

Facile Preparation of Polytopic Azoles: Synthesis, Characterization, and X-ray Powder Diffraction Studies of 1,4-Bis(pyrazol-4-yl)- and 1,4-Bis(tetrazol-5-yl)benzene

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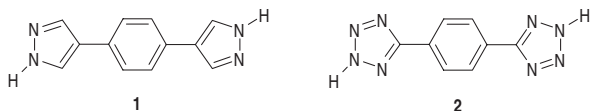
Two polytopic azoles, 1,4-bis(pyrazol-4-yl)benzene and 1,4-bis(tetrazol-5-yl)benzene, were prepared in sizable amounts by high yield syntheses employing, in mild conditions, cheap reactants and, whenever possible, aqueous solutions. The two species were characterized by ^1H and ^{13}C NMR spectroscopy and by thermal analyses, the latter evidencing their high chemical and thermal stability. X-ray powder diffraction methods disclosed their non isomorphous crystal structures, in which individual molecules interact via hydrogen bonds to form two-dimensional sheets.

Polyazoles have recently witnessed a blooming interest, due to their application in the pharmaceutical industry (as antifungal, antiprotozoal, and antihypertensive agents), as well as flame retardants¹ or corrosion inhibitors in a number of industrial processes, along with chemical mechanical planarization of semiconductors² and antifreeze formulations.³ Moreover, their deprotonated forms have been extensively used in the formation of porous coordination polymers (PCP's) capable of selective gas adsorption and sensing,⁴ or of spin crossover for high-tech applications.⁵ Therefore, the quest for novel and accessible routes to polyazoles, employing cheap reactants in mild and environmentally friendly conditions, has been widely pursued, making these species readily, and widely, available.

In the realm of PCP's, there appear very promising those polyazoles whose length can be modulated by a "linear" spacer separating the heterocycles: indeed, they can tune the distance between the polyazole-bridged transition-metal ions, thus allowing the optimization of the PCP's (electrical, magnetic, catalytic, sorptive) functional properties, as it has already been properly shown in two seminal papers by Long and co-workers.⁶

With the goal of preparing 1,4-bis(azoly)benzenes to be potentially exploited as long spacers in polynuclear coordination complexes and, possibly, nanostructured PCP's,⁶ we tailored the syntheses of 1,4-bis(pyrazol-4-yl)benzene⁷ (H_2bpb , **1**) and 1,4-bis(tetrazol-5-yl)benzene (H_2btb , **2**; see Scheme 1).⁸ The pure, crystalline phases, isolated in sizeable amounts, were fully characterized by ^1H and ^{13}C NMR spectroscopy, thermal (TG and DSC) analyses and, above all, ab initio X-ray powder diffraction (XRPD) methods.

1 could be derived by heterocyclization of *p*-phenylene-

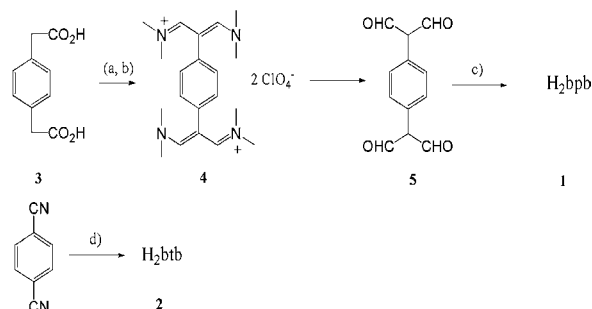


Scheme 1. Schematic drawing of the 1,4-bis(pyrazol-4-yl)-benzene (**1**, left) and 1,4-bis(tetrazol-5-yl)benzene (**2**, right) molecules.

bis(malondialdehyde) (**5**)⁹ (or its synthetic equivalents) with hydrazine. Within this context, vinamidinium salts [readily accessible through a Vilsmeier–Haack–Arnold (VHA) formylation¹⁰] have also been successfully utilized to construct substituted pyrazoles.¹¹ It is of interest to note that very few 4-aryl-substituted pyrazoles have been prepared by such procedure. Such considerations lead to the generation of the bis(vinamidinium) salt **4**⁸ as one possible intermediate (Scheme 2). Thus, **1** was best prepared from commercially available *p*-phenylenediacetic acid (**3**) by a sequence of reactions commencing with the VHA reaction (POCl_3 , DMF, 90°C , 11 h; overnight at rt) followed by quenching (H_2O , rt) and metathesis with NaClO_4 in water. Tackling the necessity of isolating the rather unstable tetraldehyde **5**, the resulting bis(perchlorate) **4** was directly reacted with hydrazine monohydrate (refluxing EtOH, 1 h) to provide the required **1** (76% over two steps). Its D_{2h} symmetry was clearly evident in its greatly simplified ^1H NMR spectrum and four-line ^{13}C NMR spectrum.⁸

Commercially available terephthalonitrile could be converted to the bistetrazole **2**, either by cycloaddition with sodium azide in the presence of triethylammonium chloride (refluxing toluene)¹² or, more preferably, by reacting it with stoichiometric NaN_3 in the presence of ZnBr_2 in refluxing water.¹³ Utilization of the Demko Sharpless protocol allowed for the conversion of terephthalonitrile to the ligand **2** in 75% yield (and 36 h) without need of organic solvents and large excess of sodium azide.

Interestingly, also the use of stoichiometric amounts of ZnCl_2 allows the recovery of **2**, although in slightly lower yield (ca. 60%). During the syntheses in aqueous environment, the already known hydrated form of 1,4-bis(tetrazol-5-yl)benzene, $\mathbf{2}\cdot\text{H}_2\text{O}$,¹⁴ is formed (XRPD and IR evidences). $\mathbf{2}\cdot\text{H}_2\text{O}$ is quantitatively transformed into **2** by heating it at 90°C overnight in an oven (XRPD and IR evidences). Differently, when toluene is employed as a solvent, the anhydrous form **2** is directly recovered.



Scheme 2. a) POCl_3 , DMF, 90°C , 11 h then H_2O ; b) NaClO_4 , H_2O c) N_2H_4 , H_2O , EtOH reflux 1 h; d) NaN_3 , ZnBr_2 , reflux 36 h.

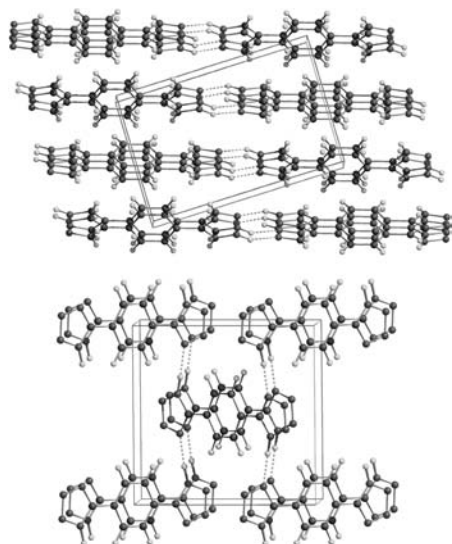


Figure 1. Crystal packing of **1** (top) and **2** (bottom) viewed approximately down [010] and [100], respectively. NH...N interactions drawn as dashed lines.

Despite sharing the same space group symmetry, crystals of **1** and **2** are not isomorphous.¹⁵ In both cases, the molecules, lying on crystallographic inversion centres, generate 2-D sheets through NH...N hydrogen-bond interactions which, however, develop in two rather different manners (Figure 1): i) through relatively weak contacts (N...N 3.05 Å) in **1**, where the molecules wind up the crystallographic 2_1 screw axis aligned with the *b* cell axis; ii) through stronger interactions (N...N 2.77 Å) in **2**, where chains of H-bonded “internal” nitrogen atoms can be envisaged, linking molecules which are related by the crystallographic *c* glide plane. This last motif closely resembles that found in the α and β polymorphs of the copper(I) pyrazolate polymer, where the hydrogen-bond interactions of **2** are formally replaced by a (nearly linear) covalent NCuN link.¹⁶ Interestingly, also **2**·H₂O crystallizes in the same space group, yet with markedly different unit cell axes and overall structure: indeed, in its extended 2-D sheets, no direct NH...N contacts are present, and the hydrogen-bond interactions between adjacent moieties are mediated by water molecules (with the strongest one involving one internal nitrogen atom, as in the anhydrous counterpart).

Notably, the extended net of hydrogen-bond interactions in **1** and **2** can be considered responsible for their very high thermal and chemical inertness and their very limited solubility. Finally, in all the cases, the torsion angles about the (formally) single CC bond are very small, and account for 9.2(3), 0.3(3), and 6.2° in **1**, **2**, and **2**·H₂O, respectively (maintaining a largely delocalized ring system).

Simultaneous TG and DSC thermal analyses indicated that both **1** and **2** crystal phases possess a rather high thermal stability: the former is stable up to ca. 360 °C, where sublimation, in air and at ambient pressure, occurs (apparently without chemical decomposition); the latter, despite of its denser structure, possesses a lower inertness (decomposing above 290 °C), probably due to the intrinsically less stable tetrazolyl, vs. pyrazolyl, heterocyclic rings ($\Delta H_{f(\text{gas})} = 320.5$ vs. 750.6 kJ mol⁻¹, respectively, for tetrazole and pyrazole).

Thermodiffraction measurements performed in situ on

powders of **2**·H₂O showed that its transformation to **2** is not fast nor simple. Indeed, at about 90 °C, a phase change to a low crystallinity material is observed, indicating that the reaction (as expected) is not topotactic and requires a heavy reorganization of the molecules within the crystal lattice.

Work can be anticipated in the direction of coupling these polyazoles with transition-metal ions, aiming at the formation of homoleptic species of $M_x(\text{bpb})$ or $M_x(\text{btb})$ formulation ($x = 1, 2$, and $2/3$). The resulting materials are expected to be chemically and thermally stable, paralleling the vast class of terephthalate-based metal–organic frameworks, which exhibit interesting functional properties ranging from gas storage and separation¹⁷ to catalytic activity¹⁸ or giant hysteretic (magnetic) effects.¹⁹

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- 15 The crystallographic data reported in this manuscript have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications Nos. 687662 and 687663. Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk). A summary of crystal data is also reported as Supporting Information (see Ref. 8).
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