Asian Journal of Chemistry; Vol. 27, No. 4 (2015), 1339-1341

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2015.17871

Synthesis, Structure and Supramolecular Properties of 1,7'-*bis*[4-(3-Methyl-2,3-dihydro-pyrazol-1-yl)phenol]-1,4,7-trioxaheptane

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Received: 22 April 2014; *Accepted*: 11 June 2014; *Published online*: 4 February 2015; AJC-16787

A new pyrazole derivative, 1,7'-*bis*[4-(3-methyl-2,3-dihydro-pyrazol-1-yl)phenol]-1,4,7-trioxaheptane with m.f. $C_{24}H_{24}N_4O_5$ has been synthesized and the crystal structure was determined by single crystal X-ray diffraction. Interestingly, the title compound are linked by intermolecular O2–H22···N2 hydrogen bonds into a 36 atoms' macro-ring which is further held together into one dimensional beaded chain *via* C–H···O hydrogen bonding between another phenol oxygen atom and one methylene carbon atom.

Keywords: Synthesis, Crystal structure, Supramolecular properties, Pyrazole.

INTRODUCTION

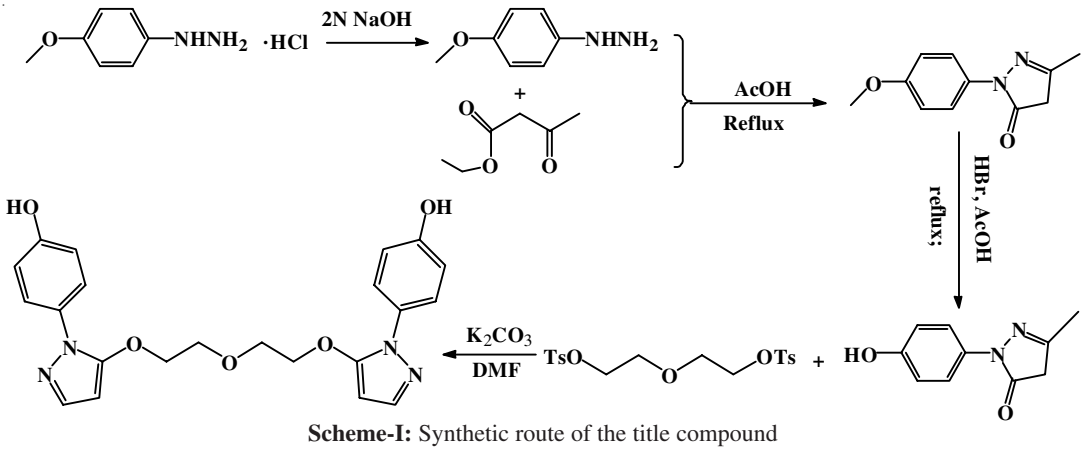
The pyrazole ring is an important heterocyclic core structure in a large number of biologically active compounds. The spectrum of pharmaceutical action of pyrazole derivatives encompasses, for example, substances acting on the central nervous system, pharmacodynamic agents, drugs aimed at metabolic diseases and chemotherapeutics[1]. Its derivatives are also reported to have a broad spectrum of biological activities, such as antitumour[2], anticoagulant[3], antihyperglycemic, analgesic, antipyretic, antimicrobial and hypoglycaemic activity[4-8]. Arylpyrazoles are important in medicinal and pesticidal chemistry[9,10]. Some arylpyrazoles have non-nucleoside HIV-1 reverse transcriptase inhibitory activity[11]. Li *et al.*[12] have reported a series of N,1,3-triphenyl-1*H*-pyrazole-4-carboxamide derivatives that exhibited potent antiproliferative activities against HTC116, MCF-7 cells and Aurora-A kinase inhibitory activities.

In view of the above-mentioned facts, we report herein the syntheses and crystal structure of a new pyrazole derivative.

EXPERIMENTAL

Commercially available chemicals were of analytical grade and were used without further purification. X-ray single crystal structure was determined on a Bruker Smart 1000 CCD area detector. Melting points were determined on a Kofler apparatus and the thermometer was uncorrected.

Synthesis of 1,7'-*bis*[4-(3-methyl-2,3-dihydro-pyrazol-1-yl)phenol]-1,4,7-trioxaheptane: The synthetic route for the compound is shown in **Scheme-I**. 2N NaOH was added to



Scheme-I: Synthetic route of the title compound

a clear aqueous solution of 10 g 4-methoxy-phenylhydrazine hydrochloride to give 4-methoxyphenylhydrazine as a pale white solid. 2-(4-Methoxy-phenyl)-5-methyl-2,4-dihydro-pyrazol-3-one, 2-(4-hydroxy-phenyl)-5-methyl-2,4-dihydro-pyrazol-3-one and diethylene glycol di-*p*-tosylate was prepared according to the literature methods[13,14], respectively.

To a stirred solution of 2-(4-hydroxy-phenyl)-5-methyl-2,4-dihydro-pyrazol-3-one (1.98 g, 10.5 mmol) in dry DMF was added 1.52 g (11 mmol) dried K_2CO_3 and the mixture was stirred for 0.5 h at room temperature, then 2.07 g (5 mmol) diethylene glycol di-*p*-tosylate in 20 mL of dry DMF was added dropwise in 0.5 h and the resulting solution stirred and heated to reflux for 24 h. After cooling down, inorganic salts were separated by filtration and the solvent removed from the filtrate under reduced pressure. The crude product was recrystallized with ethanol to give a white solid 1.03 g, Yield 46 %, m.p. 245-246 °C. The title compound (0.045 g, 0.1 mmol) was dissolved in ethanol (10 mL) and sealed for crystallization at room temperature. After about three weeks colourless crystals suitable for analysis were obtained.

X-ray structure determination: The single crystal of the title compound with the approximate dimensions of 0.34 mm × 0.28 mm × 0.21 mm was placed on a Bruker Smart 1 000 CCD area detector. The reflections were collected using a graphite monochromated MoK_α radition ($\lambda = 0.71073$ Å) at 293 K. The structure was solved by using the program SHELXL-97 and Fourier difference techniques and refined by the full-matrix least-squares method on F^2. All non-hydrogen atoms were subjected to anisotropic refinement and all hydrogen atoms were added in idealized positions and refined isotropically. Crystal data and details of the refinement are summarized in Table-1, representative bond lengths (Å) and angles (°) are presented in Table-2. CCDC reference numbers 980108.

TABLE-1
CRYSTAL DATA AND STRUCTURE REFINEMENT FOR THE TITLE COMPOUND

Empirical formula, formula weight	$C_{24}H_{26}N_4O_5$, 450.49
Temperature (K), wavelength (Å)	293(2), 0.71073
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions, (Å, deg)	20.720(10), 90.00 12.431(6), 112.89(3) 19.655(13), 90.00
Volume ($Å^3$), Z, calculated density	4664(4), 8, 1.283kg/m^3
Absorption coefficient (mm^{-1})	0.091
Index ranges, hkl	-26≤h≤16, -16≤k≤15, -25≤k≤25
θ range for data collection (°)	1.95–27.42
Reflections collected/unique	5263/2894
Data/restraints/parameters	5263/6/320
Independent reflections (R_{int})	0.0669
Goodness-of-fit indicator on F^2	0.952
Final R indices [I > 2σ(I)]	R1 = 0.0664, wR2 = 0.1701
R indices (all data)	R1 = 0.1642, wR2 = 0.2243

RESULTS AND DISCUSSION

X-ray crystal structure analyses reveal that the title compound crystallized in the monoclinic space group C2/c. As depicted in Fig. 1, the asymmetric unit consists of one title compound. Upon careful investigation of the structure, it can be seen that two title compound molecules are held together to a 36 atom macro-ring *via* strong O-H···N hydrogen bonding between one of the pyrazole N atoms (N2) and one of the phenol oxygen atoms (O4) as shown in Fig. 2. The O4···N2 distance (2.737Å), O4-H22···N2 angle (169.38) are all within the ranges of those reported O-H···N hydrogen bonds. In addition, the above mentioned macro-rings are further connected into one dimensional beaded chain *via* C–H···O hydrogen

TABLE-2
SELECTED BOND LENGTHS (Å) AND ANGLES (°) FOR THE TITLE COMPOUND

C1-C6	1.384(4)	C1-C2	1.386(4)	C2-C3	1.385(5)	C3-O5	1.361(4)
C3-C4	1.368(4)	C4-C5	1.377(4)	C5-C6	1.386(4)	C6-N1	1.431(4)
C7-C8	1.506(5)	C8-N2	1.333(4)	C8-C9	1.389(5)	C9-C10	1.353(4)
C10-O2	1.344(4)	C10-N1	1.353(4)	C13-O1	1.420(5)	C13-C14	1.464(5)
C14-O3	1.434(4)	C14-O3	1.434(4)	C15-N3	1.344(4)	C15-O3	1.346(4)
C15-C16	1.360(5)	C16-C17	1.376(5)	C17-N4	1.324(4)	C17-C18	1.512(5)
C19-C24	1.381(4)	C19-C20	1.391(4)	C19-N3	1.433(4)	C20-C21	1.386(4)
C21-C22	1.389(4)	C22-O4	1.371(4)	C22-C23	1.376(4)	C23-C24	1.384(4)
C11A-O2	1.506(11)	C12A•O1	1.282(8)			C12B•O1	1.453(10)
N1-N2	1.384(3)	N3-N4	1.383(3)				
C6–C1–C2	120.0(3)	C3–C2–C1	120.4(3)	O5–C3–C4	118.0(3)		
O5–C3–C2	122.6(3)	C4–C3–C2	119.4(3)	C3–C4–C5	120.6(3)		
C4–C5–C6	120.5(3)	C1–C6–C5	119.0(3)	C1–C6–N1	121.8(3)		
C5–C6–N1	119.2(3)	N2–C8–C9	111.7(3)	N2–C8–C7	118.8(3)		
C9–C8–C7	129.5(3)	C10–C9–C8	105.1(3)	O2–C10–C9	132.3(3)		
O2–C10–N1	118.7(3)	C9–C10–N1	109.0(3)	O1–C13–C14	112.3(3)		
O3–C14–C13	108.6(3)	N3–C15–O3	118.3(3)	N3–C15–C16	108.2(3)		
O3–C15–C16	133.4(3)	C15–C16–C17	105.4(3)	N4–C17–C16	111.8(3)		
N4–C17–C18	119.6(3)	C16–C17–C18	128.6(4)	C24–C19–C20	120.1(3)		
C24–C19–N3	121.1(3)	C20–C19–N3	118.8(3)	C21–C20–C19	119.3(3)		
C20–C21–C22	120.5(3)	O4–C22–C23	122.8(3)	O4–C22–C21	117.5(3)		
C23–C22–C21	119.7(3)	C22–C23–C24	120.2(3)	C19–C24–C23	120.2(3)		
C12A–C11A–O2	108.0(8)	O1–C12A–C11A	110.8(12)	C10–N1–N2	109.4(2)		
C10–N1–C6	132.7(3)	N2–N1–C6	117.9(2)	C8–N2–N1	104.9(3)		
C15–N3–N4	109.7(3)	C15–N3–C19	130.6(3)	N4–N3–C19	119.7(2)		
C17–N4–N3	104.9(3)	C12A–O1–C13	118.3(5)	C10–O2–C11A	108.1(4)		
C15–O3–C14	116.1(3)						

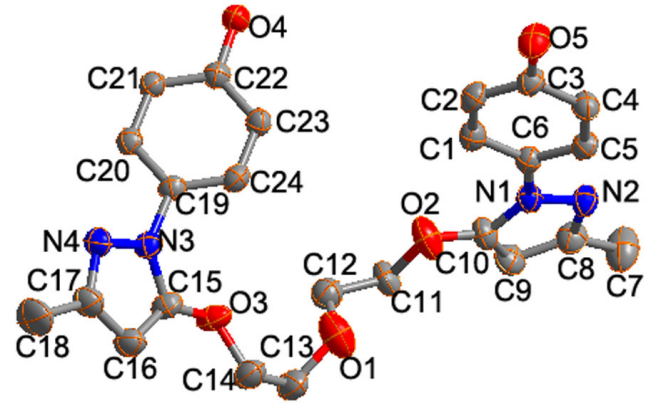


Fig. 1. Molecule structure of the title compound with thermal ellipsoids at 30 % probability (hydrogen atoms are omitted for clarity)

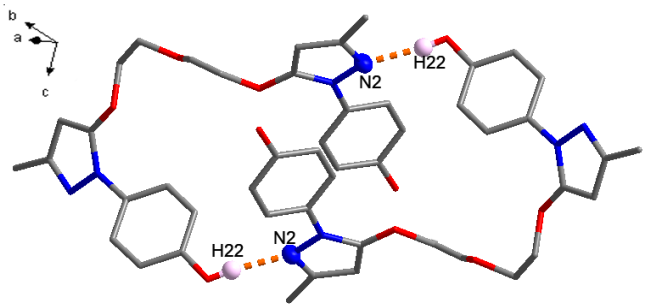


Fig. 2. View of the 36-numbered macro-ring constructed by hydrogen bonds of the title compound (hydrogen atoms, except those forming hydrogen bonds, are omitted for clarity)

bonding between another phenol oxygen atom (O_5) and one methylene carbon atom (H13B) as shown in Fig. 3. The C13···O5 distance (3.509 Å), C13-H13B···O5 angle (169.38) are also within the ranges of those reported C-H3···O hydrogen bonds[15].

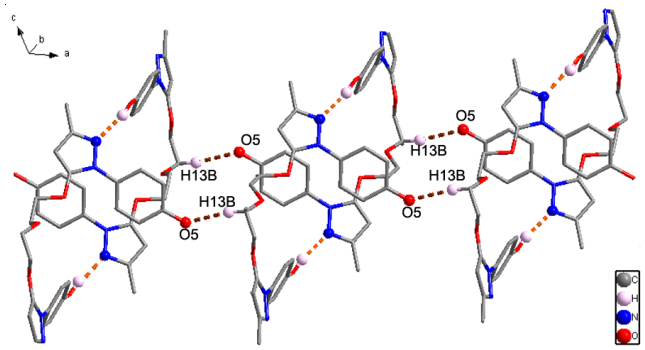


Fig. 3. View of the infinite 1D chain motif of the title compound (hydrogen atoms, except those forming hydrogen bonds, are omitted for clarity)

Conclusion

In conclusion, we have presented herein the synthesis and crystal structure of a new arylpyrazole derivative which demonstrated interesting supramolecular properties.

ACKNOWLEDGEMENTS

This work was supported by the Young Scholars Science Foundation of Lanzhou Jiaotong University (No. 2013011) and the Natural Science Foundation of Gansu Province of China (No. 1310RJZA066) .

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