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Synthesis and Crystal Structure of 1,4-Bis(2-methylphenyl)-2,5-piperazinedione

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The crystal structure of 1,4-bis(2-methylphenyl)-2,5-piperazinedione has been determined by single crystal X-ray diffraction method. The crystal belongs to monoclinic system, space group P-1 with unit cell constants a = 10.372 (3), b = 12.224 (3), c = 12.614 (3)Å, α = 95.448 (4), β = 101.751 (4), γ = 90.072 (5), V = 1558.4 (7) Å^3, Z = 2, D_c = 1.255 g/cm^3, μ = 0.083 mm^{-1}, F(000) = 624, R and wR are 0.0707 and 0.2067, respectively for 5990 unique reflections with 3580 observed reflections [I > 2σ(I)]. The title compound, $C_{18}H_{18}N_2O_2$, **(I)**, contains two independent molecules in the asymmetric unit. The dihedral angles between the two benzene rings in each molecule are 3.7 (2) and 3.2 (2)°. Molecules of (I) interact *via* weak intermolecular C—H···O interactions, forming zig-zag chains along the a-axis.

Key Words: Synthesis, Crystal structure, Piperazinedione.

INTRODUCTION

Piperazinedione and its derivatives are the smallest structural cyclodipeptides and are regarded as a by-product in the synthesis, especially in the solid-phase synthesis, of peptides[1–3]. The hydrogen bonds are one of the main modes for the interaction between drug and acceptor; and two donors and two acceptors to form hydrogen bonds are present in the molecule of piperazinedione. Its derivatives have been used widely in pharmaceutical chemistry, *e.g.*, the inhibition of the cell growth cycles of mammals[4, 5], the inhibition of glutathion-S-transferase[6] and the inhibition of the activated factor of thrombcytes[7]. In recent years, piperazinedione and its derivatives have received considerable attention due to such properties as the stable six-membered-cyclic structure and molecular diversity. In the present paper, a new piperazinedione derivative, 1,4-bis(2-methylphenyl)-2,5-piperazinedione (Fig. 1) was synthesized by the cyclocondensation reaction of N-*p*-methoxyphenyl chloroacetamide and its structure was characterized by EA, IR, ^{1}H NMR, TG and X-ray crystallographic analysis.

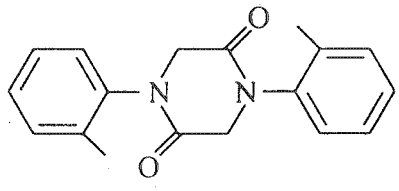

Fig. 1. 1,4-Bis(2-methylphenyl)-2,5-piperazinedione

EXPERIMENTAL

All chemicals were of analytical reagent grade and used directly without further purification. ^{1}H NMR spectrum was recorded by Bruker AC-300 with TMS as an internal standard. IR spectrum was taken by Nicolet 510P FTIR spectrometer (KBr). Elemental analysis was performed by Perkin-Elmer 240. *N*-naphthalene-1-yl chloroacetamide was prepared by the reaction of 1-naphthylamine and chloroacetyl chloride in the presence of triethylamine according to the literature method[8]. To a solution of *N*-naphthalene-1-yl chloroacetamide and *N*-*o*-methylphenyl chloroacetamide (3.3 g, 20 mmol) in acetone (30 mL), K_2CO_3 (3.04 g, 22 m mol) and NaI (0.5 g) was added and the mixture was stirred at 56°C for 5 h. The mixture was washed three times with water (50 mL) and then filtered. The filter cake was washed with a small amount of acetone and water. The title compound was obtained after dryness of the resulting white powders at room temperature for 48 h. Colourless prismatic single crystals suitable for X-ray diffraction analysis were obtained by slow evaporation at room temperature from $CHCl_3$:CH_3CH_2OH (1 : 1) after 10 d. ^{1}H NMR (400 MHz, DMSO): 4.35 (s), 7.28 (t), 7.47 (t), 7.80 (t), 7.90 (d), 8.08 (d), 8.20 (d), 8.40 (d). IR (KBr, cm^{-1}): 1597 (w), 1574 (w), 1480 (s) ν(Ar); 1643 (vs) ν(C═O); 1274 (w) ν(C—N). Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.47; H, 6.12; N, 9.52%; Found: C, 73.42; H, 6.08; N, 9.56%.

Crystal data and structure determination

A colourless single crystal with approximate dimension of 0.40 mm × 0.20 mm × 0.14 mm was mounted on a glass fibre in random orientation. The data were collected by Bruker Smart 1000 CCD diffactometer with graphite monochromated MoKα radiation (λ = 0.71073 Å) using ω scan mode in the range of $2.32 \leq \theta \leq 26.07°$ at temperature 293 ± 2 K. A total of 8564 reflections were collected with 5990 unique ones ($R_{int} = 0.0148$), of which 3589 reflections with $I > 2\sigma(I)$ were considered to be observed and used in the succeeding refinements. Intensity data were corrected for Lp factors and empirical absorption. The structure was solved by direct methods and expanded by using Fourier differential techniques with SHELXL-97[9]. All non-hydrogen atoms were located with successive difference Fourier synthesis. The structure was refined by full-matrix least-squares method on F^2 with anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms were added according to the theoretical models. Full matrix least-squares refinement gave the final R = 0.0707 and wR = 0.2067, $W = 1/[\sigma^2(F_0)^2 + (0.1123P)^2 + 0.1927P]$ where $P = (F_2^0 + 2F_c^2)$. Software used to prepare material for publication: SHELXTL, PARST[10] and PLATON[11].

RESULTS AND DISCUSSION

X-ray crystal structure

The final atomic parameters and equivalent isotropic thermal parameters for the non-hydrogen atoms are given in Table-1. Selected bond lengths and bond angles are illustrated in Tables 2 and 3, respectively. The hydrogen bonding geometries are shown in Table-4. Fig. 2 shows the molecular structure of the compound.

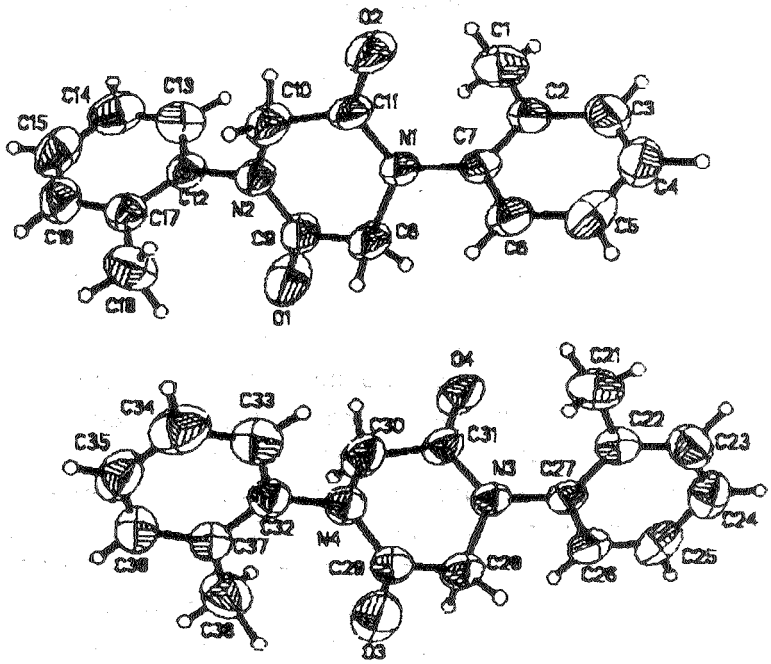

Fig. 2. Molecular structure of the title compound with the atomic numbering scheme

TABLE-1
ATOMIC COORDINATES ($\times 10^4$) AND THERMAL PARAMETERS ($Å^2 \times 10^3$)

Atom	x	y	z	Ueq
O1	0.1158(3)	0.86350(2)	1.09600(2)	0.1018(10)
O2	0.3954(2)	1.10098(17)	0.88844(18)	0.0798(9)
N1	0.2844(2)	0.94229(17)	0.89296(17)	0.0499(8)
N2	0.2334(2)	1.01888(18)	1.09531(17)	0.0514(8)
C1	0.1276(3)	1.03690(3)	0.70600(3)	0.0769(14)
C2	0.2224(3)	0.9460(2)	0.69510(2)	0.0539(10)
C3	0.2397(3)	0.9023(3)	0.59330(3)	0.0686(11)
C4	0.3241(4)	0.8196(3)	0.57980(3)	0.0718(12)
C5	0.3941(3)	0.7749(3)	0.66860(3)	0.0685(11)
C6	0.3798(3)	0.8143(2)	0.77170(2)	0.0549(10)
C7	0.2956(2)	0.9010(2)	0.78470(2)	0.0455(8)
C8	0.2453(4)	0.8638(2)	0.96170(2)	0.0720(13)
C9	0.1905(3)	0.9167(2)	1.05600(2)	0.0641(11)
C10	0.3336(3)	1.0733(2)	1.05210(3)	0.0706(11)
C11	0.3391(3)	1.0411(2)	0.9369(2)	0.0556(10)
C12	0.2044(3)	1.0711(2)	1.1943(2)	0.0505(9)
C13	0.1139(3)	1.1546(3)	1.1872(3)	0.0689(11)
C14	0.0898(4)	1.2110(3)	1.2801(4)	0.0853(16)

Atom	x	y	z	Ueq
C15	0.1565(4)	1.1826(3)	1.3799(3)	0.0864(16)
C16	0.2455(4)	1.1013(3)	1.3861(3)	0.0748(14)
C17	0.2739(3)	1.0422(2)	1.2944(2)	0.0566(10)
C18	0.3728(4)	0.9545(3)	1.3020(3)	0.0803(12)
O3	0.4357(3)	0.36580(2)	1.09978(19)	0.0992(10)
O4	0.0507(2)	0.60288(17)	0.89561(18)	0.0777(8)
N3	0.1648(2)	0.44417(17)	0.89936(17)	0.0492(7)
N4	0.3166(2)	0.52053(18)	1.10136(18)	0.0515(8)
C21	0.2300(3)	0.5434(3)	0.7155(3)	0.0749(12)
C22	0.1324(3)	0.4503(2)	0.7023(2)	0.0530(9)
C23	0.0676(3)	0.4068(3)	0.6000(3)	0.0676(11)
C24	-0.0226(3)	0.3226(3)	0.5843(3)	0.0707(12)
C25	0.0491(3)	0.2759(3)	0.6719(3)	0.0676(11)
C26	0.0137(3)	0.3146(2)	0.7751(2)	0.0549(10)
C27	0.1021(2)	0.4035(2)	0.7908(2)	0.0459(8)
C28	0.2367(3)	0.3655(2)	0.9690(2)	0.0678(11)
C29	0.3405(3)	0.4175(2)	1.0615(2)	0.0614(11)
C30	0.1939(3)	0.5736(2)	1.0600(2)	0.0664(11)
C31	0.1303(3)	0.5425(2)	0.9440(2)	0.0537(9)
C32	0.3981(3)	0.5732(2)	1.1992(2)	0.0507(9)
C33	0.4855(3)	0.6552(3)	1.1891(3)	0.0669(11)
C34	0.5601(3)	0.7100(3)	1.2818(3)	0.0834(14)
C35	0.5469(4)	0.6833(3)	1.3824(3)	0.0839(14)
C36	0.4592(3)	0.6025(3)	1.3909(3)	0.0745(12)
C37	0.3822(3)	0.5453(2)	1.3000(2)	0.0570(10)
C38	0.2845(4)	0.4589(3)	1.3101(3)	0.0813(12)

The structure of (I) consists of two crystallographically independent molecules A and B in the asymmetric unit of the centrosymmetric space group P-1 (Fig. 2.). The bond lengths and angles of A and B (Table-1) agree with each other and are comparable to those in the related compound[12], (II). Different from the planar structure of piperazinedione ring in (II), the sterically hindered effect of the *o*-methyl groups attached to the benzene rings causes the piperazinedione ring in (I) deviating from planality. However, the two aromatic rings are co-planar to each other, with the dihedral angles of 3.7(2) and 3.2(2)° in A and B, respectively. Molecules of (I) interact *via* weak intermolecular C6—H6···O3 and C26—H26···O1 interactions (Table-2) to form zig-zag chains along the a-axis. The packing is further stabilized by van der Waals' forces. Packing diagram of the title compound in a unit cell is shown in Fig. 3.

TABLE-2
SELECTED BOND LENGTHS (Å)

Bond	Dist.	Bond	Dist.
O1-C9	1.224(4)	C10-C11	1.482(4)
O2-C11	1.216(3)	C12-C17	1.398(4)
O3-C29	1.214(4)	C12-C13	1.384(4)
O4-C31	1.217(3)	C13-C14	1.370(6)
N1-C8	1.462(4)	C14-C15	1.383(6)
N1-C7	1.438(3)	C15-C16	1.354(6)
N1-C11	1.353(3)	C16-C17	1.388(5)
N2-C10	1.455(4)	C17-C18	1.481(5)
N2-C12	1.435(3)	C21-C22	1.497(4)
N2-C9	1.340(3)	C22-C23	1.384(4)
N3-C27	1.433(3)	C22-C27	1.391(4)
N3-C31	1.358(3)	C23-C24	1.363(5)
N3-C28	1.466(3)	C24-C25	1.366(5)
N4-C29	1.353(3)	C25-C26	1.371(4)
N4-C30	1.452(4)	C26-C27	1.394(4)
N4-C32	1.441(3)	C28-C29	1.507(4)
C1-C2	1.500(4)	C30-C31	1.490(4)
C2-C3	1.389(4)	C32-C33	1.383(4)
C2-C7	1.388(4)	C32-C37	1.388(4)
C3-C4	1.359(5)	C33-C34	1.377(5)
C4-C5	1.366(5)	C34-C35	1.373(5)
C5-C6	1.380(4)	C35-C36	1.368(5)
C6-C7	1.393(4)	C36-C37	1.384(4)
C8-C9	1.512(4)	C37-C38	1.495(5)

TABLE-3
SELECTED BOND ANGLES (°)

Angle	(°)	Angle	(°)
C7-N1-C8	117.3(2)	C14-C15-C16	120.7(4)
C7-N1-C11	120.0(2)	C15-C16-C17	122.5(3)
C8-N1-C11	120.7(2)	C16-C17-C18	122.1(3)
C9-N2-C10	120.8(2)	C12-C17-C18	121.9(3)
C9-N2-C12	122.1(2)	C12-C17-C16	116.0(3)
C10-N2-C12	115.9(2)	C25-C26-C27	120.0(3)
C27-N3-C28	117.5(2)	N3-C27-C22	120.2(2)
C27-N3-C31	120.2(2)	N3-C27-C26	119.2(2)
C28-N3-C31	120.2(2)	C22-C27-C26	120.2(2)
C29-N4-C32	121.5(2)	N3-C28-C29	114.1(2)

Angle	(°)	Angle	(°)
C30-N4-C32	116.6(2)	O3-C29-N4	123.4(3)
C29-N4-C30	120.9(2)	O3-C29-C28	120.4(2)
C3-C2-C7	116.9(3)	N4-C29-C28	116.1(2)
C1-C2-C7	122.3(2)	N4-C30-C31	116.9(2)
C2-C3-C4	122.7(3)	O4-C31-N3	123.9(2)
C3-C4-C5	119.8(3)	O4-C31-C30	120.1(2)
C4-C5-C6	120.0(3)	N3-C31-C30	116.0(2)
C5-C6-C7	119.7(3)	N4-C32-C33	118.1(2)
N1-C7-C6	118.7(2)	N4-C32-C37	119.9(2)
N1-C7-C2	120.4(2)	C33-C32-C37	122.0(3)
C2-C7-C6	120.9(2)	C32-C33-C34	119.0(3)
N1-C8-C9	113.9(2)	C33-C34-C35	120.1(3)
O1-C9-C8	119.4(2)	C34-C35-C36	120.1(3)
O1-C9-N2	123.4(3)	C35-C36-C37	121.8(3)
N2-C9-C8	117.1(2)	C32-C37-C36	117.0(3)
N2-C10-C11	116.9(2)	C32-C37-C38	121.6(3)
O2-C11-N1	123.6(2)	C36-C37-C38	121.4(3)
O2-C11-C10	119.7(2)	C21-C22-C23	120.8(3)
N1-C11-C10	116.7(2)	C21-C22-C27	122.3(2)
N2-C12-C17	119.7(2)	C23-C22-C27	116.8(3)
N2-C12-C13	118.3(2)	C22-C23-C24	122.8(3)
C13-C12-C17	121.9(3)	C23-C24-C25	119.7(3)
C12-C13-C14	119.9(3)	C24-C25-C26	120.0(3)
C13-C14-C15	119.0(4)		

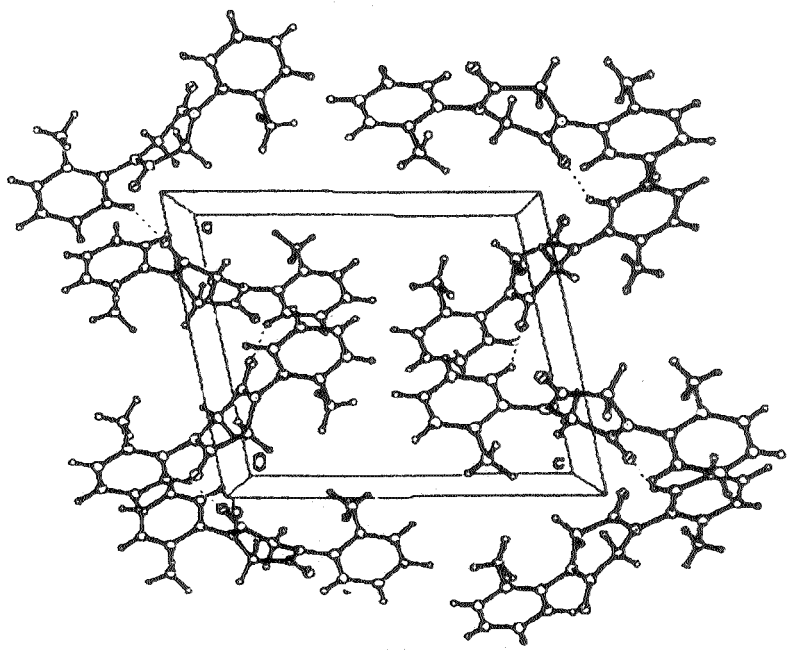

Fig. 3. View of the crystal packing for the title compound

TABLE-4
HYDROGEN BOND LENGTHS (Å) AND BOND ANGLE (°)
FOR THE TITLE COMPOUND

Donor-H···Acceptor	D-H	H···A	D···A	D-H···A
C1-H1B···O2	0.9603	2.5973	3.267(4)	127.05
C6-H6A···O3[a]	0.9306	2.4293	3.250(4)	147.05
C21-H21C···O4	0.9590	2.5749	3.250(4)	127.55
C26-H21A···O1[b]	0.9308	2.4481	3.277(4)	148.42

Symmetry code: (a) 1 – x, 1 – y, 2 – z; (b) –x, 1 – y, 2 – z

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