A MASS-SPECTROMETRIC STUDY OF 3',4'-DIHYDROXY- AND 3',4'-DIACYLOXYDIHYDROPYRANOCOUMARINS

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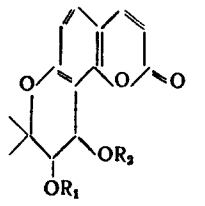
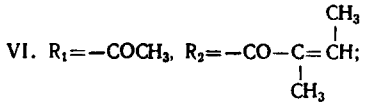
UDC 543.51 + 547.985

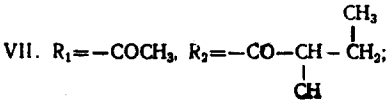
In a preceding paper we have described the fragmentation under the action of electron impact of angular and linear 3'-hydroxy- and 3'-acyloxydihydropyranocoumarins [1]. The present paper gives the results of a mass-spectrometric study of khellactone and its methoxy and diacyloxy derivatives and also of diacyloxy derivatives of isokhellactone. The compounds belong to the class of 3',4'-dihydroxy-, 3'-hydroxy-4'-methoxy, 3'-acyloxy-4'-methoxy-, and 3',4'-diacyloxydihydropyranocoumarins.



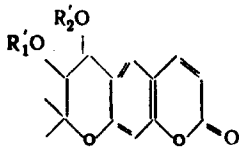
I. $R_1=R_2=-H$;
II. $R_1=R_2=-D$;
III. $R_1=-H$, $R_2=-CH_3$;
IV. $R_1=-DR_2=-CH_3$;
V. $R_1=R_2=-COCH_3$;

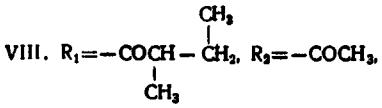


VI. $R_1=-COCH_3$, $R_2=-CO-C(CH_3)=CH-CH_3$;

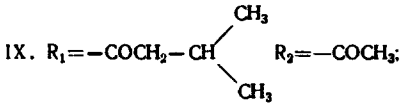


VII. $R_1=-COCH_3$, $R_2=-CO-CH(CH_3)-CH_2-CH_3$;

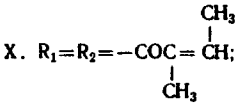




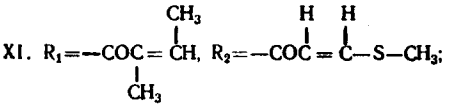
VIII. $R_1=-COCH(CH_3)-CH_2-CH_3$, $R_2=-COCH_3$,



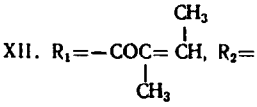
IX. $R_1=-COCH_2-CH(CH_3)-CH_3$, $R_2=-COCH_3$;



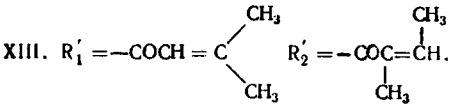
X. $R_1=R_2=-COC(CH_3)=CH-CH_3$;



XI. $R_1=-COC(CH_3)=CH-CH_3$, $R_2=-COC(H)=C(H)-S-CH_3$;



XII. $R_1=-COC(CH_3)=CH-CH_3$, $R_2=-CH_3$;



XIII. $R_1'=-COCH=C(CH_3)-CH_3$, $R_2'=-COC(CH_3)=CH-CH_3$.

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We have studied the above substances of this series: khellactone (I), [D_2]khellactone (II), methylkhellactone (III), [D]methylkhellactone (IV), khellactone diacetate (V), pteryxin (VI), dihydropteryxin (VII), visnadin (VIII), dihydrosamidin (IX), anomalin (X), floroselin (XI), the product of the methanolysis of floroselin (XII), and andelin (XIII).

Compounds (VI, VIII, IX-XI, and XIII) were isolated from the plants Libanotis condensata [2], Phlojodicarpus villosus Turcz [3], Ph. sibiricus (Steph.) K.-Pol [4], Angelica adzharica [5], Seseli sessiliflorum Schrenk [6], and Angelica decursiva [7]. Compounds (II-V, VII, and XII) were obtained synthetically from compounds (I, III, VI, and XII).

Dihydroxydihydropyranocoumarin derivatives are of interest as substances present in coumarin-bearing plants, the study of which is continuing to lead to the isolation of new substances of this class [5, 6]. Compounds such as pteryxin (VI), visnadin (VII), dihydrosamidin (IX), and anomalin (X) are used in medical practice as spasmolytics [8].

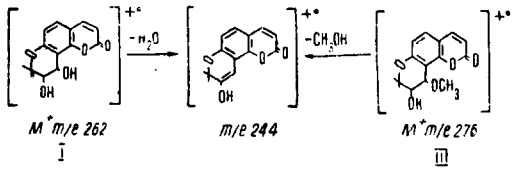
In view of this, the investigation of the fragmentation of this class of substances is important both for structural purposes and also for the purposes of their identification. The use of the mass-spectrometric method requires tenths and hundredths of a milligram of the substance under consideration, and these amounts can be obtained in practice from a single chromatographic spot.

The mass spectrum of each compound, the main fragments of which are given in Table 1, contains the peak of the molecular ion. For khellactone (I) and methylkhellactone (III) it is of medium intensity. In the case of acyl derivatives of compounds (I) and (III) the peaks of the molecular ions are of low intensity.

The nature of the fragmentation of khellactone (I) and methylkhellactone (III) differs substantially from that of acyl derivatives of khellactone. The decomposition of these compounds under the action of electron impact begins with the ejection of a molecule of water in the case of (I) and of methanol in the case of (III).

TABLE 1. Main Fragments and Their Relative Intensities in the Mass Spectra of 3',4'-Dihydroxy-, 3'-Hydroxy-4'-methoxy-,3'-Acyloxy-4'-methoxy-, and 3',4'-Diacyloxydihydropyranocoumarins

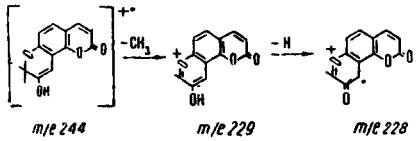
Compound	M+	Mass numbers, m/e (relative intensity, %)										
I	262 (20)	244 (2)	243 (1)	229 (3)	228 (4)	191 (100)	190 (17)	176 (6)	162 (46)	134 (30)	72 (79)	71 (58)
II	264 (19)	245 (2)	243 (1)	230 (5)	229 (7)	193 (100)	192 (18)	177 (7)	163 (30)	135 (27)	72 (42)	71 (80)
III	276 (70)	244 (4)	243 (2)	229 (2)	228 (4)	205 (100)	204 (69)	189 (26)	175 (26)	161 (12)	126 (27)	71 (46)
IV	277 (70)	245 (3)	243 (2)	230 (1)	229 (2)	206 (95)	205 (70)	204 (100)	189 (47)	175 (33)	161 (23)	126 (47)
V	346 (11)	304 (1)	305 (1)	287 (1)	286 (3)	271 (2)	261 (1)	244 (34)	229 (100)	213 (13)	191 (27)	60 (44)
VI	386 (2)	326 (7)	311 (14)	303 (3)	287 (22)	261 (6)	245 (36)	229 (37)	189 (10)	175 (14)	119 (23)	83 (100)
VII	388 (1)	328 (3)	313 (7)	303 (1)	287 (6)	261 (8)	244 (20)	229 (100)	191 (13)	100 (24)	85 (59)	83 (86)
VIII	388 (9)	332 (2)	329 (3)	328 (2)	313 (1)	286 (11)	271 (5)	261 (3)	244 (55)	229 (100)	85 (22)	71 (11)
IX	388 (6)	332 (6)	329 (1)	328 (1)	313 (3)	286 (10)	271 (7)	261 (5)	244 (59)	229 (100)	85 (59)	71 (62)
X	426 (0,1)	344 (0,5)	343 (1)	327 (32)	326 (18)	312 (4)	311 (23)	261 (5)	256 (1)	244 (10)	229 (41)	83 (100)
XI	444 (0,5)	361 (0,5)	344 (37)	329 (50)	327 (11)	316 (21)	244 (5)	229 (24)	213 (33)	118 (10)	101 (100)	83 (93)
XII	358 (3)	258 (1)	257 (2)	243 (76)	227 (5)	213 (10)	205 (20)	204 (7)	189 (10)	135 (8)	83 (73)	69 (100)
XIII	426 (3)	344 (1)	343 (0,5)	327 (9)	326 (38)	311 (29)	261 (0,5)	256 (4)	244 (6)	229 (29)	97 (20)	83 (100)



Scheme 1

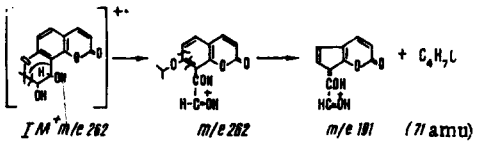
Then the fragment with m/e 244 loses a hydrogen atom, giving an ion with m/e 243. In the mass spectra of [D_2]khellactone (II) and [D]methylkhellactone (IV), the m/e 244 fragment is shifted by one mass unit in the direction of higher masses, which confirms the route of its formation. The absence of a shift for the fragment with m/e 243 in the mass spectra of (II) and (IV) shows the loss by the fragment with m/e 244 of the hydrogen atom of the hydroxy group. Then the fragment with m/e 244 splits out a CH_3 group from the gem-dimethyl grouping, forming a fragment with m/e 229, which leads to the complete aromatization of the pyran ring. The latter, ejecting a hydrogen atom, forms a fragment with m/e 228.

The shift of the ions with m/e 229 and 228 by one mass unit in the mass spectra of (II) and (IV) shows that the ion with m/e 228 is obtained only from the fragment with m/e 229, and not from that with m/e 243, and is a consequence of the loss of a hydrogen atom by the fragment with m/e 229 from position 4' with the subsequent migration to this position of the hydrogen atom of the hydroxy group. The ion with m/e 228 which appears also has a closed system of π bonds, which stabilizes it, but now as the result of the unshared electron at the 4' carbon atom. The fragments with m/e 229 and 228 lose CO groups, forming ions with m/e 201 and 200, which undergo a shift in the mass spectra of deuterated khellactone and deuterated methylkhellactone.



Scheme 2

Another direction of fragmentation of khellactone (I) and methylkhellactone (III), which is the most characteristic one for the molecules of these two substances, is the decomposition shown by the following scheme [for the case of (I)]:



Scheme 3

The fragments corresponding to this decomposition [m/e 205 for (III)] possess the highest intensity in their mass spectra. In the mass spectra of [D_2]khellactone (II) and [D]methylkhellactone (IV) they are shifted by 2 and 1 units, respectively, in the high-mass direction. Then the fragment with m/e 191, losing a HCO group, gives a fragment with m/e 162, and the fragment with m/e 205, losing a HCO group gives a fragment with m/e 176 (12%). The formation in the mass spectrum of (I) of a fragment with m/e 190 takes place in a similar manner to the formation of the fragment with m/e 191, but is accompanied by the transfer of not one but two hydrogen atoms from the fragment splitting out from the main part of the molecule. A fragment with m/e 72 appears which gives a stronger peak than the fragment with m/e 71. In the mass spectrum of [D_2] khellactone, the ion with m/e 72 is partially shifted by one mass unit in the high-mass direction. The relative intensities of the fragments with m/e 72 and 73 shows that in the formation of the fragment with m/e 72 about 48% of the hydrogen atoms are transferred to it from the hydroxy group.

In the mass spectrum of methylkhellactone, the absence of a fragment of appreciable intensity with m/e 72 permits the assumption that the fragment with m/e 204 is formed by the ejection of a hydrogen atom

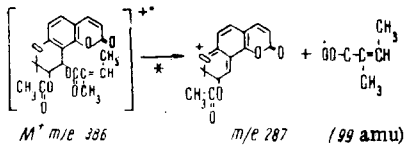
by the ion with m/e 205. The presence in the mass spectrum of [D]methylkhellactone of an ion with m/e 204 shows that the fragment with m/e 205 loses either the hydrogen atom attached to the carbon of the carbonyl group or that attached to the oxygen atom of the oxonium form.

Thus, although the fragmentations of compounds (I) and (III) coincide in the main, the presence of a methoxy group in position 4' of compound (III) in place of the hydroxy group of compound (I) leads to substantial differences in the details of the appearance of the fragments.

The mass spectra of (V-XIII), which are acyl derivatives of khellactone (I), methylkhellactone (III), and isokhellactone, differ by the magnitudes of the molecular peaks. The latter are higher for the substances the acyl residues of which have a smaller number of atoms. The molecular peaks are also stronger for the isomers containing an acyl residue having a smaller number of atoms in position 4'. In the case of compound (XIII), which belongs to the linear diacyloxydihydropyranocoumarins, the molecular ion is stronger than in compound (X).

The decomposition of the molecular ions of these compounds takes place in three directions. In all substances, the splitting out of the acid residue from position 4' is found, this being typical for a substance having a substituent in the benzyl position [9].

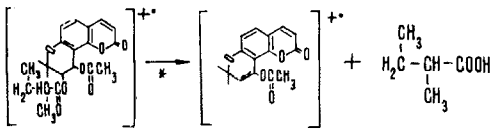
This process takes place in accordance with scheme 4, which is shown for the case of pteryxin (VIII).*



Scheme 4

Compounds containing an angeloyl group in position 4' – (VI), (X) – give stronger peaks as a result of this decomposition than compounds containing an α-methylbutyryl group, i.e., a saturated acid group, in this position (VII). In the case of substances with an acetyl group in position 4', this process gives extremely feeble peaks of approximately equal intensity for the loss of acetic acid from this position in the case of compounds (V, VIII, and IX) [fragments with m/e 328 for (VIII) and (IX)].

For all the substances (V-XIII) the predominant splitting out of the acid from position 3', which is typical for esters of carboxylic acid [10], and only to a very small extent the splitting out of acid residue are observed. The double bond so arising lengthens the system of conjugated π bonds and stabilizes the fragments formed. This decomposition takes place in accordance with Scheme 5, which is shown for the case of visnadin (VIII):



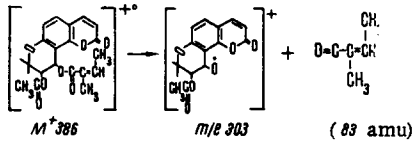
Scheme 5

Of the two processes considered (the splitting out of an acid residue from position 4' and of an acid from position 3'), as a rule that in which the acyl group with the larger number of carbon atoms splits out takes place more intensively. Anomalin (X), containing two α,β-dimethylacryloyl groups, splits out the acid residue from position 4' more strongly than from position 3'. On the other hand, andelin (XIII), with two isomeric acyl groups – α,β-dimethylacryloyl and β,β-dimethylacryloyl – and belonging to the class of linear diacyloxydihydropyranocoumarins, splits out the acid from position 3' more intensively than the acid residue from position 4'. The angelic acid also splits out more intensively from position 3' of floroselin (XI), which contains a trans-3-methylthioacryloyl group, with a larger number of atoms, in position 4'.

* An asterisk under an arrow in one of the schemes denotes a decomposition confirmed by metastable transitions.

Compounds (VI, X-XIII) with one or two residues of unsaturated acids have considerably more intensive M^+-ROO and M^+-ROOH fragments, which are described in Schemes 4 and 5, than compounds (V and VII-IX) with residues of the saturated acids, α-methylbutyric and isovaleric.

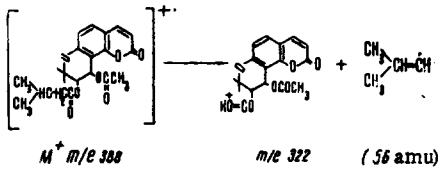
All the substances (V-XIII) give fragments of low intensity arising as the result of the splitting out of the acyl residue with the larger number of atoms. This process takes place both with and without the transfer of one hydrogen atom from the acyl group to the oxygen of the ester group, which is typical for esters of carboxylic acids [10]. It is shown in Scheme 6 for the case of pteryxin (VI).



Scheme 6

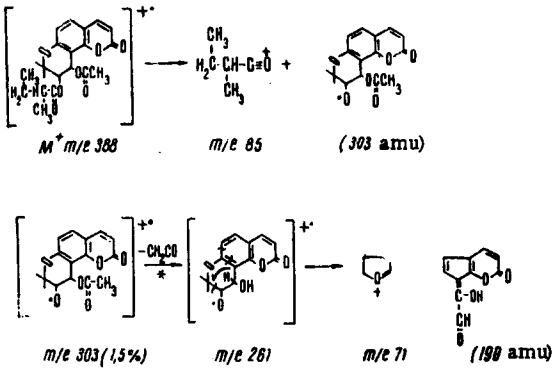
In the mass spectra of anomalin (X) and andelin (XIII) this process is represented by fragments with m/e 344 and 343, and in the mass spectrum of floroselin (XI) by fragments with m/e 371, 370, and 361.

Visnadin (VIII) and dihydrosamidin (IX), which contain residues of the saturated α-methylbutyric and isovaleric acids in position 3', also split out these acyl groups with the transfer of one or two hydrogen atoms to the acyl residue, but not conversely (Scheme 6). This forms fragments with m/e 302 and 301. The same substances, in contrast to the dihydropteryxin (VII) isomeric with them but having an α-methylbutyryl group in position 4', give a fragment with m/e 332, formed in accordance with Scheme 7, as shown for the case of dihydrosamidin (IX):



Scheme 7

In dihydrosamidin (IX) this process takes place more intensively than in its isomer visnadin (VIII). Because of the slight differences in their structure, substances (VIII) and (IX) are difficult to separate chromatographically and have simular UV spectra. The mass spectra of these substances are also almost identical in the region of large and medium masses. But in the range of low masses they differ by the relative intensities of the fragments with m/e 85 and 71. In the case of visnadin (VIII), the ratio of the intensities of the peaks with m/e 85 and m/e 71 is 2.2, while in dihydrosamidin it is 0.96. Thus, the ratio of the intensities of these fragments may be taken into account in an analysis of mixtures of these substances. Scheme 8 shows the routes of their formation for the case of visnadin.

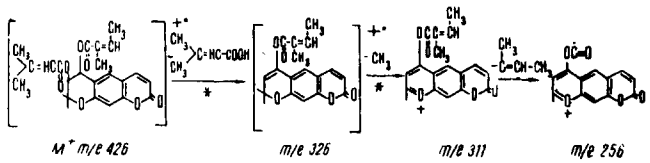


Scheme 8

The difference in the intensities of the decomposition of the ion with m/e 303 in the mass spectra of (VIII) and (IX) is due to the fact that these ions are formed from fragments which differ, even if only slightly. The ion with m/e 71 in (VIII), of lower intensity than in (IX), shows that the detachment of the α-methylbutyryl radical takes place with a greater expenditure of energy than the process for the isovaleryl radical. This affects both the intensity of the ion with m/e 85 that is split out [it is less pronounced in (VIII) than in (IX)] and also the rate of decomposition of the ion with m/e 303. The latter, which possesses the lower supply of energy in (VIII), splits out the fragment with m/e 71 to a considerably smaller extent. The stronger ester bond of the α-methylbutyric acid in (VIII) as compared with isovaleric acid in (IX) can be explained by the positive inductive influence of the α-methyl group on the ester grouping. As a result, the degree of polarization of the ester bond decreases, which leads to an increase in the electron density on this bond and, consequently, to its strengthening.

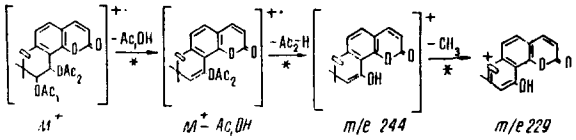
In substances (V-XIII), the fragments formed through the splitting off of the acid from position 3' lose a CH_3 group from the gem-dimethyl grouping of the dimethylchromane ring. This leads to the appearance of fragments with m/e 271 for compounds (V, VIII, and IX), with m/e 311 for (VI, X, and XIII), with m/e 329 for (XI), and with m/e 243 for (XII). Thus, the methyl of the gem-dimethyl grouping splits out only in those cases where this leads to the formation in the ring of a closed system of conjugated π bonds. Consequently, the existence of the fragment $M^+ - ROOH - CH_3$ shows the presence of an acyl residue of the acid ROOH in position 3'.

For anomalin (X) and andelin (XIII), which have similar or isomeric unsaturated acyl radicals, fragments with m/e 256 are characteristic. In the mass spectra of the two compounds they differ by the ratio of the intensities to that of the fragment with m/e 261, which is twice as intensive for (X) and 10 times less intensive for (XIII) than the fragment with m/e 256. The formation of the fragment with m/e 256 can be represented by Scheme 9, which shows the process for (XIII):



Scheme 9

The mass spectra of all the diacyloxydihydropyranocoumarins have the peaks of fragments with m/e 261, 245, 244, 243, 230, 229, 228, and 227. Their presence and intensities are characteristic for this class of compounds, and form a distinguishing feature of substances of this series. The first of these fragments (m/e 261) has a low intensity; it consists of the ion with the structure $M^+ - Ac_1 + H - Ac_2$, where Ac_1 is the acyl residue with the larger number of atoms, regardless of whether it substitutes the hydroxy group in position 3' or 4'. The structures of the following fragments and their formation can be represented by Scheme 10:



Scheme 10

In the region of medium mass numbers, the mass spectra of compounds (V-XIII) exhibit low-intensity fragments with m/e 213, 191, 190, 189, 175, and 162. In the low-mass region, strong peaks are found with m/e 85 and 83 for (VII-IX) with the saturated α-methylbutyryl and isovaleryl radicals and with m/e 83 for (VI, X, XII, and XIII) with the unsaturated angeloyl and senecioyl radicals. In the mass spectrum of floroselin (XI) in the low-mass region appear the molecular ion (M^+) of cis-3-methylthioacrylic acid (m/e 118), its fragment $M^+ - CH_3$ (m/e 103), and the acyl radical of this acid ($M^+ - OH$, m/e 101).

Thus, the mass spectra of the 3',4'-dihydroxy- and 3',4'-diacyloxydihydropyranocoumarins (I-XIII) that have been studied provide useful information on their structures which well reflects both the similarities and differences between them and can be used for the purposes of structural analysis in this class of compounds.

EXPERIMENTAL

The mass spectra of compounds (I-XIII) were recorded on an MKh-1303 instrument at an ionizing voltage of 70 V with the introduction of the samples into the ion source at the following temperatures: (I-V) 100°, (VI) 65°, (VII) 60°, (VIII) 70°, (IX) 65°, (X) 100°, (XI) 70°, (XII) 100°, (XIII) 80°. The sample-heating system ensured temperature stability with an accuracy of ±1°C.

CONCLUSIONS

The mass spectra of 13 3',4'-dihydroxy, 3'-hydroxy-4'-methoxy-, 3'-acyloxy-4'-methoxy-, and 3',4'-diacyloxydihydropyranocoumarins have been studied. Schemes of the decomposition of these compounds leading to the formation of the main fragments in their mass spectra have been proposed. It has been shown that the mass spectra of (V-XIII) indicate whether the acyloxy groups are attached to position 3' or 4' of the dihydropyran ring. Characteristic fragments with m/e 261, 245, 244, 243, 230, 229, 228, and 227 have been found, the positions and relative intensities of which form distinguishing features of the mass spectra of the diacyl derivatives of khellactone.

LITERATURE CITED

1. P. I. Zakharov, V. S. Kabanov, A. I. Ban'kovskii, G. K. Nikonov, and N. E. Ermatov, Khim. Prirodn. Soedin., 7, 398 (1971).
2. G. K. Nikonov, F. V. Babilev, and N. E. Ermatov, Khim. Prirodn. Soedin., 2, 214 (1966).
3. G. K. Nikonov and V. V. Vandyshev, Khim. Prirodn. Soedin., 5, 118 (1969).
4. F. V. Babilev and G. K. Nikonov, Khim. Prirodn. Soedin., 1, 353 (1965).
5. V. V. Vandyshev, G. K. Nikonov, and M. G. Pimenov, Khim. Prirodn. Soedin., 5, 434 (1969).
6. A. A. Savina, M. E. Perel'son, G. K. Nikonov, and A. I. Ban'kovskii, Khim. Prirodn. Soedin., 6, 517 (1970).
7. A. A. Avramenko, G. K. Nikonov, and M. G. Pimenov, Khim. Prirodn. Soedin., 6, 190 (1970).
8. B. A. Krivut, M. E. Perel'son, and V. V. Vandyshev, Khim. Prirodn. Soedin., 6, 180 (1970).
9. H. Budzikiewicz, C. Djerassi, and Dudley H. Williams, Interpretation of Mass Spectra of Organic Compounds, Holden-Day, San Francisco (1964), Chap. 9.
10. R. Ryhage and E. Stenhagen, in: Mass Spectrometry of Organic Ions (ed. F. W. McLafferty), Academic Press, New York (1963), Chap. 9.