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CHEMICAL CONSTITUENTS OF *FERULAGO NODOSA*

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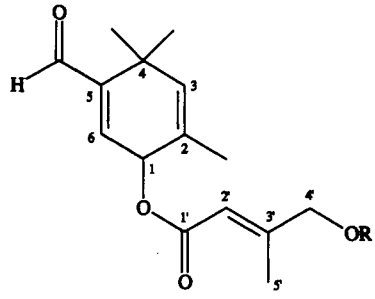
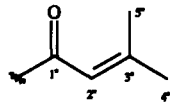
ABSTRACT.—A CH_2Cl_2 extract of the aerial parts of *Ferulago nodosa* yielded one new and two known derivatives of ferulol, as well as the coumarin ester grandivittin, and a C_{18} polyacetylenic metabolite. The structure of the new metabolite was established by spectral methods, while the identity of the known compounds was ascertained by comparison of their physical properties with those reported in the literature.

The genus *Ferulago* (1) of the family Umbelliferae, which is closely related to the more extensively studied *Ferula,* has been the subject of scant phytochemical investigations, resulting only in the isolation of coumarins, sesquiterpenes, and aromatic compounds (2–5). As part of our continuing study on the chemical constituents of Sicilian flora we have examined the lipid extract of *Ferulago nodosa* (L.) Boiss., a species indigenous to the Aegean and Balkan regions but also found in Italy in a restricted area of southern Sicily (6,7), and report here the results obtained.



1 R=H
2 R=$COCH_3$

3 R=



The CH_2Cl_2 extract of the aerial parts of *F. nodosa* was chromatographed on a Si gel column using as eluent increasing concentrations of Et_2O in hexane. Further purification of the main fractions by prep. layer chromatography yielded five pure compounds, **1–5**.

Two of the metabolites were identified, on the basis of the comparison of their spectral properties with the data reported in literature, as **1** and **2**, compounds isolated previously from other species of the Umbelliferae (8–10).

The major metabolite, **3**, comprising ca. 4% of the organic extract, was isolated as a yellow, optically active oil ($[\alpha]^{20}D$ +60°). Its spectral data (Experimental and Table 1) indicated that **3** is the 4′-*O*-senecioate of **1**, since in the ^{13}C-nmr spectrum, in addition to signals closely comparable to all those present in the spectrum of **1**, five resonances were seen for a carbonyl (δ 164.8, C-1″), two olefinic carbons (δ 114.8 and 157.8, C-2″ and C-3″), and two methyls (δ 19.8 and 26.9, C-5″ and C-4″). Definite confirmation was obtained from a complete analysis of the ^1H, COSY, and HETCOR nmr spectra of **3**. Compound **3** is a derivative of ferulol, a monocyclic irregular monoterpene present in several species of the family Umbelliferae, together with many of its analogues (8–14).

The spectral properties of compound **4** showed it to be grandivittin, a coumarin ester previously isolated from *Seseli grandivittatum* and *Eryngium campestris* (15).

Compound **5** was established as octadeca-9(*Z*),17-dien-12,14-diyn-1-

TABLE 1. Nmr Data for Compounds **1–3**.[a]

Position	Compound				
	1	**2**	**3**		
	^{13}C		^{13}C	^{1}H	L/R corr.[b]
1	67.2 d	67.4 d	66.8 d	5.96 d (3.5)	Me-2, H-3
2	125.0 s	125.0 s	124.8 s	—	Me-2, H-6, H-1
3	138.1 d	138.3 d	137.6 d	5.50 br s	Me-2, Me-4a, Me-4b
4	35.0 s	35.1 s	34.6 s	—	Me-4a, Me-4b, H-6, H-3, CHO
5	148.2 d	148.3 d	147.8 s	—	Me-4a, Me-4b, H-1, H-3, CHO
6	144.1 d	143.7 d	143.4 d	6.63 d (3.5)	H-1, CHO
2-Me ..	19.1 q	19.3 q	19.7 q	1.76 br s	H-3
4a-Me .	27.1 q	27.1 q	26.0 q	1.29 s	Me-4b
4b-Me .	26.3 q	26.4 q	26.7 q	1.24 s	Me-4a
CHO ..	193.8 d	193.5 d	193.6 d	9.44 s	H-6
1′.....	166.3 s	165.7 s	165.2 s	—	H-1
2′.....	114.3 d	114.7 d	113.8 d	5.90 m	H-4′, H-5′
3′.....	159.2 s	153.5 s	154.0 s	—	H-4′, H-5
4′.....	66.9 t	67.0 t	65.7 t	4.63 br s	H-5′
5′.....	15.7 q	15.9 q	15.5 q	2.19 d (1)	H-2′, H-4′
1″.....	—	—	164.8 s	—	H-4′
2″.....	—	—	114.8 d	5.75 m	H-4″, H-5″
3″.....	—	—	157.8 s	—	H-4″, H-5″
4″.....	—	—	26.9 q	1.92 d (1)	H-2″, H-5″
5″.....	—	—	19.8 q	2.18 d (1)	H-2″, H-4″
*C*OCH$_3$.	—	170.1 s	—	—	—
COC*H*$_3$	—	20.7 q	—	—	—

[a]^{1}H-Nmr (250.13 MHz) and ^{13}C-nmr (62.9 MHz) spectra were run in $CDCl_3$ (ppm from TMS). ^{13}C multiplicities were obtained by DEPT experiment.

[b]Long-range heteronuclear correlation.

acetoxy-11,16-diol, a known secondary metabolite of *Smyrnium olusatrum* L. (Umbelliferae) (16).

In conclusion, the pattern of the secondary metabolites of *F. nodosa* examined is comparable to that of several plants in the Umbelliferae and, in particular, it shows a strong similarity with those of many *Ferula* species. This implies that a chemotaxonomic differentiation between the genera *Ferula* and *Ferulago* is impractical and lends additional support to doubts concerning their present taxonomic separation (1).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Optical rotations were determined with Perkin-Elmer 141 and Jasco DIP-370 polarimeters using a 10-cm microcell. Mass spectra were determined with a direct inlet system at 70 eV on a Kratos MS-50S instrument. Uv and ir spectra were recorded on Perkin-Elmer model 330 and 684 spectrophotometers, respectively. Nmr spectra were measured on a Bruker AC-250 instrument, operating at 250.13 and 62.9 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts are stated in ppm relative to TMS. Multiplicities of ^{13}C-nmr resonances were determined by DEPT experiments, and 2D nmr experiments were carried out using standard Bruker microprograms. Prep. liquid chromatography was carried out on a Jobin-Yvon Miniprep-LC instrument (LiChroprep Si-60, 25–40 μm as the stationary phase).

PLANT MATERIAL.—*F. nodosa* was collected near Syracuse, Ognina, Sicily, in May 1990. A voucher specimen has been deposited at the Herbarium of the Department of Botany, University of Catania, Catania, Italy.

EXTRACTION AND ISOLATION.—Freeze-dried plant material (90 g) was extracted three times with CH_2Cl_2 at room temperature with continuous stirring, and the extracts were evaporated under reduced pressure. The oily residue (13.2 g) was subjected to chromatography in an open column (3×100 cm) containing Si gel, using a stepwise gradient of Et_2O in C_6H_{14} as the eluent. Fractions of 150 ml were examined by tlc and

appropriately pooled. Fractions 4–5 and 8 gave pure **3** and **2**, respectively. Fraction 17 was subjected to prep. tlc (Florisil, Et_2O) to give pure **1** and **4**, while fraction 19 was purified by prep. tlc [(Si gel, CH_2Cl_2-Et_2O (85:15)] to yield **5**.

Compound **1**.—Oil (58 mg, 0.064% dry wt), $[\alpha]^{20}$ (λ)(nm) +110° (589), +130° (578), +150° (546), +240° (436) (*c*=1, EtOH); ^{13}C-nmr data in Table 1.

Compound **2**.—Oil (0.47 g, 0.53% dry wt), $[\alpha]^{20}$ (λ) (nm) +30° (589), +40° (578), +50° (546), +90° (436) (*c*=1, EtOH); ^{13}C-nmr data in Table 1.

Compound **3**.—Oil (3.58 g, 3.98% dry wt), $[\alpha]^{20}$ (λ) (nm) +60° (589), +80° (578), +100° (546), +146° (436) (*c*=1, EtOH); ir ν max (film) 2715, 1720, 1695, 1655 cm^{-1}; uv λ max (EtOH) 223 nm (ε 37887); hrms 346.1785 $[M]^+$, calcd for $C_{20}H_{26}O_5$ 346.1780; ms *m/z* 346 (2), 248 (5), 233 (3), 221 (2), 205 (7), 199 (7), 181 (6), 166 (14), 149 (72), 135 (36), 121 (30), 99 (14), 83 (25), 75 (100), 73 (19), 57 (60), 43 (31), 41 (26); ^{1}H- and ^{13}C-nmr data in Table 1.

Compound **4**.—Oil (229 mg, 0.25% dry wt). Spectroscopic properties in accordance with published data (15).

Compound **5**.—Oil (22 mg, 0.024% dry wt), $[\alpha]^{20}$ (λ) (nm) +107° (589) (*c*=0.7, EtOH); ^{13}C nmr ($CDCl_3$) δ 64.7 (t, C-1), 28.4 (t, C-2), 25.7 (t, C-3), 28.0 (t, C-4), 28.8 (t, C-5), 29.1 (t, C-6), 29.0 (t, C-7), 27.5 (t, C-8), 134.2 (d, C-9), 127.8 (d, C-10), 58.4 (d, C-11), 79.7 (s, C-12), 68.8 (s, C-13), 70.2 (s, C-14), 78.3 (s, C-15), 63.3 (d, C-16), 135.8 (d, C-17), 117.1 (t, C-18), 171.1 (s, *C*OCH$_3$), 21.0 (q, CO*C*H$_3$).

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