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Crystal Structure and Structural Features of 8a-Phenylhexahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-One †

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† Presented at the 1st International Electronic Conference on Crystals, 21–31 May 2018. Available online: https://sciforum.net/conference/IECC_2018.

Published: 21 May 2018

Abstract: The crystal structure and the structural features of the 8a-phenylhexahydropyrrolo[1,2-*a*]pyrimidine-6(2*H*)-one, $C_{13}H_{16}N_2O$, obtained by condensation of 4-phenyl-4-oxobutanoic acid with 1,3-diaminopropane. Molecules are weakly linked by the intermolecular hydrogen bonds C=O···H–N into the chains. These chains are weakly linked by π-π stacking interactions to form a three-dimensional framework.

Keywords: 8a-phenylhexahydropyrrolo[1,2-*a*]pyrimidine-6(2*H*)-one; crystal structure; intermolecular hydrogen bonds; π-π stacking interactions

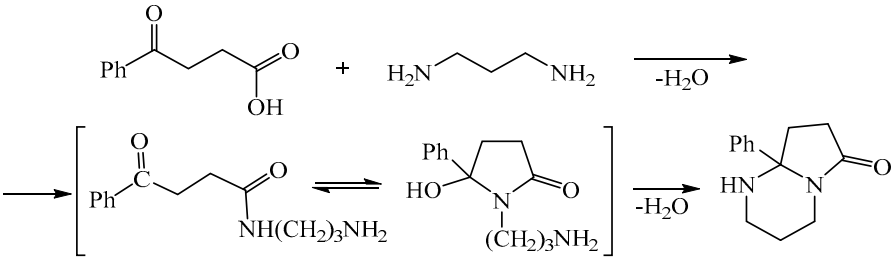
1. Introduction

The construction of heterocyclic systems including pyrrolidone (lactam) and fused imida-/oxa-/thiazolidine as well as tetrahydropyrimidine or 1,3-oxazinane fragments is quite relevant due to the broad spectrum of biological activity exhibited by these molecules. Particularly, they exhibit antimicrobial, antifungal, anti-HIV and anti-tuberculosis activity [1–3].

8a-Phenylhexahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one may be proposed to have great conformational capabilities due to the presence of two fused saturated heterocycles with the only one aromatic substituent.

2. Results

8a-Phenylhexahydropyrrolo[1,2-*a*]pyrimidine-6(2*H*)-one was obtained by condensation of 4-phenyl-4-oxobutanoic acid with 1,3-diaminopropane in toluene with azeotropic removal of water (Scheme 1):



Scheme 1. Synthesis of 8a-phenylhexahydropyrrolo[1,2-*a*]pyrimidine-6(2*H*)-one.

As was shown by the spectral data of obtaining product, the reaction didn't stop at the amide or pyrrolone stage, but goes via two heterocyclization with the formation of bicyclic system.

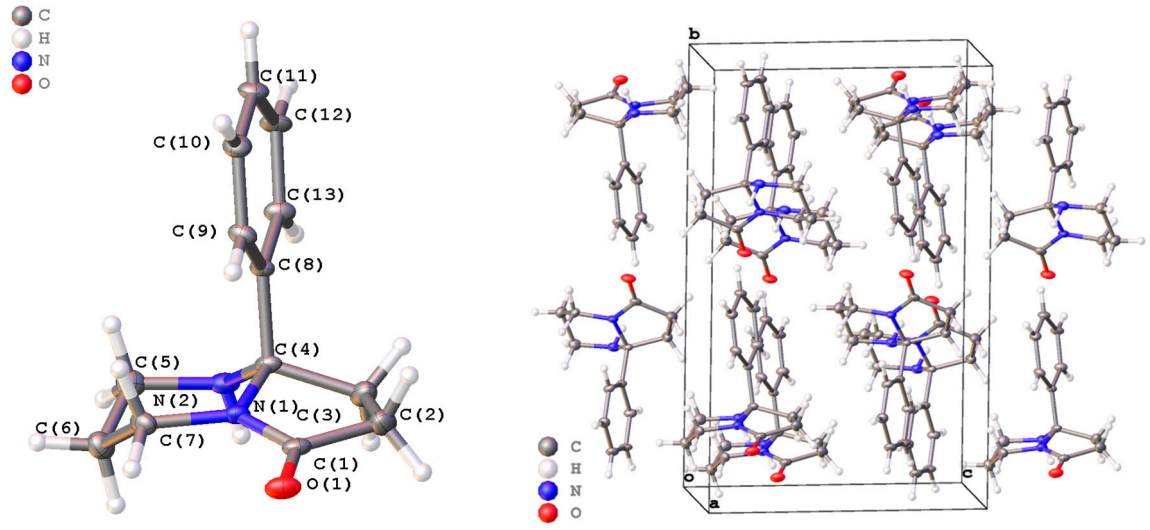
Titled compound, $C_{13}H_{16}N_2O$, crystallizes with $Z = 4$ in the space group $P2_1/n$ with cell volume of 1109.6(4) Å^3 [a = 6.0910(13) Å, b = 17.016(4) Å, c = 10.707(2) Å, β = 90.581(5)°]. The crystal structure of the titled compound with atom labaling is present on the Figure 1a, and the crystal packing is on Figure 1b.

In hexahydropyrimidine cycle, interatomic distances between carbon atoms are aroud 1.52 Å, which is in harmony with similar strutures including hexahydropyrimidine ring (CCDC codes: AFIFAX01, FOWQAK, GAXNAX). C···N distances of about 1.47 Å are typical for substituted hexahydropyrimidine (1.45–1.48 Å) [4–6]. The C(4)-N(2) distance of 1.437(4) Å is abnormally shorter than corresponding bond in mentioned above analogs. Hexahydropyrimidine cycle adopts "chair" conformation with angles in 109.6(2)–113.0(2)° range, which are comparable with corresponding cyclohexane ring angles (109°28′) and unsubstituted hexahydropyrimidine (CCDC codes: AFIFAX01, FOWQAK, GAXNAX), excluding angle C(7)-N(1)-C(4) of 119.0(2)°, which is abnormally large in comparison to mentioned structures.

Pyrrolidone cycle is non-planar and adopts twisted envelope conformation. According to the angles and dihedral angles, this portion of molecule is very similar to that in corresponding 3a-phenyl-2,3,3a,4-tetrahydro-1*H* benzo[*d*]pyrrolo[1,2-*a*]imidazol-1-one reported previously [7].

The most pronounced distinction from planarity in the whole fused molecule can be illustrated by values 47.9(3)° and 136.8(2)° of the C(5)-N(2)-C(4)-N(1) and the C(1)-N(1)-C(4)-N(2) torsion angles, correspondingly.

In the crystal there is an intermolecular hydrogen bonds between molecules with parameters given in Table 1.



(**a**) (**b**)

Figure 1. 8a-Phenylhexahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one: (**a**) Crystal structure with atom labeling. Displacement ellipsoids are drawn at the 50% probability level; (**b**) Packing diagram in crystal.

Table 1. Hydrogen bond for 8a-phenylhexahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one.

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2N)...O(1) [1]	0.90	2.27	3.098(3)	153

[1] Symmetry transformations used to generate equivalent atoms: x + 1,y,z.

3. Discussion

8a-Phenylhexahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one is a bicyclic molecule consisted of two portions, namely hexahydropyrimidine and pyrrolidone cycles. Considering hexahydropyrimidine

moiety, one can noticed that it is very similar to corresponding ones of analogues structures known from literature. The pyrrolidone cycle is also comparable with related structures based on 4-aryl-4-oxobutanoic acid and different diamino binucloephiles. The most pronounced difference is due to the enfluence of rings each to other, which manifests in increasing of planarity in this part of molecule, that restricts the conformational capabilities of the whole system.

The intermolecular arrangement of the titled compound appears as one-dimensional chains. Molecules are connected via intermolecular hydrogen bonds with H···O interatomic distance larger than expected in similar structures, so these H-bonds are relatively weak.

The aromatic rings at 8a position may take part in non-covalent π-π interactions like parallel-displaced stacking. The common parameters of these interactions such as interplanar distance, ring offset and the θ angle allow us to propose the very low energy of these interactions (data not shown). But, we believe they give some contribution into the packing of the titled molecule and play important role in stability of the crystal.

4. Materials and Methods

One g (5 mmol) of 4-phenyl-4-oxobutanoic acid and 0.562 mL (5 mmol) of 1,3-diaminopropane were placed into round-bottom flask, then 30 mL of toluene was added to the mixture and the reaction mixture was refluxed for 3–4 h. After being left to stand overnight, the separated crystals or precipitate was washed with acetone and it is placed in a vacuum desiccator for drying. If necessary, it may be recrystallized from acetone. Yield 0.74 g (61%), mp 126–129 °C. FTIR spectrum, ν, cm^{-1}: 3437 (NH), 1672 (C=O), 2985–2857 (C–H). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.39 s (1H, NH), 1.90–2.45 m, 2.00–2.15 m [2H, C(8) and C(7)], 2.55–2.96 m [2H, C(2)], 7.29–7.42 m [5H, C(8a)], 4.07 d.d.t [J = 13.2, 4.9, 1.6 Hz, 2H, C(4)]. Found, %: C 71.96; H 7.65; N 12.33. $C_{13}H_{16}N_2O$. Calculated, %: C 72.22; H 7.41; N 12.96.

X-ray diffraction was performed on an automatic three-circle diffractometer Bruker SMART Apex II (graphite monochromator, λ(MoKα) = 0.71073 Å, ω scan) at 120 K. Integration of intensities was carried out using the procedure built into the software complex SAINT [8]. Semi-empirical corrections for absorption and for systematic errors are based on the intensity of equivalent reflections in the program SADABS [9]. The structure was solved by a direct method and was refined by full-matrix least-squares versus F^2_{hkl} with anisotropic displacement parameters for all non-hydrogen atoms. The hydrogen atoms were placed in the calculated positions and were refined geometrically by using a riding model with U_{iso}(H) = 1.2 U_{iso}(C) and U_{iso}(H) = 1.5 U_{iso}(C) for methyl and other groups. Solving and refinement were carried out using the SHELX software package version 2016/6 [10]. The overlays and packing diagrams as well as parameters of non-covalent interactions were obtained using Olex2 software (ver. 1.2.8) [11].

Author Contributions: E.L. and E.K. carried out the synthesis of reported compound and obtained the single crystal, E.K. drafted the manuscript, V.G. took part in the spectral characterization of synthesized compound, prepared final version of the manuscript and translated it into English, assisted technically, A.Y. designed and supervised all experiments, and manuscript drafting. All authors read and approved the final version of the manuscript.

Acknowledgments: The work was supported by the RFBR (research project No. 16-03-00530).

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

MDPI	Multidisciplinary Digital Publishing Institute
DOAJ	Directory of open access journals
CCDC	The Cambridge Crystallographic Data Centre
RFBR	Russian Foundation for Basic Research

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