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REVISED STRUCTURE OF NEOFLAVONE IN *COUTAREA HEXANDRA*

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Abstract—A new neoflavone isolated from *Coutarea hexandra*, thought to be 5,2',5'-trihydroxy-7-methoxyneoflavone, is now shown to be 5,3',4'-trihydroxy-7-methoxyneflavone by synthesis.

From the genus *Coutarea*, several neoflavones (4-arylcoumarins) have been isolated [1, 2]. In a previous paper, a new neoflavone from *C. hexandra* Jacq. was reported and its structure deduced to be 5,2',5'-trihydroxy-7-methoxyneoflavone (**1**), based on spectral elucidation by two of us (G. R. and L.K.) [3]. Our current study on the spectral properties on neoflavones (M.I., T.T., K.H., M.M. and F.A.) show that neoflavones oxygenated at C-2' have a characteristic MS fragment $[M-18]^+$ (in the case of hydroxy) or $[M-31]^+$ (in methoxy) [4]. This fragment was not observed in our naturally occurring neoflavone, so that we had to reconsider its hydroxylation pattern. In this paper we describe the synthesis of **1**, 3',4',5-trihydroxy-7-methoxyneoflavone (**2**) and isomers (**3** and **4**) and the reassignment of structure **2** to the new compound.

Pechmann condensation of monomethylphloroglucinol [5] with 2,5-diisopropyloxybenzoylethylacetate [4] gave a 1:1 mixture of 5-hydroxy-2',5'-diisopropyloxy-7-methoxy-(**5**) and 7-hydroxy-2',5'-diisopropyloxy-5-methoxyneoflavone (**6**), which were separated by CC on silica gel. The difference between **5** and **6** was confirmed by the chemical shift of methoxy protons caused by an anisotropic effect of the side phenyl [6] (**5**: 3.73 ppm, **6**: 3.43 ppm). The respective neoflavones were deisopropylated by treatment with boron trichloride to give **1** and 7,2',5'-trihydroxy-5-methoxyneoflavone (**3**). The other desired neoflavones, **2** and **4** were obtained by condensation of monomethylphloroglucinol with 3,4-diisopropyloxybenzoylethylacetate, following by deisopropylation of **7** or **8** by the same procedures. The ^{1}H NMR (270 MHz) and the UV spectral data of the neoflavones thus obtained

Table 1. ^{1}H NMR (270 MHz) spectra in DMSO-d_6 of **1**–**4**

	1	2	3	4
3	5.74 (*s*)	5.76 (*s*)	5.72 (*s*)	5.73 (*s*)
6	6.15 (*d*)	6.24 (*d*)	6.23 (*d*)	6.30 (*d*)
	J = 2.57	J = 2.19	J = 2.19	J = 2.20
8	6.46 (*d*)	6.49 (*d*)	6.35 (*d*)	6.37 (*d*)
	J = 2.57	J = 2.19	J = 2.19	J = 2.20
2'	—	6.71 (*d*)	—	6.66 (*d*)
		J = 2.20		J = 2.20
3'	6.55 (*d*)	—	6.65 (*d*)	—
	J = 8.80		J = 8.43	
4'	6.58 (*dd*)	—	6.59 (*dd*)	—
	J = 8.80, 2.55		J = 8.43, 2.56	
5'	—	6.72 (*d*)	—	6.72 (*d*)
		J = 7.20		J = 8.06
6'	6.47 (*d*)	6.61 (*dd*)	6.53 (*d*)	6.55 (*dd*)
	J = 2.55	J = 7.20, 2.20	J = 2.56	J = 8.06, 2.20
OMe	3.87 (*s*)	3.79 (*s*)	3.40 (*s*)	3.45 (*s*)
OH	8.70 (2), 10.09	8.96, 9.07, 10.23	8.60, 8.71, 10.50	8.95, 9.06, 10.59

Table 2. UV spectra of 1–4 and bathochromic shifts on addition of reagents

	1	2	3	4
λ_{max}^{MeOH} nm (log ε)	260 (4.10) 330 (4.12)	261 (4.22) 329 (4.26)	259 (4.09), 271sh (3.83) 282sh (3.79), 333 (4.13)	260 (4.16) 333 (4.24)
+ NaOMe	275, 333, 400	278, 336, 405	271, 292sh, 380	272, 335sh, 380
+ $AlCl_3$	260, 329	260, 272sh, 330	260, 273sh, 285, 333	260, 275sh, 335
+ $AlCl_3$ + HCl	260, 329	260, 328	260, 273sh, 285, 332	260, 332
+ NaOAc	274, 330, 362sh, 400sh	278, 330, 400sh	270sh, 293sh, 380	272, 380
+ AcONa + H_3BO_3	260, 330 400sh	260, 325 400sh	260, 271sh, 285, 333	260, 335sh, 380sh

are shown in Tables 1 and 2. The spectral properties on 1 and 2, except MS, are very similar. 2 shows a strong UV fluorescence on TLC after spraying with Naturstoff-reagent (1% diphenylboric acid-β-aminoethylesster in MeOH soln) because of its *o*-dihydroxy group and can thus be conveniently distinguished from 1.

By direct comparison (co-TLC, ^{1}H NMR and mmp) of the naturally occurring neoflavone in *C. hexandra* with 1 and 2, its structure was proved to be 5,3′,4′-trihydroxy-7-methoxyneoflavone (2).

EXPERIMENTAL

Synthesis of 1 *and* 3. An ethanolic, soln of monomethylphoroglucinol (1.4 g, 10 mmol) and 2,5-diisopropyloxybenzoylethylacetate (3.1 g, 10 mmol) was satd with dry HCl under cooling. The soln was left for three days at room temp. The reactant was poured into H_2O, and then extracted with EtOAc. After evapn, the EtOAc soln was subjected to CC on silica gel (eluent; Me_2CO–benzene, 5:1) to give 5 (1.4 g) and 6 (1.5 g). 5; pale yellow oil. ^{1}H NMR (60 MHz, $CDCl_3$) δ: 1.10, 1.29 (6H, each *d*, *J* = 6.0 Hz, (Me_2CH), 3.73 (3H, *s*, OMe), 4.33–4.73 (2H, *m*, 2 × CH <), 5.93 (1H, *s*, H-3), 6.38 (1H, *d*, *J* = 2.0 Hz, H-6), 6.50 (1H, *d*, *J* = 2.0 Hz, H-8), 6.75–6.83 (3H, *m*, H-3′,4′ and 6′). 6; a colourless oil. ^{1}H NMR (60 MHz, $CDCl_3$) δ: 1.10, 1.32 (6H, each *d*, *J* = 6.0 Hz, $(Me)_2$CH), 3.43 (3H, *s*, OMe), 4.20–4.68 (2H, *m*, 2 × CH <), 6.00 (1H, *s*, H-3), 6.29 (1H, *d*, *J* = 2.0 Hz, H-6), 6.75–6.83 (4H, *m*, H-3′,4′,6′ and 8). To a CH_2Cl_2 soln (20 ml) of 5 (0.4 g), BCl_3 (0.5 ml) was added at −70°. The soln was left for 1 hr at room temp. After the usual work-up, 1 was obtained as yellow prisms (0.18 g), mp 193–194° (EtOAc). MS *m/z* (rel. int.): 300 $[M]^+$ (29.3), 284 (19.5), 283 (100), 282 (41.5), 254 (19.5), 226 (21.9), 136 (12.2). In the same way, 3 was obtained as a colourless yellow powder, mp 238–240° (EtOAc–C_6H_{16}). MS *m/z* (rel. int.): 300 $[M]^+$ (31.2), 284 (4.0), 269 (19.5), 207 (7.2), 206 (63.5), 178 (7.3), 150 (4.9), 137 (12.2), 136 (100).

Synthesis of 2 and 4. By the same condensation of monomethylphloroglucinol (1.8 g, 13 mmol) with 3,4-diisopropyloxybenzoylethylacetate (4.0 g, 13 mmol) prepared from 3,4-dihydroxyacetophenone according to our previous method [4], and following separation, 7 and 8 were obtained. 7; a brown oil, yield 800 mg. ^{1}H NMR (60 MHz, $CDCl_3$) δ: 1.35, 1.38 (6H, each *d*, *J* = 6.0 Hz, (Me_2CH), 3.80 (3H, *s*, OMe), 4.33–4.45 (2H, m, 2 × CH <), 5.95 (1H, *s*, H-3), 6.28 (1H, *d J* = 2.0 Hz, H-6), 6.50 (1H, *d*, *J* = 2.0 Hz, H-8), 6.83–6.95 (3H, *m*, H-2′,5′ and 6′). 8; a reddish oil, yield 530 mg. ^{1}H NMR (60 MHz, $CDCl_3$) δ: 1.30, 1.38 (6H, each *d*, *J* = 6.0 Hz, Me_2CH), 3.43 (3H, *s*, OMe), 4.38–4.68 (2H, *m*, 2 × CH <), 5.95 (1H, *s*, H-3), 6.25 (1H, *d*, *J* = 2.0 Hz, H-6), 6.65 (1H, *d*, *J* = 2.0 Hz, H-8), 6.88 (3H, *br s*, H-2′,5′, and 6′). Deisopropylation of 7 and 8 with BCl_3 gave 2 and 4, respectively. 2; mp 182–183° (EtOAc–C_6H_{14}), yellow prisms. MS *m/z* (rel. int.): 300 $[M]^+$ (100), 299 (13.4), 273 (16.2), 272 (93.6), 257 (22.5), 243 (7.3). 4; mp 208–210° (EtOAc–C_6H_{14}), yellow prisms. MS *m/z* (rel. int.): 300 $[M]^+$ (100), 299 (9.0), 273 (13.6), 272 (88.6), 257 (13.6).

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