APPENDIX FIVE

X-Ray Crystallography Reports Relevant to Chapter Four:

Progress Toward The Total Synthesis of Telomestatin

A5.1 Crystal Structure Analysis of 226

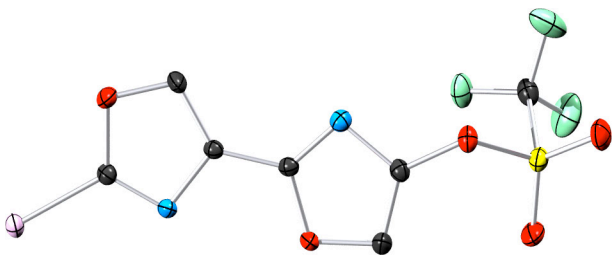

Figure A5.1.1 Iodobisoxazole triflate **226** is shown with 50% probability ellipsoids (Note: Only Molecule A is depicted). Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 282586.

Table A5.1.1 Crystal data and structure refinement for **226** (CCDC 282586)

Empirical formula	$C_7H_2F_3IN_2O_5S$
Formula weight	410.07
Crystallization Solvent	Diethylether
Crystal Habit	Plate
Crystal size	0.48 x 0.22 x 0.19 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 9170 reflections used in lattice determination	2.74 to 33.18°	
Unit cell dimensions	a = 5.3805(5) Å b = 14.4770(13) Å c = 14.8833(13) Å	α= 92.205(2)° β= 92.046(2)° γ = 90.356(2)°
Volume	1157.68(18) $Å^3$	
Z	4	
Crystal system	Triclinic	
Space group	P-1	
Density (calculated)	2.353 Mg/m^3	
F(000)	776	
Data collection program	Bruker SMART v5.630	
θ range for data collection	1.93 to 33.66°	
Completeness to θ = 33.66°	82.2 %	
Index ranges	$-8 \le h \le 7, -19 \le k \le 20, -22 \le l \le 22$	
Data collection scan type	ω scans at 5 ϕ settings	
Data reduction program	Bruker SAINT v6.45A	
Reflections collected	19450	
Independent reflections	7576 [R_{int}= 0.0597]	
Absorption coefficient	3.006 mm^{-1}	
Absorption correction	Gaussian	
Max. and min. transmission	0.91449 and 0.56264	

5.1.1 (cont.)

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	7576 / 0 / 359
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	1.034
Final R indices [I>2σ(I), 5482 reflections]	R1 = 0.0311, *w*R2 = 0.0538
R indices (all data)	R1 = 0.0539, *w*R2 = 0.0583
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.002
Average shift/error	0.000
Largest diff. peak and hole	0.827 and -0.793 e.Å^{-3}

Special Refinement Details

This molecule crystallizes with two unique conformations in the asymmetric unit, differing from each other by the torsion angles around the C(6*)-O(3*) and the O(3*)-S1* bonds, as illustrated in Figures A5.1.1 thru A5.1.4 and listed in Table A5.1.6. The difference in the environment of these two molecules is illustrated in Figure A5.1.5 and A5.1.6. A short intermolecular contact between the I1 and N(1B), distance = 3.05Å, is **NOT** present between I2 and N(1A).

Another interesting feature observed in this structure are the CH-N and CH-O hydrogen bonds listed in Table A5.1.7. Although these are not the "classical" hydrogen bonds they are not without precedent[1,2] and the values observed herein are consistent with those observed elsewhere[1].

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.

---

(1) Rahman, A. N. M. M.; Bishop, R.; Craig, D. C.; Scudder, M. L. *Eur. J. Org. Chem.* **2001**, 863–873.
(2) Jiang, L.; Lai, L. *J. Biol. Chem.* **2002**, 37732–37740.

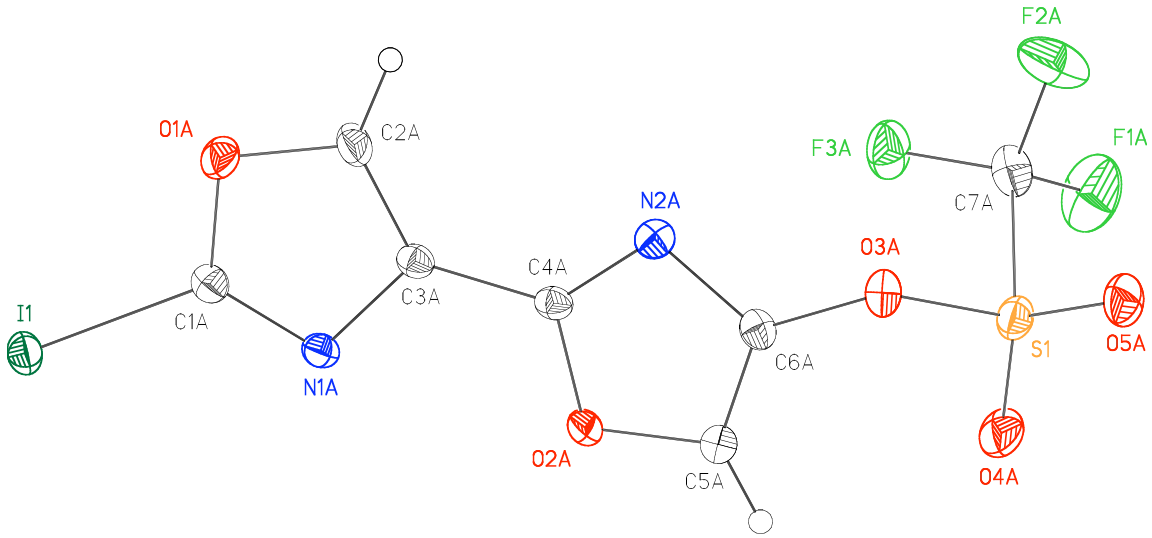

Figure A5.1.2 *Molecule A*

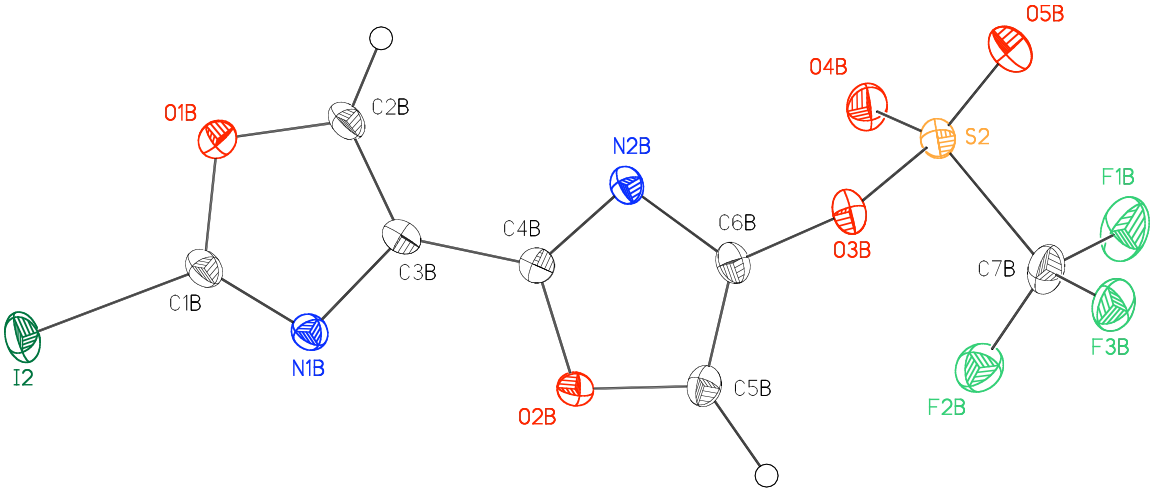

Figure A5.1.3 *Molecule B*

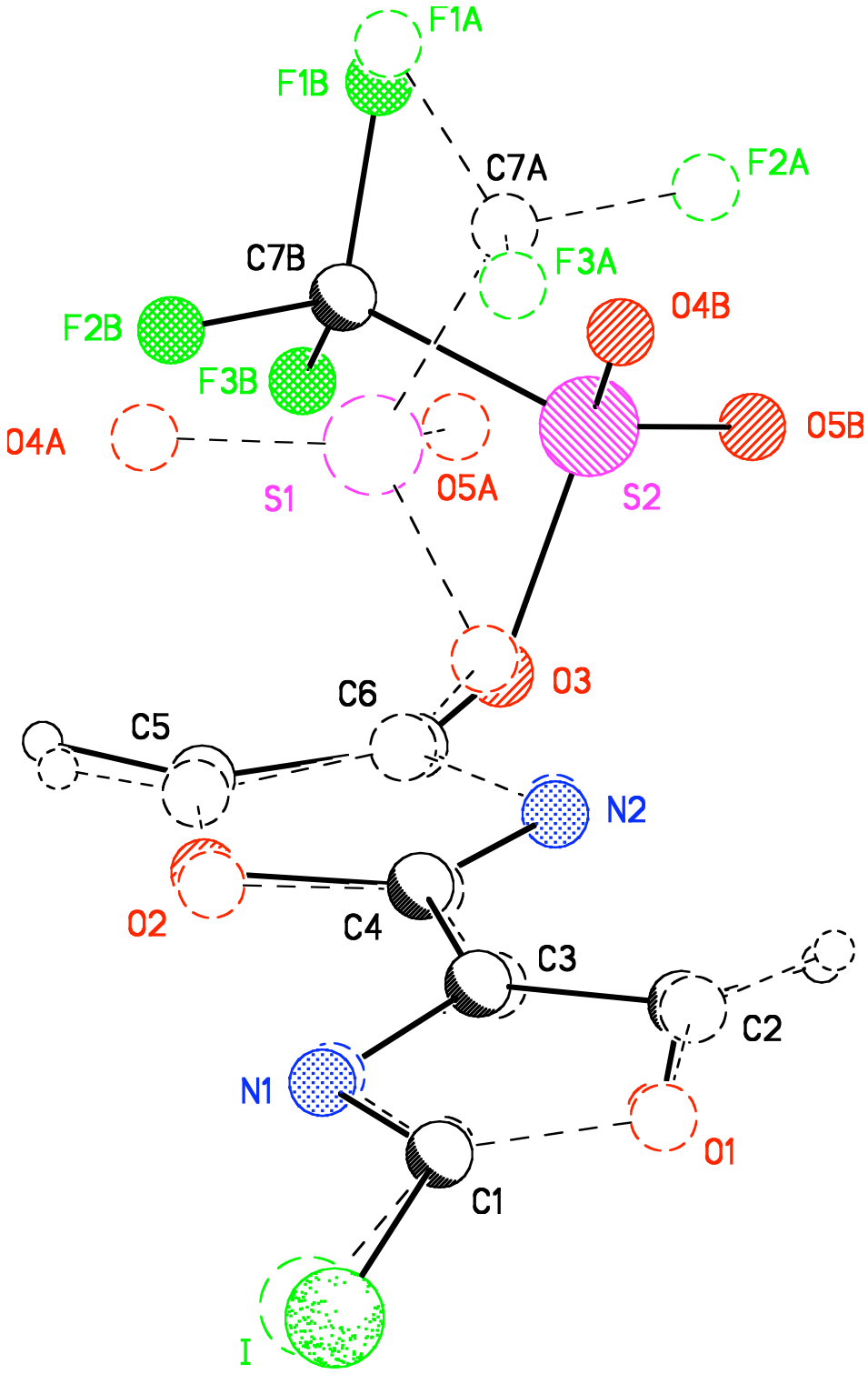

Figure A5.1.4 *Overlap of molecule A and B emphasizing the torsion angle around the C(6)-O(3) bond*

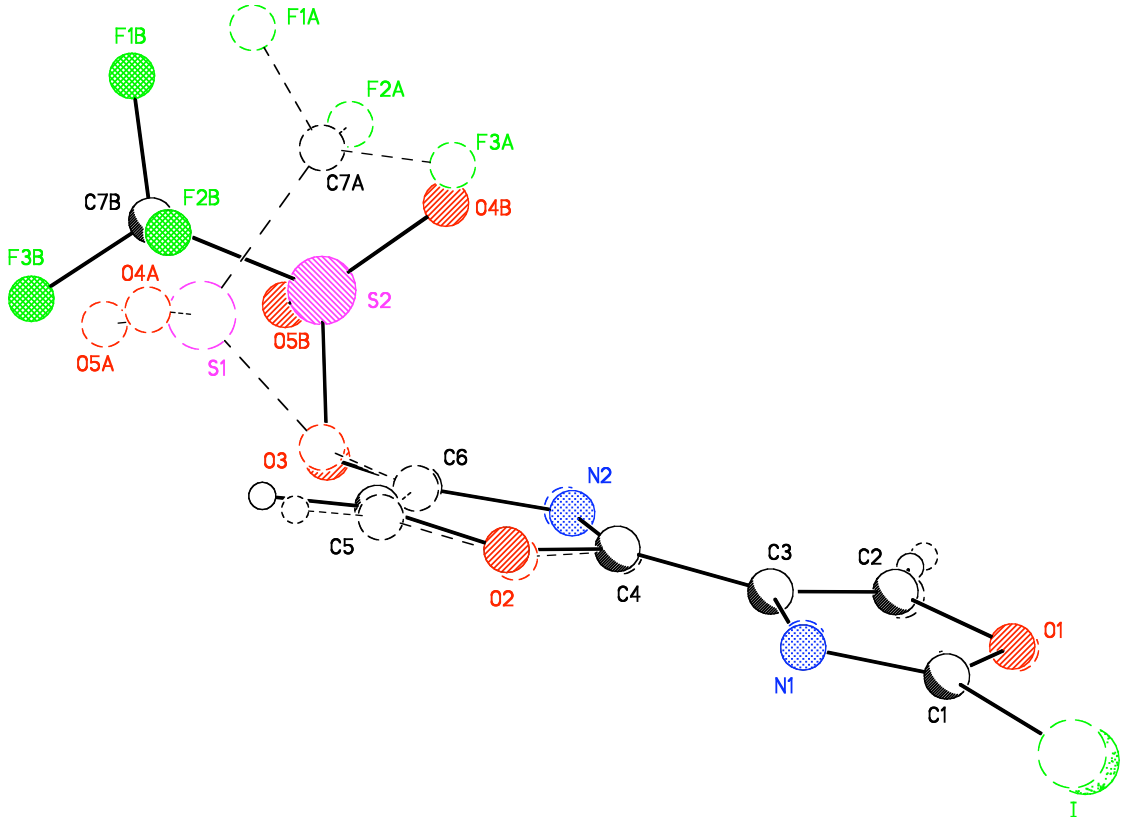

Figure A5.1.5 *Overlap of molecule A and B emphasizing the torsion angle around the O(3)-S bond*

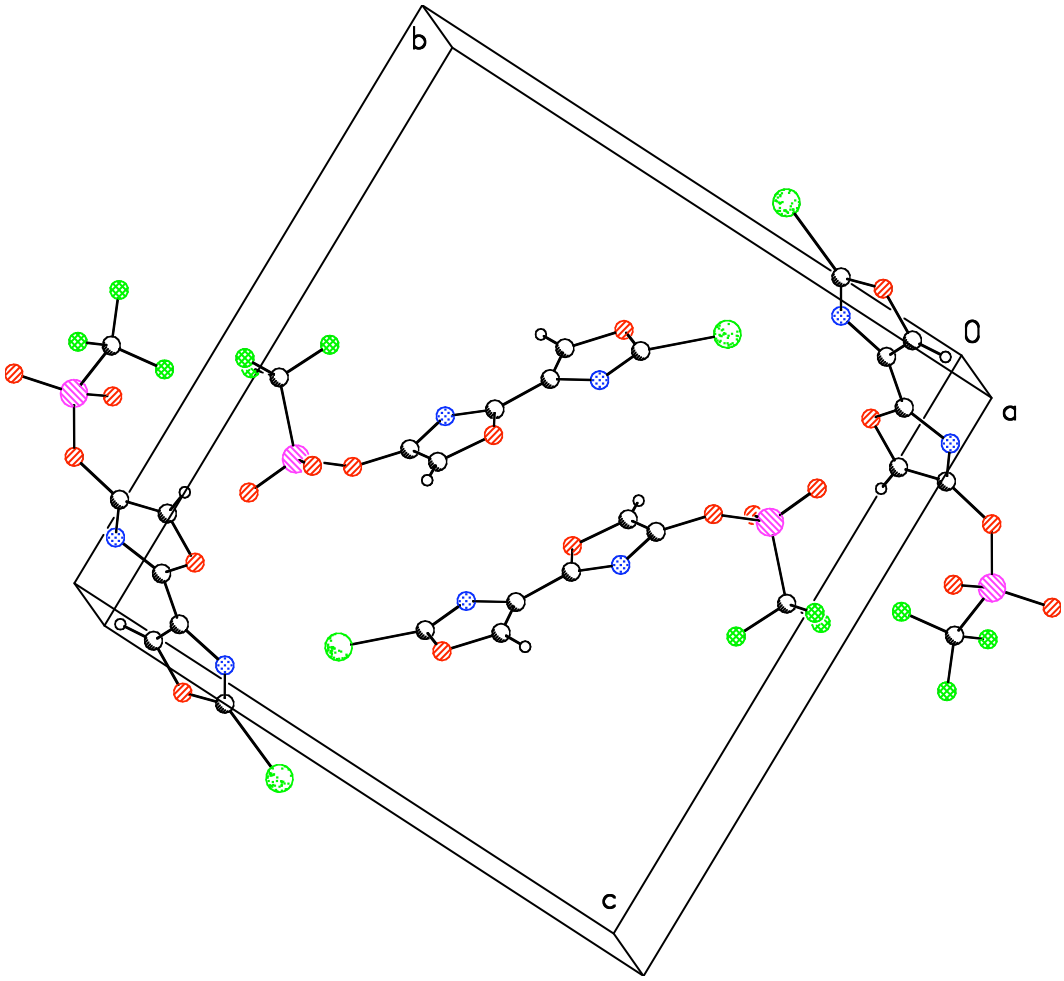

Figure A5.1.6 *Packing in the unit cell with the I(1)-N(1B) interaction emphasized*

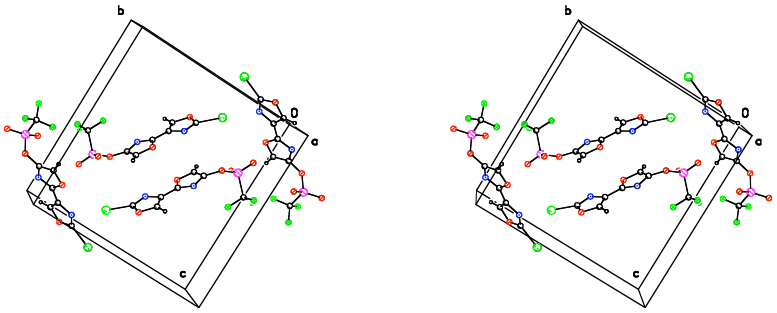

Figure A5.1.7 *Stereo view of the packing in the unit cell with the I(1)-N(1B) interaction emphasized*

Table A5.1.2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **226** (CCDC 282586). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
I(1)	2611(1)	3487(1)	1553(1)	17(1)
S(1)	2125(1)	8201(1)	6603(1)	18(1)
F(1A)	2445(4)	9715(1)	5750(1)	44(1)
F(2A)	-1292(4)	9274(1)	5935(1)	39(1)
F(3A)	903(3)	8577(1)	4943(1)	29(1)
O(1A)	-1301(3)	4609(1)	2445(1)	21(1)
O(2A)	3752(3)	5878(1)	4665(1)	19(1)
O(3A)	701(3)	7278(1)	6286(1)	17(1)
O(4A)	4719(4)	8117(2)	6483(1)	28(1)
O(5A)	1112(4)	8483(1)	7431(1)	25(1)
N(1A)	2396(4)	4804(2)	3161(1)	15(1)
N(2A)	-68(4)	6392(2)	4929(1)	16(1)
C(1A)	1153(5)	4399(2)	2502(2)	15(1)
C(2A)	-1614(5)	5227(2)	3160(2)	20(1)
C(3A)	609(5)	5342(2)	3598(2)	13(1)
C(4A)	1312(5)	5888(2)	4403(2)	13(1)
C(5A)	3925(5)	6421(2)	5442(2)	20(1)
C(6A)	1616(5)	6724(2)	5578(2)	15(1)
C(7A)	954(5)	8991(2)	5757(2)	22(1)
I(2)	2895(1)	5915(1)	10688(1)	27(1)
S(2)	3024(1)	11753(1)	7553(1)	19(1)
F(1B)	3756(3)	12036(2)	5882(1)	39(1)
F(2B)	6039(3)	10962(1)	6438(1)	27(1)
F(3B)	6889(3)	12400(1)	6769(1)	29(1)
O(1B)	596(3)	7723(1)	10466(1)	19(1)
O(2B)	6105(3)	9010(1)	8594(1)	16(1)
O(3B)	4951(3)	11381(1)	8288(1)	18(1)
O(4B)	1164(4)	11076(2)	7332(1)	26(1)
O(5B)	2497(4)	12676(2)	7808(2)	32(1)
N(1B)	4077(4)	7636(2)	9688(1)	15(1)
N(2B)	3301(4)	10062(2)	9005(1)	14(1)
C(1B)	2595(5)	7220(2)	10211(2)	17(1)
C(2B)	865(5)	8548(2)	10051(2)	17(1)
C(3B)	2946(5)	8489(2)	9579(2)	14(1)
C(4B)	4040(5)	9214(2)	9059(2)	13(1)
C(5B)	6713(5)	9817(2)	8192(2)	17(1)
C(6B)	5014(5)	10439(2)	8451(2)	15(1)
C(7B)	5080(5)	11791(2)	6599(2)	23(1)

Table A5.1.3 Bond lengths [Å] and angles [°] for **226** (CCDC 282586)

I(1)-C(1A)	2.074(3)
S(1)-O(5A)	1.4128(19)
S(1)-O(4A)	1.419(2)
S(1)-O(3A)	1.5838(19)
S(1)-C(7A)	1.833(3)
F(1A)-C(7A)	1.317(3)
F(2A)-C(7A)	1.311(3)
F(3A)-C(7A)	1.329(3)
O(1A)-C(1A)	1.357(3)
O(1A)-C(2A)	1.378(3)
O(2A)-C(4A)	1.356(3)
O(2A)-C(5A)	1.373(3)
O(3A)-C(6A)	1.404(3)
N(1A)-C(1A)	1.287(3)
N(1A)-C(3A)	1.404(3)
N(2A)-C(4A)	1.304(3)
N(2A)-C(6A)	1.372(3)
C(2A)-C(3A)	1.348(4)
C(2A)-H(2A)	0.96(3)
C(3A)-C(4A)	1.447(3)
C(5A)-C(6A)	1.340(4)
C(5A)-H(5A)	0.92(3)
I(2)-C(1B)	2.049(3)
S(2)-O(5B)	1.408(2)
S(2)-O(4B)	1.418(2)
S(2)-O(3B)	1.591(2)
S(2)-C(7B)	1.833(3)
F(1B)-C(7B)	1.323(3)
F(2B)-C(7B)	1.325(4)
F(3B)-C(7B)	1.321(3)
O(1B)-C(1B)	1.361(3)
O(1B)-C(2B)	1.374(3)
O(2B)-C(4B)	1.357(3)
O(2B)-C(5B)	1.376(3)
O(3B)-C(6B)	1.394(3)
N(1B)-C(1B)	1.295(3)
N(1B)-C(3B)	1.392(3)
N(2B)-C(4B)	1.298(3)
N(2B)-C(6B)	1.381(3)
C(2B)-C(3B)	1.345(4)
C(2B)-H(2B)	0.95(3)
C(3B)-C(4B)	1.461(4)
C(5B)-C(6B)	1.344(4)
C(5B)-H(5B)	1.14(3)
O(5A)-S(1)-O(4A)	122.97(13)
O(5A)-S(1)-O(3A)	106.06(12)
O(4A)-S(1)-O(3A)	110.99(12)
O(5A)-S(1)-C(7A)	107.22(13)
O(4A)-S(1)-C(7A)	106.61(13)
O(3A)-S(1)-C(7A)	100.73(12)

C(1A)-O(1A)-C(2A)	104.0(2)
C(4A)-O(2A)-C(5A)	105.2(2)
C(6A)-O(3A)-S(1)	119.74(17)
C(1A)-N(1A)-C(3A)	103.7(2)
C(4A)-N(2A)-C(6A)	102.6(2)
N(1A)-C(1A)-O(1A)	115.2(2)
N(1A)-C(1A)-I(1)	125.35(19)
O(1A)-C(1A)-I(1)	119.42(17)
C(3A)-C(2A)-O(1A)	107.7(2)
C(3A)-C(2A)-H(2A)	131.2(19)
O(1A)-C(2A)-H(2A)	120.6(19)
C(2A)-C(3A)-N(1A)	109.4(2)
C(2A)-C(3A)-C(4A)	130.7(2)
N(1A)-C(3A)-C(4A)	119.9(2)
N(2A)-C(4A)-O(2A)	114.1(2)
N(2A)-C(4A)-C(3A)	129.4(2)
O(2A)-C(4A)-C(3A)	116.4(2)
C(6A)-C(5A)-O(2A)	105.6(2)
C(6A)-C(5A)-H(5A)	135(2)
O(2A)-C(5A)-H(5A)	119(2)
C(5A)-C(6A)-N(2A)	112.5(2)
C(5A)-C(6A)-O(3A)	130.0(2)
N(2A)-C(6A)-O(3A)	117.5(2)
F(2A)-C(7A)-F(1A)	108.7(3)
F(2A)-C(7A)-F(3A)	108.9(2)
F(1A)-C(7A)-F(3A)	108.4(2)
F(2A)-C(7A)-S(1)	111.1(2)
F(1A)-C(7A)-S(1)	109.2(2)
F(3A)-C(7A)-S(1)	110.4(2)
O(5B)-S(2)-O(4B)	123.51(14)
O(5B)-S(2)-O(3B)	107.15(13)
O(4B)-S(2)-O(3B)	110.21(11)
O(5B)-S(2)-C(7B)	106.84(14)
O(4B)-S(2)-C(7B)	107.37(13)
O(3B)-S(2)-C(7B)	98.96(12)
C(1B)-O(1B)-C(2B)	104.3(2)
C(4B)-O(2B)-C(5B)	104.9(2)
C(6B)-O(3B)-S(2)	119.66(16)
C(1B)-N(1B)-C(3B)	103.1(2)
C(4B)-N(2B)-C(6B)	102.8(2)
N(1B)-C(1B)-O(1B)	114.9(2)
N(1B)-C(1B)-I(2)	128.2(2)
O(1B)-C(1B)-I(2)	116.89(18)
C(3B)-C(2B)-O(1B)	107.2(2)
C(3B)-C(2B)-H(2B)	131.5(18)
O(1B)-C(2B)-H(2B)	121.3(18)
C(2B)-C(3B)-N(1B)	110.5(2)
C(2B)-C(3B)-C(4B)	126.9(2)
N(1B)-C(3B)-C(4B)	122.5(2)
N(2B)-C(4B)-O(2B)	114.6(2)
N(2B)-C(4B)-C(3B)	127.2(2)
O(2B)-C(4B)-C(3B)	118.2(2)
C(6B)-C(5B)-O(2B)	105.9(2)
C(6B)-C(5B)-H(5B)	131.3(14)

O(2B)-C(5B)-H(5B)	122.7(14)
C(5B)-C(6B)-N(2B)	111.8(2)
C(5B)-C(6B)-O(3B)	128.0(2)
N(2B)-C(6B)-O(3B)	120.0(2)
F(3B)-C(7B)-F(2B)	109.7(2)
F(3B)-C(7B)-F(1B)	109.1(2)
F(2B)-C(7B)-F(1B)	109.2(2)
F(3B)-C(7B)-S(2)	110.4(2)
F(2B)-C(7B)-S(2)	109.83(19)
F(1B)-C(7B)-S(2)	108.5(2)

Table A5.1.4 Anisotropic displacement parameters ($Å^2$ x 10^4) for **226** (CCDC 282586). The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [h^2 $a^{*2}U^{11}$ + ... + 2 h k a* b* U^{12}].

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
I(1)	213(1)	135(1)	163(1)	-16(1)	4(1)	9(1)
S(1)	183(3)	205(4)	153(3)	-35(3)	0(2)	-9(3)
F(1A)	608(14)	276(11)	434(11)	62(9)	-48(10)	-215(10)
F(2A)	367(11)	449(13)	360(10)	124(9)	119(8)	207(9)
F(3A)	441(11)	258(10)	157(8)	-11(7)	8(7)	21(8)
O(1A)	131(10)	257(11)	224(10)	-80(8)	-11(8)	-7(8)
O(2A)	136(9)	185(11)	236(10)	-76(8)	-20(8)	45(8)
O(3A)	206(10)	161(10)	152(9)	-19(7)	26(7)	-28(8)
O(4A)	150(10)	334(13)	327(11)	-115(10)	-19(8)	-27(9)
O(5A)	324(12)	273(12)	146(9)	-47(8)	16(8)	33(9)
N(1A)	124(11)	134(12)	187(11)	-6(9)	-6(8)	15(8)
N(2A)	144(11)	171(12)	151(10)	12(9)	13(8)	-11(9)
C(1A)	140(13)	128(14)	174(12)	9(10)	20(10)	-9(10)
C(2A)	145(14)	194(16)	259(14)	-88(12)	25(11)	18(11)
C(3A)	118(12)	121(13)	160(12)	17(10)	12(9)	3(9)
C(4A)	124(13)	112(13)	164(12)	28(10)	-1(10)	2(9)
C(5A)	195(15)	192(16)	195(13)	-46(11)	-42(11)	41(11)
C(6A)	157(13)	135(14)	164(12)	-2(10)	29(10)	-5(10)
C(7A)	239(15)	191(16)	226(14)	-28(12)	57(11)	-15(12)
I(2)	383(1)	149(1)	293(1)	70(1)	73(1)	31(1)
S(2)	176(3)	178(4)	232(3)	67(3)	23(3)	11(3)
F(1B)	316(11)	599(14)	258(9)	217(9)	-64(8)	-25(9)
F(2B)	304(10)	273(10)	239(8)	-8(7)	55(7)	-9(8)
F(3B)	225(9)	261(10)	377(10)	80(8)	25(8)	-79(7)
O(1B)	205(10)	185(11)	195(9)	21(8)	56(8)	14(8)
O(2B)	177(10)	152(10)	161(9)	11(7)	36(7)	36(7)
O(3B)	237(10)	140(10)	158(9)	28(7)	-17(7)	-3(8)
O(4B)	143(10)	293(12)	344(11)	134(10)	-20(8)	-26(8)
O(5B)	366(13)	186(12)	423(13)	75(10)	110(10)	88(9)
N(1B)	172(12)	139(12)	150(10)	0(9)	7(9)	14(9)
N(2B)	179(12)	122(12)	129(10)	5(8)	-3(8)	5(9)
C(1B)	210(14)	129(14)	160(12)	-2(10)	1(10)	30(10)
C(2B)	222(15)	126(14)	155(12)	4(10)	2(10)	47(11)
C(3B)	145(13)	130(14)	129(11)	-25(10)	-29(9)	18(10)
C(4B)	142(13)	144(14)	106(11)	-9(9)	-12(9)	1(10)
C(5B)	187(14)	150(14)	175(12)	18(10)	18(10)	-29(10)
C(6B)	196(14)	115(14)	145(11)	0(10)	-21(10)	-10(10)
C(7B)	189(15)	260(17)	235(14)	86(12)	-16(11)	-58(12)

Table A5.1.5 Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for **226** (CCDC 282586)

	x	y	z	U_{iso}
H(2A)	-3150(60)	5540(20)	3230(20)	29(9)
H(5A)	5460(60)	6530(20)	5710(20)	31(9)
H(2B)	-260(50)	9040(20)	10145(19)	16(7)
H(5B)	8370(50)	9877(18)	7738(17)	12(7)

Table A5.1.6 Torsion angles [°] for **226** (CCDC 282586)

N(2A)-C(6A)-O(3A)-S(1)	-135.1(2)
N(2B)-C(6B)-O(3B)-S(2)	-81.0(3)
C(6A)-O(3A)-S(1)-C(7A)	81.2(2)
C(6B)-O(3B)-S(2)-C(7B)	-96.8(2)

Table A5.1.7 CH···N hydrogen bonds for **226** (CCDC 282586) [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(2A)-H(2A)...N(1A)#1	0.96(3)	2.61(3)	3.277(4)	127(2)
C(5A)-H(5A)...N(2A)#2	0.92(3)	2.72(3)	3.348(4)	127(2)
C(2B)-H(2B)...N(2B)#3	0.95(3)	2.45(3)	3.334(4)	155(2)
C(5B)-H(5B)...O(5A)#2	1.14(3)	2.54(3)	3.269(3)	120.1(17)
C(5B)-H(5B)...O(4B)#2	1.14(3)	2.40(3)	3.323(3)	136.6(18)

Symmetry transformations used to generate equivalent atoms:
#1 x-1,y,z
#2 x+1,y,z
#3 -x,-y+2,-z+2