Supporting Information

Process Development of a Suzuki Reaction used in the Manufacture of Lanabecestat

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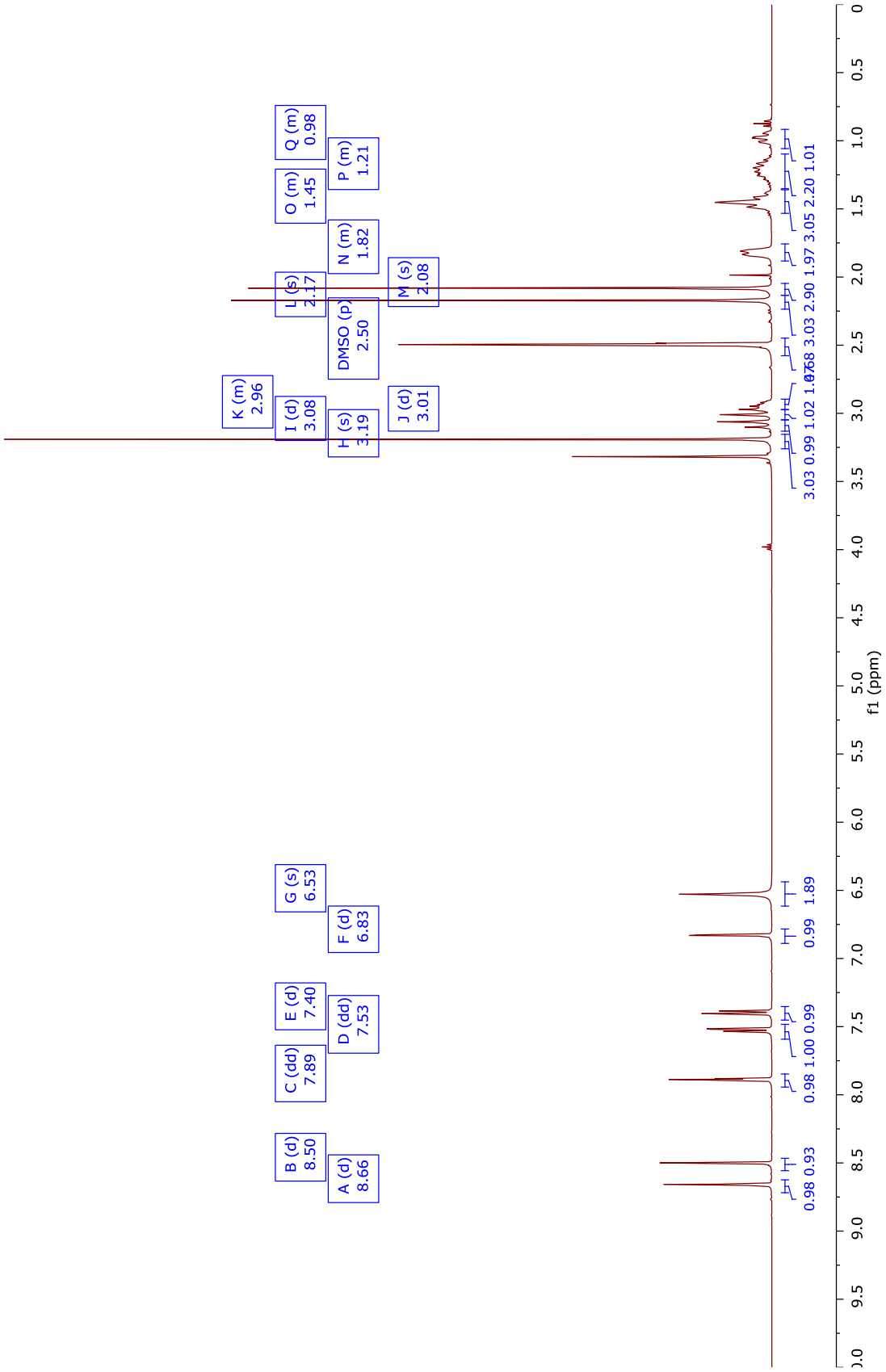
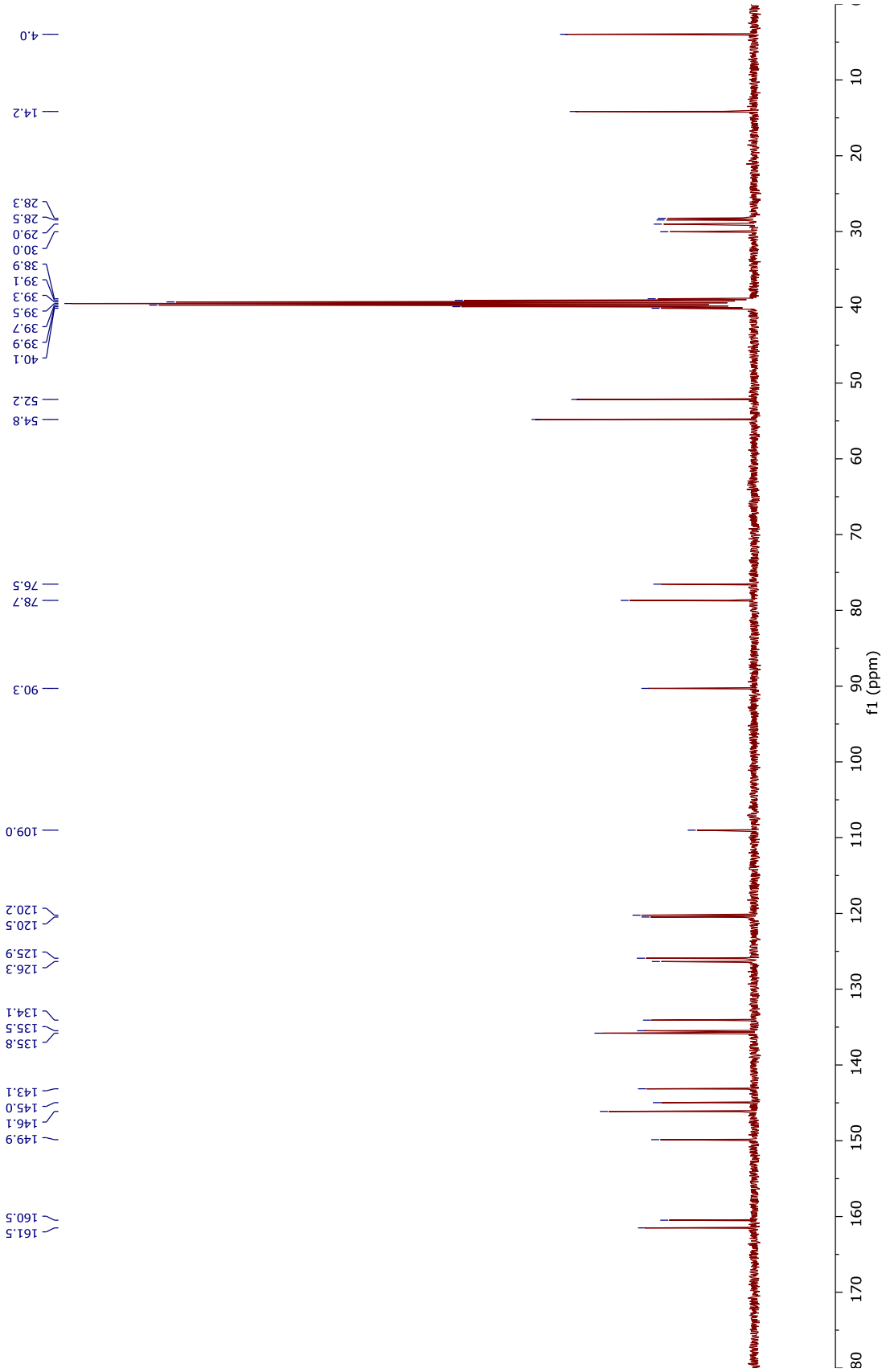
Contents of Supplementary Information:

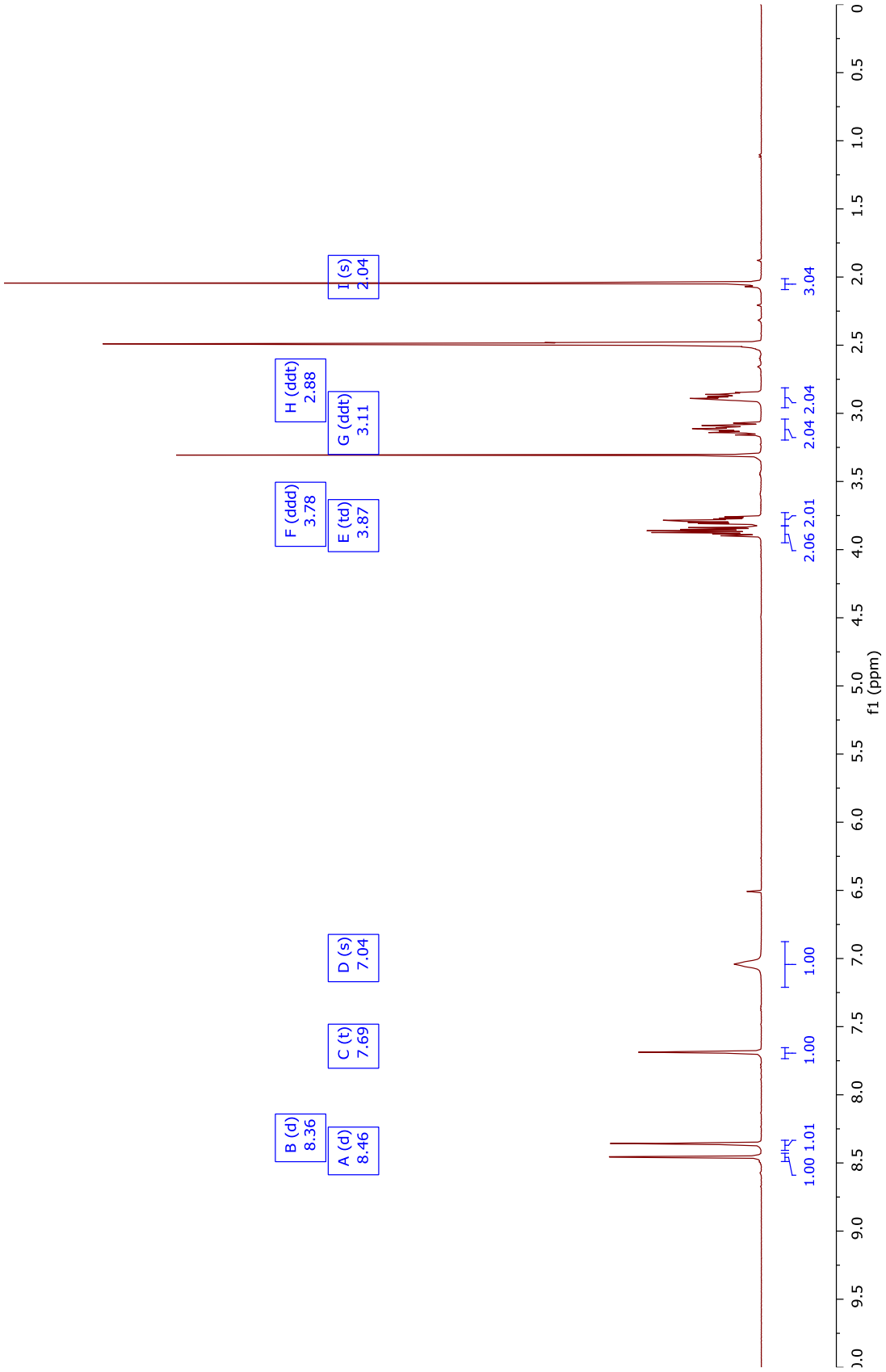
1. ^{1}H-NMR Spectra of lanabecestat (in d^{6}-DMSO)



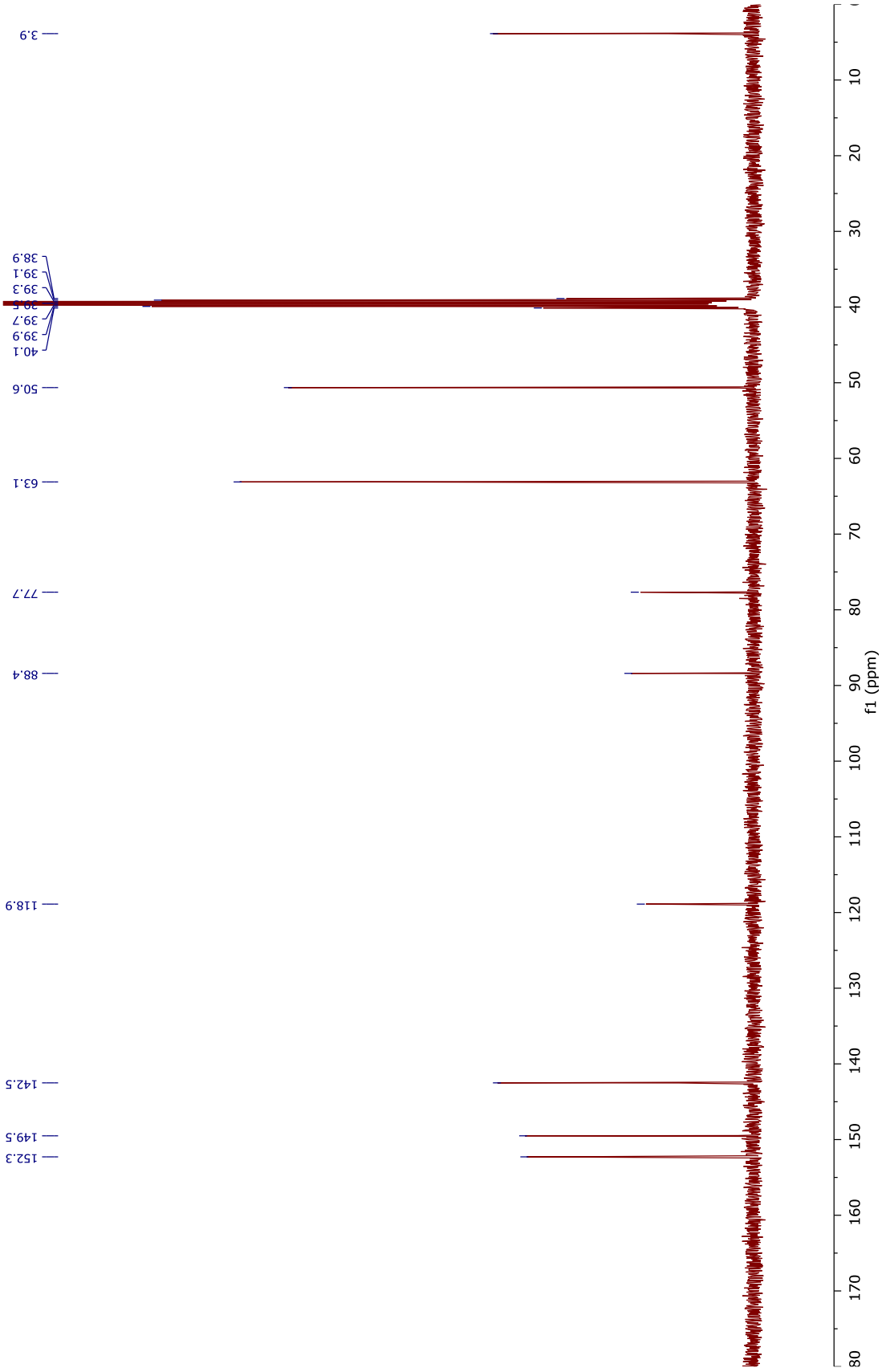
2. ^{13}C-NMR Spectra of lanabecestat (in d^6-DMSO)



3. ^{1}H-NMR Spectra of 2b (in d^{6}-DMSO)



4. ^{13}C-NMR Spectra of 2b (in d^6-DMSO)



5. Kinetic profiling data for the hydrolysis of 2b.

^{1}H-NMR profiling data were acquired on a Bruker Ultrashield AVIIIHD 500 MHz spectrometer fitted with a SmartProbe and operating with Topspin3.5pl6 software. All ^{1}H detection experiments were performed using the pulse program wetpr.2, 1 scan, acquisition time 1.6384 s, relaxation delay 3 s. NMR data were processed using Topspin3.5pl6 or Mestrenova version 11.0.2.

Time (s)	Standard Conditions (rel area%)		Standard Conditions + DEA (rel area%)	
	Boronic Ester	Boronic Acid	Boronic Ester	Boronic Acid
5			49.033	50.967
10	32.794	67.206	39.750	60.250
15	23.128	76.872	30.253	69.747
30	13.300	86.700	19.410	80.590
45	10.746	89.254	15.408	84.592
60	10.037	89.963	14.073	85.927
90	9.909	90.091	14.228	85.772
120	10.034	89.966	13.820	86.180
180	9.679	90.321	13.912	86.088
240	10.720	89.280	13.504	86.496
300	10.391	89.609	12.796	87.204

6. DynoChem® model, Process tab:

	| fitting data for boronic ester hydrolysis														
Phase	**Solution**	liquid (set volume)													
	Temperature		C												
	BE		mol/L	plot											
	BA		mol/L	plot											
	DEA		mol/L	plot											
Reactions in	**Solution**														
reaction 1	k>	0.05592	1/s	Tref	2.70E+01	C	Keq	2.03E+00	mol/L	*	BE	=	BA	+	DEA
Variables	**variables**														
	BE		mol/L												
	BA		mol/L												
	DEA		mol/L												
Finished															

7. DynoChem® Model Information, algebraic solution to equilibrium condition.

Predicting equilibrium positions for a variety of initial boronic ester (**2b**) and diethanolamine (DEA) concentrations at given water concentration:

At equilibrium:

$[BA] = x$

$[DEA] = x + [DEA]$

$[BE] = [BEi]-x$

Where DEAi = DEA in solution prior to equilibration, BEi = boronic ester before equilibration

Using:

$K_{EQ'} = [BA][DEA] / [BE]$

By substitution:

$K_{EQ}' = x([DEAi] + x) / ([BEi]-x)$

$K_{EQ}'([BEi]-x) = x([DEAi] + x)$

$K_{EQ}'[BEi] - K_{EQ'}x = x[DEAi] + x^2$

$-K_{EQ}'[BEi] + K_{EQ'}x + x[DEAi] + x^2 = 0$

$-K_{EQ}'[BEi] + x.([DEAi] + K_{EQ'}) + x^2 = 0$