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# ABSOLUTE CONFIGURATION OF (-)-STREMPELIOPINE[1]

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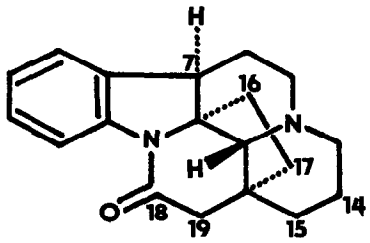
Summary: The (-)-strempeliopine was assigned the absolute configuration depicted in I on the basis of its stereospecific synthesis from (+)-18-methylenevincadifformine (II).

Soon after the isolation[2] of (-)-strempeliopine (I), the parent base of the schizozygane group of aspidospermane alkaloids, we have succeeded[3] in the total synthesis of racemic form of I. Now, we report on the determination of absolute configuration of natural (-)-base I. This assignment follows from its stereospecific synthesis from (+)-18-methylenevincadifformine (II), the absolute configuration of which was settled by circular dichroism technique.

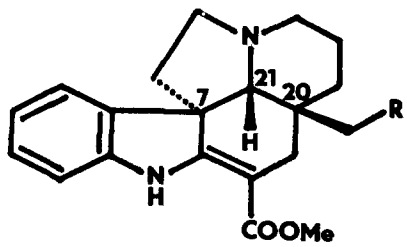
Thus, the (±)-18-methylenevincadifformine[4] (II) was smoothly resolved by using (+)-(2R,3R)-tartaric acid (1:1) as resolving agent. One recrystallization from ethanol gave a salt [ mp 137-141,5 °C; 78,6 %; $[\alpha]_{578}$ +343° (c 0.7; DMF - EtOH 2:5) ], from which (+)-II was liberated [ glass; $[\alpha]_{578}$ +560,5° (c 1.15; EtOH) ]. The absolute configuration of this base follows from CD comparative measurements of (+)-II, (+)-III[5], (-)-vincadifformine[6,7](IV) and

Table 1: Circular dichroism spectra (in methanol, 23-25 °C)

| Base | $\lambda_{max}$ [nm] ($\Delta\varepsilon$) | | |
|---|---|---|---|
| (+)-II | 324,5 (+31,3) | 285,0 (-4,3) | 236,0 (-17,5) |
| (+)-III | 325,0 (+32,3) | 285,0 (-2,4) | 237,0 (-16,6) |
| (-)-IV[6] | 324,0 (-35,7) | 286,0 (+3,2) | 237,0 (+17,2) |
| (-)-V[6] | 324,5 (-24,7) | 288,0 (+6,1) | 238,5 (+18,2) |

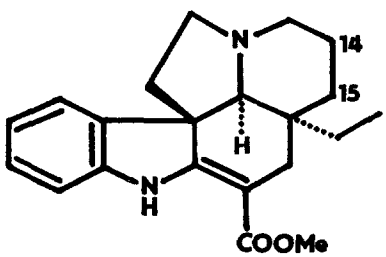


(-)-I



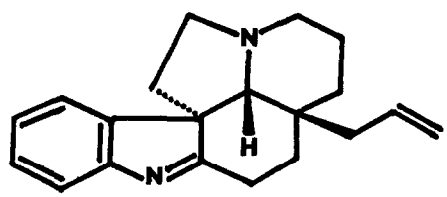
(+)-II : R = $CH{=}CH_2$

(+)-III: R = Et

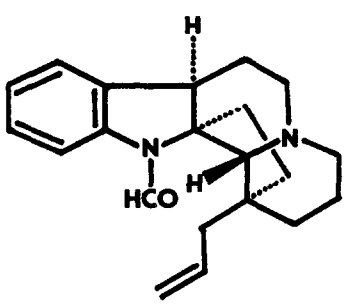


(-)-IV

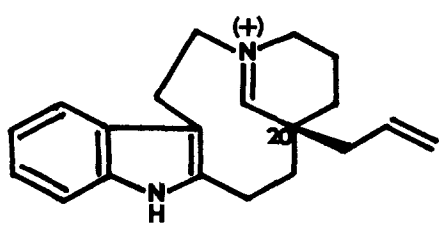
(-)-V : $\Delta^{14,15}$



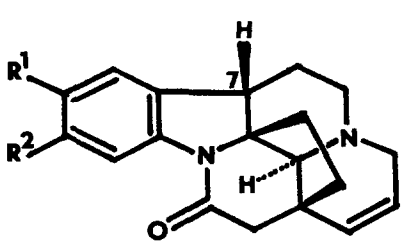
(+)-VI



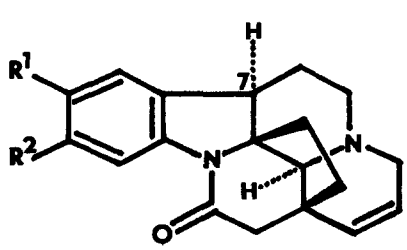
(-)-VII



VIII



IXa



IXb

(-)-tabersonine[6] (V), table 1. It is evident from the data obtained that (+)-II and (+)-III belong to the enantiomeric series with respect to (-)-IV and (-)-V, as manifested by the significant long-wavelength dichroic band at 325 nm, as well as by the entire shape of the spectra.

Subsequently, the (+)-(7S,20S,21R)-18-methylenevincadifformine (II) furnished[4], upon alkaline hydrolysis followed by decarboxylation in boiling benzene, the (+)-18-methylene-1,2-dehydroaspidospermidine (VI) [ oil; 92,4 %; $[\alpha]_{578}$ +319° (c 1.28; PhH) ], which was reductively rearranged and formylated as described previously[3] giving (-)-1-demethyl-1-formyl-18-methylenevallesamidine (VII) [ mp 94-96 °C; 41,9 %; $[\alpha]_{578}$ -27,1° (c 1.62; MeOH) ]. Finally, elaboration[3] of the allyl side chain in (-)-VII gave rise to the desired (-)-strempeliopine[8] (I) [ mp 150,5-153 °C; 34,8 %; $[\alpha]_{578}$ -25,4° (c 1.8; MeOH) ].

The assignment of relative stereochemistry to all of the previously isolated schizozygane alkaloids (IX) rests on good physico-chemical grounds[9]. Taking into account their biogenesis[10] in plant, there remains essentially no doubt that the minor bases IXb possess the same configuration as IXa at all but C(7)-center of asymmetry[11]. Having determined the absolute configuration of (-)-I we speculated about the $[\alpha]$ values of bases IXa. Here, we tentatively propose that schizozygane alkaloids belong to the enantiomeric series with respect to (-)-I, as expressed in formulae IXa and IXb.

Now, we are going to start the work aimed at the determination of absolute configuration of the other schizozygane alkaloids.

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REFERENCES and NOTES

1) On Alkaloids. XLIV. Part XLIII: Hájíček J., Trojánek J.: Collect. Czech. Chem. Commun., in press

2) Laguna A.: PhD. thesis, Prague 1980; mp 152-154 °C; $[\alpha]_D$ -120° (MeOH)

3) Hájíček J., Trojánek J.: Tetrahedron Lett. 22, 2927 (1981)

4) Hájíček J., Trojánek J.: Tetrahedron Lett. 22, 1823 (1981)

5) Obtained from (+)-II by hydrogenation ($PtO_2$, EtOH, RT) [ oil; 92,7 %; $[\alpha]_{578}$ +562° (c 0.93; EtOH) ]

6) Absolute configuration is known: Klyne W., Buckingham J.: Atlas of Stereochemistry, Oxford University Press, New York 1974, p 152, and references cited therein

7) Zsadon B., Barta M., Dancsi L., Dezséri E.: Sci. Pharm. 47, 126 (1979)

8) The reported[2] $[\alpha]$ value for (-)-I is almost with certainty a missprint because the base (+)-II is optically pure (or nearly so) and the reductive rearrangement is a C(20)-stereoconservative process (intermediacy of VIII). Unfortunately, a sample of (-)-strempeliopine, kindly supplied by Dr. M. Buděšínský (Institute of Organic Chemistry and Biochemistry, Prague), is too small to render the $[\alpha]$ measurement possible.

9) Renner U., Kernweisz P.: Helv. Chim. Acta 48, 308 (1965); Renner U.: Lloydia 27, 393 (1964)

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