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A NOVEL SYNTHESIS OF ISORHYNCHOPHYLLINE AND RHYNCHOPHYLLINE FROM SECOLOGANIN

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Recently we established novel bicylic structures for the aglycones formed by enzymatic removal of the lucose units from secologanin and its 3,4-dihydro derivative[1], and we now report that these can be used or an efficient synthesis of oxindole alkaloids. Brief warming of dihydrosecologanin aglycone (1) and oxy-tryptamine HCl in ethanol containing a few drops of Et_3N resulted in the rapid (≈ 5 mins.) formation of a ingle product in > 90% yield. This was isolated as an amorphous powder, $C_{21}H_{24}N_2O_4$, $[\alpha]_D^{25}$ +132° $CHCl_3$), and attributed the structure of an oxydihydromancunine (6) on the basis of chemical and spectral nalogies to dihydromancunine.[2] In particular, intense mass spectral peaks at $^m/e$ 267 (M-$C_4H_5O_3$) and 241 M-$C_6H_7O_3$) were attributed to ions 10 and 11 respectively and the UV spectrum was unaffected by alkali. ventually the 300 MHz NMR spectrum (see Table) allowed assignment of virtually every proton in accor-ance with structure 6, which is presumably formed from 2 in the sequence shown.

Catalytic hydrogenation of oxydihydromancunine in methanolic acetic acid resulted in the uptake of one mol. of hydrogen and the product now exhibited an immediate base shift to 275nm in the UV spectrum chara-teristic of an enolised β-dicarbonyl system. Treatment with diazomethane afforded the methyl ether, $[\alpha]_D^{25}$ 13° ($CHCl_3$), which was identical with isorhynchophylline (8) in all respects, and was readily inverted to he C-7 epimer rhynchophylline (9) m.p. 207-211°, $[\alpha]_D^{25}$ -17° ($CHCl_3$) by refluxing in glacial acetic acid or 4 hours.

Since the configuration of the chiral centres at C-3, 7 and 20 could all be changed during the reaction equence no stereochemical correlation is possible between isorhynchophylline and oxydihydromancunine. owever a positive Cotton effect at 290nm in the CD spectrum of oxydihydromancunine showed that the spiro entre at C-7 was in the B series, and another at 260nm indicated that H-3 was β.[3] The latter was con-rmed when analysis of the coupling constants of the C-3, 14, and 15 protons in the NMR spectrum proved to be trans to H-15, but the stereochemistry of H-20 remains to be established.

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TABLE

Proton	Multiplicity	J(Hz)	Chemical Shift (τ)
N-H	s		1.06
H-17	s		2.22
H-9—12	m	-	2.64 - 3.2
H-21	bs	~1,~1	4.96
O - Me	s		6.4
H_b-5	m	9,8,8	6.74
H_a-5	m	9,5,3	6.84
H-3	m	9,2.5	6.92
H-15	bs	3.5, ~2, ~1	7.3
H_b-6	m	12,8,3	7.55
H_a-6	m	12,8,5	8.0
H_2-19, H-20	m	-	8.22-8.56
H_b-14	m	12,2.5, ~ 2	8.78
H_a-14	m	12,9,3.5	8.88
H_3-18	t	7	9.08

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