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297. Stereospecific Synthesis of a 9, 11, 12, 13, 13a, 14-hexahydro-dibenzo(*f*, *h*)pyrrolo(1,2-*b*)isoquinoline-alkaloid

Preliminary communication

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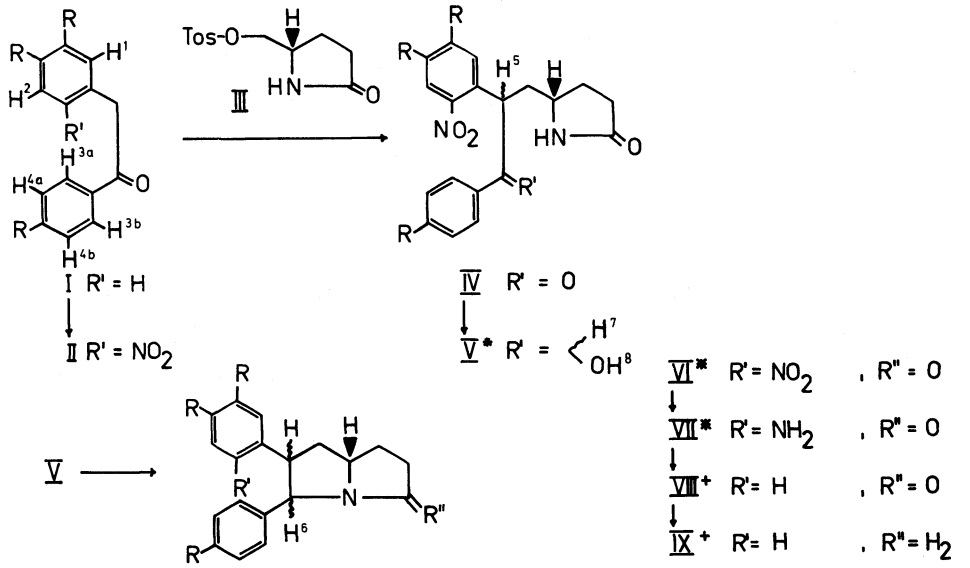
(12. XI. 73)

Several syntheses of the title-type alkaloids starting from chiral proline-derivatives, are described in the literature [1–4]. All these routes produce racemates because they include intermediates with a carbonyl-group α to the asymmetrically substituted carbon-atom C(13a). We avoided racemisation by using the proline derivative III [5] and cyclising the phenanthrene-moiety at a late stage of our synthetic route, shown in the following schemes:

Scheme 1

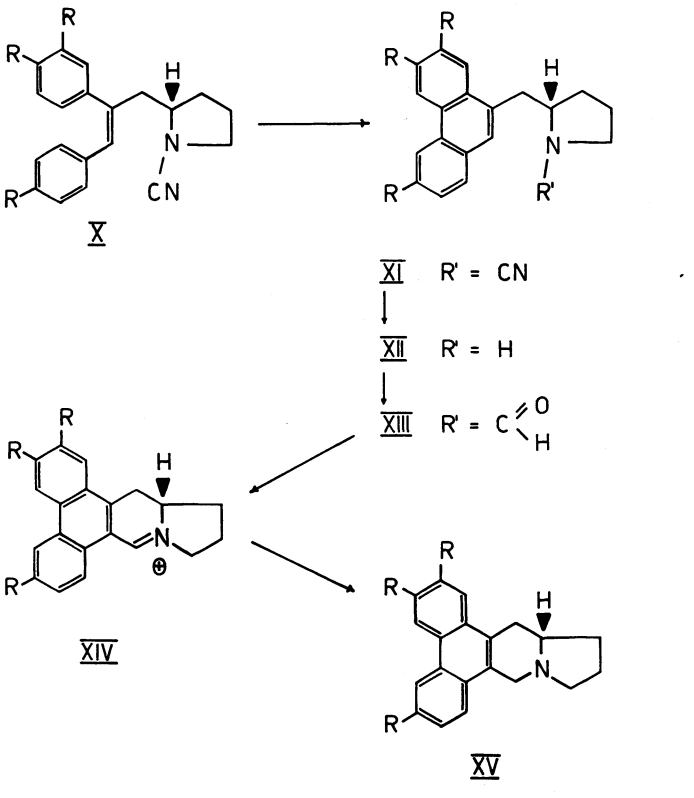


*) diastereomers were isolated +) mixture of diastereomers R = OCH_3

We obtained III by $LiBH_4$-reduction of 5-oxo-proline methyl ester to 5-oxo-prolinol which was subsequently tosylated. The optical purity of 5-oxo-prolinol was only 51% of that of *Hardegger's* [5] product, who used $LiAlH_4$. This disadvantage is compensated by a better yield of 5-oxo-prolinol, as compared with the $LiAlH_4$-reduction.

Anisole + homoveratroylchloride → I [6]. – I + 65% HNO_3 in glacial AcOH → II, m.p. 197°; NMR. (chem. shift in δ): H_1: 6.80, 1*s*; H_2: 7.83, 1*s*; $H_{3a,b}$: 8.09, 2*d* × *d*, $J_o = 7$ Hz, $J_m = 1{,}7$ Hz; $H_{4a,b}$: 7.03, 2*d* × *d*, $J_o = 7$ Hz, $J_m = 1.7$ Hz. – *II* + *III* in acetone/K_2CO_3, 110°, 4–5 atm → IV; yellow oil; M^+: 428. NMR.: H_5: 5.67, 1*t*, $J = 7.5$ Hz; $[\alpha]_D^{20} = +22°$ (MeOH). – IV + $NaBH_4$ (70% EtOH) → V. Va, low Rf., NMR.: H_7: 4.74, 1*d*, $J = 7$ Hz; H_8: 3.00, 1*s*. – Vb, high Rf, NMR.: H_7: 4.77, 1*d*, $J = 7$ Hz; H_8: 3.00, 1*s*. – V (a or b) + 1.25% HCl in glacial AcOH (20°) → VI (a or b respectively). VIa (high Rf); m.p. 152°; phenylgroups *cis*; NMR.: H_6: 5.08, 1*d*, $J = 8.5$ Hz; $[\alpha]_D^{19} = +89°$ ($CHCl_3$). – VIb (low Rf); m.p. 194°; phenylgroups *trans*; NMR.: H_6: 4.83, 1*d*, $J = 1.7$ Hz; $[\alpha]_D^{20} = +43{,}5°$ ($CHCl_3$). – VI (a or b) + H_2 (*Raney*-Ni/EtOH) → VII (a or b respectively). MS.: M^+: 382, dominating peaks at 203 and 175. – VII (mixture of diastereomers) + $NaNO_2$/2.5% aqueous HCl, followed by 30% H_3PO_2 → VIII. MS. of both diastereomers: M^+: 367, dominating peaks 203 and 175. – VIII (mixture of diastereomers) + $LiAlH_4$/THF → IX; diastereomers (colourless oils) were separated. IXa (low Rf), $[\alpha]_D^{25} = -214°$ (MeOH); IXb (high

Scheme 2



Rf), $[\alpha]_D^{25} = -173°$ (MeOH). MS. (both diastereomers): M^+ 353, base peak: 189. – IX (mixture of a and b) + BrCN in abs. $C_6H_6 \rightarrow$ X. IR. ($CHCl_3$): 2200/cm. *MS.*: M^+: 378, dominating peaks 283 and 95. – X (4.6×10^{-5} M in C_6H_{12}, saturated with air) was irradiated (254 nm) → XI; m.p. 151–2°; UV.: λ_{max} (log ε): 257 (4.73), 285 (4.44), 311 (3.90), 342 (2.89), 359 nm (2.31); $M^{\oplus}$: 376; $[\alpha]_D^{25} = +74.7$ ($CHCl_3$). – XI + $LiAlH_4$ in THF → XII (viscous oil). M^+: 351, small intensity [7], dominating peaks 349, 282 and 70; $[\alpha]_D^{22} = +8.1°$. – XII + 98% HCOOH/180° → XIII; cyclisation (without further purification) with $POCl_3$/toluene → XIV; UV.: λ_{max}: 259; 268; 282; 320; 420 nm. XIV + $NaBH_4$/MeOH → XV, m.p. 206–11°. $[\alpha]_D^{22} = +66°$ ($CHCl_3$); antofine: $[\alpha]_D^{22} = -131°$ ($CHCl_3$). XV was identical with natural antofine [8] (TLC., UV., MS., IR.) but shows opposite optical rotation, 50% in magnitude for the reason stated. Because XV has *S*-configuration, antofine is of the *R*-configuration. This is in accord with our degradation of antofine to D-proline [9].

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