SYNTHESIS OF 4-ARYL-3-CYANO-1,2,5,7-TETRAHYDROFURO[3,4-B]PYRIDINE-2,5-DIONES

Z. A. Kalme, Yu. É. Pelcher, and G. Ya. Dubur

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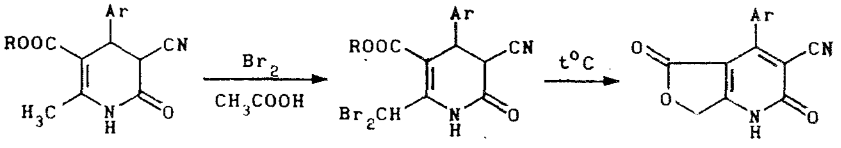
A new group of condensed 2-pyridones — 1,2,5,7-tetrahydrofuro[3,4-b]pyridine-2,5-diones III — was obtained.



I II III

I, II a $Ar=C_6H_5$, $R=C_2H_5$; b $Ar=p\text{-}ClC_6H_4$, $R=CH_3$; III a $Ar=C_6H_5$, b $Ar=p\text{-}ClC_6H_4$

Using the known methods for obtaining tetrahydrofuro[3,4-b]pyridines from 1,4-dihydropyridines [1, 2] (bromination with N-bromosuccinimide or pyridine bromide-perbromide) in the case of 3,4-dihydro-2-pyridones I we were unable to realize bromination of the methyl group and heterocyclization to give furo[3,4-b]pyridine-2,5-diones III.

The bromination of 3,4-dihydro-2-pyridones I [3] at the methyl group in the 6 position was accomplished with elementary bromine in acetic acid. The $C_{(3)}$ atom is not affected as a result of bromination, in contrast to what is observed for 5-unsubstituted 2-pyridones [4]. The resulting dibromides II are converted thermally to tetrahydrofuro[3,4-b]pyridine-2,5-diones III.

A 17.5-mmole sample of bromine was added with stirring to a suspension of 3.5 mmole of Ia, b in 7 ml of glacial acetic acid, and the mixture was allowed to stand for 3 days, after which dibromides IIa, b were removed by filtration. Solid masses, which on treatment with ethanol gave tetrahydrofuro[3,4-b]pyridine-2,5-diones IIIa, b, were formed when dibromides IIa, b were heated gradually to 170-180°C and maintained at this temperature until gas evolution ceased.

Ethyl 2-Dibromomethyl-6-oxo-4-phenyl-5-cyano-1,4,5,6-tetrahydropyridine-3-carboxylate (IIa, $C_{16}H_{14}Br_2N_2O_3$). This compound had mp 167-168°C (from ethanol). IR spectrum (KBr): 1695 (amide C=O); 1725 (ester C=O); 2262 (CN); 3200, 3280 cm^{-1} (NH). PMR spectrum (d_6-DMSO): 1.12 (3H, t, CH_3), 4.05 (2H, q, CH_2), 4.44 (1H, d, 3-H), 4.7 (1H, s, $CHBr_2$), 4.88 (1H, d, 4-H), 7.28 (5H, s, C_6H_5), 11.3 ppm (1H, s, NH). The yield was 78%.

Methyl 2-Dibromomethyl-6-oxo-4-(p-chlorophenyl)-5-cyano-1,4,5,6-tetrahydropyridine-3-carboxylate (IIb, $C_{15}H_{11}Br_2ClN_2O_3$). This compound had mp 120-122°C (from ethanol). PMR spectrum (d_6-DMSO): 3.55 (1H, s, CH_3), 4.33 (1H, d, 3-H), 4.73 (1H, s, $CHBr_2$), 4.86 (1H, d, 4-H), 7.31 (4H, d, C_6H_4), 11.31 ppm (1H, s, NH). The yield was 69%.

4-Phenyl-3-cyano-1,2,5,7-tetrahydrofuro[3,4-b]pyridine-2,5-dione (IIIa, $C_{14}H_8N_2O_3$). This compound had mp 275-280°C [dec., from ethanol—dioxane (10:1)]. IR spectrum (KBr): 1695 (lactam C=O), 1772 (lactone C=O), 2240 (CN), 3250 cm^{-1} (NH). PMR spectrum (d_6-DMSO): 5.17 (2H, s, CH_2), 7.45 (5H, s, C_6H_5), 11.55-12.04 ppm (1H, broad s, NH). The yield was 65%.

4-(p-Chlorophenyl)-3-cyano-1,2,5,7-tetrahydrofuro[3,4-b]pyridine-2,5-dione (IIIb, $C_{14}H_7ClN_2O_3$). This compound had mp 275-280°C (dec., from ethanol). IR spectrum (KBr): 1690 (lactam C=O), 1782 (lactone C=O), 2240 (CN), 3405

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cm^{-1} (NH). PMR spectrum (d_6-DMSO): 5.20 (2H, s, CH_2), 7.50 (4H, d, C_6H_4), 11.60-12.00 ppm (1H, broad s, NH). The yield was 43%.

Compounds III crystallized with a molecule of ethanol, which was split out only by drying at 120°C for 3-4 h.

The results of elementary analysis of the synthesized compounds were in agreement with the calculated values.

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