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CARDENOLIDES AND A LIGNAN FROM *ASCLEPIAS SUBULATA*

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Key Word Index—*Asclepias subulata*; Asclepiadaceae; cardiac glycosides; larciresinol glucoside; lupeol.

Abstract—Four new glycosides (three cardenolides and a lignan), nine previously reported cardenolide glycosides and a known triterpenoid were isolated from the ethyl acetate extract of the aerial parts of *Asclepias subulata*. The elucidation of the structures and stereochemistry of the new glycosides has been accomplished using mainly ^{1}H and ^{13}C NMR and mass (EI and FAB) spectral data of their acetyl derivatives and comparison of these data with those of known glycosides from the same plant as well as from other plants. The new compounds were identified as 16α-hydroxycalactin, 3β-(β-D-glucopyranosyloxy)-19-carboxy-14β-hydroxycard-20(22)-enolide, coroglaucigenin 3β-D-glucoside and 4-(β-D-glucopyranosyloxy)-larciresinol.

INTRODUCTION

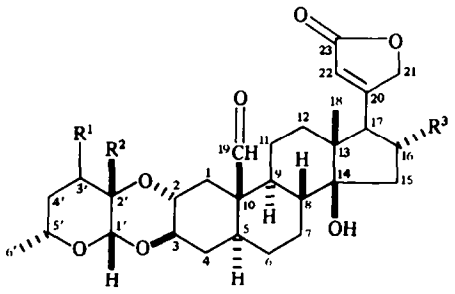
Asclepias subulata Decne (Asclepiadaceae), desert milkweed, was investigated as a source of rubber during World War II [1]. More recently, this plant was identified as a good producer of biocrude [2]. However, several other species in this genus are known sources of cytotoxic cardiac glycosides [3, 4]. Therefore, we decided to study the chemistry of *Asclepias subulata*.

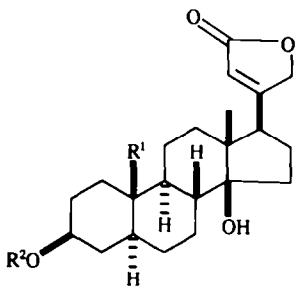
RESULTS AND DISCUSSION

Fractionation of the ethyl acetate extract of *A. subulata* following the procedure outlined in Scheme 1 afforded twelve compounds: ten cardiac glycosides (**1**–**10**), a lignan glycoside (**11**) and a triterpenoid (**12**), of which eight had already been reported: **2**–**7** and **10** from other *Asclepias* species [5, 6] and **12** from numerous sources [7]. Compounds **1**, **8**, **9** and **11**, which were difficult to isolate and purify in their free state, were converted into their corresponding acetate derivatives (**1a**, **8a**, **9a** and **11a**), purified and characterized. The identities of all the known cardiac glycosides, which include calactin (**2**) [8, 9], calotropin (**3**) [8, 9], uscharidin (**4**) [8, 9], uscharin (**5**) [8, 9], uzarigenin 3β-D-glucoside (**6**) [10], corotoxigenin 3β-D-glucoside (**7**) [11] and frugoside 4′β-D-glucoside (**10**) [12], were established by spectral evidence by comparing one with another and with literature data. The triterpenoid **12** was characterized as lupeol by direct comparison with an authentic sample in addition to its spectral evidence and those of the corresponding acetyl derivative. The new compounds, 16α-hydroxycalactin (as diacetate **1a**), 3β-(β-D-glucopyranosyloxy)-19-carboxy-14β-hydroxycard-20(22)-enolide (as tetraacetate **9a**), coroglaucigenin 3β-D-glucoside (as pentaacetate **8a**) and 4-(β-D-glucopyranosyloxy)-larciresinol (as hexaacetate **11a**), are described below. We have also included NMR and mass spectral data for **10** since very little data were reported when it was found in *Asclepias tuberosa* L. [12].

Structure of compound **1a**

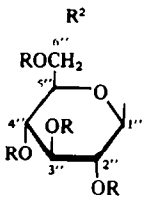
Compound **1a**, an amorphous powder, had $[\alpha]_D^{25}$ +24.0° ($CHCl_3$) and molecular formula $C_{33}H_{44}O_{12}$ (FAB high-resolution mass spectrometry). The EI mass spectrum of **1a** showed neither a molecular ion nor characteristic glucose fragments (observed in FAB mass spectra of all cardenolide glycoside acetates having a normal glycosidic linkage with one ether bridge between C-3 of the aglycone and C-1 of the sugar component) but did show a peak at *m/z* 402, corresponding to anhydrogenin, in addition to peaks with higher masses of *m/z* 426, 411 $[426 - Me]^+$ and 408 $[426 - H_2O]^+$. The absence of glucose fragments suggested that **1a** could be a cardiac glycoside with two ether bridges, as in calactin (**2**). The presence of a *m/z* 426 peak, corresponding to anhydromono-*O*-acetylgenin, in the EI mass spectrum and two acetyl groups in the molecule (loss of two molecules of acetic acid from the $[M + H - H_2O]^+$ fragment in the FAB mass spectrum, confirmed by ^{1}H NMR) suggested three possibilities for location of the acetyl groups. One was that both acetyl groups were part of the sugar moiety and the one at C-2′ underwent intermolecular migration after, or concomitant with, loss of water during heating of the sample for volatilization in the ion source [13]. The second possibility was that a compound analogous to the species generated by the thermal reaction during ionization could have formed during acetylation (Ac_2O–pyridine at room temperature) by opening the ether bridge to generate a carbonyl at C-2′ and a secondary hydroxyl group at C-2 which was then acetylated. The third possibility was that one of the two acetyl groups was part of the aglycone moiety. The second possibility was ruled out based on the ^{13}C NMR spectrum of **1a** which showed no carbonyl carbon. That both acetyl groups are on different rings (one on aglycone and the other on sugar components) was confirmed from the elemental composition of the *m/z* 229 peak (which stands out both in the EI and FAB mass spectra of **1a**) by high-



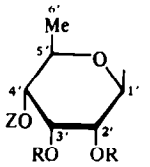


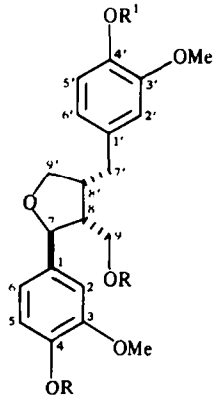
	R^1	R^2	R^3
1	β-OH	OH	OH
1a	β-OAc	OH	OAc
2	β-OH	OH	H
3	α-OH	OH	H
3a	α-OAc	OAc	H
4	=O	OH	H
5		OH	H

	R	R^1
6	H	Me
7	H	CHO
8	H	CH_2OR
8a	Ac	CH_2OR
9	H	COOH
9a	Ac	COOH
10	H	CH_2OR
10a	Ac	CH_2OR



Z



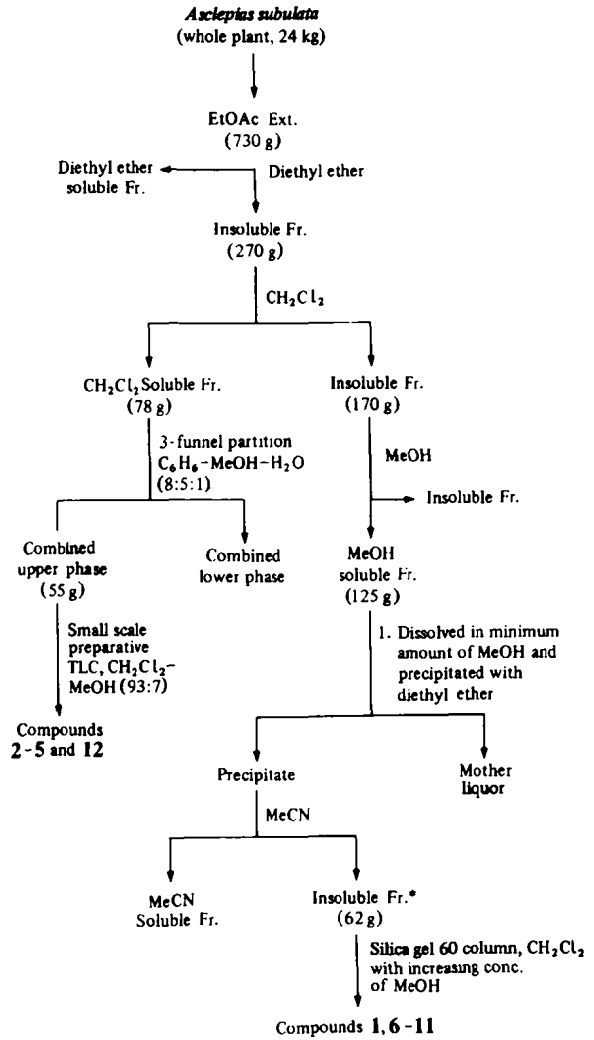


	R	R^1
11	Z	H
11a	Z	Ac
11b	H	H

resolution EIMS. The elemental composition would be $C_{10}H_{13}O_6$ if both acetyl groups were on the sugar component. Instead, $C_{15}H_{13}O_2$ for *m/z* 229 was observed; its genesis could be conceived as shown in Scheme 2. The FAB mass spectrum of **1a** gave a distinct molecular ion peak at *m/z* 633 $[M+H]^+$ and very strong peaks at *m/z* 171 (base), 143, 129, 127 and 111, corresponding to sugar fragments, as outlined in Scheme 3.

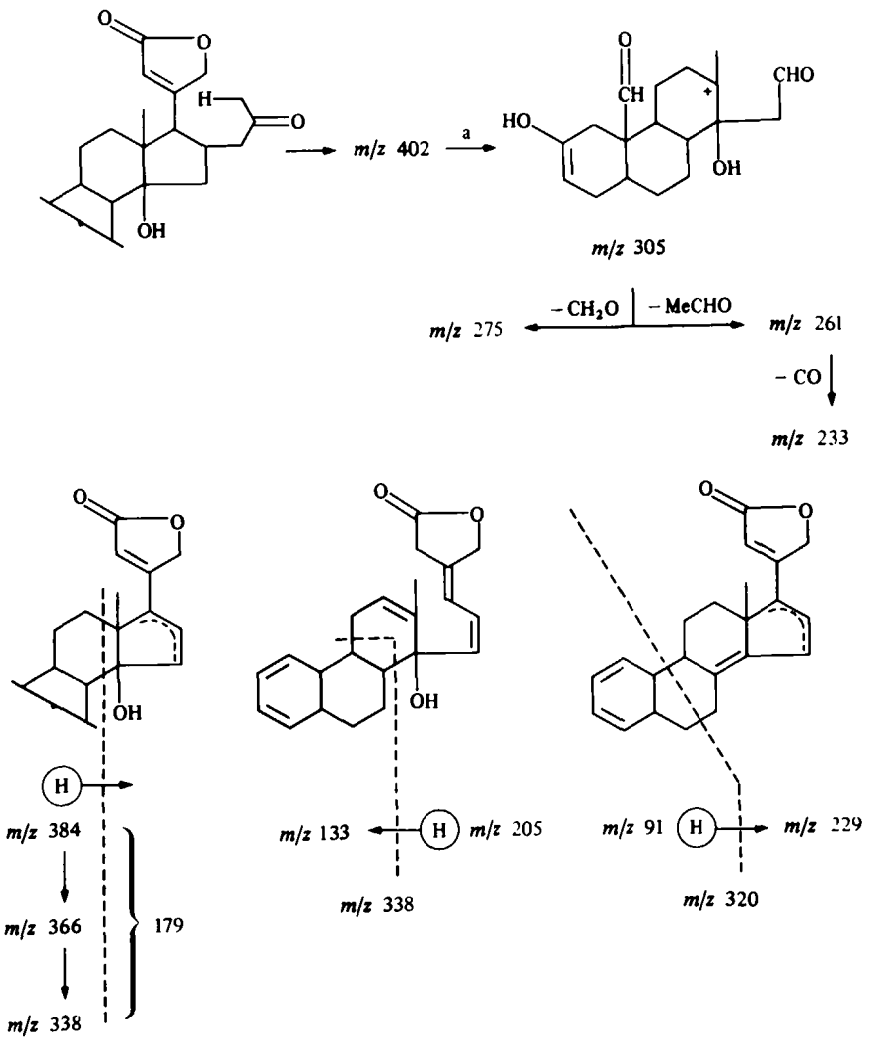
Except for the relative intensities of peaks, the EI mass spectrum of **1a** exhibited a fragmentation pattern nearly identical to that of calactin (**2**). In the upper mass region (from *m/z* 320 to 384) the major fragment ions were shifted to mass numbers lower by 2 amu (Scheme 4), while those in the lower mass region (below *m/z* 235) were unaltered. This suggested that **1** could be a dehydro derivative of **2** in which either the aglycone component was dehydrogenated or the double bond had been formed by dehydration during mass spectrometric analysis. The difference of 16 amu between calactin (**2**, *m/z* 533 $[M+H]^+$) and **1a** (*m/z* 633 $[M+H-84]^+$ indicated an extra oxygen in the aglycone moiety of the latter, presumably as a secondary hydroxyl. The fragmentation sequence *m/z* 633 $[M+H]^+ \rightarrow 615 \rightarrow 555 \rightarrow 495 \rightarrow 477$ clearly indicated that this extra hydroxyl and the one on the sugar component at C-3′ were acetylated and the remaining two unacetylated hydroxyl groups were in the same respective positions (C-2′ and C-14) as in calactin (**2**). The presence of the aglycone acetate group at C-16 appears to be the structural prerequisite for the formation of the *m/z* 305 fragment ($C_{18}H_{25}O_4$) (Scheme 2), a conclusion which was supported by ^{1}H NMR. The elemental composition of all the peaks shown in Schemes 3 and 4 were verified by high-resolution exact mass measurements.

The similarity of the ^{1}H NMR (Table 1) and ^{13}C NMR (see Experimental) spectral parameters of **1a** to those of

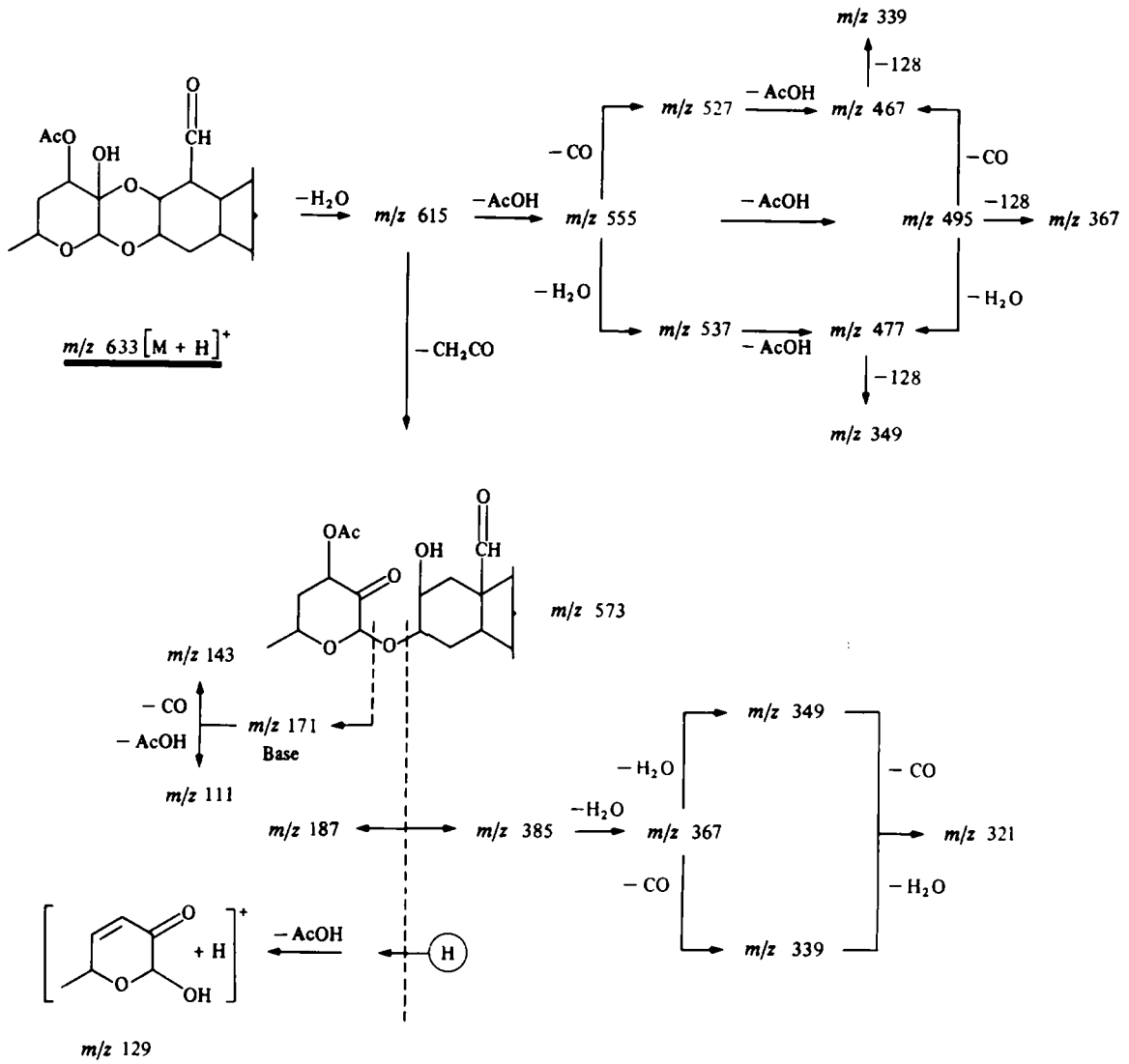


* TLC (CH_2Cl_2-MeOH, 92:8) showed the presence of **2-5**

Scheme 1. Extraction and isolation sequence.



Scheme 2. Major fragment ions in the low mass region (below m/z 300) of the EI mass spectrum of compound **1a**.

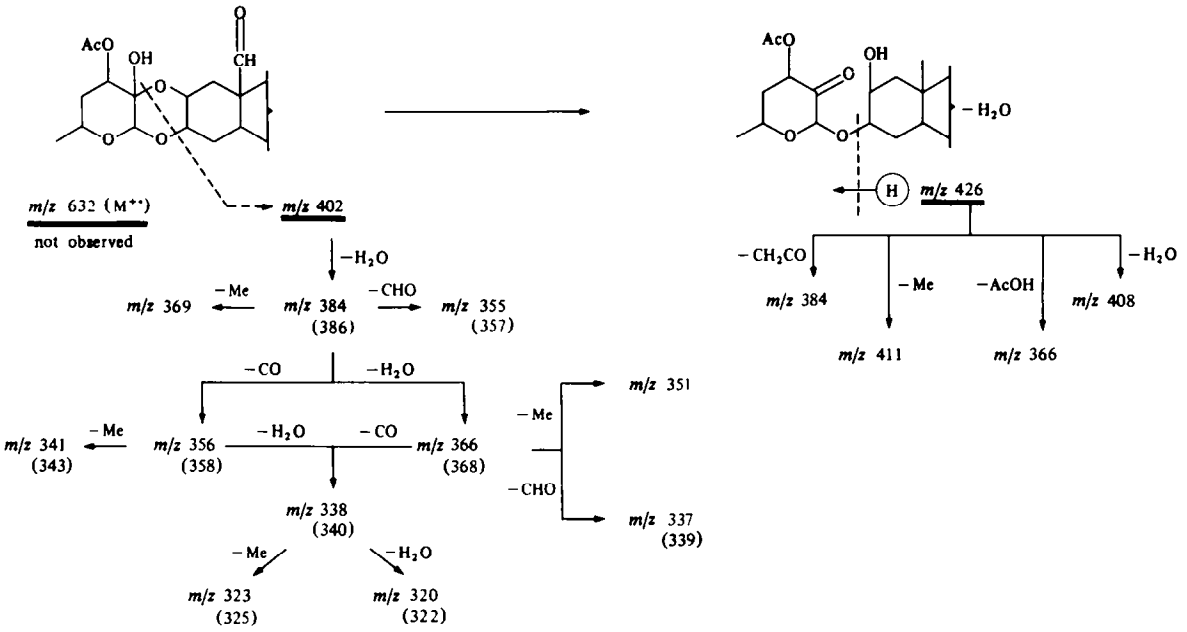


Scheme 3. Major fragment ions in the FAB mass spectrum (glycerol) of compound **1a**.

calactin (**2**) is consistent with **1** being a hydroxycalactin. The finding of the H-17 absorption of **1a** as a doublet coupled to the proton absorbing at δ5.25 indicated an acetoxyl group to be present at C-16, and the low value of $J_{H\text{-}16,H\text{-}17}$ (3.9 Hz) suggests a 16α-acetoxyl group. An X-ray study of 5β-hydroxyatoxigenin [14] shows the D-ring in this substance to approximate an enveloped configuration with C-15 at the flap. The values of $J_{16\alpha,17}$ and $J_{16\beta,17}$ in cardenolides lacking an oxygen function at C-16 are 5 and 9 Hz (Table 1); from examination of molecular models, $J_{16\beta,17}$ is the smaller one. Since the smaller coupling constant is found in **1a**, it should have a 16α-acetoxyl group. Supporting evidence that this new substance is not a 16β-acetoxycardenolide comes from the large differences in the ^{13}C NMR chemical shifts of this substance (see Experimental) and gitoxigenin 16-acetate for the D-ring carbons; the reported values for gitoxigenin 16-acetate are C-13, δ50.7; C-14, 84.1; C-15, 39.5; C-16, 75.0; C-17, 56.8 [15].

Structure of compound **9a**

The FAB mass spectrum of **9a**, $[\alpha]_D^{25}$ + 26.6° ($CHCl_3$), displayed a molecular ion peak at *m/z* 735 $[M+H]^+$, analysed for $C_{37}H_{51}O_{15}$ by high-resolution FAB mass spectrometry and a characteristic series of ions consisting of various fragments of the sugar moiety (derived from *m/z* 331, $C_{14}H_{19}O_9$, through rupture of the glycosidic bond) which suggested the presence of a glucopyranosyl tetraacetate moiety. Except for variations in the abundance of peaks, these sugar fragments dominated the entire FAB mass spectra of acetyl derivatives of all cardenolide and lignan glycosides in this study. The elemental composition of the aglycone moiety was deduced by subtracting the (sugar–H) unit from $[M+H]^+$, leaving $C_{23}H_{33}O_6$, a formula supported by a minor but structurally characteristic peak at *m/z* 405. Further fragmentation of the aglycone ion (*m/z* 405) leads to ions of lower mass at *m/z* 387 $[405-H_2O]^+$, 361 $[405-CO_2]^+$,



Scheme 4. Major fragment ions in the upper mass region (above *m/z* 300) of the EI mass spectrum of compound **1a**. The figures in parentheses represent analogous ions in the EI mass spectrum of **2**.

Table 1. H NMR chemical shifts (δ) relative to internal standard and coupling constants (J in Hz, in parentheses) for **1a**, **2** and **8a–10a** in $CDCl_3$

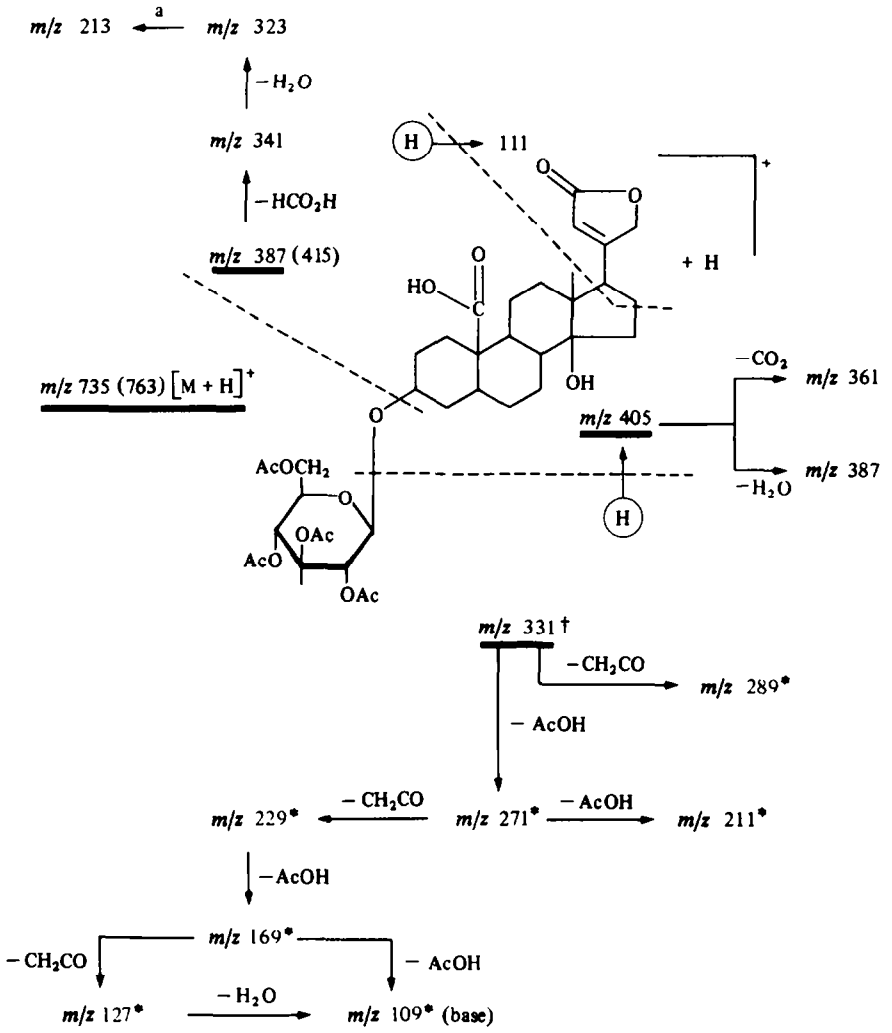
	1a	**2***	**8a**	**9a**	**10a**
1α	1.15 *t* (12.3)	1.11 (12.5)			
β	2.46 *dd* (12.3, 3.9)	2.37 (12.5, 4.4)	2.24 *dt* (13.5, 3.5)	2.48 *br d* (13.1)	2.24 *br d* (14.4)
2 }	3.85–4.05 *m*	3.82 *ddd* (11.6, 9.6, 4.4)			
3 }		3.94 *td* (10.5, 4.4)	3.63 *br m*	3.64	3.64
15	2.26 *dd* (14.0, 8.1)				
16	5.25 *td* (8.1, 3.9)				
17	2.65 *d* (3.9)	2.84 ~ *dd* (9.1, 5.1)	2.77 (9.0, 5.0)	2.77 *dd* (9.0, 5.1)	2.77 ~ *dd* (8.9, 5.1)
18	0.81 *s*	0.87	0.87	0.84	0.86
19a }	9.99 *s*	10.01	4.07 *d* (12.6)		4.11 (12.3)
19b }			4.33 *d* (12.6)		4.32 (12.3)
21a	4.83 *dd* (17.8, 1.6)	4.83 (18.2, 1.7)	4.79 (18.0, 1.7)	4.81 *br d* (18.1)	4.79 *dd* (18.1, 1.6)
21b	4.90 *dd* (17.8, 1.6)	5.00 (18.2, 1.6)	4.97 (18.0, 1.7)	4.96 *br d* (18.1)	4.97 (18.1)
22	5.94 *br s*	5.85	5.88 *t* (1.6)	5.89 *br s*	5.87
1′	4.73 *s*	4.72	4.62 *d* (8.0)	4.59 (7.9)	4.77 (8.2)
2′			4.94 *dd* (9.4, 8.0)	4.92 *t* (8.8)	4.64 *dd* (8.2, 3.0)
3′	4.96 *t* (2.9)	3.66 (3.2)	5.20 (9.4)	5.20 (9.4)	5.66 (3.0)
4′			5.09 *t* (9.5)	5.07 (9.6)	3.34 *dd* (9.5, 3.0)
5′	3.85–4.05 *m*	4.00–4.17	3.68 *ddd* (9.5, 4.6, 2.7)	3.68 (9.6, 4.7, 2.5)	3.87 *dq* (9.5, 6.2)
6′a }	1.26 *d* (6.2)	1.20 (6.9)	4.13 *dd* (12.3, 2.7)	4.12 (12.2, 2.5)	1.20 *d* (6.2)
6′b }			4.27 *dd* (12.3, 4.6)	4.26 (12.2, 4.7)	
1″					4.54 *d* (7.7)
2″					4.97 *t* (9.5)
3″					5.15 *t* (9.5)
4″					5.00 *t* (10.0)
5″					3.67 *ddd* (10.0, 4.8, 2.0)
6″a					4.02 *dd* (12.3, 2.0)
6″b					4.19 *dd* (12.3, 4.8)
MeC=O	2.04, 2.13 *s*		2.01, 2.03, 2.04, 2.06, 2.09	2.01, 2.02, 2.03, 2.08	1.98, 1.99, 2.01, 2.03 2.05, 2.08, 2.08

*Acetone-d_6 was added to dissolve sample.

341 [387 – HCO_2H]$^+$ and 323 [341 – H_2O]$^+$, indicating clearly the various oxygen functions of the molecule and supporting IR evidence for the presence of hydroxyl, carboxyl, acetoxyl and butenolide groupings. The carboxyl group was assumed to be at C-10 replacing the C-19 methyl group as in many cardenolides, an inference which was confirmed by the ^{1}H NMR spectrum of **9a** (Table 1), which was similar to that of **8a** except for the lack of the C-19 CH_2OAc absorptions at δ2.06, 4.07 and 4.33.

Structure of compound **8a**

Compound **8a**, which failed to crystallize but was judged homogeneous by TLC and its NMR spectrum, had $[\alpha]_D^{25}$ unstable ($CHCl_3$) and molecular formula $C_{39}H_{55}O_{15}$ (FAB high-resolution mass spectrometry). In the IR spectrum of **8a** neither CHO nor COOH was seen but there were characteristic enone and hydroxyl bands as for other cardiac glycosides found in this plant. The FAB mass spectrum of **8a** exhibited readily interpretable fragmentation peaks as depicted in Scheme 5. The nature of the sugar and aglycone components in **8a** was deduced by correlation with **9a** which differs from **8a** only at C-10. That **8a** possesses the sugar component with the same elemental composition ($C_{14}H_{19}O_9$) as does **9a** was clear from the ubiquitous sugar fragments shown in Scheme 5. Subtracting this (sugar–H) moiety from $[M+H]^+$ left $C_{25}H_{37}O_6$ (*m/z* 433). This unit was not discernible, but a peak was observed at *m/z* 415 [433 – H_2O]$^+$ for the anhydrogenin. The presence of tertiary hydroxyl and acetoxyl groupings in the aglycone residue was clearly marked by the appearance of characteristic peaks at *m/z* 397 [415 – H_2O]$^+$, 355 [415 – HOAc]$^+$ and 337 [397 – HOAc]$^+$ or [355 – H_2O]$^+$. Unlike **9a**, whose

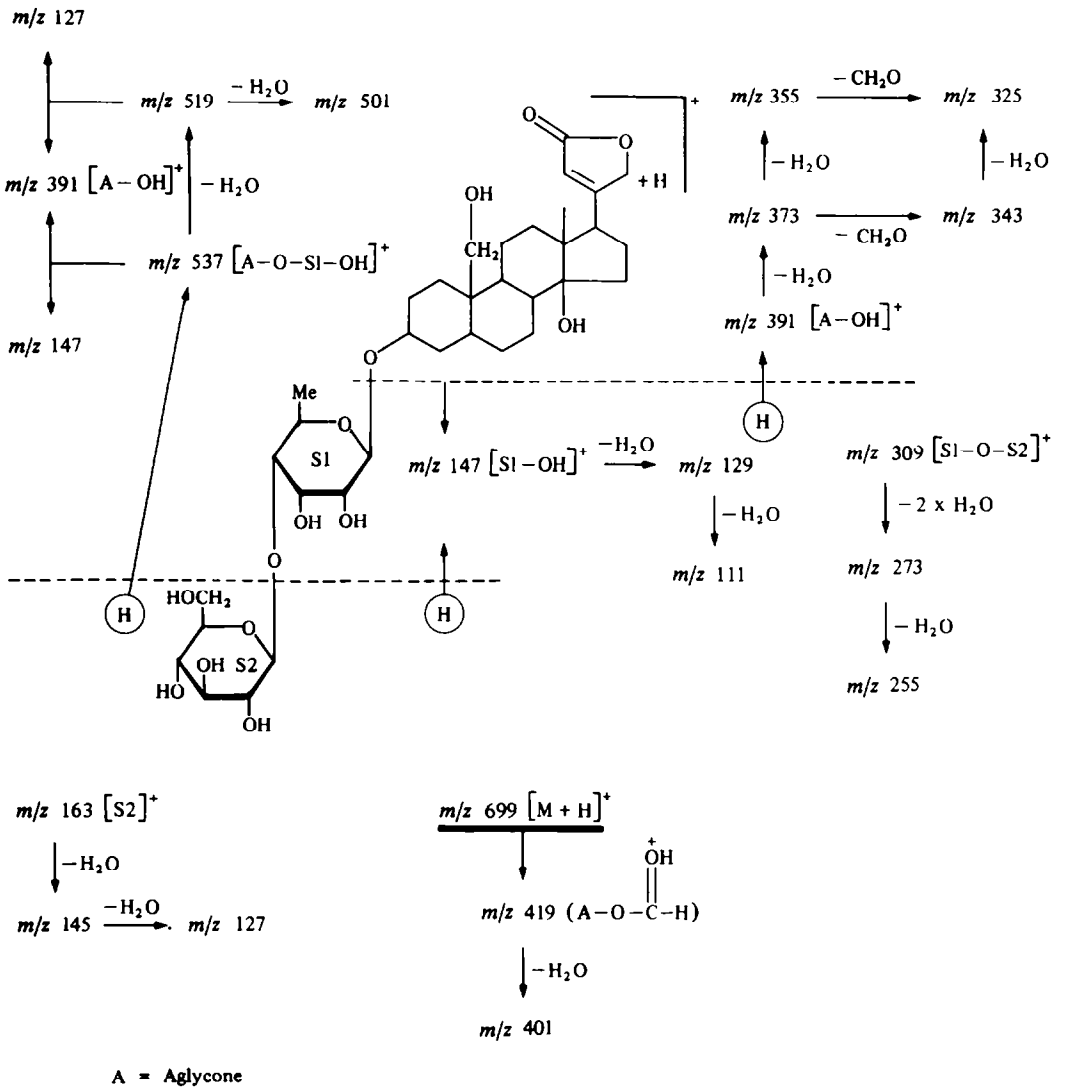


Scheme 5. Major fragment ions in the FAB mass spectrum (glycerol) of compound **9a**. The figures in parentheses represent analogous ions in the FAB mass spectrum (sulfolane) of compound **8a**. *Observed for **8a**. † Base peak for **8a**.

^{1}H NMR spectrum showed four acetates (three secondary and one primary) all confined to the sugar component, there were five acetates (three secondary and two primary) in the ^{1}H NMR spectrum of **8a**; the extra primary acetate must be in the aglycone component. The difference of 28 amu between the molecular weight of **8a** (*m/z* 763 $[M+H]^+$) and **9a** (*m/z* 735 $[M+H]^+$) confirmed this finding. The ^{1}H NMR and ^{13}C NMR spectra of **8a** and **9a** were very similar except for the C-19 absorptions, strongly indicating that **8** and **9** differ only in that **8** has CH_2OH at C-10 whereas **9** has COOH. This close correspondence also suggests that the stereochemistry of coroglaucigenin, the aglycone component in **8a**, has been established [16–18], **8** must be coroglaucigenin 3β-D-glucoside as depicted.

Structure of compound **10**

Compound **10**, ill-defined mp, heptaacetate (**10a**), $[\alpha]_D^{25}$ −37.7°(MeOH), was identified as 3β-[6′-deoxy-4′-(β-D-pyranosyloxy)-β-D-allopyranosyloxy]-5β-14,19-dihydroxycard-20(22)-enolide (or 4′β-D-glucofrugoside), which had been previously reported from *Asclepias tuberosa* as having mp 187–190°/265–287°, $[\alpha]_D^{25}$ −7.2° (MeOH) [12]. As the NMR and mass spectral data of this compound have not been reported, they are presented here. Except for stereochemistry, the structure of **10** was deduced from its FAB mass spectrum. The EI mass spectrum of **10** did not display a molecular ion peak but showed characteristic ions in the upper mass region at *m/z* 419 (30 amu higher than the mass of the genin), which contains the genin, C-1′, and the sugar ether oxygen [observed in the EI mass spectrum of **6** (*m/z* 403) and **7** (*m/z* 417)], 390, 382, 372, 364, 354, 342, 341, 336, 324, 323, 321 and 308. The mass spectrum acquired with the FAB technique using a glycerol matrix was very informative. It not only established unequivocally the molecular weight of **10** (*m/z* 699 $[M+H]^+$), but also suggested the sequence in which the sugar moieties are linked to the genin. Fission of the ether linkages between sugar (S1) and sugar (S2), and between sugar (S1) and aglycone (A) moieties gave pairs of peaks adding up to the molecular weight: *m/z* 537 − 163 (−2 amu) and *m/z* 391 − 309



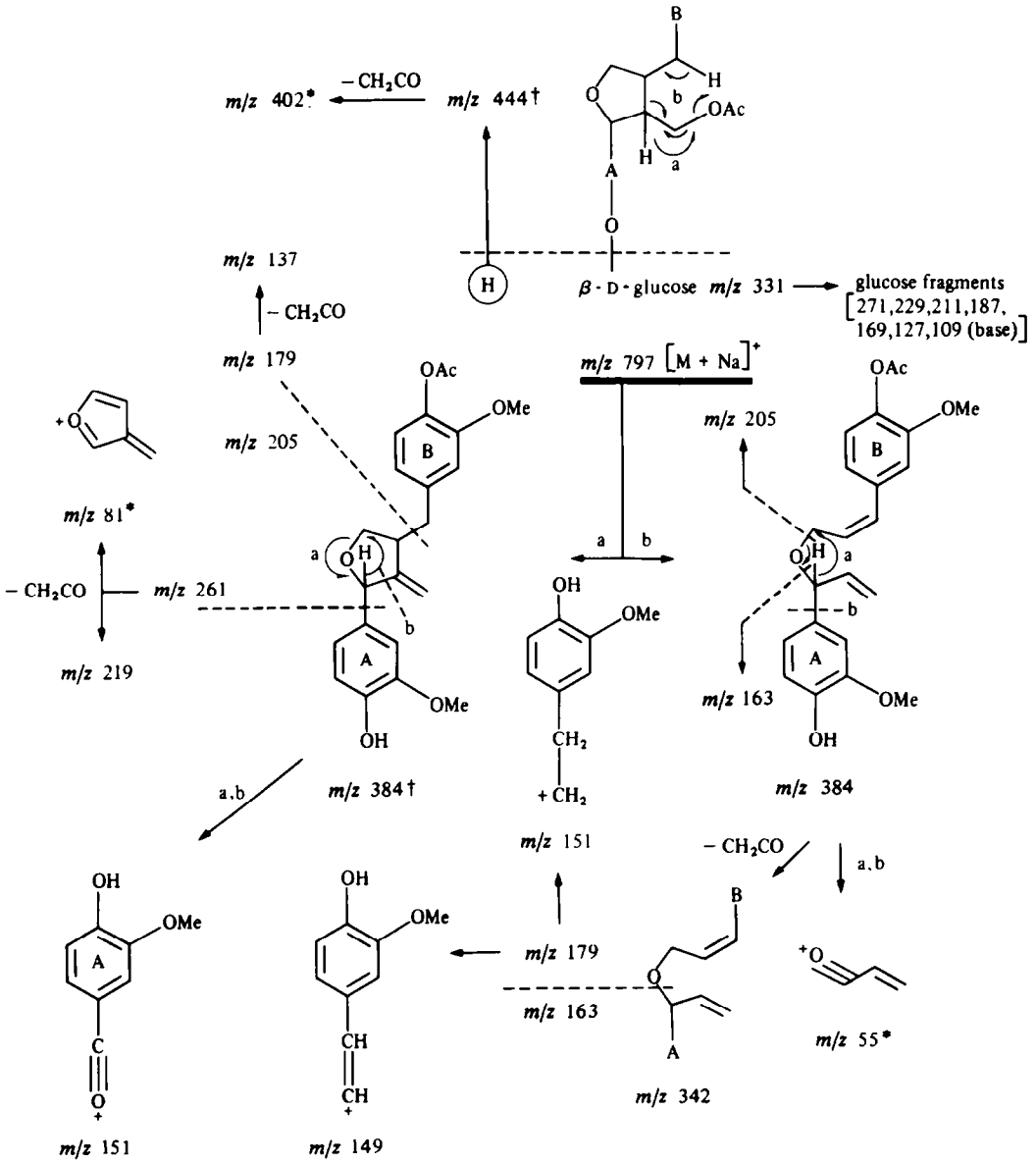
Scheme 6. Major fragment ions in the FAB mass spectrum (glycerol) of compound **10**.

(−2 amu). The appearance of *m/z* 537 and 519 peaks, derived from $[M+H]^+ - 162$ (S2) and $[M+H]^+ - 180$ (S-OH) (or $537 - H_2O$), respectively, clearly supported the proposal that glucopyranose (S2) was linked to allomethylose (S1) which in turn was linked to the aglycone (A). Further fragmentation of the *m/z* 537 ion via glycosidic bond cleavage with charge retention (i) by the allomethylase (S1) followed by loss of water gave two abundant diagnostically important ions at *m/z* 147 (base) and 129, and (ii) by the genin gave a series of peaks depicted in Scheme 6.

The ^{1}H NMR parameters of **10a** (Table 1) strongly support the proposed structure. The aglycone parameters closely match those of **8a**, and in addition there are slightly displaced tetraacetyl-β-glucopyranoside absorptions. The additional peaks in the spectrum of **10a** fit very well for the additional sugar grouping with the stereochemistry shown. The large values of $J_{1'2'}$ and $J_{4'5'}$ require the substituents at positions 1', 2', 4' and 5' to be equatorial; the small values of $J_{2'3'}$ and $J_{3'4'}$ then indicate the acetoxyl group at C-3' to be axial.

Structure of compound **11a**

Compound **11a** was isolated as an amorphous powder, $C_{38}H_{46}O_7$ (FAB mass spectrometry; sulfolane, thiogly-



* Not observed in FABMS

† Not observed in EIMS and FABMS but mechanistically plausible intermediates

Scheme 7. Major fragment ions in the EI and FAB mass spectra of **11a**.

cerol): *m/z* 797 $[M+Na]^+$, hexaacetate $[\alpha]_D^{25} -7.8°$ ($CHCl_3$). The IR spectrum of **11a** suggested the presence of phenyl (1600 and 1510 cm^{-1}), CH_2O (1420 cm^{-1}), β-sugar (900 cm^{-1}), acetyl carbonyl (1750 cm^{-1}) and methyl (1370 cm^{-1}) groups. Its ^1H NMR spectrum showed the presence of a β-glucopyranoside, two 1,2,4-trisubstituted benzenes and protons whose chemical shifts and coupling pattern suggested the central grouping of the lignan lariciresinol (**11b**) [19, 20] to be present. Acetate groupings were clearly present at C-9 from the downfield location of the C-9 proton absorptions, and on the 4- or 4'-position from the downfield location of the 5- or 5'-proton absorption. The ^{13}C NMR spectrum was in full accord with structure **11a** for this new substance.

The sugar was located with the aid of mass spectral evidence. The EI mass spectrum of **11a** did not display a recognizable molecular ion peak but did exhibit characteristic peaks at *m/z* 402, corresponding to the aglycone ($-CH_2CO$) component and *m/z* 331, corresponding to the sugar component, derived from $[M]^{+\cdot}$ by fission at the glucoside linkage with and without transfer of a hydrogen, respectively. These aglycone (*m/z* 444, not observed) and sugar (*m/z* 331) fragment ions then give rise to all the principal fragment ions depicted in Scheme 7. The elemental compositions of the ions at *m/z* 402, 219, 151 and 137 were verified by high-resolution exact mass measurements which showed the *m/z* 151 peak to consist of $C_9H_{11}O_2$ and $C_8H_7O_3$ in a 3:1 ratio and the remaining peaks to be due solely to single compositions. The observed fragmentation peaks show that the methoxyl groups are on different rings, and are presumed to be in the 3 and 3'-positions, as is usual for many lignans of this type (e.g. **11b**); this was consistent with the NMR evidence that the aryl acetoxy grouping was at the 4- or 4'-position. The remaining question of whether the sugar is at 4 or 4' was deduced from the fragmentation pattern of **11a** in the EI and FAB mode. The absence of a mass spectral peak at *m/z* 165 for A^+ in the EI and FAB mass spectra, which would be expected if R were Ac, suggested that the sugar was at position 4. Instead, peaks at *m/z* 179 for B–CH_2 (R_1 = Ac) (this peak is seen more clearly in the FAB mass spectrum) and *m/z* 137 (after the loss of CH_2CO) were observed, and the structure is apparently **11a**.

EXPERIMENTAL

General. For instrumental procedures see ref. [21].

Plant material. Plant material used in this study was harvested during October 1981 from the University of Arizona's Overpass Farm. The field was planted from seeds collected in Sentinel, Arizona on 6 June 1979 and 6 miles east of Altar, Sonora, Mexico on 22 February 1980 (S. P. McLaughlin 2190 and 2416). Herbarium specimens have been deposited at the University of Arizona. All plant material was air-dried, ground to 3 mm particle size and stored at 5° prior to extraction.

Extraction, fractionation and isolation. The ground *A. subulata* (24 kg) was extracted, fractionated and chromatographed as shown in Scheme 1. Individual compounds from various CC fractions (52, 500 ml size) were isolated qualitatively. Where necessary (see text), isolation and purification were accomplished by converting compounds into their corresponding acetyl derivatives followed by prep. TLC using CH_2Cl_2–EtOAc–MeOH (16:7:1) or CH_2Cl_2–EtOAc (3:1) as developing solvent systems.

All the isolated new compounds were amorphous but were judged homogeneous by TLC. The ^{13}C NMR data for **1a** and **11a** and the ^1H NMR data for **11a** are described below; the NMR spectral data for the other compounds are described in the text.

Calactin 16α-acetate (**1a**). ^{13}C NMR ($CDCl_3$): δ36.1 (C-1), 69.2 (C-2), 71.5 (C-3), 33.1 (C-4), 43.4 (C-5), 27.4 (C-6), 27.3 (C-7), 42.2 (C-8), 48.5 (C-9), 52.6 (C-10), 21.9 (C-11), 39.5 (C-12), 48.8 (C-13), 84.6 (C-14), 38.8 (C-15), 78.2 (C-16), 57.7 (C-17), 15.5 (C-18), 206.09 (C-19), 171.8 (C-20), 73.7 (C-21), 118.5 (C-22), 174.2 (C-23), 94.0 (C-1'), 90.1 (C-2'), 72.6 (C-3'), 35.3 (C-4'), 66.8 (C-5'), 20.6 (C-6'), 20.1 and 20.9 ($\underline{C}H_3CO$), 170.6 and 170.8 ($CH_3\underline{C}O$).

4-(β-D-Glucopyranosyloxy)-lariciresinol hexaacetate (**11a**). ^1H NMR ($CDCl_3$): δ6.94 (*d*, *J* = 1.8 Hz, H-2), 6.99 (*d*, *J* = 8.1 Hz, H-5), 6.86 (*dd*, *J* = 8.1, *J* = 1.8 Hz, H-6), 4.86 (*d*, *J* = 5.5 Hz, H-7), 2.55 (*m*, H-8), 4.38 (*dd*, *J* = 11.3, *J* = 6.5 Hz, H-9a), 4.20 (*dd*, *J* = 11.3 Hz, *J* = 7.7 Hz, H-9b), 6.69 (*d*, *J* = 2.1 Hz, H-2'), 7.04 (*d*, *J* = 7.9 Hz, H-5'), 6.67 (*dd*, *J* = 2.1, *J* = 7.9 Hz, H-6'), 2.55 (*m*, *J* = 12.7, *J* = 12.0 Hz, H-7'a), 2.84 (*dd*, *J* = 12.7, *J* = 4.6 Hz, H-7'b), 2.69 (*m*, H-8'), 3.73 (*dd*, *J* = 8.6, *J* = 6.9 Hz, H-9'a), 4.06 (*dd*, *J* = 8.6, *J* = 6.4 Hz, H-9'b), 4.93 (~ *d*, *J* = 7.9 Hz, H-1''), 5.28 (*d*, *J* = 7.9 Hz, H-2''), 5.28 (*d*, *J* = 9.7 Hz, H-3''), 5.16 (~ *t*, *J* = 9.7 Hz, H-4''), 3.76 (*m*, *J* = 9.7, *J* = 5.0, *J* = 2.5 Hz, H-5''), 4.28 (*dd*, *J* = 12.3, *J* = 5.0 Hz, H-6''a), 4.16 (*dd*, *J* = 12.3, *J* = 2.5 Hz, H-6''b), 3.80 and 3.83 (*s*, OMe), 2 × 2.03, 2.04, 2 × 2.08, 2.30 (*s*, MeCO); ^{13}C NMR ($CDCl_3$): δ136.6 (C-1), 113.3 (C-2), 150.7 (C-3), 144.7 (C-4), 108.8 (C-5), 120.4 (C-6), 82.9 (C-7), 56.2 (C-8), 72.8 (C-9), 141.6 (C-1'), 117.8 (C-2'), 151.1 (C-3'), 139.1 (C-4'), 122.7 (C-5'), 120.6 (C-6'), 33.3 (C-7'), 55.9 (C-8'), 62.7 (C-9'), 100.9 (C-1''), 68.5, 71.3, 72.0, 72.7 (C-2'', C-3'', C-4'', C-5'')*, 62.0 (C-6''), 42.2 and 49.0 ($O\underline{C}H_3$), 5 × 20.6, 20.8 ($\underline{C}H_3CO$), 169.1, 169.3, 170.3, 170.6, 170.9 (C=O).

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