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# MONOTERPENE ALKALOIDS, IRIDOIDS AND PHENYLPROPANOID GLYCOSIDES FROM *OSMANTHUS AUSTROCALEDONICA**

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IN HONOUR OF THE RETIREMENT OF PROFESSOR ANDRÉ CAVÉ

**Key Word Index**—*Osmanthus austrocaledonica*; Oleaceae; monoterpene alkaloids; iridoids; flavonoids; phenylpropanoid glycosides; structure elucidation.

**Abstract**—Six monoterpene alkaloids have been isolated from the aerial parts of *Osmanthus austrocaledonica*. Two of these, dihydrojasminine and austrodimerine, are novel compounds. Their structures have been elucidated on the basis of their spectral data and molecular modeling. Seven iridoids and six phenolic compounds have been also isolated from the same plant. Two of these, austrosmoside and 6′-*O*-β-(*E*)-cinnamoylverbascoside, are novel compounds. Their structures have been deduced from their spectral data and confirmed by chemical correlations. 

## INTRODUCTION

The genus *Osmanthus* Lour. belongs to the family *Oleaceae* and includes some 30 species of small trees and shrubs from Northern America, Eastern Europe, South-east Asia and the Pacific Islands [2, 3]. Several Asian species have been studied from a chemical point of view and shown to contain lignans, iridoids and phenylpropanoid glycosides [4–11].

*O. austrocaledonica* (Vieill.) Knolb. is a shrub endemic to New Caledonia, which was first described as belonging to the genus *Notolaea* Vent. by Vieillard [12], but whose position within the genus *Osmanthus* is now widely accepted [13–15]. Preliminary chemical tests (JP and TS) conducted on this species indicated the presence of alkaloids and iridoids in the aerial parts. These early results prompted us to study the alkaloidal and neutral contents of this shrub, in a continuation of our investigations on New Caledonian plants.

## RESULTS AND DISCUSSION

Classical extraction conducted in the presence of ammonia followed by repeated column chromatography led to the isolation of six monoterpene alkaloids. Four of them were identified as the known 4-methyl-5,5′-[(1-methyltrimethylene)di](methylnicotinate) [16], 4,4′-bis-methyl-5,5′-[(1-methyltrimethylene)di](methylnicotinate) [16], 4-hydroxy-β-phenylethyl 5-ethyl-3-methoxycarbonyl-4-pyridinyl acetate [17], and jasminine (**1**) [17–19] previously isolated from various *Oleaceae* species. The two remaining alkaloids, dihydrojasminine (**2**) and austrodimerine (**3**), were novel.

Alkaloid **2**, $[\alpha]_D^{20}+300°$, exhibited an $[M]^+$ at m/z 222.100440 (HREIMS) corresponding to the empirical formula $C_{11}H_{14}N_2O_3$. Its UV spectrum showed absorptions corresponding to a 1,4-dihydropyridine system [20]. The $^1H$ NMR spectrum exhibited a double doublet ($J = 5$ and 3.5 Hz) at $\delta$ 6.24 exchangeable upon $D_2O$ addition, and two doublets at $\delta$ 7.22 ($J = 5$ Hz) and 5.93 ($J = 3.5$ Hz) transformed into singlets upon deuterium exchange, accounting for the NH and the two α-$^1H$ of a 3,5-disubstituted-1,4-dihydropyridine unit. The coupling patterns of the remaining signals appeared to be similar to those found in the lactam ring of jasminine (**1**) (Table 1) except for the

* Part 145 in the series "Plants of New-Caledonia". For part 144, see Ref. [1].

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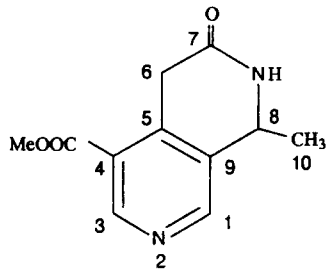
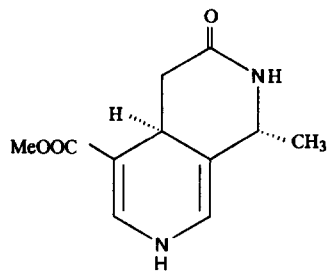


**1**



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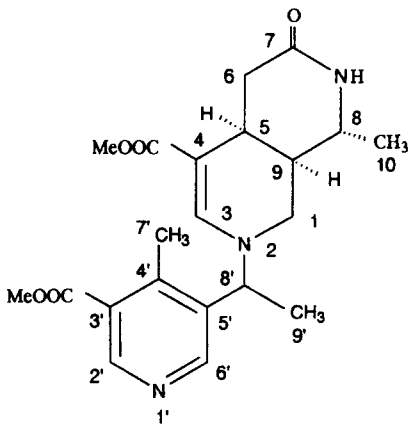

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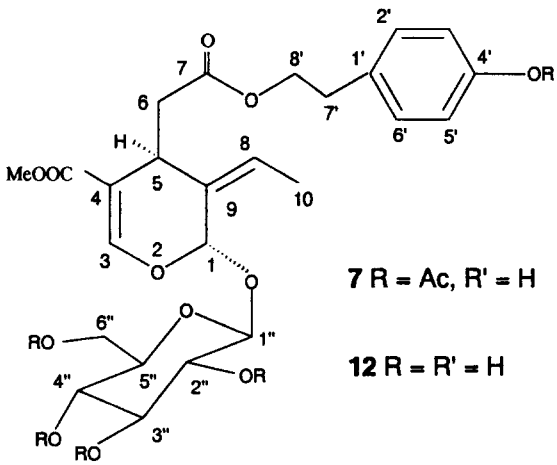
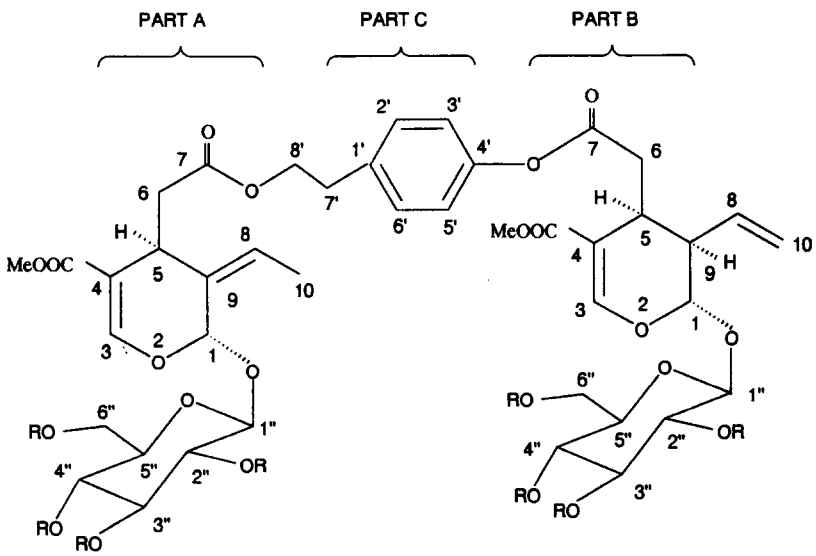


**7** R = Ac, R' = H

**12** R = R' = H

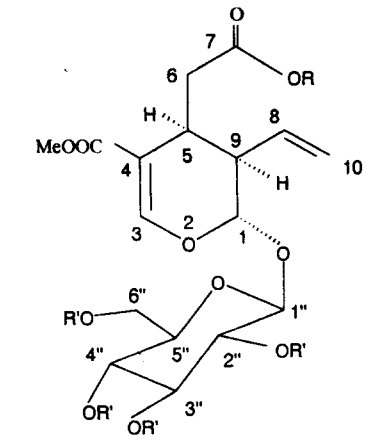


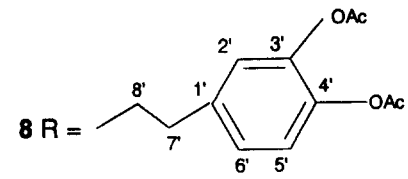

**4** R= H

**6** R = Ac

shift differences expected when an aromatic ring is present in the latter. On the basis of these data, the structure of **2** was determined as 2,5-dihydrojasminine. The relative configuration at C-9 and C-8 was established on the basis of a NOESY cross-peak, observed between H-5 and $CH_3$-10.

Alkaloid **3**, $[\alpha]_D^{20}+75°$, exhibited an $[M]^+$ at $m/z$ 401.195071 (HREIMS) corresponding to the empiri-

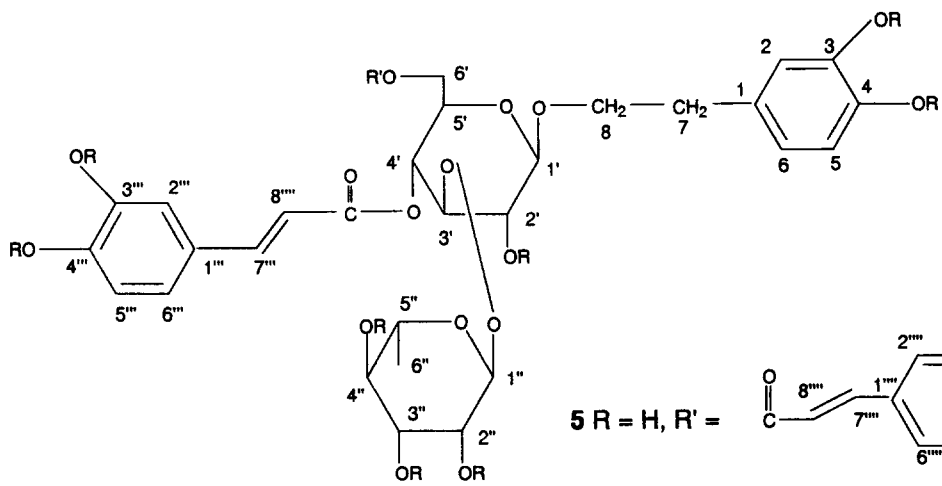




**8** R = R' = Ac

**9** R = $CH_3$ R' = Ac

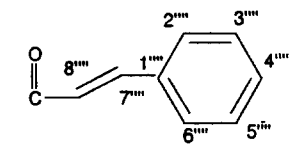
**13** R = $CH_3$ R' = H



**5** R = H, R' =



**11** R = Ac, R' =



**10** R = R' = H

cal formula $C_{21}H_{27}N_3O_5$, and two prominent fragment ions at *m/z* 223 ($C_{11}H_{15}N_2O_3$) and 178 ($C_{10}H_{12}NO_2$). These two ions suggested a dimeric structure made up of a tetrahydrojasminine moiety and a carbomethoxy-methyl-ethyl-pyridine moiety [16]. In support of this, two series of signals were observed in the $^1H$ NMR (Table 1) and in the $^{13}C$ NMR spectra. The first series was attributable to an *N*-substituted-1,2,5,9-tetrahydrojasminine unit, and the second to a 3-carbomethoxy-5-ethyl-4-methyl pyridine system previously encountered in several *Oleaceae* alkaloids [16]. The position of linkage between N-2 on the tetrahydrojasminine moiety and C-8′ on the pyridine moiety was unambiguously deduced from cross peaks observed on the 2D phase sensitive NOESY spectrum (mixing time 700 ms) between H-3 and H-8′, and H-3 and $CH_3$-9′. Further information on the linkage position was obtained from the results of the long range $^1H$–$^{13}C$ correlations in the HMBC spectrum, where it was clear that the proton at $\delta$ 4.77 (H-8′) had long range coupling with the carbon signals at $\delta$ 142 and 39.4 (C-3 and C-1, respectively). The structure of this new alkaloid, named austrodimerine, was therefore established as **3**. The relative configurations at C-5 and C-9 were determined on the basis of the NOESY cross-peak observed between H-5 and H-9. In addition, the *cis* relationship between H-5 and H-9 was in full agreement with that previously established for the iridoid precursors of the monoterpene alkaloids [21, 22]. The relative configuration at C-9 and

Table 1. $^1$H NMR spectral data of compounds **1**–**3*** (270 MHz, $CDCl_3$, TMS)

| H | 1 | 2 | 3 |
|---|---|---|---|
| 1 | 8.62 (*s*) | 5.93 (*d*, 3.5) | 2.83 (*m*), 3.05 (*m*) |
| 2 | | 6.24 (*dd*, 5, 3.5) | |
| 3 | 9.09 (*s*) | 7.22 (*d*, 5) | 7.59 (*s*) |
| 5 | | 3.80 (*dd*, 11, 5) | 3.05 (*m*) |
| 6a | 4.16 (*d*, 21) | 2.92 (*dd*, 17, 5) | 2.83 (*m*) |
| 6b | 4.00 (*d*, 21) | 2.29 (*dd*, 17, 11) | 1.94 (*m*) |
| CO-NH | 7.56 (*s*) | 6.44 (*s*) | 6.41 (*s*) |
| 8 | 4.80 (*q*, 7) | 3.95 (*q*, 6) | 3.89 (*qd*, 7, 0.5) |
| 9 | | | 1.94 (*m*) |
| $CH_3$-10 | 1.60 (*d*, 7) | 1.29 (*d*, 6) | 1.09 (*d*, 7) |
| $CH_3OOC_{-4}$ | 3.96 (*s*) | 3.70 (*s*) | 3.71 (*s*) |
| 2′ | | | 8.98 (*s*) |
| 6′ | | | 8.56 (*s*) |
| $CH_3$-7′ | | | 2.55 (*s*) |
| 8′ | | | 4.77 (*q*, 7) |
| $CH_3$-9′ | | | 1.58 (*d*, 7) |
| $CH_3OOC_{-4'}$ | | | 3.96 (*s*) |

* Multiplicities and coupling constants (in Hz) are in parentheses.

C-8 was established by semiempirical quantum mechanics calculations and $J$ coupling constants. Calculation of the energy was performed using the MOPAC AM1 method with geometry optimization. The lowest energy structures were calculated for the two isomers, with $CH_3$-10 in the $\alpha$ or $\beta$ position, **3** or **3′**, respectively. The dihedral angle between H-9 and H-8 was determined for these two stereoisomers, and was found to be $-78.5°$ for **3** and $48.9°$ for **3′**. For these values, the coupling constants were calculated using Karplus equations and were found 0.8 Hz for **3** and 4.4 Hz for **3′**. The relative stereochemistry between C-9 and C-8 was therefore established as in **3** since there is a good agreement between the measured and the calculated coupling constants for this isomer ($J_{cal} = 0.8$; $J_{mes} = 0.5$ Hz). The absolute configurations of compounds **2** and **3** could not be determined, due to the high instability of these two alkaloids and to the small amounts of products isolated.

The known artifactual origin of numerous monoterpene alkaloids [23] led us to repeat the extraction using $Na_2CO_3$ as the alkaline agent. The same alkaloids were isolated, so an artifactual origin of these alkaloids could be excluded.

Finally, the fractionation of a methanolic extract of the aerial parts afforded eight iridoids and six phenolic compounds. Seven of the iridoids were identified with the known loganin [24], 7-oxologanin [25, 26], loganic acid [24], ligstroside [27], oleuropein [27], secoxyloganin [28, 29] and with the iridoid GI5 previously isolated from *Fraxinus americana* [27], on the basis of their spectral data and those of their acetyl derivatives. One of the iridoids isolated, austrosmoside (**4**), was a new compound. Phenolic products were identified with the known 7-*O*-$\beta$-D-glucosylapigenin [30], 4′-*O*-$\beta$-D-glucosylapigenin [30], 7-*O*-$\beta$-D-neohesperidosylapigenin [30], salidroside [27], and verbascoside [31], while 6′-*O*-(*E*)-cinnamoylverbascoside (**5**) was a novel phenylpropanoid glycoside.

Austrosmoside (**4**) exhibited in its HRFAB mass spectrum a pseudomolecular ion, $[M+H]^+$, at 911.31846, indicating the empirical formula $C_{42}H_{54}O_{22}$. The $^1$H NMR spectrum exhibited signals accounting for an ethylidene, a vinyl, a *p*-disubstituted aromatic ring, two glucose anomeric protons, and two carbomethoxy groups, in agreement with a bis-iridoid structure. Acetylation afforded an octacetyl derivative **6**, which on FAB-MS gave pseudomolecular ions at $m/z$ 1269 $[M+Na]^+$ and 1247 $[M+H]^+$, corresponding to the empirical formula $C_{58}H_{70}O_{30}$. The $^1$H NMR spectrum of **6** exhibited two series of signals (Table 2). The first series was identical with the signals observed in the spectrum of pentacetyl-ligstroside (**7**). The second one was closely related to the spectra of hexacetyl-oleuroside (**8**) and of tetracetyl-secoxyloganin methyl ester (**9**) [26]. Nevertheless, striking differences were observed regarding the chemical shifts of the $CH_2$-6 signals of **6** ($\delta$ 2.55 and 3.20) when compared to those of **8** ($\delta$ 2.28 and 2.96) and **9** ($\delta$ 2.28 and 2.96). These differences clearly established esterification of the carboxy group at C-6 on the secoxyloganin part of austrosmoside and established the presence of a phenolic function. This permitted the structure **4** to be assigned to this novel compound. Finally, the chemical structure was confirmed by chemical correlation. Methanolysis of **4** afforded ligstroside (**12**) and secoxyloganin methyl ester (**13**). During the preparation of this manuscript a new secoiridoid glucoside with a very similar structure, but with the presence of an additional glucoside unit was isolated from *Jasminum polyanthum* [32].

6′-*O*-(*E*)-Cinnamoylverbascoside (**5**) on

Table 2. $^1$H NMR spectral data of compounds **6–9*** (270 MHz, $CDCl_3$, TMS)

| H | 6 | 7 | 8 | 9 |
|---|---|---|---|---|
| Part A | | | | |
| 1 | 5.70 (*s*) | 5.69 (*s*) | | |
| 3 | 7.44 (*s*) | 7.47 (*s*) | | |
| 5 | 3.94 (*dd*, 8, 4) | 3.73 (*s*) | | |
| 6a | 2.40 (*dd*, 16, 8) | 2.40 (*dd*, 16, 8) | | |
| 6b | 2.72 (*dd*, 16, 4) | 2.73 (*dd*, 16, 4) | | |
| 8 | 5.99 (*q*, 7) | 5.99 (*q*, 7) | | |
| $CH_3$-10 | 1.69 (*d*, 7) | 1.67 (*d*, 7) | | |
| $CH_3OOC_4$ | 3.75 (*s*) | 3.73 (*s*) | | |
| 1″ | 5.01 (*d*, 8) | 5.03 (*d*, 8) | | |
| 2″ | 5.18–5.13 (*m*)† | 5.18–5.13 (*m*)† | | |
| 3″ | 5.18–5.13 (*m*)† | 5.18–5.13 (*m*)† | | |
| 4″ | 5.18–5.13 (*m*)† | 5.18–5.13 (*m*)† | | |
| 5″ | 3.76 (*m*)† | 3.78 (*m*)† | | |
| 6″a | 4.27 (*dd*, 12, 5) | 4.32 (*dd*, 13, 5) | | |
| 6″b | 4.11 (*dd*, 12, 3) | 4.11 (*dd*, 13, 3) | | |
| Part B | | | | |
| 1 | 5.25 (*d*, 3) | | 5.23 (*d*, 3) | 5.27 (*d*, 3) |
| 3 | 7.40 (*d*, 2) | | 7.46 (*d*, 2) | 7.47 (*d*, 2) |
| 5 | 3.29 (*dtd*, 9, 5, 3) | | 3.15 (*dtd*, 9, 5, 2) | 3.18 (*dtd*, 9, 5, 2) |
| 6a | 2.55 (*dd*, 17, 9) | | 2.28 (*dd*, 16, 9) | 2.28 (*dd*, 16, 9) |
| 6b | 3.20 (*dd*, 17, 5) | | 2.96 (*dd*, 16, 5) | 2.96 (*dd*, 16, 5) |
| 8 | 5.55 (*ddd*, 17, 10, 9) | | 5.45 (*ddd*, 16, 11, 10) | 5.53 (*dt*, 17, 10) |
| 9 | 2.94 (*m*) | | 2.76 (*ddd*, 10, 5, 3) | 2.85 (*ddd*, 10, 5, 3) |
| 10a | 5.15–5.25 (*m*)† | | 5.11 (*d*, 11) | 5.23 (*d*, 10) |
| 10b | 5.25–5.30 (*m*)† | | 5.16 (*d*, 16) | 5.21 (*d*, 17) |
| $CH_3OOC$-4 | 3.65 (*s*) | | 3.65 (*s*) | 3.68 (*s*) |
| 1″ | 4.85 (*d*, 8) | | 4.84 (*d*, 8) | 4.88 (*d*, 8) |
| 2″ | 5.00 (*dd*, 9, 8) | | 5.01 (*dd*, 9, 8) | 5.00 (*dd*, 9, 8) |
| 3″ | 5.23 (*t*, 9) | | 5.20 (*t*, 9) | 5.18 (*t*, 9) |
| 4″ | 5.13–5.18 (*m*)† | | 5.08 (*t*, 9) | 5.11 (*t*, 9) |
| 5″ | 3.79 (*m*)† | | 3.72 (*m*) | 3.73 (*m*) |
| 6″a | 4.10–4.30 (*m*)† | | 4.28 (*dd*, 12, 5) | 4.29 (*dd*, 12, 5) |
| | 4.10–4.30 (*m*)‡ | | 4.11 (*dd*, 12, 2) | 4.14 (12, 2) |
| Part C | | | | |
| 2′ | 7.18 (*d*, 9) | 7.21 (*d*, 9) | 7.01 (*d*, 1.5) | |
| 3′ | 6.97 (*d*, 9) | 7.02 (*d*, 9) | | |
| 5′ | 6.97 (*d*, 9) | 7.02 (*d*, 9) | 7.06 (*d*, 9) | |
| 6′ | 7.18 (*d*, 9) | 7.21 (*d*, 9) | 7.10 (*dd*, 9, 1.5) | |
| 7′ | 2.90 (2H, *t*, 7) | 2.91 (2H, *t*, 7) | 2.91 (2H, *t*, 7) | |
| 8′ | 4.26–4.16 | 4.27 (*dt*, 11, 7) | 4.24 (2H, *t*, 7) | |
| | (2H, *m*)† | 4.18 (*dt*, 11, 7) | | |
| $CH_3OOC$-7 | | | | 3.65 (*s*) |

* Multiplicities and coupling constants (in Hz) are in parentheses.
† Signal patterns unclear due to overlapping.

HRFABMS gave a pseudomolecular ion at *m/z* 755.25508 $[M+H]^+$, suggesting the empirical formula $C_{38}H_{42}O_{16}$. The $^1$H NMR spectrum was closely related to that of verbascoside (**10**), with two main differences: (i) an additional series of signals corresponding to an (*E*)-cinnamoyl unit appeared in the olefinic and aromatic regions of the spectrum of **5**; (ii) the $CH_2$-6′ resonances of the glucose unit of **5** were clearly individualised as two double doublets at $\delta$ 4.32 and 4.27, while the corresponding signals in **10** resonated in the non-anomeric sugar protons region of the spectrum ($\delta$ 3.20 to 4.00). Acetylation furnished an octa-acetyl derivative **11**. Thorough study of the $^1$H- and $^{13}$C-NMR spectra of this derivative permitted the position of the linkage of the rhamnose unit on the glucose moiety ($\delta$H-3′ 3.90, $\delta$ C-3′ 80.9) to be determined and unambiguously established that the acids belonging to the cinnamic series esterified the glucose unit at

positions 4′ (δH-4′ 5.29) and 6′ (δ CH2-6′ 4.33). Linkage of the caffeic unit at position 4′ and of the cinnamic unit at position 6′ were finally determined by chemical correlation. Treatment of verbascoside (**10**) by one equivalent of (*E*)-cinnamoyl chloride in pyridine led to 6′-*O*(*E*)-cinnamoyl verbascoside, identical with natural compound **5**.

## EXPERIMENTAL

### *General*

UV: MeOH; NMR: Bruker AC 270, Bruker AC 200 and a Bruker DRX 400 spectrometers [$^1$H (270, 200 and 400 MHz) and $^{13}$C (50 MHz)], with TMS was the int standard. Chemical shifts are reported in δ (ppm) values. The signals of $^1$H and $^{13}$C spectra were unambiguously assigned by using DEPT and 2D NMR techniques: COSY, NOESY, HMQC and HMBC. These 2D experiments were performed using standard Bruker microprograms. EIMS and DICMS (using $NH_3$ as reagent gas): Nermag R 10-10C spectrometer. FABMS: ZAB HF in glycerol matrix with NaCl as additive for positive ion mode. HRMS and HRFABMS: AEI MS-902 spectrometer. CC: silica gel [Merck 60H, 0.04–0.06 mm (flash), 0.015–0.04 mm in normal and C18 reversed phase]. MPLC: Büchi model 688 apparatus. The geometry optimization was performed using the Polack-Ribiere conjugate gradient with a termination condition of 0.1 kcal/mol.

### *Plant material*

This was collected on Mont Taom (New Caledonia) in July 1989. The species was identified by one of us (T.S.) and herbarium samples (Gouco 369) are retained in the herbaria of the Centre ORSTOM of Nouméa.

### *Extraction and isolation of alkaloids*

Dried, pulverized aerial parts of *O. austrocaledonica* (1 kg) were basified with $NH_4OH$ (or a satd soln of $Na_2CO_3$) and extracted with $CH_2Cl_2$ (2L × 4). The residue of the $CH_2Cl_2$ extract was washed with 1N HCl (10 l). The aq solns were basified with $NH_4OH$ (or a satd soln of $Na_2CO_3$) and extracted with $CH_2Cl_2$ (1L × 3). After drying over $Na_2SO_4$, the organic solvent was removed *in vacuo* to give a crude alkaloid mixture (1.1 g) which was chromatographed over a silica gel 60 H column, using AcOEt–MeOH mixts of increasing polarity. Fractions (20 ml) were collected and chromatography was monitored on TLC ($CH_2Cl_2$–MeOH–$NH_4OH$; 95:5:0.1). Solns yielding pure compounds were immediately dried by careful evaporation ($T < 40°$) and stored under an $N_2$ atmosphere. Yields: 4-methyl-5,5′-[(1-methyltrimethylene)di](methylnicotinate), 40 mg; 4,4′-bis-methyl-5,5′-[(1-methyltrimethylene)di](methylnicotinate), 50 mg; 4-hydroxy-β-phenylethyl 5-ethyl-3-methoxycarbonyl-4-pyridinyl acetate, 20 mg; jasminine (**1**), 100 mg, 2,5-dihydrojasminine (**2**), 50 mg and austrodimerine (**3**), 30 mg.

### 2,5-*Dihydrojasminine* (**2**)

$[\alpha]_D^{20}$ +300° (c 0.01, $CHCl_3$); UV $\lambda_{max}$ (log ε) (MeOH) 344 (3.83), 206 (4.27) nm; IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3400, 2920, 2860, 1640, 1500, 1440, 1385, 1180, 1100, 975, 920, 620; $^1$H NMR: Table 1; DCIMS *m/z* 240 $[M+NH4]^+$, 223 $[M+H]^+$; EI *m/z* (rel. int.): 222 (35); HREIMS found: 222.100440 calcd: 222.100435 ($C_{11}H_{14}N_2O_3$).

### *Austrodimerine* (**3**)

$[\alpha]_D^{20}$ +75° (c 1, $CHCl_3$); UV $\lambda_{max}$ (log ε) (MeOH) 290 (4.17), 232 (3.79), 207 (4.27) nm; IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3400, 2850, 1720, 1660, 1295, 1135, 980; $^1$H NMR: Table 1; DCIMS *m/z* 402 $[M+H]^+$; EI *m/z* (rel. int.): 401 (85), 386 (20), 370 (27), 315 (5), 223 (74), 178 (100); HREIMS found: 401.195071 calcd: 401.195058 ($C_{21}H_{27}N_3O_5$); $^{13}$C NMR ($CDCl_3$, 50 MHz): δ 15.6 (C-7′), 18.8 (2C, C-9′, C-10), 29.6 (C-5), 34.3 (C-9), 35.4 (C-6), 39.4 (C-1), 49.2 (C-8), 51.2 ($CH_3OOC$-4), 52.8 ($CH_3OOC$-4′), 58.8 (C-8′), 100.7 (C-4), 127.3 (C-3′), 134.9 (C-5′), 142.3 (C-3), 147.4 (C-4′), 150 (C-6′), 151 (C-2′), 167.1 (MeOOC-4′), 168.1 (MeOOC-4), 171 (C-7).

### *Extraction and isolation of iridoids and phenolic compounds*

Dried and pulverized aerial parts of *O. austrocaledonica* (1 kg) were first defatted with $CH_2Cl_2$ and then extracted with MeOH (2L × 5). The MeOH-soluble extract was evaporated under reduced pressure to give a residue (120 g), a portion of which (30 g) was dissolved in about 200 ml of MeOH, which was added to silica gel (60 g, 0.06–0.230 mm) and evaporated on a rotavapor. The mixture was subjected to VLC on silica gel 60 H. Elution with a $CH_2Cl_2$–MeOH gradient yielded 13 fractions. Fractions 5–6 were chromatographed (silica gel 0.015–0.04 mm; $CH_2Cl_2$–MeOH, 24:1) to afford ligstroside (3.4 g) and oleuropein (7.26 g). Fractions 7–8 were chromatographed (silica gel 60 H; $CH_2Cl_2$–MeOH gradient) to afford 7-oxologanin (30 mg), loganin (50 mg), 7-*O*-β-D-neohesperidosylapigenin (20 mg), and loganic acid (60 mg). Fraction 9 was chromatographed (silica gel C-18 0.015–0.04 mm; $H_2O$–MeOH gradient) to afford secoxyloganin (25 mg), GI5 (20 mg), salidroside (10 mg), and 6′-*O*-(*E*)-cinnamoylverbascoside (15 mg). Fractions 10–11 were chromatographed under the same conditions to afford austrosmoside (**4**, 20 mg), verbascoside (25 mg) and 4′-*O*-β-D-glucosylapigenin (30 mg).

*Austrosmoside* (**4**)

$[\alpha]_D^{20}$ −78° (c 0.07, MeOH); UV $\lambda_{max}$ (log ε) (MeOH) 243 (3.48); $^1$H NMR (DMSO-$d_6$, 270 MHz): δ 7.50 (*d*, *J* = 1 Hz, H-3A), 7.43 (*d*, *J* = 2 Hz, H-3B), 7.28 (2H, *d*, *J* = 8 Hz, H-2′C, H-6′C), 7.04 (2H, *d*, *J* = 8 Hz, H-3′C, H-5′C), 5.94 (*q*, *J* = 7 Hz, H-8A), 5.77 (*s*, H-1A), 5.64 (*ddd*, *J* = 16 Hz, *J′* = 10 Hz, *J″* = 9 Hz, H-8B), 5.45 (*d*, *J* = 4 Hz, H-1B), 5.35 (2H, *m*, Ha-10B, Hb-10B), 4.52 (2H, *d*, *J* = 8 Hz, H-1″A, H-1″B), 3.65 (3H, *s*, $COOCH_3$-4A), 3.63 (3H, *s*, $COOCH_3$-4B), 1.67 (3H, *d*, *J* = 7 Hz, $CH_3$-10A); FABMS *m/z*: 911 $[M+H]^+$, 854, 796, 738, 680, 504. HRFABMS found: 911.31846 calcd: 911.31847.

*Acetylation of* **4**

Treatment of **4** (10 mg) with $Ac_2O$ (1 ml) and pyridine (1 ml) at room temp overnight followed by flash CC (hexane-EtOAc, 7:3) gave the octaacetate **6** (90%); $[\alpha]_D^{20}$ −102° (c 0.17, $CHCl_3$); UV $\lambda_{max}$ (log ε) (MeOH) 241 (4.30); $^1$H NMR: Table 2; FABMS *m/z*: 1269 $[M+Na]^+$, 1247 $[M+H]^+$, 899, 825, 700, 555, 461.

*Methanolysis of* **4**

Treatment of **4** (8 mg) with 0.1 N MeONa (2 ml) at room temp overnight, followed by flash CC ($CH_2Cl_2$-MeOH 9:1) gave secoxyloganin methyl ester (4 mg) and ligstroside (2 mg).

6′-O-(E)-*Cinnamoylverbascoside* (**5**)

$[\alpha]_D^{20}$ −52° (c 0.05, MeOH); UV $\lambda_{max}$ (MeOH) 283; $^1$H NMR ($CDCl_3$, 270 MHz): δ 7.88 (*d*, *J* = 16 Hz, H-7‴), 7.70 (*d*, *J* = 16 Hz, H-7″), 7.63–6.53 (11H, *m*), 6.45 (*d*, *J* = 16 Hz, H-8‴), 6.29 (*d*, *J* = 16 Hz, H-8″), 5.22 (*d*, *J* = 1.5 Hz, H-1″), 4.83 (*t*, *J* = 8 Hz, H-4′), 4.37 (*d*, *J* = 8 Hz, H-1′), 4.32 (*dd*, *J* = 13 Hz, *J′* = 6 Hz, H-6′a), 4.27 (*dd*, *J* = 13 Hz, *J′* = 4 Hz, H-6′b), 4.10–4.32 (11H, *m*), 2.78 (2H, *t*, *J* = 7 Hz, $CH_2$-7), 1.11 (3H, *d*, *J* = 6 Hz, $CH_3$-6″); FABMS *m/z* 755 $[M+H]^+$. HRFABMS found: 755.25508 calcd: 755.25509.

*Acetylation of* **5**

Treatment of **5** (10 mg) with $Ac_2O$ (1 ml) and pyridine (1 ml) at room temp overnight followed by flash CC (hexane–EtOAc 7:3) gave the octaacetate **11** (90%); $[\alpha]_D^{20}$ −12° (c 0.5, MeOH); UV $\lambda_{max}$ (log ε) (MeOH) 277 (4.75); $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.73 (*d*, *J* = 16 Hz, H-7‴), 7.65 (*d*, *J* = 16 Hz, H-7⁗), 7.39 (*dd*, *J* = 8 Hz, *J′* = 1 Hz, H-6‴), 7.36 (*d*, *J* = 1 Hz, H-2‴), 7.32–7.23 (5H, *m*), 7.19 (*d*, *J* = 8 Hz, H-5‴), 7.09 (2H, *m*, H-5, H-6), 7.03 (*d*, *J* = 1 Hz, H-2), 6.45 (*d*, *J* = 16 Hz, H-8‴), 6.37 (*d*, *J* = 16 Hz, H-8⁗), 5.29 (*t*, *J* = 9 Hz, H-4′), 5.12 (*dd*, *J* = 9 Hz, *J′* = 3 Hz, H-3″), 5.08 (*dd*, *J* = 9 Hz, *J′* = 8 Hz, H-2′), 5.03 (*dd*, *J* = 3, *J′* = 1 H-2″), 4.97 (*t*, *J* = 9 Hz, H-4″), 4.84 (*d*, *J* = 1 Hz, H-1″), 4.45 (*d*, *J* = 8 Hz, H-1′), 4.32 (*dd*, *J* = 12 Hz, *J′* = 3 Hz, H-6′b), 4.27 (*dd*, *J* = 12 hz, *J′* = 5 Hz, H-6′a), 4.13 (*m*, H-8b), 3.90 (*t*, *J* = 9 Hz, H-3′), 3.80 (*m*, H-5″), 3.72 (*m*, H-5′), 3.67 (*m*, H-8a), 2.90 (2H, *m*, $CH_2$-7), 2.34–2.29 (4*s*, 4 Ar-OAc), 2.10–1.89 (12H, *s*, 4 R-OAc), 1.04 (*d*, *J* = 7 Hz, $CH_3$-6″); $^{13}$C NMR ($CDCl_3$, 50 MHz): δ 17.45 (C-6″), 20.6 (5C, $OCOCH_3$), 20.7 (3C, $OCOCH_3$), 35.4 (C-7), 62.7 (C-6′), 67.3 (C-5″), 68.6 (C-4′), 69.7 (C-8), 70.0 (2C, C-2″, C-3″), 71.9 (C-4″), 72.1 (2C, C-2′, C-5′), 80.9 (C-3′), 99.1 (C-1″), 100.7 (C-1′), 117.2 (C-8⁗), 118.2 (C-8‴), 122.8 (C-2‴), 123.8 (C-5), 123.1 (C-2), 124.1 (C-5‴), 126.4 (C-6‴), 127.2 (C-6), 128.2 (2C, C-2⁗, C-6⁗), 129.9 (2C, C-3⁗, C-5⁗), 130.5 (C-4⁗), 132.8 (C-1‴), 134 (C-1⁗), 137.5 (C-1), 140.6 (C-4), 141.9 (C-3), 142.6 (C-3‴), 143.9 (C-4‴), 144.4 (C-7‴), 145.6 C-7⁗), 164.9 (C-9‴), 166.5 (C-9⁗), 167.9–170.3 (8C, MeCO); FABMS *m/z* 1113 $[M+Na]^+$, 1091 $[M+H]^+$, 1072, 853.

*Acylation of verbascoside* (**10**)

Treatment of **10** (25 mg) with (*E*)-cinnamoyl chloride (40 mg) and pyridine (5 ml) at 0° overnight followed by flash CC (hexane–EtOAc 1:1) gave 6′-*O*(*E*)-cinnamoylverbascoside (**5**) (25%).

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