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CONDOXINE: A NOVEL OXINDOLE SYSTEM FROM SECOLOGANIN AGLYCONE.

Richard T. Brown and Ray Platt

Department of Chemistry, The University, Manchester M 13 9 PL

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Recently we reported that condensation of 2-oxytryptamine (1) and 3,4-dihydrosecologanin aglycone (2a) afforded oxydihydromancunine, subsequently shown to have the unique pseudo structure (3a).[1,2] We have now found that similar reaction of (1) with secologanin aglycone (2b) takes a different course to give the novel compound (4), which we have termed condoxine, rather than the anticipated oxymancunine (3b/5) or heteroyohimbine (6) structures.

Treatment of an equimolar mixture of oxytryptamine hydrochloride and secologanin aglycone in ethanol with a few drops of triethylamine at room temperature for five minutes gave largely one product. Removal of the solvent, chromatography on silica and recrystallisation from chloroform/cyclohexane afforded prisms m.p. 142-5°, $[\alpha]_D^{25}$ -14° ($CHCl_3$). As anticipated, mass measurement gave a molecular formula $C_{21}H_{22}N_2O_4$, and the oxindole and β-alkoxyacrylate chromophores were still present with a UV maximum at 247 nm and IR bands at 1720 and 1627 cm^{-1}. Furthermore a strong mass spectral fragment at m/e 265 due to the loss of $C_4H_5O_3$ from the molecular ion was in accord with 3b, 5 or 6. However, the CD spectrum displayed a positive Cotton effect at 310 nm and a negative one at 260 nm indicating 7B and 3α configurations respectively. Due to severe steric interactions the latter is not compatible with a mancunine type structure 3b or 5 which was thus eliminated on these and other grounds.

On the other hand, attempts to interpret the NMR spectrum on the basis of structure 6 revealed several inconsistencies which led to its exclusion. For example, there was no signal readily attributable to H-21 in 6, whereas that at τ 4.7 matched H-21 in 3 but was coupled to a methylene group corresponding to C-14. Eventually interchange of the masked aldehyde functions at C-3 and C-21 gave structure 4, which had a chair form piperidine ring with a mancunine type ether bridge and could also account for the α-configuration at the centre between N-4 and C-7 indicated by the CD spectrum. It allowed assignment of every signal in the NMR spectrum (see Table) with the aid of decoupling and benzene induced shifts. Moreover, the observed coupling constants could be fitted to values estimated from a Dreiding model incorporating

the known absolute configurations. In particular, the high field shift of H-19 and the long-range interaction between Me-18 and H-21 were explained by the indicated ethylidene configuration.

A precedent for the interchange of C-3 and C-21 is afforded by the indole alkaloids related to condylocarpine (7), and the process can be visualised as involving an intermediate such as 8. However there is no obvious reason why 4 should be formed to the apparent exclusion of 5 and 6.

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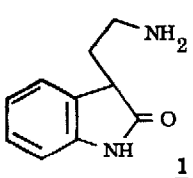
TABLE NMR Spectrum at 300MHz.

Proton	Multiplicity	J(Hz)	$\tau(CDCl_3)$	$\tau(CDCl_3/C_6D_6$ 1:1)
N-H	s		1.25	
H-17	s		2.15	
H9 - 12	m		2.7-3.2	
H-3	bs	3.5, ~2, ~1	4.70	
H - 19	qd	7, 1.8, < 1	5.60	
H - 15	m	3.5, ~2, ~1, < 1	(6.15)	6.18
H - 21	dd	1.8, 2.0	(6.15)	6.08
O-Me	s		6.35	
Ha - 5	m	13, 11, 5	6.60	
Hb - 5	m	13, 9, 6	6.75	
Ha - 6	m	9, 9, 5	7.65	
Hb - 6	m	11, 9, 6	8.06	
Ha - 14	dt	13, 3.5, 3.5	7.98	
Hb - 14	dt	13, ~2, ~2	8.13	
H_3 - 18	dd	7, 2.0	8.52	

References

1. R. T. Brown, C. L. Chapple and R. Platt, Tetrahedron Letters, 1401 (1976).
2. R. T. Brown, and R. Platt, J.C.S. Chem. Comm., in press (1976).



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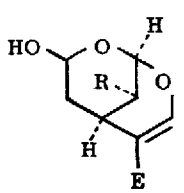
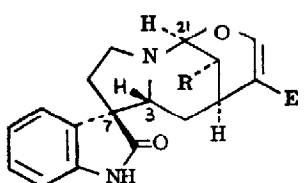
E = CO_2Me



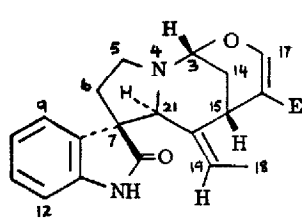
R

2a: Et
b: $CH{:}CH_2$



R

3a: Et
b: $CH{:}CH_2$



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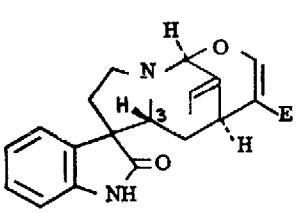

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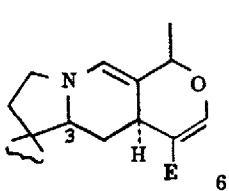

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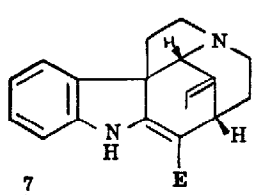

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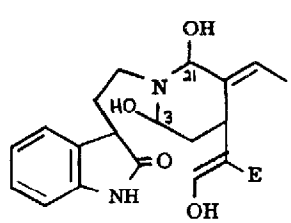

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