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PYRANOCOUMARINS FROM *ARRACACIA NELSONII**

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Key Word Index—*Arracacia nelsonii*; Umbelliferae; angular pyranocoumarins; khellactone derivatives; 3′-angeloyl-4′-oxo-khellactone.

Abstract—(+)-Suksdorfin, (−)-isosamidin, (−)-3′-angeloyl-*cis*-khellactone, and a new pyranocoumarin, (3′*S*)-3′-angeloyl-4′-oxo-khellactone, were isolated from the aerial parts of *Arracacia nelsonii*. Their structures were established by chemical and spectroscopic means.

INTRODUCTION

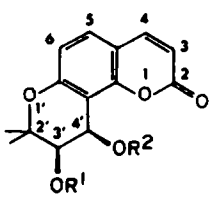
Phthalides [1], coumarins [2], terpenoids [3] and flavonoids [4] are the main secondary plant constituents found in the Umbelliferae, and chemosystematic relationships have been suggested [5]. However, knowledge of the chemistry of the genus *Arracacia* (subfamily Apioideae, tribe Smyrnieae) appears to be limited to one species [6]. In continuation of our investigation of Mexican plants [7, 8], we now report the isolation and structure determination from *A. nelsonii* of several angular pyranocoumarins.

RESULTS AND DISCUSSION

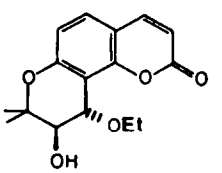
Extensive chromatography of the chloroform extract of the aerial parts of *A. nelsonii* yielded the known compounds (+)-suksdorfin (**1**) [9] and (−)-isosamidin (**2**) [10], which were identified by comparing their physical constants with those of authentic samples. The ^{1}H NMR data of **3**, also isolated as a natural product, were essentially the same as those of **1** and **2**, if allowance was made for the different substitution patterns at C-3′ and C-4′. This information together with the molecular formula $C_{19}H_{20}O_6$ established a hydroxyl at C-4′ (geminal proton: δ5.18, *d*, J = 5 Hz) and an angelate at C-3′ (geminal proton: δ5.44, *d*, J = 5 Hz) with a *cis* relationship. A product with this structure was described some years ago [11], but the complete spectral data of this substance were not published and showed differences with our **3** (see Experimental). Although direct comparison of the two samples was not possible, acetylation of **3** afforded **4**, identical in all respects with (+)-isopteryxin [9], thus confirming structure **3** for (−)-3′-angeloyl-*cis*-khellactone.

The 3′*R*,4′*S* configuration of **3** was determined by the fact that basic hydrolysis in ethanol of **4** yielded (+)-*cis*-ethyl-khellactone (**5**) and (−)-*trans*-ethyl-khellactone (**6**) as described for khellactone diesters [9] and whose absolute stereochemistry has been previously established [12].

The new pyranocoumarin **7** had the molecular formula $C_{19}H_{18}O_6$ (elemental analysis and mass spectrometry). Its IR, UV and ^{13}C NMR spectra (see Experimental) indicated the presence of three carbonyls and a coumarin nucleus. The ^{1}H NMR spectrum of **7** showed an AB system (δ7.58, *d*, J = 9.5 Hz, H-4 and 6.29, *d*, J = 9.5, H-3) characteristic of the protons of a δ-lactone, and a second AB system (δ7.53, *d*, J = 8.5 Hz, H-5 and 6.87, *d*, J = 8.5 Hz, H-6) for the *ortho* protons of a benzenoid nucleus. The signals of a geminal dimethyl linked to oxygen (δ1.42 and 1.59), a one-proton singlet at δ5.60 (H-3′) as well as the characteristic signals of an angelate ester chain (δ6.18, 1H, *m*, H-3″; 2.03, 3H, *dq*, J = 7, 1.2 Hz, H-4″; 1.99, 3H, *s* (*br*), H-5″) gave evidence of the presence of a secondary ester at C-3′ and a carbonyl at C-4′ of an angular pyranocoumarin, thus establishing structure **7**, in



	R^1	R^2
1	Ac	*i*-Val
2	Ac	Sen
3	Ang	H
4	Ang	Ac
5	H	Et



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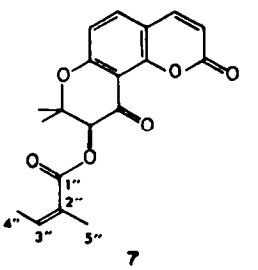

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accordance with the molecular formula requirements. The downfield shifts of H-5 ($\Delta\delta = 0.24$) and H-3′ ($\Delta\delta = 0.42$) of **7** with respect to **3** are due to the resonance and inductive effects, respectively, of the carbonyl located at C-4′.

The ^{13}C NMR data of **7** are listed in the Experimental and the assignments were made by comparison with those of related compounds [13]. Manganese dioxide oxidation of **3** afforded a substance identical in all respects with **7**, thus securing the proposed structure, and determining the *S*-configuration at C-3′, in accordance with the above-described correlations.

Although coumarins seem to be common in the Umbelliferae, this is the first report of the occurrence of angular pyranocoumarins in the tribe Smyrnieae. An investigation of other Mexican species of this family is currently underway.

EXPERIMENTAL

Mps. are uncorr. *A. nelsonii* C. & R. was collected in the State of Chiapas, México. A voucher has been deposited at the National Herbarium, Instituto de Biología de la Universidad Nacional Autónoma de México, M-6817.

Extraction and chromatography of A. nelsonii. Air-dried aerial parts (4.2 kg) were extracted twice at room temp. with Me_2CO for 2 weeks, then the Me_2CO extract was evaporated to dryness under red. pres. and the residue was partitioned between H_2O and $CHCl_3$. Elimination of the organic solvent gave 150 g extract, which was chromatographed on a silica gel (2 kg) column using a $CHCl_3$–Me_2CO gradient elution system, 1 l. fractions being collected. The components isolated from the different fractions were: $CHCl_3$, hydrocarbons, fats and waxes (rejected); $CHCl_3$–Me_2CO (19:1) stigmasterol (0.012% of dry wt), identified by standard sample comparison; $CHCl_3$–Me_2CO (9:1), (+)-suksdorfin (**1**) and (−)-isosamidin (**2**); $CHCl_3$–Me_2CO (17:3), (−)-isosamidin (**2**) and (3′*S*)-3′-angeloyl-4′-oxo-khellactone (**7**); $CHCl_3$–Me_2CO (4:1), (3′*S*)-3′-angeloyl-4′-oxo-khellactone (**7**) and (−)-3′-angeloyl-*cis*-khellactone (**3**); $CHCl_3$–Me_2CO (7:3), (−)-3′-angeloyl-*cis*-khellactone (**3**).

As the first chromatographic separation was not clear-cut, purifications on smaller columns or prep. TLC were required.

(+)-Suksdorfin (**1**). Isolated as colourless crystals, mp 137–139° (lit. [9] 140°); EIMS (not previously reported) *m/z* (rel. int.): 388 (6) $[M]^+$, 287 (4), 261 (7), 244 (25), 229 (100), 85 (22), 57 (25), 43 (28). This substance was identified by comparison with the data ($[\alpha]_D$, mp, IR, UV, ^1H NMR) reported in the literature [9, 14]. The total yield was 0.115% of the dry wt.

(−)-Isosamidin (**2**). Crystallized when triturated with EtOAc–*n*-hexane. Mp 119–120° (lit. [10] 120°) (0.030% yield of dry wt); EIMS (not previously reported) *m/z* (rel. int.): 386 (3) $[M]^+$, 326 (21), 311 (10), 229 (17), 83 (100), 55 (12), 43 (13). Comparison with reported data confirmed the structure of this substance [10, 14].

(−)-3′-Angeloyl-cis-khellactone (**3**). Isolated in 0.031% yield of dry wt, and crystallized slowly from a mixture of Me_2CO–*i*-Pr_2O. Mp 149–151°; $[\alpha]_D^{25}$ −49.0° ($CHCl_3$; *c* 0.02); UV λ_{max}^{MeOH} nm (log ε): 205 (3.42), 217 (3.20), 255 (3.41), 324 (4.06); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3604, 3089, 3007, 2986, 1726, 1606, 1392, 1457, 1405, 1386, 1351, 1284, 1145, 1114, 1085, 1050, 1028, 1004, 893, 836; ^1H NMR (80 MHz, $CDCl_3$): δ7.58 (1H, *d*, *J* = 9 Hz, H-5), 6.75 (1H, *d*, *J* = 9 Hz, H-6), 6.22 (1H, *d*, *J* = 9.5 Hz, H-3), 6.10 (1H, *m*, H-3″), 5.44 (1H, *d*, *J* = 5 Hz, H-4′), 5.18 (1H, *d*, *J* = 5 Hz, H-3′), 2.57 (1H, *s* (*br*), OH), 1.99 (3H, *dq*, *J* = 6, 1.3 Hz, 4″-Me), 1.93 (3H, *s* (*br*), 5″-Me), 1.50 and 1.43 (3H each, *s*, geminal Me at C-2′); EIMS *m/z* (rel. int.): 344 (11) $[M]^+$, 229 (13), 191 (8), 134 (7), 83 (100), 55 (35), 39 (6).

(3′S)-3′-angeloyl-4′-oxo-khellactone (**7**). Isolated as crystals with mp 198–201° (from Me_2CO–*i*-Pr_2O) in 0.002% yield of the dry wt, $[\alpha]_{589}^{25}$ −30°, $[\alpha]_{578}^{25}$ −32.5°, $[\alpha]_{546}^{25}$ −34.5°, $[\alpha]_{436}^{25}$ −49°, ($CHCl_3$; *c* 0.021); UV λ_{max}^{MeOH} nm (log ε): 212 (4.39), 265 (3.85), 271 (3.91), 305 (3.90), 333 (3.86), 346 (3.87); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2980, 2920, 1735, 1715, 1610, 1600, 1555, 1480, 1455, 1420, 1400, 1390, 1370, 1350, 1300, 1240, 1140, 1115, 1095, 915; ^1H NMR (80 MHz, $CDCl_3$): see text; ^{13}C NMR (20 MHz, $CDCl_3$): δ184.38 (*s*, C-4′), 166.12 (*s*, C-1″), 162.09 (*s*, C-2), 159.46 (*s*, C-7), 153.85 (*s*, C-8a), 143.00 (*d*, C-4), 139.75 (*d*, C-3″), 134.78 (*d*, C-5), 127.06 (*s*, C-2″), 114.89 (*d*, C-3), 114.16 (*d*, C-6), 113.06 (*s*, C-4a), 108.37 (*s*, C-8), 82.46 (*s*, C-2′), 76.54 (*d*, C-3′), 26.25 (*q*, C-5″), 20.43 and 19.80 (*q* each, geminal Me at C-2′), 15.95 (*q*, C-4″); EIMS *m/z* (rel. int.): 342 (6) $[M]^+$, 271 (3), 242 (16), 189 (22), 160 (8), 83 (100), 55 (31). (Found: C, 65.49; H, 5.38. $C_{19}H_{18}O_6$ requires: C, 66.66; H, 5.30.)

Acetylation of compound **3**. 100 mg **3** was acetylated with acetyl chloride (0.6 ml) and C_5H_5N (0.6 ml) at room temp. The product (96 mg) was homogeneous on TLC and was crystallized by maintaining the oily residue under vacuum for several days. Mp 80–81° (lit. [9] 81.5–82.5°); $[\alpha]_D^{22}$ +9.3° (EtOH; *c* 0.61). The spectral data corresponded to those reported previously for (+)-isopteryxin (**4**).

Hydrolysis of **4**. 90 mg **4** was dissolved in 10 ml EtOH and ethanolic NaOH (60 mg NaOH in 2 ml EtOH). The reaction was continued with stirring for 1 hr at room temp. under Ar. The soln was acidified, evaporated at red. pres., diluted with H_2O, and extracted with EtOAc. The washed and dried extract was evaporated and the residue was chromatographed over silica gel eluting with hexane–EtOAc. (+)-*cis*-Ethyl-khellactone (**5**) eluted first. Mp 126–128° (lit. [9] 127–128°); $[\alpha]_D^{25}$ +133° (EtOH; *c* 0.002); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3585, 2981, 1728, 1605, 1404, 1371, 1353, 1308, 1238, 1243, 1199, 1182, 1112, 1059; ^1H NMR (80 MHz, $CDCl_3$): δ7.58 (1H, *d*, *J* = 10 Hz, H-4), 7.27 (1H, *d*, *J* = 9 Hz, H-5), 6.72 (1H, *d*, *J* = 9 Hz, H-6), 6.22 (1H, *d*, *J* = 10 Hz, H-3), 4.78 (1H, *d*, *J* = 6 Hz, H-4′), 4.13 (2H, *q*, *J* = 7 Hz, Me–C$\underline{H}_2$–O–), 3.82 (1H, *d*, *J* = 6 Hz, H-3′), 2.93 (1H, *s*, OH), 1.35 and 1.44 (3H each, *s*, geminal Me at C-2′), 1.29 (3H, *t*, *J* = 7 Hz, C$\underline{H}_3$–CH_2–O–); EIMS *m/z* (rel. int.): 290 (71) $[M]^+$, 219 (69), 218 (85), 191 (100), 190 (60), 162 (60), 134 (39), 63 (18), 43 (15).

Further elution gave (−)-*trans*-ethylkhellactone (**6**). Mp 160–161° (lit. [9] 161–162°); $[\alpha]_D^{25}$ −56° (EtOH; *c* 0.0019); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580, 2980, 1727, 1606, 1491, 1467, 1405, 1373, 1355, 1289, 1238, 1199, 1116, 1081, 1058, 1021, 982; ^1H NMR (80 MHz, $CDCl_3$): δ7.57 (1H, *d*, *J* = 10 Hz, H-4), 7.28 (1H, *d*, *J* = 9 Hz, H-5), 6.75 (1H, *d*, *J* = 9 Hz, H-6), 6.22 (1H, *d*, *J* = 10 Hz, H-3), 4.63 (1H, *d*, *J* = 5 Hz, H-4′), 4.00 (2H, *q*, *J* = 7 Hz, Me–CH_2–O), 3.88 (1H, *d*, *J* = 5 Hz, H-3′), 1.86 (1H, *s*, OH), 1.47 (6H, *s*, geminal Me at C-2′), 1.30 (3H, *t*, C$\underline{H}_3$–CH_2–O–); EIMS *m/z* (rel. int.): 290 (32) $[M]^+$, 218 (65), 191 (100), 162 (89), 134 (52), 89 (32), 77 (40), 57 (50), 43 (69).

Oxidation of compound **3**. To a soln of **3** (100 mg) in $CHCl_3$ (10 ml) was added activated MnO_2 (1 g) and the mixture stirred at room temp. for 4 hr. After usual work-up, the residue was purified by CC to give 65 mg **7**, mp and mmp 198–201°, identified by direct comparison with the natural product.

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