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PARACOTOIN DERIVATIVES FROM LEAVES OF *TICOREA PEDICELLATA**

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Key Word Index—*Ticorea pedicellata*; Rutaceae; 4,5-dimethoxyparacotoin; 4,5,2′-trimethoxyparacotoin; 4,2′-dimethoxyparacotoin; chemotaxonomy.

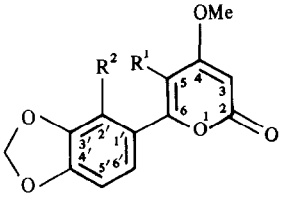
Abstract—Three new paracotoin derivatives have been isolated from the leaves of *Ticorea pedicellata* and identified as 4,5-dimethoxyparacotoin, 4,5,2′-trimethoxyparacotoin and 4,2′-dimethoxyparacotoin by full spectral analysis. The chemotaxonomic implications of the occurrence of paracotoin-type compounds in the Rutaceae are briefly discussed.

INTRODUCTION

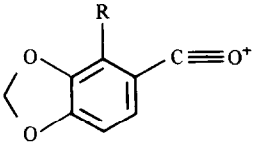
The small genus *Ticorea* Aubl., belonging to the tribe Cusparieae (Rutaceae), is found in the rain forests of French Guyana [1]. Compared with many other tribes of the Rutaceae, the Cusparieae has not been widely investigated and, as far as we can ascertain, there are no reports of any phytochemical studies on *Ticorea*. In this paper we report the isolation of three novel paracotoin derivatives from the leaves of *T. pedicellata* Dec. Compounds of this type have not previously been recorded in the Rutaceae and their presence is of considerable chemotaxonomic interest.

RESULTS AND DISCUSSION

Three compounds were obtained from the leaves by initial extraction into ethanol and subsequent partitioning into chloroform followed by column chromatography. The major compound, Ti-1 (yield 0.0004%), analysed for $C_{14}H_{12}O_6$. The IR spectrum showed a strong band at 1740 cm^{-1} suggesting the presence of a lactone carbonyl. The ^1H NMR spectrum revealed signals for all 12 protons. Signals for three aromatic protons, showing both *ortho*- and *meta*-coupling, together with a 2H singlet at δ6.01 were typical of a substituted piperonyl system and this was confirmed by the presence of a strong fragment at *m/z* 121 in the electron-impact mass spectrum. The remaining signals consisted of two methoxyl resonances at δ3.91 and 3.66 and a 1H singlet at δ5.54. These data suggested that the non-piperonyl moiety was a dimethoxy unsaturated α-pyrone. The strongly shielded resonance for the single lactone-ring proton required its assignment to C-3, α to the carbonyl, leaving the two methoxyl groups and attachment to the piperonyl ring to fill C-4 to C-6. Placement of the point of attachment at C-6 was indicated by the occurrence of the base peak *m/z* 149 (**5**) in the electron-impact mass spectrum. This fragment could only be derived if C-6 was linked to the lactone-ring oxygen and leads to the assignment of structure **2** to Ti-1. This compound is closely related to the known 4-methoxyparacotoin (**1**) (λ_{max} 336 nm, ν_{max} 1739 cm^{-1}) which has been isolated from several species of the genus *Aniba* (Lauraceae) [2].



	R^1	R^2
1	H	H
2	OMe	H
3	OMe	OMe
4	H	OMe



	R
5	H
6	OMe

*Part 17 in the series "Chemosystematics in the Rutaceae". For Part 16 see Waterman, P. G. and Hussain, R. A. (1983) *Bot. J. Linn. Soc.* **86**, 227.

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The ^{13}C NMR spectrum of **2** was in complete agreement with the proposed structure. Resonances for the piperonyl ring system were established by comparison with published data [3]. For the lactone ring, the resonances at δ_C 162.1 and 167.7 could be assigned to C-2 and C-4, with the occurrence of the carbonyl resonance at less than 170 ppm being further support for an α-lactone rather than a γ-lactone [4]. The highly shielded doublet at δ_C 89.1 was typical of C-3 of a C-4 oxygenated coumarin [5], while the deshielded position of one of the methoxyl resonances (δ_C 60.8) required its placement at C-5, with both *ortho* positions substituted [6].

The second most abundant compound, Ti-4 (yield 0.0002%), analysed for $C_{15}H_{14}O_7$ and gave UV and IR spectra similar to **2**. The major changes in the ^1H NMR spectrum were a third methoxyl resonance at δ4.00 and a simplification of the aromatic region by the loss of one proton, leaving an AB quartet for two *ortho*-coupled protons. These data suggested that Ti-4 was **3**, the 2′-methoxy derivative of **2** and this was confirmed by the electron-impact mass spectrum which gave a base peak at *m/z* 179 (**6**).

A third compound, Ti-3, was obtained in trace amounts only and analysed for $C_{14}H_{12}O_6$, identical to **2**. High-field ^1H NMR revealed two methoxyl resonances at δ4.03 and 3.81. The former of these was typical of the 2′-methoxy signal in **3** and together with the occurrence of a simple AB quartet (J = 8 Hz) in the aromatic region and a major fragment at *m/z* 179 in the electron-impact mass spectrum indicated that Ti-3 had the same 2-methoxypiperonyl system as **3**. This left only a single methoxyl for the lactone ring which, in the light of signals at δ5.49 and 6.71 (1H each) showing *meta*-coupling (J = 2 Hz) similar to that seen in 4-methoxyparacotoin [7], must be assigned structure **4**.

Finally the structure of **2** was further confirmed by means of ^1H NMR experiments using the lanthanide shift reagent Eu(fod)$_3$. With steric hindrance inhibiting the binding of the shift reagent to the *ortho*-situated methoxyl groups at C-4 and C-5, observed effects were solely the product of interaction of Eu(fod)$_3$ with the C-2 carbonyl. As anticipated from previous experiments with coumarins [8], the greatest effect was seen at H-3, with the effect on H-2′ and H-6′ *ca* 30% of this level. The much smaller relative shift for the 4-methoxyl group can be attributed to the very large angle between this substituent and the Eu–O=C bond. The shifts for all protons, which compared well with calculated values [8], are given in the Experimental.

The isolation of **2**–**4** from *T. pedicellata* is of considerable chemotaxonomic interest. Whilst these three compounds appear to be novel, and are of a type not previously recorded in the Rutaceae, the parent compounds of the group, 6-phenylpyran-2-one, paracotoin and 4-methoxyparacotoin (**1**), are highly characteristic products of the genus *Aniba* (Lauraceae) [9], and they and related styrylpyran-2-ones are found in Lauraceae, Annonaceae, Piperaceae and the more primitive Psilopsida [9]. The co-occurrence of various classes of 1-benzyltetrahydroisoquinoline alkaloids in the Rutaceae and in primitive families of the Magnoliidae (Polycarpicae), such as the Lauraceae and Annonaceae, has been cited as evidence for a direct phylogenetic link between these taxa [10, 11]. Now the co-occurrence of 6-phenylpyran-2-ones offers further biochemical evidence, biogenetically unrelated to that of the alkaloids, that supports the proposed relationship between the Magnoliidae and Rutaceae.

EXPERIMENTAL

Plant material. T. pedicellata was collected in August 1981 from the Region de Saül, French Guyana. A voucher specimen, C. Moretti 1234, has been deposited at the herbarium of O.R.S.T.O.M. in Cayenne, French Guyana.

Extraction and isolation of compounds. Ground leaves (1.5 kg) were extracted with petrol (bp 40–60°) followed by EtOH. The conc. EtOH extract was washed with acid and then base, and finally washed with $CHCl_3$ to give a crude mixture (1.57 g). This mixture was subjected to CC on Al_2O_3 (Woelm, activity II–III). Elution with C_6H_6–$CHCl_3$ (1:1) and $CHCl_3$ gave a mixture of blue fluorescent compounds which, on recrystallization from MeOH, gave Ti-1 (**2**, 55 mg). Repeated CC of the supernatant yielded a blue fluorescent band which on recrystallization from MeOH gave Ti-4 (**3**, 30 mg). Subsequent recrystallization of the supernatant of Ti-4 from $CHCl_3$ gave Ti-3, in trace amounts only.

4,5-*Dimethoxyparacotoin* (**2**). Recrystallized as needles from MeOH, mp 184°. Found $[M]^+$ 276.0610; $C_{14}H_{12}O_6$ requires 276.0634. UV λ_{max}^{EtOH} nm: 236, 334. IR ν_{max}^{KCl} cm^{-1}: 1740. ^1H NMR (360 MHz, $CDCl_3$): δ7.58 (1H, *dd*, J_1 = 8.3 Hz, J_2 = 1.8 Hz, H-6′), 7.52 (1H, *d*, J = 1.8 Hz, H-2′), 6.86 (1H, *d*, J = 8.3 Hz, H-5′), 6.01 (2H, *s*, O–CH_2–O), 5.54 (1H, *s*, H-3), 3.91 (3H, *s*, OMe-4), 3.66 (3H, *s*, OMe-5). ^{13}C NMR (90.56 MHz, $CDCl_3$): δ167.7 (*s*, C-4), 162.1 (*s*, C-2), 150.6 (*s*, C-6), 149.1, 147.9 (2 × *s*, C-3′ and C-4′), 134.0 (*s*, C-5), 124.0 (*s*, C-1′), 122.8 (*d*, C-6′), 108.3, 108.0 (2 × *d*, C-2′ and C-5′), 101.4 (*t*, O–CH_2–O), 89.1 (*d*, C-3), 60.8 (*q*, OMe-5), 56.4 (*q*, OMe-4). EIMS (probe) 70 eV, *m/z* (rel. int.): 276 $[M]^+$ (79), 261 $[M-Me]^+$ (36), 248 $[M-CO]^+$ (14), 233 $[M-CO-Me]^+$ (55), 149 $[C_8H_5O_3]^+$ (100), 121 $[C_7H_5O_2]^+$ (37). ^1H NMR–Eu(fod)$_3$ experiment (90 MHz, $CDCl_3$, molar ratio of Eu(fod)$_3$ to **2** *ca* 0.42, shifts quoted relative to a value of 1.0 for H-3 [8]): 4-OMe (0.09), 5-OMe (0.16), H-2′ (0.26), 3′,4′–O–CH_2–O (0.04), H-5′ (0.07), H-6′ (0.30).

4,5,2′-*Trimethoxyparacotoin* (**3**). From MeOH as an amorphous solid. Found $[M]^+$ 306.0745; $C_{15}H_{14}O_7$ requires 306.0739. IR ν_{max}^{KCl} cm^{-1}: 1730. ^1H NMR (90 MHz, $CDCl_3$): δ6.90, 6.58 (2H, AB*q*, J = 8 Hz, H-5′ and H-6′), 6.00 (2H, *s*, O–CH_2–O), 5.58 (1H, *s*, H-3), 4.00 (3H, *s*, OMe-2′), 3.90 (3H, *s*, OMe-4), 3.55 (3H, *s*, OMe-5). EIMS (probe) 70 eV, *m/z* (rel. int.): 306 $[M]^+$ (84), 291 $[M-Me]^+$ (9), 278 $[M-CO]^+$ (2), 276 $[M-OMe]^+$ (34), 263 $[M-CO-Me]^+$ (59), 179 $[C_9H_7O_4]^+$ (100).

4,2′,-*Dimethoxyparacotoin* (**4**). From MeOH as an amorphous solid. Found $[M]^+$ 276.0623; $C_{14}H_{12}O_6$ requires 276.0634. ^1H NMR (400 MHz, $CDCl_3$): δ7.45, 6.61 (2H, AB*q*, J = 8 Hz, H-5′ and H-6′), 6.71, 5.49 (2H, AB*q*, J = 2 Hz, H-5 and H-3), 6.00 (2H, *s*, O–CH_2–O), 4.03 (3H, *s*, OMe-2′), 3.81 (3H, *s*, OMe-4). EIMS (probe) 70 eV, *m/z* (rel. int.): 276 $[M]^+$ (100), 261 $[M-Me]^+$ (2), 248 $[M-CO]^+$ (98), 233 $[M-CO-Me]^+$ (51), 179 $[C_9H_7O_4]^+$ (52).

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REFERENCES

1. Lemée, A. (1952) *Flore de la Guyane Française*, Tome II. Imprimerie Commerciale Administrative, Brest.
2. Mors, W. B., Taveira Magalhaes, M. and Gottlieb, O. R. (1962) *Fortschr. Chem. Org. Naturst.* **20**, 131.
3. Wehrli, F. W. and Nishida, T. (1979) *Fortschr. Chem. Org. Naturst.* **36**, 70.

4. Pelter, A., Ward, R. S. and Gray, T. I. (1976) *J. Chem. Soc. Perkin Trans.* 1, 2475.
5. Khalid, S. A. and Waterman, P. G. (1983) *Phytochemistry* **22**, 1001.
6. Panichpol, K. and Waterman, P. G. (1978) *Phytochemistry* **17**, 1363.
7. Rezende, C. M. A. de M., von Bulow, M. V., Gottlieb, O. R., Pinho, S. L. V. and Da Rocha, A. I. (1971) *Phytochemistry* **10**, 3167.
8. Gray, A. I., Waigh, R. D. and Waterman, P. G. (1978) *J. Chem. Soc. Perkin Trans.* 2, 391.
9. Gottlieb, O. R. (1972) *Phytochemistry* **11**, 1537.
10. Hegnauer, R. (1973) *Chemotaxonomie der Pflanzen*, Vol. 6, p. 174. Birkhäuser, Basle.
11. Waterman, P. G. and Khalid, S. A. (1981) *Biochem. Syst. Ecol.* **9**, 45.

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FLAVANONES FROM *HELICHRYSUM THAPSUS*

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Key Word Index—*Helichrysum thapsus*; Compositae; flavanones; prenylated flavanones; 3α-hydroxy-6-geranyl-pinocembrin.

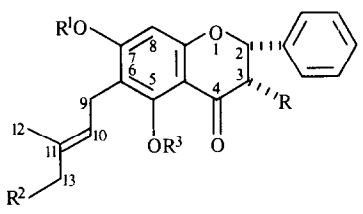
Abstract—The aerial parts of *Helichrysum thapsus* afforded three new flavanone derivatives all derived from pinocembrin.

In continuation of our studies of representatives of the large genus *Helichrysum* (Compositae, tribe Inuleae) we now have investigated *H. thapsus* (O. Kuntze) Moeser. The polar fractions contained a complex mixture of flavanones which could be separated by a combination of repeated TLC and HPLC. Finally four compounds were obtained, the known prenylated flavanone **6** [1], the 3α-hydroxy derivative **1**, the geranyl derivative **4** and the β-acetoxy flavanone **5**.

The structure of **1** followed from the molecular formula, the ^{1}H NMR spectral data (Table 1) and those of the acetates **2** and **3** obtained by acetylation **1**. The nature of the side chain could be deduced from the typical ^{1}H NMR signals which were nearly identical with those of **6** where the position of the prenyl residue was established unambiguously [1]. The signals of H-12 and H-13 collapse to a singlet if the side chain is at C-8 [1] while compounds with a prenyl group at C-6 showed separated methyl signals. The presence of a 3α-hydroxy group was deduced from the chemical shift and the coupling of the doublet at δ 4.75. The latter was shifted down field in the spectrum of the corresponding acetates **2** and **3**. As the second doublet in the spectrum of **2** was slightly broadened the signals of H-2 and H-3 could be assigned. It may be of interest to note that the chemical shifts of H-3 and H-8 differed in the spectra of **2** and **3** obviously due to the presence of a hydrogen bond in **2**.

The molecular formula of **4** was $C_{25}H_{28}O_5$ indicating that **4** may differ from **1** by an additional prenyl group. The ^{1}H NMR spectrum (Table 1), however, clearly showed that the prenyl side chain was replaced by a geranyl residue as followed from the characteristic side chain signals which were close to those of similar phenolic geranyl derivatives. The presence of a 3α-hydroxy group again could be deduced from the couplings of a pair of doublets which showed the same chemical shifts as **1**. Accordingly, **4** was closely related to **1** and most likely the side chain again was at C-6 though the position of the latter could not be established with certainty as acid catalysed cyclization failed.

The structure of **5** also followed from the molecular formula and the ^{1}H NMR spectrum (Table 1) which



	1	2	3	4	5	6
R	αOH	αOAc	αOAc	αOH	βOAc	H
R^1	H	Ac	Ac	H	H	H
R^2	H	H	H	$CH_2CH{=}CMe_2$	H	H
R^3	H	H	Ac	H	H	H