



Reaction Profile of $\text{Pd}(0) + 2 \text{PH}_3 + \text{H}_2$

Practice Session

Pd⁰(PR₃)₂

```
%CHK=/starchk/chemistry/ch_res/eclab/jamal/class_PdPH32.chk
%nproc=16
%mem=24GB
# b3lyp/gen empiricaldispersion=gd3bj pseudo=read optcyc=99 nosymm
  opt freq=noraman
```

Title Card Required

```
0 1
Pd      -1.89777385   1.57389907   0.92659901
P       -0.02304064   2.22509022   2.09577695
P       -3.77846000   0.92160400  -0.24680000
H       -3.83594400   1.04753800  -1.65796000
H       -4.23811700  -0.41889300  -0.19850900
H       -5.03863100   1.51995100   0.00715100
H        1.10545636   2.75834122   1.42296695
H       -0.09780964   3.23747122   3.08573995
H        0.70053236   1.29704522   2.8868019
```

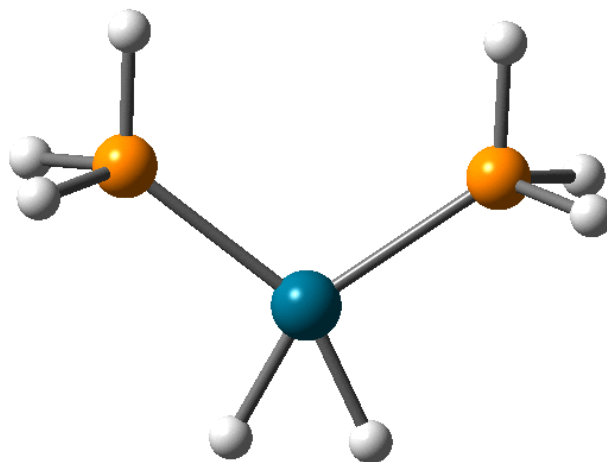
```
Pd 0
lanl2dz
****
```

Transition state

1. Do `freq=noraman` calculation of rough Transition state structure
2. The first imaginary frequency should relate your reaction coordinate.
3. If so, read previously calculated frequencies and performed the `opt=(ts noeig readfc)`.
4. At the optimized TS structure run the `freq=noraman` calculation, again

M = Pd: Transition State

$$V_i = -643.58 \text{ cm}^{-1}$$





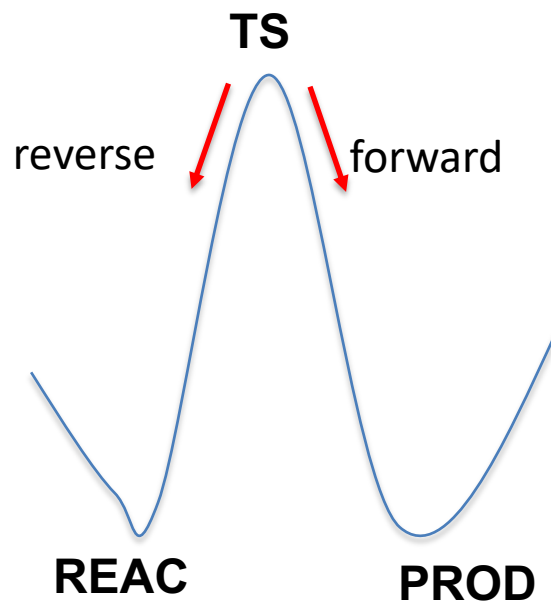
IRC CALCULATIONS

5. Intrinsic Reaction Coordinate calculations from the optimized TS:

a. Forward: IRC=(RCFC forward maxpoint=@@) guess=read

b. Reverse: IRC=(RCFC reverse maxpoint=@@) guess=read

Run from TRUE transition state (with ONE imaginary frequency)



Fundamental Concepts of the Carbene Transfer Catalysis

“Direct” C-H bond oxidation, amination or alkylation is 2e-oxidation process:

- X = CRR', NR and O groups have triplet ground states and 2-el, and
- $X + H-[C] \longrightarrow H-X-[C]$ is highly exothermic

Glorius, F.; et. al., *Nature*, **2014**, 510 (7506), 485.

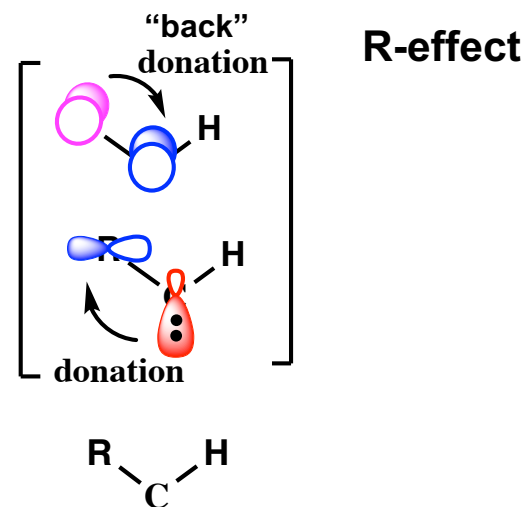
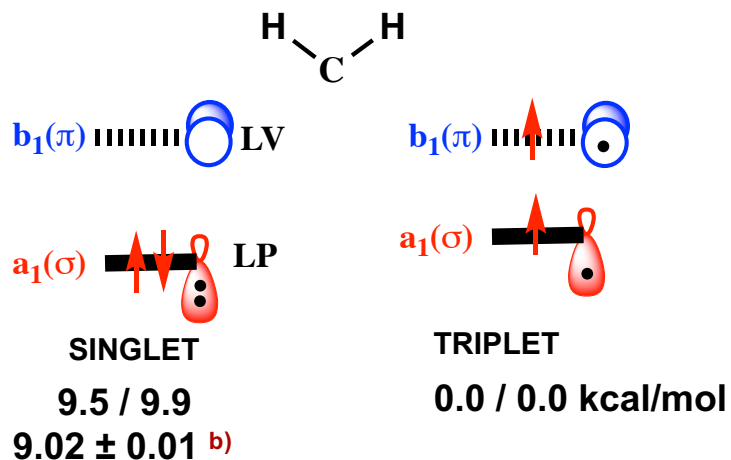
Tomioka, H.; et. al. *Nature*, **2001**, 412 (6847), 626

and **MANY MORE...**

Bertrand, G.; et. al. : *Organometallics*, **2011**, 30, 5304

Bertrand, G.; et. al. : *Nat. Chem.*, **2009**, 1, 265

Bertrand, G.; et. al. : *Science*, **2007**, 316, 439



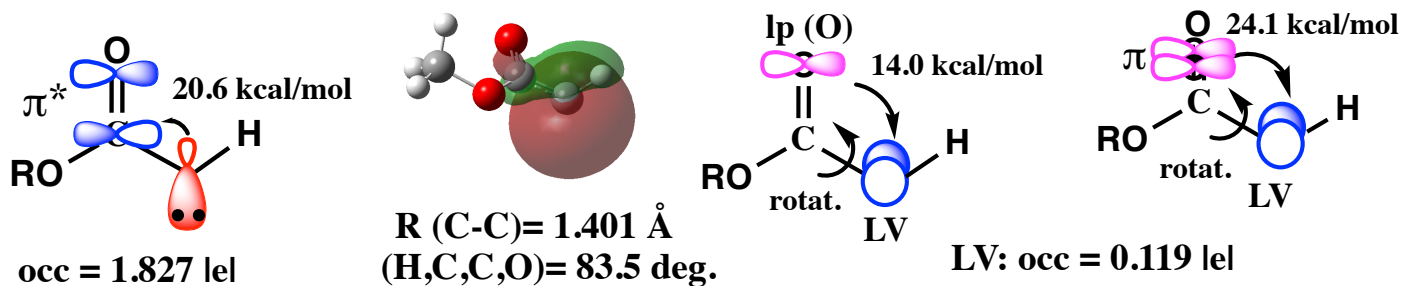
Musaev, D. G.; et. al. *J. Phys. Chem.*, **1993**, 97, 4064

^{b)} Exp: Bunker, P. R.; Jensen, P.; Kraemer, W. P.; Beardsworth, R. *J. Chem. Phys.*, **1986**, 85, 3724

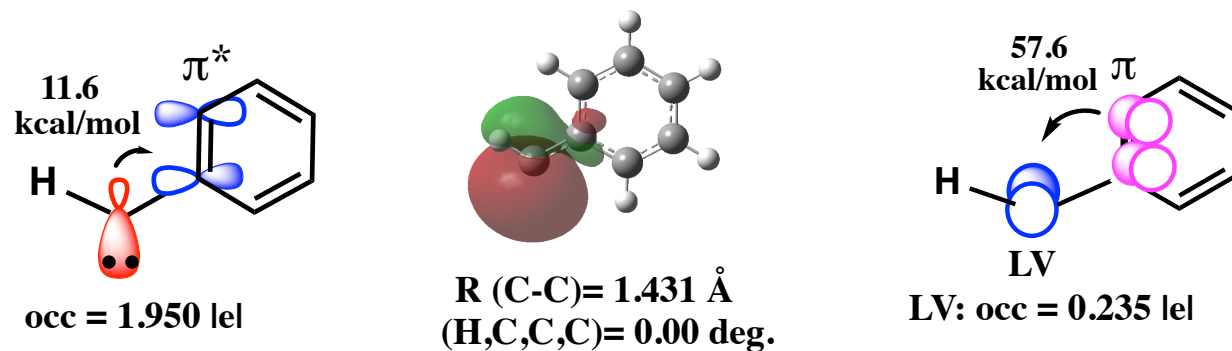
Fundamental Concepts of the Carbene Transfer Catalysis:

Acceptor and Donor Carbenes

A



D

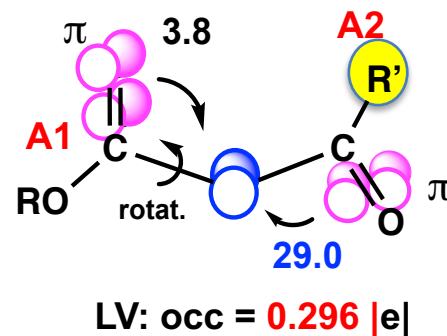
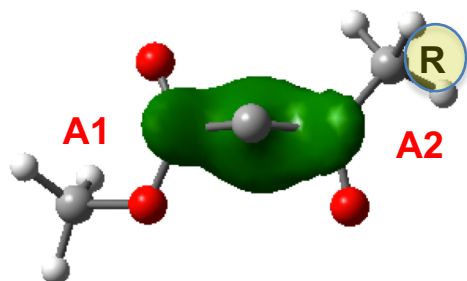
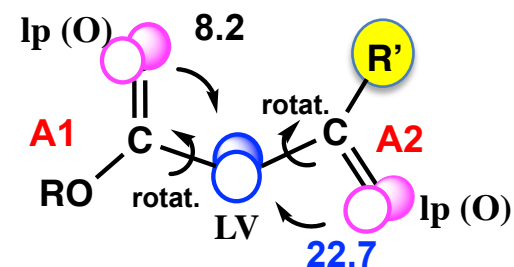
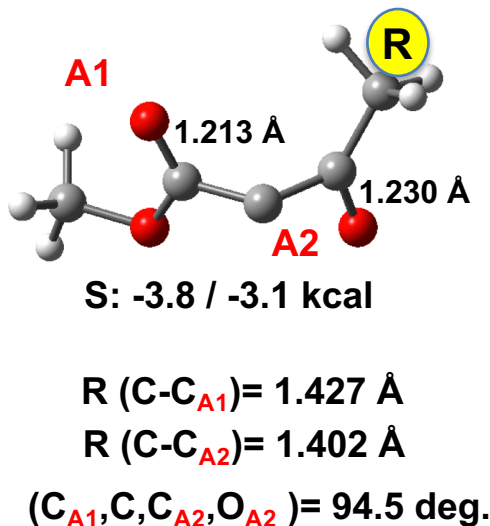
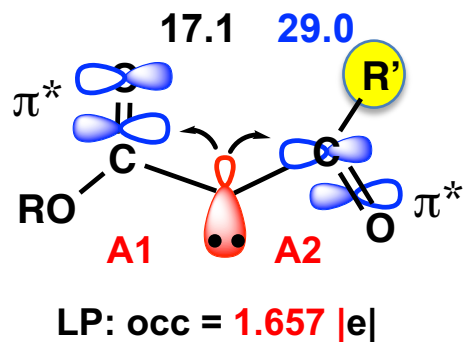


A Predictive Model for the $[\text{Rh}_2(\text{esp})_2]$ -catalyzed Intermol. $\text{C}(\text{sp}^3)\text{-H}$ Bond Insertion of β -carbonyl Ester Carbenes

Acceptor/Acceptor Carbenes



B. McLarney

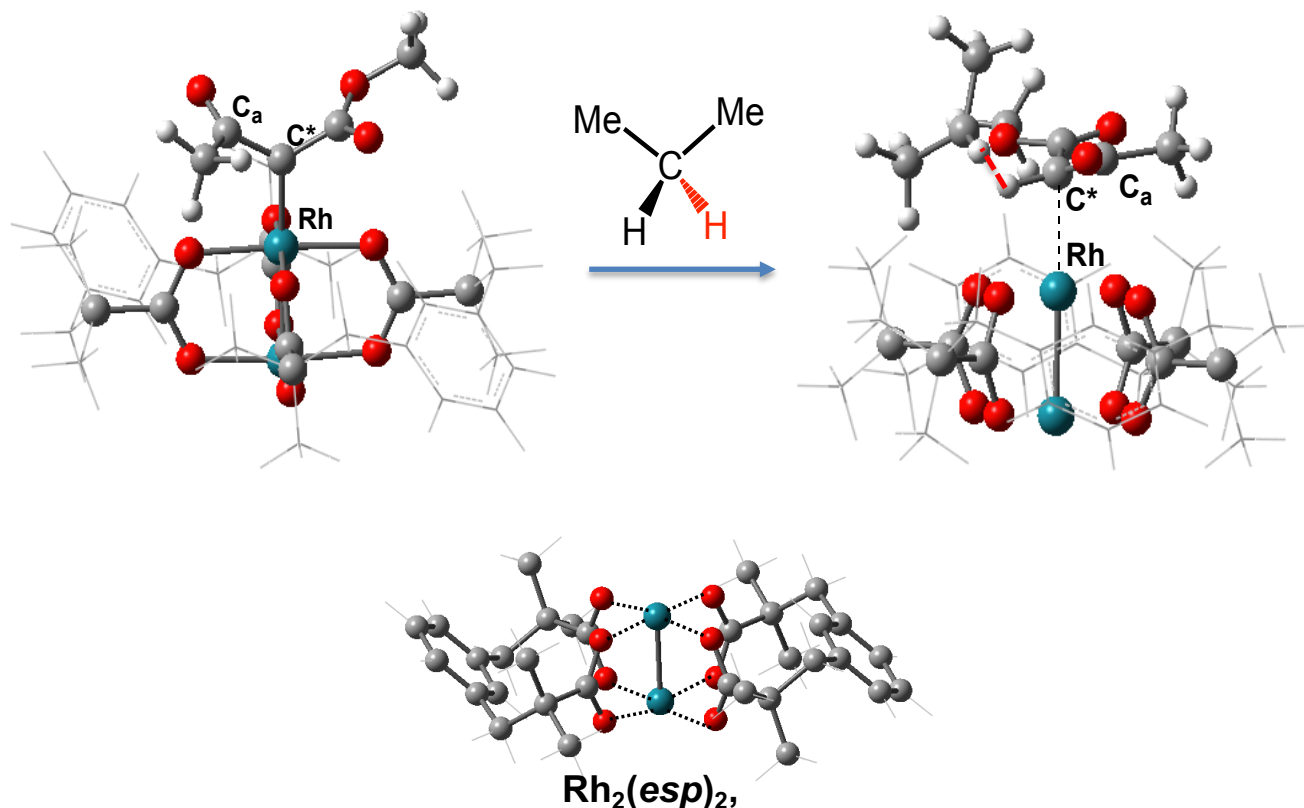


ACS Catalysis, 2019, 9, 4526-4538.

EC lecture series 2020

[Rh₂(esp)₂]-catalyzed Intermolecular C(sp³)-H Bond Insertion of β-carbonyl Ester Carbenes

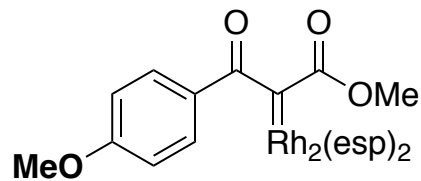
ACS Catalysis, 2019, 9, 4526-4538.



J. Du Bois and coworkers:
JACS, 2004, 126, 15378

esp = α,α,α',α'-tetramethyl-
(1,3)-benzenedipropionate

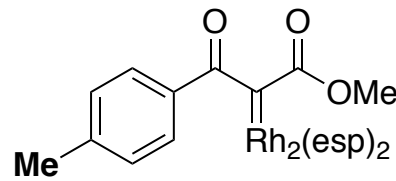
Electronic nature of the carbonyl plays an important role in determining the C–H activation barriers



2a

$$\sigma_p = -0.268$$

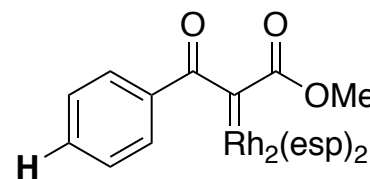
$$\Delta H^\ddagger = 3.1 \text{ kcal/mol}$$



2b

$$\sigma_p = -0.170$$

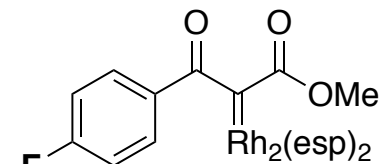
$$\Delta H^\ddagger = 2.4 \text{ kcal/mol}$$



2c

$$\sigma_p = 0$$

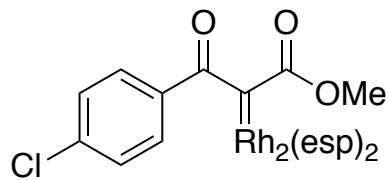
$$\Delta H^\ddagger = 1.9 \text{ kcal/mol}$$



2d

$$\sigma_p = 0.062$$

$$\Delta H^\ddagger = 1.3 \text{ kcal/mol}$$

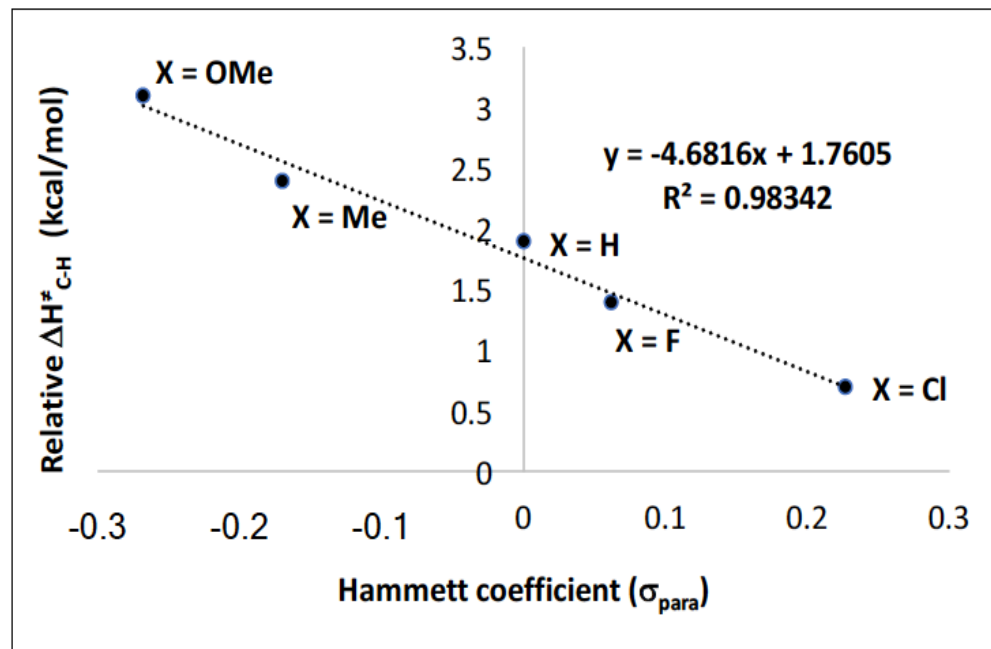


2e

$$\sigma_p = 0.227$$

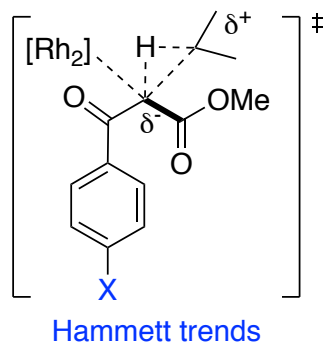
$$\Delta H^\ddagger = 0.5 \text{ kcal/mol}$$

As the Ph becomes electron deficient, the C–H activation barrier decreases.

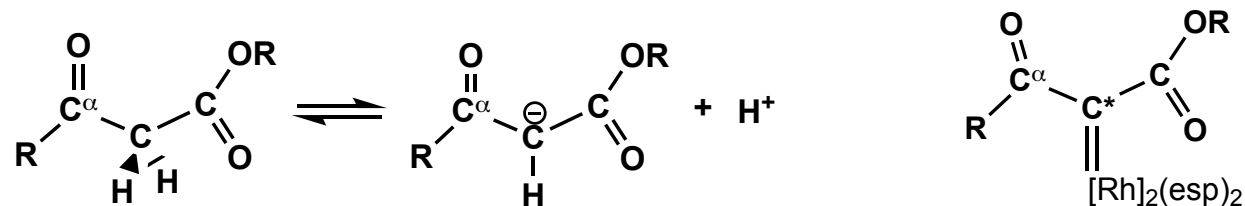


Accessible Parameters of Carbonyl Substituent Impacting the Stability of the Carbene Transfer TS

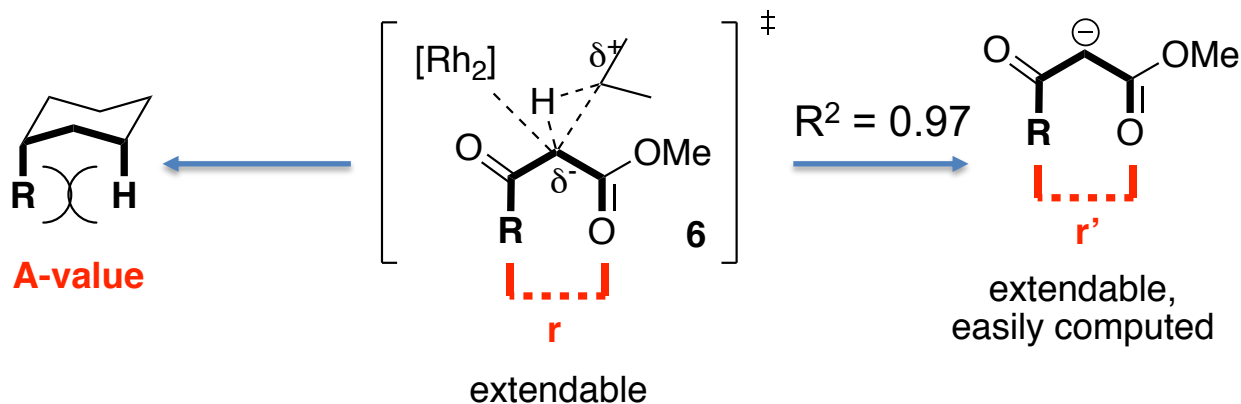
Determining Parameter for Electronics



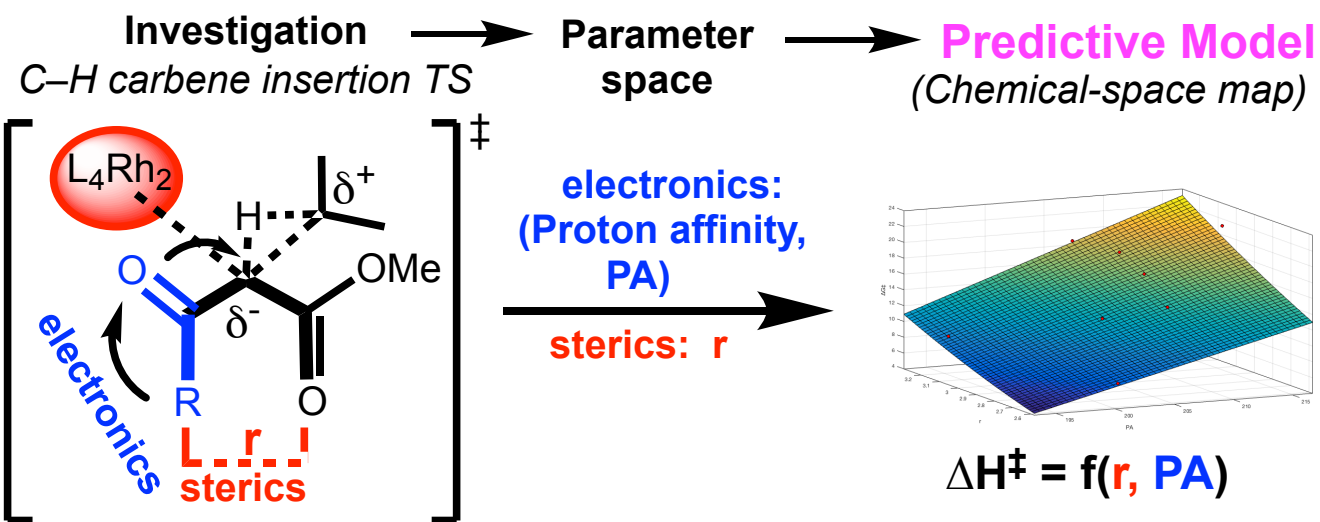
Proton Affinity (PA)



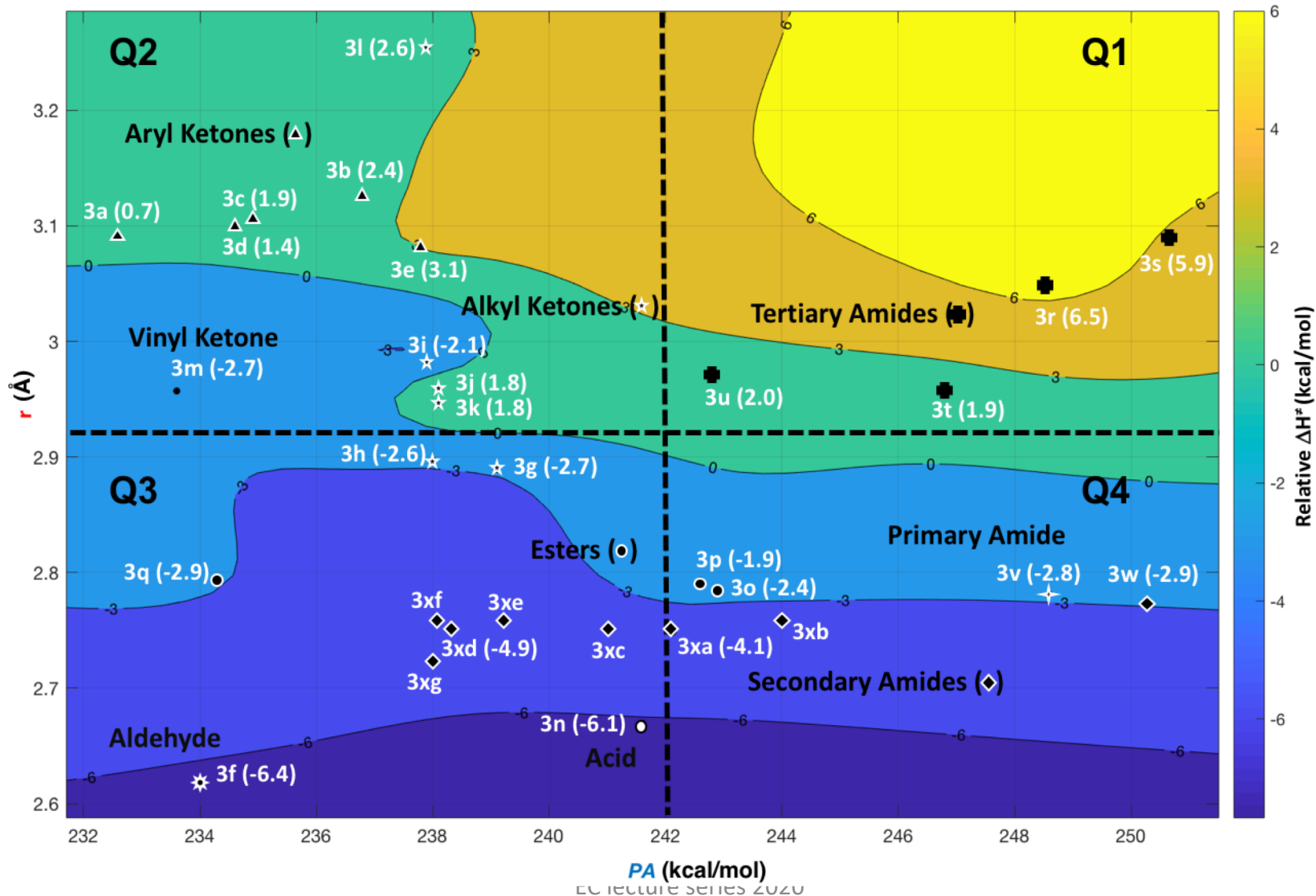
Determining Parameter for Sterics



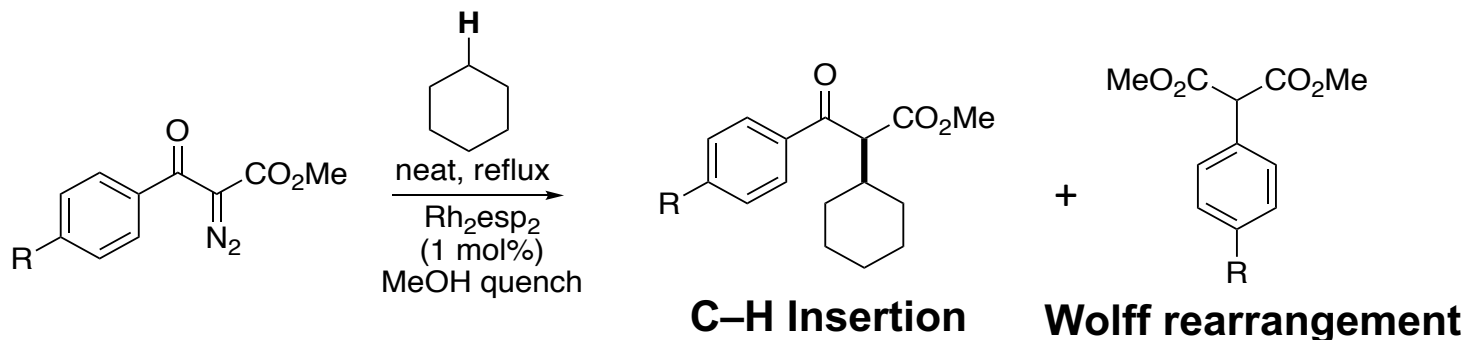
From the **Parameter Space** to the **Chemical-space**



The Developed Chemical Space Map



Experimental Validation-1: Aryl Ketones

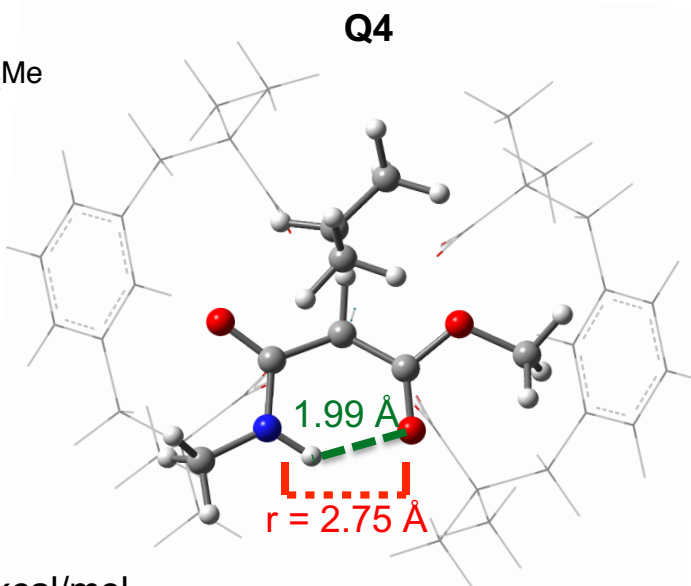
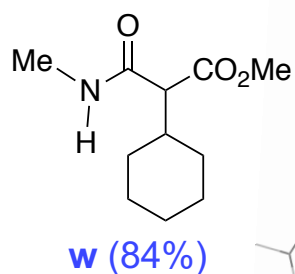
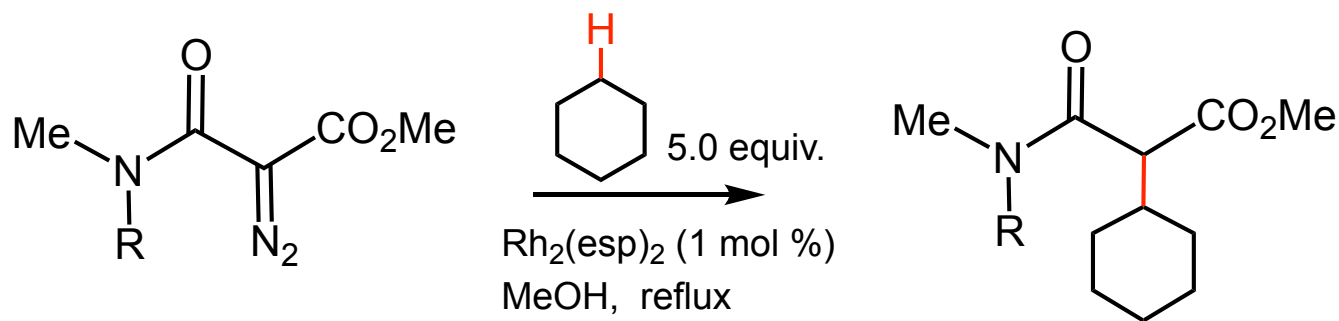


% isolated yield

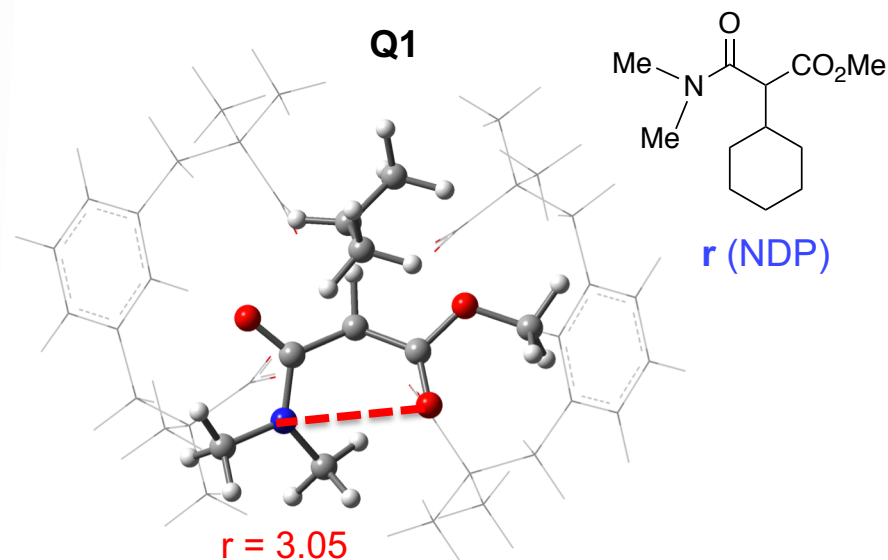
R = OMe (a),	PA = 237.8	0	96
Me (b),	PA = 236.8	21	71
H (c),	PA = 234.9	34	60
F (d),	PA = 234.6	49	47
Cl (e),	PA = 232.6	62	32

the carbenes with more electron deficient phenyl rings (i.e. with a smaller PA value) should be more selective for C – H insertion vs. Wolff rearrangement.

1,6-Hydrogen Bonding Facilitates Carbene Insertion into the C–H bond

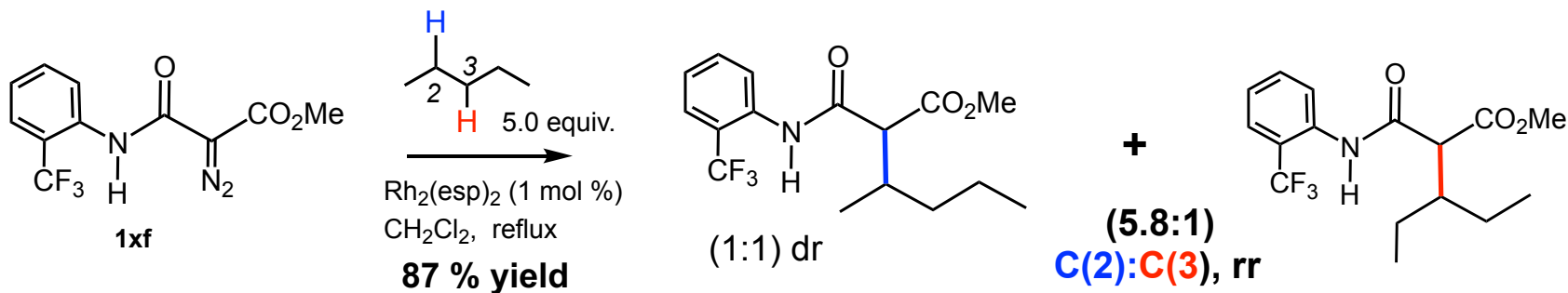
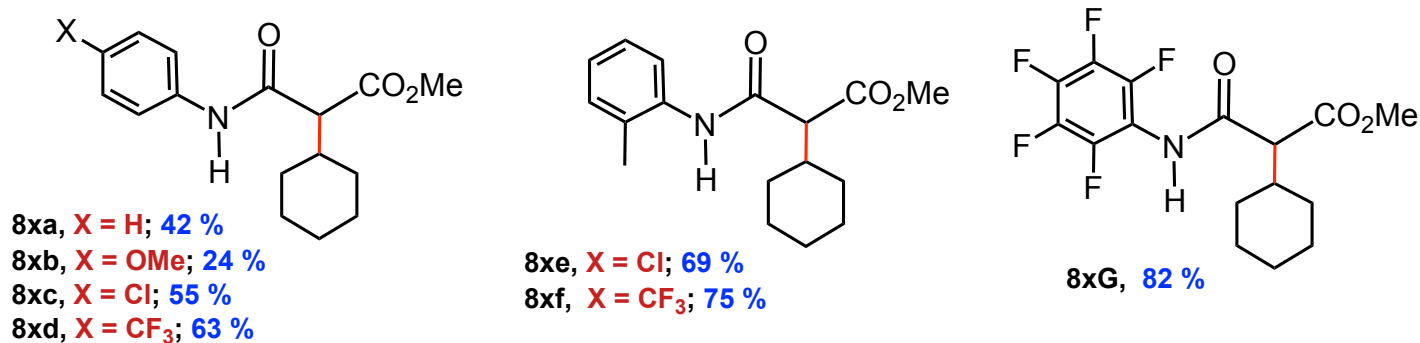
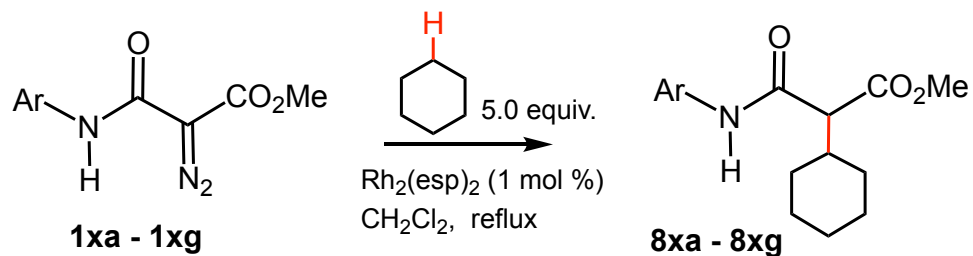


PA = 250.3 kcal/mol
 $\Delta H^\ddagger = -2.9$ kcal/mol



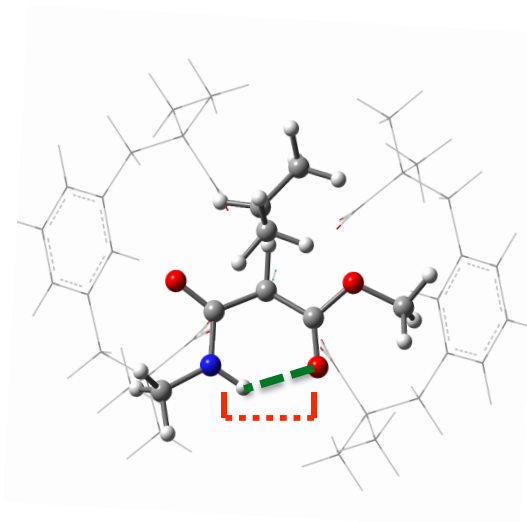
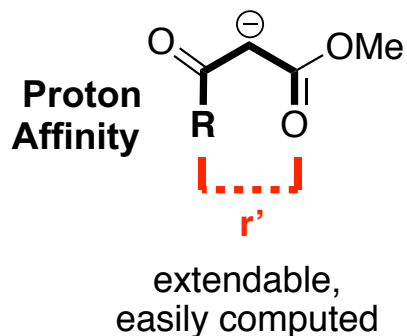
PA = 248.5 kcal/mol
 $\Delta H^\ddagger = 6.5$ kcal/mol

Generality of the Discovered C(sp³)-H Bond Alkylation rxn: Expanding it to other Secondary N-aryl α -diazo- β -amide esters, and Different Substrates



CONCLUSIONS:

Developed Predictive Model for $[\text{Rh}_2(\text{esp})_2]$ -catalyzed β -carbonyl ester carbene insertion into the $\text{C}(\text{sp}^3)\text{-H}$ bond



Demonstrated Simplest Path for Discovery of new and effective carbene transfer catalysis.