Total Synthesis of the Lycopodium Alkaloid (±)-Serratinine

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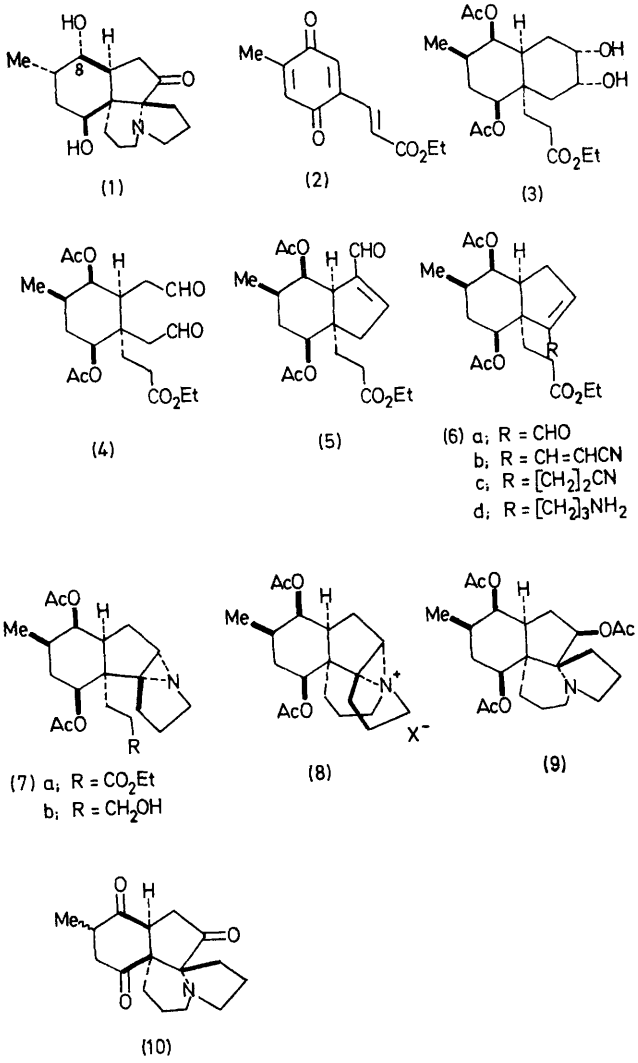
Summary Serratinine (**1**) isolated from *Lycopodium serratum* Thunb. var. *serratum* f. *serratum* has been synthesized.

AMONG lycopodium alkaloids, serratinine (**1**)[1] has a unique skeleton, because of its complicated stereochemistry (six chiral centres) and the presence of two adjacent quaternary carbon atoms. We report here a complete synthesis of serratinine.

We have reported previously[2,3] that Diels–Alder reaction of (**2**)[2] with butadiene, followed by Zn–AcOH reduction, $NaBH_4$ reduction, acetylation, OsO_4–$NaClO_3$ oxidation,[4] and catalytic hydrogenation provided the diol (**3**),[3] which gave the dialdehyde (**4**)[3] on oxidation with periodic acid. Treatment of (**4**) with basic alumina or piperidinium acetate in dry benzene[5] gave selectively the aldehyde (**5**), whereas treatment with excess of pyrrolidine and AcOH in dry MeOH[3] afforded selectively the aldehyde (**6a**).

Wittig reaction of (**6a**) with $(EtO)_2P(O)$-CH_2CN gave the conjugated nitrile (**6b**) (66%), ν_{max} 2230 cm^{-1}, as a *cis-trans*-mixture, which was selectively hydrogenated over $(Ph_3P)_3RhCl$ to afford the nitrile (**6c**) (75%) δ 5·65 (1H, m, olefinic-H). Reduction of (**6c**) with $CoCl_2$–$NaBH_4$[6] gave the primary amine (**6d**) which was treated with *N*-chlorosuccinimide and Cu_2Cl_2 to give two stereoisomeric aziridines; one (**7a**) (20%) had m.p. 127—129°, δ 4·83—5·25 (2H, m, CHOAc), 4·12 (2H, q, *J* 7 Hz, $CO_2CH_2CH_3$), 2·02 and 2·04 (each 3H, s, OAc), 1·23 (3H, t, *J* 7 Hz, $CO_2CH_2CH_3$), and 1·11 (3H, d, *J* 7 Hz, $CHCH_3$), the other (with a different configuration of the aziridine ring) (3%) had m.p. 82—84°. Selective reduction of (**7a**) with $LiBH_4$ provided the primary alcohol (**7b**) (74%), δ 3·61 (2H, m, CH_2OH), 2·65—3·05 (1H, m, exchangable with D_2O), 2·01 and 2·03 (each 3H, s, OAc), and 1·10 (3H, d, *J* 7 Hz, $CHCH_3$). Reaction of (**7b**) with *p*-$MeC_6H_4SO_2Cl$–pyridine afforded the aziridinium salt (**8**) which without isolation was treated with KOAc in EtOH to give the triacetate (**9**) (34%), m.p. 161—163°, δ 5·11 (2H, m, CHOAc), 4·82 (1H, m, CHOAc), 203 (3H, s, OAc), and 2·09 (6H, s, 2 × OAc). Alkaline hydrolysis of (**9**), followed by oxidation with Jones' reagent



afforded the triketone (**10**) (35%), m.p. 143—146°. Reduction of (**10**) with $NaBH_4$ gave (±)-serratinine (18%) (**1**: racemate), m.p. 202—203°, and (±)-8-*epi*-serratinine, (20%), m.p. 205—207°. These compounds were identical with authentic specimens of natural serratinine and 8-*epi*-serratinine[1] derived from serratinine, respectively, in all respects except the m.p. and the specific rotation.

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