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SHORT COMMUNICATIONS

Tautomerism of 3(5)-Amino-4-cyano- and 3(5)-Amino-4-thiocyanatopyrazoles

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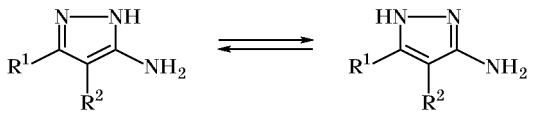
The $N^1H-N^2 \rightleftarrows N^1-N^2H$ tautomerism of pyrazoles has been studied in sufficient detail by various physical methods [1–7]. However, the tautomeric properties of α-aminopyrazoles were examined only for a very limited number of compounds [8–10]. α-Aminopyrazoles are key compounds in the synthesis of fused heterocyclic compounds, and determination of the state of their tautomeric equilibria is important for estimation of the relative stability of particular tautomers, comparison of various calculated parameters with those found experimentally, and study of the mechanism of their cyclocondensation reactions with difunctional electrophiles. Puello *et al.* [10] revealed the existence of two different tautomers of crystalline 3(5)-amino-5(3)-(4-X-phenyl)pyrazoles. In solution they also exist as mixtures of two tautomers, which was usually confirmed by the data of indirect methods [1, 2, 10].

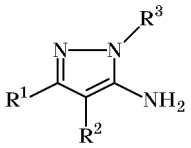
We have found that introduction of a cyano or thiocyanato group into position *4* of 3(5)-aminopyrazole reduces the rate of tautomeric transformation, so that separate signals from each tautomeric form can be observed in the ^1H and ^{13}C NMR spectra in DMSO:



3A **5A**

R^2 = CN, SCN.

The ^1H NMR spectra of 3(5)-amino-4-cyano-5(3)-methylpyrazole (**Ia**) and 3(5)-amino-5(3)-aryl-4-thiocyanatopyrazoles **IIa**–**IIc** contained doubled signals from the NH and NH_2 protons, and compound **Ia** shows in the ^{13}C NMR spectrum doubled signals from the CR^1 and CNH_2 carbon atoms (see table). In the ^1H and ^{13}C NMR spectra of **Ib** (R^1 = H) we observed signals belonging to only one tautomer. Addition of a catalytic amount of acetic acid to a solution of **IIa** in DMSO leads to coalescence of the NH and NH_2 signals in the ^1H NMR spectrum (see table). In order to unambiguously assign signals to each tautomer (3- and 5-amino, **3A** and **5A**) of pyrazoles **Ia**, **Ib**, and **IIa**–**IIc** we have synthesized model compounds **IIIa**, **IIIb**, and **IV**b, whose structure was reliably determined on the basis of the ^{13}C NMR spectra using long-range $^{13}C-^1H$ coupling constants (with successive selective heteronuclear decoupling from the CH_3, CH_2, and NH_2 protons; see table).



The observed pattern of heteronuclear coupling allowed us to assign the structure of 5-aminopyrazoles to compounds **IIIa** and **IIIb**, in agreement with the data of [11]. By comparing the chemical shifts of the pyrazole ring carbon atoms in compounds **Ia** and **Ib** with those found for **IIIa** and **IIIb** we have identified the corresponding tautomers **3A** and **5A** of **Ia** and **Ib** (see table). Tautomers **3A** and **5A** of compounds **IIa**–**IIc** were identified by comparing the chemical shifts of the NH and NH_2 protons in the ^1H NMR spectra of **Ia**, **Ib**, and **IIa**–**IIc**: **3A**: δ(NH_2) 5.30–5.50 ppm, δ(NH) 12.7 ppm; **5A**: δ(NH_2) 6.20 ppm, δ(NH) 12.10–12.20 ppm.

Analysis of the spectral data showed that solutions of pyrazoles **Ia**, **Ib**, and **IIa**–**IIc** in DMSO contain mainly the corresponding 5-amino tautomer. Very

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^{1}H and ^{13}C NMR spectra of 3- and 5-aminopyrazoles **I**–**IV**

Comp. no.	R^1	R^2	R^3	Isomer (fraction)	^{1}H NMR spectrum, δ, ppm	^{13}C NMR spectrum, δ_C, ppm (J_{CH}, Hz)
Ia	Me	CN	H	**3A** (37%)	2.09 br.s (3H, Me), 5.31 br.s (2H, NH_2), 12.75 br.s (1H, N^1H)	10.21 (Me), 76.97 br.s (C^4), 115.70 (CN), 145.16 br.s (CMe), 157.25 br.s (CNH_2)
				5A (63%)	2.18 br.s (3H, Me), 6.23 br.s (2H, NH_2), 12.06 br.s (1H, N^1H)	12.72 (Me), 72.16 br.s (C^4), 115.70 (CN), 149.49 br.s (CMe), 153.39 br.s (CNH_2)
Ib	H	CN	H	**5A** (100%)	6.06 br.s (2H, NH_2), 7.69 br.s (1H, 3-H), 12.10 br.s (1H, N^1H)	74.32 br.s (C^4), 116.21 (CN), 139.71 br.s (CH), 155.29 br.s (CNH_2)
IIa	Ph	SCN	H	**3A** (29%)	5.42 br.s (2H, NH_2), 7.07–8.07 m (5H, H_{arom}), 12.71 br.s (1H, N^1H)	[a]
				5A (71%)	6.15 br.s (2H, NH_2), 7.07–8.07 m (5H, H_{arom}), 12.16 br.s (1H, N^1H)	
IIa	Ph	SCN	H	**3A** + **5A**[b]	5.94 br.s (2H, NH_2), 7.07–8.07 m (5H, H_{arom}), 12.31 br.s (1H, N^1H)	72.20 br.s (C^4), 112.76 (SCN), 127.33, 128.69 (C^o, C^m, C^p), 132.36 br.s (C^i), 150.55 br.s (CPh), 153.41 br.s (CNH_2)
IIb	4-ClC_6H_4	SCN	H	**3A** (13%)	5.39 br (2H, NH_2), 7.55–7.82 m (4H, H_{arom}), 12.72 br.s (1H, N^1H)	
				5A (87%)	6.15 br.s (2H, NH_2), 7.55–7.82 m (4H, H_{arom}), 12.23 br.s (1H, N^1H)	
IIc	4-BrC_6H_4	SCN	H	**3A** (18%)	5.50 br.s (2H, NH_2), 7.68–7.75 m (4H, H_{arom}), 12.71 br.s (1H, N^1H)	
				5A (82%)	6.19 br.s (2H, NH_2), 7.68–7.75 m (4H, H_{arom}), 12.24 br.s (1H, N^1H)	
IIIa	Me	CN	1-CH_2Ph	**5A**	2.30 (Me), 4.10 (2H, CH_2), 5.12 (2H, NH_2), 7.12–7.45 m (5H, H_{arom})	12.70 q (Me, J = 127.9), 49.76 t.t (CH_2, J = 133.2, ^3J = 4.3), 72.50 q.t (C^4, ^3J = 3.6, ^3J = 2.9), 115.55 (CN), 137.00, 128.54, 127.45, 127.37 (Ph), 148.97 q (CMe, ^2J = 6.5), 152.04 t (CNH_2, ^3J = 2.6)
IIIb	H	CN	1-CH_2-C_6H_4Cl-4	**5A**	5.15 (2H, CH_2), 6.75 (2H, NH_2), 7.15–7.42 (4H, H_{arom}), 7.59 (1H, 3-H)	48.39 t.t (CH_2, J = 130.2, ^3J = 4.1), 72.36 d.t (C^4, ^2J = 10.1, ^3J = 3.O), 115.23 (CN), 136.74, 132.24, 129.28, 128.57 (Ph), 140.85 d (C^3, J = 191.9), 151.73 (CNH_2)
IV	Ph	SCN	1-CH_2Ph	**5A**	5.27 (2H, CH_2), 6.56 (2H, NH_2), 6.96–7.94 (10H, H_{arom})	51.57 (CH_2), 72.96 (C^4), 113.66 (SCN), 128.30, 129.33, 133.00, 137.70 (2Ph), 151.10 (C^3), 152.67 (C^5)

[a] Common broadened signals are observed.

[b] A catalytic amount of acetic acid was added.

broad separate signals of tautomers **3A** and **5A** were observed previously [10] for only one aminopyrazole derivative, 3(5)-amino-5(3)-phenylpyrazole (ultrapure DMSO-d_6, **3A**:**5A** ratio ~1:1).

Thus, 3(5)-amino-4-cyano- and -4-thiocyanatopyrazoles exist in DMSO-d_6 at 20°C as mixtures of two tautomers which give separate signals in the ^{1}H and ^{13}C NMR spectra.

Compounds **I**–**IV** were synthesized by the procedures reported in [12, 13]. Compounds **Ia**, **Ib**, and **IIa** were described previously [12].

3(5)-Amino-5(3)-(4-chlorophenyl)-4-thiocyanatopyrazole (IIb). Yield 75%. mp 164°C. Found, %: C 47.71; H 2.93. $C_{10}H_7ClN_4O_2$. Calculated, %: C 47.91; H 2.81.

3(5)-Amino-5(3)-(4-bromophenyl)-4-thiocyanatopyrazole (IIc). Yield 68%. mp 187°C. Found, %: C 40.83; H 2.60. $C_{10}H_7BrN_4$. Calculated, %: C 40.69; H 2.39.

5-Amino-1-(4-chlorobenzyl)-4-cyanopyrazole (IIIa). Yield 86%. mp 174°C. Found, %: C 56.71; H 4.03. $C_{11}H_9ClN_4$. Calculated, %: C 56.78; H 3.90.

5-Amino-1-benzyl-4-cyano-3-methylpyrazole (IIIb). Yield 85%. mp 121°C. Found, %: C 67.75; H 5.85. $C_{12}H_{12}N_4$. Calculated, %: C 67.90; H 5.70.

5-Amino-1-benzyl-3-phenyl-4-thiocyanatopyrazole (IV). Yield 57%. mp 118°C. Found, %: C 64.12; H 4.25. $C_{15}H_{12}N_4S$. Calculated, %: C 64.26; H 4.31.

The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DPX-300 spectrometer at 300.13 and 75.47 MHz, respectively.

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