Crystal structure of 1,3-dicyclohexyl-1-(tetrahydrothiophene-2-carbonyl)urea, $C_{18}H_{26}N_2O_2S$

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Abstract

$C_{18}H_{26}N_2O_2S$, orthorhombic, $Pna2_1$ (no. 33), $a = 11.779(2)$ Å, $b = 16.454(3)$ Å, $c = 9.601(2)$ Å, $V = 1860.7$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.072$, $wR_{\text{ref}}(F^2) = 0.151$, $T = 298$ K.

Source of material

1,3-Dicyclohexyl-1-(tetrahydrothiophene-2-carbonyl)urea was prepared by reacting of thiophene-2-carboxylic acid (0.01 mol) and dicyclohexylcarbodiimide (0.01 mol) in dichloromethane over 24 hours (353 K to reflux), followed by aqueous work-up and extraction. The product was crystallized by dissolving the crude material in hot ethanol solution, and slow cooling to the room temperature.

Experimental details

All H atoms were positioned geometrically and allowed to ride on their parent atoms at distances of $d(\text{Csp}^2\text{—H}) = 0.93$ Å with $U_{\text{iso}} = 1.2 U_{\text{eq}}(\text{parent atom})$, $d(\text{Csp}^3\text{—H}) = 0.97$ Å with $U_{\text{iso}} = 1.5$

$U_{\text{eq}}(\text{parent atom})$ and $d(\text{N—H}) = 0.86$ Å with $U_{\text{iso}} = 1.2 U_{\text{eq}}(\text{parent atom})$

Discussion

In recent years, more and more attention has been focused on synthesis and properties of thiophene carboxylic acid derivatives, which not only play an important role in constructing coordination polymers with attractive topological structure but also have been found applications in a large number of organic reactions and widely employed in organic synthesis and reported to be potential anticancer agents [1–3]. Especially thiophene-2-carboxylic acids, such as 3-arylsulfonylamino-5-phenylthiophene-2-carboxylic acid, have been discovered as potent inhibitors of HCV NS5B polymerase and HCV subgenomic RNA replication [4,5].

The bond lengths and angles in the title molecule (figure, top) are within normal ranges. The thiophene ring (C1/C2/C3/C4/ S1) is slightly puckered, with an r.m.s. deviation of 0.019(2) Å. The four atoms N1, C5, C6 and O1 are coplanar (r.m.s. deviation = 0.028(2) Å, plane p1) and the atoms N2, C12, C13 and O2 are coplanar (r.m.s. deviation = 0.023(1) Å, plane p2). The dihedral angles formed by the thiophene ring with p1 and p2 are 60.7(3)° and 43.1(3)°, respectively. The cyclohexyl groups are in a chair conformation. It should be noted that the hydrogen bonding interactions plays an important role in the crystal structure of the title compound. As shown in bottom figure, adjacent molecules are linked by intermolecular $\text{N2—H2} \cdots \text{O2}^i$ (symmetry code i: $2-x, 2-y, -1/2+z$) hydrogen bond interactions to form chains stabilizing the crystal structure.

Table 1. Data collection and handling.

Crystal:	colorless block, size 0.12 × 0.14 × 0.29 mm
Wavelength:	Mo K_{α} radiation (0.71073 Å)
μ :	1.85 cm ^{−1}
Diffractometer, scan mode:	Bruker APEX CCD, ϕ/ω
$2\theta_{\text{max}}$:	50.04°
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$:	9350, 3243
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2691
$N(\text{param})_{\text{refined}}$:	208
Programs:	SHELXS-97 [6], SHELXL-97 [7], SHELXTL [8], ORTEP [9]

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Table 2. Atomic coordinates and displacement parameters (in Å²).

Atom	Site	x	y	z	U _{iso}
H(2)	4a	1.0428	0.9769	0.7642	0.050
H(1)	4a	1.3827	1.1803	0.8262	0.109
H(2A)	4a	1.3163	1.1525	1.0529	0.095
H(3)	4a	1.1104	1.1334	1.0611	0.058
H(6)	4a	0.7786	1.1184	0.7742	0.056
H(7A)	4a	0.7666	1.1568	1.0050	0.089
H(7B)	4a	0.7564	1.0655	1.0509	0.089
H(8A)	4a	0.5737	1.1209	1.0437	0.113
H(8B)	4a	0.5922	1.1500	0.8896	0.113
H(9A)	4a	0.4845	1.0343	0.8859	0.110
H(9B)	4a	0.5747	0.9878	0.9758	0.110
H(10A)	4a	0.6063	1.0391	0.6997	0.101
H(10B)	4a	0.5955	0.9483	0.7484	0.101

Table 2. Continued.

Atom	Site	x	y	z	U _{iso}
H(11A)	4a	0.7696	0.9560	0.8646	0.089
H(11B)	4a	0.7886	0.9831	0.7095	0.089
H(13)	4a	1.0870	0.8864	0.9957	0.053
H(14A)	4a	1.2488	0.9588	0.9487	0.073
H(14B)	4a	1.2513	0.9256	0.7954	0.073
H(15A)	4a	1.3797	0.8489	0.9273	0.099
H(15B)	4a	1.2855	0.8289	1.0377	0.099
H(16A)	4a	1.2879	0.7696	0.7602	0.106
H(16B)	4a	1.3085	0.7160	0.8931	0.106
H(17A)	4a	1.1232	0.7338	0.9630	0.103
H(17B)	4a	1.1237	0.6996	0.8103	0.103
H(18A)	4a	1.0894	0.8292	0.7198	0.080
H(18B)	4a	0.9947	0.8096	0.8297	0.080

Table 3. Atomic coordinates and displacement parameters (in Å²).

Atom	Site	x	y	z	U ₁₁	U ₂₂	U ₃₃	U ₁₂	U ₁₃	U ₂₃
S(1)	4a	1.2060(3)	1.1684(2)	0.7265(4)	0.076(2)	0.118(3)	0.100(3)	-0.012(2)	0.019(2)	0.042(2)
O(1)	4a	0.9449(5)	1.1862(4)	0.7186(7)	0.064(4)	0.046(3)	0.059(4)	0.018(3)	-0.007(3)	0.010(3)
O(2)	4a	0.9520(6)	0.9935(4)	1.0528(6)	0.066(4)	0.063(4)	0.024(3)	0.017(3)	0.011(3)	0.008(2)
N(1)	4a	0.9217(5)	1.0768(4)	0.8626(7)	0.039(3)	0.044(3)	0.034(3)	0.002(3)	0.003(3)	0.002(3)
N(2)	4a	1.0395(5)	0.9642(4)	0.8510(6)	0.049(4)	0.053(4)	0.022(3)	0.013(3)	0.008(3)	0.007(3)
C(1)	4a	1.3069(9)	1.1698(7)	0.847(2)	0.043(5)	0.086(8)	0.14(1)	-0.023(5)	-0.011(7)	0.040(8)
C(2)	4a	1.269(1)	1.1545(7)	0.975(1)	0.087(8)	0.074(7)	0.076(8)	-0.006(6)	-0.033(7)	0.003(6)
C(3)	4a	1.1521(7)	1.1418(5)	0.9801(9)	0.042(4)	0.059(5)	0.044(4)	-0.006(4)	-0.015(4)	0.010(4)
C(4)	4a	1.1065(8)	1.1436(5)	0.846(1)	0.063(6)	0.035(4)	0.053(4)	-0.005(4)	0.008(4)	0.002(4)
C(5)	4a	0.9849(7)	1.1371(5)	0.8000(8)	0.044(4)	0.041(4)	0.035(4)	0.022(3)	-0.002(3)	-0.014(3)
C(6)	4a	0.7967(7)	1.0780(5)	0.8458(9)	0.046(4)	0.055(5)	0.040(4)	0.007(4)	-0.009(4)	0.011(4)
C(7)	4a	0.7388(8)	1.1037(7)	0.977(1)	0.050(5)	0.084(7)	0.087(8)	0.008(5)	0.005(5)	-0.028(6)
C(8)	4a	0.6101(9)	1.1075(9)	0.956(2)	0.049(6)	0.12(1)	0.12(1)	0.002(6)	0.013(6)	-0.038(9)
C(9)	4a	0.5651(9)	1.0288(9)	0.904(2)	0.044(6)	0.11(1)	0.12(1)	0.006(6)	0.003(6)	0.024(9)
C(10)	4a	0.624(1)	1.0016(8)	0.775(2)	0.062(6)	0.080(7)	0.109(9)	-0.008(5)	-0.029(6)	-0.013(7)
C(11)	4a	0.7519(9)	0.9977(7)	0.796(1)	0.059(6)	0.086(7)	0.077(7)	0.010(5)	-0.006(5)	-0.031(6)
C(12)	4a	0.9741(6)	1.0085(5)	0.9320(8)	0.039(4)	0.050(4)	0.027(4)	-0.004(3)	0.003(3)	0.005(3)
C(13)	4a	1.1061(7)	0.8960(5)	0.8978(8)	0.050(5)	0.054(5)	0.028(4)	0.021(4)	0.019(3)	0.001(3)
C(14)	4a	1.2306(8)	0.9124(7)	0.891(1)	0.057(5)	0.073(6)	0.051(6)	-0.002(4)	-0.007(4)	-0.002(4)
C(15)	4a	1.299(1)	0.8381(7)	0.939(1)	0.071(7)	0.11(1)	0.072(7)	0.029(6)	-0.001(6)	0.014(6)
C(16)	4a	1.267(1)	0.7623(7)	0.857(2)	0.094(8)	0.089(9)	0.082(7)	0.044(7)	0.031(7)	-0.005(7)
C(17)	4a	1.143(1)	0.7463(6)	0.867(2)	0.11(1)	0.043(5)	0.100(9)	0.018(6)	0.027(8)	-0.004(6)
C(18)	4a	1.0752(8)	0.8203(6)	0.818(1)	0.056(5)	0.071(7)	0.073(7)	-0.009(5)	0.014(5)	-0.010(5)

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References

- Chen, Z.; Zuo, Y.; Li, X. H.; Wang, H.; Zhao, B.; Shi, W.; Cheng, P.: Structure and luminescent property of novel 2D indium(III) and 1D cadmium(II) coordination polymers based on thiophene-2,5-dicarboxylic acid. *J. Mol. Struct.* **888** (2008) 360-365.
- Akenbach, H. J.; Brauer, D. J.; Merhof, G. F.: Synthesis of 1-Deoxy-4-thio-D-ribose starting from Thiophene-2-carboxylic acid. *Tetrahedron* **53** (1997) 6019-6026.
- Babu, G.; Yu, H. M.; Yanga, S. M.; Fang, J. M.: Carbazothienophene-2-carboxylic acid derivatives as endothelin receptor antagonists. *Bioorg. Med. Chem. Lett.* **14** (2004) 1129-1132.
- Chan, L.; Das, S. K.; Reddy, T. J.; Poisson, C.; Proulx, M.; Pereira, O.; Courchesne, M.; Roy, C.; Wang, W.; Siddiqui, A.; Yannopoulos, C. G.; Nguyen-Ba, N.; Labrecque, D.; Bethell, R.; Hamel, M.; Courtemanche-Asselin, P.; LHeureux, L.; David, M.; Nicolas, O.; Brunette, S.; Bilimoria, D.; Bédard, J.: Discovery of thiophene-2-carboxylic acids as potent inhibitors of HCV NS5B polymerase and HCV subgenomic RNA replication. Part 1: Sulfonamides. *Bioorg. Med. Chem. Lett.* **14** (2004) 793-796.
- Chan, L.; Pereira, O.; Reddy, T. J.; Das, S. K.; Poisson, C.; Courchesne, M.; Proulx, M.; Siddiqui, A.; Yannopoulos, C. G.; Nguyen-Ba, N.; Roy, C.; Nasturica, D.; Moinet, C.; Bethell, R.; Hamel, M.; LHeureux, L.; David, M.; Nicolas, O.; Courtemanche-Asselin, P.; Brunette, S.; Bilimoria, D.; Bédard, J.: Discovery of thiophene-2-carboxylic acids as potent inhibitors of HCV NS5B polymerase and HCV subgenomic RNA replication. Part 2: Tertiary amides. *Bioorg. Med. Chem. Lett.* **14** (2004) 797-800.
- Sheldrick, G. M.: SHELXS-97. Program for the Solution of Crystal Structures. University of Göttingen, Germany 1997.
- Sheldrick, G. M.: SHELXL-97. Program for the Refinement of Crystal Structures. University of Göttingen, Germany 1997.
- Sheldrick, G. M.: SHELXTL. Structure Determination Software Suite. Version 6.14. Bruker AXS, Madison, Wisconsin, USA 2000.
- Johnson, C. K.: ORTEP-II. Report ORNL-5138. Oak Ridge National Laboratory, Oak Ridge, Tennessee, USA 1976.