organic compounds

Methyl 5-[*N,N*-bis(methoxycarbonyl-methyl)amino]-4-cyano-2-methoxy-carbonyl-3-thiopheneethanoate

Qiang Wang, Zhong-Shu Li and Bai-Wang Sun*

Ordered Matter Science Research Center, College of Chemistry and Chemical Engineering, Southeast University, Nanjing 210096, People's Republic of China

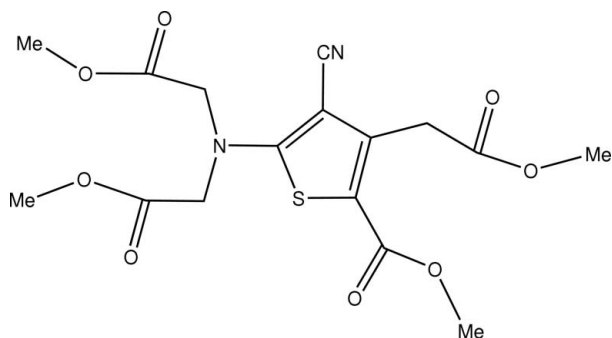Correspondence e-mail: chmsunbw@seu.edu.cn

In the title compound, $C_{16}H_{18}N_2O_8S$, derived from ranelic acid, there is a highly substituted thiophene ring. The crystal structure involves intermolecular C—H···O and C—H···S hydrogen bonds.

Related literature

For related literature, see: Bonnelye *et al.* (2008); Fonseca (2008).

Experimental

Crystal data

$C_{16}H_{18}N_2O_8S$	$\gamma = 95.81\ (3)°$
$M_r = 398.38$	$V = 944.5\ (3)$ Å^3
Triclinic, $P\bar{1}$	$Z = 2$
$a = 9.7164\ (19)$ Å	Mo $K\alpha$ radiation
$b = 9.790\ (2)$ Å	$\mu = 0.22$ mm^{-1}
$c = 10.170\ (2)$ Å	$T = 293\ (2)$ K
$\alpha = 98.05\ (3)°$	$0.25 \times 0.20 \times 0.18$ mm
$\beta = 96.71\ (3)°$	

Data collection

Rigaku SCXmini diffractometer	9976 measured reflections
Absorption correction: multi-scan (*CrystalClear*; Rigaku, 2005)	4313 independent reflections
$T_{min} = 0.942$, $T_{max} = 0.988$	3561 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.027$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.048$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.130$	
$S = 1.03$	
4313 reflections	$\Delta\rho_{max} = 0.33$ e Å^{-3}
246 parameters	$\Delta\rho_{min} = -0.38$ e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
C3—H3A···O3^i	0.97	2.51	3.355 (3)	146
C16—H16A···O5^{ii}	0.96	2.57	3.421 (3)	148
C16—H16C···S^{ii}	0.96	2.87	3.727 (3)	149

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

Data collection: *CrystalClear* (Rigaku, 2005); cell refinement: *CrystalClear*; data reduction: *CrystalClear*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXL97*.

References

Bonnelye, E., Chabadel, A., Saltel, F. & Jurdic, P. (2008). *Bone*, **42**, 129–138.
Fonseca, J. E. (2008). *Rheumatology*, **47**, iv17–iv19.
Rigaku. (2005). *CrystalClear*. Rigaku Corporation, Tokyo, Japan.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

supplementary materials

Methyl 5-[*N,N*-bis(methoxycarbonylmethyl)amino]-4-cyano-2-methoxycarbonyl-3-thiopheneethanoate

Q. Wang, Z.-S. Li and B.-W. Sun

Comment

The title compound, (I), $C_{16}H_{18}O_8N_2S$, is an important intermediate in the synthesis of strontium ranelate, a medicine for the treatment of osteoporosis (Bonnelye *et al.*, 2008; Fonseca, 2008). Strontium ranelate is composed of two stable strontium ions combined with the anion of organic ranelic acid. The ranelic acid is a carrier that makes the treatment palatable, and the strontium is the active component with regard to the bone. We report here the crystal structure of the title compound. The molecular structure of (I) is shown in Fig. 1 and geometric parameters are given in Table 1. In the crystal (Fig. 2 and Table 2), there are intermolecular C—H···O and C—H···S hydrogen bonds leading to a one-dimensional structure.

Experimental

All chemicals used (reagent grade) were commercially available. Methyl 5-[bis(methoxycarbonylmethyl)amino]-4-cyano-3-(methoxycarbonyl)-2-thiophene- carboxylate (0.426 g, 0.1 mmol) was added to a solution containing ethanol (8 ml) and acetone (4 ml). The mixture was stirred at room temperature for 10 min and then filtered off. Colorless crystals suitable for X-ray analysis were obtained by slow evaporation at room temperature over several days.

Refinement

All H atoms attached to C and N atom were fixed geometrically and treated as riding with C—H = 0.97 Å with $U_{iso}(H)$ =$1.2U_{eq}(C)$.
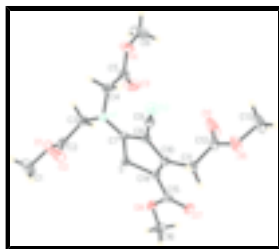
Figures

Fig. 1. The molecular structure of the title molecule, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.
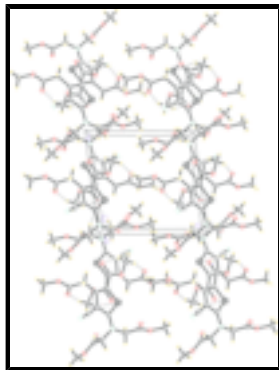
supplementary materials

Fig. 2. Crystal packing of the compound (I) viewed along the *b* axis. Hydrogen bonds are shown as dashed lines.

methyl 5-[*N*,*N*-bis(methoxycarbonylmethyl)amino]-4-cyano-2- methoxycarbonyl-3-thiophene-ethanoate

Crystal data

$C_{16}H_{18}N_2O_8S$	$Z = 2$
$M_r = 398.38$	$F_{000} = 416$
Triclinic, $P\bar{1}$	$D_x = 1.401$ Mg m^{-3}
Hall symbol: -P 1	Mo $K\alpha$ radiation $\lambda = 0.71073$ Å
$a = 9.7164$ (19) Å	Cell parameters from 6733 reflections
$b = 9.790$ (2) Å	$\theta = 3.3$–27.3º
$c = 10.170$ (2) Å	$\mu = 0.22$ mm^{-1}
$\alpha = 98.05$ (3)º	$T = 293$ (2) K
$\beta = 96.71$ (3)º	Prism, colorless
$\gamma = 95.81$ (3)º	$0.25 \times 0.20 \times 0.18$ mm
$V = 944.5$ (3) Å^3	

Data collection

Rigaku SCXmini diffractometer	4313 independent reflections
Radiation source: fine-focus sealed tube	3561 reflections with $I > 2\sigma(I)$
Monochromator: graphite	$R_{int} = 0.027$
Detector resolution: 8.192 pixels mm^{-1}	$\theta_{max} = 27.5$º
$T = 293(2)$ K	$\theta_{min} = 3.1$º
ω scans	$h = -12 \rightarrow 12$
Absorption correction: multi-scan (CrystalClear; Rigaku, 2005)	$k = -12 \rightarrow 12$
$T_{min} = 0.942$, $T_{max} = 0.988$	$l = -13 \rightarrow 13$
9976 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites

$R[F^2 > 2\sigma(F^2)] = 0.048$

$wR(F^2) = 0.130$

$S = 1.03$

4313 reflections

246 parameters

Primary atom site location: structure-invariant direct methods

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.062P)^2 + 0.411P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max} = 0.33$ e Å^{-3}

$\Delta\rho_{min} = -0.38$ e Å^{-3}

Extinction correction: none

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 $F^2 > \sigma(F^2)$ 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}
C1	0.0925 (5)	0.8277 (4)	0.4871 (3)	0.0967 (13)
H1A	0.165 (3)	0.894 (3)	0.4933 (6)	0.145*
H1B	0.116 (3)	0.7635 (17)	0.5387 (14)	0.145*
H1C	0.018 (2)	0.866 (3)	0.5154 (12)	0.145*
C2	0.0887 (2)	0.8372 (2)	0.2560 (2)	0.0414 (5)
C3	0.03705 (19)	0.7542 (2)	0.11943 (19)	0.0374 (4)
H3A	0.0661	0.6620	0.1164	0.045*
H3B	−0.0642	0.7441	0.1059	0.045*
C4	−0.01502 (19)	0.8243 (2)	−0.1025 (2)	0.0366 (4)
H4A	0.0231	0.8874	−0.1582	0.044*
H4B	−0.0962	0.8606	−0.0702	0.044*
C5	−0.0589 (2)	0.6829 (2)	−0.1857 (2)	0.0427 (5)
C6	−0.2176 (5)	0.5578 (4)	−0.3673 (4)	0.1086 (14)
H6A	−0.2891	0.5740	−0.4348	0.163*
H6B	−0.2567	0.4957	−0.3126	0.163*
H6C	−0.1448	0.5171	−0.4094	0.163*
C7	0.22416 (18)	0.80692 (18)	−0.00849 (18)	0.0312 (4)
C8	0.30195 (18)	0.86329 (19)	−0.09923 (18)	0.0321 (4)
C9	0.2567 (2)	0.9617 (2)	−0.18082 (19)	0.0369 (4)
C10	0.43987 (18)	0.82416 (19)	−0.09451 (18)	0.0335 (4)
C11	0.5374 (2)	0.8694 (2)	−0.18941 (19)	0.0404 (4)
H11A	0.5404	0.9690	−0.1876	0.048*
H11B	0.6307	0.8498	−0.1592	0.048*

C12	0.4935 (2)	0.7974 (2)	−0.3310 (2)	0.0446 (5)
C13	0.5241 (4)	0.8027 (4)	−0.5571 (3)	0.0940 (11)
H13A	0.5736	0.8606	−0.6092	0.141*
H13B	0.4257	0.7956	−0.5864	0.141*
H13C	0.5541	0.7119	−0.5686	0.141*
C14	0.46807 (18)	0.7442 (2)	0.00257 (18)	0.0335 (4)
C15	0.59750 (19)	0.6869 (2)	0.04245 (19)	0.0360 (4)
C16	0.7100 (2)	0.5700 (2)	0.2060 (2)	0.0501 (5)
H16A	0.6891	0.5245	0.2802	0.075*
H16B	0.7815	0.6466	0.2366	0.075*
H16C	0.7418	0.5053	0.1396	0.075*
O1	0.0564 (2)	0.76176 (18)	0.34904 (16)	0.0637 (5)
O2	0.1471 (2)	0.95261 (18)	0.27677 (18)	0.0673 (5)
O3	−0.0096 (2)	0.57999 (18)	−0.1647 (2)	0.0719 (6)
O4	−0.15997 (19)	0.68911 (18)	−0.28405 (17)	0.0626 (5)
O5	0.4141 (3)	0.6943 (2)	−0.3638 (2)	0.1020 (9)
O6	0.5525 (2)	0.8633 (2)	−0.41698 (17)	0.0695 (5)
O7	0.70142 (14)	0.69773 (18)	−0.01103 (16)	0.0520 (4)
O8	0.58547 (14)	0.62078 (16)	0.14789 (15)	0.0438 (3)
N1	0.08891 (15)	0.81812 (17)	0.01103 (16)	0.0346 (3)
N2	0.2253 (2)	1.0438 (2)	−0.2444 (2)	0.0535 (5)
S	0.32536 (5)	0.71175 (5)	0.08736 (5)	0.03457 (14)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.151 (4)	0.103 (3)	0.0364 (14)	0.029 (2)	0.0078 (17)	0.0058 (15)
C2	0.0371 (10)	0.0491 (12)	0.0399 (11)	0.0130 (9)	0.0055 (8)	0.0071 (9)
C3	0.0266 (9)	0.0471 (11)	0.0394 (10)	0.0020 (7)	0.0078 (7)	0.0087 (8)
C4	0.0280 (9)	0.0392 (10)	0.0447 (11)	0.0078 (7)	0.0016 (8)	0.0136 (8)
C5	0.0412 (11)	0.0444 (11)	0.0418 (11)	0.0083 (9)	−0.0004 (8)	0.0071 (9)
C6	0.132 (3)	0.080 (2)	0.088 (2)	0.010 (2)	−0.054 (2)	−0.0192 (19)
C7	0.0275 (8)	0.0346 (9)	0.0308 (9)	0.0026 (7)	0.0019 (7)	0.0052 (7)
C8	0.0301 (9)	0.0364 (9)	0.0297 (9)	0.0015 (7)	0.0031 (7)	0.0069 (7)
C9	0.0335 (9)	0.0429 (10)	0.0348 (10)	0.0016 (8)	0.0064 (7)	0.0084 (8)
C10	0.0292 (9)	0.0388 (10)	0.0312 (9)	−0.0010 (7)	0.0047 (7)	0.0039 (8)
C11	0.0329 (10)	0.0530 (12)	0.0366 (10)	−0.0014 (8)	0.0081 (8)	0.0128 (9)
C12	0.0494 (12)	0.0491 (12)	0.0391 (11)	0.0046 (10)	0.0171 (9)	0.0112 (9)
C13	0.137 (3)	0.106 (3)	0.0417 (15)	−0.002 (2)	0.0369 (17)	0.0125 (16)
C14	0.0259 (8)	0.0432 (10)	0.0318 (9)	0.0027 (7)	0.0055 (7)	0.0068 (8)
C15	0.0280 (9)	0.0429 (10)	0.0358 (10)	0.0015 (7)	0.0030 (7)	0.0045 (8)
C16	0.0396 (11)	0.0547 (13)	0.0573 (13)	0.0102 (9)	−0.0046 (10)	0.0188 (11)
O1	0.0920 (13)	0.0632 (11)	0.0376 (8)	0.0077 (9)	0.0124 (8)	0.0119 (8)
O2	0.0858 (13)	0.0538 (10)	0.0547 (10)	−0.0060 (9)	−0.0015 (9)	0.0011 (8)
O3	0.0808 (13)	0.0454 (9)	0.0806 (13)	0.0218 (9)	−0.0235 (10)	−0.0024 (9)
O4	0.0680 (11)	0.0608 (10)	0.0513 (10)	0.0112 (8)	−0.0206 (8)	0.0029 (8)
O5	0.161 (2)	0.0805 (14)	0.0505 (11)	−0.0555 (15)	0.0369 (13)	−0.0065 (10)
O6	0.0858 (13)	0.0810 (12)	0.0413 (9)	−0.0148 (10)	0.0204 (9)	0.0163 (9)

O7	0.0305 (7)	0.0792 (11)	0.0519 (9)	0.0127 (7)	0.0118 (6)	0.0202 (8)
O8	0.0322 (7)	0.0563 (9)	0.0478 (8)	0.0104 (6)	0.0060 (6)	0.0207 (7)
N1	0.0255 (7)	0.0430 (9)	0.0366 (8)	0.0047 (6)	0.0049 (6)	0.0094 (7)
N2	0.0579 (12)	0.0532 (11)	0.0536 (11)	0.0069 (9)	0.0061 (9)	0.0237 (9)
S	0.0279 (2)	0.0437 (3)	0.0358 (3)	0.00654 (18)	0.00741 (17)	0.0147 (2)

Geometric parameters (Å, °)

C1—O1	1.448 (3)	C8—C9	1.427 (3)
C1—H1A	0.9033	C8—C10	1.428 (3)
C1—H1B	0.9033	C9—N2	1.143 (3)
C1—H1C	0.9033	C10—C14	1.363 (3)
C2—O2	1.191 (3)	C10—C11	1.508 (3)
C2—O1	1.325 (3)	C11—C12	1.504 (3)
C2—C3	1.510 (3)	C11—H11A	0.9700
C3—N1	1.456 (2)	C11—H11B	0.9700
C3—H3A	0.9700	C12—O5	1.189 (3)
C3—H3B	0.9700	C12—O6	1.308 (3)
C4—N1	1.455 (2)	C13—O6	1.448 (3)
C4—C5	1.511 (3)	C13—H13A	0.9600
C4—H4A	0.9700	C13—H13B	0.9600
C4—H4B	0.9700	C13—H13C	0.9600
C5—O3	1.193 (3)	C14—C15	1.466 (3)
C5—O4	1.330 (2)	C14—S	1.7420 (18)
C6—O4	1.457 (3)	C15—O7	1.204 (2)
C6—H6A	0.9600	C15—O8	1.338 (2)
C6—H6B	0.9600	C16—O8	1.448 (2)
C6—H6C	0.9600	C16—H16A	0.9600
C7—N1	1.365 (2)	C16—H16B	0.9600
C7—C8	1.396 (2)	C16—H16C	0.9600
C7—S	1.7323 (19)		
O1—C1—H1A	109.5	C14—C10—C11	126.48 (17)
O1—C1—H1B	109.5	C8—C10—C11	121.39 (17)
H1A—C1—H1B	109.5	C12—C11—C10	112.45 (16)
O1—C1—H1C	109.5	C12—C11—H11A	109.1
H1A—C1—H1C	109.5	C10—C11—H11A	109.1
H1B—C1—H1C	109.5	C12—C11—H11B	109.1
O2—C2—O1	125.5 (2)	C10—C11—H11B	109.1
O2—C2—C3	125.5 (2)	H11A—C11—H11B	107.8
O1—C2—C3	108.99 (18)	O5—C12—O6	122.9 (2)
N1—C3—C2	112.93 (16)	O5—C12—C11	125.5 (2)
N1—C3—H3A	109.0	O6—C12—C11	111.64 (19)
C2—C3—H3A	109.0	O6—C13—H13A	109.5
N1—C3—H3B	109.0	O6—C13—H13B	109.5
C2—C3—H3B	109.0	H13A—C13—H13B	109.5
H3A—C3—H3B	107.8	O6—C13—H13C	109.5
N1—C4—C5	111.64 (16)	H13A—C13—H13C	109.5
N1—C4—H4A	109.3	H13B—C13—H13C	109.5
C5—C4—H4A	109.3	C10—C14—C15	129.21 (17)

N1—C4—H4B	109.3	C10—C14—S	112.01 (14)
C5—C4—H4B	109.3	C15—C14—S	118.78 (14)
H4A—C4—H4B	108.0	O7—C15—O8	124.03 (18)
O3—C5—O4	125.0 (2)	O7—C15—C14	125.19 (18)
O3—C5—C4	124.21 (19)	O8—C15—C14	110.78 (16)
O4—C5—C4	110.76 (17)	O8—C16—H16A	109.5
O4—C6—H6A	109.5	O8—C16—H16B	109.5
O4—C6—H6B	109.5	H16A—C16—H16B	109.5
H6A—C6—H6B	109.5	O8—C16—H16C	109.5
O4—C6—H6C	109.5	H16A—C16—H16C	109.5
H6A—C6—H6C	109.5	H16B—C16—H16C	109.5
H6B—C6—H6C	109.5	C2—O1—C1	116.7 (2)
N1—C7—C8	129.48 (17)	C5—O4—C6	116.3 (2)
N1—C7—S	120.44 (14)	C12—O6—C13	117.7 (2)
C8—C7—S	110.07 (13)	C15—O8—C16	116.74 (16)
C7—C8—C9	124.59 (17)	C7—N1—C4	119.77 (16)
C7—C8—C10	113.62 (16)	C7—N1—C3	117.45 (15)
C9—C8—C10	121.51 (16)	C4—N1—C3	115.49 (15)
N2—C9—C8	177.3 (2)	C7—S—C14	92.11 (9)
C14—C10—C8	112.12 (16)		
O2—C2—C3—N1	11.3 (3)	S—C14—C15—O7	177.27 (17)
O1—C2—C3—N1	−169.76 (17)	C10—C14—C15—O8	176.21 (19)
N1—C4—C5—O3	−3.4 (3)	S—C14—C15—O8	−3.1 (2)
N1—C4—C5—O4	176.17 (17)	O2—C2—O1—C1	1.7 (4)
N1—C7—C8—C9	8.5 (3)	C3—C2—O1—C1	−177.2 (2)
S—C7—C8—C9	−171.41 (15)	O3—C5—O4—C6	3.0 (4)
N1—C7—C8—C10	−177.50 (17)	C4—C5—O4—C6	−176.6 (3)
S—C7—C8—C10	2.6 (2)	O5—C12—O6—C13	−3.2 (4)
C7—C8—C9—N2	129 (5)	C11—C12—O6—C13	177.7 (2)
C10—C8—C9—N2	−45 (5)	O7—C15—O8—C16	5.2 (3)
C7—C8—C10—C14	−2.7 (2)	C14—C15—O8—C16	−174.41 (17)
C9—C8—C10—C14	171.57 (17)	C8—C7—N1—C4	34.7 (3)
C7—C8—C10—C11	177.14 (16)	S—C7—N1—C4	−145.47 (15)
C9—C8—C10—C11	−8.6 (3)	C8—C7—N1—C3	−176.48 (18)
C14—C10—C11—C12	109.2 (2)	S—C7—N1—C3	3.4 (2)
C8—C10—C11—C12	−70.6 (2)	C5—C4—N1—C7	76.6 (2)
C10—C11—C12—O5	−17.2 (4)	C5—C4—N1—C3	−72.8 (2)
C10—C11—C12—O6	161.94 (19)	C2—C3—N1—C7	76.1 (2)
C8—C10—C14—C15	−177.92 (18)	C2—C3—N1—C4	−133.71 (17)
C11—C10—C14—C15	2.3 (3)	N1—C7—S—C14	178.60 (15)
C8—C10—C14—S	1.4 (2)	C8—C7—S—C14	−1.50 (14)
C11—C10—C14—S	−178.35 (15)	C10—C14—S—C7	0.03 (15)
C10—C14—C15—O7	−3.4 (3)	C15—C14—S—C7	179.46 (15)

Hydrogen-bond geometry (Å, °)

D—H···A	D—H	H···A	D···A	D—H···A
C3—H3A···O3[i]	0.97	2.51	3.355 (3)	146

| C16—H16A···O5[ii] | 0.96 | 2.57 | 3.421 (3) | 148 |
| C16—H16C···S[ii] | 0.96 | 2.87 | 3.727 (3) | 149 |

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

Fig. 1

Fig. 2