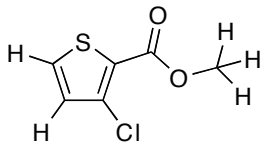
Appendix A

X-ray Crystal Structure of methyl 3-chlorothiophene-2-carboxylate

X-ray crystallographic diffraction, data collection and data work-up run by Dr. Michael W. Day at the X-Ray Crystallography Laboratory of the Beckman Institute at the California Institute of Technology.

Methyl 3-chlorothiophene-2-carboxylate (see Figure A.1 for the structure) was synthesized as previously described,[1] in preparation for use in polyamides that target the HIF-1α binding sequence.[2–5] During *in vacuo* concentration of the methyl 3-chlorothiophene-2-carboxylate, a large rectangular crystal formed inside the round bottom flask. The crystal was harvested and submitted for X-ray crystallographic analysis at the X-ray Crystallography Laboratory of the Beckman Institute at the California Institute of Technology. Dr. Michael W. Day performed the analyses. The results are described in Tables A.1–A.5 and Figures A.2 (ORTEP diagram)[6] and A.3 (crystal packing diagram, prepared in Cambridge Crystallographic Data Centre's Mercury software).[7] As of May 2009, no known crystal structures of this compound are in the Cambridge Structural Database.[8]



1

Figure A.1. Chemical structure of methyl 3-chlorothiophene-2-carboxylate (**1**)

Table A.1. Crystal data and structure refinement for **1** (CCDC 621056)

Empirical formula	$C_6H_5O_2ClS$
Formula weight	176.61
Crystallization Solvent	Diethylether
Crystal Habit	Block
Crystal size	0.27 x 0.22 x 0.11 mm^3
Crystal color	Colorless

Data Collection

Type of diffractometer	Bruker SMART 1000	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	100(2) K	
θ range for 4568 reflections used in lattice determination	2.95 to 32.85°	
Unit cell dimensions	a = 3.9030(4) Å b = 7.0415(7) Å c = 14.1389(15) Å	α = 101.291(2)° β = 92.911(2)° γ = 103.851(2)°
Volume	368.03(7) $Å^3$	
Z	2	
Crystal system	Triclinic	
Space group	P-1	
Density (calculated)	1.594 Mg/m^3	
F(000)	180	
Data collection program	Bruker SMART v5.630	
θ range for data collection	2.95 to 33.07°	
Completeness to θ = 33.07°	84.5 %	
Index ranges	$-5 \le h \le 5$, $-10 \le k \le 10$, $-19 \le l \le 19$	
Data collection scan type	ω scans at 7 ϕ settings	
Data reduction program	Bruker SAINT v6.45A	
Reflections collected	7841	
Independent reflections	2339 [R_{int}= 0.0528]	
Absorption coefficient	0.732 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	0.9238 and 0.8268	

Table A.1. **(cont.)**

Structure solution and Refinement

Structure solution program	Bruker XS v6.12
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	Bruker XL v6.12
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	2339 / 0 / 111
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	1.548
Final R indices [I>2σ(I), 1821 reflections]	R1 = 0.0335, *w*R2 = 0.0632
R indices (all data)	R1 = 0.0467, *w*R2 = 0.0646
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.000
Average shift/error	0.000
Largest diff. peak and hole	0.412 and -0.315 e.Å^{-3}

Special Refinement Details

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) 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 $F^2 > 2\sigma(F^2)$ 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.

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

Table A.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **1** (CCDC 621056). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor

	x	y	z	U_{eq}
S(1)	2592(1)	3029(1)	2079(1)	28(1)
Cl(1)	9437(1)	7820(1)	4119(1)	36(1)
O(1)	7587(3)	8581(2)	2092(1)	41(1)
O(2)	3446(3)	6220(1)	1056(1)	33(1)
C(1)	3599(4)	2345(2)	3129(1)	31(1)
C(2)	5821(4)	3874(2)	3783(1)	30(1)
C(3)	6728(3)	5637(2)	3420(1)	25(1)
C(4)	5223(3)	5433(2)	2496(1)	23(1)
C(5)	5610(4)	6934(2)	1894(1)	25(1)
C(6)	3584(5)	7601(3)	419(1)	39(1)

Table A.3. Bond lengths [Å] and angles [°] for **1** (CCDC 621056)

S(1)-C(1)	1.7041(15)	C(1)-S(1)-C(4)	92.00(7)
S(1)-C(4)	1.7276(12)	C(5)-O(2)-C(6)	115.38(11)
Cl(1)-C(3)	1.7260(12)	C(2)-C(1)-S(1)	112.46(11)
O(1)-C(5)	1.2005(16)	C(2)-C(1)-H(1)	128.8(10)
O(2)-C(5)	1.3531(15)	S(1)-C(1)-H(1)	118.7(10)
O(2)-C(6)	1.4436(18)	C(1)-C(2)-C(3)	111.74(12)
C(1)-C(2)	1.3589(19)	C(1)-C(2)-H(2)	126.3(9)
C(1)-H(1)	0.943(18)	C(3)-C(2)-H(2)	122.0(9)
C(2)-C(3)	1.4100(18)	C(4)-C(3)-C(2)	113.87(11)
C(2)-H(2)	0.928(14)	C(4)-C(3)-Cl(1)	125.06(10)
C(3)-C(4)	1.3720(18)	C(2)-C(3)-Cl(1)	121.06(10)
C(4)-C(5)	1.4670(18)	C(3)-C(4)-C(5)	128.64(11)
C(6)-H(6A)	0.978(16)	C(3)-C(4)-S(1)	109.92(9)
C(6)-H(6B)	0.938(18)	C(5)-C(4)-S(1)	121.44(9)
C(6)-H(6C)	0.96(2)	O(1)-C(5)-O(2)	123.00(12)
		O(1)-C(5)-C(4)	125.90(12)
		O(2)-C(5)-C(4)	111.09(11)
		O(2)-C(6)-H(6A)	111.1(10)
		O(2)-C(6)-H(6B)	108.8(11)
		H(6A)-C(6)-H(6B)	108.0(14)
		O(2)-C(6)-H(6C)	111.2(12)
		H(6A)-C(6)-H(6C)	110.1(15)
		H(6B)-C(6)-H(6C)	107.5(15)

Table A.4. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for **1** (CCDC 621056). The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	292(2)	213(2)	283(2)	22(1)	-24(1)	-12(1)
Cl(1)	399(2)	280(2)	287(2)	12(1)	-73(1)	-49(2)
O(1)	476(7)	268(5)	394(6)	108(4)	-91(5)	-63(5)
O(2)	391(6)	283(5)	281(5)	73(4)	-76(4)	27(4)
C(1)	338(8)	245(7)	343(7)	97(6)	38(6)	20(6)
C(2)	337(8)	290(7)	250(7)	78(5)	15(6)	44(6)
C(3)	232(7)	215(6)	250(6)	7(5)	14(5)	18(5)
C(4)	210(6)	185(6)	264(6)	19(5)	12(5)	19(5)
C(5)	266(7)	228(6)	254(6)	39(5)	18(5)	58(5)
C(6)	469(10)	402(9)	324(8)	155(7)	-32(7)	107(8)

Table A.5. Hydrogen coordinates ($x\ 10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$) for **1** (CCDC 621056)

	x	y	z	U_{iso}
H(1)	2630(40)	1010(30)	3186(11)	45(5)
H(2)	6670(40)	3820(20)	4400(10)	30(4)
H(6A)	2860(40)	8790(30)	729(11)	48(5)
H(6B)	2010(50)	6970(30)	-139(13)	56(5)
H(6C)	5910(60)	7980(30)	215(13)	70(6)

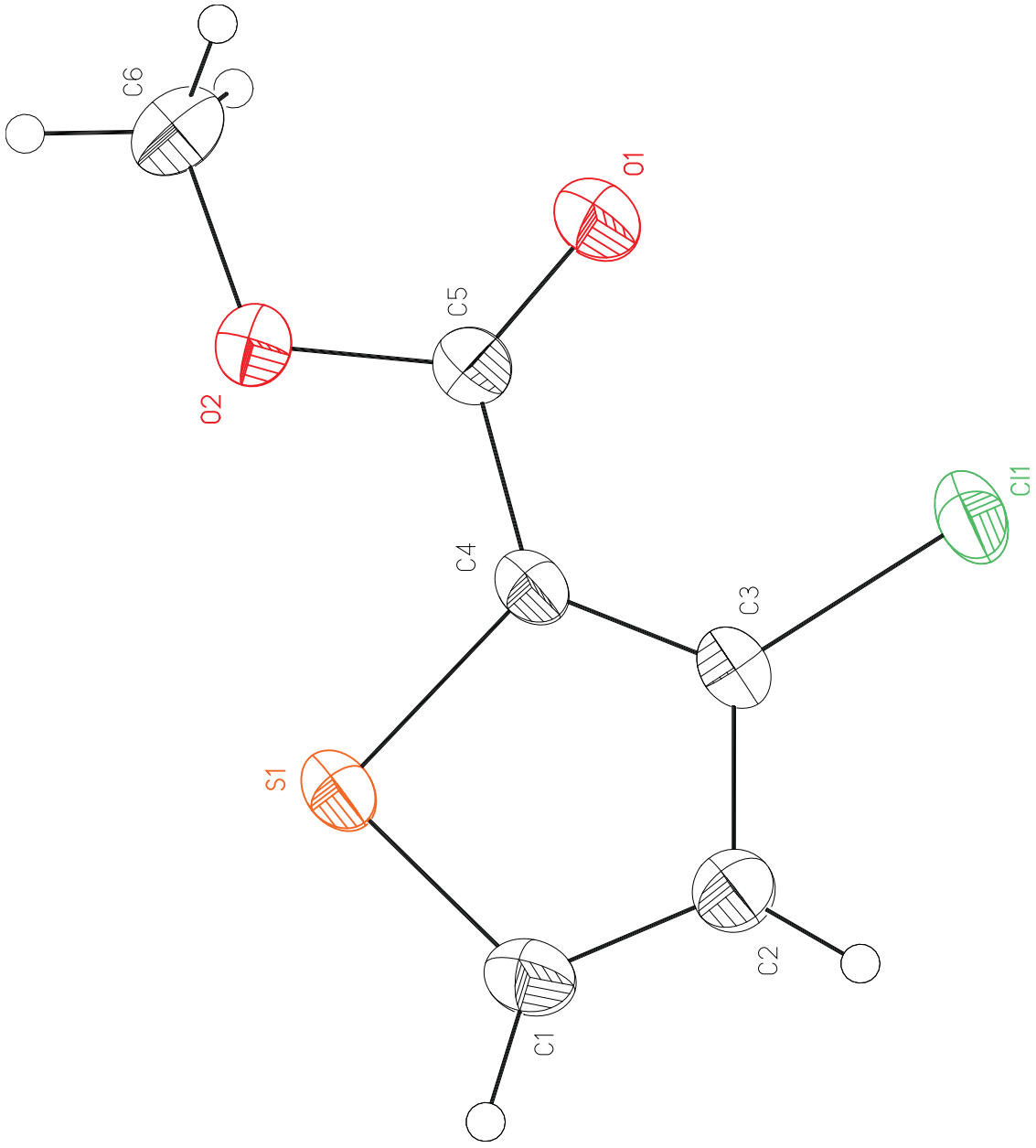


Figure A.2. ORTEP representation of methyl 3-chlorothiophene-2-carboxylate

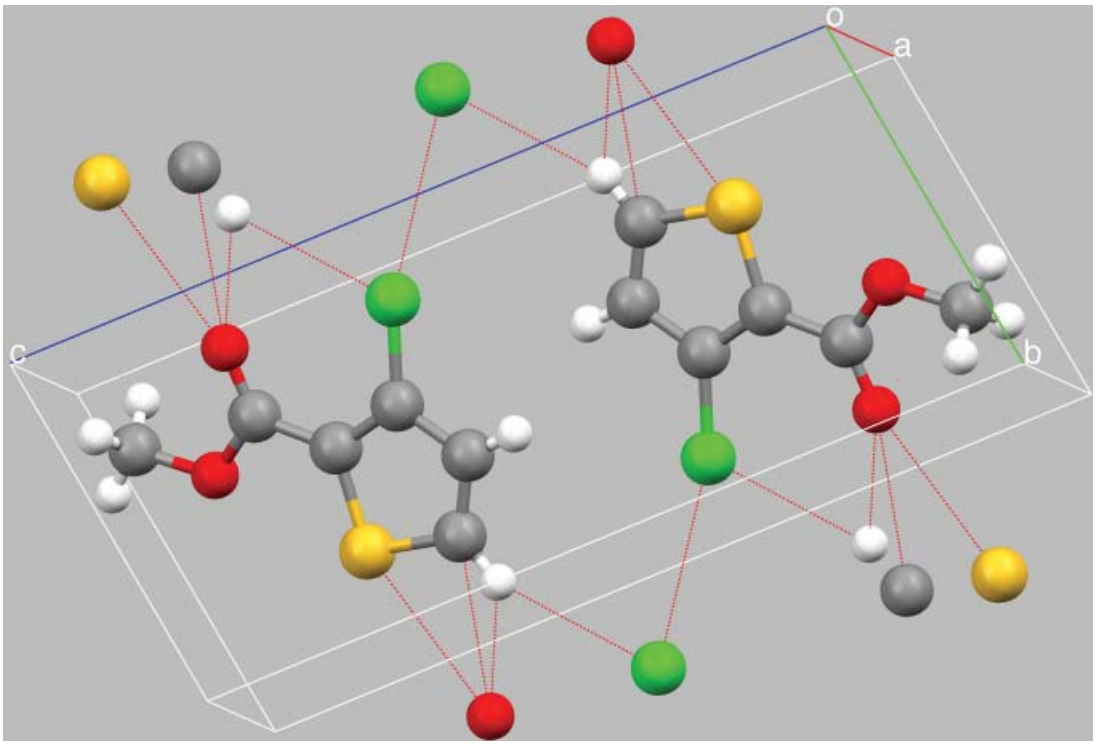


Figure A.3. Crystal packing and van der Waal's contacts for methyl 3-chlorothiophene-2-carboxylate

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