

Reactions of hydroxycarbenes with simple aldehydes and ketones

group seminar talk

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AG Schreiner

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Outline

① Introduction

② Reaction studies

Precursor

MeCOH and aldehydes

MeCOH and acetone

A new carbene

③ Closure

Difficulties

Outlook

Summary

literature

A long story^[1]



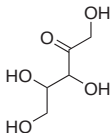
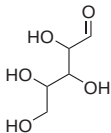
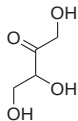
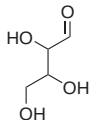
Aleksandr Mikhailovich Butlerov (1828 – 1886)

- Discoverer of formaldehyde
- Condensation of formaldehyde
- Butlerov reaction
- Formose reaction

products of the butlerov reaction^[2]



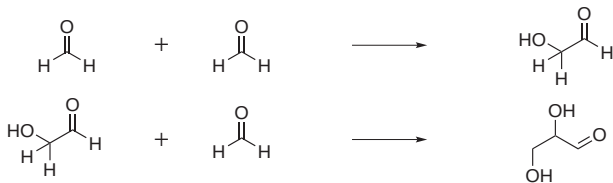
- Glycolaldehyde (up to 50% yield)
- Glycerinaldehyde
- Dihydroxyacetone
- Tetrulose
- Aldotetrose
- Ribulose
- Ribose



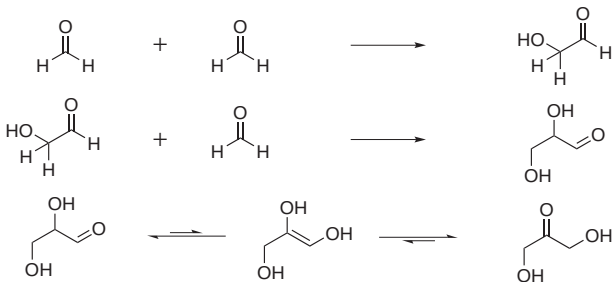
reaction steps



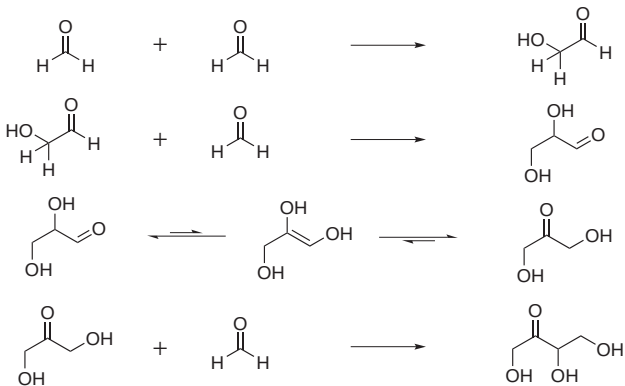
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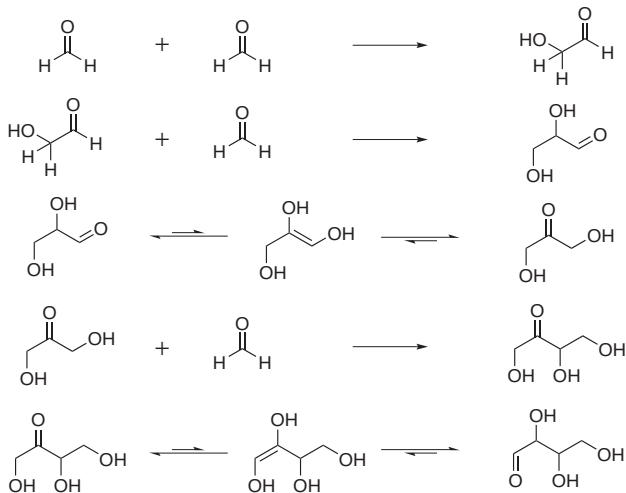
reaction steps



reaction steps



reaction steps



sugar in space

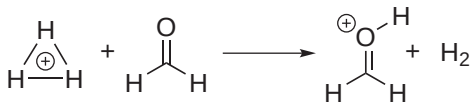
Conditions

- Formaldehyde and glycolaldehyde were found in interstellar medium^[3]
- High-energy radiation
- Cyclic H_3^+ ion suspected to act as proton donor^[4]

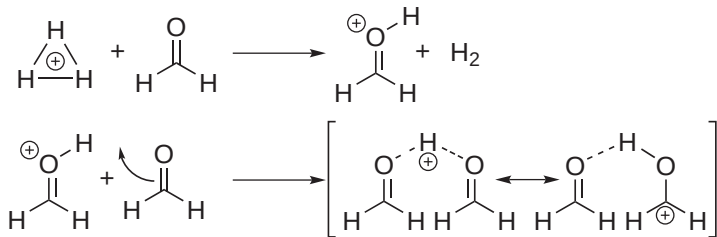
Restrictions

- Few intermolecular collisions due to low particle densities in interstellar medium^[5]
- Several decades, up to a few hours between two intermolecular collisions
- Hydroxycarbene half life time: ≈ 2 h (vanishes through tunneling)^[6]

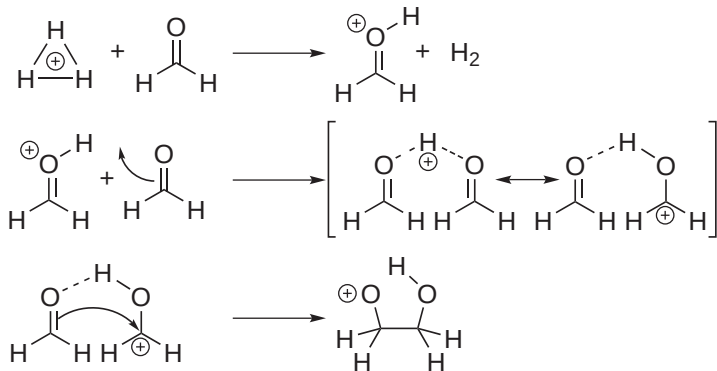
Acetaldehyde condensation in ISM^[7]



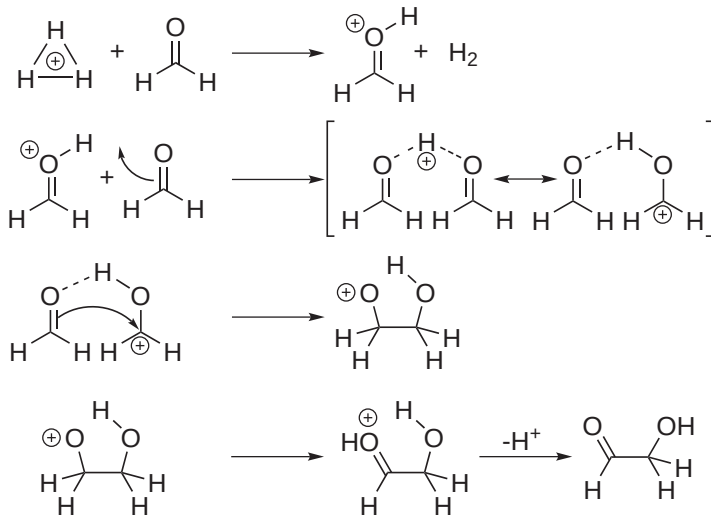
Acetaldehyde condensation in ISM^[7]



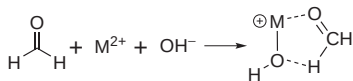
Acetaldehyde condensation in ISM^[7]



Acetaldehyde condensation in ISM^[7]



In solution: Unknown catalyst



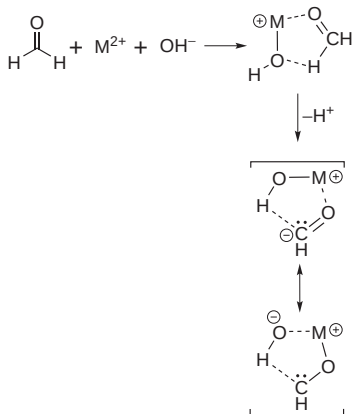
Lack of knowledge

- Reaction starts very slowly
- Final phase of the reaction is well known
- Reaction products much are more reactive towards formaldehyde, than itself is
- First step still unclear

Wanzlick's suggestion

Reaktion through a metal-stabilized carben-anion!^[8]

In solution: Unknown catalyst



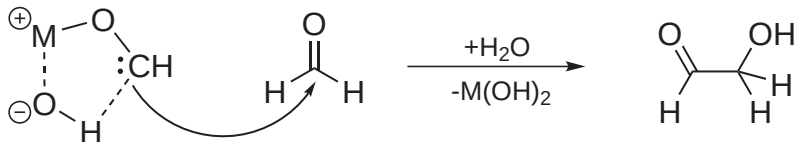
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Base-mediated Umpolung?



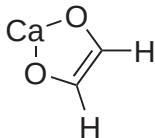
Poor description

- Deprotonation of formaldehyde in aqueous medium
- Umpolung through a base

Already proven

- Higher sugars form catalytically active complexes with metal-ions ^[9]

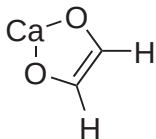
Autocatalysis?



The role of Ca-Compounds

- Ca^{2+} stabilized Enol form acts as catalyst
- Ca-Compounds of several C_6 -sugars could be isolated^[9]

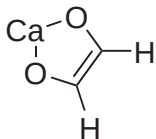
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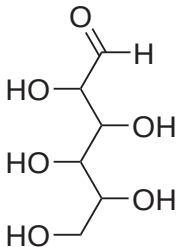
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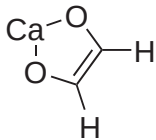


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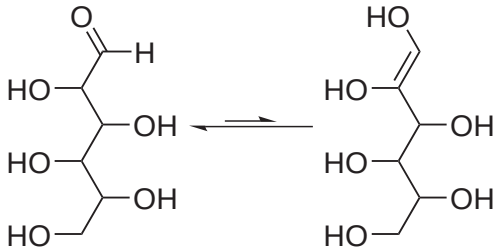


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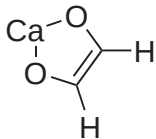


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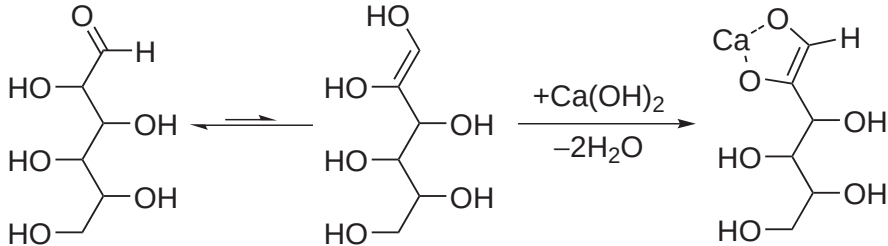


Autocatalysis?

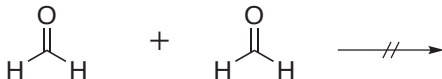


The role of Ca-Compounds

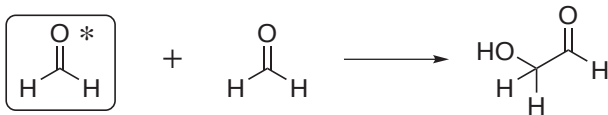
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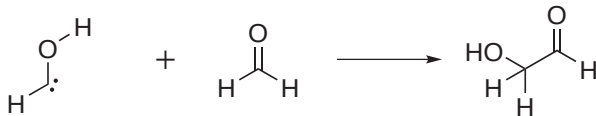
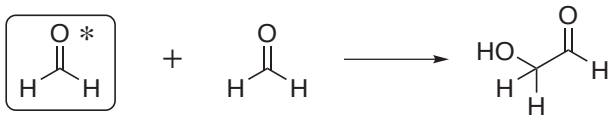
Activated aldehyde



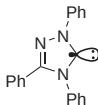
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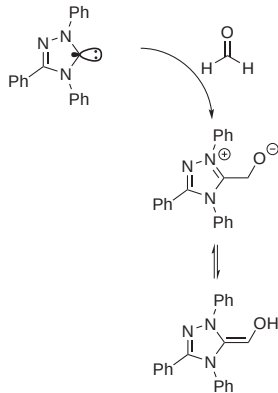


Activated aldehyde



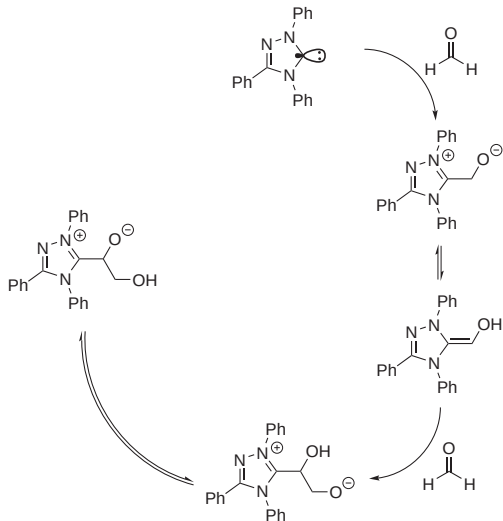
Carbene as organocatalyst^[10]



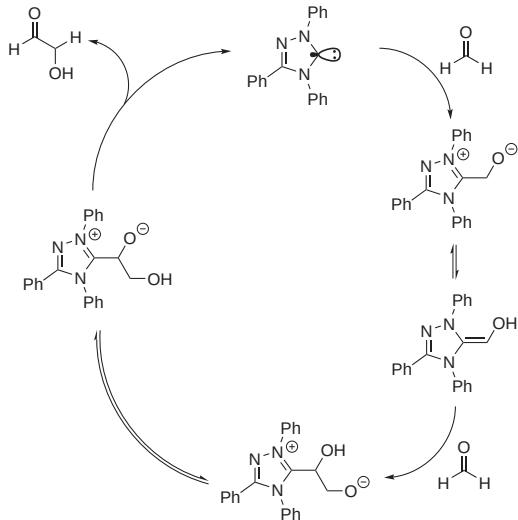




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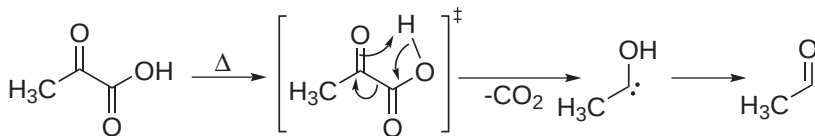
Carbene as organocatalyst^[10]



Question

- Could Hydroxycarbenes act as activated aldehyde?
- Reaction of hydroxycarbenes with aldehydes/ketones possible?
- Mechanism?

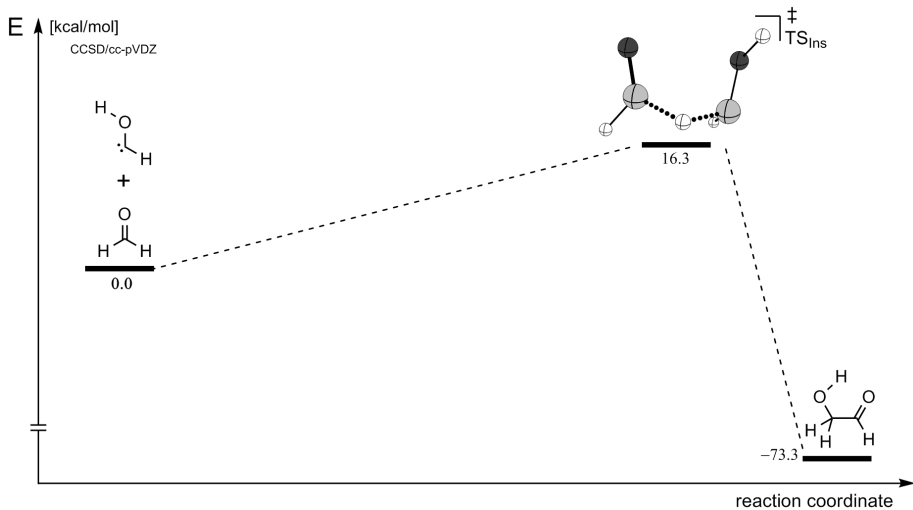
preparation of the hydroxycarbene



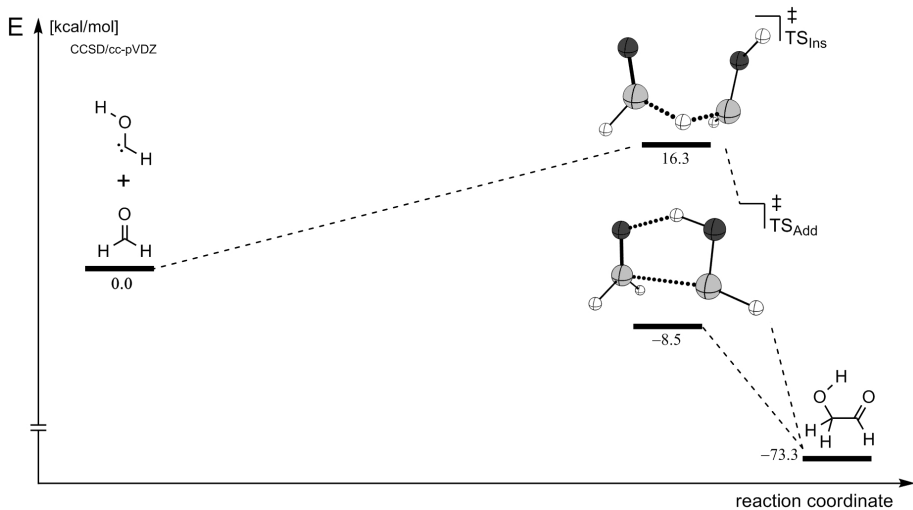
Decomposition of pyruvic acid

- Distillable without decomposition ($\theta_{\text{vap}} \approx 165^\circ\text{C}$)
- High vacuum flash pyrolysis: $\theta_{\text{dec}} \approx 700^\circ\text{C}$
- Barrier for decomposition: ca. 40 kcal/mol
- Methylhydroxycarbene could already be isolated in Ar Matrix

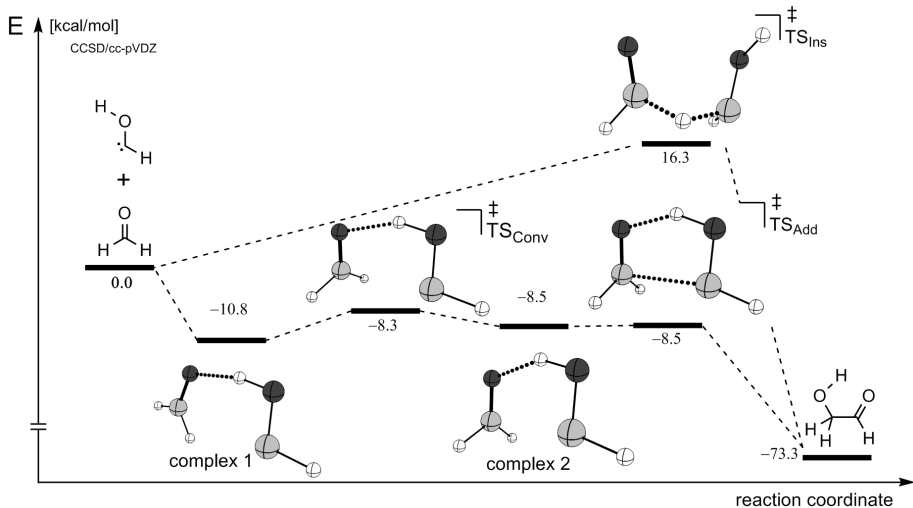
Glycolaldehyd PES



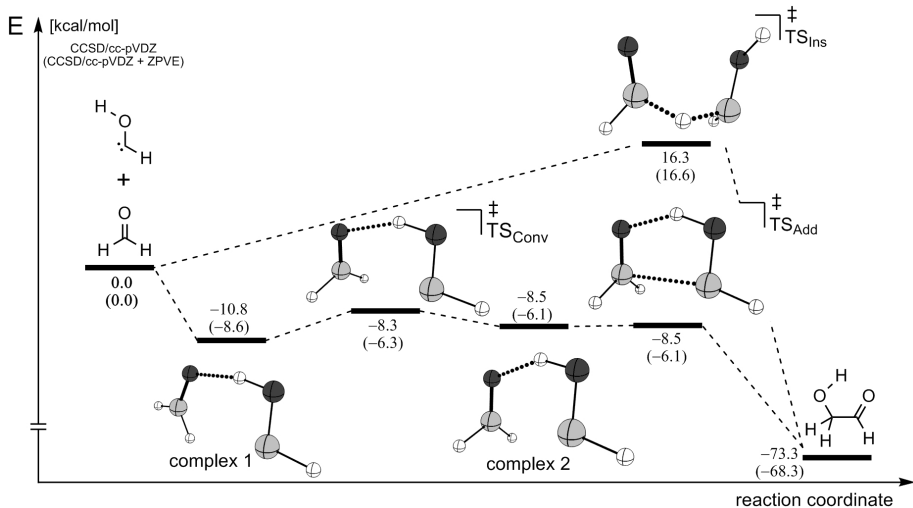
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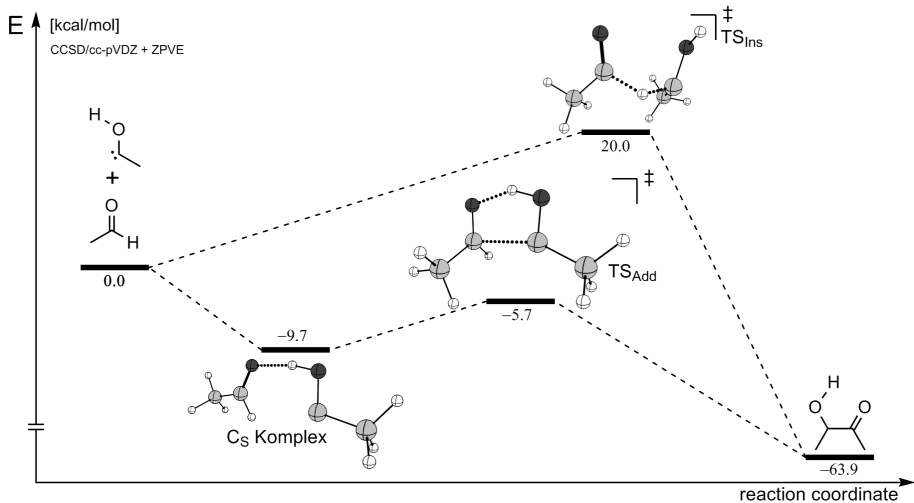
Glycolaldehyd PES



Glycolaldehyd PES



Acetoin PES



Static systems

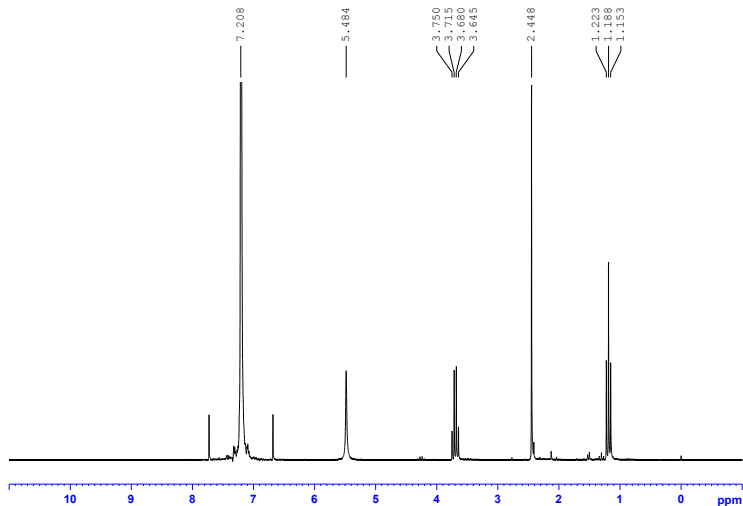
Experimental setup

- Evacuated 250 mL round bottom flask
- 60 μL (9.0 mmol) pyruvic acid
- (150 mbar (1.5 mmol) acetaldehyde)
- $p \leq 500$ mbar (estimated pressure at 200°C)

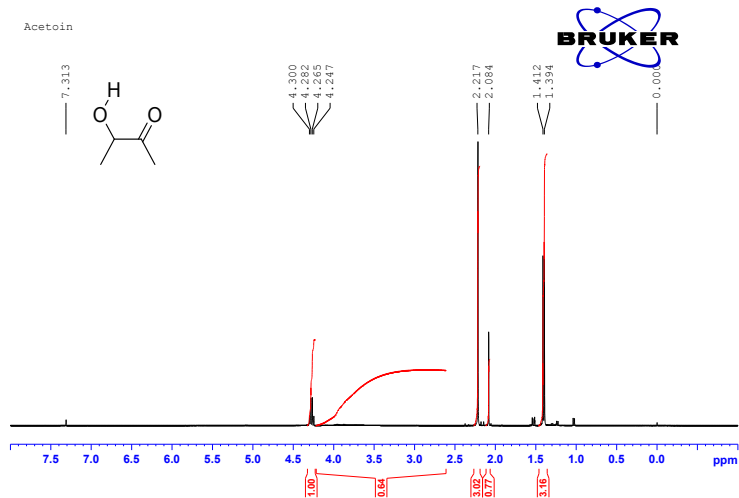
No results

- Brown substance on the glass surface
- Poor solubility in CDCl_3
- NMR indicates no success
- Probably another decomposition in the condensed phase occurred

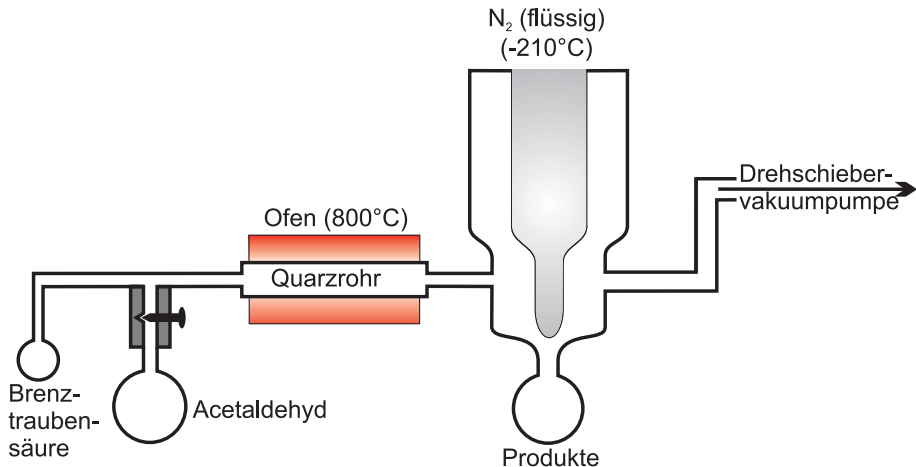
NMR spectrum: products of static pyrolysis



NMR spectrum: pure acetoin



Pyrolysis in flow systems



Typical experiment

Setup

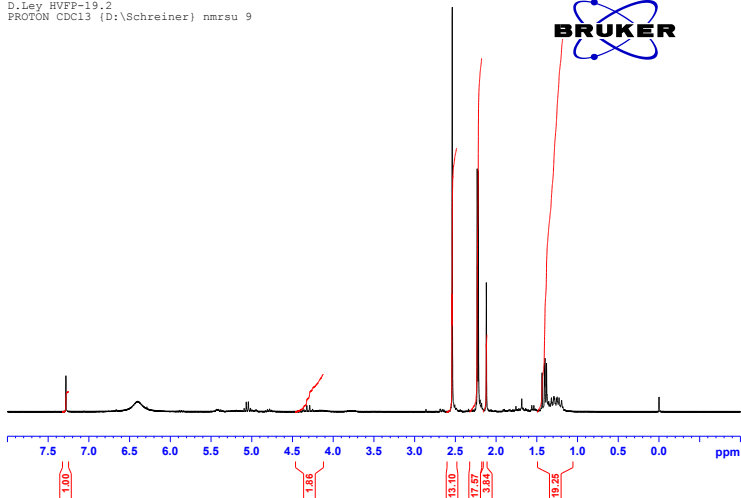
- 1.18 g (13.2 mmol) pyruvic acid
- 9.7 g (220 mmol) acetaldehyde
- $t = 6.5$ h
- $\theta \approx 800^\circ\text{C}$

Successful

- NMR: (10.2 ± 2.9) mg (≈ 0.1 mmol) Acetoin
- Yield: 0.8% with respect to pyruvic acid

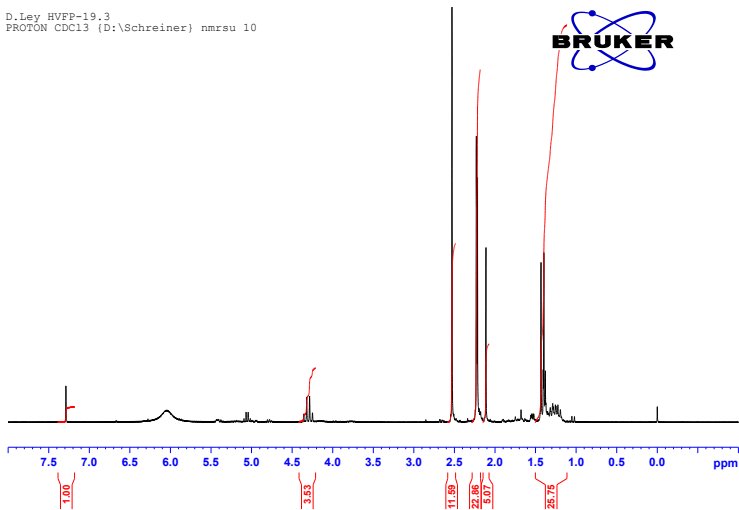
Quantitation via NMR

D.Ley HVFP-19.2
PROTON CDC13 {D:\Schreiner} nmrsu 9



Quantitation via NMR

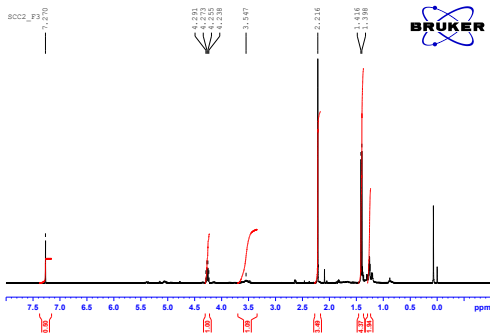
D.Ley HVFP-19.3
PROTON CDC13 {D:\Schreiner} nmrsu 10



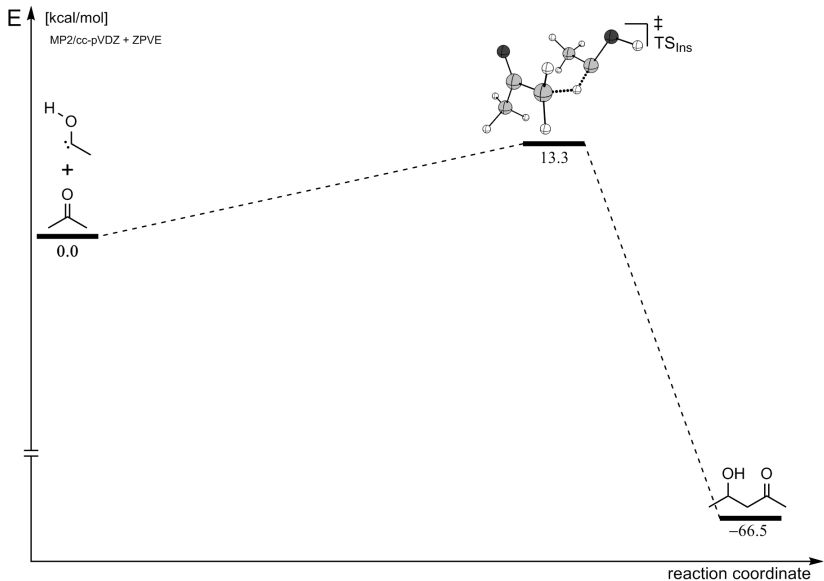
Another experiment

Same reaction conditions

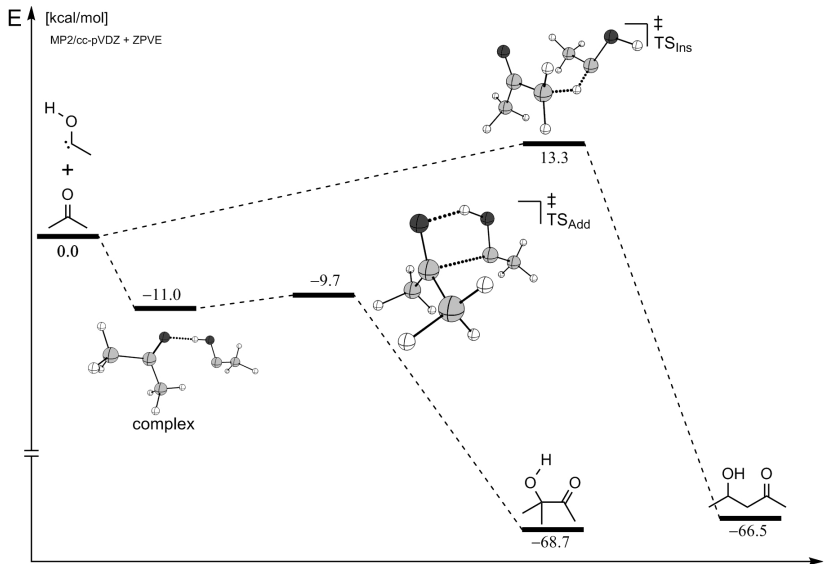
- 1.84 g (20.9 mmol) pyruvic acid
- 9.8 g (154 mmol) acetaldehyde
- Purification by column chromatography



Methylhydroxycarben and acetone



Methylhydroxycarben and acetone



Experiment

Setup

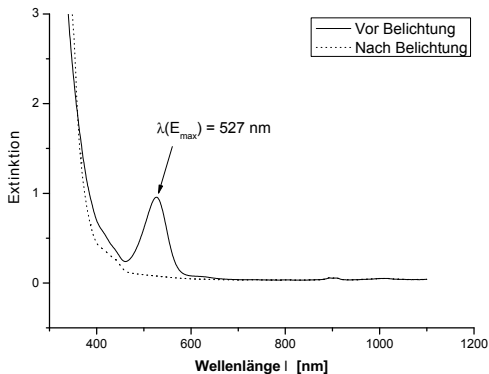
- 2.29 g (26.0 mmol) pyruvic acid
- 8.36 g (144.1 mmol) acetone

Successful

- (0.66 ± 0.18) mg product
- yield: ca. 1/4 %

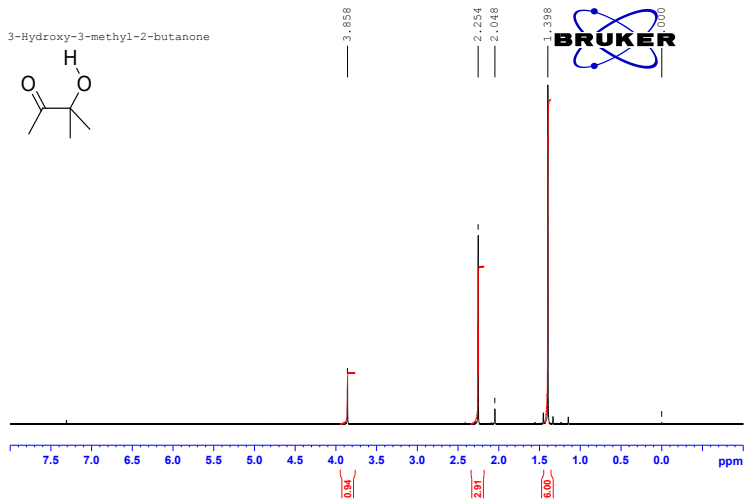
Surprise

Colorless reaction product turned red afert 10 h in the dark!



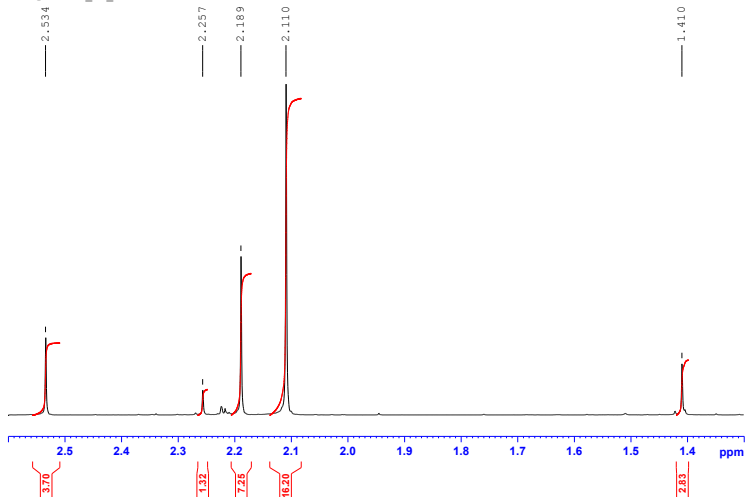
3-hydroxy-3-methyl-2-butanone

3-Hydroxy-3-methyl-2-butanone



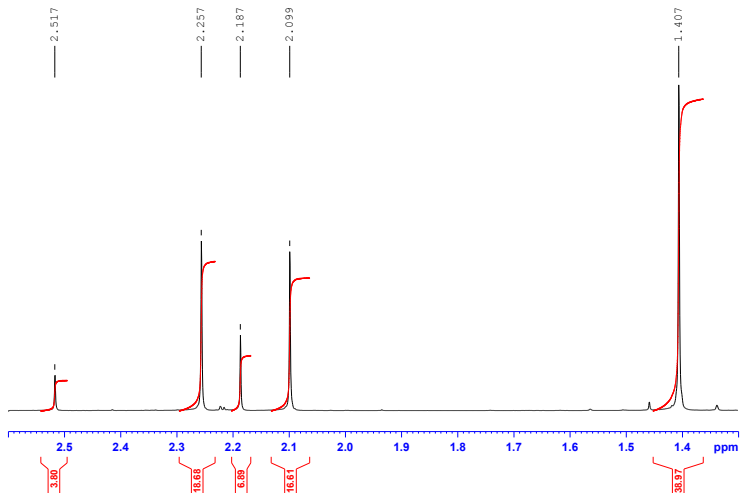
3-hydroxy-3-methyl-2-butanone

D.Ley, HVFP_22_1

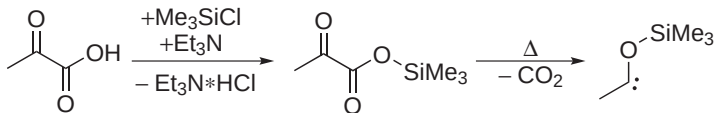


3-hydroxy-3-methyl-2-butanone

D.Ley, HVFP_22_2

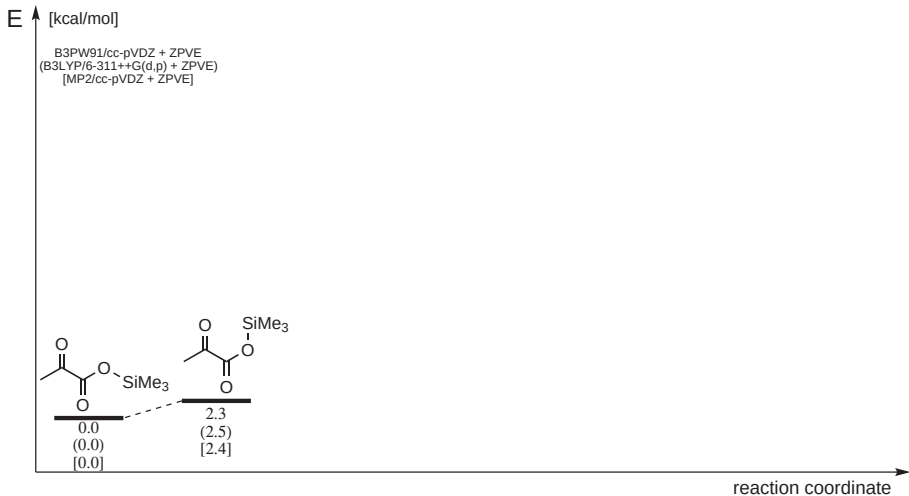


Methyl-trimethylsilyloxycarbene

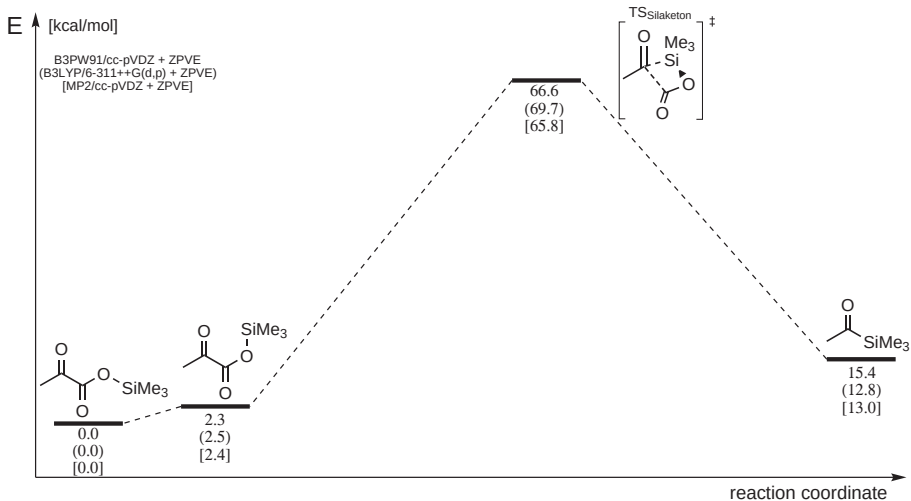


- Silylation of pyruvic acid leads to its silylester
- Decarboxylation barrier: $E^\ddagger \approx 40 \text{ kcal/mol}$
- Compound is volatile and moisture sensitive

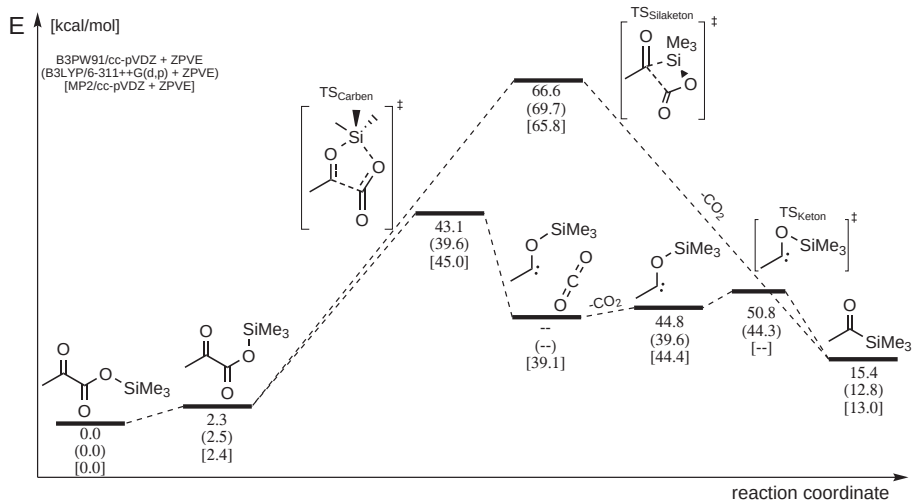
PES of the carbene precursor



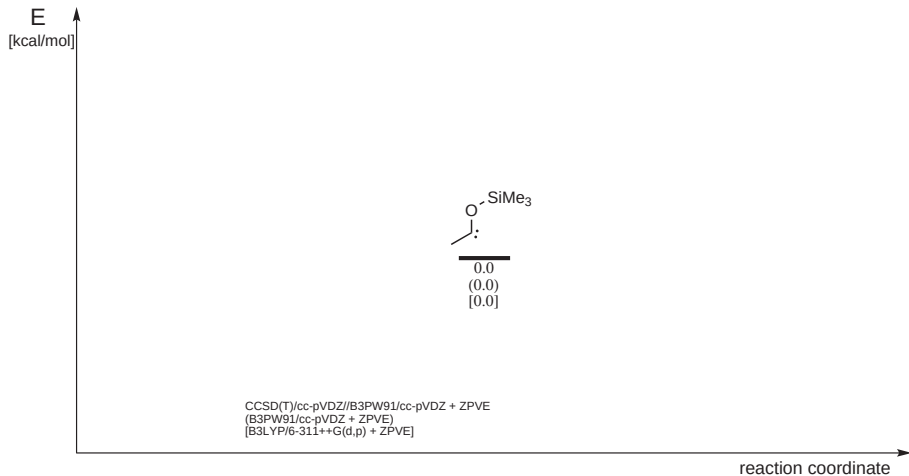
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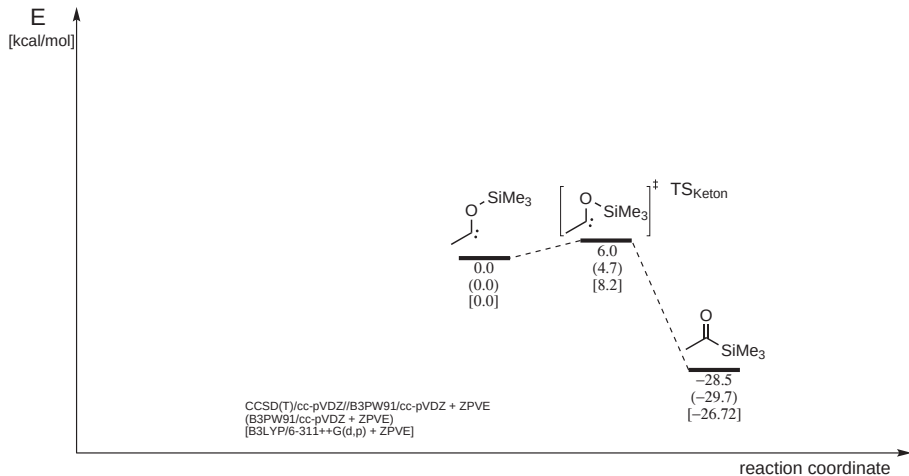
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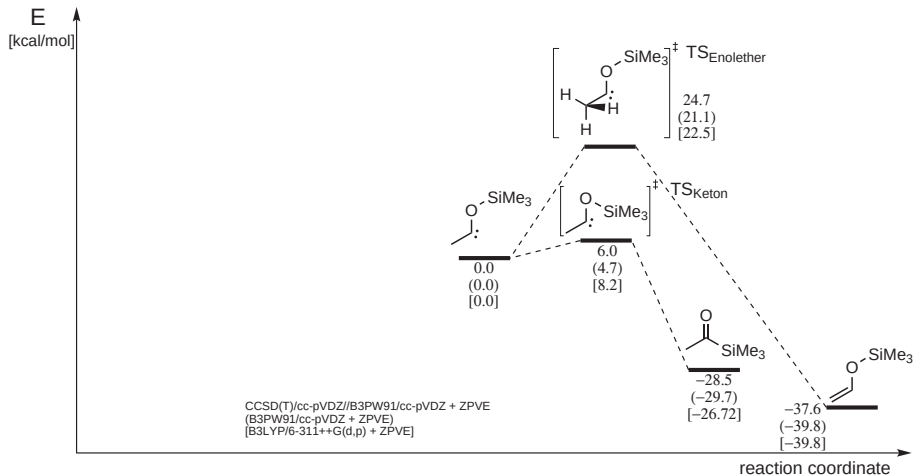
PES of the silylated carbene



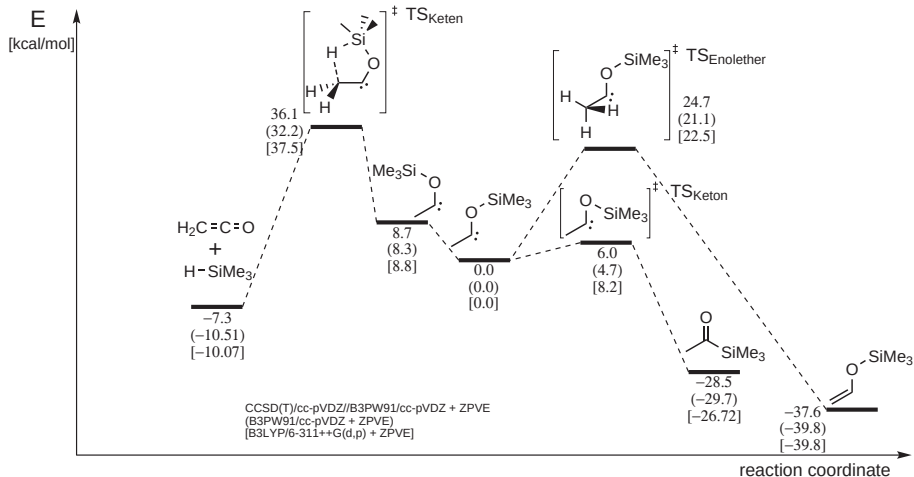
PES of the silylated carbene



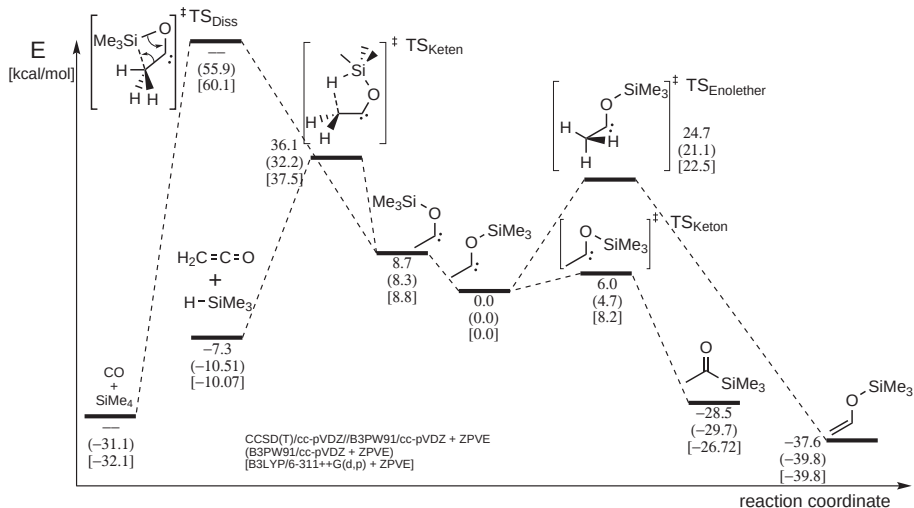
PES of the silylated carbene



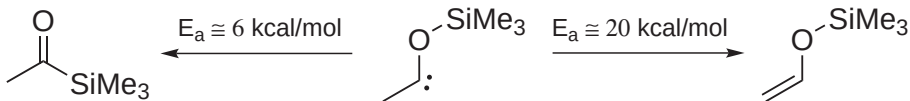
PES of the silylated carbene



PES of the silylated carbene



Matrix isolation experiments



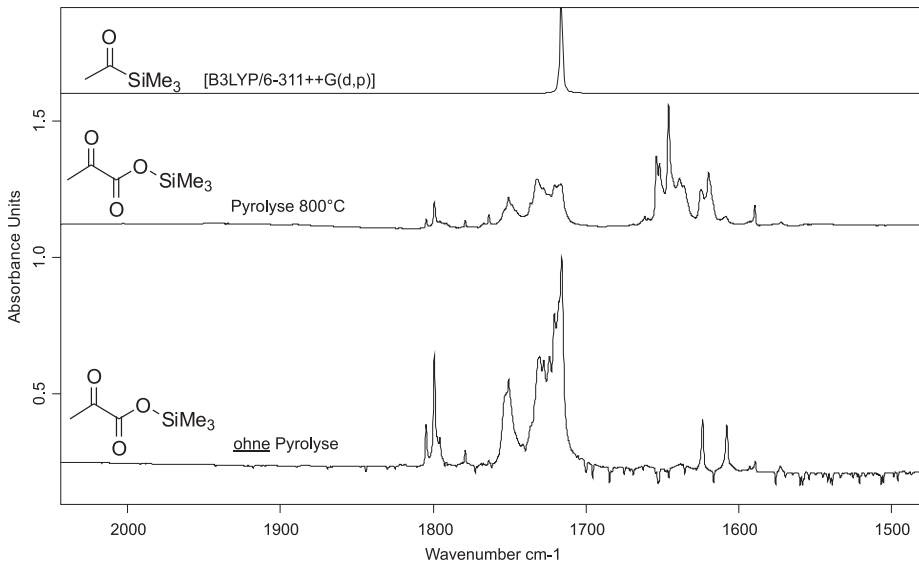
Methyl-trimethylsilyloxycarbene should...

- Be accesible due to decarboxylation of its precursor
- Be thermodynamically stable under matrix conditions
- Vanish after exposure to $\lambda \approx 390 \text{ nm}$ ($\triangleq 73 \text{ kcal/mol}$)

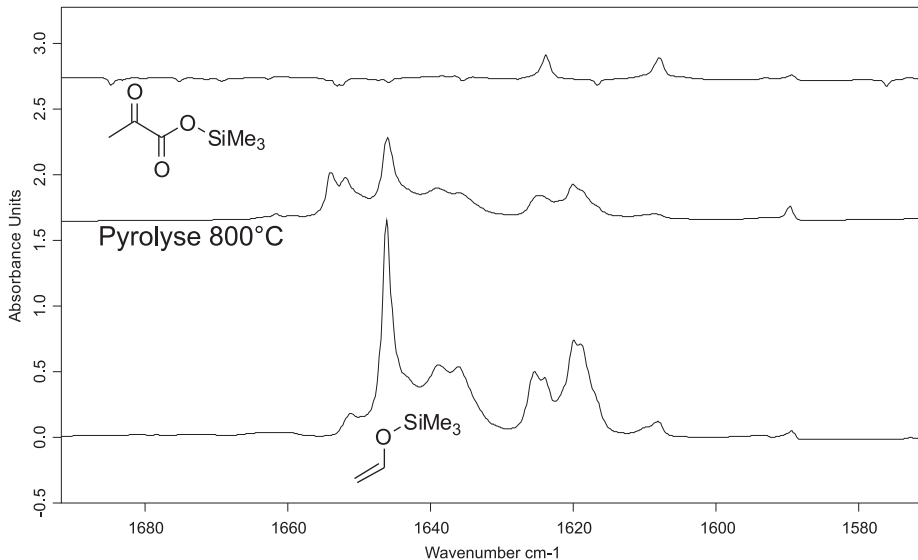
But:

- Several experiments showed no evidence for the carbenes presence
- The kinetically less favorable product could be found

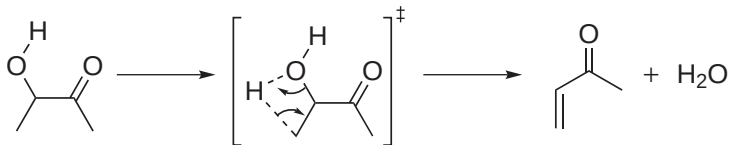
Matrix IR spectra



Matrix IR spectra

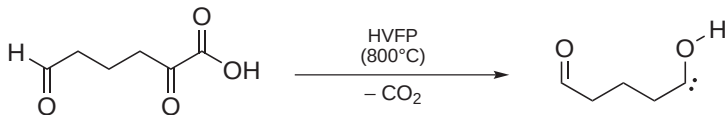


Experimental problems



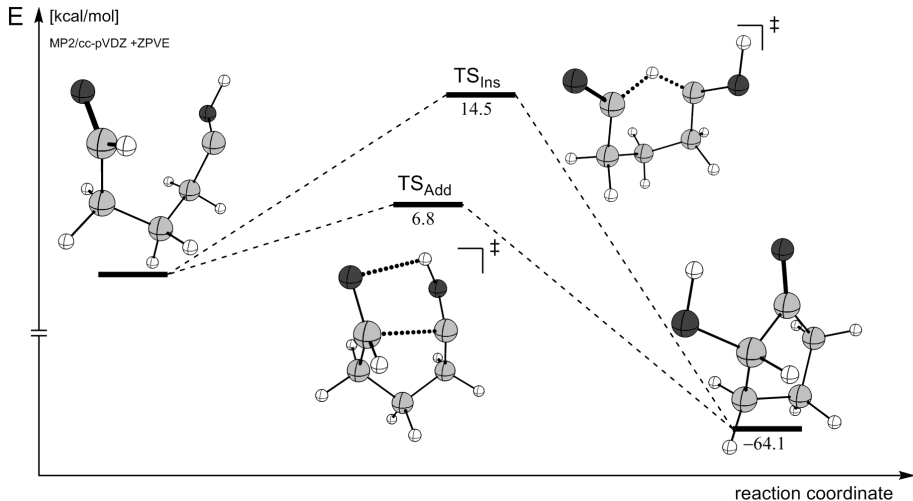
- Acetoin decomposes at the given conditions
- No Acetoin could be isolated via GC
- Quantitation via NMR is unreliable
- Many modifiable parameters
- Matrix isolation studies impossible

Intramolecular carbene-carbonyl addition

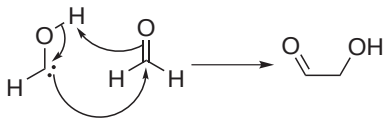


- Precursor's vapor pressure is expected to be sufficient
- Matrix isolation experiments should be possible
- Maybe even kinetical studies are accesible

Intramolecular carbene-carbonyl addition



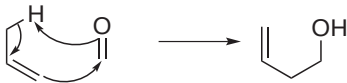
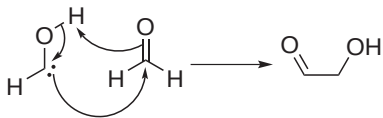
Similar reactions



- Similarity to the (hetero-)ene-reaction^[11, 12]
- Heteroatoms stabilize the transition state

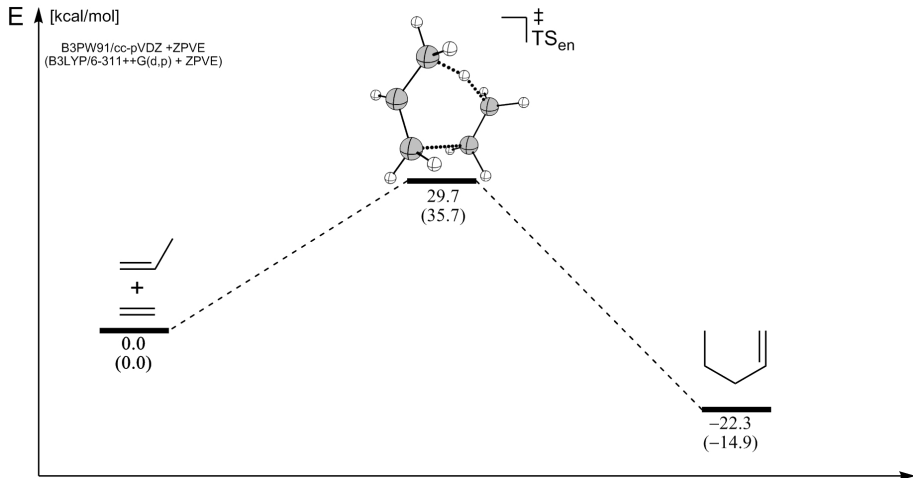


Similar reactions

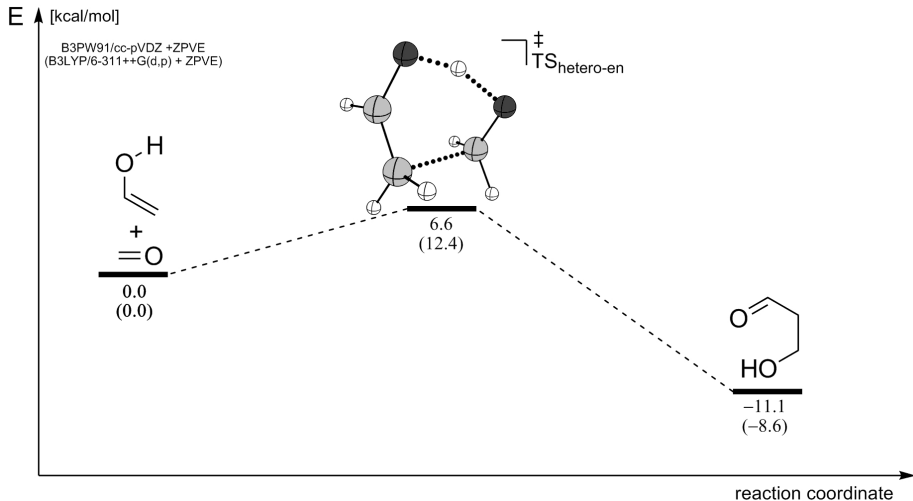


- Similarity to the (hetero-)ene-reaction^[11, 12]
- Heteroatoms stabilize the transition state
- Dihetero-ene-reaction?
- Restriction: stable enols required
- Phenol, Acetylacetone

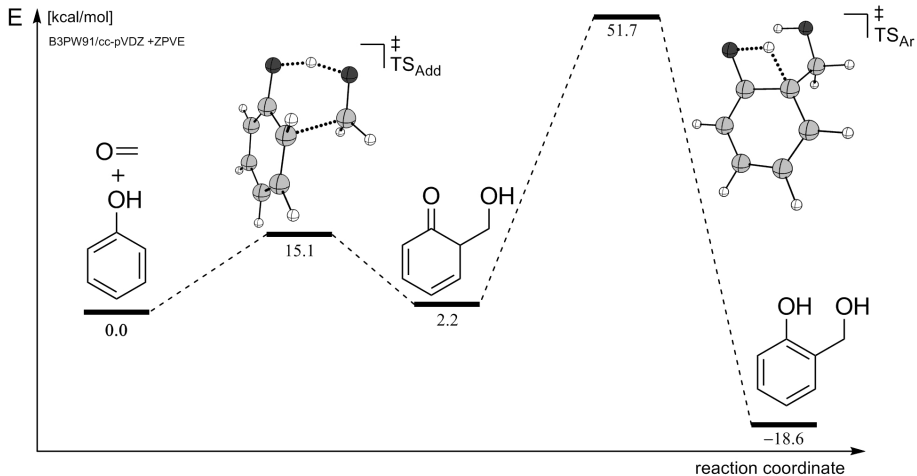
Comparism



Comparism



Comparism



Summary

- First step of the formose reaction is still unclear
- Hydroxycarbenes behave as activated aldehydes
- Addition of Hydroxycarbenes on carbonyl groups is possible
- Relation to ene-reaction/hetero-ene-reaction
- Dihetero-ene-reaction?

acknowledgement

- Prof. Dr. Schreiner
- Dr. Reisenauer
- Dr. Röcker
- Dennis Gerbig
- Volker Lutz
- Christian Suchomski & Sebastian Dold
- Ali Masoudi Alavi & Julian Weber

References

- [1] A. M. Butlerov, *Annalen* **1861**, 120, 295.
- [2] R. Breslow, *Tetrahedron Lett.* **1959**, 21, 22-26.
- [3] J. M. Hollis, F. J. Lovas, P. R. Jewell, *Astrophys. J.* **2001**, 551, 803-806.
- [4] M. J. H. de Groot, H. J. G. L. M. Lamers, *Nature* **1992**, 355, 420-422.
- [5] T. P. Snow, V. M. Bierbaum, *Annu. Rev. Anal. Chem.* **2008**, 1, 229-259.
- [6] P. R. Schreiner, H. P. Reisenauer, F. C. Pickard, A. C. Simmonett, W. D. Allen, E. Mátyus, A. G. Czásár, *Nature* **2008**, 453, 906-909.
- [7] D. T. Halfen, A. J. Apponi, N. Woolf, R. Polt, L. M. Ziurys, *Astrophys. J.* **2006**, 639, 237-245.
- [8] H.-W. Wanzlick, *Angew. Chem* **1962**, 74, 129.
- [9] A. N. Simonov, O. P. Pestunova, L. G. Matvienko, and V. N. Parmon, *Kinet. Katal.* **2007**, 48, 261-270.
- [10] D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, 107, 5606-5655.
- [11] K. Alder, F. Pascher, A. Schmitz *Ber. Dtsch. Chem. Ges.* **1943**, 76, 27-53.
- [12] C. K. Z. Andrade, O. E. Vercillo, J. P. Rodrigues, D. P. Silveira *J. Braz. Chem. Soc.* **2004**, 15, 813-817.