Crystal structure of 4-chloro-*N*-[2-(5-methyl-4,6-dioxo-3-phenyl-hexahydro-pyrrolo-[3,4-*d*]isoxazol-2-yl)-ethyl]-benzenesulfonamide, C₂₀H₂₀ClN₃O₅S

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Abstract

C₂₀H₂₀ClN₃O₅S, orthorhombic, *Fdd2* (no. 43), *a* = 39.856(4) Å, *b* = 19.058(1) Å, *c* = 10.5849(8) Å, *V* = 8039.9 Å³, *Z* = 16, *R*_{gt}(*F*) = 0.061, *wR*_{obs}(*F*²) = 0.173, *T* = 160 K.

Source of material

All chemicals used for the preparation of the fused-ring compound were of reagent grade quality. The title compound was prepared by a procedure that reported in the literature [1] which involved first converting aziridine and oxime into a corresponding nitron and then 1,3-dipolar cycloaddition with *N*-methylmaleimide as dipolarophile. The compound was recrystallized from: petroleum ether/ethyl acetate (b.p. 60–80 °C) afforded the title compound (m.p. 196–198 °C).

Elemental analysis: found – C, 53.05 %; H, 4.5 %; N, 9.6 %; calc. for C₂₀H₂₀N₃O₅ClS – C, 53.35 %; H, 4.5 %; N, 9.35 %.

Discussion

The use of 1,3-dipolar cycloaddition cascades for the synthesis of cyclic rings containing a nitrogen atom, such as pyrrolizidines, indolizidines and quinolizidines is important as they occur in a number of alkaloids [2–4]. Some of the *N*-heterocyclic bearing isoxazolidine rings possess various biological activity [5,6]. We have recently published a range of aza-cyclic *N*-heterocycles including isoxazolidine and pyrrolidine ring compounds [7–9]. The title compound is another example of our newly synthesized isoxazolidine derivatives that contains two fused five-membered rings, i.e. a 1,2-oxazolidine and an *N*-methylpyrrolidine ring. The title cycloadduct, 4-chloro-*N*-[2-(5-methyl-4,6-dioxo-3-phenyl-hexahydro-pyrrolo[3,4-*d*]isoxazol-2-yl)-ethyl]-benzenesulfonamide, has been synthesized via electrophile induced oxime → nitron → cycloaddition cascades.

The title compound contains two fused five membered rings; a nearly planar pyrrolidine ring and oxazolidine ring in an envelope conformation with the N1 atom in the flap position. The oxazolidine system, by contrast, is a puckered ring. The relevant torsion angles are ∠N1–C1–C2–C3 = 23.4(5)° and ∠N1–O1–C3–C2 = –35.4(5)°. The pyrrolidine and isoxazolidine rings are not in plane, viz. ∠O1–C3–C4–N2 = –121.0(4)° and ∠C1–C2–C5–N2 = 103.4(4)°. The bond lengths of the C–N and C–C bonds, viz. *d*(N2–C4) = 1.386(7) Å, *d*(N2–C5) = 1.379(7) Å, *d*(C3–C4) = 1.514(8) Å and *d*(C2–C5) = 1.517(7) Å, in the pyrrolidine ring are all shorter than the average of C–N and C–C single bonds, respectively. These results indicate extensive delocalization of electrons within the pyrrolidine ring. On the contrary, the bond lengths of the isoxazolidine ring, viz. *d*(C3–O1) = 1.429(6) Å, *d*(O1–N1) = 1.470(5) Å, *d*(N1–C1) = 1.483(6) Å, *d*(C1–C2) = 1.550(7) Å and *d*(C2–C3) = 1.533(7) Å, are within the average single bonds. These results agree with similar distances obtained in previously reported structure [1,10]. All the other bond lengths and angles fall within the expected range. The absolute structure is confirmed by the Flack *x* parameter of 0.04(2).

Table 1. Data collection and handling.

Crystal:	colorless, prismatic, size 0.12 × 0.27 × 0.38 mm
Wavelength:	Cu K α radiation (1.54184 Å)
μ :	29.97 cm ^{–1}
Diffraction, scan mode:	Stoe STADIA, ω – θ
2 θ _{max} :	129.0°
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} :	3271, 2969
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ (<i>I</i> _{obs}), 2898
<i>N</i> (<i>param</i>) _{refined} :	276
Programs:	SHELXS-86 [11], SHELXL-93 [12]

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

Atom	Site	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso}
H(3N)	16b	0.248(2)	0.159(3)	0.600(6)	0.04(2)
H(1)	16b	0.3085	–0.0249	0.4641	0.030
H(2)	16b	0.3569	–0.0276	0.5811	0.031
H(3)	16b	0.3297	–0.0330	0.7697	0.037
H(6A)	16b	0.3609	0.2172	0.7057	0.061
H(6B)	16b	0.3925	0.1771	0.7652	0.061
H(6C)	16b	0.3598	0.1912	0.8493	0.061
H(8)	16b	0.3116	0.1639	0.4676	0.034

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Table 2. Continued.

Atom	Site	x	y	z	U _{iso}
H(9)	16b	0.3240	0.2318	0.2913	0.035
H(10)	16b	0.3421	0.1808	0.1038	0.039
H(11)	16b	0.3481	0.0585	0.0926	0.040
H(12)	16b	0.3359	-0.0111	0.2669	0.033
H(13A)	16b	0.2506	-0.0149	0.5091	0.031
H(13B)	16b	0.2530	0.0568	0.4305	0.031

Table 2. Continued.

Atom	Site	x	y	z	U _{iso}
H(14A)	16b	0.2042	0.0541	0.5618	0.031
H(14B)	16b	0.2279	0.0493	0.6838	0.031
H(16)	16b	0.2614	0.1627	0.8303	0.030
H(17)	16b	0.2705	0.1520	1.0500	0.033
H(19)	16b	0.1706	0.1723	1.1125	0.033
H(20)	16b	0.1615	0.1815	0.8918	0.031

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
Cl(1)	16b	0.22840(3)	0.15954(7)	0.2606(1)	0.0494(7)	0.0383(7)	0.0251(7)	0.0009(6)	-0.0049(6)	0.0022(6)
S(1)	16b	0.20321(2)	0.18989(6)	0.6799(1)	0.0171(5)	0.0253(6)	0.0227(6)	0.0004(4)	-0.0006(4)	0.0011(5)
N(1)	16b	0.2868(1)	0.0506(2)	0.5732(4)	0.023(2)	0.026(2)	0.021(2)	0.000(2)	0.003(2)	0.004(2)
N(2)	16b	0.3540(1)	0.1135(2)	0.7235(4)	0.026(2)	0.037(2)	0.026(2)	0.009(2)	-0.002(2)	-0.003(2)
N(3)	16b	0.2294(1)	0.1446(2)	0.5980(4)	0.020(2)	0.027(2)	0.025(2)	-0.002(2)	0.002(2)	-0.002(2)
O(1)	16b	0.28810(8)	0.0044(2)	0.6842(4)	0.026(2)	0.039(2)	0.032(2)	0.001(1)	0.004(2)	0.012(2)
O(2)	16b	0.38590(9)	0.1024(2)	0.5451(4)	0.027(2)	0.045(2)	0.033(2)	-0.005(2)	0.004(2)	0.001(2)
O(3)	16b	0.3164(1)	0.0968(3)	0.8861(4)	0.039(2)	0.087(3)	0.026(2)	0.019(2)	-0.002(2)	-0.010(2)
O(4)	16b	0.17015(8)	0.1645(2)	0.6522(4)	0.021(2)	0.038(2)	0.033(2)	-0.002(1)	-0.001(1)	-0.003(2)
O(5)	16b	0.21039(8)	0.2629(2)	0.6560(3)	0.025(2)	0.024(2)	0.027(2)	0.001(1)	-0.001(1)	0.004(2)
C(1)	16b	0.3148(1)	0.0228(2)	0.4956(5)	0.023(2)	0.026(2)	0.025(3)	0.003(2)	0.004(2)	-0.005(2)
C(2)	16b	0.3428(1)	0.0148(2)	0.5964(5)	0.025(2)	0.025(2)	0.027(3)	0.007(2)	0.003(2)	0.001(2)
C(3)	16b	0.3227(1)	0.0089(3)	0.7194(5)	0.027(2)	0.039(3)	0.027(3)	0.007(2)	0.003(2)	0.011(2)
C(4)	16b	0.3298(1)	0.0764(3)	0.7897(5)	0.024(2)	0.053(3)	0.022(3)	0.013(2)	-0.002(2)	0.004(3)
C(5)	16b	0.3639(1)	0.0804(3)	0.6138(5)	0.022(2)	0.034(3)	0.027(3)	0.006(2)	-0.001(2)	0.000(2)
C(6)	16b	0.3679(1)	0.1801(3)	0.7642(6)	0.037(3)	0.038(3)	0.048(4)	0.010(2)	-0.016(3)	-0.015(3)
C(7)	16b	0.3224(1)	0.0686(2)	0.3854(5)	0.017(2)	0.027(2)	0.024(2)	-0.001(2)	0.000(2)	-0.001(2)
C(8)	16b	0.3190(1)	0.1421(3)	0.3917(5)	0.029(2)	0.030(2)	0.027(3)	-0.001(2)	0.003(2)	-0.004(2)
C(9)	16b	0.3264(1)	0.1823(3)	0.2866(5)	0.023(2)	0.030(2)	0.034(3)	-0.004(2)	-0.002(2)	0.005(2)
C(10)	16b	0.3371(1)	0.1524(3)	0.1751(6)	0.028(2)	0.046(3)	0.025(3)	-0.002(2)	-0.003(2)	0.008(3)
C(11)	16b	0.3406(1)	0.0798(3)	0.1688(6)	0.028(2)	0.047(3)	0.025(3)	0.003(2)	0.000(2)	-0.005(3)
C(12)	16b	0.3334(1)	0.0383(3)	0.2725(5)	0.024(2)	0.031(3)	0.027(3)	0.003(2)	-0.003(2)	-0.004(2)
C(13)	16b	0.2539(1)	0.0364(2)	0.5165(5)	0.025(2)	0.022(2)	0.031(3)	-0.002(2)	0.001(2)	-0.004(2)
C(14)	16b	0.2263(1)	0.0676(3)	0.5965(5)	0.024(2)	0.025(2)	0.028(3)	-0.002(2)	0.005(2)	0.003(2)
C(15)	16b	0.2107(1)	0.1745(2)	0.8424(5)	0.023(2)	0.022(2)	0.020(3)	-0.001(2)	0.002(2)	0.003(2)
C(16)	16b	0.2431(1)	0.1651(3)	0.8874(5)	0.018(2)	0.028(2)	0.030(3)	-0.001(2)	0.004(2)	0.001(2)
C(17)	16b	0.2485(1)	0.1591(2)	1.0178(5)	0.027(2)	0.022(3)	0.034(3)	0.001(2)	-0.008(2)	0.005(2)
C(18)	16b	0.2215(1)	0.1637(2)	1.0983(5)	0.035(3)	0.022(3)	0.020(3)	0.001(2)	0.001(2)	0.004(2)
C(19)	16b	0.1889(1)	0.1710(3)	1.0551(5)	0.030(3)	0.027(2)	0.024(3)	0.000(2)	0.008(2)	0.003(2)
C(20)	16b	0.1836(1)	0.1765(3)	0.9241(5)	0.019(2)	0.029(2)	0.030(3)	0.003(2)	0.004(2)	-0.002(2)

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References

- Dondas, H. A.; Cummins, J. E.; Grigg, R.; Thornton-Pett, M.: Sequential Nucleophilic Substitution 1,3-Dipolar Cycloaddition Reactions of Z-Oxime Anions with Aziridine and Dipolarophiles. *Tetrahedron* **57** (2001) 7951-7964.
- Frank, E.; Wolfling, J.; Auzsi, B.; König, V.; Schneider, T. R.; Schneider, G.: Stereoselective synthesis of some novel heterocyclic estore derivatives by intramolecular 1,3-dipolar cycloaddition. *Tetrahedron* **58** (2002) 6843-6849.
- Iwasa, S.; Tsushima, S.; Shimada, T.; Nishiyama, H.: Synthesis of 2,6-bis(4*R*-trialkylsiloxy-methyloxazolonyl) pyridines and their use in catalytic asymmetric 1,3-dipolar cycloaddition reactions of nitrones and activated alkenes. *Tetrahedron Lett.* **42** (2001) 6715-6717.
- Gothelf, K. V.; Jorgensen, K. A.: Catalytic enantioselective 1,3-Dipolar Cycloaddition reactions of nitrones. *Chem. Commun.* (2000) 1449-1458.
- Hong, C. Y.; Kim, Y. K.; Chang, J. H.; Kim, S. H.; Choi, H.; Nam, D. H.; Kim, Y. Z.; Kwak, J. J.: Novel fluoroquinolone antibacterial agents containing oxime-substituted (aminomethyl)pyrrolidines: Synthesis and antibacterial activity of 7-(4-(aminomethyl)-3-(methoxyimino)pyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro[1,8]naphthyridine-3-carboxylic acid. *J. Med. Chem.* **40** (1997) 3584-3593.
- Kim, D. J.; Seo, K. J.; Lee, K. S.; Shin, K. J.; Yoo, K. H.; Kim, D. C.; Park, S. W.: Novel fluoroquinolone antibacterial agents containing oxime-substituted (aminomethyl) pyrrolidines: Synthesis and antibacterial activity of 7-(4-(aminomethyl)-3-(methoxyimino)pyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro[1,8]naphthyridine-3-carboxylic acid. *Bioorg. Med. Chem.* **10** (2000) 2799-2802.
- Dondas, H. A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Kennewell, P.; Thornton-Pett, M.: Halogen-induced inter- and intra-molecular formation of nitrones from oximes and alkenes. *Tetrahedron* **57** (2001) 1119-1128.
- Dondas, H. A.; Grigg, R.; Markandu, J.; Perrier, T.; Suzuki, T.; Thibault, S.; Thomas, W. A.; Thornton-Pett, M.: Stereoselective electrophile-induced mono- and bis-cyclisation-fragmentation reactions of oxime *O*-Allyl and *O*-Benzyl Ethers. Synthesis of Dihydropyridine. *Tetrahedron* **58** (2002) 161-173.
- Dondas, H. A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Thomas, W. A.; Kennewell, P.: Phenylselenyl halide induced formation of cyclic nitrones from alkenyl oximes. *Tetrahedron* **56** (2000) 10087-10096.
- Dondas, H. A.; Thornton-Pett, M.: Crystal structure of two brom containing aza-tetracyclic fused-ring *N*-heterocycles including isoxazolidine ring. *J. Chem. Crystallogr.* **34** (2004) 459-463.
- Sheldrick, G. M.: Phase annealing in SHELX-90: direct methods for larger structures. *Acta Crystallogr. A* **46** (1990) 467-473.
- Sheldrick, G. M.: SHELXL-93. Program for the Refinement of Crystal Structures. University of Göttingen, Germany 1993.