

## NMR analysis of a series of substituted pyrazolo[3,4-*d*]pyrimidines-

### 4-amines

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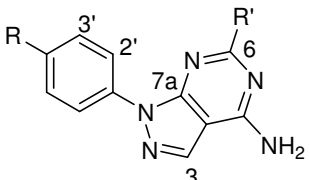
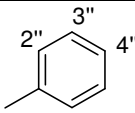
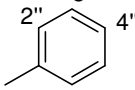
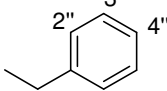
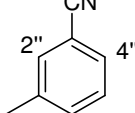
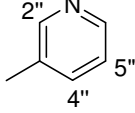
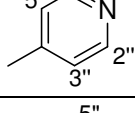
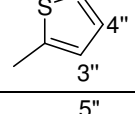
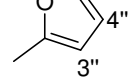
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**A series of twenty one substituted pyrazolo[3,4-*d*]pyrimidines-4-amines were studied by <sup>1</sup>H and <sup>13</sup>C NMR. The application of two-dimensional techniques, HMQC and HMBC, allowed the complete assignment of the spectra for all the compounds.**

**KEYWORDS:** NMR; 2D NMR; <sup>1</sup>H NMR; <sup>13</sup>C NMR; pyrazolo[3,4-*d*]pyrimidines-4-[amines](#)

Structure	Compound	R	R'
	<b>1a</b>	H	
	<b>2a</b>	Cl	
	<b>3a</b>	Br	
	<b>1b</b>	H	
	<b>2b</b>	Cl	
	<b>3b</b>	Br	
	<b>1c</b>	H	
	<b>2c</b>	Cl	
	<b>3c</b>	Br	
	<b>1d</b>	H	
	<b>2d</b>	Cl	
	<b>3d</b>	Br	
	<b>1e</b>	H	
	<b>2e</b>	Cl	
	<b>3e</b>	Br	
	<b>1f</b>	H	
	<b>2f</b>	Cl	
	<b>3f</b>	Br	
	<b>1g</b>	H	
	<b>2g</b>	Cl	
	<b>3g</b>	Br	

**Figure 1.** Structures and numbering for compounds

## INTRODUCTION

As part of our ongoing research program on heterocyclic compounds which may serve as leads for designing novel chemotherapeutic agents, we have been involved on the preparation of pyrazolopyrimidines [1, 2]. These compounds and other related fused heterocycles are known to exhibit biological activity of several types such as CNS depressant [3], neuroleptic [4], tuberculostatic [5], antibacterial and antifungal [2, 6]. It was also reported that pyrazolo[3,4-*d*]pyrimidines inhibit xanthine oxidase [7, 1].

## RESULTS AND DISCUSSION

The compounds described (Figure 1) constitute a series of pyrazolo[3,4-*d*]pyrimidines containing in position 1 a *p*-substituted phenyl group and in position 6 a heterocyclic or aryl ring.

The  $^1\text{H}$  NMR signals of the aryl substituent on position 1, the proton 3 and  $\text{NH}_2$  were readily attributed.

The assignment of the remaining protons and the  $^{13}\text{C}$  signals was achieved by concerted application of proton-detected (C,H) 1-bond (HMQC) and long range (HMBC) heteronuclear two-dimensional chemical shift correlation experiments.

The proton and carbon chemical shifts assignments are presented in tables 1 and 2.

## EXPERIMENTAL

$^1\text{H}$  NMR spectra were recorded at 300 MHz and  $^{13}\text{C}$  NMR spectra at 75.4 MHz both on a Varian Unity Plus Spectrometer. The spectra were obtained at 298 K, in 5 mm tubes, using  $\text{DMSO-}d_6$  or acetone-  $d_6$ , with the solvent (residual) peak as internal reference:  $\text{DMSO-}d_6$ :  $\delta$  2.49 ( $^1\text{H}$ ) and  $\delta$  39.5 ( $^{13}\text{C}$ ); acetone-  $d_6$ :  $\delta$  2.05 ( $^1\text{H}$ ) and  $\delta$  29.9 ( $^{13}\text{C}$ ).

$^1\text{H}$  NMR parameters were as follows: spectral width, 4000 Hz; data points, 32 K; pulse width  $45^\circ$ , acquisition time 2.8 s.  $^{13}\text{C}$  NMR parameters were as follows: spectral width, 18850; data points, 64K; pulse width  $45^\circ$ , acquisition time 1.8 s; delay 1 s.

Heteronuclear  $^1\text{H-}^{13}\text{C}$  HMQC and HMBC experiments were carried out using standard procedures. The spectra widths were  $F_1 = 18100$  Hz and  $F_2 = 5000$  Hz. The spectra were collected as 2048 x 256 block data and processed using a sinusoidal multiplication in each dimension. HMQC was optimized for  $^1\text{J}$  ( $^{13}\text{C}$ ,  $^1\text{H} = 140$  Hz) and HMBC for long-range  $^{13}\text{C}$ ,  $^1\text{H}$  coupling constants of 8 Hz.

## Materials

The pyrazolo[3,4-d]pyrimidine derivatives used in this study were prepared in our laboratory [2].

## Acknowledgments

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**Table 1.**  $^1\text{H}$  chemical shifts<sup>a</sup> (multiplicities, coupling constants in Hertz) of pyrazolopyrimidines

	H3	NH <sub>2</sub>	H-2' H6'	H3' H5'	H4'	H2''	H6''	H3''	H5''	H4''
<b>1a</b>	8.36 (s)	7.92(vbrs)	8.32(d, 9.0)	7.59(t, 8.2)	7.35(t, 7.2)		8.47-8.40 (m)		7.51-7.47(m)	7.51-7.47 8m)
<b>2a</b>	8.30 (s)	7.97(vbrs)	8.38(d, 8.7)	7.65(d, 9.0)	-		8.46-8.41(m)		7.54-7.47 (m)	7.54-7.47 (m)
<b>3a</b>	8.38 (s)	7.98(vbrs)	8.31(d, 9.0)	7.78(d, 9.0)	-		8.47-8.39 (m)		7.54-7.47 (m)	7.54-7.47 (m)
<b>1b*</b>	8.28 (s)	7.80(vbrs)	8.20(dt, 7.5, 1.5)	7.51(t, 7.5)	7.17(tt, 7.2, 1.2)		7.35-7.22 (m)		7.35-7.22 (m)	7.35-7.22 (m)
<b>2b*</b>	8.29 (s)	7.85(brs)	8.27(d, 7.0)	7.58(d, 7.0)	-		7.38-7.14 (m)		7.28(t, 7.5)	7.18(t, 7.2)
<b>3b*</b>	8.33 (s)	7.84(vbrs)	8.22(d, 8.7)	7.71(d, 8.7)	-		7.36-7.23 (m)		7.36-7.23 (m)	7.18(tt, 6.9, 1.2)
<b>1c</b>	8.38 (s)	8.14(vbrs)	8.26(dd, 8.7, 1.2)	7.59(t, 8.0)	7.36(tt, 7.5,1.2)	8.66-8.73 (m)	7.96(dt, 7.5, 1.5)	-	7.73(t, 8.8)	8.66-8.73 (m)
<b>2c</b>	8.39 (s)	8.20;8.00(2 brs)	8.32(dd, 7.2, 2.1)	7.65(dd, 6.9, 2.1)	-	8.66-8.64 (m)	7.95(dt, 7.8, 1.5)	-	7.73(t, 7.8)	8.66-8.64 (m)
<b>3c</b>	8.38 (s)	8.18(vbrs)	8.26(d, 8.7)	7.76(d, 8.7)	-	8.72-8.66 (m)	7.95(dt, 7.5, 1.2)	-	7.71(t, 8.1)	8.72-8.66 (m)
<b>1d</b>	8.39 (s)	8.16;7.96(2 brs)	8.30(dd, 8.7, 1.2)	7.52-7.64(m)	7.52-7.64(m)	9.54(d, 2.1)	8.67-8.64 (m)	-	7.36(t, 7.5)	8.67-8.64 (m)
<b>2d</b>	8.39 (s)	8.16;8.00(2 brs)	8.36(d, 9.0)	7.65(d, 9.0)	-	9.50(brs)	8.73-8.65 (m)	-	7.58-7.50 (m)	8.73-8.65 (m)
<b>3d</b>	8.41 (s)	8.17 (brs)	8.31(d, 9.0)	7.79(d, 9.0)	-	9.56(d, 2.1)	8.68(d, 7.0)	-	7.58-7.52 (m)	8.68(d, 7.0)
<b>1e</b>	8.41 (s)	8.18;8.01(2 brs)	8.32-8.21(m)	7.60(tt, 7.5, 2.0)	7.36(tt, 7.2, 1.2)		8.74(brd, 6.0)		8.32-8.21(m)	-
<b>2e</b>	8.42 (s)	8.20;8.00(2 brs)	8.34(d, 9.0)	7.66(d, 6.5)	-		8.74(d, 6.3)		8.28(d, 6.3)	-
<b>3e</b>	8.41 (s)	8.22;8.04(2 brs)	8.29(d, 8.7)	7.77(d, 8.7)	-		8.74(d, 4.7)		8.26(d, 4.8)	-
<b>1f</b>	8.33 (s)	7.93(vbrs)	8.30(dd, 7.5, 1.5)	7.57(t, 7.5)	7.34(t, 7.5)	-	-	7.93 (dd, 3.6, 1.2)	7.69(dd, 5.3, 1.5)	7.18(dd, 5.0, 3.9)

<b>2f</b>	8.34 (s)	7.97(vbrs)	8.33(d, 9.0)	7.62(d, 9.3)	-	-	-	7.94(dd, 3.9, 1.2)	7.70(dd, 5.1, 1.2)	7.18(dd, 5.1, 3.9)
<b>3f**</b>	8.34 (s)	7.37(brs)	8.47(d, 9.0)	7.78(d, 9.0)	-	-	-	8.06(dd, 3.9, 1.2)	7.65(dd, 5.1, 1.2)	7.20(dd, 5.1, 3.9)
<b>1g</b>	8.78 (s)	7.87(brs)	8.92(d, 7.8)	8.03(t, 8.0)	8.40-7.76(m)	-	-	8.40-7.76 (m)	8.25-8.20 (m)	7.10(dd, 3.6, 1.5)
<b>2g</b>	8.35 (s)	8.00(brs)	8.53(d, 9.3)	7.62(d, 9.3)	-	-	-	7.34(dd, 3.3, 0.9)	7.90-7.70 (m)	6.66(dd, 3.3, 1.8)
<b>3g</b>	8.35 (s)	8.00(vbrs)	8.28(d, 9.3)	7.75(d, 9.0)	-	-	-	7.26(dd, 3.3, 0.9)	7.90-7.87 (m)	6.67(dd, 3.3, 1.5)

<sup>a</sup> In ppm from the solvent peak \*CH<sub>2</sub> 4.01; 4.01; 4.02 (for compounds 1b, 2b, 3b, respectively); \*\*Acetone-*d*<sub>6</sub>. Vbrs-very broad singlet

**Table 2.** <sup>13</sup>C chemical shifts of pyrazolopyrimidines

Compound	C-2' C6'	C3' C5'	C4'	C1'	C3	C3a	C4	C6	C7a	C1''	C2''	C6''	C3''	C5''	C4''
<b>1a</b>	120.5	129.3	126.0	139.3	134.3	100.4	158.3	162.0	154.6	138.0	128.2	128.2	128.4	128.4	130.5
<b>2a</b>	121.8	129.2	130.5	137.8	134.6	100.3	158.2	162.0	154.7	138.0	128.1	128.1	128.3	128.3	129.9
<b>3a</b>	122.2	132.2	118.3	137.9	134.7	100.4	158.3	162.1	154.8	138.5	128.4	128.4	128.2	128.2	130.6
<b>1b*</b>	120.4	129.2	126.2 or 4''	139.2	134.1	99.8	158.4	167.7	154.4	139.0	129.1	129.1	128.3	128.3	126.0 or 4'')
<b>2b*</b>	121.6	129.1	129.8	138.0	134.4	99.8	158.3	167.8	154.4	138.8	129.0	129.0	128.2	128.2	126.2
<b>3b*</b>	121.9	132.0	118.0	138.5	134.5	99.8	158.3	167.8	154.5	138.8	129.0	129.0	128.2	128.2	126.2
<b>1c**</b>	120.7	129.4	126.2	139.0	134.3	100.7	158.4	159.8	154.2	111.6	131.5	133.8	139.2	129.9	132.6
<b>2c**</b>	122.0	129.3	130.1	137.8	134.6	100.7	158.3	159.9	154.3	111.6	131.4	133.8	139.0	129.8	132.6
<b>3c**</b>	122.4	132.2	118.8	138.3	134.7	100.7	158.3	159.9	154.3	111.6	131.5	133.9	139.0	129.9	132.6
<b>1d</b>	120.6	129.3	126.2	139.1	134.3	100.6	158.4	160.2	154.2	--	151.1	135.4	133.4	123.6	149.4
<b>2d</b>	122.0	129.3	130.1	137.9	134.7	100.6	158.4	160.4	154.4	--	149.4	135.5	133.3	123.6	151.1
<b>3d</b>	122.2	132.2	118.3	138.3	135.4	100.6	158.3	160.3	154.3	--	151.1	134.7	133.2	123.6	149.4
<b>1e</b>	120.6	129.3	126.2	139.0	134.3	100.9	158.4	159.9	154.1	--	150.2	150.2	122.0	122.0	145.2
<b>2e</b>	122.0	129.3	130.2	137.8	134.7	101.0	158.4	160.0	157.4	--	150.2	150.2	122.0	122.0	145.1
<b>3e</b>	122.3	132.2	118.4	138.2	134.7	101.0	158.4	160.0	154.3	--	150.2	150.2	122.0	122.0	145.1
<b>1f</b>	120.2	129.2	125.9	139.2	134.3	100.1	158.1	158.6	154.0	--	144.0	--	128.5	130.1	128.2

<b>2f</b>	121.8	129.4	128.4	138.1	134.8	100.3	158.3	158.9	154.3	--	143.9	--	130.4	128.8	130.1
<b>3f***</b>	122.9	132.8	119.1	139.9	134.8	101.3	159.3	160.1	155.6	--	145.2	--	130.5	128.7	129.6
<b>1g</b>	121.3	129.7	126.6	140.7	134.2	101.3	156.4	159.4	155.5	--	154.1	--	113.8	145.5	112.7
<b>2g</b>	122.6	129.8	131.3	139.5	134.7	101.3	156.6	159.4	154.0	--	145.6	--	114.0	141.8	112.7
<b>3g</b>	122.0	132.1	118.2	138.4	134.7	100.2	155.3	158.2	154.2	--	152.4	--	113.2	145.2	112.2

<sup>a</sup> In ppm from the solvent peak \*CH<sub>2</sub> 45.5; 45.4; 45.4 (for compounds 1b, 2b, 3b, respectively); \*\* CN 118.8; 118.7; 118.4 (for compounds 1c, 2c, 3c, respectively) \*\*\*Acetone-*d*<sub>6</sub>