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AN INFORMAL SYNTHESIS OF ± LYSERGINE

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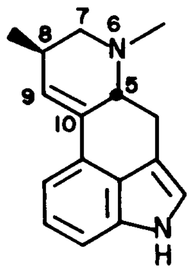
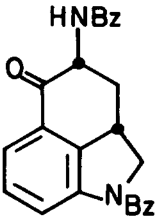
ABSTRACT *The synthesis of lysergine from tryptophane is described.*

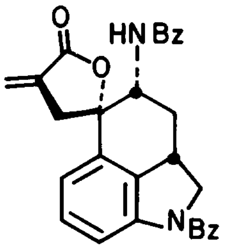
The ergot alkaloid lysergine was identified as a natural product in 1961.[1] Syntheses of this substance have been quite formal involving isomerization of agroclavine[2,3], reduction of lysergene[2-4] or even reduction of lysergic acid *via* elymoclavine [4] Here we describe a less formal synthesis from a somewhat more accessible starting material



Lysergine



1 Bz = Benzoyl



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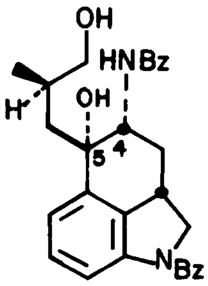
The ketone **1**, readily available from tryptophane, was converted to the lactone **2** in one step as described previously [5] Reduction of **2** with either $NaBH_4$/MeOH or hydrogenation (Pd/C) followed by Vitride gave the diol **3** with 90-97% stereochemical control of the center which is destined to become C_8 in lysergine. Either method caused some loss of the N_1 benzoyl, but this group could be fully restored by mild benzoylation (BzCl/MeOH) on workup (88% overall yield). Treatment of **3** with excess $MsCl/Et_3N$ gave the olefin **4**, mp 183-184°, as the major product along with the isomeric enamine



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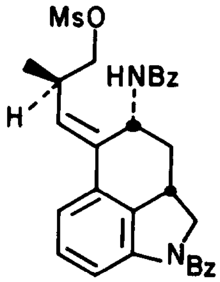

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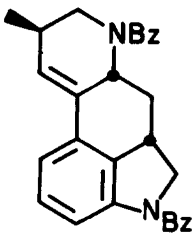

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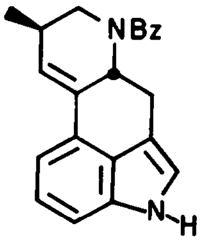

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Base induced cyclization (NaH/DMF) produced **5** (mp. 217-218°, 88%)[6] from which the indole **6** (mp. 262° dec; 92%)[6] was obtained directly on exposure to the conditions described by Gassman[7] for amide cleavage (*t*-BuOK/THF/H_2O). The identity of the oxidant required for this cheerful result is unknown to us. The N_6 benzoyl was cleaved with dibal/THF[8] (73%), and methylation was best accomplished with NaH_3BCN/H_2CO[9] to give racemic lysergine (mp 227-229°, 71%). This material showed identical tlc behavior and ir, uv and 300 MHz nmr spectra superimposable with those of a sample of lysergine obtained from lysergic acid at the Eli Lilly Laboratories.

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References and Notes

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