Electronic Supplementary Material (ESI) for ChemComm.


Supporting Information for

# Understanding Viral Neuraminidase Inhibition by Substituted Difluorosialic Acids – Supplementary Information

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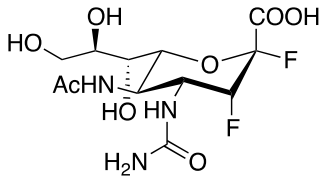
**Content**

# General information

Unless otherwise stated, all reagents were obtained from commercial suppliers and were used without further purification. Column chromatography was performed with silica gel (230-400 mesh). TLC was performed on pre-coated silica plates and visualized using UV light and/or by applying a solution of cer-ammonium-molybdate in $H_2SO_4$ followed by heating. Moisture sensitive reactions were carried out under an atmosphere of dry argon. MeOH was distilled over magnesium. All NMR spectra were acquired on Bruker AV-300, Bruker AV-400INV or Bruker AV-400DIR. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane ($^1$H NMR) using the residual solvent signal as reference, or relative to $CFCl_3$ ($^{19}$F NMR) using TFA as reference. The fluorine concentrations were measured with an Orion Fluoride Ion Selective Electrode (ISE) from Thermo Scientific calibrated with NaF standard solution from Thermo Scientific, using Logger Pro 2.2.1 as software.

**4-Ureido-2eq3ax-difluorosialic acid sodium salt (7)**

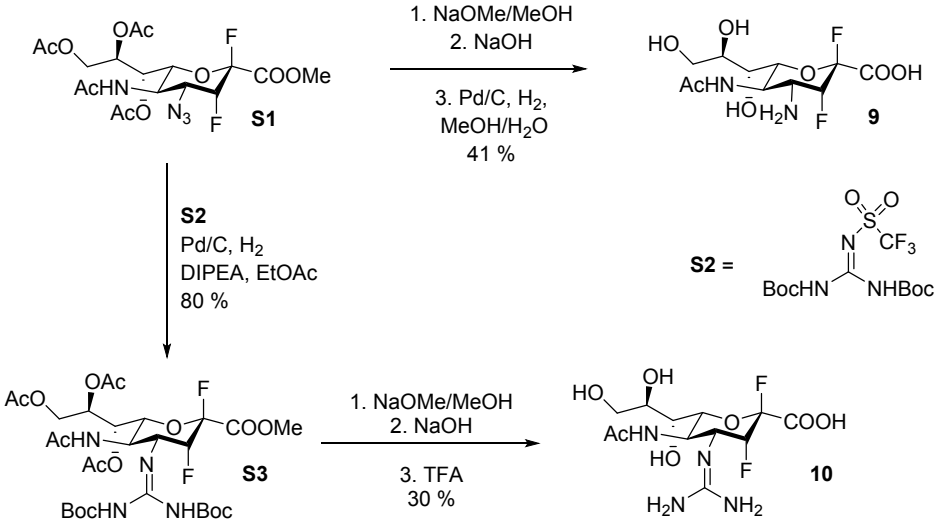



To a solution of 4-amino-2eq3ax-difluorosialic acid-methyl ester[7] (50 mg, 0.146 mmol) in acetonitrile (1.5 mL) was added TMS-isocyanate (30 μL, 0.219 mmol) and the solution heated at 80°C for 2h, after which a white precipitate had formed. The mixture concentrated to give a sticky residue which was triturated with ether containing a few drops of methanol. Solids were filtered and dried under high vac to give 4-Ureido-2eq3ax-difluorosialic acid-methyl ester as a colourless solid (50 mg, 0.117 mmol, 89%). $R_f$ = 0.3 (EtOAc/MeOH/$H_2O$ 12:2:1). $^1$H NMR (400 MHz, MeOD): δ = 7.99 (d, *J* = 8.7 Hz, 1H, NH), 5.03 (dd, *J* = 50.0 Hz, 2.3 Hz, 1H), 4.43 – 4.26 (m, 2H), 3.97 – 3.86 (m, 4H), 3.82 – 3.75 (m, 2H), 3.64 (dd, *J* = 12.1, 5.8 Hz, 1H), 3.54 – 3.48 (m, 1H), 1.96 (s, 3H) ppm. $^{13}$C NMR (100 MHz, MeOD); δ = 173.28, 172.16 (d, *J* = 13 Hz), 159.94, 88.25 (d, *J* = 18 Hz), 87.33 (dd, *J* = 184 Hz, *J* = 18 Hz), 74.33 (d, *J* = 3 Hz), 69.96, 68.21, 63.45, 52.55, 50.91 (dd, *J* = 5 Hz, *J* = 1 Hz), 45.34 (d, *J* = 3 Hz), 21.27 ppm. ESI-MS (pos): *m/z* (%) = 386.3 (100) $[M+H]^+$.

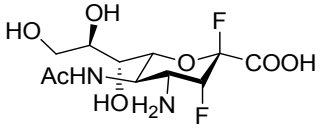
To the 4-ureido-2eq3ax-difluorosialic acid-methyl ester (14 mg, 0.036 mmol) in methanol (0.5 mL) was added 6 M NaOH solution (6 μL 0.036 mmol) and the solution stirred at RT for 1 h. The solution was concentrated and dried under high vac to give the title compound (**7**) as an off white solid (13 mg, 0.033 mmol, 93%). $^1$H NMR (400 MHz, MeOD); δ = 5.15 (dt, *J* = 51.9 Hz, *J* = 2.1 Hz, 1H), 4.28 (dd, *J* = 31.0 Hz, *J* = 11.4 Hz, 1H), 4.15 (t, *J* = 10.8 Hz, 1H), 3.88 (ddd, *J* = 8.6 Hz, *J* = 5.6 Hz, *J* = 2.6 Hz, 1H), 3.82 (dd, *J* = 11.4 Hz, *J* = 2.6 Hz, 1H), 3.77 (d, *J* = 10.4 Hz,

1H), 3.62 (dd, $J$ = 11.4 Hz, $J$ = 5.7 Hz, 1H), 3.54 (d, $J$ = 12 Hz, $J$ = 4 Hz, 1H), 1.95 (s, 3H). ESI-MS (pos): *m/z* (%) = 372.0 (100) $[M+H]^+$.

# Synthesis of the diaxial-DFSAs



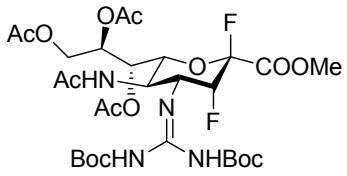

**4-Amino-2ax3ax-difluorosialic acid (9)**



The protected 4-azido-2ax3ax-difluorosialic acid **S1** (218 mg, 0.437 mmol), was dissolved in dry MeOH (15 mL) under Ar-atmosphere. NaOMe (5.4 M in MeOH, 5 drops) were added and the mixture was stirred at room temperature for 18 h. NaOH (1 M, 0.5 mL) was added and the solution was stirred for 2 h. Dowex 50WX8 (ion exchanger, $H^*$, strong) is added, the suspension stirred for 10 minutes, the resin was filtered off and washed extensively with MeOH. The filtrates are combined and the solvent was removed yielding the deprotected azide (approx. 140 mg), that is used without any further purification. The azide is dissolved in MeOH/$H_2O$ (1:1, 20 mL), Pd/C (10 wt%, 15 mg) was added and the mixture was degassed (evacuated and filled with Ar). The reaction flask was evacuated and filled with $H_2$ (balloon) and the reaction was stirred at room temperature for 18 h. Pd/C was filtered off and washed extensively with MeOH. The filtrates were combined, the solvent was removed *in vacuo* and the residue was purified by flash-chromatography on silica gel (EtOAc/MeOH/$H_2O$ 7:2:1 + 1 % AcOH). The title compound **9** was obtained as the acetate salt (66 mg, 0.201 mmol, 46%). $R_f$ = 0.05 (EtOAc/MeOH/$H_2O$ 7:2:1). $^1$H NMR (400 MHz,$D_2O$): δ = 5.24 (d, $J_{H,F}$ = 49.6 Hz, $J_{3,4}$ = 1.4 Hz, 1H, H-3), 4.53 (t, $J_{4,5,6}$ = 11.0 Hz, 1H, H-5), 4.30 (d, $J_{5,6}$ = 10.5 Hz, 1H, H-6), 4.03 (bdd, $J_{H,F}$ = 30.2, $J_{4,5}$ = 11.0 Hz,

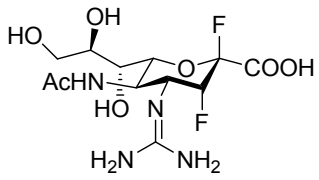
1H, H-4), 3.95–3.86 (m, 2H, H-8, H-9a), 3.68 (dd, $J$ = 12.4 Hz, $J_{8,9b}$ = 6.5 Hz, 1H, H-9b), 3.60 (d, $J_{7,8}$ = 9.3 Hz, 1H, H-7), 1.95 (s, 3H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, D2O): δ = 22.4 (NHAc), 43.7 (C-5), 50.8 (d, $J$ = 18.4 Hz, C-4), 63.3 (C-9), 68.1 (C-7), 69.8 (C-8), 72.1 (C-6), 85.3 (dd, $J$ = 46.7, $J$ = 178.1 Hz, C-3), 105.4 (dd, $J$ =28.9, $J$ = 225.2 Hz, C-2), 169.2 (d, $J$ = 23.1 Hz, C-1), 175.2 (CO) ppm. $^{19}$F NMR (282 MHz, $D_2O$) δ = –123.69 (d, $J$ = 12.9 Hz, 1F, F-2), -207.99 (ddd, $J$ = 47.7, $J$ = 30.2, $J$ = 12.9 Hz, 1F, F-3) ppm. ESI-MS (pos): *m/z* (%) = 351.2 (100) $[M+Na]^+$. ESI-MS (neg): *m/z* (%) = 327 (100) $[M–H]^–$.

**7,8,9-Tri-*O*-acetyl-4-(*N,N*-diboc-guanidino)-2ax3ax-difluorosialic acid-methyl ester (S3)**




The protected 4-azido-2ax3ax-difluorosialic acid **S1** (300 mg 0.607 mmol), the di-boc-guanidine-triflate (**S2**, 280 mg, 0.715 mmol) and DIPEA (160 µL, 0.913 mmol) were dissolved in EtOAc (HPLC. 15 mL). Pd/C (10 wt%, 60 mg) was added and the mixture was degassed (evacuated and filled with Ar). The flask was evacuated and filled with $H_2$ (balloon) and the reaction was stirred for 22 h at room temperature. The Pd/C was filtered off and washed with acetone. The filtrates were combined and the solvent was removed *in vacu*o. The crude product was purified by flash chromatography ($CH_2Cl_2$/acetone 15:1) giving the title compound as a colorless foam (334 mg, 0.470 mmol, 77%). $R_f$ = 0.30 ($CH_2Cl_2$/acetone 15:1). $^1$H NMR (300 MHz, $CDCl_3$): δ = 11.33 (s, 1H, NH), 8.92 (d, $J$ = 7.5 Hz, 1H, NH), 6.31 (d, $J$ = 8.8 Hz, 1H, NH), 5.31 (d, $J$ = 28.2 Hz, 2H, H-4, H-5), 5.04 (d, $J_{H,F}$ = 48.0 Hz, 1H, H-3), 4.87 – 4.61 (m, 1H, H-6), 4.56 – 4.34 (m, 2H, H-8, H-9a), 4.20 (d, $J_{7,8}$ = 10.0 Hz, 1H, H-7), 4.09 (dd, $J$ = 12.2, $J_{8,9b}$ = 6.2 Hz, 1H, H-9b), 3.88 (s, 3H, $OCH_3$), 2.15 (s, 3H, $CH_3$), 2.07 (s, 3H, $CH_3$), 2.05 (s, 3H, $CH_3$), 1.85 (s, 3H, $CH_3$), 1.49 (s, 18H, 6x$CH_3$) ppm. $^{19}$F NMR (282 MHz, $CDCl_3$): δ = -121.36 (d, $J$ = 15.5 Hz, 1F, F-2), -205.08 (ddd, $J$ = 47.4 Hz, $J$ = 31.6 Hz, $J$ = 15.6 Hz, 1F, F-3) ppm. ESI-MS (pos): *m/z* (%) = 733.4 (100) $[M+Na]^+$. ESI-MS (neg): *m/z* (%) = 709 (90) $[M–H]^–$, 745.4 (100) $[M+Cl]^–$.

**4-Guanidino-2ax3ax-difluorosialic acid (10)**



The protected 4-guanidino-DFSA **S3** (300 mg, 0.422) was dissolved in dry MeOH under Ar-atmosphere. NaOMe (5.4 M in MeOH, 10 drops) was added and the reaction was stirred for 16 h at room temperature. NaOH (1 M, 250 µL) was added and the solution was stirred for 1 h. Dowex 50WX8 (ion exchanger, $H^*$, strong) was added, the suspension stirred for 5 minutes, the resin was filtered off and washed extensively with MeOH. The filtrates were combined and the solvent was removed *in vacu*o. The crude product (~ 222 mg) was dissolved in neat TFA (20 mL) at 0 °C and stirred for 2 h. TFA was co-evaporated with toluene and the crude product was purified by flash-chromatography on silica gel (EtOAc/MeOH/$H_2O$ 7:2:1), giving the title compound **10** (65 mg, 0.176 mmol, 42%) as a colorless solid. $R_f$ = 0.15 (EtOAc/MeOH/$H_2O$ 7:2:1). $^1$H NMR (400 MHz, $D_2O$): δ = 5.08 (d, $J_{H,F}$ = 47.6 Hz, 1H, H-3), 4.38 – 4.06 (m, 3H, H-4, H-5 H-6), 3.87 – 3.81 (m, 2H, H-8, H-9a), 3.64-3.55 (m, 2H, H-9b, H-7), 1.99 (s, 3H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, $D_2O$): δ = 22.2 (NHAc), 45.5 (C-5), 52.1 (d, *J* = 19.2 Hz, C-4), 63.4 (C-9), 68.3 (C-7), 69.9 (C-8), 72.2 (C-6), 86.7 (dd, *J* = 47.6, *J* = 176.3 Hz, C-3), 105.9 (dd, *J* = 29.3, *J* = 224.0 Hz, C-2), 157.3 (NC($NH_2$)), 169.6 (d, *J* = 23.3 Hz, C-1), 174.9 (CO) ppm. $^{19}$F NMR (282 MHz, $D_2O$): = δ -123.23 (d, *J* = 12.8 Hz, 1F, F-2), -206.70 (ddd, *J* = 42.8 Hz, *J* = 29.5 Hz, *J* = 12.6 Hz, 1F, F-3). ESI-MS (pos): *m/z* (%) = 371.2 (100) $[M+H]^+$, 393.3 (50) $[M+Na]^+$, 763.4 (90) $[2M+Na]^+$. ESI-MS (neg): *m/z* (%) = 369.2 (100) $[M–H]^–$, 739.3 (90) $[2M–H]^–$.

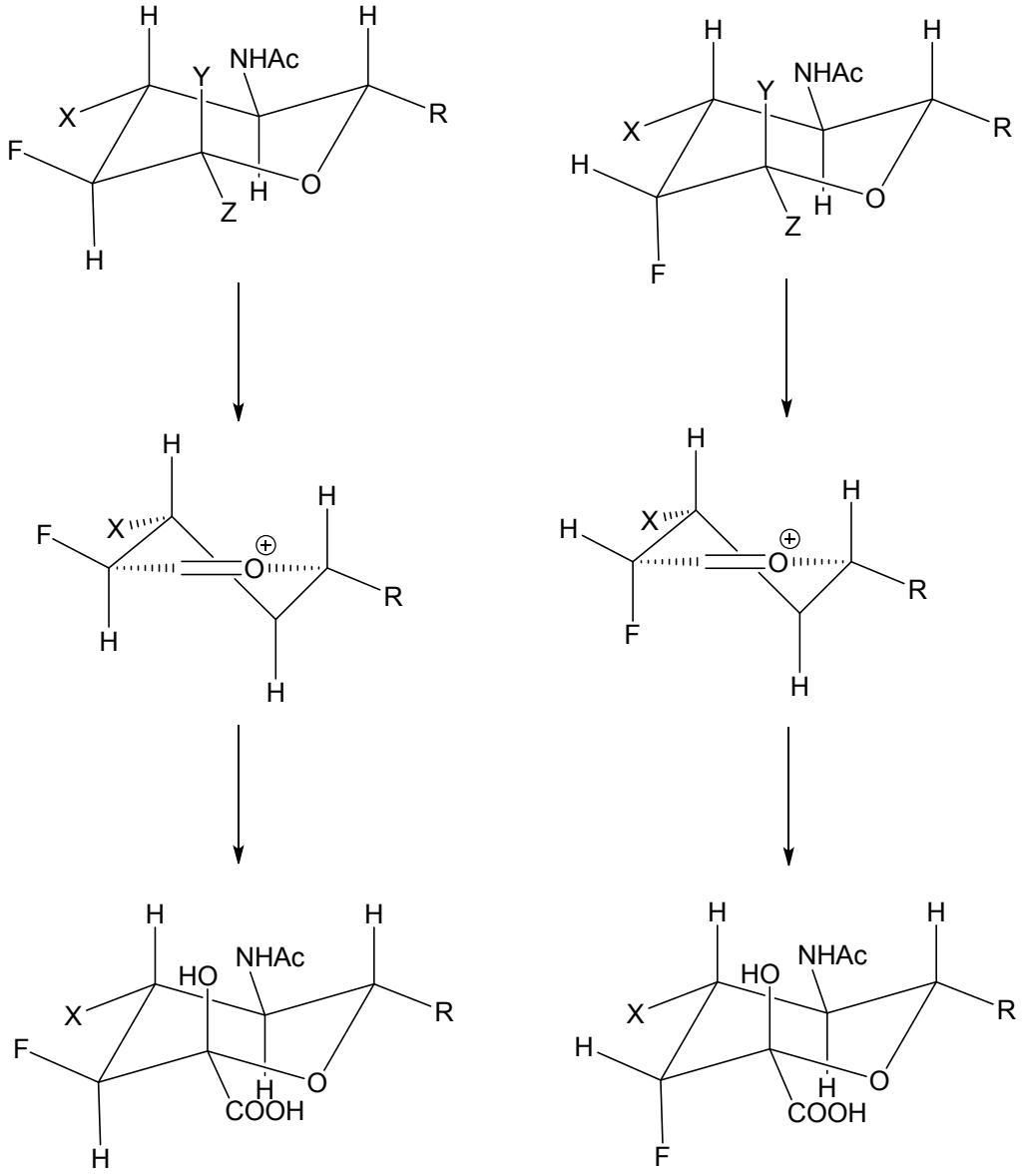
## Experimental procedure for kinetic analysis: complete spontaneous hydrolysis

Solutions of compounds **2**, **3**, **4**, **5** & **6** (1.919 ml, final concentration 5 mM) were prepared in 50 mM phosphate buffer pH 7.08 at 20 °C (pH 7.0 at 50 °C) containing 1 M $NaClO_4$ and incubated at 50°C in parafilmed 1.5 mL screw-top plastic vials with O-ring seals. Aliquots (75 μL) were removed at regular time intervals, diluted 4-fold into the same buffer and frozen immediately. The fluoride concentration was determined at the end of the experiment (4 weeks) using a VWR Symphony fluoride electrode interfaced with Logger Pro 2.2.1 analysis software (Vernier, Inc.). The electrode was calibrated with 10 mM and 0.01 mM standard fluoride solutions in the appropriate buffer containing 1 M $NaClO_4$. First-order rate constants for hydrolysis (*k*) were determined by direct fit of the [$F^-$] versus time data to a first-order rate equation $A_t = A_\infty(1 - e^{-kt}) + \text{offset}$.

## Experimental procedure for the initial rate methodology

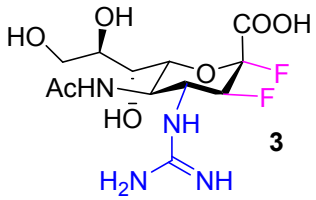
Specifically solutions of compounds **3**, **4**, **5**, **6**, **9**, **10** (0.8 mL at the concentrations of 2.5, 5, 7.5 and 10 mM) & **7** (0.8 mL at the concentrations of 0.5, 1, 1.5 and 2 mM) in 50 mM buffer containing 1 M $NaClO_4$ were prepared and incubated at 50°C in parafilmed 1.5 mL screw-top plastic vials with O-ring seals. The hydrolysis of compound **6** was studied at different pHs using acetate buffer pH 5 (50 °C), phosphate buffer pH 7 (50 °C), and Tris buffer pH 8.1(50 °C). The buffers were prepared at 20°C and the following temperature coefficients were used to calculate the pH at 50°C: -0.0002 per °C (acetate buffer), -0.0028 per °C (phosphate buffer), -0.028 per °C (Tris buffer). All other compounds were only studied in phosphate buffer at pH 7. Aliquots (75 μL) were removed at different time intervals, diluted 4-fold into the same buffer and frozen immediately. The fluoride concentration was determined at the end of the experiment (4 weeks) using a VWR Symphony fluoride electrode interfaced with Logger Pro 2.2.1 analysis software (Vernier, Inc.). The electrode was calibrated with 10 mM and 0.01 mM standard fluoride solutions in the appropriate buffer containing 1 M $NaClO_4$. Initial rates at each concentration were determined from a linear fit of the [$F^-$] versus time data. Re-plot of the initial rates versus inactivator concentration allowed the determination of the rate constants for hydrolysis (k) by fit to the equation: rate = k [substrate].

Figure 1. Angular relationship between neuraminic acid substituents

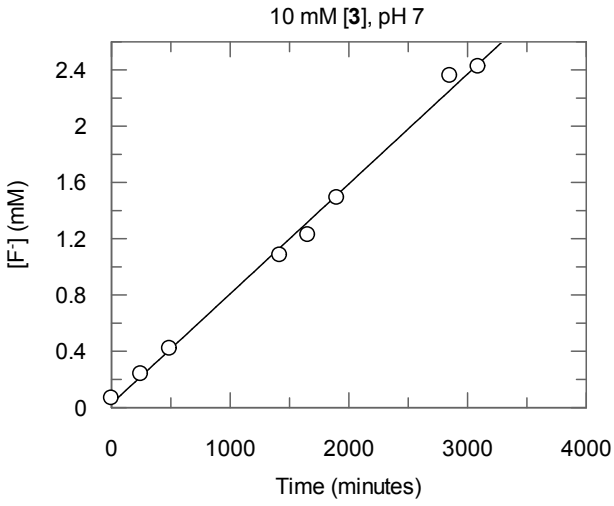



X = OH, $NH_2$, $NHC(NH)NH_2$, $NHC(O)NH_2$
Y = F,H Z = H,F

# Spontaneous Hydrolysis Plots/Results (3, 4, 5, 6, 7, 9, 10)




**3**

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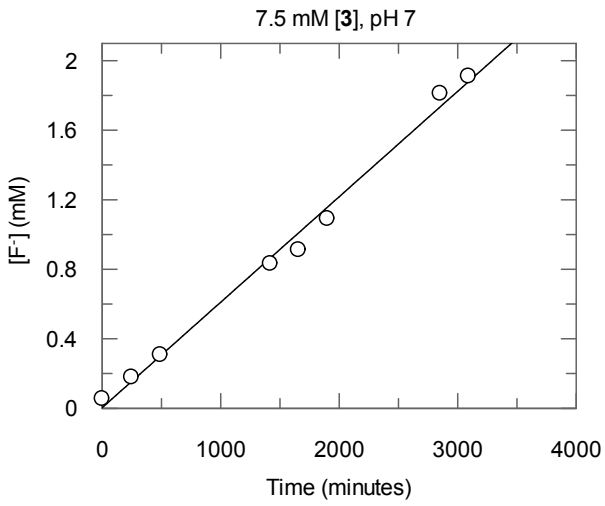


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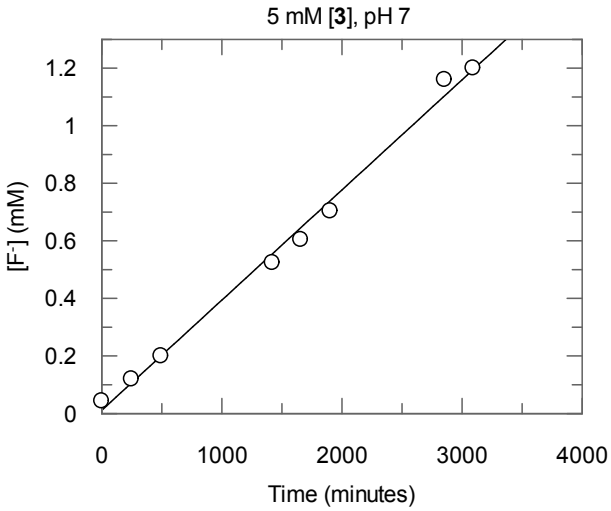


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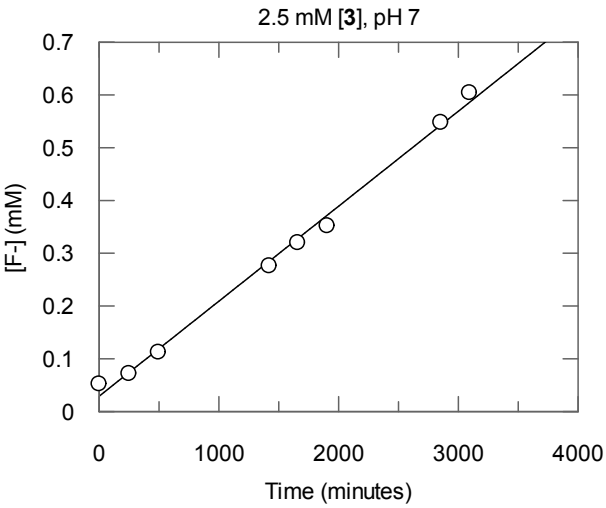


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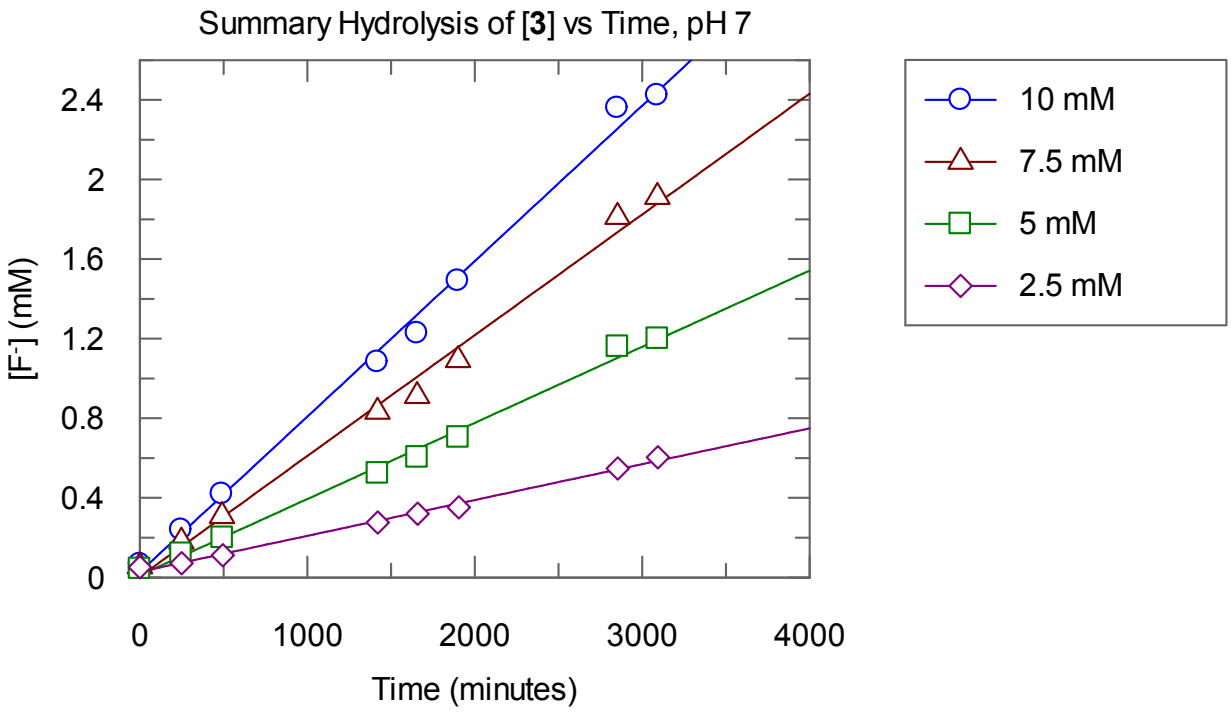


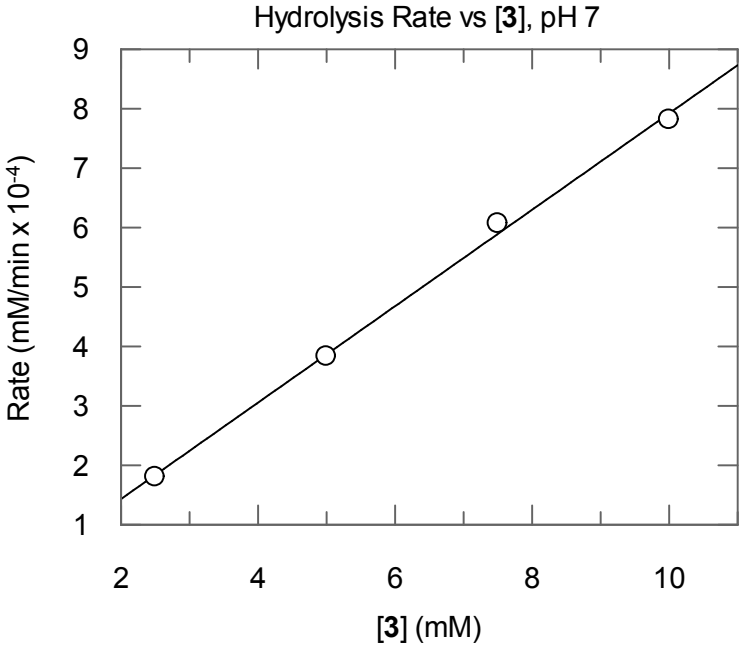


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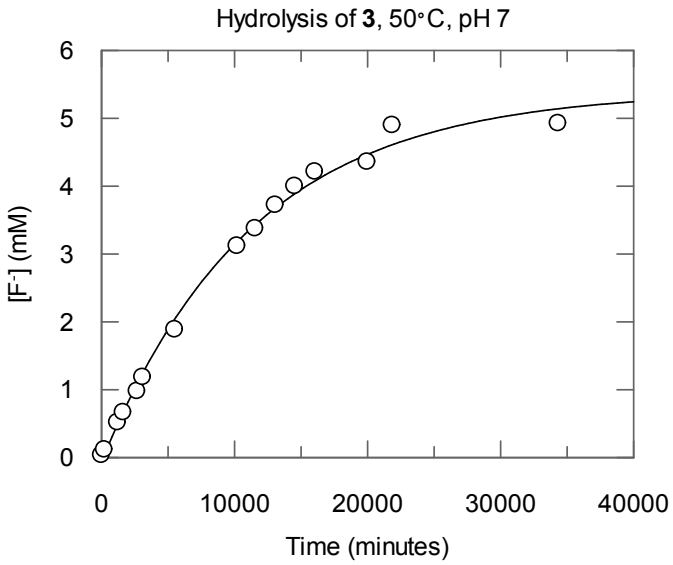


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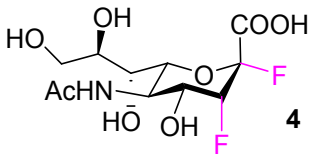
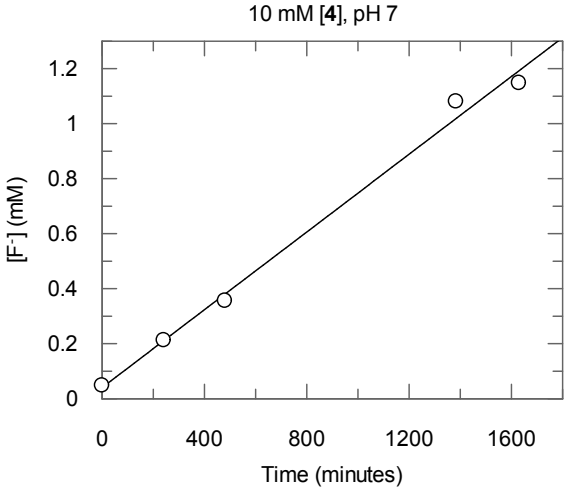



**4**

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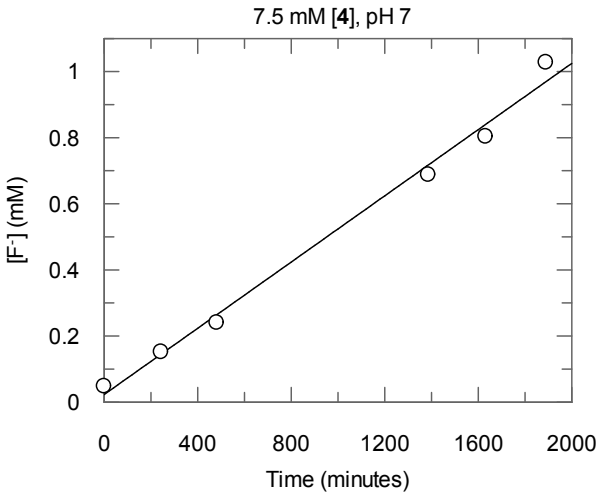


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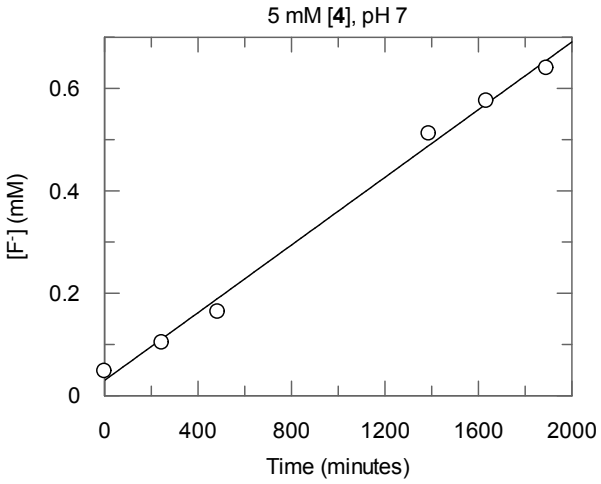


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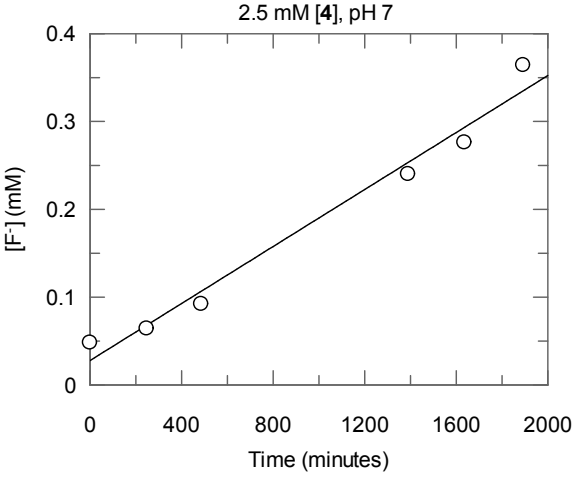


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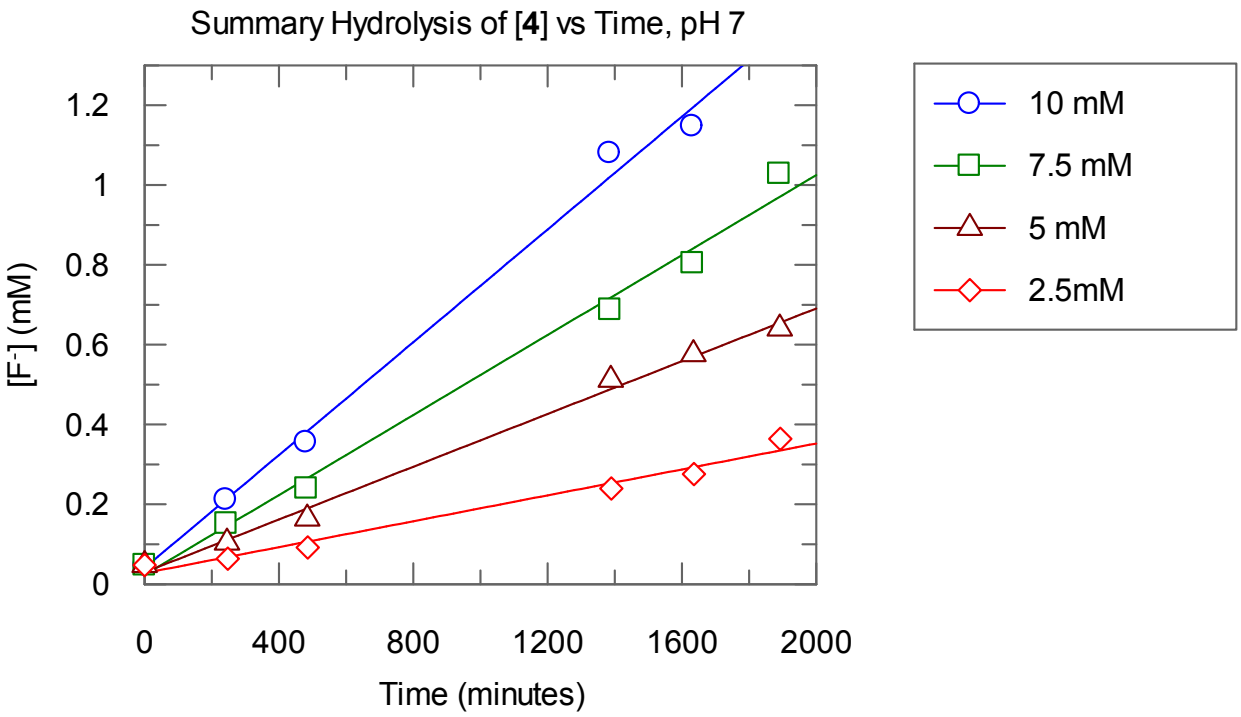


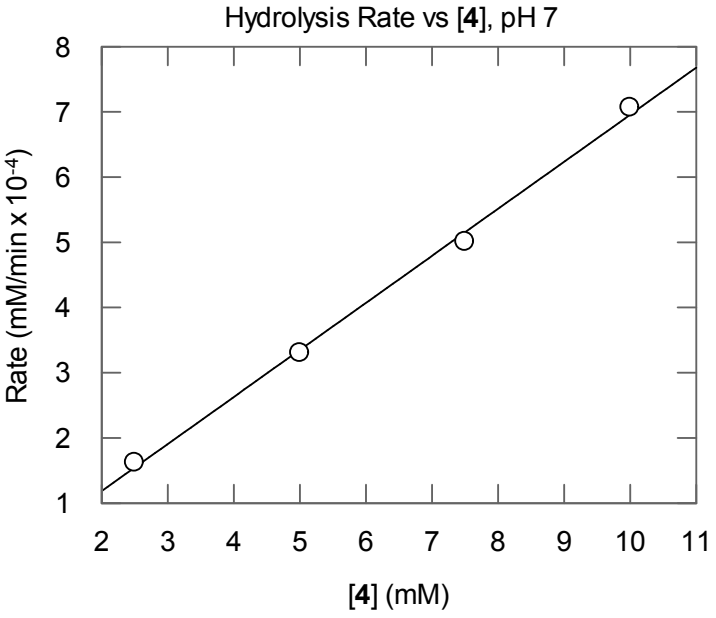


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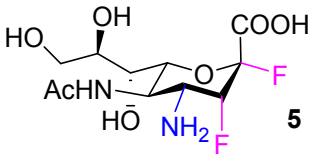
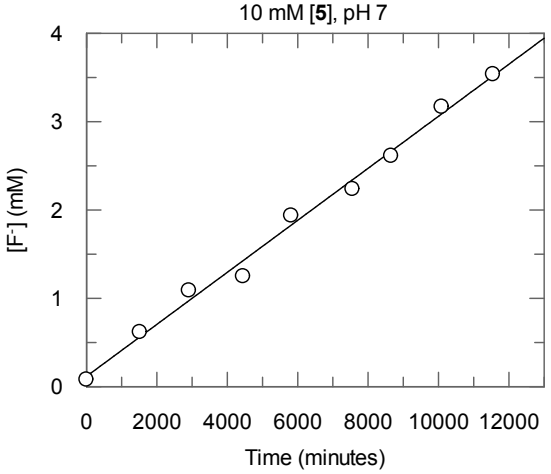
| a (intercept) | -0.2582 | 0.1751 |
| b (gradient) | 0.7214 | 0.0256 |



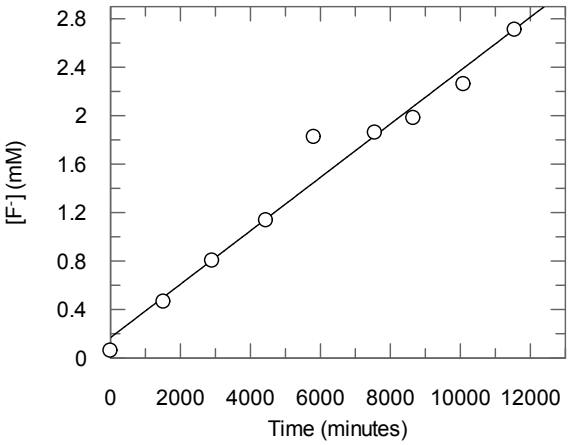

**5**

10 mM [**5**], pH 7



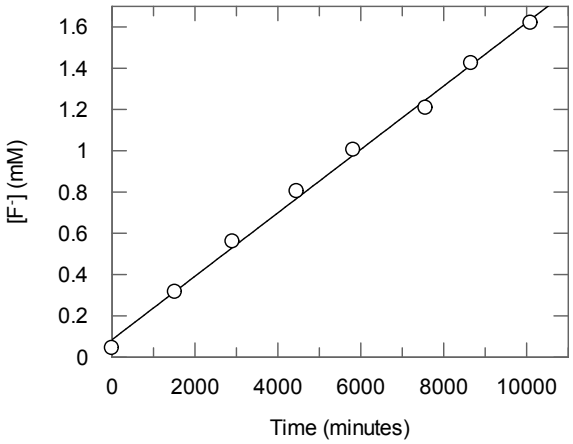

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 1.16148e-001 | 6.69129e-002 |
| b (gradient) | 2.94430e-004 | 9.65941e-006 |

7.5 mM [**5**], pH 7



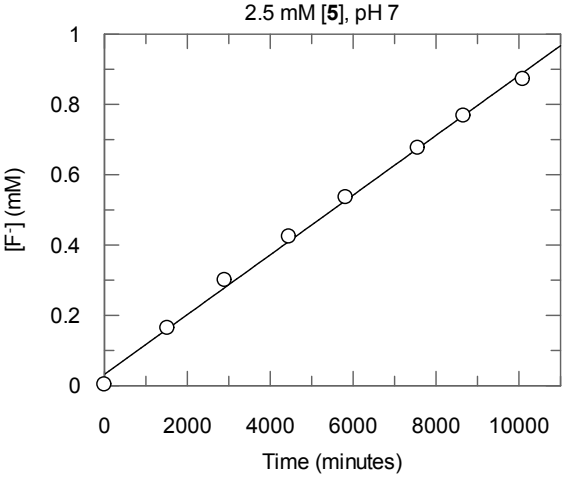

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 1.68413e-001 | 9.95703e-002 |
| b (gradient) | 2.20317e-004 | 1.43724e-005 |

5 mM [**5**], pH 7

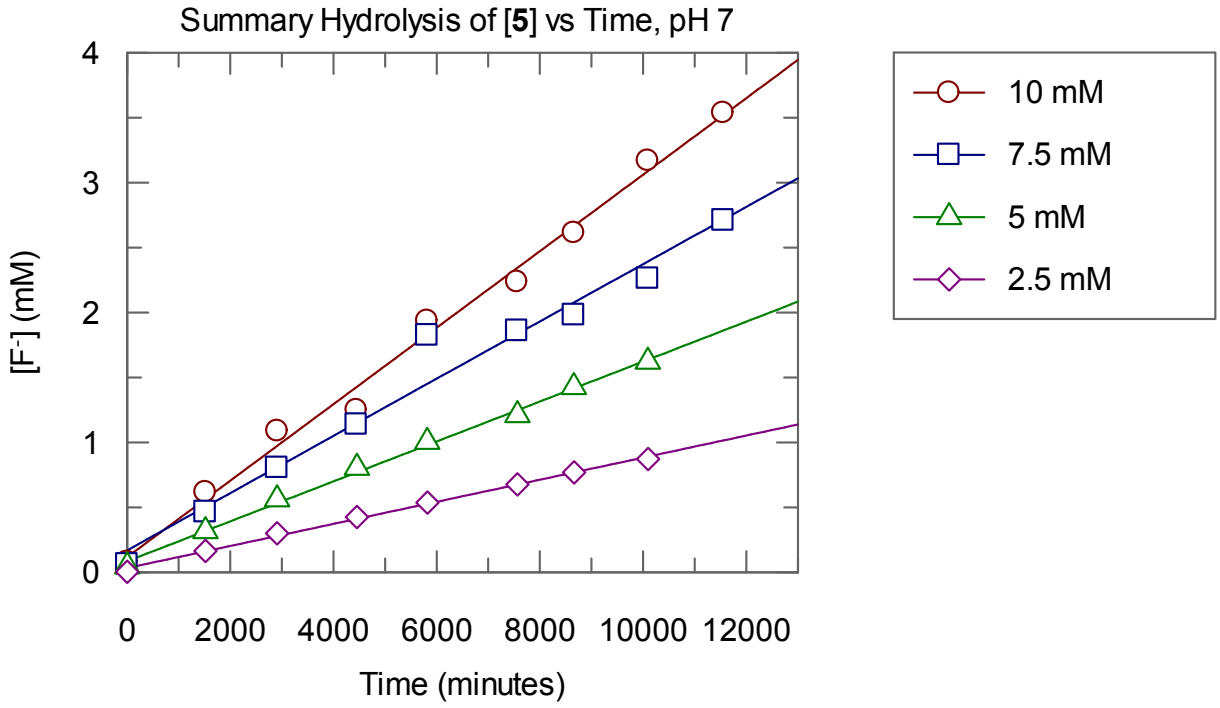


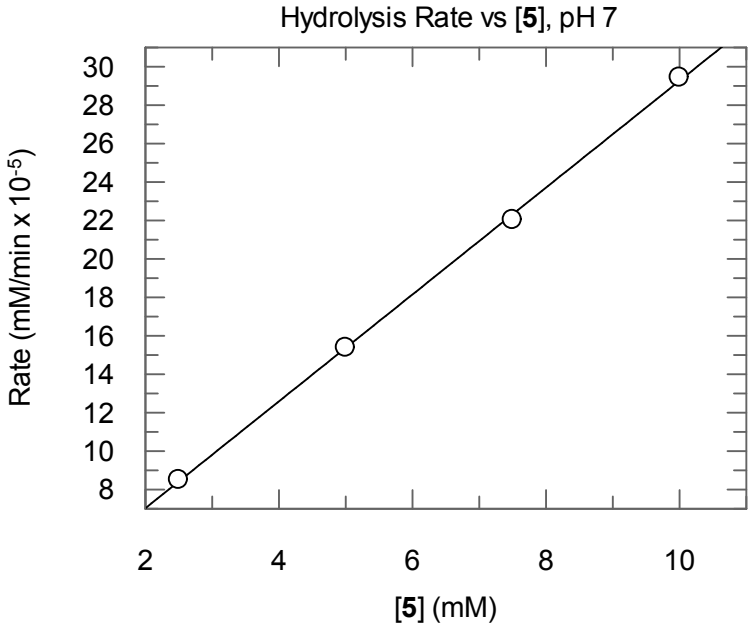

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 8.43684e-002 | 2.08297e-002 |
| b (gradient) | 1.53707e-004 | 3.40954e-006 |

2.5 mM [**5**], pH 7

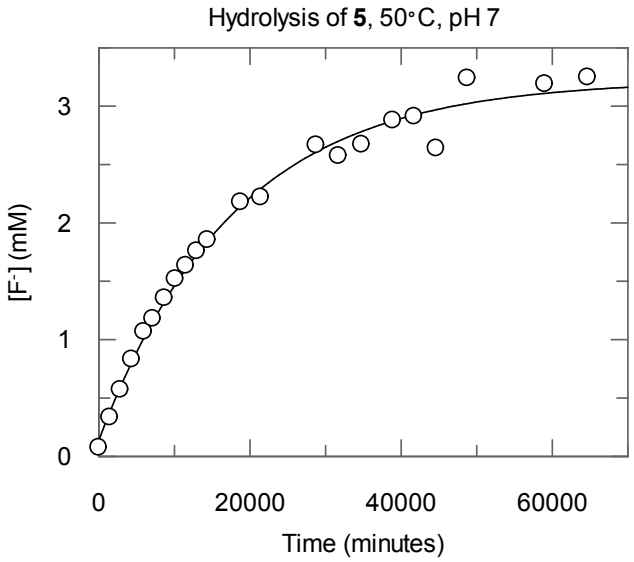



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0320 | 0.0115 |
| b (gradient) | 8.50007e-005 | 1.88128e-006 |

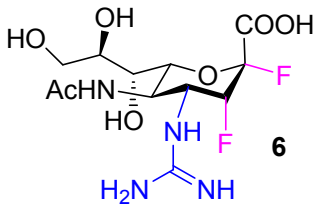


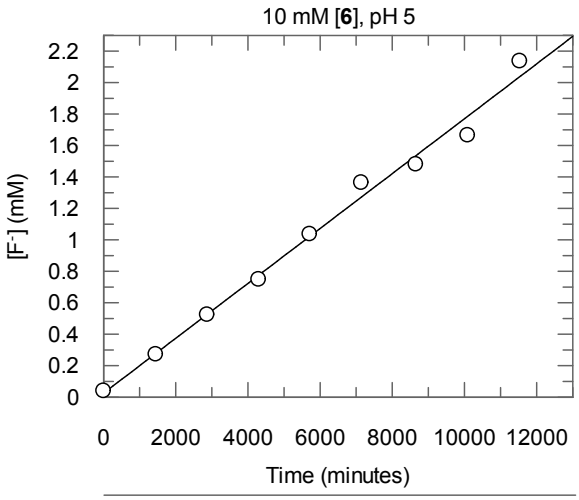




| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 1.4640 | 0.2989 |
| b (gradient) | 2.7796 | 0.0437 |

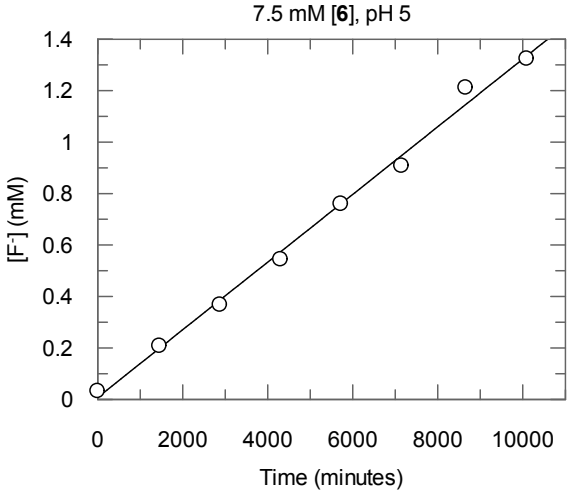



| Parameter | Value | Std. Error |
|---|---|---|
| Limit | 3.0857 | 0.0784 |
| Rate constant | 5.59174e-005 | 4.29495e-006 |
| Offset | 0.1379 | 0.0681 |

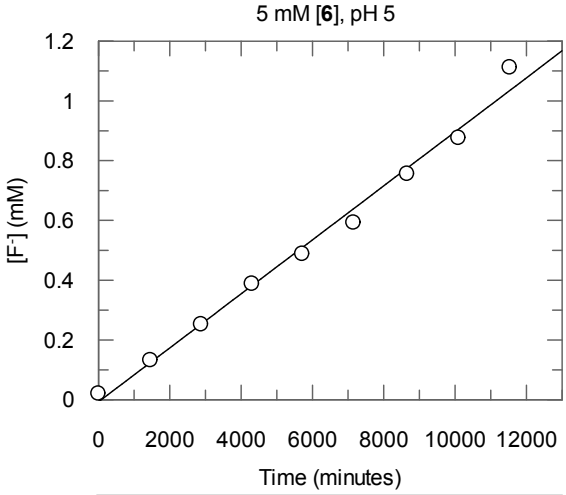


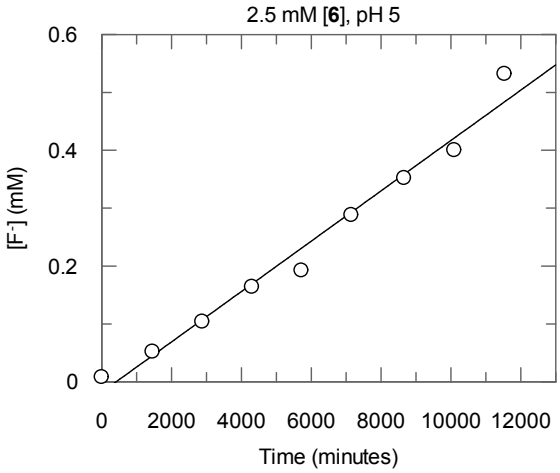

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 2.57291e-002 | 4.48786e-002 |
| b (gradient) | 1.74425e-004 | 6.54936e-006 |



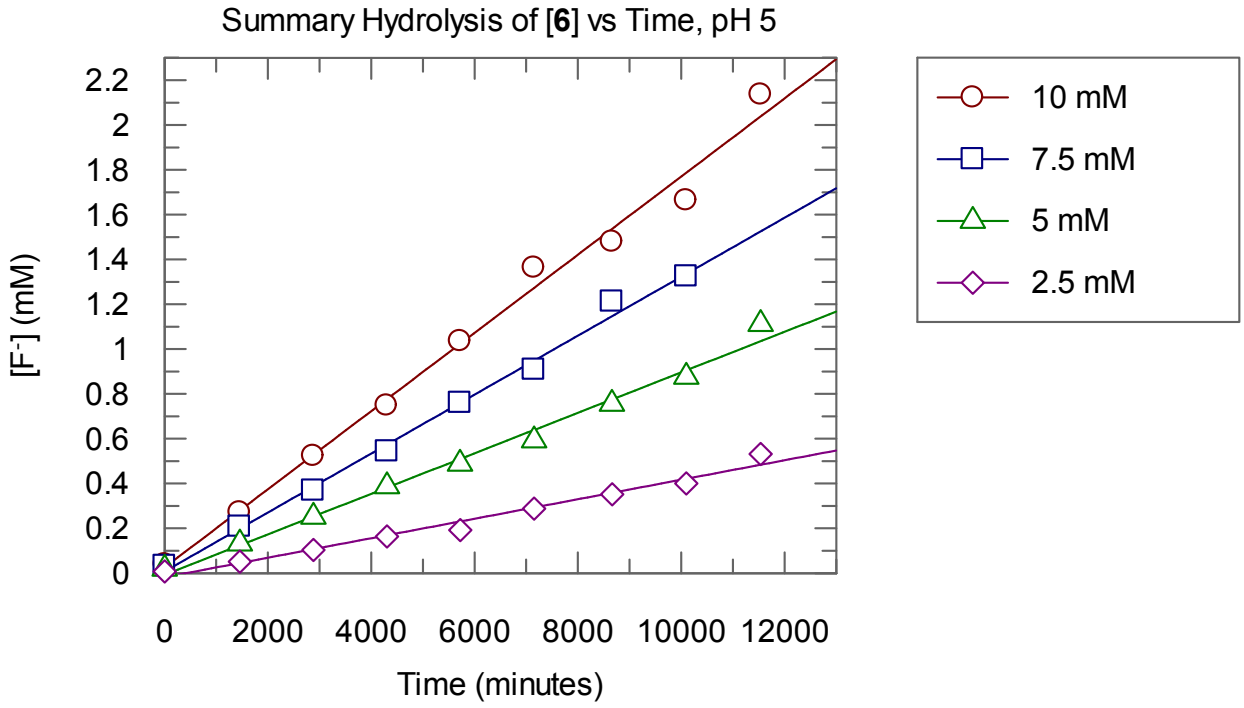

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 7.61374e-003 | 2.33804e-002 |
| b (gradient) | 1.31532e-004 | 3.88582e-006 |

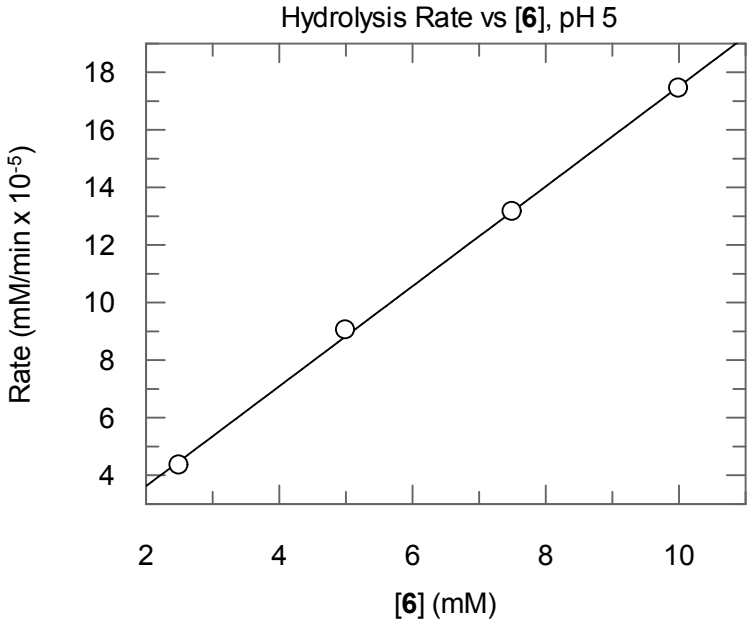



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | -0.0072 | 0.0239 |
| b (gradient) | 9.03551e-005 | 3.48707e-006 |

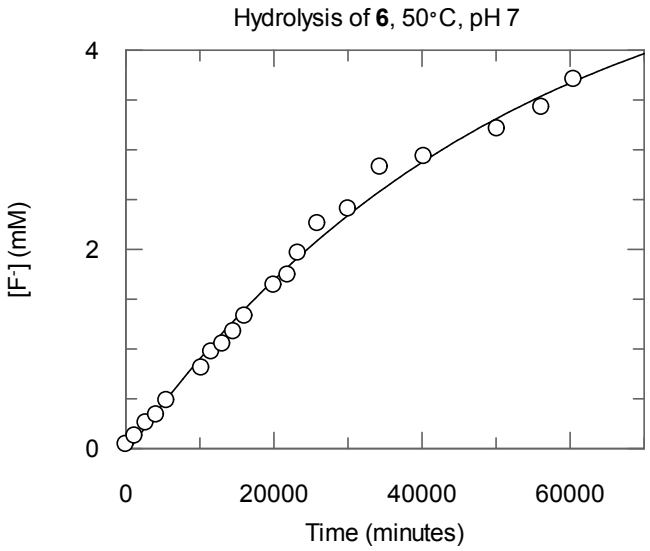



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | -0.0180 | 0.0166 |
| b (gradient) | 4.34925e-005 | 2.41904e-006 |

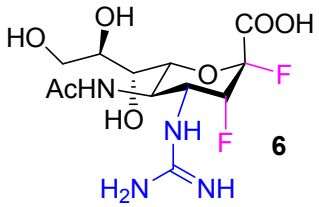


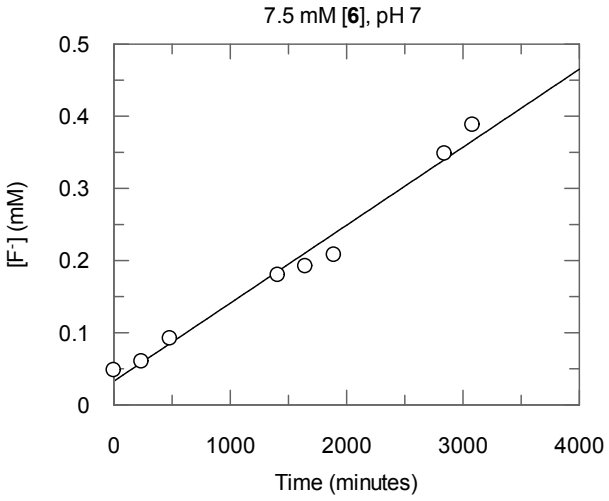

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.1460 | 0.2239 |
| b (gradient) | 1.7358 | 0.0327 |



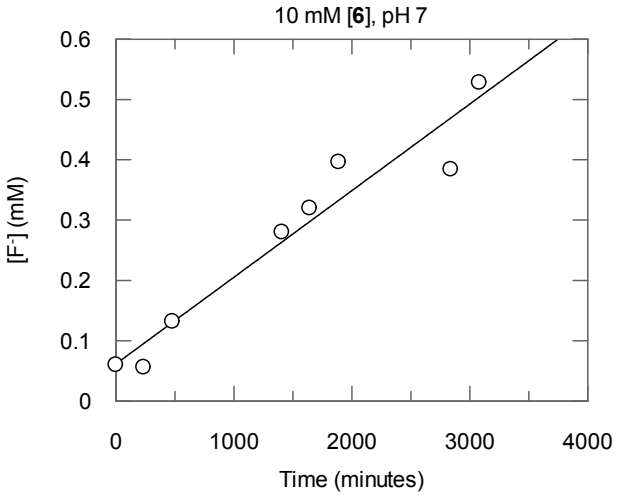

| Parameter | Value | Std. Error |
|---|---|---|
| Limit | 5.3792 | 0.3876 |
| Rate constant | 1.96938e-005 | 2.50454e-006 |
| Offset | -0.0605 | 0.0562 |



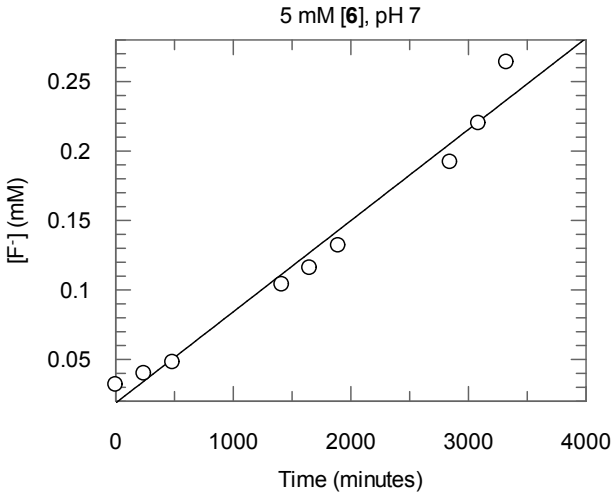

**6**



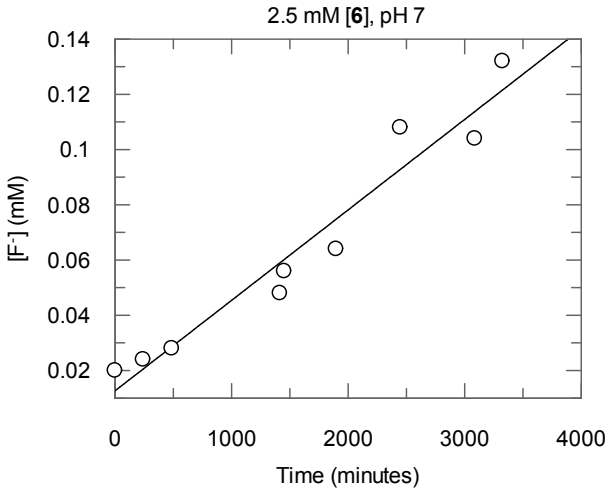

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 3.28398e-002 | 1.09921e-002 |
| b (gradient) | 1.08047e-004 | 6.07736e-006 |



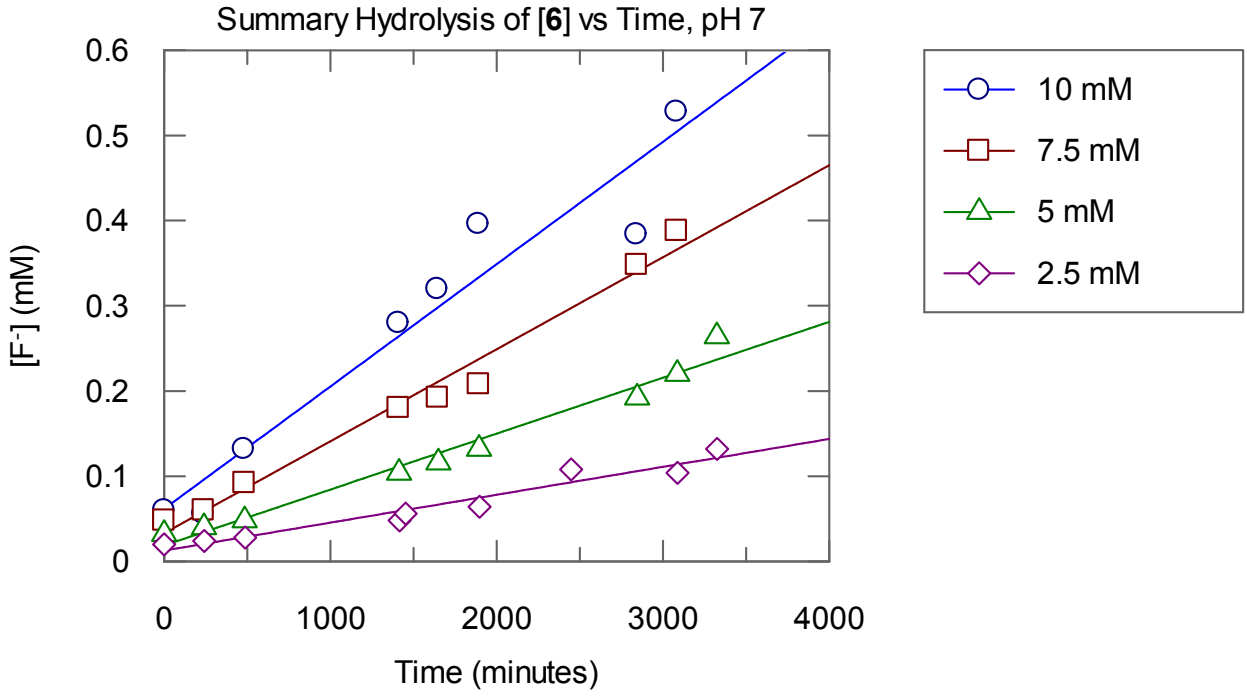

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 6.15567e-002 | 2.87327e-002 |
| b (gradient) | 1.43637e-004 | 1.59040e-005 |

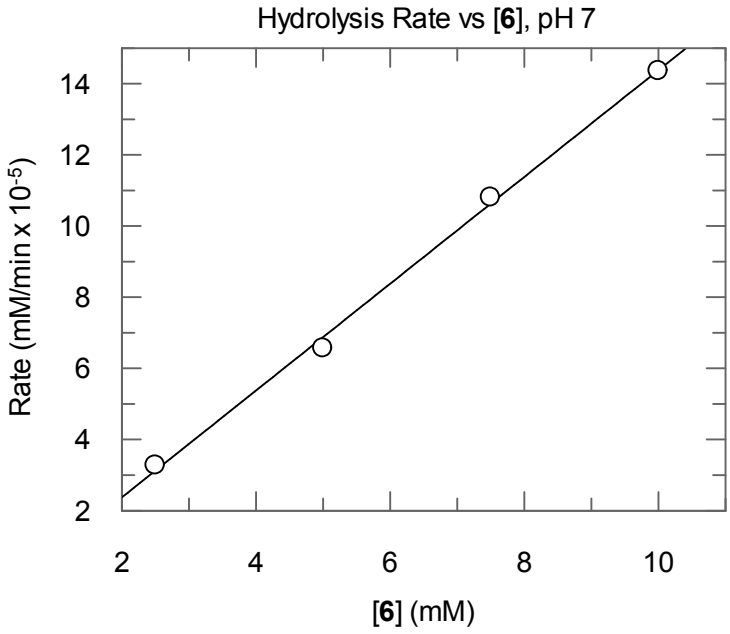



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0186 | 0.0082 |
| b (gradient) | 6.56193e-005 | 4.04556e-006 |

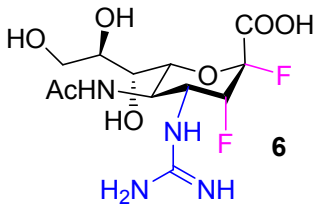



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0126 | 0.0060 |
| b (gradient) | 3.27509e-005 | 3.03861e-006 |

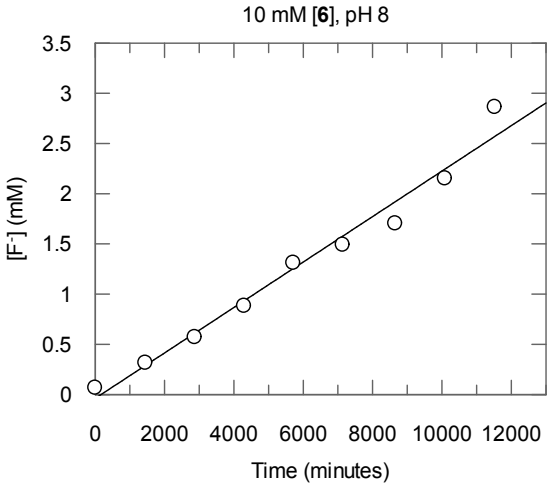




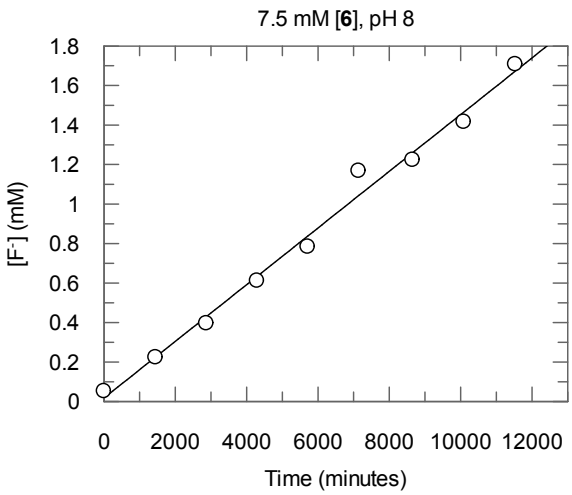

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | -0.6258 | 0.3387 |
| b (gradient) | 1.5003 | 0.0495 |



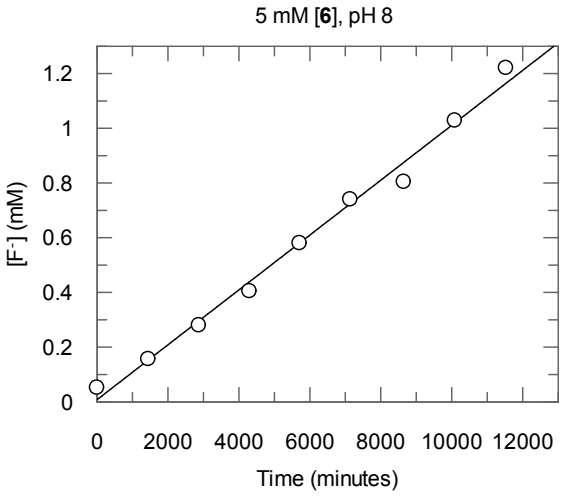

**6**



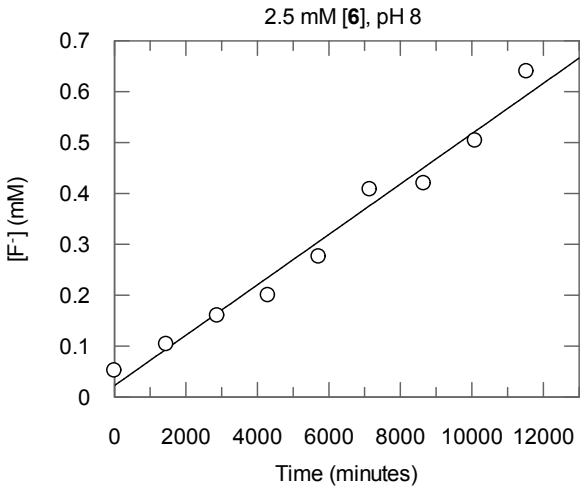

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | -3.81714e-002 | 9.49945e-002 |
| b (gradient) | 2.26307e-004 | 1.38735e-005 |



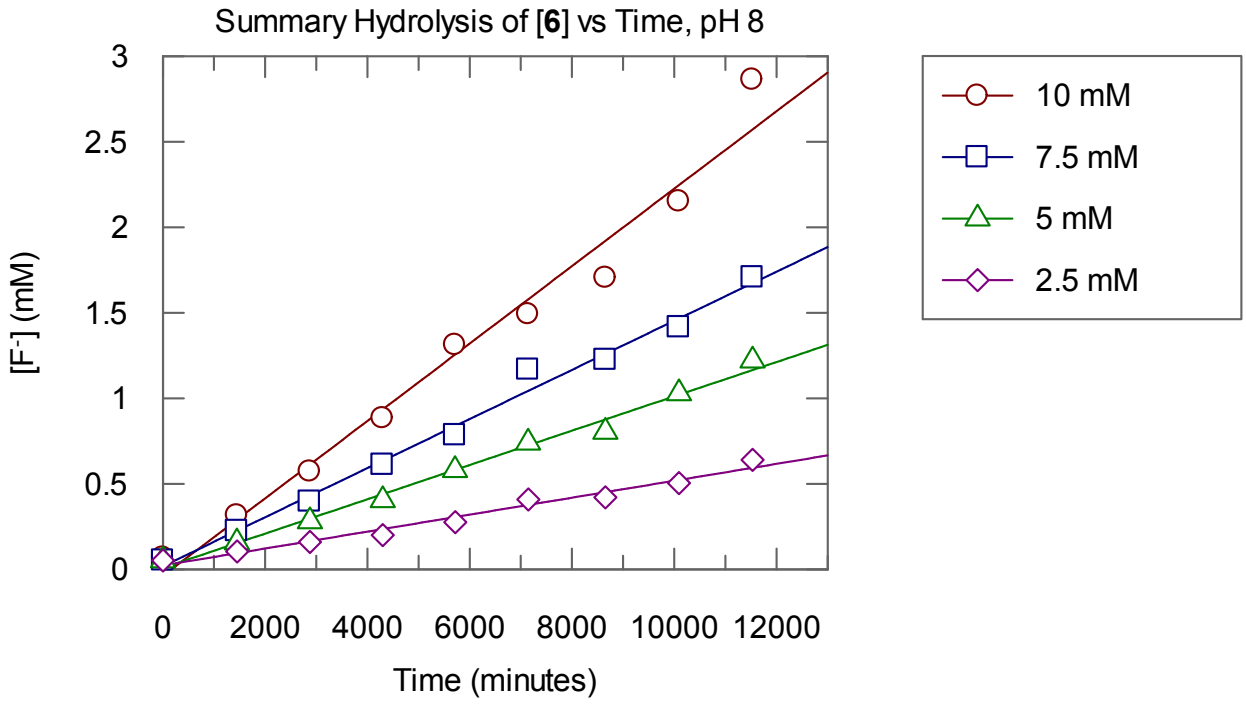

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 1.74459e-002 | 3.76931e-002 |
| b (gradient) | 1.43531e-004 | 5.50408e-006 |

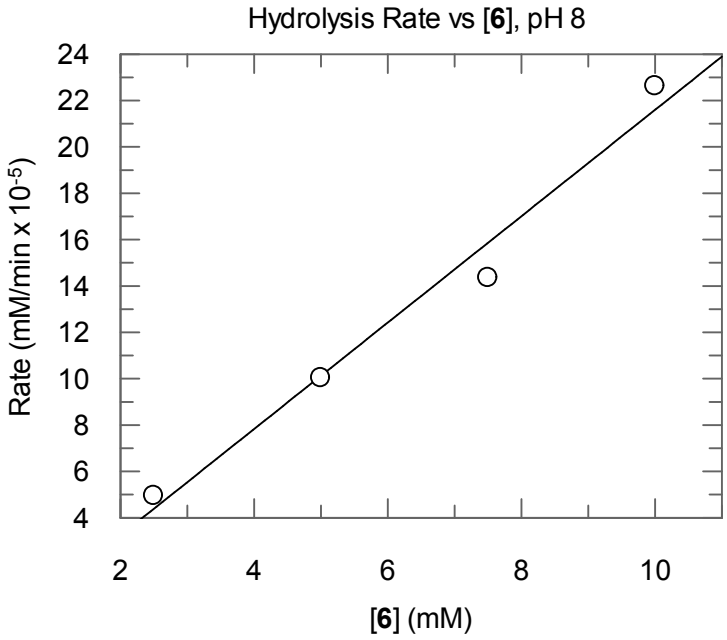



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 8.08746e-003 | 2.54145e-002 |
| b (gradient) | 1.00294e-004 | 3.71023e-006 |

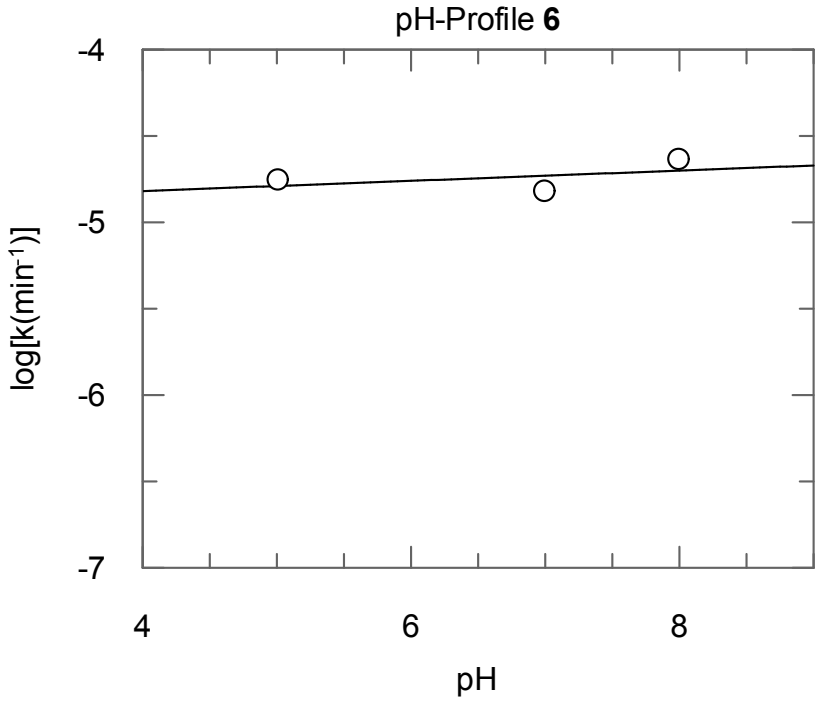


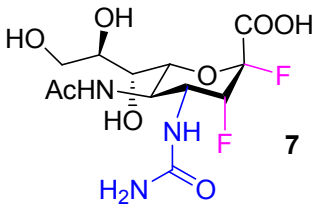

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0224 | 0.0202 |
| b (gradient) | 4.95000e-005 | 2.94722e-006 |





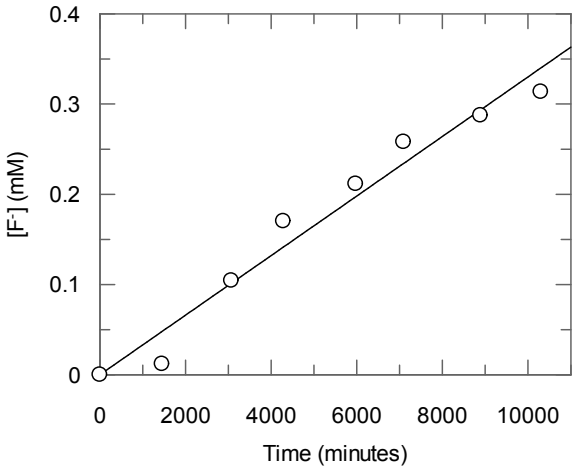

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | -1.3507 | 1.6583 |
| b (gradient) | 2.2946 | 0.2422 |





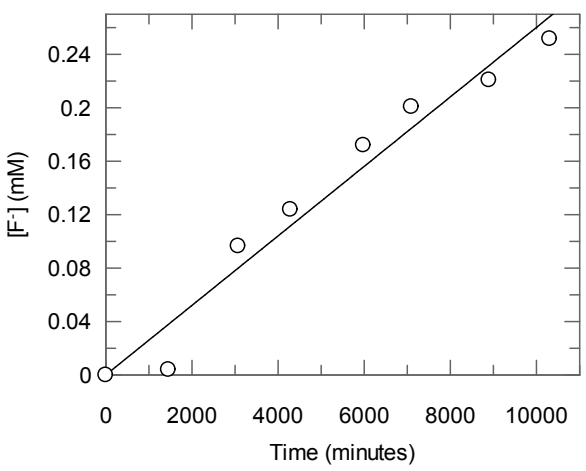

**7**

2 mM [**7**], pH 7



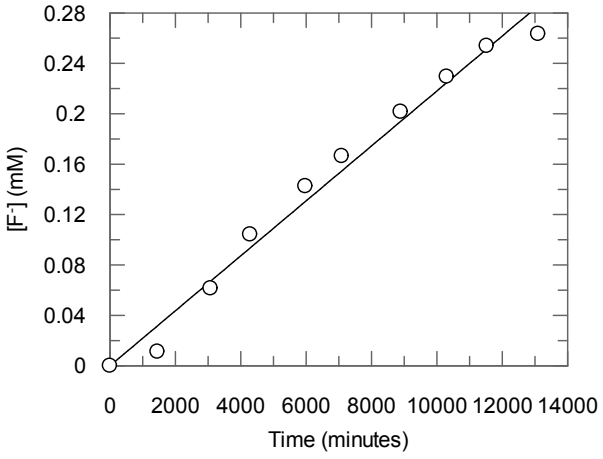

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | -5.52608e-011 | 0.0159 |
| b (gradient) | 3.30063e-005 | 2.59100e-006 |

1.5 mM [**7**], pH 7



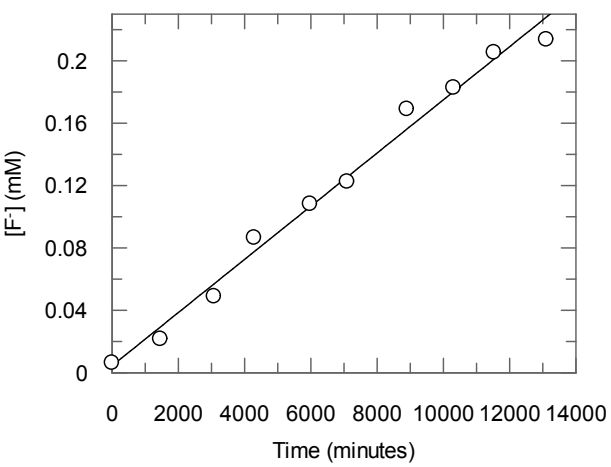

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 7.40104e-011 | 0.0131 |
| b (gradient) | 2.60151e-005 | 2.14049e-006 |

1 mM [**7**], pH 7

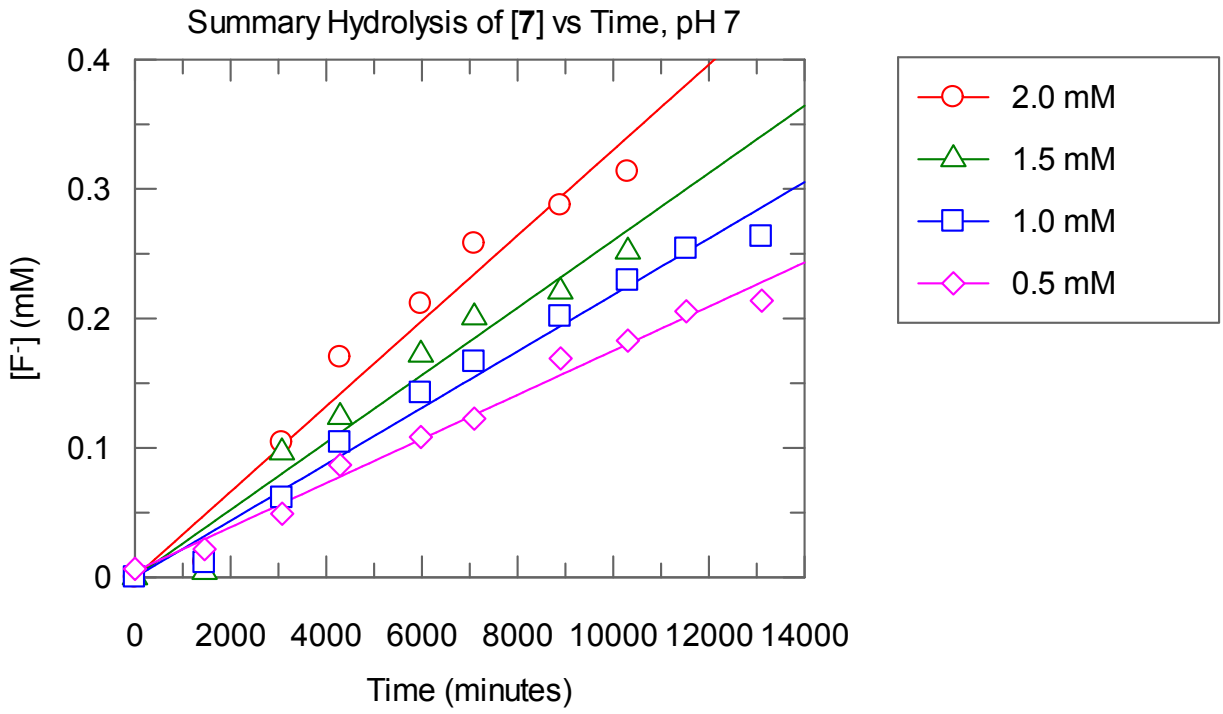


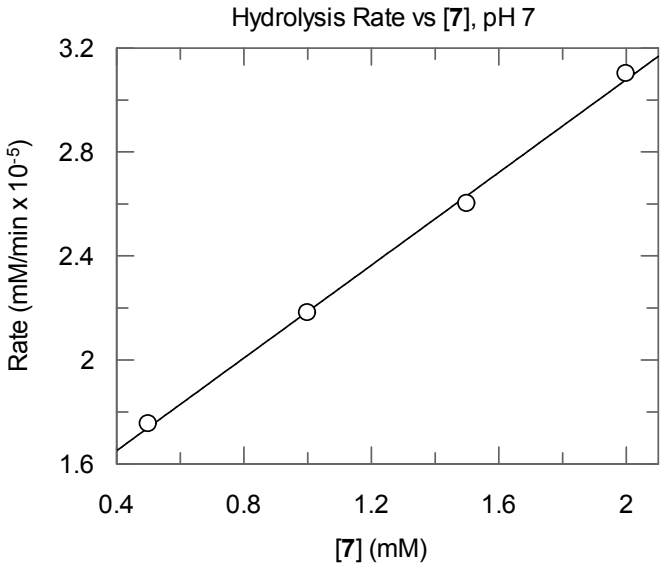

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | -6.86137e-011 | 0.0079 |
| b (gradient) | 2.18062e-005 | 1.01707e-006 |

0.5 mM [**7**], pH 7

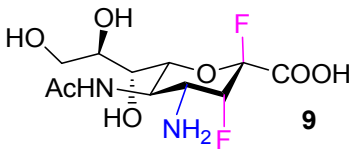



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0045 | 0.0052 |
| b (gradient) | 1.70478e-005 | 6.63583e-007 |



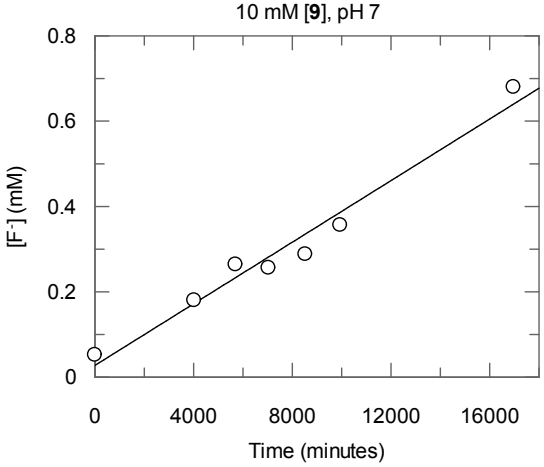




| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 1.19349e-005 | 1.30025e-006 |
| b (gradient) | 1.01246e-005 | 9.49566e-007 |



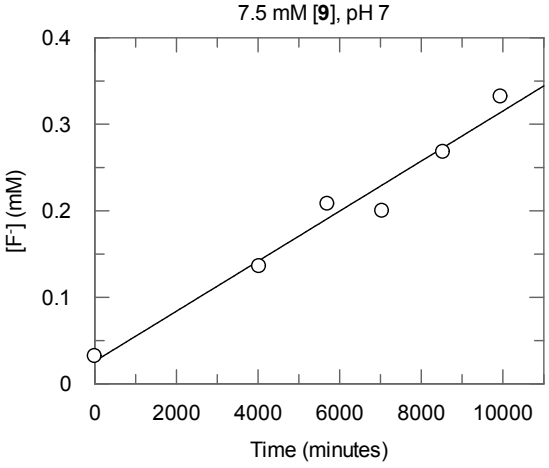

**9**

10 mM [**9**], pH 7



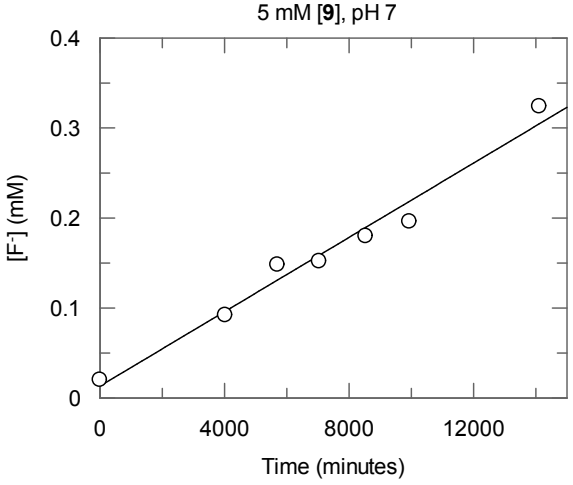

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0273 | 0.0258 |
| b (gradient) | 3.60993e-005 | 2.88750e-006 |

7.5 mM [**9**], pH 7



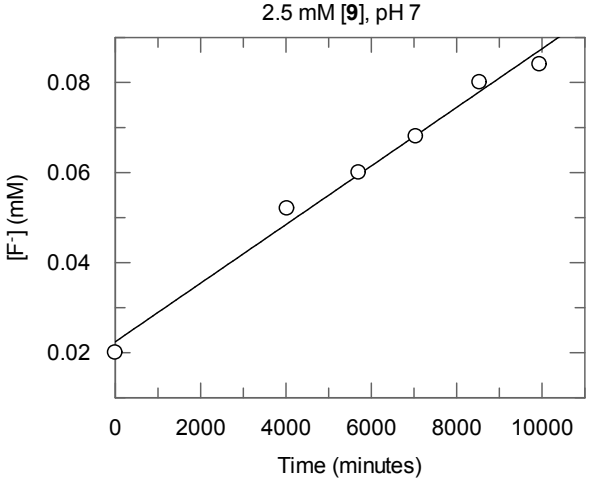

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0260 | 0.0170 |
| b (gradient) | 2.89320e-005 | 2.53049e-006 |

5 mM [**9**], pH 7

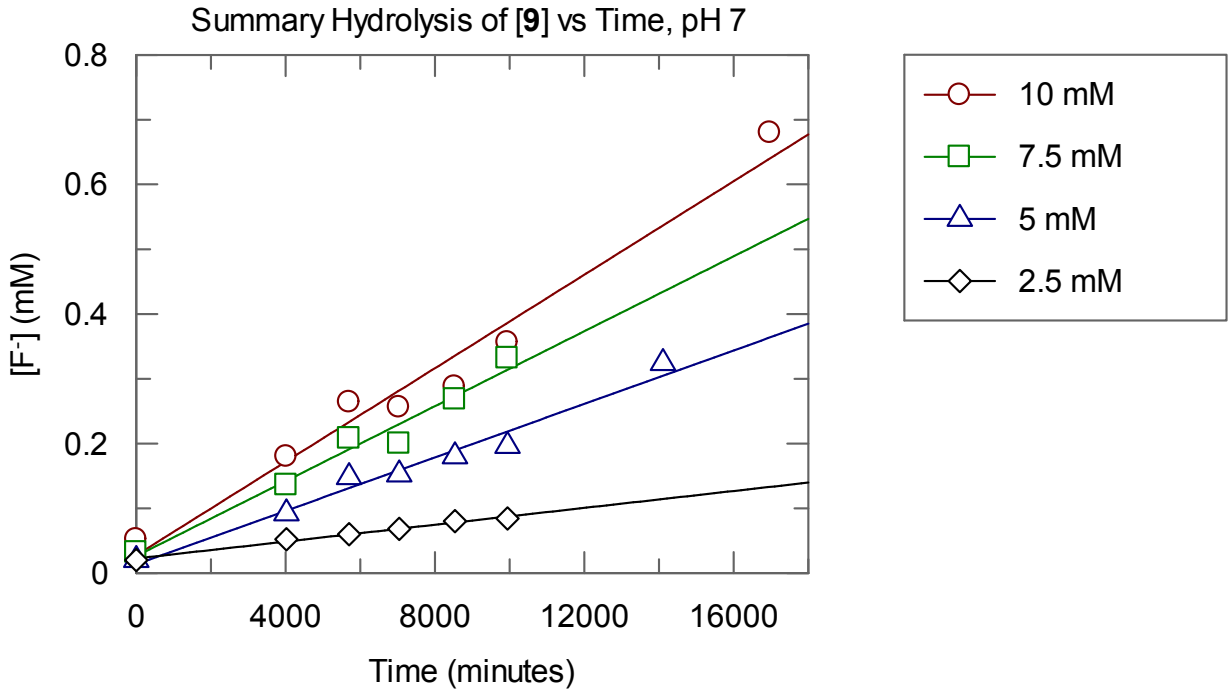


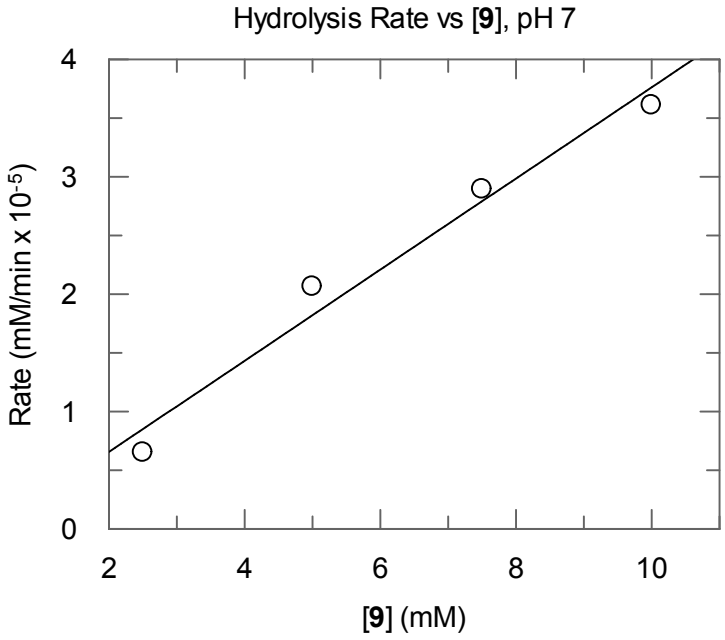

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0132 | 0.0123 |
| b (gradient) | 2.06456e-005 | 1.50622e-006 |

2.5 mM [**9**], pH 7

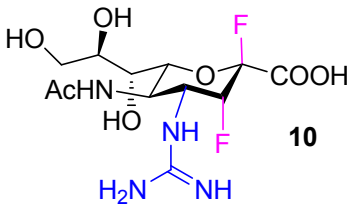



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0224 | 0.0024 |
| b (gradient) | 6.50955e-006 | 3.53250e-007 |

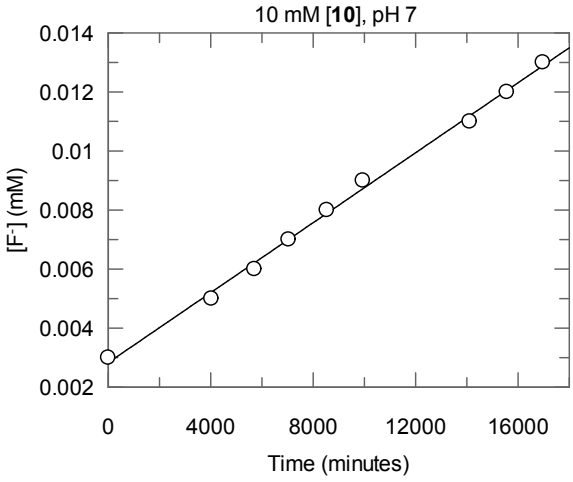



| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | -0.1217 | 0.3154 |
| b (gradient) | 0.3882 | 0.0461 |

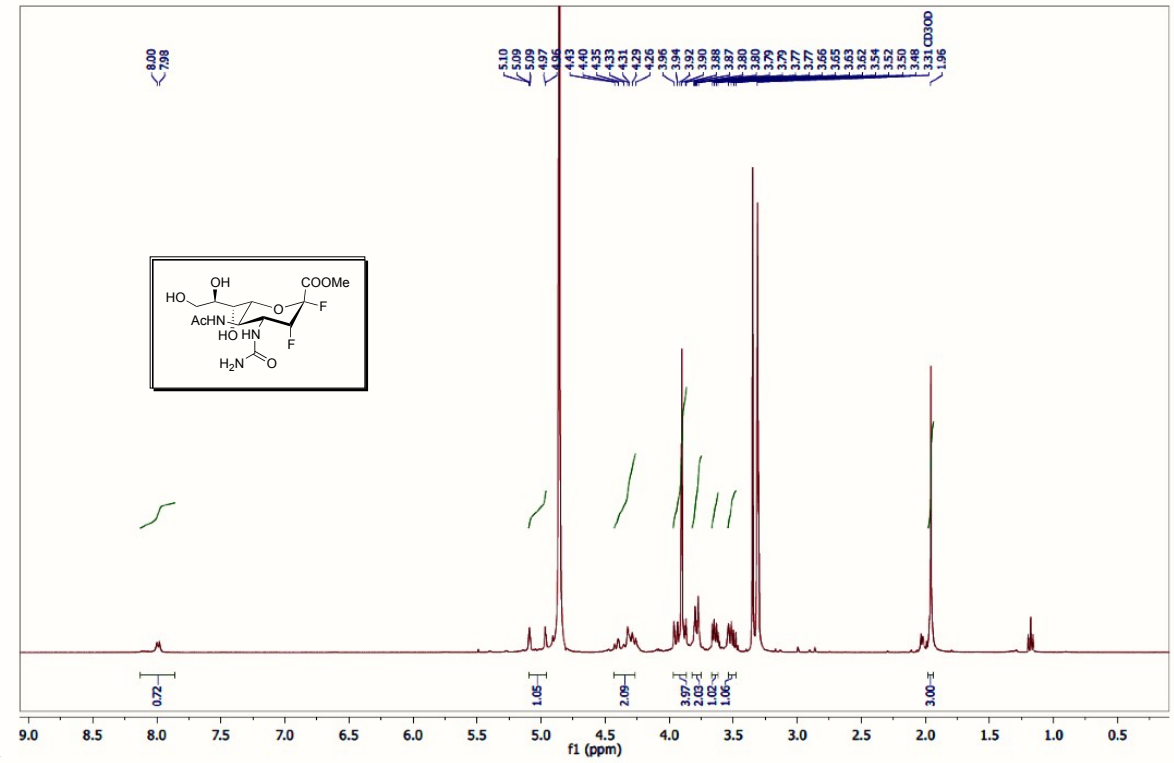


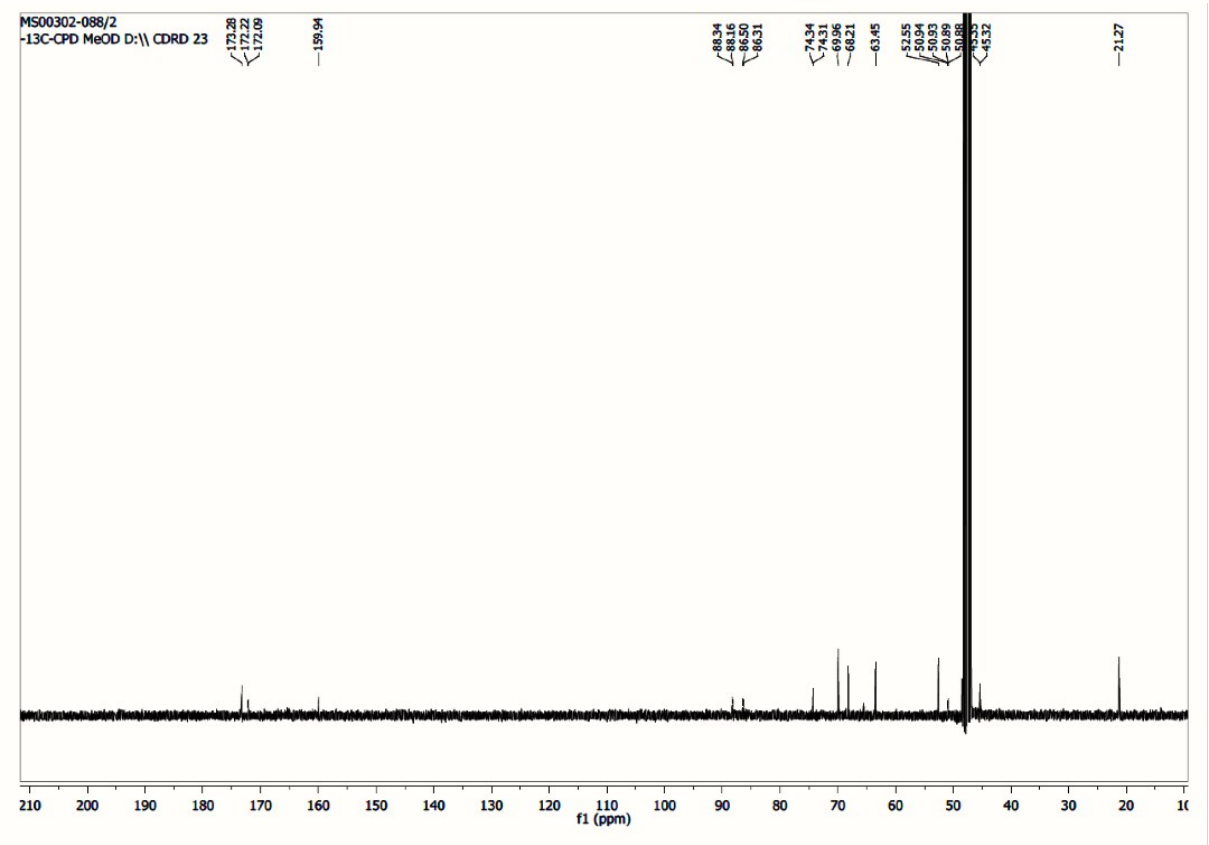

**10**

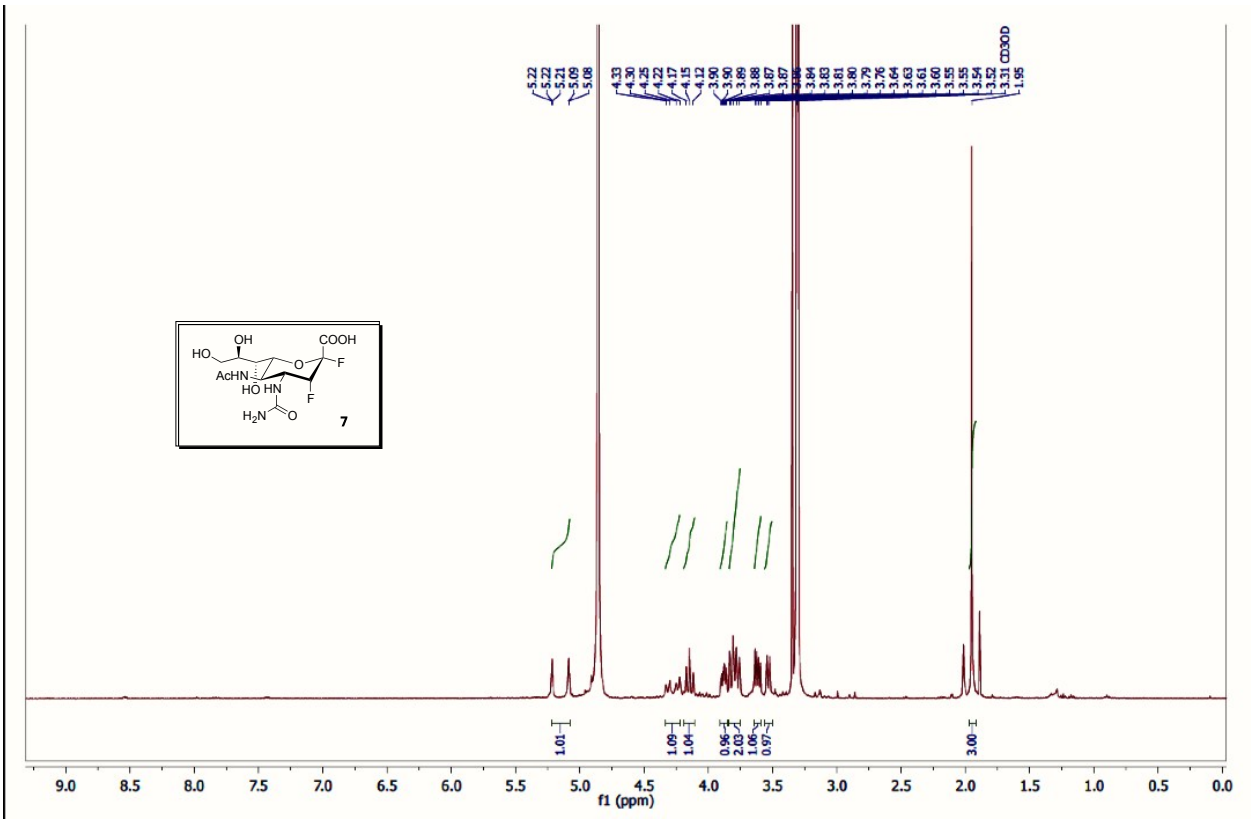


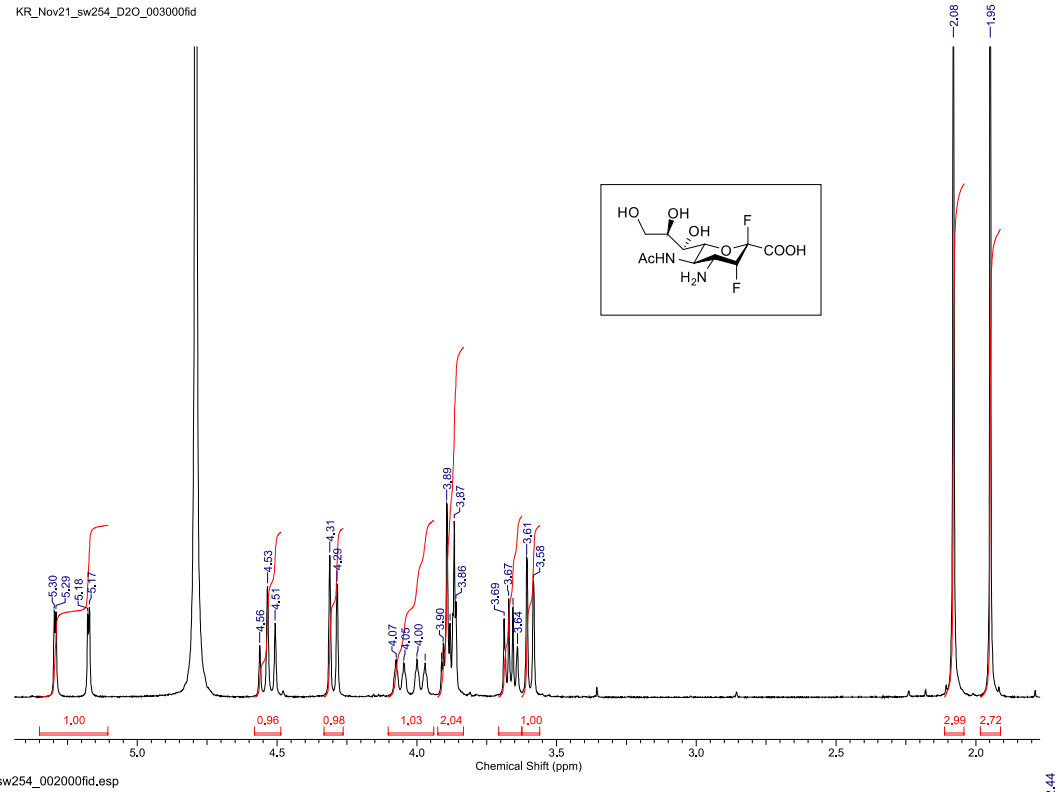

| Parameter | Value | Std. Error |
|---|---|---|
| a (intercept) | 0.0028 | 0.0001 |
| b (gradient) | 5.92538e-007 | 1.21303e-008 |

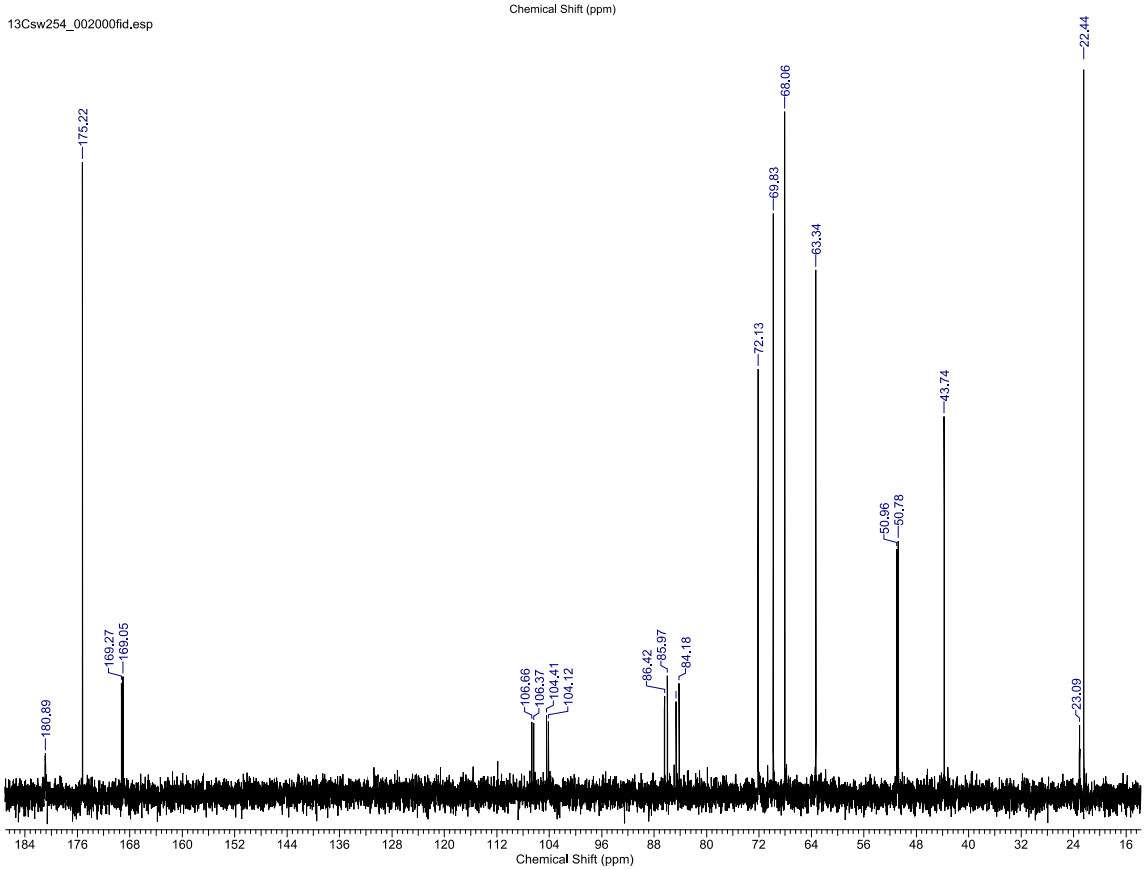
# NMR Spectra

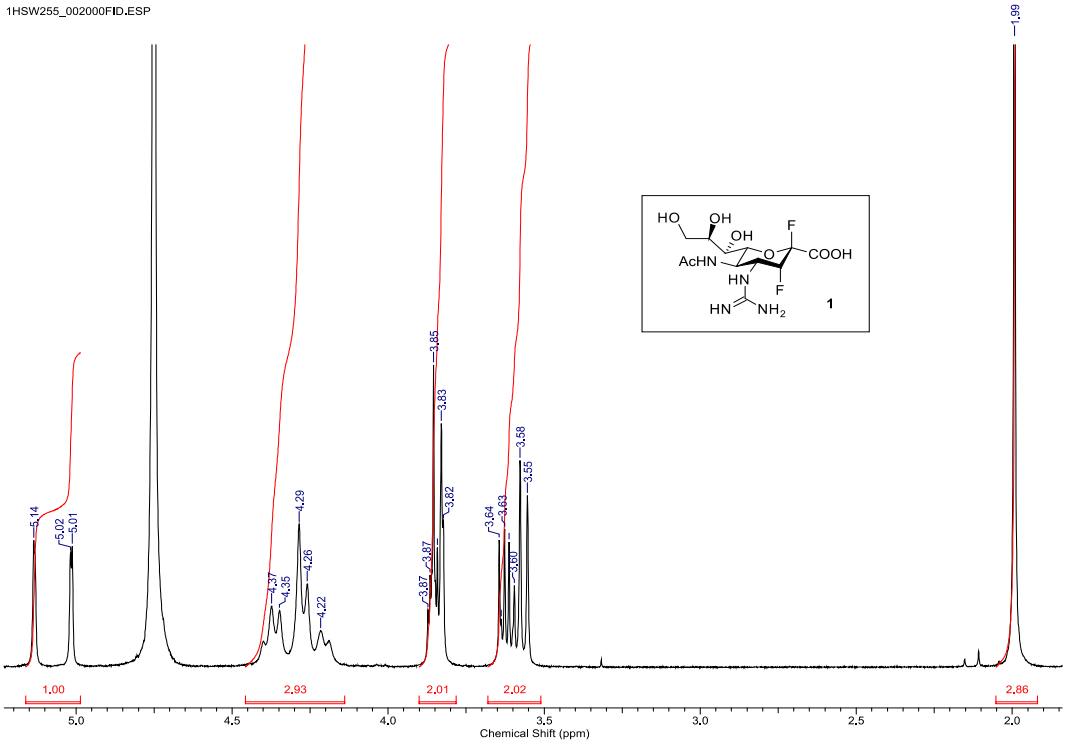

8.00
7.98
5.10
5.09
5.09
4.97
4.96
4.43
4.40
4.35
4.33
4.31
4.29
4.26
3.96
3.94
3.92
3.90
3.88
3.87
3.80
3.80
3.79
3.79
3.77
3.77
3.66
3.65
3.63
3.62
3.54
3.52
3.50
3.48
3.31 CD3OD
1.96
OH
COOMe
HO
O
F
AcHN
HO HN
F
H2N
O
0.72
1.05
2.09
3.97
2.03
1.02
1.06
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

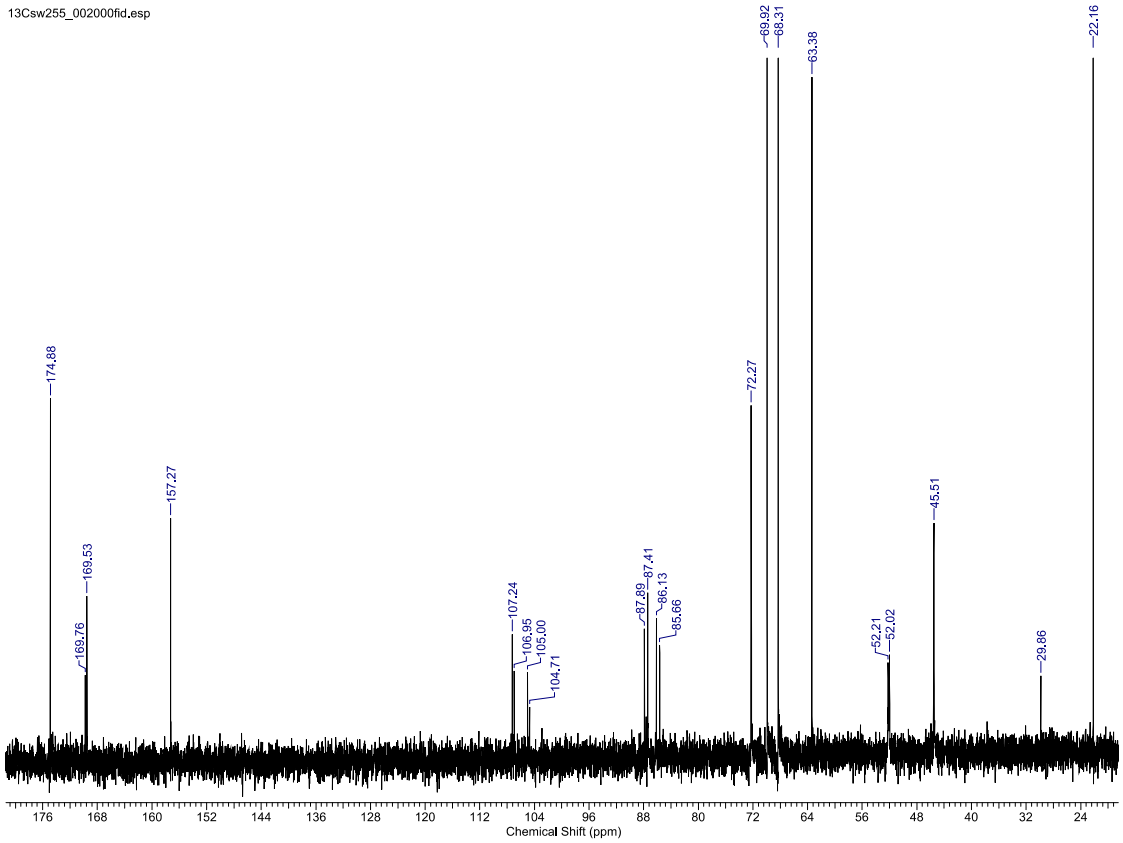

MS00302-088/2
-13C-CPD MeOD D:\\ CDRD 23
173.28
172.22
172.09
159.94
88.34
88.16
86.50
86.31
74.34
74.31
69.96
68.21
63.45
52.55
50.94
50.93
50.89
50.88
45.33
45.32
21.27
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


5.22
5.22
5.21
5.09
5.08
4.33
4.30
4.25
4.22
4.17
4.15
4.12
3.90
3.90
3.89
3.88
3.87
3.87
3.86
3.84
3.83
3.81
3.80
3.79
3.76
3.64
3.63
3.61
3.60
3.55
3.55
3.54
3.52
3.31 CD3OD
1.95
OH
COOH
HO
O
F
AcHN
HO HN
F
H2N
O
7
1.01
1.09
1.04
0.96
2.03
1.06
0.97
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


KR_Nov21_sw254_D2O_003000fid
HO
OH
OH
F
AcHN
O
COOH
H2N
F
2.08
1.95
5.30
5.29
5.18
5.17
4.56
4.53
4.51
4.31
4.29
4.07
4.05
4.00
3.90
3.89
3.87
3.86
3.69
3.67
3.65
3.61
3.58
1.00
0.96
0.98
1.03
2.04
1.00
2.99
2.72
5.0
4.5
4.0
3.5
3.0
2.5
2.0
Chemical Shift (ppm)


13Csw254_002000fid.esp
22.44
175.22
68.06
69.83
63.34
72.13
43.74
50.96
50.78
180.89
169.27
169.05
106.66
106.37
104.41
104.12
86.42
85.97
84.18
23.09
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


1HSW255_002000FID.ESP
1.99
5.14
5.02
5.01
4.37
4.35
4.29
4.26
4.22
3.87
3.87
3.85
3.83
3.82
3.64
3.63
3.60
3.58
3.55
HO
OH
OH
F
AcHN
O
COOH
HN
F
HN
NH2
1
1.00
2.93
2.01
2.02
2.86
5.0
4.5
4.0
3.5
3.0
2.5
2.0
Chemical Shift (ppm)


13Csw255_002000fid.esp
69.92
68.31
63.38
22.16
174.88
169.53
169.76
157.27
107.24
106.95
105.00
104.71
87.89
87.41
86.13
85.66
72.27
52.21
52.02
45.51
29.86
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)