Short Communication

Synthesis of 4-Arylamino-1*H*-pyrazolo[3,4-*d*]pyrimidines

Lene Andersen and Erik B. Pedersen

Department of Chemistry, Odense University, DK-5230 Odense M, Denmark

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4-Substituted pyrazolo[3,4-*d*]pyrimidines have long been known to possess antitumor activity.[1,2] As early as 1956 Robins[3] and later on Skipper *et al.*[4] reported the synthesis and biological activity of 4-alkylaminopyrazolo[3,4-*d*]pyrimidines. Recently, the corresponding nucleosides have been shown to be anticoccidial agents.[5] Therefore, it would be of interest to find an easy synthesis of 4-arylamino-1*H*-pyrazolo-[3,4-*d*]pyrimidine derivatives as candidates for biological screening.

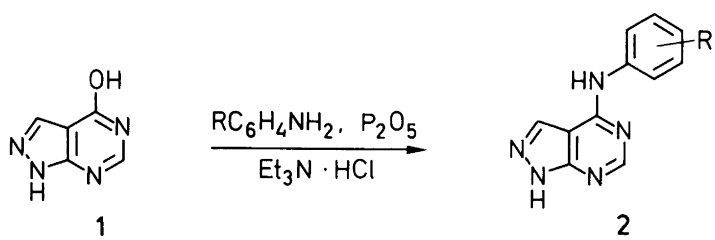
Commercially available 1*H*-pyrazolo[3,4-*d*]-pyrimidine-4-ol (**1**) was treated with a mixture of triethylamine hydrochloride, phosphorus pentaoxide, and an arylamine, at 150–200 °C for 1.5–24 h to give the corresponding amino compounds (**2**) in 21–59 % yield (see Table 1).

Correct microanalysis, mass, IR, ^{1}H NMR and ^{13}C NMR spectra were obtained for all new compounds.

The interpretation of the ^{13}C NMR spectra was made by comparison with the spectra of other 4-substituted 1*H*-pyrazolo[3,4-*d*]pyrimidines[6] and with ^{13}C NMR spectra of anilines, and by inspection of undecoupled spectra.

Experimental

*4-(3-Trifluoromethylanilino)1*H*-pyrazolo[3,4-*d*]pyrimidine* (**2e**). *Typical experiment.* 3-Trifluoromethylaniline (0.16 mol) was added with stirring to a mixture of phosphorus pentaoxide (27.2 g, 0.16 mol) and triethylamine hydrochloride (22.0 g, 0.16 mol) protected with a $CaCl_2$ drying tube. The mixture was placed in a preheated oil bath at 200 °C. When the mixture had turned into a homogeneous melt (15–30 min), (**1**) (5.44 g, 0.04 mol) was added and the mixture was stirred at 200 °C for 24 h. The reaction mixture was allowed to cool to about 100 °C, 2 **M** sodium hydroxide was added until a pH of 9–10 was reached and the mixture was stirred for 1 h at ambient temperature. The digested product was filtered off, washed with water and recrystallized from 96 % ethanol to give 6.6 g (59 %) of (**2e**). MS [*m/z* (% rel. int.)] 279 (79, *M*), 278 (100), 258 (12), 145 (19). ^{1}H NMR (60 MHz; [$^2H_6$]Me_2SO): δ 7.42 (d, 1 H, *J* = 8 Hz), 7.64 (t, 1 H, *J* = 8 Hz), 8.20 (d, 1 H, *J* = 8 Hz), 8.36 (s, 1 H), 8.57 (s, 1 H), 10.32 (NH), 13.76 (NH). ^{13}C NMR



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Scheme 1.

Table 1. Preparation of (**2a–g**).

Compound	Ar	Reaction			
		Time/h	Temp./°C	Yield/%	M.p./°C
(**2a**)	C_6H_5	1.5	150	21	253[a]
(**2b**)	4-ClC_6H_4	2.5	200	26	259
(**2c**)	3-ClC_6H_4	3	200	50	298–299
(**2d**)	3-CF_3, 4-ClC_6H_3	3	200	56	300
(**2e**)	3-$CF_3C_6H_4$	24	200	59	301
(**2f**)	3,5-$(CH_3)_2C_6H_3$	3	150	48	282–284
(**2g**)	4-FC_6H_4	3	150	31	264–265

[a]Lit. m.p. 263–264 °C.[3]

(15 MHz; [$^2H_6$]Me_2SO): δ 100.7 (C–3a), 132.1 (C–3), 153.9, 154.7 (C–4, C–7a), 154.9 (C–6), 116.5, 119.0, 124.0, 126.5, 129.6, 140.2 (Ar), 121.0 (CF_3). IR(KBr) 1640 cm^{-1}. Anal. $C_{12}H_8F_3N_5$: C, H, N.

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