[12] The C protonation and C–P bond formation in **10** is complete within 2 min in the presence of NH_4Cl. If the phenol is protected, as in **6**, then no reaction occurs upon treatment with NH_4Cl/H_2O at room temperature (30 min). An *o*,*o*′-dihydroxy analogue of **10** is quite stable.[2e] Hence, the nucleophilicity of the phosphanyl group and the proton-donor capability of the phenol are important for the high reactivity of **10**.

[13] Rearrangement of an alkinyloxyphosphorane to a benzophosphole is structurally related to the title reaction: H. J. Bestmann, K. Roth, R. W. Saalfrank, *Angew. Chem.* **1977**, *89*, 915; *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 877; we thank a referee for this reference.

Detection of Reaction Selectivity on Catalyst Libraries by Spatially Resolved Mass Spectrometry**

Matthias Orschel, Jens Klein, Hans-Werner Schmidt, and Wilhelm F. Maier*

While combinatorial chemistry has established its importance for drug development,[1–3] combinatorial methods are just starting to be applied increasingly in the field of materials research and catalyst development.[4–6, 16] In analogy to the development of new drugs, the major problems are not centered on the synthesis of new libraries—25 000 different components on a few square centimeters have already been realized[4]—but on the reliable, fast, and spatially resolved detection of the desired properties of the library components.[7, 8]

For the combinatorial development of new catalyst materials, the catalytic activity and selectivity of the library components have to be determined quickly and reliably. Very few examples for the determination of reactivity behavior of the components of combinatorial libraries have been reported. A very sensitive and fast method for investigating catalytic activity is emissivity-corrected IR thermography,[9] which allows the reliable and spatially resolved detection of the heat change on heterogeneous catalysts in gas-phase reactions[9] as well as the heat change of homogeneously catalyzed reactions in the liquid phase.[10] Although the relative activity of catalysts is easily determined by such thermographic methods, no information on catalytic selectivity is obtained. A mass spectrometer specially developed for high-throughput screening in combinatorial catalyst development has been applied by Weinberg et al. to catalyst libraries generated in situ by evaporation techniques.[11, 12] Disadvantages of such a solution are its high cost and that it is not accessible to general synthetic or academic laboratories. Although mass spectrometry should be able to identify reaction selectivities, only catalytic activities have been reported. The identification of selectivity differences of heterogeneous catalysts on libraries by spatially resolved mass spectrometry has not yet been demonstrated.

The aim of our study was the detection of selectivity changes on the different components of a catalyst library in the product distribution of a gas-phase reaction by spatially resolved mass spectrometry. The components used for this task were a commercially available gas analyzer and a synthesis robot. The basic idea was to exchange the pipetting unit of the robot for the capillary of the inlet system of a conventional gas analyzer. This combination allows use of the spatial library information of the synthesis robot for the product analysis. To allow the investigation of general gas-phase reactions the MS capillary had to be combined with another capillary providing the feed gas (capillary bundle).

In Figure 1 the experimental setup is shown schematically. The pipetting unit of the commercial robot (spatial resolution in *x*,*y*,*z* direction 0.1 mm) was exchanged for the capillary

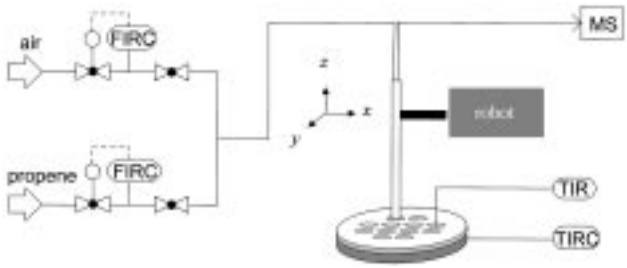

Figure 1. Schematic representation of the setup for spatially resolved mass spectrometry on a catalyst library with control of the capillary bundle with a pipetting robot. FIRC = mass-flow controller, TIR = temperature indicator, TIRC = temperature controller.

bundle (Figure 2). The capillary bundle (length 15 cm) consists of an outer steel capillary (outer diameter 2.0 mm, inner diameter 1.5), two inner steel capillaries (outer diameter

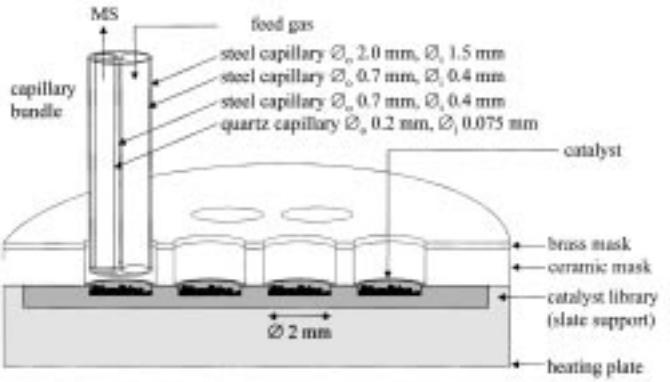

Figure 2. Schematic representation of the positioning of the capillary bundle in the library compartments. $\varnothing_o$ = outer diameter, $\varnothing_i$ = inner diameter.

0.7 mm, inner diameter 0.4 mm), and the MS capillary (quartz capillary, outer diameter 0.2 mm). One of the inner capillaries is used for feed gas supply, and the other one is principally available for other uses, depending on the reaction conditions. In the present case the second inner steel capillary simply

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hosts the MS capillary. A simple gas analyzer (Pfeiffer/Balzers) controlled by the Quadstar software was used as mass spectrometer; it continuously analyzes product gas sampled through the 2 m long quartz capillary (inner diameter 75 μm).

Figure 2 shows the schematic setup of the detection system in connection with the catalyst library. Unusual is the open construction, where the feed gas flow is directed onto the surface of the library component and the mass spectrometer thus samples and analyzes a mixture of feed gas and products. The excess of this mixture, which effectively displaces the air above the library component, leaves through the space between the capillary bundle and the drill hole wall of the ceramic mask. The library is heated directly from below with an electric heating plate. The temperature is controlled through thermocouples in the heating plate and a hole directly in the library. Radiative losses above the library are reduced by an additional ceramic mask placed on top of the library. Its hole pattern (hole diameter 2.4 mm) matches that of the library, thus enlarging the "reactor volume" above the catalyst components. This allows the capillary bundle to sink more deeply into each library compartment, thus shielding the reactants more effectively from the laboratory air. On top of the ceramic mask an additional brass plate mask is positioned. Its conical holes, which match that of the ceramic mask, help to guide the capillary bundle into the library compartments. The capillary bundle is positioned in the compartment so that it touches the outer surface of the library, which ensures a uniform distance of 2 mm from the end of the capillary bundle to the compartment bottom. With this setup the library has been transformed into an array of extremely simple microreactors. It should be emphasized that the present activities in the field of microreactors are not only of general interest as a new reactor technology,[13] but may very well become relevant for future aspects of combinatorial catalyst research.

The precise dosage of the reactants is achieved by an electronic mass flow controller, allowing precise feed flow adjustments ($>100\ \mu L\,min^{-1}$). The feed gases can be mixed before entering the capillary bundle or, by feeding through separate capillaries, directly above the component in the library compartment. With this construction the feed gas only reaches the component investigated and is isolated from the rest of the library. The feed gases are supplied to the capillary bundle through a flexible polymer tube (inner diameter 2 mm) that does not hinder the movement of the robot. Product compositions can be monitored continuously through the MS capillary. The library can be investigated sequentially or by following well-defined components of interest. In this investigation product composition was monitored by mass spectrometry for 15 to 180 s following a sequential pattern under isothermal conditions as well as with a change in temperature for selected library components. Data acquisition and storage was achieved by the controlling computer with commercial software.

To demonstrate the performance of this setup, the selective oxidation of propene with air was selected as a model reaction of technical interest. Besides CO_2, the undesired product of total oxidation, the following oxidation products are selectively formed: acrolein, 1,5-hexadiene, benzene, allyl alcohol, and propylene oxide. The selectivities for propene oxidation of several AMM-type catalysts (AMM = amorphous microporous mixed oxide), observed by Orzesek et al. in the gas phase at normal pressure in a conventional gas-phase flow reactor, were used as a reference.[14] For the screening study a sol–gel catalyst library was prepared on a slate substrate, as summarized in Table 1. The slate plate contained component holes of 2 mm diameter and 2 mm depth, similar to the library described earlier.[5] The holes were filled with 2 mg each of the AMM catalysts. A matrix of 33 catalysts was selected for the experiment. The molar catalyst compositions are given in Table 1. At a total feed flow of $7\ mL\,min^{-1}$ a propene/air composition of 0.4 was continuously dosed through the capillary bundle. Because of the low flow rate of the feed gases and the low total feed gas volume, there was no special safety concern, and the experiments could be conducted in the laboratory air.

Table 1. AMM catalyst library.

	1	2	3	4	5	6
1	Sc_2Si	Y_2Si	V_5Si	Ta_2Si	Cr_2Si	Fe_2Si
2	Co_2Si	Rh_2Si	Ni_2Si	Cu_6Si	Ag_2Si	Au_2Si
3	In_2Si	Si	Sn_5Si	$Bi_{10}Si$	Te_2Si	W_3Ti
4	W_3Zr	Mo_3Ti	Mo_3Zr	Sb_3Ti	Sb_3Zr	Cu_3Ti
5	Cu_3Zr	In_3Ti	In_3Zr	Re_3Ti	Re_3Zr	Cr_3Ti
6	Cr_3Zr	Fe_3Ti	Fe_3Zr			

In Figure 3 the mass spectra (after correction by subtraction of the mass spectrum of the feed gas) obtained for the Cu-containing catalyst AMM-$Cu_6^{II}Si$ are shown as a function of the reaction temperature. The temperature axis is not linear

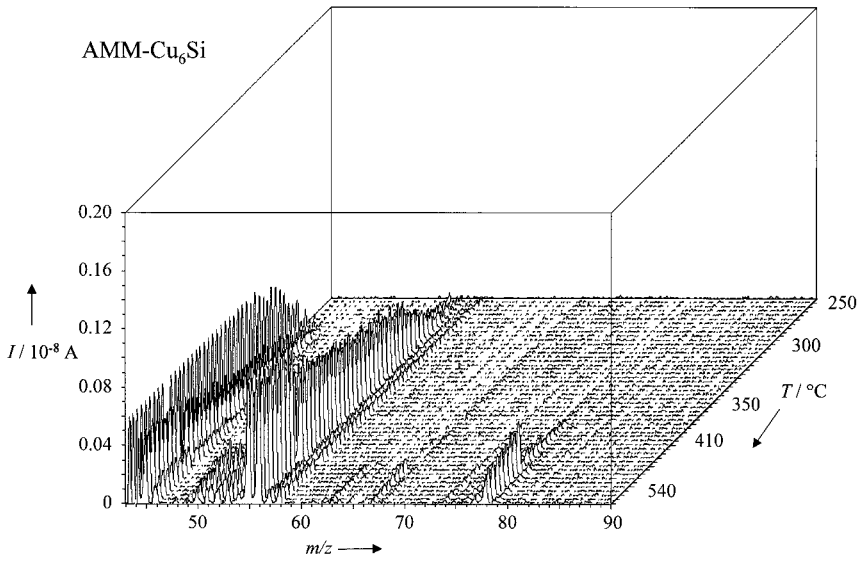

Figure 3. Change in the mass spectra with increasing temperature for a library compartment containing the AMM-Cu_3Si catalyst. Clearly visible is the increase in intensity I for mass peaks $m/z = 55$ and 56, typical for acrolein.

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since a constant heating rate was not chosen. The reaction was carried out by decreasing the temperature from 550 to 250 °C in 15 min. Selective oxidation of propene starts around 255 °C.

At low conversion below 300 °C exclusive formation of acrolein ($m/z = 55, 56$) is observed. Total oxidation, identified by production of CO_2 ($m/z = 44$), starts at 300 °C and remains a minor side reaction. Around 400 °C the beginning of benzene formation ($m/z = 78$) can be recognized. At 550 °C, in addition to the products observed at lower temperatures, 1,5-hexadiene ($m/z = 67$) appears. In further experiments the catalytic response of the catalyst with time was studied at 500 °C. It was found that the relatively high initial activity for the formation of acrolein dropped within 4 min to about 40 % and remained constant for another 4 min. Reactivation of the catalyst with air resulted in an increase to about 80 % of the initial activity, which again dropped to about 40 % after 4 min. Apparently the observation of activity changes with time or regeneration phenomena can be studied readily on selected components.

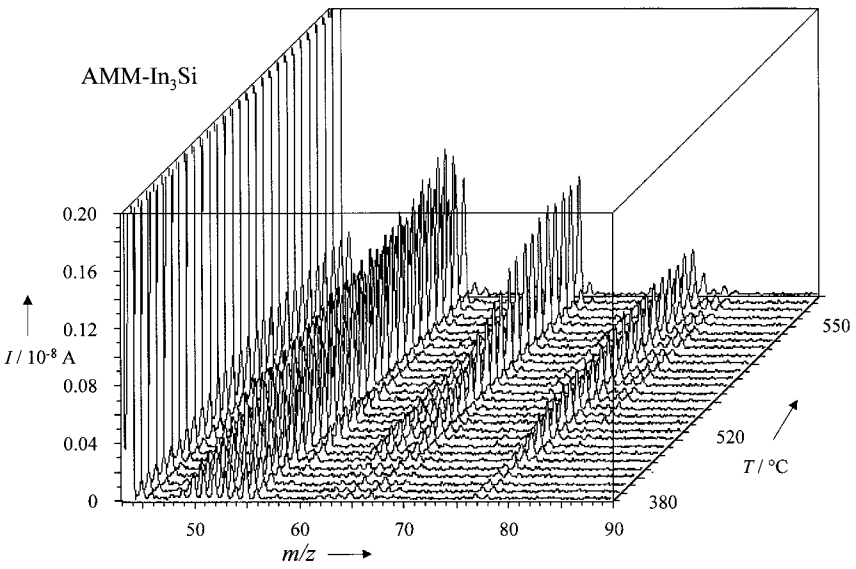

Figure 4. Change in the mass spectra with increasing temperature for a library compartment containing the AMM-In_3Si catalyst. Clearly visible is the increase in intensity I for mass peak $m/z = 67$, typical for 1,5-hexadiene.

The spectra obtained for the In-containing catalyst AMM-In_3Si under identical conditions, but with an increase in temperature from 380 to 550 °C (the library was heated at the maximum rate, total time 8 min), shows a significantly different reaction behavior (Figure 4). Product formation starts only at 380 °C with total oxidation (CO_2) as the dominant reaction accompanied by production of acrolein. At 420 °C traces of 1,5-hexadiene and benzene appear (the peaks at $m/z = 50-55$ are fragmentation peaks of these two products). Relative to the Cu-containing catalyst, 1,5-hexadiene formation is significantly increased. These results confirm the data obtained previously with the same catalysts in a conventional gas-phase flow reactor.[14, 15] The unusual selective formation of 1,5-hexadiene on the In-containing catalyst under conventional reaction conditions has also been described in more detail.[15]

These studies of individual component behavior in a catalytic reaction also demonstrate that component performance can readily be studied over an increased time interval or a wider temperature range, an option of potential importance for the investigation of induction, regeneration, or deactivation phenomena. Nevertheless, such time-consuming experiments should be carried out under conventional reaction conditions, since more detailed studies are required to judge the feasibility of combinatorial screening studies aimed at such phenomena.

In the third experiment shown here the catalytic performance of the library components was studied sequentially at 500 °C in one-minute intervals. The total time required for all catalysts studied was therefore only 33 minutes. Although due to the high reaction temperature the spectra are dominated by the peak at $m/z = 44$ for the product of total oxidation (CO_2), the selectivities observed at the higher mass range perfectly reproduce those identified earlier under conventional reaction conditions.[14] The spectra displayed in Figure 5 document the different catalytic selectivities. For comparison the product composition of the propene oxidation on pure microporous silicon dioxide is also shown. Besides AMM-Cu_6Si (Figure 3) and AMM-Cr_2Si, the AMM-Te_2Si catalyst shows the highest selectivity for acrolein formation. While such a selectivity is well known for Cu- and Cr-containing catalysts, it had not been observed for Te-containing silica. In

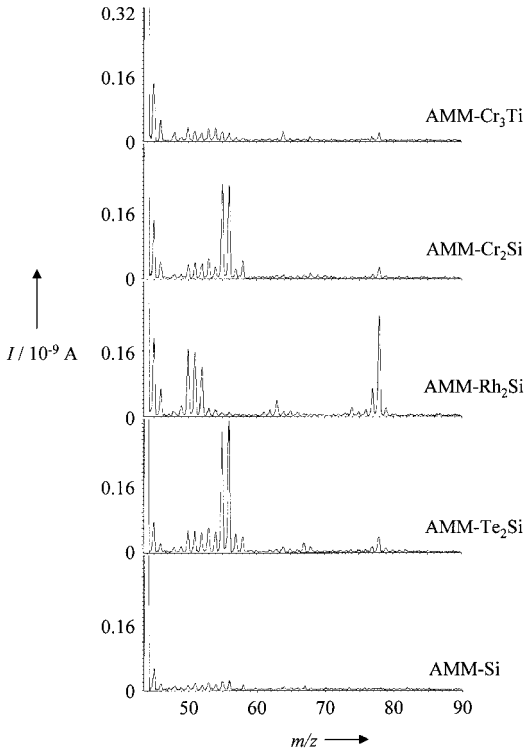

Figure 5. Mass spectra for the reaction of propene with air obtained automatically on selected library components at 500 °C. The different catalytic selectivity is documented.

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contrast to the silica-based AMM-Cr_2Si, the titania-based AMM-Cr_2Ti shows no significant selectivity for formation of acrolein or another product at this temperature, indicating a strong matrix effect on the catalyst activity and selectivity of the active site element Cr. In contrast to the other catalysts, the Rh-containing AMM-Rh_2Si shows a high selectivity for benzene formation from propene, indicative of an oxidative dehydrocyclization.

It has been shown here for the first time that significantly different selectivities of the components on catalyst libraries can be automatically detected by spatially resolved mass spectrometry. Advantages of the setup shown are the relatively low cost owing to the use of a commercial quadrupole-based gas analyzer, a commercial pipetting robot to control spatial resolution and analysis time, and the direct analysis of catalytic performance on the library without the need for a special reactor. This combination also allows reuse of the spatial information of the synthesis program as an integral part the screening procedure. Prerequisite for the use of such high-throughput screening procedures are the absence of induction periods of the catalysis studied. New catalysts requiring time-consuming activations cannot be discovered by such fast methods. However, this may not necessarily be a disadvantage since catalysts without an induction period are also of interest.

A disadvantage of the protocol presented here is its limitation to normal pressure. The fact that the complete library can be heated to the reaction temperature may be an advantage in oxidation reactions (regeneration of all components not under investigation), but a disadvantage for reduction reactions, where catalysts may have to be reduced to be active for hydrogenation reactions. Simple hydrogenation reactions, however, have already been conducted in our setup without problem. Presumably the small total amount of catalyst is reduced rapidly with the hydrogen-containing feed gas.

This investigation also opens the door for further developments of combinatorial methods in catalyst development. Especially the direct combination of IR thermography with spatially resolved mass spectrometry seems attractive, since on large libraries with several hundred or thousand components only active components can be selected for mass spectrometric identification of selectivity. Furthermore, the setup used can be readily modified, and by variation of the capillaries attached to the capillary bundle in the robot a large number of analytical techniques such as GC, GC-MS, IR, UV/VIS, and Raman spectroscopy, and capillary electrophoresis can be applied to libraries in a spatially resolved manner.

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High-Throughput Testing of Heterogeneous Catalyst Libraries Using Array Microreactors and Mass Spectrometry**

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Combinatorial chemistry holds the promise to significantly accelerate the pace of research for the discovery and optimization of heterogeneous catalysts and to contribute to our understanding of catalytic function. However, to realize this potential advances must be made in two complementary areas: 1) the rapid generation and processing of a large diversity of structurally and compositionally different solid-state materials, and 2) high-throughput testing of these libraries for desired catalytic properties.[1]

Solid-state libraries can be prepared using techniques that can basically be categorized into two major groups: 1) thin film deposition based methods of synthesis,[2–4] and 2) solution-based methods for preparation of combinatorial libraries.[5–7] These techniques recently were used for the discovery

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