Equilibration of *cis*- and *trans*-9-Methylthioxanthene 10-Oxides (3).—Typically, 0.10 g of either *cis* or *trans* **3** was treated with 8 ml (at 0–5°) of dry (phosphorus pentoxide) dinitrogen tetroxide. After 3 hr at 0°, the excess dinitrogen tetroxide was removed under reduced pressure and the residue was analyzed by nmr spectroscopy. The product was essentially free of decomposition products (as determined by nmr) and consisted of a mixture of 30% *cis* **3** and 70% *trans* **3**.[27]

***cis*- and *trans*-9-Methyl-9-hydroxythioxanthene 10-Oxides (13).**—A solution of *m*-chloroperbenzoic acid (2.84 g, 0.0131 mol assuming 80% purity) in methylene chloride (100 ml) was added to a cold (0–5°) solution of 9-methylthioxanthen-9-ol (3.00 g, 0.0132 mol) in 200 ml of methylene chloride. The resulting mixture was stirred for 18 hr and then washed with saturated sodium bicarbonate solution. The organic layer was dried (magnesium sulfate) and the solvent was removed (stream of nitrogen) to afford 3.20 g of a light yellow oil that solidified upon standing. Thin layer chromatography indicated the presence of two major and one minor component.

This solid was extracted with hot benzene (200 ml) and the benzene solution was cooled to 25°. The benzene-insoluble material and the substance which precipitated upon cooling of the benzene solution were combined and recrystallized from ethyl acetate to afford 0.79 g (0.0032 mol, 25% yield) of α **13**, mp 199.5–202.5 dec. This material was homogeneous to tlc.

Anal. Calcd for $C_{14}H_{12}O_2S$: C, 68.82; H, 4.95; S, 13.13. Found: C, 68.61; H, 4.81; S, 13.31.

The benzene solution which remained was concentrated (steam bath) to 35 ml. Two types of crystals deposited upon cooling and these were separated mechanically. This procedure afforded 0.40 g (0.0016 mol, 13%) of crude β **13**, mp 195–197° dec. Thin layer chromatography indicated that this material was essentially homogeneous. One recrystallization from acetone afforded β **13**, mp 201.5–202.5°.

Anal. Found: C, 68.60; H, 4.88; S, 12.98.

While the melting points of α **13** and β **13** are quite similar, their electronic spectra prove that they are not the same material.[28]

Registry No.—**1**, 10133-81-0; **3** (*cis*), 19018-80-5; **3** (*trans*), 19018-81-6; **4**, 19019-06-8; **5**, 19019-07-9; **6**, 19019-08-0; **7**, 16860-11-0; **8**, 261-31-4; **9**, 19019-10-4; **10**, 3166-16-3; **11**, 19019-12-6; **12**, 19019-13-7; α **13**, 19018-82-7; β **13**, 19018-83-8; 1-methyl-4-chlorothioxanthene, 19019-14-8; 1,6-dichloro-4-methylthioxanthene, 19019-15-9.

(27) Attempted equilibration using a dioxane–hydrochloric acid mixture resulted in some decomposition; however, the use of morpholine led to the clean equilibration of *cis* and *trans* **3**. The results were similar to those obtained with dinitrogen tetroxide.

(28) On the basis of their electronic spectra (see above), we have tentatively assigned the *cis* (sulfoxide–alcohol) configuration to α **13** and the *trans* configuration to β **13**.

The Mass Spectra of Pseudoguaianolides Related to Helenalin

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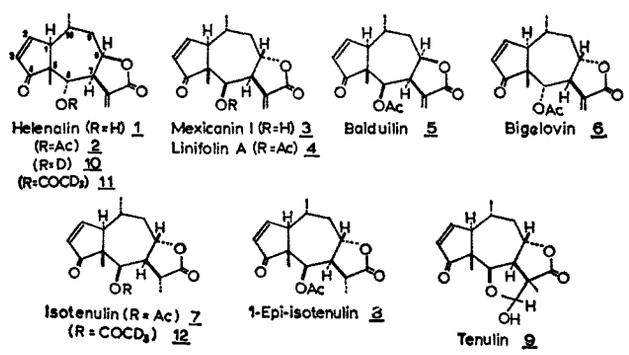
Received May 7, 1968

Examination of the mass spectra of 11 pseudoguaianolide sesquiterpenoid lactones bearing oxygen substituents at the 4, 6, and 8 positions reveal characteristic peaks at *m/e* 95, 96, 122, 123, and 124, compositions of which have been determined by high-resolution studies. Fragmentation mechanisms leading to these peaks are postulated and supported by the mass spectra of four deuterated derivatives.

The mass spectrometric study of fragmentation patterns of organic compounds under electron impact can yield fundamental information and also provide a diagnostic tool for the structural study of related compounds. Pseudoguaianolide sesquiterpenoid lactones[4] whose spectra have not been previously described[5] constitute an extensive series of closely related compounds which is eminently suitable for such studies. In this initial communication we report studies on pseudoguaianolides bearing the 4-, 6-, and 8-oxygenation pattern which occurs frequently within this family. Most significantly, peaks of *m/e* 95, 96, 122, 123, and 124 are common to this group of spectra. These peaks appear to be of diagnostic value and also seem capable of being interpreted rationally. [The complete spectra of the compounds **1–9** (Chart I) are shown in Figures 1–9.[6]]

CHART I



(1) Constituents of *Helenium* Species. XXII. Previous paper: W. Herz, C. M. Gast, and P. S. Subramaniam, *J. Org. Chem.*, **33**, 2780 (1968). Studies at Florida State University were supported by grants from the National Institutes of Health (GM-05814) and the National Science Foundation (GP-6362).

(2) National Heart Institute.

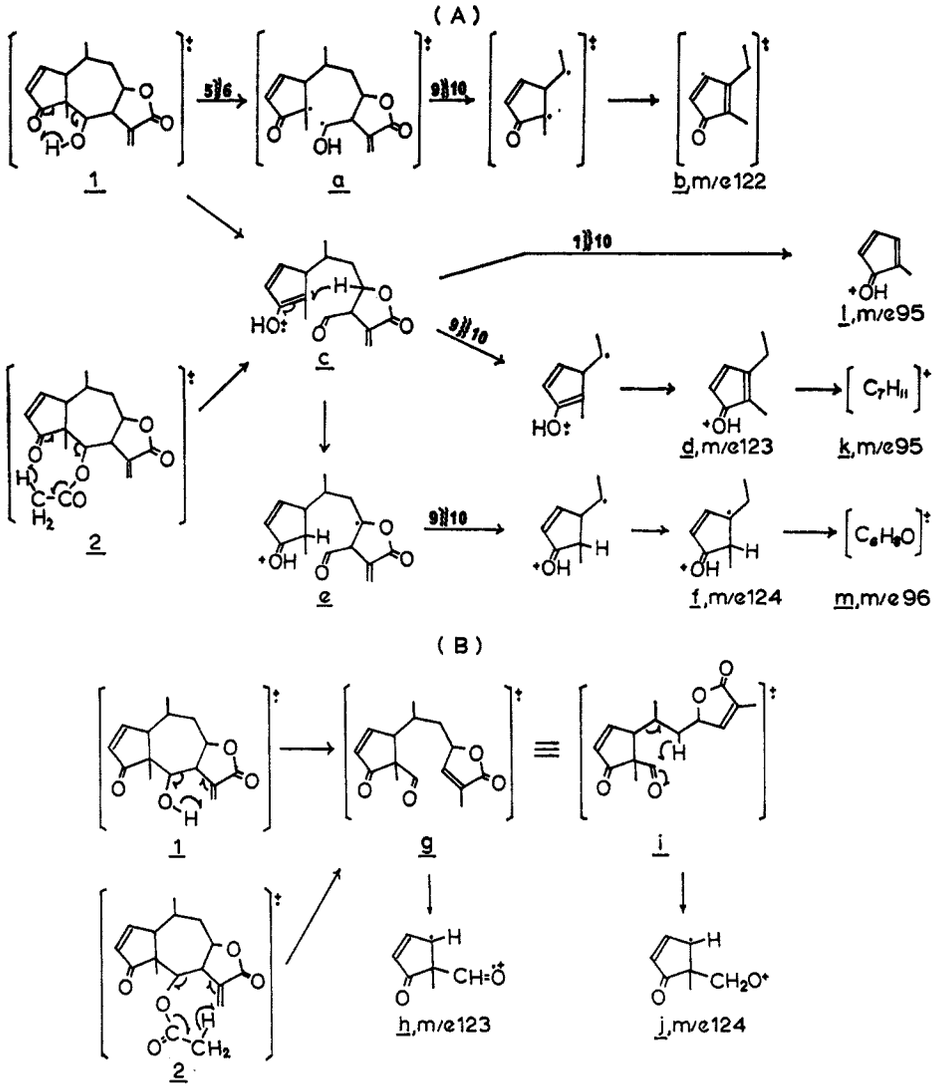
(3) Department of Chemistry, Florida State University.

(4) *Cf.* W. Herz, Abstracts of the 19th Symposium on Organic Chemistry, Tempe, Ariz., 1965, pp 67–75.

(5) Mass spectrometric studies of other sesquiterpene lactones have been reported: (a) santonin and related compounds by D. G. B. Boocock and E. S. Waight, *Chem. Comm.*, 90 (1960), and by T. Tsuchiya, E. Yoshii, and T. E. Watanabe, *Tetrahedron*, **23**, 4623 (1967); (b) elephantopin and its relatives by S. M. Kupchan, Y. Aynehchi, J. M. Cassady, A. T. McPhail, G. A. Sim, H. K. Schnoes, and A. L. Burlingame, *J. Amer. Chem. Soc.*, **88**, 3674 (1966); (c) gaillardin and its derivatives by S. M. Kupchan, J. M. Cassady, J. E. Kelsey, H. K. Schnoes, D. H. Smith, and A. L. Burlingame, *ibid.*, **88**, 5292 (1966); (d) achillin by S. J. Smolenski, C. L. Bell, and L. Bauer, *Lloydia*, **30**, 144 (1967).

(6) For Figures 1–15 and Table II, order document NAPS-00178 from ASIS-National Auxiliary Publications Service, c/o CCM Information Sciences, Inc., 22 West 34th Street, New York, N. Y. 10001, remitting $1.00 for microfiche or $3.00 for photocopies.

SCHEME I



All of the compounds of the series show weak parent peaks, with peaks of slightly lower *m/e* values (244, 234, 229, 216, and 210) arising by such familiar processes as the loss of methyl and acetyl groups and of water. Most of the peaks at *m/e* value below 90 result from elimination of all oxygen atoms. The loss of ketene (42 mass units) is responsible for an intense peak in the spectra of the acetates (**2**, **4**, **5**, **6**, and **8**), while the most intense peak of high *m/e* value in the spectrum of **7** arises from the loss of acetyl (43 mass units) to produce *m/e* 263. No facile explanation for this somewhat trivial difference seems to be apparent.

The high resolution mass spectra of helenalin (**1**), and isotenulin (**7**) were selected for detailed study (Table II).[6] As anticipated, the accurate masses of the peaks of high *m/e* values correspond to the trivial elimination of water (*m/e* 244) and carbon monoxide (*m/e* 234), the subsequent loss of methyl (*m/e* 229), and combinations of these.

The most prominent feature of the spectra (Figures 1–9)[6] is the group of peaks of *m/e* 95, 96, 122, 123, and 124. In each of the compounds these have been examined at high resolution; the composition of the ions involved and their *m/e* values in each case are tabulated in Table I. A survey[7] of the spectra of naturally occurring pseudoguaianolides devoid of the 4-, 6-, and 8-oxygenation pattern characteristic of the compounds of this study suggests that this group of peaks constitutes *prima facie* evidence of this oxygenation pattern.[8]

Clearly these peaks must arise from cleavages peculiarly favored by their common structural feature. Scheme I presents postulated routes leading to ions of the compositions observed, helenalin (**1**) being employed as a paradigm.

m/e **95, 96, 122, 123, and 124.**—Among the cleavages to fragments which should be stabilized by the double bonds and oxygen substituents of **1**, a provides one starting point. This intermediate can then fragment by cleavage of the 9,10 bond to *m/e* 122, $C_8H_{10}O$, which may be represented as b. In order to explain the formation of the fragment $C_8H_{11}O$ at *m/e* 123 it is necessary to postulate the transfer of a proton from the portion of the molecule ultimately eliminated as a neutral moiety; it is attractive to consider that the hydroxylic proton

(7) L. Tsai, R. J. Highet, and W. Herz, unpublished results.

(8) All pseudoguaianolides isolated from *Helenium* species so far have the lactone ring closed to C-8, and this study is confined to such compounds. As might be anticipated from the cleavage mechanisms here discussed, compounds possessing lactones closed to C-6 display a different cleavage pattern.

TABLE I

COMPOSITION OF CHARACTERISTIC PEAKS

m/e		1	10	2	11	3	4	5	6	7	12	8	9
125	$C_8H_{11}DO$		40		35						100		
	$C_7H_7DO_2$		60		65								
124	$C_8H_{12}O$	40	33[a]	33	33[a]	50	86	50	67	92	100[a]	95	92
	$C_7H_8O_2$	60	67[a]	67	67[a]	50	14	50	33	8		5	8
123	$C_8H_{11}O$	90	80	80	80	83	91	83	67	100	100	100	97
	$C_7H_7O_2$	10	20	20	20	17	9	17	33				3
97	C_6H_7DO		100		100						100		
96	C_6H_8O	100	100[a]	100	100[a]	100	100	100	100	100	100[a]	86	100
	C_7H_{12}											14	
95	C_6H_7O	50	50	50	50	75	60	67	75	60	50	50	83
	C_7H_{11}	50	50	50	50	25	40	33	25	40	50	50	17

[a] Resolution of the instrument does not allow direct determination of deuterium content in these peaks; *e.g.*, $C_8H_{10}DO$ and $C_8H_{12}O$ are not distinguishable.

is involved forming c from l, followed by cleavage of the 9,10 bond; the resulting diradical may be stabilized by rearrangement to the ion d. Subsequent decarbonylation forms the ion k at *m/e* 95. The formation of the fragment at *m/e* 124 must involve further proton transfer from c, probably *via* a six-membered cyclic transition involving H-8 to the oxygen stabilized radical e; again cleavage of the 9,10 bond produces the ion observed, f.

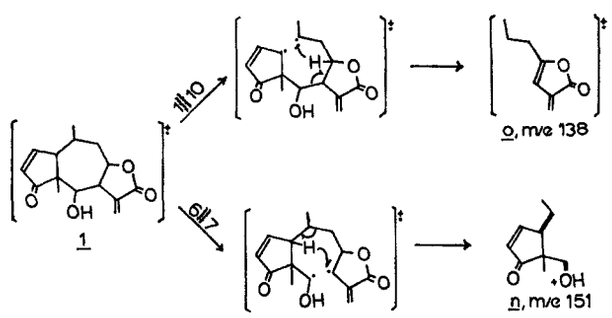
Helenalin (**1**), bearing an exocyclic methylene group at C-11, displays an alternative mode of fragmentation (B in Scheme I) leading to peaks of *m/e* 123 and 124, which appear in the high resolution spectrum as doublets. Cleavage of the 6,7 bond is evidently initiated by a proton transfer from the hydroxy group to form g. Dissociation of the 1,10 bond leads to the ion h, of *m/e* 123. Fragmentation with proton transfer, probably from C-9 (*cf.* i) leads to the ion j, of *m/e* 124. In the compounds with a C-11 methyl group, the second mode of scission is not favored, and the peaks at *m/e* 123 and 124 are essentially singlets (see Table I). The appearance of oxygenated peaks at *m/e* 95 and 96 (l and m) in the spectra of these compounds suggests that these fragments may result from scission of 1,10 bonds in c and f, respectively.

Compounds **2, 4, 6, 7,** and **8** bear acetoxy groups at C-6; the intermediates discussed above may be reached by a proton transfer from the acetyl group either to the carbonyl of C-4, leading to c, or to the exocyclic methylene of C-11, leading to g. Neutral ketene is formed concomitantly. Although the acetyl group is generally responsible for the strongest peak of the spectra, the remainder of the spectra closely resemble those of the parent alcohols.

m/e **151 and 138.**—At intermediate *m/e* values, the fragments of *m/e* 151 are a doublet. The major component, $C_9H_{11}O_2$, can be represented as n (Scheme II), but the character of the minor component, $C_8H_7O_3$, remains obscure. The peak at *m/e* 138, $C_8H_{10}O_2$, can be explained satisfactorily by assuming that it is derived from the lactone portion of the molecule and can be represented as o (Scheme II). So far this is the only fragment resulting from the lactone moiety.

To learn whether the above schemes actually operate, the mass spectra of helenalin-OD (**10**) and trideuterioacetylhelenalin (**11**) were determined. These spectra (Figures 10 and 11)[6] show strong peaks at *m/e* 125 and 97 and demonstrate that the proton transfer from the

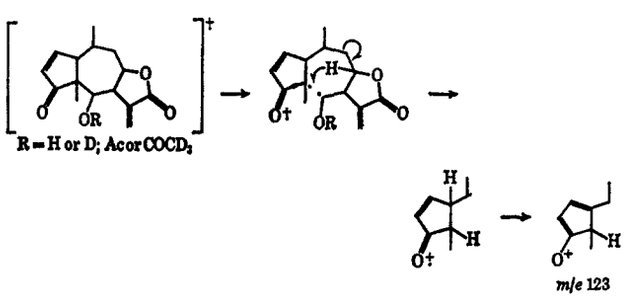
SCHEME II



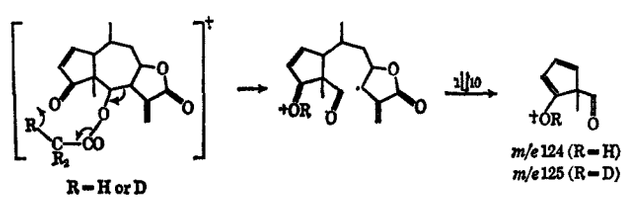
hydroxyl and acetate groups postulated occurs; however, the relative strengths of the peaks and their compositions within the groups are altered (see Table I), and reveal that the hydrogen transfer from other sites leading to these fragments does occur to a lesser extent.[9]

Although the list of compounds studied includes several epimeric pairs, no consistent behavior traceable to steric sources has been observed. Thus, helenalin (**1**) and mexicanin I (**3**), which differ in stereochemistry both at C-6 and C-8, present very similar spectra. However, a difference does appear in the spectra of the isomeric acetates. Acetylhelenalin (**2**) and bigelovin

(9) (a) For instance, a portion of the ions of *m/e* 123 may arise by the following mechanism.



(b) The observation that the $C_7H_8O_2$ fragment (*m/e* 124) is partially shifted to *m/e* 125 may indicate the following variation of the fragmentation parthways.

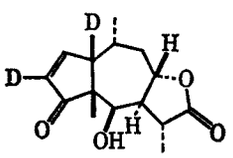


(6), both with an acetyl group *cis* to the proton at C-7, show a prominent peak at *m/e* 244 arising from elimination of acetic acid. This peak is much weaker in the spectra of linifolin A (4), balduilin (5), and isotenulin (7), which lack this *cis* juxtaposition. If this explanation is accepted, the relative strong peak at *m/e* 246 in the spectrum of 1-epiiostenulin (8) appears to be anomalous. It is tempting to speculate that the loss of acetic acid is rendered more facile in the case of 8 by the stereochemistry of the 7–5 ring junction.

The spectra of the dihydro compounds, 7, 8, and 9, serve to support the speculation on the origins of the fragments. The peaks above *m/e* 180 are shifted by 2 mass units to higher *m/e* values as anticipated. Below *m/e* 180 the spectra are similar to those of the compounds containing the C-11 methylene group. This confirms our supposition that the low *m/e* value peaks are derived from the cyclopentenone portion of the molecule. In the absence of the exocyclic double bond, the fragmentation path B in Scheme I does not occur, and the peaks of *m/e* 123 and 124 are singlets. The spectrum of trideuterioacetyldesacetylisotenulin (12, Figure 12)[6] shows shifts of the peaks to higher *m/e* values consistent with the mechanisms discussed above.

The spectra of 7 and 8 which are enantiomeric at C-1 do not differ significantly, although isotenulin shows a somewhat surprising reversal in the relative intensities of the M − 42 and M − 43 peaks. This similarity suggests that fragmentation of the molecules does not involve cleavage of bonds leading to C-1, and is consistent with the mechanisms here postulated.

The availability of 1,3-dideuterio-1-epidesacetylisotenulin[10] (13) permitted a confirming study The mass

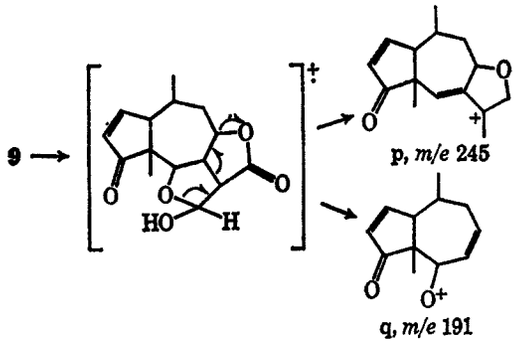


13

spectrum of 13 (Figure 13)[6] shows the shift of the most prominent peaks by two mass units to higher *m/e* values as anticipated. The peak at *m/e* 151, attributed to the fragment n (Scheme II) formed with the transfer of H-1 to the neutral fragment, is shifted by only 1 mass unit.

Although the structure of tenulin (9) might reasonably be anticipated to give rise to a strikingly different spectrum, the loss of ketene to *m/e* 264 is followed by the familiar fragmentation to strong peaks at *m/e* 95, 123, and 124. Of the two unusual peaks at *m/e* 245 and 191, the former corresponds to the loss of acetic acid and a proton, resulting in ion p, while the latter [*m/e* (observed) 191.1052; $C_{12}H_{15}O_2$ requires 191.1072] may result from the cleavage of the lactone–hemiketal system to form the ion q.

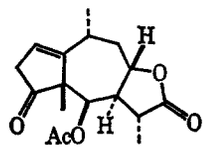
The spectra of the Δ-1 isomers, compound 14 and mexicanin A (15) (Figures 14 and 15),[6] which closely resemble the spectra of the normal series, exemplify the



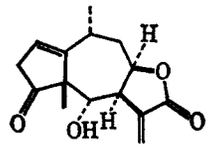
p, *m/e* 245

q, *m/e* 191

frequent observation that double-bond position does not necessarily affect the course of the fragmentation.



14



mexicanin A, 15

This study demonstrates the strict requirement of the functional groups, *viz.*, the 4,6,8-oxygen substituents and the double bond in the five-membered ring, of a pseudoguaianolide to furnish the characteristic peaks at *m/e* 95, 96, 122, 123, and 124 in the mass spectrum of this type of compounds. Thus these groups of peaks can be taken as one of the criteria for structural elucidation of a pseudoguaianolide of as yet unknown structure.

Experimental Section

All spectra were determined with an AEI MS 9 mass spectrometer operating at 70 eV and using a direct inlet system at about 210°. High resolution spectra were measured at a resolution of 10,000.

Helenalin-OD (10).—Helenalin was dissolved in methanol-OD, the solution was evaporated to dryness under nitrogen, and the dried solid was applied at once to the probe and introduced to the mass spectrometer.[11]

Trideuterioacetylhelenalin (11).—A mixture of 100 mg of helenalin, 0.6 ml of pyridine, and 0.6 ml hexadeuterioacetic anhydride was heated on the steam bath for 1 hr and allowed to stand at room temperature for 6 hr. Addition of ice water precipitated the acetyl derivative as a crystalline solid. It was filtered, washed with water, dried *in vacuo*, and crystallized from benzene–hexane giving 90 mg of colorless plates, mp 176–177°. The sample had the same ir and nmr spectra (except for changes introduced by deuteration) as authentic acetylhelenalin, mp 179.5–180.5°.[12]

Trideuterioacetyldesacetylisotenulin (12).—This substance was prepared from desacetylisotenulin and hexadeuterioacetic anhydride in the manner described in the previous section. It melted at 156–158° after recrystallization from benzene–hexane and had the same ir and nmr spectra (except for changes introduced by deuteration) as an authentic sample of isotenulin, mp 156–158°.[13]

Registry No.—1, 6754-13-8; 2, 10180-86-6; 3, 5945-41-5; 4, 5988-99-8; 5, 6895-47-2; 6, 3668-14-2; 7, 10092-04-3; 8, 19202-91-6; 9, 19202-92-7; 10, 19202-93-8; 11, 19202-94-9; 12, 19202-95-0.

(10) A. Romo de Vivar, L. Rodriguez-Hahn, J. Romo, M. V. Lakshmikantham, R. N. Mirrington, J. Kagan, and W. Herz, *Tetrahedron*, **22**, 3279 (1966).

(11) There was probably some back-exchange during this operation as indicated by the presence of weak *m/e* 262 and other peaks due to helenalin (see Figure 10).

(12) R. Adams and W. Herz, *J. Amer. Chem. Soc.*, **71**, 2546 (1949).

(13) B. H. Braun, W. Herz, and K. Rabindran, *ibid.*, **78**, 4423 (1956).