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STEREOCHEMISTRY OF CHAPLIATRIN AND ITS CONGENERS FROM *LIATRIS GRACILIS*

WERNER HERZ, KINZO WATANABE and JOHN F. BLOUNT*

Department of Chemistry, The Florida State University, Tallahassee, FL 32306, U.S.A.; *Research Division, Hoffmann-La Roche Inc., Nutley, NJ 07110, U.S.A.

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Ke Word Index—*Liatris gracilis*; Compositae; Eupatorieae; 5,10-epoxygermacranolides; sesquiterpene lactones; chapliatrin; isochapliatrin; X-ray analysis.

Abstract—Re-examination of *Liatris gracilis* afforded the known sesquiterpene lactones chapliatrin, isochapliatrin, acetlisochapliatrin, five new closely related 5,10-epoxygermacranolides and a new eudesmanolide. The stereochemistry of the 5,10-epoxygermacranolides has been settled by an X-ray analysis of isochapliatrin.

INTRODUCTION

As part of our study of *Liatris* species which elaborate a number of cytotoxic and antitumor sesquiterpene lactones [1] we earlier described [2] three closely related 5,10-epoxygermacranolides chapliatrin, isochapliatrin and acetylisochapliatrin from *L. chapmanii* T&G and *L. gracilis* Pursh. Chapliatrin was subsequently found also in *L. tenuifolia* Nutt., together with the guaianolide spicatin [3], and exhibited confirmed activity in the P-388 lymphocytic leukemia and Lewis lung carcinoma test systems†.

The structures proposed for these compounds in 1975 are reproduced in formulas **1a**–**1c**. It was pointed out [2, 3] that the configurations assigned to C-3, C-4 and C-10 were tentative‡. In the intervening years several unsuccessful attempts were made to secure more convincing evidence for the stereochemistry at these centers. Re-examination of *L. gracilis* to provide more material for chemical and biological studies has now resulted in the isolation not only of chapliatrin and acetylchapliatrin previously found in this species, but also of isochapliatrin and five minor closely-related 5,10-epoxygermacranolides as well as a new eudesmanolide **4**. As the result of an X-ray analysis of isochapliatrin, the three previously known members of this series can now be represented as **2a**–**2c** and the five new ones on **2d**–**2g** and **3**.

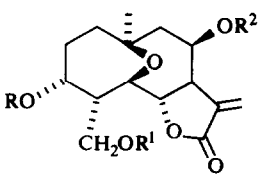
RESULTS AND DISCUSSION

To facilitate the discussion, we present first the results of our X-ray analysis of isochapliatrin which offered a certain number of difficulities. The crystals were less satisfactory than usual, giving rise to broad diffracted peaks which required a wide scan for data collection. The unit cell contained two independent molecules of isochapliatrin whose conformations are similar, but not the same. Both molecules suffered from disorder in the substituent at C-8 and an attempt to account for the disorder by refining certain atoms as pairs of half-atoms met with only limited success. Figure 1 contains stereoscopic drawings of the two molecules which represent the relative configuration drawn in the plane as **2b**. The stereochemistry at C-5, C-6, C-7, C-8 and C-10 (see previous footnote) is that deduced earlier, but the stereochemistry at C-3 and C-4 is reversed.

Tables 1–4 list final atomic parameters and final anisotropic thermal parameters, bond lengths, bond angles and selected torsion angles for the two molecules. Table 5 shows that the molecules differ significantly in the C(1)–C(2)–C(3)–C(4), C(2)–C(3)–C(4)–C(5), C(7)–C(8)–C(9)–C(10) and C(8)–C(9)–C(10)–C(1) torsion angles and in the conformations of the α,β-unsaturated lactone ring although the sum of the internal torison angles is approximately the same (90° vs. 89°). In the primed molecule (Fig. 1, bottom) the lactone ring approximates an envelope with C-7 as the flap, whereas that of Fig. 1 (top) is somewhat more puckered and can be likened to a twist envelope. In both molecules the sign of the O(6)–C(12)–C(11)–C(13) torsion angle (ω_2) is paired with the sign of the O(5)–C(6)–C(7)–C(11) torsion angle (ω_3) [4] and corresponds to the sign of the negative Cotton effect associated with the n,π^*-transition of the α,β-unsaturated lactone which isochapliatrin exhibits in solution. Consequently our assumption [2] that **2b** also represents the absolute configuration of isochapliatrin

†These tests were carried out under the auspices of the Developmental Therapeutics Program, Division of Cancer Treatment of the National Cancer Institute.

‡The dotted C-10, O bond of formulas **1a**–**1c** was based on a then common misinterpretation of what constitutes an α-oriented and a β-orientated bond emanating from C-10 of certain germacranolides when a three-dimensional model is transformed into a two-dimensional figure. In fact, the correct representation in the plane of our structures for chapliatrin and its congeners should have been the one shown below.



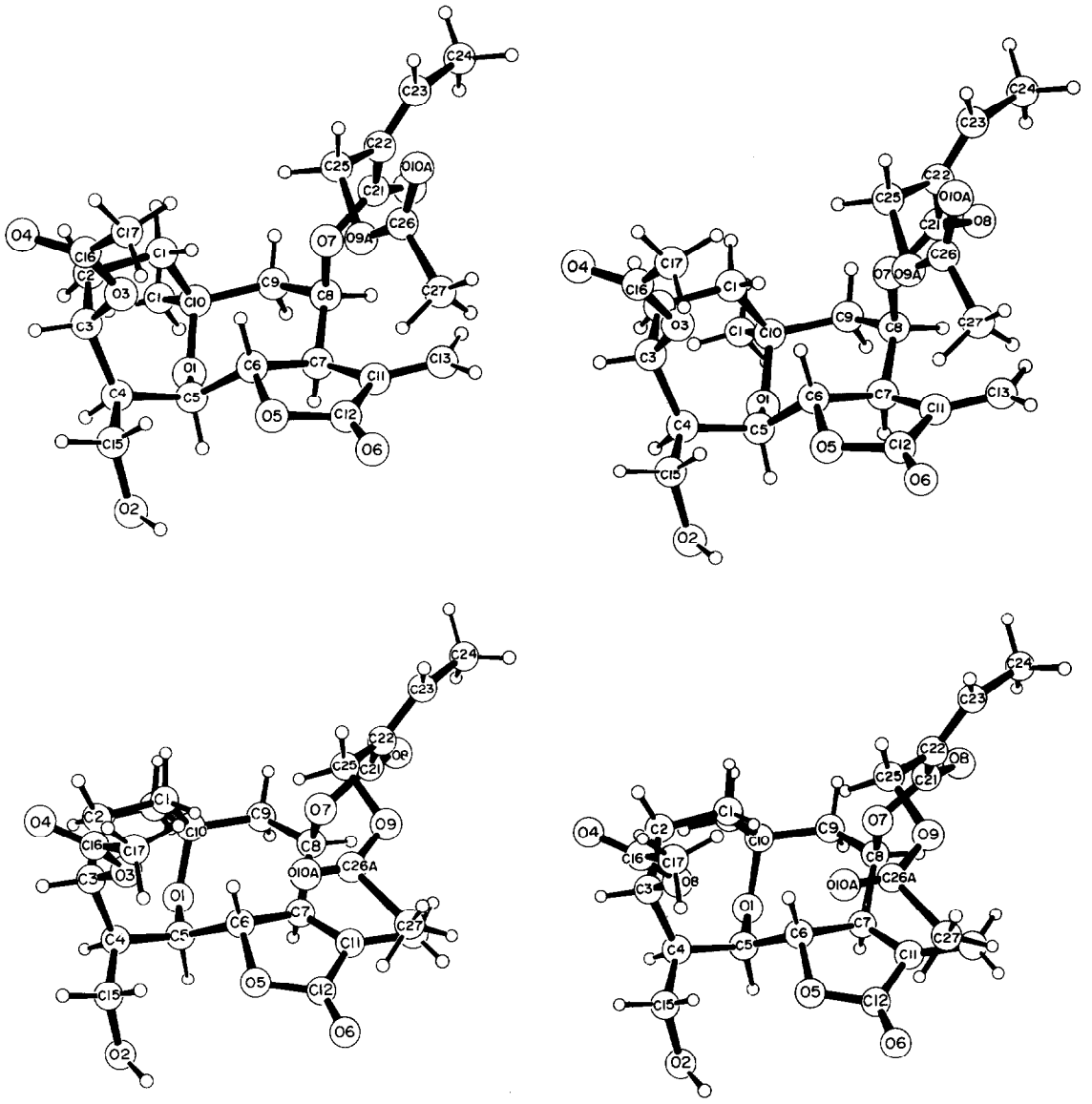


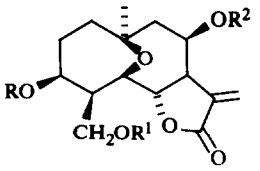
Fig. 1. Stereoscopic view of isochapliatrin molecules with ellipsoids of thermal motion. Top unprimed molecule, bottom primed molecule.

(3*S*, 4*S*, 5*R*, 6*S*, 7*R*, 8*R*, 10*S*) is probably correct. An attempt to provide independent evidence for this by applying the Horeau method [4–7] to chapliatrin was unsuccessful.

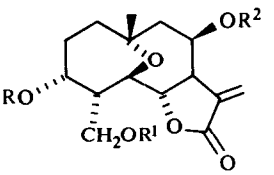
From structure **2b** for isochapliatrin, formulas **2a** and **2c** follow for chapliatrin and acetylchapliatrin [2] and formulas **2d**–**2g** can be deduced for four of the six new minor lactones from *L. gracilis*. Comparison of their ^1H and ^{13}C NMR spectra which are listed in Tables 6 and 8 with the spectra of **2a**–**2c** listed in ref. [2] shows that **2d**, **2f** and **2g** are analogs of chapliatrin (**2a**) containing respectively a sarracenate, an angelate and a γ-acetoxyangelate ester side chain on C-8, whereas **2e** is an analog of isochapliatrin (**2b**) with a sarracenate ester side chain on C-8.

That the fifth new lactone was the anhydro derivative **3** of chapliatrin was apparent from the IR, ^1H and ^{13}C NMR spectra (Tables 6 and 8) which evidenced the absence of hydroxyl absorption (IR) and the presence of a double bond linking C-3 and C-4. In the ^{13}C NMR spectrum the C-3 and C-4 doublets were replaced by signals of two olefinic carbons at δ 131.29 and 137.76 and the frequencies of C-2, C-5 and C-15 were shifted to lower field. Decoupling experiments in $CDCl_3$ and C_6D_6 solution showed that the stereochemistry at C-5, C-6, C-7 and C-8, and hence that at C-10, corresponded to that of the other 5,10-epoxygermacranolides. The unsaturated ester was placed at C-8 and the acetoxy group on C-15 because of the chemical shifts of H-8 and C-8 which remained essentially constant throughout the series.

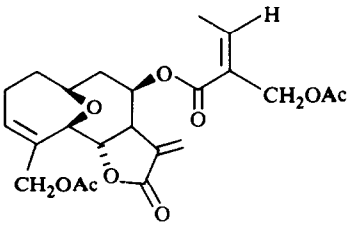
The remaining sesquiterpene lactone **4**, $C_{24}H_{32}O_{11}$, contained a γ-acetoxyangelate and an extra acetate (^1H and ^{13}C NMR spectra, Tables 7 and 8), one of which esterified a secondary hydroxyl (*dt* at δ 5.64) and the



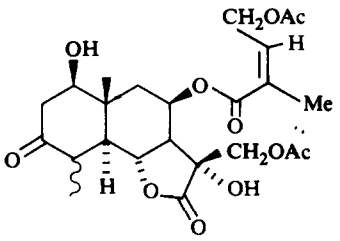
2a R = H, R^1 = Ac, R^2 = A
2b R = Ac, R^1 = H, R^2 = A
2c R , R^1 = Ac, R^2 = A
2d R = H, R^1 = Ac, R^2 = B
2e R = Ac , R^1 = H, R^2 = B
2f R = H , R^1 = Ac , R^2 = C
2g R = H, R^1 = Ac , R^2 = D



1a R = H , R^1 = Ac , R^2 = A
1b R = Ac , R^1 = H, R^2 = A
1c R , R^1 = Ac , R^2 = A



3



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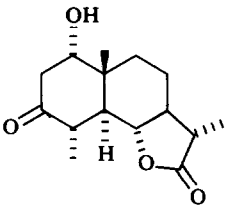

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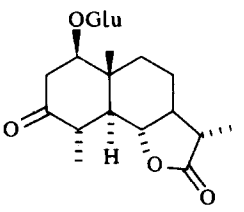

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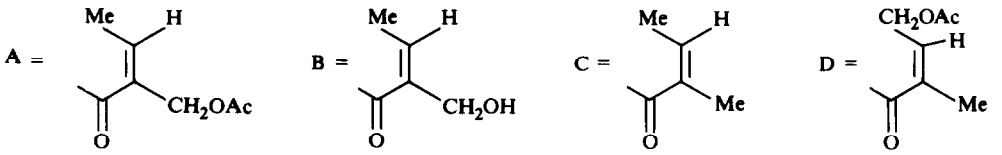
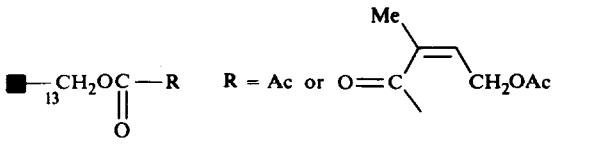
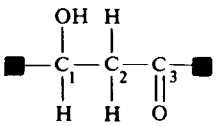
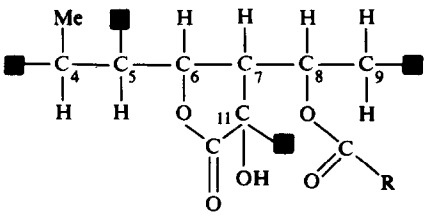




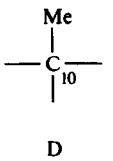
A



B



C



D

Table 1. Final atomic parameters for **2b** with standard deviations in parentheses

Atom	X	Y	Z	B
O(1)	0.5158(4)	0.4480(3)	0.716(1)	*
O(2)	0.7103(4)	0.5291(4)	0.444(1)	*
O(3)	0.6189(3)	0.6116(3)	0.916(1)	*
O(4)	0.6960(5)	06321(4)	1.159(1)	*
O(5)	0.5352(3)	0.6029	0.461(1)	*
O(6)	0.4847(4)	0.6666(4)	0.240(1)	*
O(7)	0.3530(4)	0.5915(3)	0.793(1)	*
O(8)	0.2186(6)	0.5832(6)	0.815(2)	*
O(9)A	0.3951(10)	0.7349(8)	0..698(2)	*
O(9)B	0.3385(16)	0.7520(19)	0.719(4)	*
O(10)A	0.3507(16)	0.8407(9)	0.744(3)	*
O(10)B	0.4440(35)	0.7663(61)	0.701(6)	*
O(1)′	0.9975(4)	0.5221(3)	1.207(1)	*
O(2)′	0.8020(4)	0.4443(4)	0.932(1)	*
O(3)′	0.8898(3)	0.3597(3)	1.409(1)	*
O(4)′	0.8138(5)	0.3408(4)	1.652(1)	*
O(5)′	0.9746(4)	0.3648(3)	0.955(1)	*
O(6)′	1.0226(4)	0.2994(4)	0.739(1)	*
O(7)′	1.1622(4)	0.3755(3)	1.287(1)	*
O(8)′	1.2969(5)	0.3889(5)	1.312(2)	*
O(9)′	1.1593(7)	0.2157(6)	1.226(2)	*
O(10)A′	1.0371(14)	0.2212(17)	1.217(3)	*
O(10)B′	1.0974(38)	0.1393(22)	1.248(5)	*
C(1)	0.4963(7)	0.5068(5)	1.008(1)	*
C(2)	0.5874(7)	0.5039(5)	1.051(1)	*
C(3)	0.6401(5)	0.5409(5)	0.921(1)	*
C(4)	0.6414(5)	0.5147(5)	0.729(1)	*
C(5)	0.5572(6)	0.5023(4)	0.637(1)	*
C(6)	0.5023(5)	0.5615(4)	0.610(1)	*
C(7)	0.4177(5)	0.5409(5)	0.543(1)	*
C(8)	0.3564(6)	0.5286(5)	0.696(2)	*
C(9)	0.3747(7)	0.4685(5)	0.812(1)	*
C(10)	0.4649(7)	0.4538(5)	0.876(1)	*
C(11)	0.3952(6)	0.5957(5)	0.417(1)	*
C(12)	0.4704(6)	0.6275(6)	0.358(2)	*
C(13)	0.3230(7)	0.6177(7)	0.362(2)	*
C(14)	0.4672(8)	0.3845(6)	0.959(2)	*
C(15)	0.6977(5)	0.5574(6)	0.613(1)	*
C(16)	0.6531(6)	0.6530(5)	1.034(2)	*
C(17)	0.6318(6)	0.7234(5)	0.999(1)	*
C(21)	0.2797(9)	0.6159(7)	0.839(2)	*
C(22)	0.2832(10)	0.6850(7)	0.904(2)	*
C(23)	0.2233(12)	0.7154(8)	0.978(2)	*
C(24)	0.1352(14)	0.6897(11)	1.010(2)	*
C(25)	0.3649(12)	0.7200(7)	0.895(2)	*
C(26)	0.3769(11)	0.7947(11)	0.656(3)	*
C(27)	0.3886(9)	0.8069(7)	0.458(3)	*
C(1)′	1.0182(6)	0.4616(5)	1.495(1)	*
C(2)′	0.9293(7)	0.4666(5)	1.514(1)	*
C(3)′	0.8701(6)	0.4310(5)	1.414(1)	*
C(4)′	0.8713(6)	0.4568(4)	1.217(1)	*
C(5)′	0.9546(6)	0.4674(5)	1.131(1)	*
C(6)′	1.0096(5)	0.4067(5)	1.104(1)	*
C(7)′	1.0948(5)	0.4253(5)	1.036(1)	*
C(8)′	1.1575(6)	0.4375(5)	1.188(2)	*
C(9)′	1.1386(6)	0.4976(5)	1.301(1)	*
C(10)′	1.0528(6)	0.5118(5)	1.371(2)	*
C(11)′	1.1136(6)	0.3697(6)	0.913(1)	*
C(12)′	1.0374(7)	0.3422(6)	0.851(1)	*
C(13)′	1.1859(7)	0.3451(8)	0.856(1)	*
C(14)′	1.0491(8)	0.5823(5)	1.450(2)	*
C(15)′	0.8131(6)	0.4135(5)	1.108(2)	*
C(16)′	0.8543(6)	0.3218(5)	1.528(1)	*
C(17)′	0.8687(7)	0.2485(5)	1.493(1)	*
C(21)′	1.2385(8)	0.3539(6)	1.334(2)	*
C(22)′	1.2384(9)	0.2860(6)	1.406(2)	*
C(23)′	1.3066(9)	0.2599(6)	1.488(1)	*
C(24)′	1.3909(9)	0.2879(8)	1.498(2)	*
C(25)′	1.1603(10)	0.2476(7)	1.410(2)	*
C(26)A′	1.0919(23)	0.2131(36)	1.174(5)	*
C(26)B′	1.1087(17)	0.1785(14)	1.154(5)	*
C(27)′	1.1017(9)	0.1581(8)	0.981(3)	*
HO(2)	0.706	0.560	0.36	7.0
H(1)A	0.485	0.551	0.96	6.0
H(1)B	0.467	0.501	1.12	6.0
H(2)A	0.603	0.456	1.05	6.0
H(2)B	0.595	0.524	1.17	6.0
H(3)	0.697	0.537	0.97	5.0
H(4)	0.668	0.470	0.74	5.0
H(5)	0.570	0.486	0.51	5.0
H(6)	0.498	0.589	0.72	5.0
H(7)	0.424	0.498	0.47	5.0
H(8)	0.301	0.521	0.64	6.0
H(9)A	0.357	0.428	0.74	6.0
H(9)B	0.341	0.473	0.92	6.0
H(13)A	0.271	0.596	0.41	8.0
H(13)B	0.319	0.658	0.28	8.0
H(14)A	0.525	0.373	0.99	8.0
H(14)B	0.447	0.351	0.87	8.0
H(14)C	0.432	0.383	1.07	8.0
H(15)A	0.673	0.604	0.60	6.0
H(15)B	0.752	0.563	0.68	6.0
H(17)A	0.659	0.752	1.09	7.0
H(17)B	0.571	0.729	1.01	7.0
H(17)C	0.651	0.736	0.88	7.0
H(23)	0.234	0.763	1.03	12.0
H(24)A	0.130	0.642	0.96	16.0
H(24)B	0.093	0.718	0.94	16.0
H(24)C	0.120	0.690	1.14	16.0
H(25)AB	0.363	0.764	0.96	10.0
H(25)AA	0.409	0.691	0.96	10.0
H(25)BB	0.380	0.749	1.00	10.0
H(25)BA	0.414	0.690	0.87	10.0
H(27)AC′	1.147	0.165	0.89	12.0
H(27)AB′	1.107	0.111	1.03	12.0
H(27)AA′	1.048	0.162	0.92	12.0
H(27)AC	0.448	0.799	0.43	12.0
H(27)AB	0.354	0.778	0.38	12.0
H(27)AA	0.377	0.856	0.43	12.0
H(27)BC′	1.111	0.196	0.90	12.0
H(27)BB′	1.150	0.126	0.97	12.0
H(27)BA′	1.051	0.132	0.94	12.0
H(27)BC	0.407	0.765	0.40	12.0
H(27)BB	0.338	0.824	0.40	12.0
H(27)BA	0.434	0.843	0.44	12.0
HO(2)′	0.805	0.412	0.85	7.0
H(1)A′	1.050	0.463	1.61	6.0
H(1)B′	1.027	0.416	1.44	6.0
H(2)A′	0.915	0.515	1.54	6.0
H(2)B′	0.922	0.447	1.66	6.0
H(3)′	0.813	0.436	1.46	5.0
H(4)′	0.846	0.502	1.22	5.0
H(5)′	0.942	0.482	1.01	5.0
H(6)′	1.013	0.380	1.22	5.0

Table 1 (*Contd.*)

Atom	X	Y	Z	B
H(7)′	1.090	0.468	0.96	5.0
H(8)′	1.211	0.445	1.13	6.0
H(9)A′	1.156	0.537	1.23	6.0
H(9)B′	1.176	0.493	1.41	6.0
H(13)A′	1.238	0.365	0.90	9.0
H(13)B′	1.186	0.306	0.77	9.0
H(14)A′	0.992	0.595	1.48	9.0
H(14)B′	1.070	0.616	1.36	9.0
H(14)C′	1.085	0.586	1.56	9.0
H(15)A′	0.837	0.368	1.10	6.0
H(15)B′	0.760	0.411	1.17	6.0
H(17)A′	0.841	0.220	1.59	7.0
H(17)B′	0.928	0.238	1.50	7.0
H(17)C′	0.845	0.236	1.37	7.0
H(23)′	1.299	0.216	1.55	8.0
H(24)A′	1.391	0.334	1.44	10.0
H(24)B′	1.430	0.258	1.44	10.0
H(24)C′	1.406	0.296	1.63	10.0
H(25)A′	1.112	0.277	1.43	10.0
H(25)B′	1.160	0.212	1.51	10.0

*Anisotropic thermal parameters are given in Table 2.

second a primary hydroxyl group next to a quaternary center (AB system at δ4.67*d* and 4.11*d*, second carbon triplet near δ63). This is represented by partial structure **A**. NMR spectrometry also indicated the presence of a secondary and a tertiary hydroxyl group. The former was evidenced by a one-proton *dd* at δ3.74 which experienced the expected paramagnetic shift on addition of trichloroacetylisocyanate (TAI) [8], the latter was revealed only after addition of TAI, which produced two, rather than only one, NH frequencies in the ^{1}H NMR spectrum (Table 7), and appeared to be associated with a carbon singlet at δ75.30. As the ^{13}C NMR spectrum also exhibited two carbonyl signals at δ210.09 and δ174.59, in addition to the three ester carbonyls at δ165.04, 170.87 and 171.08, and exhibited three C–O doublets in the δ67–77 range, two of which were assignable to the carbons bearing one of the esters and the secondary hydroxyl, the array of functional groups was completed by invoking the presence of a cycloalkanone and a γ-lactone, the latter accounting for an IR band at 1790 cm^{-1}.

Extensive spin decoupling experiments in $CDCl_3$ and C_6D_6 solution led to partial structure **B**, where C-2 (numbering as in final structure) was placed next to the ketone group because of its chemical shift (triplet at δ44.21) and the chemical shifts of its hydrogens, and C where the lactone ring is closed to C-6 and the ester

Table 2. Final anisotropic thermal parameters for **2b** with standard deviations in parentheses

Atom	B11 × 10^4	B22 × 10^3	B33 × 10^3	B12 × 10^4	B13 × 10^4	B23 × 10^3
O(1)	62(3)	3(0)	24(1)	−4(2)	25(6)	−1(0)
O(2)	73(4)	5(0)	24(2)	20(3)	29(6)	1(1)
O(3)	45(3)	2(0)	22(1)	3(2)	1(5)	0(0)
O(4)	67(4)	4(0)	27(2)	3(3)	−16(7)	0(1)
O(5)	38(3)	4(0)	20(1)	4(2)	14(5)	1(0)
O(6)	58(4)	5(0)	26(2)	−2(3)	12(6)	3(1)
O(7)	45(3)	3(0)	28(2)	−1(2)	16(5)	−1(0)
O(8)	61(5)	9(1)	62(4)	−1(4)	25(10)	−9(1)
O(9)A	42(7)	2(0)	30(4)	2(4)	−2(14)	−1(1)
O(9)B	85(14)	11(2)	60(8)	−33(14)	−45(29)	15(3)
O(10)A	175(20)	3(1)	49(6)	45(9)	58(26)	−3(1)
O(10)B	251(44)	88(16)	58(12)	−385(78)	−30(64)	22(10)
O(1)′	62(3)	2(0)	29(2)	−4(2)	−17(6)	1(0)
O(2)′	69(4)	5(0)	25(2)	16(3)	−31(6)	0(1)
O(3)′	49(3)	2(0)	22(1)	5(2)	0(5)	0(0)
O(4)′	66(4)	4(0)	22(2)	−4(3)	19(7)	1(1)
O(5)′	46(3)	3(0)	24(1)	0(2)	−12(5)	−1(0)
O(6)′	62(4)	5(0)	31(2)	10(3)	−2(7)	−3(1)
O(7)′	45(3)	4(0)	28(2)	−3(2)	−18(6)	1(1)
O(8)′	48(4)	7(0)	72(4)	−8(3)	−38(9)	9(1)
O(9)′	99(7)	7(0)	54(4)	−17(5)	57(13)	−5(1)
O(10)A′	49(9)	15(2)	61(8)	−3(11)	−23(21)	−16(3)
O(10)B′	447(67)	12(2)	43(9)	−128(34)	−17(58)	4(4)
C(1)	68(5)	3(0)	18(2)	−10(3)	18(8)	0(1)
C(2)	70(6)	3(0)	18(2)	1(3)	0(9)	0(1)
C(3)	46(4)	3(0)	16(2)	11(3)	9(7)	0(1)
C(4)	46(4)	3(0)	22(2)	8(3)	5(8)	0(1)
C(5)	59(5)	2(0)	16(2)	2(3)	8(8)	0(1)
C(6)	44(4)	3(0)	17(2)	−5(3)	23(7)	−2(1)
C(7)	46(4)	3(0)	15(2)	−8(3)	22(7)	−1(1)
C(8)	44(5)	3(0)	41(3)	1(3)	−4(10)	−2(1)
C(9)	65(6)	3(0)	23(2)	−15(3)	44(9)	−1(1)
C(10)	69(6)	2(0)	33(3)	−12(3)	39(11)	0(1)

Table 2. (*Contd.*)

Atom	B11 × 10^4	B22 × 10^3	B33 × 10^3	B12 × 10^4	B13 × 10^4	B23 × 10^3
C(11)	44(5)	4(0)	21(2)	−4(3)	−18(8)	−1(1)
C(12)	42(5)	3(0)	26(3)	2(3)	24(9)	0(1)
C(13)	46(5)	6(1)	35(3)	−5(4)	−12(10)	4(1)
C(14)	91(7)	4(0)	31(3)	−9(4)	46(12)	1(1)
C(15)	37(4)	5(0)	18(2)	11(3)	29(7)	1(1)
C(16)	46(5)	2(0)	34(3)	−5(3)	42(10)	−2(1)
C(17)	64(6)	3(0)	31(3)	−7(3)	21(10)	−1(1)
C(21)	60(6)	5(1)	30(3)	13(5)	−26(12)	0(1)
C(22)	93(8)	4(0)	29(3)	28(5)	−16(13)	−1(1)
C(23)	127(11)	7(1)	28(3)	46(8)	5(16)	1(1)
C(24)	181(15)	13(1)	15(3)	103(12)	25(17)	2(1)
C(25)	141(12)	4(0)	40(4)	1(6)	−39(19)	−2(1)
C(26)	66(9)	7(1)	58(7)	−23(8)	0(20)	1(2)
C(27)	79(8)	5(1)	75(7)	1(5)	56(19)	5(2)
C(1)′	60(5)	3(0)	21(2)	0(3)	−24(9)	−1(1)
C(2)′	81(6)	3(0)	22(2)	0(4)	−13(10)	0(1)
C(3)′	57(5)	3(0)	16(2)	5(3)	12(8)	0(1)
C(4)′	59(5)	2(0)	20(2)	9(3)	0(8)	0(1)
C(5)′	51(5)	3(0)	15(2)	2(3)	1(7)	0(1)
C(6)′	44(4)	3(0)	21(2)	2(3)	−38(8)	1(1)
C(7)′	33(4)	4(0)	23(2)	−3(3)	−1(8)	1(1)
C(8)′	46(5)	3(0)	36(3)	−13(3)	−20(10)	1(1)
C(9)′	57(5)	3(0)	28(3)	−12(3)	−35(10)	0(1)
C(10)′	59(5)	2(0)	37(3)	−8(3)	−43(11)	0(1)
C(11)′	50(5)	5(0)	19(2)	5(4)	18(8)	0(1)
C(12)′	50(5)	4(0)	25(3)	3(4)	19(10)	−1(1)
C(13)′	55(6)	8(1)	22(2)	−3(5)	22(9)	−2(1)
C(14)′	108(8)	2(0)	44(4)	−15(4)	−57(14)	−1(1)
C(15)′	48(5)	3(0)	32(3)	1(3)	2(9)	0(1)
C(16)′	43(5)	3(0)	21(2)	−9(3)	−9(9)	2(1)
C(17)′	74(6)	3(0)	30(3)	−5(4)	−2(10)	0(1)
C(21)′	53(6)	4(0)	31(3)	4(4)	−12(10)	0(1)
C(22)′	99(8)	3(0)	27(3)	−5(5)	31(12)	−1(1)
C(23)′	97(8)	5(0)	19(2)	32(5)	31(12)	2(1)
C(24)′	81(8)	8(1)	40(4)	28(6)	−73(14)	−1(1)
C(25)′	121(10)	5(0)	23(3)	12(6)	29(13)	1(1)
C(26)A′	23(13)	22(4)	26(7)	82(19)	−4(22)	4(5)
C(26)B′	10(10)	4(1)	43(10)	−16(8)	23(24)	3(3)
C(27)′	96(9)	5(1)	55(5)	−2(6)	−77(17)	−7(1)

The anisotropic temperature factor has the form

$$\exp[-(h^2B11 + k^2B22 - l^2B33 + 2hkB12 + 2hlB13 + 2klB23)].$$

function is placed on C-8 because of the chemical shifts of H- (δ 4.75) and H-8 (δ 5.64). The tertiary hydroxyl group was placed next to the lactone carbonyl because of the unusually high lactone frequency. The remaining two carbon atoms required by the empirical formula and the ^{13}C NMR spectrum were accounted for by partial structure **D**.

Combination of **A**, **B**, **C** ane **D** to give the eudesmanolide structure **4** was not only logical on biogenetic grounds, but also satisfied the following observations: (1) The chemical shifts of H-4 (δ 2.75) and C-4 (δ 55.93) were sufficiently low to indicate that C-4 is α to a carbonyl group; (2) Addition of acid to a solution of **4** produced a change in the CD curve (see Experimental) characteristic of dehydration to an α,β-unsaturated ketone as observed for other 1-hydroxy-3-ketoeudesmanolids [9, 10]; (3) Addition of TAI produced a paramagnetic shift of the methylene signal of partial structure **A**, but not in the frequency of the methyl signal of **D**. Consequently partial structure **A** is located on C-11; (4) Placement of the unsaturated ester function at C-8 is based on analogy and on the shift of C-8 which corresponds to that of similarly constituted eudesmanolides carrying α,β-unsaturated esters on C-8 [1].

The stereochemistry assigned to **4** is based on the following evidence: (1) The values of $J_{5,6}$ (12 Hz), $J_{6,7}$ (12 Hz) and $J_{7,8}$ (2.5 Hz) indicate that H-5 and H-6, and H-6 and H-7, are *trans* and that H-7 and H-8 are *cis*, as in other lactones of this type [1]; (2) Addition of TAI produced a large paramagnetic shift in the frequency of H-7 (Table 7), hence H-7 is *cis* to the hydroxyl group on C-11; (3) The coupling constants involving H-1 and H-2 (10

Table 3. Bond lengths (A) in **2b** with standard deviations in parentheses

	Unprimed	Primed
O(1)–C(5)	1.406(11)	1.411(11)
O(1)–C(10)	1.457(12)	1.531(13)
O(2)–C(15)	1.396(12)	1.459(13)
O(3)–C(3)	1.450(11)	1.456(11)
O(3)–C(16)	1.322(13)	1.301(12)
O(4)–C(16)	1.234(14)	1.197(13)
O(5)–C(6)	1.487(10)	1.494(11)
O(5)–C(12)	1.392(12)	1.368(13)
O(6)–C(12)	1.194(13)	1.213(14)
O(7)–C(8)	1.448(12)	1.437(13)
O(7)–C(21)	1.339(15)	1.366(14)
O(8)–C(21)	1.206(18)	1.194(15)
O(9)–C(25)		1.503(17)
C(1)–C(2)	1.524(15)	1.501(15)
C(1)–C(10)	1.528(14)	1.473(14)
C(2)–C(3)	1.493(13)	1.529(14)
C(3)–C(4)	1.518(12)	1.550(12)
C(4)–C(5)	1.554(13)	1.521(13)
C(4)–C(15)	1.525(13)	1.517(14)
C(5)–C(6)	1.495(13)	1.522(13)
C(6)–C(7)	1.524(12)	1.529(12)
C(7)–C(8)	1.536(14)	1.546(14)
C(7)–C(11)	1.484(14)	1.468(15)
C(8)–C(9)	1.505(15)	1.493(15)
C(9)–C(10)	1.575(15)	1.526(15)
C(10)–C(14)	1.512(15)	1.522(15)
C(11)–C(12)	1.453(14)	1.435(15)
C(11)–C(13)	1.324(15)	1.350(16)
C(16)–C(17)	1.468(14)	1.502(14)
C(21)–C(22)	1.457(19)	1.452(17)
C(22)–C(23)	1.280(23)	1.373(20)
C(22)–C(25)	1.509(24)	1.490(21)
C(23)–C(24)	1.549(29)	1.488(21)
C(26)–C(27)	1.506(32)	
For those atoms which were refined as two half atoms (A and B), only the distances for the A atoms are shown		
O(9)A–C(25)	1.576(22)	
O(9)A–C(26)	1.266(26)	
O(9)–C(26)A		1.169(39)
O(10)A–C(26)A		0.966(45)
O(10)A–C(26)	1.202(30)	
C(26)A–C(27)		1.813(56).

Table 4. Bond angles (°) in **2b** with standard deviations in parentheses

	Unprimed	Primed
C(5)–O(1)–C(10)	123.9(7)	120.4(7)
C(3)–O(3)–C(16)	119.3(7)	116.8(7)
C(6)–O(5)–C(12)	109.1(7)	108.5(7)
C(8)–O(7)–C(21)	118.6(8)	116.8(8)
C(2)–C(1)–C(10)	115.9(8)	118.3(8)
C(1)–C(2)–C(3)	114.3(8)	115.9(8)
O(3)–C(3)–C(2)	110.8(7)	109.0(7)
O(3)–C(3)–C(4)	108.5(7)	107.5(7)
C(2)–C(3)–C(4)	116.7(8)	114.9(8)
C(3)–C(4)–C(5)	116.8(7)	117.2(8)
C(3)–C(4)–C(15)	110.4(7)	107.6(8)
C(5)–C(4)–C(15)	112.1(7)	114.6(8)
O(1)–C(5)–C(4)	111.5(7)	112.6(7)
O(1)–C(5)–C(6)	111.9(7)	111.9(7)
C(4)–C(5)–C(6)	117.7(7)	118.6(7)
O(5)–C(6)–C(5)	108.5(7)	108.5(7)
O(5)–C(6)–C(7)	103.7(6)	103.8(7)
C(5)–C(6)–C(7)	112.0(7)	113.1(8)
C(6)–C(7)–C(8)	113.4(7)	113.5(8)
C(6)–C(7)–C(11)	103.3(7)	102.5(8)
C(8)–C(7)–C(11)	114.9(8)	115.7(8)
O(7)–C(8)–C(7)	105.0(7)	105.8(8)
O(7)–C(8)–C(9)	114.1(9)	114.4(9)
C(7)–C(8)–C(9)	114.9(8)	113.5(8)
C(8)–C(9)–C(10)	120.3(8)	122.3(8)
O(1)–C(10)–C(1)	112.6(8)	111.2(8)
O(1)–C(10)–C(9)	107.9(8)	107.0(8)
O(1)–C(10)–C(14)	104.2(8)	99.1(8)
C(1)–C(10)–C(9)	112.2(8)	116.4(8)
C(1)–C(10)–C(14)	111.2(9)	111.8(9)
C(9)–C(10)–C(14)	108.4(9)	110.0(9)
C(7)–C(11)–C(12)	107.7(8)	107.7(9)
C(7)–C(11)–C(13)	131.1(10)	130.9(10)
C(12)–C(11)–C(13)	121.2(10)	121.4(11)
O(5)–C(12)–O(6)	118.7(8)	118.2(9)
O(5)–C(12)–C(11)	108.9(8)	110.1(9)
O(6)–C(12)–C(11)	132.4(9)	131.2(10)
O(2)–C(15)–C(4)	112.1(8)	108.4(8)
O(3)–C(16)–O(4)	121.7(8)	126.0(9)
O(3)–C(16)–C(17)	112.3(9)	111.9(9)
O(4)–C(16)–C(17)	126.0(10)	122.1(9)
O(7)–C(21)–O(8)	120.5(12)	120.7(11)
O(7)–C(21)–C(22)	113.2(12)	112.7(10)
O(8)–C(21)–C(22)	126.1(14)	126.6(12)
C(21)–C(22)–C(23)	124.1(15)	120.9(12)
C(21)–C(22)–C(25)	117.0(13)	119.2(12)
C(23)–C(22)–C(25)	118.7(13)	119.5(11)
C(22)–C(23)–C(24)	128.5(16)	129.1(12)
O(9)–C(25)–C(22)		101.9(11)
For those atoms which were refined as two half atoms (A and B), only the angles for the A atoms are shown		
C(25)–O(9)A–C(26)	109.2(25)	
C(25)–O(9)–C(26)A		109.1(25)
O(9)A–C(25)–C(22)	114.1(13)	
O(9)A–C(26)–O(10)A	132.1(23)	
O(9)–C(26)A–O(10)A		139.2(47)
O(9)–C(26)A–C(27)		101.8(32)
O(10)A–C(26)A–C(27)		116.6(42)
O(9)A–C(26)–C(27)	111.0(18)	
O(10)A–C(26)–C(27)	116.9(19)	

and 8.5 Hz) indicate that the hydroxyl group on C-1 is equatorial and β-orientated if the absolute configuration corresponds to that shown in the formula*. That this is the case follows from the CD curve which exhibits a weak positive Cotton effect in the ketone n, π region similar in sign to that of ring A/B *trans*-fused tetrahydrosantonins of known absolute configuration [10].

As for the stereochemistry at C-4, $J_{4,5}$ is 7.5 Hz. This value seems too large to accommodate the C-4 methyl

*The H-1 signal of arsanin (**5**) is reported as δ 3.78 (*br t*, J = 3 Hz) [11]; artecalin $J_{1,2}$ = 11, 6.5 Hz.

Table 5. Torsion angles (°) in **2b** with standard deviations in parentheses

	Unprimed	Primed
C(10)–C(1)–C(2)–C(3)	85.8(10)	87.4(11)
C(1)–C(2)–C(3)–C(4)	−64.3(11)	−60.9(11)
C(2)–C(3)–C(4)–C(5)	50.4(11)	45.9(11)
C(3)–C(4)–C(5)–C(6)	62.4(10)	63.8(10)
C(4)–C(5)–C(6)–C(7)	−172.0(7)	−173.7(7)
C(5)–C(6)–C(7)–C(8)	91.4(9)	90.7(9)
C(6)–C(7)–C(8)–C(9)	−67.6(11)	−66.0(11)
C(7)–C(8)–C(9)–C(10)	42.9(13)	45.7(13)
C(8)–C(9)–(10)–C(1)	67.5(12)	62.5(13)
C(9)–C(10)–C(1)–C(2)	−169.5(8)	−169.2(9)
C(6)–C(7)–C(11)–C(12)	22.5(10)	25.2(10)
C(7)–C(11)–C(12)–O(5)	−9.3(11)	−14.4(12)
C(11)–C(12)–O(5)–C(6)	−8.7(10)	−3.5(11)
C(12)–O(5)–C(6)–C(7)	22.5(8)	19.0(9)
O(5)–C(6)–C(7)–C(11)	−26.8(8)	−26.4(9)
O(6)–C(12)–C(11)–C(13)	−13.8(19)	−5.1(20)

group in the less stable β-orientation, but is considerably smaller than the 11 Hz figure recently reported for $J_{4,5}$ in eudesmanolide **6** [12]. As the coupling constants given for H-1 of **6** are also somewhat different, we tentatively ascribe the divergence to slightly different conformations of ring A in **4** and **6** rather than to a difference in C-4 stereochemistry. This is supported by the chemical shifts of H-4 and H-15 in **4** which are both somewhat lower than those in **6**, but otherwise comparable. An attempt to investigate a possible epimerization at C-4 was foiled by the ease with which **4** undergoes dehydration.

EXPERIMENTAL

Extraction of Liatris gracilis. Above ground material of *L. gracilis* Pursh (0.9 kg), collected by Dr. R. K. Godfrey on September 28, 1980, in the Apalachicola National Forest off State Route 20 west of Tallahassee, Leon Co., Florida (Godfrey voucher No. 78183 on deposit in herbarium of Florida State University) was extracted with $CHCl_3$ and worked up in the usual fashion [13]. The extract (40 g) was preadsorbed on 90 g of silica gel (Merck #60, particle size 0.063–0.200 mm) and chromatographed over 1 kg of the same adsorbent packed in *n*-hexane. Fractions were collected as follows: Fraction 1–5 (hexane), 6–10 (hexane–EtOAc, 19:1), 10–15 (hexane–EtOAc, 9:1), 16–20 (hexane–EtOAc, 4:1), 21–25 (hexane–EtOAc 1:1), 26–30 (hexane–EtOAc, 1:3), 31–35 (EtOAc) 36–40 (EtOAc–MeOH, 19:1), 41–45 (EtOAc–MeOH, 3:1) and 46–50 (MeOH).

Fractions 14 and 15 were combined and rechromatographed (prep. TLC, C_6H_6–EtOAc, 19:1) to give 5 g lupeol. Fractions 25 and 26 were combined and purified by prep. TLC (C_6H_6–EtOAc, 7:3 and 3:2) to give 0.40 g acetylisochapliatrin (**2c**) and 0.10 g **3**. The properties of **2c** have been reported [2]. Lactone **3** was a gum, $[\alpha]_D^{26}$ + 134.9° (*c* 1.02, $CHCl_3$); CD curve (MeOH), $[\theta]_{326}$ −95,

Table 6. ^{1}H NMR spectra of **2d**–**2g** and **3***

	2d	2e	2f	2g	3	3†
H-1a	1.37 *ddbr* (16, 7)	1.46 *ddbr*	1.34 *ddbr*	1.37 *ddbr*	1.55‡	1.31 *m*‡
1b	2.77 *ddbr* (16, 12)	2.54 *ddbr*	2.77 *ddbr*	2.75 *ddbr* (15,11)	2.47‡	2.35 *m*‡
2a	~2‡	‡	‡	‡	2.62‡	2.27 *m*‡
2b	~2‡	‡	‡	‡	2.22 *dtbr* (17.5, 6.5)	1.84 *m*
3	4.03 *m*	5.49 *m*	4.03 *m*	4.07 *m*	5.84‡	5.63 *dbr* (6.5)
4	2.19 *m*	2.35 *m*	2.19 *m*	2.19 *m*	—	—
5	3.94 *dd* (10, 3)	4.00 *dd*	3.92 *dd*	3.95 *dd*	4.36 *d* (9.5)	4.35 *d* (10)
6	5.71 *t* (10)	5.37 *t*	5.72 *t*	5.72 *t*	4.92 *t* (9.5)	4.90 *t* (10)
7	3.31 *dm* (10)	3.40 *dm*	3.28 *dm*	3.31 *dm*	3.47 *dm* (9.5)	2.87 *dddd* (10, 3, 3.5, 1.5)
8	5.76 *ddd* (5, 2.5, 2)	5.82 *ddd*	5.74 *ddd*	5.74 *m*	5.86 *m*	5.56 *ddd* (4.5, 2.5, 1.5)
9a	1.97 *dd* (15.5, 4.5)	~2‡	‡	‡	‡	1.69 *dd* (16, 2.5)
9b	2.15 *dd* (15.5, 2.5)	~2‡	‡	‡	‡	1.51 *dd* (16, 4.5)
13a	6.29*d* (3)	6.30 *d*	6.27 *d*	6.28 *d*	6.31 *d* (3.5)	6.17 *d* (3)
13b	5.58*d* (3)	5.60 *d* (2.5)	5.56 *d* (3)	5.55 *d*	5.64 *d* (3)	5.28 *d* (2.5)
14§	1.26	1.24	1.21	1.23	1.30	1.02
15a	4.77 *dd* (12, 10.5)	3.65‖	4.78 *dd*	4.75 *dd* (12, 9.5)	4.71 *dbr* (12)	4.77 *d*
15b	4.00 *dd* (12, 5)		4.00 *dd*	4.04 *dd* (12, 5.5)	4.54 *dbr* (12)	4.63 *d*
3′	6.41 *q* (7)	6.41 *q*	6.10 *qq* (7, 1.5)	6.04 *tq* (5, 1.5)	6.50 *q* (7)	6.00 *q*
4′	2.05 *d* (7)§	2.05 *q*§	1.95 *dq*§ (7, 1.5)	5.00 *dq*‖ (5, 1.5)	2.07 *d* (7)§	1.88 *d*§
5′	4.23*d* (12.5)	4.25 *d*	1.84 *quint*§ (1.5)	1.90*q* (1.5)§	4.67 *d* (12.5)	4.67 *d*
	4.16 *d* (12.5)	4.17 *d*			4.55 *d* (12.5)	4.35 *d*
Ac§	2.08	2.11	2.08	2.07, 2.09	1.95, 2.06	1.72, 1.73

*Run at 270 MHz in $CDCl_3$, unless otherwise specified, with TMS as internal standard. Unmarked signals are singlets. Figures in parentheses are coupling constants in Hz and are not listed if they correspond to those in preceding column.

†Run in C_6D_6.

‡In multiplet or obscured.

§Intensity three protons.

‖ Intensity two protons (AB system).

Table 7. ^{1}H NMR spectrum of 4*

	4 ($CDCl_3$)	4 ($CDCl_3$–C_6D_6, 2:3)	4 + TAI ($CDCl_3$)
H-1	3.74 *dd* (10, 8.5)	2.95 *dd* (11, 7)	5.04 *dd* (9, 7.5)
2a	2.65‡	2.32 *dd* (17, 7)	3.06 *dd* (18, 7.5)
2b		2.22 *dd* (17, 11)	2.62 *dd* (18, 9)
4	2.75 *quint* (7.5)	2.56 *quint*	2.89 *quint*
5	1.94 *dd* (12, 7.5)	~1.05	2.44 *dd* (11, 7.5)
6	4.75 *t* (12)	4.46 *t*	4.80 *t* (11)
7	2.49 *dd* (12, 2.5)	2.04 *dd* (12, 2)	3.49 *dbr* (11)
8	5.65 *dt* (3, 2.5)	5.49 *dt* (2, 25)	5.73 *m*
9a	2.46 *dd* (15, 3)	2.14 *dd* (15.5, 2.5)	2.26 *dd* (15, 2.5)
9b	1.55 *ddbr* (15, 2.5)	0.83 *dd* (15.5, 2.5)	1.77 *dbr* (15)
13a	4.67 *d* (12)	4.55 *d*	4.77 *d*
13b	4.11 *d* (12)	3.92 *d*	4.32 *d*
14†	1.22	0.89	1.25
15†	1.31 *d* (7.5)	1.06 *d*	1.36 *d*
3′	6.14 *tq* (5, 1.5)	5.86 *tq*	6.11 *m*
4′	5.06 *dq* (5, 1.5)‡	5.11 *dq*‡	4.89 *dm* (17), 5.21 *ddbr* (17, 7.5)
5′†	2.00 *q* (1.5)	1.72 *q* (2)	1.98 *dbr* (2)
Ac†	2.08, 2.09	1.75, 1.76	2.07, 2.08
Misc.	—	—	8.77, 8.69 (NH)

*Run at 270 MHz using TMS as internal standard. Unmarked signals are singlets. Figures in parentheses are coupling constants in Hz and are not listed if they correspond to those in preceding column.

†Intensity three protons.

‡Center of AB system, intensity two protons.

Table 8. ^{13}C NMR Spectra of **2d**, **2g**, **3** and **4***

	2d	2g	3§	4
C-1	29.97*t*	30.02*t*	24.73*t*	77.20*t*†
2	288.8*t*	29.20*t*	36.46*t*	44.21*t*
3	67.45*d*	67.62*d*	131.29*d*	210.09
4	49.83*d*	49.82*d*	137.76	55.93*d*
5	78.57*d*	78.71*d*	82.53*d*	42.96*d*
6	77.48*d*	77.62*d*	76.82*d*	72.44*t*
7	47.24*d*	47.29*d*	46.37*d*	47.35*d*
8	67.29*d*	67.31*d*	66.89*d*	67.04*d*
9	45.17*t*	45.33*t*	45.38*t*	42.61*t*
10	79.63	79.52	79.67	40.67
11	134.91	134.88	134.48	75.30
12	168.93	168.88	168.73	174.59
13	121.62*t*	121.45*t*	122.02*t*	63.20*t*‡
14	30.51*q*	30.51*q*	29.23*q*	13.75*q*
15	62.74*t*	62.74*t*†	65.48*t*	15.88*q*
1′	165.64	165.74	164.48	165.04
2′	131.10	128.10	126.80	126.98
3′	143.45*d*	139.86*d*	147.21*d*	142.24*d*
4′	15.85*q*	62.99*t*†	15.98*q*	63.04*t*‡
5′	64.54*t*	19.92*q*	66.89*t*	19.69*q*
Ac	172.15	171.85	170.77	171.08
	20.92*q*	170.80	170.65	170.87
		20.92*q*(2)	21.06*q*	20.89*q*
			20.72*q*	20.49*q*

*Run at 67.89 MHz in $CDCl_3$ with TMS as internal standard. Unmarked signals are singlets.

† ‡Assignments are interchangeable.

§Run at 37.71 MHz.

$[\theta]_{305}$ −50 (neg max), $[\theta]_{262}$ −563 (neg min), $[\theta]_{247}$ 0, $[\theta]_{235}$ +1060 (max), $[\theta]_{228}$ 0, $[\theta]_{223}$ −4360 (last reading); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780, 1735 and 1650; MS *m/z* (%) 463 ($[M+H]^+$, 2.3), 462 ($[M]^+$, 2.8), 420 (3.6), 419 (2.9), 403 (3.3), 360 (2.1), 342 (2.0), 321 (3.8), 244 (19.0), 141 (93.6), 99 (32.2), 81 (100). [Calc. for $C_{24}H_{31}O_9$: MW + H, 463.1974; Calc. for $C_{24}H_{30}O_9$: MW, 462.1827. Found: MW + H (MS), 463.1980; MW: 462.1766.] ^{1}H and ^{13}C NMR spectra are listed in Tables 6 and 8.

Fractions 27–29 were combined and separated by prep. TLC (C_6H_6–EtOAc, 3:2, and $CHCl_3$–MeOH, 19:1) to give 1.4 g **2c**, 30 mg **2f**, 0.10 g **2g**, 1.2 g chapliatrin (**2a**) and 2.1 g isochapliatrin (**2b**). Properties of **2a** and **2b** have been reported [2]. Lactone **2f** was a gum; CD curve (MeOH) $[\theta]_{267}$ −617 (neg max), $[\theta]_{257}$ 0; $[\theta]_{236}$ +2940 (max), $[\theta]_{228}$ 0, $[\theta]_{213}$ −17700 (last reading); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3510, 1770, 1720 and 1650; MS *m/z* (%) 423 [M + H]$^+$, (4.2), 422 [M]$^+$, (1.1) 405 (3.9), 404 (1.9), 362 (1.8), 322 (12.3), 262 (8.3), 111 (19.3), 83 (100), 55 (93.5). [Calc. for $C_{22}H_{30}O_8$: MW, 422.1938. Found: MW (MS, peak matching), 422.1941.] The ^{1}H NMR spectrum is listed in Table 6. Lactone **2g** also was a gum; CD curve (MeOH) $[\theta]_{325}$ +254 (very broad max), $[\theta]_{293}$ 0, $[\theta]_{257}$ −693 (sh), $[\theta]_{233}$ −1210 (sh), $[\theta]_{207}$ −6840 (last reading); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3510, 1775, 1735 and 1655; MS *m/z* (%) 481 $[M^- + H]^+$, (2.0), 480 [M]$^+$, 01), 463 (1.4), 462 (0.5), 421 (1.0), 199 (26.2), 139 (28.2), 99 (63.8), 81 (41.5), 55 (38.4), 43 (100), [Calc. for $C_{24}H_{32}O_{10}$: MW, 480.1992. Found: MW (MS, peak matching), 480.1994.] ^{1}H and ^{13}C NMR spectra are listed in Tables 1 and 3.

Fractions 30–32 contained 2.0 g of a 1:1 mixture of **2a** and **2b**. Fractions 33–36 were combined and purified by prep. TLC ($CHCl_3$–MeOH, 19:1, 93:7 and 9:1) to give a small amount of **2a** and **2b**, 70 mg of **2d**, 50 mg of **2e** and 100 mg of **4**. Lactone **2d** was a gum $[\alpha]_D^{26}$ −50.2° (*c* 0.53, $CHCl_3$); CD curve (MeOH) $[\theta]$ −303 (neg. max), $[\theta]_{259}$ 0, $[\theta]_{231}$ +2650 (max), $[\theta]_{224}$ 0, $[\theta]_{208}$

-13400 (last reading); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3480, 1775, 1725 and 1650; MS m/z (%) 439 $[M+H]^+$, (1.4), 421 (2.5), 322 (20.0), 262 (14.5), 244 (8.8), 199 (16.3), 111 (37.5), 99 (100), 81 (69.3), 55 (63.1). [Calc. for $C_{22}H_{30}O_9$: MW, 438.1887. Found: MW (MS, peak matching), 438.1873.] ^1H and ^{13}C NMR spectra are listed in Tables 6 and 8. The ^1H NMR spectrum of **2e** is also listed; decomposition during processing of the ^{13}C NMR spectrum prevented determination of its IR and ^{13}C NMR spectra and the MS.

Lactone **4** was a gum whose ^1H and ^{13}C NMR spectra are listed in Tables 7 and 8; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 1790, 1740, 1720 and 1650; CD curve (MeOH), $[\theta]_{314}$ -140 (neg max), $[\theta]_{303}$ 0, $[\theta]_{271}$ $+765$ (max), $[\theta]_{255}$ 600 (min), $[\theta]_{236}$ $+2680$ (last reading); CD curve 4.5 hr after acidification with two drops HCl, $[\theta]_{340}$ -850 (neg max), $[\theta]_{331}$ -800 (sh), $[\theta]_{303}$ 0, $[\theta]_{278}$ $+530$ (max), $[\theta]_{258}$ $+380$ (min), $[\theta]_{240}$ $+775$ (last reading); CD 5 days after acidification $[\theta]_{340}$ -1800 (neg max), $[\theta]_{300}$ 0, $[\theta]_{283}$ $+320$ (max), $[\theta]_{259}$ $+145$ (min), $[\theta]_{243}$ $+1940$ (last reading); MS (NCI) m/z (%) 496 $[M]^+$, (100), 478 (13); MS(EI) m/z (%) 497 $[M+H]^+$, (0.2), 496 $[M]^+$, (0.3), 479 (0.4), 339 (3.1), 321 (4.6), 294 (9.9), 276 (4.8), 234 (13.9), 221 (17.1), 175 (11.8), 161 (12.9), 159 (14.9), 158 (18.4), 140 (33.4), 121 (77.9), 99 (100), 82 (95.0). The molecular ion was too weak to be detected by high resolution mass spectrometry.

Attempted application of Horeau's method. Reaction of 118.3 mg (0.246 mmol) **2a** with 278.1 mg α-phenylbutyric anhydride (0.897 mmol) in the usual manner [7] furnished 202.8 mg α-phenylbutyric anhydride which when dissolved in 5 ml $CHCl_3$ ($c = 4.06$) exhibited zero rotation.

X-Ray analysis of **2b**. Crystals of **2b** were monoclinic, space group $P2_1$, with $a = 16.358$ (7), $b = 19.912$ (10), $c = 7.435$ (4) Å, $\beta = 90.24$ (4)°, and $d_{calcd} = 1.318$ g/cm^3 for $Z = 4$ ($C_{24}H_{32}O_{10}$; $M = 480.51$). The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). The size of the crystal used for data collection was approximately 0.6 × 0.6 × 1.0 mm. A total of 3357 independent reflections were measured for $[\theta] < 57°$, of which 2917 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure [14] and was refined by block-diagonal least squares in which the matrix was partitioned into two blocks. In an attempt to account for disorder in the substituents at C-8 in both independent molecules, atoms O-9 and O-10 of the unprimed molecule and atoms C-26′ and O-10′ of the primed molecule were each refined as a pair of half-weighted atoms. In the final refinement, anisotropic thermal parameters were used for the non-hydrogen atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations but their parameters were not refined. The final discrepancy indices are $R = 0.082$ and $wR = 0.085$ for the 2917 observed reflections. The final difference map has no peaks greater than $\pm 0.4 eÅ^{-3}$.

REFERENCES

1. Herz, W. and Kulanthaivel, P. (1983) *Phytochemistry* **22**, 715.
2. Herz, W., Wahlberg, I., Stevens, C. S. and Kalyanaraman, P. S. (1975) *Phytochemistry* **14**, 1803.
3. Herz, W. and Sharma, R. P. (1976) *J. Org. Chem.* **41**, 1248.
4. McPhail, A. T. and Sim, G. A. (1973) *Tetrahedron* **29**, 1751.
5. Horeau, A. (1961) *Tetrahedron Letters* 506.
6. Horeau, A. (1962) *Tetrahedron Letters* 965.
7. Herz, W. and Kagan, H. (1967) *J. Org. Chem.* **32**, 216.
8. Samek, Z. and Buděšinský, M. (1979) *Collect. Czech. Chem. Commun.* **43**, 2444.
9. Moiseeva, G. P., Akhyev, B., Kasymov, Sh. Z. and Sidyakin G. P. (1973) *Khim. Prir. Soedin.* **9**, 167.
10. Moiseeva, G. P., Kasymov, Sh. Z., Yagudaev, M. R. and Sidyakin, G. P. (1980) *Khim. Prir. Soedin* **16**, 343.
11. Yamakawa, K. and Nishitani, K. (1978) *Chem. Pharm. Bull. (Tokyo)* **24**, 2810.
12. Hänsel, R., Kartharahardia, M., Huang, J.-T. and Bohlmann, F. (1980) *Phytochemistry* **19**, 857.
13. Herz, W. and Högenauer, G. (1962) *J. Org. Chem.* **27**, 905.
14. Germain, G., Main, P. and Woolfson, M. M. (1971) *Acta Crystallogr. Sect. A* **27**, 368.