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REVERSIBLE TRAPPING OF LABILE 21-DEHYDROHETEROYOHIMBINES AS 21-CYANO ADDUCTS.

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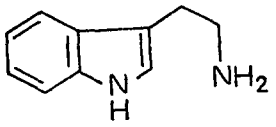
Recently we reported the biomimetic conversion of strictosidine (3a) into tetrahydroalstonine (8a) and vincoside (3b) into akuammigine (8b).[1] Both were kinetically controlled reactions where the more rapidly formed, N_4-C_{21} cyclised intermediates were reduced before rearrangement could occur to the thermodynamically more stable vallesiachotamine isomers (4) with N_4-C_{17} bonds. The labile intermediates were considered to be 21-dehydroheteroyohimbines (5) or the related enamines (6) which we have now confirmed by trapping as their stable, crystalline cyanide adducts (7) from which the dehydro compounds can be subsequently regenerated.

A mixture of vincoside and strictosidine was prepared by condensation of tryptamine (1) and secologanin (2) in pH4.0 citrate/phosphate buffer. After the pH had been adjusted to 5.5, β-glucosidase and a two-fold excess of KCN were added, and the solution left to stand overnight. The products were isolated by chloroform extraction and crystallisation from methanol afforded one compound $C_{21}H_{24}N_3O_3$ (M^+ 277.1789), m.p. 231-2° $[\alpha]_D^{25}$ -170° ($CHCl_3$) in ca. 10% yield. The basic heteroyohimbine structure was evident from mass spectral fragments as was the presence of a cyano group, which also showed an i.r. band at 2240 cm^{-1}; a positive Cotton effect in the c.d. spectrum at 295 n.m. indicated that H-3 was α. After a detailed analysis of the p.m.r. spectrum (see Table) the structure was assigned as 21-cyano-tetrahydroalstonine (7a) which was confirmed by reduction to tetrahydroalstonine after prolonged treatment with $NaBH_4$ in ethanol at 40° for 24 hrs.[2] Treatment of an ethanolic solution of (7a) overnight with silver acetate liberated the labile 20,21-dehydroajmalicine (6a), identified from its spectral data and by its rapid reduction to tetrahydroalstonine (8a) with $NaBH_4$.[3]

Proton	21-Cyano-akuammigine τ	Multiplicity	J (Hz)	21-Cyano-tetrahydroalstonine τ	Multiplicity	J (Hz)
NH	2.13	s		2.15	s	
H-3	6.70	d + f.c.	13 (H-14α), 2 (H-14β), 1 (H-6)	6.00	d + f.c.	12 (H-14β), 3.6 (H-14α) 2 (H-6's)
H-5α	6.34	q + f.c.	11.5 (H-5β), 6 (H-6α), 1.2 (H-6β)			
H-5β	7.40	t of d's	11.5 (H-5α), 11.5 (H-6α), 4.2 (H-6β)	7.06	M (3H)	
H-6α	7.00	m	15.5 (H-6β), 11.5 (H-5β), 6 (H-5α)	7.24	M (1H)	
H-6β	7.24	d + f.c.	15.5 (H-6α), 4.2 (H-5β), 1.2 (H-5α)			
H-14α	8.26	t of d's	15.5 (H-14β), 13 (H-3), 4.2 (H-15)	7.44	d of t's	13 (H-14β), 4.5 (H-15), 3.6 (H-3)
H-14β	6.75	d of t's	15.5 (H-14α), 2.5 (H-3), 2.5 (H-15)	8.49	q	13 (H-14α), 12 (H-3), 12 (H-15)
H-15	6.91	broad s	6.4 (H-20), 4.2 (H-14α), 2.5 (H-14β)	6.86	d of t's	12 (H-14β), 4.5 (H-14α), 4.5 (H-20)
H-17	2.38	s		2.23	s	
H-18 (Me)	8.65	d	6.5 (H-19)	8.37	d	6 Hz (H-19)
H-19	5.23	q + f.c.	6.5 (H-18), 1 (H-20)	5.57	sextet	10.2 (H-20), 6 Hz (H-18's)
H-20	7.72	q + f.c.	11.5 (H-21), 5.4 (H-13), 1 (H-19)	8.03	d of d's	10.2 (H-19), 4.5 (H-15), 1.5 Hz (H-21)
H-21	6.63	d	11.5 (H-20)	5.84	d	1.5 (H-20)
CO_2Me	6.27	s		6.21	s	



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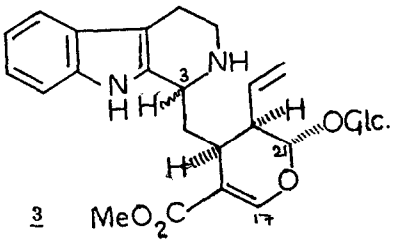

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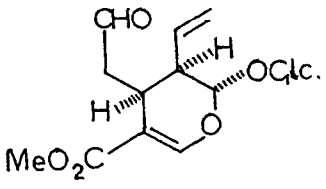

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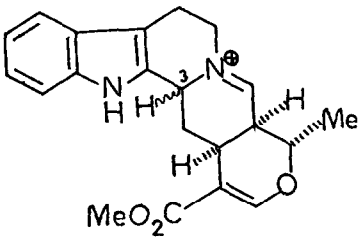

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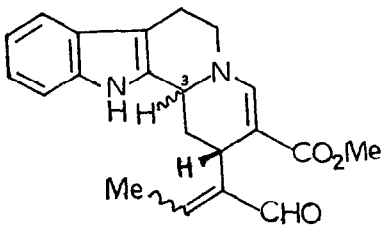
3-H

a: α

b: β



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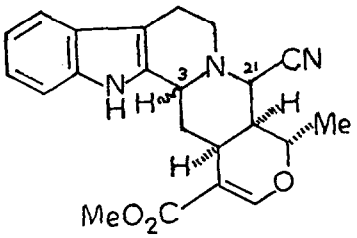

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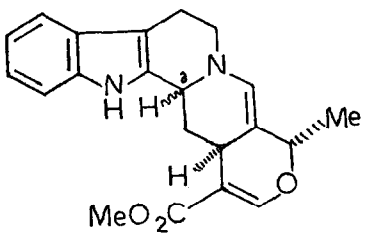

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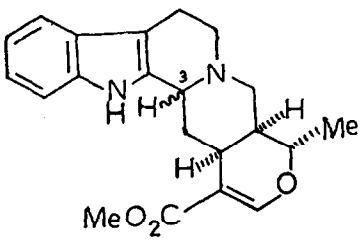

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Chromatography of the mother liquors afforded more (7a) and an isomeric compound m.p. 189-190°. The latter was assigned the structure of 21-cyanoakuammigine (7b) from u.v., i.r., c.d. and m.s. spectra and a detailed p.m.r. analysis (see Table) as before, and confirmed by reduction to akuammigine (8b) in the same way.

Overall the yield of crystalline cyano-alkaloids was ca. 20%, with a greater proportion of the 3α isomer. The simplicity and reversibility of the procedure make it an attractive method for preparing the previously inaccessible 21-dehydro alkaloids, and in particular labelled compounds, for further biosynthetic studies.

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