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# 3-(2-Fluorophenyl)-6-(phenoxymethyl)-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazole

**Melanie Holm,[a] Dieter Schollmeyer[b] and Stefan Laufer[a]***

[a]Institute of Pharmacy, Department of Pharmaceutical and Medicinal Chemistry, Eberhard-Karls-University Tübingen, Auf der Morgenstelle 8, 72076 Tübingen, Germany, and [b]Department of Organic Chemistry, Johannes Gutenberg-University Mainz, Duesbergweg 10-14, D-55099 Mainz, Germany
Correspondence e-mail: stefan.laufer@uni-tuebingen.de

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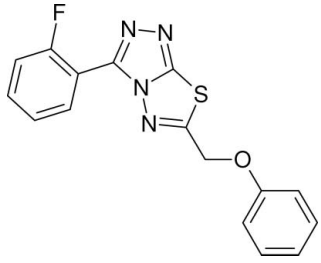
Key indicators: single-crystal X-ray study; $T$ = 193 K; mean $\sigma$(C–C) = 0.003 Å; $R$ factor = 0.048; $wR$ factor = 0.136; data-to-parameter ratio = 13.1.

The crystal structure of the title compound, $C_{16}H_{11}FN_4OS$, was synthesized in the course of our studies on 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazoles as inhibitors of p38 mitogen-activated protein kinase (MAPK). The three-dimensional data obtained were used to generate a three-dimensional pharmacophore model for *in silico* database screening. The dihedral angles between the central heterocylic system and the fluorophenyl and phenyl rings are 20.21 (3) and 5.43 (1)°, respectively; the dihedral angle between the two benzene rings is 15.80 (4)°.

## Related literature

Protein kinases (PK) are favoured targets for the development of new drugs (Hopkins & Groon, 2002) because the reversible protein-phosphorylation by PK is an important control mechanism in the signal pathways of a cell (Laufer *et al.*, 2005). The [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole nucleus is associated with diverse biological activities (Malhotra *et al.*, 2003). For the preparation of the title compound, see: Invidiata *et al.* (1997); Malhotra *et al.* (2003).




## Experimental

### Crystal data

$C_{16}H_{11}FN_4OS$
$M_r$ = 326.35
Monoclinic, $P2_1/n$
$a$ = 10.8551 (6) Å
$b$ = 12.1899 (3) Å
$c$ = 11.6667 (6) Å
$\beta$ = 110.857 (5)°
$V$ = 1442.61 (11) Å$^3$
$Z$ = 4
Cu $K\alpha$ radiation
$\mu$ = 2.19 mm$^{-1}$
$T$ = 193 (2) K
0.58 × 0.51 × 0.26 mm

### Data collection

Enraf–Nonius CAD-4 diffractometer
Absorption correction: $\psi$ scan (*CORINC*; Dräger & Gattow, 1971)
$T_{min}$ = 0.61, $T_{max}$ = 0.99
(expected range = 0.348–0.565)
2883 measured reflections
2736 independent reflections
2583 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.037
3 standard reflections
frequency: 60 min
intensity decay: 4%

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.135
$S$ = 1.06
2736 reflections
209 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.43 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.43 e Å$^{-3}$

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *CORINC* (Dräger & Gattow, 1971); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: BT2678).

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# supplementary materials

*Acta Cryst.* (2008). E**64**, o700 [ **doi:10.1107/S1600536808003917** ]

# 3-(2-Fluorophenyl)-6-(phenoxymethyl)-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazole

**M. Holm, D. Schollmeyer and S. Laufer**

## Comment

Continued interest in development of small molecule inhibitors of p38 mitogen-activated protein (MAP) kinase is based on the central role of this enzyme in inflammatory cell signalling. Activation of p38 leads to an increase production of pro-inflammatory cytokines such as TNF-alpha and IL-1beta. Many different diseases have their seeds in an overactive immune response. Prominent examples like psoriasis, rheumatoid arthritis and inflammatory bowel disease turn it into a still prominent target for antiinflammatory drug discovery. 3-(2-chlorophenyl)-6-((4-methoxyphenoxy)methyl)-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole was identified as potential hit in a virtual screening and the [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole core therefore chosen as starting point for a medicinal chemistry program. To gain more information about structure-activity relationship, a series of compounds were synthesized and tested.

The synthesis of **1** (Figure 1) was started from the substituted hydrazide, which was treated with carbon disulfide. Cyclization followed by reaction with hydrazine. The final product **2** was synthesized by reaction of **1** with 2-phenoxyacetic acid in presence of phosphorus oxychloride.

Of special interest was the proposed binding mode of disubstituted compound and a crystal structure of compound **2** was prepared (Figure 2).

## Experimental

The synthesis of 3-(2-fluorophenyl)-6-(phenoxymethyl)-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole was started from 2-fluorobenzohydrazide. Carbon disulfide (55.0 mmol) was added slowly to a solution of the hydrazide (36.0 mmol) in absolute ethanol (70 ml) containing potassium hydroxid (55.0 mmol). The resulting mixture was stirred over night at room temperature, then cooled and diluted with ether (100 ml). Potassium 2-(2-fluorobenzoyl)hydrazinecarbodithioate precipitated and was collected by filtration, washed with diethyl ether and dried.

A mixture containing potassium dithiocarbazinate (16.0 mmol) suspended in water (2 ml) and hydrazine hydrate (99%, 32.0 mmol) was heated under gentle reflux for 2 h. It was cooled to room temperature and diluted with water (80 ml) and acidified with concentrated hydrochloric acid. Thick white solid mass separated out. It was collected by filtration, washed with water and recrystallized from ethanol to get 4-amino-5-(2-fluorophenyl)-4*H*-1,2,4-triazole-3-thiol **1**. (Invidiata *et al.*, 1997)

For the preparation of the title compound, a mixture of **1** (5.0 mmol), 2-phenoxyacetic acid (1.0 mmol) and phosphorus oxychloride (10 ml) was refluxed for 6 h, cooled to room temperature and poured onto crushed ice. The solid product separated out and was collected by filtration, washed with aqueous NaOH solution (20 ml, 2 *M*) and then with water, dried and recrystallized from ethanol **2**. (Malhotra *et al.*, 2003)

Crystals of **2** for X-ray analysis precipitated slowly as brown platelets from ethanol at room temperature.

### Refinement

Hydrogen atoms were placed at calculated positions with C—H=0.95A% (aromatic) or 0.99 Å ($sp^3$ C-atom). All H atoms were refined with isotropic displacement parameters set at 1.2 times of the $U_{eq}$ of the parent atom.

### Figures

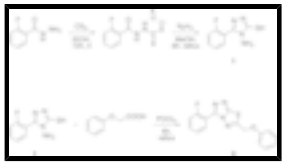


Fig. 1. Synthesis of compounds **1** and **2**.

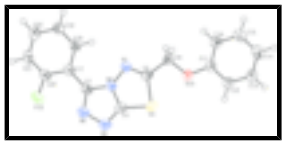


Fig. 2. Perspective view of **2**. Displacement ellipsoids are drawn at the 50% probability level. H atoms are depicted as circles of arbitrary size.

### 3-(2-Fluorophenyl)-6-(phenoxymethyl)-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazole

*Crystal data*

| | |
|---|---|
| $C_{16}H_{11}FN_4OS$ | $F_{000}$ = 672 |
| $M_r$ = 326.35 | $D_x$ = 1.503 Mg m$^{-3}$ |
| Monoclinic, $P2_1/n$ | Cu $K\alpha$ radiation<br>λ = 1.54178 Å |
| Hall symbol: -P 2yn | Cell parameters from 25 reflections |
| $a$ = 10.8551 (6) Å | θ = 65–70º |
| $b$ = 12.1899 (3) Å | μ = 2.19 mm$^{-1}$ |
| $c$ = 11.6667 (6) Å | $T$ = 193 (2) K |
| β = 110.857 (5)º | Plate, light brown |
| $V$ = 1442.61 (11) Å$^3$ | 0.58 × 0.51 × 0.26 mm |
| $Z$ = 4 | |

*Data collection*

| | |
|---|---|
| Enraf–Nonius CAD-4 diffractometer | $R_{int}$ = 0.037 |
| Monochromator: graphite | $\theta_{max}$ = 69.9º |
| $T$ = 193(2) K | $\theta_{min}$ = 4.8º |
| ω/2θ scans | $h$ = 0→13 |
| Absorption correction: ψ scan (CORINC; Dräger & Gattow, 1971) | $k$ = 0→14 |
| $T_{min}$ = 0.61, $T_{max}$ = 0.99 | $l$ = −14→13 |
| 2883 measured reflections | 3 standard reflections |
| 2736 independent reflections | every 60 min |
| 2583 reflections with $I$ > 2s($I$) | intensity decay: 4% |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | Hydrogen site location: inferred from neighbouring sites |
| Least-squares matrix: full | H-atom parameters constrained |
| $R[F^2 > 2\sigma(F^2)] = 0.048$ | $w = 1/[\sigma^2(F_o^2) + (0.0847P)^2 + 0.6884P]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $wR(F^2) = 0.135$ | $(\Delta/\sigma)_{max} < 0.001$ |
| $S = 1.06$ | $\Delta\rho_{max} = 0.43$ e Å$^{-3}$ |
| 2736 reflections | $\Delta\rho_{min} = -0.43$ e Å$^{-3}$ |
| 209 parameters | Extinction correction: SHELXL97 (Sheldrick, 2008), $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$ |
| Primary atom site location: structure-invariant direct methods | Extinction coefficient: 0.0071 (8) |
| Secondary atom site location: difference Fourier map | |

*Special details*

**Geometry**. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

**Refinement**. Refinement of $F^2$ against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on $F^2$, conventional *R*-factors *R* are based on F, with F set to zero for negative $F^2$. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on $F^2$ are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å$^2$)*

| | *x* | *y* | *z* | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| N1 | 0.65749 (15) | 0.29912 (12) | 0.27951 (14) | 0.0311 (4) |
| C2 | 0.62295 (17) | 0.25592 (16) | 0.17147 (17) | 0.0324 (4) |
| S3 | 0.63057 (5) | 0.11269 (4) | 0.16086 (4) | 0.0375 (2) |
| C4 | 0.68622 (19) | 0.11015 (15) | 0.31907 (19) | 0.0358 (4) |
| N5 | 0.72177 (18) | 0.03789 (14) | 0.40767 (17) | 0.0445 (4) |
| N6 | 0.75709 (18) | 0.09854 (14) | 0.51539 (17) | 0.0426 (4) |
| C7 | 0.74119 (17) | 0.20439 (15) | 0.48900 (18) | 0.0331 (4) |
| N8 | 0.69477 (14) | 0.21442 (12) | 0.36353 (14) | 0.0306 (4) |
| C9 | 0.58296 (19) | 0.32345 (16) | 0.05735 (17) | 0.0358 (4) |
| H9A | 0.5190 | 0.3806 | 0.0593 | 0.043* |
| H9B | 0.6607 | 0.3596 | 0.0484 | 0.043* |
| O10 | 0.52441 (15) | 0.24906 (12) | −0.04087 (12) | 0.0433 (4) |
| C11 | 0.50482 (17) | 0.28429 (16) | −0.15846 (17) | 0.0326 (4) |
| C12 | 0.45545 (19) | 0.20490 (17) | −0.24815 (18) | 0.0376 (4) |
| H12 | 0.4366 | 0.1333 | −0.2266 | 0.045* |
| C13 | 0.4337 (2) | 0.23046 (19) | −0.36915 (19) | 0.0436 (5) |

| | | | | |
|---|---|---|---|---|
| H13 | 0.4012 | 0.1759 | −0.4308 | 0.052* |
| C14 | 0.4591 (2) | 0.3350 (2) | −0.40103 (19) | 0.0451 (5) |
| H14 | 0.4442 | 0.3524 | −0.4843 | 0.054* |
| C15 | 0.5060 (2) | 0.41365 (19) | −0.3114 (2) | 0.0439 (5) |
| H15 | 0.5220 | 0.4858 | −0.3336 | 0.053* |
| C16 | 0.5303 (2) | 0.38932 (16) | −0.1887 (2) | 0.0378 (5) |
| H16 | 0.5637 | 0.4437 | −0.1271 | 0.045* |
| C17 | 0.77445 (17) | 0.29576 (16) | 0.57653 (17) | 0.0323 (4) |
| C18 | 0.76314 (19) | 0.40498 (16) | 0.53692 (18) | 0.0345 (4) |
| H18 | 0.7312 | 0.4204 | 0.4515 | 0.041* |
| C19 | 0.79764 (19) | 0.49076 (17) | 0.61989 (18) | 0.0390 (4) |
| H19 | 0.7895 | 0.5642 | 0.5909 | 0.047* |
| C20 | 0.8439 (2) | 0.47064 (19) | 0.74481 (19) | 0.0426 (5) |
| H20 | 0.8664 | 0.5297 | 0.8016 | 0.051* |
| C21 | 0.8569 (2) | 0.3633 (2) | 0.78588 (19) | 0.0451 (5) |
| H21 | 0.8895 | 0.3480 | 0.8713 | 0.054* |
| C22 | 0.8224 (2) | 0.27895 (18) | 0.70268 (19) | 0.0399 (5) |
| F23 | 0.83678 (15) | 0.17577 (12) | 0.74746 (12) | 0.0608 (4) |

*Atomic displacement parameters (Å$^2$)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| N1 | 0.0311 (7) | 0.0273 (8) | 0.0325 (8) | 0.0000 (6) | 0.0082 (6) | 0.0011 (6) |
| C2 | 0.0281 (8) | 0.0299 (9) | 0.0381 (10) | −0.0027 (7) | 0.0105 (7) | −0.0040 (7) |
| S3 | 0.0402 (3) | 0.0294 (3) | 0.0430 (3) | −0.00168 (17) | 0.0147 (2) | −0.00653 (18) |
| C4 | 0.0330 (10) | 0.0276 (10) | 0.0457 (11) | −0.0003 (7) | 0.0126 (8) | −0.0033 (8) |
| N5 | 0.0482 (10) | 0.0293 (9) | 0.0522 (10) | 0.0041 (7) | 0.0134 (8) | 0.0039 (7) |
| N6 | 0.0453 (10) | 0.0317 (9) | 0.0464 (10) | 0.0027 (7) | 0.0111 (8) | 0.0066 (7) |
| C7 | 0.0283 (8) | 0.0320 (10) | 0.0375 (10) | 0.0007 (7) | 0.0099 (7) | 0.0059 (7) |
| N8 | 0.0279 (7) | 0.0244 (7) | 0.0375 (8) | 0.0009 (6) | 0.0092 (6) | 0.0011 (6) |
| C9 | 0.0390 (10) | 0.0318 (10) | 0.0325 (10) | −0.0051 (7) | 0.0075 (8) | −0.0044 (7) |
| O10 | 0.0606 (9) | 0.0355 (8) | 0.0316 (7) | −0.0147 (6) | 0.0137 (6) | −0.0050 (6) |
| C11 | 0.0304 (9) | 0.0348 (10) | 0.0322 (9) | 0.0007 (7) | 0.0107 (7) | −0.0011 (7) |
| C12 | 0.0398 (10) | 0.0348 (10) | 0.0375 (10) | −0.0024 (8) | 0.0129 (8) | −0.0026 (8) |
| C13 | 0.0416 (10) | 0.0532 (13) | 0.0341 (10) | 0.0000 (9) | 0.0112 (8) | −0.0062 (9) |
| C14 | 0.0370 (10) | 0.0612 (14) | 0.0369 (11) | 0.0034 (10) | 0.0129 (8) | 0.0081 (10) |
| C15 | 0.0377 (10) | 0.0433 (11) | 0.0495 (12) | 0.0011 (9) | 0.0141 (9) | 0.0132 (9) |
| C16 | 0.0358 (10) | 0.0340 (11) | 0.0425 (11) | −0.0018 (7) | 0.0125 (8) | −0.0018 (8) |
| C17 | 0.0262 (8) | 0.0365 (10) | 0.0334 (9) | 0.0009 (7) | 0.0097 (7) | 0.0038 (7) |
| C18 | 0.0345 (9) | 0.0356 (10) | 0.0314 (9) | 0.0036 (8) | 0.0094 (7) | 0.0030 (7) |
| C19 | 0.0412 (10) | 0.0364 (10) | 0.0378 (10) | 0.0054 (8) | 0.0119 (8) | 0.0006 (8) |
| C20 | 0.0404 (10) | 0.0500 (13) | 0.0377 (10) | 0.0005 (9) | 0.0144 (8) | −0.0083 (9) |
| C21 | 0.0468 (11) | 0.0600 (14) | 0.0293 (10) | −0.0021 (10) | 0.0144 (8) | 0.0045 (9) |
| C22 | 0.0384 (10) | 0.0428 (11) | 0.0384 (10) | −0.0014 (8) | 0.0136 (8) | 0.0110 (9) |
| F23 | 0.0822 (10) | 0.0482 (8) | 0.0443 (7) | −0.0076 (7) | 0.0128 (7) | 0.0186 (6) |

*Geometric parameters (Å, °)*

| | | | |
|---|---|---|---|
| N1—C2 | 1.292 (2) | C13—C14 | 1.382 (3) |

| | | | |
|---|---|---|---|
| N1—N8 | 1.381 (2) | C13—H13 | 0.9500 |
| C2—C9 | 1.492 (3) | C14—C15 | 1.376 (3) |
| C2—S3 | 1.7544 (19) | C14—H14 | 0.9500 |
| S3—C4 | 1.726 (2) | C15—C16 | 1.392 (3) |
| C4—N5 | 1.307 (3) | C15—H15 | 0.9500 |
| C4—N8 | 1.363 (2) | C16—H16 | 0.9500 |
| N5—N6 | 1.389 (3) | C17—C22 | 1.391 (3) |
| N6—C7 | 1.324 (2) | C17—C18 | 1.400 (3) |
| C7—N8 | 1.373 (2) | C18—C19 | 1.383 (3) |
| C7—C17 | 1.467 (3) | C18—H18 | 0.9500 |
| C9—O10 | 1.422 (2) | C19—C20 | 1.384 (3) |
| C9—H9A | 0.9900 | C19—H19 | 0.9500 |
| C9—H9B | 0.9900 | C20—C21 | 1.384 (3) |
| O10—C11 | 1.380 (2) | C20—H20 | 0.9500 |
| C11—C16 | 1.382 (3) | C21—C22 | 1.371 (3) |
| C11—C12 | 1.385 (3) | C21—H21 | 0.9500 |
| C12—C13 | 1.381 (3) | C22—F23 | 1.349 (2) |
| C12—H12 | 0.9500 | | |
| C2—N1—N8 | 107.31 (15) | C12—C13—H13 | 119.8 |
| N1—C2—C9 | 122.45 (17) | C14—C13—H13 | 119.8 |
| N1—C2—S3 | 118.02 (15) | C15—C14—C13 | 119.5 (2) |
| C9—C2—S3 | 119.48 (13) | C15—C14—H14 | 120.2 |
| C4—S3—C2 | 87.12 (9) | C13—C14—H14 | 120.2 |
| N5—C4—N8 | 111.49 (18) | C14—C15—C16 | 121.1 (2) |
| N5—C4—S3 | 138.59 (15) | C14—C15—H15 | 119.4 |
| N8—C4—S3 | 109.92 (14) | C16—C15—H15 | 119.4 |
| C4—N5—N6 | 105.39 (16) | C11—C16—C15 | 118.55 (19) |
| C7—N6—N5 | 109.71 (16) | C11—C16—H16 | 120.7 |
| N6—C7—N8 | 107.62 (17) | C15—C16—H16 | 120.7 |
| N6—C7—C17 | 126.80 (18) | C22—C17—C18 | 116.43 (19) |
| N8—C7—C17 | 125.48 (17) | C22—C17—C7 | 122.11 (18) |
| C4—N8—C7 | 105.78 (16) | C18—C17—C7 | 121.42 (17) |
| C4—N8—N1 | 117.63 (15) | C19—C18—C17 | 121.19 (18) |
| C7—N8—N1 | 136.59 (15) | C19—C18—H18 | 119.4 |
| O10—C9—C2 | 105.77 (15) | C17—C18—H18 | 119.4 |
| O10—C9—H9A | 110.6 | C18—C19—C20 | 120.62 (19) |
| C2—C9—H9A | 110.6 | C18—C19—H19 | 119.7 |
| O10—C9—H9B | 110.6 | C20—C19—H19 | 119.7 |
| C2—C9—H9B | 110.6 | C21—C20—C19 | 119.1 (2) |
| H9A—C9—H9B | 108.7 | C21—C20—H20 | 120.4 |
| C11—O10—C9 | 117.99 (15) | C19—C20—H20 | 120.4 |
| O10—C11—C16 | 124.62 (17) | C22—C21—C20 | 119.70 (19) |
| O10—C11—C12 | 114.51 (17) | C22—C21—H21 | 120.2 |
| C16—C11—C12 | 120.87 (18) | C20—C21—H21 | 120.2 |
| C13—C12—C11 | 119.58 (19) | F23—C22—C21 | 117.38 (19) |
| C13—C12—H12 | 120.2 | F23—C22—C17 | 119.7 (2) |
| C11—C12—H12 | 120.2 | C21—C22—C17 | 122.9 (2) |
| C12—C13—C14 | 120.3 (2) | | |

| | | | |
|---|---|---|---|
| N8—N1—C2—C9 | −176.82 (15) | C9—O10—C11—C12 | 175.96 (17) |
| N8—N1—C2—S3 | 0.50 (19) | O10—C11—C12—C13 | −179.06 (17) |
| N1—C2—S3—C4 | 0.04 (15) | C16—C11—C12—C13 | 1.2 (3) |
| C9—C2—S3—C4 | 177.45 (15) | C11—C12—C13—C14 | −1.0 (3) |
| C2—S3—C4—N5 | 179.1 (2) | C12—C13—C14—C15 | −0.1 (3) |
| C2—S3—C4—N8 | −0.59 (14) | C13—C14—C15—C16 | 1.0 (3) |
| N8—C4—N5—N6 | −0.9 (2) | O10—C11—C16—C15 | 179.97 (18) |
| S3—C4—N5—N6 | 179.41 (19) | C12—C11—C16—C15 | −0.4 (3) |
| C4—N5—N6—C7 | 0.4 (2) | C14—C15—C16—C11 | −0.8 (3) |
| N5—N6—C7—N8 | 0.2 (2) | N6—C7—C17—C22 | −3.4 (3) |
| N5—N6—C7—C17 | −176.25 (17) | N8—C7—C17—C22 | −179.30 (17) |
| N5—C4—N8—C7 | 1.0 (2) | N6—C7—C17—C18 | 174.60 (19) |
| S3—C4—N8—C7 | −179.19 (12) | N8—C7—C17—C18 | −1.2 (3) |
| N5—C4—N8—N1 | −178.73 (15) | C22—C17—C18—C19 | −0.3 (3) |
| S3—C4—N8—N1 | 1.1 (2) | C7—C17—C18—C19 | −178.43 (17) |
| N6—C7—N8—C4 | −0.7 (2) | C17—C18—C19—C20 | −0.3 (3) |
| C17—C7—N8—C4 | 175.79 (17) | C18—C19—C20—C21 | 0.9 (3) |
| N6—C7—N8—N1 | 178.96 (18) | C19—C20—C21—C22 | −0.8 (3) |
| C17—C7—N8—N1 | −4.5 (3) | C20—C21—C22—F23 | −179.92 (18) |
| C2—N1—N8—C4 | −1.0 (2) | C20—C21—C22—C17 | 0.2 (3) |
| C2—N1—N8—C7 | 179.34 (19) | C18—C17—C22—F23 | −179.53 (17) |
| N1—C2—C9—O10 | −167.07 (16) | C7—C17—C22—F23 | −1.4 (3) |
| S3—C2—C9—O10 | 15.6 (2) | C18—C17—C22—C21 | 0.3 (3) |
| C2—C9—O10—C11 | −165.85 (15) | C7—C17—C22—C21 | 178.45 (19) |
| C9—O10—C11—C16 | −4.3 (3) | | |

**Fig. 1**

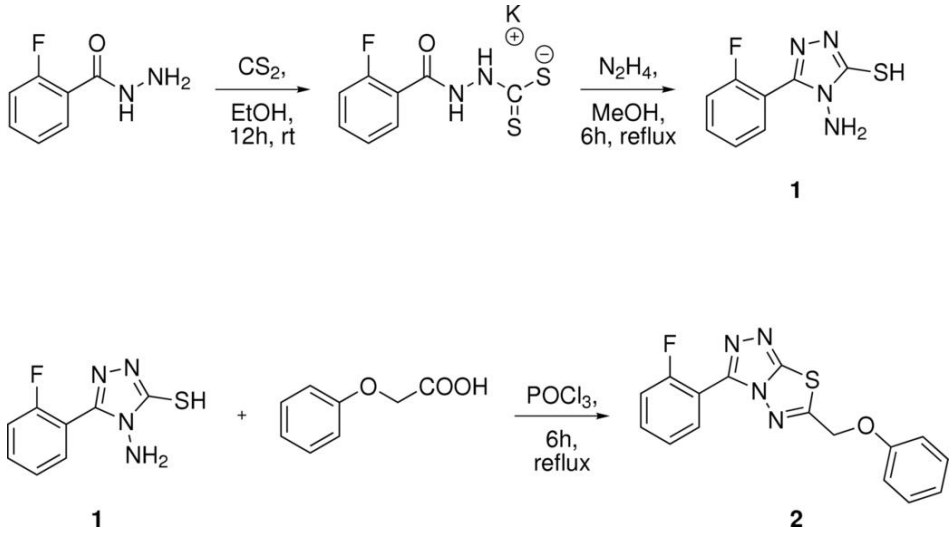
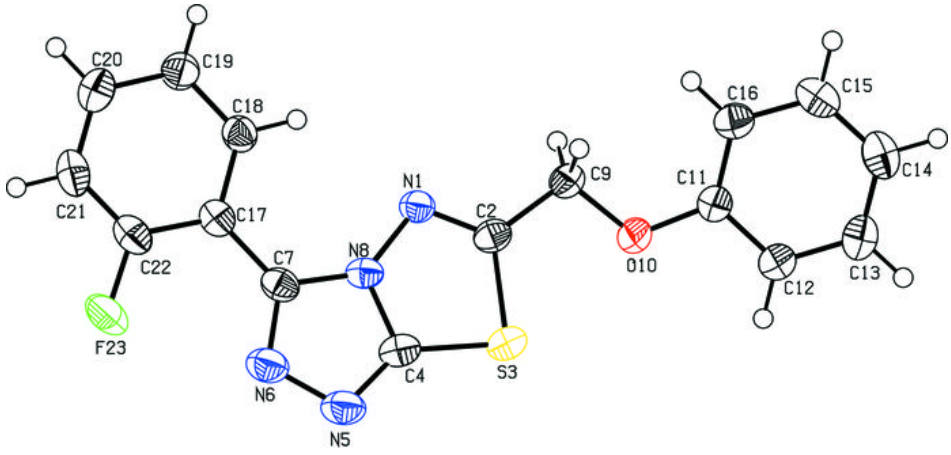

F
O
NH2
N
H
CS2,
EtOH,
12h, rt
K
S
S
N2H4,
MeOH,
6h, reflux
SH
N
NH2
1
COOH
POCl3,
6h,
reflux
2

**Fig. 2**


C20
C19
C18
C21
C17
C22
F23
C7
N8
N1
C2
C9
O10
C11
C16
C15
C14
C13
C12
N6
N5
C4
S3