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TOTAL SYNTHESIS OF THE HOMOERYTHRINAN ALKALOIDS, 6βH,7-DIHYDROSCHELHAMMERIDINE (ALKALOID A) AND 6βH,7-DIHYDRO-3-EPISCHELHAMMERIDINE (ALKALOID 1): REVISION OF THE PROPOSED STEREOCHEMISTRY[1]

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Abstract--The stereo-controlled total syntheses established that alkaloid A (of Schelhammera pedunculata) and alkaloid 1 (of Phelline comosa) are 6βH-homoerythrinan derivatives.

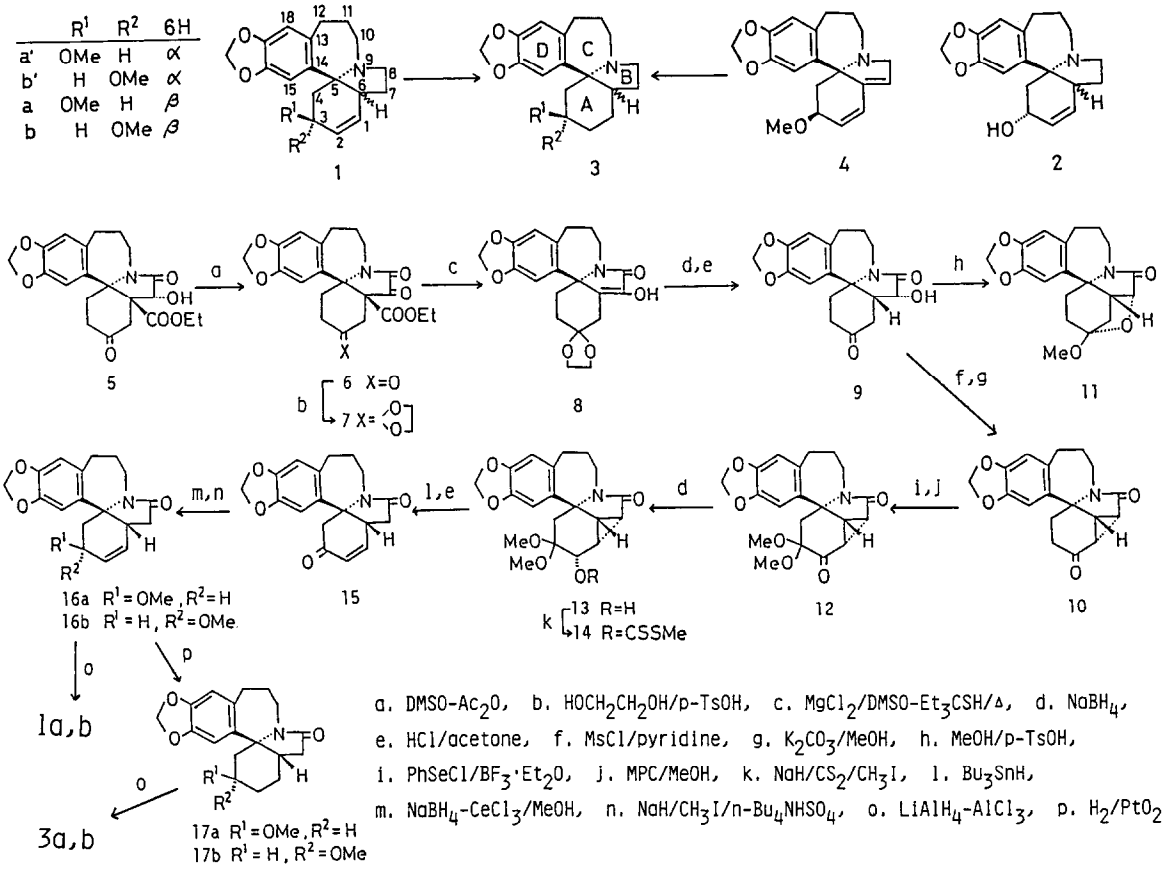
6,7-Dihydroschelhammeridine (alkaloid A) is one of the homoerythrinan alkaloid occurring in Schelhammera pedunculata (Liliaceae).[2] Its 3-epimer, 6,7-dihydro-3-epischelhammeridine (alkaloid 1), is also found in Phelline comosa (Aquifoliaceae).[3] Both alkaloids give the same allylic alcohol **2** on hydrolysis with hydrochloric acid.[2,3] The proposed structure **1a'** of alkaloid A (and hence **1b'** of alkaloid 1) is based on the fact that it is hydrogenated quantitatively to tetrahydroschelhammeridine[2] which is also obtained by hydrogenation of schelhammeridine **4**.[4] The assignment of the 6αH-configuration for tetrahydroschelhammeridine **3a'** depends upon the argument that steric compressions would prefer the attack from the α-side in the hydrogenation of schelhammeridine.[4] However, Mondon and Seidel[5] doubted this assignment because they found that in erythrinan series the same hydrogenation always gave cis-fused perhydroindoles predominantly, thus suggesting that alkaloid A (and hence also alkaloid 1) could be an A/B-cis 6βH-homoerythrinan derivative.

This communication describes the stereo-controlled total synthesis of the compounds of 6βH-configuration, **1a** and **1b**, and shows their identities with the natural alkaloids, alkaloid A and alkaloid 1 (comosine)[6], respectively.

The homoerythrinan derivative **5**[7] was oxidized with DMSO-Ac_2O to the trioxo compound **6** (95%), mp 185-189°C,[8] which on acetalization with 1,2-ethanediol gave the mono-ethyleneacetal **7**, mp 257-260°C (99%). This was deethoxycarbonylated to **8** (91%) and then converted to the cyclohomoerythrinan **10**, mp 278-280°C, by the procedure described in erythrinan series[9] in overall yield 66% from **8**. The 6β-H stereochemistry of the intermediate keto-alcohol **9**, hence that of **10**, was rigidly established by a quantitative formation of the cyclic acetal **11**, mp 206-207°C, on short treatment of **9** with methanol in presence of a catalytic amount of p-TsOH.

The compound **10** was transformed to the enone **15**, mp 212-214°C, in overall yield 50%, by a similar procedure described in the synthesis of schelhammericine.[7]

Reduction of the enone **15** with $NaBH_4$-$CeCl_3$[10] in methanol yielded a 2:1 mixture of the unsaturated alcohols which were separated after methylation to the O-methyl derivatives, **16a** (mp 175-176°C, 54%) and **16b** (mp 236-237°C, 25%). AlH_3 reduction of **16a** gave the amine **1a**, gum, whose ^1H-NMR spectrum was identical with that of alkaloid A reported by Johns et al.[2] Similarly **16b** gave the 3-epimer **1b**, gum, which was identified (TLC and spectral comparisons) with alkaloid 1 (comosine).



Catalytic hydrogenation of **16a** and **16b** in ethanol over platinum oxide gave the dihydro-derivative, **17a** (mp 149-150°C) and **17b** (mp 175-176°C), respectively. They were similarly reduced to the amine, **3a** and **3b**, which were found to be identical with tetrahydroschelhammeridine[2] and dihydrocomosine[3] on comparisons of their ^{1}H-NMR spectra with the reported data, respectively. Therefore the stereochemistry of tetrahydroschelhammeridine, the major product of catalytic hydrogenation of schelhammeridine **4**,[5] must also be revised to 6βH-configuration.

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