Sustainable synthesis of enantiopure fluorolactam derivatives by a selective direct fluorination - amidase strategy

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SUPPORTING INFORMATION 4

X-ray Crystallography

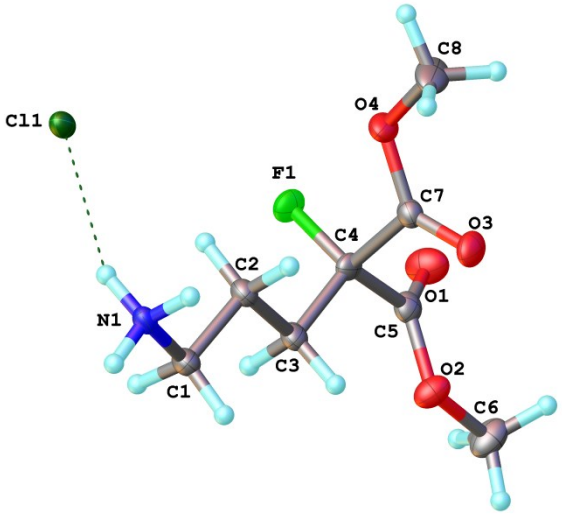
The X-ray single crystal data have been collected using λCuKα- (λ = 1.54178Å, compounds **2b** and **2c**) and λMoKα-radiation (λ =0.71073Å, compounds **8** and **9**) on a Bruker D8Venture (Photon100 CMOS detector, IμS-microsource, focusing mirrors) diffractometer. For compounds **4c** and **4d** the data were collected on an Agilent XCalibur (Sapphire-3 CCD detector, fine-focus sealed tube, graphite monochromator, λMoKα-radiation, λ =0.71073Å) diffractometer. The temperature 120.0(2)K was maintained by a Cryostream (Oxford Cryosystems) open-flow nitrogen cryostats. All structures were solved by direct method and refined by full-matrix least squares on F^2 for all data using Olex2 [1] and SHELXTL [2] software. All non-hydrogen atoms were refined anisotropically, hydrogen atoms in all structures except **4c** were refined isotropically, the hydrogen atoms in molecule **4c** were placed in the calculated positions and refined in riding mode. Crystal data and parameters of refinement are listed in SI.

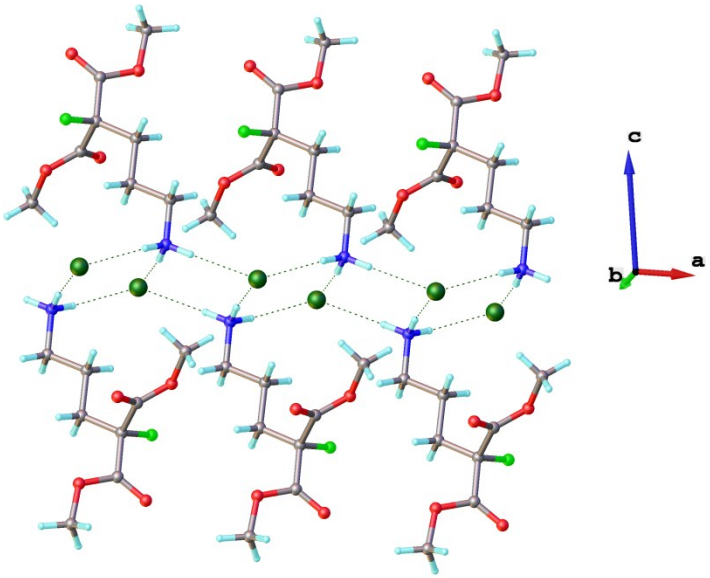
Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC-1401917-1401922.

[1] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339-341.

[2] G.M. Sheldrick, *Acta Cryst.,* 2008, **A64**, 112-122.

SI-4.1 Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt **4c**





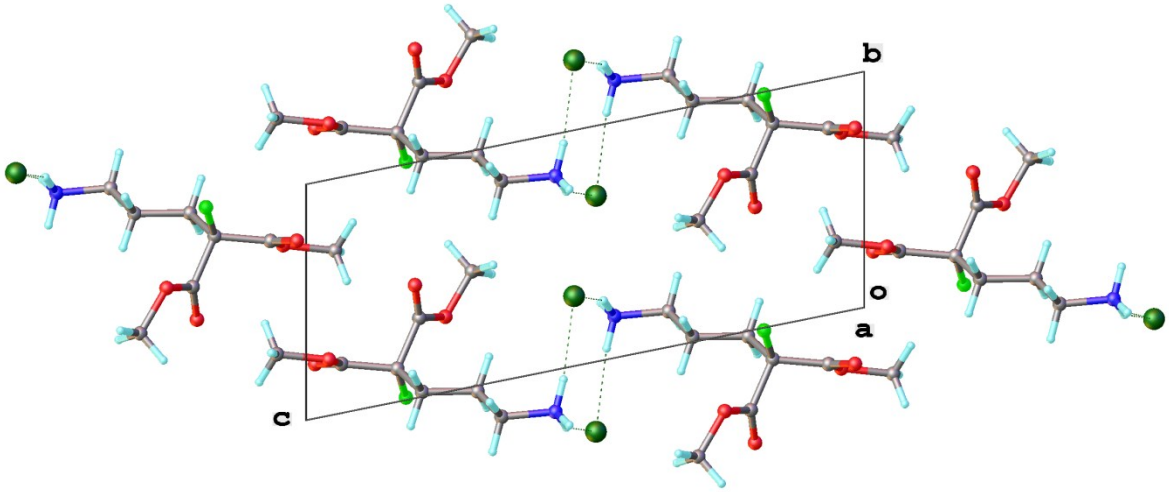


Table 1 Crystal data and structure refinement for 15srv065.	
Identification code	15srv065
Empirical formula	$C_8H_{15}FNO_4^+ \times Cl^-$
Formula weight	243.66
Temperature/K	120.0
Crystal system	triclinic
Space group	P-1
a/Å	5.8210(4)
b/Å	6.4875(5)
c/Å	15.7485(12)
α/°	100.738(7)
β/°	96.625(6)
γ/°	94.612(6)
Volume/Å^3	577.23(7)
Z	2
ρ_{calc}g/cm^3	1.402
μ/mm^{-1}	0.340
F(000)	256.0
Crystal size/mm^3	0.36 × 0.21 × 0.05
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.32 to 56
Index ranges	$-7 \leq h \leq 7$, $-8 \leq k \leq 8$, $-20 \leq l \leq 20$
Reflections collected	8623
Independent reflections	2785 [R_{int} = 0.0419, R_{sigma} = 0.0444]
Data/restraints/parameters	2785/0/139
Goodness-of-fit on F^2	1.165
Final R indexes [I>=2σ (I)]	R_1 = 0.0521, wR_2 = 0.1240
Final R indexes [all data]	R_1 = 0.0626, wR_2 = 0.1289
Largest diff. peak/hole / e Å^{-3}	0.56/-0.27

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 15srv065. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Cl1	7541.8(10)	12967.3(9)	5196.0(4)	20.11(16)
F1	6831(3)	9887(2)	1791.7(10)	24.8(4)
O1	5595(4)	7691(4)	162.9(14)	35.3(5)
O2	1871(3)	7620(3)	407.2(12)	25.6(4)
O3	3597(3)	5205(3)	1952.9(13)	27.3(4)
O4	7177(3)	6800(3)	2497.0(13)	28.6(5)
N1	2217(4)	11772(3)	4469.5(14)	19.5(4)
C1	1745(5)	11523(4)	3504.7(17)	22.7(5)
C2	3501(4)	10233(4)	3072.4(17)	20.3(5)
C3	2916(5)	9785(4)	2079.7(17)	20.6(5)
C4	4737(4)	8589(4)	1636.2(17)	18.8(5)
C5	4151(5)	7910(4)	635.4(17)	21.5(5)
C6	1074(6)	6948(5)	-520.2(18)	32.0(7)
C7	5104(4)	6631(4)	2030.0(16)	19.6(5)
C8	7546(7)	5106(5)	2970(2)	45.0(9)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 15srv065. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	16.0(3)	14.3(3)	30.2(3)	5.0(2)	2.8(2)	1.2(2)
F1	21.1(8)	21.0(8)	31.8(9)	8.6(6)	1.5(6)	-6.4(6)
O1	29.5(11)	48.4(13)	28.8(11)	5.6(10)	7.7(9)	7.1(10)
O2	22.7(10)	31.9(10)	21.5(10)	8.1(8)	0.0(7)	-3.8(8)
O3	31.4(11)	16.1(9)	33.1(11)	7.9(8)	-2.0(8)	-3.8(8)
O4	29.0(11)	17.2(9)	37.2(11)	7.1(8)	-8.9(9)	3.7(8)
N1	17.2(10)	13.9(9)	27.2(11)	2.0(8)	4.3(8)	2.9(8)
C1	21.9(13)	19.2(12)	26.3(13)	2.5(10)	0.4(10)	6(1)
C2	21.4(13)	16.7(11)	22.9(13)	3.8(10)	1.7(10)	5.3(10)
C3	22.9(13)	15.9(11)	23.2(13)	4.8(10)	0.7(10)	4.7(10)
C4	16.5(12)	13.9(11)	25.5(13)	6.4(10)	0.5(10)	-2.7(9)
C5	25.9(14)	15.9(11)	23.5(13)	6.6(10)	2.2(10)	1.6(10)

C6	34.8(16)	36.9(16)	21.6(14)	8.2(12)	-3.7(12)	-7.5(13)
C7	22.1(13)	16.2(11)	20.3(12)	2.6(9)	2.3(10)	3.5(10)
C8	55(2)	21.5(14)	53(2)	12.1(14)	-27.2(17)	6.9(14)

Table 4 Bond Lengths for 15srv065.

Atom	**Atom**	**Length/Å**		**Atom**	**Atom**	**Length/Å**
F1	C4	1.394(3)		N1	C1	1.488(3)
O1	C5	1.185(3)		C1	C2	1.515(3)
O2	C5	1.323(3)		C2	C3	1.528(4)
O2	C6	1.453(3)		C3	C4	1.521(4)
O3	C7	1.202(3)		C4	C5	1.545(4)
O4	C7	1.324(3)		C4	C7	1.533(3)
O4	C8	1.454(3)				

Table 5 Bond Angles for 15srv065.

Atom	**Atom**	**Atom**	**Angle/°**		**Atom**	**Atom**	**Atom**	**Angle/°**
C5	O2	C6	116.1(2)		C3	C4	C7	109.2(2)
C7	O4	C8	114.7(2)		C7	C4	C5	109.1(2)
N1	C1	C2	110.3(2)		O1	C5	O2	126.8(3)
C1	C2	C3	111.2(2)		O1	C5	C4	122.9(3)
C4	C3	C2	111.7(2)		O2	C5	C4	110.3(2)
F1	C4	C3	108.8(2)		O3	C7	O4	125.8(2)
F1	C4	C5	106.4(2)		O3	C7	C4	122.2(2)
F1	C4	C7	108.5(2)		O4	C7	C4	111.8(2)
C3	C4	C5	114.6(2)					

Table 6 Hydrogen Bonds for 15srv065.

D	**H**	**A**	**d(D-H)/Å**	**d(H-A)/Å**	**d(D-A)/Å**	**D-H-A/°**
N1	H1A	Cl1[1]	0.91	2.32	3.226(2)	172.2
N1	H1B	Cl1[2]	0.91	2.30	3.169(2)	158.9
N1	H1C	Cl1	0.91	2.31	3.160(2)	154.7

[1]1-X,2-Y,1-Z; [2]-1+X,+Y,+Z

Table 7 Torsion Angles for 15srv065.										
A	**B**	**C**	**D**	**Angle/°**		**A**	**B**	**C**	**D**	**Angle/°**
F1	C4	C5	O1	31.3(3)		C3	C4	C7	O3	65.0(3)
F1	C4	C5	O2	-148.9(2)		C3	C4	C7	O4	-110.8(2)
F1	C4	C7	O3	-176.5(2)		C5	C4	C7	O3	-60.9(3)
F1	C4	C7	O4	7.7(3)		C5	C4	C7	O4	123.2(2)
N1	C1	C2	C3	174.8(2)		C6	O2	C5	O1	0.5(4)
C1	C2	C3	C4	177.0(2)		C6	O2	C5	C4	-179.3(2)
C2	C3	C4	F1	-66.2(3)		C7	C4	C5	O1	-85.7(3)
C2	C3	C4	C5	174.9(2)		C7	C4	C5	O2	94.1(2)
C2	C3	C4	C7	52.2(3)		C8	O4	C7	O3	-2.2(4)
C3	C4	C5	O1	151.6(3)		C8	O4	C7	C4	173.4(2)
C3	C4	C5	O2	-28.6(3)						

Table 8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 15srv065.				
Atom	***x***	***y***	***z***	**U(eq)**
H1A	2229	10478	4613	23
H1B	1086	12461	4719	23
H1C	3623	12530	4666	23
H1D	1831	12930	3345	27
H1E	157	10812	3295	27
H2A	3518	8882	3278	24
H2B	5072	11009	3242	24
H3A	1380	8946	1910	25
H3B	2815	11136	1878	25
H6A	1722	7978	-835	48
H6B	-628	6848	-620	48
H6C	1590	5566	-731	48
H8A	7465	3767	2554	68
H8B	6342	5019	3352	68

H8C	9080	5391	3322	68

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:

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1.                                Fixed                                Uiso
 At                    1.2                    times                     of:
  All        C(H,H)         groups,         All        N(H,H,H)         groups
 At                    1.5                    times                     of:
  All                             C(H,H,H)                             groups
2.a     Secondary     CH2     refined     with     riding     coordinates:
 C1(H1D,H1E),                    C2(H2A,H2B),                    C3(H3A,H3B)
2.b      Idealised      Me      refined      as      rotating      group:
 N1(H1A,H1B,H1C), C6(H6A,H6B,H6C), C8(H8A,H8B,H8C)
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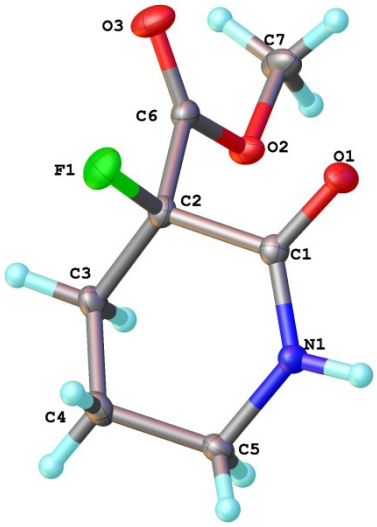
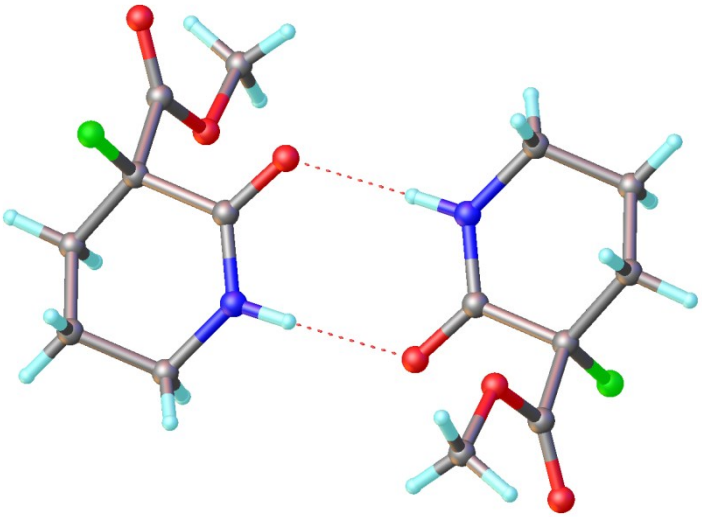
SI-4.2 Racemic methyl 3-fluoro-2-oxopiperidine-3-carboxylate **4d**





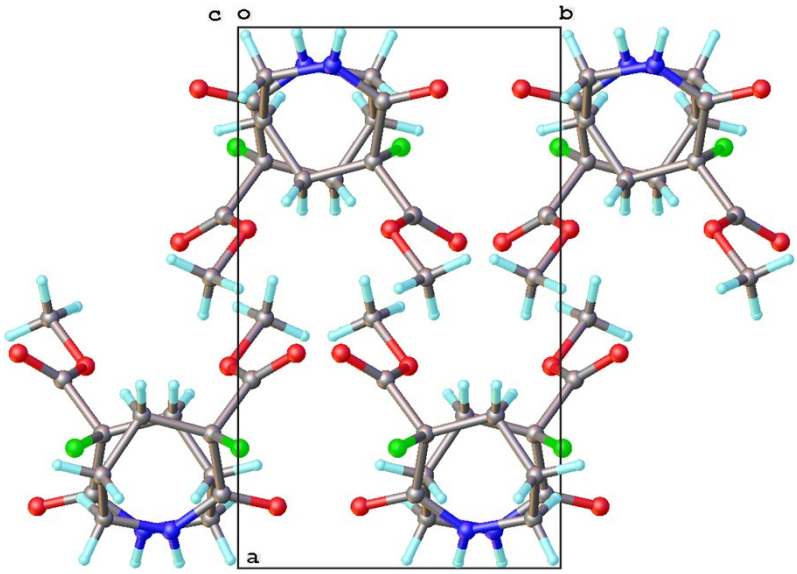


Table 1 Crystal data and structure refinement for 14srv042.	
Identification code	14srv042
Empirical formula	$C_7H_{10}NO_3F$
Formula weight	175.16
Temperature/K	120.0
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.2560(4)
b/Å	6.72544(17)
c/Å	10.4787(4)
α/°	90.00
β/°	113.193(4)
γ/°	90.00
Volume/Å^3	793.93(4)
Z	4
ρ_{calc}mg/mm^3	1.465
m/mm^{-1}	0.129
F(000)	368.0
Crystal size/mm^3	0.31 × 0.26 × 0.17
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection	7.06 to 59.98°
Index ranges	$-17 \leq h \leq 17$, $-9 \leq k \leq 9$, $-14 \leq l \leq 14$
Reflections collected	14038
Independent reflections	2324 [R_{int} = 0.0385, R_{sigma} = 0.0236]
Data/restraints/parameters	2324/0/149
Goodness-of-fit on F^2	1.028
Final R indexes [I>=2σ (I)]	R_1 = 0.0346, wR_2 = 0.0902
Final R indexes [all data]	R_1 = 0.0410, wR_2 = 0.0942
Largest diff. peak/hole / e Å^{-3}	0.47/-0.23

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 14srv042. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
F1	7779.8(6)	10055.9(10)	7218.2(6)	23.13(16)
O1	8858.9(7)	11213.8(10)	5334.4(8)	20.62(17)
O2	6266.6(6)	9718.6(10)	3585.0(7)	17.04(16)
O3	6028.8(7)	11804.4(12)	5143.8(8)	25.13(19)
N1	9301.7(7)	7922.9(12)	5640.6(9)	15.82(17)
C1	8632.1(8)	9499.9(14)	5596(1)	14.08(18)
C2	7518.3(8)	9193.5(14)	5912.6(9)	14.46(18)
C3	7177.6(9)	7025.3(15)	5968.8(11)	19.2(2)
C4	8284.1(9)	5778.4(16)	6731.3(11)	18.9(2)
C5	9075.2(9)	5851.9(14)	5928.8(11)	17.4(2)
C6	6513.9(8)	10424.6(14)	4859.7(10)	15.09(19)
C7	5379.2(10)	10827.8(18)	2466.8(11)	23.5(2)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 14srv042. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
F1	24.4(3)	31.2(3)	14.1(3)	-5.1(2)	7.9(2)	0.9(3)
O1	20.5(4)	12.5(3)	32.8(4)	0.6(3)	14.7(3)	-1.6(3)
O2	18.7(3)	16.9(3)	14.5(3)	1.1(2)	5.4(3)	5.5(2)
O3	26.9(4)	24.5(4)	24.9(4)	-3.6(3)	11.2(3)	8.7(3)
N1	14.9(4)	13.2(4)	21.3(4)	1.1(3)	9.2(3)	-0.3(3)
C1	13.2(4)	14.5(4)	14.1(4)	-1.4(3)	4.9(3)	-2.2(3)
C2	14.6(4)	16.3(4)	13.2(4)	-0.7(3)	6.2(3)	-1.1(3)
C3	16.2(4)	18.0(4)	24.4(5)	5.6(4)	9.1(4)	-1.5(3)
C4	20.1(5)	18.1(4)	18.6(5)	6.0(4)	7.7(4)	0.4(4)
C5	18.9(4)	12.9(4)	20.7(5)	2.9(3)	8.2(4)	0.9(3)
C6	14.8(4)	14.6(4)	17.5(4)	-0.1(3)	8.1(3)	-0.7(3)

C7	25.7(5)	25.5(5)	18.0(5)	6.0(4)	7.4(4)	11.5(4)

Table 4 Bond Lengths for 14srv042.

Atom	**Atom**	**Length/Å**		**Atom**	**Atom**	**Length/Å**
F1	C2	1.4020(11)		N1	C5	1.4746(12)
O1	C1	1.2414(12)		C1	C2	1.5403(13)
O2	C6	1.3352(12)		C2	C3	1.5243(13)
O2	C7	1.4521(12)		C2	C6	1.5325(13)
O3	C6	1.2011(12)		C3	C4	1.5255(14)
N1	C1	1.3305(12)		C4	C5	1.5139(15)

Table 5 Bond Angles for 14srv042.

Atom	**Atom**	**Atom**	**Angle/°**		**Atom**	**Atom**	**Atom**	**Angle/°**
C6	O2	C7	115.30(8)		C3	C2	C6	112.96(8)
C1	N1	C5	126.65(8)		C6	C2	C1	107.54(8)
O1	C1	N1	124.00(9)		C2	C3	C4	110.22(8)
O1	C1	C2	117.79(8)		C5	C4	C3	108.83(8)
N1	C1	C2	118.19(8)		N1	C5	C4	110.97(8)
F1	C2	C1	105.87(7)		O2	C6	C2	109.25(8)
F1	C2	C3	108.60(8)		O3	C6	O2	125.68(9)
F1	C2	C6	106.80(8)		O3	C6	C2	125.08(9)
C3	C2	C1	114.57(8)					

Table 6 Hydrogen Bonds for 14srv042.

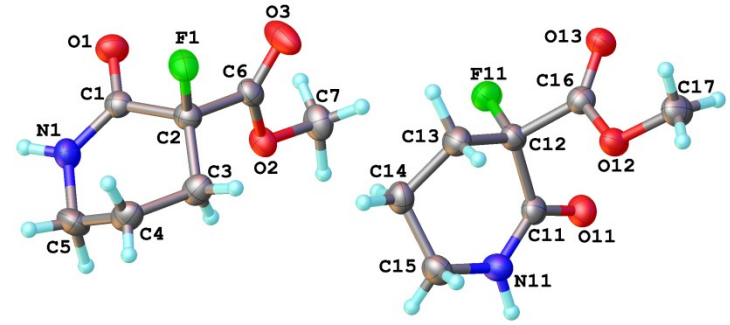
D	**H**	**A**	**d(D-H)/Å**	**d(H-A)/Å**	**d(D-A)/Å**	**D-H-A/°**
N1	H1	O1[1]	0.881(16)	1.998(16)	2.8770(11)	175.7(14)

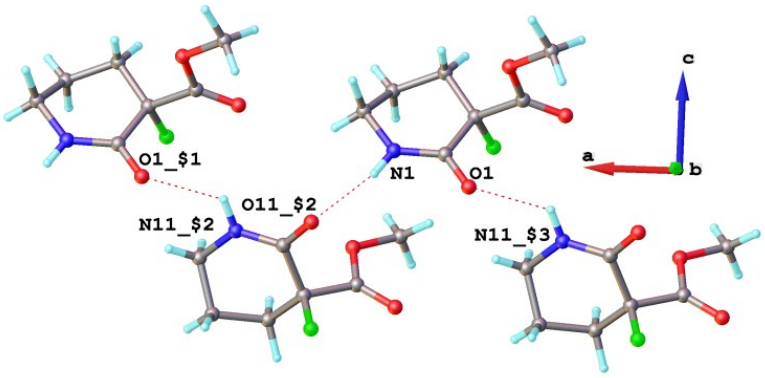
[1]2-X,2-Y,1-Z

Table 7 Torsion Angles for 14srv042.										
A	**B**	**C**	**D**	**Angle/°**		**A**	**B**	**C**	**D**	**Angle/°**
F1	C2	C3	C4	-76.45(10)		C1	C2	C6	O2	63.90(10)
F1	C2	C6	O2	177.17(7)		C1	C2	C6	O3	-116.16(11)
F1	C2	C6	O3	-2.89(13)		C2	C3	C4	C5	-62.56(11)
O1	C1	C2	F1	-70.70(11)		C3	C2	C6	O2	-63.50(10)
O1	C1	C2	C3	169.66(9)		C3	C2	C6	O3	116.43(11)
O1	C1	C2	C6	43.19(11)		C3	C4	C5	N1	52.18(11)
N1	C1	C2	F1	108.25(9)		C5	N1	C1	O1	-179.27(9)
N1	C1	C2	C3	-11.39(12)		C5	N1	C1	C2	1.85(14)
N1	C1	C2	C6	-137.85(9)		C6	C2	C3	C4	165.27(8)
C1	N1	C5	C4	-23.07(14)		C7	O2	C6	O3	3.87(15)
C1	C2	C3	C4	41.65(11)		C7	O2	C6	C2	-176.19(8)

Table 8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 14srv042.				
Atom	***x***	***y***	***z***	**U(eq)**
H1	9892(14)	8180(20)	5387(15)	28(4)
H3A	6781(13)	6510(20)	5013(15)	23(3)
H3B	6619(14)	6990(20)	6431(16)	31(4)
H4A	8094(13)	4420(20)	6855(15)	25(3)
H4B	8707(13)	6300(20)	7655(16)	27(4)
H5A	8708(13)	5150(20)	5032(15)	23(3)
H5B	9843(14)	5240(20)	6432(16)	26(4)
H7A	4688(14)	11070(20)	2659(15)	30(4)
H7B	5707(15)	12050(30)	2357(17)	37(4)
H7C	5167(15)	9990(20)	1637(17)	33(4)

SI-4.3 (*S*)-methyl 3-fluoro-2-oxopiperidine-3-carboxylate **2b**





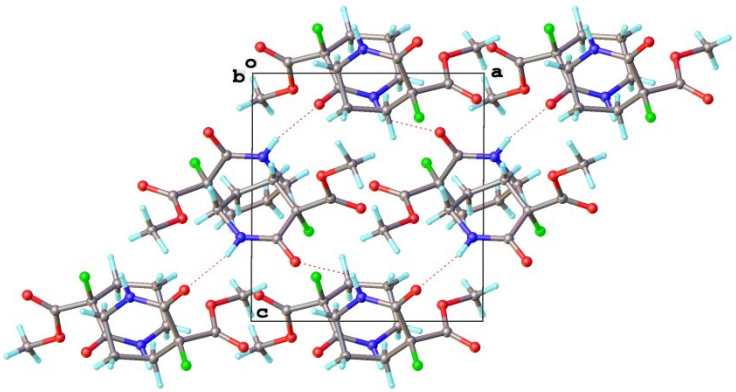


Table 1 Crystal data and structure refinement for 14srv257	
Identification code	14srv257
Empirical formula	$C_7H_{10}FNO_3$
Formula weight	175.16
Temperature/K	120.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.5224(4)
b/Å	10.3050(5)
c/Å	9.1442(4)
α/°	90.00
β/°	90.3404(11)
γ/°	90.00
Volume/Å^3	803.06(6)
Z	4
ρ_{calc}g/cm^3	1.449
μ/mm^{-1}	1.105
F(000)	368.0
Crystal size/mm^3	0.53 × 0.35 × 0.29
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	9.68 to 144.92
Index ranges	$-9 \le h \le 9$, $-12 \le k \le 12$, $-11 \le l \le 9$
Reflections collected	7399
Independent reflections	2833 [R_{int} = 0.0612, R_{sigma} = 0.0576]
Data/restraints/parameters	2833/1/297
Goodness-of-fit on F^2	1.005
Final R indexes [I>=2σ (I)]	R_1 = 0.0547, wR_2 = 0.1520
Final R indexes [all data]	R_1 = 0.0547, wR_2 = 0.1520
Largest diff. peak/hole / e Å^{-3}	0.24/-0.24
Flack parameter	0.1(2)
Hooft parameter	0.02(7)

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 14srv257. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.				
Atom	***x***	***y***	***z***	**U(eq)**
F1	7533(2)	4806.2(18)	3623(2)	36.2(4)
O1	8108(3)	7298(2)	2396(2)	37.7(5)
O2	6992(2)	7552(2)	5858(2)	30.9(5)
O3	5292(3)	6351(3)	4548(3)	51.6(7)
N1	10467(3)	6772(3)	3379(3)	36.2(6)
C1	8905(4)	6734(3)	3319(3)	27.9(6)
C2	8069(3)	5869(3)	4447(3)	29.9(6)
C3	9074(4)	5363(4)	5693(4)	35.6(7)
C4	10664(4)	4980(4)	5137(4)	38.8(7)
C5	11465(4)	6158(4)	4497(4)	44.5(9)
C6	6594(3)	6595(3)	4946(3)	29.1(6)
C7	5692(4)	8382(3)	6321(4)	39.3(8)
F11	2797(2)	6620.1(19)	8214.7(19)	37.3(4)
O11	2890(3)	7040(2)	11254(2)	36.4(5)
O12	1743(2)	4135(2)	10648(2)	33.2(5)
O13	326(3)	5222(2)	8952(2)	36.6(5)
N11	5238(3)	6050(3)	10965(3)	34.0(6)
C11	3759(3)	6296(3)	10590(3)	28.4(6)
C12	3111(3)	5620(3)	9204(3)	28.0(6)
C13	4223(4)	4644(4)	8494(4)	36.0(7)
C14	5908(4)	5122(3)	8589(3)	35.3(7)
C15	6367(4)	5246(4)	10182(4)	36.0(7)
C16	1539(4)	4991(3)	9564(3)	30.2(6)
C17	352(4)	3397(4)	11030(4)	38.9(8)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 14srv257. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.						
Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
F1	35.3(10)	33(1)	40.3(9)	-8.5(8)	4.2(7)	-4.8(7)
O1	37.3(12)	39.1(13)	36.6(11)	5.8(10)	-5.3(9)	0.2(10)
O2	25.9(10)	28.6(11)	38.2(11)	-3.6(9)	3.1(8)	1.0(8)
O3	27.9(13)	60.1(17)	66.7(17)	-28.0(14)	-1.7(10)	2.5(11)
N1	29.9(14)	44.1(16)	34.5(13)	3.2(12)	4.3(11)	-3.4(11)
C1	29.4(15)	26.9(14)	27.2(13)	-3.4(12)	-0.1(10)	2.0(11)
C2	28.7(15)	29.8(15)	31.1(15)	-2.2(12)	-0.3(11)	1.4(12)
C3	39.5(18)	34.9(18)	32.5(16)	0.7(14)	1.3(13)	9.5(13)
C4	38.2(18)	44.0(19)	34.0(16)	1.7(16)	-2.7(13)	14.0(15)
C5	24.8(16)	63(2)	45.4(18)	-0.4(18)	-6.9(13)	1.3(15)
C6	24.0(14)	29.7(14)	33.5(14)	2.3(12)	1.2(10)	-3.6(11)
C7	35.3(17)	34.1(17)	49(2)	-3.9(16)	8.3(14)	5.1(13)
F11	37.5(10)	41.5(10)	32.9(9)	8.4(8)	-1.0(7)	-2.8(8)
O11	34.1(11)	37.3(12)	37.7(11)	-5.1(9)	4.0(9)	0.3(9)
O12	29.9(11)	36.2(12)	33.7(11)	6.8(9)	-1.9(8)	-3.3(9)
O13	28.1(12)	44.9(13)	36.8(11)	3.5(10)	-2.3(9)	0.1(9)
N11	30.8(14)	37.7(15)	33.4(14)	-4.4(11)	-3.2(10)	2.9(11)
C11	28.8(14)	27.3(14)	29.1(14)	1.7(11)	3.9(11)	-3.3(11)
C12	25.3(15)	30.1(15)	28.8(14)	3.4(11)	0.6(10)	0.8(11)
C13	34.4(17)	41.6(18)	32.2(15)	-5.1(14)	1.3(11)	1.5(13)
C14	30.9(17)	38.6(17)	36.6(16)	2.2(14)	6.7(12)	3.6(13)
C15	28.9(17)	37.4(19)	41.8(18)	1.4(15)	-1.1(12)	3.9(13)
C16	31.9(15)	28.9(15)	29.9(14)	-0.8(12)	-0.4(11)	-1.4(11)
C17	37.9(19)	37.0(18)	41.8(19)	7.3(15)	-0.2(14)	-9.0(15)

Table 4 Bond Lengths for 14srv257.						
Atom	**Atom**	**Length/Å**		**Atom**	**Atom**	**Length/Å**
F1	C2	1.404(4)		F11	C12	1.396(3)
O1	C1	1.226(4)		O11	C11	1.229(4)
O2	C6	1.333(4)		O12	C16	1.337(4)
O2	C7	1.465(4)		O12	C17	1.454(4)
O3	C6	1.193(4)		O13	C16	1.196(4)
N1	C1	1.333(4)		N11	C11	1.328(4)
N1	C5	1.469(5)		N11	C15	1.461(4)
C1	C2	1.541(4)		C11	C12	1.546(4)
C2	C3	1.514(4)		C12	C13	1.529(4)
C2	C6	1.535(4)		C12	C16	1.526(4)
C3	C4	1.503(5)		C13	C14	1.521(5)
C4	C5	1.513(6)		C14	C15	1.511(5)

Table 5 Bond Angles for 14srv257.								
Atom	**Atom**	**Atom**	**Angle/°**		**Atom**	**Atom**	**Atom**	**Angle/°**
C6	O2	C7	115.0(2)		C16	O12	C17	114.9(2)
C1	N1	C5	126.2(3)		C11	N11	C15	127.4(3)
O1	C1	N1	124.3(3)		O11	C11	N11	124.4(3)
O1	C1	C2	118.6(3)		O11	C11	C12	118.2(3)
N1	C1	C2	117.1(3)		N11	C11	C12	117.4(3)
F1	C2	C1	104.1(2)		F11	C12	C11	105.3(2)
F1	C2	C3	108.4(3)		F11	C12	C13	109.1(2)
F1	C2	C6	106.0(2)		F11	C12	C16	106.7(2)
C3	C2	C1	116.2(3)		C13	C12	C11	115.2(2)
C3	C2	C6	113.8(2)		C16	C12	C11	108.9(2)
C6	C2	C1	107.4(2)		C16	C12	C13	111.1(3)
C4	C3	C2	110.1(3)		C14	C13	C12	110.5(3)
C3	C4	C5	109.2(3)		C15	C14	C13	108.7(3)
N1	C5	C4	110.8(3)		N11	C15	C14	110.7(3)
O2	C6	C2	109.9(2)		O12	C16	C12	109.2(2)
O3	C6	O2	125.4(3)		O13	C16	O12	125.9(3)
O3	C6	C2	124.6(3)		O13	C16	C12	124.9(3)

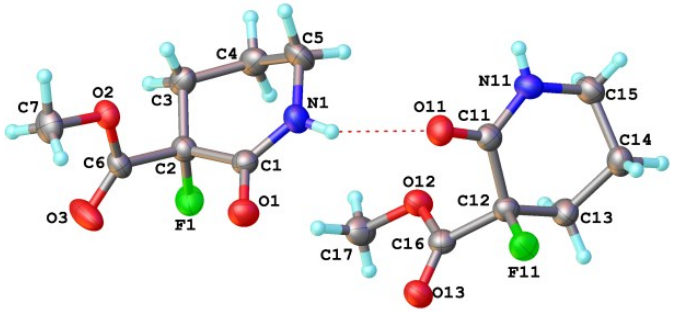
Table 6 Hydrogen Bonds for 14srv257.						
D	**H**	**A**	**d(D-H)/Å**	**d(H-A)/Å**	**d(D-A)/Å**	**D-H-A/°**
N1	H1	O11[1]	0.86(5)	2.08(4)	2.857(4)	150(4)
N11	H11	O1[2]	0.93(5)	2.37(4)	3.051(3)	130(3)

[1]1+X,+Y,-1+Z; [2]+X,+Y,1+Z

Table 7 Torsion Angles for 14srv257.										
A	**B**	**C**	**D**	**Angle/°**		**A**	**B**	**C**	**D**	**Angle/°**
F1	C2	C3	C4	76.8(3)		F11	C12	C13	C14	80.9(3)
F1	C2	C6	O2	174.0(2)		F11	C12	C16	O12	-172.2(2)
F1	C2	C6	O3	-7.5(4)		F11	C12	C16	O13	8.8(4)
O1	C1	C2	F1	69.8(3)		O11	C11	C12	F11	63.5(3)
O1	C1	C2	C3	-171.0(3)		O11	C11	C12	C13	-176.2(3)
O1	C1	C2	C6	-42.3(3)		O11	C11	C12	C16	-50.7(4)
N1	C1	C2	F1	-107.3(3)		N11	C11	C12	F11	-115.2(3)
N1	C1	C2	C3	11.9(4)		N11	C11	C12	C13	5.1(4)
N1	C1	C2	C6	140.6(3)		N11	C11	C12	C16	130.6(3)
C1	N1	C5	C4	27.5(5)		C11	N11	C15	C14	22.3(5)
C1	C2	C3	C4	-39.9(4)		C11	C12	C13	C14	-37.3(4)
C1	C2	C6	O2	-75.3(3)		C11	C12	C16	O12	-58.9(3)
C1	C2	C6	O3	103.3(4)		C11	C12	C16	O13	122.0(3)
C2	C3	C4	C5	61.3(4)		C12	C13	C14	C15	61.8(4)
C3	C2	C6	O2	54.9(3)		C13	C12	C16	O12	69.0(3)
C3	C2	C6	O3	-126.6(4)		C13	C12	C16	O13	-110.1(4)
C3	C4	C5	N1	-54.4(4)		C13	C14	C15	N11	-53.6(4)
C5	N1	C1	O1	177.4(3)		C15	N11	C11	O11	-175.8(3)
C5	N1	C1	C2	-5.7(5)		C15	N11	C11	C12	2.8(5)
C6	C2	C3	C4	-165.5(3)		C16	C12	C13	C14	-161.7(3)
C7	O2	C6	O3	-3.2(5)		C17	O12	C16	O13	3.2(5)
C7	O2	C6	C2	175.4(2)		C17	O12	C16	C12	-175.8(3)

Table 8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 14srv257.				
Atom	***x***	***y***	***z***	**U(eq)**
H1	11020(50)	7120(40)	2700(50)	36(10)
H3A	9170(50)	5960(40)	6290(50)	36(10)
H3B	8520(50)	4690(50)	6190(50)	50(12)
H4A	10590(40)	4250(40)	4390(40)	29(9)
H4B	11250(60)	4650(60)	5750(60)	63(14)
H5A	11800(50)	6900(40)	5330(40)	38(10)
H5B	12330(50)	5900(40)	4010(40)	37(10)
H7A	5310(50)	8840(50)	5450(50)	41(10)
H7B	4820(50)	7890(40)	6670(40)	37(10)
H7C	6280(50)	8980(40)	7160(50)	44(11)
H11	5620(50)	6390(50)	11830(50)	44(11)
H13A	4240(40)	3910(40)	9060(40)	29(9)
H13B	3910(50)	4450(50)	7420(50)	48(11)
H14A	6670(50)	4520(50)	8160(50)	52(12)
H14B	6070(40)	6080(30)	8180(40)	22(7)
H15A	7270(50)	5670(40)	10390(40)	40(10)
H15B	6340(40)	4460(40)	10620(40)	25(8)
H17A	-540(60)	3920(60)	11410(60)	62(14)
H17B	800(60)	2740(60)	11570(60)	60(13)
H17C	10(60)	2870(50)	10260(60)	53(13)

SI-4.4 (*R*)-Methyl 3-fluoro-2-oxopiperidine-3-carboxylate **2c**



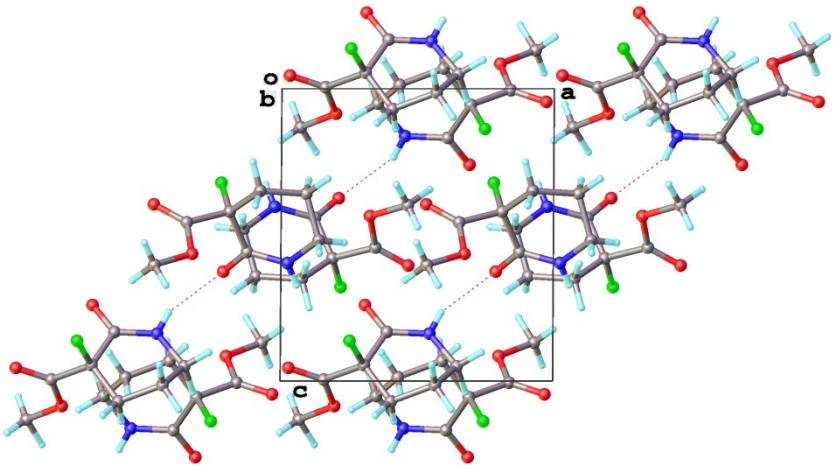


Table 1 Crystal data and structure refinement for 14srv258	
Identification code	14srv258
Empirical formula	$C_7H_{10}FNO_3$
Formula weight	175.16
Temperature/K	120.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.5211(3)
b/Å	10.3039(3)
c/Å	9.1547(3)
α/°	90.00
β/°	90.3650(8)
γ/°	90.00
Volume/Å^3	803.77(5)
Z	4
ρ_{calc}g/cm^3	1.447
μ/mm^{-1}	1.104
F(000)	368.0
Crystal size/mm^3	0.32 × 0.3 × 0.24
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	9.66 to 144.94
Index ranges	-9 ≤ h ≤ 10, -12 ≤ k ≤ 12, -11 ≤ l ≤ 11
Reflections collected	6957
Independent reflections	2916 [R_{int} = 0.0579, R_{sigma} = 0.0613]
Data/restraints/parameters	2916/1/297
Goodness-of-fit on F^2	1.103
Final R indexes [I>=2σ (I)]	R_1 = 0.0513, wR_2 = 0.1451
Final R indexes [all data]	R_1 = 0.0515, wR_2 = 0.1455
Largest diff. peak/hole / e Å^{-3}	0.33/-0.26
Flack parameter	-0.01(16)
Hooft parameter	0.00(7)

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 14srv258. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.				
Atom	***x***	***y***	***z***	**U(eq)**
F1	7463.4(17)	5472.8(15)	1375.6(16)	36.8(4)
O1	6903(2)	2983.0(19)	2600(2)	37.3(4)
O2	8010.5(19)	2734.7(17)	-854.1(19)	31.1(4)
O3	9704(2)	3938(3)	451(3)	52.8(6)
N1	4532(3)	3510(2)	1621(2)	35.8(5)
C1	6094(3)	3546(2)	1680(2)	28.6(5)
C2	6929(3)	4414(2)	549(3)	29.0(5)
C3	5934(3)	4920(3)	-694(3)	34.6(6)
C4	4317(3)	5305(3)	-134(3)	37.9(6)
C5	3524(3)	4125(3)	507(3)	44.0(7)
C6	8403(3)	3682(2)	53(3)	29.9(5)
C7	9305(3)	1902(3)	-1316(3)	39.6(6)
F11	2198.4(18)	3662.2(16)	6783.9(16)	37.5(4)
O11	2110(2)	3242.7(19)	3745(2)	36.0(4)
O12	3261(2)	6149.0(19)	4352.9(19)	34.2(4)
O13	4675(2)	5059.7(19)	6046(2)	35.5(4)
N11	-241(2)	4225(2)	4037(2)	33.8(5)
C11	1242(3)	3988(2)	4416(3)	29.8(5)
C12	1891(3)	4664(2)	5796(3)	28.9(5)
C13	769(3)	5633(3)	6508(3)	35.4(5)
C14	-918(3)	5154(3)	6408(3)	35.4(5)
C15	-1381(3)	5033(3)	4817(3)	36.1(6)
C16	3466(3)	5293(2)	5431(2)	29.7(5)
C17	4646(3)	6888(3)	3979(3)	39.1(6)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 14srv258. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.						
Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
F1	36.6(8)	33.2(8)	40.6(8)	-8.9(6)	4.4(6)	-3.4(6)
O1	36.4(9)	39.5(10)	35.9(9)	5.0(8)	-4.7(7)	1.1(8)
O2	26.1(8)	28.5(8)	38.8(9)	-2.8(7)	2.7(6)	2.2(7)
O3	25.2(9)	62.1(14)	71.1(15)	-27.7(12)	-6.0(8)	2.6(9)
N1	28(1)	43.6(12)	35.8(11)	3.9(10)	1.9(8)	-0.2(9)
C1	29.3(11)	29.7(11)	26.9(10)	-2.4(9)	-1.8(8)	1.4(9)
C2	26.7(11)	29.5(11)	30.8(11)	-1.4(9)	-0.1(8)	1.2(10)
C3	33.8(13)	39.0(14)	30.8(12)	0.8(11)	1.4(10)	10.4(10)
C4	34.7(13)	43.7(14)	35.2(12)	0.6(12)	-2.7(10)	12.5(11)
C5	22.4(11)	60.0(19)	49.5(15)	1.0(14)	-6.3(10)	3.0(12)
C6	21.6(10)	32.5(11)	35.6(11)	1.9(10)	1.0(8)	-0.4(9)
C7	34.6(13)	34.4(13)	49.9(15)	-3.8(13)	7.7(11)	7.4(11)
F11	37.6(7)	40.8(8)	34.2(7)	10.3(6)	-1.2(6)	-1.5(6)
O11	33.9(9)	36.4(9)	37.9(9)	-4.6(7)	4.5(7)	1.5(7)
O12	31.7(9)	37.0(9)	33.9(9)	6.7(7)	-3.3(7)	-4.5(7)
O13	29.2(9)	40(1)	37.4(9)	4.2(8)	-2.8(7)	-1.3(7)
N11	30.4(10)	37.1(12)	33.8(11)	-3.0(9)	-5.2(8)	0.9(9)
C11	30.0(11)	27.9(11)	31.5(11)	1.6(9)	1.8(9)	-3.9(9)
C12	28.5(12)	29.5(12)	28.6(11)	2.6(9)	-2.3(8)	0.5(9)
C13	31.9(12)	40.6(14)	33.8(12)	-6.9(11)	1.7(9)	-1(1)
C14	30.7(12)	39.1(14)	36.5(12)	3.2(11)	4.1(9)	3.8(10)
C15	29.5(12)	39.6(14)	39.3(13)	0.3(11)	-3.0(9)	3.0(11)
C16	31.0(11)	29.4(11)	28.7(10)	-2.4(9)	-2.6(8)	-1.3(9)
C17	39.8(14)	38.5(14)	39.1(14)	6.3(12)	-1.5(11)	-11.9(12)

Table 4 Bond Lengths for 14srv258.						
Atom	**Atom**	**Length/Å**		**Atom**	**Atom**	**Length/Å**
F1	C2	1.402(3)		F11	C12	1.396(3)
O1	C1	1.230(3)		O11	C11	1.234(3)
O2	C6	1.323(3)		O12	C16	1.334(3)
O2	C7	1.462(3)		O12	C17	1.447(3)
O3	C6	1.195(3)		O13	C16	1.195(3)
N1	C1	1.332(3)		N11	C11	1.331(3)
N1	C5	1.472(4)		N11	C15	1.468(3)
C1	C2	1.545(3)		C11	C12	1.542(3)
C2	C3	1.507(3)		C12	C13	1.530(3)
C2	C6	1.536(3)		C12	C16	1.529(3)
C3	C4	1.525(4)		C13	C14	1.522(4)
C4	C5	1.512(4)		C14	C15	1.512(4)

Table 5 Bond Angles for 14srv258.								
Atom	**Atom**	**Atom**	**Angle/°**		**Atom**	**Atom**	**Atom**	**Angle/°**
C6	O2	C7	115.23(19)		C16	O12	C17	114.81(19)
C1	N1	C5	126.5(2)		C11	N11	C15	127.4(2)
O1	C1	N1	124.8(2)		O11	C11	N11	123.7(2)
O1	C1	C2	118.3(2)		O11	C11	C12	118.5(2)
N1	C1	C2	116.9(2)		N11	C11	C12	117.8(2)
F1	C2	C1	103.74(18)		F11	C12	C11	105.15(19)
F1	C2	C3	108.5(2)		F11	C12	C13	108.76(19)
F1	C2	C6	106.14(18)		F11	C12	C16	107.08(18)
C3	C2	C1	116.5(2)		C13	C12	C11	114.9(2)
C3	C2	C6	113.84(19)		C16	C12	C11	108.84(19)
C6	C2	C1	107.14(19)		C16	C12	C13	111.6(2)
C2	C3	C4	109.9(2)		C14	C13	C12	110.8(2)
C5	C4	C3	109.2(2)		C15	C14	C13	109.0(2)
N1	C5	C4	110.7(2)		N11	C15	C14	110.3(2)
O2	C6	C2	110.10(19)		O12	C16	C12	109.32(19)
O3	C6	O2	125.8(2)		O13	C16	O12	126.1(2)
O3	C6	C2	124.1(2)		O13	C16	C12	124.5(2)

Table 6 Hydrogen Bonds for 14srv258.						
D	**H**	**A**	**d(D-H)/Å**	**d(H-A)/Å**	**d(D-A)/Å**	**D-H-A/°**
N1	H1	O11	0.82(4)	2.14(4)	2.858(3)	145(3)
N11	H11	O1[1]	0.79(4)	2.46(4)	3.042(3)	132(3)

[1]-1+X,+Y,+Z

Table 7 Torsion Angles for 14srv258.										
A	**B**	**C**	**D**	**Angle/°**		**A**	**B**	**C**	**D**	**Angle/°**
F1	C2	C3	C4	-77.0(3)		F11	C12	C13	C14	-80.8(2)
F1	C2	C6	O2	-174.02(19)		F11	C12	C16	O12	172.25(19)
F1	C2	C6	O3	6.6(3)		F11	C12	C16	O13	-9.0(3)
O1	C1	C2	F1	-69.9(3)		O11	C11	C12	F11	-63.9(3)
O1	C1	C2	C3	170.9(2)		O11	C11	C12	C13	176.5(2)
O1	C1	C2	C6	42.1(3)		O11	C11	C12	C16	50.5(3)
N1	C1	C2	F1	107.3(2)		N11	C11	C12	F11	114.7(2)
N1	C1	C2	C3	-11.9(3)		N11	C11	C12	C13	-4.9(3)
N1	C1	C2	C6	-140.7(2)		N11	C11	C12	C16	-130.9(2)
C1	N1	C5	C4	-27.6(4)		C11	N11	C15	C14	-22.7(4)
C1	C2	C3	C4	39.6(3)		C11	C12	C13	C14	36.7(3)
C1	C2	C6	O2	75.6(2)		C11	C12	C16	O12	59.1(3)
C1	C2	C6	O3	-103.8(3)		C11	C12	C16	O13	-122.2(3)
C2	C3	C4	C5	-60.9(3)		C12	C13	C14	C15	-61.7(3)
C3	C2	C6	O2	-54.7(3)		C13	C12	C16	O12	-68.8(2)
C3	C2	C6	O3	125.9(3)		C13	C12	C16	O13	109.9(3)
C3	C4	C5	N1	54.0(3)		C13	C14	C15	N11	53.6(3)
C5	N1	C1	O1	-177.3(3)		C15	N11	C11	O11	176.1(2)
C5	N1	C1	C2	5.7(4)		C15	N11	C11	C12	-2.4(4)
C6	C2	C3	C4	165.1(2)		C16	C12	C13	C14	161.3(2)
C7	O2	C6	O3	3.9(4)		C17	O12	C16	O13	-3.3(4)
C7	O2	C6	C2	-175.51(19)		C17	O12	C16	C12	175.4(2)

Table 8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 14srv258.				
Atom	***x***	***y***	***z***	**U(eq)**
H1	4110(40)	3190(40)	2340(40)	36(8)
H3A	5820(50)	4320(40)	-1370(40)	52(10)
H3B	6500(50)	5630(40)	-1170(40)	51(10)
H4A	4440(40)	5990(30)	550(40)	31(7)
H4B	3710(30)	5600(30)	-970(30)	19(6)
H5A	2630(40)	4440(40)	980(40)	38(8)
H5B	3210(40)	3440(40)	-370(40)	46(9)
H7A	8740(40)	1370(30)	-2170(40)	35(8)
H7B	9610(50)	1390(50)	-550(50)	56(11)
H7C	10010(50)	2440(40)	-1770(40)	47(9)
H11	-570(40)	3960(40)	3290(40)	45(9)
H13A	950(40)	6470(40)	6000(40)	36(8)
H13B	1040(50)	5840(40)	7490(50)	57(11)
H14A	-1700(40)	5760(40)	6920(40)	40(8)
H14B	-1010(40)	4330(40)	6870(40)	38(8)
H15A	-1410(30)	5910(30)	4380(30)	19(6)
H15B	-2310(40)	4610(40)	4730(40)	37(8)
H17A	4220(40)	7420(50)	3280(40)	50(10)
H17B	5440(60)	6250(60)	3450(60)	83(15)
H17C	5020(40)	7260(40)	4720(40)	39(9)