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STRUCTURE OF ORGANIC  
COMPOUNDS

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## Crystal Structure and Computational Study of 5-Ethyl-4-(4-Methoxyphenethyl)-4,5-Dihydro-3*H*-1,2,4- Triazol-3-One and 4-(4-Methoxyphenethyl)-5- Propyl-4,5-Dihydro-3*H*-1,2,4-Triazol-3-One

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**Abstract**—Molecular structures of compounds 5-ethyl-4-(4-methoxyphenethyl)-4,5-dihydro-3*H*-1,2,4-triazol-3-one, (C<sub>13</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>) (**I**) and 4-(4-methoxyphenethyl)-5-propyl-4,5-dihydro-3*H*-1,2,4-triazol-3-one, (C<sub>14</sub>H<sub>19</sub>N<sub>3</sub>O<sub>2</sub>) (**II**) were studied by single crystal X-ray diffraction. Molecular compound **I** crystallizes in the monoclinic space group *P*2<sub>1</sub> with *Z* = 2, while molecular compound **II** crystallizes in the monoclinic space group *P*2<sub>1</sub>/*c* with *Z* = 4. The molecular geometries of the compounds **I** and **II** were optimized using computational quantum mechanical methods: the density functional theory and the Hartree–Fock approximation. Theoretical values of bond lengths, bond angles, and torsion angles were obtained using the BL3YP functional and the 6-31G+(d) basis. The results show that theoretical values are consistent with experimental values.

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### INTRODUCTION

Five-membered heterocycles are increasingly important in medical chemistry. Especially 1,2,4-triazole derivatives have a wide spectrum of biological activity, including anti-tuberculosis, antimalarial, antioxidant, antimicrobial, anti-inflammatory, antiviral, cytotoxic, anticonvulsant, antiproliferative, anti-depressant, hypoglycemic, anticancer, antipyretic and analgesic activities [1–4]. In addition, flucanazole and itraconazole, which have a triazole nucleus, are effective against fungal growth in biological systems [5]. Due to the importance of the items researched in this work, the results of experimental and theoretical studies were compared to determine the structure details.

### EXPERIMENTAL

#### *Synthesis*

The compounds were synthesized according to [6].

#### *X-Ray Data Collection*

X-ray diffraction patterns were obtained on a Bruker diffractometer [7, 8]. Single crystals of com-

pounds **I** and **II** were grown in the form of blocks. Crystals with approximate sizes of 0.500 × 0.300 × 0.200 mm for **I** and 0.55 × 0.50 × 0.45 mm for **II** were chosen for further measurements (MoK<sub>α</sub> radiation, λ = 0.71073 Å, ω scan technique at 293 K). Data reduction was performed using the APEX2 [8] and SAINT software [7]. The crystal structures of the title compounds were solved and refined by direct methods and full-matrix least square procedure using the SHELXS-97 [9, 10] and SHELXL-97 programs [9, 10]. The ORTEP-3 program [11] for MS Windows has been preferred for the visualization of figures. WinGX [11] was used to prepare data for publication.

The parameters of all atoms of compounds **I** and **II**, except hydrogen, were refined in the anisotropic approximation of atomic displacements. The H1 atoms attached to N1 and N2 atoms were localized from difference Fourier map and their parameters were refined in the isotropic approximation. Other H atoms were positioned with idealized geometry and refined using isotropic temperature factors and C–H distances of 0.93–0.96–0.97 Å with *U*<sub>iso</sub>(H) = 1.2*U*<sub>eq</sub>(C) and 1.5*U*<sub>eq</sub>(C). Crystallographic data, struc-

**Table 1.** Crystal data, details of data collection, and results of structure refinement for the compounds  $C_{13}H_{17}N_3O_2$  (**I**) and  $C_{14}H_{19}N_3O_2$  (**II**)

	Compound <b>I</b>	Compound <b>II</b>
Formula	$C_{13}H_{17}N_3O_2$	$C_{14}H_{19}N_3O_2$
<i>M</i>	247.30	261.32
<i>T</i> , K	293	293
Crystal system, sp. gr., <i>Z</i>	Monoclinic, $P2_1$ , 2	Monoclinic, $P2_1/c$ , 4
<i>a</i> , <i>b</i> , <i>c</i> , Å	7.3529(2), 7.7617(2), 11.3557(2)	7.9592(7), 6.4084(4), 28.7320(19)
$\beta$ , deg	95.142(2)	104.787(7)
<i>V</i> , Å <sup>3</sup>	645.47(3)	1416.96(18)
$\mu$ , mm <sup>-1</sup>	0.088	0.084
<i>F</i> (000)	264	560
$\theta_{\min}$ , $\theta_{\max}$ , deg	1.80, 26.50	3.26, 26.48
Limiting indices <i>h</i> , <i>k</i> , <i>l</i>	$-9 \leq h \leq 8$ , $-9 \leq k \leq 5$ , $-13 \leq l \leq 14$	$-9 \leq h \leq 9$ , $-7 \leq k \leq 6$ , $-36 \leq l \leq 29$
Reflections used	1739	2822
<i>R</i> <sub>1</sub>	0.038	0.075
<i>S</i>	1.079	1.019
$\Delta\rho_{\min}/\Delta\rho_{\max}$ , e/Å <sup>3</sup>	-0.285/0.208	-0.163/0.126

ture solution and refinement results are listed in Table 1, the CCDC reference numbers are 1957024 and 1957025 for crystals **I** and **II**, respectively.

used as initial atomic parameters in theoretical calculations.

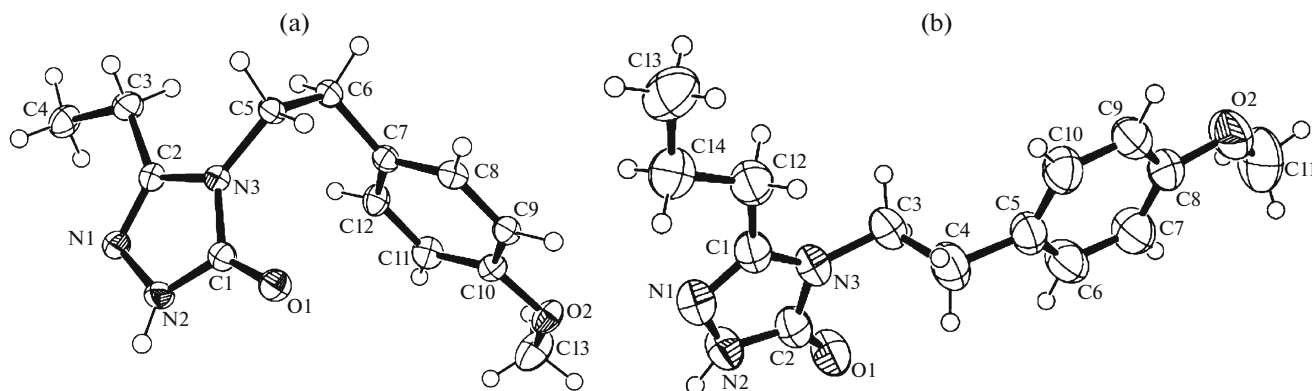
### Theoretical Analysis

The geometry was optimized for the compounds **I** and **II** of triazole derivatives in gas phases using the density functional theory (DFT) with the B3LYP functional and Hartree–Fock (HF) approximation with the 6-31G+(d) basis [12–15]. Theoretical calculations were performed using the Gaussian03 program [16]. For this aim, X-ray diffraction (XRD) data are

## RESULTS AND DISCUSSION

### X-Ray Diffraction Study

The molecular structures of compounds **I** and **II** were obtained by single crystal XRD technique. Compound **I** crystallizes in the monoclinic sp. gr.  $P2_1$  with  $Z = 2$ , while compound **II** crystallizes in the sp. gr.  $P2_1/c$  with  $Z = 4$ . The asymmetric unit in both compounds contains one molecule (Fig. 1). The bond lengths and



**Fig. 1.** Molecules of (a)  $C_{13}H_{17}N_3O_2$  and (b)  $C_{14}H_{19}N_3O_2$ .

**Table 2.** Hydrogen bond geometry for compound **I**

$D-H\cdots A$	$D-H$ , Å	$H\cdots A$ , Å	$D\cdots A$ , Å	$D-H\cdots A$ , deg
$N2-H1\cdots O1^i$	0.85(3)	1.90(3)	2.754(2)	175(2)
$C5-H5A\cdots O1^{ii}$	0.97	2.60	3.513(2)	157.2
$C6-H6A\cdots O2^{iii}$	0.97	2.56	3.457(2)	153.5
$C8-H8\cdots O1^{ii}$	0.93	2.53	3.392(2)	154.1

Symmetry code: (i)  $-x + 1, y - 1/2, -z + 1$ ; (ii)  $-x + 1, y + 1/2, -z + 1$ ; (iii)  $x + 1, y, z$ .

**Table 3.** Hydrogen bond geometry for compound **II**

$D-H\cdots A$	$D-H$ , Å	$H\cdots A$ , Å	$D\cdots A$ , Å	$D-H\cdots A$ , deg
$N2-H1\cdots O1^i$	0.91(2)	1.89(2)	2.789(2)	167(2)

Symmetry code: (i)  $-x + 2, -y + 2, -z + 1$ .

angles in **I** and **II** have normal values [17, 18]. In **I**, the triazole ring is twisted by  $63.17(1)^\circ$  with respect to the benzene ring, whereas in compound **II** the corresponding dihedral angle is only  $2.71(1)^\circ$ , which indicates that both ring systems are almost coplanar.

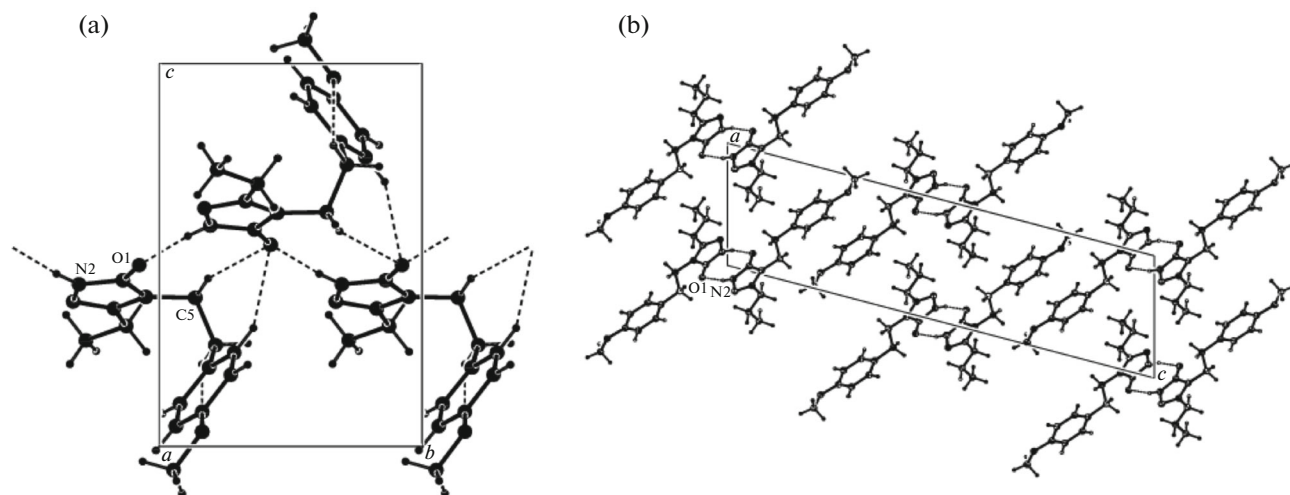
In **I**, the crystal packing is consolidated by the  $N-H\cdots O$  and  $C-H\cdots O$  hydrogen bonds, namely,  $N2-H1\cdots O1$ ,  $C5-H5A\cdots O1$ ,  $C6-H6A\cdots O2$ , and  $C8-H8\cdots O1$ , which generate eight-membered ring, producing  $R_2^2(9)$  and  $R_2^1(7)$  motifs [17] (Table 2). In **II**, molecules are joined by hydrogen bonds of the  $N-H\cdots O$  type (Table 3), namely,  $N2-H1\cdots O1$  (symmetry code:  $-x - 1, -y - 2, -z - 1$ ), which links molecules into centrosymmetric pairs, forming a  $R_2^2(8)$  motif [19]. The molecule packing in both compounds is shown in Fig. 2.

### Optimized Geometry

Geometric parameters, such as bond lengths, bond angles, and torsion angles, were tested with the basis set 6-31G+(d) using DFT/B3YLP and HF methods to determine if they are compatible with the experimental values. The results showed that, although most of the parametric values were almost close to the experimental data, the bridge  $C7-C6-C5-N3$  torsion angle in compound **I** was calculated as  $60.68^\circ$  and  $59.40^\circ$  using DFT/BYLP and HF, respectively. The bridge torsion angle  $N3-C3-C4-C5$  in compound **II** was calculated as  $177.03^\circ$  and  $177.96^\circ$  using DFT/BYLP and HF, respectively. The XDR values of these torsion angles are  $63.3(4)^\circ$  and  $172.47(15)^\circ$  for compounds **I** and **II**, respectively.

The root mean square errors were calculated for bond lengths and angles. The calculated values with the selected basis set of DFT/B3YLP and HF methods were  $0.014$  Å and  $0.88^\circ$ ,  $0.015$  Å and  $0.87^\circ$  for compound **I**,  $0.019$  Å and  $0.59^\circ$ ,  $0.016$  Å and  $0.57^\circ$  for compound **II**, respectively. The results showed that the HF method gives the best results for the studied molecular structures, although both methods give approximate results. Some selected geometric parameters are shown in Tables 4 and 5.

The structure determined by XRD and geometry optimized by DFT/B3YLP and HF methods with the



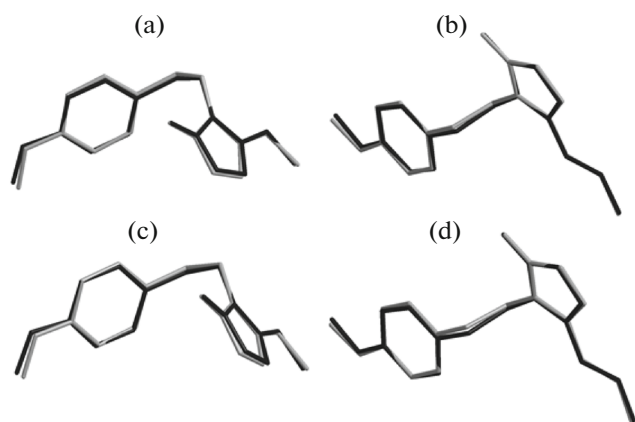
**Fig. 2.** Packing of the molecules of (a)  $C_{13}H_{17}N_3O_2$  and (b)  $C_{14}H_{19}N_3O_2$ .

**Table 4.** The experimental and calculated values of selected bond lengths (Å), bond angles, and torsion angles (deg) for I

Parameter	XRD	DFT	HF
O1–C1	1.240(3)	1.2252	1.2033
N3–C1	1.381(3)	1.4054	1.3807
N3–C2	1.378(3)	1.3871	1.3799
N3–C5	1.465(2)	1.4572	1.4527
C1–N2	1.349(3)	1.3739	1.3497
N2–N1	1.391(2)	1.3784	1.3677
C7–C6	1.515(3)	1.5135	1.5132
O2–C10	1.374(2)	1.368	1.349
O2–C13	1.427(3)	1.4206	1.3992
C6–C5	1.529(3)	1.5452	1.5357
N1–C2	1.297(3)	1.3041	1.2717
C1–N3–C2	107.63(17)	108.1114	107.528
C1–N3–C5	123.91(17)	122.3629	122.8555
C2–N3–C5	128.32(17)	129.4806	129.5567
O1–C1–N2	128.3(2)	129.8808	129.3561
O1–C1–N3	127.91(19)	128.1759	127.9036
C10–O2–C13	117.02(17)	118.5115	119.8867
C7–C6–C5	115.20(16)	114.7571	114.9528
O2–C10–C11	124.65(19)	124.6679	124.7299
O2–C10–C9	115.43(18)	115.8176	115.9295
N3–C5–C6	113.57(17)	114.6572	114.6259
C2–C3–C4	113.9(2)	113.3728	113.2599
C12–C7–C6–C5	–109.0(4)	99.1841	103.2898
C8–C7–C6–C5	72.9(4)	80.0799	76.6462
C13–O2–C10–C11	–2.6(6)	1.7228	1.912
C13–O2–C10–C9	177.9(4)	178.5846	178.3356
C1–N3–C5–C6	–107.1(3)	107.5582	105.9452
C2–N3–C5–C6	76.1(4)	75.1877	77.2327
N1–C2–C3–C4	6.7(6)	–6.5569	3.9511
N3–C2–C3–C4	–176.2(3)	172.2429	174.823

**Table 5.** The experimental and calculated values of selected bond lengths (Å), bond angles, and torsion angles (deg) for II

Parameter	XRD	DFT	HF
C1–N1	1.298(2)	1.3046	1.2723
C1–N3	1.376(2)	1.3862	1.3786
C2–O1	1.237(2)	1.2275	1.2056
C2–N2	1.347(2)	1.3733	1.3485
C2–N3	1.376(2)	1.4017	1.3772
C3–N3	1.459(2)	1.4581	1.4539
C3–C4	1.515(3)	1.5436	1.5333
C4–C5	1.508(2)	1.5134	1.5132
C11–O2	1.410(3)	1.4214	1.4001
N1–N2	1.389(2)	1.3792	1.3688
C8–O2	1.375(2)	1.3679	1.3489
O1–C2–N2	129.57(17)	130.119	129.6601
O1–C2–N3	126.67(15)	127.870	127.5244
N3–C3–C4	112.49(14)	112.8912	112.5807
C5–C4–C3	110.91(14)	111.8208	111.9279
C7–C8–O2	124.71(18)	124.6518	124.6742
O2–C8–C9	115.77(17)	115.8602	116.0141
C1–C12–C13	114.54(15)	113.7557	113.6713
C12–C13–C14	111.96(17)	111.9998	111.6656
C1–N3–C2	107.95(13)	108.2598	107.6813
C1–N3–C3	129.38(14)	129.4874	129.5919
C2–N3–C3	122.36(15)	122.218	122.7105
C8–O2–C11	118.17(17)	118.537	119.9303
C3–C4–C5–C6	–84.4(2)	85.6204	–86.8301
C3–C4–C5–C10	93.3(2)	92.6504	91.9281
N1–C1–C12–C13	–2.2(3)	2.5558	3.4102
N3–C1–C12–C13	176.15(16)	178.5771	–177.4477
C4–C3–N3–C1	86.5(2)	93.5828	94.9801
C4–C3–N3–C2	–86.3(2)	84.0084	–83.3612
C7–C8–O2–C11	5.1(3)	0.0187	–0.1684
C9–C8–O2–C11	–174.6(2)	179.7383	179.6105



**Fig. 3.** Superimposed images of the structures of compounds (a, c) **I** and (b, d) **II** according to XRD (black) and theoretical values (grey) obtained using (a, b) DFT and (c, d) HF.

6-31G+(d) basis set are superimposed in Fig 3. Although the overall superimposition is in good agreement, most deviations from the superimposition were observed in the triazole ring for compound **I**. These deviations are assumed to occur because the theoretical calculations are based on the gas phase of the compound, while the experimental results are based on its solid phase.

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#### REFERENCES

1. Y. Ünver, S. Deniz, F. Çelik, et al., *J. Enzym Inhib. Med. Chem.* **31** (3S), 89 (2016).
2. Y. Ünver and E. Bektaş, *Lett. Drug Design Discovery*, **15** (7), 706 (2018).
3. Y. Ünver, E. Bektaş, and Ş. Direkel, *Russ. J. Gen. Chem.* **88**, 2616 (2018).
4. Y. Ünver and H. Tanak, *Crystallogr. Rep.* **53**, 585 (2018).
5. F. Çelik, Y. Ünver, B. Barut, et al., *Med. Chem.* **14**, 230 (2018).
6. Y. Ünver, S. Meydanal, K. Sancak, et al., *Turk. J. Chem.* **35**, 265 (2011).
7. Bruker, *SAINT* (Bruker AXS Inc., Madison, Wisconsin, USA, 2002).
8. Bruker, *APEX2* (Bruker AXS Inc., Madison, Wisconsin, USA, 2005).
9. G. M. Sheldrick, *Acta Crystallogr. A* **64**, 112 (2008).
10. G. M. Sheldrick, *Acta Crystallogr. C* **71**, 3 (2015).
11. L. J. Farrugia, *J. Appl. Crystallogr.* **45**, 849 (2012).
12. A. D. Becke, *J. Chem. Phys.* **98** (7), 5648 (1993).
13. C. Lee, W. Yang, and R. G. Parr, *Phys. Rev. B* **37** (2), 785 (1998).
14. H. B. Schlegel, *J. Comput. Chem.* **3** (2), 214 (1982).
15. C. Peng, P. Y. Ayala, H. B. Schlegel, and M. J. Frisch, *J. Comput. Chem.* **17** (1), 49 (1996).
16. M. J. Frisch, G. W. Trucks, H. B. Schlegel, et al., *Gaussian 03* (Wallingford, Conn., USA, 2004).
17. S. Öztürk Yildirim, R. J. Butcher, D. Ünlüer, and Y. Köysal, *Acta Crystallogr. E* **68**, o1651 (2012).
18. F. H. Allen, O. Kennard, D. G. Watson, et al., *R. J. Chem. Soc. Perkin Trans. 2*, S1 (1987).
19. J. Bernstein, R. E. Davies, L. Shimoni, and N.-L. Chang, *Angew. Chem. Int. Ed. Engl.* **34**, 1555 (1995).