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New bis-Pyrazole Derivatives Synthesized From Aryl- and Xylyl-Linked bis(β-Diketone) Precursors

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New bis-Pyrazole Derivatives Synthesized From Aryl- and Xylyl-Linked bis(β-Diketone) Precursors

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Abstract: The synthesis and characterization of six new aryl-linked, and in one instance xylyl-linked, bis-pyrazoles are reported. The X-ray structures of two of these derivatives are also presented.

Keywords: bis-Pyrazole, diketone, supramolecular, X-ray

INTRODUCTION

Our group has been investigating the use of aryl- and xylyl-linked bis-β-diketone derivatives as components for constructing new multinuclear metallo assemblies.[1,2] In an extension of this work we are currently undertaking related studies employing bis-pyrazole derivatives derived from these bis-β-diketones. It has long been known that pyrazole derivatives can be readily prepared from β-diketones via condensation with hydrazine,[3,4] and the preparation of the new bis-pyrazoles described in this report was based on this synthetic procedure.

Although the preparation of pyrazole derivatives is well documented for simple β-diketone precursors, there are only limited reports bis-β-diketones being employed as precursors for bis-pyrazole derivatives.[5,6]

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We now report the synthesis and characterization of **1**–**7**, which incorporate both *meta*- and *para*-substituted phenylene spacers (**1**–**6**) as well as, in the case of **7**, a *meta*-xylyl spacer (Schemes 1 and 2). This structural variation, together with the use of different terminal R groups, gives the opportunity to selectively "tune" the electronic and steric properties of these products (and when used as ligands, also of any metal complexes derived from them) as well as providing some control of their solubilities in different solvents.

RESULTS AND DISCUSSION

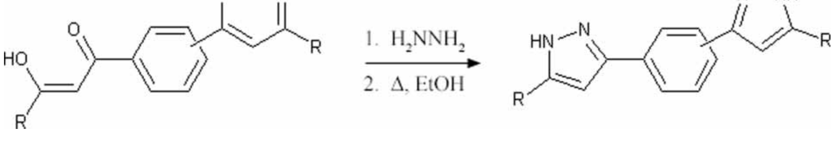
Compounds **1**–**7** were prepared from the corresponding bis(β-diketone) species **8**–**13**[2] and **14**,[7] obtained by the published procedures. Nucleophilic attack of two equivalents of hydrazine with the required bis(β-diketone) precursor in hot ethanol in each case led to formation of the required bis-pyrazole, with isolation of the product involving a solvent extraction step (water/chloroform) followed by recrystallization from ethanol (except for **3**, which was obtained pure from the extraction step); yields ranged from 25 to 72% (Schemes 1 and 2).

All products were characterized by elemental microanalysis, FTIR spectroscopy, ^{1}H NMR spectroscopy, and ESI-MS. Crystals of **5** and **7** were obtained by slow evaporation of pyridine and methanol solutions, respectively, and were used for X-ray diffraction studies to verify the nature of the compounds in the solid state.

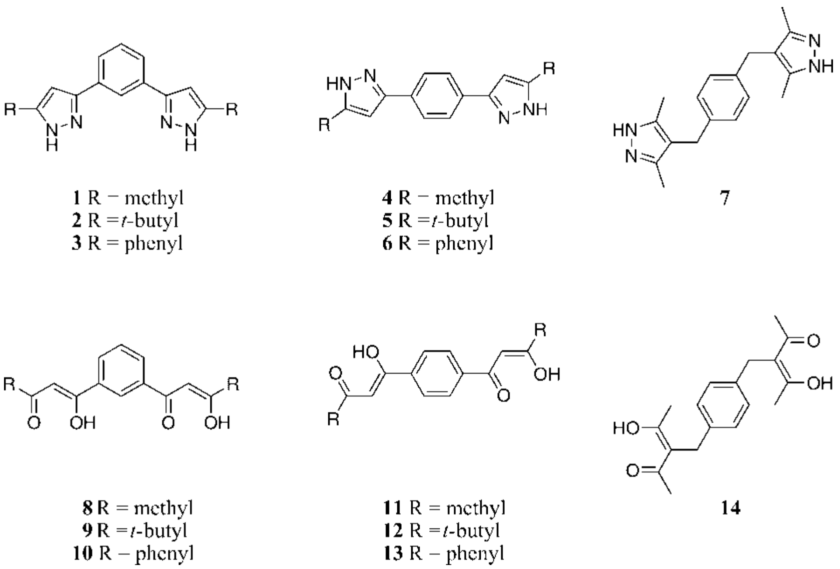
An ORTEP[8] plot of the X-ray structure of **5** is shown in Figure 1. The pyrazole nitrogens are aligned mutually *trans* to each other. The molecule crystallizes as a one-dimensional polymer, involving intermolecular hydrogen bonding within the lattice. Figure 2 shows the hydrogen bonding pattern for **5**. In this case two molecules of the ligand are linked via two water molecules; the remaining hydrogen atom on each molecule of water hydrogen bonds to a lattice pyridine nitrogen forming a one-dimensional polymeric chain.

An ORTEP[8] representation of the X-ray crystal structure of **7** is given in Figure 3. The pyrazole groups either side of the *m*-xylylene unit are aligned at 180° to each other.

The lattice structure takes the form of a two-dimensional polymer formed from hydrogen bonding interactions. One pyrazole group of the molecule hydrogen bonds to two methanol solvent molecules, which in turn interact



Scheme 1. General synthesis of bis-pyrazole ligands **1**–**7**.



1 R = methyl
2 R = *t*-butyl
3 R = phenyl

4 R = methyl
5 R = *t*-butyl
6 R = phenyl

7

8 R = methyl
9 R = *t*-butyl
10 R = phenyl

11 R = methyl
12 R = *t*-butyl
13 R = phenyl

14

Scheme 2.

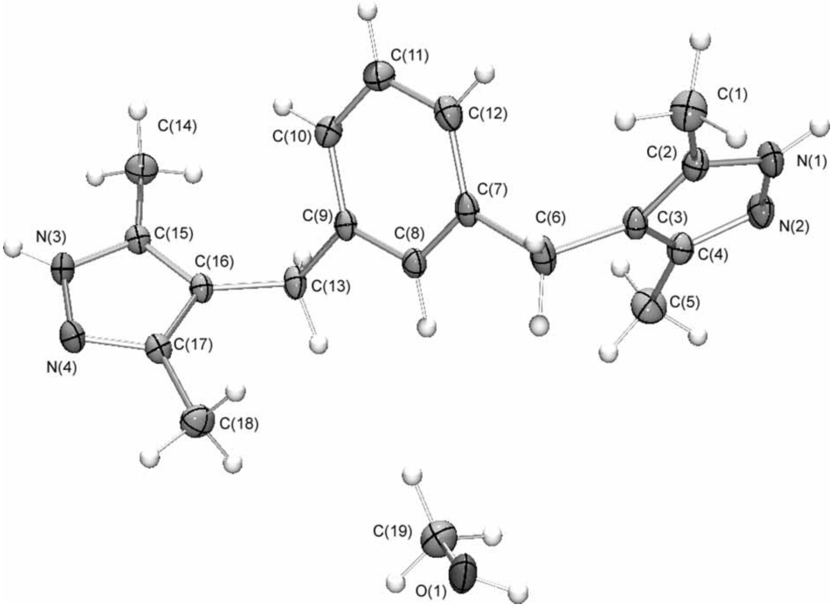


Figure 1. ORTEP plot of **5** shown with 50% probability ellipsoids. Solvate molecules are omitted for clarity.

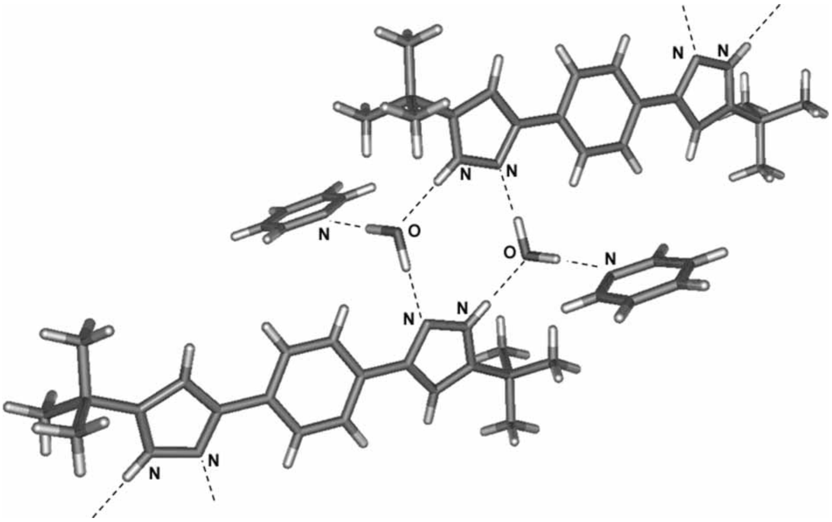


Figure 2. Schematic representation of **5** showing hydrogen bonding to form a one-dimensional chain. Hydrogen bond distances: N(2)-O(1) 2.7891(16) Å, O(1)-N(1)^{i} 2.8472(17) Å, O(1)-N(3)^{ii} 2.8716(19) Å. i $-x+2$, $-y+2$, $-z+1$; ii $-x+1$, $y+1/2$, $-z+3/2$.

with the another molecule. The other pyrazole interacts with adjacent pyrazoles in the lattice resulting in the formation of infinite two-dimensional sheets. Part of one of these sheets showing the hydrogen bonding interactions is shown in Figure 4.

X-RAY STRUCTURE DETERMINATIONS

Data for **5** were collected at 150(2) K with ω scans to approximately 56° 2θ using a Bruker SMART 1000 diffractometer employing graphite-monochromated

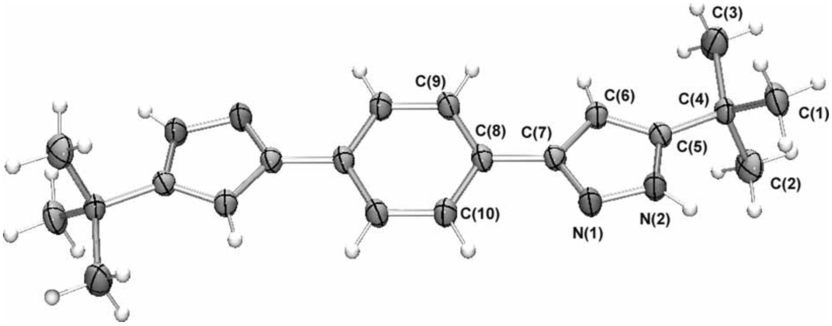


Figure 3. ORTEP plot of **7** shown with 50% probability ellipsoids.

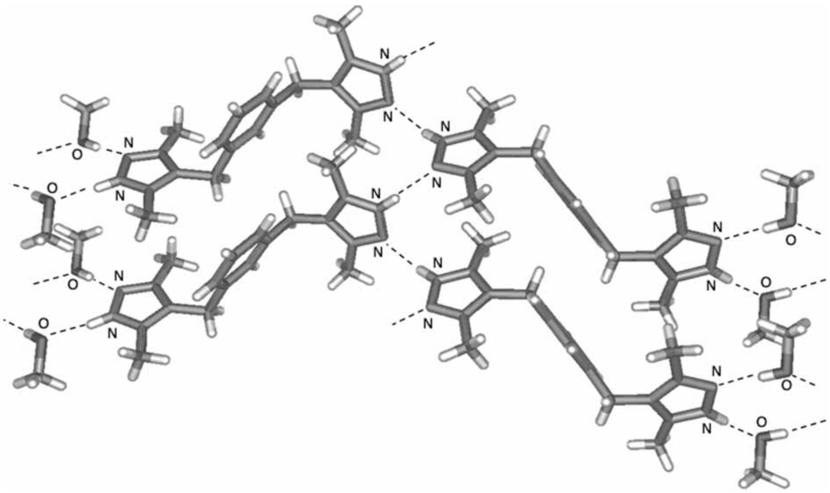


Figure 4. Representation of the X-ray crystal structure of **7** showing the intermolecular hydrogen bonding as well as the hydrogen bonding to methanol solvate molecules to produce a two-dimensional chain. Hydrogen bond distances: N(1)-O(1)^{i} 2.7929(11) Å, N(3)-N(4)^{ii} 2.8953(11) Å, O(1)-N(2)^{iii} 2.7410(11) Å. i. x, $-y-1/2$, $z-1/2$; ii. $-x+1$, $y+1/2$, $-z+3/2$; iii. $-x$, $y-1/2$, $-z+1$.

Mo-Kα radiation generated from a sealed tube (0.71073 Å). For **7**, data were collected at 150(2) K with φ and ω scans to approximately 56° 2θ using a Bruker-Nonius APEX2-X8-FR591 diffractometer employing graphite-monochromated Mo-Kα radiation generated from a rotating anode (0.71073 Å). Data integration and reduction were undertaken with SAINT and XPREP[9,10] and subsequent computations were carried out using the WinGX-32 graphical user interface.[11] Multiscan empirical absorption corrections were applied to the data using the program SADABS.[12] The structures were solved by direct methods using SIR97[13] and then refined and extended with SHELXL-97.[14] Nonhydrogen atoms were refined anisotropically. Carbon-bound hydrogen atoms were included in idealized positions and refined using a riding model. Oxygen-bound hydrogen atoms were first located in the difference Fourier map and were refined with bond length and angle restraints.

Crystal Structure and Refinement Data

$R1 = \Sigma\|F_o|-|F_c\|/\Sigma|F_o|$ for $F_o > 2\sigma(F_o)$ and $wR2 = \{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_c^2)^2]\}^{1/2}$ where $w = 1/[\sigma^2(F_o^2)+(AP)^2+BP]$, $P = (F_o^2+2F_c^2)/3$, and A and B are listed with the crystal data for each structure.

5 · 2Py · 2(H$_2$O). Formula $C_{20}H_{26}N_4 \cdot 2Py \cdot 2(H_2O)$, $M = 516.68$, monoclinic, space group $P2_1/c$, $a = 10.1140(18)$, $b = 14.021(2)$, $c = 11.0090(19)$ Å,

$\beta = 110.963(3)^\circ$, $V = 1457.8(4)$ Å^3, $Dc = 1.177\,\mathrm{g\,cm^{-3}}$, $Z = 2$, crystal size $0.615 \times 0.466 \times 0.125$ mm, colorless, habit blade, temperature 150(2) K, $\lambda(\mathrm{MoK}\alpha) = 0.71073$ Å, $\mu(\mathrm{MoK}\alpha)$ $0.076\,\mathrm{mm^{-1}}$, $T(\mathrm{empirical})_{\mathrm{min,max}} = 0.877117, 1.00000$, $2\theta_{\mathrm{max}} = 56.64$, *hkl* range -13 to 13, -18 to 18, -14 to 14, $N = 14083$, $N_{\mathrm{ind}} = 3510$ (R_{merge} 0.0218), $N_{\mathrm{obs}} = 2897$ ($I > 2\sigma(\mathrm{I})$), $N_{\mathrm{var}} = 111$, residuals $R1$ ($F, 2\sigma$) $= 0.0512$, $wR2$ (F^2, all) $= 0.1399$, $A = 0.0838$, $B = 0.4638$, GoF (all) $= 1.036$, $\Delta\rho_{\mathrm{min,max}} = 0.681, -0.193\,\mathrm{e^-}$ Å^{-3}.

7 · MeOH. Formula $C_{18}H_{22}N_4 \cdot \mathrm{MeOH}$, $M = 326.44$, monoclinic, space group $P2_1/c$, $a = 17.887(2)$, $b = 5.5530(7)$, $c = 19.796(2)$ Å, $\beta = 114.991(6)^\circ$, $V = 1782.2(4)$ Å^3, $Dc = 1.217\,\mathrm{g\,cm^{-3}}$, $Z = 4$, crystal size $0.3 \times 0.25 \times 0.15$ mm, colorless, habit prism, temperature 150(2) K, λ $(\mathrm{MoK}\alpha) = 0.71073$ Å, μ $(\mathrm{MoK}\alpha)$ $0.078\,\mathrm{mm^{-1}}$, T $(\mathrm{empirical})_{\mathrm{min,max}} = 0.90558666, 0.99000$, $2\theta_{\mathrm{max}} = 66.64$, *hkl* range -27 to 27, -8 to 8, -30 to 30, $N = 26834$, $N_{\mathrm{ind}} = 6826$ (R_{merge} 0.0320), $N_{\mathrm{obs}} = 5400$ ($I > 2\sigma(\mathrm{I})$), $N_{\mathrm{var}} = 223$, residuals $R1$ ($F, 2\sigma$) $= 0.0471$, $wR2$ (F^2, all) $= 0.1409$, $A = 0.090$, $B = 0.3123$, GoF (all) $= 1.050$, $\Delta\rho_{\mathrm{min,max}} = 0.438, -0.329\,\mathrm{e^-}$ Å^{-3}.

EXPERIMENTAL

General

^{1}H NMR spectra were recorded in d^6-DMSO at 300 K on a Bruker Avance DPX300 spectrometer at 300 MHz. δH values are recorded in ppm and are relative to $\mathrm{Me_4Si}$ at 0 ppm. Low-resolution electrospray ionisation mass spectra (ESI-MS) were obtained on a Finnigan LCQ-8 spectrometer. FT-IR (KBr) spectra were collected using a Bio-Rad FTS-40 spectrometer.

General Synthesis for Compounds 1–7

Hydrazine monohydrate (2.5 mol equiv) in ethanol (10 mL) was added dropwise to a refluxing ethanol (40 mL) solution of the appropriate bis(β-diketone) (1 mol equiv). The solution was refluxed for 3 h and cooled before partitioning between chloroform (400 mL) and water (400 mL). The organic phase was separated, washed with water (2×200 mL), and dried ($\mathrm{MgSO_4}$) before concentrating under reduced pressure. Pure samples of the corresponding bis(pyrazole) compounds were then obtained by recrystallization from ethanol, except in the case of **3**, which was obtained pure directly from evaporation of the chloroform solution.

1,3-di(3-Methyl-5-pyrazolyl)-benzene (1) (57%) as pale yellow needles. Elemental analysis found: C, 65.37; H, 6.26; N, 21.41%. Calc. for $C_{14}H_{14}N_4 \cdot H_2O$: C, 65.60; H, 6.29; N, 21.86%. ^{1}H NMR δ: 11.73 (br *s*, –NH, 2H), 7.28 (*s*, aromatic, H), 6.79 (*dd*, aromatic, 2H), 6.53 (*t*, aromatic, H), 5.65 (*s*, Hγ, 2H), 1.43 (*s*, $-CH_3$, 6H). (ESI-MS): m/z 239.3 $[M+H]^+$. FTIR (KBr): 3191, 3001, 2933, 1576, 1448, 1285, 1156, 687 cm^{-1}.

1,3-di(3-tert-butyl-5-pyrazolyl)-benzene (2) (72%), as a white microcrystalline powder. Elemental analysis found: C, 74.33; H, 8.10; N 17.20%. Calc. for $C_{20}H_{26}N_4$: C, 74.50; H, 8.13; N, 17.38%. ^{1}H NMR δ: 12.65 (br *s*, $-NH$, 2H), 8.14 (*s*, aromatic, H), 7.67 (*dd*, aromatic, 2H), 7.39 (*t*, aromatic, H), 6.55 (*s*, Hγ, 2H), 1.32 (*s*, $-CH_3$, 18H). (ESI-MS): m/z 323.5 $[M+H]^+$. FTIR (KBr): 3218, 2962, 1457, 1279, 1170, 790 cm^{-1}.

1,3-di(3-Phenyl-5-pyrazolyl)-benzene (3) (25%) as a white powder. Elemetal analysis found: C, 71.55; H, 4.61; N, 13.63%. Calc. for $C_{24}H_{18}N_4 \cdot 0.4CHCl_3$: C, 71.44; H, 4.52; N, 13.66%. ^{1}H NMR δ: 13.47 (br *s*, $-NH$, 2H), 8.38 (*s*, aromatic, H), 8.35 (*s*, chloroform, 3H) 7.86 (*t*, aromatic, 4H), 7.82 (*d*, aromatic, 2H), 7.55(*d*, aromatic, 4H), 7.48 (*t*, aromatic, H), 7.36 (*dd*, aromatic, 2H), 7.29 ppm (*s*, Hγ, 2H). (ESI-MS): m/z 363.5 $[M+H]^+$. FTIR (KBr): 3634, 3073, 2986, 2889, 1457, 1175, 759 cm^{-1}.

1,4-di(3-Methyl-5-pyrazolyl)-benzene (4) (38%) as pale yellow needles. Elemental analysis found: C, 68.93; H, 5.92; N, 21.82%. Calc. for $C_{14}H_{14}N_4 \cdot 0.4EtOH$: C, 69.24; H, 6.42; N, 21.82%. ^{1}H NMR δ: 12.54 (br *s*, $-NH$, 2H), 7.75 (*s*, aromatic, 4H), 6.45 (*s*, Hγ, 2H), 2.04 ppm (*s*, $-CH_3$, 6H). (ESI-MS): m/z 239.3 $[M+H]^+$. FTIR (KBr): 3218, 1585, 1455, 848, 790 cm^{-1}.

1,4-di(3-*tert*-Butyl-l,5-pyrazolyl)-benzene (5) (69%) as a white microcrystalline powder. Elemental analysis found: C, 74.55; H, 8.07; N, 16.79%. Calc. for $C_{20}H_{26}N_4$: C, 74.50; H, 8.13; N, 17.38%. ^{1}H NMR δ: 12.59 (br *s*, $-NH$, 2H), 7.78 (*s*, aromatic, 4H), 6.49 (*s*, Hγ, 2H), 1.23 (*s*, $-CH_3$, 18H). (ESI-MS): m/z 323.5 $[M+H]^+$. FTIR (KBr): 3216, 2964, 1558, 1457, 1244, 794 cm^{-1}. Crystals of sufficient quality for an X-ray structure analysis of formula $C_{20}H_{26}N_4 \cdot 2Py \cdot 2(H_2O)$ were obtained by slow evaporation of a pyridine solution over several days.

1,4-di(3-Phenyl-5-pyrazolyl)-benzene (6) (38%) as a yellow microcrystalline powder. Elemental analysis found: C, 79.38; H, 5.18; N, 15.17%. Calc. for $C_{24}H_{18}N_4$: C, 79.54; H, 5.01; N, 15.46%. ^{1}H NMR δ: 13.82 (br *s*, $-NH$, 2H), 8.35 (*s*, aromatic, 4H), 8.27 (*d*, aromatic, 4H), 7.83 (*t*, aromatic, 4H), 7.75 (*d*, aromatic, 2H), 7.66 (*s*, Hγ, 2H). (ESI-MS): m/z 363.5 $[M+H]^+$. FTIR (KBr): 3141, 3092, 2889, 2829, 1472, 1184, 974, 753 cm^{-1}.

3,3′-(1,3-Xylylene)-bis(3-methyl-5-pyrazolyl) (7) (63%) as pale yellow needles. Elemental analysis found: C, 72.62; H, 7.68; N, 18.46%. Calc. for $C_{18}H_{22}N_4 \cdot 0.2EtOH$: C, 72.78; H, 7.71; N, 18.46%. ^{1}H NMR δ: 11.94 (br *s*, $-NH$, 2H), 7.13 (*t*, aromatic, H), 6.89 (*dd*, aromatic, 2H), 6.87 (*s*, aromatic, H), 3.58 (*s*, $-CH_2$, 4H), 2.01 ppm (*s*, $-CH_3$, 6H). (ESI-MS): m/z 295.4 $[M+H]^+$. FTIR (KBr): 3108, 2966, 2906, 1586, 1298, 1046, 811 cm^{-1}. Crystals of sufficient quality for X-ray structure analysis of formula $C_{18}H_{22}N_4 \cdot MeOH$ were obtained by the slow evaporation of a methanol solution over several days.

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