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5-METHYLCOUMARINS FROM *NASSAUVIA* SPECIES

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Key Word Index—*Nassauvia* species; Compositae; Mutisieae; 5-methylcoumarins, sesquiterpenes; dithiophenes.

Abstract—The investigation of the aerial parts of five *Nassauvia* species afforded, in addition to known compounds, three new derivatives of 5-methyl-4-hydroxycoumarins, a dithiophene acetylene diol and the farnesyl ether of coniferyl alcohol. The structures were elucidated by high field NMR techniques.

INTRODUCTION

The shrubby genus *Nassauvia* (Compositae, tribe Mutisieae) with *ca* 40 species in the Andes from S. Bolivia to Patagonia is placed in the subtribe Nassauviinae [1]. So far only one species has been studied chemically [2] which, as many other genera of the tribe, also gave derivatives of 5-methylcoumarin. We now have studied five further species from Chile. The results are discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *N. magellanica* J. F. Gmel. afforded the 5-methylcoumarin derivatives **7**, **8** and **5** [3] together with the isomer of the latter, the exomethylene derivative **4**. The aerial parts of *N. pygmaea* (Cass.) Hook. also gave **7** and **8** as well as the 5′-desoxy derivative **6** [3]. From the extract of the aerial parts of *N. revoluta* D. Don, in addition to widespread compounds, the 5-methylcoumarins **1**–**3**, the dithiophene derivatives **9** and **10** [4] and the geranyl derivative **11** were isolated. The aerial parts of *N. lagascae* (D. Don.) Meigen only gave lupeol, taraxasterol and α-amyrin, while those of *N. darwinii* (H. et A.) O. Hoffm. et Dusen afforded some sesquiterpene hydrocarbons, *ent*-kaurenic acid and its Δ^9-derivative and lupeol.

The structure of **4** followed from the molecular formula ($C_{14}H_{12}O_3$) and its ^{1}H NMR spectrum (Table 1) which differed characteristically from that of **5** [3]. The chemical shifts of the low field broadened singlets indicated the presence of an exomethylene group where one of the protons was strongly deshielded by the coumarin carbonyl group. The pair of triplets at δ4.47 and 2.70 required the proposed structure, especially as the latter broadened triplet was sharpened on irradiation of the frequencies of the exomethylene protons. This coumarin **4** was an isomer of triptospinocoumarin (**5**) [3] but it is most likely an artifact, as it is also formed from **5** on standing in $CDCl_3$, probably due to traces of acid.

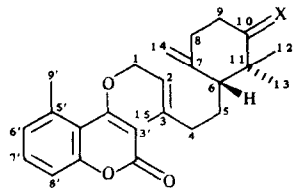
The structures of the coumarins **1**–**3** also followed from the ^{1}H NMR spectra (Table 1) which were in the terpene part similar to those of the corresponding sesquiterpene ethers of umbelliferone which are widespread in the Umbelliferae. In the case of **1**, in addition to the typical signals of a 5-methyl-4-hydroxycoumarin derivative, those for a seco-drimane derivative were visible. Spin decoupling shows that the 4-hydroxy group was connected with a prenyl unit [δ4.65 *br d* (2H), 5.49 *br t* (1H, J = 7 Hz)]. Furthermore the couplings of a double doublet at δ3.41 indicated the presence of an equatorial hydroxy group and the broadened singlets at δ4.90 and 4.60 required an exomethylene group. The ^{13}C NMR spectrum (see Experimental) also agreed with the proposed structure.

The ^{1}H NMR data of **2** were close to those of **1**. However, due to the presence of keto group, several signals were shifted down field and the H-10 signal was missing. The couplings of H-6 showed that the side chain at the corresponding carbon was equatorially orientated. The absolute configuration followed from the observed Cotton-effect as most likely the octant rule is valid in this case.

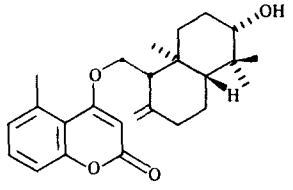
The ^{1}H NMR data of **3** differed from those of **1** and **2**. The presence of three singlets for methyls at sp^3 carbons indicated a drimane derivative. Accordingly, the signals of the sesquiterpene moiety were similar to those of the corresponding scopoletin ether [5]. Compounds **1**–**3** we have named nassauvirevolutin A–C.

The ^{1}H NMR spectrum of **11** (see Experimental) was very close to that of **12** which was isolated from a *Gyptothamnium* species [6]. Due to the additional aromatic proton the typical picture of a 1,2,4-trisubstituted benzene derivative was visible.

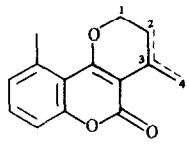
The chemistry of the genus *Nassauvia* supports a close relationship to *Triptilion* [3] which is placed by A. Cabrera [1] in the same group, however, together with *Polyachyris* and *Moscharia* which both contain other constituents. The former afforded highly oxygenated eudesmanes [7] while the latter contains isocedrene derivatives typical for the subtribe [8]. As already pointed out previously [6] the taxonomy of the complicated tribe Mutisieae may need further studied. Most likely the unique 5-methylcoumarins and the isocedrenes are of interest for final delimitations of the subtribes.



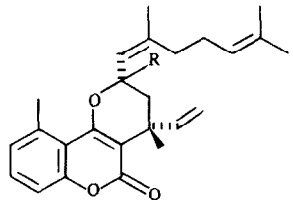
1 X = αOH,H
2 X = O



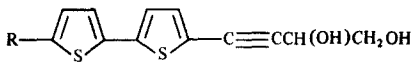
3



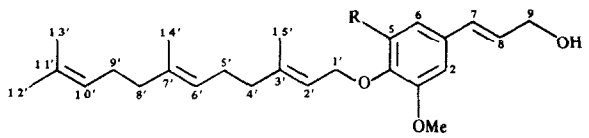
4 Δ^3
5 Δ^2



6 R = H
7 R = OH
8 R = OH (6,7-epoxide)



9 R = Me
10 R = H



11 R = H
12 R = OMe

The extract of the aerial parts (510 g) of *N. magellanica* (voucher A. Landeros 724) gave 2 mg **7**, 3 mg **8**, 2 mg **4** and 2 mg **5** by CC and TLC. **4** and **5** could only be enriched by HPLC (RP 8, MeOH–H_2O, 4:1, R_t 10.3 min).

The extract of the aerial parts (418 g) of *N. pygmaea* (voucher A. Landeros 718) gave 9 mg aromadendrene, 25 mg **6**, 20 mg **7** and 300 mg **8** by CC and TLC.

The extract of the aerial parts (190 g) of *N. lagascae* (voucher A. Landeros 717) gave 50 mg lupeol, 50 mg taraxasterol and 30 mg α-amyrin, while the extract of the aerial parts (460 g) of *N. darwinii* (voucher A. Landeros 712) afforded 55 mg of a mixture of germacrene D, α-humulene and silphinene, 50 mg *ent*-kaurenic acid, 20 mg of its Δ^9-derivative and 10 mg lupeol.

Nassauvirevolutin A (**1**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 1705, 1615, 1595 (coumarin); MS *m/z* (rel. int.): 396 $[M]^+$ (3) ($C_{25}H_{32}O_4$), 381 (1.5), 378 (1.3), 363 (4), 177 (100), 135 (40); ^{13}C NMR ($CDCl_3$): 15.9 *q*, 16.6 *q*, 23.3 *t*, 23.4 *q*, 25.9 *q*, 32.0 *t*, 32.4 *t*, 38.2 *t*, 40.3 *s*, 50.8 *d*, 66.1 *t*, 76.7 *d*, 90.4 *d*, 108.5 *t*, 114.5 *s*, 115.2 *d*, 117.0 *d*, 127.4 *d*, 131 .3 *d*, 137.0 *s*, 144.1 *s*, 146.9 *s*, 154.7 *s*, 162.7 *s*, 168.3 *s*; $[\alpha]_D^{24}$ +2.1 ($CHCl_3$; *c* 0.83).

Nassauvirevolutin B (**2**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705, 1615, 1605, 1565, 1465, 1450, 1390, 1370, 1250, 1145, 1095, 1055, 960, 910; MS *m/z* (rel. int.): 394.214 $[M]^+$ (12) (calcd for $C_{25}H_{30}O_4$: 394.214), 379 (3), 229 (50), 177 (21), 135 (36), 57 (100); CD (MeCN): $\Delta\varepsilon_{280} - 0.5$.

Nassauvirevolutin C (**3**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560 (OH), 1710, 1615 (coumarin); MS *m/z* (rel. int.): 396.230 $[M]^+$ (4) (calc. for $C_{25}H_{32}O_4$: 396.230), 381 (2.5), 177 (42), 135 (100).

Isotriptospinocoumarin (**4**). Colourless oil, not free from **5**; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710, 1600 (coumarin); MS *m/z* (rel. int.): 228.079 $[M]^+$ (90) (calc. for $C_{14}H_{12}O_3$: 228.079), 213 (30), 189 (45), 135 (53), 69 (100).

2-[3,4-*Dihydroxybut*-1-*inyl*]-5′-*methyldithiophene* (**9**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3595 (OH), 2190 (C≡C); MS *m/z* (rel. int.): 264 $[M]^+$ (5) ($C_{13}H_{12}O_2S_2$), 233 $[M-CH_2OH]^+$ (10), 97 (45), 71 (100); ^1H NMR ($CDCl_3$): 3.87 and 3.79 (*dd*, H-1), 5.02 (*dd*, H-2), 6.90 (*d*, H-6), 7.13 (*d*, H-7), 7.07 (*d*, H-10), 6.65 (*d*, H-11), 2.48 (*s*, H-13); (*J* [Hz]: 1,2 = 3.5; 1′,2 = 7; 6,7 = 10,11 = 3.5).

Coniferylalcohol-4-O-*farnesyl ether* (**11**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1605 (C=C), 960 (tr CH=CH); MS *m/z* (rel. int.). 353 $[M-CH_2OH]^+$ (2), 180 [coniferylalcohol]$^+$ (64), 69 $[C_5H_9]^+$ (100); ^1H NMR ($CDCl_3$): δ6.94 (*d*, H-2), 6.81 (*d*, H-5), 6.89 (*dd*, H-6), 6.54 (*br d*, H-7), 6.34 (*dt*, H-8), 4.30 (*br d*, H-9); 4.61 (*br d*, H-1′), 5.51 (*br t*, H-2′), 2.11 (*br t*, H-4′), 2.05 (*br q*, H-5′, H-9′), 5.10 (*br t*, H-6′), 1.97 (*br t*, H-8′), 5.08 (*br t*, H-10′), 1.67 (*br s*, H-12′), 1.59 (*br s*, H-13′, H-14′), 1.72 (*br s*, H-15′); (*J* [Hz]: 2,5 = 2; 5,6 = 8.5; 7,8 = 16; 8,9 = 6; 1′,2′ = 4′,5′ = 5′,6′ = 8′,9′ = 9′,10′ = 7).

EXPERIMENTAL

The air-dried plant material was collected in the provincia Ultima Esperanza, Sierra de los Baguales, Chile; vouchers are deposited in the Herbarium of the University of Concepcion. After cutting, the material was extracted at 20° with MeOH–Et_2O–petrol (1:1:1). The extracts were treated with MeOH to remove satd compounds. The soluble parts were separated first by CC (silica gel) and further by TLC and HPLC as reported previously [9]. The aerial parts (494 g) of *N. revoluta* (voucher A. Landeros 725) gave by CC and TLC 2 mg vanillyl alcohol and 3 mg benzoic acid. TLC of the CC fraction with Et_2O gave (Et_2O–petrol, 1:1, two developments) 7 mg **1** (R_f 0.25), 4 mg **2** (R_f 0.50) and 4 mg **11** (R_f 0.40). The more polar CC fraction gave by TLC (Et_2O–petrol, 9:1) 3 mg **3** (R_f 0.65) and a mixture of **9** and **10** which was separated by HPLC (RP 8, MeOH–H_2O, 7:3, flow rate 3 ml/min) to give 2 mg **10** and 2 mg **9** (R_t 12.3 min).

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Table 1. ^{1}H NMR spectral data of **1–4** ($CDCl_3$, 400 MHz, δ-values)

H	1	2*	3	4
1_1	4.65 *br d*	4.63 *br d*	4.30 *dd*	4.47 *t*
1_2			4.22 *dd*	
2	5.49 *br t*	5.48 *br t*	2.32 *br d*	2.70 *br t*
4_1	1.97 *m*	2.01 *ddd*	2.18 *m*	6.44 *br s*
4_2	2.21 *m*	1.89 *ddd*	2.49 *m*	5.16 *q*
9_1	1.86 *dq*	2.31 *dt*	1.87 *m*	—
9_2	1.53 *dddd*	2.64 *ddd*	1.73 *m*	—
10	3.41 *dd*	—	3.32 *dd*	—
12	1.02 *s*	1.20 *s*	1.04 *s*	—
13	0.74 *s*	1.04 *s*	0.83 *s*	—
14_1	4.90 *br s*	5.05 *br s*	4.95 *br s*	—
14_2	4.60 *br s*	4.85 *br s*	4.52 *br s*	—
15	1.76 *br s*	1.72 *br s*	0.82 *s*	—
3′	5.65 *s*	5.63 *s*	5.67 *s*	—
6′	7.02 *br d*	7.02 *br d*	7.00 *br d*	7.00 *br d*
7′	7.37 *t*	7.37 *t*	7.37 *t*	7.35 *t*
8′	7.17 *br d*	7.17 *br d*	7.17 *br d*	7.15 *br d*
9′	2.66 *s*	2.66 *s*	2.57 *s*	2.68 *s*

*H-5_1 1.68 *dddd*, H-5_2 1.22 m, H-6 2.17 *dd*.

J [Hz]: 6′,7′ = 7′,8′ = 8; compounds **1** and **2**: 1,2 = 7; (compound **1**: $8_1,9_1 = 8_2,9_1 = 8_1,9_2 = 9_1,10$ 4; $8_1,8_2 = 8_2,9_2 = 9_1,9_2 = 12$; $9_2$10 = 9.5; compound **2**: $4_1,5_1 = 5_1,5_2 = 5_1,6 = 12$; $4_2,5_1 = 5_2,6 = 4$; $8_1,9_1 = 4$; $8_1,9_2 = 8$; $8_2,9_1 = 4$; $8_2,9_2 = 8$; $9_1,9_2 - 14$); compound **3**: $1_1,2_2 = 1_2,2 = 10$; $1_1,2 = 3$; $9_1,10 = 4$; $9_2,10 = 11$; compound **4**: 1,2 = 5.5; $2_1,4 = 2_2,4 = 4_1,4_2 = 1$.

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