Short Note

5-Dimethylamino-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one

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Abstract: The title compound was prepared by treatment of 5-fluoro-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one with aqueous dimethylamine. Detailed spectroscopic data (1H NMR, 13C NMR, 15N NMR, IR, MS) are presented.

Keywords: chromeno[2,3-c]pyrazol-4(1H)-one; nucleophilic substitution; DMF

In the course of a program devoted to the synthesis of new heterocyclic scaffolds we recently presented the synthesis of various heterocyclic xanthone analogues of type A containing a [5,6]pyran[2,3-c]pyrazol-4(1H)-one substructure (Figure 1) [1-7]. In these compounds, one benzene ring of the parent xanthone is replaced by a pyrazole system and the other one by a variable heteroaromatic moiety or by a (substituted) benzene ring.

Figure 1.

Due to the importance of fluorinated compounds in medicinal chemistry [8-12] we also synthesized appropriate congeners B carrying fluoro substituents at different positions of a chromeno[2,3-c]pyrazol-4(1H)-one scaffold, for instance at positions 5, 6, 7 and 8 (Figure 1) [13]. During the synthesis of 5-fluoro-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (3, Scheme 1) we observed an
interesting phenomenon. The preparation of 3 was accomplished by cyclization of intermediate 2, which was obtained upon reaction of 1-phenyl-2-pyrazolin-5-one (1) with 2,6-difluorobenzoyl chloride under the conditions described by Jensen for the C-4 acylation of pyrazolones (calcium hydroxide, dioxane, reflux) [14]. When the cyclization of 2 (NaH/DMF) was carried out under forced conditions and prolonged heating, besides the desired fluoro compound 3 also the corresponding dimethylamino congener 4 was obtained in increasing extent (Scheme 1). This finding can be accounted to the known decomposition of DMF (N,N-dimethylformamide) at its boiling temperature, leading to the liberation of dimethylamine [15]. This process can also occur at lower temperatures when catalyzed by basic or acidic materials [15]. Also the conversion of active haloheteroarenes into the corresponding N,N-dimethylamino compounds has been described in this way, as an example the synthesis of 6-chloro-3-(dimethylamino)pyridazine from 3,6-dichloropyridazine (95% yield) via 48 hours reflux in DMF solution may serve [16].

For comparison purposes, we prepared amine 4 in an alternative way, i.e. by reaction of 3 with excess aqueous dimethylamine. The latter procedure is definitely advantageous compared to the above mentioned one, as here the title compound is smoothly obtained under mild conditions without any by-products, thus superseding a chromatographic separation (Scheme 1).

**Scheme 1. Synthesis of compounds 3 and 4.**

A detailed characterization of compound 4 including IR, MS and NMR (1H, 13C, 15N) spectral data as well as microanalytical data is given in the Experimental. Full and unambiguous assignment of all 1H, 13C and 15N NMR resonances was achieved by combined application of standard NMR spectroscopic techniques such as 1H-coupled 13C-NMR (gated decoupling), APT, COSY, NOESY, gs-HSQC and gs-HMBC [17].

**Experimental**

The melting point was determined on a Kofler hot-stage microscope and is uncorrected. The mass spectrum was obtained on a Shimadzu QP 1000 instrument (EI, 70 eV), the IR spectrum on a Perkin-Elmer FTIR 1605 spectrophotometer (KBr-disc). The elemental analysis was performed at the Microanalytical Laboratory, University of Vienna. All NMR spectra were recorded from CDCl3.
solutions on a Bruker Avance 500 instrument with a ‘directly’ detecting broadband observe probe (BBFO) at 298 K (500.13 MHz for $^1$H, 125.76 MHz for $^{13}$C, 50.68 MHz for $^{15}$N). The centre of the solvent signal was used as an internal standard which was related to TMS with $\delta = 7.26$ ppm ($^1$H in CDCl$_3$) and $\delta = 77.0$ ppm ($^{13}$C in CDCl$_3$). The digital resolutions were 0.2 Hz/data point in the $^1$H and 0.4 Hz/data point in the $^1$H-coupled $^{13}$C-NMR spectra (gated decoupling). The $^{15}$N NMR spectrum (gradient-selected $^{15}$N,$^1$H-HMBC) was referenced against external nitromethane.

5-Dimethylamino-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (4)

In a reaction flask closed with a balloon, to a solution of 5-fluoro-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (3) (28 mg, 0.1 mmol) in 1,4-dioxane (4 mL) was portionwise added an aqueous solution (40%) of dimethylamine (400 $\mu$L) via syringe. Then the mixture was stirred at room temperature for 3 hours. Evaporation of the solvents under reduced pressure produced a light-colored residue which was washed with water and dried to afford 23 mg (75%) of chromatographically pure 4. For analytical purposes the material was recrystallized from EtOH to give 19 mg (62%) of 4 as yellowish crystals with mp 184–186 °C.

IR (KBr) ν (cm$^{-1}$): 1651 (C=O).

MS (EI, 70 eV): (m/z, %) 305 (M$^+$, 32), 291 (20), 290 (100), 276 (52), 121 (15), 77 (31) 51 (28).

$^1$H NMR (CDCl$_3$): $\delta$ (ppm) 2.98 (s, 6H, NMe$_2$), 6.90 (dd, 1H, H-6, $^3$J(H6,H7) = 8.3 Hz, $^4$J(H6,H8) = 1.0 Hz), 6.96 (dd, 1H, H-8, $^3$J(H8,H7) = 8.2 Hz, $^4$J(H8,H6) = 1.0 Hz), 7.40 (m, 1H, Ph H-4), 7.47 (dd, 1H, H-7, $^3$J(H7,H6) = 8.3 Hz, $^3$J(H7,H8) = 8.2 Hz), 7.55 (m, 2H, Ph H-3.5), 7.90 (m, 2H, Ph H-2.6), 8.18 (s, 1H, H-3).

$^{13}$C NMR (CDCl$_3$): $\delta$ (ppm) 44.8 (NMe$_2$), $^1$J = 136.3 Hz, $^3$J = 4.1 Hz), 107.7 (C-3a, $^3$J(C3a,H3) = 9.8 Hz), 108.1 (C-8), 112.9 (C-6), 113.4 (C-4a), 121.0 (Ph C-2.6), 127.4 (Ph C-4), 129.4 (Ph C-3.5), 133.2 (C-7, $^1$J = 160.9 Hz), 136.8 (C-3, $^1$J = 193.6 Hz), 137.3 (Ph C-1), 151.6 (C-9a, $^3$J(C9a,H3) = 4.8 Hz), 154.4 (C-5), 157.9 (C-8a), 172.6 (C-4).

$^{15}$N NMR (CDCl$_3$): $\delta$ (ppm) −325.5 (NMe), −188.8 (N-1), −91.7 (N-2).

Anal. Calcd for $C_{13}H_{18}N_3O_2$: C, 70.81%; H, 4.95%; N, 13.76%. Found: C, 70.47%; H, 4.73%; N 13.54%.

References and Notes


