

Application of High Throughput Screening to Heterogeneous Liquid and Gas Phase Oxidation Catalysis

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Abstract: The application of combinatorial methods to oxidation catalysis in the liquid and gas phases is described. New lead materials have been discovered for the selective liquid phase oxidation of alcohols to aldehydes/ketones catalyzed by vanadium supported on carbon, for the low temperature CO oxidation/light off for cold start automotive emissions control over supported noble metals and perovskites, for volatile organic compound (VOC) removal using CoCr oxide catalysts, and for the selective gas phase oxidation of propane to acrylic acid and acrylonitrile

using mixed metal oxides. Catalyst discovery libraries were screened in 96-well batch reactors, in a rapid serial scanning mass spectrometer and in a massively parallel microfluidic reactor as primary screens. Promising hits were scaled up in conventional autoclaves or in multi-channel fixed bed secondary/tertiary screening reactors.

Keywords: acrylonitrile; alcohol oxidation; ammoxidation; combinatorial chemistry; CO oxidation; heterogeneous catalysis; high-throughput screening

Introduction

The application of combinatorial methodologies to heterogeneous catalysis continues to increase at a rapid rate in academic and industrial laboratories.^[1–46] For industry, this is mainly being driven by the need to reduce the time-to-market for new and optimized catalysts and processes, and to do so in a more efficient manner. The number of experiments that can now be performed using state-of-the-art high-throughput workflows can be orders of magnitude higher than was recently possible using conventional research techniques. Combinatorial methods are also allowing the exploration of very large and diverse compositional, structural, and process spaces, much of which would otherwise go unexplored, but from which new and unexpected discoveries often arise. These two key factors are increasing the probability of discovering new catalysts, facilitating catalyst and process optimization, and rapidly providing large amounts of information to aid scientists in the development of new heterogeneous catalysts.

The high-throughput experimental process in heterogeneous catalysis involves the design, synthesis, and testing of high-density libraries aimed at efficiently exploring very large numbers of diverse materials. Although early research in the field goes back at least 30 years,^[47,48] work beginning in the mid 1990s^[49–53] has significantly advanced the field and initiated the many

efforts that are currently underway. Today, combinatorial catalysis includes computer-assisted design of materials arrays^[54] and high-throughput synthesis, characterization, and screening techniques that are characterized by the use of robotics and advanced software.^[55] The integrated synthesis and screening of a plurality of catalysts in library format has been recognized as an essential factor.^[56] These techniques, along with integrated data management systems,^[57] represent a powerful research strategy when applied to problems where a large parameter space controls the properties of a product or material, such as in heterogeneous catalysis.

The high throughput workflow can be divided into primary, secondary, and tertiary synthesis and screening.^[1,2,8,58] Primary screening is qualitative or semi-quantitative, characterized by very high throughput, and is most often focused on discovery. Secondary screening is utilized for confirmation of primary screening results, lead optimization, or discovery. Tertiary screening is performed using conventional fixed-bed microreactors with full reactant and product detection and full mass balance, and in some cases is also parallelized.

This paper describes the application of combinatorial catalysis to liquid-phase batch as well as continuous flow gas-phase oxidation reactions. It provides an overview of our combinatorial screening methodologies, reactor technologies, and integrated synthesis and screening workflows,^[1,2,59–72] with a focus on the chemistries and

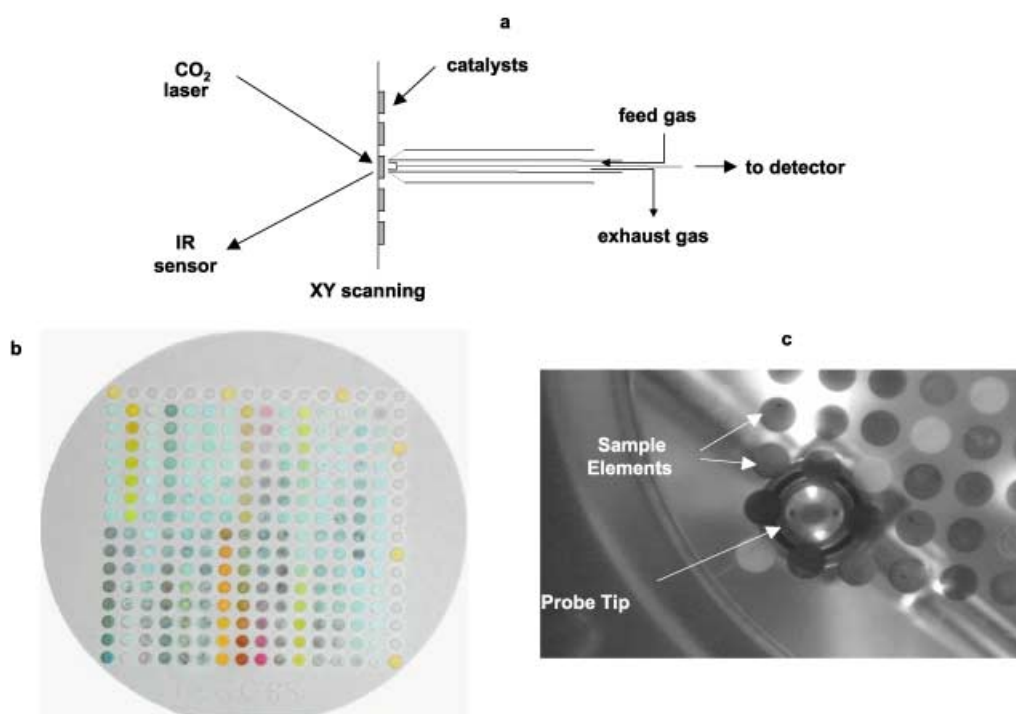


Figure 1. (a) Drawing and (b) photo of 4" wafer with 16×16 catalyst matrix and (c) photo of scanning mass spectrometer probe tip and catalyst array.

new lead materials discovered. Specifically, these include materials for the selective liquid phase oxidation of alcohols to aldehydes/ketones catalyzed by vanadium supported on carbon, for low temperature CO oxidation/light off in cold start automotive emissions over supported noble metals and perovskites, for VOC removal with butane as model feed using CoCr oxide catalysts, and for the selective gas phase oxidation of propane to acrylic acid and acrylonitrile using mixed metal oxides.

Results and Discussion

Catalyst discovery libraries were screened in 96-well batch reactors, in a rapid serial scanning mass spectrometer (Figure 1) and in a massively parallel microfluidic reactor (Figure 2) as the primary screens. Promising hits were scaled up in conventional autoclaves or in multi-channel fixed bed secondary/tertiary screening reactors (Figure 3). More details regarding the screening equipment are given in the experimental section.

Selective Oxidation of Benzylic Alcohols to Aldehydes/Ketones

The selective liquid-phase oxidation of alcohols to the corresponding aldehydes/ketones is a desirable transformation of significant commercial interest in the fine

chemicals and pharmaceutical industries. Sustainable catalysts that operate under mild reaction conditions and allow for high selectivities are preferred. New developments in catalytic alcohol oxidations have been reviewed.^[73–78]

We have developed combinatorial screening workflows for several alcohol oxidation platforms, including use of homogeneous ligated Pd complexes^[79,80] as well as heterogeneous systems based on polyoxometallates (POMs), redox sieves and supported redox metals (oxometals and metal ions)^[81,82] using air and H_2O_2 as oxidants. Libraries consisting of 96 catalysts are prepared in multi-well reactors and screened for catalytic activity using various analytical methods (a modified TLC procedure,^[83] fast serial GC, and NMR). Hits identified in the high throughput primary screens are scaled up and optimized in conventional laboratory test units (Parr bombs for pressure reactions and refluxers for ambient pressure). We found that well-dispersed V-based redox catalysts, in particular V supported on active carbon, mixed addenda ammonium-PVMO-POM supported on active carbon, and V-MCM-41 redox molecular sieves were among the most active materials identified and applicable for broad generic classes of alcohol substrates. The activity is based on well-dispersed vanadium species in various matrices or supports. Vanadium site distribution appears to be mainly responsible for the activities and concomitant high selectivities of these catalysts. Accordingly, the method of achieving the site distribution, either by incorpora-

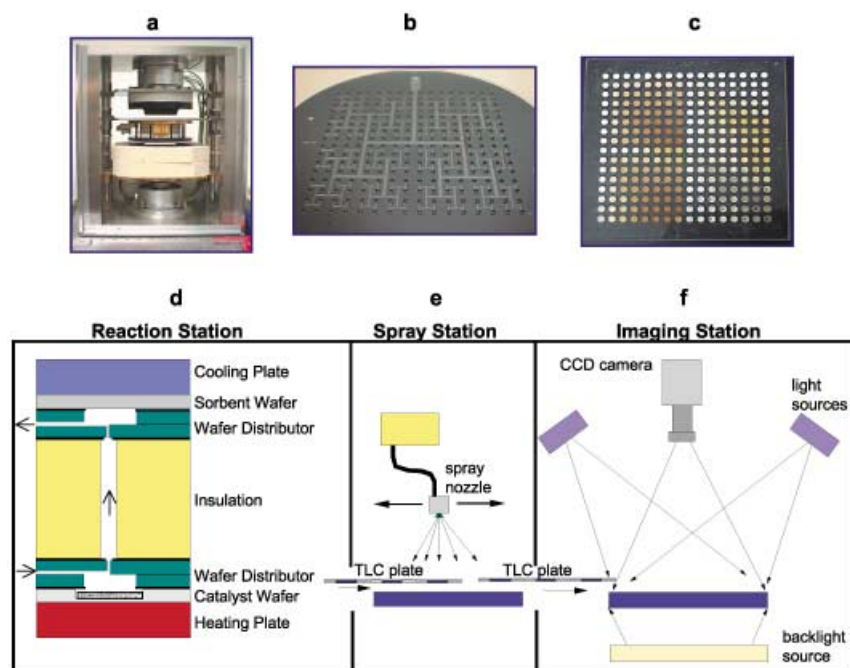


Figure 2. Photographs of the (a) microfluidic parallel screening reactor, (b) gas distribution wafer, and (c) example catalyst wafer. Schematic representation of microfluidic parallel screening reactor system showing the (d) reaction station, (e) spray station, and (f) imaging station.

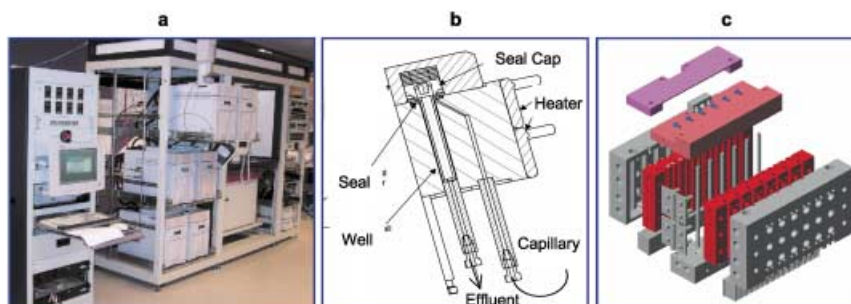


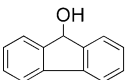
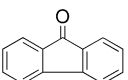
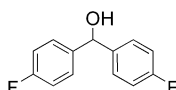
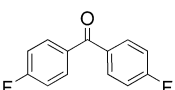
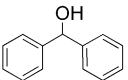
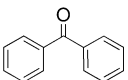
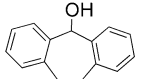
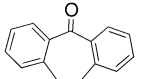
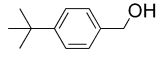
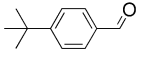
Figure 3. (a) 48-channel fixed-bed reactor system (beds arranged in 6×8 array or in 6 modules of 8 reactors each). (b) Cross-section of single reactor in 48-channel fixed-bed reactor. (c) 6-channel secondary/tertiary screening reactor. All items are described in detail in the text.

tion in well-defined POM or MCM units or simply by supporting on high surface area carriers plays a crucial role.

For the supported metal platform, the catalysts obtained by drying the supported metal salts (supported metal ions) were generally less active than those obtained by calcination (supported oxometal, e.g., V_2O_5). V/C (about 1.0–2.5 wt % V loading) was selected for further scale-up. Complete conversion could be accomplished for many alcohol substrates in less than an 8 h reaction time at moderate temperatures of less than 150 °C and air pressure of about 15 bar in EtOAc or MIBK solvents. For instance, V/C was shown to selectively oxidize the non-activated secondary alcohol 1,5-dimethylbicyclo[3.2.1]octan-8-ol to the ketone at 140 °C and 500 psi air in chlorobenzene solvent.^[14,81] Moreover,

carbon supported V catalyst libraries were found to be a convenient and efficient platform for the general aerobic oxidation of benzylic alcohols to aldehydes and ketones even at ambient pressure.^[14] The general experimental procedure involves heating the reaction mixture in MIBK solvent under an atmosphere of oxygen at ambient pressure. The desired aldehyde and ketone products were isolated in excellent yields by simple filtration of the reaction mixture followed by concentration under reduced pressure. High isolated yields >90% confirmed the preliminary NMR and GC results.^[14] Because the benzylic protons are activated, a reaction temperature of only 105 °C was sufficient for the transformation. Lower reaction temperatures of < 100 °C resulted in dramatically longer reaction times, whereas higher temperatures (~ 140 °C) led to side-

Table 1. Aerobic oxidation of alcohols to aldehydes and ketones.^[a] 2.2 wt % V on active carbon.

Entry	Alcohol	Product	Yield [%]	Time [h]
1			91	8
2			92	36
3			91	24
4			92	8
5			70 ^[b]	48

^[a] Reaction conditions: temperature = 105 °C, 1 atm O₂, MIBK solvent. Yields correspond to isolated material of >95% purity.

^[b] Yield based on GC-MS, GC-MS selectivity = 100%.

product formation as well as oxidative cleavage of the solvent. In addition, we have shown that these reactions can be carried out at ambient pressure, and therefore high-pressure equipment is not needed to accomplish the selective oxidation. Termination of the reaction at the stage of complete alcohol conversion is essential for high selectivities. Typical results are summarized in Table 1.

The active carbon carrier, as obtained from commercial sources, contributed about 10–20% of the overall activity due to the transition metal impurities present in the carbon carrier (as revealed by XRF analysis of the as supplied carbon supports). Screening various types of carbon showed that carriers from Norit and Silcarbon are suitable supports for this reaction.

Leaching experiments indicate that loss of vanadium from the carbon carrier is negligible. Refluxing the catalyst for 66 h in MIBK (10 times longer than typical reaction time) resulted in less than 10% of V leaching, as analyzed by atomic absorption. The supernatant was also tested for its catalytic activity and showed that the homogeneous contribution to the oxidation of 2-butyl-5-hydroxymethylimidazole by leached V is only slightly higher than background (pure solvent). Therefore, the oxidation is predominantly heterogeneously catalyzed.

Low Temperature CO Light Off for Cold Start Automotive Emissions Control

Vehicle emissions of CO, NO_x and uncombusted hydrocarbons are highest under cold start conditions, i.e., when the engine is still cold and the catalytic converter has not yet warmed up to steady-state operating temperature. Therefore, cold start automotive emissions control is of considerable interest for the protection of the environment. Several solutions to address the high emissions during the first 2 minutes after engine start up have been proposed, among them an additional catalyst stage for CO oxidation (in the presence of NO, water and uncombusted fuel) at low temperatures of ca. 200 °C. Perovskite catalysts have been shown to be active for CO oxidation^[84,85] and allow significant noble metal savings over supported catalysts. We have conducted a primary screening program in our scanning mass spectrometer (SMS) searching for low temperature CO oxidation perovskite catalysts using a realistic ‘cold start’ feed consisting of 1% CO/10% O₂/1% NO/10% H₂O and 1% Kr as internal standard in 77% Ar carrier gas.

We have attempted to rank catalyst activities and map out light off curves using shallow temperature ramps in the range of 180 °C to 250 °C and gradients in metal loading. As an example, Figure 4 shows SMS results for the Nd_{0.8}Sr_{0.2}Mn_{0.9}Ni_{0.04}Pd_{0.06}O_x perovskite (synthesized in bulk, XRD analyzed, slurry dispensed to wafers using various dispense, loading and dilution levels – see Experimental Section). The Pd-doped perovskite begins igniting at about 225 °C whereas at 200 °C the catalyst is still inactive and at 250 °C most of the catalyst spots are already lit off (with respect to the so-called light off temperature T₂ where the activity suddenly jumps from about 10% to full CO conversion). Above light off T₂, the reaction becomes mass transport limited rendering catalyst discrimination meaningless. Note that the absolute numbers for light off temperature depend somewhat on catalyst loading/well (space velocity), i.e., light off curves can be offset by about ± 20 °C, however, the relative ranking remains unaffected (for the same catalyst loading).

The light off curves from 180 °C to 240 °C in 10 °C increments for the three perovskite catalysts Nd_{0.8}Sr_{0.2}Mn_{0.9}Ni_{0.04}Pd_{0.06}O_x, Nd_{0.5}Sr_{0.5}Mn_{0.95}Pt_{0.05}O_x, and Nd_{0.5}Sr_{0.5}Mn_{0.98}Rh_{0.02}O_x with 5 wt % Pt/Al₂O₃ as a reference are shown in Figure 5. Blanks as well as pure alumina carrier are inactive. Pd and Pt doped perovskites are seen to light off at about 220–230 °C well below the light off of the Rh-containing sample. The presence of water and NO in the feed tends to lower the overall activity, with the signal intensity for mass 30 (NO) mostly unchanged and no additional peak at mass 46 (NO₂) observed (N₂ cannot be detected due to overlap with CO in QMS). In summary, perovskites have been found to effectively catalyze the oxidation of CO under

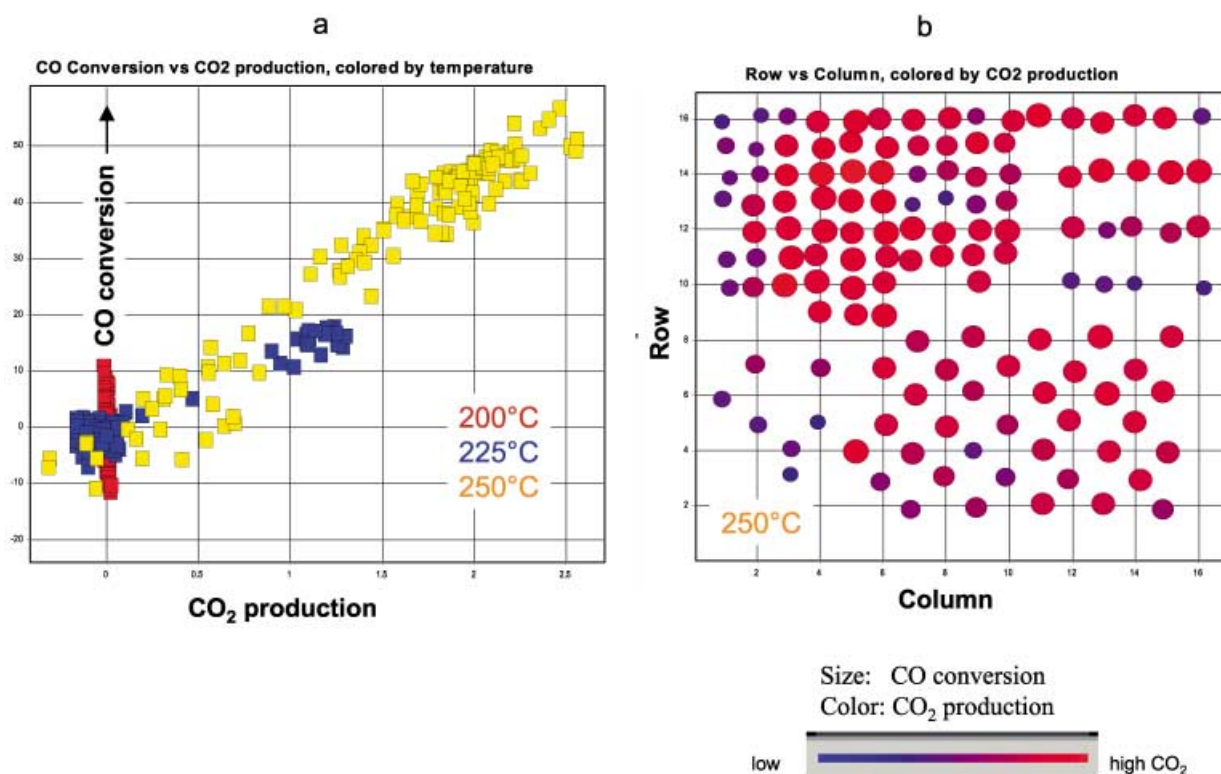


Figure 4. $\text{Nd}_{0.8}\text{Sr}_{0.2}\text{Mn}_{0.9}\text{Ni}_{0.04}\text{Pd}_{0.06}\text{O}_x$ perovskite on 4" wafer (synthesized in bulk, XRD analyzed, slurry dispensed to wafer); various dispense, loading and dilution levels. (a) CO conversion versus CO_2 production, colored by temperature. (b) Rows versus columns; CO_2 production by color, CO conversion by size.

cold start conditions and are proposed as a competitive alternative to supported noble metal systems.

VOC Removal using Butane as Model Feed

Volatile organic compounds (VOCs) are considered an important group of air pollutants. Catalytic decomposition represents an effective tool for reducing VOC emissions from stationary and mobile sources. Nobel metal supported catalysts,^[86,87] LaMO_3 perovskites with $\text{M} = \text{Mn}, \text{Co}$,^[88] and Cr-exchanged zeolites^[89] have been proposed. Commercial catalysts for VOC removal, odor abatement and tail gas purification are composed of Ni (ICI Katalco), Pd or Pt on alumina (BASF), CuCr on titania (BASF), metal oxide supported precious metal (Haldor Topsoe), CuCr on alumina (Katalizator), AlCrMgFe oxides (Boreskov Institute), Pd-Pt on alumina (KataLeuna), unsupported CuCr (Boreskov Institute). Cr has been identified as the most active metal among the transition metals for VOC decomposition.

We have targeted more efficient VOC removal catalysts with high activity for total combustion at low temperature, negligible organics slip and high selectivity to CO_2 without production of intermediate CO, oxygenates or cracking products. Butane was used as model feed for VOC in the SMS using 3 inch \times 3 inch wafers

with 11×11 arrays at 350°C reaction temperature, approximately 1 s contact time, 60 s analysis time, 8 s purge per catalyst, and roughly 3.5 h total screening time per wafer. The feed composition was 60% butane and 40% oxygen, i.e., oxygen deficient conditions were used deliberately in order to limit the conversion and thus better discriminate catalyst activities, allow identification of reaction intermediates and accelerate accumulation of coke on the catalysts. More than 6000 catalysts were screened in a two month period. The screening protocol encompassed bulk (unsupported) mixed metal oxides calcined in air at 400°C . Transition metals M^1 known to have some oxidation activity $\text{M}^1 = \text{Ti}, \text{V}, \text{Cr}, \text{Mo}, \text{W}, \text{Mn}, \text{Re}, \text{Fe}, \text{Co}, \text{Ni}, \text{Cu}$, and Ag were combined with each other into binaries as well as doped with $\text{M}^2 = \text{K}, \text{Cs}, \text{Mg}, \text{Sr}, \text{Sc}, \text{Y}, \text{Ce}, \text{Sm}, \text{Zr}, \text{Nb}, \text{Ta}, \text{Zn}, \text{Cd}, \text{B}, \text{Al}, \text{In}, \text{Sn}, \text{Pb}, \text{P}, \text{Sb}, \text{Bi}$, and Te using 5-point compositional gradients (5 different compositions per binary).

As an example, Figure 6 summarizes screening results for $\text{M}^1 \times \text{M}^1$ binaries and Figure 7 for $\text{M}^1 \times \text{M}^2$ binaries. Five m/z values were recorded, namely 44, 68, 70, 72, and 98. In Figures 6 and 7, the intensity of the MS signal at the specified m/z is given for the best M^1M^1 or M^1M^2 catalyst (composition) tested. CO_2 at specific mass 44 is the dominant product, and only traces of oxygenates are formed. Co, Cr, Ni, Mn, and Cu are identified as the most active metals.

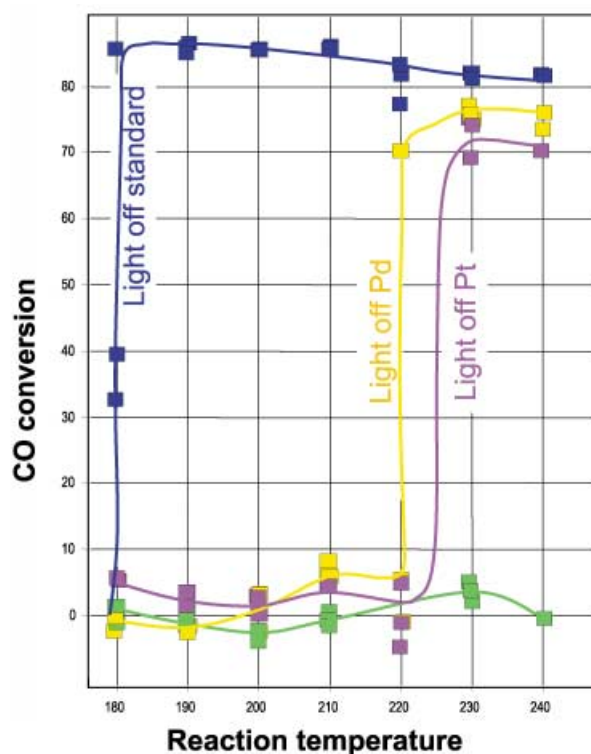


Figure 5. Mapping out CO light off curves from 180 °C to 240 °C for 3 perovskite catalysts $\text{Nd}_{0.8}\text{Sr}_{0.2}\text{Mn}_{0.9}\text{Ni}_{0.04}\text{Pd}_{0.06}\text{O}_x$, $\text{Nd}_{0.5}\text{Sr}_{0.5}\text{Mn}_{0.95}\text{Pt}_{0.05}\text{O}_x$, $\text{Nd}_{0.5}\text{Sr}_{0.5}\text{Mn}_{0.98}\text{Rh}_{0.02}\text{O}_x$ and the 5 wt % $\text{Pt}/\text{Al}_2\text{O}_3$ reference in ScanMS.

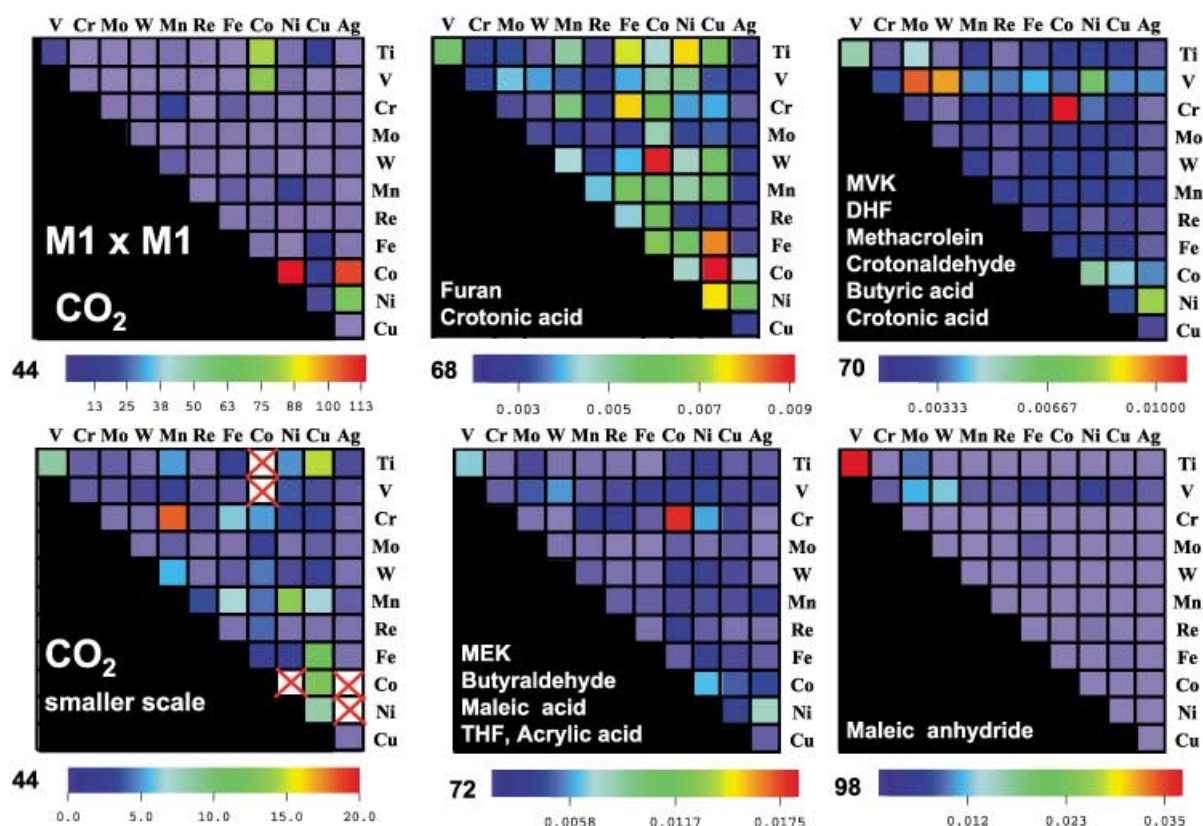


Figure 6. VOC removal screening protocol for $M^1 \times M^1$ binaries: SMS signal intensities (amperes) at masses 44 (CO_2), 68, 70, 72, 98.

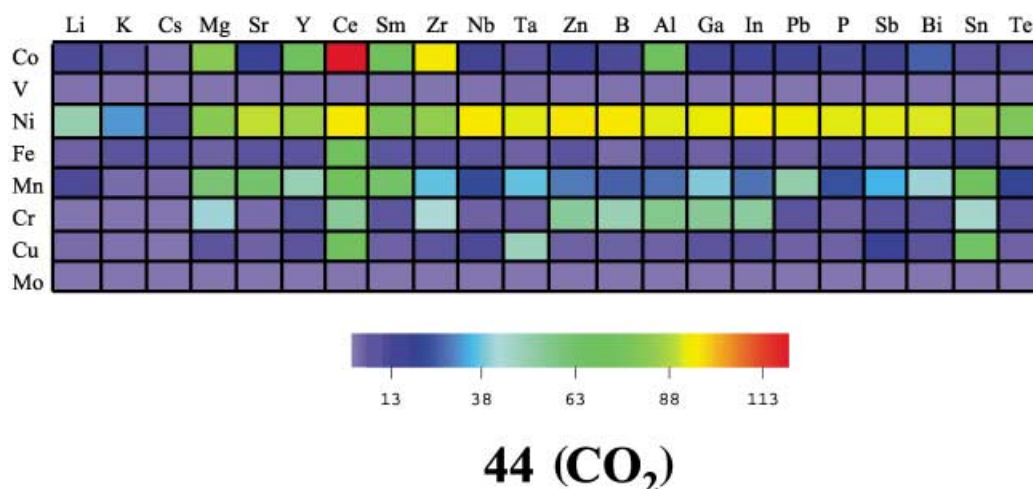


Figure 7. VOC removal screening protocol for $M^1 \times M^2$ binaries: SMS signal intensities (amperes) at mass 44 (CO₂).

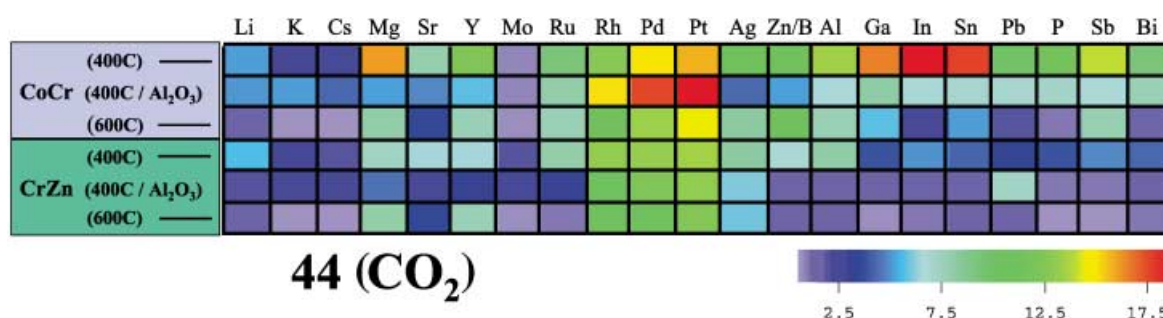


Figure 8. VOC removal screening results for CoCrM² and CrZnM³ ternaries: SMS signal intensities (amperes) at mass 44 (CO₂).

Next, CoCrM³ and CrZnM³ ternaries were synthesized and screened with M³ selected from Li, K, Cs, Mg, Sr, Y, Mo, Ru, Rh, Pd, Pt, Ag, Zn, Al, Ga, In, Sn, Pb, P, Sb, and Bi (M³ < 10%, 15 different compositions/ternaries; 3 copies: (a) unsupported, calcined at 400 °C, (b) unsupported, calcined at 600 °C, (c) Al₂O₃ supported, calcined at 400 °C) as well as CoCr ternaries from the Symyx library archive. Results are given in Figure 8 showing high CO₂ production for the CoCr/400 °C systems. Catalyst compositions were then optimized in focus libraries. Figure 9 shows an example for a CoCrSi/CoVSi bis-ternary focus library. VPO catalysts on the diagonal were used as ‘standards’ to establish the correlation between primary and tertiary screening. High CO₂ signals are observed for Co-rich CoCr and CoCrSi systems. Note that in Figures 6–9 raw SMS data are used for screening and thus comparisons are only valid within a library and at a given *m/z*.

Best CoCr-based SMS hits were scaled up and more quantitatively evaluated in tertiary screening (tubular fixed bed reactor/GC detection) at 300 °C and 0.5 s contact time with 60% butane/40% oxygen feed composition. Bulk (unsupported) CoCr achieved 93% selectivity to CO₂, 2% selectivity to CO, 5% selectivity to C₄ olefins and isomers at 8.7% butane conversion,

whereas bulk CoZn gave 88%, 7% and 4% selectivity to CO₂, CO, C₄-ene/iso, respectively, at 9% conversion. Yields of oxygenates were negligible. The activity and selectivity of supported CoCrSi systems were found to strongly depend on the synthesis method (precipitation versus spray drying versus impregnation). Spray dried CoCrSi was the most active with 10% conversion and 80%, 10% and 7% selectivity to CO₂, CO and C₄-ene/iso, respectively. Conversions are quantitative when using oxygen-rich ‘real’ feed. In summary, bulk and supported CoCr mixed oxides promote total butane combustion and are proposed as catalyst systems for VOC removal.

Selective Oxidation of Propane to Acrylic acid and Acrylonitrile

Acrylonitrile is currently produced from the ammoxidation of propylene by the SOHIO/BP process. A significant reduction in acrylonitrile production cost can be obtained by the implementation of a propane to acrylonitrile process. Significant cost savings can also be achieved by developing a direct oxidation of propane to acrylic acid to replace the current two-step process

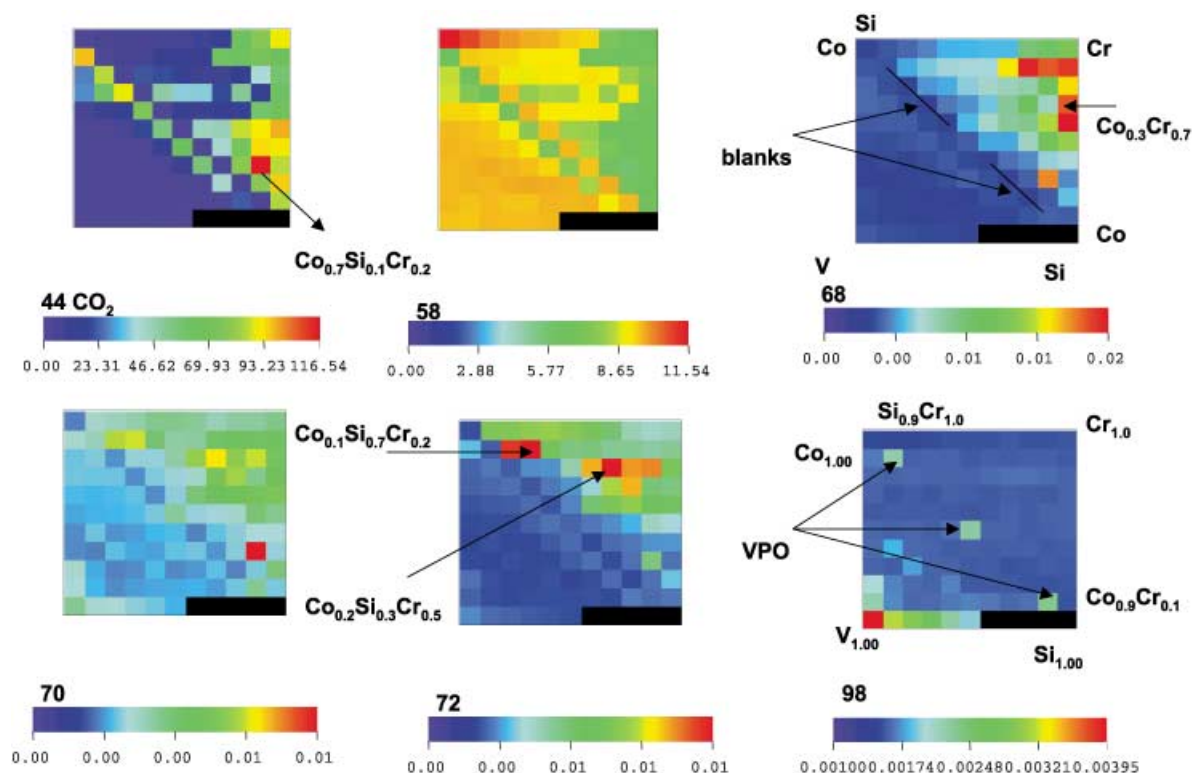


Figure 9. SMS screening results for a CoCrSi/CoVSi bistrinary 11×11 library on 3" wafer: SMS signal intensities (amperes) at masses 44 (CO_2), 58, 68, 70, 72, 98.

where the first step is the oxidation of propylene to acrolein and the second step is the oxidation of acrolein to acrylic acid. The current best catalysts for these chemistries are the VSbO_4 system developed at Standard Oil^[90] (ammoxidation) and the MoVNbTe mixed oxide systems developed at Mitsubishi (oxidation and ammoxidation).^[91–93] This molybdate system is quite difficult to prepare. It took several years for other groups to reproduce the Mitsubishi work successfully. Some of the critical aspects of the syntheses are the homogeneity of the catalyst precursor mixture, the control of the oxidation states of the metals throughout the synthesis, and control of the volatile components of the catalyst mixture. Our automated catalyst synthesis tools and workflows are capable of controlling the variables required to prepare this and other complex mixed metal oxide catalysts. Thus a well developed suite of catalysts discovery tools can automate the enormous effort that is required to discover and optimize a complex catalytic system such as the MoVNbTe system.

The composition of the MoVNbTe oxide propane ammoxidation catalyst was optimized by primary screening using the massively parallel microfluidic reactor. A library of 510 catalysts was prepared with precursor compositions in the range $\text{Mo}_1\text{V}_x\text{Nb}_y\text{Te}_z\text{O}_n$ where $x = 0.2–0.375$, $y = 0.05–0.2$, $z = 0.1–0.33$. Figure 10a shows a CCD image of an exposed and developed detection plate. The darker spots correspond to a higher

yield of acrylonitrile. The four groupings of dark spots are a result of how the 3-dimensional composition space was laid out on a 2-dimensional catalyst library. The dark point in the center of the plate is the location of the standard catalyst by which the data are normalized. This provides a correction for plate-to-plate variations, and is a gauge of the consistency of the entire screening workflow. Figure 10b shows the performance data for the complete library, where large blue markers indicate higher acrylonitrile yield. The red circle indicates the location of the optimal composition found by secondary screening. The data show a distinct performance optimum over a narrow range of compositions. The sample with the highest yield has a composition ($\text{Mo}_1\text{V}_{0.28}\text{Nb}_{0.11}\text{Te}_{0.26}$) that is reasonably close to the optimum found by secondary screening ($\text{Mo}_1\text{V}_{0.32}\text{Nb}_{0.15}\text{Te}_{0.23}$). The primary screen is intended primarily to eliminate the large compositional regions that are inactive. The catalyst discovery workflow typically includes the reoptimization of the compositional and processing optimum found with the primary screen in a secondary screen using fewer samples. Thus, the accuracy of the primary screen is more than adequate.

The same MoVNbTe library was screened for the oxidation of propane to acrylic acid. The results are shown in Figure 10c. Again the optimum composition found by primary screening, $\text{Mo}_1\text{V}_{0.30}\text{Nb}_{0.09}\text{Te}_{0.26}$, is very

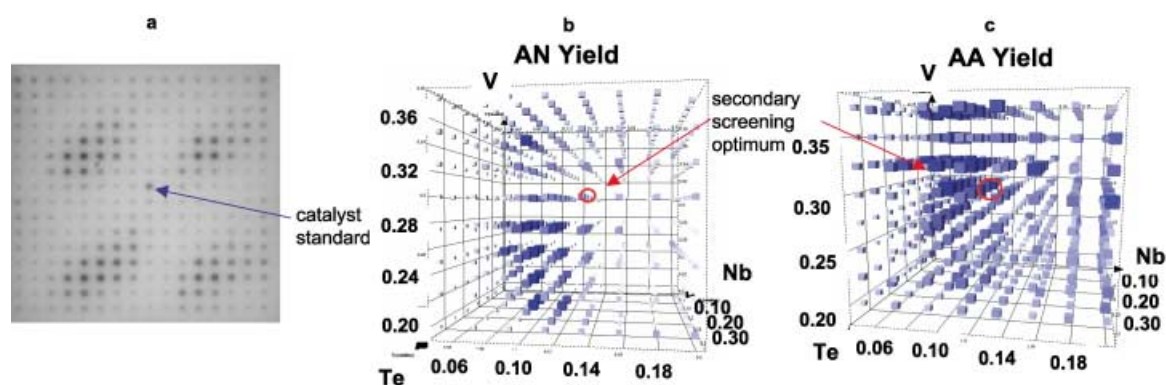


Figure 10. a) Image of raw microfluidic reactor data for the acrylonitrile (AN) experiment. Note the standard at the center of the plate. b) Plot of acrylonitrile yield vs. composition of $\text{Mo}_1\text{V}_x\text{Nb}_y\text{Te}_z$. c) Plot of acrylic acid (AA) yield vs. composition of $\text{Mo}_1\text{V}_x\text{Nb}_y\text{Te}_z$. Yield increases with increasing size and darkness of marker. Red circle indicates optimal composition as determined by the secondary screen.

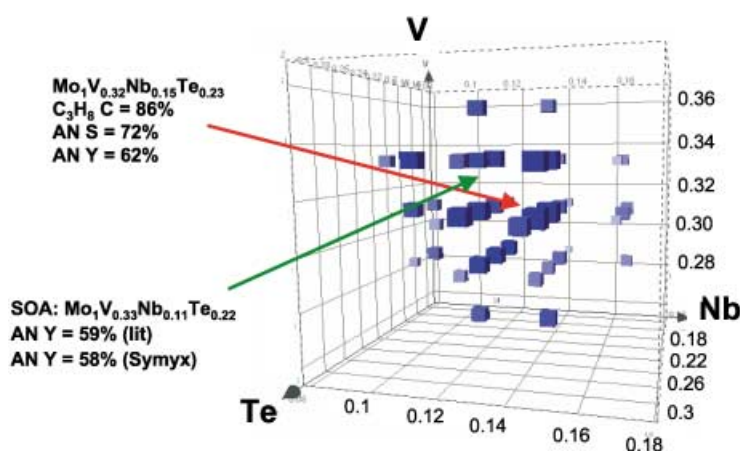


Figure 11. Compositional optimization of MoVNbTe oxide (red arrow). Acrylonitrile (AN) selectivity increases with size of the marker and propane conversion increases with brightness. The literature state-of-the-art results are also shown (blue arrow).

close to the optimum found by secondary screening, $\text{Mo}_1\text{V}_{0.31}\text{Nb}_{0.12}\text{Te}_{0.27}$ (indicated by a red circle in Figure 10c).

In Figure 11 are shown the secondary screening results of the compositional optimization of $\text{Mo}_1\text{V}_x\text{Nb}_y\text{Te}_z\text{O}_n$ where $x = 0.27 - 0.36$, $y = 0.09 - 0.17$, $z = 0.17 - 0.3$. The optimal composition, with the processing conditions used here, was found to be $\text{Mo}_1\text{V}_{0.32}\text{Nb}_{0.15}\text{Te}_{0.23}$. This catalyst gave an acrylonitrile yield of 62%. The literature state of the art composition, $\text{Mo}_1\text{V}_{0.33}\text{Nb}_{0.11}\text{Te}_{0.22}$, gave an acrylonitrile yield of 58% in the secondary screen, close to literature yield of 59%. At the secondary screening level XRD data are collected for a large portion of the samples. XRD patterns for samples with $\text{Mo}_1\text{V}_{0.32}\text{Nb}_y\text{Te}_x\text{O}_n$ are shown in Figure 12. The XRD pattern of the sample $\text{Mo}_1\text{V}_{0.32}\text{Nb}_{0.09}\text{Te}_{0.27}$ reveals a single crystalline phase having a pseudo-hexagonal structure. The sample $\text{Mo}_1\text{V}_{0.32}\text{Nb}_{0.14}\text{Te}_{0.2}$, containing more Nb and less Te, consists primarily of an orthorhombic phase. The samples with an intermediate

composition contain both phases. The highest yield of acrylonitrile is obtained from catalysts containing both phases ($\text{Mo}_1\text{V}_{0.32}\text{Nb}_{0.14}\text{Te}_{0.23}$). This study allowed us to quickly identify synthesis parameters which produce the individual phases of the optimal catalyst. The structure of the orthorhombic phase has been published^[94] and the structure of the pseudo-hexagonal phase will be published shortly. We have published a detailed discussion of the function of these phases.^[95]

The massively parallel microfluidic reactor is also useful for testing catalyst processing conditions such as calcination temperature on a large set of chemically diverse samples. The large number of samples contained on a single wafer allows the rapid screening of dopants as well. For example, on a single catalyst wafer 31 dopants with 8 concentrations each can be screened at once. As an example, a VSbO_4 -based propane ammoxidation catalyst originally developed by Standard Oil Co., now BP, was used.^[90] A sample of VSbO_4 on 50 wt % $\text{Al}_2\text{O}_3\text{-SiO}_2$ was prepared as described in the Experimental

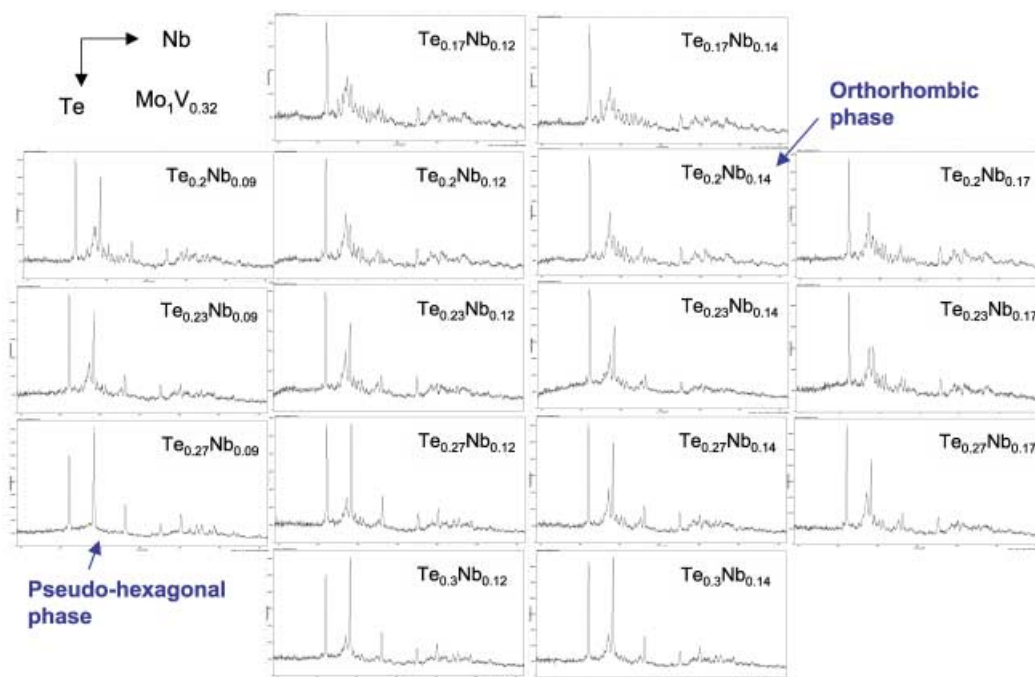


Figure 12. XRD patterns of $\text{Mo}_1\text{V}_{0.32}\text{Nb}_x\text{Te}_y$ catalysts.

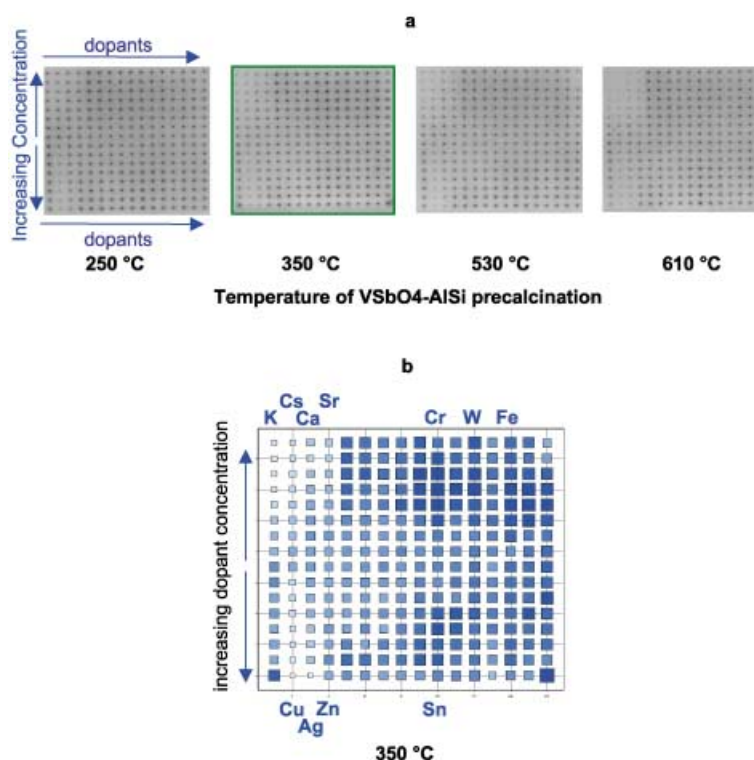


Figure 13. Optimization of dopants and precalcination temperature for VSbO_4 on 50 wt % Al_2O_3 - SiO_2 catalysts for propane ammoxidation to acrylonitrile. **a)** Photograph of detection plates for libraries with indicated precalcination temperatures; **b)** integrated intensities for the library precalcined at 350°C .

Section and portions were calcined at four different temperatures. Four catalyst wafers were prepared, each containing one of the precalcined VSbO_4 samples in

every well. Each wafer was then impregnated with the same set of dopants (31 elements, 8 concentrations each) and recalcined at 620°C . Figure 13a shows CCD images

of the developed detection plates along with compositional information in Figure 13b. The most dramatic difference between these libraries is the effect of a basic dopant as a function of the precalcination temperature. The top halves of the first four columns are doped with K, Cs, Ca and Sr, which are expected to be deactivating. As the precalcination temperature increases the VSbO₄ sinters and crystallizes and thus the dopants are confined to the surface of the catalyst where they have a more pronounced effect on the acrylonitrile yield. Figure 13b shows the performance of the catalysts that were subjected to a precalcination treatment at 350 °C. Basic dopants deactivate the catalyst. Copper decomposes NH₃, thus leading to a low acrylonitrile yield. In agreement with literature reports, Cr, W, Fe, and Sn increase the acrylonitrile yield.^[96–99] Active catalysts that are not marked have not been previously reported and cannot be disclosed at this time.

Conclusions

We have demonstrated the applicability of primary and secondary high throughput synthesis and screening to oxidation chemistries of current interest and importance. Transition metals supported on carbon are low-cost, simple and robust but efficient catalyst systems for the selective oxidation of broad generic classes of activated and benzylic alcohols and even secondary aliphatic alcohols in the absence of alpha-protons. V/C, in particular, is proposed as a new alcohol oxidation platform and less sensitive alternative to polyoxometallates and redox sieves since the activity of V-based redox catalysts is mainly a function of the V distribution and less dependent on the nature of the dispersant. PtPdRh dispersed in perovskites have been demonstrated to be active and stable for the low temperature CO oxidation and allow for significant noble metal savings as compared to the corresponding supported noble metal catalysts. CoCr-based mixed oxides have been identified as highly active for the total combustion of butane with negligible CO and oxygenate formation and are proposed for VOC removal as alternative to noble metal catalysts. The synthesis and chemical composition of the MoVNbTe mixed metal oxide system for the selective oxidation of propane to acrylonitrile has been successfully optimized on a 100- μ g scale. The primary screening results correlate well with secondary screening, thus validating the workflow for the discovery of complex mixed metal oxide catalysts.

Experimental Section

Liquid-Phase Oxidations

Catalyst preparation: The carbon-supported vanadia catalysts were prepared as follows: Active carbon (Norit RBI pellets, available from Aldrich 33,128–7; oven dried at 200–250 °C for 2 h) was impregnated to incipient wetness with a warm solution of NH₄VO₃ in water (500 mg NH₄VO₃ in 10 mL hot water, i.e., 0.427 M V stock solution, 1 mL/g pore volume of (pre-dried) active carbon carrier), dried at 120–150 °C for 24 h, and then optionally calcined at 400 °C for 4 h.^[56] The V loading varied between 1 and 2.2 wt % V.

General aerobic oxidations: Ninety-six-well high-throughput high-pressure batch reactors were designed and built. Details have been given elsewhere.^[14] The reactor vials were filled with calculated amounts of reagent/solvent and the reactor block was pressurized, either by sealing and heating to the required temperature to generate high pressure in the sealed vials or by pressurizing with reactants or inert gas through the common headspace. Following the reaction, the reactor block was cooled and the reaction products were analyzed by a modified TLC procedure, fast serial GC, and NMR.^[70,71]

A typical experimental procedure for the scale-up experiments was as follows: 100 mL commercial stainless steel reactors from Parr Instruments were loaded with the reactants, solvent, and the catalysts. The reactor was sealed, pressurized with air, and was heated at the reaction temperature for the required number of hours. The oxidized product was recovered by filtering the solid catalyst residue. The product retained in the catalyst was recovered by washing with a suitable solvent (e.g., methanol). The combined filtrate was then concentrated and analyzed (see below).

Example for ambient pressure reaction: aerobic oxidation of imidazole alcohol with carbon supported vanadia in methyl isobutyl ketone (MIBK): 67 mg catalyst (2 wt % V on carbon, 1.3 mg, 0.027 mmol) and 41 mg of 2-butyl-5-hydroxymethylimidazole (41 mg, 0.27 mmol) were reacted in 2.7 mL MIBK solvent (0.1 M solution) at 105 °C and 1 bar oxygen for 6 h. GC-MS data showed complete conversion with 100% selectivity for the desired product.

Leaching experiments: After stirring 1 g catalyst (2 wt % V on carbon, 20 mg, 0.4 mmol) in 10 mL of MIBK at 105 °C for 66 h, the catalyst was filtered from the supernatant MIBK. Analysis of the supernatant by atomic absorption spectroscopy gave 64 ppm of V (1.8 mg in 10 mL), which corresponds to less than 10% of leached metal.

In addition, the supernatant was analyzed for its catalytic ability towards oxidation of 2-butyl-5-hydroxymethylimidazole (homogeneous catalysis). Therefore, a 0.1 M solution of the substrate was stirred at 105 °C and 1 bar oxygen for 6 h. GC-MS data showed about 20% conversion for the desired product which is about twice as much as the background. The filtered V/C had the same activity as un-leached V/C catalyst.

Gas Phase Oxidations

Catalyst preparation (primary methods): Wafer-formatted primary screening catalyst libraries used for screening on both the scanning mass spectrometer and the massively

parallel microfluidic reactor were designed and synthesized using Symyx Proprietary Library Studio® and Impressionist® software.^[57,58] Commercial 3 inch × 3 inch quartz wafers were first bead-blasted through steel masks with α -Al₂O₃ powder to produce 11 × 11 or 16 × 16 arrays of wells. The metal precursors typically used for the synthesis of primary screening libraries were aqueous metal nitrates (alkali, earth alkali, rare earth, Group IIIB, IB, IIB metals, Zr, Cr, Mn, Fe, Co, Ni, Al, Ga, In, Pb, Bi, Ru, Rh, Pd, and Pt), oxalates (Ti, V, Nb, Ta, Mo, Sn, and Ge), ammonium salts (vanadate, tungstate, and Sb oxalate), acids (boric, perhenic, telluric, selenic, and phosphoric), and in some cases chlorides (Hf, Sn, Ir, and Pt). The precursor solutions were premixed in microtiter plates and then transferred to the catalyst wafers by automated liquid handling robots, either in a rapid serial or parallel manner.^[56] If the synthesis of a catalyst library required sets of incompatible precursor solutions the sets of solutions were transferred to the wafer sequentially followed by a rapid drying of the solution mixtures in a vacuum oven. For supported catalysts, carriers were predispensed on the wafer as slurries and dried prior to impregnation.^[72] When multiple impregnations of a support were required the catalysts were dried before each additional impregnation. This drying step was fast enough to avoid precipitation.

Single phase perovskite catalysts for CO oxidation were synthesized according to a modified literature recipe^[84] by dissolving metal nitrates in water (Nd, Sr, Mn, Ni, Pd, Rh nitrates and Pt tetraammine nitrate), adding malic acid to the mixed metal nitrate solution, heating to 90 °C to form a viscous syrup, further heat treating the syrup at 200 °C for 1 h to convert the syrup into a solid foam, and calcining the solid foam at 800 °C for 8 h in air to form the perovskite. The mixed lanthanide source in ref.^[84] was replaced by pure Nd. On chip perovskite synthesis in the wafer wells as well as slurry dispensing of preformed perovskite powders to wafers has been applied.^[56] Bulk and supported perovskites powders have been prepared. The BET surface areas of bulk perovskites were in the range of about 10 to about 20 m²/g. On chip XRD characterization was performed to confirm perovskite formation.

A library of mixed metal oxide catalysts was prepared and evaluated for oxidation and ammoxidation of propane to acrylic acid and acrylonitrile, respectively. The precursor compositions investigated were in the range Mo₁V_xNb_yTe_zO_n where $x = 0.2 - 0.375$, $y = 0.05 - 0.2$, $z = 0.1 - 0.33$. The catalysts were dried at 120 °C and calcined under N₂ at 600 °C for 2 h. Doped VSbO₄ propane ammoxidation catalysts were also prepared for primary screening. A sample of VSbO₄ on 50 wt % Al₂O₃-SiO₂ was prepared according to published procedures.^[90] To 35 mL water were added Ludox AS-40 (2.50 g) followed by Al(OH)₃ (7.55 g). To this mixture was added Sb₂O₃ (3.08 g). The mixture was heated at reflux and a solution of NH₄VO₃ dissolved in hot water was added. The combined mixture was heated for 20 h with stirring. The water was removed under reduced pressure and the resulting powder was dried at 120 °C in air. Portions of the powder were calcined in air for 6 h at 250 °C, 350 °C, 530 °C, and 610 °C. Each powder was ground and transferred to wells of a catalyst wafer by slurry dispensing techniques. The final weight of VSbO₄-Al₂O₃-SiO₂ was 200 µg per well. The powders were impregnated with 31 dopants (8 concentrations each) and calcined again at 620 °C in air for 2 h.

Catalyst preparation (secondary methods): As with primary screening, catalyst libraries for secondary and tertiary screening are designed using custom software tools. The synthesis is carried out using a variety of liquid handling, solid handling, and solid processing tools. All weighing and dispensing steps are computer-controlled while all other steps are parallelized to such a degree that the catalyst synthesis throughput matches the screening throughput.

A series of catalytic materials for the oxidation and ammoxidation of propane was prepared with the general precursor composition Mo₁V_xNb_yTe_zO_n where $x = 0.27 - 0.36$, $y = 0.09 - 0.17$, $z = 0.17 - 0.3$ using published methods.^[90-93] The variables x , y , and z were varied independently.

Catalyst Screening

Scanning mass spectrometer: The scanning mass spectrometer, a rapid serial primary screen, was used to test low temperature catalysts for both CO oxidation and butane oxidation (Figure 1). Details of the reactor have been published previously.^[1,2,59-65] The reactor set-up permitted the introduction of up to four different gases and one liquid feed. Catalyst libraries were prepared on either 3" or 4" wafers, producing 121 or 256 element libraries, as described above. For screening, the wafers were mounted on an x-y stage that registers the catalyst to be tested below the reactor head. The catalyst being tested is heated by a CO₂ laser to the desired reaction temperature. Temperatures in the range from 200–500 °C were obtained using standard quartz wafers, with a thickness of ~1300 µm. Temperatures up to 700 °C can be accessed using thinner wafers of < 500 µm. The chamber pressure is maintained at constant pressure of 30 psig, using argon dilution gas and a pressure controller. The reactants are mixed in the head and delivered through two small ports on either side of the catalyst element being analyzed. At the center of the head, a small fraction of the reaction gas is removed through a heated 'sniffer' capillary. This capillary delivers a constant sample stream to the Bruker Quadrupole Mass Spectrometer. Custom Symyx software was written to operate both the reactor and QMS, enabling independent reactor operation (with one wafer) for periods of over a week. Up to 20 quadrupole masses could be monitored for a given experiment.

With both heat and reactant streams delivered to each catalyst independently, initial activity and selectivity were measured. For CO oxidation, the feed gas consisted of 1% CO, 1% NO, 10% H₂O, 10% O₂, 1% Kr and 77% argon, with monitored product m/z of 18 (water), 28 (CO), 30 (NO), 32 (O₂), 44 (CO₂), 46 (NO₂) and 84 (Kr). The contribution of nitrogen (28) to the signal at $m/z = 28$ was assumed to be negligible. Experimental SMS conditions for CO oxidation were 3–5 min time-on-stream per well, signal averaging over the final 20% of analysis time. For CO- and NO-containing feed, selection of reactor materials is crucial, and a Teflon-coated aluminum nozzle body, gold-coated nozzle tip and surface, silico-steel-coated gas feed transfer lines, fused silica liquid transfer line, fused silica product transfer line proved to be necessary to get consistent and reproducible results.

For butane oxidation, the feed gas consisted of butane/oxygen ratios from 2/1 to 3/1, with product $m/z =$ of 18 (water), 32 (O₂), 44 (CO₂), 58, 68, 70, 72, 98 and 84 (Kr) being monitored. Molecular peaks or fragmentation patterns of

potential reaction products are butane/acetone (58), CO₂ (44), furan/crotonaldehyde/DHF/methacrolein (68), methacrolein/crotonaldehyde/DHF/MVK (70), MEK/acrylic acid/butyraldehyde/THF (72), maleic anhydride/maleic acid (98). The Kr signal at $m/z = 84$ was used as the internal standard. Each wafer contained at least 6 blank elements and 6 standard catalysts, in order to assess the quality of the data as well as the relative conversion and selectivity for the catalyst array within each wafer.

The measurement requires from one to three minutes per sample, depending on the catalyst stabilization time and number of masses being analyzed. A single 256-element wafer can be screened at two temperatures over the course of one day.

Massively parallel microfluidic reactor system: High throughput screening of combinatorial libraries for propane oxidation and ammoxidation were performed using a massively parallel microfluidic reactor system. Details of the reactor have been published previously.^[44,66–69] The reactor is based on a microfluidic flow distribution device, 256-element catalyst array, and colorimetric detection methodology allowing fully parallel reaction and detection (Figure 2). A single reaction feed stream provided by conventional flow controllers and vaporizers is divided into 256 equal streams by employing a fluidic device constructed using microfabrication technologies^[66] (Figure 2b). Each individual stream is allowed to contact a 2-mm diameter \times \sim 0.2 mm deep well containing approximately one milligram of catalyst. All 256 individual reaction streams then flow through a temperature gradient before making contact with an absorbent plate (for example a 3 \times 3 inch glass plate coated with silica, e.g., a TLC plate) or array where the products of interest are trapped either by absorption, chemical reaction, and/or condensation. After sufficient amounts of products have accumulated, the absorbent array is removed from the reactor and sprayed with a dye solution in a separate spray station (Figure 2e). A dye is chosen that selectively interacts with the reaction product of interest to cause a change in the absorption spectrum or the enhancement or bleach of fluorescence. The developed absorbent array is then imaged by a high-resolution CCD camera (Figure 2f). The image integration and data processing are done such that the final figure of merit for a catalyst is in units of absorbance and thus proportional to concentration. A standard catalyst is included on all catalyst libraries and catalyst performance is normalized to the performance of the standard. The relative variation in yield (1σ /average yield) was periodically checked by running a library of up to 256 identical acrylonitrile or acetic acid catalysts and was less than 15%, including variations due to catalyst synthesis, reactor residence time, reaction temperature non-uniformities, adsorbent thickness variation, dye spray inhomogeneity, and data integration and processing. This range of data scatter does not inhibit our ability to discriminate between catalysts. The integral detection scheme (signal accumulation over TLC exposure time) and the amplification of performance differences when monitoring initial kinetics (maximum kinetic rates) also help in ranking the catalysts.

Catalyst libraries designed for the oxidation and ammoxidation of propane were screened in the massively parallel microfluidic reactor under conditions similar to those used for secondary screening (see below). For the ammoxidation of propane the reaction temperature was 420 °C and the feed was 6% C₃H₈, 7% NH₃, 17% O₂ and 70% He. For the oxidation of

propane the reaction temperature was 340 °C and the feed was 15% C₃H₈, 18% O₂ and 67% He. Due to catalyst size and flow rate limitations the contact time was about 0.4 sec, compared to about 2 sec in the secondary screening reactor for both reactions. The catalyst libraries were placed in the reactor, heated to reaction temperature under feed gas, and conditioned on stream for 20 min before the reaction products were collected.

Multi-channel fixed-bed reactor: Several secondary and tertiary screening reactors have been developed at Symyx, some of which are depicted in Figure 3.^[67] These reactors include a single feed system that supplies reactants to a set of flow restrictors. The flow restrictors divide the flows evenly among the reactors or supply a gradient of flow rates (or a gradient of partial pressures with even flow rate). The back pressure created by the flow restrictors is large compared to any back pressure caused by the catalyst bed or down-stream plumbing thus ensuring even flows. Analysis is typically performed by gas chromatography.^[71] What differentiates a secondary screen from a tertiary screen is primarily the amount of data collected for each sample. For secondary screening a fast GC method is used that quantifies a few key reaction products. For tertiary screening a longer GC method is used that quantifies all the important reaction products and allows a carbon balance to be measured. Tertiary screening typically also entails testing all samples under several reaction conditions.

Secondary screening libraries of catalytic materials prepared for the oxidation and ammoxidation of propane were tested on a six-channel reactor module (Figure 3c). A specific weight of catalyst (150 mg) was diluted with SiC (about 3 \times volume of catalyst) to establish a consistent bed height. The reaction conditions for propane oxidation were: 150 mg catalyst charge to each channel, 15 psig, 350 °C, WHSV (weight hourly space velocity = feed rate in units of weight/time divided by catalyst weight) = 0.6 h⁻¹, feed ratio C₃H₈/O₂/He/H₂O = 1/1.2/3.8/0.67. The reaction conditions for propane ammoxidation were: 150 mg catalyst charge to each channel, atmospheric pressure, 420 °C, WHSV = 0.148 h⁻¹, feed ratio C₃H₈/NH₃/O₂/He = 1/1.2/3/12. The effluent of the reactor was analyzed by gas chromatography using a plot-Q and a molsieve column with FID and TCD detectors, respectively. Conversion, selectivity, and yield are defined as: Conversion = (moles C₃H₈ consumed/moles C₃H₈ charged) \times 100, Selectivity = (moles product/moles C₃H₈ consumed) \times (# C atoms in product/3) \times 100, Yield = (moles product/moles C₃H₈ charged) \times (# C atoms in product/3) \times 100.

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