Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Ethyl 4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

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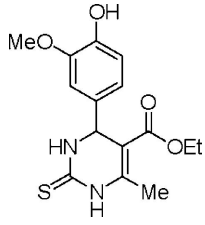
Received 23 September 2007; accepted 23 September 2007

Key indicators: single-crystal X-ray study; T = 294 K; mean σ(C–C) = 0.004 Å; R factor = 0.040; wR factor = 0.107; data-to-parameter ratio = 12.8.

In the title compound, $C_{15}H_{18}N_2O_4S$, the packing is consolidated by an intra/intermolecular bifurcated O—H···(O,O) and intermolecular N—H···S hydrogen bonds. The tetrahydropyrimidin-2-one ring is twisted.

Related literature

For background, see: Kappe (1993).



Experimental

Crystal data

$C_{15}H_{18}N_2O_4S$
M_r = 322.37
Triclinic, $P\overline{1}$
a = 8.469 (2) Å
b = 9.362 (3) Å
c = 11.183 (3) Å
α = 97.935 (4)°
β = 107.783 (4)°
γ = 108.777 (4)°
V = 771.4 (4) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.23 mm^{-1}
T = 294 (2) K
0.20 × 0.18 × 0.18 mm

Data collection

Bruker SMART CCD diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 1997)
T_{min} = 0.956, T_{max} = 0.960
3996 measured reflections
2693 independent reflections
2011 reflections with $I > 2\sigma(I)$
R_{int} = 0.018

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.107
S = 1.02
2693 reflections
211 parameters
2 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O1^{i}	0.82	2.07	2.788 (2)	147
O3—H3···O4	0.82	2.25	2.690 (3)	114
N2—H2···S1^{ii}	0.90 (3)	2.44 (3)	3.326 (2)	167 (2)
N1—H1···S1^{iii}	0.891 (10)	2.531 (11)	3.417 (2)	173 (2)

Symmetry codes: (i) $-x+1, -y, -z$; (ii) $-x+2, -y+1, -z+1$; (iii) $-x+3, -y+1, -z+1$.

Data collection: *SMART* (Bruker, 1997); cell refinement: *SAINT* (Bruker, 1997); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXTL*.

The author thanks the Outstanding Young Scholar funds of Hebei University of Science and Technology.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HB2552).

References

Bruker (1997). *SADABS*, *SMART*, *SAINT* and *SHELXTL*. Bruker AXS Inc., Madison, Wisconsin, USA.
Kappe, C. O. (1993). *Tetrahedron*, **49**, 6937–6963.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.

  doi:10.1107/S1600536807046752

supplementary materials

Acta Cryst. (2007). E**63**, o4172 [**doi:10.1107/S1600536807046752**]

Ethyl 4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

Z.-H. Shang, Y. Xiu and Y.-Y. Lin

Comment

Dihydropyrimidinones (DHPMs) and their derivatives exhibit a wide range of pharmacological and biological activities such as antibacterial, antiviral, antitumor and anti-inflamatory actions (Kappe, 1993).

The title compound, (I), (Fig. 1), was synthesized by the one-pot reaction of 4-hydroxy-3-methoxybenzaldehyde, thiourea and ethyl 3-oxobutanoate in ethanol under reflux. In the arbitrarily chosen asymmetric molecule, C4 has S configuration, but crystal symmetry generates a racemic mixture of enantiomers. The tetrahydropyrimidin-2-one ring is significantly twisted [C3—N2—C4—C5 = 32.8 (3)°]; the phenyl ring is almost perpendicular to the tetrahydropyrimidin-2-one ring [C3—N2—C4—C9 = −93.5 (2)° and C9—C4—C5—C2 = 99.7 (2)°]. The crystal structure is stabilized mainly through intermolecular N—H···S and O—H···O hydrogen bonds (Table 1).

Experimental

A solution of ethyl 3-oxobutanoate (1.95 g, 15 mmol), 4-hydroxy-3-methoxybenzaldehyde (1.52 g, 10.0 mmol) and thiourea (0.76 g, 10 mmol) in ethanol (10 ml) was heated under reflux in the presence of a catalytic amount of HCl for 5 h. The reaction mixture was cooled and filtered. The solid product was recrystallized from ethanol to afford the pure product which was then dissolved in 100 ml absolute ethanol and crystals suitable for X-ray analysis were grown by slow evaporation over a period of 15 d.

Refinement

The C and O-bound H atoms were positioned geometrically, with C—H = 0.93–0.97Å and O—H = 0.82 Å, and refined in a riding model, with U_{iso}(H)= 1.2U_{eq}(C, O) or 1.5U_{eq}(methyl C). The positional parameters of the nitrogen-bound H atoms were refined freely, with U_{iso}(H) = 1.2U_{eq}(N).

Figures

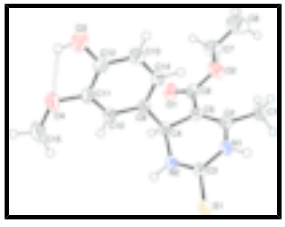


Fig. 1. The molecular structure of (I), drawn with 50% probability ellipsoids (arbitrary spheres for the H atoms). The hydrogen bond is indicated by a double-dashed line.

Fig. 2. The formation of the title compound.

Ethyl 4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo- 1,2,3,4-tetrahydropyrimidine-5-carboxylate

Crystal data

$C_{15}H_{18}N_2O_4S$	$Z = 2$
$M_r = 322.37$	$F_{000} = 340$
Triclinic, $P\overline{1}$	$D_x = 1.388$ Mg m^{-3}
Hall symbol: -P 1	Melting point: 518-520 K
$a = 8.469$ (2) Å	Mo $K\alpha$ radiation $\lambda = 0.71073$ Å
$b = 9.362$ (3) Å	Cell parameters from 1562 reflections
$c = 11.183$ (3) Å	$\theta = 2.4$–26.1º
$\alpha = 97.935$ (4)º	$\mu = 0.23$ mm^{-1}
$\beta = 107.783$ (4)º	$T = 294$ (2) K
$\gamma = 108.777$ (4)º	Prism, colorless
$V = 771.4$ (4) Å^3	0.20 × 0.18 × 0.18 mm

Data collection

Bruker SMART CCD diffractometer	2693 independent reflections
Radiation source: fine-focus sealed tube	2011 reflections with $I > 2\sigma(I)$
Monochromator: graphite	$R_{int} = 0.018$
$T = 294$(2) K	$\theta_{max} = 25.0$º
ω scans	$\theta_{min} = 2.0$º
Absorption correction: multi-scan (SADABS; Bruker, 1997)	$h = -10 \rightarrow 4$
$T_{min} = 0.956$, $T_{max} = 0.960$	$k = -11 \rightarrow 11$
3996 measured reflections	$l = -12 \rightarrow 13$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: difmap and geom
$R[F^2 > 2\sigma(F^2)] = 0.040$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.107$	$w = 1/[\sigma^2(F_o^2) + (0.0443P)^2 + 0.4122P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.02$	$(\Delta/\sigma)_{max} = 0.001$
2693 reflections	$\Delta\rho_{max} = 0.23$ e Å^{-3}
211 parameters	$\Delta\rho_{min} = -0.26$ e Å^{-3}
2 restraints	Extinction correction: none
Primary atom site location: structure-invariant direct methods	

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}
S1	1.28452 (8)	0.56315 (7)	0.51735 (7)	0.0443 (2)
O1	0.7638 (2)	−0.18798 (19)	0.30554 (17)	0.0447 (4)
O2	1.0003 (2)	−0.20831 (18)	0.26755 (18)	0.0465 (5)
O3	0.5754 (2)	0.1860 (3)	−0.18247 (17)	0.0547 (5)
H3	0.4890	0.2102	−0.1883	0.082*
O4	0.4557 (2)	0.2693 (2)	0.00204 (17)	0.0524 (5)
N1	1.2645 (2)	0.2813 (2)	0.41844 (19)	0.0345 (5)
N2	1.0002 (2)	0.2943 (2)	0.41542 (18)	0.0329 (5)
C1	1.3338 (3)	0.0517 (3)	0.4109 (3)	0.0441 (6)
H1A	1.2797	−0.0582	0.4025	0.066*
H1B	1.4214	0.1029	0.4974	0.066*
H1C	1.3914	0.0677	0.3493	0.066*
C2	1.1921 (3)	0.1183 (2)	0.3851 (2)	0.0307 (5)
C3	1.1748 (3)	0.3695 (3)	0.4455 (2)	0.0308 (5)
C4	0.8943 (3)	0.1362 (2)	0.3277 (2)	0.0295 (5)
H4	0.7970	0.0855	0.3565	0.035*
C5	1.0128 (3)	0.0437 (3)	0.3421 (2)	0.0300 (5)
C6	0.9129 (3)	−0.1276 (3)	0.3051 (2)	0.0323 (5)
C7	0.9108 (4)	−0.3780 (3)	0.2279 (3)	0.0479 (7)
H7A	0.7905	−0.4098	0.1638	0.058*
H7B	0.9020	−0.4176	0.3024	0.058*
C8	1.0197 (5)	−0.4392 (3)	0.1721 (3)	0.0728 (10)
H8A	1.0180	−0.4073	0.0939	0.109*
H8B	0.9709	−0.5513	0.1522	0.109*
H8C	1.1412	−0.3990	0.2337	0.109*
C9	0.8087 (3)	0.1452 (2)	0.1891 (2)	0.0293 (5)
C10	0.6679 (3)	0.1976 (3)	0.1605 (2)	0.0325 (5)
H10	0.6255	0.2213	0.2251	0.039*
C11	0.5909 (3)	0.2150 (3)	0.0391 (2)	0.0349 (5)
C12	0.6507 (3)	0.1751 (3)	−0.0592 (2)	0.0366 (6)
C13	0.7897 (3)	0.1247 (3)	−0.0315 (2)	0.0401 (6)
H13	0.8311	0.0998	−0.0963	0.048*
C14	0.8694 (3)	0.1104 (3)	0.0923 (2)	0.0355 (5)

H14	0.9644	0.0771	0.1099	0.043*
C15	0.3902 (4)	0.3151 (4)	0.0975 (3)	0.0637 (9)
H15A	0.3406	0.2269	0.1284	0.096*
H15B	0.2987	0.3528	0.0598	0.096*
H15C	0.4872	0.3966	0.1689	0.096*
H2	0.937 (3)	0.349 (3)	0.435 (2)	0.049 (7)*
H1	1.3834 (14)	0.327 (3)	0.443 (2)	0.046 (7)*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0291 (3)	0.0336 (3)	0.0617 (4)	0.0114 (3)	0.0146 (3)	−0.0064 (3)
O1	0.0307 (9)	0.0437 (10)	0.0550 (11)	0.0108 (8)	0.0130 (8)	0.0142 (8)
O2	0.0449 (10)	0.0259 (9)	0.0694 (12)	0.0104 (7)	0.0286 (9)	0.0058 (8)
O3	0.0470 (11)	0.0894 (15)	0.0380 (10)	0.0360 (11)	0.0156 (9)	0.0246 (10)
O4	0.0481 (10)	0.0796 (14)	0.0451 (11)	0.0438 (10)	0.0160 (9)	0.0205 (10)
N1	0.0229 (10)	0.0318 (11)	0.0484 (12)	0.0126 (8)	0.0137 (9)	0.0033 (9)
N2	0.0233 (10)	0.0351 (11)	0.0372 (11)	0.0142 (8)	0.0090 (8)	−0.0012 (9)
C1	0.0322 (13)	0.0393 (14)	0.0563 (17)	0.0185 (11)	0.0088 (12)	0.0051 (12)
C2	0.0309 (12)	0.0303 (12)	0.0316 (12)	0.0156 (10)	0.0105 (10)	0.0041 (10)
C3	0.0270 (11)	0.0355 (12)	0.0307 (12)	0.0149 (10)	0.0105 (9)	0.0053 (10)
C4	0.0227 (11)	0.0304 (12)	0.0330 (12)	0.0091 (9)	0.0099 (9)	0.0048 (10)
C5	0.0286 (12)	0.0322 (12)	0.0289 (12)	0.0131 (10)	0.0092 (9)	0.0075 (10)
C6	0.0323 (13)	0.0364 (13)	0.0277 (12)	0.0150 (10)	0.0075 (10)	0.0114 (10)
C7	0.0550 (16)	0.0281 (13)	0.0557 (17)	0.0090 (12)	0.0226 (13)	0.0081 (12)
C8	0.094 (3)	0.0384 (16)	0.088 (2)	0.0178 (16)	0.049 (2)	0.0084 (16)
C9	0.0226 (11)	0.0247 (11)	0.0354 (13)	0.0070 (9)	0.0080 (9)	0.0040 (9)
C10	0.0291 (12)	0.0342 (12)	0.0347 (13)	0.0132 (10)	0.0135 (10)	0.0045 (10)
C11	0.0269 (12)	0.0380 (13)	0.0372 (14)	0.0143 (10)	0.0070 (10)	0.0089 (10)
C12	0.0312 (12)	0.0420 (14)	0.0329 (13)	0.0126 (11)	0.0089 (10)	0.0095 (11)
C13	0.0377 (13)	0.0499 (15)	0.0375 (14)	0.0205 (12)	0.0172 (11)	0.0099 (12)
C14	0.0295 (12)	0.0398 (13)	0.0404 (14)	0.0184 (10)	0.0128 (10)	0.0085 (11)
C15	0.0586 (18)	0.096 (2)	0.0614 (19)	0.0567 (18)	0.0254 (15)	0.0233 (18)

Geometric parameters (Å, °)

S1—C3	1.689 (2)	C4—H4	0.9800
O1—C6	1.208 (3)	C5—C6	1.479 (3)
O2—C6	1.326 (3)	C7—C8	1.470 (4)
O2—C7	1.456 (3)	C7—H7A	0.9700
O3—C12	1.364 (3)	C7—H7B	0.9700
O3—H3	0.8200	C8—H8A	0.9600
O4—C11	1.373 (3)	C8—H8B	0.9600
O4—C15	1.421 (3)	C8—H8C	0.9600
N1—C3	1.352 (3)	C9—C14	1.375 (3)
N1—C2	1.395 (3)	C9—C10	1.397 (3)
N1—H1	0.891 (10)	C10—C11	1.372 (3)
N2—C3	1.325 (3)	C10—H10	0.9300
N2—C4	1.471 (3)	C11—C12	1.398 (3)

N2—H2	0.90 (3)	C12—C13	1.371 (3)
C1—C2	1.494 (3)	C13—C14	1.389 (3)
C1—H1A	0.9600	C13—H13	0.9300
C1—H1B	0.9600	C14—H14	0.9300
C1—H1C	0.9600	C15—H15A	0.9600
C2—C5	1.343 (3)	C15—H15B	0.9600
C4—C5	1.510 (3)	C15—H15C	0.9600
C4—C9	1.524 (3)		
C6—O2—C7	117.25 (19)	C8—C7—H7A	110.3
C12—O3—H3	109.5	O2—C7—H7B	110.3
C11—O4—C15	117.87 (19)	C8—C7—H7B	110.3
C3—N1—C2	123.52 (18)	H7A—C7—H7B	108.6
C3—N1—H1	118.4 (17)	C7—C8—H8A	109.5
C2—N1—H1	116.1 (17)	C7—C8—H8B	109.5
C3—N2—C4	124.04 (18)	H8A—C8—H8B	109.5
C3—N2—H2	118.4 (17)	C7—C8—H8C	109.5
C4—N2—H2	116.3 (17)	H8A—C8—H8C	109.5
C2—C1—H1A	109.5	H8B—C8—H8C	109.5
C2—C1—H1B	109.5	C14—C9—C10	118.5 (2)
H1A—C1—H1B	109.5	C14—C9—C4	122.74 (19)
C2—C1—H1C	109.5	C10—C9—C4	118.7 (2)
H1A—C1—H1C	109.5	C11—C10—C9	121.4 (2)
H1B—C1—H1C	109.5	C11—C10—H10	119.3
C5—C2—N1	118.47 (19)	C9—C10—H10	119.3
C5—C2—C1	129.1 (2)	C10—C11—O4	126.0 (2)
N1—C2—C1	112.37 (18)	C10—C11—C12	119.4 (2)
N2—C3—N1	116.1 (2)	O4—C11—C12	114.6 (2)
N2—C3—S1	123.25 (16)	O3—C12—C13	118.8 (2)
N1—C3—S1	120.65 (16)	O3—C12—C11	121.8 (2)
N2—C4—C5	108.71 (16)	C13—C12—C11	119.5 (2)
N2—C4—C9	110.28 (17)	C12—C13—C14	120.8 (2)
C5—C4—C9	114.55 (18)	C12—C13—H13	119.6
N2—C4—H4	107.7	C14—C13—H13	119.6
C5—C4—H4	107.7	C9—C14—C13	120.4 (2)
C9—C4—H4	107.7	C9—C14—H14	119.8
C2—C5—C6	126.0 (2)	C13—C14—H14	119.8
C2—C5—C4	119.97 (19)	O4—C15—H15A	109.5
C6—C5—C4	114.02 (18)	O4—C15—H15B	109.5
O1—C6—O2	123.2 (2)	H15A—C15—H15B	109.5
O1—C6—C5	123.2 (2)	O4—C15—H15C	109.5
O2—C6—C5	113.57 (19)	H15A—C15—H15C	109.5
O2—C7—C8	107.1 (2)	H15B—C15—H15C	109.5
O2—C7—H7A	110.3		
C3—N1—C2—C5	19.3 (3)	C4—C5—C6—O2	154.47 (19)
C3—N1—C2—C1	−157.4 (2)	C6—O2—C7—C8	171.4 (2)
C4—N2—C3—N1	−16.1 (3)	N2—C4—C9—C14	106.3 (2)
C4—N2—C3—S1	165.59 (17)	C5—C4—C9—C14	−16.8 (3)
C2—N1—C3—N2	−12.3 (3)	N2—C4—C9—C10	−70.8 (2)

C2—N1—C3—S1	166.09 (17)	C5—C4—C9—C10	166.18 (19)
C3—N2—C4—C5	32.8 (3)	C14—C9—C10—C11	−0.2 (3)
C3—N2—C4—C9	−93.5 (2)	C4—C9—C10—C11	177.04 (19)
N1—C2—C5—C6	−178.7 (2)	C9—C10—C11—O4	−178.2 (2)
C1—C2—C5—C6	−2.5 (4)	C9—C10—C11—C12	1.9 (3)
N1—C2—C5—C4	1.5 (3)	C15—O4—C11—C10	1.3 (4)
C1—C2—C5—C4	177.7 (2)	C15—O4—C11—C12	−178.8 (2)
N2—C4—C5—C2	−24.2 (3)	C10—C11—C12—O3	178.2 (2)
C9—C4—C5—C2	99.7 (2)	O4—C11—C12—O3	−1.8 (3)
N2—C4—C5—C6	155.99 (18)	C10—C11—C12—C13	−2.4 (3)
C9—C4—C5—C6	−80.2 (2)	O4—C11—C12—C13	177.7 (2)
C7—O2—C6—O1	−1.3 (3)	O3—C12—C13—C14	−179.4 (2)
C7—O2—C6—C5	−179.36 (19)	C11—C12—C13—C14	1.1 (4)
C2—C5—C6—O1	156.6 (2)	C10—C9—C14—C13	−1.1 (3)
C4—C5—C6—O1	−23.6 (3)	C4—C9—C14—C13	−178.2 (2)
C2—C5—C6—O2	−25.3 (3)	C12—C13—C14—C9	0.7 (4)

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3···O1^{i}	0.82	2.07	2.788 (2)	147
O3—H3···O4	0.82	2.25	2.690 (3)	114
N2—H2···S1^{ii}	0.90 (3)	2.44 (3)	3.326 (2)	167 (2)
N1—H1···S1^{iii}	0.891 (10)	2.531 (11)	3.417 (2)	173 (2)

Symmetry codes: (i) −*x*+1, −*y*, −*z*; (ii) −*x*+2, −*y*+1, −*z*+1; (iii) −*x*+3, −*y*+1, −*z*+1.

Fig. 1

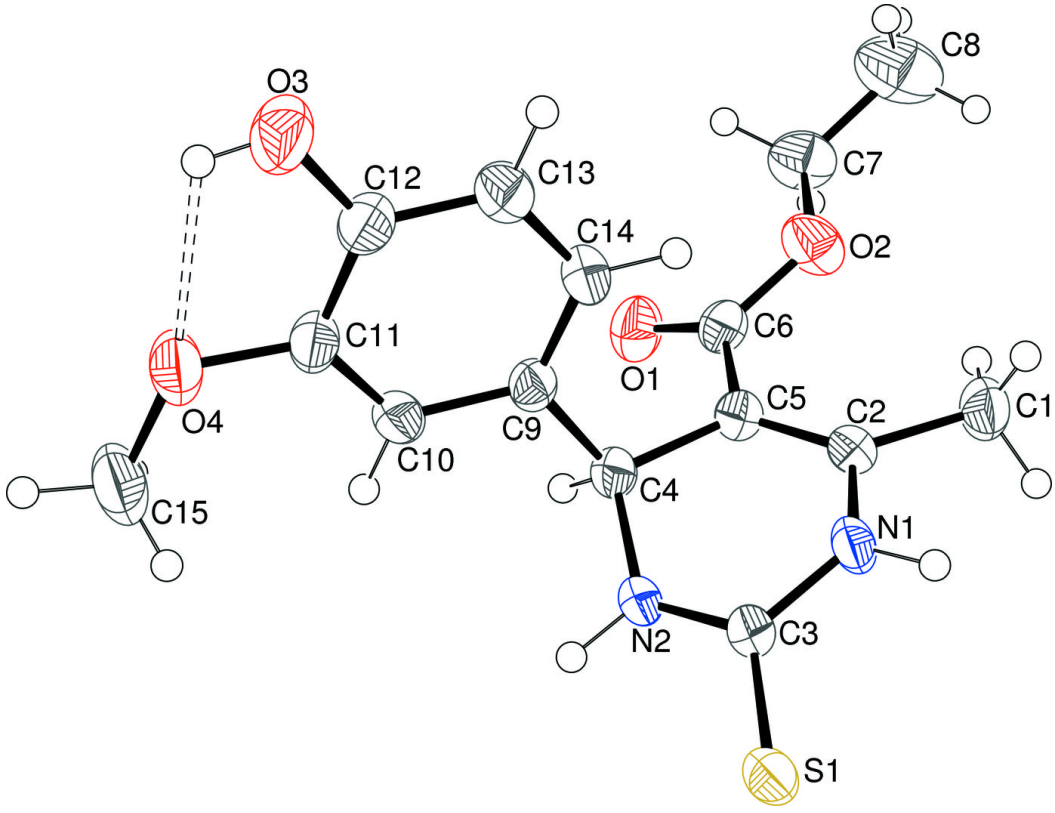
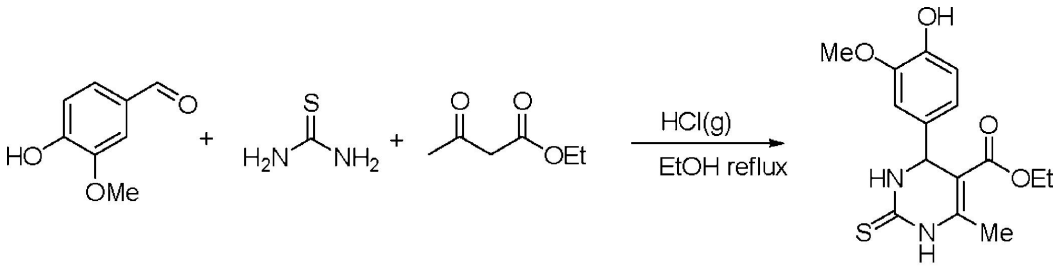

C8
O3
C7
C12
C13
C14
O2
C6
C11
O1
C5
C2
C1
O4
C9
C10
C4
C15
N1
N2
C3
S1

Fig. 2



(I)