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HETEROYOHIMBINES AND THEIR CORRESPONDING OXINDOLES,III (1).

A CHEMICAL CORRELATION THROUGH SECO-OXINDOLES

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Seco-oxindoles were obtained both from oxindoles and 7-chloro indolenines through reduction with a 1:1 mixture of formic acid and formamide.

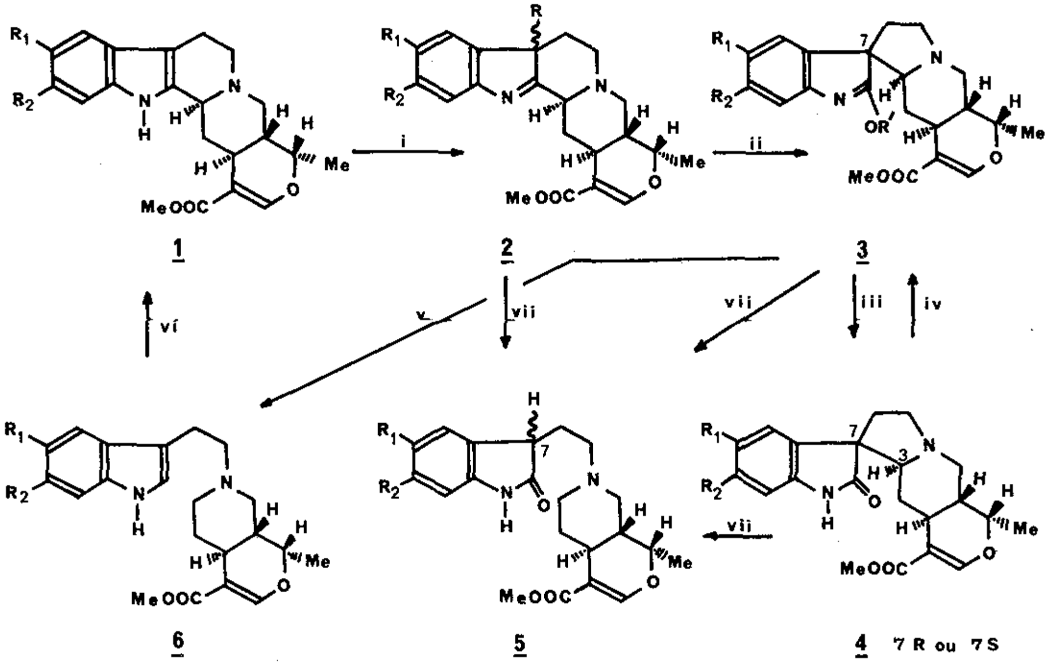
Structure elucidation of oxindole alkaloïds 4 mainly rests on two inverse pathways of chemical correlations, i.e. (table 1):

a) The oxidative pathway described by Finch and Taylor(2), leading from indolic heteroyohimbines 1 to oxindoles 4 *via* 7-chloro- or 7-acetoxy-indolenines 2 and imidoethers 3.

b) The reductive pathway described by Aimi,Yamanaka,Endo,Sakai and Haginiwa(3), leading from oxindoles 4 *via* imidoethers 3 to 2,3-secoindoles 6, which are further oxidised and cyclised to 1.

Seco-oxindoles 5 were thought to be interesting derivatives in view of similar correlations. They were easily obtained in one step through reduction, by means of a refluxing 1:1 mixture of formic acid and formamide(4), either of oxindoles 4 or of 7-chloro indolenines 2 (R = Cl) derived from heteroyohimbines. Generation in acidic medium of the *same* immonium *n* from (7R)-oxindoles ("B"-type) or (7S)-oxindoles ("A"-type) explains the reductive formation of seco-oxindoles *p* (table 2). In the case of 7-chloro indolenines *r* derived from indoles *q*, the intermediacy of species *s*, *t*, *l*-*m*, and *n* may be admitted.

TABLE 1



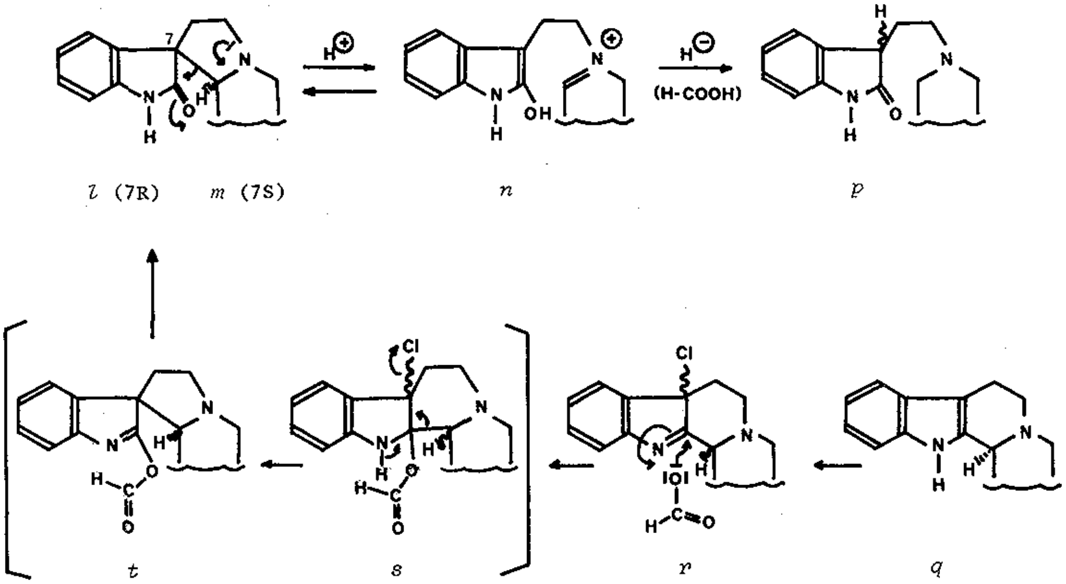
(a) R_1,R_2=H; (b) R_1=OMe,R_2=H ; (c) R_1=H,R_2=OMe ; (d) R_1,R_2=OMe.

i, R=Cl(^{t}BuOCl, Et_3N) or R=OAc($Pb(OAc)_4$) ; ii,KOH/MeOH ; iii,5% AcOH ; iv, $Et_3O^+BF_4^-$ (R'=Et) ; v, $NaBH_4$/AcOH ; vi, $Hg(OAc)_2$ or Potier's modified Polonovski's reaction on N-oxide ; vii, $HCO_2H/HCONH_2$, reflux.

When applied in the *normal* series to (19 S)-oxindoles of the "B"-type : 4a (mitraphylline), 4b and 4c (hemisynthetic from cabucine 1b and from tetraphylline 1c (1b)) and of the "A"-type : dimethoxy-10,11 isomitraphylline 4d this method (4) afforded the corresponding seco-oxindoles 5a, b, c, d in approximatively 90 % yields. When applied to 7-chloro indolenines 2b and 2c, respectively derived from 1b and 1c, the same reductive method afforded 5b and 5c in approximatively 75 % yields (5).

Seco-oxindoles 5a, b, c, d could not be crystallised (6). Their molecular weights (M.S.) and spectral data are in complete agreement with the depicted structures. The main feature in their mass spectra is a typical m/e 224 peak (base peak) arising from the $C_{(5)}$-$C_{(6)}$ bond breakage.

T A B L E 2



l (7R) *m* (7S) *n* *p*

t *s* *r* *q*

References and Footnotes

1. Preceding publications in this series:-a,I.,F.Titeux, L.Le Men-Olivier and J.Le Men, Phytochemistry, 1975,14,565; -b, II., F.Titeux, L.Le Men-Olivier and J.Le Men, Bull.Soc.chim.France, 1976,1473.
2. -a, N.Finch and W.I.Taylor, J.amer.chem.Soc.,1962,84, 1318 and 3871; -b,J.Shavel and H.Zinnes, J.amer.chem.Soc.,1962,84,1320;-c,N.Finch, C.W.Gemenden,I.H.Hsu and W.I.Taylor, J.amer.chem.Soc.,1963,85,1520; -d,N.Finch,C.W.Gemenden,I.H.Hsu;A.Kerr,G.A.Sim and W.I.Taylor, J.amer.chem.Soc.,1965,87,2229.
3. -a, N.Aimi,E.Yamanaka,J.Endo,S.I.Sakai and J.Haginiwa,Tetrahedron Letters,1972,1081;-b,N.Aimi,E.Yamanaka,J.Endo,S.I.Sakai and J.Haginiwa, Tetrahedron Letters,1973,2015;-c,S.I.Sakai,Heterocycles,1976, 131.
4. M.-J.Hoizey,L.Olivier,J.Lévy and J.Le Men, Tetrahedron Letters,1971, 1011.
5. The remaining 25 % mainly consist of the corresponding yohimbines.
6. Probably due to tautomerism between (7R)- and (7S)-2-oxo indolines, through 2-hydroxy indoles .

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