VIII Summer School on Green Chemistry, Venice / Italy, 4-10 September 2005

Microwave-Assisted Organic Synthesis in Near-Critical Water at 300 °C. A Proof-of-Concept Study.

Jennifer M. Kremsner and C. Oliver Kappe

Institute of Chemistry, Organic and Bioorganic Chemistry, Karl-Franzens-University Graz, Heinrichstrasse 28, A-8010 Graz, Austria
email: jenny.kremsner@uni-graz.at *website: http://www.maos.net*

❶ Why Near Critical Water (NCW) ??

- ☺ non-toxic
- ☺ non-flammable
- ☺ environmentally benign
- ☺ readily available
- ☺ cheap

Properties of NCW

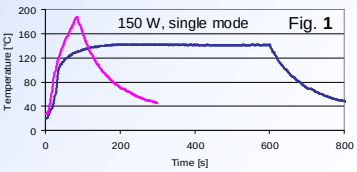
fluid	ordinary water (T < 150 °C) (p < 4 bar)	near-critical water (NCW) (T = 150-350 °C) (p = 4-200 bar)	supercritical water (SCW) (T > 374 °C) (p > 221 bar)
temperature (°C)	25	250	400
pressure (bar)	1	50	250
density (g cm^{-3})	1	0.8	0.17
dielectric constant, ε'	78.5	**27.1**	5.9
pK_w	14	**11.2**	19.4

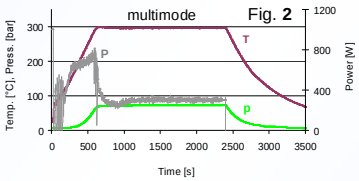
Krammer, P.; Vogel H. *J. Supercrit.Fluids*, **2000**, *16*, 189-206

- ☺ solubility of organic compounds (ε' = 27.1) ⇨ NCW is a pseudo-organic solvent
- ☺ strong acid and base at 250 °C (pK_W = 11.2)
- ☺ simple post-reaction product isolation
- ☺ "tune" properties of NCW through changing temperature and pressure

❷ NCW and Microwave (MW) Irradiation

In the mid 1990s C. R. Strauss pioneered the use of microwave energy to heat reaction mixtures utilizing water as solvent.[1]
Due to the dramatic changes of the dielectric properties at higher temperatures NCW is virtually transparent to microwave radiation. It therefore needs a 0.03 M sodium chloride solution (Fig. **1**) to generate NCW (300 °C, 80 bar) which can be maintained for several hours at a 15-400 ml scale (Fig. **2**). [2]





*Microwave heating profiles for **pure water** and **0.03 M NaCl** solution (Fig. **1**), and heating curve for the generation of near critical water under microwave conditions (Fig. **2**)*

[1] C. R. Strauss, R. W. Trainor, *Aust. J. Chem.* **1995**, *48*, 1665-1692; C. R. Strauss, *Aust. J. Chem.* **1999**, *52*, 83-96
[2] J. M. Kremsner, C. O. Kappe, *Eur. J. Org. Chem.* **2005**, 3672-3679

❸ Instrumentation

Synthos 3000™ (Multimode)

www.anton-paar.com

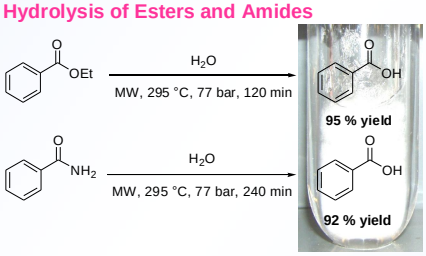
Reactor Specifications:

- Continuous microwave output power 0-1400 W
- 8 or 16 reactions in parallel
- up to 300 °C and 80 bar
- up to 60 ml filling volume per vessel
- quartz or teflon vessels
- temperature monitoring by IR thermography and immersing gas balloon thermometer
- built-in forced-air cooling
- wireless remote sensor technology
- hydraulic system for simultaneous pressure sensing

❹ Chemistry Examples

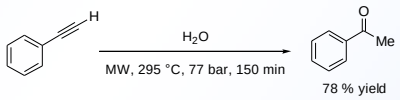
Several different transformations were successfully performed in MW-NCW without the addition of an acid or basic catalyst.

Hydrolysis of Esters and Amides



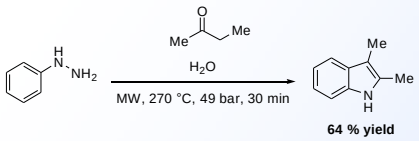
- in gerneral only possible in the presence of strong mineral acids or bases
- no reaction observed below 200 °C
- autocatalytic mechanism

Hydration of Acetylenes



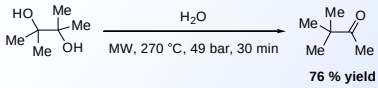
- di – and trimeric self-condensation by-products
- no reaction below 200 °C
- isolated as 2-(2,4-dinitrophenyl)hydrazone

Fischer Indole Synthesis



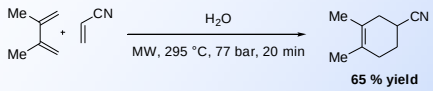
- significant interest due to the broad applications of indoles
- no reaction below 200 °C
- previously investigated by C. R. Strauss [1]

Pinacol Rearrangement



- usually catalyzed by strong acids
- significantly accelerated by raising the temperature
- isolated as 2-(2,4-dinitrophenyl)hydrazone

Diels Alder Cycloaddition



- reaction yield enhanced due to solubility of starting materials in NCW
- no hydrophobic effects
- no reaction below 200 °C

❺ Conclusion

Our proof-of-principle studies have demonstrated

- ❖ the technical feasibility to perform microwave synthesis in NCW which extends the accessible temperature / pressure range for microwave-assisted organic synthesis compared to currently used microwave instrumentation.
- ❖ that it was possible to reproduce or improve the results comparing previously published data obtained from thermal NCW experiments with the results obtained in MW-NCW.
- ❖ that in most cases the unique strongly acidic properties of NCW were exploited to perform transformations that normally would require the presence of a strong acid.
- ❖ that MW–NCW technology is therefore ideally suited to perform organic synthesis in this high temperature region, combining the advantages of MW chemistry with the benefits of using water as solvent under near-critical conditions.

Acknowledgement

We gratefully acknowledge support for this work by the Austrian Science Fund (FWF, Project 15582) and would like to thank Anton Paar GmbH for providing microwave instrumentation and technical support.