Neoclerodane Diterpenoids from *Scutellaria polyodon*†

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Nine new neoclerodane diterpenoids, scupolins A−I, have been isolated from an Me_2CO extract of the aerial parts of *Scutellaria polyodon* (**3**−**11**), together with the known neoclerodanes jodrellin B (**1**) and scutecolumnin A (**2**). Structures **3**−**11** were established by spectroscopic means and by comparison with closely related compounds.

A large number of neoclerodane[1] diterpenoids have been isolated from plants and microorganisms in the past few years.[2−4] These compounds have attracted interest because of their biological activities, especially as antifeedants against some economically important lepidopterous pests,[2,5] and as antifungal, antitumor, antimicrobial, and molluscicidal agents.[2] The species of the genus *Scutellaria* (family Labiatae) are the source of the most potent neoclerodane insect antifeedants known so far.[6−8] In continuation of our studies on *Scutellaria* plants[8−10] we report here on the isolation and structure elucidation of nine new neoclerodane derivatives isolated from *Scutellaria polyodon* Juz.

Results and Discussion

An Me_2CO extract of the aerial parts of *S. polyodon* was subjected to extensive chromatography to yield the known neoclerodanes jodrellin B[6] (**1**) and scutecolumnin A[11] (**2**), together with nine new diterpenoids, scupolins A−I, whose structures (**3**−**11**, respectively) were established as follows.

Scupolin A (**3**) had the molecular formula $C_{27}H_{40}O_9$, and its ^{1}H- and ^{13}C-NMR spectra (see Tables 1 and 2, respectively) were almost identical with those of scutorientalin B (**12**, $C_{26}H_{38}O_9$), a neoclerodane diterpene recently isolated from *Scutellaria orientalis* subsp. *pinnatifida*.[12] The observed differences between the ^{1}H- and ^{13}C-NMR spectra of **3** and **12** were consistent with the presence in the former of a 2-methylbutanoyloxy substituent at the C-6α position[11] [δ_H 2.31, 1H, sext (H-2′), 1.68 and 1.46, 1H each, both ddq (H_A-3′ and H_B-3′), 0.90, 3H, t (Me-4′), and 1.12, 3H, d (Me-5′); δ_C 175.1 s (C-1′), 41.4 d (C-2′), 26.4 t (C-3′), 11.4 q (C-4′), and 16.5 q (C-5′)] instead of the isobutyrate ester of the latter[12] [δ_H 2.49, 1H, sept (H-2′), and 1.15 and 1.18, 3H each, both d (Me-3′ and Me-4′); δ_C 174.1 s (C-1′), 34.1 d (C-2′), 20.2 q (C-3′), and 21.0 q (C-4′)]. In particular, the location of the acetate group at the C-11 position is in agreement with the chemical shifts and coupling constants shown by the C-11 and C-12 protons of **3** (see Table 1), which were identical with those reported[12−15] for other neoclerodanes having an 11*S*-acetoxyl substituent and an α,β-unsaturated 15,16-γ-lactone moiety, previously isolated from *Scutellaria* plants.

The ^{1}H-NMR spectrum of scupolin B (**4**, $C_{26}H_{36}O_{10}$) showed characteristic signals for a neoclerodane diterpenoid possessing a 4α,18-oxirane, an α,β-unsaturated 15,16-γ-lactone, and a hydroxyl group at the C-8β position. The proton spectrum of **4** was very similar to that of **3** (see Table 1), except for three acetoxyl groups (δ 2.09, 2.00, and 1.93, 3H each, singlets) and no 2-methylbutanoyloxy group. The acetates must be attached to the C-6α, C-11, and C-19 positions, because the signals of their geminal protons appeared at identical field and with the same coupling values ($\delta_{H-6\beta}$ 5.14 dd, $J_{6\beta,7\alpha} = 11.9$ Hz, $J_{6\beta,7\beta} = 4.7$ Hz; δ_{H-11} 5.53 dd, $J_{11,12A} = 10.7$ Hz, $J_{11,12B} = 1.5$ Hz; δ_{H-19} 4.39 and 4.85 d, $J_{gem} = 12.0$ Hz) as those observed for other (11*S*)-6α,11,19-tris(acyloxy)-4α,18-epoxy-8β-hydroxyneoclerod-14-en-15,16-olide derivatives found in *Scutellaria* species.[12,14,15]

Scupolin C (**5**) had the molecular formula $C_{36}H_{40}O_{10}$, and its IR spectrum showed hydroxyl (3450 cm^{-1}), α,β-unsaturated γ-lactone (3105, 1780, 1640 cm^{-1}), acetate (1740, 1240 cm^{-1}), and benzoate group (3060, 1720 br, 1600, 1580 cm^{-1}) absorptions.[9,10,15] The UV spectrum of **5** [λ_{max} nm (log ϵ) 225 (4.38), 273 (3.29)] corroborated the presence of benzoate esters in this diterpenoid.[9,10,15] The ^{1}H- and ^{13}C-NMR spectra of **5** (see Tables 1 and 2) described the presence of an acetoxyl group, two benzoates, and a neoclerodane framework with the same functionalities as those found in **3** and **4**. The attachment of the acetoxyl group at the C-11 position and the two benzoates at the C-6α and C-19 positions was in agreement with the chemical shifts of the geminal protons of the ester groups, as compared with those of the 6α,11*S*,19-triacetoxy derivative **4** [$\Delta\delta = \delta$(**4**) − δ(**5**), +0.34 (H-6β), +0.07 (H-11), +0.43 (H_A-19), and +0.17 ppm (H_B-19)], because the C-6 and C-19 protons are shifted downfield in **5** and the C-11 proton resonates at an almost identical chemical shift in both compounds. Thus, scupolin C had structure **5**.

Scupolins D (**6**) and E (**7**) had the same molecular formula $C_{27}H_{40}O_{10}$, and their ^{1}H- and ^{13}C-NMR spectra (see Tables 1 and 2) were almost identical, showing characteristic signals for a neoclerodane structure having a 4α,18-oxirane, an α,β-unsaturated 15,16-γ-lactone,

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Table 1. ^{1}H-NMR Spectral Data of Compounds **3**−**8**

proton(s)	**3**	**4**	**5**	**6**	**7**	**8**
H-1α	∼1.65[a]	*a*	*a*	1.66 (dddd)	*a*	*a*
H-1*β*	1.89 (dddd)	∼1.90[a]	*a*	1.88 (dddd)	∼1.90[a]	*a*
H-2α	∼2.00[a]	*a*	*a*	∼2.03[a]	*a*	*a*
H-2*β*	∼1.50[a]	*a*	*a*	1.50 (ddddd)	*a*	*a*
H-3α	2.37 (dddd)	*a*	*a*	2.29 (tdd)	*a*	2.97 (tdd)
H-3*β*	∼1.15[a]	∼1.15[a]	*a*	1.16 (ddd)	∼1.10[a]	*a*
H-6*β*	5.20 (ddd)	5.14 (br dd)	5.48 (dd)	3.83 (dd)	5.04 (d)	5.37 (dd)
H-7α	2.05 (dd)	*a*	*a*	5.41 (d)	3.78 (dd)	*a*
H-7*β*	1.55 (dd)	1.51 (dd)	1.76 (dd)			*a*
H-10*β*	2.15 (dd)	*a*	2.40 (dd)	2.06 (dd)	2.14 (dd)	*a*
H-11	5.52 (dd)	5.53 (dd)	5.60 (dd)	5.53 (dd)	5.57 (dd)	*a*
H_A-12	2.54 (dd)	2.53 (dd)	2.60 (dd)	2.54 (dd)	2.55 (dd)	*a*
H_B-12	3.50 (dd	3.52 (dd)	3.62 (dd)	3.46 (dd)	3.54 (dd)	*a*
H-14	5.84 (br t)	5.84 (br t)	5.87 (br t)	5.84 (br t)	5.85 (br t)	5.81 (br t)
H_A-16	4.65 (dd)	4.64 (dd)	4.68 (dd)	4.63 (dd)	4.65 (dd)	4.72 (2H, d)
H_B 16	4.85 (dd)	4.86 (dd)	4.89 (dd)	4.84 (dd)	4.87 (dd)	
Me-17	1.30 (3H, s)	1.30 (3H, s)	1.34 (3H, s)	1.23 (3H, s)	1.36 (3H, s)	1.21 (3H, s)
H_A-18[b]	2.29 (d)	2.25 (d)	2.34 (d)	2.49 (d)	2.28 (d)	2.58 (d)
H_B-18[c]	2.98 (dd)	3.01 (dd)	3.18 (dd)	3.21 (dd)	3.04 (dd)	3.17 (dd)
H_A-19	4.11 (td)[d]	4.39 (br d)	4.82 (d)	4.12 (dd)[e]	4.12 (dd)[e]	
H_B-19	4.28 (dd)[e]	4.85 (d)	5.02 (d)	4.29 (dd)[e]	4.22 (dd)[e]	
Me-20	0.70 (3H, s)	0.76 (3H, s)	0.86 (3H, s)	0.84 (3H, s)	0.74 (3H, s)	1.01 (3H, s)
OAc-6α		1.93 (3H, s)				
OAc-11	2.00 (3H, s)	2.00 (3H, s)	2.03 (3H, s)	2.01 (3H, s)	2.01 (3H, s)	
OAc-19		2.09 (3H, s)				
H-2′	2.31 (sext)			2.43 (sext)	2.38 (sext)	2.35 (sext)
H_A-3′	1.46 (ddq)			1.48 (ddq)	∼1.50[a]	*a*
H_B-3′	1.68 (ddq)			1.72 (ddq)	∼1.70[a]	*a*
Me-4′	0.90 (3H, t)			0.92 (3H, t)	0.94 (3H, t)	0.91 (3H, t)
Me-5′	1.12 (3H, d)			1.18 (3H, d)	1.18 (3H, d)	1.14 (3H, d)
OBz						
H-2′,6′			8.12 (2H, dd)			
H-3′,5′			7.31 (2H, td)			
H-4′			7.49 (tt)			
H-2″,6″			7.77 (2H, dd)			
H-3″,5″			6.90 (2H, td)			
H-4″			7.26 (tt)			
OH-6α				3.15 (d)		
OH-7*β*					2.68 (s)	
OH-8*β*	*a*	*a*	*a*	2.00 (s)	*a*	*a*
OH-19	2.46 (dd)			2.69 (dd)	*a*	*a*

$J_{H,H\ (Hz)}$	**3**	**4**	**5**	**6**	**7**	**8**
1α,1*β*	13.4	*a*	*a*	13.9	*a*	*a*
1α,2α	*a*	*a*	*a*	3.5	*a*	*a*
1α,2*β*	*a*	*a*	*a*	13.9	*a*	*a*
1α,10*β*	11.7	*a*	12.2	12.3	11.9	*a*
1*β*,2α	2.7	*a*	*a*	2.6	*a*	*a*
1*β*,2*β*	4.2	*a*	*a*	4.1	*a*	*a*
1*β*,10*β*	2.8	*a*	2.7	2.5	2.4	*a*
2α,2*β*	*a*	*a*	*a*	13.9	*a*	*a*
2α,3α	4.1	*a*	*a*	4.3	*a*	4.1
2α,3*β*	*a*	*a*	*a*	2.6	*a*	*a*
2*β*,3α	13.4	*a*	*a*	13.4	*a*	14.0
2*β*,3*β*	*a*	*a*	*a*	4.1	*a*	*a*
3α,3*β*	13.4	*a*	*a*	13.4	*a*	14.0
6*β*,7α	11.4	11.9	11.8	10.0	9.6	12.1
6*β*,7*β*	4.8	4.7	4.6			3.9
7α,7*β*	14.3	14.3	14.4			*a*
11,12A	10.7	10.7	10.9	10.7	10.8	*a*
11,12B	1.4	1.5	1.3	1.2	1.4	*a*
12A,12B	15.4	15.3	15.1	15.1	15.4	*a*
14,16A	1.8	1.8	1.2	1.7	1.8	1.7
14,16B	1.8	1.8	1.3	1.7	1.8	1.7
16A,16B	17.4	17.4	17.4	17.4	17.4	0
18A,18B	3.8	4.0	3.9	3.1	3.7	3.7
18B,3α	2.4	2.2	1.9	2.3	2.4	2.4
19A,19B	11.5	12.0	12.2	12.5	12.0	
19A,6*β*	0.9	<0.5	0	0	0	
6*β*,OH-6α				1.9		
19A,OH-19	11.5			8.8	10.1	
19B,OH-19	1.3			5.6	2.7	
7α,OH-8*β*	0	0	0	0	4.2	
2′,3′	7.0			7.1	7.0	6.9
2′,5′	7.0			6.8	7.0	7.0
3′A,3′B	13.8			13.7	*a*	*a*
3′,4′	7.4			7.3	7.4	7.4
OBz						
2′,3′(2″,3″)			7.4			
2′,4′(2″,4″)			1.3			
3′,4′(3″,4″)			7.6			

[a] Overlapped signal. [b] Exo hydrogen with respect to ring B. [c] Endo hydrogen with respect to ring B. [d] Collapsed into a doublet of doublets after addition of D_2O. [e] Collapsed into a doublet after addition of D_2O.

Table 2. ^{13}C-NMR Spectral Data of Compounds **3** and **5**−**11**

carbon	**3**	**5**[a]	**6**	**7**	**8**	**9**	**10**	**11**
C-1	23.0 (t)	23.3 (t)	22.6 (t)	23.0 (t)	22.2 (t)	22.6 (t)	29.0 (t)	28.9 (t)
C-2	24.8 (t)	24.8 (t)	24.7 (t)	24.7 (t)	24.7 (t)	70.1 (d)	66.7 (d)	66.7 (d)
C-3	32.6 (t)	33.0 (t)	31.6 (t)	32.4 (t)	33.1 (t)	71.0 (d)	37.0 (t)	37.0 (t)
C-4	65.1 (s)	64.9 (s)	67.4 (s)	65.3 (s)	64.4 (s)	65.8 (s)	60.8 (s)	60.7 (s)
C-5	46.4 (s)[b]	45.6 (s)	47.2 (s)	46.8 (s)	55.1 (s)	42.4 (s)	42.7 (s)	42.7 (s)
C-6	71.0 (d)	69.7 (d)	72.1 (d)	74.2 (d)	69.3 (d)	68.4 (d)	68.2 (d)	68.3 (d)
C-7	40.0 (t)	40.2 (t)	74.6 (d)	73.5 (d)	40.8 (t)	33.4 (t)	33.6 (t)	33.6 (t)
C-8	76.4 (s)	76.5 (s)	78.3 (s)	78.6 (s)	77.4 (s)	35.4 (d)	35.7 (d)	35.4 (d)
C-9	46.2 (s)[b]	46.5 (s)	46.1 (s)	46.2 (s)	42.3 (s)	41.3 (s)	41.0 (s)	41.0 (s)
C-10	43.1 (d)	43.5 (d)	41.8 (d)	42.6 (d)	45.5 (d)	41.0 (d)	41.3 (d)	41.1 (d)
C-11	74.3 (d)	74.1 (d)	74.9 (d)	74.9 (d)	34.8 (t)	86.3 (d)	85.6 (d)	84.2 (d)
C-12	33.1 (t)	33.1 (t)	33.1 (t)	33.0 (t)	25.4 (t)	32.6 (t)	32.3 (t)	33.5 (t)
C-13	168.1 (s)	167.9 (s)	167.5 (s)	167.6 (s)	171.4 (s)[c]	41.9 (d)	45.7 (d)	40.2 (d)
C-14	116.5 (d)	116.7 (d)	116.9 (d)	116.6 (d)	114.6 (d)	33.4 (t)	102.0 (d)	39.6 (t)
C-15	173.9 (s)	173.9 (s)	173.6 (s)	173.8 (s)	174.2 (s)	68.2 (t)	146.7 (d)	104.7 (d)
C-16	73.1 (t)	73.1 (t)	73.0 (t)	73.1 (t)	73.1 (t)	108.2 (d)	108.2 (d)	109.7 (d)
C-17	26.5 (q)	26.7 (q)	22.5 (q)	22.0 (q)	26.3 (q)	16.5 (q)	16.7 (q)	16.7 (q)
C-18	47.5 (t)	48.2 (t)	49.2 (t)	48.0 (t)	51.7 (t)	44.0 (t)	49.8 (t)	49.8 (t)
C-19	61.3 (t)	62.3 (t)	62.3 (t)	62.6 (t)	171.6 (s)[c]	91.1 (d)	100.3 (d)	100.3 (d)
C-20	15.9 (q)	16.0 (q)	15.3 (q)	15.7 (q)	22.3 (q)	14.3 (q)	14.1 (q)	13.9 (q)
OAc	170.7 (s)	170.7 (s)	170.6 (s)	170.6 (s)		169.9 (s)	170.4 (s)	170.4 (s)
	20.7 (q)	20.8 (q)	20.7 (q)	20.7 (q)		21.3 (q)	21.2 (q)	21.2 (q)
C-1′	175.1 (s)		175.7 (s)	176.9 (s)	175.0 (s)	175.3 (s)		
C-2′	41.4 (d)		41.5 (d)	41.6 (d)	41.4 (d)	34.2 (d)		
C-3′	26.4 (t)		26.7 (t)	26.4 (t)	26.2 (t)	18.9 (q)		
C-4′	11.4 (q)		11.7 (q)	11.5 (q)	11.4 (q)	18.3 (q)		
C-5′	16.5 (q)		16.9 (q)	16.7 (q)	16.2 (q)			
OMe-15β								54.5 (q)
OMe-19β							55.3 (q)	55.2 (q)

[a] OBz-6α: COO 166.1 (s), C-1′ 130.1 (s), C-2′,C-6′ 129.7 (d), C-3′,C-5′ 128.3 (d), C-4′ 132.9 (d). OBz-19: COO 167.1 (s), C-1″ 129.84 (s), C-2″,C-6″ 129.79 (d), C-3″,C-5″ 127.8 (d), C-4″ 132.6 (d). [b,c] These assignments may be reversed.

Table 3. ^{1}H-NMR Spectral Data of Compounds **9**, **10**, and **11**

proton(s)	**9**	**10**	**11**	$J_{H,H}$ (Hz)	**9**	**10**	**11**
H-2β	4.32 (m)[a]	4.10 (m)[b]	4.08 (m)[b]	1α,3α	3.2	2.9	2.9
H-3α	3.95 (dd)	2.53 (dt)	2.54 (dt)	1α,10β	*c*	*c*	13.2
H-6β	4.64 (dd)	4.62 (dd)	4.62 (dd)	1β,10β	*c*	*c*	9.5
H-10β	*c*	*c*	2.18 (dd)	2β,3α	4.1	2.9	2.9
H-11α	4.06 (dd)	3.99 (dd)	3.99 (dd)	3α,3β		14.1	14.1
H-13β	2.83 (m)[d]	3.53 (m)[e]	2.94 (m)[e]	6β,7α	11.5	11.3	10.9
H-14	*c*	4.81 (t)	*c*	6β,7β	4.6	4.5	4.5
H-15	3.85 (2H, m)	6.45 (t)	5.10 (br d)	8β,17	6.3	6.0	5.9
H-16β	5.61 (d)	6.01 (d)	5.72 (d)	11α,12A	10.9	11.5	11.5
Me-17	0.88 (3H, d)	0.89 (3H, d)	0.90 (3H, d)	11α,12B	5.7	4.7	4.7
H_A-18	2.85 (d)	2.37 (d)	2.35 (d)	13β,14	*c*	2.4	*c*
H_B-18	3.05 (d)	2.94 (d)	2.94 (d)	13β-15	*c*	2.4	0
H-19α	6.65 (s)	5.11 (s)	5.11 (s)	13β,16β	5.1	6.2	5.4
Me-20	1.15 (3H, s)	1.12 (3H, s)	1.11 (3H, s)	14,15	*c*	2.4	
OAc	1.92 (3H, s)	2.02 (3H, s)	2.02 (3H, s)	14A,15α	*c*		4.1
H-2′	2.54 (sept)			14B,15α	*c*		<0.5
Me-3′	1.22 (3H, d)			18A,18B	4.4	4.4	4.4
Me-4′	1.19 (3H, d)			2′,3′(4′)	7.1		
OMe-15β			3.33 (3H, s)				
OMe-19β		3.50 (3H, s)	3.50 (3H, s)				

[a] $W_{1/2}$ = 4.5 Hz. [b] $W_{1/2}$ = 8 Hz. [c] Overlapped signal. [d] $W_{1/2}$ = 24 Hz. [e] $W_{1/2}$ = 20 Hz.

a C-11*S* acetoxyl group, a tertiary alcohol at the C-8β position, a primary hydroxyl group at C-19, and a 2-methylbutanoate ester group. In addition, the ^{1}H-NMR spectra of **6** and **7** (see Table 1) displayed signals for an AB system corresponding to the C-6β and C-7α axial protons[9,10,13,15] [**6** δ 3.83 dd (collapsed into a d after addition of D_2O) and 5.41 d, J_{vic} = 10.0 Hz; **7** δ 5.04 and 3.78 dd (transformed into a d by addition of D_2O), J_{vic} = 9.6 Hz, respectively] instead of the ABX pattern shown by the H-6β and C-7 methylene protons of scupolin A (**3**, see Table 1). Apart from the above data, the presence of an oxygen substituent at the C-7β position in **6** and **7** was supported by their ^{13}C-NMR spectra when compared with that of **3** (see Table 2): downfield shift of the C-6, C-7, and C-8 carbons (Δδ **6** +1.1, +34.6, and +1.9; **7** +3.2, +33.5, and +2.2 ppm, respectively) and upfield resonance of the C-17 carbon (Δδ −4.0 and −4.5 ppm for **6** and **7**, respectively, γ-gauche effect).

From all the above data, it was evident that the structures of scupolins D and E differred only in the attachment of the 2-methylbutyryloxy group, which, probably, is at the C-7β position in **6** and at the C-6α position in **7**. This hypothesis was supported by the downfield resonance of the Me-17 protons in **7** (δ 1.36 s, 7β-OH regioisomer) with respect to **6** (δ 1.23 s, ester group at the C-7β position), as well as by the variation of the chemical shifts of the C-18 oxiranic protons in both compounds (**6** δ 2.49 and 3.21 dd, **7** δ 2.28 and 3.04 dd). It is known[16,17] that esterification of the C-6α equatorial alcohol in 4α,18-epoxy-6α-hydroxyneoclerodane derivatives causes a noticeable diamagnetic shift of the C-18 protons.

The HMBC spectrum of **6** showed correlations through

three bonds between the H-11 proton (δ 5.53) and the carbonyl carbon of the acetoxyl group (δ 170.6 s), and between the H-7α proton (δ 5.41) and the carbonyl carbon belonging to the 2-methylbutanoate (δ 175.7 s), thus confirming the location of the ester groups. Moreover, the C-7 carbon (δ 74.6 d, bearing proton at δ 5.41, HMQC spectrum) correlated with the Me-17 protons (δ 1.23), whereas the C-6 carbon (δ 72.1 d, attached proton at δ 3.83) showed connectivities with the H-7α and both C-19 methylene protons (δ 4.12 and 4.29). These results firmly support a 2-methylbutyryloxy substituent at the C-7β position in **6**. Additionally, the H-6β and H-7α protons were unambiguously distinguished by the NOESY spectrum of **6**, which displayed cross peaks of NOE between the H-6β proton (δ 3.83) and the H-10β (δ 2.06) and H_B-18 (δ 3.21) protons, as well as between the H-7α proton (δ 5.41) and the H_B-19 (δ 4.29), Me-17 (δ 1.23), and Me-20 (δ 0.84) protons. All the above data were only compatible with the structure depicted in **6** for scupolin D and consequently, its regioisomer scupolin E must possess structure **7**.

The IR spectrum of scupolin F (**8**, $C_{25}H_{36}O_8$) showed absorptions attributable to hydroxyl (3500 cm^{-1}), α,β-unsaturated γ-lactone (1740, 1625 cm^{-1}), and carboxyl (3300−2900 br, 1725 cm^{-1}) groups. The ^{1}H- and ^{13}C-NMR spectra of **8** (see Tables 1 and 2) revealed the presence of a 4α,18-oxirane, an α,β-unsaturated 15,16-γ-lactone, a tertiary 8β-hydroxyl group, and a 2-methylbutyryloxy substituent at the C-6α position, all signals identical with those found in **3**. Comparison of the ^{1}H- and ^{13}C-NMR spectra of **3** and **8** indicated the absence of an 11-acetoxyl substituent in **8** and also that the C-19 hydroxymethylene group of **3** was oxidized in **8** to a carboxyl group (δ_{C-19} 171.6 s). The observed differences in the C-4, C-5, C-6, C-18, and C-19 carbon atom resonances of **8** as compared with those of **3** ($\Delta\delta$ −0.7, +8.7, −1.7, +4.2, and +110.3 ppm, respectively), together with the downfield shift shown by the axial H-3α and Me-20 protons of **8** ($\delta_{H-3\alpha}$ 2.97, δ_{Me-20} 1.01) with respect to those of **3** ($\delta_{H-3\alpha}$ 2.37, δ_{Me-20} 0.70), further supported the location of the carboxyl group of **8** at the C-19 axial position. Therefore, scupolin F possessed structure **8**.

Scupolin G (**9**) had the molecular formula $C_{26}H_{38}O_9$, and its IR spectrum showed hydroxyl (3400 cm^{-1}) and ester group (1740, 1700, 1250 cm^{-1}) absorptions. The ^{1}H NMR spectrum of **9** was very similar to that of scutecolumnin B (**13**), a neoclerodane derivative previously isolated from *Scutellaria columnae*.[11] In fact, both **9** and **13** showed ^{1}H NMR signals corresponding to a 6α-acetoxyl group, a 4α,18-oxirane, an esterified 19,2α-hemiacetal function, and a hexahydrofurofuran structural part in which the C-11−C-16 carbons of the neoclerodane framework are involved (see Table 3 and de la Torre et al.[11]). However, the acyloxy group at C-19 was different in both compounds: an isobutyryloxy group is established in **9** [δ_H 2.54, 1H, sept, J = 7.1 Hz (H-2′) and 1.22 and 1.19, 3H each, both d, J = 7.1 Hz (Me-3′ and Me-4′); δ_C 175.3 s (C-1′), 34.2 d (C-2′), and 18.9 q and 18.3 q (C-3′ and C-4′)][6,12] instead of the 2-methylbutanoate present in **13**.[11] In addition, scupolin G (**9**) possessed a secondary hydroxyl group (ν_{OH} 3400 cm^{-1}, geminal proton at δ 3.95 dd, J = 4.1, 3.2 Hz, methine carbon bearing an oxygen atom at δ 70.1 d), which must be placed at the C-3β axial position on the basis of the following data.

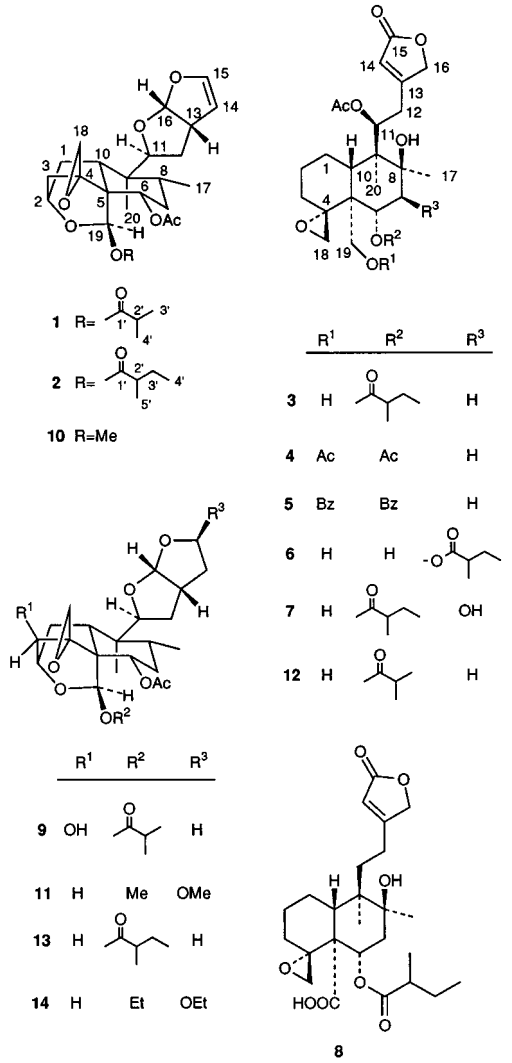
The C-5−C-17, C-19, and C-20 carbon atom resonances of **9** (see Table 2) were identical with those of **13**.[11] This places the secondary alcohol of scupolin G at C-3 or, less probably, at C-1. The placement of the hydroxyl at C-3 is supported by the downfield resonance of the H-2β proton in **9** (δ 4.32) with respect to that of **13** (δ 4.17).[11] Irradiation at δ 4.32 (H-2β proton of **9**) transformed the double doublet signal at δ 3.95 (J = 4.1, 3.2 Hz) into a doublet (J = 3.2 Hz), which must be due to the existence of a *W*-type coupling between the H-1α and H-3α equatorial protons.[6] Therefore, the hydroxyl group of **9** must be axial and placed at the C-1β or C-3β position. Comparison of the ^{13}C NMR spectra of **9** (Table 2) and **13**[11] unambiguously established that the hydroxyl group of the former was located at the C-3β position, because downfield resonances of the C-2, C-3, and C-4 carbons ($\Delta\delta$ +2.9, +34.2, and +5.4 ppm, respectively) and diamagnetic shift of the C-1 and C-18 carbons ($\Delta\delta$ −5.8 and −6.1 ppm, respectively, shielding γ-effect) were observed, whereas the C-10 carbon resonated at an identical chemical shift in both compounds (δ 41.0).

All the above conclusions on structure **9** for scupolin G were in complete agreement with its HMBC and NOESY spectra. In particular, the HMBC spectrum showed connectivities between the H-6β proton (δ 4.64 dd) and the carboxyl carbon of the acetate (δ 169.9 s), and between the C-19 proton (δ 6.65 s) and the carboxyl carbon of the isobutyrate (δ 175.3 s), whereas the NOESY spectrum displayed NOE cross peaks between the H-19α and Me-20 protons, thus establishing the relative stereochemistry of the C-19 asymmetric center as *R*. Moreover, the H-3α equatorial proton (δ 3.95) showed NOE with the H-2β proton (δ 4.32), and neither of the C-18 oxiranic protons (δ 2.85 and 3.05) showed NOE with the H-3α proton. These results further supported the stereochemistry of the hydroxyl group of scupolin G as it is depicted in formula **9** (axial 3β-OH).

The ^{1}H- and ^{13}C-NMR spectra of scupolin H (**10**, $C_{23}H_{32}O_7$, see Tables 2 and 3) were identical with those of jodrellin B[6] (**1**) except for the upfield shift shown by the C-19 proton (δ 5.11 and 6.70 s in **10** and **1**, respectively) and for the presence in **10** of a 19-*O*-methyl-19,2α-acetal group [δ_H 3.50, 3H, s (OMe), δ_C 100.3 d (C-19) and 55.3 q (OCH_3)] instead of the (19-*O*-isobutyryl)-19,2α-hemiacetal of **1**,[6] the rest of the spectra being identical in both compounds. Irradiation at δ 5.11 (C-19 proton) under the NOE experimental conditions caused an NOE enhancement in the signal of the Me-20 protons (δ 1.12), establishing a cis spatial relationship between these hydrogens, as it is shown in **10**.

The last of the diterpenoids isolated from *S. polyodon*, scupolin I (**11**), had the molecular formula $C_{24}H_{36}O_8$, and its ^{1}H- and ^{13}C-NMR spectra were very similar to those of **10** (see Tables 2 and 3), except for the C-14−C-15 structural part. The signals associated with a vinyl ether group in **10** were absent in **11**, while those corresponding to a hemiacetal [δ_H 5.10 br d, J = 4.1 Hz (H-15α), δ_C 39.6 t (C-14) and 104.7 d (C-15)] and an additional methoxyl group (δ_H 3.33, 3H, s; δ_C 54.5 q) were observed, indicating that **11** was the 15-methoxy-14,15-dihydro derivative of **10**. The stereochemistry at the C-15 position was established by an NOE experiment, in which an NOE was observed between the H-15 and the H-11α endo proton, and consequently the

H-15 hydrogen of **11** must be also in an endo configuration. This conclusion was also in agreement with the chemical shift of the H-11α proton of **11**, which resonated at δ 3.99, a value almost identical with those reported for 15β-hydroxy[10,18] or ethoxy[19] derivatives (δ 3.95 or 4.09, respectively) and very different from those observed in the corresponding 15α epimers[10,18,19] (δ 4.50 and 4.54, respectively). Finally, structure **11** for scupolin I was also supported by comparing its NMR spectroscopic data (see Tables 2 and 3) with those of **14**, a 15β,19β-diethoxy derivative recently isolated from *Scutellaria discolor*.[19] Apart from the signals due to the methoxyl (**11**) or ethoxyl (**14**) groups, the ^{1}H- and ^{13}C-NMR spectra of both compounds were identical.



The absolute stereochemistry of the clerodane framework of **3**−**11** and that of the C-2′ stereogenic center of the 2-methylbutanoate group of **3**, **6**, **7**, and **8** was not ascertained. However, on biogenetic grounds, we hypothesize that all the new compounds belong to the neoclerodane[1] series and therefore possess a 2′*S* absolute configuration at the C-2′ chiral center of **3**, **6**, **7**, and **8**. This stereochemical assignment would be in agreement with that of other neoclerodanes previously isolated from *Scutellaria* species, whose structures, including their absolute configuration, are well known.[8−10,15,19−21]

It should be noted that scupolin I (**11**), which possesses a methoxyl group at C-15, could be an artifact formed in the course of the extraction and/or isolation. It is known[19,22,23] that the C-14−C-15 double bond of compounds such as **1**, **2**, and **10** is very sensitive even to solvation in the presence of weak acids or bases. Moreover, the methoxyl group at C-19 in **10** and **11** (and the C-19 ethoxy substituent of **14**) is a rare structural feature in neoclerodane diterpenoids,[2−4,6,11,19,23−25] and it could also be considered as unnatural, taking into account that the hydrolysis of an ester group of a hemiacetalic function[20,23,24] (like that of **1**, **2**, and **9**) or its nucleophilic substitution by an alkoxyl group[26,27] is achieved very easily by acid catalysis. In fact, in the majority of the articles reporting the isolation of 15-hydroxy, methoxy, or ethoxyneoclerodane derivatives such as **11** and **14**, these compounds were found as mixtures of 15α and 15β epimers,[2−4,10,18,19,23,25] but in some cases, they were isolated as single products,[22] and this has been considered as a proof for defining these substances as natural products in their own right.[22,25] In the present work, it is difficult to establish if **10** and **11** are natural compounds or artifacts arising from **1** and/or **2**,[25] because MeOH was not used in the extraction or processing procedures, and **10** and **11** were detected in a fresh Me_2CO extract of the plant by TLC. However, minute amounts of the 15α epimer of **11** were also detected,[28] and this seems to indicate[19,22] that at least **11** could be an artifact from **10**.

Experimental Section

General Experimental Procedures. Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 MC polarimeter. IR spectra (KBr) were obtained on a Perkin-Elmer 681 spectrophotometer. UV spectra were recorded on a Perkin-Elmer Lambda 2 spectrophotometer. ^{1}H-NMR spectra were recorded in $CDCl_3$ solution using Varian INOVA-400, Varian INOVA-300, or Bruker AM-200 apparatus at 400, 300, or 200 MHz, respectively, and chemical shifts are reported with respect to residual $CHCl_3$ (δ 7.25). ^{13}C NMR spectra were recorded in $CDCl_3$ at 100.5, 75.4, or 50.3 MHz, and chemical shifts are reported with respect to solvent signals (δ_{CDCl_3} 77.00). ^{13}C-NMR assignments were determined by DEPT, HMQC, and, in some cases, HMBC spectra. MS were recorded in the positive EI mode on a VG MASSLAB 12−250 instrument. Elemental analyses were made with a Carlo Erba EA 1108 apparatus. Merck Si gel no. 7734 (70−230 mesh) deactivated with 15% H_2O, w/v, was used for column chromatography.

Plant Collection. *S. polyodon* Juz. was cultivated in the Orto Botanico dell′Università di Milano, at Tuscolano, Brescia, Italy. Seeds of the species were provided by the Jardin Botanique de Lausanne, Lausanne, Switzerland. Plant materials were collected in August 1995, and voucher specimens have been deposited in the Herbarium of the Dipartimento di Biologia, Università di Milano, Italy.

Extraction and Isolation. Dried and finely powdered aerial parts of *S. polyodon* (2.7 kg) were extracted with Me_2CO (3 × 10 L) at room temperature for 1 week. After concentration of the Me_2CO extract *in vacuo* at low temperature (35 °C), 89 g of residue remained. This residue was subjected to dry column chromatography on Si gel with a solvent gradient from 100% petroleum ether (bp 50−70 °C) to 100% EtOAc. The residue

obtained (870 mg) from the fractions eluted with EtOAc−petroleum ether (1:1) was rechromatographed [radial chromatography, Si gel disk, EtOAc−petroleum ether (3:2) as eluent] yielding the following compounds in order of increasing chromatographic polarity: scutecolumnin A[11] (**2**, 10 mg), jodrellin B[6] (**1**, 68 mg), scupolin H (**10**, 70 mg), and scupolin I (**11**, 82 mg).

The fractions eluted with EtOAc−petroleum ether (7:3)(1.8 g) were subjected to radial chromatography [Si gel disk, EtOAc−petroleum ether (4:1) as eluent] giving the following compounds in order of increasing chromatographic polarity: scupolin C (**5**, 72 mg), scupolin A (**3**, 640 mg), scupolin F (**8**, 38 mg), scupolin G (**9**, 95 mg), scupolin E (**7**, 25 mg), scupolin D (**6**, 700 mg), and scupolin B (**4**, 16 mg).

The chromatographic fractions containing diterpenoids were decolored by filtration through a pad of a mixture (1:1) of activated charcoal and Celite, eluting with EtOAc.

The previously known compounds, jodrellin B[6] (**1**) and scutecolumnin A[11] (**2**), were identified by their $[\alpha]_D$, IR, ^{1}H-NMR, and mass spectra, and by comparison (TLC) with authentic samples.

Scupolin A (3), (11*S*)-11-acetoxy-6α-[(2′-methylbutyryl)oxy]-4α,18-epoxy-8*β*,19-dihydroxyneoclerod-13-en-15,16-olide: mp 205−207 °C (EtOAc−*n*-hexane); $[\alpha]^{19}_D$ +2.3° (*c* 0.631, $CHCl_3$); IR (KBr) ν_{max} 3580, 3480 (OH), 3110, 1785, 1745, 1630 (α,*β*-unsaturated *γ*-lactone), 3060 (oxirane), 1725, 1720, 1235 (ester groups), 2960, 2940, 1460, 1370, 1075, 1020, 960, 890, 860, 840, 800 cm^{-1}; ^{1}H NMR (300 MHz), see Table 1; ^{13}C NMR (50.3 MHz), see Table 2; EIMS (70 eV, direct inlet) *m*/*z* (rel int) $[M]^+$ absent, 480 $[M - C_2H_4]^+$ (1.5), 450 (1), 418 (1), 394 (7), 347 (7), 334 (6), 329 (8), 316 (17), 298 (6), 259 (10), 178 (13), 177 (16), 172 (11), 153 (10), 146 (11), 133 (13), 119 (14), 117 (15), 105 (19), 93 (15), 91 (26), 85 (21), 79 (24), 57 (100), 55 (19), 45 (17), 43 (88), 41 (35); *anal*. C 63.59%, H 7.89%, calcd for $C_{27}H_{40}O_9$, C 63.76%, H 7.93%.

Scupolin B (4), (11*S*)-6α,11,19-triacetoxy-4α,18-epoxy-8*β*-hydroxyneoclerod-13-en-15,16-olide: mp 98−104 °C, amorphous solid; $[\alpha]^{19}_D$−6.6° (*c* 0.198, $CHCl_3$); IR (KBr) ν_{max} 3460 (OH), 3100, 1780, 1640 (α,*β*-unsaturated *γ*-lactone), 1740, 1240 (OAc), 2940, 1450, 1370, 1090, 1020, 965, 890, 860, 840, 800 cm^{-1}; ^{1}H NMR (200 MHz), see Table 1; EIMS (70 eV, direct inlet) *m*/*z* (rel int) 508 $[M]^+$ (0.05), 448 $[M - AcOH]^+$ (0.2), 357 (2), 333 (4), 328 (2), 285 (3), 189 (2), 183 (2), 176 (11), 131 (7), 117 (9), 105 (12), 93 (9), 91 (17), 79 (11), 77 (8), 55 (9), 43 (100); *anal*. C 61.51%, H 7.29%, calcd for $C_{26}H_{36}O_{10}$, C 61.40%, H 7.14%.

Scupolin C (5), (11*S*)-11-acetoxy-6α,19-bis(benzoyloxy)-4α,18-epoxy-8*β*-hydroxyneoclerod-13-en-15,16-olide: mp 244−246 °C (EtOAc−*n*-hexane); $[\alpha]^{19}_D$ +43.1° (*c* 0.438, $CHCl_3$); IR (KBr) ν_{max} 3450 (OH), 3105, 1780, 1640 (α,*β*-unsaturated *γ*-lactone), 3060, 1740 br, 1720 br, 1600, 1580 (OBz), 1740, 1240 (OAc), 2950, 2880, 1450, 1370, 1280, 1180, 1120, 1070, 1025, 960, 750, 710 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 225 (4.38), 273 (3.29) nm; ^{1}H NMR (300 MHz), see Table 1; ^{13}C NMR (75.4 MHz), see Table 2; EIMS (70 eV, direct inlet) *m*/*z* (rel int) 632 $[M]^+$ (0.05), 554 $[M - AcOH - H_2O]^+$ (0.05), 510 $[M - BzOH]^+$ (0.05), 450 $[M - AcOH - BzOH]^+$ (0.2), 328 $[M - AcOH - 2\ BzOH]^+$ (0.3), 202 (5), 189 (7), 173 (5), 171 (24), 159 (7), 156 (9), 122 (5), 105 $[Bz]^+$ (100), 91 (10), 77 (47), 51 (10), 43 (19); *anal*. C 68.12%, H 6.51%, calcd for $C_{36}H_{40}O_{10}$, C 68.34%, H 6.37%.

Scupolin D (6), (11*S*)-11-acetoxy-7*β*-[(2′-methylbutyryl)oxy]-4α,18-epoxy-6α,8*β*,19-trihydroxyneoclerod-13-en-15,16-olide: mp 193−195 °C (EtOAc−*n*-hexane); $[\alpha]^{19}_D$−6.7° (*c* 0.372, $CHCl_3$); IR (KBr) ν_{max} 3580, 3460 (OH), 3100, 1770, 1635 (α,*β*-unsaturated *γ*-lactone), 3060 (oxirane), 1740, 1730, 1230 (ester groups), 2960, 2940, 1460, 1370, 1170, 1140, 1080, 1030, 1025, 965, 900, 840 cm^{-1}; ^{1}H NMR (400 MHz), see Table 1; ^{13}C NMR (100.5 MHz), see Table 2; EIMS (70 eV, direct inlet) *m*/*z* (rel int) 524 $[M]^+$ (0.05), 506 $[M - H_2O]^+$ (0.1), 464 $[M - AcOH]^+$ (0.4), 362 (5), 344 (6), 331 (3), 314 (3), 301 (6), 283 (5), 271 (14), 177 (15), 176 (26), 121 (13), 119 (11), 105 (15), 93 (13), 91 (20), 85 (38), 79 (17), 57 (100), 55 (14), 43 (38), 41 (23); *anal*. C 61.69%, H 7.80%, calcd for $C_{27}H_{40}O_{10}$, C 61.81%, H 7.69%.

Scupolin E (7), (11*S*)-11-acetoxy-6α-[(2′-methylbutyryl)oxy]-4α,18-epoxy-7*β*,8*β*,19-trihydroxyneoclerod-13-en-15,16-olide: mp 185−188 °C (EtOAc−*n*-hexane); $[\alpha]^{19}_D$−10.5° (*c* 0.153, $CHCl_3$); IR (KBr) ν_{max} 3560, 3460 (OH), 3100, 1780, 1640 (α,*β*-unsaturated *γ*-lactone), 3075 (oxirane), 1740, 1240 (ester groups), 2970, 2940, 1450, 1370, 1185, 1150, 1080, 1025, 970, 850 cm^{-1}; ^{1}H NMR (200 MHz), see Table 1; ^{13}C NMR (50.3 MHz), see Table 2; EIMS (70 eV, direct inlet) *m*/*z* (rel int) $[M]^+$ absent, 506 $[M - H_2O]^+$ (0.05), 464 $[M - AcOH]^+$ (0.4), 446 $[M - H_2O - AcOH]^+$ (0.5), 415 (0.6), 362 (6), 344 (4), 301 (6), 271 (12), 177 (12), 176 (19), 121 (12), 119 (11), 105 (4), 95 (10), 93 (14), 91 (22), 85 (30), 79 (14), 77 (11), 57 (100), 55 (17), 43 (45), 41 (29); *anal*. C 61.96%, H 7.73%, calcd for $C_{27}H_{40}O_{10}$, C 61.81%, H 7.69%.

Scupolin F (8), 6α-[(2′-methylbutyryl)oxy]-19-carboxy-4α,18-epoxy-8*β*-hydroxyneoclerod-13-en-15,16-olide: mp 158−161 °C (EtOAc−*n*-hexane); $[\alpha]^{19}_D$ +22.6° (*c* 0.354, $CHCl_3$); IR (KBr) ν_{max} 3500 (OH), 3300−2900, 1725 (COOH), 1740, 1625 (α,*β*-unsaturated *γ*-lactone), 1725 (ester), 2960, 1460, 1440, 1375, 1200, 1130, 1090, 1030, 1020, 910, 845, 730 cm^{-1}; ^{1}H NMR (200 MHz), see Table 1; ^{13}C NMR (50.3 MHz), see Table 2; EIMS (70 eV, direct inlet) *m*/*z* (rel int) 464 $[M]^+$ (0.1), 446 $[M - H_2O]^+$ (0.1), 318 (2), 305 (7), 300 (10), 287 (13), 203 (12), 189 (12), 185 (11), 171 (51), 165 (19), 161 (21), 159 (11), 157 (13), 156 (14), 147 (14), 145 (17), 143 (16), 136 (17), 121 (22), 119 (29), 117 (33), 107 (24), 105 (34), 98 (59), 93 (24), 91 (55), 85 (34), 79 (38), 77 (32), 67 (26), 57 (79), 55 (36), 43 (100), 41 (59); *anal*. C 64.49%, H 7.84%, calcd for $C_{25}H_{36}O_8$, C 64.63%, H 7.81%.

Scupolin G (9), (11*S*,13*R*,16*S*,19*R*)-6α-acetoxy-19-(isobutyryloxy)-2α,19;4α,18;11,16;15,16-tetraepoxyneoclerodan-3*β*-ol: mp 192−194 °C (EtOAc−*n*-hexane); $[\alpha]^{19}_D$ +27.6° (*c* 0.156, $CHCl_3$); IR (KBr) ν_{max} 3400 (OH), 1740, 1700, 1250 (ester groups), 2960, 1465, 1380, 1290, 1150, 1080, 1015, 960, 915, 900, 770 cm^{-1}; ^{1}H NMR (300 MHz), see Table 3; ^{13}C NMR (50.3 MHz), see Table 2; EIMS (70 eV, direct inlet) *m*/*z* (rel int) 494 $[M]^+$ (0.1), 407 $[M - OCOCHMe_2]^+$ (11), 294 (3), 234 (19), 206 (5), 188 (11), 159 (13), 113 [side chain at C-9]$^+$ (100), 105 (7), 91 (7), 83 (17), 69 (67), 67 (12), 55 (21), 43 (57), 41 (13); *anal*. C 63.26%, H 7.62%, calcd for $C_{26}H_{38}O_9$, C 63.14%, H 7.75%.

Scupolin H (10), (11*S*,13*S*,16*S*,19*S*)-6α-acetoxy-2α,19;4α,18;11,16;15,16-tetraepoxy-19-methoxyneoclerod-14-ene: mp 204−207 °C (EtOAc−*n*-hexane); $[\alpha]^{19}_D$−30.2° (*c* 0.126, $CHCl_3$); IR (KBr) ν_{max} 3110, 1620

(vinyl ether), 3040 (oxirane), 1730, 1250 (OAc), 2960, 1450, 1370, 1100, 1090, 1080, 1020, 990, 950, 905, 875, 780, 750 cm^{-1}; ^1H NMR (200 MHz), see Table 3; ^{13}C NMR (50.3 MHz), see Table 2; EIMS (70 eV, direct inlet) *m/z* (rel int) 420 $[M]^+$ (0.7), 389 $[M - MeO]^+$ (3), 388 $[M - MeOH]^+$ (4), 300 (3), 288 (5), 249 (3), 218 (7), 207 (6), 201 (7), 190 (51), 189 (29), 175 (28), 173 (30), 172 (33), 171 (26), 161 (27), 159 (31), 157 (36), 145 (22), 119 (26), 111 [side chain at C-9]$^+$ (90), 105 (25), 91 (32), 83 (27), 69 (32), 55 (50), 43 (100), 41 (22); *anal*. C 65.61%, H 7.83%, calcd for $C_{23}H_{32}O_7$, C 65.69%, H 7.67%.

Scupolin I (11), (11*S*,13*S*,15*R*,16*R*,19*S*)-6α-acetoxy-2α,19;4α,18;11,16;15,16-tetraepoxy-15,19-dimethoxyneoclerodane: mp 195−198 °C (EtOAc−*n*-hexane); $[\alpha]^{19}_D$−36.3° (*c* 0.108, $CHCl_3$); IR (KBr) ν_{max} 3040 (oxirane), 1720, 1250 (OAc), 2950, 1450, 1370, 1220, 1190, 1150, 1100, 1090, 1060, 1020, 990, 950, 900, 825, 790 cm^{-1}; ^1H NMR (200 MHz), see Table 3; ^{13}C NMR (50.3 MHz), see Table 2; EIMS (70 eV, direct inlet) *m/z* (rel int) 452 $[M]^+$ (0.05), 421 $[M - MeO]^+$ (3), 420 $[M - MeOH]^+$ (3), 392 $[M - AcOH]^+$ (0.3), 360 $[M - AcOH - MeOH]^+$ (0.5), 232 (1), 218 (3), 190 (10), 189 (6), 172 (12), 143 [side chain at C-9]$^+$ (30), 111 [C-9 side chain − MeOH]$^+$ (100), 91 (8), 83 (13), 71 (9), 55 (13), 43 (25), 41 (18); *anal*. C 63.59%, H 7.91%, calcd for $C_{24}H_{36}O_8$, C 63.70%, H 8.02%.

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References and Notes

(1) Although the hydrocarbon skeleton of these diterpenoids is biogenetically derived from an *ent*-labdane, and they should be named *ent*-clerodanes, we prefer to use the term "neoclerodane" proposed by Rogers et al. (Rogers, D.; Unal, G. G.; Williams, D. J.; Ley, S. V.; Sim, G. A.; Joshi, B. S.; Ravindranath, K. R. *J. Chem. Soc., Chem. Commun*. **1979**, 97−99) because it is the nomenclature used in the majority of the articles published on this subject since 1979.
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(28) Compound **11** was purified by crystallization (see Experimental Section), and the ^1H-NMR spectrum of the material remaining in the mother liquors (9 mg) showed minute amounts (∼5%, measured from the ^1H-NMR spectrum) of the 15α-methoxy epimer[10,18,19] of **11**, although it was homogeneous on TLC. The scarcity of the sample available precluded the complete characterization of this substance.

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