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A 2,2-DIMETHYLPYRANOFLAVONOL FROM *CITRUS NOBILIS*

TIAN-SHUNG WU

Department of Applied Chemistry, Providence College of Arts and Science, Taichung, Taiwan 40211, R.O.C.

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Key Word Index—*Citrus nobilis* var. *sunki*; Rutaceae; citrusinol; flavonoids; coumarins; sesquiterpene; acridone alkaloids; homoacridone alkaloids.

Abstract—An investigation of the root bark constituents of *Citrus nobilis* var. *sunki* has afforded a sesquiterpene [elemol], six coumarins [suberosin, suberenol, crenulatin, xanthyletin, xanthoxyletin and nordentatin], and four acridone alkaloids [citropone-A, 5-hydroxynoracronycine, citrusinine-I and citracridone-I] together with *p*-hydroquinone. A new 2,2-dimethylpyranoflavonol was also isolated, identified and named citrusinol.

INTRODUCTION

In continuation of my chemical investigation of the genus *Citrus* [1], I have now examined *Citrus nobilis* Lour var. *sunki* Hort. The root bark of this plant afforded a new flavonol (1), together with 12 other known constituents.

RESULTS AND DISCUSSION

Citrusinol (**1**) gave a dark green colour with methanolic ferric chloride and a positive magnesium–hydrochloric acid test. The UV spectrum of **1** was similar to those of other flavonols, and gave a bathochromic shift with aluminum chloride. These findings suggest that **1** is a flavonol [2]. The IR spectrum indicated the presence of a chelated hydroxyl group at 3360 cm^{-1} and a carbonyl group at 1620 cm^{-1}. This assumption was substatiated by the ^1H NMR spectrum of citrusinol, in which a 5-hydroxyl signal was observed at $\delta 12.24$ (1H, *brs*; disappeared on D_2O). The ^1H NMR spectrum of **1** showed A_2B_2 pattern signals at $\delta 7.08$ and 8.23 (each 2H, *d*, $J = 8$ Hz) due to H-3′,5′ and H-2′,6′ of the B-ring. Compound **2**, an acetylated derivative of **1**, showed marked downfield shifts of the H-3′,5′ and upfield shifts of the H-2′,6′ signals (Table 1) consistent with the presence of a free 4′-hydroxyl in **1**. On the other hand, AB-type quartets at $\delta 5.80$ and 6.94 ($J = 10$ Hz) together with a six-proton singlet at $\delta 1.50$ indicate a 2,2-dimethylpyran ring attached to the A ring. Acetylation of **1** caused a downfield shift of the lone aromatic proton at $\delta 6.21$ (H-6) to $\delta 6.55$, but had no effect on the olefinic protons of the 2,2-dimethylpyran ring [3], suggesting the location of the dimethylpyran ring at an angular orientation. Thus, citrusional may be represented by a **1**.

In order to confirm this structure acetylcitrusinol (**2**) was subjected to catalytic hydrogenation with Pd/C to give a product whose IR, ^1H NMR, and mass spectra were in agreement with **3** which was prepared from amuresin (**5**) [4] by the hydrolysis and acetylation.

Known compounds, elemol (**6**) [6], suberosin (**7**) [5], suberenol (**8**) [6], crenulatin (**9**) [6], xanthyletin (**10**) [5, 6], xanthoxyletin (**11**) [6], nordentatin (**12**) [6], citropone-A(**13**) [7], 5-hydroxynoracronycine (**14**) [5], citrusinine-I(**15**) [6], citracridone-I(**16**) [5, 6] and *p*-hydorquinone [6] were isolated and identified by ^1H NMR, IR and MS spectra comparisons, mmp and TLC determinations with authentic samples.

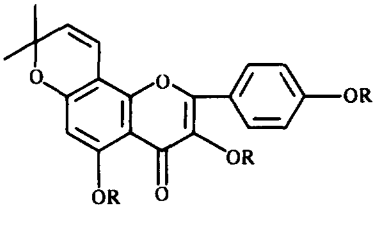
This is the first report of a 2,2-dimethyl pyranflavonoid in a *Citrus* species.

EXPERIMENTAL

Mps are uncorr. ^1H NMR (100 MHz) were recorded in $CDCl_3$ except where noted. Chemical shifts are shown in ppm (δ) with TMS as int. standard. MS were determined using a direct inlet system. UV were measured in MeOH and IR recorded in KBr expect where stated.

Plant material. Root bark of *Citrus nobilis* Lour *var. sunki* Hort was collected in Taiwan, during October, 1981. A voucher specimen has been deposited in the herbarium of the Chia-Nan Junior College of Pharmacy, Tainan, Taiwan.

Extraction and separation. Powdered root bark (0.45 kg) was extracted with Me_2CO. A 100 ml of the Me_2CO extract was adsorbed on silica gel, transfered to a silica gel column packed in $CHCl_3$–Me_2CO (9:1) and eluted with the same solvent to yield six fractions. Vacuum distillation (bp 116°/4 mmHg) of fraction 1 afforded, on standing, colourless micro-needles **6** (2.1 g). CC of the residue over silica gel, and elution with *n*-hexane–EtOAc (4:1) gave **7** (5.2 g), **10** (3.3 g), **11** (2.3 g), **13** (2 mg), **a** (8 mg), and **12** (13 mg), successively. Fraction 2 was rechromatographed on a silica gel column with iso-Pr_2O to afford successively **17** (20 mg),



1 R = H
2 R = Ac

Table 1. ^{1}H NMR of Citrusinol and its derivatives

	1*	**1**†	**2***	**3**‡	**5**§
H-6	6.18 (1H, *s*)	6.21 (1H, *s*)	6.55 (1H, *s*)	6.49 (1H, *s*)	6.09 (1H, *s*)
H-3′, 5′	7.03 (2H, *d*, *J* = 8 Hz)	7.08 (2H, *d*, *J* = 8 Hz)	7.30 (2H, *d*, *J* = 8 Hz)	7.20 (2H, *d*, *J* = 9 Hz)	6.92 (2H, *d*, *J* = 9 Hz)
H-2′, 6′	8.17 (2H, *d*, *J* = 8 Hz)	8.23 (2H, *d*, *J* = 8 Hz)	7.89 (2H, *d*, *J* = 8 Hz)	7.82 (2H, *d*, *J* = 9 Hz)	8.08 (2H, *d*, *J* = 9 Hz)
H-1″	6.89 (1H, *d*, *J* = 10 Hz)	6.94 (1H, *d*, *J* = 10 Hz)	6.85 (1H, *d*, *J* = 10 Hz)	2.88 (1H, *t*, *J* = 7 Hz)	2.87 (1H, *t*, *J* = 7 Hz)
H-2″	5.74 (1H, *d*, *J* = 10 Hz)	5.80 (1H, *d*, *J* = 10 Hz)	5.79 (1H, *d*, *J* = 10 Hz)	1.88 (1H, *t*, *J* = 7 Hz)	1.88 (1H, *t*, *J* = 7 Hz)
Me	1.50 (6H, *s*)	1.50 (6H, *s*)	1.54 (6H, *s*)	1.40 (6H, *s*)	1.35 (6H, *s*)
OH-5		12.24 (1H, *br*, *s*)‖			12.17 (1H, *s*)‖
OAc			2.32 (3H, *s*) 2.35 (3H, *s*) 2.40 (3H, *s*)	2.29 (3H, *s*) 2.32 (3H, *s*) 2.38 (3H, *s*)	

*Recorded in $CDCl_3$ + $(CD_3)_2CO$.
†Recorded in $(CD_3)_2CO$.
‡Recorded in $CDCl_3$.
§Recorded in $CDCl_3$ + $(CD_3)_2SO$.
‖These signals disappeared on addition of D_2O.

b (10 mg), steroids (40 mg), **1** (17 mg), **15** (8 mg), **14** (4 mg) and **16** (12 mg). Fraction 3 was subjected to florisil CC and elution with $CHCl_3$ to give **8** (46 mg).

Citrusinol (**1**). Yellow needles from Me_2CO, mp 252–254°. Calc. for $C_{20}H_{16}O_6 \cdot H_2O$: C, 64.86; H, 4.90; Found: C, 64.99; H, 4.82%. UV λ_{max} nm (log ε): 206 (4.19), 240 (4.42), 282 (4.40), 313 (4.03), 333 (4.09), 385 (4.07). $\lambda_{max}^{+AlCl_3}$ nm (log ε): 206 (4.25), 230 (sh, 4.29), 248 (4.44), 291 (4.38), 315 (sh, 3.85), 366 (4.09), 446 (4.17). $\lambda_{max}^{+AlCl_3, +HCl}$ nm (log ε): 206 (4.27), 230 (4.34 sh), 248 (4.44), 291 (4.38), 315 (3.89 sh), 366 (4.11), 450 (4.15). λ_{max}^{+NaOMe} nm (log ε): 208 (4.36), 230 (4.23 sh), 253 (4.43), 281 (sh, 4.27), 338 (3.74 sh), 412 (4.26). λ_{max}^{+NaOAc} nm (log ε): 245 (4.44), 282 (4.36), 334 (4.00), 395 (4.10). IR ν_{max} cm^{-1}: 3360, 3180, 1620, 1575, 1535. MS m/z (%): 352 $[M]^+$, 35), 337 (100), 323 (3), 308 (4), 281 (10), 203 (36), 168 (9), 135 (9), 121 (21).

Acetylation of citrusional (**1**). **1** (12 mg) was treated with Ac_2O (0.5 ml) and NaOAc (30 mg), the mixture was allowed to stand overnight and poured into ice H_2O. The ppt. was recryst. from Me_2CO to give **2** (12 mg) as colourless plates, mp 203–205°. UV_{max} nm: 208 (sh), 233, 271, 325 (sh). IR $\nu_{max}^{CHCl_2}$ cm^{-1}: 1765, 1750, 1635, 1600, 1575. MS m/z: 478 $[M]^+$, 450, 436, 421, 408, 394, 379 (100%), 365, 351, 347, 323, 308, 203, 121.

Hydrogenation of **2**. A solution of **2** (10 mg) in THF (10 ml) was stirred under H_2 in the presence of 5% Pd/C (10 mg) at room temp. for 1 hr. The soln was filtered and the conc. filtrate recryst. from Me_2CO gave **3** (10 mg) as colourless plates, mp 213–215°. UV λ_{max} nm: 216, 262, 312. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1630, 1610, 1580. MS m/z: 480 $[M]^+$, 438, 396, 354, 339, 325, 300, 270, 165, 121.

Hydrolysis of amurensin (**5**). 100 mg of amurensin (**5**) was hydrolysed with 5 ml of conc HCl for 30 min at 100°, filtered and washed with H_2O. The aglycone (**4**) cryst. from MeOH (yield 52 mg) as pale yellow needles, mp 303–304°. UV λ_{max} nm: 211, 227 (sh), 256 (sh), 273, 310 (sh), 330 (sh), 371, 432 (sh). IR ν_{max} cm^{-1}: 3290, 1645, 1605, 1537, 1510. MS m/z: 354 $[M]^+$, 339, 299, 279, 167, 129.

Acetylation of (**4**). 40 mg of **4** was treated as described for (**1**) to yield a colourless plates, mp 214–215° which were identified as **3** by the comparison of mp, IR, ^{1}H NMR, MS and TLC.

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