overreact
a tool for creating *ab initio* microkinetic models

Felipe S. S. Schneider

28th March 2022

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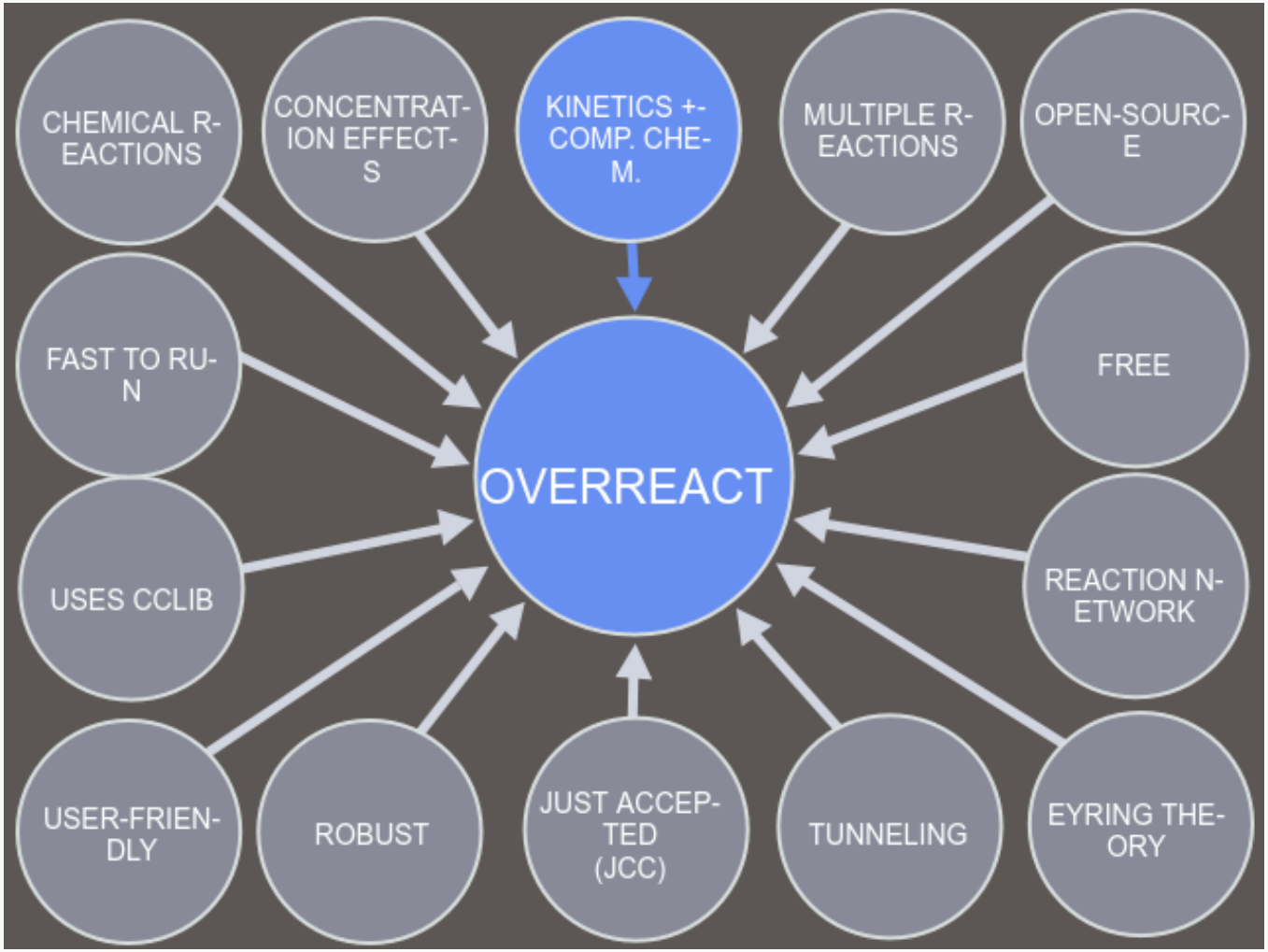
CHEMICAL R-EACTIONS
CONCENTRAT-ION EFFECT-S
KINETICS +- COMP. CHE-M.
MULTIPLE R-EACTIONS
OPEN-SOURC-E
FAST TO RU-N
FREE
OVERREACT
USES CCLIB
REACTION N-ETWORK
USER-FRIEN-DLY
ROBUST
JUST ACCEP-TED (JCC)
TUNNELING
EYRING THE-ORY

The problem in a nutshell

OL | Organic Letters

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The Challenge of Reproducing with Calculations Raw Experimental Kinetic Data for an Organic Reaction

Raúl Pérez-Soto, Maria Besora,* and Feliu Maseras*

Cite This: *Org. Lett.* 2020, 22, 2873–2877 Read Online

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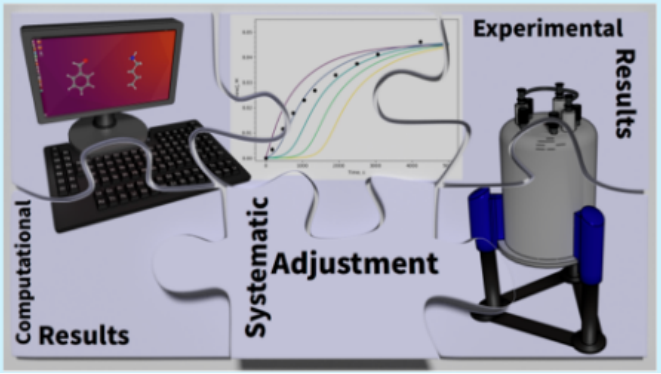
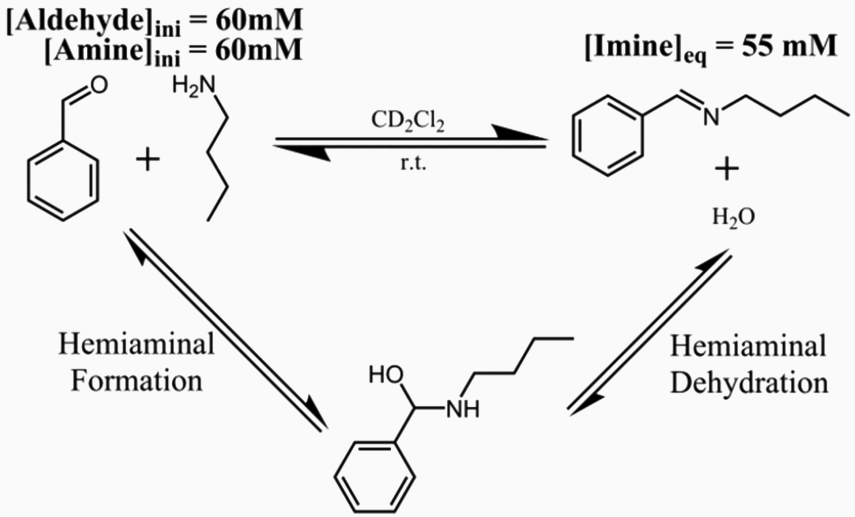
ABSTRACT: DFT calculations and microkinetic simulations are applied to the reproduction of previously reported experimental results on the evolution of product concentration versus time in the condensation reaction of *n*-butylamine and benzaldehyde. The mechanism is complicated by the role played by water impurities as proton shuttles. Several functionals and other approaches are tested, yet good agreement is only achieved upon the usage of an adjustment consisting of a directed biasing of the computed DFT free energies.



Pérez-Soto, R. et al. *Organic Letters* **2020**, *22*, 2873–2877

What they did



- B3LYP-D3/cc-pVTZ (Gaussian09)

Pérez-Soto, R. et al. *Organic Letters* **2020**, *22*, 2873–2877

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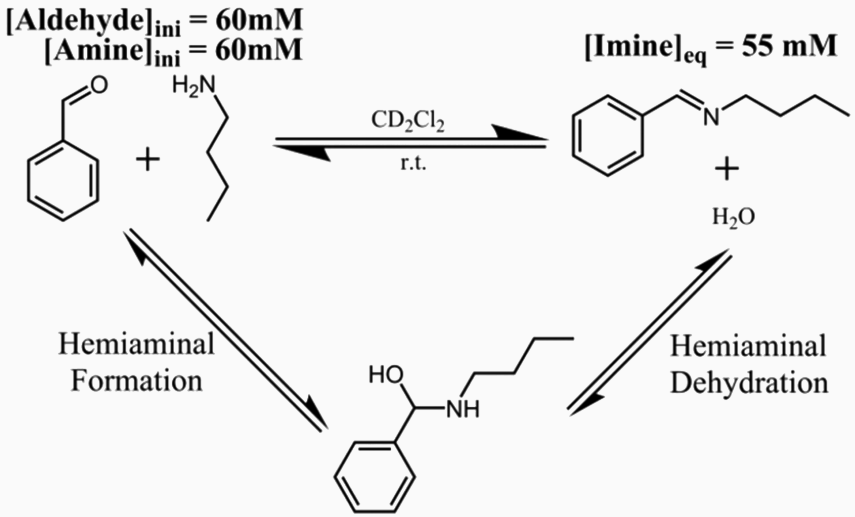

- B3LYP-D3/cc-pVTZ (Gaussian09)
- *Rigid-Rotor Harmonic Approximation* (RRHO)

Pérez-Soto, R. et al. *Organic Letters* **2020**, *22*, 2873–2877

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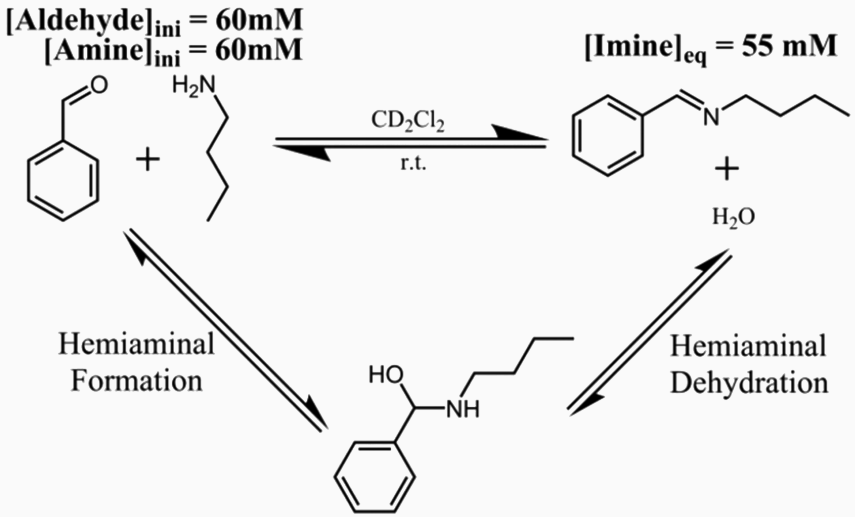
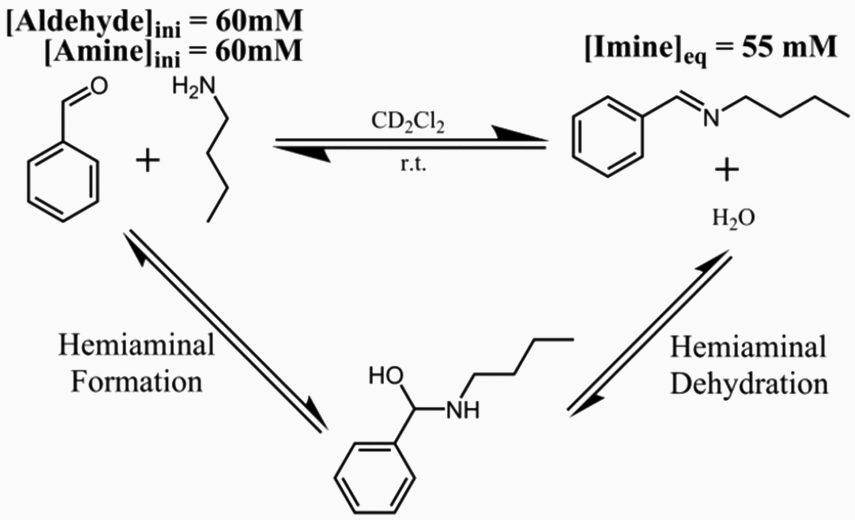


- B3LYP-D3/cc-pVTZ (Gaussian09)
- *Rigid-Rotor Harmonic Approximation* (RRHO)
- SMD (dichloromethane)

Pérez-Soto, R. et al. *Organic Letters* **2020**, *22*, 2873–2877

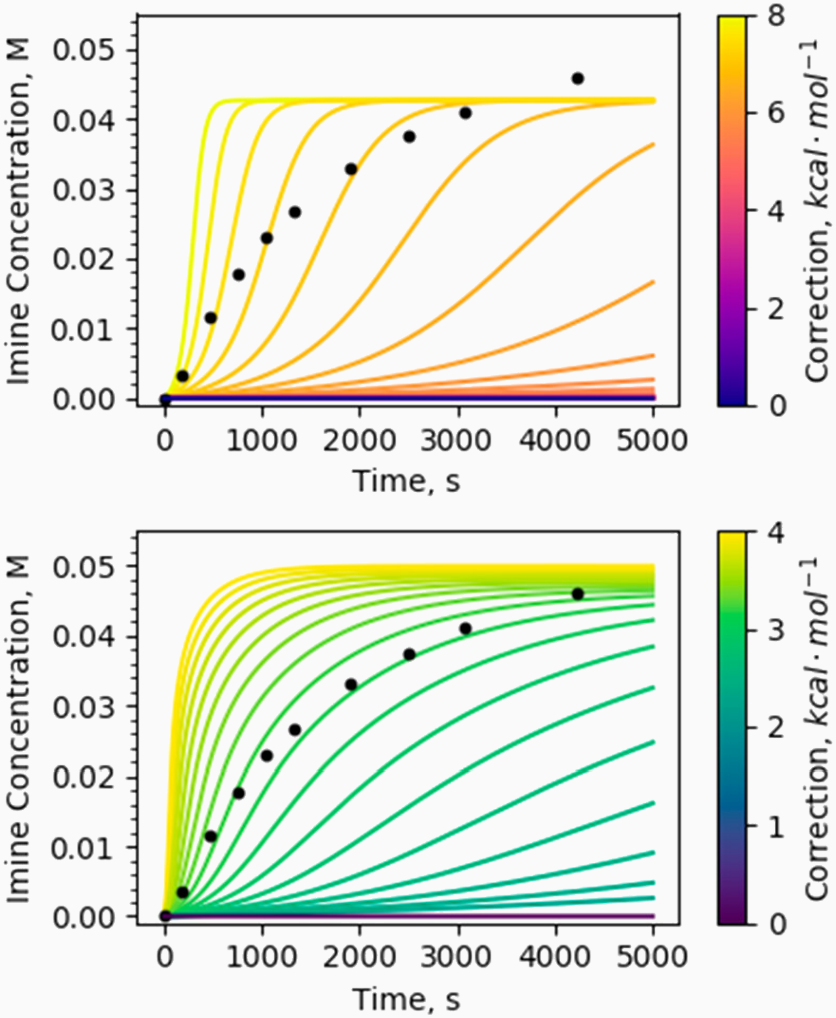
What they did



- B3LYP-D3/cc-pVTZ (Gaussian09)
- *Rigid-Rotor Harmonic Approximation* (RRHO)
- SMD (dichloromethane)
- 1 atm → 1 M correction

Pérez-Soto, R. et al. *Organic Letters* **2020**, *22*, 2873–2877

Their results



Two hypotheses:

- H1: adjusting transition state energies only

Plus: water impurities (1 mM) should be considered!

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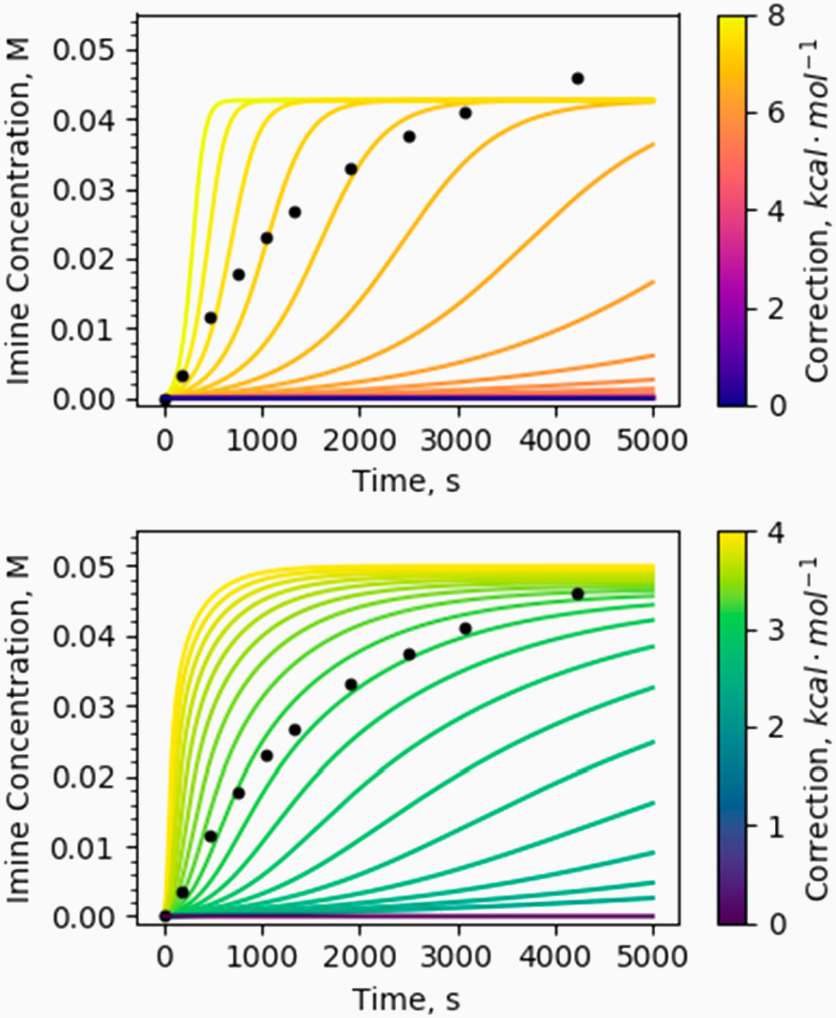
Their results



Two hypotheses:

- H1: adjusting transition state energies only
- H2: adjusting *all* structures

Plus: water impurities (1 mM) should be considered!

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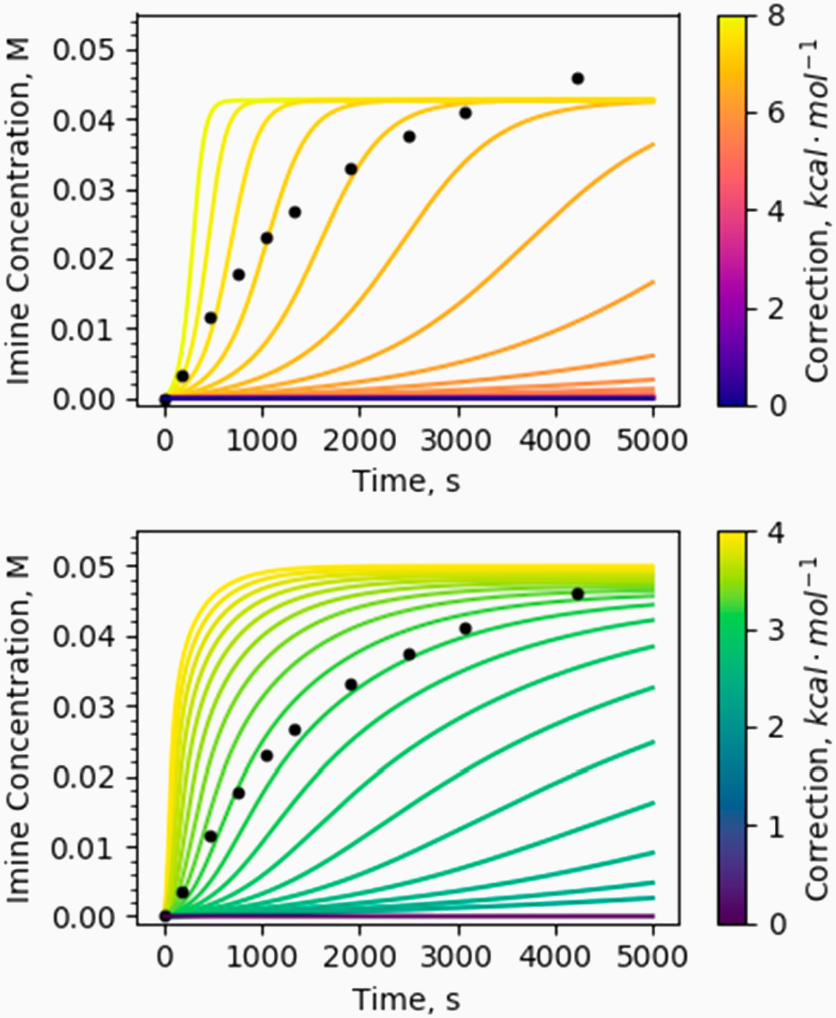
Their results



Two hypotheses:

- H1: adjusting transition state energies only
- H2: adjusting *all* structures
  - 3.2 kcal/mol

Plus: water impurities (1 mM) should be considered!

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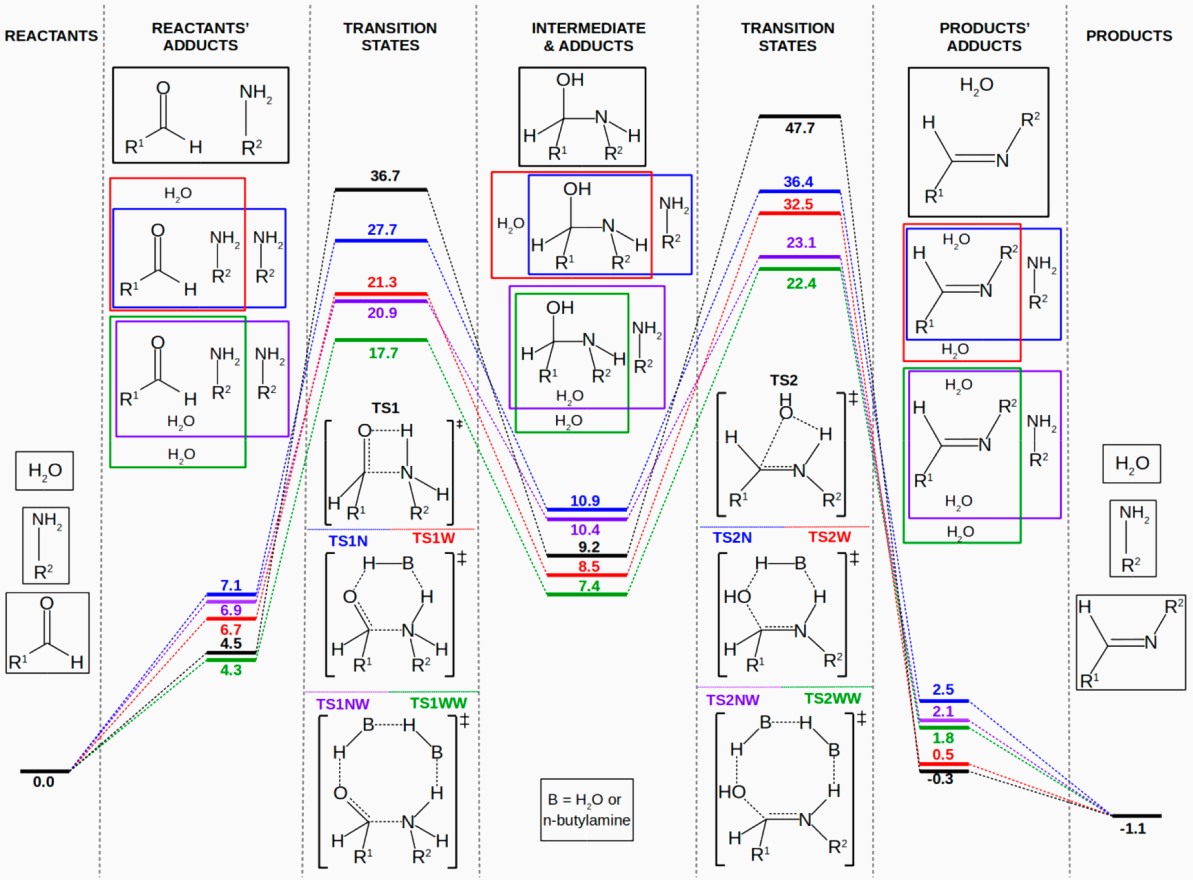
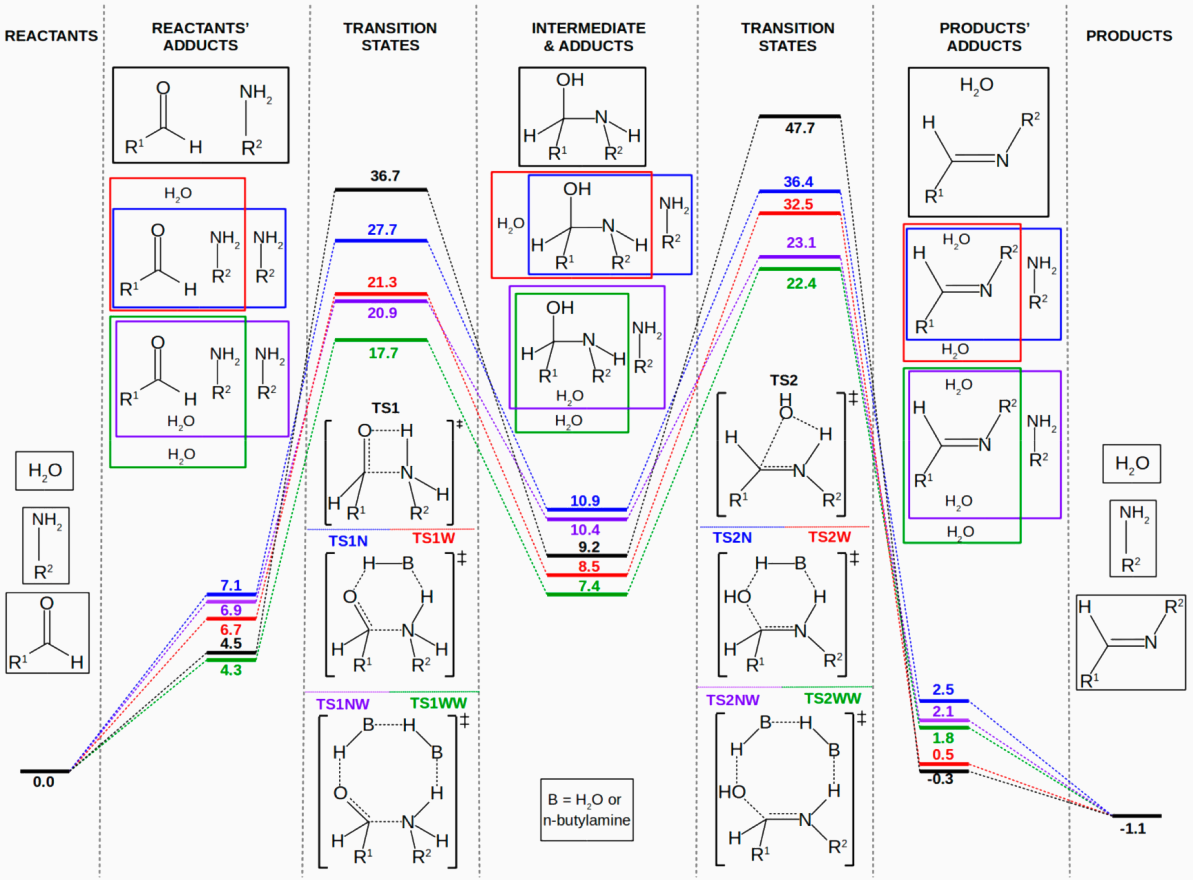
Going forward



- Quantum tunneling?

Pérez-Soto, R. et al. *Organic Letters* **2020**, *22*, 2873–2877

Going forward



- Quantum tunneling?
- Quasi-RRHO?

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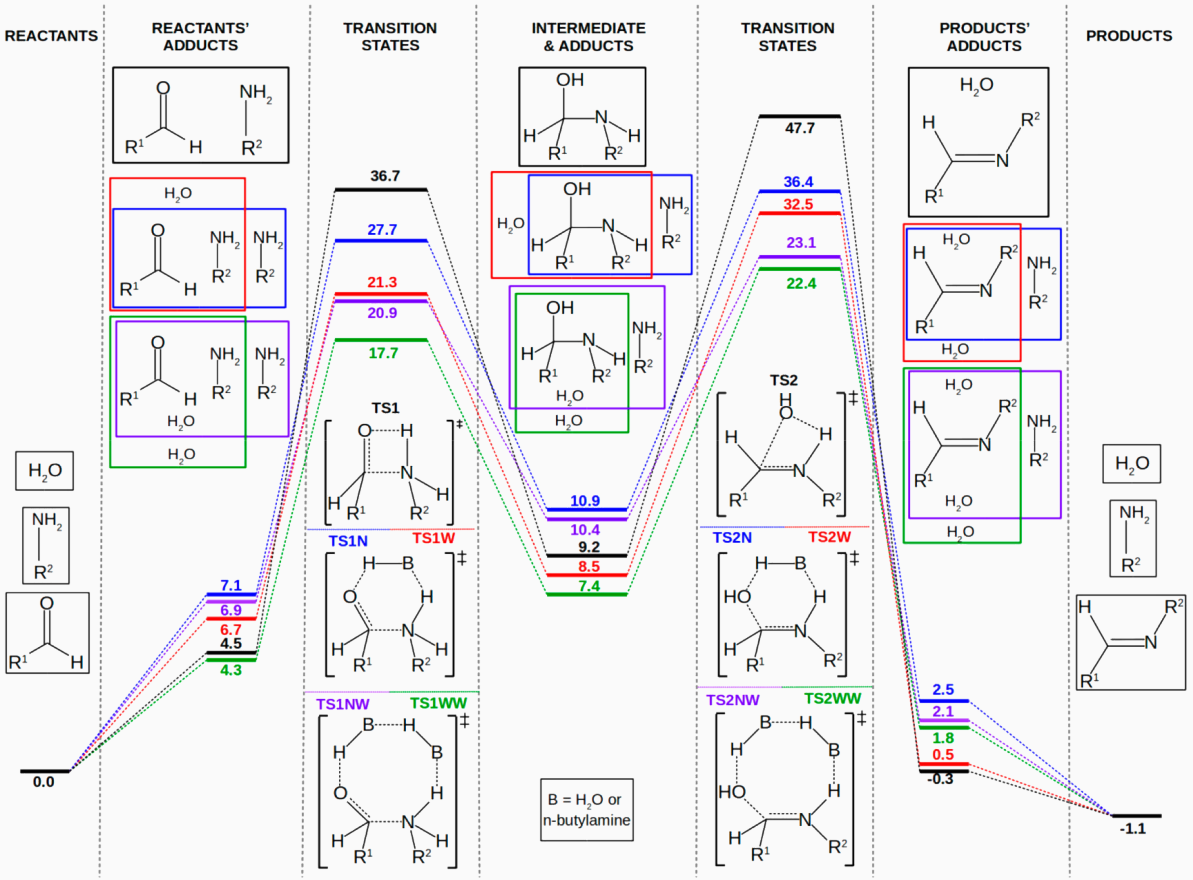

- Quantum tunneling?
- Quasi-RRHO?
- Automation?

```
#Constants
k00 = 1.1520016141e+08
k01 = 2.1243982518e+11
k02 = 4.6522262685e+09
k03 = 2.1243982518e+11
k04 = 2.1243982518e+11
k05 = 1.0627425113e+11
k06 = 2.3472075016e+08
k07 = 2.1243982518e+11
k08 = 2.8944452758e+10
k09 = 2.1243982518e+11
k10 = 1.2474135377e+06
k11 = 2.1243982518e+11
k12 = 1.2524507574e+09
k13 = 2.1243982518e+11
k14 = 1.6652981977e+09
k15 = 2.1243982518e+11
k16 = 2.5518729986e+09
```

...

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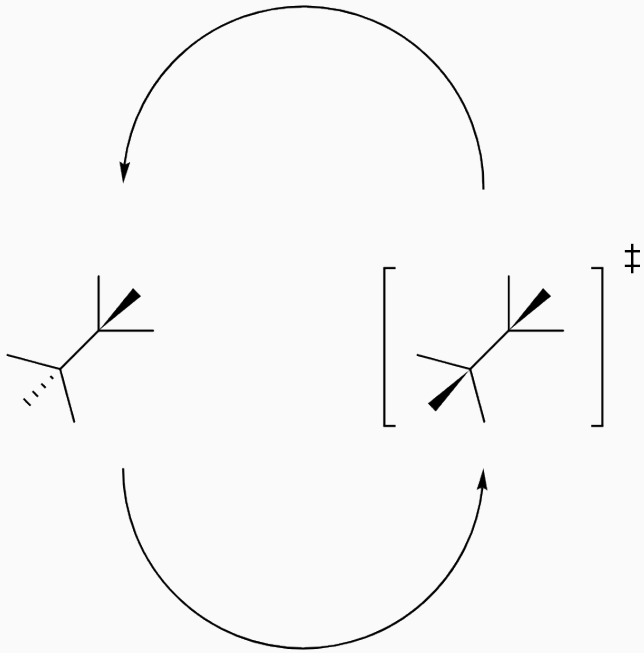
The idea

Meet overreact, the tool

```
$scheme
 // Reactions
 S -> ‡E -> S
$end

$compounds
 // Species: logfile
 S: staggered.out‡
 E: eclipsed.out
$end
```

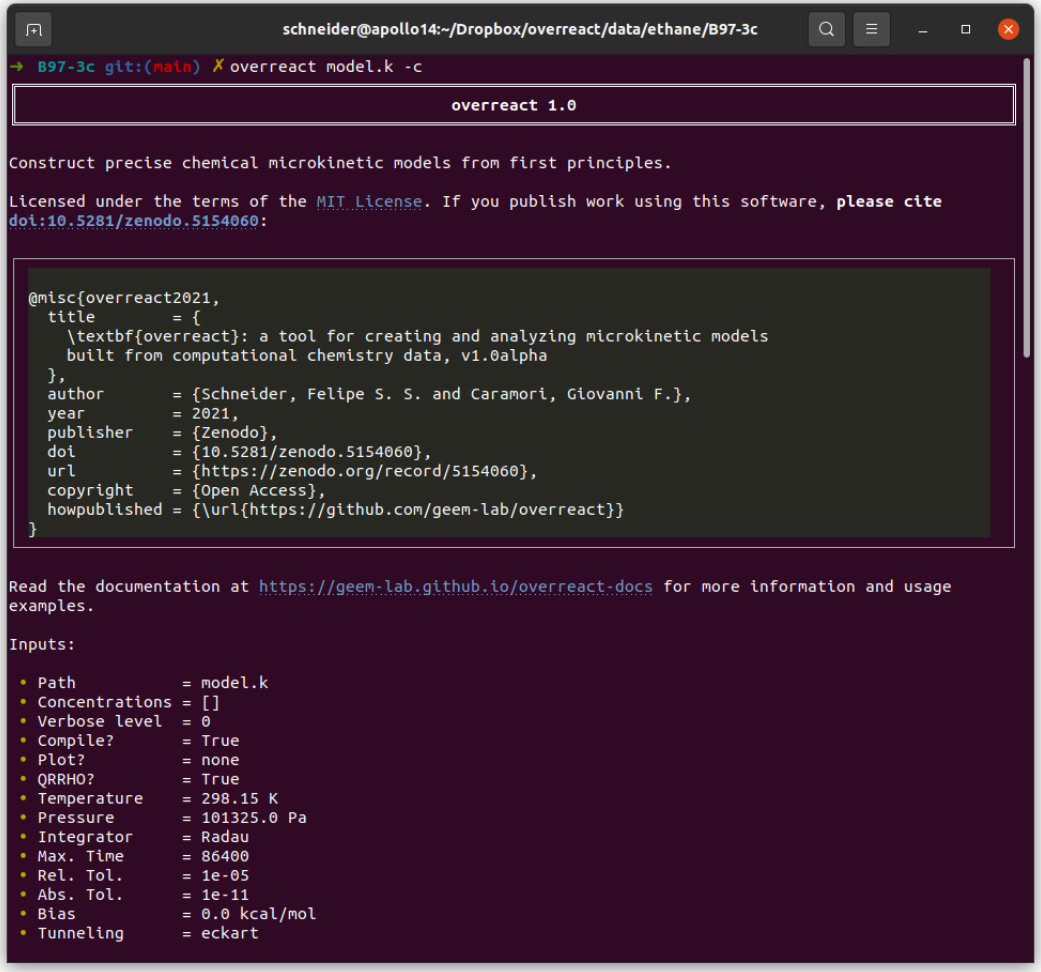


Ethane internal rotation

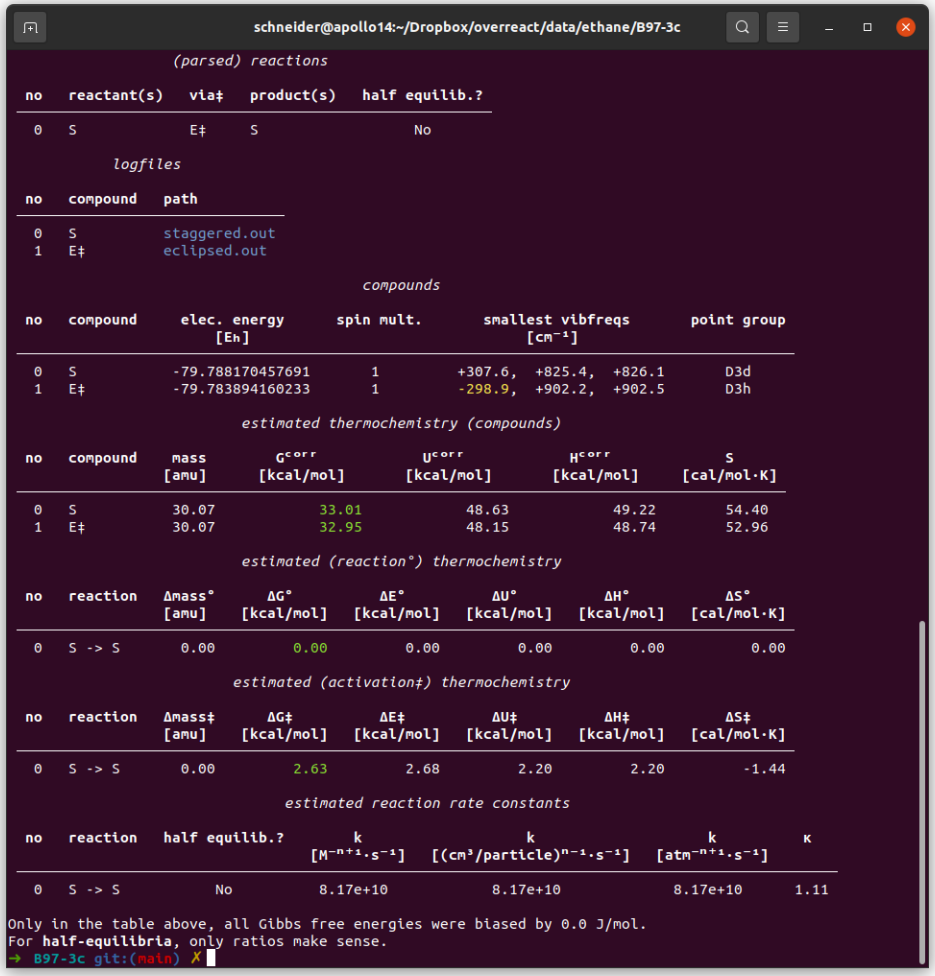
(B97-3c @ ORCA 4.2.1)

Schneider, F. S. S. and Caramori, G. F. **overreact**, an *in silico* lab: automated quantum chemical microkinetic simulations. *In preparation* **2021**.

Meet overreact, the tool: user-friendly



Meet overreact, the tool: detailed output



Experimental: $\frac{1}{12\times10^{-12}}\,\mathrm{s}^{-1} = 8.333\times10^{10}\,\mathrm{s}^{-1}$ ($\Delta G^{\ddagger}$: 2.88 kcal/mol)

Zheng, J. *Science* **2006**, *313*, 1951–1955

Hirota, E. et al. *The Journal of Chemical Physics* **1979**, *71*, 1183–1187

Meet overreact, the tool: indicating solvent

```
$scheme
 NH3(w??)+OH·(w) -> NH3·OH#(w) -> NH2·(w) + H2O(w)

$compounds
 NH3(w): NH3.out
 OH·(w): OH·.out
 NH2·(w): NH2·.out
 H2O(w): H2O.out
 NH3·OH#(w): NH3·OH.out
  // symmetry=3 // extra symmetries
```

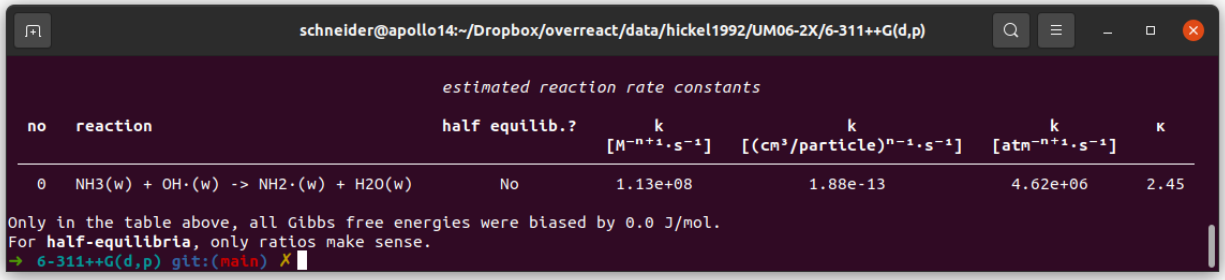
$$NH_{3(w)} + OH\cdot_{(w)} \longrightarrow NH_2\cdot_{(w)} + H_2O_{(w)}$$

(M062X-D3(0)/6-311++G(d,p)/SMD(water) @ ORCA 4.2.1)

Meet overreact, the tool: results in solvent

$$NH_{3(w)} + OH\cdot_{(w)} \longrightarrow NH_2\cdot_{(w)} + H_2O_{(w)}$$

	$k\ (M^{-1}s^{-1})$
Hickel and Sehested[1] (exp.)	9.7×10^7
Men'kin et al.[2] (exp.)	7.0×10^7
Neta et al.[3] (exp.)	9.0×10^7
Ours (ORCA 4.2.1)	$\mathbf{1.1 \times 10^8}$
Dzib et al.[4] (Gaussian09)	2.3×10^7



[1] Hickel, B.; Sehested, K. *International Journal of Radiation Applications and Instrumentation. Part C. Radiation Physics and Chemistry* **1992**, *39*, 355–357.

[2] Men'kin, V. et al. *High Energy Chemistry (English Translation)* **1989**, *22*, 333–336.

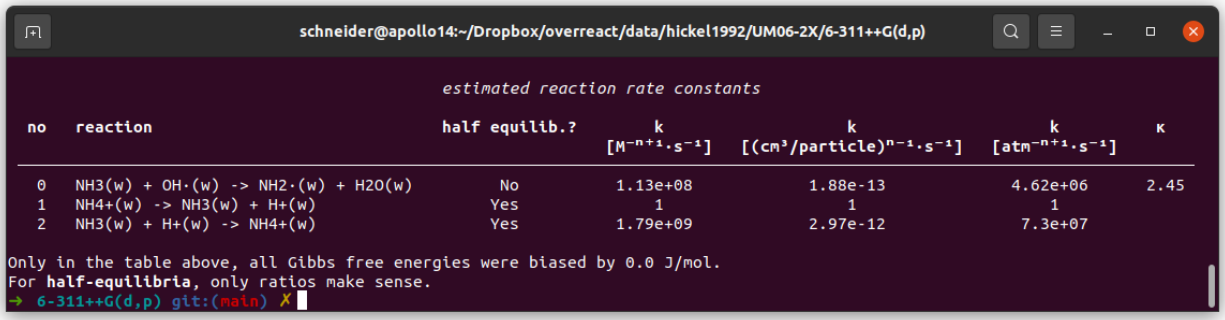
[3] Neta, P. et al. *The Journal of Physical Chemistry* **1978**, *82*, 1875–1878.

[4] Dzib, E. et al. *International Journal of Quantum Chemistry* **2018**, *119*, e25686.

Meet overreact, the tool: equilibria

```
$scheme
 NH3(w??)+OH·(w) -> NH3·OH#(w) -> NH2·(w) + H2O(w)
 NH4+(w) <=> NH3(w) + H+(w) // pK = 9.25

$compounds
 NH3(w): NH3.out
 OH·(w): OH·.out
 NH2·(w): NH2·.out
 H2O(w): H2O.out
 NH3·OH#(w): NH3·OH.out
  // symmetry=3 // extra symmetries
 NH4+(w): NH4+.out
 H+(w):
  // energy=0.0
  // energy=-1112525.6 // J == -265.9 kcal/mol (proton solvation from doi:10.1021/jp810292n)
  energy=-1094746.6 // J == -261.7 kcal/mol (the value that adjusts the pK)
  mult=1
  atomnos=[1]
  atommasses=[1.008]
  atomcoords=[[0.0, 0.0, 0.0]]
```



Meet overreact, the library

- Parsing of **multiple reactions**

$$A \rightleftharpoons B \longrightarrow \dots$$

$$B \longrightarrow C \longrightarrow \dots$$

[1] Brown, R. *JOURNAL OF RESEARCH of the National Bureau of Standards* **1981**, *86*, 357
[2] Bell, R. P. *Transactions of the Faraday Society* **1959**, *55*, 1

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- Eyring-Evans-Polanyi equation

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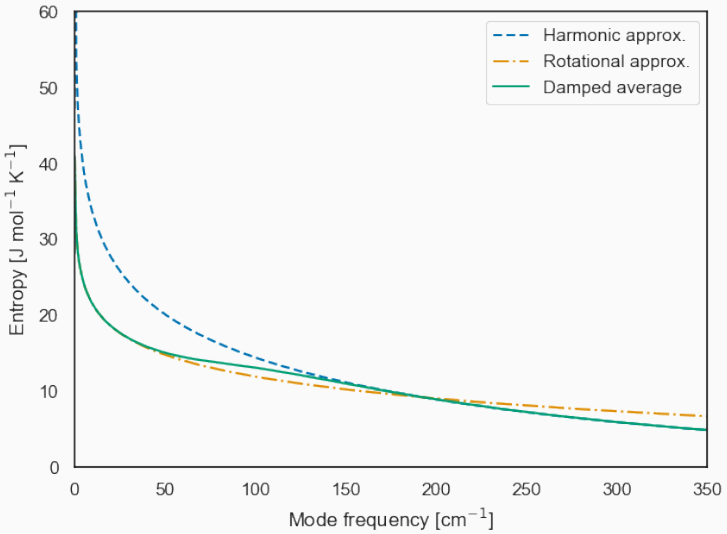
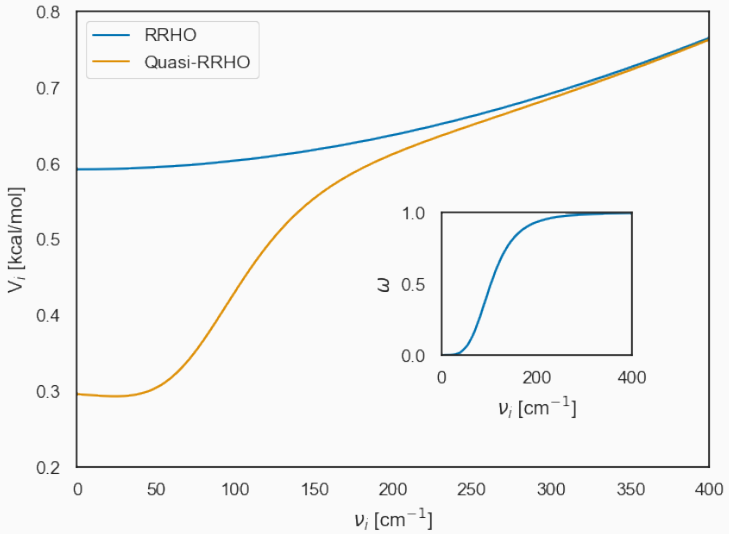
- Rigid rotor-harmonic oscillator approximation (**RRHO**)
- **Automatic** 1 atm → 1 M correction
- Eyring-Evans-Polanyi equation
- **Eckart**[1]**transmission coefficients** (Wigner[2]also implemented)

[1] Brown, R. *JOURNAL OF RESEARCH of the National Bureau of Standards* **1981**, *86*, 357
[2] Bell, R. P. *Transactions of the Faraday Society* **1959**, *55*, 1

Meet overreact, the library: quasi-RRHO

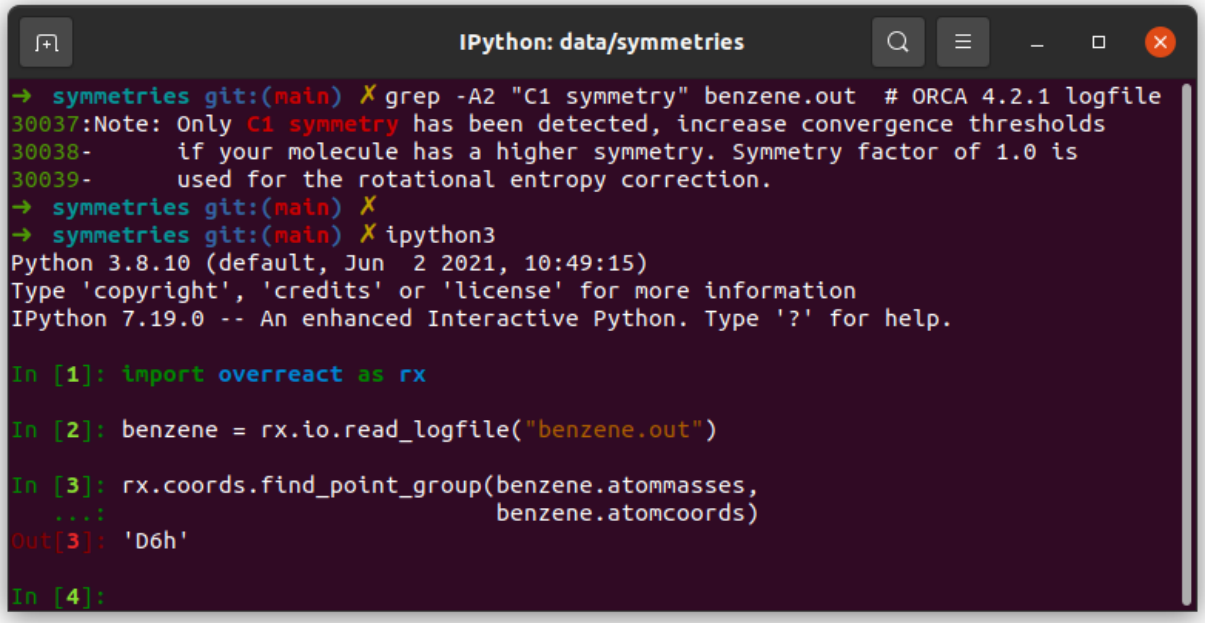
- Quasi-RRHO for both vibrational entropies[1] and enthalpies[2]





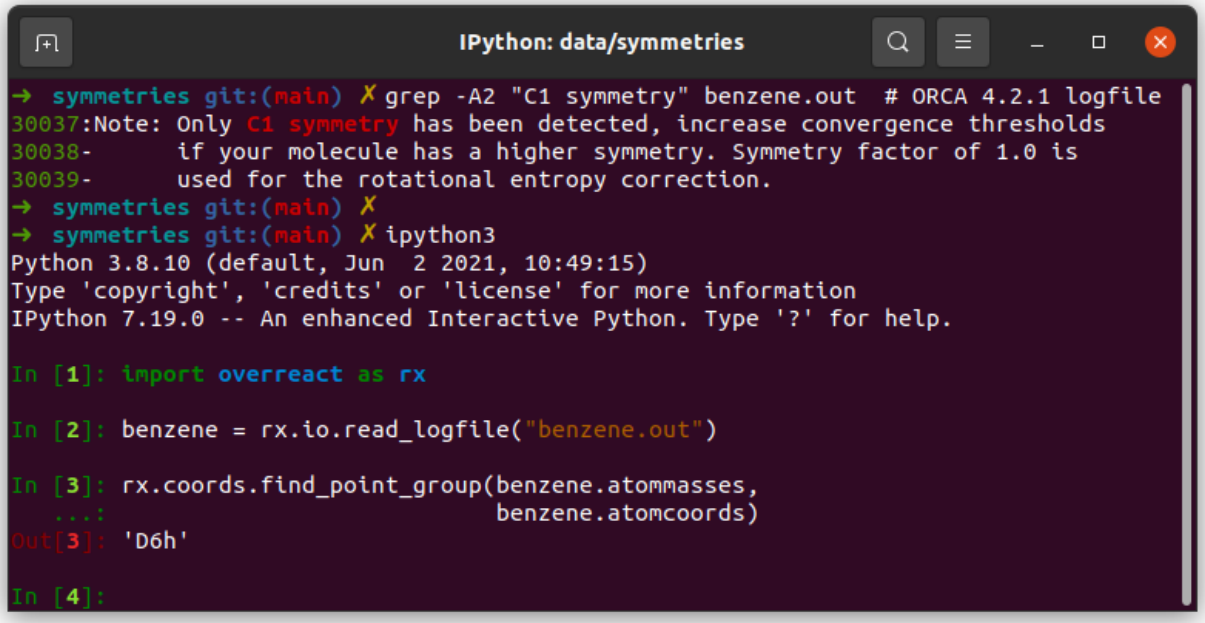
[1] Grimme, S. *Chemistry - A European Journal* **2012**, *18*, 9955–9964.
[2] Li, Y.-P. et al. *The Journal of Physical Chemistry C* **2015**, *119*, 1840–1850.

Meet overreact, the library: symmetries



- Robust code for the determination of point groups and rotational symmetry numbers

Meet overreact, the library: symmetries



- Robust code for the determination of point groups and rotational symmetry numbers
- (The above implies an error of $RT \ln\left(\frac{12}{1}\right) \approx 1.5$ kcal/mol @ 25°C)

Meet overreact, the library

- Automatic generation of the required differential equations

$$\frac{dy}{dt} = f(t, y)$$

[1] Virtanen, P. et al. *Nature Methods* **2020**, *17*, 261–272

[2] O'boyle, N. M. et al. *Journal of Computational Chemistry* **2008**, *29*, 839–845

Meet overreact, the library

- Automatic generation of the required differential equations

$$\frac{dy}{dt} = f(t, y)$$

- Solution via standard methods (via `scipy`[1])

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Meet overreact, the library

- Automatic generation of the required differential equations

$$\frac{dy}{dt} = f(t, y)$$

- Solution via standard methods (via `scipy`[1])
- Compatible with **many** packages (via `cclib`[2])

  - ADF (versions 2007 and 2013)
  - DALTON (versions 2013 and 2015)
  - Firefly, formerly known as PC GAMESS (version 8.0)
  - GAMESS (US) (versions 2014 and 2017)
  - GAMESS-UK (versions 7.0 and 8.0)
  - Gaussian (versions 09 and 16)
  - Jaguar (versions 7.0 and 8.3)
  - Molcas (version 18.0)
  - Molpro (versions 2006 and 2012)
  - MOPAC (version 2016)
  - NWChem (versions 6.0, 6.1, 6.5 and 6.6)
  - ORCA (versions 4.0 and 4.1)
  - Psi4 (versions 1.0 and 1.2.1)
  - Q-Chem (versions 4.2 and 5.1)
  - Turbomole (versions 5.9 and 7.2)

[1] Virtanen, P. et al. *Nature Methods* **2020**, *17*, 261–272

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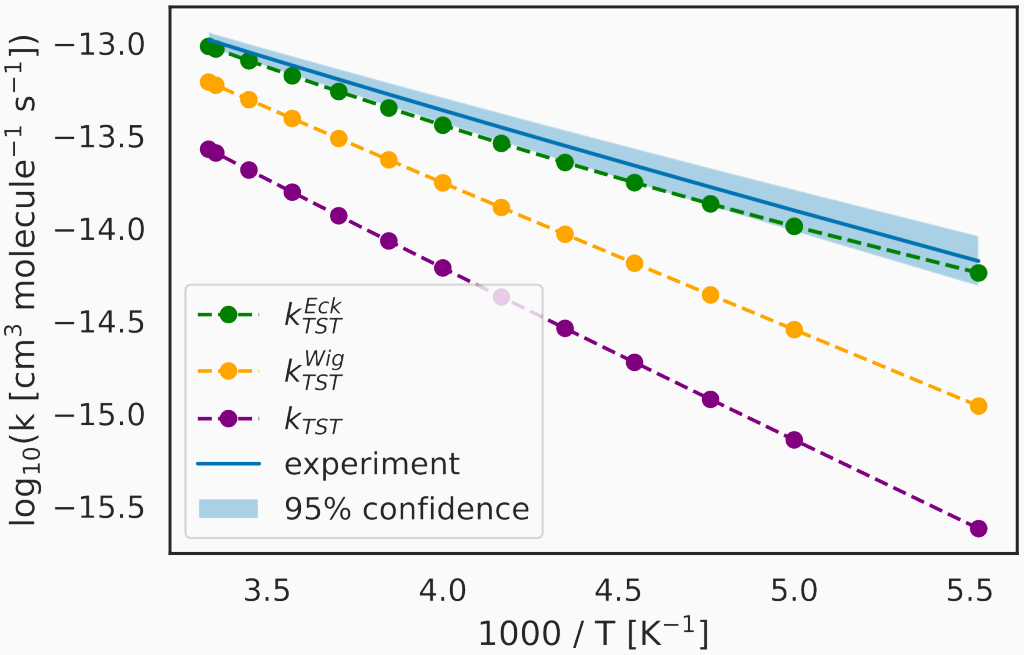
- **Microkinetic modelling**

[1] Virtanen, P. et al. *Nature Methods* **2020**, *17*, 261–272
[2] O'boyle, N. M. et al. *Journal of Computational Chemistry* **2008**, *29*, 839–845

Two solved problems

$CH_4 + Cl\cdot \longrightarrow CH_3\cdot + HCl$



$$k^{exp} = 1.03 \times 10^{-13} \text{cm}^3\text{molecule}^{-1}\text{s}^{-1}$$

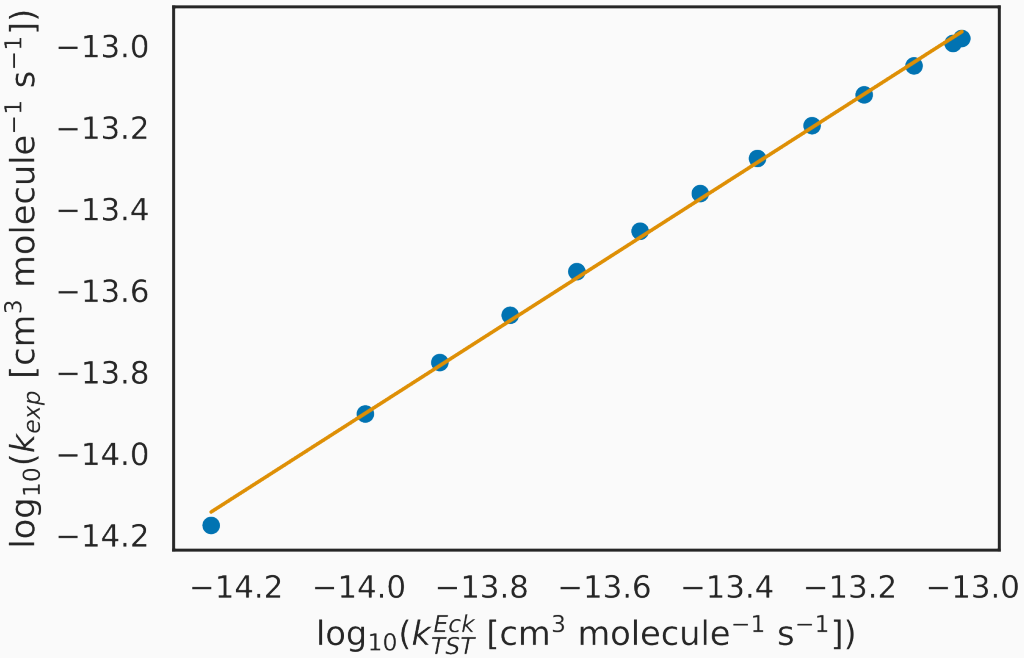
$$k^{\text{UMP2/cc-pVTZ}} = 9.29 \times 10^{-14} \text{cm}^3\text{molecule}^{-1}\text{s}^{-1}$$

Burkholder, J. et al. *Chemical kinetics and photochemical data for use in atmospheric studies; evaluation number 19*, tech. rep.; Pasadena, CA: Jet Propulsion Laboratory, National Aeronautics and Space Agency, 2020

Tanaka, N. et al. *Journal of Atmospheric Chemistry* **1996**, *23*, 37–49

Jupyter notebook: `https://git.io/JBjLB`

$CH_4 + Cl\cdot \longrightarrow CH_3\cdot + HCl$



$$\log_{10} k^{exp} = 0.9633 \times \log_{10} k^{\text{UMP2/cc-pVTZ}} - 0.4256 \qquad (r^2 = 0.9984)$$

Burkholder, J. et al. *Chemical kinetics and photochemical data for use in atmospheric studies; evaluation number 19*, tech. rep.; Pasadena, CA: Jet Propulsion Laboratory, National Aeronautics and Space Agency, 2020

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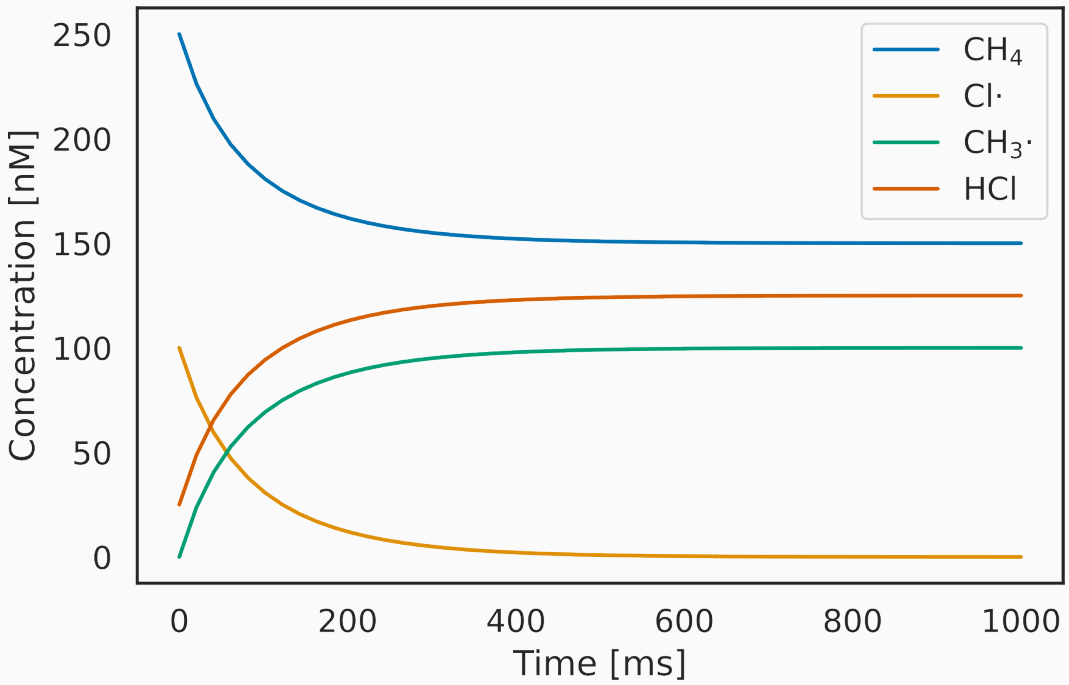


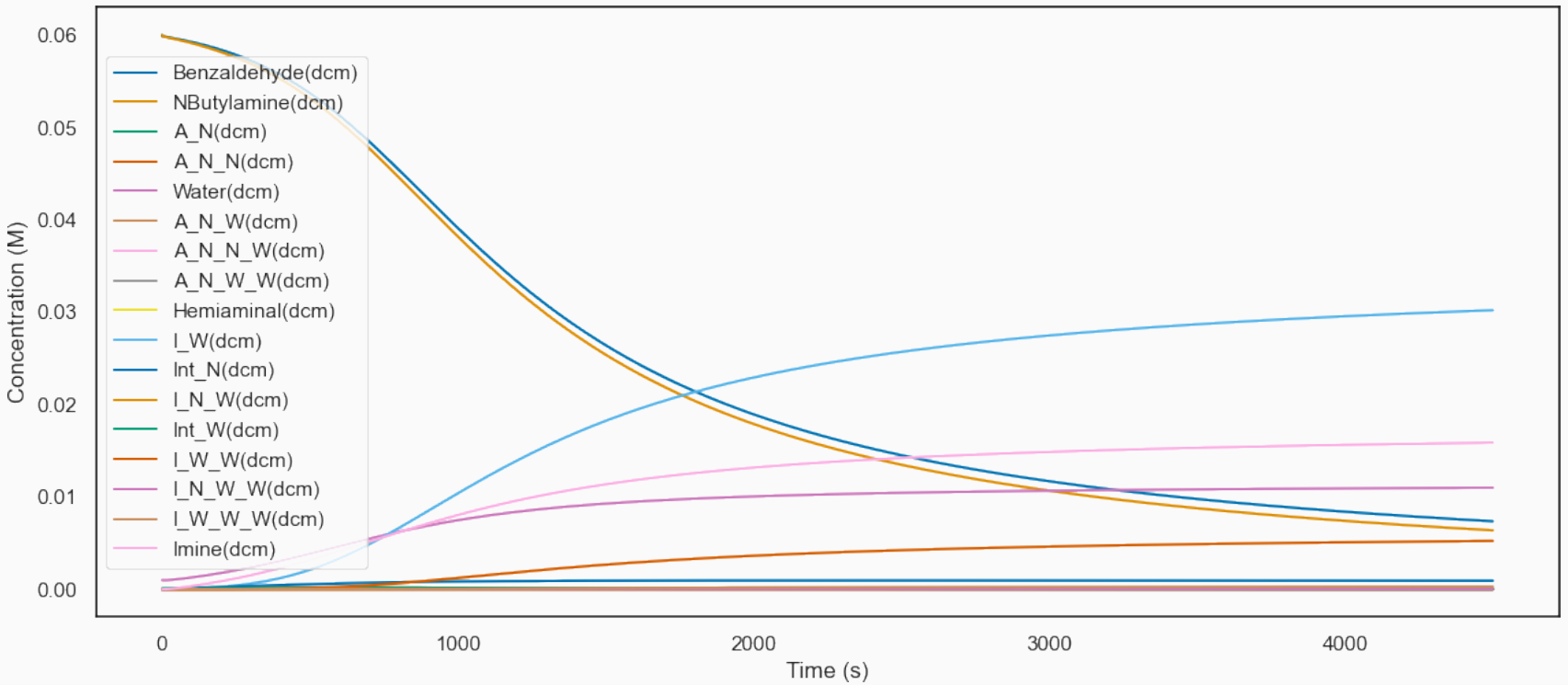
(Arbitrarily) starting from:

$$y_0^{Cl\cdot} = 1 \times 10^{-7} M, \quad y_0^{CH_4} = 2.5 y_0^{Cl\cdot}, \quad y_0^{HCl} = 0.25 y_0^{Cl\cdot}$$

Jupyter notebook: `https://git.io/JBjLQ`

Reproducing the work of Pérez-Soto et al.

```
$ overreact model.k "Benzaldehyde(dcm): 0.06" "NButylamine(dcm) : 0.06" 'Water(dcm): 0.001' \
    --bias=3.2 --plot=active --max-time 5000
```



Pérez-Soto, R. et al. *Organic Letters* **2020**, *22*, 2873–2877

Reproducing the work of Pérez-Soto et al.

```
$ overreact model.k "Benzaldehyde(dcm): 0.06" "NButylamine(dcm) : 0.06" 'Water(dcm): 0.001' \
    --bias=3.2 --plot=active --max-time 5000
```

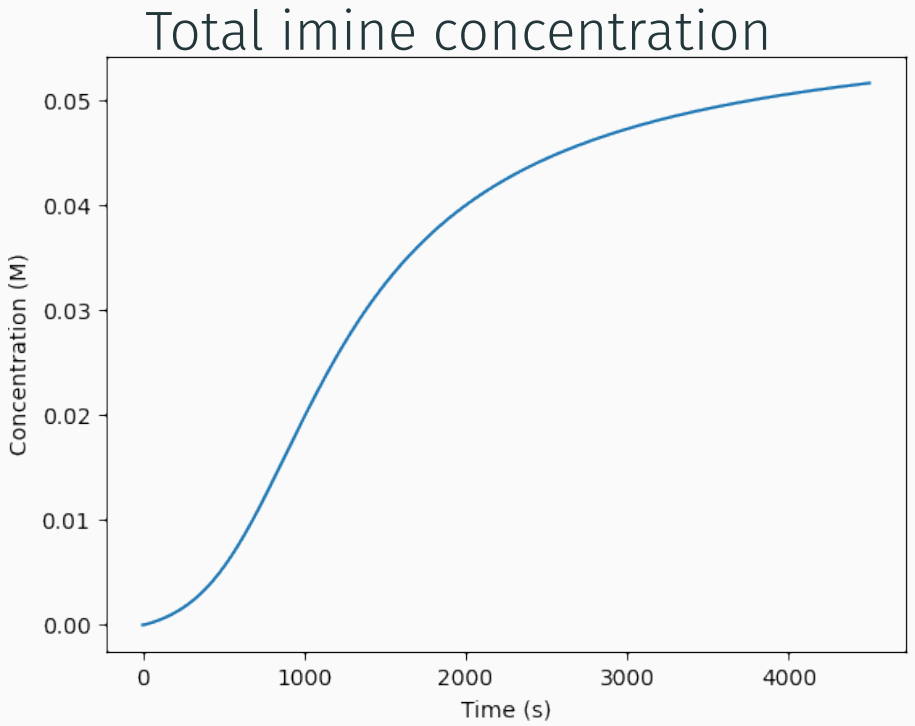
schneider

initial and final concentrations [M]

no	compound	t = 0 s	t = 5e+03 s
0	Benzaldehyde(dcm)	0.060	0.007
1	NButylamine(dcm)	0.060	0.006
2	A_N(dcm)	0.000	0.000
3	A_N_N(dcm)	0.000	0.000
4	Water(dcm)	0.001	0.011
5	A_N_W(dcm)	0.000	0.000
6	A_N_N_W(dcm)	0.000	0.000
7	A_N_W_W(dcm)	0.000	0.000
8	TS1_#(dcm)	0.000	0.000
9	Hemiaminal(dcm)	0.000	0.000
10	TS2_#(dcm)	0.000	0.000
11	I_W(dcm)	0.000	0.031
12	TS1N_#(dcm)	0.000	0.000
13	Int_N(dcm)	0.000	0.001
14	TS2N_#(dcm)	0.000	0.000
15	I_N_W(dcm)	0.000	0.000
16	TS1W_#(dcm)	0.000	0.000
17	Int_W(dcm)	0.000	0.000
18	TS2W_#(dcm)	0.000	0.000
19	I_W_W(dcm)	0.000	0.005
20	TS1NW_#(dcm)	0.000	0.000
21	Int_N_W(dcm)	0.000	0.000
22	TS2NW_#(dcm)	0.000	0.000
23	I_N_W_W(dcm)	0.000	0.000
24	TS1WW_#(dcm)	0.000	0.000
25	Int_W_W(dcm)	0.000	0.000
26	TS2WW_#(dcm)	0.000	0.000
27	I_W_W_W(dcm)	0.000	0.000
28	Imine(dcm)	0.000	0.016

Simulation data was saved to **model.csv**

→ cc-pVTZ git:(main) ✗



Pérez-Soto, R. et al. *Organic Letters* **2020**, *22*, 2873–2877

Perspectives

Future work

- Improved tunneling corrections

[1] Tanaka, N. et al. *Journal of Atmospheric Chemistry* **1996**, *23*, 37–49.
[2] Garza, A. J. *Journal of Chemical Theory and Computation* **2019**, *15*, 3204–3214.

Future work

- Improved tunneling corrections
- **Kinetic isotope effects** (KIE)[1]

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- **Time-resolved spectroscopy**

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Questions?

https://geem-lab.github.io/overreact-docs/