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КРАТКИЕ СООБЩЕНИЯ

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CRYSTAL STRUCTURES OF 1-ARYL-4-(BIARYLMETHYLENE)PIPERAZINE AND PIPERIDINE, STRUCTURALLY RELATED TO ADOPRAZINE

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8-(1-([1,1′-Biphenyl]-4-ylmethyl)piperidin-4-yl)-3,4-dihydroquinolin-2(1*H*)-one (**1**) and 8-(4-([1,1′-biphenyl]-4-ylmethyl)piperazin-1-yl)quinolin-2(1*H*)-one (**2**) are prepared in the crystalline state and studied by X-ray diffraction. The crystal packing drawing of compound (**1**) indicates that individual molecules are linked by pairs of N—H···O hydrogen bonds forming A—A and B—B inversion dimers, with $R_2^2(8)$ ring motifs. These dimers are stabilized by N—H···O hydrogen bonds and linked via C—H···O short contact interactions forming a two-dimensional network. In the case of compound (**2**), there are two independent molecules A and B linked by pairs of N—H···O hydrogen bonds forming A—A and B—B inversion dimers, with $R_2^2(8)$ ring motifs. These dimers are stabilized by N—H···O hydrogen bonds and linked via C—H···O short contact interactions forming a two-dimensional network.

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Schizophrenia is a severe psychiatric illness afflicting 1 % of the population worldwide. The symptoms of the disease can be grouped as positive and negative, which include disorganized thought, delusions and auditory hallucinations whereas the negative symptoms are emotional flattening, poverty of speech and motivational deficits [1]. The first generation antipsychotics possess side effects such as extrapyramidal symptoms (EPS) and hyperprolactinemia [2] and atypical antipsychotics suffer from limitations such as weight gain, diabetes and an increased risk of seizures and agranulocytosis [3]. A combination of the D2 receptor blockade with the 5-HT1A receptor activation rather than antagonism has been a subject of recent research attention [4, 5]. Indeed, numerous mechanistic considerations [6—8] and preclinical evidence [9—11] support the potential of such a combination. In an ongoing effort, we have synthesized and disclosed dual D2 and 5-HT1A receptor binding affinities of a series of compounds that are the structural analogs of adoprazine and bifeprunox [12, 13].

Herein we wish to report the crystal structure of compounds (**1**) and (**2**) (Fig. 1) obtained by X-ray diffraction studies. The synthesis of these compounds was accomplished as per our earlier reported procedures [14].

Experimental. Suitable crystals for the X-ray analysis of compounds (**1**) and (**2**) were obtained by recrystallization of the final products using a mixture of dichloromethane and methanol in the ratios 2:8 and 8.5:1.5 respectively.

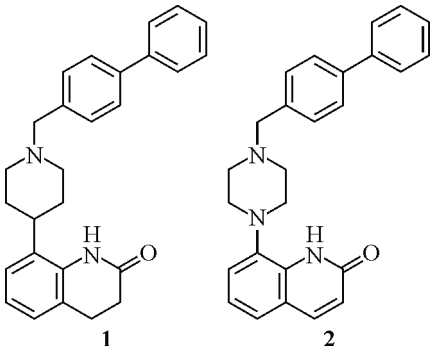

Fig. 1. Chemical structures of compounds (**1**) and (**2**)

X-ray diffraction study. Single crystal data collection for complexes (**1**) and (**2**) were performed at 173 K (–100 °C) on a Stoe Mark II-IPD System [14] equipped with a two-circle goniometer and using MoK_α graphite monochromated radiation. Diffraction data for (**1**) and (**2**) were collected using ω rotation scans of 0—180° at ϕ = 0° and of 0—180° at ϕ = 90° with a step Δω = 1.0°, an exposures of 1 min per image, 2θ range = 2.29—59.53° and $d_{min} – d_{max}$ = 17.779—0.716 Å. The distance between the imaging plate and the sample was 100 mm. The structures were solved by direct methods using the SHELXS program [15]; the refinement and further calculations were carried out using SHELXL [15]. For compound (**1**), the H atoms were included in the calculated positions and treated as riding atoms using SHELXL default parameters. A numerical absorption correction was applied using the X-SHAPE program [14]. For compound (**2**), the bound H atoms were included in the calculated positions and treated as riding atoms using SHELXL default parameters. A semi-empirical absorption correction was applied using the MULSCAN routine in PLATON [16]. For both (**1**) and (**2**) the non-H atoms were refined anisotropically, using the weighted full matrix least squares technique on F^2. Crystal data and refinement details are summarized in Table 1. The molecular structures of (**1**) and (**2**), along with the crystallographic numbering schemes are illustrated in the ORTEP [17] drawings

T a b l e 1

Crystal data and details of the structure refinement for compounds **1** *and* **2**

Compound	**1**	**2**
Formula	$C_{27}H_{28}N_2O$	$C_{26}H_{25}N_3O$
Formula weight	396.51	395.49
Crystal system	Monoclinic	Triclinic
Space group	*P*21/*c*	*P*–1
a, *b*, *c*, Å	13.6265(18), 5.4055(5), 28.282(4)	6.0195(6), 17.5195(17), 19.8616(18)
α, β, γ, deg.	β 95.73(1)	80.820(8), 89.342(8), 88.967(8)
V, Å^3	2072.8(4)	2067.3(3)
Z	4	4
D_x, g/cm^3	1.271	1.271
μ, mm^{-1}	0.08	0.08
F(000)	848	840
Crystal size, mm	0.45×0.30×0.09	0.45×0.29×0.10
Temperature, K	173(2)	173(2)
λMoK_α, Å	0.71073	0.71073
θ_{min}—θ_{max}, deg.	1.5—25.7	1.4—26.1
Range of indices *h*, *k*, *l*	$-16 \le h \le 16$, $-6 \le k \le 6$, $-34 \le l \le 34$	$-7 \le h \le 6$, $-21 \le k \le 21$, $-24 \le l \le 24$
Reflections collected / unique	16914 / 3921, R_{int} = 0.081	23347 / 7831, R_{int} = 0.082
Observed data [$I > 2\sigma(I)$]	1713	4033
T_{min}, T_{max}	0.949, 1.000	0.521, 1.000
N_{ref}, N_{par}	3921, 309	7831, 542
R_1, wR_2, S [$I > 2\sigma(I)$]	0.034, 0.066, 0.63	0.035, 0.073, 0.70
Largest diff. peak / hole, e/Å^3	0.14 / –0.13	0.18 / –0.14

N o t e: $w = [\sigma^2(F_0^2) + (aP)^2 + bP]^{-1}$, where $P = (F_0^2 + 2F_c^2)/3$.

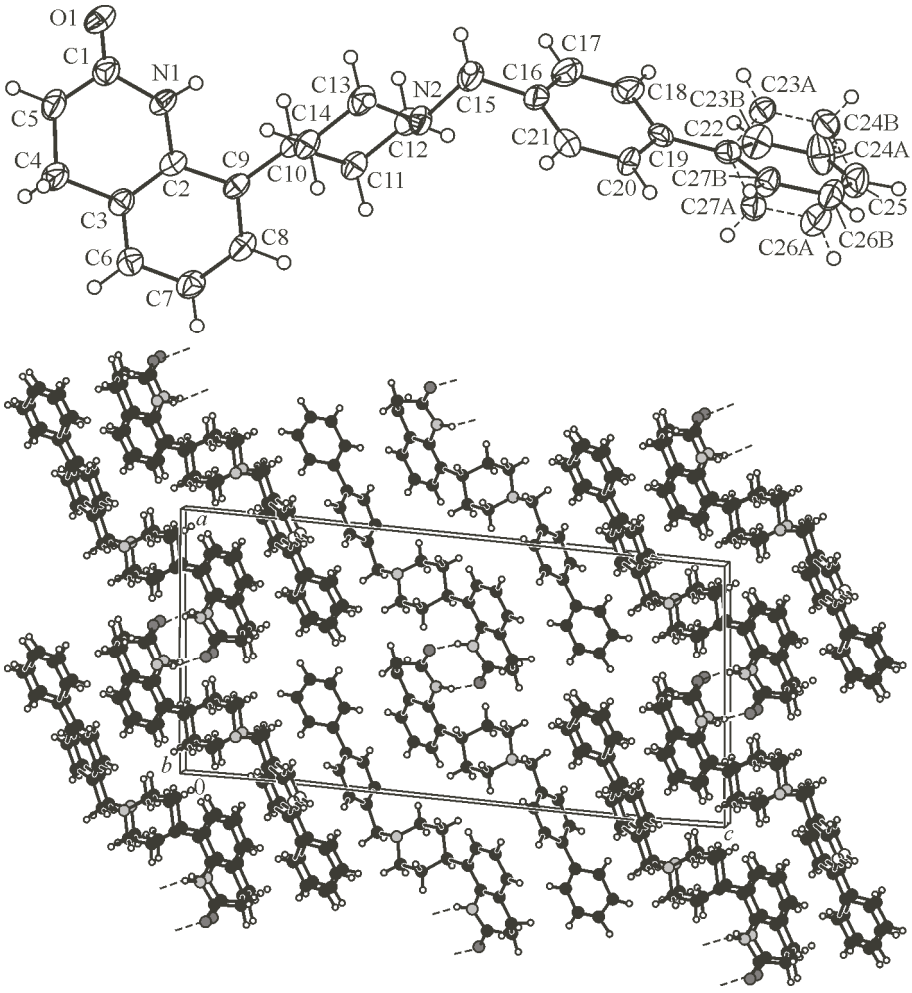

Fig. 2. An ORTEP view of the molecular structure of compound **1** with the atom labeling scheme and a disordered phenyl ring. Displacement ellipsoids are drawn at the 50 % probability level and H atoms are shown as small spheres of arbitrary radii. (O1—C1, 1.226(2) Å; N1—C1, 1.366(2) Å; N2—C15, 1.466(2) Å; C1—N1—C2, 124.34(17)°; C12—N2—C15, 110.35(15)°; O1—C1—N1; 121.29(19)°) (*a*). Crystal packing drawing of compound **1** with a dotted line showing hydrogen bonding interactions (*b*)

(Figs. 2 and 3 respectively). The crystal packing for (**1**) and (**2**) is illustrated in the PLATON [16] drawing (Figs. 2, *b* and 3, *b* respectively).

Results and discussion. The molecular structure of compound (**1**) (molecular formula $C_{27}H_{28}N_2O$) is illustrated in Fig. 2. In the asymmetric unit of compound (**1**) there is an organic molecule with one disordered phenyl ring of the biphenyl moiety, as shown in Fig. 2. The suitable crystal for the X-ray analysis was obtained by recrystallization of the final product using a mixture of dichloromethane and methanol (2:8). The bridging piperidine ring has a *chair* conformation whereas two piperidin-2-one rings of the quinoline moiety have screw *boat* conformations. The mean plane of the central piperidine ring is inclined to the benzene ring of the quinoline moiety by 51.59(10)°, while it is inclined to the adjacent benzene ring of the biphenyl group by 65.58(9)°. In the crystal, individual molecules are linked by pairs of N—H···O hydrogen bonds, forming A—A and B—B inversion dimers with $R_2^2(8)$ ring motifs [18—20]. These dimers are stabilized by N—H···O hydrogen bonds and linked via C—H···O short contact interactions, forming a two-dimensional network. The network is further stabilized by a number of C—H—π interactions, as shown in Fig. 2, *b*. The hydrogen bond angles and bond lengths of compound (**1**) are given in Table 2.

Table 2

Hydrogen-bond geometry (Å, deg.) *in compound* **1**

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*···O1^{i}	0.88	2.14	2.964(2)	155
C13—H13*A*···O1^{i}	0.99	2.53	3.235(2)	128

Symmetry codes: ^{i} $-x+1, -y, -z$.

The molecular structure of compound (**2**) with the molecular formula $C_{26}H_{25}N_3O$ is shown in Fig. 3. The suitable crystal of the compound for the X-ray analysis was obtained by recrystallization from a mixture of CH_2Cl_2 and CH_3OH in the 8:2 ratio. In the asymmetric unit of the compound $C_{26}H_{25}N_3O$, there are two independent molecules (A and B). The conformation of the two molecules is very similar. Each of the bridging piperazine rings has a *chair* conformation. The two benzene rings of the biphenyl moiety are inclined to one another by 39.54(8) and 19.16(9)° in both molecules A and B. The mean plane of the central piperazine ring is inclined to the benzene ring of the quinoline moiety by 72.75(8)° in A and 63.33(8)° in B, while it is inclined to the adjacent benzene ring of the biphenyl group by 69.38(8)° in A and 84.74(9)°, in B. In the crystal, individual molecules are linked by pairs of N—H···O hydrogen bonds, forming A—A and B—B inversion dimers, with $R_2^2(8)$ ring motifs [18—20]. These dimers are stabilized by N—H···O hydrogen bonds and linked via C—H···O short contact interactions forming a two-dimensional network. The network is further stabilized by a number of C—H···π interactions, as shown in Fig. 3, *b*. The hydrogen bond angles and bond lengths of com-

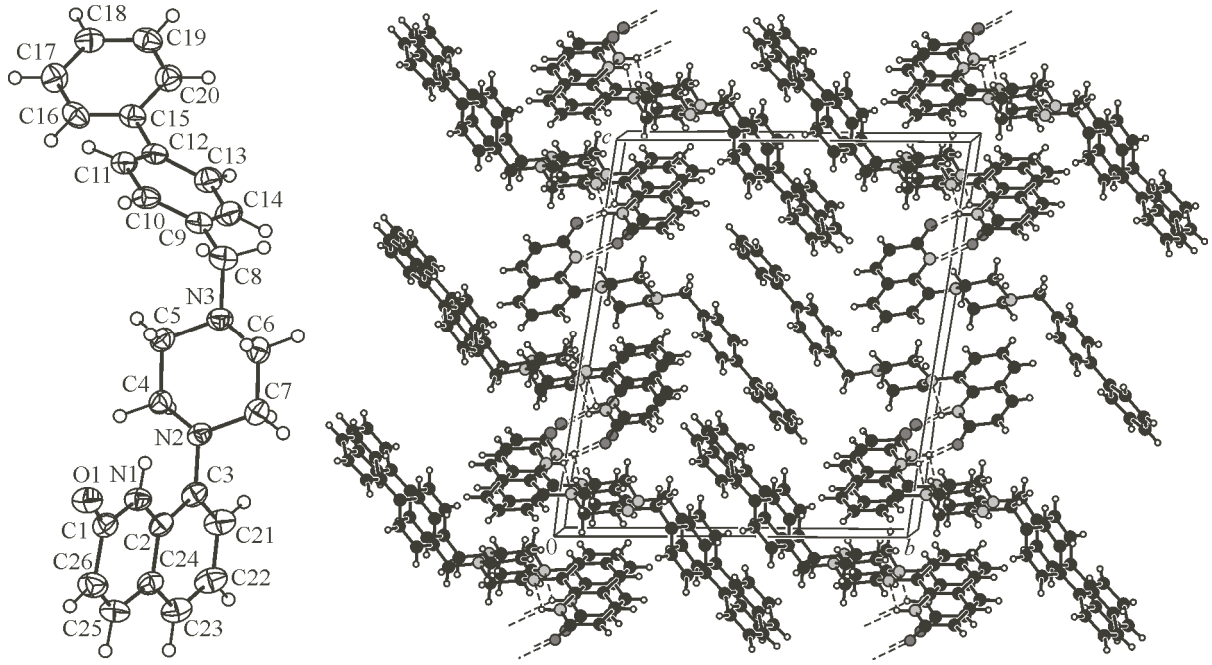

Fig. 3. An ORTEP structure with atom labeling of compound **2**. Displacement ellipsoids are drawn at the 50 % probability level and H atoms are shown as small spheres of arbitrary radii. One of the two independent molecules is removed for clarity of the structure. (The average bond distances and bond angles: O—C 1.238(2) Å; N—CO 1.370(2) Å; N—CC 1.391(2) Å; O—C—N 121.75(16)°; O—C—C 123.04(17)° of the quinoline moiety of A and B type molecules of compound **2**) (*a*). A view of the crystal packing of compound **2**, showing N—H…O Hydrogen bonding and C—H…O short contact interaction resulting in the formation of a two-dimensional network (*b*)

Table 3

Hydrogen-bond geometry (Å, deg.) *in compound* **2**

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*···N2	0.88	2.40	2.772(2)	106
N1—H1*N*···O2^{i}	0.88	2.09	2.9300(18)	160
C7—H7*B*···O1^{ii}	0.99	2.55	3.528(2)	168
N4—H4*N*···O1^{i}	0.88	2.13	2.9516(18)	155
C30—H30*B*···O2^{ii}	0.99	2.64	3.550(2)	152
C32—H32*B*···O1^{i}	0.99	2.50	3.362(2)	146

Symmetry codes: ^{i} $-x, -y, -z+1$; ^{ii} $x+1, y, z$.

pound (**2**) are given in Table 3. In conclusion, the bond lengths and bond angles of compounds (**1**) and (**2**) are very close to the corresponding ones found in the Cambridge structural database [19—20].

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Supplementary crystallographic data of CCDC deposit number are 990357 and 990358 for complexes **1** and **2** respectively and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by e-mailing data_request@ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(0)1223-336033.

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