Uncovering the Mechanism of the Silver(I)/Persulfate-Catalyzed Cross-Coupling of Arylboronic Acids with Heteroarenes

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Supporting Information

Instrumentation

GC analyzes were done using a Shimadzu Gas Chromatograph GC-14B. Proton, carbon, and boron NMR were recorded on a Bruker 500 MHz spectrometer. GC-MS analyses were done with an HP 5890 Series II Gas Chromatograph with an HP Mass Selector Detector. Column chromatography was performed using the automated CombiFlash® Rf system from Teledyne Isco, Inc. Products were separated using prepacked silica gel columns with a gradient elution of ethyl acetate and hexanes.

Materials for synthetic and kinetic studies

$AgNO_3$, $K_2S_2O_8$, $Na_2S_2O_8$ were purchased from Acros Organics. **1** was purchased from Oakwood Products, Inc. **2** was purchased from TCI Fine Chemicals. TFA and **4** was purchased from Alfa Aesar. All chemicals were used without further purification.

Procedure for degassing solvents

CH_2Cl_2 was purified by a Solvent Purification system (Innovative Technology Inc.; MA). H_2O was degassed by bubbling through with argon overnight.

Procedure for synthesis of 3

In a 25 mL round bottom flask with a magnetic stirring bar, **1**, TFA, and **2** were dissolved in 10 mL CH_2Cl_2. To the flask, 5 mL degassed H2O was added. $AgNO_3$ was dissolved in 5 mL degassed water and added to the reaction. $K_2S_2O_8$ was added to the reaction as a solid. The flask was then evacuated of air, a septum was attached, and was back-filled with Ar. The reaction was allowed to stir overnight. Reaction workup involved diluting the reaction with 10 mL CH_2Cl_2 and quenching with 10 mL saturated bicarbonate solution. The organic layer was separated and run through a plug of neutral alumina. The alumina was washed with ethyl acetate. Product formation was confirmed by GC-MS. The organic layer was rotary evaporated to dryness. Crude

product formation was observed by ^{1}H NMR in $CDCl_3$. Product was purified via automated flash chromatography and characterized by ^{1}H NMR and ^{13}C NMR.

Procedure for Reaction Progress Kinetic Analysis[1] Studies

In a 100 mL round bottom flask with a magnetic stirring bar, **1**, TFA, and **2** were dissolved in 30 mL CH_2Cl_2. To the flask, 15 mL degassed H2O was added. $AgNO_3$ was dissolved in 15 mL degassed water and added to the reaction. $K_2S_2O_8$ was added to the reaction as a solid. The flask was then evacuated of air, a septum was attached, and was back-filled with Ar. The reaction was stopped and 0.5 mL aliquots were taken from the organic layer during the course of the reaction. Aliquots taken were quenched with 1.0 mL saturated bicarbonate solution, and 0.5 mL of biphenyl in ethyl acetate solution was added as an internal standard. The organic layer was extracted and analyzed by GC.

Procedure for pyridine ^{1}H NMR studies

^{1}H NMR spectra were obtained for four solutions: 1) In a vial, 28.75 μL (0.25 mmol) of **1** was dissolved in 1.0 mL $CDCl_3$. 2) In a vial, 28.75 μL (0.25 mmol) of **1** and 18.575 μL (0.25 mmol) of TFA was dissolved in 1.0 mL $CDCl_3$. 3) In a vial, 28.75 μL (0.25 mmol) of **1**, 18.575 μL (0.25 mmol) of TFA, and 42.475 mg (0.25 mmol) of $AgNO_3$ were dissolved in 1.0 mL $CDCl_3$. 4) In a vial, 28.75 μL (0.25 mmol) of **1** and 42.475 mg (0.25 mmol) of $AgNO_3$ were dissolved in 1.0 mL $CDCl_3$.

Procedure for ^{11}B NMR studies

^{11}B NMR studies were done using quartz NMR tubes. Spectra were obtained for the following solutions: 1) **2** dissolved in D_2O. 2) In a vial, 0.15 mmol of **4**, 0.1 mmol of **1**, 0.1 mmol of TFA, and 0.02mmol of $AgNO_3$ was dissolved in 1mL D_2O. The solution was then transferred

[1] (a) Mathew, J S.; Klussman, M.; Iwamura, H.; Valera, F.; Futran, A.; Emanuelsson, E. A. C.; Blackmond, D. G. *J. Org. Chem. 2006*, 71, 4711-4722. (b) Blackmond, D. G. *Angew. Chem. Int. Ed.* **2005**, 44, 4302-4320. (c) Devery, J. J., III.; Conrad, J. C.; MacMillan, D. W. C.; Flowers, R. A., II. *Angew. Chem. Int. Ed.* **2010**, 49, 6106-6110. (d) Choquette, K. A.; Sadasivam, D. V.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2011**, 133, 10655-10661. (reference 7 in paper)

to a quartz NMR tube. A ^{11}B NMR spectrum was immediately obtained. After letting the previous sample sit for 4h, a ^{11}B NMR spectrum was obtained again, showing some hydrolysis of **4** to **2**. 3) In a vial, 0.15 mmol of **4**, 0.1 mmol of TFA, and 0.02mmol of $AgNO_3$ was dissolved in 1mL D_2O. The solution was then transferred to a quartz NMR tube. A ^{11}B NMR spectrum was immediately obtained. After letting the previous sample sit for 4h, a ^{11}B NMR spectrum was obtained again, showing some hydrolysis of **4** to **2**.

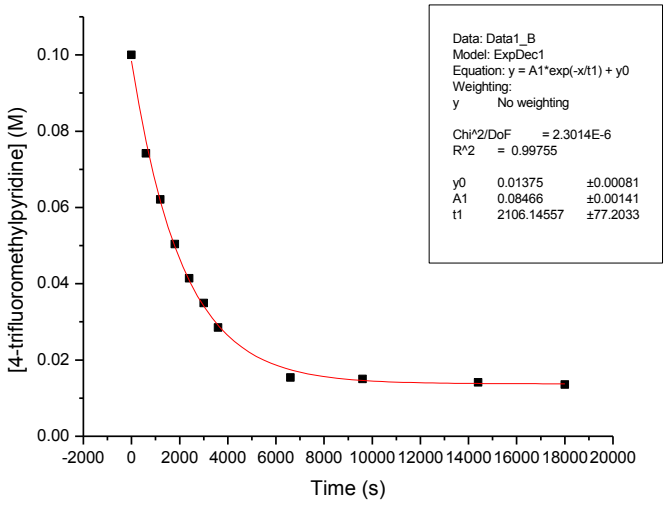
Spectroscopic data for 3

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.85 (1H, d), 7.93 (3H), 7.42 (1H, d), 7.32 (2H, d), 2.43 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 158.85, 150.54, 140.04, 139.08, 135.32, 129.69, 126.92, 121.95, 117.13, 115.63, 21.31; GC/MS *m/z* (rel. abundance) 237 (100), 91 (13).

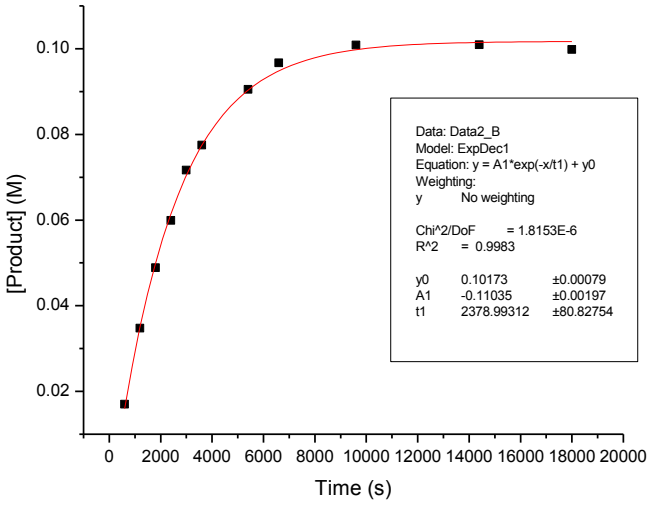
Conditions for same excess experiments (Run 1 and 2)

Run	[1] (M)	[2] (M)	[e] (M)	$K_2S_2O_8$ (M)	[e] (M)	$AgNO_3$ (M)
1-100%	0.1	0.15	0.05	0.3	0.2	0.02
2-50%	0.05	0.1	0.05	0.25	0.2	0.02

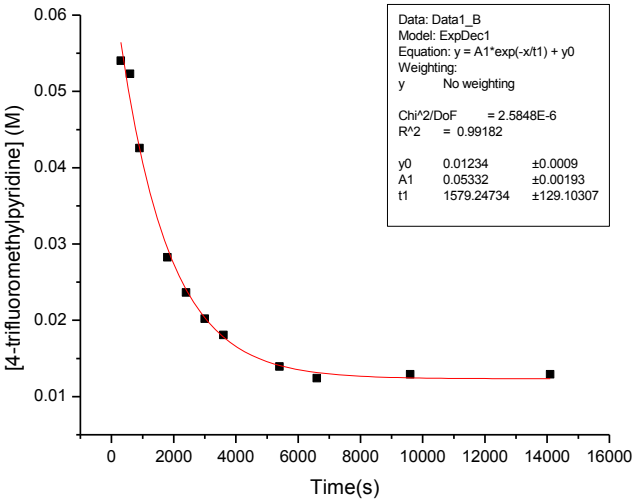
Decay data for Run 1



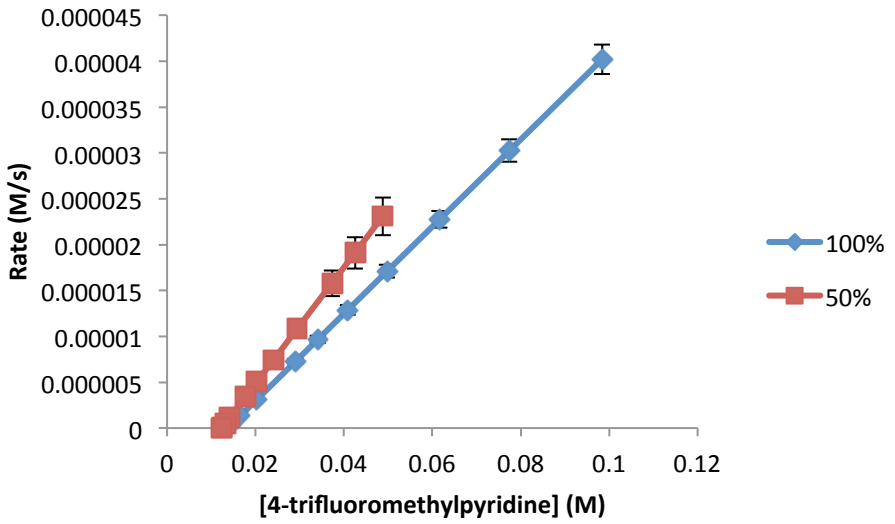
Growth data for Run 1



Decay data for Run 2



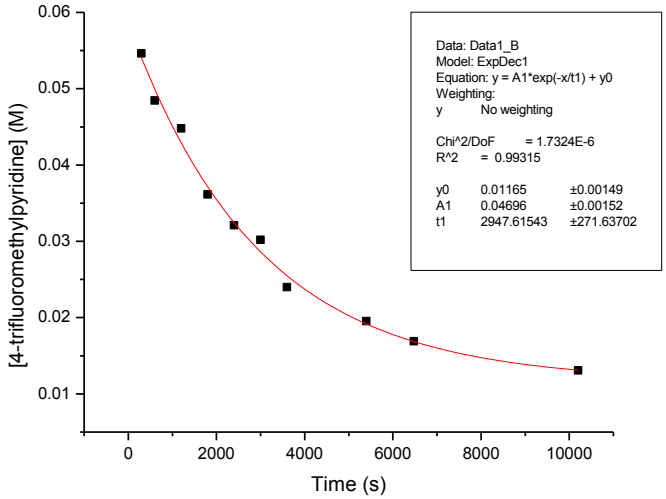
Plot of rate vs. [1] for catalyst stability



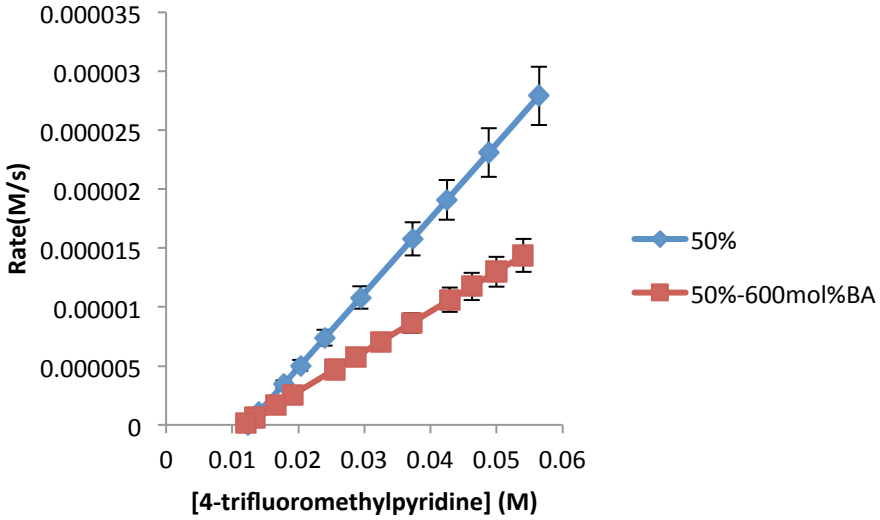
Conditions for different excess experiments for rate order for 2

Run	[1] (M)	[2] (M)	[e] (M)	$K_2S_2O_8$ (M)	$AgNO_3$ (M)
2-50%	0.05	0.1	0.05	0.25	0.02
3-Diff xs	0.05	0.3	0.25	0.25	0.02

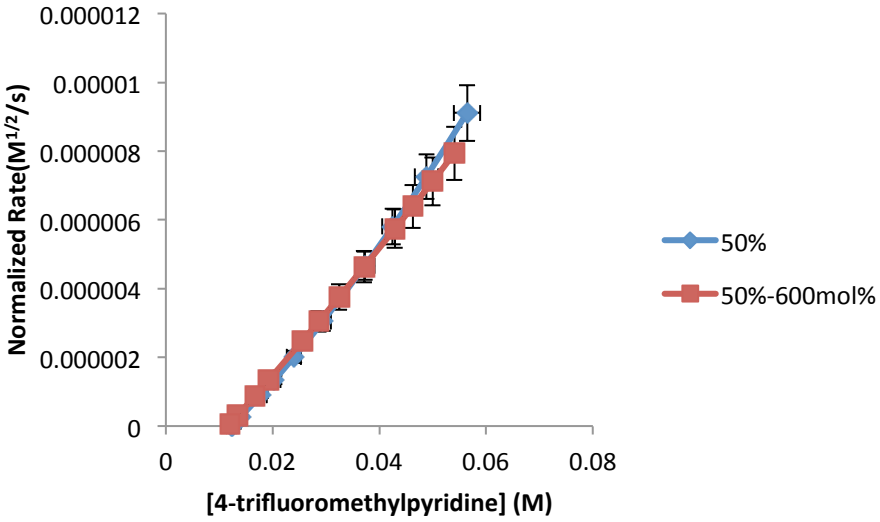
Decay data for Run 3



Plot of rate vs. [1] for rate order for 2 – Run 3



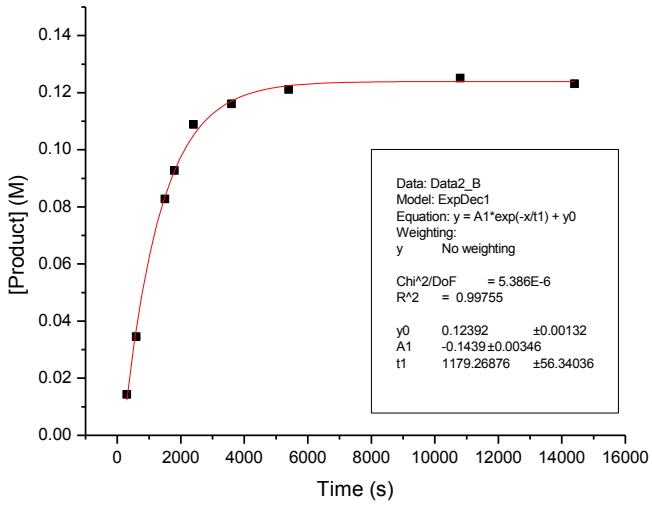
Plot of normalized rate vs. [1] for rate order for 2 – Run 3



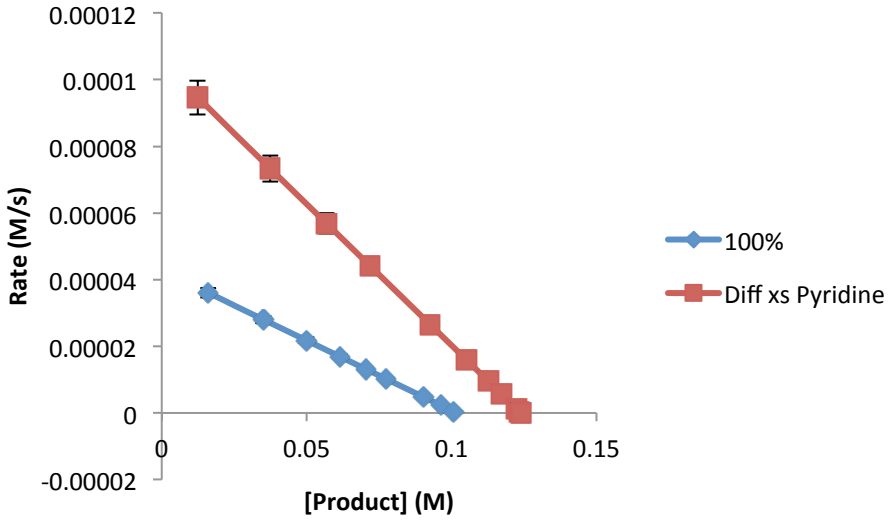
Conditions for different excess experiments for rate order for 1

Run	[1] (M)	[2] (M)	$K_2S_2O_8$ (M)	$AgNO_3$ (M)
1-100%	0.1	0.15	0.3	0.02
4-Diff xs	0.2	0.15	0.3	0.02

Growth data for Run 4



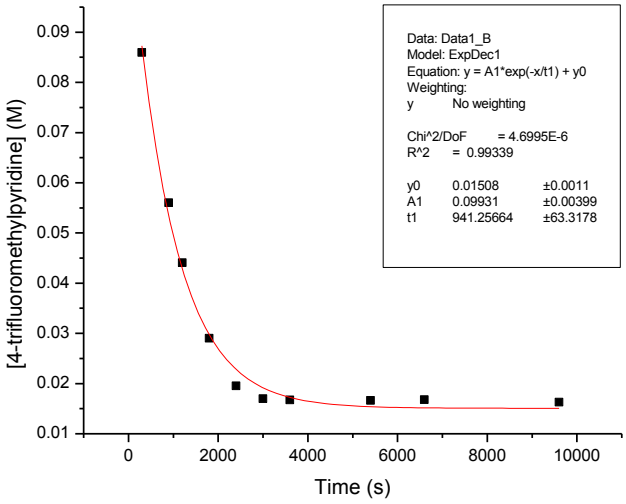
Plot of rate vs. [3] for rate order of 1



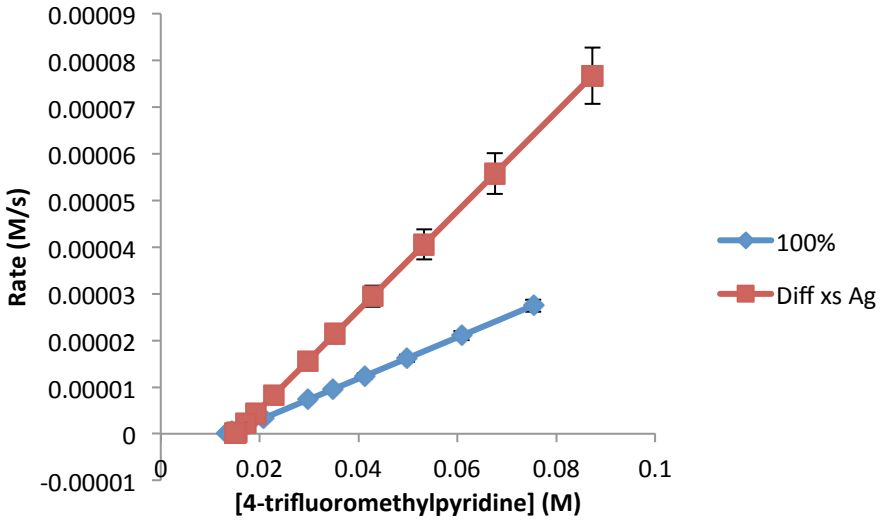
Conditions for different excess experiments for rate order for $AgNO_3$

Run	[1] (M)	[2] (M)	$K_2S_2O_8$ (M)	$AgNO_3$ (M)	[e] (M)
1-100%	0.1	0.15	0.3	0.02	0.08
5-Diff xs	0.1	0.15	0.3	0.04	0.06

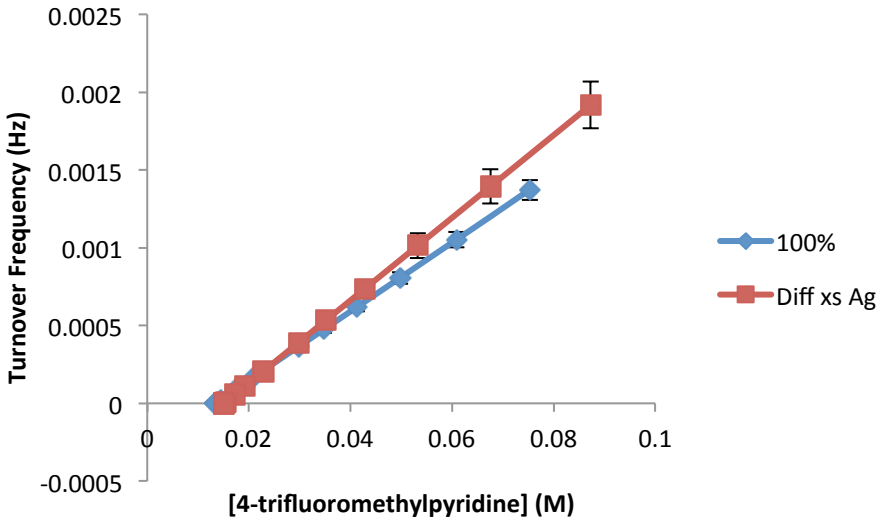
Decay data for Run 5



Plot of rate vs. [1] for rate order for $AgNO_3$



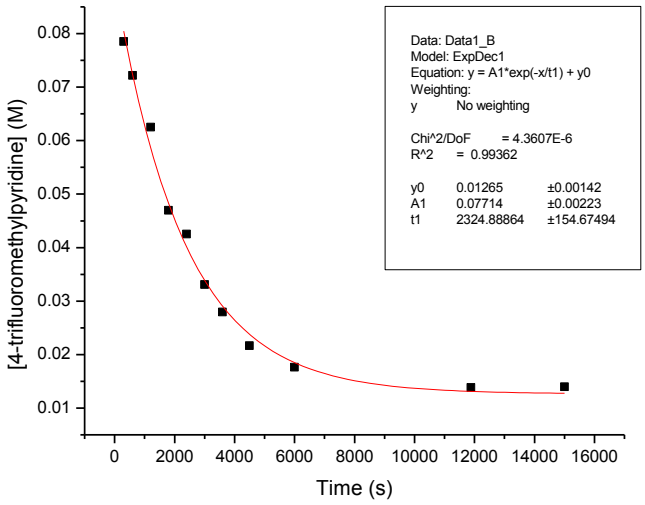
Plot of normalized rate vs. [1] for rate order of $AgNO_3$



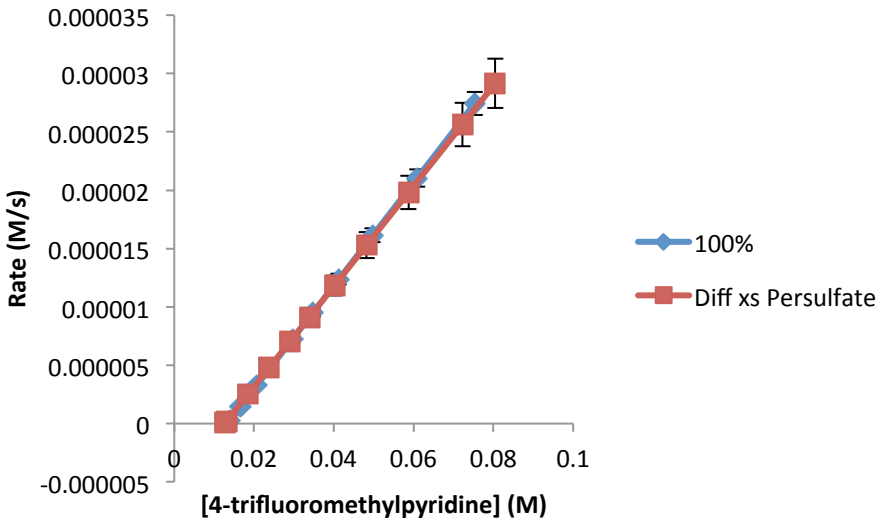
Conditions for different excess experiments for rate order for $K_2S_2O_8$

Run	[1] (M)	[2] (M)	$K_2S_2O_8$ (M)	[e] (M)	$AgNO_3$ (M)
1-100%	0.1	0.15	0.3	0.2	0.02
6-Diff xs	0.1	0.15	0.6	0.5	0.02

Decay data for Run 6



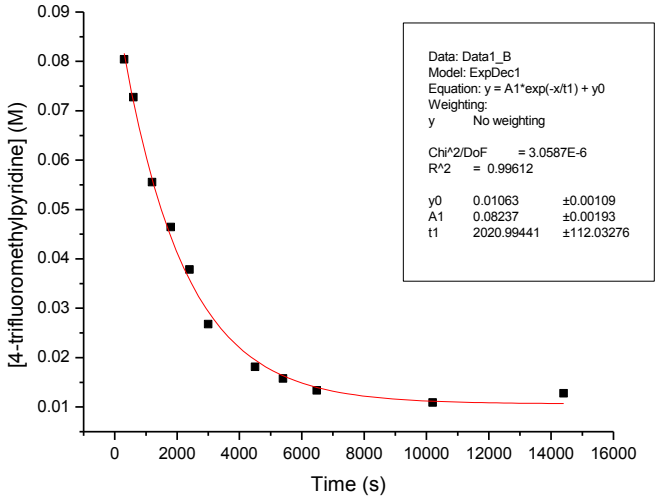
Plot of rate vs. [1] for rate order for $K_2S_2O_8$



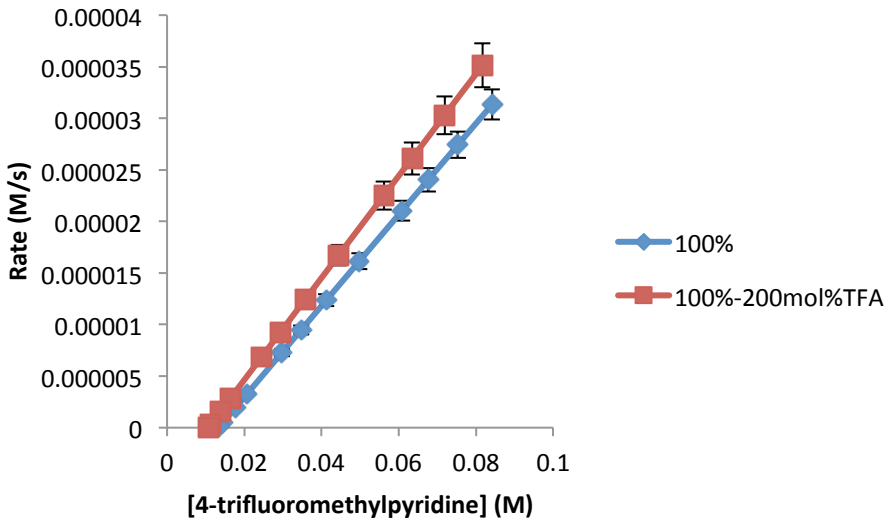
Conditions for different excess experiments for rate order for TFA

Run	[1] (M)	[2] (M)	$K_2S_2O_8$ (M)	$AgNO_3$ (M)	TFA (M)
1-100%	0.1	0.15	0.3	0.02	0.1
7-Diff xs	0.1	0.15	0.3	0.02	0.2

Decay data for Run 7



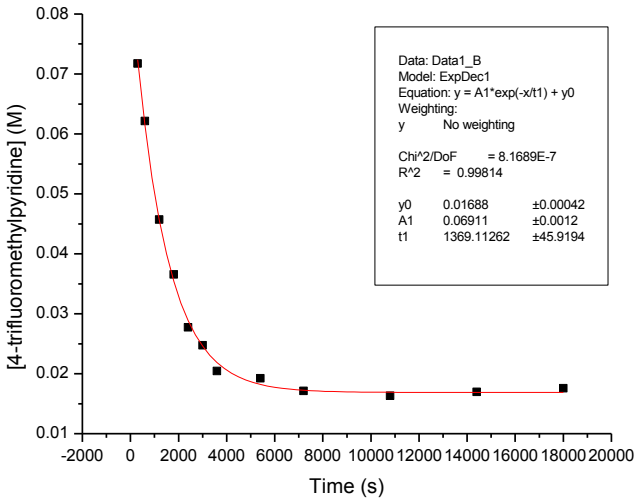
Plot of rate vs. [1] for rate order for TFA



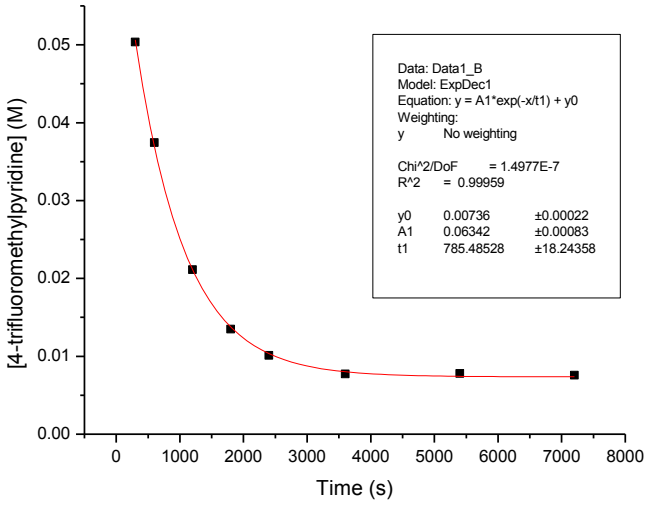
Conditions for different excess experiments for rate order for $Na_2S_2O_8$

Run	[1] (M)	[2] (M)	$Na_2S_2O_8$ (M)	[e] (M)	$AgNO_3$ (M)
8-100%	0.1	0.15	0.3	0.2	0.02
9-Diff xs	0.1	0.15	0.6	0.5	0.02

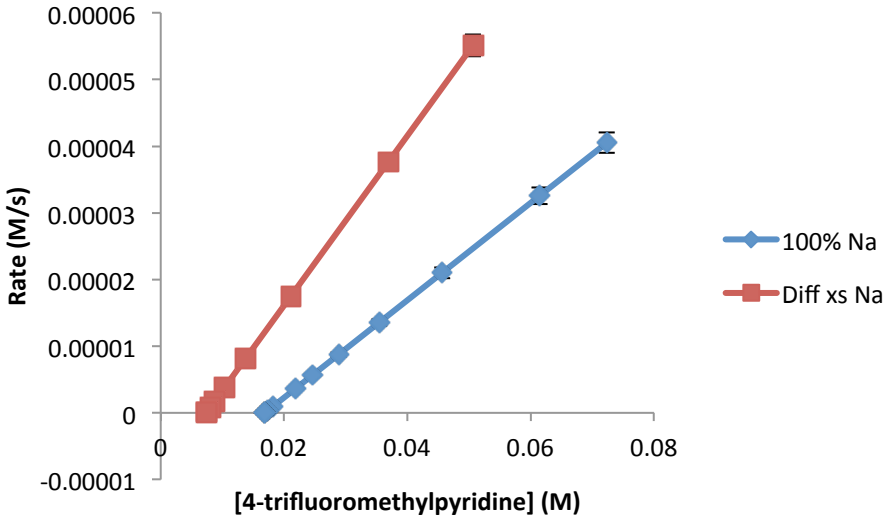
Decay data for Run 8



Decay data for Run 9



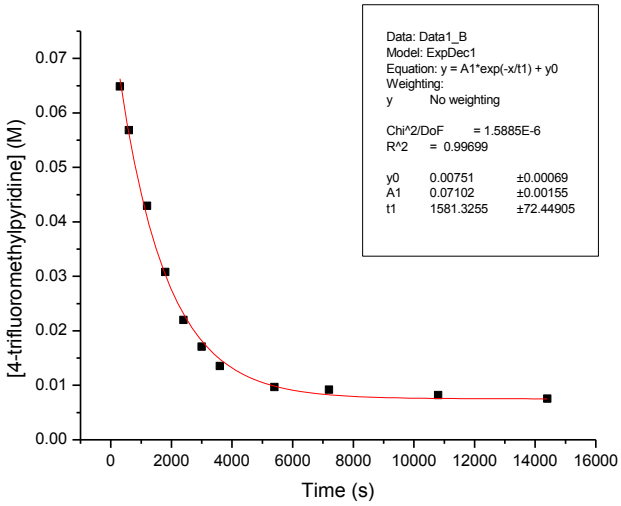
Plot of rate vs. [1] for rate order for $Na_2S_2O_8$



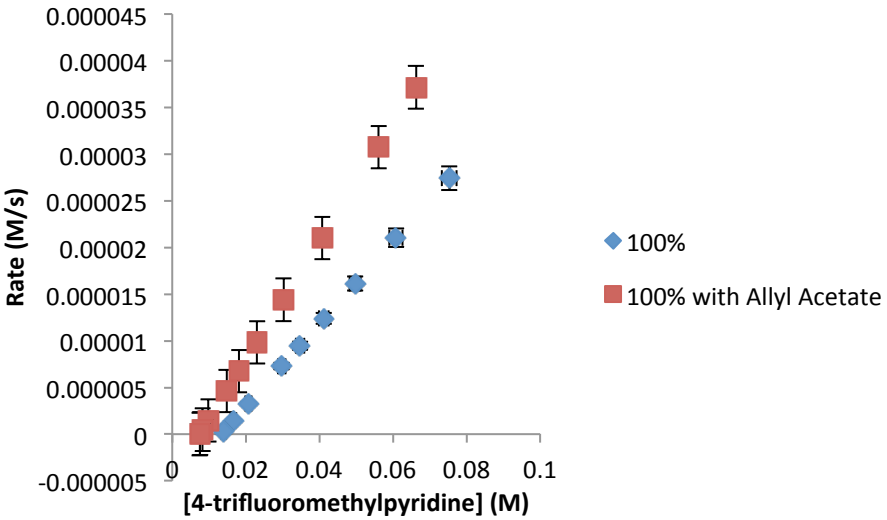
Conditions for experiments using allyl acetate as sulfate radical anion trap

Run	[1] (M)	[2] (M)	$Na_2S_2O_8$ (M)	$AgNO_3$ (M)	Allyl Acetate (M)
1-100%	0.1	0.15	0.3	0.02	0.0
10-AllylAc	0.1	0.15	0.3	0.02	0.6

Decay plot for Run 10



Plot of rate vs. [1] comparing Run 1 (100% run) to Run 10 (100% run with Allyl Acetate)



Calculation of conversion of rate data and error

Concentration samples at specific time points are plotted as [**1**] (M) vs. time (s). The data are then fit to a first order exponential decay using Equation 1.

$$[1] = y_0 + Ae^{\frac{-time}{t}} \tag{1}$$

The standard deviation of the [**1**] resulting from curve fitting is determined using Equation 2.

$$\sigma_{[1]} = Ae^{\frac{-time}{t}} \sqrt{\left(\frac{-e^{\frac{-time}{t}}}{t}\right)^2 + \left(\frac{\sigma_A}{A}\right)^2} + \sigma_{y_0} \tag{2}$$

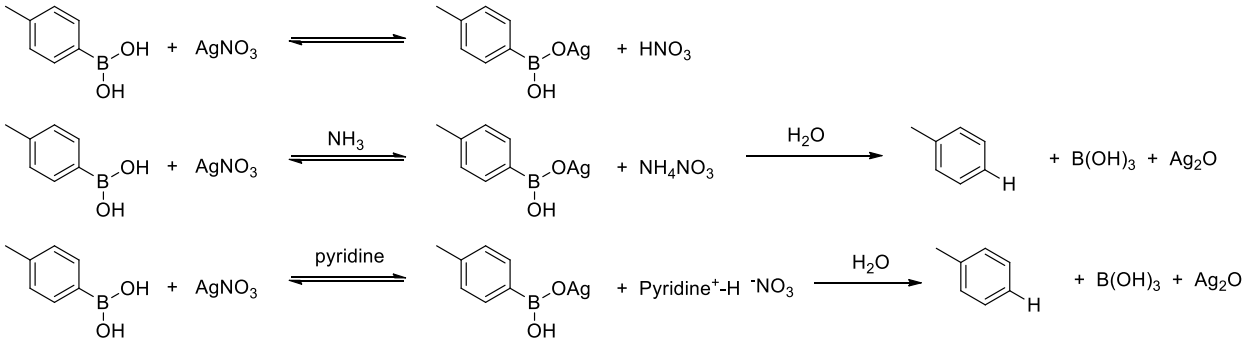
The derivative of Equation 1 provides the equation for the rate of change in [**1**] and is given in Equation 3.

$$-\frac{d[1]}{dt} = \frac{Ae^{\frac{-time}{t}}}{-t} \tag{3}$$

The standard deviation of $-d[\mathbf{1}]/dt$ resulting from Equation 3 is determined using Equation 4.

$$\sigma_{\frac{d[1]}{dt}} = \frac{Ae^{\frac{-time}{t}}}{-t} \sqrt{\left(\frac{-e^{\frac{-time}{t}}}{t}\frac{time}{\sigma_t}\right)^2 + \left(\frac{\sigma_A}{A}\right)^2 + \left(\frac{\sigma_t}{t}\right)^2} \tag{4}$$

Reactions of boronic acid with silver nitrate



Derivation of rate law

Rate Equation:

$$-\frac{d\,[CF_3C_5H_4N]}{dt} = k_2[CF_3C_5H_4N - Ag^I]\,[S_2O_8]$$

The interaction between silver(I) and pyridine was assumed to be at steady state:

$$[CF_3C_5H_4N - Ag^I] = \frac{k_1[CF_3C_5H_4N][Ag^I]}{k_{-1}+k_2[S_2O_8{}^{2-}]+k_3[Ar{-}B(OH)_2]}$$

$$-\frac{d\,[CF_3C_5H_4N]}{dt} = \frac{k_1k_2[CF_3C_5H_4N][Ag^I]\,[S_2O_8]}{k_{-1}+k_2[S_2O_8{}^{2-}]+k_3[Ar{-}B(OH)_2]}$$

A mass balance was written for the silver complexes in the system:

$$[Ag^I]_{tot} = [Ag^I] + [CF_3C_5H_4N - Ag^I]$$

[Ag^I] was solved for and inserted into the rate law:

$$-\frac{d\,[CF_3C_5H_4N]}{dt} =$$

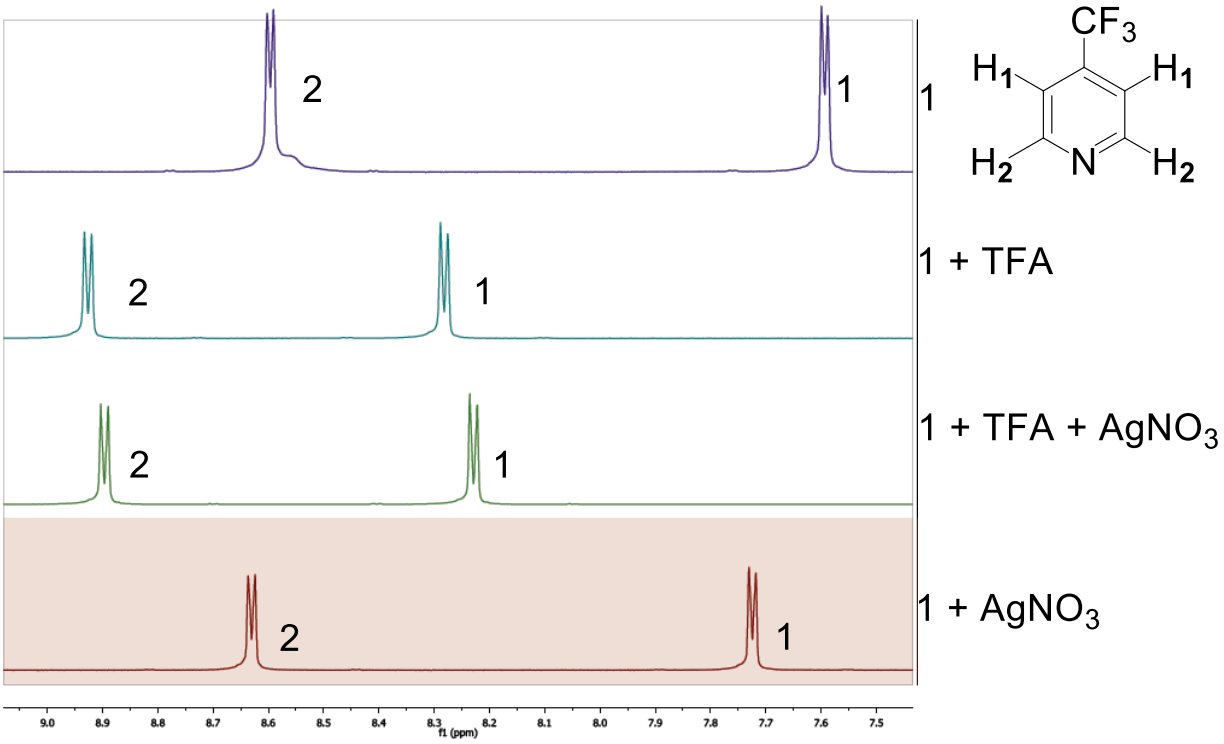
$$\left(\frac{k_1k_2[CF_3C_5H_4N][S_2O_8]}{k_{-1}+k_2[S_2O_8{}^{2-}]+k_3[Ar{-}B(OH)_2]}\right)\left(\frac{k_{-1}[Ag^I]_{tot}+k_2[S_2O_8{}^{2-}][Ag^I]_{tot}+k_3[Ar{-}B(OH)_2][Ag^I]_{tot}}{k_{-1}+k_2[S_2O_8{}^{2-}]+k_3[[Ar{-}B(OH)_2]]+k_1[CF_3C_5H_4N]}\right)$$

Assuming $k_2 << k_{-1}$, $k_2 << k_3$, $k_2 << k_1$, and that Ag^I is the resting state of the catalyst:

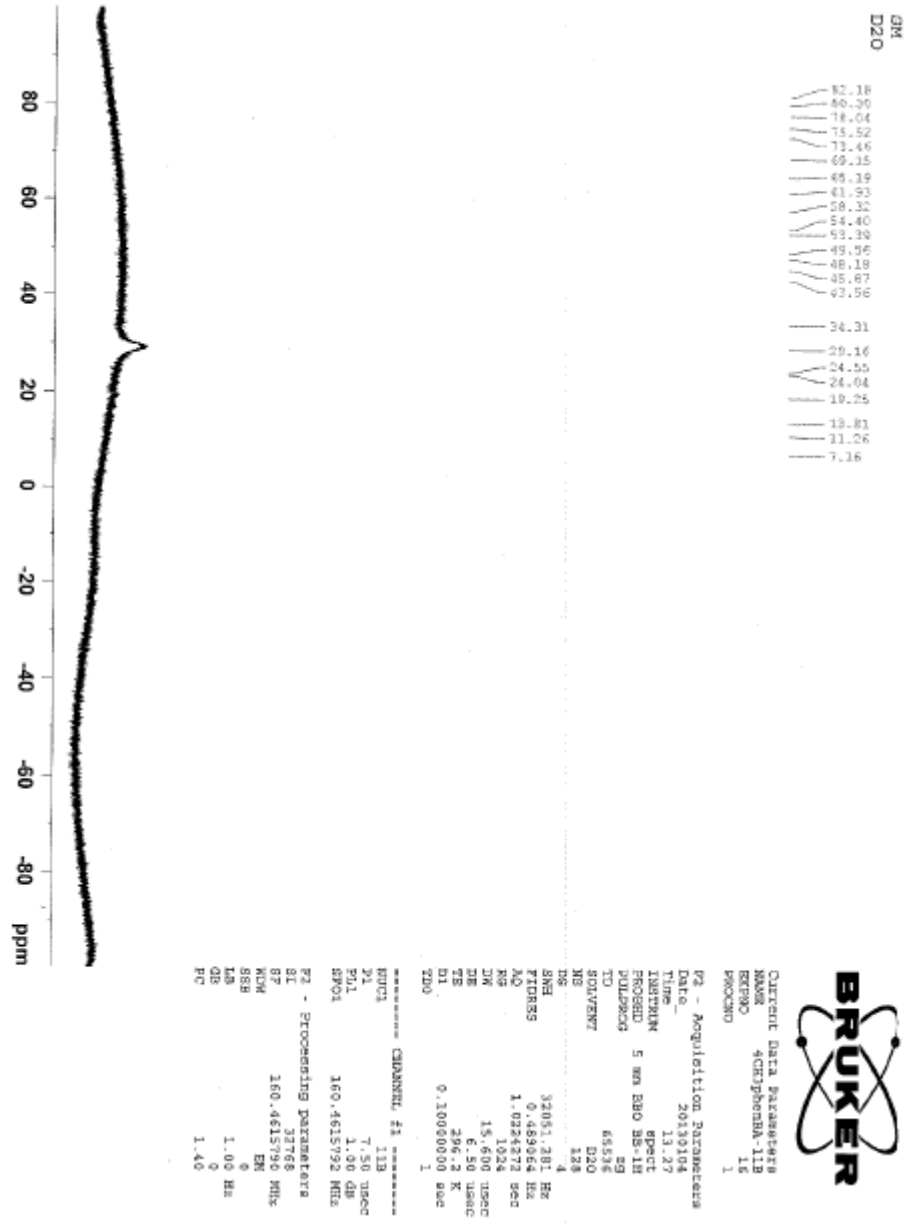
$$-\frac{d\,[CF_3C_5H_4N]}{dt} = k_1k_2[CF_3C_5H_4N][S_2O_8{}^{2-}][Ag^I]_{tot}\left(\frac{k_{-1}+k_2[S_2O_8{}^{2-}]+k_3[Ar{-}B(OH)_2]}{k_{-1}{}^2+2k_{-1}k_3[[Ar{-}B(OH)_2]]+k_3{}^2[Ar{-}B(OH)_2]^2}\right)$$

$$\approx k_{obs}\frac{[CF_3C_5H_4N][S_2O_8{}^{2-}][Ag^I]_{tot}}{[Ar{-}B(OH)_2]^{0.5}}$$

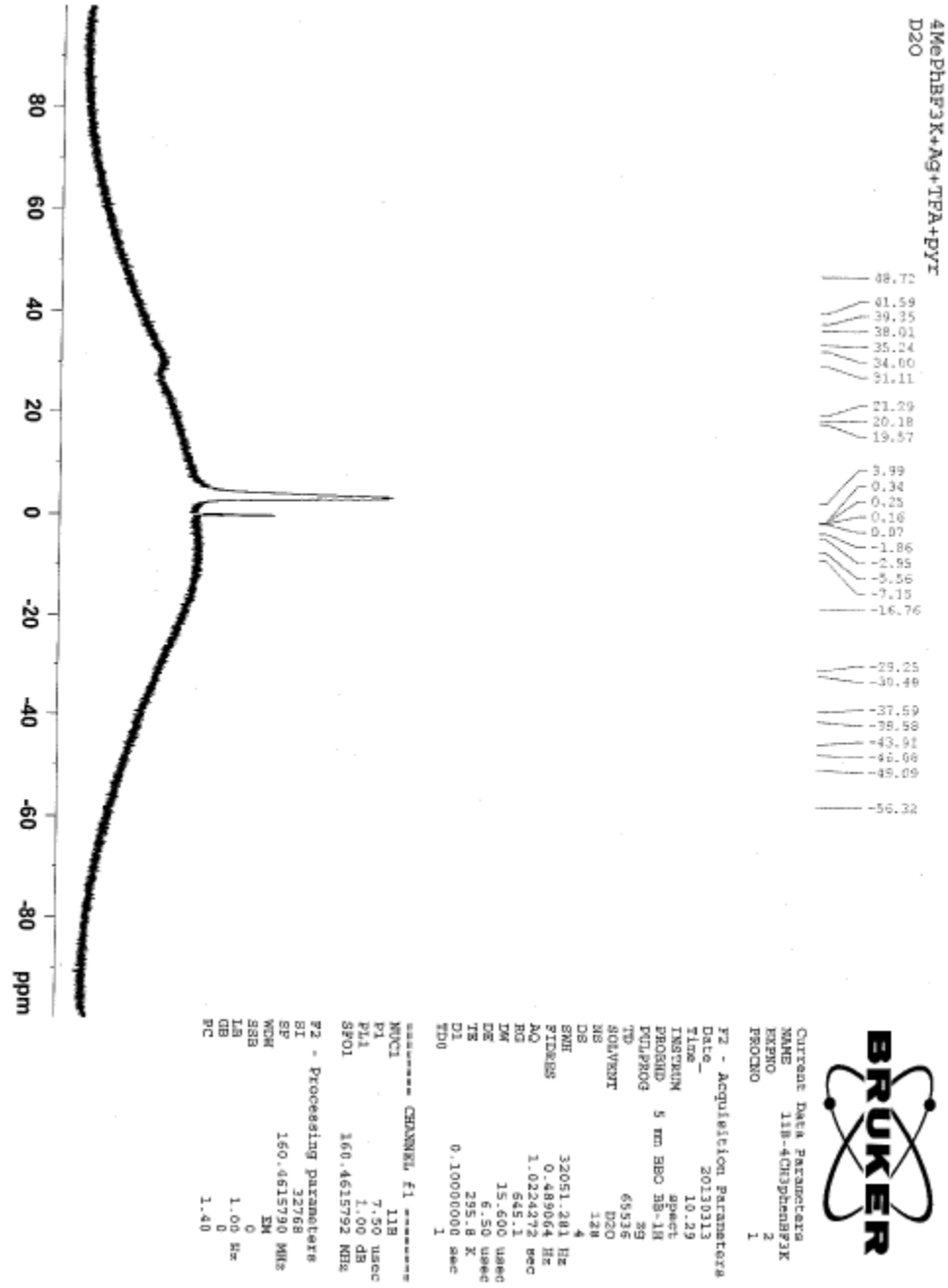
Spectral data for pyridine ^{1}H NMR studies



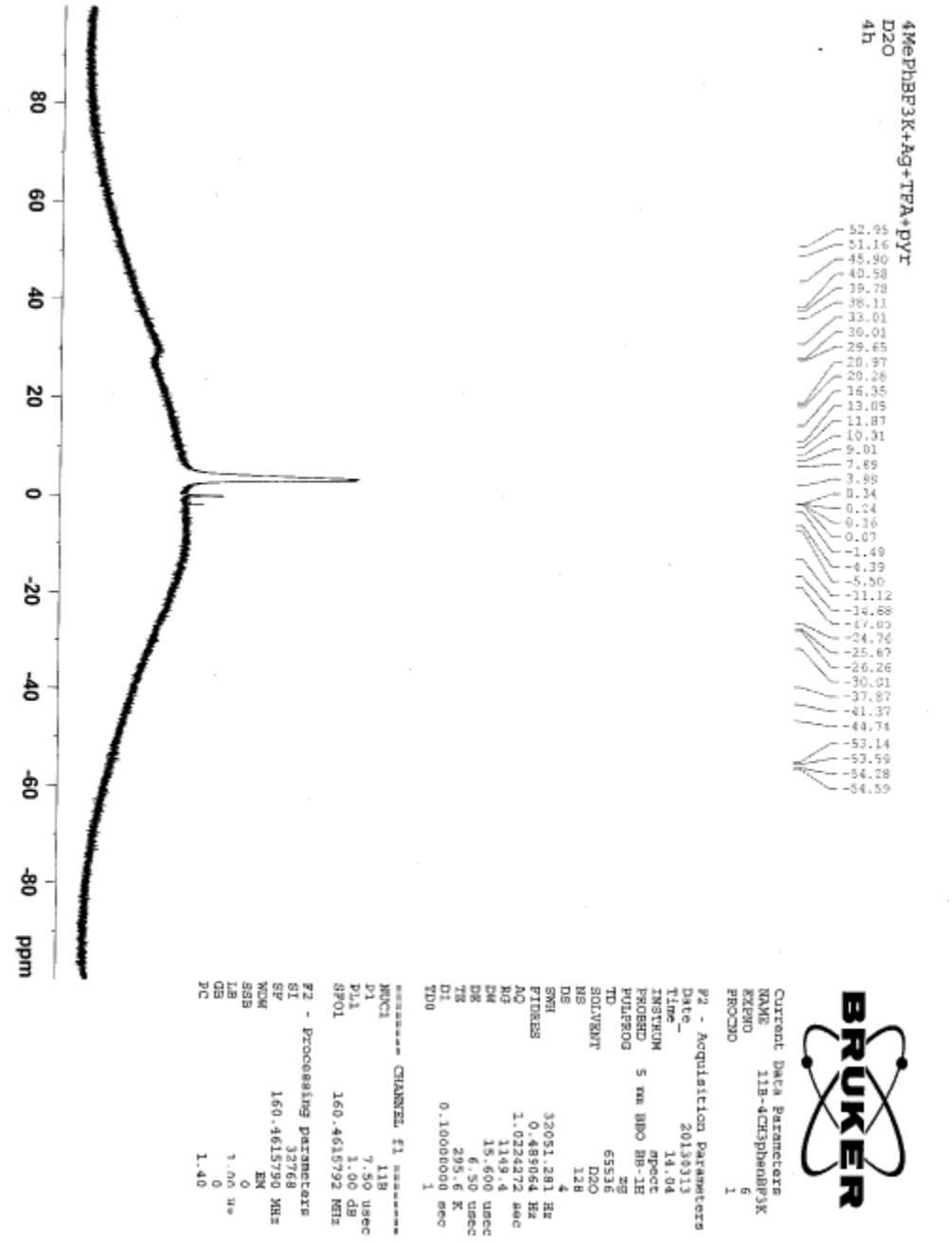
^{11}B NMR spectrum of **2**



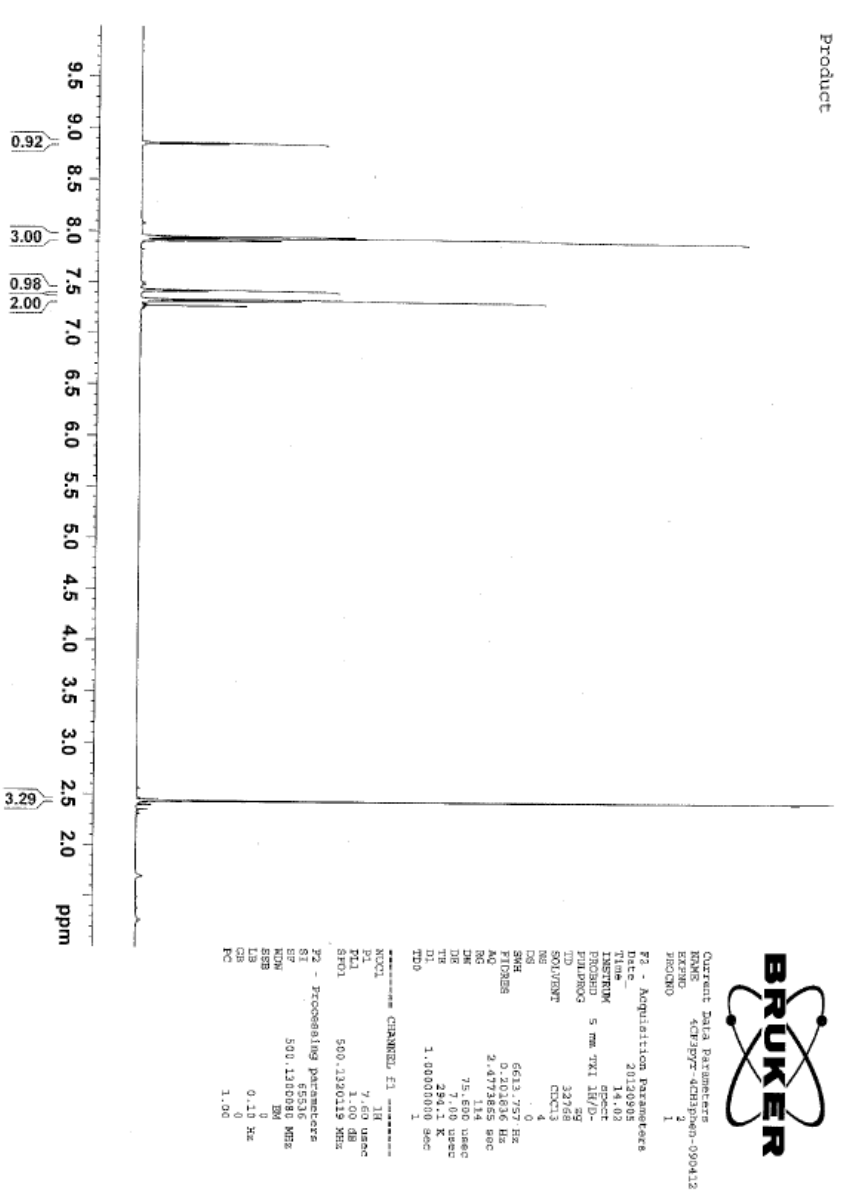
^{11}B NMR spectrum of **4** under reaction conditions at t = 0mins

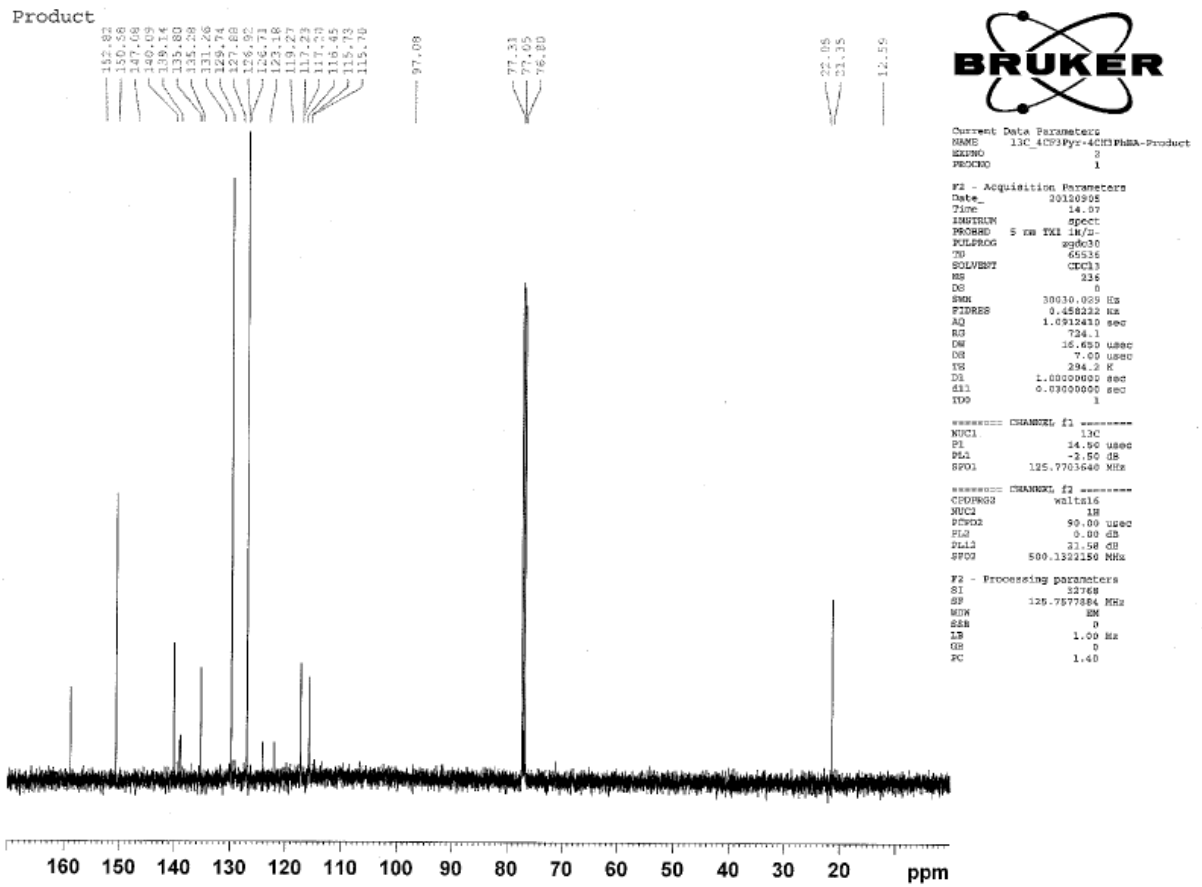


^{11}B NMR spectrum of **4** under reaction conditions at t = 4h



^{1}H and ^{13}C NMR spectra for cross-coupled product **3**

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140.09
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135.80
135.28
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129.74
127.88
126.90
126.71
123.18
119.27
117.23
117.00
116.45
115.73
115.70
97.08
77.31
77.05
76.80
22.06
21.35
12.59
BRUKER
Current Data Parameters
NAME 13C_4CF3Pyz-4CH3PhMA-Product
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120905
Time 14.07
INSTRUM spect
PROBHD 5 mm TXI 1H/D-
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TD 65536
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NS 236
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RG 724.1
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DE 7.00 usec
TE 294.2 K
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d11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 14.50 usec
PL1 -2.50 dB
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CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 33.58 dB
SFO2 500.1322150 MHz
F2 - Processing parameters
SI 32768
SF 125.7577884 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm