Supporting Information

Scalable Continuous Flow Process for the Synthesis of Eflornithine using Fluoroform as Difluoromethyl Source

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Contents

1. Flow Reactor Setups

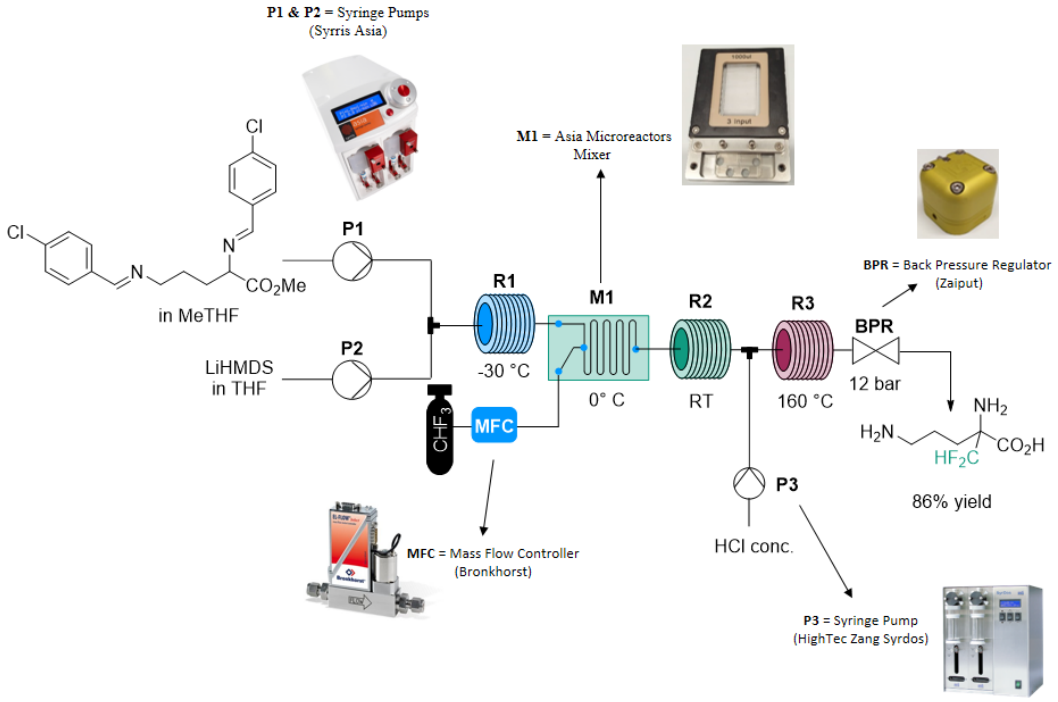


Figure S1. Continuous-flow setup (schematic) for the telescoped reaction.

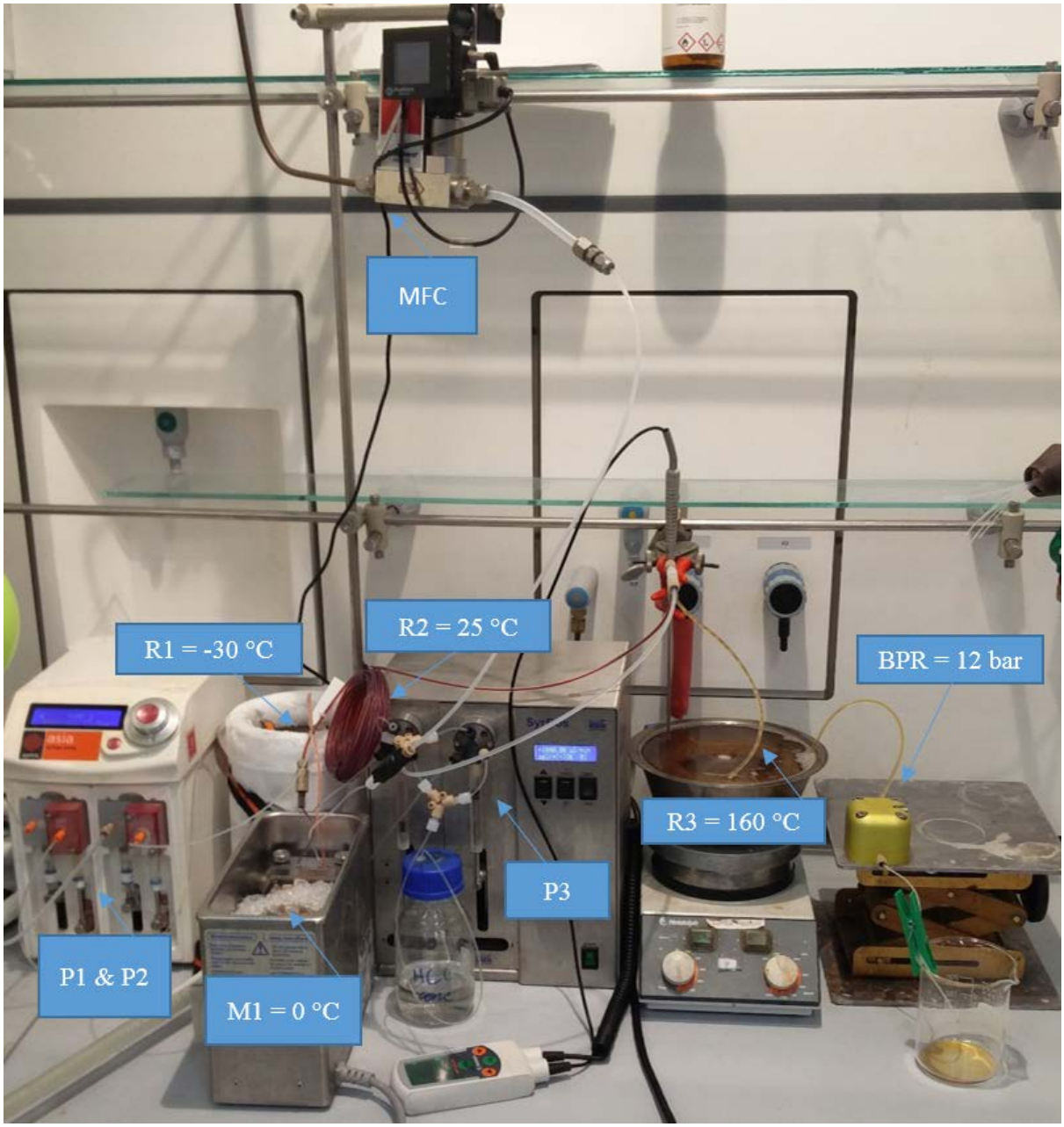


Figure S2. Image of continuous-flow setup for the telescoped reaction.

1. Base Screening

A screening for a suitable alternative to LiHMDS was conducted using optimized flow conditions with a 0.5 M solution of **8** in 2-MeTHF as substrate solution.

Table S1. Screening for an alternative to LiHMDS.

Entry	Base	equiv	**Yield [%]**[a]
1	LiHMDS	3	87
2	*n*-BuLi	3	0
3	LDA	3	1-2
4	KO*t*Bu	3	0
5	LiO*t*Bu	3	0
6	$LiN(cyHex)_2$	3	5
7	$LiN(cyHex)_2$	5	10
8	$LiN(cyHex)_2$	10	0

[a]Analyzed by ^{19}F NMR (α, α, α,-trifluorotoluene as internal standard)

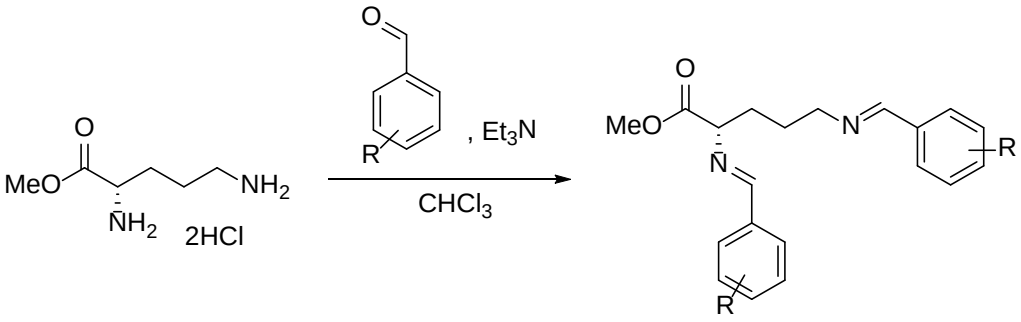
2. Protection Group Screening

A screening for a suitable protecting group for the NH_2-residues of ornithine methyl ester was conducted using different benzaldehyde analogues. As the obtained bisimines are not stable towards chromatography, the yield and purity was determined through ^{1}H NMR using nitromethane as internal standard.

General experimental procedure:

A dry 10 mL round bottom flask with magnetic stirring bar was charged with (S)-methyl 2,5-diaminopentanoate dihydrochloride (0.50 g, 2.282 mmol) and the corresponding benzaldehyde derivative (2 equiv, 4.564 mmol), sealed and flushed with argon three times. Chloroform (5 mL) was added and the stirred, colorless reaction mixture was cooled to 0 °C. After addition of triethylamine (632 µL, 4.564 mmol) over 10 min the reaction mixture was allowed to warm to room temperature and stirred for 18 h. The solvent was removed under reduced pressure. The slightly yellow residue was treated with Et_2O to precipitate $Et_3N{\cdot}HCl$. The formed colorless precipitate was filtered off and the obtained filtrated was concentrated in vacuo. The residue was checked for purity in ^{1}H NMR.

Table S2. Yields and Melting points of various bisimine protected ornithine methyl ester.



R = 2-OMe, 3-OMe, 4-OMe, 2-Cl, 3-Cl, 4-Cl, 2,3-Cl, 4-NO_2, 4-CN, 4-Br, 4-Tfm, 4-OH, 4-Me

Entry	Benzaldehyde	Melting point [°C]	**Yield [%]**[a]
1	2-OMe	-	4
2	3-OMe	-	65
3	4-OMe	-	88
4	2-Cl	-	50
5	3-Cl	-	81
6	4-Cl	89-91	92
7	2,3-Cl	-	87
8	4-NO_2	-	-
9	4-CN	-	82
10	4-Br	74-77	92
11	4-Tfm	-	93
12	4-OH	-	-
13	4-Me	66-69	85

[a]Analyzed by ^{1}H NMR via internal standard (CH_3NO_2), corrected for purity.

3. Stability and Water Content of Compound 8

To determine stability of bisimine compound **8,** eight NMR tubes were charged with 100 mg of compound **8** and 10 mg CH_3NO_2 as internal standard, sealed with a cap and stored at −30 °C. The purity of samples was then determined by ^{1}H NMR over the course of 10 days. There was no significant degradation of compound **8** detected.

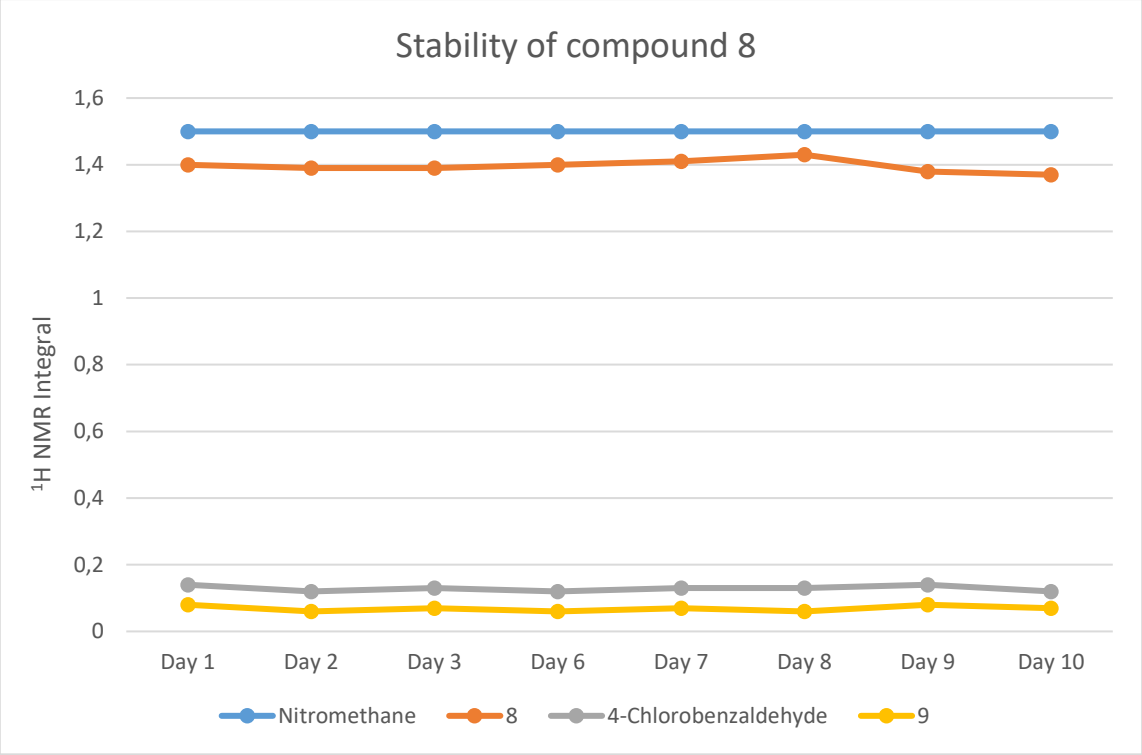


Figure S3. ^{1}H NMR intensities of compound **8**, **9**, benzaldehyde and nitromethane over time.

Additionally the water content of compound **8** was determined by Karl Fischer Titration on a Metrohm Coulometer "Aquaster Combi Coulomat fritless"

Table S3. Water content of compound **8**.

Measurment #	H_2O content [ppm]
1	1585
2	1263
3	1567
4	1484
Average (mean)	**1475**

4. X-ray Crystallography

All crystals suitable for single crystal X-ray diffractometry were removed from a vial and immediately covered with a layer of silicone oil. A single crystal was selected, mounted on a glass rod on a copper pin, and placed in the cold N_2 stream provided by an Oxford Cryosystems cryostream. XRD data collection was performed for compounds **8 & 9**, on a Bruker APEX II diffractometer with use of an Incoatec microfocus sealed tube of Mo Kα radiation (λ= 0.71073 Å) and a CCD area detector. Empirical absorption corrections were applied using SADABS.[1, 2] The structures were solved with use of the intrinsic phasing option in SHELXT and refined by the full-matrix least-squares procedures in SHELXL.[3-5] The space group assignments and structural solutions were evaluated using PLATON.[6,7] Non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located in a difference map and refined isotropically. All crystal structures representations were made with the program Diamond. CCDC S7-S21 contain the supplementary crystallographic data for compounds **8 & 9** respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. Table **S4** contains crystallographic data and details of measurements and refinement for compds **8 & 9**.

Table S4. Crystallographic data and details of measurements for compounds **8 &9** Mo Kα (λ=0.71073Å). $R_1 = \Sigma/ |F_o| - |F_c|/|\Sigma|F_d$; $wR2 = [\Sigma_w(F_o^2-F_2^2)^2/\Sigma_w(F_o^2)^2]^{1/2}$

Compound	**9**	**8**
Formula	$C_{12}H_{13}ClN_2O$	$C_{20}H_{20}Cl_2N_2O_2$
Fw (g mol^{-1})	236.69	391.28
a (Å)	9.5078(5)	6.4075(2)
b (Å)	10.2795(5)	7.4469(3)
c (Å)	12.2956(6)	20.0123(7)
α (°)	101.780(3)	90
β (°)	105.312(2)	94.277(2)
γ (°)	90.288(3)	90
V (Å^3)	1132.43(10)	952.25(6)
Z	4	2
Crystal size (mm)	0.05 × 0.05 × 0.05	0.08 × 0.08 × 0.06
Crystal habit	Block, colourless	Block, colourless
Crystal system	Triclinic	Monoclinic
Space group	*P*1	$P2_1$
d_{calc} (mg/m^3)	1.388	1.365
μ (mm^{-1})	0.32	0.36
T (K)	100(2)	100(2)
2θ range (°)	2.4–33.0	2.9–31.8
F(000)	496	408
R_{int}	0.076	0.096
independent reflns	8622	7286
No. of params	393	315
R1, wR2 (all data)[a]	R1 = 0.0496 wR2 = 0.1079	R1 = 0.0623 wR2 = 0.0410
R1, wR2 (>2σ)[b]	R1 = 0.0375 wR2 = 0.0978	R1 = 0.1008 wR2 = 0.0907

Synthesis and Crystallization of Compound 8

Compound **8** was synthesised according to the procedure given in the experimental section. A crystal was obtained by slow evaporation at 5 °C from petroleum ether/EtOAc for 5 days.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1.

Results

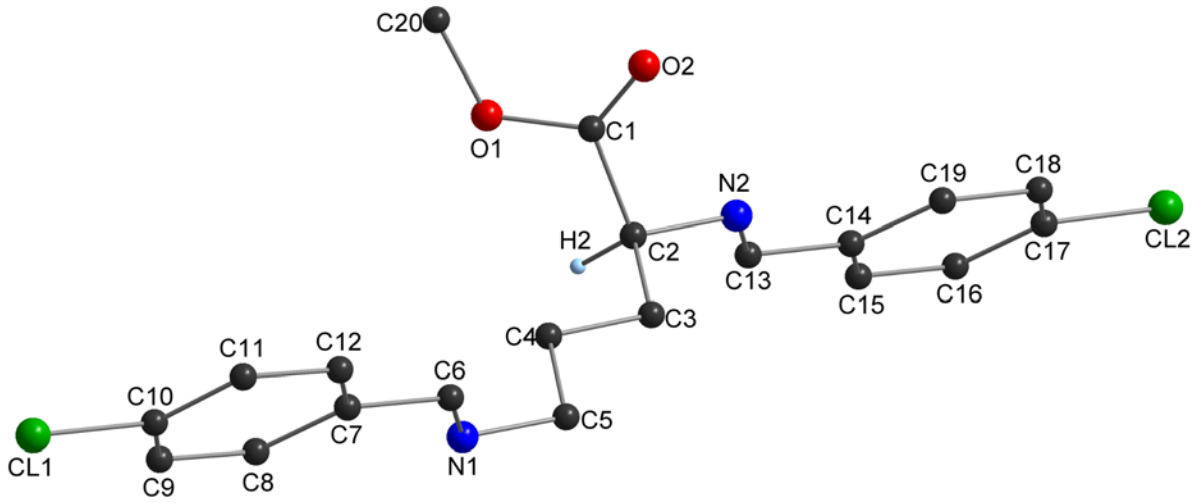


Figure S4. Crystal structure of **8**

Computing details

Data collection: Bruker *APEX2*; cell refinement: Bruker *SAINT* v8.37A (Bruker, 2015); data reduction: Bruker *SAINT* v8.37A (Bruker, 2015); program(s) used to solve structure: SHELXT-2014/5; program(s) used to refine structure: *SHELXL2014*/7 (Sheldrick, 2014); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

8

Crystal data

$C_{20}H_{20}Cl_2N_2O_2$	$F(000)$ = 408
M_r = 391.28	D_x = 1.365 Mg m^{-3}
Monoclinic, $P2_1$	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 6.4075 (2) Å	Cell parameters from 9875 reflections

b = 7.4469 (3) Å	θ = 2.9–31.8°
c = 20.0123 (7) Å	μ = 0.36 mm^{-1}
β = 94.277 (2)°	T = 100 K
V = 952.25 (6) Å^3	Block, colourless
Z = 2	0.08 × 0.08 × 0.06 mm

Data collection

Bruker APEX-II CCD diffractometer	7286 independent reflections
Radiation source: Incoatec microfocus sealed tube	5694 reflections with $I > 2\sigma(I)$
Multilayer monochromator	R_{int} = 0.096
ϕ and ω scans	θ_{max} = 33.2°, θ_{min} = 2.9°
Absorption correction: multi-scan *SADABS*	h = -9→9
T_{min} = 0.638, T_{max} = 0.746	k = -11→11
57041 measured reflections	l = -30→30

Refinement

Refinement on F^2	Hydrogen site location: difference Fourier map
Least-squares matrix: full	All H-atom parameters refined
$R[F^2 > 2\sigma(F^2)]$ = 0.041	$w = 1/[\sigma^2(F_o^2) + (0.0378P)^2 + 0.0838P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.101	$(\Delta/\sigma)_{max}$ = 0.001
S = 1.02	$\Delta\rangle_{max}$ = 0.46 e Å^{-3}
7286 reflections	$\Delta\rangle_{min}$ = -0.23 e Å^{-3}
315 parameters	Absolute structure: Flack x determined using 2189 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
1 restraint	Absolute structure parameter: -0.03 (4)

Special details

Geometry. 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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2) for (AT782_b)

	x	*y*	*z*	U_{iso}*/U_{eq}
Cl1	1.18049 (9)	0.90139 (9)	0.62696 (3)	0.02355 (16)
Cl2	-0.67848 (9)	0.22490 (9)	-0.12419 (3)	0.02014 (14)
O1	0.5383 (2)	0.2401 (3)	0.20889 (8)	0.0224 (3)
O2	0.2308 (3)	0.1313 (3)	0.23844 (9)	0.0250 (4)
N1	0.4424 (4)	0.7932 (3)	0.37161 (11)	0.0197 (5)
N2	0.0571 (3)	0.3488 (3)	0.12994 (10)	0.0187 (5)
C1	0.3294 (3)	0.2423 (3)	0.21038 (11)	0.0179 (4)
C2	0.2368 (4)	0.4063 (4)	0.17411 (12)	0.0173 (5)
C3	0.1610 (4)	0.5389 (4)	0.22617 (13)	0.0184 (5)
C4	0.3364 (4)	0.5996 (4)	0.27717 (13)	0.0188 (5)
C5	0.2624 (4)	0.7352 (4)	0.32727 (13)	0.0196 (5)
C6	0.4514 (4)	0.7371 (4)	0.43164 (12)	0.0173 (5)
C7	0.6314 (4)	0.7781 (3)	0.47941 (13)	0.0159 (5)
C8	0.8082 (4)	0.8668 (4)	0.45868 (13)	0.0176 (5)
C9	0.9768 (4)	0.9029 (4)	0.50384 (13)	0.0183 (5)
C10	0.9689 (4)	0.8508 (4)	0.57048 (13)	0.0179 (5)
C11	0.7975 (4)	0.7606 (3)	0.59257 (13)	0.0178 (5)
C12	0.6287 (4)	0.7251 (4)	0.54654 (12)	0.0179 (5)
C13	0.0488 (4)	0.4046 (4)	0.06981 (12)	0.0154 (5)
C14	-0.1302 (4)	0.3607 (3)	0.02184 (12)	0.0142 (5)
C15	-0.1258 (4)	0.4060 (4)	-0.04555 (11)	0.0148 (5)
C16	-0.2943 (4)	0.3657 (3)	-0.09163 (12)	0.0159 (5)
C17	-0.4669 (4)	0.2805 (3)	-0.06831 (12)	0.0150 (5)
C18	-0.4762 (4)	0.2337 (4)	-0.00129 (12)	0.0163 (5)
C19	-0.3077 (4)	0.2749 (3)	0.04392 (12)	0.0159 (5)
C20	0.6457 (4)	0.0958 (4)	0.24602 (14)	0.0267 (5)
H2	0.347 (4)	0.465 (4)	0.1486 (14)	0.016 (8)*
H3A	0.103 (4)	0.646 (4)	0.2033 (14)	0.018 (7)*
H3B	0.048 (4)	0.481 (5)	0.2485 (14)	0.015 (7)*
H4A	0.398 (4)	0.499 (5)	0.3008 (14)	0.023 (8)*
H4B	0.453 (5)	0.644 (5)	0.2557 (15)	0.026 (8)*
H5A	0.147 (4)	0.684 (4)	0.3530 (15)	0.024 (8)*
H5B	0.205 (4)	0.831 (4)	0.3075 (14)	0.013 (7)*
H6	0.341 (4)	0.659 (4)	0.4495 (15)	0.021 (8)*
H8	0.818 (4)	0.907 (5)	0.4129 (15)	0.027 (8)*
H9	1.090 (4)	0.972 (5)	0.4913 (15)	0.019 (8)*
H11	0.795 (4)	0.718 (5)	0.6369 (15)	0.022 (8)*
H12	0.512 (5)	0.659 (5)	0.5604 (15)	0.025 (8)*
H13	0.161 (4)	0.481 (4)	0.0524 (14)	0.016 (8)*

H19	-0.310 (5)	0.248 (5)	0.0911 (16)	0.029 (9)*
H18	-0.598 (4)	0.178 (4)	0.0113 (15)	0.017 (8)*
H16	-0.287 (5)	0.399 (5)	-0.1380 (16)	0.026 (8)*
H15	-0.004 (4)	0.462 (4)	-0.0606 (14)	0.018 (8)*
H20A	0.614 (4)	0.101 (4)	0.2925 (14)	0.023 (7)*
H20B	0.797 (5)	0.106 (4)	0.2416 (14)	0.025 (8)*
H20C	0.605 (5)	-0.024 (5)	0.2267 (15)	0.031 (8)*

Atomic displacement parameters (Å²) for (AT782_b)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0190 (3)	0.0291 (4)	0.0220 (3)	0.0014 (3)	-0.0024 (2)	-0.0017 (3)
Cl2	0.0167 (3)	0.0248 (3)	0.0186 (3)	-0.0010 (3)	-0.0013 (2)	-0.0006 (3)
O1	0.0202 (7)	0.0239 (9)	0.0229 (8)	0.0018 (7)	-0.0005 (6)	0.0012 (7)
O2	0.0268 (9)	0.0208 (9)	0.0274 (9)	-0.0031 (7)	0.0017 (7)	0.0071 (7)
N1	0.0218 (11)	0.0151 (11)	0.0219 (11)	-0.0032 (9)	-0.0008 (9)	-0.0014 (9)
N2	0.0191 (10)	0.0205 (12)	0.0160 (10)	-0.0014 (9)	-0.0012 (8)	0.0017 (8)
C1	0.0208 (10)	0.0191 (11)	0.0136 (9)	-0.0007 (8)	-0.0004 (7)	-0.0019 (8)
C2	0.0177 (11)	0.0188 (12)	0.0153 (10)	-0.0031 (11)	0.0000 (8)	0.0034 (10)
C3	0.0200 (13)	0.0166 (12)	0.0183 (12)	0.0000 (10)	-0.0008 (10)	0.0005 (10)
C4	0.0183 (12)	0.0203 (13)	0.0176 (11)	-0.0035 (10)	-0.0011 (9)	0.0006 (10)
C5	0.0193 (12)	0.0180 (12)	0.0211 (11)	-0.0024 (12)	-0.0020 (9)	-0.0011 (12)
C6	0.0186 (11)	0.0137 (12)	0.0198 (11)	-0.0017 (11)	0.0025 (9)	-0.0030 (11)
C7	0.0174 (12)	0.0127 (12)	0.0179 (11)	-0.0002 (9)	0.0026 (9)	-0.0017 (9)
C8	0.0204 (12)	0.0150 (13)	0.0179 (11)	-0.0007 (10)	0.0044 (9)	0.0011 (10)
C9	0.0168 (12)	0.0161 (12)	0.0224 (12)	-0.0006 (11)	0.0042 (9)	0.0004 (11)
C10	0.0179 (13)	0.0176 (14)	0.0179 (11)	0.0016 (10)	-0.0001 (9)	-0.0012 (10)
C11	0.0214 (12)	0.0167 (14)	0.0159 (11)	0.0013 (10)	0.0047 (9)	-0.0006 (9)
C12	0.0205 (12)	0.0156 (12)	0.0184 (11)	0.0004 (12)	0.0057 (9)	-0.0013 (12)
C13	0.0161 (11)	0.0137 (11)	0.0163 (10)	0.0009 (10)	0.0015 (8)	-0.0001 (10)
C14	0.0161 (11)	0.0123 (12)	0.0141 (10)	0.0011 (9)	0.0009 (9)	0.0000 (9)
C15	0.0159 (11)	0.0129 (12)	0.0159 (10)	-0.0002 (11)	0.0029 (8)	0.0013 (10)
C16	0.0196 (12)	0.0142 (12)	0.0143 (10)	0.0009 (10)	0.0029 (9)	0.0013 (9)
C17	0.0138 (11)	0.0142 (12)	0.0169 (11)	0.0014 (9)	0.0010 (9)	-0.0017 (9)
C18	0.0155 (11)	0.0177 (12)	0.0159 (10)	-0.0004 (11)	0.0034 (8)	0.0012 (11)
C19	0.0171 (11)	0.0172 (13)	0.0136 (10)	-0.0003 (9)	0.0024 (9)	0.0003 (9)
C20	0.0280 (13)	0.0237 (13)	0.0273 (13)	0.0071 (10)	-0.0062 (10)	-0.0024 (10)

Geometric parameters (Å, º) for (AT782_b)

Cl1—C10	1.741 (2)	C8—C9	1.382 (4)

Cl2—C17	1.742 (2)	C8—H8	0.97 (3)
O1—C1	1.341 (3)	C9—C10	1.393 (4)
O1—C20	1.451 (3)	C9—H9	0.94 (3)
O2—C1	1.204 (3)	C10—C11	1.387 (4)
N1—C6	1.269 (3)	C11—C12	1.393 (3)
N1—C5	1.466 (3)	C11—H11	0.94 (3)
N2—C13	1.270 (3)	C12—H12	0.96 (3)
N2—C2	1.462 (3)	C13—C14	1.477 (3)
C1—C2	1.519 (4)	C13—H13	1.00 (3)
C2—C3	1.540 (4)	C14—C15	1.393 (3)
C2—H2	1.00 (3)	C14—C19	1.404 (3)
C3—C4	1.529 (3)	C15—C16	1.400 (3)
C3—H3A	0.98 (3)	C15—H15	0.95 (3)
C3—H3B	0.98 (3)	C16—C17	1.386 (3)
C4—C5	1.523 (4)	C16—H16	0.97 (3)
C4—H4A	0.96 (3)	C17—C18	1.391 (3)
C4—H4B	0.95 (3)	C18—C19	1.390 (3)
C5—H5A	1.01 (3)	C18—H18	0.94 (3)
C5—H5B	0.88 (3)	C19—H19	0.97 (3)
C6—C7	1.474 (4)	C20—H20A	0.97 (3)
C6—H6	1.00 (3)	C20—H20B	0.99 (3)
C7—C8	1.400 (3)	C20—H20C	1.00 (3)
C7—C12	1.402 (3)		
C1—O1—C20	115.7 (2)	C8—C9—C10	119.3 (2)
C6—N1—C5	117.0 (2)	C8—C9—H9	120.9 (18)
C13—N2—C2	116.9 (2)	C10—C9—H9	119.5 (18)
O2—C1—O1	124.1 (2)	C11—C10—C9	121.7 (2)
O2—C1—C2	125.1 (2)	C11—C10—Cl1	119.64 (19)
O1—C1—C2	110.8 (2)	C9—C10—Cl1	118.6 (2)
N2—C2—C1	108.4 (2)	C10—C11—C12	118.4 (2)
N2—C2—C3	108.9 (2)	C10—C11—H11	122.0 (18)
C1—C2—C3	108.90 (19)	C12—C11—H11	119.5 (19)
N2—C2—H2	112.0 (16)	C11—C12—C7	121.0 (2)
C1—C2—H2	109.1 (17)	C11—C12—H12	119.6 (18)
C3—C2—H2	109.5 (18)	C7—C12—H12	119.3 (18)
C4—C3—C2	112.86 (18)	N2—C13—C14	121.3 (2)
C4—C3—H3A	107.7 (17)	N2—C13—H13	122.4 (16)
C2—C3—H3A	109.6 (16)	C14—C13—H13	116.3 (16)
C4—C3—H3B	110.9 (16)	C15—C14—C19	119.4 (2)

C2—C3—H3B	107.8 (19)	C15—C14—C13	120.3 (2)
H3A—C3—H3B	108 (2)	C19—C14—C13	120.3 (2)
C5—C4—C3	112.74 (18)	C14—C15—C16	121.0 (2)
C5—C4—H4A	109.5 (18)	C14—C15—H15	119.3 (17)
C3—C4—H4A	110.7 (18)	C16—C15—H15	119.7 (17)
C5—C4—H4B	111 (2)	C17—C16—C15	118.2 (2)
C3—C4—H4B	111.6 (18)	C17—C16—H16	122.6 (18)
H4A—C4—H4B	101 (3)	C15—C16—H16	119.2 (19)
N1—C5—C4	108.9 (2)	C16—C17—C18	122.1 (2)
N1—C5—H5A	112.2 (17)	C16—C17—Cl2	119.67 (19)
C4—C5—H5A	111.3 (19)	C18—C17—Cl2	118.17 (19)
N1—C5—H5B	108.5 (18)	C19—C18—C17	119.0 (2)
C4—C5—H5B	112.3 (18)	C19—C18—H18	123.2 (18)
H5A—C5—H5B	104 (2)	C17—C18—H18	117.8 (18)
N1—C6—C7	121.6 (3)	C18—C19—C14	120.2 (2)
N1—C6—H6	123.1 (17)	C18—C19—H19	121.3 (18)
C7—C6—H6	115.3 (17)	C14—C19—H19	118.5 (18)
C8—C7—C12	119.0 (2)	O1—C20—H20A	109.6 (18)
C8—C7—C6	121.1 (2)	O1—C20—H20B	109.2 (19)
C12—C7—C6	119.9 (2)	H20A—C20—H20B	111 (2)
C9—C8—C7	120.5 (2)	O1—C20—H20C	111.3 (18)
C9—C8—H8	117.1 (18)	H20A—C20—H20C	110 (3)
C7—C8—H8	122.3 (18)	H20B—C20—H20C	106 (3)
C20—O1—C1—O2	-2.1 (3)	C8—C9—C10—Cl1	-178.7 (2)
C20—O1—C1—C2	175.9 (2)	C9—C10—C11—C12	-1.2 (4)
C13—N2—C2—C1	-131.4 (3)	Cl1—C10—C11—C12	178.7 (2)
C13—N2—C2—C3	110.2 (3)	C10—C11—C12—C7	0.3 (4)
O2—C1—C2—N2	-48.3 (3)	C8—C7—C12—C11	0.5 (4)
O1—C1—C2—N2	133.7 (2)	C6—C7—C12—C11	179.4 (3)
O2—C1—C2—C3	70.0 (3)	C2—N2—C13—C14	-177.4 (2)
O1—C1—C2—C3	-108.0 (2)	N2—C13—C14—C15	-172.9 (3)
N2—C2—C3—C4	177.02 (19)	N2—C13—C14—C19	8.0 (4)
C1—C2—C3—C4	59.0 (2)	C19—C14—C15—C16	-0.7 (4)
C2—C3—C4—C5	178.2 (3)	C13—C14—C15—C16	-179.9 (2)
C6—N1—C5—C4	-108.2 (3)	C14—C15—C16—C17	0.5 (4)
C3—C4—C5—N1	-176.9 (2)	C15—C16—C17—C18	-0.4 (4)

C5—N1—C6—C7	176.3 (2)	C15—C16—C17—Cl2	-179.1 (2)
N1—C6—C7—C8	-5.9 (4)	C16—C17—C18—C19	0.5 (4)
N1—C6—C7—C12	175.3 (3)	Cl2—C17—C18—C19	179.2 (2)
C12—C7—C8—C9	-0.5 (4)	C17—C18—C19—C14	-0.7 (4)
C6—C7—C8—C9	-179.4 (3)	C15—C14—C19—C18	0.8 (4)
C7—C8—C9—C10	-0.3 (4)	C13—C14—C19—C18	180.0 (3)
C8—C9—C10—C11	1.2 (4)		

Hydrogen-bond geometry (Å, º) for (AT782_b)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2···Cl2^{i}	1.00 (3)	2.94 (3)	3.881 (3)	157 (2)
C5—H5*B*···O2^{ii}	0.88 (3)	2.64 (3)	3.442 (4)	152 (2)
C11—H11···O2^{iii}	0.94 (3)	2.59 (3)	3.534 (3)	174 (3)
C20—H20*C*···Cl2^{iv}	1.00 (3)	2.84 (3)	3.701 (3)	145 (2)

Symmetry codes: (i) -*x*, *y*+1/2, -*z*; (ii) *x*, *y*+1, *z*; (iii) -*x*+1, *y*+1/2, -*z*+1; (iv) -*x*, *y*-1/2, -*z*.

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Synthesis and Crystallization of Compound 9

Compound **9** was obtained by concentrating the filtrate of compound **10** under vacuo and dissolving it in EtOAc at elevated temperatures. A crystal was obtained by slow evaporation of solvent at 5 °C for 3 days.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1.

Results

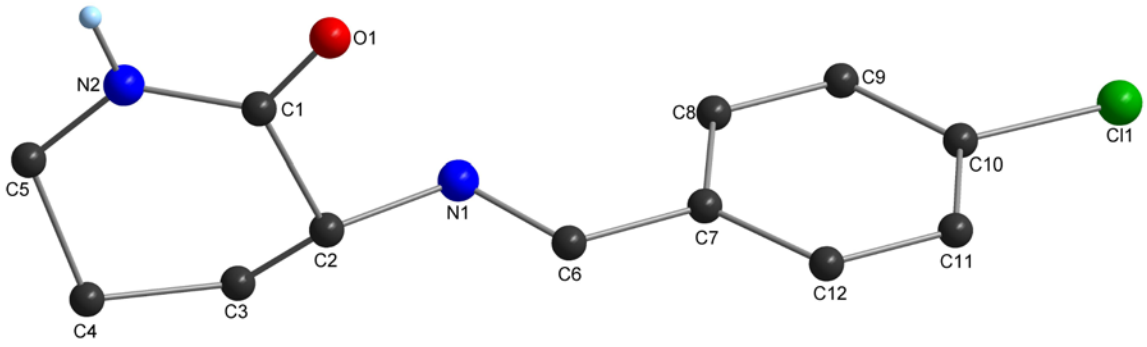

Figure S5. Crystal structure of **9**

Computing details

Data collection: Bruker *APEX2*; cell refinement: Bruker *SAINT* v8.37A (Bruker, 2015); data reduction: Bruker *SAINT* v8.37A (Bruker, 2015); program(s) used to solve structure: SHELXT-2014/5; program(s) used to refine structure: *SHELXL2014*/7 (Sheldrick, 2014); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

(9)

Crystal data

$C_{12}H_{13}ClN_2O$	Z = 4
M_r = 236.69	F(000) = 496
Triclinic, $P\bar{1}$	D_x = 1.388 Mg m^{-3}
a = 9.5078 (5) Å	Mo $K\alpha$ radiation, λ = 0.71073 Å
b = 10.2795 (5) Å	Cell parameters from 9903 reflections
c = 12.2956 (6) Å	θ = 2.4–33.0°

α = 101.780 (3)°	μ = 0.32 mm^{-1}
β = 105.312 (2)°	T = 100 K
γ = 90.288 (3)°	Block, colourless
V = 1132.43 (10) Å^3	0.05 × 0.05 × 0.05 mm

Data collection

Bruker APEX-II CCD diffractometer	8622 independent reflections
Radiation source: Incoatec microfocus sealed tube	7018 reflections with $I > 2\sigma(I)$
Multilayer monochromator	R_{int} = 0.076
ϕ and ω scans	θ_{max} = 33.2°, θ_{min} = 2.4°
Absorption correction: multi-scan *SADABS*	h = -14→14
T_{min} = 0.624, T_{max} = 0.746	k = -15→15
98076 measured reflections	l = -18→18

Refinement

Refinement on F^2	0 restraints
Least-squares matrix: full	Hydrogen site location: difference Fourier map
$R[F^2 > 2\sigma(F^2)]$ = 0.038	All H-atom parameters refined
$wR(F^2)$ = 0.108	$w = 1/[\sigma^2(F_o^2) + (0.0502P)^2 + 0.3756P]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 1.03	$(\Delta/\sigma)_{max}$ = 0.001
8622 reflections	$\Delta\rangle_{max}$ = 0.72 e Å^{-3}
393 parameters	$\Delta\rangle_{min}$ = -0.32 e Å^{-3}

Special details

Geometry. 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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2) for (AT779_a)

	x	y	z	U_{iso}*/U_{eq}
Cl1	0.18856 (4)	0.86447 (3)	-0.32596 (3)	0.03391 (8)
Cl2	0.86397 (3)	0.70162 (3)	1.33615 (2)	0.02479 (6)

O1	0.49955 (9)	0.63035 (8)	0.33302 (7)	0.02356 (15)
O2	0.53636 (9)	0.73994 (8)	0.63756 (7)	0.02349 (15)
N1	0.26026 (10)	0.59243 (9)	0.13867 (8)	0.02003 (16)
N2	0.35064 (10)	0.57177 (9)	0.43222 (8)	0.01933 (16)
N3	0.71612 (10)	0.90883 (9)	0.83458 (8)	0.02079 (16)
N4	0.64550 (10)	0.84035 (9)	0.53180 (8)	0.01992 (16)
C1	0.38375 (11)	0.57481 (9)	0.33404 (8)	0.01746 (16)
C2	0.27718 (11)	0.50423 (9)	0.21996 (8)	0.01816 (17)
C3	0.12583 (12)	0.47152 (11)	0.23226 (10)	0.02250 (19)
C4	0.13679 (12)	0.41255 (11)	0.33759 (10)	0.0235 (2)
C5	0.21850 (12)	0.51092 (12)	0.44591 (10)	0.0242 (2)
C6	0.29475 (10)	0.55063 (10)	0.04487 (9)	0.01789 (17)
C7	0.27106 (10)	0.62982 (9)	-0.04509 (8)	0.01693 (16)
C8	0.19378 (11)	0.74555 (10)	-0.03632 (9)	0.01876 (17)
C9	0.16879 (12)	0.81836 (10)	-0.12209 (9)	0.02080 (18)
C10	0.22363 (12)	0.77513 (11)	-0.21686 (9)	0.02204 (19)
C11	0.30327 (12)	0.66288 (11)	-0.22693 (9)	0.02254 (19)
C12	0.32523 (11)	0.58945 (10)	-0.14103 (9)	0.01983 (18)
C13	0.65198 (12)	0.95699 (10)	0.73005 (9)	0.02065 (18)
C14	0.60782 (11)	0.83618 (10)	0.62842 (8)	0.01821 (17)
C15	0.72915 (14)	0.94888 (11)	0.51208 (10)	0.0250 (2)
C16	0.72167 (14)	1.07926 (11)	0.59285 (10)	0.0265 (2)
C17	0.76090 (14)	1.05830 (11)	0.71544 (10)	0.0256 (2)
C18	0.63292 (11)	0.88796 (9)	0.89570 (9)	0.01793 (17)
C19	0.68957 (10)	0.83895 (9)	1.00261 (8)	0.01680 (16)
C20	0.59678 (11)	0.82147 (10)	1.07020 (9)	0.01823 (17)
C21	0.64863 (11)	0.77754 (10)	1.17290 (9)	0.01952 (17)
C22	0.79532 (11)	0.75252 (10)	1.20665 (9)	0.01847 (17)
C23	0.88983 (11)	0.76617 (10)	1.13971 (9)	0.01942 (17)
C24	0.83608 (11)	0.80986 (10)	1.03787 (9)	0.01875 (17)
H1	0.3158 (16)	0.4274 (15)	0.1935 (13)	0.020 (3)*
H2	0.0675 (17)	0.4115 (16)	0.1606 (14)	0.025 (4)*
H3	0.0751 (18)	0.5525 (18)	0.2417 (15)	0.034 (4)*
H4	0.1886 (19)	0.3279 (18)	0.3284 (15)	0.036 (4)*
H5	0.0374 (19)	0.3872 (17)	0.3396 (14)	0.032 (4)*
H6	0.2496 (16)	0.4657 (15)	0.5111 (13)	0.023 (4)*
H7	0.1550 (17)	0.5793 (16)	0.4662 (14)	0.027 (4)*
H8	0.4111 (18)	0.6126 (16)	0.4934 (14)	0.026 (4)*
H9	0.3353 (17)	0.4617 (16)	0.0269 (14)	0.025 (4)*
H10	0.1591 (17)	0.7778 (16)	0.0317 (14)	0.027 (4)*

H11	0.1137 (16)	0.8932 (15)	-0.1186 (13)	0.024 (4)*
H12	0.3439 (18)	0.6390 (16)	-0.2891 (15)	0.030 (4)*
H13	0.3783 (18)	0.5096 (16)	-0.1490 (14)	0.028 (4)*
H14	0.5628 (16)	0.9912 (14)	0.7324 (12)	0.018 (3)*
H15	0.757 (2)	1.1420 (19)	0.7707 (16)	0.040 (5)*
H16	0.866 (2)	1.0213 (18)	0.7320 (15)	0.037 (4)*
H17	0.799 (2)	1.1468 (19)	0.5891 (16)	0.039 (5)*
H18	0.617 (2)	1.1102 (19)	0.5709 (16)	0.042 (5)*
H19	0.8298 (18)	0.9265 (16)	0.5214 (14)	0.029 (4)*
H20	0.692 (2)	0.9605 (18)	0.4322 (16)	0.038 (5)*
H21	0.6154 (18)	0.7729 (17)	0.4750 (15)	0.031 (4)*
H22	0.5291 (18)	0.9022 (16)	0.8755 (14)	0.028 (4)*
H23	0.4935 (17)	0.8377 (16)	1.0453 (14)	0.027 (4)*
H24	0.5820 (17)	0.7653 (16)	1.2167 (14)	0.028 (4)*
H25	0.9924 (17)	0.7448 (16)	1.1640 (14)	0.026 (4)*
H26	0.8956 (19)	0.8222 (17)	0.9891 (15)	0.036 (4)*

Atomic displacement parameters (Å^2) for (AT779_a)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.04414 (17)	0.03297 (15)	0.02917 (14)	0.00038 (12)	0.01019 (12)	0.01661 (11)
Cl2	0.02810 (13)	0.02813 (13)	0.01942 (11)	0.00626 (9)	0.00693 (9)	0.00717 (9)
O1	0.0224 (4)	0.0265 (4)	0.0204 (3)	-0.0061 (3)	0.0061 (3)	0.0016 (3)
O2	0.0260 (4)	0.0229 (3)	0.0204 (3)	-0.0046 (3)	0.0057 (3)	0.0030 (3)
N1	0.0248 (4)	0.0173 (3)	0.0167 (4)	0.0021 (3)	0.0034 (3)	0.0032 (3)
N2	0.0187 (4)	0.0214 (4)	0.0162 (4)	-0.0036 (3)	0.0022 (3)	0.0036 (3)
N3	0.0217 (4)	0.0225 (4)	0.0163 (4)	0.0005 (3)	0.0030 (3)	0.0029 (3)
N4	0.0237 (4)	0.0176 (4)	0.0172 (4)	-0.0019 (3)	0.0050 (3)	0.0017 (3)
C1	0.0188 (4)	0.0154 (4)	0.0169 (4)	0.0008 (3)	0.0032 (3)	0.0026 (3)
C2	0.0202 (4)	0.0153 (4)	0.0171 (4)	0.0015 (3)	0.0025 (3)	0.0024 (3)
C3	0.0184 (4)	0.0241 (5)	0.0219 (5)	-0.0002 (4)	0.0003 (4)	0.0049 (4)
C4	0.0185 (4)	0.0233 (5)	0.0276 (5)	-0.0034 (4)	0.0022 (4)	0.0079 (4)
C5	0.0221 (5)	0.0292 (5)	0.0220 (5)	-0.0050 (4)	0.0057 (4)	0.0070 (4)
C6	0.0160 (4)	0.0171 (4)	0.0182 (4)	0.0000 (3)	0.0019 (3)	0.0020 (3)
C7	0.0149 (4)	0.0173 (4)	0.0163 (4)	-0.0012 (3)	0.0018 (3)	0.0015 (3)
C8	0.0182 (4)	0.0194 (4)	0.0170 (4)	0.0004 (3)	0.0032 (3)	0.0022 (3)
C9	0.0206 (4)	0.0185 (4)	0.0217 (4)	0.0007 (3)	0.0031 (3)	0.0041 (3)
C10	0.0234 (5)	0.0216 (4)	0.0202 (4)	-0.0045 (4)	0.0030 (4)	0.0062 (3)
C11	0.0243 (5)	0.0238 (5)	0.0195 (4)	-0.0027 (4)	0.0077 (4)	0.0023 (4)
C12	0.0194 (4)	0.0192 (4)	0.0194 (4)	0.0002 (3)	0.0051 (3)	0.0009 (3)

C13	0.0235 (5)	0.0192 (4)	0.0167 (4)	0.0018 (3)	0.0024 (3)	0.0021 (3)
C14	0.0183 (4)	0.0180 (4)	0.0164 (4)	0.0017 (3)	0.0022 (3)	0.0027 (3)
C15	0.0317 (5)	0.0202 (4)	0.0231 (5)	-0.0052 (4)	0.0090 (4)	0.0027 (4)
C16	0.0331 (6)	0.0195 (4)	0.0249 (5)	-0.0015 (4)	0.0046 (4)	0.0050 (4)
C17	0.0303 (5)	0.0205 (4)	0.0220 (5)	-0.0034 (4)	0.0020 (4)	0.0023 (4)
C18	0.0174 (4)	0.0148 (4)	0.0191 (4)	0.0011 (3)	0.0026 (3)	0.0010 (3)
C19	0.0157 (4)	0.0145 (4)	0.0189 (4)	0.0000 (3)	0.0039 (3)	0.0018 (3)
C20	0.0155 (4)	0.0166 (4)	0.0218 (4)	0.0005 (3)	0.0053 (3)	0.0018 (3)
C21	0.0194 (4)	0.0180 (4)	0.0220 (4)	0.0011 (3)	0.0083 (3)	0.0025 (3)
C22	0.0204 (4)	0.0164 (4)	0.0181 (4)	0.0014 (3)	0.0048 (3)	0.0031 (3)
C23	0.0158 (4)	0.0206 (4)	0.0218 (4)	0.0015 (3)	0.0044 (3)	0.0053 (3)
C24	0.0164 (4)	0.0195 (4)	0.0211 (4)	0.0007 (3)	0.0060 (3)	0.0049 (3)

Geometric parameters (Å, º) for (AT779_a)

Cl1—C10	1.7389 (11)	C8—H10	0.975 (16)
Cl2—C22	1.7407 (10)	C9—C10	1.3925 (16)
O1—C1	1.2418 (12)	C9—H11	0.933 (15)
O2—C14	1.2377 (13)	C10—C11	1.3856 (16)
N1—C6	1.2733 (13)	C11—C12	1.3927 (15)
N1—C2	1.4606 (13)	C11—H12	0.934 (17)
N2—C1	1.3318 (13)	C12—H13	0.967 (16)
N2—C5	1.4645 (14)	C13—C17	1.5340 (16)
N2—H8	0.844 (17)	C13—C14	1.5375 (14)
N3—C18	1.2707 (14)	C13—H14	0.925 (15)
N3—C13	1.4553 (13)	C15—C16	1.5107 (16)
N4—C14	1.3367 (13)	C15—H19	0.968 (16)
N4—C15	1.4626 (14)	C15—H20	0.984 (19)
N4—H21	0.863 (17)	C16—C17	1.5146 (16)
C1—C2	1.5319 (14)	C16—H17	1.027 (19)
C2—C3	1.5289 (15)	C16—H18	1.033 (19)
C2—H1	0.909 (15)	C17—H15	0.988 (19)
C3—C4	1.5184 (16)	C17—H16	1.054 (18)
C3—H2	0.990 (16)	C18—C19	1.4735 (14)
C3—H3	0.966 (17)	C18—H22	0.972 (16)
C4—C5	1.5152 (16)	C19—C20	1.3956 (14)
C4—H4	1.003 (18)	C19—C24	1.3986 (14)
C4—H5	0.987 (17)	C20—C21	1.3956 (15)
C5—H6	0.987 (15)	C20—H23	0.975 (16)
C5—H7	0.966 (16)	C21—C22	1.3875 (14)

C6—C7	1.4747 (14)	C21—H24	0.956 (16)
C6—H9	1.000 (16)	C22—C23	1.3932 (14)
C7—C12	1.3973 (14)	C23—C24	1.3874 (14)
C7—C8	1.4018 (14)	C23—H25	0.982 (16)
C8—C9	1.3859 (14)	C24—H26	0.952 (18)
C6—N1—C2	117.96 (9)	C12—C11—H12	121.0 (10)
C1—N2—C5	127.49 (9)	C11—C12—C7	120.71 (10)
C1—N2—H8	116.2 (11)	C11—C12—H13	118.9 (10)
C5—N2—H8	116.3 (11)	C7—C12—H13	120.4 (10)
C18—N3—C13	118.00 (9)	N3—C13—C17	109.07 (9)
C14—N4—C15	126.53 (9)	N3—C13—C14	108.27 (8)
C14—N4—H21	116.4 (11)	C17—C13—C14	113.83 (9)
C15—N4—H21	117.1 (11)	N3—C13—H14	110.2 (9)
O1—C1—N2	121.79 (9)	C17—C13—H14	113.0 (9)
O1—C1—C2	119.59 (9)	C14—C13—H14	102.2 (9)
N2—C1—C2	118.60 (9)	O2—C14—N4	122.22 (9)
N1—C2—C3	107.95 (8)	O2—C14—C13	119.31 (9)
N1—C2—C1	108.12 (8)	N4—C14—C13	118.46 (9)
C3—C2—C1	113.04 (8)	N4—C15—C16	111.78 (9)
N1—C2—H1	110.8 (9)	N4—C15—H19	109.5 (10)
C3—C2—H1	109.0 (9)	C16—C15—H19	110.1 (10)
C1—C2—H1	108.0 (9)	N4—C15—H20	110.7 (11)
C4—C3—C2	111.25 (9)	C16—C15—H20	108.5 (11)
C4—C3—H2	111.8 (9)	H19—C15—H20	106.2 (14)
C2—C3—H2	109.8 (9)	C15—C16—C17	108.89 (10)
C4—C3—H3	107.9 (10)	C15—C16—H17	109.0 (10)
C2—C3—H3	109.1 (10)	C17—C16—H17	106.8 (10)
H2—C3—H3	106.9 (13)	C15—C16—H18	108.8 (11)
C5—C4—C3	110.08 (9)	C17—C16—H18	110.0 (10)
C5—C4—H4	110.7 (10)	H17—C16—H18	113.3 (15)
C3—C4—H4	108.6 (10)	C16—C17—C13	111.00 (9)
C5—C4—H5	112.3 (10)	C16—C17—H15	111.0 (11)
C3—C4—H5	108.8 (10)	C13—C17—H15	106.6 (11)
H4—C4—H5	106.3 (14)	C16—C17—H16	107.2 (10)
N2—C5—C4	112.05 (9)	C13—C17—H16	109.2 (10)
N2—C5—H6	107.0 (9)	H15—C17—H16	111.9 (14)
C4—C5—H6	110.4 (9)	N3—C18—C19	121.24 (9)
N2—C5—H7	109.8 (10)	N3—C18—H22	123.0 (10)
C4—C5—H7	109.7 (10)	C19—C18—H22	115.7 (10)

H6—C5—H7	107.8 (13)	C20—C19—C24	119.23 (9)
N1—C6—C7	121.18 (9)	C20—C19—C18	119.99 (9)
N1—C6—H9	122.2 (9)	C24—C19—C18	120.79 (9)
C7—C6—H9	116.6 (9)	C21—C20—C19	121.00 (9)
C12—C7—C8	119.07 (9)	C21—C20—H23	118.6 (9)
C12—C7—C6	120.03 (9)	C19—C20—H23	120.3 (9)
C8—C7—C6	120.90 (9)	C22—C21—C20	118.26 (9)
C9—C8—C7	120.89 (9)	C22—C21—H24	122.8 (10)
C9—C8—H10	118.7 (9)	C20—C21—H24	119.0 (10)
C7—C8—H10	120.4 (9)	C21—C22—C23	122.04 (9)
C8—C9—C10	118.62 (10)	C21—C22—Cl2	119.25 (8)
C8—C9—H11	121.4 (10)	C23—C22—Cl2	118.71 (8)
C10—C9—H11	119.9 (10)	C24—C23—C22	118.76 (9)
C11—C10—C9	121.95 (10)	C24—C23—H25	120.6 (9)
C11—C10—Cl1	119.51 (9)	C22—C23—H25	120.6 (9)
C9—C10—Cl1	118.54 (9)	C23—C24—C19	120.68 (9)
C10—C11—C12	118.74 (10)	C23—C24—H26	122.6 (11)
C10—C11—H12	120.2 (10)	C19—C24—H26	116.7 (11)
C5—N2—C1—O1	179.60 (10)	C18—N3—C13—C17	142.13 (10)
C5—N2—C1—C2	-2.10 (16)	C18—N3—C13—C14	-93.51 (11)
C6—N1—C2—C3	-116.91 (10)	C15—N4—C14—O2	179.89 (11)
C6—N1—C2—C1	120.49 (10)	C15—N4—C14—C13	1.44 (16)
O1—C1—C2—N1	-46.30 (12)	N3—C13—C14—O2	48.87 (13)
N2—C1—C2—N1	135.36 (9)	C17—C13—C14—O2	170.34 (10)
O1—C1—C2—C3	-165.74 (9)	N3—C13—C14—N4	-132.63 (10)
N2—C1—C2—C3	15.93 (13)	C17—C13—C14—N4	-11.17 (14)
N1—C2—C3—C4	-164.51 (9)	C14—N4—C15—C16	-22.11 (16)
C1—C2—C3—C4	-44.97 (12)	N4—C15—C16—C17	51.07 (13)
C2—C3—C4—C5	60.43 (12)	C15—C16—C17—C13	-61.75 (13)
C1—N2—C5—C4	17.35 (16)	N3—C13—C17—C16	162.47 (9)
C3—C4—C5—N2	-45.34 (13)	C14—C13—C17—C16	41.45 (13)
C2—N1—C6—C7	175.65 (8)	C13—N3—C18—C19	179.88 (8)
N1—C6—C7—C12	172.49 (9)	N3—C18—C19—C20	177.69 (9)
N1—C6—C7—C8	-7.85 (15)	N3—C18—C19—C24	-2.09 (15)
C12—C7—C8—C9	1.07 (14)	C24—C19—C20—C21	1.00 (15)
C6—C7—C8—C9	-178.59 (9)	C18—C19—C20—C21	-178.80 (9)

C7—C8—C9—C10	-0.77 (15)	C19—C20—C21—C22	0.45 (15)
C8—C9—C10—C11	-0.71 (16)	C20—C21—C22—C23	-1.93 (15)
C8—C9—C10—Cl1	178.54 (8)	C20—C21—C22—Cl2	178.41 (7)
C9—C10—C11—C12	1.83 (16)	C21—C22—C23—C24	1.90 (15)
Cl1—C10—C11—C12	-177.41 (8)	Cl2—C22—C23—C24	-178.44 (8)
C10—C11—C12—C7	-1.50 (16)	C22—C23—C24—C19	-0.37 (15)
C8—C7—C12—C11	0.09 (15)	C20—C19—C24—C23	-1.04 (15)
C6—C7—C12—C11	179.75 (9)	C18—C19—C24—C23	178.75 (9)

Hydrogen-bond geometry (Å, º) for (AT779_a)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C3—H3···Cl2^{i}	0.966 (17)	2.875 (17)	3.7324 (12)	148.5 (13)
C4—H4···O2^{ii}	1.003 (18)	2.657 (18)	3.4570 (14)	136.8 (13)
N2—H8···O2	0.844 (17)	2.049 (17)	2.8833 (12)	169.9 (15)
C11—H12···O2^{iii}	0.934 (17)	2.544 (17)	3.2843 (13)	136.3 (13)
C16—H18···N4^{iv}	1.033 (19)	2.584 (19)	3.5971 (16)	166.7 (14)
C15—H19···Cl2^{iii}	0.968 (16)	2.981 (16)	3.4692 (12)	112.5 (11)
C15—H20···Cl1^{v}	0.984 (19)	2.818 (18)	3.5006 (12)	127.1 (13)
N4—H21···O1	0.863 (17)	2.081 (18)	2.9299 (12)	167.4 (16)
C21—H24···O1^{vi}	0.956 (16)	2.445 (16)	3.2928 (13)	147.7 (13)

Symmetry codes: (i) *x*-1, *y*, *z*-1; (ii) -*x*+1, -*y*+1, -*z*+1; (iii) *x*, *y*, *z*-1; (iv) -*x*+1, -*y*+2, -*z*+1; (v) -*x*+1, -*y*+2, -*z*; (vi) *x*, *y*, *z*+1.

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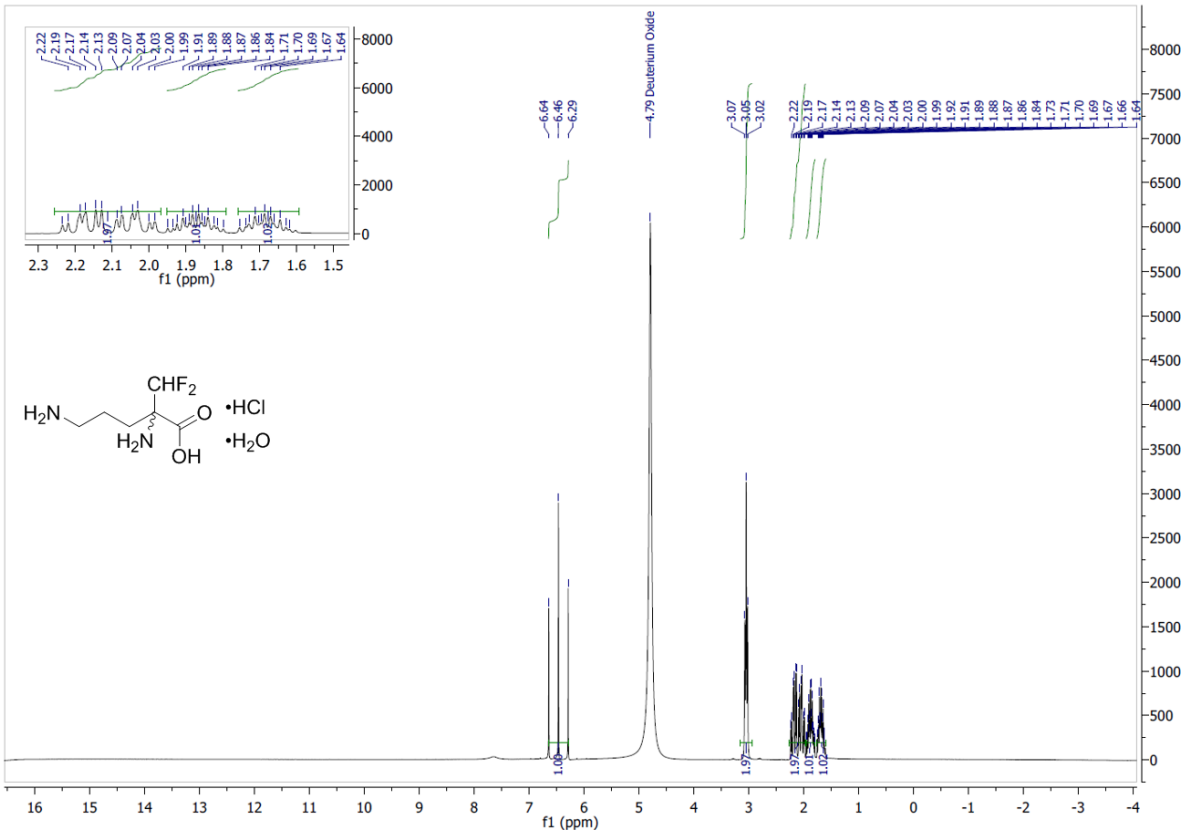
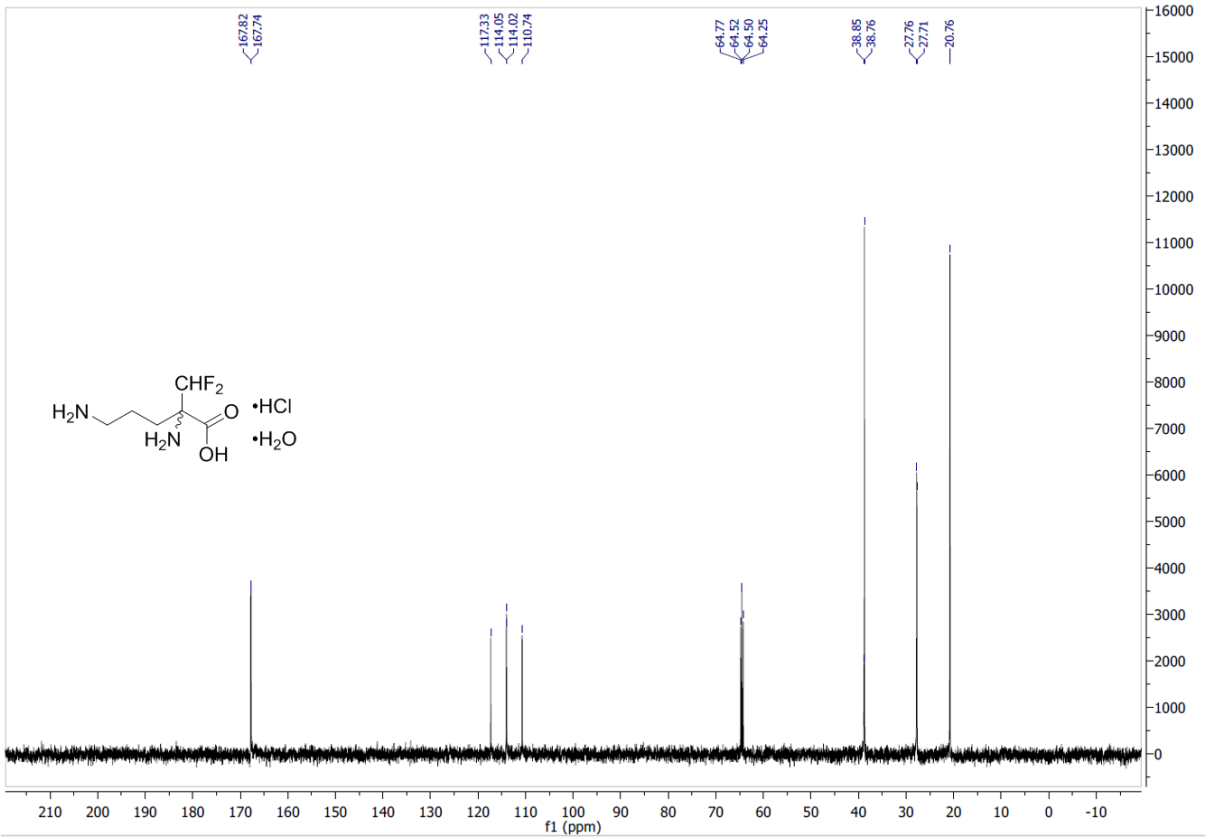
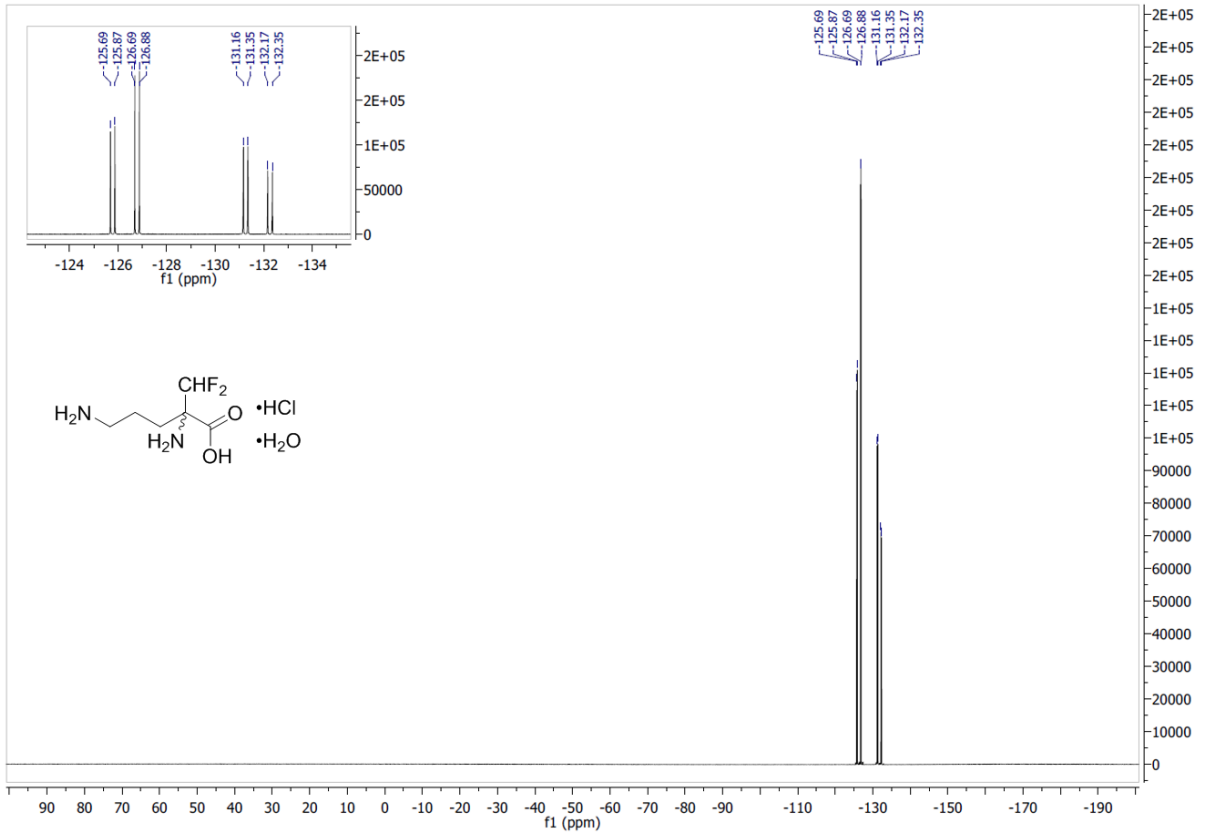
5. 1H-NMR and 13C-NMR Spectra

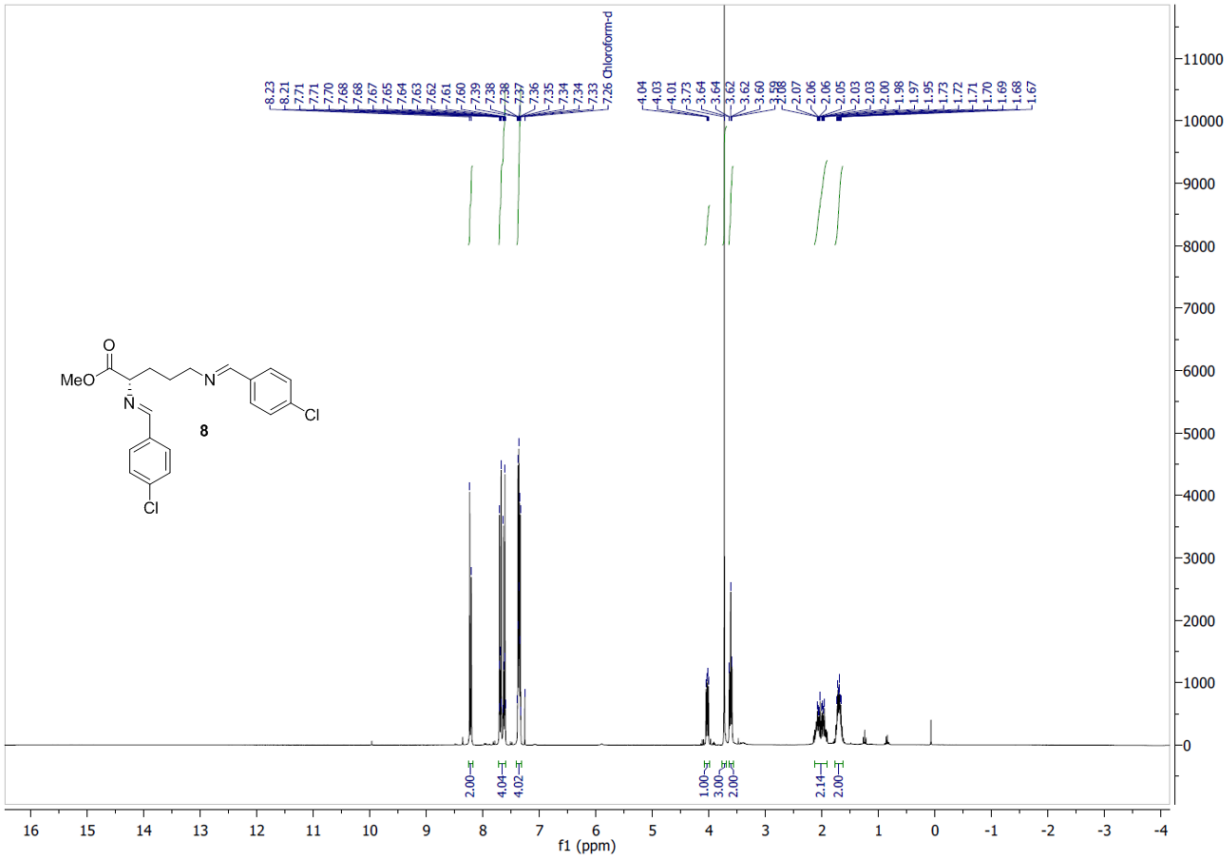
Eflornithine hydrochloride monohydrate (1):

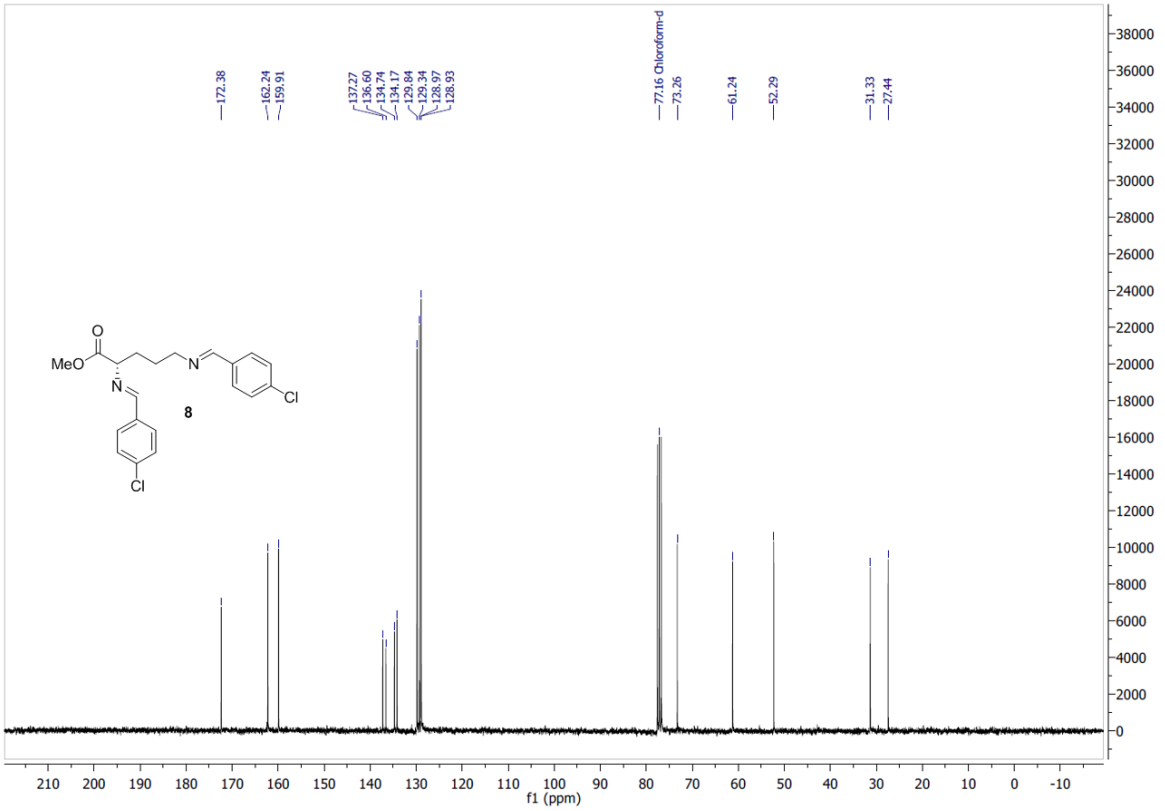



167.82
167.74
117.33
114.05
114.02
110.74
64.77
64.52
64.50
64.25
38.85
38.76
27.76
27.71
20.76
CHF2
H2N
O
•HCl
H2N
OH
•H2O
f1 (ppm)


125.69
125.87
126.69
126.88
131.16
131.35
132.17
132.35
f1 (ppm)
CHF2
H2N
O
•HCl
H2N
OH
•H2O
f1 (ppm)

(S)-2,5-bis(((E)-4-chlorobenzylidene)amino)pentanoate (8):





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