

Mono- and Tri-Ester Hydrogenolysis using Tandem Catalysis. Scope and Mechanism

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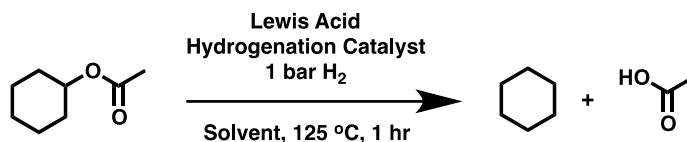
Supplementary Materials

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Activation parameters were calculated using the following Eyring expression (T = temperature, k = rate constant, R = gas constant, k_B = Boltzman constant, and h = Planck's constant).

$$\ln\left(\frac{k}{T}\right) = -\frac{\Delta H^\ddagger}{R} \cdot \frac{1}{T} + \frac{\Delta S^\ddagger}{R} + \ln\left(\frac{k_B}{h}\right)$$

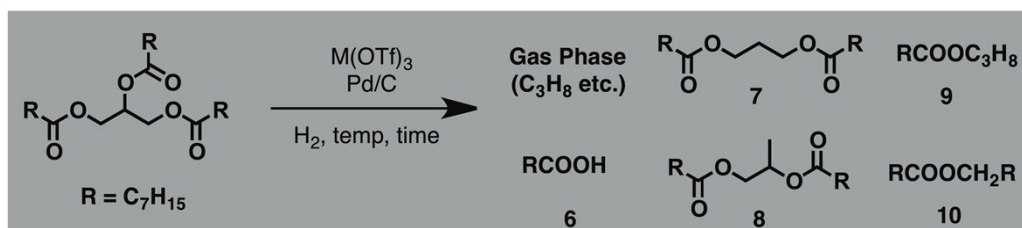
Table S1. Screening of tandem hydrogenolysis catalysts and conditions



	Acid	Hydrog. Cat.	Solvent	Conv.(%) ^b
1 ^c	-	10% Pd/C	neat	N.R.
2 ^c	La(OTf) ₃	10% Pd/C	neat	N.R.
3 ^c	Yb(OTf) ₃	10% Pd/C	neat	N.R.
4 ^c	Sc(OTf) ₃	10% Pd/C	neat	N.R.
5	Ce(OTf) ₄	10% Pd/C	neat	5
6	Fe(OTf) ₃	10% Pd/C	neat	33
7	Al(OTf) ₃	10% Pd/C	neat	56
8	Zr(OTf) ₄	10% Pd/C	neat	56
9	Hf(OTf) ₄	10% Pd/C	neat	89
10	HOTf	10% Pd/C	neat	20
11 ^c	HOAc	10% Pd/C	neat	N.R.
12	Hf(OTf) ₄	5% Pd/SiO ₂	neat	85
13	Hf(OTf) ₄	5% Pd/TiO ₂	neat	74
14	Hf(OTf) ₄	5% Pd/Al ₂ O ₃	neat	31
15	Hf(OTf) ₄	5% Pd/BaSO ₄	neat	15
16	Hf(OTf) ₄	5% Pt/C	neat	52
17 ^d	Hf(OTf) ₄	10% Pd/C	neat	24
18 ^d	Hf(OTf) ₄	10% Pd/C	<i>n</i> -Octane	5
19 ^d	Hf(OTf) ₄	10% Pd/C	CHCl ₃	5
20 ^d	Hf(OTf) ₄	10% Pd/C	THF	N.R.
21 ^d	Hf(OTf) ₄	10% Pd/C	DMF	N.R.
22 ^d	Hf(OTf) ₄	10% Pd/C	MeOH	N.R.
23 ^d	Hf(OTf) ₄	10% Pd/C	H ₂ O	N.R.

^a All reactions performed with 0.5 mol% acid catalyst, 0.2 mol% metal hydrogenation catalyst, and 1 bar of H₂ in a balloon at 125 °C for 1 h unless otherwise noted. OTf = trifluoromethanesulfonate, CF₃SO₂-. HOAc = acetic acid. THF = tetrahydrofuran. DMF = *N,N*-dimethylformamide. MeOH = methanol. ^b NMR conversion vs. mesitylene internal standard. N.R. = no reaction. ^c N.R. entries run for 4 h. ^d 60 °C, 46 hours.

Table S3. Catalytic hydrogenolysis of triglycerides (Runs at 150 °C for 6 hr and 200 °C for 2 hr)



	Substrate	M(OTf) _n	p(H ₂) (bar)	T (°C)	Conv (%)	Liquid Phase Yield(%)					“RCOO” Balance (%)
						6	7	8	9	10	
1 ^b	5a	Hf	1	150	27.3	14.1	0.3	11.8	2.8	-	96
2 ^b	5a	Hf	1	200	48.7	37.4	1.6	1.2	3.9	1.2	93
3 ^b	5a	Hf	30	150	70.9	40.4	1.7	9.6	10.8	11.0	92
4 ^b	5a	Hf	30	150	96.7	69.8	4.5	0.6	20.9	12.6	94
5 ^{bc}	5a	Hf	1	200	25.2	10.8	-	-	-	-	86
6 ^d	5a	Hf	1	200	20.1	12.5	0.9	8.5	5.8	2.3	100
7	5a	Hf	1	200	86.2	48.9	4.0	2.5	5.5	3.6	72
8	5a	Al	1	150	40	23	1.8	12.6	5.7	5.7	99
9	5a	Al	1	200	41	37.1	3.9	6.3	4.5	3	100
10	5a	Al	30	150	55	19.3	1.6	12	10.9	10.4	88
11	5a	Al	30	200	94	25.4	1.8	-	25	22.8	93
12	5a	Ce	1	150	0	-	-	-	-	-	99
13	5a	Ce	1	200	20	8.5	2.2	5.4	6.1	2.4	97
14	5a	Sc	1	150	0	-	-	-	-	-	99
15	5a	Sc	1	200	15	6.3	0.5	4.2	2.1	0.7	98
16	5a	H	1	150	76	72	-	-	-	-	96
17	5a	H	1	200	73	52.5	-	-	2	-	81
18	glycerol	Hf	1	200	Complex mixture + coke + water					-	

^a Conditions unless otherwise noted: 1.5 mol % M(OTf)_n, 0.6 mol% Pd/C and 1 mmol substrate for 2 hr at 200 °C and 6 hr at 150 °C. Conversion and liquid phase yield determined by ¹H-NMR. RCOO Balance determined by taking all carboxylate-containing species (5-10) into account versus starting material. See example in Fig. S7 and Table S7. “-” = not detected. Reactions performed at 30 bar H₂ included 2 mL cyclohexane as solvent added to the Parr reactor. ^b Catalyst loadings reduced: 0.5 mol% Hf(OTf)₄ and 0.2 mol% Pd/C and reactions at 150 °C were run at 2 hours. ^c No Pd/C. ^d 15 mol% *N,N*-dimethylacetamide added.

Table S4. Gas phase selectivity for entries in Table S3.

Entry	Substrate	Gas Phase Selectivity(%)					
		CO ₂	CH ₄	C ₂ H ₄	C ₂ H ₆	C ₃ H ₆	C ₃ H ₈
4	5a	0.7	-	-	3.3	-	96.0
7	5a	0.2	-	-	2.3	5.8	91.7
5	5a	trace	-	-	-	-	-

12	glycerol	20.0	-	4.7	28.3	14.4	32.6
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Gas phase selectivity determined by GC-TCD. “-” = not detected.

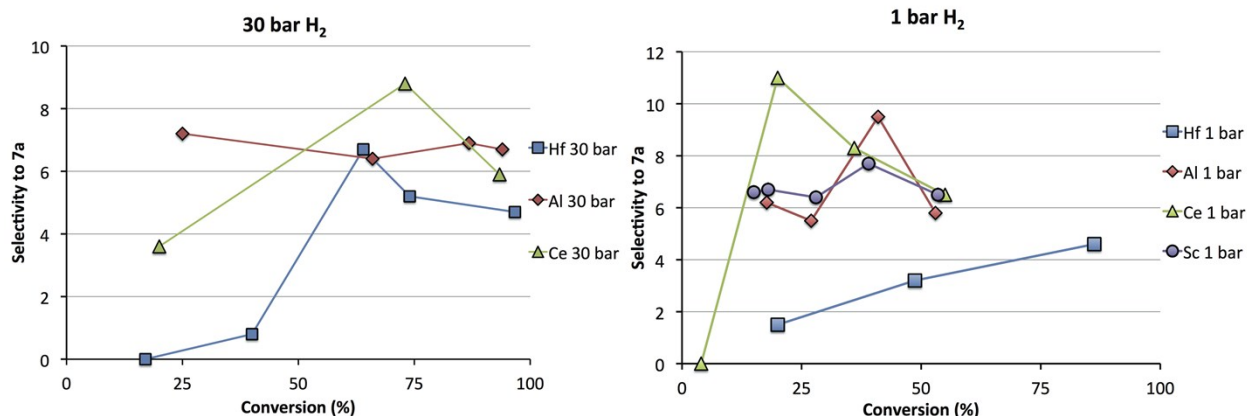


Figure S1. Selectivity to 7a for different M(OTf)_n catalysts over a range of conversions at 30 bar (left) and 1 bar (right) H₂. Reactions performed at 30 bar H₂ included additional 2 mL of cyclohexane in the Parr reactor to make up sufficient volume for the mechanical stirring apparatus. Conditions: 1.5 mol% M(OTf)_n, 0.6 mol% Pd/C (10 wt %), 200 °C, 30 minutes to 5 hours.

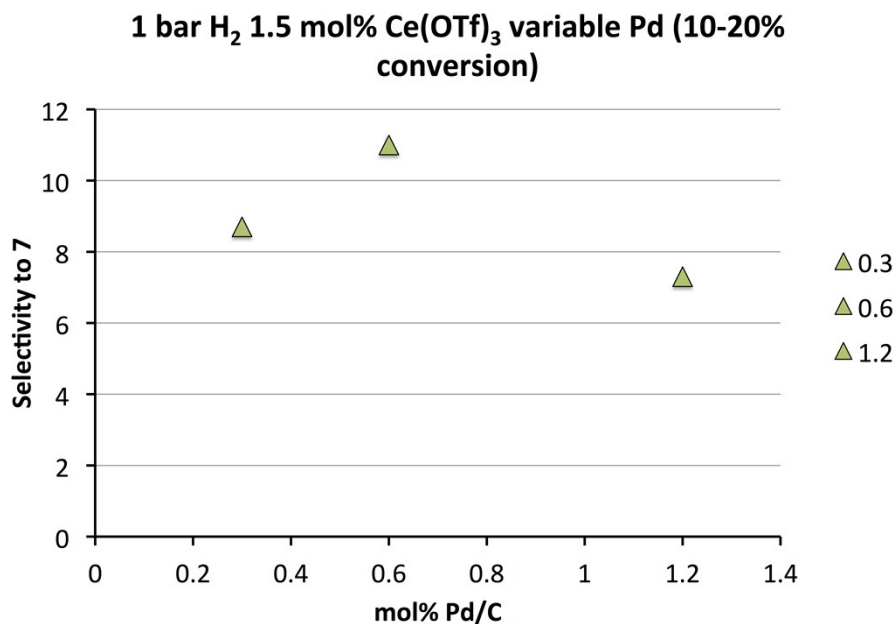


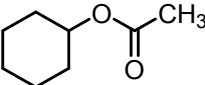
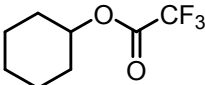
Figure S2. Selectivity to 7a at varying ratios of Ce(OTf)₃ to Pd/C (10 wt %). Conditions: 1.5 mol% Ce(OTf)₃, 0.3, 0.6, and 1.2 mol% Pd/C (10 wt %), 200 °C, 1 bar H₂, 2 hours.

Table S5. Conversion (Figure 5) of cyclohexyl acetate at different pressures of H₂ by ¹H NMR versus 1,1,2,2-tetrachloroethane internal standard. Conditions: 100 °C, 0.5 mol % Hf(OTf)₄, 0.2 mol % Pd/C (10 wt %), neat cyclohexyl acetate.

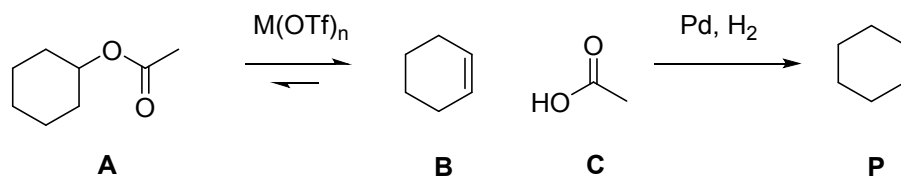
H ₂ Pressure (bar)	Conversion
1	12.4 %
10	14 %
20	14 %
30 ^a	15 and 13 %
40	13 %
50	15 %

^a Duplicate run.

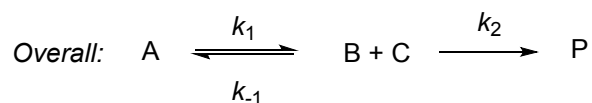
Table S6. Computed enthalpy and free energy profiles for the Hf(IV) triflate catalyzed RC(O)O-R' bond cleavage of cyclohexyl acetate and cyclohexyltrifluoroacetate at the B3LYP level of theory. Reaction coordinate A → G for the cyclohexylacetate substrate is presented in Figures 8 and 10.

Reaction Coordinate Structure				
	ΔH(soln), Kcal/mol	ΔG(soln), Kcal/mol	ΔH(soln), Kcal/mol	ΔG(soln), Kcal/mol
A	0.0	0.0	0.0	0.0
B	-23.4	-12.3	-15.0	-3.0
C (TS)	-8.1	4.1	-4.4	13.5
D	-14.3	-5.5	-11.4	-0.6
E (TS)	1.2	15.4	6.2	22.1
F	-12.5	-3.0	-5.6	5.3
G	-10.6	-11.6	-2.8	-3.6

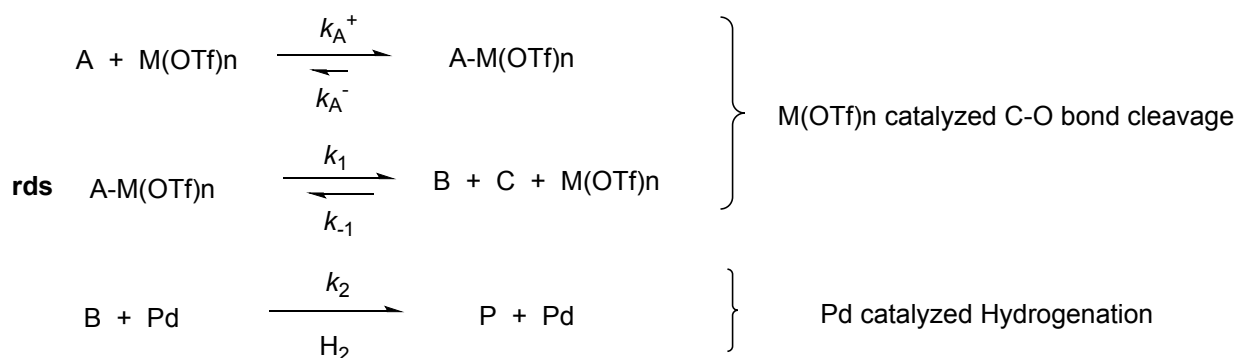
Rate Law Derivation:



The experimental data suggest that the reaction is zero order in A and H₂ and first order in M(OTf)_n catalyst. Based on this, and the very exothermic binding of substrate A to M(OTf)_n (-23.4 kcal/mol) calculated by DFT, it appears the reaction is operating similar to enzyme kinetics.



Breaking down the C-O cleavage step and simplifying the Pd catalyzed hydrogenation (we have condensed substrate adsorption/desorption, the hydrogenation on the surface, and the desorption of cyclohexane from Pd into a single step represented by k₂ because this is after the rate limiting step):



Where k_A⁺ and k_A⁻ are the rates of substrate adsorption and desorption to the M(OTf)_n respectively.

The conservation of species:

$$[\text{M(OTf)}_n]_{\text{total}} = [\text{M(OTf)}_n] + [\text{A-M(OTf)}_n]$$

The rate of formation of product (cyclohexane) is:

$$\text{rate} = \frac{d[\text{P}]}{dt} = k_2[\text{B}]$$

Applying the steady state approximation to [B]:

$$\frac{d[B]}{dt} = k_1[A-M(OTf)_n] - k_{-1}[M(OTf)_n][B][C] - k_2[B] = 0$$

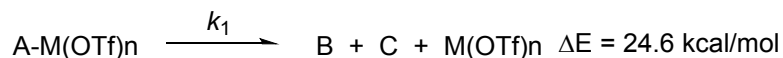
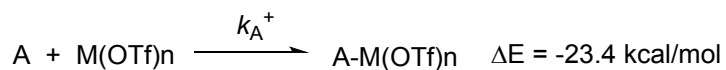
And to [A-M(OTf)_n]:

$$\frac{d[A-M(OTf)_n]}{dt} = k_A^+[A]([M(OTf)_n]_{total} - [A-M(OTf)_n]) + k_{-1}[B][C]([M(OTf)_n]_{total} - [A-M(OTf)_n]) - [A-M(OTf)_n](k_A^- + k_1) = 0$$

We can solve for [A-M(OTf)_n]:

$$[A-M(OTf)_n] = \frac{[M(OTf)_n]_{total}(k_A^+[A] + k_{-1}[B][C])}{(k_A^+[A] + k_{-1}[B][C]) + k_A^- + k_1}$$

The following steps were calculated by DFT,



Therefore, it is reasonable for $k_A^+, k_{-1} \gg \gg k_A^-, k_1$ yielding:

$$[A-M(OTf)_n] = [M(OTf)_n]_{total}$$

Placing back into the steady state equation for [B] we have:

$$\frac{d[B]}{dt} = k_1[M(OTf)_n]_{total} - k_{-1}[M(OTf)_n][B][C] - k_2[B] = 0$$

$$[B] = \frac{k_1[M(OTf)_n]_{total}}{k_{-1}[M(OTf)_n][C] + k_2}$$

Therefore the overall rate is:

$$rate = \frac{d[P]}{dt} = \frac{k_2 k_1 [M(OTf)_n]_{total}}{k_{-1} [M(OTf)_n][C] + k_2}$$

If we assume that the rate of hydrogenation (k_2) is much greater than C-O bond formation (k_{-1}), or if $[C] \sim 0$ in solution phase early under reaction conditions, then the rate becomes:

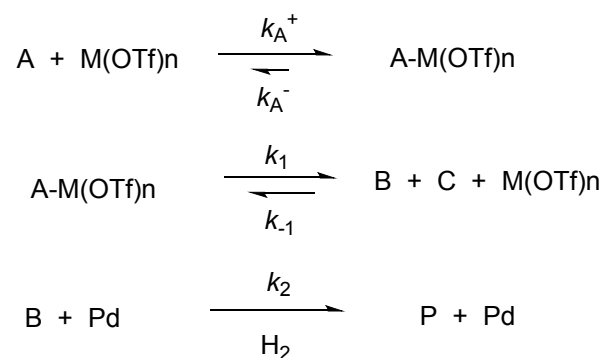
$$rate = \frac{d[P]}{dt} = k_1 [M(OTf)_n]_{total}$$

Yielding a reaction that is overall zero order in substrate $[A]$ and H_2 (included in the term k_2) and first order in $M(OTf)_n$.

DynoChem Modelling

The kinetic plot of cyclohexyl acetate consumption at 125 °C was modelled with Dyno Chem software (Scale up Systems) to find a good fit.

Using the same model:



Experimentally obtained value:

$$k_1 = 0.089 \text{ s}^{-1}$$

DFT computed values:

$$\Delta G^\circ = -RT\ln(K)$$

ΔG° for catalyst complexation is + 15.36 kcalmol⁻¹, which yields K_A of 4.67×10^6 .

ΔG° for conversion of A-M(OTf)_n to B + C + M(OTf)_n is -15.36 kcalmol⁻¹, which yields K_1 of 2×10^{-7} .

Fitting Values (see plot below):

Setting these values into a kinetic profile with experimental data for the consumption of A, k_2 was found to be $0.1409 \pm 0.0003 \text{ s}^{-1}$. The confidence intervals for k_A^+ were very large, indicating that the effect on the model from changing k_A^+ was very small and that a range of values would give similar results. This was confirmed by running the model with different values of k_A^+ and observing no change in fitting behavior. For the example below, k_A^+ was arbitrarily set at 1 s^{-1} .

Reactions Kinetics

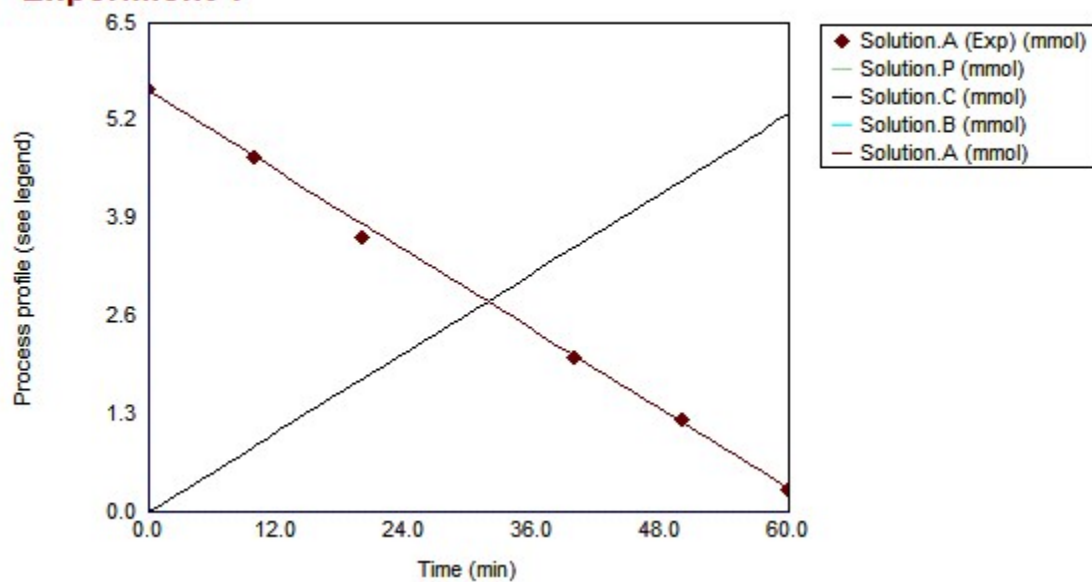
Reaction	Equation	Rate Expression	kref	Value	units
Rxn1	A + M(OTf) _n <-> AM(OTf) _n	$k_A^+[M(OTf)_n]$	k_A^+	1	1/s
		$[AM(OTf)_n]/[A][M(OTf)_n]$	K_A	4.687E+6	
Rxn2	AM(OTf) _n <-> B + C + M(OTf) _n	$k_1[AM(OTf)_n]$	k_1	0.089	1/s
		$[B][C][M(OTf)_n]/[AM(OTf)_n]$	K_1	2.0E-7	
Rxn3	B + Pd --> P + Pd	$k_2[Pd]$	k_2	0.1409	1/s

Model Parameters

Phase	Variable Name	Initial Value	Units
Solution	P	0.0	mmol
Solution	C	0.0	mmol
Solution	B	0.0	mmol
Solution	Pd	0.0105	mmol
Solution	M(OTf) _n	0.0263	mmol
Solution	A	5.62	mmol
Solution	Volume	9.0E-4	L
Solution	AM(OTf) _n	0.0	mmol
Solution	Pressure	1.0	bar

Simulation Plot:

Experiment 1



	Solution	Solution	Solution	Solution	Solution
Time	A (Exp)	P	C	B	A
min	mmol	mmol	mmol	mmol	mmol
0.0	5.62	0.0	0.0	0.0	5.62
1.667E-12		7.552E-14	1.001E-20	0.0	5.62
1.667E-10		7.552E-12	1.27E-19	0.0	5.62
1.667E-8		7.552E-10	1.17E-15	0.0	5.62
1.667E-6		7.552E-8	0.0	0.0	5.62
1.667E-4		4.906E-7	1.163E-7	0.0	5.62
0.0167		7.977E-4	7.974E-4	3.604E-15	5.603
1.224		0.1073	0.1073	1.032E-14	5.488
2.449		0.2153	0.2153	4.231E-15	5.38

3.673		0.3233	0.3233	2.812E-15	5.272
4.898		0.4313	0.4313	2.102E-15	5.164
6.122		0.5393	0.5393	1.686E-15	5.056
7.347		0.6473	0.6473	1.397E-15	4.948
8.571		0.7553	0.7553	1.205E-15	4.84
9.796		0.8633	0.8633	1.043E-15	4.732
10.0	4.72	0.8813	0.8813	1.024E-15	4.714
11.02		0.9713	0.9713	9.356E-16	4.624
12.245		1.079	1.079	8.323E-16	4.516
13.469		1.187	1.187	7.241E-16	4.408
14.694		1.295	1.295	5.941E-16	4.3
15.918		1.403	1.403	6.198E-16	4.192
17.143		1.511	1.511	6.202E-16	4.084
18.367		1.619	1.619	6.33E-16	3.976
19.592		1.727	1.727	6.557E-16	3.868
20.0	3.66	1.763	1.763	6.649E-16	3.832
20.816		1.835	1.835	5.417E-16	3.76
22.041		1.943	1.943	4.742E-16	3.652
23.265		2.051	2.051	4.011E-16	3.544
24.49		2.159	2.159	3.211E-16	3.436
25.714		2.267	2.267	2.329E-16	3.328
26.939		2.375	2.375	1.35E-16	3.22
28.163		2.483	2.483	2.611E-17	3.112
29.388		2.591	2.591	0.0	3.004
30.612		2.698	2.698	3.381E-16	2.897
31.837		2.806	2.806	3.251E-16	2.789
33.061		2.914	2.914	3.13E-16	2.681
34.286		3.022	3.022	3.017E-16	2.573
35.51		3.13	3.13	2.913E-16	2.465
36.735		3.238	3.238	2.816E-16	2.357
37.959		3.346	3.346	2.724E-16	2.249

39.184		3.454	3.454	2.636E-16	2.141
40.0	2.04	3.526	3.526	2.584E-16	2.069
40.408		3.562	3.562	2.56E-16	2.033
41.633		3.67	3.67	2.484E-16	1.925
42.857		3.778	3.778	2.411E-16	1.817
44.082		3.886	3.886	2.34E-16	1.709
45.306		3.994	3.994	2.279E-16	1.601
46.531		4.102	4.102	2.219E-16	1.493
47.755		4.21	4.21	2.162E-16	1.385
48.98		4.318	4.318	2.106E-16	1.277
50.0	1.22	4.408	4.408	2.061E-16	1.187
50.204		4.426	4.426	2.057E-16	1.169
51.429		4.534	4.534	2.009E-16	1.061
52.653		4.642	4.642	1.962E-16	0.9532
53.878		4.75	4.75	1.916E-16	0.8452
55.102		4.858	4.858	1.875E-16	0.7372
56.327		4.966	4.966	1.834E-16	0.6292
57.551		5.074	5.074	1.795E-16	0.5212
58.776		5.182	5.182	1.757E-16	0.4132
60.0	0.28	5.29	5.29	1.72E-16	0.3052

Procedure for Error Analysis

The errors reported for all rate constants and activation parameters were determined using Regression Analysis workbook in Excel (Rodney Carr, Deakin University, Australia and Neville Hunt, Coventry University, UK as part of the **OATBRAN** project). All data is reported at the 95 % confidence interval. An example excel analysis is provided below (125 °C, 0.5 mol % Hf(OTf)₄, 0.2 mol % Pd/C, 1 bar H₂, neat cyclohexyl acetate).

Input Data (x = time in s, y = mmol cyclohexyl acetate).

Data	
X	Y
0	5.6200448
600	4.7168233
1200	3.6630649
2400	2.0406115
3000	1.2210216
3600	0.2676212

Output Data (regression analysis)

Regression Statistics						
Observations	6					
s	0.082976929					
Corr	-0.9994					
R Square	99.87%					
R Square (adj)	99.84%					

Coefficients and Tests						
	Estimate	St.Error	t-ratio	P-value	95% Lower	95% Upper
Const	5.564887782	0.057970847	95.99459182	0.0000	5.403934908	5.725840656
X	-0.001468531	2.61353E-05	-56.18962677	0.0000	-0.001541095	-0.001395968

Fitted Values and Residuals						
	X	Y	Fitted	Residual	St.resid	Nscore
	0	5.620044827	5.564887782	0.055157044	0.929071293	1.281551566
	600	4.716823337	4.683768935	0.033054402	0.479399516	0.201893479
	1200	3.663064932	3.802650087	-0.139585155	-1.883580199	-1.281551566
	2400	2.040611514	2.040412391	0.000199123	0.00268699	-0.201893479
	3000	1.221021644	1.159293544	0.0617281	0.895264156	0.643345405
	3600	0.267621182	0.278174696	-0.010553514	-0.177764543	-0.643345405

The error (\pm) was estimated as taking half of the magnitude of the difference between the 95% lower and upper limits.

References

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