Novel Dimeric Indole Alkaloids from *Aristotelia australasica*. Structural Determination and Synthesis[1]

J.-C. Quirion, C. Kan, I. R. C. Bick,[2] and H.-P. Husson*

Institut de Chimie des Substances Naturelles du CNRS, 91190 Gif-sur-Yvette, France

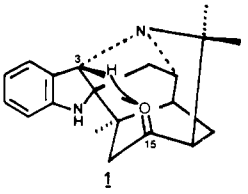
Received February 26, 1987

The structures of the two dimeric indole alkaloids **2** and **3** derived from aristone (**1**) have been determined from ^1H NMR, ^{13}C NMR, and mass spectrometric data. A biogenetic hypothesis is proposed to account for the formation of a C–N bond between the two halves of the dimers, and a partial synthesis of **3** based on this hypothesis has been carried out by a coupling process involving radicals generated by chemical or photochemical reactions.

Introduction

The genus *Aristotelia* (Elaeocarpaceae) comprises species that grow in temperate regions of the South Pacific (Australia, New Zealand, and Chile). From the four species studied previously,[3] *A. peduncularis*, *A. serrata*, *A. fructicosa*, and *A. chilensis*, 25 bases have been isolated, which belong to the group of indole alkaloids formed by union of a tryptamine with a nonrearranged monoterpene unit.

A. australasica F.V.M. (local name: mountain wineberry) is endemic in mountainous regions of north-eastern New South Wales (Australia). From leaves and branchlets of this plant we have isolated 16 monomeric alkaloids, 12 of which are new,[4] together with the two dimeric alkaloids **2** and **3** that are the subject of this report. The structures proposed for the latter on the basis of spectroscopic data have been confirmed by a partial synthesis of **3** that starts with aristone (**1**) and involves a radical process that follows the proposed scheme of biogenesis.

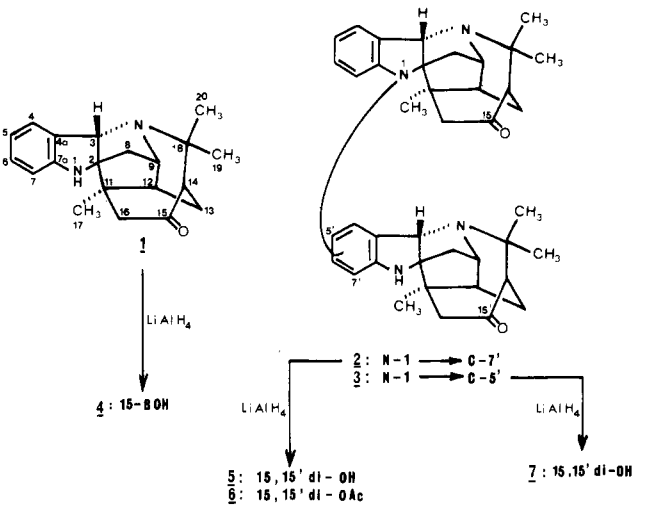


1

Results and Discussion

A. Structural Determination. Bisaristone A (2) $C_{40}H_{46}N_4O_2$ (high resolution MS, exact mass $M^{+\cdot}$ 614.3619, calcd 614.3620). Compound **2** (Scheme I) has the following spectroscopic characteristics: IR ($CHCl_3$) 1710 cm^{-1}; UV (ethanol) λ_{max} 215, 239, 294 nm. The very low solubility of **2** did not permit a well-resolved ^1H NMR spectrum to be obtained, but the ^{13}C spectrum (CF_3CO_2D) (Table I) shows the presence of two carbonyls at 219.2 and 218.4 ppm and five quaternary aromatic carbons at 153.1, 152.0, 134.3, 132.4, and 130.5 ppm. The seven tertiary aromatic carbon peaks are paired, except for a unique signal that can readily be assigned to C-7 (113.5 ppm). These data point to a dimeric structure with an aromatic carbon as one of the points of attachment. The signals from the aliphatic residues can all be grouped in pairs, and their chemical shifts are close to those recorded for aristone (**1**, Table I), which has been isolated from the same plant.[4] No change in multiplicity is observed in this part of the spectrum as compared to **1**, indicating that the second point of attachment of the dimer is not associated with these carbons. The only remaining possibility is thus a junction between the nitrogen atom N-1 and an aromatic carbon atom.

Scheme I



In order to confirm C-7′ as the point of substitution in the aromatic nucleus, we sought a suitable derivative that would furnish an adequate ^1H NMR spectrum. Reduction of **2** with $LiAlH_4$ in warm THF led to a single compound **5** ($M^{+\cdot}$ 618) corresponding to the reduction of the two carbonyl groups. A β pseudoequatorial stereochemistry for the two hydroxyl groups of **5** was deduced from examination of its ^1H NMR spectrum (only one signal at 4.51 ppm for H-15 and H-15′, J = 10 Hz, J' = 8 Hz, J'' = 3 Hz). Aristone (**1**) was likewise reduced to the alcohol **4**, exhibiting the same configuration at C-15, to allow the proton in the reduced dimer **5** to be identified. The latter, as expected, shows seven aromatic proton signals that can be assigned from decoupling experiments. A signal corresponding to the proton on C-7′ is lacking; that for the C-7 proton suffers considerable shielding (δ = 5.83 ppm) owing to the anisotropic effect of the aromatic nucleus in the second half of the dimer:[5] a Dreiding model shows that the two indole nuclei are practically perpendicular to one another.

The hypothesis of an N-1 linkage to C-7′ is supported by a comparison of the ^{13}C and ^1H NMR spectra of **4** and **5** (Table I), which shows that atoms in the vicinity of N-1, namely, C-2, C-4, C-6, C-7, C-7a, C-11, and C-17, suffer the greatest variations in chemical shift.

(1) This work forms part of the thesis of J.-C. Quirion presented on April 22, 1986, for a Doctorat ès-Sciences at the Université de Paris-Sud (Centre d'Orsay).

(2) Present address: Chemistry Department, University of Tasmania, Hobart, Tas., Australia 7001.

(3) (a) Bick, I. R. C.; Hai, M. A. *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, 1985; Vol. XXIV. (b) Zabel, V.; Watson, W. H.; Bittner, M.; Silva, M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2842.

(4) Quirion, J.-C.; Kan, C.; Bick, I. R. C.; Husson, H.-P., unpublished work.

(5) A similar shielding has also been observed for the dimeric indole alkaloid ervafoline, whose mode of coupling involves one of the nitrogen atoms (N-1): Henriques, A.; Kan, C.; Chiaroni, A.; Riche, C.; Husson, H.-P.; Kan, S. W. Lounasmaa, M. *J. Org. Chem.* **1982**, *47*, 803.

0022-3263/87/1952-4527$01.50/0

Table I. ^{13}C NMR Chemical Shifts (in ppm) in $CDCl_3$ (Except for Compound 2) Downfield from TMS ($\delta = 0$) (Signals Bearing * May Be Reversed)

	C-2	C-3	C-4a	C-4	C-5	C-6	C-7	C-7a	C-8	C-9	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18	C-19	C-20
aristone (1)	80.1	67.9	132.1	124.3	120.1	127.8	111.3	148.8	36.0	57.2	37.7	41.6	22.3	51.3	213.6	45.6	28.0*	58.8	27.0*	25.6*
bisaristone A (2)	82.9	73.4	132.4	124.4	122.0	126.4	113.5	152.0	36.0	65.7	40.1	42.7	21.2	52.1	218.4	47.0	26.7*	68.2	26.7*	25.8*
(CF_3CO_2D)	87.1	73.4	134.3	125.5	122.0	127.8	130.5	153.1	38.0	66.2	41.6	42.9	21.5	52.2	219.2	47.3	27.1*	68.2	26.7*	26.0*
alcohol 4	79.9	65.8	134.2	124.6	120.1	127.2	111.1	149.2	37.7	57.6	40.1	41.6	24.4	39.1	73.1	36.6	27.6*	57.5	29.7*	30.3*
alcohol 5	79.6	66.3	132.4	126.5	119.3	123.3	109.2	149.7	37.4	57.8	39.8	41.5	23.9	39.4	72.8	34.8	27.6*	57.6	29.9*	29.1*
	84.7	66.6	134.3	127.6	120.4	124.2	128.7	151.7	37.9	57.8	41.6	42.0	24.2	39.4	73.0	36.6	28.1*	57.6	30.0*	29.2*

The diacetyl derivative **6** was prepared in order to confirm some of the assignments in the ^{13}C NMR spectrum of **5**, in which certain signals overlap.

Bisaristone B (3) $C_{40}H_{46}N_4O_2$ (high resolution MS, exact mass $M^{+\cdot}$ 614.3695, calcd 614.3620). Alkaloid **3** (Scheme I) shows spectroscopic characteristics very close to those of bisaristone A (**2**) with which it is isomeric. In the ^1H NMR spectrum of **3**, however, a doubling of certain peaks is observed, probably as a result of hindered rotation between the two halves of the molecule. Integration of the aromatic portions shows that the rotamers exist in the proportion of 65:35.

Selective irradiation of the aromatic protons allows the identification of a singlet at 6.85 ppm that may be assigned to the hydrogen at C-4′ or C-7′. In the ^{13}C NMR spectrum, only the signal at 119.0 ppm corresponding to C-5′ is not paired. Reduction of **3** furnishes the diol **7**, analogous to **5**, which likewise exists in the form of two rotamers. Structure **3** may thus be put forward for bisaristone B.

Since suitable crystals of **2** or **3** could not be obtained, confirmation of their structures by X-ray analysis was precluded; however, the biogenetic considerations that follow and a partial synthesis leave no doubt concerning the complete structure and stereochemistry of **2** and **3**.

B. Biogenetic Considerations. The formation of alkaloids **2** and **3** implies a radical-type coupling between an amine and an aromatic nucleus, of which no example to our knowledge exists in the field of natural products. The formation, by analogy with the oxidative coupling of phenols,[6] of the amino radical **8** may be considered to take place from **1**; this radical could in turn lead to the mesomeric para and ortho forms **9** and **10** which are capable of dimerization (Scheme II).

In view of the considerable quantity of dimeric bases isolated from the plant material (31% of total alkaloids), their formation as artefacts during the extraction is precluded.

An attempt to dimerize aristone (**1**) by means of peroxidase from horseradish under the classical conditions used for biomimetic oxidative coupling of phenols[7] gave no result. The enzymatic system responsible for this reaction deserves to be better understood, and studies are in progress in our laboratory designed to isolate it from in vitro cultures.

C. Partial Synthesis of Bisaristone B (3). The first known reaction involving a free-radical amine, the Hofmann–Löffler cyclization, dates from the end of the 19th century,[8] but the mechanism was only established later.[9] However, examples of the cyclization of a chloramine onto an aromatic nucleus are more numerous.[10] We preferred the approach of generating the radicals directly by a chemical method, which has proved effective in biomimetic coupling reactions of phenols. Vanadium oxychloride, used successfully in the synthesis of morphine,[11] leads in the case of aristone (**1**) to the formation of a dimer (yield 8%) whose mass spectrum shows molecular ions at m/e 686, 684, and 682. This result clearly indicates the presence of two chlorine atoms in the molecule, although the exact structure could not be defined; however, the appearance of a single dihydroindolic NH absorption and of five aromatic proton signals in the ^1H NMR spectrum of the dimer shows that the latter is indeed of the expected type and that the two chlorine atoms are located in the aromatic nuclei.

Treatment of aristone (**1**) with potassium ferricyanide in alkaline medium [(two-phase system: CH_2Cl_2, H_2O, $NaHCO_3$, $N(Bu)_4HSO_4$)] furnishes bisaristone B (**3**) in excellent yield (71%) as the only prooduct.[12] The bisaristone B obtained is identical with the natural product, in particular, the specific rotation: $[\alpha]^{20}_D$ −75° ($CHCl_3$), cf. −89° for naturally occuring **3**.

The absolute configuration represented in **1** (Scheme I) is that deduced from an X-ray crystallographic study;[3b] no value for the optical rotation of **1**, however, has been given in the literature. If the (−)-aristone isolated by us from the same plant as the dimer and used in the present study is assumed to have the same stereochemistry as that shown in **1**, then the absolute configuration of **2** and **3** can also be deduced.

The above-mentioned reaction is of the same type as the reaction observed by P. Welzel et al. for arylamines;[13] to our knowledge, dimerization involving the formation of a C–N linkage, in the presence of potassium ferricyanide, is a new reaction.

An example of the photochemical dimerization of aromatic amines has been described:[14] Harman (**11**) when irradiated in methylene chloride solution forms the dimers **12** and **13** (Scheme III). Although **11** is not closely analogous to our alkaloids, the example has led us to attempt the same type of reaction. Methylene chloride was employed as solvent, the only medium suitable as far as both solubility and photochemical reactions are concerned, but its influence could not be ignored, since it is potentially capable of generating chlorine radicals that in turn could initiate the formation of amino radicals; the authors cited previously[14] did not take this possibility into account.

Irradiation of a solution of (−)-aristone (**1**) in CH_2Cl_2 (500-W lamp, 2 h) leads to the formation of 10% bisaristone B (**3**) and to the recovery of 60% of starting material. Prolongation of the reaction time does not lead to an increase in yield of **3**, which suggests the presence of secondary products in the reaction medium that act as an internal filter.

(6) Barton, D. H. R. *Chem. Brit.* **1967**, *3*, 330.
(7) Husson, H.-P.; Poupat, C.; Rodriguez, B.; Potier, P. *Tetrahedron* **1973**, *29*, 1405.
(8) Hofmann, A. W. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 109.
(9) Corey, E. J.; Hertler, W. R. *J. Am. Chem. Soc.* **1960**, *82*, 1657.
(10) Minisci, F.; Galli, R. *Tetrahedron Lett.* **1966**, 2531.
(11) Schwartz, M. A.; Holton, R. A.; Scott, S. W. *J. Am. Chem. Soc.* **1969**, *91*, 2800.
(12) Potassium ferricyanide has been used for the oxidative coupling of phenols: Haynes, C. G.; Turner, A. H.; Waters, W. A. *J. Chem. Soc.* **1956**, 2823. It has recently been observed that this reagent is also efficient for radical coupling of aromatic amines: Quirion, J. C.; Husson, H.-P., to be published.
(13) Welzel, P.; Muther I.; Volk, H. *Tetrahedron Lett.* **1977**, 745.
(14) Balsells, R. E.; Frasca, A. R. *Tetrahedron* **1983**, *39*, 33.

Some observations are in order concerning the formation of **3** under photochemical conditions, as this type of reaction has not previously been reported in the dihydroindole series; aristone could constitute a special case. From a Dreiding model of aristone (**1**, Scheme IV) it can be seen that the carbonyl group at C-15 is located sufficiently close to H-3 to strip the latter off in a Norrish type II reaction[15] and produce the biradical **14** (Scheme IV). The generation of **14** by either an intra- or intermolecular reaction leads to **15** and so to the ortho and para mesomeric forms (Scheme II) which yield **3** after coupling and oxidation of the alcohol radical.

This hypothesis is supported by the fact that irradiation of the alcohol **4** (Scheme I) derived from aristone (**1**) does not lead to the formation of the dimers **5** or **7**.

Experimental Section

Infrared spectra (IR) were recorded on an Infracord Perkin-Elmer spectrophotometer. Ultraviolet spectra (UV) were run in ethanol solution on a Bausch and Lomb Spectronic 505 spectrophotometer. ^1H nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ (TMS as an internal standard, $\delta = 0$ ppm) on either a Brüker WP-200 (200 MHz) or Brüker WP-400 (400 MHz) instrument. ^{13}C NMR spectra were recorded in $CDCl_3$ or CF_3CO_2D on a Brüker WP-200 (50.33 MHz) instrument and high-resolution mass spectrometry (MS) was performed on an AEI MS 50 spectrometer.

Isolation of the Alkaloids. Extraction the dry aerial parts of *Aristotelia australasica* (3.5 kg) in the classical manner gave 13 g of crude alkaloids. Bisaristone A (4 g) (**2**) crystallized from chloroform. After dissolution of the mother liquors in the mixture $CHCl_3$–CH_3OH (50/50) and filtration through a column of Sephadex LH 20, the monomeric and dimeric alkaloids were separated. The dimers were further purified by column chromatography and preparative TLC on silica gel and crystallization, yielding bisaristone A (**2**) (500 mg), bisaristone B (**3**) (45 mg), and aristone (**1**) (1.41 g).

The alkaloids exhibited the following characteristics:

Aristone (1): mp 268–270 °C (acetone); UV (EtOH) λ_{max} (log ϵ) 213 (3.35), 239 (2.32), 293 (0.82) nm; $[\alpha]^{20}_D$ −130° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) 3300, 1660 cm^{-1}; MS (70 eV), *m/e* (relative intensity) 308 ($M^{+\bullet}$, 100), 293 (43), 251 (20), 250 (26), 198 (47), 197 (52), 194 (65), 181 (56), 130 (26), 129 (47); ^1H NMR ($CDCl_3$) δ 1.21, 1.37, 1.40 (3 Me, s), 1.62 (1 H, dd, J = 10, 1 Hz, H-8), 1.85 (1 H, ddd, J = 3.5, 2.5, 1 Hz, H-12) 1.89 (1 H, ddd, J = 13.5, 3.5, 3.5 Hz, H-13), 2.04 (1 H, dd, J = 10, 1.5 Hz, H-8), 2.11 (1 H, dd, J = 3.5, 2.5 Hz, H-14), 2.13 (1 H, d, J = 18.5 Hz, H-16), 2.32 (1 H, ddd, J = 13.5, 2.5, 2.5 Hz, H-13), 2.80 (1 H, d, J = 18.5 Hz, H-16), 3.51 (1 H, ddd, J = 1.5, 1, 1 Hz, H-9), 3.54 (1 H, s, H-3), 3.68 (1 H, s, N1-H), 6.63 (1 H, d, J = 7.5 Hz, H-7) 6.76 (1 H, t, J = 7.5 Hz, H-5), 7.05 (1 H, t, J = 7.5 Hz, H-6), 7.14 (1 H, d, J = 7.5 Hz, H-4); ^{13}C NMR, see Table I.

Bisaristone A (2): mp 303–305 °C (methanol); UV (EtOH) λ_{max} (log ϵ) 209 (4.41), 245 (3.97), 299 (3.50) nm; IR (film) 3350, 1710, 1600, 1450 cm^{-1}; MS (70 eV), *m/e* (relative intensity) 614 ($M^{+\bullet}$, 100), 600 (8), 599 (18), 558 (17), 557 (9), 543 (6), 529 (6), 504 (8), 500 (9), 488 (5), 376 (17), 307 (5), 178 (13); exact mass 614.3619 (calcd for $C_{40}H_{46}N_4O_2$ 614.3620); ^{13}C NMR, see Table I.

Bisaristone B (3): amorphous; UV (EtOH) λ_{max} (log ϵ) 208 (4.43), 248 (3.99), 299 (3.50) nm; $[\alpha]^{20}_D$ −89° (*c* 0.64, $CHCl_3$); IR (film) 3350, 1710, 1605, 1460 cm^{-1}; MS (70 eV), *m/e* (relative intensity) 614 ($M^{+\bullet}$, 100), 600 (7), 599 (16), 558 (7), 557 (4), 543 (3), 529 (3), 504 (3), 500 (7), 488 (4), 437 (4), 376 (4), 178 (8), 91 (11); exact mass 614.3695 (calcd for $C_{40}H_{46}N_4O_2$ 614.3620); ^1H NMR ($CDCl_3$) δ 0.81 (3 H, s, Me 17), 1.26, 1.28, 1.33, 1.35, 1.40, 1.41, 1.45 (s, Me-17′, Me-19, Me-19′, Me-20, Me-20′), 1.65–1.75 (3 H, m, H-8, H-8′, H-12), 1.88 (1 H, dt, J = 12, 3 Hz, H-13′), 1.90 (1 H, m, H-12′), 1.92 (1 H, dt, J = 12, 3 Hz, H-13), 2.10 (3 H, m, H-8, H-8′, H-14′), 2.15 (1 H, d, J = 18.5 Hz, H-16), 2.17 (1 H, d, J = 18.5 Hz, H-16′), 2.33 (3 H, m, H-13, H-13′, H-14), 2.83 (1 H, d, J = 18.5 Hz, H-16′), 2.95 and 3.00 (1 H, 2 d, J = 18.5 Hz, H-16), 3.50 (1 H, br s, H-9), 3.53 (1 H, s, H-3), 3.59 (1 H, br s, H-9′), 3.72 and 3.74 (1 H, 2 s, H-3′), 3.76 (1 H, br s, N_1-H), 5.98 and 6.05 (1 H, 2 d, J = 7.5 Hz, H-7), 6.62 and 6.63 (1 H, 2 d, J = 7.5 Hz, H-6′), 6.69 (1 H, t, J = 7.5 Hz, H-5), 6.82 and 6.97 (1 H, 2 d, J = 7.5 Hz, H-7′), 6.85 (1 H, t, J = 7.5 Hz, H-4′), 6.94 and 6.99 (1 H, 2 t, J = 7.5 Hz, H-6), 7.10 (1 H, d, J = 7.5 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 21.9 and 22.3 (C-13 and C-13′), 25.7, 26.7, 26.9, 27.8, 27.9, 28.0, 28.1 (C-17, C-17′, C-19, C-19′, C-20, C-20′), 34.4, 34.6, 35.8, and 35.9 (C-8 and C-8′), 37.8, 39.3, and 39.4 (C-11 and C-11′), 41.5, 41.9, and 42.0 (C-12 and C-12′), 45.6 and 46.3 (C-16 and C-16′), 51.2 and 51.3 (C-14 and C-14′), 57.3, 58.7, and 59.0 (C-9, C-9′, C-18, and C-18′), 68.0, 68.1, and 68.7 (C-3 and C-3′), 80.6 (C-2′), 84.2 and 84.4 (C-2), 109.6, 110.0, 111.4 and 112.0 (C-7 and C-7′), 119.0 (C-5), 123.2 and 123.4 (C-6 and C-6′), 126.8 (C-5), 127.9 and 128.0 (C-4), 130.2 (C-4′a), 131.7 (C-4′), 133.7 (C-4a), 136.9 (C-7a), 147.6 (C-7′a), 152.0 and 152.2 (C-5′), 213.5, 213.6, 213.8, and 214.0 (C-15 and C-15′).

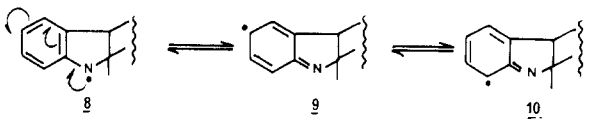
Preparation of Alcohol 4. Aristone (**1**) (42 mg, 1.36×10^{-4} mol) and $LiAlH_4$ (25 mg) in THF (5 mL) were refluxed under nitrogen for 6 h. After cooling, AcOEt (2 mL) was added and normal extractive workup furnished an oil which was purified by flash chromatography on silica gel to yield alcohol **4** (27 mg, 64%): amorphous; UV (EtOH) λ_{max} 213, 246, 298 nm; $[\alpha]^{20}_D$ +2° (*c* 0.74, $CHCl_3$); IR (film) 3300, 1590, 1440 cm^{-1}; MS (70 eV), *m/e* (relative intensity) 310 ($M^{+\bullet}$, 100), 295 (52), 293 (13), 198 (85), 183 (35), 182 (38); ^1H NMR ($CDCl_3$) δ 1.06 (3 H, s, Me), 1.32 (3 H, s, Me), 1.35 (1 H, ddd, J = 14.5, 4.5, 2 Hz, H-12), 1.50 (1 H, dd, J = 9.5, 1 Hz, H-8), 1.55 (3 H, s, Me), 1.70 (2 H, m, H-13 and H-14), 1.79 (1 H, dd, J = 16, 10 Hz, H-16), 1.86 (1 H, dd, J = 16, 3 Hz, H-16), 2.01 (1 H, dd, J = 9.5, 2 Hz, H-8), 2.13 (1 H, ddd, J = 14, 4.5, 3 Hz, H-13), 3.40 (1 H, dd, J = 2, 1 Hz, H-9), 3.65 (1 H, br s, OH), 4.50 (1 H, ddd, J = 10, 8, 3 Hz, H-15), 4.73 (1 H, s, H-3), 6.68 (1 H, d, J = 7.5 Hz, H-7), 6.80 (1 H, t, J = 7.5 Hz, H-5), 7.01 (1 H, t, J = 7.5 Hz, H-6), 7.14 (1 H, d, J = 7.5 Hz, H-4); ^{13}C NMR, see Table I.

Preparation of Diol 5. The reduction of bisaristone A(**2**) (42 mg, 6.81×10^{-5} mol) with $LiAlH_4$ as above gave after normal extractive workup alcohol **5** (37 mg, 87%): amorphous; UV (EtOH) λ_{max} (log ϵ) 209 (4.38), 247 (3.93), 297 (3.60) nm; IR (film) 3300, 1590, 1440 cm^{-1}; MS (70 eV), *m/e* (relative intensity) 618 ($M^{+\bullet}$, 100), 616 (17), 603 (28), 601 (9), 506 (9), 491 (9), 208 (12), 197 (10), 180 (11), 149 (26), 134 (11), 120 (11); ^1H NMR ($CDCl_3$) δ 0.86 (3H, s, Me-17′), 1.06 (3 H, s, Me-17), 1.33, 1.35, 1.58, and 1.61 (4 s, Me-19, Me-19′, Me-20, and Me-20′), 1.5–2.3 (16 H, m), 3.43 (1 H, br s, H-9′), 3.48 (1 H, br s, H-9), 4.10 (1 H, br s, N_1-H), 4.51 (2 H, ddd, J = 10, 8, 3 Hz, H-15 and H-15′), 4.78 (1 H, s, H-3′), 4.90 (1 H, s, H-3), 5.83 (1 H, d, J = 7.5 Hz, H-7), 6.79 (3 H, m, H-4′, H-6, and H-6′), 6.93 (1 H, t, J = 7.5 Hz, H-5), 7.15 (1 H, t, J = 7.5 Hz, H-5′), 7.25 (1 H, d, J = 7.5 Hz, H-4); ^{13}C NMR, see Table I.

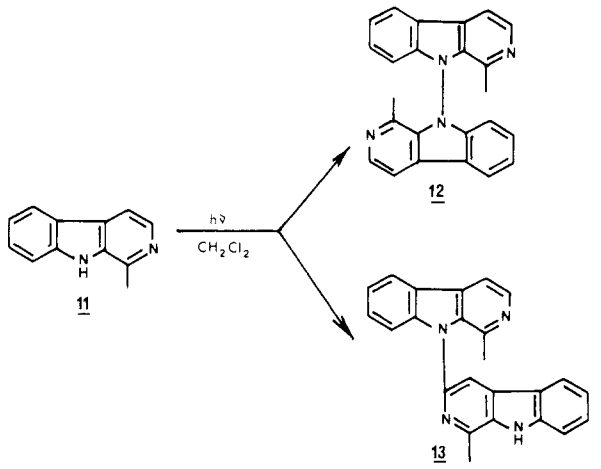
Preparation of Diacetate 6. Alcohol **5** (30 mg, 4.85×10^{-5} mol) was acetylated with acetic anhydride (0.1 mL) in pyridine (2 mL) at reflux for 18 h. The reaction mixture was then concentrated in vacuo to give a crude product which was purified by flash chromatography on silica gel to yield diacetate **6** (29 mg, 87%): amorphous; UV (EtOH) λ_{max} 214, 247, 296 nm; IR ($CHCl_3$) 3350, 1720, 1590, 1440 cm^{-1}; mass spectrum, *m/e* 702 ($M^{+\bullet}$, 100), 687 (10), 658 (2), 643 (50), 627 (2), 599 (2), 586 (16), 583 (14), 550 (3), 526 (9), 499 (6), 415 (7), 293 (6), 292 (23), 181 (10); ^1H NMR ($CDCl_3$) δ 0.87 (3 H, s, Me-17′), 1.07 (3 H, s, Me-17), 1.35, 1.37, 1.45, and 1.46 (4 s, Me-19, Me-19′, Me-20, and Me-20′), 1.4–2.4 (16 H, m), 1.98 and 2.05 (2 s, OAc), 3.43 (1 H, br s, H-9′), 3.48 (1 H, br s, H-9), 4.10 (1 H, br s, N_1-H), 4.53 (1 H, s, H-3′), 4.67 (1 H, s, H-3), 5.40 (2 H, ddd, J = 10, 7.5, 2 Hz, H-15 and H-15′), 5.88 (1 H, d, J = 7.5 Hz, H-7), 6.80 (3 H, m, H-4′, H-6, and H-6′), 6.99 (1 H, t, J = 7.5 Hz, H-5), 7.17 (1 H, d, J = 7.5 Hz, H-5′), 7.25 (1 H, d, J = 7.5 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 23.8 and 24.2 (C-13 and C-13′), 27.5 and 27.6 (CO_2CH_3), 29.3 and 29.4 (C-17, C-17′, C-19, C-19′, C-20, and C-20′), 35.8 and 36.1 (C-14 and C-14′), 34.3, 34.4, 34.8, and 36.7 (C-8, C-8′, C-16, and C-16′), 39.5 and 41.0 (C-11 and C-11′), 41.4 and 42.3 (C-12 and C-12′), 57.2 (C-18 and C-18′), 57.3 and 57.7 (C-9 and C-9′), 65.9 and 66.4 (C-3 and C-3′), 74.4 and 74.8 (C-15 and C-15′), 79.8 (C-2′), 84.8 (C-2), 109.4 (C-7), 119.5 and 120.6 (C-5 and C-5′), 123.1 and 124.1 (C-4 and C-4′), 126.5 and 127.6 (C-6 and C-6′), 128.8 (C-7′), 132.2 and 134.8 (C-4a and

(15) Coyle, J. D. *J. Chem. Soc.* **1971**, 2254.

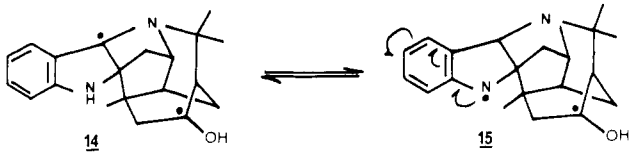
Scheme II



Scheme III



Scheme IV



C-4'a), 149.8 and 152.0 (C-7a and C-7'a), 170.5 and 170.7 (C=O).

Preparation of Diol 7. The reduction of bisaristone B (**3**) (20 mg, 3.35×10^{-5} mol) with $LiAlH_4$ in THF as above gave, after purification on a short column chromatography of silica gel, diol **7** (18 mg, 90%): amorphous; UV (EtOH) λ_{max} (log ϵ) 210 (4.25), 248 (3.95), 295 (3.50) nm; IR (film) 3300, 1590, 1450 cm^{-1}; MS (70 eV), *m/e* (relative intensity) 618 ($M^{+\bullet}$, 50), 616 (19), 603 (16), 601 (7), 585 (4), 562 (3), 561 (3), 544 (3), 506 (11), 490 (5), 465 (5), 439 (3), 149 (8), 94 (100); ^{13}C NMR ($CDCl_3$) δ 23.4 and 23.7 (C-13 and C-13'), 27.3, 28.5, 28.6, 29.2, 29.4, and 29.5 (C-17, C-17', C-19, C-19', C-20, and C-20'), 35.9, 36.2, 36.8, 36.9, 37.5, 37.8, 38.8, 39.0, 39.1, and 39.8 (C-8, C-8', C-14, C-14', C-16, and C-16'), 41.0 and 41.1 (C-11 and C-11'), 41.5 and 41.6 (C-12 and C-12'), 57.4, 57.5, and 57.7 (C-9 and C-9'), 57.8 and 57.9 (C-18 and C-18'), 65.7, 66.0, 66.2, and 66.4 (C-3 and C-3'), 72.1, 72.2, and 72.4 (C-15 and C-15'), 79.7 and 79.9 (C-2'), 83.8 and 83.9 (C-2), 108.8 and 109.6 (C-7), 111.3 and 112.0 (C-7'), 118.3 and 118.5 (C-5), 123.4 and 123.5 (C-6'), 126.4 and 127.2 (C-6), 127.3 and 128.1 (C-4), 130.6 and 130.7 (C-4'a), 131.2 (C-4'), 133.7 and 134.8 (C-4a), 137.0 and 137.1 (C-5'), 147.7 and 147.8 (C-7'a), 152.4 and 152.7 (C-7a).

Partial Synthesis of 3. (a) Potassium Ferricyanide Oxidation of 1. Aristone (**1**) (31 mg, 10^{-4} mol), $K_3Fe(CN)_6$ (150 mg, 4.6×10^{-4} mol), and NBu_4HSO_4 (3 mg) were allowed to react in a two-phase system: CH_2Cl_2 (10 mL)/$NaHCO_3$ 5% aqueous solution (10 mL) with rapid stirring for 4 days. The resultant two-phase reaction mixture was then extracted with CH_2Cl_2. The combined organic layers were washed with water, dried over anhydrous sodium sulfate, and concentrated to give a crude product which was purified by flash chromatography on silica gel (CH_2Cl_2/MeOH, 95/5), yielding bisaristone B (**3**) (22 mg, 71%) and unreacted aristone (**1**) (5 mg). Bisaristone B (**3**), amorphous, was identical with the natural product (MS, ^1H NMR, IR): $[\alpha]^{20}_D$ −75° (*c* 2.2, $CHCl_3$).

(b) Irradiation of 1. A solution of aristone (**1**) (125 mg, 4×10^{-4} mol) in CH_2Cl_2 (5 mL) was irradiated for 2 h in a Pyrex glass vessel using a medium pressure mercury lamp (Hanau, 500 W).

After distillation of the solvant, the crude product was purified by flash chromatography on silica gel, yielding starting material **1** (70 mg) and bisaristone B (**3**) (12 mg, 10%) identical with the natural product $[\alpha]^{20}_D$ −65° (*c* 1.1, $CHCl_3$).

(c) $VOCl_3$ Oxidation of 1. A solution of **1** (40 mg, 1.29×10^{-4} mol) in anhydrous ether (3 mL) was added slowly to a solution of vanadium oxytrichloride (56 mg, 3.23×10^{-4} mol) in ether (5 mL) at −78 °C under nitrogen atmosphere. The resulting dark solution was stirred at −78 °C for 24 h and refluxed for 6 h. The reaction mixture was then diluted with ether (10 mL) and the organic layer was washed with water, dried over anhydrous sodium sulfate, and concentrated. The crude product was purified by TLC. A pure dimer (3 mg) was obtained as an amorphous solid: MS (70 eV), *m/e* (relative intensity) 686 (11), 685 (19), 684 (39), 682 (52), 279 (4), 207 (4), 178 (29), 149 (13), 94 (95), 91 (100); ^1H NMR ($CDCl_3$) δ 1.24 and 1.27 (s, Me-17 and Me-17'), 1.37 and 1.41 (s, Me-19, Me-19', Me-20, and Me-20'), 1.87 (m, 2 H, H-12 and H-12'), 1.90 (m, 2 H, H-13 and H-13'), 2.05 (dd, 2 H, H-8 and H8', J = 10, 1.5 Hz), 2.12 (m, 2 H, H-14 and H-14'), 2.15 (d, 2 H, H-16 and H-16', J = 18 Hz), 2.35 (m, 2 H, H-13 and H-13'), 2.81 (d, 2 H, H-16 and H-16', J = 18 Hz), 3.58 (br s, 2 H, H-9 and H-9'), 3.65 (br s, 2 H, H-3 and H-3'), 3.90 (1 H, s, N_1-H), 7.17 (1 H, s), 7.2–7.3 (4 H, m).

Acknowledgment. We thank MM. C. Mackowski and T. W. Tweedie, New South Wales Forestry Commission, for their invaluable assistance in collecting and identifying the plant material.