



Crystal and Molecular Structure of 7-Methyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*]pyrimidin-4[3*H*]one

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Abstract: X-ray characterization of 7-methyl-5,6,7,8- tetrahydro[1]benzothieno [2,3-*d*]pyrimidin-4[3*H*]one is described. The compound crystallizes in the monoclinic space group $P2_1/c$ with $a=7.0013(2)\text{\AA}$, $b=8.3116(3)\text{\AA}$, $c=18.374(6)\text{\AA}$, $\beta=91.746(2)^\circ$, $V=1068.76(6)\text{\AA}^3$, $z=4$. The structure was solved using the direct method and refined to reliability R-factor of 0.0639 using 3180 independent reflections. The crystal structure is further stabilized by intermolecular C-H...N, N-H...N, C-H...O, N-H...O, and π - π interactions.

Keywords: Benzothiophene derivatives, crystal structure, weak interactions C-H...N, N-H...N, C-H...O, N-H...O, and π - π interactions.

Introduction

The pyrimidine ring is a frequent partner in polycyclic heterocyclic systems of biological significance¹. Compounds containing a fused pyrimidine ring make up a broad class that has attracted attention in the past few years owing to its wide range of biological activities. Many potential drugs have been modelled on these compounds, particularly in cancer and virus research²⁻⁴. On the other hand, thienopyrimidine, heterocyclic ring systems, has also attracted attention because of their promising biological activities. These derivatives have been reported to possess analgesic⁵, antipyretic⁶, antianaphilactic^{7,8}, and anti-inflammatory activities^{9,10}. Also, some are clinically effective antiallergic¹¹, potentially antineoplastic agents¹², or have significant hypocholesterolemic activity¹³. These aspects prompted us to prepare new polyheterocyclic fused systems containing the thienopyrimidine moiety with potential biological activity during our search for new compounds of pharmacological interest¹⁴⁻¹⁶.

Experimental

Crystal of 7-methyl-5,6,7,8- tetrahydro[1]benzothieno[2,3-*d*]pyrimidin-4[3*H*]one was prepared by slow evaporation method using ethyl acetate solvent. Crystals are stable for a long-time in normal conditions of temperature and humidity. The chemical formula was determined when resolving the crystal structure by X-ray diffraction spectroscopy.

Investigation techniques

X-ray diffraction

The X-ray diffraction data were collected on a Bruker Smart CCD Area Detector System. Intensity data were collected up to a maximum of 30.51° for the compound in the ω - ϕ scan mode. The data were reduced using SAINTPLUS¹⁷. A total of 8472 reflections were collected, resulting in 3180 independent reflections of which the number of reflections satisfying $I > 2\sigma(I)$ criteria were 2098. These were treated as observed. The structure was solved by direct methods using SHELXS97¹⁸ and difference Fourier synthesis using SHELXL97¹⁹. The positions and anisotropic displacement parameters of all non-hydrogen atoms were included in the full-matrix least-square refinement using SHELXL97¹⁹ and the procedure were carried out for a few cycles until convergence was reached. The H atoms were placed at calculated positions in the riding model approximation (C---H 0.93Å), with their temperature factors set to 1.2 times those of the equivalent isotropic temperature factors of the parent atoms. All other non-H atoms were refined anisotropically. The R factor after final convergence was 0.0639 and the maximum and minimum values of residual electron density were 0.939 and -0.908 eÅ⁻³. Molecular diagrams were generated using ORTEP²⁰. The mean plane calculation was done using the program PARST²¹. The drawings were made with Diamond16. Crystallographic data (CIF) for the structure reported in this paper have been deposited in the Cambridge Crystallographic Data centre as supplementary materials No 725038. Table 1 summarizes the crystal data, intensity data collection and refinement details for the title compound. The atomic coordinates of the nonhydrogen atoms with their equivalent temperature factors for the compound are presented in Table 2.

Table 1. Crystal data and structure refinement.

Empirical formula	C ₁₁ H ₁₃ N ₂ OS
Formula weight	221.29
Temperature	293(2) K
Wavelength (Å)	0.71073
Crystal system, space group	Monoclinic, P2 ₁ /c
Unit cell dimensions	
a (Å)	7.0013(2)
b (Å)	8.3116(3)
c (Å)	18.374(5)
β (°)	91.746(2)
Volume (Å ³)	1068.76(6)
Z	4
Calculated density (Mg/m ³)	1.375
Absorption coefficient (mm ⁻¹)	0.276
	<i>Condt...</i>
F(000)	468
Crystal size	0.4 mm x 0.35 mm x 0.3 mm
Theta range for data collection	2.22 to 30.51°
Limiting indices	-5 ≤ h ≤ 9, -11 ≤ k ≤ 11, -24 ≤ l ≤ 26

Reflections collected / unique	8472 / 3180 [R(int) = 0.0262]
Completeness to theta	30.51 97.7 %
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3180 / 0 / 141
Goodness-of-fit on F ²	1.063
Final R indices [I > 2σ(I)]	R1 = 0.0639, wR2 = 0.1550
R indices (all data)	R1 = 0.0995, wR2 = 0.1757
Largest diff. peak and hole (e Å ⁻³)	0.939 and -0.908

Table 2. Atomic Coordinates (x 10⁴) and Equivalent Isotropic Displacement Parameter (x 10³) Non-Hydrogen Atoms.

Atoms	x	y	z	U(eq)
C(1)	-1937(4)	798(4)	3881(1)	43(1)
C(2)	245(3)	2193(3)	4523(1)	34(1)
C(3)	756(3)	2151(3)	5161(1)	32(1)
C(4)	-2561(3)	1325(3)	5148(1)	34(1)
C(5)	-437(4)	3086(4)	6526(1)	46(1)
C(6)	897(7)	4115(9)	6977(2)	132(1)
C(7)	2768(6)	4319(7)	6827(2)	85(1)
C(8)	3341(4)	4431(4)	6044(2)	46(1)
C(9)	4100(5)	5238(6)	7334(2)	75(1)
C(10)	1937(4)	3560(3)	5553(1)	37(1)
C(11)	232(3)	2943(3)	5757(1)	33(1)
C(1)	-294(3)	1529(3)	3866(1)	43(1)
C(2)	-3045(3)	677(3)	4467(1)	40(1)
C(1)	2385(1)	3203(1)	4640(1)	43(1)
C(1)	3646(3)	1165(3)	5662(1)	46(1)

Results and Discussion

Structure description

The main geometrical features of different entities are reported in Table 3. The ORTEP diagram of the molecule is shown in Figure 1. The Benzothieno and pyrimidine rings are coplanar with an angular tilt of 15° between them, the Methyl group is almost orthogonal to cyclohexene plane with an angle of 85°. Thiophene ring is planar while cyclohexene ring is in half-chair conformation.

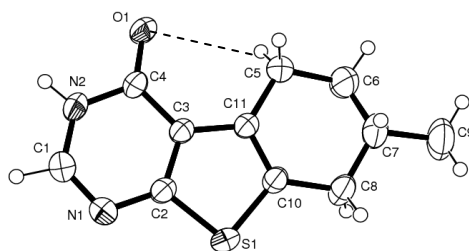


Figure 1. Ortep view of title compound, showing 50% probability ellipsoids and the atom numbering scheme. Dotted line indicates intramolecular C5-H5A...O1 interactions.

The total puckering amplitude²² of the cyclohexyl ring is $QT = 0.4323(9) \text{ \AA}$, and the value of the lowest displacement asymmetry parameter ΔC_2 (C1–C2) = $0.0492(0) \text{ \AA}$ are indicative of chair conformation. The plane calculation shows that the atoms C6 and C7 deviate from the mean plane C5/C8/C10/C11 constituting the ring by 0.1917 \AA and $-0.1643(2) \text{ \AA}$, respectively, indicating that the conformation of the ring is that of a half-chair, with the atom C6 and C7 being displaced by this overall planarity of the rest to the ring. The ring puckering parameters for the cyclohexene ring in the title compound are $Q(2) = 0.1874(7) \text{ \AA}$, $\varphi(2) = 96.07(2)^\circ$ and $\theta = 50.27(1)^\circ$ respectively. In most of the benzothiophene ring systems the cyclohexene ring adopts half-chair conformation²³.

Table 3. Selected bond lengths (\AA) and angles ($^\circ$) in 7-methyl-5,6,7,8- tetrahydro[1]benzothieno[2,3-*d*]pyrimidin-4[3*H*]one.

C(1)-N(1)	1.301(4)	C(4)-O(1)	1.237(3)
C(1)-N(2)	1.350(4)	C(4)-N(2)	1.394(3)
C(2)-N(1)	1.370(3)	C(5)-C(6)	1.498(5)
C(2)-C(3)	1.385(3)	C(5)-C(11)	1.507(3)
C(2)-S(1)	1.725(2)	C(7)-C(8)	1.508(4)
C(3)-C(11)	1.437(3)	C(8)-C(10)	1.500(4)
C(3)-C(4)	1.438(3)	C(10)-C(11)	1.363(3)
C(4)-O(1)	1.237(3)	C(10)-S(1)	1.742(3)
C(4)-N(2)	1.394(3)		
N(1)-C(1)-N(2)	125.6(2)	C(6)-C(7)-C(8)	119.2(3)
N(1)-C(2)-C(3)	127.1(2)	C(9)-C(7)-C(8)	112.5(3)
N(1)-C(2)-S(1)	121.39(19)	C(10)-C(8)-C(7)	110.8(2)
C(3)-C(2)-S(1)	111.46(18)	C(11)-C(10)-C(8)	125.4(2)
C(2)-C(3)-C(11)	113.0(2)	C(11)-C(10)-S(1)	112.72(18)
C(2)-C(3)-C(4)	117.6(2)	C(8)-C(10)-S(1)	121.8(2)
C(11)-C(3)-C(4)	129.4(2)	C(10)-C(11)-C(3)	111.6(2)
O(1)-C(4)-N(2)	120.3(2)	C(10)-C(11)-C(5)	121.9(2)
O(1)-C(4)-C(3)	126.7(2)	C(3)-C(11)-C(5)	126.5(2)
N(2)-C(4)-C(3)	113.0(2)	C(1)-N(1)-C(2)	112.8(2)
C(6)-C(5)-C(11)	110.9(3)	C(1)-N(2)-C(4)	123.8(2)
C(7)-C(6)-C(5)	123.2(4)	C(2)-S(1)-C(10)	91.27(12)
C(6)-C(7)-C(9)	121.3(4)		

The molecular structures are primarily stabilized by weak intramolecular C5-H5A...O1 hydrogen bond [C5-H5A = $0.970(3) \text{ \AA}$, H5A...O1 = $2.857(2) \text{ \AA}$, C5...O1 = $3.146(3) \text{ \AA}$ and the angle C5-H5A...O1 = 98 \AA] leading to the formation of a pseudo-six-membered ring with graph set S(6) according to Etter's analysis²⁴. These interactions appear to play a predominant role in shaping the molecular structures and thus locking the molecular conformation and eliminating conformation flexibility.

The crystal structure is stabilized by intermolecular interactions of the type C-H...N, N-H...N, C-H...O, and N-H...O. The C-H...N interactions forms a tape like pattern along '*a*' axis Figure 2. The N-H...N forms zig-zag ribbon structure along crystallographic '*a*' axis Figure 3. The two C-H...O and one N-H...O interactions form trifurcated bonds from three donors C8, C9 and N2 to the same acceptor, O1 along '*b*' axis Figure 4. Apart from these trifurcated hydrogen bond interaction, the N-H...O interaction generates centrosymmetric head-to-head dimers corresponding to graph set notation of $R_2^2(8)$ ²⁴, along crystallographic '*b*' axis Figure 4 resulting in one dimensional tape like structure. The π - π stacking

interaction Figure 5 between the benzothieno and pyrimidine rings with C3-C10 atoms of two molecules being separated by a distance of $3.879(3)\text{\AA}$ (symmetry code: $-x, 1-y, 1-z$) further strengthens the supramolecular structure.

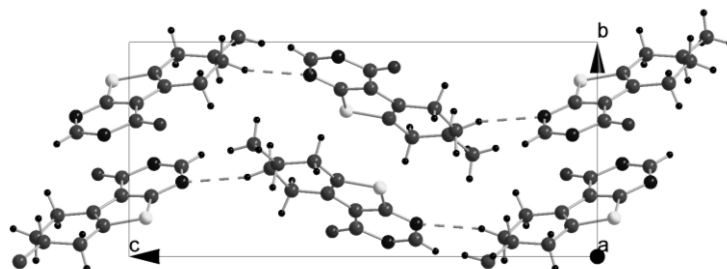


Figure 2. Crystal structure of title compound viewed along 'a' axis. Dotted lines indicate intermolecular C-H...N interaction.

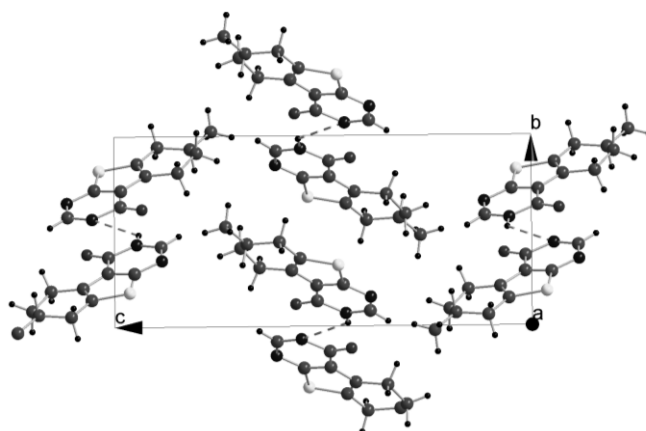


Figure 3. Crystal structure of title compound viewed along 'a' axis. Dotted lines indicate intermolecular N-H...N interactions.

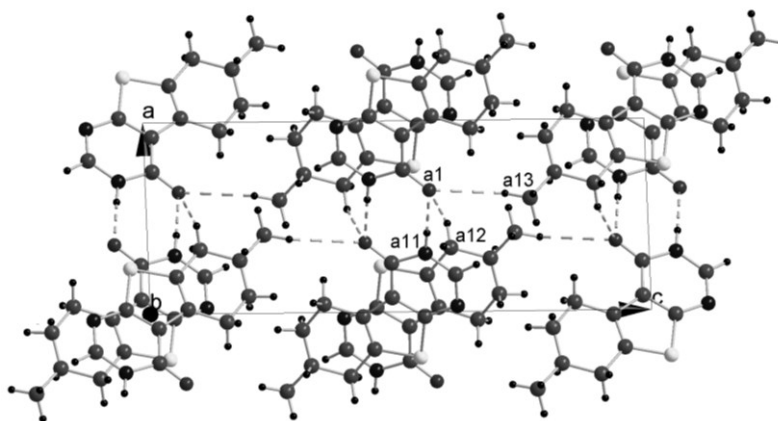


Figure 4. Crystal structure of title compound viewed along 'b' axis. Dotted lines indicate N-H...O (a11-a1) and C-H...O (a12, a13-a1) intermolecular interactions.

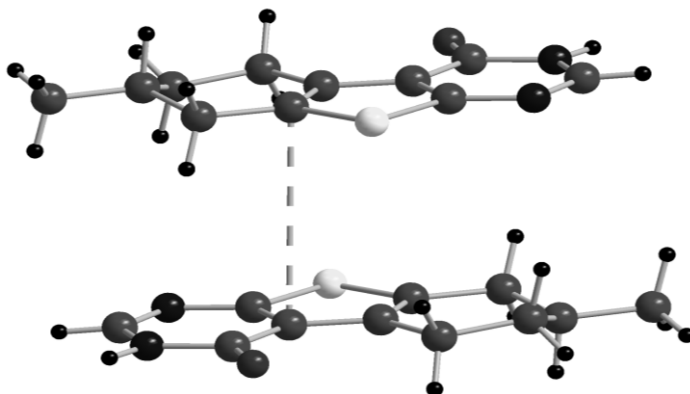


Figure 5. π - π stacking interactions between the benzothieno and pyrimidine rings.

Table 4. Non-bonded interactions and possible hydrogen bonds (\AA , $^\circ$). (*D*-donor; *A*-acceptor; *H*-hydrogen).

D—H \cdots A	D—H	H \cdots A	D \cdots A	D—H \cdots A
C5-H5A \cdots O1	0.970(3)	2.857(2)	3.146(3)	113
C6-H6B \cdots N1 ⁱ	0.970(4)	2.722(2)	3.632(4)	156
N2-H2 \cdots N2 ⁱⁱ	0.860(2)	2.984(2)	3.595(3)	129
N2-H2 \cdots O1 ⁱⁱ	0.860(2)	1.924(2)	2.782(3)	173
C8-H8B \cdots O1 ⁱⁱⁱ	0.970(3)	2.711(2)	3.522(4)	141
C9-H9C \cdots O1 ^{iv}	0.960(4)	2.955(2)	3.784(4)	145

Symmetry code: ⁱ $x, -y+1/2, +z+1/2$; ⁱⁱ $-x-1, -y, -z+1$; ⁱⁱⁱ $x+1, +y, +z$, ^{iv} $-x, +y+1/2, -z+1/2+1$.

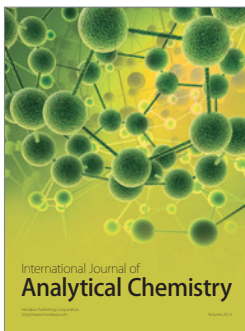
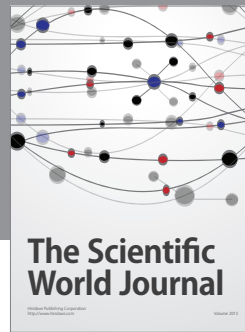
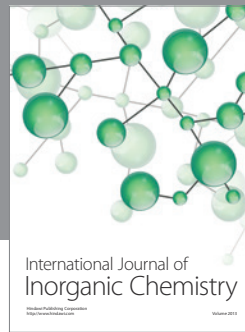
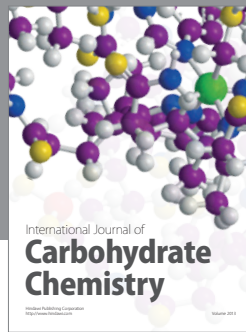
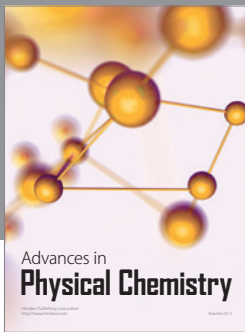
Conclusion

Good quality single crystals of 7-Methyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*]pyrimidin-4[3*H*]one were grown by slow evaporation technique at room temperature. The crystal structure of the title compound is stabilized by different types of intramolecular, intermolecular particularly an interesting H-bond network and π - π stacking interactions.

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