

SYNTHESIS OF NEW HETEROCYCLIC PHENOLS : 9-HYDROXY-PYRIDO [1,2-a] PYRIMIDINE-4- ONE AND
 9-HYDROXY-PYRIMIDO [1,6-a] PYRIMIDINE-4-ONE

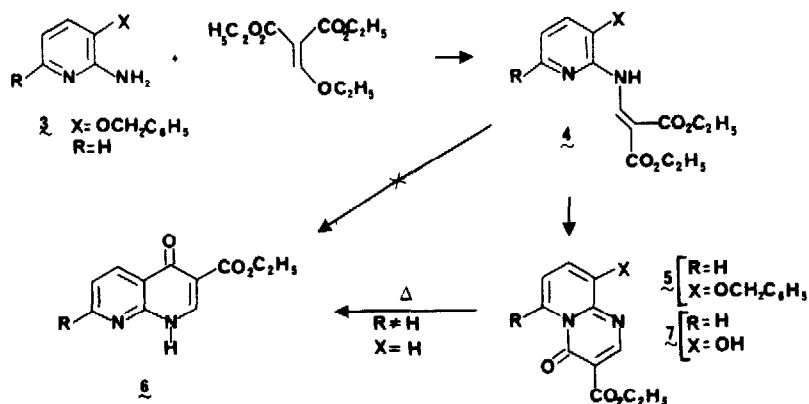
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Summary : The novel title phenols have been prepared by condensation of a derivative of Meldrum acid with 3-benzyloxy-2-amino-pyridine or 5-benzyloxy-4-amino-pyrimidine, and subsequent hydrogenolysis of the protecting group.

We have previously outlined the interest deserved to heterocyclic "phenols" both for their physicochemical properties (zwitterionic tautomers¹, complexing properties²) and for their enhanced reactivity³. Pursuing our work on fused heterocycles derived from 3-hydroxy-pyridine⁴ and 5-hydroxy-pyrimidine⁵ we have now extended the field of our investigation to the synthesis of 9-hydroxy-pyrido [1,2-a] pyrimidine-4-one 1 and 9-hydroxy-pyrimido [1,6-a]pyrimidine-4-one 2 which is reported here.

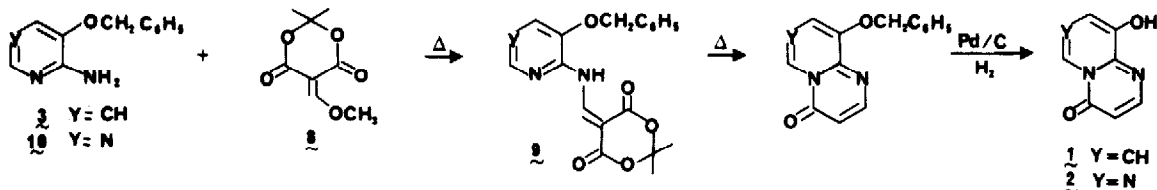
Condensation of 3-benzyloxy-2-amino-pyridine 3 prepared according to Bristol *et al*⁶, with diethyl ethoxymethylenemalonate yielded first the condensation product 4 (97 %) which readily underwent cyclisation to the pyrido[1,2-a]pyrimidone 5 (85 %). Obviously the presence



of the benzyloxy group prevents the rearrangement to the pyrido[2,3-b]pyridine 6 to take place as it is usually observed upon heating in the case where $R \neq H$ and $X = H$ ⁷.

Subsequent hydrogenolysis of the benzyl protecting group provided 3-ethoxycarbonyl-9-hydroxy-pyrido[1,2-a]pyrimidine-4-one 7 (25 %)⁸. Saponification of the compound 5 or 7 and subsequent decarboxylation were unsuccessful to obtain the expected product 1. In all cases, we observe a ring cleavage in basic media, leading to an N-aryl amino acrylic acid from which the starting product 3-benzyloxy-2-amino-pyridine was recovered.

Substituting diethyl ethoxymethylenemalonate for isopropylidene methoxymethylene-malonate 8 (prepared *in situ* by condensation of methyl formate with Meldrum acid in presence of zinc chloride)⁹, we could obtain by condensation with 2-amino-3-benzyloxy-pyridine the isopropylidene N-(3-benzyloxy-2-pyridyl) aminomethylenemalonate 9 (68 %). Further heating at 250° (47 %) and subsequent hydrogenolysis of the benzyl group provided 9-hydroxy-pyrido[1,2-a]pyrimidine-4-one 1 (30 %)⁸. The above synthesis could be extended to 5-benzyloxy-4-amino-pyrimidine 10¹⁰ which reacted with identical reagents under similar conditions, afforded the final 9-hydroxy-pyrimido[1,6-a]pyrimidine-4-one 2.



All the new compounds described in this report show the expected spectral properties in UV, IR and ¹H NMR and gave satisfactory mass spectrum and elemental analysis.

Further syntheses involving replacement of isopropylidene methoxy methylene malonate by 1,1,3,3-tetramethoxypropan and ring closure in perchloric acid¹¹ as well as extension of these condensations to pyrazine are under investigation.

References and Notes

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