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TEN *CIS*-CLERODANE-TYPE DITERPENE LACTONES FROM *GUTIERREZIA TEXANA*

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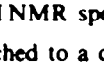
Key Word Index—*Gutierrezia texana*; Compositae; *cis*-clerodane derivatives; diterpene lactones; structural determination; NMR.

Abstract—Ten new 5α,10α-*cis*-clerodane-type diterpene lactones were isolated from the aerial parts of *Gutierrezia texana*. Using NMR techniques and some chemical transformations, the structures were established as 6α,18-dihydroxy-*cis*-cleroda-3,13(14)-diene-15,16-olide; 18,19-dihydroxy-*cis*-cleroda-3,13(14)-diene-15,16-olide; *cis*-cleroda-3,13(14)-diene-15,16:18,19-diolide; 18,19-epoxy-19α-hydroxy-*cis*-cleroda-3,13(14)-diene-15,16-olide; 3α,4:18,19-diepoxy-18β,19α-dihydroxy-*cis*-cleroda-13(14)-ene-15,16-olide; 3α,4-epoxy-19α-hydroxy-*cis*-cleroda-13(14)-ene-15,16:18,19-diolide; 3α,4:18,19-diepoxy-19α-hydroxy-*cis*-cleroda-13(14)-ene-15,16-olide; 3α,4β,19α-trihydroxy-18,19-epoxy-*cis*-cleroda-13(14)-ene-15,16-olide; 19-*O*-α-L-arabinopyranosyl-*cis*-cleroda-3,3,13(14)-diene-15,16-olide-19-oic ester and 2β,6α-dihydroxy-*cis*-cleroda-3,13(14)-diene-15,16:18,6α-diolide. One of the structures was also confirmed by X-ray crystallographic analysis.

INTRODUCTION

We previously reported furano-*ent*-labdane-type diterpenoids from *Gutierrezia grandis* (Compositae) [1] and some diterpene glycosides from *G. sphaerocephala* [2] while Cruse and James reported a novel chloroditerpenoid lactone from *G. dracunculoides* [3]. Here, we report from an annual *Gutierrezia* species native to Texas, *G. texana*, 10 new 5α,10α-*cis*-clerodane-type diterpene lactones (**1**–**10**).

RESULTS AND DISCUSSION

The IR spectrum of compound **1** (mass spectrum: *m/z* 334 for $C_{20}H_{30}O_4$, $[\alpha]_D^{23} - 6.4°$) indicated the presence of hydroxyl group(s) (ν_{max}^{KBr} 3400 cm^{-1}). A β-substituted butenolide moiety was evident by IR peaks at 1780, 1750 and 1640 cm^{-1}, ^{1}H NMR signals at δ5.82 (*br s*, 1H) and δ4.73 (*br s*, 2H) and a fragment in the electron impact mass spectrum at *m/z* 111 [CH_2CH_2– ]$^+$. In the ^{1}H NMR spectrum of **1**, signals for a carbinol group attached to a double bond were present [broadened AB pattern at δ4.28 and 4.10, see Table 1, and the vinylic proton signal at δ5.59 (*br t*, *J* = 3 Hz, 1H)]. The presence of three methyl groups in **1** was confirmed by the two three-proton singlets of δ1.31, 0.81 and a three-proton doublet at δ0.79 (*J* = 7 Hz). In the ^{13}C NMR spectrum (Table 6) of **1**, a β-substituted butenolide group was indicated by the characteristic signals at δ171.1 (*s*, C-13), 115.0 (*d*, C-14), 174.2 (*s*, C-15) and 73.0 (*t*, C-16). The presence of another pair of sp^2 carbon signals at δ129.4 (*d*, C-3), 141.4 (*s*, C-4) and a triplet at δ67.6 indicated an α,β-unsaturated carbinol function in **1**. The doublet signal at δ79.7 supported a secondary hydroxyl group in **1**. The formation of the diacetate **11** was in accord with the presence of the two hydroxyl groups. All the above data suggested a clerodane-type skeleton for **1** [4–9]. In the ^{1}H NMR spectrum of **1**, the double doublet signal at δ3.42 (1H, *dd*, *J* = 4, 11 Hz) (Table 1) indicated a secondary hydroxyl group which could only be attached at C-6 judging from the coupling pattern; moreover, the coupling constants (4 and 11 Hz) suggested an equatorial orientation of this hydroxyl group. In order to assign the stereochemistry at the C-5 and C-10 positions, **1** was correlated with the reported compound **26**. In the AB ring portion of the structure, while the ^{1}H NMR data of **1** were very similar to those of **26** except for the coupling pattern of H-6, they exhibited opposite optical rotation, −6.4 and +23°, respectively [8]. When **1** was converted into **21** (**25** was also obtained) and one then compared the ^{1}H NMR data and the optical rotation of **21** with those of the well established structure **27** [8, 10], the chemical shift (δ1.25) of H-19 in **21** appeared at lower field than the H-19 in **27** (δ1.15) and **21** and **27** again exhibited opposite optical rotation, −22.4 and +34°, respectively [8]. These indicated most probably that the C-5 methyl was α-orientated, that is, opposite to that of **27**. The AB ring *cis*-fusion was correlated with **3** and **4** which were deduced from NOE results outlined below. Therefore, **1** was assigned as 6α,18-dihydroxy-5α,10α-*cis*-cleroda-3,13(14)-diene-15,16-olide.

The IR spectrum of **2**, one of the major components in the extract, was similar to that of **1** except that the hydroxyl absorptions were broader at ν_{max}^{KBr} 3200–3400 cm^{-1}, thus indicating hydrogen bonding. In the ^{1}H NMR spectrum of **2**, signals were observed for a β-substituted butenolide and an α,β-unsaturated carbinol group as observed for **1** (Table 1). Instead of a downfield signal for a C-5 methyl as in **1** a sharp AB quartet appeared

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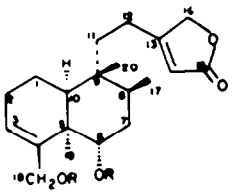
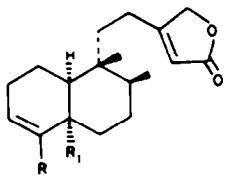
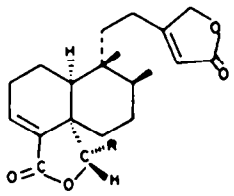


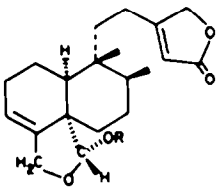
R	
1	H
11	Ac



	R	R_1
2	CH_2OH	CH_2OH
9	CH_3	COOX
	(X = α-L-arabinosyl)	
12	CH_2OAc	CH_2OAc
14	CH_2OAc	CHO
19	CH_3	COOH
24	CHO	CHO



R	
3	H
23	OH



R	
4	H
13	Ac

at δ3.60 (d, J = 10 Hz) and δ3.24 (d, J = 10 Hz) which was unambiguously assignable to a C-19 primary hydroxyl group. In the mass spectrum, a fragment for an ethylbutenolide was also present. The ^{13}C NMR data of 2 and that of its diacetate supported the structure of 2, a compound which could be easily converted into the natural diolide 3 discussed below.

The ^{1}H NMR spectrum of 3 ($C_{20}H_{26}O_4$, 330; $[\alpha]_D^{30}$ +41.4°) again indicated the presence of a butenolide group. While an AB system was also indicated, both the coupling constants and the chemical shifts (Table 1) were different from those for both AB systems in 2. A signal for H-18 as exhibited by 2 was not observed. The H-3 vinylic proton was deshielded ($\Delta\delta$ = 0.99) when compared with those in 2. These data indicated a second lactone function at C-18,19 in 3 as opposed to 2. A 2D Cosy spectrum (500 MHz) established the signal assignments. A long range coupling between H-6β and H-19α was observed in the 2D Cosy spectrum; inspection of Dreiding models indicated a W-coupling. The same couplings were observed for kerlin and kerlinolide, structures which have been confirmed by X-ray analysis [11]. In the ^{13}C NMR spectrum of 3, the C-18 carbonyl group was confirmed by a signal at δ170.9. Other ^{13}C NMR signals and all the spectral data were in accord with 3 being a 15,16:18,19-diolide. It is noteworthy that 3 could be prepared in quantitative yield from 2 by Jones reagent (see Experimental). The transformation of 2 into 3 strongly supported all the above structural assignments. In order to establish the stereochemistry, NOE experiments were conducted at 500 MHz on 3. Irradiation of the signal at

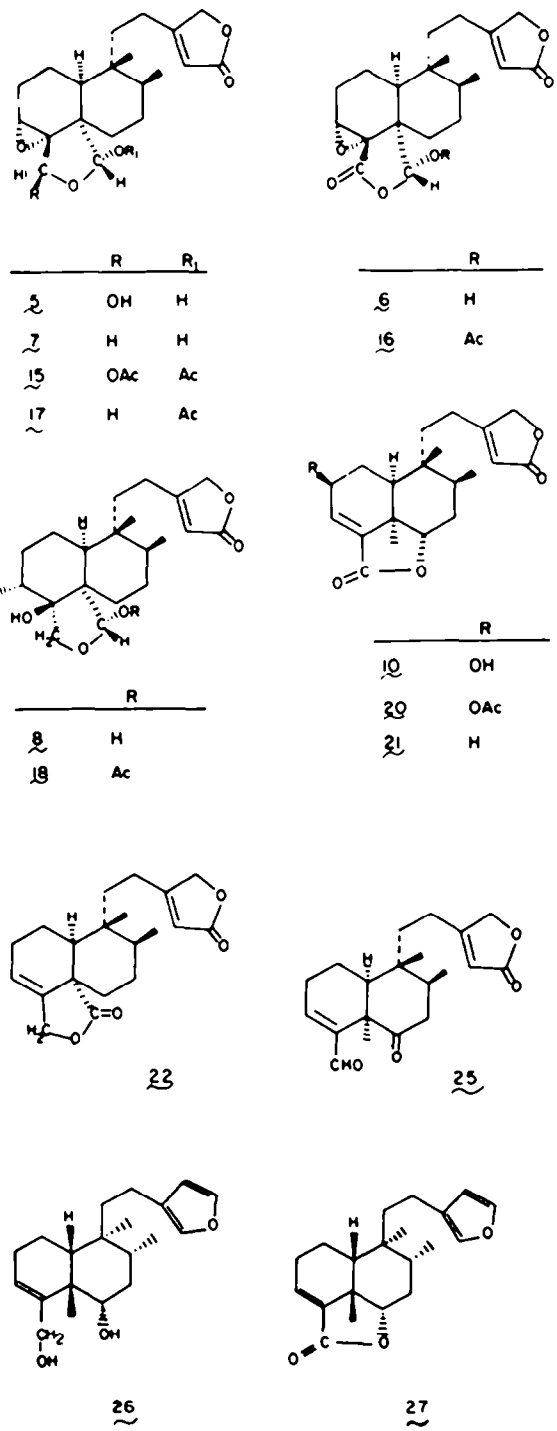
Table 1. ^{1}H NMR data of compounds 1–5 (recorded at 500 MHz, $CDCl_3$, TMS)*

H	1	2	3	4	5
1α	—	1.87 *m*	1.92	1.79 *br m*	1.45
1β	—	—	1.72 *ddd*	1.66	1.45
2α	—	2.18 *br m*	2.11 *m*	2.07	1.58
2β	—	2.18 *br m*	2.38 *m*	2.02	2.06 *br d* (14)
3	5.59 *br t* (3)	5.80	6.79	5.64 *br m* (wl/2:8)	3.52 *br s*
6α	—	—	1.67 *br s*	1.60 *ddd* (4, 14, 14)	1.77
6β	3.42 *dd* (4, 11)	—	1.56 *br s*	1.52 *dt* (4, 4, 14)	1.60
7α	—	—	1.93 —	1.91 *m*	1.78
7β	—	—	1.42 *ddd* (3, 7, 14)	1.33	1.32
8	—	1.40 *br m*	1.60	1.53	1.45
10	—	1.49 —	1.37 *dd* (2, 11)	1.65	1.62
11	—	—	1.50 *ddd* (3, 14, 14)	1.87	1.60
11′	—	—	1.50 *ddd* (5, 14, 14)	1.37	1.45
12	2.23 —	2.26 —	2.33 *ddd* (3, 14, 14)	2.51	2.40
12′	2.13 —	2.26 —	2.33 *ddd* (5, 14, 14)	2.30	2.27
14	5.82 *br s*	5.80	5.80	5.77	5.79
16†	4.73 *br s*	4.72 *d* (1.2)	4.72	4.69 *br s*	4.71
17‡	0.79 *d* (7)	0.76	1.05	1.04	0.91
18	4.28 *br d* (12)	4.20 *br d* (11)	—	4.23 *br d* (11)	5.18 *br s*
18′	4.10 *br d* 12)	3.93 *br d* (11)	—	4.37 *ddd* (3, 5, 11)	—
19	1.31 *s*‡	3.60 *d* (10)	3.72 *dd* (1, 8)	5.44 *d* (4)	5.51 *br s*
19′	—	3.24 *d* (10)	4.54 *d* (8)	—	—
20‡	0.81 *s*	0.75	0.97	0.93	0.80

*Coupling pattern and coupling constants (value in Hz in parentheses) are not repeated if identical with the proceeding column.

†Intensity for two protons.

‡Intensity for three protons.



δ3.72 (H-19α) markedly enhanced the signal at δ1.37 (H-10), and also some enhancement of H-11 (δ1.50), H-16 (δ4.72) and H-12 (δ2.33) was observed. This evidence indicated that the A-B ring was *cis*-fused and that the lactone side chain at C-9 should have an α-orientation. Irradiation of the signal at δ4.54 (H-19β) enhanced the signal for H-7α (δ1.93) and also to some extent the signal for H-16 (δ4.72). Irradiation of the signal at δ1.05 (H-17) gave NOE on the signals for H-6β, H-7β and H-1β. Irradiation of the signal for H-20 (δ0.97) dramatically enhanced the signal at δ1.92 (H-1α) and also the signal for H-10 (δ1.37); models indicated spatial proximity of H-10α and the C-9β methyl group. All these results suggested the A-B ring *cis*-fusion and the C-8β and C-9β methyl groups. From biogenetic considerations, compounds **1**–**4** should be closely related to each other. But while **1**, **2** and **4** had negative optical rotation, **3** exhibited positive optical rotation. Therefore, NOE experiments were also conducted on **4** and the NOE results proved that the AB rings in **4** were also *cis*-fused. Thus, we assigned the stereochemistry for **1** and **2** to be the same as that for **3** and **4** based on NOE results for the later two compounds. The 5α,10α-configuration was also proposed for **2** **10** based on the arguments for **1** and the biogenetic origin.

Compound **4** was the major constituent. Its ^{1}H NMR spectrum, in which a total number of 28 proton signals were unambiguously observed, indicated the presence of a butenolide group and an AB system with allylic coupling (Table 1). In addition to the vinylic proton signal at δ5.64 (*br m*, 1H) for H-3, two doublet signals with the same coupling constants of 4 Hz appeared at δ5.44 and δ3.44. Upon addition of D_2O, the signal at δ3.44 disappeared and the signal at δ5.44 became a singlet. A 2D Cosy spectrum (500 MHz) clearly indicated that the signal at δ5.77 (H-14) was coupled with the signal at δ4.69 (H-16), and the signal at δ5.64 (H-3) was coupled with that for H-2α at δ2.07. The AB quartet (*m* actually) showed further coupling with H-3 and H-2α. Moreover, the downfield part of the AB system was also coupled with H-2β at δ2.02. The signal at δ5.44 was coupled only with the hydroxyl signal at δ3.44. Intensive spin decoupling experiments supported the above assignments. Accordingly, a hemiacetal group could be tentatively assigned to C-19. A C-19 hemiacetal function was confirmed by the Jones oxidation* of the hemiacetal group in **4** into the corresponding lactone function in **22**, the C-18,C-19 structural isomer of **3**. Moreover, **23** and **24** were produced along with **22** in the oxidation. Normal acetylation of **4** yielded, in addition to a normal acetylation product **13**, a by-product **14**, all in accord with a C-19 hemiacetal function. In the ^{13}C NMR spectra of **4**, the hemiacetal function was unambiguously indicated by the resonance at δ101.3 (*d*). The above evidence plus the ^{13}C-^{1}H chemical shift correlations (500 MHz), which confirmed the chemical shift assignments, all supported the structure of **4**. The stereochemistry of **4** was also deduced from NOE results (500 MHz). Irradiation of the doublet methyl signal at δ1.04 enhanced signals at δ1.66 (H-1β), 1.33 (H-7β) and 1.52 (H-6β). Irradiation of the methyl singlet at δ0.93 enhanced signals for H-1α,12,11′ and H-10. Irradiation of the signal at δ4.37 (H-18β) enhanced the signal for H-6α. All these results supported **4** having the same A,B ring *cis*-fusion as **3**. For a final proof, compound **4** was submitted for X-ray crystallographic analysis and the results [W. H. Watson *et al.*, personal communication] confirmed that A,B-ring is *cis*-fused, the hydroxyl group at the C-19 position is α-located and the other chiral centres are as depicted.

Spectral data for **5** indicated that it had a similar skeleton as **4**; however, in the ^{1}H NMR spectrum of **5**, the C-3 vinylic proton signal exhibited by **4** was replaced by a broadened singlet at δ3.52 which did not disappear upon

*This successful reaction is noteworthy because earlier attempts to oxidize a similar hemiacetal group into a corresponding lactone were not successful [5].

addition of D_2O. This evidence suggested a C-3,C-4 epoxy function, a conclusion which was also supported by spin decoupling experiments. In the ^1H NMR spectrum, in addition to the H-19 signal at δ5.51 (*s*) similar to the one exhibited by **4**, another broad singlet at δ5.18 suggested a second hemiacetal group at C-18. In the ^{13}C NMR spectrum, the ^{13}C–^1H chemical shift correlations (500 MHz) established the signal assignments while the C-18,C-19 dihemiacetal groups and the C-3,C-4 epoxy system were confirmed by the signals at δ97.8 (*d*), 102.7 (*d*) and δ57.3 (*d*), 70.6 (*s*). The stereochemistry at C-3 and C-4 is tentatively assigned based on the following arguments. Firstly, from biogenetic considerations, compound **5** should have the same 5α,10α-A,B -ring *cis*-fusion system as **3** and **4** had, and thus, the C-3α,C-4 epoxy, a less hindered position, should be favoured. Secondly, the ^1H NMR data of H-3 (δ3.52, *br s*, $W_{1/2} < 2$ Hz) were more similar to those reported for a 3α-epoxide rather than those (*d*, $J \approx 5.5$ Hz) for a 3β-epoxide [8]. Thirdly, a 3α-hydroxy analogue, **8**, which was most likely derived from the 3α-epoxy compound by epoxy ring opening, was also isolated from this extract. The hydroxyl group at the C-19 position in **5** (and also in **6**, **7** and **8**) was correlated with that in **4** in which a C-19 hydroxy was confirmed by X-ray analysis. However, the β-hydroxyl group at the C-18 position was assigned on the basis of NOE experiments since irradiation of the signal at δ 5.18 enhanced only the signal for H-3 at δ3.52. This indicated a C-18β hydroxy group since if irradiation of C-18β proton signal enhanced the H-3 signal, inspection of molecular models indicated that it should also enhance a signal for H-6. As expected, irradiation of the signal at δ5.51 (H-19) did not enhance the H-3 signal. These NOE results, together with the ^{13}C–^1H chemical shift correlations, also helped to confirm the ^{13}C NMR and ^1H NMR signal assignments (Tables 1–3 and 6) at the C-18 and the C-19 positions in **5**–**8**. As expected, **5** readily gave the diacetate **15** on acetylation. Therefore, we assigned compound **5** as 3α,4:18,19-diepoxy-18β,19α-dihydroxy-*cis*-cleroda-13(14)-ene-15,16-olide.

^1H NMR data for compound **6** were similar to those for **5** except that one of the two singlet signals for the

Table 2. ^1H NMR data of compounds **6**–**8**, **16**–**18** (200 MHz, $CDCl_3$, TMS)*

	6	16	7	17	8	18
H-3	3.61 *br s*	3.65	3.29	3.33	3.74 *dd* (5, 11)	4.91
H-14	5.84 *br t* (1.5)	5.80	5.81	5.79	5.85	5.85
H-16†	4.77 *d* (1.7)	4.71	4.75	4.70	4.77	4.82
H-17‡	0.99 *d* (7)	0.92	1.00	0.92	1.03	0.97
H-18	--	--	4.00 *d* (10)	3.94	4.29 *d* (11)	4.33
	—	—	3.83 *d* (10)	3.88	3.99 *d* (11)	3.96
H-19	5.92 *br s*	6.70 *s*	5.55 *br s*	6.42 *s*	5.50 *br s*	6.51 *s*
H-20‡	0.88 *s*	0.86	0.87	0.85	0.94	0.92
OAc‡		2.17 *s*	—	2.09 *s*	--	2.05 *s*
OAc‡		--	—			1.99 *s*

*Coupling pattern and coupling constants (value in Hz in parentheses) are not repeated if identical with the proceeding column.

†Intensity for two protons.

‡Intensity for three protons.

Table 3. ^1H NMR data of compounds **10**–**15** and **20** (200 MHz, $CDCl_3$, TMS)*

H	10	20	11	12	13	14	15
2	4.64 *ddd* (3, 9, 9)	5.64	—	—	–	—	—
3	6.72 *d* (3)	6.66	5.71 *br t* (3)	5.91	5.65 *br m* (w1/2: 8)	6.18 *br t* (3)	3.54 *br s*
6	4.32 *dd* (7, 11)	4.32	4.6–4.9	—	.	—	—
14	5.88 *br t* (1.5)	5.87	5.86	5.86	5.78	5.85	5.79
16†	4.76 *d* (1.7)	4.75	4.76	4.77	4.70	4.75	4.70
17‡	0.86 *d* (7)	0.87	0.83	0.80	1.04	0.96	0.91
18	—	—	4.6–4.9	4.62 *br s*	4.24 *ddd* (2, 3, 11)	4.58 *br s*	6.19 *s*
	—	--	4.6–4.9	4.62 *br s*	4.43 *ddd* (3, 5, 11)	4.58 *br s*	—
19	1.38 *s*‡	1.39‡	1.16‡	3.96 *d* (11)	6.39 *s*	9.38	6.44
	—	--	—	3.87 *d* (11)	—	--	—
20‡	0.75 *s*	0.81	0.87	0.83	0.96	0.91	0.85
OAc‡	—	2.10 *s*	2.07	2.07	2.01	2.04	2.07
OAc‡	--	—	2.08 *s*	2.08	—	—	2.11 *s*

*Coupling pattern and coupling constants (value in Hz in parentheses) are not repeated if identical with the proceeding column.

†Intensity for two protons.

‡Intensity for three protons.

hemiacetal groups observed for **5** was not present. The ^{13}C NMR data for **6** were also similar to those for **5** except for some differences for C-18, C-4, C-3 and C-19 (Table 6). Instead of two doublet hemiacetal signals as in **5**, **6** exhibited only one hemiacetal doublet signal at δ 101.3 but another singlet at δ 175.6 was observed. This evidence suggested that one of the hemiacetal groups in **5** was oxidized into a carbonyl group to yield **6**. That C-18 was oxidized to a carbonyl group was evident from the following data. In the ^{13}C NMR spectrum, the C-5 signal (δ45.1) in **6** remained almost unchanged when compared with the C-5 signal (δ45.9) in **5**. In contrast, the C-4 signal was greatly shielded ($\Delta\delta$9.9) and the C-3 signal was slightly deshielded ($\Delta\delta$2.2). As expected, **6** gave only the monoacetate **16** on acetylation. By comparing all the available data, **6** could be deduced to be 3α,4-epoxy-19α-hydroxy-*cis*-cleroda-13(14)-ene-15,16:18,19-diolide.

Spectral properties of **7** were similar to those for **5** and **6**. One hemiacetal group was deduced based on the signals at δ5.55 (*br s*) and the AB quartet (δ4.00 and 3.83, two *d*, J = 10 Hz) in its ^1H NMR spectrum and this was also supported by spectral properties of the monoacetate **17** derived from **7**. That the hemiacetal group was attached at the position of C-19 rather than C-18 followed from the following evidence. The chemical shift for the hemiacetal signal at δ5.55 was closer to the value for the H-19 signal at δ5.51 rather than the value for the H-18 signal at δ5.18 in **5**. Moreover, the ^{13}C NMR data (Table 6) indicated that the C-5 and C-19 signals were not shifted in comparison to the data for **5** and **7**, while the C-4 signal shifted up-field from δ70.6 in **5** to 67.2 in **7** and the C-3 signal shifted down-field from δ57.3 in **5** to δ60.2 in **7**. Furthermore, NOE results (500 MHz) were in good agreement with the above analysis since irradiation of the epoxy signal at δ3.29 dramatically enhanced part of the AB quartet at δ4.00 (and also the H-2 signals at δ2.10 and 1.65); the reciprocal irradiation of the signal at δ4.00 enhanced the signal at δ3.29; irradiation on the signal at δ5.55 did not enhance the signal at δ3.29. Therefore, **7** was deduced to be 3α,4:18,19-diepoxy-19α-hydroxy-*cis*-cleroda-13(14)-ene-15,16-olide.

^1H NMR data of **8** indicated that it should be closely related to **7** (Table 2). While a hemiacetal signal at δ5.50 was similar to that (δ5.55) exhibited by **7**, the signal for H-3 (δ3.29) for **7** shifted downfield to δ3.74 in **8**. Moreover, the coupling pattern of this signal changed from a *br s* in **7** to a *dd* (J = 5, 11 Hz) in **8**. Obviously, the signal at δ3.74 was attributable to a proton attached to a carbon atom bearing a free hydroxyl group; this was confirmed by the formation of the diacetate **18**. Consequently, a C-3,C-4 dihydroxy function could be proposed. In the ^{13}C NMR spectrum, a hemiacetal doublet signal was present at δ104.1. Two free hydroxy-bearing carbon signals (one *d* and one *s*) were observed at δ72.7 and 85.1. It was clear that the deshielding effect on C-3 and C-4 was due to the epoxy-ring opening on the basis of comparing the data for **8** with those for **7**. A 3α-hydroxyl group followed from the H-3 coupling (J = 5, 11 Hz) and a C-4β-hydroxyl group could only be assigned based on the A,B ring *cis*-fusion and the C-18,C-19 five-member ring construction. This is probably due to the epoxy ring opening of **7** to form a *trans*-diol system found in **8**. Similar *trans*-diaxial openings of this type of epoxide were previously reported [5]. **7** and **4** are the likely precursors of **8** and, therefore, we proposed the stereochemistry of **8** as depicted.

^{13}C NMR data of **9** indicated that it was a pentoside of a clerodane-butenolide (an anomeric doublet at δ95.2, a triplet at δ66.9 and three other oxygen-bearing doublets at δ68.1, 73.3 and 70.4). ^1H NMR data of **9** at 500 MHz showed clearly all signals of the pentosyl moiety. The coupling pattern and coupling constants (Table 4) were in accord with those of other arabinopyranosides isolated from *Gutierrezia* [2]. Moreover, acid hydrolysis of **9** yielded arabinose and an aglycone **19**. The α-L-arabinosyl linkage was deduced based on $J(1',2')$ = 7.5 Hz. The vinylic methyl signal at δ1.59 (*br s*, 3H) left only position C-19 for the arabinosyl group. All spectral data, including those for the aglycone **19**, supported the structure of **9** as 19-*O*-α-L-arabinopyranosyl-*cis*-cleroda-3,13(14)-diene-15,16-olide-19-oic ester.

Compound **10** was a minor constituent. The ^1H NMR signals at δ4.32 (*dd*, J = 7, 11 Hz) and 6.72 (*d*, J = 3 Hz) suggested that a C-18,6α lactone was present when these data were compared with relevant data for **1**. One secondary hydroxyl group in **10** was confirmed by the formation of a monoacetate **20**. The C-2 hydroxyl group followed from the signal for H-3 (*d*, J = 3 Hz) and spin decoupling experiments on **10**: irradiation on the signal for H-3 (δ6.72) collapsed the signal at δ4.64 into a triplet (J = 9 Hz). Irradiation of the signal at δ4.64 collapsed the doublet at δ6.72 into a singlet. That the C-2 hydroxul group should have a β-orientation was indicated by inspection of models and consideration of coupling constants.

EXPERIMENTAL

Gutierrezia texana (DC) T. and G. var. *texana* was collected by M. Leidig and F. Gao on 3 Sept. 1984 in Travis Co., TX, off Highway 183, near the bridge over Cottonmouth Creek. The material was identified by Meredith A. Lane, Department of Botany, University of Colorado, Boulder. A voucher specimen (MAL2009) is on deposit in the Herbarium of the University of Texas at Austin.

Isolation of compounds. Aerial parts (529 g) of *G. texana* were extracted with CH_2Cl_2 (10 l.; 30 min × 2). The combined extract when evapd afforded a residue which was dissolved in Me_2CO (1.4 l.); the soln was stored in a refrigerator overnight. After

Table 4. ^1H NMR data of compounds **9** (recorded at 500 MHz) and **19** (recorded at 200 MHz) ($CDCl_3$, TMS)

H	9	19
3	5.56 *br m*	5.63 *br m*
14	5.88 *br s*	5.84 *br t* (1.5)
16	4.77 *dd* (1.5, 17)	4.74 *d* (1.7)
	4.72 *dd* (1.5, 17)	4.74 *d* (1.7)
17*	0.92 *d* (7)	0.93 *d* (7)
18*	1.59 *br s*	1.73 *br s*
20*	0.89 *s*	0.91 *s*
Arabinosyl		
1'	5.32 *d* (7.5)	—
2'	3.76 *dd* (7.5, 9)	—
3'	3.64 *dd* (3, 9)	—
4'	3.94 *br s*	—
5'a	3.60 *br d* (12)	—
5'b	3.90 *dd* (2, 12)	—

*Intensity for three protons.

Table 5. ^{1}H NMR data of compounds 21–25 (90 MHz, $CDCl_3$, TMS)*

H	21	22	23	24	25
3	6.86 *t* (3)	5.85	6.91	7.03 *dd* (3,6)	6.91 *t* (3)
6	4.31 *dd* (7,11)	—	-	—	—
14	5.86 *br t* (1.5)	5.85	5.82	5.82	5.74
16†	4.73 *d* (1.5)	4.80 *br s*	4.76	4.73	4.71
17‡	0.81 *d* (6)	0.98	1.08	0.97	0.85
18	—	4.47 *br d* (10)		10.12 *br s*	9.40
	—	4.95 *d* (10)	—	—	
19‡	1.25 *s*	—	5.98 *br s*	9.28 *s*	1.25
20‡	0.75 *s*	0.98	1.00	0.94	0.93

*Coupling pattern and coupling constants (value in Hz in parentheses) are not repeated if identical with the preceding column.

†Intensity for two protons.

‡Intensity for three protons.

Table 6. ^{13}C NMR data of compounds 1–9 [22.6 MHz (4 and 5 at 125.8 MHz), $CDCl_3$, TMS]*

C No.	1	2	3	4†	5†	6	7	8	9
1	17.0 *t*	17.2	24.4	23.0	17.8 *p*	17.9 *t*	18.3	17.2	21.9
2	35.1 *t*	31.1	27.2	26.2	26.4 *p*	26.2 *t*	27.0	30.4	26.5
3	129.4 *d*	131.0	136.6	119.6	57.3 *n*	59.5 *d*	60.2	72.7	125.7
4	141.4 *s*	139.8	135.2	140.9	70.6 *p*	60.7 *s*	67.2	85.1	135.3
5	42.4 *s*	41.5	43.6	49.1	45.9 *p*	45.1 *s*	45.4	54.7	51.4
6	79.7 *d*	27.9 *t*	25.7	23.7	19.8 *p*	19.6 *t*	19.8	26.2	26.0
7	21.9 *t*	21.9	25.5	25.9	25.2 *p*	24.5 *t*	25 5	25.1	25.5
8	36.0 *d*	36.9	35.8	37.1	35.1 *n*	34.5 *d*	35.7	36.8	35.0
9	40.0 *s*	39.9	38.8	37.8	37.4 *p*	37.3 *s*	37.6	39.2	38.9
10	45.5 *d*	40.6	45.3	38.5	37.9 *n*	36.7 *d*	38.0	40.3	42.9
11	37.5 *t*	34.8	40.0	39.9	39.0 *p*	38.8 *t*	39.2	41.4	37.4
12	23.5 *t*	23.6	22.6	23.8	23.6 *p*	23.5 *t*	23.9	23.6	23.3
13	171.1 *s*	171.4	171.1	173 1	172.9 *s*	172.8 *s*	173.1	171.4	173 2
14	115.0 *d*	114.8	115 7	114.3	114.3 *n*	114.5 *d*	114.5	115.2	114.5
15	174.2 *s*	174.3	174.4	175.1	175.3 *p*	174.2 *s*	175.3	174.7	175.8
16	73.0 *t*	73.1	76.6	73.5	73.6 *p*	73 8 *t*	73.7	73.5	73.9
17	15.5 *q*	15.7	18.3	17.7	16.7 *n*	16.4 *q*	17.0	17.0	16.8
18	67.6 *t*	75.2	170.9 *s*	67.4 *t*	102.7 *n*	175.6 *s*	66.7 *t*	66.7	19.4 *q*
19	31.0 *q*	64.8 *t*	77.0	101 1 *d*	97.8 *n*	101.3 *d*	102.6 *d*	104.1	176.5 *s*
20	17.6 *q*	17.2	22.7	22.3	21.8 *n*	21.4 *q*	22.2	23.6	21.0
Arabinosyl									
1'	—	—	—		—		—	—	95.2 *d*
2'				—	—	—	-	—	68.1 *d*
3'		-		—	—	—	--	—	73.3 *d*
4'	.	.		—	-	—	.	—	70.4 *d*
5'	—	—	—	--	-	—	—		66.9 *t*

*Multiplicities are not repeated if identical with the preceding column.

†Assignments for 4 and 5 were confirmed by ^{13}C–^{1}H chemical shift correlation and for 5 also by attached proton test. The APT results are given at the right within the column for 5: *p* = positive signal (two protons or no proton attached); *n* = negative signal (one or three protons).

filtering through celite, the soln was evapd to yield 28.2 g of a dark brown syrup which was applied onto a silica gel column. The column was eluted with a hexane–EtOAc gradient to yield, after further separation and purification over a Sephadex LH-20 column packed in cyclohexane CH_2Cl_2–MeOH (7:4:1), compounds 3, 4 and 7. Further elution of the silica gel column with MeOH–EtOAc (9:1) yielded a complex mixture. The mixture was first passed through a Sephadex LH-20 column. Final separations were achieved by HPLC using the following conditions: semi prep. silica gel column (10 mm × 25 cm); RI detector; EtOAc as eluting solvent; flow rate: 2.8 ml/min. Compounds 1 (60 mg), 2 (200 mg), 5 (300 mg), 6 (26 mg), 8 (39 mg), 9 (110 mg) and 10 (10 mg) were obtained.

6α,18-*Dihydroxy*-cis-*cleroda*-3,13(14)-*diene*-15,16-*olide* (1). $[\alpha]_D^{23}$ – 6.4° ($CHCl_3$, *c* 1.2). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 3100, 3030, 1780, 1640 (C=C), 1750 (C=O), 1030, 1010, 760. EIMS (probe)

70 eV, *m/z* (rel. int.): 316 [M – H_2O]$^+$ ($C_{20}H_{30}O_4$, 334), (17), 301 [316 – Me]$^+$ (100), 111 [$C_6H_7O_2$]$^+$ (22).

Oxidation of **1**. **1** (44 mg in 3 ml Me_2O) was treated with three drops of Jones reagent for 5 min. After removal of most of the Me_2O, the reaction mixture was poured into H_2O and extracted with EtOAc. The crude products obtained in the usual work-up were separated by HPLC (conditions as described above but using hexane–EtOAc, 1:1) to obtain **21** (7 mg), **25** (6 mg) and a minor compound (unidentified). The diolide **21** had $[\alpha]_D^{24}$ – 22.4° ($CHCl_3$; *c* 0.66); EIMS (probe) 70 eV, *m/z* (rel. int.): 330 [M]$^+$ ($C_{20}H_{26}O_4$] (78), 315 [M – Me]$^+$ (99), 219 [M – $C_6H_7O_2$]$^+$ (98), 149 (100), 111 [$C_6H_7O_2$]$^+$ (46). The aldehydic ketone **25** had $[\alpha]_D^{25}$ – 44.7° ($CHCl_3$; *c* 0.55); EIMS (probe) 70 eV, *m/z* (rel. int.): 330 [M]$^+$ ($C_{20}H_{26}O_4$) (8), 315 [M – Me]$^+$ (19), 220 [M – $C_6H_6O_2$]$^+$ (22), 111 [$C_6H_7O_2$] (71), 69 (100).

Acetylation of **1**. Compound **1** (15 mg) was acetylated with Ac_2O pyridine to yield diacetate **11** (16 mg). EIMS (probe) 70 eV *m/z* (rel. int.): 316 [M – MeCOO – MeCO]$^+$ (3), 301 [316 – Me]$^+$ (10), 283 [301 – H_2O]$^+$ (7), 43 [MeCO]$^+$ (100).

18,19-*Dihydroxy*-cis-*cleroda*-3,13(14)-*diene*-15,16-*olide* (**2**). Colourless prisms from EtOAc, mp 149–150°. $[\alpha]_D^{25}$ – 29.7° (MeOH, *c* 0.75). IR ν_{max}^{KBr} cm^{-1}: 3200–3400 (*br* OH), 3000, 1780, 1640, (C=C), 1750 (C=O), 1060, 1030, 1000, 890, 860. EIMS (probe) 70 eV, *m/z* (rel. int.): 316 [M – H_2O]$^+$ ($C_{20}H_{30}O_4$, 334) (6), 298 [M – $2H_2O$]$^+$ (3), 285 [316–CH_2OH]$^+$ (72), 173 [316 – MeOH – $C_6H_7O_2$]$^+$ (93), 111 [$C_6H_7O_2$] (43), 105 (100%).

Acetylation of **2**. Compound **2** (32 mg) was acetylated with Ac_2O pyridine to afford 33 mg of the diacetate **12**. EIMS (probe) 70 eV, *m/z* (rel. int.): 316 [M – MeCOO – MeCO]$^+$ (3), 298 [M – 2 × MeCOOH]$^+$ (20), 285 [316 – CH_2OH]$^+$ (100), 43 [MeCO]$^+$ (62).

Oxidation of **2**. Compound **2** (34 mg) in 3 ml Me_2O, was treated with 4.5 drops of Jones reagent added under magnetic stirring at room temp within 5 min. After removal of most of the Me_2O, H_2O was added to the reaction mixture. Usual work-up yielded 31 mg of almost pure **3** (identity to the natural compound was confirmed by ^{1}H NMR and TLC).

cis-*Cleroda*-3,13(14)-*diene*-15,16:18,19-*diolide* (**3**). White needles (64 mg) from EtOAc, mp 195–196°. $[\alpha]_D^{30}$ + 41.4° ($CHCl_3$; *c* 1.3). IR ν_{max}^{KBr} cm^{-1}: 3100, 1770, 1680, 1630 (C=C), 1740 (vs, 2 × C=O), 1200, 1030, 980, 890, 760. EIMS (probe) 70 eV, *m/z* (rel. int.): 330 [M]$^+$ ($C_{20}H_{26}O_4$) (5), 219 [M – $C_6H_7O_2$]$^+$ (3), 111 [$C_6H_7O_2$]$^+$ (19), 91 (100%).

18,19-*Epoxy*-19α-*hydroxy*-cis-*cleroda*-3,13(14)-*diene*-15,16-*olide* (**4**). Colourless prisms (390 mg) from EtOAc, mp 151–153°. $[\alpha]_D^{25}$ – 59.2° (MeOH; *c* 1.2); $[\alpha]_D^{24}$ – 49.1° ($CHCl_3$, *c* 1.2). IR ν_{max}^{KBr} cm^{-1}: 3360 (OH), 3100, 1790, 1620, (C=C), 1720 (C=O), 1160, 1040, 1000, 910, 890. EIMS (probe) 70 eV, *m/z* (rel. int.): 314 [M – H_2O]$^+$ ($C_{20}H_{28}O_4$, 332) (100), 299 [314 – Me]$^+$ (8), 285 (68), 111 [$C_6H_7O_2$]$^+$ (50).

Acetylation of **4**. Compound **4** (93 mg) was acetylated with Ac_2O pyridine at *ca* 50° for 7 hr. After usual work-up, the reaction products **13** (69 mg) and **14** (18 mg) were separated by HPLC using a semi-prep. silica gel column (10 mm × 25 cm), RI detector, hexane EtOAc (2:1) as solvent at a flow rate of 2.8 ml/min. The monoacetate **13**, EIMS (probe) 70 eV, *m/z* (rel. int.): 315 [M$^+$ – MeCOO]$^+$ ($C_{22}H_{30}O_5$, 374) (20), 285 [315 – CH_2O]$^+$ (39), 173 [285 – $C_6H_8O_2$]$^+$ (88), 105 (100). The aldehydic acetate **14**, IR ν_{max}^{KBr} cm^{-1}: 3100, 1780, 1640 (C=C), 2700 (CHO), 1730 (vs, 2 × C=O), 1240 (COOR). EIMS (probe) 70 eV, *m/z* (rel. int.): 285 [M – HOAc – CHO]$^+$ ($C_{22}H_{30}O_5$, 374) (32), 173 [285 – $C_6H_8O_2$]$^+$ (59), 105 (100).

Oxidation of **4**. Compound **4** (62 mg) was dissolved in 4 ml Me_2O. Jones reagent (seven drops) was added under magnetic stirring at room temp within 40 min. Work-up gave 57 mg crude products (three major spots). Separation was made on HPLC using the conditions described above with the solvent system hexane–EtOAc (1:1); **22** (8 mg), **23** (8 mg) and **24** (9 mg) were obtained. **23**: $[\alpha]_D^{21}$ – 21° ($CHCl_3$, *c* 1.0); **24**: $[\alpha]_D^{24}$ – 21.8° ($CHCl_3$, *c* 0.5). EIMS (probe) 70 eV, *m/z* (rel. int.) for **22**: 330 [M]$^+$ ($C_{20}H_{26}O_4$) (4), 285 [M – COOH]$^+$ (15), 220 [M – $C_6H_6O_2$]$^+$ (90), 175 [285 – $C_6H_6O_2$]$^+$ (89), 111 [$C_6H_7O_2$]$^+$ (95), 105 (100); for **23**: 364 [M]$^+$ ($C_{20}H_{28}O_5$) (1), 314 [M – MeOH]$^+$ (3), 301 [M – COOH]$^+$ (11), 271 [M – $C_2H_3O_3$]$^+$ (23), 190 [M – $C_6H_7O_2$]$^+$ (100), 111 [$C_6H_7O_2$]$^+$ (86); for **24**: 330 [M]$^+$ ($C_{20}H_{26}O_4$) (2), 298 [M – MeOH]$^+$ (59), 192 (100), 111 [$C_6H_7O_2$]$^+$ (85).

3α,4:18,19-*Diepoxy*-18β,19α-*dihydroxy*-cis-*cleroda*-13(14)-*ene*-15,16-*olide* (**5**). $[\alpha]_D^{30}$ + 19.9° ($CHCl_3$, *c* 0.8). IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 3120, 1780, 1640 (C=C), 1750 (C=O), 1120, 1010, 960, 940, 900, 850. EIMS (probe) 70 eV, *m/z* (rel. int.): 347 [M – OH]$^+$ ($C_{20}H_{28}O_6$, 364) (2), 346 [M – H_2O]$^+$ (1), 328 [M – 2 × H_2O]$^+$ (1), 111 ($C_6H_7O_2$]$^+$ (100).

Acetylation of **5**. Compound **5** (25 mg) was acetylated with Ac_2O pyridine in the usual manner to give 25 mg diacetate **15**. EIMS (probe) 70 eV, *m/z* (rel. int.): 389 [M – MeCOO]$^+$ ($C_{24}H_{32}O_8$, 448) (3), 360 [389 – CHO]$^+$ (3), 347 [389 – C_2H_2O]$^+$ (36), 328 [M – 2 × $MeCO_2H$]$^+$ (5), 318 [347 – CHO]$^+$ (46), 300 [318 – H_2O]$^+$ (22), 111 [$C_6H_7O_2$]$^+$ (84), 43 [MeCO]$^+$ (100).

3α,4-*Epoxy*-19α-*hydroxy*-cis-*cleroda*-13(14)-*ene*-15,16:18,19-*diolide* (**6**). IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 1780, 1640 (C=C), 1740 (vs, 2 × C=O), 1130, 1030, 910, 760. EIMS (probe) 70 eV, *m/z* (rel. int.): 289 [M – C_2HO_3]$^+$ ($C_{20}H_{26}O_6$, 362) (39), 271 [289 – H_2O]$^+$ (13), 111 [$C_6H_7O_2$]$^+$ (100).

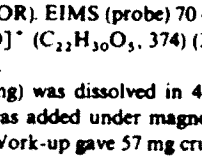
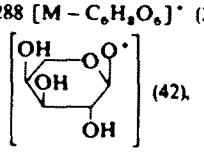
Acetylation of **6**. Compound **6** (14 mg) was acetylated with Ac_2O–pyridine in the usual way to give 12 mg of **16**. $[\alpha]_D^{23}$ – 5° ($CHCl_3$, *c* 1.2). EIMS (probe) 70 eV, *m/z* (rel. int.): 344 [M – MeCOOH]$^+$ ($C_{22}H_{28}O_7$, 404) (10), 315 [344 – CHO]$^+$ (18), 233 [344 – $C_6H_7O_2$]$^+$ (58), 177 (99), 43 [MeCO]$^+$ (100).

3α,4:18,19-*Diepoxy*-19-*hydroxy*-cis-*cleroda*-13(14)-*ene*-15,16-*olide* (**7**). Compound **7** (190 mg) had the following properties: $[\alpha]_D^{25}$ – 21.8° ($CHCl_3$, *c* 3.1). IR ν_{max}^{KBr} cm^{-1}: 3420, 1040 (OH), 3120, 1780, 1640 (C=C), 1750, (C=O), 940, 890, 840, 770. EIMS (probe) 70 eV, *m/z* (rel. int.): 330 [M – H_2O]$^+$ ($C_{20}H_{28}O_5$, 348) (6), 312 [M – 2 × H_2O]$^+$ (5), 111 [$C_6H_7O_2$]$^+$ (100).

Acetylation of **7**. Compound **7** (14 mg) was acetylated with Ac_2O–pyridine for 6 hr. After usual work-up, 14 mg of **17** were obtained. IR ν_{max}^{KBr} cm^{-1}: 3120, 1780, 1640 (C=C), 1750 (C=O), 1250, 890. EIMS (probe) 70 eV, *m/z* (rel. int.): 331 [M – MeCOO]$^+$ (4), 111 [$C_6H_7O_2$]$^+$ (55), 43 [MeCO]$^+$ (100).

3α,4β,19α-*Trihydroxy*-18,19-*epoxy*-cis-*cleroda*-13(14)-*ene*-15,16-*olide* (**8**). IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 3120, 1780, 1640 (C=C), 1740 (C=O), 1030, 760. EIMS (probe) 70 eV, *m/z* (rel. int.): 314 [M – H_2O – 2 × OH]$^+$ ($C_{20}H_{30}O_6$, 366) (1), 312 [M – 3 × H_2O]$^+$ (1), 173 (22), 111 [$C_6H_7O_2$]$^+$ (100).

Acetylation of **8**. Compound **8** (14 mg) was acetylated with Ac_2O pyridine for 3 hr to give 10 mg **18**. $[\alpha]_D^{23}$ + 14.1° ($CHCl_3$, *c* 1.2). EIMS (probe) 70 eV, *m/z* (rel. int.): 391 [M – MeCOO]$^+$ ($C_{24}H_{34}O_8$, 450) (2), 330 [M – 2 × MeCOOH]$^+$ (4), 111 [$C_6H_7O_2$]$^+$ (84), 43 [MeCO]$^+$ (100).

19-*O*-α-L-*Arabinopyranosyl*-cis-*cleroda*-3,13(14)-*diene*-15,16-*olide*-(19-*oic ester*) (**9**). $[\alpha]_D^{26}$ – 19° (MeOH, *c* 0.77). IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 3120, 1780, 1640 (C=C), 1740 (vs, 2 × C=O), 1080, 1030, 950, 790. EIMS (probe) 70 eV, *m/z* (rel. int.) 332 [M – $C_5H_8O_4$]$^+$ ($C_{25}H_{36}O_8$, 464) (2), 288 [M – $C_6H_8O_6$]$^+$ (25), 177  (70), 149  (42), 111 [$C_6H_7O_2$]$^+$ (27), 109 (100).

Acid hydrolysis of **9**. Compound **9** (12 mg) was dissolved in 0.5 ml MeOH and 1.5 ml 5% HCl was added. The mixture was stirred at 80° for 2 days. The reaction mixture was then extracted with EtOAc to yield an EtOAc extract and a H_2O layer. The EtOAc extract yielded an aglycone **19** (8 mg). IR ν_{max}^{KBr} cm^{-1}: 3400–2600 (COOH), 1780–1680 (2 × C=O), 1630 (C=C), 1180, 1130, 1030, 750. EIMS (probe) 70 eV, *m/z* (rel. int.): 332 $[M]^+$ ($C_{20}H_{28}O_4$) (7), 302 $[M - 2 \times Me]^+$ (3), 288 $[M - CO_2]$ (40), 287 $[M - COOH]^+$ (39), 175 (100), 111 $[C_6H_7O_2]^+$ (81). The H_2O layer yielded one sugar, arabinose (identified by cellulose TLC, in pyridine–EtOAc–HOAc–H_2O, 36:36:7:21. Hydrogen aniline phthalate was used for visualization).

2β,6α-Dihydroxy-cis-cleroda-3,13(14)-diene-15,16:18,6α-diolide (**10**). IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 3120, 1780, 1640 (C=C), 1750 (C=O), 1030, 970, 770, 760. EIMS (probe) 70 eV, *m/z* (rel. int.): 346 $[M]^+$ ($C_{20}H_{26}O_5$) (1), 331 $[M - Me]^+$ (88), 313 $[331 - H_2O]^+$ (45), 119 (100), 111 $[C_6H_7O_2]^+$ (93).

Acetylation of **10**. Compound **10** (10 mg) was acetylated with Ac_2O–pyridine in the usual manner to give 9 mg monoacetate **20**. EIMS (probe) 70 eV, *m/z* (rel. int.): 346 $[M - MeCOO]^+$ (38), 331 $[346 - Me]^+$ (13), 313 $[331 - H_2O]^+$ (19), 43 $[MeCO]^+$ (100).

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