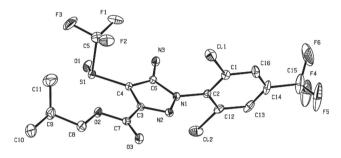
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The synthesis and crystal structure of isobutyl 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-((trifluoromethyl)sulfinyl)-1H-pyrazole-3carboxylate, C₁₆H₁₃Cl₂F₆N₃O₃S



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Abstract

 $C_{16}H_{13}Cl_2F_6N_3O_3S$, monoclinic, $P2_1/n$ (no. 14), a = 5.8650(10) Å,b = 30.196(5) Å,c = 11.777(2) Å, $\beta = 96.619(2)^{\circ}$, $V = 2071.8(6) \text{ Å}^3$, Z = 4, $R_{gt}(F) = 0.0521$, $wR_{\rm ref}(F^2) = 0.1211, T = 173 \text{ K}.$

CCDC no.: 1920921

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 including fipronil were of analytical grade quality, which were obtained from commercial suppliers and used directly without further purification (Wuhan Guoyao Chemical Reagent Co., Ltd.). The synthesis process of the target product involves the following steps by an improved Pinner reaction. Firstly, to a 250 mL three-necked bottle, added 0.01 mol (4.37 g) fipronil

Table 1: Data collection and handling.

| Crystal: | Colourless block |
|--|--|
| Size: | $0.12\times0.10\times0.07~\text{mm}$ |
| Wavelength: | Mo $K\alpha$ radiation (0.71073 Å) |
| μ : | $0.49 \; \text{mm}^{-1}$ |
| Diffractometer, scan mode: | CCD, φ and ω -scans |
| $\theta_{\sf max}$, completeness: | 26.4°, >99% |
| $N(hkl)_{\text{measured}}, N(hkl)_{\text{unique}}, R_{\text{int}}$: | 15720, 4233, 0.041 |
| Criterion for I_{obs} , $N(hkl)_{gt}$: | $I_{\rm obs} > 2 \ \sigma(I_{\rm obs})$, 3370 |
| N(param) _{refined} : | 282 |
| Programs: | Bruker [1], SHELX [2, 3], |
| | Diamond [4] |

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å2).

| х | V | Z | U _{iso} */U _{ea} |
|------------|---|---|---|
| | <u> </u> | | 0.0316(2) |
| | | | 0.0316(2) |
| | | | |
| ` ' | ` , | ` , | 0.01874(17) 0.0433(5) |
| ` , | ` , | | ` ' |
| ` , | ` , | ` ' | 0.0417(5) |
| ` , | ` ' | ` ' | 0.0566(6) |
| ` , | ` , | ` , | 0.0917(11) |
| ` , | ` , | ` ' | 0.1048(13) |
| . , | ` , | ` ' | 0.1043(12) |
| ` , | ` , | ` , | 0.0268(5) |
| ` , | ` ' | ` , | 0.0216(4) |
| 0.6658(3) | 0.66245(7) | 0.73301(16) | 0.0235(5) |
| 0.3989(4) | 0.75131(7) | 0.49104(18) | 0.0154(5) |
| 0.5007(4) | 0.72835(8) | 0.58411(18) | 0.0165(5) |
| 0.1727(4) | 0.74014(8) | 0.31342(19) | 0.0208(5) |
| 0.161985 | 0.768221 | 0.302337 | 0.025* |
| 0.106985 | 0.722121 | 0.263337 | 0.025* |
| 0.2111(5) | 0.81497(10) | 0.5649(2) | 0.0194(6) |
| 0.3750(4) | 0.79788(9) | 0.5002(2) | 0.0158(6) |
| 0.4624(4) | 0.68636(9) | 0.5581(2) | 0.0152(5) |
| 0.3317(4) | 0.68134(9) | 0.4490(2) | 0.0154(6) |
| -0.0389(6) | 0.63015(11) | 0.4100(3) | 0.0306(7) |
| 0.2918(4) | 0.72429(9) | 0.4091(2) | 0.0160(6) |
| 0.5530(5) | 0.65337(9) | 0.6443(2) | 0.0168(6) |
| 0.5814(5) | 0.57675(10) | 0.6884(3) | 0.0260(7) |
| 0.528995 | 0.580884 | 0.764661 | 0.031* |
| 0.751323 | 0.577059 | 0.697354 | 0.031* |
| 0.4942(6) | 0.53363(10) | 0.6377(3) | 0.0325(8) |
| 0.535656 | 0.532141 | 0.557767 | 0.039* |
| 0.6128(7) | 0.49519(11) | 0.7045(3) | 0.0429(9) |
| ` , | 0.497710 | 0.704012 | 0.064* |
| 0.559522 | 0.467142 | 0.668981 | 0.064* |
| 0.575912 | 0.496021 | 0.783572 | 0.064* |
| | 0.5007(4) 0.1727(4) 0.161985 0.106985 0.2111(5) 0.3750(4) 0.4624(4) 0.3317(4) -0.0389(6) 0.2918(4) 0.5530(5) 0.5814(5) 0.528995 0.751323 0.4942(6) 0.535656 0.6128(7) 0.779295 0.559522 | 0.04011(14) 0.77877(3) 0.70487(13) 0.80621(3) 0.25821(12) 0.63290(2) -0.1676(3) 0.66337(7) -0.0452(3) 0.62899(7) -0.1378(4) 0.59258(8) 0.3827(7) 0.96016(8) 0.3646(7) 0.95215(8) 0.0659(7) 0.94870(9) 0.2263(4) 0.64386(7) 0.4919(3) 0.61221(6) 0.6658(3) 0.66245(7) 0.3989(4) 0.75131(7) 0.5007(4) 0.72835(8) 0.1727(4) 0.74014(8) 0.161985 0.768221 0.106985 0.722121 0.2111(5) 0.81497(10) 0.3750(4) 0.79788(9) 0.4624(4) 0.68636(9) 0.3317(4) 0.68134(9) -0.0389(6) 0.63015(11) 0.2918(4) 0.72429(9) 0.5530(5) 0.65337(9) 0.5814(5) 0.57675(10) 0.528995 0.580884 0.751323 0.577059 0.4942(6) 0.53363(10) 0.535656 0.532141 0.6128(7) 0.49519(11) 0.779295 0.497710 0.559522 0.467142 | 0.04011(14) 0.77877(3) 0.63055(7) 0.70487(13) 0.80621(3) 0.36042(7) 0.25821(12) 0.63290(2) 0.37233(6) -0.1676(3) 0.66337(7) 0.36723(18) -0.0452(3) 0.62899(7) 0.52224(16) -0.1378(4) 0.59258(8) 0.3664(2) 0.3827(7) 0.96016(8) 0.4564(2) 0.3646(7) 0.95215(8) 0.6342(2) 0.0659(7) 0.94870(9) 0.5147(3) 0.2263(4) 0.64386(7) 0.24872(16) 0.4919(3) 0.61221(6) 0.61135(16) 0.6658(3) 0.66245(7) 0.73301(16) 0.3989(4) 0.75131(7) 0.49104(18) 0.5007(4) 0.72835(8) 0.58411(18) 0.1727(4) 0.74014(8) 0.31342(19) 0.161985 0.768221 0.302337 0.106985 0.722121 0.263337 0.2111(5) 0.81497(10) 0.5649(2) 0.3750(4) 0.79788(9) 0.5002(2) 0.4624(4) 0.68636(9) 0.5581(2) 0.3317(4) 0.68134(9) 0.4490(2) -0.0389(6) 0.63015(11) 0.4100(3) 0.2918(4) 0.72429(9) 0.4091(2) 0.5530(5) 0.65337(9) 0.6443(2) 0.5814(5) 0.57675(10) 0.6884(3) 0.528995 0.580884 0.764661 0.751323 0.577059 0.697354 0.4942(6) 0.53363(10) 0.6377(3) 0.535656 0.532141 0.557767 0.6128(7) 0.49519(11) 0.7045(3) 0.779295 0.497710 0.704012 0.559522 0.467142 0.668981 |

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Table 2 (continued)

| Atom | X | y | Z | $U_{iso}*/U_{eq}$ |
|------|------------|-------------|-----------|-------------------|
| C11 | 0.2373(7) | 0.52951(14) | 0.6321(5) | 0.0660(14) |
| H11A | 0.191410 | 0.532069 | 0.709273 | 0.099* |
| H11B | 0.188995 | 0.500652 | 0.599703 | 0.099* |
| H11C | 0.164258 | 0.553130 | 0.583744 | 0.099* |
| C12 | 0.5094(5) | 0.82674(10) | 0.4451(2) | 0.0216(6) |
| C13 | 0.4847(6) | 0.87218(10) | 0.4564(3) | 0.0294(7) |
| H13 | 0.578475 | 0.892076 | 0.419955 | 0.035* |
| C14 | 0.3209(6) | 0.88800(10) | 0.5219(3) | 0.0308(8) |
| C15 | 0.2889(10) | 0.93731(13) | 0.5339(3) | 0.0560(12) |
| C16 | 0.1830(6) | 0.85995(10) | 0.5763(2) | 0.0260(7) |
| H16 | 0.071064 | 0.871411 | 0.620638 | 0.031* |

and then dissolved by 30 mL isobutyl alcohol, 0.02 mol of anhydrous ferric chloride in batches was added as a catalyst, ultrasonic stirring for 0.5 h, the reaction mixture was reacted at 100 °C for 9 h. The resulting solution was then cooled to room temperature, and removed excess solvent to give a tan cream. Secondly, 100 mL of distilled water and 50 mL of ethyl acetate were added to the tan cream one by one, and extracted three times. The organic phases were combined and washed with saturated sodium carbonate solution (30 mL), distilled water and brine, respectively, and then dried over MgSO4. The filtrate was concentrated, swirled and adsorbed onto 6 g of activated silica gel. Finally, the crude product was obtained by column chromatography on silica gel with $V_{\rm ethyl\,acetate}/V_{\rm petroleum\,ether}$ (1:4) the eluent, which was dried under vacuum to give the title compound. Yield: 91.2%, ¹H NMR (CDCl₃, 400 MHz, ppm) δ 7.79 (s, 2H, Ar-H), 5.17 (s, 2H, C-NH₂), 4.15 (d, J = 8.0 Hz, 2H, C-CH₂), 2.08 (td, J = 20.0, 12.0 Hz, 1H, C-CH), 0.99 (dd, I = 8.0, 8.0 Hz, 6H, C-CH₃). **IR** (KBr, ν , cm⁻¹): 3451, 3328 (N-H), 2970 (Ar-H), 1728 (C=O), 1618 (-C=N), 1497 (benzene ring skeleton vibration), 1326 (C-F), 1144, 1065 (C-O-C), 875, 816 (C-H), 657 (aromatic ring C-H). MS (FAB): m/e, 512 (M^+).

After allowing the V_{ethyl} acetate $V_{\text{petroleum ether}}$ (1:5) to stand in air for 8 days, transparent colorless block crystals of the title compound formed by slow evaporation of the solvent. The crystals were isolated, washed with light petroleum and dried in vacuum (yield 89.6%).

Experimental details

All H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms with C-H distances in the range 0.93–0.98 Å, and with $U_{\rm iso}({\rm H}) = 1.2 \, U_{\rm eq}$ for aryl and nitrogen H atoms and 1.5 $U_{\rm eq}$ for the methyl H atoms. The special instructions are as follows:

Fixed U_{iso} , At 1.2 times of: All C(H) groups, All C(H, H) groups, All N(H, H) groups

- At 1.5 times of: All C(H, H, H) groups
- 2.a Riding coordinates: N3(H3A, H3B)
- 2.b Ternary CH refined with riding coordinates: C9(H9)
- 2.c Secondary CH₂ refined with riding coordinates: C8(H8A, H8B)
- 2.d Aromatic/amide H refined with riding coordinates: C13(H13), C16(H16)
- 2.e Idealised Me refined as rotating group: C10(H10A, H10B, H10C), C11(H11A, H11B, H11C).

Comment

Phenylpyrazole derivatives have attracted increasing attention owing to their excellent biological activities [5]. In the field of pesticides, they play a fundamental role in the rapid development of insecticides, and in the field of medicine, their derivatives can reduce analgesia and inflammation [6]. In the agricultural field, phenylpyrazole compounds are mainly used to deal with soil insects such as gold nematodes, aquatic insects such as rice, and control of aphids [7]. In addition, phenylpyrazole heterocycle derivatives are useful inter-mediates and ligands, from which many macrocyclic compounds with high fluorescence quantum yield and supermolecular structures with extended conjugated aromatic system can be constructed. Heterocyclic ester derivatives and its complexes are important chemical reagents, which can act as a foundational role of a wide range of applications in the fields of catalysis, biochemistry, functional materials, medicine and other research areas [8]. However, to our best knowledge, only a few phenylpyrazole ester compounds have been reported. Considering on the advantages of high stability, long duration of action, good solubility and small side effects for phenylpyrazole ester derivatives, the title compound has been synthesized by an improved Pinner reaction using FeCl₃ as green catalyst, and isobutyl alcohol as solvent and reactant [9].

The molecular structure consists of a pyrazole ring, including a trifluoromethanesulfinyl group and carboxylic acid isobutyl ester group linked on the peripheral part, and a phenyl ring, which is bridged with C-N bond 1.418(3) Å formed by N1—C2 single bond to the 2,6-dichloro-4-trifluoromethylphenyl moiety. The S1-C4 bond distance is 1.747(3) Å, significantly longer than the double bond length of S1–O1 (1.484(2) Å), which is the single bond connecting 5-membered heterocyclic pyrazole ring. The 2,6-dichloro-4-(trifluoromethyl)phenyl moiety is twisted out of the plane of pyrazole ring and the two heterocyclic rings makes a dihedral angle of 73.38(3)° [10]. The isobutylate group is coplanar to the plane of pyrazole ring due to the carboxyl planar structure. However the CF₃ group in the trifluoromethanesulfinyl moiety is almost perpendicular to the pyrazole plane and the angle of C4-S1-C5 is 95.56(14)° [11]. The N2-C3 bond

distance is 1.318(4) Å, which is the shortest carbon-nitrogen double bond. The C5-F1, C5-F2 and C5-F3 bond distance (CF₃ group connecting with phenyl moiety) are 1.320(4) Å. 1.327(4) Å and 1.349(4) Å, respectively and their average bond distance is slightly larger than the average value of the other CF₃ group in the trifluoromethanesulfinyl moiety. Generally the geometric parameters are similar to fibronil [12].

There are some non-classical hydrogen bonds in the packing crystal structure of the title compound, which is partially facilitated by F-H interactions between neighboring molecules. The two most prominent F-H interactions are F2-H11C (bond distance 2.660(2) Å) and F3-H11B (bond distance 2.8640(25) Å), which acts in centrosymmetric pairs between adjacent molecules, connecting these molecules to chains along the b axis of the unit cell. The other hydrogen bond F4—H10C has 2.8787(29) Å bond distance along the c axis and connects these chains with each other. The F-H interactions F1—H3B (bond distance 2.7735(21) Å) is along the a axis, working with other three kinds of hydrogen bonds and building up a perfect two-dimensional structure.

The bioactivities of the title compound and model phenylpyrazole insecticide (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. Two kinds of compounds were dissolved in organic solvent (acetone) and suspended in distilled water containing Triton X-100. Leaf discs were dipped in each test solution for 35 s and allowed to dry for 2.5 h. The treated leaf discs were placed into 10 cm diameter Petri dishes. Then, ten 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 24 °C and 80% relative humidity under a photoperiod of 16:8 h light: dark. All treatments were replicated three times. Mortalities were determined 24 h after treatment. The death rate of each treatment group was determined. LC₅₀ value was calculated by the SPSS. Bioactivity result exhibited that the activities of the title compound against Plutella xylostella after 24 h is 15.26 mg·L⁻¹, better than that of fipronil 27.24 mg·L⁻¹. These researches propose a novel insight to provide some novel phenylpyrazole insecticide by an improved pinner reaction.

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