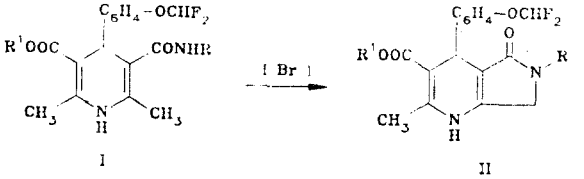
BROMINATION OF AMIDES OF 2,6-DIMETHYL-1,4-DIHYDROPYRIDINE-5-CARBOXYLIC ACIDS

I. P. Skrastin'sh, V. V. Kastron, and G. Ya. Dubur

UDC 547.822.1

We have shown that on bromination of amide Ia or anilide Ib by the procedure we developed earlier for the bromination of the corresponding esters of the acids with dioxane dibromide and N-bromosuccinimide [1, 2], and also with pyridine bromide—perbromide [3], the attack takes place at the 6-CH_3 with subsequent cyclization to pyrrolo[3,4-b]pyridines, II.



I, II a R=H, R'=CH_3; b R=C_6H_5, R'=C_2H_5

The formation of pyrrolo[3,4-b]pyridines on bromination of amides of type I is not described in the literature. On bromination of amides of 1,4-dihydropyridine-3,5-dicarboxylic acids, oxidation of the 1,4-dihydropyridine ring takes place.

2-Methyl-3-methoxycarbonyl-4-(2-difluoromethoxyphenyl)-5-oxo-1,4,5,6,7-pentahydro-pyrrolo[3,4-b]pyridine (IIa) is obtained on th bromination of amide Ia with pyridine bromide—perbromide (yield 32%); with N-bromosuccinimide (yield 46%); with dioxane dibromide (yield 40%). Mp 236-238°C. R_f 0.20 (acetone—methanol—water 8:2:1). IR spectrum: 1660, 1701, 3170, 3190 cm^{-1}. UV spectrum, λ_{max} (log ε): 233 (4.24), 357 nm (3.81). NMR spectrum (in DMSO-d_6): 2.27 (3H, s, 2-CH_3), 3.50 (3H, s, OCH_3), 5.10 (1H, s, 4-H), 5.44 (2H, s, CH_2), 7.20 (1H, q, $OCHF_2$, J_{FH} = 72, J_{FH} = 74 Hz); 7.25 (5H, m, ArH and NH), 10.73 ppm (1H, s, NH). Mass spectrum, m/z (I, %): 350 (9.5) M^+, 335 (10.8) $[M-CH_3]^+$, 319 (5.2) $[M-OCH_3]^+$, 291 (3.3) $[M—COOCH_3]^+$, 283 (8.9) $[M-OCHF_2]^+$, 281 (5.9) $[283-2H]^+$, 207 (100) $[M-C_6H_4OCHF_2]^+$.

2-Methyl-3-ethoxycarbonyl-4-(2-difluoromethoxyphenyl)-5-oxo-6-phenyl-1,4,5,7-tetrahydropyrrolo[3,4-b]pyridine (IIb). Mp 210-212°C. R_f 0.42 (ethyl acetate—acetic acid 10:1). IR spectrum: 1620, 1690, 3140 cm^{-1}. UV spectrum, λ_{max} (log ε): 230 (4.13), 360 nm (3.95). NMR spectrum (in $CDCl_3$): 1.14 (3H, t, CH_2CH_3); 2.61 (3H, s, 2-CH_3), 4.02 (2H, q, CH_2CH_3), 5.58 (1H s, 4-H), 5.75 (2H, s, CH_2), 6.78 (1H, q, $OCHF_2$, J_{FH} = 72.0, J_{FH} = 74.0 Hz);, 7.35 (4H, m, ArH), 9.95 ppm (1H, s, NH). Mass spectrum, m/z (I, %): 440 (60) M^+, 438 (40) $[M-H_2]^+$, 411 (14.9) $[M-CH_2H_5]^+$, 396 (6.3) $[M-OC_2H_5]^+$, 373 (29) $[M-OCHF_2]^+$, 371 (76) $[373-H_2]^+$, 342 (64) $[371-C_2H_5]^+$, 297 (100) $[M-C_6H_4OCHF_2]^+$.

LITERATURE CITED

1. I. P. Skrastin'sh, V. V. Kastron, G. Ya. Dubur, I. B. Mazheika, and V. P. Kadysh, *Khim. Geterotsikl. Soedin.*, No. 9, 1227 (1987).
2. I. P. Skrastin'sh, V. V. Kastron, G. Ya. Dubur, I. B. Mazheika, and É. É. Liepin'sh, *Khim. Geterotsikl. Soedin.*, No. 7, 948 (1989).
3. S. D. Young, *Synthesis*, No. 7, 617 (1984).

Institute of Organic Synthesis, Latvian Academy of Sciences, Riga 226006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, p. 1276, September, 1991. Original article submitted January 10, 1991.

0009-3122/91/2709-1031$12.50