Coumarins XIV: High-Resolution Mass Spectra of 3′,4′-Disubstituted 3′,4′-Dihydroseselins

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Abstract □ High-resolution mass spectra of 14 3′,4′-disubstituted 3′,4′-dihydroseselins were examined. The nature of the substituents determines the mode of fragmentation. Compounds having one or two acyloxy substituents fragment mainly by a pathway leading to the stable coumarinopyrilium ion. Coumarins with alkoxy or hydroxy substituents proceed by way of fission of the chroman ring, accompanied by the loss of two ring carbon atoms. Several generalizations are formulated which will aid in the interpretation of the mass spectra of this class of coumarins from a structural standpoint.

Keyphrases □ 3′,4′-Dihydroseselins, 3′,4′-disubstituted—high-resolution mass spectra, mode of fragmentation, structural interpretation □ Coumarins, substituted—high-resolution mass spectra, mode of fragmentation, structural interpretation □ Mass spectroscopy, high resolution—3′,4′-disubstituted 3′,4′-dihydroseselins, mode of fragmentation, structural interpretation

In earlier mass spectral studies, fragmentation patterns of several linear furano- (1), angular dihydrofurano-, and dihydropyranocoumarins (2–5) were examined. As an extension of these studies, high-resolution mass spectra of 14 3′,4′-disubstituted 3′,4′-dihydroseselins (I–XIV, Table I) were examined. The examples selected provide the data needed to give substance to certain general fragmentation pathways based on the structural types examined. These pathways are supported by exact mass measurements and provide some interesting generalizations which may be of value for the structural elucidation of coumarins.

DISCUSSION

Two major routes of fragmentation were evident.

Pathway A—This process involves loss of ROH in one or two steps, *i.e.*, loss of RO· followed by H·, to generate a chromene system followed by a ·CH_3 expulsion to provide a stable coumarinopyrilium ion (6) (Scheme I). Subsequent fragmentations take place without destruction of this stable ring system. This mode of fragmentation is of major consequence in the spectra of esters of lomatin but is of minor consequence for lomatin itself (4).

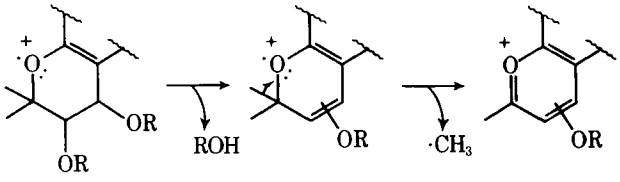
Pathway B—Fission of the chroman ring with the loss of two ring carbons (2′ and 3′) along with their respective substituents is an alternative mode of fragmentation (7) (Scheme II). This retro Diels–Alder-type fragmentation occurs with or without a hydrogen transfer and constitutes the principal mode of fragmentation (with one and/or two hydrogen transfers) in the spectrum of lomatin (4, 8).

The group behavior was as follows.

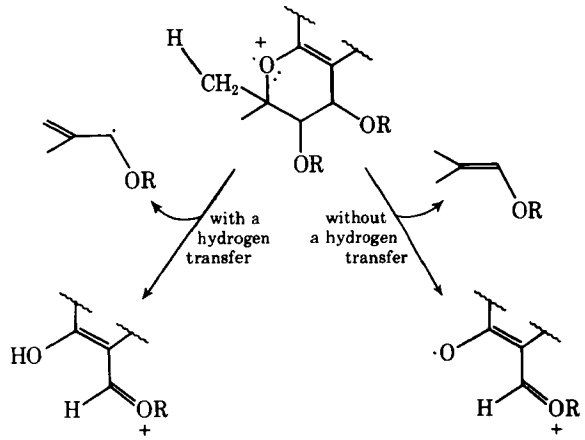
Group 1—Anomalin (I) and calipteryxin (II) exhibit similar spectra (Table I) with no molecular ion (M^+), presumably because the bulkiness of both substituents renders them unstable[1]. The base peak at *m/e* 83 is derived from the angeloyl and/or senecioyl groups. Pathway A is the major fragmentation route. Scheme III shows the major fragmentation routes of I as an example. Bohlmann and coworkers (9, 10) reported the mass spectra of several compounds that could be classified in Group 1, and their fragmentation conforms to pathway A expectations.

Groups 2–4—Compounds III–VII exhibit moderately intense molecular ion peaks and fragment predominantly *via* pathway A. Compounds III and IV exhibit base peaks at *m/e* 83 due to the relatively stable ion derived from the unsaturated five-carbon acid substituents. The base peak appears at *m/e* 229 when one substituent is a saturated five-carbon acyloxy group and the other is an acetoxy group, as in the spectra of V and VI. This is also true when both substituents are acetoxy groups, as in VII.

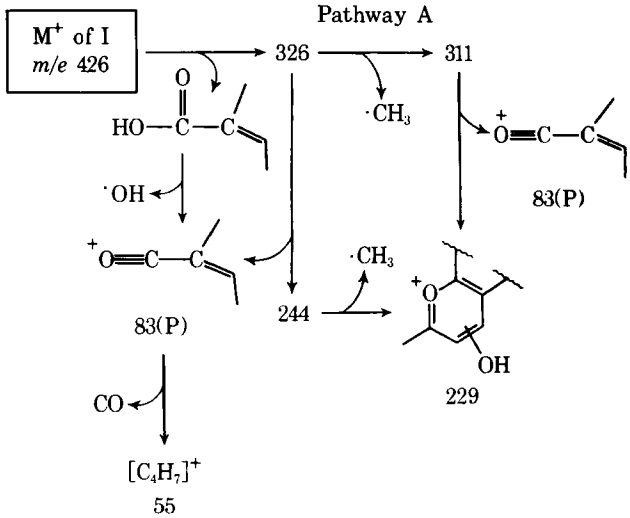
An M − 60 peak due to the loss of acetic acid is present in the spectrum of pteryxin (III) (Scheme IV) but not in the spectrum for isopteryxin (IV) (Scheme V); this difference indicates that the loss of the 3′-substituent (as the acid) is preferred over the loss of the 4′-substituent. In addition, the loss of five-carbon acids seems to be favored over the loss of acetic acid. Similar conclusions are reached when the spectra of suksdorfin (V) (Scheme VI) and visnadin (VI) (Scheme VII) are compared. These two observations permit differ-



Scheme I—Pathway A



Scheme II—Pathway B



Scheme III

[1] These peaks were visible at 15 ev.

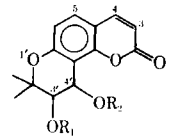


Table I—High-Resolution Mass Measurements of the Major Fragments for Compounds I–XIV[a]

Compound	R_1	R_2	m/e	Elemental Composition	Calculated Mass	Measured Mass	Relative Intensity, %
Anomalin[b] (I)			327	$C_{19}H_{19}O_5$	327.1232	327.1198	28
			326	$C_{19}H_{18}O_5$	326.1153	326.1157	12
			311	$C_{18}H_{15}O_5$	311.0918	311.0904	15
			244	$C_{14}H_{12}O_4$	244.0735	244.0741	9
			243	$C_{14}H_{11}O_4$	243.0657	243.0678	7
			229	$C_{13}H_9O_4$	229.0500	229.0449	32
			83 (P)	C_5H_7O	83.0496	83.0493	100
			55	C_4H_7	55.0546	55.0538	40
Calipteryxin[b] (II)			327	$C_{19}H_{19}O_5$	327.1232	327.1269	6
			326	$C_{19}H_{18}O_5$	326.1153	326.1150	16
			311	$C_{18}H_{15}O_5$	311.0918	311.0910	10
			244	$C_{14}H_{12}O_4$	244.0735	244.0728	8
			243	$C_{14}H_{11}O_4$	243.0657	243.0644	6
			229	$C_{13}H_9O_4$	229.0500	229.0505	28
			83 (P)	C_5H_7O	83.0496	83.0500	100
			55	C_4H_7	55.0546	55.0549	30
Pteryxin[c] (III)	CH_3CO		386 (M)	$C_{21}H_{22}O_7$	386.1364	386.1400	6
			326	$C_{19}H_{18}O_5$	326.1153	327.1200	14
			311	$C_{18}H_{15}O_5$	311.0918	311.0927	14
			287	$C_{16}H_{15}O_5$	287.0919	287.0879	42
			261	$C_{14}H_{13}O_5$	261.0762	261.0746	28
			245	$C_{14}H_{13}O_4$	245.0813	245.0751	46
			244	$C_{14}H_{12}O_4$	244.0735	244.0738	9
			229	$C_{13}H_9O_4$	229.0500	229.0467	38
			191	$C_{10}H_7O_4$	191.0343	191.0343	5
			83 (P)	C_5H_7O	83.0496	83.0502	100
			55	C_4H_7	55.0546	55.0547	40
			43	C_2H_3O	43.0284	43.0276	26
Isopteryxin[b] (IV)		CH_3CO	386 (M)	$C_{21}H_{22}O_7$	386.1364	386.1348	22
			326	$C_{19}H_{18}O_5$	326.1153	—	—
			311	$C_{18}H_{15}O_5$	311.0918	—	—
			287	$C_{16}H_{15}O_5$	287.0919	287.0869	6
			261	$C_{14}H_{13}O_5$	261.0762	261.0762	5
			245	$C_{14}H_{13}O_4$	245.0813	245.0688	24
			244	$C_{14}H_{12}O_4$	244.0735	244.0724	34
			229	$C_{13}H_9O_4$	229.0500	229.0532	72
			191	$C_{10}H_7O_4$	191.0343	191.0334	18
			83 (P)	C_5H_7O	83.0496	83.0487	100
			55	C_4H_7	55.0546	55.0539	44
			43	C_2H_3O	43.0284	43.0290	26
Suksdorfin[c] (V)	CH_3CO		388 (M)	$C_{21}H_{24}O_7$	388.1520	388.1524	22
			328	$C_{19}H_{20}O_5$	328.1309	328.1322	16
			313	$C_{18}H_{17}O_5$	313.1074	313.1067	12
			286	$C_{16}H_{14}O_5$	286.0840	286.0829	11
			261	$C_{14}H_{13}O_5$	261.0762	261.0756	21
			245	$C_{14}H_{13}O_4$	245.0813	245.0787	25
			244	$C_{14}H_{12}O_4$	244.0735	244.0731	48
			229 (P)	$C_{13}H_9O_4$	229.0500	229.0527	100
			191	$C_{10}H_7O_4$	191.0343	191.0325	18
			190	$C_{10}H_6O_4$	190.0265	190.0286	12
			85	C_5H_9O	85.0653	85.0654	22
			57	C_4H_9	57.0702	57.0704	26
			43	C_2H_3O	43.0284	43.0288	26
Visnadin (provismine)[d] (VI)		CH_3CO	388 (M)	$C_{21}H_{24}O_7$	388.1520	388.1540	12
			328	$C_{19}H_{20}O_5$	328.1309	—	—
			313	$C_{18}H_{17}O_5$	313.1074	—	—
			286	$C_{16}H_{14}O_5$	286.0840	286.0831	5
			261	$C_{14}H_{13}O_5$	261.0762	261.0746	13
			245	$C_{14}H_{13}O_4$	245.0813	245.0766	10
			244	$C_{14}H_{12}O_4$	244.0735	244.0720	65
			229 (P)	$C_{13}H_9O_4$	229.0500	229.0464	100
			191	$C_{10}H_7O_4$	191.0343	191.0329	25
			190	$C_{10}H_6O_4$	190.0265	190.0245	22
			85	C_5H_9O	85.0653	85.0653	26
			57	C_4H_9	57.0702	57.0701	28
			43	C_2H_3O	43.0284	43.0289	26
trans-Khellactone diacetate[d] (VII)	CH_3CO	CH_3CO	346 (M)	$C_{18}H_{18}O_7$	346.1052	346.1056	18
			286	$C_{16}H_{14}O_5$	286.0840	286.0847	5
			245	$C_{14}H_{13}O_4$	245.0813	245.0779	10
			244	$C_{14}H_{12}O_4$	244.0735	244.0708	36
			229 (P)	$C_{13}H_9O_4$	229.0500	229.0514	100
			213	$C_{13}H_9O_3$	213.0551	213.0547	20
			191	$C_{10}H_7O_4$	191.0343	191.0346	26
			190	$C_{10}H_6O_4$	190.0265	190.0272	14

(continued)

Table I—(*Continued*)

Compound	R_1	R_2	*m/e*	Elemental Composition	Calculated Mass	Measured Mass	Relative Intensity, %
			60	$C_2H_4O_2$	60.0300	60.0289	30
			43	C_2H_3O	43.0284	43.0282	35
cis-4′-*O*-Ethylkhellactone acetate[c] (VIII)	CH_3CO	CH_3CH_2	333 (M + 1)	$C_{18}H_{21}O_6$	333.1337	333.1358	7
			332 (M)	$C_{18}H_{20}O_6$	332.1259	332.1273	16
			258	$C_{15}H_{14}O_4$	258.0891	258.0854	12
			257 (P)	$C_{15}H_{13}O_4$	257.0813	257.0806	100
			245	$C_{14}H_{13}O_4$	245.0813	245.0835	5
			229	$C_{13}H_9O_4$	229.0500	229.0483	52
			219	$C_{12}H_{11}O_4$	219.0657	219.0663	26
			218	$C_{12}H_{10}O_4$	218.0579	218.0562	43
			213	$C_{13}H_9O_3$	213.0551	213.0578	14
			191	$C_{10}H_7O_4$	191.0343	191.0346	65
			190	$C_{10}H_6O_4$	190.0265	190.0248	48
			176	$C_{10}H_8O_3$	176.0473	176.0454	12
			162	$C_9H_6O_3$	162.0316	162.0307	57
			134	$C_8H_6O_2$	134.0367	134.0369	36
			43	C_2H_3O	43.0284	43.0292	35
trans-4′-*O*-Ethylkhellactone acetate[c] (IX)	CH_3CO	CH_3CH_2	333 (M + 1)	$C_{18}H_{21}O_6$	333.1337	333.1349	5
			332 (M)	$C_{18}H_{20}O_6$	332.1259	332.1252	30
			258	$C_{15}H_{14}O_4$	258.0891	258.0878	15
			257 (P)	$C_{15}H_{13}O_4$	257.0813	257.0852	100
			245	$C_{14}H_{13}O_4$	245.0813	245.0809	11
			229	$C_{13}H_9O_4$	229.0500	229.0495	66
			219	$C_{12}H_{11}O_4$	219.0657	219.0617	42
			218	$C_{12}H_{10}O_4$	218.0579	218.0584	82
			213	$C_{13}H_9O_3$	213.0551	213.0537	24
			191	$C_{10}H_7O_4$	191.0343	191.0334	72
			190	$C_{10}H_6O_4$	190.0265	190.0261	55
			176	$C_{10}H_8O_3$	176.0473	176.0485	21
			162	$C_9H_6O_3$	162.0316	162.0319	92
			134	$C_8H_6O_2$	134.0367	134.0361	40
			43	C_2H_3O	43.0284	43.0277	30
cis-4′-*O*-Methylkhellactone[c] (X)	H	CH_3	277 (M + 1)	$C_{15}H_{17}O_5$	277.1075	277.1044	8
			276 (M)	$C_{15}H_{16}O_5$	276.0997	276.1017	44
trans-4′-*O*-Methylkhellactone[c,e] (XI)	H	CH_3	229	$C_{13}H_9O_4$	229.0500	229.0448	9
			205 (P)	$C_{11}H_9O_4$	205.0500	205.0507	100
			204	$C_{11}H_8O_4$	204.0422	204.0424	66
			189	$C_{10}H_5O_4$	189.0187	189.0178	30
			176	$C_{10}H_8O_3$	176.0473	176.0443	20
			175	$C_{10}H_7O_3$	175.0394	175.0357	8
			161	$C_9H_5O_3$	161.0238	161.0254	16
			77	C_6H_5	77.0391	77.0393	8
			73	C_4H_9O	73.0653	73.0671	14
cis-4′-*O*-Ethylkhellactone[c] (XII)	H	CH_3CH_2	291 (M + 1)	$C_{16}H_{19}O_5$	291.1231	291.1218	10
			290 (M)	$C_{16}H_{18}O_5$	290.1153	290.1178	43
trans-4′-*O*-Ethylkhellactone[c,e] (XIII)	H	CH_3CH_2	219	$C_{12}H_{11}O_4$	219.0657	219.0660	56
			218 (P)	$C_{12}H_{10}O_4$	218.0579	218.0579	100
			203	$C_{13}H_9O_3$	203.0551	203.0562	8
			191	$C_{10}H_7O_4$	191.0343	191.0353	74
			190	$C_{10}H_6O_4$	190.0265	190.0273	41
			176	$C_{10}H_8O_3$	176.0473	176.0478	5
			175	$C_{10}H_7O_3$	175.0394	175.0379	5
			162	$C_9H_6O_3$	162.0316	162.0324	46
			134	$C_8H_6O_2$	134.0367	134.0378	15
trans-Khellactone[d] (XIV)	H	H	262 (M)	$C_{14}H_{14}O_5$	262.0840	262.0840	15
			192	$C_9{}^{13}CH_7O_4$	192.0377	192.0388	12
			191 (P)	$C_{10}H_7O_4$	191.0343	191.0347	100
			190	$C_{10}H_6O_4$	190.0265	190.0255	16
			162	$C_9H_6O_3$	162.0316	162.0311	17
			134	$C_8H_6O_2$	134.0367	134.0377	17
			107	C_7H_7O	107.0496	107.0492	7

[a] Fragments with a relative abundance of less than 5% of the parent peak were not considered. [b] Reference 12. [c] Reference 13. [d] Reference 14. [e] The accurate mass measurements for XI and XIII are not included. The relative intensities of the low-resolution peaks as compared to X and XII, respectively, were almost identical and, therefore, are not included.

entiation of positional isomers, a problem frequently encountered in this class of coumarins. Obviously, when the diacetate (VII) fragments (Scheme VIII), it is impossible to tell which acetoxy group is eliminated, although one would suggest loss of the 3′-moiety by analogy to V and VI.

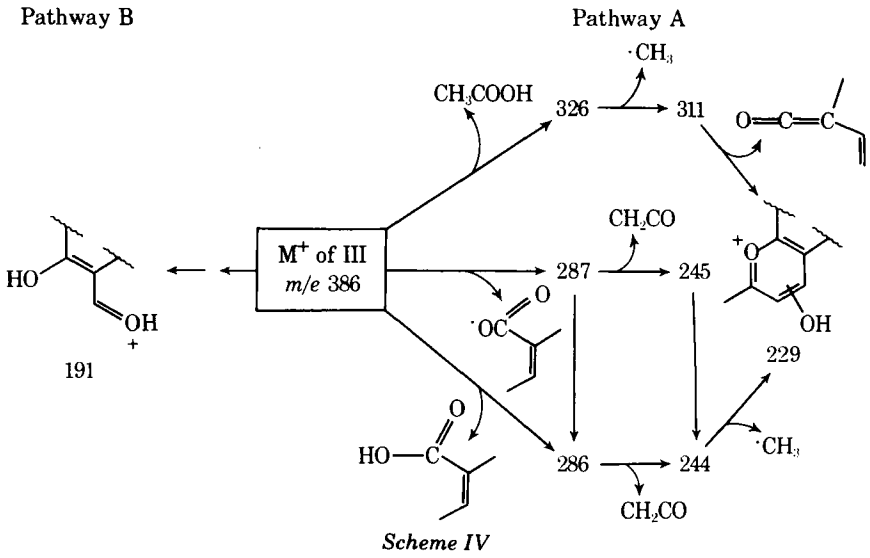
It is also of interest to compare the spectra of Group 1 and 2 compounds with those of Group 3. In this case, peaks due to the loss of $C_4H_7COO\cdot$ are present in the spectra of I–IV but not in the spectra of V and VI. Das *et al.* (11) reported fragmentation patterns for visnadin (VI) that are in accord with the results of this study.

Group 5—Pathways A and B seem to be equally important in the spectra of VIII and IX. The presence of an acetoxy group apparently is necessary for the observation of Pathway A (Scheme IX). Only small differences in peak height are observed in the spectra of VIII and IX.

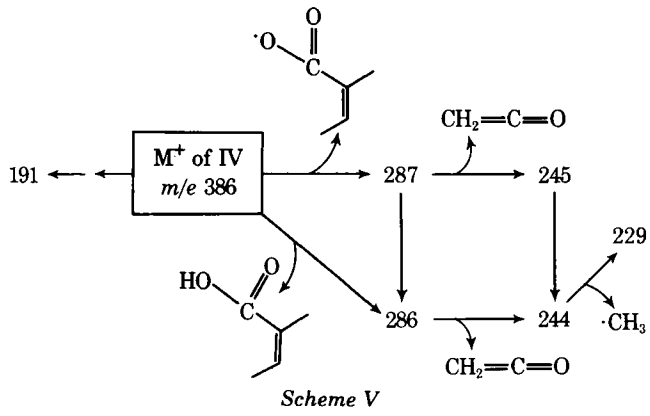
Groups 6 and 7—Compounds X–XIV exhibit sizable molecular ion peaks, although ethers X–XIII also exhibit $M^+ + 1$ peaks. Pathway A seems to be of little or no consequence (Schemes X–XII). A stepwise loss of carbon monoxide, characteristic of coumarins, was observed from Pathway B fragmentation.

The following generalizations will aid in the interpretation of the mass spectra of this class of coumarins and, hopefully, will lead to the effective use of these results in the structural elucidation of unknown coumarins.

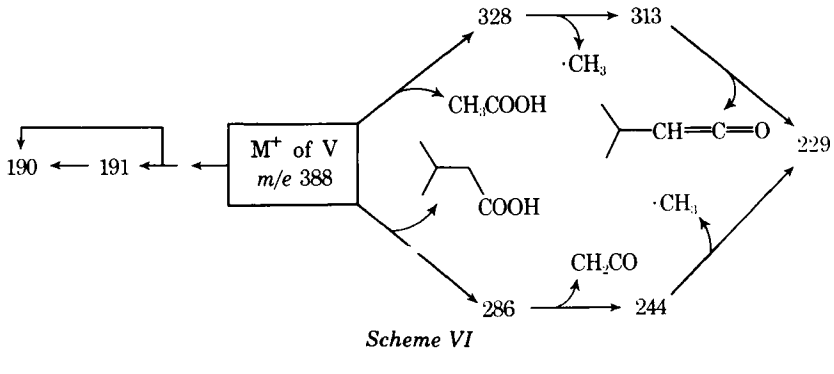
1. All compounds exhibit M^+, except when R_1 and R_2 are both



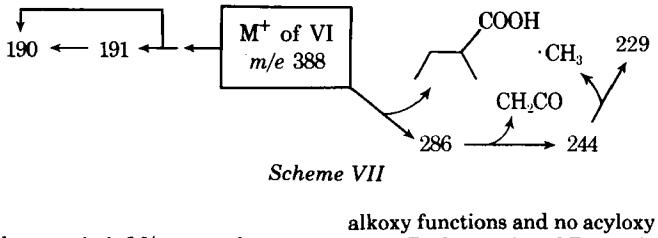
Scheme IV



Scheme V



Scheme VI



Scheme VII

bulky (Group 1).

2. When R_2 is an alkoxy group, characteristic $M^+ + 1$ peaks appear.

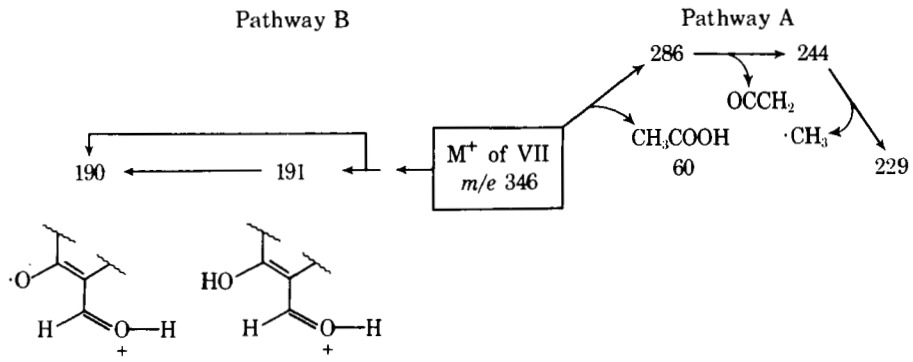
3. Pathway A predominates when both substituents are acyloxy groups (Groups 1–4).

4. Pathway B predominates in compounds with hydroxy and alkoxy functions and no acyloxy substituent.

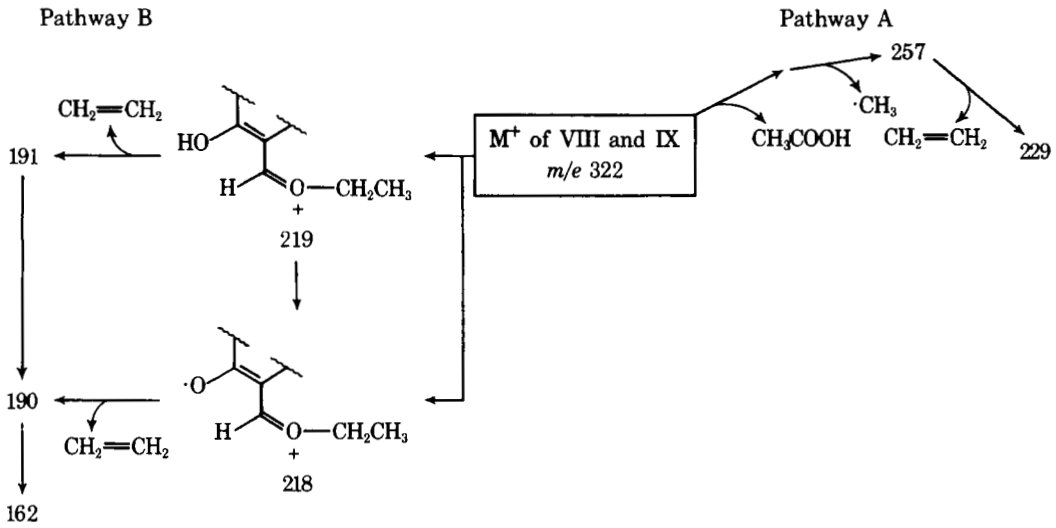
5. Pathways A and B are of equal importance when one substituent is an acyloxy function (*e.g.*, Group 5).

6. Loss of a 3′-acyloxy substituent is preferred over loss of a 4′-acyloxy moiety.

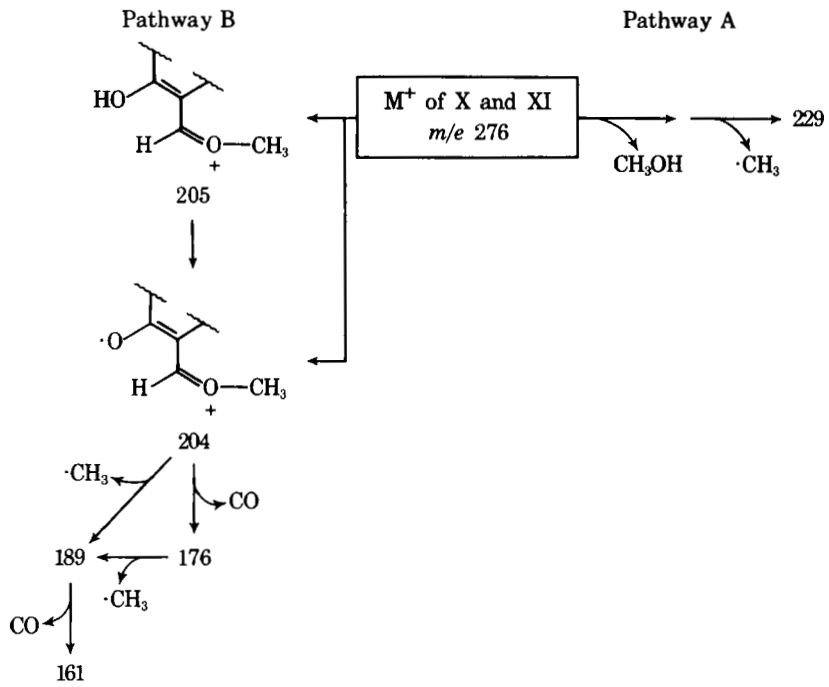
7. Loss of five-carbon acids is more facile than loss of acetic acid.



Scheme VIII



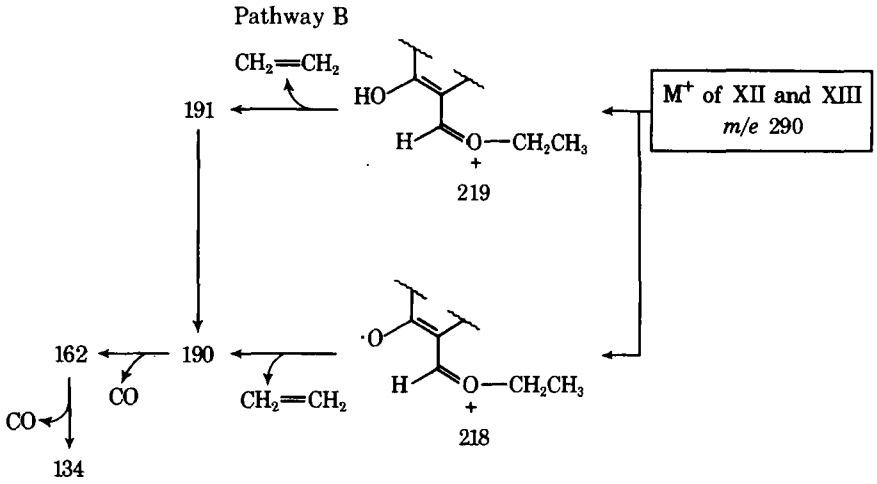
Scheme IX



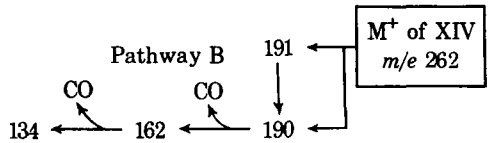
Scheme X

8. Loss of an unsaturated five-carbon acyloxy substituent occurs more readily than loss of a corresponding five-carbon saturated analog.

9. The acyloxy substituents give rise to their respective characteristic peaks. For example, angelates and/or senecioates show peaks at *m/e* 83 and 55, isovalerates and α-methylbutyrates show peaks at



Scheme XI



Scheme XII

m/e 85 and 57, and acetates show a peak at *m/e* 43.

10. No significant differences are observed in the spectra of *cis*- and *trans*-isomers.

EXPERIMENTAL

Materials—Compounds I–XIV were available from previous studies (12–14).

Mass Spectra[2]—The mass spectrometer was operated at an ionizing voltage of 70 ev, a source temperature of 200°, and an unheated direct inlet. Perfluorokerosene was used as the internal standard.

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[2] Determined by Dr. N. Shaath and Dr. R. Upham, Mass Spectrometry Laboratory, Department of Chemistry, University of Minnesota, employing an AEI MS30 high-resolution mass spectrometer. Preliminary mass spectral data were obtained using a Hitachi Perkin-Elmer RMU-6D mass spectrometer.