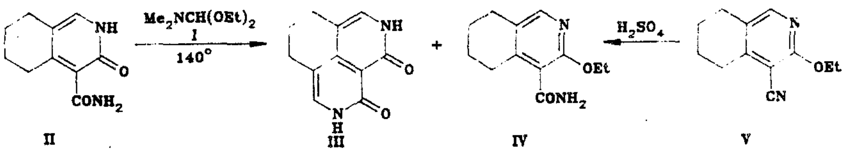
UNEXPECTED O-ALKYLATION OF 2,3,5,6,7,8-HEXAHYDRO-3-OXOISOQUINOLINE-4-CARBOXAMIDE BY DIMETHYLFORMAMIDE DIETHYLACETAL

L. T. Guss, L. V. Ershov,
and V. G. Granik

UDC 547.833.6.04

Uracils and related compounds undergo N-alkylation when treated with DMF diethylacetal (I) [1]. O-Alkylation of aromatic lactams by this reagent has not been observed up to this time. We have now shown that heating 2,3,5,6,7,8-hexahydro-3-oxoisoquinoline-4-carboxamide (II, mp 299-301°C, from water) with acetal I at 140°C (with distillation of the evolved alcohol) gives both 1,2,7,8-tetrahydro-4,5-trimethylene-2,7-naphthyridine-1,8-dione (III, 69% yield, mp > 300°C, from water) and 5,6,7,8-tetrahydro-3-ethoxyisoquinoline-4-carboxamide (IV, 10% yield, mp 174-176°C, from CH_3CN). The structure of IV was proved by independent synthesis from 5,6,7,8-tetrahydro-4-cyano-3-ethoxyisoquinoline (V, mp 78-79°C, from hexane) which, in turn, was prepared in 71% yield from the previously described [2] 3-chloro derivative using sodium ethylate.



The previously proposed N-alkylation mechanism for uracils with acetal I includes initial formation of an O-[(dimethylamino)ethoxymethyl]aromatic heterocycle [1] but does not account for a direct O-alkylation.

Elemental analytical data agreed with that calculated.

LITERATURE CITED

1. R. F. Abdulla and R. S. Brinkmeyer, Tetrahedron, 35, 1675 (1975).
2. N. I. Smetskaya, A. M. Zhidkova, N. O. Mukhina, and V. G. Granik, Khim. Geterotsikl. Soedin., No. 9, 1287 (1984).

S. Ordzhonikidze All-Union Research Institute for Pharmaceutical Chemistry, Moscow 119021. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, p. 1696, December, 1987. Original article submitted May 20, 1987.

0009-3122/87/2312-1368$12.50