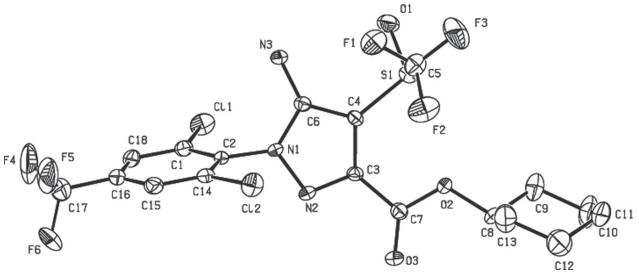
Lianqing Chen* and Xiaoshan Wei

The synthysis and crystal structure of cyclohexyl 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-((trifluoromethyl)sulfinyl)-1*H*-pyrazole-3-carboxylate, $C_{18}H_{15}N_3Cl_2F_6O_3S$



https://doi.org/10.1515/ncrs-2019-0148
Received February 28, 2019; accepted April 5, 2019; available online May 8, 2019

Abstract

$C_{18}H_{15}N_3Cl_2F_6O_3S$, monoclinic, $P2_1/n$ (no. 14), $a = 5.6682(7)$ Å, $b = 31.130(4)$ Å, $c = 12.2829(16)$ Å, $\beta = 98.328(2)°$, $V = 2144.5(5)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0535$, $wR_{ref}(F^2) = 0.1133$, $T = 173$ K.

CCDC no.: 1908255

The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

All chemical reagents and solvents were of analytical grade quality and obtained from commercial suppliers and used directly without further purification (Wuhan Guoyao Chemical Reagent Co. Ltd.). Doubly distilled water was used throughout all experiments.

Fipronil (systematic name: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-((trifluoromethyl)sulfinyl)-1*H*-pyrazole-3-carbonitrile, 4.55 g, 10 mmol) was dissolved in

***Corresponding author: Lianqing Chen,** Key Laboratory of Catalysis and Materials Science of the State, Ethnic Affairs Commission and Ministry of Education, South-Central University for Nationalities, Wuhan 430074, P.R. China, e-mail: lqchen@mail.scuec.edu.cn, chenlia@uwplatt.edu
Xiaoshan Wei: Key Laboratory of Catalysis and Materials Science of the State, Ethnic Affairs Commission and Ministry of Education, South-Central University for Nationalities, Wuhan 430074, P.R. China

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.13 × 0.10 × 0.08 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.48 mm^{-1}
Diffractometer, scan mode:	CCD,
θ_{max}, completeness:	27.6°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	12742, 4881, 0.042
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3550
$N(param)_{refined}$:	326
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3], Diamond [4]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
Cl1	0.18202(14)	0.19273(3)	0.64316(6)	0.0313(2)
Cl2	0.84484(14)	0.22254(3)	0.38067(7)	0.0313(2)
S1	0.61958(13)	0.36151(2)	0.64006(6)	0.02034(17)
F1	1.0614(3)	0.33309(6)	0.64888(16)	0.0382(5)
F2	0.9362(3)	0.36871(7)	0.50270(16)	0.0461(5)
F3	1.0286(4)	0.40138(7)	0.6569(2)	0.0543(6)
F4[a]	0.510(3)	0.0451(4)	0.5346(11)	0.074(3)
F5[a]	0.8119(17)	0.0568(2)	0.4524(8)	0.065(2)
F6[a]	0.465(3)	0.05585(19)	0.3623(6)	0.098(4)
O1	0.6526(4)	0.34991(7)	0.75781(16)	0.0297(5)
O2	0.4073(4)	0.38274(6)	0.40977(16)	0.0248(5)
O3	0.2380(4)	0.33638(6)	0.28040(16)	0.0266(5)
N1	0.4832(4)	0.24747(7)	0.51708(17)	0.0166(5)
N2	0.3834(4)	0.27019(7)	0.42658(18)	0.0185(5)
N3	0.7045(4)	0.25739(8)	0.69439(18)	0.0216(5)
H3A	0.715436	0.230051	0.704293	0.026*
H3B	0.768526	0.274641	0.744994	0.026*
C1	0.3760(5)	0.17380(9)	0.5587(2)	0.0206(6)
C2	0.5093(5)	0.20246(8)	0.5064(2)	0.0160(6)
C3	0.4209(5)	0.31064(9)	0.4548(2)	0.0165(6)
C4	0.5477(5)	0.31509(8)	0.5628(2)	0.0179(6)
C5	0.9276(5)	0.36590(11)	0.6095(3)	0.0297(7)
C6	0.5881(5)	0.27311(9)	0.6006(2)	0.0171(6)
C7	0.3420(5)	0.34381(9)	0.3711(2)	0.0195(6)
C8	0.3675(6)	0.41964(10)	0.3361(2)	0.0306(8)
H8	0.233947	0.413500	0.275516	0.037*
C9	0.3036(6)	0.45674(10)	0.4040(3)	0.0376(8)
H9A	0.425538	0.459858	0.469866	0.045*
H9B	0.148215	0.451108	0.429025	0.045*
C10	0.2886(8)	0.49820(12)	0.3374(4)	0.0546(11)

Table 2 (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
H10A	0.154452	0.496196	0.276321	0.066*
H10B	0.256103	0.522493	0.385104	0.066*
C11	0.5163(8)	0.50680(11)	0.2911(3)	0.0482(10)
H11A	0.647287	0.512030	0.352229	0.058*
H11B	0.496772	0.532969	0.244871	0.058*
C12	0.5812(9)	0.46943(13)	0.2228(3)	0.0592(12)
H12A	0.737044	0.475087	0.198186	0.071*
H12B	0.459988	0.466422	0.156659	0.071*
C13	0.5955(7)	0.42782(11)	0.2887(3)	0.0455(10)
H13A	0.625352	0.403548	0.240488	0.055*
H13B	0.730778	0.429467	0.349377	0.055*
C14	0.6715(5)	0.18680(9)	0.4409(2)	0.0196(6)
C15	0.6964(6)	0.14327(9)	0.4250(2)	0.0262(7)
H15	0.806576	0.132674	0.380061	0.031*
C16	0.5564(6)	0.11536(9)	0.4762(2)	0.0281(7)
C17	0.5739(9)	0.06817(12)	0.4567(3)	0.0488(10)
C18	0.3985(6)	0.13011(9)	0.5430(2)	0.0264(7)
H18	0.305772	0.110405	0.577984	0.032*
F6A[b]	0.714(6)	0.0550(6)	0.405(3)	0.081(6)
F4A[b]	0.341(4)	0.0544(6)	0.402(3)	0.082(6)
F5A[b]	0.561(7)	0.0451(11)	0.549(2)	0.050(5)

[a]Occupancy: 0.73(3), [b]Occupancy: 0.27(3).

30 mL cyclohexanol solution, and anhydrous ferric chloride (3.24 g, 20 mmol) was added portionwise. After ultrasonic stirring for 0.5 h, the reaction mixture was reacted at 100 °C for 9 h. The reaction solution was cooled to room temperature, and replaced with a distillation apparatus to remove excess solvent to obtain a brown paste. Distilled water (100 mL) and ethyl acetate (500 mL) were successively added to the tan paste, and then extracted three times to combine the organic phases. After drying over $MgSO_4$, the mixture was filtered, and the filtrate was concentrated by rotary evaporation and applied to the activated silica powder (5.0 g). The crude product was isolated by column chromatography, the crude material was washed several times with petroleum ether, filtered and dried to give the title compound. Yield: 3.10 g (68.1%), **^{1}H NMR** ($CDCl_3$, 400 MHz, ppm) δ 7.79 (s, 2H, Ar—H), 5.16 (s, 2H, C—NH_2), 5.02 (dd, J = 12.4, 7.6 Hz, 1H, C—CH), 1.99 (s, 2H, C—CH_2), 1.77 (s, 2H, C—CH_2), 1.58—1.47 (m, 2H, C—CH_2), 1.43—1.31 (m, 2H, C—CH_2), 1.28 (d, J = 12.0 Hz, 2H, C—CH_2). **IR** (KBr, ν, cm^{-1}): 3451 and 3333 (N—H stretching vibration), 2947 (C—H), 1725 (C=O), 1618 (C=N), 1454 and 1401 (benzene ring skeleton vibration), 1325 (C—F), 1141 and 1064 (C—O—C), 874 and 817(aromatic ring C—H). **MS (FAB)**: m/e, 537 (M^+).

After allowing the $V_{\text{ethyl acetate}}/V_{\text{petroleum ether}}$ (1:3) to stand in air for 10 days, transparent block colorless crystals formed by slowly evaporating of the solvent. The crystals of the title compound were isolated, washed with light petroleum and dried in vacuum (yield 82.3%)

Experimental details

All H atoms are geometrically positioned and refined using the riding model. The C—H constraint distance is from 0.95 Å to 1.00 Å, and U_{iso}(H) is limited to 1.5 U_{iso}(C) methyl H atoms and 1.2 U_{eq}(C) are aryl H atoms, allowing the rotation of the C—C bond. The CF_3 group was refined by a disordered model. It was found that the atoms F4, F5 and F6 of the CF_3 moiety were disordered at three positions (F4/F4A, F5/F5A and F6/F6A) and split into two positions with occupancies of 0.728 and 0.272 and refined anisotropically.

Comment

Phenylpyrazole derivatives have attracted increasing attention owing to their excellent biological activities and play a fundamental role in the rapid development of pesticides [5]. Fipronil is the first commercial phenylpyrazole insecticide introduced for pest control, which is highly effective against soil insects, such as wireworms and aquatic insects, with extended use in the control of many agricultural vermin on various crops, such as water rice weevil and locust [6]. Its mechanism of action is to inhibit insecticidal α-amino butyric acid, thereby blocking the gated chloride channel to kill insects [7]. Ester compounds are of great significance in the field of medicinal chemistry, especially ester prodrugs have high stability, long duration of action, good solvent and low toxic side effects [8]. However, there was very few phenylpyrazole ester derivatives reported, and it still remains a great challenge to find some novel phenylpyrazole ester pesticides [9]. There is an urgent need to design and develop a general green approach to provide more luminescent phenylpyrazole ester insecticides.

The core structure of the title molecule consists of a pyrazole ring. A trifluoromethanesulfinyl group and a cyclohexyl ester group are linked on the peripheral part, and a phenyl ring, which is bridged to the pyrazole ring with N1—C2 bond 1.417(3) Å. The bond distances of C17—F4, C17—F5 and C17—F6 (CF_3 groups attached to the phenyl moiety) are 1.290(12) Å, 1.403(9) Å and 1.291(6) Å, respectively and their average bond distance is slightly shorter than the average value of the other CF_3 group in the trifluoromethanesulfinyl moiety. The S1—C4 bond distance is 1.744(3) Å, significantly larger than the double bond length of S1—O1 (1.476(2) Å), which is the single bond connecting 5-membered heterocyclic pyrazole ring [10]. The bond length of O3—C7 is 1.205(3) Å, which is shorter than the bond length of O2—C8, 1.460(3) Å. In the crystal structure of title compound, the 2,6-dichloro-4-(trifluoromethyl)phenyl ring is twisted out of the plane of pyrazole ring and the two heterocyclic rings makes a dihedral angle of 74.53(2)°. The ester group is coplanar to the plane of pyrazole ring. However, CF_3 group in the trifluoromethanesulfinyl moiety is almost perpendicular to the pyrazole plane

and the angle of C4—S1—C5 is 95.97(14)° [11]. The N2—C3 bond distance is 1.315(3) Å, which is the shortest carbon-nitrogen bond.

The packing of the title structure is partially facilitated by π–π conjugated interactions between aromatic rings in neighboring molecules. The two most prominent such interactions are given in the π–π ones (*Cg*1 represents the pyrazole ring N1/N2/C3/C4/C6, *Cg*2 that of C1/C2/C14/C15/C16/C18) benzene ring. The first of these interactions, *C(g)*1···*C(g)*1 acts in centrosymmetric pairs between two aromatic rings of neighboring molecules, connecting the molecules to infinite chains along the *a* axis of the unit cell. The second *C(g)*2···*C(g)*2 π–π interaction connects these chains with each other. There are no classic H-bonds.

The bioactivities of the title compound and fipronil against the 3rd instar larvae of *Plutella xylostella* were investigated by the leaf disc-dipping assay. Leaves of Chinese cabbage grown in the greenhouse were collected, and discs (5 cm diameter) were punched from each leaf. The compounds were dissolved in acetone and suspended in distilled water containing Triton X-100. Leaf discs were dipped in each test solution for 30 s and allowed to dry for 2.8 h. The treated leaf discs were placed into Petri dishes (10.0 cm diameter). Then, 15 *Plutella xylostella* larvae were introduced into each dish. Doubly distilled water containing acetone-Triton X-100 solution was used as the control. Petri dishes were kept in incubator at 26 °C and 86% relative humidity under a photoperiod of 15:9 h light: dark. All treatments were replicated three times. Mortalities were determined 24 h after treatment. The death rate of each treatment group was confirmed. LC_{50} value was calculated by the SPSS. Bioactivity result exhibited that the activities of the title compound against *Plutella xylostella* after 24 h is 17.28 $mg{\cdot}L^{-1}$ which is slightly better than that of fipronil 27.45 $mg{\cdot}L^{-1}$. This result proposes a novel insight to provide more novel phenylpyrazole ester pesticides by a general green method.

Acknowledgements: The authors thank the National Natural Science Foundation of China (Grant Nos. 20702064, 21177161 and 31402137); Natural Science Foundation of Hubei province for Distinguished Young Scholars (No. 2013CFA034); the Program for Excellent Talents in Hubei Province (RCJH15001); the Opening Project of Key Laboratory of Green Catalysis of Sichuan Institutes of High Education (LYZ1107) and the Fundamental Research Funds for the Central University, South-Central University for Nationalities (CZP17077).

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