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FLAVONOIDS OF *CHROMOLAENA ODORATA*

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Key Word Index—*Chromolaena odorata*; Compositae; flavonoids; methylated chalcones; 5,6,7-trimethoxy-4′-hydroxyflavanone, scutellarein tetramethyl ether; sinensetin.

Abstract—A dichloromethane extract of *Chromolaena odorata* has yielded 2′-hydroxy-3,4,4′,5′,6′-pentamethoxychalcone, 2′,4-dihydroxy-4′,5′,6′-trimethoxychalcone, an optically inactive flavanone, scutellarein tetramethyl ether and sinensetin, in addition to the previously reported 2′-hydroxy-4,4′,5′,6′-tetramethoxychalcone.

INTRODUCTION

Chromolaena odorata (L.) King & Robinson (syn. *Eupatorium odoratum* L.) has been the subject of chemical examination by several groups [1–5], constituents being reported including some sesquiterpenes, isosakuranetin, 2′-hydroxy-4,4′,5′,6′-tetramethoxychalcone (**6**)‡, salvigenin (**7**), lupeol and β-amyrin. In the course of systematic search for sesquiterpene lactones in the Compositae, we isolated from *Chromolaena odorata* the chalcones (**4**) and (**5**) in addition to (**6**), an optically inactive flavanone (**3**) and the flavones (**1**) and (**2**). Although chalcone (**5**) and flavanone (**3**) have been synthesized [6, 7], this appears to be the first report of their isolation from a natural source.

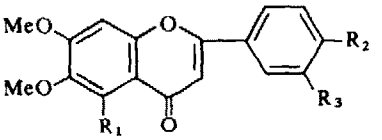
RESULTS AND DISCUSSION

The least polar substance (**6**), mp 140–142°, was identified as 2′-hydroxy-4,4′,5′,6′-tetramethoxychalcone by comparison of its physical properties with those reported in the literature [3] and additionally by converting it to salvigenin (**7**), identical in all respects to an authentic sample (mp, TLC, IR and NMR spectra).

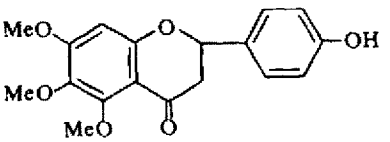
The molecular formula of (**5**), was established as $C_{20}H_{22}O_7$ by high resolution MS. Its UV spectrum was characteristic of a chalcone. The NMR spectrum revealed the presence of a chelated hydroxyl at 13.55 ppm which indicated its position *ortho* to the carbonyl. The presence of five methoxyls between 3.71 and 3.87 ppm was also clear from the NMR spectrum and three of these were located in ring A by comparing the results of electron impact MS on (**5**) and (**6**). Both (**5**) and (**6**) gave a high intensity peak at *m/e* 210 which could be attributed to cleavage α to the carbonyl function. That the other two methoxyls were in ring B was obvious from the pattern of NMR signals displayed at 6.77 *d* (J = 8.5 Hz, H-5), 7.17 *d* (J = 8.5 Hz, H-6) and 7.10 broad singlet (H-2). Final confirmation for this structure was obtained by converting (**5**) to sinensetin (**1**) by selenium dioxide oxidation.

Compound (**3**) had a UV spectrum characteristic of a flavanone. Also the NMR spectrum showed a doublet of doublets at 5.30 (J = 11.5, 5 Hz, H-2) and two overlapping proton signals at 2.90 ppm for H-3^{cis} and H-3^{trans}. In the NMR spectrum there were three methoxyls at 3.85, 3.92 and 4.00 ppm; a high intensity peak at *m/e* 210 in the high resolution MS suggested that all three were in ring A. Since ring B was monosubstituted at the 4′-position (A_2B_2 system of H-2′, H-3′, H-5′ and H-6′ at 6.90 and 7.30 ppm), the remaining oxygen function was placed as a hydroxyl which at 4′ was revealed by the IR spectrum as a broad band at 3400 cm^{-1}. The proposed structure was confirmed by conversion of (**3**) to (**6**) with diazomethane followed by treatment with acetic acid.

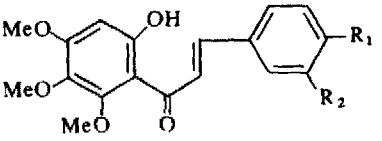
Compound (**4**), had a UV spectrum characteristic of a chalcone. Since its molecular formula $C_{18}H_{18}O_6$ (high resolution MS) was identical with that of flavanone (**3**) it was suspected that (**4**) was derived from (**3**). This was proved by treating (**4**) with conc H_2SO_4 when (**3**) was obtained in 90% yield.



(**1**) $R_1 = R_2 = R_3 = OMe$
(**2**) $R_1 = R_2 = OMe$ $R_3 = H$
(**7**) $R_1 = OH$ $R_2 = OMe$ $R_3 = H$



(**3**)



(**4**) $R_1 = OH$ $R_2 = H$
(**5**) $R_1 = R_2 = OMe$
(**6**) $R_1 = OMe$ $R_2 = H$

Flavanone (**3**) was optically inactive which is perhaps not surprising in view of the literature report [9] that optically active 4′-hydroxyflavanones containing a blocked 5-hydroxyl are very susceptible to racemization. However, the conformation of (**3**) was evident from the NMR spectrum which showed that ring B is equatorially substituted on ring C ($J_{2,3}^{trans}$ = 11.5 Hz, $J_{2,3}^{cis}$ = 5 Hz) as in all the flavanones reported up to 1970 [9].

‡ The name odoratin given by Bose *et al.* [3] to this chalcone is inappropriate as it is preempted by a triterpene [8].

In addition, two known flavones were isolated. The less polar one was identified as scutellarein tetramethyl ether (2) by converting it to salvigenin (7) [4] which was identical with an authentic sample in all respects (mp, TLC, IR and NMR spectra). The second flavone was identified as sinensetin (1) by comparing its physical properties with those reported in the literature [10]; its IR and NMR spectra were superimposable on those of an authentic sample.

EXPERIMENTAL

Mps are uncorr. NMR spectra were measured on a T-60 instrument (values given in ppm); low resolution mass spectra were obtained on a MS-30 mass spectrometer, high resolution mass spectra on a MS-902 mass spectrometer, UV spectra in EtOH, for preparative TLC Si gel G was used.

Extraction of Chromolaena odorata. Above ground parts of *C. odorata* (L.) King & Robinson wt. 1 kg, were extracted with CH_2Cl_2 (5 l.) for 24 hr. After evapn of the solvent, the residue was dissolved in 700 ml hot EtOH and diluted with 1 l. H_2O. It was then treated with 14 g lead acetate in 40 ml H_2O containing 4 ml HOAc and left overnight at room temp. The supernatant was filtered and coned under red. pres. to remove most of the EtOH when some precipitation occurred. It was extracted with CH_2Cl_2 (5 × 200 ml); removal of the solvent furnished a very viscous liquid (12 g) which was chromatographed over 500 g Al_2O_3 (Brockmann grade 1), the following fractions being collected: 1–5 (C_6H_6), 6–15 (C_6H_6–$CHCl_3$ 10:1), 16–25 (C_6H_6–$CHCl_3$ 1:1), 26–35 (C_6H_6–$CHCl_3$ 1:10), 36–45 ($CHCl_3$), 46–50 ($CHCl_3$–MeOH 99:1). Fractions 6–25 were a mixture of 3 compounds as indicated by TLC; these were separated by preparative TLC (C_6H_6–EtOAc, 9:1).

The least polar compound (**6**) (R_f 0.8) was crystallized from MeOH as orange needles, yield 0.215 g, mp 140–142°, (lit mp 142–144°) [3], IR, UV, MS and NMR as reported in the lit.

The second band (**5**) (R_f 0.7) was crystallized from EtOAc as orange needles, yield 0.235 g, mp 135–136° (lit mp 136°) [6]. IR (Nujol): 1630, 1580 and 1550 cm^{-1}; UV λ_{max}: 375 (log ε 4.38), 260 nm (log ε 4.11); NMR (CCl_4): 5 methoxyls between 3.71 and 3.87 (overlapping signals), 7.72 (H-α and H-β), 6.14 (H-3'), 6.77 *d* (J = 8.5 Hz, H-5), 7.17 *d* (J = 8.5 Hz, H-6), 7.10 *br s* (H-2) and a *br s* at 13.55 ppm (OH) which disappeared on D_2O exchange. MS: Calcd. for $C_{20}H_{22}O_7$: MW 374.1365. Found: 374.1346, other significant peaks at *m/e* (Comp, %) 210 ($C_{10}H_{10}O_5$, 100) 195 ($C_9H_7O_5$, 78.9), 167 ($C_8H_7O_4$, 24.7), 164 ($C_{10}H_{12}O_2$, 63.5), 151 ($C_9H_{11}O_2$, 37.8), 91 (C_7H_7, 43.8).

The third band (**4**) (R_f 0.50) was crystallized from EtOAc as orange needles, yield 0.205 g, mp 147–148°. IR ($CHCl_3$): 3400 (br), 1635, 1610 and 1550 cm^{-1}; UV λ_{max}: 370 (log ε 4.23) and 2.35 nm (log 3.95), NMR ($CDCl_3$): 3.77 (3H, OCH_3), 3.90 (6H, 2-OCH_3), 7.80 (H-α and H-β), 6.27 (H-3'), 6.87 *d* (J = 8.5 Hz, H-3 and H-5), 7.6 *d* (J = 8.5 Hz, H-2 and H-6) and a *br s* at 13.75 ppm (OH) which disappears on D_2O exchange. MS: Calcd for $C_{18}H_{18}O_6$: MW 330.1102. Found: 330.1094 (42.7%). Other significant peaks at *m/e* (Comp, %) 210 ($C_{10}H_{10}O_5$, 100), 195 ($C_9H_7O_5$, 82.1), 167 ($C_8H_7O_4$, 52.8), 120 (C_8H_8O, 7.1), 119 (C_8H_7O, 9.6), 91 (C_7H_7, 15.1).

Fractions 26–35 on further purification by preparative TLC (C_6H_6–EtOAc 5:1) yielded the flavanone (**3**) yield 0.250 g, mp 202–204° (lit. mp 190–192°) [7]. IR (Nujol): 3400 (br), 1650, 1580 and 1550 cm^{-1}; UV λ_{max}: 275 (log ε 4.12) and 320 nm (sh, log ε 3.54), NMR ($CDCl_3$): 3.85, 3.92 and 4.0 (3-methoxyls) 5.30 *dd* (J = 11.5, 5 Hz, H-2), 2.90 (2H overlapping signals H-3^{cis} and H-3^{trans}), 6.33 (H-8), 6.9 *d* (J = 8.5 Hz, H-3' and H-5'), 7.3 *d* (J = 8.5 Hz, H-2' and H-6'). MS: Calcd for $C_{18}H_{18}O_6$: MW 330.1102. Found: MW 330.1084. Other significant peaks at *m/e* (Comp, %) 210 ($C_{10}H_{10}O_5$, 89.8), 195 ($C_9H_7O_5$, 100) 167 ($C_8H_7O_4$, 54.6), 112 ($C_7H_4O_4$, 74.5), 149 ($C_8H_5O_3$, 17.5), 120 (C_8H_8O, 8.9), 9.1 (C_7H_7, 11.7).

Fractions 36–45 were a mixture of (**2**) and (**1**), these were separated on preparative TLC (C_6H_6–EtOAc 4:1). The less polar band (**2**) was crystallized from EtOAc yield 0.10 g, mp 140–141° (lit. mp 141–142°) [11, 12] spectral data as in lit.

The more polar band (**1**) was crystallized from MeOH–EtOAc to yield 0.60 g, mp 166–168° (lit. mp 166–168°) [10].

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