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# A NEW FLAVONE FROM *AGERATUM CONYZOIDES*

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**Key Word Index**—*Ageratum conyzoides*; Compositae: 5′-methoxynobiletin; heptamethoxyflavone.

**Abstract**—A new flavone has been isolated from *Ageratum conyzoides* and identified as 5,6,7,8,3′,4′,5′-heptamethoxyflavone on the basis of spectroscopic and degradative evidence and the assignment is confirmed by synthesis.

## INTRODUCTION

We recently reported the isolation from the stem and leaves of *Ageratum conyzoides* of sitosterol, stigmasterol, dotriacontene, 7-methoxy-2,2-dimethylchromen, including a new flavone conyzorigun (**1**) [1]. Since this herb is used in many parts of Nigeria to promote wound healing and because preliminary experiments with rabbits showed that the crude plant extract was significantly superior to vaseline gauze as a wound dressing material [2], we attempted to identify the substance responsible for promoting wound healing. The chromatographic fractions of the petrol extract of the stem and leaves of *A. conyzoides* that showed the greatest activity contained more than 90% of another new flavone.

## RESULTS AND DISCUSSION

After due allowance has been made for the substitutions in their B-ring, the NMR spectra of conyzorigun and the new flavone are very similar indeed. The latter has seven aromatic methoxy signals between δ 3.99 and 4.08, a two-proton singlet at 7.18 and a vinyl H at 6.62. However unlike conyzorigun the formation of yellow colour with dilute HCl was immediate, suggestive of a flavone nucleus. Moreover, it analysed for $C_{22}H_{24}O_9$ ($M^+$ 432) and therefore is one oxygen short of the trimethoxy-ring B substituted analogue of conyzorigun. Alkaline hydrolysis yielded'2,3,4,5-tetramethoxy-6-hydroxyacetophenone (in 92% yield) and 3,4,5-trimethoxybenzoic acid (25% was isolated, the remainder was not eluted from the column), the structures of both being confirmed by synthesis. The new flavone must therefore be 5′-methoxynobiletin (**2**).*

The assigned structure **2** was confirmed by synthesis. 3,4,5-Trimethoxybenzaldehyde was condensed with 2,3,4,5-tetramethoxy-6-hydroxyacetophenone to give a mixture which on the basis of spectra data must be the expected chalcone and flavanone. The mixture was then subjected to $SeO_2$ oxidation; the reaction product after chromatography gave 5,6,7,8,3′,4′,5′-heptamethoxyflavone identical in all respects with natural material.

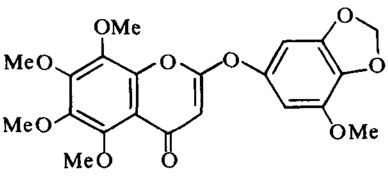
Preliminary results on the crystalline **2** are not as impressive as those with the oil as a wound dressing promoting substance. This may have something to do with the mode of testing. However the fact that nobiletin, 5,6,7,8,3′,4′-hexamethoxyflavone, is antifungal provides additional incentive to find an effective method of testing 5′-methoxynobiletin.

It is interesting that our new compound is one of the few flavones in herbaceous plants which are oxygenated at the 3′,4′ and 5′ positions [3].

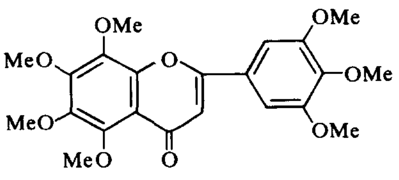
## EXPERIMENTAL

*Isolation of 5′-methoxynobiletin.* The air-dried, powdered stem and leaves of *A. conyzoides* was extracted with petrol and the concentrate taken in 90% MeOH. After concn to one-third the original vol., the remaining aq. alcoholic soln was extracted with $C_6H_6$. The $C_6H_6$ extract was chromatographed on Si gel column. In addition to eluting the previously reported compounds: sitosterol, stigmasterol, dotriacontene, 7-methoxy-2,2-dimethylchromen and conyzorigun [1], $Et_2O$–petrol (1:1) eluted 5′-methoxynobiletin (0.017% dry plant wt), mp 109–111°, $M^+$ 432. (Found: C, 61.01; H, 5.56. $C_{22}H_{24}O_9$ requires: C, 61.11; H, 5.56%). $\nu_{max}^{nujol}$ cm$^{-1}$: 1635, 1590, 1440, 1245, 1120, 850. $^1$H NMR ($CDCl_3$): δ 7.18 (2H, *s*, aromatic H), 6.62 (1H, *s*, vinyl H) and 7 aromatic OMe at 4.08 (3H, *s*), 4.03 (3H, *s*) and 3.99 (15H, *s*).

*Hydrolysis.* The above flavone (100 mg) in *n*-PrOH (10 ml) was refluxed with NaOH (6 g in 35 ml *n*-PrOH) for 6 hr. Work-up gave a gum which was taken up in $C_6H_6$. A solid



**1**



**2**

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*The same compound has been independently identified as a new flavone in *Eupatorium coelestinum* (see preceding paper).

which separated from the $C_6H_6$ soln as colourless crystals (13 mg) was characterized as 3,4,5-trimethoxybenzoic acid, mp 165–167° (lit. 167° [4]) on the basis of spectra and physical data and synthesis. The $C_6H_6$ soln on chromatography gave an oil (55 mg—92% of theory) which was confirmed to be 2,3,4,5-tetramethoxy-6-hydroxyacetophenone by comparison with a synthetic material. The 3,4,5-trimethoxybenzoic acid which dissolved in $C_6H_6$ was not eluted from the column.

*Synthesis.* 2,3,4,5-Tetramethoxy-6-hydroxyacetophenone and 3,4,5-trimethoxybenzaldehyde were synthesized by the methods of refs. [5] and [6], respectively. 2,3,4,5-Tetramethoxy-6-hydroxyacetophenone (110 mg) and 3,4,5-trimethoxybenzaldehyde (200 mg) were dissolved in MeOH (3 ml) and KOH (50%, 2 ml) added. The mixture was stirred at room temp. for 20 hr. Addition of $H_2O$ was followed by washing with $Et_2O$. The aldehyde-free aq. layer was acidified and the $Et_2O$ extract gave a mixture of chalcone and the flavanone. The mixture was heated with $SeO_2$ (55 mg) in amyl alcohol (3 ml) under reflux for 2 days. After filtration and steam distillation, an oil was obtained which was chromatographed on Si gel. 5,6,7,8,3′,4′,5′-Heptamethoxyflavone (35 mg) identical in all respects with the natural compound was eluted with $Et_2O$–petrol (1:2).

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