Structure and Biogenetic-type Synthesis of Andranginine: an Indole Alkaloid of a New Type

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Summary The isolation and structure of andranginine (**1**), an indole alkaloid of a new type is described; the transformation of precondylocarpine acetate (**5**) into this novel alkaloid has been achieved.

ANDRANGININE (**1**), $C_{21}H_{22}N_2O_2$ (M^+ 334), m.p. 240°, $[\alpha]^{25}$ (300—600 nm) = 0°, is one of the indole alkaloids isolated from *Craspidospermum verticillatum Boj. var. petiolare*.† The spectroscopic properties of (**1**) revealed an indolic chromophore, λ_{max} (EtOH) 225 (log ϵ 4·02), 285 (3·76), and 293 (3·55) nm, and an ester function ν_{max} (Nujol) 1700 cm^{-1}; furthermore, the ^{13}C n.m.r. assignments of the natural product (**1**) and ^1H n.m.r. data for the corresponding $LiAlH_4$ reduction product (**2**), $C_{20}H_{22}ON_2$ (M^+ 306), m.p. 224°, are consistent with the proposed structure (see Table).

The mass spectrum of andranginine (1) confirms the molecular formula and exhibits significant peaks at *m/e* 105, 119, 120, 133 (base peak), 214, and 229 compatible with the structure in terms of (**1**) and (**3**).

Andranginine (**1**) had been independently synthesized (A.I.S., C.C.W.) during the course of previous studies[1–4] on the formation and reaction of dihydropyridine-acrylic esters of the secodine series. Thermolysis of precondylocarpine acetate (**5**)[4] at 100° in ethyl acetate solution afforded a racemic compound (28% yield) which was identical with andranginine (**1**). It is noteworthy that a concerted

† Details of other alkaloids from this plant will be published in *Bull. Soc. chim. France*, C. Kan-Fan, B. C. Das, H.-P. Husson, and P. Potier.

TABLE

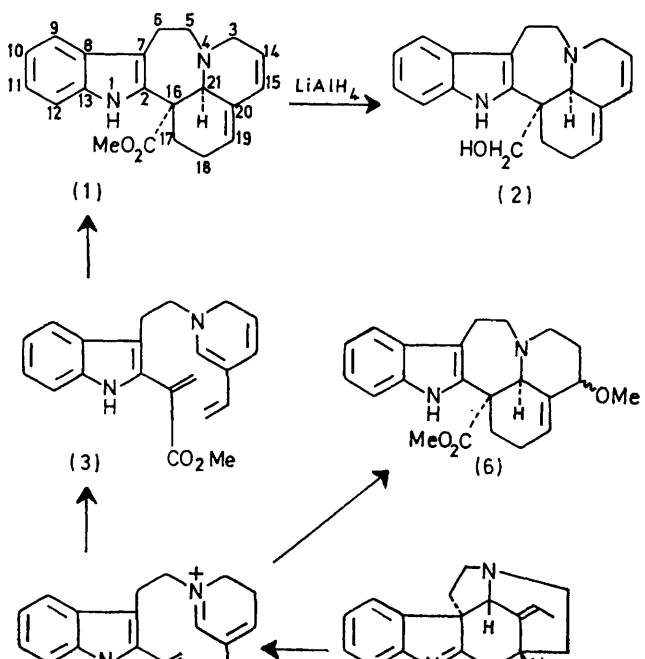
Assignment of ^{13}C chemical shifts[a]

	Compound (1)	Compound (2)
C-2	137·2	141·2
C-3	54·0	55·2
C-5	54·9	57·9
C-6	17·8(a)	17·8(c)
C-7	114·4	113·9
C-8	127·6	127·7
C-9	118·2	117·8
C-10	121·7	121·2
C-11	119·1	119·0
C-12	110·7	110·6
C-13	134·9(b)	134·8(d)
C-14	128·8	125·2
C-15	128·0	128·5
C-16	48·2	42·8
C-17	33·7	30·5
C-18	22·8(a)	22·4(c)
C-19	122·5	124·9
C-20	135·3(b)	134·2(d)
C-21	64·9	63·4
CH_3 (ester)	52·3	—
CO (ester)	171·8	—
CH_2 (alcohol)	—	63·4

^1H Chemical shifts for the alcohol (2)[b]

	δ p.p.m.	Coupling constants Hz
3α-H (pseudo ax.)	3·55	^2J 16(d)
3β-H (pseudo eq.)	3·15	^2J 16, ^3J 5(q)
5α-H (eq.)	3·10	^2J 14, ^3J 5(q)
5β-H (ax.)	3·60	^2J 14, ^3J 11(q)
6α-H (ax.)	3·05	^2J 16, ^3J 11(q)
6β-H (eq.)	2·75	^2J 16, ^3J 5(q)
14-H	5·70	^3J 10, $^3J'$5(q)
15-H	6·05	^3J 10(d)
17α-H (eq.)	2·55	^2J 15, ^3J 6(q)
17β-H (ax.)	1·66	^2J 15, ^3J 15, $^3J'$6(m)
18α-H (ax.)	2·33	^2J 18, ^3J 15(m)
18β-H (eq.)	2·15	^2J 18, ^3J 6, $^3J'$ 6, $^3J''$ 5(m)
19-H	5·65[c]	
21-H	3·70[d]	

[a] The ^{13}C n.m.r. spectra were obtained using a Bruker HX90E pulsed FT spectrometer at 22·63 MHz in deuteriochloroform; $\delta(Me_4Si) = \delta(CDCl_3) + 76·9$; (a), (b), (c), and (d) values could be interchanged. [b] In $CDCl_3$–CF_3CO_2H (99 : 1) against Me_4Si internal standard (δ = 0), spectra recorded at 240 MHz (due to the courtesy of Drs. S. K. Kan, P. Gonord, C. Duret, Institut d'Electronique Fondamentale, 91-Orsay, France). Assignments made after decoupling experiments. [c] Broad signal, $W_{\frac{1}{2}}$ 12 Hz. [d] Singlet.



cycloaddition of (3) leads to the observed stereospecificity‡ and further that the increased yield compared with the thermal reactions involving other dihydropyridine acrylic esters[4] may be ascribed to stabilization of species (3) or (4) by the presence of the vinyl substituent generated from the ethylidene group of (5) during the rearrangement which must follow a course similar to that described earlier.[1,4] Further support for the proposed mechanism was obtained by carrying out the thermolysis in methanol to yield racemic compound (6),§ a result of trapping the intermediate immonium species (4).

The simultaneous and independent discovery of a new type of alkaloid from natural sources and from the simple and relatively high yielding partial synthesis described above brings further evidence to bear on the role of secodihydropyridine systems in the biosynthesis of the more complex indole alkaloids and once again[4] opens the possibility of cycloaddition chemistry in the formation of this type of natural product. As discussed elsewhere[5] the operation of extended Mannich chemistry also rationalizes the reaction (3) → (1).

The lack of optical activity in both natural and synthetic product is of considerable interest and suggests that the achiral secodine-type precursor (3) is transformed into (1) in a non-enzymatic process in *C. verticillatum*.

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‡ Although direct evidence for the assignment of configurations at C-16 and C-21 is lacking, previous work in this field of alkaloids[1–4] makes it logical to draw analogy and represent stereochemistry at these centres as depicted in (1). However, this point will be clarified from *X*-ray analysis of (1) which is currently under investigation.

§ Compound (6) showed an indole chromophore and *m/e* 366 (M^+), 335 (M^+ — OMe), 334 (M^+ — MeOH), 229, and 152.

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[5] A. I. Scott and C. C. Wei, *Bio-organic Chemistry*, 1974, in the press.