RMG Study Group

Solvent effects in RMG (Java + π)

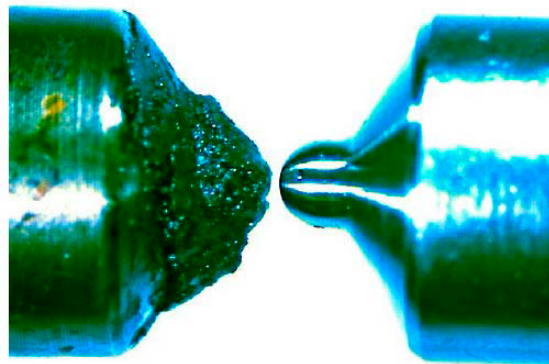### Belinda Slakman and Amrit Jalan
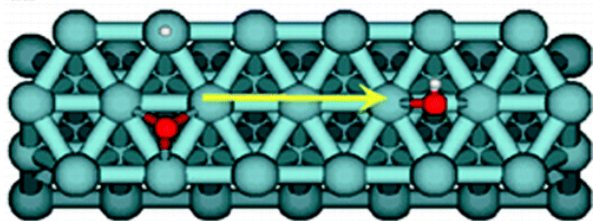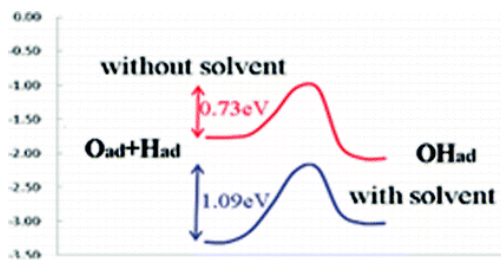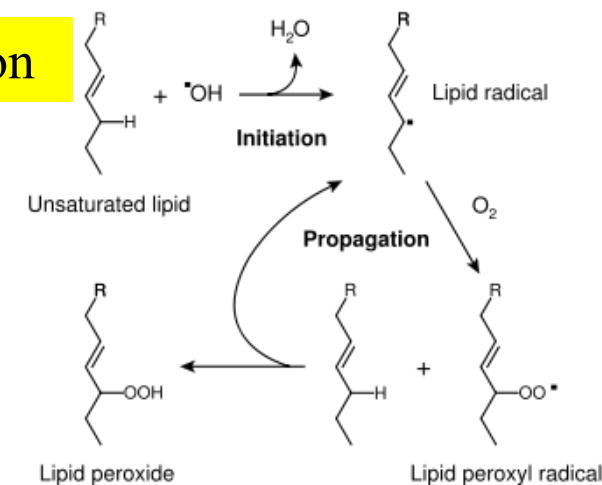
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Northeastern University

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Solvent effects are important in many chemical systems of practical interest

Engines: gumming and clogging in diesel injectors

Biological oxidation

Catalysis, Fuel cells

Thermal stability under storage conditions

Detailed kinetic modeling of solution phase systems is still fairly fictional

2

Objective: to boldly swim where no one has swum before

RMG System Overview
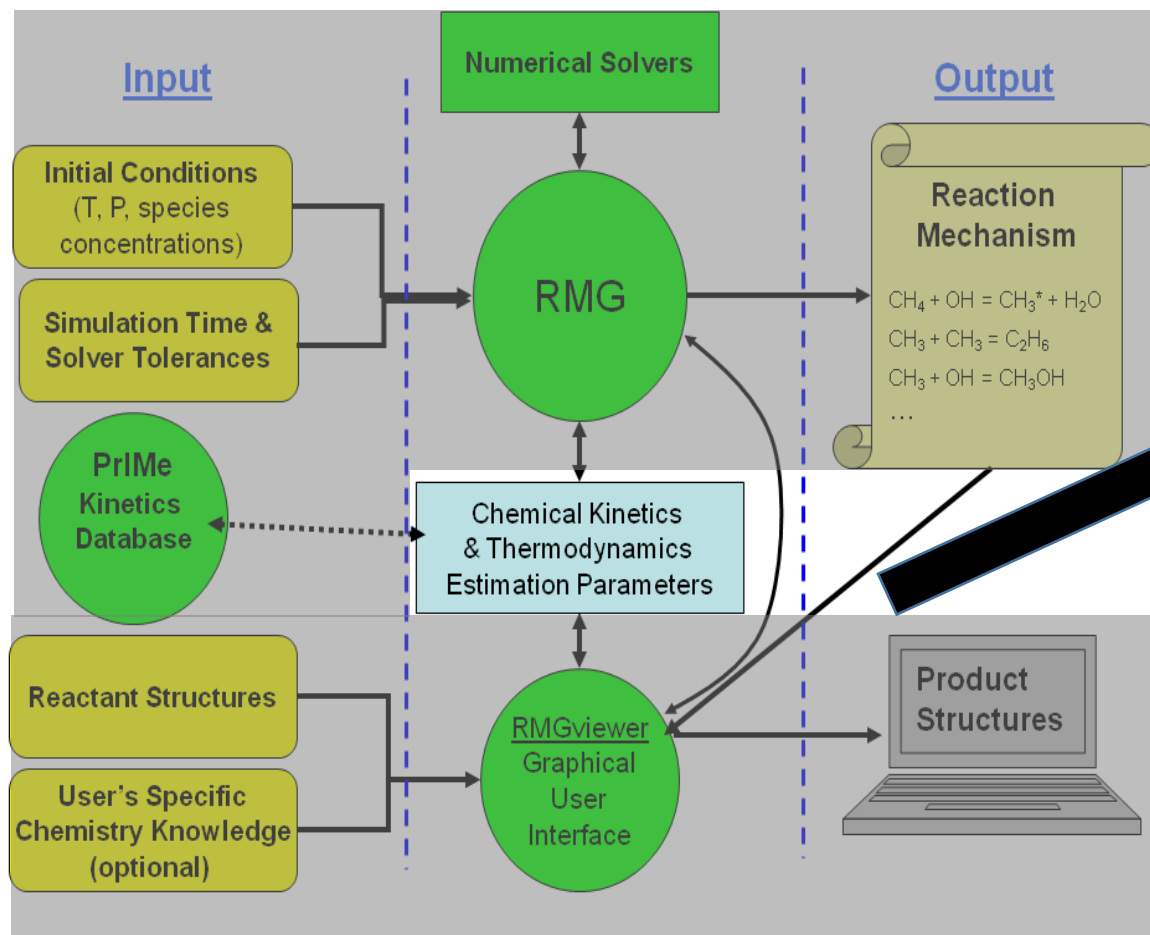
Requires modifications to handle different solvents

Automatic estimation of solvent effects on:

1) Species thermochemistry
2) Reaction rate parameters

Our application demands both accuracy and high-throughput

System	Reactions	Species
Butanol oxidation	3381	263
Jet Fuel oxidation	7715	317
Methyl formate oxidation	1550	285
Hexane pyrolysis	1178	60

Actual number of reactions and species considered can be $\sim 10^6$

Structure-activity relations are already used in gas-phase RMG for high-throughput parameter estimation

e.g. Group additivity & Evans Polanyi relations

We are looking for similar methods for solution phase thermochemistry and kinetics

Outline

We want quick estimates of $G_i(T)$ and k in different solvents

- Solution phase thermochemistry

- Solution Phase kinetics

Metrics: Accuracy and high-throughput

Solvation thermodynamics involves cavity formation and solute-solvent interactions

Digging a hole
in the solvent

- Dipolarity/ polarizability
- Hydrogen bonding

Free energy change of entire process = ΔG^0_{solv}

Existing theoretical models for ΔG^0_{solv} are fairly accurate but computationally expensive

- Implicit solvation models
  - QM description of solute, solvent as bulk continuum
  - Model both kinetics and thermochemistry
- Explicit solvent molecular mechanics
  - Use force fields to model solute solvent interactions
- Parameterized using experimental data

1. On-the-fly quantum calculations: computationally expensive

2. Gas phase approach: Perform QM calculations and fit groups for each solvent
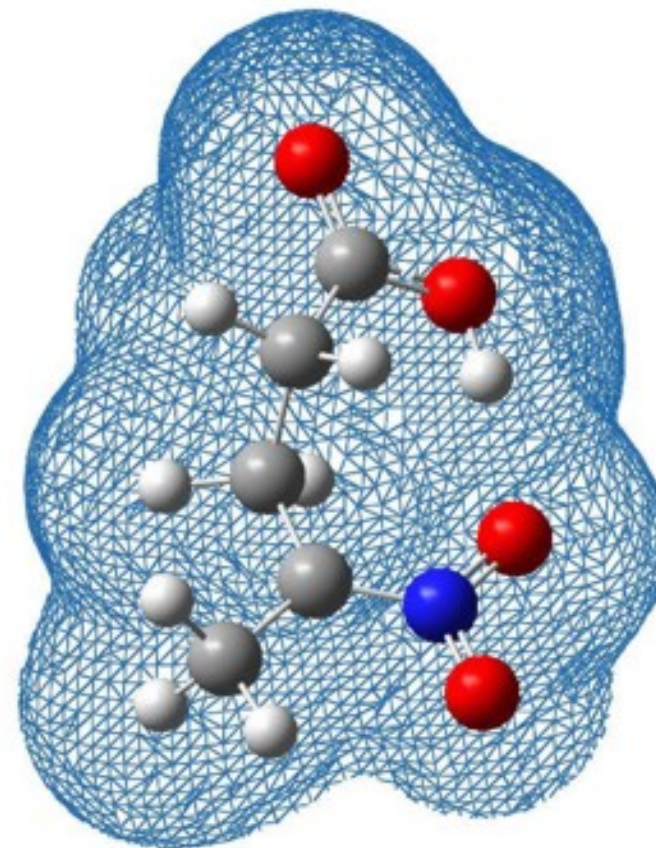
Empirical models of solvation use solute/solvent descriptors to model ΔG^0_{solv}

The Abraham model

- Linear Solvation Energy Relationships (LSER)
- Use molecular descriptors to quantify different interactions

$$-\frac{\Delta G^0_{solv}}{2.303RT} = c + eE + sS + aA + bB + lL$$

■ Solute descriptor
■ Solvent dependent coefficients

Electrostatic (dipolarity, polarizability)

Hydrogen bonding

Cavity Formation

A,B,E,S,L : available for over 5000 solutes
c,a,b,e,s,l : available for >50 solvents

LSER approach is attractive if we can estimate solute descriptors for an arbitrary molecule

Platts *et al.* developed a group additivity approach
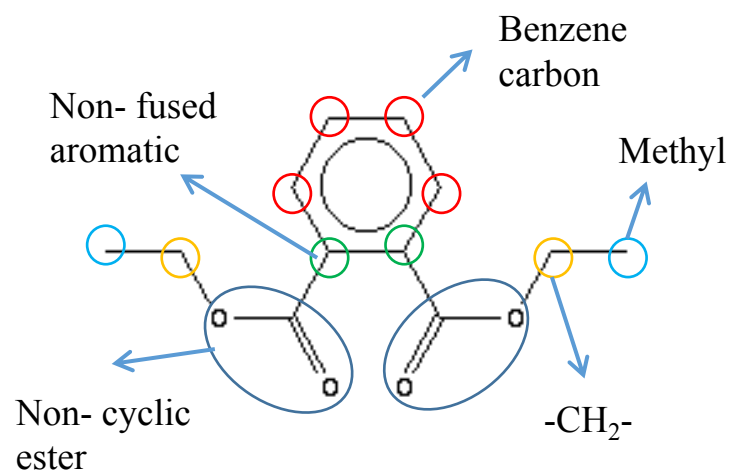
Descriptor	Value
A	0.003
B	0.807
E	0.752
S	1.391
L	7.072

Solvent	ΔG^0_{solv} (kcal/mol)
Hexane	-9.68
Water	-7.58
CH_3CN	-11.65
DMSO	-11.57

2D molecular structure $\longrightarrow$ Solute descriptors $\longrightarrow$ ΔG^0_{solv}

Negligible cost per computation => high-throughput

LSER reproduce experimental ΔG^0_{solv} for a variety of solute-solvent pairs
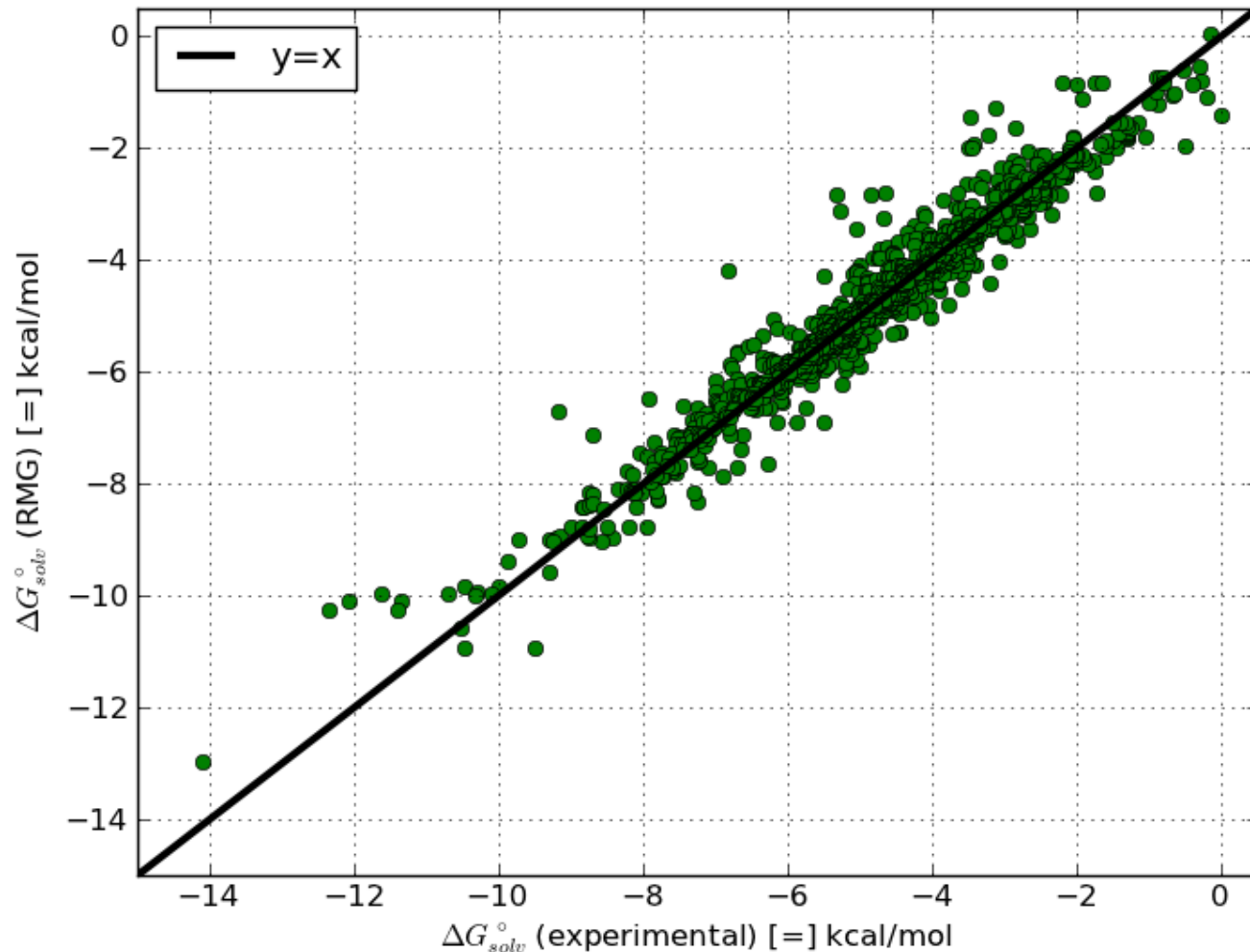
- Minnesota Solvation Database: 935 experimental data points (130 solutes, 35 solvents)
- RMS error (RMSE) = 0.47 kcal/mol
- Outliers: solute-solvent pairs with strong H-bonding

Temperature dependence: decomposition of ΔG_{solv}^0 into ΔH_{solv}^0 & ΔS_{solv}^0

$$\Delta G_{\text{solv}}(T) = \Delta H^0_{\text{solv}} - T\Delta S^0_{\text{solv}}$$

<u>Method 1</u>: Analytical expressions from hard-sphere models

$$\Delta S^0_{\text{solv}} \approx \Delta S^0_{\text{cav}} = -\left(\frac{\partial \Delta G^0_{\text{cav}}}{\partial T}\right) = K'_0 + K'_1 r_{\text{cav}} + K'_2 r^2_{\text{cav}}$$

- Input parameters: $r_{\text{solute}}, r_{\text{solvent}}, \rho, T$

<u>Method 2</u>: Empirical correlations for ΔH_{solv}^0 developed by Mintz *et al.**

$$\Delta H_{solv}^0 = c' + e'E + s'S + a'A + b'B + l'L$$

- No new input parameters, may not be available for all solvent of interest
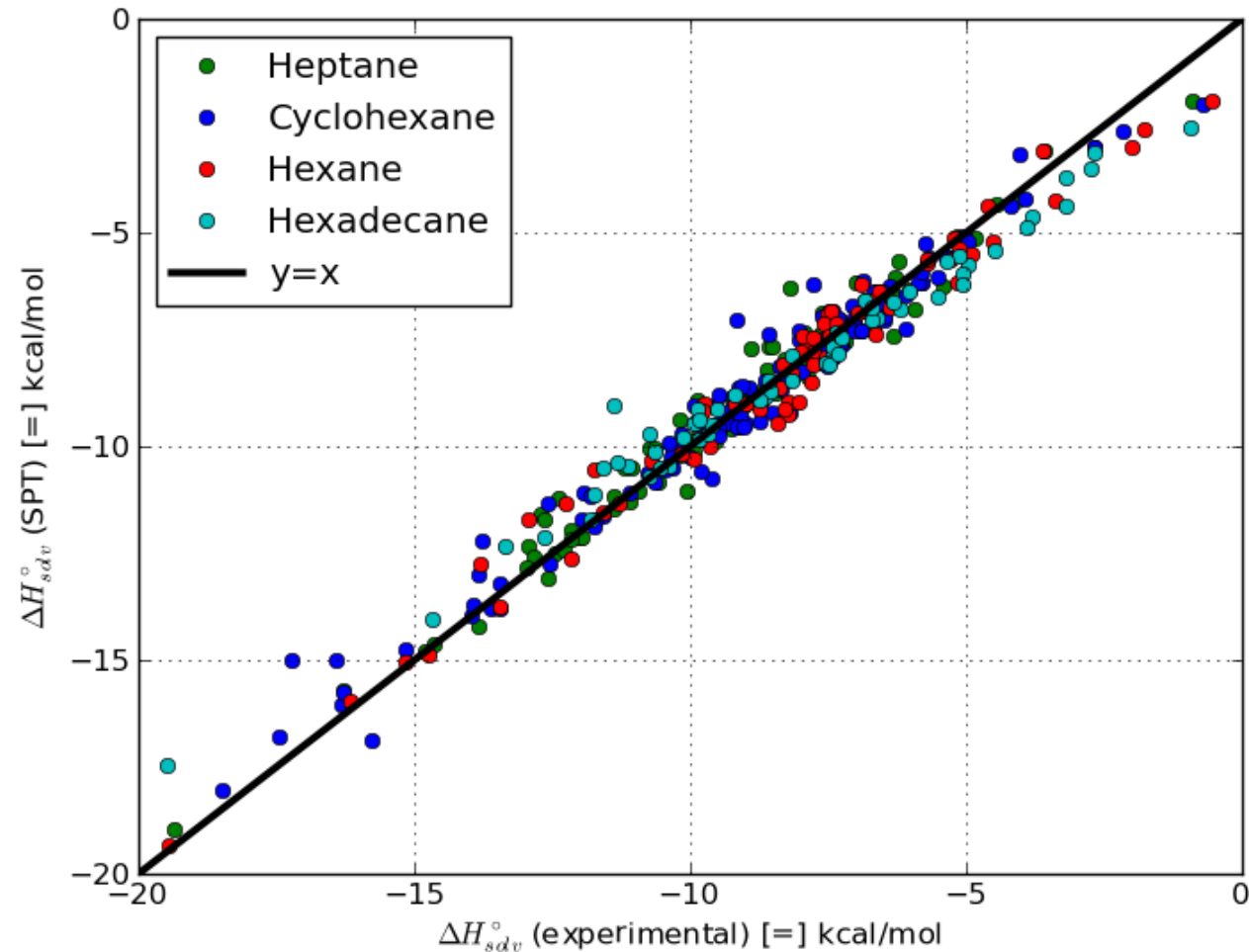
Testing the accuracy of hard sphere models: alkane solvents
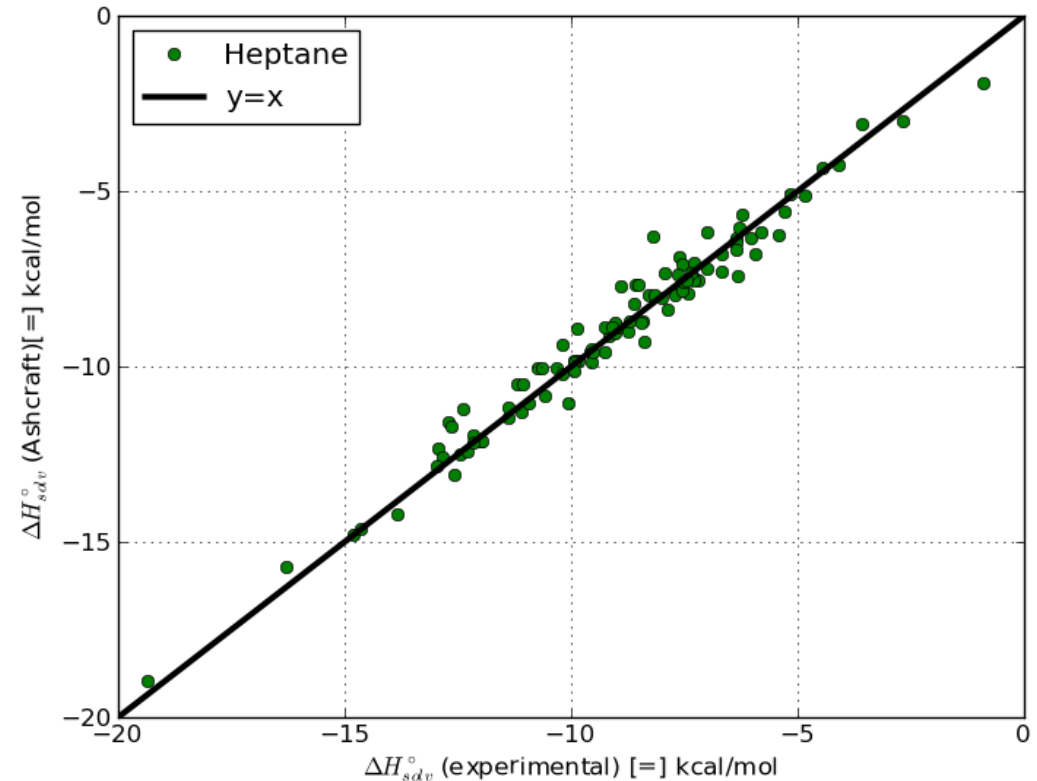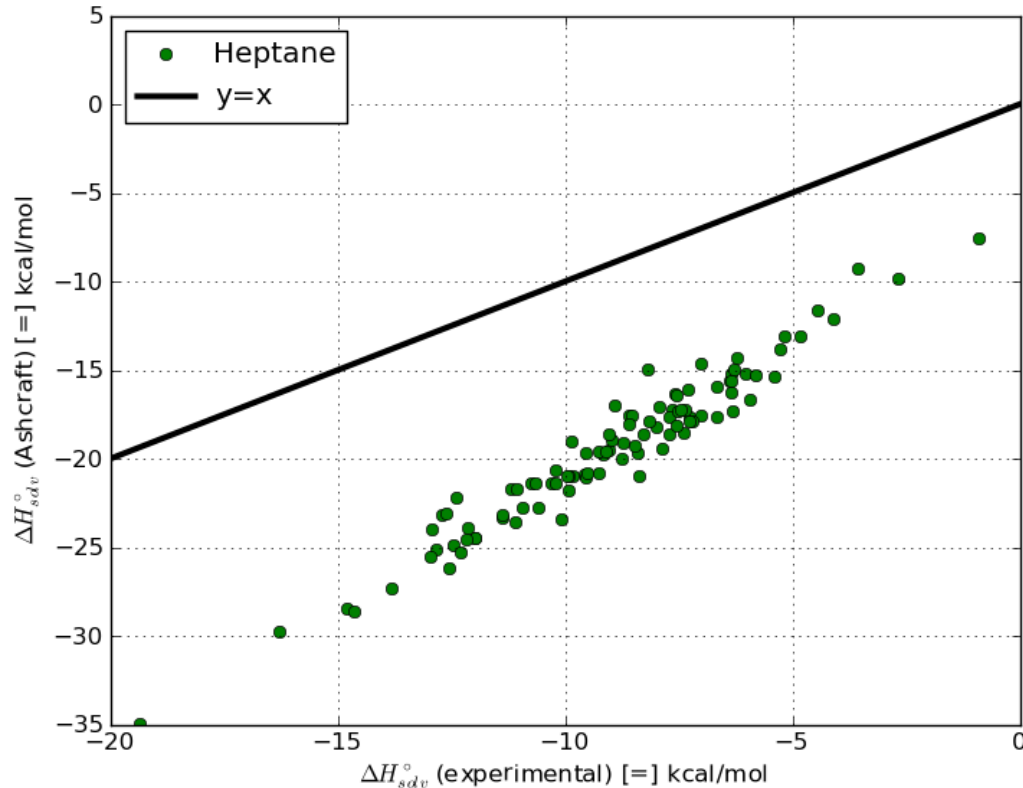
Use of correction factors drastically improves agreement with experimental data:
- Heptane: $\alpha = 1.38\ A^0$, $\beta = 0.95$
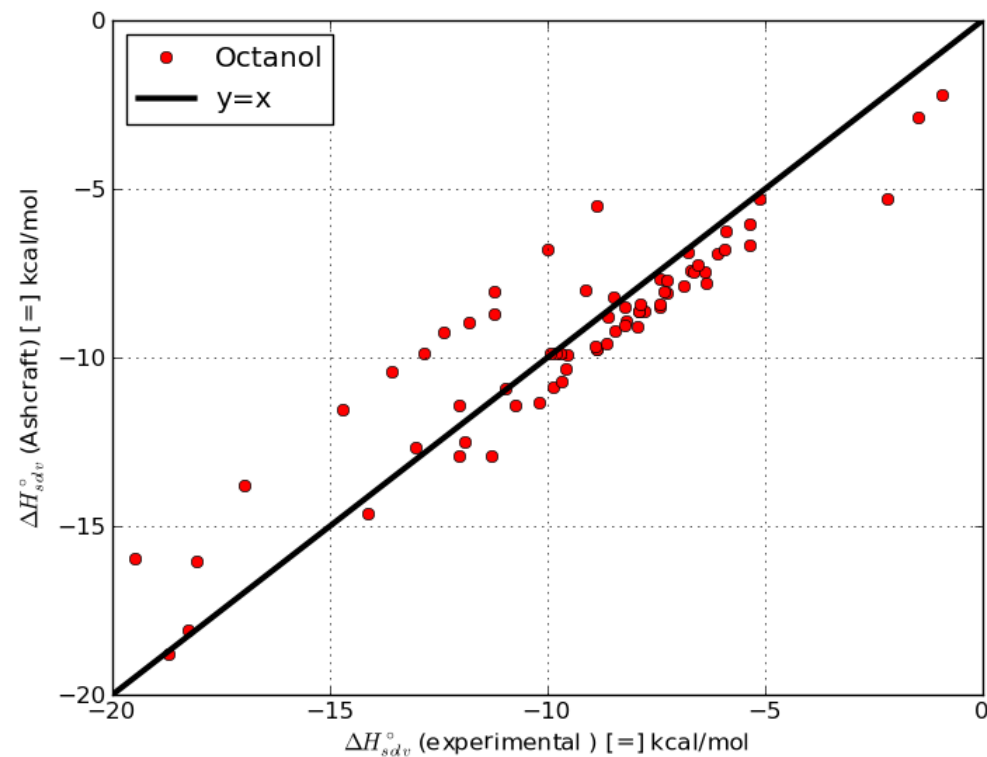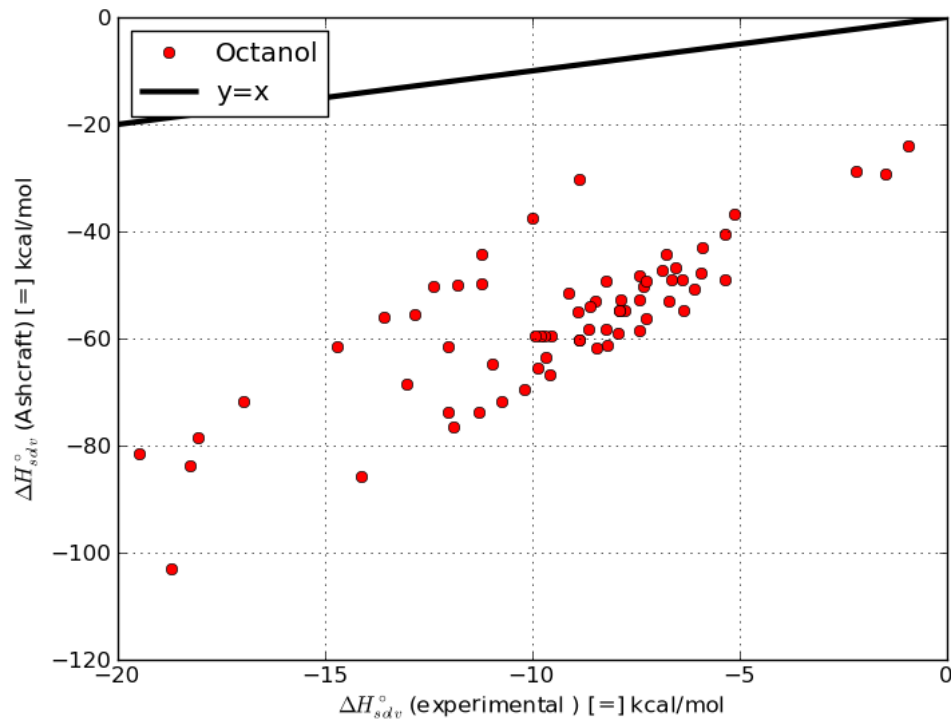- High sensitivity to molecular radii

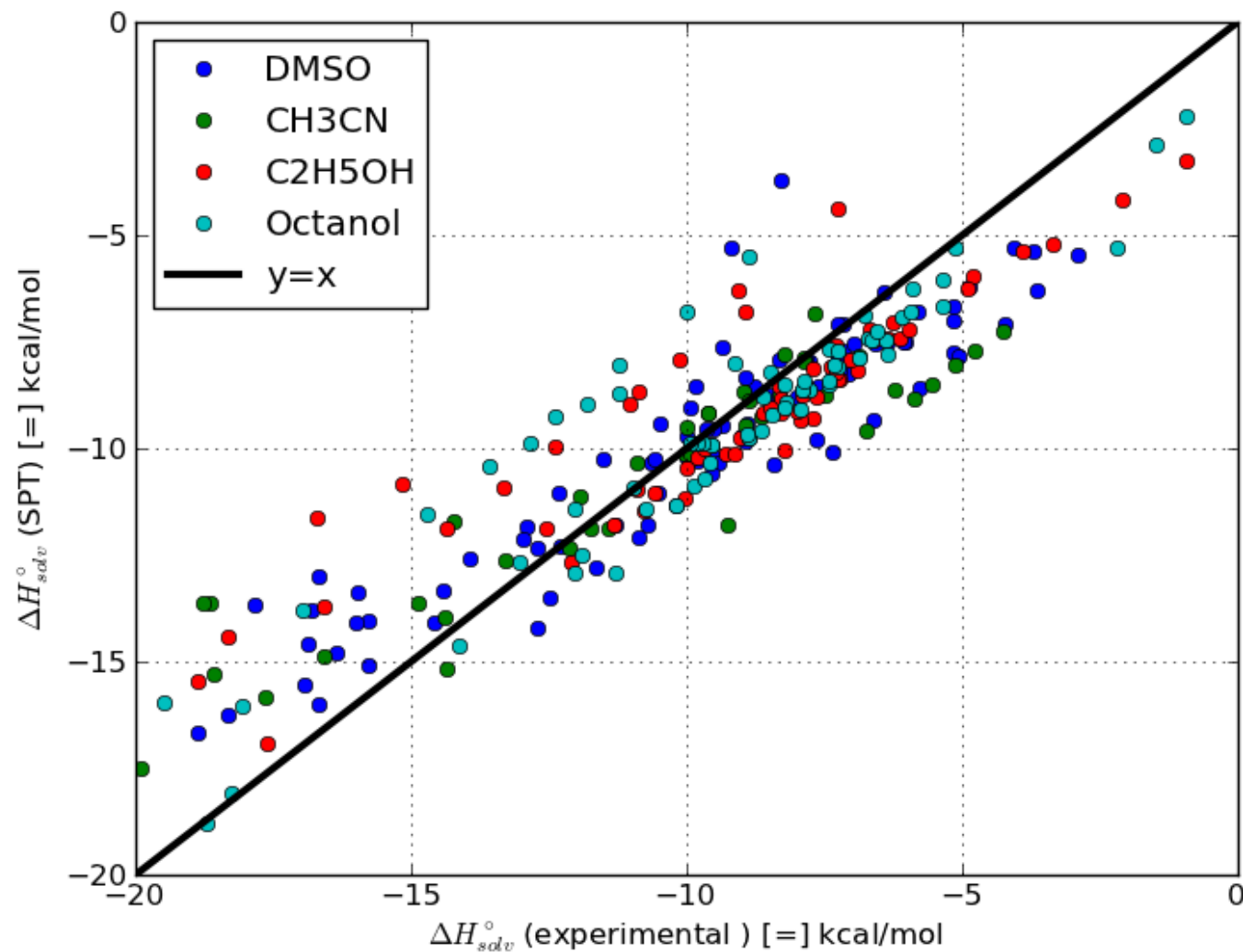# Testing the accuracy of hard sphere models: alkane solvents

Testing the accuracy of hard sphere models: protic solvents

Correction factors improve agreement: Octanol: $\alpha = -1.72\ A^0, \beta = 0.91$
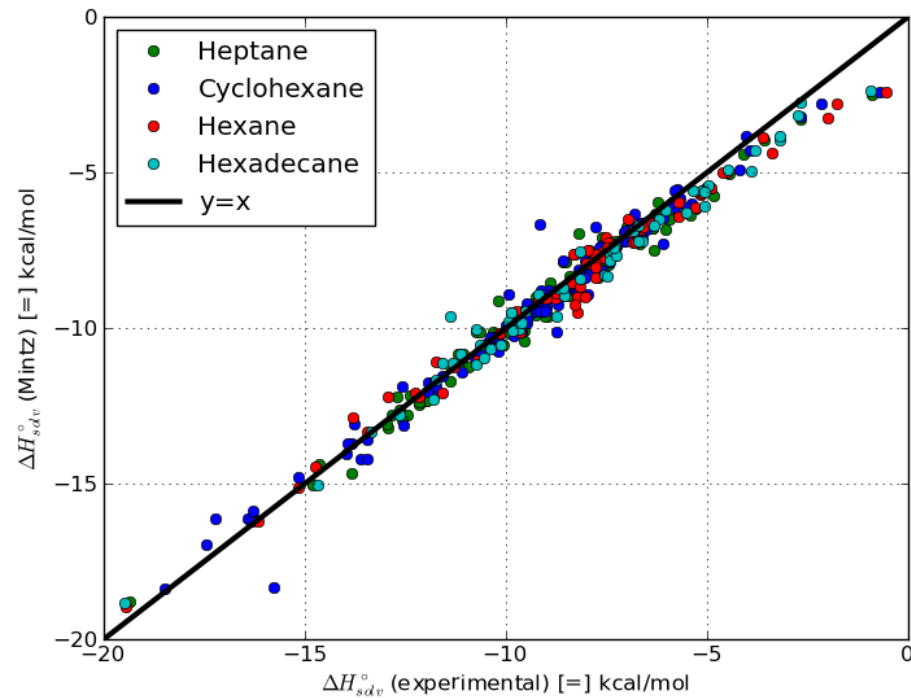- Species with strong H-bonding are main outliers

Testing the accuracy of hard sphere models: protic solvents
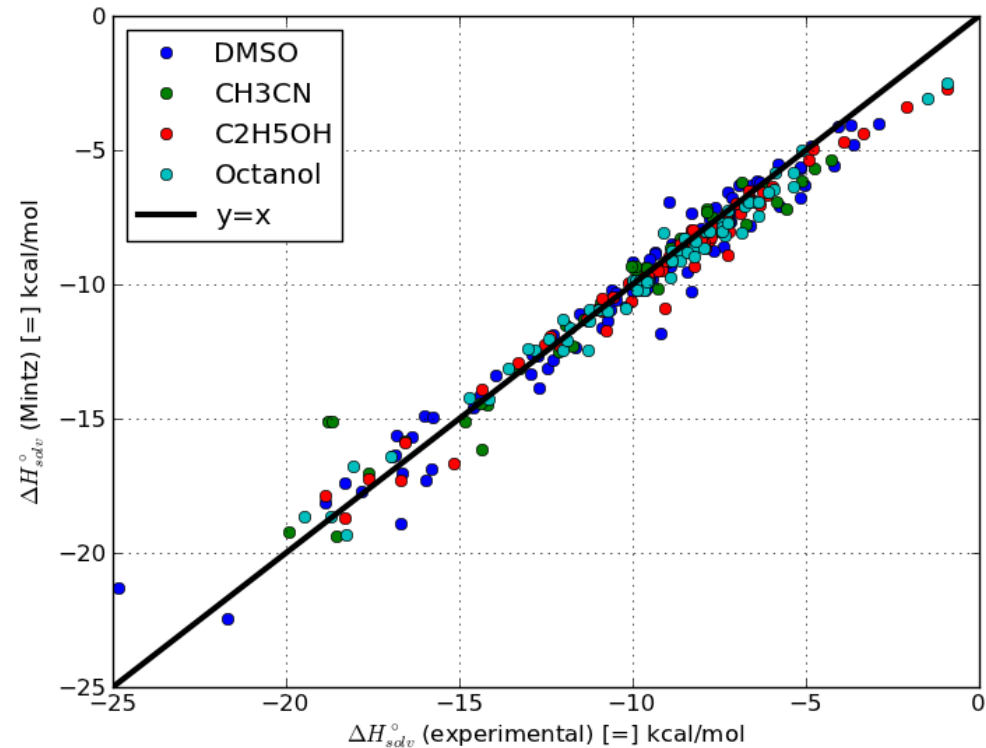
Empirical correlations work for both alkane and protic solvents

$$\Delta H^0_{solv} = c' + e'E + s'S + a'A + b'B + l'L$$

Mintz estimates for alkane solvents with RMG descriptors

Mintz estimates for protic solvents with RMG descriptors

Simple approximations are used to estimate solvation of free radical intermediates

- Corrections using Platts' group values are being used
  - correct for H-bond donating ability (A) of saturated species
  - all other descriptors assumed to be the same
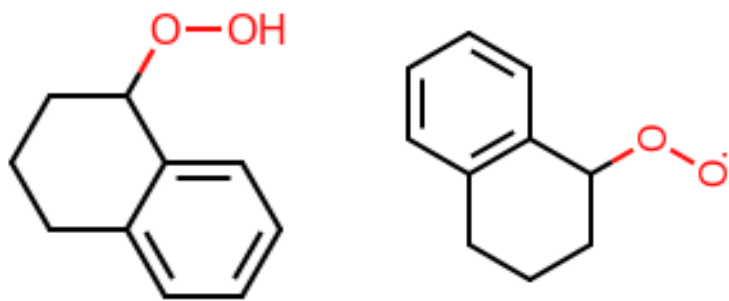
Species	E	S	A	B	L
ROOH	1.044	1.147	0.348	0.644	6.232
ROO.	1.044	1.147	0.003	0.644	6.232

These radical corrections are implemented in a manner similar to gas phase thermo.

Species	ΔG^0_{hyd} (k_H)	ΔG^0_{hyd} (RMG)
HO.	-3.9	-4.7
HOO.	-6.8	-7.5

*values in kcal/mol

Outline

We want quick estimates of $G_i(T)$ and k in different solvents

- Solution phase thermochemistry

Abraham/Platts/Mintz + some QM

Solvent dependent structure activity relationships

- Solution Phase kinetics
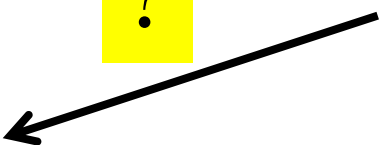
Metrics: Accuracy and high-throughput

Outline

We want quick estimates of $G_i(T)$ and k in different solvents

- Solution phase thermochemistry

? Solvent dependent structure activity relationships

- Solution Phase kinetics

Metrics: Accuracy and high-throughput

Prevailing view:
Solvents do not influence radical reaction rates

TUTORIAL REVIEW

The frequently overlooked importance of solvent in free radical syntheses

Grzegorz Litwinienko,[a] A. L. J. Beckwith[b] and K. U. Ingold*[c]

Kinetic solvent effects on peroxyl radical reactions†
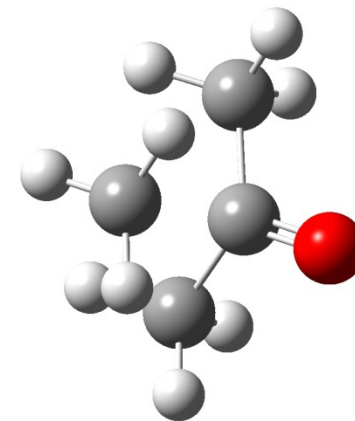
Mukund Jha and Derek A. Pratt*

Solvent can affect elementary reaction rates primarily through two routes

1. Differential solvation of transition state vs. reactants
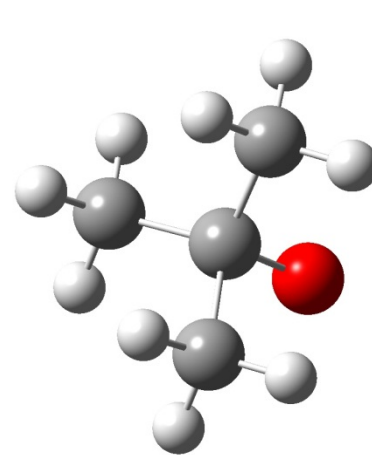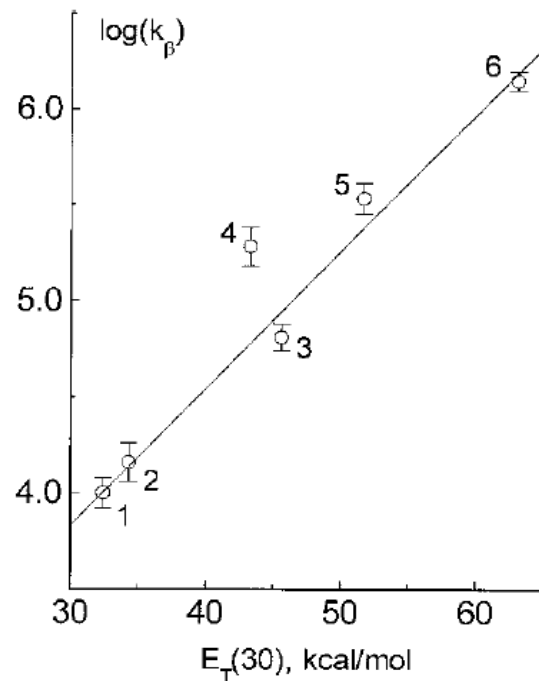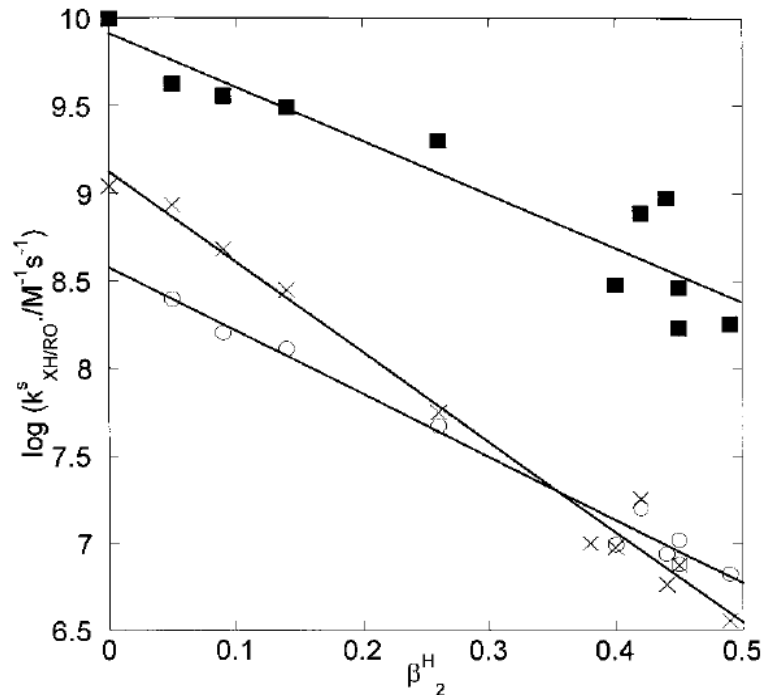

Reactant
$\mu = 1.97$ Debye
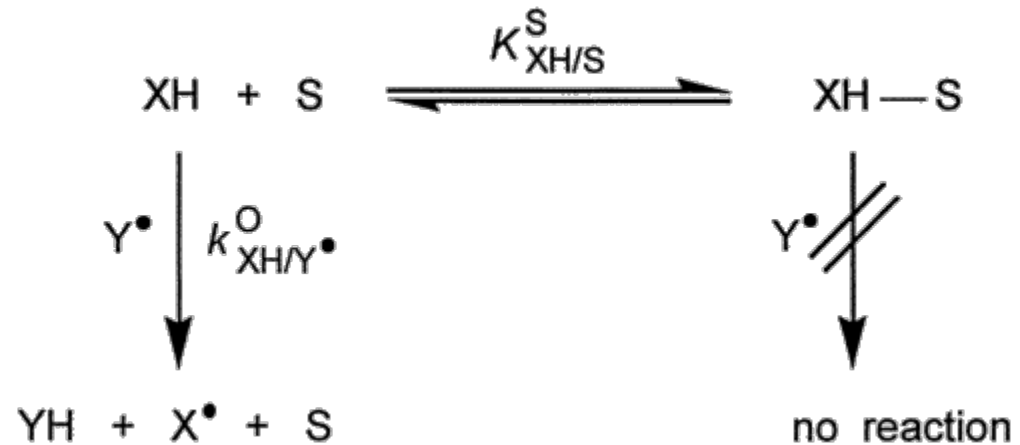
Transition state
$\mu = 2.64$ Debye

β-scission rates $\Leftrightarrow$ electrostatic descriptors

Solvents can affect elementary reaction rates primarily through two routes

2. Formation of reactant-solvent complexes
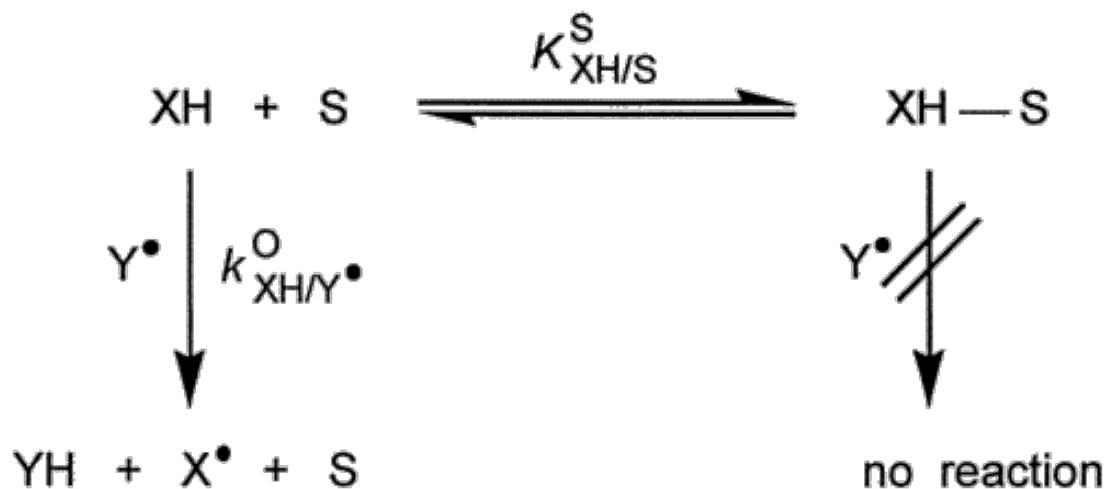

$$\log k_S = \log k_0 - 8.3AB$$

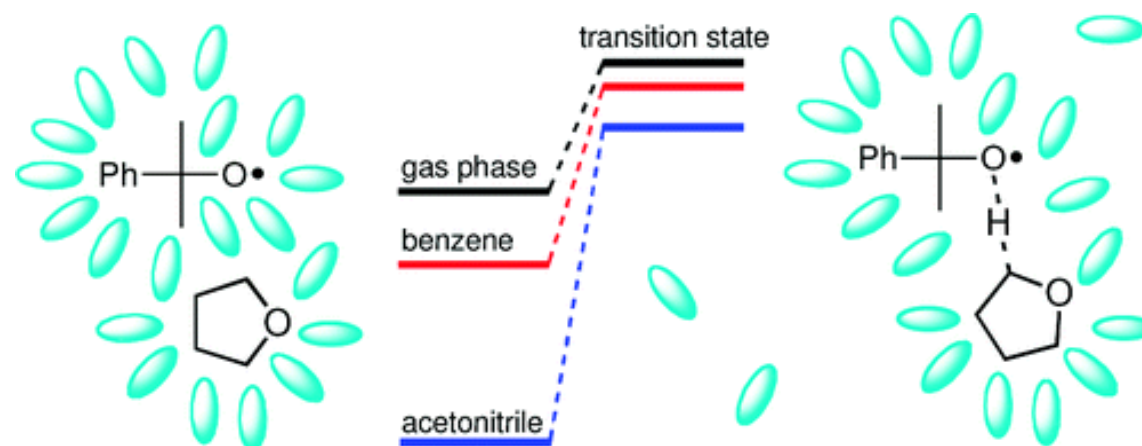H-Abstraction ⟺ H-bonding descriptors

Complexation with solvent can reduce availability of free reactants

It is also possible that both effects operate simultaneously

Differential solvation and reactant-solvent complexes

Snelgrove *et al.*, 2001

El-Sheshtawy *et al.*, 2011

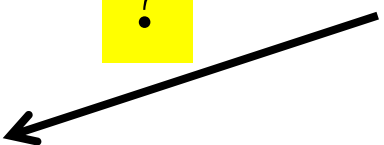To what extent can computational modeling help us quantify these effects?

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?   Solvent dependent structure activity relationships

- Solution Phase kinetics

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