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PARTIAL SYNTHESIS OF BALOXINE

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Abstract - Baloxine 1 (19S-hydroxy 14-oxo vincadifformine) was obtained from vindolinine 2.

The structure of baloxine 1, an alkaloid of the leaves of *Melodinus balansae* Baill. has been inferred from its spectroscopic properties (1), except for the configuration of C(19). It seemed obvious to prepare baloxine (19-hydroxy 14-oxo vincadifformine) through hydroboration-oxidation (*viz* 2,3,4) and further transformation of a suitable precursor.

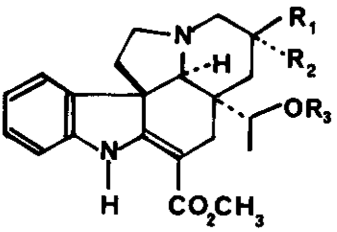
Vindolinine 2 was transformed (5,6) into 19 R- and 19 S-hydroxytabersonine 3 and 4 of known structure and configuration, the respective tetrahydropyranyl derivatives of which were prepared : 5 and 6. 5 as well as 6 were shown (NMR) to be a diastereoisomeric mixture due to the tetrahydropyranyl substituent.

Hydroboration of 5 - 1) $Et_3O^+BF_4^-$; 2) $NaBH_4$,THF - followed by oxidation (H_2O_2, NaOH) yielded only an untractable mixture, while 6 gave under these conditions results similar to those gained with tabersonine (3) : a mixture of two derivatives was thus obtained (72 %). Their mass spectra ($M^{+\cdot}$454) spectroscopic data and further transformations showed them to be the stereoisomeric alcohols 7a and 7b.

Oxidation of the mixture of 7a and 7b under Albright and Goldman's conditions (DMSO, Ac_2O) (7) yielded (60%) the ketone 9,I.R.$_{CHCl_3}$ 1730, 1680, 1610 cm^{-1}, $M^{+\cdot}$452, S.M. m/z 238 (100%), 214 (85%), 138 (75%) plus the methylthiomethyl derivatives 8a,b ($M^{+\cdot}$514) as by-products (12%).

Finally, hydrolysis (HCl-H_2O-EtOH, .05:.05:1, 5 minutes) of 9 gave 19S-hydroxy 14-oxo vincadifformine 1 (60%) $(\alpha)_D$=-120° ($CHCl_3$, c=0.1) ; I.R.$_{CHCl_3}$: 3450, 1735, 1680, 1610 cm^{-1} ; S.M. : m/z 368 ($M^{+\cdot}$), 350, 323, 214, 154 (100%) ; N.M.R. : 1.01 (d,3H,C(18)-H_3) ; 3.75 (s,3H,$COOCH_3$).

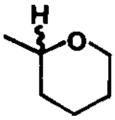
Its U.V., I.R. and mass spectra were superimposable with those of baloxine. Baloxine is thus shown to be 19S-hydroxy 14-oxo vincadifformine (8).

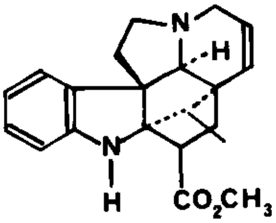


1

	R_1	R_2	R_3
1	=O		THP
7a	H	OH	THP
7b	OH	H	THP
8a	H	H_3C–O–S–	THP
8b	H_3C–O–S–	H	THP
9	=O		THP

THP =





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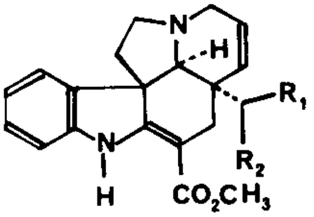

3

	R_1	R_2	
3	CH_3	OH	(19R)
4	OH	CH_3	(19S)
5	CH_3	OTHP	(19R)
6	OTHP	CH_3	(19S)

REFERENCES AND NOTE

1 . M.H.Mehri, M.Koch, M.Plat and P.Potier, Bull.Soc.Chim.Fr., 1972, 3291.

2 . G.Lukacs, M. de Bellefon, L.Le Men-Olivier, J.Lévy and J.Le Men, Tetrahedron Letters,1974,487.

3 . C.Caron -Sigaut, L.Le Men-Olivier, G.Hugel, J.Lévy and J.Le Men, Tetrahedron, 1979, **35**, 957.

4 . C.Caron-Sigaut, Thèse de Doctorat d'Etat, Reims, 1980.

5 . P.Rasoanaivo, N.Langlois and P.Potier, Tetrahedron Letters, 1974, 3669.

6 . N.Langlois and R.Z.Andriamialisoa, J.Org.Chem., 1979, **44**, 2468.

7 . J.D.Albright and L.Goldmann, J.Am.Chem.Soc., 1967, **89**, 2416.

8 . This work was initiated by the late Professor J.Le Men.

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