A Scalable Synthesis of the Difluoromethyl-*allo*-threonyl hydroxamate-based LpxC Inhibitor LPC-058

Xiaofei Liang[1], Ramesh Gopalaswamy[1]*, Frank Navas III[1], Eric J.Toone[1,2], Pei Zhou[1,2]*

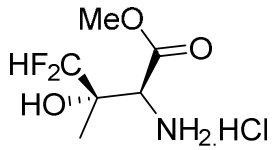
[1]Department of Chemistry, Duke University, Durham, NC, 27708, USA

[2]Department of Biochemistry, Duke University Medical Center, Durham, NC 27710, USA

SUPPORTING INFORMATION

Table of Contents

Crystal Structure Report for rds037 (Compound 11)



A colorless blade-like specimen of $C_6H_{12}ClF_2NO_3$, approximate dimensions 0.180 mm x 0.300 mm x 0.380 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

Table 1: Data collection details for rds037 (Compound 11)

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Phi	38.143	24.74	0.00	-190.75	23.00	0.50	721	10.00	0.71073	50	30.0	n/a
Omega	38.143	52.96	-36.64	-46.34	76.78	0.50	177	10.00	0.71073	50	30.0	n/a
Omega	38.143	56.39	-24.68	-237.44	59.81	0.50	160	10.00	0.71073	50	30.0	n/a
Omega	38.143	54.43	-25.41	-91.25	5.99	0.50	159	10.00	0.71073	50	30.0	n/a
Omega	38.143	55.46	-47.65	-169.93	55.06	0.50	204	10.00	0.71073	50	30.0	n/a
Omega	38.143	52.71	-9.17	-157.39	11.29	0.50	122	10.00	0.71073	50	30.0	n/a

A total of 1543 frames were collected. The total exposure time was 4.29 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 17754 reflections to a maximum θ angle of 30.50° (0.70 Å resolution), of which 5902 were independent (average redundancy 3.008, completeness = 100.0%, R_{int} = 2.71%, R_{sig} = 2.88%) and 5465 (92.60%) were greater than $2\sigma(F^2)$. The final cell constants of a = 12.4761(5) Å, b = 5.4881(2) Å, c = 14.5393(5) Å, β = 103.817(2)°, volume = 966.70(6) $Å^3$, are based upon the refinement of the XYZ-centroids of 8013 reflections above 20 σ(I) with 6.655° < 2θ < 62.86°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.891. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6652 and 0.7462.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21 1, with Z = 4 for the formula unit, $C_6H_{12}ClF_2NO_3$. The final anisotropic full-matrix least-squares refinement on F^2 with 243 variables converged at R1 = 2.67%, for the observed data and wR2 = 6.75% for all data. The goodness-of-fit was 1.037. The largest peak in the final difference electron density synthesis was 0.393 $e^-/Å^3$ and the largest hole was -0.261 $e^-/Å^3$ with an RMS deviation of 0.050 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.509 g/cm^3 and F(000), 456 e^-.

Table 2. Sample and crystal data for rds037.

Identification code	rds037
Chemical formula	$C_6H_{12}ClF_2NO_3$
Formula weight	219.62
Temperature	110(2) K
Wavelength	0.71073 Å
Crystal size	0.180 x 0.300 x 0.380 mm

Crystal habit	colorless blade	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 12.4761(5) Å	α = 90°
	b = 5.4881(2) Å	β = 103.817(2)°
	c = 14.5393(5) Å	γ = 90°
Volume	966.70(6) $Å^3$	
Z	4	
Density (calculated)	1.509 g/cm^3	
Absorption coefficient	0.403 mm^{-1}	
F(000)	456	

Table 3. Data collection and structure refinement for rds037.

Theta range for data collection	1.44 to 30.50°
Index ranges	-16<=h<=17, -7<=k<=7, -18<=l<=20
Reflections collected	17754
Independent reflections	5902 [R(int) = 0.0271]
Coverage of independent reflections	100.0%
Absorption correction	multi-scan
Max. and min. transmission	0.7462 and 0.6652
Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick, 2008)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-97 (Sheldrick, 2008)
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	5902 / 1 / 243
Goodness-of-fit on F^2	1.037
Δ/σ_{max}	0.001
Final R indices	5465 data; I>2σ(I) R1 = 0.0267, wR2 = 0.0654
	all data R1 = 0.0305, wR2 = 0.0675
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0361P)^2+0.1095P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	0.0(0)
Largest diff. peak and hole	0.393 and -0.261 $eÅ^{-3}$
R.M.S. deviation from mean	0.050 $eÅ^{-3}$

Table 4. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for rds037.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Cl1	0.77524(2)	0.85891(6)	0.41563(2)	0.01896(7)
Cl2	0.68987(2)	0.35823(6)	0.106275(19)	0.01829(7)
F1	0.10368(7)	0.57067(17)	0.22751(6)	0.02596(19)
F2	0.22715(6)	0.40278(17)	0.34101(6)	0.02516(19)
O1	0.85325(7)	0.91040(17)	0.21090(7)	0.01707(19)
O2	0.95416(8)	0.11068(19)	0.12578(7)	0.01927(19)
O3	0.03998(7)	0.47692(17)	0.39956(7)	0.01473(17)
N1	0.84034(8)	0.3224(2)	0.31514(7)	0.01345(19)
C1	0.90478(9)	0.0861(2)	0.19684(9)	0.0137(2)
C2	0.92743(9)	0.3070(2)	0.26175(9)	0.0126(2)
C3	0.04253(10)	0.2941(2)	0.33194(9)	0.0128(2)
C4	0.12989(9)	0.3588(3)	0.27747(9)	0.0184(2)
C5	0.93615(14)	0.9121(3)	0.05807(10)	0.0273(3)
C6	0.06856(11)	0.0441(2)	0.37675(10)	0.0192(3)
F3	0.23110(6)	0.88177(19)	0.12623(6)	0.02647(19)
F4	0.33468(7)	0.06900(18)	0.24767(6)	0.0277(2)
O4	0.59998(8)	0.41591(17)	0.30488(7)	0.01784(19)
O5	0.47357(8)	0.60423(18)	0.36726(7)	0.01769(18)
O6	0.43628(7)	0.97991(16)	0.09908(6)	0.01429(18)
N2	0.62538(8)	0.8270(2)	0.20443(7)	0.0135(2)
C7	0.53994(9)	0.5861(2)	0.30846(8)	0.0136(2)
C8	0.52694(9)	0.8073(2)	0.24406(9)	0.0124(2)
C9	0.42134(10)	0.7932(2)	0.16107(9)	0.0123(2)
C10	0.32062(9)	0.8513(3)	0.20034(9)	0.0184(2)
C11	0.47854(12)	0.4008(3)	0.43224(9)	0.0217(3)
C12	0.40499(11)	0.5442(2)	0.11444(10)	0.0181(3)

Table 5. Bond lengths (Å) for rds037.

F1-C4	1.3685(17)	F2-C4	1.3596(14)
O1-C1	1.2032(16)	O2-C1	1.3300(15)
O2-C5	1.4499(17)	O3-C3	1.4105(15)
O3-H3	0.84	N1-C2	1.4809(15)
N1-H1A	0.91	N1-H1B	0.91
N1-H1C	0.91	C1-C2	1.5209(17)
C2-C3	1.5520(16)	C2-H2	1.0

C3-C6	1.5203(17)	C3-C4	1.5341(17)
C4-H4	1.0	C5-H5A	0.98
C5-H5B	0.98	C5-H5C	0.98
C6-H6A	0.98	C6-H6B	0.98
C6-H6C	0.98	F3-C10	1.3644(14)
F4-C10	1.3690(18)	O4-C7	1.2061(15)
O5-C7	1.3284(15)	O5-C11	1.4541(16)
O6-C9	1.4061(14)	O6-H6	0.84
N2-C8	1.4798(15)	N2-H2A	0.91
N2-H2B	0.91	N2-H2C	0.91
C7-C8	1.5180(17)	C8-C9	1.5615(16)
C8-H8	1.0	C9-C12	1.5172(17)
C9-C10	1.5328(17)	C10-H10	1.0
C11-H11A	0.98	C11-H11B	0.98
C11-H11C	0.98	C12-H12A	0.98
C12-H12B	0.98	C12-H12C	0.98

Table 6. Bond angles (°) for rds037.

C1-O2-C5	115.20(11)	C3-O3-H3	109.5
C2-N1-H1A	109.5	C2-N1-H1B	109.5
H1A-N1-H1B	109.5	C2-N1-H1C	109.5
H1A-N1-H1C	109.5	H1B-N1-H1C	109.5
O1-C1-O2	125.36(12)	O1-C1-C2	124.13(11)
O2-C1-C2	110.44(10)	N1-C2-C1	108.65(9)
N1-C2-C3	109.72(10)	C1-C2-C3	112.16(10)
N1-C2-H2	108.8	C1-C2-H2	108.8
C3-C2-H2	108.8	O3-C3-C6	112.42(10)
O3-C3-C4	109.39(10)	C6-C3-C4	108.96(11)
O3-C3-C2	104.74(9)	C6-C3-C2	113.11(10)
C4-C3-C2	108.05(10)	F2-C4-F1	105.74(11)
F2-C4-C3	108.62(10)	F1-C4-C3	111.21(10)
F2-C4-H4	110.4	F1-C4-H4	110.4
C3-C4-H4	110.4	O2-C5-H5A	109.5
O2-C5-H5B	109.5	H5A-C5-H5B	109.5
O2-C5-H5C	109.5	H5A-C5-H5C	109.5
H5B-C5-H5C	109.5	C3-C6-H6A	109.5
C3-C6-H6B	109.5	H6A-C6-H6B	109.5
C3-C6-H6C	109.5	H6A-C6-H6C	109.5
H6B-C6-H6C	109.5	C7-O5-C11	115.10(10)

C9-O6-H6	109.5	C8-N2-H2A	109.5
C8-N2-H2B	109.5	H2A-N2-H2B	109.5
C8-N2-H2C	109.5	H2A-N2-H2C	109.5
H2B-N2-H2C	109.5	O4-C7-O5	125.09(12)
O4-C7-C8	124.65(11)	O5-C7-C8	110.23(10)
N2-C8-C7	108.79(9)	N2-C8-C9	109.17(10)
C7-C8-C9	112.53(9)	N2-C8-H8	108.8
C7-C8-H8	108.8	C9-C8-H8	108.8
O6-C9-C12	113.21(10)	O6-C9-C10	109.45(10)
C12-C9-C10	108.60(11)	O6-C9-C8	104.04(9)
C12-C9-C8	112.86(10)	C10-C9-C8	108.50(10)
F3-C10-F4	105.81(11)	F3-C10-C9	108.70(10)
F4-C10-C9	110.54(10)	F3-C10-H10	110.6
F4-C10-H10	110.6	C9-C10-H10	110.6
O5-C11-H11A	109.5	O5-C11-H11B	109.5
H11A-C11-H11B	109.5	O5-C11-H11C	109.5
H11A-C11-H11C	109.5	H11B-C11-H11C	109.5
C9-C12-H12A	109.5	C9-C12-H12B	109.5
H12A-C12-H12B	109.5	C9-C12-H12C	109.5
H12A-C12-H12C	109.5	H12B-C12-H12C	109.5

Table 7. Torsion angles (°) for rds037.

C5-O2-C1-O1	4.25(18)	C5-O2-C1-C2	-178.75(11)
O1-C1-C2-N1	-24.87(16)	O2-C1-C2-N1	158.08(10)
O1-C1-C2-C3	96.59(14)	O2-C1-C2-C3	-80.46(12)
N1-C2-C3-O3	-45.94(12)	C1-C2-C3-O3	-166.78(10)
N1-C2-C3-C6	76.82(13)	C1-C2-C3-C6	-44.02(15)
N1-C2-C3-C4	-162.47(10)	C1-C2-C3-C4	76.68(13)
O3-C3-C4-F2	52.78(14)	C6-C3-C4-F2	-70.48(14)
C2-C3-C4-F2	166.26(11)	O3-C3-C4-F1	-63.17(12)
C6-C3-C4-F1	173.56(10)	C2-C3-C4-F1	50.30(13)
C11-O5-C7-O4	1.38(17)	C11-O5-C7-C8	179.65(10)
O4-C7-C8-N2	-21.37(16)	O5-C7-C8-N2	160.35(9)
O4-C7-C8-C9	99.73(14)	O5-C7-C8-C9	-78.55(12)
N2-C8-C9-O6	-46.42(12)	C7-C8-C9-O6	-167.31(10)
N2-C8-C9-C12	76.70(13)	C7-C8-C9-C12	-44.19(14)
N2-C8-C9-C10	-162.89(10)	C7-C8-C9-C10	76.22(13)
O6-C9-C10-F3	56.46(14)	C12-C9-C10-F3	-67.59(14)
C8-C9-C10-F3	169.39(11)	O6-C9-C10-F4	-59.26(13)
C12-C9-C10-F4	176.69(10)	C8-C9-C10-F4	53.67(13)

Table 8. Anisotropic atomic displacement parameters (Å^2) for rds037.

The anisotropic atomic 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}
Cl1	0.01898(13)	0.01959(14)	0.01566(12)	0.00305(13)	-0.00110(10)	-0.00442(13)
Cl2	0.01859(12)	0.01909(14)	0.01464(12)	-0.00249(13)	-0.00109(9)	0.00448(13)
F1	0.0235(4)	0.0252(4)	0.0307(5)	0.0073(4)	0.0094(3)	-0.0052(4)
F2	0.0118(3)	0.0320(5)	0.0303(4)	-0.0068(4)	0.0024(3)	-0.0051(3)
O1	0.0161(4)	0.0133(4)	0.0216(4)	-0.0028(3)	0.0041(3)	-0.0025(3)
O2	0.0240(5)	0.0179(5)	0.0171(4)	-0.0034(4)	0.0071(4)	-0.0029(4)
O3	0.0148(4)	0.0112(4)	0.0160(4)	-0.0036(3)	-0.0008(3)	0.0019(3)
N1	0.0120(4)	0.0119(5)	0.0158(4)	-0.0012(4)	0.0020(3)	0.0001(4)
C1	0.0116(5)	0.0137(5)	0.0145(5)	-0.0010(5)	0.0005(4)	0.0020(4)
C2	0.0114(5)	0.0110(6)	0.0151(5)	0.0003(4)	0.0024(4)	-0.0002(4)
C3	0.0112(5)	0.0099(5)	0.0163(5)	-0.0018(4)	0.0011(4)	-0.0001(4)
C4	0.0129(5)	0.0195(6)	0.0225(5)	-0.0011(6)	0.0035(4)	-0.0010(5)
C5	0.0387(8)	0.0248(8)	0.0190(6)	-0.0087(6)	0.0084(6)	-0.0006(6)
C6	0.0185(6)	0.0109(6)	0.0244(7)	0.0007(5)	-0.0022(5)	0.0021(4)
F3	0.0124(3)	0.0355(5)	0.0288(4)	0.0072(4)	-0.0004(3)	0.0040(4)
F4	0.0238(4)	0.0283(5)	0.0320(5)	-0.0074(4)	0.0085(4)	0.0078(4)
O4	0.0184(4)	0.0133(4)	0.0207(4)	0.0033(3)	0.0026(3)	0.0027(3)
O5	0.0220(4)	0.0165(5)	0.0148(4)	0.0032(4)	0.0049(3)	0.0012(4)
O6	0.0161(4)	0.0101(4)	0.0144(4)	0.0028(3)	-0.0010(3)	-0.0024(3)
N2	0.0115(4)	0.0123(5)	0.0156(4)	0.0011(4)	0.0010(3)	-0.0011(4)
C7	0.0132(5)	0.0133(5)	0.0123(5)	-0.0005(4)	-0.0009(4)	-0.0019(4)
C8	0.0119(5)	0.0100(6)	0.0145(5)	0.0000(4)	0.0017(4)	-0.0004(4)
C9	0.0113(5)	0.0092(5)	0.0149(5)	0.0017(4)	0.0002(4)	-0.0005(4)
C10	0.0126(5)	0.0213(6)	0.0207(5)	0.0026(6)	0.0027(4)	0.0010(5)
C11	0.0301(7)	0.0191(7)	0.0153(6)	0.0057(5)	0.0043(5)	-0.0030(5)
C12	0.0178(5)	0.0100(6)	0.0225(6)	-0.0017(5)	-0.0034(5)	-0.0015(5)

Table 9. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2) for rds037.

	x/a	y/b	z/c	U(eq)
H3	1.0908	0.4523	0.4481	0.022

	x/a	y/b	z/c	U(eq)
H1A	0.8562	0.4461	0.3579	0.016
H1B	0.8372	0.1794	0.3461	0.016
H1C	0.7740	0.3511	0.2742	0.016
H2	0.9241	0.4569	0.2220	0.015
H4	1.1385	0.2226	0.2341	0.022
H5A	0.9589	-0.2417	0.0913	0.041
H5B	0.9797	-0.0600	0.0112	0.041
H5C	0.8577	-0.0963	0.0260	0.041
H6A	1.1397	0.0497	0.4233	0.029
H6B	1.0722	-0.0755	0.3275	0.029
H6C	1.0105	-0.0032	0.4083	0.029
H6	0.3957	0.9537	0.0450	0.021
H2A	0.6864	0.8504	0.2523	0.016
H2B	0.6170	0.9553	0.1637	0.016
H2C	0.6332	0.6873	0.1729	0.016
H8	0.5223	0.9564	0.2825	0.015
H10	0.3071	0.7174	0.2428	0.022
H11A	0.4263	0.4283	0.4719	0.032
H11B	0.5534	0.3872	0.4725	0.032
H11C	0.4592	0.2499	0.3961	0.032
H12A	0.3431	0.5508	0.0585	0.027
H12B	0.3891	0.4244	0.1594	0.027
H12C	0.4723	0.4967	0.0954	0.027

Table 10. Hydrogen bond distances (Å) and angles (°) for rds037.

	Donor-H	Acceptor-H	Donor-Acceptor	Angle
O3-H3···Cl1#3	0.84	2.32	3.1617(9)	175.9
N1-H1A···Cl1#1	0.91	2.70	3.4687(11)	143.4
N1-H1B···Cl1	0.91	2.26	3.1354(11)	162.5
N1-H1C···O4	0.91	2.35	3.0107(13)	129.8
N1-H1C···Cl2	0.91	2.42	3.1720(10)	140.5
O6-H6···Cl2#2	0.84	2.26	3.0973(9)	171.1
N2-H2A···O1#1	0.91	2.32	2.8589(13)	117.4
N2-H2A···Cl1#1	0.91	2.37	3.1958(10)	151.1
N2-H2B···Cl2#1	0.91	2.60	3.4254(11)	150.7

Symmetry transformations used to generate equivalent atoms:

#1 x, y+1, z

#2 -x+1, y+1/2, -z

#3 -x+2, y+1/2, -z+1

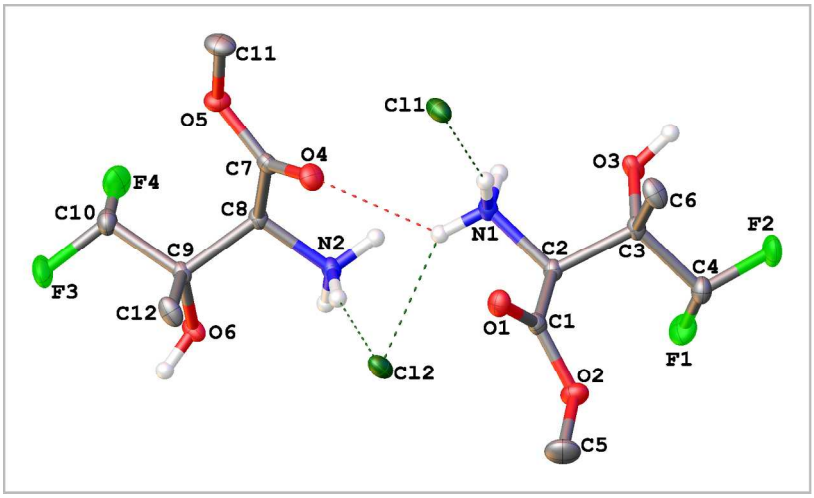
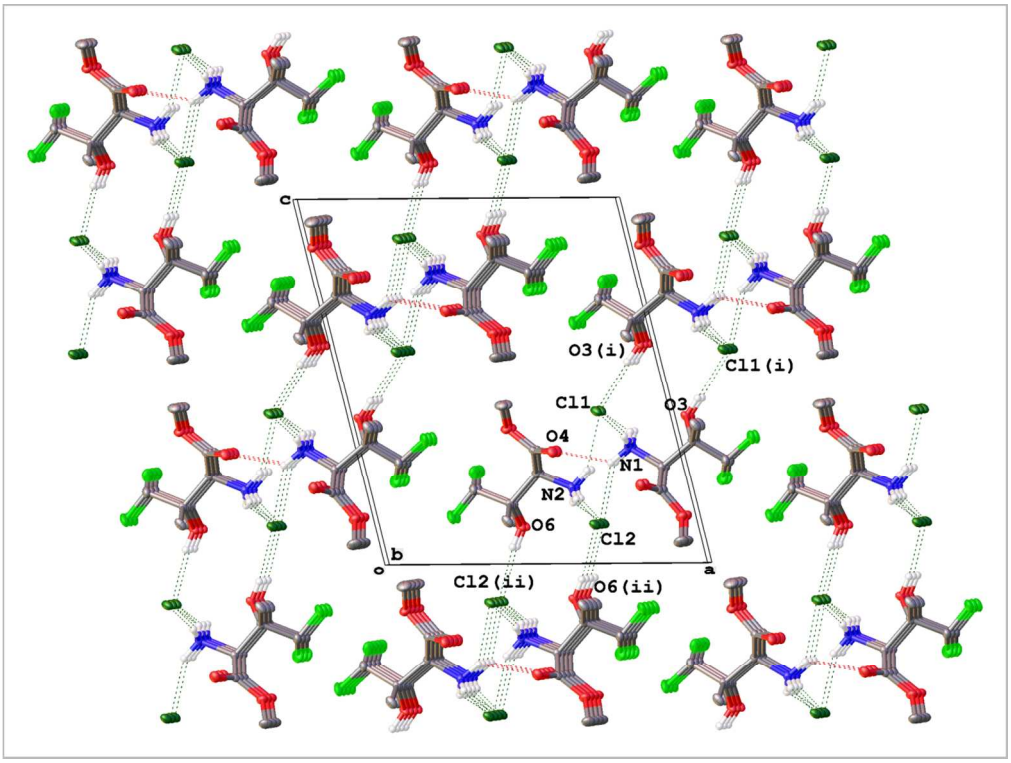


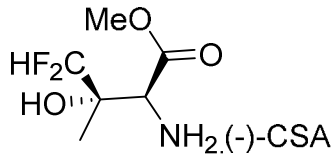
Figure A. Thermal Ellipsoid plot of rds037 drawn at 50% probability. H atoms on carbon are removed for clarity.

Figure B. Packing diagram of rds037 viewed along a axis of unit cell, showing hydrogen bond interactions with neighboring sulfonate anions. Only hydrogen bond donor and acceptor atoms labeled.



Ellipsoids drawn at 50% probability. H atoms on carbon are removed and O5(i) label excluded for clarity. (Symmetry operations i: 2-x, ½ + y, 1-z; ii: 1 – x, ½ +y, -z)

Crystal Structure Report for rds041 (Compound 21)



A colorless rod-like specimen of $C_{16}H_{27}F_2NO_7S$, approximate dimensions 0.070 mm x 0.070 mm x 0.340 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

Table 1: Data collection details for rds041 (Compound 21).

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Times	Wavelength Å	Voltage kV	Current / mA	T/K
Phi	38.160	25.79	0.00	-172.00	23.00	0.50	622	30.00	0.71073	50	30.0	n/a
Omega	38.160	53.74	-50.39	84.58	64.98	0.50	206	30.00	0.71073	50	30.0	n/a
Omega	38.160	-62.69	-61.82	-77.83	-14.56	0.50	165	30.00	0.71073	50	30.0	n/a
Omega	38.160	62.43	-21.38	28.70	15.40	0.50	166	30.00	0.71073	50	30.0	n/a
Omega	38.160	-56.38	-55.44	-146.33	-54.46	0.50	204	30.00	0.71073	50	30.0	n/a
Omega	38.160	-15.43	-9.26	-135.04	-80.56	0.50	63	30.00	0.71073	50	30.0	n/a
Omega	38.160	60.99	-43.63	-78.37	57.56	0.50	207	30.00	0.71073	50	30.0	n/a

A total of 1633 frames were collected. The total exposure time was 13.61 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 27049 reflections to a maximum θ angle of 27.40° (0.77 Å resolution), of which 4195 were independent (average redundancy 6.448, completeness = 99.6%, R_{int} = 6.06%, R_{sig} = 3.57%) and 3755 (89.51%) were greater than $2\sigma(F^2)$. The final cell constants of a = 6.3347(2) Å, b = 12.7819(4) Å, c = 22.8824(7) Å, volume = 1852.78(10) $Å^3$, are based upon the refinement of the XYZ-centroids of 4987 reflections above 20 σ(I) with 4.778° < 2θ < 53.48°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.857. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6387 and 0.7455.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 21 21 21, with Z = 4 for the formula unit, $C_{16}H_{27}F_2NO_7S$. The final anisotropic full-matrix least-squares refinement on F^2 with 250 variables converged at R1 = 3.03%, for the observed data and wR2 = 7.08% for all data. The goodness-of-fit was 1.024. The largest peak in the final difference electron density synthesis was 0.286 $e^-/Å^3$ and the largest hole was -0.278 $e^-/Å^3$ with an RMS deviation of 0.046 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.489 g/cm^3 and F(000), 880 e^-.

Table 2. Sample and crystal data for rds041.

Identification code	rds041	
Chemical formula	$C_{16}H_{27}F_2NO_7S$	
Formula weight	415.45	
Wavelength	0.71073 Å	
Crystal size	0.070 x 0.070 x 0.340 mm	
Crystal habit	colorless rod	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.3347(2) Å	α = 90°
	b = 12.7819(4) Å	β = 90°
	c = 22.8824(7) Å	γ = 90°
Volume	1852.78(10) $Å^3$	
Z	4	
Density (calculated)	1.489 g/cm^3	
Absorption coefficient	0.234 mm^{-1}	
F(000)	880	

Table 3. Data collection and structure refinement for rds041.

Theta range for data collection	1.78 to 27.40°
Index ranges	-8<=h<=8, -16<=k<=16, -26<=l<=29
Reflections collected	27049
Independent reflections	4195 [R(int) = 0.0606]
Coverage of independent reflections	99.6%
Absorption correction	multi-scan
Max. and min. transmission	0.7455 and 0.6387
Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick, 2008)
Refinement method	Full-matrix least-squares on F^2
Refinement program	XL, G.M. Sheldrick, Acta Cryst. (2008). A64, 112-122
Function minimized	$\Sigma\ w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	4195 / 0 / 250

Goodness-of-fit on F^2	1.024	
Δ/σ_{max}	0.001	
Final R indices	3755 data; I>2σ(I)	R1 = 0.0303, wR2 = 0.0676
	all data	R1 = 0.0379, wR2 = 0.0708
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0372P)^2+0.2708P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	-0.0(1)	
Largest diff. peak and hole	0.286 and -0.278 eÅ^{-3}	
R.M.S. deviation from mean	0.046 eÅ^{-3}	

Table 4. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for rds041.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
S1	0.57368(7)	0.28632(3)	0.593476(18)	0.01258(9)
F1	0.65601(17)	0.61596(9)	0.50106(5)	0.0254(3)
F2	0.81001(18)	0.74054(8)	0.54991(5)	0.0229(3)
O2	0.3185(2)	0.46397(11)	0.46531(5)	0.0177(3)
O1	0.0331(2)	0.52411(11)	0.41729(5)	0.0217(3)
O3	0.8412(2)	0.54708(10)	0.60399(5)	0.0166(3)
O4	0.5022(2)	0.23812(10)	0.53919(5)	0.0178(3)
O5	0.79407(19)	0.26702(10)	0.60725(5)	0.0173(3)
O6	0.52121(18)	0.39834(9)	0.59501(5)	0.0151(3)
O7	0.1456(2)	0.39524(11)	0.68299(5)	0.0190(3)
N1	0.1034(2)	0.39000(12)	0.55284(6)	0.0134(3)
C6	0.1709(3)	0.61763(15)	0.57648(8)	0.0175(4)
C3	0.9634(3)	0.57184(14)	0.55446(7)	0.0137(4)
C2	0.9961(3)	0.47109(14)	0.51737(7)	0.0129(3)
C1	0.1164(3)	0.48935(14)	0.46034(7)	0.0145(4)
C5	0.4438(3)	0.47617(16)	0.41256(8)	0.0223(4)
C4	0.8488(3)	0.65310(15)	0.51709(8)	0.0176(4)
C15	0.5328(3)	0.10401(16)	0.76838(8)	0.0212(4)
C14	0.3674(3)	0.18913(14)	0.75983(7)	0.0152(4)
C8	0.4204(3)	0.26782(13)	0.70934(7)	0.0126(3)
C7	0.4188(3)	0.22209(14)	0.64789(7)	0.0131(3)
C11	0.3733(3)	0.27457(15)	0.80815(7)	0.0172(4)

	x/a	y/b	z/c	U(eq)
C12	0.5950(3)	0.32275(16)	0.79960(7)	0.0184(4)
C13	0.6246(3)	0.32071(14)	0.73215(7)	0.0146(4)
C10	0.2149(3)	0.35560(16)	0.78572(7)	0.0192(4)
C9	0.2456(3)	0.34845(14)	0.71963(7)	0.0134(4)
C16	0.1525(3)	0.13542(16)	0.75224(8)	0.0197(4)

Table 5. Bond lengths (Å) for rds041.

S1-O4	1.4585(12)	S1-O5	1.4523(13)
S1-O6	1.4704(13)	S1-C7	1.7852(17)
F1-C4	1.361(2)	F2-C4	1.369(2)
O2-C1	1.326(2)	O2-C5	1.453(2)
O1-C1	1.202(2)	O3-H3	0.84
O3-C3	1.409(2)	O7-C9	1.209(2)
N1-H1A	0.91	N1-H1B	0.91
N1-H1C	0.91	N1-C2	1.482(2)
C6-H6A	0.98	C6-H6B	0.98
C6-H6C	0.98	C6-C3	1.524(2)
C3-C2	1.556(2)	C3-C4	1.529(3)
C2-H2	1.0	C2-C1	1.529(2)
C5-H5A	0.98	C5-H5B	0.98
C5-H5C	0.98	C4-H4	1.0
C15-H15A	0.98	C15-H15B	0.98
C15-H15C	0.98	C15-C14	1.523(3)
C14-C8	1.568(2)	C14-C11	1.555(3)
C14-C16	1.535(3)	C8-C7	1.523(2)
C8-C13	1.550(2)	C8-C9	1.531(2)
C7-H7A	0.99	C7-H7B	0.99
C11-H11	1.0	C11-C12	1.545(2)
C11-C10	1.531(3)	C12-H12A	0.99
C12-H12B	0.99	C12-C13	1.555(2)
C13-H13A	0.99	C13-H13B	0.99
C10-H10A	0.99	C10-H10B	0.99
C10-C9	1.527(2)	C16-H16A	0.98
C16-H16B	0.98	C16-H16C	0.98

Table 6. Bond angles (°) for rds041.

O4-S1-O6	111.19(8)	O4-S1-C7	103.25(8)
O5-S1-O4	114.29(8)	O5-S1-O6	112.18(7)
O5-S1-C7	107.39(8)	O6-S1-C7	107.88(8)
C1-O2-C5	115.47(14)	C3-O3-H3	109.5
H1A-N1-H1B	109.5	H1A-N1-H1C	109.5
H1B-N1-H1C	109.5	C2-N1-H1A	109.5
C2-N1-H1B	109.5	C2-N1-H1C	109.5
H6A-C6-H6B	109.5	H6A-C6-H6C	109.5
H6B-C6-H6C	109.5	C3-C6-H6A	109.5
C3-C6-H6B	109.5	C3-C6-H6C	109.5
O3-C3-C6	107.13(13)	O3-C3-C2	109.02(14)
O3-C3-C4	109.96(14)	C6-C3-C2	112.55(15)
C6-C3-C4	109.49(15)	C4-C3-C2	108.67(13)
N1-C2-C3	109.94(13)	N1-C2-H2	107.5
N1-C2-C1	110.22(14)	C3-C2-H2	107.5
C1-C2-C3	113.91(15)	C1-C2-H2	107.5
O2-C1-C2	111.77(14)	O1-C1-O2	125.74(16)
O1-C1-C2	122.48(16)	O2-C5-H5A	109.5
O2-C5-H5B	109.5	O2-C5-H5C	109.5
H5A-C5-H5B	109.5	H5A-C5-H5C	109.5
H5B-C5-H5C	109.5	F1-C4-F2	105.76(15)
F1-C4-C3	109.88(15)	F1-C4-H4	110.5
F2-C4-C3	109.45(14)	F2-C4-H4	110.5
C3-C4-H4	110.5	H15A-C15-H15B	109.5
H15A-C15-H15C	109.5	H15B-C15-H15C	109.5
C14-C15-H15A	109.5	C14-C15-H15B	109.5
C14-C15-H15C	109.5	C15-C14-C8	113.93(15)
C15-C14-C11	113.20(15)	C15-C14-C16	107.79(15)
C11-C14-C8	93.91(13)	C16-C14-C8	113.15(14)
C16-C14-C11	114.59(14)	C7-C8-C14	115.64(14)
C7-C8-C13	118.93(15)	C7-C8-C9	113.32(14)
C13-C8-C14	102.13(13)	C9-C8-C14	99.43(13)
C9-C8-C13	104.96(13)	S1-C7-H7A	107.9
S1-C7-H7B	107.9	C8-C7-S1	117.64(12)
C8-C7-H7A	107.9	C8-C7-H7B	107.9
H7A-C7-H7B	107.2	C14-C11-H11	114.6
C12-C11-C14	102.23(13)	C12-C11-H11	114.6
C10-C11-C14	102.77(14)	C10-C11-H11	114.6
C10-C11-C12	106.48(16)	C11-C12-H12A	111.1

C11-C12-H12B	111.1	C11-C12-C13	103.21(14)
H12A-C12-H12B	109.1	C13-C12-H12A	111.1
C13-C12-H12B	111.1	C8-C13-C12	103.94(14)
C8-C13-H13A	111.0	C8-C13-H13B	111.0
C12-C13-H13A	111.0	C12-C13-H13B	111.0
H13A-C13-H13B	109.0	C11-C10-H10A	111.4
C11-C10-H10B	111.4	H10A-C10-H10B	109.2
C9-C10-C11	101.99(14)	C9-C10-H10A	111.4
C9-C10-H10B	111.4	O7-C9-C8	127.24(15)
O7-C9-C10	126.17(16)	C10-C9-C8	106.55(14)
C14-C16-H16A	109.5	C14-C16-H16B	109.5
C14-C16-H16C	109.5	H16A-C16-H16B	109.5
H16A-C16-H16C	109.5	H16B-C16-H16C	109.5

Table 7. Anisotropic atomic displacement parameters ($Å^2$) for rds041.

The anisotropic atomic 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}
S1	0.01235(18)	0.0137(2)	0.01169(17)	-0.00052(16)	0.00151(16)	-0.00043(17)
F1	0.0186(5)	0.0249(6)	0.0328(6)	-0.0004(5)	-0.0080(5)	0.0038(5)
F2	0.0290(6)	0.0152(6)	0.0245(5)	-0.0017(4)	0.0033(5)	0.0054(5)
O2	0.0152(6)	0.0237(7)	0.0144(6)	0.0014(5)	0.0024(5)	-0.0016(6)
O1	0.0252(7)	0.0261(8)	0.0139(6)	0.0034(5)	-0.0014(5)	0.0049(6)
O3	0.0185(6)	0.0180(7)	0.0133(6)	-0.0014(5)	0.0028(5)	-0.0035(5)
O4	0.0201(6)	0.0196(7)	0.0138(6)	-0.0039(5)	0.0017(5)	-0.0019(5)
O5	0.0130(6)	0.0200(7)	0.0188(6)	0.0009(5)	0.0039(5)	0.0020(5)
O6	0.0144(6)	0.0125(6)	0.0184(6)	0.0008(5)	-0.0002(5)	-0.0005(5)
O7	0.0162(6)	0.0209(7)	0.0199(6)	0.0024(5)	-0.0005(5)	0.0034(6)
N1	0.0133(7)	0.0134(8)	0.0136(6)	0.0004(6)	0.0009(6)	0.0012(6)
C6	0.0161(9)	0.0168(9)	0.0196(9)	-0.0029(7)	-0.0022(7)	-0.0023(8)
C3	0.0160(9)	0.0124(9)	0.0126(8)	-0.0016(7)	0.0009(7)	-0.0009(7)
C2	0.0119(8)	0.0134(9)	0.0133(8)	0.0000(7)	-0.0016(6)	0.0002(7)
C1	0.0197(10)	0.0105(9)	0.0131(8)	-0.0020(6)	-0.0003(7)	-0.0021(7)
C5	0.0199(9)	0.0308(11)	0.0160(8)	0.0004(8)	0.0045(8)	-0.0049(9)
C4	0.0175(9)	0.0163(9)	0.0191(8)	-0.0008(7)	-0.0002(7)	0.0019(8)
C15	0.0210(10)	0.0179(10)	0.0248(9)	0.0066(8)	-0.0015(8)	-0.0004(8)
C14	0.0131(9)	0.0168(9)	0.0158(8)	0.0040(7)	-0.0007(6)	0.0000(7)
C8	0.0135(8)	0.0127(9)	0.0115(7)	0.0002(6)	-0.0001(6)	-0.0007(7)
C7	0.0128(8)	0.0111(8)	0.0153(7)	-0.0009(7)	0.0022(7)	-0.0023(8)
C11	0.0178(9)	0.0226(10)	0.0112(7)	0.0026(7)	0.0022(6)	-0.0017(8)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C12	0.0177(9)	0.0226(10)	0.0149(8)	-0.0010(7)	-0.0020(7)	-0.0027(8)
C13	0.0127(9)	0.0154(9)	0.0156(8)	0.0007(7)	0.0002(6)	-0.0014(7)
C10	0.0181(10)	0.0228(11)	0.0168(8)	-0.0023(7)	0.0042(7)	0.0020(8)
C9	0.0124(8)	0.0125(9)	0.0154(8)	-0.0007(7)	0.0012(7)	-0.0029(7)
C16	0.0174(9)	0.0210(10)	0.0206(9)	0.0046(8)	0.0002(7)	-0.0014(8)

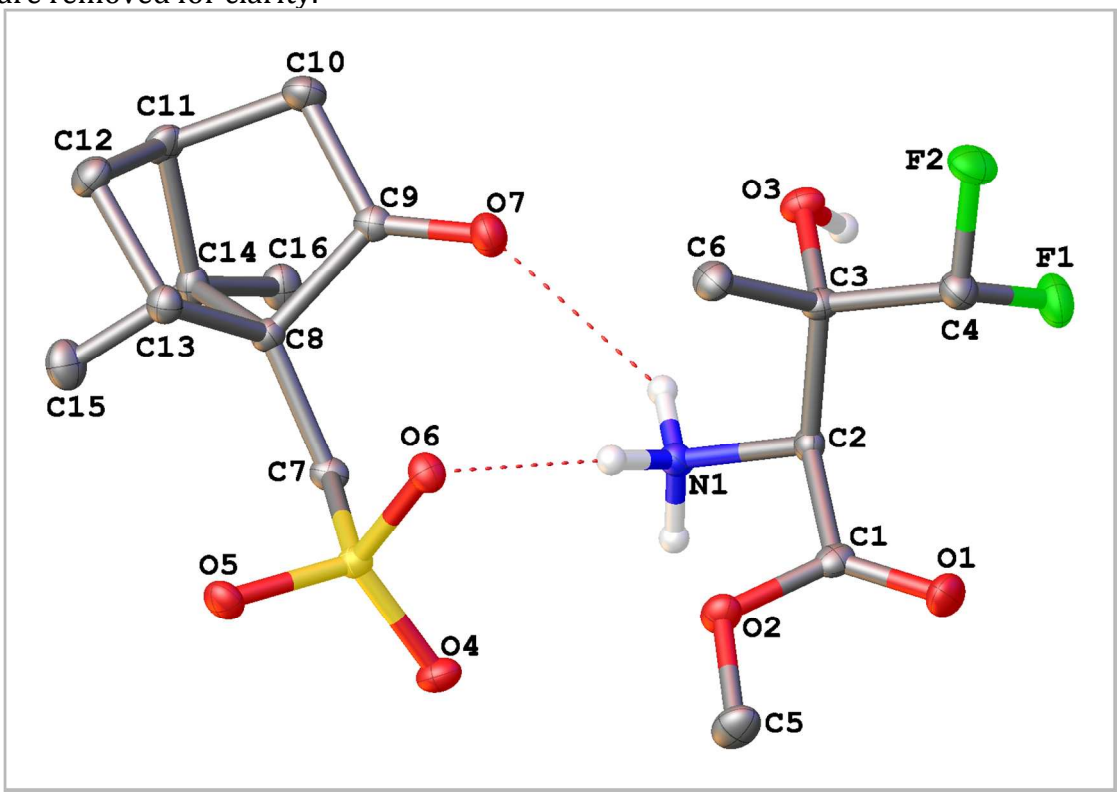
Table 8. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$) for rds041.

	x/a	y/b	z/c	U(eq)
H3	-0.2563	0.5060	0.5944	0.025
H1A	0.1090	0.3291	0.5323	0.02
H1B	0.0303	0.3796	0.5866	0.02
H1C	0.2368	0.4115	0.5614	0.02
H6A	0.1432	0.6835	0.5970	0.026
H6B	0.2650	0.6307	0.5433	0.026
H6C	0.2381	0.5681	0.6034	0.026
H2	-0.1469	0.4436	0.5069	0.015
H5A	0.3845	0.4325	0.3814	0.033
H5B	0.5895	0.4546	0.4204	0.033
H5C	0.4418	0.5496	0.4003	0.033
H4	-0.0655	0.6712	0.4818	0.021
H15A	0.5015	0.0648	0.8041	0.032
H15B	0.6728	0.1361	0.7717	0.032
H15C	0.5306	0.0564	0.7348	0.032
H7A	0.2707	0.2207	0.6341	0.016
H7B	0.4673	0.1486	0.6505	0.016
H11	0.3445	0.2483	0.8485	0.021
H12A	0.7045	0.2803	0.8194	0.022
H12B	0.6005	0.3952	0.8148	0.022
H13A	0.6390	0.3925	0.7164	0.017
H13B	0.7510	0.2796	0.7212	0.017
H10A	0.0687	0.3372	0.7971	0.023
H10B	0.2484	0.4265	0.8004	0.023
H16A	0.1599	0.0857	0.7197	0.03
H16B	0.0444	0.1883	0.7440	0.03
H16C	0.1159	0.0980	0.7882	0.03

Table 9. Hydrogen bond distances (Å) and angles (°) for rds041.

	Donor-H	Acceptor-H	Donor-Acceptor	Angle
O3-H3···O6	0.84	1.97	2.7864(18)	163.9
N1-H1A···O4	0.91	1.97	2.7435(19)	142.1
N1-H1B···O5	0.91	2.13	2.8036(19)	130.1
N1-H1B···O7	0.91	2.33	2.9909(18)	129.1
N1-H1C···O6	0.91	1.97	2.8192(19)	155.5

Figure C. Thermal Ellipsoid plot of rds041 drawn at 50% probablility. H atoms on carbon are removed for clarity.



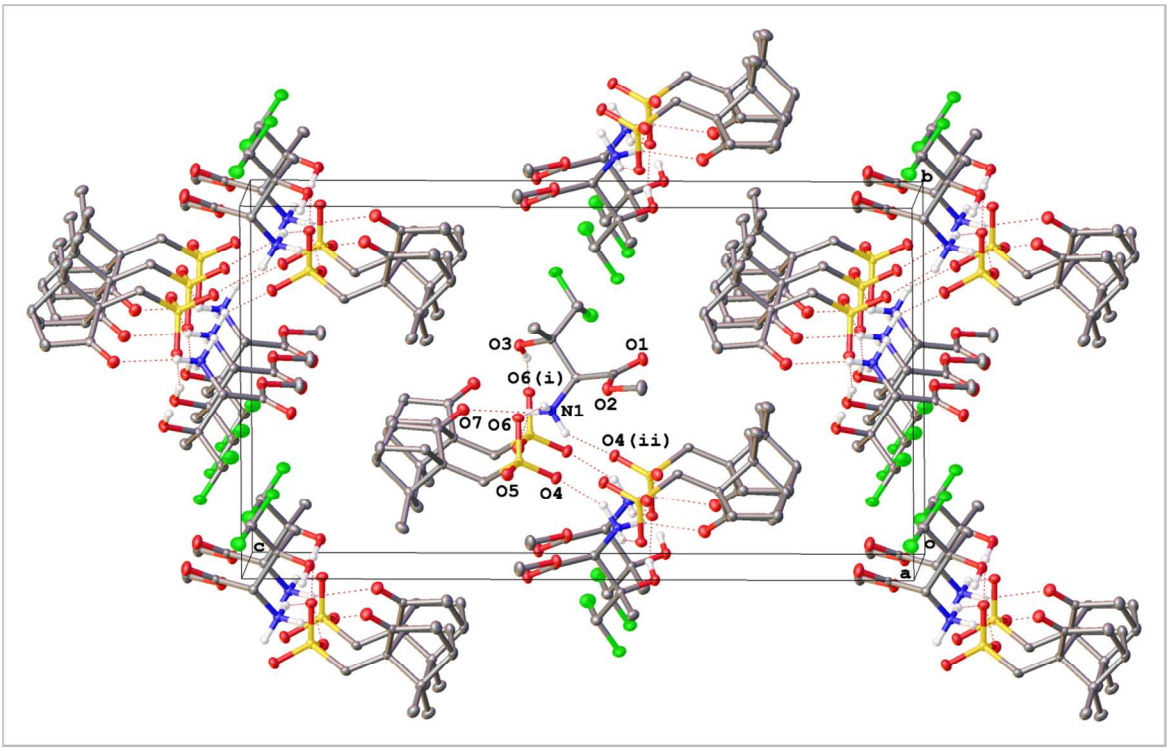
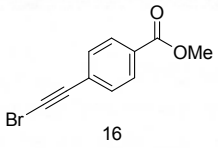


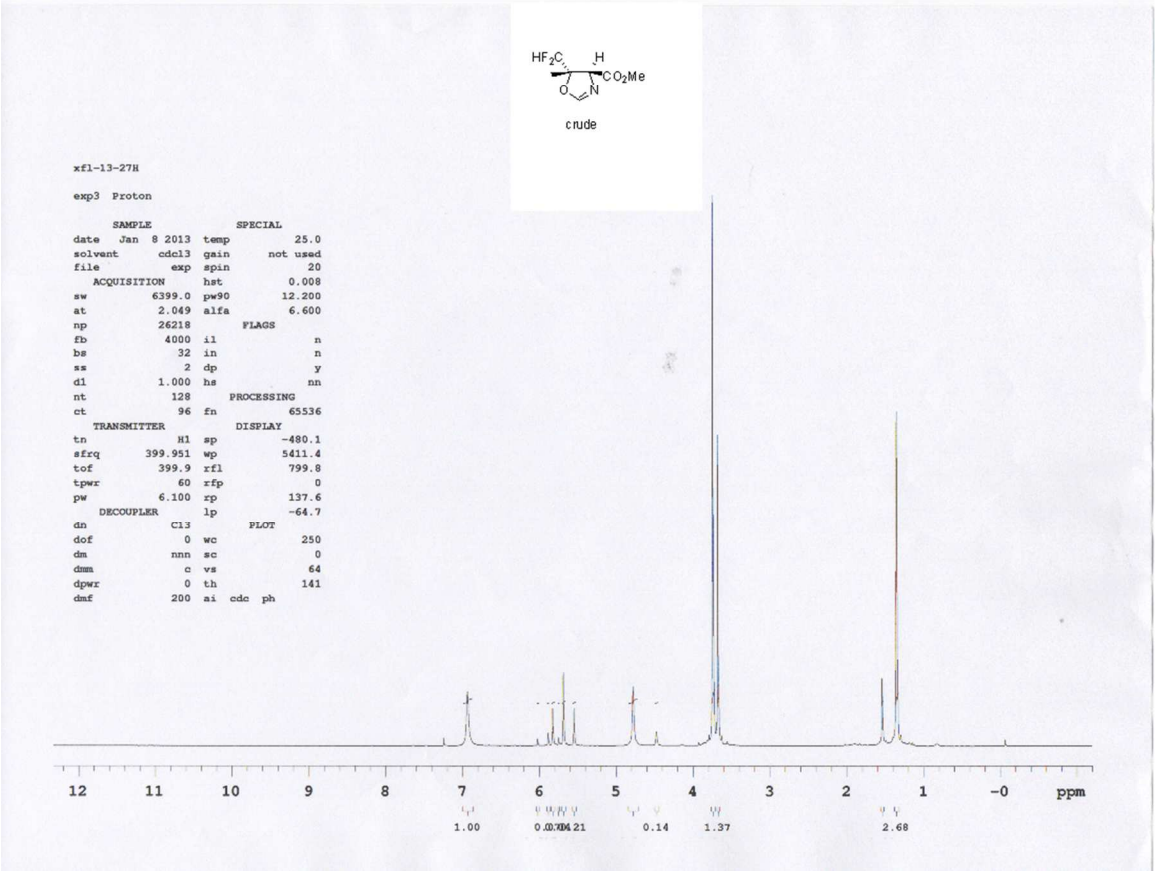
Figure D. Packing diagram of rds041 viewed along a axis of unit cell, showing hydrogen bond interactions with neighboring sulfonate anions . Only hydrogen bond donor and acceptor atoms labeled. Ellipsoids drawn at 50% probablility. H atoms on carbon are removed and O5(i) label excluded for clarity. (Symmetry operations i: -1+x, y, z; ii: 1/2 +x, ½ -y, 1-z)

Compound **16** 1H NMR

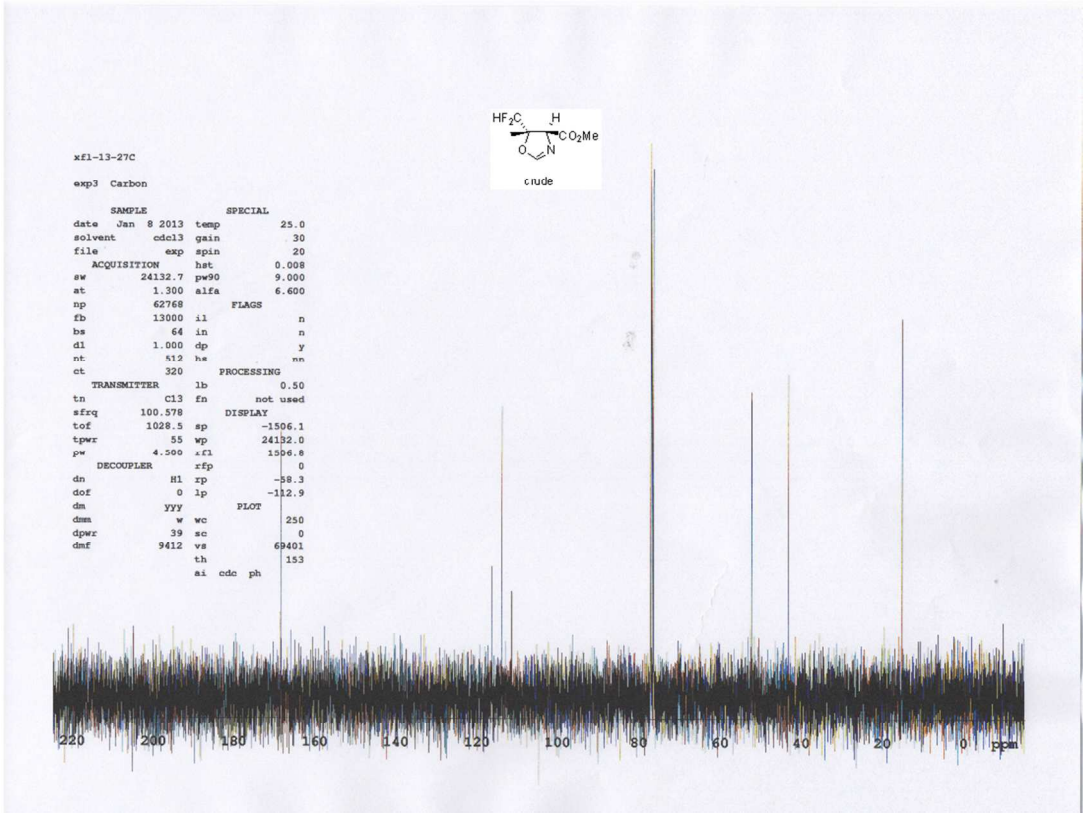


16

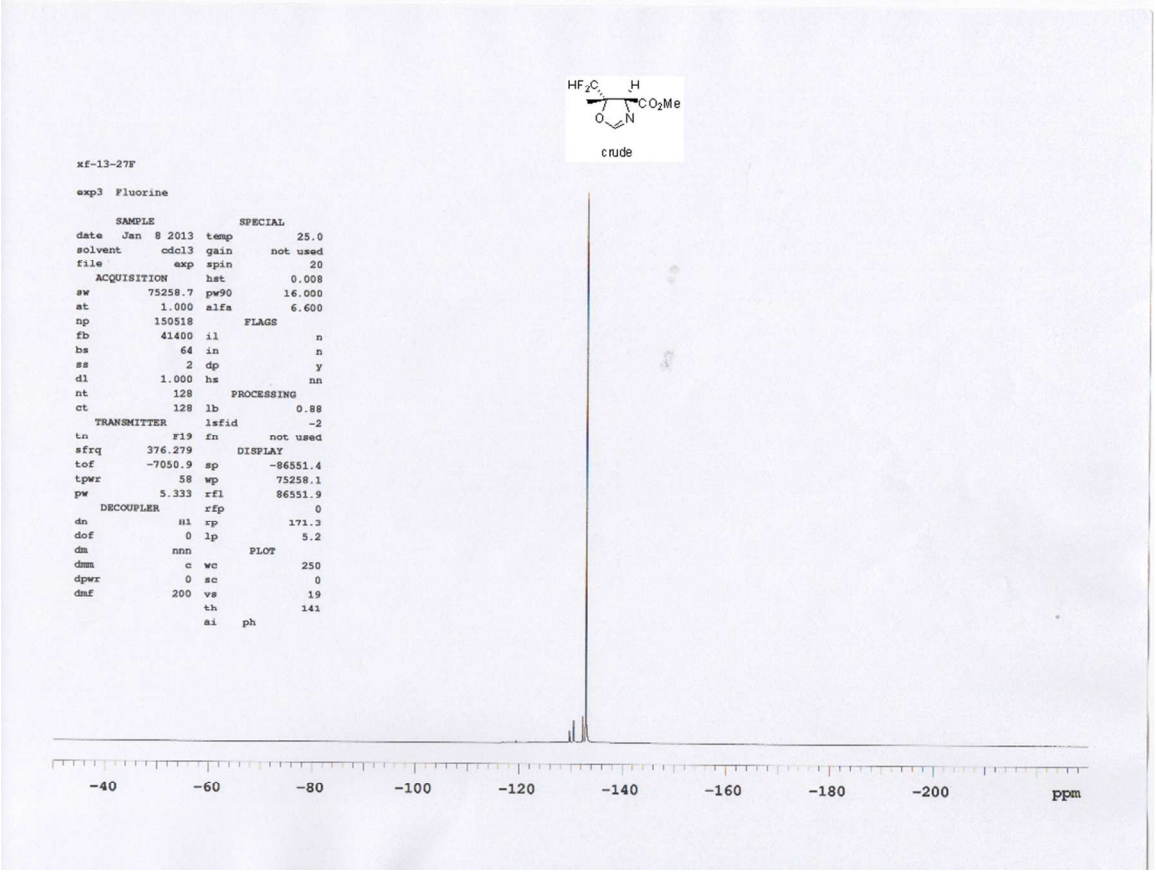
Mixture of diastereomers **19 a & b (9:1)** 1H NMR



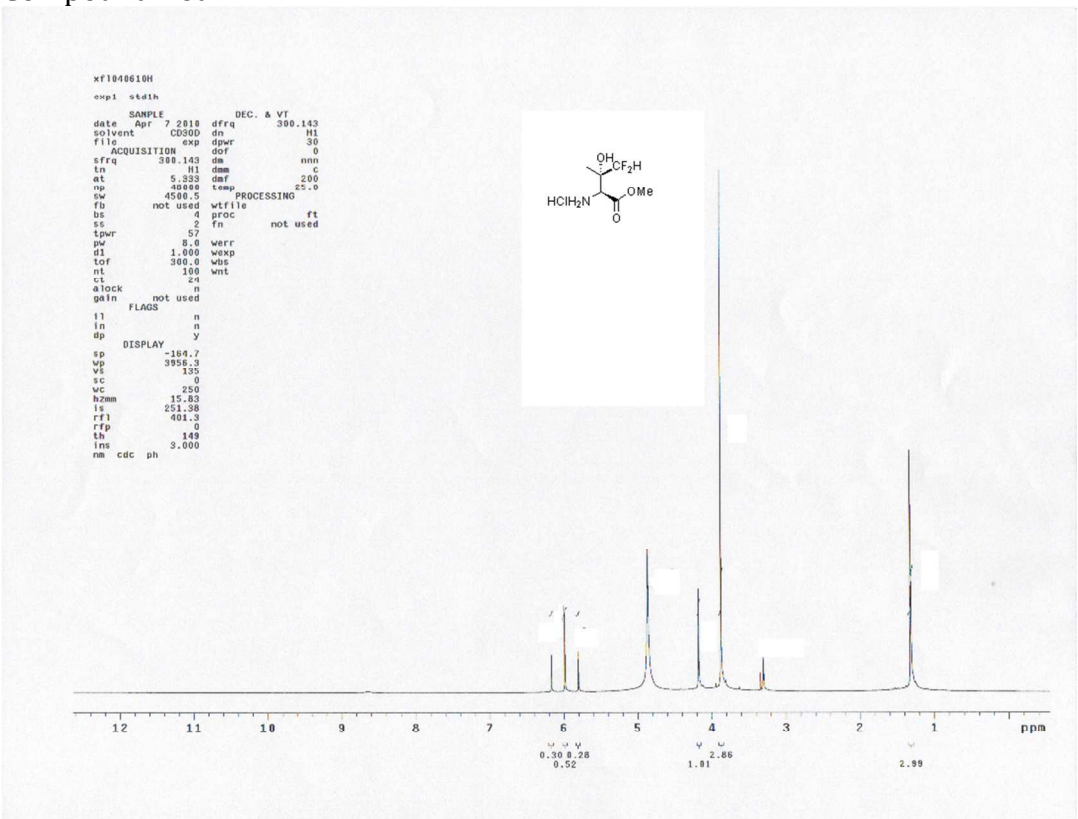
Mixture of diastereomers **19 a & b (9:1)** 13C NMR



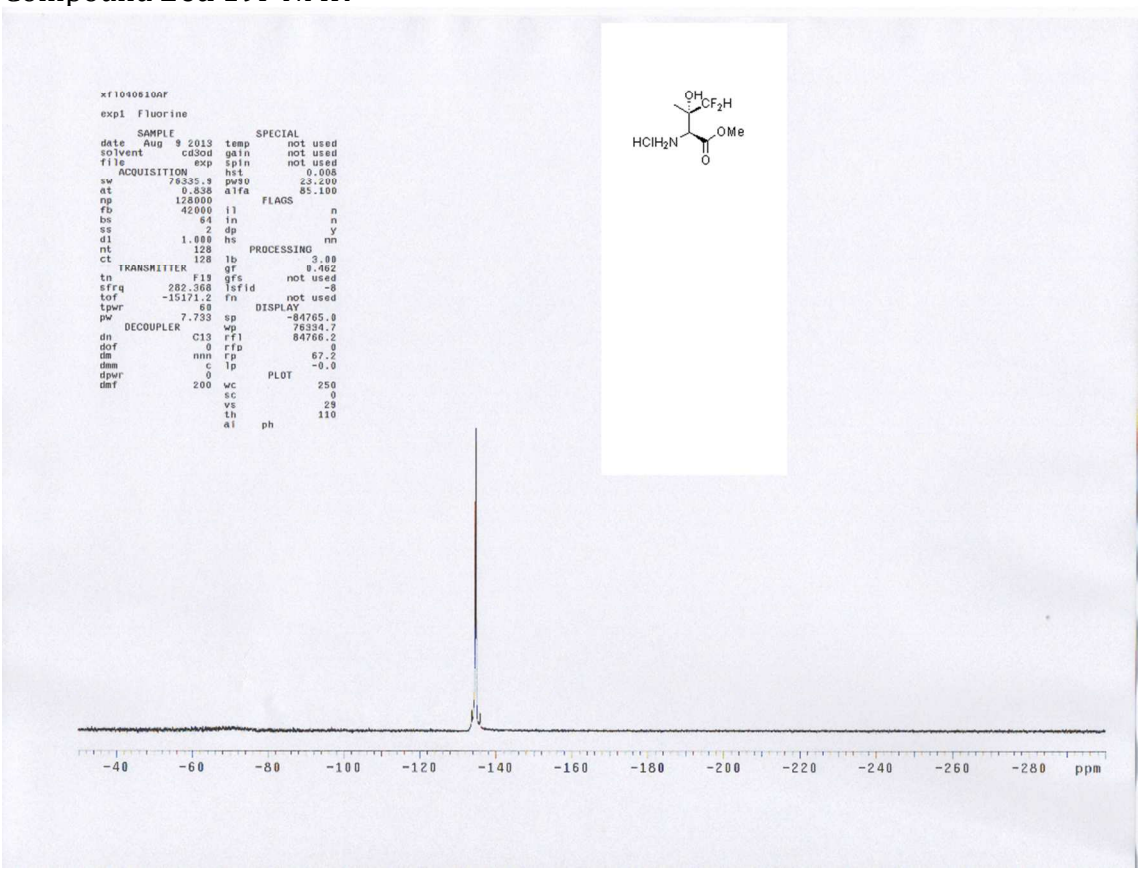
Mixture of diastereomers **19 a & b (9:1)** 19F NMR



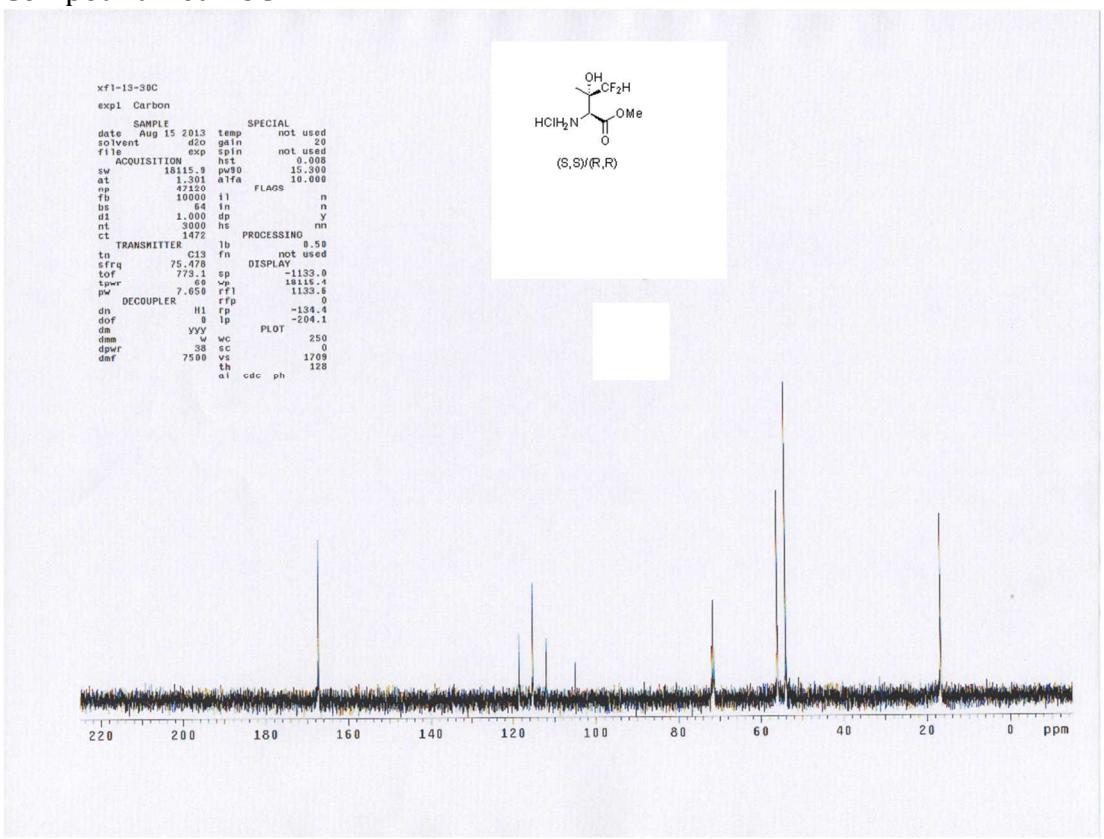
Compound **20a** 1H NMR



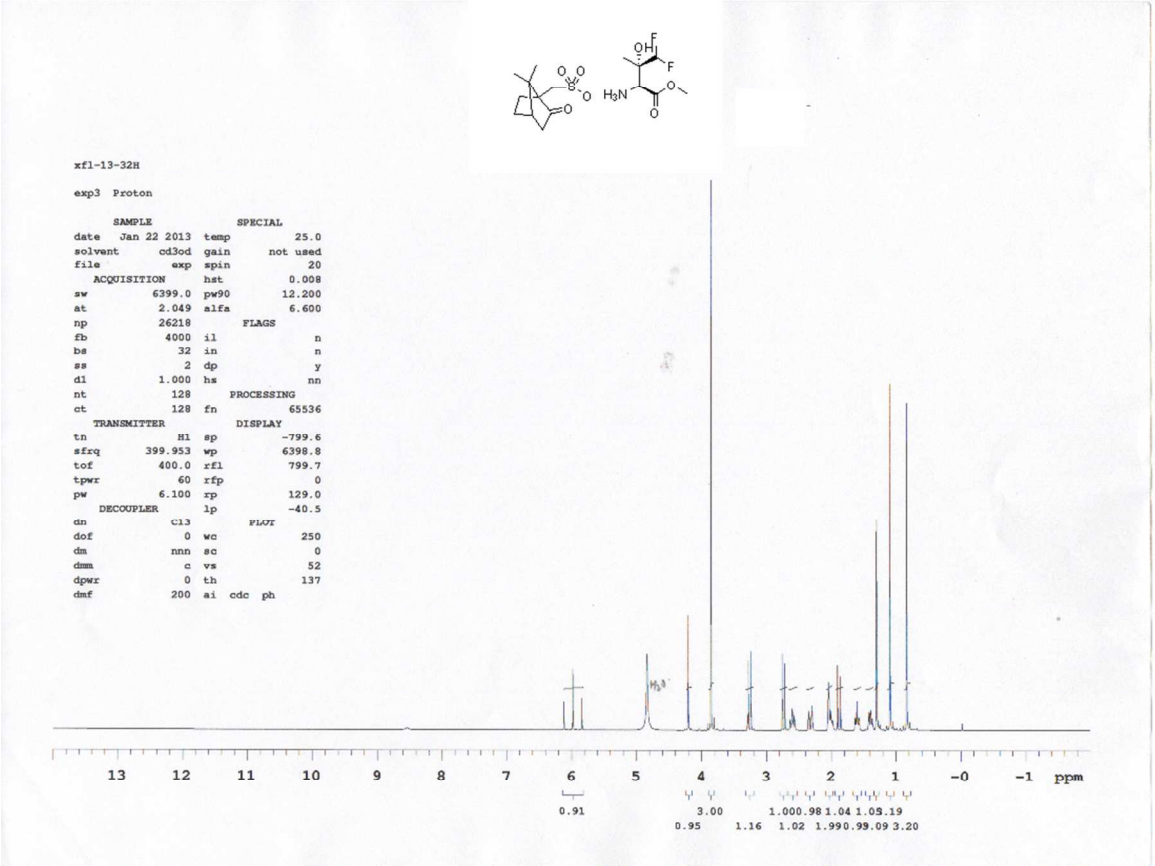
Compound **20a** 19F NMR



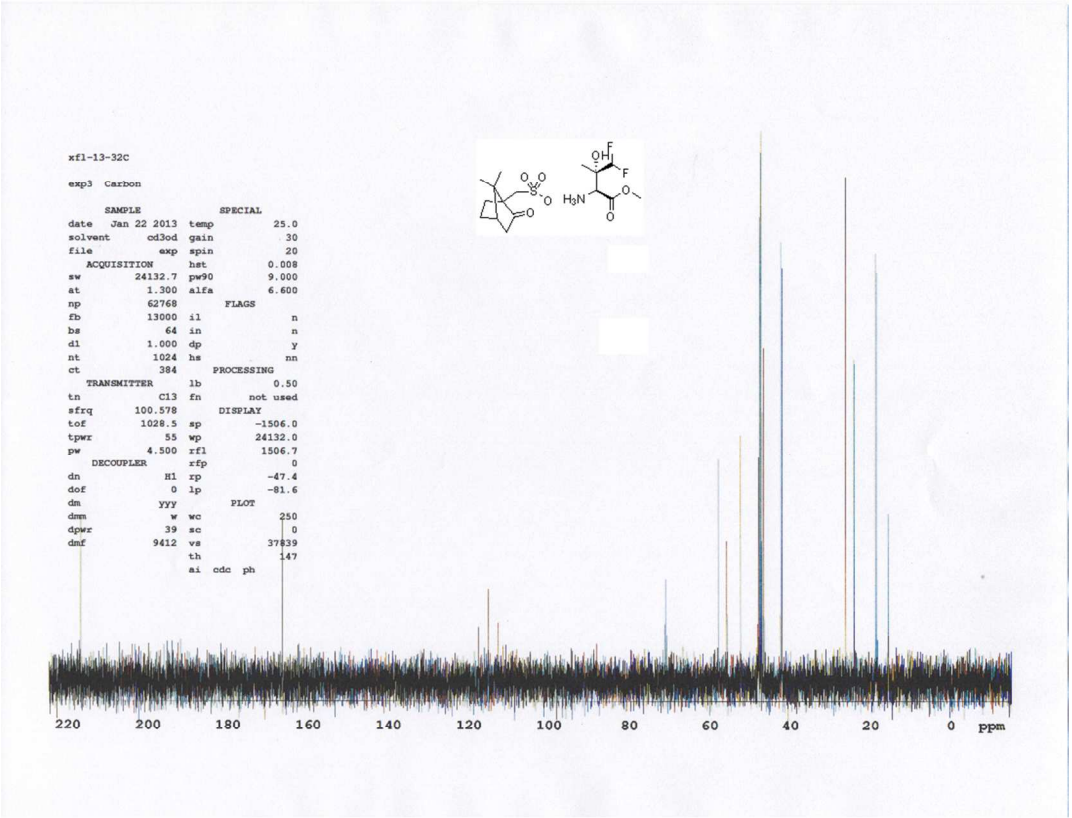
Compound **20a** 13C NMR



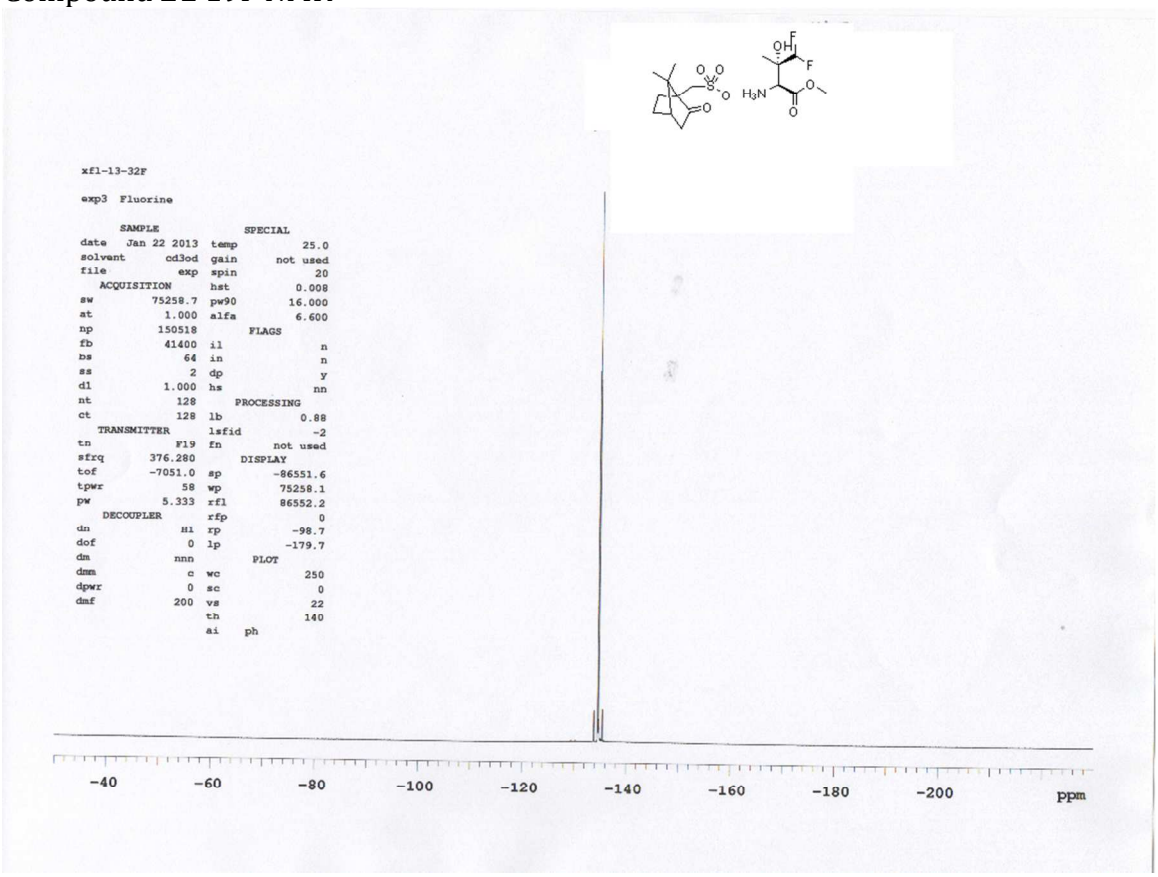
Compound **21** 1H NMR



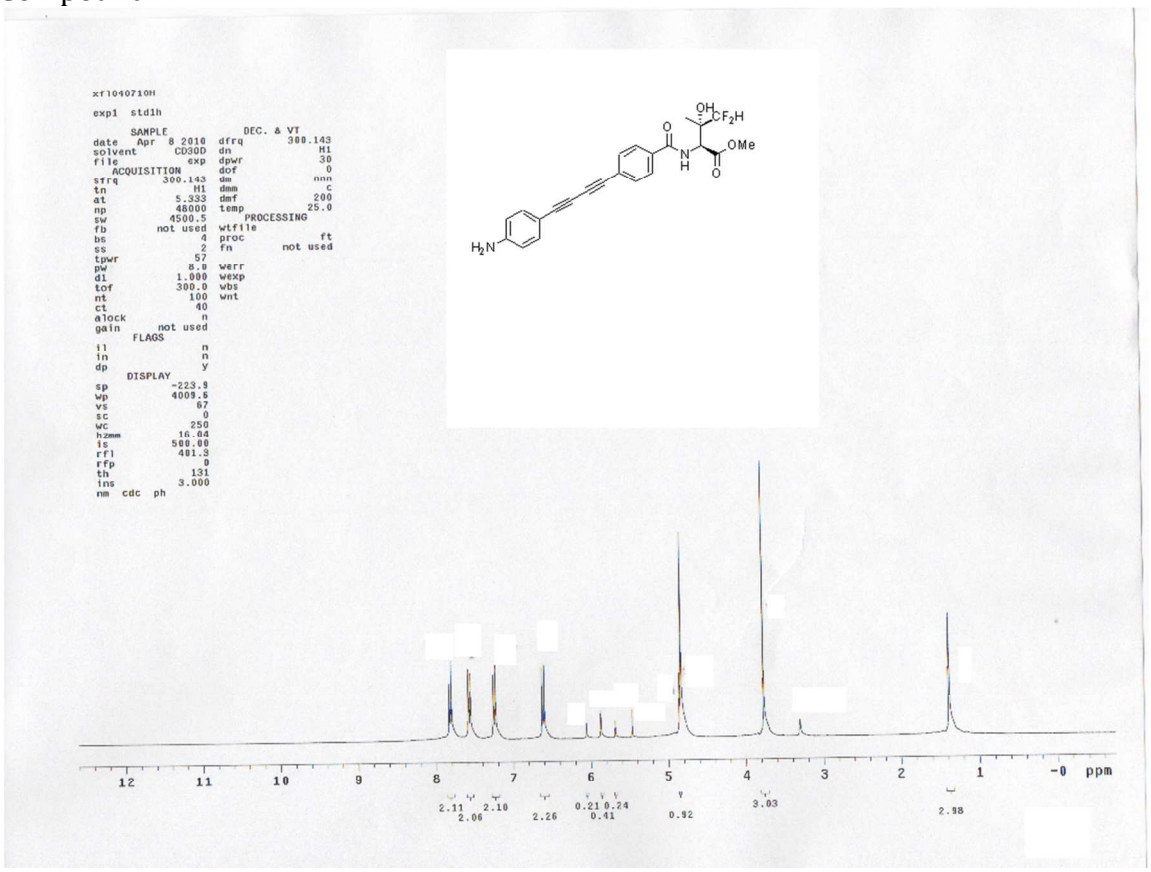
Compound **21** 13C NMR



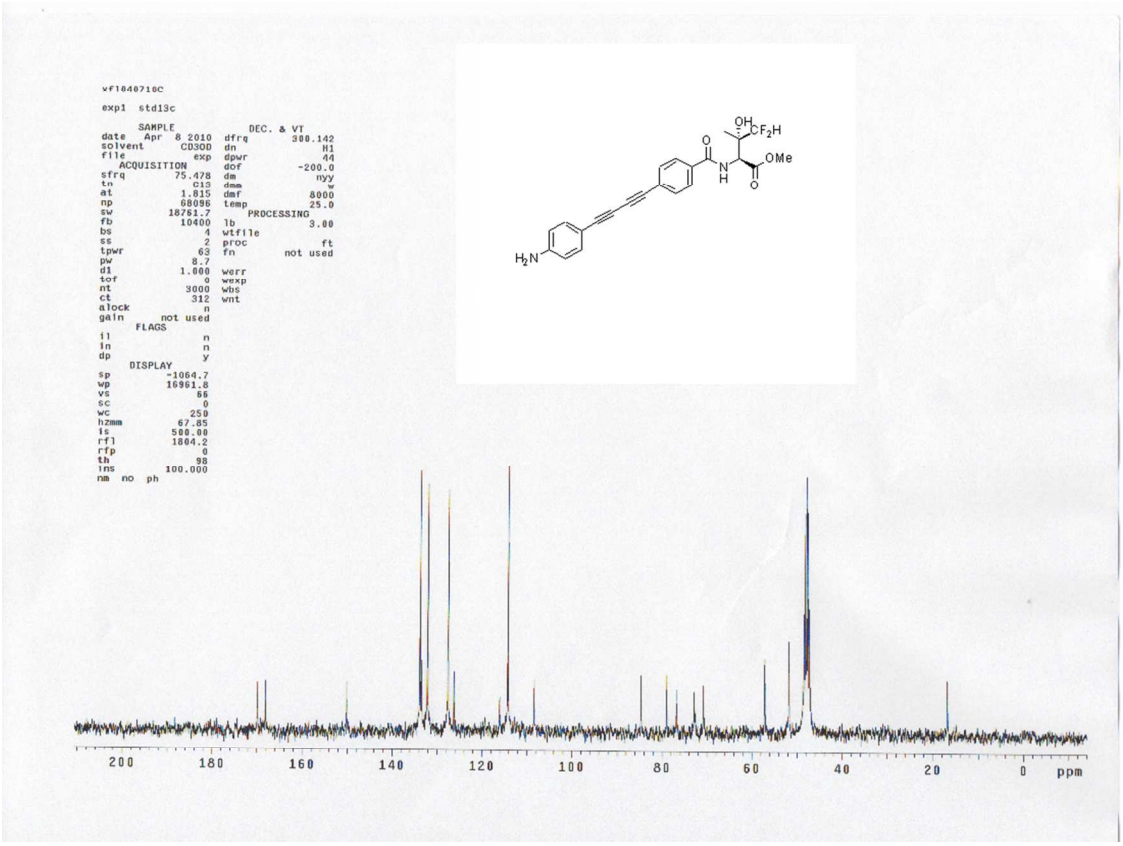
Compound **21** 19F NMR



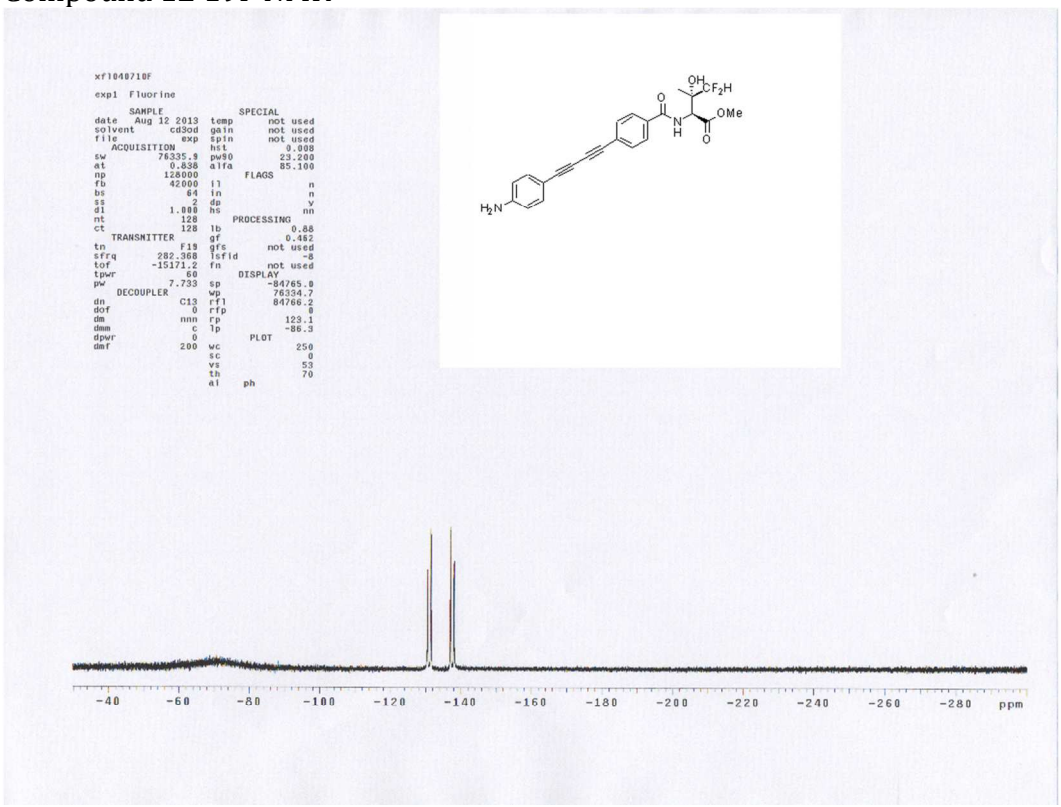
Compound **12** 1H NMR



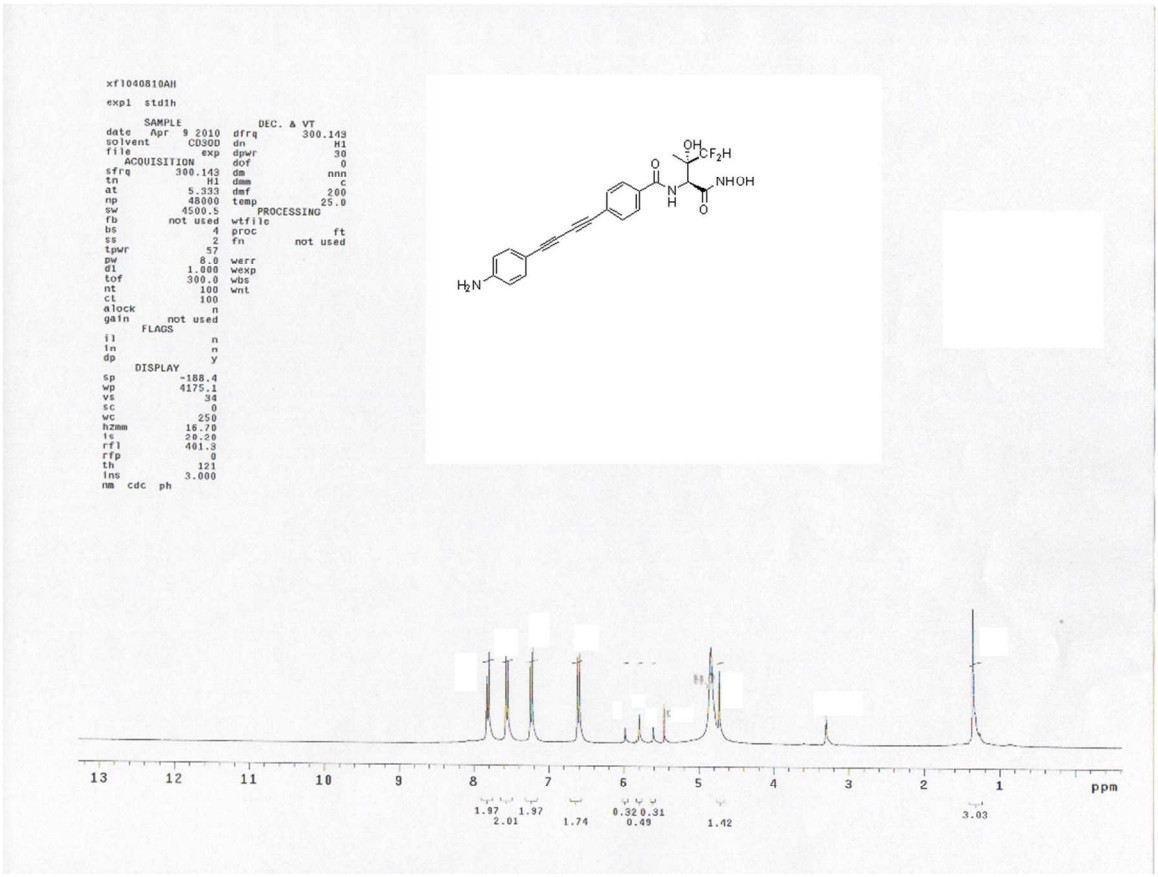
Compound 1**2** 13C NMR



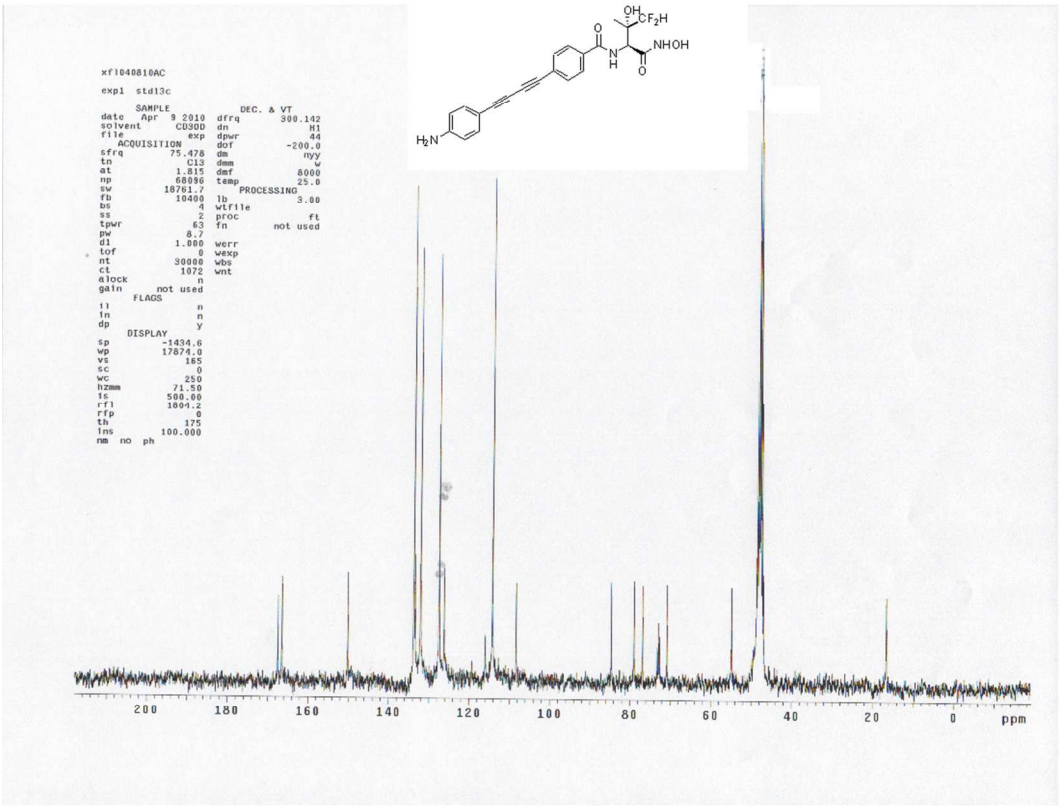
Compound 1**2** 19F NMR



LPC-058 1H NMR



LPC-058 13C NMR



LPC-058 19F NMR