

A Short Stereospecific Synthesis of (\pm)-1,12b-Didehydrolycorane

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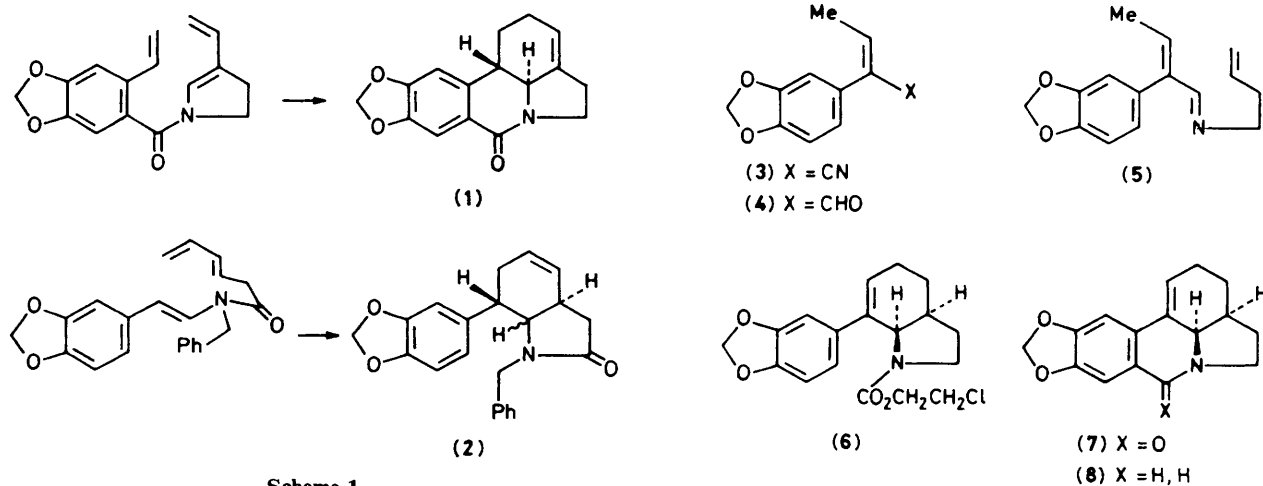
The imine (5), on treatment with 2-chloroethyl chloroformate in the presence of di-isopropylethylamine, followed by heating at 140 °C gave (6), which was converted into 1,12b-didehydrolycorane to prove the stereochemistry of (6).

Recently two intramolecular [2 + 4] cycloaddition approaches to the synthesis of the lycorane skeleton have been reported. The first is stereospecific, giving only the *trans*-isomer (1) (50%),¹ while the second gave (2) (45–50%) as a 1:1.5 mixture of *cis*- and *trans*-stereoisomers² (Scheme 1).

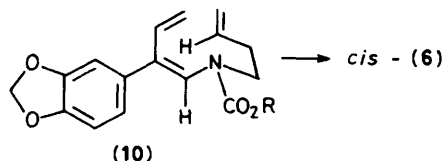
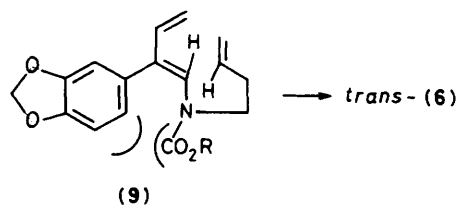
In any strategy that involves an intramolecular or intermolecular [2 + 4] cycloaddition process, there are, in principle, six possible ways of making the cyclohexene ring.

Here we report an alternative to those in Scheme 1 that provides a very short and stereospecific synthesis of 1,12b-didehydrolycorane (8).³

Treatment of a mixture of piperonylacetonitrile and acetaldehyde with Triton B–MeOH gave (3) (46%), m.p. 79–80 °C. Reduction of (3) with di-isobutylaluminium hydride gave the aldehyde (4) (56%), which was directly condensed with but-3-enylamine to give the imine (5). When



Scheme 1



the imine (5) was treated with NPr_2Et (2.0 equiv.)– $\text{ClCH}_2\text{CH}_2\text{OC(O)Cl}$ (2.0 equiv.) in chlorobenzene for 42 h then heated to 140 °C for 7 h the carbamate (6) was isolated in 53% yield from (4).⁴ We were unable to detect (within 5%) any other stereoisomers. To confirm the *cis*-stereochemistry for the product (6), it was converted into (8) as follows. Treatment of (6) with POCl_3 at 75–90 °C for 40 h gave the amide (7) (86%), m.p. 145–147 °C (CH_2Cl_2 –hexane). Reduction of (7) with LiAlH_4 – Et_2O gave (\pm)-1,12b-didehydrolycorane (8) (72%), m.p. 104–105.5 °C (CH_2Cl_2 –hexane, lit.³ 106–107 °C).

The exclusive formation of the *cis*-fused adduct (6) is in interesting contrast to the Stork case (1). If one assumes an *exo*-type transition state, then the stereochemical outcome is determined by the geometry of the diene. The transition state (9) causes a severe steric interaction between the carbamate group and the piperonyl group, whereas the alternative geo-

metry (10) does not. The nitrogen atom lone pair in (10) is out of plane with respect to the diene.

This short and convergent route [5 steps from piperonyl acetonitrile to (7)] provides a convenient synthesis of the basic lycorane alkaloids.[†]

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References

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[†] All new compounds gave satisfactory spectral and micro-analytical combustion analysis data.