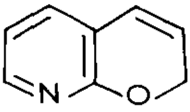
HETEROCYCLES, Vol.12, No 4, 1979

SYNTHESIS OF NEW FUNDAMENTAL HETEROCYCLES IX
SYNTHESIS OF 2H-PYRANO|3,2-b|PYRIDINE[1]

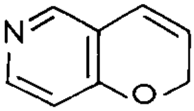
Henri Sliwa* and Klaus Peter Krings†
Laboratoire de Chimie Organique II, Université des Sciences et
Techniques de Lille, BP 36, 59650 Villeneuve d'Ascq, France

Abstract - Reductive ring opening of 5-aza-2-chromanol hydrochloride (**6**) followed by ring closure afforded 5-azachroman (**9**) which has been converted to the fundamental parent heterocycle (**3**) through acetoxylation of its N-oxide and subsequent pyrolysis.

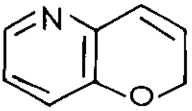
Among the condensed heterocycles which contain a pyran ring fused to a pyridine nucleus, the only ones known as fundamental heterocycles (i.e. as unsubstituted and most fully unsaturated heterocycles) are 2H-pyrano|2,3-b|pyridine (**1**)[2] and 2H-pyrano|3,2-c|pyridine (**2**).[3,4]



1



2

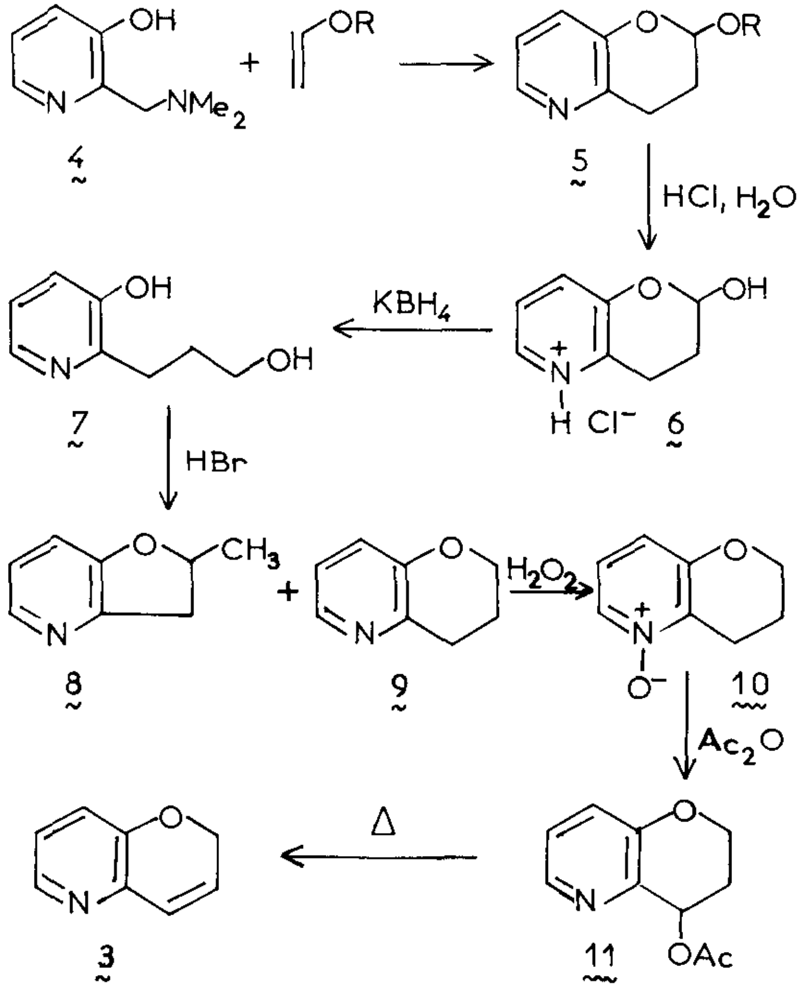


3

We report in the present note the synthesis of a third member of the series, 2H-pyrano|3,2-b|pyridine (**3**) which can be considered as derived from 3-hydroxypyridine while the former are formally derivatives of 2- or 4-hydroxypyridine.

† Granted-in-Aid from the "Institut de Chimie Pharmaceutique" of Lille, France.

The synthesis has been achieved according the following scheme :



The condensation, we recently reported[5,6] of the Mannich base of 3-hydroxypyridine (4) with vinyl ethers was used in order to synthesize 2-alcoxy-5-azachromans (5) ; hydrolysis of the latter afforded 5-aza-2-chromanol isolated as hydrochloride (6). Although, in the solid state, the compound (6) only presents the cyclic hemiacetal structure[6], reduction by KBH$_4$ occured on the open tautomer leading to the open diol (7) with an 81 % yield. Recyclization was brought about by heating at 150°C in a sealed tube a solution of the compound (7) in 48 % aqueous HBr. A 50 % yield of a mixture consisting of 5-azachroman (92 %) and 2-methyl-2,3-dihydrofuro|3,2-b|-pyridine (8 %) was thus obtained. Separation of the two components was conveniently achieved by distillation with a spinning band apparatus.

5-Azachroman (**9**) was quantitatively transformed into its N-oxide (**10**) by 30 % hydrogen peroxide in acetic acid. Treatment of the latter by acetic anhydride[7] afforded 4-acetoxy-5-azachroman (**11**, 70 % yield) which was subjected to pyrolysis. By heating, under a stream of nitrogen, to 465°C in an helice glass packed tube, the acetoxy derivative (**11**) diluted in benzene underwent the expected elimination. In this manner 2H- pyrano|3,2-c|pyridine was obtained together with some unaffected starting material (87 % yield in crude product containing 70 % of the fundamental heterocycle (**3**)). Distillation under reduced pressure afforded pure (**3**) which was characterized by the following data : bp 56°C/0.8 torr ; ir (film, cm^{-1}): 3050 (ν C-H), 2840 (ν CH_2), 1635 (ν C=C), 1580, 1560, 1460, 1440 (ν pyridine), 1225 (ν C-O arylic ether), 1195, 1120 (ν C-O cyclic ether), 1060, 1030 (ν O-CH_2), 800 (δ CH pyridine), 690 (δ = C-H) ; pmr ($CDCl_3$, δ from TMS) : 4.85 (d d, 2H, CH_2, J_{2-3} = 3.5 Hz, J_{2-4} = 1.9 Hz), 5.98 (d t, 1 H, 3-H, J_{3-4} = 5.3. Hz), 6.58 (d t, 1 H, 4-H), 6.98 (m of d appearance, 2H, 7-H and 8-H), 8.07 (m of t appearance, 1 H, 6-H).

Attempts to improve the yield of this synthesis, especially in the recyclization step, and by performing base promoted eliminations on a suitably functionalized 5-azachroman are presently under investigation.

REFERENCES

1. Part VIII : G. Cordonnier and H. Sliwa, *J. Chem. Research*, 1979, in press ; Part VII : H. Sliwa and G. Cordonnier, *J. Heterocyclic Chem.*, 1977, **14**, 169.
2. H. Sliwa, *C.R. Acad. Sci.*, Ser. C, 1967, **264**, 1893 ; *Bull. Soc. chim. France*, 1970, 631.
3. G. Lhommet, H. Sliwa, and P. Maitte, *C.R. Acad. Sci.*, Ser. C, 1971, **272**, 2197 ; *Bull. Soc. chim. France*, 1972, 1435.
4. G. Cordonnier and H. Sliwa, *J. Chem. Research*, 1979, in press.
5. H. Sliwa and D. Blondeau, *J. Heterocyclic Chem.*, 1976, **13**, 419.
6. D. Blondeau and H. Sliwa, *J. Chem. Research* (M), 1979, 117.
7. G. Kobayashi and S. Furukawa, *Pharm. Bull.* (Japan), 1953, **1**, 347.

Received, 8th January, 1979