Sesquiterpene Coumarins and Related Derivatives from *Ferula pallida*

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Six new compounds—two sesquiterpene coumarins, pallidones A and B (**1**, **2**), and four related derivatives, pallidones C−F (**3**−**6**), as well as two known sesquiterpene coumarins, feselol (**7**) and conferol (**8**), have been isolated from the EtOAc extracts of the roots of *Ferula pallida*. All structures of these compounds were determined on the basis of spectral evidence, especially 2D NMR (^{1}H−^{1}H COSY, HSQC, HMBC, and NOESY) and HRMS. The possible biosynthetic pathway of pallidones C−F (**3**−**6**) is discussed.

The chemical constituents of the genus *Ferula* (Umbelliferae) have been studied by many groups in the past. Compounds commonly found in this genus are sesquiterpenes[1−6] (especially daucanes, humulanes, himachalanes, and guaianes) and sesquiterpene coumarins.[7] A recent chemical study of *F. sinaica* also showed the main components to be sesquiterpene coumarins and sesquiterpenes.[8] Here we wish to report the isolation and structure elucidation of six new compounds: two sesquiterpene coumarins, pallidones A (**1**) and B (**2**), and four related sesquiterpene derivatives, pallidones C−F (**3**−**6**) (Chart 1), along with the two known sesquiterpene coumarins, feselol (**7**) and conferol (**8**) (Chart 2). A possible biosynthetic pathway for pallidones C−F (**3**−**6**) is also discussed.

Results and Discussion

The EtOAc extracts (55 g) of the roots of *F. pallida* (1.6 kg) were separated using repeated Si gel column chromatography, HPLC, and gel permeation chromatography (GPC) to give compounds **1**−**8**.

Compound **1** was obtained as a colorless oil. The EIMS showed a molecular ion peak at *m*/*z* 412, which, together with its ^{1}H, and ^{13}C NMR, and DEPT (Table 1) spectral data, suggested a molecular formula of $C_{25}H_{32}O_5$. This was supported by HREIMS (*m*/*z* 412.2273). The ^{1}H NMR spectral data of **1** showed the presence of a 1,2,4-trisubstituted benzene ring at δ_H 7.63 (1H, d, J = 8.8 Hz, H-5), 6.82 (1H, dd, J = 8.8, 2.2 Hz, H-6), 6.76 (1H, d, J = 2.2 Hz, H-8), a methoxy group at δ_H 3.85, and other signals characteristic of the sesquiterpene unit, which were determined on the basis of the correlations of ^{1}H−^{1}H COSY, HSQC, HMBC, and NOESY NMR spectra. The remaining ^{1}H and ^{13}C NMR data of **1**, except for those of the sesquiterpene unit, showed it to be a 7-oxygen-substituted coumarin compound. The correlations of δ_H 3.85 (OMe) with δ_C 164.0 (C-7), 112.1 (C-6), and 100.2 (C-8) in the HMBC spectrum, and the correlations of δ_H 3.85 (OMe) with δ_H 6.82 (H-6) and 6.76 (H-8) in the NOESY spectrum, suggested the methoxy group was connected to C-7.

In the HMBC spectrum of **1**, the correlations of δ_H 3.78 (H-1′) with δ_C 167.0 (C-2), 104.3 (C-3), 162.8 (C-4), 140.5 (C-2′), and 126.0 (C-3′); δ_H 1.34 (H-15′) with δ_C 104.3 (C-3) and 140.5 (C-2′); and δ_H 7.66 (OH) with δ_C 104.3 (C-3), 162.8 (C-4), and 109.4 (C-10) confirmed that the sesquiterpene unit is connected to C-3 of the coumarin unit and that a hydroxy group is connected to C-4. The chemical shifts of C-3 and C-4 are very close to those reported for similar compounds previously isolated from *F. communis*.[9] The configurations of the two double bonds of the sesquiterpene unit were determined as 2′*E* and 6′*Z* based on the ^{13}C NMR spectral data (δ_C 25.4, C-13′; δ_C 16.9, C-14′).[10−12] These configurations were verified by the observed correlations of δ_H 6.11 (H-7′) with δ_H 1.91 (H-13′), δ_H 2.73 (H-4′) with δ_H 1.74 (H-14′), and δ_H 5.83 (H-3′) with δ_H 3.78 (H-1′) in NOESY spectrum of **1**. The ^{1}H and ^{13}C NMR spectral assignments were made using ^{1}H−^{1}H COSY, HSQC, and HMBC NMR data. Thus, the structure of **1** has been determined as shown and given the name pallidone A.

Table 1. NMR Spectral Data of Compounds **1** and **2** (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, δ, ppm)[a]

	compound **1**		compound **2**	
no.	H	C	H	C
2		167.0 s		165.6 s
3		104.3 s		106.1 s
4		162.8 s		160.6 s
5	7.63, d (8.8)[b]	124.0 d	7.54, d (9.3)	123.8 d
6	6.82, dd (8.8, 2.2)	112.1 d	6.82−6.84, m	112.3 d
7		164.0 s		163.3 s
8	6.76, d (2.2)	100.2 d	6.82−6.84, m	100.7 d
9		154.4 s		157.0 s
10		109.4 s		106.2 s
1′	3.78, q (6.9)	34.0 d	4.86, q (6.6)	89.7 d
2′		140.5 s		47.1 s
3′	5.83, t (6.8)	126.0 d	1.69, m; 1.91, m	38.0 t
4′	2.73, m	26.6 t	1.95, m	23.7 t
5′	2.68, 2.75, m	23.1 t	5.24, t (6.7)	129.6 d
6′		157.2 s		129.0 s
7′	6.11, s	125.0 d	2.97, br s	54.4 t
8′		200.8 s		209.4 s
9′	2.29, d (6.8)	53.6 t	2.27, d (6.7)	50.7 t
10′	2.34, m	25.2 d	2.25, m	24.5 d
11′	0.92, d (6.6)	22.7 q	0.88, d (6.7)	22.6 q
12′	0.92, d (6.6)	22.7 q	0.88, d (6.7)	22.6 q
13′	1.91, s	25.4 q	1.57, s	16.4 q
14′	1.74, s	16.9 q	1.29, s	19.3 q
15′	1.34, d (6.9)	16.2 q	1.45, d (6.6)	15.8 q
−OH	7.66, s			
OMe	3.85, s	55.8 q		55.8 q

[a] $CDCl_3$ as solvents, TMS as internal standard. [b] Figures in parentheses are coupling constants in Hz.

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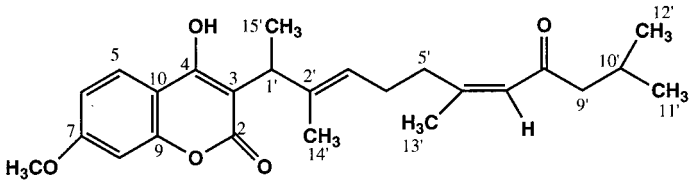
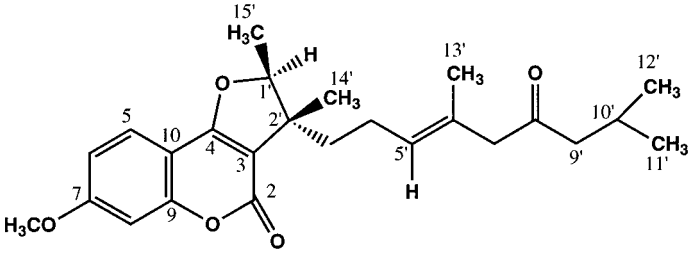
Chart 1



1



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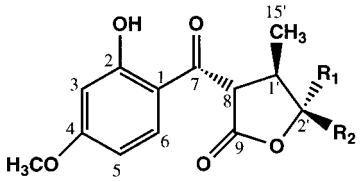
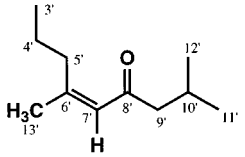
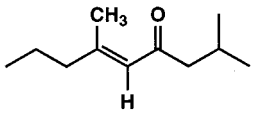
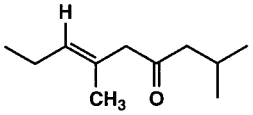
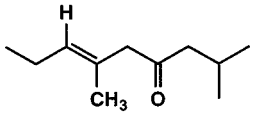


Compound	R_1	R_2
3	CH_3	
4		CH_3
5	CH_3	
6		CH_3

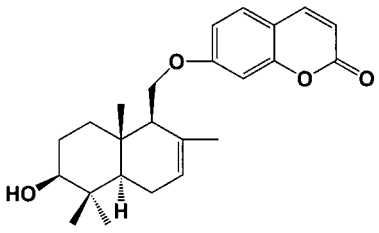
Compound **2** was obtained as a colorless oil. The ^1H and ^{13}C NMR spectral data (Table 1) of **2** were similar to those of **1**. HREIMS of **2** gave a molecular ion peak at *m*/*z* 412.2233, consistent with the same molecular formula ($C_{25}H_{32}O_5$) as **1**. The differences evident between **1** and **2** were signals assigned to the sesquiterpene units. The ^1H and ^{13}C NMR data showed that the sesquiterpene unit of **2** contained only one double bond, compared with two double bonds present in the sesquiterpene unit of **1**, thus suggesting the presence of an additional ring in compound **2**. Furthermore, the chemical shifts of the carbonyl carbon (δ_C 209.4) and the double bond (δ_C 129.6, 129.0) in **2** indicated that the double bond is not conjugated with the carbonyl group. Additionally, the ^1H and ^{13}C NMR spectral data of **2** showed signals for another carbonyl α-methylene (δ_H 2.97, br s, H-7′, 2H; δ_C 54.4, C-7′, CH_2), which was confirmed by correlations observed in the HMBC spectrum of **2**: δ_H 1.45 (H-15′) with δ_C 89.7 (C-1′) and 47.1 (C-2′) and δ_H 1.29 (H-14′) with δ_C 89.7 (C-1′), 47.1 (C-2′), 38.0 (C-3′), and 106.1 (C-3). These correlations suggested C-2′ is connected to C-3. That C-1′ is connected to C-4 by an ether bond can be deduced according to the unsaturation value and the chemical shifts of C-1′ (δ_C 89.7) and C-4 (δ_C 160.6). The relative stereochemistry of C-1′ and C-2′ were determined as 1′*S** and 2′*R** on the basis of observed correlations between δ_H 4.86 (H-1′) and δ_H 1.69 and 1.91 (H-3′) and between δ_H 1.45 (H-15′) and δ_H 1.29 (H-14′) in the NOESY spectrum of **2**. The configuration of the double bond of the sesquiterpene unit was assigned as 5′*E* on the basis of the chemical shift of C-13′, which is at relatively higher field (δ_C 16.4).[10−12] Compound **2** is named pallidone B, and the structure has been determined as shown.

Table 2. ^{1}H NMR Spectral Data of Compounds **3**−**6** (400 MHz, δ, ppm)[a]

H	3	4	5	6
3	6.45, d (2.4)	6.44, d (2.4)	6.45, d (2.4)	6.46, d (2.4)
5	6.52, dd (9.0, 2.4)	6.51, dd (9.0, 2.4)	6.52, dd (9.0, 2.4)	6.52, dd (9.0, 2.4)
6	7.72, d (9.0)	7.68, d (9.0)	7.70, d (9.0)	7.69, d (9.0)
8	4.28, d (12.0)	4.24, d (11.8)	4.26, d (12.0)	4.25, d (12.0)
1′	3.10, dq (12.0, 6.8)	3.11, dq (11.8, 6.8)	3.12, dq (12.0, 6.8)	3.16, dq (12.0, 6.8)
3′	1.58−1.72, m	1.66, m	1.63, m	1.79−1.87, m
4′	1.58−1.72, m	1.70, m	2.26, m	2.26, m
5′	2.48, m; 2.78, m	2.16, m	5.25, t (6.4)	5.25, t (6.4)
7′	6.10, s	6.06, s	3.06, s	3.04, s
9′	2.30, d (6.8)	2.30, d (6.8)	2.31, d (6.8)	2.31, d (6.8)
10′	2.14, m	2.13, m	2.15, m	2.14, m
11′, 12′	0.94, d (6.6)	0.93, d (6.6)	0.93, d (6.6)	0.92, d (6.6)
13′	1.90, s	2.14, s	1.66, s	1.65, s
14′	1.50, s	1.34, s	1.53, s	1.36, s
15′	1.08, d (6.8)	1.07, d (6.8)	1.09, d (6.8)	1.08, d (6.8)
Ar−OH	12.47, s	12.44, s	12.46, s	12.46, s
OMe	3.87, s	3.88, s	3.87, s	3.86, s

[a] $CDCl_3$ as solvents, TMS as internal standard. [b] Figures in parentheses are coupling constants in Hz.

Chart 2



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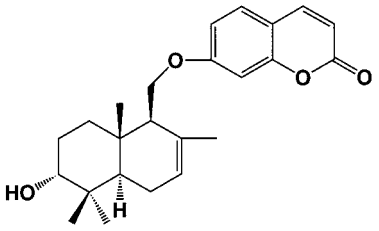

8

Compound **3** was obtained as a colorless oil. The HRE-IMS showed the molecular ion peak at *m*/*z* 430.2386, which suggested a molecular formula of $C_{25}H_{34}O_6$. The ^{1}H NMR spectral data (Table 2) of **3** showed the presence of a 1,2,4-trisubstituted benzene ring at δ_H 6.45 (^{1}H, d, J = 2.4 Hz, H-3), 6.52 (1H, dd, J = 9.0, 2.4 Hz, H-5), and 7.72 (1H, d, J = 9.0 Hz, H-6); a methoxy group at δ_H 3.87; a chelated phenolic hydroxyl group at δ_H 12.47 (Ar−OH); and other signals due to a sesquiterpene unit, which were similar to those of compounds **1** and **2**. The ^{13}C NMR spectral data (Table 3) were in good agreement with the above analysis, showing three carbonyl groups (δ_C 196.2, C-7; δ_C 171.3, C-9; δ_C 200.9, C-8′), two of which (C-7 and C-8′) were keto carbonyl groups conjugated with the aromatic ring and the double bond and the other (C-9), an ester carbonyl group, based on its chemical shift. These were confirmed by the observed correlations in HMBC spectrum.

After determination of the structure of the sesquiterpene unit on the basis of the correlations of ^{1}H−^{1}H COSY, HSQC, HMBC, and NOESY NMR spectra, there remained only 10 carbon signals to be assigned. These remaining signals could be attributed to an aromatic ring, two carbonyl groups (C-7 and C-9), a methine (C-8), and a methoxy group. The HMBC correlations of δ_H 3.87 (OMe) with δ_C 167.0 (C-4), 101.0 (C-3), and 108.4 (C-5); δ_H 7.72 (H-6) with δ_C 167.0 (C-4), 166.4 (C-2), and 196.2 (C-7); and

Table 3. ^{13}C NMR and DEPT Spectral Data of Compounds **3**−**6** (100 MHz, δ, ppm)[a]

C	3	4	5	6
1	114.1 s	113.9 s	114.0 s	114.0 s
2	166.4 s	166.3 s	166.3 s	166.4 s
3	101.0 d	100.9 d	101.0 d	101.0 d
4	167.0 s	167.1 s	167.1 s	167.1 s
5	108.4 d	108.5 d	108.5 d	108.4 d
6	133.2 d	133.0 d	133.1 d	133.0 d
7	196.2 s	195.9 s	196.0 s	196.0 s
8	54.6 d	54.5 d	54.5 d	54.6 d
9	171.3 s	171.0 s	171.1 s	171.1 s
1′	44.2 d	41.4 d	44.1 d	41.3 d
2′	87.7 s	87.6 s	87.4 s	87.7 s
3′	35.2 t	39.2 t	35.2 t	39.4 t
4′	22.2 t	21.6 t	22.3 t	22.6 t
5′	33.8 t	41.0 t	128.3 d	128.2 d
6′	158.1 s	157.0 s	130.4 s	130.2 s
7′	124.7 d	124.1 d	54.1 t	54.3 t
8′	200.9 s	201.4 s	209.3 s	209.3 s
9′	53.7 t	53.6 t	51.2 t	50.9 t
10′	25.2 d	25.2 d	24.6 d	24.6 d
11′	22.7 q	22.7 q	22.7 q	22.6 q
12′	22.7 q	22.7 q	22.7 q	22.6 q
13′	25.4 q	19.2 q	16.7 q	16.6q
14′	24.1 q	20.6 q	23.8 q	20.7 q
15′	12.8 q	13.5 q	12.8 q	13.5 q
OMe	55.8 q	55.8 q	55.8 q	55.8 q

[a] $CDCl_3$ as solvents, TMS as internal standard.

δ_H 12.47 (Ar−OH) with δ_C 114.1 (C-1), 166.4 (C-2), and 101.1 (C-3), and the NOESY correlations of δ_H 3.87 (OMe) with δ_H 6.45 (H-3) and 6.52 (H-5) suggested that the methoxy and the hydroxy groups were connected to C-4 and C-2, respectively, and the carbonyl group at δ_C 196.2 (C-7) was conjugated with the aromatic ring. In the ^{1}H−^{1}H COSY spectrum of **3**, H-8 (δ_H 4.28, d, J = 12.0 Hz, 1H) was strongly correlated with H-1′ (δ_H 3.10, dq, J = 12.0, 6.8 Hz, 1H), and when considered in combination with the observed HMBC correlations of δ_H 3.10 (H-1′) with δ_C 196.2 (C-7), 54.6 (C-8), and 171.3 (C-9) and δ_H 1.08 (H-15′) with δ_C 54.6 (C-8) and 87.7 (C-2′), verified that C-1′ was connected to C-8. On the basis of the above analysis and the chemical shifts of C-9 and C-2′, the ester group of C-9 must be connected to C-2′. This linkage was supported by the HMBC correlations of δ_H 3.10 (H-1′) with δ_C 196.2 (C-7), 54.6 (C-8), and 171.3 (C-9). The configuration of the double bond of the sesquiterpene unit was assigned as 6′-*Z* based on the ^{13}C NMR spectral data (δ_C 25.4, C-13′).[10−12] The relative stereochemistry of H-8 and H-1′ of compound **3** can be deduced as trans, based on the magnitude of the coupling constant ($J_{8,1'}$ = 12.0 Hz). Furthermore, in the

NOESY spectrum of **3**, δ_H 4.28 (H-8) correlated with δ_H 1.58−1.72 (H-3′) and 1.08 (H-15′) and δ_H 3.10 (H-1′) correlated with δ_H 1.50 (H-14′), supporting the relative stereochemistry of compound **3** as 8*S**, 1′*R**, and 2′*R**. The complete ^{1}H and ^{13}C NMR spectral data were assigned using correlations in the ^{1}H−^{1}H COSY, NOESY, HSQC, and HMBC spectra. Thus, the structure of **3** has been determined as shown, and named pallidone C.

Compound **4**, obtained as a colorless oil. Its ^{1}H (Table 2) and ^{13}C NMR (Table 3) spectral data were very similar to those of compound **3**. HREIMS gave the molecular ion peak at *m*/*z* 430.2379, suggesting a molecular formula of $C_{25}H_{34}O_6$, the same as that of **3**. The differences in the ^{13}C NMR spectral data between compounds **3** and **4** are the chemical shifts of C-1′, C-3′, C-5′, C-13′, and C-14′ (Table 3).

The chemical shifts of C-5′ (δ_C 41.0 for **4**, 33.8 for **3**) and C-13′ (δ_C 19.2 for **4**, 25.4 for **3**) of compound **4** are downfield and upfield, respectively relative to those of compound **3**. This suggested that the double bond of the sesquiterpene unit of compound **4** is of the *E* configuration.[10−12] As in compound **3**, H-8 and H-1′ of compound **4** are in trans relationship ($J_{8,1'}$ = 11.8 Hz). Thus, the differences in the chemical shifts of C-1′, C-3′, and C-14′ in compounds **3** and **4** may be the result of the different configurations of C-3′ in two compounds. In the NOESY spectrum of compound **4**, clear correlations of δ_H 4.24 (H-8) with δ_H 1.34 (H-14′) and 1.07 (H-15′) and δ_H 3.11 (H-1′) with δ_H 1.66 (H-3′) suggested the relative stereochemistry of compound **4** as 8*S**, 1′*R**, and 2′*S**. Therefore, **4** is an isomer of **3**. 2D NMR correlations (^{1}H−^{1}H COSY, NOESY, HSQC, and HMBC) were used to assign the ^{1}H and ^{13}C NMR data and confirm the structure of **4**, which is named pallidone D.

Compound **5**, obtained as a colorless oil, shows ^{1}H (Table 2) and ^{13}C NMR (Table 3) spectral data nearly identical with those of compound **3**. HREIMS (*m*/*z* 430.2379) indicated the molecular formula of $C_{25}H_{34}O_6$, the same as for **3** and **4**. The chemical shift of C-8′ of compound **5** is significantly downfield in comparison with that of compound **3** (**5**, δ_C 209.3; **3**, δ_C 200.9), as was the case for the sesquiterpene unit of compound **2**. This verified that the double bond was not conjugated with the carbonyl group in compound **5**. Furthermore, the ^{1}H and ^{13}C NMR spectral data of **5** displayed signals for a second carbonyl α-methylene (δ_H 3.06, s, H-7′, 2H; δ_C 54.1, C-7′, CH_2) in addition to C-9′. The existence of two α-methylenes (C-7′ and C-9′) in **5** was also confirmed by the DEPT spectrum and HSQC and HMBC correlations. The double bond is proposed to be of the *E* configuration based on the chemical shifts of C-4′ (δ_C 22.3) and C-13′ (δ_C 16.7).[10−12] The relative configuration has been determined as 8*S**, 1′*R**, and 2′*R** by comparison of the ^{13}C NMR spectral data with those of compound **3** and confirmed by the correlations observed in the NOESY spectrum. Thus, the structure of pallidone E has been identified as shown in **5**.

Compound **6**, obtained as a colorless oil, has ^{1}H (Table 2) and ^{13}C NMR (Table 3) spectral data nearly identical with those of compound **5**. HREIMS also gave the molecular formula $C_{25}H_{34}O_6$. The double bond is of the *E* configuration based on the chemical shifts of C-4′ (δ_C 22.6) and C-13′ (δ_C 16.6).[10−12] The main differences between compounds **5** and **6** are the chemical shifts of C-1′, C-3′, C-14′, and C-15′ (Table 3), which, in compound **6**, are almost identical with those of compound **4**, while in compound **5** are similar to those in compound **3**. Hence, the relative configuration of compound **6** has been determined as 8*S**, 1′*R**, and 2′*S** and confirmed by the correlations observed in the NOESY spectrum. Thus, the structure of pallidone F has been identified as shown in **6**.

Table 4. NMR Spectral Data of Compounds **7** and **8** (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, δ, ppm)

	compound **8**		compound **7**	
no.	H	C	H	C
2		161.3 s		161.3 s
3	6.25, d (9.4)	113.1 d	6.23, d (9.5)	113.2 d
4	7.63, d (9.4)	143.5 d	7.63, d (9.5)	143.5 d
5	7.26, d (8.3)	132.4 d	7.36, d (8.3)	132.5 d
6	6.83, dd (8.3, 2.0)	113.2 d	6.83, dd (8.3, 2.1)	112.9 d
7		162.1 s		162.1 s
8	6.81, d (2.0)	101.4 d	6.81, d (2.1)	101.4 d
9		156.0 s		155.9 s
10		112.6 s		112.5 s
1′	2.01, m; 1.35, dd (8.8, 5.7)	37.9 t	1.66, m	31.8 t
2′	1.67, m	27.4 t	1.95, m; 1.63, m	25.2 t
3′	3.29, dd (10.8, 4.8)	78.9 d	3.47, brs	75.7 d
4′		38.8 s		37.2 s
5′	1.28, dd (10.9, 5.5)	49.5 d	1.71, m	43.4 d
6′	2.10, m	23.4 t	1.97, m	23.2 t
7′	5.56, br s	128.8 d	5.45, br s	128.7 d
8′		132.4 s		132.5 s
9′	2.23, br s	53.9 d	2.32, br s	53.5 d
10′		35.9 s		35.6 s
11′	4.17, dd (9.6, 3.3); 4.02, dd (9.6, 5.9)	67.1 t	4.17, dd (9.7, 3.3); 4.02, dd (9.7, 5.9)	67.1 t
12′	1.70, br s	21.7 q	1.70, br s	21.8 q
13′	1.01, s	28.1 q	0.97, s	28.1 q
14′	0.90, s	15.3 q	0.93, s	22.4 q
15′	0.91, s	14.9 q	0.92, s	14.8 q

[a] $CDCl_3$ as solvents, TMS as internal standard. [b] Figures in parentheses are coupling constants in Hz.

Two known isomeric sesquiterpene coumarins, feselol (**7**)[13−15] and conferol (**8**)[14−16] were also isolated. Although they have been reported several times from the *Ferula* genus, their full NMR spectral data have not been previously reported and are reported herein (Table 4).

Structures of the type seen in pallidones C−F (**3**−**6**) are rare in nature. Many previous studies on the genus *Ferula* have verified that sesquiterpenes and coumarins are the main components of this genus. It is interesting to note that pallidones C−F were isolated along with sesquiterpene coumarin derivatives (**1**, **2**, **7**, **8**) from this species. We believe that both these sesquiterpene coumarin derivatives (**1**, **2**, **7**, **8**) and pallidones C−F (**3**−**6**) could be derived from a common biosynthetic precursor, 2-hydroxy-4-methoxycinnamic acid, which combines with the appropriate sesquiterpenes via the following possible pathway (Figure 1).

Experimental Section

General Experimental Procedures. NMR (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, both using TMS as internal standard) were measured on a Bruker AM 400 spectrometer, and MS spectra were recorded on a JEOL JMSD-300 instrument. Column chromatography: Si gel 60 (Merck); HPLC: GPC (Shodex H-2001, 2002, $CHCl_3$), Si gel (Si 60, Hibar RT 250−25). IR spectra were recorded on a 1720 infrared Fourier transform spectrometer (Perkin-Elmer), UV spectra on a UV2100 UV−Vis recording spectrometer (Shimadzu). Optical rotations were measured with a JASCO DIP-370 digital polarimeter.

Plant Material. The roots of *Ferula pallida* (1.6 kg, dried wt) were collected in Uzbekistan, in August 1997, and identified by Dr. Olimjon K. Kodzhimatov. A voucher specimen is preserved at the Herbarium of Institute of Botany, Academy of Sciences, Uzbekistan.

Extraction and Isolation of Compounds. The powdered, air-dried roots (1.6 kg) of *F. pallida* were extracted three times

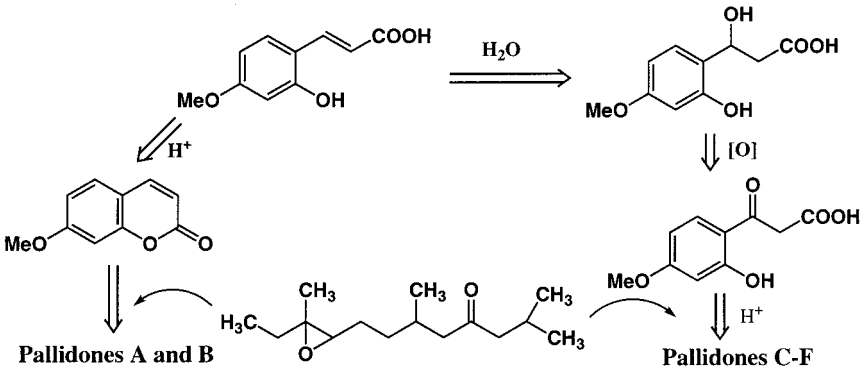

Figure 1.

with *n*-hexane (7 L), EtOAc (7 L), and MeOH (7 L) at a temperature of about 60 °C, 24 h each time.

The EtOAc extract (55 g) was chromatographed over a Si gel column (10 × 50 cm, Merck Si gel 60, 1.2 kg) and eluted with *n*-hexanes−EtOAc (10:1 to 1:1), then with pure EtOAc. Ten fractions were obtained. Fraction 1 (1.1 g) was purified by GPC ($CHCl_3$), then HPLC (silica, hexanes−EtOAc, 6:1), to give compounds **1** (31 mg), **2** (22 mg), and **3** (7 mg). Fraction 5 (300 mg) was separated by HPLC (silica, hexanes−EtOAc, 6:1), and 14 fractions (fractions 5.01−5.14) were obtained. Fractions 5.02, 5.05, 5.06, and 5.14 were purified by GPC ($CHCl_3$) to give compounds **5** (10 mg), **6** (18 mg), **4** (17 mg), and **7** (52 mg). Fraction 7 (400 mg) was separated by HPLC (silica, hexanes−EtOAc, 3:1) to give 13 fractions (fractions 7.01−7.13), and compound **8** (15 mg) was obtained after the purification of fraction 7.12 by GPC ($CHCl_3$).

Pallidone A (1): obtained as a colorless oil; $[\alpha]^{25}_D$ +14.90° (*c* 0.95, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 241 (4.11), 286 (2.79), 315 (3.98) nm; IR ($CHCl_3$) ν_{max} 3334, 3033, 2963, 1693, 1620, 1514, 1428, 1368, 1275, 1196, 1160, 1029, 840, 695 cm^{-1}; EIMS *m/z* (rel int) 412 $[M]^+$ (8.1), 394 (13.7), 355 (10.1), 327 (11.2), 313 (8.3), 274 (44.9), 273 (100), 259 (18.3), 257 (36.9), 245 (98.2), 231 (45.5), 220 (48.3), 219 (98), 217 (28.8), 205 (77.1), 193 (75.0), 187 (22.9), 175 (17.6), 163 (20.7), 151 (94.6), 137 (25.5), 135 (38.6), 122 (53.8), 121 (27.8), 109 (36.9), 107 (46.0), 95 (85), 79 (59), 67 (54.9), 57 (97.3), 43 (97.5), 41 (97.3); HREIMS *m/z* 412.2273 (calcd for $C_{25}H_{32}O_5$, 412.2250); ^1H and ^{13}C NMR and DEPT data, see Table 1.

Pallidone B (2): obtained as a colorless oil; $[\alpha]^{25}_D$ +39.70° (*c* 1.12, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 242 (3.78), 286 (2.85), 319 (3.96) nm; IR ($CHCl_3$) ν_{max} 3025, 2962, 2873, 1708, 1636, 1615, 1562, 1520, 1451, 1417, 1386, 1334, 1274, 1159, 1103, 1030, 989, 842 cm^{-1}; EIMS *m/z* (rel int) 412 $[M]^+$ (16.4), 193 (37.8), 355 (7.9), 259 (7.3), 247 (54.4), 246 (97.4), 245 (93.7), 231 (81.5), 217 (44.9), 205 (25.7), 189 (33.1), 158 (33.1), 151 (100), 115 (19.6), 107 (17.6), 95 (21.7), 85 (48.3), 79 (26.7), 67 (26.9), 57 (98.0), 43 (50.8), 41 (97.1); HREIMS *m/z* 412.2233 (calcd for $C_{25}H_{32}O_5$, 412.2250); ^1H and ^{13}C NMR and DEPT data, see Table 1.

Pallidone C (3): obtained as a colorless oil; $[\alpha]^{25}_D$ +28.60° (*c* 0.38, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 241 (4.08), 285 (4.06), 320 (3.82) nm; IR ($CHCl_3$) ν_{max} 3025, 2957, 2359, 1736, 1678, 1627, 1510, 1466, 1370, 1275, 1231, 1201, 1126, 963, 796, 751 cm^{-1}; EIMS *m/z* (rel int) 430 $[M]^+$ (14.6), 373 (6.0), 355 (5.1), 273 (4.8), 263 (7.1), 247 (4.6), 246 (25.0), 245 (22.1), 221 (6.1), 205 (10.1), 192 (17.9), 177 (20.4), 152 (26.0), 151 (100), 135 (16.8), 109 (17.0), 108 (21.2), 95 (57.3), 85 (16.5), 69 (25.0), 57 (33.7), 43 (37.8), 41 (39.6); HREIMS *m/z* 430.2386 (calcd for $C_{25}H_{34}O_6$, 430.2355); ^1H NMR data, see Table 2; ^{13}C NMR and DEPT, data see Table 3.

Pallidone D (4): obtained as a colorless oil; $[\alpha]^{25}_D$ +11.90° (*c* 0.75, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 241 (3.75), 285 (4.04), 320 (3.76) nm; IR ($CHCl_3$) ν_{max} 3030, 3013, 2960, 1766, 1682, 1626, 1510, 1466, 1444, 1370, 1273, 1230, 1201, 1158, 1126, 1057, 1031, 964, 910, 843, 796 cm^{-1}; EIMS *m/z* (rel int) 430 $[M]^+$ (49.8), 373 (40.3), 345 (25.7), 327 (14.6), 291 (9.9), 279 (7.7), 273 (24.9), 245 (16.4), 221 (32.6), 210 (68.2), 192 (85.6), 177 (78.5), 163 (24.0), 152 (92.8), 151 (87.1), 135 (100), 124 (37.8), 121 (33.6), 109 (40.9), 108 (82.1), 107 (60.4), 95 (96.8), 93 (47.6), 85 (56.9), 82 (50.5), 79 (46.9), 69 (95.2), 67 (92.0), 57 (95.5), 43 (95.8), 41 (94.6); HREIMS *m/z* 430.2379 (calcd for $C_{25}H_{34}O_6$, 430.2355); ^1H NMR data, see Table 2; ^{13}C NMR and DEPT data, see Table 3.

Pallidone E (5): obtained as a colorless oil; $[\alpha]^{25}_D$ +29.50° (*c* 0.94, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 241 (3.85), 285 (3.82), 320 (3.62) nm; IR ($CHCl_3$) ν_{max} 3031, 3025, 2962, 2360, 1766, 1709, 1627, 1510, 1465, 1444, 1371, 1275, 12311201, 1126, 1071, 1030, 964, 796 cm^{-1}; EIMS *m/z* (rel int) 430 $[M]^+$ (7.5), 346 (7.8), 345 (6.4), 329 (6.8), 263 (7.9), 262 (11.9), 245 (5.9), 219 (6.8), 192 (10.0), 151 (100), 136 (17.9), 135 (11.4), 108 (20.3), 107 (11.5), 95 (22.1), 85 (59.8), 69 (16.6), 57 (95.9), 43 (32.6), 41 (57.0); HREIMS *m/z* 430.2379 (calcd for $C_{25}H_{34}O_6$, 430.2355); ^1H NMR data, see Table 2; ^{13}C NMR and DEPT data, see Table 3.

Pallidone F (6): obtained as a colorless oil; $[\alpha]^{25}_D$ +12.60° (*c* 1.04, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 241 (3.99), 285 (3.92), 320 (3.72) nm; IR ($CHCl_3$) ν_{max} 2960, 1766, 1708, 1627, 1510, 1465, 1371, 1275, 1230, 1214, 1201, 1072, 1017 cm^{-1}; EIMS *m/z* (rel int) 430 $[M]^+$ (7.4), 373 (6.3), 345 (4.2), 245 (3.4), 221 (3.6), 210 (10.0), 177 (13.0), 151 (100), 135 (19.7), 108 (10.1), 95 (37.7), 69 (11.0), 67 (11.5), 57 (13.2), 43 (19.6), 41 (17.9); HREIMS *m/z* 430.2377 (calcd for $C_{25}H_{34}O_6$, 430.2355); ^1H NMR data, see Table 2; ^{13}C NMR and DEPT data, see Table 3.

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