

NOVEL RING TRANSFORMATION OF A 4H-PYRIDO(1,2-a)PYRIMIDINE INTO
A 1,8-NAPHTHYRIDINE¹

István Hermeicz*, and Zoltán Hésczáros

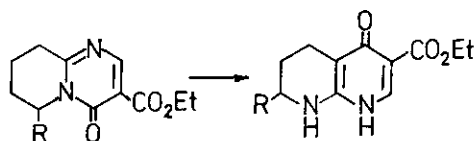
CHINOIN Pharmaceutical and Chemical Works, Research Centre,

H-1325 Budapest, Ujpest 1 P.O.Box 110, Hungary

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 reported² 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.

We found that the pyridopyrimidine 1b³



1 a/ R = Me
 b/ R = Et

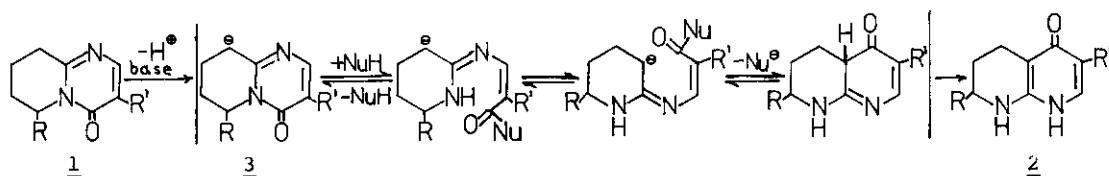
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/an oil/ kept at ambient temperature gradually - in a period of half a year - converts into 2b, a new naphthyridine derivative /m.p. 189-190°C; EtOH/.

Similarly from the clear aqueous solution

of the pyridopyrimidine 1a³, the white crystals of the naphthyridine started to precipitated after a few years 2a [m.p. 181-182°C, EtOH, ν_{\max} /KBr/ between 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, 1E, 7-H, J_{6e7a} 4Hz, J_{6a7a} 9,5 Hz, J_{7a7-He} 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 group⁴ 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 mechanism⁵ from pyridopyrimidine 1/ via the carbanion form 3/. Bases with stronger nucleophilic character /i.e. NH₃, NH₂OH/ react³ 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.

REFERENCES

1. Nitrogen Bridgehead Compounds, Part 13 and Ringtransformation Part 6.; see Part 12: see ref 4b, and Part 5: I. Hermeecz, J. Engler, Z. Mészáros, and G. Tóth, Tetrahedron Lett., 1979, 1337.
2. a./ Z. Mészáros and I. Hermeecz, Tetrahedron Lett., 1975, 1019;
b./ I. Hermeecz, Z. Mészáros, L. Vasvári-Debreczy, Á. Horváth, G. Horvátn, and M. Pongor-Csákvári, J. C. S. Perkin I, 1977, 789;
c./ G. Bernáth, F. Fülöp, I. Hermeecz, Z. Mészáros, and G. Tóth, J. Hetero-cyclic Chem., 1979, 16, 137;
d./ L. Vasvári-Debreczy, I. Hermeecz, Z. Mészáros, P. Dvortsák, and G. Tóth, J. C. S. Perkin I, in press;
e./ F. Fülöp, I. Hermeecz, Z. Mészáros, Gy. Dombi, and G. Bernáth, J. Hetero-cyclic Chem., 1979, 16, 457.
3. Z. Mészáros, J. Knoll, P. Szentmiklósi, Á. Dávid, G. Horváth, and I. Hermeecz, Arzneim.-Forsch., 1972, 22, 815.
4. a./ G. Náráy-Szabó, I. Hermeecz, and Z. Mészáros, J. C. S. Perkin I, 1974, 1753;
b./ I. Hermeecz, I. Bitter, Á. Horváth, G. Tóth, and Z. Mészáros, Tetrahedron Lett., 1979, 2557.
5. a./ H. C. van der Plas: Accounts of Chemical Research 1978, 11, 462;
b./ A. N. Kost, R. S. Sagitullin, and S.P. Gromof, Khim. Geterots. Soed., 1978, 1141;
c./ R.S. Sagitullin; A. N. Kost, and G. G. Danagulyan, Tetrahedron Lett., 1978, 4135.

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