Chemistry of Heterocyclic Compounds, Vol. 32, No. 8, 1996

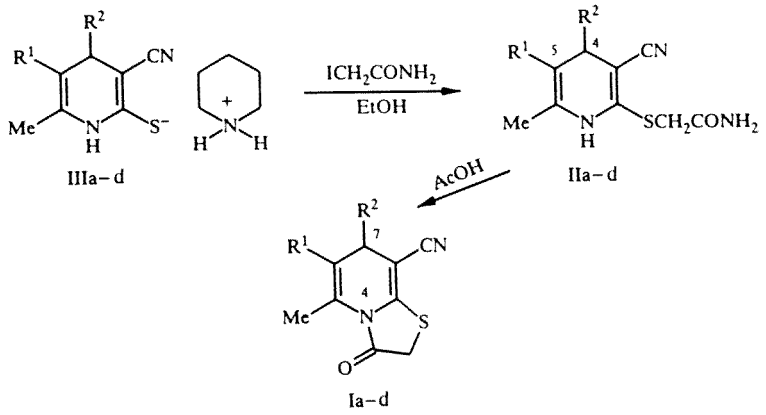
METHOD FOR PREPARATION OF 3-OXO-2,3,4,7-TETRAHYDROTHIAZOLO[3,2-*a*]PYRIDINES

A. Krauze and G. Duburs

It has been shown previously that 2-carbamoylmethylthio-1,4-dihydropyridines are dehydrated in a mixture of hydrochloric and acetic acids to give 2-cyanomethylthio-1,4-dihydropyridines (I). It has also been shown that 7-(4-pyridyl)-2,3,4,7-tetrahydrothiazolo[3,2-*a*]pyridine (Ia) was obtained as a byproduct (29%) of the oxidation of 4-(4-pyridyl substituted 3-cyano-2-carbamoylmethylthio-1,4-dihydropyridine with sodium nitrite in acetic acid along with the required pyridine [2].

We have found that 2,3,4,7-tetrahydrothiazolo[3,2-*a*]pyridines Ia and Ib-Id are formed on boiling 2-carbamoylmethylthio-1,4-dihydropyridines IIa-IId in acetic acid with no other additive. Compounds IIa-IId were prepared by alkylating the corresponding thiolates IIIa-IIId with iodoacetamide.

Compounds Ia-Ic were obtained in 70-85% yields from the 4- or 5-pyridyl substituted compounds IIa-IIc. The reaction occurred considerably more slowly with the 4-(*p*-chlorophenyl)-5-ethoxycarbonyl substituted dihydropyridine IId: after boiling for 8 h the principal component in the reaction mixture was the starting material and the yield of the thiazolopyridine Id was only 25%. Evidently the nucleophilic center of the pyridyl substituents in compounds IIa-IIc is protonated in acetic acid and the cation formed is a strong acceptor which facilitates an increased yield of products Ia-Ic.



I—III a R^1 = COOMe, R^2 = 4-C_5H_4N; b R^1 = $CONH_2$, R^2 = 4-C_5H_4N; c R^1 = 4-C_5H_4N, R^2 = 3-$NO_2C_6H_4$; d R^1 = COOEt, R^2 = 4-ClC_6H_4

The simple reaction described here is a suitable method for the preparation of tetrahydrothiazino[3,2-*a*]pyridines. The limits to its use are the subject of further study.

5-Carbamoyl-2-carbamoylmethylthio-6-methyl-4-(4-pyridyl)-3-cyano-1,4-dihydropyridine (IIb, $C_{15}H_{15}N_5O_2S$). Yield 84%. mp 228-230°C. IR Spectrum: 3410, 3368, 3280 sh, 3148 (NH_2), 2196 (CN), 1682, 1672, 1650 cm^{-1} (CO). ^1H NMR Spectrum (DMSO-D_6): 2.12 (3H, s, 6-CH_3), 3.58 and 3.70 (2H, 2d, J = 14.4 Hz, SCH_2), 4.67 (1 H, s, 4-H), 7.0 (2 H, br. s, 5-$CONH_2$), 7.15 and 8.47 (4H, 2dd, 4-C_5H_4N), 7.52 and 7.82 (2H, 2s, SCH_2CONH_2), 9.92 ppm (1H, s, NH).

5-Methyl-6-methoxycarbonyl-3-oxo-7-(4-pyridyl)-8-cyano-2,3,4,7-tetrahydrothiazolo[3,2-*a*]pyridine (Ia). Yield 70%. mp 173-175°C [2].

6-Carbamoyl-5-methyl-3-oxo-7-(4-pyridyl)-8-cyano-2,3,4,7-tetrahydrothiazolo[3,2-*a*]pyridine(Ib,$C_{15}H_{12}N_4O_2S$). Yield 74%. mp 240-242°C. IR Spectrum: 3376, 3196 (NH_2), 2196 (CN), 1730, 1668 cm^{-1} (CO). ^1H NMR Spectrum (DMSO-D_6): 2.34 (3H, s, 5-CH_3), 4.12 (2H, s, SCH_2CO), 4.68 (1H, s, 7-H), 7.28 and 8.46 (4H, 2dd, 7-C_5H_4N), 7.32 and 7.60 ppm (2H, 2s, $CONH_2$).

Latvian Institute of Organic Synthesis, Riga LV 1006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1134-1135, August, 1996. Original article submitted July 1, 1996.

 0009-3122/96/3208-0982$15.00

5-Methyl-7-(3-nitrophenyl-3-oxo-6-(4-pyridyl)-8-cyano-2,3,4,7-tetrahydrothiazolo[3,2-*a*]pyridine (Ic, $C_{20}H_{14}N_4O_3S$). Yield 85%. mp 215-217°C. IR Spectrum: 2201 (CN), 1744 cm^{-1} (CO). ^1H NMR Spectrum (DMSO-D_6): 2.14 (3H, s, 5-CH_3), 4.16, 2H, s, SCH_2CO), 5.06 (1H, s, 7-H), 7.14 and 8.44 (4H, 2dd, 6-C_5H_4N), 7.5-8.1 ppm (4H, m, 7-$NO_2C_6H_4$).

5-Methyl-3-oxo-7-(4-chlorophenyl)-8-cyano-6-ethoxycarbonyl-2,3,4,7-tetrahydro[3,2-*a*]pyridine (Id, $C_{18}H_{15}N_2ClO_3S$). Yield 25%. mp 154-156°C. IR Spectrum: 2200 (CN), 1740, 1710, 1664 cm^{-1} (CO). ^1H NMR Spectrum (DMSO-D_6): 1.04 (3H, t, $CH_2\underline{CH_3}$), 4.02 (2H, q, $\underline{CH_2}CH_3$), 4.14 (2H, s, SCH_2CO), 4.74 (1H, s, 7-H), 7.28 and 7.42 ppm (4H, 2dd, 7-ClC_6H_4).

REFERENCES

1. A. A. Krauze, É. É. Liepin'sh, Yu. É. Pelcher, and G. Ya. Dubur, Khim. Geterotsikl. Soedin., No. 1, 124 (1987).
2. A. Krauze and G. Duburs, Latv. Khim. Zh., No. 1, 92 (1994).