P_1 and P_0 Silicas. These were of the same grade and from the same supplier as the silicas called P_1H_1 and P_0H_1 in ref 1. Before use they were heated at 125 °C for 3-4 days and allowed to cool in a vacuum desiccator.

Adsorption of Indicators. The slurry evaporation method[1] was used. The indicator was applied in ether dried over 4-Å molecular sieves, except for 4-nitroaniline and 4-nitrophenol, which were applied with dry acetone. After removal of solvent on a rotary evaporator, the container was connected to a vacuum pump and pumped for 6 to 12 h to remove any remaining solvent.

The Reflectance Spectra. The instrument was a Cary Model 14 spectrophotometer equipped with an integrating sphere. The integrating sphere was freshly coated with successive layers of white primer, several water-soluble top coats, 15 sprayed coats of $BaSO_4$ suspended in water, and finally with 10 coats of MgO from a burning Mg ribbon.[24]

The silica samples with the adsorbed indicator were poured onto microscope slides previously sprayed with a clear polyurethane and allowed to dry for 4-5 min. The sample port of the integrating sphere was covered with clear plastic wrap to keep any loose silica from contaminating the sphere. The sample slide then was placed over the port and clamped in place with a block of $MgCO_3$. Another block of $MgCO_3$ was placed over the reference port. Each spectrum was scanned 3 times.

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Structures of the Ratibidanolides, Sesquiterpene Lactones with a New Carbon Skeleton, and Unusual Xanthanolides from *Ratibida columnifera*[1]

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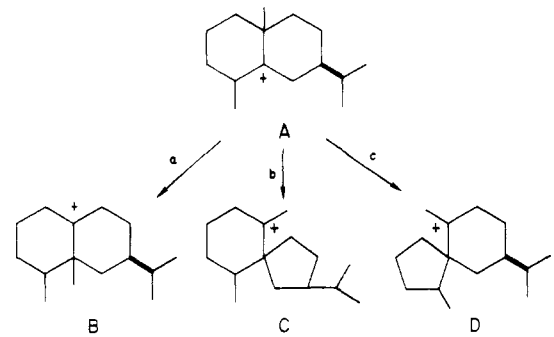
Structures and stereochemistry of two sesquiterpene lactones from *Ratibida columnifera* which possess a new rearranged eudesmane derived carbon skeleton were deduced by NMR spectroscopy and X-ray diffraction. The main lactone fraction of this plant consisted of a family of unusual xanthanolides whose structures were established in the same manner. Other constituents included the new nerolidol derivative (3*S**,5*R**)-(-)-5-hydroxy-9-oxonerolidol.

The eudesmane cation A and its epimers, or their biological equivalents, have been invoked[2-4] as progenitors of the eremophilane and spirovetivane classes of sequiterpenes, angular methyl migration (path a) leading to the eremophilanes and nootkatanes (B), and ring contraction of the six-membered ring bearing the isopropyl substituent leading to the hinesanes, solavetivanes, and agarospiranes (C). We now describe two representatives **1** and **5** of the previously unknown carbon skeleton D which results from the third possible rearrangement mode of A, namely ring contraction of the six-membered ring bearing the methyl substituent (path c). Lactones **1** and **5** were isolated from the common prairie coneflower *Ratibida columnifera* (Nutt.) Woot. & Standl.[5] together with isolantolactone (**8**), the elemadienolide **9**, a family of unusual xantholides **10a-f**, **11**, **12a,b**, and **14a-d**, the new nerol derivative **15a**, the thiophene acetylenes **17**[7] and **18**[7] and the flavone hispidulin (**19**).[8,9]

We discuss first the structure elucidation of **1** and **5**, members of the new class of ratibidanolides, which are based on what we propose to name the ratibidane carbon



skeleton. That the two compounds were α-methylene-α,β-unsaturated-γ-lactones and double bond isomers, with **1** possessing partial structure E (numbering as in final formula) and **5** the corresponding structure with an endocyclic double bond between C-9 and C-10, was clear from inspection of the ^1H NMR spectra (Table I) and spin decoupling experiments. By irradiating at the frequencies of the typical narrowly split doublets of H-13a,b near δ 6.25 and 5.65 the signal of H-7 was located at δ 3.04; this signal was split so as to indicate the presence of three vicinal protons. Two of these, H-6a and H-6b, constituted the AB part of an ABX system and hence represented two protons next to a quarternary center. The third, H-8 near δ 4.6 and hence the proton under the lactone oxygen, was in the case of **1** additionally coupled to two mutually coupled protons (H-9a,b) whose chemical shift indicated that they were allylic to a nonconjugated $=CH_2$ group made evident by the ^1H and ^{13}C NMR spectra (Table II). In the case of **5**, H-8 was additionally coupled to a vinylic proton which in turn was allylically coupled to the protons of a vinylic methyl group. Reaction of the α-methylene-α,β-unsaturated-γ-lactone function of **1** with diazomethane to give pyrazoline **2** and with 4-bromothiophenol to give adduct **3** produced the expected spectral changes as did ep-

(1) Initial work on this problem was supported in part by a grant from the U.S. Public Health Service (CA-13121) through the National Cancer Institute.

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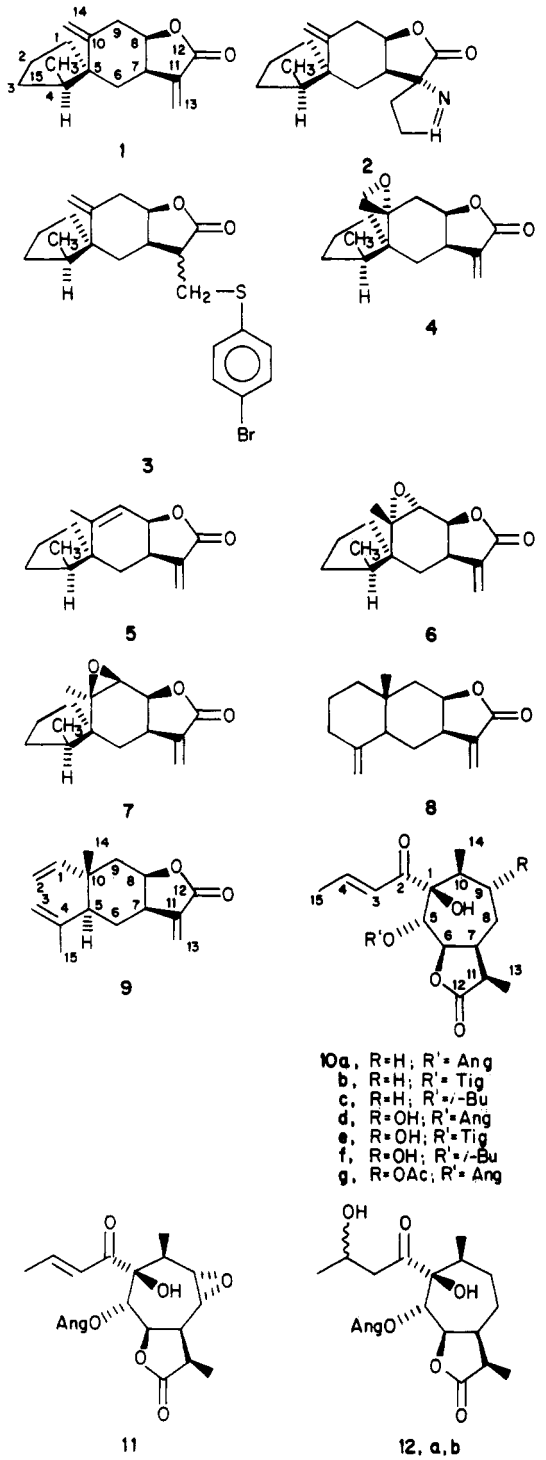
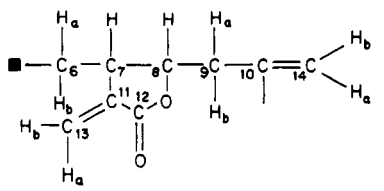
0022-3263/85/1950-0610$01.50/0

Chart I



oxidation of **1** which gave a single epoxide **4** and epoxidation of **5** which furnished a major epoxide **6** and a minor epoxide **7**.



E

^{13}C NMR spectroscopy (Table II) showed that the remaining six carbons and ten hydrogens of **1**, not yet in-

Table I. ^1H NMR Spectra of 1-7 ($CDCl_3$, 270 MHz)

	1	2	3	4	5	5[a]	6	7
H-2a,b	1.45-1.85 m, 1.97 m	1.4-1.85 m, 1.99 m	1.4-1.85 m, 1.97 m	1.1-1.9 m	1.45-1.95 m	1.45-1.95 m	1.3-2.25 m	1.4-2.1 m
H-3a,b								
H-4	1.97 t (13.5)	1.77 t (14)	1.58 t (13.5)		1.38 dd (13.5, 5)	0.91 dd		
H-6β	1.40 dd (13.5, 5)	1.13 dd (14, 3.5)	1.37 dd (13.5, 3.3)					
H-6α								
H-7	3.04 dddd (13.5, 7.5,[d] 5, 2.5, 2)	2.46 ddd (14, 6, 3.5)	2.50 m	3.22 dddd (13.5, 7, 5, 2.5, 2)	3.03 dddd (12.5, 6, 5, 1.5, 1.5)	2.40 dddd	3.22[d]	3.00 m
H-8	4.57 dt (10, 7.5)	5.31 dt (6, 8)	4.55 dt (6, 8)	4.82 dt (9.5, 7)	4.66 ddq (6, 5, 1)	4.13 ddq	4.97 dd (9.5, 2)	4.81 dd (8, 3.5)
H-9α	2.70 dd (12, 7.5)	2.89 dd (13, 8)	2.74 dd (13, 8)	2.06 dd (12, 7)	5.60[d]	5.37 dq (5, 1)	3.26 d (2)	3.03 d (3.5)
H-9β	2.26 dddd (12, 10, 1.8, 0.8)	2.38 ddbr (13, 8)	2.25 ddbr (13, 8)	1.1-1.9 m	-	-	-	-
H-13α	6.25 d (2.5)	2.07 ddd (13, 8, 4.5)	3.48 dd (12.5, 3)	6.27 d (2.5)	6.18 d (1.5)	6.15 dd (1.8, 0.5)	6.13 d (3.5)	6.21 d (2)
H-13β	5.62 d (2)	c	2.78 t (12.5)	5.65 d (2)	5.60 d (1.5)	5.03 dd (1.5, 0.5)	5.68 d (3)	5.55 d (2)
H-14	5.08 br, 4.77 t (0.8)	5.13 br, 4.79 br	5.05 br, 4.75 br	2.84 d (4), 2.67 d (4)	1.80 t (1)[b]	1.49 t[b]	1.36[b]	1.42[b]
H-15[b]	0.82 d (7)	0.88 d (6.5)	0.85 d (6.5)	0.96 d (7)	0.96 d (7)	0.72 d	0.94 d	1.14 d
misc		4.81 ddd[e] (18, 8, 4.5), 4.65 ddd[e] (18, 9.5, 8)	2.90 ddd[f] (12, 7.5, 3), 7.43,[g] 7.24[g]					

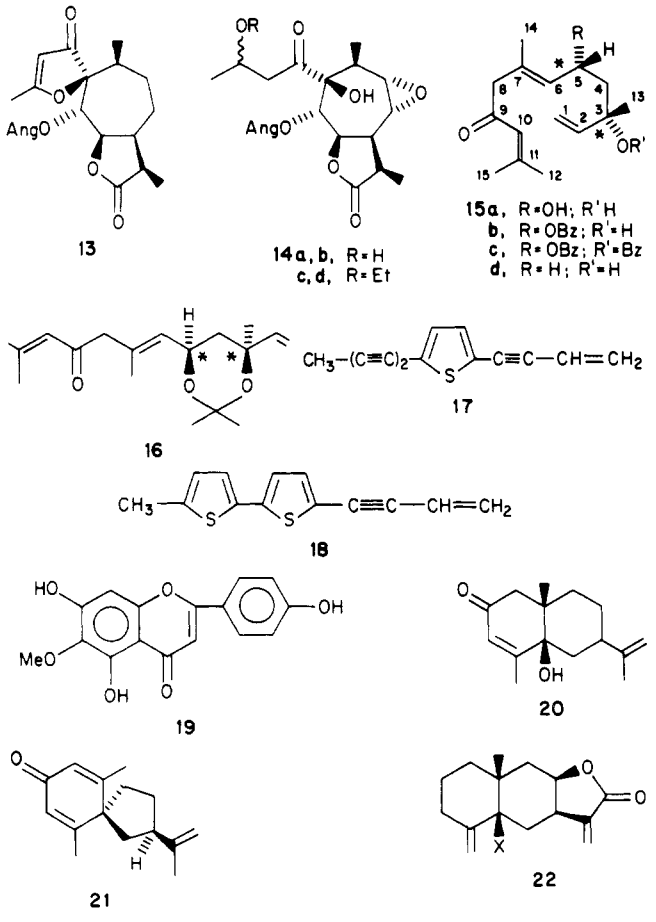
[a] In C_6D_6. [b] Intensity three protons. [c] Obscured, in region 1.4-1.85. [d] Obscured. [e] H-16. [f] H-11. [g] Aromatic protons.

Table II. ^{13}C NMR Spectra ($CDCl_3$, 67.89 MHz)

C	1	4	10a	10d	11	12a	12b	13a[a]	14c	14d
1	32.44 c[b]	31.96 t	84.35	86.70	84.43	85.07	85.05	93.47	84.44	84.32
2	22.41 t	22.27 t	201.73	199.21	201.00	216.67	216.80	204.20	213.60	212.56
3	33.91 t[b]	40.00 t	129.18 d	125.76 d	125.53 d	49.10 t	49.10 t	105.16	48.80 t	47.79 t
4	44.72 d	44.22 d	145.13 d	145.62 d	146.64 d	63.60 d	63.75 d	190.51	72.02 d	71.38 d
5	49.67	46.17	79.65 d[c]	79.17 d	80.55 d[c]	79.72 d	79.72 d	72.04	78.85 d	78.85 d
6	41.45 t[c]	34.12 t	79.56 d[c]	79.17 d	78.96 d[c]	79.15 d	79.06 d	77.78	78.60 d	78.60 d
7	37.15 d	37.17 d	38.61 d	33.47 d	42.64 d[c]	38.61 d	38.64 d	38.77	42.9 d	42.39 d
8	77.67 d	75.49 d	26.91 t	31.07 t	55.65 d	26.62 t	26.42 t	27.07	55.65 d	55.59 d
9	38.77 t[c]	35.11 t[c]	19.39 t	69.74 d	50.56 d	19.25 t	19.22 t	18.88	50.65 d	50.65 d
10	148.37	58.74	35.08 d[c]	41.36 d[c]	40.00 d[c]	35.47 d	35.52 d	34.30	39.62	39.62
11	139.41	139.03	37.65 d	37.81 d	37.98 d[c]	37.64 d	37.59 d	37.97	37.85 d	37.81 d
12	170.40	170.17	177.92	178.58	176.87	177.69	177.87	177.61	176.85	176.85
13	122.21 t	121.84 t	10.32 q[c]	9.89 q[c]	10.20 q	10.20 q	10.10 q	9.95	9.88 q	9.88 q
14	113.68 t	50.04 t	15.73 q[c]	12.53 q	12.23 q	16.05 q	16.03 q	14.67	16.01 q	16.01 q
15	14.79 q	15.92 q	18.52 q	18.52 q	18.70 q	22.47 q	22.56 q	16.48	19.69 q	19.26 q
1[1]			168.27	167.50	168.91	168.78	168.67	165.87	167.42	167.29
2[1]			126.84	126.67	126.58	126.52	126.51	126.89	126.60	125.68
3[1]			140.58 d	140.64 d	141.87 d	141.82 d	141.61 d	139.81	141.33 d	141.13 d
4[1]			15.88 q	15.83 q	16.02 q	15.84 q	15.83 q	15.79	15.35 q	15.35 q
5			20.21 q	20.06 q	20.17 q	20.31 q	20.30 q	20.27	20.32 q	20.32 q

[a] Quaternary carbon, CH, CH_2, and CH_3 were identified by DEPT sequence. [b] Assignments may be interchanged. [c] Assignments made by selective spin decoupling. [d] 63.91 t and 12.51 q, OEt. [e] 64.08 t and 12.51 q, OEt.

Chart II



corporated in E, consisted of a $CH–CH_3$ residue, three methylenes, and a quaternary carbon. The quaternary carbon was required to join C-6 and C-10, thus leaving formula 1 (exclusive of stereochemistry) or biogenetically implausible alternatives with the methyl group on C-2 or C-3. These were excluded by the results of NOE difference spectrometry which will be detailed in the sequel.

The magnitudes of $J_{7,13}$ in 1 and 5 and the derived epoxides 4, 6, and 7 indicated that we are dealing with cis- rather than trans-fused γ-lactones. On the other hand the values of $J_{8,9a}$ and $J_{8,9b}$ in 1–4 differed significantly from

Table III. NOE Difference Spectrum of 1

saturatn	obs NOE (%)
H-9α	H-9β (21), H-8 (8), H-14b (8.3)
H-9β	H-9α (22.8), H6β (2.9), H-15 (4)
H-14b	H-14a (13.5), H-9a (7.4)
H-15	H-9β (2), H-6β (2)

those commonly found in isoalantolactone derivatives. This observation could be rationalized by assuming that the cyclohexane ring was a boat rather than a chair, possibly to minimize interactions between C-14 and a β-orientated methyl group on C-1 or C-4. That this was so and that the methyl group was on C-4 and β-orientated was evidenced by the NOE experiments detailed in Table III; assignments of α- and β-configuration to the components of the H-6 and H-9 pairs is based on the magnitudes of the coupling constants to neighboring H-7 (in the case of H-6α,β) and H-8 (in the case of H-9α,β).

From the model it follows that 1 should furnish mainly or exclusively one epoxide as was observed and that this should be the α-epoxide 4. The paramagnetic shifts of H-7 (Δδ 0.18) and H-8 (Δδ 0.25) bear this out; the model also indicates that a somewhat smaller paramagnetic shift of H-15 (Δδ 0.14) can be attributed to its lying in the plane of the epoxide ring and to its rear. The major epoxide formed from 5 should be 6 and the minor epoxide 7; this is borne out by the paramagnetic shifts of H-7 and H-8 (Δδ 0.18 and 0.40) and the constancy of H-15 in 6 and by the constancy of H-7 and the paramagnetic shift of H-15 (Δδ 0.18) in 7 (see Table I).

To verify the conclusions drawn from NMR spectrometry an X-ray analysis of 4 was undertaken. Crystal data are listed in the Experimental Section. Figure 1 is a stereoscopic view of the molecule which shows that the stereochemistry depicted in formula 4 is correct. Tables IV–VIII listing final atomic and final anisotropic thermal parameters, bond lengths, bond angles, and selected torsion angles are available as supplementary material. The cyclohexane ring is indeed a somewhat distorted boat and the cyclopentane ring is a half-chair. For the lactone ring the sum of the internal torsion angles is 77°; it is best viewed as a half-chair with C-8 above and C-7 below the plane formed by C-11, C-12, and O-2. The sign of the O-3, C-12, C-11, C-13 torsion angle (ω_2 = −6.2°) is paired with the sign of the O-2, C-8, C-7, C-11 torsion angle (ω_3 = −22.9°)[10] and negative and corresponds to the sign of the

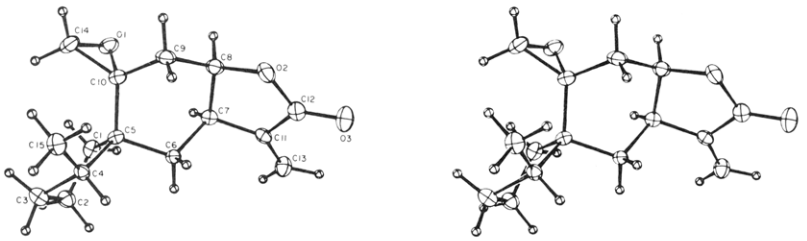


Figure 1. Stereoscopic view of **4** molecule with ellipsoids of thermal motion.

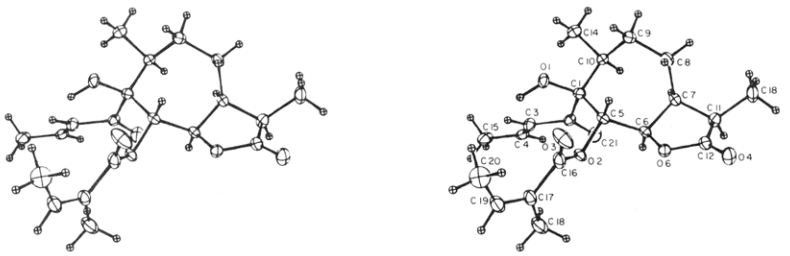
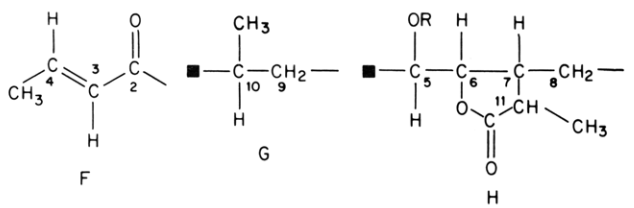


Figure 2. Streoscopic view of **10a** molecule with ellipsoids of thermal motion.

negative Cotton effect associated with the n,π*-transition of the γ-lactone which both **1** and **4** exhibit in solution.[11,12] This indicates that Figure 1 also corresponds to the absolute configuration of the molecule.

We now consider the structures of the various xantholides which as a group constitute the main secondary metabolites isolated from *R. columnifera*, with lactones **10a**, **10d**, and **11** as the dominant members. In lactones **10a–f** and **11**, the presence of partial structure F (numbering as in final formula) was evident from the IR, ^{1}H, and ^{13}C NMR spectra (Tables II and IX); further analysis of the NMR spectrum and spin decoupling also established the presence in **10a** of partial structures G and H, whose R is an angelyl residue. As the methylene group of G was different from the methylene group of H, the remaining carbon atom of **10a**, which was quaternary and which because of its chemical shift (δ 84.35) carried the hydroxyl group revealed by the IR spectrum, had to be attached to C-2, C-5, and C-10 of F, G, and H, thus leading to formula **10a**. In **10b**, which was only obtained admixed with **10a**, and in **10c** the angelate was replaced by a tiglate and by an isobutyrate ester.



As regards the stereochemistry, the significant paramagnetic shift of the H-5 signal ($\Delta\delta$ 0.82) on acylation of **10a** with trichloroacetyl isocyanate (TAI)[13] demonstrated that H-5 and the tertiary hydroxyl were cis; the only other shifts of note were experienced by H-10 ($\Delta\delta$ 0.4) and H-14 ($\Delta\delta$ 0.23), an observation which unfortunately shed no light on the stereochemistry at C-10. From the values of $J_{5,6}$ (9.5 Hz) and $J_{6,7}$ (6 Hz) it could be deduced that H-5 and H-6 were trans and H-6 and H-7 cis, respectively (model); likewise, from the magnitudes of $J_{7,11}$ (9 Hz) and $J_{9,10}$ (12 and 3 Hz) it was estimated that H-7 and H-11 were cis and the C-10 methyl group β in the absolute configuration depicted in the formula. These deductions were supported by the NOE difference spectrum of **10a** (Table X) which showed that the pairs H-7 and H-10, H-6 and H-7, and OH and H-5 were cis. No signal enhancement was noted between OH and H-6, H-7, or H-10, an observation which confirmed that the OH group was trans to these three protons.

To put these conclusions on a firm basis and to gain information on the conformations of xantholides in general, an X-ray analysis of **10a** was undertaken.[14] Crystal data are listed in the Experimental Section. Figure 2 is a stereoscopic view of the molecule which shows that the stereochemistry deduced for **10a** is correct. Tables XI–XIV with final atomic and final anisotropic thermal parameters, bond lengths, bond angles, and selected torsion angles are available as supplementary material. The cycloheptane ring is very close to a perfect boat ($\Sigma_s = 21°$)[10], with the C_s axis bisecting C-5 and the C-8, C-9 bond, and the lactone ring is close to a perfect envelope ($\Sigma |w| = 115°$) with C-7 as the flap. The conformation of **10a** in the solid state is probably not significantly different from that in solution, to judge from the coupling constants listed in Table IX which conform to those estimated from the figure, from the reaction with TAI which reveals a paramagnetic shift of H-3, and from the NOE difference spectrum (Table X) which shows that there exist significant interactions between H-3, on the one hand, and the hydroxyl proton and H-5 on the other.

The molecular formulas of **10d–f**, their ^{1}H NMR spectra, the ^{13}C NMR spectrum of **10d**, and the formation of acetate **10g** from **10d** revealed that these substances contained a secondary hydroxyl group on C-9 which because of the magnitudes of $J_{8,9}$ and $J_{9,10}$ must be α-orientated. The three compounds differed from each other in the nature of the ester residue on C-5; however, **10e** was only obtained in admixture with **10d**. Another major lactone constituent with an angelate ester function on C-5 was the 8,9-epoxide **11** (Tables II and IX); its reaction with TAI permitted observation of the coupling constants involving H-7, H-8, H-9, and H-10 which showed that the epoxide was cis and α.

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(14) For X-ray analyses of other xantholides see: (a) Parthemollin: Sundararaman, P.; McEwen, R. S. *J. Chem. Soc., Perkin Trans. 2* **1975**, 440. (b) Ivalbin: Herz, W.; Kumar, N.; Blount, J. F. *J. Org. Chem.* **1979**, *44*, 4437.

Table IX. ^{1}H NMR Spectra of 10a–g and 11 ($CDCl_3$, 270 MHz)

	10a	10a + TAI	10b[a]	10[c]	10[d]	10e[a]	10f	10g	11	11 + TAI
3	6.74 dq (15.5, 1.5)	6.93 dq	6.77 dq	6.74 dq	6.61 dq		6.60 dq	6.65 dq	6.76 dq	7.34 dq
4	7.03 dq (15.5, 7)	7.09 dq	7.03 dq	7.06 dq	7.05 dq		7.12 dq	7.08 dq	7.05 dq	7.11 dq
5	5.28 d (9.5)	6.10 d	5.28 d	5.18 d	5.31 d (10)	5.28 d	5.23 d	5.29 d	5.51 d (9.2)	6.23 d
6	4.93 dd (9.5, 6)	4.92 dd	4.93 dd	4.88 dd	4.90 dd (10, 7)		4.89 dd	4.98 dd	4.85 dd (9.2, 6.3)	4.65 dd
7	2.97 m	2.95 m	2.97 m	2.96 m	3.20 dddd (14, 10, 7, 2)		3.22 dddd	3.17 dddd	2.82 ddd (9, 7.5, 6.3)	2.83 ddd
8α	1.5–2.0 m		1.53–1.95 m	1.5–1.95 m	1.80 dt (16, 2)		1.81 dt	1.83 dt		
8β					2.12 m		2.13 m	2.14 ddd (16, 14, 5.5)	3.13[g]	3.19 dd (7.5, 4.5)
9α										
9β					3.90 ddd (10, 5.5, 2)		3.93 ddd	5.09 ddd (10, 5.5, 2)	3.10[g]	3.59 dd (8, 4.5)
10	2.33 ddq (12, 3, 6.5)	2.73 ddq	2.36 ddq	2.31 ddq	2.12 m		2.13 m	2.41 dq (10, 7)	2.00 dq (8.5, 6.5)	2.44 dq (8, 7)
11	2.90 dq (9.7)	2.95 m	2.92 dq	2.89 dq	2.91 dq (10, 7.5)		2.94 dq	2.94 dq	3.05 dq (9, 7)	3.06 dq
13[b]	1.18 d (7)	1.19 d	1.18 d	1.18 d	1.22 d		1.25 d	1.22 d	1.44 d (7)	1.45 d
14[b]	0.80 d (6.5)	1.03 d	0.81 d	0.78 d	0.89 d		0.91 d	0.82 d	1.09 d (6.5)	1.14 d
15[b]	1.92 dd (7, 1.5)	1.96 dd	1.92 dd	1.94 dd	1.91 dd		1.97 dd	1.93 dd	1.92 dd	2.00 dd
3′	6.13 qq (7, 1.5)	6.13 qq	6.82 qbr (7)	1.13 d[b] (7)	6.08 qq (7, 1.5)	6.75 qbr	1.11 d (7)	6.12 qq (7, 1.5)	6.17 qq	6.11 qq
4′[b]	1.96 dq (7, 1.5)	1.94 dq	1.78 dbr (7)	1.09 d (7)	1.91 dq	1.76 dbr	1.07 d (7)	1.94 dbr	1.95 dq	1.89 dq
5′[b]	1.79 quint	1.80 quint	1.76 br	2.52 sept[e] (7)	1.72 quint (1.5)	1.74 br	2.48 sept[e] (7)	1.76 quint (1.5)	1.79 quint	1.76 quint
misc	4.20[c]	8.46[d]	4.26[c]	4.07[c]	4.46[c]	4.48[c]	4.42[c]	4.53[c] 2.06[f]	4.44[c]	8.68[d]

[a] Shifts obtained from mixture, signals not listed are the same as in the preceding column. [b] Intensity three protons. [c] OH. [d] NH. [e] H-2′. [f] Ac. [g] Overlapping AB part of ABXY system.

Scheme I

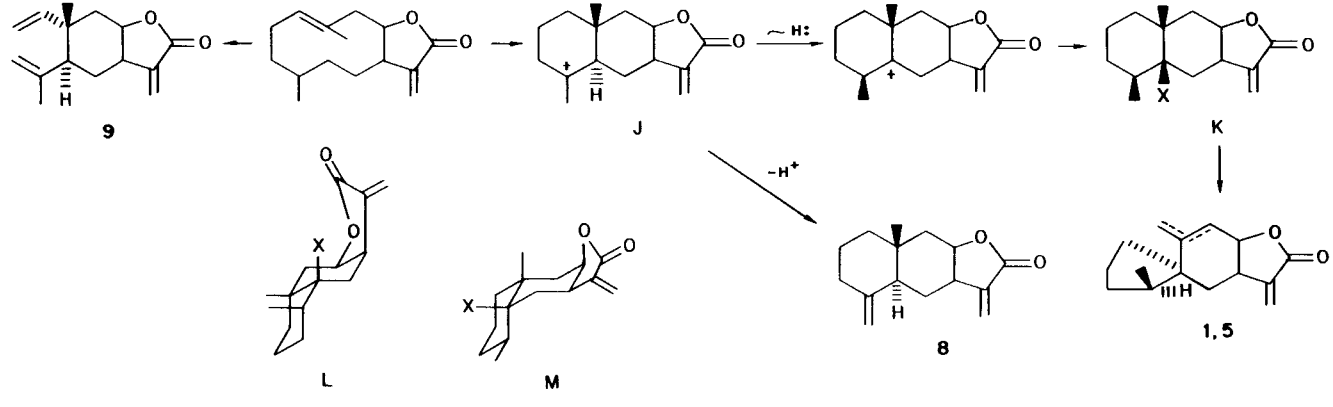
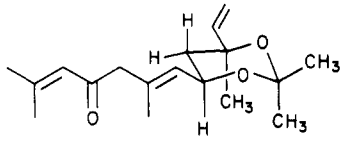


Table X. NOE Difference Spectrum of 10a

saturatn	obsd NOE (%)
H-5	OH (13)
H-6	H-7 (11), H-3 (6.1)
OH	H-5 (12.7), H-3 (4.9)
H-10	H-7 (15)

Lactones **12a** and **12b** were C-4 epimeric β-hydroxy ketones formally derived from **10a** (Tables II and XVI); an attempt to use Horeau's method for distinguishing between the two epimers resulted in dehydration to **10a**. Oxidation of a mixture of **12a,b** with Jones reagent gave the spiro lactone **13**. The corresponding 8,9α-epoxides **14a** and **14b** were also found as was an inseparable mixture of ethers **14c** and **14d**. The latter may be artefacts.

The structure of the nerolidol derivative **15a** ($[\alpha]_D$ −39°) was established by analysis of its ^1H and ^{13}C NMR spectrum, the NMR spectra of its monobenzoate and dibenzoate **15b** ($[\alpha]_D$ −23° and **15c** $[\alpha]_D$ +29°) (Table XVII), and comparison with the ^{13}C NMR spectrum of (*S*)-(+)-9-oxonerolidol (**15d**).[15] The relative configuration was deduced from the ^1H NMR spectrum of the derived acetonide **16**. On the reasonable assumption that the 1,3-dioxolan ring is in the chair conformation, the values of $J_{4a,5}$ and $J_{4b,5}$ indicated that H-5 was axial. The NOE difference spectrum of **16** showed no interaction between H-5 and H-1a,b or H-2; consequently, the stereochemistry of **16** is represented by I or its mirror image and the parent substance is (3*S**,5*R**)-(−)-5-hydroxy-9-oxonerolidol.[16] The absolute configuration remains uncertain as the influence of the additional asymmetric center at C-5 on the specific rotation of (*S*)-(+)-nerolidol cannot be assessed. However, a (−)-5-acetoxy-9-oxonerolidol of unspecified configuration isolated earlier from *Anthemis austriaca*[17] is probably related to **15a** configurationally and is therefore **15d**.



I

We conclude with a comment on the biogenesis of the ratibidanolides. The co-occurrence of **1**, **5**, **8**, and **9**, all at the same oxidation level, suggests a biogenetic pathway from a single germacradienolide precursor or its equivalent (Scheme I). Cope rearrangement gives **9** while H^+ cyclization produces eudesmane cation J which can eliminate to give **8**. However the stereochemistry of the ratibidanolides cannot be rationalized by a fully concerted sequence of all trans-antiparallel hydride and methylene shifts from J. As the ions involved are tertiary, conformational relaxation and rearrangement without rigid antiperplanar alignments may occur. Alternatively an intermediate stage, conceivably a decalin of type K (X = leaving group or enzyme) in the nonsteroid-like conformation L, may intervene. Compounds of type K are known. While β-rotunol (**20**) appears to possess the steroid-like conformation M as evidenced by its facile conversion to **21**,[19] recent work on *cis*-decalin-type eudesmanolides **22** from *Artemisia umbelliformis*[20] which are closely related to the compounds under consideration here indicates that whether conformation L or M is preferred depends on the nature of X.

Experimental Section

Isolation of *R. columnifera* Constituents. Above ground parts of dried *Ratibida columnifera* (Nutt.) Woot. & Standl., collected by D. Gage and J. Gershenzon on May 3, 1981 inside the Austin City limits, Travis Co., Texas (voucher on deposit in the University of Texas herbarium) wt. 15.3 kg, were extracted with $CHCl_3$ and worked up in the usual fashion.[21] Half (95 g) of the crude gum was absorbed on 150 g of silicic acid (Mallinckrodt, 100 mesh) and chromatographed over 1.2 kg of the same absorbent packed in hexane, 500-mL fractions being collected as follows. Fraction 1–4 (hexane), 5–12 (hexane–EtOAc, 19:1), 13–20 (hexane–EtOAc, 9:1), 21–28 (hexane–EtOAc, 4:1), 29–36 (hexane–EtOAc, 3:2), 37–44 (hexane–EtOAc, 1:1), 45–52 (hexane–EtOAc, 2:3), 53–60 (hexane–EtOAc, 1:4), 61–64 (EtOAc), 65–68 (EtOAc–MeOH 19:1), 69–72 (EtOAc–MeOH, 9:1).

Fraction 4 which showed mainly one spot on TLC (hexane–EtOAc, 39:1) gave on purification by preparative TLC a 4:1 mixture of the acetylenes **17** (M^+, 196)[6] and **18** (M^+, 230)[6] in 0.1-g yield. Fraction 9 when filtered through Al_2O_3 gave slightly impure (by ^1H NMR criteria) gummy lactone **1** (2.2 g). Similar treatment of fraction 10 gave 2.8 g of **1**. Preparative TLC (benzene–EtOAc, 39:1) afforded spectroscopically pure **1** which could not be induced to crystallize. Fractions 12 and 13 were combined (2.1 g); purification by TLC (benzene–EtOAc, 39:1) gave a fraction whose NMR spectrum showed it to be a lactone mixture. Separation of this fraction by HPLC (4% EtOAc in hexane) afforded only one substance **9** in reasonably pure form (12 mg). Column chromatography of fractions rich in one compound from the HPLC experiment furnished 17 mg of **5** and 24 mg of **8** contaminated by **5**, ^1H NMR spectrum of **8** δ 6.13 and 5.59 (each d, J = 1.5 Hz, H-13a,b), 4.77 and 4.44 (each q, J = 1.5 Hz, 15a,b), 4.50 (dt, J = 2.5 Hz, H-8), 2.99 (dddbr, J = 14, 2, 2, 1.5, H-3a), 2.20 (dd, J = 16.2 Hz, H-9a), 2.0 (m, H-3b), 0.83 (3 H, H-14).

Fraction 15 on standing deposited 0.145 g of a mixture of β-sitosterol and stigmasterol. Trituration of fractions 23 and 24 with hexane–EtOAc gave 1.89 g of **10a**. Fractions 25–28 and the mother liquor from fraction 24 were combined and rechromatographed over silica gel ($CHCl_3$–MeOH, 99:1) to give in fractions 5–9 an inseparable mixture of **10a** and **10b** (1.5 g), in fractions 10, 11 a mixture of **10a–c**, and in fractions 12–16 a mixture of **10b** and **10c** (0.4 g). Fraction 17 after purification by preparative TLC ($CHCl_3$–MeOH–EtOAc, 18:1:1) afforded reasonably pure (85%) **10c** (18 mg). Fractions 20–24 afforded 1.3 g of **11**. The last fractions of the rechromatogram, fractions 27–29, afforded an inseparable mixture of epimers **14c** and **14d** (0.7 g).

Fractions 30–32 of the original chromatogram were combined and rechromatographed over silica gel ($CHCl_3$–MeOH, 99:1). The only substance isolated was **15a** (0.3 g) which could not be induced to crystallize. Fractions 34 and 35 on standing deposited 0.30 g of hispidulin (**19**) which was identified by comparison with authentic material. The mother liquors were combined with fraction 36 and rechromatographed over silica gel to yield from fractions 2 and 3 of the rechromatogram 0.35 of **12a** which could not be induced to crystallize. Fractions 5 and 6 were mainly **12b**; rechromatography afforded 0.26 g of gummy **12b**. Fraction 8 gave after repurification by TLC ($CHCl_3$–MeOH–EtOAc, 8:1:1) 20 mg of **14a**. Fractions 9–11 afforded 0.27 g of a **14a,b** mixture.

Fractions 43–45 of the original chromatogram contained mainly one lactone component. Rechromatography (silica gel, $CHCl_3$–MeOH 49:1) afforded 4.6 g of **10d**, 0.21 g of a mixture of **10d**, **10e**, and **10f**, 0.14 g of a mixture of **10e** and **10f**, and a small amount (15 mg) of **10f**. Fractions 41 and 42 (9.3 g) were also mainly **10d**.

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(16) Proximity of the methyl singlet in the NMR spectrum of **16**, regardless of solvent, interfered with unequivocal determination of the NOE's involving H-5 and the methyl singlet although it appears that two of them interacted with H-5 as demanded by I. There was also an NOE involving H-5 and H-14, but not H-6 which indicated that in I the conformation of the α,β-unsaturated ketone side chain is approximately as in the solid state.

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(18) Hikino, H.; Aota, K.; Kuwano, D.; Takemoto, T. *Tetrahedron* **1971**, *27*, 4881.

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(21) Bohlmann, F.; Dutta, L. *Phytochemistry* **1979**, *8*, 1228.

Table XVI. ^{1}H NMR Spectra of 12a,b, 13, and 14a–d

H	12a	12b	13	14a	14b	14c[a]	14d[a]
3a	2.86 dd (19, 3)	2.76 dd (18.5, 4.5)	5.44 br	2.85 dd (19, 3)	2.83 dd (18, 8.5)	3.18 dd (15.5, 8)	2.89 dd (15.5, 5)
3b	2.56 dd (19,9)	2.68 dd (18.5, 1.5)		2.58 dd (19, 9)	2.62 dd (18, 3)	2.36 dd (15.5, 4.5)	2.65 dd (15.5, 6)
4	4.20 ddq (9, 3, 7)	4.16[d]		4.20 ddq (9, 3, 7)	4.17 m	3.79 ddq (8, 4.5, 6.5)	3.89 ddq (6, 5, 6.5)
5	5.25 d (10)	5.26 d	5.72 d (9.5)	5.46 d	5.47 d	5.57 d	5.57 d
6	4.89 dd (10, 6)	4.84 dd	4.97 dd (9.5, 6)	4.97 dd (10, 6)	4.78 dd	4.67 dd (10, 7)	4.74 dd
7	2.95 m	2.88 m	3.05 m	2.76 m	2.75 m	2.78 dt (9, 7)	2.78 dt
8	1.45–1.80 m	1.45–1.75 m	1.5–2.0 m	3.10[e]	3.10[e]	3.12[e]	3.12[e]
9							
10	2.29 ddq (12, 3, 6.5)	2.31 ddq	2.29 ddq (11.5, 2.5, 7)	1.95[d]	1.95[d]	2.04 m	2.04 m
11	2.95 m	3.01 m	2.94 dq (9, 7.5)	3.03 dq	3.02 dq	3.01 dq	3.02 dq
13[b]	1.16 d (7)	1.15 d	1.16 d	1.45 d	1.44 d	1.44 d	1.45 d
14[b]	0.83 d (6.5)	0.83 d	0.89 d	1.13 d	1.13 d	1.10 d	1.10 d
15[b]	1.19 d (7)	1.19 d	2.16 br	1.21 d (7)	1.21 d	1.20 d	1.18 d
3′	6.21 qq (7, 1.5)	6.21 qq	6.09 qq	6.26 qq	6.25 qq	6.19 qq	6.19 qq
4′[b]	1.99 dq (7, 1.5)	1.98 dq	1.95 dq	2.00 dq	2.00 dq	2.00 dq	2.00 dq
5′[b]	1.86 quint (1.5)	1.84 quint	1.79 quint	1.87 quint	1.85 quint	1.86 quint	1.86 quint
misc	4.27[c]	4.19[c]		4.60[c]	4.49[c]	4.96,[c] *f*	4.93,[c] *f*

[a] Chemical shifts obtained from mixture. [b] Intensity three protons. [c] OH. [d] Partially obscured. [e] Center of A_2B_2 system. [f] 3.59 dq (9, 7) and 3.35 dq (9, 7) OCH_2CH_3; 1.18 t (7) CH_2CH_3.

Table XVII. ^{1}H NMR Spectra of 15a–c and 16 ($CDCl_3$, 270 MHz)

H	15a	15b	15c	16
1a	5.03 dd (11, 1.5)	5.04 dd	5.18 dd	4.99 dd
1b	5.25 (dd (17, 1.5)	5.34 dd	5.32 dd	5.17 dd
2	5.95 dd (17, 11)	6.01 dd	6.13 dd	5.92 dd
4a	1.85 dd (14.5, 9.5)	2.19 dd (14, 6)	2.65 dd (14, 7.5)	1.70 dd (14, 11)
4b	1.62 dd (14.5, 4)	2.06 dd (14, 7.5)	2.47 dd (14, 4.5)	1.57 dd (14, 3)
5	4.78 dt (4, 9.5)	5.90 ddd (9.5, 7.5, 6)	6.02[d]	4.77 ddd (11, 8, 3)
6	5.32 dq (9.5, 1.5)	5.39 dq	5.37 d	5.30 dq (8, 1.5)
8a	3.09 br[b]	3.11 br[b]	2.96 d (15)	3.10 br[b]
8b			2.84 d (15)	
10	6.10 qq (1.5, 1.5)	6.07 qq	6.01 qq	6.11 qq
12a	2.14 d (1.5)	2.15 d	2.09 d	2.15 d
13a	1.89 d (1.5)	1.86 d	1.78 d	1.89 d
14a	1.39	1.32	1.76	1.53 or 1.43
15a	1.68 d (1.5)	1.78 d	1.78 d	1.74 d
misc		8.00,[b,c] 7.55,[c] 7.43[b,c]	7.94,[c,c] 7.45,[b,c] 7.33[c,e]	1.53[f] or 1.53[a] and 1.43[a]

[a] Intensity three protons. [b] Intensity two protons. [c,D] Benzoate protons. [e] Intensity four protons. [f] Intensity six protons.

Properties of (4*S*,5*S*,7*R*,8*R*)-Ratibida-10(14),11(13)-dien-8,12-olide (1). 1 was a gum which could not be induced to crystallize: CD curve (MeOH) $[\theta]_{257}$ −5110, $[\theta]_{242}$ 0, $[\theta]_{220}$ +25 200 (last reading); IR ($CHCl_3$) 1750, 1650, 1635 cm^{-1}; ^{1}H and ^{13}C NMR spectra in Tables I and II; M_r calcd for $C_{15}H_{20}O_2$, 232.1464, found (MS), 232.1447 (relative intensity 3.6). Other significant peaks in the high-resolution MS were at m/z (composition, relative intensity) 217 ($C_{14}H_{17}O_2$, 7.2), 176 ($C_{11}H_{12}O_2$, 3), 147 ($C_{10}H_{11}O$, 8.9), 131 ($C_{10}H_{11}$, 13), 121 C_9H_{13}, 10), 107 (C_8H_{11}, 20.5), 91 (C_7H_7, 18).

Reaction of 50 mg of 1 in ether with excess CH_2N_2 for 20 min at room temperature followed by removal of the solvent gave 52 mg of noncrystalline pyrazoline **2** whose ^{1}H NMR spectrum is listed in Table I. The low-resolution MS did not exhibit the molecular ion, but a relatively sharp peak at m/z 246 ($M^+ - N_2$, relative intensity 46.2).

A solution of 50 mg of 1 and 150 mg of 4-bromothiophenol in 2 mL of benzene and a few drops of piperidine was stirred for 30 min. Removal of solvent and purification of the residue by TLC (benzene–EtOAc, 39:1) gave 45 mg of **3**, mp 89–90 °C (hexane–EtOAc) whose ^{1}H NMR spectrum is listed in Table I; MS, m/z (relative intensity) 422 and 420 (M^+, 22.9 and 21.5).

Epoxidation of 0.200 g of 1 in 10 mL of $CHCl_3$ with 0.500 g of *m*-chloropenbenzoic acid at room temperature overnight, dilution with 150 mL of EtOAc, washing with 5% $NaHSO_3$, 5% $NaHCO_3$, and H_2O, and evaporation of the organic layer followed by crystallization from hexane–EtOAc gave 0.185 g of **4**: mp 112–115 °C; CD curve (MeOH) $[\theta]_{255}$ −3255, $[\theta]_{239}$ 0, $[\theta]_{212}$ +44 600 (last reading); IR (KBr) 1760, 1660 cm^{-1}; ^{1}H and ^{13}C NMR spectra in Tables I and II; M_r calcd for $C_{15}H_{20}O_3$, 248.1412, found (MS, peak matching), 248.1410. Significant peaks in the high-resolution MS were at m/z (composition, relative intensity) 218 ($C_{14}H_{18}O_2$, 9.9), 207 ($C_{12}H_{15}O_3$, 3.3) 193 ($C_{11}H_{13}O_3$, 11.8), 133 ($C_{10}H_{13}$), 107 (C_8H_{11}, 63), 91 (C_7H_7, 78.5), 81 (C_6H_9, 85.6).

Properties of (4*S*,5*S*,7*R*,8*R*)-Ratibida-9,11(13)-dien-8,12-olide (5). The substance could not be induced to crystallize: CD curve (MeOH) $[\theta]_{253}$ −4510, $[\theta]_{236}$ 0, $[\theta]_{215}$ +30 900 (last reading); IR ($CHCl_3$) 1750, 1635 br cm^{-1}; ^{1}H NMR spectrum in Table I; M_r calcd for $C_{15}H_{20}O_2$, 232.1464, found (MS), 232.1465 (relative intensity 7.1). Other significant peaks in the high-resolution MS were at m/z (composition, relative intensity) 217 ($C_{14}H_{17}O_2$, 9.2), 176 ($C_{11}H_{12}O_2$, 25.9), 148 ($C_{10}H_{12}O$, 5.8), 136 ($C_8H_8O_2$), 91 (C_7H_7, 24).

Reaction of 0.120 g of a fraction rich in **5** with 0.400 g of *m*-chloroperbenzoic acid as detailed for 1 and separation of the epoxide mixture by TLC (benzene–EtOAc, 19:1) gave 35 mg of pure **6** and 12 mg of slightly contaminated **7**. Epoxide **6** melted at 118–120 °C (hexane–EtOAc), CD curve (MeOH) $[\theta]_{219}$ +45 000 (last reading); IR (KBr) 1755, 1640 cm^{-1}; ^{1}H NMR spectrum in Table I; M_r calcd for $C_{15}H_{20}O_3$, 248.1412, found (MS, peak matching), 248.1410. Other significant peaks in the low-resolution MS were at m/z (relative intensity) 233 (6.1), 219 (1.9), 189 (2.6), 188 (2.6), 161 (7), 159 (2.2), 147 (2.5), 135 (4.4), 123 (96.9), 109 (24), 97 (28.7), 95 (23.9), 91 (22.1), 81 (100), 77 (44.7). Isomer **7** could not be induced to crystallize; ^{1}H NMR spectrum in Table I; M_r calcd for $C_{15}H_{20}O_{31}$, 248.1412, found (MS), 248.1434 (relative intensity 2.1). Other significant peaks in the high-resolution MS were at m/z (composition, relative intensity) 233 ($C_{14}H_{17}O_3$, 100), 220 ($C_{14}H_{20}O_2$, 17), 219 ($C_{14}H_{19}O_2$, 18.3), 195 ($C_{11}H_{15}O_3$, 19.5), 147 ($C_{11}H_{15}$, 22.7), 133 ($C_{11}H_{13}$), 123 (C_9H_{15}, 42.4), 119 (C_9H_{11}, 10.3).

(5*R*,7*R*,8*R*,10*S*)-Elema-1,3,11(13)-trien-8,12-olide (9). This substance was a gum: IR ($CHCl_3$) 1752, 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) 5.82 (dd, J = 17.5, 10.5 Hz, H-1), 4.98 (dd, J = 10.5, 1 Hz, H-2a), 4.97 (dd, J = 17.51 Hz, H-2b), 4.86 (quint, J = 1.5 Hz, H-3a), 4.61 (br, H-3b), 2.05 (dd, J = 12.5, 3 Hz, H-5), 1.72 (m, H-6a,b), 3.04 (ddddd, J = 11, 7, 6, 2, 1.5 Hz, H-7), 4.58 (ddd, J = 6, 5, 4.5 Hz, H-8), 1.90 (dd, J = 14, 5 Hz, H 9a), 1.78 (dd, J = 14, 4.5, H-9b), 6.18 (d, J = 2 Hz, H-13a), 5.58 (d, J = 1.5 Hz, H-13b), 1.04 (H-14), 1.71 (br, H-15); ^{1}H NMR (C_6D_6) 5.55 (dd, H-1), 4.84 (dd, H-2a), 4.79 (dd, H-2b), 4.79 (quint, H-3a), 4.47 (br, H-3b), 1.2–1.7 (c, H-5, H-6a,b, H-9a,b), 2.18 (ddddd, H-7), 3.92 (q, J = 5 Hz, H-8), 6.08 (d, H-13a), 4.97 (d, H-13b), 0.89 (H-14), 1.54 (br, H-15); M_r calcd for $C_{15}H_{20}O_2$, 232.1464, found (MS), 232.1490 (relative intensity 1.2). Other significant peaks in the high-resolution MS were at m/z (composition, relative intensity) 217 ($C_{14}H_{17}O_2$, 2.1), 190 ($C_{12}H_{14}O_2$, 2.6), 176 ($C_{11}H_{12}O_2$, 1.5), 161 ($C_{11}H_{13}O$, 0.3), 145 ($C_{11}H_{13}$, 4.9), 121 (C_8H_9O, 2.6), 107 (C_8H_{11}, 11.5), 91 (C_7H_7, 50). The substance appears to be identical

with an impure elemadienolide isolated earlier from *Liatris platylepis*.[21]

(1*S*,5*S*,6*R*,7*S*,10*S*,11*R*)-1-Hydroxy-2-oxo-5-(acyloxy)-xanth-3-en-6,12-olides (10a–c). Lactone **10a** was crystalline: mp 102–102.5 °C (colorless rods, hexane–EtOAc); CD curve (MeOH) $[\theta]_{340}$ +840, $[\theta]_{302}$ 0, $[\theta]_{270}$, −180 (sh), $[\theta]_{218}$ −21 600 (last reading); IR (KBr) 3480, 1762, 1725, 1682, 1640, 1620 cm^{-1}; ^{1}H and ^{13}C NMR spectra in Tables IX and II; M_r calcd for $C_{20}H_{28}O_6$, 364.1885, found (MS), 364.1877 (relative intensity 0.3). Other significant peaks were at m/z (composition, relative intensity) 295 ($C_{16}H_{23}O_5$, 6.6) and 83 (C_5H_7O, 100). Lactone **10b** was only obtained in admixture with **10a**; its ^{1}H NMR spectrum is listed in Table IX. Lactone **10c** was obtained only in approximately 85% purity; its ^{1}H NMR spectrum is listed in Table IX.

(1*S*,5*S*,6*R*,7*S*,9*R*,10*S*,11*R*)-1,9-Dihydroxy-2-oxo-5-(acyloxy)xanth-3-en-6,12-olides (10d–f). Lactone **10d** was a gum: CD curve (MeOH) $[\theta]_{343}$ +408, $[\theta]_{312}$ 0, $[\theta]_{284}$ −544 (sh), $[\theta]_{220}$ −18 100 (last reading); IR ($CHCl_3$) 3420, 1765, 1720, 1685, 1620 cm^{-1}; ^{1}H and ^{13}C NMR spectra in Tables IX and II; M_r calcd for $C_{20}H_{28}O_7$, 380.1835, found (MS), 380.1855 (relative intensity 0.1). Other significant peaks in the high-resolution MS were at m/z (composition, relative intensity) 311 ($C_{16}H_{23}O_6$, 2.7), 211 ($C_{11}H_{15}O_4$, O_4), 83 (C_5H_7O, 100). Acetylation (acetic anhydride–pyridine) and workup in the usual manner gave a gummy acetate **10g** whose ^{1}H NMR spectrum is listed in Table IX. Lactone **10e** was obtained only in admixture with **10d**; its ^{1}H NMR spectrum is listed in Table IX. Lactone **10f** was also a gum; ^{1}H NMR spectrum in Table IX; MS (low resolution), m/z (relative intensity) 369 (M + 1, 7.9), 311 (0.8), 299 (28.9), 211 (17.6), 193 (11.4), 71 (100), 69 (42.7).

(1*S*,5*S*,6*R*,7*R*,8*R*,9*S*,10*S*,11*R*)-8,9-Epoxy-1-hydroxy-2-oxo-5-angeloxyxanth-3-en-6,12-olide (11). This substance was recrystallized from hexane–EtOAc, mp 135–137 °C; CD curve (MeOH) $[\theta]_{365}$ +121, $[\theta]_{347}$ 0, $[\theta]_{311}$ −424, $[\theta]_{217}$ −22 900 (last reading); IR (KBr) 3380, 1755, 1730, 1670, 1615 cm^{-1}; ^{1}H and ^{13}C NMR spectra in Tables IX and II; M_r calcd for $C_{20}H_{26}O_7$, 378.1676, found (MS, peak matching), 378.1673. Other significant peaks in the low-resolution MS were at m/z (relative intensity) 309 (32.5), 209 (1), 83 (100), 69 (47.7), 55 (74.5).

(1*S*,4*R*,5*S*,6*R*,7*S*,10*S*,11*R*)-1,4-Dihydroxy-2-oxo-5-angeloxyxanthan-6,12-olide and Its 4(*S*)-Epimer (12a,b). Lactones **12a** and **12b** could not be induced to crystallize: CD curve of **12a** (MeOH) $[\theta]_{296}$ +1800, $[\theta]_{260}$ +407 (min), $[\theta]_{244}$ +1800, $[\theta]_{244}$ +1800, $[\theta]_{216}$ −17 450 (last reading); IR ($CHCl_3$) 3440, 1765, 1700 cm^{-1}, ^{1}H and ^{13}C NMR spectra in Tables XVI and II; M_r calcd for $C_{20}H_{30}O_7$, 382.1989, found (MS, peak matching), 382.1990. Significant peaks in the low-resolution MS were at m/z (relative intensity) 383 (M + 1, 4.3), 365 (32.7), 295 (54.5), 283 (3.7), 195 (4.6), 83 (100), 69 (16.4), 55 (86.3). CD curve of **12b** (MeOH) $[\theta]_{294}$ +1620, $[\theta]_{265}$ +579 (min), $[\theta]_{243}$ +2007, $[\theta]_{235}$ 0, $[\theta]_{215}$ −13 100 (last reading), IR ($CHCl_3$) 3440, 1765, 1700 cm^{-1}; ^{1}H and ^{13}C NMR spectra in Tables XVI and II; M_r calcd for $C_{20}H_{30}O_7$, 382.1989, found (MS, peak matching), 382.1990. Significant ions in the low-resolution MS were at m/z (relative intensity) 383 (M + 1, 4.3), 365 (32.7), 295 (54.5), 283 (3.7), 195 (4.6), 83 (100), 69 (16.4), 55 (83.6).

A solution of 0.1 g of a mixture (approximately 1:1) of **12a** and **12b** in 10 mL of acetone was stirred with 0.2 mL of Jones reagent at 0 °C. The usual workup followed by preparative TLC (CHCl–MeOH–EtOAc, 18:1:1) afforded 24 mg of **13**, mp 166–167 °C (hexane–EtOAc); IR (KBr) 1767, 1710, 1692 and 1602 cm^{-1}; ^{1}H NMR and ^{13}C NMR spectra in Tables XVI and II; M_r calcd for $C_{20}H_{26}O_6$, 362.1729, found (MS), 362.1720 (relative intensity 2.3). Other significant peaks in the high-resolution MS were at m/z (composition relative intensity) 262 ($C_{15}H_{18}O_4$, 8.8), 247 ($C_{14}H_{15}O_4$, 3.9), 83 (C_5H_7O, 100).

(1*S*,4*R*,5*S*,6*R*,7*R*,8*R*,9*S*,10*S*,11*R*)-8,9-Epoxy-1-hydroxy-(and 1-ethoxy)-2-oxo-5-angeloxyxanthan-6,12-olides and Their 4(*S*)-Epimers (14a–d). Lactone **14a** was a gum: CD curve (MeOH) $[\theta]_{282}$ −1005, $[\theta]_{265}$ 0, $[\theta]_{245}$ +3116, $[\theta]_{235}$ 0, $[\theta]_{213}$ −18 100 (last reading); IR (KBr) 3440, 1755, 1735, 1715 cm^{-1}; ^{1}H NMR spectrum in Table XVI. The low-resolution MS exhibited a very weak M + 1 ion at m/z 397 (relative intensity 0.01) and further ions at m/z 309 (15.8), 297 (2.7), 209 (0.5), 83 (100), 69 (6.5), 55 (51.8). The positive CI MS exhibited ions at m/z 397 (M + H$^+$, 7.4), 379 (28.7), 309 (3.4), 297 (100), 83 (38.7). Lactone **14b** was only obtained in admixture with **14a**: the ^{1}H NMR spectrum is listed in Table XVI. Lactones **14c,d** were an inseparable mixture (approximately 1:1) whose ^{1}H NMR and ^{13}C NMR spectra are listed in Tables XVI and II. The low-resolution MS did not exhibit the molecular ions, but had significant peaks at m/z (relative intensity) 309 (3.8), 209 (0.1), and 83 (100).

(−)-(3*S,5*R**)-5-Hydroxy-9-oxonerolidol (15a).** The substance was an oil; $[\alpha]_D$ −39° ($CHCl_3$); IR ($CHCl_3$) 3450, 1675, 1615 cm^{-1}; ^{1}H NMR spectrum in Table XVII; ^{13}C NMR spectrum ($CDCl_3$) 111.42 (t, C-1), 145.65 (d, C-2), 73.26 (C-3), 47.11 (t, C-4), 66.09 (d, C-5), 123.00 (d, C-6) 131.98 (C-7), 54.69 (t, C-8), 198.69 (C-9), 132.41 (d, C-10), 156.79 (C-11), 26.98 (q) and 27.74 (q, C-12 and C-13), 17.12 (q, C-14), 20.87 (q, C-15); MS (low resolution), m/z (relative intensity) 234 (M$^+$ − 18, 0.1), 195 (2.3), 167 (1.3), 139 (2.2), 134 (1.1), 125 (1.2), 121 (4.3), 109 (2.3), 101 (6.2), 84 (14) and 83 (100). Benzoylation of 50 mg of **15a** in the usual way and separation of the products by preparative TLC (benzene–EtOAc, 9:1) gave 24 mg of **15b**, $[\alpha]_D$ −23° ($CHCl_3$), and 28 mg of **15c**, $[\alpha]_D$ +29° ($CHCl_3$) as gums whose ^{1}H NMR spectra are listed in Table XVII.

A mixture of 25 mg of **15a**, 2 mL of 2,2-dimethoxypropane, and 2 mg of *o*-toluenesulfonic acid was stirred at room temperature for 4 h. Evaporation at reduced pressure and purification of the residue by TLC (benzene–EtOAc, 9:1) gave 19 mg of **16** as a gum whose ^{1}H NMR spectrum is listed in Table XVIII. The low-resolution MS exhibited the molecular ion as a very weak peak at m/z 292 (relative intensity 0.03); other significant peaks were found at m/z 277 (0.8), 217 (3.4), 166 (7.1), 165 (3.8), 151 (2.2), 135 (5.1), 134 (9.9), 123 (3), 119 (9.4), 109 (2.8), 107 (6.8), 93 (10), 84 (26.4), 83 (100).

X-ray Analyses. (a) Single crystals of **4** were prepared by slow evaporation from ethyl acetate–hexane. They were orthorhombic, space group $P2_12_12_1$, with a = 7.102 (4) Å, b = 9.975 (3) Å, c = 18.166 (13) Å, and d_{calcd} = 1.282 g cm^{-3} for Z = 4 (M_r 248.32). The intensity data were measured on a CAD4 Enraf Nonius diffractometer (Mo radiation, monochromated, $\theta - 2\theta$ scans). The size of the crystal used for data collection was approximately 0.3 × 0.3 × 0.3 mm^3. No absorption correction was necessary (μ = 0.82). A total of 1355 independent reflections were measured for $\theta \leq 25°$, of which 985 were considered to be observed [$I \geq 2\alpha(I)$]. The structure was solved by direct methods by using MULTAN 78 and refined by full-matrix least-squares methods. In the final refinement anisotropic thermal parameters were used for non-hydrogen atoms. Methyl hydrogen atoms were located from a difference Fourier map; the remaining hydrogen atom parameters were calculated assuming idealized geometry. Hydrogens atom contributions were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices were R = 5.0 and R_w = 5.7 for the 985 observed reflections. The final difference Fourier map was essentially featureless with no peaks greater than ±0.2 eÅ^{-3}

(b) Single crystals of **12a** were prepared by slow evaporation from ethyl acetate–hexane. They were orthorhombic, space group $P2_12_12_1$, with a = 10.778 (4) Å, b = 10.869 (5) Å, c = 16.649 (6) Å, and d_{calcd} = 1.24 g cm^{-3} for Z = 4 (M_r 364.4). The procedure used was the same as in the preceding paragraph with a crystal of approximately 0.3 × 0.3 × 0.3 mm^3, no absorption correction (μ = 0.85), and 1983 reflections of which 1286 were considered to be observed. The final discrepancy indices were R = 6.0 and R_w = 5.9 for the 1286 observed reflections. The final difference Fourier map had no peaks greater than ±0.2 eÅ^{-3}.

Registry No. **1**, 94137-79-8; **2**, 94137-80-1; **3**, 94137-81-2; **4**, 94137-82-3; **5**, 94137-83-4; **6**, 94137-84-5; **7**, 94161-32-7; **8**, 470-17-7; **9**, 69855-24-9; **10a**, 94137-85-6; **10b**, 94346-33-5; **10c**, 94161-33-8; **10d**, 94137-86-7; **10e**, 94233-52-0; **10f**, 94137-87-8; **11**, 94137-88-9; **12a** (isomer I), 94137-89-0; **12a** (isomer II), 94233-53-1; **13**, 94137-90-3; **14** (R = H) (isomer I), 94137-91-4; **14** (R = H) (isomer II), 94233-54-2; **14** (R = Et) (isomer I), 94137-92-5; **14** (R = Et) (isomer II), 94233-55-3; **15a**, 94161-19-0; **16**, 94161-34-9; **17**, 1205-94-3; **18**, 1137-83-3; **19**, 1447-88-7.

Supplementary Material Available: Tables IV–VIII and Tables XI–XV listing final atomic parameters, final anisotropic thermal parameters, bond lengths, bond angles, and selected torsion angles for compounds **4** and **10a** (12 pages). Ordering information is given on any current masthead page.