

Synthesis of small molecules with hydroxycarbenes as precursor

Seminar talk presented by
Felix Keul

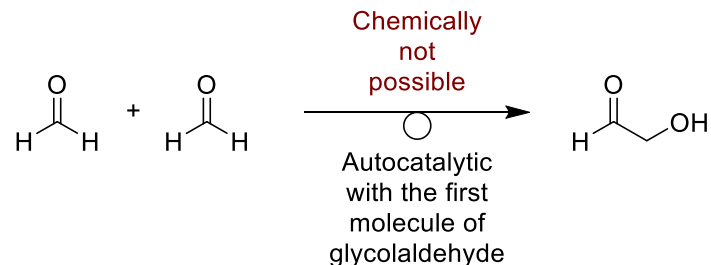
September 7th, 2018

*Institute of Organic Chemistry
Justus-Liebig University Giessen*

Famous Formose (Butlerow) reaction



- Glycolaldehyde is the first entry in the formose reaction



- needs liquid water, strong bases, high concentrations and ambient temperatures
 - no long term stability and no stereochemical purity
- ➔ less relevant for forming sugars in prebiotic and extraterrestrial context

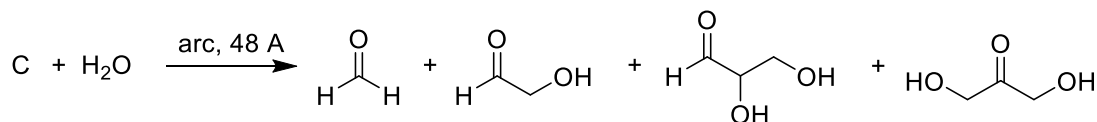
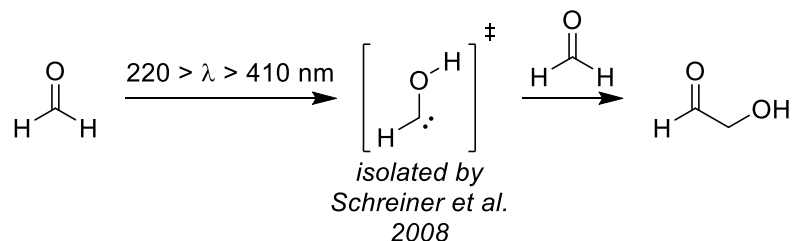


R. Breslow, *Tetrahedron Lett.*, **1959**, 1, 22-26; A. Butlerow, *Justus Liebig Ann. Chem.*, **1861**, 120, 295-298; R. F. Socha, A. H. Weiss, M. M. Sakharov, *React. Kinet. Catal. Lett.*, **1980**, 14, 119-128; R. Larralde, M. P. Robertson, S. L. Miller, *Proc. Natl. Acad. Sci. U. S. A.*, **1995**, 92, 8158-8160; S. Toxvaerd, *Orig. Life Evol. Biosph.*, **2013**, 43, 391-409

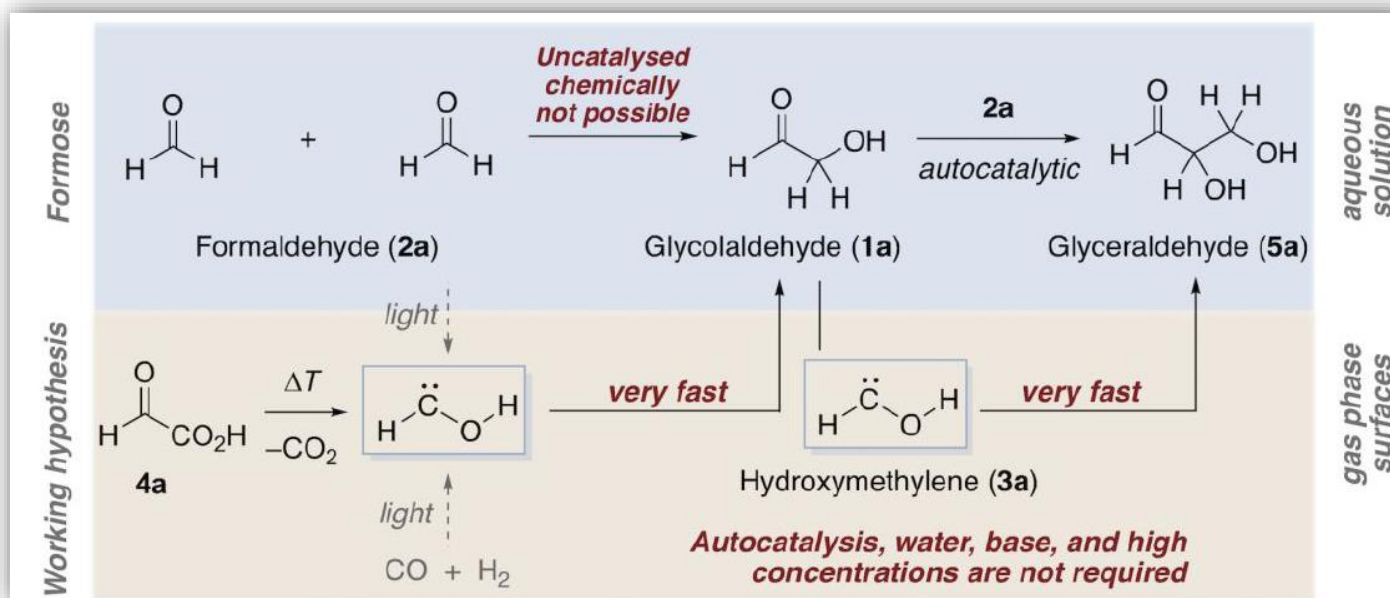
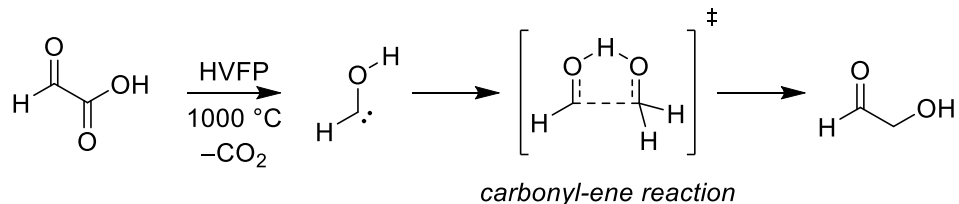


- Murchison and Murry meteorites containing sugar related compounds

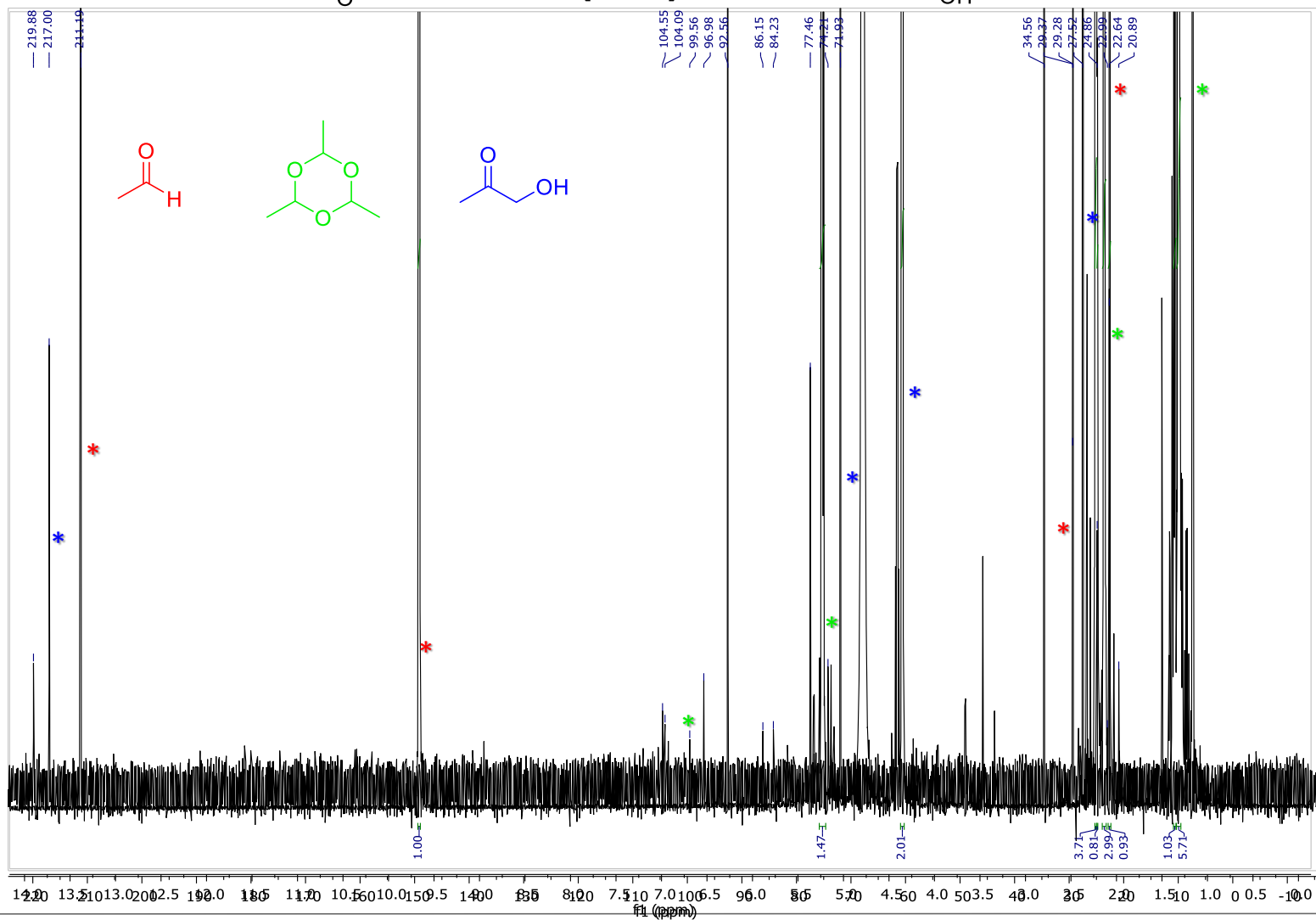
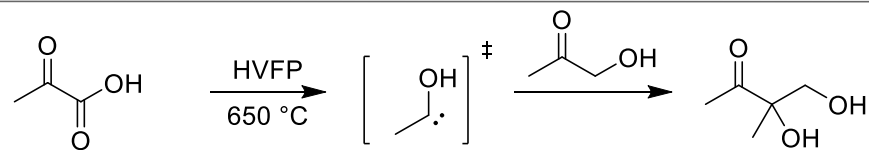
“polyols were present on the early Earth and therefore at least available for incorporation into the first forms of life”



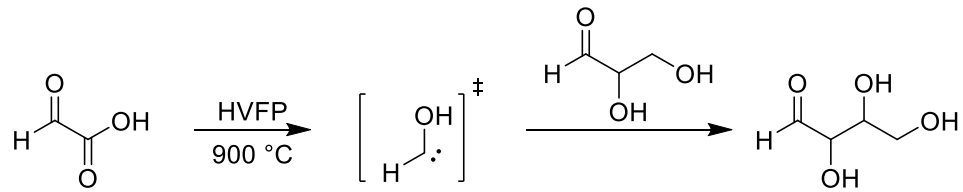
G. Cooper, N. Kimmich, W. Belisle, J. Sarinana, K. Brabham, L. Garrel, *Nature*, **2001**, 414, 879-883; Y. Kebukawa, A. L. D. Kilcoyne, G. D. Cody, *Astrophys. J.*, **2013**, 771, 19; J. M. Hollis, F. J. Lovas, P. R. Jewell, *Astrophys. J.*, **2000**, 540, 107-110; J. R. Sodeau, E. K. C. Lee, *Chem. Phys. Lett.*, **1978**, 57, 71-74; P. R. Schreiner, H. P. Reisenauer, F. C. Pickard IV, A. C. Simmonett, W. D. Allen, *Nature*, **2008**, 453, 906-909; S. N. Ahmed, M. L. McKee, P. B. Shevlin, *J. Am. Chem. Soc.*, **1985**, 107, 1320-1324

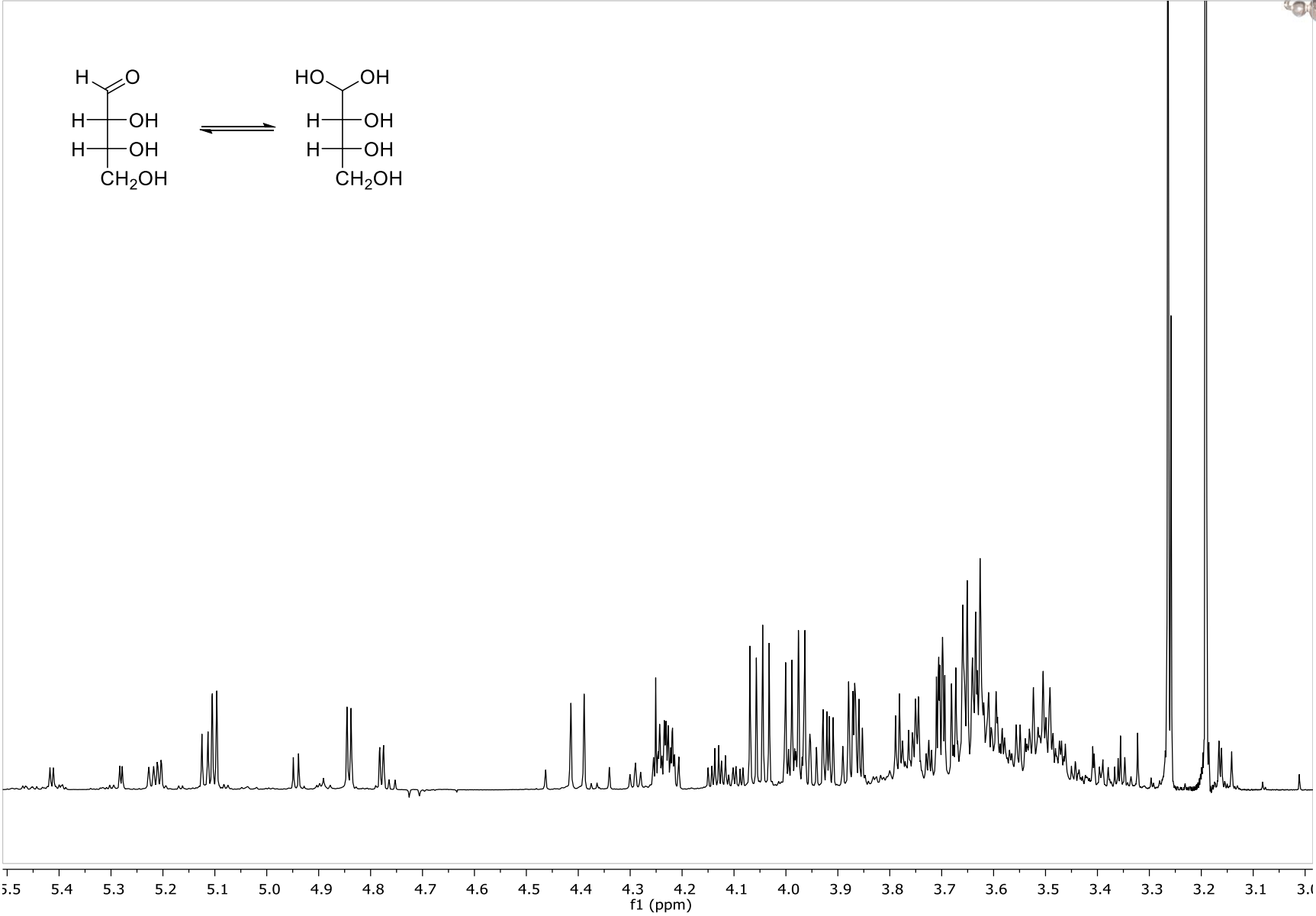


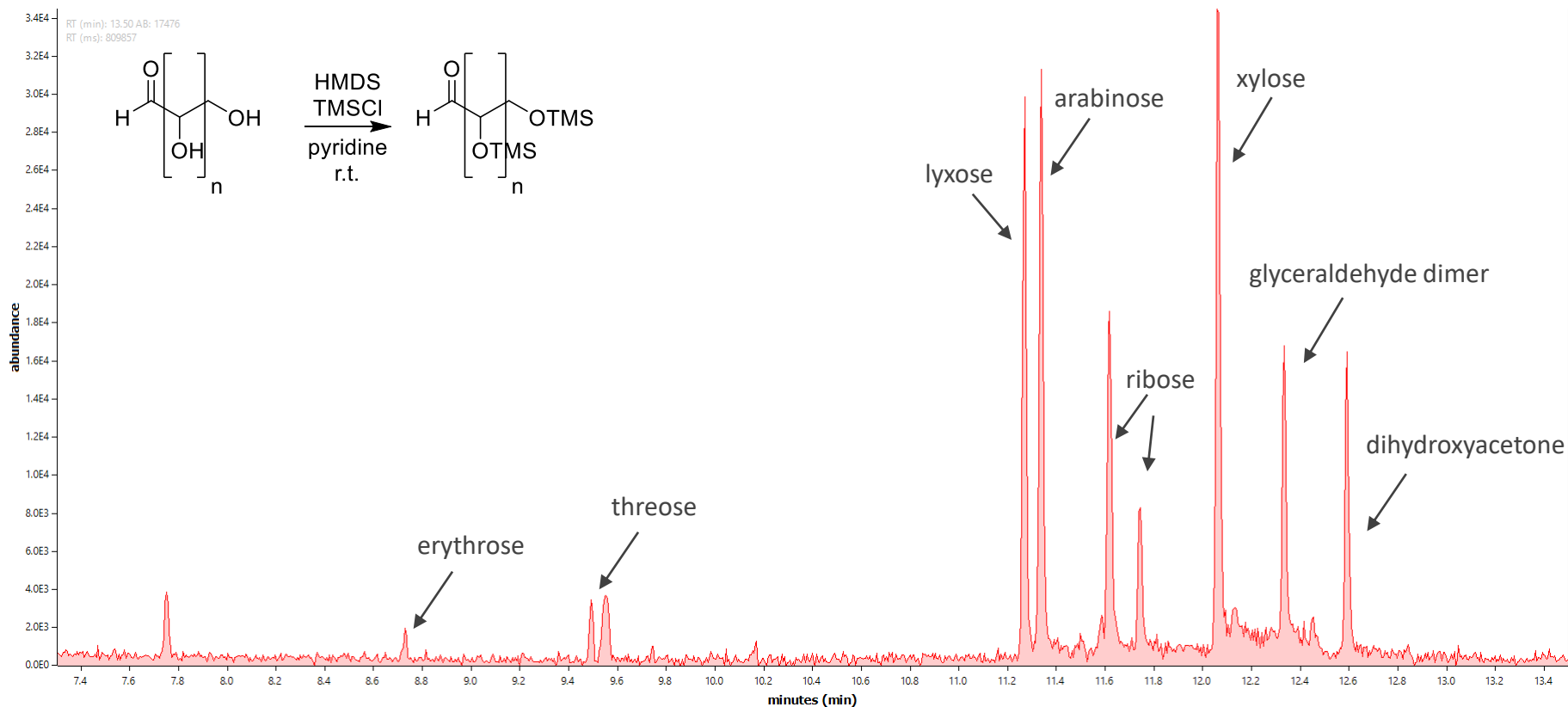
High vacuum flash pyrolysis







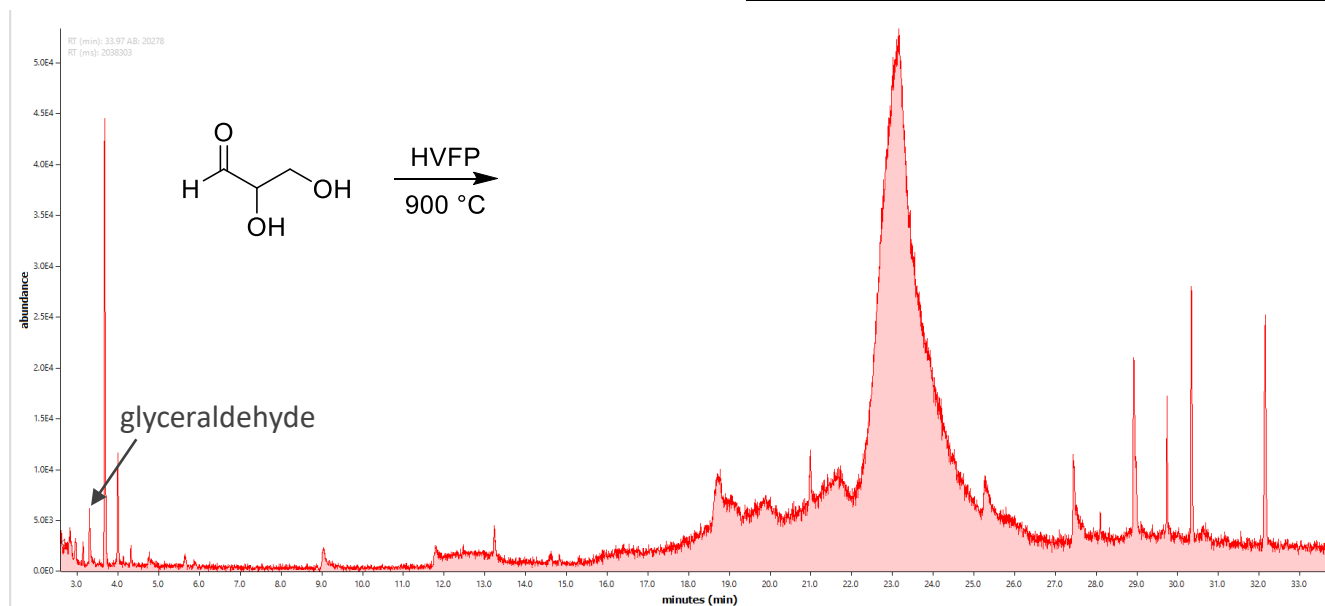
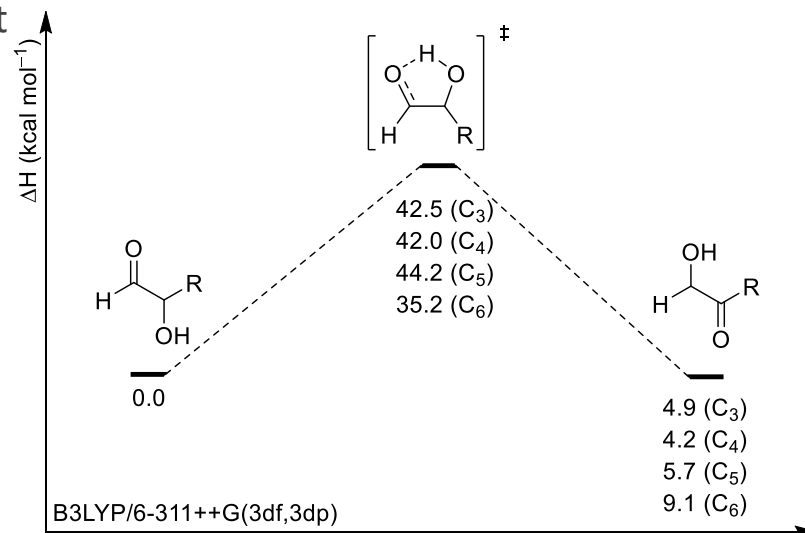
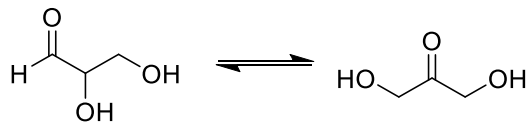


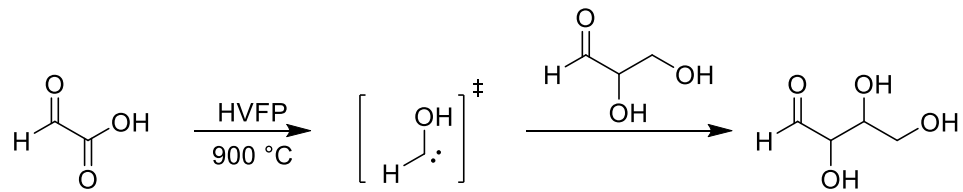


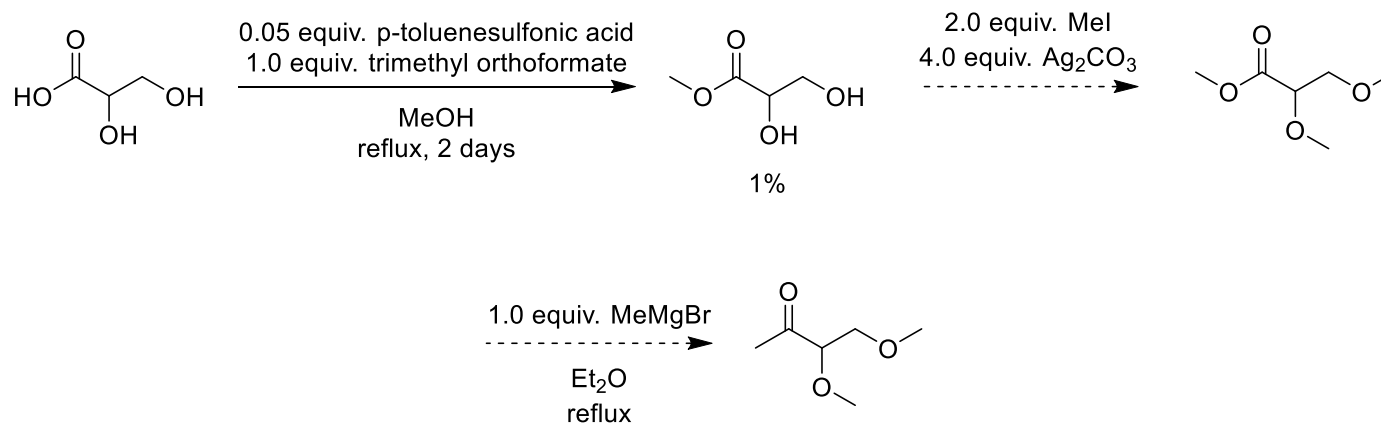
Testing the stability of glyceraldehyde



Lobry De Bruyn- Alberda van Ekenstein rearrangement

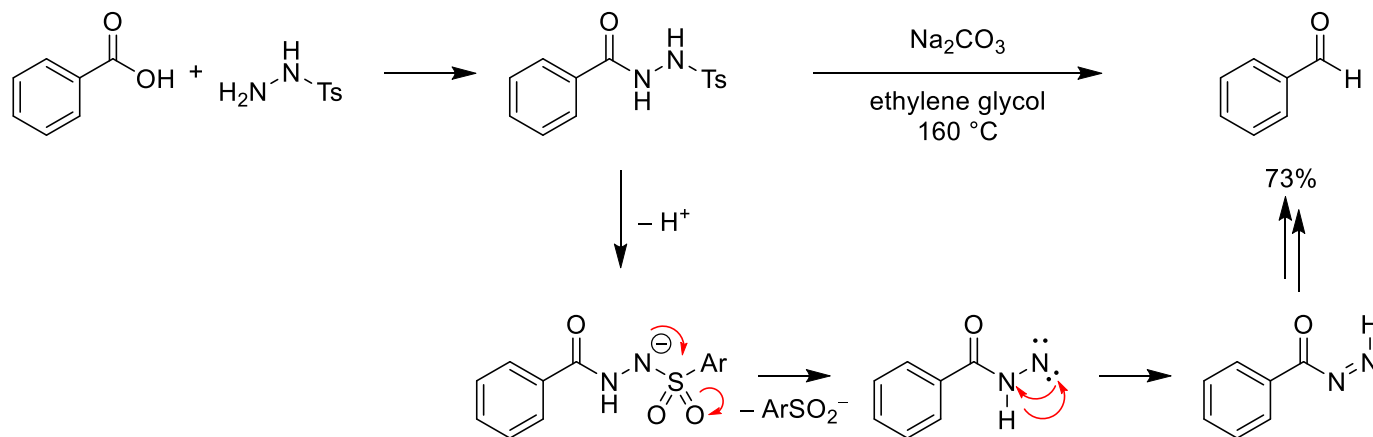




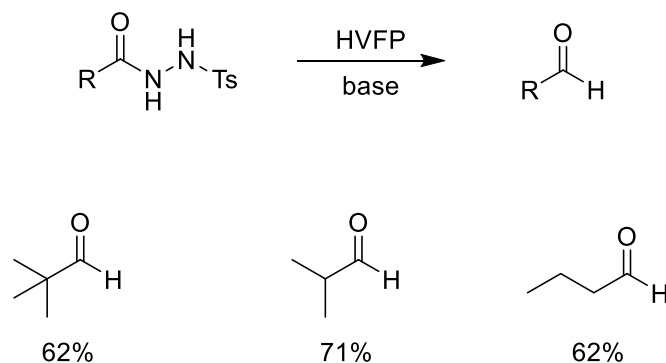




- Method to synthesis aldehydes from carboxylic acids

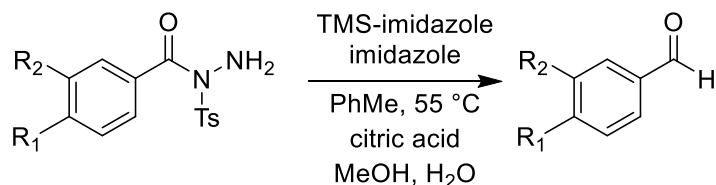
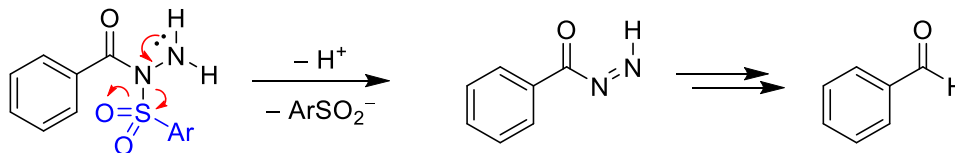


- Even aliphatic aldehydes can be synthesized in an alkaline environment





- Modified version of Fukuyama *et al.*



$R_1 = \text{I}$ (92%), CO_2Me (82%), CF_3 (80%), CN (60%), OMe (78%), NO_2 (0%)
 $R_2 = \text{OMe}$ (92%), NO_2 (66%), Bpin (80%)

Chemical Science

RSC Publishing

EDGE ARTICLE

[View Article Online](#)
[View Journal](#) | [View Issue](#)

Modified McFadyen-Stevens reaction for a versatile synthesis of aliphatic/aromatic aldehydes: design, optimization, and mechanistic investigation†

Yuri Iwai, Takashi Ozaki, Ryo Takita, Masanobu Uchiyama, Jun Shimokawa and Tohru Fukuyama*

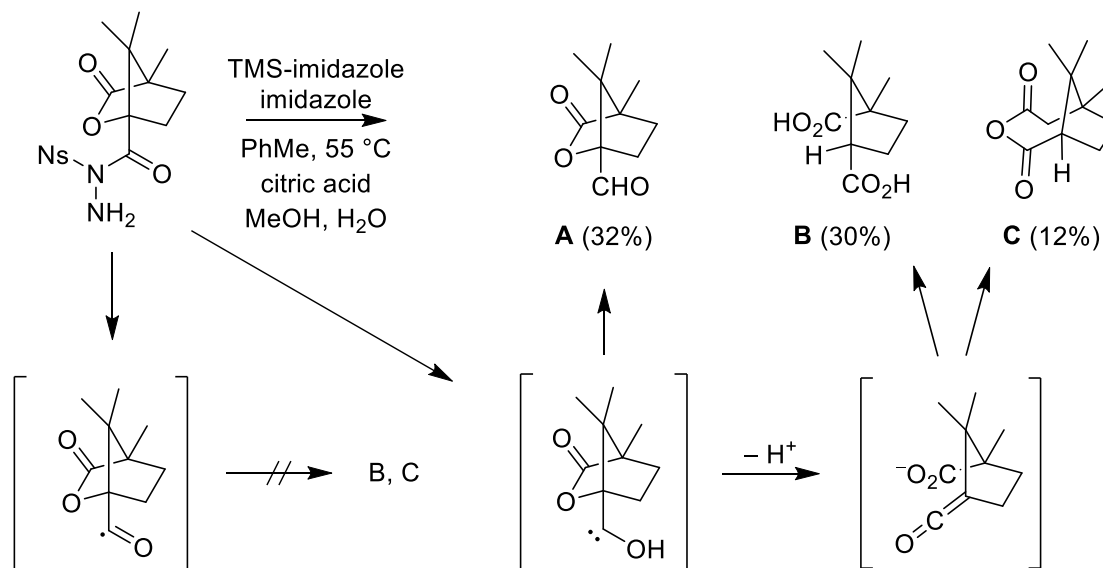
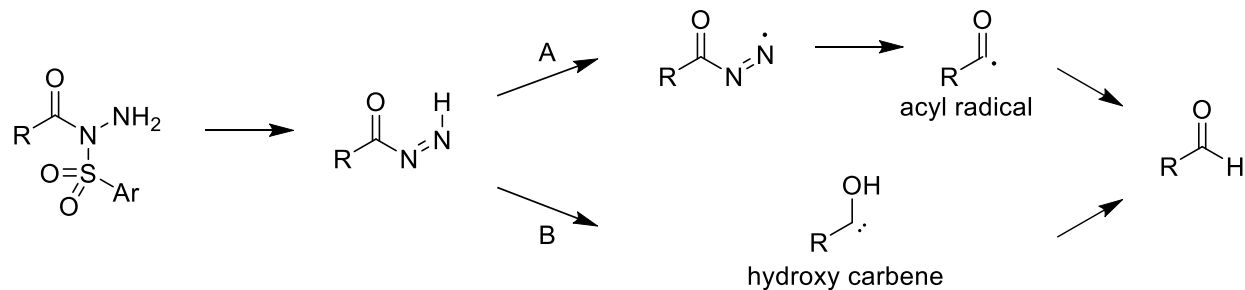
The traditional McFadyen-Stevens reaction requires harsh alkaline reaction conditions, thus precluding application to the synthesis of aliphatic aldehydes. Our modified McFadyen-Stevens reaction enables the transformation from the *N,N*-acylsulfonyl hydrazine to the corresponding aldehyde upon treatment with an imidazole-TMS imidazole combination without relying on oxidative or reductive reagents. The reduced basicity and *in situ* protection of the resulting aldehyde widens the substrate scope to include aliphatic aldehydes, even ones bearing an α -hydrogen atom. Close examination of the side reactions for particular substrates in combination with theoretical considerations *via* DFT calculations led to a mechanistic understanding of the McFadyen-Stevens reaction involving an acyl diazene and a hydroxy carbene as reasonable intermediates.

Received 22nd November 2012
 Accepted 7th December 2012

DOI: 10.1039/c2sc22045h
www.rsc.org/chemicalscience

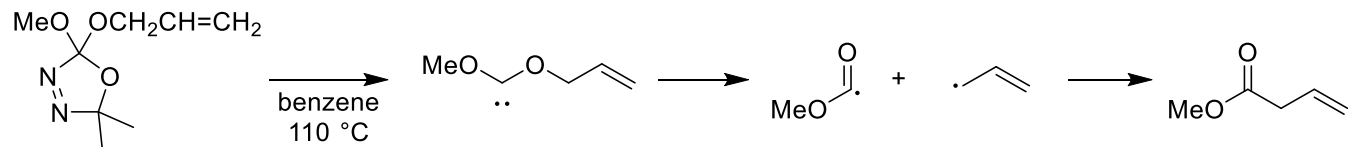


- Two possible pathways

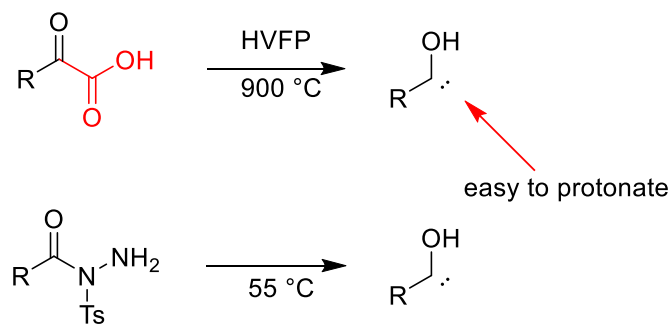


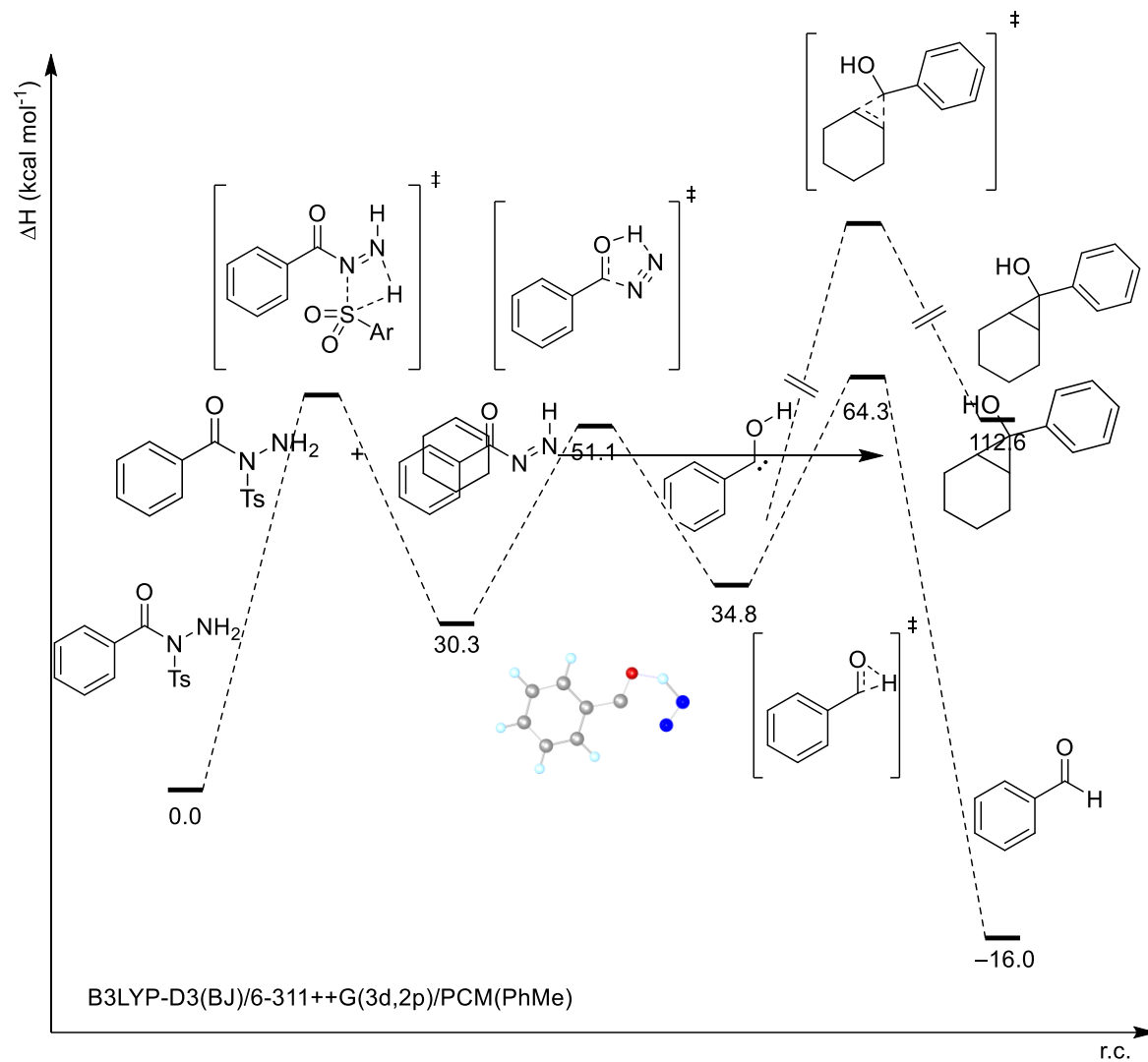


- Carbene in solution



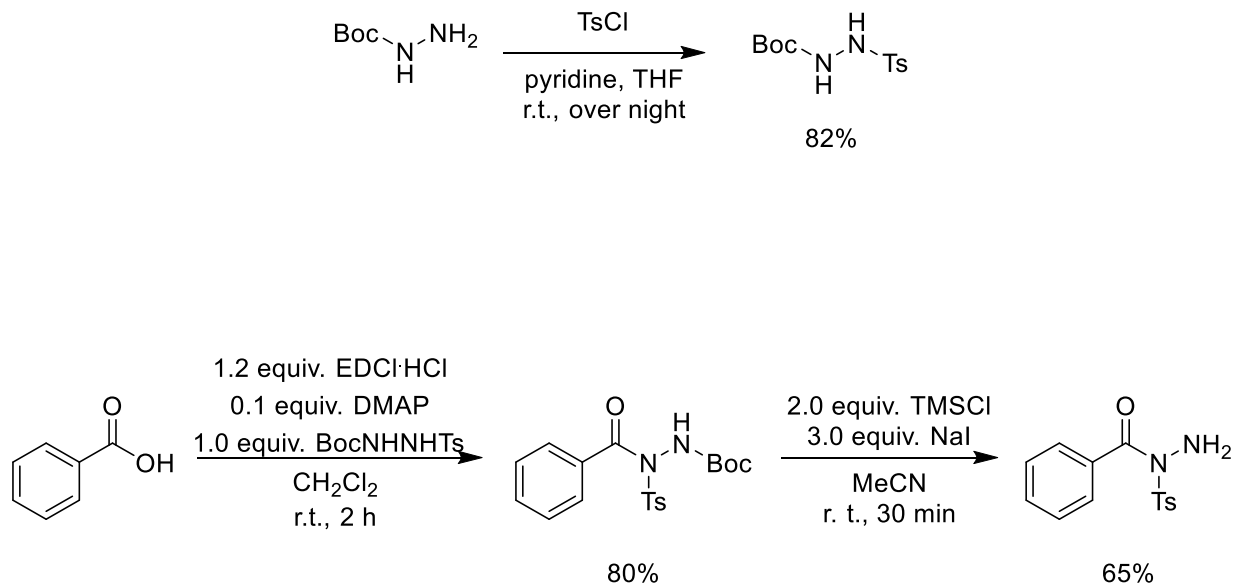
- McFayden-Stevens starting material as possible precursor for hydroxycarbene in solution





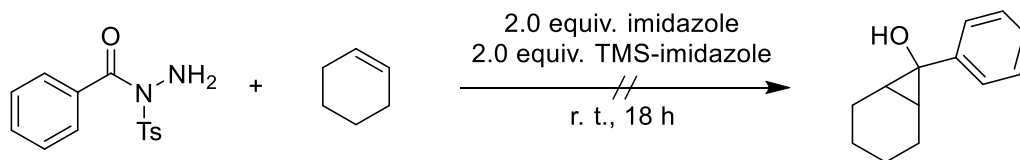
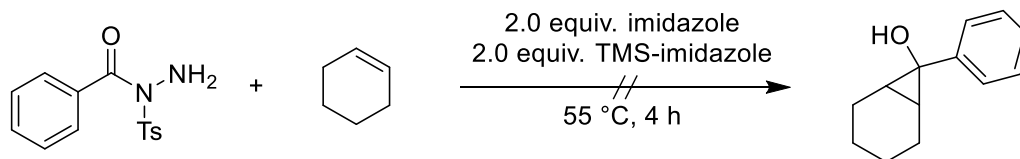


- Route after Fukuyama *et al.*

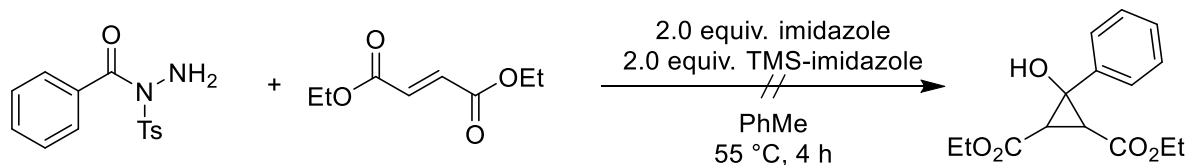




- Cyclohexen as carben scavenger

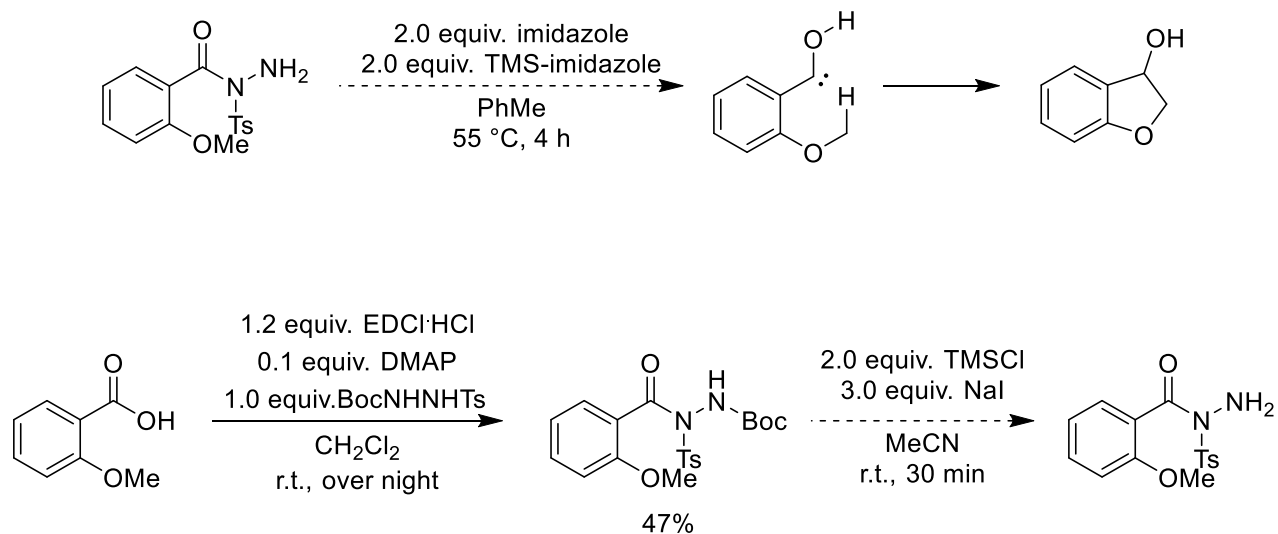


- Starting material is not soluble in cyclohexen at room temperature
- More electrophilic carbene scavenger



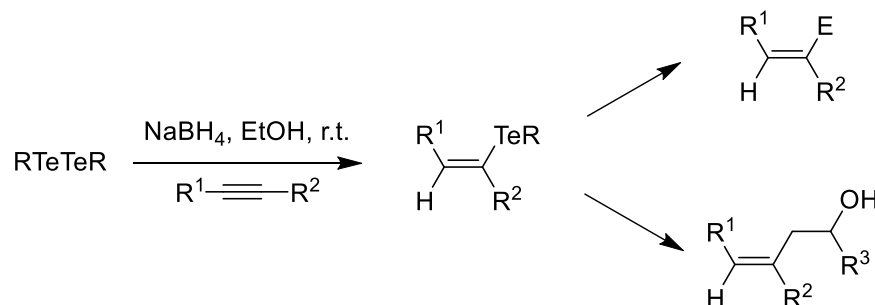


- Intramolecular reaction

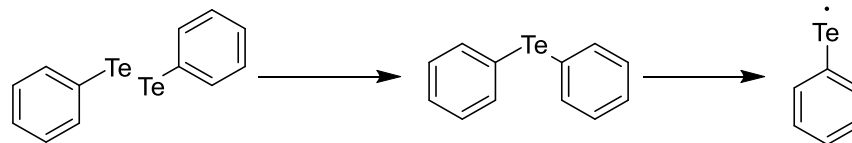




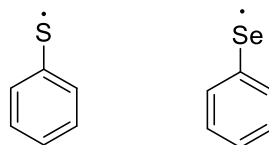
- Organotellurium compounds involved in cross-coupling reactions and living radical polymerizations

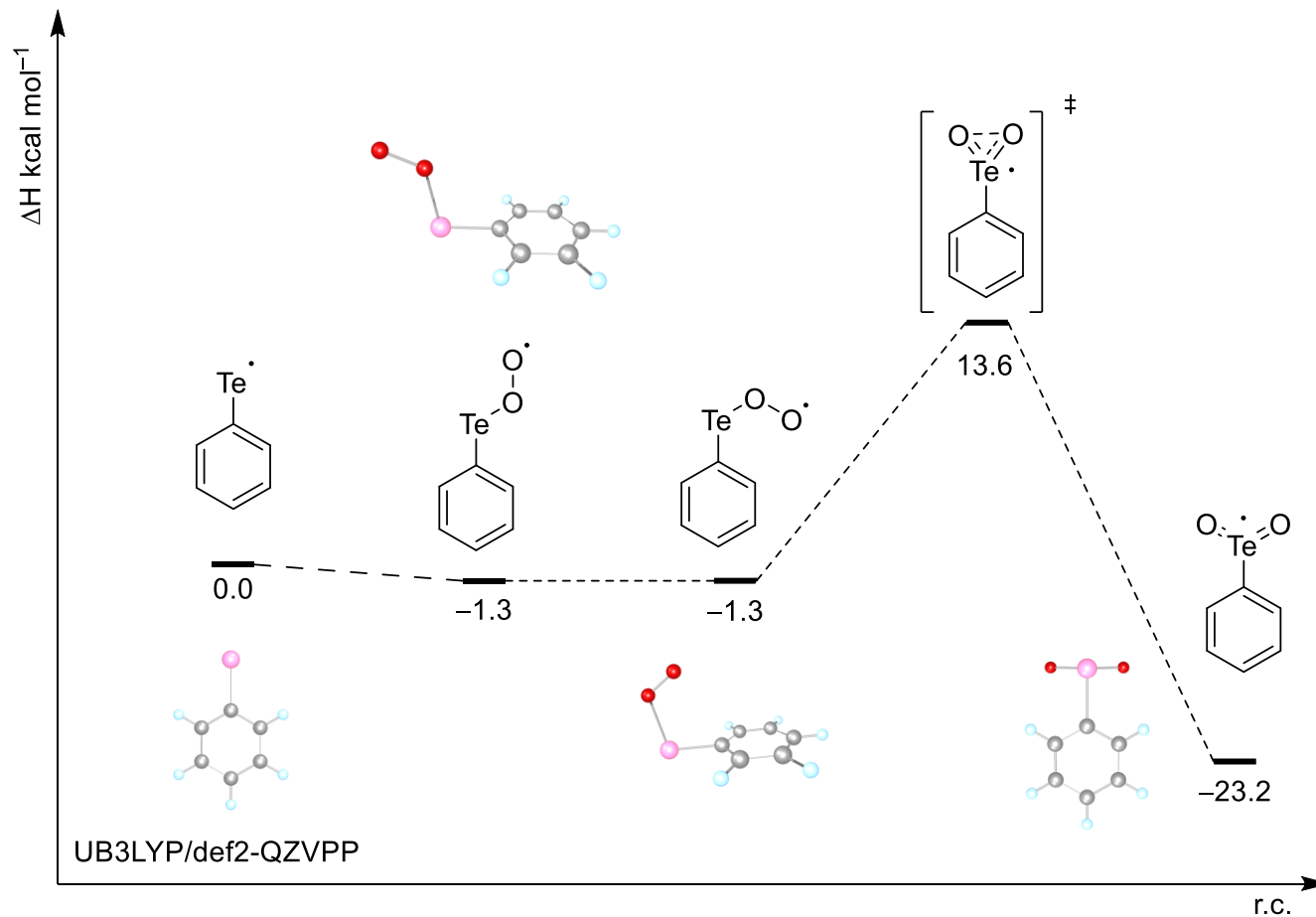


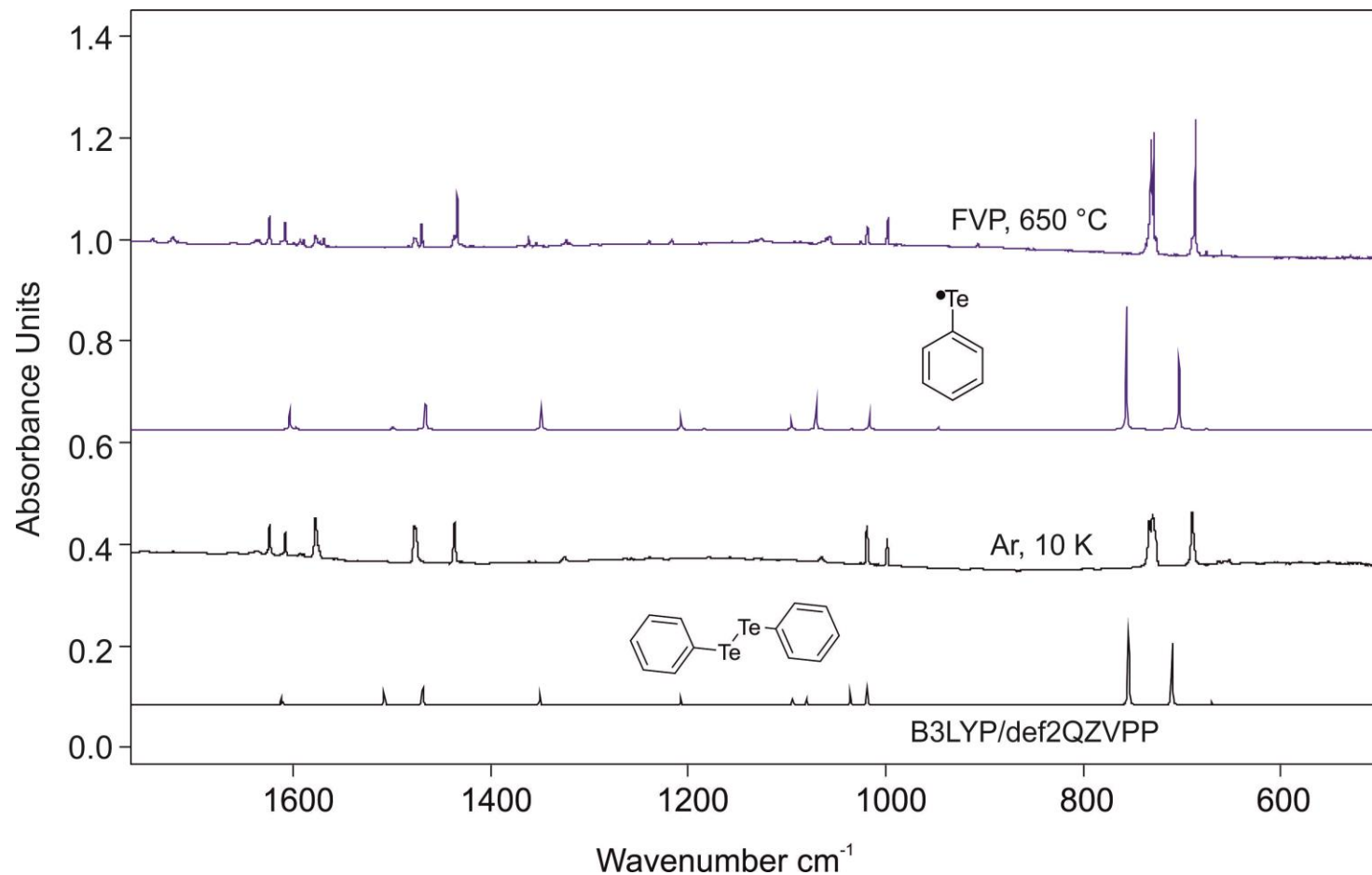
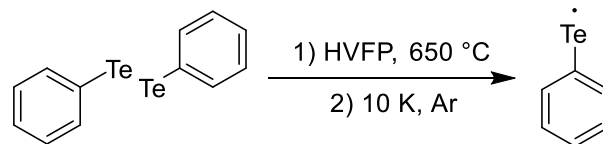
- Formation of phenyltelluryl-radical are studied with EPR-technique

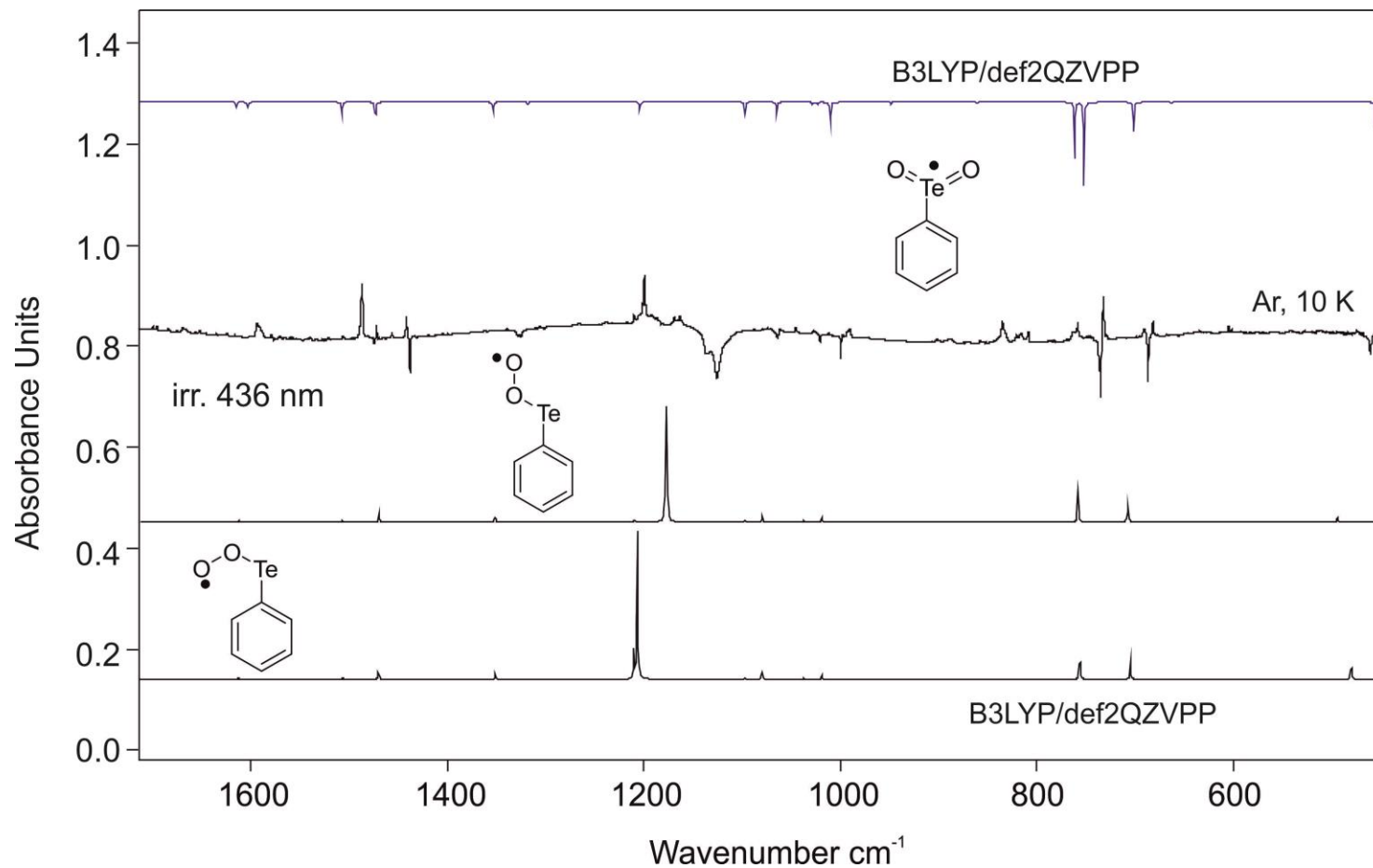
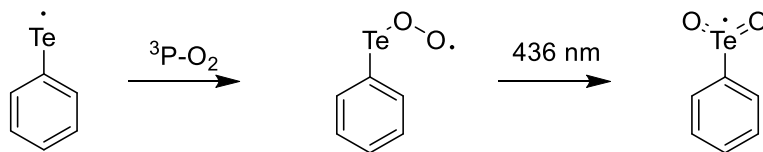


- Former studies









Acknowledgement



Prof. Dr. Peter R. Schreiner

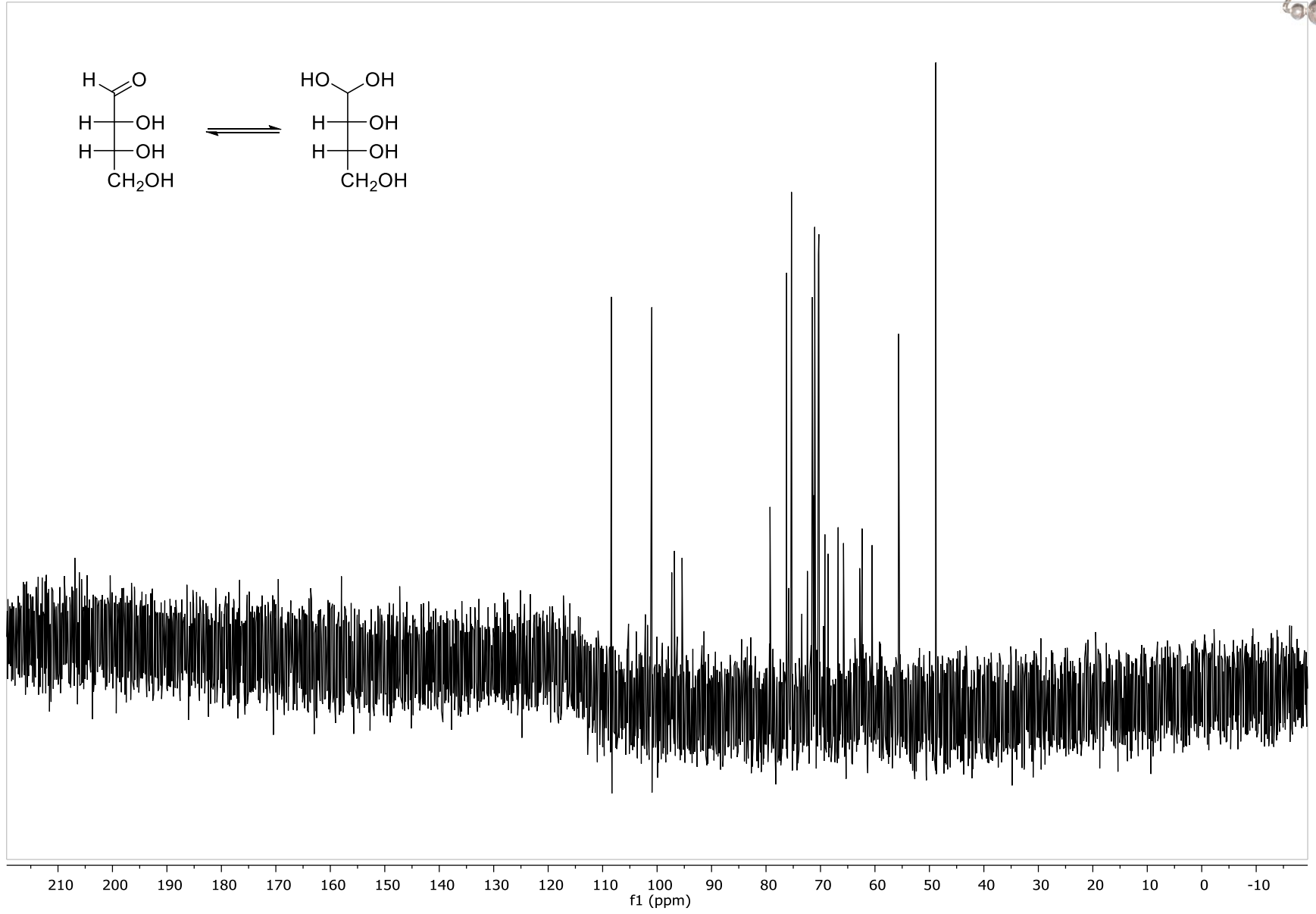
Artur

Raffi, Henrik, André

Alex, Lukas, Markus, Fred, Dominik, Jan, Eschi, JPB

PRS Group







- Intramolecular reaction

