Tetrahedron Letters No. 35, pp 3029 - 3030 , 1977. Pergamon Press. Printed in Great Britain.

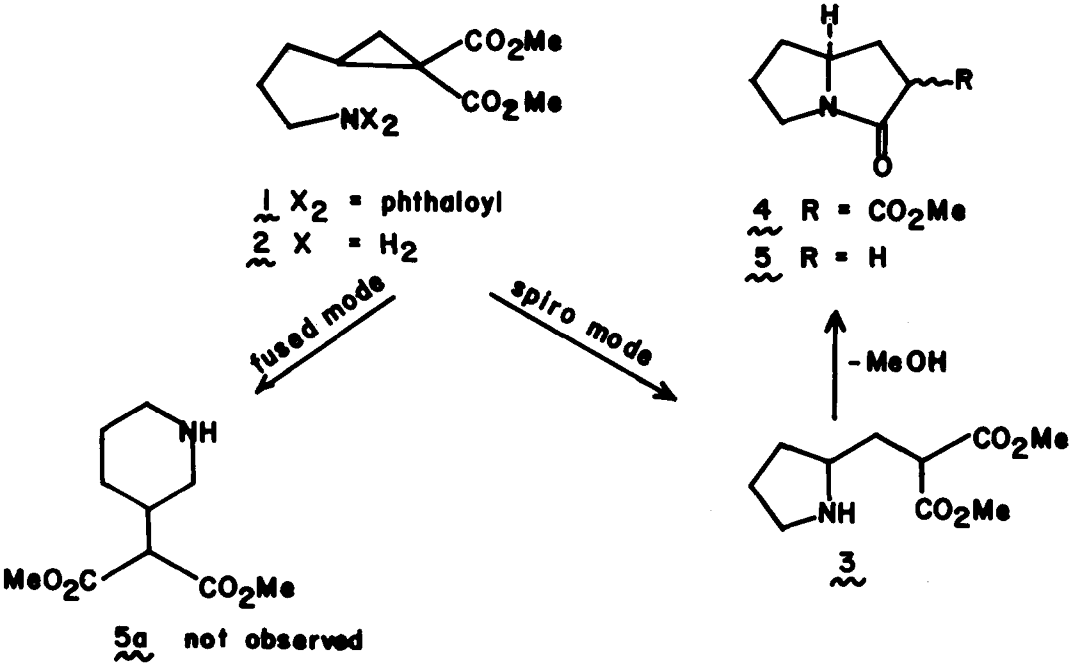
# A SIMPLE APPROACH TO THE PYRROLOINDOLINE SYSTEM

Samuel Danishefsky* and Robert Doehner

Department of Chemistry, University of Pittsburgh, Pittsburgh, Penna. 15260

(Received in USA 20 June 1977; received in UK for publication 7 July 1977)

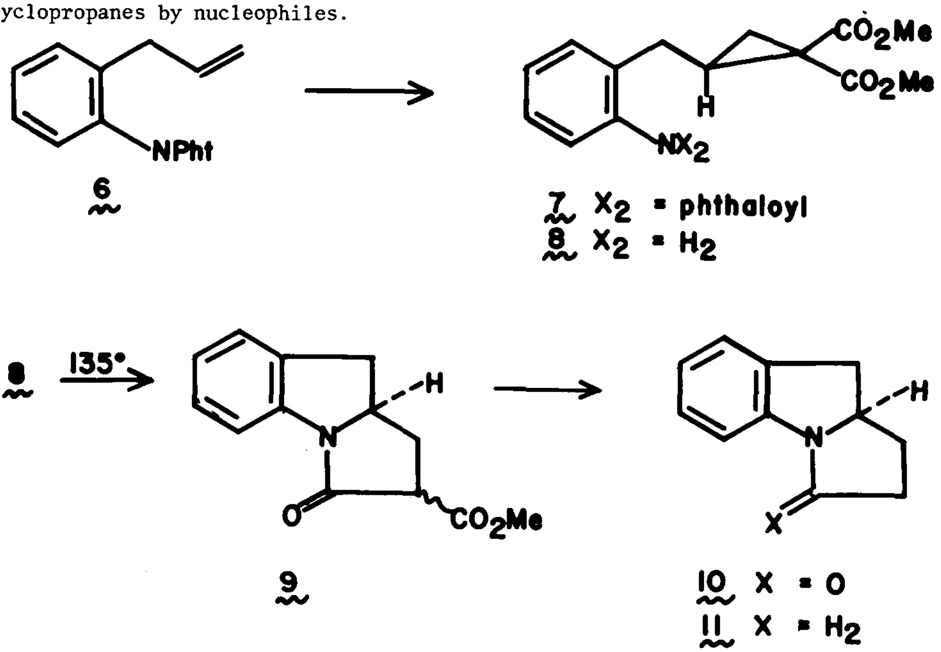
Recently we reported[1a] a new entry to the pyrrolizidine system. Treatment of a phthalimidocyclopropane 1 with 1.1 eq of hydrazine in hot methanol released an amine (2) which underwent spontaneous ring mutation strictly in the spiro mode,[1b] thereby leading to 3, and thence 4 and 5 (90% overall yield). In this sequence, one did not detect any fused mode product, 5a.



It was of interest to examine the feasibility of the process in the instance where the activated cyclopropycarbinyl group is ortho to an aromatic amino function. Examination of Drieding models suggested to us that the transition state for spiro mode of attack would involve considerable angle strain. In contrast, the fused mode of opening would involve much less strain. On the other hand, in the fused mode the angle between the nitrogen nucleophile and the vulnerable C-C bond of the cyclopropane, approaches 180°[2] only when the nitrogen and carbon atoms approach each other at rather close distances. In the spiro mode, the corresponding angles may be achieved with potentially less repulsion. The results of our investigation which bear on this question are summarized below.

*Ortho*-allylaniline[3] was converted to 6, mp 91-92°.[4] Reaction of 6 with dimethyl diazomalonate (1.1 eq of copper bronze, 1.5 eq of diazo cpd-xylene-reflux, 16 hr) afforded a 62% yield of 7,[4] mp 120-123°. Treatment of 7 with 1:1 eq of hydrazine in methanol, under reflux, afforded the amine, 8.[4] It will be noted[1a] that under these conditions amine 2 cyclizes to give 4.

The amine, 8, was heated at 135° (neat) to afford carbomethoxylactam 9 as a mixture of epimers.[4] Decarbomethoxylation of 9 (wet dimethylsulfoxide[5]-180°, 2 hr) afforded 10, mp 139-140°. The yield of homogeneous 10 from 6 was 59%. In addition to its spectral properties, the structure of 10 was proven by its reduction to the known 11,[6] picrate mp 135-136°, lit[6] 133-134°. No aminodiesters which would have resulted from a fused mode opening could be detected. In summary, a viable route to the 1,2-trimethyleneindoline system has been developed.[7] Moreover, a clear preference for the spiro mode of ring opening of systems of the type 8 is apparent, though the reasons must await a more precise knowledge of the trajectory of attack in the opening of activated cyclopropanes by nucleophiles.



---

* This work was supported by CA-12107-13.

1a. S. Danishefsky and J. Dynak, J. Org. Chem., 39, 1979 (1974); (b) S. Danishefsky and J. Dynak, W. E. Hatch and M. Yamamoto, J. Amer. Chem. Soc., 96, 1256 (1974).
2. L. Tenud, S. Farooq, J. Seibl and A. Eschenmoser, Helv. Chim. Acta., 53, 2050 (1970).
3. C. D. Hurd and W. M. Jenkins, J. Org. Chem., 22, 1418 (1957).
4. The structure of the product is in accord with its infrared, nmr and mass spectra.
5. C. L. Liotta and F. L. Cook, Tetrahedron Lett., 1095 (1974).
6. E. Laschtuvka and R. Huisgen, Chem. Ber., 93, 81 (1960).
7. For another route see: R. Garner, Tetrahedron Lett., 221 (1968).