Structural Studies of 2-Methyl-7-substituted Pyrazolo[1,5-*a*]pyrimidines

Clarissa P. Frizzo,[a]* Marcos A. P. Martins,[a] Mara R. B. Marzari,[a] Patrick T. Campos,[a] Rosa M. Claramunt,[b] M. Ángeles García,[b] Dionisia Sanz,[b]* Ibon Alkorta,[c] and José Elguero[c]

[a]Núcleo de Química de Heterociclos (NUQUIMHE), Departamento de Química, Universidade Federal de Santa Maria, 97105-900 Santa Maria-RS, Brazil
[b]Departamento de Química Orgánica y Bio-Orgánica, Facultad de Ciencias, UNED, Senda del Rey 9, E-28040 Madrid, Spain
[c]Instituto de Química Médica, CSIC, Juan de la Cierva, 3, E-28006 Madrid, Spain
*E-mail: clarissa.frizzo@mail.ufsm.br or dsanz@ccia.uned.es Additional Supporting Information may be found in the online version of this article.

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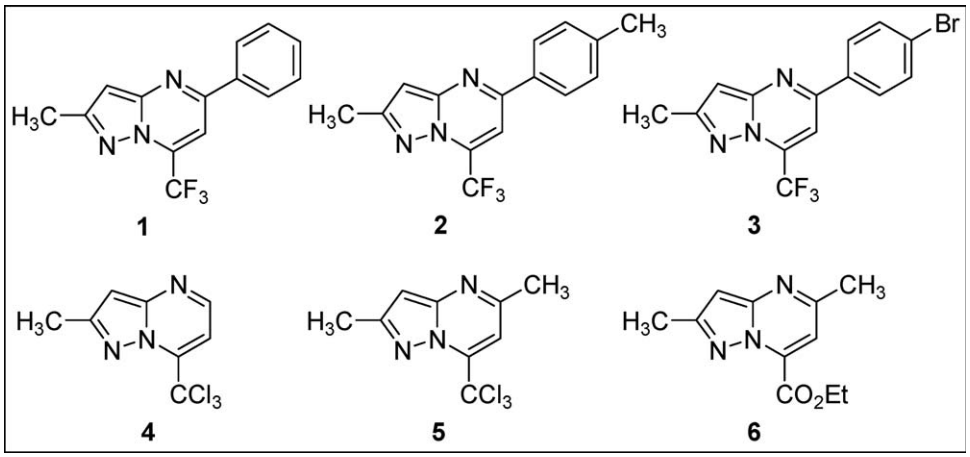
Dedicated to our friend Professor Luis Castedo on the occasion of his 70th birthday.



Six pyrazolo[1,5-*a*]pyrimidines bearing a 7-trifluoromethyl (three compounds), a 7-trichloromethyl (two compounds), and a 7-ethoxycarbonyl (one compound) have been structurally characterized. The new X-ray structures of 2-methyl-5-(*p*-bromophenyl)-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidine (**3**) and 2-methyl-7-trichloromethylpyrazolo[1,5-*a*]pyrimidine (**4**) are reported. The combined use of GIAO/B3LYP/6-311++G(d,p) calculations with NMR spectroscopy in solution and in the solid state allows to establish some general rules that can be useful for characterizing related compounds. Compounds **3** and **4** present in the solid-state interesting intra- and intermolecular halogen bonds.

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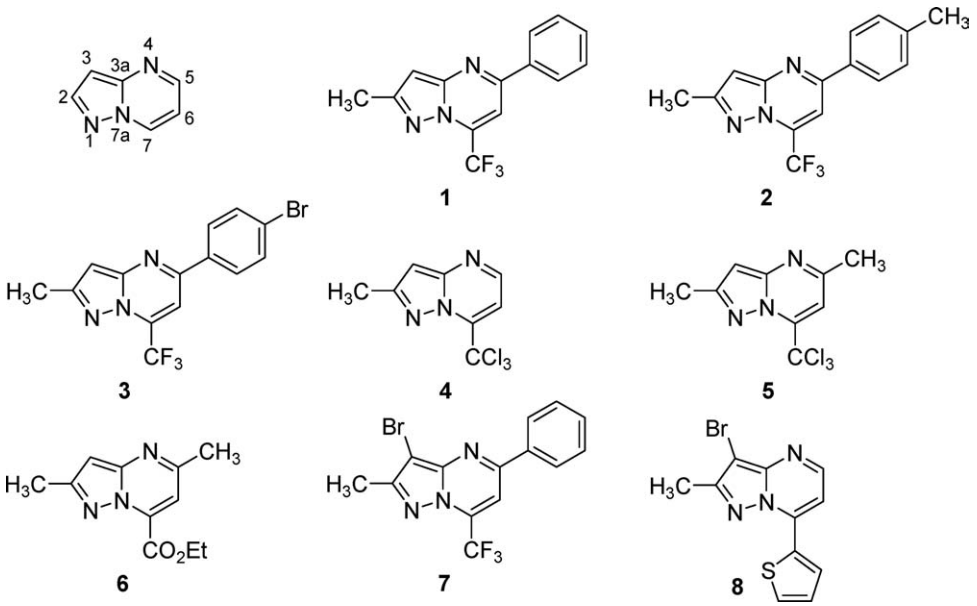
INTRODUCTION

Pyrazolo[1,5-*a*]pyrimidines are purine analogues and as such have useful properties as antimetabolites in purine biochemical reactions. Compounds of this class have attracted wide pharmaceutical interest because their activity as inhibitors of HMG-CoA reductase [1], COX-2 [2], AMP phosphodiesterase [3], KDR kinase [4], and as selective peripheral benzodiazepine receptor ligands [5] as well as antianxiety agents [6]. Recently, other pharmaceutical activities have been reported, for example, as compounds for the treatment of sleep disorders [7], as oncological agents [8], and estrogen receptor ligands [9]. Other activities include hypnotic [10] inhibitors of human cyclin-dependent kinase 2 [11] and high affinity for $GABA_A$ receptors [12].

These examples explain the high interest in variously substituted pyrazolo[1,5-*a*]pyrimidines. As a consequence, the synthesis of these compounds has been approached by different methods [13]. In the literature, there is a large number and variety of such type of fused heterocycles bearing a CF_3 substituent at position 7 [14] but 7-trichloromethyl substituted pyrazolo[1,5-*a*]pyrimidines are much less frequent [15].

Because most studies on these compounds are related to their synthesis or to their biological properties, we decided to devote one paper to a structural study to establish the general patterns for their characterization. The six compounds **1–6** that we have analyzed are reported in Scheme 1 together with their atom numbering.

Scheme 1



RESULTS AND DISCUSSION

The synthesis of the following compounds was already described: 2-methyl-5-phenyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidine (**1**) [14], 2-methyl-5-(*p*-tolyl)-7-trifluoromethylpyrazolo [1,5-*a*]pyrimidine (**2**) [16], 2-methyl-7-trichloromethylpyrazolo[1,5-*a*]pyrimidine (**4**) [17], and 2,5-dimethyl-7-trichloromethylpyrazolo[1,5-*a*]pyrimidine (**5**) [17,18].

Even if 2-methyl-5-(*p*-bromophenyl)-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidine (**3**) is commercially available (from Asinex), it was never described before and our preparation has been included here. Ethyl 2,5-dimethylpyrazolo[1,5-*a*]pyrimidine-7-carboxylate (**6**) is a new compound.

Some of us already reported the X-ray molecular structures of derivatives **2** and **5** [16,18] and those of compounds **7** (a 3-bromo derivative of **1**) and **8** had also been published [14a,17].

Crystallography. In the molecule of the title compounds (Scheme 1 and Fig. 1), the bond lengths are within the related range (Table 1) [19–22]. In particular, the formally single C(3a)-N(4) and C(7)-N(7a) bonds are only slightly longer than the formally double C(2)-N(1) bond, although each of these single bonds is significantly shorter than the formally single C(3a)-N(7a) bond. Similarly, the lengths of the C(2)-C(3) and C(3)-C(3a) bonds, formally single and double bonds, respectively, differ by less than 0.02 Å. These observations, together with the planarity at atom N1, suggest that this heterocyclic system exhibits a degree of naphthalene-type delocalization, involving a peripheral system of 10 π electrons with only modest participation by the cross-

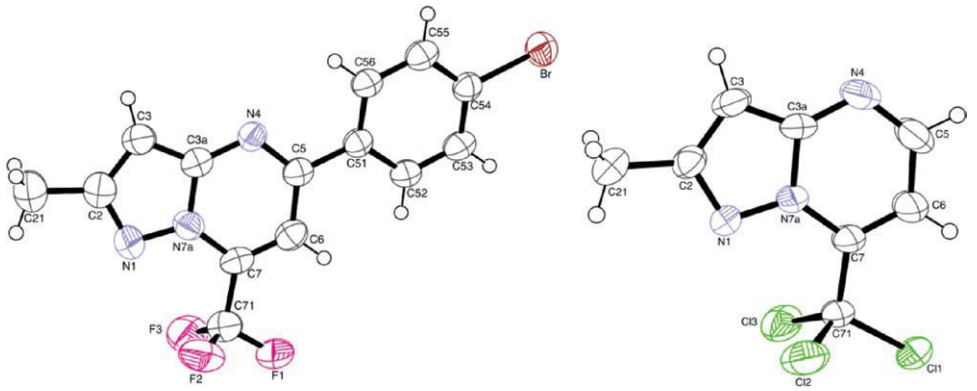


Figure 1. The X-ray molecular structures of compounds **3** and **4** (ORTEP plot, 50% probability for the ellipsoids. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table 1
Selected bond lengths (Å) and bond angles (°).

	3	4
N(7a)-N(1)	1.355(6)	1.351(3)
N(1)-C(2)	1.333(8)	1.343(4)
C(2)-C(3)	1.395(8)	1.386(5)
C(3)-C(3a)	1.376(8)	1.372(5)
C(3a)-N(4)	1.346(7)	1.341(5)
N(4)-C(5)	1.314(7)	1.320(7)
C(5)-C(6)	1.423(8)	1.393(6)
C(6)-C(7)	1.340(8)	1.349(6)
C(7)-N(7a)	1.361(7)	1.367(4)
N(7a)-C(3a)	1.400(8)	1.409(4)
N(7a)-N(1)-C(2)	103.7(5)	104.0(2)
N(1)-C(2)-C(3)	113.1(5)	113.1(3)
C(2)-C(3)-C(3a)	105.7(6)	105.6(3)
C(3)-C(3a)-N(4)	132.8(6)	132.9(3)
C(3a)-N(4)-C(5)	117.5(5)	115.7(3)
N(4)-C(5)-C(6)	122.2(5)	125.0(5)
C(5)-C(6)-C(7)	119.7(6)	119.9(4)
C(6)-C(7)-N(7a)	118.7(5)	116.4(3)
C(7)-N(7a)-N(1)	127.9(5)	126.8(2)
N(7a)-C(3a)-C(3)	104.9(5)	105.5(3)
N(7a)-C(3a)-N(4)	122.3(5)	121.5(3)
N(1)-N(7a)-C(3a)	112.6(5)	111.7(2)
C(7)-N(7a)-C(3a)	119.5(5)	121.4(3)

ring bond (C3a-N7a) [23]. Five-membered pyrazole ring is planar with r.m.s. deviations from the plane of 0.0015 and 0.0025 Å in compounds **3** and **4**, respectively. The six-membered pyrimidine ring is also planar with r.m.s. deviations from the plane of 0.0062 and 0.0131 Å in compounds **3** and **4**, respectively. The angle torsion N(1)-N(7a)-C(3a)-N(4) for compounds **3** and **4** is –179.4(5) and 178.1(17)°, showing that the pyrazole and pyrimidine rings are in the same plane. The geometry of the pyrazolopyrimidine system is similar to that reported in the literature [16].

The molecular structure of compounds **3** and **4** reveals that the intermolecular interactions are related to the nature of substituent. Compound **4** that is not substituted in position 5 of the pyrazolopyrimidine ring shows intra- and intermolecular interactions similar to those found in a related compound with a 5-methyl group [18]: it shows two intramolecular interactions between Cl(2)···N(1) and Cl(3)···N(1) with interatomic distances of 3.097(6) and 3.093(6) Å, respectively. In this molecule, the crystal packing forms an infinite chain along plane *ab* through the intermolecular interaction Cl(1)···N(4) with interatomic distances of 3.115(3) Å ($x+1/2, -y+1, z$) (Fig. 2).

The crystal structure of compound **3** shows that the pyrazolopyrimidine and phenyl rings are almost in the same plane with a C(6)-C(5)-C(51)-C(52) torsion angle of 11.2(8)°. This finding indicates that there is a small π-resonance between the pyrazolopyrimidine system and the aryl ring [18,24,25]. In addition, interesting intermolecular interactions between the halogens atoms as F(1) atom of the trifluoromethyl group of one molecule and the F(3) atom of the trifluoro methyl group of another molecule, with an interatomic distance of 2.899(6) Å ($x+1,y,z$) are observed.

The fluorine atom as halogen bonding has been related to noncovalent interactions, however, while, the Ar-ArF stacking motif formed between nonfluorinated and perfluorinated aromatic rings is rated an important supramolecular synthon [26], the contacts of C-F···H [27,28], C-F···F [29] and C-F···πF [30] type are not yet sufficiently clear [31,32]. On the other hand, the ability of the fluorine–fluorine intermolecular interactions in directing the supramolecular structure of synthons concerning atoms of aliphatic systems is unknown. Thus,

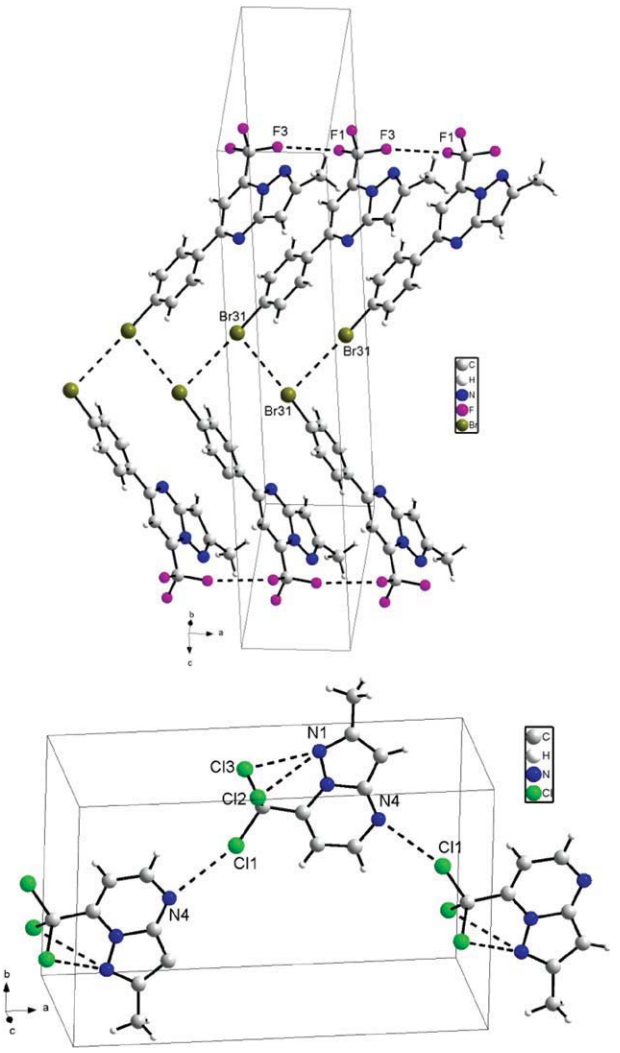


Figure 2. A stereoview of part of the crystal structure of **3** and **4** showing the packing along the *ab* plane. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

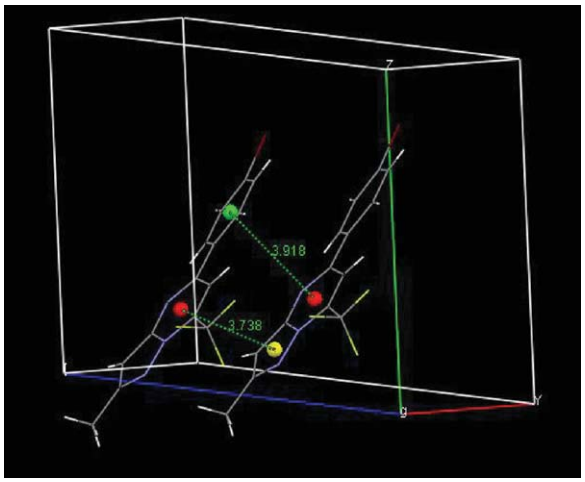


Figure 3. A 3D-view of part of the crystal structure of compound **3** showing π-π interactions between pyrazole···pyrimidine and pyrimidine···phenyl ring-centroid. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

we present here, for the first time, an intermolecular noncovalent interaction between fluorine atoms of aliphatic systems that fix the supramolecular structure of a pyrazolopyrimidine bearing a trifluoromethyl group. The interatomic distance appeared to be less than the sum of van der Waals radii of the atoms involved in the interaction [33].

The bromine atoms are also involved in the molecular packing of compound **3**, which forms an infinite chain along plane *ab* through the intermolecular interaction Br(31)···Br(31) with an interatomic distance of 3.6584(9) Å ($x+1/2,-y+3/2,-z+2$) (Fig. 2). In case of bromine–bromine intermolecular interaction, the interatomic distance also appeared to be less than the sum of van der Waals radii of the atoms involved in the interaction [33]. Recently, we have reported intermolecular Br···Br contacts of about 3.9 Å in crystals of bromopyrazoles [34]. Moreover, pyrazolopyrimidines are interlinked by noncovalent π-π stacking interactions between aromatic rings. As a result, the molecules of **3** and **4** form chains by means of F···F, Br···Br, and Cl···N interactions, respectively, and these chains are themselves linked into sheets by π-π stacking interaction.

In **3**, the weak π-π stacking interactions involve the pyrimidine rings of two adjacent molecules at (x, y, z) and ($1+x$, y, z), where the ring-centroid separation with the pyrazole ring is 3.738 Å; the ring-centroid separation between the pyrimidine and the phenyl is 3.918 Å (Fig. 3). In **4**, the π-π stacking interaction involves the fused heterocyclic rings of the molecules at (x, y, z) and ($1.5-x$, $-y$, $-0.5+z$), with a ring-centroid separation of 3.813 Å between the pyrimidines and of 3.631 Å between the pyrazoles (Fig. 4). These values are similar to those reported in the literature for similar compounds [35].

NMR. We have reported in Tables 2–4 the NMR results concerning compounds **1–6**.

The CPMAS chemical shifts, although less precise (some signals overlap) than those in solution, are linearly related to the DMSO-d_6 values: CPMAS (ppm) = (0.993 ± 0.002) DMSO (ppm), $n = 79$, $R^2 = 0.9997$.This means that the structures in solution (mainly the torsion angles) are similar to those in the solid-state determined by X-ray crystallography.

Computational studies. Initially, we optimized the geometries of pyrazolo[1,5-*a*]pyrimidines **1-6** at the B3LYP/6-31G(d) level verifying that they correspond to the minima (frequency calculations). A further optimization was carried out at the B3LYP/6-311++G(d,p) level and represented the result in Figure 5.

The calculated geometries are very similar (bond distances and bond angles) to those determined experimentally for compounds **2**, **3**, **4**, and **5**; even the sensitive torsion angles are much alike. On these geometries, we calculated [GIAO/B3LYP/6-311++G(d,p)//B3LYP/6-311++ G(d,p)] the absolute shieldings (σ, ppm) and transformed them into chemical shifts (δ, ppm) by means of the following three equations: $\delta^1H = 31.0 - 0.970\ \sigma^1H$; $\delta^{13}C = 175.7 - 0.963\ \sigma^{13}C$; $\delta^{15}N = -152.0 - 0.946\ \sigma^{15}N$ that we have previously devised based on a statistic analysis of many data [36].

In these works, we established that the absolute shieldings corresponding to carbon atoms bearing halogen atoms systematically deviate. In this article and based on the previous reports[36], we have corrected the C-Br atom in *para* position of compound **3** by –20.1

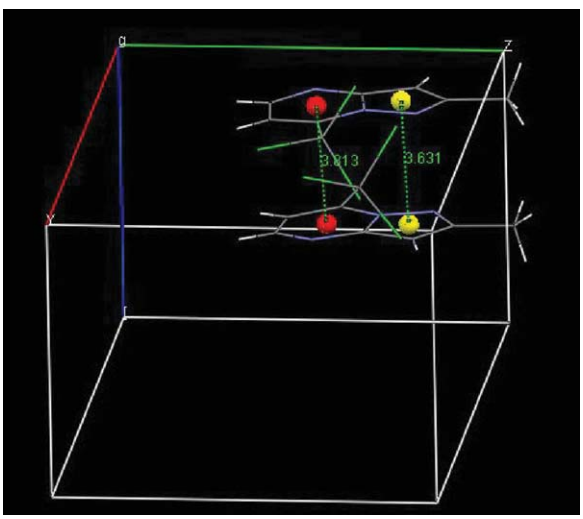


Figure 4. A 3D-view of part of the crystal structure of compound **4** showing π-π interactions between pyrazole···pyrazole and pyrimidine··· pyrimidine ring-centroid. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table 2

^{1}H NMR data in DMSO-d_6 of compounds **1–6** (chemical shifts δ in ppm and coupling constants *J* in Hz).

Nuclei	**1**	**2**	**3**	**4**	**5**	**6**
Me-2	2.47 (s)	2.47 (s)	2.48 (s)	2.52 (s)	2.47(s)	2.40
H-3	6.78 (s)	6.74 (s)	6.80 (s)	6.84 (s)	6.64 (s)	6.49
H-6	8.00 (s)	7.96 (s)	8.04 (s)	7.67 (d)	7.55 (s)	7.20
R-5	7.56 (m, 3H, H3′, H4′, H5′) 8.26 (m, 2H, H2′, H6′)	2.37 (CH_3); 7.34 (m, 2H, H3′,H5′) 8.16 (m, 2H, H2′, H6′)	7.74 (m, 2H,H3′,H5′) 8.22 (m, 2H, H2′, H6′)	8.70 (d), $^3J_{5,6} = 4.5$	2.63 (s,CH_3)	2.53 (s, CH_3)
R-7	–	–	–	–	–	1.35 (t, CH_3); 4.44 (q,CH_2O)

Table 3

^{13}C and ^{15}N NMR data in DMSO-d_6 of compounds **1–6** (chemical shifts δ in ppm and coupling constants *J* in Hz).

Nuclei	**1**	**2**	**3**	**4**	**5**	**6**
N1[a]	−105.1	−105.4	−105.0	−99.8	−101.6	−104.0
C2	156.0	155.9	156.1	154.4	154.1	154.6
C3	97.3	97.1	97.5	97.1	95.9	95.2
C3a	149.5	149.5	149.4	150.4	150.2	149.3
N4[a]	−101.7	−103.4	−101.4	−90.7	−96.2	−96.3
C5	154.6	154.6	153.5	149.0	158.7	158.3
C6	103.6 $^3J_{CF} = 3.8$	103.4 $^3J_{CF} = 4.2$	103.5 $^3J_{CF} = 3.8$	104.7	105.5	108.5
C7	132.4 $^2J_{CF} = 37.7$	132.4 $^2J_{CF} = 36.4$	132.4 $^2J_{CF} = 36.4$	141.1	140.7	134.9
N7a[a]	−172.4	−172.7	−171.9	−171.2	−172.9	−169.5
Me-2	14.3 ^1J= 125.4[b]	14.3 ^1J= 129.9[b]	14.3 ^1J= 128.3[b]	14.5 ^1J= 125.9[b]	14.5 ^1J = 126.8[b]	14.3 ^1J = 129.0[b]
R-5	135.7 (C1′) 127.4 (C2′) 129.0 (C3′) 131.0 (C4′)	133.0 (C1′) 127.3 (C2′) 129.6 (C3′) 141.1 (C4′) 20.9 (CH_3)	134.9 (C1′) 129.3 (C2′) 131.9 (C3′) 124.9 (C4′)	–	24.5 ^1J = 129.7[b]	24.1 ^1J = 125.8[b]
R-7	119. 6 $^1J_{CF} = 273.9$	119. 6 $^1J_{CF} = 275.0$	119.5 $^1J_{CF} = 273.8$	88.7[b]	88.7[b]	160.1 (CO) 62.6 (CH_2) 13.8 (CH_3)

[a] Observed in the (^{1}H-^{15}N) gs-HMBC spectra.
[b] Observed in the (^{1}H-^{13}C) gs-HMBC spectra.

Table 4

^{13}C and ^{15}N CPMAS NMR data of compounds **1–6** (chemical shifts δ in ppm).

Nuclei	**1**	**2**	**3**	**4**	**5**	**6**
N1	−99.7	−100.3	−103.3	−92.5	−99.5	−94.5
C2	157.2	155.4	156.3	153.0	153.4	153.9
C3	92.2	99.2	97.8	95.7	93.6	93.7
C3a	148.2	150.1	149.2	149.1	148.2	151.1
N4	−99.7	−100.3	−103.3	−92.5	−99.5	−94.5
C5	152.0	152.5	153.6 (br)	145.4	156.2	157.6
C6	102.3	99.2	101.0 (br)	104.4	104.9	112.3
C7	131.7	131.8	133.6	141.2	139.0	131.7
N7a	−171.0	−171.7	−170.3	−168.3	−173.3	−166.2
Me-2	13.2	12.9	14.0/13.0	17.4	14.8	14.7
R-5	136.2 (C1′) 128.6 (C2′, C3′, C4′)	131.8 (C1′) 127.5/124.9 (C2′) 131.8/128.7 (C3′) 141.7 (C4′) 20.8 (CH_3)	133.6 (C1′, C3′) 128.5 (C2′, C4′)	–	26.4	24.6
R-7	119.9 (br)	120 (vbr)	120.4 (br)	[a]	[a]	161.8 (CO) 63.8 (CH_2) 14.0 (CH_3)

[a] Not observed.

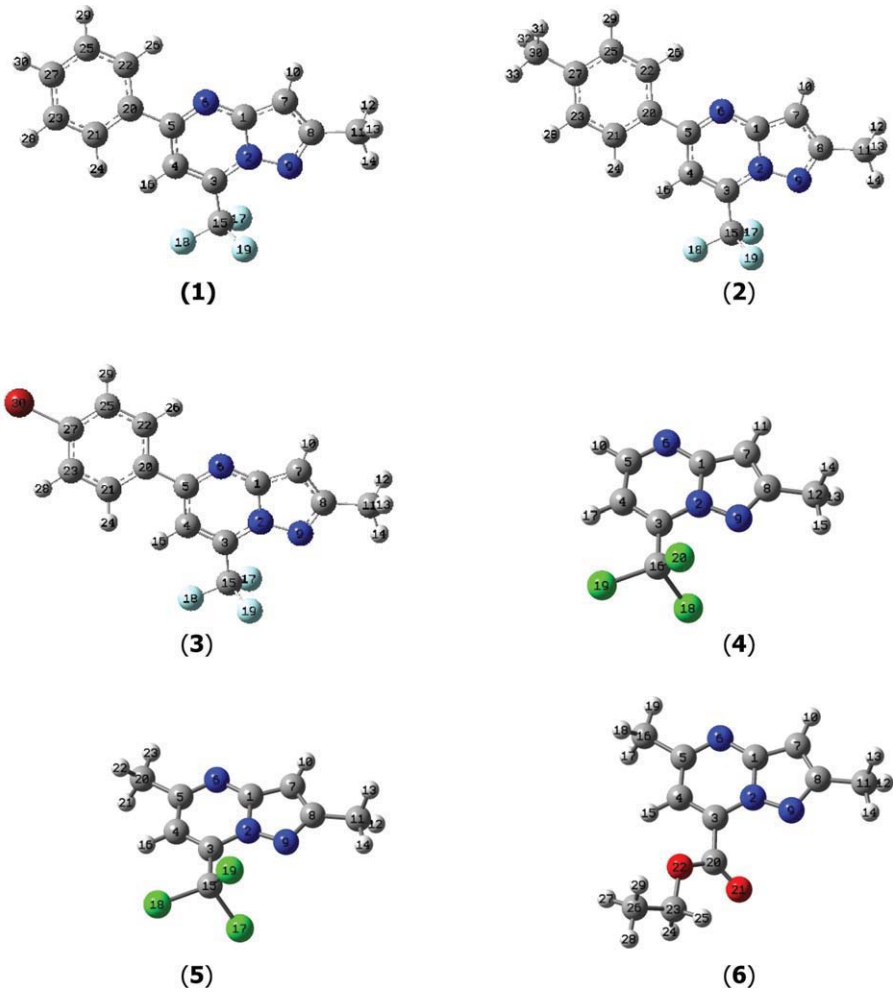


Figure 5. The six optimized structures. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

ppm, the CF_3 atoms of compounds **1**, **2**, and **3** by +2.8 ppm and the CCl_3 atoms of compounds **4** and **5** by –33.3 ppm. With these corrections, we obtained the plot of Figure 6. The trendline corresponds to Exp. DMSO-d_6 (ppm) = (0.999 ± 0.001) Calc. (ppm), n = 114, R^2 = 0.9998. The very good quality of this regression verifies the signals assignment.

In solution, the *ortho* and *meta* signals correspond to averaged values (the same for the H atoms of the methyl groups) but in the solid state the splittings present in compound **2** probably correspond to the absence of free rotation of the *p*-tolyl group at position 5 (Scheme 2).

CONCLUSIONS

The main conclusions of our investigations are:

1. In the gas-phase, theoretical calculations [B3LYP/6-311++G(d,p) optimized geometries and GIAO/B3LYP/6-311++G(d,p)//B3LYP/6-311++G(d,p) abso-

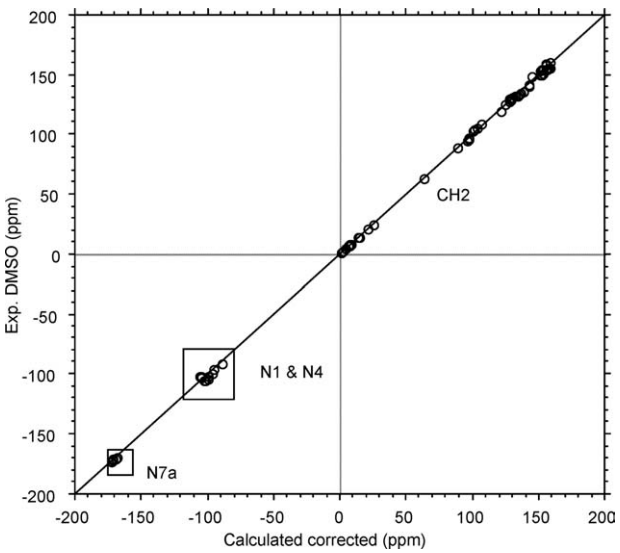
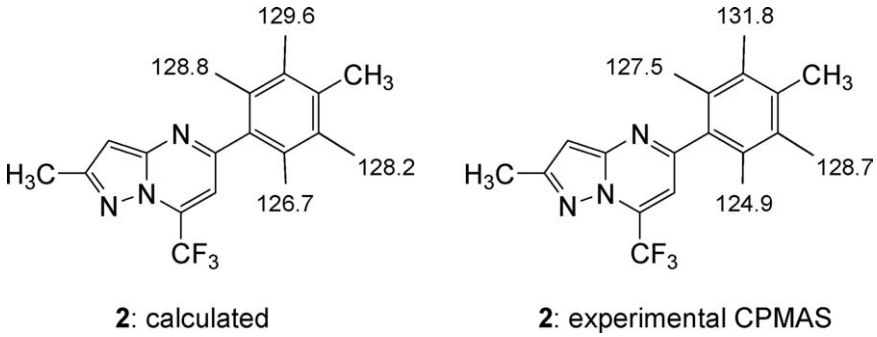


Figure 6. Plot of experimental *vs.* calculated chemical shifts.

Scheme 2



2: calculated **2**: experimental CPMAS

lute shieldings] of each monomer account well for the properties in condensed phases: solution (NMR) and solid state (NMR and crystallography).

2. In DMSO-d6 solution, NMR results are consistent with the proposed structures providing chemical shifts (in brackets mean values in ppm) useful for characterizing new series of pyrazolo[1,5-a]pyrimidines: δN7a(−172) < δN1(−103.5) < δN4(−98); δC2-Me(155) ≈ δC5-Ar(154) > δC7(135) > δC6(105); δC2-Me(155) > δC5-H(149) > δC7(135) > δC6(105); δC5-Me(158) > δC2-Me(155) > δC7(135) > δC6(105). The CPMAS data show similar trends, meaning that the structures in solution are close to those in the solid state.
3. X-Ray crystallographic studies show interesting halogen interactions (X...X, X...N), both the F···F at 2.90 Å and the Br...Br at 3.66 Å for 3 and the Cl...N at 3.115 Å for 4, of great importance in crystal engineering [37,38].

EXPERIMENTAL

General. 3-Amino-5-methyl-1*H*-pyrazole was obtained commercially from Aldrich (ACS grade) and used without further purification. The heterocyclic precursors were synthesized in accordance with methodologies developed in our laboratory [37]. The crystals used for the data collection were obtained by crystallization of compounds from hexane followed by slow evaporation at room temperature. All solvents (Merck) were dried in accordance with procedures carried out in our laboratory [38]. Melting points were determined on a Microquimica MQAPF–302 melting point apparatus.

2-Methyl-7-trifluoromethyl-5-(p-bromophenyl)pyrazolo[1,5-a]pyrimidine (3). A solution of 3-amino-5-methyl-1*H*-pyrazole (1.0 mmol) in acetic acid (5 mL) was added to a stirred solution of 4-(*p*-bromophenyl)-1,1,1-trifluoro-4-methoxy-3-buten-2-one (1.0 mmol) in acetic acid (5 mL). The mixture was stirred for 16 h and after the reaction time the product was extracted with chloroform (3 × 10 mL), washed with distilled water (3 × 10 mL), and dried on magnesium sulfate. The solvent was removed in a rotary evaporator and compound **3** was purified by recrystallization from hexane, and was obtained in 86% yield. M.p. 171–173°C.

Ethyl 2,5-dimethylpyrazolo[1,5-a]pyrimidine-7-carboxylate (6). A solution of 3-amino-5-methyl-1*H*-pyrazole (1.0 mmol) in acetic acid (5 mL) was added to a stirred solution of ethyl 4-methoxy-2-oxo-3-pentenoate (1.0 mmol) in acetic acid (5 mL). The mixture was stirred for 16 h and after the reaction time, the product was extracted with chloroform (3 × 10 mL), washed with distilled water (3 × 10 mL), and dried on magnesium sulfate. The solvent was removed in a rotary evaporator and the product was purified by crystallization from hexane, and was obtained in 91% yield. M.p. 74–76°C.

Crystallography. The diffraction measurements were carried out by graphite-monochromated Mo Kα radiation with λ = 0.71073 Å on a Bruker SMART CCD diffractometer [39]. The structures were solved with direct methods using the SHELXS-97 program and refined on *F2* by full-matrix least-squares with the SHELXL97 package [40]. Absorption correction was performed by the Gaussian method [41]. Anisotropic displacement parameters for nonhydrogen atoms were applied. The hydrogen atoms were placed at calculated positions with 0.96 Å (methyl CH3), 0.97 Å (methylene CH2), 0.98 Å (methyne CH), 0.93 Å (aromatic CH) and 0.82 Å (OH) using a riding model. Hydrogen isotropic thermal parameters were kept equal to *U*iso(H) = *xU*eq (carrier C atom), with $x = 1.5$ for methyl groups and $x = 1.2$ otherwise. The valence angles C—C—H and H—C—H of methyl groups were set to 109.5° and H atoms were allowed to rotate around the C—C bond. Molecular graphics were prepared using ORTEP for Windows [42]. The crystal data and details concerning data collection and structure refinement are given in Table 5.

Crystallographic data for structures have been deposited with the Cambridge Crystallographic Data Center (2-methyl-7-trichloromethylpyrazolo[1,5-*a*]pyrimidine CCDC 734995; 2-methyl-5-(*p*-bromophenyl)-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidine CCDC 734998). Copies of the data can be obtained, free of charge, on application to CCDC 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

NMR measurements. ^{1}H (400.13 MHz), ^{13}C (100.61 MHz), and ^{15}N (40.56 MHz) spectra in solution were obtained with a Bruker DRX-400 instrument, with a 5-mm inverse-detection H-X probe equipped with a gradient coil, at 300 K. Chemical shifts (δ in ppm) are given from solvent DMSO-d_6 2.49 for ^{1}H and 39.5 for ^{13}C, external nitromethane (0.00) for ^{15}N NMR. Coupling constants (*J* in Hz) are accurate to ± 0.2

Table 5

Crystal data and structure refinement for compounds **4** and **3**.

	3	**4**
Formula	C_{14} H_9 Br F_3 N_3	C_8 H_6 Cl_3 N_3
Mr	356.15	250.51
CCDC	734,998	734,995
Temperature (K)	293 (2)	296 (2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Orthorhombic	Orthorhombic
Space Group	$P2_12_12_1$	$Pca2_1$
Unit cell parameters		
a (Å)	4.7574 (7)	15.307 (2)
b (Å)	11.0476 (17)	9.4510 (14)
c (Å)	26.177 (5)	6.9446 (10)
α (°)	90	90
β (°)	90	90
γ (°)	90	90
V (Å^3)	1375.8 (4)	1004.7 (3)
Z	4	4
Density (calculated) (g/cm^3)	1.719	1.656
Absorption coefficient (mm^{-1})	3.018	0.871
F (000)	704	504
Crystal size (mm)	0.758 × 0.088 × 0.05	0.35 × 0.25 × 0.13
θ range for data collection (°)	2.00 to 27.36	2.15 to 28.33
h,k,l range	$-6 \leq h \leq 6$	$-20 \leq h \leq 20$
	$-14 \leq k \leq 14$	$-12 \leq k \leq 11$
	$-33 \leq l \leq 33$	$-5 \leq l \leq 9$
T_{max}/T_{min}	0.9330/0.5595	0.8951/0.7502
Reflections collected	13211	9557
Independent reflections	3093 [R(int) = 0.0623]	2091 [R(int) = 0.0396]
Data/restraints/parameters	3093/0/190	2091/1/127
Absorption correction	Gaussian	Gaussian
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Final R indices [I>2σ(I)]	$R1 = 0.0441$, w$R2 = 0.0991$	$R1 = 0.0459$, w$R2 = 0.1196$
R indices (all data)	$R1 = 0.0905$, w$R2 = 0.1262$	$R1 = 0.0682$, w$R2 = 0.1342$
Goodness of fit on F^2	1.008	1.052
Largest diff. peak and hole (eÅ^{-3})	0.280 and –0.391	0.466 and –0.291

Hz for ^{1}H and ± 0.6 Hz for ^{13}C and ^{15}N. 2D-inverse-proton-detected heteronuclear-shift-correlation spectra (^{1}H-^{13}C) gs-HMQC, (^{1}H-^{13}C) gs-HMBC and (^{1}H-^{15}N) gs-HMBC were acquired and processed using standard pulse sequences [43]. Solid-state ^{13}C (100.73 MHz) and ^{15}N (40.60 MHz) CPMAS-NMR spectra have been obtained with a Bruker WB-400 spectrometer at 300 K with a wide-bore 4-mm DVT probehead. Samples were carefully packed in ZrO_2 rotors. ^{13}C spectra were originally referenced to a glycine sample and then the chemical shifts were recalculated to the Me_4Si [for the carbonyl atom δ (glycine) = 176.1 ppm] and ^{15}N spectra to $^{15}NH_4Cl$ and then converted to nitromethane scale using the relationship: δ ^{15}N ($MeNO_2$) = δ ^{15}N(NH_4Cl)-338.1 ppm. Typical acquisition parameters for ^{13}C CPMAS were: spectral width, 40 kHz; recycle delay, 5–60 s; acquisition time, 30 ms; contact time, 2–4 ms; and spin rate, 12 kHz. In order to distinguish protonated and unprotonated carbon atoms, the NQS (Non-Quaternary Suppression) experiment by conventional cross-polarization was recorded; before the acquisition the decoupler is switched off for a very short time of 25 (s. Typical acquisition parameters for ^{15}N CPMAS were: spectral width, 40 kHz; recycle delay, 5–60 s; acquisition time, 35 ms; contact time, 7 ms; and spin rate, 6 kHz [44].

Computational details. The optimization of the geometries of the structures were first carried out at the B3LYP/6-31G(d) and afterwards reoptimized at the B3LYP/6-311++G(d,p) computational level [45–50] within the Gaussian-03 package [51]. Frequency calculations at the first level were carried out to confirm that the obtained structures correspond to energy minima. GIAO absolute shieldings [52,53] were calculated on the B3LYP/6-311++G(d,p) optimized geometries.

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