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Cooperative association of pyrazoles and phenols: A versatile binary system†

Ishtvan Boldog,[a] Eduard B. Rusanov,[a] Joachim Sieler[b] and Konstantin V. Domasevitch*[a]

[a] *Inorganic Chemistry Department, Kiev University, Volodimirska Street 64, Kiev 01033, Ukraine. E-mail: dk@anorgchemie.univ.kiev.ua*
[b] *Institut für Anorganische Chemie, Universität Leipzig, Linnéstraße 3, D-04103, Leipzig, Deutschland*

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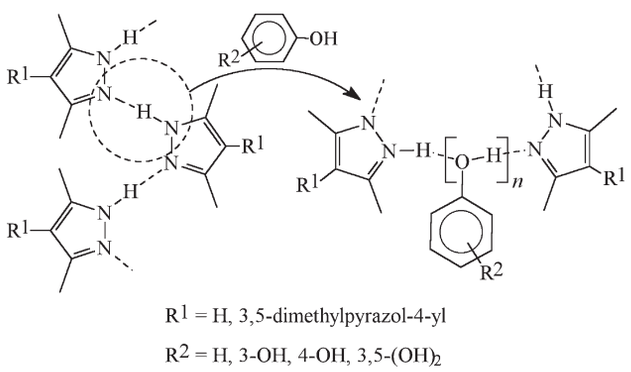
The ability of self-complementary H-bond donor/acceptor phenol (OH/O) and pyrazole (NH/N) molecules for cooperative association allowed the developing of a range of binary compounds, in which the molecular counterparts are integrated by hydrogen bonding. Complexes involving either monofunctional 3,5-dimethylpyrazole and phenol and polyfunctional 3,3′,5,5′-tetramethyl-4,4′-bipyrazole, hydroquinone and phloroglucinol are based on mixed phenol–pyrazole chains. They reveal common features allowing high level of control over the entire connectivity and dimensionality. Unprecedented NH···π pyrazole hydrogen bonding was essential for the structure of the resorcinol complex.

Introduction

Developing of multicomponent organic systems is an outlook of solid state organic chemistry[1] that offers a significant potential for construction of materials in which single molecular functionalities are rationally integrated and may also present a major contribution to the better understanding of complex supramolecular relations, dynamics and reactivity in chemistry and biology.[2,3] Proper handling of binary organic/organic relations is important also from a synthetic perspective as the existence of stable and concomitant molecular combinations can significantly complicate or, *vice versa*, simplify many isolation and purification strategies.

The ability of certain complementary donor and acceptor organic molecules to afford binary complexes is well known and widely used for supramolecular synthesis.[1–4] A special, highly illustrative example of a binary organic system may arise if one achieves a cooperative association of different self-complementary molecules, *i.e.* the species combining both donor and acceptor binding sites in equal proportions.[5] In this case incorporation of an extra component does not effect an alteration of a given connectivity (for example, topology of intermolecular hydrogen bonding) and it assumes the existence of the classes of binary compounds based upon the complementary combination of the H-bonding donating/accepting sites: $\{[-X^1H-]\} \otimes \{[-X^2H-]\} \Rightarrow \{[-X^1H-]_n[-X^2H-]_m\}$, a meccano-like principle (Scheme 1).[6] Thus both the components possess a parity of structural functions and hence an equally rich and overlapping potential from the design perspective for the motif propagation and control over the structure dimensionality. Herein we report a family of binary compounds formed by the most paradigmatic and general self-complementary species, pyrazoles[7,8] and phenols,[9,10] that combine NH/N and OH/O hydrogen bond donor/acceptor functionalities.



Scheme 1 Illustration of how an additional self-complementary component can be incorporated into the structure without alteration of the connectivity.

Results and discussion

The binary composite $(pyrazole)_n(phenol)_m$ consists of molecular components with maximum one/one H-bond donor/acceptor; therefore a completely interconnected structure may contain cyclic or 1D chain motifs. Control over the structure dimensionality is feasible by evolution from mono- to polyfunctional species considering either pyrazole and phenol counterparts. As an especially suitable bipyrazole tecton we have examined 3,3′,5,5′-tetramethyl-4,4′-bipyrazole Me_4bpz. This conformationally flexible molecule is easily adaptable to the crystal environment demands and also minimizes effects of the π···π stacking interactions owing to its non-planar structure.[11] Me_4bpz and its monofuctional analogue 3,5-dimethylpyrazole Me_2pz easily co-crystallize with a representative range of species: phenol, hydroquinone, resorcinol and phloroglucinol, yielding binary molecular complexes by a set of DH···A (D,A = O,N) interactions.

The simplest binary composite sustained with two monofunctional tectons, $Me_2pz{\cdot}PhOH$ **1**, affords a 1D zig-zag chain of alternating components and it is a prototype for cooperative assembly of pyrazoles and phenols (Fig. 1, A). The geometry

† Electronic supplementary information (ESI) available: Details for crystal structure determination and refinement and geometry of hydrogen bonding in structures. See http://www.rsc.org/suppdata/nj/b3/b317104c/

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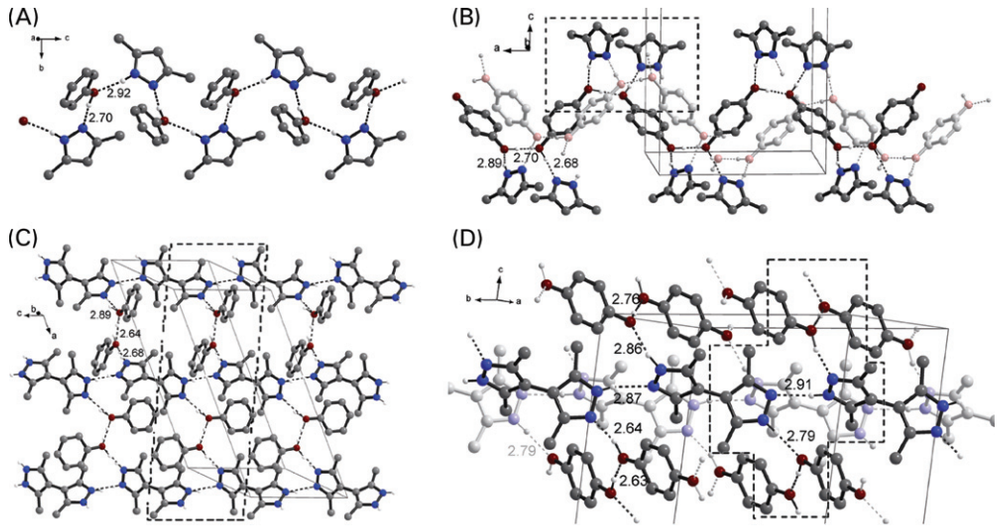

Fig. 1 Crystal structures of $Me_2pz{\cdot}PhOH$ **1** (A), $Me_2pz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **2** (B), $Me_4bpz{\cdot}2PhOH$ **3** (C), $Me_4bpz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **4** (D). **2**–**4** can be viewed as propagation of H-bonded pyrazole–phenol motif of **1** (marked with dotted borders) by means of doubling of the molecular functionality. Numeric parameters here and below indicate D···A (D,A = N,O) separations of the hydrogen bonding.

of the intermolecular bonding is characteristic for hydrogen bonds of the types NH···O (O···N 2.916(3) Å ∠NH···O 173(3)°) and OH···N (O···N 2.700(3) Å, ∠OH···N 170(2)°), the latter were observed for adducts of phenols and pyridines.[12]

The binary complex of bifunctional pyrazole $Me_4bpz{\cdot}2PhOH$ **3** possesses the same pyrazole/phenol ratio and its structure can be thought as a result of simple propagation of the array in a second direction. Partial rearrangement of the chain motif yields $AA(BBAA)_n$ connectivity mode that enables the satisfaction of steric demands by longer $(PhOH)_2$ bridge (O···O 2.647(3) Å). In that sense, the structure **3** is also built up from zigzag chains, but with doubled $[(pyrazole)_2(PhOH)_2]$ unique fragment. Chains are connected by means of carbon–carbon bonds within a frame of bipyrazole molecules in 2D puckered sheets (Fig. 1c) that are separated at $\frac{1}{2}b$ (*ca.* 7.3 Å) by protruding phenyl groups. The dimensionality of the architecture apparently grows by one after two pyrazole functions are collected within a single molecule. X-Ray data clearly suggest the possibility of solid state tautomerism of the compound as all NH and OH protons were disordered over two possible positions, which is a sign for solid state proton transfer. Both phenomena are typical for cyclic pyrazole patterns, in contrast to catameric structures where the hydrogen atoms in NH···N bridges are ordered and immobile.[13] Inclusion of the strongly binding phenolic O–H group enhances the strength of the partial bonding contributors. This effect, known as σ-bond cooperativity or polarization enhanced hydrogen bonding,[14] can in principle promote the rather promising proton dynamics in catamer patterns: NH···OH···N to N···HO···HN, and thought as a design tool.

Considering the parity of structural roles of pyrazole and phenol counterparts, doubling of the phenolic function has the same impact for the motif expansion. $Me_2pz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **2** and $Me_4bpz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **4** comprising hydroquinone as the phenolic component are an evolution of parent adducts **1** and **3**. The connection is most clear in the 3D structure of **4**, where $[C_6H_4(OH)_2]_2$ bridges, functionally analogous to $[PhOH]_2$ bridges in **3**, are the part of the H-bonded hydroquinone thread that fuses the pack of 2D sheets, similar to the main topology of **3** (Fig. 1D). In other words, two protruding phenyl groups of prototypal 2D sheets are coinciding by means of the common ring of hydroquinone that increases the dimensionality of the structure (2D → 3D). 2D structure **2** is composed from extended chains of $[(Me_2pz)\text{-}(C_6H_4(OH)_2)_2]_n$ those are resemblant to the $[(Me_2pz)(PhOH)]_n$ chains in **1**, fused by the analogous $[p\text{-}C_6H_4(OH)_2]_n$ thread (Fig. 1B) (O···O 2.763(3) Å, ∠OH···O 168(3)°). A similar feature of both structures of **2** and **4** is the important role of $[p\text{-}C_6H_4(OH)_2]_n$ thread that runs angle-wise to the basic phenol–pyrazole chain and the *para*-disposition of OH functionalities can be thought as a main reason of such inheritance. The only previously known catameric phenol/pyrazole adduct, $Me_2pz{\cdot}$1,1-bis(*p*-hydroxyphenyl)cyclohexane[15] is an analogue of $Me_2pz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **2** in the sense of functionalities ratio. Both structures comprise clearly related 2D sheets consisting of $[Me_2pz{\cdot}R(OH)_2]_n$ chains. It is rather surprising that self-complementary 4-(*p*-hydroxyphenyl)-3,5-dimethylpyrazole displays no direct interaction between principal pyrazole and phenol functions in the crystal.[16]

The above observations are applicable also for the more complicated binary complex $2Me_4bpz{\cdot}(1,3,5\text{-}C_6H_3(OH)_3){\cdot}H_2O$ **6**, containing trifunctional phloroglucinol as the phenolic component: phloroglucinol molecules form helices that are encompassed by eight characteristic $(Me_4bpz)_n$ threads (Fig. 2). Such a high number of neighboring threads is provided by water molecules that extend the H-bonding bridge for two of these threads. An extra hydrogen bond donating OH (H_2O) group is not involved in the entire strong H-bonding linkage but unprecedentedly utilizes a neighboring pyrazole cycle as a π-acceptor system (Fig. 3) thus uniting two bipyrazole threads. Such a π-accepting function is also known for imidazole compounds.[17] Interconnection of pyrazole and OH functions in a $AA(BBAA)_n$ fashion yields a large cycle involving eight pyrazole, six phenol and two water molecules. In contrast, the structure of the resorcinol complex $Me_4bpz{\cdot}(m\text{-}C_6H_4(OH)_2)$ **5** displays no homomolecular association and in this sense it does not follow the general scheme. It is based upon cyclic H-bonded fragments with two phenol and two pyrazole molecules that afford a puckered 2D sheet (Fig. 4). Steric demands of the packing are essential for the structure and they result in surprising "π-confusion" of the connectivity involving NH···π bonding pyrazole/resorcinol, instead of the anticipated NH···O scheme. This clear and illustrative π-hydrogen bonding pattern is unique for pyrazoles, despite of its significant role for related heterocycles,[2,18] particularly for pyrrole.[19] In **5** the NH···π interacting pyrazole and resorcinol cycles are actually orthogonal (dihedral angle 102.6°) and the distance between N(2) and the plane of the resorcinol molecule, 3.27 Å, is shorter than the closest N···C contact at 3.38 Å.

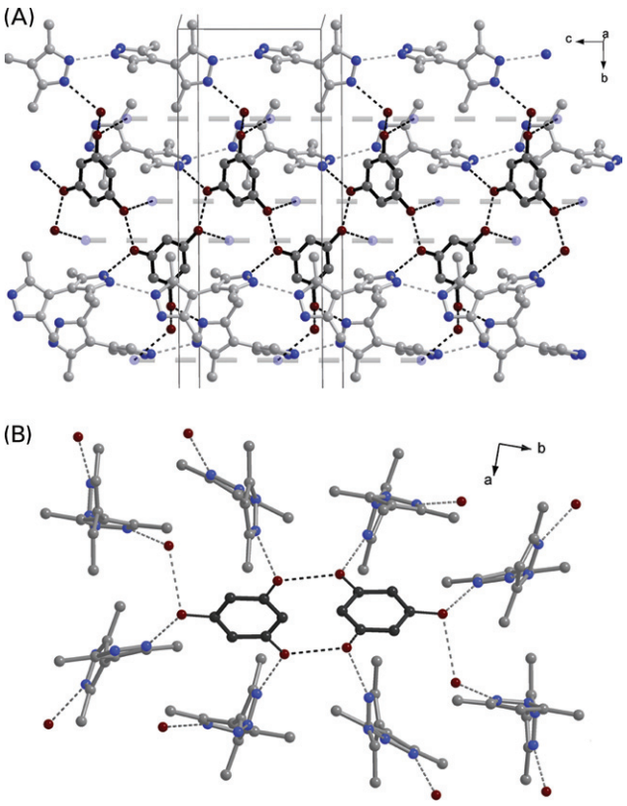

Fig. 2 $2Me_4bpz{\cdot}(1,3,5\text{-}C_6H_3(OH)_3){\cdot}H_2O$ **6** adduct: A–phloroglucinol helix associates with linear chains of bipyrazoles (part of the chains are represented with hatched lines for clarity), all running along *c* axis. B–View down *c* axis showing eight closest neighbors.

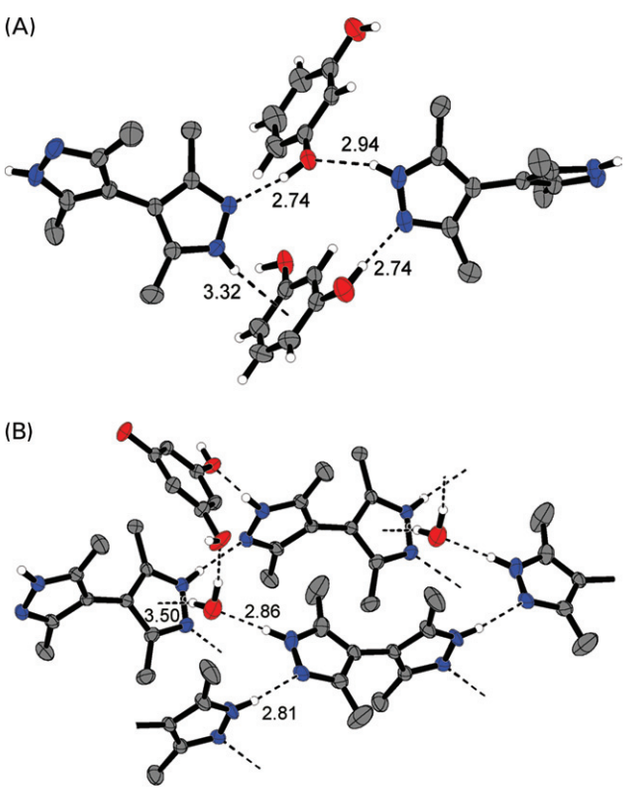

Fig. 3 π-Hydrogen bonding involving pyrazole nuclei either as donor or acceptor seen in binary compounds **5** (A) and **6** (B). Separations H···π and angles D–H···π are 2.65 Å, 149° (**5**) and 2.61 Å, 157° (**6**).

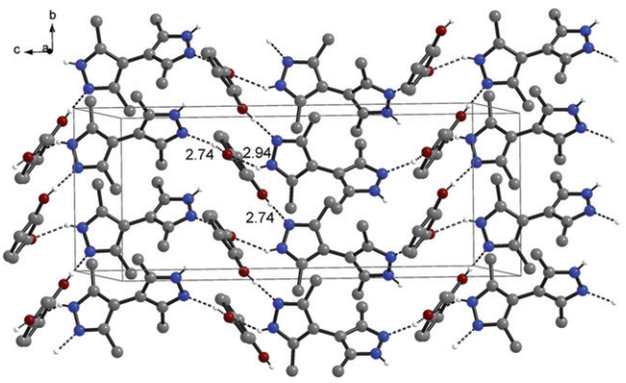

Fig. 4 2D sheets constituting the structure of $Me_4bpz{\cdot}(m\text{-}C_6H_4(OH)_2)$ **5** showing alteration of the molecular components.

In summary, we believe that the common features of **1**–**5** are applicable for preparation of a wide variety of binary pyrazole/phenol composites and may be categorized as follows: combination of two monofunctional molecules affords an alternating 1D chain; bifunctional molecules themselves form homomolecular threads that are interlinked by bridges of monofunctional molecules forming a 2D structure, while a combination of two bifunctional molecules yields a 3D interlinked ensemble of two sorts of homomolecular threads, and both $A(BA)_n$ and $AA(BBAA)_n$ motifs of pyrazole–phenol interactions are feasible. In that sense the structural functions of the two components are equal. The existence of such alternating patterns clearly demonstrates the prospect for developing multidimensional systems with H-bonding properties presumably intermediate between the ones for individual components, with a special impact for supramolecular devices with mobile protons. The $Me_4bpz{\cdot}2PhOH$ **3** complex provides a possible and encouraging prototype of infinite NH···OH···N architecture with disordered protons and potential for long range proton transfer.

Experimental

Starting compounds were materials of reagent grade used without further purification. 3,3′,5,5′-tetramethyl-4,4′-bipyrazole Me_4bpz was synthesized according to the literature method.[20]

Binary compounds $Me_2pz{\cdot}PhOH$ **1**, $Me_2pz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **2**, $Me_4bpz{\cdot}2PhOH$ **3**, $Me_4bpz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **4**, $2Me_4bpz{\cdot}(1,3,5\text{-}C_6H_3(OH)_3){\cdot}H_2O$ **6** were prepared from methanolic solutions of molecular components given in 1:1 molar ratio, the yields of colorless large block shaped crystals were 30–60%. Bipyrazole and resorcinol do not form adducts under these conditions, but readily co-crystallize from chloroform as 1:1 complex $Me_4bpz{\cdot}(m\text{-}C_6H_4(OH)_2)$ **5**.

Crystal data are presented in Table 1.‡ X-ray diffraction data for **1** were collected using a Stoe STADI-4 diffractometer; psi-scan based semi-empirical absorption correction was applied. The data for **2**–**6** were collected using a Siemens SMART CCD diffractometer (absorption correction using SADABS[21]) (graphite monochromated Mo–Kα radiation, $\lambda = 0.71073$ Å). The structures were solved by direct methods and refined in the anisotropic approximation using SHELX-97.[22] In structure **3** the orientation of two unique phenol molecules (dihedral angle 4.5°) forming unequal hydrogen bonds (N···O 2.681(4) and 2.887(3) Å) lowers the entire symmetry and eliminates a possible center of inversion. The refinement in centrosymmetric space group $C2/c$ led only to poor convergence at $R1 = 0.12$ and large atomic thermal parameters.

‡ CCDC reference numbers 22877–22782. See http://www.rsc.org/suppdata/nj/b3/b317104c/ for crystallographic data in .cif or other electronic format.

Table 1 Crystal data for $Me_2pz{\cdot}PhOH$ **1**, $Me_2pz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **2**, $Me_4bpz{\cdot}2PhOH$ **3**, $Me_4bpz{\cdot}(p\text{-}C_6H_4(OH)_2)$ **4**, $Me_4bpz{\cdot}(m\text{-}C_6H_4(OH)_2)$ **5**, and $2Me_4bpz{\cdot}(1,3,5\text{-}C_6H_3(OH)_3){\cdot}H_2O$ **6**

	1	2	3	4	5	6
Formula	$C_{11}H_{14}N_2O$	$C_{11}H_{14}N_2O_2$	$C_{22}H_{26}N_4O_2$	$C_{16}H_{20}N_4O_2$	$C_{16}H_{20}N_4O_2$	$C_{26}H_{36}N_8O_4$
Formula weight	190.24	206.24	378.47	300.36	300.36	524.63
Temperature, K	293	223	223	223	223	223
Crystal system	Monoclinic	Orthorhombic	Monoclinic	Triclinic	Orthorhombic	Orthorhombic
Space group, Z	$P2_1/c$, 4	*Pbca*, 8	*Cc*, 4	$P\bar{1}$, 4	*Pbca*, 8	*Fdd*2, 16
a/Å	8.043(1)	11.901(2)	19.065(2)	7.3717(7)	18.270(3)	29.564(3)
b/Å	15.116(1)	9.902(2)	14.725(2)	14.192(1)	8.528(1)	46.197(6)
c/Å	8.934(1)	18.667(4)	8.583(1)	16.436(2)	21.054(4)	8.554(1)
α/°				98.782(2)		
β/°	96.650(12)		114.80(2)	94.460(2)		
γ/°				103.055(2)		
U/Å^3	1078.9(2)	2199.8(7)	2187.3(5)	1644.1(3)	3280.4(9)	11 683(2)
μ(Mo-Kα), cm^{-1}	0.77	0.87	0.75	0.83	0.83	0.83
$2\theta_{max}$/°	52.0	54.6	51.0	51.4	51.4	52.7
Meas/Unique reflns	2377/1344	12 807/2465	5869/2838	9068/6141	17 024/3119	15 462/5317
R_{int}	0.025	0.023	0.024	0.021	0.044	0.039
R1, *w*R2 [$I > 2\sigma(I)$][a]	0.036, 0.090	0.036, 0.091	0.042, 0.119	0.051, 0.135	0.049, 0.128	0.043, 0.106
R1, *w*R2 (all data)	0.079, 0.103	0.044, 0.096	0.048, 0.126	0.089, 0.151	0.072, 0.141	0.055, 0.111

[a] All unique reflections were used in the refinements.

In **3** all NH and OH hydrogen atoms were located to be disordered over two positions. Attempted refinement led to unreasonable elongation of N–H and O–H bonds and high thermal values for hydrogen atoms that may be suggestive of dynamic character of proton disordering. For this reason, the hydrogen atoms were fixed and the partial occupancies were set at 0.5. Other structures did not show any sign of solid state tautomerism, and all NH and OH hydrogen atoms were located and refined isotropically. CH hydrogen atoms were constrained geometrically and considered in riding model with isotropic *U* values at 1.2–1.5 times the equivalent isotropic *U* value of the atoms to which they are attached. Disordering of CH_3 hydrogen atoms was relevant for refinement of **1** and **2** and was accounted using a symmetric binary model.

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