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Miniaturization of screening devices for the combinatorial development of heterogeneous catalysts

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Abstract

The present work is focused on the determination of the advantages, bottlenecks and challenges of miniaturized screening systems which are essential to the success of combinatorial high-throughput methodologies in heterogeneous catalysis. Two different reactor configurations with different degrees of miniaturization were developed for the parallel and fast screening of heterogeneously catalyzed gas phase reactions: a monolithic reactor system acting as a multichannel reactor and a microreaction system based on microfabrication techniques. In both cases, a scanning mass spectrometry technique was successfully applied for quantitative product analysis within 60 s per catalyst. Due to its flexibility and high spatial resolution, this three dimensional scanning MS can be used with different and highly parallel reactor arrays. Many experiments were carried out to study the efficiency and reliability of the different screening systems, with the oxidation of methane, the oxidation of CO, and the oxidative dehydrogenation of *i*-butane as model reactions. Moreover, chip modules in silicon–glass technology having a number of parallel microchannels were developed, each of them containing a different catalyst. Using this approach, "catalysis-on-a-chip" proved in methane oxidation was possible. Finally, a multibatch reactor consisting of a number of parallel mini autoclaves was developed and tested in the liquid-phase hydrogenation of citral in order to overcome the lack of parallel and fast screening procedures for heterogeneously catalyzed gas–liquid reactions widely spread in the chemical industry.

Keywords: Combinatorial catalysis; High-throughput screening of catalysts; Miniaturization; Scanning mass spectrometry; Microchannel reactor; Catalysis-on-a-chip; Multibatch hydrogenation

1. Introduction

The miniaturization of chemical and physical processes and their integration onto a microchip for a specific application are definitely reality. Already today, the emerging high-throughput screening of combinatorial libraries revolutionize the drug discovery in the same way that microchips have influenced the epochal development of computers and electronics. The pharmaceutical industry is, indeed, the main driver of developing process miniaturization and integration.

Obviously, there are very strong analogies between the development of combinatorial chemistry for drug discovery and combinatorial material science, including combinatorial catalysis as an important part. It is well worthwhile to read an excellent paper of Lebl [1] about the development of combinatorial chemistry and to compare it with today's situation

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in combinatorial material science. The first papers in combinatorial chemistry were published in the mid 1980s. Since that exponentially growing activities in the field have been observed, fundamentally changing the old research paradigms. The first companies in this field were founded in the late 1980s and beginning of 1990s. Combinatorial chemistry and high-throughput screening are now core technologies in all major pharmaceutical companies. In 1995, a landmark paper of Xiang et al. [2] was published extending the application of combinatorial chemistry to the discovery of solid state materials.

However, many of the current research activities in combinatorial catalysis concentrate on miniaturized analytical and microreactor systems as well as high-throughput catalyst screening. In contrast to conventional bench-scale systems, high-throughput and the application of very small amounts of materials are the two major advantages of catalyst screening using miniaturized chemical devices. Three key concepts will determine the near future progress in this field, namely miniaturization, automation and parallel processing.

The high-throughput catalyst screening should be able to substitute totally or at least partially the time-consuming and man power-consuming conventional screening methods. This is the motivation for the ongoing research in two screening stages, viz. catalyst discovery as the first stage and catalyst optimization as the second one. In both stages, the application of either catalyst particles used in a multitude of parallel fixed beds or catalytic active walls of several microflow channels in parallel is carried out. Screening results obtained with the former are appropriate, in particular, for catalyst scale-up procedures preparing industrial usable fixed bed catalysts. Their preparation is carried out predominantly by well-known conventional methods, e.g. impregnation, ion-exchange, grafting. Screening results from the latter are directly applicable to microchannel reactors and catalytic wall reactors in general. The preparation techniques used include a wide variety of surface treatment and deposition methods, e.g. sputtering, CVD, PVD, chemical and electrochemical deposition, plasma-chemical and anodic oxidation, sol–gel-deposition.

During the last 3 years a number of library screening techniques for heterogeneous catalysts have been developed by a few research groups. The most important contributions were published by Symyx Technologies in Santa Clara, CA, the Max-Planck-Institut für Kohlenforschung Mülheim, Germany, the Chemnitz University of Technology, Germany, the Institute for Applied Chemistry Berlin, Germany, and the Department of Chemical Engineering, University of California, Los Angeles.

Among the screening methods optical ones and mass spectrometry have been most frequently used. An easy and rapid method to detect the optical properties of a material library is the use of a CCD camera [3] or, in the simplest way in the case of liquid phase reactions, the application of a color indicator method. For example, by in situ monitoring of the production of protons via the color change of a fluorescent pH indicator in the presence of UV light, Reddington et al. [4] developed a new heterogeneous catalyst (Pt_{44}–Ru_{41}–Os_{10}–Ir_5) for the electrooxidation of methanol resulting in 40% higher current densities than the standard methanol fuel cell catalyst $Pt_{50}Ru_{50}$.

By emission corrected infrared (IR) thermography, Maier and co-workers [5] used IR cameras with high temperature resolution to spatially resolve reaction heats of the hydrogenation of 1-hexyne, the oxidation of isooctane, and the oxidation of toluene over catalysts of a library consisting of 37 combinations of transition metals on amorphous microporous mixed oxides. Clearly, the identification of reaction products and, thus, the estimation of selectivities is not possible but these techniques are especially useful to detect the catalyst activity in a very sensitive and effective way during primary screening in combinatorial catalyst development.

Among the optical screening methods, resonance-enhanced multiphoton ionization (REMPI) can, in principle, provide information about the reaction products, if the absorption and ionization features of the latter are known [6]. Senkan and Ozturk combined microreactors with REMPI as an optical screening tool to detect the catalytic properties of 72 Pt–Pd catalysts [6] and a ternary Pt–Pd–In/γ-Al_2O_3 library (66 catalysts [7]) for the simple dehydrogenation of cyclohexane to benzene. Up to date, the use of REMPI for screening reactions with more complicated product mixtures is not known.

To overcome the drawbacks of the optical methods mass spectrometry is often applied as qualitative and quantitative detection tool for the products formed during the catalytic reaction and facilitates the estimation

of product selectivities and reactant conversion. Two basic concepts for the application of scanning mass spectrometers have been published: Scanning a catalyst library wafer with two concentrical capillaries in a transient mode [8] and scanning a continuously operated reactor array [9], as described in detail later. Catalyst screening techniques based on mass spectrometry were applied to several reactions as the partial oxidation of propene over a sol–gel derived catalyst library with 33 mixed oxides [10], the oxidation of CO over 120 ternary thin film Pt–Pd–Rh and Pd–Rh–Cu catalysts [8] and over supported gold catalysts [11,12], oxidative dehydrogenation of ethane over 66 ternary combinations of Mo, V and Nb oxides [13], dehydrogenation of cyclohexane over 66 combinations of alumina supported Pt, Pd and In [14] and oxidative dimerization of methane over 30 binary combinations of silica supported W and Mn oxides [12].

Due to the enormous industrial impact of the development of better catalysts a number of new companies is already active in the field of combinatorial catalysis, namely Symyx Technologies in Santa Clara, CA, hte Aktiengesellschaft in Heidelberg, Germany, and Avantium in Amsterdam, The Netherlands.

Based on the experiences of the authors in the preparation of heterogeneous catalysts for hydrogenation and oxidation reactions and in the development of microchannel reactors, different catalyst screening approaches have been developed. This methodological work is focused on the determination of the advantages, bottlenecks and challenges in catalyst screening systems. Therefore, a lot of work was done to adapt analysis tools, to allow reproducible tests, to investigate suitable degrees of miniaturization and to reduce cross talking between adjacent microreactors.

This contribution, however, deals with in house developments of screening devices for catalyst discovery using both fixed bed catalysts and catalytic active walls, with the catalyst preparation as well as with the performance of these catalyst screening devices for heterogeneously catalyzed gas phase oxidation and hydrogenation reactions. The screening approaches are presented in a top-down-order concerning size, i.e. beginning with a monolithic reactor module screening fixed-bed catalysts in millimeter-sized parallel channels, secondly, a microreaction system with the catalysts as catalytic active coatings on several microchannels, and finally, the catalysis-on-a-chip approach with the most advanced reactor miniaturization to date.

In addition, a novel multibatch reactor system for the screening of heterogeneous catalysts in gas–liquid hydrogenations is shortly introduced.

2. Scanning mass spectrometry

A key component in high-throughput catalyst screening systems is a suitable product analysis technique. There is indeed high demand for fast and parallel product analysis tools as can be seen from a lot of patents in combinatorial catalysis. The number of parallel reactors in catalyst screening is, in most cases, limited by the speed of the product analysis. As reported later, we use a scanning mass spectrometer in continuously operated parallel gas phase reactions, first described by Zech et al. [9] and shortly later adapted by Senkan et al. [14] and others.

The scanning mass spectrometer consists of a mass spectrometer having a capillary sample inlet and a sampling device that positions the capillary in *X*–*Y*–*Z*-direction at defined positions within the parallel reactor configuration. The gas samples are continuously transferred to the mass spectrometer through the inlet capillary allowing a very fast online analysis. Based on our experience with this type of analysis tools, the scanning MS can be regarded as an almost universal analysis technique for gas phase reactions in combinatorial catalysis. It can be used with virtually every reactor configuration and application, where time and spatially resolved sampling is needed and complex gaseous mixtures have to be analyzed.

The principle functioning of the sampling device is illustrated in Fig. 1 [15]. The sample is taken by a replaceable silica capillary in a gas-tight housing. Fig. 2 shows the capillary in front of the product outlets of different reactors.

The capillary can be positioned with an accuracy of about 10 μm under hazardous chemical conditions and high thermal demands. During the sampling the capillary moves first in *X*-direction and *Y*-direction to the corresponding microreactor and afterwards in *Z*-direction a certain depth into the product outlet of that microreactor. The moving parameters and the position of the capillary, adjusted and supervized by a CCD camera equipped with magnifying optics, are

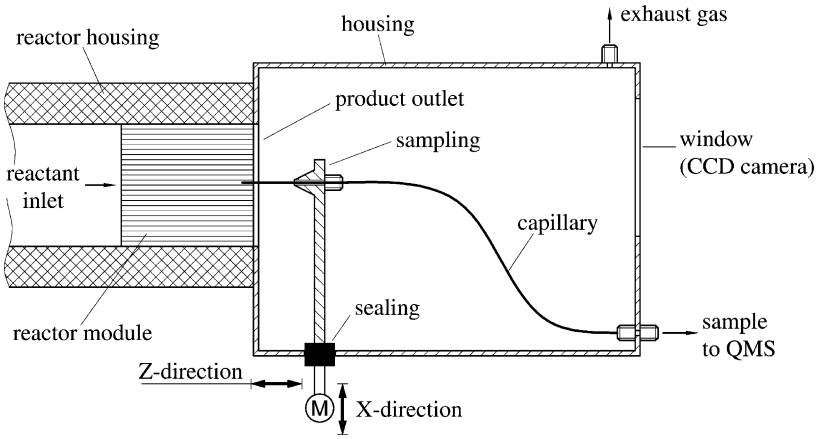

Fig. 1. Principle functioning of the developed sampling device. The sample is taken by the capillary.

freely programmable. The materials of the housing and the sealing were carefully chosen to withstand temperatures up to 450°C. The analysis speed can be determined by choosing the right MS conditions and the application of short and small inlet capillaries. Depending of course on the nature of the products of interest, analysis times of less than 60 s can easily be achieved. Therefore, this scanning mass spectrometry technique is very interesting for primary screening approaches, i.e. screening very large reactor arrays within a short time. By choosing the right capillary and housing configurations it is also possible to apply this technique in high temperature and high pressure environments.

In primary screening, miniaturization is essential to increase the number of tested catalysts. The question was how far one can miniaturize the catalytic reactors while maintaining a good analysis speed and pure samples with the described scanning MS. Therefore, a sample structure consisting of a static micromixer was investigated [16]. The outlet of the micromixer consists of a very large number of parallel microchannels having a cross section of 100 m × 100 m on a pitch of only 200 μm. Each of these microchannels is delivering a separate gas stream. The composition of each of these substreams should be analyzed by the scanning MS. A CCD-picture of the channel outlets is shown in Fig. 3. In the picture lines of light and dark channel outlets can be observed resulting from light reflection due to different outlet angles. In an experiment, microchannels with light channel outlets are delivering Ar, microchannels with black channel outlets are delivering N_2, respectively. On the right-hand side of Fig. 3, the capillary scanning the mixer at a distance of 50 μm can be seen.

A sampling capillary with an outer diameter of 30 μm and an inner diameter of 20 μm was used. It was necessary to use such a narrow capillary to achieve a high spatial resolution and to avoid disturbance of the fluid flow as much as possible. In a typical experiment, the capillary scanned the fluid composition in different positions and distances from the channel outlets. All the time the mass spectrometer was analyzing the samples at a rate of about three samples per second resulting in about 60,000 data sets per experiment. The fluid temperature was kept constant at 25°C.

A typical result of the scanning of the microchannel array in *X*-direction at a defined distance of 50 μm is shown in Fig. 4. The diagram shows the molar concentration of argon in the fluid versus the capillary position. Strong variations in the argon concentration can be observed. The variations are very regular and represent the structure of the microchannel array at the outlet very well. When the capillary passes in front of a microchannel that delivers Ar, the Ar concentration in the diagram increases to a value of almost 1. Similarly, the Ar concentration decreases to almost 0 when the capillary passes a microchannel with a N_2 substream.

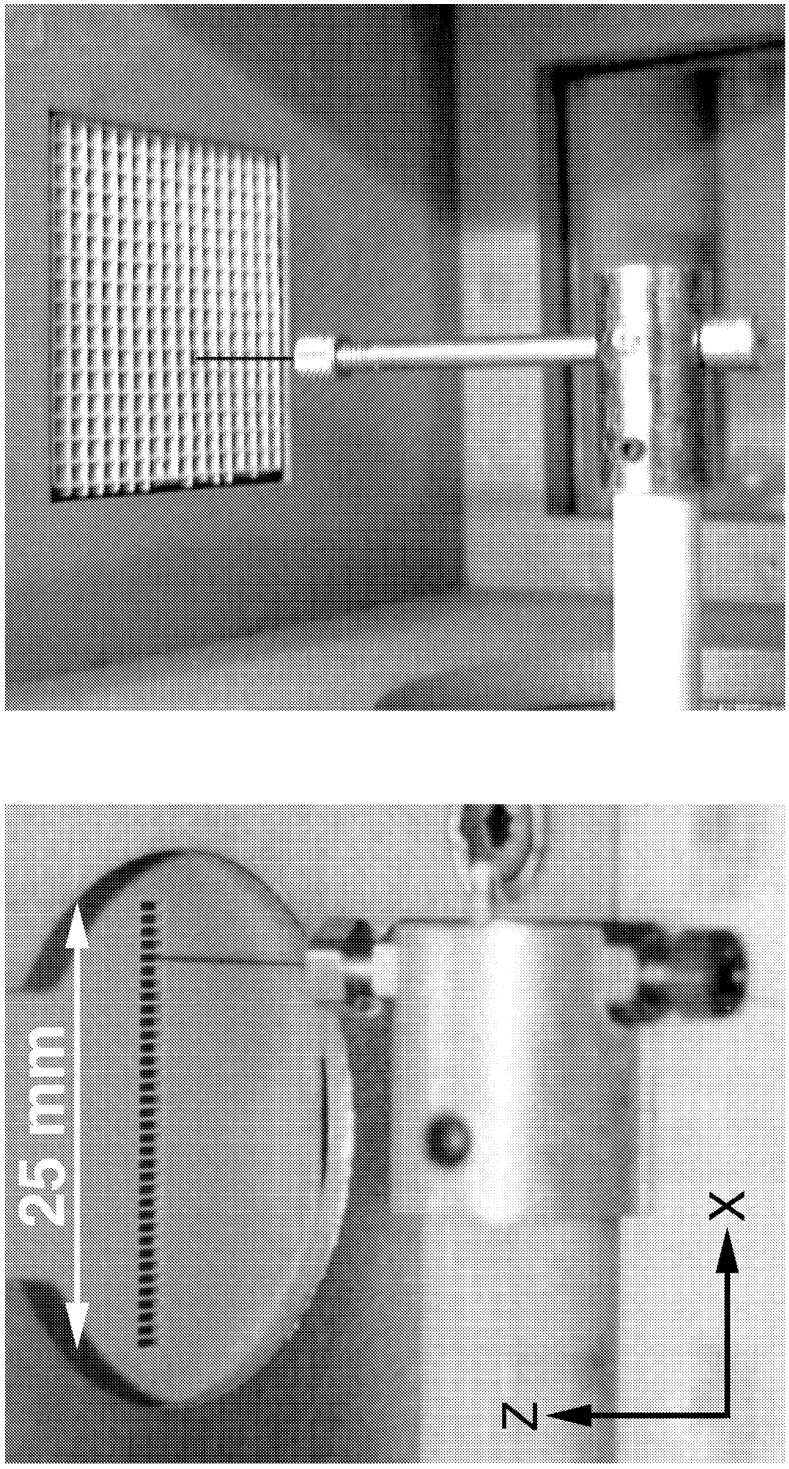

Fig. 2. The sampling capillary in front of different reactor configurations.

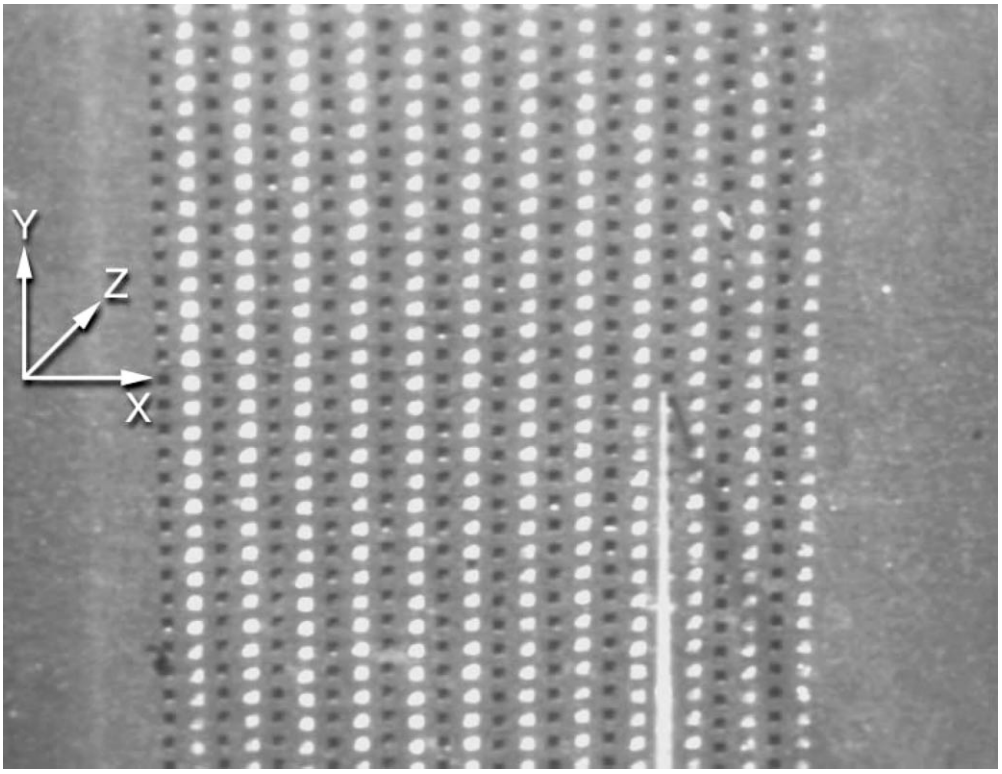

Fig. 3. CCD picture of the microchannel array and the scanning capillary.

That means, that even an extremely miniaturized reactor array on a pitch of 200 μm can be screened by means of the scanning MS while still yielding rather pure samples.

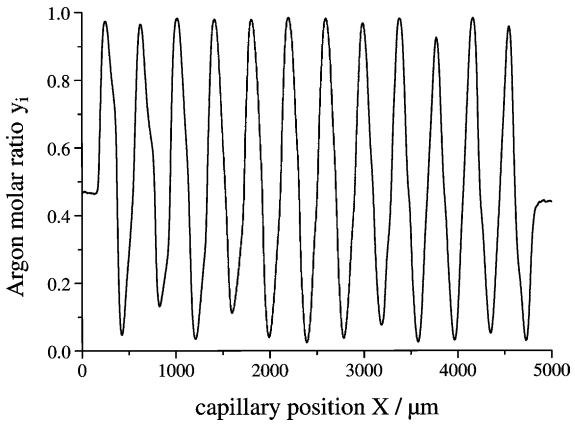

Fig. 4. Scanning data at a capillary distance of 50 μm.

3. Screening of fixed bed catalysts in monoliths as multichannel reactor

3.1. Experimental equipment and procedure

Recently, Rodemerck et al. [12] presented a multitubular reactor containing 15 tubular quartz reactors equipped with an on-line mass spectrometer. Beside information about the products formed during the catalytic reaction, other main advantages of this system are that the time for catalyst screening can be decreased by a factor of 10 compared to traditional test equipment (single fixed-bed reactor), and that catalyst powder or small catalyst particles (size up to 1 mm) can be exposed to a gaseous reactant mixture which passes the catalyst bed in the plug-flow mode. This means that the catalyst screening can be carried out under nearly industrial conditions. The latter is definitively not the case if, firstly, the catalyst library consists only of sites of thin film patches [8] exhibiting

different structural, morphological and, thus, probably chemical and catalytic properties in comparison with conventionally prepared heterogeneous catalysts. Secondly, if the gaseous reactants are transported to and then from these catalyst patches by means of a system of capillaries [8] gas flow through the catalyst bulk is not ensured.

For further miniaturization and, thus, increased speed of the catalyst screening a ceramic monolith reactor module was developed by Rodemerck et al. [17]. Each channel of the monolith (2.2 mm × 2.2 mm, 150 mm long each, arranged in 16 columns and 16 rows) represents a single fixed-bed reactor and contains a different catalyst material, again in the form of powder or catalyst particles, so that up to 256 catalyst compositions can be tested in parallel.

The gas composition produced by the catalytic reaction in each channel of the monolith can be analyzed sequentially by a quadrupole mass spectrometer (QMS, Pfeiffer Vakuumtechnik). For that purpose, the QMS inlet capillary is moved in *X*- and *Y*-direction of the catalyst array and then into the particular channel (*Z*-direction) by a three-dimensional (3D) positioning system based on the experiences of Zech et al. [15]. The position of the capillary above a monolith channel can be automatically changed by using the three stepping motors of the positioning system supervized by a CCD camera and exactly controlled by the software. Fig. 5 shows the principle of the reactor system which is fully automated so that catalyst tests run automatically. The 3D positioning system works at temperatures up to 600°C so that catalytic properties at high-temperature conditions can be screened.

Before the catalytic data obtained for each catalyst during the screening procedure can be compared with

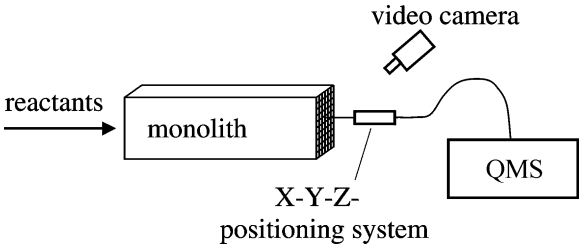

Fig. 5. Principle of the monolithic reactor system for parallel screening of heterogeneous catalysts.

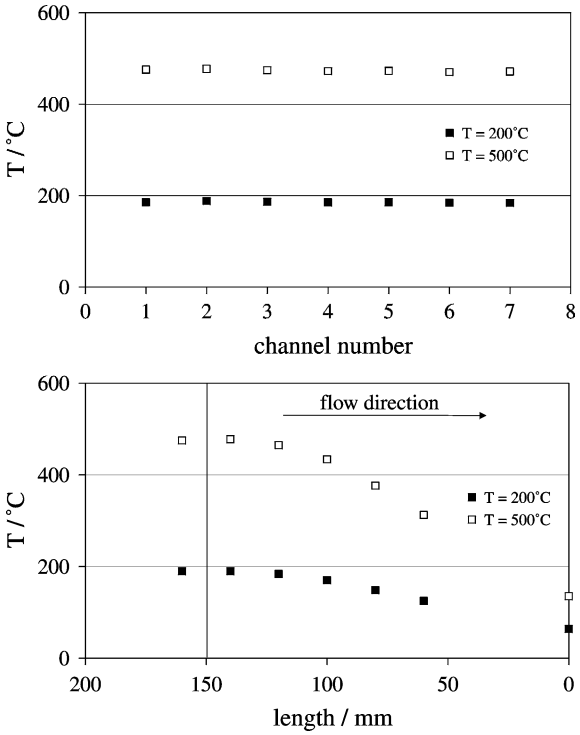

Fig. 6. Axial and radial temperature profiles in the monolith. The catalysts were settled in each channel between 110 and 140 mm in length. Only the first-half of the monolith (75–150 mm) is heated.

those of the other catalysts of the array to decide which catalyst of an array is the most active or selective, the reliability of the experiments has to be ensured. Therefore, a number of experiments concerning, e.g. temperature profiles and interference from gaseous components from the open ends of adjacent channels were conducted, represented exemplary in Figs. 6 and 7. The axial and radial temperature profiles (Fig. 6) measured without catalysts showed that the differences between the channels did not exceed 5 K and that an axial isothermal zone of approximately 4 cm exists [17]. Fig. 7 shows that penetration of gases into the channel by counter-current diffusion (measured via diffusion of air into the channel outlets versus a He-stream) strongly depends on the flow rate and on the position of the QMS inlet capillary. Optimal conditions with respect to flow rate (minimum 5 ml/min) and capillary position (25 mm from channel outlet) for catalyst screening experiments were found. Moreover,

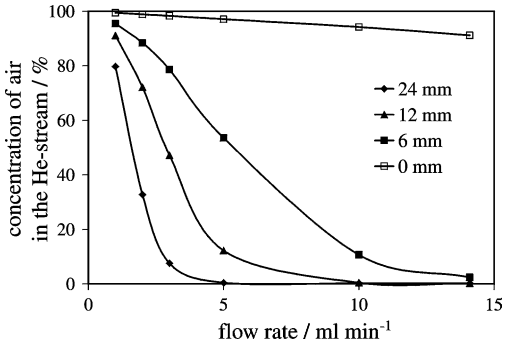

Fig. 7. Back diffusion of air into a channel of the monolith flowed through by a stream of He.

as the diffusion of air into the channel outlets depends on the flow rate in each individual channel, differences in flow rate can be measured by differences in the concentration of air at a position of 25 mm from the end of the channels. From this type of experiment it followed that the flow rates, experimentally proved for 36 channels filled with differently composed catalysts, differed by about 10%. From these non-catalytic experiments it can be concluded that the experimental conditions can be adjusted well enough to compare different catalysts enabling the use of this reactor system for parallel screening experiments of heterogeneous catalysts.

3.2. Methane oxidation

3.2.1. Library preparation

A catalyst library was prepared via the incipient wetness method by the combination of different amounts of Pt, Zr and V, via their acetylacetonates, on Al_2O_3 by means of an automatic liquid handler (Gilson). The library contains 36 Pt/Zr/V/Al_2O_3 catalysts (a combination of 0, 0.01, 0.1, 0.5 wt.% Pt; 0, 0.1, 0.5 wt.% Zr and 0, 0.1, 0.5 wt.% V [17]). After dissolving the Pt, Zr, and V precursors in $CHCl_3$, the calculated volumes of the precursor solutions were mixed and diluted followed by soaking γ–Al_2O_3 (Aluperl type 1540, Kali-Chemie AG) by the mixture. After drying at ambient temperature the catalyst precursors were pretreated by calcination in air for 3 h at 450°C in the channels of the monolithic reactor.

3.2.2. Screening results

Methane oxidation at 450°C was chosen to test the Pt/Zr/V/Al_2O_3 catalysts in the monolithic reactor in parallel. In Fig. 8, the screening results of the 36-member-array are compared with those obtained in the multitubular reactor system (15 fixed bed reactors of 3.5 mm ID, for details see [12]). In both screening systems only the catalysts which contain 0.5 wt.% Pt were active catalyzing the total oxidation of methane to carbon oxides. Selective oxidation products were not detected by the MS. The catalysts containing Pt amounts up to 0.1 wt.% were found to give only very small methane conversion. There is need for further explanation of other features of the screening results. Firstly, the lower conversion degree in the monolithic reactor (see Fig. 8) is caused by a higher gas flow. Secondly, due to differences in the gas velocity in the individual channels the methane conversion differs more than in the multitube reactor. Thirdly, in the monolithic reactor catalysts with lower Pt contents gave

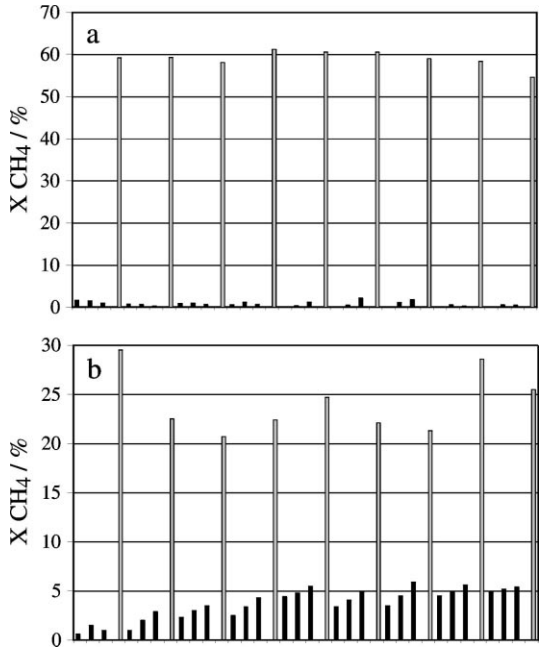

Fig. 8. Methane conversion degree of 36 Pt/Zr/V/Al_2O_3 catalysts of different compositions (grey: catalysts containing 0.5% Pt, black: 0–0.1% Pt), $T = 450°C$, feed: 6% CH_4, 6% O_2, 10% Ar, 78% He. (a) Test in the multitubular reactor, 200 mg each catalyst, GHSV = 6600 ml h^{-1} g^{-1}; (b) test in the monolithic reactor, 26 mg each catalyst, GHSV = 18,000 ml h^{-1} g^{-1}.

conversion degrees up to 7%. Note that the conversion degree measured at these inactive catalysts was increased with screening time (catalysts on the left side of the diagram were tested first). This effect is due to the fact that carbon oxides are accumulated and methane concentration is decreased in the chamber at the end of the channels, where the MS capillary is moved in. A part of this gas mixture can penetrate the end of the channels by diffusion as described above and, therefore, the concentration of carbon oxides is increased in the channels containing inactive catalysts whereas the concentration of methane is decreased implying a higher conversion degree.

However, the results obtained with a $Pt/Zr/V/Al_2O_3$ library clearly show that it is possible to select the more active or selective catalysts from a catalyst library. The monolithic reactor is considered to be an efficient tool for a fast catalyst pre-screening (often called phase 1) distinguishing between poor and good catalysts. Applying this system one catalyst can be tested in less than 1 min. Thus, this reactor system can speed up the screening of catalysts by a factor of 100 compared to the traditional equipment. The accuracy of the results, however, is lower mainly due to difficulties in generating equal gas flows in all channels of the monolith and, under certain experimental conditions, due to the diffusion of exhausted gases from adjacent catalysts into the end of a channel containing the catalyst which is actually under screening.

Therefore, it can be concluded that an efficient strategy of catalyst development was found consisting of selecting the best catalyst or good candidates from a library in a very short time by the developed monolithic reactor operating in a parallel screening mode and to test these catalysts then once more in a more precise manner in the multitube reactor to obtain quantitative results at desired reaction conditions.

3.3. CO oxidation

3.3.1. Library preparation

Different supported gold catalysts originally prepared and applied for the selective hydrogenation of unsaturated aldehydes [18,19] were obtained by the following methods: precipitation (P), deposition–precipitation (DP), impregnation (I) and sol–gel technique (SG). Details of the preparation procedure and pretreatment conditions were reported elsewhere [12,18,19]. Their uniform internal pretreatment in the channels of the monolith were simultaneously conducted at 650°C.

3.3.2. Screening results

The gold catalysts were tested in CO oxidation at temperatures between 25 and 250°C. For the quantitative product analysis during the parallel testing of the catalysts, the mass numbers 28 (CO), 32 (O_2), 40 (Ar, internal standard) and 44 (CO_2) were used. The results are shown in Fig. 9 using the yield of carbon dioxide as the measure of activity. It can be seen that, as expected [20], in particular gold catalysts on the basis of ZrO_2 and TiO_2 were active at lower temperatures. Surprisingly, Au/Nd_2O_3 gave significantly higher activities in the temperature range of between 150 and 250°C than the other supported (titania and zirconia free) gold catalysts. Comparing the screening results with those obtained in the multitube reactor [21], the same samples were identified as the best catalysts and the similar trend in activity (Au/TiO_2-DP>Au/TiO_2-I>Au/Nd_2O_3) was observed which shows again it is possible to select the best catalysts from a catalyst library by screening in the monolith reactor. Moreover, this is connected with a considerable gain of time, because the screening procedure of one catalyst is finished after approximately 1 min.

4. Microreaction system for the development of catalysts for microchannel reactors

Due to advancements in microfabrication techniques, new types of chemical reactors, namely microchannel reactors, were developed several years ago [22]. Such a reactor consists of a very large number of parallel microchannels having a cross section of, for instance, 500 m × 500 m. By means of such small channel dimensions, very large heat and mass transfer rates can be achieved. Furthermore, explosive and dangerous reactions can reasonably be carried out in microchannel reactors. Obviously, microchannel reactors for heterogeneously catalyzed reactions gain increasing importance because of higher conversion degrees and selectivities as well as process intensification. The approach we present here is, therefore, focused on the combinatorial screening of catalysts, where the catalytic active species are immobilized

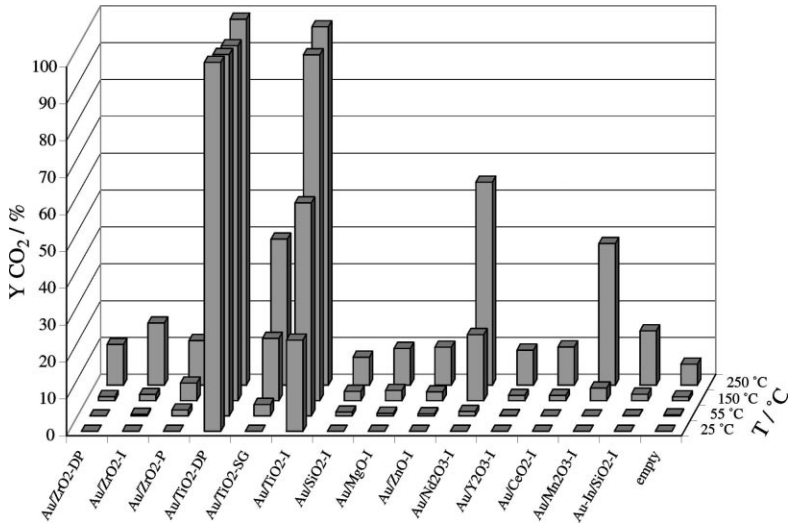

Fig. 9. Screening results of CO oxidation over supported gold catalysts in the monolith reactor (feed: 1% CO, 75% He, 20% O_2, 4% Ar; $\tau = 0.18\,\mathrm{g\,s\,ml^{-1}}$).

on the channel walls of the microchannels. The key elements of this approach are, as stated above, a suitable reactor module and the analysis technique. Regarding the catalysts on the surface of such microchannels there are of course a number of challenges, such as the adhesion of these catalytic active coatings onto the channel walls, the catalytic activity due to often lower surface areas and the long term behavior.

4.1. Reactor module and microstructured catalyst inlays

The first and simplest generation of the reactor module consists of a stack of metallic frames, as shown in Fig. 10 [15]. Stacking these metallic frames together, several parallel and independent microreactors are formed. The prototype consists of 35 microreactors. Each microreactor is then filled with a microstructured inlay containing one catalyst as catalytic active coating on top of its microchannels. It is, therefore, possible to screen 35 different catalysts in parallel. A photograph of the reactor module is shown in Fig. 11.

In order to test the catalytic properties of the prepared catalysts, the reactants are uniformly distributed to all parallel microreactors. Then, the reactants flow through the microchannels of the microstructured inlays, react on the catalytic active surface of the microchannels and the products are withdrawn through the product outlets.

The catalysts can easily be removed and replaced with a new set of catalysts. The module is heated externally to achieve reaction temperatures up to 450°C. The product outlet at the end of each microreactor has a cross section of 2–0.5 mm. It is obvious that the design of the reactor module can be further improved, e.g. by designing the module as cross-flow heat exchanger [23] to ensure a constant temperature along the reaction channels and the height of the reactor module.

The reactor module design allows the use of replaceable microstructured catalyst inlays made of different materials such as metals, silicon, ceramics, and glass. That is an important strength increasing the flexibility of the system. This allows many different catalyst synthesis procedures as well as microchannel geometries being essential to the generation of suitable catalyst libraries for different heterogenously catalyzed reactions. Fig. 12 presents a typical microstructured support and some examples of catalysts prepared on different substrates.

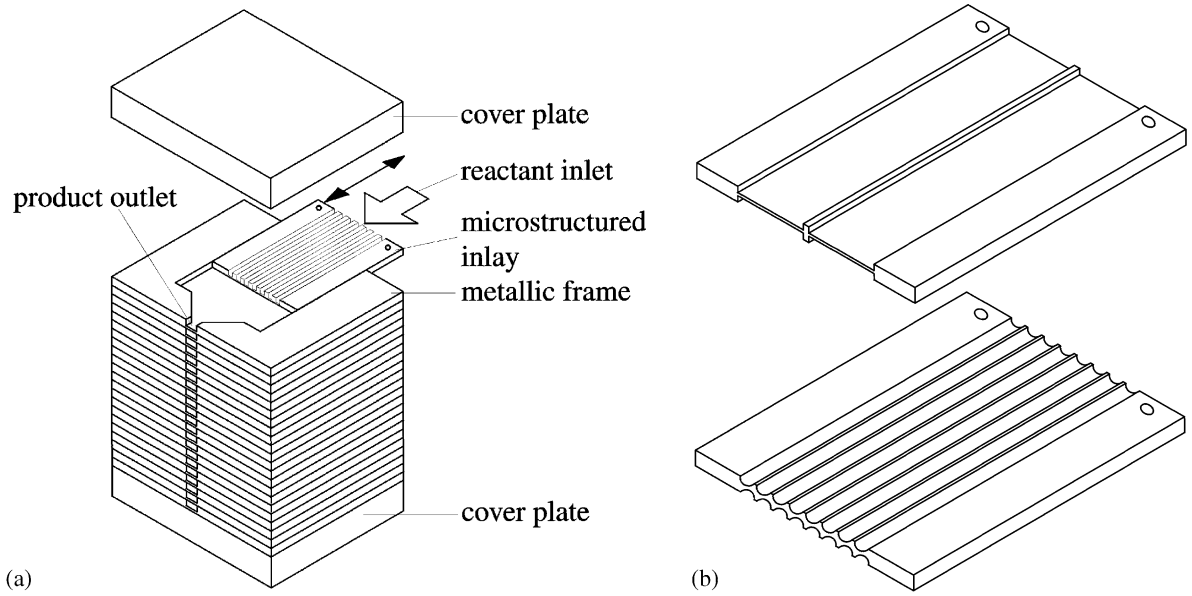

Fig. 10. (a) Reactor module consisting of 35 stacked metallic frames. The catalyst inlays are mounted and removed in the directions of the arrow. (b) Microstructured catalyst inlays made of aluminum either by mechanical micromilling by wet etching (channel radius: 130 μm).

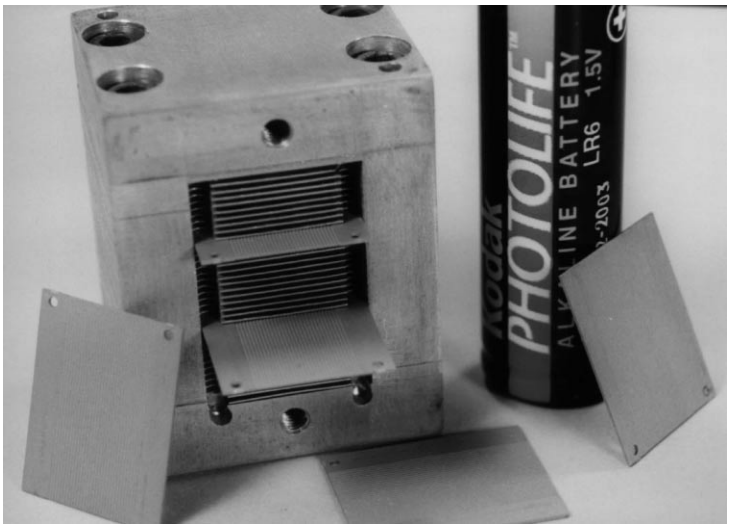

Fig. 11. Photograph of the reactor module and the microstructured inlays.

4.2. Flowsheet of the catalyst screening unit

The catalyst screening unit consists of several mass flow controllers (Brooks) supplying the reactant gases and the described reactor module in a housing that is externally heated. Furthermore, there is a scanning mass spectrometer consisting of a sampling device and a quadrupole mass spectrometer (Hiden Analytical), as described earlier. The parallel product outlets of the reactor module lie very close together which implies

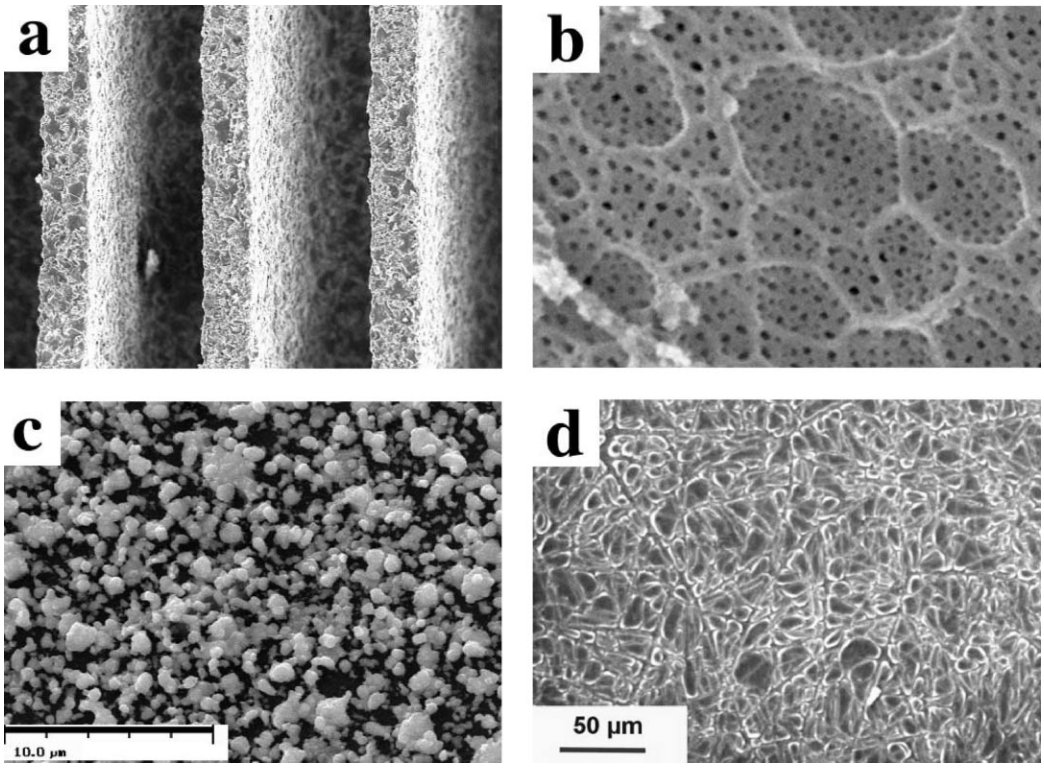

Fig. 12. (a) Typical microstructure with a channel width of 300 μm manufactured by electrodischarge micromachining [26]; (b) Al_2O_3-layer prepared by anodic oxidation, pore diameter approx. 40 nm; (c) activated silver catalyst on Al_2O_3 prepared by sputtering [30]; (d) Ru–Al_2O_3-catalyst prepared by the SG technique.

that the reactor module can almost be considered as a static micromixer. Thus, products from an individual microreactor are mixed immediately with the products from the adjacent microreactor when leaving the corresponding reactor. As the products from each catalyst should be analyzed with low background noise from the other ones, the sample has to be taken inside the product outlet of the corresponding microreactor.

A PC finally controls the reaction, the product sampling and the data acquisition (Fig. 13).

4.3. Automation and data processing

As stated above systems for high-throughput catalysts screening have to be automated. Therefore, the complete screening procedure is automated in our setup. The system can be run overnight or longer without the need for observing the screening progress. That means, that the moving parameters and the position of the capillary is controlled by appropriate software and supervized by a CCD camera while, at the same time, the mass spectrometer analyzes the gas samples according to the capillary position. It is possible to run a predefined program varying the sampling parameters. Furthermore, reaction conditions including residence time, reactant concentration, reactor temperature and pressure are controlled and can be varied during screening.

The catalyst preparation procedure is carried out in parallel for 35 catalysts, however, not yet automated. Presently, 35 catalysts can be produced per day, being in accordance with the time for screening these catalysts under different reaction conditions. In the future, an automated liquid dispensing robot will be used to facilitate the catalyst preparation procedure. Nevertheless, it is very difficult and probably not necessary to

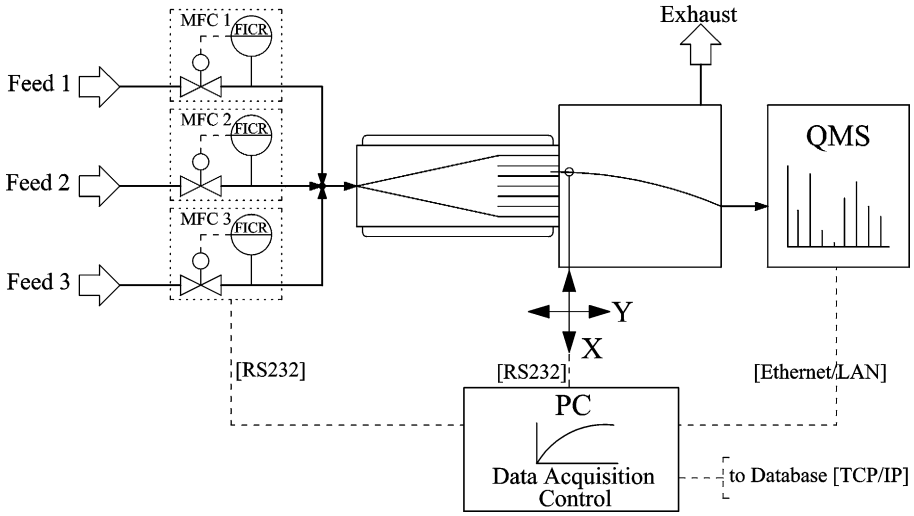

Fig. 13. Simplified flowsheet and communication links of the catalyst screening unit consisting of: gas supply, reactor, sampling device, mass spectrometer and PC.

automate the whole workflow in an academic institution as this is coupled with very high investments in both, capital and labor. Data processing is realized by using the powerful relational database from Oracle, an industry standard in combinatorics. All parameters characterizing the catalyst libraries are registered in the database. Again, it is very difficult for academic institutions to set up a complete data management system.

4.4. Efficiency and reliability of screening experiments

4.4.1. Reactant distribution

When operating a number of reactors in parallel in order to compare the performance of these rectors it has to be ensured that each reactor and each catalyst is exposed to the same reaction conditions, especially equal amounts of reactants at the same residence times. A number of experiments was carried out to investigate the reactant distribution in the screening system used [24]. For this purpose, identical catalysts were prepared, mounted into the reactor module and tested for catalytic activity in methane oxidation. Identical catalysts should then yield the same results. At the beginning, a conventional standard diffusor was used to distribute the reactants over the entire cross section of the reactor module. The results are shown in Fig. 14. It can be seen, that with these identical catalysts very different conversions represented by the CO_2-signal and measured by the mass spectrometer could be observed. This is due to non-uniform reactant distribution leading to different residence times within the microfluidic reactors.

In the next step, the standard diffusor was modified. The results obtained with the modified diffusor are also shown in Fig. 14. Obviously, the deviations achieved by modifying the incoming flow are far lower compared to the ones with the un-modified diffusor. The remaining deviations are below 10%. This is sufficiently low for the screening experiments. However, it is predicted that an even better reactant distribution can be achieved by further improving the incoming flow distribution.

4.4.2. Signal-to-noise ratio

In order to achieve results with high accuracy the products from one catalyst should be analyzed with low interference from products from adjacent catalysts. That means, that the cross talking or signal-to-noise ratio between the reactors spaced by a distance of only 200 μm in this approach should be as low as possible.

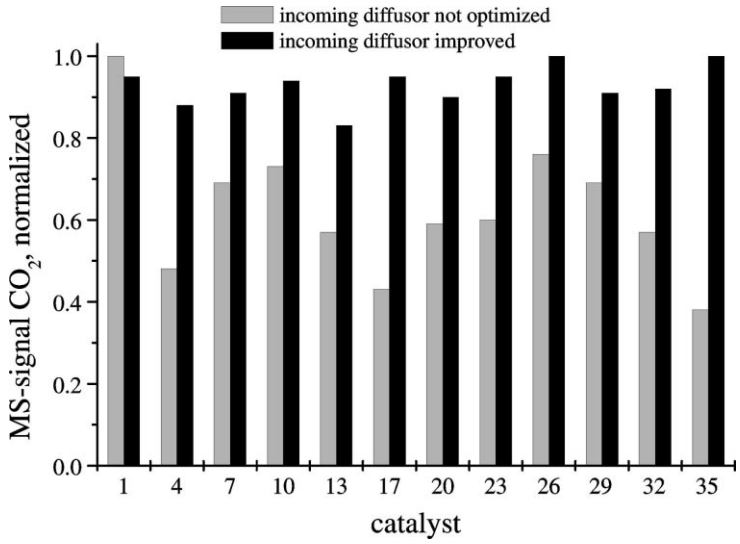

Fig. 14. Reactant distribution expressed as behavior of identical catalysts with and without modification of the incoming flow by different diffusor types.

In order to check the cross talking between the catalysts, an active catalyst was prepared and placed next to inactive ones. Then, a screening was carried out. The results are summarized in Fig. 15, where the detected MS-signal for CO_2 is plotted against the catalyst position. The active catalyst was placed at position 18. Screening time for each catalyst was only 60 s. It can be seen, that the active catalyst produces CO_2. Its neighbors in the library cause only very small amounts of CO_2. The detected amount is in the range of 2% of the amount of the active catalyst which is a really good result. The value of the signal-to-noise ratio can also be measured at longer residence times and hence lower gas velocities, as shown in the second part

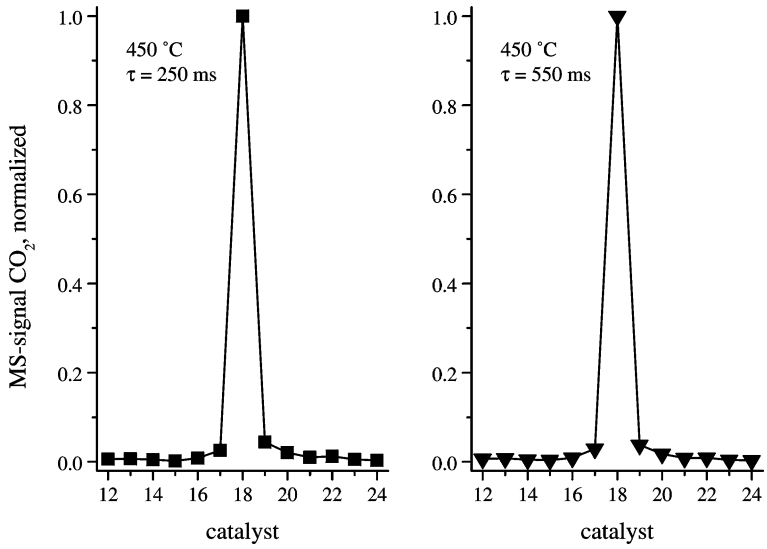

Fig. 15. Signal-to-noise ratio measured as crosstalking between different catalysts at residence times of 250 and 550 ms.

of Fig. 5. It can be assumed that this value further decreases with longer screening times as the noise seems to be produced mainly by the inertia of the analysis system.

4.4.3. Response time

The catalyst screening system developed is used to screen catalysts for microchannel reactors at different process conditions. In order to speed up the discovery process, the tested catalysts must react to changes of the process conditions immediately.

To investigate this property, the behavior of one catalyst in the library was observed while changing the process conditions. The diagram in Fig. 16 shows the step response of the catalyst and the analysis system represented by the normalized MS-signals caused by a step in the reactant concentration in methane oxidation at 450°C. Obviously, the signals of CH_4, O_2 and CO_2 reach a new steady state rapidly, i.e. after approximately 30 s. In contrast, the signal of H_2O takes much longer (about 200 s) to achieve a new steady state. The latter phenomena is caused by adsorption effects within the analysis system.

Having investigated the system behavior, it can be concluded that it is possible to carry out the screening of catalysts with the described setup within very short times for each catalyst under steady state in heterogeneously catalyzed reactions under harsh chemical conditions.

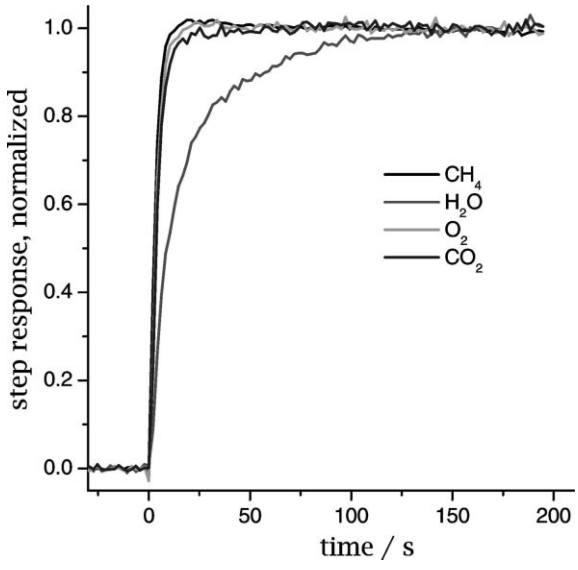

Fig. 16. Step response of one catalyst initiated by changes of the reactant concentration in methane oxidation at 450°C.

4.5. Methane oxidation

4.5.1. Library preparation

As an example, a library of 52 catalysts containing different concentrations of Pt, Zr and V was prepared [24]. First, a Al_2O_3-layer onto microstructured Al-inlays having flow channel diameters of 250 μm was formed by anodic oxidation in sulfuric acid or oxalic acid. This Al_2O_3-layer has a regular pore system with adjustable parameters regarding pore diameter and pore length and is used as catalyst support [25]. Then, the catalytic active species were immobilized by wet impregnation into the Al_2O_3-layer.

Mixtures of different active components (Pt, V, Zr) were obtained by sequential wet impregnation with precursor solutions and calcination at 450°C after every impregnation step. 26 catalysts with an Al_2O_3-layer formed by anodic oxidation in sulfuric acid and 26 catalysts with an Al_2O_3-layer formed by anodic oxidation in oxalic acid were prepared.

Certainly, it is also possible to use other methods for coating the channel walls with a catalytic active layer, e.g. by applying SG, CVD, or PVD technologies.

4.5.2. Screening results

The library was tested in methane oxidation at 450°C and 1.1 bar. The methane-to-oxygen ratio in the feed was 1 in order to find out the potential of the catalysts to form intermediate products. Fig. 17 illustrates the results for a residence time of 550 ms and a screening time of 60 s for each catalyst. One sample cycle, i.e. sampling each of the 35 catalyst inlays once, can, therefore, be carried out within about 35 min. Statistic calculations of the mass spectra reveal that a variation coefficient of the corresponding *M*/*Z*-peaks of less than 1% can be achieved within that short period of time under reaction conditions.

The graph points out the conversion degree of methane for all library members. As can be seen, there are some catalyst inlays that show a very high conversion degree while others are much less active

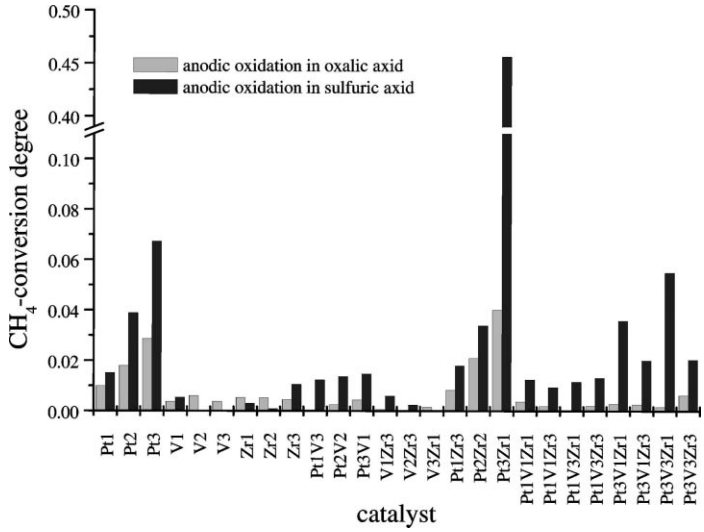

Fig. 17. Conversion degree of the prepared catalysts in methane oxidation at 450°C and 1.1 bar.

under the reaction conditions applied. The active catalysts always contain Pt. The higher the Pt content is the higher the conversion degree will be. Furthermore, the addition of Zr increases while V decreases the conversion degree. Catalysts with an Al_2O_3-layer formed by anodic oxidation in sulfuric acid generally show higher activity. This is caused by smaller pore diameters and hence higher surface areas compared to an Al_2O_3-layer formed by anodic oxidation in oxalic acid.

4.5.3. Reproducibility

Some members of the same library were tested at the same reaction conditions in reproduced experiments. The results of this reproducibility tests are shown in Fig. 18. As can be seen in the diagram, the variations of the measured conversion degree in repeated experiments is indeed in the range of the measurement error. Thus, it is possible to carry out catalytic experiments with excellent reproducibility with the developed screening system.

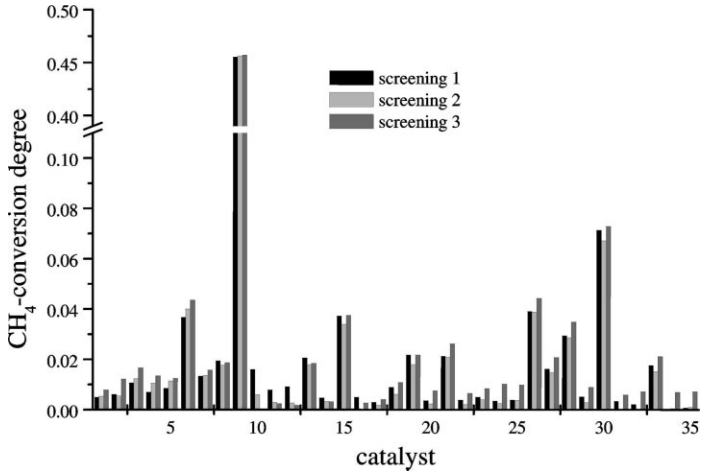

Fig. 18. Reproducibility test for the prepared catalysts in methane oxidation at 450°C and 1.1 bar.

4.6. Oxidative dehydrogenation of i-butane to i-butene

As another model reaction the oxidative dehydrogenation of *i*-butane to *i*-butene was chosen. The reaction was carried out at 450°C, 1.1 bar and a residence time of 450 ms. Several hundred catalysts containing different concentrations of up to three active components on different supports were screened. Fig. 19 illustrates preliminary results for the ternary system V–Zr–Mn on a Al_2O_3-support prepared by anodic oxidation in oxalic acid.

4.7. Optimization tools for microchannel reactors

Having tested large numbers of different catalysts in primary screening there is still need to optimize hits in secondary screening. This also concerns the presented microreaction system although the conditions and catalysts applied are already very close to those found in conventional microchannel reactors. However, suitable optimization tools can provide possibilities to investigate in detail the activation and desactivation as well as the long term behavior of promising catalysts. Furthermore, the catalysts can be exposed to more extreme reaction conditions, e.g. higher pressures, higher temperatures and reactant concentrations

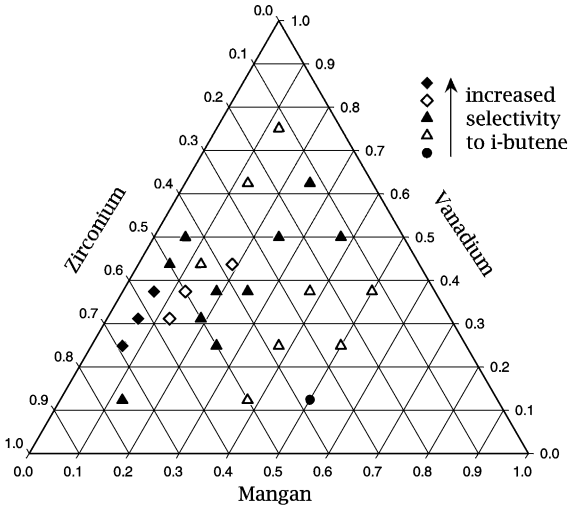

Fig. 19. Selectivity to *i*-butene in the oxydehydrogenation of *i*-butane for the ternary system V–Zr–Mn at 450°C and 1.1 bar.

Fig. 20. Modular reactors for the optimization of catalysts for microchannel reactors.

in the explosion regime. Therefore, some modular microreactor configurations were developed at Chemnitz University of Technology [26]. Two examples are presented in Fig. 20. They are generally used to test larger catalyst quantities and different microchannel geometries, meanwhile, extending the parameter space for the variation of the process conditions.

5. Catalysis-on-a-chip

Having learned the lessons from combinatorial chemistry, it is obvious that there will be an ever increasing demand for more and more material tests to be carried out in combinatorial catalysis. The process of miniaturization while increasing the array density, e.g. multiplying the number of wells on microtiter plates to multiply the number of tested substances while miniaturizing the reaction volumes, will be necessary also for catalyst screening systems.

The motivation for the development of the catalysis-on-a-chip approach follows similar footsteps. We want

to carry out a lot more and faster catalytic tests with less material in the discovery mode. Furthermore, we intend to extend the application of these chip-based systems to multiphase catalytic processes. These are very ambitious targets but miniaturization has indeed important strengths that will be worthwhile. Small scale or chip-based systems allow efficient thermal control, short response times and reduce the inertia of the whole system. Furthermore, miniaturized systems are far easier to automate. By reducing the size of the libraries it becomes possible to use high precision engineering technologies for both, the catalyst preparation and the reactor fabrication. This is followed by a standardization of the screening workflow facilitating the comparison between library members and the reproducibility of the experiments.

The challenges of developing highly parallel chip-based screening systems for combinatorial catalysis are the catalyst design, the sampling and the product analysis as well as the integration of microchemical and electronic components on the chip. Furthermore, it has to be ensured that catalytic results gained on chip-basis can be compared with experiments on a larger scale.

In a first run, chip modules in silicon–glass technology were developed. Each of these chip modules contains a number of parallel microchannels having a cross section of, for instance, 500 m × 200 m, see Figs. 21 and 22. Each microchannel contains a different catalyst. Catalyst synthesis is realized by a micropipetting system known from biotechnological applications. Firstly, a porous catalyst support is synthesized by the SG technique. This support is in the second step impregnated with different precursor solutions to yield different catalysts.

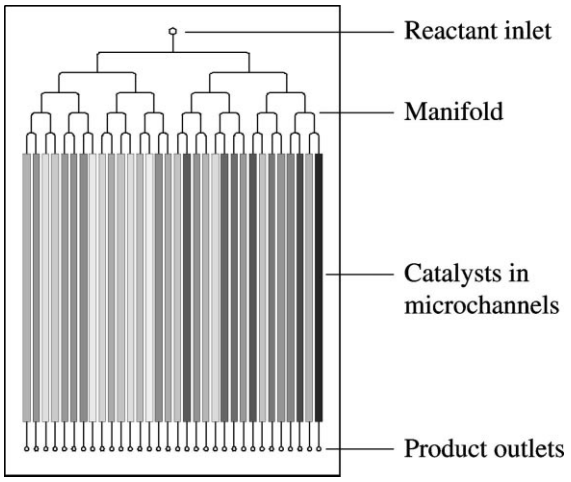

Fig. 21. Principle of the catalysis-on-a-chip approach.

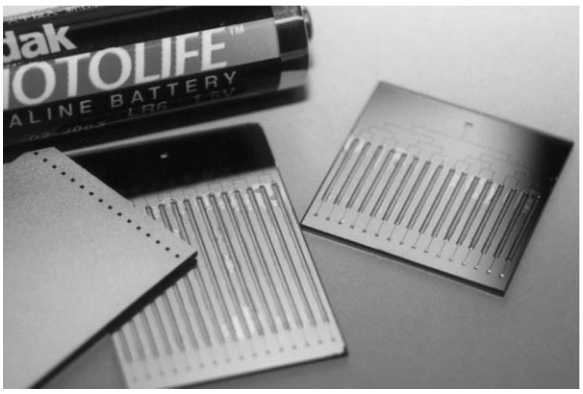

Fig. 22. Prototypes of the chip modules having parallel microchannels.

A uniform distribution of the reactants to all the catalysts is achieved by a microfabricated manifold on the chip. The products leave the chip separately through small holes on the back of the chip and can be analyzed by the scanning MS as described in detail above. The first chip modules contain 16 or 8 parallel channels having different cross sections and channel lengths and they are currently tested in methane oxidation.

6. Multibatch reactor for the fast screening of gas–liquid reactions

As shown before, a number of effective screening tools to detect the catalytic properties of solid materials in gas phase reactions has successfully been developed. However, there is still a lack of parallel and fast screening methods for heterogeneously catalyzed gas–liquid phase reactions although this type of reaction is widely spread in the chemical industry, e.g. if new catalysts for fine chemicals synthesis are needed. Therefore, the development of rapid screening methods for catalytic materials applied in gas–liquid reactions is a challenging task.

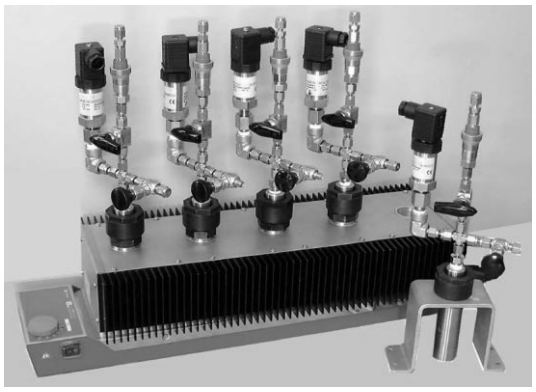

Fig. 23. Reactor modul consisting of five mini autoclaves for fast screening of heterogeneously catalyzed gas–liquid reactions in a multibatch reactor.

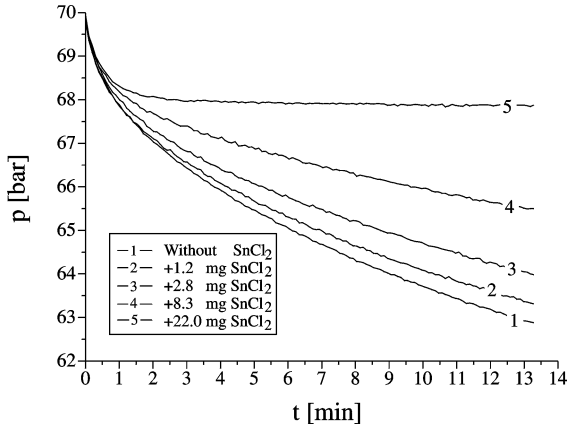

Fig. 24. Parallel screening of heterogeneously catalyzed gas–liquid phase reactions: pressure–time curves of the hydrogenation of citral over 5% Rh/Al_2O_3 with and without addition of $SnCl_2$ as promoter ($T = 298\,K$, $p_{H_2} = 70\,bar$, 840 rpm, reactant: 10.7 mmol citral, solvent: 7.5 ml *n*-hexane, internal standard: 0.67 ml dodecane, catalyst mass: 200 mg).

In this paper, first results of a multibatch reactor system [27] developed to screen heterogeneously catalyzed gas–liquid reactions in a much faster mode are presented. The multibatch system (Fig. 23) consists of 15 parallel working mini autoclaves (reactor volume: 45 ml) which are arranged in three arrays. Each array can be heated and stirred independently from the others. Each autoclave is equipped with a high-precision pressure receptor whose signal is analyzed by a personal computer operating with a self-written software. Thus, fast on-line monitoring of the catalyst activity via pressure–time dependencies is realized and allows an effective comparison with the results obtained in the other autoclaves already during the experiment. Exportation of the data in other software tools and data bases is possible.

In the present configuration, it is possible to screen 15 different catalysts for gas–liquid reactions, e.g. for selective hydrogenations, in parallel for extended periods of time, or to vary typical conditions of such reactions (temperature, pressure, stirring rate, type of solvent, concentrations of the organic components and catalysts) in a very short time. It is obvious that the traditional experimental technique, i.e. catalyst testing in one batch reactor of 100 ml or higher reactor volume, would have taken days or months to get the results. Enlarging the present system to 200 autoclaves in modules of five autoclaves can easily be achieved. The actual specifications of this multibatch system are characterized by:

- pressure: up to 117 bar;
- temperature: 25–300°C;
- stirring rate: up to 1200 rpm;
- volume of the liquid phase: 5–20 ml;
- size per array (five mini autoclaves): 55 cm × 38 cm × 18 cm.

To obtain product selectivities and conversions, catalyst screening is presently accomplished by analyzing the reaction products off-line by gas chromatography, however, automated on-line analysis of each autoclave is in preparation. An example of parallel screening of heterogeneously catalyzed gas–liquid reactions is shown in Fig. 24. The hydrogenation of citral was conducted at room temperature and 70 bar hydrogen pressure over an alumina supported Rh catalyst with and without addition of $SnCl_2$. Tin is known to be a promoter for rhodium, platinum and ruthenium catalysts [28] and acts via oxidized tin species or tin containing alloys which give rise to higher selectivities to the desired unsaturated alcohols (geraniol and nerol in the case of citral hydrogenation). Beside the ex-situ synthesis of Rh–Sn catalysts via controlled surface reaction (CSR) method which gave selectively acting catalysts [29], the addition of a tin containing precursor is the simplest way to prepare in situ a bimetallic

Table 1
Parallel screening of hydrogenation of citral over 5% Rh/Al_2O_3 with and without addition of $SnCl_2$; reaction conditions: $T = 298$ K, $p_{H_2} = 70$ bar, stirring rate = 840 rpm, reactant: 10.7 mmol citral, solvent: 7.5 ml *n*-hexane, internal standard: 0.67 ml dodecane, catalyst mass: 200 mg; product analysis after 15 min

Batch reactor	1	2	3	4	5
Amount of $SnCl_2$ added (mg)	0	1.2	2.8	8.3	22.0
Citral conversion (%)	84.0	76.0	65.9	41.1	1.6
Selectivities (%)					
Citronellal	98.2	97.5	96.4	91.6	50.0
Citronellol	1.4	1.6	1.8	2.8	0
Geraniol + nerol	0.4	0.9	1.8	5.6	50.0

catalyst [28]. Without a separate reduction step, $SnCl_2$ was added in different amounts to the monometallic catalyst suspended in a citral/solvent/internal standard mixture prior to the start of the reaction by pressurizing the autoclave. The pressure–time curves of Fig. 24 allow a rapid discrimination between the activities of the catalysts formed after addition of different amounts of $SnCl_2$. Beside the variable promoter concentration in this example, other reaction conditions can be varied in parallel in the same fast way. By analyzing the product mixtures obtained after a reaction time of 15 min by means of gas chromatography rapid estimation of the selectivities and conversions for each batch reactor (see Table 1) was possible. With this multibatch reactor specification the time for the screening of heterogeneous catalysts for gas–liquid phase reaction can be decreased by a factor of 5 compared to traditional catalytic experiments in only one autoclave.

7. Conclusion

Already today, the application of combinatorial methods is fundamentally changing the research paradigms in catalysis. In the present work, we have shown that miniaturization is a key issue in designing efficient tools for high-throughput catalyst screening. Different miniaturized reactor arrays were successfully developed and studied in heterogeneously catalyzed gas phase reactions, namely monolithic reactors, microchannel reactors and chip-based systems. Furthermore, a flexible scanning MS technique applicable in many screening configurations was presented and described in detail. In addition, a multibatch reactor system was successfully realized allowing the parallel and efficient development of heterogeneous catalysts for gas–liquid reactions. These developments combined with robotic synthesis and scientific data management strategies can have an enormous impact on the chemical industry by dramatically saving the time needed for the discovery and optimization of novel catalytic materials.

Acknowledgements

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