NOVEL RING TRANSFORMATION OF A 4H-PYRIDO(1,2-a)PYRIMIDINE INTO A 1,8-NAPHTHYRIDINE[1]

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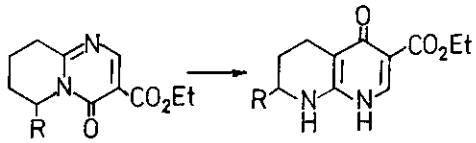
Abstract — Ethyl 4-oxo-6,7,8,9-tetrahydro-4H-pyrido(1,2-a)pyrimidine-3-carboxylates /1/ can be converted into ethyl 4-oxo--1,4,5,6,7,8-hexahydro-1,8-naphthyridine-3-carboxylates /2/ under basic conditions.

Recently we have reported[2] that 6-substituted 4H-pyrido(1,2-a)pyrimidin-4-ones can be converted thermally into 7-substituted 1,4-dihydro-1,8-naphthyridin-4--ones. We now wish to report an other type of transformation of tetrahydro-4H--pyrido(1,2-a)pyrimidin-4-ones /1/ into hexahydro-1,8-naphthyridin-4-ones /2/.

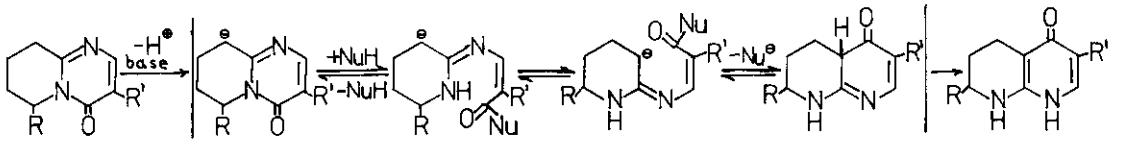


1 a/ R = Me b/ R = Et 2

We found that the pyridopyrimidine /1b/[3] /an oil/ kept at ambient temperature gradually - in a period of half a year - converts into 2b, a new naphthyridine derivative /m.p. 189-190°C; EtOH/.

Similarly from the clear aqueous soliton of the pyridopyrimidine /1a/[3], the white crystals of the naphthyridine started to precipitated after a few years /2a/ [m.p. 181-182°C, EtOH, ν_{max} /KBr/ beetwen 3140-3270 broad, 1710, 1640 cm^{-1}, λ_{max} /EtOH/ 266 /9200/, 327 /14300/, 337 /15200/ and 357 nm /14100/; δ /$CDCl_3$:CF_3COOH 1:1/ 1,43 /d, 3H, 7-Me/, 1,49 /t, 3H, Me/, 1,77 /m, 1H, 6-H_{ax}/, 2,21 /m, 1H, 6-H_{eq}/, 2,92 /m, 2H, 5-CH_2/, 3,89 /m, 1H, 7-H, J_{6e7a} 4Hz, J_{6a7a} 9,5 Hz, $J_{7a7\text{-}Me}$ 5Hz/, 4,55 /q, 2H, O-CH_2/ 7,60 /br, 1H/, 7,89 /s, 1H, 2-H/].

The same transformation was accomplished in 2 hours in a yield of 60-90 %, when the pyridopyrimidine /1a/ was heated in the presence of a secondary amine /i.e. pyrrolidine, piperidine/. This fact suggests, that the active 9-methylene group[4] of the tetrahydro-4H-pyrido(1,2-a)pyrimidin-4-ones /1/ plays an important role in that type of ring transformation reaction. The naphthyridine /2/ may be formed



according to the ANRORC mechanism[5] from pyridopyrimidine /1/ via the carbanion form /3/. Bases with stronger nucleophilic character /i.e. NH_3, NH_2OH/ react[3] with the 3-ester group of the pyridopyrimidines /1/.

The ring transformation of the tetrahydro-4H-pyrido(1,2-a)pyrimidin-4-ones may provide a facile method for the preparation of the hexahydro-1,8-naphthyridin-4--ones.

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