Exploring Quantum Tunneling In Organic Reactions

José P. L. Roque

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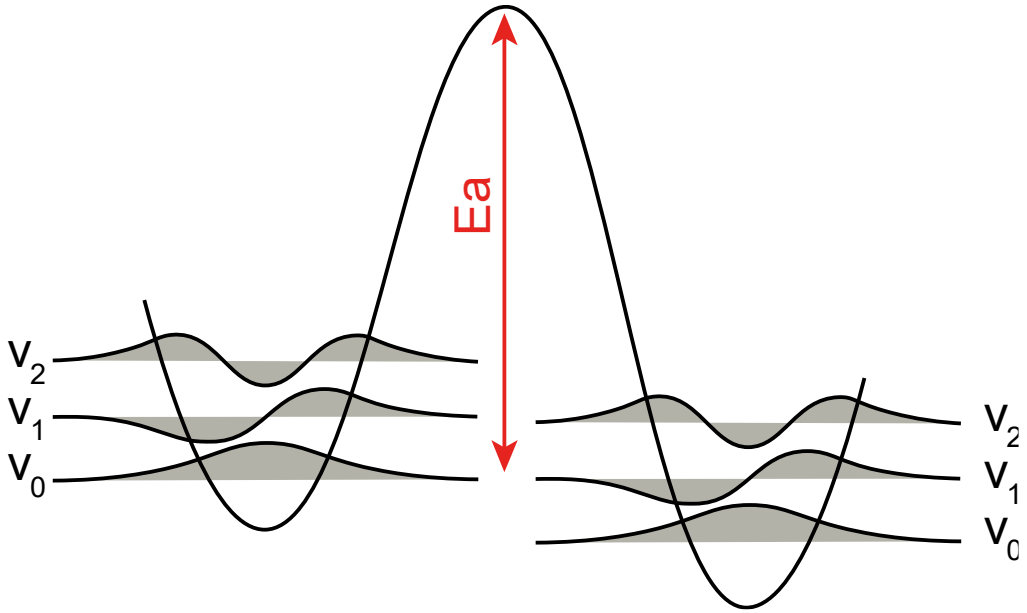
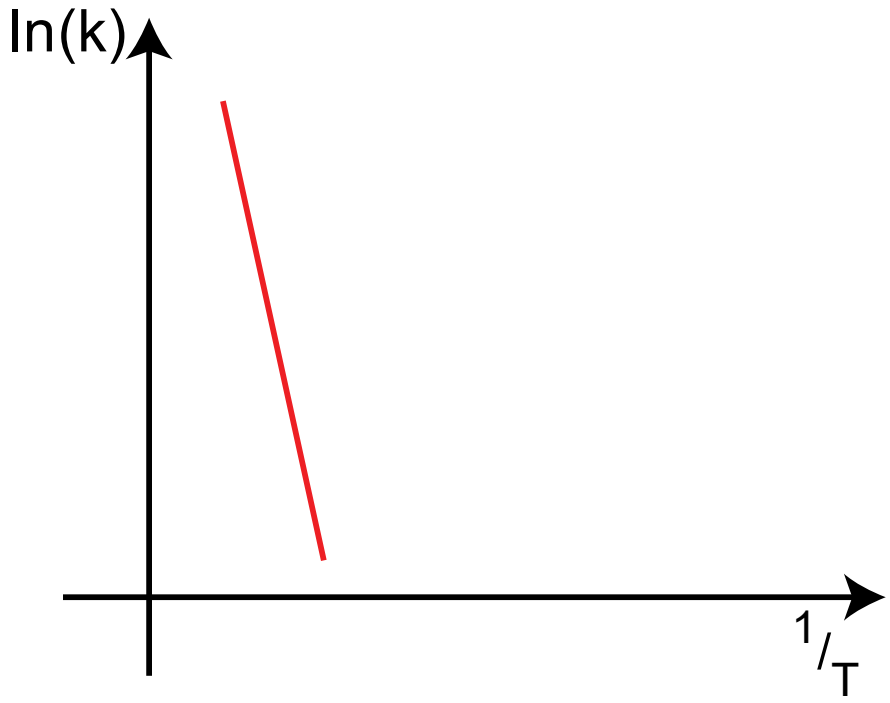
UNIVERSIDADE D COIMBRA

Over-the-barrier Reactivity

Double-well Potential



Arrhenius Plot



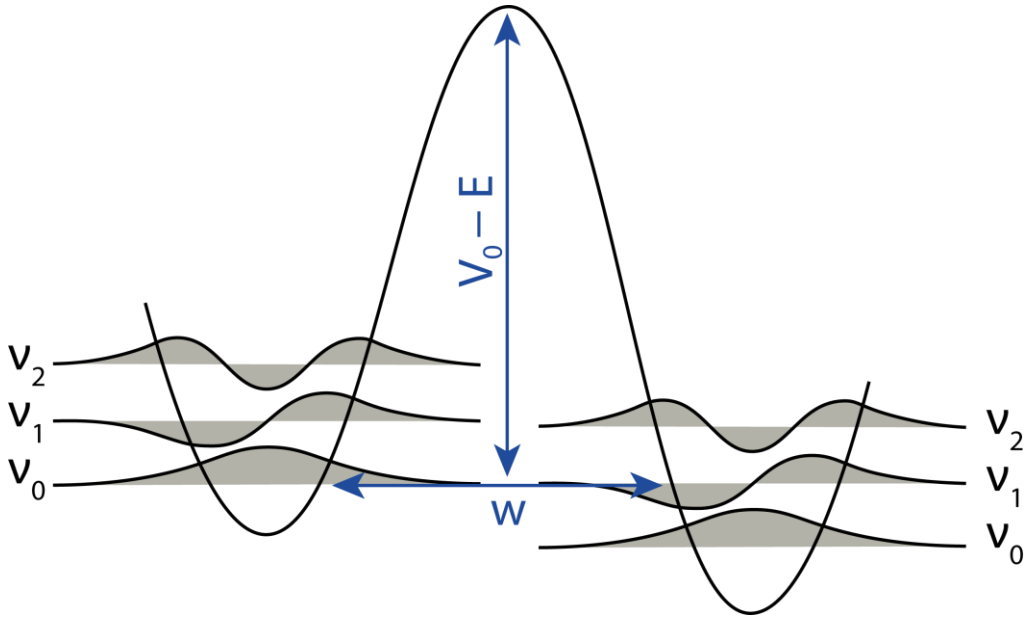
Arrhenius Equation

$$k = A \cdot e^{\frac{-Ea}{RT}}$$

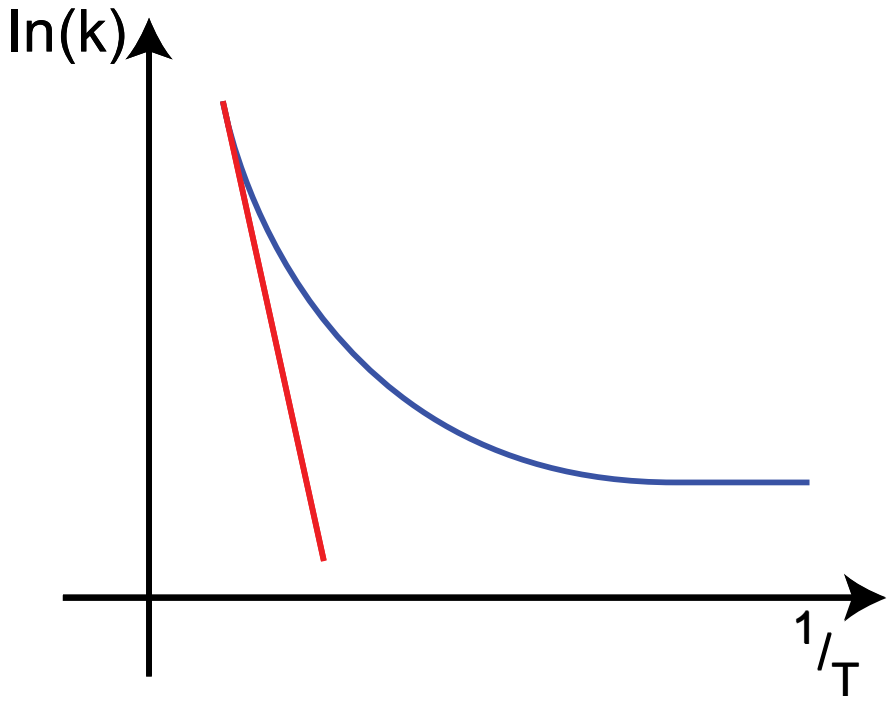
$$\ln(k) = \ln(A) - \frac{Ea}{R}\left(\frac{1}{T}\right)$$

Quantum Tunneling: The phenomena

Double-well Potential



Arrhenius Plot



Tunneling Contribution

$$K = \mathrm{e}\left(-\pi^2 w \sqrt{\frac{2m}{\mathrm{h}^2}(V_0 - E)}\right).v$$

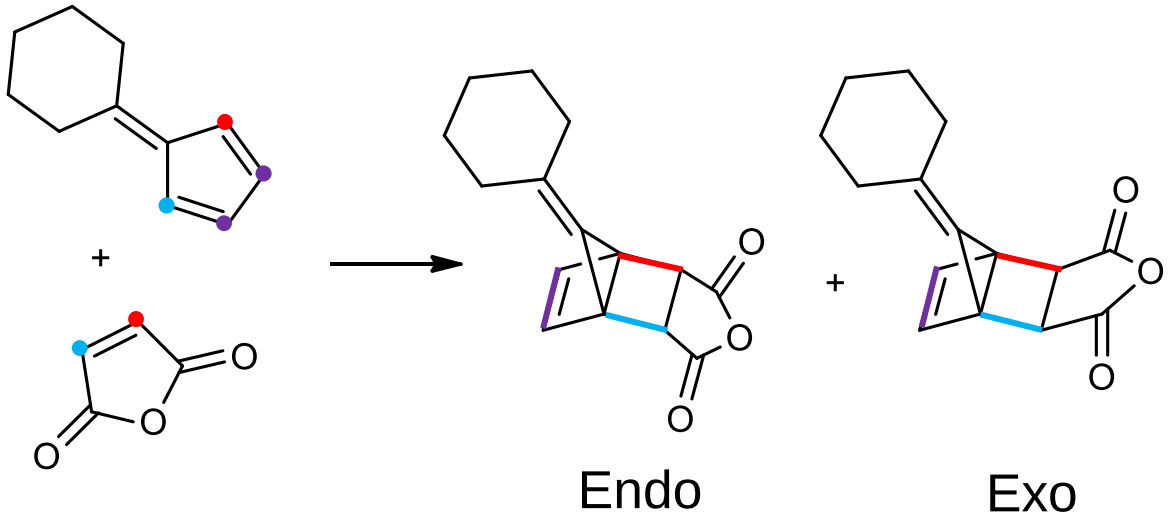
Arrhenius Equation

$$k = A\,.\,\mathrm{e}^{\frac{-Ea}{\mathrm{R}T}}$$

$$\ln(k) = \ln(A) - \frac{Ea}{R}\left(\frac{1}{T}\right)$$

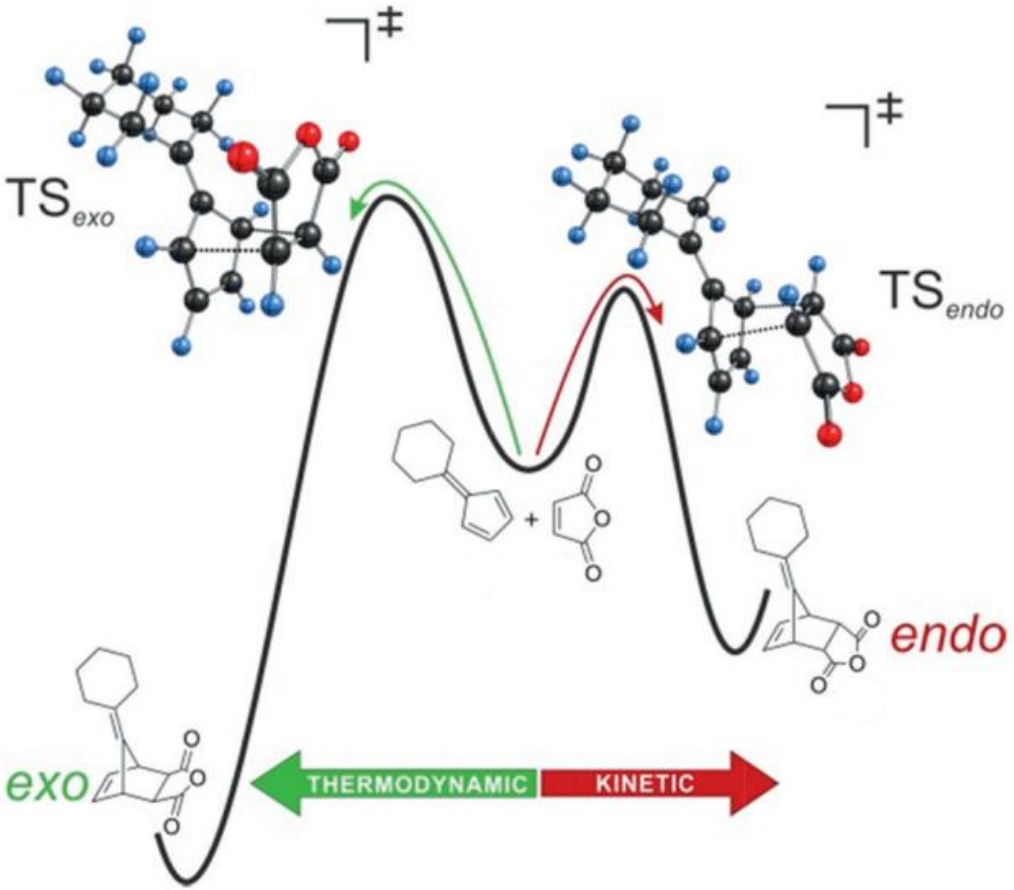
Selectivity in Chemistry: Classical Interpretation

Diels-Alder Reaction



Endo

Exo



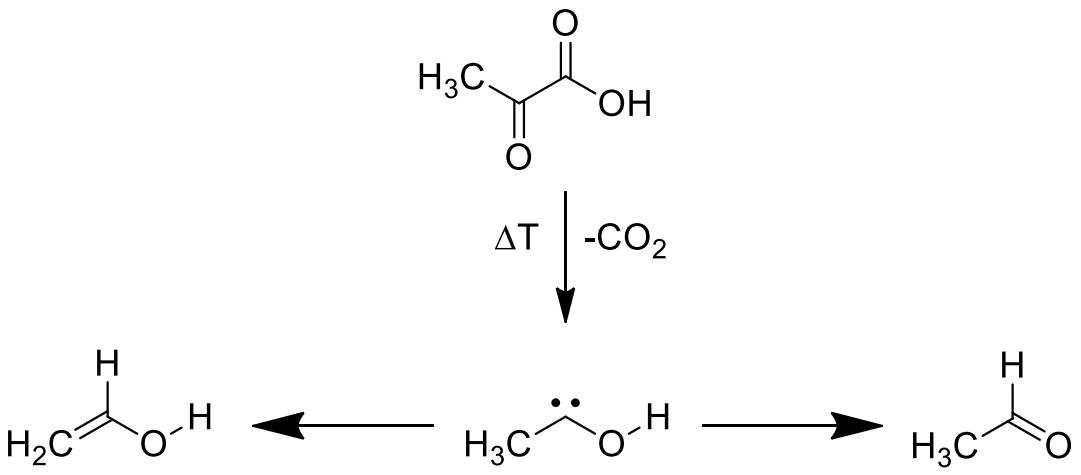
Endo Preference until T ~ 25º C

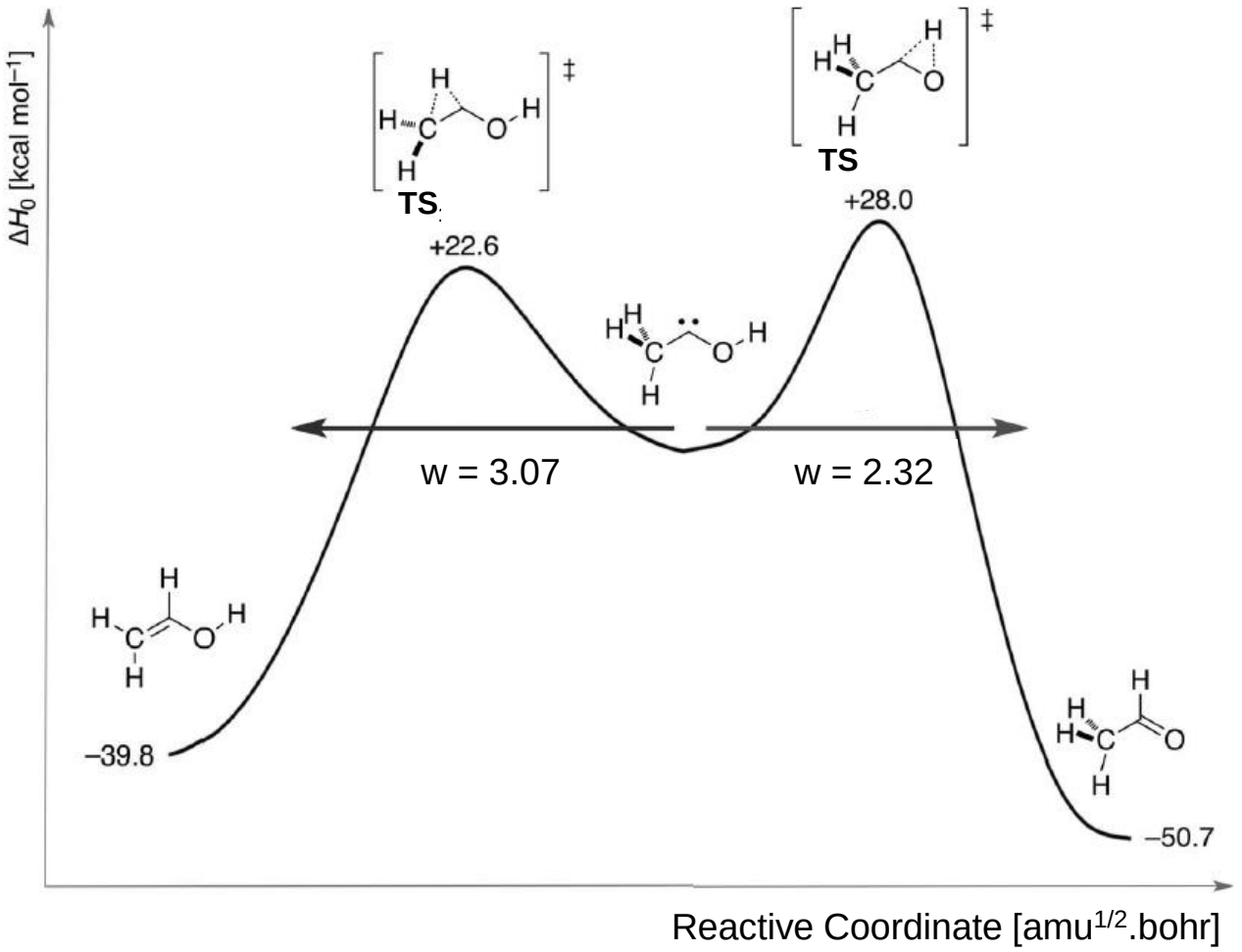
Exo Preference from T > 25º C

Ley, D.; Gerbig, D.; Schreiner, P. R.; *Org. Biomol. Chem.* **2012**, 10, 3781-3790.

Tunneling Control: The Game Changer

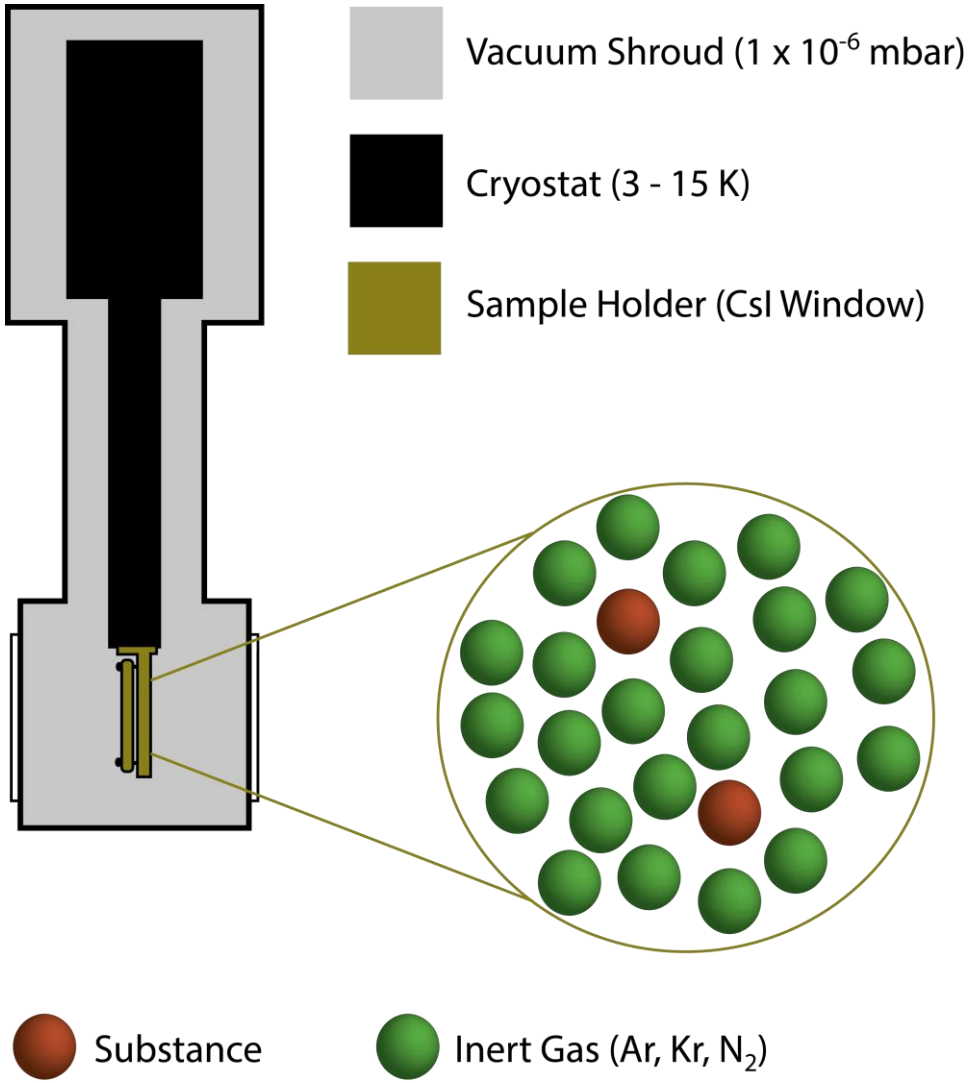
Decay of Methylhydroxycarbene in Cryogenic Matrix



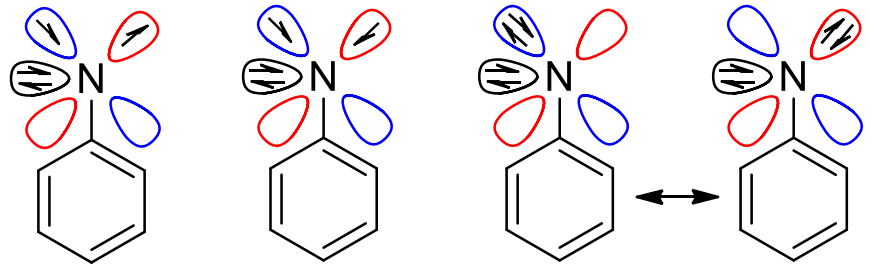


Schreiner, P. R.; Reisenauer, H. P.; Ley, D.; Gerbig, D.; Wu, C.; Allen, W. D.; *Science*, **2011**, 332, 1300-1303.

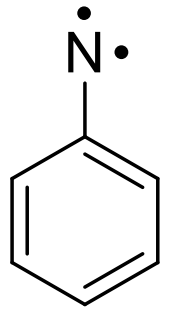
Matrix-Isolation and Phenylnitrenes



CASPT2N/6-311G(2d,p)
(kcal mol^{-1})



^{3}A" (0.0) ^{1}A" (18.5) ^{1}A' (36.9)

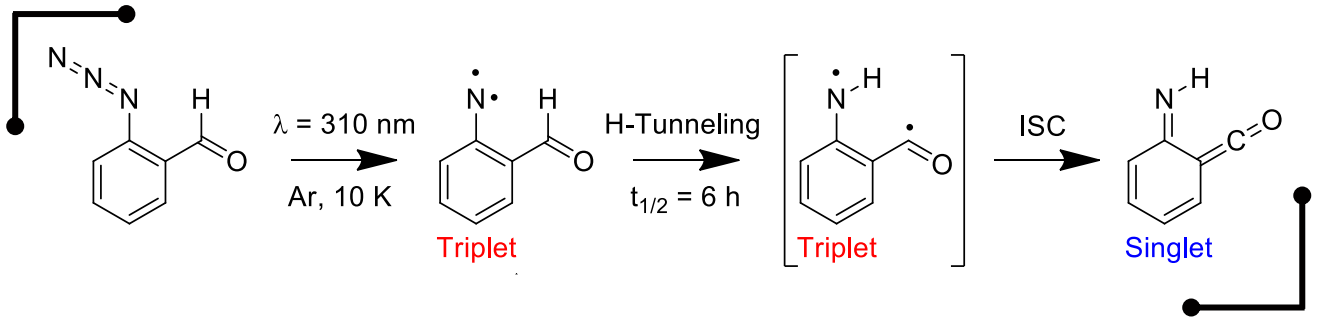


Tunneling in Nitrenes: The Proof of Concept

J|A|C|S
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Evidence of a Nitrene Tunneling Reaction: Spontaneous Rearrangement of 2-Formyl Phenylnitrene to an Imino Ketene in Low-Temperature Matrixes

Cláudio M. Nunes,[†] Stephanie N. Knezz,[‡] Igor Reva,*[,†] Rui Fausto,[†] and Robert J. McMahon*[,‡]



1 **Direct Observation**

Computed Barrier above 17 kcal mol^{-1}

2 **Temperature Independency**

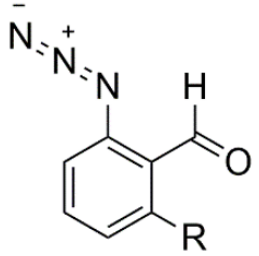
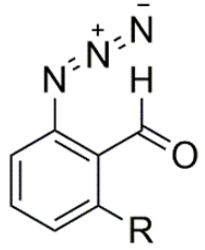
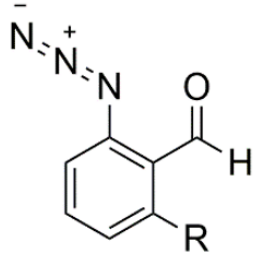
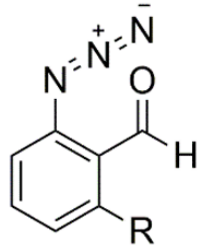
Similar Kinetic profiles at 10 and 20 K

3 **Large Kinetic Isotope Effect**

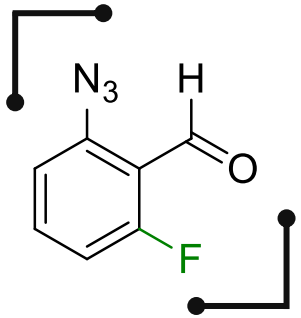
No reaction for Deuterated isotopologue

Nunes, C. M.; Knezz, S.; Reva, I.; Fausto, R.; McMahon, R. J. *J. Am. Chem. Soc.* **2016**, 138, 15287-15290.

Tunneling Control in Nitrenes: The Strategy

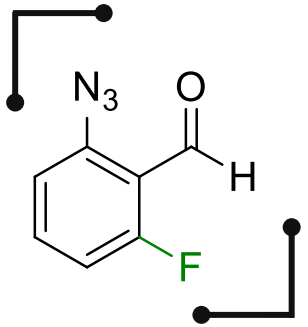
Structure R = H , F				
	H | F	H | F	H | F	H | F
ΔG_{298K} (B3LYP)	0.0 | 0.0	4.1 | 4.4	2.5 | 0.3	3.4 | 1.3
ΔG_{298K} (CBS-QB3)	0.0 | 0.0	3.6 | 3.5	2.7 | 0.4	2.9 | 0.6
Pop_{298K}	98 | 55	0 | 0	1 | 26	1 | 19

Energies are given in kcal mol^{-1} and Boltzmann populations in %.



anti-CHO

≈ 55%

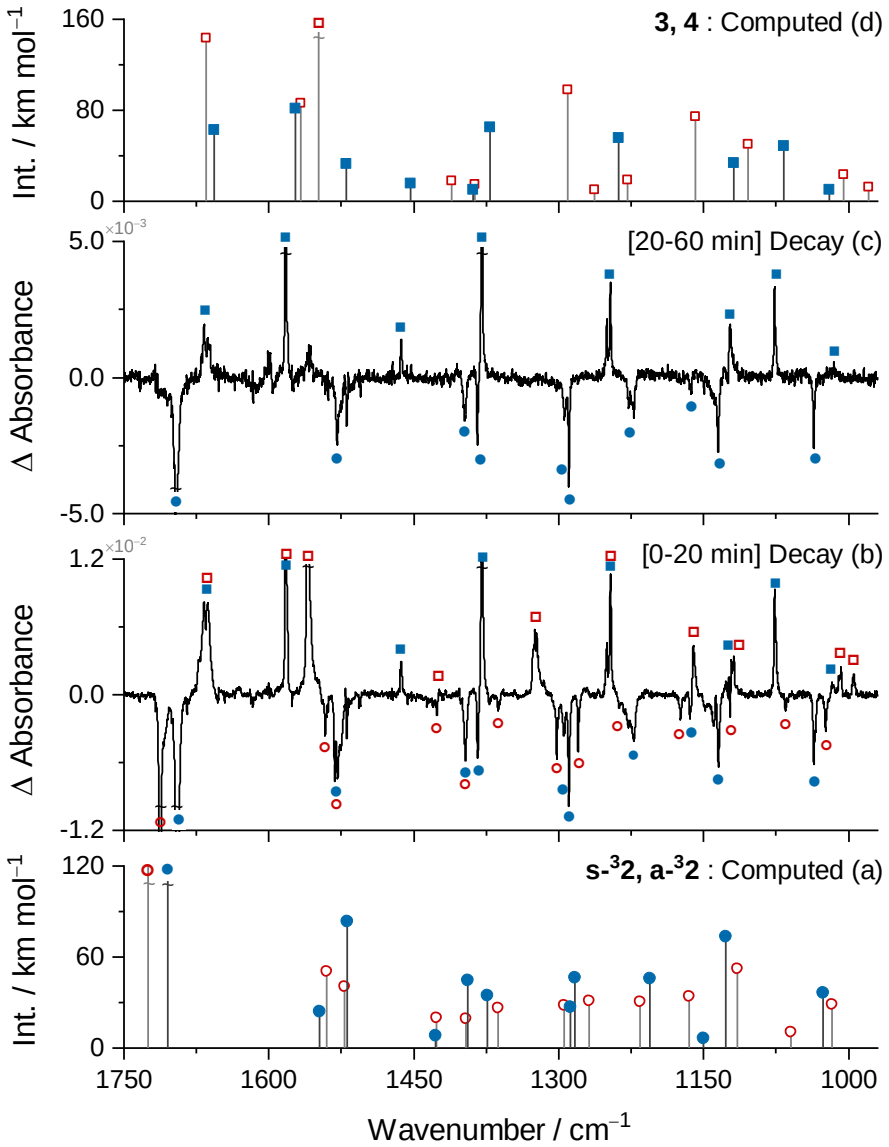


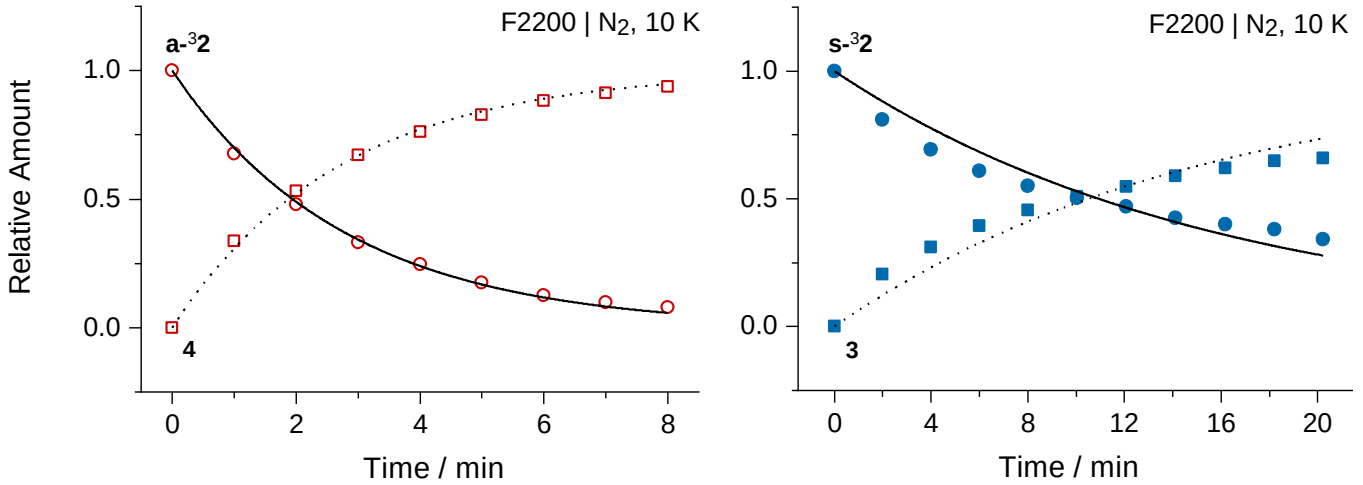
syn-CHO

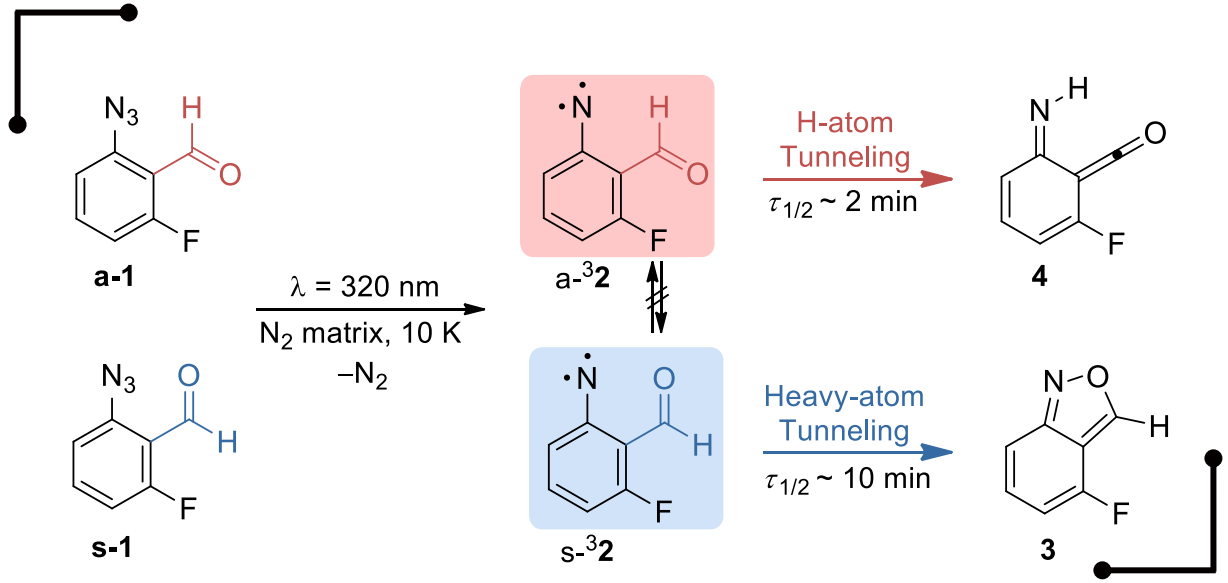
≈ 45%

Nunes, C. M.; Roque, J. P. L.; Doddipatla, S.; Wood, S. A.; McMahon, R. J.; Fausto, R. *J. Am. Chem. Soc.* **2022**, 144, 20866-20874.

Tunneling Control in Nitrenes







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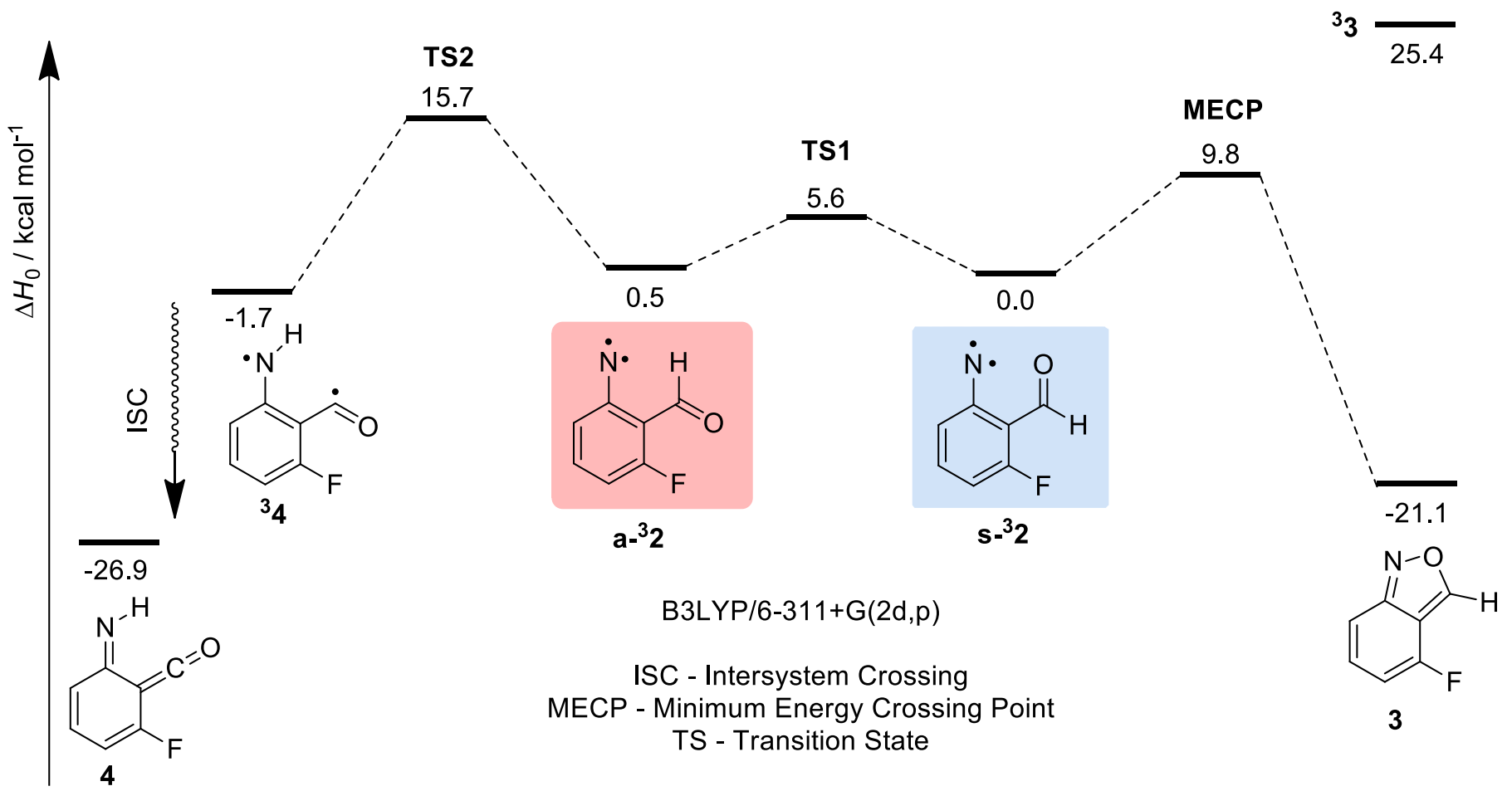
Tunneling Control in Nitrenes



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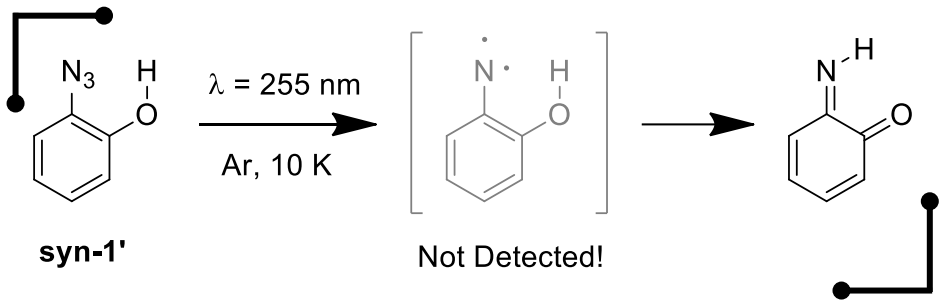
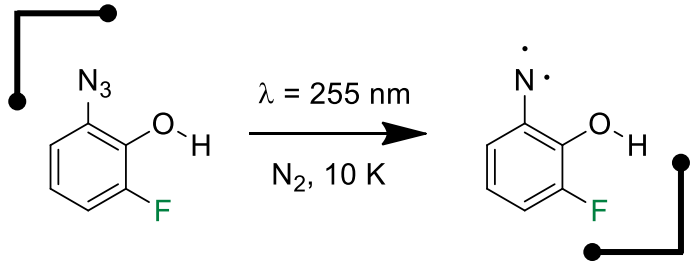
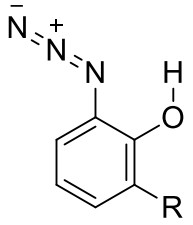
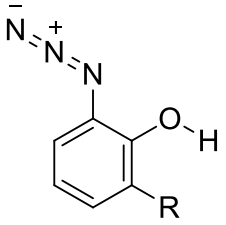
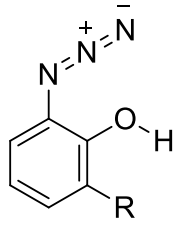
Switching on Tunneling Reactions: The Strategy



syn-1'

Liebigs Ann. **1996**, 2029–2037.
Liebigs Ann. **1996**, 1971–1980.

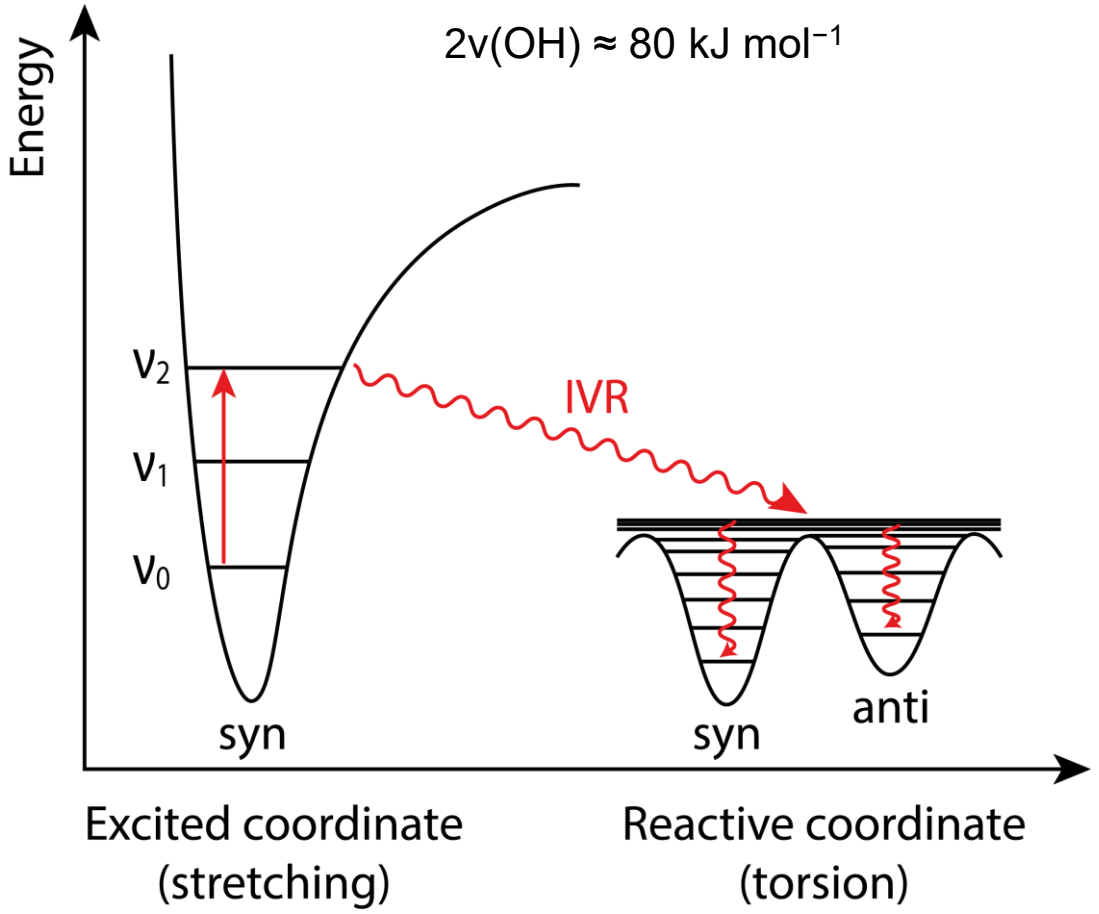


	syn-OH		*anti*-OH
Structures **1′**, **1** R = H, F			
Name	H | F	H | F	H | F
ΔG_{298K} (CBS-QB3)	0.0 | 0.0	15.5 | 4.5	12.8 | 2.6
Pop_{298K}	99.2 | 66.1	0.2 | 10.7	0.6 | 23.1

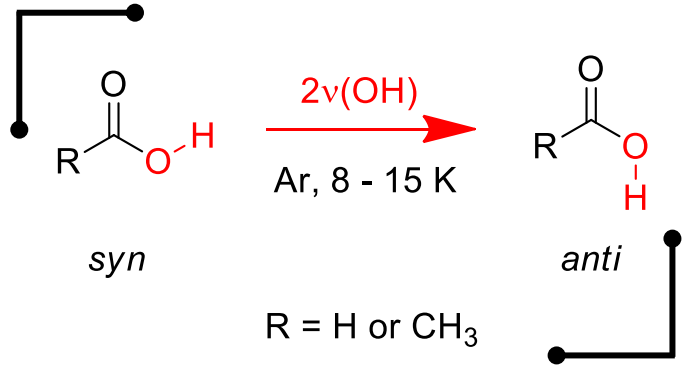
Energies are given in kcal mol^{-1} and Boltzmann populations in %.

Roque, J. P. L.; Nunes, C. M.; Viegas, L. P.; Pereira, N. A. M.; Pinho e Melo, T. M. V. D.; Schreiner, P. R.; Fausto, R. *J. Am. Chem. Soc.* **2021**, 143, 8266-8271.

Vibrational Excitation: Mastering Conformations

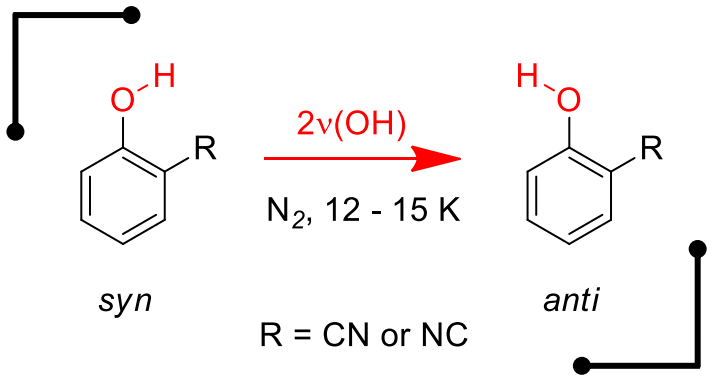


$\Delta G^{\ddagger} \approx 50$ kJ mol^{-1}



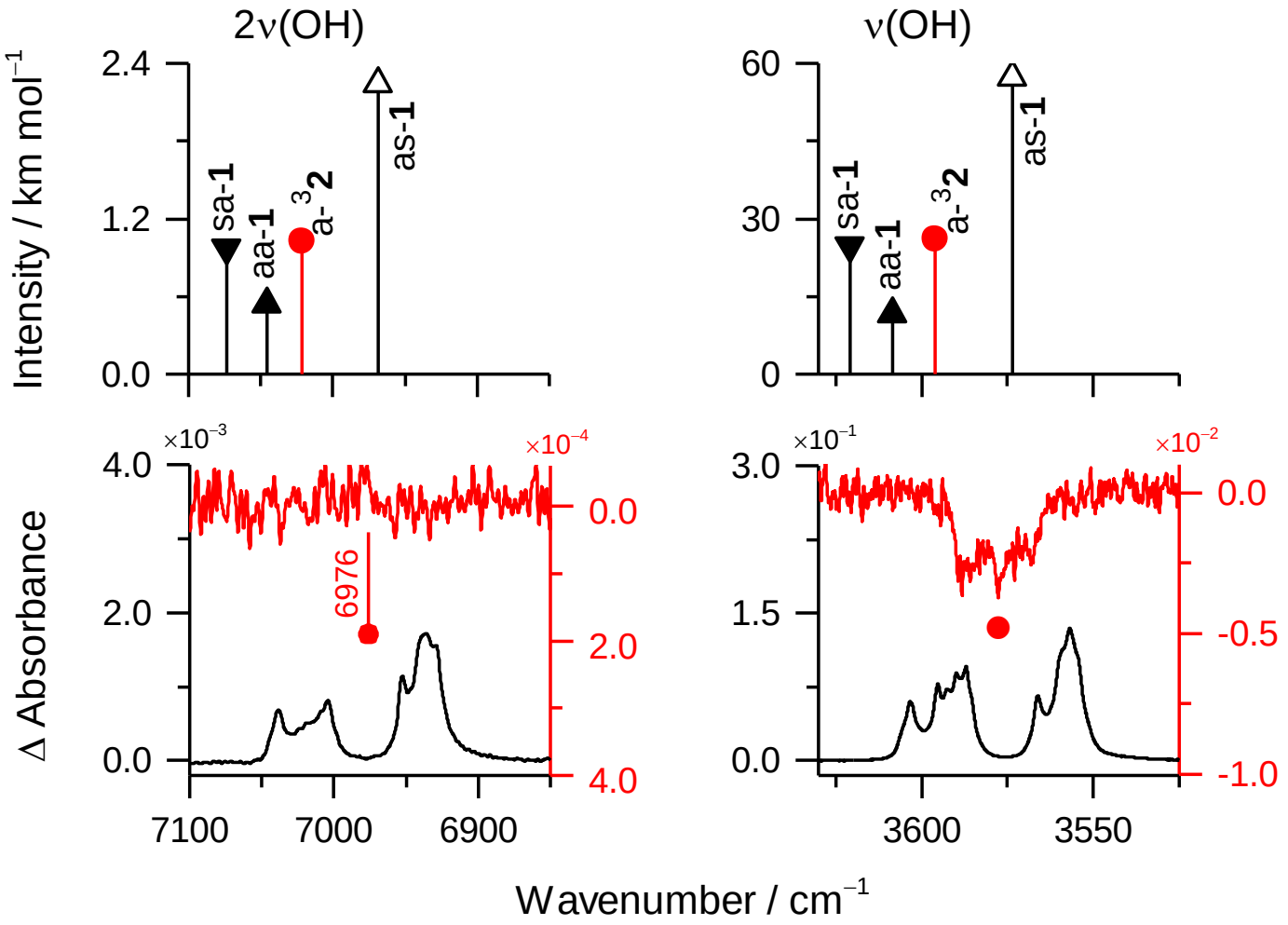
J. Am. Chem. Soc. **1997**, 119, 11715-11716.
J. Am. Chem. Soc. **2003**, 125, 16188-16189.

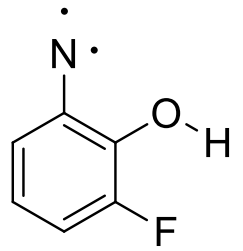
$\Delta G^{\ddagger} \approx 25$ kJ mol^{-1}



J. Phys. Chem. A. **2019**, 123, 4396−4405
Chem. Phys. Lett. **2020**, 747, 137069.

Switching on Tunneling Reactions



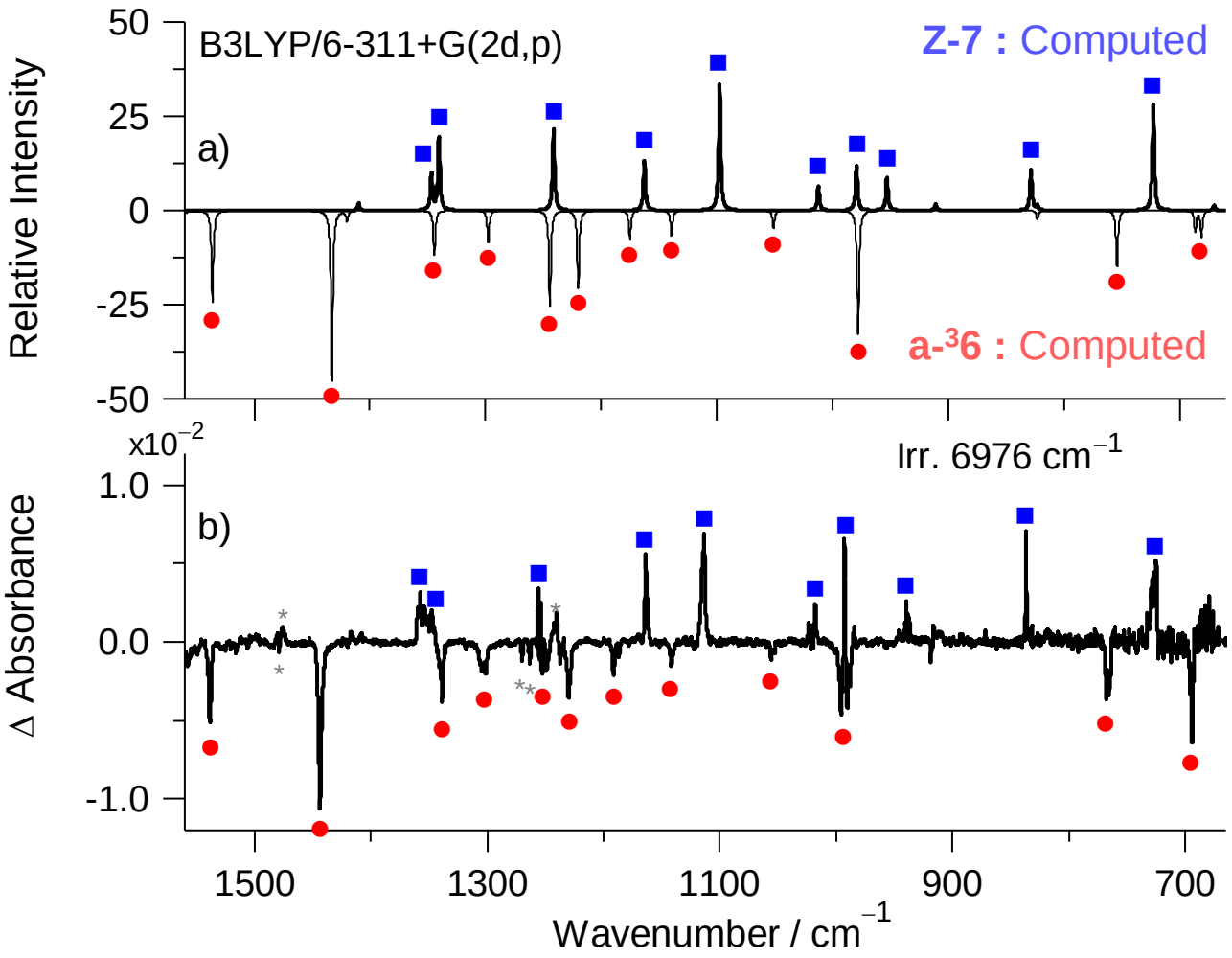


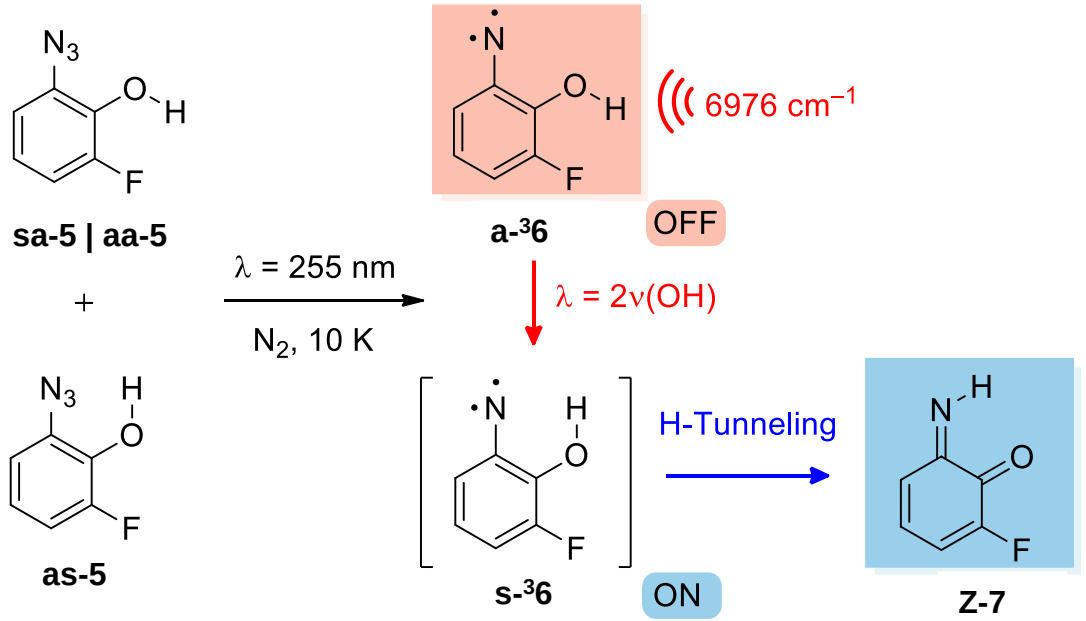
anti-³6

2ν(OH) = 6976 cm^{-1}

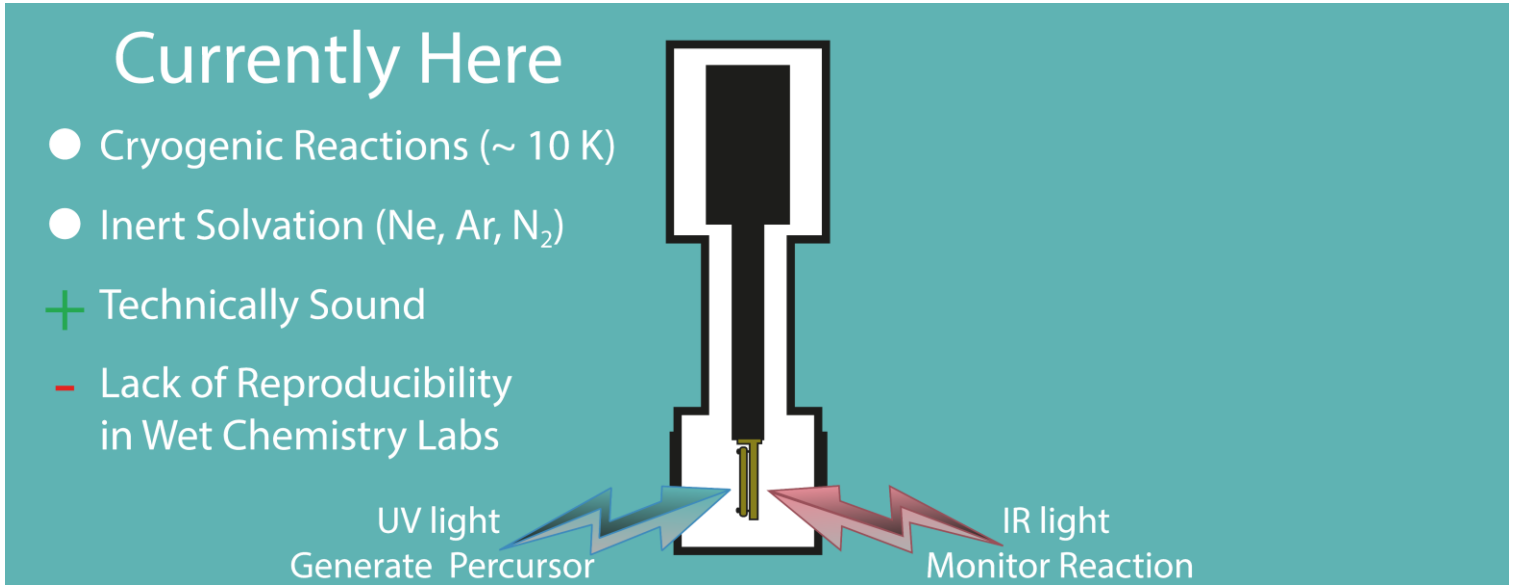
Roque, J. P. L.; Nunes, C. M.; Viegas, L. P.; Pereira, N. A. M.; Pinho e Melo, T. M. V. D.; Schreiner, P. R.; Fausto, R. *J. Am. Chem. Soc.* **2021**, 143, 8266-8271.

Switching on Tunneling Reactions





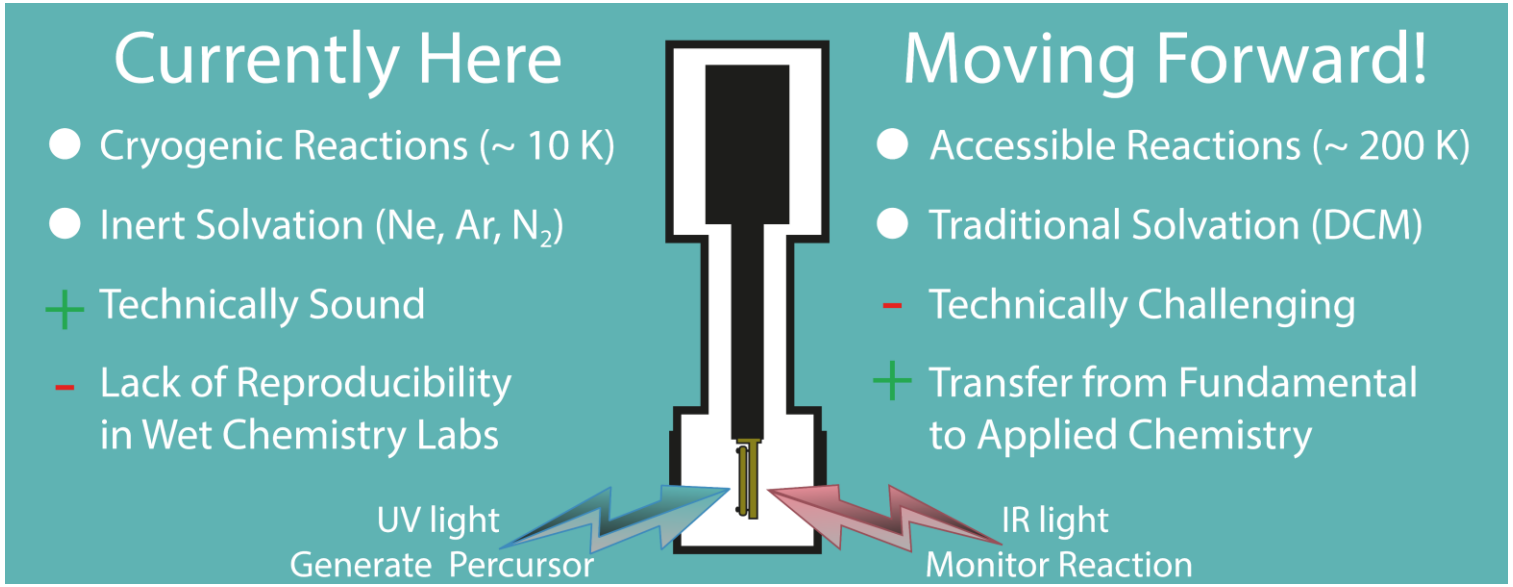
Conclusions and Outlook



Developments in Tunneling Reactivity

- Limitations of TST
- Role of Conformations

Conclusions and Outlook



Developments in Tunneling Reactivity

- Limitations of TST
- Role of Conformations

Design of Molecules and Synthesis Planning

- Unleash Tunneling Control

Acknowledgments

Supervisors and Colleagues

Rui Fausto
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Nelson Pereira
Luís Viegas
Stephanie Knezz
Samuel Wood

UNIVERSIDADE D
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Fundação
para a Ciência
e a Tecnologia

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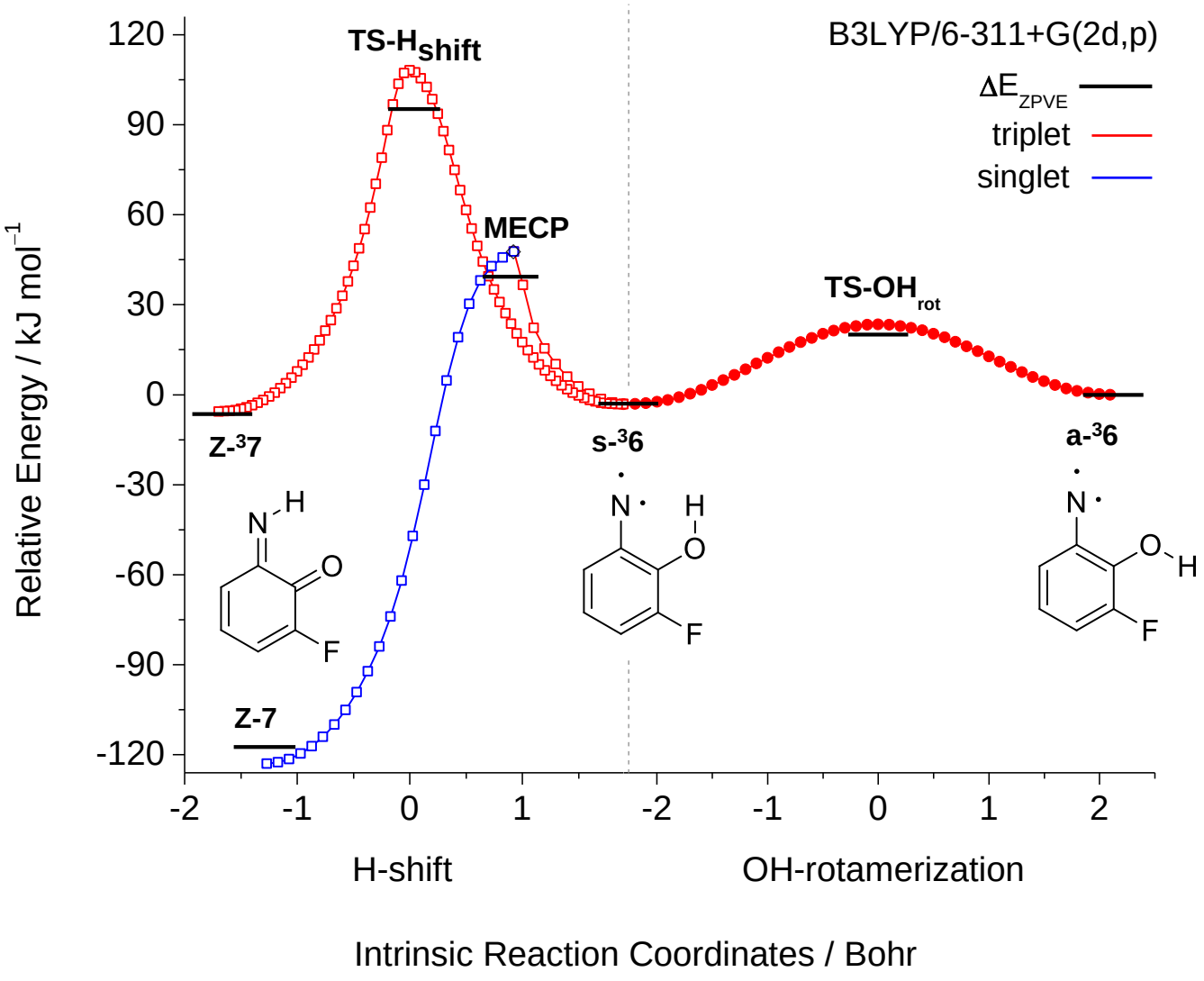
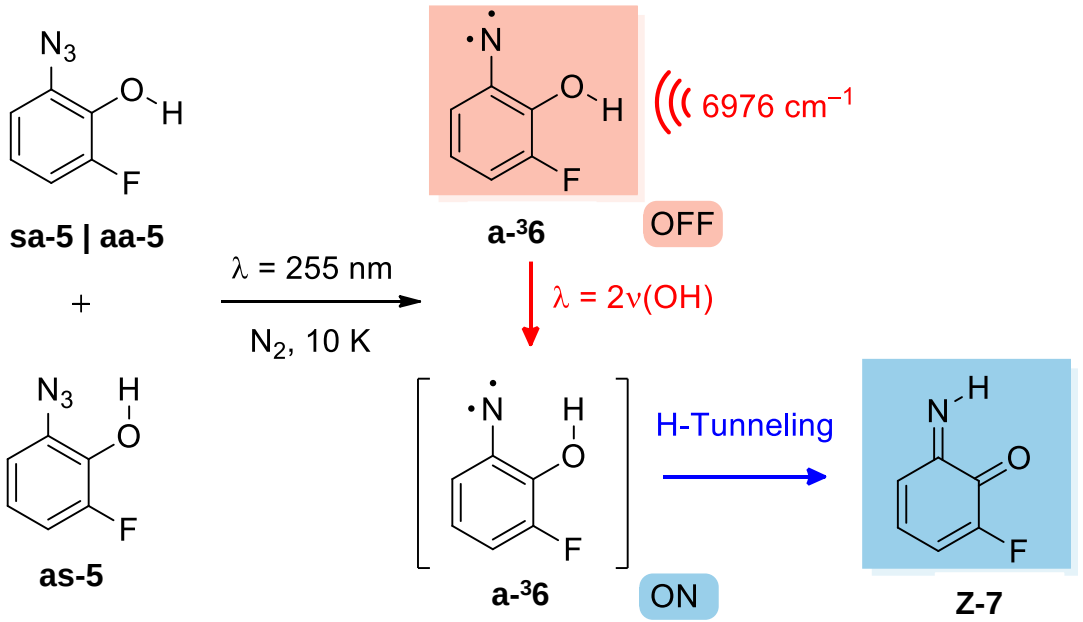
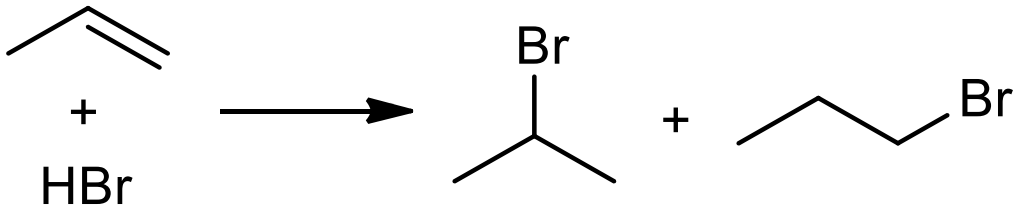
Switching on Tunneling Reactions

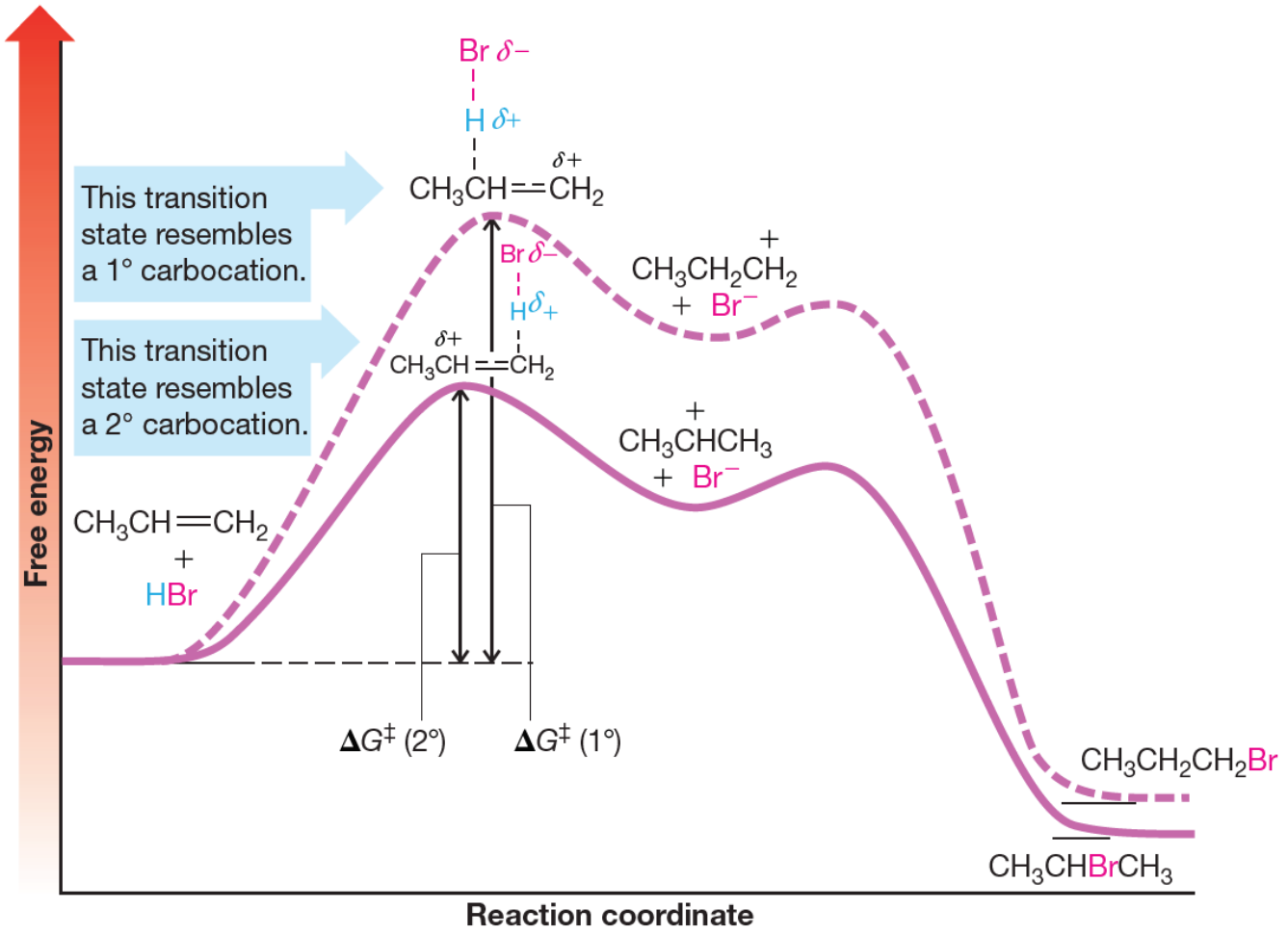




Selectivity in Chemistry: Classical Interpretation

Addition of Alkyl Halides to Asymmetric Alkenes





T. W. G. Solomons, C. B. Fryhle, S. A. Snyder, *Organic Chemistry*, 12th Edn, John Wiley & Sons, **2016**.