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ADDITIONAL ALKALOIDS FROM *LAURELIA PHILIPPIANA* AND *L. NOVAE-ZELANDIAE*

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Key Word Index—*Laurelia philippiana*; *L. novae-zelandiae*; Atherospermataceae; alkaloids; asimilobine; anonaine; norcorydine; nornantenine; (+)-reticuline; 4-hydroxyanonaine; obovanine; oxoputerine; (−)-romneine.

Abstract—Asimilobine, anonaine, norcorydine, nornantenine, (+)-reticuline and the new alkaloid, 4-hydroxyanonaine, were isolated from *Laurelia philippiana* bark. The biogenetically related obovanine, oxoputerine and (−)-romneine, not known as a natural product, were obtained from the bark of *L. novae-zelandiae*. The occurrence of (*R*)-norlaudanosoline-derived alkaloids in *L. novae-zelandiae* is a distinctive feature of this tree. Neither *L. novae-zelandiae* nor *L. philippiana* accumulate dimeric benzylisoquinoline alkaloids to any appreciable extent in the trunk bark, differing in this respect from *L. sempervirens*, the only other *Laurelia* species.

INTRODUCTION

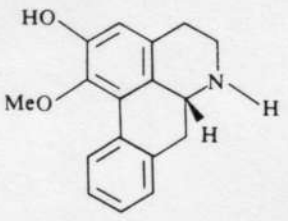
In a chemotaxonomic discussion of the alkaloids of the Atherospermataceae it was pointed out that the Chilean tree *Laurelia sempervirens* accumulates bisbenzylisoquinolines, while these dimeric compounds appear to be absent from the other two species of this genus, *L. philippiana* (= *Laureliopsis philippiana*, 'tepa') of Chile and *L. novae-zelandiae* ('pukatea') of New Zealand [1]. A preliminary analysis of *L. sempervirens* bark showed that bisbenzylisoquinoline alkaloids made up at least 25% of the total bases [2], but the alkaloids described for *L. philippiana* [2, 3] and *L. novae-zelandiae* [4, 6], were all monomeric aporphinoids. As this difference could be of taxonomic significance, a re-examination of these trees was begun. This communication reports the isolation and characterization of several additional alkaloids, all monomers, from the two latter species.

RESULTS AND DISCUSSION

Asimilobine (**1**), anonaine (**2a**), norcorydine (**3**), nornantenine (**4a**) and (+)-reticuline (**5**), now isolated from *L. philippiana* bark, had not been found previously in this species; nornantenine, however, is a major alkaloid in *L. sempervirens* [2]. ^{1}H NMR evidence is also adduced for the presence of the undescribed 4-hydroxyanonaine (**2b**) in the same material. It seems reasonable to postulate that this compound lies on or near the biosynthetic route to liriodenine (**7**), present in all three species of *Laurelia* [2, 6], and that 4-hydroxynornantenine (**4b**), already described for *L. philippiana* [3] may be similarly related to oxonantenine (**8**), found in *L. sempervirens* [2].

Obovanine (**9a**), oxoputerine (**10**) and (−)-romneine (**6**) are the newly identified compounds of *L. novae-zelandiae* bark. Pukateine (**9b**) was the main alkaloid in this tissue, and laureline (**11**), which had not been found in a commercial pukatea extract [4], was isolated once again. Although obovanine and oxoputerine had not been reported before in the Atherospermataceae, their clear biogenetic relationship to pukateine makes their occurrence unremarkable.

Dextrorotatory romneine had been isolated before from *Romneya coulteri* (Papaveraceae), where it co-occurs with levorotatory reticuline [7], and its (−)-



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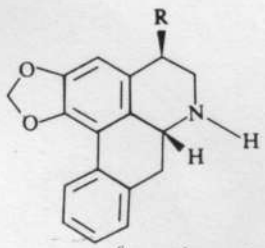

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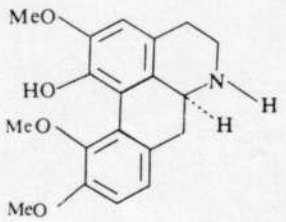

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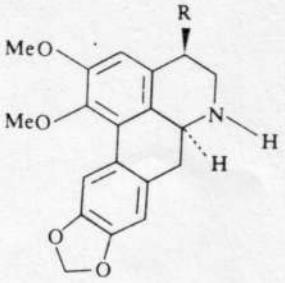

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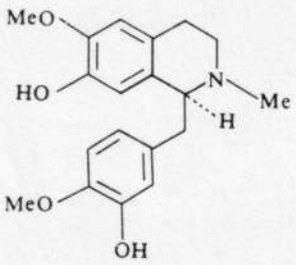

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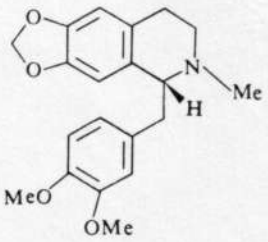

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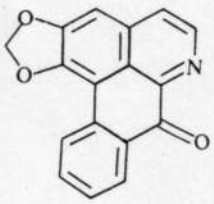

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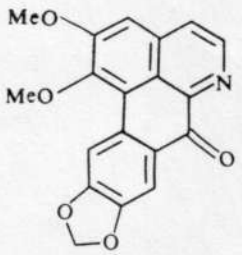

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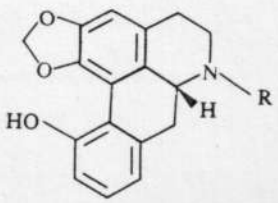

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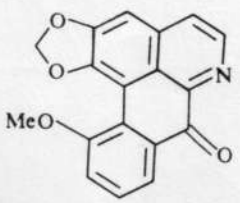
9b R = Me



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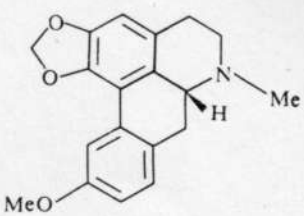

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metho salt had been found in several other members of the Papaveraceae [8]. This is the first report on the isolation of (*R*)(−)-romneine from a natural source, and its presence in *L. novae-zelandiae* underscores the exceptional capability of this species of (formally) utilizing (*R*)-norlaudanosoline [1]. It seems possible that (*R*)- and (*S*)-norreticulines are interconverted in pukatea and, as in the case of some Papaveraceae, the configuration of each enantiomer directs its further biosynthetic elaboration: thus, (*R*)-norreticuline would lead to (*R*)(−)-romneine and the (*R*)(−)-1,2,11-trioxygenated aporphinoids of *L. novae-zelandiae*, obovanine, pukateine, *O*-methylpukateine and oxoputerine, presumably via puterine (*O*-methylobovanine); (*S*)-norreticuline would lead to the (*S*)(+)-1,2,9,10- and 1,2,9,11-tetraoxygenated aporphinoids laurolitsine, boldine and isoboldine of *L. novae-zelandiae*, and nornantenine, oxonantenine and norcorydine of the Chilean species.

The absolute value of the specific rotation of (−)-romneine hydrobromide obtained from *L. novae-zelandiae* (75°) is considerably larger than those reported for the material from *Romneya coulteri* (40°) [7] and for the bases prepared from the norroemerine enantiomers obtained by crystallization of diastereomeric salts (43°) [9]. This discrepancy suggests the possibility that the literature values correspond to stereochemically impure samples. Such a hypothesis receives support from the low specific rotation of the (+)-laudanosine with which the romneine from *R. coulteri* was chemically correlated, and should be regarded together with the lack of enantiomeric purity of the reticuline isolated from the same source [7].

Repeated TLC of the *L. philippiana* fraction containing 4-hydroxynornantenine afforded an amorphous material which darkened rapidly in contact with air. The ^{1}H NMR spectrum of this product in $CDCl_3$ showed that it was a mixture of *rel*-(4*R*, 6a*S*)-4-hydroxynornantenine [3, 10], and a larger amount of another noraporphine with no methoxy groups, a 1,2-methylenedioxy signal centred at 6.02 ppm, an aromatic proton singlet at 7.00 ppm, an aromatic proton multiplet overlapping the $CHCl_3$ signal and another (one proton) multiplet centered at 8.05 ppm and obscuring the 4-hydroxynornantenine singlet at 7.89 ppm. The spectrum also exhibited a multiplet centred at 4.83 ppm, considerably downfield from the 4-hydroxynornantenine H-4 signal. The singlet at 7.00 ppm corresponds to the H-3 resonance shifted downfield by the presence of a hydroxyl group at C-4, as is always the case in 4-oxygenated aporphinoids. The large chemical shift of H-4 is diagnostic of its *trans* relationship to H-6a as in episteporphine [11], pachystaudine and norpachystaudine [12], and (synthetic) epicataline [13]. As the absolute configuration of a natural ring D unsubstituted aporphinoid can be presumed to be (6a*R*) [1], it follows that the new compound isolated from *L. philippiana is rel*-(4*R*, 6a*R*)-4-hydroxyanonaine, the nor-counterpart of episteporphine.

The identification of norcorydine is largely based upon the ^{1}H NMR spectrum of its *N,O*-diacetyl derivative. In this compound the H-8 and H-9 resonances are separated by 0.25 ppm, while in the corresponding norisocorydine derivative these signals would be expected to appear very close to each other. The mass spectra of *N,O*-diacetylnorcorydine and asimilobine show a high intensity peak due to the initial loss of ketene from the *O*-acetyl group, as proven by high resolution measurements. The fragmentation then continues with the loss of 59 and 72 mass units, as has been observed for the naturally occurring *N*-acetylasimilobine and *N*-acetylnornuciferine [14].

200 MHz ^{1}H NMR spectra were recorded for obovanine and pukateine, allowing the H-9 resonance to be assigned unequivocally as the low-field component of the aromatic proton pattern. The H-6a doublet of doublets appears at 3.79 ppm in the obovanine spectrum and at 3.14 ppm in the case of pukateine. These signals had not been identified previously in the ^{1}H NMR spectra of nonquaternary aporphines or noraporphines lacking a C-7 oxygen substituent, and the H-6a/H-7 coupling constants can be expected to prove useful for the study of the conformations of these compounds in solution.

EXPERIMENTAL

All mps are uncorr. IR and ^{1}H NMR spectra (TMS as internal standard) were determined in KBr and $CDCl_3$, respectively. MS were recorded using electron impact ionization at 70 eV and 170–200°. CC and TLC were carried out on Si gel using $CHCl_3$ with increasing concns of MeOH or EtOH.

The alkaloids were extracted and fractionated as described previously [2]. Individual fractions were submitted to column and prep. TLC and the eluted bands were monitored by ^{1}H NMR for compounds not isolated by us from these plants. Acetyl derivatives of noraporphines were prepared using Ac_2O–pyridine at room temp.

Asimilobine (**1**). ^{1}H NMR as in ref. [19]. Identified as the *N,O*-diacetyl derivative, mp 141–144° (lit. 143–144°) [15], $[\alpha]_D^{15}$ −344° (*c* = 1.21, $CHCl_3$); ^{1}H NMR: δ 2.20 *s* (3H, NAc), 2.36 *s* (3H, OAc), 3.60 *s* (3H, OMe), 6.86 *s* (1H, H-3), 8.31 *m* (1H, H-11); MS: *m/z* 351.1461 (M^+, 59%, $C_{21}H_{21}NO_4$ requires 351.1471), 309.1370 ($M^+ - CH_2CO$, 30%, $C_{19}H_{19}NO_3$ requires 309.1364), 250.0999 ($M^+ - CH_2CO - C_2H_5NO$, 100%, $C_{17}H_{14}O_2$ requires 250.0993), 238.0994 ($M^+ - CH_2CO - C_3H_5NO$, 58%, $C_{16}H_{14}O_2$ requires 238.0994), 237.0925 ($M^+ - CH_2CO - C_3H_5NO - H$, 83%, $C_{16}H_{13}O_2$ requires 237.0915); and comparison with a ref. sample (mmp, IR, R_f)[15].

Anonaine (**2a**). *N*-Acetyl derivative, mp 231–233° (lit. 229–230°) [15], $[\alpha]_D^{23}$ −354.0° (*c* = 0.21, $CHCl_3$) (lit. −356°) [15], ^{1}H NMR as in ref. [15]. Identified by comparison with a ref. sample (mmp, IR, R_f) [15].

Norcorydine (**3**). *N,O*-Diacetyl derivative, amorphous, $[\alpha]_D^{16}$ +266° (*c* = 0.76, $CHCl_3$); IR: $\tilde{\nu}_{max}$ 1720, 1640 cm^{-1}; ^{1}H NMR: δ 2.16 *s* (3H, NAc), 2.25 *s* (3H, OAc), 3.45 *s* (3H, C-11 OMe), 3.85 *s* (3H, OMe), 3.88 *s* (3H, OMe), 6.70 *s* (1H, H-3), 6.88 *d*, *J* = 8 Hz (1H, H-8 or H-9), 7.13 *d*, *J* = 8 Hz (1H, H-9 or H-8); MS: *m/z* 411.1684 (M^+, 78%, $C_{23}H_{25}NO_6$ requires 411.1682), 369.1566 ($M^+ - CH_2CO$, 88%, $C_{21}H_{23}NO_5$ requires 369.1576), 310.1209 ($M^+ - CH_2CO - C_2H_5NO$, 99%, $C_{19}H_{18}O_4$ requires 310.1205), 297.1132 ($M^+ - CH_2CO - C_3H_5NO - H$, 100%, $C_{18}H_{17}O_4$ requires 297.1127).

Nornantenine (**4a**). *N*-Acetyl derivative, mp 283–284° (lit. 285°, 294°) [2, 16], $[\alpha]_D^{26}$ +340° (*c* = 0.50, $CHCl_3$) (lit. +349°) [16], identified by comparison with an authentic sample available in our laboratory (mmp, IR, R_f).

(+)-*Reticuline* (**5**). Perchlorate, mp 202–204°, $[\alpha]_D^{22}$ +85° (*c* = 0.42, EtOH), and comparison with an authentic sample available in our laboratory (mmp, IR, R_f).

rel-(4*R*, 6a*R*)-4-*Hydroxyanonaine* (**2b**). Amorphous, contaminated with *rel*-(4*R*, 6a*S*)-4-hydroxynornantenine; ^{1}H NMR: δ 4.83 *m*, (1H, H-4), 5.95 *d*, J = 1.5 Hz (1H, OCH_2O), 6.08 *d*, J = 1.5 Hz (1H, OCH_2O), 7.0 *s* (1H, H-3), 7.06–7.43 unresolved (H-8, H-9 and H-10), 8.05 *dd* (1H, H-11).

(−)-*Romneine* (**6**). Amorphous; ^{1}H NMR: δ 2.50 *s* (3H, NMe), 3.81 *s* (3H, OMe), 3.85 *s* (3H, OMe), 5.85 *s* (2H, OCH_2O), 6.25 *s* (1H, H-8), 6.51 *s* (1H, H-5), 6.61 *d*, J = 2 Hz (1H, H-5′ or H-6′), 6.70 *d*, J = 2 Hz (1H, H-6′ or H-5′), 6.71 *s* (1H, H-2′); comparison with ref. ^{1}H NMR spectrum [7]. Hydrobromide, mp 223–225° (lit. 226–228°) [7], $[\alpha]_D^{15}$ −75° (c = 0.2, EtOH); comparison with ref. IR spectrum [7].

Obovanine (**9a**). ^{1}H NMR (200 MHz): δ 3.79 *dd*, J = 13.5, J' = 4.3 Hz (1H, H-6a), 5.97 *d*, J = 1.1 Hz (1H, OCH_2O), 6.12 *d*, J = 1.1 Hz (1H, OCH_2O), 6.66 *s* (1H, H-3), 6.88 *dd*, J = 7.2, J' = 0.9 Hz (1H, H-8 or H-10), 6.97 *dd*, J = 9.2, J' = 1.3 Hz (1H, H-10 or H-8), 7.21 *dd*, J = 8.2, J' = 7.3 Hz (1H, H-9); MS: *m*/*z* 281 (M^+, 70%), 280 (M^+ − H, 100%), 264 (M^+ − OH, 10%), 252 (M^+ − CH_2NH, 22%), 251 (M^+ − H − CH_2NH, 21%), 222 (20%). Hydrochloride, short needles, mp 250° *d* (lit. 260–262°) [18], $[\alpha]_D^{12}$ −263° (c = 0.11, MeOH) (lit. −164°) [18].

Pukateine (**9b**). Mp 210–211° (lit. 208–212°) [4]. $[\alpha]_D^{15}$ −257° (c = 1.0, EtOH) (lit. 240.4 ± 3°) [4]; ^{1}H NMR (200 MHz): δ 2.55 *s* (3H, NMe), 3.14 *dd*, J = 13.3, J' = 3.4 Hz (1H, H-6a), 5.98 *d*, J = 1.3 Hz (1H, OCH_2O), 6.13 *d*, J = 1.3 Hz (1H, OCH_2O), 6.65 *s* (1H, H-3), 6.91 *dd*, J = 7.2, J' = 1 Hz (1H, H-8 or H-10), 6.98 *dd*, J = 6.9, J' = 1 Hz (1H, H-10 or H-8), 7.22 *dd*, J = 8.3, J' = 7.3 Hz (1H, H-9); MS: *m*/*z* 295 (M^+, 100%), 294 (M^+ − H, 100%), 280 (15%), 278 (M^+ − OH, 15%), 265 (45%), 252 (M^+ − CH_2NMe, 40%), 236 (15%), 222 (10%), 215.3 m* (295 → 252), 196.3 m* (251 → 222); and comparison with a ref. sample (mmp, IR, R_f) [5].

Oxoputerine (**10**), Mp 242–244° (lit. 241–243°) [19]; IR: $\bar{\nu}_{max}$ 1650 cm^{-1}; ^{1}H NMR as in ref. [19]; MS: *m*/*z* 305.0696 ($C_{18}H_{11}NO_4$ requires 305.0704); comparison with ref. sample (mmp, IR, R_f) [19].

Laureline (**11**). Amorphous; ^{1}H NMR as in ref. [17]; (+)-tartrate, mp 208–210° (lit. 211°) [20], $[\alpha]_D^{15}$ −59° (c = 0.10, EtOH) (lit. −25.1 ± 3.1°) [20].

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