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## Five New Modified 6,7-Secolabthane Diterpenoids from *Cluytia richardiana*

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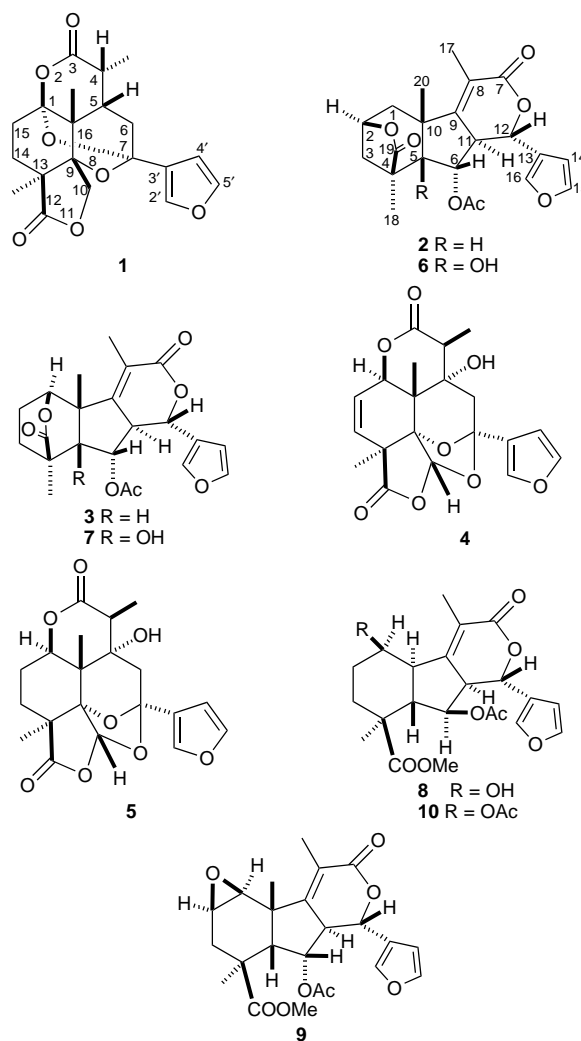
The aerial parts of *Cluytia richardiana* yielded five new modified 6,7-secolabthane diterpene derivatives, saudinolide (**4**), dihydrosaudinolide (**5**), 5 $\beta$ -hydroxyrichardianidin **1** (**6**), and 5 $\beta$ -hydroxyrichardianidin **2** (**7**), and the 6,7-seco-6,11-cyclo-20-norlabthane cluytene F (**8**). The structural assignments of the diterpenoids were based on their spectral data, including 2D NMR experiments, and chemical derivatization. X-ray crystallographic analyses provided unambiguous characterization of the structures and relative stereochemistries of **4**, **6**, **7**, and 1-*O*-acetylcluytene F (**10**).

In our previous reports,<sup>1,2</sup> we described the structures of five new modified labthane diterpenoids, namely, the 6(7),9(10)-biseco-6(11),1(9)-bicyclobabdanes, cluytenes A and C, and the 6,7-seco-6,11-cyclobabdanes, cluytenes B, D, and E, isolated from the aerial parts of *Cluytia richardiana* L. (Euphorbiaceae). Earlier investigations have reported on the isolation of other 6,7-secolabdanes, including saudin (**1**),<sup>3</sup> richardianidin **1** (**2**), and richardianidin **2** (**3**);<sup>4</sup> the structures of **1** and **2** were unambiguously established by X-ray crystallography. Furthermore, saudin (**1**) was found to possess a significant hypoglycemic effect in nonalloxanized rather than alloxanized fasted mice.<sup>3,5</sup> Examination of the same source<sup>1,2</sup> has now led to the isolation and characterization of five additional structurally related new diterpenoids, namely, the two saudin derivatives, saudinolide (**4**) and its dihydro derivative **5**, the 5 $\beta$ -hydroxyrichardianidin derivatives **6** and **7**, as well as the 6,7-seco-6,11-cyclo-20-norlabthane, cluytene F (**8**) (Chart 1).

### Results and Discussion

The EtOAc precipitate, obtained from the defatted EtOAc extract of *C. richardiana* (see the Experimental Section)<sup>1,2</sup> was flash chromatographed over Si gel to give, in crystalline form, the major diterpenoids **4** and **5** in 0.03% and 0.015% yields, respectively. Saudinolide (**4**), C<sub>20</sub>H<sub>20</sub>O<sub>8</sub>, was found to have a  $\gamma$ -lactone ( $\nu_{\max}$  1780 cm<sup>-1</sup>;  $\delta_C$  174.7) and a  $\delta$ -lactone ( $\nu_{\max}$  1720 cm<sup>-1</sup>;  $\delta_C$  172.7); a monosubstituted furan ring, as previously encountered in all diterpenoids isolated from this plant, was also present. The <sup>1</sup>H- and <sup>13</sup>C-NMR spectral data (Table 1) were generally similar to those of the earlier reported 6,7-secolabthane diterpene saudin (**1**),<sup>3</sup> except for signals indicating the presence of a hydroxyl group at C-5 ( $\nu_{\max}$  3520 cm<sup>-1</sup>;  $\delta_C$  72.5, s), a disubstituted double bond at C-14(15) ( $\delta_{C-14}$  126.2,  $\delta_{C-15}$  132.3), and an oxide bridge at C-7(10) ( $\delta_{C-7}$  108.4;  $\delta_{C-10}$  100.6). Since

Chart 1



the <sup>1</sup>H- and <sup>13</sup>C NMR data of **1** were unambiguously assigned,<sup>3</sup> the placement of the tertiary hydroxyl group at C-5 was straightforward, as the ABC system due to the methylene group at C-6 in saudin (**1**) [ $\delta$  1.82, dd,  $J$  = 3.0 and 13.6 Hz (H6a);  $\delta$  2.44, dd,  $J$  = 10.8 and 13.6 Hz (H6b)] was replaced in **4** by an AB system as a dd

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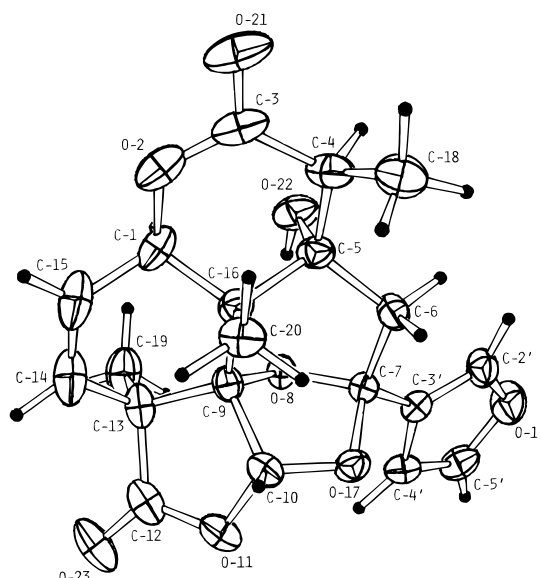
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**Table 1.**  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR Chemical Shift Values (in ppm) for Diterpenes **4** and **5**<sup>a</sup>

proton/ carbon	<b>4</b>		<b>5</b>	
	$^1\text{H}$	$^{13}\text{C}$	$^1\text{H}$	$^{13}\text{C}$
1	5.93 <sup>b</sup>	73.0 d <sup>c</sup>	5.58 brt (8.6, 9.9)	71.6 d
3		172.7 s		172.9 s
4	2.9 dq (1.3, 8.0) <sup>d</sup>	47.7 d	2.86 dq (1.3, 8.1)	47.2 d
5		72.5 s		72.7 s
6	2.61 d (15.0)	42.3 t	2.59 d (15.1)	42.6 t
	2.54 d (15.0)		2.52 d (15.1)	
7		108.4 s		108.6 s
9		89.7 s		91.1 s
10	5.93 s <sup>b</sup>	100.6 d	6.11 s	100.1 d
12		174.7 s		176.1 s
13		44.3 s		40.7 s
14	5.91 d (3.9)	126.2 d	1.98 m	25.2 t
			1.84 m	
15	6.22 dd (3.9, 8.0)	132.3 d	2.44 m	20.5 t
			1.84 m	
16		48.8 s		46.2 s
2'	7.68 br d (1.0)	141.9 d	7.66 br d (1.0)	141.9 d
3'		124.3 s		124.5 s
4'	6.52 dd (1.0, 1.8)	108.7 d	6.50 dd (1.0, 1.9)	108.8 d
5'	7.48 t (1.8)	144.4 d	7.46 t (1.9)	144.4 d
C(4)-Me	1.41 d (8.0)	15.5 q	1.39 d (8.1)	15.4 q
C(13)-Me	1.19 s	19.6 q	1.29 s	17.4 q
C(16)-Me	1.46 s	16.5 q	1.45 s	15.7 q
OH	4.10 d (1.3)		4.0 d (1.3)	

<sup>a</sup> Spectra recorded for **4** and **5** at 300 MHz ( $^1\text{H}$ ) and 75 MHz ( $^{13}\text{C}$ ). <sup>b</sup> Signal superimposed on each other,  $J$  unresolved. <sup>c</sup> Multiplicities of the carbon signals were determined by APT and DEPT experiments, also aided by 2D NMR COSY and HETCOR experiments. <sup>d</sup> Values in the parentheses are coupling constants, in Hz.

centered at  $\delta$  2.58,  $J$  = 15 Hz. Furthermore, a COSY 2D NMR experiment suggested the presence of the system  $-\text{CH}=\text{CHCH}(\text{O})-$  in **4**, and this was confirmed by a 2D NMR HETCOR experiment and other  $^{13}\text{C}$  NMR data, which showed signals at  $\delta_{\text{C}}$  73.0 (d), 44.3 (s), 126.2 (d), 132.3 (d), and 48.8 (s) assigned to C-1, C-13–15, and C-16, respectively. Moreover, the NMR data of **4** did not show the oxygenated methylene of **1** at C-10. A higher degree of oxygenation at this center in **4** was indicated by the fact that the resonances for position 10 of **1** were replaced by a low-field methine signal ( $\delta_{\text{H}}$  5.93, s;  $\delta_{\text{C}}$  100.6). This last piece of information, together with the fact that the C-7 signal occurred at  $\delta_{\text{C}}$  108.4, indicating the same level of oxygenation as in **1**, suggested the gross structure of saudinolide (**4**). X-ray crystallographic analysis established the complete structure and relative stereochemistry of **4**. Non-hydrogen atom fractional coordinates are listed in Table 2. Bond lengths are in accord with expectations.<sup>6</sup> A view of the solid-state conformation is presented in Figure 1 [endocyclic torsion angles  $\omega_{ij}$  ( $\sigma$  0.3–0.5°) about the bonds

**Figure 1.** ORTEP diagram (40% probability ellipsoids) showing the crystallographic atom numbering scheme and solid-state conformation of saudinolide (**4**); small filled circles represent hydrogen atoms.

between atoms  $i$  and  $j$  follow:  $\omega_{1,2}$  34.7,  $\omega_{2,3}$  -7.1,  $\omega_{3,4}$  8.6,  $\omega_{4,5}$  -37.2,  $\omega_{5,16}$  64.7,  $\omega_{16,1}$  -62.7° in  $\delta$ -lactone ring A;  $\omega_{5,6}$  49.2,  $\omega_{6,7}$  10.3,  $\omega_{7,8}$  -71.5,  $\omega_{8,9}$  73.3,  $\omega_{9,16}$  -12.1,  $\omega_{16,5}$  -48.2° in tetrahydropyran ring B;  $\omega_{1,16}$  57.5,  $\omega_{16,9}$  -21.9,  $\omega_{9,13}$  -24.4,  $\omega_{13,14}$  38.9,  $\omega_{14,15}$  -2.1,  $\omega_{15,1}$  -48.7° in cyclohexene ring C;  $\omega_{7,8}$  45.5,  $\omega_{8,9}$  -47.5,  $\omega_{9,10}$  32.7,  $\omega_{10,17}$  -5.7,  $\omega_{17,7}$  -23.9° in 1,3-dioxalane ring D;  $\omega_{9,10}$  27.0,  $\omega_{10,11}$  -27.1,  $\omega_{11,12}$  16.0,  $\omega_{12,13}$  1.8,  $\omega_{13,9}$  -17.5° in  $\gamma$ -lactone ring E;  $\omega_{1',2'}$  -0.6,  $\omega_{2',3'}$  -0.2,  $\omega_{3',4'}$  0.3,  $\omega_{4',5'}$  -0.7,  $\omega_{5',1'}$  0.8° in furan ring F]. Ring A approximates to an envelope (1,2-diplanar, half-boat) form with C-16 as the out-of-plane atom while ring B has a distorted boat (1,4-diplanar) form. Ring C is best described as being intermediate between 1,3- and 1,4-diplanar (boat) forms. Rings D and E both have envelope conformations with O-8 and C-10, respectively, as the out-of-plane atoms; ring F is essentially planar. The hydroxyl group at C-5 is intramolecularly hydrogen bonded to O-8 [ $\text{O} \cdots \text{O} = 2.613(4)$  Å]. While structure **1** for saudin was assumed to depict its absolute stereochemistry, solely on a biogenetic basis,<sup>3</sup> noteworthy differences of stereochemistry at positions 4 and 7 of **1** and **4** are apparent despite their overall structural similarities.

Dihydrosaudinolide (**5**),  $\text{C}_{20}\text{H}_{22}\text{O}_8$ , possesses a  $\gamma$ - and  $\delta$ -two-lactone system ( $\nu_{\text{max}}$  1780  $\text{cm}^{-1}$ , 1725  $\text{cm}^{-1}$ ;  $\delta_{\text{C}}$  176.1, 172.9) and a furan ring, as found in **4**. Compari-

**Table 2.** Non-Hydrogen Atom Fractional Coordinates for Saudinolide (**4**), with Estimated Standard Deviations in Parentheses

atom	x	y	z	atom	x	y	z
C-1	0.2585(4)	0.3279(1)	-0.1153(5)	C-15	0.1429(4)	0.3599(2)	-0.1968(7)
O-2	0.2725(4)	0.2841(1)	-0.2270(4)	C-16	0.4018(4)	0.3546(1)	-0.1140(4)
C-3	0.3976(5)	0.2587(1)	-0.2281(6)	O-17	0.6093(3)	0.4380(1)	0.0112(3)
C-4	0.5370(5)	0.2767(1)	-0.1323(5)	C-18	0.6633(6)	0.2756(1)	-0.2759(7)
C-5	0.5137(4)	0.3220(1)	-0.0116(4)	C-19	0.1583(4)	0.4079(2)	0.2276(6)
C-6	0.6490(3)	0.3511(1)	0.0404(4)	C-20	0.4461(4)	0.3657(1)	-0.3252(4)
C-7	0.6038(3)	0.3979(1)	0.1441(4)	O-21	0.3952(5)	0.2210(1)	-0.3107(5)
O-8	0.4518(2)	0.3959(1)	0.1912(3)	O-22	0.4526(3)	0.3028(1)	0.1634(3)
C-9	0.3846(3)	0.4007(1)	0.0042(4)	O-23	0.1682(3)	0.5052(1)	0.0597(5)
C-10	0.4727(4)	0.4432(1)	-0.0700(4)	O-1'	0.8415(3)	0.4087(1)	0.5661(4)
O-11	0.3980(3)	0.4849(1)	0.0047(4)	C-2'	0.7930(4)	0.3852(1)	0.4057(5)
C-12	0.2568(4)	0.4749(1)	0.0314(5)	C-3'	0.6871(3)	0.4102(1)	0.3203(4)
C-13	0.2293(4)	0.4204(1)	0.0304(5)	C-4'	0.6669(4)	0.4525(1)	0.4329(5)
C-14	0.1313(4)	0.4038(2)	-0.1296(6)	C-5'	0.7631(4)	0.4498(1)	0.5775(5)

**Table 3.**  $^1\text{H}$ -NMR Chemical Shift Values (in ppm) and Coupling Constants (in Hz, in Parentheses) for Diterpenes **6–8** and **10**<sup>a</sup>

proton	<b>6</b>	<b>7</b>	<b>8</b>	<b>10</b>
1	2.55 m 2.19 m	4.68 m	4.68 m	5.58 m
2	4.81 m	2.01 m 1.67 m	1.81 m 1.70 m	2.15 m 1.60 m
3	2.49 td (2.8, 15.1) 1.92 dd (1.7, 15.1)	1.96 m 1.84 m	2.26 m 1.41 td (2.8, 4.0, 13.5)	1.98 dd (4.1, 13.6) 1.45 dd (2.7, 13.6)
5			2.97 dd (10.1, 14.3)	2.93 dd (10.3, 14.0)
6	5.29 d (8.7)	5.0 d (8.3)	5.41 t (10.1, 10.2)	5.43 t (10.3, 10.3)
10			2.49 dd (1.7, 14.3)	2.58 br dd (1.3, 14.0)
11	3.18 qdd (2.5, 8.7, 11.8)	3.31 qdd (2.5, 8.3, 8.4)	3.29 qdd (2.0, 10.2, 12.8)	3.30 br qdd (2.0, 10.3, 12.5)
12	5.12 d (11.8)	4.99 d (8.3)	5.26 d (12.8)	5.27 d (12.5)
14	6.45 br d (1.3)	6.49	6.40 dd (1.0, 1.8)	6.39 dd (1.2, 1.8)
15	7.41 t (1.6)	7.45 m	7.37 t (1.8)	7.38 t (1.8)
16	7.49 br s	7.48 m	7.44 br s	7.45 br s
17	2.08 d (2.5)	2.06 d (2.5)	2.12 d (2.0)	1.86 d (2.0)
18	1.18 s	1.21 s	1.23 s	1.25 s
20	1.57 s	1.53 s		
OAc	1.75 s	1.72 s	1.53 s	2.12, 1.56 (2 × s)
OMe			3.59 s	3.60 s
OH	2.65 br s			

<sup>a</sup> Spectra for **6–8** and **10** recorded at 300 MHz.**Table 4.**  $^{13}\text{C}$ -NMR Spectral Data for Diterpenoids **6–8** and **10**<sup>a</sup>

carbon	compound			
	<b>6</b>	<b>7</b>	<b>8</b>	<b>10</b>
1	39.9 t <sup>b</sup>	79.3 d	64.8 d	68.2 d
2	75.0 d	24.9 t	29.1 t	25.1 t
3	41.6 t	23.4 t	29.6 t	30.3 t
4	47.0 s	47.6 s	44.2 s	43.7 s
5	84.2 s	83.5 s	46.6 d	48.0 d
6	80.5 d	82.2 d	72.1 d	68.6 d
7	165.9 s	165.1 s <sup>c</sup>	165.7 s	165.3 s
8	121.2 s <sup>d</sup>	121.4 s	119.8 s	120.1 s
9	159.2 s	155.0 s	152.4 s	151.0 s
10	50.9 s	53.4 s	45.5 d	43.5 s
11	49.1 s	47.7 d	42.7 d	42.5 d
12	74.4 d	75.2	69.1 d	71.9 d
13	121.6 s <sup>d</sup>	122.0 s <sup>c</sup>	122.8 s	122.7 s
14	108.7 d	109.0 d	109.3 d	109.2 d
15	143.7 d	144.0 d	143.5 d	143.6 d
16	142.3 d	141.3 d	141.5 d	141.5 d
17	12.9 q	13.8 q	11.9 q	11.9 q
18	16.2 q	15.5 q	13.4 q	13.4 q
19	179.2 s	173.7 s	176.4 s	176.3 s
20	25.0 q	18.4 q		
OAc	168.4 s	172.3 s	169.5 s	170.1, 169.3 (2 × s)
	25.0 q	20.0 q	19.9 q	21.3, 19.9 (2 × q)
OMe			51.9 q	52.0 q

<sup>a</sup> Spectra recorded for **6–8** and **10** at 75 MHz. <sup>b</sup> Multiplicities of the carbon signals of all compounds were determined by APT and DEPT experiments, also aided by 2D-NMR COSY and HETCOR experiments. <sup>c,d</sup> Interchangeable signals.

son of the  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectral data of **4** and **5** (Table 1) suggested that **5** was likely to be the C-14-(15)-dihydro derivative of **4**, since a 2D NMR COSY experiment established the system  $-\text{CH}_2\text{CH}_2\text{CH}(\text{O})-$  in **5**. Chemical correlation with **4** confirmed the structure and relative stereochemistry of **5**. Thus, hydrogenation of **4**, using  $\text{Pd}/\text{CaCO}_3$  as a catalyst, afforded the corresponding dihydro derivative **5** in 85% yield.

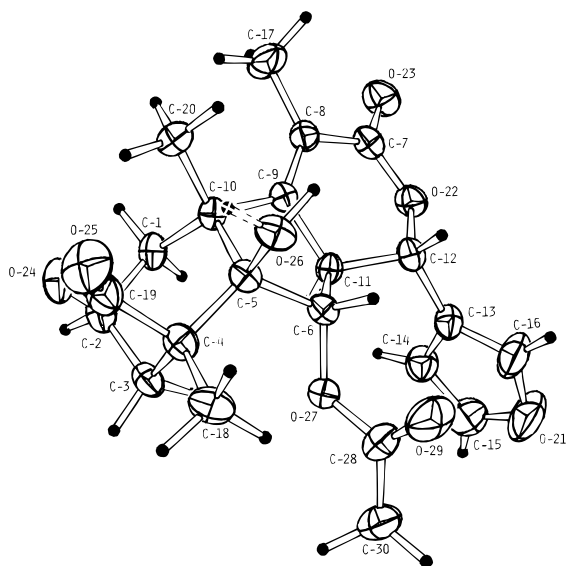
In addition, three minor diterpenoids **6–8** were isolated in crystalline form in 0.003%, 0.004%, and 0.007% yields, respectively. One of these, 5 $\beta$ -hydroxy-richardianidin **1** (**6**),  $\text{C}_{22}\text{H}_{24}\text{O}_8$ , was found to contain a  $\gamma$ -lactone ( $\nu_{\text{max}}$  1770  $\text{cm}^{-1}$ ;  $\delta_{\text{C}}$  179.2), an  $\alpha,\beta$ -unsaturated  $\delta$ -lactone ( $\nu_{\text{max}}$  1700  $\text{cm}^{-1}$ ;  $\delta_{\text{C}}$  165.9), and a furan ring. The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of **6** (Tables 3 and 4) were found to be generally similar to those reported for richardianidin **1** (**2**),<sup>4</sup> save for the differences associated with the presence of a tertiary hydroxyl group at C-5

( $\nu_{\text{max}}$  3400  $\text{cm}^{-1}$ ;  $\delta_{\text{C}}$  84.2, s). Therefore, the presence of the C-2(4)- $\gamma$ -lactone was inferred from the spectroscopic data ( $\delta_{\text{C}-2}$  75.0,  $\delta_{\text{C}-19}$  179.2; versus  $\delta_{\text{C}-2}$  75.2,  $\delta_{\text{C}-19}$  180.2 in **2**). The COSY 2D NMR spectrum suggested the presence of the systems  $-\text{CH}(\text{OAc})\text{CHCH}(\text{O})-$  and  $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$  in **6**, and this was confirmed by a 2D NMR HETCOR experiment (Tables 3 and 4). In addition, the  $^{13}\text{C}$ -NMR spectrum revealed the deshielding of C-4, -6, and -10 to  $\delta_{\text{C}}$  47.0, 80.5, and 50.9, respectively (versus corresponding values of  $\delta_{\text{C}}$  41.8, 71.9, and 44.9 for **2**), due to the presence of the hydroxyl group at C-5. X-ray crystallographic analysis of **6** confirmed the overall structure and determined the relative stereochemistry at C-5. The asymmetric crystal unit consists of two independent molecules for which non-hydrogen atom fractional coordinates are listed in Table 5. Corresponding bond lengths in each of the molecules do not differ significantly and, in general, lie close to the expected values.<sup>6</sup> Bond strain is, however, reflected in several elongated bonds involving C-5 and C-10 [C-1–C-10 = 1.568(6), 1.567(7) Å; C-5–C-6 = 1.567(7), 1.567-(6) Å; C-5–C-10 = 1.588(7), 1.590(6) Å in the pair of molecules]. A view of the solid-state conformation of one molecule is illustrated in Figure 2. Corresponding torsion angles in the pair of crystallographically independent molecules are very similar ( $\Delta_{\text{max}} = 5.0^\circ$ ;  $\Delta_{\text{mean}} = 1.3^\circ$ ), and thus, their conformations do not differ significantly. Endocyclic torsion angles characterizing ring conformations are summarized in Table 6. The C-2(4)-bridged cyclohexane ring A has a chair conformation flattened around C-10, the cyclopentane ring B is in an envelope form with C-9 as the out-of-plane atom, the  $\delta$ -lactone ring C approximates more closely to a 1,2-diplanar (half-boat, envelope) than to a 1,3-diplanar form, and the furan ring D is planar. Torsion angles ( $\sigma$  0.4–0.5°) in the  $\gamma$ -lactone ring [values for the unprimed molecule, with corresponding values for the primed molecule in parentheses follow:  $\omega_{2,3}$  –42.2 (–43.4),  $\omega_{3,4}$  39.2 (40.4),  $\omega_{4,19}$  –24.2 (–25.1),  $\omega_{19,24}$  –2.6 (–2.1),  $\omega_{24,2}$  28.9 (29.1)°] are related by an approximate mirror plane of symmetry passing through C-3 and the mid-point of the C-19–O-24 bond and, accordingly, this ring has an envelope conformation. Molecules of **6** are associated in the solid state by an O–H...O hydrogen bond. The hydroxyl hydrogen atom of each molecule is disordered

**Table 5.** Non-Hydrogen Atom Fractional Coordinates for the Two Molecules of 5 $\beta$ -Hydroxyrichardianidin 1 (**6**) in the Asymmetric Crystal Unit, with Estimated Standard Deviations in Parentheses

atom	x	y	z	atom	x	y	z
C-1	0.3427(3)	-0.1615(5)	0.6094(4)	C-1'	0.0141(3)	0.4016(5)	0.2799(4)
C-2	0.4177(3)	-0.1004(5)	0.6918(4)	C-2'	-0.0642(3)	0.3411(5)	0.2070(5)
C-3	0.4701(3)	-0.0375(5)	0.6156(4)	C-3'	-0.0475(3)	0.2743(5)	0.0964(4)
C-4	0.4152(3)	0.0735(5)	0.5741(4)	C-4'	-0.0009(3)	0.1631(5)	0.1603(4)
C-5	0.3362(3)	0.0354(4)	0.4767(4)	C-5'	0.0876(2)	0.2028(4)	0.2329(4)
C-6	0.3514(3)	-0.0080(4)	0.3497(4)	C-6'	0.1480(2)	0.2439(4)	0.1505(4)
C-7	0.1630(3)	-0.2659(5)	0.2416(4)	C-7'	0.2931(3)	0.5036(5)	0.3813(5)
C-8	0.1762(3)	-0.1994(5)	0.3613(4)	C-8'	0.2215(3)	0.4394(5)	0.4154(4)
C-9	0.2481(3)	-0.1386(4)	0.4005(4)	C-9'	0.1686(2)	0.3757(4)	0.3274(4)
C-10	0.2843(3)	-0.0709(4)	0.5206(4)	C-10'	0.0874(3)	0.3104(4)	0.3285(4)
C-11	0.3115(3)	-0.1336(4)	0.3227(4)	C-11'	0.1827(2)	0.3673(4)	0.1991(3)
C-12	0.2736(3)	-0.1491(4)	0.1857(4)	C-12'	0.2728(3)	0.3830(5)	0.1935(5)
C-13	0.3366(3)	-0.1774(5)	0.1129(4)	C-13'	0.2827(3)	0.4111(5)	0.0667(5)
C-14	0.3953(3)	-0.2750(6)	0.1342(5)	C-14'	0.2458(3)	0.5103(6)	-0.0083(4)
C-15	0.4415(4)	-0.2643(8)	0.0526(6)	C-15'	0.2673(4)	0.4986(7)	-0.1160(5)
C-16	0.3523(4)	-0.1149(8)	0.0191(5)	C-16'	0.3243(4)	0.3469(7)	-0.0037(6)
C-17	0.1059(3)	-0.2160(7)	0.4252(5)	C-17'	0.2172(4)	0.4603(7)	0.5474(5)
C-18	0.4591(3)	0.1859(5)	0.5343(5)	C-18'	-0.0001(3)	0.0487(5)	0.0824(5)
C-19	0.3859(3)	0.1019(6)	0.6917(5)	C-19'	-0.0532(3)	0.1387(6)	0.2551(5)
C-20	0.2183(3)	-0.0206(5)	0.5865(4)	C-20'	0.0820(3)	0.2602(5)	0.4563(4)
O-21	0.4171(3)	-0.1656(6)	-0.0209(4)	O-21'	0.3153(3)	0.3986(6)	-0.1151(4)
O-22	0.2156(2)	-0.2522(4)	0.1679(3)	O-22'	0.3096(2)	0.4858(4)	0.2708(3)
O-23	0.1072(2)	-0.3404(4)	0.2091(4)	O-23'	0.3364(2)	0.5752(4)	0.4477(4)
O-24	0.3901(2)	0.0000(-) <sup>a</sup>	0.7600(3)	O-24'	-0.0906(2)	0.2427(4)	0.2784(3)
O-25	0.3591(3)	0.1969(4)	0.7189(4)	O-25'	-0.0625(3)	0.0432(4)	0.3063(4)
O-26	0.2840(2)	0.1423(3)	0.4463(3)	O-26'	0.1237(2)	0.0943(3)	0.2967(3)
O-27	0.4368(2)	-0.0168(3)	0.3426(3)	O-27'	0.1132(2)	0.2543(3)	0.0208(3)
C-28	0.4653(3)	0.0569(5)	0.2642(5)	C-28'	0.1425(3)	0.1795(5)	-0.0559(4)
O-29	0.4236(3)	0.1405(5)	0.2092(4)	O-29'	0.1871(3)	0.0936(4)	-0.0219(4)
C-30	0.5502(3)	0.0218(7)	0.2547(6)	C-30'	0.1103(4)	0.2174(7)	-0.1864(5)

<sup>a</sup> The y-coordinate of O-24 was held constant throughout the least-squares parameter refinement to define the space group origin in this direction.

**Figure 2.** ORTEP diagram (40% probability ellipsoids) showing the crystallographic atom numbering scheme and solid-state conformation of the unprimed molecule of 5 $\beta$ -hydroxyrichardianidin (**6**); the hydroxyl hydrogen atom is disordered over two positions. Small filled circles represent hydrogen atoms.

over two orientations such that it is involved (1:1) in intramolecular [O(25)···O(26) = 3.069(5) Å, O(25')···O(26') = 3.147(6) Å] and intermolecular [O(26)···O(26') = 2.836(4) Å] hydrogen bonds.

The <sup>1</sup>H- and <sup>13</sup>C-NMR spectral data (Tables 3 and 4) for the second minor diterpenoid, 5 $\beta$ -hydroxyrichardianidin 2 (**7**), C<sub>22</sub>H<sub>24</sub>O<sub>8</sub>, were remarkably similar to those of **6** but lacked signals associated with the C-2(4)- $\gamma$ -lactone ring. Instead, **7**, like **3**, was concluded to have a C-1(4)- $\delta$ -lactone group, as suggested by its <sup>13</sup>C-NMR spectral data ( $\delta_{C-1}$  79.3,  $\delta_{C-19}$  173.7 versus  $\delta_{C-1}$  78.07,

**Table 6.** Endocyclic Torsion Angles ( $\omega_{ij}$ , deg) about the Bonds between Atoms *i* and *j* in **6**, **7**, and **10**; Estimated Standard Deviations are in Parentheses

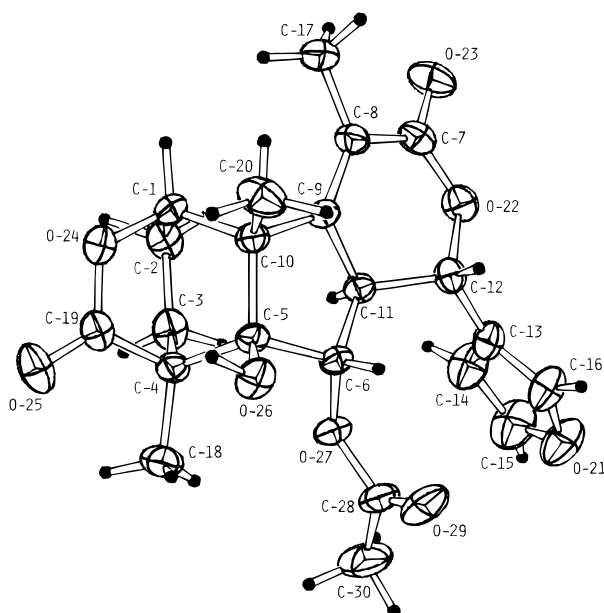
	<b>6</b>		<b>7</b>	<b>10</b>
	unprimed molecule	primed molecule		
cyclohexane ring A				
$\omega_{1,2}$	-59.3(6)	-59.0(5)	57.5(3)	53.4(3)
$\omega_{2,3}$	75.4(5)	74.9(5)	4.9(3)	-57.9(3)
$\omega_{3,4}$	-72.4(4)	-71.7(4)	-61.9(2)	56.6(3)
$\omega_{4,5}$	54.8(5)	55.1(5)	56.4(2)	-56.0(2)
$\omega_{5,10}$	-32.7(5)	-34.0(5)	2.5(2)	56.1(2)
$\omega_{10,1}$	34.3(5)	35.1(5)	-61.1(2)	-52.2(2)
cyclopentane ring B				
$\omega_{5,6}$	-0.8(5)	1.6(4)	-25.6(2)	25.8(1)
$\omega_{6,11}$	21.7(5)	19.2(4)	28.8(2)	-0.8(1)
$\omega_{11,9}$	-35.8(5)	-34.3(4)	-20.8(2)	-25.4(2)
$\omega_{9,10}$	34.7(5)	34.1(4)	4.9(2)	41.0(2)
$\omega_{10,5}$	-19.9(5)	-21.2(4)	12.5(2)	-41.1(2)
$\alpha,\beta$ -unsaturated $\delta$ -lactone ring C <sup>b</sup>				
$\omega_{7,8}$	-8.8(7)	-8.0(8)	-19.1(3)	-8.5(3)
$\omega_{8,9}$	2.7(7)	1.4(7)	0.5(3)	-1.1(3)
$\omega_{9,11}$	25.8(6)	25.8(6)	37.6(3)	29.6(2)
$\omega_{11,12}$	-46.5(5)	-44.8(5)	-57.1(2)	-47.1(2)
$\omega_{12,22}$	43.4(6)	41.4(6)	43.0(3)	41.6(2)
$\omega_{22,7}$	-16.4(7)	-15.3(7)	-4.8(3)	-13.8(3)
furan ring D				
$\omega_{13,14}$	0.0(7)	0.1(7)	-0.3(4)	0.9(3)
$\omega_{14,15}$	0.2(8)	0.1(7)	0.5(4)	-0.2(3)
$\omega_{15,21}$	-0.3(8)	-0.3(8)	-0.6(4)	-0.5(3)
$\omega_{21,16}$	0.2(8)	0.4(8)	0.4(4)	1.1(3)
$\omega_{16,13}$	-0.1(7)	-0.3(7)	-0.0(4)	-1.3(3)

<sup>a</sup> The torsion angle A-B-C-D is defined as positive if, when viewed along the B-C bond, atom A must be rotated clockwise to eclipse atom D. <sup>b</sup>  $\Delta C_5(1,2\text{-dipolar}) = |\omega_{7,8}| + |\omega_{8,9}| + |\omega_{9,11}| + |\omega_{22,7}| + |\omega_{11,12}| + |\omega_{12,22}| = 24.0^\circ$  and  $23.3^\circ$ , respectively, for the unprimed and primed molecules of **6**; =  $30.9^\circ$  for **10**;  $\Delta C_2(1,3\text{-dipolar}) = |\omega_{8,9}| + |\omega_{22,7}| + |\omega_{9,11} - \omega_{12,22}| = 36.7^\circ$  and  $32.3^\circ$  for, respectively, the unprimed and primed molecules of **6**, =  $26.9^\circ$  for **10**.

$\delta_{C-19}$  175.63 in **3**). A 2D NMR COSY experiment established the system -CH<sub>2</sub>CH<sub>2</sub>CH(O)- in ring A of **7**, and this was confirmed by a 2D NMR HETCOR

**Table 7.** Non-Hydrogen Atom Fractional Coordinates for 5 $\beta$ -Hydroxyrichardianidin 2 (**7**) with Estimated Standard Deviations in Parentheses

atom	x	y	z	atom	x	y	z
C-1	0.3290(3)	0.44916(7)	-0.2387(3)	C-16	0.6738(4)	0.29015(7)	0.2196(5)
C-2	0.2272(3)	0.41712(9)	-0.3224(3)	C-17	0.7226(3)	0.43496(7)	-0.4106(4)
C-3	0.1289(3)	0.39779(7)	-0.1654(3)	C-18	0.0316(3)	0.40513(9)	0.1713(4)
C-4	0.1539(2)	0.41929(6)	0.0220(3)	C-19	0.1143(3)	0.46110(6)	-0.0242(3)
C-5	0.3380(2)	0.41833(5)	0.0836(3)	C-20	0.5564(3)	0.46932(7)	-0.0132(5)
C-6	0.4157(2)	0.37824(5)	0.1203(3)	O-21	0.6107(3)	0.25469(5)	0.2594(4)
C-7	0.7429(3)	0.36435(7)	-0.3370(4)	O-22	0.7291(2)	0.33457(4)	-0.2147(3)
C-8	0.6678(3)	0.40207(6)	-0.2890(3)	O-23	0.8197(2)	0.35892(5)	-0.4820(3)
C-9	0.5498(2)	0.40248(5)	-0.1555(3)	O-24	0.2152(2)	0.47706(5)	-0.1547(3)
C-10	0.4475(3)	0.43591(5)	-0.0812(3)	O-25	0.0041(2)	0.47993(5)	0.0392(3)
C-11	0.5002(2)	0.36562(5)	-0.0605(3)	O-26	0.3543(2)	0.43832(4)	0.2580(2)
C-12	0.6520(3)	0.34090(6)	-0.0312(3)	O-27	0.3000(2)	0.34963(4)	0.1772(2)
C-13	0.6182(3)	0.30255(6)	0.0523(4)	C-28	0.3129(3)	0.33423(6)	0.3536(3)
C-14	0.5127(4)	0.27297(7)	-0.0192(5)	O-29	0.4135(3)	0.34384(6)	0.4657(3)
C-15	0.5140(5)	0.24512(8)	0.1103(7)	C-30	0.1807(5)	0.30480(9)	0.3829(6)

**Figure 3.** ORTEP diagram (40% probability ellipsoids) showing the crystallographic atom numbering scheme and solid-state conformation of 5 $\beta$ -hydroxyrichardianidin 2 (**7**); small filled circles represent hydrogen atoms.

experiment and other  $^{13}\text{C}$  NMR data, which revealed signals at  $\delta_{\text{C}}$  79.3, 24.9, 23.4, 47.6, and 53.4 assigned to C-1-4 and C-10, respectively. On the basis of the foregoing data, this minor diterpenoid was formulated as **7**. The relative stereochemistry at C-5 was confirmed by X-ray crystallography. Carbon and oxygen atom fractional coordinates are listed in Table 7. Bond lengths, other than the elongated C-5–C-10 bond at 1.590(3) Å, are not unusual.<sup>6</sup> A view of the solid-state conformation is presented in Figure 3, while endocyclic torsion angles characterizing the shapes of rings A–D are provided in Table 6. The C-1(4)-bridged cyclohexane ring A has a boat conformation, while the cyclopentane ring B is intermediate between an envelope form with C-6 as the out-of-plane atom and a half-chair form with its  $\text{C}_2$ -symmetry axis passing through C-10 and the midpoint of the C-6–C-11 bond. The  $\delta$ -lactone ring C has a 1,3-diplanar form; the furan ring D is planar. In the solid state, an O–H $\cdots$ O hydrogen bond [O-26 $\cdots$ O-24 = 3.060(2) Å] associates molecules of **7** related by the  $2_1$  screw axis along the  $c$ -direction.

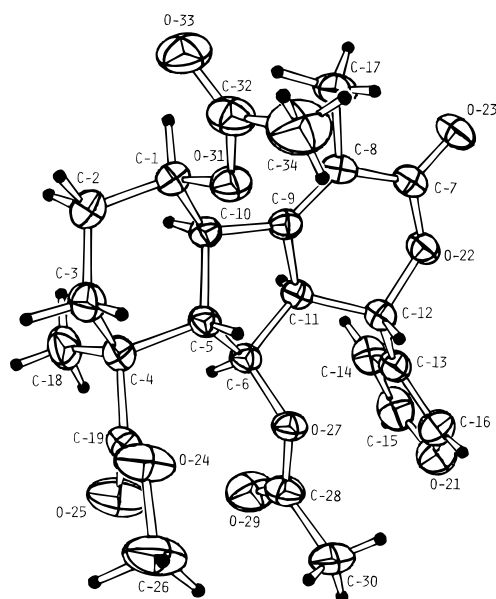
The third minor diterpenoid cluytene F (**8**),  $\text{C}_{22}\text{H}_{26}\text{O}_8$ , was found to have an acetate group ( $\delta_{\text{C}}$  169.5, 19.9), a

methyl ester function ( $\delta_{\text{C}}$  176.4, 51.9), an  $\alpha,\beta$ -unsaturated  $\delta$ -lactone group ( $\delta_{\text{C}}$  165.7), and a furan ring. Comparison of the spectral data of **8** (Tables 3 and 4) with those of cluytene D (**9**)<sup>2</sup> led to the conclusion that **8** contained the 6,7-seco-6,11-cyclo-20-norlabdane skeletal backbone with the additional presence of a secondary hydroxyl group ( $\delta_{\text{C}}$  64.8; C-1) and a methine proton ( $\delta_{\text{C}}$  45.5; C-10) instead of the C-1(2)-epoxide and the Me-20 group, respectively, in **9**. On acetylation, **8** afforded the corresponding acetate **10** ( $\delta_{\text{C}}$  170.1, 21.3), with the  $^1\text{H}$  NMR spectrum showing the anticipated deshielding of H-1 to a multiplet at  $\delta$  5.58 (versus  $\delta_{\text{H-1}}$  4.68 in **8**), thus confirming the presence of a hydroxyl group at C-1 in **8**. A 2D NMR COSY experiment showed that the signal at  $\delta$  4.68 (H-1) was coupled to two C-2 protons at  $\delta$  1.81 and 1.70 and the methine proton at  $\delta$  2.49 (H-10), with the latter showing additional coupling with H-5 ( $\delta$  2.97), suggesting the presence of the system  $-\text{CH}_2\text{CH}(\text{OH})\text{CHCH}-$  in **8**. Furthermore, the placement of the OAc group at C-6 ( $\delta$  5.41, t,  $J$  = 10.1 and 10.2 Hz, H-6) was also corroborated from the 2D NMR COSY experiment, which established the system  $-\text{CHCH}(\text{OAc})\text{CHCH}(\text{O})-$  in **8**, as well as in its mono-acetate **10**. Both systems were further confirmed by the 2D NMR HETCOR experiments on **8** and **10** and by  $^{13}\text{C}$  NMR data of earlier compounds,<sup>1,2</sup> which helped formulate structure **8** for cluytene F. X-ray crystallographic analysis of **10** unambiguously established the structure and relative stereochemistry of compound **8**, which did not crystallize in a suitable form. Fractional coordinates for the carbon and oxygen atoms are listed in Table 8. A view of the solid-state conformation is illustrated in Figure 4. Bond lengths are in good agreement with expected values.<sup>6</sup> Endocyclic torsion angles (Table 6) indicate that the cyclohexane ring A has a chair conformation, the cyclopentane ring B is in an envelope form with C-10 as the out-of-plane atom, the  $\delta$ -lactone ring C is intermediate between 1,2- and 1,3-diplanar forms, and the furan ring D is planar.

It is noteworthy that the stereochemistry of the acetate-bearing carbon of **8**, namely, C-6, is inverted as compared to that of **6**, **7**, and other related cluytenes previously isolated from the same source. Furthermore, the  $^1\text{H}$ -NMR chemical shift values and multiplicities of H-6 in **8** and other related cluytenes are only marginally different.<sup>2,4</sup> Therefore, without X-ray crystallographic analysis, a prejudicial assignment of the stereochemis-

**Table 8.** Non-Hydrogen Atom Fractional Coordinates for 1-*O*-Acetylcluytene F (**10**) with Estimated Standard Deviations in Parentheses

atom	x	y	z	atom	x	y	z
C-1	0.3068(1)	0.2484(2)	0.5086(2)	C-18	0.3921(2)	0.1668(2)	0.1999(3)
C-2	0.3814(2)	0.2933(2)	0.4272(2)	C-19	0.2663(2)	0.2563(2)	0.1031(2)
C-3	0.3452(2)	0.3143(2)	0.2968(2)	O-21	-0.0641(1)	-0.1278(1)	0.1843(2)
C-4	0.3104(2)	0.2312(1)	0.2278(2)	O-22	0.0234(1)	0.0070(1)	0.5228(1)
C-5	0.2323(1)	0.1881(1)	0.3101(2)	O-23	0.0243(1)	0.0367(1)	0.7209(1)
C-6	0.1854(1)	0.1014(1)	0.2666(2)	O-24	0.2237(2)	0.3342(1)	0.1038(2)
C-7	0.0598(2)	0.0512(1)	0.6208(2)	O-25	0.2654(2)	0.2096(1)	0.0133(2)
C-8	0.1412(2)	0.1124(1)	0.6036(2)	C-26	0.1775(3)	0.3619(2)	-0.0103(3)
C-9	0.1848(1)	0.1138(1)	0.4933(2)	O-27	0.1058(1)	0.1259(1)	0.1894(1)
C-10	0.2674(1)	0.1667(1)	0.4431(2)	C-28	0.0931(2)	0.0814(2)	0.0809(2)
C-11	0.1536(1)	0.0536(1)	0.3886(2)	O-29	0.1412(2)	0.0208(1)	0.0483(2)
C-12	0.0481(2)	0.0326(1)	0.3959(2)	C-30	0.0106(2)	0.1198(2)	0.0121(2)
C-13	0.0177(2)	-0.0442(1)	0.3173(2)	O-31	0.2280(1)	0.3097(1)	0.5281(1)
C-14	0.0598(2)	-0.1308(2)	0.3139(3)	C-32	0.2381(2)	0.3694(2)	0.6197(2)
C-15	0.0084(2)	-0.1783(2)	0.2327(3)	O-33	0.3079(2)	0.3731(1)	0.6859(2)
C-16	-0.0567(2)	-0.0462(2)	0.2395(3)	C-34	0.1538(3)	0.4288(2)	0.6291(3)
C-17	0.1678(2)	0.1623(2)	0.7194(2)				

**Figure 4.** ORTEP diagram (40% probability ellipsoids) showing the crystallographic atom numbering scheme and solid-state conformation of 1-*O*-acetylcluytene F (**10**); small filled circles represent hydrogen atoms.

try at C-6 on the basis of biogenetic grounds would have led to the wrong conclusion.

## Experimental Section

**General Experimental Procedures.** Melting points were recorded on an Electrothermal 9100 instrument. UV spectra were obtained in MeOH, using a Varian DMS 90 spectrophotometer, and IR spectra were taken as KBr disks on a Perkin-Elmer 5808 spectrophotometer. The NMR spectra were taken on a Varian VXR 300 instrument at 300 MHz ( $^1\text{H}$ ) and 75 MHz ( $^{13}\text{C}$ ) in  $\text{CDCl}_3$ , using tetramethylsilane (TMS) as internal standard. Spectral editing (APT and DEPTGL) and 2D NMR spectra (COSY and HETCOR) were obtained using standard Varian software. CIMS were recorded on a Finnigan MAT 300 mass spectrometer, using  $\text{CH}_4$  as ionizing gas. Optical rotations were recorded in  $\text{CHCl}_3$ , unless otherwise stated, at ambient temperature using a Perkin-Elmer 241 MC polarimeter. TLC was performed on Si gel 60 F 254, using  $\text{CHCl}_3$ - $\text{Me}_2\text{CO}$  (9:1) as solvent, with visualization using 1% vanillin/ $\text{H}_2\text{SO}_4$  spray reagent.

**Plant Material.** The aerial parts of *C. richardiana*<sup>7</sup> were collected in Abha, Saudi Arabia, in June 1991. A voucher specimen (no. 10362) is deposited at the herbarium of MAPPRC, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia.

**Extraction and Isolation of Diterpenoids.** The initial isolation procedure for the diterpenoids obtained from cold defatted EtOAc extract of *C. richardiana* was as previously described.<sup>1,2</sup> Elution with petroleum ether (60–80 °C)-EtOAc (8.5:1.5) from a Si gel column yielded saudinolide (**4**) as granules [1.05 g;  $R_f$  0.59, solvent  $\text{CHCl}_3$ - $\text{Me}_2\text{CO}$  (9:1)], followed by dihydrosaudinolide (**5**) as plates (509 mg;  $R_f$  0.50). Further elution with petroleum ether-EtOAc (4:2) gave 5 $\beta$ -hydroxyrichardianidin 2 (**7**) as plates (130 mg;  $R_f$  0.31), followed by 5 $\beta$ -hydroxyrichardianidin 1 (**6**) as needles (91 mg;  $R_f$  0.30) and cluytene F (**8**) as colorless granules (235 mg;  $R_f$  0.29).

**Saudinolide (4):** colorless granules from petroleum ether/EtOAc and (off-white) needles from hot EtOAc: mp 231–35 °C;  $[\alpha]_D^{+98}$  ( $c$  0.142,  $\text{CHCl}_3$ ); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 220 (4.30), 265 (3.90) nm; IR (KBr)  $\nu_{\text{max}}$  3520 (OH), 1780 ( $\gamma$ -lactone), 1720 ( $\delta$ -lactone), 1510, 1450, 1380 (br), 1200, 1190, 1050, 970, 860, 830, 735  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Table 1; CIMS  $m/z$   $[\text{M} + 29]^+$  417 (20),  $[\text{MH}]^+$  389 [ $\text{C}_{20}\text{H}_{20}\text{O}_8 + \text{H}]^+$  (100), 371 ( $[\text{MH}]^+ - \text{H}_2\text{O}$ ) (25), 343 (5), 215 (5), 154 (10).

**Dihydrosaudinolide (5):** plates from petroleum ether/EtOAc; mp 262–64 °C;  $[\alpha]_D^{+73}$  ( $c$  0.118,  $\text{CHCl}_3$ ); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 218 (4.32), 258 (3.00) nm; IR (KBr)  $\nu_{\text{max}}$  3515 (OH), 1780 ( $\gamma$ -lactone), 1725 ( $\delta$ -lactone), 1510, 1470, 1390 (br), 1200, 1190, 1050, 970, 860, 735  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Table 1; CIMS  $m/z$   $[\text{M} + 29]^+$  419 (5),  $[\text{MH}]^+$  391 [ $[\text{C}_{20}\text{H}_{22}\text{O}_8 + \text{H}]^+$ , 100], 373 ( $[\text{MH}]^+ - \text{H}_2\text{O}$ , 20), 301 (5).

**5 $\beta$ -Hydroxyrichardianidin 1 (6):** colorless needles from petroleum ether/EtOAc: mp 246–47 °C;  $[\alpha]_D^{+42}$  ( $c$  0.05,  $\text{CHCl}_3$ ); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 220 (4.15), 275 (3.90) nm; IR (KBr)  $\nu_{\text{max}}$  3400 (OH), 1770 ( $\gamma$ -lactone), 1745 (OAc), 1700 ( $\alpha,\beta$ -unsaturated  $\delta$ -lactone), 1505, 1465, 1370, 1220, 1075, 1015, 820, 710  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Tables 3 and 4, respectively; CIMS  $m/z$   $[\text{M} + 29]^+$  445 (5),  $[\text{MH}]^+$  417 [ $[\text{C}_{22}\text{H}_{24}\text{O}_8 + \text{H}]^+$  (5), 399 ( $[\text{MH}]^+ - \text{H}_2\text{O}$ ) (10), 385 (20), 357 ( $[\text{MH}]^+ - 60$ ) (100), 339 ( $m/z$  357 -  $\text{H}_2\text{O}$ ) (58), 302 (5).

**5 $\beta$ -Hydroxyrichardianidin 2 (7):** colorless plates

from petroleum ether/EtOAc; mp 298–300 °C;  $[\alpha]_D^{+17}$  ( $c$  0.067,  $\text{CHCl}_3$ ); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 220 (4.18), 273 (3.92) nm; IR (KBr)  $\nu_{\text{max}}$  3520 (OH), 1750 ( $\delta$ -lactone), 1740 (OAc), 1705 ( $\alpha,\beta$ -unsaturated  $\delta$ -lactone), 1500, 1465, 1370, 1220, 1065, 1010, 815, 710  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Tables 3 and 4, respectively; CIMS  $m/z$   $[\text{M} + 29]^+$  445 (10),  $[\text{MH}]^+$  417  $[(\text{C}_{22}\text{H}_{24}\text{O}_8 + \text{H})^+]$  (55), 399  $[(\text{MH})^+ - \text{H}_2\text{O}]$  (5), 385 (15), 357  $[(\text{MH})^+ - 60]$  (100), 339 ( $m/z$  357 –  $\text{H}_2\text{O}$ ) (5), 311 (5).

**Cluytene F (8):** colorless granules from petroleum ether/EtOAc; mp 216–18 °C;  $[\alpha]_D -58$  ( $c$  0.16, EtOH); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 218 (4.24), 268 (3.98) nm; IR (KBr)  $\nu_{\text{max}}$  3440 (OH), 1740 and 1730 (COOMe and OAc), 1690 ( $\alpha,\beta$ -unsaturated  $\delta$ -lactone), 1500, 1320, 1230 (br), 1140, 1120, 1020, 860, 750  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Tables 3 and 4, respectively; CIMS  $m/z$   $[\text{M} + 29]^+$  447 (5),  $[\text{MH}]^+$  419  $[(\text{C}_{22}\text{H}_{26}\text{O}_8 + \text{H})^+]$ , 45, 399 (5), 387 (20), 359  $[(\text{MH})^+ - 60]$ , 100, 341 ( $m/z$  359 –  $\text{H}_2\text{O}$ ), 25, 262 (5), 245 (5).

**Hydrogenation of Saudinolid (4) to 5.** Compound **4** (100 mg) in MeOH (10 mL) was stirred for 3 h under  $\text{H}_2$  at 0.5 psi, using Pd/CaCO<sub>3</sub> as catalyst. The resulting mixture was filtered through Celite and dried *in vacuo* to leave a residue (85 mg), from which the major product (**5**) was obtained by crystallization (petroleum ether/EtOAc) as colorless plates (65 mg); mp 263–65 °C;  $[\alpha]_D +66$  ( $c$  0.118,  $\text{CHCl}_3$ ). The physical (mp,  $[\alpha]_D$ , and mmp) and spectroscopic (NMR, IR, CIMS) data were indistinguishable from those of the natural product **5**.

**Acetylation of Cluytene F (8).** Compound **8** (100 mg) was dissolved in pyridine and treated with Ac<sub>2</sub>O at room temperature for 12 h. Regular workup gave a single product, **10** (95 mg), which was purified by recrystallization (petroleum ether/EtOAc) to give colorless needles (80 mg); mp 235–37 °C;  $[\alpha]_D +30$  ( $c$  0.13,  $\text{CHCl}_3$ ); IR (KBr)  $\nu_{\text{max}}$  1750, 1720 (br, COOMe, OAc), 1700 ( $\alpha,\beta$ -unsaturated  $\delta$ -lactone), 1500, 1430, 1370, 1240, 1220, 1190, 1115, 1070, 1010, 870, 810, 770, 735  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR, see Tables 3 and 4, respectively; CIMS  $m/z$   $[\text{MH}]^+$  461 (22), 401  $[(\text{MH})^+ - 60]$  (100), 341 (45).

**X-ray Crystal Structure Analysis of Saudinolid 1 (4), 5 $\beta$ -hydroxyrichardianidin 1 (6), 5 $\beta$ -hydroxy-richardianidin 2 (7), and 1-*O*-acetylcluytene F (10).** Crystal data for **4**:  $\text{C}_{20}\text{H}_{20}\text{O}_8$ ; MW 388.38, orthorhombic, space group  $P2_12_12_1(D_2^4)$  No. 19 from the Laue symmetry and systematic absences  $h00$  when  $h \neq 2n$ ,  $0k0$  when  $k \neq 2n$ ,  $00l$  when  $l \neq 2n$ ,  $a = 9.205(2)$  Å,  $b = 27.985(4)$  Å,  $c = 6.919(1)$  Å,  $V = 1782.3(9)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.447$  g cm<sup>-3</sup>,  $\mu(\text{Cu K}\alpha \text{ radiation}, \lambda = 1.5418 \text{ Å}) = 9.1$  cm<sup>-1</sup>; crystal dimensions:  $0.04 \times 0.14 \times 0.60$  mm.

Crystal data for **6**:  $\text{C}_{22}\text{H}_{24}\text{O}_8$ ; MW 416.43, monoclinic, space group  $P2_1(C_2^2)$  No. 4 from the Laue symmetry, systematic absences  $0k0$  when  $k \neq 2n$ , and **6** is chiral,  $a = 16.492(3)$  Å,  $b = 10.962(2)$  Å,  $c = 11.150(2)$  Å,  $\beta = 103.16(2)^\circ$ ,  $V = 1963(1)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.409$  g cm<sup>-3</sup>,  $\mu(\text{Cu K}\alpha \text{ radiation}) = 8.6$  cm<sup>-1</sup>; crystal dimensions:  $0.04 \times 0.14 \times 0.60$  mm.

Crystal data for **7**:  $\text{C}_{20}\text{H}_{24}\text{O}_8$ ; MW 416.43, orthorhombic, space group  $P2_12_12_1(D_2^4)$  No. 19 as for **4** above,  $a = 8.126(1)$  Å,  $b = 34.780(5)$  Å,  $c = 7.084(1)$  Å,  $V = 2002.1(8)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.381$  g cm<sup>-3</sup>,  $\mu(\text{Cu K}\alpha \text{ radiation}) = 8.4$  cm<sup>-1</sup>; crystal dimensions:  $0.14 \times 0.18 \times 0.60$  mm.

Crystal data for **10**:  $\text{C}_{24}\text{H}_{28}\text{O}_9$ ; MW 460.49, orthor-

hombic, space group  $P2_12_12_1(D_2^4)$  No. 19 as for **4** above,  $a = 14.066(2)$  Å,  $b = 15.009(2)$  Å,  $c = 10.777(1)$  Å,  $V = 2275.2(8)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.344$  g cm<sup>-3</sup>,  $\mu(\text{Cu K}\alpha \text{ radiation}) = 8.2$  cm<sup>-1</sup>; crystal dimensions:  $0.08 \times 0.36 \times 0.50$  mm.

Preliminary unit-cell dimensions and space group information were derived in each case from oscillation and Weissenberg photographs. Intensity data (4246 nonequivalent  $\pm h, +k, +l$  reflections for **6**; 2140, 2398, and 2648  $+h, +k, +l$  reflections for **4**, **7**, and **10**, respectively) were recorded on an Enraf-Nonius CAD-4 diffractometer [Cu K $\alpha$  radiation, graphite monochromator;  $\omega - 2\theta$  scans,  $\theta_{\text{max}} = 75^\circ$ ; scanwidths  $(0.90 + 0.14 \tan \theta)^\circ$  for **4**  $(0.80 + 0.14 \tan \theta)^\circ$  for **6**, **7**, and **10**]. The intensities of four reference reflections from each crystal, monitored every 2 h during data collection, showed no significant variation ( $<1\%$  overall). Refined unit-cell parameters were computed from the diffractometer setting angles for 25 reflections ( $36^\circ < \theta < 40^\circ$ ) widely separated in reciprocal space. The usual Lorentz and polarization corrections were applied to the intensity data. Empirical absorption corrections, based on the  $\phi$ -dependency of the intensities of several reflections with  $\chi$  ca.  $90^\circ$ , were also made to the data for **4**, **6**, and **10**. Those 1702, 3183, 2172, and 2266 reflections for **4**, **6**, **7**, and **10**, respectively, with  $I > 3.0\sigma(I)$  were retained for the structure analyses.

The crystal structures were solved by direct methods (MULTAN11/82). Initial coordinates for all non-hydrogen atoms of **4**, **7**, and **10** were obtained from  $E$ -maps. For **6**, the asymmetric unit consists of two crystallographically independent molecules for which approximate coordinates were obtained in part from an  $E$ -map and from a series of weighted  $F_o$  Fourier syntheses phased successively by an increasing number of atoms. Non-hydrogen atom positional and thermal parameters (at first isotropic and then anisotropic) were adjusted by means of several rounds of full-matrix least-squares calculations. In the later iterations, hydrogen atoms in **4** and **6** were incorporated at their calculated positions, whereas for **7** and **10** hydrogen atom positional and isotropic thermal parameters were included as variables; an extinction correction  $g$  was also refined during the final cycles for **7** and **10**. The parameter refinements converged (max. shift: esd = 0.03) at  $R = 0.047$  ( $R_w = 0.064$ , GOF = 1.53) for **4**,  $R = 0.053$  ( $R_w = 0.072$ , GOF = 1.58) for **6**,  $R = 0.043$  [ $R_w = 0.058$ , GOF = 1.57,  $g = 2.7(3) \times 10^{-6}$ ] for **7**, and  $R = 0.034$  ( $R_w = 0.047$ , GOF = 1.30,  $g = 1.3(2) \times 10^{-6}$ ) for **10**, where  $R = \sum |F_o| - |F_c| / \sum |F_o|$ ;  $R_w = [\sum w(|F_o| - |F_c|)^2 / \sum |F_o|^2]^{1/2}$ , GOF =  $[\sum w(|F_o| - |F_c|)^2 / (N_{\text{observns}} - N_{\text{param}})]^{1/2}$ . Final difference Fourier syntheses contained no unusual features. Atomic parameters, bond lengths, bond angles, and torsion angles for **4**, **6**, **7**, and **10** have been deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

Crystallographic calculations were performed on PDP11/44 and Micro VAX computers by use of the Enraf-Nonius Structure Determination Package (SDP). For all structure-factor calculations, neutral atom scattering factors and their anomalous dispersion corrections were taken from the literature.<sup>8</sup> In the least-squares iterations,  $\sum w\delta^2$  [ $w = 1/\sigma^2(|F_o|)$ ,  $\Delta = (|F_o| - |F_c|)$ ] was minimized.



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