High-Throughput Screening Techniques in Catalysis

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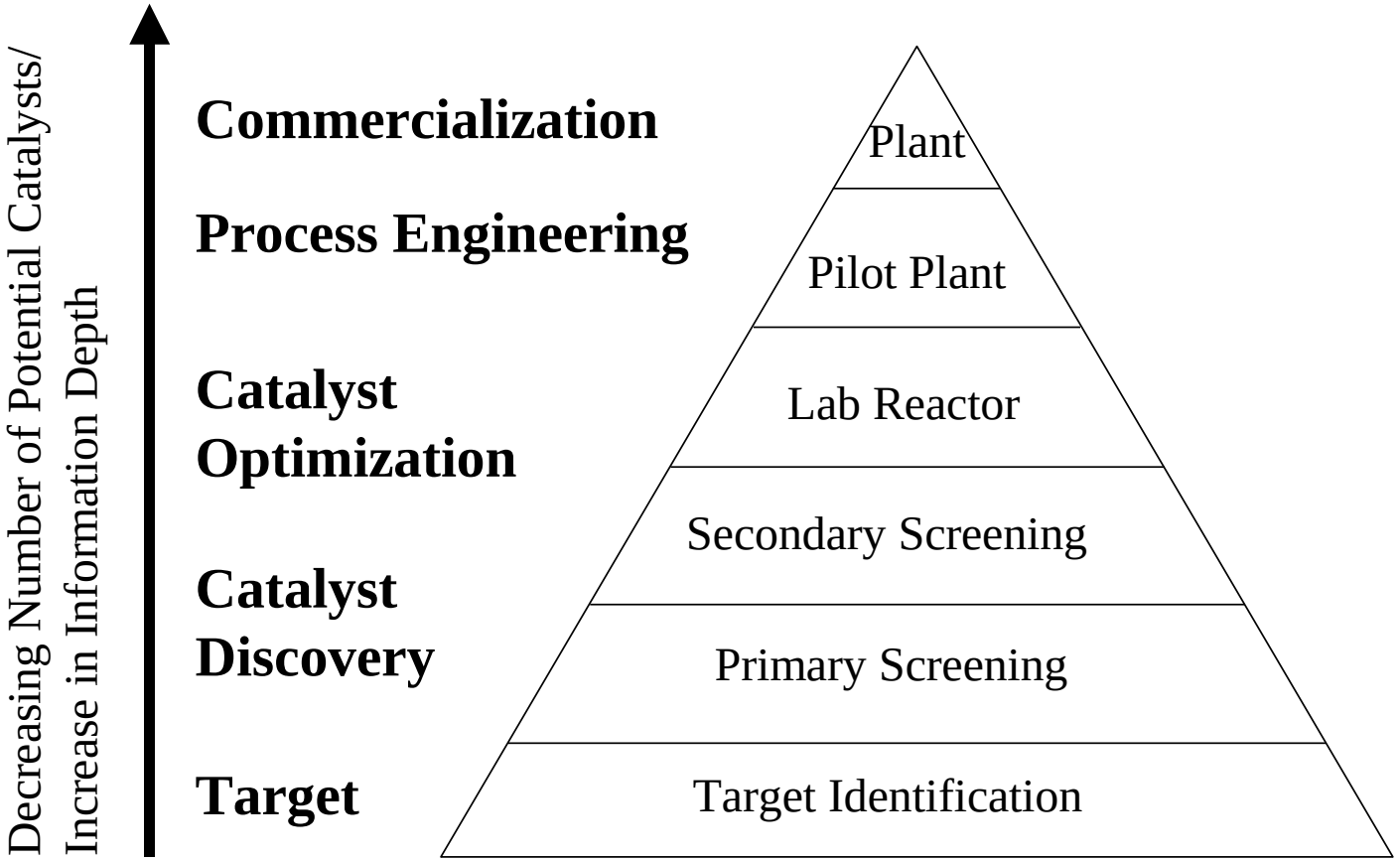
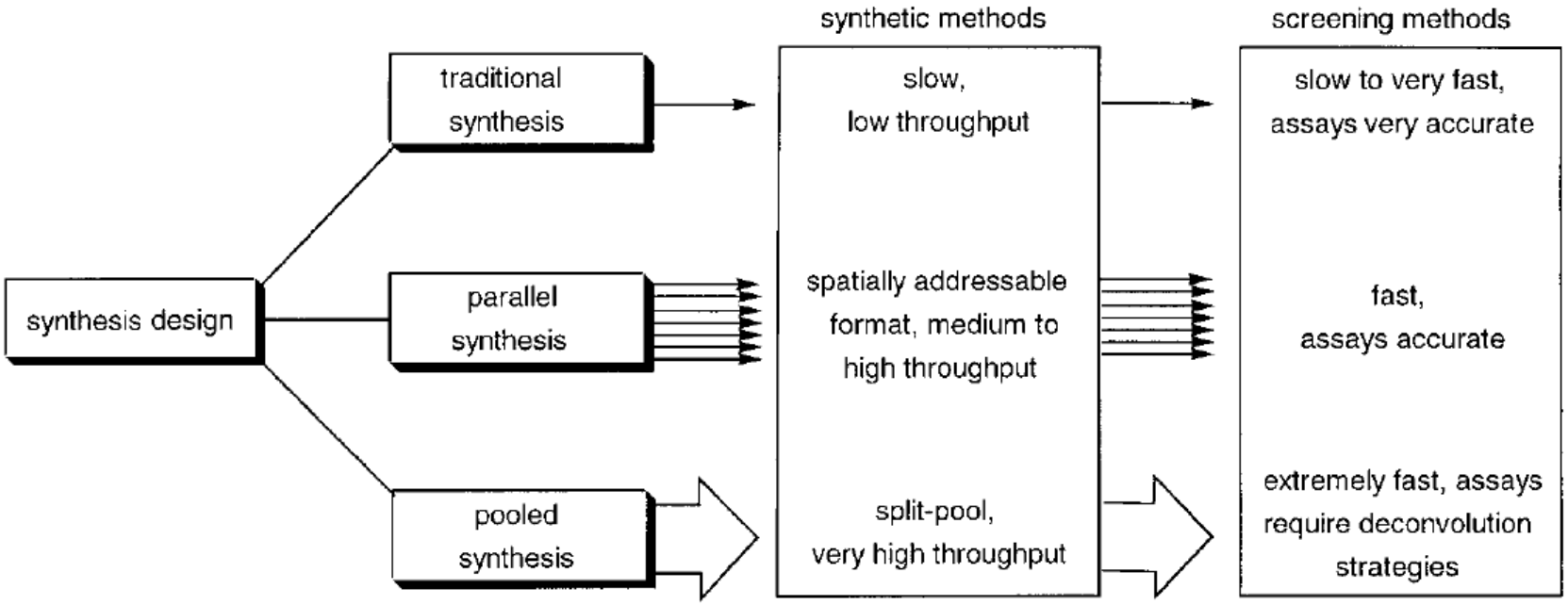
Discovery and Optimization Process



Adapted from B. Jandeleit et al., *Angew. Chem. Int. Ed.* ***1999, 38, 2494-2532.***

Synthesis & Screening



B. Jandeleit et al., *Angew. Chem. Int. Ed.* ***1999, 38, 2494-2532.***

Analytical High-Throughput Techniques I

- (Time-resolved) infrared thermography: reaction rates of exothermic reactions
- Resonance-enhanced multiphoton ionization (REMPI): High-throughput screening of combinatorial catalyst libraries. The technique is based on the in situ photoionization of the reaction products by a tunable UV laser. The resulting photoelectrons or photoions under the conditions of resonance-enhanced multiphoton ionization (REMPI) are detected by an array of microelectrodes
- Scanning mass spectrometry: Investigation of selectivities
- Reactive dyes: Most straightforward method to qualitatively screen for catalytic activities.

Analytical High-Throughput Techniques II

- UV/Vis-spectroscopy: Parallel monitoring of reactions; wavelength tuned to the absorption band of the analyte of interest. Sensitivity can be improved using fluorescence based assays.
- Non-dispersive infrared (NDIR) analysis: Parallelized on-line analysis of gas streams. Limited to not too complex samples.
- Circular dichroism (CD) has been largely used for screening of enantioselective catalysts, often in conjunction with liquid chromatography for more complex samples.

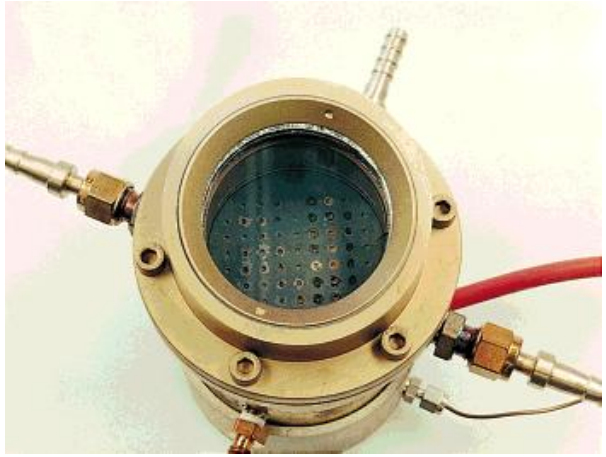
Analytical High-Throughput Techniques III

- Acoustic-wave sensor systems have been used as analytical high-throughput screening system for the identification and quantification of volatile substances in combinatorial chemical libraries. Measurements are performed using arrays of acoustic-wave thickness-shear mode sensors in the MHz-range coated with different chemically sensitive films.
- Flow-through NMR

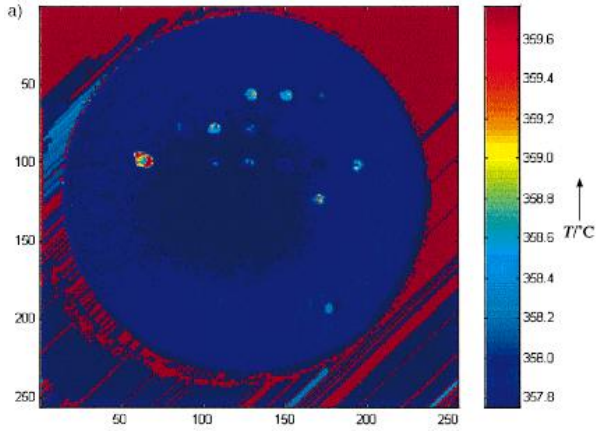
Analytical High-Throughput Techniques IV

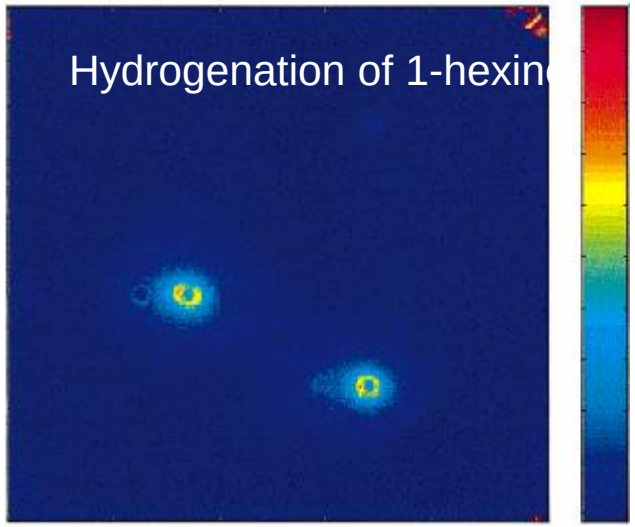
- Microfluidic devices, which integrate chemical transformations and analysis on the same chip represent a promising approach for parallelized high-throughput screening of catalysts with minute material consumption.
- Chromatography and electrophoresis

IR-Thermography

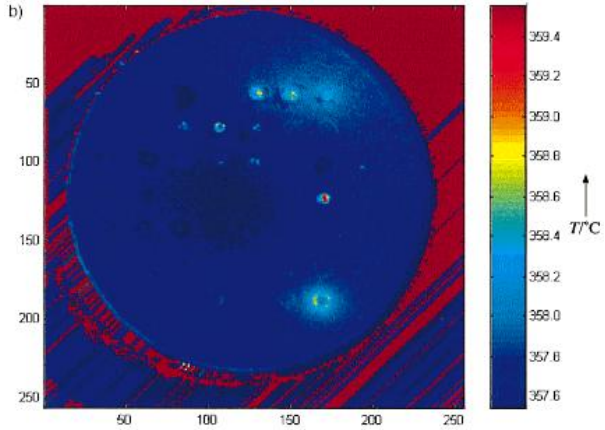


Oxidation of isooctane



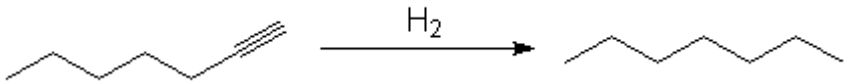


Oxidation of toluene

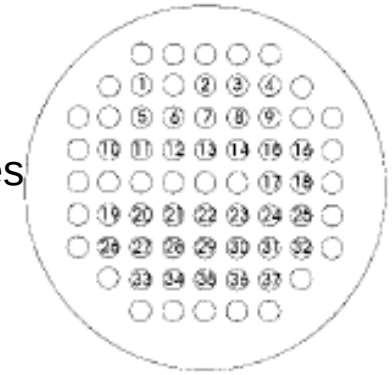


A. Holzwarth, H.-W. Schmidt, W.F. Maier, *Angew. Chem.* ***1998, 110, 2788-2792.***

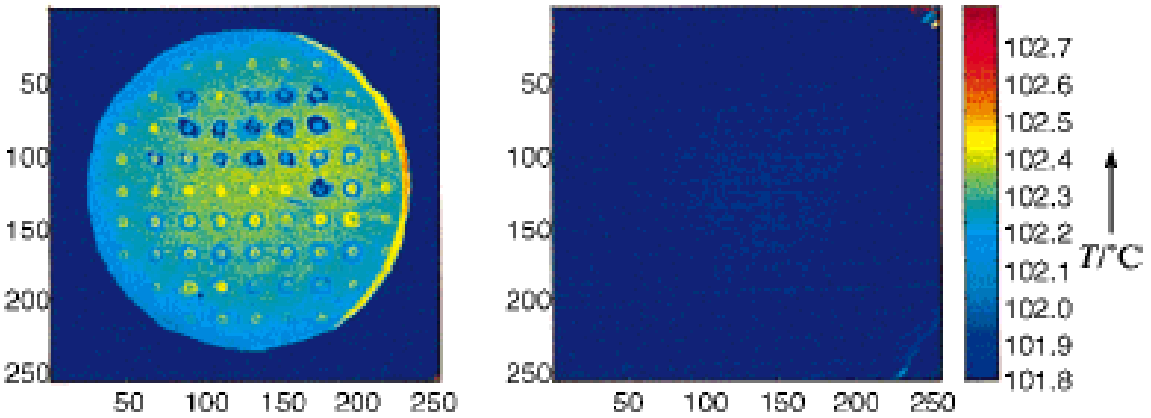
IR-Thermography



Catalysts:
amorphous
microporous mixed oxides
(AMM)

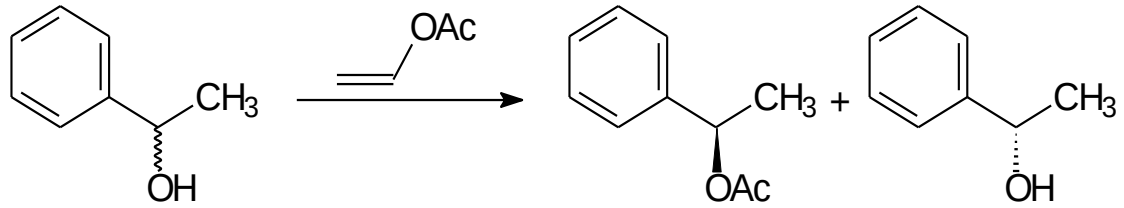


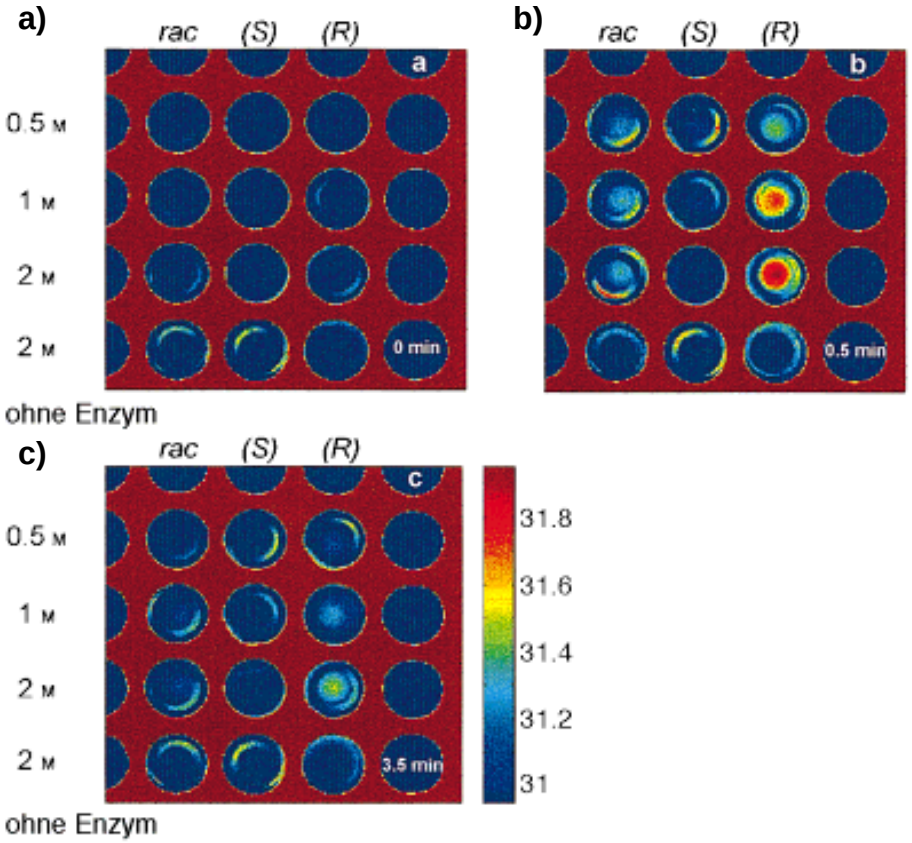
1	Ir_1Ti	14	Ni_5Ti	27	Zn_5Si
2	Pt_1Ti	15	Rh_5Ti	28	V_5Si
3	Pt_2Ti	16	Ru_5Ti	29	Mn_3Si
4	Pt_5Ti	17	Cu_5Ti	30	Mn_5Si
5	Zn_5Ti	18	Cu_5Si	31	Fe_5Si
6	V_5Ti	19	Pd_1Si	32	$Fe_{10}Si$
7	Mn_3Ti	20	Pd_5Si	33	Ir_2Si
8	Mn_5Ti	21	Cr_5Si	34	Ir_5Si
9	Fe_5Ti	22	Co_5Si	35	Pt_1Si
10	Pd_1Ti	23	Ni_5Si	36	Pt_2Si
11	Pd_5Ti	24	Rh_5Si	37	Pt_5Si
12	Cr_5Ti	25	Ru_5Si		
13	Co_5Ti	26	Ti_5Si		



A. Holzwarth, H.-W. Schmidt, W.F. Maier, *Angew. Chem.* ***1998, 110, 2788-2792.***

IR-Thermographie

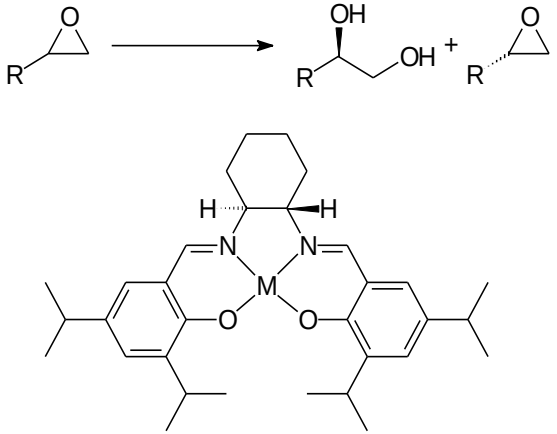


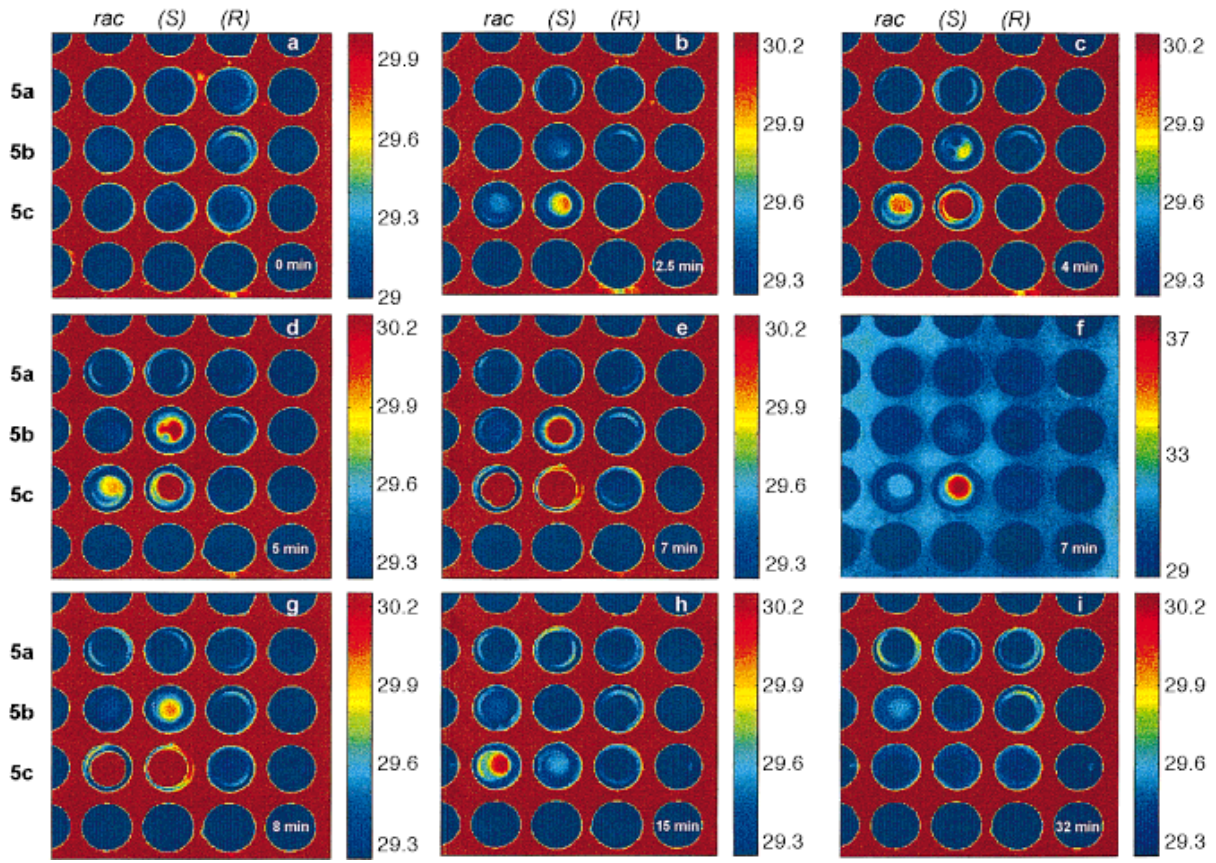


Time resolved IR thermography: Lipase catalyzed enantioselective acylation of 1-phenylethanol after a) 0, b) 0.5 and c) 3.5 min.

M.T. Reetz, M.H. Becker, K.M. Kühling, A. Holzwarth, *Angew. Chem.* ***1998, 110, 2792-2795.***

IR-Thermography

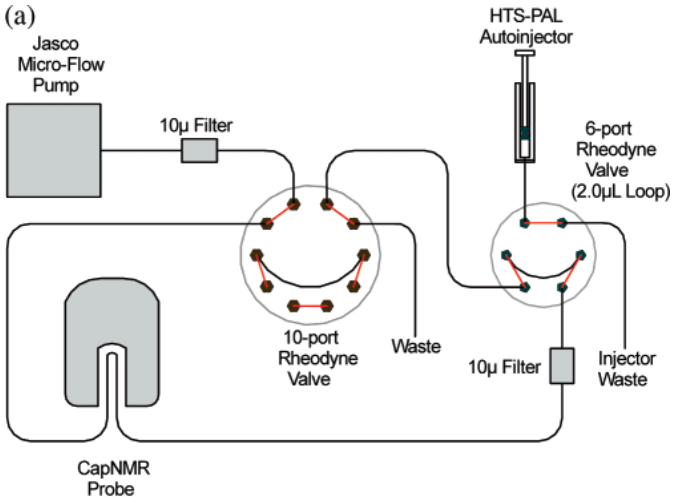


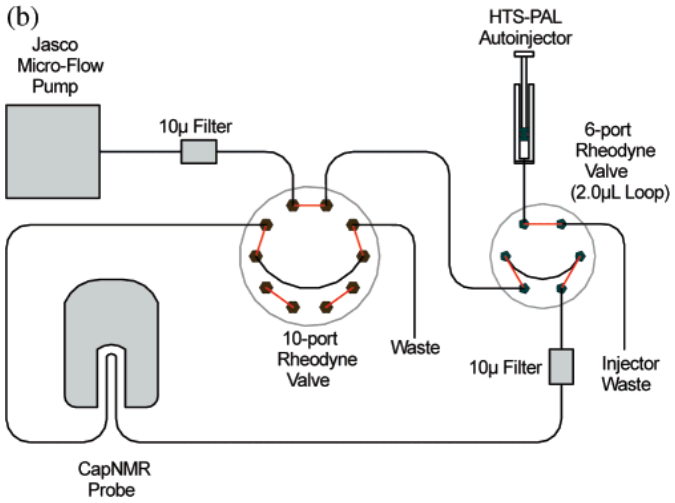


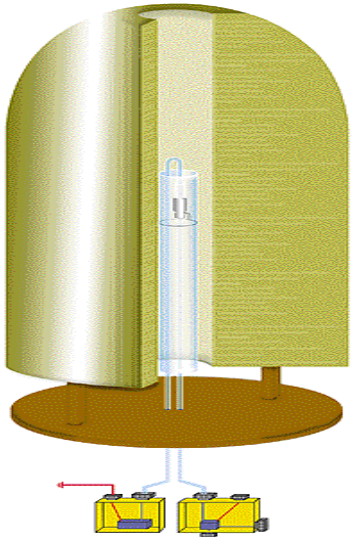
Zeitaufgelöste IR-thermographische Aufnahme der Hydrolyse Von Benzylglycidol, katalysiert durch die Metallkomplexe (S,S)-Mn-Salen (a), (S,S)-Cr-Salen (b), (S,S)-Co-Salen (c) nach a) 0, b) 2.5, c) 4, d) 5, e) 7, g) 8, h) 15 und i) 32 min. In (f) ist dasselbe Bild wie in (e) gezeigt, die Temperaturskala erstreckt sich hier aber über 10 K. Neben den Balken sind die zu den jeweiligen Farben gehörenden Temperaturen [°C] angegeben.

M.T. Reetz, M.H. Becker, K.M. Kühling, A. Holzwarth, *Angew. Chem.* ***1998, 110, 2792-2795.***

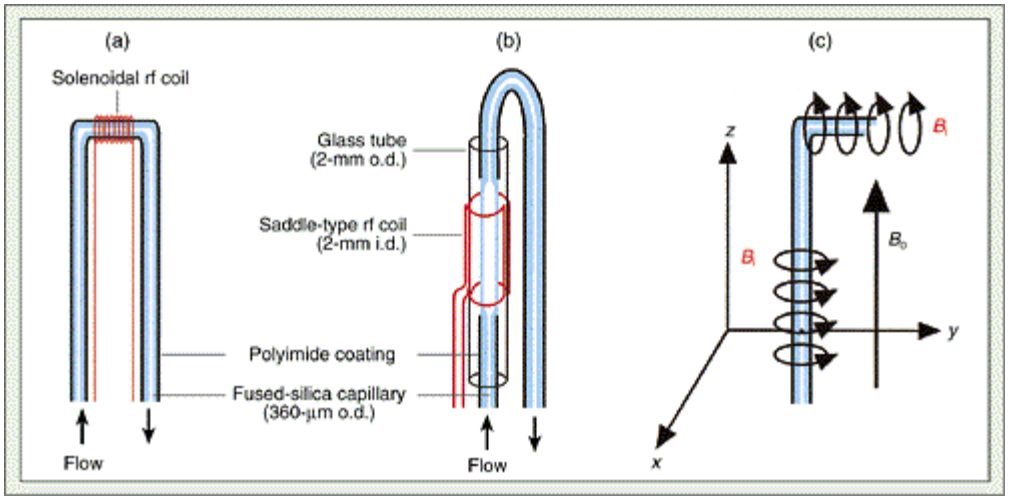
On-line NMR







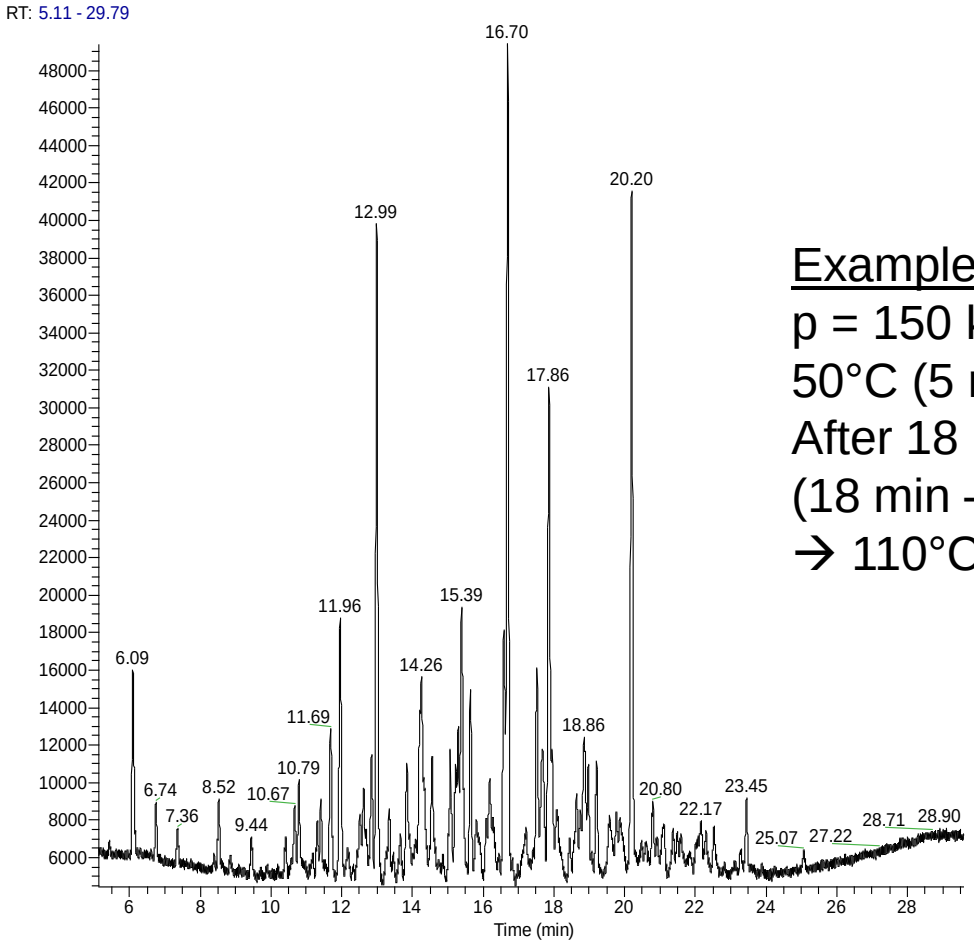
P. Gfrörer, J. Schewitz, K. Pusecker, E. Bayer, *Anal. Chem.* ***1999, 71, 315A-321A.***



Chromatography

- Why Gas Chromatography (GC) in High-Throughput Screening?
- Sample Properties
- Separation Efficiency
- Sample Throughput
- Techniques to Screen Reactions
- Future Developments: How to Increase the Sample Throughput?

Gasoline Analysis



Example: Gasoline Fraction

p = 150 kPa,

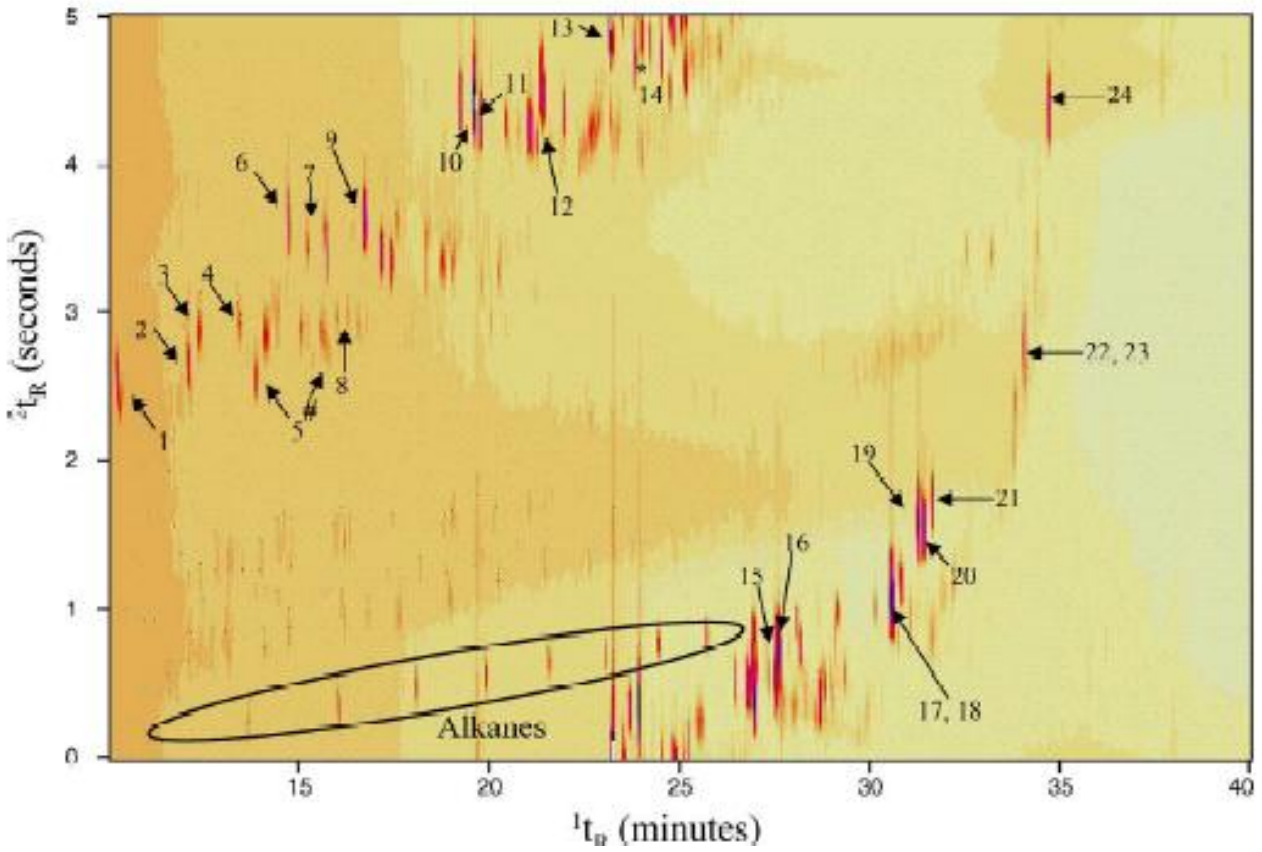
50°C (5 min) → 200°C @ 5 K/ min

After 18 min everything is eluted:

(18 min – 2 min) * 5 K/ min = 80 K

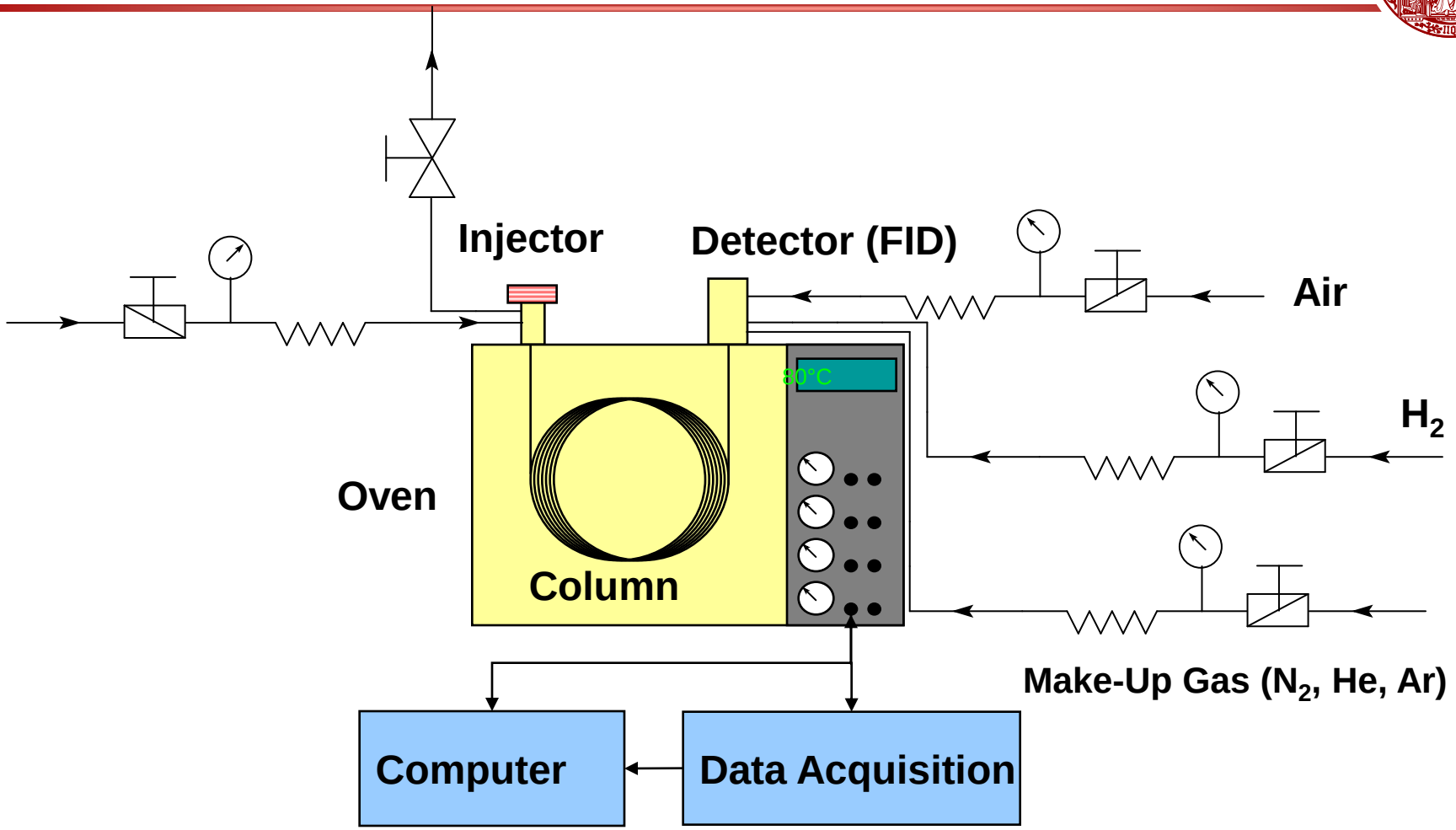
→ 110°C, T_{iso} = 80°C

2D Mapping: Crude Oil Analysis



R. Ong, S. Lundstedt, P. Haglund, P. Marriott, *J. Chromatogr. A* **2003**, *1019*, 221-232.

GC Instrumentation



Injection Techniques:General

- Biggest impact on separation **efficiency**, **reproducibility** and **correctness**
- Small **sample volume** (separation efficiency , overloading). For packed columns, sample size ranges 0.1 µl up to 20 µl. Capillary columns typically need around 0.1 µl
- No influence on **carrier gas flow**
- Amount and volume should be **reproducible → internal standard**
- Sample must **not decompose** (except for pyrolysis GC)
- No **fractioning in the injector** (split flow!)
- The temperature of the sample port is usually about **50°C** higher than the boiling point of the least volatile component of the sample

Combined Sample Injection Techniques

Headspace-Technique: suitable for volatile analytes of medium concentration, solid samples, destructive matrix

Purge-and-Trap-Technique: suitable for highly volatile analytes of low concentration, solid samples, destructive matrix

Pyrolysis: suitable for non-volatile samples, wanted thermal degradation

SPME solid phase micro-extraction: suitable for volatile analytes of medium concentration, solid samples, destructive matrix, selective extraction, reduction of organic solvents

‘Non-volatile Compounds’

GC analysis desirable because of

- high separation efficiency
- short analysis time
- already existing protocols
- no other technique available
- personal preference
- improving sensitivity
- labelling functional groups

→ **Derivatization**

Derivatization

- Lowering polarity
- Increasing volatility
- Increasing stability
- No side-reactions
- Fast & complete
- Improving chromatographic properties: sharp peaks
- GC-MS: simple/ characteristic fragmentation pattern
- Spectroscopic properties: GC-FT-IR

Detection

- Short response time: TCD: 0.1 s, FID: 0.001 s
- Small detection volume, no mixing of separated analytes
- Classification:

  Concentration dependent detectors

  Mass flow dependent detectors
- Sensitivity and Response

  high responsitivity: signal-to-substance amount

  low detectivity: reciprocal of limit of detection (LOD)
- Linearity: signal linear dependent on concentration or mass flow
- Selectivity: relative sensitivity of the detector for two substances or substance classes

$$\text{selectivity} = a_i/a_j$$

Signal

Concentration dependent detectors

- Signal influenced by physical properties of the carrier gas and analytes
- TCD, ECD, GC-MS (SIM-mode)

$$y_i = a_i' c_i = a_i \frac{dQ_i}{dV}$$

Mass flow dependent detectors

- Signal influenced only by physical properties of analytes
- FID, TID, FPD

$$y_i = a_i \frac{dQ_i}{dt}$$

$$A_i = \int_S^E y_i dt$$

y_i = signal
c_i = concentration of i
a_i = response factor
Q_i = total amount of i
A_i = peak area

Response

Signal-to-Substance Amount

Concentration dependent detectors

- TCD, ECD, GC-MS (SIM-mode)

$$a_i = \frac{y_i}{c_i}\left[\frac{mV}{mg/ml}\right]$$

Mass flow dependent detectors

- FID, TID, FPD

$$a_i = \frac{y_i}{m_i}\left[\frac{A}{g/s}\right]$$

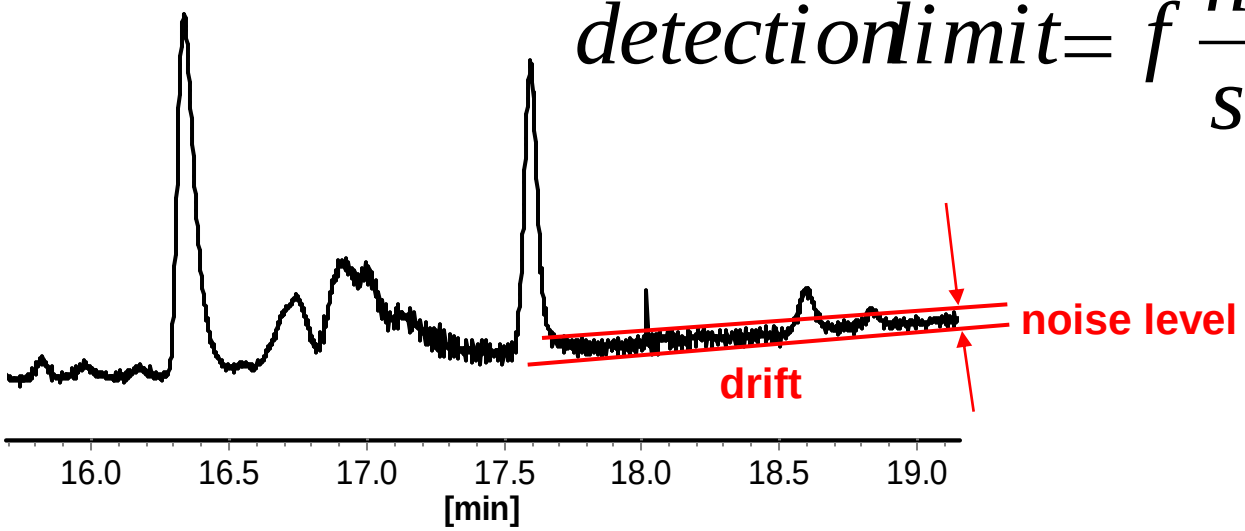
y_i = signal
c_i = concentration of i
a_i = response factor
m_i = mass flow

Response is substance dependent and detector specific

Limit of Detection (LOD)

Peak: at least twice as high as the noise level!

$$detection\,limit = f\,\frac{noise\,level}{sensitivity}$$

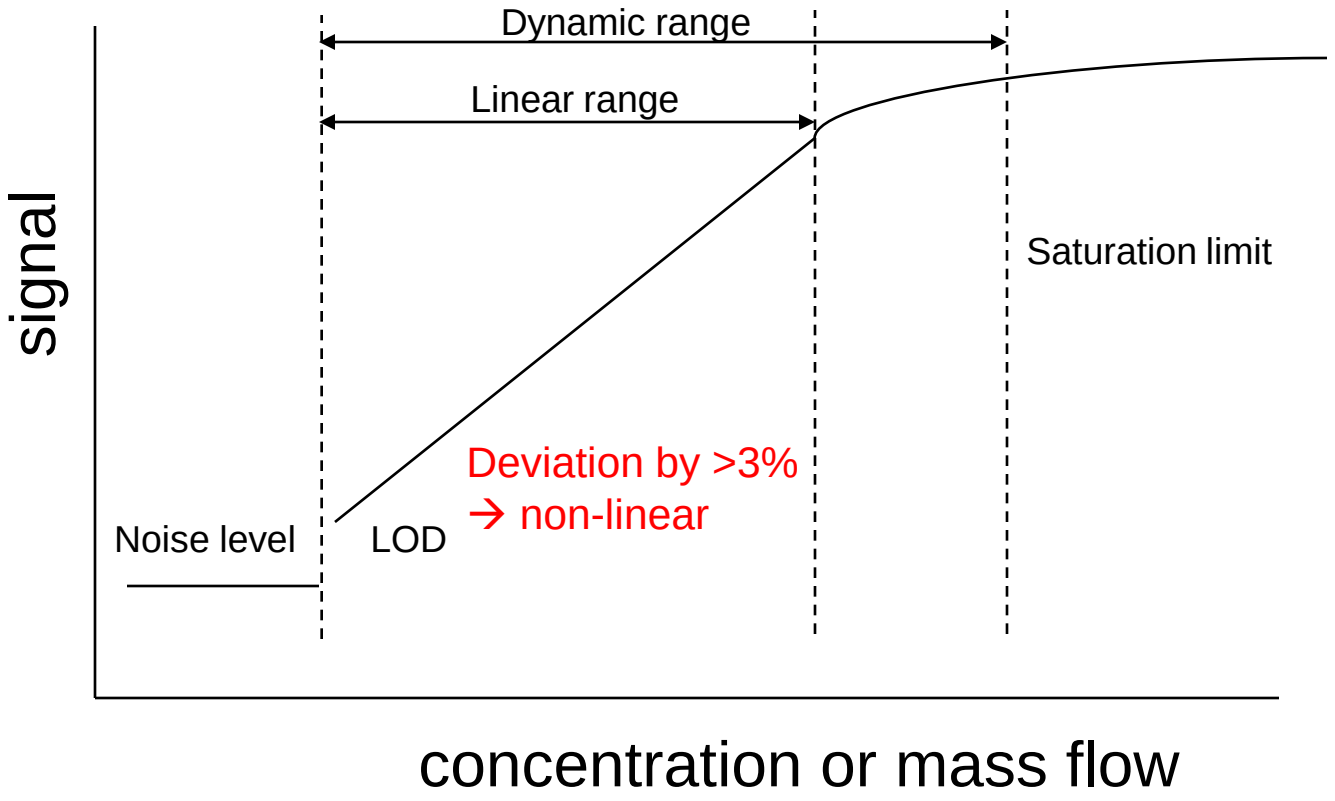


- Noise level: statistical,high frequent ripple of signal
- Drift: change of baseline (not caused by detector!)
- Periodcal unsteadiness: caused by electronics

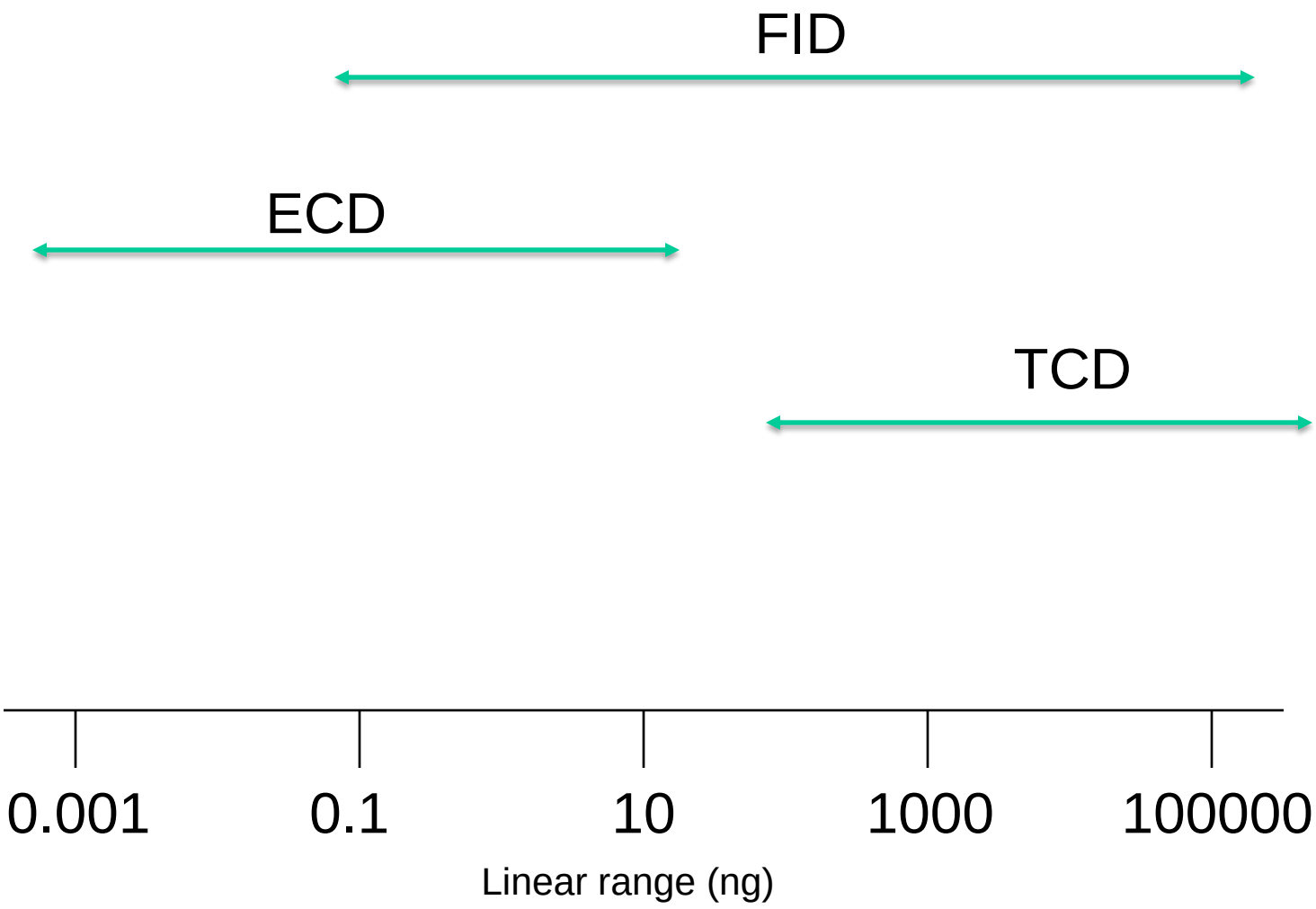
Linearity

Ideal: signal ~ concentration or mass flow

→ peak area ~ sample amount



Comparison of Dynamic Ranges



Finding the Separation Optimum

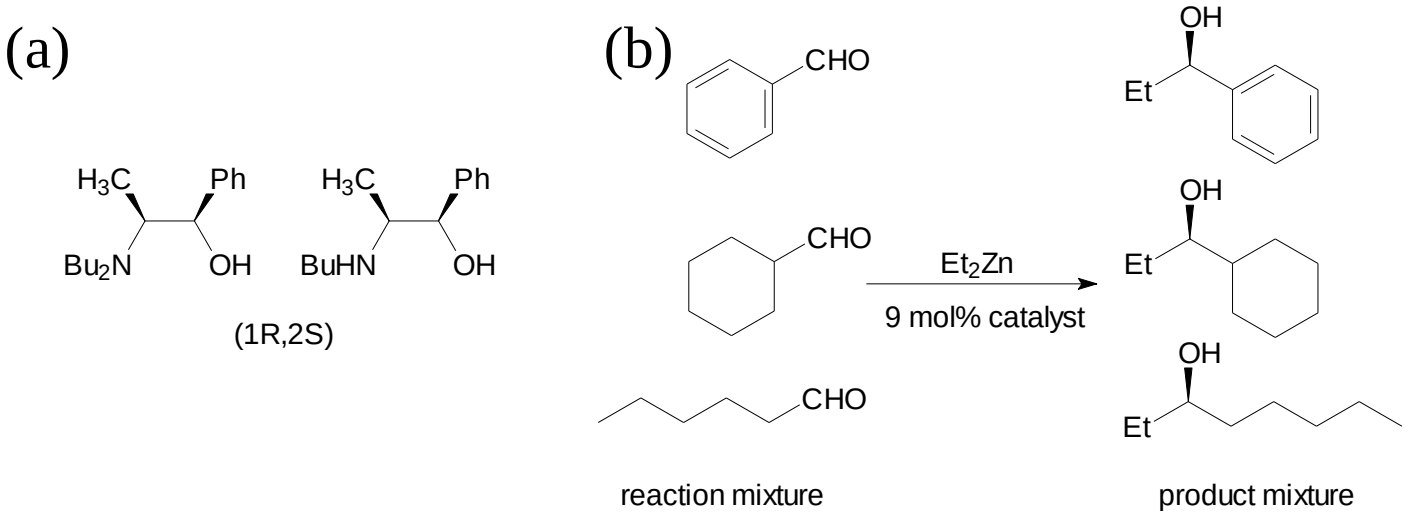
Four steps are necessary:

1. Selection of Stationary Phase (SP)
   a) Polarity
   b) (Enantio-) Selectivity (Achiral/ Chiral CSP)
2. Selection of Carrier Gas
   a) Depending on Detector
   b) Influences the Efficiency
3. Optimum Separation Temperature
   a) Isothermal Separation
   b) Temperature Program
4. Optimum Carrier Gas Flow
   a) Isobar
   b) Pressure Program

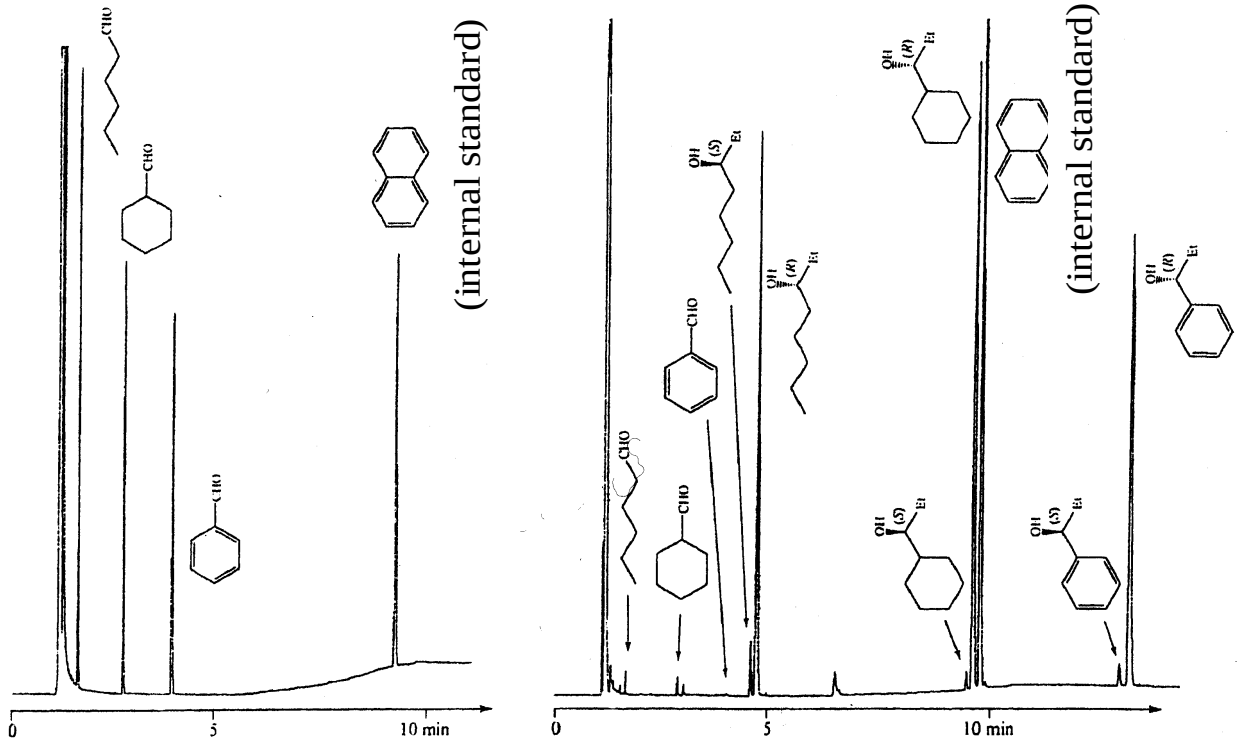
Screening Techniques

- Off-line Screening
  - Sequential Analysis
  - Parallelized Analysis
- On-line Screening
  - Sequential Analysis in Batch Reactors
  - Parallelized Reactors
  - HT-Multiplexing GC
- Integration of Reaction and Separation

Off-Line Screening: Sequential Analysis

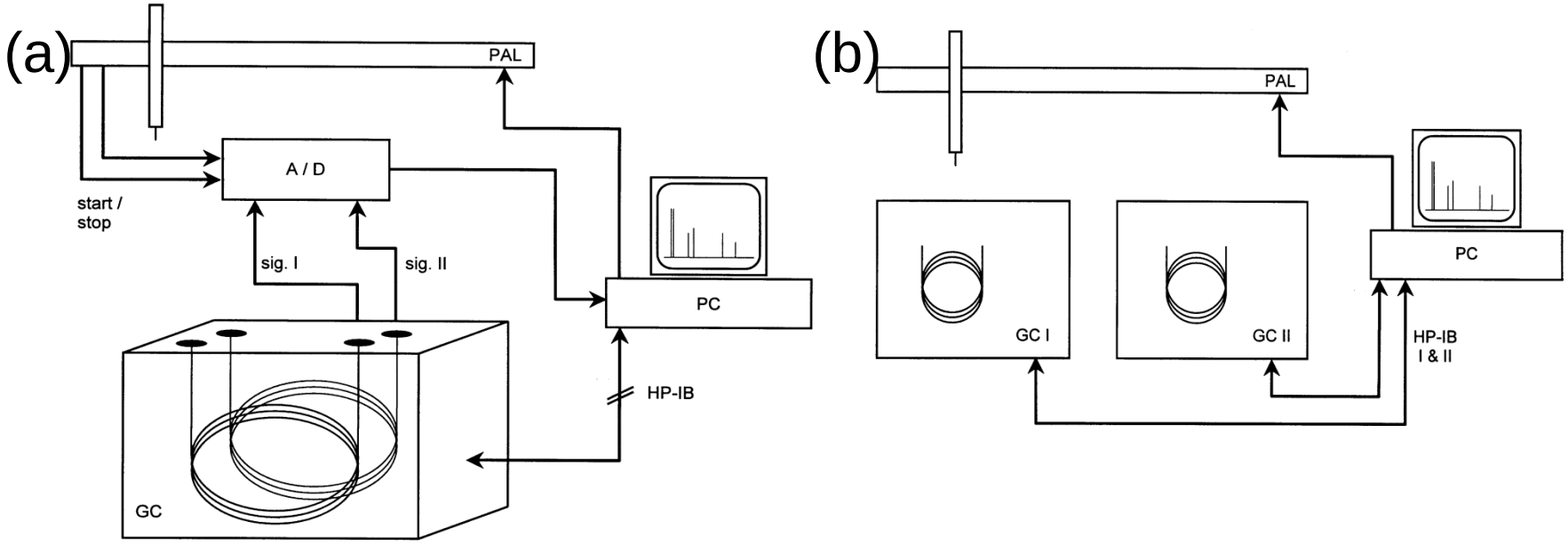


Off-Line Screening: Sequential Analysis

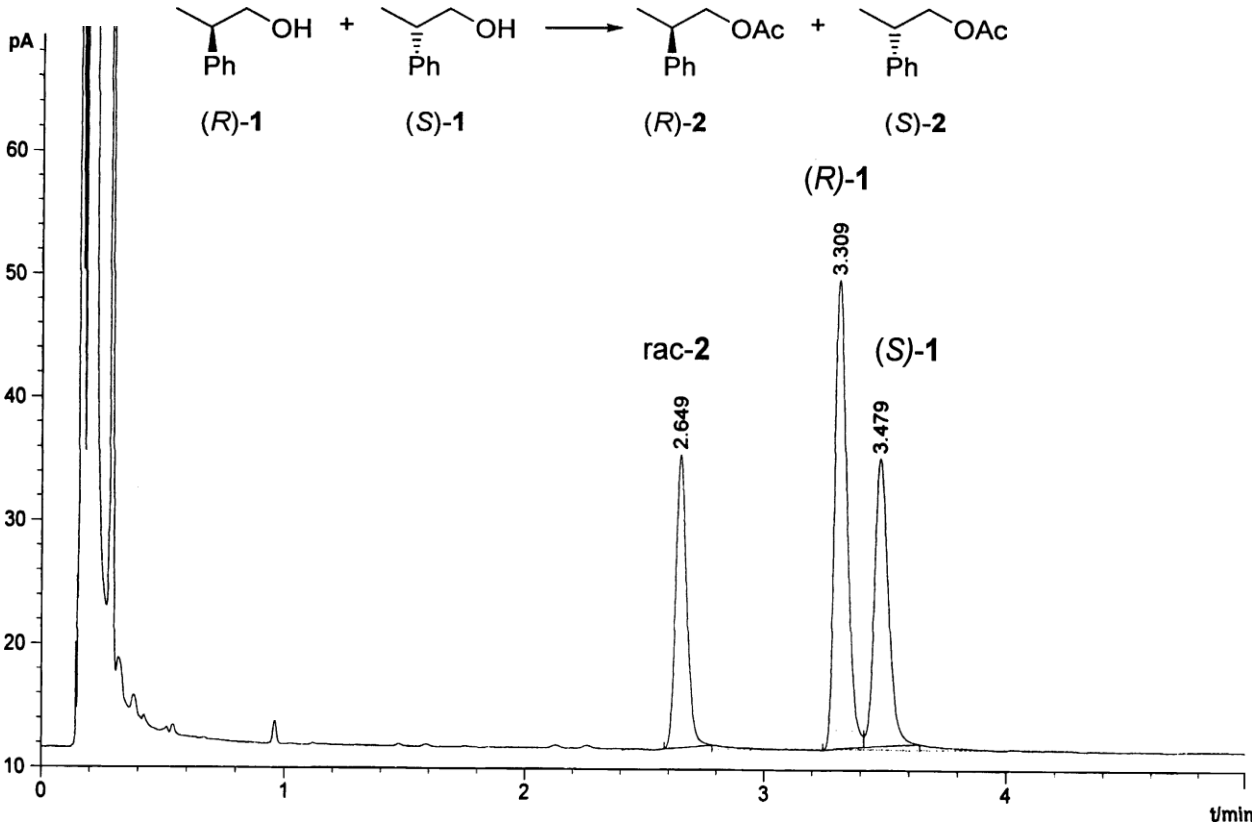


Gas chromatogram of the reaction mixture (left) and GC separation of a representative product mixture obtained by multisubstrate high-throughput screening using (1*R*,2*S*)-N,N'-dibutylnorephedrine as the catalyst (right)

Off-Line Screening: Parallelized Analysis

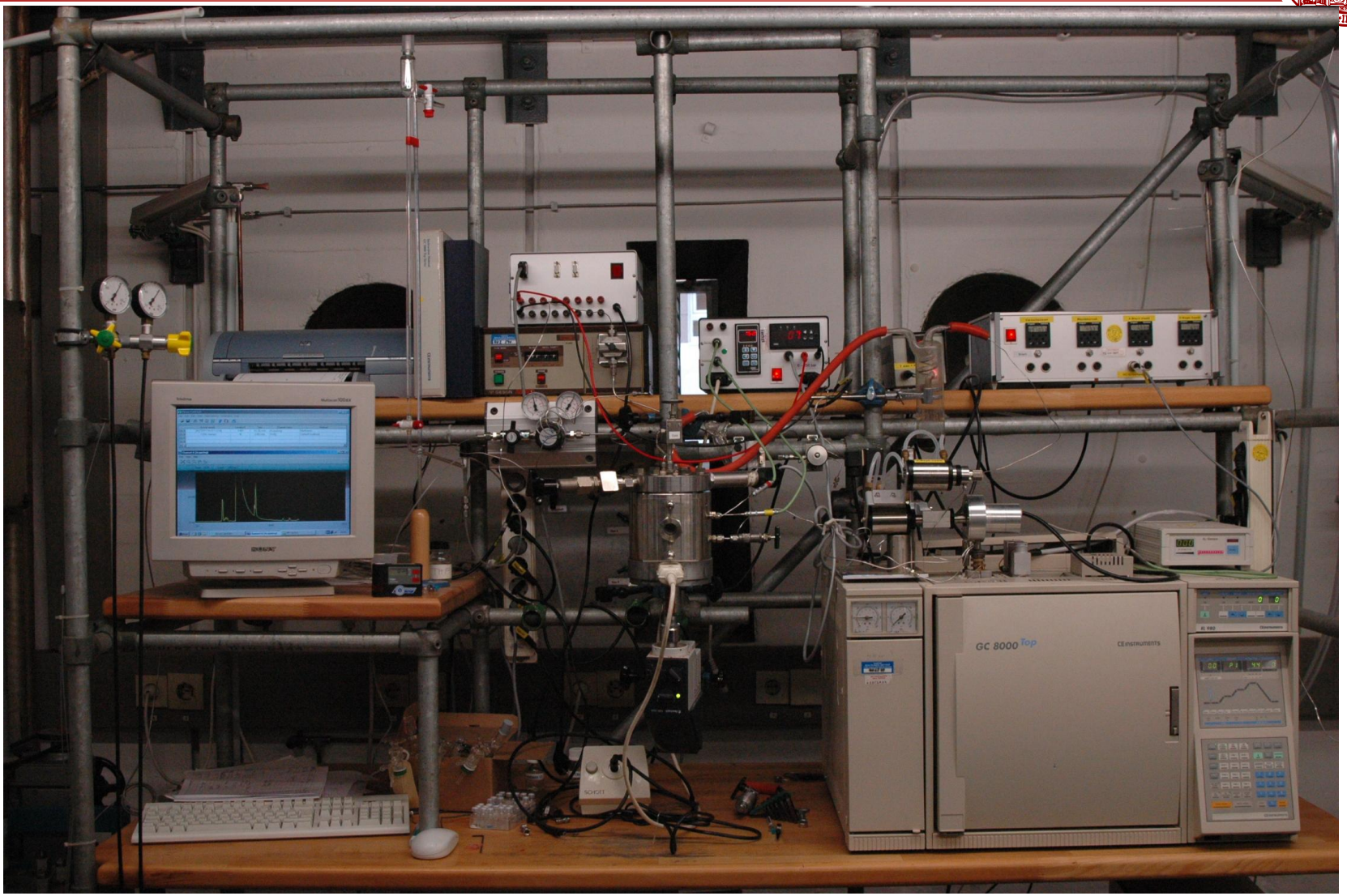


Off-Line Screening: Parallelized Analysis

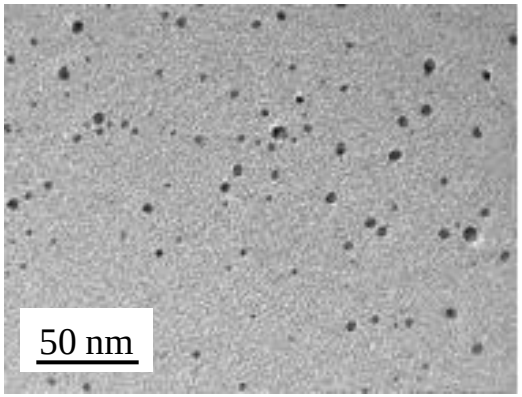


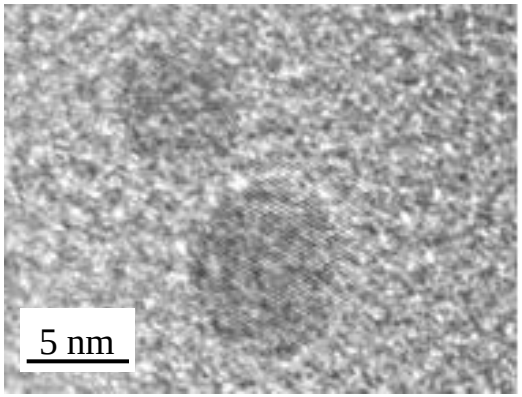
Gas chromatogram of the reaction mixture of the acylation-based kinetic resolution of (R)- and (S)-2-phenyl-1-propanol. 2,3-Di-O-ethyl-6-O-tert.-butyldimethylsilyl-β-cyclodextrin was used as CSP

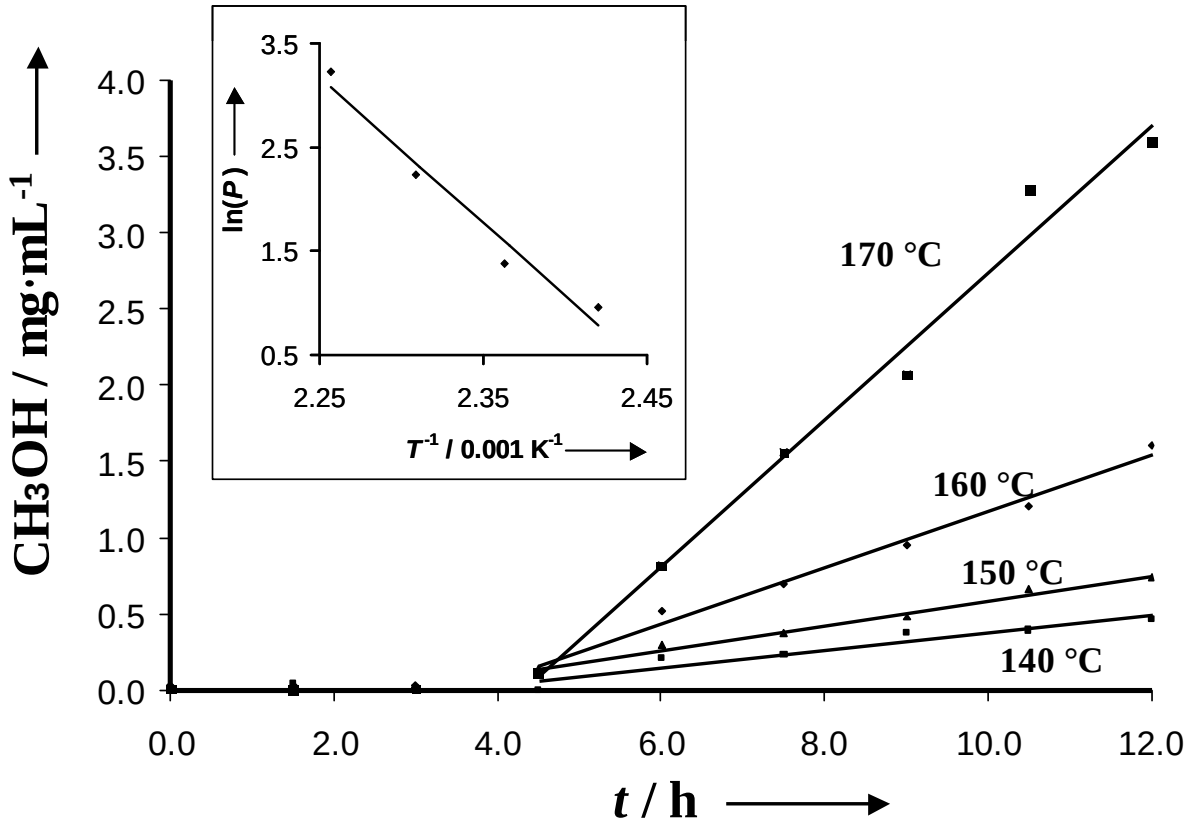
On-Line Screening: Sequential Analysis



Methanol Synthesis







S. Vukojevic, O. Trapp, J.-D. Grunwaldt, C. Kiener, F. Schüth, *Angew. Chem.* **2005**, *117*, 8192 -8195.

Integration of Reaction and Separation

Modes to Integrate Catalysis and Separation

Microreactor/ Flow-Reactor Approach

- ✓ Offline analysis
- ✓ Preparative mode

S.V. Ley, K.F. Jensen, A. Kirschning
G. Jas, A. Kirschning, *Chem. Eur. J.* **2003**, *9*, 5708-5723.

Chromatographic Microreactor Approach

- ✓ Online analysis, online kinetics
- ✓ Easy to couple with analytical techniques
- ✓ Ideal to study fast processes ($k > 10^{-2}\ s^{-1}$)

On-column Reaction Chromatography

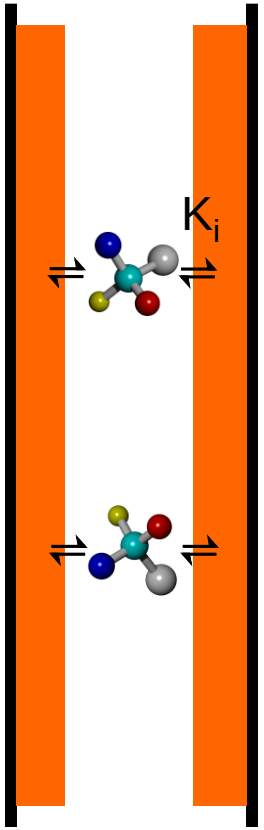
- ✓ Online analysis, online kinetics
- ✓ Selectivity of stationary phase
- ✓ Easy to couple with analytical techniques
- ✓ Ideal to study slower processes ($k < 10^{-2}\ s^{-1}$)
- ✓ Unified equation

- ➢ Educt purity
- ➢ Kinetics
- ➢ Thermodynamics
- ➢ No competing reactions
- ➢ Educt libraries
- ➢ High-throughput possible

O. Trapp, *J. Chromatogr. A* **2008**, *1184*, 160-190.

Thermodynamics & Kinetics

Thermodynamics



k‘, *K*
Van-Deemter-Golay
(Diffusion)

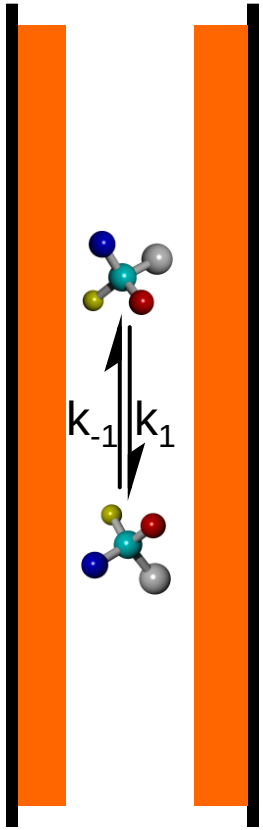
$$H = A + \frac{B}{u} + Cu$$

$$H = \frac{B}{u} + (C_M + C_S)u$$

$$H = \frac{2D_M}{u} + \left(\frac{1 + 6k' + 11k'^2}{96(1+k')^2} \cdot \frac{d_c^2}{D_M} + \frac{2k'}{3(1+k')^2} \cdot \frac{d_f^2}{D_S} \right) u$$

Retention increment
($\Delta\Delta G$, $\Delta\Delta S$, $\Delta\Delta H$)

Kinetics



k(*T*), $\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$
Unified Equation

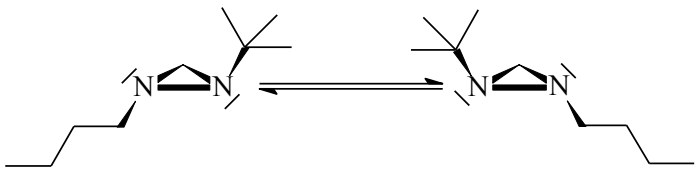
→**Interconversions**
(Dynamic Chromatography)

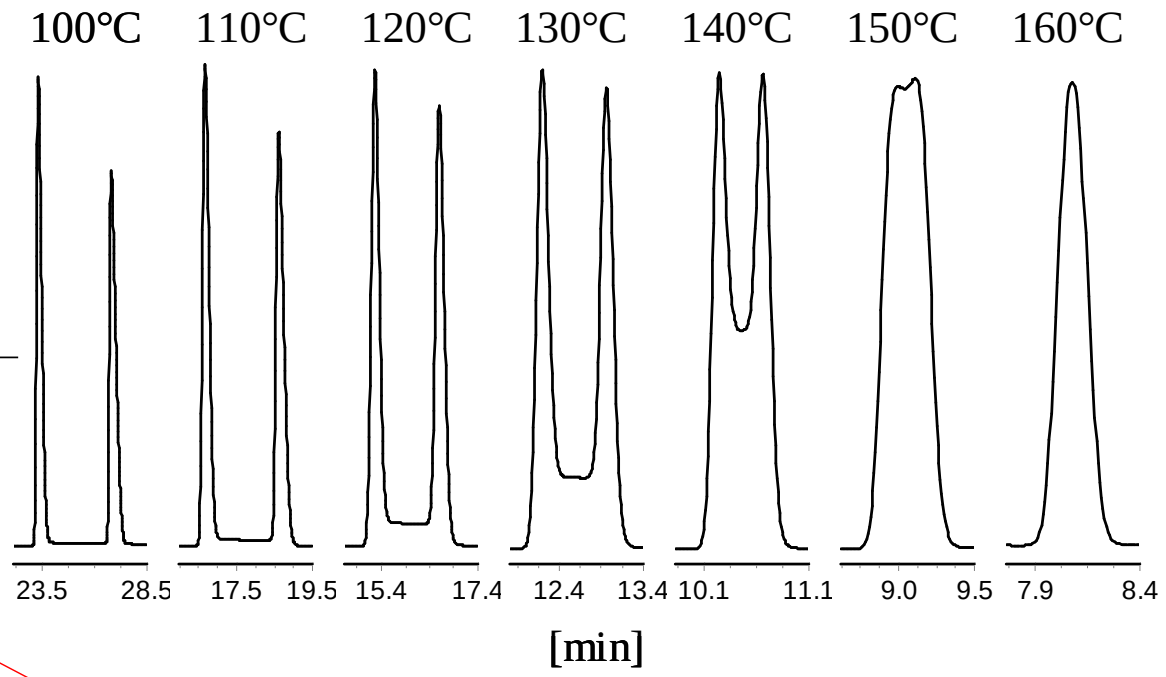
→**Conversions**
(on-column Reaction Chromatography)

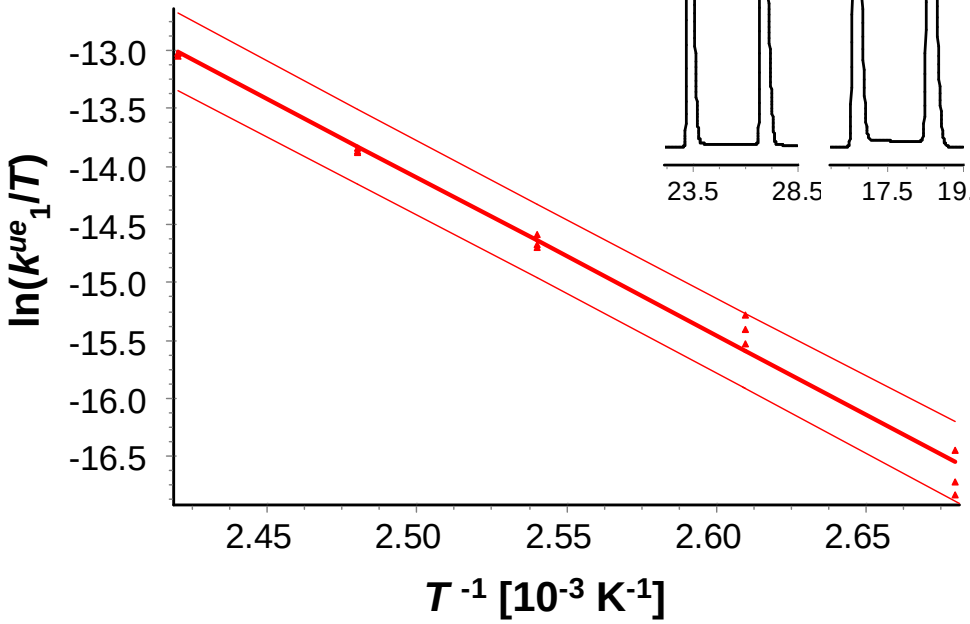
1-*n*-Butyl-2-*tert.*-butyldiaziridine

DGC Experiment

25 m Chirasil-ß-Dex 500 nm





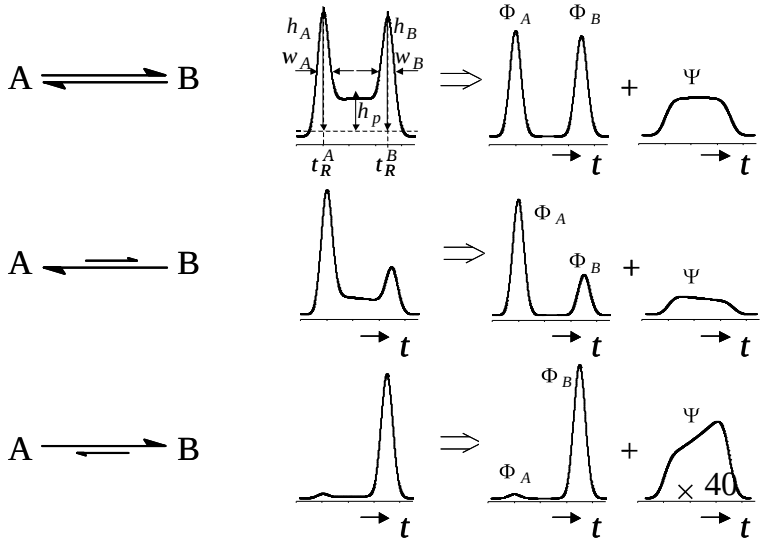


$\Delta H^{\ddagger} = 112.6 \pm 2.5$ kJ/mol

$\Delta S^{\ddagger} = -27 \pm 2$ J/(K mol)

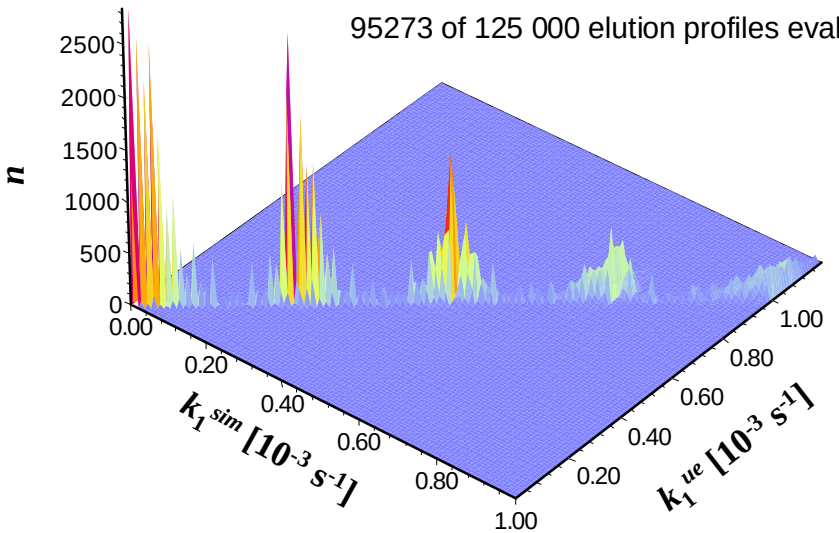
O. Trapp, Chirality **2006**, *18*, 489-497.

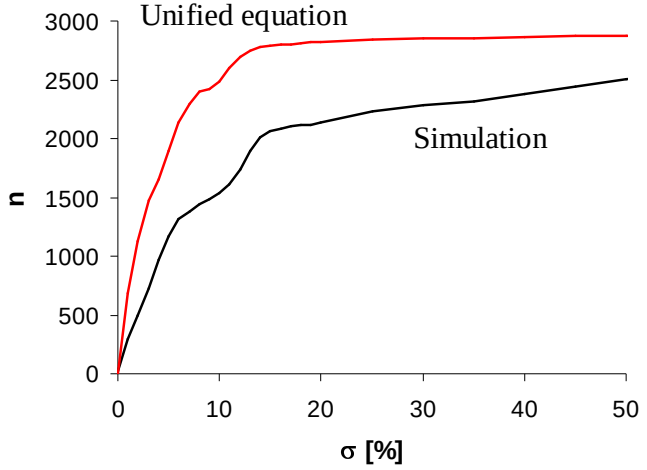
Unified Equation



$$k_1^{ue} = -\frac{1}{t_R^A}\left(\ln\left(B_0 e^{-\frac{A_\infty}{B_\infty}k_1^{ue}t_R^i}\left(\frac{100e^{-\frac{(t_R^B-t_R^A)^2}{8\sigma_B^2}} - h_p e^{-\frac{(t_R^B-t_R^A)^2}{2\sigma_B^2}}}{\sigma_B\sqrt{2\pi}} - \frac{100}{t_R^B-t_R^A}\right) + \frac{100B_0 + A_0\left(100 - h_p\left(1+\sqrt{\frac{2}{\pi N}}\right)\right)}{t_R^B - t_R^A}\right) - \ln\left(A_0\left(\frac{h_p - 100e^{-\frac{(t_R^A-t_R^B)^2}{8\sigma_A^2}}}{\sigma_A\sqrt{2\pi}} + \frac{100 - h_p\left(1+\sqrt{\frac{2}{\pi N}}\right)}{t_R^B - t_R^A}\right)\right)\right)$$

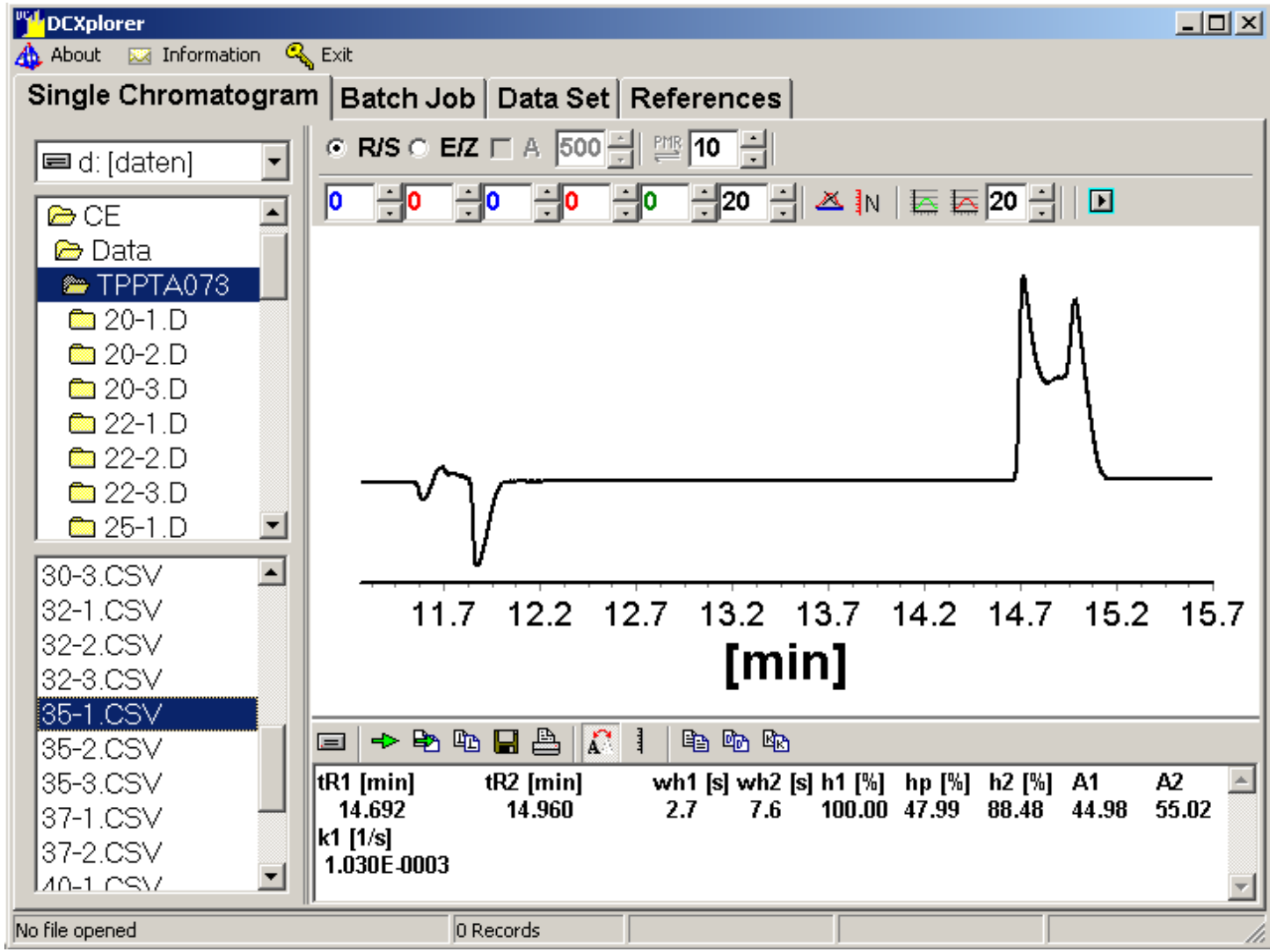
95273 of 125 000 elution profiles evaluated





O. Trapp, Anal. Chem. **2006**, *78*, 189-198.

DCXplorer


DCXplorer
About
Information
Exit
Single Chromatogram
Batch Job
Data Set
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35-2.CSV
35-3.CSV
37-1.CSV
37-2.CSV
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13.2
13.7
14.2
14.7
15.2
15.7
[min]
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tR2 [min]
wh1 [s]
wh2 [s]
h1 [%]
hp [%]
h2 [%]
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A2
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14.960
2.7
7.6
100.00
47.99
88.48
44.98
55.02
k1 [1/s]
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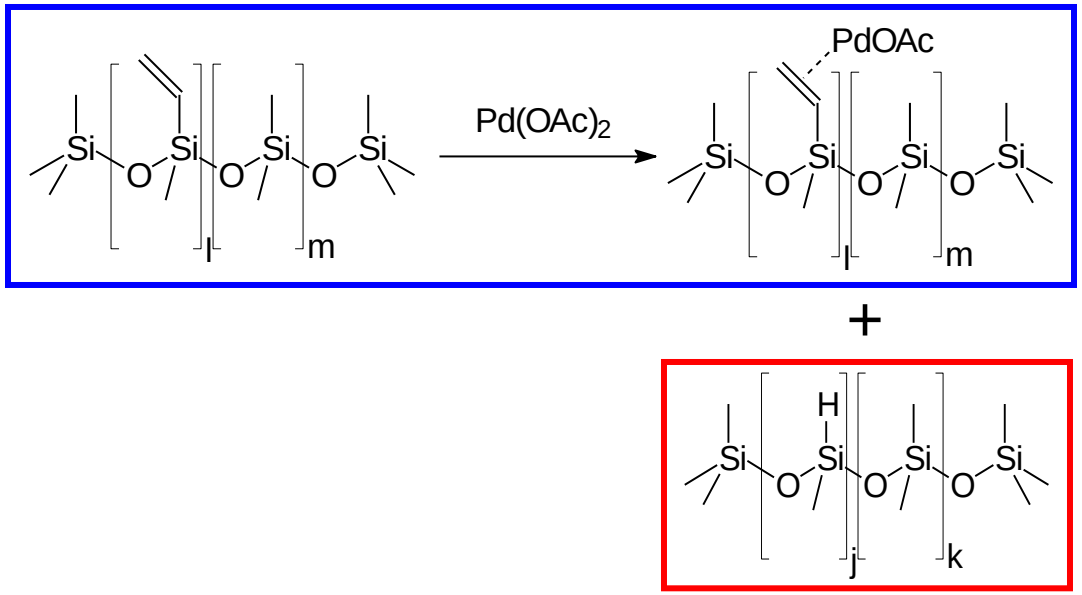
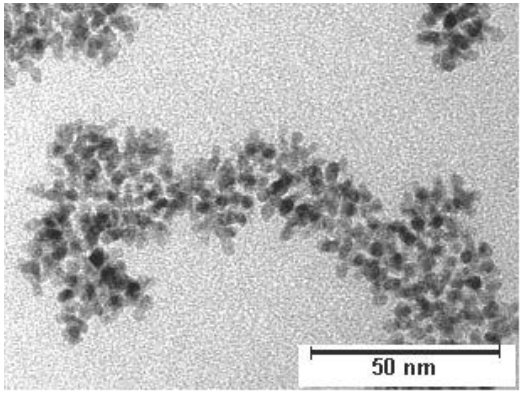
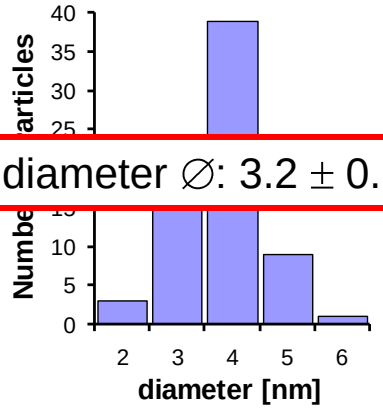
Catalysis

- Matching catalyst and reaction
- How fast?
- Kinetics, selectivity
- Activation parameters
- Mechanism
- Understanding → rational design
- High-throughput screening: large data sets
- Economic use of resources

Pd Nanoparticles





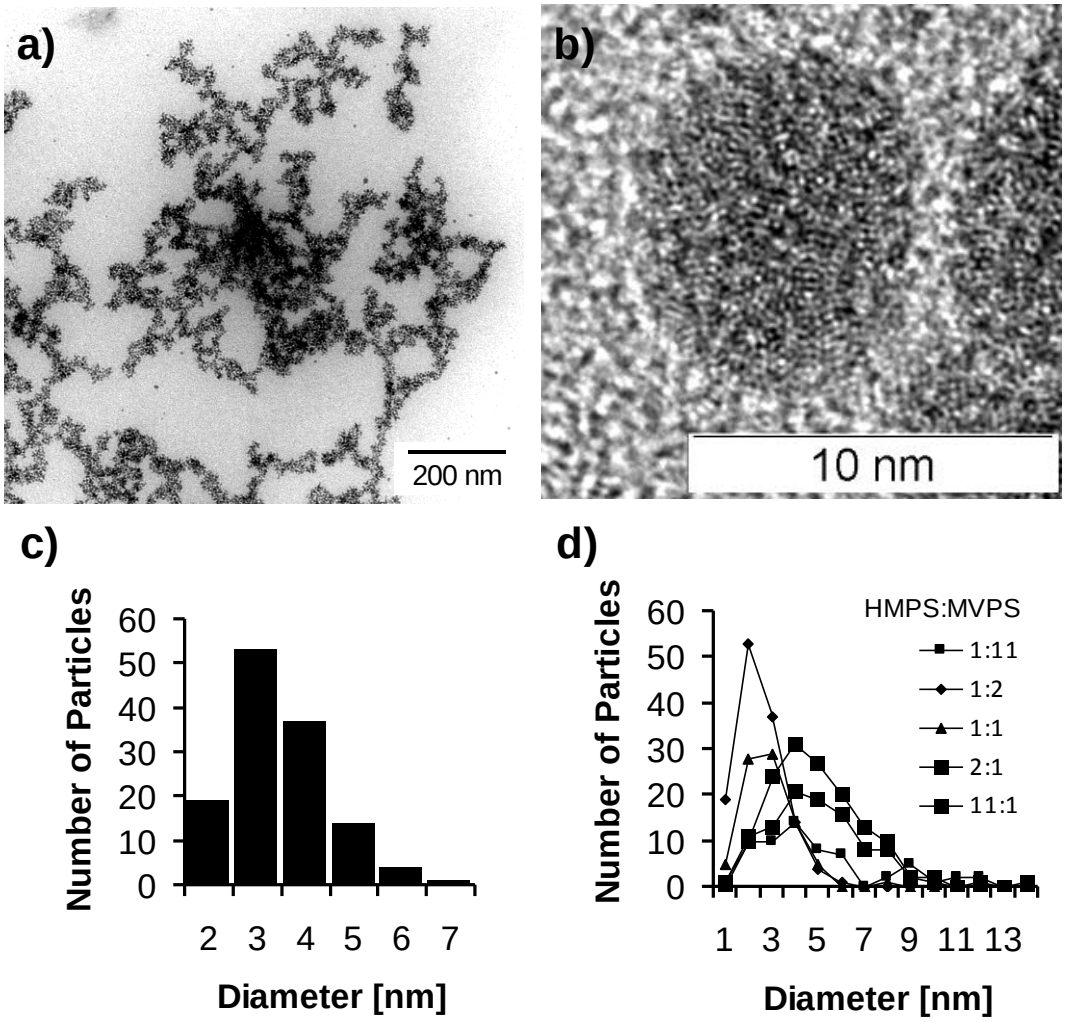


Mean diameter ∅: 3.2 ± 0.7 nm

- Reduction to Pd nanoparticles by Si-H
- Hydrosilylation → cross-linking of polysiloxanes
- Stabilization of particles by polysiloxane matrix
- free Si-OH groups on glass surfaces react with Si-H groups
  → permanently bonded

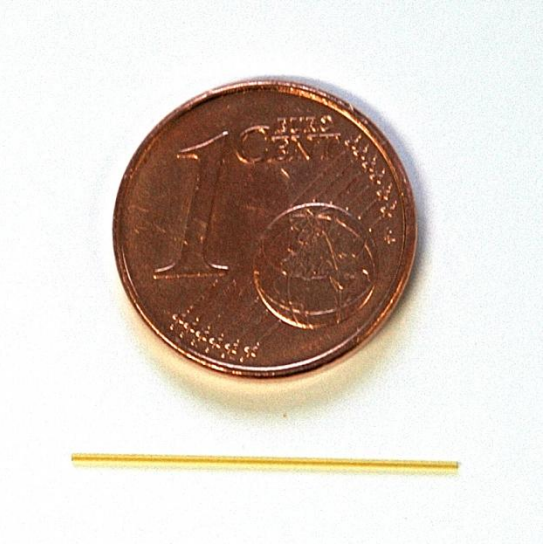
O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

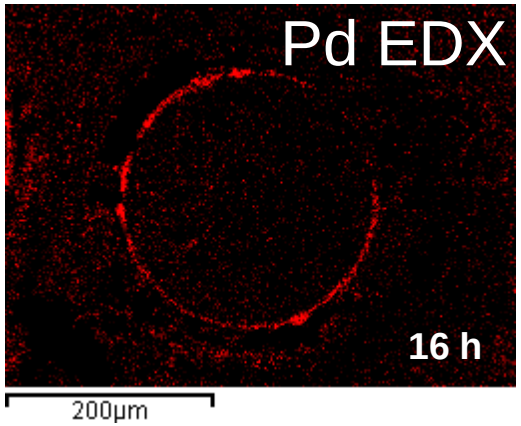
Property Tuning of Pd Nanoparticles



O. Trapp, S.K. Weber, S. Bauch, T. Bäcker, W. Hofstadt, B. Spliethoff, *Chem. Eur. J.* **2008,** 14, 4657-4666.

Hydrogenations with Pd Nanoparticles in a Capillary





Length: 2 cm fused-silica column

i.d. 250 µm, 250 nm film thickness

7.8 ng Pd/ cm → 0.73 pmol/ cm

= 26.6 billions Pd-nanoparticles/ cm

Coupled to a separation column:

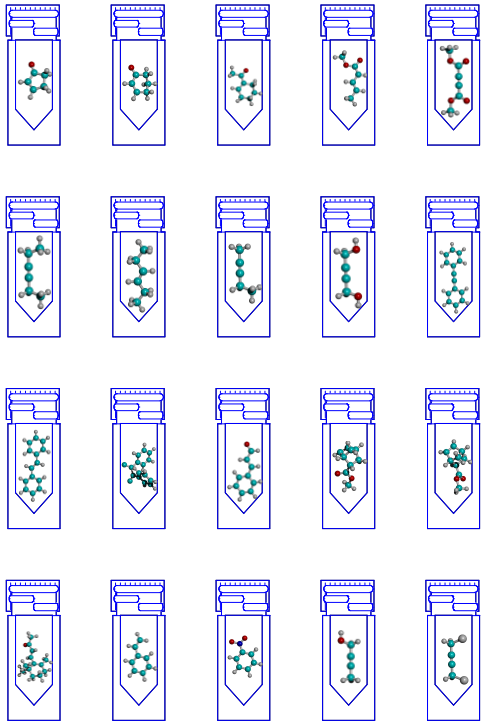
25 m GE SE-52 250 nm film thickness

(Poly(95%-dimethyl 5%-diphenyl)siloxane)

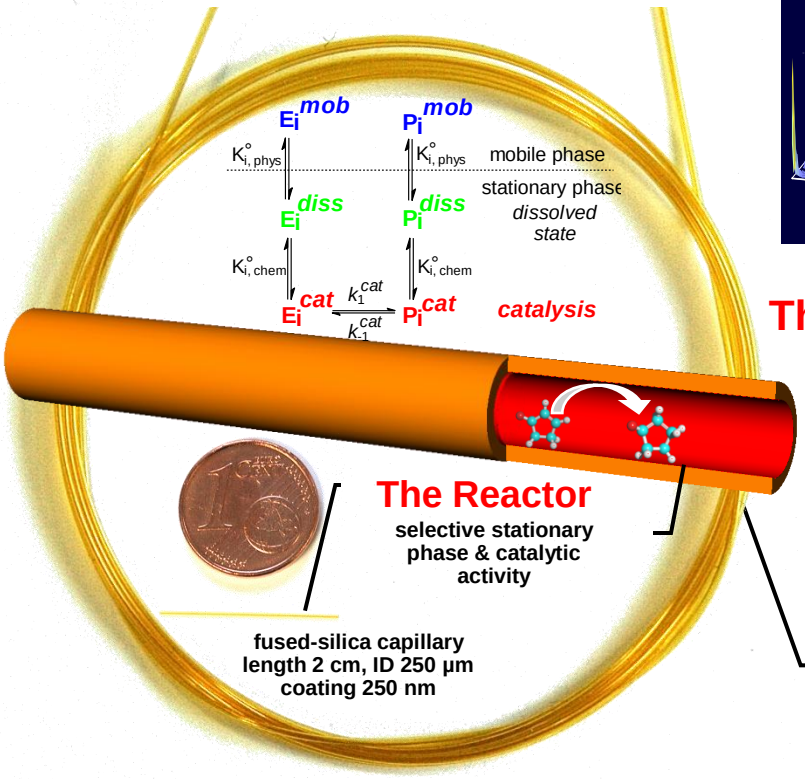
Carrier gas: H_2

On-column Reaction Chromatography

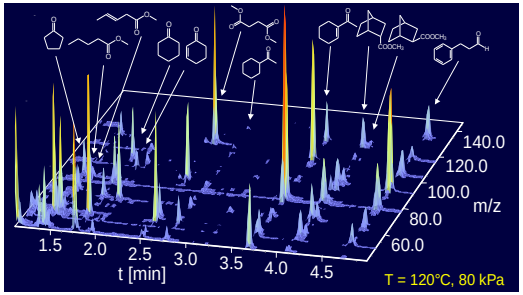
Reaction Library



On-column Synthesis & Separation



GC-MS Measurements

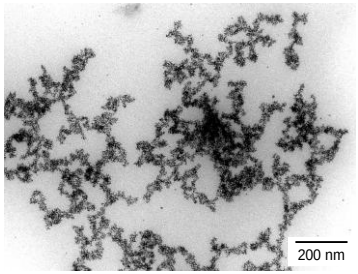


Thermodynamics & Kinetics

k, $\Delta G^\ddagger$, $\Delta H^\ddagger$, $\Delta S^\ddagger$

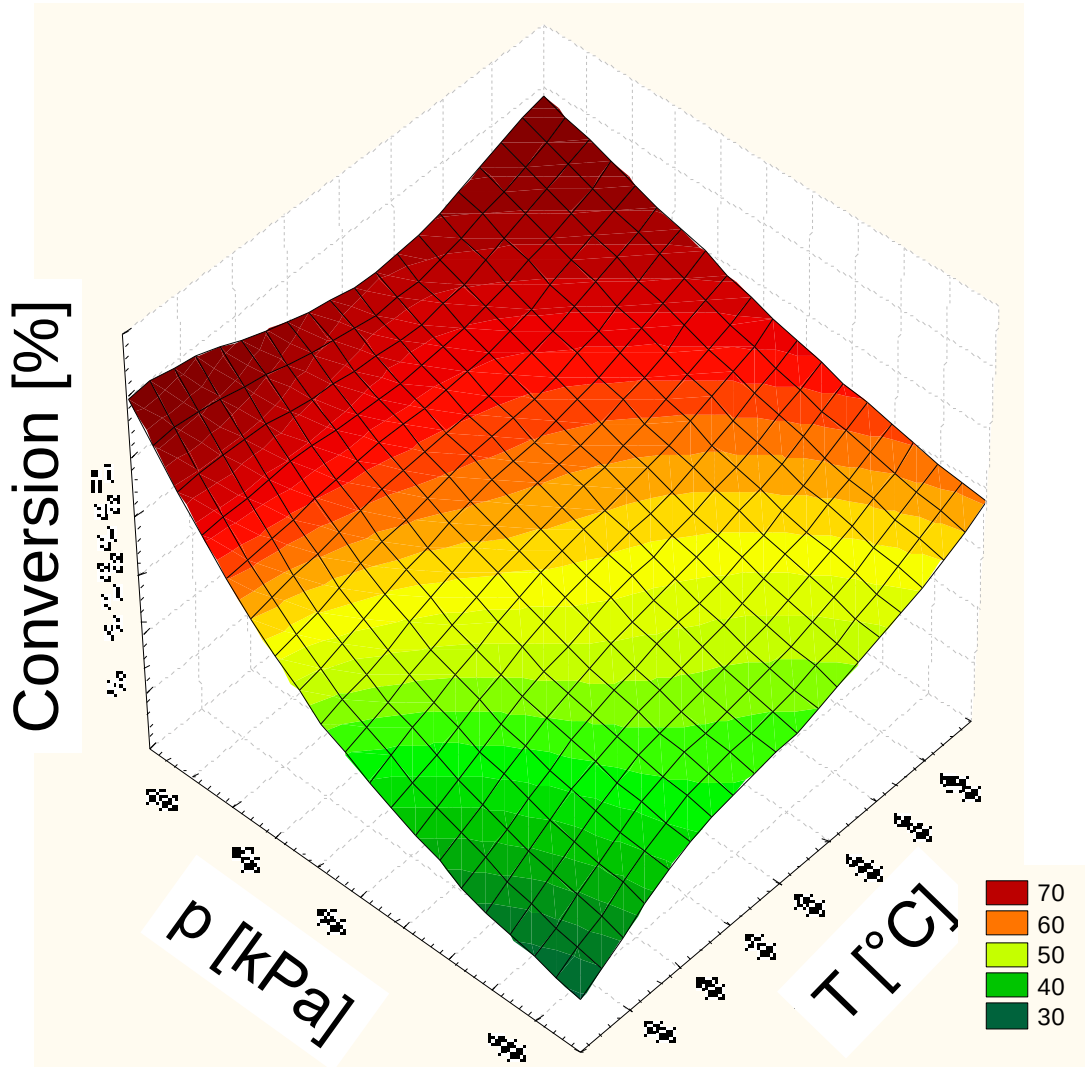
Structure Correlation

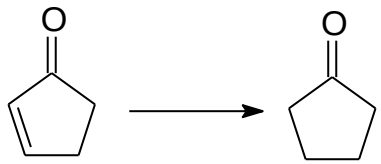
Characterization



O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

Hydrogenation of 2-Cyclopentenon

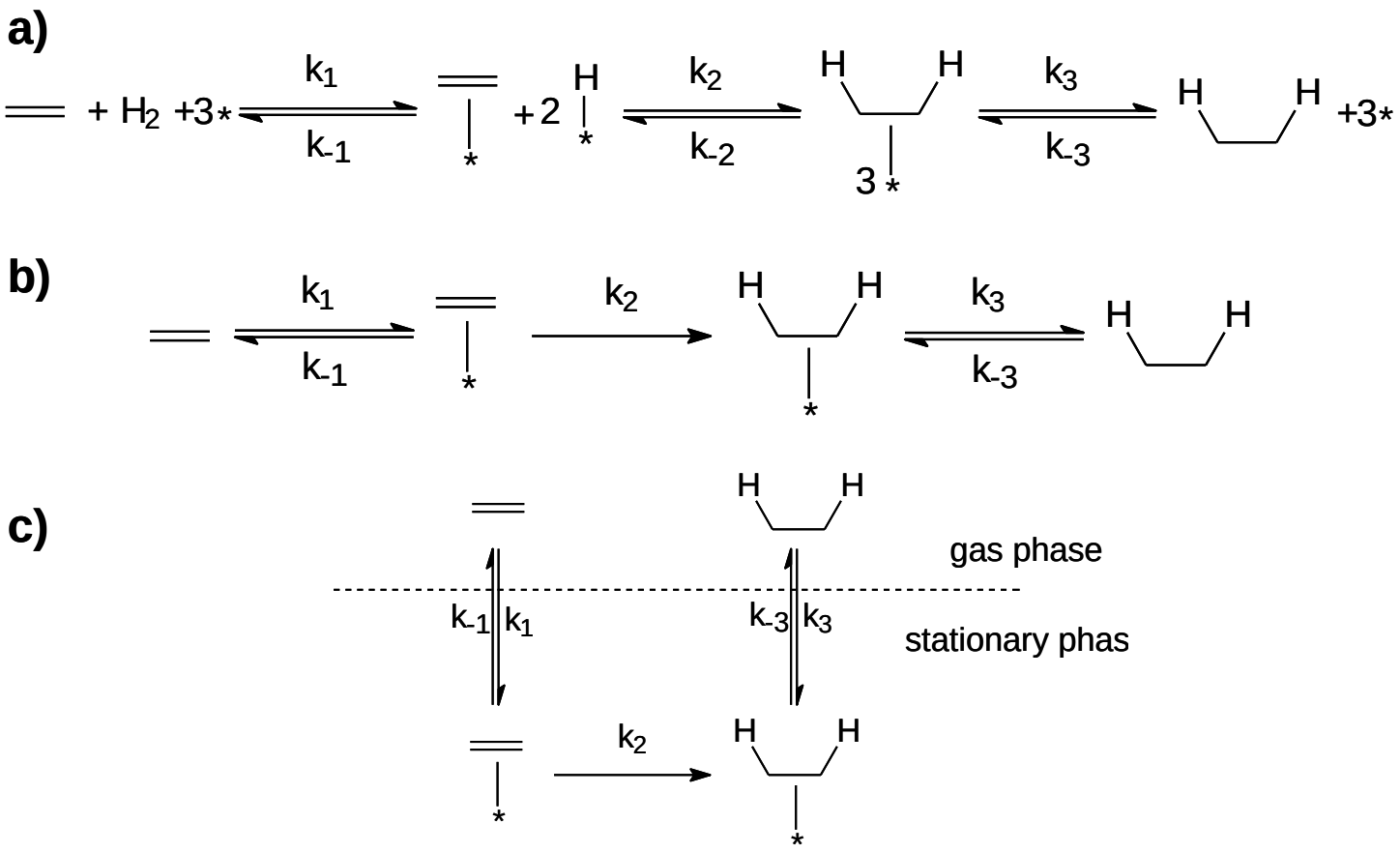




- Kinetics
- Diffusion
- Activation parameters

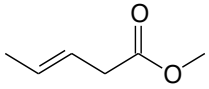
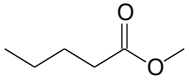
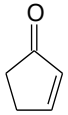
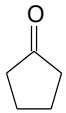
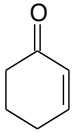
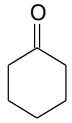
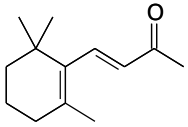
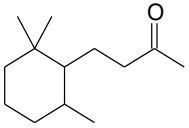
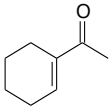
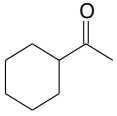
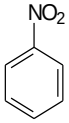
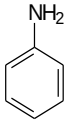
$k = 8.9\ s^{-1}$ (80°C)

Mechanism: Langmuir-Hinshelwood in a Chromatographic Reactor



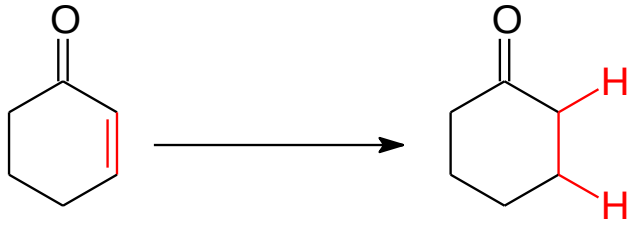
O. Trapp, S.K. Weber, S. Bauch, T. Bäcker, W. Hofstadt, B. Spliethoff, *Chem. Eur. J.* **2008,** 14, 4657-4666.

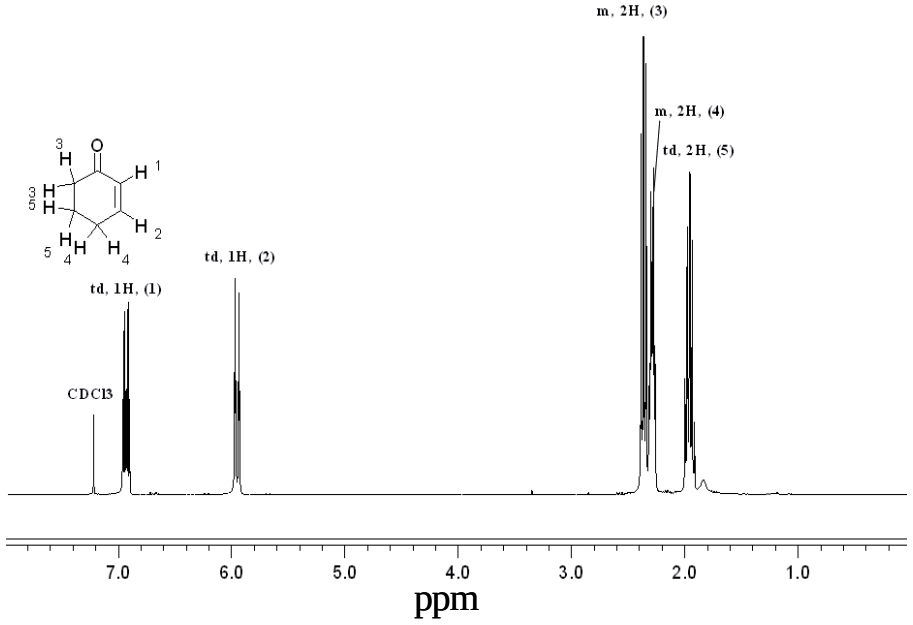
Activation Parameters

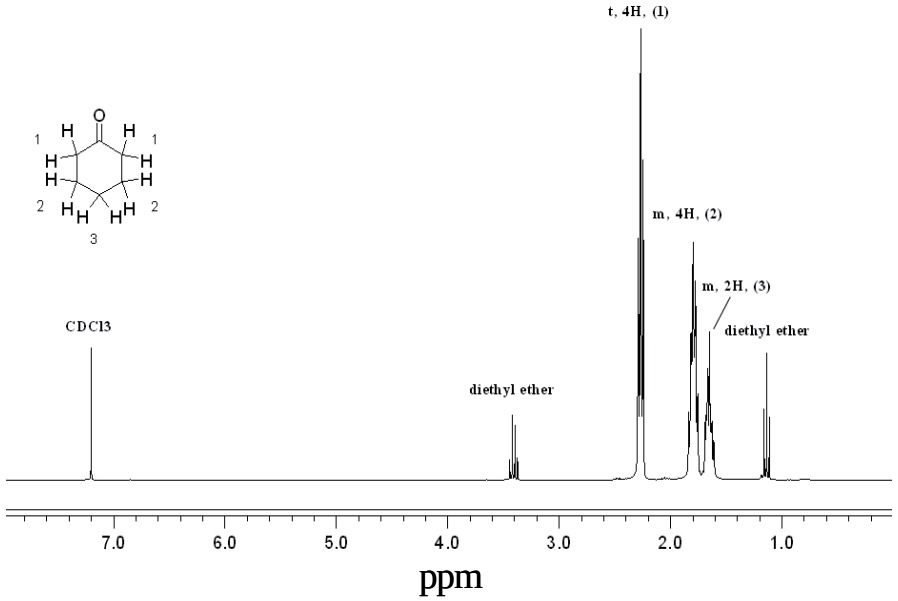
	Substrate	Produkte	C [%]	k [1/s]	$\Delta G^{\#}_{25°C}$ [kJ/mol]	$\Delta H^{\#}$	$\Delta S^{\#}$ [J/K·mol]	r	s.d.
1			11	194.1	67.8	30.1 ± 0.5	-126 ± 3	0.997	0.057
2			62	42.1	70.4	25.2 ± 0.5	-152 ± 4	0.996	0.052
3			47	36.4	71.4	27.2 ± 0.7	-148 ± 6	0.996	0.046
4			22	3.7	82.3	56.0 ± 1.0	-94 ± 2	0.998	0.020
5			13	43.9	73.4	37.5 ± 0.6	-121 ± 3	0.999	0.025
6			36	23.0	75.3	38.3 ± 1.5	-124 ± 7	0.985	0.116

O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

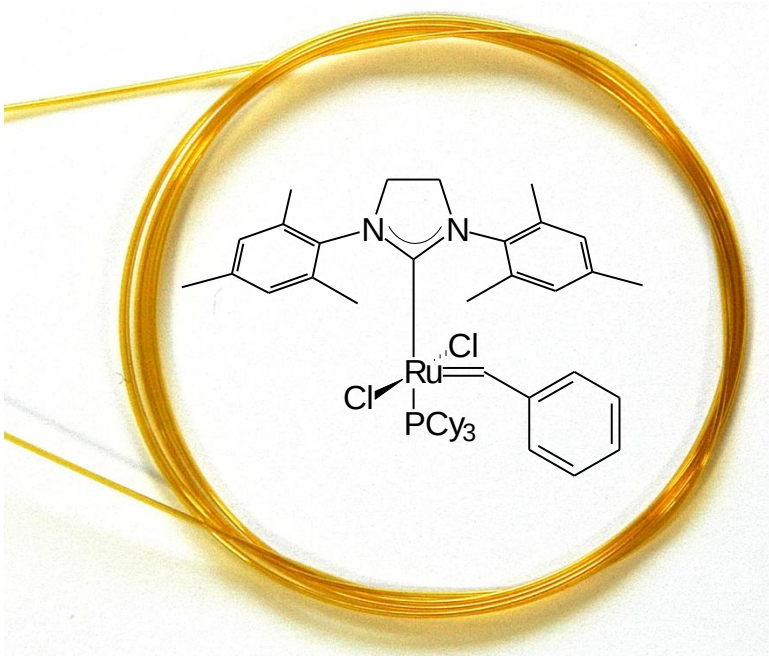
‘Lab-in-a-Capillary‘: Preparative Hydrogenations







Ring Closure Metathesis (RCM)



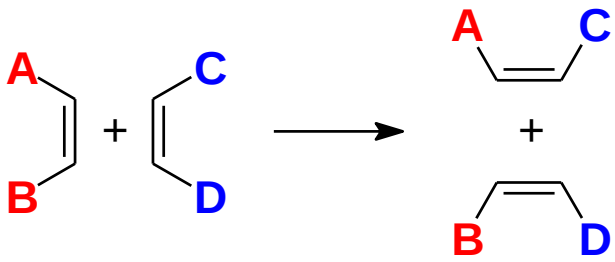
Combination of separation selectivity and catalytic activity

Length: 10 m fs-capillary

I.D. 250 µm, 500 nm film thickness

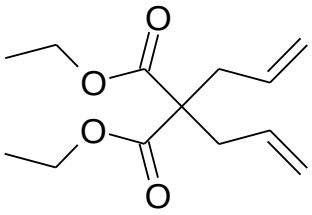
Grubbs 2nd generation catalyst dissolved in GE SE-30

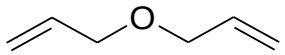
1.6 µg catalyst/ m → 1.9 nmol/ m

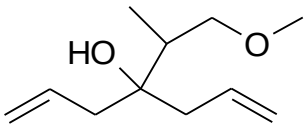


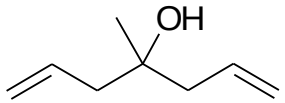
O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

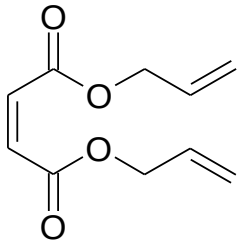
RCM: Educts

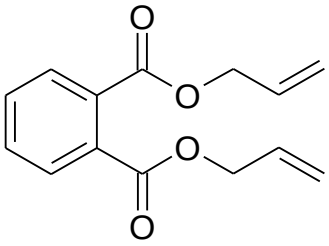


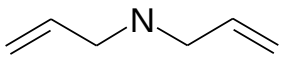


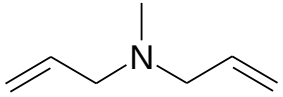


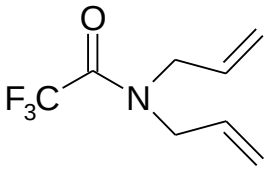


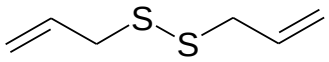


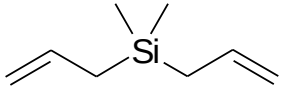


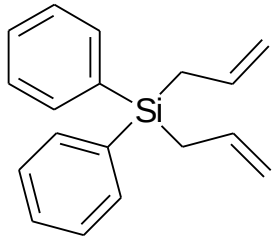






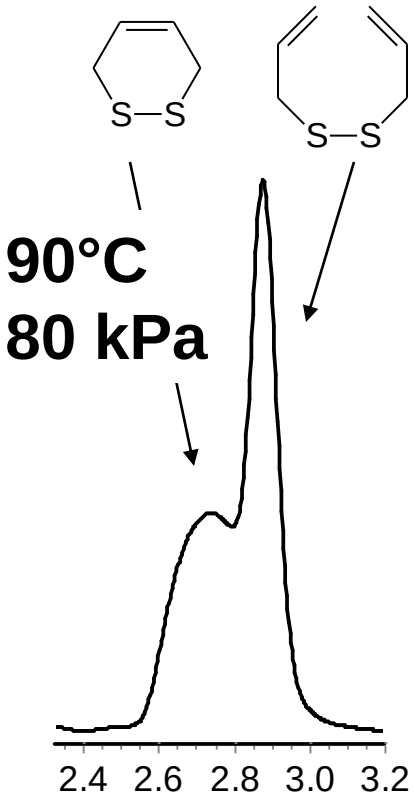


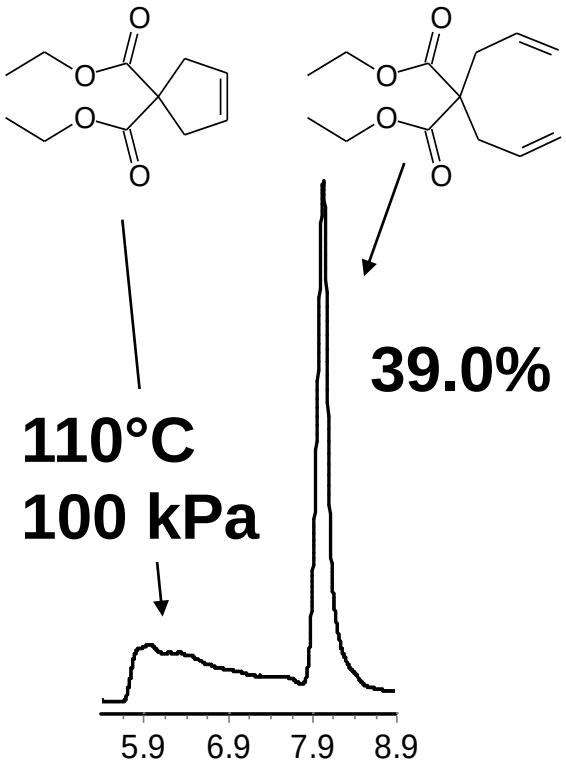


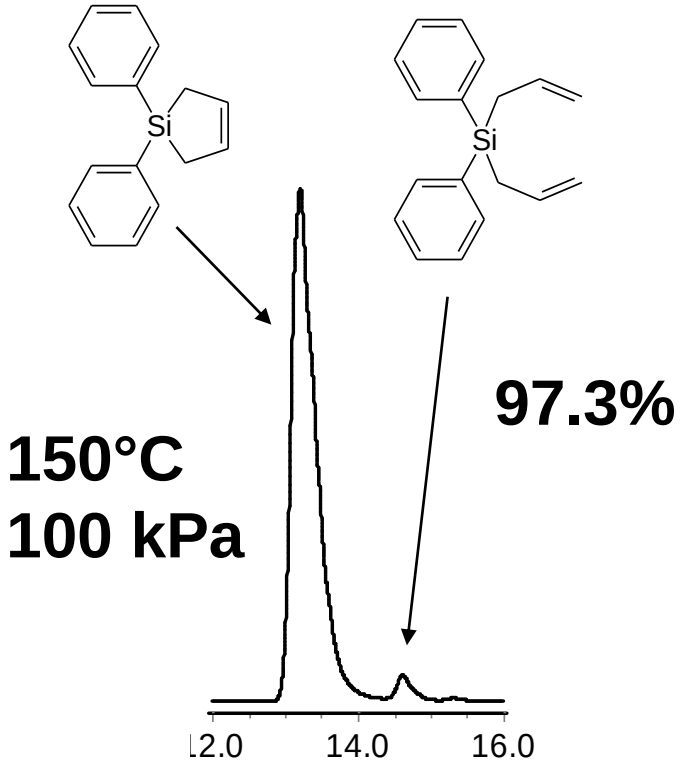


O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

Metathesis: Interconversion Profiles

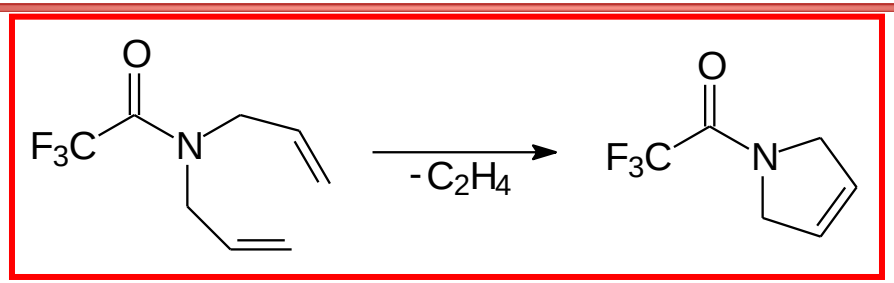






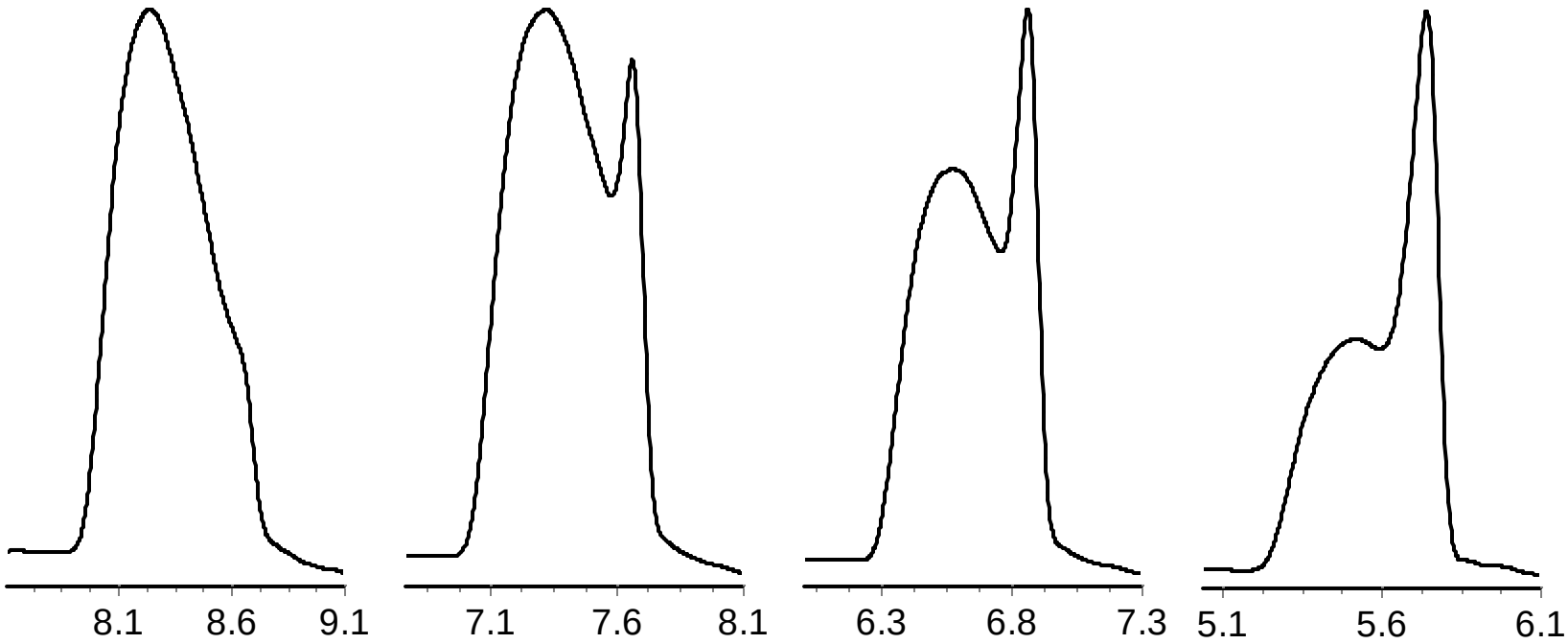
O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

Metathesis – Contact Time Variation

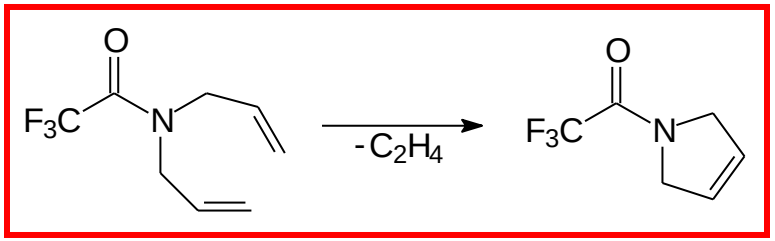


50°C

60 kPa **70 kPa** **80 kPa** **100 kPa**

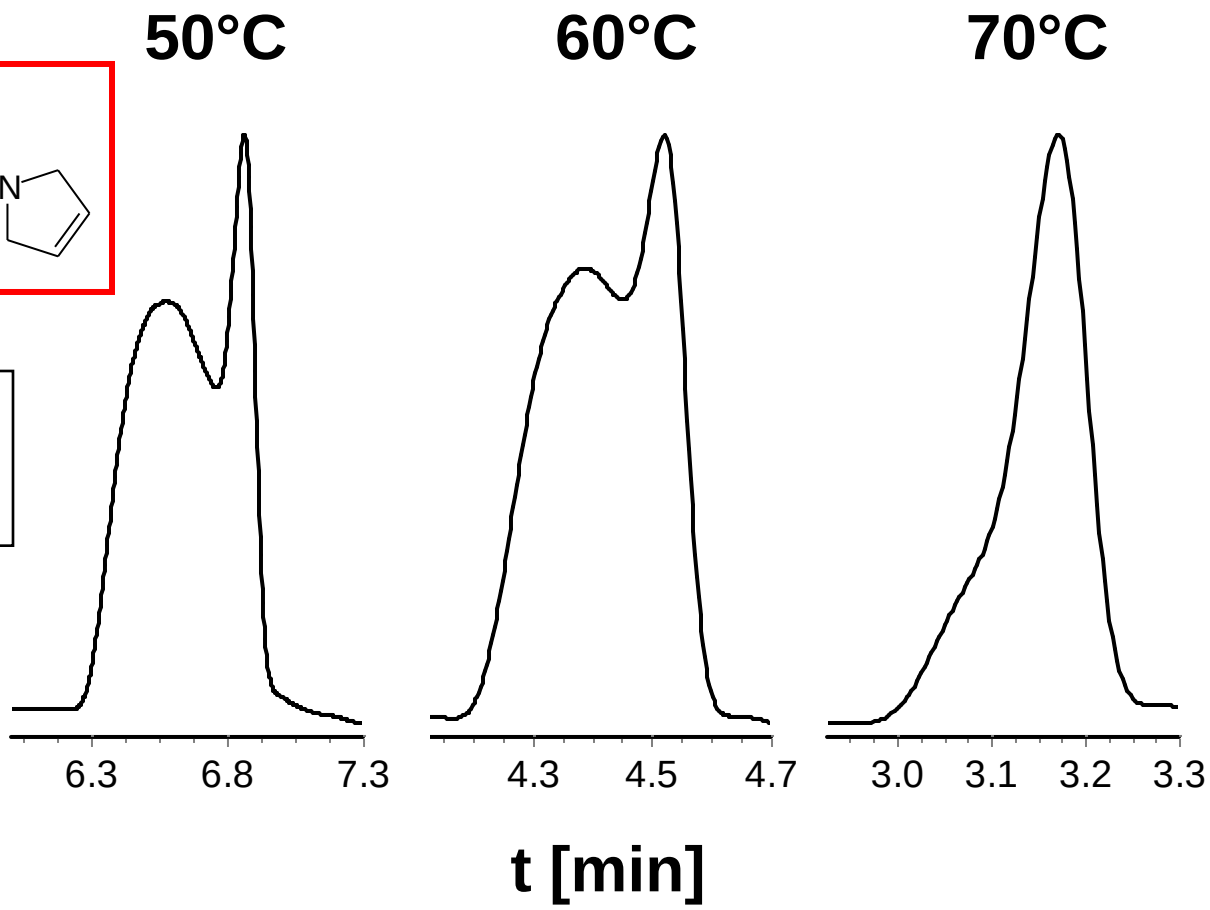


Metathesis – Activation Parameters



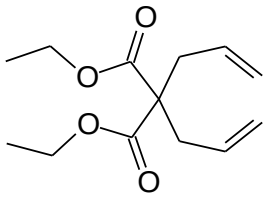
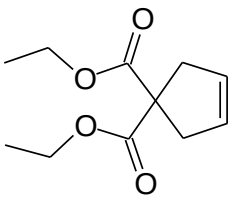
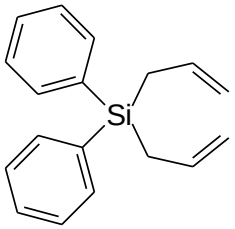
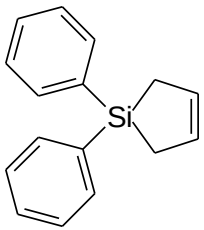
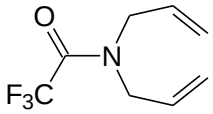
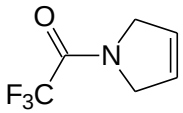
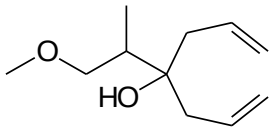
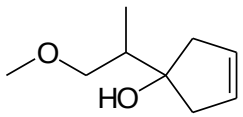
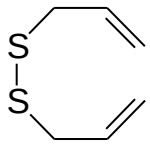
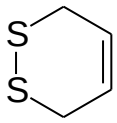
$\Delta H^{\ddagger}$ = 15.5 kJ/mol
$\Delta S^{\ddagger}$ = -230 J/(Kmol)

80 kPa



O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

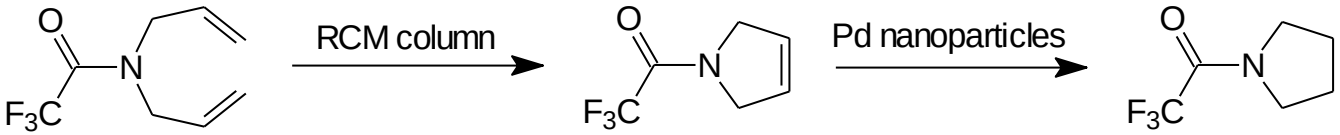
Activation Barriers

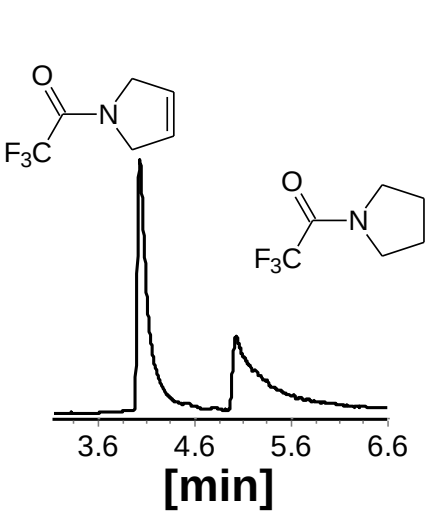
	Substrate	Product	T [°C]	C [%]	k [1/s]	$\Delta G^{\#}$ [kJ/mol]
1			110.0	39.0	$2.2 \cdot 10^{-3}$	114.1
2			150.0	97.3	$3.4 \cdot 10^{-3}$	124.9
4			50.0	62.5	$8.6 \cdot 10^{-3}$	89.8
5			120.0	59.5	$7.7 \cdot 10^{-3}$	113.1
6			90.0	51.0	$4.9 \cdot 10^{-3}$	105.6

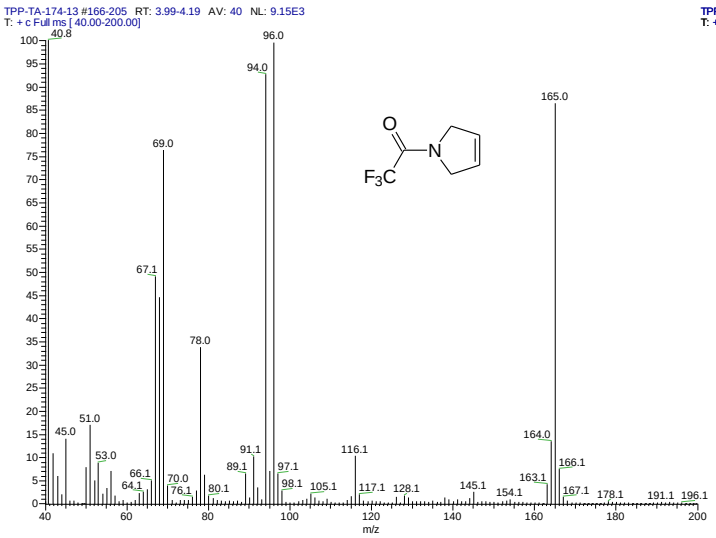
O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

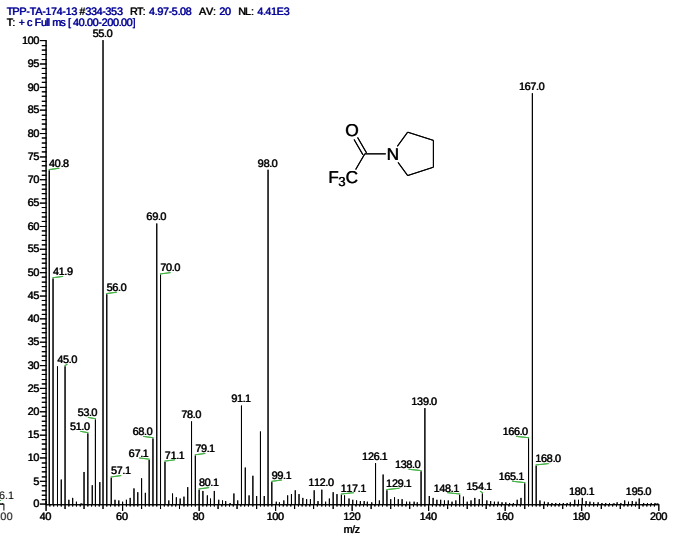
Reaction Cascades

<6 min









O. Trapp, S.K. Weber, S. Bauch, W. Hofstadt, *Angew. Chem.* **2007**, *119*, 7447-7451.

Conclusions & Outlook

- Combining separation selectivity & (enantioselective) catalysis
- Determination of reaction rate constants
- High-throughput screening of catalysts and reactions

  → currently 5880 reactions in 40 h!
- Minute substrate consumption
- Continuous tuning of solvent properties
- Preparative synthesis possible (20 mg/ h) – micro plants

→ **(R)evolution of chemist's toolkit**

On-Line Screening: ht-Multiplexing GC

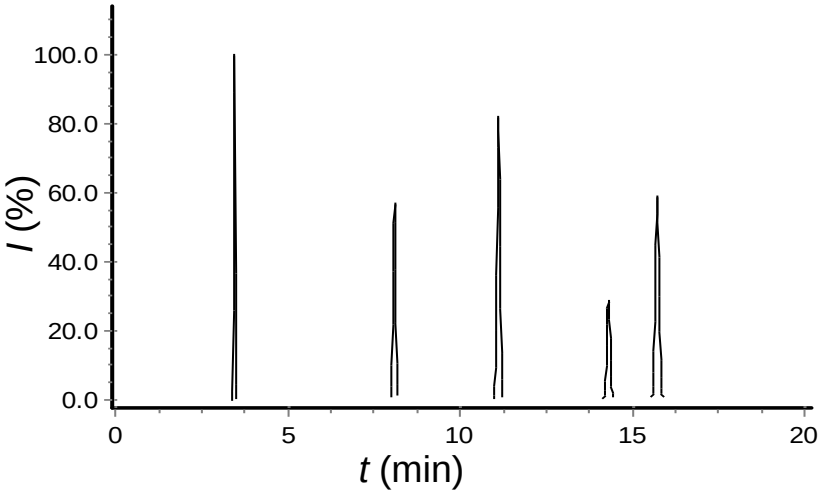
High-Throughput Analysis

- Reaction monitoring
  - → continuous sample analysis in real-time
  - → not only one reaction, side reactions
  - → complex samples, separation required
  - → kinetics
- High-throughput screening
  - → reaction monitoring in parallel reactors
  - → combinatorial approaches
  - → material properties
- Improvement of sensitivity
- Cost/ sample

Maximization of Information ↔ Minimization of Analysis Time

→ Chromatography

How to Increase the Duty Cycle?



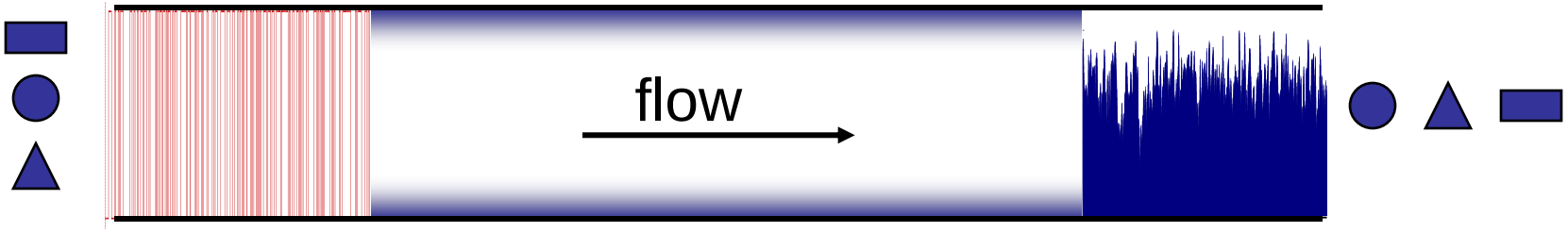
$$Duty\ Cycle = \frac{\sum_{i=1}^{n} (w_b^i)}{t_R^n} \times f$$

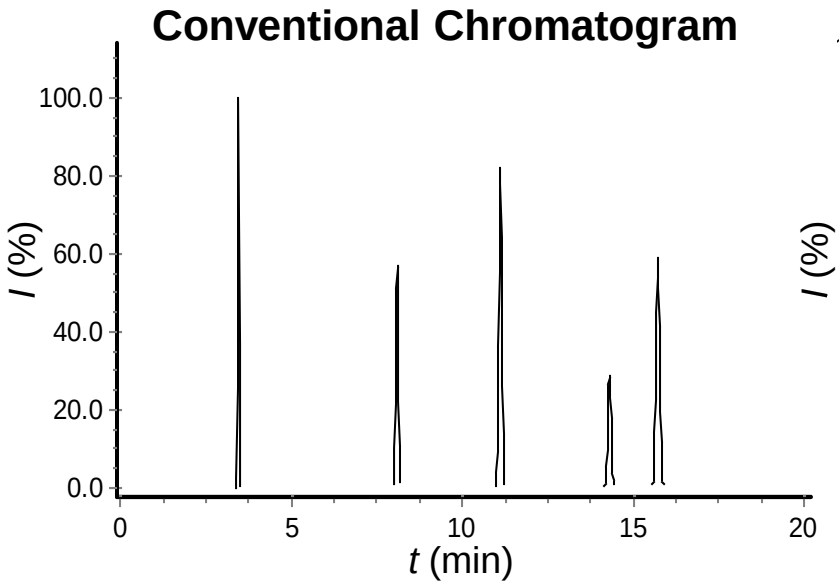
- Consecutive sample injections
  → Process analysis (f ≤10)
- Parallel analysis
  → f = N
  → high cost: N instruments

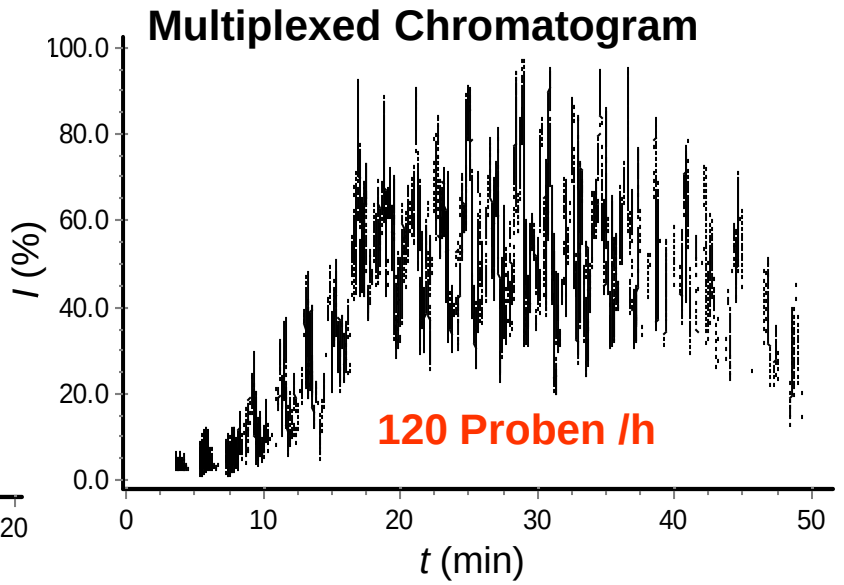
- Fast separation techniques
- Correlation techniques
- Multiplexing techniques
  → Information technology
  (Telecommunication, FT-Spectroscopy, HT-TOF-MS)

O. Trapp, J.R. Kimmel, O.K. Yoon, I.A. Zuleta, F.M. Fernandez, R.N. Zare, A*ngew. Chem. Int. Ed.* **2004**, *43*, 6541-6544.

Multiplexing Chromatography







Binary Pseudo-Random Sequences

Jacques Salomon Hadamard
8. Dezember 1865, Versailles
- 17 Oktober 1963, Paris

Omit first row and column

$$H := \begin{bmatrix} 1 & 1 & 1 & 1 & 1 & 1 & 1 & 1 \\ 1 & -1 & -1 & -1 & 1 & -1 & 1 & 1 \\ 1 & -1 & -1 & 1 & -1 & 1 & 1 & -1 \\ 1 & -1 & 1 & -1 & 1 & 1 & -1 & -1 \\ 1 & 1 & -1 & 1 & 1 & -1 & -1 & -1 \\ 1 & -1 & 1 & 1 & -1 & -1 & -1 & 1 \\ 1 & 1 & 1 & -1 & -1 & -1 & 1 & -1 \\ 1 & 1 & -1 & -1 & -1 & 1 & -1 & 1 \end{bmatrix}$$

Change
–1 to 1
1 to 0

Sequence to modulate the analytes

$$S := \begin{bmatrix} 1 & 1 & 1 & 0 & 1 & 0 & 0 \\ 1 & 1 & 0 & 1 & 0 & 0 & 1 \\ 1 & 0 & 1 & 0 & 0 & 1 & 1 \\ 0 & 1 & 0 & 0 & 1 & 1 & 1 \\ 1 & 0 & 0 & 1 & 1 & 1 & 0 \\ 0 & 0 & 1 & 1 & 1 & 0 & 1 \\ 0 & 1 & 1 & 1 & 0 & 1 & 0 \end{bmatrix}$$

Simplex matrix

Mathematical Background

Raw Chromatogram:
Simplex Matrix x Chromatogram

$$\left[Z \right] = \left[S \right]_n \times \left[t_R \right]$$

Deconvoluted Chromatogram:
Invers Simplex Matrix x Raw Chromatogram

$$\left[t_R \right] = \left[S \right]_n^{-1} \times \left[Z \right]$$

Multiplexing Advantage

Improvement of the Signal-to-Noise Ratio
(N = Sequence Length)

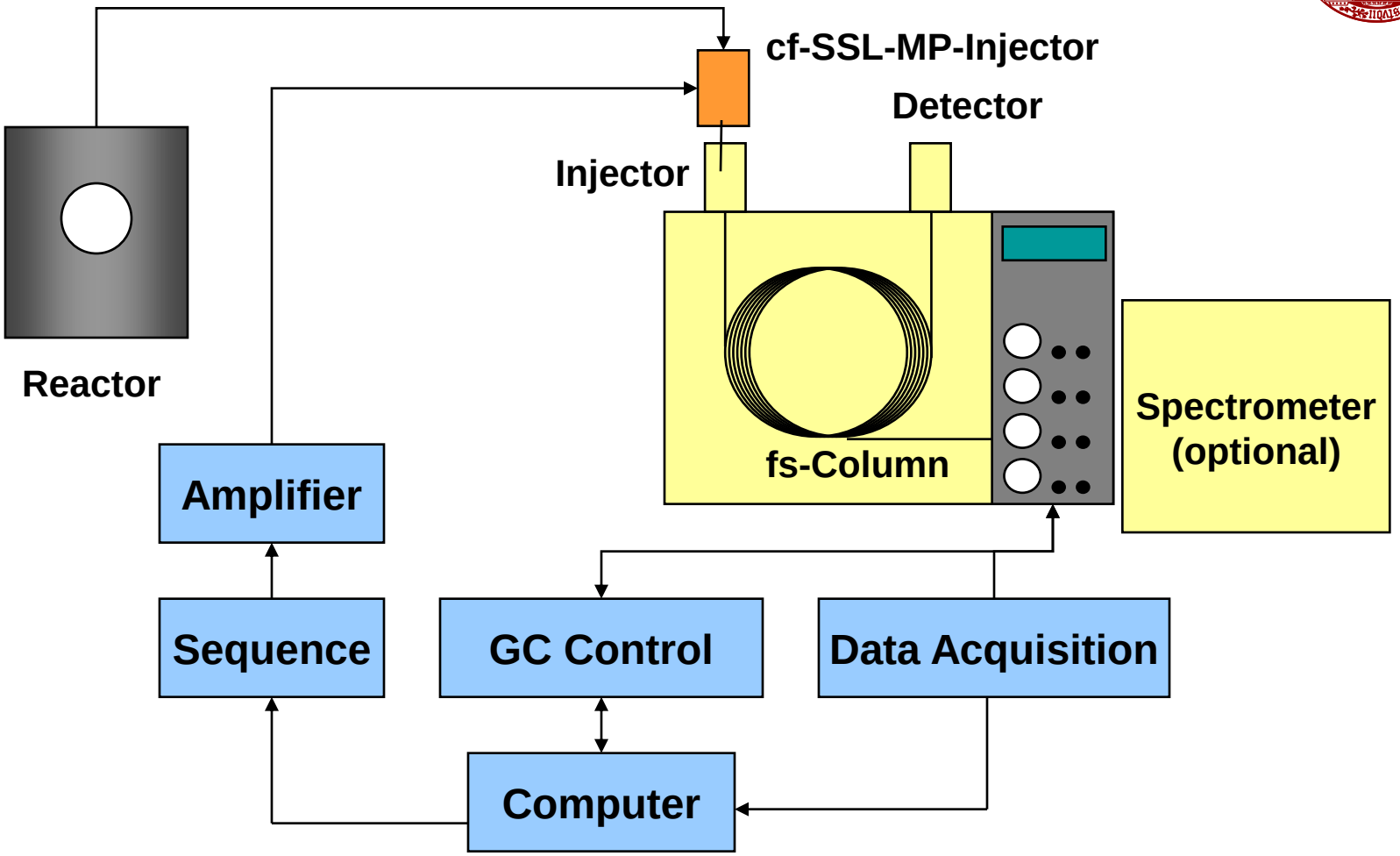
$$\sqrt{\frac{N}{2}} > SNR > \frac{\sqrt{N}}{2} \qquad G_{\max}(SNR) = \frac{\sqrt{N}}{2}$$

Advantageous

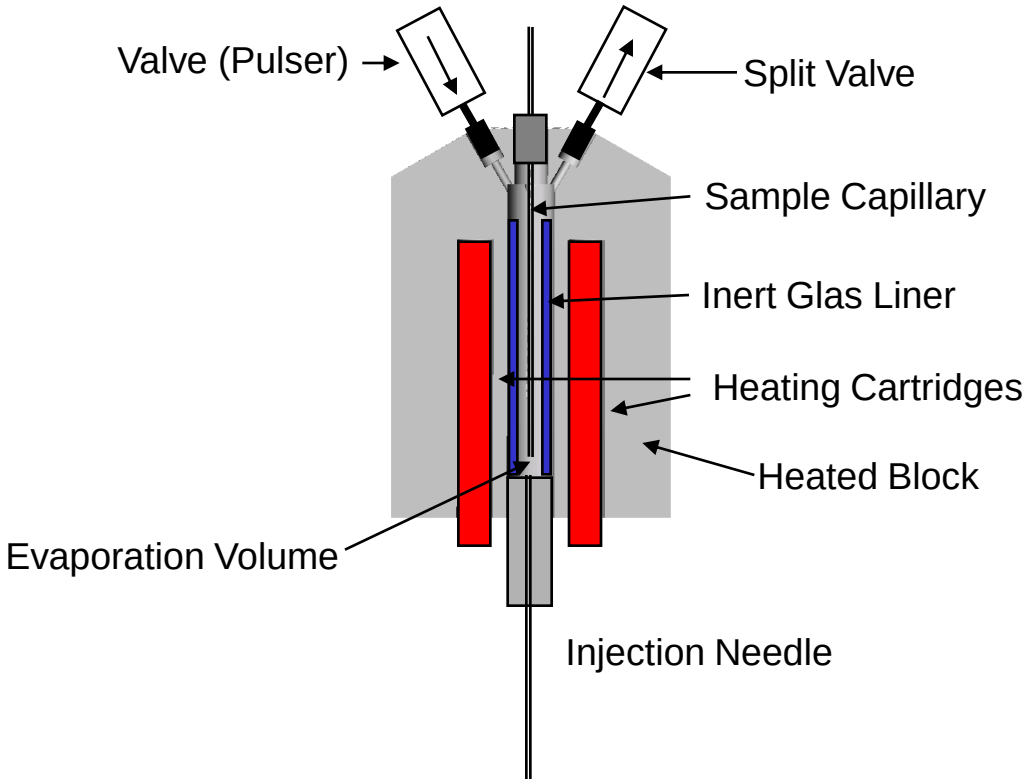
11-bit (N=2047, G=22),
12-bit (N=4095, G=32),
13-bit (N=8191, G=45) …
sequences!

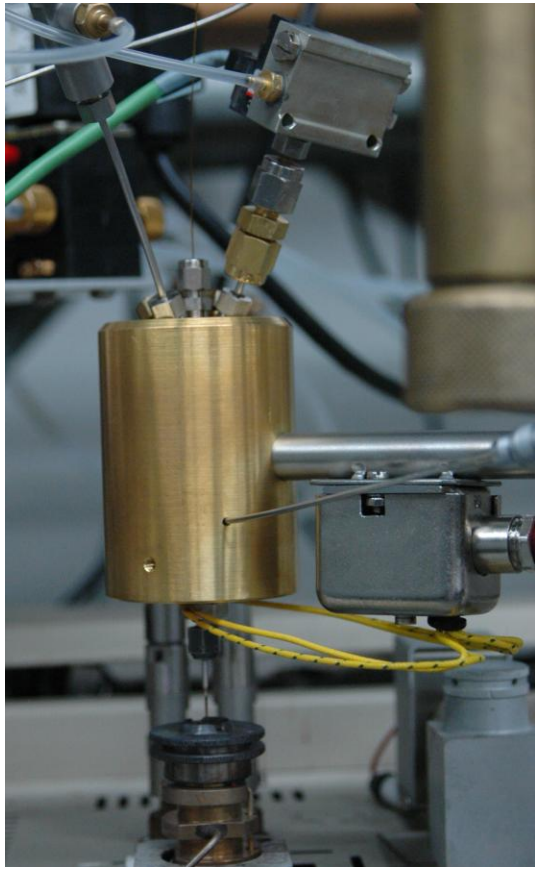
→ Pre-requisite: Fast Modulation!

Experimental Setup



cf-SSL-MP Injector

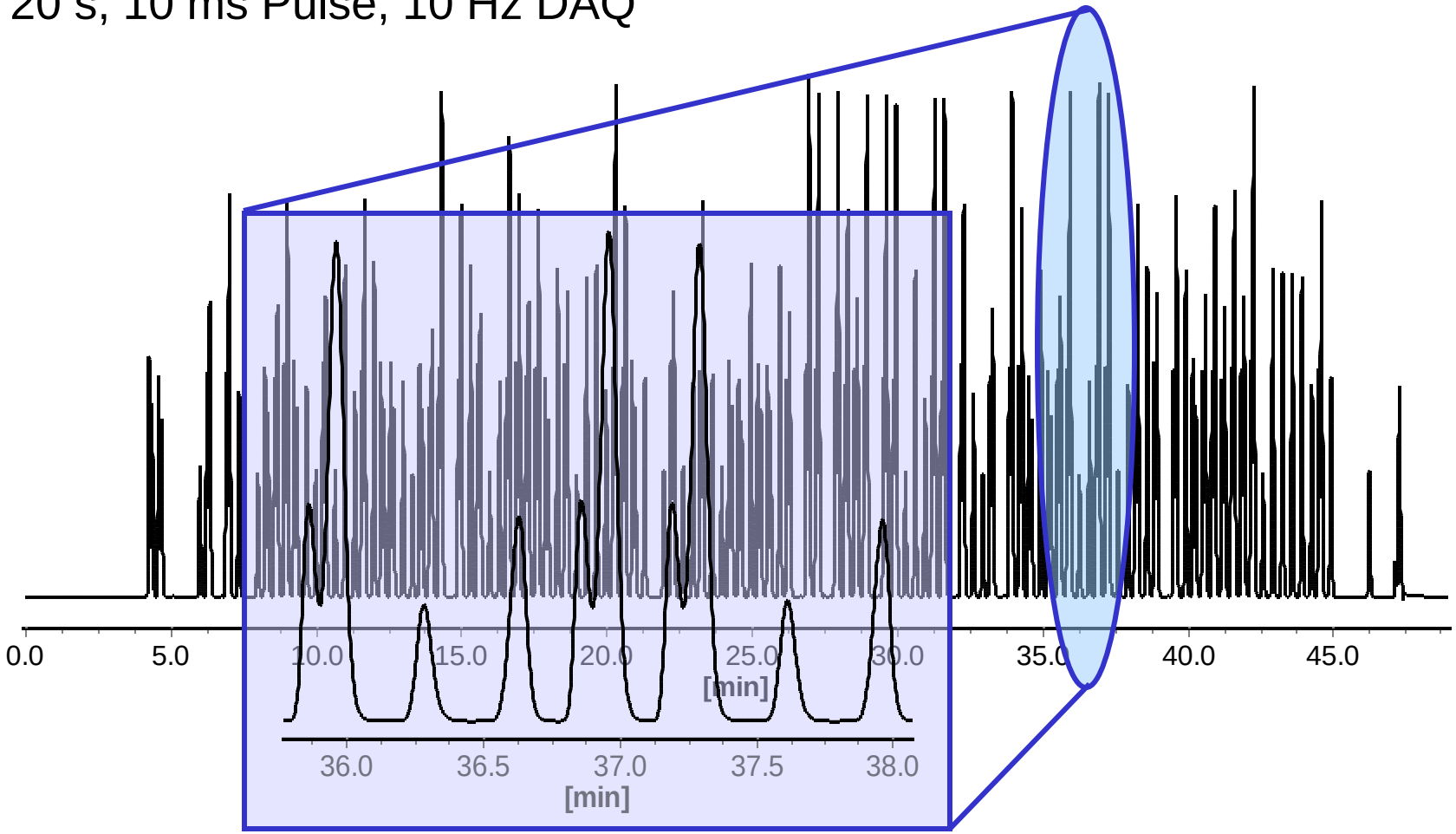




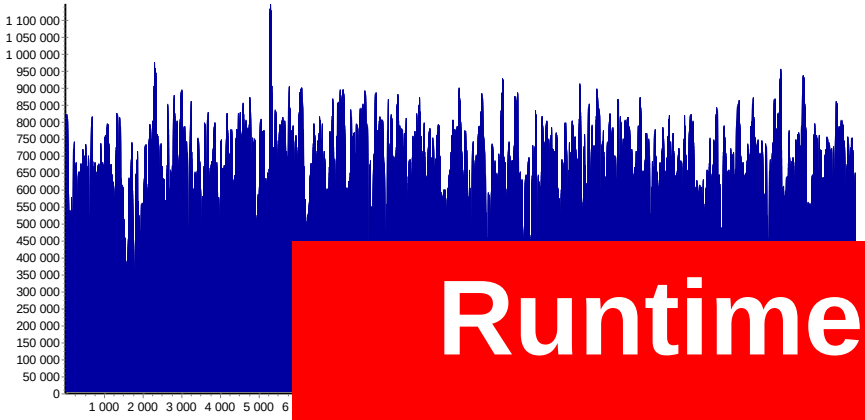
Injection Stability

7-bit Sequence (127 Elements),

Δt = 20 s, 10 ms Pulse, 10 Hz DAQ



MPGC: 11-bit, Δt = 1 s, 2 ms



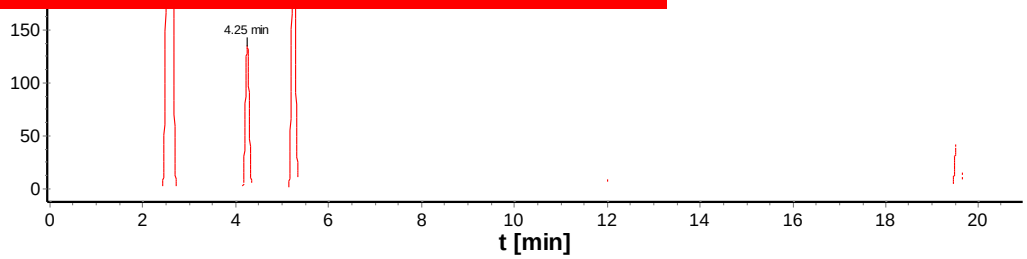
20 m SE30 (ID 250 µm, film thickness 250 nm), 40 °C, 0.5 kPa He
11 bit, Δt = 1 s, 2 ms Pulse
ne, n-heptane

Runtime: 34 min

1023 injections

⇒ 1800 injections/h

Transformation



High-Throughput Catalysis

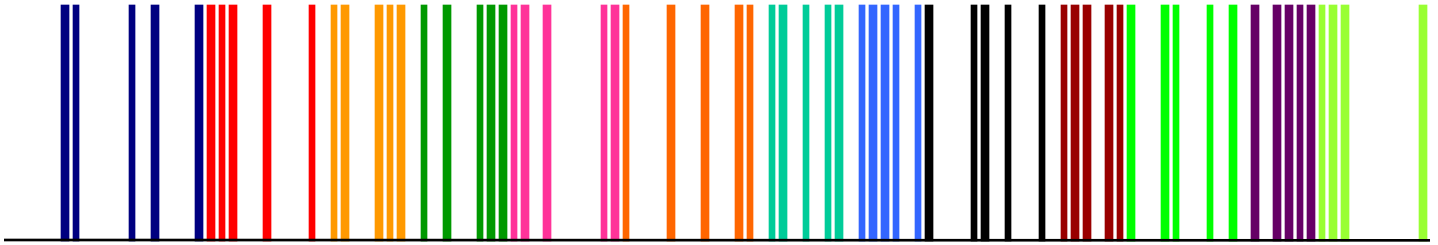




F. Schüth *et al.*, *Catal. Today* **2006**, *117*, 284.
O. Trapp, *J. Chromatogr. A* **2008,** *1184*, 160-190.

High-Throughput Analysis

A_i Samples

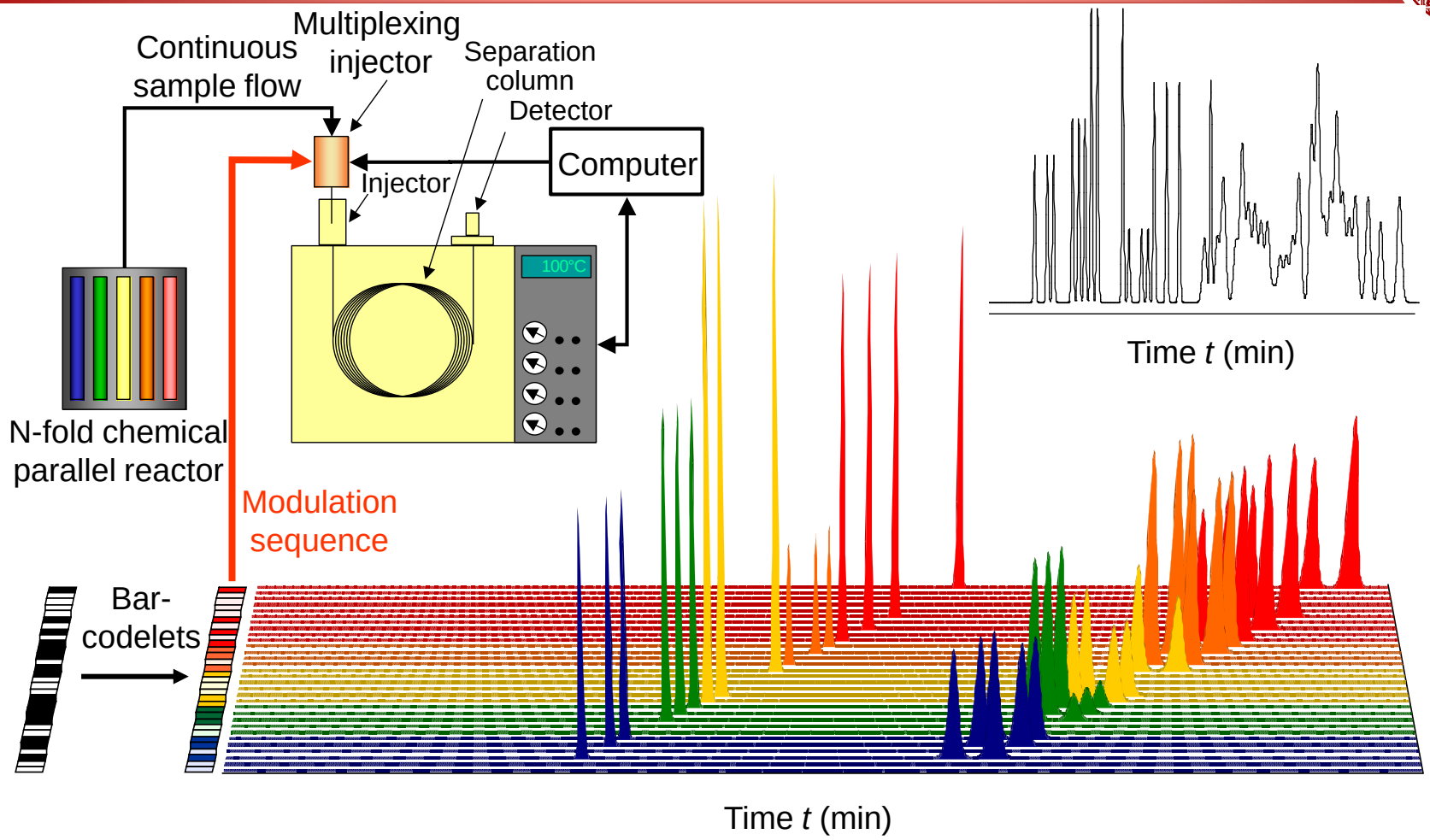


A_1 A_2 A_3 A_4 A_5 A_6 A_7 A_8 A_9 A_{10} A_{11} A_{12} A_{13}

Encoding	Gain	Information
Bar-Code 	Duty Cycle	Conserves Chemical Information (Composition)
Bar-Codelets 	Throughput	Conserves Information of Samples (Concentration)

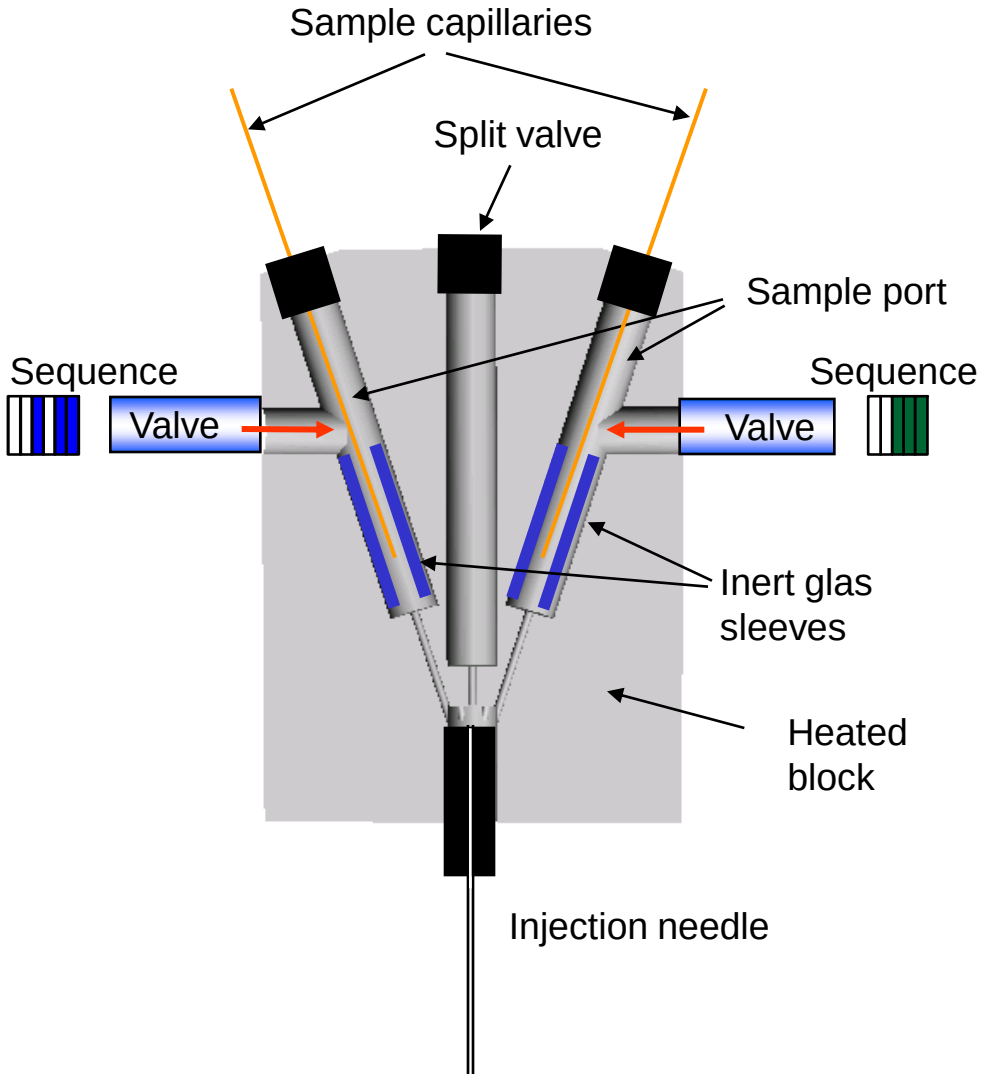
O. Trapp, *PCT Patent Application* WO2007045224A2, **2007**.
O. Trapp, *Angew. Chem. Int. Ed.* **2007**, *46*, 5609-5613.

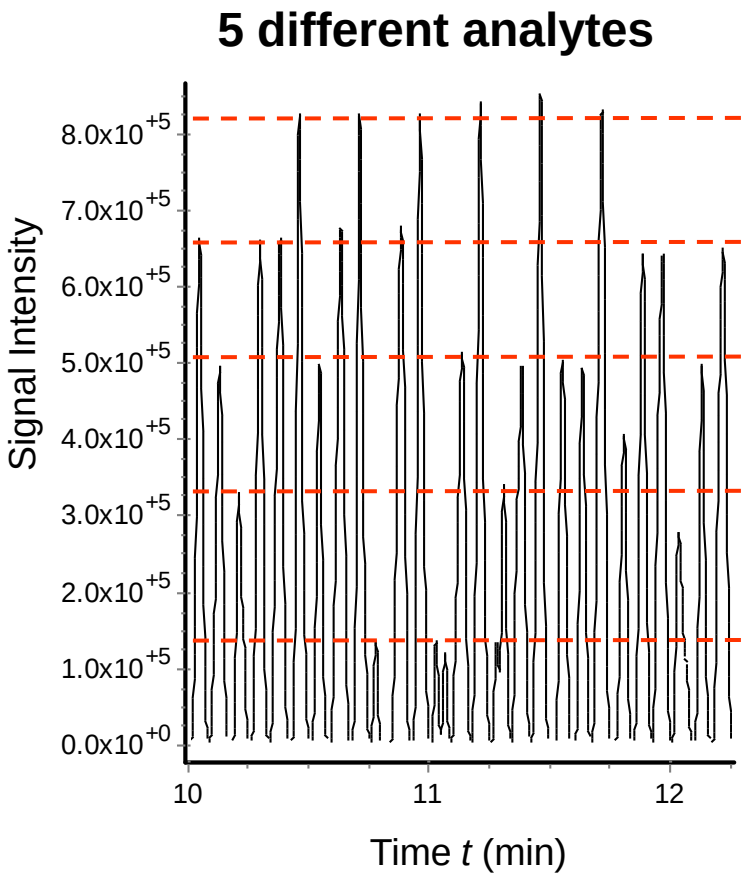
High-Throughput Multiplexing Chromatography (htMPC) – The Principle



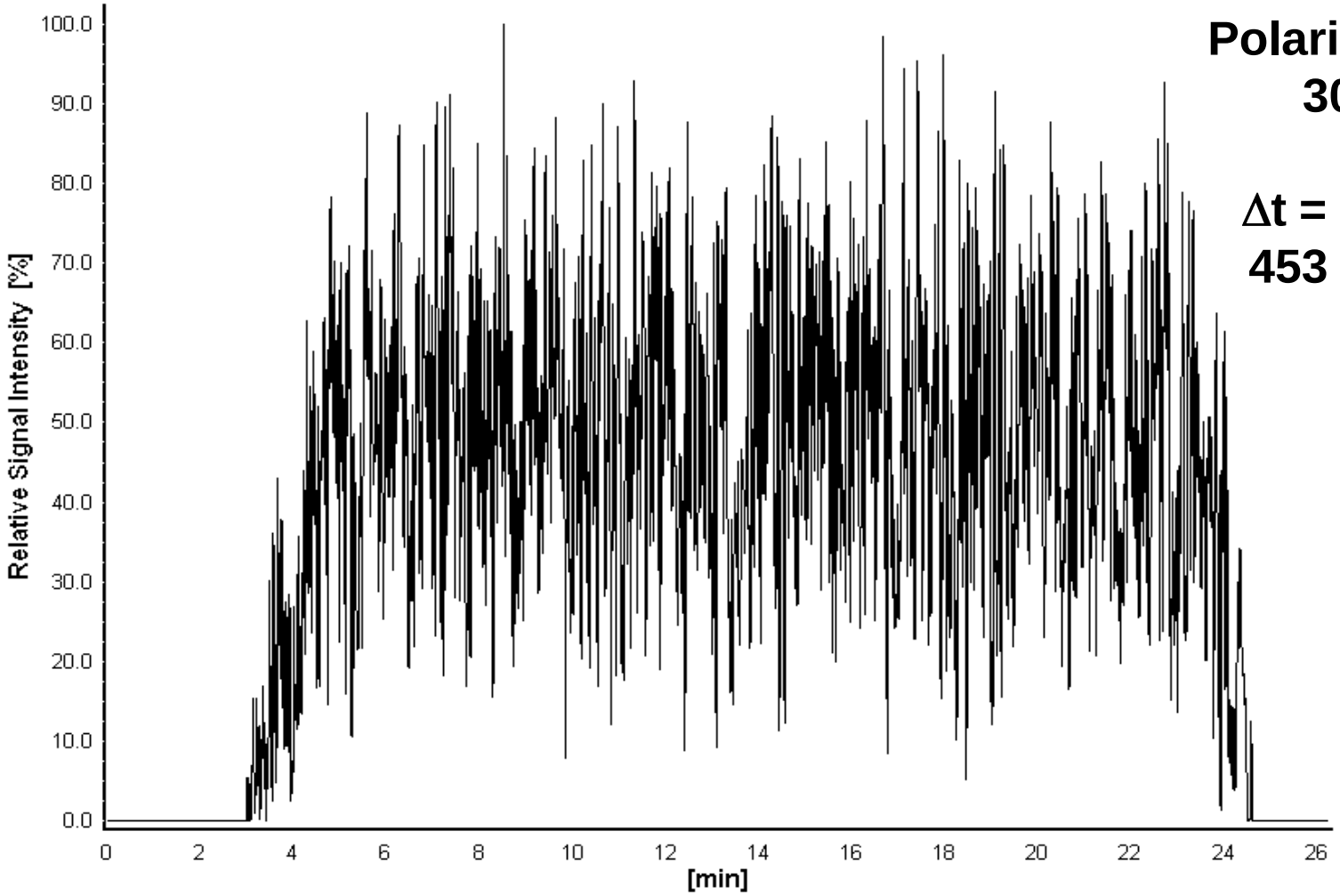
O. Trapp, *Angew. Chem.* **2007**, *119*, 5706-5710.

Rapid Sample Injections



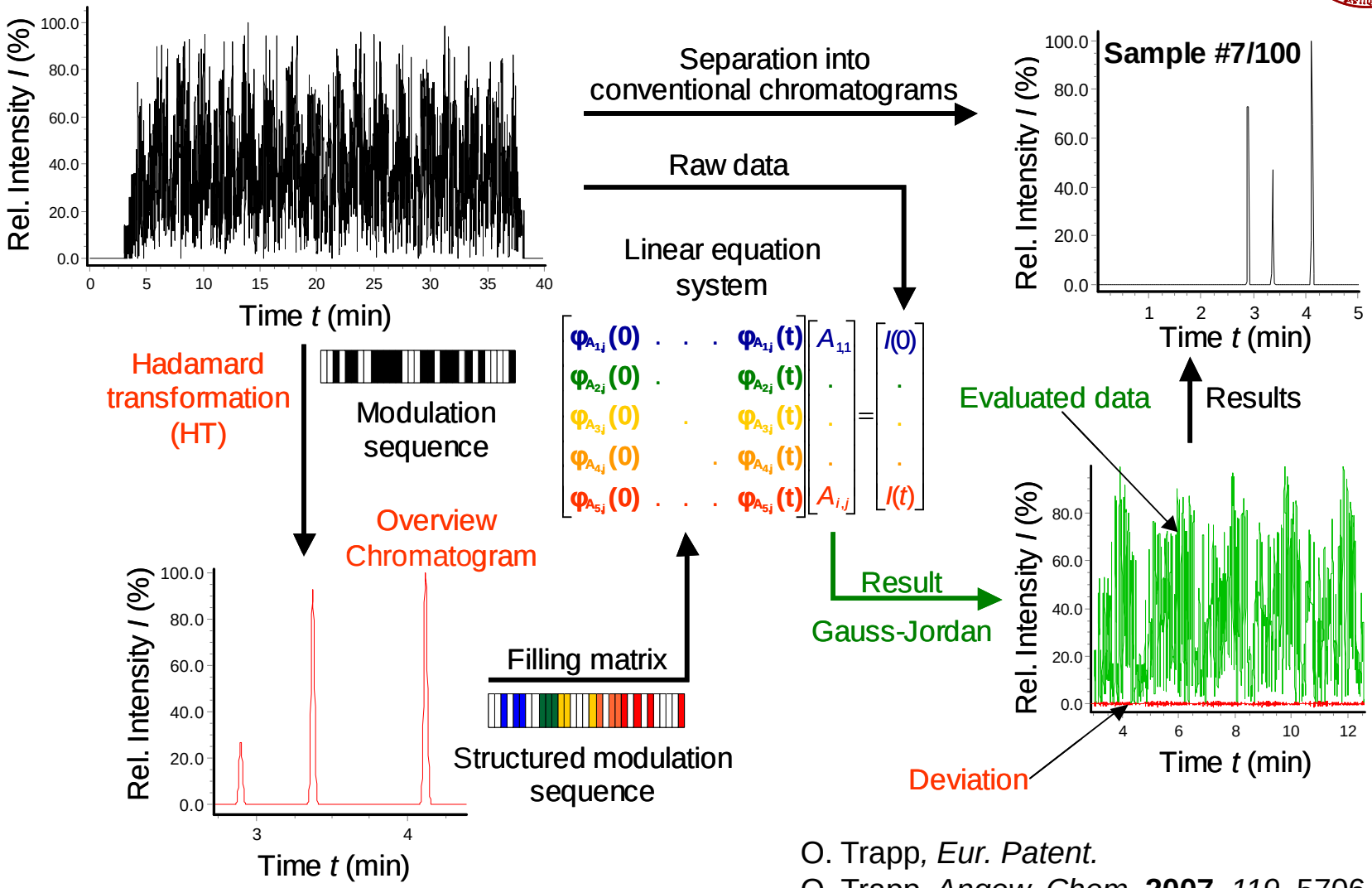


htMPGC: 200 Samples



PolarisQ-Trace GC
30 m HP-5
11-bit,
Δt = 600 ms, 5x,
453 samples/ h

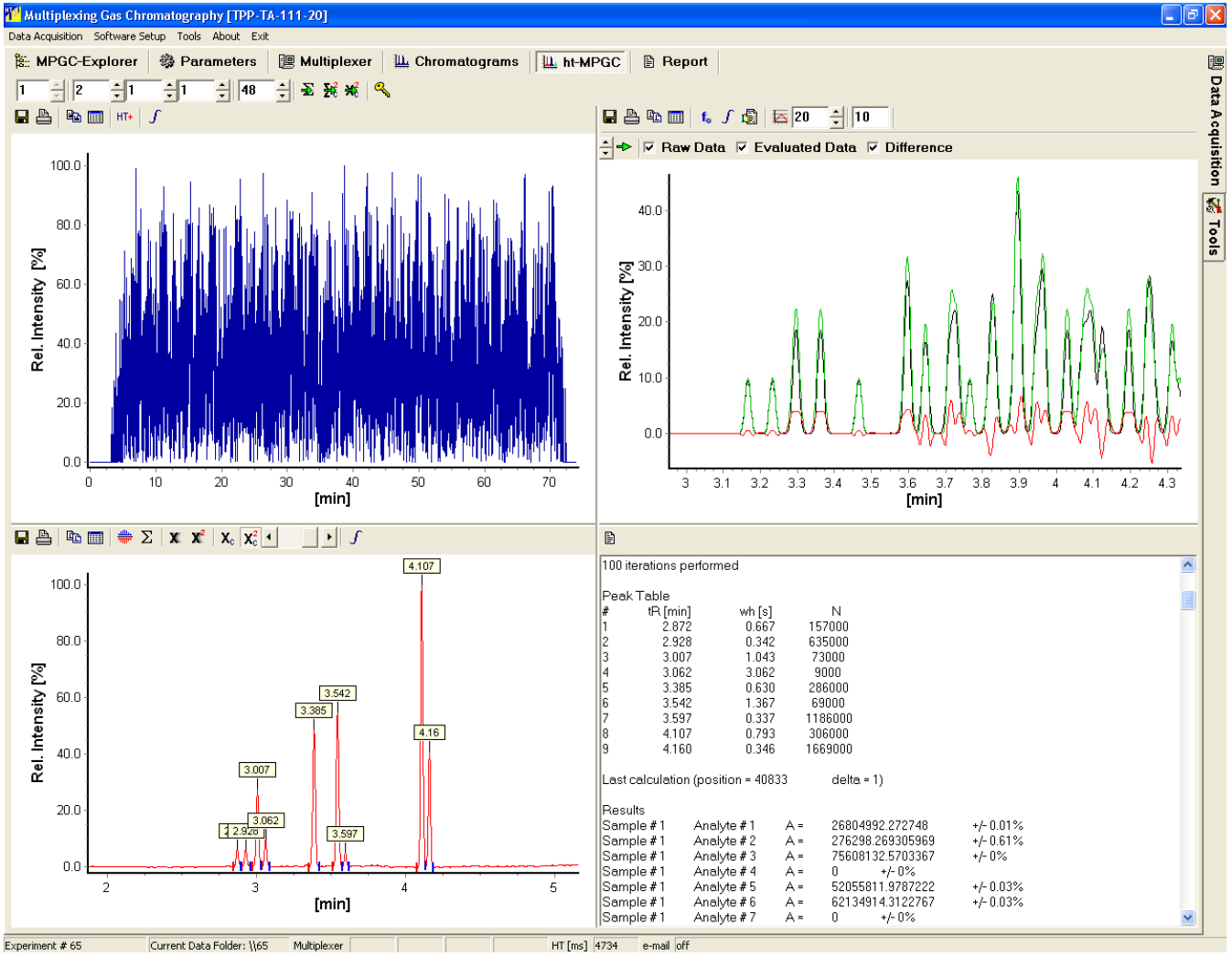
htMPC: Data Deconvolution



O. Trapp, *Eur. Patent.*

O. Trapp, *Angew. Chem.* **2007**, *119*, 5706-5710.

Software: htMPGC



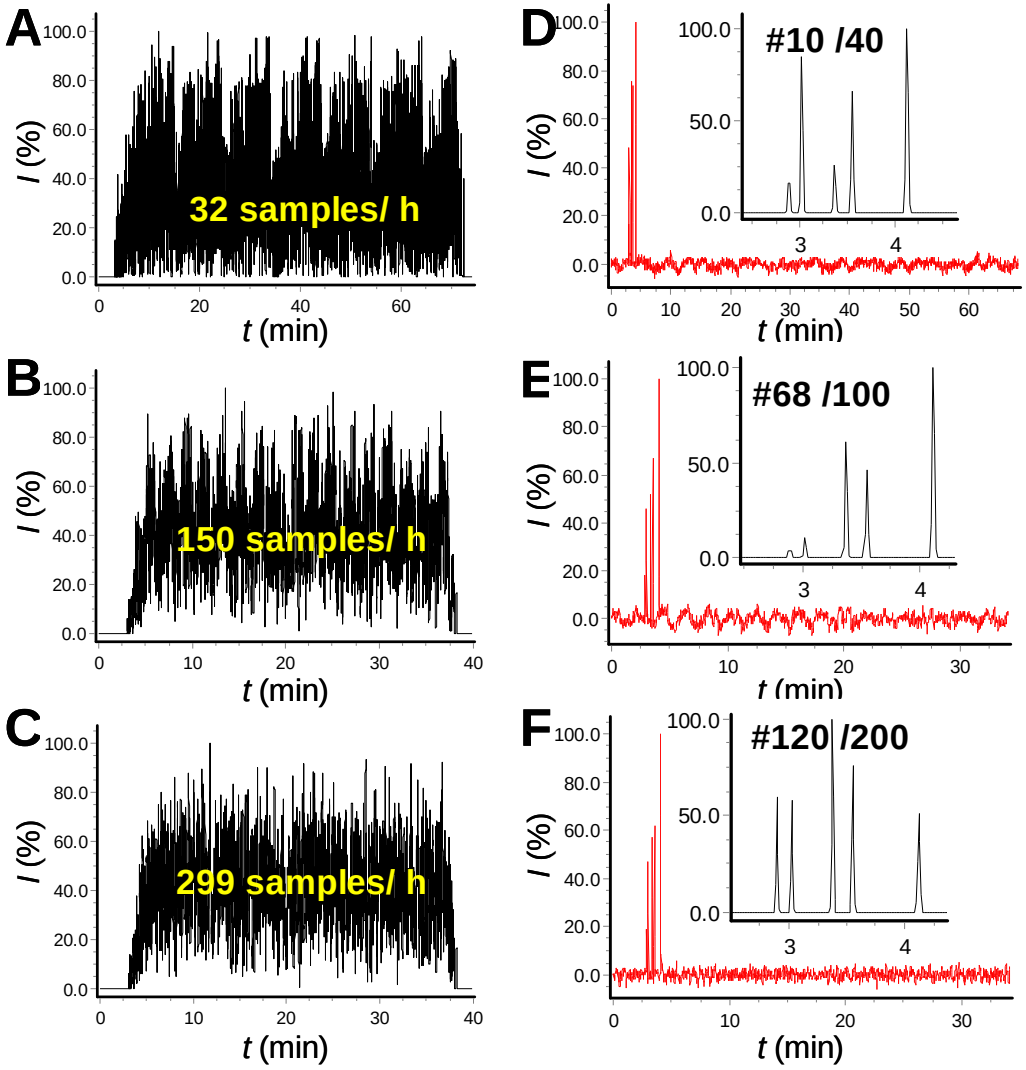
htMPGC: Examples

modulation interval Δt = 2 s,
900 injections/ h,
25 injections/ sample

modulation interval Δt = 1 s,
1,800 injections/ h,
10 injections/ sample

modulation interval Δt = 1 s,
1,800 injections/ h,
5 injections/ sample

11-bit modulation sequence



Conclusions & Outlook

- High-throughput analysis in catalysis (parallel reactors, product analysis, *ee*)
- Time-resolved acquisition of kinetic data
- Investment, maintenance & space

- Extension to HPLC, CE and SFC
- 2D Experiments: MPGCxGC, MPGC-MS
- Intermolecular Interactions, non-linear Effects