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SYNTHESIS OF FUNDAMENTAL HETEROCYCLES C_5O-C_5N :[1] 2H-PYRANO[3,2-b]PYRIDINE AND 2H-PYRANO[2,3-c] PYRIDINE.

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Summary : An intramolecular modified Wittig type reaction using a solid liquid transfer process has been tested in the preparation of 2H-1-benzopyrans and extended to the synthesis of the title compounds.

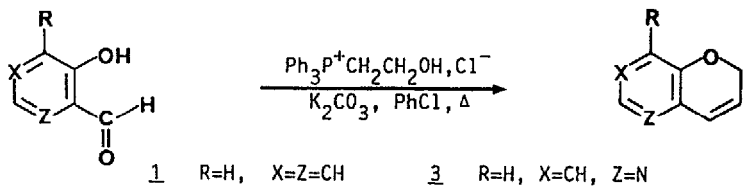
Intramolecular Wittig type reactions have been used to prepare various unsaturated rings and the efficiency of the method has been outlined by the synthesis of strained bridgehead olefins.[5] Extension to the heterocyclic field has been made by several authors,[6-8] especially by Schweizer et al[9] who prepared 2H-1-benzopyran using a "non classical" Wittig reaction. In this elegant procedure the addition of the in situ formed sodium salt of salicyladehyde on vinyltriphenylphosphonium bromide generated the required phosphorane which underwent ring closure by intramolecular attack on the formyl group.

It can be noted that this reaction has not been used to prepare pyranopyridines for which orthoformyl substituted 3-hydroxy pyridines appear to be promising starting materials. But, as we have experienced, attempted preparations of pyrano [3,2-b] pyridine from 2-formyl-3-hydroxy-pyridine and vinyltriphenylphosphonium bromide utilizing the above procedure were unsuccessful. So we turned our attention on a recently reported simplified Wittig synthesis using a solid liquid transfer process for the conversion of aromatic and heteroaromatic aldehydes into allylic ethers, as summarized by the following reaction.[10]

$$ArCHO + Ph_3P^+CH_2CH_2OH, X^- + ROH \xrightarrow{K_2CO_3} ArCH = CH-CH_2OR + Ph_3PO$$

We first applied this method to salicylaldehyde in order to test the efficiency of its intramolecular extension for the synthesis of 2H-1-benzopyran. This latter was obtained in 37 % yield by the general following procedure.

To a stirred mixture of salicylaldehyde ($25\ 10^{-3}$ mole), potassium carbonate ($50\ 10^{-3}$ mole) and chlorobenzene (30 ml) heated to 110°C, 2-hydroxyethyl-triphenylphosphonium chloride ($25\ 10^{-3}$ mole) was added in small portions over a period of an hour. The resulting mixture was allowed to stand with continous heating and stirring for 19 hours. After cooling and filtration, diethyl ether was added to the filtrate in order to cause the precipitation of triphenylphosphine oxide which was separated by filtration. The organic liquid phase was evaporated and distilled under reduced pressure affording the expected compound 1.



1 R=H, X=Z=CH 3 R=H, X=CH, Z=N

2 R=OCH_3, X=Z=CH 4 R=H, X=N, Z=CH

8-Methoxy-2H-1-benzopyran 2 and 3H-naphto [2,1-b] pyran were similarly prepared in 20 % yield, starting respectively from 2-hydroxy-3-methoxy-benzaldehyde and 2-hydroxy-1-naphthaldehyde. But the condensation was unsuccessful with 2-hydroxy-acetophenone in accordance with the previous Schweizer's results.[9]

Although the observed yields, which have not been optimized, were generally lower than those reported by Schweizer (71 %, 57 % and 14 % respectively) our modified procedure could be applied with success to the synthesis of pyranopyridines. So, condensation with 2-formyl-3-hydroxy-pyridine[11] afforded the already described by one of us[2] 2H-pyrano [3,2-b] pyridine 3 in 15 % yield, and the new fundamental heterocycle 2H-pyrano [2,3-c] pyridine 4 was obtained in 50 % yield from 3-hydroxy-4-formyl-pyridine.[12] These results show that this procedure is a method of choice for the convenient synthesis of these fused heterocycles in a single reaction step.

The purity and the structure of the synthesized compounds were ascertained by elemental analysis, mass spectrometry and nmr study (^1H and ^{13}C). As an example, the new heterocycle 4 showed the following nmr data : ^1H nmr (deuterochloroform) δ , ppm : 4.81 (2H, H-2, dd), 5.87 (1H, H-3, td), 6.30 (1H, H-4, td), 6.74 (1H, H-5, d), 8.03 (1H, H-6, d), 8.02 (1H, H-8, s), J_{H2-H3} = 3.2 Hz, J_{H2-H4} = 1.5Hz, J_{H3-H4} = 10.0 Hz, J_{H5-H6} = 4.9 Hz ; ^{13}C nmr (deuterochloroform) δ ppm : 65.8 (C_2), 119.8 (C_3), 122.6 (C_4), 128.3 (C_{4a}), 127.4 (C_5), 143.2 (C_6), 138.0 (C_8), 150.1 (C_{8a}); Eb_4=95°C; n_D^{20}=1,5906.

Improvements and application of this method to other heterocyclic orthohydroxyaldehydes are in progress.

References and Notes :

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