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SHORT COMMUNICATION

SYNTHESIS AND CRYSTAL STRUCTURE OF 1-[2-(3-ETHYL-2,2-DIMETHYLCYCLOBUTYL)ACETYL]-3-PHENYLTHIOUREA

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ABSTRACT. The title compound 1-[2-(3-ethyl-2,2-dimethylcyclobutyl)acetyl]-3-phenylthiourea has been synthesized and its crystal structure was studied. The crystal belongs to triclinic system, space group *P*-1, a = 10.200(2) Å, b = 12.395(3) Å, c = 15.679(3) Å, α = 92.99(2)°, β = 106.00(3)°, γ = 111.95(3)°, V = 1740.4(6) Å^3, Z = 2, μ = 0.187 mm^{-1}, D_c = 1.162 g/cm^3, F(000) = 656, R = 0.0784, $wR2$ = 0.1505, formula unit $C_{17}H_{24}N_2OS$. The title compound has a fragment of 2,2-dimethylcyclobutane and its conformation represents *semi-chair*. The intermolecular and intramolecular hydrogen bonds are revealed.

KEY WORDS: Synthesis, Single crystal X-ray diffraction, Crystal structure, 2,2-Dimethylcyclobutane

INTRODUCTION

Many thiourea compounds exhibit strong structure stabilization and interesting biological activities. So in recent years the synthesis and their biological activities have been studied. Many cyclobutyl analogues also have favorable bioactivities [1-3]. So the thiourea compounds containing cyclobutane ring may have interesting biological activities. In this paper we reported the synthesis and crystal structure of 1-[2-(3-ethyl-2,2-dimethylcyclobutyl)acetyl]-3-phenyl-thiourea. In the present contribution the synthesis of the title compound has been performed according to the scheme shown in Figure 1.

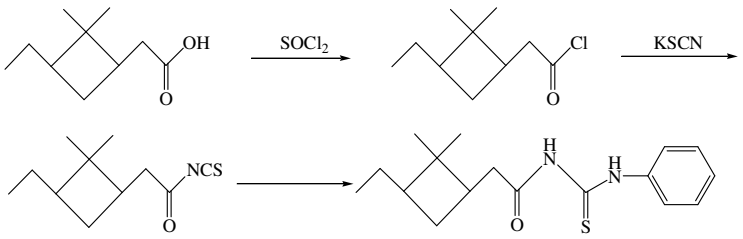

Figure 1. The synthesis scheme of the title compound

In order to determine the structure and configuration of the title compound X-ray diffraction study has been carried out.

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EXPERIMENTAL

Synthesis. 2,2-Dimethyl-3-ethylcyclobutaneacetic acid was prepared in our laboratory according to literature [4]. The title compound was synthesized according to following method: 2,2-dimethyl-3-ethylcyclo-butaneacetic acid (5.0 g, 0.029 mol) was dissolved in the mixture of dichloromethane (40 mL) and $SOCl_2$ (4.5 mL, 0.062 mol), and the mixture was stirred and refluxed for 4 h. Then the excessive solution was removed by decompression distillation. The residue was added dropwise to the mixture of KSCN (3.0 g, 0.030 mol) and acetonitrile (30 mL). The resulting mixture was stirred for 4 h at room temperature. Aniline (2.70 g, 0.029 mol) was added into the mixture. The reaction mixture was refluxed for 7 h. Then the excessive solution was removed by decompression distillation and the residue was poured into water (70 mL). Finally pumping filtration left the crude product as yellow powder. The solid was purified by recrystallization with ethanol in 83.9% yield. Melting point: 99.0-100.0 °C. IR (KBr) ν: cm^{-1} 3191 (N-H), 3036 (C=H), 1695 (C=O), 1252 (C-N), 1164 (C=S). ^{1}H NMR (δ, ppm, $CDCl_3$): 12.38 (s, 1H, NH), 9.05 (s, 1H, NH), 7.65 (d, 2H, C_6H_5), 7.38 (m, 2H, C_6H_5), 7.25 (m, 1H, C_6H_5), 2.51, 2.30 (m, 2H, CH_2), 2.40,2.18 (m, 2H, CH_2), 1.77 (m, 2H, CH_2), 1.35 (m, 1H, CH), 1.20 (m, 1H, CH), 1.08-0.89 (m, 6H, CH_3), 0.80 (q, 3H, CH_3).

X-ray diffraction study. Experimental X-ray diffraction data were obtained on a Enraf-Nonius CAD4 diffractometer (graphite-monochromated MoK_α radiation, λ = 0.71073 Å) by ω/2θ scanning. Data were collected in the θ range of 1.4–25.3° (range of indices: $0 \le h \le 12$, $-14 \le k \le 13$, $-18 \le l \le 18$). The structure was solved and refined with SHELX-97 software. 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 729335.

Table 1. Selected crystallographic data and experiment parameters.

Gross formula	$C_{17}H_{24}N_2OS$
Molecular weight	304.44
Temperature, K	293(2)
Symmetry and space group	Triclinic, *P*-1
a, b, c, Å	10.200(2), 12.395(3), 15.679(3)
α, β, γ, deg	92.99(2), 106.00(3), 111.95(3)
V, $Å^3$	1740.4(6)
Z	2
P_{calc}, g/cm^3	1.162
Crystal dimensions, mm	0.30 × 0.20 × 0.10 mm
Absorption coefficient, mm^{-1}	0.187
Measured/observed reflections	6718/6332
R_{int}	0.0310
Refined parameters	349
R factor [$I > 2\sigma(I)$]	$R1 = 0.0784$, $wR2 = 0.1505$
R factor (all data)	$R1 = 0.1498$, $wR2 = 0.1774$
Goof value	1.011

RESULTS AND DISCUSSION

The IR and ^{1}H NMR for the product are in good agreement with the title compound. In order to determine the structure and configuration of title compound X-ray diffraction study has been carried out. Figure 2 illustrates the structure of the title compound. As a whole, the molecule is substantially non-planar. 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 unsubstituted C atom, with a dihedral angle of 17.5°. This is a little different from other compounds containing cyclobutane rings. In (±)-2-[(1*S*,3*S*)-3-acetyl-2,2-dimethylcyclobutyl]-N-(*p*-tolyl)acetamide the dihedral angle is 23.7° [5]; in (±)-*cis*-pinonic acid [6] and *(*1*S, 3S)*-(+)-*cis*-3-acetyl-2,2-dimethylcyclobutaneacetic acid [7] the dihedral angle is 29.8°; in (+)-*trans*-pinonic acid [8] 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 [9] the angle is 18.6°; in (-)-*cis*-3-acetyl-2,2-dimethylcyclobutanecarboxylic acid [10] the angle is 25.5°. The selected bond lengths and bond angles are listed in Table 2 and 3.

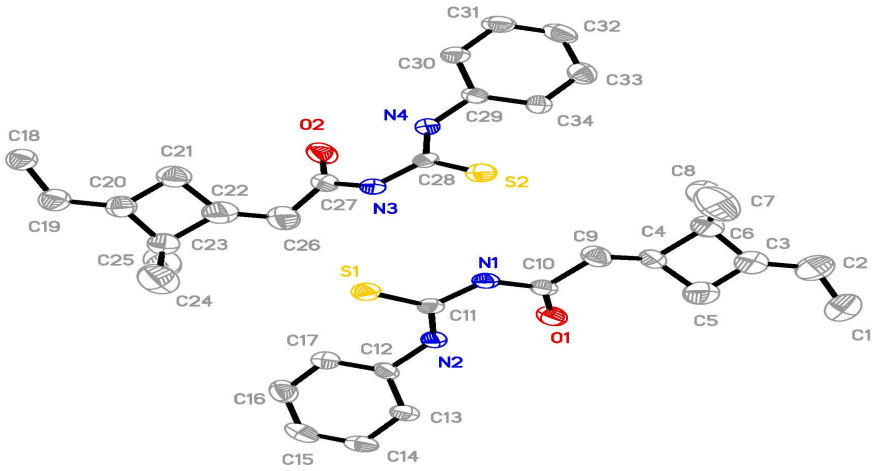

Figure 2. View of the structure of the title compound. Ellipsoids are drawn at the 50% probability level.

Table 2. Selected bond lengths (Å).

Bond	Length	Bond	Length	Bond	Length	Bond	Length
S1-C11	1.642(7)	O1-C10	1.222(8)	C7-H7C	0.9600	C8-H8A	0.9600
N1-C10	1.377(8)	N1-C11	1.399(8)	C8-H8B	0.9600	C8-H8C	0.9600
N1-H1A	0.8600	N2-C11	1.312(8)	C9-C10	1.512(9)	C9-H9A	0.9700
N2-C12	1.430(8)	N2-H2A	0.8600	C9-H9B	0.9700	C12-C17	1.370(10)
C1-C2	1.473(8)	C1-H1B	0.9600	C12-C13	1.373(9)	C13-C14	1.399(10)
C1-H1C	0.9600	C1-H1D	0.9600	C13-C18	1.551(10)	C14-C15	1.359(11)
C2-C3	1.450(7)	C2-H2B	0.9700	C14-H14A	0.9300	C15-C16	1.350(11)
C2-H2C	0.9700	C3-C6	1.461(10)	C6-C7	1.466(7)	C16-C17	1.392(10)
C3-C4	1.560(10)	C3-H3A	0.9800	N4-H4C	0.8600	C6-C8	1.533(11)
C4-C5	1.634(10)	C4-H4A	0.9700	C7-H7A	0.9600	C7-H7B	0.9600
C4-H4B	0.9700	C5-C6	1.469(10)	C5-C9	1.502(10)	C5-H5A	0.9800

Table 3. Selected bond angles and torsion angles.

Angles	(°)	Angles	(°)	Angles	(°)
C10-N1-C11	129.5(6)	C10-N1-H1A	115.2	C3-C2-C1	116.6(8)
C11-N1-H1A	115.2	C11-N2-C12	128.1(6)	C1-C2-H2B	108.1
C11-N2-H2A	115.9	C12-N2-H2A	115.9	C3-C2-H2B	108.1
C2-C1-H1B	109.5	C2-C1-H1C	109.5	C3-C2-H2C	108.1
H1B-C1-H1C	109.5	C2-C1-H1D	109.5	C1-C2-H2C	108.1
H1B-C1-H1D	109.5	H1C-C1-H1D	109.5	H2B-C2-H2C	107.3
C1-C2-C3-C5	5.6(16)	C1-C2-C3-C6	-174.4(10)	C5-C4-C9-C10	-72.3(10)
C6-C4-C9-C10	172.1(6)	C6-C4-C5-C3	-11.8(7)	C6-C3-C5-C4	12.2(7)
H4A-C4-C5-H5B	-22	H4A-C4-C6-C3	-95	H4A-C4-C6-C7	150
H4A-C4-C6-C8,	25	C2-C3-C5-C4	-167.8(10)	C6-C3-C5-C4	12.2(7)
C2-C3-C6-C4	168.3(12)	C2-C3-C6-C7	-77.4(13)	C2-C3-C6-C8	49.6(16)
C5-C3-C6-C4	-11.7(6)	C5-C3-C6-C7	102.6(8)	C5-C3-C6-C8	-130.4(8)

The C12 atom containing in the benzene ring, S1, N1, N2 and C11 are in the same plane. The dihedral angel between the plane and the benzene ring is 49.9(2)°. There are two intramolecular hydrogen bonds and two intermolecular hydrogen bonds in the title compound which contributes to the stabilization of the crystal structure. The hydrogen bonds are shown in the Figure 3 and Table 4.

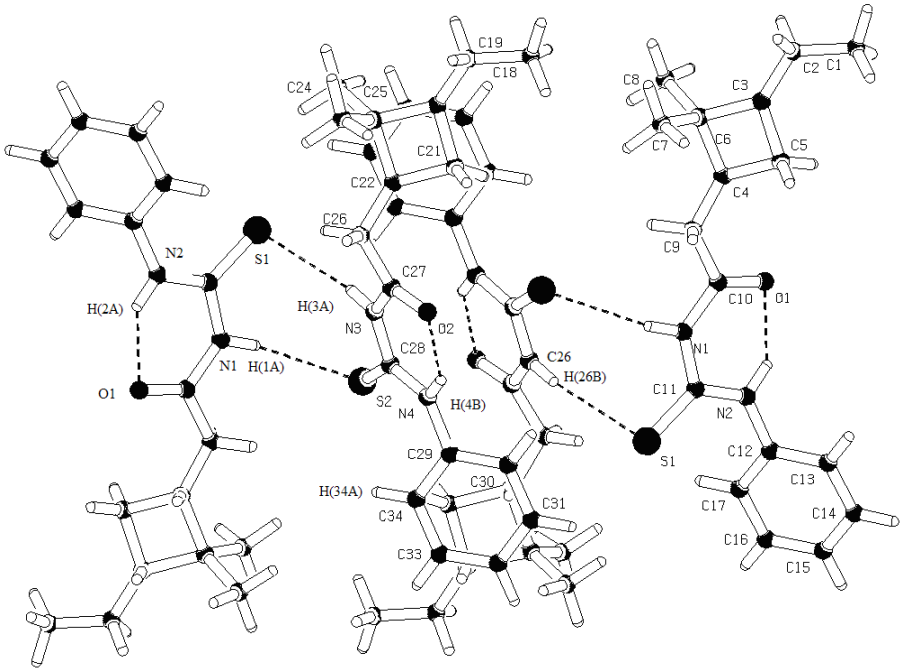

Figure 3. The hydrogen bonds of the title compound.

N4, H4B and O2 form a intramolecular hydrogen bond and on account of the hydrogen bond N4, C28, N3, C27 and O2 form a 6-membered ring. The C-N bond length on the sides of C28=S2 bond are varied greatly. The bond length of C28-N4 (1.326(7) Å) is shorter than that of

C28-N3 (1.383(7) Å). The bond length of C28=S2 is 1.66 (6) Å longer than the normal bond length of C=S H(1A) due to the intermolecular hydrogen bond of N(1)—H(1A)…S(2).

Table 4. Hydrogen-bond geometry (Å, °) of the title compound.

D—H…A	D—H	H…A	D…A	D—H…A
N(1)—H(1A)…S(2)[a,b]	0.86	2.62	3.460(6)	165
N(2)—H(2A)…O(1)[c]	0.86	1.96	2.666(5)	138
N(3)—H(3A)…S(1)[a,b]	0.86	2.64	3.466(5)	163
N(4)—H(4B)…O(2)[c]	0.86	1.92	2.637(7)	140
C(26)—H(26B)…S(1)[a,b]	0.97	2.78	3.701(8)	159
C(34)—H(34A)…S(2)[c]	0.93	2.81	3.267(6)	111

Note. Elements of symmetry transformation: [a] 1-x, -y, 1-z ; [b] intermolecular hydrogen bond; [c] intramolecular hydrogen bond.

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