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TERPENOIDS AND A COUMARIN FROM *FERULA SINAICA*

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Key Word Index—*Ferula sinaica*; Umbelliferae; sesquiterpene esters; a coumarin derivative; 3-methoxy-4,5-methylenedioxypropiophenone.

Abstract—A new coumarin has been isolated from the root of *Ferula sinaica*, together with known compounds ferutidin, a sesquiterpene alcohol and 3-methoxy-4,5-methylenedioxypropiophenone. The structures were elucidated mostly by spectroscopic methods.

INTRODUCTION

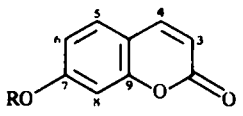
Ferula sinaica (Umbelliferae) is abundant in the Khibar region of Saudi Arabia. No chemical investigations have been reported on this plant, although systematic studies have been carried out on a number of other species of this genus [1]. *Ferula* species are a rich source of coumarins especially umbelliferone (7-hydroxycoumarin) sesquiterpene ethers [2]. We have now isolated the previously known compounds, ferutidin (**4**), the sesquiterpene alcohol **5** and 3-methoxy-4,5-methylenedioxypropiophenone (**6**) and a new coumarin **2** from the benzene extract of the roots of *Ferula sinaica*.

RESULTS AND DISCUSSION

The spectral data suggested that **2**, $C_{29}H_{36}O_6$, is a coumarin, since it gave a UV λ_{max} at 320 nm ($\log \varepsilon$ 4.1) and the IR spectrum showed the presence of a hydroxyl function (3450 and 1120 cm^{-1}) and a strong carbonyl band at 1715 cm^{-1}. However, most evidence for the suggested structure for **2** came from its ^1H NMR spectrum. The low field region of this spectrum showed two pairs of doublets at δ7.63 and 6.23 (J = 9 Hz for both) corresponding to two *ortho*-related protons. Irradiation of each one of the doublets collapsed the other to a singlet. The resonances of these two protons with 1.4 ppm difference in chemical shifts suggested that the two hydrogens were at positions 3 and 4 in a coumarin ring [3]. The ^1H NMR also contained three signals for three aromatic protons, one of them is *meta*-coupled while the other two are *ortho*-coupled protons. The spin decoupling experiments identified the proton at C-6 which in turn is *meta*-coupled to the proton at C-8. From the chemical shifts of the aromatic protons, it is clear that there is 7-oxygenation in the coumarin ring. Indeed acid hydrolysis of **2** gave umbelliferone (**1**) identified by direct comparison (mmp, TLC, UV and ^1H NMR) with an authentic sample.

Based on spectral data, **2** was shown to be a bicyclic diterpene linked to the 7-hydroxyl of umbelliferone. The ^1H NMR spectrum of **2** is very similar to that of **3**, a coumarin which has been recently isolated from *Ferula loscosii* [4], the only difference being an additional olefinic signal which integrated for one proton and another D_2O exchangeable one; the latter is assigned to the proton of the hydroxyl group which also appeared in the IR spectrum of **2**. The location of this hydroxyl group could be inferred unambigously from the mass spectrum which showed peaks at m/z 480 $[M]^+$, 462 $[M-H_2O]^+$ and 380 [M – β-hydroxyisovaleryl group]$^+$, thus clearly showing that it is in the isovaleryl moiety. Further support came from the ^1H NMR which showed five methyl-singlets. Occasional irradiation in the region of complex signals between δ2.3 and 1.4 did not affect the methyl singlets. Moreover, two methyl singlets shifted from δ1.2 and 1.02 to δ2.15 and 2.05 in the ^1H NMR spectrum on addition of Eu(fod-d_9)$_3$ (molar concentration ratio of reagent:substrate = 0.2:1.0, respectively); this large shift indicates the close proximity of the oxygen function to two methyls in the isovaleryl moiety. The ^1H NMR spectrum of **2** also showed two broad singlets at δ4.92 and 4.54 assigned for the methylene protons at C-12′. The configuration of the CH_2O-7 coumarinyl group on C-9′ in **2** is inferred from the comparison of the chemical shifts of C-11′ protons (δ4.19, *d*, J = 6.0 Hz) of this compound with those for the same protons in coladonin and isovaleryl coladonin (**3**) (δ4.15, *d*, J = 6.0 Hz) [4].

The ^{13}C NMR spectrum of **2** demonstrated the presence of two double bonds, one disubstituted and the other trisubstituted. The only possible location of the latter is as in structure **2**; i.e. between the carbons 5′ and 6′. The assignment of coumarinyl ^{13}C signals in **2** was based on the data described for 7-hydroxycoumarin [5], and by the aid of the single frequency off-resonance decoupling (SFORD) technique while the assignment of the olefinic and oxygenated carbons can be made in a straightforward



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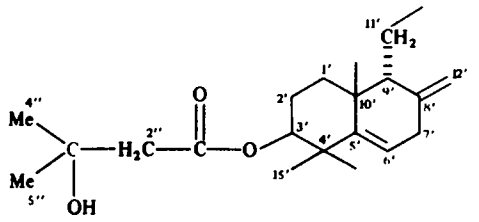

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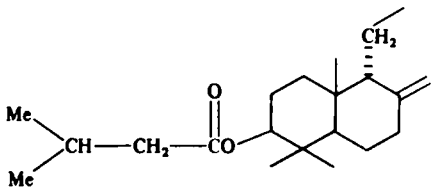

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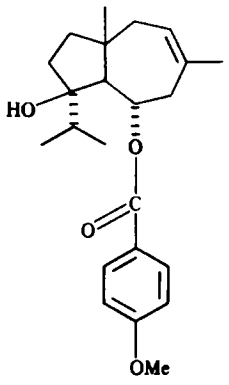

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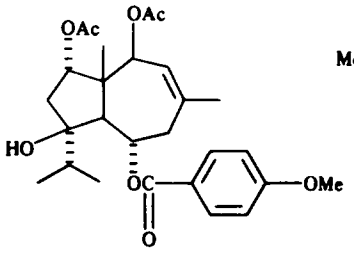

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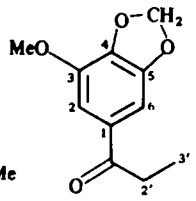

6

manner, based on multiplicities and chemical shifts. The SFORD technique was not very helpful in the assignment of aliphatic carbon signals, due to overlapping. However, the assignment of these signals (see Experimental) is based on comparison with those of a similar skeleton [6] in naturally occurring coumarinyl ethers.

Ferutidin (the *p*-anisic acid ester of jaeschkeanadiol) (**4**) which is widely distributed in *Ferula* species [7–10] was identified in *Ferula sinaica* by comparison of its IR, ^{1}H NMR [8] and ^{13}C NMR spectrum [9]. Compound **5**, $C_{27}H_{36}O_8$, has identical spectral data (MS, ^{1}H NMR and ^{13}C NMR) to the compound recently isolated for the first time from *Ferula communis* [9].

Compound **6** ([M]$^+$ at *m/z* 208) gave a mass spectrum very similar to that reported for the naturally occurring 3-hydroxy analogue recently isolated from *F. elaeochytris* [10]. The mass spectrum showed a base peak at *m/z* 208 together with prominent signals at *m/z* 179, 151 [M − COEt] and 121. The ^{1}H NMR spectrum of **6** corroborates the structure. The ^{13}C NMR spectrum is also consistent with the structure and is presented here (see Experimental), since it has not previously been reported. Compound **6** was previously identified from *Ferula ugamica* [11].

EXPERIMENTAL

Mps are uncorr. NMR spectra were obtained in $CDCl_3$ on a Jeol 100 MHz with TMS as int. reference. Chemical shifts are expressed in δ (ppm). MS were obtained with a direct inlet system at 70 eV.

Isolation and identification of the compounds. Dried and coarsely powdered roots (300 g) of *Ferula sinaica* (identified by Dr. Hassan M. Hassan, Department of Botany, King Saud University, Riyadh, Saudi Arabia) were extracted with C_6H_6 (2 l.) for 7 days at room temp. The extract was filtered and concd *in vacuo* to give a waxy residue, which was chromatographed on a silica gel column (200 g) packed in $CHCl_3$ and eluted with $CHCl_3$–EtOAc, collecting 100 ml fractions. The fractions were compared by TLC (silica gel using $CHCl_3$ as solvent), and those

giving similar spots were combined and further purified on silica gel (Merck) to give compounds **2** and **4–6**.

Compound **2**. Crystals, mp 91–94° (hexane–Et_2O); UV λ_{max}^{MeOH} nm (log ε): 209 (4.3), 260 sh (3.2) and 320 (4.1); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 3050, 2940, 1715, 1610, 1580, 1510, 1450 and 1120; ^1H NMR: δ7.63 (*d*, J = 9.5 Hz, H-4), 7.36 (*d*, J = 9.1 Hz, H-5), 6.8 (2H, H-6 and H-8), 6.23 (*d*, J = 9.5 Hz, H-3), 5.5 (*br s*, H-6'), 4.92 (1H, *br s*, one C-12' proton), 4.5 (*br s*, one C-12' proton), 4.19 (*d*, J = 6.0 Hz, C-11' protons), 4.0 (1H, *m*, H-3'), 3.27 (1H, exchangeable proton), 1.2 (*s*, 3H), and between 1.02 and 0.84 Me signals integrated for 12H; EIMS *m/z* (rel. int.): 480 $[M]^+$ (0.1), 464 (0.3), 462 (0.5), 452 (2.0), 424 (2.1), 410 (3.8), 382 (16.6), 380 (2.2), 220 (19.3), 162 (34.6), 57 (53.7); ^{13}C NMR ($CDCl_3$): δ162.1 (*s*, C=O), 161.8 (*s*, C-2), 161.1 (*s*, C-7), 155 (*s*, C-9), 146.2 (*s*, C-8'), 143.34 (*d*, C-4), 132.2 (*s*, C-5'), 128.66 (*d*, C-5), 122.8 (*d*, C-6'), 113.04 (*d*, C-6), 113.02 (*s*, C-10), 112.0 (*d*, C-3), 107.7 (*t*, C-12'), 101.3 (*d*, C-8), 78.8 (*d*, C-3'), 76.3 (*s*, C–O), 65.6 (*t*, C-11'), 54.75 (C-9'), 39.1 (C-2''), 38.8 (C-7'), 38.7 (C-4'), 37.2 (C-10'), 35.8 (C-1'), 23.4 (C-2'), 28.3 (C-15'), 23.4 (C-4''), 21.6 (C-5''), 15.5 (C-14'), 15.3 (C-13').

Compound **4**. Mp 106–108° (lit. [8] 109–110°). IR and ^1H NMR data identical with those [10] for the same compound.

Compound **5**. Gum, $C_{27}H_{36}O_8$, identical spectral data (MS, ^1H NMR, ^{13}C NMR) with the same compound [9]; EIMS *m/z* (rel. int.): 488 $[M]^+$ (0.03), 445 (13), 337 (5), 293 (6), 277 (8), 259 (12), 217 (62), 199 (36), 191 (58), 135 (100); ^{13}C NMR ($CDCl_3$): δ170.37 and 170.8 (2 MeCO), 166.32 (*s*, C-1'), 163 (*s*, C-5'), 131.7 (*d*, C-3' and C-7'), 131.5 (*s*, C-8), 128.4 (*d*, C-9), 122.2 (*s*, C-1'), 113.8 (*d*, C-4' and C-6'), 85.7 (*s*, C-4), 79.2 (*d*, C-2), 75.1 (*d*, C-10), 69.45 (*d*, C-6), 55.48 (*d*, C-5), 54.48 (*q*, OMe), 51.08 (*s*, C-1), 41.04 (*t*, C-3), 39.4 (*t*, C-7), 37.1 (C-11), 26.07 (*q*, C-14), 21.07 (2 MeCO), 18.1 (*q*, C-15), 17.55 and 15.08 (each *q*, C-12 and C-13).

Compound **6**. $C_{11}H_{12}O_4$. EIMS *m/z* (rel. int.): 208 $[M]^+$ (90%), 179 $[M-Et]^+$ (100), 151 $[M-COEt]^+$ (82), 121 (45) and 83 (88); ^{13}C NMR ($CDCl_3$): δ198.76 (*s*, C=O), 148.89 (*s*, C-5), 143.48 (*s*, C-3), 138.99 (*s*, C-4), 131.8 (*s*, C-1), 108.46 (*d*, C-6), 102.27 (*d*, C-2), 102.6 (*t*, OCH_2O), 56.6 (*q*, OMe), 31.6 (*t*, C-2'), 8.48 (*q*, C-3').

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