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SESQUITERPENE LACTONES FROM *LIATRIS ACIDOTA*, *L. ASPERA* AND *L. MUCRONATA**

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Key Word Index—*Liatris acidota*; *L. aspera*; *L. mucronata*; Compositae; Eupatorieae; sesquiterpene lactones; heliangolides; germacradienolides; flavones; 3β-acetoxytaraxaster-20-en-30-aldehyde; benzofurans.

Abstract—Examination of *Liatris mucronata* gave the known 15-hydroxylated heliangolides liscundin, liscunditrin, punctaliatrin and two new closely related heliangolides. *Liatris acidota* furnished six new similar but 15-deoxygenated heliangolides as well as euparin and 3β-acetoxytaraxaster-20-en-30-aldehyde. *Liatris aspera* gave a known glycosidic germacradienolide and a new germacradienolide as well as several known flavones and a known benzofuran. Structures were established by spectroscopic methods and chemical transformations.

INTRODUCTION

As part of our study of *Liatris* species (Compositae, Eupatorieae) which elaborate a variety of cytotoxic and antileukemic sesquiterpene lactones [1–17] we have investigated *L. acidota*, *L. aspera* and *L. mucronata* and hereby report isolation of a number of new heliangolides and one new germacradienolide from these species in addition to known lactones, benzofurans and flavones and the triterpene 3β-acetoxytaraxaster-20-en-30-aldehyde.

RESULTS AND DISCUSSION

We begin with *Liatris mucronata* DC., which occurs chiefly in Texas and adjacent Oklahoma and Mexico [18], and gave in addition to plant sterol glycosides and triterpenes, mainly lupeol, the heliangolides **1a**–**1c**, **2a** (the major lactone constituent) and **2b**. Compounds **1a** and **1b** are liscundin and liscunditrin which were previously [10] isolated from *L. secunda* Ell. Their 270 MHz ^{1}H and ^{13}C NMR spectra are listed in Tables 1 and 2 as are those of **2b** (punctaliatrin) previously [4] found in *L. punctata* Hook.†

As is evident from inspection of Tables 1 and 2, **1c** differed from liscundin and liscunditrin only in the nature of the ester side chain and was in fact 5′-deacetylliscunditrin as shown by the lack of acetate signals, the upfield shift of the H-5′ signal in the ^{1}H NMR spectrum and the characteristic changes in the ^{13}C NMR spectrum. Likewise the nature of the side chain in **2a** became evident on comparing its ^{1}H and ^{13}C NMR spectra with those of punctaliatrin. The same side chain is found in eleganin (**1e**) from *Liatris elegans* (Walt.) Michx. [10] and *L. scabra* Willd. [12] and in the guaianolides graminiliatrin and deoxygraminiliatrin from *L. graminifolia* [7].‡

In each case the sequence of protons on the carbon skeleton was established by extensive decoupling. To permit a more facile distinction between the signals arising from H-15 and C-15 of the sesquiterpene nucleus and H-4′ and C-4′ (or H-5′ and C-5′) of the ester side chain, **1b**, **1c** and **2b** were oxidized with manganese dioxide to **3a**, **3b** and **4**; the selective attack on C-15 in the case of **1c** and **2b** is of interest. Hydrolysis of **1c** under mild conditions was difficult and gave a mixture containing some **1e** whose ^{1}H NMR spectrum is also listed in Table 1.

Liatris acidota Engelm. and A. Gray, which occurs in the coastal plain of Texas and Louisiana [18], gave a series of very similar heliangolides **1f**, **1g**, **2c** and **5**–**7** as well as euparin (**10**), the pseudotaraxasterol derivative, **11**, and mixtures of lupeol, taraxerol, lupenone and taraxerone. That **1f** and **1g** were 15-deoxy analogs of **1c** and **1e** was clear from the ^{1}H and ^{13}C NMR spectra given in Tables 1 and 2; **1f** and **1h** have recently been isolated from the very closely related *Hartwigia floridana* A. Gray [22]. Similarly, **2c** was the 15-deoxy derivative of punctaliatrin. In all these cases the broadened two-proton singlet of H-15 near δ4.3 was replaced by a vinylic methyl singlet near

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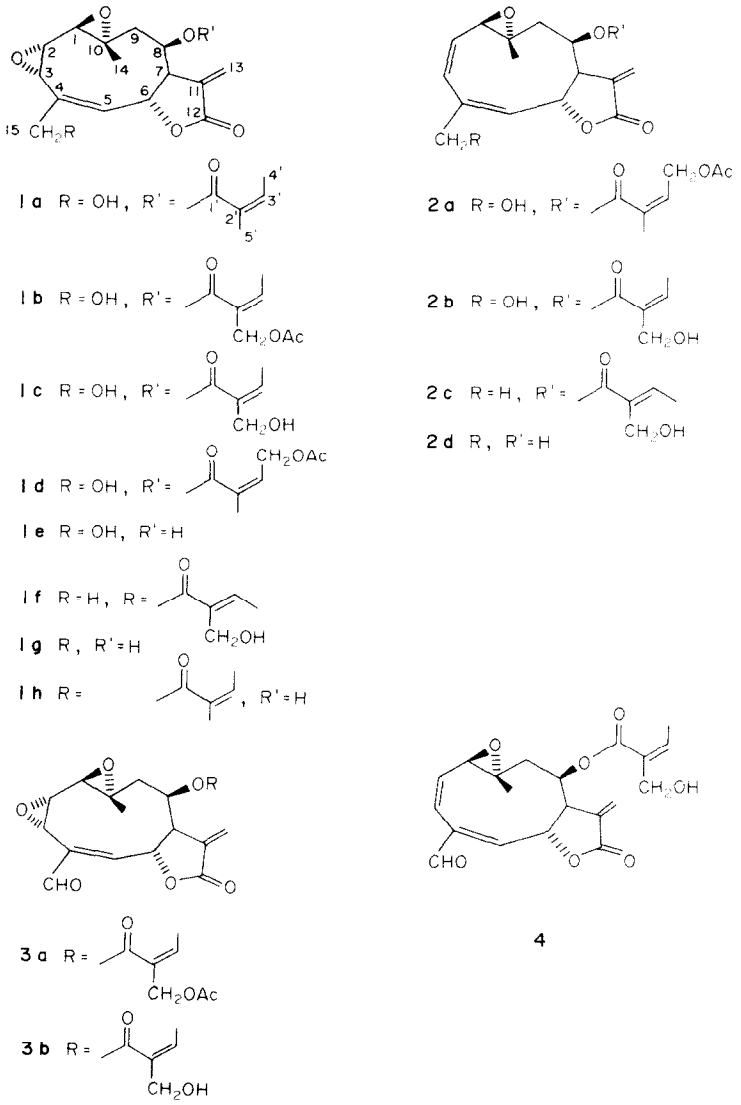
†As has been pointed out in a recent article [19] literature ^{13}C NMR spectral assignments for the methyl groups of the angelic ester side chain present in **1a** and many other sesquiterpene lactones are inconsistent. This was originally due to differences in the way the carbon atoms of the side chain were numbered, but as time went by this was overlooked in publications from our laboratory and resulted in misassignment of C-4′ and C-5′. That the quartet near δ20 is that of C-5′ (present numbering) and the one near δ16 that of C-4 as listed in Table 1 has been confirmed by selective decoupling experiments.

‡Ref. [19] also comments on a discrepancy in the ^{13}C NMR spectra reported for this side chain by us [20] and others [21]. As the values reported by us are fully in accord with expectations for the *Z*-stereochemistry shown in **2a**, as the *Z*-stereochemistry of the ester side chain is also borne out by the chemical shift of H-3′ (near δ6.9 in the *E*-isomer) and as irradiation at the frequency of H-5′ collapses the methyl quartet near δ19 (C-5′) to a singlet, we are unable to explain the conclusions of the Japanese authors [20] about the nature of the side chain in eupalinin B and D.



δ1.9 broadened by coupling to H-5 and H-6; appropriate alterations in the ^{13}C NMR spectra were also observed. Lactones **5** and **7** (Tables 3 and 4) were 11,13-dihydro derivatives of **2d** and **1g**, respectively; assignments in the ^{1}H and ^{13}C NMR spectra of **7** were clarified by decoupling and oxidation (Jones' reagent) to **8**. The C-11 stereochemistry assigned to **5**, **7** and **8** is based on the small value of $J_{7,11}$ (2.5Hz) which required pseudoequatorial (or α if the absolute configuration is as depicted in the formulae) orientation of the C-11 methyl group (model).

Lactone **6** was a chlorohydrin (MS) formally derived from 2c by addition of hydrochloric acid to the 11,13-double bond as evidenced by the ^{1}H NMR spectrum (Table 3). The chemical shift of H-13 indicated that the halogen was on C-13. Conceivably **6** is an artefact arising by ring opening, during the extraction procedure, of an intermediate 11,13-epoxide, **9**. The latter was prepared in low yield by exposure of **6** to basic alumina; its ^{1}H NMR spectrum is also listed in Table 3.

The C-11 stereochemistry, shown in formula **6**, is based on the following arguments. In the aliphatic region of the ^{13}C NMR spectrum (Table 4), **6** exhibited three triplets at δ54.00, 45.43 and 40.89, the last triplet being assignable to C-9 by comparison with other lactones of this series. The triplet at δ54.00 could be assigned to C-5′ of the ester side chain by comparison with **1c**, **1f**, **2b** and **2c** and by selective decoupling through irradiation at the frequency of H-5′. Hence the triplet at δ45.43 was that of C-13 and was appreciably upfield ($ca\Delta\delta$10) from its location in the spectra of compounds with similar functionality. The upfield shift can be ascribed to β-orientation of the $-CH_2Cl$ group which would place it within the shielding zone of the ester carbonyl on C-8; on the other hand the upfield shift of C-8 relative to C-8 of **3** seems to be characteristic of compounds carrying a C-11 substituent. α-Orientation of the 11-hydroxyl, which brings it into close proximity to H-5 (model), can also be invoked to explain the unusual chemical shift of H-5 (δ6.13), particularly as conversion of **6** to **9** results in restoration of the normal H-5 frequency.

Triterpene aldehyde **11**, $C_{32}H_5O_3$, was obtained in small amount from the non-polar fraction of the extract of *L. acidota*. The ^{1}H NMR spectrum in conjunction with the mass spectrum (see Experimental) indicated the presence of partial structure $-C(CHO)=CH-CH_2-$ and an equatorially oriented acetate at C-3 of a pentacyclic

Table 1. ^{1}H NMR spectra of 1–4*

H No.	1a	1b	1c	1e†	1f	1g†	2a	2b	2c	3a	3b‡	4
1	2.54 *d* (8.5)	2.57 *d*	2.56 *d*	2.52 *d*	2.56 *d*	2.51 *d*	3.26 *br d* (7.5)	3.27 *d*	3.28 *br d*	2.44 *d* (8.5)	2.46 *d*	3.14 *d* (7.5)
2	3.11 *dd* (8.5, 4)	3.12 *dd*	3.13 *dd*	3.12 *dd*	3.12 *dd*	3.13 *dd*	5.69 *dd* (12, 7.5)	5.70 *dd*	5.55 *dd*	3.14 *dd* (8.5, 4)	3.14 *dd*	5.87 *dd* (11, 7.5)
3	3.69 *br d* (4)	3.70 *br d*	3.70 *br d*	3.69 *br d*	3.58 *br d*	3.56 *br d*	6.12 *br d* (12)	6.17 *br d*	6.14 *br d*	3.88 *dd* (4, 1)	3.86 *dd*	6.32 *d* (11)
5	5.59 *br d* (10.5)	5.59 *br d*	5.60 *br d*	5.59 *br d*	5.27 *br d* (11)	5.24 *br d*	5.60 *br d* (10.5)	5.61 *br d*	5.31 *br d* (11)	6.32 *dd* (10.5, 1)	6.34 *dd*	6.53 *dd* (10.5, 1)
6	5.46 *br d* (10.5)	5.44 *br d*	5.49 *br d*	5.45 *br d*	5.47 *br d* (11)	5.39 *br d*	5.14 *br d* (10.5)	5.15 *br d*	5.13 *dd* (11, 1)	5.61 *dd* (10.5, 1)	5.64 *dd*	5.33 *dd* (10.5, 1)
7	2.87 *m* (1.5, 1.5, 1)	2.94 *m*	2.95 *m*	2.69 *m*	2.85 *m*	2.65 *m*	3.01 *m*	3.04 *m*	2.98 *m*	3.01 *m* (1.8, 1.5, 1)	3.05 *m*	3.19 *m* (1.5, 1, 1)
8	5.19 *m* (4, 2, 1)	5.29 *m*	5.22 *m*	4.07 *m*	5.17 *m*	4.06 *m*	5.22 *m*	5.26 *m*	5.21 *m*	5.37 *m* (4, 2.5, 1)	5.28 *m*	5.34 *m* (4, 2, 1)
9a	2.81 *dd* (15, 4)	2.83 *dd*	2.86 *dd*	2.54 *dd*	2.87 (14.5, 4.5)	2.55 *dd*	2.78 *dd* (15, 4)	2.85 *dd*	2.85 *dd* (14.5, 4.5)	2.86 *dd* (15, 4)	2.90 *dd*	2.88 *dd*
9b	1.37 *dd* (15, 2)	1.44 *dd*	1.42 *dd*	1.27 *br d*	1.39 *dd* (14.5, 2)	1.28 *br dd*	1.37 *dd* (0.5, 2)	1.40 *dd*	1.39 *br dd* (14.5, 2)	1.45 *br dd* (15, 2.5)	1.44 *br dd*	1.46 *dd* (15, 2)
13a	6.40 *d* (1.5)	6.41 *d*	6.41 *br*	6.36 *br*	6.39 *d*	6.37 *d*	6.40 *d*	6.41 *br*	6.39 *d*	6.52 *d* (1.8)	6.50 *d*	6.51 *d*
13b	5.82 *d* (1.57)	5.86 *d*	5.83 *br*	5.74 *br*	5.81 *d*	5.72 *d*	5.82 *d*	5.86 *d*	5.81 *d*	5.95 *d*	5.95 *d*	5.96 *d*
14§	1.57 *br*	1.61 *br*	1.59 *br*	1.71 *br*	1.56 *br*	1.71 *br*	1.38 *br*	1.38 *br*	1.38 *br*	1.38 *br*	1.64 *br*	1.44 *br*
15	4.31 *br*‖	4.30 *br*‖	4.28¶	4.24¶	1.97 *br*§	1.93 *br*§	4.16 *br*‖	4.16 *br*‖	1.89 *br*§	9.66	9.60	9.56
3′	6.14 *br q* (7)	6.56 *q*	6.44 *q*	—	6.98 *q*	—	6.04 *br t* (5.5)	6.40 *q* (7)	6.93 *q*	6.59 *q*	6.47 *q*	6.44 *q*
4′	1.97 *br d*§ (7)	2.10 *d*§	2.04 *d*	—	1.93 *d*	—	4.99¶	2.01 *d* (7)	1.90 *d*	2.11 *d*	2.06 *d*	2.04 *d*§
5′	1.84 *br*§	4.67¶	4.19¶	—	4.33¶	—	1.84 *br*	4.17¶	4.32¶	4.21¶	4.21¶	4.18¶
Ac	—	2.06	—				2.04			2.07		

*Run at 270 MHz in $CDCl_3$ unless otherwise specified. Unmarked signals are singlets. Frequencies in δ-values downfield from TMS as internal standard. Coupling constants (Hz) (in parentheses) are not given if they correspond to those in preceding column.

†Run in $CDCl_3$ with DMSO-d_6 and a little H_2O.

‡Run in $CDCl_3$ with two drops of DMSO-d_6.

§Intensity three protons.

‖Intensity two protons.

¶Center of AB system.

Table 2. ^{13}C NMR spectra of **1** and **2***

C No.	1a	1b	1c	1f	1g†	2a	2b	2c
1	61.53 *d*‡	61.44 *d*	61.53 *d*	61.67 *d*	60.78 *d*	60.36 *d*‡	60.42 *d*	60.38 *d*
2	55.08 *d*‡	55.00 *d*	55.16 *d*	56.34 *d*	56.07 *d*	131.24 *d*‡	131.32 *d*	132.25 *d*
3	51.73 *d*‡	51.69 *d*	51.73 *d*	53.78 *d*	53.48 *d*	128.63 *d*‡	128.57 *d*	128.42 *d*
4	135.98§	135.97§	136.33	133.68	131.25	139.33	139.49	137.21§
5	124.97*d*	124.80 *d*	124.65 *d*	125.75 *d*	126.59 *d*	124.73 *d*‡	124.54 *d*	125.95 *d*
6	74.64 *d*‡	74.51 *d*	74.89 *d*	75.03 *d*	74.56 *d*	75.31 *d*‡	75.59 *d*	75.93 *d*
7	49.38 *d*	49.25 *d*	49.39 *d*	49.72 *d*	49.96 *d*	50.12 *d*‡	50.15 *d*	50.44 *d*
8	74.93 *d*‡	75.36 *d*	75.65 *d*	76.08 *d*	73.31 *d*‡	77.69 *d*‡	77.68 *d*	78.02 *d*
9	42.47 *d*	42.53 *t*	42.44 *t*	42.47 *t*	45.25 *t*	42.82 *t*	42.82 *t*	42.83 *t*
10	56.68	56.53	56.68	56.50	57.59	61.45	61.58	61.28
11	136.41§	136.19§	136.33	136.45	139.59	136.93	136.99	136.19§
12	169.07	168.83	169.51	168.99	169.56	169.19	169.70	169.25
13	125.63 *t*	125.78 *t*	125.96 *t*	125.50 *t*	122.54 *t*	125.33 *t*	125.22 *t*	124.94 *t*
14	19.85 *q*	19.87 *q*	19.80 *q*	19.97 *q*	20.10 *q*‡	19.67 *q*‡	19.59 *q*	19.70 *q*
15	63.88 *t*	63.75 *t*	63.88 *t*§	21.57 *q*	20.95 *q*‡	65.32 *t*‡	65.24 *t*	23.73 *q*
1′	166.05	164.38	165.37	165.99	—	165.20	165.40	166.06
2′	126.40	126.48	130.86	131.39	—	127.40	130.91	131.38
3′	141.21 *d*	142.63 *d*	147.78 *d*	142.89	—	141.40 *d*	142.50	142.71 *d*
4′	15.78 *q*‡	15.63 *q*	15.78 *q*	14.60 *q*	—	62.86 *t*	15.60 *q*	14.60 *q*
5′	20.24 *q*	64.98 *t*	63.80 *t*§	56.56 *t*	—	19.40 *q*‡	64.01 *t*	56.62 *t*
1″	—	170.74	—	—	—	170.71	—	—
2″	—	20.93 *q*	—	—	—	20.87 *q*	—	—

*Run at 67.89 MHz in $CDCl_3$ unless specified otherwise. Unmarked signals are singlets. Frequencies in δ-values downfield from TMS as internal standard.

†Run in DMSO-d_6.

‡Assignment by selective decoupling at frequency of appropriate proton.

§Assignments may be interchanged.

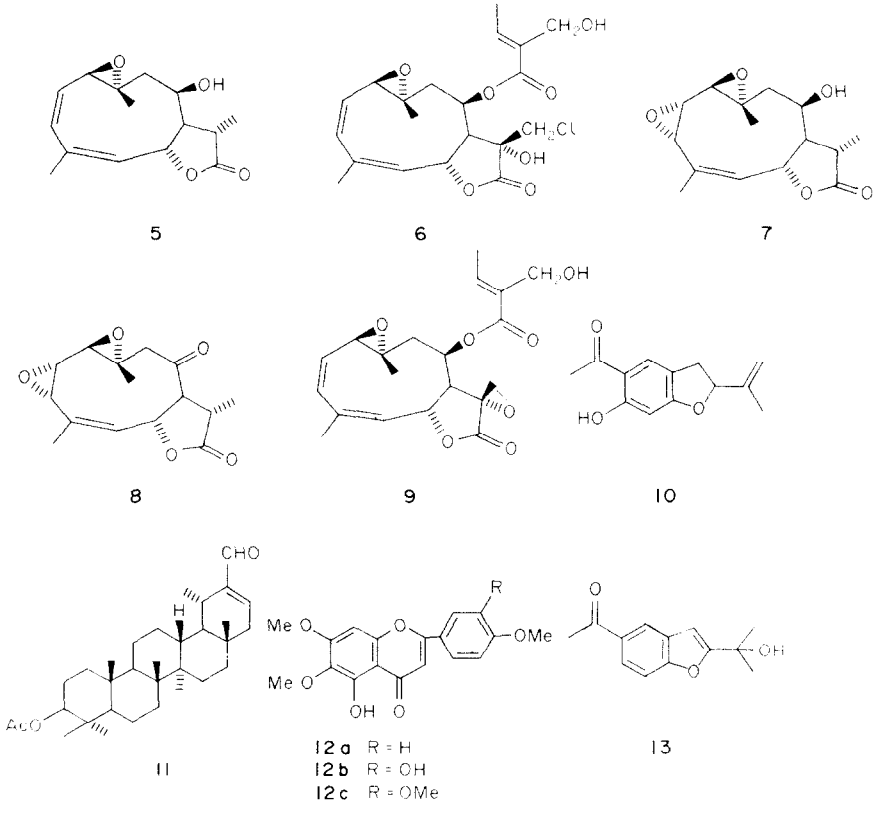


Table 3. ^{1}H NMR spectra of **5–9***

H No.	5	6†	7†	8	9
1	3.24 *br d* (7.5)	3.32 *br d*	2.51 *d* (8.5)	2.85 *d*	3.26 *br d* (7.5)
2	5.52 *dd* (12, 7.5)	5.52 *dd*	3.12 *dd* (8.5, 4)	3.10 *dd*	5.56 *dd* (12, 7.5)
3	6.08 *br d* (12)	6.06 *br d*	3.53 *br d* (4)	3.56 *br d*	6.17 *br d* (12)
5	5.44 *br d* (11)	6.13 *br d*	5.42 *br d*	5.46 *br d*	5.58 *br d*
6	4.98 *dd* (11, 1)	5.17 *br d*	5.28 *br d*	4.99 *dd*	5.30 *br d*
7	2.02 *m* (2, 1, 1)	2.50 *br*	1.87 *m*	2.96 *dd*	2.29
8	4.11 *m* (4, 2, 1)	5.48 *m*	3.97 *m*	—	5.37 *m*
9a	2.47 *dd* (15, 4)	2.91 *dd*	2.51 *dd*	3.09 *d* (11)	2.80 *dd* (15, 4)
9b	1.25 *br d* (15, 2)	1.33 *br dd*	1.21 *br dd*	2.39 *br d* (11)	1.32 *br dd* (15, 2)
11	2.61 *dq* (2, 7.5)	—	2.62 *dq* (2.5, 7.5)	3.22 *dq*	—
13	1.49 *d* (7.5)	3.66 §	1.44 *d* (7.5)	1.42 *d*	3.26 §
14‡	1.50 *br*	1.31 *br*	1.69 *br*	1.50 *br*	1.41 *br*
15‡	1.89 *br*	1.91 *br*	1.96 *br*	2.00 *br*	1.94 *br*
3′	—	6.94 *q* (7)	—	—	6.96 *q*
4′	—	1.92 *d* (7)	—	—	1.93 *d*
5′	—	4.30 §	—	—	4.34 §

*Conditions are the same as those given in Table 1.
† Run in $CDCl_3$ with two drops of DMSO-d_6.
‡Intensity three protons.
§Center of AB system.

Table 4. ^{13}C NMR spectra of **5–8***

C No.	5	6†	7‡	8
1	60.53 *d*	59.90 *d*	60.91 *q*	61.54 *d*
2	131.72 *d*	131.50 *d*	55.93 *d*	55.87 *d*
3	128.50 *d*	128.64 *d*	53.62 *d*	50.31 *d*
4	135.37	135.13	131.14	134.27
5	127.40 *d*	126.60 *d*	127.55 *d*	126.62 *d*
6	77.03 *d*	76.85 *d*‡	75.57 *d*‡	75.49 *d*
7	54.20 *d*	52.82 *d*	51.81 *d*	59.81 *d*
8	73.81 *d*	70.64 *d*‡	70.47 *d*‡	203.20
9	46.38 *t*	40.89 *t*	44.81 *t*	55.19 *t*
10	62.07	60.61	57.51	56.33
11	42.73 *d*	75.25	41.03 *d*	36.01 *d*
12	180.41	173.95	179.53	177.86
13	18.65 *q*	45.43 *t*	17.82 *q*	17.48 *q*§
14	20.27 *q*	23.62 *q*	20.08 *q*‡	17.33 *q*§
15	24.04 *q*	23.62 *q*	21.12 *q*‡	21.66 *q*
1′	—	165.11	—	—
2′	—	132.18	—	—
3′	—	141.99 *d*	—	—
4′	—	14.27 *q*	—	—
5′	—	54.00 *t*‡	—	
—				

*Conditions are the same as those given in Table 2.
† Run in DMSO-d_6.
‡Assignments by selective decoupling at frequency of appropriate proton.
§Assignments may be interchanged.

triterpene skeleton carrying six methyl singlets and a methyl doublet. A logical structure satisfying these requirements and the ^{13}C NMR spectrum (Table 5) was the pseudotaraxasterane derivative, **11**, which has been prepared recently by oxidation of taraxasterol acetate [23], but is new as a natural product. Repetition of the oxidation produced material identical with the substance from *L. acidota*.

Table 5. ^{13}C NMR spectrum of **11***

C No.		C No.	
1	38.48 *t*	17	34.82
2	23.71 *t*	18	48.28 *d*
3	80.96 *d*	19	29.43 *d*
4	37.82	20	148.51
5	55.44 *d*	21	148.96 *d*
6	18.20 *t*	22	36.51 *t*
7	34.19 *t*	23	27.95 *q*
8	41.09	24	16.50 *q*
9	50.36 *d*	25	16.00 *q*
10	37.06	26	16.33 *q*
11	21.48 *t*	27	14.70 *q*
12	27.28 *t*	28	23.17 *q*
13	39.06 *d*	29	17.51 *q*
14	42.30	30	193.89 *d*
15	26.91 *t*	31	170.94
16	43.03 *t*	32	21.28 *q*

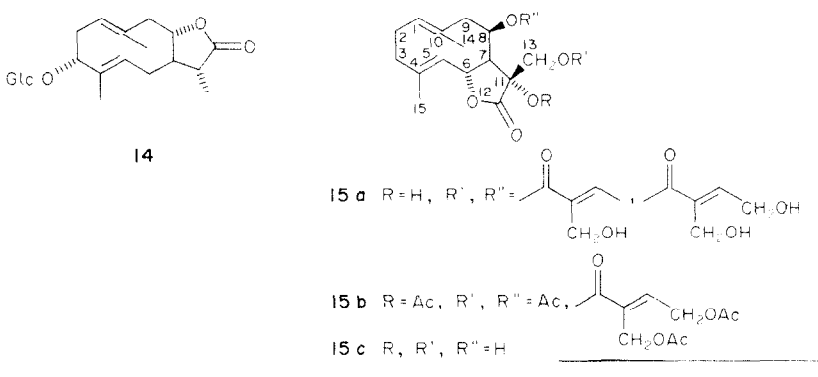
*Conditions specified in Table 2 apply. Assignments by comparison with spectra of taraxasterol and taraxasterol acetate. Our assignments for these compounds differ somewhat from those reported recently [29] due to errors in the multiplicities ascribed to several signals [Herz, W. and Watanabe, K., unpublished].

A Louisiana collection of *L. aspera* Michx. which is widely distributed in central and eastern U.S.A. [18] furnished the known substances salvigenin (**12a**), eupatorin (**12b**), 5-hydroxy-6,7,3',4'-tetramethoxyflavone (**12c**), the benzofuran **13**, a mixture of taraxasteryl and lupeyl acetates, taraxasterol and lupeol, plant sterol glycosides and a germacradienolide, **14**, previously encountered [24] in *Eupatorium altissimum* L.

Lactone **15a** was new; presence of the germacradienolide skeleton was indicated by the NMR spectra of **15a**, an acetate **15b** formed in very low yield under the usual acetylation conditions, but with displacement of the *cis*-sarracenyl moiety, and the hydrolysis product **15c** (Table 6) and was confirmed in the usual way by spin decoupling which established the sequences H-1 through H-3 and H-5 through H-9. Analysis of the ^1H NMR spectra of **15(a–c)** and the ^{13}C NMR spectrum of **15a** (Table 7) also revealed that C-8 and C-13 carried acyl functions. The AB system of H-13a,b, centered near δ4.2, and the broadened doublet of H-8 near δ 5.6 in **15a** and **15b** experienced significant diamagnetic shifts on hydrolysis to **15c**. The multiplicity of H-7 and H-13a,b demonstrated that the hydroxyl group, whose presence was indicated by the IR spectrum, was located on C-11. The nature of the two acyl functions of **15a** was also clear from the spectroscopic evidence; however, their distribution over C-8 and C-13 remains uncertain as attempts at selective hydrolysis failed. The relatively facile displacement of the *cis*-sarracenyl residue by acetate under the usual acetylation conditions to form **15b** suggests that it esterifies the C-11 rather than the C-8 hydroxyl group.

The stereochemistry of the groups attached to the 10-membered ring of **15a** is defined by the coupling constants involving H-5 through H-9 which are consonant with a *trans*-lactone and a C-8 acyl group *cis* to the C-7 side chain. The C-11 stereochemistry is apparent from the significant downfield shift of H-7 ($\Delta\delta$ 0.63), on conversion of **15a** to **15b**, which can be rationalized only if the hydroxyl group is *cis* to H-7 (model). The absolute configuration is as shown because as in costunolide and other *trans*, *trans*-germacra-1(10),4-dienolides of established absolute configuration, interaction between the double bonds in the 10-membered ring gives rise to a strongly positive Cotton effect below 215 nm [25].

The taxonomically difficult genus *Liatris* [18] also presents a rather confusing picture if viewed in the light of its sesquiterpene lactone chemistry. Of the 20 species examined so far (21 if the closely related *Hartwigia floridana* is included) five, *L. graminifolora* [7], *pycnostachya* [7], *spicata* [7], *squarrosa* [17] and *tenuifolia* [12], furnished identical, or very similar, guaianolides as major lactone constituents.* Seven (*L. acidota* and *mucronata* (present work), *elegans* [10], *punctata* [4], *scabra* [12], *secunda* [10] and *H. floridana* [22]) gave identical, or very similar heliangolides of type **1** or **2** and three others (*L. cylindracea* [14], *platylepis* [15]† and *provincialis* [4]‡) produced very similar heliangolides of a different type.



*L. *tenuifolia* also contained lactones found in *L. chapmanii* and *gracilis*.

†This species is not recognized by Gaiser.

‡This species was identified [26] subsequent to Gaiser's treatment.

Table 6. ^{1}H NMR spectra of **15(a–c)***

H No.	**15a**	**15b**	**15c**
1	4.90 *br dd* (10.5, 3)	4.89 *br dd*	4.77 *br dd*
2a	‡	‖	2.32 *m*
2b	‡	‖	2.18 *m*
3a	‡	‖	2.28 *m*
3b	‡	‖	2.04 *dt* (12, 6)
5	4.79 *br d* (10)	4.89 *br d*	4.69 *br d*
6	5.48 *t* (10)	5.32 *t*	5.29 (*t*)
7	2.59 *d* (9.5)	3.23 *d*	2.36 *d*
8	5.64 *br d* (5.5)	5.62 *br d*	4.59 *br d*
9a	2.88 *dd* (14, 5.5)	2.93 *dd*	2.65 *dd*
9b	‡	‖	2.18 *br d* (5.5)
13	4.25 (12)	4.25 (12)	3.88 (12)
14†	1.42 *br*	1.45 *br*	1.61 *br*
15	1.73 *br*	1.73 *br*	1.66 *br*
3′	6.86 *t* (6)	6.73 *t*	—
4′	§	4.77	—
5′	§	4.89	—
3″	7.00 *q* (7)	6.73 *t*	—
4″	1.91 *d* (7)	2.17, 2.09, 2.02, 1.92¶	—
5″	§	—	—

*Conditions specified in Table 1 apply.
†Intensity three protons.
‡In complex five-proton multiplet from δ2.06–2.44.
§In complex six-proton multiplet from δ4.14–4.46.
‖In complex five-proton multiplet from δ1.94–2.44. Center of AB system.
¶Acetate methyls.

Table 7. ^{13}C NMR spectrum of **15a***

C No.		C No.	
1	127.66 *d*	14	19.12 *q*
2	25.77 *t*	15	16.89 *q*
3	39.12 *t*	1′	166.61
4	141.70	2′	131.18†
5	131.25 *d*	3′	144.09 *d*‡
6	74.75 *d*	4′	14.60 *q*
7	57.97 *d*	5′	55.71 *t*§
8	71.26 *d*	1″	165.36
9	44.02 *t*	2″	131.01‡
10	132.53	3″	145.56 *d*‡
11	76.12	4″	58.47 *t*
12	176.20	5″	56.47 *t*§
13	64.80 *t*		

*Conditions specified in Table 2 apply.
§, †, ‡Assignments with similar signs may be interchanged.

The sesquiterpene lactone chemistry of *L. chapmanii* [1, 11] and *gracilis* [11] appears to be somewhat similar and differs from that of *L. aspera*, treated in the present report, which elaborates small amounts of germacradienolides. Finally, *L. earlei* [12], *L. pauciflora* [12] and *L. scariosa* [16] gave no identifiable lactones. Aside from the work on *L. mucronata* and *L. punctata*, *these results cannot be fitted satisfactorily into Gaiser's treatment [18] of the genus. Further taxonomic and chemical studies are clearly needed.

*The suggestion has been made [27] that *L. mucronata* should be treated as a variety of *L. punctata*.

EXPERIMENTAL

Extraction of Liatris mucronata. Aerial parts of *L. mucronata* DC., wt 5.8 kg, collected by D. Gage and J. Gershenzon on 26 Oct. 1980, on the north side of Texas Highway 71, 5 miles west of the Pedernales River, Burnet Co., Texas (voucher on deposit in Herbarium of University of Texas) was extracted with $CHCl_3$ and worked-up in the usual manner [28]. The crude gum (150 g) was preadsorbed on 150 g silicic acid (Mallinckrodt 100 mesh) and chromatographed over 1 kg silicic acid set in C_6H_6–$CHCl_3$ (1:1). Fractions were collected as follows: 1–12 ($CHCl_3$–C_6H_6, 7:1, 6 l.); 13–20 ($CHCl_3$, 4 l.); 21–28 ($CHCl_3$–MeOH, 99:1, 4 l.); 29–48 ($CHCl_3$–MeOH, 49:1, 10 l.) and 49–58 ($CHCl_3$–MeOH, 19:1, 5 l.).

Fractions 5–8 (15 g) gave a mixture of triterpenes, the major one being identified as lupeol. Fraction 32 (650 mg) contained two major constituents which were separated by TLC (Et_2O–MeOH, 19:1). The upper band yielded gummy **1a** [10] (90 mg). The ^{1}H and ^{13}C NMR spectra are listed in Tables 1 and 2. The lower band gave **2a** (110 mg) which was recrystallized from EtOAc–hexane, mp 140–141°, CD curve (MeOH) $[\theta]_{220}$ −12800. [Calc. for $C_{22}H_{26}O_8$: MW, 418.1628. Found. MW (MS), 418.1628.] The low resolution MS had significant peaks at *m/z* (%) 418 (very weak), 359 (1), 277 (4), 260 (5) and 99 (100). ^{1}H and ^{13}C NMR spectra are given in Tables 1 and 2. Fractions 33–36 (11 g) contained predominantly **2a**.

Fraction 37 exhibited one major spot on TLC; purification by prep. TLC (Et_2O–MeOH, 19:1) gave 1.3 g of gummy **1b** [10] whose ^{1}H and ^{13}C NMR are listed in Tables 1 and 2. Fraction 39

(12 g) showed one major spot on TLC; purification of 150 mg of the crude fraction by TLC ($CHCl_3$–MeOH–EtOAc, 7:1:2) and crystallization from EtOAc–hexane gave needles of punctaliatrin (**2b**) [4] whose ^1H and ^{13}C NMR are listed in Tables 1 and 2. Fractions 42–45 (10 g) which showed mainly one spot were combined. Purification of 100 mg of this material by TLC ($CHCl_3$–MeOH–EtOAc, 17:1:2, developed twice) gave 60 mg of gummy **1c**, CD curve (MeOH) $[\theta]_{238}$ + 540. The low resolution MS showed no peak corresponding to M^+ and only a very weak peak for $[M+1]^+$. Other significant peaks were at *m/z* (%) 277 (1), 259 (2), 99 (100) and 81 (69). The ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

Fraction 55 on trituration with MeOH gave 135 mg of a mixture of sitosterol- and stigmasterol β-D-glucosides which was characterized by preparation of the tetra-acetates and comparison with the ^1H NMR spectra of authentic samples of the tetra-acetates.

Oxidations of **1b**, **1b** *and* **2b**. Solns of 100 mg **1b** or **1c** in 5ml $CHCl_3$ were oxidized with active MnO_2 in the manner described for eleganin [10]. Filtration followed by the usual work-up afforded 45 mg **3a** and **3b**, respectively, **3b** being considerably more polar than **3a**. The ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2. Oxidation of 200 mg of **2b** in the same way gave 95 mg **4** after purification by TLC. The ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

Hydrolysis of **1c**. A soln of 0.15 g **1c** in 3 ml dioxane and some H_2O containing 0.15 g K_2CO_3 was stirred at room temp. for 10 days, diluted with H_2O and extracted with EtOAc. Evaporation of solvent gave a residue whose ^1H NMR spectrum showed it to be a 2:1 mixture of **1c** and **1e**. The spectrum of the latter is listed in Table 1.

Extraction of Liatris acidota. Aerial parts of *L. acidota* Engelm. and A. Gray, wt 4.9 kg, collected by Dr. R. K. Godfrey and Mr. D. Gage on 30 Aug. 1979, 13 miles SE. of Oakdale, Evangeline Parish, Louisiana (Godfrey No. 77194 on deposit in the Herbarium of Florida State University) was extracted with $CHCl_3$ and worked-up in the usual manner [28]. The crude gum (63 g) was preadsorbed on 70 g silicic acid and chromatographed on 750 g of the same adsorbent packed in C_6H_6. Fractions were collected as follows: 1–8 (C_6H_6, 4 l.), 9–14 (C_6H_6–$CHCl_3$, 1:1, 3 l.); 15–20 ($CHCl_3$, 3 l.); 21–26 ($CHCl_3$–MeOH, 99:1, 3 l.); 27–32 ($CHCl_3$–MeOH, 41:1, 3 l.) and 33–40 ($CHCl_3$–MeOH, 19:1, 4 l.).

Purification of fraction 4 (175 mg) by TLC (C_6H_6–EtOAc, 19:1) gave two bands. The less polar material (35 mg) was identified as euparin (**10**) by direct comparison. The more polar material was a mixture of lupenone and taraxerone. Fraction 11 (710 mg) on purification by TLC (C_6H_6–EtOAc, 9:1) yielded a mixture of lupeol and taraxerol. Fraction 20 (220 mg) contained several substances (TLC). Purification by TLC with the solvent system C_6H_6–EtOAc (19:1) twice and crystallization from hexane furnished 3β-acetoxytaraxaster-20-en-30-aldehyde (**11**) (25 mg) which melted unsharply at 240–256° (lit. mp 258–260° [23]). Further crystallization from hexane did not improve the mp. The IR spectrum (KBr) had bands at 1735, 1690, 1645 cm^{-1}; the ^1H NMR spectrum ($CDCl_3$, 270 MHz) exhibited signals at δ9.39 (H-30), 6.70 (*dd*, *J* = 6, 3 Hz, H-21), 4.49 (*m*, H-3α), 2.27 (*br t*, *J* = 8 Hz, H-22), 2.05 (Ac), 1.04, 0.97, 0.88, 0.86, 0.85 and 0.67 (H-23–H-28), 1.03 (*d*, *J* = 7 Hz, H-29). The ^{13}C NMR spectrum is listed in Table 5. [Calc. for $C_{32}H_{50}O_3$: MW, 482.3759. Found: MW (MS), 482.3707.] Other significant peaks in the high resolution MS were at *m/z* (composition, %) 422 ($C_{30}H_{46}O$, 27.6), 407 ($C_{29}H_{43}O$, 12.2), 249 ($C_{16}H_{25}O_2$, 0.6) and 189 ($C_{14}H_{21}$, 73.3). The substance was identical in all respects (TLC, IR, ^1H NMR) with material prepared by oxidation of 10 mg taraxasteryl acetate in 5 ml Me_2CO–C_6H_6 (1:1) with 0.2 ml Jones' reagent for 8 hr at room temp. followed by the usual work-up and purification by TLC [23].

Fraction 26 (7 g) showed many spots on TLC. Purification of 0.5 g by TLC ($CHCl_3$–MeOH–EtOAc, 8:1:1) gave only one homogeneous fraction. Repurification by TLC using the same solvent mixture gave **2c** (55 mg) as a gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765, 1705; CD curve (MeOH); $[\theta]_{231}$ − 80 200 (last reading). [Calc. for $C_{20}H_{24}O_6$: MW, 360.1573. Found: MW (MS), 360.1567.] Other significant ions in the low resolution MS were at *m/z* (%) 244 (5), 99 (100) and 81 (50). ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

Fraction 27 (3 g) showed one predominant spot. Purification by TLC ($CHCl_3$–MeOH–EtOAc, 18:1:1, two developments) afforded pure **1f** as a gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765, 1705; CD curve (MeOH), $[\theta]_{236}$ + 7160. [Calc. for $C_{20}H_{24}O_5$: MW, 376.1522. Found: MW (MS), 376.1516.] ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

Purification of fraction 29 (270 mg) by TLC ($CHCl_3$–MeOH EtOAc, 8:1:1, two developments) and crystallization from EtOAc gave **5** (95 mg), mp 195–198°, IR ν_{max}^{KBr} cm^{-1}: 3425, 1755; CD curve (MeOH), $[\theta]_{232}$ − 34 000 (last reading). [Calc. for $C_{15}H_{20}O_4$: MW, 264, 1361. Found: MW (MS) 264, 1356.] ^1H and ^{13}C NMR spectra are listed in Tables 3 and 4.

Fraction 30 on trituration with Et_2O afforded 210 mg of solid. Purification by TLC ($CHCl_3$–MeOH–EtOAc, 7:1:2 once and $CHCl_3$–MeOH–EtOAc, 5:2:3 twice) permitted isolation of crystalline **6** (60 mg) and **1g** (125 mg). The former was recrystallized from EtOAc, mp 222–225° (dec); IR ν_{max}^{KBr} cm^{-1}: 3425, 1770, 1710; CD curve (MeOH) $[\theta]_{272}$ + 159, $[\theta]_{232}$ − 70 900 (last reading). [Calc. for $C_{20}H_{25}O_7{}^{35}Cl$ and $C_{20}H_{25}O_7{}^{37}Cl$: MW, 412.1289 and 414.1259. Found: MW (MS), 412.1383 and 414.1237.] Other significant peaks in the low resolution MS were at *m/z* (%) 296 (2.3), 99 (100) and 81 (53.6). The ^1H and ^{13}C NMR spectra are listed in Tables 3 and 4.

Compound **1g** was recrystallized from EtOAc–MeOH, mp 240–243° (dec); IR ν_{max}^{KBr} cm^{-1}: 3475, 1750; CD curve (MeOH), $[\theta]_{260}$ + 1640, $[\theta]_{226}$ − 22 300 (last reading). The low resolution MS exhibited only a very weak peak for $[M+1]^+$ at *m/z* 279 (0.01 %). ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

Fraction 32 on trituration with Et_2O gave solid **7** (210 mg) which was recrystallized from MeOH, mp 305–308° (dec); IR ν_{max}^{KBr} cm^{-1}: 3440, 1752; CD curve (MeOH) $[\theta]_{258}$ + 277, $[\theta]_{210}$ − 14 700 (last reading). [Calc. for $C_{15}H_{20}O_5$: MW, 280.1311. Found: MW (MS), 280.1305.] ^1H and ^{13}C NMR spectra are listed in Tables 3 and 4. Fraction 31 also yielded solid material whose NMR spectrum showed it to be a mixture of **7** (major component) and **1g**.

Oxidation of **7**. A soln of 70 mg **7** in 12 ml Me_2CO was stirred with 0.1 ml Jones' reagent for 45 min at 0°. The usual work-up followed by recrystallization from EtOAc gave 61 mg **8**, mp 225–226°; IR ν_{max}^{KBr} cm^{-1}: 1765, 1710. [Calc. for $C_{15}H_{18}O_5$: MW, 278.1154. Found: MW (MS), 278.1146.] ^1H and ^{13}C NMR spectra are listed in Tables 3 and 4.

Conversion of **6** *to* **9**. A soln of 10 mg **6** in $CHCl_3$ was passed through a column of basic alumina (10 g). The eluate showed two spots on TLC. Purification by TLC ($CHCl_3$–MeOH–EtOAc, 8:1:1) gave mainly starting material and 1 mg **9** whose ^1H NMR spectrum is listed in Table 3.

Extraction of Liatris aspera. Aerial parts of *L. aspera* Michx (5.9 kg) collected by Dr. R. K. Godfrey and D. Gage on 1 Sept. 1979 along Arkansas Rt 29 between Bardley and Canfield, Lafayette Co., Arkansas (Godfrey No. 77199 on deposit in the Herbarium of Florida State University) was extracted with $CHCl_3$ and worked-up as usual [28]. The crude gum (72 g) was preadsorbed on 100 g silicic acid and chromatographed on 750 g

silicic acid packed in C_6H_6. Fractions were collected as follows: 1–10 (C_6H_6, 5 l.); 11–18 (C_6H_6–$CHCl_3$, 1:1, 4 l.); 19–28 ($CHCl_3$, 5 l.); 29–34 ($CHCl_3$–MeOH, 99:1, 3 l.); 35–40 ($CHCl_3$–MeOH, 49:1, 3 l.); 41–50 ($CHCl_3$–MeOH, 19:1, 5 l.) and 51–58 ($CHCl_3$–MeOH, 9:1, 4 l.).

Fraction 1 (650 mg) gave a mixture of taraxasteryl and lupeyl acetates. Fractions 2–10 (1.4 g) were a mixture of lupeol and taraxasterol. Purification of 300 mg of fraction 33 (total wt 3.1 g) by TLC ($CHCl_3$–MeOH–EtOAc, 8:1:1) gave three bands. The upper band was repurified by TLC (EtOAc–C_6H_6, 1:4, two developments) to yield 45 mg salvigenin (**12a**) mp 186–188° and 65 mg 5-hydroxy-6,7,3′,4′-tetramethoxyflavone (**12c**) which were identified by direct comparison with authentic material. The middle band on repurification by TLC ($CHCl_3$–MeOH–EtOAc, 8:1:1, two developments) gave 5 mg of gummy eupatorin (**12b**) identified as such by comparison with NMR of authentic material. Repurification of the lowest band by TLC using the same solvent system gave 6 mg of oily **13** whose NMR spectrum tallied with that described in the literature.

Fraction 48 (750 mg) was purified by TLC ($CHCl_3$–MeOH–EtOAc, 7:1:2, two developments). The only homogeneous fraction obtained in this fashion was repurified using the same solvent system (three developments) to give gummy **15a** (175 mg) which had IR $\nu_{max}^{CHCl_3}$ cm^{-1}: at 3410, 1775, 1700, 1650; CD curve (MeOH), $[\theta]_{220} + 107\,900$ (last reading). The low resolution MS exhibited only a very weak $[M+1]^+$ ion at m/z 495 (0.05%). ^1H and ^{13}C NMR spectra are listed in Tables 6 and 7.

Fractions 57 and 58 (4.3 g) were rechromatographed over Si gel (110 g). Fractions eluted with $CHCl_3$–MeOH (9:1) contained one major compound. TLC ($CHCl_3$–MeOH–EtOAc, 6:2:2, two developments) afforded gummy material which was identified as **14** by spectroscopic comparison with an authentic sample [24]. Fraction 49 on trituration with MeOH afforded 170 mg of the usual mixture of sitosterol and stigmasterol β-D-glucosides.

Reactions of **15a**. (a) A mixture of 75 mg **15a** and 4 ml 1.5% aq. KOH was stirred for 15 hr under N_2, acidified with dil. HCl, satd with NaCl and extracted with EtOAc. The crude product was purified by TLC ($CHCl_3$–MeOH–EtOAc, 8:1:1) to give spectroscopically pure **15c** (20 mg). [Calc. for $C_{15}H_{22}O_5$: MW, 282.150. Found: MW (MS), 282.151.] The ^1H NMR spectrum is listed in Table 6.

(b) Acetylation of 40 mg **15a** with 0.5 ml Ac_2O in 0.5 ml of pyridine overnight at room temp. followed by the usual work-up gave a gum which showed many spots on TLC. Purification by TLC (EtOAc–C_6H_6, 1:5) and isolation of a fraction with R_f 0.5 yielded 2 mg of a gummy substance which was pure by NMR criteria and whose spectrum, listed in Table 6, was consistent with structure **15b**. Acetylation of **15a** at 0° gave the same mixture of products.

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