Tetrahedron Letters No. 18, pp 1579 - 1580, 1978.   0040-4039/78/0429-1579. $02.00/0.

A SYNTHESIS OF TABERSONINE

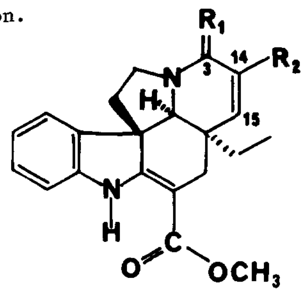
Jean Lévy*, Jean-Yves Laronze, Jacqueline Laronze and Jean Le Men

Laboratoire de Transformations et Synthèse de Substances Naturelles,
Faculté de Pharmacie, 51 rue Cognacq-Jay, 51096 REIMS CEDEX, FRANCE-ERA au CNRS n° 319

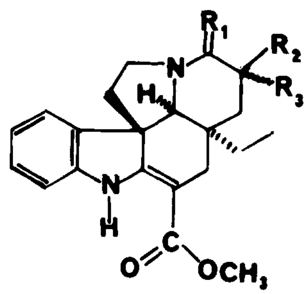
(Received in UK 21 February 1978; accepted for publication 17 March 1978)

Tabersonine 1[1,2] has been synthesised by Ziegler[3]. The present communication deals with a new synthetic access to this alkaloid. In a previous report[4] from these laboratories, the three-step synthesis of (±)-3-oxovincadifformine 3 from 2-hydroxytryptamine was described, together with its conversion to (±)-vincadifformine 5. Compound 3 appeared a suitable key intermediate for introduction of the 14,15-double bond. We now present preliminary results to this effect using (-)-3 (obtained[5] from natural (-)-tabersonine 1).

The dianion of 3, generated in a 20:1 mixture of THF/HMPA(v/v) at -78°C with lithium diisopropylamide, was treated with a large excess of phenylselenyl chloride (ØSeCl)[6] to yield the disubstituted derivative 7[7] (47%). Elimination of one substituent by oxidation with MCPBA[8] yielded (88%) the unsaturated monosubstituted derivative 6, which did not undergo catalytic hydrogenation.



	R1	R2
1	H_2	H
2	O	H
6	O	SeΦ



	R1	R2	R3
3	O	H	H
4a	O	SeΦ	H
4b	O	H	SeΦ
5	H_2	H	H
7	O	SeΦ	SeΦ

The non-oxidative abstraction of one ØSe group in 7 was achieved by attack with phenylsulfide anion, generated from thiophenol[9]. Derivatives 4a and 4b, differing in the orientation of the ØSe substituent were thus obtained (85%). Oxidative elimination[8] of the remaining ØSe was effected on the mixture of 4a,b and afforded 2, which was shown to be identical with authentic (-)-3-oxotabersonine. Finally, the selective removal of the lactam carbonyl through controlled reduction of 2 with $LiAlH_4$ in THF at 0°C for 4 hours yielded (-)-tabersonine 1 (38%), along with unchanged starting material (55%).

TABLE

Compound	m.p. °C	$(\alpha)^{\circ}_D(CHCl_3)$	$M^{\cdot +}$	λmax^{MeOH}_{nm}	$\nu^{KBr}_{cm^{-1}}$
7	215	- 171	660,662,664	225,295,325	$1600,1620,1640_{sh},1675$
6	230	- 79	504,506	230,295,325	$1600,1620,1640_{sh},1675$
4a (less polar)	205	- 148	506,508	216,295,330	$1605,1635_{sh},1650,1665_{sh}$
4b (more polar)	105-10	- 70	506,508	225,298,330	$1605,1635_{sh},1650,1670_{sh}$

NOTES AND REFERENCES

1. M.-M.Janot,H.Pourrat and J.Le Men, Bull.Soc.Chim.France,707 (1954).

2. M.Plat,J.Le Men,M.-M.Janot,H.Budzikiewicz,J.M.Wilson,L.J.Durham and C.Djerassi, Bull.Soc. Chim.France, 2237 (1962).

3. F.E.Ziegler and G.B.Bennett, J.Amer.Chem.Soc.,93,5390(1971); 95,7458 (1973).

4. J.-Y.Laronze,J.Laronze-Fontaine,J.Lévy and J.Le Men,Tetrahedron Lett.,491(1974).

5. S.Sakaï, Heterocycles, 4,131(1976).

6. P.A.Zoretic and P.Soja, J.Org.Chem.,41,3587(1976);P.G.Gassman and R.J.Balchunis, J.Org. Chem.,42,3236(1977).

7. All new compounds are listed in Table.

8. D.L.J.Clive, Chem.Comm.,695(1973);H.J.Reich,I.L.Reich and J.M.Renga,J.Amer.Chem.Soc., 95,5813(1973);K.B.Sharpless,R.F.Lauer and A.Y.Teranishi,J.Amer.Chem.Soc.,95,6137(1973).

9. G.Massiot(whom we thank for this suggestion), to be published.