A NOVEL SYNTHESIS OF ASPIDOSPERMA ALKALOIDS USING SIMULTANEOUS CYCLIZATION AT 2 AND 3 POSITIONS OF INDOLE RING

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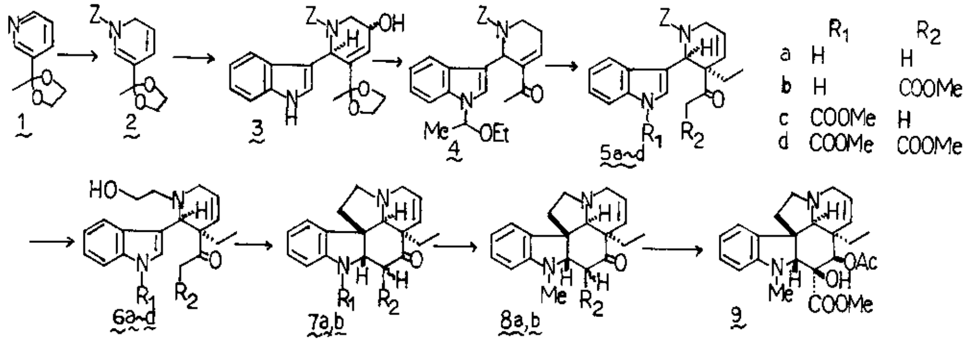
A formal synthesis of (±)-vindorosine (9) was performed by a novel type of cyclization reaction (6a,6d → 7a,7b) which consists of two carbon-carbon bond formations at the C-2 and C-3 positions in the indole ring. The key compounds (6a and 6d) were prepared as follows. The ketal (1) was reduced with a bulky reducing reagent, $NaAl(OCH_2CH_2OMe)_2H_2$, in the presence of $ClCOOCH_2Ph$ in THF to afford 1,6-dihydropyridine derivative (2), which was submitted to our oxygenative nucleophile introduction rection[1] to form compound (3). 3 was converted to 5a via 4 in six steps and the desired compound (6a) was obtained from 5a through 5c. The methanesulfonate of 6a was treated with $(Me_3Si)_2NK$, in THF at -70°C at first then at room temperature for 1 h to give the pentacyclic compound (7a). Alternatively, 6d derived from 5a by way of 5d [i) $(Me_3Si)_2NK$, THF; ii) CO_2; iii) CH_2N_2], was subjected to the same cyclization reaction using t-BuOK in place of $(Me_3Si)_2NK$ to furnish a more functionalized compound (7b). 7a and 7b were methylated with CH_2O and $NaBH_3CN$ to afford 8a and 8b, which were identified with Büchi's samples[2] which were transformed to (±)-vindorosine (9).



REFERENCES

1) M. Natsume, et al, Tetrahedron Lett., 3473 (1979).

2) G. Büchi, et al, J. Am. Chem. Soc., 93, 3299 (1971).