

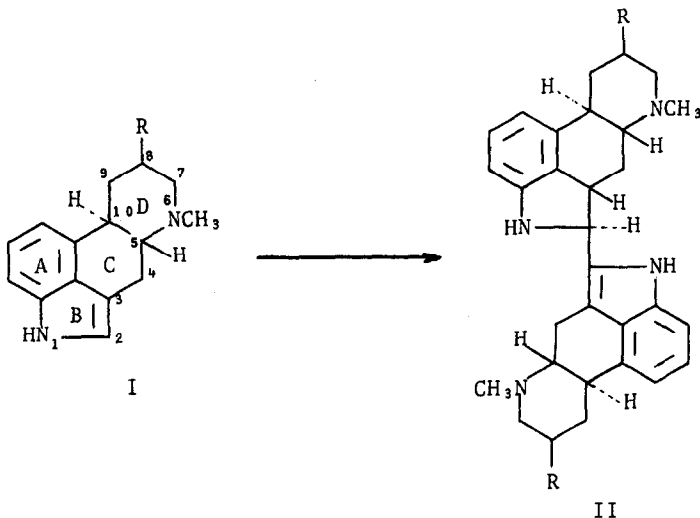
DIMERIZATION OF ERGOT DERIVATIVES

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In the conversion of 9,10-dihydrolysergol (I, R=CH₂OH) to the chloride² (I, R=CH₂Cl) using phosphorous oxychloride, we have isolated



significant quantities of the dimer II (R=CH₂Cl) in addition to the desired product. Subsequent attempts to repeat the dimerization led to erratic results, possibly because acidic impurities in different samples of phosphorous oxychloride were the real catalysts for the dimerization. Therefore, a study was undertaken to find an acidic reagent which would reliably effect the conversion I → II. The result of this work was the discovery that a mixture of trifluoroacetic acid and boronfluoride etherate would cause efficient dimerization of a wide variety of ergot alkaloid derivatives.

Dimerization was observed with these reagents regardless of the nature of the side chain substituent R, or the presence or absence of a double bond in ring D. Several of the characterized dimers are listed as follows:

<u>R</u>	<u>Double bond Ring D</u>	<u>Dimer Formula</u>
COOCH ₃	9,10	C ₃₄ H ₃₆ N ₄ O ₄
COOCH ₃	--	C ₃₄ H ₄₀ N ₄ O ₄
COOCH ₃ ³	7,8	C ₃₄ H ₃₆ N ₄ O ₄
CH ₃	8,9	C ₃₂ H ₃₆ N ₄
CH ₂ Cl	--	C ₃₂ H ₃₈ Cl ₂ N ₄
CH ₂ CN ²	--	C ₃₄ H ₃₈ N ₆

Evidence supporting the dimeric structures, which are analogous to that of skatole dimer⁴, was as follows:

1. Mass spectra showed molecular ion peaks double that of the monomers.
2. Acetylation of the dimers gave mono-N-acetyl derivatives (i.r. 1655 cm⁻¹) under conditions in which the monomers were inert.
3. The u.v. spectra are a summation of the indole and indoline moieties.
4. Evidence for the configuration of the 2,3 hydrogens in the indoline portion is lacking; however, we favor the trans arrangement with the minimal steric hindrance⁴.

The general dimerization procedure follows: To a solution of 0.90 g of methyl 9,10-dihydrolysergate in 25 ml CF₃COOH, was added 5 ml BF₃-ether. The mixture was stirred at room temperature for 30 min. Water and excess NH₄OH were added, and the product was extracted with EtOAc. The extract was washed with H₂O, dried (Na₂SO₄), and the solvent was removed. The product was crystallized from MeOH, m.p. 242-245° dec.; yield, 0.78 g.

Anal. Calcd. for C₃₄H₄₀N₄O₄: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.64; H, 7.19; N, 9.85.

NOTES AND REFERENCES

1. Author to whom inquiries should be addressed.
2. M. Semonsky and N. Kucharczyk, Coll. Czech. Chem. Commun., **33** 577 (1968).
3. The preparation of this monomer will be described in another publication by Dr. W. L. Garbrecht of these laboratories.
4. G. F. Smith and A. E. Walters, J. Chem. Soc. 940 (1961); G. Berti, A. Da Settimo, D. Segnini, Tetrahedron Letters No. 26, p. 13 (1960).