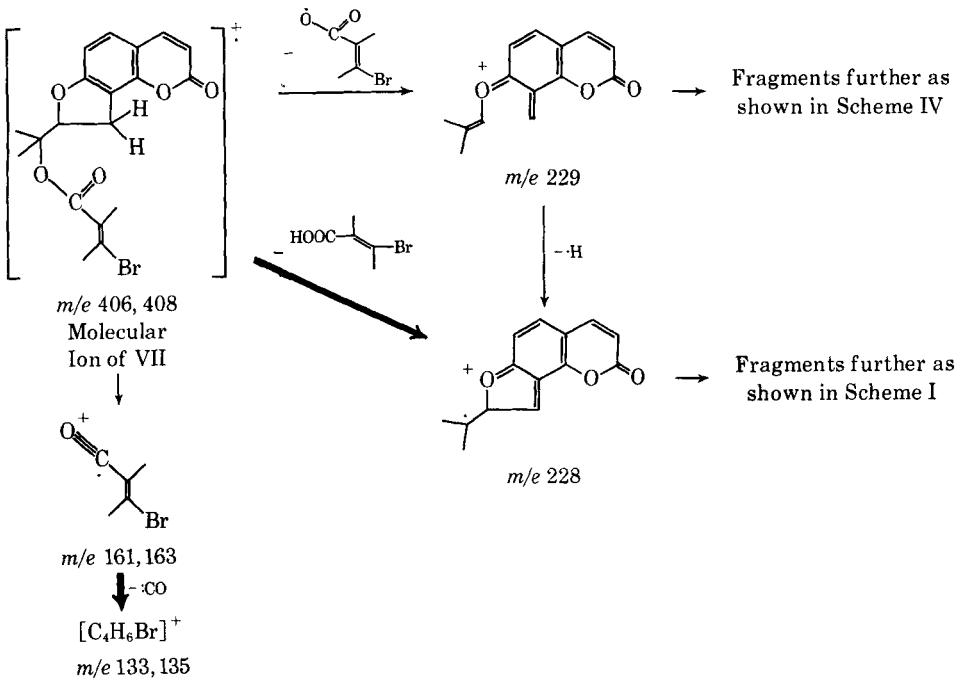


Fig. 5—Mass spectrum of VII.

[1] The peak at *m/e* 229 is extremely small in the case of III. However, this peak (corrected for the *P* + 1 satellite peak of 228) is observable in the case of the esters of III. This is probably due to the expulsion of ·OOC—R radical as against ·OH radical, the former being much more stable.



Scheme VI

same *m/e* units as in the case of II. Once again, the ion of *m/e* 213 forms the base peak. However, the peak at *m/e* 83 in the case of II which arises from the acid part is displaced to *m/e* 161 and 163. Similarly, the peak at *m/e* 55 is displaced to *m/e* 133 and 135.

EXPERIMENTAL

Materials—Columbianetin (III) and its acetate (V), angelate (II), tiglate (VI), and 3-bromoangelate (VII) were available in these laboratories as products isolated or synthesized during the studies of Willette and Soine (2) on *Lomatium columbianum* Mathias and Const.

Mass Spectra—These were carried out by Mr. A. R. Swanson and Mr. R. D. Berg, School of Chemistry, University of Minnesota, employing a Hitachi Perkin-Elmer RMU-6D mass spectrometer. The instrument was operated with a source temperature of 250° and an ionizing voltage of 50 ev. The sample inlet temperature was 70° in the case of columbianetin, 90° for the acetate, 120° in the case of the angelate, and 125° for the tiglate and 3-bromoangelate. Assistance in the interpretation of the spectra was given by Dr. Thomas Watson, Pharmacy Department, University of Sydney, Sydney, Australia.

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Keyphrases

Coumarins
Columbianetin—structure
Esters, columbianetin—synthesis
Mass spectrometry—structure