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КРАТКИЕ СООБЩЕНИЯ

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CRYSTAL AND MOLECULAR STRUCTURE OF (±)-2-[(1*S*,3*S*)-3-ACETYL-2,2-DIMETHYLCYCLOBUTYL]-N-(*p*-TOLYL)ACETAMIDE

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The structure of (±)-2-[(1*S*,3*S*)-3-acetyl-2,2-dimethylcyclobutyl]-N-(*p*-tolyl)acetamide has been determined by single crystal X-ray diffraction analysis. The crystal belongs to triclinic system, space group *P*-1, a = 8.8700(18) Å, b = 10.331(2) Å, c = 10.363(2) Å, α = 71.11(3)°, β = 65.06(3)°, γ = 72.18(3)°, V = 798.6(3) Å^3, Z = 2, formula unit $C_{17}H_{23}NO_2$. The title compound has a fragment of 2,2-dimethylcyclobutane and its conformation represents *semi-chair*. The intermolecular hydrogen bonds N—H···O and C—H···O are revealed.

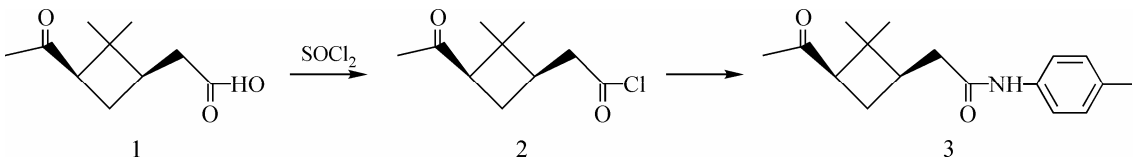
K e y w o r d s: single crystal X-ray diffraction, crystal structure, terpenes, pinonic acid, cyclobutane fragment, hydrogen bond.

Terpenes are convenient chiral precursors due to their availability and low cost; among them, α-pinene (both enantiomers) and verbenone are prominent. For instance, α-pinene has been used as starting material for the production of some compounds of industrial interest [1]. Chiral cyclobutane compound, pinonic acid, can be synthesized from α-pinene. Many derivatives of pinonic acid have interesting biological properties. For instance, the synthesis of cyclobutane analogues of the nucleoside oxetanocin has been the subject of great interest during the last years because of their activity against the human immunodeficiency virus (HIV) [2].

We synthesized several derivatives of pinonic acid. In our previous works we have reported the crystal structure of 2-[(1*S*,3*S*)-3-acetyl-2,2-dimethylcyclobutyl]-N-(2,6-difluorophenyl)acetamide and 2-[(1*S*,3*S*)-3-acetyl-2,2-dimethylcyclobutyl]-N-(*m*-tolyl)acetamide [3, 4]. In the present contribution, the synthesis of an acetamide derivative of pinonic acid has been performed according to the scheme shown in Fig. 1.

In order to determine the structure and configuration of compound **3**, single-crystal X-ray diffraction study has been carried out.

Experimental. Synthesis. Pinonic acid (27 mmol) and thionyl chloride (32 mmol) were dissolved in dichloromethane (50 ml). The resulting mixture was refluxed for 8 h. After refluxing the solvent was distilled away under vacuum and the remainder was 2-(3-acetyl-2,2-dimethylcyclobutyl)acetyl chloride. The acetyl chloride reacted with *p*-toluidine (27 mmol) for 24 h using dichloro-



1 2 3

Fig. 1. Synthetic route for the title compound

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Table 1

Selected Crystallographic Data and Experimental Parameters

Gross formula	$C_{17}H_{23}NO_2$
M	273.36
Temperature, K	293(2)
Crystal system, space group	Triclinic, P-1
a, b, c, Å	8.8700(18), 10.331(2), 10.363(2)
α, β, γ, deg.	71.11(3), 65.06(3), 72.18(3)
V, Å^3	798.6(3)
Z	2
D_{calc}, g/cm^3	1.137
Crystal dimensions, mm	0.40×0.30×0.20
Absorption coefficient, mm^{-1}	0.074
Measured / observed reflections	3084 / 2882
R_{int}	0.0643
Refined parameters	181
R factors [$I > 2\sigma(I)$]	$R1 = 0.0841$, $wR2 = 0.2017$
R factors (all data)	$R1 = 0.1399$, $wR2 = 0.2734$
CCDC deposition number	672003

methane as solvent. After the reaction was complete, the solvent was distilled away and the crude title compound was isolated. The pure compound was obtained by crystallizing from a mixture of ethanol (40 ml) and water (40 ml). The yield of the title compound was 36.4 %. Crystals of the title compound suitable for X-ray diffraction were obtained by slow evaporation of its solution in ethanol.

X-ray diffraction study. Experimental X-ray diffraction data were obtained on an Enraf-Nonius CAD4 diffractometer (graphite-monochromated MoK_α radiation, $\lambda = 0.71073$ Å) by $\omega/2\theta$ scanning. Data were collected in the θ-range of 2.1—25.2° (range of indices: $-9 \le h \le 10$, $-11 \le k \le 12$, $0 \le l \le 12$). The structure was solved and refined with SHELX-97 software [5]. All H atoms were placed geometrically, with the C—H distances in the range 0.93—0.98 Å and N—H distances 0.86 Å, and included in the refinement in riding motion approximation with $U_{iso}(H) = 1.2$ or $1.5U_{eq}(H)$ of the carrier atom.

Selected crystallographic data and experiment parameters are listed in Table 1. Full crystallographic data for the compound of this study have been deposited with Cambridge Crystallographic Data Centre (www.ccdc.cam.ac.uk), CCDC deposition number 672003. These data are available free of charge at www.ccdc.cam.ac.uk/data_request.cif.

Results and Discussion. The raw material, pinonic acid, was synthesized according to early classical procedures described in the literature for the oxidation of α-pinene. However the epimerization of the cyclobutane carbon C3 linked to the ketone carbonyl occurs in the process of oxidation. Therefore, pinonic acid is a mixture of two diastereomers. The presence of these isomers is evidenced by the absorption signals for the CH_3 protons of C7 and C8 which show two sets of singlets at 0.89/1.34 (major) and 0.99/1.21 ppm (minor) in the ^{1}H NMR spectrum of the title product. This is consistent with previously reported results [6].

Fig. 2 illustrates the structure of a crystallographically independent molecule of (±)-2-[(1*S*,3*S*)-3-acetyl-2,2-dimethylcyclobutyl]-N-(p-tolyl)acetamide. As a whole, the molecule is substantially nonplanar. Carbon atoms of benzene ring, C11, C12, C13, C14, C15, C16, and substituted C17 are situated virtually in one plane while C10, C11, N are in another plane. The dihedral angle between the planes is 13.1°.

The 2,2-dimethylcyclobutane fragment is not flat and the conformation represents *semi-chair*. The cyclobutane ring is flexed as though folded from the dimethylsubstituted C atom to the unsubsti-

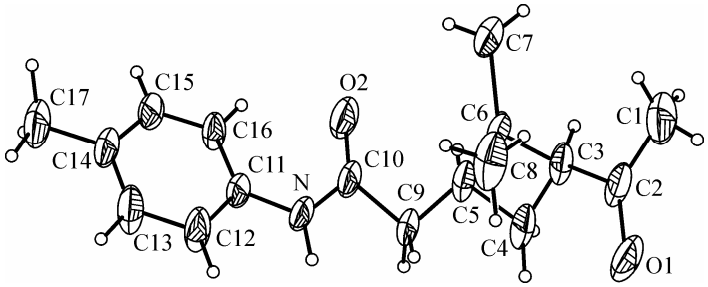

Fig. 2. View of molecular structure of the title compound. Thermal ellipsoids are drawn at 30 % probability level

Table 2

Hydrogen Bond Geometry (Å, deg.)

D—H…A	D—H	H…A	D…A	D—H…A
N—H0A…O1*	0.86	2.15	2.998(7)	169
C16—H16A…O2	0.93	2.33	2.903(6)	120

Note. Elements of symmetry transformation: * 1–*x*, 2–*y*, –*z*.

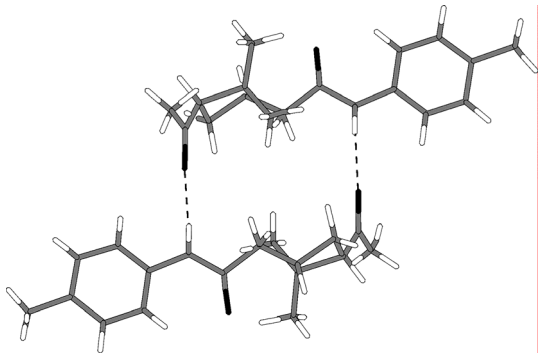

Fig. 3. Hydrogen bonding between two molecules of the title compound

tuted C atom, with the dihedral angle of 23.7°. This is slightly different from other compounds containing the cyclobutane ring. In (±)-*cis*-pinonic acid [7] and (1*S*,3*S*)-(+)-*cis*-3-acetyl-2,2-dimethylcyclobutaneacetic acid [8] the dihedral angle is 29.8°; in (+)-*trans*-pinonic acid [9] the angle is 19.1°; in methyl (±)-2-((1*R*,3*R*)-3-{2-[(3*S*)-1-ethyl-3-hydroxy-2-oxo-2,3-dihydro-1*H*-3-indolyl]acetyl}-2,2-dimethylcyclobutyl)acetate [10] the angle is 18.6°; in (–)-*cis*-3-acetyl-2,2-dimethylcyclobutanecarboxylic acid [11] the angle is 25.5°. The ketone carbonyl is aimed away from the *gem*-dimethyl group. The acetyl group (C3—C2—O1—C1) forms a dihedral angle of 63.9° with its half of the cyclobutane ring (C3—C4—C6). The corresponding values in (±)-*cis*-pinonic acid and (–)-*cis*-3-acetyl-2,2-dimethylcyclobutanecarboxylic acid are 57.4° and 62.3°. The dihedral angle between C1—C2—O1 and C2—C3—C4 planes is 7.5°, while in (±)-*cis*-pinonic acid and (–)-*cis*-3-acetyl-2,2-dimethylcyclobutanecarboxylic acid the values are 1.9° and 6.5°.

The two chiral centers lie on C3 and C5. The values of torsion angles O1—C2—C3—C4, O1—C2—C3—C6, O1—C2—C3—H3A, H9A—C9—C5—C4, H9A—C9—C5—C6 and H9A—C9—C5—H5A, are equal to –6.2°, –83.5°, –135.5°, 62.3°, –43.9°, –172.8° respectively. Stereochemistry of the asymmetric centers C3 and C5 can be characterized by the values of torsion angles H3A—C3—C6—C5 and H5A—C5—C4—C3 which are equal to 93.5° and 92.4°, respectively. The corresponding values in methyl (±)-2-((1*R*,3*R*)-3-{2-[(3*S*)-1-ethyl-3-hydroxy-2-oxo-2,3-dihydro-1*H*-3-indolyl]acetyl}-2,2-dimethylcyclobutyl) acetate are 92.2° and 90.8°, respectively.

The crystal structure is stabilized by N—H···O and C—H···O hydrogen bonding interactions (Fig. 3). Parameters of the hydrogen bonds are presented in Table 2.

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