Phytochemistry, 1978, Vol 17, pp 1686–1687 © Pergamon Press Ltd Printed in England. 0031-9422/78/0901 1686 $02.00/0

ADINA ALKALOIDS: ISOLATION OF DESOXYCORDIFOLINE

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(*Received* 13 *January* 1978)

Key Word Index—*Adina rubescens*; Rubiaceae; carboxy β-carboline glucoside

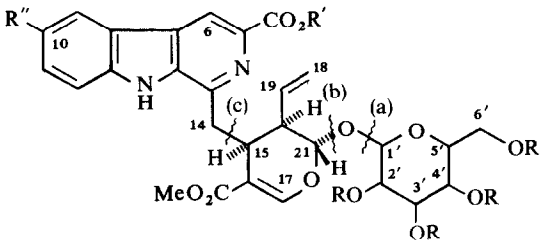
The Malaysian tree *Adina rubescens* has been shown to contain an extensive series [2–8] of carboxy indole alkaloids. We now report the isolation from *A. rubescens* of pure crystalline desoxycordifoline (**1a**) previously obtained only as the methyl tetraacetate derivative [1, 3] (**1b**) from *Adina cordifolia*.

A combination of ion exchange and gel permeation chromatography of a methanolic extract of *A. rubescens* heartwood afforded a light yellowish crystalline glucoalkaloid $C_{28}H_{30}NO_{11}$ $[\alpha]_D^{25}$ −212° (H_2O); mp 178–180°. Its UV spectrum was the sum of an aromatic β-carboline and β-alkoxyacrylate chromophores, the latter accounting for two peaks at 1650 and 1635 cm^{-1} in the IR spectrum in addition to carboxylic acid, hydroxyl and indolic N—H bands at 3000–2500, 3300–3120 and 3400 cm^{-1} respectively. NMR signals for a carboxylic acid proton at τ −1.10, an indolic N—H at τ 0.89 as well as five aromatic protons in the region τ 1.10–3.0 confirmed the above observations. Three olefinic proton signals overlaid the sugar protons H-1′-4′ in the region τ 4.2–5.5, while a singlet at τ 2.35 corresponded to the vinylic proton of a β-alkoxyacrylate system and a methoxyl singlet at 6.46 overlaying the sugar hydroxyls in the region τ 6.0–6.55 was consistent with a methyl ester. Cleavage with β-glucosidase established that the sugar moiety was β-D-glucose.

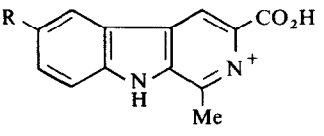
Acetylation gave the tetraacetate derivative (**1c**) whose NMR spectrum was similar to that of the known [1] methyl tetraacetate derivative (**1b**) except for the presence in the spectrum of (**1c**) of a carboxylic acid proton signal at τ 3.50 and the absence of an extra methoxy signal. The IR spectrum showed N—H, carboxylic acid and carbonyl absorptions at 3400, 3000–2500 and 1750 cm^{-1} respectively. The three proton vinylic group was further confirmed by the mass spectrum of (**1c**) which showed a strong peak at *m/e* 165 ($C_9H_9O_3$) corresponding to the pyrylium ion (**3**). Comparison of the rest of the mass spectrum of (**1c**) with that of cordifoline pentaacetate (**1d**) [9] showed some very striking similarities in the types of fragments and pattern of fragmentation. Both spectra showed a very intense sugar fragment at *m/e* 331 ($C_{14}H_{19}O_9$) attributed to the oxonium ion (**4**) and complementary ions at M −331 ($C_{14}H_{19}O_9$) and M −347 ($C_{14}H_{19}O_{10}$) corresponding to cleavages (a) and (b). The spectra of (**1c**) and (**1d**) showed peaks at *m/e* 284 ($C_{15}H_{12}O_4N_2$) and *m/e* 226 ($C_{13}H_{10}N_2O_2$) respectively. The latter two fragments corresponded to the β-carboline ions (**2a**) and (**2b**) which resulted from the favourable cleavage (c) and hydrogen transfer. It was thus becoming increasingly apparent that we were dealing with an analogue of cordifoline. This inference was subsequently confirmed when methylation of (**1c**) gave a product which was identical (NMR, UV, IR and TLC) with an authentic sample of methyl desoxycordifoline tetraacetate (**1b**). We have thus correlated the glucoalkaloid structure (**1a**) with that of its 10-acetoxy analogue (**1d**) and its known methyl tetraacetate derivative (**1b**).

EXPERIMENTAL

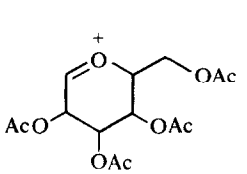
Isolation of desoxycordifoline (**1a**). Finely ground heartwood (900 g) of *A. rubescens* was extracted with methanol (6 l.), and the solvent was removed under red. pres. to give an amorphous brown powder (101 g). The latter was taken up in MeOH and passed down an Amberlyst A15(H^+) resin column. Elution with MeOH–NMe_3 afforded a basic concentrate (22 g). Further ion exchange chromatography of the above concentrate on an Amberlyst A26 (OH^-) column, eluting with MeOH–dil. HOAc gave an amino acid concentrate (16 g). Half of this was taken up in MeOH and chromatographed on Sephadex LH20 gel (600 g) eluting with MeOH. 120 × 20 ml fractions were collected and monitored by UV and TLC assay. Fractions 39–43 were combined and the solvent vol reduced to about



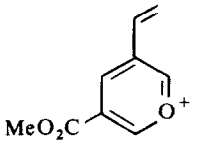
	R	*R′*	*R″*
(**1a**)	H	H	H
(**1b**)	Ac	Me	H
(**1c**)	Ac	H	H
(**1d**)	Ac	H	OAc



(**2a**) R = OAc
(**2b**) R = H



(**4**) *m/e* 331



(**3**) *m/e* 165

50 ml, when addition of Me_2CO precipitated desoxycordifoline (0.60 g). This was recrystallized from Me_2CO–MeOH (1:1), mp 178–180°; $[\alpha]_D^{25}$ −212° (H_2O); UV λ_{max}^{MeOH} nm: 238, 268, 305, 347; IR ν_{max}^{Nujol} cm^{-1}: 3400 (N—H), 3300–3000 (OH), 3000–2500 (—CO_2H), 1650, 1635 ($MeO_2C.C{=}CH{-}O$). τ(CD_3COCD_3): 1.10, (1H, *s*, CO_2H); 0.6–1.0 (1H, *br s*, N—H), 1.25 (1H, *s*, H-6). 1.7 (1H, *d*, H-9) 2.20–3.0 (4H, *m*, H-17, 10, 11, 12) 4.2–5.5 (3H, *m*, H-18 and 19), 5.00–5.40 (5H, *m*, H-21 and H-1′-4′), 6.0–6.55 (7H, sugar OH, H-5′, H_2-6′), 6.46 (3H, *s*, OMe), 6.70 (2H, *m*, H_2-14), 7.35 (1H, *m*, H-15).

Acetylation (Ac_2O/Py) gave desoxycordifoline tetraacetate (**1c**) ($C_{36}H_{38}N_2O_{15}$); $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (indole N—H), 3000–2500 (CO_2H), 1750, 1700, 1695 (CO) λ_{max}^{EtOH} nm: 238, 268, 305, 347. τ ($CDCl_3$): 1.13 (1H, *s*, H-6), 1.75 (1H, *d*, H-9) 2.20–2.9 (5H, *m*, Ar_3, indole N—H, H-17), 3.5 (1H, *br s*, —CO_2H), 4.00–4.3 (1H, *m*, H-19); 4.30–5.3 (7H, *m*, H-21, H_2-18, H_4-1′-4′); 5.86 (2H, *br s*, H-6′); 6.20 (3H, *s*, —OCH_3), 6.30–7.00 (4H, *m*, H_2-14, H-5′, H-15), 7.35 (1H, *m*, H-20), 8.0 (4× 3H, *s*, —CO—CH_3).

MS: *m/e* 739, 738 (M^+), 721, 693, 450, 407, 391, 347, 331, 271, 226, 181, 169, 165, 127, 109.

Subsequent methylation of (**1c**) with diazomethane gave a product that was identical (NMR, MS, IR, TLC) with the authentic methyl desoxycordifoline tetraacetate (**1b**) [1, 3].

Acknowledgements—We thank the SRC and The Commonwealth Scholarship Commission in the U.K. for financial support of this work.

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Phytochemistry, 1978, Vol. 17, pp 1687–1689 © Pergamon Press Ltd Printed in England 0031-9422/78/0901-1687 $02.00/0

ALKALOIDS FROM *STRYCHNOS USAMBARENSIS*: REVISED STRUCTURE FOR USAMBARINE

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(*Received* 26 *January* 1978; *received for publication* 17 *March* 1978)

Key Word Index—*Strychnos usambarensis*; Loganiaceae; bis-indole alkaloids; usambarine.

Abstract—Synthesis has shown an error in the structural determination of usambarine. A further examination of IR and PMR spectra indicates a revised structure for this alkaloid. Stereochemistry (3*S*, 4*R*, 15*S*, 17*S*, 20*R*) has been advanced from the CD curve and biosynthetic considerations.

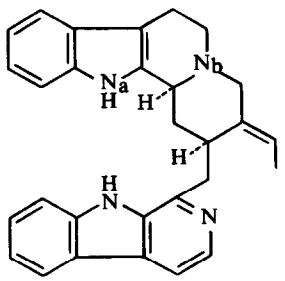
INTRODUCTION

In 1971, some new bis-indole alkaloids were isolated from the roots of *Strychnos usambarensis*: usambarensine (**1**), 3′,4′ dihydrousambarensine (**2**) and their N_b-metho derivatives [1]. Usambarine (**3**) was obtained from leaves of the same species [2]. In 1975, the structure and absolute configuration of usambarensine was proved by X-Ray analysis [3]; the structure and stereochemistry of 3′,4′ dihydrousambarensine were also established by synthesis from (±)-geissoschizoic acid [4].

The synthesis of usambarine was then carried out. The four stereoisomers of formula (**3**) (epimeric at C-3 and C-17) were synthesized and none was identical with natural usambarine, by comparison of PMR and IR spectra: moreover none was present in the leaves of *Strychnos usambarensis*. These facts suggested that the structure (**3**) for usambarine needed reconsideration.

RESULTS AND DISCUSSION

The synthetic bases were prepared by condensation of (±)-geissoschizal (or (±)-3-epi-geissoschizal) and N_b-methyltryptamine in 0.3 M H_2SO_4 at 103–105°. The



1 usambarensine